Applications of C_2-Symmetric Bis(azaferrocenes) in Asymmetric Copper-Catalyzed Reactions

by

Michael Man-chu Lo

B. Eng. (Mech.), University of Hong Kong, 1993
M. Phil. (Chem.), Hong Kong University of Science and Technology, 1996

SUBMITTED TO THE DEPARTMENT OF CHEMISTRY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

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FEBRUARY 2002

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Submitted to the Department of Chemistry on November 5, 2001
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Doctor of Philosophy in Organic Chemistry

ABSTRACT

Based on a strategy developed in our group for the desymmetrization of planar heterocycles, we have designed, synthesized, and resolved a number of bidentate, C_2-symmetric planar-chiral bis(azaferrocenes) that bear a structural resemblance to the highly versatile bis(oxazolines). These bis(azaferrocenes) have their stereogenic elements directly connected to their ligating atoms, which should help these heterocycles exert better stereodifferentiating ability when they are applied as ligands in metal-catalyzed processes.

To validate the ligand design, we first applied our C_2-symmetric bis(azaferrocenes) as ligands in the asymmetric copper-catalyzed cyclopropanation of olefins. We discovered that one of these ligands is particularly effective, and using a hindered diazo ester, an array of monosubstituted olefins has been cyclopropanated with excellent diastereo- as well as enantioselectivity. The level of stereoselection achieved is comparable to some of the best ligands reported to date. Preliminary studies also showed that trans and trisubstituted olefins can be excellent substrates for the ligand.

The same copper–bis(azaferrocene) complex also catalyzes the ring expansion of oxetanes into tetrahydrofurans with high stereoselection. In the optimization process, we have developed a new hindered diazo ester that may also prove useful in other asymmetric carbene transfer processes. With the catalyst controlling the stereochemistry of the newly established C2 carbon and the oxetane substrate defining the configuration at the C3 carbon, the ring expansion furnishes either diastereomer of a 3-substituted tetrahydrofuran-2-carboxylate with high stereoselectivity.

The Kinugasa reaction, which is the copper-mediated reaction between nitrones and terminal alkynes, is an underexplored synthetic pathway to 2-azetidinones. Using a bis(azaferrocene) as the ligand, we have successfully improved the Kinugasa reaction in the following aspects: (1) the reaction is catalytic in copper; (2) the reaction gives high cis diastereoselectivity; and, (3) the reaction is highly enantioselective with a variety of nitrones and alkynes. Combined with a subsequent epimerization, our enantioselective process represents the first general, catalytic system for the Kinugasa reaction, which provides stereoselective access to all four of the possible isomers.

Thesis Supervisor: Gregory C. Fu
Title: Professor of Chemistry

Portions of this dissertation have appeared in the following publications:

Lo, M. M.-C.; Fu, G. C. "A New Class of Planar-Chiral Ligands: Synthesis of a C_2-Symmetric Bisazaferrocene and Its Application in the Enantioselective Cu(I)-Catalyzed Cyclopropanation of Olefins" *J. Am. Chem. Soc.* **1998**, *120*, 10270–10271.

Lo, M. M.-C.; Fu, G. C. "Applications of Planar-Chiral Heterocycles in Enantioselective Catalysis: Cu(I)/Bisazaferrocene-Catalyzed Asymmetric Ring Expansion of Oxetanes to Tetrahydrofurans" *Tetrahedron* **2001**, *57*, 2621–2634.

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I am indebted to the first generation of graduate students for their mentorship. I thank Dr. Diego Hoic, for teaching me a great deal of things about X-ray crystallography; Dr. David Hays, for setting a good example for being meticulous in details; Dr. Jack Liang, for his wisdom and maintaining the glove box well while tolerating my trespasses against his reasonable rules; Dr. Shuang Qiao, for her friendship and her passion of things that she holds dear; Dr. Craig Ruble, for discussions on azaferrocenes and showing me how to use the HPLC machines.

My baymates, Dr. Jordi Tormo, Brian Hodous, Beata Tao, Michael Smith, and Dr. Jan Kirchhoff, are praised for tolerating the mess that I created in my work area. Beata deserves special recognition for her willingness to disagree and argue with me about everything from chemistry to philosophy, and both Beata and Desmond are thanked for their friendship. Michael Smith taught me a lot of things about America. Dr. Stéphane Bellemin-Laponnaz, Dr. Shigeru Arai, and Dr. Jens Hildebrand were always great to talk to about chemistry and lives in other lands. Dr. Matthew Netherton impressed me with his precision in writing and his high standards in chemistry. Dr. Ken Tanaka demonstrated how to accomplish the amount of work required for a Ph.D. in two years. Michael Choi offered help whenever I asked for it. My heartfelt gratitude goes to all these individuals, who have contributed to make my life at MIT memorable. I also feel privileged to be working along with these gifted and dedicated individuals: Adam Littke, Shih-Yuan Liu, Ryo Shintani, Ivory Hills, and Ara Mermerian, and I learnt a lot from them. For individuals outside the lab, I thank Jane Dunphy, for brushing up

my English and improving my scientific writing skills; and Dr. William Davis, for training in X-ray crystallography.

I want to express my gratitude to Haiyang Liu and Yi Zhang; and also the group at Harvard, Eddie Hui, Dr. Barry Cheung, Ming-sum Lee, and Denis Yu, for their friendship.

Special thanks go to my team of proofreaders, Beata, Ivory, Jens, Matthew and Priscilla, who make the preparation of this dissertation as rapidly and as painlessly as it has been.

My family is the source of strength that powers me through the years as a graduate student. My parents have never quite understood a number of decisions in my life, yet without questioning my sanity, they embraced them fully. I cannot ask for more from them, and I truly appreciate their trust in me. I thank my brother, Joseph, for his encouragement during rough times, and I am indebted to him for assuming my responsibility of taking care of my parents. What a wonderful job he has done!

Last and most importantly, I am forever grateful to my wife, Priscilla, for staying beside me and brightening my days through these years. Being the spouse of a graduate student in organic chemistry is never easy, and without Priscilla, finishing all the work described in this dissertation would have been impossible. I was hardly a good husband, but I promise that better and sunnier days lie ahead of us.

As I leave the stressful days behind, the following poem by the Chinese poet Li Bai (701–762) can best describe my state of mind:

朝辭白帝彩雲間，
千里江陵一日還。
兩岸猿聲啼不盡，
輕舟已過萬重山。

It translates as:
"At dawn, amidst the iridescent clouds, I bade farewell to the fortress of *Baidi*,
to finish the thousand-mile journey back to *Jiangning* in a day's time.
Under the incessant howls of apes along the banks,
my light boat has breezed through the myriad mountains."

To Mum, Dad, Joseph, and Priscilla

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Abbreviations

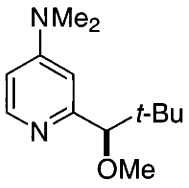
BHA	butylated hydroxyanisole, or 2,6-di-*t*-butyl-4-methoxyphenol
BHT	butylated hydroxytoluene, or 2,6-di-*t*-butyl-4-methylphenol
BTPP	*t*-butyliminotri(pyrrolidino)phosphorane
Cp*	pentamethylcyclopentadienyl
Cp'	substituted cyclopentadienyl
CSA	chiral solvating agent
DABCO	1,4-diazabicyclo[2.2.2]octane
DMAN	1,8-bis(*N*,*N*-dimethylamino)naphthalene
DMAP	4-(*N*,*N*-dimethylamino)pyridine
Men	menthyl
MTBE	methyl *t*-butyl ether
n.d.	not determined
PMP	1,2,2,6,6-pentamethylpiperidine
PhthN	phthalimido
pybox	2,6-bis(oxazolinyl)pyridine
r.t.	room temperature
salen	*N*,*N*'-bis(salicylaldehydo)ethylenediamine
SAR	structure–activity relationship
TEMPO	2,2,6,6-tetramethyl-1-piperidinyloxy, free radical

Chapter 1

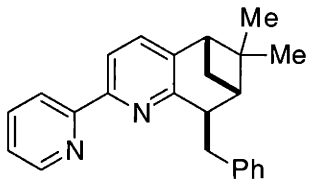
Design, Synthesis, and Resolution of C_2-Symmetric Bis(azaferrocenes)

A. Introduction.

Heterocycles that possess sp^2-hybridized nitrogen atoms, such as pyridines and imidazoles, are commonly applied in catalysis and asymmetric synthesis. To desymmetrize these compounds, the common approach is to install central-chiral stereogenic centers close to the heteroatom, examples of which are shown below.[1]



Vedejs (1996)



Chelucci (1998)

Our alternative approach is illustrated with pyridine as an example (Figure 1.1). Pyridine is achiral because of the existence of mirror planes, one in the plane of the pyridine ring, and one that bisects the pyridine ring through the nitrogen. To obtain a chiral derivative of pyridine, we eliminate the two mirror planes by π-complexation of the pyridine ring to a metal fragment (ML_n), and by incorporation of a substituent (R) in the 2-position of the pyridine ring.[2] As a result, no more mirror planes can be found in the resultant derivative **1.1**, and hence the heterocycle becomes chiral. Complexes having this type of chirality are often described as "planar-chiral."[3]

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1 (a) Vedejs, E.; Chen, X. *J. Am. Chem. Soc.* **1996**, *118*, 1809–1810. (b) Chelucci, G.; Pinna, G. A.; Saba, A. *Tetrahedron: Asymmetry* **1998**, *9*, 531–534.

2 Fu, G. C. *Acc. Chem. Res.* **2000**, *33*, 412–420.

3 "A chiral plane is caused if a plane of symmetry is destroyed in such a way that chirality arises only by the difference of both sides of the plane." Cahn, R. S.; Ingold, C. K.; Prelog, V. *Experientia* **1956**, *12*, 81–94. For a review, see: Schlögl, K. *Top. Curr. Chem.* **1984**, *125*, 29–62.

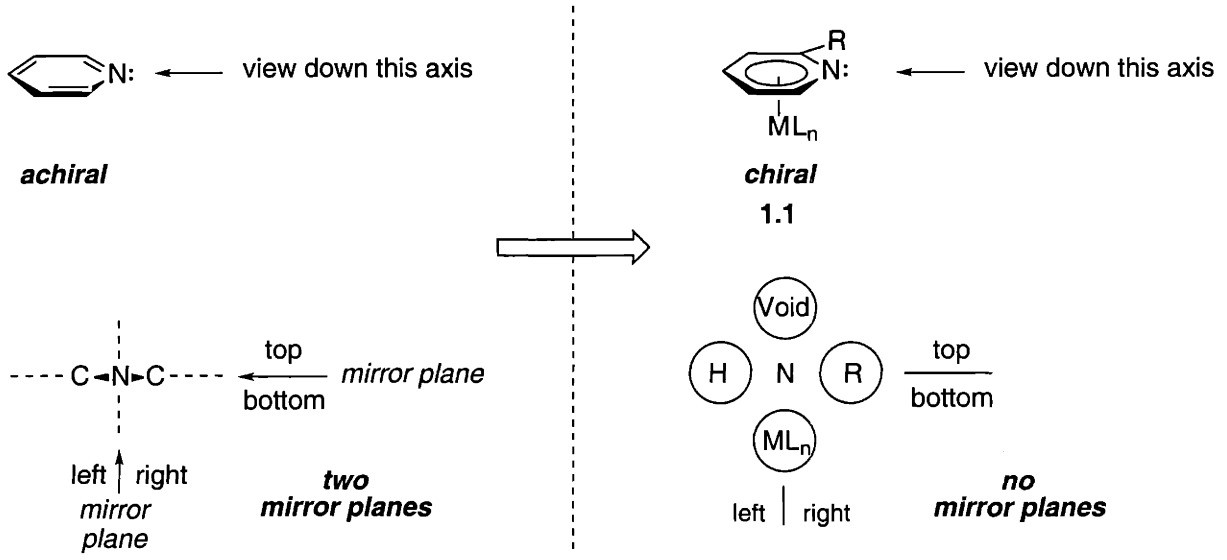

Figure 1.1. Desymmetrization of planar heterocycles.

The design of **1.1** allows for facile adjustment on the ligand properties. It offers two methods of tuning the steric environment around the heteroatom: either by discriminating the hydrogen on the left from the 2-substituent on the right, or by differentiating the void on top of the heterocycle from the metal fragment below. In addition, the electronic nature of the ligand can be readily changed by the incorporation of substituents on the heterocycle or by the use of another metal fragment. This versatility in our design should enable the ligand framework to be broadly applicable in a variety of reactions.

With respect to the choice of the metal fragment ML_n, the iron cyclopentadienyl group (FeCp')[4] appears to be the best candidate, due to "its high stability and the well-established methods for its incorporation into more complex structures."[5] In addition, its steric and electronic properties, as well as the solubility of the resultant complex, can be modified through the substituents on the Cp ring.

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4 Cp': substituted cyclopentadienyl.

5 Togni, A.; Hayashi, T. In *Ferrocenes: Homogeneous Catalysis, Organic Synthesis, Materials Science*; Togni, A., Hayashi, T., Eds.; VCH: New York, 1995; pp V–VI.

However, η^6-complexation of a pyridine ring to FeCp' furnishes a 19-electron complex, which has one electron more than the stable 18-electron configuration. To retain our ligand design while lowering the electron count to 18, we decided to explore two modifications: (1) Replace the η^6-bound neutral pyridine ring by a η^5-bound pyrrolyl anion. (2) Fuse the neutral pyridine ring to cyclopentadiene, which is then π-complexed to the iron cyclopentadienyl group (Figure 1.2).

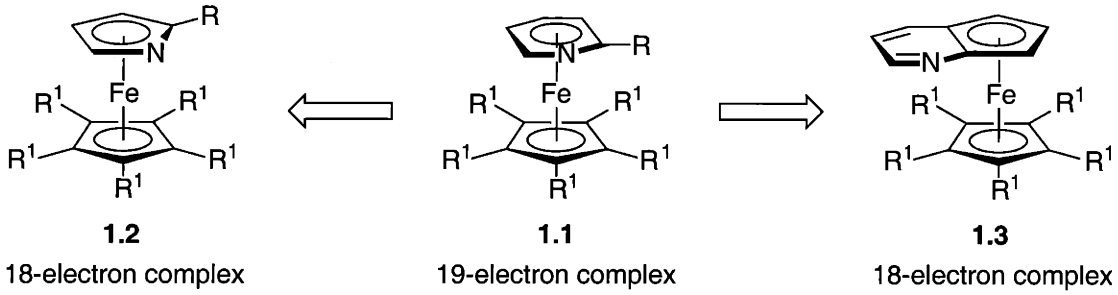

Figure 1.2. Modification of the initial ligand design to generate robust transition-metal complexes.

With the structure of the modified complexes in mind, tremendous efforts have been spent by our group to synthesize and resolve numerous planar-chiral azaferrocenes (**1.2**)[6] and planar-chiral pyrindinyl complexes (**1.3**).[7] A few of them (**1.4–1.7**) prove to be very effective asymmetric nucleophilic catalysts.

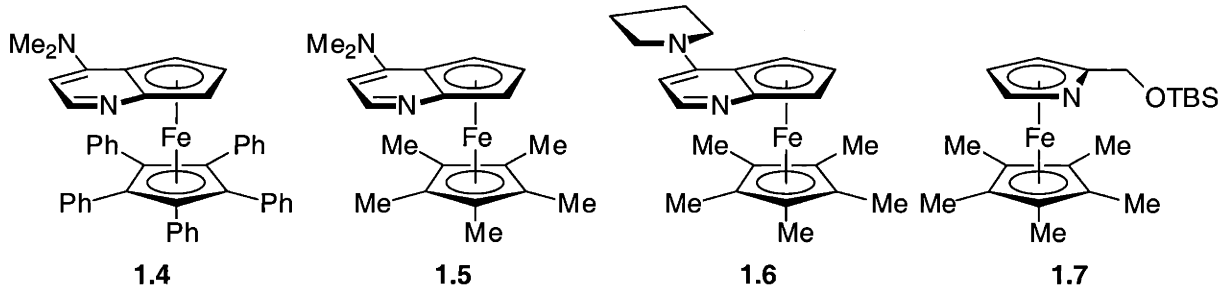

Figure 1.3. Planar-chiral heterocycles that have been shown to be effective nucleophilic catalysts.

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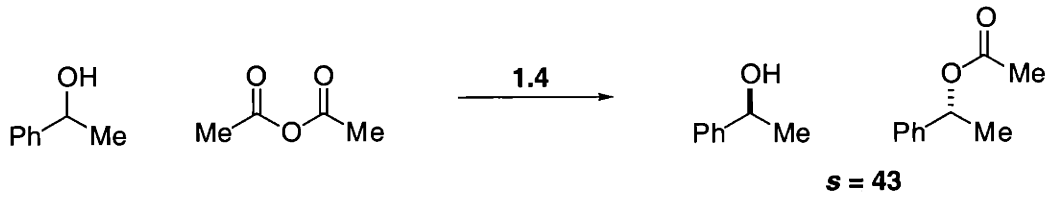
6 For the first report of azaferrocene, see: (a) King, R. B.; Bisnette, M. B. *Inorg. Chem.* **1964**, *8*, 796–800. (b) Joshi, K. K.; Pauson, P. L.; Qazi, A. R.; Stubbs, W. H. *J. Organomet. Chem.* **1964**, *1*, 471–475.

7 Before our work began in this area, there had been no report of any η^5-pyrindinyl complex with FeCp'. The only η^5-pyrindinyl complex known then was with $Mn(CO)_3$. See: Ji, L.-N.; Kershner, D. L.; Rerek, M. E.; Basolo, F. *J. Organomet. Chem.* **1985**, *296*, 83–94.

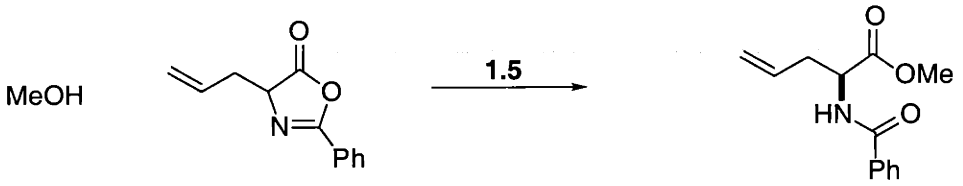
Listed in the following are reactions that are subject to enantioselective catalysis by the above planar-chiral heterocycles **1.4–1.7**:

1. kinetic resolution of secondary alcohols through acylation with anhydrides (eq 1.1)[8]



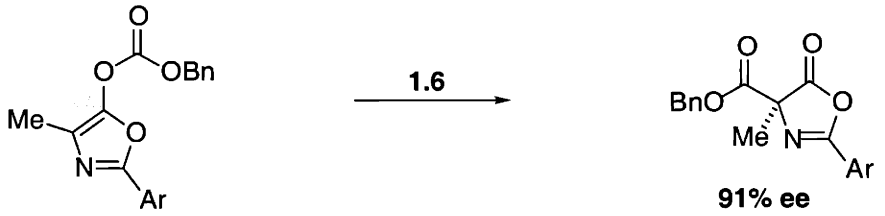
s = 43 (1.1)

2. dynamic kinetic resolution of azlactones through solvolysis (eq 1.2)[9]



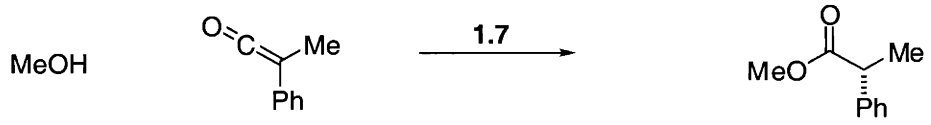
61% ee (1.2)

3. rearrangement of O-acylated azlactones (eq 1.3)[10]



91% ee (1.3)

4. addition of alcohols to ketenes (eq 1.4)[11]



77% ee (1.4)

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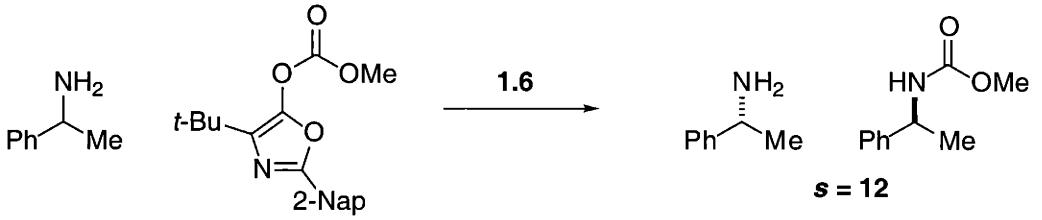
8 (a) Ruble, J. C.; Latham, H. A; Fu, G. C. *J. Am. Chem. Soc.* **1997**, *119*, 1492–1493. (b) Ruble, J. C.; Tweddell, J.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 2794–2795. (c) Tao, B.; Ruble, J. C.; Hoic, D. A.; Fu, G. C. *J. Am. Chem. Soc.* **1999**, *121*, 5091–5092. (d) Bellemin-Laponnaz, S.; Tweddell, J.; Ruble, J. C.; Breitling, F. M.; Fu, G. C. *Chem. Commun.* **2000**, 1009–1010.

9 Liang, J.; Ruble, J. C.; Fu, G.C. *J. Org. Chem.* **1998**, *63*, 3154–3155.

10 Ruble, J. C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 11532–11533.

11 Hodous, B. L.; Ruble, J. C.; Fu, G. C. *J. Am. Chem. Soc.* **1999**, *121*, 2637–2638.

5. kinetic resolution of amines through acylation with O-acylated azlactones (eq 1.5)[12]



(1.5)

For some of these reactions (eq 1.2, 1.3, and 1.5), our planar-chiral heterocycles remain the only reported catalysts that give good enantioselectivities.

Apart from being applied as asymmetric nucleophilic catalysts, these planar-chiral heterocycles can also be effective chiral ligands for transition metals.[13] Figure 1.4 compares again the two approaches of desymmetrization. In the first approach, the stereogenic center is two bonds away from the ligating atom, whereas in the second approach, the stereogenic element is *directly* connected to it. With the stereogenic element in closer proximity to the heteroatom, the heterocycle can conceivably exert better stereodifferentiating ability.[14]

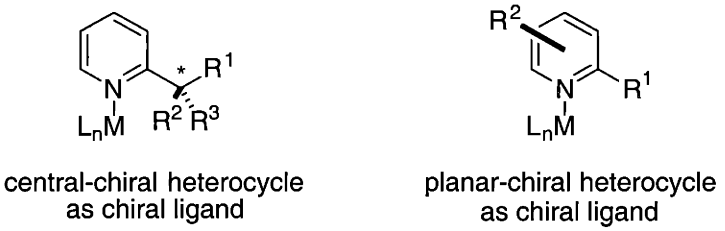


Figure 1.4. Comparison of two desymmetrization approaches with respect to the stereogenic element.

While this crude analysis may be an oversimplification of the origin of asymmetric induction in myriad catalytic enantioselective reactions, we hope that this unique way of

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12 Arai, S.; Bellemin-Laponnaz, S.; Fu, G. C. *Angew. Chem. Int. Ed.* **2001**, *40*, 234–236.

13 The lone pair on the sp^2-heteroatom of heterocycles that are π-complexed to metals can also serve as a σ-donor to transition metals. For a review of σ,π-complexes of five-membered monoheterocycles, see: Sadimenko, A. P.; Garnovskii, A. D.; Retta, N. *Coord. Chem. Rev.* **1993**, *126*, 237–318.

14 Ganter expressed a similar idea when he discussed his design of chelate ligands with planar chirality. See: Ganter, C.; Brassat, L.; Glinsböckel, C.; Ganter, B. *Organometallics* **1997**, *16*, 2862–2867.

looking at ligand design will produce chiral ligands that complement the existing "privileged" ones.[15]

Between the two planar-chiral ligand frameworks, azaferrocene **1.2** is the preferred design to test our hypothesis, since its stereogenic element is directly connected to the ligating atom.[16,17] The popularity of phosphine ligands in asymmetric catalysis soon expanded our initial focus on azaferrocenes to include the analogous phosphaferrocene framework as well. Through the efforts of our group, the following C_1-symmetric complexes (**1.8–1.11**) have been shown to be effective ligands in transition-metal based asymmetric catalysis.

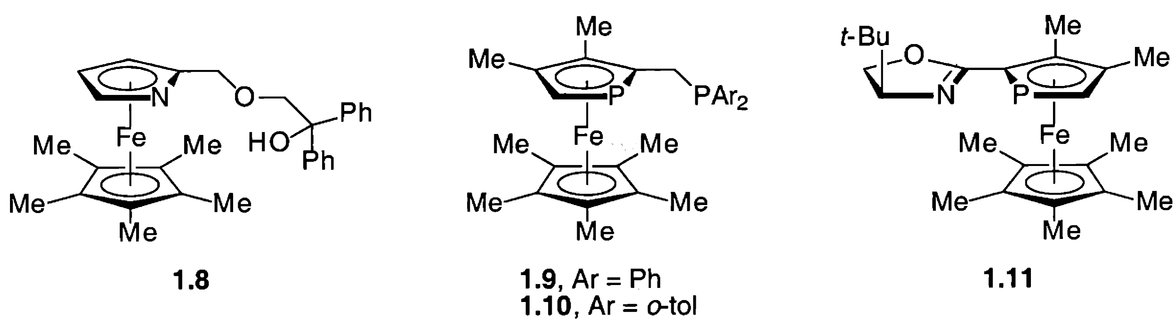

Figure 1.5. Planar-chiral heterocycles that have been shown to be effective ligands for metal-based reactions.

Summarized below are the reactions that involve the use of **1.8–1.11**. They represent the first applications of heteroferrocene complexes as chiral ligands in asymmetric catalysis.[18]

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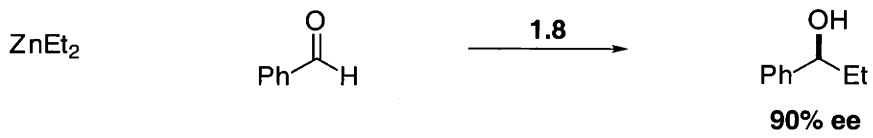
15 "Privileged" chiral ligands refer to those that enjoy both generality and effectiveness, e.g., BINAP and salen.

16 Dr. Jack Liang has explored the syntheses and applications of C_2-symmetric planar-chiral 2,2'-bipyridines that are based on the framework **1.3**. For an account of the work, see: Liang, J. Ph.D. Thesis, Massachusetts Institute of Technology, 1999.

17 These heteroferrocenes are known to act as Lewis bases to transition metals. For the first report of N-coordination of an azaferrocene to a transition metal, see: (a) Pyshnograeva, N. I.; Setkina, V. N.; Kursanov, D. N. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1984**, *33*, 2544–2546. For the first report of P-coordination of a phosphaferrocene to a transition metal, see: (b) Mathey, F. *J. Organomet. Chem.* **1978**, *154*, C13–C15.

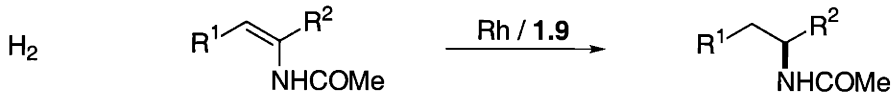
18 At the outset of our research program in 1995, no azaferrocene or phosphaferrocene complexes had been reported as chiral ligands in asymmetric catalysis.

1. addition of diethylzinc to aldehydes (eq 1.6)[19]



(1.6)

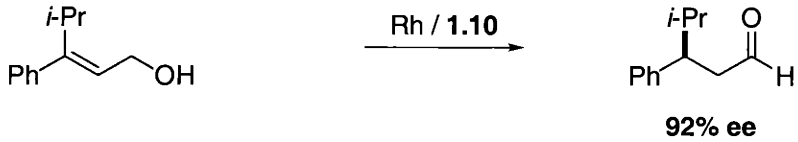
2. rhodium-catalyzed hydrogenation of functionalized olefins (eq 1.7)[20]



(1.7)

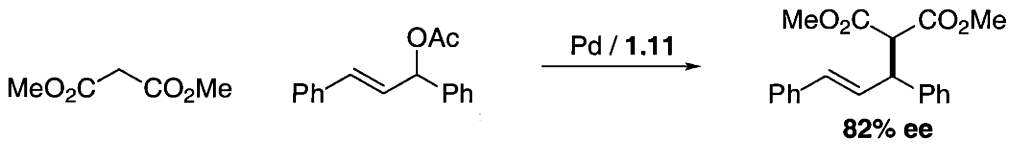
R^1	R^2	% ee
Et	CO_2Me	96
H	Ph	96

3. rhodium-catalyzed isomerization of allylic alcohols (eq 1.8)[21]



(1.8)

4. palladium-catalyzed allylic alkylation of malonates (eq 1.9)[22]



(1.9)

We have been interested in employing our design in the development of C_2-symmetric ligands as well. The inclusion of a C_2-symmetry axis within a chiral ligand is believed to "serve the very important function of dramatically reducing the number of

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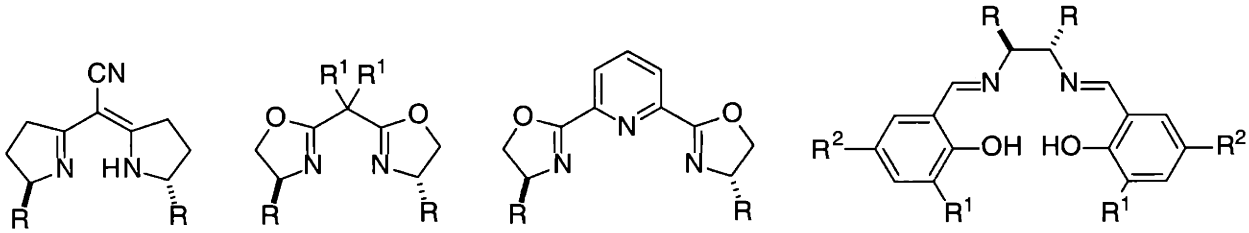
19 Dosa, P. I.; Ruble, J. C.; Fu, G. C. *J. Org. Chem.* **1997**, *62*, 444–445.

20 (a) Dehydroamino acids: Qiao, S.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 4168–4169. (b) Enamides: Qiao, S. Ph.D. Thesis, Massachusetts Institute of Technology, 1999.

21 (a) Tanaka, K.; Qiao, S.; Tobisu, M.; Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 9870–9871. (b) Tanaka, K.; Fu, G. C. *J. Org. Chem.* in press.

22 Shintani, R.; Lo, M. M.-C.; Fu, G. C. *Org. Lett.* **2000**, *2*, 3695–3697.

possible competing, diastereomeric transition states."[23] Consistent with this assertion, the following ligands with sp^2-hybridized nitrogens (semicorrin,[24] bis(oxazoline),[25] pybox,[26] and salen[27]) are among the most general and effective chiral ligands that have been reported to date.



semicorrin bis(oxazoline) pybox salen

To illustrate the general effectiveness of these ligands, we adapt Figure 1.6 from the work of Andersson, which summarizes the state-of-the-art in the application of bis(oxazolines) as chiral ligands/auxiliaries at the time we began our investigation.[28]

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23 Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581–1590.

24 For a review, see: Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339–345.

25 For reviews, see: (a) Bolm, C. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 542–543. (b) Ghosh, A. K.; Mathivanan, P.; Cappiello, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1–45. (c) Johnson, J. S.; Evans, D. A. *Acc. Chem. Res.* **2000**, *33*, 325–335.

26 The use of pybox was first reported by Nishiyama in the rhodium-catalyzed asymmetric hydrosilylation of ketones. See: (a) Nishiyama, H.; Sakaguchi, H.; Nakamura, T.; Horihata, M.; Kondo, M.; Itoh, K. *Organometallics* **1989**, *8*, 846–848. (b) Nishiyama, H.; Kondo, M.; Nakamura, T.; Itoh, K. *Organometallics* **1991**, *10*, 500–508.

27 For reviews, see: (a) Katsuki, T. *Coord. Chem. Rev.* **1995**, *140*, 189–214. (b) Canali, L.; Sherrington, D. C. *Chem. Soc. Rev.* **1999**, *28*, 85–93. (c) Jacobsen, E. N. *Acc. Chem. Res.* **2000**, *33*, 421–431.

28 Bedekar, A. V.; Koroleva, E. B.; Andersson, P. G. *J. Org. Chem.* **1997**, *62*, 2518–2526.

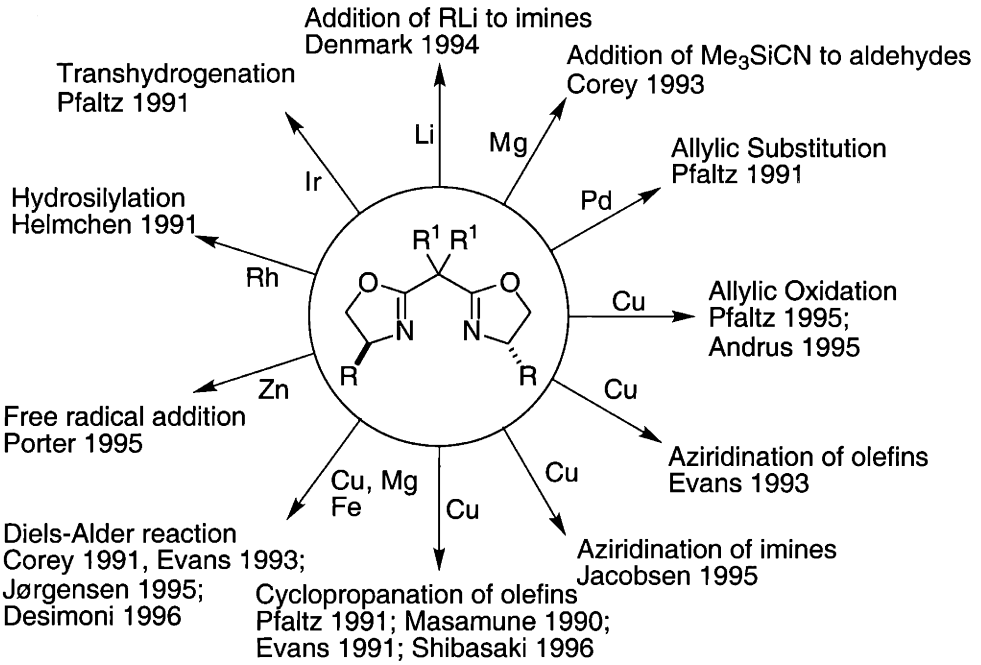
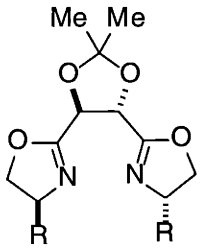


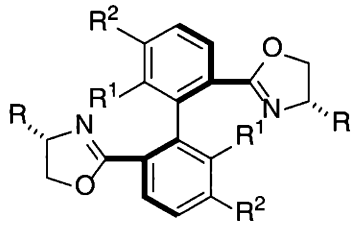
Figure 1.6. Applications of bis(oxazolines) in asymmetric synthesis (1997).

In view of the success of the ligand, numerous attempts have been made to modify the bis(oxazoline) structure by incorporating different types of chirality, e.g., stereogenic centers on the carbon backbone,[29] axial chirality,[30] and planar chirality[31] into the framework.



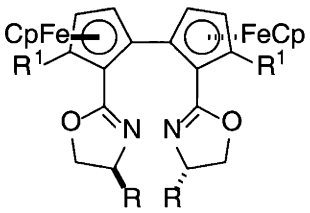
Andersson/
Ikeda/Knight (1996)

stereogenic centers
on the carbon backbone



Corey (1995)/
Hayashi (1996)

axial chirality



Ahn (1997)

planar chirality

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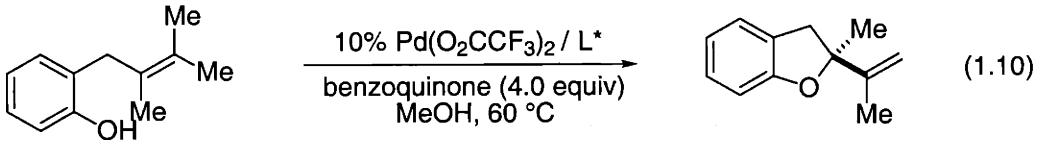
29 (a) Bedekar, A. V.; Andersson, P. G. *Tetrahedron Lett.* **1996**, *37*, 4073–4076. (b) Imai, Y.; Zhang, W.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *Tetrahedron: Asymmetry* **1996**, *7*, 2453–2462. (c) Harm, A. M.; Knight, J. G.; Stemp, G. *Synlett* **1996**, 677–678.

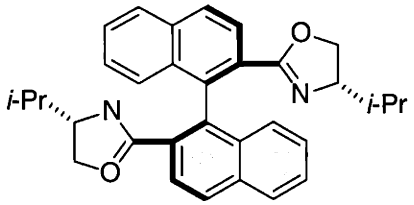
30 (a) Gant, T. G.; Noe, M. C.; Corey, E. J. *Tetrahedron Lett.* **1995**, *36*, 8745–8748. (b) Uozumi, Y.; Kyota, H.; Kishi, E.; Kitayama, K.; Hayashi, T. *Tetrahedron: Asymmetry* **1996**, *7*, 1603–1606.

31 Kim, S.-G.; Cho, C.-W.; Ahn, K. H. *Tetrahedron: Asymmetry* **1997**, *8*, 1023–1026.

These modifications, at times, lead to ligands that exert better stereoselection than the "conventional" bis(oxazolines), as exemplified by the following asymmetric Wacker-type cyclization of Uozumi and Hayashi (eq 1.10).[32]

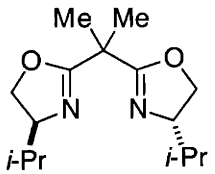


(1.10)



1.12

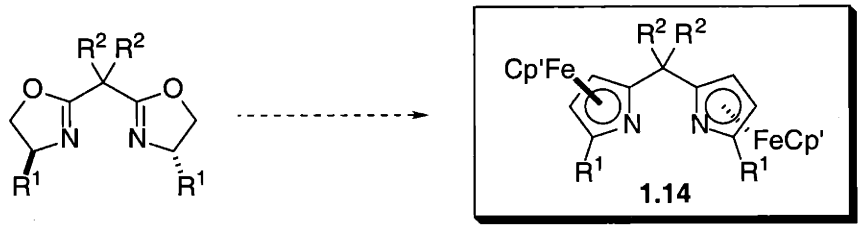
96% ee



1.13

35% ee

Our approach to develop analogs for the bis(oxazoline) framework is to extend our concept for the desymmetrization of planar heterocycles into building novel C_2-symmetric planar-chiral bis(azaferrocenes) **1.14**:



Ligand **1.14** has the following features:

1. The size of the chelate ring with metal is the same as in the parent bis(oxazoline) system, in contrast with the aforementioned structural analogs in which seven- or nine-membered rings are formed.
2. The only stereogenic element in the ligand is planar-chirality, and it is connected directly to the ligating atoms.

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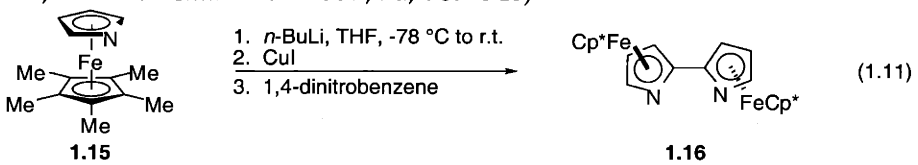
32 Uozumi, Y.; Kato, K.; Hayashi, T. *J. Org. Chem.* **1998**, *63*, 5071–5075.

3. The design is modular as the steric and electronic demand of the ligand can be varied by changing Cp', R^1, and R^2.[33]

In this chapter, we detail the synthesis of several members of **1.14** and our different methods to access these compounds in enantiomerically pure form. X-ray structures with **1.14** functioning as bidentate ligands for copper(I) are also presented to gain better understanding of the steric environment that these chiral ligands create around the metal atom.

---

33 At the beginning of the project, we explored the possibility of synthesizing a C_2-symmetric bisazaferrocene with a zero-atom linker. Bis(azaferrocene) **1.16** would be an analog for the tetrahydrobi(oxazole) that Pfaltz has used in his enantioselective iridium-catalyzed transfer hydrogenation of ketones and palladium-catalyzed allylic substitutions (Müller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232–240).



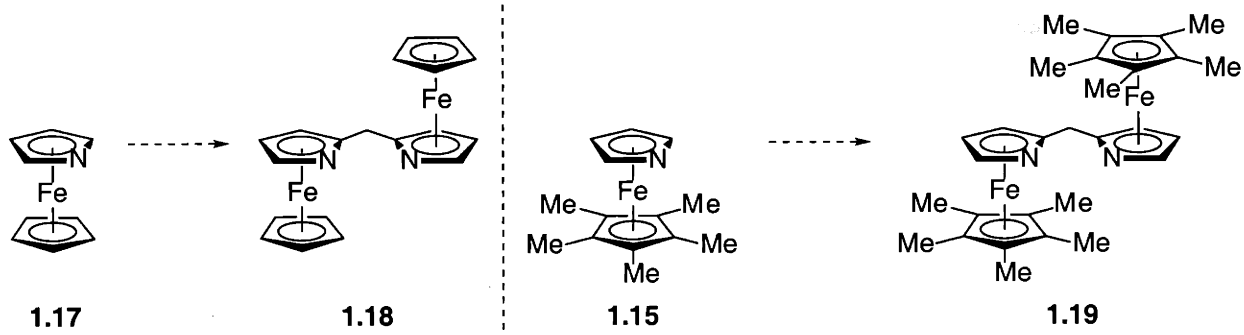
1.15 **1.16** (1.11)

Bis(azaferrocene) **1.16** was indeed synthesized and characterized, but unfortunately it is not stable enough to be manipulated in air.

B. Results and Discussion.

I. Synthesis of Racemic C_2-Symmetric Bis(azaferrocenes) 1.14.

Based on the known instability of azaferrocene (**1.17**) to air and light, we suspected that the simpler bis(azaferrocene) **1.18** is not stable enough to be conveniently applied in catalysis.[34] Hence, as the starting point, we choose **1.19** as our target complex. In addition to increased stability, the larger Cp* fragment may improve the steric differentiation of **1.19** as a chiral ligand (cf. Figure 1.1).



Scheme 1.1 summarizes the two general approaches for the synthesis of C_2-symmetric bis(azaferrocenes) **1.14**. A pyrrole is first π-complexed to a FeCp' fragment to afford an azaferrocene, which is then metalated at the 5-position and linked to another azaferrocene (eq 1.12). If either one of the azaferrocenes is resolved, the rac product should also be enantiomerically pure; and if both azaferrocenes are resolved, the resultant bis(azaferrocene) will be obtained as a single stereoisomer.

Alternatively, two pyrroles are first linked to furnish a di(pyrrol-2-yl)alkane, which is then π-complexed to *two* FeCp' fragments (eq 1.13). However, the diastereoselectivity of the complexation has to be controlled to minimize the formation

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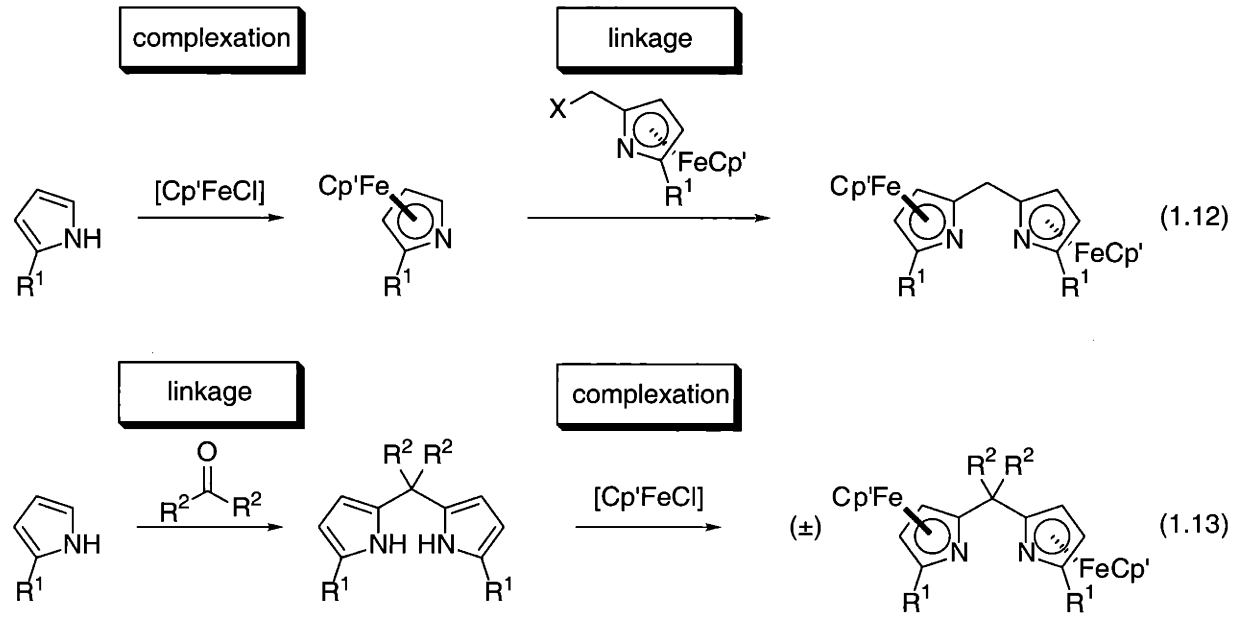
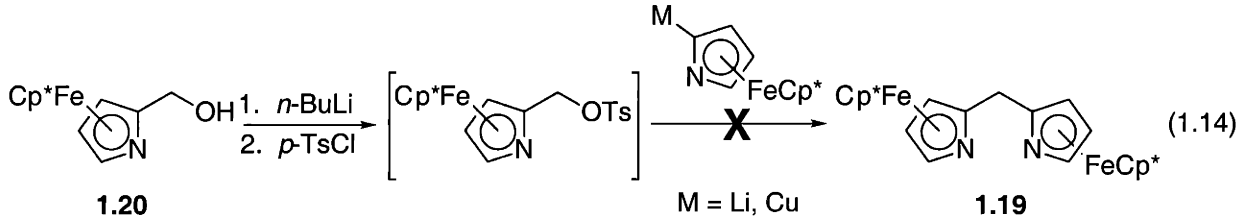
34 The stability of a metal complex is often enhanced upon substituting the η^5-Cp ring with an η^5-Cp* ring. For leading references, see: Kerber, R. C. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: New York, 1995; Vol. 7, Chapter 2.

of the meso product, and methods for resolving the enantiomers of the rac product have to be developed.



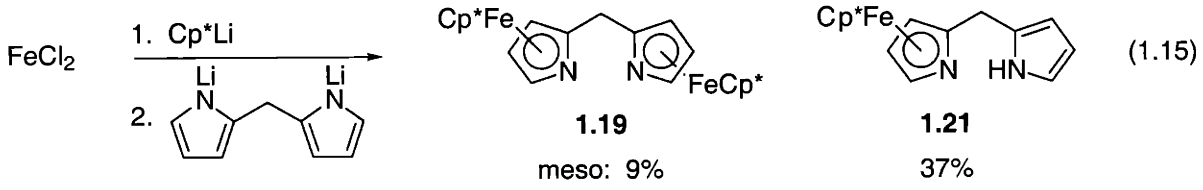
Scheme 1.1. General approaches to the synthesis of C_2-symmetric bis(azaferrocenes).

As **1.20** was available in enantiomerically pure form,[19] we attempted the synthesis of (±)-**1.19** using the first approach. Unfortunately, neither the lithiated azaferrocene nor the copper-transmetalated complex afforded any desired product (eq 1.14).



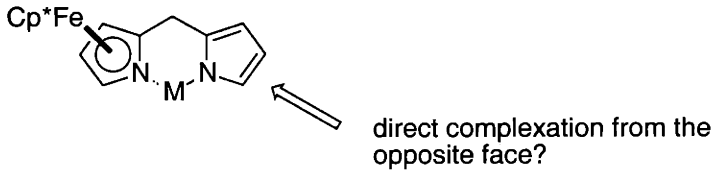
1.20 **1.19**

The second approach also apparently failed, as treatment of $FeCl_2$ with Cp*Li followed by the addition of the dilithio salt of di(pyrrol-2-yl)methane affords predominantly azaferrocene **1.21** and bis(azaferrocene) *meso*-**1.19** (eq 1.15).

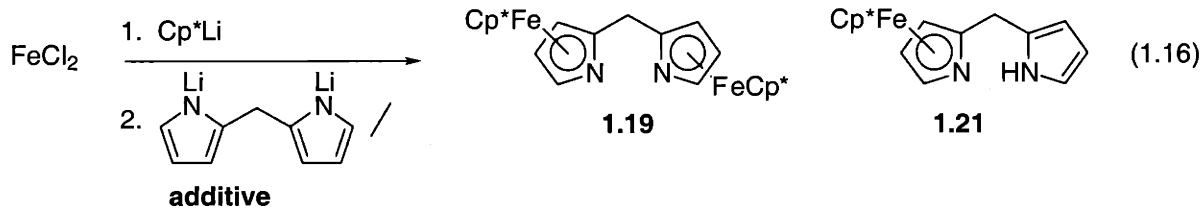


(1.15)

After scrutinizing the ^{1}H NMR spectrum of the crude product, we noticed signals that suggested the presence of a trace amount of *rac*-**1.19**. To enhance its formation, we speculated that the replacement of the hard lithium by a soft transition metal at the mono-complexation stage would serve to chelate **1.21** and direct the second complexation to take place at the *opposite* face.



By adding different transition metal salts to the dilithio salt of di(pyrrol-2-yl)methane and repeating the reaction illustrated in eq 1.15, we can indeed alter the diastereomeric composition of **1.19** (Table 1.1).

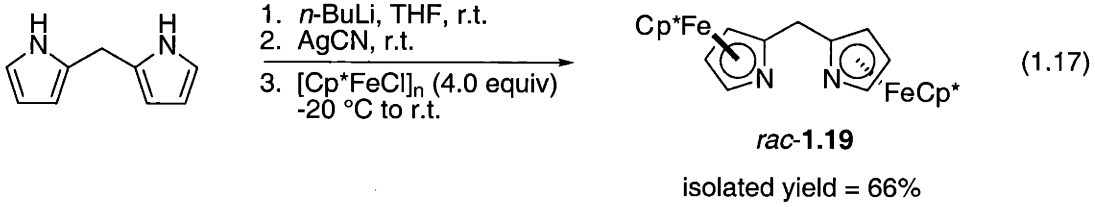


(1.16)

Table 1.1. Effect of transition metal salts in the synthesis of **1.19** (eq 1.16).

		NMR yield (%)		
entry	**additive**	*rac*-**1.19**	*meso*-**1.19**	**1.21**
1	none	trace	5	39
2	$NiCl_2$	25	54	21
3	CuCN	27	16	26
4	AgCN	35	10	48
5	$ZnCl_2$	20	13	8

AgCN affords the best diastereoselectivity (rac:meso = 78:22, entry 4). By increasing the amount of $[Cp^*FeCl]_n$, we can further suppress the formation of **1.21** and enhance the formation of *rac*-**1.19** (eq 1.17).



rac-**1.19**

isolated yield = 66%

(1.17)

After successfully obtaining the first member of the bis(azaferrocene) family, we were eager to extend the synthetic approach to some other members as well. The installation of a substituent at the 5-position of the azaferrocene can increase the steric bulk around the metal center (M), while substitution at the bridging carbon can decrease the bite angle of the ligand.[35,36] These properties could prove beneficial in the future applications of **1.14** as chiral ligands in asymmetric catalysis (Figure 1.7)

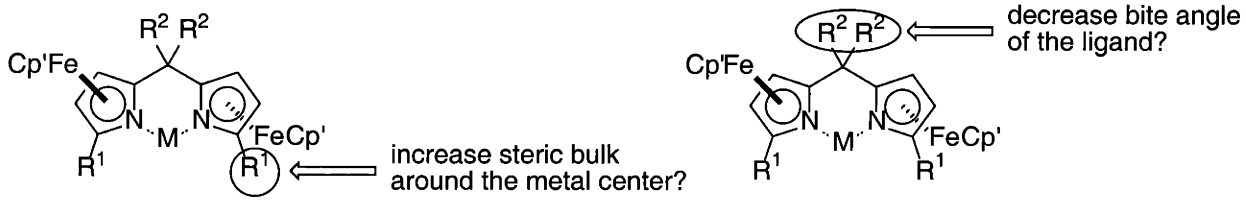


Figure 1.7. Effects of substituents R^1 and R^2 on ligand properties.

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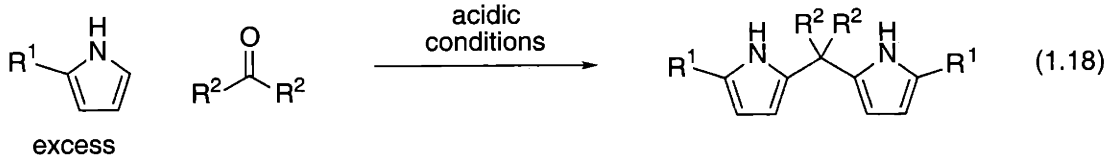
35 For a review on the effect of ligand bite angle in metal-catalyzed C–C bond formation, see: (a) van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741–2769.

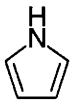
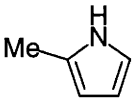
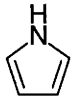
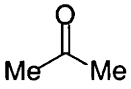
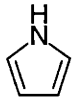
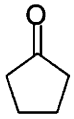
36 Davies has conducted a systematic study on the influence of the ligand bite angle on the enantioselectivity of a Cu(II)-catalyzed Diels–Alder reaction. The ligand geometry in a series of spirobis(oxazolines) was perturbed through substitution at the bridging atom, and a significant correlation between the bite angle and the enantioselectivity was deduced. For the original account and the subsequent theoretical analyses, see: (a) Davies, I. W.; Gerena, L.; Castonguay, L.; Senanayake, C. H.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *Chem. Commun.* **1996**, 1753–1754. (b) Davies, I. W.; Deeth, R. J.; Larsen, R. D.; Reider, P. J. *Tetrahedron Lett.* **1999**, *40*, 1233–1236. (c) Lipkowitz, K. B.; Schefzick, S.; Avnir, D. *J. Am. Chem. Soc.* **2001**, *123*, 6710–6711. Denmark has performed a similar study with the addition of methyllithium to imines. See: (d) Denmark, S. E.; Stiff, C. M. *J. Org. Chem.* **2000**, *65*, 5875–5878.

The synthesis of these new bis(azaferrocenes) requires the corresponding di(pyrrol-2-yl)alkanes, which are prepared by the condensation of pyrrole and the corresponding carbonyl compound under acidic conditions (Table 1.2):



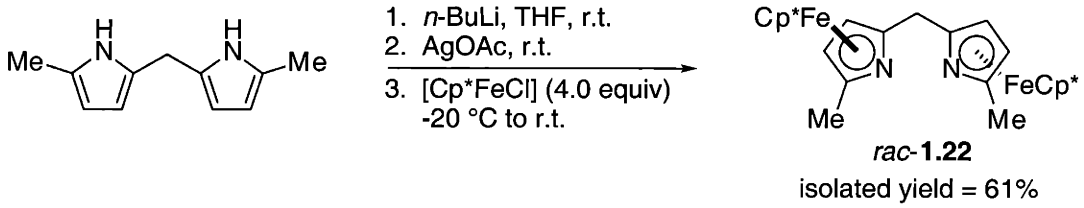
(1.18)

Table 1.2. Synthesis of di(pyrrol-2-yl)alkanes (eq 1.18).

entry	pyrrole	carbonyl compound	isolated yield (%)
1		$(HCHO)_n$	21
2		$(HCHO)_n$	36
3			19
4			4

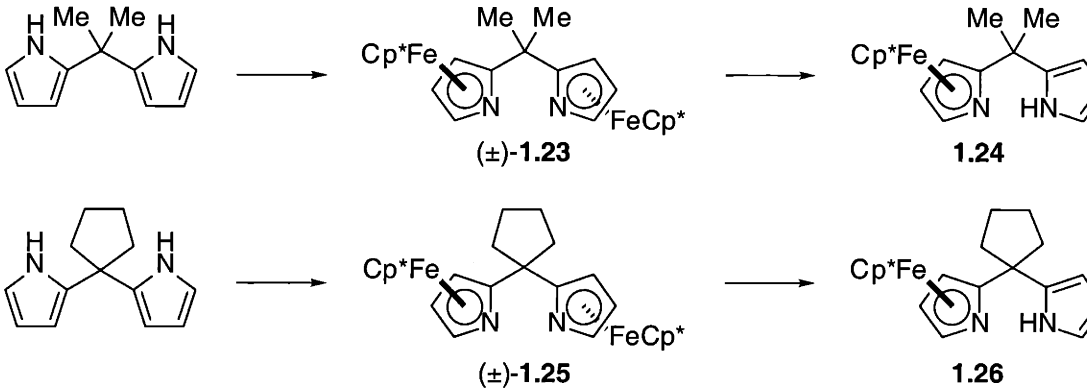
Although the isolated yields are generally poor, the starting materials are inexpensive and readily available. The products are isolated in a straightforward manner by first distilling the excess pyrrole from the crude reaction mixture, followed by reduced-pressure distillation. This method leaves the oligomeric products in the crude mixture and circumvents the need for flash chromatography, which can lead to further decomposition of the product, as the di(pyrrol-2-yl)alkanes are prone to air-oxidation in solution. Gram-quantities of the products can be made available via this route.

The synthesis of bis(azaferrocene) *rac*-**1.22**, which contains no substitution on the bridging carbon, was accomplished similarly (eq 1.19).



(1.19)

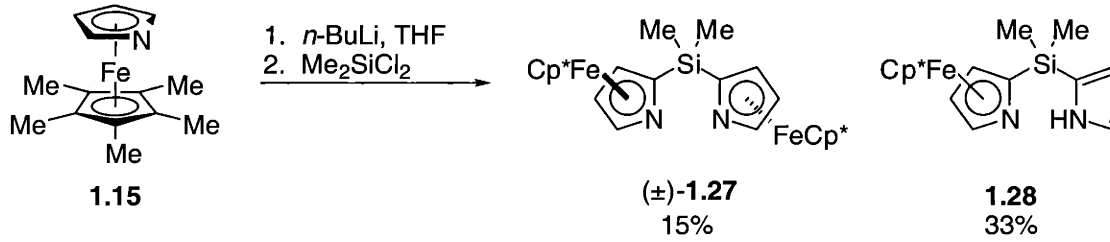
When the bridging carbon is substituted, the bis(azaferrocenes) become much less stable. Bis(azaferrocenes) *rac*-**1.23** and *rac*-**1.25** were synthesized and characterized by ^{1}H NMR, but attempts to isolate them resulted in the decomplexation of one of the FeCp* fragments.[37]



(1.20)

(1.21)

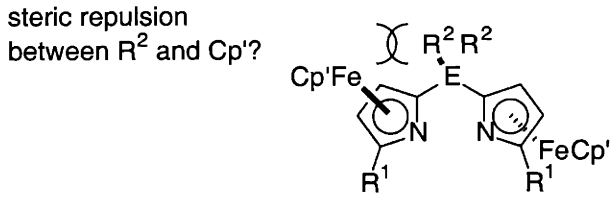
Replacing the bridging carbon with a silicon tether in *rac*-**1.23** does not improve the stability of the resultant bis(azaferrocene); after isolation, *rac*-**1.27** undergoes similar decomposition to **1.28** (eq 1.22).



(1.22)

37 Bisazaferrocene *rac*-**1.25** is stable enough to be trapped as a [CuOTf•ligand•styrene] complex and characterized crystallographically (*vide infra*).

We attributed the ease with which gem-disubstituted bis(azaferrocenes) *rac*-**1.23**, *rac*-**1.25**, and *rac*-**1.27** undergo decomplexation to the steric interactions between the substituent R^2 and the methyl groups of the Cp* ring.



We were also interested in obtaining bis(azaferrocenes) that bear different FeCp' fragments. The change from Cp* to a more sterically demanding Cp' such as pentaphenylcyclopentadienyl should improve the top/bottom differentiation of the heterocycle (cf. Figure 1.1) and increase the steric bulk of the ligand (Figure 1.8).

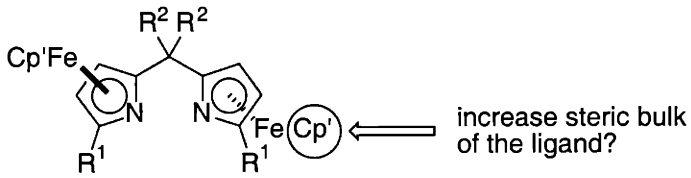
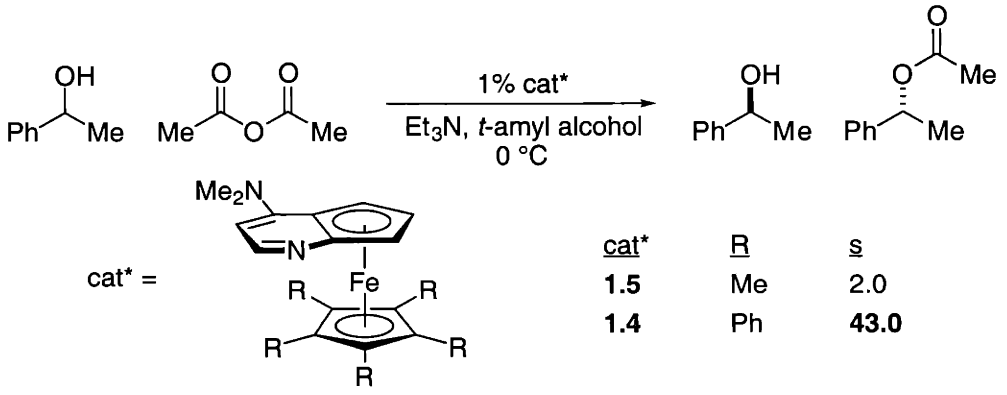


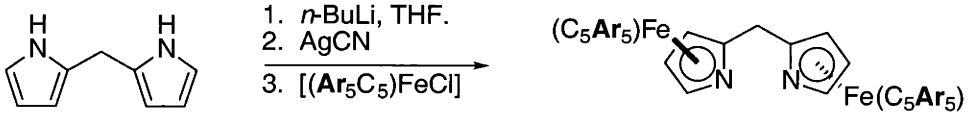
Figure 1.8. Effects of FeCp' on ligand properties.

The beneficial effect of this change is best illustrated by the following example from our study on the kinetic resolution of secondary alcohols, in which a dramatic improvement in stereodifferentiation was observed by increasing the size of Cp' in a planar-chiral pyrindinyl complex.[8a]



cat*	R	s
1.5	Me	2.0
1.4	Ph	**43.0**

The report by Miura and Dyker on a simple synthesis of pentaarylcyclopentadienes facilitated our task of varying the FeCp' fragment.[38,39] As a result, pentaarylcyclopentadienes of different steric and electronic properties can be obtained in a single step from zirconocene dichloride and aryl bromides. With a number of them in hand, we synthesized and isolated a variety of rac decaarylbis(azaferrocenes) **1.29–1.33** in low to moderate yields (Table 1.3).[40]



(1.23)

Table 1.3. Synthesis of decaarylbis(azaferrocenes) **1.29–1.33** (eq 1.23).

entry	Ar	bis(azaferrocene)	rac : meso	isolated yield, rac (%)
1	Ph	**1.29**	64 : 36	20
2	3,5-$Me_2C_6H_3$	**1.30**	70 : 30	50
3	4-MeC_6H_4	**1.31**	57 : 43	28
4	4-(MeO)C_6H_4	**1.32**	n.d.	22
5	4-(*i*-PrO)C_6H_4	**1.33**	63 : 37	45

II. Access to Enantiomerically Pure C_2-Symmetric Bis(azaferrocenes).

The method of choice for the resolution of planar-chiral heterocycles in our group is chiral HPLC, as we can rapidly obtain sufficient quantities of enantiomerically pure material to explore its potential in asymmetric catalysis. Screening our

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38 (a) Miura, M. Pivsa-Art, S.; Dyker, G.; Heiermann, J.; Satoh, T.; Nomura, M. *Chem. Commun.* **1998**, 1889–1890. (b) Dyker, G.; Heiermann, J.; Miura, M.; Inoh, J.-I.; Pivsa-Art, S.; Satoh, T.; Nomura, M. *Chem. Eur. J.* **2000**, *6*, 3426–3433.

39 Prior to the report by Miura and Dyker, pentaphenylcyclopentadiene was the only readily accessible pentaarylcyclopentadiene. It can be purchased from Aldrich or synthesized in two steps from tetraphenylcyclopentadienone and phenylmagnesium bromide. See: Field, L. D.; Ho, K. M.; Lindall, C. M.; Masters, A. F.; Webb, A. G. *Aust. J. Chem.* **1990**, *43*, 281–291.

40 The pentaarylcyclopentadienes used in this study were provided by Dr. Jack Liang.

bis(azaferrocenes) against different chiral columns for separation revealed that complexes **1.19, 1.22, 1.31,** and **1.33** can be resolved by this method. Figure 1.9 features the analytical HPLC chromatogram of **1.19**.

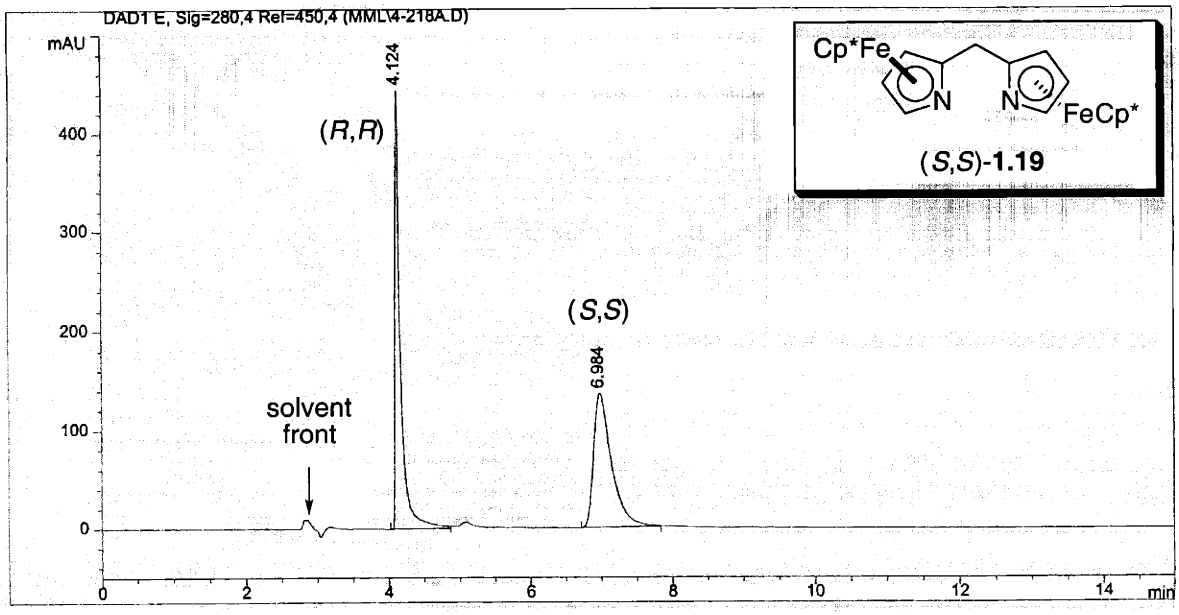


Figure 1.9. HPLC chromatogram of (±)-**1.19** on a Chiralcel OD column.

In this particular case, the separation is highly efficient ($\alpha \approx 3.2$).[41] Translating this factor into practical terms, a gram of racemic material can easily be resolved using a 1.0 cm x 25 cm column within one day.

The absolute configurations of the resolved enantiomers of **1.19** (Figure 1.10) and **1.22** (Figure 1.11) have been determined unambiguously by X-ray crystallography.

---

41 The selectivity factor α is a measurement of how well two species are separated, and it is experimentally determined by the following ratio $[(t_R)_B - t_M] / [(t_R)_A - t_M]$, where t_R is the retention time and t_M is the dead time.

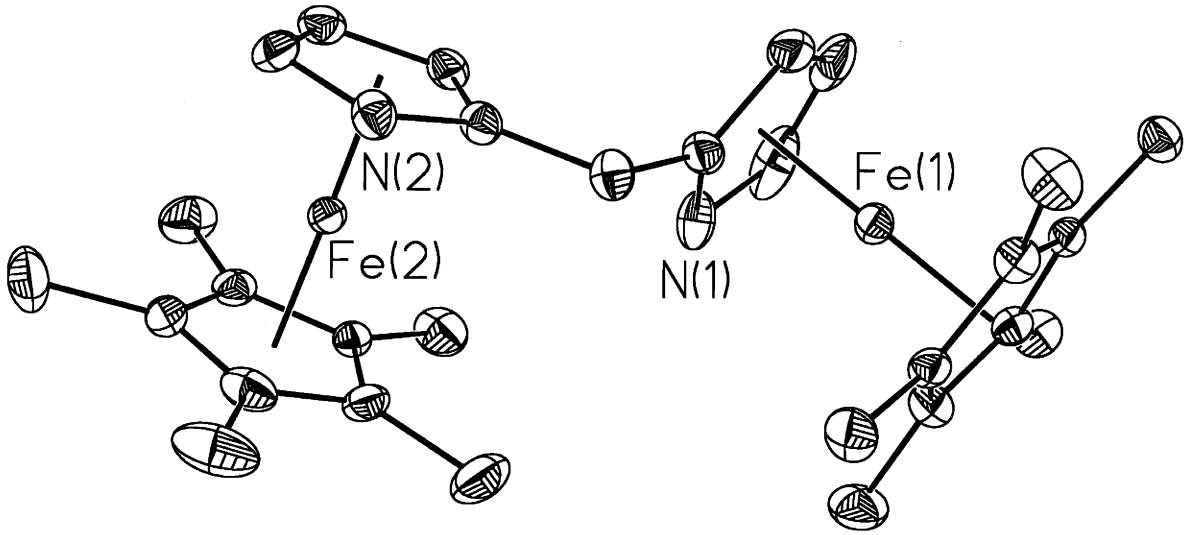


Figure 1.10. ORTEP plot of (*R*,*R*)-**1.19**, with thermal ellipsoids drawn at the 35% probability level.

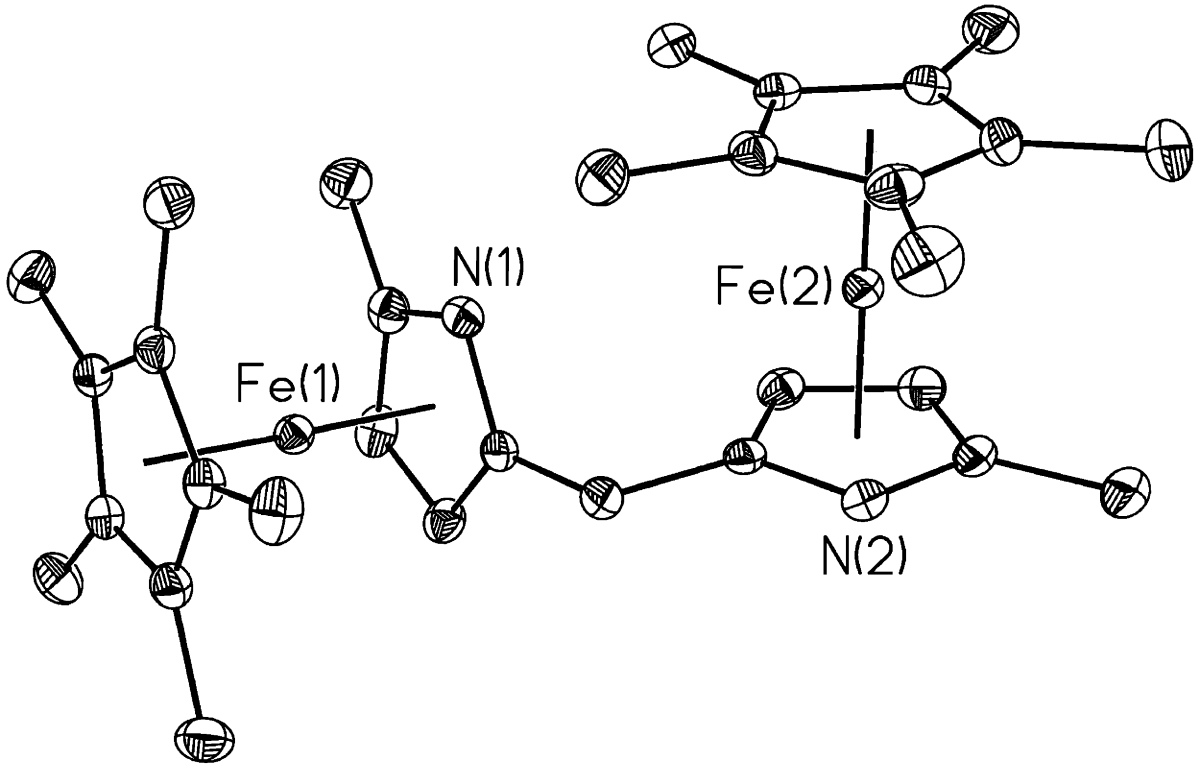
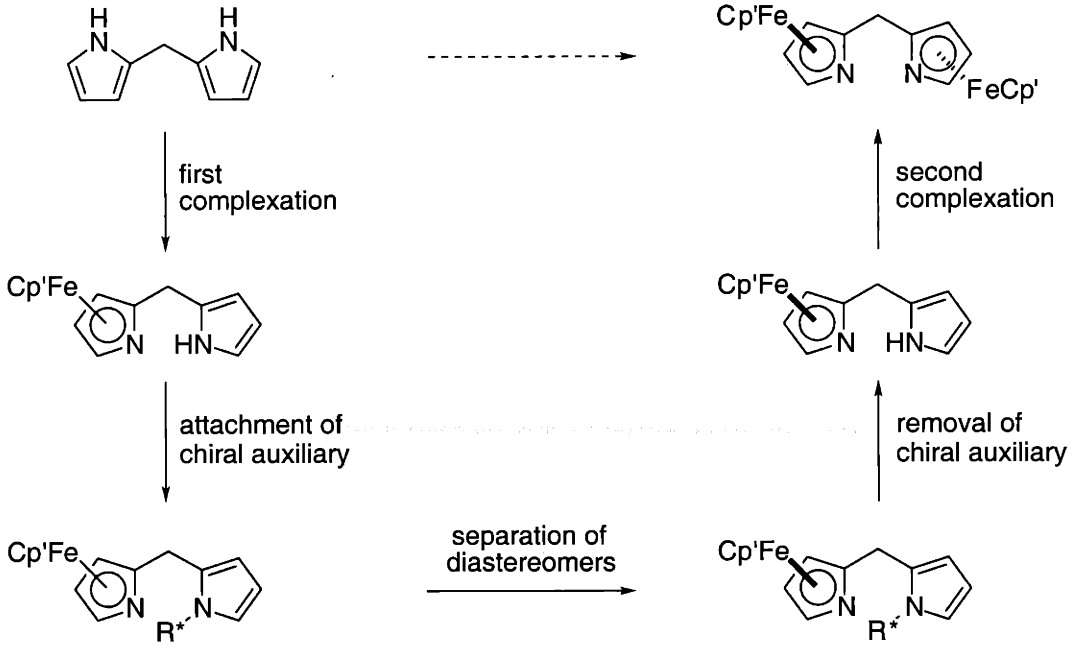


Figure 1.11. ORTEP plot of (*R*,*R*)-**1.22**, with thermal ellipsoids drawn at the 35% probability level.

Both of the depicted enantiomers have the (*R*,*R*) configuration.[42,43] There are no unusual structural features in these bis(azaferrocenes): The iron atom is 1.64–1.66 Å from the pyrrolyl ring and the cyclopentadienyl ring, and these rings are roughly parallel to each other (angle of deviation < 2°).

We have devised the following alternative route involving diastereomeric derivatives to circumvent the need for HPLC (Scheme 1.2). This route is useful when either the bis(azaferrocene) cannot be resolved by chiral HPLC or when a large quantity of a single enantiomer is required.



Scheme 1.2. Alternative method to prepare enantiomerically pure bis(azaferrocenes).

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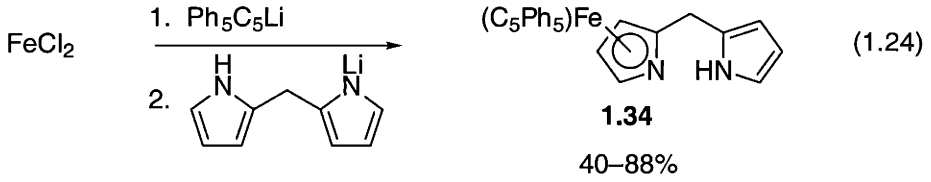
42 There have been confusion and conflict in the assignment of stereochemical descriptors to metallocene-type planar-chiral complexes. Schlögl originally proposed a system in which the metal atom is always viewed beneath the plane (Schlögl, K.; Pelousek, H.; Mohar, A. *Monatsh. Chem.* **1961**, *92*, 533–541), but later Cahn, Ingold, and Prelog extended their rules for central-chiral compounds to these compounds as well (Cahn, R. S.; Ingold, C.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385–415). The two systems do not agree with each other, and Schlögl later withdrew his model in favor of the Cahn–Ingold–Prelog system (Schlögl, K. *Top. Stereochem.* **1967**, *1*, 39–91). Despite Schlögl's decision, many chemists still adhere to the Schlögl system. For example, see: Hayashi, T. In *Ferrocenes: Homogeneous Catalysis, Organic Synthesis, Materials Science*; Togni, A., Hayashi, T., Eds.; VCH: New York, 1995; Chapter 2.

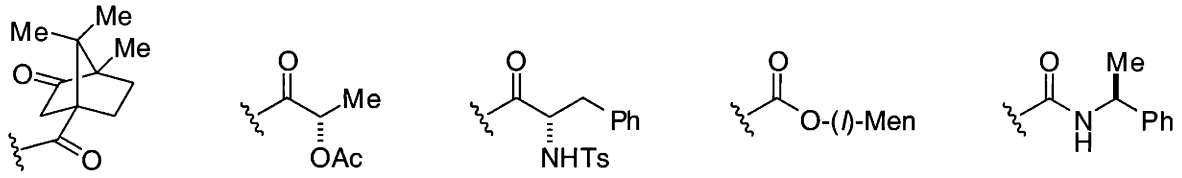
43 All stereochemical descriptors used in this dissertation are based on the Cahn–Ingold–Prelog system.

We sought to validate our scheme by applying it to **1.29**, since the bis(azaferrocene) cannot be resolved by chiral HPLC.[44] Treatment of $FeCl_2$ with the lithiated pentaphenylcyclopentdiene, followed by the monolithio salt of di(pyrrol-2-yl)methane affords azaferrocene (±)-**1.34** in varying yields (40–88%) (eq 1.24).



(1.24)

Many chiral auxiliaries have been investigated for their effectiveness, and those whose diastereomeric azaferrocene adducts can be separated either by flash chromatography or HPLC are listed in Figure 1.12:[45]



1.35 **1.36** **1.37** **1.38** **1.39**

Figure 1.12. Chiral auxiliaries whose diastereomeric azaferrocenes can be separated.

Among these auxiliaries, we determined **1.38** to be the auxiliary of choice. Thus, azaferrocene **1.40** was prepared in quantitative yield by deprotonating (±)-**1.34** and subsequently acylating it with (*l*)-menthyl chloroformate (eq 1.25).

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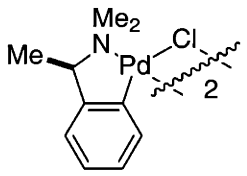
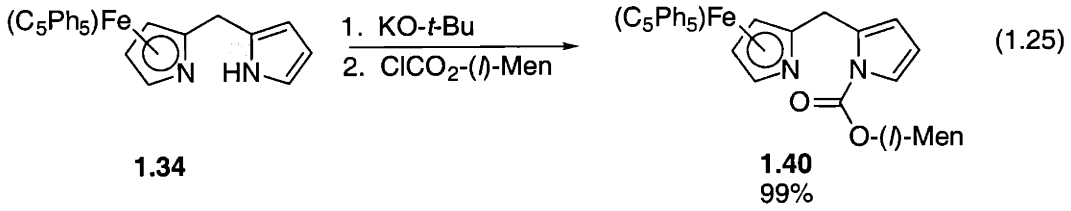
44 We have attempted in vain to resolve (±)-**1.29** by crystallization with tartaric acid and complexation with the following palladium complex.

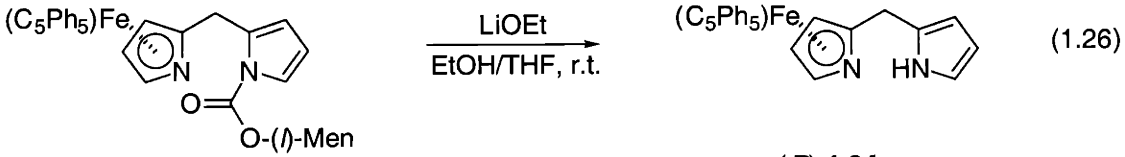


45 See Experimental for further discussions on the separation of these diastereomeric azaferrocene adducts.



1.34 **1.40** 99% (1.25)

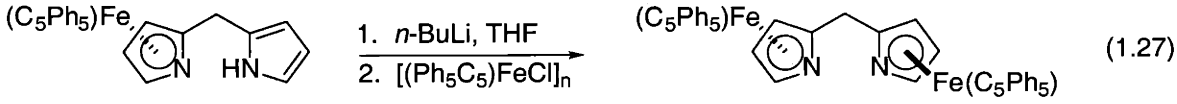
The diastereomeric azaferrocenes **1.40** were separated,[46] and the chiral auxiliary was removed by deacylation with LiOEt in ethanol/THF. No loss in optical purity was detected (eq 1.26).



(*R,l*)-**1.40** 93% de

(*R*)-**1.34** 92% ee 100% yield (1.26)

To complete the synthesis of (*R,R*)-**1.29**,[47] azaferrocene (*R*)-**1.34** was deprotonated and treated with $[(Ph_5C_5)FeCl]_n$ (eq 1.27). AgCN was omitted in this step as it leads to substantial racemization of the product **1.29**.



(*R*)-**1.34** 92% ee

(*R,R*)-**1.29** 88% ee 30% yield (1.27)

The enantiomeric excess of **1.29** was determined by ^{1}H NMR using (*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol as a chiral solvating agent (CSA).[48] Figure 1.13 shows how the protons at the 5-position (H_a) are rendered non-equivalent under the influence of the chiral alcohol.

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46 Ironically, the most efficient method that we have found to separate the diastereomers of **1.40** is *still* chiral HPLC.

47 The assignment of absolute stereochemistry is based on its sense of asymmetric induction in copper-catalyzed reactions. See Experimetal for details.

48 For a review on chiral solvating agents, see: Pirkle, W. H.; Hoover, D. J. *Top. Stereochem.* **1982**, *13*, 263–331.

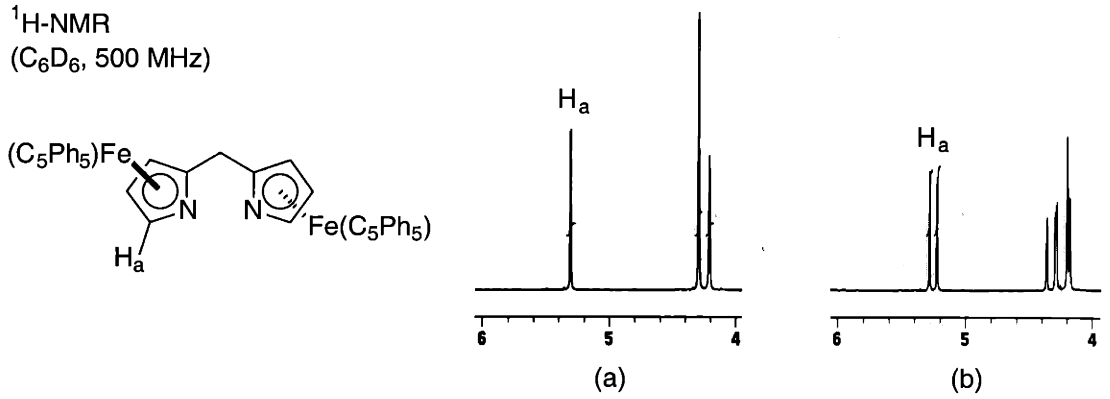

Figure 1.13. ^{1}H NMR spectra of (a) (±)-**1.29**, (b) (±)-**1.29** and (*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol.

III. X-ray Crystal Structures of [Metal•Bis(azaferrocene)] Complexes.

After a number of C_2-symmetric bis(azaferrocenes) had been successful synthesized, we became interested in the steric environment that these bidentate ligands create with a metal center, and whether the designated structural perturbations actually change the ligand geometry. A literature survey showed only one example in which the substituent effect on the bridging atom can be deduced from analogous metal•bis(oxazoline) complexes.[49]

In our investigation of the copper-catalyzed asymmetric cyclopropanation of olefins, we discovered that Cu(I)-bis(azaferrocene) complexes have a tendency to form highly crystalline solids with styrene, even when the bis(azaferrocene) itself is not stable. We have characterized three of those complexes (derived from **1.19**, **1.25**, and **1.29**) by X-ray crystallography.[50] Shown in the following are the ORTEP plots of these structures with the olefin, counterion, and solvent molecules omitted (Figures 1.14–1.16).[51]

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49 The metal•bis(oxazoline) complexes have the structure [$W(CO)_4$•bis(oxazoline)]. See: Bennett, S.; Brown, S. M.; Conole, G.; Kessler, M.; Rowling, S.; Sinn, E.; Woodward, S. *J. Chem. Soc., Dalton Trans.* **1995**, 367–376.

50 For the first report of a [CuOTf•ligand•olefin] complex, see: Quan, R. W.; Li, Z.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1996**, *118*, 8156–8157.

51 The ORTEP plots show the copper complexes as C_2-symmetric, but in reality they are C_1-symmetric because of the presence of a π-bound styrene.

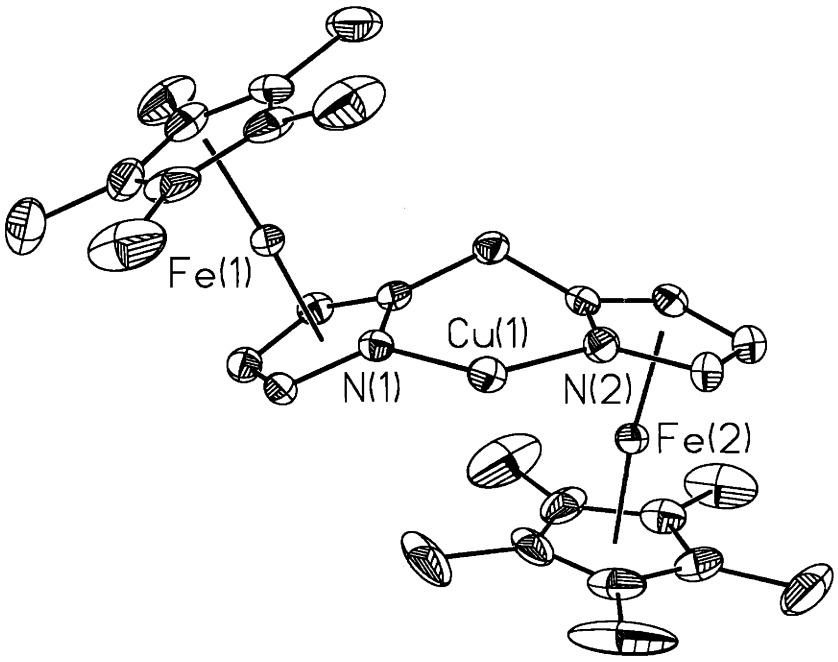


Figure 1.14. ORTEP plot of [CuOTf•(*S*,*S*)-**1.19**] complex, with thermal ellipsoids drawn at the 35% probability level.

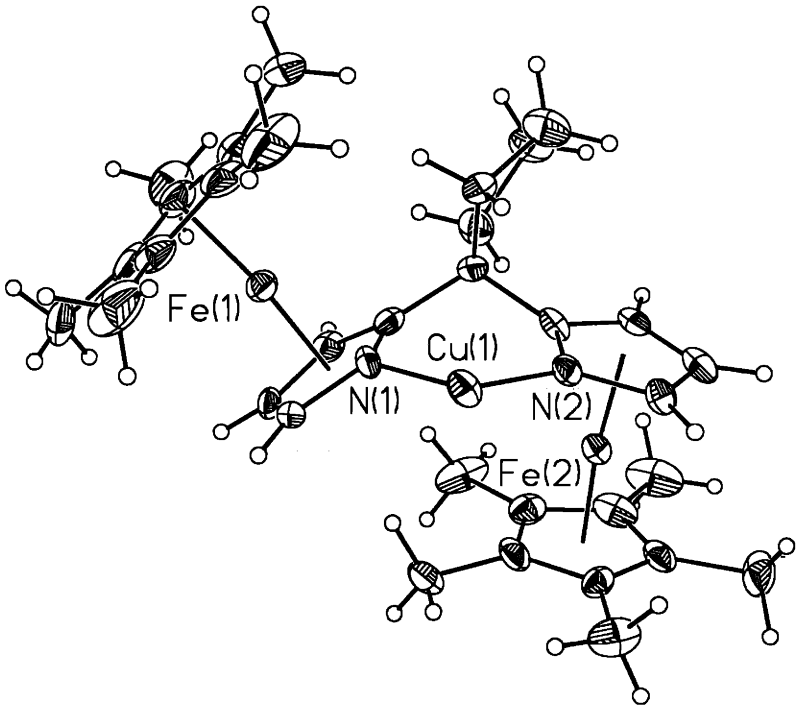


Figure 1.15. ORTEP plot of [CuOTf•(±)-**1.25**] complex, with thermal ellipsoids drawn at the 35% probability level.

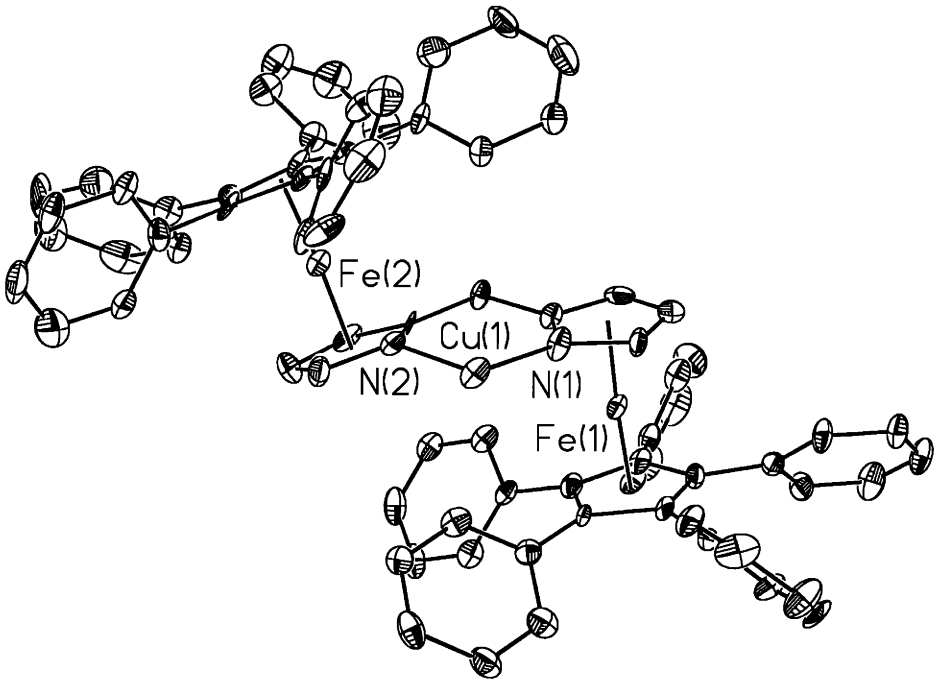


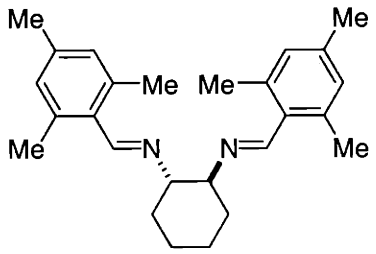
Figure 1.16. ORTEP plot of [CuOTf•(±)-**1.29**] complex, with thermal ellipsoids drawn at the 35% probability level.

Listed in Table 1.4 are some of the interesting structural parameters, such as the metal–nitrogen distances, the ligand bite angle (∠ N–Cu–N) θ, the ∠ C(azaferrocene)–C(bridging)–C(azaferrocene) angle Φ, the iron–cyclopentadiene distance, the iron–pyrrole distance, and the angle between the cyclopentadiene ring and the pyrrole ring.

Table 1.4. Comparison of some structural parameters in [CuOTf•bis(azaferrocene)•styrene] complexes.

ligand	**1.19**	**1.25**	**1.29**
Cu–N (Å)	1.946(4), 1.954(3)	1.963(8), 1.966(7)	1.96(1), 1.98 (1)
Φ (°)	117.3(3)	110.5(7)	119.4(11)
θ (°)	97.6(1)	96.3(3)	97.0(5)
Fe – Cp (Å)	1.646(2), 1.655(2)	1.657(4), 1.658(4)	1.664(6), 1.666(6)
Fe – pyrrole (Å)	1.659(2), 1.661(2)	1.670(4), 1.673(4)	1.688(7), 1.691(6)
∠ Cp – pyrrole (°)	3.8(2), 6.5(2)	7.5(6), 10.1(5)	3.3(3), 4.2(4)

On average, the complexes from bis(azaferrocenes) **1.19**, **1.25**, and **1.29** have shorter Cu–N distances (1.94–1.98 Å) than the Jacobsen diimine **1.41** (1.99(1), 2.00(1) Å).[50]

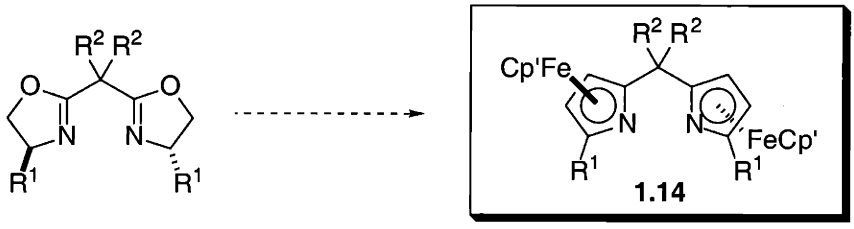


1.41

Substitution at the bridging carbon decreases Φ (117° → 111°), but the decrease does not change the ligand bite angle (98° → 96°) to the same extent. In addition, the substitution causes the cyclopentadiene ring and the pyrrole ring to deviate more from coplanarity (3.8°, 6.5° → 7.5°, 10.1°); this may be due to repulsion between the carbon atom of the spiro bridge and the methyl group of the Cp* ring. Replacing the Cp* ring by a more electron-deficient and sterically demanding Ph_5C_5 ring pushes the iron atom slightly further from the pyrrole ring (1.66 Å → 1.69 Å).

C. Conclusions.

We have discussed the evolution of our ligand design from planar-chiral heterocycles to C_2-symmetric bis(azaferrocenes), as well as their relationship with the bis(oxazolines). The first member in the bis(azaferrocene) family, **1.19** (R^1 = H, R^2 = H, Cp' = Cp*), was synthesized after we discovered that transition metals can improve the diastereoselection during the double π-complexation of di(pyrrol-2-yl)methane. Analogs bearing different R^1 and Cp' were also synthesized, but attempts to introduce substituents at the bridging carbon (R^2) failed to give a bis(azaferrocene) that is stable enough for further manipulation.



Two methods have been developed to obtain the bis(azaferrocenes) in enantiomerically pure form. Separation of the enantiomers by chiral HPLC gives access to a small amount of material rapidly, while the preparation of diastereomeric derivatives can be used for a large quantity of a single enantiomer, or when the bis(azaferrocene) is not resolvable by chiral HPLC.

Some of these bis(azaferrocenes) have been characterized by X-ray crystallography, either in the free form or bound to [CuOTf•styrene]. The structural information thus revealed improves our understanding of the effect of different substituents on the properties of bis(azaferrocenes) as ligands.

D. Experimental.

I. General.

^{1}H and ^{13}C nuclear magnetic resonance spectra were recorded on a Varian Unity-300 or a Varian VXR-500 NMR spectrometer at ambient temperature. ^{1}H data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane (δ scale), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, and br = broadened), integration, and coupling constant (Hz). ^{13}C chemical shifts are reported in parts per million downfield from tetramethylsilane (δ scale). All ^{13}C spectra were determined with broadband ^{1}H decoupling.

Infrared spectra were obtained on a Perkin-Elmer Series 1600 FT-IR spectrophotometer. High resolution mass spectra were recorded on a Finnegan MAT System 8200 spectrometer or a Bruker Daltonics Apex FT-ICR-MS (3 Tesla). Melting points were obtained on a Thomas Hoover Unimelt capillary melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter and are reported as follows: $[\alpha]^{\text{Temp }(^{\circ}C)}_{\lambda\ (nm)}$ (*c* solvent, enantiomeric purity).

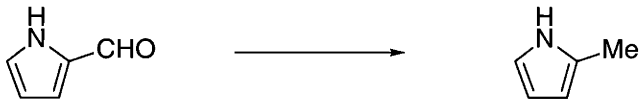
Analytical chiral HPLC was performed on either a Daicel Chiralcel OD column (4.6 mm x 25 cm), Daicel Chiralpak AD column (4.6 mm x 25 cm), or a Regis (*R,R*) Whelk-O 2 column (4.6 mm x 25 cm). Semi-preparative chiral HPLC was performed on either a Daicel Chiralcel OD column (1.0 cm x 25 cm) or a Daicel Chiralpak AD column (1.0 cm x 25 cm). Analytical TLC was performed using EM Science 0.25 mm silica gel 60 plates and visualized with UV light. Flash chromatography was performed on EM Science silica gel 60 (230–400 mesh).

Solvents were distilled under nitrogen from the indicated drying agents: THF (Na/benzophenone); Et_2O (Na/benzophenone).

Unless otherwise stated, all reagents were purchased from commercial suppliers and used as received. Di(pyrrol-2-yl)methane,[52] 2,2-di(pyrrol-2-yl)propane,[53] **1.15**,[54] and pentaarylcyclopentadienes[38b] were synthesized according to literature procedures.

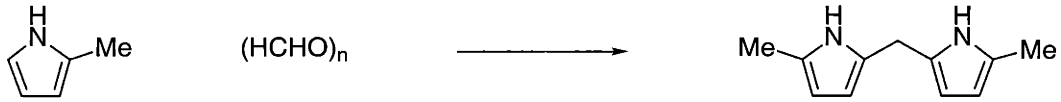
All reactions were carried out with magnetic stirring in oven-dried glassware under an atmosphere of argon (manifold) or under an atmosphere of nitrogen (Vaccum Atmospheres glove box), unless otherwise noted.

II. Preparation of Di(pyrrol-2-yl)alkanes.



2-Methylpyrrole. Pyrrole-2-carboxaldehyde (20.0 g, 0.210 mol) and KOH (40.6 g, 0.724 mol) were dissolved in 300 mL ethylene glycol. Hydrazine hydrate (27 mL, 0.87 mol) was added, turning the reaction mixture into a thick yellow slurry. The reaction mixture was then brought to reflux for 1 h, during which the yellow solid dissolved. Distillation under reduced pressure afforded water and the product (11.3 g, 66 % yield) as a colorless liquid in separate phases.

The ^{1}H NMR spectrum of the product matched the literature data.[55]



Di(5-methylpyrrol-2-yl)methane. The procedure was modified from the procedure of Lee for the synthesis of di(pyrrol-2-yl)methane.[56] 2-Methylpyrrole (11.9 g, 146 mmol) and aqueous formaldehyde (2.53 g, 31.2 mmol) were mixed and stirred for 5

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52 Wang, Q. M.; Bruce, D. W. *Synlett* **1995**, 1267–1268.
53 Brown, W. H.; French, W. N. *Can. J. Chem.* **1958**, *36*, 372–377.
54 Ruble, J. C.; Fu, G. C. *J. Org. Chem.* **1996**, *61*, 7230–7231.
55 Lash, T. D.; Richter, D. T.; Shiner, C. M. *J. Org. Chem.* **1999**, *64*, 7973–7982.
56 Ka, J.-W.; Lee, C.-H. *Tetrahedron Lett.* **2000**, *41*, 4609–4613.

min at 60 °C. Trifluoroacetic acid (0.25 mL, 3.3 mmol) was added dropwise, rapidly turning the slight yellow reaction mixture to deep brown. After 30 min, the reaction mixture was quenched with 1M NaOH, diluted with water, and extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$) and concentrated in vacuo to afford a brown liquid. Distillation of the crude product first removed excess 2-methylpyrrole, and then the desired product as a brown liquid (1.94 g, 36% yield).

The ^1H NMR spectrum of the product matched the literature data.[57] ^{13}C NMR (126 MHz, $CDCl_3$): δ 13.2, 26.8, 105.9, 106.4, 127.5, 128.1.

1,1-Di(pyrrol-2-yl)cyclopentane. Pyrrole (27 mL, 0.39 mol) was dissolved in EtOH (50 mL) and cooled to 0 °C. Concentrated HCl (2 mL) was added dropwise, followed by cyclopentanone (8.5 mL, 0.096 mol). The resultant dark green solution was stirred at r.t.. After 2 days, the reaction mixture was quenched with K_2CO_3, diluted with water, and extracted with EtOAc. The organic layer was dried (K_2CO_3) and concentrated in vacuo to afford a dark brown liquid. Distillation of the crude product first removed excess pyrrole and cyclopentanone, and then the desired product as a yellow liquid (2.20 g, 4.4% yield).

^1H NMR (500 MHz, $CDCl_3$): δ 1.74–1.78 (m, 4H), 2.12–2.18 (m, 4H), 6.08–6.10 (m, 2H), 6.10–6.12 (m, 2H), 6.58–6.60 (m, 2H), 7.66 (s br, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 24.0, 39.5, 47.3, 104.4, 107.8, 117.4, 137.8. mp 93–95 °C. HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{16}N_2$, 223.1206; found, 223.1206.

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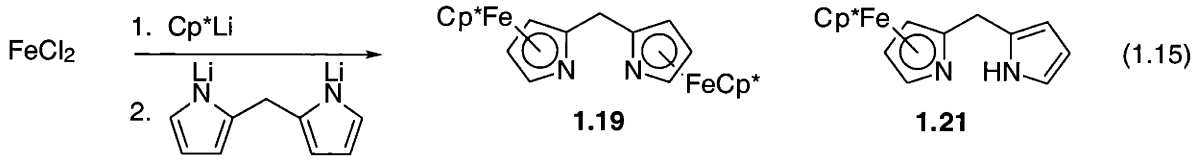
57 Butler, A. R.; Shepherd, P. T. *J. Chem. Soc., Perkin Trans. 2* **1980**, 113–116.

III. Diastereoselective Complexation of Cp*Fe to Di(pyrrol-2-yl)methane: Effect of Transition Metal Salts.



(1.15)

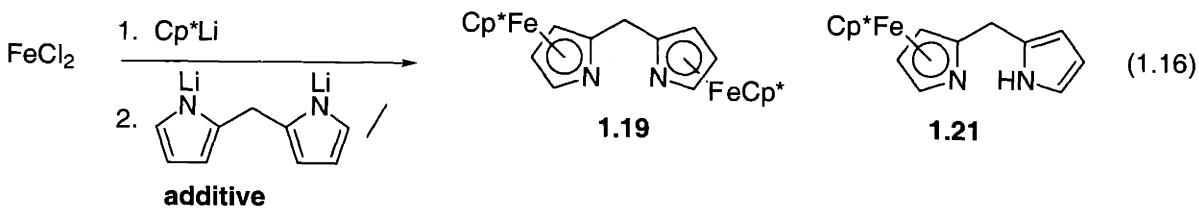
n-BuLi (1.6 M in hexanes; 0.65 mL, 1.04 mmol) was added to a solution of Cp*H (140 mg, 1.03 mmol) in THF (10 mL), forming a creamy yellow slurry. After stirring for 15 min at r.t., the slurry was transferred by cannula to a rapidly stirring suspension of $FeCl_2$ (128 mg, 1.01 mmol) in THF (10 mL) at 0 °C, affording a green solution of $[Cp^*FeCl]_n$.

n-BuLi (1.6 M in hexanes; 0.65 mL, 1.04 mmol) was added to a solution of di(pyrrol-2-yl)methane (74.5 mg, 0.510 mmol) in THF (5 mL). The resulting brown solution was stirred for 15 min, and then this solution was transferred by cannula to the 0 °C solution of $[Cp^*FeCl]_n$ (*vide supra*), resulting in a brown reaction mixture. The reaction was allowed to warm to r.t. and stirred for 6 days. It was then quenched by the addition of MeOH and concentrated in vacuo to afford the crude product, which was purified by flash chromatography (5/30/65 Et_3N/EtOAc/hexanes → 5/95/0 → 5/15/80 Et_3N/MeOH/EtOAc) to give two fractions: (±)-**1.21** (125 mg, 37% yield) with a trace amount of (±)-**1.19**, and *meso*-**1.19** (45.8 mg, 9% yield).

(±)-**1.19.** ^1H NMR (500 MHz, C_6D_6): δ 1.88 (s, 30H), 3.73 (d, 2H, J = 2.0), 3.86 (d, 2H, J = 2.0), 4.04 (s, 2H), 4.83 (s, 2H). ^{13}C NMR (75 MHz, C_6D_6): δ 11.8, 30.4, 73.2, 75.8, 81.1, 92.7, 107.0. IR (KBr): 2965, 2903, 1476, 1445, 1380, 1142, 1030, 922, 809 cm^{-1}. mp 150 °C dec. HRMS–EI (*m/z*): M^+ calcd for $C_{29}H_{38}Fe_2N_2$, 526.1734; found, 526.1733. Anal. Calcd for $C_{29}H_{38}Fe_2N_2$: C, 66.18; H, 7.28; N, 5.32. Found: C, 66.13; H, 7.45; N, 5.55.

meso-**1.19.** ^{1}H NMR (300 MHz, C_6D_6): δ 1.83 (s, 30H), 3.82 (s, 2H), 3.98 (d, 1H, J = 15.7), 4.04 (s, 2H), 4.12 (d, 1H, J = 15.7), 4.84 (s, 2H). ^{13}C NMR (75 MHz, C_6D_6): δ 11.4, 29.6, 73.1, 75.3, 80.7, 92.6, 106.3.

1.21. ^{1}H NMR (500 MHz, C_6D_6): δ 1.69 (s, 15H), 3.63 (d, 1H, J = 2.1), 3.73 (d, 1H, J = 1.5), 3.73 (d, 1H, J = 16.2), 3.84 (d, 1H, J = 16.5), 4.78 (s, 1H), 6.22 (s, 1H), 6.35 (q, 1H, J = 3.0), 6.48 (q, 1H, J = 2.1), 9.39 (s br, 1H). ^{13}C NMR (126 MHz, C_6D_6): δ 11.1, 27.2, 72.8, 75.4, 81.1, 92.0, 105.6, 106.1, 108.5, 116.9, 130.0. HRMS–ESI (m/z): $[M + H]^+$ calcd for $C_{19}H_{24}FeN_2$, 337.1362; found, 337.1357.



(1.16)

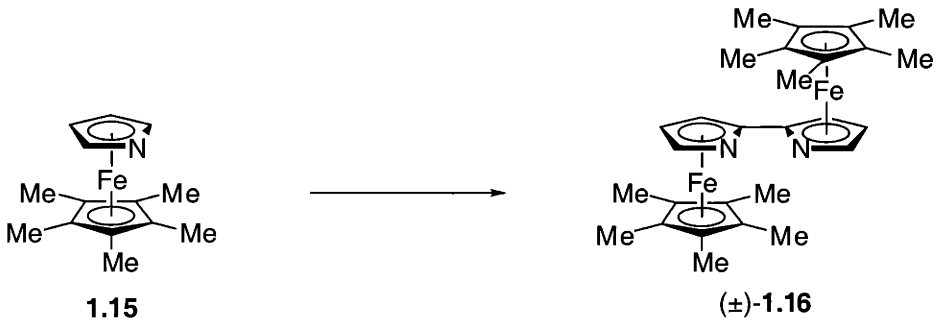
General procedure. *n*-BuLi (1.6 M in hexanes; 1.33 mL, 2.13 mmol) was added to a solution of Cp*H (277 mg, 2.03 mmol) in THF (20 mL), forming a creamy yellow slurry. After stirring for 15 min at r.t., the slurry was transferred by cannula to a rapidly stirring suspension of $FeCl_2$ (263 mg, 2.08 mmol) in THF (20 mL) at -20 °C, affording a green solution of $[Cp^*FeCl]_n$.

n-BuLi (1.6 M in hexanes; 0.67 mL, 1.07 mmol) was added to a solution of di(pyrrol-2-yl)methane (74.7 mg, 0.511 mmol) in THF (10 mL). The resulting brown solution was stirred for 15 min, and then half of it was transferred to a suspension of the additive (0.26 mmol) in THF (10 mL). After 30 min, this solution was transferred by cannula to half of the -20 °C solution of $[Cp^*FeCl]_n$ (*vide supra*), resulting in a brown reaction mixture. The reaction was allowed to warm to r.t. and stirred for 6 h. It was then quenched by the addition of a solution of 2,2′-bipyridine (123 mg, 0.788 mmol) in

MeOH (10 mL). The reaction mixture was filtered through a plug of silica gel with Et_2O as the eluant to afford the crude product for NMR analysis.

	NMR yield (%)		
additive	*rac*-**1.19**	*meso*-**1.19**	**1.21**
$NiCl_2$	25	54	21
CuCN	27	16	26
AgCN	35	10	48
$ZnCl_2$	20	13	8

IV. Preparation of C_2-Symmetric Bisazaferrocenes.

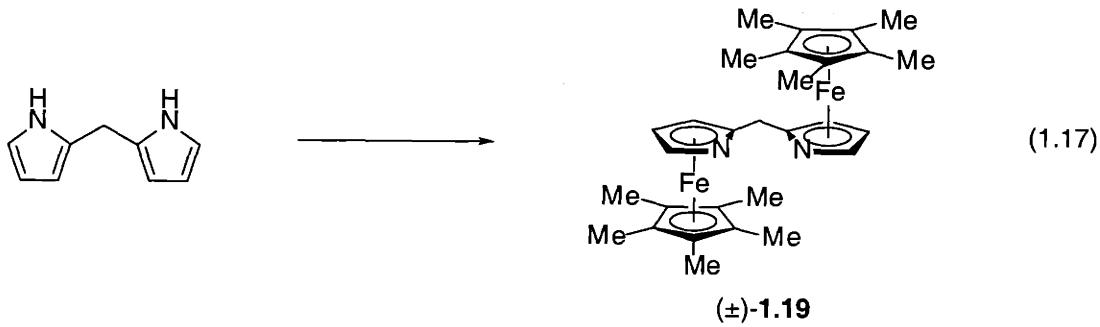


1.15 (±)-**1.16** (1.11)

Synthesis of (±)-1.16. *n*-BuLi (1.6 M in hexanes; 0.34 mL, 0.54 mmol) was added to a solution of **1.15** (127 mg, 0.494 mmol) in THF (10 mL) at -78 °C, and warmed up to 0 °C for 15 min. The solution was transferred by cannula to a stirring suspension of CuI (96.9 mg, 0.509 mmol) in THF (10 mL) at -78 °C, and again warmed up to 0 °C for 15 min. A solution of 1,4-dinitrobenzene (255 mg, 1.52 mmol) in THF (1 mL) was introduced to the reaction mixture, which was then brought to reflux for 18 h. It was cooled down to r.t., quenched by a solution of 2,2'-bipyridine (265 mg, 1.70 mmol), filtered through a plug of silica with EtOAc as the eluant to afford the crude product. Initial purification by flash chromatography (30/70 EtOAc/hexanes) afforded (±)-**1.16** as

a brown solid (17.6 mg, 21% yield after corrected for impurities). The analytical sample was obtained through purification by flash chromatography inside the glove box.

(±)-**1.16.** ^{1}H NMR (300 MHz, C_6D_6): δ 1.71 (s, 30 H), 4.07 (d, 2H, J = 1.8), 4.73 (d, 2H, J = 1.8), 5.08 (s, 2H). ^{13}C NMR (75 MHz, C_6D_6): δ 11.3, 71.3, 75.7, 81.5, 92.8, 102.3. HRMS–EI (m/z): M^+ calcd for $C_{28}H_{36}Fe_2N_2$, 512.1577; found, 512.1574.



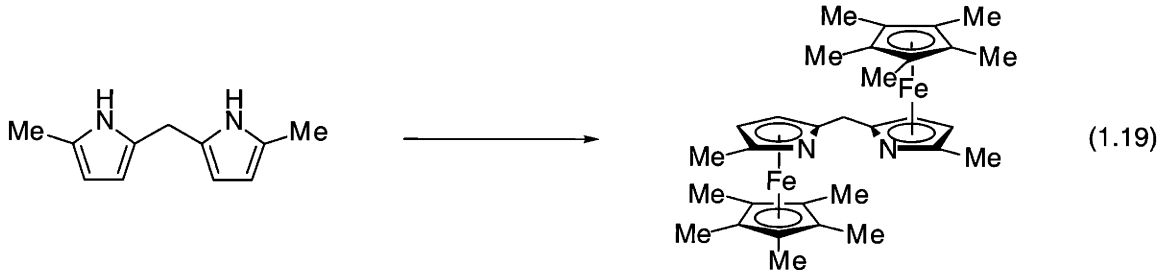
(1.17)

(±)-**1.19**

Synthesis of (±)-1.19. *n*-BuLi (1.6 M in hexanes; 15.2 mL, 24.3 mmol) was added to a solution of Cp*H (3.33 g, 24.4 mmol) in THF (150 mL), forming a creamy yellow slurry. After stirring for 15 min at r.t., the slurry was transferred by cannula to a rapidly stirring suspension of $FeCl_2$ (3.24 g, 25.5 mmol) in THF (100 mL) at -20 °C, affording a green solution of $[Cp^*FeCl]_n$.

n-BuLi (1.6 M in hexanes; 8.00 mL, 12.8 mmol) was added to a solution of di(pyrrol-2-yl)methane (0.895 g, 6.10 mmol) in THF (40 mL). The resulting brown solution was stirred for 15 min, and then it was transferred by cannula to a stirring suspension of AgCN (0.841 g, 6.30 mmol) in THF (20 mL). The white AgCN dissolved slowly, producing a deep-brown reaction mixture. This solution was transferred by cannula to the -20 °C solution of $[Cp^*FeCl]_n$ (*vide supra*), resulting in a brown reaction mixture. The reaction was allowed to warm to r.t. and stirred for 6 h. It was then quenched by the addition of a solution of 2,2′-bipyridine (2.46 g, 15.7 mmol) in MeOH (10 mL). The reaction mixture was filtered through a plug of silica gel, thereby removing a sticky,

purple-red solid. The filtrate was concentrated to give a purple solid, which was purified by flash chromatography (5/25/75 Et_3N/EtOAc/hexanes → 5/75/25 → 5/100 Et_3N/hexanes). Yellow decamethylferrocene eluted first, followed by (±)-**1.19** (removal of solvent afforded a deep-red solid: 2.12 g, 66% yield), and then *meso*-**1.19** (0.81 g, 25% yield).



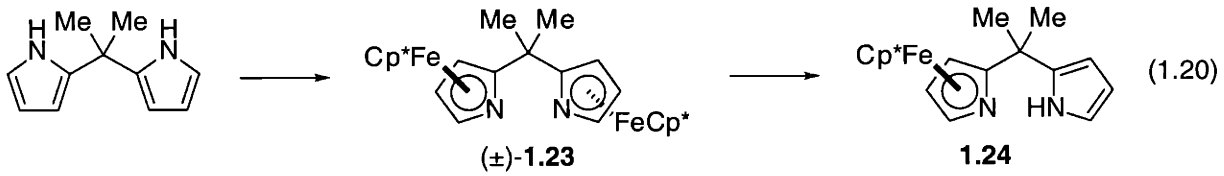
(1.19)

(±)-**1.22**

Synthesis of (±)-1.22. A slurry of Cp*Li (4.56 g, 32.0 mmol) was transferred by cannula to a rapidly stirring suspension of $FeCl_2$ (4.16 g, 32.8 mmol) in THF (300 mL) at -10 °C, affording a green solution of $[Cp^*FeCl]_n$.

n-BuLi (1.6 M in hexanes; 11.0 mL, 17.6 mmol) was added to a solution of di(5-methylpyrrol-2-yl)methane (1.41 g, 8.07 mmol) in THF (60 mL). The resulting brown solution was stirred for 1 hour, and transferred to AgOAc (1.36 g, 8.12 mmol). The white AgOAc dissolved slowly, producing a black reaction mixture. This solution was transferred by cannula to the -10 °C solution of $[Cp^*FeCl]_n$ (*vide supra*), resulting in a brown reaction mixture. The reaction was allowed to warm to r.t. and stirred for 40 h. It was then quenched by the addition of a solution of 2,2'-bipyridine (6.34 g, 40.6 mmol) in MeOH (20 mL). The reaction mixture was filtered through a plug of silica gel, thereby removing a sticky, purple-red solid. The filtrate was concentrated to give a brown solid, which was purified by flash chromatography (1/30/70 Et_3N/MTBE/hexanes) to afford (±)-**1.22** as an orange solid (2.73 g, 61% yield).

(±)-**1.22.** ^{1}H NMR (500 MHz, C_6D_6): δ 1.86 (s, 30H), 2.06 (s, 6H), 3.54 (d, 2H, J = 2.1), 3.86 (d, 2H, J = 2.1), 4.00 (s, 2H). ^{13}C NMR (126 MHz, C_6D_6): δ 11.1, 14.8, 30.5, 73.5, 74.0, 80.5, 102.5, 106.2. IR (KBr): 3084 (w), 2973 (m), 2950 (m), 2903 (s), 1480 (m), 1444 (m), 1419 (m), 1381 (s), 1369 (m), 1271 (m), 1032 (m), 941 (m), 821 (m) cm^{-1}. HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{31}H_{42}Fe_2N_2$, 555.2120; found, 555.2116.



(±)-**1.23** **1.24** (1.20)

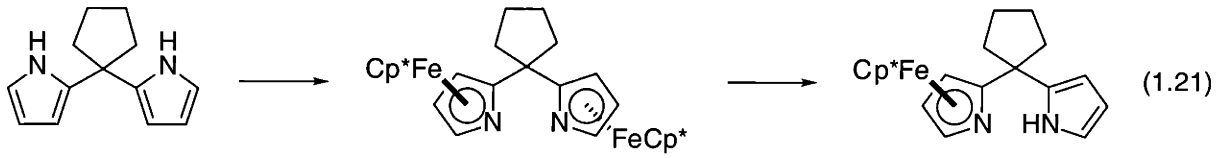
Attempted synthesis of (±)-1.23. Cp*Li (328 mg, 2.31 mmol) and $FeCl_2$ (377 mg, 2.32 mmol) were mixed in a round-bottom flask and cooled to -20 °C. THF (20 mL) was slowly introduced, affording a green solution of $[Cp^*FeCl]_n$.

n-BuLi (1.48 M in hexanes; 0.82 mL, 1.21 mmol) was added to a solution of 2,2-di(pyrrol-2-yl)propane (99.9 mg, 0.580 mmol) in THF (5 mL). The resulting brown solution was stirred for 45 min, and then it was added to AgCN (78.2 mg, 0.58 mmol). After 30 min, this solution was transferred by cannula to the -20 °C solution of $[Cp^*FeCl]_n$ (*vide supra*), resulting in a brown reaction mixture. The reaction was allowed to warm to r.t. and stirred for 5 days. It was then quenched by the addition of a solution of 2,2′-bipyridine (450 mg, 2.88 mmol) in MeOH (5 mL). The reaction mixture was filtered through a plug of silica, and **1.24** was found to be the major azaferrocene in the crude product. It was purified by flash chromatography (1/100 Et_3N/hexanes → 1/5/95 Et_3N/EtOAc/hexanes → 1/20/80; 1/100 Et_3N/hexanes → 1/2/98 Et_3N/MTBE/hexanes → 1/4/96) to afford **1.24** as an orange solid (81.8 mg, 39% yield).

Azaferrocene (±)-**1.24** was resubjected to the above reaction conditions and the crude product was examined by ^{1}H NMR. Signals consistent with (±)-**1.23** were identified.

(±)-**1.23.** ^{1}H NMR (500 MHz, C_6D_6): δ 1.82 (s, 30H), 2.30 (s, 6H), 3.68 (d, 2H, J = 2), 3.88 (d, 2H, J = 2), 4.75 (s, 2H).

1.24. ^{1}H NMR (500 MHz, C_6D_6): δ 1.42 (s, 3H), 1.58 (s, 15H), 1.83 (s, 3H), 3.74–3.76 (m, 2H), 4.79 (s, 1H), 6.28–6.31 (m, 1H), 6.42 (q, 1H, J = 3.0), 6.69–6.71 (m, 1H), 10.86 (s br, 1H). ^{13}C NMR (126 MHz, C_6D_6): δ 11.2, 26.1, 35.9, 38.2, 68.7, 69.0, 75.5, 81.1, 92.1, 103.5, 107.9, 116.4, 140.0.



(±)-**1.25** **1.26** (1.21)

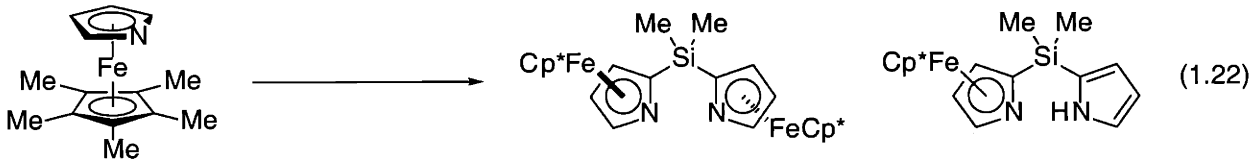
Attempted synthesis of (±)-1.25. Cp*Li (1.46 g, 10.3 mmol) and $FeCl_2$ (1.67 g, 10.3 mmol) were mixed in a round-bottom flask and cooled to -20 °C. THF (50 mL) was slowly introduced, affording a green solution of $[Cp^*FeCl]_n$.

n-BuLi (1.48 M in hexanes; 1.46 mL, 2.16 mmol) was added to a solution of 1,1-di(pyrrol-2-yl)cyclopentane (204 mg, 1.03 mmol) in THF (5 mL). The resulting brown solution was stirred for 30 min, and then it was added to AgCN (139 mg, 1.04 mmol). After 45 min, this solution was transferred by cannula to the -20 °C solution of $[Cp^*FeCl]_n$ (*vide supra*), resulting in a brown reaction mixture. The reaction was allowed to warm to r.t. and stirred for 1 day. It was then quenched by the addition of a solution of 2,2′-bipyridine (~ 4.5 g) in MeOH (20 mL). The reaction mixture was filtered through a plug of Celite, and ^{1}H NMR showed that the azaferrocene product consists mainly of (±)-**1.25** and a smaller amount of **1.26**.

Attempts to purify the crude product by flash chromatography with neutral alumina (5/95 EtOAc/hexanes → 10/90) afforded only **1.26**. Fractional recrystallization of the crude product in pentane at -35 °C afforded (±)-**1.25** with some 2,2'-bipyridine. On standing, (±)-**1.25** slowly decomposes to give **1.26**.

(±)-**1.25.** ^{1}H NMR (500 MHz, C_6D_6): δ 1.86 (s, 30 H), 2.26–2.46 (m, 6H), 2.92–3.02 (m, 2H), 3.59 (d, 2H, J = 2.1), 3.79 (d, 2H, J = 2.4), 4.93 (s, 2H).

1.26. ^{1}H NMR (500 MHz, C_6D_6): δ 1.4–1.8 (m, 4H), 1.65 (s, 15H), 1.8–2.0 (m, 2H), 2.3–2.4 (m, 1H), 2.6–2.8 (m, 1H), 3.71 (d, 1H, J = 2), 3.76 (d, 1H, J = 2), 4.79 (s, 1H), 6.25 (s, 1H), 6.4 (s, 1H), 6.7 (s, 1H), 11.1 (s br, 1H).



1.15 (±)-**1.27** **1.28** (1.22)

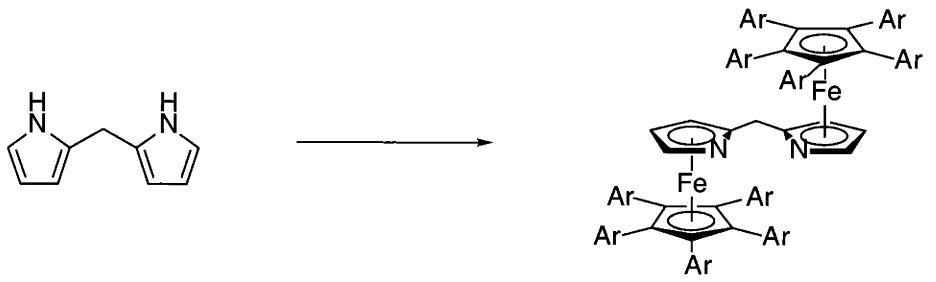
Attempted synthesis of (±)-1.27. *n*-BuLi (1.6 M in hexanes; 0.34 mL, 0.54 mmol) was added to a solution of **1.15** (127 mg, 0.494 mmol) in THF (10 mL) at -78 °C, and warmed up to 0 °C for 15 min. Me_2SiCl_2 (30 μL, 0.25 mmol) was added to the reaction mixture, and it was stirred at r.t. overnight. The reaction mixture was concentrated in vacuo to give a brown solid. This was purified by flash chromatography (25/75 EtOAc/hexanes) to afford **1.28** as a less polar orange film (30.8 mg, 33% yield) and a brown solid, which on further purification (flash chromatography, 80/20 EtOAc/acetone → 10/90 Et_3N/EtOAc) afforded (±)-**1.27** as an orange crystalline solid (20.5 mg, 15% yield). One week after (±)-**1.27** was purified and stored in the glove box, azaferrocene **1.28** was detected in the product.

(±)-**1.27.** ^{1}H NMR (300 MHz, C_6D_6): δ 1.02 (s, 6H), 1.82 (s, 30H), 3.90 (d, 2H, J = 2.1), 3.94 (d, 2H, J = 2.4), 5.12 (s, 2H). ^{13}C NMR (75 MHz, C_6D_6): δ 1.5, 11.8, 77.5, 79.8, 80.7, 97.8. HRMS–EI (*m/z*): M^+ calcd for $C_{30}H_{42}Fe_2N_2Si$, 570.1816; found, 570.1815.

1.28. ^{1}H NMR (300 MHz, C_6D_6): δ 0.29 (s, 3H), 0.74 (s, 3H), 1.59 (s, 15H), 3.88 (d, 1H, J = 2.4), 3.99 (d, 1H, J = 2.0), 5.05 (d, 1H, J = 2.0), 6.5–6.6 (m, 1H), 6.75–6.85 (m, 1H), 6.95–

7.0 (m, 1H), 11.1 (s br, 1H). ^{13}C NMR (75 MHz, C_6D_6): δ 2.4, 3.6, 11.1, 77.3, 78.9, 80.9, 96.5, 109.6, 117.4, 117.4, 121.2.

Synthesis of decaarylbis(azaferrocenes) (Table 1.3).



(1.23)

General procedure. *n*-BuLi (1.48 M in hexanes; 0.88 mL, 1.30 mmol) was added to a solution of Ar_5C_5H (1.24 mmol) in THF (10 mL). After stirring for 30 min at r.t., the solution was transferred to a rapidly stirring suspension of $FeCl_2$ (155 mg, 1.22 mmol) in THF (10 mL), affording a green solution of $[(Ar_5C_5)FeCl]_n$.

n-BuLi (1.48 M in hexanes; 0.40 mL, 0.59 mmol) was added to a solution of di(pyrrol-2-yl)methane (41.4 mg, 0.284 mmol) in THF (10 mL). The resulting brown solution was stirred for 15 min, and then it was transferred to AgCN (38.4 mg, 0.287 mmol). After 1 h, this solution was transferred to the solution of $[(Ar_5C_5)FeCl]_n$ (*vide supra*), and heated to 70 °C for 8 h. The reaction was cooled to warm to r.t. and quenched by the addition of a solution of 2,2'-bipyridine (~ 1.2 g) in MeOH (10 mL). The reaction mixture was filtered through a plug of silica with 50/50 EtOAc/hexanes as the eluant to afford the crude product for NMR analysis.

Entry 1, Ar = Ph. The general procedure was followed, except for the generation of $[(Ar_5C_5)FeCl]_n$: In a Schlenk tube, *n*-BuLi (1.45 M in hexanes; 1.37 mL, 2.03 mmol) and Ph_5C_5H (863 mg, 1.93 mmol) were dissolved in toluene (20 mL) and heated to 100 °C for 1 h. Solvent was removed in vacuo, and the residue was redissolved in THF (20

mL). This solution was transferred to $FeCl_2$ (245 mg, 1.93 mmol), and the resultant solution of $[(Ph_5C_5)FeCl]_n$ was stirred at r.t. for another 2 h.

^1H NMR revealed that the crude product was a 64:36 rac:meso mixture. Purification by flash chromatography (1/99 Et_2O/benzene → 5/95) afforded (±)-**1.29** as an orange solid (107.3 mg, 20% yield).

(±)-**1.29.** ^1H NMR (500 MHz, C_6D_6): δ 4.21 (s, 2H), 4.29 (s, 4H), 5.31 (s, 2H), 6.8–7.0 (m, 30H), 7.35 (d, 20H, J = 7.6). ^{13}C NMR (126 MHz, C_6D_6): δ 28.7, 75.6, 79.6, 87.9, 94.8, 109.7, 126.7, 127.5, 132.5, 134.8. HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{79}H_{58}Fe_2N_2$, 1147.3372; found, 1147.3351.

Entry 2, Ar = 3,5-$Me_2C_6H_3$. The general procedure was followed. ^1H NMR revealed that the crude product was a 70:30 rac:meso mixture. Purification by flash chromatography (2/98 Et_2O/benzene → 12/88) twice afforded (±)-**1.30** as an orange solid (50% yield).

(±)-**1.30.** ^1H NMR (500 MHz, $CDCl_3$): δ 1.98 (s, 60 H), 3.87 (s, 2H), 4.28 (d, 2H, J = 1.5), 4.39 (d, 2H, J = 1.5), 5.20 (s, 2H), 6.66 (s, 10H), 6.70 (s, 20H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.3, 31.8, 76.4, 79.5, 87.9, 94.5, 110.2, 127.9, 130.4, 135.0, 136.0. HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{99}H_{98}Fe_2N_2$, 1427.6502; found, 1427.6468.

Entry 3, Ar = 4-MeC_6H_4. The general procedure was followed. ^1H NMR revealed that the crude product was a 57:43 rac:meso mixture. Purification by flash chromatography (10/90 Et_2O/benzene → 25/75) twice afforded (±)-**1.31** as an orange solid (28% yield).

(±)-**1.31.** ^1H NMR (300 MHz, $CDCl_3$): δ 2.22 (s, 30H), 3.75 (s, 2H), 4.27 (s, 2H), 4.36 (s, 2H), 5.19 (s, 2H), 6.77 (d, 20H, J = 7.8), 6.94 (d, 20H, J = 7.8). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 29.0, 75.4, 79.3, 87.4, 94.7, 109.5, 128.1, 132.0, 132.2, 135.7. HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{89}H_{78}Fe_2N_2$, 1287.4937; found, 1287.4978.

Entry 4, Ar = 4-(MeO)C_6H_4. The general procedure was followed. Purification by flash chromatography (1/30/70 Et_3N/EtOAc/hexanes → 1/50/50) twice afforded (±)-**1.32** as an orange solid (22% yield).

(±)-**1.32.** ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.69 (s, 30H), 3.80 (s, 2H), 4.28 (d, 2H, J = 1.8), 4.35 (d, 2H, J = 1.8), 5.17 (s, 2H), 6.55 (d, 20H, J = 8.9), 7.01 (d, 20H, J = 8.9). ^{13}C NMR (126 MHz, $CDCl_3$): δ 29.2, 55.2, 75.2, 79.2, 86.9, 94.5, 109.2, 112.9, 127.2, 133.5, 158.1. HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{89}H_{78}Fe_2N_2O_{10}$, 1447.4428; found, 1447.4447.

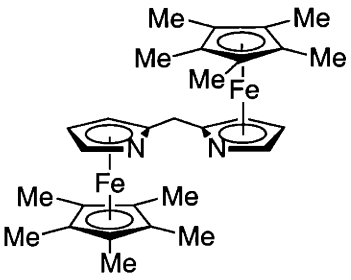
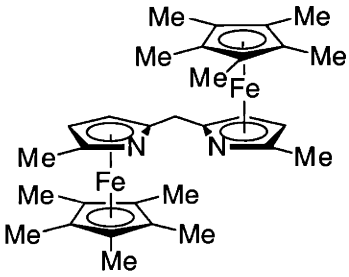
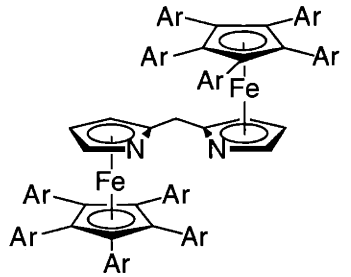
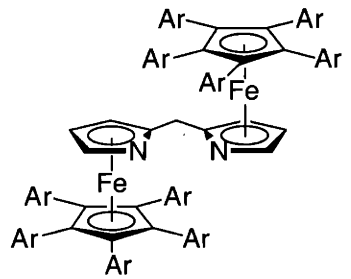
Entry 5, Ar = 4-(*i*-PrO)C_6H_4. The general procedure was followed. ^{1}H NMR revealed that the crude product was a 63:37 rac:meso mixture. Purification by flash chromatography (35/65 Et_2O/pentane) afforded (±)-**1.33** as an orange solid (45% yield).

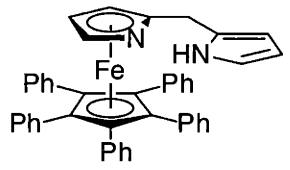
(±)-**1.33**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.28 (d, 60 H, J = 5.8), 3.86 (s, 2H), 4.26 (s, 2H), 4.35 (s, 2H), 4.42 (sept, 10H, J = 6.0), 5.15 (s, 2H), 6.52 (d, 20H, J = 8.2), 6.97 (d, 20H, J = 8.2). ^{13}C NMR (126 MHz, C_6D_6): δ 22.3, 29.1, 69.6, 75.4, 79.1, 86.8, 94.6, 109.2, 114.5, 127.0, 133.5, 156.4.

V. HPLC Resolution of C_2-Symmetric Bis(azaferrocenes).

The HPLC conditions used for resolving C_2-symmetric bis(azaferrocenes) and their precursors are summarized in Table 1.5. All eluant flow is at 1.0 mL/min.

Table 1.5. HPLC resolution conditions for C_2-symmetric bis(azaferrocenes).

substrate	column	conditions	indicated config. t_R (min)	opposite config. t_R (min)
	Chiralcel OD	0.1% Et_2NH, 4% *i*-PrOH, 95.9% hexanes	4.1	7.0
	Chiralcel OD Chiralpak AD	0.1% Et_2NH, 10% EtOAc, 95.9% hexanes 0.2% Et_2NH, 1% *i*-PrOH, 98.8% hexanes	10.8 9.2	7.4 10.4
 Ar = 4-MeC_6H_4	(*R*,*R*) Whelk-O 2	0.2% Et_2NH, 5% CH_2Cl_2, 94.8% pentane	15.8, 20.0	
 Ar = 4-(*i*-PrO)C_6H_4	Chiralcel OD	0.2% Et_2NH, 15% $CHCl_3$, 84.8% hexanes	5.9	9.7

	Chiralpak AD	2.5% *i*-PrOH, 97.5% hexanes	7.3	12.3

Optical rotation data for resolved C_2-symmetric bis(azaferrocenes).

(*R,R*)-1.19. $[\alpha]^{20}_D$ +108° (*c* 1.00, C_6H_6).

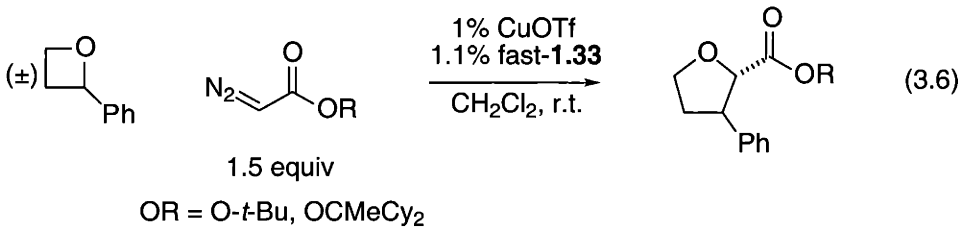
(*R,R*)-1.22. $[\alpha]^{20}_D$ +174° (*c* 1.07, C_6D_6).

(*R,R*)-1.33. $[\alpha]^{20}_D$ +95° (*c* 0.31, C_6H_6).

Assignment of absolute stereochemistry.

1. The absolute configurations of (*R,R*)-**1.19** and (*R,R*)-**1.22** are assigned unambiguously by X-ray crystallography. See Appendix for details.
2. For the bis(azaferrocene) **1.33**, the absolute configurations of the enantiomers are assigned by analogy through the following reactions:

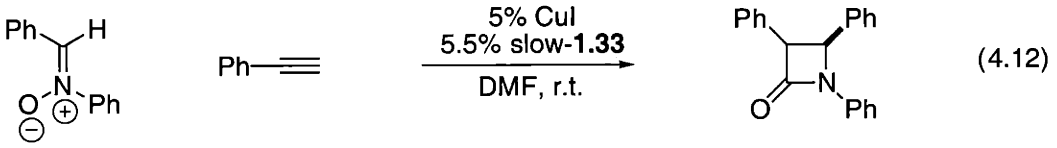
a. The fast enantiomer was employed as the ligand in the ring expansion of (±)-2-phenyloxetane (cf. Chapter 3):



(3.6)

For both diazo esters, the major enantiomers of the tetrahydrofuran products have the (2*S*) configuration; hence, according to our stereochemical model, the ligand has the (*R,R*) configuration.

b. The slow enantiomer was employed as the ligand in the Kinugasa reaction between *N*,α-diphenylnitrone and phenylacetylene (cf. Chapter 4):



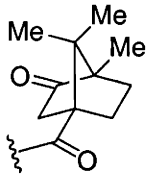
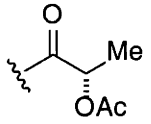
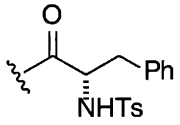
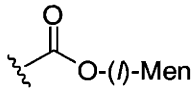
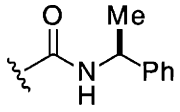
(4.12)

The major enantiomers of the 2-azetidinone products have the (4*S*) configuration; hence, according to our stereochemical model, the ligand has the (*S*,*S*) configuration.

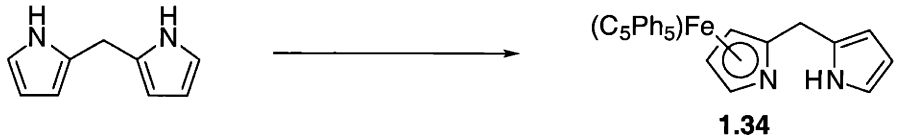
VI. Enantiomerically Pure Bis(azaferrocenes) through Diastereomeric Derivatives.

Details on the chiral auxiliaries whose diastereomeric azaferrocene adducts with **1.34** can be separated are listed in Table 1.6:

Table 1.6. Diastereomeric azaferrocenes for the preparation of enantiomerically pure **1.29**.

auxiliary	medium	conditions	problems
	achiral HPLC silica	25% MTBE, 75% hexanes	inefficient separation
	achiral HPLC silica	1% *i*-PrOH, 99% $CHCl_3$	poor yield in attaching the chiral auxiliary
	silica gel flash chromatography	10/90 EtOAc/hexanes → 25/75	poor yield in attaching the chiral auxiliary
	chiral HPLC Chiralpak AD	1% *i*-PrOH, 99% hexanes	inefficient separation
	achiral HPLC silica	1%Et_2NH, 30% MTBE, 69% hexanes	detachment of the chiral auxiliary during HPLC separation

First complexation.



(1.24)

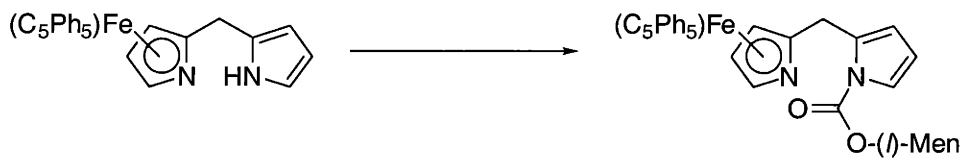
1.34

In a Schlenk tube, *n*-BuLi (1.48 M in hexanes; 6.6 mL, 9.77 mmol) and Ph_5C_5H (4.00 g, 8.96 mmol) were dissolved in toluene (25 mL) and heated to 100 °C for 1 h. The Schlenk tube was cooled to r.t., solvent was removed in vacuo, and the residue was redissolved in THF (50 mL). This solution was transferred to $FeCl_2$ (1.10 g, 8.70 mmol), and the resultant solution of $[(Ph_5C_5)FeCl]_n$ was stirred for another 1.5 h.

n-BuLi (1.48 M in hexanes; 2.9 mL, 4.29 mmol) was added to a solution of di(pyrrol-2-yl)methane (659 mg, 4.51 mmol) in THF (5 mL). After 45 min, this solution was transferred to the solution of $[(Ph_5C_5)FeCl]_n$ (*vide supra*) and stirred for 40 h. The reaction mixture was filtered through a plug of silica with 50/50 $CHCl_3$/hexanes as the eluant. The crude product was purified by flash chromatography (50/50 $CHCl_3$/hexanes; 50/50 CH_2Cl_2/hexanes → 5/15/85 Et_3N/EtOAc/hexanes → 5/30/70) to afford **1.34** as an orange solid (2.58 g, 88% yield).

1.34. ^1H NMR (500 MHz, C_6D_6): δ 3.86 (d, 1H, J = 16.2), 3.94 (d, 1H, J = 16.2), 4.24 (d, 1H, J = 1.8), 4.27 (s, 1H), 5.30 (s, 1H), 6.05 (s, 1H), 6.23 (q, 1H, J = 2.9), 6.3 (s, 1H), 6.9–7.0 (m, 15H), 7.32–7.37 (m, 10H), 8.13 (s br, 1H). ^{13}C NMR (126 MHz, C_6D_6): δ 27.5, 76.8, 79.5, 88.6, 95.5, 107.1, 108.7, 109.6, 117.7, 127.3, 128.7, 129.0, 133.2, 135.7. HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{44}H_{34}FeN_2$, 647.2144; found, 647.2122.

Attachment of chiral auxiliary.



(1.25)

1.34 **1.40**

In a 100-mL round bottom flask, azaferrocene **1.34** (405 mg, 0.625 mmol) and KO-*t*-Bu (87.9 mg, 0.783 mmol) were dissolved in THF (40 mL). After being stirred for 10 min, the reaction mixture was charged with (*l*)-menthyl chloroformate (343 mg, 1.57 mmol) and stirred overnight. It was filtered through a plug of silica with 50/50 $CHCl_3$/EtOAc and concentrated in vacuo to afford a red liquid. This crude product was purified by flash chromatography (10/90 EtOAc/hexanes → 20/80) to afford **1.40** as a mixture of diastereomers (515 mg, 99% yield).

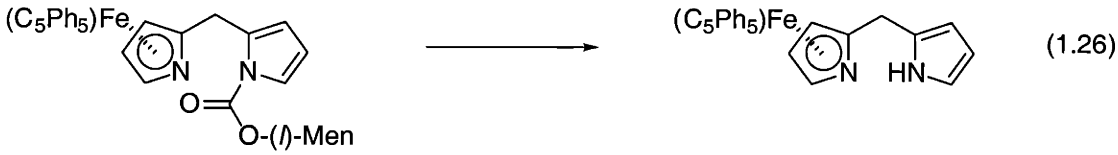
1.40. HRMS–ESI (*m*/*z*): $[M + H]^+$ calcd for $C_{55}H_{52}FeN_2O_2$, 829.3451; found, 829.3427.

The diastereomers of **1.40** were separated using semi-preparative HPLC (Daicel Chiralpak AD, 1 cm x 25 cm; 1/99 *i*-PrOH/hexanes, 2.5 mL/min; 4 mg per injection). The (*R,l*) diastereomer was collected from 7.2 min to 8.9 min, and the (*S,l*) diastereomer was collected from 9.2 min to 10.6 min.

(*R,l*)-**1.40.** ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.72 (d, 3H, *J* = 6.8), 0.83 (d, 3H, *J* = 6.8), 0.91 (d, 3H, *J* = 6.5), 0.9–2.1 (m, 9H), 3.92 (d, 1H, *J* = 16.1), 4.26 (d, 1H, *J* = 16.3), 4.55 (s, 1H), 4.57 (s, 1H), 4.74 (dt, 1H, *J* = 4.4, 10.9), 5.38 (s, 1H), 5.70 (dd, 1H, *J* = 1.7, 3.0), 6.00 (t, 1H, *J* = 3.3), 7.0–7.2 (m, 26H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.5, 21.0, 22.2, 23.5, 26.4, 28.2, 31.6, 34.2, 40.9, 47.2, 64.3, 76.6, 79.0, 88.0, 94.7, 108.7, 110.5, 113.3, 121.1, 126.6, 127.5, 132.5, 133.8, 135.0, 150.3.

(*S,l*)-**1.40.** ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.74 (d, 3H, *J* = 6.9), 0.8–2.0 (m, 15H), 3.95 (d, 1H, *J* = 16.5), 4.22 (d, 1H, *J* = 16.5), 4.52 (d, 1H, *J* = 2.2), 4.56 (d, 1H, *J* = 2.2), 4.72 (dt, 1H, *J* = 4.1, 10.9), 5.38 (s, 1H), 5.66 (s, 1H), 6.01 (t, 1H, *J* = 3.3), 7.0–7.3 (m, 26H).

Removal of chiral auxiliary.



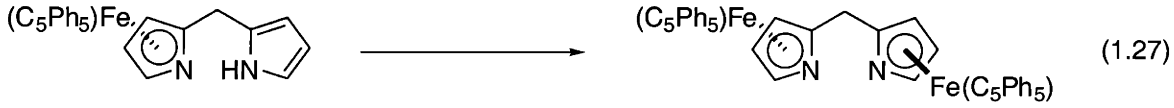
(1.26)

(*R,l*)-**1.40** (*R*)-**1.34**

In a vial, (*R,l*)-**1.40** (180 mg, 0.217 mmol; 93% de) was dissolved in a mixture of EtOH/THF (4:1) and charged to LiOEt (119 mg, 2.30 mmol). The reaction was monitored by TLC, and no **1.40** was detected after 18 hours. The reaction mixture was filtered through a plug of silica with 20/80 EtOAc/$CHCl_3$ as the eluant. The filtrate was concentrated in vacuo to afford a crude product, which was purified by flash chromatography (60/40 CH_2Cl_2/hexanes → 100/0) to afford (*R*)-**1.34** as an orange solid (144 mg, 100% yield; 92% ee).

(*S*)-1.34. $[\alpha]^{20}_D$ -17° (*c* 0.50, $CHCl_3$; 87% ee).

Second complexation.



(1.27)

(*R*)-**1.34** (*R,R*)-**1.29**

In a Schlenk tube, *n*-BuLi (1.48 M in hexanes; 0.12 mL, 0.18 mmol) and Ph_5C_5H (79.9 g, 0.179 mmol) were dissolved in toluene (5 mL) and heated to 100 °C for 1 h. The Schlenk tube was cooled to r.t., solvent was removed in vacuo, and the residue was redissolved in THF (5 mL). This solution was transferred to $FeCl_2$ (28.9 mg, 0.178 mmol), and the resultant solution of $[(Ph_5C_5)FeCl]_n$ was stirred for another 1.5 h.

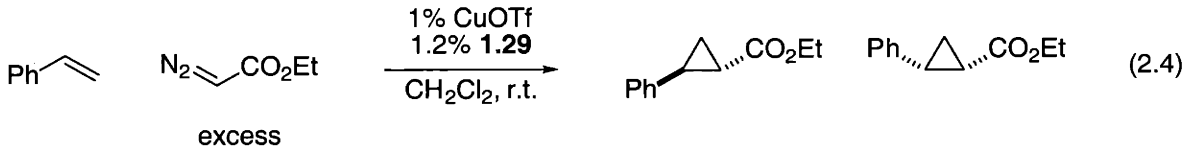
n-BuLi (1.48 M in hexanes; 0.05 mL, 0.074 mmol) was added to a solution of (*R*)-**1.34** (22.2 mg, 0.0343 mmol) in THF (5 mL). After 10 min, the solution of $[(Ph_5C_5)FeCl]_n$ (*vide supra*) was transferred to this solution and stirred for 2 days. The reaction mixture

was filtered through a plug of silica with 20/80 EtOAc/$CHCl_3$ as the eluant. The crude product was purified by flash chromatography (80/20 benzene/hexanes → 100/0 → 1/99 Et_2O/benzene → 4/96) to afford (*R,R*)-**1.34** as an orange solid (12.2 mg, 31% yield; 88% ee, corrected for the ee of the CSA).

Assignment of absolute stereochemistry.

The absolute configuration of bis(azaferrocene) **1.29** that is obtained from the above route is assigned by analogy through the following reactions:

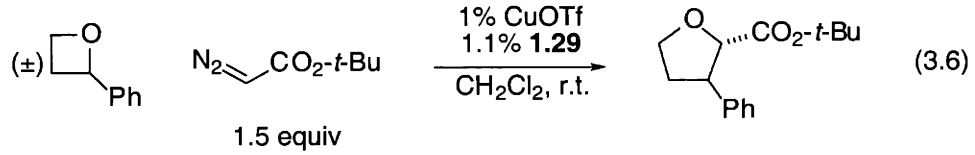
a. The bis(azaferrocene) **1.29** was employed as the ligand in the cyclopropanation of styrene (cf. Chapter 2):



(2.4)

The major enantiomers of the cyclopropane products have the (1*S*) configuration; hence, according to our stereochemical model, the ligand has the (*R,R*) configuration.

b. The bis(azaferrocene) **1.29** was employed as the ligand in the ring expansion of (±)-2-phenyloxetane (cf. Chapter 3):



(3.6)

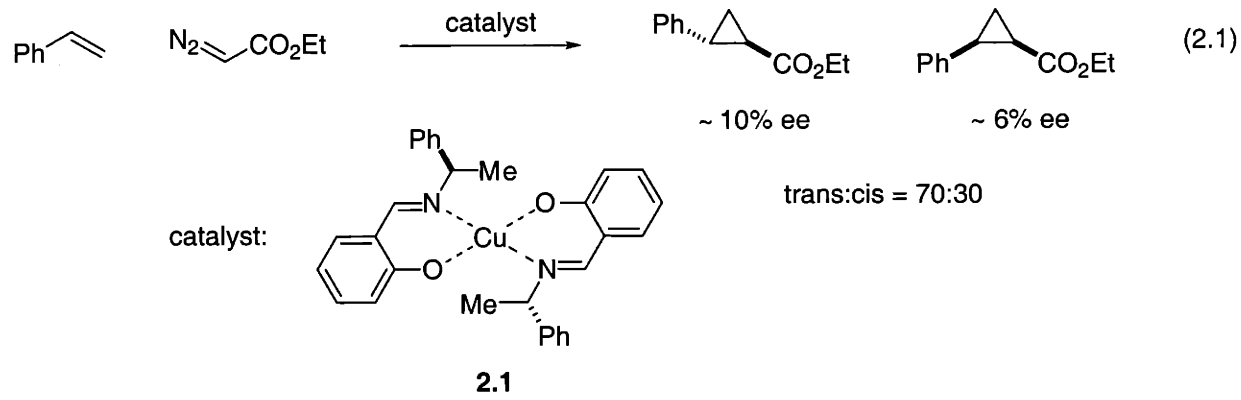
The major enantiomers of the tetrahydrofuran products have the (2*S*) configuration; hence, according to our stereochemical model, the ligand has the (*R,R*) configuration.

Chapter 2

Copper-Catalyzed Asymmetric Cyclopropanation of Olefins with Diazo Esters

A. Introduction.

By virtue of their ring strain, cyclopropanes have attracted attention both as compounds of theoretical interest and of practical importance.[1] As a result, great efforts have been made to develop stereoselective methods for their construction.[2] To this end, metal-catalyzed cyclopropanation of olefins with diazo compounds stands out as a versatile method.[3] Moreover, the report by Nozaki on the use of copper(II)–Schiff base complex **2.1** to catalyze the cyclopropanation of styrene holds a special status as the first example of enantioselective metal-catalyzed reaction (eq 2.1).[4]



2.1

Although the enantioselectivity of the reaction is low, the principle that chiral transition-metal catalysts can induce asymmetry in the products was firmly established. Building on these results, Aratani developed the first generation of highly

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1 For reviews, see: (a) *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: New York, 1987. (b) Baird, M. S. *Top. Curr. Chem.* **1988**, *144*, 137–209. (c) Wong, H. N. C.; Hon, M.-Y.; Tse, C.-W.; Yip, Y.-C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165–198.

2 Salaün, J. *Chem. Rev.* **1989**, *89*, 1247–1270.

3 For reviews, see: (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*; John Wiley: New York, 1998; Chapter 4. (b) Doyle, M. P. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: New York, 2000; Chapter 5. (c) Pfaltz, A. In *Comprehensive Asymmetric Catalysis*; Springer: New York, 1999; Vol. 2, Chapter 16.1.

4 Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1966**, *7*, 5239–5244.

enantioselective cyclopropanation catalysts **2.2** for the synthesis of several industrially important cyclopropanecarboxylic acids and their derivatives (Figure 2.1).[5]

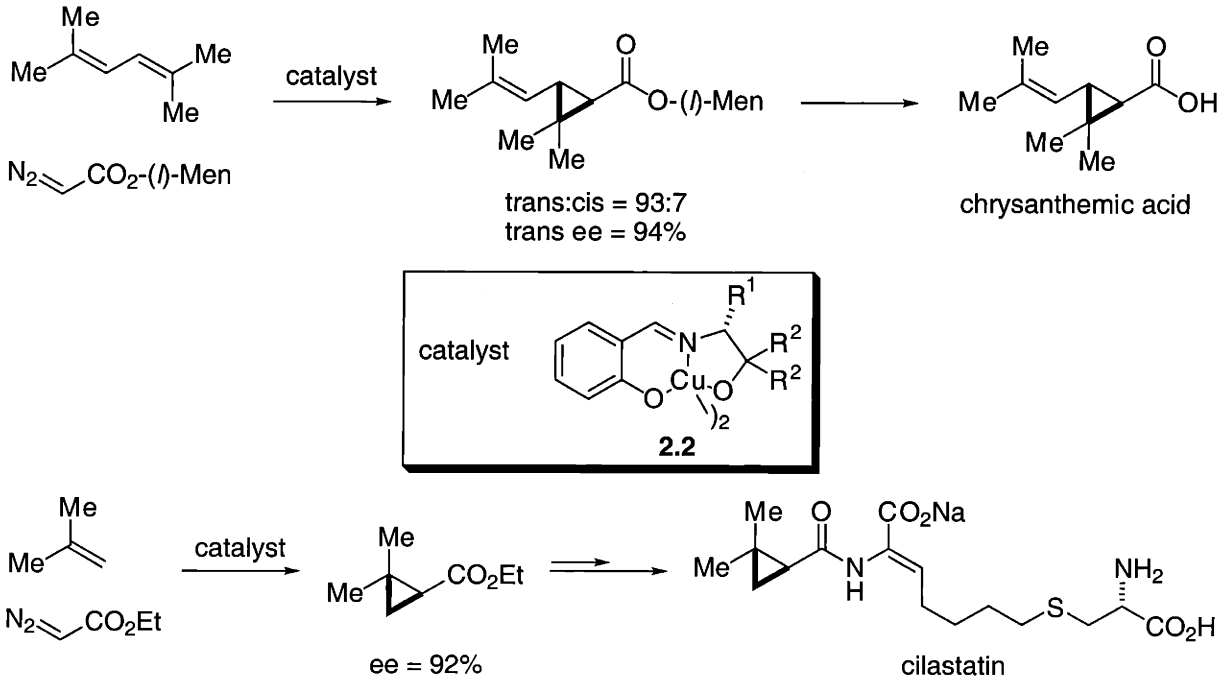

Figure 2.1. Highly effective cyclopropanation catalysts developed by Aratani.

Further improvement to the copper catalysts came from the development of C_2-symmetric bidentate nitrogen ligands. Semicorrins, reported by Pfaltz[6] in 1986, and bis(oxazolines), reported simultaneously by Masamune,[7] Pfaltz,[8] and Evans[9] in the early 1990s, were demonstrated to provide excellent enantioselection in copper-catalyzed asymmetric cyclopropanation. Shown in Figure 2.2 is a comparison of these ligands in the cyclopropanation of styrene with ethyl diazoacetate.

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5 (a) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1975**, *16*, 1707–1710. (b) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1977**, *18*, 2599–2602. (c) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1982**, *23*, 685–688. (d) Aratani, T. *Pure Appl. Chem.* **1985**, *57*, 1839–1844.

6 (a) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1005–1006. (b) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Helv. Chim. Acta* **1988**, *71*, 1553–1565.

7 Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6005–6008.

8 Müller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232–240.

9 Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726–728.

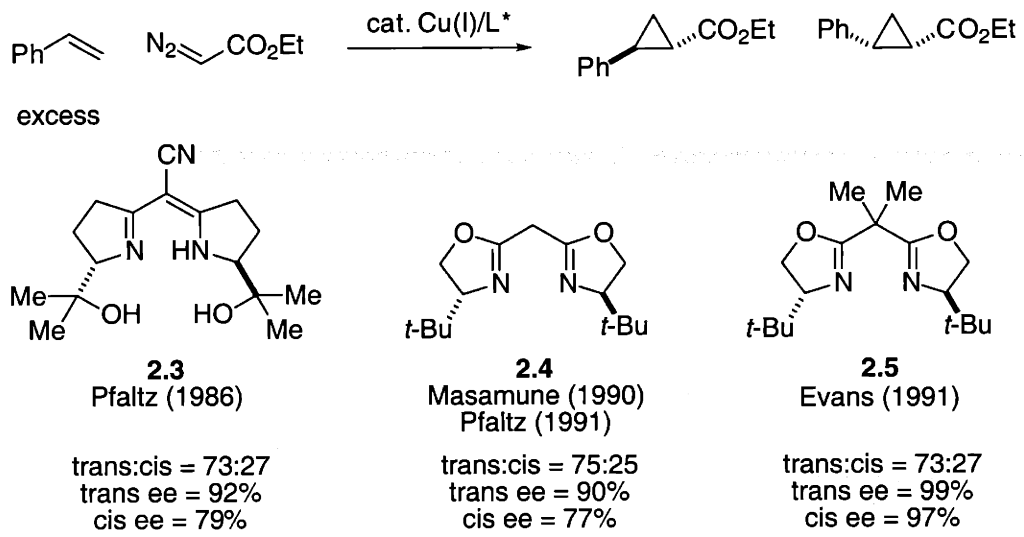
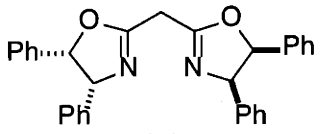
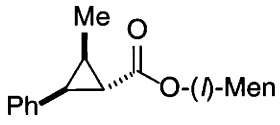


Figure 2.2. C_2-symmetric bidentate ligands for asymmetric cyclopropanation of styrene.

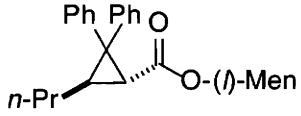
These ligands have a wider substrate scope than the Aratani catalysts, but not every class of olefins reacts with the same excellent enantioselectivity. For example, Evans' bis(oxazoline) **2.5** works well for mono, 1,1-di-, and trans-substituted olefins, but not for cis- or trisubstituted olefins.[10] Structural modifications have been made to address this limitation, e.g., Masamune developed **2.6**, which is highly effective for the asymmetric cyclopropanation of cis- and trisubstituted olefins.[11]



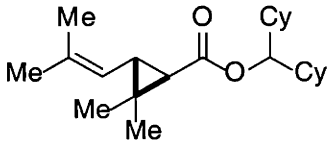
2.6



trans:cis = 88:12
trans ee = 92%



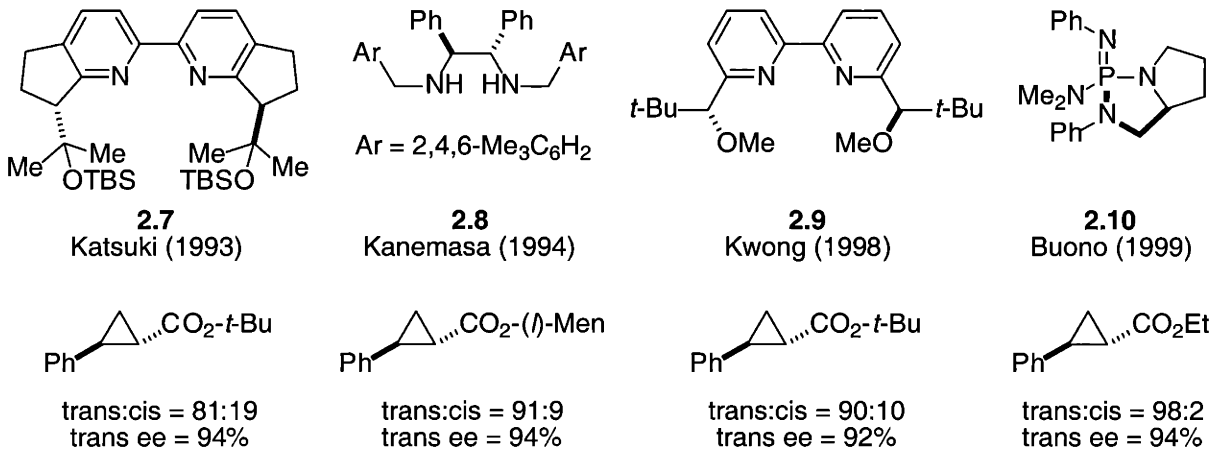
trans:cis = 98:2
trans ee = 84%



trans:cis = 95:5
trans ee = 94%

10 Woerpel, K. A. Ph.D. Thesis, Harvard University, 1992.
11 Lowenthal, R. E.; Masamune, S. *Tetrahedron Lett.* **1991**, *32*, 7373–7376.

The success of C_2-symmetric bis(oxazolines) as ligands for asymmetric cyclopropanation soon spurred the development of various structural analogs to surpass the results achieved with **2.3–2.5**. Figure 2.3 highlights those that have achieved excellent enantioselectivity with styrene.[12]



2.7
Katsuki (1993)

2.8
Kanemasa (1994)

2.9
Kwong (1998)

2.10
Buono (1999)

Figure 2.3. Some recently reported examples of highly enantioselective ligands for copper-catalyzed asymmetric cyclopropanation.

Given the popularity of the reaction, copper-catalyzed cyclopropanation would provide a good testing ground for validating the ligand design of our C_2-symmetric bis(azaferrocenes) and comparing them with the well-established ligand systems. In this chapter, we describe our investigations to this end. In addition, the copper•ligand•styrene complexes have been studied by ^{1}H NMR and X-ray crystallography, and their relevance to the mechanism of the reaction is discussed.

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12 (a) **2.7**: Ito, K.; Katsuki, T. *Tetrahedron Lett.* **1993**, *34*, 2661–2664. (b) **2.8**: Kanemasa, S.; Hamura, S.; Harada, E.; Yamamoto, H. *Tetrahedron Lett.* **1994**, *35*, 7985–7988. (c) **2.9**: Kwong, H.-L.; Lee, W.-S.; Ng, H.-F.; Chiu, W.-H.; Wong, W.-T. *J. Chem. Soc., Dalton Trans.* **1998**, 1043–1046. (d) **2.10**: Brunel, J. M.; Legrand, O.; Reymond, S.; Buono, G. *J. Am. Chem. Soc.* **1999**, *121*, 5807–5808.

B. Results and Discussion.

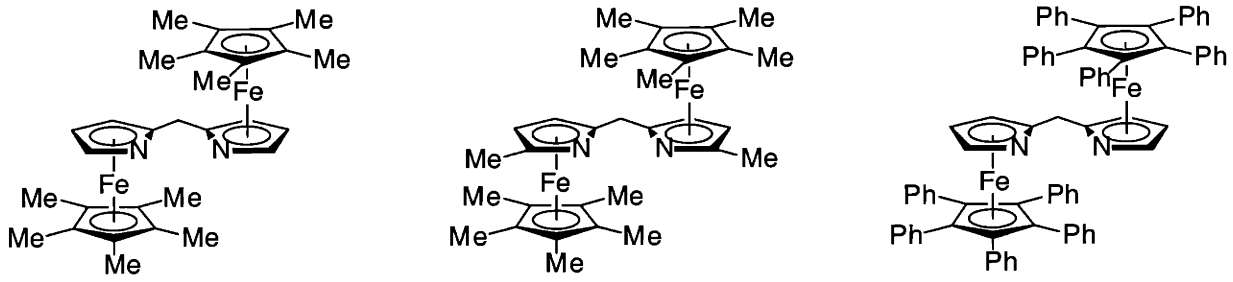


Figure 2.4. C_2-Symmetric bis(azaferrocenes) investigated in this chapter.

I. Development of Reaction Conditions.

We first studied two methods of generating the active copper catalyst: (1) directly from a copper(I) salt; and, (2) in situ reduction of a copper(II) salt (Table 2.1).

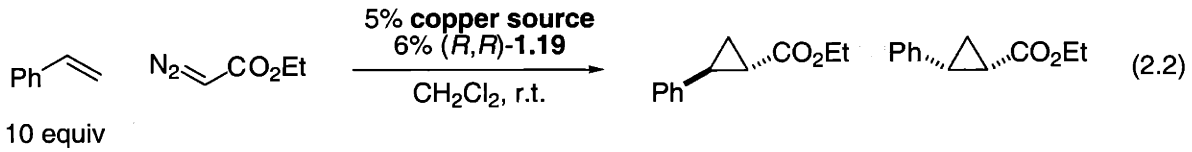


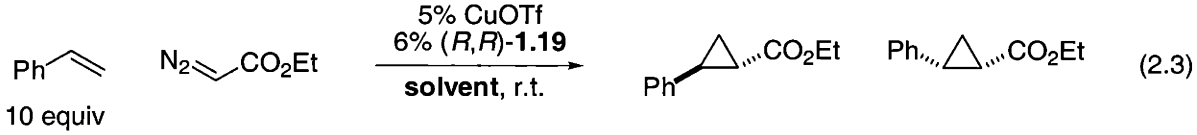
Table 2.1. Asymmetric cyclopropanation of styrene as a function of the copper source (eq 2.2).

				% ee[a]	
entry	**copper source**	NMR yield (%)	trans : cis	trans	cis
1	CuCN	trace	61 : 39	49	54
2	CuI	21	76 : 24	56	35
3	$CuOTf \bullet 0.5C_6H_6$	64	74 : 26	64	36
4	$Cu(MeCN)_4PF_6$	80	72 : 28	59	29
5	$CuCl + AgPF_6$	73	77 : 23	61	37
6	$CuCl + AgSbF_6$	36	78 : 22	64	37
7	$Cu(OTf)_2 + PhNHNH_2$	78	70 : 30	41	20

[a] The enantioselectivities reported in this study are lower than the later ones, and the probable reason is the ligand being less enantiomerically enriched.

The coordinating ability of the anion influences the activity of the catalyst: cyanide and iodide are quite unreactive (entries 1 and 2), while triflate, hexafluorophosphate, and hexafluoroantimonate are effective (entries 3–6). Good levels of enantioselectivity are obtained when the catalyst is generated directly from copper(I) triflate and copper(I) hexafluorophosphate (entries 3 and 4). The active copper catalysts can be obtained alternatively by anion metathesis, but this more cumbersome procedure offers no significant improvement (entry 4 vs entry 5). Finally, in situ reduction of copper(II) triflate by phenylhydrazine furnishes a catalytic species that is only moderately enantioselective (entry 7).

After identifying CuOTf as the optimal copper source, we compared the reaction in different hydrocarbon and halogenated solvents (Table 2.2).[13]



(2.3)

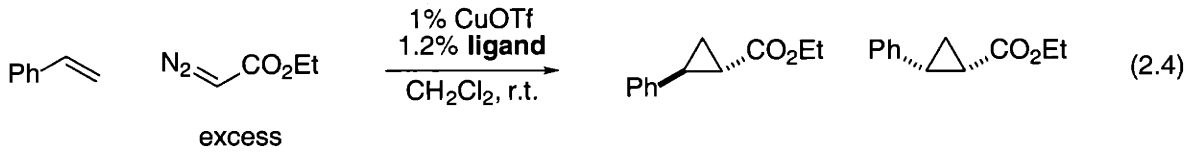
Table 2.2. Asymmetric cyclopropanation of styrene as a function of the solvent (eq 2.3).

				% ee	
entry	**solvent**	NMR yield (%)	trans : cis	trans	cis
1	C_6H_{14}	39	53 : 47	17	9
2	PhH	67	76 : 24	75	50
3	$PhCH_3$	32	76 : 24	76	50
4	$PhCF_3$	52	74 : 26	57	26
5	CH_2Cl_2	77	77 : 23	76	46
6	$CHCl_3$	93	76 : 24	70	38
7	$ClCH_2CH_2Cl$	70	75 : 25	70	42

13 Woerpel and Evans have explored the use of polar solvents, and they have noticed various complications, e.g., C–H insertion in THF, "explosive" reaction in MeCN, and complex product mixtures in $MeNO_2$ (Ref. 10).

The best enantioselectivity is obtained in CH_2Cl_2 (entry 5), benzene (entry 2), and toluene (entry 3), with the trans diastereomer furnished in 75–76% ee. Halogenated solvents other than CH_2Cl_2 afford poorer enantioselectivities (entries 4, 6, and 7). Considering other factors such as yield and compatibility,[14] we concluded that CH_2Cl_2 is the solvent of choice.[15]

The effect of ligand structure on the enantioselectivity of the reaction was then examined. In this study, we decided to change the reaction conditions closer to our final target by lowering the catalyst loading to 1% and using the olefin instead of the diazo ester as the limiting reagent.[16] However, the analogs of **1.19** do not improve the stereoselection of the reaction (Table 2.4).



(2.4)

Table 2.3. Asymmetric cyclopropanation of styrene as a function of the ligand (eq 2.4).

			% ee	
entry	**ligand**	trans : cis	trans	cis
1	**1.19**	76 : 24	73	44
2	**1.22** (96% ee)	65 : 35	62(64)	41(42)
3	**1.29** (88% ee)	53 : 47	65(74)	57(64)

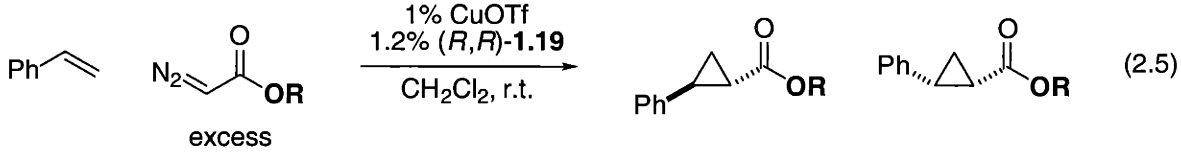
The values in parentheses refer to values after correction for the ligand ee.

14 Aromatic hydrocarbons can undergo aromatic cycloaddition/substitution with diazo esters.

15 Woerpel and Evans have reported in reference 10 that the best solvent for the cyclopropanation of styrene with a bis(oxazoline) as the ligand for copper is $CHCl_3$ (98% ee), with CH_2Cl_2 faring worse (88% ee).

16 The predominant side reaction is the dimerization of the diazo ester. In most studies, this deleterious dimerization is minimized by using a large excess of olefin (the diazo ester is the limiting reagent). We decided to use the olefin as the limiting reagent instead, since we envision in most synthetic applications that the olefin is the component carried from the previous step, while the diazo ester can either be purchased or easily synthesized.

At this point, the stereoselection achieved through our catalyst system still leaves much to be desired. Studies employing semicorrins and bis(oxazolines) as chiral ligands in copper-catalyzed cyclopropanation have demonstrated that the stereoselectivity can be improved by increasing the steric demand of the diazo ester.[6–9] With our bis(azaferrocene) **1.19**, we observed parallel behavior (Table 2.4).



(2.5)

Table 2.4. Asymmetric cyclopropanation of styrene as a function of the diazo ester (eq 2.5).[a]

entry	OR	trans : cis	% ee trans	% ee cis	isolated yield, trans (%)[b]
1	OEt	76 : 24	73	44	39
2	O-*t*-Bu	86 : 14	87	82	63
3	O-(*d*)-Men	88 : 12	87[c]	81[c]	67
4	O-(*l*)-Men	85 : 15	89[c]	84[c]	66
5	BHT	96 : 4	94	n.d.	79
6	$OCMeCy_2$	92 : 8	92	94	n.d.

Abbreviations: Men = menthyl; BHT = butylated hydroxytoluene, or 2,6-di-*t*-butyl-4-methylphenol. [a] Except for entry 6, all data represent the average of two runs, one with each enantiomer of the ligand. [b] The reported isolated yields are based on the use of 3.2 equiv of diazo ester, except entry 5 in which only 1.2 equiv was used. [c] after correction for the ee of the starting menthol.

By changing the ethyl group to a *t*-butyl group in the diazoacetate, we improve both the stereoselectivity and the yield (entry 2). Menthyl diazoacetates give similar results as *t*-butyl diazoacetate, and the stereochemistry in the chiral ester group has little impact on the selectivity imposed by the ligand **1.19** (entries 3 and 4).[17] Excellent

17 A control experiment with the achiral ligand 2,2'-bipyridine shows that the asymmetry induced by the menthyl group is negligible (trans ee = 4%, cis ee = 13%).

diastereo- and enantioselectivity are obtained when the BHT ester of diazoacetic acid is used (entry 5).[18] The use of this hindered diazo ester also decreases the formation of maleates and fumerates; hence, a good yield of the trans cyclopropane is obtained with only a slight excess of the diazo ester.

In terms of versatility, the cyclopropane esters derived from BHT diazoacetate are difficult to hydrolyze.[19] The only facile method to remove the BHT from these products is by reduction with $LiAlH_4$ to give the corresponding cyclopropylmethanols. Hence, we include the results from another hindered diazo ester, 1,1-dicyclohexylethyl diazoacetate, for comparison (entry 6).[20] Its stereoselectivity is slightly inferior to that provided by BHT diazoacetate, but the tertiary ester group in its products is readily converted to the corresponding cyclopropanecarboxylic acid by treatment with CF_3CO_2H at room temperature. It can be used as an alternative carbene source if the ease of product functionalization is more important than the overall stereoselectivity.[21]

II. Scope of the Reaction.

With the BHT diazoacetate as the carbene source and CuOTf•**1.19** as the catalyst, we investigated the asymmetric cyclopropanation of an array of monosubstituted olefins (Table 2.5).

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18 Doyle first described the use of BHT diazo ester to achieve excellent trans diastereoselectivity in cyclopropanation. See: Doyle, M. P.; Bagheri, V.; Wandless, T. J.; Harn, N. K.; Brinker, D. A.; Eagle, C. T.; Loh, K.-L. *J. Am. Chem. Soc.* **1990**, *112*, 1906–1912.

19 Seebach has reported the hydrolysis of *α-substituted* BHT cyclopropanecarboxylates under vigorous conditions (KO-*t*-Bu in THF/H_2O, 120 °C). See: Häner, R.; Maetzke, T.; Seebach, D. *Helv. Chim. Acta* **1986**, *69*, 1655–1665. Woerpel and Evans reported that they were unable to hydrolyze the cyclopropanation product from styrene and BHT diazoacetate (Ref. 10).

20 This new diazo ester was developed primarily to improve the stereoselection in the asymmetric ring expansions of oxetanes. See Chapter 3 for more discussion.

21 Woerpel and Evans have proposed another solution by the use of BHA (butylated hydroxyanisole) diazoacetate as a substitute for BHT diazaoacetate. The two diazo esters showed similar stereoselection in the asymmetric cyclopropanation of styrene, but the BHA group can be readily removed from the cyclopropanecarboxylic acid by oxidation with CAN (Ref. 10).

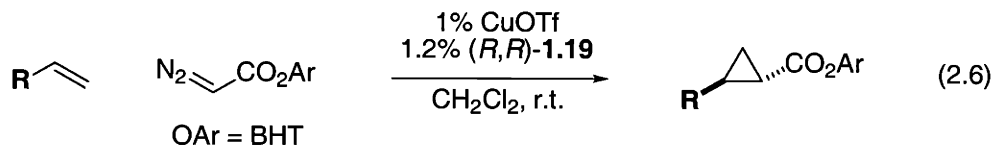

Table 2.5. Asymmetric cyclopropanation of monosubstituted olefins (eq 2.6).[a]

entry	R	trans : cis	% ee, trans	isolated yield (%)[b]
1	Ph	96 : 4	94	79
2	4-(MeO)C_6H_4	94 : 6	87	90
3	4-(F_3C)C_6H_4	94 : 6	96	81
4	$PhCH_2$	94 : 6	91	78
5	*n*-C_6H_{13}	93 : 7	90	80
6[c]	Et_3Si	99 : 1	95	64

[a] All data represent the average of two runs, one with each enantiomer of the ligand. [b] For entries 1, 4–6, the isolated yield refers to the trans diasteromer, while for entries 2 and 3, it refers to a mixture of trans and cis diastereomers. [c] 2% catalyst was used.

We have established that for styrene derivatives, the enantioselectivity is moderately sensitive to electronic effects.[22] Thus, electron-poor 4-trifluoromethylstyrene (entry 3) undergoes cyclopropanation with higher enantioselectivity but lower reactivity than electron-neutral styrene (entry 1) or electron-rich 4-methoxystyrene (entry 2).[23] We have also demonstrated that alkyl-substituted olefins, such as allylbenzene (entry 4) and 1-octene (entry 5), as well as silyl-substituted olefins, such as vinyltriethylsilane (entry 6), react with the diazo ester to furnish cyclopropanes with excellent stereoselection.

Using a higher catalyst loading (5%) and the BHT diazoacetate as the carbene source, we have also briefly examined olefins of higher substitution patterns (Figure 2.5). The

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22 A Hammett study of the electronic effect in styrenes has been reported for a copper-catalyzed asymmetric cyclopropanation of olefins using a chiral 2,2'-bipyridine. See: Wong, H. L.; Tian, Y.; Chan, K. S. *Tetrahedron Lett.* **2000**, *41*, 7723–7726.

23 A less reactive olefin requires more BHT diazoacetate to go to completion.

trans cyclopropane from (*E*)-1-phenylpropene (eq 2.7) and the cis cyclopropane from 2-methyl-2-butene were formed in good enantiomeric excess (eq 2.9). On the other hand, the enantiomeric excesses of the trans cyclopropanes formed from (*Z*)-1-phenylpropene (eq 2.8) and 2-methyl-2-butene (eq 2.9) are mediocre.

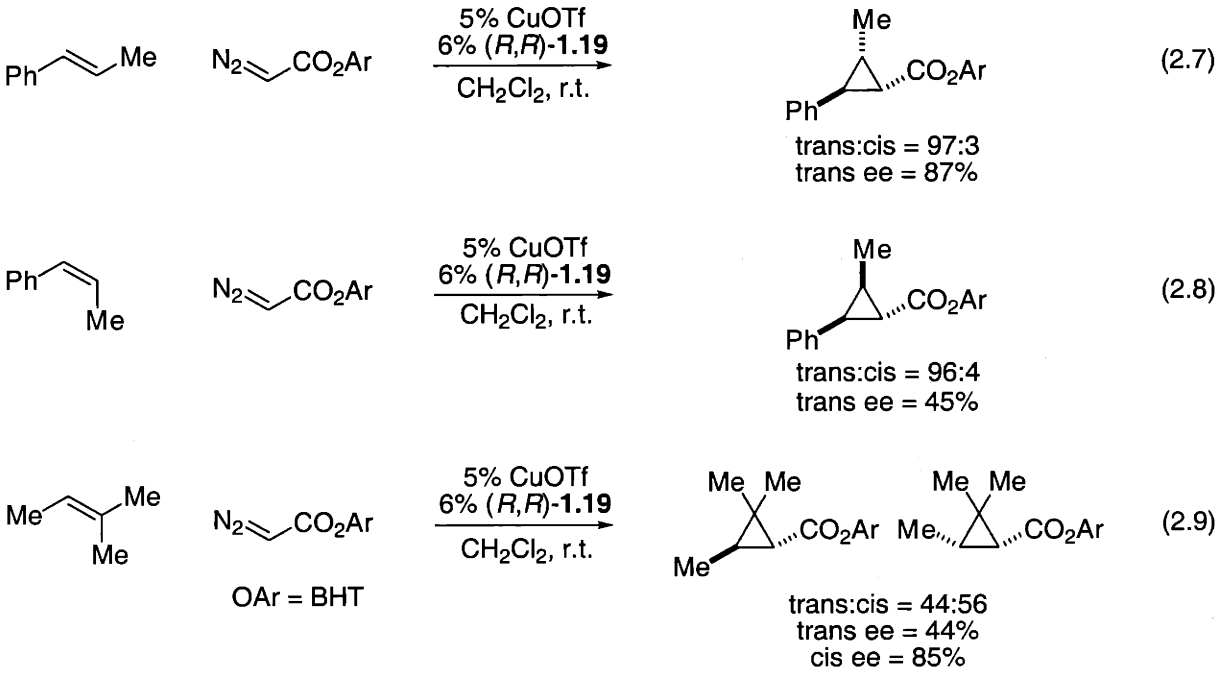

Figure 2.5. Asymmetric cyclopropanation of trans-, cis-, and trisubstituted olefins using catalyst CuOTf/**1.19**.

To explore different frameworks of C_2-symmetric planar-chiral ligands, Dr. Jack Liang synthesized 2,2'-bipyridine derivative **2.11** and obtained it in enantiomerically pure form. In Table 2.6, we compare the stereoselection in the copper-catalyzed asymmetric cyclopropanation obtained from **1.19** and **2.11**, and examine the effect of changing the ligand framework from azaferrocene to π-bound pyrindinyl complex.[24]

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24 The cyclopropanation was investigated by Dr. Jack Liang and Mr. Ramon Rios. For an account of the work, see: Rios, R.; Liang, J.; Lo, M. M.-C.; Fu, G. C. *Chem. Commun.* **2000**, 377–378.

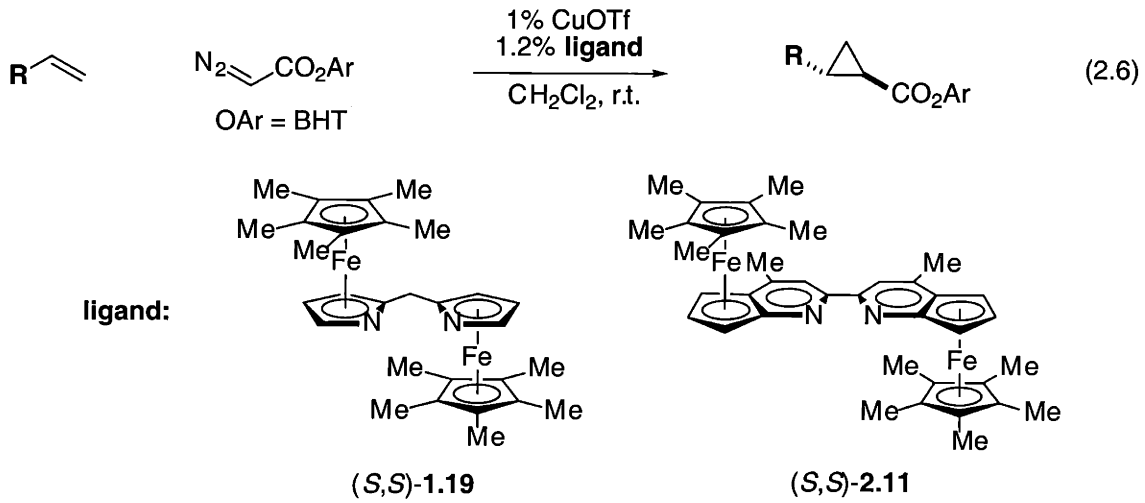


Table 2.6. Comparison of **1.19** and **2.11** in copper-catalyzed asymmetric cyclopropanation of monosubstituted olefins (eq 2.6).[a]

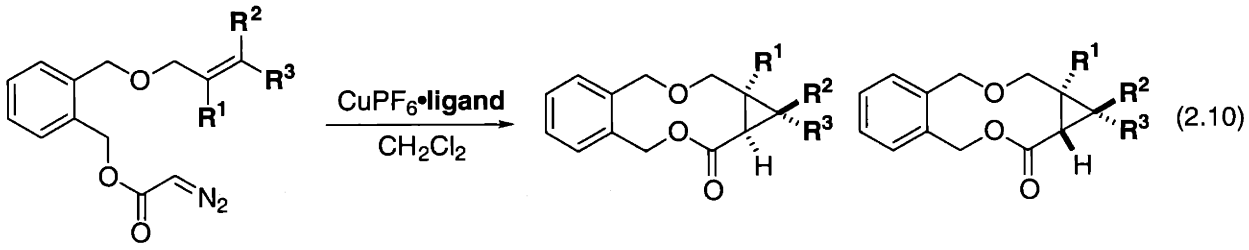
		1.19		**2.11**	
entry	**R**	trans : cis	% ee, trans	trans : cis	% ee, trans
1	Ph	96 : 4	94	97 : 3	87
2	4-(MeO)C_6H_4	94 : 6	87	95 : 5	75
3	4-(F_3C)C_6H_4	94 : 6	96	94 : 6	94
4	*n*-C_6H_{13}	93 : 7	90	94 : 6	78
5	Et_3Si	99 : 1	95	96 : 4	80

[a] All data represents the average of two runs, one with each enantiomer of the ligand.

C_2-Symmetric ligands **2.11** and **1.19** display similar levels of diastereoselectivity, but **2.11** appears to be less enantioselective for most monosubstituted olefins. The better performance of **1.19** may be attributed to the proximity between the stereogenic element and the ligating atom.

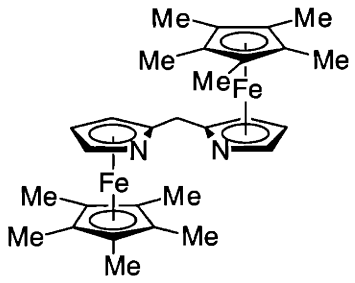
Doyle has also evaluated the stereocontrol of **1.19** in the intramolecular cyclopropanation of diazo esters (Table 2.7).[25]

25 Doyle, M. P.; Hu, W.; Chapman, B.; Marnett, A. B.; Peterson, C. S.; Vitale, J. P.; Stanley, S. A. *J. Am. Chem. Soc.* **2000**, *122*, 5718–5728.

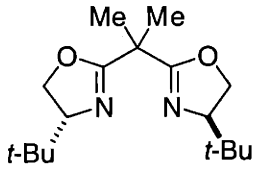


2.12 **2.13** **2.14**

ligand:



1.19



2.5

Table 2.7. Comparison of **1.19** and **2.5** in copper-catalyzed asymmetric intramolecular cyclopropanation of olefins (eq 2.10).

				$CuPF_6$•**1.19**		$CuPF_6$•**2.5**	
entry	R^1	R^2	R^3	**2.13 : 2.14**	% ee, **2.13**	**2.13 : 2.14**	% ee, **2.13**
1	H	H	H	> 99 : 1	53	> 99 : 1	80
2	Me	H	H	> 99 : 1	36	> 99 : 1	90
3	H	H	*n*-Pr	> 99 : 1	80	> 99 : 1	84
4	H	*n*-Pr	H	92 : 8	6	51 : 49	17
5	H	Me	Me	96 : 4	90	92 : 8	18

Olefins of different substitution patterns were surveyed, and **1.19** displays good enantiocontrol when the olefin is trans substituted (entry 3) and trisubstituted (entry 5). In the case of trisubstituted olefins, the selectivity achieved by **1.19** is significantly better than Evans' bis(oxazoline) **2.5** and several chiral dirhodium(II)–carboxamidate catalysts that Doyle examined (54–63% ee). The combined results from intramolecular and intermolecular cyclopropanation suggest that trisubsituted olefins can be excellent substrates for our catalyst.

III. Copper•Ligand•Olefin Complexes and Their Relevance to the Mechanism of Copper-Catalyzed Cyclopropanation.

In Chapter 1, we reported that CuOTf•**1.19** forms highly crystalline material with olefins. In this chapter, we reexamine the crystal structures of our catalyst CuOTf•(*S,S*)-**1.19** with styrene and allylbenzene in light of their potential relevance to the mechanism of copper-catalyzed cyclopropanation.[26] Jacobsen has reported the X-ray structure of a related complex [$CuPF_6$•**1.42**•styrene] and observed structural features that "may hold broader implications for the design of ligands for asymmetric catalysis."[27] Hence, it would be interesting to see whether we can identify similar features in our complexes (Figures 2.6 and 2.7).

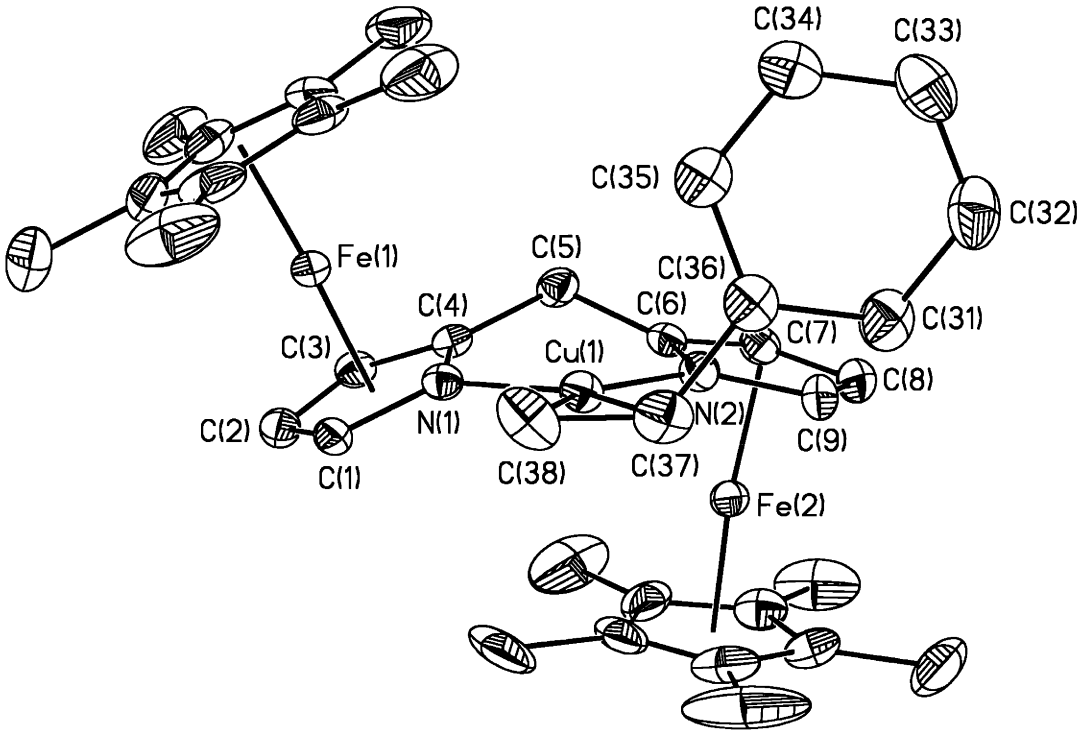


Figure 2.6. ORTEP plot of [CuOTf•(*S,S*)-**1.19**•styrene].

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26 For example, Woerpel and Evans suggested that the X-ray structure of a catalyst•olefin complex helps clarify the number of olefins associated with the catalyst in the resting state (Ref. 10).

27 Quan, R. W.; Li, Z.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1996**, *118*, 8156–8157.

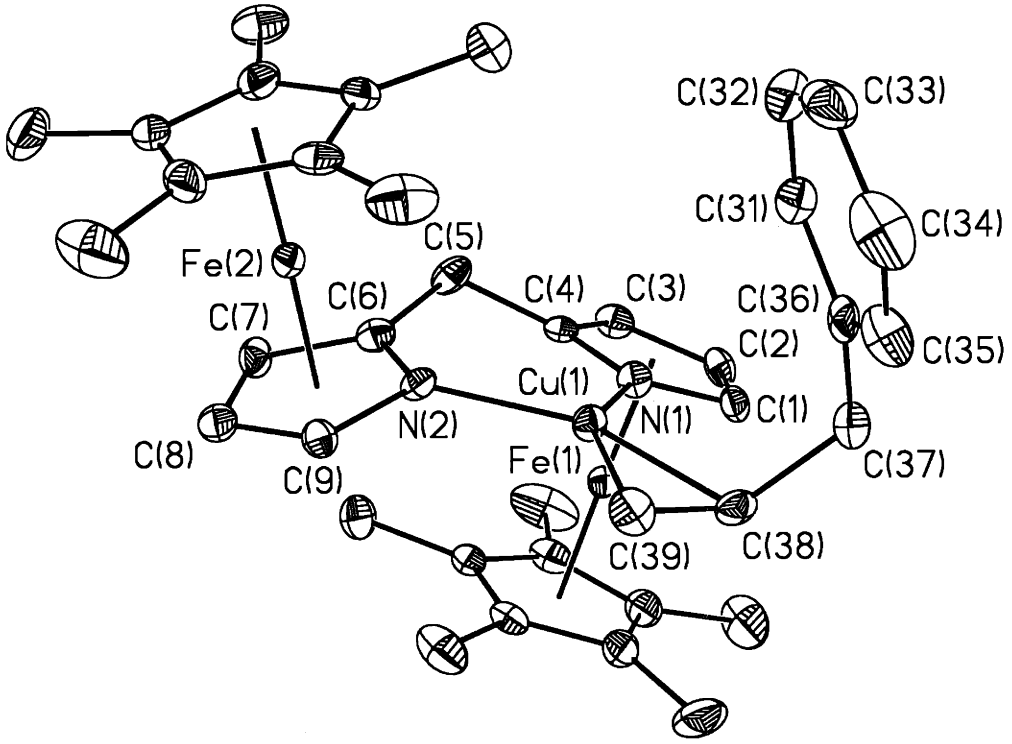


Figure 2.7. ORTEP plot of [CuOTf•(*S*,*S*)-**1.19**•allylbenzene].

Each of the X-ray structures reveals that the copper center has a square-planar geometry, with bis(azaferrocene) **1.19** acting as a bidentate σ-ligand and the C=C double bond of the olefin as a π-ligand. The triflate anion is non-coordinating, and for the major trans cyclopropane product, *the olefin face that is bound to the copper is not the face that undergoes cyclopropanation.* The bond length data (Cu–C(sp^2) = 1.99–2.02 Å, C(sp^2)–C(sp^2) = 1.38–1.39 Å) suggest that there is little back-bonding from the copper. The phenyl group of the olefin is positioned in the empty quadrant such that its steric interactions with the methyl groups of the Cp* ring are minimized. In none of the complexes can we detect any face–face or edge–face aromatic interactions that are identified in the Jacobsen structure, presumably because the rigidity of our complexes causes the repulsive steric forces to dominate their overall structures.

The crystal structures indicate that our catalyst binds to only *one* prochiral face of the olefin in the crystal. Being well aware of the pitfall for discussing solution phenomenon

based on solid-state results, we investigated the selectivity of the binding between the prochiral faces of styrene and CuOTf•(*S*,*S*)-**1.19** by ^{1}H NMR (Figure 2.8).

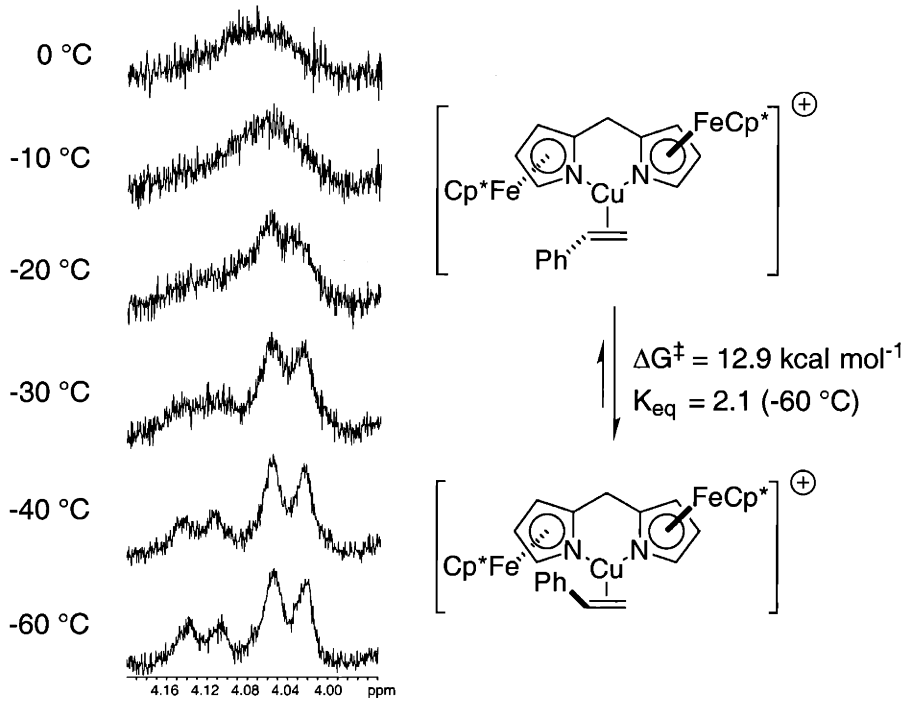
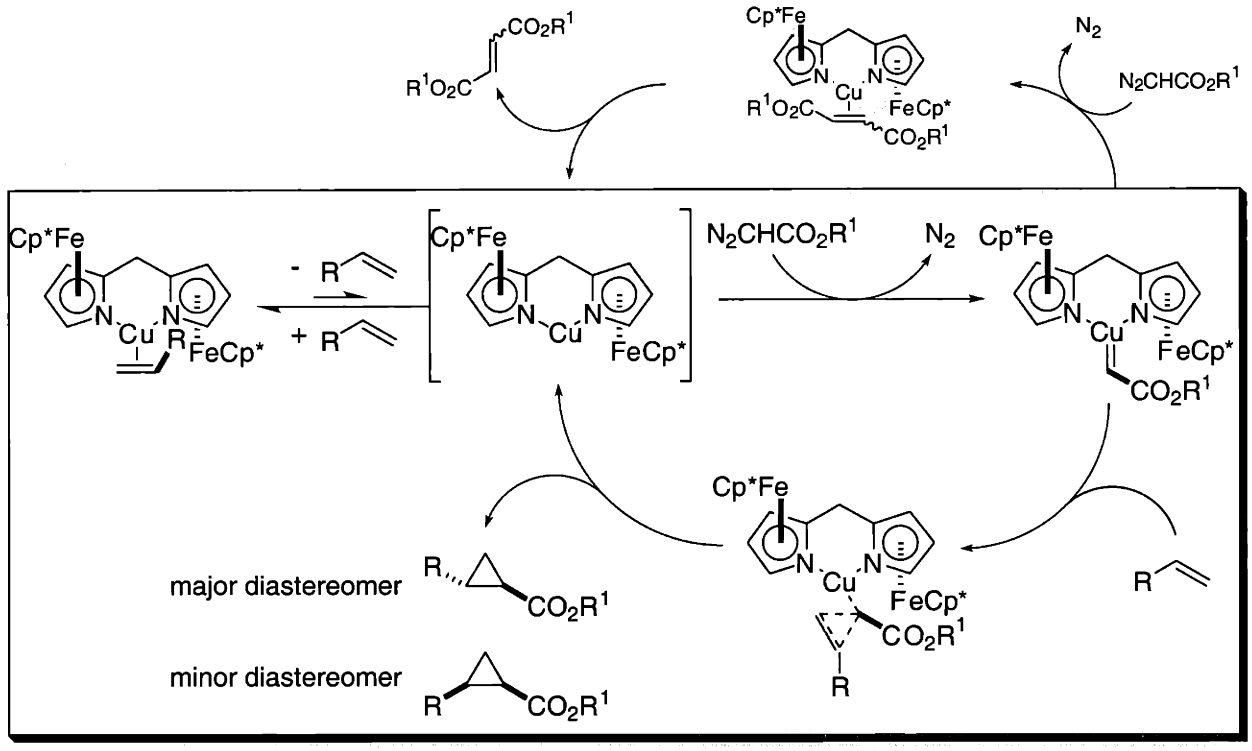


Figure 2.8. Variable temperature ^{1}H NMR study of the solution structure of [CuOTf•(*R*,*R*)-**1.19**• styrene] complex.

The coordination of the copper complex to styrene causes its three vinylic protons to be upfield shifted to the region 4.0–4.2 ppm. At 0 °C, the signals are broad, indicating rapid exchange of the resonances. Upon cooling, the ^{1}H NMR signals start to decoalesce and reveal the presence of the two diastereomeric catalyst•olefin complexes. The diastereomeric ratio is 2.1 at -60 °C; hence, unlike the Jacobsen complex (facial selectivity > 98:2),[27] our catalyst displays only poor enantiofacial selectivity in its binding to the prochiral faces of styrene. In addition, the energy barrier for interconversion between the two diastereomeric complexes is ~ 13 kcal mol^{-1}, which indicates that the binding of the olefin to the metal center is rapidly *reversible* at room temperature.

The dichotomy between the poor enantiofacial selectivity that our catalyst exhibits in its binding to the prochiral faces of styrene and the excellent enantioselectivity that it achieves in its catalysis of the cyclopropanation of styrene can be rationalized with the following conclusion: *The olefin has to dissociate from the copper center before it can participate in the reaction leading to the trans cyclopropane product* (Scheme 2.1).[28]



Scheme 2.1. Proposed mechanism for the copper-catalyzed asymmetric cyclopropanation of olefins.

The active catalyst of the system is generated by the dissociation of the olefin from the resting-state complex, which then reacts with the diazo ester to give the copper

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28 Similar conclusions have appeared in some recent discussions on the mechanism of copper-catalyzed cyclopropanation. For kinetic studies on the reaction, see: (a) Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Prieto, F.; Pérez, P. J. *Organometallics* **1999**, *18*, 2601–2609. For theoretical studies on the mechanism, see: (b) Fraile, J. M.; García, J. I.; Martínez-Merino, V.; Mayoral, J. A.; Salvatella, L. *J. Am. Chem. Soc.* **2001**, *123*, 7616–7625.

carbene.[29,30] This step stands in contrast with the Evans/Woerpel mechanism, in which the catalyst•olefin complex reacts directly with the diazo ester to generate a copper•olefin•carbene complex.[10]

The subsequent step is stereodetermining. Among the various stereochemical models that have been proposed, the one by Pfaltz can correctly account for the favored enantiomers in both diastereomers (Figure 2.9).[6b] As the olefin approaches the carbene, bonding interactions develop between the two moieties with concomitant pyramidalization of the carbon atoms that are involved in those interactions. Repulsive interactions between the ester group R^1 and the methyl groups of the Cp* ring differentiate the two prochiral faces of the *copper carbene*, leading to the formation of two stereoisomers that have *the same configuration at C1*.

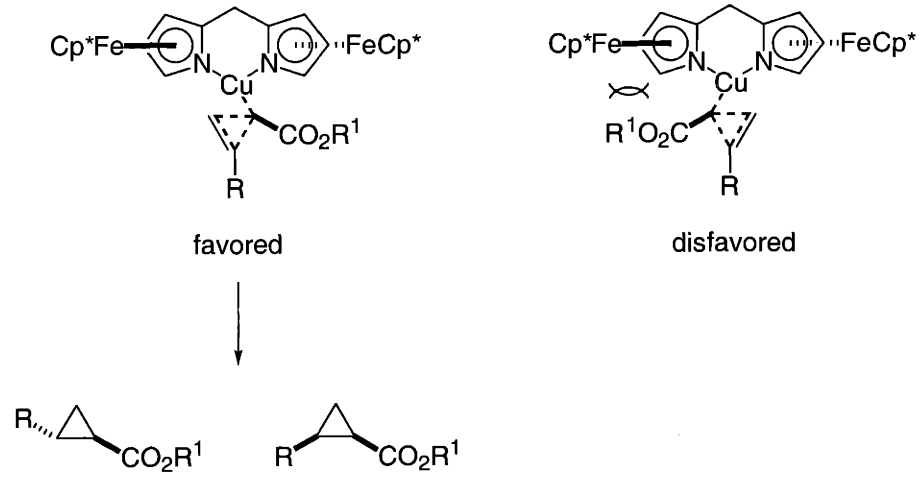

Figure 2.9. Pfaltz model for predicting the stereochemical outcome in copper-catalyzed asymmetric cyclopropanations of olefins.

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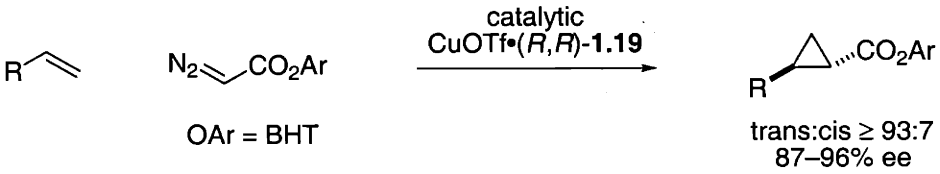
29 In his theoretical study, Salvatella suggested the following alternative sequence of events: (1) The diazo ester coordinates to the copper•ligand•olefin complex. (2) The olefin dissociates from the copper center. (3) Nitrogen extrusion takes place to afford the copper carbene (Ref. 28b).

30 Copper carbenes that can participate in cyclopropanation with olefins used to be considered as elusive, but Hofmann has recently synthesized and characterized spectroscopically a copper carbene complex that can undergo cyclopropanation with styrene. For details, see: Straub, B. F.; Hofmann, P. *Angew. Chem. Int. Ed.* **2001**, *40*, 1288–1290.

C. Conclusions.

We have demonstrated that bis(azaferrocene) **1.19** serves as an effective ligand for the copper-catalyzed asymmetric cyclopropanation of olefins. Using a hindered diazo ester, BHT diazoacetate, an array of monosubstituted olefins has been cyclopropanated with excellent diastereo- as well as enantioselectivity. The level of stereoselection achieved by **1.19** ranks close to some of the best ligands reported to date. Encouraging results have also been obtained with olefins of higher substitution pattern, and they suggest that these substrates merit further investigation.



The CuOTf•(*S*,*S*)-**1.19**•olefin complexes have been investigated by ^{1}H NMR and X-ray crystallography. The solid state structure suggests that the complex binds to the prochiral face of the olefin that does not undergo cyclopropanation, while the NMR studies reveal that the complex binds to the olefin reversibly at room temperature and with low enantiofacial selectivity. Hence, we conclude that the olefin complex is likely to be the resting state of the catalyst, and that the olefin has to dissociate before it reacts to form the cyclopropane product.

D. Experimental.

I. General.

^{1}H and ^{13}C nuclear magnetic resonance spectra were recorded on a Varian Unity-300 or a Varian VXR-500 NMR spectrometer at ambient temperature. ^{1}H data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane (δ scale), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broadened), integration, and coupling constant (Hz). ^{13}C chemical shifts are reported in parts per million downfield from tetramethylsilane (δ scale). All ^{13}C spectra were determined with broadband ^{1}H decoupling.

Infrared spectra were obtained on a Perkin-Elmer Series 1600 FT-IR spectrophotometer. High resolution mass spectra were recorded on a Finnegan MAT System 8200 spectrometer or a Bruker Daltonics Apex FT-ICR-MS (3 Tesla). Melting points were obtained on a Thomas Hoover Unimelt capillary melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter and are reported as follows: $[\alpha]^{\text{Temp }(^{\circ}C)}_{\lambda\ (nm)}$ (*c*, solvent, enantiomeric purity).

Preparative achiral HPLC was performed on an Alltech Econosphere Silica 10U column (22 mm x 250 mm). Analytical chiral HPLC was performed on a Daicel Chiralcel OD column (4.6 mm x 25 cm). Analytical achiral GC was performed on a J & W Scientific DB-1701 column (0.25 mm x 30 m). Analytical chiral GC was performed on either a Chiraldex G-TA column (0.25 mm x 20 m) or a Chiraldex B-PH column (0.25 mm x 20 m). Analytical TLC was performed using EM Science 0.25 mm silica gel 60 plates and visualized with either UV light or ethanolic phosphomolybdic acid. Flash chromatography was performed on EM Science silica gel 60 (230–400 mesh).

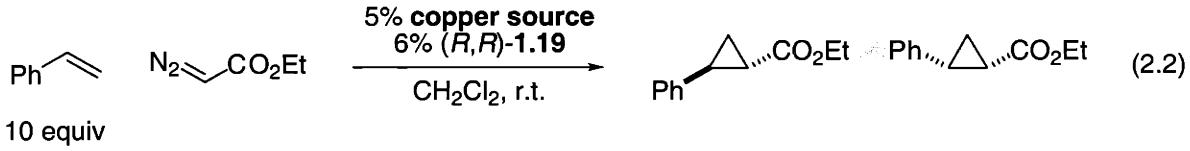
Solvents were distilled under nitrogen from the indicated drying agents: C_6H_{14} (Na); PhH (Na); $PhCH_3$ (Na); $PhCF_3(CaH_2)$; CH_2Cl_2 (CaH_2); $CHCl_3$ (CaH_2); $ClCH_2CH_2Cl$ (CaH_2).

Unless otherwise stated, all reagents were purchased from commercial suppliers and used as received. Olefins (Aldrich) were purified by distillation from calcium hydride under reduced pressure. Ethyl diazoacetate (Aldrich) was purified by flash chromatography prior to use. *t*-Butyl diazoacetate,[31] (*d*)-menthyl and (*l*)-menthyl diazoacetate,[6b] 2,6-di-*t*-butyl-4-methylphenyl diazoacetate,[18] and (Z)-1-phenylpropene[32] were synthesized according to literature procedures.

All reactions were carried out with magnetic stirring in oven-dried glassware under an atmosphere of argon (manifold) or under an atmosphere of nitrogen (Vaccum Atmospheres glove box), unless otherwise noted.

II. Development of Reaction Conditions.

1. Copper Source (Table 2.1).



(2.2)

General procedure for entries 1–4. A solution was prepared of the copper source (12 μmol) and (*R,R*)-**1.19** (6.8 mg, 13 μmol) in CH_2Cl_2 (5 mL). After 30 min, styrene (0.27 mL, 2.4 mmol) was added to this catalyst solution, and then a solution of ethyl diazoacetate (25 μL, 0.24 mmol) in CH_2Cl_2 (10 mL) was added by syringe pump to the reaction mixture over 4 h. After 16 h (total) of stirring at r.t., the reaction mixture was

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31 Takamura, N.; Mizoguchi, T.; Koga, K.; Yamada, S. *Tetrahedron* **1975**, *31*, 227–230.
32 Davies, D. E.; Gilchrist, T. L.; Roberts, T. G. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1275–1281.

filtered through a plug of silica with 15/85 EtOAc/hexanes to afford the crude product for analysis.

copper source	NMR yield (%)	trans : cis	trans ee	cis ee
CuCN	trace	61 : 39	49	54
CuI	21	76 : 24	56	35
$CuOTf•0.5C_6H_6$	64	74 : 26	64	36
$Cu(MeCN)_4PF_6$	80	72 : 28	59	29

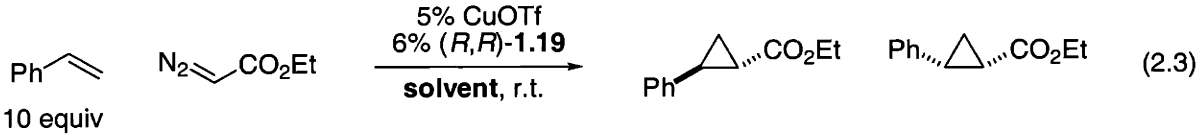
General procedure for entries 5,6. A mixture of CuCl (1.5 mg, 15 μmol), AgX (18 μmol), and (*R,R*)-**1.19** (9.6 mg, 17 μmol) were dissolved in 10 mL CH_2Cl_2. After 30 min, the catalyst solution was filtered through acrodisc and added to styrene (0.35 mL, 3.1 mmol). A 10 mL CH_2Cl_2 solution of ethyl diazoacetate (32 μL, 0.30 mmol) was added slowly over 4 h. After 16 h (total) of stirring at r.t., the reaction mixture was filtered through a plug of silica with 15/85 EtOAc/hexanes to afford the crude product for analysis.

X	NMR yield (%)	trans : cis	trans ee	cis ee
PF_6	73	77 : 23	61	37
SbF_6	36	78 : 22	64	37

Entry 7. A solution of $Cu(OTf)_2$ (7.7 mg, 21 μmol) and (*R,R*)-**1.19** (12 mg, 22 μmol) was prepared in CH_2Cl_2 (10 mL). After 15 min, $PhNHNH_2$ (2.1 μL, 21 μmol) in CH_2Cl_2 (0.1 mL) was added, turning the brown solution to orange. After another 15 min, styrene (0.49 mL, 4.3 mmol) was added, and then a solution of ethyl diazoacetate (45 μL, 0.43 mmol) in CH_2Cl_2 (10 mL) was added by syringe pump to the reaction mixture over 4 h. After 16 h (total) of stirring at r.t., the reaction mixture was filtered through a plug of silica with 15/85 EtOAc/hexanes. GC analysis of the crude product revealed a

70:30 trans:cis mixture, and that the trans product was formed in 41% ee (major enantiomer: 1*S*,2*S*), and the cis product was formed in 20% ee (major enantiomer: 1*S*,2*R*). NMR analysis of the crude product showed that the yield was 78%.

2. Solvent (Table 2.2).

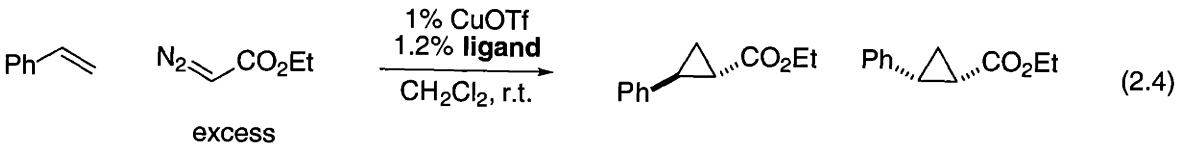


(2.3)

General procedure. A solution of CuOTf•0.5C_6H_6 (2.7 mg, 11 μmol) and (*R*,*R*)-**1.19** (6.2 mg, 12 μmol) was prepared in the solvent (5 mL). After 30 min, styrene (0.25 mL, 2.2 mmol) was added to this catalyst solution, and then a solution of ethyl diazoacetate (22 μL, 0.21 mmol) in the solvent (20 mL) was added by syringe pump to the reaction mixture over 8 h. After 16 h (total) of stirring at r.t., the reaction mixture was filtered through a plug of silica with 15/85 EtOAc/hexanes to afford the crude product for analysis.

			% ee	
solvent	NMR yield (%)	trans : cis	trans	cis
C_6H_{14}	39	53 : 47	17	9
PhH	67	76 : 24	75	50
$PhCH_3$	32	76 : 24	76	50
$PhCF_3$	52	74 : 26	57	26
CH_2Cl_2	77	77 : 23	76	46
$CHCl_3$	93	76 : 24	70	38
$ClCH_2CH_2Cl$	70	75 : 25	70	42

3. **Ligand (Table 2.3).**

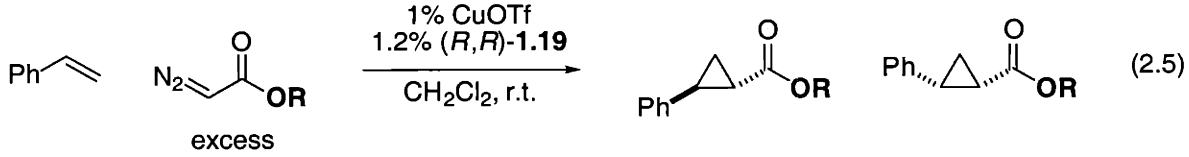


(2.4)

Entry 2. A solution of CuOTf•0.5C_6H_6 (3.5 mg, 14 μmol) and (*S,S*)-**1.22** (9.1 mg, 16 μmol) was prepared in CH_2Cl_2 (1 mL). After 30 min, half of this catalyst solution was transferred to a solution of styrene (71.8 mg, 0.689 mmol) in CH_2Cl_2 (5 mL), and then a solution of ethyl diazoacetate (257 mg, 2.25 mmol) in CH_2Cl_2 (1 mL) was added by syringe pump to the reaction mixture over 4 h. After 18 h (total) of stirring at r.t., the reaction mixture was filtered through a plug of silica with 15/85 EtOAc/hexanes as the eluant. GC analysis showed that the crude product was a 65:35 trans:cis mixture of isomers, and that the cis product was of 41% ee. The crude product was converted to the corresponding cyclopropylmethanol derivatives (*vide infra*), and the trans product was shown to be of 62% ee (major enantiomer: 1*R*,2*R*).

Entry 3. A solution of CuOTf•0.5C_6H_6 (1.4 mg, 5.6 μmol) and (*R,R*)-**1.29** (6.1 mg, 5.3 μmol) was prepared in CH_2Cl_2 (1 mL). After 30 min, the catalyst solution was transferred to a solution of styrene (60.6 mg, 0.582 mmol) in CH_2Cl_2 (5 mL), and then a solution of ethyl diazoacetate (206 mg, 1.80 mmol) in CH_2Cl_2 (2 mL) was added by syringe pump to the reaction mixture over 8 h. After 18 h (total) of stirring at r.t., the reaction mixture was filtered through a plug of silica with 30/70 EtOAc/hexanes as the eluant. GC analysis showed that the crude product was a 53:47 trans:cis mixture of isomers, and that the cis product was of 57% ee. The crude product was converted to the corresponding cyclopropylmethanol derivatives (*vide infra*), and the trans product was shown to be of 65% ee (major enantiomer: 1*S*,2*S*).

III. Asymmetric Cyclopropanation of Styrene as a Function of the Diazo Ester (Table 2.4).



(2.5)

All diastereoselectivities, enantioselectivities, and yields that are reported in Table 2.4 are the average of two runs, one with each enantiomer of bisazaferrocene **1.19**.

Entry 1, OR = OEt. A solution of $CuOTf \cdot 0.5C_6H_6$ (3.6 mg, 14 μmol) and (*R,R*)-**1.19** (8.8 mg, 17 μmol) was prepared in CH_2Cl_2 (1.4 mL). After 30 min, half of this catalyst solution was transferred to a flask containing styrene (74.1 mg, 0.711 mmol). The resulting solution was stirred for 5 min, and then a solution of ethyl diazoacetate (259 mg, 2.27 mmol) in CH_2Cl_2 (0.8 mL) was added by syringe pump to the reaction mixture over 4 h. After 18 h (total) of stirring at r.t., the reaction mixture was filtered through a plug of silica with 15/85 EtOAc/hexanes as the eluant. GC analysis showed that the crude product was a 76:24 trans:cis mixture of isomers. The product was purified by repeated flash chromatography (50% $CHCl_3$/hexanes; 5% EtOAc/hexanes) to afford pure trans cyclopropane (48.3 mg, 36% yield; 74% ee, major enantiomer: 1*S*,2*S*) and pure cis cyclopropane (10.0 mg, 5% yield; 44% ee, major enantiomer: 1*S*,2*R*).

The reaction was run under identical conditions with (*S,S*)-**1.19**. GC analysis showed that the crude product was a 75:25 trans:cis mixture. Flash chromatography afforded a 43% yield of trans cyclopropane (73% ee, major enantiomer: 1*R*,2*R*) and a 4% yield of cis cyclopropane (43% ee, major enantiomer: 1*R*,2*S*).

The ^1H NMR spectra of the diastereomers matched the literature data.[9]

Entry 2, OR = O-*t*-Bu. The asymmetric cyclopropanation of styrene with *t*-butyl diazoacetate was carried out according to the procedure given for entry 1. *t*-Butyl diazoacetate was added to the reaction mixture over 12 h. GC analysis showed that the crude product was an 86:14 trans:cis mixture, and that the cis cyclopropane was formed in 81% ee (major enantiomer: 1*S*,2*R*). The product was purified by flash chromatography (1/99 Et_2O/pentane) to afford the trans cyclopropane (83.3 mg, 54% yield; 87% ee, major enantiomer: 1*S*,2*S*).

The reaction was repeated under identical conditions with (*S*,*S*)-**1.19**. GC analysis showed that the crude product was an 86:14 trans:cis mixture, and that the cis cyclopropane was formed in 83% ee (major enantiomer: 1*R*,2*S*). Flash chromatography afforded a 71% yield of trans cyclopropane (88% ee, major enantiomer: 1*R*,2*R*).

The ^1H NMR spectrum of the trans cyclopropane matched the literature data.[10]

Entry 3, OR = O-(*d*)-Men. A solution of CuOTf•0.5C_6H_6 (4.2 mg, 17 μmol) and (*R*,*R*)-**1.19** (11 mg, 20 μmol) was prepared in CH_2Cl_2 (1.6 mL). After 30 min, half of this catalyst solution was transferred to a flask containing styrene (85.6 mg, 0.822 mmol). The solution was stirred for 5 min, and then (*d*)-menthyl diazoacetate (74.4 mg, 0.332 mmol, 0.40 equiv) was added to the reaction mixture. TLC showed that the consumption of (*d*)-menthyl diazoacetate was complete in 4 h. The remaining 2.8 equiv of (*d*)-menthyl diazoacetate was added in batches of 0.40 equiv every 4 h. After 36 h (total), the reaction mixture was filtered through a plug of silica with 15/85 EtOAc/hexanes as the eluant. GC analysis showed that the crude product was an 88:12 trans:cis mixture, and that the trans product was formed in 89% ee (major diastereomer: 1*S*,2*S*) and the cis product was formed in 83% ee (major diastereomer: 1*S*,2*R*). The product was purified by repeated flash chromatography (40/60 $CHCl_3$/hexanes; 30/70 CH_2Cl_2/hexanes) to afford the trans cyclopropane (168 mg, 68% yield).

The ^{1}H NMR data of the trans cyclopropane matched the literature data.[6b]

The reaction was repeated under identical conditions with (*S,S*)-**1.19**. GC analysis showed that the crude product was an 85:15 trans:cis mixture, and that the trans product was formed in 89% ee (major diastereomer: 1*R*,2*R*) and the cis product was formed in 84% ee (major diastereomer: 1*R*,2*S*). Flash chromatography afforded a 66% yield of trans cyclopropane. *This reaction actually corresponds to the enantiomeric version of entry 4, run 1.*

Entry 4, OR = O-(*l*)-Men. The asymmetric cyclopropanation of styrene with (*l*)-menthyl diazoacetate was carried out according to the procedure given for entry 3. A total of 3.2 equiv of (*l*)-menthyl diazoacetate was used, and the reaction was complete in 36 h. GC analysis showed that the crude product was an 85:15 trans:cis mixture, and that the trans product was formed in 90% ee (major diastereomer: 1*S*,2*S*) and the cis product was formed in 85% ee (major diastereomer: 1*S*,2*R*). The product was purified by repeated flash chromatography (40/60 $CHCl_3$/hexanes; 30/70 CH_2Cl_2/hexanes) to afford a 66% yield of trans cyclopropane.

The ^{1}H NMR data of the trans cyclopropane matched the literature data.[6b]

The reaction was repeated under identical conditions with (*S,S*)-**1.19**. GC analysis showed that the crude product was an 88:12 trans:cis mixture, and that the trans product was formed in 86% ee (major diastereomer: 1*R*,2*R*) and the cis product was formed in 80% ee (major diastereomer: 1*R*,2*S*). Flash chromatography afforded a 67% yield of trans cyclopropane. *This reaction actually corresponds to the enantiomeric version of entry 3, run 1.*

Entry 5, OR = BHT. A solution of CuOTf•0.5C_6H_6 (2.6 mg, 10 μmol) and (*R,R*)-**1.19** (6.5 mg, 12 μmol) was prepared in CH_2Cl_2 (1.0 mL). After 30 min, half of this catalyst solution was transferred to a flask containing styrene (54.3 mg, 0.521 mmol). The

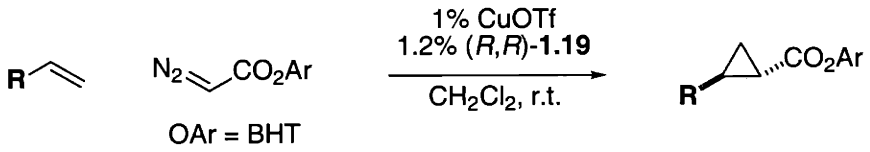
solution was stirred for 5 min, and then the BHT ester of diazoacetic acid (60.0 mg, 0.208 mmol, 0.40 equiv) was added to the reaction mixture. TLC showed that the consumption of the diazo ester was complete in 10 h. The remaining 0.8 equiv of the diazo ester was added in batches of 0.40 equiv at 10 h intervals. After a total of 36 h, TLC showed no residual styrene or diazo ester. The reaction mixture was filtered through a plug of silica with 15/85 EtOAc/hexanes as the eluant. GC analysis showed that the crude product was a 97:3 trans:cis mixture. The crude product was purified first by flash chromatography (40/60 $CHCl_3$/hexanes) and then by preparative HPLC (0.8/99.2 MTBE/hexanes), which afforded the trans cyclopropane as a colorless liquid (162 mg, 85% yield; 94% ee, major enantiomer: 1*S*,2*S*).

The reaction was repeated with (*S*,*S*)-**1.19**. GC analysis of the crude reaction product showed a 96:4 trans:cis ratio. Purification afforded a 74% yield of trans cyclopropane (95% ee, major enantiomer: 1*R*,2*R*).

The ^1H NMR data of the trans cyclopropane matched the literature data.[18]

Entry 6, OR = OCMeCy$_2$. A solution of CuOTf•0.5C_6H_6 (2.2 mg, 8.7 μmol) and (*R*,*R*)-**1.19** (5.1 mg, 9.7 μmol) was prepared in CH_2Cl_2 (1.0 mL). After 30 min, half of this catalyst solution was transferred to a vial containing styrene (45.3 mg, 0.435 mmol). The solution was stirred for 5 min, and then 1,1-dicyclohexylethyl diazoacetate (48.6 mg, 0.175 mmol, 0.40 equiv) was added to the reaction mixture. The remaining 1.23 equiv of the diazo ester was added in batches of 0.40 equiv at 12-h intervals. After a total of 48 h, the reaction mixture was filtered through a plug of silica with Et_2O as the eluant. The crude product was converted to the corresponding methyl ester (*vide infra*). GC analysis showed that the derivative was a 92:8 trans:cis mixture, and that the trans product was formed in 92% ee (major enantiomer: 1*S*,2*S*) and the cis product was formed in 94% ee (major enantiomer: 1*S*,2*R*).

IV. Asymmetric Cyclopropanation of Monosubstituted Olefins (Table 2.5).

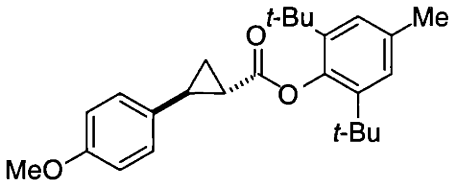


(2.6)

All diastereoselectivities, enantioselectivities, and yields that are reported in Table 2.5 are the average of two runs, one with each enantiomer of bisazaferrocene **1.19**.

Entry 2, R = 4-(MeO)C_6H_4. The asymmetric cyclopropanation of 4-methoxystyrene was carried out according to the procedure given for Table 2.4, entry 5. A total of 1.2 equiv of the diazo ester was used, and the reaction was complete in 36 h. GC analysis of the crude product revealed a 94:6 trans:cis mixture. The product was purified by flash chromatography (50/50 $CHCl_3$/hexanes), which afforded the trans and cis cyclopropanes as a yellow solid (189 mg, 92% yield; trans ee: 84%, major enantiomer: 1*S*,2*S*).

The reaction was repeated with (*S*,*S*)-**1.19**. GC analysis of the crude reaction product showed a 94:6 trans:cis ratio. Flash chromatography afforded an 87% yield of trans and cis cyclopropanes (trans ee: 89%, major enantiomer: 1*R*,2*R*).

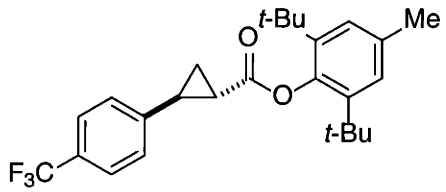


2,6-Di-*t*-butyl-4-methylphenyl (1*S*,2*S*)-2-(4-methoxyphenyl)cyclopropane carboxylate. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.35 (s, 9H), 1.36 (s, 9H), 1.47 (ddd, 1H, *J* = 4.0, 6.7, 8.2), 1.70 (td, 1H, *J* = 4.7, 9.5), 2.09 (ddd, 1 H, *J* = 4.0, 4.9, 8.3), 2.31 (s, 3H), 2.66 (ddd, 1H, *J* = 4.3, 6.7, 9.5), 3.81 (s, 3H), 6.86 (d, 2H, *J* = 8.9), 7.11 (s, 2H), 7.12 (d, 2H, *J* = 8.5). ^{13}C NMR (126 MHz, $CDCl_3$): δ 16.6, 21.8, 25.2, 26.8, 31.7, 35.5, 55.5, 114.2, 127.2,

128.0, 131.8, 134.6, 142.3, 146.2, 158.7, 174.0. IR (neat): 2961, 1744, 1613, 1598, 1250, 1141, 1109, 1039, 825, 737 cm^{-1}. $[\alpha]^{20}_D$ +212° (*c* 0.79, CH_2Cl_2; trans:cis = 94:6, 84% ee). HRMS–EI (*m/z*): M^+ calcd for $C_{26}H_{34}O_3$, 394.2508; found, 394.2508.

Entry 3, R = 4-(F_3C)C_6H_4. The asymmetric cyclopropanation of 4-trifluoromethylstyrene was carried out according to the procedure given for Table 2.4, entry 5. A total of 2.0 equiv of the diazo ester was used, and the reaction was complete in 48 h. GC analysis of the crude product revealed a 94:6 trans:cis mixture. The product was purified by flash chromatography (25/75 CH_2Cl_2/hexanes), which afforded the trans and cis cyclopropanes as a white solid (181 mg, 80% yield; trans ee: 94%, major enantiomer: 1*S*,2*S*).

The reaction was repeated with (*S*,*S*)-**1.19**. GC analysis of the crude reaction product showed a 95:5 trans:cis ratio. Flash chromatography afforded an 81% yield of trans and cis cyclopropanes (trans ee: 97%, major enantiomer: 1*R*,2*R*).



2,6-Di-*t*-butyl-4-methylphenyl (1*S*,2*S*)-2-(4-trifluoromethylphenyl)cyclopropane carboxylate. ^1H NMR (500 MHz, $CDCl_3$): δ 1.34 (s, 9H), 1.36 (s, 9H), 1.55 (ddd, 1H, *J* = 4.9, 6.4, 8.4), 1.80 (td, 1H, *J* = 4.9, 8.3), 2.22 (ddd, 1H, *J* = 4.4, 5.4, 8.6), 2.32 (s, 3H), 2.72 (ddd, 1H, *J* = 4.3, 6.6, 9.0), 7.11 (s, 2H), 7.28 (d, 2H, *J* = 8.3), 7.58 (d, 2H, *J* = 8.2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 17.2, 21.8, 25.8, 26.8, 31.7, 35.5, 124.3 (q, $^1J_{C-F}$ = 270), 125.8 (q, $^3J_{C-F}$ = 3.8), 126.9, 127.2, 129.2 (q, $^2J_{C-F}$ = 32), 134.8, 142.2, 144.0, 146.1, 173.4. IR (KBr): 2967, 1745, 1618, 1322, 1147, 1122 cm^{-1}. mp 169-173 °C. $[\alpha]^{20}_D$ +188° (*c* 1.01, CH_2Cl_2; trans:cis = 94:6, 94% ee). HRMS–EI (*m/z*): M^+ calcd for $C_{26}H_{31}F_3O_2$, 432.2276; found, 432.2275.

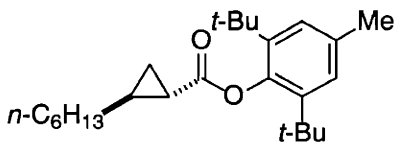
Entry 4, R = $PhCH_2$. The asymmetric cyclopropanation of allylbenzene was carried out according to the procedure given for Table 2.4, entry 5. A total of 2.0 equiv of the diazo ester was used, and the reaction was complete in 48 h. GC analysis of the crude product revealed a 94:6 trans:cis mixture. The product was purified first by flash chromatography (40/60 $CHCl_3$/hexanes) and then by preparative HPLC (30/70 $CHCl_3$/hexanes), thereby affording the trans cyclopropane (155 mg, 78% yield; 90% ee, major enantiomer: 1*S*,2*R*).

The reaction was repeated with (*S*,*S*)-**1.19**. GC analysis of the crude reaction product revealed a 94:6 trans:cis mixture. Flash chromatography followed by preparative HPLC afforded the trans cyclopropane in 78% yield (92% ee, major enantiomer: 1*R*,2*S*).[33]

The ^1H NMR spectrum of the trans cyclopropane matched the literature data.[10]

Entry 5, R = *n*-C_6H_{13}. The asymmetric cyclopropanation of 1-octene was carried out according to the procedure given for Table 2.4, entry 5. A total of 2.0 equiv of the diazo ester was used, and the reaction was complete in 54 h. GC analysis of the crude product revealed a 93:7 trans:cis mixture. The product was purified by flash chromatography (40/60 $CHCl_3$/hexanes; 2/98 Et_2O/hexanes), which afforded the trans cyclopropane as a colorless oil (172 mg, 80% yield; 89% ee, major enantiomer: 1*S*,2*S*).

The reaction was repeated with (*S*,*S*)-**1.19**. GC analysis of the crude reaction product revealed a 93:7 trans:cis mixture. Flash chromatography afforded the trans cyclopropane in 80% yield (90% ee, major enantiomer: 1*R*,2*R*).

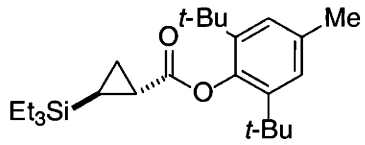


33 The stereodescriptor for this enantiomer was misassigned as (1*R*,2*R*) in reference 10.

2,6-Di-*t*-butyl-4-methylphenyl (1*S*,2*S*)-2-*n*-hexylcyclopropanecarboxylate. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.88 (m, 1H), 0.90 (t, 3H, J = 6.8), 1.2–1.6 (m, 12H), 1.33 (s, 9H), 1.34 (s, 9H), 1.66 (td, 1H, J = 4.1, 8.1), 2.23 (s, 3H), 7.09 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.3, 16.5, 21.7, 21.8, 22.9, 24.2, 29.3, 29.4, 31.7, 32.1, 33.5, 35.5, 127.1, 134.4, 142.3, 146.3, 174.9. IR (neat): 2956, 2925, 1747, 1598, 1403, 1364, 1140, 1110 cm^{-1}. $[\alpha]^{20}_D$ +66.7° (*c* 1.02, CH_2Cl_2; 89% ee). HRMS–EI (*m/z*): M^+ calcd for $C_{25}H_{40}O_2$, 372.3028; found, 372.3027.

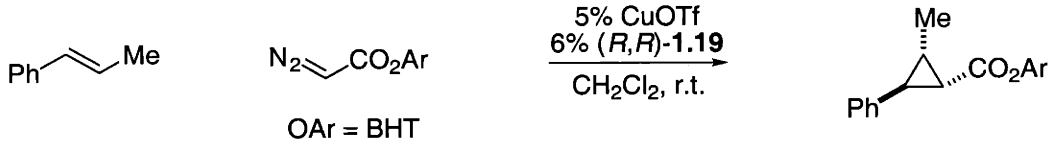
Entry 6, R = Et$_3$Si. A solution of CuOTf•0.5C_6H_6 (3.0 mg, 12 μmol) and (*R*,*R*)-**1.19** (7.4 mg, 14 μmol) in CH_2Cl_2 (0.6 mL) was added to triethylvinylsilane (82.9 mg, 0.582 mmol). The resulting solution was stirred for 5 min, and then the BHT ester of diazoacetic acid (66.5 mg, 0.231 mmol, 0.40 equiv) was added to the reaction mixture. TLC showed that consumption of the diazo ester was complete in 24 h. The remaining 2.8 equiv of the diazo ester were added in batches of 0.40 equiv at 12-h intervals. After a total of 5 days, the reaction mixture was filtered through a plug of silica (15/85 EtOAc/hexanes and 40/60 $CHCl_3$/hexanes as the eluants). GC analysis of the crude product revealed a 99:1 trans:cis mixture. The product was purified by repeated flash chromatography (40/60 $CHCl_3$/hexanes; 30/70 $CHCl_3$/hexanes) to afford the trans cyclopropane as a colorless oil (148 mg, 63% yield; 94% ee, major enantiomer: 1*R*,2*S*).

The reaction was repeated with (*S*,*S*)-**1.19**. GC analysis of the crude reaction product revealed a 99:1 trans:cis mixture. Flash chromatography afforded the trans cyclopropane in 65% yield (96% ee, major enantiomer: 1*S*,2*R*).



2,6-Di-*t*-butyl-4-methylphenyl (1*R*,2*S*)-2-(triethylsilyl)cyclopropanecarboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.42 (q, 6H, *J* = 7.9), 0.67–0.78 (m, 2H), 0.93 (t, 9H, *J* = 7.9), 1.45 (ddd, 1H, *J* = 2.8, 3.9, 10.6), 1.47 (s, 9H), 1.4-1.5 (m, 1H), 1.50 (s, 9H), 2.19 (s, 3H), 7.16 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 2.9, 7.3, 7.6, 12.9, 17.7, 21.8, 31.7, 35.5, 127.1, 134.5, 142.2, 146.4, 175.7. IR (neat): 2957, 2941, 1749, 1139, 1109 cm^{-1}. $[\alpha]^{20}_D$ +90.1° (*c* 0.71, CH_2Cl_2; 94% ee). HRMS–EI (*m/z*): [M$^+$] calcd for $C_{25}H_{42}O_2Si$, 402.2954; found, 402.2955.

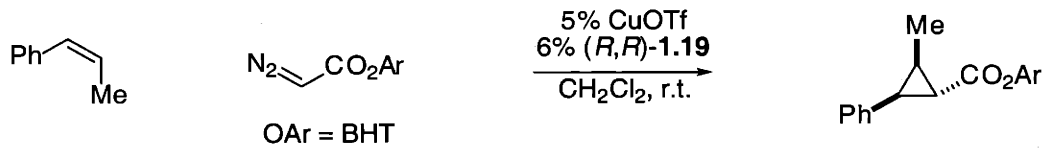
V. Asymmetric Cyclopropanation of Other Olefins.



(2.7)

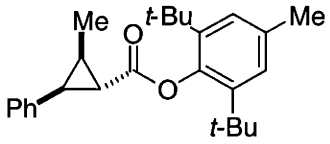
A solution of CuOTf•0.5C_6H_6 (3.4 mg, 14 μmol) and (*R*,*R*)-**1.19** (8.2 mg, 16 μmol) was prepared in CH_2Cl_2 (1.0 mL). After 30 min, (*E*)-1-phenylpropene (64.7 mg, 0.547 mmol) was added, followed by the BHT ester of diazoacetic acid (78.7 mg, 0.273 mmol) was added to the reaction mixture. TLC showed that the consumption of the diazo ester was complete in 24 h. The reaction mixture was filtered through a plug of silica with 15/85 EtOAc/hexanes as the eluant. GC analysis showed that the crude product was a 97:3 trans:cis mixture. The crude product was purified by flash chromatography (40/60 $CHCl_3$/hexanes) to afford the trans cyclopropane as a colorless liquid (36.1 mg, 35% yield; 87% ee, major enantiomer: 1*S*,2*S*,3*S*).

The ^{1}H NMR spectrum of the trans cyclopropane matched the literature data.[10]

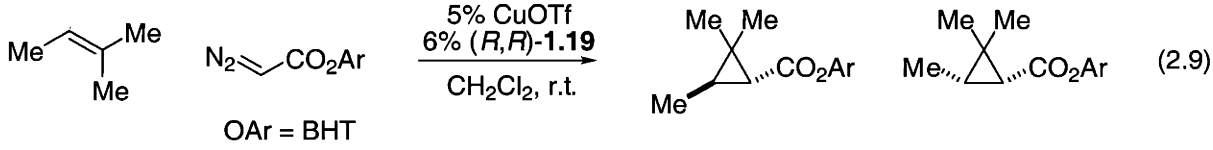


(2.8)

A solution of CuOTf•0.5C_6H_6 (3.6 mg, 14 μmol) and (*R,R*)-**1.19** (8.3 mg, 16 μmol) was prepared in CH_2Cl_2 (1.0 mL). After 30 min, (*Z*)-1-phenylpropene (69.4 mg, 0.587 mmol) was added, followed by the BHT ester of diazoacetic acid (83.8 mg, 0.291 mmol) was added to the reaction mixture. TLC showed that the consumption of the diazo ester was complete in 24 h. The reaction mixture was filtered through a plug of silica with 15/85 EtOAc/hexanes as the eluant. GC analysis showed that the crude product was a 96:4 trans:cis mixture. The crude product was partially purified by flash chromatography (40/60 $CHCl_3$/hexanes), and HPLC analysis showed that the trans product was formed in 45% ee (major enantiomer: 1*S*,2*R*,3*S*).



2,6-Di-*t*-butyl-4-methylphenyl (1*S*,2*R*,3*S*)-2-methyl-3-phenylcyclopropane carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.80 (d, 3H, *J* = 6.4), 1.44 (s, 9H), 1.48 (s, 9H), 1.94 (dqd, 1H, *J* = 4.5, 6.3, 9.6), 2.14 (t, 1H, *J* = 7.3), 2.19 (s, 3H), 3.01 (dd, 1H, *J* = 4.9, 9.8), 7.0–7.2 (m, 7H). ^{13}C NMR (126 MHz, C_6D_6): δ 13.1, 21.9, 24.5, 28.5, 32.1, 32.2, 33.2, 35.9, 127.3, 127.6, 127.6, 129.0, 129.8, 134.9, 136.8, 143.0, 143.0, 147.3, 174.2. IR (KBr): 3072 (w), 2969 (m), 1747 (s), 1737 (s), 1421 (m), 1152 (s), 1136 (s), 1107 (s), 745 (m), 699 (m) cm^{-1}. HRMS–ESI (*m/z*): [M + Na]$^+$ calcd for $C_{26}H_{34}O_2$, 401.2451; found, 401.2440.

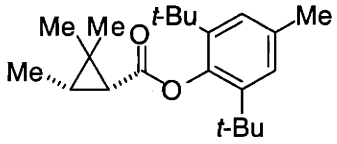


(2.9)

A solution of CuOTf•0.5C_6H_6 (3.4 mg, 14 μmol) and (*R,R*)-**1.19** (8.8 mg, 17 μmol) was prepared in CH_2Cl_2 (0.5 mL). After 30 min, 2-methyl-2-butene (58 μL, 0.55 mmol) was added, followed by the BHT ester of diazoacetic acid (79.1 mg, 0.274 mmol) was

added to the reaction mixture. TLC showed that the consumption of the diazo ester was complete in 24 h. The reaction mixture was filtered through a plug of silica with 15/85 EtOAc/hexanes as the eluant. GC analysis showed that the crude product was a 44:56 trans:cis mixture. The crude product was purified by flash chromatography (1/99 Et_2O/pentane) to afford a mixture of trans and cis cyclopropane as a white solid (31.5 mg, 35% yield; trans ee: 44%, major enantiomer: 1*R*,3*R*; cis ee: 85%, major enantiomer: 1*R*,3*S*).

The ^1H NMR spectrum of the trans cyclopropane matched the literature data.[18]

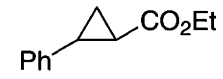
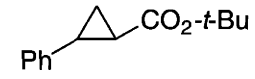
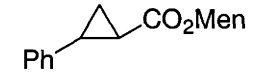
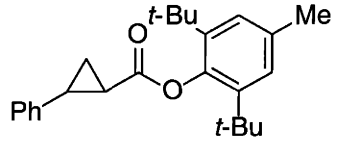
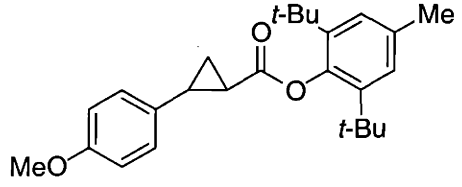
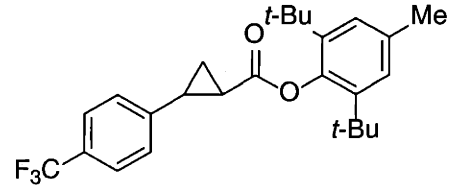
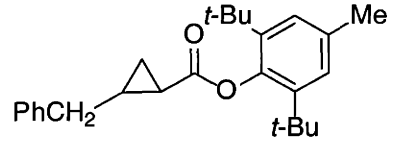
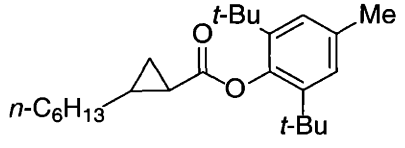
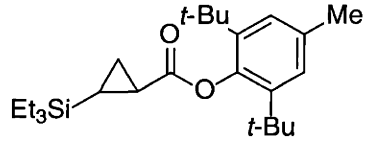


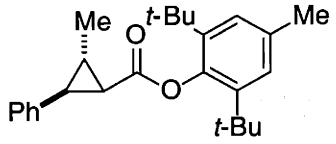
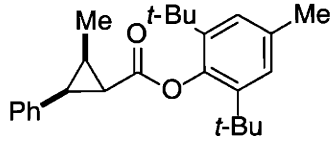
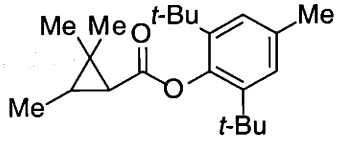
2,6-Di-*t*-butyl-4-methylphenyl (1*R*,3*S*)-2,2,3-trimethylcyclopropanecarboxylate. ^1H NMR (500 MHz, C_6D_6): δ 0.98 (s, 3H), 1.03 (qd, 1H, *J* = 6.5, 8.7), 1.27 (d, 3H, *J* = 6.4), 1.31 (s, 3H), 1.44 (s, 9H), 1.46 (s, 9H), 1.68 (d, 1H, *J* = 8.9), 2.19 (s, 3H), 7.16 (s, 2H). ^{13}C NMR (126 MHz, C_6D_6): δ 8.4, 14.4, 21.9, 27.0, 29.2, 30.1, 32.2, 32.2, 35.7, 35.8, 127.4, 127.5, 134.5, 143.1, 143.1, 147.0, 171.9. R (KBr): 3003 (w), 2954 (m), 2871 (w), 1733 (s), 1411 (m), 1362 (m), 1155 (m), 1088 (s), 871 (m), 743 (m) cm^{-1}. HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{22}H_{34}O_2$, 353.2451; found, 353.2447.

VI. Assay of Diastereoselectivity.

The diastereomeric ratio of the cyclopropanes were all determined by GC chromatography. Table 2.8 summarizes the GC assay conditions for the trans and cis cyclopropanes:

Table 2.8. Achiral GC data for diastereomeric cyclopropanecarboxylate esters.

reaction product	column	conditions	trans t_R (min)	cis t_R (min)
	DB-1701	140 °C, He, 1.0 mL/min	8.5	7.3
	DB-1701	150 °C, He, 1.0 mL/min	7.2	6.3
	DB-1701	180 °C, He, 1.0 mL/min	22.6, 23.8	19.3, 19.7
	DB-1701	220 °C, He, 1.72 mL/min	9.8	10.3
	DB-1701	240 °C, He, 1.72 mL/min	10.1	9.6
	DB-1701	220 °C, He, 1.72 mL/min	9.1	9.3
	DB-1701	220 °C, He, 1.72 mL/min	13.0	14.0
	DB-1701	200 °C, He, 1.72 mL/min	13.8	13.5
	DB-1701	240 °C He, 1.0 mL/min	6.4	6.0

	DB-1	210 °C He, 1.72 mL/min	13.3	11.8
	DB-1	210 °C He, 1.72 mL/min	12.5	13.2
	DB-1	180 °C He, 1.72 mL/min	8.5	8.0

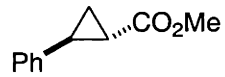
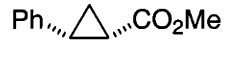
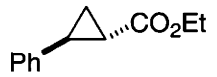
VII. Assay of Enantioselectivity.

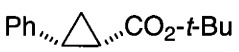
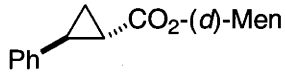
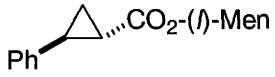
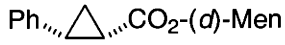
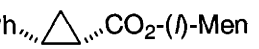
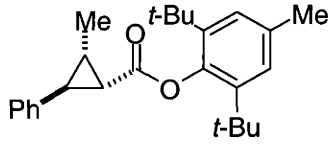
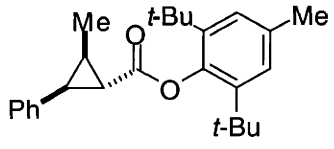
The enantiomeric excess of the cyclopropanes were assayed in either one of the following methods:

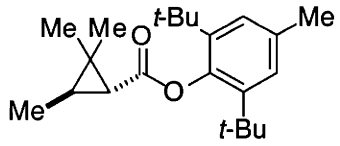
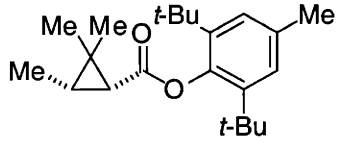
a. direct analysis

Table 2.9 summaries the assay conditions for cyclopropanecarboxylate esters:

Table 2.9. Resolution conditions for enantiomeric cyclopropanecarboxylate esters.

substrate	column	conditions	indicated config. t_R (min)	opposite config. t_R (min)
	GC Chiraldex G-TA	90 °C, H_2, 1.0 mL/min	41.9	40.3
	GC Chiraldex G-TA	90 °C, H_2, 1.0 mL/min	47.6	37.1
	GC Chiraldex B-PH	85 °C He, 2.0 mL/min	99.9	97.1

	GC Chiraldex B-PH	85 °C He, 2.0 mL/min	81.4	85.9
	GC Chiraldex G-TA	90 °C, H_2, 1.5 mL/min	53.3	42.0
	GC Chiraldex G-TA	100 °C, H_2, 1.5 mL/min	28.1	24.7
	GC DB-1701	180 °C He, 1.0 mL/min	22.6	22.6
	GC Chiraldex B-PH	140 °C He, 2.0 mL/min	56.5	56.0
	GC DB-1701	180 °C He, 1.0 mL/min	23.8	23.8
	GC Chiraldex B-PH	140 °C He, 2.0 mL/min	62.0	63.2
	GC DB-1701	180 °C He, 1.0 mL/min	19.7	19.7
	GC DB-1701	180 °C He, 1.0 mL/min	19.3	19.3
	HPLC Chiralcel OD	0.01% *i*-PrOH/hexanes, 1.0 mL/min	17.7	15.1
	HPLC Chiralcel OD	0.2% *i*-PrOH/hexanes, 1.0 mL/min	8.1	10.7

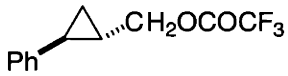
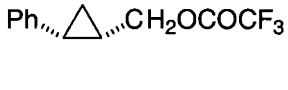
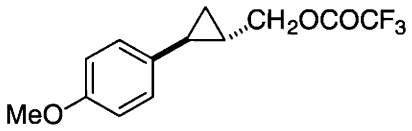
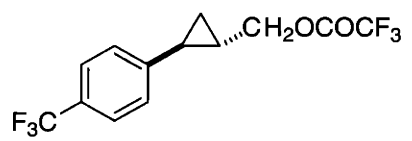
	HPLC Chiralcel OD	0.02% *i*-PrOH/hexanes, 1.0 mL/min	10.9	18.5
	HPLC Chiralcel OD	0.02% *i*-PrOH/hexanes, 1.0 mL/min	9.0	8.3

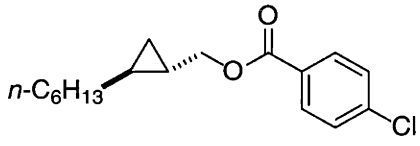
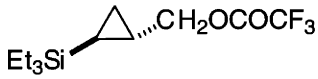
The stereoselectivity for the reactions of menthyl-derived diazo esters were measured by GC analysis of the crude reaction products on a DB-1701 column, and corrected for the ee of the starting menthol: (*d*)-menthol: 98% ee; (*l*)-menthol: 99% ee.

b. reduction by $LiAlH_4$ to the alcohol, followed by derivatization.

Table 2.10 summarizes the assay conditions for cyclopropylmethanols.

Table 2.10. Resolution conditions for enantiomeric cyclopropylmethanols.

substrate	column	conditions	indicated config. t_R (min)	opposite config. t_R (min)
	GC Chiraldex G-TA	90 °C, H_2, 1.5 mL/min	21.8	20.2
	GC Chiraldex G-TA	90 °C, H_2, 1.5 mL/min	14.4	16.9
	GC Chiraldex G-TA	100 °C, H_2, 1.5 mL/min	63.1	58.4
	GC Chiraldex G-TA	100 °C, H_2, 1.5 mL/min	28.6	26.8

	HPLC Chiralcel OD	10% *i*-PrOH/hexanes, 1.0 mL/min	15.1	9.3
	HPLC Chiralcel OD	0.05% *i*-PrOH/hexanes, 1.0 mL/min	22.0	25.3
	GC Chiraldex B-PH	60 °C He, 2.0 mL/min	17.0	18.3

Assignment of absolute stereochemistry.

Table 2.4, trans products. For Table 2.4, entry 6, the sign of the optical rotation of the trans cyclopropane product formed in the presence of bis(azaferrocene) (*R,R*)-**1.19** is positive, and the absolute stereochemistry of the predominant trans cyclopropane is therefore (1*S*,2*S*).[10] The major enantiomer of the alcohol that results from the reduction of this ester is the same as the major enantiomer that is produced from the corresponding reductions of the other trans cyclopropane products in Table 2.4; hence the (1*S*,2*S*) stereochemistry is produced preferentially for all of the cyclopropanations illustrated in Table 2.4.

Table 2.4, cis products. For Table 2.4, entry 1, the sign of the optical rotation of the cis cyclopropane product formed in the presence of bis(azaferrocene) (*R,R*)-**1.19** is positive, and the absolute stereochemistry of the predominant cis cyclopropane is therefore (1*S*,2*R*).[10] The absolute stereochemistry of the major enantiomer of the other cis cyclopropanes was assigned by analogy.

Table 2.5. For Table 2.5, entry 1, the sign of the optical rotation of the trans cyclopropane product formed in the presence of bis(azaferrocene) (*R,R*)-**1.19** is positive, and the absolute stereochemistry of the predominant trans cyclopropane is therefore (1*S*,2*S*).[10] The absolute stereochemistry of the product of Table 2.5, entry 4, was also

assigned by optical rotation (1*S*,2*R*).[10] The absolute stereochemistry of the other products were assigned by analogy.

Eq 2.7–2.9. The absolute stereochemistry of the cyclopropanes are assigned by assuming that (*R*,*R*)-**1.19** and (*R*,*R*)-**2.5** have the same sense of asymmetric induction.[10]

Chapter 3

Chiral Ylides Catalytically Generated by Copper Complexes and Their Subsequent Rearrangements: Asymmetric Ring Expansion of Oxetanes to Tetrahydrofurans

A. Introduction.

An ylide is a compound in which a positively charged atom from groups 15–17 is connected to a carbon atom carrying an unshared pair of electrons.[1] It can be regarded as a special type of zwitterion in which the structure, or at least one canonical form, contains both positive and negative charges on adjacent atoms. Some ylides are stable enough to be isolated, but the others, once formed, will subsequently undergo a plethora of transformations, e.g. [1,2]- or [2,3]-sigmatropic rearrangement,[2] dipolar cycloaddition, β-hydrogen elimination, etc. Most of these reactions create one or two additional stereogenic centers; hence, their effective asymmetric versions should be versatile synthetic tools (Figure 3.1).

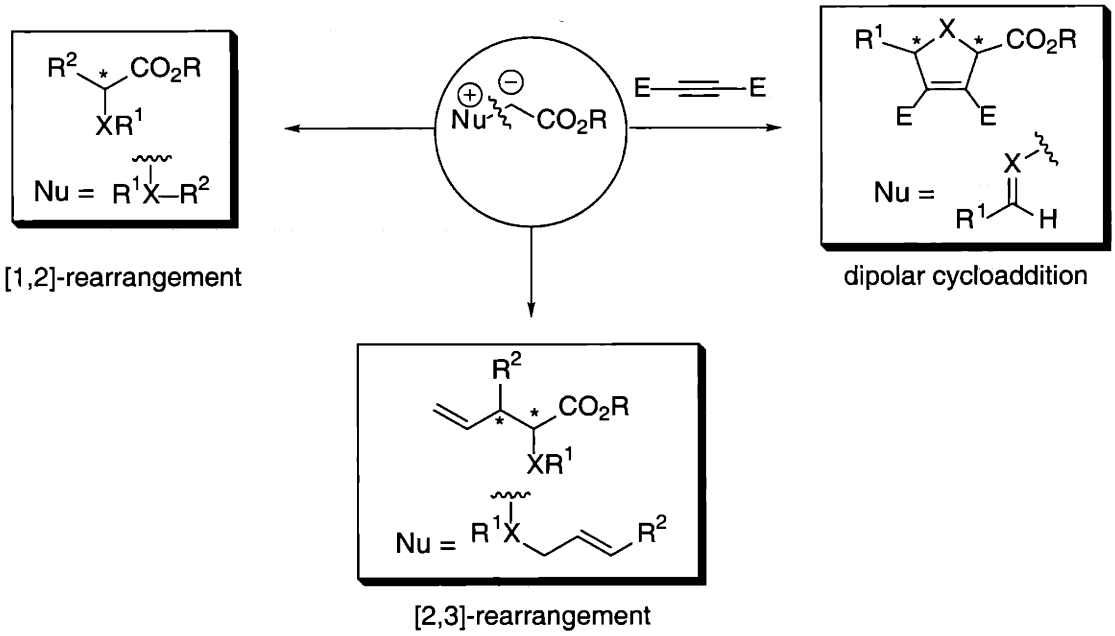


Figure 3.1. Examples of ylide transformations that create additional stereogenic centers.

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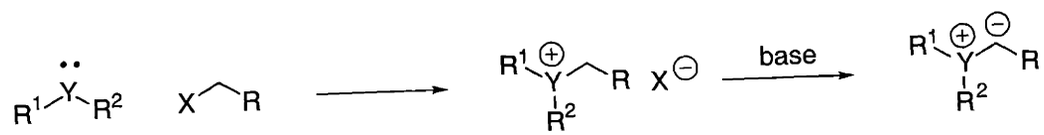
1 For reviews of ylide chemistry, see: (a) Johnson, A. W. In *Ylid Chemistry*; Blomquist, A. T., Ed.; Academic Press: New York and London, 1966. (b) Morris, D. G. *Surv. Prog. Chem.* **1983**, *10*, 189–257. (c) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263–309.

2 For reviews of rearrangement chemistry, see: (a) Markó, I. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Volume 3, Chapter 3.10, pp 913–974. (b) Brückner, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Volume 6, Chapter 4.6, pp 873–908.

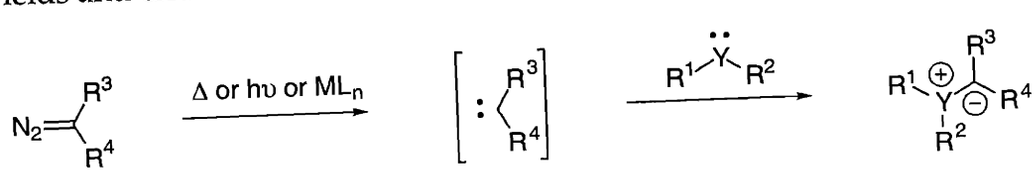
There are two general methods of ylide formation. The older and the more common method is called the "salt method", in which a sulfonium or ammonium cation, generated by the alkylation of the corresponding nucleophile, is deprotonated by a strong base.



Y = S, NR^3

Several factors render the modification of the transformation to a catalytic asymmetric version difficult: (1) The reaction often requires forcing conditions such as heating, strong alkylating agents, and strong bases, e.g., *n*-BuLi or $NaNH_2$. (2) Side reactions such as dealkylation of the cations and Hoffmann elimination can interfere. (3) When R^1 or R^2 contains α-hydrogen atoms, problems with regioselectivity arise during deprotonation.

The second approach involves the addition of carbenes to the nucleophile for the direct generation of the ylide. Pioneering work by Ando[3] and Doyle[4] established the effectiveness of this approach. They explored the generation of carbenes from diazo compounds through different routes, and found that metal-catalyzed reactions give better yields and cleaner reaction mixtures than thermal or photochemical pathways.



The carbene approach addresses some of the difficulties concerning the salt method: (1) The ambiguity in the regioselectivity for the deprotonation of ylides is now removed, as the anionic charge resides on the carbon from the carbene source. (2) The

3 Ando, W. *Acc. Chem. Res.* **1977**, *10*, 179–185.
4 Doyle, M. P. *Acc. Chem. Res.* **1986**, *19*, 348–356.

mild and neutral conditions under which the ylides are generated disfavor elimination and ensure higher functional group tolerance. (3) The scope of the reaction is expanded, as less nucleophilic bases such as carbonyl compounds or ethers also participate in the generation of ylides.

However, the development of metal catalysts for ylide generation remains a challenging problem. Since the Lewis bases themselves are often good ligands for the metal center, they tend to inhibit the decomposition of diazo compounds. Thus elevated temperatures are often needed, especially when the Lewis bases are highly nucleophilic . Furthermore, a variety of competing reaction pathways are available for metal carbenes, and factors favoring ylide formation are not well explored or understood (Figure 3.2).

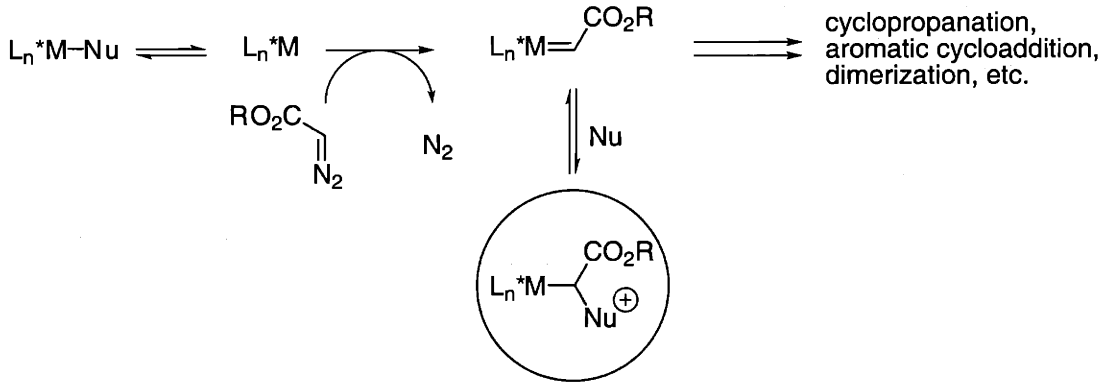


Figure 3.2. Metal-catalyzed decomposition of diazo esters in the presence of Lewis bases.

In Chapter 2, we have demonstrated that our bis(azaferrocenes) are effective ligands for the copper-catalyzed asymmetric cyclopropanation of olefins. We hypothesize that the high stereoselectivity originates from the chiral environment of the putative copper carbene, which allows only one prochiral face of the carbene to participate in the formation of cyclopropanes. The same chiral environment can conceivably direct the enantioselective formation of ylides from Lewis bases (Figure 3.3).

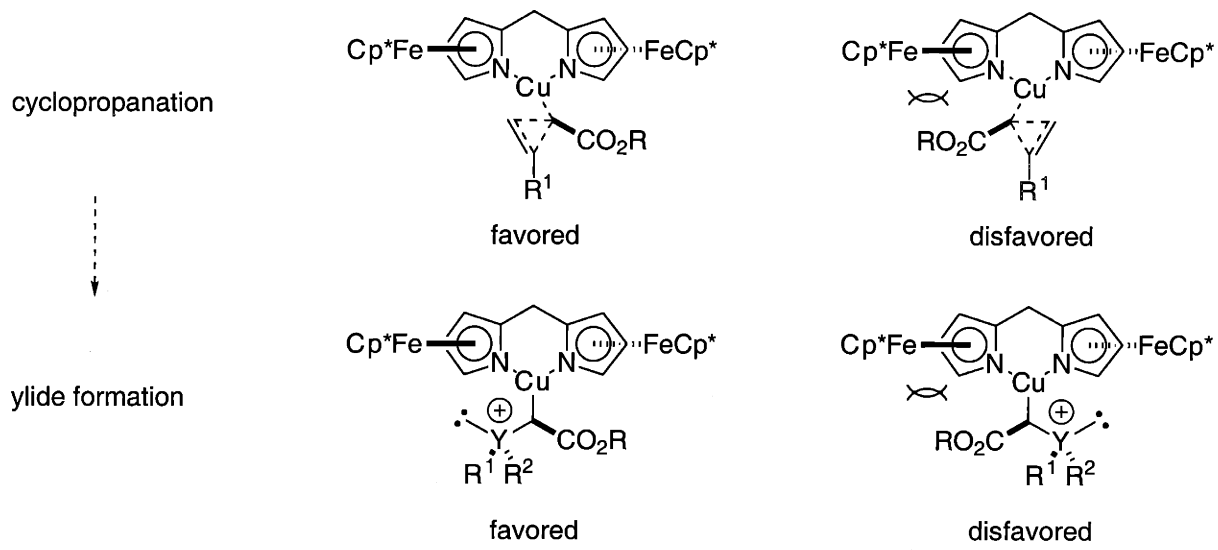


Figure 3.3. Stereodifferentiation by a copper carbene in cyclopropanation and ylide formation.

Copper catalysts are believed to be less effective for ylide formation than rhodium.[5] One notable exception is the report by Nozaki on copper-catalyzed carbon–oxygen insertion of diazo esters into oxetanes to form tetrahydrofurans (eq 3.1).[6] The reaction is a result of a [1,2]-rearrangement (Stevens) of the oxonium ylide formed between the diazo ester and the oxetane.[7] Later, Nozaki also attempted to induce asymmetry in the reaction by using the chiral catalyst **2.1**. The optical rotation data of the products suggests that there is some stereoselection in the reaction, but the level remains unclear.[8]

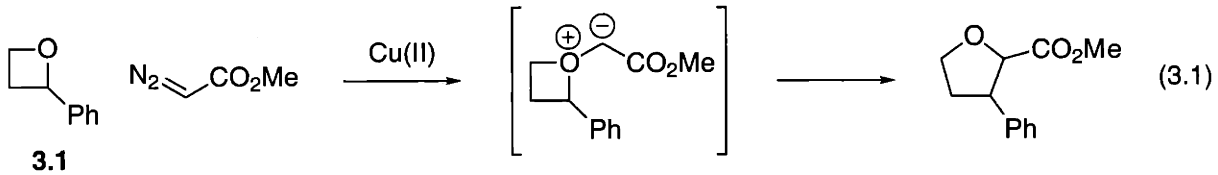
---

5 For a comparison of the performance between copper and rhodium catalysts in ylide formation, see: Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*; John Wiley: New York, 1998; Chapter 7.

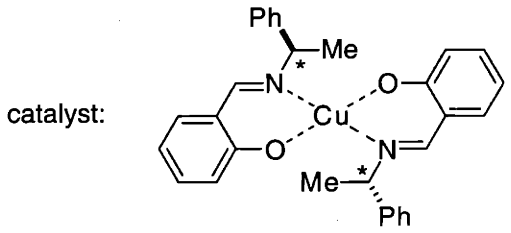
6 Nozaki, H.; Takaya, H.; Noyori, R. *Tetrahedron* **1966**, *22*, 3393–3401.

7 Ethers are relatively unreactive towards ylide formation because of their unfavorable equilibrium with metal carbenes (cf. Figure 3.2). Oxetanes represent an exception to this rule since their ring strain provides a large driving force for their subsequent rearrangements.

8 (a) Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1966**, *7*, 5239–5244. (b) Nozaki, H.; Takaya, H.; Moriuti, S.; Noyori, R. *Tetrahedron* **1968**, *24*, 3655–3669.

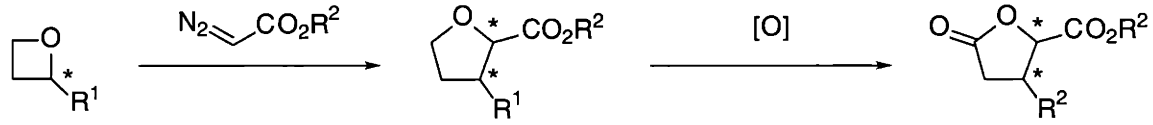


3.1



2.1

Since this initial work, only Katsuki has described further investigations of this interesting transformation.[9] This lack of attention is surprising, since the reaction is the only example of an asymmetric [1,2]-rearrangement of ylides that are generated in a catalytic and intermolecular fashion.[10] In addition, the reaction represents an expeditious route to optically pure tetrahydrofurans and γ-lactones.[11]



oxetane **tetrahydrofuran** **γ-lactone**

For his ring expansion of oxetanes, Katsuki used the C_2-symmetric bipyridine **3.2**, which he developed initially for the asymmetric cyclopropanation of olefins (Table 3.1):

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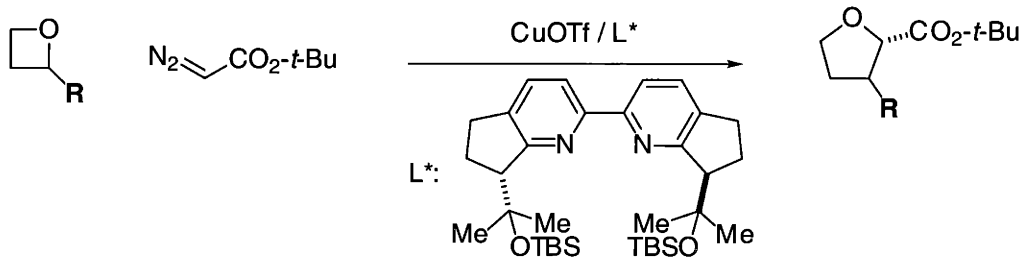
9 (a) Ito, K.; Katsuki, T. *Chem. Lett.* **1994**, 1857–1860. (b) Ito, K.; Yoshitake, M.; Katsuki, T. *Heterocycles* **1996**, *42*, 305–317.

10 For a review on stereoselective ylide rearrangements, see ref. 5 and: (a) Li, A. H.; Dai, L. X.; Aggarwal. V. K. *Chem. Rev.* **1997**, *97*, 2341–2372. (b) Hodgson, D. M.; Pierard, F. Y. T. M.; Stupple, P. A. *Chem. Soc. Rev.* **2001**, *30*, 50–61. Below listed some examples of asymmetric [2,3]-rearrangements of ylides that are generated intermolecularly. Oxygen, Iodine: (c) Doyle, M. P.; Forbes, D. C.; Vasbinder, M. M.; Peterson, C. S. *J. Am. Chem. Soc.* **1998**, *120*, 7653–7654. Sulfur: (d) Nishibayashi, Y.; Ohe, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1995**, 1245–1246. (e) Fukuda, T.; Katsuki, T. *Tetrahedron Lett.* **1997**, *38*, 3435–3438. (f) Fukuda, T.; Irie, R.; Katsuki, T. *Tetrahedron* **1999**, *55*, 649–664. (g) McMillen, D. W.; Varga, N.; Reed, B. A.; King, C. *J. Org. Chem.* **2000**, *65*, 2532–2536.

11 For a survey of stereocontrolled methods for the synthesis of tetrahydrofurans, see: Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309–3362.



(3.2)

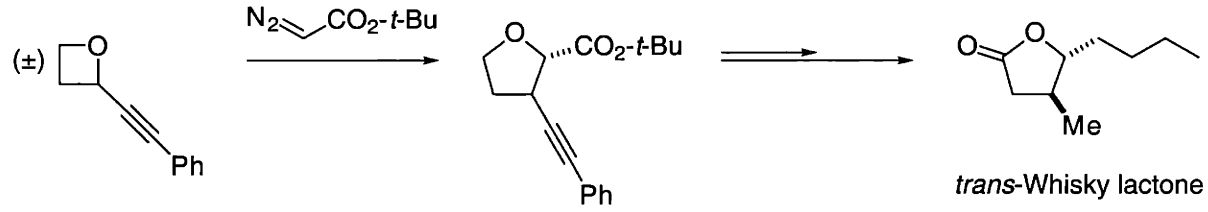
3.2

Table 3.1. Asymmetric ring expansion of 2-substituted oxetanes to tetrahydrofurans in the presence of **3.2** (eq 3.2).

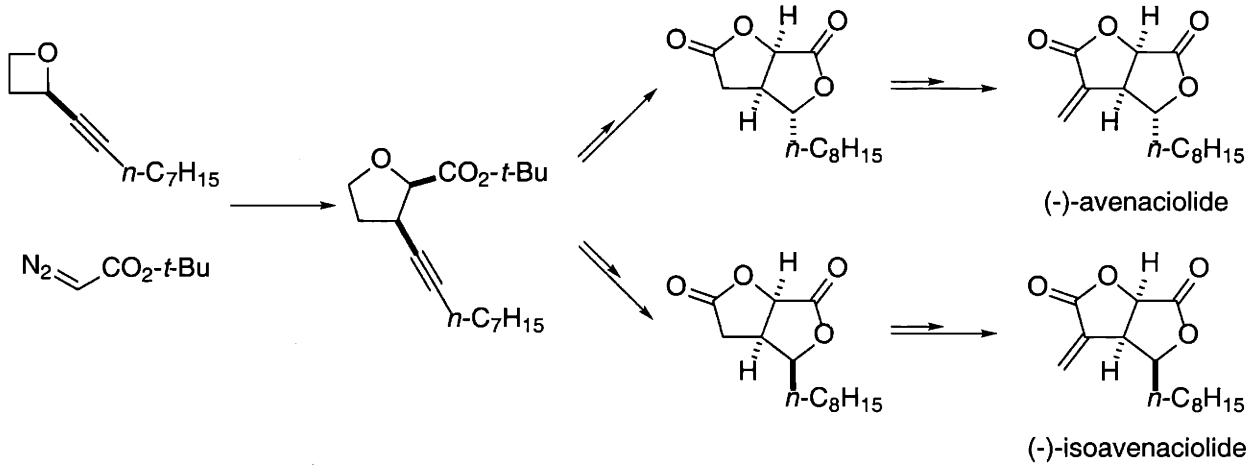
		oxetane	tetrahydrofuran product			
entry	**R**	% ee	trans : cis	% ee, trans	% ee, cis	yield (%)
1	Ph	0	59 : 41	75	81	72
2	4-ClC_6H_4	0	54 : 46	75	80	80
3	4-MeC_6H_4	0	50 : 50	50	76	62
4	PhC≡C	0	59 : 41	75	71	76
5	Ph	89 (*R*)	89 : 11	92	16	70
6	Ph	85 (*S*)	25 : 75	11	93	60
7	$nC_7H_{15}C$≡C	93 (*S*)	15 : 85	n.d.	72	69

With racemic oxetanes, good levels of stereoselectivity are obtained for both diastereomeric products when the 2-substituent is aromatic or alkynyl (entries 1–4). The use of enantiomerically enriched oxetanes results in the diastereoselective formation of either tetrahydrofuran in high enantiomeric excess (entries 5–7). *For the tetrahydrofuran product, the catalyst controls the stereochemistry at C2, while the oxetane substrate determines the configuration at C3.*

Katsuki further demonstrated the utility of the reaction by applying it in the total synthesis of *trans*-Whisky lactone (Scheme 3.1)[12] and the formal total synthesis of (-)-avenaciolide and (-)-isoavenaciolide (Scheme 3.2).[13]



Scheme 3.1. Total synthesis of *trans*-Whisky lactone.



Scheme 3.2. Formal total synthesis of bislactone structures (-)-avenaciolide and (-)-isoavenaciolide.

In this chapter, we discuss our investigations into the use of bis(azaferrocenes) as ligands for copper to catalyze the ring expansion of oxetanes to tetrahydrofurans. New diazo esters, which may prove useful in other carbene transfer reactions, have been developed to enhance the stereoselectivity. Finally, a mathematical analysis of the reaction is presented to further our understanding of its mechanistic aspects.

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12 (a) Ito, K.; Yoshitake, M.; Katsuki, T. *Chem. Lett.* **1995**, 1027–1028. (b) Ito, K.; Yoshitake, M.; Katsuki, T. *Tetrahedron* **1996**, *52*, 3905–3920.

13 (a) Ito, K.; Fukuda, T.; Katsuki, T. *Synlett* **1997**, 387–389. (b) Ito, K.; Fukuda, T.; Katsuki, T. *Heterocycles* **1997**, *46*, 401–411.

B. Results and Discussion.

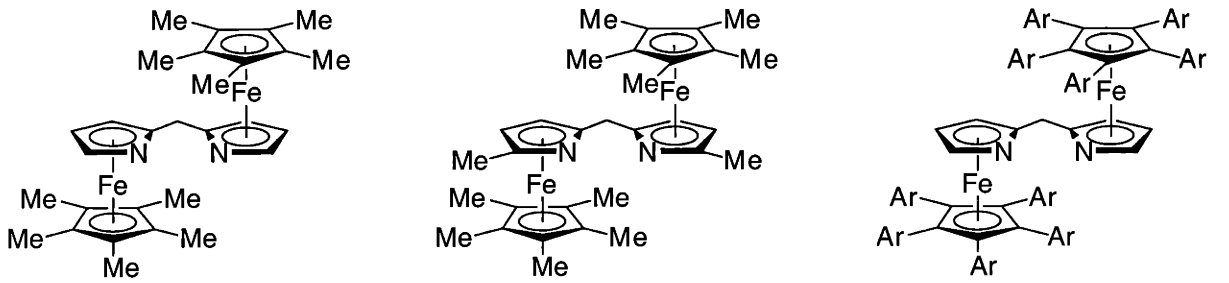
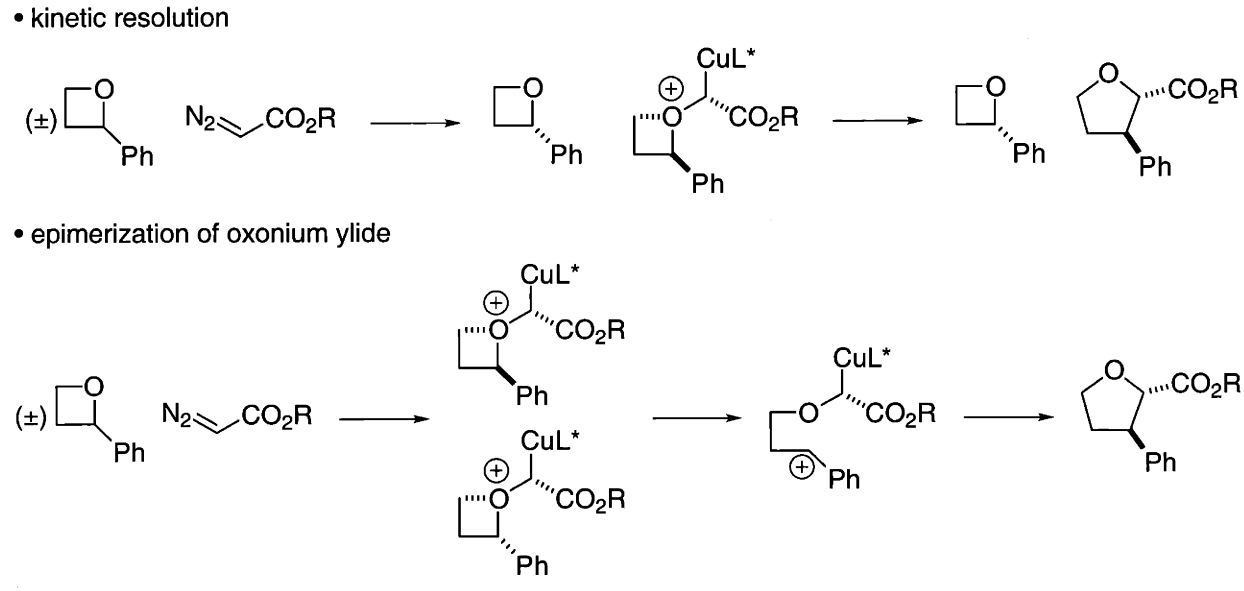


Figure 3.4. C_2-Symmetric bis(azaferrocenes) investigated in this chapter.

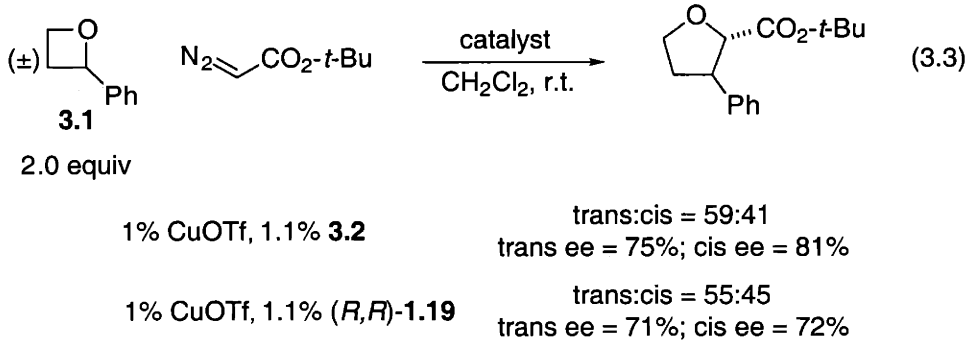
I. Development of Reaction Conditions.

The first improvement to the ring expansion of oxetanes that we intended to achieve was the control of diastereoselectivity, through either one of the following pathways: (1) kinetic resolution of oxetanes, in which the reacted enantiomer forms one diastereomeric tetrahydrofuran; (2) epimerization at C2 of the oxonium ylide to give the thermodynamically favored trans diastereomer (Scheme 3.3).



Scheme 3.3. Possible scenarios for the diastereomeric ring expansion to tetrahydrofurans.

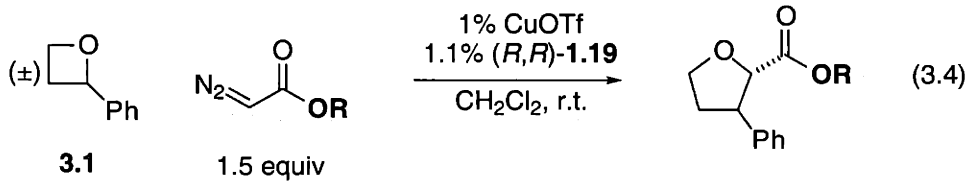
To examine the feasibility of these pathways, we repeated the ring expansion under the Katsuki conditions, with bipyridine **3.2** replaced by bis(azaferrocene) **1.19** (eq 3.3).



(3.3)

The results indicate that our system is very similar to the Katsuki system: (1) The residual oxetane is racemic, suggesting the absence of kinetic resolution. (2) The diastereomeric tetrahydrofurans are furnished in similar amounts. (3) Both diastereomeric products are formed in good enantiomeric excess and have the same configuration at C2. Hence, we were forced to conclude that neither scenario for the diasteroselective ring expansion to tetrahydrofurans is operating, but our catalyst still provides good enantioselection in the process.

To enhance this enantioselection, we decided to examine the reaction with the diazo esters that we have tried in our cyclopropanation, hoping that a larger ester group would provide a better carbene facial selectivity during the ylide formation (cf. Figure 3.3). Since we had already established that there is no kinetic resolution of the oxetane in our system, the reaction was performed with the oxetane as the limiting reagent (Table 3.2).



(3.4)

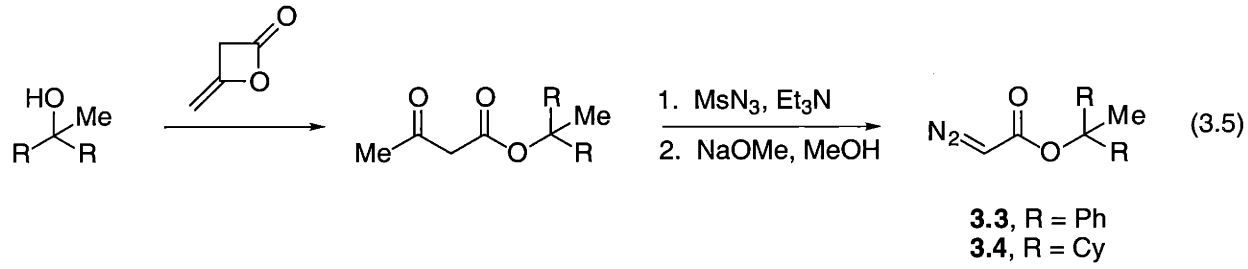
Table 3.2. Enantioselectivity in the ring expansion of (±)-**3.1** as a function of the diazo ester (eq 3.4).

entry	OR	trans : cis	% ee		% ee, trans cyclopropanation[a]
			trans	cis	
1	OEt	55 : 45	47	n.d.	73
2	O-*t*-Bu	56 : 44	70	69	87
3	O-(*d*)-Men	57 : 43	51	n.d.	87
4	O-(*l*)-Men	61 : 39	48	n.d.	89
5	BHT	61 : 39	65	n.d.	94

[a] With styrene.

Examination of the above results reveals that the trends of the two carbene transfer reactions are not completely parallel. For example, the two menthyl diazoacetates give better selectivity than ethyl diazoacetate in the cyclopropanation of styrene, yet all three diazo esters have essentially the same stereoselection in the ring expansion of (±)-**3.1** (entries 1, 3, and 4). The best diazo ester for cyclopropanation, BHT (entry 5), affords lower selectivity than *t*-butyl diazoacetate (entry 2).

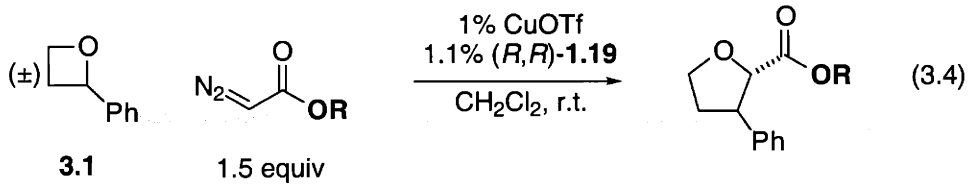
Since the best stereoselection that we have obtained is from *t*-butyl diazoacetate, we decided to develop new diazo esters based on this motif. The steric bulk of the diazo ester can be further increased by replacing the two methyl substituents on the *t*-butyl group with larger ones such as phenyl and cyclohexyl. The synthesis of these new diazo esters follows the usual sequence of acyl transfer to the alcohol to form the corresponding acetoacetate ester, diazo transfer, and finally deacetylation (eq 3.5).



(3.5)

3.3, R = Ph
3.4, R = Cy

With diazo esters **3.3** and **3.4**, we were delighted to find further improvement to the enantioselectivity of the ring expansion with (±)-**3.1** (Table 3.3). The best result was achieved with the ester group 1,1-dicyclohexylethyl (entry 3).



(3.4)

Table 3.3. Enantioselectivity in the ring expansion of (±)-**3.1** as a function of the diazo ester (eq 3.4).

			% ee	
entry	**OR**	trans : cis	trans	cis
1	O-*t*-Bu	56 : 44	70	69
2	$OCMePh_2$	56 : 44	80	78
3	$OCMeCy_2$	57 : 43	84	84

In addition to improved enantioselectivity, these diazo esters also furnish products that are much easier to deprotect. Treatment of the above carboxylate esters with CF_3CO_2H in CH_2Cl_2 affords the corresponding carboxylic acids in 10 minutes, with no cleavage or epimerization of the tetrahydrofuran ring.[14] In contrast, the principal method to functionalize the other tetrahydrofuran esters is by reducing them to the primary alcohols. Basic hydrolysis of these esters to the carboxylic acids is either impossible (when OR = BHT), or epimerizes the newly established stereogenic center in the products. Thus, diazo esters **3.3** and **3.4** have the potential to be useful carbene sources because of their high steric demand and the ease of functionalization of their products.[15,16]

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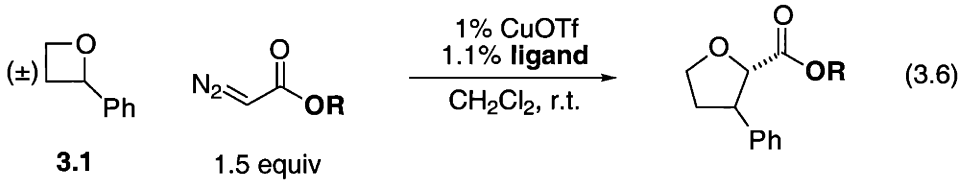
14 The hydrolysis can also be effected with TMSI, but low temperature (0 °C) and a precise amount of the Lewis acid (1.2 equiv) are required to avoid cleavage of the THF ring.

15 The various modes of intramolecular reactions that these diazo esters can participate in complicate their use in carbene transfer reactions. For instance, **3.3** can undergo intramolecular cyclopropanation/ring expansion with its phenyl ring to give a number of cycloheptatrienyl esters,

Next, various bis(azaferrocenes) were evaluated as the ligand for the ring expansion of (±)-**3.1** (Table 3.4).



(3.6)

Table 3.4. Enantioselectivity in the ring expansion of (±)-**3.1** as a function of the ligand (eq 3.6).

				% ee	
entry	**ligand**	**OR**	trans : cis	trans	cis
1	**1.19**	O-*t*-Bu	56 : 44	70	69
2	**1.22**	O-*t*-Bu	58 : 42	68	80
3	**1.29** (88% ee)	O-*t*-Bu	n.d.	75(85)	68(77)
4	**1.33**	O-*t*-Bu	50 : 50	78	70
5	**1.19**	$OCMeCy_2$	57 : 43	84	84
6	**1.22**	$OCMeCy_2$	61 : 39	81	85
7	**1.33**	$OCMeCy_2$	52 : 48	53	59

The values in parentheses refer to values after correction for the ligand ee.

The ligand structure has some influence on the diastereoselectivity of the reaction. While the decamethylbis(azaferrocenes) **1.19** and **1.22** offer similar diastereoselection in the ring expansion (entries 1, 2, 5, and 6), the decaarylbis(azaferrocene) **1.33** furnishes the diastereomeric products in equal amounts (entries 4 and 7). This contrast may be related to the electronic properties of the bis(azaferrocene) ligand.

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while the tertiary hydrogens of the cyclohexyl ring of **3.4** are prone to intramolecular C–H insertions. Thus, their use might be limited to those intermolecular processes that proceed readily.

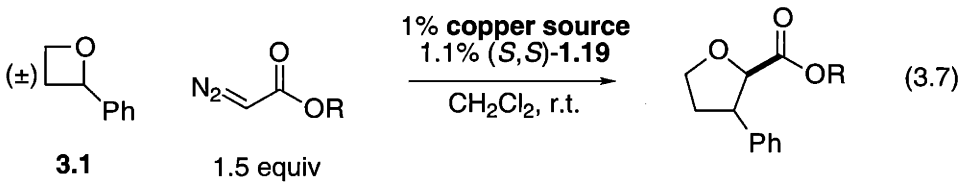
16 Diazo ester **3.4** and BHT diazoacetate provide similar levels of enantioselectivity in the asymmetric cyclopropanation of styrene (cf. Chapter 2, Section B).

With respect to enantioselectivity, the decaarylbis(azaferrocenes) **1.29** and **1.33** are better for the trans tetrahydrofuran with *t*-butyl diazoacetate (entries 3 and 4 vs entries 1 and 2), but similar enantioselectivities are also provided by the decamethylbis(azaferrocenes) **1.19** and **1.22** with the more hindered diazo ester **3.4** (entries 5 and 6). These ligands also offer the best enantioselection for the formation of the cis tetrahydrofuran. After considering the availability of these bis(azaferrocenes) in enantiomerically pure form, we decided to continue with the use of **1.19** as the ligand of choice.

The reaction proceeds quite readily at room temperature with only 1% catalyst loading, so we sought to enhance the stereoselectivity by lowering the reaction temperature. However, the reaction at 0 °C gives products of similar ee, suggesting that the selectivity of the reaction is not very sensitive to the temperature.

In our study on copper-catalyzed asymmetric cyclopropanation of olefins, we observed that all copper(I) salts with weakly coordinating anions give essentially the same stereoselectivity. To check whether the same behavior holds for the ring expansion of oxetanes, we studied the reaction with the copper source generated in two different ways: (a) direct use of a copper salt; and, (b) anion metathesis from CuCl + MX (Table 3.5).

In general, the identity of the anion has little effect on the reaction, except for perchlorate, which, perhaps due to its oxidizing power, causes a precipitous drop in both yield and enantioselectivity. For triflate, tetrafluoroborate, and hexafluorophosphate, the two methods to generate the copper source were compared, and only in the case of hexafluorophosphate was a significant difference observed. Finally, we decided to keep $CuOTf \bullet 0.5C_6H_6$ as the copper source, although it should be noted that another commercially available copper(I) source, $Cu(MeCN)_4PF_6$, can be used interchangeably.



(3.7)

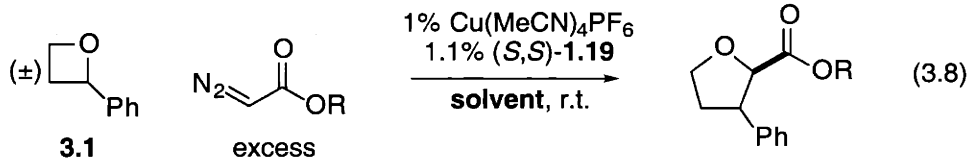
Table 3.5. Enantioselectivity in the ring expansion of (±)-**3.1** as a function of the copper source (eq 3.7).

copper source	OR = O-*t*-Bu			OR = OCMeCy$_2$		
	trans : cis	trans ee	cis ee	conv.[a]	trans : cis	trans ee
CuCl	56 : 44	64	69	55	57 : 43	62
CuCl + $AgClO_4$	57 : 43	22	31	43	59 : 41	35
CuCl + $AgSbF_6$	58 : 42	69	73	100	59 : 41	66
CuCl + AgO_2CCF_3	58 : 42	69	70	29	57 : 43	79
CuCl + AgOTs	55 : 45	70	73	96	57 : 43	83
CuCl + NaBARF[b]	55 : 45	69	73	97	58 : 42	83
CuCl + AgOTf	55 : 45	68	72	100	58 : 42	84
CuOTf•0.5C_6H_6	53 : 47	70	74	100	57 : 43	82
CuCl + $AgBF_4$	55 : 45	68	72	86	57 : 43	84
Cu(MeCN)$_4BF_4$	56 : 44	70	74	94	58 : 42	84
CuCl + $AgPF_6$	55 : 45	63	67	100	59 : 41	60
Cu(MeCN)$_4PF_6$	56 : 44	70	73	98	57 : 43	83

[a] conv. = conversion. [b] BARF = B(3,5-(F_3C)$_2C_6H_3$)$_4$.

Solvent is an important variable in cyclopropanation reactions. CH_2Cl_2 proves to be the best solvent for our system, which is consistent with the widely held belief that halogenated hydrocarbons are the solvents of choice for reactions of diazo esters. Solvents with Lewis basic sites, including alkenes or aromatic hydrocarbons, are thought to be less useful because of their ability to bind to transition metal catalysts and inhibit diazo decomposition.

However, a wider range of solvents might be usable in the ring expansion of oxetanes, due to their higher nucleophilicity. Thus, we carried out a comprehensive investigation using $Cu(MeCN)_4PF_6$ as the copper source. Solvents of three categories were examined: halogenated, aromatic, and polar (Table 3.6).



(3.8)

Table 3.6. Enantioselectivity in the ring expansion of (±)-**3.1** as a function of the solvent (eq 3.8).

	OR = O-*t*-Bu			OR = $OCMeCy_2$		
solvent	trans : cis	trans ee	cis ee	conv.	trans : cis	trans ee
CH_2Cl_2[a]	56 : 44	70	73	98	57 : 43	83
$CHCl_3$	55 : 45	68	74	97	57 : 43	82
PhCl	/	/	/	100	55 : 45	84
$ClCH_2CH_2Cl$	/	/	/	100	57 : 43	83
PhH[a]	54 : 46	74	81	98	55 : 45	87
$PhCH_3$[a]	54 : 46	73	81	100	55 : 45	86
$PhCF_3$[a]	54 : 46	70	73	100	56 : 44	83
C_6F_6	/	/	/	99	57 : 43	86
n-BuOAc	/	/	/	90	55 : 45	87
EtOAc[a]	55 : 45	75	80	99	56 : 44	87
MeO_2CPh	54 : 46	69	74	100	55 : 45	84
$MeNO_2$	55 : 45	75	77	59	57 : 43	88
$MeCONMe_2$	55 : 45	69	74	54	57 : 43	80
MeCN	56 : 44	73	76	36	58 : 42	86
MeCOEt	56 : 44	74	76	26	59 : 41	n.d.

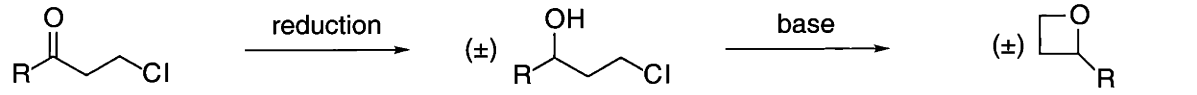
[a] The reaction was repeated with $CuOTf \bullet 0.5C_6H_6$ as the copper source and *t*-butyl diazoacetate as the carbene source, and the ee's observed were all ±2% of the corresponding values with $Cu(MeCN)_4PF_6$.

All four halogenated solvents give complete conversion of the oxetane and essentially the same level of stereoselectivity. Complete conversion is also achieved in all four aromatic solvents, and most of them are marginally better than CH_2Cl_2 in terms of stereoselectivity. The conversion varies for polar solvents—it is high in esters (*n*-BuOAc, EtOAc, MeO_2CPh), but drops for nitromethane and *N,N*-dimethylacetamide, and decreases further for acetonitrile and methyl ethyl ketone. Ethyl acetate provides the best stereoselectivity among the esters screened, so it was chosen as the best solvent.[17]

II. Ring Expansion of Racemic Oxetanes and Analogous Heterocycles.

With the ligand, solvent, and copper source optimized for the ring expansion of (±)-**3.1**, and using the newly developed diazo ester **3.4** as the carbene source, we were ready to examine the ring expansion of other oxetanes.

The synthesis of various racemic 2-substituted oxetanes starts from β-chloroketones. These ketones were prepared either by Friedel–Crafts type electrophilic substitutions (**3.5, 3.7, 3.8**), or by a Stille coupling between an arylstannane and an acid chloride (**3.6**). Reductions of the β-chloroketones by $NaBH_4$ give γ-chloroalcohols **3.9–3.12**, which can then be cyclized upon treatment with KH to afford the desired oxetanes **3.13–3.16**.



3.5, R = 4-(MeO)C_6H_4
3.6, R = 4-(F_3C)C_6H_4
3.7, R = 1-Naphthyl
3.8, R = *n*-$C_7H_{15}C{\equiv}C$

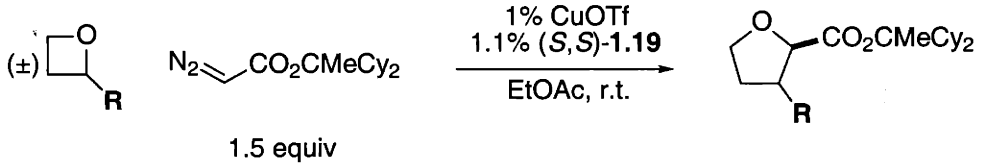
3.9, R = 4-(MeO)C_6H_4
3.10, R = 4-(F_3C)C_6H_4
3.11, R = 1-Naphthyl
3.12, R = *n*-$C_7H_{15}C{\equiv}C$

3.13, R = 4-(MeO)C_6H_4
3.14, R = 4-(F_3C)C_6H_4
3.15, R = 1-Naphthyl
3.16, R = *n*-$C_7H_{15}C{\equiv}C$

---

17 The use of ethyl acetate as the solvent for carbene transfer is somewhat unusual, since the ester group is known to react with diazo esters. For an example of the intramolecular formation of carbonyl ylide from an ester group, see: Hildebrandt, K.; Debärdemäker, T.; Friedrichsen, W. *Tetrahedron Lett.* **1988**, *29*, 2045–2046.

The ring expansion was examined under conditions optimized for (±)-**3.1** (Table 3.7):

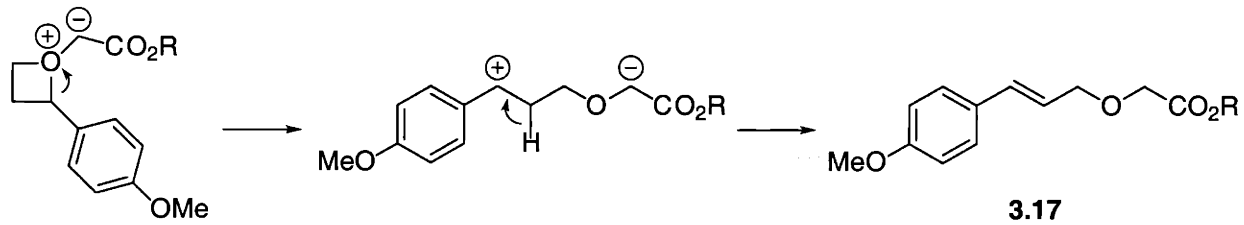


(3.9)

Table 3.7. Asymmetric ring expansion of racemic oxetanes to tetrahydrofurans: Scope of the C2 substituent (eq 3.9).

				% ee	
entry	**R**	NMR yield	trans : cis	trans	cis
1	Ph	85	56 : 44	87	88
2	4-(MeO)C_6H_4	47	55 : 45	51	45
3	4-(F_3C)C_6H_4	94	53 : 47	89	90
4	1-Naphthyl	87	49 : 51	80	83
5	*n*-$C_7H_{15}C{\equiv}C$	66	54 : 46	85	87

Incorporation of an electron-withdrawing substituent increases the enantioselectivity marginally (entry 3), while a naphthyl group decreases it (entry 4). Replacing the hydrogen at the 4-position of the phenyl ring by a methoxy group has a deleterious effect on both the yield and the enantioselectivity of the ring expansion (entry 2).[18] The isolation of **3.17** from the reaction suggests that β-hydrogen elimination is a side reaction.[19]



3.17

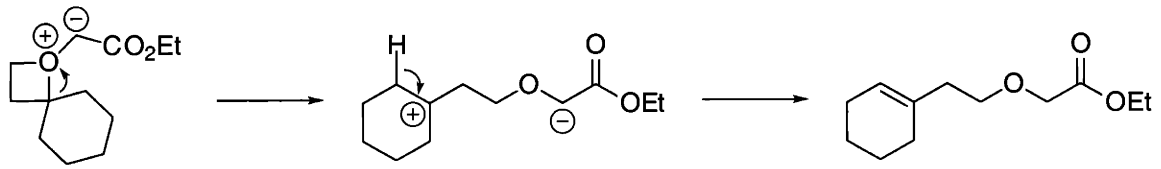
18 We have reexamined the reaction of (±)-**3.13** in other solvents and with different copper sources, but none of the changes improved the reaction. In addition, the catalyst decomposes (±)-**3.13** even in the absence of diazo esters.

19 An E2 mechanism is also possible.

To account for the influence of an electron-donating group, we believe that it stabilizes the carbocationic character at the benzylic carbon in the zwitterionic intermediate and disfavors a rapid intramolecular nucleophilic attack to form the tetrahydrofuran product. The impediment in the desired reaction pathway opens up the opportunity for other side reactions such as β-hydrogen elimination.[20]

As a 2-substituent of the oxetane, an alkynyl group works as well as an electron-neutral or an electron-deficient aromatic system in terms of enantioselectivity, although the yield drops by about 20% (entry 5). The alkynyl group serves as a useful handle for derivatization into alkyl, alkenyl, or other functional groups.

To gain further information about the role of the C2 substituent, we examined the ring expansion of a 2,2-dialkyl-substituted oxetane, 1-oxaspiro[3.5]nonane, in which C2 is a tertiary carbon. However, similar to **3.13**, it reacts with ethyl diazoacetate by the β-hydrogen elimination pathway to afford **3.18**.



3.18

The aforementioned experiments confirm that substituents stabilizing carbocationic character at C2 of the oxetane direct the reaction towards the β-hydrogen elimination pathway instead of the desired ring expansion. We have also examined oxetanes in which there are *no* substituents at C2, the parent oxetane and 3,3-dimethyloxetane, but neither one participates in any reaction with ethyl diazoacetate. The only products

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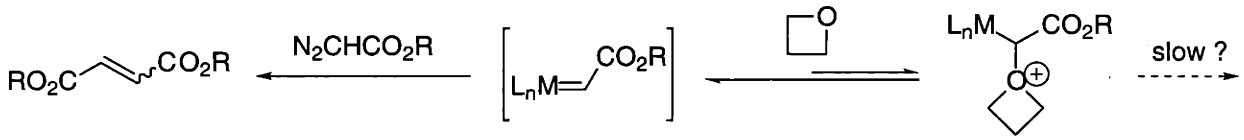
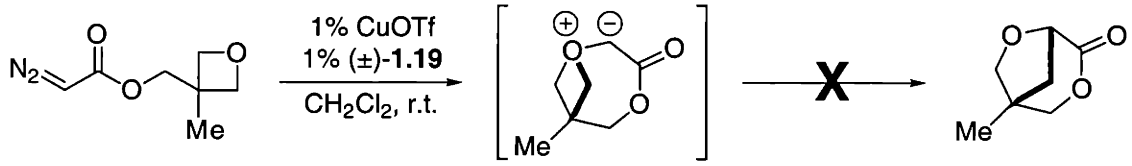
20 In his study of the kinetics of [1,2]-rearrangement of ammonium ylides, Stevens showed that *electron-withdrawing* substituents enhance the ability of a benzyl group to migrate by establishing the following order: 4-(O_2N) > 4-X > 4-Me > 4-(MeO). As a result, a heterolytic bond-cleavage pathway was proposed. See: (a) Thomson, T.; Stevens, T. S. *J. Chem. Soc.* **1932**, 55–73. (b) Dunn, J. L.; Stevens, T. S. *J. Chem. Soc.* **1932**, 1926–1931.

found were maleates and fumerates that are derived from the dimerization of the diazo ester.



The absence of a substituent at C2 should enhance the formation of the oxonium ylide because the oxygen is less hindered. However, the subsequent rearrangement step must be extremely slow, and the oxonium ylide reverts back to the metal carbene and the oxetane. To promote the equilibrium between the oxetane and the metal carbene towards the oxonium ylide, we synthesized oxetane **3.19**[21] and subjected it to the catalyst. The bicyclic nature of the intermediate oxonium ylide should impose extra strain in the system, and thus favor the subsequent [1,2]-rearrangement by relieving a large part of that strain. However, no desired product could be identified (eq 3.10).



3.19 (3.10)

We have also investigated the possibility of analogous ring expansions with other four-membered heterocycles as well. To the best of our knowledge, only two studies have been reported. One was carried out by Hata and Watanabe on azetidines (eq 3.12),[22]

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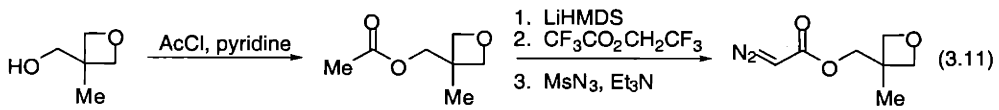
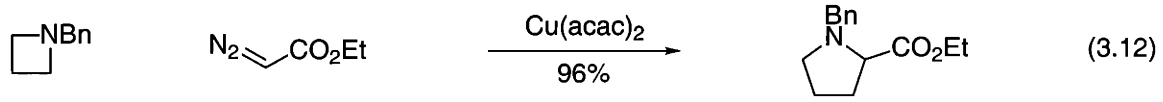
21 Oxetane **3.19** was synthesized according to eq 3.11:



(3.11)

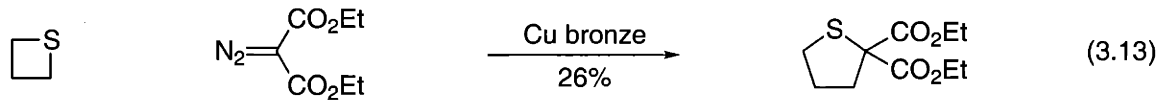
3.19

22 Hata, Y.; Watanabe, M. *Tetrahedron Lett.* **1972**, *13*, 4659–4660.



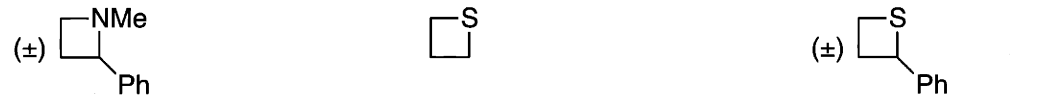
(3.12)

and another one by Ando on thietanes (eq 3.13):[23]



(3.13)

We have examined several azetidines and thietanes, and those that undergo the desired ring expansion are listed in Figure 3.5. Despite the structural similarity among **3.1**, **3.20**, and **3.22**, we were disappointed to find out that none of the ring expansion proceeds with even moderate enantioselectivity in the presence of **1.19**.



3.20
trans:cis = 54:46
trans ee = 16%

3.21
racemic

3.22
trans:cis = 55:45
trans ee = 1%, cis ee = 2%

Figure 3.5. Four-membered heterocycles that undergo analogous ring expansion.

III. Ring Expansion of Enantiomerically Pure Oxetanes: Diastereoselective Formation of 3-Substituted Tetrahydrofuran-2-Carboxylates.

Katsuki has shown that the absolute stereochemistry at C3 of the tetrahydrofuran product is largely determined by that of C2 of the oxetane substrate. With our catalyst, results with the racemic oxetanes suggest that our system behaves similarly. Therefore, to obtain one stereoisomer of the tetrahydrofuran out of the possible four, optically pure oxetanes have to be used.

In the ring expansion of racemic oxetanes, the extent of epimerization of the oxonium ylides during the ring expansion has little impact on the enantiomeric excesses

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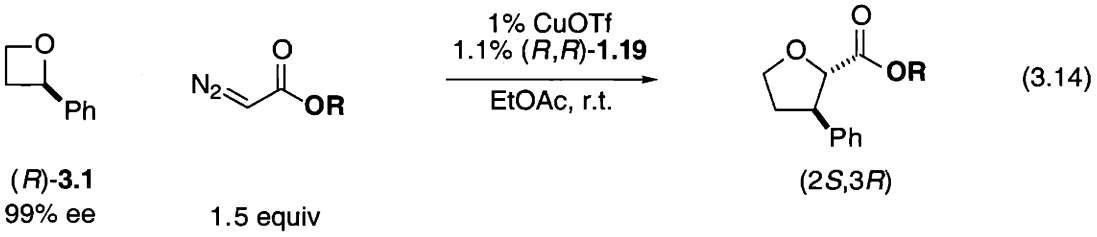
23 Ando, W.; Yagihara, T.; Tozune, S.; Imai, I.; Suzuki, J.; Toyama, T.; Nakaido, S.; Migita, T. *J. Org. Chem.* **1972**, *37*, 1721–1727.

of the tetrahydrofuran products, because these numbers mostly reflect the facial selectivities of the carbene transfer (*vide infra*). However, when the oxetane is enantiomerically pure, such epimerization will lead to a substantial loss of the favored stereoisomer. Hence, in order to have a highly stereoselective process, both a high carbene facial selectivity and a small extent of epimerization are required. On the other hand, to achieve the same level of stereoselection, a lower carbene facial selectivity can be compensated by a smaller extent of epimerization of the oxonium ylide. Hence, it is important to reexamine the effect of diazo esters of different steric demand towards the stereoselectivity of the reaction with enantiomerically pure oxetanes.

We tested most of the diazo esters with (*R*)-**3.1** and (*R,R*)-**1.19** to confirm that diazo ester **3.4** still provides the best stereoselectivity for the diastereoselective formation of trans tetrahydrofurans (Table 3.8):



(*R*)-**3.1**
99% ee

1.5 equiv

(2*S*,3*R*)

(3.14)

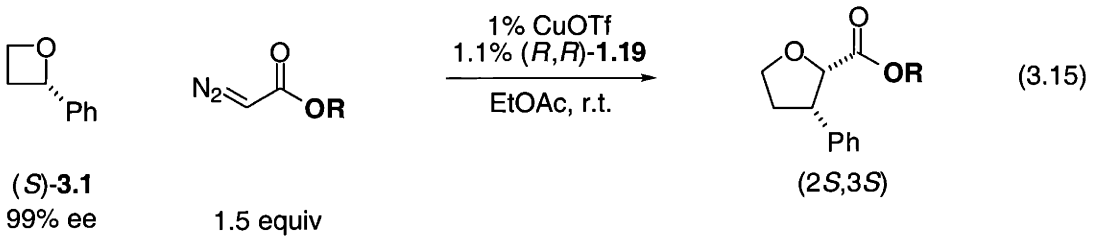
Table 3.8. Asymmetric ring expansion of (*R*)-**3.1** as a function of the diazo ester: Stereoselective formation of trans tetrahydrofurans (eq 3.14).[a]

entry	**OR**	NMR yield (%)	trans : cis	% ee, trans
1	OEt	53	82 : 18	92
2	O-*t*-Bu	57	90 : 10	97
3	O-(*d*)-Men	82	90 : 10	95
4	O-(*l*)-Men	85	90 : 10	97
5	$OCMeCy_2$	77	95 : 5	98

[a] All selectivity data represent the average of two runs, one with each enantiomer of the ligand.

The above combination of the (*R*)-oxetane and the (*R,R*)-ligand can be described as the "matched" process, in which the stereochemistry of the substrate and the catalyst cooperate to generate the more thermodynamically favored trans tetrahydrofuran. Ethyl diazoacetate is still the least selective carbene source (entry 1). Unlike the case with (±)-**3.1**, the enantiomeric menthyl diazoacetates (entries 3,4) give similar diastereoselectivity (90 : 10) to *t*-butyl diazoacetate (entry 2), and the stereochemistry of the menthyl group has no influence on the selectivity. Diazo ester **3.4** still gives the best stereoselection for (*R*)-**3.1** (entry 5). The yields reflect the advantage of using hindered diazo esters, such as menthyl diazoacetates or **3.4**, to minimize dimerization.

The effect of the diazo ester in the diastereoselective formation of cis tetrahydrofurans was examined with the opposite enantiomer of the substrate, (*S*)-**3.1**, and the same enantiomer of the chiral ligand, (*R,R*)-**1.19** (Table 3.9):



(3.15)

Table 3.9. Asymmetric ring expansion of (*S*)-**3.1** as a function of the diazo ester: Stereoselective formation of cis tetrahydrofurans (eq 3.15).

entry	**OR**	NMR yield (%)	trans : cis	% ee, cis
1	OEt	52	29 : 71	94
2	O-*t*-Bu	63	17 : 83	96
3	O-(*d*)-Men	74	21 : 79	99
4	O-(*l*)-Men	67	28 : 72	94
5	$OCMeCy_2$	74	16 : 84	95

The cis (2*S*,3*S*)-tetrahydrofuran is formed diastereoselectively, although the selectivity is lower than the corresponding value for the trans tetrahydrofuran. *The*

(2S)-configuration of the product shows again that it is under catalyst control. The size of the diazo ester has some effect on the diastereoselectivity of the ring expansion, but not on the enantiomeric excess of the cis tetrahydrofuran products. Ethyl (entry 1) and (*l*)-menthyl diazoacetate (entry 4) are the least diastereoselective carbene sources, while the two tertiary diazo esters, *t*-butyl (entry 2) and **3.4** (entry 5), give the best stereoselection. Contrary to what is observed for the formation of the trans tetrahydrofurans, the stereochemistry of the menthyl group does have a marked effect on the stereoselectivity of the reaction (entry 3 vs entry 4).

To conclude the results obtained from the study of racemic and enantiomerically pure oxetanes, the stereoselection of the process improves with more sterically demanding diazo esters, up to a point where this improvement is counteracted by the increased epimerization during the rearrangement of the oxonium ylide. From a practical point of view, 1,1-dicyclohexylethyl diazoacetate (**3.4**) remains the best choice for the stereoselective formation of either diastereomeric tetrahydrofuran, but *t*-butyl diazoacetate can be used almost interchangeably for the diastereoselective formation of the cis product.[24]

After confirming that **3.4** is the optimal diazo ester for the ring expansion of enantiomerically pure oxetanes, we proceeded to study other 2-substituted oxetanes. The synthesis of enantiomerically pure oxetanes **3.13–3.16** is actually not much more difficult than the racemic ones. The same synthetic pathway for the racemic oxetanes was used, with racemic γ-chloroalcohols **3.9–3.12** replaced by enantiomerically pure ones, which in turn can be obtained from the asymmetric reduction of β-chloroketones **3.5–3.8**.

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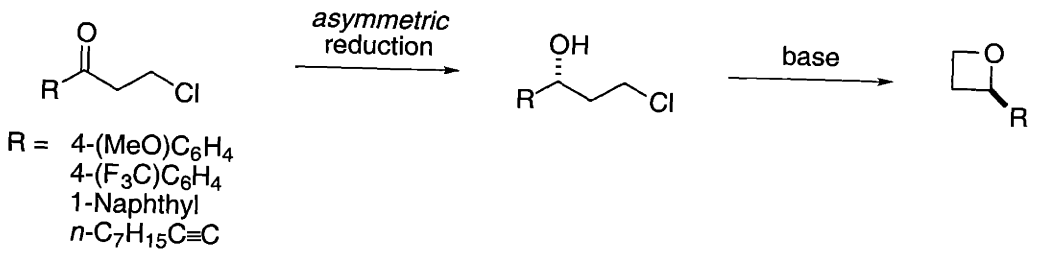
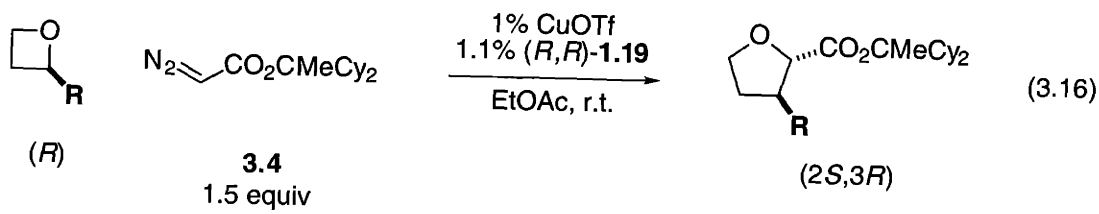
24 *t*-Butyl diazoacetate is commercially available from Aldrich.



DIP–Cl was the chiral reducing agent used when R is an aryl group.[25] All three alcohols were obtained with greater than 95% ee (**3.9**, 96% ee; **3.10**, 98% ee; **3.11**, 97% ee). DIP–Cl was not effective for alkynyl ketone **3.8**, however (12% ee). So, we examined other chiral reducing agents that have been used for various alkynyl ketones (Chirald/$LiAlH_4$,[26] 45% ee; BINAL–H,[27] 12% ee), and we eventually found that neat Alpine–Borane[28] gives **3.12** in 89% ee. To improve the enantiomeric excess of **3.12**, the crude product was derivatized as the 3,5-dinitrobenzoate and recrystallized to enantiomerically purity.

With the (*R*)-oxetanes synthesized in high enantiomeric excess, we carried out their ring expansions using (*R*,*R*)-**1.19** (Table 3.10):



(3.16)

25 Srebnik, M.; Ramachandran, P. V.; Brown, H. C. *J. Org. Chem.* **1988**, *53*, 2916–2920.
26 Yamaguchi, S.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 1870–1877.
27 Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6717–6725.
28 Brown, H. C.; Pai, G. G. *J. Org. Chem.* **1985**, *50*, 1384–1394.

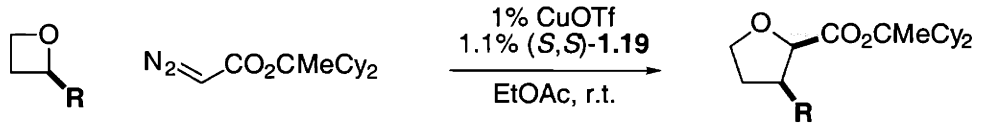
Table 3.10. Asymmetric ring expansion of oxetanes:
Stereoselective formation of trans tetrahydrofurans (eq 3.16).[a]

			tetrahydrofuran product		
entry	R	oxetane % ee	trans : cis	% ee, trans	isolated yield (%)
1	Ph	99	95 : 5	98	74[b]
2	4-(MeO)C_6H_4	98	75 : 25	69	29
3	4-(F_3C)C_6H_4	97	94 : 6	98	81
4	1-Naphthyl	> 99	86 : 14	91	75
5	*n*-$C_7H_{15}C{\equiv}C$	> 99	89 : 11	97	64

[a] All data represent the average of two runs. [b] Mixture of diastereomers.

The trends observed for the enantiomerically pure 2-substituted oxetanes mirror closely to the racemic case (cf. Table 3.7). The incorporation of an electron-withdrawing group has no effect on the diastereoselectivity (entry 3), while an electron-donating group leads to a poor reaction, both in terms of stereoselectivity and yield (entry 2). Naphthyl- (entry 4) and alkynyl-substituted (entry 5) oxetanes undergo the reaction with slightly diminished stereoselection.

Switching the configuration of the ligand from (*R*,*R*) to (*S*,*S*), we expected the diastereoselective formation of the cis tetrahydrofurans with a (2*R*)-configuration. This prediction was indeed borne out by experiment, confirming that the catalyst controls the configuration of the new stereocenter (Table 3.11).



(*R*) **3.4** 1.5 equiv (2*R*,3*R*) (3.17)

Table 3.11. Asymmetric ring expansion of oxetanes:
Stereoselective formation of cis tetrahydrofurans (eq 3.17).

			tetrahydrofuran product		
entry	**R**	oxetane % ee	trans : cis	% ee, cis	isolated yield (%)
1	Ph	99	16 : 84	95	74[a]
2	4-(MeO)C_6H_4	98	42 : 58	82	20
3	4-(F_3C)C_6H_4	97	14 : 86	95	52
4	1-Naphthyl	> 99	15 : 85	95	72
5	*n*-$C_7H_{15}C{\equiv}C$	> 99	16 : 84	94	60

[a] Mixture of diastereomers.

Irrespective of the nature of the substituent, oxetanes that participate well in the ring expansion give essentially the same level of stereoselection (entries 1, 3–5), with the cis products formed in excellent enantiomeric excess (% ee ~ 95%). The reaction with the problematic substrate **3.13** gives poor yield and is only slightly diastereoselective (entry 2). Hydrolysis of the alkynyl tetrahydrofuran ester generated in entry 5 furnishes the carboxylic acid that is an intermediate in the Katsuki formal synthesis of (-)-avenaciolide and (-)-isoavenaciolide. The stereoselectivity obtained with **1.19** (trans:cis = 16:84, cis ee = 94%) is an improvement over that obtained with the Katsuki bipyridine **3.2** (trans:cis = 15:85, cis ee = 72%).[13]

IV. Mathematical Analysis of the Ring Expansion.

As discussed before, the ring expansion of oxetanes is thought to proceed through the formation of the oxonium ylides, followed by a [1,2]-rearrangement to form the tetrahydrofuran product. We follow the mathematical analysis that was proposed by Katsuki to gain more insight into the reaction (Figure 3.6).[9]

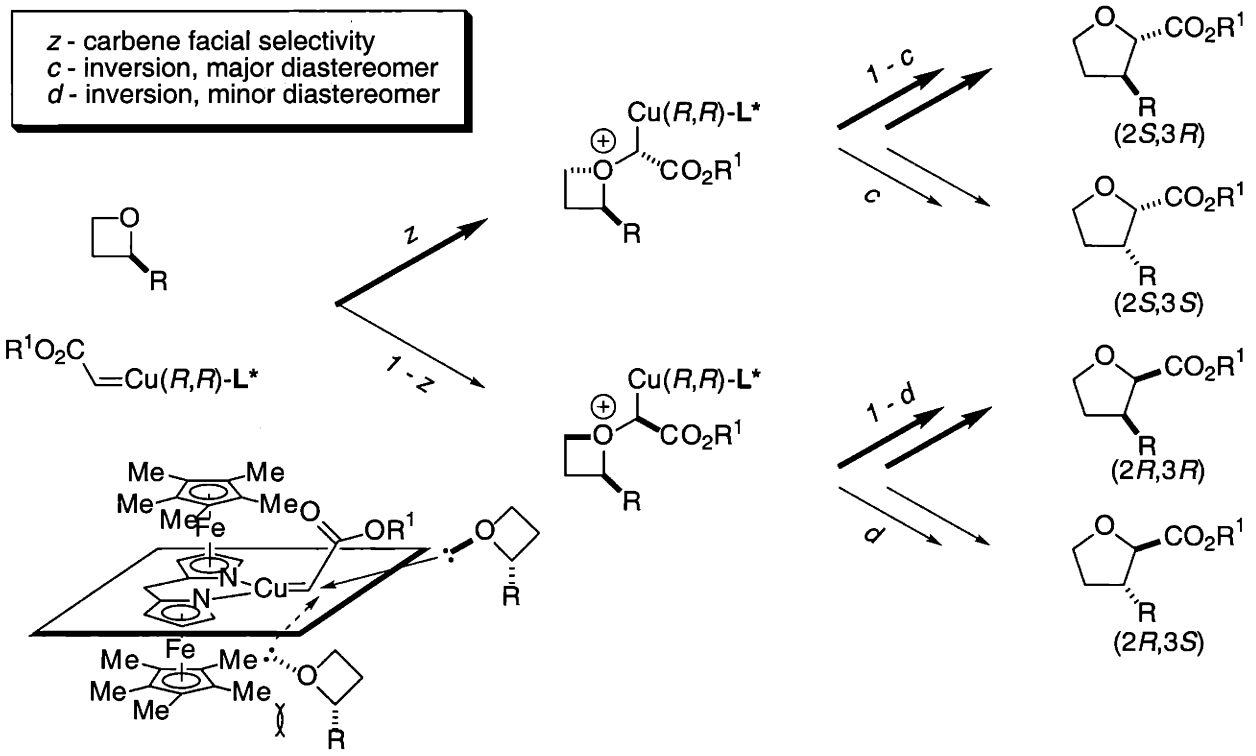


Figure 3.6. The "matched" case: Reaction pathways for (*R*)-oxetane catalyzed by Cu/(*R*,*R*)-**1.19**.

The overall stereoselection of the reaction is factored into:

1. facial selectivity for the formation of the oxonium ylide

   The steric environment of the copper carbene favors the reaction of one of its prochiral faces over the other, the selectivity of which is denoted by *z*.

2. degree of epimerization at C2 of the oxetane during rearrangement

   The two diastereomeric oxonium ylides undergo [1,2]-rearrangement, during which some epimerization occurs at C2 of the oxetane. The degree of inversion is denoted by *c* for the major diastereomer and *d* for the minor diastereomer.

As indicated by Figure 3.6, the trans (2*S*,3*R*)-tetrahydrofuran is the predominant product from (*R*)-oxetane and (*R*,*R*)-catalyst. A similar analysis can be constructed to describe the reaction of (*S*)-oxetane (Figure 3.7).

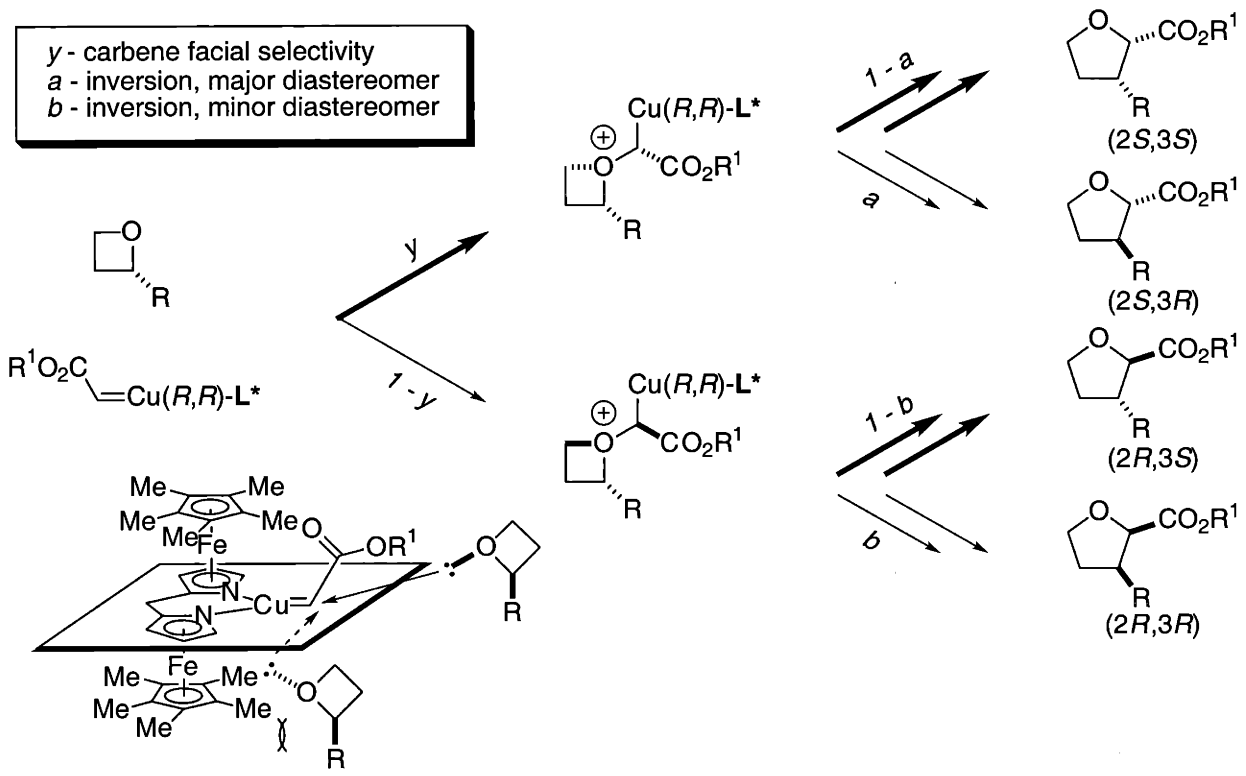


Figure 3.7. The "mismatched" case: Reaction pathways for (*S*)-oxetane catalyzed by Cu/(*R*,*R*)-**1.19**.

In this case, the cis (2*S*,3*S*)-tetrahydrofuran is the preferred product. The parameters *z*, *c*, *d* are now replaced by *y*, *a*, *b*. According to our definition, the ideal system would have $y = z = 1$, denoting complete facial selection and $a = b = c = d = 0$, denoting complete retention of stereochemistry at C2 of the oxetane. A completely non-selective carbene transfer will have $y = z = 0.5$, while complete epimerization at C2 will make $a = b = c = d = 0.5$.

Since the experimental results suggest that (*R*)- and (*S*)-oxetanes react in the same rate, we can describe the formation of the four stereoisomers by the following set of equations:

$$(2S,3R) = f_R * z * (1 - c) + f_S * y * a$$

$$(2S,3S) = f_R * z * c + f_S * y * (1 - a)$$

$$(2R,3S) = f_R * (1 - z) * d + f_S * (1 - y) * (1 - b)$$

$$(2R,3R) = f_R * (1 - z) * (1 - d) + f_S * (1 - y) * b$$

where f_R and f_S represent the fraction of (*R*)- and (*S*)-enantiomer of the oxetane

$\therefore\ f_R + f_S = 1,\quad$ ee (oxetane) $= f_R - f_S$

There are *six* variables altogether (y, z, a, b, c, d), and within the set of simultaneous equations, *three* of them are independent. To determine the value of the variables under one set of conditions, we need to run *at least two* reactions with the oxetane at different ee, and determine the distribution of the four stereoisomers of the tetrahydrofuran product.

In our first analysis, we compare our system with the Katsuki system using the substrate **3.1**, and examine the effect of different diazo esters, copper sources, and solvents towards the reaction parameters (Table 3.12).

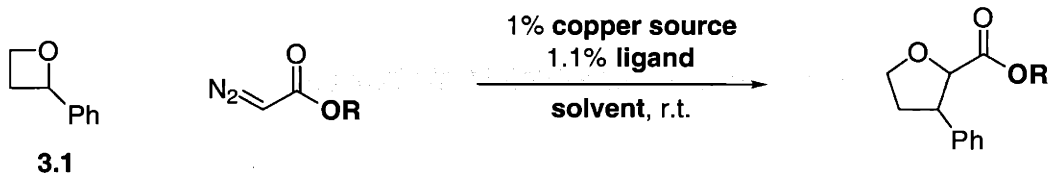


Table 3.12. Influence of copper sources, ligands, solvents, and diazo esters on the reaction parameters of **3.1**.

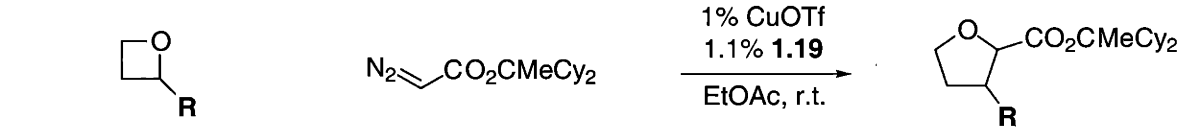
copper source	ligand	solvent	OR	*y*	*z*	*a*	*b*	*c*	*d*
$CuOTf \bullet 0.5C_6H_6$	**3.2**	CH_2Cl_2	O-*t*-Bu	0.86	0.92	0.090	0.16	0.024	0.39
$Cu(MeCN)_4PF_6$[a]	**1.19**	CH_2Cl_2	O-*t*-Bu	0.83	0.89	0.074	0.14	0.026	0.20
$CuOTf \bullet 0.5C_6H_6$	**1.19**	EtOAc	O-*t*-Bu	0.86	0.91	0.069	0.13	0.030	0.19
$CuOTf \bullet 0.5C_6H_6$	**1.19**	EtOAc	$OCMeCy_2$	0.92	0.96	0.107	0.25	0.021	0.26

[a] $CuOTf \bullet 0.5C_6H_6$ under these conditions gives similar values for all the parameters.

Under the same conditions (solvent: CH_2Cl_2; diazo ester: N_2CHCO_2-*t*-Bu), our ligand **1.19** is slightly inferior to the Katsuki ligand **3.2** in terms of carbene facial selectivities (y, z; rows 1 and 2). However, **1.19** lowers the extent of epimerization, especially for the minor diastereomer in the matched case (d). Both facial selectivities y and z are increased by either a change of solvent from CH_2Cl_2 to EtOAc (row 3), or by

a change of diazo ester from *t*-butyl to **3.4** (row 4). However, the larger size of the ester group causes more epimerization, especially for those minor diastereomeric ylides (*b*, *d*).

In our second analysis, we analyze the effect of the oxetane 2-substituent towards those parameters (Table 3.13):[29]



3.1, R = Ph
3.14, R = 4-(F_3C)C_6H_4
3.15, R = 1-Naphthyl
3.16, R = *n*-$C_7H_{15}C{\equiv}C$

3.4

Table 3.13. Comparison between various 2-substituted oxetanes.[30]

R	*y*	*z*	*a*	*b*	*c*	*d*
Ph	0.92	0.96	0.107	0.25	0.021	0.26
4-(F_3C)C_6H_4	0.92	0.97	0.079	0.25	0.023	0.18
1-Naphthyl	0.92	0.90	0.094	0.28	0.084	0.39
n-$C_7H_{15}C{\equiv}C$	0.91	0.93	0.099	0.27	0.051	0.18

In general, *y* is slightly smaller than *z*, denoting that the facial selectivity of the carbene transfer to the matched (*R*)-oxetane is higher. This can be rationalized by comparing the transition states between the reaction of (*R*)- and (*S*)-oxetanes (Figure 3.8). As the mismatched oxetane approaches the copper carbene, the 2-substituent of the oxetane is oriented towards the methyl groups of the Cp* ring, creating additional steric interactions that *increase* the energy of the favored pathway, and thus lowering

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29 The parameters are determined by two reactions running with the opposite enantiomers of the oxetane (or the catalyst). To check whether these parameters are correct, the selectivity in the racemic case is calculated and compared with the experimental values. The parameters obtained with **3.13** cannot be analyzed this way.

30 Instead of running the reaction with an oxetane of different ee, the catalyst was inverted. The mathematical analysis is the same, except that all the absolute configurations of the products need to be inverted.

the facial selectivity. Similar interactions are absent during the formation of the trans product, since the 2-substituent is oriented away from the Cp* ring.

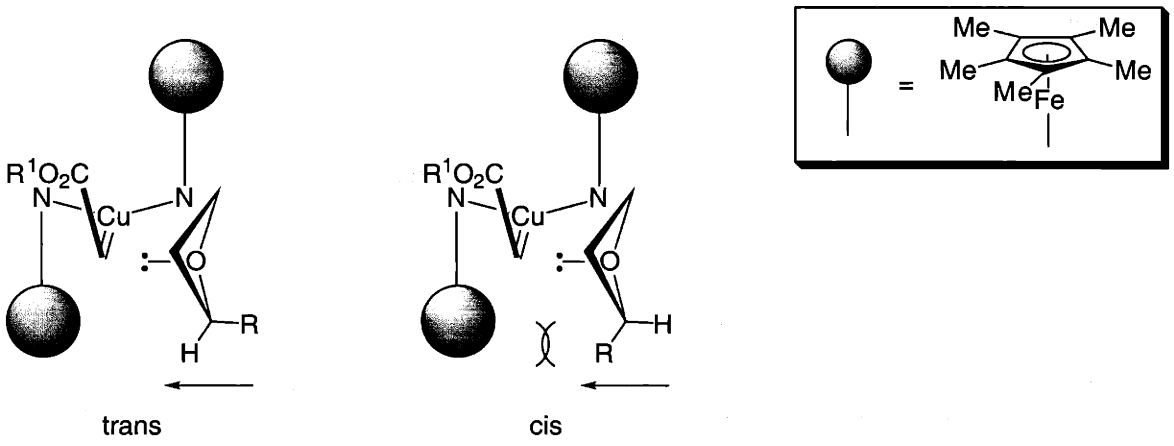

Figure 3.8. Comparison of the transition states between the reaction of (*R*)- and (*S*)-oxetanes

The order $d \approx b > a > c$ is obtained by comparing their magnitudes. From this, we can conclude that:

1. The primary driving force for epimerization comes from the mismatch between the substrate configuration and the ligand configuration (*d*, *b*).
2. The secondary force is the thermodynamics of the process, as the cis → trans epimerization (*a*) is more favorable than the trans → cis process (*c*).

Since the primary factor is related to the configuration of the ligand, but not the thermodynamics of the final product, it provides a compelling piece of evidence that the chiral metal catalyst is associated with the oxonium ylide before the rearrangement takes place. Doyle has described such association to be "necessary for asymmetric catalysis" (Figure 3.9).[31]

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31 Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911–935.

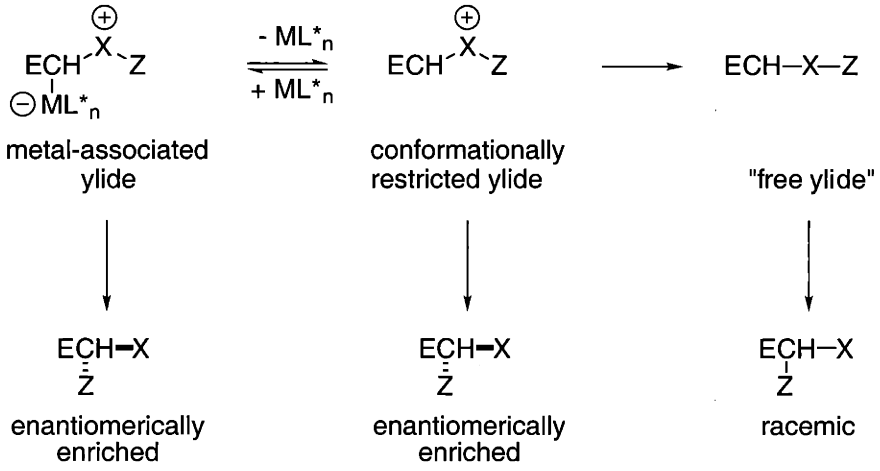


Figure 3.9. Relationship between metal–ylide association and stereochemical outcome.

Using our mathematical model, we can simulate the scenario in which there is no ligand influence on the degree of epimerization. Consider the reaction between **3.1** and **3.4** catalyzed by CuOTf/(*R*,*R*)-**1.19**. Since there is no influence from the ligand during the rearrangement step, the parameters for the mismatched case should be equal to those for the matched case. Hence, $d = a = 0.107$, and $b = c = 0.021$. Putting these numbers into the model, we obtain the simulated selectivities (Table 3.14). Under this hypothetical scenario, the enantiomeric excess of the products would have improved in the diastereoselective formation of tetrahydrofurans from optically pure oxetanes.

Table 3.14. Comparison between simulated data and experimental results.

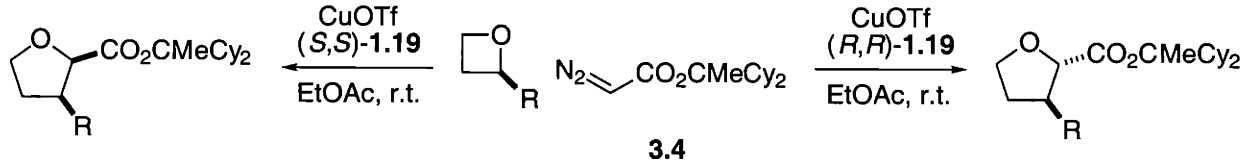
			tetrahydrofuran product		
entry	scenario	oxetane % ee	trans : cis	% ee, trans	% ee, cis
1	(a)	0	56 : 44	85	91
2	(a)	100 (*R*)	94 : 6	99	/
3	(a)	100 (*S*)	18 : 82	/	100
4	(b)	0	56 : 44	87	88
5	(b)	100 (*R*)	95 : 5	98	/
6	(b)	100 (*S*)	16 : 84	/	95

(a) Simulated data with no ligand influence on epimerization. (b) Experimental results.

C. Conclusions.

We have demonstrated that C_2-symmetric bis(azaferrocenes) serve as effective ligands for copper-catalyzed asymmetric ring expansions of oxetanes to tetrahydrofurans. In the optimization process, we showed that the steric demand of the diazo ester has a significant impact on the stereoselection. As a result, a new diazo ester, 1,1-dicyclohexylethyl diazoacetate, was developed to improve stereoselection. The ester group in the product can be easily deprotected, making this diazo ester an attractive carbene source in other applications.

Under our optimized conditions, bis(azaferrocene) **1.19** offers an improvement to the state-of-the-art. The ring expansion works well with 2-substituted oxetanes bearing an alkynyl group or an electron-neutral to -deficient aromatic ring. Racemic oxetanes give a mixture of diastereomeric tetrahydrofuran products in equal proportions and with the ee of each diastereomer up to 90%. From enantiomerically pure oxetanes, which are synthesized in two steps from β-chloroketones, the reaction furnishes either diastereomeric tetrahydrofuran in high enantiomeric excess. The configuration of the new stereocenter is controlled by the catalyst. Unfortunately, efforts to catalyze analogous ring expansion in other heterocycles with similar stereoselection did not bear fruit.



Building on the Katsuki model, we have factored the overall stereoselection into the facial selectivity of the carbene transfer to the oxetane and the extent of epimerization of the resultant ylides. The magnitudes of these reaction parameters indicate that the chiral metal fragment stays associated with the ylide throughout the reaction.

D. Experimental.

I. General.

^{1}H and ^{13}C nuclear magnetic resonance spectra were recorded on a Varian VXR-500 NMR spectrometer at ambient temperature. ^{1}H data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane (δ scale), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qnt = quintet, sept = septet, m = multiplet, and br = broadened), integration, and coupling constant (Hz). ^{13}C chemical shifts are reported in parts per million downfield from tetramethylsilane (δ scale). All ^{13}C spectra were determined with broadband ^{1}H decoupling.

Infrared spectra were obtained on a Perkin-Elmer Series 1600 FT-IR spectrophotometer. High resolution mass spectra were recorded on a Finnegan MAT System 8200 spectrometer or a Bruker Daltonics Apex FT-ICR-MS (3 Tesla). Melting points were obtained on a Thomas Hoover Unimelt capillary melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter and are reported as follows: $[\alpha]^{Temp\ (^{\circ}C)}_{\lambda\ (nm)}$ (*c* solvent, enantiomeric purity).

Analytical chiral HPLC was performed on either a Daicel Chiralcel OD column (4.6 mm x 25 cm) or a Daicel Chiralpak AD column (4.6 mm x 25 cm). Analytical achiral GC was performed on a J & W Scientific DB-1701 column (0.25 mm x 30 m). Analytical chiral GC was performed on either a Chiraldex B-PH column (0.25 mm x 20 m) or a Chiraldex G-TA column (0.25 mm x 20 m). Analytical TLC was performed using EM Science 0.25 mm silica gel 60 plates and visualized with either UV light or ethanolic phosphomolybdic acid. Flash chromatography was performed on EM Science silica gel 60 (230–400 mesh).

Solvents were distilled under nitrogen from the indicated drying agents: CH_2Cl_2 (CaH_2); PhCl (CaH_2); $ClCH_2CH_2Cl$ (CaH_2); PhH (Na); $PhCH_3$ (Na); $PhCF_3$ (CaH_2);

C_6F_6 (CaH_2); MeO_2CPh (CaH_2); MeCOEt (K_2CO_3). Anhydrous $CHCl_3$, EtOAc, *n*-BuOAc, $MeCONMe_2$, and MeCN were obtained from Aldrich.

Unless otherwise stated, all reagents were purchased from commercial suppliers and used as received. The following reagents were distilled under reduced pressure from the indicated drying agents: dicyclohexyl ketone (Aldrich, $MgSO_4$), diketene (Aldrich, CaH_2). Potassium hydride (Strem) was obtained as a suspension in paraffin oil, and the oil-free compound was obtained after repeated washing with pentane in a glove box and drying in vacuo. Ethyl diazoacetate (Aldrich) was purified by flash chromatography prior to use. *t*-Butyl diazoacetate,[32] (*d*)-menthyl diazoacetate, (*l*)-menthyl diazoacetate,[33] 2,6-di-*t*-butyl-4-methylphenyl diazoacetate,[34] methanesulfonyl azide,[35] (±)-2-phenyloxetane,[36] $Cu(MeCN)_4BF_4$,[37] (4-trifluoromethylphenyl)tri-*n*-butylstannane,[38] 1-vinylcyclohexanol,[39] (3'-methyl-3'-oxetane)methyl acetate,[40] (±)-4-phenylazetidin-2-one,[41] (±)-2-phenylazetidine,[42] (1-bromo-3-chloro)propylbenzene,[43] (±)-2-phenylthietane[44] were synthesized according to literature procedures.

All reactions were carried out with magnetic stirring in oven-dried glassware under an atmosphere of argon (manifold) or under an atmosphere of nitrogen (Vaccum Atmospheres glove box), unless otherwise noted.

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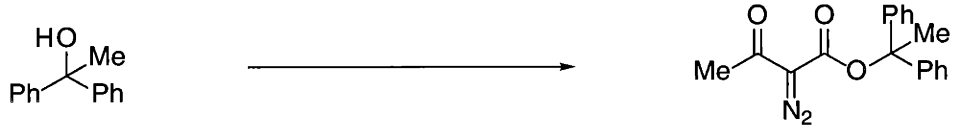
II. Synthesis of Diazo Esters.

1. 1,1-Diphenylethyl Diazoacetate.



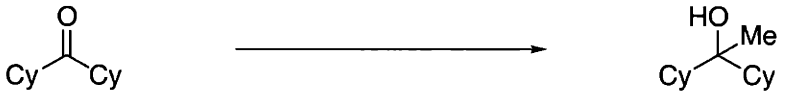
1,1-Diphenylethyl 2-diazo-3-oxobutanoate. In a 100-mL two-necked round-bottom flask equipped with an addition funnel and a condenser, 1,1-diphenylethanol (3.61 g, 18.2 mmol), DMAP (0.271 g, 2.22 mmol) and Et_3N (0.189 g, 1.87 mmol) were mixed and dissolved in 50 mL MeCN. The mixture was then brought to reflux. To this was added a 15-mL MeCN solution of diketene (3.03 g, 36.0 mmol) through an addition funnel over 30 min. The refluxing dark red reaction mixture was cooled down to r.t. and stirred for another 3 h. Et_3N (5.0 mL, 36 mmol) and a 15-mL MeCN solution of methanesulfonyl azide (4.17 g, 34.4 mmol) was then charged to the reaction mixture. After 12 h, TLC indicated only the product spot. The reaction mixture was poured into a mixture of Et_2O/water. The aqueous layer was extracted with Et_2O (4 x 100 mL), and the combined organic extracts were washed with 2M KOH, brine, dried ($MgSO_4$), and concentrated in vacuo to afford an orange solid. This material was purified by flash chromatography (10/90 Et_2O/benzene) to afford a yellow powder (3.85 g, 69% yield).

^1H NMR (500 MHz, $CDCl_3$): δ 2.29 (s, 3H), 2.38 (s, 3H), 7.26–7.30 (m, 6H), 7.30–7.36 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 27.7, 28.4, 87.1, 125.9, 127.8, 128.5, 145.0, 159.7, 190.6. IR (KBr): 3062 (w), 2143 (s), 1716 (s), 1654 (s), 1496 (m), 1449 (s), 1367 (s), 1257 (s), 1153 (s), 1057 (s), 970 (m), 772 (s), 742 (s), 703 (s) cm^{-1}. mp 114 °C dec.

1,1-Diphenylethyl diazoacetate. 1,1-Diphenylethyl 2-diazo-3-oxobutanoate (1.89 g, 6.12 mmol) was dissolved in a mixture of MeOH (50 mL) and MeCN (5 mL) to form a yellow suspension. A solution of NaOMe (0.506 g, 9.37 mmol) in MeOH (15 mL) was then added. The yellow suspension was stirred at 0 °C for 0.5 h, and at r.t. for another 0.5 h. TLC showed no more residual starting diazo ester, and the reaction mixture was poured into a mixture of water and CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL), and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford a yellow liquid (1.55 g, 95% crude yield). Purification by flash chromatography (15/85 Et_2O/pentane, 2/98 Et_2O/benzene) gave a yellow solid, which on further recrystallization from Et_2O/pentane afforded the analytically pure compound.

^1H NMR (500 MHz, $CDCl_3$): δ 2.24 (s, 3H), 4.77 (br, 1H), 7.20–7.32 (m, 10H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 27.4, 47.2, 85.4, 125.8, 127.2, 128.1, 145.5, 165.2. IR (KBr): 3123 (m), 3089 (w), 2983 (w), 2113 (s), 1682 (s), 1496 (m), 1448 (m), 1371 (m), 1345 (s), 1256 (s), 1216 (s), 1053 (s), 977 (m), 735 (s), 696 (s) cm^{-1}. mp 56–57 °C.

2. 1,1-Dicyclohexylethyl Diazoacetate.



1,1-Dicyclohexylethanol. To a solution of dicyclohexyl ketone (27.4 g, 0.141 mol) in Et_2O (300 mL) at 0 °C was slowly added 3.0 M MeMgBr (70 mL, 0.21 mol) over 40 min. The reaction mixture was then allowed to warm up to r.t., stirred for 3 days, and quenched with saturated NH_4Cl solution. It was then diluted with 1 M HCl and extracted with Et_2O. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford the desired alcohol as a yellow liquid (23.0 g, 78% yield).

The ^{1}H NMR spectrum of the product matched the literature data.[45] ^{13}C NMR (126 MHz, $CDCl_3$): δ 20.2, 26.4, 26.9, 27.0, 27.1, 27.5, 44.4, 75.9.

1,1-Dicyclohexylethyl 2-diazo-3-oxobutanoate. The title compound was synthesized similar to the procedure for 1,1-diphenylethyl 2-diazo-3-oxobutanoate.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.0–1.3 (m, 11H), 1.48 (s, 3H), 1.6–2.0 (m, 11H), 2.45 (s, 3H).

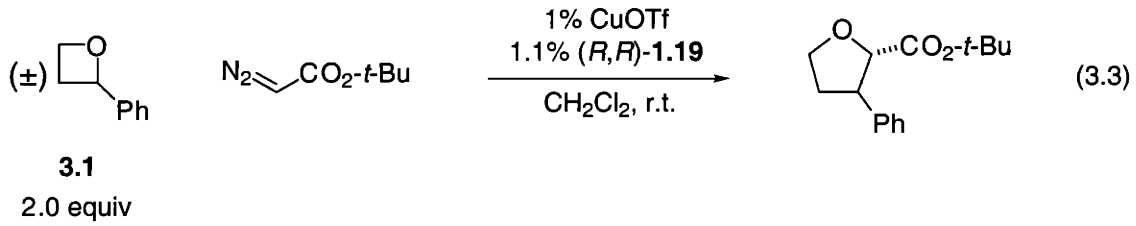
1,1-Dicyclohexylethyl diazoacetate. The crude product from the previous step was dissolved in 100 mL MeOH. NaOMe (2.5 equiv) was added batchwise, turning the reaction mixture brown. After 12 h, the reaction mixture was diluted with water and saturated with NaCl. This was extracted with Et_2O, and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford a yellow slurry. Purification by flash chromatography (5/95 Et_2O/pentane) afforded a yellow viscous liquid, which slowly solidified to a yellow solid upon storage at low temperature.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.0–1.3 (m, 10H), 1.42 (s, 3H), 1.62–1.69 (m, 2H), 1.70–1.80 (m, 8H), 1.86 (tt, 2H, J = 2.9, 11.4), 4.60 (br, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 19.5, 26.6, 27.1, 27.7, 28.3, 45.1, 46.7, 91.8, 166.5. IR (KBr): 3136 (m), 2998 (m), 2955 (s), 2922 (s), 2850 (s), 2107 (s), 1693 (s), 1671 (s), 1450 (m), 1340 (s), 1244 (s), 1128 (m), 1050

45 Bestmann, H. J.; Röder, T.; Sühs, K. *Chem. Ber.* **1988**, *121*, 1509–1517.

(m), 997 (m), 737 (m) cm^{-1}. mp 48–49 °C. HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{26}N_2O_2$, 301.1886; found, 301.1885.

III. Ring Expansion of Racemic 2-Phenyloxetane under Katsuki Conditions (eq 3.3).



(3.3)

A solution of (*R*,*R*)-**1.19** (5.4 mg, 10 μmol) in CH_2Cl_2 (2 mL) was added to CuOTf•0.5C_6H_6 (2.4 mg, 9.5 μmol) and stirred for 90 min. The catalyst solution was then filtered through acrodisc to afford an orange solution. Half of this solution was transferred to a flask containing (±)-**3.1** (128 mg, 0.955 mmol), and more CH_2Cl_2 was added until the total volume is 2.5 mL. *t*-Butyl diazoacetate (67.6 mg, 0.476 mmol), dissolved in CH_2Cl_2 (0.75 mL), was added over 45 min to the reaction mixture using a syringe pump. After 1 more h, the reaction mixture was filtered through a plug of silica with 1% Et_3N/Et_2O as the eluant. GC analysis showed that the product was a 55:45 trans:cis mixture, and that both diastereomeric products were formed in 71% ee. The residual starting oxetane has an ee of less than 1%.

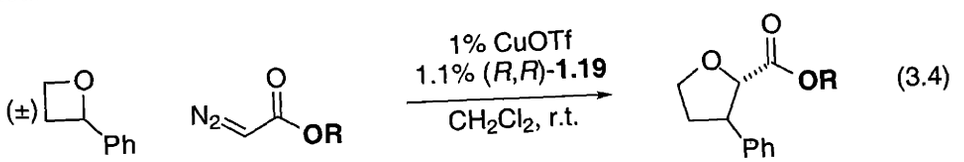
The reaction was repeated with (*S*,*S*)-**1.19**. GC analysis of the crude reaction product revealed a 55:45 trans:cis mixture, and that the trans product was formed in 71% ee and the cis product was formed in 73% ee. The residual starting oxetane has an ee of less than 1%.

The ^1H NMR spectra of the diastereomers matched the literature data.[9b]

***t*-Butyl (2*S*,3*R*)-3-phenyltetrahydrofuran-2-carboxylate.** ^{13}C NMR (126 MHz, $CDCl_3$): δ 28.2, 35.1, 50.1, 69.6, 81.6, 84.0, 127.0, 127.5, 128.8, 142.1, 172.1.

***t*-Butyl (2*S*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate.** ^{13}C NMR (126 MHz, C_6D_6): δ 27.7, 31.8, 48.1, 68.9, 81.2, 81.8, 127.1, 128.4, 128.6, 139.5, 170.2.

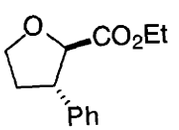
IV. Carbene Insertion into Racemic 2-Phenyloxetane: Stereoselectivity as a Function of Diazo Ester (Tables 3.2, 3.3).



(3.4)

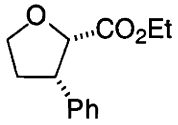
General procedure. CuOTf•0.5C_6H_6 (2.6 mg, 10 μmol) and (*R*,*R*)-**1.19** (6.8 mg, 13 μmol) were dissolved in CH_2Cl_2 (4 mL). Half of this catalyst solution was added to a 3 mL CH_2Cl_2 solution of (±)-**3.1** (69.3 mg, 0.516 mmol). To this reaction mixture a solution of the diazo ester (0.79 mmol) in CH_2Cl_2 (10 mL) was added slowly over 1 h. The reaction was then stirred at r.t. for another 9 h, then filtered through a plug of silica with 1/10/10 Et_3N/Et_2O/pentane to afford the crude product for analysis.

Table 3.2, entry 1, OR = OEt. The general procedure was followed using ethyl diazoacetate (89.9 mg, 0.788 mmol). GC analysis of the crude reaction product revealed a 55:45 trans:cis mixture, and that the trans product was formed in 47% ee (major enantiomer: 2*S*,3*R*).



Ethyl (2*R*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, C_6D_6): δ 0.85 (t, 3H, *J* = 7.2), 1.68 (qd, 1H, *J* = 7.8, 12.4), 1.99 (dtd, 1H, *J* = 4.6, 7.5, 12.2), 3.45 (dt, 1H, *J* = 6.0, 7.7), 3.90 (m, 3H), 4.02 (dt, 1H, *J* = 6.7, 8.2), 4.52 (d, 1H, *J* = 5.8), 7.00–7.06 (m, 1H), 7.08 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.4, 35.1, 49.8, 61.2, 69.7, 83.6, 127.1,

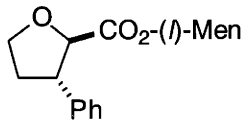
127.4, 128.9, 141.9, 172.9. IR (neat): 3030 (w), 2979 (m), 2878 (m), 1747 (s), 1603 (w), 1493 (w), 1455 (w), 1266 (m), 1192 (s), 1098 (s), 759 (m), 700 (s) cm^{-1}. $[\alpha]^{20}_D$ -99° (*c* 0.99, EtOH; 92% ee). HRMS–FAB (*m/z*): M^+ calcd for $C_{13}H_{16}O_3$, 220.1099; found, 220.1105.



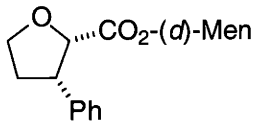
Ethyl (2*S*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, C_6D_6): δ 0.54 (t, 3H, *J* = 7.0), 1.72 (dtd, 1H, *J* = 3.4, 7.4, 12.1), 2.26 (tdd, 1H, *J* = 8.6, 9.8, 12.0), 3.25 (td, 1H, *J* = 8.0, 9.6), 3.52–3.62 (m, 2H), 3.71 (dt, 1H, *J* = 7.2, 8.3), 4.31 (dt, 1H, *J* = 3.4, 8.4), 4.59 (d, 1H, *J* = 8.2), 7.01 (tt, 1H, *J* = 2.0, 6.8), 7.05–7.15 (m, 4H). ^{13}C NMR (126 MHz, C_6D_6): δ 14.1, 31.3, 49.0, 60.2, 69.4, 82.1, 127.5, 128.7, 128.8, 139.2, 171.4. IR (thin film): 2979 (w), 2882 (w), 1741 (s), 1199 (s), 1102 (s), 1086 (s), 699 (m) cm^{-1}. $[\alpha]^{20}_D$ +117° (*c* 0.54, EtOH; 94% ee). HRMS–ESI (*m/z*): $\{M + Na\}^+$ calcd for $C_{13}H_{16}O_3$, 243.0992; found, 243.0980.

Table 3.2, entry 2, OR = O-*t*-Bu. The general procedure was followed using *t*-butyl diazoacetate (113 mg, 0.791 mmol). GC analysis of the crude reaction product revealed a 56:44 trans:cis mixture, and that the trans product was formed in 70% ee (major enantiomer: 2*S*,3*R*) and the cis product was formed in 69% ee (major enantiomer: 2*S*,3*S*).

Table 3.2, entry 3, OR = O-(*d*)-Men. The general procedure was followed using (*d*)-menthyl diazoacetate (188 mg, 0.838 mmol). GC analysis of the crude reaction product revealed a 57:43 trans:cis mixture. The crude product was converted to the acetate (*vide infra*), and GC analysis showed that the trans diastereomer is of 51% ee (major diastereomer: 2*S*,3*R*).

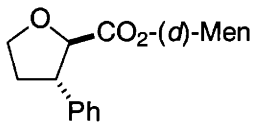


(*l*)-Menthyl (2*R*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.58 (dq, 1H, *J* = 3.9, 12.7), 0.72 (d, 3H, *J* = 6.4), 0.76 (d, 3H, *J* = 4.9), 0.78 (d, 3H, *J* = 4.9), 0.75–0.82 (m, 1H), 0.86 (q, 1H, *J* = 11.6), 1.08–1.18 (m, 1H), 1.21 (tdd, 1H, *J* = 3.1, 11.0, 12.3), 1.36–1.44 (m, 2H), 1.71 (ddd, 1H, *J* = 8.5, 12.2, 16.5), 1.77 (dtd, 1H, *J* = 2.8, 7.2, 14.4), 1.98–2.05 (m, 2H), 3.53 (dt, 1H, *J* = 6.6, 8.0), 3.94 (dt, 1H, *J* = 3.8, 8.0), 4.06 (dt, 1H, *J* = 6.6, 8.5), 4.58 (d, 1H, *J* = 6.4), 4.85 (dt, 1H, *J* = 4.3, 10.8), 7.00–7.06 (m, 1H), 7.10–7.14 (m, 4H). ^{13}C NMR (126 MHz, C_6D_6): δ 16.6, 21.2, 22.4, 23.8, 26.5, 31.8, 34.7, 36.1, 41.4, 47.4, 51.0, 70.0, 74.9, 84.6, 127.4, 127.9, 129.3, 142.4, 172.8. IR (neat): 3063 (w), 3029 (w), 2954 (s), 2870 (s), 1742 (s), 1604 (w), 1494 (m), 1455 (s), 1371 (m), 1265 (m), 1193 (s), 1099 (s), 986 (m), 758 (m), 700 (s) cm^{-1}. $[\alpha]^{20}_D$ -135° (*c* 1.29, EtOH; 96% de). HRMS–FAB (*m/z*): M^+ calcd for $C_{21}H_{30}O_3$, 330.2195; found, 330.2205.

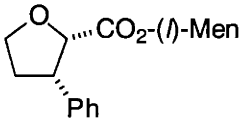


(*d*)-Menthyl (2*S*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.37 (d, 3H, *J* = 6.7), 0.67 (d, 3H, *J* = 7.0), 0.74 (q, 1H, *J* = 11.8), 0.75 (dq, 1H, *J* = 3.4, 12.4), 0.81(d, 3H, *J* = 6.7), 0.87 (dq, 1H, *J* = 2.8, 12.8), 1.07 (d sept, 1H, *J* = 2.8, 6.9), 1.14–1.24 (m, 1H), 1.26–1.38 (m, 1H), 1.50–1.62 (m, 2H), 1.62–1.70 (m, 1H), 2.30–2.43 (m, 2H), 3.72 (q, 1H, *J* = 7.4), 4.04 (q, 1H, *J* = 7.8), 4.37 (dt, 1H, *J* = 4.9, 8.2), 4.44 (dt, 1H, *J* = 4.6, 10.9), 4.64 (d, 1H, *J* = 7.3), 7.2–7.3 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 15.9, 21.2, 22.1, 23.0, 25.3, 31.4, 32.4, 34.3, 40.7, 46.6, 48.0, 68.6, 74.9, 82.3, 127.2, 128.2, 128.6, 139.4, 170.6. IR (KBr): 2956 (s), 2932 (s), 2870 (m), 1734 (s), 1456 (m), 1386 (m), 1203 (s), 1105 (s), 1082 (s), 752 (m), 701 (m) cm^{-1}. mp 72–73 °C. $[\alpha]^{20}_D$ +112° (*c* 0.55, EtOH). HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{21}H_{30}O_3$, 353.2087; found, 353.2076.

Table 3.2, entry 4, OR = O-(*l*)-Men. The general procedure was followed using *(l)*-menthyl diazoacetate (186 mg, 0.829 mmol). GC analysis of the crude reaction product revealed a 61:39 trans:cis mixture. The crude product was converted to the acetate (*vide infra*), and GC analysis showed that the trans diastereomer is of 48% ee (major diastereomer: 2*S*,3*R*).



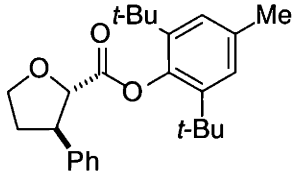
(*d*)-Menthyl (2*R*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.59 (dq, 1H, *J* = 3.8, 12.7), 0.75 (d, 3H, *J* = 6.4), 0.79 (d, 3H, *J* = 4.9), 0.80 (d, 3H, *J* = 4.6), 0.7–0.85 (m, 1H), 0.89 (q, 1H, *J* = 11.7), 1.1–1.2 (m, 1H), 1.26 (tdd, 1H, *J* = 3.1, 11.0, 12.4), 1.36–1.44 (m, 2H), 1.71 (qd, 1H, *J* = 7.8, 12.4), 1.93–2.08 (m, 3H), 3.56 (dt, 1H, *J* = 5.8, 7.6), 3.94 (dt, 1H, *J* = 4.3, 8.1), 4.08 (dt, 1H, *J* = 7.0, 8.2), 4.60 (d, 1H, *J* = 5.8), 4.93 (dt, 1H, *J* = 4.4, 10.9), 7.08 (tt, 1H, *J* = 1.8, 6.9), 7.09–7.15 (m, 4H). ^{13}C NMR (126 MHz, C_6D_6): δ 16.8, 21.2, 22.5, 23.9, 26.8, 31.8, 34.7, 35.5, 41.5, 47.5, 50.5, 69.8, 74.8, 84.5, 127.4, 127.9, 129.3, 143.0, 172.5. IR (neat): 3063 (w), 3029 (w), 2954 (s), 2870 (s), 1743 (s), 1604 (w), 1494 (m), 1455 (s), 1370 (m), 1264 (s), 1194 (s), 1100 (s), 986 (m), 758 (m), 700 (m) cm^{-1}. $[\alpha]^{20}_D$ -38° (*c* 1.10, EtOH). HRMS–FAB (*m/z*): M^+ calcd for $C_{21}H_{30}O_3$, 330.2195; found, 330.2202.



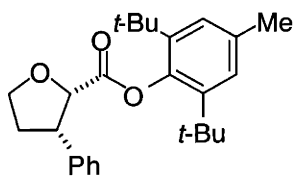
(*l*)-Menthyl (2*S*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.15 (dt, 1H, *J* = 11.0, 12.5), 0.64 (d, 3H, *J* = 6.7), 0.64–0.70 (m, 1H), 0.69 (d, 3H, *J* = 6.7), 0.81 (d, 3H, *J* = 7.0), 0.85–1.00 (m, 2H), 1.1–1.3 (m, 2H), 1.5–1.6 (m, 2H), 1.6–1.7 (m, 1H), 2.35–2.45 (m, 2H), 3.73 (q, 1H, *J* = 7.9), 4.01 (q, 1H, *J* = 8.0), 4.39–4.47 (m, 2H), 4.65 (d, 1H, *J* = 7.9), 7.2–7.3 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 16.3, 20.9, 21.9, 23.3, 26.1,

31.2, 32.2, 34.2, 39.7, 46.9, 48.2, 68.9, 74.4, 81.6, 127.2, 128.5, 128.6, 139.4, 170.6. IR (KBr): 2956 (m), 2914 (m), 2867 (m), 1732 (s), 1452 (m), 1200 (s), 1086 (s), 700 (m) cm^{-1}. mp 102–103 °C. $[\alpha]^{20}_D$ +34° (*c* 0.65, EtOH; 98% de). HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{21}H_{30}O_3$, 353.2087; found, 353.2077.

Table 3.2, entry 5, OR = BHT. The general procedure was followed using 2,6-di-*t*-butyl-4-methylphenyl diazoacetate (256 mg, 0.889 mmol). GC analysis of the crude reaction product revealed a 60:40 trans:cis mixture. The crude product was converted to the acetate (*vide infra*), and GC analysis showed that the trans diastereomer is of 65% ee (major enantiomer: 2*S*,3*R*).

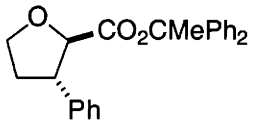


2,6-Di-*t*-butyl-4-methylphenyl (2*S*,3*R*)-3-phenyltetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, $CDCl_3$): δ 1.23 (s, 9H), 1.33 (s, 9H), 2.15 (qd, 1H, *J* = 7.4, 12.7), 2.31 (s, 3H), 2.54 (dtd, 1H, *J* = 5.2, 7.5, 12.6), 3.92 (ddd, 1H, *J* = 5.5, 7.0, 7.9), 4.22 (q, 1H, *J* = 7.7), 4.26 (dt, 1H, *J* = 5.0, 8.0), 4.79 (d, 1H, *J* = 5.5), 7.09 (dd, 1H, *J* = 0.6, 2.1), 7.11 (dd, 1H, *J* = 0.6, 2.1), 7.24–7.28 (m, 1H), 7.34–7.36 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.7, 31.6, 31.6, 35.4, 35.5, 35.8, 48.3, 69.8, 84.8, 127.2, 127.3, 127.6, 129.0, 134.9, 142.0, 142.2, 142.3, 146.2, 172.7 IR (thin film): 3064 (w), 2962 (s), 2916 (s), 2873 (s), 1760 (s), 1600 (m), 1421 (m), 1364 (m), 1268 (m), 1183 (s), 1147 (s), 1106 (s), 860 (m), 756 (m), 700 (s) cm^{-1}. $[\alpha]^{20}_D$ +61° (*c* 1.16, EtOH; 69% ee). HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{26}H_{34}O_3$, 417.2400; found, 417.2381.



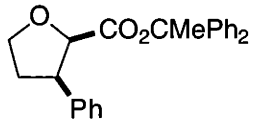
2,6-Di-*t*-butyl-4-methylphenyl (2*S*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.94 (s, 9H), 1.25 (s, 9H), 2.24 (s, 3H), 2.41 (dtd, 1H, *J* = 4.5, 7.8, 12.2), 2.65 (dtd, 1H, *J* = 7.2, 8.6, 12.2), 3.79 (dt, 1H, *J* = 6.7, 7.8), 4.16 (q, 1H, *J* = 7.9), 4.32 (dt, 1H, *J* = 4.7, 8.6), 4.91 (d, 1H, *J* = 6.1), 6.99 (d, 1H, *J* = 1.8), 7.05 (d, 1H, *J* = 1.8), 7.16–7.21 (m, 1H), 7.22–7.28 (m, 2H), 7.38–7.42 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.6, 31.3, 31.3, 31.4, 35.0, 35.4, 47.9, 68.2, 82.0, 127.1, 127.2, 127.3, 128.5, 129.5, 134.7, 137.7, 142.2, 142.5, 142.9, 169.3 IR (thin film): 2960 (s), 1757 (s), 1599 (w), 1420 (m), 1364 (m), 1268 (m), 1180 (s), 1149 (s), 1106 (s), 1046 (s), 859 (w), 697 (m) cm^{-1}. mp 78–81 °C. $[\alpha]^{20}_D$ +55° (*c* 1.06, EtOH; 77% ee). HRMS–ESI (*m/z*): M^+ calcd for $C_{26}H_{34}O_3$, 417.2400; found, 417.2408.

Table 3.3, entry 2, OR = $OCMePh_2$. The general procedure was followed using (*S*,*S*)-**1.19** (3.9 mg, 7.3 μmol) and 1,1-diphenylethyl diazoacetate (176 mg, 0.660 mmol). NMR analysis of the crude reaction product revealed a 56:44 trans:cis mixture. The crude product was converted to the methyl ester (*vide infra*), and GC analysis showed that the trans diastereomer is of 80% ee (major enantiomer: 2*R*,3*S*) and the cis diastereomer is of 78% ee (major enantiomer: 2*R*,3*R*).



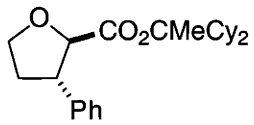
1,1-Diphenylethyl (2*R*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.10 (qd, 1H, *J* = 8.3, 12.5), 2.18 (s, 3H), 2.39 (m, 1H), 3.48 (q, 1H, *J* = 7.6), 4.11 (dt, 1H, *J* = 6.7, 8.5), 4.19 (dt, 1H, *J* = 3.8, 8.2), 4.55 (d, 1H, *J* = 7.0), 7.06–7.10 (m, 2H), 7.16–7.25 (m, 8H), 7.27–7.40 (m, 5H). ^{13}C NMR (126 MHz, C_6D_6): δ 27.3, 35.9, 50.3, 69.8, 84.7, 85.5, 126.7, 126.9, 127.4, 127.6, 127.7, 128.1, 128.7, 128.7, 129.3, 142.7, 146.3, 146.4, 170.7 IR (neat): 3088 (m), 3060 (m), 3028 (m), 2979 (m), 2943 (m), 2879 (m), 1755 (s), 1602 (w), 1494 (s), 1448 (s), 1179 (s), 1094 (s), 1049 (s), 756 (s), 699 (s) cm^{-1}. $[\alpha]^{20}_D$ -42° (*c* 0.52,

EtOH; 80% ee). HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{25}H_{24}O_3$, 395.1618; found, 395.1608.



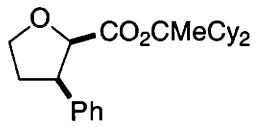
1,1-Diphenylethyl (2*R*,3*R*)-3-phenyltetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, $CDCl_3$): δ 1.62 (s, 3H), 2.32–2.46 (m, 2H), 3.82 (q, 1H, *J* = 8.0), 4.03 (q, 1H, *J* = 7.9), 4.37 (dt, 1H, *J* = 4.3, 8.2), 4.75 (d, 1H, *J* = 7.9), 6.78–6.83 (m, 2H), 7.12–7.26 (m, 9 H), 7.29–7.36 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 26.1, 31.5, 48.3, 68.9, 81.9, 85.5, 125.8, 126.3, 127.0, 127.3, 127.4, 128.0, 128.2, 128.6, 128.8, 138.9, 144.6, 145.9, 169.2. IR (film): 2930 (s), 2852 (s), 1732 (s), 1449 (s), 1381 (m), 1243 (s), 1193 (s), 1101 (s), 1083 (s), 698 (s) cm^{-1}. $[\alpha]^{20}_D$ -44° (*c* 0.65, EtOH; 95% ee). HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{25}H_{24}O_3$, 395.1618; found, 395.1630.

Table 3.3, entry 3, OR = OCMeCy$_2$. The general procedure was followed using 1,1-dicyclohexylethyl diazoacetate (79.2 mg, 0.284 mmol). NMR analysis of the crude reaction product revealed a 57:43 trans:cis mixture. The crude product was converted first to the alcohol then to two different derivatives (*vide infra*). GC analysis showed that the trans diastereomer is of 84% ee (acetate, major diastereomer: 2*S*,3*R*) and the cis diastereomer is of 84% ee (trifluoroacetate, major diastereomer: 2*S*,3*S*).



1,1-Dicyclohexylethyl (2*R*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, C_6D_6): δ 0.9–1.2 (m, 10H), 1.43 (s, 3H), 1.5–1.8 (m, 11H), 1.85 (t qnt, 2H, *J* = 2.8, 11.6), 2.03 (dddd, 1H, *J* = 4.3, 6.7, 7.6, 11.9), 3.54 (dt, 1H, *J* = 6.4, 7.9), 3.93 (dt, 1H, *J* = 4.0, 8.1), 4.04 (dt, 1H, *J* = 6.7, 8.5), 4.51 (d, 1H, *J* = 6.4), 7.02–7.06 (m, 1H), 7.10– 7.16 (m,

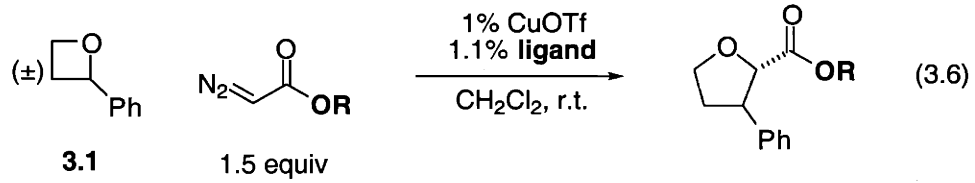
4H). ^{13}C NMR (125 MHz, C_6D_6): δ 19.8, 27.2, 27.5, 27.6, 28.2, 28.2, 28.6, 28.7, 36.0, 45.5, 50.6, 69.8, 85.2, 91.1, 127.3, 128.0, 129.2, 142.9, 172.2. IR (neat): 2929 (s), 2852 (s), 1742 (s), 1449 (s), 1190 (s), 1100 (s), 755 (m), 700 (s) cm^{-1}. $[\alpha]^{20}_D$ -63° (*c* 1.00, EtOH; 98% ee). HRMS–FAB (*m/z*): $[M + H]^+$ calcd for $C_{25}H_{36}O_3$, 385.2743; found; 385.2732.



1,1-Dicyclohexylethyl (2*R*,3*R*)-3-phenyltetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, C_6D_6): δ 0.71 (dq, 1H, *J* = 3.4, 12.4), 0.86–1.16 (m, 9H), 1.24 (s, 3H), 1.4–1.5 (m, 2H), 1.5–1.7 (m, 9H), 1.73–1.9 (m, 2H), 2.29 (qd, 1H, *J* = 8.7, 11.9), 3.27 (q, 1H, *J* = 8.1), 3.74 (q, 1H, *J* = 7.8), 4.26 (dt, 1H, *J* =3.7, 8.4), 4.58 (d, 1H, *J* = 7.6), 7.05 (m, 1H), 7.14 (t, 2H, *J* = 7.6), 7.20 (d, 2H, *J* = 8.2). ^{13}C NMR (126 MHz, C_6D_6): δ 19.5, 27.2, 27.2, 27.6, 27.6, 27.7, 27.8, 28.2, 28.2, 28.6, 31.6, 45.3, 45.4, 48.6, 68.8, 83.0, 91.0, 127.4, 128.8, 129.2, 139.5, 170.6. IR (neat): 2930 (s), 2852 (s), 1732 (s), 1449 (s), 1381 (m), 1243 (s), 1193 (s), 1101 (s), 1083 (s), 698 (s) cm^{-1}. $[\alpha]^{20}_D$ -44° (*c* 0.65, EtOH; 95% ee). HRMS–FAB (*m/z*): $[M + H]^+$ calcd for $C_{25}H_{36}O_3$, 385.2743; found, 385.2735.

V. Development of Reaction Conditions.

1. Ligand (Table 3.4).



General procedure. $CuOTf \cdot 0.5C_6H_6$ (2.2 mg, 8.7 μmol) and the ligand (9.9 μmol) were dissolved in CH_2Cl_2 (1 mL). Half of this catalyst solution was added to a solution of (±)-**3.1** (57.3 mg, 0.427 mmol) in CH_2Cl_2 (3 mL). To this reaction mixture a solution of the diazo ester (0.53 mmol) in CH_2Cl_2 (1 mL) was added slowly over 15 min. The

reaction was then stirred at r.t. for another hour, then filtered through a plug of silica with 1/10/10 Et_3N/Et_2O/pentane as the eluant to afford the crude product for analysis.

Entry 2. The general procedure was followed using (*R,R*)-**1.22** as the ligand and *t*-butyl diazoacetate as the diazo ester. GC analysis of the crude reaction product revealed a 58:42 trans : cis mixture, and that the trans product was formed in 68% ee (major enantiomer: 2*S*,3*R*) and the cis product was formed in 80% ee (major enantiomer: 2*S*,3*S*).

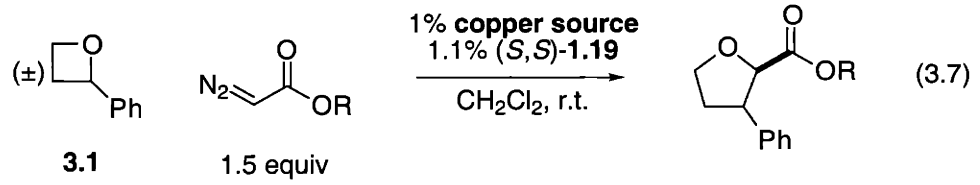
Entry 3. The general procedure was followed using (*R,R*)-**1.29** as the ligand and *t*-butyl diazoacetate as the diazo ester. GC analysis of the crude reaction product revealed that the trans product was formed in 75% ee (major enantiomer: 2*S*,3*R*) and the cis product was formed in 68% ee (major enantiomer: 2*S*,3*S*).

Entry 4. The general procedure was followed using (*R,R*)-**1.33** as the ligand and *t*-butyl diazoacetate as the diazo ester. GC analysis of the crude reaction product revealed a 50:50 trans:cis mixture, and that the trans product was formed in 78% ee (major enantiomer: 2*S*,3*R*) and the cis product was formed in 70% ee (major enantiomer: 2*S*,3*S*).

Entry 6. The general procedure was followed using (*R,R*)-**1.22** as the ligand and **3.4** as the diazo ester. NMR analysis of the crude reaction product revealed a 61:39 trans:cis mixture. The crude product was converted to the methyl ester (*vide infra*), and HPLC analysis showed that the trans diastereomer is of 81% ee (major enantiomer: 2*S*,3*R*) and the cis diastereomer is of 85% ee (major enantiomer: 2*S*,3*S*).

Entry 7. The general procedure was followed using (*R,R*)-**1.33** as the ligand and **3.4** as the diazo ester. NMR analysis of the crude reaction product revealed a 52:48 trans:cis mixture. The crude product was converted to the methyl ester (*vide infra*), and HPLC analysis showed that the trans diastereomer is of 53% ee (major enantiomer: 2*S*,3*R*) and the cis diastereomer is of 59% ee (major enantiomer: 2*S*,3*S*).

2. Copper Source (Table 3.5).



(3.7)

General procedure A. The copper source (16 μmol) and (*S,S*)-**1.19** (10 mg, 19 μmol) were dissolved in CH_2Cl_2 (2 mL). A quarter of this catalyst solution was added to a solution of (±)-**3.1** (55.0 mg, 0.410 mmol) in CH_2Cl_2 (3 mL). To this reaction mixture a solution of the diazo ester (0.57 mmol) in CH_2Cl_2 (1 mL) was added slowly over 15 min. The reaction was then stirred at r.t. for another hour, then filtered through a plug of silica with 50/50 Et_2O/pentane as the eluant to afford the crude product for analysis.

OR = O-*t*-Bu. The general procedure was followed using *t*-butyl diazoacetate as the diazo ester. The crude reaction product was analyzed by GC to determine the diastereomeric ratio and the ee of each diastereomer.

copper source	trans : cis	trans ee	cis ee
CuCl	56 : 44	64	69
CuOTf•0.5C_6H_6	53 : 47	70	74
$Cu(MeCN)_4BF_4$	56 : 44	70	74
$Cu(MeCN)_4PF_6$	56 : 44	70	73

OR = OCMeCy$_2$. The general procedure was followed using **3.4** as the diazo ester. The crude reaction product was analyzed by ^{1}H NMR to determine the conversion and the diastereomeric ratio. The crude product was then converted to the acetate (*vide infra*) for determination of the trans ee.

copper source	conversion (%)	trans : cis	trans ee
CuCl	55 (52 h)	57 : 43	62
CuOTf•0.5C$_6$H$_6$	100	57 : 43	82
Cu(MeCN)$_4$BF$_4$	94	58 : 42	84
Cu(MeCN)$_4$PF$_6$	98	57 : 43	83

General procedure B. CuCl (1.5 mg, 15 μmol) and (*S,S*)-**1.19** (9.6 mg, 18 μmol) were dissolved in CH_2Cl_2 (2 mL). After 1 h, one quarter of this catalyst solution was added to a stirring suspension of MX (4.1 μmol).and stirred in dark for 3 h. The catalyst solution was filtered through acrodisc and added to (±)-**3.1** (50.1 mg, 0.373 mmol). To this reaction mixture a solution of the diazo ester (0.53 mmol) in CH_2Cl_2 (1 mL) was added slowly over 15 min. The reaction was then stirred at r.t. for another 60 min, then filtered through a plug of silica with 50/50 Et_2O/pentane to afford the crude product for analysis.

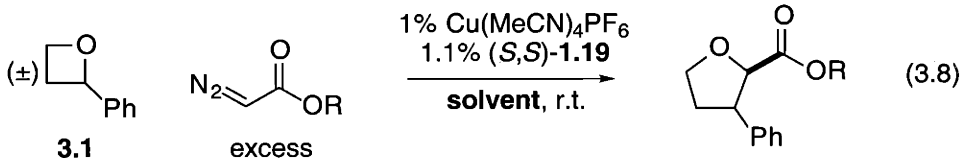
OR = O-*t*-Bu. The general procedure was followed using *t*-butyl diazoacetate as the diazo ester. The crude reaction product was analyzed by GC to determine the diastereomeric ratio and the ee of each diastereomer.

anion source	trans : cis	trans ee	cis ee
AgO_2CCF_3	58 : 42	69	70
AgOTs	55 : 45	70	73
AgOTf	55 : 45	68	72
$AgClO_4$	57 : 43	22	31
$AgBF_4$	55 : 45	68	72
$AgPF_6$	55 : 45	63	67
$AgSbF_6$	58 : 42	69	73
NaBARF	55 : 45	69	73

OR = $OCMeCy_2$. The general procedure was followed using **3.4** as the diazo ester. The crude reaction product was analyzed by ^1H NMR to determine the conversion and the diastereomeric ratio. The crude product was then converted to the acetate (*vide infra*) for determination of the trans ee.

anion source	conversion (%)	trans : cis	trans ee
AgO_2CCF_3	29	57 : 43	79
AgOTs	96	57 : 43	83
AgOTf	100	58 : 42	84
$AgClO_4$	43	59 : 41	35
$AgBF_4$	86	57 : 43	84
$AgPF_6$	100	59 : 41	60
$AgSbF_6$	100	59 : 41	66
NaBARF	97	58 : 42	83

3. **Solvent (Table 3.6).**



(3.8)

General procedure. $Cu(MeCN)_4PF_6$ (7.3 mg, 20 μmol) and (*S,S*)-**1.19** (12.2 mg, 23 μmol) were dissolved in CH_2Cl_2 (2 mL) and stirred for 1 h. The catalyst solution was filtered through acrodisc, divided into 5 equal parts and solvent was removed in vacuo. One part of Cu[(*S,S*)-**1.19**]PF_6 thus prepared was dissolved in the solvent being investigated and added to (±)-**3.1** (52.4 mg, 0.391 mmol). After 30 min, a solution of the diazo ester (0.49 mmol) in 1 mL of solvent was added slowly over 15 min. The reaction was then stirred at r.t. for another 2 h, then filtered through a plug of silica with 50/50 Et_2O/pentane as the eluant to afford the crude product for analysis.

OR = O-*t*-Bu. The general procedure was followed using *t*-butyl diazoacetate as the diazo ester. The crude reaction product was analyzed by GC to determine the diastereomeric ratio and the ee of each diastereomer.

solvent	trans : cis	trans ee	cis ee
$CHCl_3$	55 : 45	68	74
PhH	54 : 46	74	81
$PhCH_3$	54 : 46	73	81
$PhCF_3$	54 : 46	70	73
EtOAc	55 : 45	75	80
MeO_2CPh	54 : 46	69	74
$MeNO_2$	55 : 45	75	77
$MeCONMe_2$	55 : 45	69	74

MeCN	56 : 44	73	76
MeCOEt	56 : 44	74	76

OR = $OCMeCy_2$. The general procedure was followed using **3.4** as the diazo ester. The crude reaction product was analyzed by ^1H NMR to determine the conversion and the diastereomeric ratio. The crude product was then converted to the acetate (*vide infra*) for determination of the trans ee.

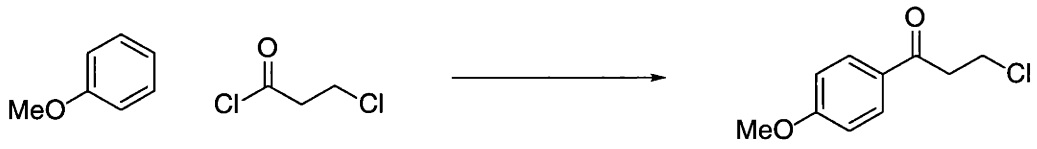
solvent	conversion (%)	trans : cis	trans ee
$CHCl_3$	97	57 : 43	82
PhCl	100	55 : 45	84
$ClCH_2CH_2Cl$	100	57 : 43	83
PhH	98	55 : 45	87
$PhCH_3$	100	56 : 44	86
$PhCF_3$	100	56 : 44	83
C_6F_6	99	57 : 43	86
n-BuOAc	90	55 : 45	87
EtOAc	99	56 : 44	87
MeO_2CPh	100	55 : 45	84
$MeNO_2$	59	57 : 43	88
$MeCONMe_2$	54	57 : 43	80
MeCN	36	58 : 42	86
MeCOEt	26	59 : 41	n.d.

VI. Synthesis of Racemic Oxetanes.

1. Preparation of β-Chloroketones.

General. The β-chloroketones were prepared by two methods: (1) Friedel–Crafts acylation of the arene (**3.5, 3.7**) or the alkynylsilane (**3.8**) by 3-chloropropionyl chloride. (2) Stille coupling of the arylstannane (**3.6**) to the acid chloride. On standing, the β-chloroketones slowly eliminates HCl to afford the corresponding α,β-unsaturated ketones, which in most cases cannot be completely removed from the desired product.

All yields are unoptimized.



3-Chloro-1-(4-methoxyphenyl)propan-1-one. To a solution of $AlCl_3$ (20.0 g, 0.150 mol) in $PhNO_2$ (150 mL) was added anisole (13.5 mL, 0.124 mol), followed by 3-chloropropionyl chloride (12.5 mL, 0.118 mol). After 2 h, TLC showed no residual anisole. The reaction mixture was quenched by pouring it into a mixture of ice and water (300 mL). The aqueous layer was extracted with CH_2Cl_2 (4 x 300 mL), and the combined organic layer was washed with saturated Na_2CO_3 solution, dried ($MgSO_4$), and concentrated in vacuo (70–80 °C, 2 torr) to afford a mixture of brown oil and white solid. Recrystallization of this crude product from Et_2O/hexanes afforded the desired product as pale brown crystals (13.5 g, 55% yield).

^1H NMR (500 MHz, $CDCl_3$): δ 3.42 (t, 2H, J = 6.9), 3.88 (s, 3H), 3.92 (t, 2H, J = 6.9), 6.95 (d, 2H, J = 9.2), 7.95 (d, 2H, J = 8.9).[46] ^{13}C NMR (126 MHz, $CDCl_3$): δ 39.2, 41.1,

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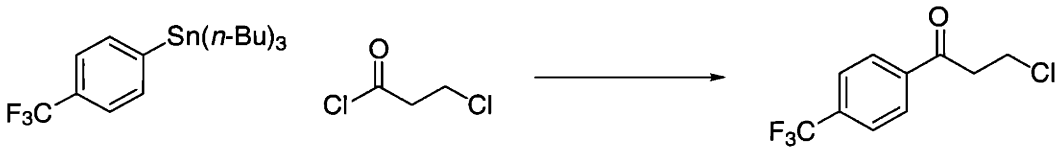
46 The ^1H NMR data matches all but one signals reported by Ruotsalainen (Ruotsalainen, H. *Suomen Komistilehli B***1973**, *46*, 215–220). The discrepancy for the chemical shift of the methoxy group is probably due to a typographical error in the original report.

55.7, 114.1, 129.6, 130.6, 164.0, 195.4. HRMS–EI (*m*/z): M^+ calcd for $C_{10}H_{11}ClO_2$, 198.0448; found, 198.0444.



3-Chloro-1-(4-trifluoromethylphenyl)propan-1-one. To a solution of $Pd_2(dba)_3$ (1.15 g, 1.26 mmol) in CH_2Cl_2 (20 mL) was added a solution of P(*t*-Bu)$_3$ (0.612 g, 3.02 mmol) in CH_2Cl_2 (30 mL). It was cooled to 0 °C, and charged with 3-chloropropionyl chloride (12.0 mL, 0.126 mol). The purple solution slowly turns brown. After 15 min, degassed (4-trifluoromethylphenyl)tri-*n*-butylstannane (21.8 g, 50.1 mmol) was added to the reaction mixture, which was then stirred at 0 °C for 12 h and at r.t. for another 36 h. The reaction mixture was filtered through a plug of silica with Et_2O as the eluant, and concentration of the filtrate in vacuo afforded a red liquid. The crude product was purified by flash chromatography (2.5/97.5 Et_2O/pentane) to afford the desired product as a yellow liquid (7.79 g, ~ 66% yield), which slowly solidified to a white solid on standing at 0 °C.[47] ^{1}H NMR analysis showed that there is only a small amount of residual organotin impurity.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.49 (t, 2H, *J* = 6.7), 3.94 (t, 2H, *J* = 6.7), 7.76 (d, 2H, *J* = 8.9), 8.07 (d, 2H, *J* = 7.9). ^{13}C NMR (126 MHz, $CDCl_3$): δ 38.4, 41.7, 123.7 (q, $^1J_{C-F}$ = 273), 126.0 (q, $^3J_{C-F}$ = 3.9), 128.6, 134.9 (q, $^2J_{C-F}$ = 32.6), 139.1, 195.9. IR (KBr): 1686 (s), 1513 (m), 1414 (m), 1326 (s), 1129 (s), 1067 (s), 853 (m), 834 (m), 714 (m), 653 (m) cm^{-1}. HRMS–EI (*m*/z): M^+ calcd for $C_{10}H_8ClF_3O$, 236.0216; found, 236.0211.

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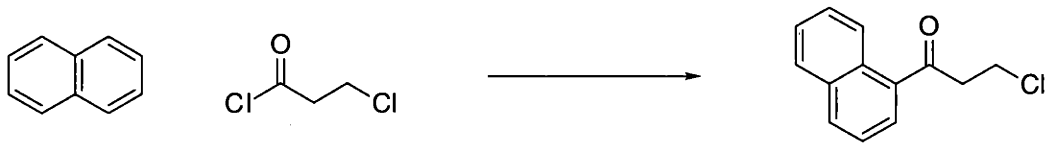
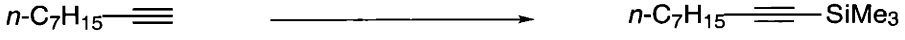
47 We first attempted the Stille coupling using the procedure of Stille *et al.* (Labadie, J. W.; Tueting, D.; Stille, J. K. *J. Org. Chem.* **1983**, *48*, 4634–4642.) and Pd(Bn)(Cl)(PPh$_3$)$_2$ as the catalyst. Di(4-(trifluoromethyl)phenyl)methanone was formed instead as the major product. We then switched to $Pd_2(dba)_3$ / P(*t*-Bu)$_3$ as the catalyst and we were gratified to find that the formation of the side product is much reduced, and the desired β-chloroketone was formed in moderate yield.



3-Chloro-1-(1-naphthyl)propan-1-one. 3-Chloropropionyl chloride (25.7 g, 0.216 mol) was added to a suspension of $AlCl_3$ (34.2 g, 0.257 mol) in CH_2Cl_2 (300 mL). It was cooled to 0 °C, then naphthalene (25.7 g, 0.201 mol) was added batchwise over 15 min to the reaction mixture.[48] A lot of white solid precipitated out, which on further stirring redissolved again. After 12 h, the reaction mixture was poured into ice. The aqueous layer was extracted with CH_2Cl_2 (3 x 300 mL), and the combined organic layer was washed with saturated $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated in vacuo to afford an emerald green liquid. This was purified by flash chromatography (5/20/75 Et_2O/CH_2Cl_2/pentane) to afford a yellow oil (45.60 g). ^1H NMR analysis showed that there is only a trace amount of the 2-isomer (1-isomer:2-isomer ~ 10:1).

^1H NMR (500 MHz, $CDCl_3$): δ 3.51 (t, 2H, J = 6.6), 3.97 (t, 2H, J = 6.6), 7.49 (dd, 1H, J = 7.3, 8.2), 7.53 (ddd, 1H, J = 1.2, 6.9, 8.1), 7.59 (ddd, 1H, J = 1.4, 6.7, 8.7), 7.86 (d, 2H, J = 7.6), 7.99 (d, 1H, J = 8.2), 8.66 (d, 1H, J = 8.2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 39.3, 44.4, 124.5, 125.9, 126.8, 128.2, 128.4, 128.6, 130.2, 133.5, 134.1, 135.1, 200.6. IR (neat): 3050 (w), 2968 (w), 1682 (s), 1593 (m), 1573 (m), 1508 (s), 1337 (s), 1236 (s), 1099 (s), 944 (m), 801 (s), 776 (s) cm^{-1}. HRMS–EI (m/z): M^+ calcd for $C_{13}H_{11}ClO$, 218.0498; found, 218.0495.



(Non-1-ynyl)trimethylsilane. The synthesis of the title compound was adapted from the procedure described by Hanack and Haβdentenfel for various

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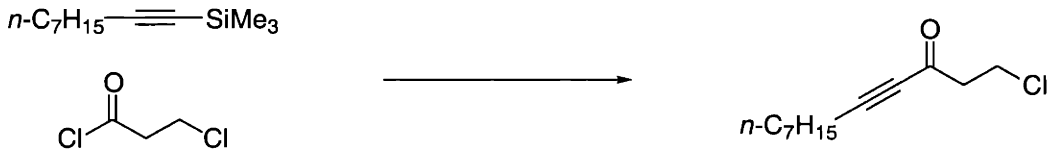
48 We found that the sequence of the addition of reagents can have significant effect on the regioselectivity of the Friedel–Crafts acylation. The procedure we reported here is referred as the Perrier procedure, which involves the pre-formation of the Lewis acid–acid chloride complex followed by the addition of the arene to the complex.

alkynyltrimethylsilanes.[49] The crude product was distilled under reduced pressure (65–68 °C, 0.6 torr) to afford the product as a colorless liquid (12.82 g, 90% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.14 (s, 9H), 0.88 (t, 3H, *J* = 6.9), 1.2–1.4 (m, 8H), 1.51 (qnt, 2H, *J* = 7.3), 2.21 (t, 2H, *J* = 7.2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 0.4, 14.3, 20.1, 22.8, 28.8, 29.0, 31.9, 84.4, 108.0. IR (neat): 2958 (s), 2931 (s), 2856 (s), 2176 (s), 1466 (m), 1249 (s), 1033 (m), 841 (s) cm^{-1}. HRMS–EI (*m/z*): $[M - CH_3]^+$ calcd for $C_{12}H_{24}Si$, 181.1413; found, 181.1409.



1-Chlorododec-4-yn-3-one. To a stirring suspension of $AlCl_3$ (9.50 g, 71.2 mmol) in CH_2Cl_2 (150 mL) at 0 °C was added slowly a mixture of (non-1-ynyl)trimethylsilane (12.7 g, 64.7 mmol) and 3-chloropropionyl chloride (8.23 g, 64.8 mmol) over 10 min. The yellow suspension slowly dissolved to form a brown solution. After the addition finished, the reaction mixture was allowed to warm up to r.t. and stirred for 1 h. It was poured into a mixture of ice and CH_2Cl_2. The aqueous layer was extracted with more CH_2Cl_2 (2 x 150 mL), and the combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford a brown liquid. This crude product was purified by flash chromatography (30/70 $CHCl_3$/hexanes → 75/25) to afford a yellow oil (10.90 g).

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J* = 7.0), 1.2–1.5 (m, 8H), 1.59 (qnt, 2H, *J* = 7.3), 2.38 (t, 2H, *J* = 7.2), 3.01 (t, 2H, *J* = 7.2), 3.79 (t, 2H, *J* = 6.7). ^{13}C NMR (126 MHz, C_6D_6): δ 14.1, 19.1, 22.7, 27.7, 28.8, 28.9, 31.7, 38.0, 47.8, 80.4, 96.3, 184.0. IR (neat): 2929 (s), 2857 (m), 2212 (m), 1678 (s), 1649 (m) cm^{-1}. HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{19}ClO$, 237.1017; found, 237.1026.

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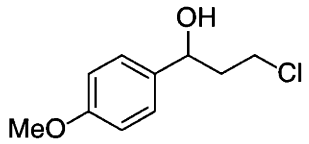
2. Preparation of Racemic γ-Chloroalcohols.

General. The procedure given below for the reduction of **3.5** is representative. The reduction is always accompanied by the formation of a small amount of the fully reduced product. However, it can be removed easily by flash chromatography once the γ-chloroalcohol is cyclized to give the oxetane.

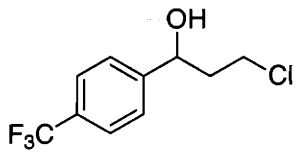
All yields are unoptimized.



(±)-3-Chloro-1-(4-methoxyphenyl)propan-1-ol. To a solution of **3.5** (5.00 g, 25.2 mmol) in a mixture of THF (75 mL) and EtOH (75 mL) at 0 °C was added $NaBH_4$ (1.18 g, 31.2 mmol) over 7 min. The reaction mixture was stirred at 0 °C, and after 3 h, TLC showed no starting ketone. The reaction mixture was poured into a mixture of saturated NH_4Cl solution and ice (300 mL). The aqueous layer was extracted by Et_2O (4 x 300 mL), and the combined organic extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford a pale yellow solid. This was purified by flash chromatography twice (25/75 Et_2O/pentane; 10/90 Et_2O/benzene) to afford the desired compound as a pale yellow solid (3.99 g, 79% yield).

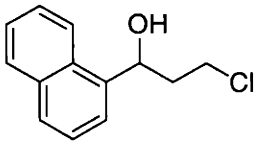
^1H NMR (500 MHz, $CDCl_3$): δ 1.90 (dd, 1H, J = 0.9, 3.4), 2.06 (m, 1H), 2.24 (tdd, 1H, J = 5.8, 8.2, 14.3), 3.54 (td, 1H, J = 6.0, 11.0), 3.72 (ddd, 1H, J = 5.7, 8.1, 10.8), 3.81 (s, 3H), 4.90 (ddd, 1H, J = 3.6, 4.7, 8.2), 6.90 (d, 2H, J = 8.9), 7.29 (d, 2H, J = 8.5). ^{13}C NMR (126 MHz, $CDCl_3$): δ 41.5, 42.0, 55.5, 71.2, 114.2, 127.3, 136.0, 159.5. IR (KBr): 3293 (m br),

2960 (w), 2904 (w), 1612 (m), 1516 (m), 1288 (m), 1253 (s), 1179 (m), 1032 (m), 834 (m), 652 (m) cm^{-1}. HRMS–FAB (*m/z*): M^+ calcd for $C_{10}H_{13}ClO_2$, 200.0604; found, 200.0608.



(±)-3-Chloro-1-(4-trifluoromethylphenyl)propan-1-ol. The general procedure was followed using **3.6** (2.99 g, 12.6 mmol). The crude product was purified by flash chromatography (4/96 Et_2O/benzene) to afford the desired product as a colorless liquid (1.70 g, 55% yield).

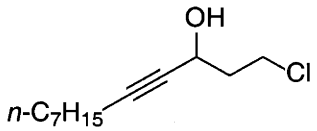
^1H NMR (500 MHz, $CDCl_3$): δ 2.08 (m, 1H), 2.12 (d, 1H, *J* = 3.7), 2.21 (tdd, 1H, *J* = 5.4, 8.9, 14.5), 3.58 (td, 1H, *J* = 5.7, 11.0), 3.78 (ddd, 1H, *J* = 5.2, 8.5, 11.0), 5.05 (td, 1H, *J* = 4.0, 8.9), 7.50 (d, 2H, *J* = 8.2), 7.63 (d, 2H, *J* = 8.2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 41.6, 41.6, 70.8, 124.3 (q, $^1J_{C-F}$ = 272), 125.8 (q, $^3J_{C-F}$ = 3.8), 126.3, 130.3 (q, $^2J_{C-F}$ = 32), 147.9. IR (neat): 3369 (m, br), 2967 (w), 2916 (w), 1621 (m), 1420 (m), 1327 (s), 1167 (s), 1127 (s), 1069 (s), 1017 (s), 840 (s) cm^{-1}. HRMS–EI (*m/z*): M^+ calcd for $C_{10}H_{10}ClF_3O$, 238.0372; found, 238.0367.



(±)-3-Chloro-1-(1-naphthyl)propan-1-ol. The general procedure was followed using **3.7** (12.1 g, 55.1 mmol). The crude product was purified by flash chromatography (2.5/97.5 MTBE/hexanes; 90/10 benzene/hexanes) to afford two fractions, one cleaner with less contamination from the 2-isomer and α,β-unsaturated alcohol (5.71 g), and the

other with more contamination (3.29 g). This was carried on to the next step without further purification.

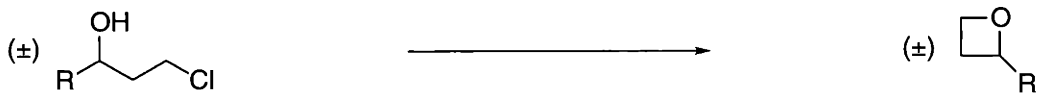
^{1}H NMR (500 MHz, C_6D_6): δ 1.35 (dd, 1H, *J* = 1.2, 3.7), 1.87 (tdd, 1H, *J* = 4.7, 9.6, 14.5), 2.0 (m, 1H), 3.23 (ddd, 1H, *J* = 4.6, 5.8, 10.7), 3.63 (ddd, 1H, *J* = 4.7, 9.8, 10.5), 5.37 (td, 1H, *J* = 3.4, 9.2), 7.24–7.28 (m, 2H), 7.31 (ddd, 1H, *J* = 1.2, 6.7, 8.5), 7.50 (d, 1H, *J* = 7.0), 7.56 (d, 1H, *J* = 8.2), 7.65 (d, 1H, *J* = 8.5), 8.09 (d, 1H, *J* = 8.2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 40.9, 42.5, 68.1, 122.9, 123.1, 125.7, 125.9, 126.5, 128.5, 129.2, 130.2, 134.0, 139.7. IR (neat): 3382 (m, br), 3051 (w), 2962 (w), 1597 (w), 1511 (m), 1281 (m), 1070 (s), 801 (s), 778 (s) cm^{-1}. HRMS–EI (*m/z*): M^+ calcd for $C_{13}H_{13}ClO$, 220.0655; found, 220.0660.



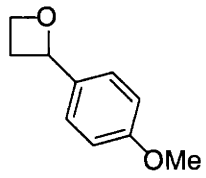
(±)-1-Chlorododec-4-yn-3-ol. The general procedure was followed using **3.8** (5.15 g, 24.0 mmol). The crude product was purified by flash chromatography (7.5/92.5 Et_2O/pentane → 15/85) to afford the desired product as a colorless liquid (3.39 g).

^{1}H NMR (500 MHz, C_6D_6): δ 0.89 (t, 3H, *J* = 7.2), 1.15–1.30 (m, 8H), 1.38 (qnt, 2H, *J* = 7.2), 1.68 (d, 1H, *J* = 5.2), 1.86–2.00 (m, 2H), 2.02 (dt, 2H, *J* = 2.0, 7.1), 3.38 (td, 1H, *J* = 6.3, 10.8), 3.46 (ddd, 1H, *J* = 6.4, 7.3, 11.0), 4.44 (m, 1H). ^{13}C NMR (126 MHz, C_6D_6): δ 14.7, 19.2, 23.4, 29.3, 29.5, 29.5, 32.4, 41.4, 41.4, 60.2, 81.4, 86.2. IR (neat): 3346 (m, br), 2930 (s), 2857 (s), 2228 (w), 1456 (m), 1285 (m), 1045 (m), 662 (m) cm^{-1}.

3. Preparation of Oxetanes.

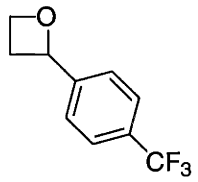


General. The procedure given below for the cyclization of (±)-**3.9** is representative for the synthesis of racemic oxetanes from γ-chloroalcohols. All yields are unoptimized. The addition of Et_3N to the eluent (~ 1%) helps preventing the partial decomposition of the oxetanes during flash chromatography.



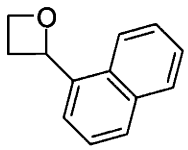
(±)-2-(4-Methoxyphenyl)oxetane. KH (233 mg, 5.80 mmol) was suspended in THF (50 mL). It was cooled to 0 °C, then a solution of (±)-**3.9** (973 mg, 4.85 mmol) in THF (6 mL) was slowly added from a syringe. The reaction mixture was then warmed up to r.t. and stirred for 16 h. It was poured into a mixture of 200 mL Et_2O / 100 mL H_2O, and the aqueous layer was extracted with more Et_2O (2 x 100 mL). The combined organic layer was washed with brine, dried (K_2CO_3), and concentrated in vacuo to afford a yellow liquid. This was purified by flash chromatography (1/10/89 Et_3N/Et_2O/pentane) to afford the desired compound as a colorless liquid (572 mg, 72% yield).

^1H NMR (500 MHz, C_6D_6): δ 2.28 (tdd, 1H, *J* = 7.6, 9.3, 10.8), 2.43 (dtd, 1H, *J* = 5.4, 8.0, 10.7), 3.30 (s, 3H), 4.32 (td, 1H, *J* = 5.7, 9.2), 4.47 (dt, 1H, *J* = 5.7, 8.0), 5.59(t, 1H, *J* = 7.5), 6.83 (d, 2H, *J* = 8.5), 7.31 (d, 2H, *J* = 8.9). ^{13}C NMR (126 MHz, C_6D_6): δ 31.3, 54.8, 67.4, 82.4, 114.1, 127.0, 136.7, 159.8. IR (KBr): 3059 (m), 2972 (m), 2881 (s), 1593 (m), 1508 (m), 1328 (m), 1048 (m), 977 (s), 927 (s), 800 (s), 781 (s) cm^{-1}. HRMS–EI (*m/z*): M^+ calcd for $C_{10}H_{12}O_2$, 164.0837; found, 164.0840.



(±)-2-(4-Trifluoromethylphenyl)oxetane. The general procedure was followed using (±)-**3.10** (1.60 g, 6.71 mmol). The crude product was purified by flash chromatography (1/10/89 Et_3N/Et_2O/pentane) to afford the desired product as a colorless liquid (727 mg, 54% yield).

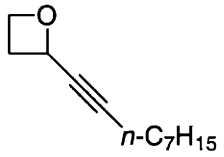
^1H NMR (500 MHz, C_6D_6): δ 1.97 (dddd, 1H, J = 7.0, 7.6, 9.1, 11.0), 2.33 (dtd, 1H, J = 5.8, 8.2, 11.0), 4.19 (td, 1H, J = 5.8, 9.2), 4.38 (dt, 1H, J = 5.8, 7.9), 5.38 (t, 1H, J = 7.6), 7.10 (d, 2H, J = 8.5), 7.37 (d, 2H, J = 8.2). ^{13}C NMR (126 MHz, C_6D_6): δ 30.9, 68.2, 81.8, 125.4 (q, $^1J_{C-F}$ = 272), 125.7, 125.9 (q, $^3J_{C-F}$ = 3.9), 130.0 (q, $^2J_{C-F}$ = 32), 148.8. IR (neat): 2965 (w), 2887 (w), 1619 (w), 1325 (s), 1165 (s), 1124 (s), 1067 (s), 983 (s), 838 (m) cm^{-1}. HRMS–EI (*m/z*): M^+ calcd for $C_{10}H_9F_3O$, 202.0606; found, 202.0609.



(±)-2-(1-Naphthyl)oxetane. The general procedure was followed using (±)-**3.11** (5.71 g, 25.9 mmol) The crude product was purified by flash chromatography (1/4/96 Et_3N/Et_2O/pentane) to afford a white solid (2.63 g, 55% yield).

^1H NMR (500 MHz, C_6D_6): δ 2.18 (tdd, 1H, J = 7.3, 8.9, 10.7), 2.62 (dtd, 1H, J = 5.8, 8.2, 10.7), 4.32 (td, 1H, J = 5.8, 9.2), 4.52 (ddd, 1H, J = 5.7, 7.5, 8.2), 6.22 (t, 1H, J = 7.6), 7.2–7.3 (m, 2H), 7.35–7.42 (m, 2H), 7.59 (d, 1H, J = 8.2), 7.66–7.70 (m, 1H), 8.06 (td, 1H, J = 1.2, 7.0). ^{13}C NMR (126 MHz, C_6D_6): δ 30.7, 68.5, 80.8, 122.2, 123.5, 126.1, 126.3, 126.4, 128.1, 129.5, 129.8, 134.5, 140.6. IR (KBr): 2999 (w), 2958 (m), 2882 (m), 1611 (m), 1514 (s), 1250

(s), 1034 (m), 957 (m), 832 (m) cm^{-1}. HRMS–FAB (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{12}O$, 185.0966; found, 185.0963.



(±)-2-(Non-1-ynyl)oxetane. The general procedure was followed using (±)-**3.12** (2.31 g, 10.7 mmol). The crude product was purified by flash chromatography (1/4/95 Et_3N/Et_2O/pentane) to afford a yellow liquid (200 mg, 10% yield).

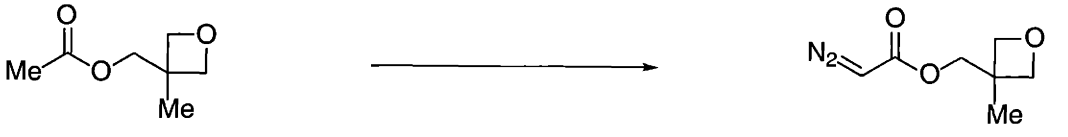
The ^1H NMR spectrum matched the literature data.[13b] ^{13}C NMR (126 MHz, C_6D_6): δ 14.7, 19.5, 23.3, 29.3, 29.5, 29.5, 30.5, 32.4, 68,4, 70.5, 81.9, 89.6. HRMS–EI (*m/z*): M^+ calcd for $C_{12}H_{20}O$, 180.1514; found, 180.1511.

(2-Hydroxyethyl)cyclohexan-1-ol To a solution of 9-BBN dimer (9.59 g, 39.3 mmol) in THF (200 mL) at 0 °C was added 1-vinylcyclohexanol (4.92 g, 38.9 mmol) over 3 min. The resulting white suspension was allowed to warm to r.t. slowly. After being stirred for 3 h, the reaction mixture was cooled to 0 °C and charged with 2.5 M NaOH solution (100 mL). After 30 min, 30 wt% H_2O_2 (30 mL, 0.26 mol) was cautiously added to the reaction mixture. It was then warmed to r.t., and the aqueous layer was extracted with EtOAc (3 x 150 mL). The combined organic extract was washed with brine, dried (K_2CO_3), and concentrated in vacuo to afford a colorless viscous liquid. This was further purified by flash chromatography (50/50 EtOAc/hexanes) to afford a colorless liquid (3.62 g, 64% yield).

The ^{1}H NMR spectrum of the product matched the literature data.[50]

1-Oxaspiro[3.5]nonane. The title compound was synthesized according to the procedure of Moulines.[36]

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.2–1.45 (m, 4H), 1.6–1.7 (m, 4H), 1.8–1.9 (m, 2H), 2.32 (t, 2H, J = 7.8), 4.50 (t, 2H, J = 7.8). ^{13}C NMR (126 MHz, $CDCl_3$): δ 22.7, 25.3, 32.6, 38.8, 65.0, 86.8.



(3'-Methyl-3'-oxetane)methyl diazoacetate. (3'-Methyl-3'-oxetane)methyl acetate (2.45 g, 17.0 mmol) was dissolved in THF (30 mL) and cooled to -78 °C. The reaction mixture was charged with a solution of LDA (2.00 g, 18.7 mmol) in THF (17 mL), stirred for 1.5 h, and charged with $CF_3CO_2CH_2CF_3$ (6.73 g, 34.4 mmol). It was stirred at -78 °C for 2 h, warmed up to r.t., and poured into a mixture of Et_2O and water. The aqueous layer was extracted with Et_2O (2 x 100 mL), and the combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford a brown liquid.

The crude product obtained in the above step was dissolved in MeCN (50 mL). The reaction mixture was charged with methanesulfonyl azide (3.08 g, 25.4 mmol) and Et_3N (4.8 mL, 34 mmol), and stirred under Ar for 24 h. It was then poured into a mixture of Et_2O and 2M KOH solution. The aqueous layer was extracted with Et_2O (3 x 50 mL), and the combined organic layer was washed with brine, dried (K_2CO_3) and

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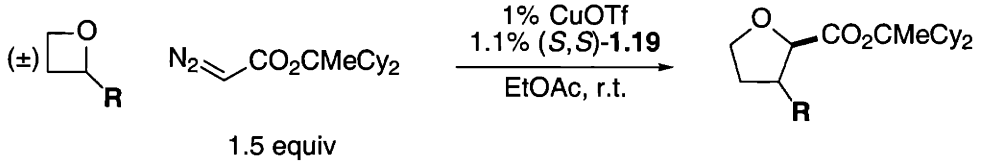
50 Klos, A. M.; Heintzelman, G. R.; Weinreb, S. M. *J. Org. Chem.* **1997**, *62*, 3758–3761.

concentrated in vacuo to afford a brown liquid. Part of the crude product was purified by flash chromatography (1/20/80 Et_3N/EtOAc/hexanes → 1/25/75)

^1H NMR (500 MHz, $CDCl_3$): δ 1.34 (s, 3H), 4.26 (s, 2H), 4.39 (d, 2H, J = 6.1), 4.52 (d, 2H, J = 5.8), 4.83 (br, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.2, 39.4, 46.5, 69.0, 79.6. HRMS–ESI (m/z): $[M + Na]^+$ calcd for $C_7H_{10}N_2O_3$, 193.0584; found, 193.0591.

VII. Ring Expansion of Oxetanes.

1. Carbene Insertion into Racemic 2-Substituted Oxetanes: Influence of the 2-Substituent on the Ring Expansion (Table 3.7).

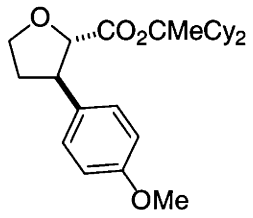


(3.9)

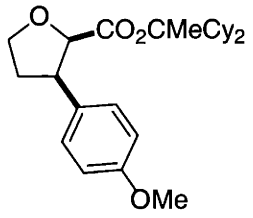
General procedure. A solution of (*S*,*S*)-**1.19** (4.3 mg, 8.2 μmol) in EtOAc (2 mL) was added to CuOTf•0.5C_6H_6 (1.9 mg, 7.5 μmol) and stirred for 30 min. The catalyst solution was then filtered through acrodisc to afford an orange solution. Half of this solution was transferred to a flask containing the oxetane (0.39 mmol), and more EtOAc was added until the total volume is 4 mL. The solution was stirred for 5 min in a water bath maintained at 20 °C, and then **3.4** (172 mg, 0.618 mmol), dissolved in 1 mL of EtOAc, was added slowly over 5 min to the reaction mixture. After 4 h, the reaction mixture was filtered through a plug of silica with Et_2O as the eluant to afford the crude product.

Entry 2, R = 4-(MeO)C_6H_4. The general procedure was followed using (±)-**3.13** (73.7 mg, 0.449 mmol). 1,3-Diisopropylbenzene (51.4 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans and cis tetrahydrofurans was 47% (C_6D_6). The NMR analysis also showed that the product was

a 55:45 trans:cis mixture. The crude product was purified by flash chromatography (10/90 Et_2O/pentane) and converted to the methyl ester (trans ee: 51%, major enantiomer: 2*R*,3*S*; cis ee: 45%, major enantiomer: 2*R*,3*R*).



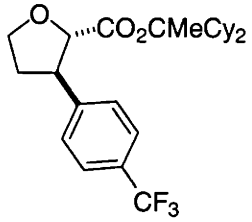
1,1-Dicyclohexylethyl (2*S*,3*R*)-3-(4-methoxyphenyl)tetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, C_6D_6): δ 0.95–1.20 (m, 10H), 1.45 (s, 3H), 1.55–1.61 (m, 2H), 1.63–1.94 (m, 11H), 2.04 (dddd, 1H, *J* = 4.0, 7.0, 7.6, 11.9), 3.31 (s, 3H), 3.54 (dt, 1H, *J* = 6.7, 8.1), 3.96 (dt, 1H, *J* = 3.8, 8.0), 4.06 (dt, 1H, *J* = 6.7, 8.5), 4.50 (d, 1H, *J* = 6.4), 6.76 (d, 2H, *J* = 8.8), 7.08 (d, 2H, *J* = 8.5). ^{13}C NMR (126 MHz, C_6D_6): δ 19.8, 27.2, 27.2, 27.6, 27.6, 28.2, 28.3, 28.7, 28.7, 36.2, 45.5, 50.0, 55.1, 69.8, 85.4, 91.0, 114.7, 129.0, 134.6, 159.4, 172.3. IR (neat): 2929 (s), 2852 (s), 1741 (s), 1613 (m), 1514 (s), 1448 (m), 1249 (s), 1180 (s), 1098 (s), 1036 (m), 827 (m) cm^{-1}. $[\alpha]^{20}_D$ +43° (*c* 0.86, EtOH; 70% ee). HRMS–FAB (*m/z*): $[M + K]^+$ calcd for $C_{26}H_{38}O_4$, 453.2407; found, 453.2417.



1,1-Dicyclohexylethyl (2*R*,3*R*)-3-(4-methoxyphenyl)tetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, C_6D_6): δ 0.73 (dq, 1H, *J* = 3.5, 12.5), 0.9–1.2 (m, 9H), 1.29 (s, 3H), 1.4–1.5 (m, 2H), 1.5–1.7 (m, 9H), 1.75–1.85 (m, 2H), 2.31 (qd, 1H, *J* = 8.7, 11.8), 3.28 (q, 1H, *J* = 9.2), 3.34 (s, 3H), 3.77 (q, 1H, *J* = 7.8), 4.29 (dt, 1H, *J* = 3.7, 8.4), 4.59 (d, 1H, *J* = 7.6), 6.78 (d, 2H, *J* = 8.5), 7.14 (d, 2H, *J* = 8.6). ^{13}C NMR (126 MHz, C_6D_6): δ 19.5, 27.2, 27.2, 27.6, 27.6, 27.7, 27.8, 28.2, 28.2, 28.6, 31.8, 45.3, 45.5, 47.9, 55.1, 68.9, 83.1,

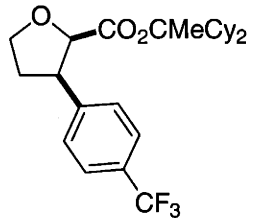
91.0, 114.3, 130.2, 131.4, 159.5, 170.8. IR (thin film): 2929 (s), 2851 (s), 1733 (s), 1613 (w), 1514 (s), 1448 (m), 1248 (s), 1181 (m), 1096 (m), 1073 (m), 1036 (m), 840 (w), 806 (w) cm^{-1}. $[\alpha]^{20}_D$ -33° (*c* 0.91, EtOH; 82% ee). HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{26}H_{38}O_4$, 437.2662; found, 437.2649.

Entry 3, R = 4-(F_3C)C_6H_4. The general procedure was followed using (±)-**3.14** (77.9 mg, 0.385 mmol). 1,3-Diisopropylbenzene (37.4 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans and cis tetrahydrofurans was 94% (C_6D_6). The NMR analysis also showed that the product was a 53:47 trans:cis mixture. The crude product was purified first by flash chromatography (C_6H_6), then by preparative achiral HPLC (15/85 EtOAc/hexanes) to afford both tetrahydrofurans in diastereomerically pure form (trans ee: 89%, major enantiomer: 2*R*,3*S*; cis ee: 90%, major enantiomer: 2*R*,3*R*).



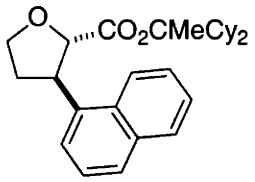
1,1-Dicyclohexylethyl (2*S*,3*R*)-3-(4-trifluoromethylphenyl)tetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, C_6D_6): δ 0.9–1.2 (m, 10H), 1.41 (s, 3H), 1.52 (qd, 1H, *J* = 8.1, 12.2), 1.55–1.75 (m, 11H), 1.94 (dtd, 1H, *J* = 4.4, 7.5, 12.0), 3.40 (dt, 1H, *J* = 6.4, 7.9), 3.86 (dt, 1H, *J* = 4.0, 8.1), 3.99 (dt, 1H, *J* = 6.9, 8.3), 4.35 (d, 1H, *J* = 6.1), 6.93 (d, 2H, *J* = 7.9), 7.31 (d, 2H, *J* = 7.9). ^{13}C NMR (126 MHz, $CDCl_3$): δ 19.3, 26.6, 26.7, 27.0, 27.0, 27.0, 27.6, 27.6, 28.1, 28.2, 35.8, 44.9, 44.9, 49.9, 69.5, 83.9, 92.3, 124.3 (q, $^1J_{C-F}$ = 272), 125.8 (q, $^3J_{C-F}$ = 3.8), 127.9, 129.4 (q, $^2J_{C-F}$ = 32.3), 146.3, 171.7. IR (neat): 2933 (s), 2854 (s), 1745 (s), 1620 (m), 1449 (s), 1327 (s), 1165 (s), 1124 (s), 1069 (s), 1017 (m), 834 (m) cm^{-1}. $[\alpha]^{20}_D$

+52° (*c* 1.05, EtOH; 99% ee). HRMS–FAB (*m/z*): M^+ calcd for $C_{26}H_{35}F_3O_3$, 452.2538; found, 452.2546.

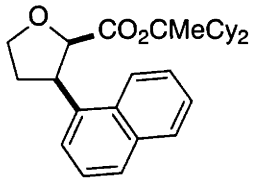


1,1-Dicyclohexylethyl (2*R*,3*R*)-3-(4-trifluoromethylphenyl)tetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, C_6D_6): δ 0.63 (dq, 1H, *J* = 3.3, 12.3), 0.8–0.9 (m, 2H), 0.95–1.1 (m, 7H), 1.18 (s, 3H), 1.3–1.4 (m, 2H), 1.5–1.8 (m, 11H), 2.07 (qd, 1H, *J* = 8.4, 12.0), 3.10 (q, 1H, *J* = 7.9), 3.68 (q, 1H, *J* = 7.9), 4.17 (dt, 1H, *J* = 4.0, 8.4), 4.45 (d, 1H, *J* = 7.6), 7.05 (d, 2H, *J* = 7.9), 7.36 (d, 2H, *J* = 8.2). ^{13}C NMR (126 MHz, C_6D_6): δ 19.0, 26.8, 26.8, 27.1, 27.1, 27.2, 27.2, 27.4, 27.8, 27.9, 28.2, 31.3, 44.9, 45.0, 47.8, 68.3, 82.3, 91.3, 125.0 (q, $^1J_{C-F}$ = 272), 125.4 (q, $^3J_{C-F}$ = 3.8), 129.2, 129.3 (q, $^2J_{C-F}$ = 32.2), 143.6, 169.7. IR (neat): 2932 (s), 2854 (s), 1733 (s), 1619 (m), 1449 (m), 1327 (s), 1165 (s), 1125 (s), 1070 (s), 849 (m) cm^{-1}. $[\alpha]^{20}_D$ -32° (*c* 0.62, EtOH; 95% ee). HRMS–FAB (*m/z*): M^+ calcd for $C_{26}H_{35}F_3O_3$, 452.2538; found, 452.2528.

Entry 4, R = 1-Naphthyl. The general procedure was followed using (±)-**3.15** (60.4 mg, 0.328 mmol). Anisole (34.7 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans and cis tetrahydrofurans was 87% (C_6D_6). The NMR analysis also showed that the product was a 49:51 trans:cis mixture. The crude product was purified first by flash chromatography (5/95 Et_2O/pentane → 10/90), then by preparative achiral HPLC (25/75 $CHCl_3$/hexanes) to afford both tetrahydrofurans in diastereomerically pure form (trans ee: 80%, major enantiomer: 2*R*,3*S*; cis ee: 83%, major enantiomer: 2*R*,3*R*).



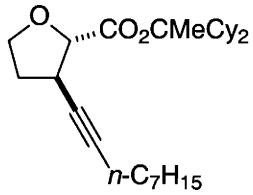
1,1-Dicyclohexylethyl (2*S*,3*R*)-3-(1-naphthyl)tetrahydrofuran-2-carboxylate ^{1}H NMR (500 MHz, C_6D_6): δ 0.8–1.2 (m, 10H), 1.44 (s, 3H), 1.5–1.9 (m, 13H), 2.27 (tdd, 1H, *J* = 6.6, 7.9, 13.1), 4.02 (dt, 1H, *J* = 5.8, 7.9), 4.24 (dt, 1H, *J* = 6.6, 8.0), 4.41 (td, 1H, *J* = 5.0, 8.2), 4.79 (d, 1H, *J* = 4.3), 7.23 (t, 1H, *J* = 7.6), 7.28 (ddd, 1H, *J* = 1.2, 6.9, 8.1), 7.32 (d, 1H, *J* = 6.4), 7.37 (ddd, 1H, *J* = 1.4, 6.9, 8.5), 7.55 (d, 1H, *J* = 8.2), 7.66 (d, 1H, *J* = 7.9), 8.21 (d, 1H, *J* = 8.5). ^{13}C NMR (126 MHz, C_6D_6): δ 19.4, 26.8, 26.8, 27.1, 27.2, 27.2, 27.8, 27.9, 28.3, 28.4, 34.0, 45.1, 45.1, 45.3, 69.3, 84.0, 90.9, 123.7, 123.8, 125.8, 125.8, 126.3, 127.7, 129.4, 132.3, 134.6, 138.7, 172.1. IR (neat): 3048 (m), 2926 (s), 2852 (s), 1738 (s), 1598 (m), 1512 (m), 1383 (s), 1279 (s), 1193 (s), 1106 (s), 1086 (s), 933 (m), 778 (s) cm^{-1}. $[\alpha]^{20}_D$ +32.8° (*c* 1.02, EtOH; 91% ee). HRMS–FAB (*m/z*): M^+ calcd for $C_{29}H_{38}O_3$, 434.2828; found, 434.2828.



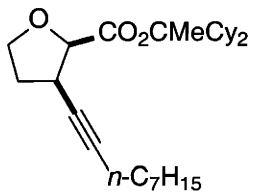
1,1-Dicyclohexylethyl (2*R*,3*R*)-3-(1-naphthyl)tetrahydrofuran-2-carboxylate ^{1}H NMR (500 MHz, C_6D_6): δ 0.11 (dq, 1H, *J* = 3.5, 12.5), 0.47 (dq, 1H, *J* = 3.2, 12.4), 0.7–1.1 (m, 10H), 1.02 (s, 3H), 1.1–1.2 (m, 1H), 1.35–1.6 (m, 8H), 1.69 (tt, 1H, *J* = 2.7, 11.9), 1.75–1.80 (m, 1H), 2.73 (tt, 1H, *J* = 9.0, 11.0), 3.86 (td, 1H, *J* = 7.6, 8.4), 4.00 (td, 1H, *J* = 7.3, 10.7), 4.41 (dt, 1H, *J* = 2.6, 8.2), 4.96 (d, 1H , *J* = 7.6), 7.22–7.34 (m, 3H), 7.52 (d, 1H, *J* = 7.3), 7.54 (d, 1H, *J* = 8.2), 7.63 (d, 1H, *J* = 7.9), 7.84 (d, 1H, *J* = 8.5). ^{13}C NMR (126 MHz, C_6D_6): δ 19.5, 26.9, 27.1, 27.4, 27.4, 27.6, 27.7, 27.7, 28.1, 28.5, 30.2, 44.8, 45.1, 45.5, 68.6, 81.4, 90.5, 124.3, 125.0, 126.0, 126.1, 126.6, 128.3, 129.4, 133.7, 134.5, 134.7, 171.1. IR (neat): 3045 (w),

2928 (s), 2852 (s), 1732 (s), 1447 (m), 1212 (m), 1192 (m), 1077 (m), 778 (m) cm^{-1}. $[\alpha]^{20}_D$ -140° (*c* 0.60, EtOH; 95% ee). HRMS–FAB (*m/z*): $[M + K]^+$ calcd for $C_{29}H_{38}O_3$, 473.2458; found, 473.2450.

Entry 5, R = *n*-$C_7H_{15}C{\equiv}C$. The general procedure was followed using (±)-**3.16** (68.0 mg, 0.377 mmol). 1,3-Diisopropylbenzene (38.9 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans and cis tetrahydrofurans was 66% (C_6D_6). The NMR analysis also showed that the product was a 54:46 trans:cis mixture. The crude product was purified first by flash chromatography (4/96 Et_2O/pentane), and then converted to the methyl esters (trans ee: 85%, major enantiomer: 2*R*,3*S*; cis ee: 87%, major enantiomer: 2*R*,3*R*).

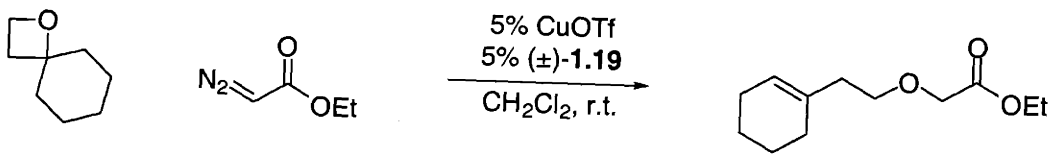


1,1-Dicyclohexylethyl (2*S*,3*R*)-3-(non-1-ynyl)tetrahydrofuran-2-carboxylate. ^1H NMR (500 MHz, C_6D_6): δ 0.89 (t, 3H, *J* = 7.0), 1.0–1.4 (m, 18H), 1.41 (m, 2H), 1.47 (s, 3H), 1.60 (m, 2H), 1.65–2.00 (m, 12H), 2.07 (dt, 2H, *J* = 2.3, 7.1), 3.30 (ttd, 1H, *J* = 2.0, 5.6, 9.7), 3.84 (m, 2H), 4.58 (d, 1H, *J* = 6.1). ^{13}C NMR (126 MHz, C_6D_6): δ 14.7, 19.5, 19.8, 23.4, 27.3, 27.3, 27.6, 27.6, 27.7, 28.3, 28.3, 28.8, 28.8, 29.5, 29.6, 29.6, 32.5, 34.7, 36.1, 45.5, 45.5, 69.3, 80.6, 83.0, 84.5, 91.4, 171.4. IR (neat): 2927 (s), 2853 (s), 1745 (s), 1449 (s), 1380 (m), 1283 (m), 1251 (m), 1191 (s), 1098 (s) cm^{-1}. $[\alpha]^{20}_D$ +72° (*c* 1.11, EtOH; 97% ee). HRMS–ESI (*m/z*): M^+ calcd for $C_{28}H_{46}O_3$, 453.3339; found, 453.3328.



1,1-Dicyclohexylethyl (2*R*,3*R*)-3-(non-1-ynyl)tetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.89 (t, 3H, *J* = 7.0), 1.1–1.4 (m, 18H), 1.49 (qnt, 2H, *J* = 7.3), 1.60 (s, 3H), 1.61–2.20 (m, 14H), 2.14 (dt, 2H, *J* = 2.1, 7.2), 2.95 (tq, 1H, *J* = 2.2, 7.9), 3.58 (q, 1H, *J* = 7.5), 4.16 (dt, 1H, *J* = 4.9, 8.2), 4.45 (d, 1H, *J* = 7.3). ^{13}C NMR (126 MHz, C_6D_6): δ 14.3, 19.4, 19.6, 23.0, 27.0, 27.0, 27.3, 27.4, 27.4, 27.9, 28.1, 28.3, 28.4, 29.3, 29.3, 32.1, 33.2, 34.6, 45.4, 45.5, 68.6, 77.9, 81.5, 84.1, 90.8, 170.2 IR (neat): 2927 (s), 2853 (s), 1732 (s), 1449 (s), 1379 (m), 1300 (m), 1210 (m), 1097 (s) cm^{-1}. $[\alpha]^{20}_D$ +5.8° ± 0.3° (*c* 0.95, EtOH; 94% ee). HRMS–FAB (*m/z*): $[M + K]^+$ calcd for $C_{28}H_{46}O_3$, 469.3084; found, 469.3068.

2. Carbene Insertion into 2,2-Dialkyl-Substituted Oxetanes.

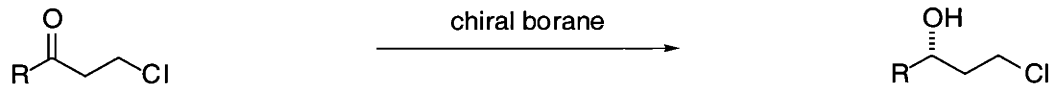


$CuOTf•0.5C_6H_6$ (5.4 mg, 21 μmol) and (±)-**1.19** (11.8 mg, 22.4 μmol) was dissolved in CH_2Cl_2 (6 mL) and stirred for 15 min. Half of this solution was transferred to a flask containing 1-oxaspiro[3.5]nonane (53.2 mg, 0.422 mmol), and ethyl diazoacetate (53.8 mg, 0.472 mmol), dissolved in 1 mL of CH_2Cl_2, was added slowly over 12 h to the reaction mixture. The reaction mixture was filtered through a plug of silica with Et_2O as the eluant to afford the crude product. This was further purified by flash chromatography (5/95 Et_2O/pentane → 10/90) to afford a colorless liquid (53.3 mg, 60% yield).

Ethyl 2-(cyclohex-1-enyl)ethoxyacetate. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.29 (t, 3H, *J* = 7.2), 1.5–1.6 (m, 2H), 1.6–1.65 (m, 2H), 1.9–2.0 (m, 4H), 2.28 (t, 2H, *J* = 6.9), 3.61 (t, 2H, *J* = 7.0), 4.08 (s, 2H), 4.22 (q, 2H, *J* = 7.1), 5.49 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.4, 22.5, 23.1, 25.4, 28.7, 38.1, 61.0, 68.5, 70.7, 123.0, 134.5, 170.8.

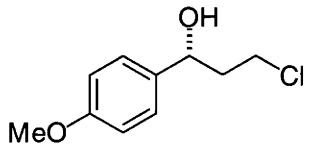
VIII. Synthesis of Enantiomerically Enriched Oxetanes.

1. Preparation of Enantiomerically Enriched γ-Chloroalcohols.



General. The enantiomerically enriched γ-chloroalcohols were obtained by the asymmetric reduction of the corresponding β-chloroketones with a stoichiometric amount of chiral organoboranes, DIP–Cl for aryl ketones **3.5–3.7** and neat Alpine-Borane for propargylic ketone **3.8**. Excellent yields were reported by Brown for the application of both organoboranes in the asymmetric reduction of ketones. However, we can only obtain mediocre yields from our β-chloroketones, and the products are invariably contaminated with some pinene-derived alcohols. No significant improvement in yield was observed when we changed the boron-scavenging reagent from ethanolamine or (diethanol)amine to MoO_5•py•HMPA.

The procedure given below for the asymmetric reduction of **3.5** is representative for those using DIP–Cl as the chiral reducing reagent. All yields are unoptimized.



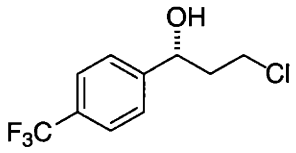
(*R*)-3-Chloro-1-(4-methoxyphenyl)propan-1-ol. To a solution of (+)-DIP–Cl (4.87 g, 15.2 mmol) in THF (10 mL) at 0 °C was added a solution of **3.5** (2.50 g, 12.6 mmol) in THF (15 mL). After 14 h, TLC showed only a trace amount of starting ketone. The reaction mixture was warmed up to r.t. and solvent was removed in vacuo. The crude product was then redissolved in Et_2O and added to $HN(CH_2CH_2OH)_2$ (3.01 g, 28.7 mmol). A large amount of white solid slowly precipitated, which was later removed by filtration. The filtrate was concentrated in vacuo to a yellow oil, which was then

purified by flash chromatography (25/75 Et_2O/pentane) to afford the purified product as a white solid (2.90 g). GC analysis of the acetate derivative showed that the product is of 96% ee.

Recrystallization (Et_2O/pentane, -10 °C) afforded a white cotton-like solid (618 mg). GC analysis of the acetate derivative showed that the product is enantiomerically pure (>99% ee). ^1H NMR showed that the solid was still contaminated with impurities, but this was carried on to the next step without further purification.

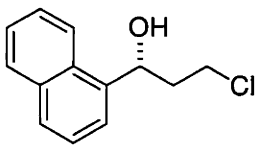
The analytical sample was obtained by repeating the recrystallization.

mp 60 °C. $[\alpha]^{20}_D$ +16° (*c* 1.03, $CHCl_3$).



(*R*)-3-Chloro-1-(4-trifluoromethylphenyl)propan-1-ol. The general procedure was followed using **3.6** (2.08 g, 8.81 mmol). The crude product was purified by flash chromatography (4/96 Et_2O/benzene) to afford the desired product as a colorless liquid (1.46 g, 67% yield; 98% ee).

$[\alpha]^{20}_D$ +15° (*c* 0.56, $CHCl_3$; 98% ee).

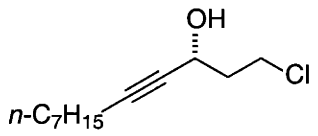


(*R*)-3-Chloro-1-(1-naphthyl)propan-1-ol. The general procedure was followed using **3.7** (3.21 g, 14.7 mmol). The crude product was purified by flash chromatography (15/85 Et_2O/pentane) to afford a yellow liquid (1.26 g). ^1H NMR showed that the

product was still contaminated with impurities, but this was carried on to the next step without further purification.

The analytical sample was obtained by purifying the alcohol as its 3,5-dinitrobenzoate and then hydrolyzing the ester back to the alcohol. The procedure followed that described for (*R*)-**3.12** (*vide infra*). HPLC analysis showed that the product is of 97% ee.

$[\alpha]^{20}_{D}$ +40° (*c* 0.64, $CHCl_3$; 97% ee).



(*R*)-1-Chlorododec-4-yn-3-ol. To neat **3.8** (4.52 g, 21.1 mmol) at -20 °C was slowly added neat (*R*)-Alpine-Borane (11.5 mL, 42.2 mmol). The reaction mixture was stirred at -15 to -20 °C for 4 days and 0 °C for 1 day. Afterwards, the reaction mixture was diluted with Et_2O and quenched by the addition of acetaldehyde (2 mL). Ethanolamine (~ 1.4 g) was then added to the stirring mixture. The white precipitate was removed by filtration, and concentration of the filtrate in vacuo afforded the crude product, which was then purified twice by flash chromatography (10/90 Et_2O/pentane) to obtain a yellow liquid (2.10 g, 89% ee).

The product was dissolved in 50 mL CH_2Cl_2, and charged with a suspension of 3,5-$(O_2N)C_6H_3COCl$ (3.34 g, 14.5 mmol) and DMAP (129 mg, 1.05 mmol) in CH_2Cl_2 (20 mL). The reaction mixture was then cooled to 0 °C and Et_3N (2.0 mL, 14.3 mmol) was slowly added, which rapidly turned the yellow heterogeneous suspension into a brown solution. After 2 h, TLC showed no starting alcohol. The reaction mixture was diluted with CH_2Cl_2 (300 mL), washed with 1M HCl, saturated $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated in vacuo to afford a yellow oil. Purification through flash

chromatography (5/95 Et_2O/pentane → 10/90) afforded the 3,5-dinitrobenzoate as a pale yellow solid (1.49 g, 37% overall yield from ketone). Recrystallization of this yellow solid from Et_2O/pentane afforded white fine needles (1.00 g, >99% ee).

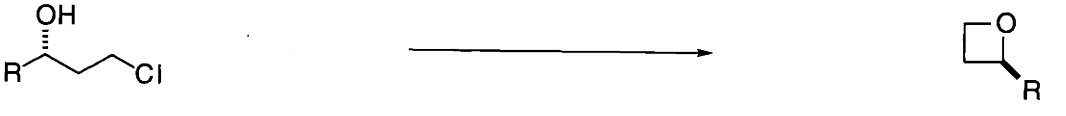
The purified 3,5-dinitrobenzoate (989 mg, 2.41 mmol) was dissolved in a mixture of MeOH (15 mL) and CH_2Cl_2 (2 mL). $NaHCO_3$ (155.5 mg, 1.85 mmol) was added and the reaction mixture was stirred at r.t.. After 1 h, TLC showed no starting ester. The reaction mixture was diluted with 200 mL 1 M HCl, washed with 1M HCl, dried ($MgSO_4$), and concentrated in vacuo to afford a white solid. This was purified by flash chromatography (90/10 benzene/pentane) to afford the desired product as a colorless liquid (471 mg, 90% yield; >99% ee).

$[\alpha]^{20}_D$ -3.1° (*c* 1.09, $CHCl_3$).

Assignment of absolute stereochemistry. The 3-chloro-1-arylpropan-1-ols obtained from (+)-DIP–Cl were assigned to be (*R*) based on the model proposed by Brown,[28] while 1-chlorododec-4-yn-3-ol from (*R*)-Alpine Borane was also assigned to be (*R*) based on the model proposed by Midland.[51]

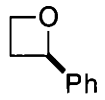
The assignments were subsequently verified with the ring expansion, as the oxetanes derived from these alcohols all give the (2*S*,3*R*) tetrahydrofuran preferentially with (*R*,*R*)-**1.19** (*vide infra*).

2. Preparation of Enantiomerically Enriched 2-Substituted Oxetanes



51 Midland, M. M.; Tramontano, A.; Kazubski, A.; Graham, R. S.; Tsai, D. J. S.; Cardin, D. B. *Tetrahedron* **1984**, *40*, 1371–1380.

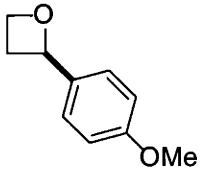
General. The same procedure for the synthesis of racemic oxetanes was used (*vide supra*), with the racemic γ-chloroalcohols replaced by the enantiomerically enriched ones. All yields are unoptimized.



(*R*)-2-Phenyloxetane. The general procedure was followed using (*R*)-3-chloro-1-phenylpropan-1-ol (943 mg, 5.53 mmol). The crude product was purified by flash chromatography (1/4/96 Et_3N/Et_2O/pentane) to afford the desired product as a yellow liquid (564 mg, 76% yield; >99% ee).

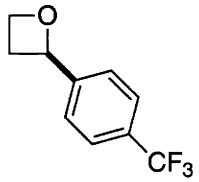
$[\alpha]^{20}_D$ + 180° (*c* 1.52, EtOH).

(*S*)-2-Phenyloxetane was prepared similarly from (*S*)-3-chloro-1-phenylpropan-1-ol (2.09 g, 12.3 mmol) with a 78% isolated yield. GC analysis showed that the product is enantiomerically pure (>99% ee).



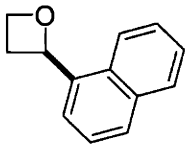
(*R*)-2-(4-Methoxyphenyl)oxetane. The general procedure was followed using (*R*)-**3.9**. The crude product was purified by flash chromatography (1/10/89 Et_3N/Et_2O/pentane) twice to afford the desired product as a pale yellow liquid, which on standing solidified to a white solid (265 mg, 98% ee).

mp 49 °C. $[\alpha]^{20}_D$ +141° (*c* 1.04, EtOH; 98% ee).



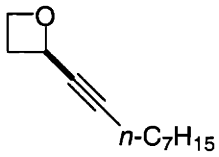
(*R*)-2-(4-Trifluoromethylphenyl)oxetane. The general procedure was followed using (*R*)-**3.10**. The crude product was purified by flash chromatography (1/9/90 Et_3N/Et_2O/pentane) to afford the desired product as a colorless liquid (636 mg, 54% yield; 97% ee).

$[\alpha]^{20}_D$ +113° (*c* 2.64, EtOH; 97% ee).



(*R*)-2-(1-Naphthyl)oxetane. The general procedure was followed using (*R*)-**3.11**. The crude product was purified by flash chromatography (1/4/95 Et_3N/Et_2O/pentane) to afford a white solid (695 mg, 70% yield). HPLC analysis showed that the product is of 97% ee. This was recrystallized from Et_2O/pentane at -35 °C to afford a crystalline white solid (439 mg, >99% ee).

mp 74 °C. $[\alpha]^{20}_D$ +250° (*c* 1.05, EtOH).



(*R*)-2-(Non-1-ynyl)oxetane. The general procedure was followed using (*R*)-**3.12**. The crude product was purified by flash chromatography (1/4/95 Et_3N/Et_2O/pentane) to afford a yellow liquid (148.8 mg, 38% yield).

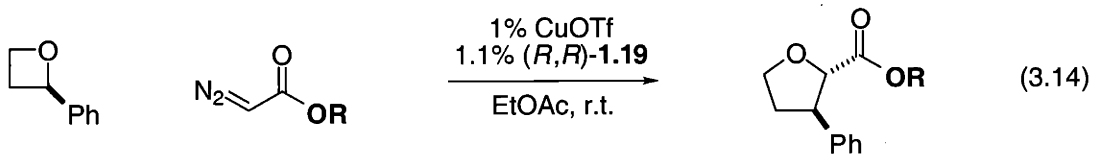
$[\alpha]^{20}_D$ +92° (*c* 1.7, $CHCl_3$). lit.[13b] $[\alpha]^{20}_D$ +33.3° (*c* 1.51, $CHCl_3$).

Assignment of absolute stereochemistry. The assignment was made based on the absolute configuration of the γ-chloroalcohols. In addition, the sign of the optical rotation for the synthesized 2-(non-1-ynyl)oxetane is positive, and the absolute stereochemistry of the oxetane is therefore (*R*).[13b]

IX. Carbene Insertion into Enantiopure 2-Phenyloxetane: Stereoselectivity as a Function of Diazo Ester.

General. Negative enantiomeric excess indicates that the major enantiomer has an opposite absolute stereochemistry at C2 of the tetrahydrofuran to the expected one based on the absolute configuration of the catalyst. Such a "reversal" of asymmetric induction only occurs for the minor diastereomer.

1. Stereoselective Formation of trans Tetrahydrofurans (Table 3.8).



(3.14)

(*R*)-**3.1**
99% ee

1.5 equiv

(2*S*,3*R*)

All diastereoselectivities and enantioselectivities that are reported in Table 3.8 are the average of two runs, one with each enantiomer of bisazaferrocene **1.19**.

General procedure. A solution of (*R,R*)-**1.19** (4.4 mg, 8.4 μmol) in EtOAc (2 mL) was added to CuOTf•0.5C_6H_6 (1.8 mg, 7.2 μmol) and stirred for 30 minutes. The catalyst solution was then filtered through acrodisc to afford an orange solution. Half of this

solution was transferred to a flask containing (*R*)-**3.1** (48.7 mg, 0.36 mmol), and more EtOAc was added until the total volume is 2.5 mL. The solution was stirred for 5 minutes in a water bath maintained at 20 °C, and then diazo ester (0.48 mmol), dissolved in 1 mL of EtOAc, was added slowly over 5 minutes to the reaction mixture. After 30 minutes, the reaction mixture was filtered through a plug of silica with Et_2O as the eluant to afford the crude product.

Entry 1, OR = OEt. The general procedure was followed. Run 1 was carried out with (*R,R*)-**1.19** (2.2 mg, 4.2 μmol), (*R*)-**3.1** (48.7 mg, 0.363 mmol), and ethyl diazoacetate (55.0 mg, 0.482 mmol). GC analysis showed that the product was an 81:19 trans:cis mixture, and that the trans product was formed in 91% ee (major enantiomer: 2*S*,3*R*). 1,3-Diisopropylbenzene (54.1 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans tetrahydrofuran was 53% (C_6D_6).

Run 2 was carried out with (*S,S*)-**1.19** (2.6 mg, 4.9 μmol), (*S*)-**3.1** (60.5 mg, 0.451 mmol), and ethyl diazoacetate (67.8 mg, 0.594 mmol). GC analysis of the crude reaction product revealed an 82:18 trans:cis mixture, and that the trans product was formed in 92% ee (major enantiomer: 2*R*,3*S*). The crude product was purified by flash chromatography (1/7 *i*-Pr_2O/pentane, 20/80 Et_2O/pentane) to afford a 44% yield of trans tetrahydrofuran as a colorless liquid.

Entry 2, OR = O-*t*-Bu. The general procedure was followed. Run 1 was carried out with (*R,R*)-**1.19** (2.2 mg, 4.2 μmol), (*R*)-**3.1** (48.5 mg, 0.361 mmol), and *t*-butyl diazoacetate (66.8 mg, 0.470 mmol). GC analysis showed that the product was a 90:10 trans:cis mixture, and that the trans product was formed in 97% ee (major enantiomer: 2*S*,3*R*) and the cis product was formed in -47% ee (major enantiomer: 2*R*,3*R*). 1,3-Diisopropylbenzene (68.5 mg) was added to the crude product as an internal NMR

standard, and the NMR yield thus determined for the trans tetrahydrofuran was 57% (C_6D_6).

Run 2 was carried out with (*S,S*)-**1.19** (2.6 mg, 4.9 μmol), (*S*)-**3.1** (61.7 mg, 0.460 mmol) and *t*-butyl diazoacetate (86.2 mg, 0.606 mmol). GC analysis of the crude reaction product revealed a 90:10 trans:cis mixture, and that the trans product was formed in 97% ee (major enantiomer: 2*R*,3*S*) and the cis product was formed in -44% ee (major enantiomer: 2*S*,3*S*). The crude product was purified by flash chromatography (5/95 Et_2O/pentane) to afford a 54% yield of trans tetrahydrofuran as a colorless liquid.

Entry 3, OR = O-(*d*)-Men. The general procedure was followed. Run 1 was carried out with (*R,R*)-**1.19** (2.1 mg, 3.9 μmol), (*R*)-**3.1** (47.3 mg, 0.353 mmol), and (*d*)-menthyl diazoacetate (104 mg, 0.462 mmol). GC analysis showed that the product was a 90:10 trans:cis mixture, and that the trans product was formed in 95% ee (major diastereomer: 2*S*,3*R*). 1,3-Diisopropylbenzene (50.4 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans tetrahydrofuran was 82% (C_6D_6).

Run 2 was carried out with (*S,S*)-**1.19** (3.2 mg, 6.1 μmol), (*S*)-**3.1** (69.6 mg, 0.519 mmol), and (*d*)-menthyl diazoacetate (152 mg, 0.678 mmol). GC analysis of the crude reaction product revealed a 90:10 trans:cis mixture, and that the trans product was formed in 97% ee (major diastereomer: 2*R*,3*S*). The crude product was purified by flash chromatography (5/95 Et_2O/pentane) to afford a 73% yield of trans tetrahydrofuran as a colorless liquid. *This reaction actually corresponds to the enantiomeric version of entry 4, run 1.*

Entry 4, OR = O-(*l*)-Men. The general procedure was followed. Run 1 was carried out with (*R,R*)-**1.19** (2.1 mg, 3.9 μmol), (*R*)-**3.1** (46.4 mg, 0.346 mmol), and (*l*)-menthyl diazoacetate (102 mg, 0.455 mmol). GC analysis showed that the product was a 91:9

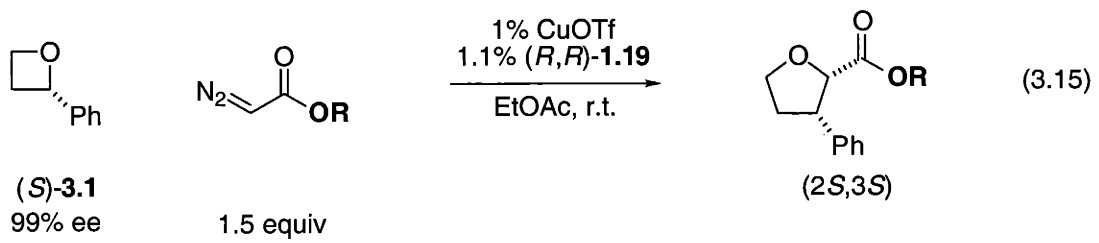
trans:cis mixture, and that the trans product was formed in 97% ee (major diastereomer: 2*S*,3*R*). 1,3-Diisopropylbenzene (58.5 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans tetrahydrofuran was 85% (C_6D_6).

Run 2 was carried out with (*S*,*S*)-**1.19** (3.2 mg, 6.1 μmol), (*S*)-**3.1** (70.3 mg, 0.524 mmol), and (*l*)-menthyl diazoacetate (153 mg, 0.683 mmol). GC analysis of the crude reaction product revealed a 90:10 trans:cis mixture, and that the trans product was formed in 95% ee (major diastereomer: 2*R*,3*S*). The crude product was purified by flash chromatography (5/95 Et_2O/pentane) to afford a 68% yield of trans tetrahydrofuran as a colorless liquid. *This reaction actually corresponds to the enantiomeric version of entry 3, run 1.*

Entry 5, OR = OCMeCy$_2$. The general procedure was followed. Run 1 was carried out with (*R*,*R*)-**1.19** (3.3 mg, 6.2 μmol), (*R*)-**3.1** (77.1 mg, 0.575 mmol), and **3.4** (207 mg, 0.744 mmol). 1,3-Diisopropylbenzene (111.2 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans tetrahydrofuran was 77% (C_6D_6). The NMR analysis also showed that the product was a 95:5 trans:cis mixture. The crude product was purified by flash chromatography (5/95 Et_2O/pentane), which afforded a mixture of trans and cis tetrahydrofurans as a colorless liquid (145.0 mg, 66% yield; trans ee: 98%, major enantiomer: 2*S*,3*R*; cis ee: -20%, major enantiomer: 2*R*,3*R*).

Run 2 was carried out with (*S*,*S*)-**1.19** (2.6 mg, 4.9 μmol), (*S*)-**3.1** (61.3 mg, 0.457 mmol) and **3.4** (166 mg, 0.597 mmol). NMR analysis showed that the product was a 95:5 trans:cis mixture. Flash chromatography afforded an 83% yield of trans and cis tetrahydrofurans (trans ee: 98%, major enantiomer: 2*R*,3*S*; cis ee: -22%, major enantiomer: 2*S*,3*S*).

2. Stereoselective Formation of cis Tetrahydrofurans (Table 3.9).



(3.15)

(*S*)-**3.1**
99% ee

1.5 equiv

(2*S*,3*S*)

Entry 1, OR = OEt. The general procedure was followed using (*R*,*R*)-**1.19** (2.3 mg, 4.4 μmol), (*S*)-**3.1** (53.5 mg, 0.399 mmol) and ethyl diazoacetate (67.7 mg, 0.593 mmol). GC analysis showed that the product was a 28:72 trans:cis mixture. 1,3-Diisopropylbenzene (51.2 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis tetrahydrofuran was 52% (C_6D_6). The crude product was purified by flash chromatography (10/90 Et_2O/pentane → 12.5/87.5), then by preparative achiral HPLC (12.5/87.5 EtOAc/hexanes) to afford the cis tetrahydrofuran as a colorless liquid (94% ee, major enantiomer: 2*S*,3*S*).

Entry 2, OR = O-*t*-Bu. The general procedure was followed using (*R*,*R*)-**1.19** (2.3 mg, 4.4 μmol), (*S*)-**3.1** (53.5 mg, 0.399 mmol) and *t*-butyl diazoacetate (85.2 mg, 0.599 mmol). GC analysis showed that the product was a 17:83 trans:cis mixture. 1,3-Diisopropylbenzene (56.8 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis tetrahydrofuran was 63% (C_6D_6). The crude product was purified by flash chromatography (5/95 Et_2O/pentane), then by preparative achiral HPLC (12.5/87.5 EtOAc/hexanes) to afford the cis tetrahydrofuran as a colorless gum (96% ee, major enantiomer: 2*S*,3*S*).

Entry 3, OR = O-(*d*)-Men. The general procedure was followed using (*R*,*R*)-**1.19** (1.9 mg, 3.7 μmol), (*S*)-**3.1** (45.1 mg, 0.336 mmol) and (*d*)-menthyl diazoacetate (116 mg,

0.515 mmol). GC analysis showed that the product was a 20:80 trans:cis mixture. 1,3-Diisopropylbenzene (34.1 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis tetrahydrofuran was 74% (C_6D_6). Part of the crude product was purified by flash chromatography (5/95 Et_2O/pentane), then by preparative achiral HPLC (5/95 EtOAc/hexanes) to afford the cis tetrahydrofuran as a white solid.

The crude product was reduced to the alcohol and derivatized as the trifluoroacetate (*vide infra*), and GC analysis showed that the cis product was formed in 99% ee (major diastereomer: 2*S*,3*S*).

Entry 4, OR = O-(*l*)-Men. The general procedure was followed using (*R*,*R*)-**1.19** (1.9 mg, 3.7 μmol), (*S*)-**3.1** (44.5 mg, 0.332 mmol) and (*l*)-menthyl diazoacetate (115 mg, 0.514 mmol). GC analysis showed that the product was a 27:73 trans:cis mixture. 1,3-Diisopropylbenzene (47.9 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis tetrahydrofuran was 67% (C_6D_6). Part of the crude product was purified by flash chromatography (5/95 Et_2O/pentane), then by preparative achiral HPLC (5/95 EtOAc/hexanes) to afford the cis tetrahydrofuran as a white solid.

The crude product was reduced to the alcohol and derivatized as the trifluoroacetate (*vide infra*), and GC analysis showed that the cis product was formed in 94% ee (major diastereomer: 2*S*,3*S*).

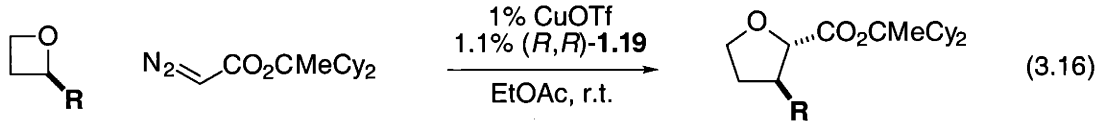
Entry 5, OR = $OCMeCy_2$. The general procedure was followed. Run 1 was carried out with (*S*,*S*)-**1.19** (2.6 mg, 4.9 μmol), (*R*)-**3.1** (61.5 mg, 0.458 mmol) and **3.4** (166 mg, 0.597 mmol). NMR analysis showed that the product was a 16:84 trans:cis mixture. The crude product was purified by flash chromatography (5/95 Et_2O/pentane), which

afforded a mixture of trans and cis tetrahydrofurans as a colorless liquid (120 mg, 68% yield; trans ee: 24%, major enantiomer: 2*R*,3*S*; cis ee: 95%, major enantiomer: 2*R*,3*R*).

Run 2 was carried out with (*R*,*R*)-**1.19** (3.3 mg, 6.2 μmol), (*S*)-**3.1** (78.4 mg, 0.584 mmol) and **3.4** (212 mg, 0.760 mmol). 1,3-Diisopropylbenzene (135.0 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis tetrahydrofuran was 74% (C_6D_6). The NMR analysis also showed that the product was a 16:84 trans:cis mixture. Flash chromatography afforded an 81% yield of trans and cis tetrahydrofurans (trans ee: 23%, major enantiomer: 2*S*,3*R*; cis ee: 95%, major enantiomer: 2*S*,3*S*).

X. Carbene Insertion into Enantiopure 2-Substituted Oxetanes: Influence of the 2-Substituent on the Ring Expansion.

1. Stereoselective Formation of trans Tetrahydrofurans (Table 3.10).



(3.16)

All diastereoselectivities, enantioselectivities, and yields that are reported in Table 3.10 are the average of two runs.

General procedure. To CuOTf•0.5C_6H_6 (1.9 mg, 7.5 μmol) was added a solution of (*R*,*R*)-**1.19** (4.7 mg, 8.9 μmol) in EtOAc (1 mL), and the catalyst solution was stirred for 1 h. It was then filtered through acrodisc to afford an orange solution. Half of this solution was added to the oxetane (0.39 mmol), and more EtOAc was added until the total volume is 0.8 mL. The solution was stirred for 5 min in a water bath maintained at 20 °C, and then diazo ester **3.4** (0.62 mmol), dissolved in 1 mL of EtOAc, was added in 4

batches over 3 h to the reaction mixture. After another hour, the reaction mixture was filtered through a plug of silica with Et_2O as the eluant to afford the crude product.

Entry 2, R = 4-(MeO)C_6H_4. The same procedure was used to prepare the catalyst solution. In a 4-mL vial, (*R*)-**3.13** (39.0 mg, 0.238 mmol) and **3.4** (99.4 mg, 0.357 mmol) were dissolved in EtOAc (0.5 mL) and stirred for 5 min in a water bath maintained at 20 °C. The catalyst solution was added to the stirring reaction mixture, and after 1 h, it was filtered through a plug of silica with Et_2O as the eluant. 1,3-Diisopropylbenzene (51.4 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans tetrahydrofuran was 32% (C_6D_6). The NMR analysis also showed that the product was a 75:25 trans:cis mixture. The crude product was purified first by flash chromatography (10/90 Et_2O/pentane), then by preparative achiral HPLC (10/90 EtOAc/hexanes), which afforded the trans tetrahydrofuran (25.9 mg, 26% yield; 68% ee, major enantiomer: 2*S*,3*R*) and the cis tetrahydrofuran (-53% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

Run 2 was carried out similarly. NMR analysis revealed that the crude product was a 76:24 trans:cis mixture, and that the yield of the trans tetrahydrofuran based on 1,3-diisopropylbenzene was 36% (C_6D_6). Flash chromatography followed by preparative achiral HPLC afforded the trans tetrahydrofuran in 32% yield (70% ee, major enantiomer: 2*S*,3*R*) and the cis tetrahydrofuran (-52% ee, major enantiomer: 2*R*,3*R*).

Entry 3, R = 4-(F_3C)C_6H_4. The general procedure was followed. Run 1 was carried out using (*R*)-**3.14** (78.1 mg, 0.386 mmol) and **3.4** (172 mg, 0.617 mmol). 1,3-Diisopropylbenzene (69.4 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans tetrahydrofuran was 91% (C_6D_6). The NMR analysis also showed that the product was a 94:6 trans:cis mixture. The crude product was purified first by flash chromatography (10/90 EtOAc/hexanes),

then by preparative achiral HPLC (15/85 EtOAc/hexanes), which afforded the trans tetrahydrofuran (138.6 mg, 79% yield; 99% ee, major enantiomer: 2*S*,3*R*) and the cis tetrahydrofuran (-7% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

Run 2 was carried out similarly. NMR analysis revealed that the crude product was a 94:6 trans:cis mixture, and that the yield of the trans tetrahydrofuran based on 1,3-diisopropylbenzene was 89% (C_6D_6). Flash chromatography followed by preparative achiral HPLC afforded the trans tetrahydrofuran in 82% yield (98% ee, major enantiomer: 2*S*,3*R*) and the cis tetrahydrofuran (1% ee, major enantiomer: 2*S*,3*S*).

Entry 4, R = 1-Naphthyl. The general procedure was followed. Run 1 was carried out using (*R*)-**3.15** (69.5 mg, 0.377 mmol) and **3.4** (170 mg, 0.611 mmol). Anisole (81.1 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans tetrahydrofuran was 74% (C_6D_6). The NMR analysis also showed that the product was a 86:14 trans:cis mixture. The crude product was purified first by flash chromatography (10/90 Et_2O/pentane), then by preparative achiral HPLC (1/99 *i*-PrOH/hexanes), which afforded the trans tetrahydrofuran (126.4 mg, 77% yield; 91% ee, major enantiomer: 2*S*,3*R*) and the cis tetrahydrofuran (7% ee, major enantiomer: 2*S*,3*S*) as colorless liquids.

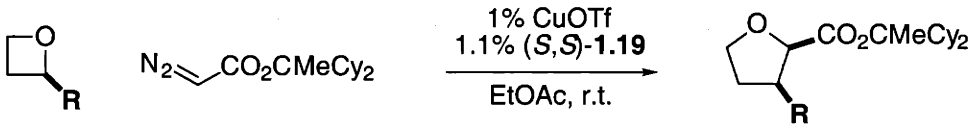
Run 2 was carried out similarly. NMR analysis revealed that the crude product was a 86:14 trans:cis mixture, and that the yield of the trans tetrahydrofuran based on anisole was 72% (C_6D_6). Flash chromatography followed by preparative achiral HPLC afforded the trans tetrahydrofuran in 73% yield (91% ee, major enantiomer: 2*S*,3*R*) and the cis tetrahydrofuran (14% ee, major enantiomer: 2*S*,3*S*).

Entry 5, R = *n*-$C_7H_{15}C{\equiv}C$. The general procedure was followed. Run 1 was carried out using (*R*)-**3.16** (46.3 mg, 0.257 mmol) and **3.4** (108 mg, 0.386 mmol). 1,3-Diisopropylbenzene (23.2 mg) was added to the crude product as an internal NMR

standard, and the NMR yield thus determined for the trans tetrahydrofuran was 68% (C_6D_6). The NMR analysis also showed that the product was a 87:13 trans:cis mixture. The crude product was purified by flash chromatography (4/96 Et_2O/pentane), which afforded the trans tetrahydrofuran (65.2 mg, 59% yield; 96% ee, major enantiomer: 2*S*,3*R*) and the cis tetrahydrofuran (-17% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

Run 2 was carried out similarly. NMR analysis revealed that the crude product was a 90:10 trans:cis mixture, and that the yield of the trans tetrahydrofuran based on 1,3-diisopropylbenzene was 76% (C_6D_6). Flash chromatography afforded the trans tetrahydrofuran in 69% yield (97% ee, major enantiomer: 2*S*,3*R*) and the cis tetrahydrofuran (-8% ee, major enantiomer: 2*R*,3*R*).

2. Stereoselective Formation of cis Tetrahydrofurans (Table 3.11).



(3.17)

Entry 2, R = 4-(MeO)C_6H_4. The same procedure for the formation of the corresponding trans tetrahydrofuran was followed using (*S*,*S*)-**1.19** (0.72 mg, 1.4 μmol), (*R*)-**3.13** (19.7 mg, 0.120 mmol), and **3.4** (50.3 mg, 0.181 mmol). 1,3-Diisopropylbenzene (18.3 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis tetrahydrofuran was 29% (C_6D_6). The NMR analysis also showed that the product was a 42:58 trans:cis mixture. The crude product was purified first by flash chromatography (10/90 Et_2O/pentane), then by preparative achiral HPLC (10/90 EtOAc/hexanes), which afforded the trans tetrahydrofuran (-36%

ee, major enantiomer: 2*S*,3*R*) and the cis tetrahydrofuran (9.8 mg, 20% yield; 82% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

Entry 3, R = 4-(F_3C)C_6H_4. The general procedure was followed using (*S*,*S*)-**1.19** (0.9 mg, 1.7 μmol) and (*R*)-**3.14** (32.5 mg, 0.161 mmol). 1,3-Diisopropylbenzene (32.9 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis tetrahydrofuran was 62% (C_6D_6). The NMR analysis also showed that the product was a 14:86 trans:cis mixture. The crude product was purified first by flash chromatography (10/90 EtOAc/hexanes), then by preparative achiral HPLC (15/85 EtOAc/hexanes), which afforded the trans tetrahydrofuran (17% ee, major enantiomer: 2*R*,3*S*) and the cis tetrahydrofuran (37.8 mg, 52% yield; 95% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

Entry 4, R = 1-Naphthyl. The general procedure was followed using (*S*,*S*)-**1.19** (0.9 mg, 1.7 μmol) and (*R*)-**3.15** (29.5 mg, 0.160 mmol). Anisole (28.1 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis tetrahydrofuran was 70% (C_6D_6). The NMR analysis also showed that the product was a 15:85 trans:cis mixture. The crude product was purified first by flash chromatography (10/90 Et_2O/pentane), then by preparative achiral HPLC (1/99 *i*-PrOH/hexanes), which afforded the trans tetrahydrofuran (18% ee, major enantiomer: 2*R*,3*S*) and the cis tetrahydrofuran (49.9 mg, 72% yield; 95% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

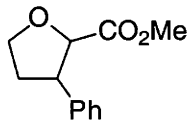
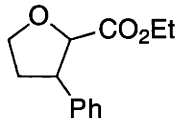
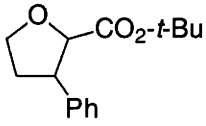
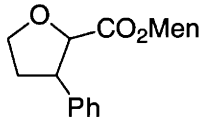
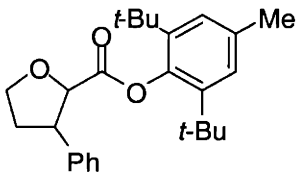
Entry 5, R = *n*-$C_7H_{15}C{\equiv}C$. The general procedure was followed using (*S*,*S*)-**1.19** (0.9 mg, 1.7 μmol) and (*R*)-**3.16** (28.0 mg, 0.155 mmol). 1,3-Diisopropylbenzene (20.6 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis tetrahydrofuran was 62% (C_6D_6). The NMR analysis also

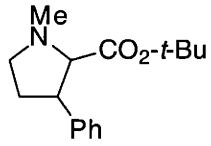
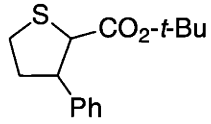
showed that the product was a 16:84 trans:cis mixture. The crude product was purified by flash chromatography (4/96 Et_2O/pentane), which afforded the trans tetrahydrofuran (15% ee, major enantiomer: 2*R*,3*S*) and the cis tetrahydrofuran (39.9 mg, 60% yield; 94% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

XI. Assay of Diastereoselectivity.

Table 3.15 summarizes the assay conditions for the diastereomeric five-membered heterocycles that can be resolved on a DB-1701 GC column:

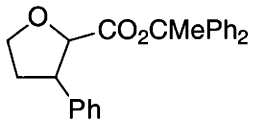
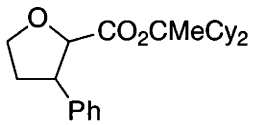
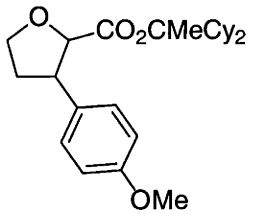
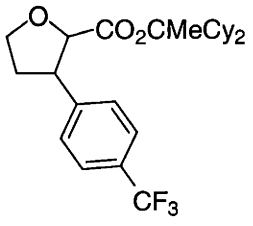
Table 3.15. GC data for diastereomeric five-membered heterocycles.

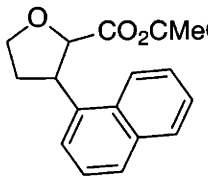
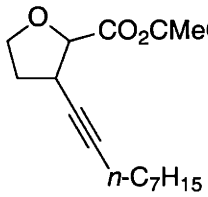
reaction product	temperature (°C)	carrier gas flow (mL/min)	trans t_R (min)	cis t_R (min)
	140	He, 1.0	16.1	14.8
	140	He, 1.0	20.7	19.4
	130	He, 1.0	40.3	39.3
	180	He, 1.0	47.7, 48.0	44.2, 44.8
	280	He, 1.0	4.0	4.2

	140	H_2, 1.0	17.4	14.8
	150	H_2, 1.0	23.2	22.4

The diastereomeric ratios of the tetrahydrofurans that cannot be analyzed by GC were determined by integration of the ^1H NMR spectrum (delay time = 30 seconds). Table 3.16 lists the peaks used for integration:

Table 3.16. NMR data for diastereomeric tetrahydrofurans.

reaction product	solvent	trans δ (ppm)	cis δ (ppm)
	C_6D_6	3.42 (dt)	3.75 (q)
	C_6D_6	4.51 (d)	4.58 (d)
	C_6D_6	3.54 (dt) (H5)	4.59 (d)
	C_6D_6	4.35 (d)	4.45 (d)

	C_6D_6	4.79 (d)	4.96 (d)
	C_6D_6	4.58 (d)	4.45 (d)

Assignment of relative stereochemistry. The assignment for *t*-butyl 3-phenyltetrahydrofuran-2-carboxylate is based on comparison with the NMR data of Katsuki.[9b] The other assignments are based on analogy. It appears that all of the diastereomers possess the following properties:

a. $(J_{2,3})_{trans} < (J_{2,3})_{cis}$;

b. The ester group of the cis diastereomer is more shielded than the ester group of the trans diastereomer;

c. With the (*R*)-oxetane and the (*R*,*R*)-ligand, the trans diastereomer is formed preferentially.

XII. Assay of Enantioselectivity.

The enantiomeric excess of the γ-chloroalcohols was assayed either directly or as the acetate derivative (Ac_2O/pyridine/Et_3N in CH_2Cl_2). Table 3.17 summarizes the assay conditions:

Table 3.17. Resolution conditions for enantiomeric γ-chloroalcohols.

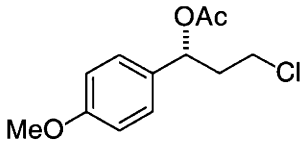
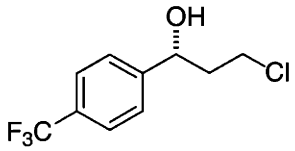
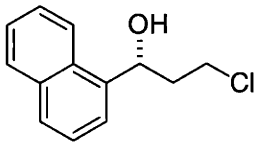
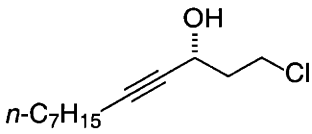
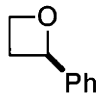
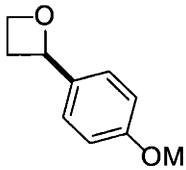
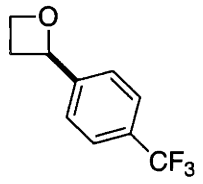
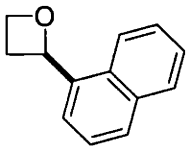
substrate	column	conditions	indicated config. t_R (min)	opposite config. t_R (min)
	GC Chiraldex B-PH	130 °C H_2, 1.0 mL/min	59.4	57.0
	GC Chiraldex B-PH	120 °C He, 1.0 mL/min	70.9	73.8
	HPLC Chiralcel OD	10% *i*-PrOH/hexanes 1.0 mL/min	27.0	10.0
	GC Chiraldex G-TA	120 °C H_2, 1.0 mL/min	48.4	52.2

Table 3.18 summarizes the assay conditions for the oxetanes:

Table 3.18. Resolution conditions for enantiomeric oxetanes.

substrate	column	conditions	indicated config. t_R (min)	opposite config. t_R (min)
	GC Chiraldex G-TA	120 °C He, 1.5 mL/min	6.1	7.7
	HPLC Chiralcel OD	1% *i*-PrOH/hexanes 1.0 mL/min	14.1	13.2

	GC Chiraldex G-TA	100 °C He, 1.0 mL/min	7.8	8.4
	HPLC Chiralcel OD	3% *i*-PrOH/hexanes 1.0 mL/min	18.9	8.4

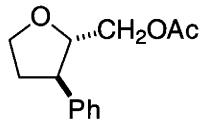
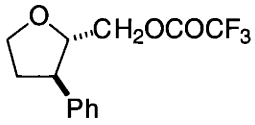
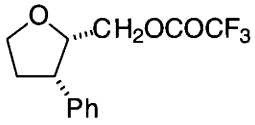
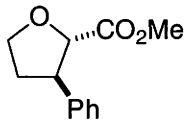
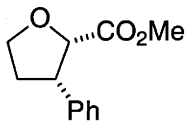
The enantiomeric excess of the tetrahydrofurans were assayed by one of the three methods:

a. reduction to the alcohol ($LiAlH_4$), followed by acetylation (Ac_2O/pyridine); for *trans*-3-phenyltetrahydrofuran-2-carboxylates in the presence of the cis diastereomer.
b. reduction to the alcohol ($LiAlH_4$), followed by trifluoroacetylation ($(CF_3CO)_2O$); for diastereomerically pure *cis*-3-phenyltetrahydrofuran-2-carboxylates.
c. hydrolysis to the carboxylic acid (CF_3CO_2H), followed by methylation ($TMSCHN_2$); for tetrahydrofurans bearing a tertiary ester group.

For products that require derivatization for the analysis of ee, they were first purified if the ester group is achiral. The ee of menthyl trans-3-phenyltetrahydrofuran-2-carboxylates can be assayed directly, but not the corresponding cis diastereomers. Instead the crude product was first reduced to the diastereomeric alcohols, which were then purified, separated by preparative achiral HPLC, and derivatized as trifluoroacetates.

Table 3.19 summarizes the assay conditions for enantiomeric five-membered heterocycles:

Table 3.19. Resolution conditions for enantiomeric five-membered heterocycles.

substrate	column	conditions	indicated config. t_R (min)	opposite config. t_R (min)
	GC Chiraldex B-PH	110 °C H_2, 2.0 mL/min	57.4	59.5
	GC Chiraldex G-TA	90 °C He, 1.0 mL/min	81.7	77.5
	GC Chiraldex G-TA	90 °C He, 1.0 mL/min	74.1	83.2
	GC Chiraldex G-TA	120 °C, He, 0.5 mL/min	58.9	67.7
	HPLC	1% *i*-PrOH/hexanes 1.0 mL/min	19.1	24.6
	GC Chiraldex G-TA	120 °C, He, 0.5 mL/min	56.1	64.3
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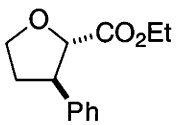
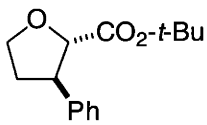
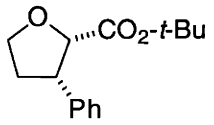
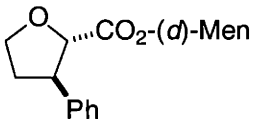
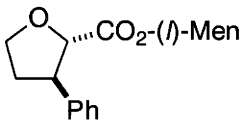
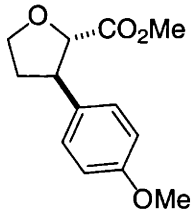
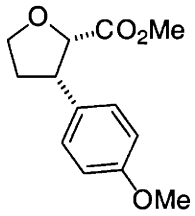
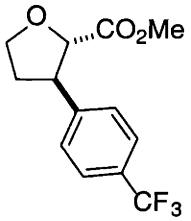
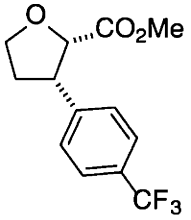
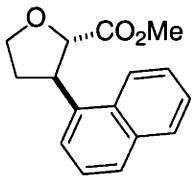
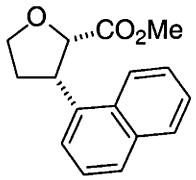
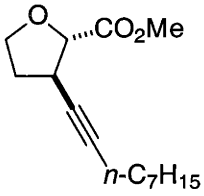
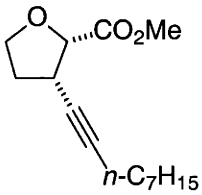
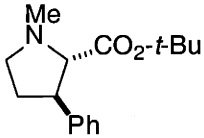
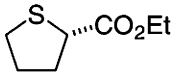
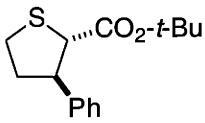
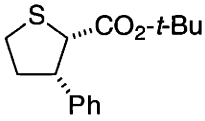
	GC Chiraldex B-PH	110 °C He, 1.0 mL/min	68.3	70.4
	GC Chiraldex B-PH	120 °C H_2, 1.0 mL/min	41.6	44.0

	GC Chiraldex B-PH	120 °C H_2, 2.0 mL/min	50.1	51.3
	GC Chiraldex B-PH	150 °C, He, 1.0 mL/min	134.0	138.0
	GC Chiraldex B-PH	150 °C, He, 1.0 mL/min	131.8	135.6
	GC Chiraldex G-TA	130 °C, He, 1.0 mL/min	92.9	86.3
	GC Chiraldex G-TA	130 °C, He, 1.0 mL/min	73.2	70.6
	GC Chiraldex G-TA	130 °C, He, 1.0 mL/min	31.3	24.2
	GC Chiraldex G-TA	130 °C, He, 1.0 mL/min	21.8	19.6
	HPLC Chiralcel AD	1% EtOH/hexanes 1.0 mL/min	19.6	15.2

	HPLC Chiralcel AD	1% EtOH/hexanes 1.0 mL/min	21.6	27.4
	GC Chiraldex G-TA	120 °C, He, 1.0 mL/min	110.4	92.3
	GC Chiraldex G-TA	120 °C, He, 1.0 mL/min	105.8	95.4
	GC Chiraldex B-PH	100 °C H_2, 1.0 mL/min	77.7	83.7
	GC Chiraldex G-TA	100 °C H_2, 1.5 mL/min	8.9, 13.6	
	GC Chiraldex B-PH	100 °C H_2, 1.0 mL/min	77.2, 80.1	
	GC Chiraldex B-PH	100 °C H_2, 1.0 mL/min	66.1, 67.7	

Assignment of absolute stereochemistry. The sign of the optical rotation of the trans tetrahydrofuran derived from the reaction of (*S*)-**3.1** and *t*-butyl diazoacetate in the presence of (*S,S*)-**1.19** is negative; the absolute stereochemistry of the predominant enantiomer of the trans tetrahydrofuran is therefore (2*R*,3*S*).[9b] The absolute stereochemistry of the other trans products that are derived from (*S*)-**3.1** was

confirmed by either comparing the tetrahydrofuran alcohols (from reduction) or the tetrahydrofuran carboxylic acids (from hydrolysis). The absolute stereochemistry of the trans products that are derived from other 2-substituted oxetanes were assigned by analogy.

The sign of the optical rotation of the cis tetrahydrofuran derived from (*S*)-**3.1** and *t*-butyl diazoacetate in the presence of (*R,R*)-**1.19** is positive; the absolute stereochemistry of the predominant enantiomer of the cis tetrahydrofuran is therefore (2*S*,3*S*).[9b] The absolute stereochemistry of the other cis products that are derived from (*S*)-**3.1** was confirmed by either comparing the tetrahydrofuran alcohols (from reduction) or the tetrahydrofuran carboxylic acids (from hydrolysis). The absolute stereochemistry of the cis products that are derived from other 2-substituted oxetanes were assigned by analogy.

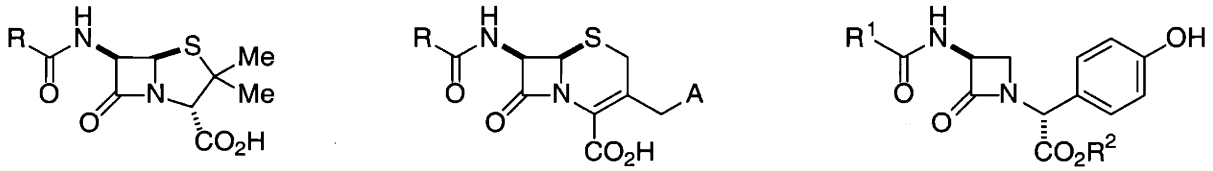
Chapter 4

Copper-Catalyzed Kinugasa Reaction:

Asymmetric 2-Azetidinone Formation from Nitrones and Terminal Alkynes

A. Introduction.

The 2-azetidinone (β-lactam) moiety has been extensively investigated as a result of the interesting biological activities found in its derivatives. Most notably, penicillins (**4.1**) and cephalosporins (**4.2**) belong to the earliest antibacterial agents, while nocardicins (**4.3**) have been identified to be a new class of antibiotics (Figure 4.1).[1]



penicillins (**4.1**) cephalosporins (**4.2**) nocardicins (**4.3**)

Figure 4.1. Important classes of antibacterial agents containing the 2-azetidinone moiety.

2-Azetidinones have other interesting biological activities. For example, various 3-alkyl-1,4-diaryl-2-azetidinones have been demonstrated to be potent cholesterol absorption inhibitors (Figure 4.2).[2] In particular, Merck and Schering-Plough are currently codeveloping SCH 58235 as Ezetimibe. Phase III clinical trial showed that Ezetimibe significantly reduces levels of low-density lipoprotein (LDL) or "bad" cholesterol in patients without affecting the absorption of the fat-soluble vitamins that are needed by the human body.[3]

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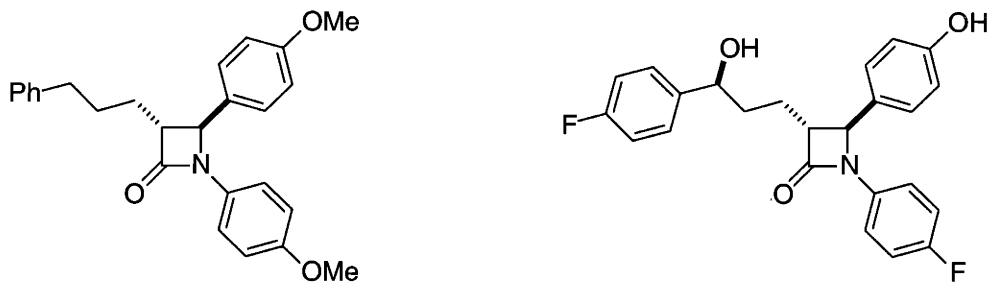
1 For general reviews, see: (a) Davies, D. E.; Storr, R. C. In *Comprehensive Heterocyclic Chemistry*; Katritsky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 7, pp 247–267. (b) De Kimpe, N. In *Comprehensive Heterocyclic Chemistry II*; Katritsky, A. R., Rees, C. W., Scriven, E. F. V., Padwa, A., Eds.; Pergamon: Oxford, 1996; Vol. 1B, pp 536–572. (c) *The Organic Chemistry of β-Lactams* Georg, G.I., Ed.; VCH: New York, 1992.

2 For accounts of the discovery of the pharmological activity and structure–activity relationships on the 2-azetidinone core, see: (a) Burnett, D. A.; Caplen, M. A.; Davis, H. R., Jr.; Burrier, R. E.; Clader, J. W. *J. Med. Chem.* **1994**, *37*, 1733–1736. (b) Clader, J. W.; Burnett, D. A.; Caplen, M. A.; Domalski, M. S.; Dugar, S.; Vaccaro, W.; Sher, R.; Browne, M. E.; Zhao, H.; Burrier, R. E.; Salisbury, B.; Davis, H. R., Jr. *J. Med. Chem.* **1996**, *39*, 3684–2693. (c) Rosenblum, S. B.; Huynh, T.; Afonso, A.; Davis, H. R., Jr.; Yumibe, N.; Clader, J. W.; Burnett, D. A. *J. Med. Chem.* **1998**, *41*, 973–980.

3 Merck/Schering-Plough Pharmaceuticals Press Release. http://www.sch-plough.com/news/research/2001/05-21-01.html (accessed October 2001).

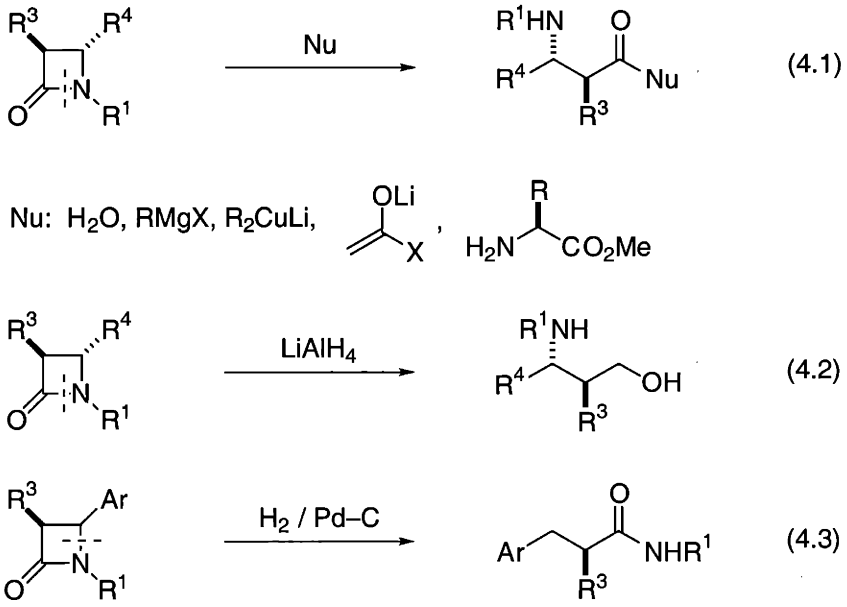


SCH 48461

SCH 58235
Ezetimibe

Figure 4.2. Some 3-alkyl-1,4-diaryl-2-azetidinones that have been identified to be potent cholesterol absorption inhibitors.

2-Azetidinones also serve as useful synthetic intermediates by virtue of the strain energy stored in their 4-membered ring system (Scheme 4.1).[4]



Scheme 4.1. Synthetic utility of 2-azetidinones.

The amide bond N1-C2 can be cleaved by various nucleophiles, such as water, Grignard reagents, organocuprates, lithiated enolates, and amino acids to afford β-

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4 For reviews, see: (a) Ojima, I. *Acc. Chem. Res.* **1995**, *28*, 383–389. (b) Ojima, I.; Delaloge, F. *Chem. Soc. Rev.* **1997**, *26*, 377–386.

amino acid derivatives (eq 4.1). Many of these products have found important uses, such as the synthesis of paclitaxel (Taxol) and its analogs,[5] or as monomeric building blocks for β-peptides.[6] Reduction of N-substituted 2-azetidinones by $LiAlH_4$ gives γ-aminoalcohols (eq 4.2),[7] while hydrogenolysis furnishes aromatic α-amino acids (eq 4.3).[8]

Given the importance of the moiety, many reactions have been developed for its synthesis, such as the hydroxamate cyclization,[9] the metalloester enolate–imine condensation,[10] the chromium carbene–imine reaction,[11] the isocyanate–alkene cycloaddition,[12] and the ketene–imine cycloaddition, commonly known as the Staudinger reaction.[13] Despite the maturity of these methods, asymmetric variants are rare, and in most cases, asymmetric induction arises from the use of chiral auxiliaries.[14]

A general solution for the catalytic stereoselective synthesis of 2-azetidinones from achiral, readily available starting materials remains to be found. So far, only two approaches can be found in the literature with some degree of success.[15] The first one,

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5 The commercial semi-synthesis of the anti-cancer agent paclitaxel (Taxol) employs a 2-azetidinone for the installation of the β-amino acid-derived sidechain. See: Holton, R. A.; Biediger, R. J.; Boatman, P. D. In *Taxol: Science and Applications*; Suffness, M., Ed.; CRC Press: Boca Raton, FL, 1995; p 97.

6 β-Peptides have attracted a lot of interest due to their potential applications in novel drug design. See: (a) Seebach, D.; Matthews, J. L. *Chem. Commun.* **1997**, 2015–2022. (b) Gellman, S. H. *Acc. Chem. Res.* **1998**, *31*, 173–180.

7 The γ-aminoalcohol/γ-aminoether moiety is found in antidepressants such as Prozac or Paxil.

8 Ojima, I.; Shimizu, N. *J. Am. Chem. Soc.* **1986**, *108*, 3100–3102.

9 Miller, M. J. *Acc. Chem. Res.* **1986**, *19*, 49–56.

10 Hart, D. J.; Ha, D. C. *Chem. Rev.* **1989**, *89*, 1447–1465.

11 Hegedus, L. S. *Acc. Chem. Res.* **1995**, *28*, 299–305.

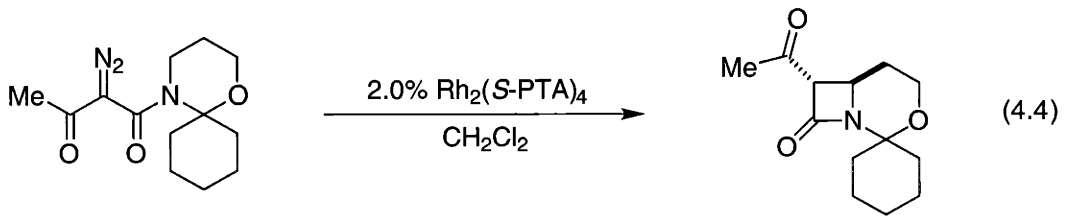
12 Chmielewski, M.; Kaluza, Z.; Furman, B. *Chem. Commun.* **1996**, 2689–2696.

13 Staudinger, H. *Liebigs Ann. Chem.* **1907**, *356*, 51–123.

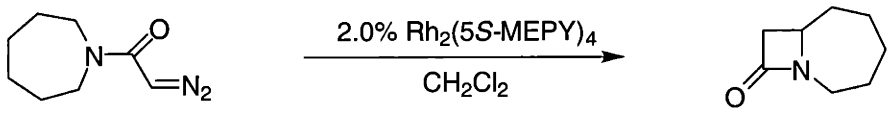
14 For a general review on asymmetric synthesis by the Staudinger reaction, see: (a) Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M. *Eur. J. Org. Chem.* **1999**, 3223–3235. For other examples: (b) chromium carbene–imine cycloaddition: Hegedus L. S.; Imwinkelried, R.; Alarid-Sargent, M.; Dvorak, D.; Satoh, Y. *J. Am. Chem. Soc.* **1990**, *112*, 1109–1117. (c) metalloester enolate–imine condensation: Hattori, K.; Yamamoto, H. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 2337–2342.

15 Apart from the two approaches mentioned in the main text, Alper has reported an unusual kinetic resolution of chiral, racemic aziridines that is mediated by a *catalytic* amount of metal and a *stoichiometric* amount of menthol to afford 2-azetidinones in high optical yield. See: Calet, S.; Urso, F.; Alper, H. *J. Am. Chem. Soc.* **1989**, *111*, 931–934.

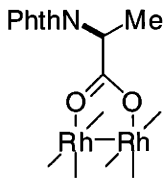
reported by McKervey,[16] Hashimoto[17] (eq 4.4), and Doyle[18] (eq 4.5), involves the asymmetric C–H insertions of α-diazo amides catalyzed by chiral carboxamide–dirhodium(II) complexes.



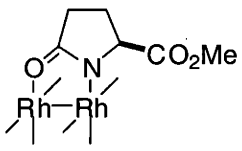
96% ee (4.4)



97% ee (4.5)



Rh_2(*S*-PTA)$_4$



Rh_2(5*S*-MEPY)$_4$

The main drawback of this approach is the narrow scope of the reaction. Diazo insertion into the β C–H bonds to form γ-lactams often competes with the desired pathway. This problem in regioselectivity is especially pronounced for α-

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16 McCarthy, N.; McKervey, M. A.; Ye, T.; McCann, M.; Murphy, E.; Doyle, M. P. *Tetrahedron Lett.* **1992**, *33*, 5983–5986.

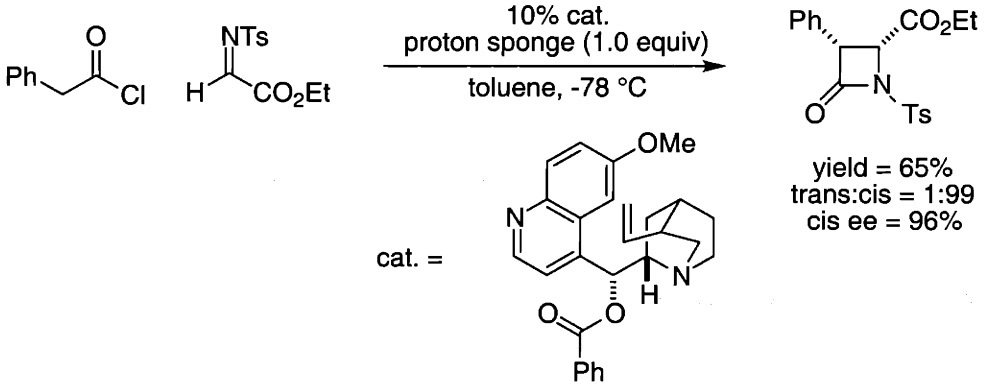
17 (a) Watanabe, N.; Anada, M.; Hashimoto, S.-i.; Ikegami, S. *Synlett* **1994**, 1031–1033. (b) Hashimoto, S.-i.; Watanabe, N.; Anada, M.; Ikegami, S. *Yuki Gosei Kagaku Kyokaishi* **1996**, *54*, 988–999. (c) Anada, M.; Watanabe, N.; Hashimoto, S.-i. *Chem. Commun.* **1998**, 1517–1518. (d) Anada, M.; Hashimoto, S.-i. *Tetrahedron Lett.* **1998**, *39*, 9063–9066.

18 (a) Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Daniel, K. L. *Tetrahedron Lett.* **1992**, *33*, 7819–7822. (b) Doyle, M. P.; Kalinin, A. V. *Synlett* **1995**, 1075–1076.

19 Only two α-diazoacetamides, which are derived from *cis*-2,6-dimethylpiperidine and azepane, have been reported by Doyle to produce the desired bicyclic 2-azetidinones with high regioselectivity. A mixture of regioisomeric products (selectivity ~ 2:1 to 1:3) were observed for the

diazoacetamides, and only substrates that are biased by either conformational constraints[19] or electronic effects[20] undergo the desired C–H insertions.

Another approach is through asymmetric nucleophilic catalysis of the Staudinger reaction. Leckta recently reported that the reaction can be catalyzed by a chiral quinine derivative with excellent stereoselectivity (eq 4.6).[21] However, the imine component is limited to an activated *N*-sulfonyl imino ester. Also, the yields are generally moderate (36–65% for 1 imine substrate), a fact which Leckta attributed to the slow polymerization of the imine.[22]



(4.6)

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corrresponding diazo compound that is derived from azocane, and no product was formed from those that are derived from pyrrolidine, piperidine, or morpholine (Ref. 18b).

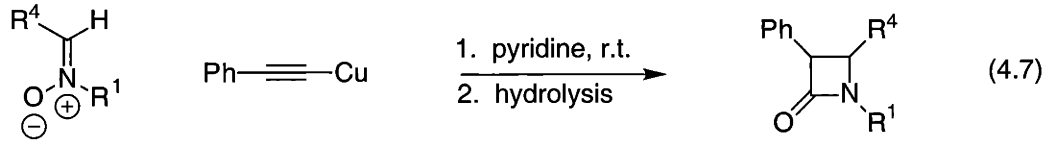
20 An electron-withdrawing group (carboethoxy) γ-to the carbonyl group disfavors diazo insertion into the β C–H bonds (Ref. 18a).

21 Taggi, A. E.; Hafez, A. M.; Wack, H.; Young, B.; Drury, W. J., III.; Lectka, T. *J. Am. Chem. Soc.* **2000**, *122*, 7831–7832.

22 Our group is also exploring a similar approach in the catalytic asymmetric synthesis of 2-azetidinones through the use of planar-chiral pyridine derivatives as the nucleophilic catalyst. The substrate scope is broadened relative to the Lectka study, as aryl alkyl ketenes and symmetrical dialkyl ketenes react with high enantioselectivity with *N*-sulfonyl imines. Hodous, B. L.; Fu, G. C. *J. Am. Chem. Soc.*, submitted for publication, 2001.

23 This mode of reaction is unique for copper. Most metal acetylides add as nucleophiles to the electrophilic carbon of the nitrone to form substituted hydroxylamines. For a review, see: (a)

A third possibility is the copper(I)-mediated reaction[23] between nitrones and terminal alkynes, which was first reported by Kinugasa and Hashimoto in 1972 (eq 4.7).[24,25]



(4.7)

These workers showed that copper phenylacetylide reacts with various *N*,α-diarylnitrones in dry pyridine to afford the corresponding 2-azetidinones in 50–60% yield. Subsequent work of Irwin,[26] Sandhu,[27] Miura,[28] and Basak[29] further extended the utility of the reaction through substrates with a wide range of alkyl, aryl and heteroaryl substituents. Figure 4.3 shows a sample of products that have been synthesized by the Kinugasa reaction.

Volkmann, R. A. In *Comprehensive Organic Synthesis: Selectivity, Strategy, and Efficiency in Modern Organic Chemistry*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, Chapter 1.12, pp 391–393. For specific asymmetric examples, see: (b) Lithium: Merino, P.; Franco, S.; Merchan, F. L.; Tejero, T. *J. Org. Chem.* **1998**, *63*, 5627–5630. (c) Magnesium: Merino, P.; Franco, S.; Gascon, J. M.; Merchan, F. L.; Tejero, T. *Tetrahedron: Asymmetry* **1999**, *10*, 1867–1871. (d) Zinc: Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **1999**, *121*, 11245–11246.

24 Kinugasa, M.; Hashimoto, S. *J. Chem. Soc., Chem. Commun.* **1972**, 466–467.

25 The reaction probably involves the 1,3-dipolar cycloaddition between a copper acetylide and a nitrone. See Part B, Section III for mechanistic discussions.

26 Ding, L. K.; Irwin, W. J. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2382–2386.

27 (a) Dutta, D. K.; Boruah, R. C.; Sandhu, J. S. *Indian J. Chem.* **1986**, *25B*, 350–353. (b) Dutta, D. K.; Boruah, R. C.; Sandhu, J. S. *Heterocycles* **1986**, *24*, 655–658.

28 (a) Okuro, K.; Enna, M.; Miura, M.; Nomura, M. *J. Chem. Soc., Chem. Commun.* **1993**, 1107–1108. (b) Miura, M.; Enna, M.; Okuro, K.; Nomura, M. *J. Org. Chem.* **1995**, *60*, 4999–5004.

29 (a) Basak, A.; Mahato, T.; Bhattacharya, G.; Mukherjee, B. *Tetrahedron Lett.* **1997**, *38*, 643–646. (b) Basak, A.; Bhattacharya, G.; Bdour, H. M. M. *Tetrahedron* **1998**, 6529–6538.

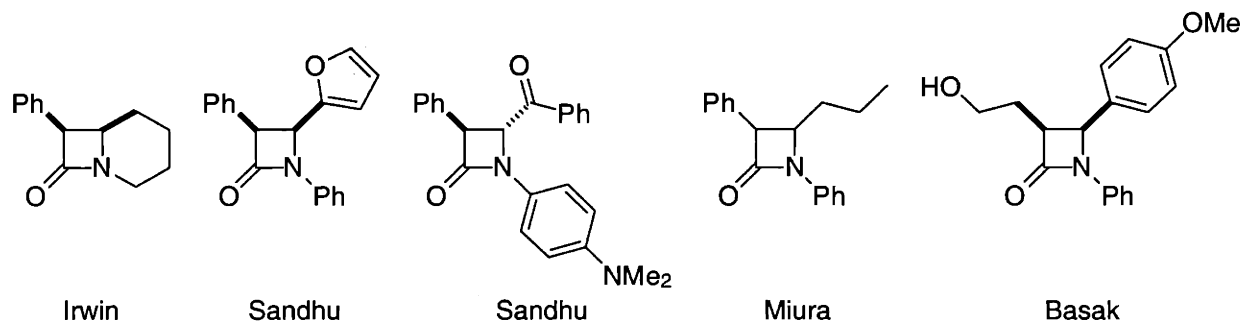
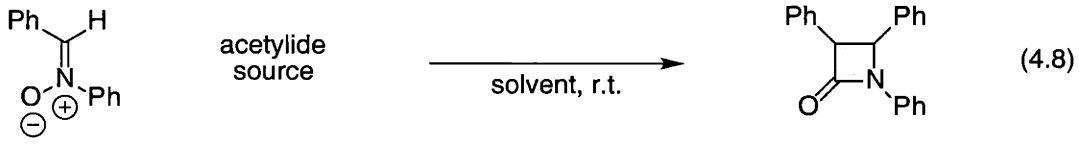


Figure 4.3. A sample of products that have been synthesized by the Kinugasa reaction.

The following features render the Kinugasa reaction an appealing convergent route to 2-azetidinones: (1) nitrone preparation is straightforward; (2) nitrones are typically crystalline materials that are stable and easily purified; (3) numerous alkynes with widely varying substituents are commercially available; and, (4) functional groups such as alcohols, amines, halides and esters are compatible with the reaction conditions.

There are still problems associated with the reaction; for example, the issue of diastereoselectivity has not been clearly resolved nor effectively controlled. In early work, the diastereomeric ratios of the product were either not reported, or the cis product was reported to be formed exclusively.[30] Since crystallization was the usual method for product isolation, these reports are not reliable. Later studies suggest that the reaction is in fact moderately cis-diastereoselective. This confusion is best illustrated by the following example for the synthesis of 1,3,4-triphenyl-2-azetidinone (Table 4.1).

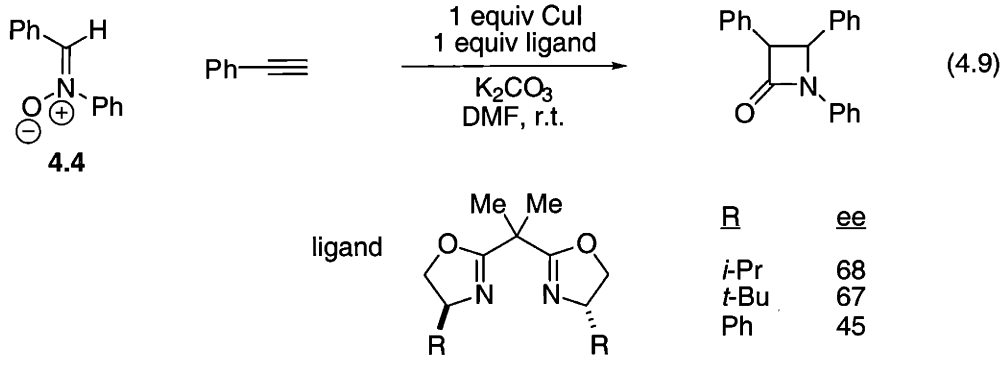


30 For example, Kinugasa assigned all his 2-azetidinone products as cis, but his reported coupling constants between H3 and H4 suggest that two of the four products are in fact trans.

Table 4.1. Diastereoselection reported for the synthesis of 1,3,4-triphenyl-2-azetidinone (eq 4.8).

author	acetylide source	solvent	yield (%)	trans : cis
Kinugasa[24]	CuC≡CPh	pyridine	55	0 : 100
Irwin[26]	CuC≡CPh	pyridine	32	38 : 62
Miura[28b]	CuI/PhC≡CH/K_2CO_3	DMF	65	34 : 66

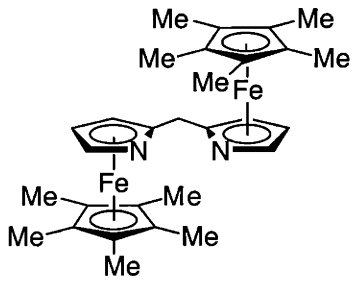
Perhaps discouraged by the use of stoichiometric copper, few have ventured to develop an asymmetric version of the reaction. Miura reported the first and only example by employing a *stoichiometric* amount of a chiral bis(oxazoline) as the ligand in the reaction between *N*,α-diphenylnitrone and phenylacetylene (eq 4.9). The enantiomeric excess of the product was found to be 68%, which dropped to 57% when a substoichiometric amount of ligand (20%) was used.[28b] Clearly, there is room for improvement in terms of both catalyst turnover and overall stereoselectivity.



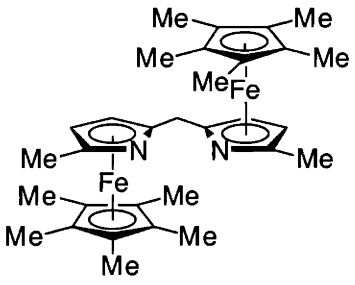
Miura also demonstrated that the diastereomeric mixture can be epimerized by heating it with K_2CO_3 in DMF to give the trans diastereomer exclusively. The product has the same ee as the starting material, indicating that *both diastereomers have the same absolute configuration at C4.*

In this chapter, we describe our efforts to improve the following aspects of the reaction: (1) lower the amount of copper used from stoichiometric to catalytic, (2) improve the cis diastereoselectivity of the reaction; and, (3) induce high enantioselectivity in the reaction through the use of our bis(azaferrocenes).

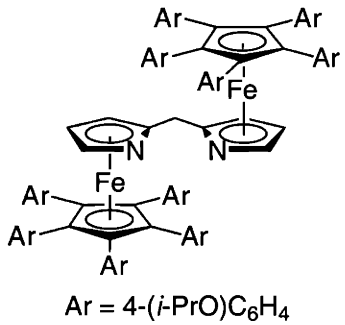
B. Results and Discussion.



(*R*,*R*)-**1.19**

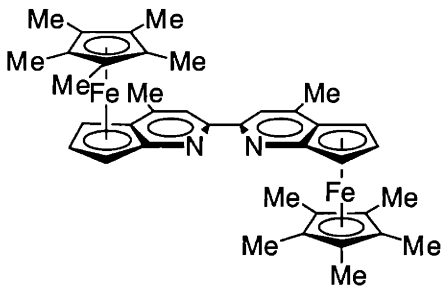


(*R*,*R*)-**1.22**



Ar = 4-(*i*-PrO)C_6H_4

(*R*,*R*)-**1.33**

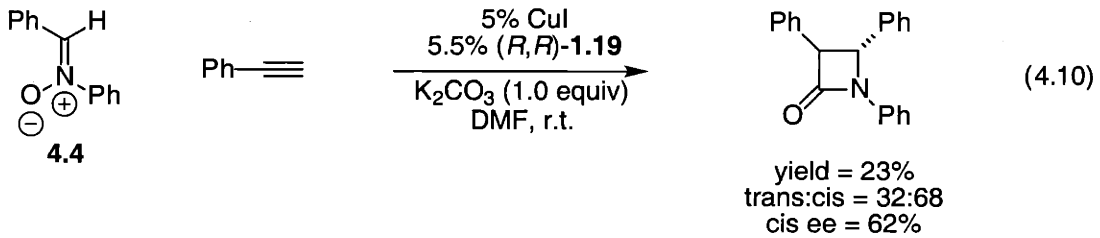


(*S*,*S*)-**2.11**

Figure 4.4. C_2-Symmetric planar-chiral ligands investigated in this chapter.

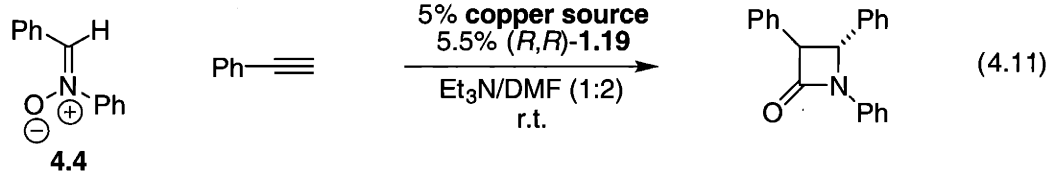
I. Development of Reaction Conditions.

Our initial evaluation of the copper–bis(azaferrocene) catalyst focused on the reaction between *N*,α-diphenylnitrone with phenylacetylene, as it was the most studied by others. We first carried out the reaction under the Miura conditions, with the bis(oxazoline) ligand replaced by bis(azaferrocene) **1.19** (eq 4.10).[28b]



(4.10)

We were encouraged by the observed enantioselectivity (cis ee: 62%), which matches the values reported for various bis(oxazolines). Similar to Miura's observations, both diastereomers have the same configuration (4*R*). However, the system was still plagued by two major problems, a disappointing yield and poor diastereoselectivity. Inspired by Carreira's success in generating zinc acetylides with amine bases,[31] we decided to replace K_2CO_3 with Et_3N, and to examine the efficacy of different copper sources (Table 4.2).[32]



(4.11)

Table 4.2. Asymmetric Kinugasa reaction as a function of the copper source (eq 4.11).

entry	**copper source**	GC yield (%)	trans : cis	% ee, cis
1	CuI	56% at 18.5 h	47 : 53	58 (61)
2	CuCN	45% at 230 h	80 : 20	57 (62)
3	CuOAc	32% at 4.5 h	46 : 54	52 (55)
4	CuCl	38% at 16 h	21 : 79	57 (67)
5	$Cu(MeCN)_4PF_6$	31% at 24 h	43 : 57	45 (28)

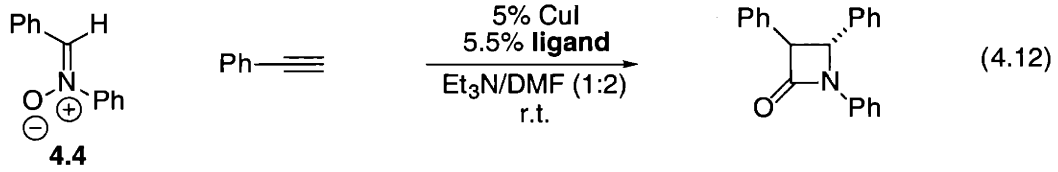
The % ee in parentheses refers to the reaction *without* any added base.

When compared to the results in eq 4.10, the reaction with CuI shows a substantial improvement in yield without any loss of enantioselectivity (entry 1). The coordinating ability of the anion does not seem to have any relationship with the activity of the copper source, as both the most active, CuOAc (entry 3), and the least active, CuCN (entry 2), have strongly coordinating anions. The study was repeated without any

31 Frantz, D. E.; Fässler, R.; Tomooka, C. S.; Carreira, E. M. *Acc. Chem. Res.* **2000**, *33*, 373–381.
32 Neither silver(I) nor gold(I) complexes gives any desired products.

added base, and most of the reactions slow down significantly with slight increases in enantioselectivity.

To determine the best ligand for the reaction, we examined three representative members from the bis(azaferrocene) family and the C_2-symmetric planar-chiral bipyridine derivative **2.11** (Table 4.3).



(4.12)

Table 4.3. Asymmetric Kinugasa reaction as a function of the ligand (eq 4.12).

entry	**ligand**	GC yield (%)	trans : cis	% ee, cis
1	**1.19**	56% at 18.5 h	47 : 53	58 (61)
2	**1.22**	62% at 69 h	40 : 60	70 (67)
3	**1.33**	40% at 450 h	75 : 25	2 (53)
4	**2.11**	59% at 25 h	23 : 77	40 (47)

The % ee in parentheses refers to the reaction *without* any added base.

The incorporation of methyl groups at the 5-positions of bis(azaferrocene) **1.19** improves the cis enantioselectivity of the reaction (entry 2). Bipyridine **2.11** is less effective than bis(azaferrocene) **1.19**, perhaps due to the fact that the stereogenic element is more distant from the ligating atom (entry 4). The results from **1.33** are intriguing (entry 3), since the reaction is moderately enantioselective in the *absence* of an added base, but the presence of Et_3N leads to racemic product and does not accelerate the reaction (without Et_3N: 42% GC yield at 136 h). One interpretation of this phenomenon is that Et_3N competes with the bis(azaferrocene) for complexation with the copper source, and the resultant achiral $Cu(Et_3N)_n^+$ complex becomes the operating catalyst. If the Cu/bis(azaferrocene) complex is not very reactive, as in the case of **1.33**, the excess amine will decrease the enantioselectivity of the reaction. On the other hand,

if the ligand forms a complex with copper that is more reactive, e.g., **1.19**, this decrease will be smaller. However, the amine can still have a deleterious effect on the reaction because the effective concentration of the catalyst is lowered by the scavenging action of the excess amine (Figure 4.5).

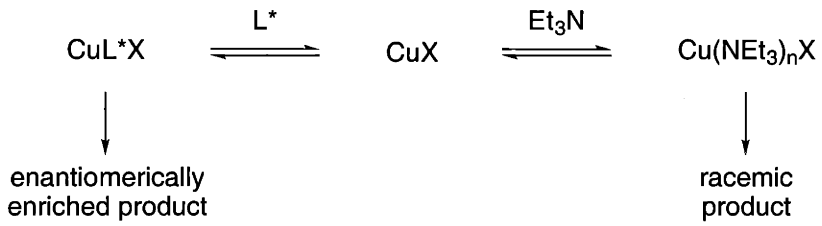
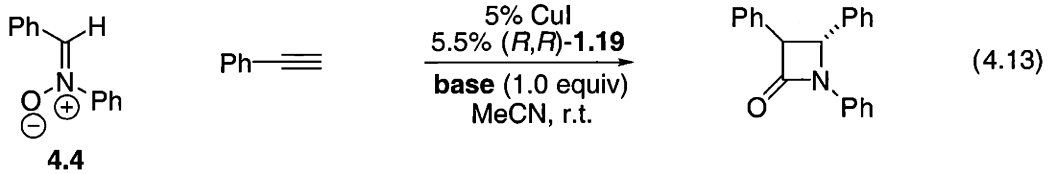


Figure 4.5. Deleterious effect of excess amine.

Hence, in our next systematic study of the effect of base, we limited the amount of added base to only 1.0 equivalent (Table 4.4).[33] We were pleasantly surprised to discover that *both the rate and the cis-diastereoselectivity can be improved significantly by lowering the amount of added base.*[34] Trialkylamines have the proper basicity to bring about this improvement (68–77% GC yield, ~ 20–85 fold increase in rate), since less basic $PhNMe_2$ does not accelerate the reaction (entry 1), and more basic phosphazene base BTPP shuts down the reaction (entry 2). Increasing the steric demand of the amine appears to improve the cis diastereoselectivity, but it has only a small effect on the enantioselectivity (entries 4–10).



(4.13)

33 We found in a preliminary screen that MeCN is a better solvent than DMF in terms of yield. A more detailed solvent study will be presented later.

34 We have further lowered the amount of the amine (Cy_2NMe) to 0.1 equiv, but there appears to be no additional beneficial effect in terms of rate and cis-diastereoselectivity.

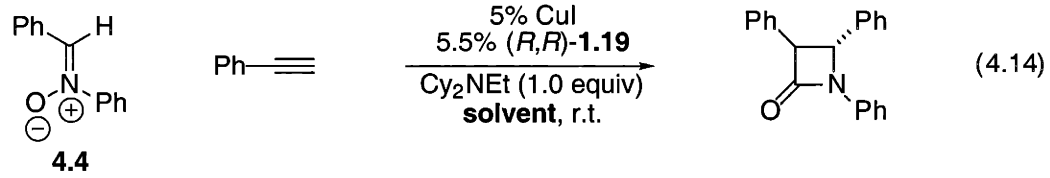
Table 4.4. Asymmetric Kinugasa reaction as a function of the added base (eq 4.13).

entry	base	GC yield (%)	trans : cis	% ee, cis
1	$PhNMe_2$	23	very slow reaction	
2	BTPP	0	no reaction	
3	DMAN	62	26 : 74	57
4	DABCO	77	17 : 83	55
5	Et_3N	74	11 : 89	58
6	$(i\text{-Pr})_2N(i\text{-Bu})$	68	8 : 92	57
7	Cy_2NMe	71	7 : 93	58
8	Cy_2NEt	71	3 : 97	57
9	$(t\text{-Bu})(i\text{-Pr})NMe$	72	3 : 97	56
10	PMP	72	2 : 98	56

Abbreviations: BTPP = *t*-butyliminotri(pyrrolidino)phosphorane; DMAN = 1,8-bis(*N*,*N*-dimethylamino)naphthalene; DABCO = 1,4-diazabicyclo[2.2.2]octane; PMP = 1,2,2,6,6-pentamethylpiperidine.

With the two major issues of the reaction (yield and cis diastereoselectivity) resolved, we sought to optimize the enantioselectivity of the reaction by exploring other solvents (Table 4.5). Solvents other than MeCN do provide better enantioselectivity, but none can compete with MeCN in terms of yield (entries 3–10). The solvent polarity has no bearing on the performance, as a polar solvent (EtOAc, entry 9) and a non-polar solvent (toluene, entry 10) give the same poor yield and enhanced enantioselectivity. CH_2Cl_2 is a choice that maintains some balance between yield and enantioselectivity (entry 8). We have tried to improve the yield in this solvent by screening different compounds as additives. Some of them do increase the rate of

the reaction without affecting its enantioselectivity, but none provides a yield in CH_2Cl_2 that is similar to that observed in MeCN.[35]



(4.14)

Table 4.5 Asymmetric Kinugasa reaction as a function of the solvent (eq 4.14).

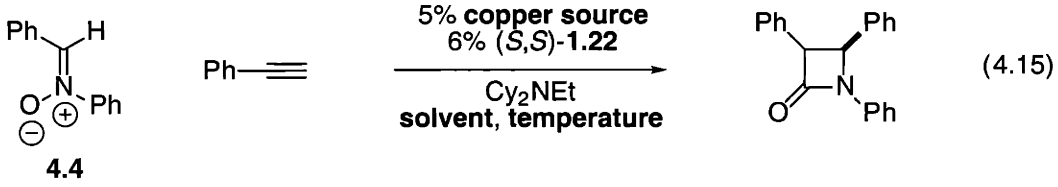
entry	**solvent**	GC yield (%)	trans : cis	% ee, cis
1	PhCN	57	9 : 91	52
2	MeCN	71	3 : 97	57
3	acetone	30	9 : 91	64
4	THF	18	7 : 93	67
5	$PhCF_3$	19	9 : 91	67
6	$CHCl_3$	26	16 : 84	68
7	HCO_2Me	20	11 : 89	69
8[a]	CH_2Cl_2	42	8 : 92	69
9	EtOAc	16	7 : 93	72
10	toluene	14	11 : 89	74

[a] Cy_2NMe was used instead of Cy_2NEt.

Having failed to secure any improvement to our catalytic system by a change of solvent, we decided to focus on the ligand **1.22**, since results from Table 4.3 show that **1.22** provides a better enantioselectivity than **1.19**. To overcome the concomitant lower activity of **1.22**, we reexamined the use of different copper sources (Table 4.6). CuCl was found to enhance the reactivity of the catalyst and afford a good yield in MeCN

35 Additives that have been examined and shown to accelerate the reaction or improve the final yield in CH_2Cl_2: Me_3N–O, *N*-methylmorpholine *N*-oxide, TEMPO, $(t\text{-BuO})_2$, and 2-azetidinone.

(entry 4). This change of copper source allows the reaction temperature to be lowered, further enhancing the yield and the enantioselectivity (entries 4–6).[36]



4.4

(4.15)

Table 4.6. Optimization for **1.22** as a ligand for the asymmetric Kinugasa reaction (eq 4.15).

entry	copper source	solvent	temperature	crude yield[a] (%)	trans : cis	% ee, cis
1	CuI	CH_2Cl_2	r.t.	32	11 : 89	83
2	CuCl	CH_2Cl_2	r.t.	29	9 : 91	82
3	$Cu(MeCN)_4PF_6$	MeCN	r.t.	57	< 5 : 95	75
4	CuCl	MeCN	r.t.	70	5 : 95	72
5[b]	CuCl	MeCN	0 °C	71	5 : 95	75
6	CuCl	MeCN	-20 °C	58[c]	< 5 : 95	77

[a] For all entries except entry 1, crude yield refers to yield by NMR. For entry 1, a yield by GC is reported. [b] Cy_2NMe was used as the base. [c] The reaction was incomplete.

II. Scope of the Reaction.

We expanded our study to other nitrones using the optimal conditions for the reaction between *N*,α-diphenylnitrone and phenylacetylene.[37] The nitrones that we used were prepared by two routes: (1) tandem reduction of a nitroarene[38]/condensation with an aldehyde (eq 4.16); and, (2) alkylation of a nitrosoarene in the presence of base (eq 4.17).

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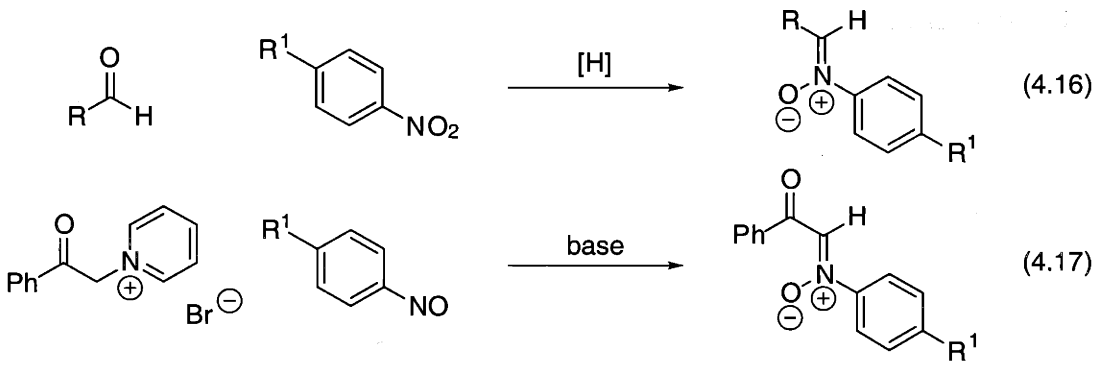
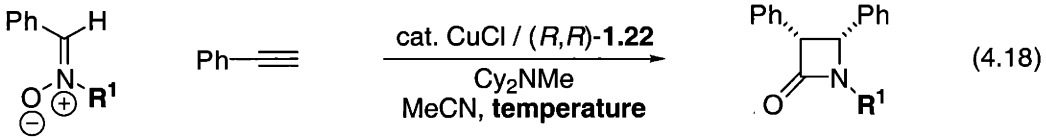
36 The principal side reaction that reduces the yield is the deoxygenation of the nitrone substrate to give the corresponding imine. This process can be minimized by lowering the reaction temperature.

37 Cy_2NMe is the base of choice because it gives a slightly faster and more reliable reaction than Cy_2NEt at temperatures lower than room temperature. A substoichiometric amount (20-fold relative to CuCl) is used in our optimized reactions.

38 The reduction is carried out either by H_2 with catalytic Pt/C, or by Zn dust.



We found that nitrones with *N*-aryl groups of different electronic nature undergo the reaction with good enantioselectivity.[39] The catalyst loading can be lowered to 2.5% for most *N*-aryl nitrones and to 1% for highly reactive nitrones (Table 4.7).



4.4, R^1 = Ph
4.5, R^1 = 4-(MeO)C_6H_4
4.6, R^1 = 4-(Br)C_6H_4
4.7, R^1 = 4-(EtO_2C)C_6H_4

Table 4.7. Catalytic asymmetric Kinugasa reaction: Influence of the N1-substituent (eq 4.18).[a,b]

entry	R^1	temperature	trans : cis	% ee, cis	isolated yield, cis (%)
1[c]	Ph	0 °C	5 : 95	77	69
2[d]	4-(MeO)C_6H_4	0 °C	5 : 95	85	53
3[d]	4-(Br)C_6H_4	0 °C	6 : 94	72	74
4[c]	4-(EtO_2C)C_6H_4	0 °C	6 : 94	67	79
5[d]	4-(EtO_2C)C_6H_4	-20 °C	5 : 95	71	91

[a] Cy_2NMe was used in 20-fold excess relative to CuCl. [b] All data represent the average of two runs, one with each enantiomer of the ligand. [c] 1% catalyst loading. [d] 2.5% catalyst loading.

39 *N*-Benzyl-α-phenylnitrone (R^1 = CH_2Ph) and *N*-(*t*-butyl)-α-phenylnitrone (R^1 = *t*-Bu) also react to some extent with phenylacetylene under the reaction conditions, but the rates appear to be slower, and hence these nitrones were not investigated further.

Electron-withdrawing substituents on the *N*-aryl ring furnish higher reactivity and yields, but lower enantioselectivity. Thus, at 0 °C, phenylacetylene reacts with the electron-rich nitrone **4.5** to give the product in 53% yield and 85% ee (entry 2) and with the electron-poor nitrone **4.7** in better yield (79%) but lower enantioselectivity (67%) (entry 4). The high cis diastereoselectivity, on the other hand, is not affected by the electronic nature of the *N*-aryl group.

To improve the reaction with **4.7**, we can take advantage of its reactivity and lower the reaction temperature to -20 °C (entry 5). The enantioselectivity improves from 67% to 71%, and the yield increases to 91%. This result illustrates a general feature of the reaction: *To maximize the yield and the stereoselectivity, the reaction should be carried out at the lowest possible temperature within the constraints of acceptable reaction time.*

It would be desirable to use an *N*-aryl group that can be easily removed from the products to furnish the N-unsubstituted 2-azetidinones. The 4-(MeO)C_6H_4 group (entry 2) has been used as one of the standard protecting groups for the nitrogen atom of 2-azetidinones, since it can be oxidatively removed by CAN. In principle, the 4-(Br)C_6H_4 group (entry 3) can be converted to an electron-rich aromatic ring through palladium-catalyzed amination or aryl ether formation, and subsequently removed by CAN oxidation.[40] This circuitous approach can be useful when the target nitrone requires stabilization from electron-deficient *N*-aryl groups.[41]

We then investigated the influence of the C4-substituent using nitrones with 4-(MeO)C_6H_4 as the *N*-aryl group and found that the reaction is not limited to nitrones bearing an α-aryl group (Table 4.8).

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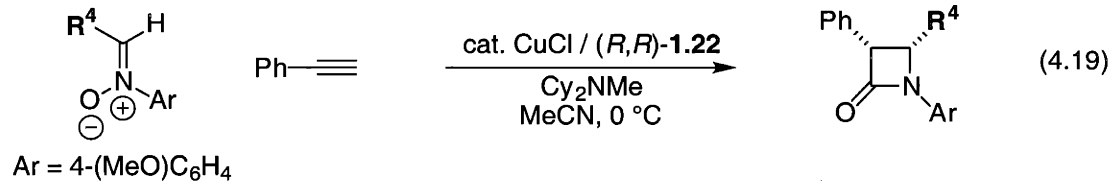
40 For a recent example on how a similar approach is used in a protective group strategy, see: Plante, O. J.; Buchwald, S. L.; Seeberger, P. H. *J. Am. Chem. Soc.* **2000**, *122*, 7148–7149.

41 Nitrones with electron-rich *N*-aryl groups are less stable and more difficult to be prepared.



(4.19)

Ar = 4-(MeO)C_6H_4

4.5, R^4 = Ph
4.8, R^4 = 4-(MeO)C_6H_4
4.9, R^4 = 4-(F_3C)C_6H_4
4.10, R^4 = Cy
4.11, R^4 = PhCO

Table 4.8. Catalytic asymmetric Kinugasa reaction: Influence of the C4-substituent (eq 4.19).[a,b]

entry	R^4	trans : cis	% ee, cis	isolated yield, cis (%)
1[c]	Ph	5 : 95	85	53
2[c,e]	4-(MeO)C_6H_4	7 : 93	90	50
3[c]	4-(F_3C)C_6H_4	7 : 93	83	46
4[d]	Cy	7 : 93	89	57
5[d]	PhCO	9 : 91	72	42

[a] Cy_2NMe was used in 20-fold excess relative to CuCl. [b] All data represent the average of two runs, one with each enantiomer of the ligand. [c] 2.5% catalyst loading. [d] 1% catalyst loading. [e] Reaction at r.t..

The reactivity of the nitrone is also quite sensitive to electronic effects of the α-substituent. Thus, nitrone **4.8** is less reactive than **4.5**, and its reaction has to be carried out at r.t. (entry 2). Both α-aliphatic (entry 4) and α-keto nitrones (entry 5) are more reactive than **4.5**; hence, the catalyst loading for their reaction can be decreased to 1%. The cis diastereomer is obtained with excellent stereoselectivity in most cases. The nature of the C4-substituent does not affect the enantioselectivity significantly, as nitrones with aryl groups of different electronic nature (entries 1–3) and aliphatic groups (entry 4) react with phenylacetylene to give the cis products in good enantiomeric excess. A phenacyl group, however, decreases the enantioselectivity (entry 5).

Some of the products that are formed from phenylacetylene and other nitrones under the catalysis of Cu/**1.22** are shown in Figure 4.6.

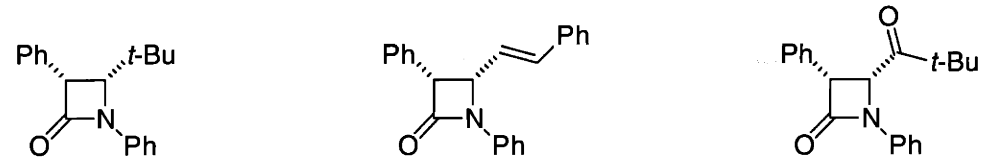


Figure 4.6. Products that are formed from phenylacetylene and other nitrones under the catalysis of Cu/**1.22**.

The scope of the reaction with respect to alkynes was examined with nitrones bearing the more reactive cyclohexyl group (**4.10**) and phenacyl group (**4.12**) (Table 4.9). In general, the reactivity of the alkynes $R^3C{\equiv}CH$ ranks roughly as follows: R^3 = electron-poor aromatic > electron-rich aromatic ~ 1° aliphatic > alkenyl > 3° silyl > 2° aliphatic > 3° aliphatic.[42] The nitrones **4.10** and **4.12** are reactive enough to allow the reaction to be conducted at 1% catalyst loading and at lower temperatures. Aromatic alkynes (entries 1–3, 6) and alkenyl alkynes (entries 5 and 7) are good substrates for these nitrones, furnishing the cis product in excellent stereoselectivity. The electronic nature of the aromatic ring of the alkyne affects only the reactivity but not the stereoselectivity (entries 1–3). Alkynes bearing primary alkyl groups, such as 3-phenylpropyne, afford products in significantly lower diastereoselectivity, although these products are still formed in good enantiomeric excess (entry 4).

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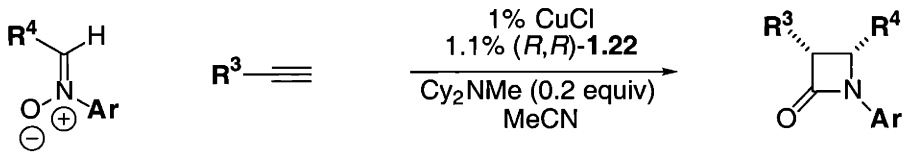
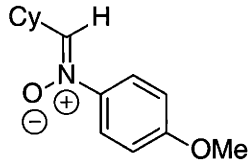
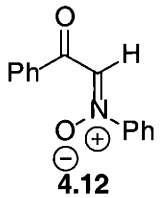
42 Alkynes with electron-withdrawing groups react with tertiary amines by some other pathway, and hence the desired reaction with nitrones only takes place in the *absence* of base. The few exploratory experiments with *N*,α-diphenylnitrone and ethyl propiolate indicate that the enantioselectivity is poor.



(4.20)



4.10



4.12

Table 4.9. Catalytic asymmetric Kinugasa reaction:
Scope of the alkynes with respect to **4.10** and **4.12** (eq 4.20).[a]

entry	nitrone	R^3	trans : cis	% ee, cis	isolated yield, cis (%)
1[b]	**4.10**	Ph	< 5 : 95	92	65
2[b]	**4.10**	4-(MeO)C_6H_4	8 : 92	91	60
3[b]	**4.10**	4-(F_3C)C_6H_4	< 5 : 95	93	57
4[b]	**4.10**	$PhCH_2$	29 : 71	73 (70)	43 (17)
5[b]	**4.10**	1-cyclohexenyl	< 5 : 95	84	63
6[c]	**4.12**	Ph	10 : 90	90	56
7[c]	**4.12**	1-cyclohexenyl	10 : 90	91	45

[a] Except for entry 5, all data represent the average of two runs, one with each enantiomer of the ligand. The values in parentheses refer to those corresponding to the trans product. [b] Reaction at -20 °C. [c] Reaction at -40 °C.

Some of the less successful examples that are formed under the catalysis of Cu/**1.22** are shown in Figure 4.7.

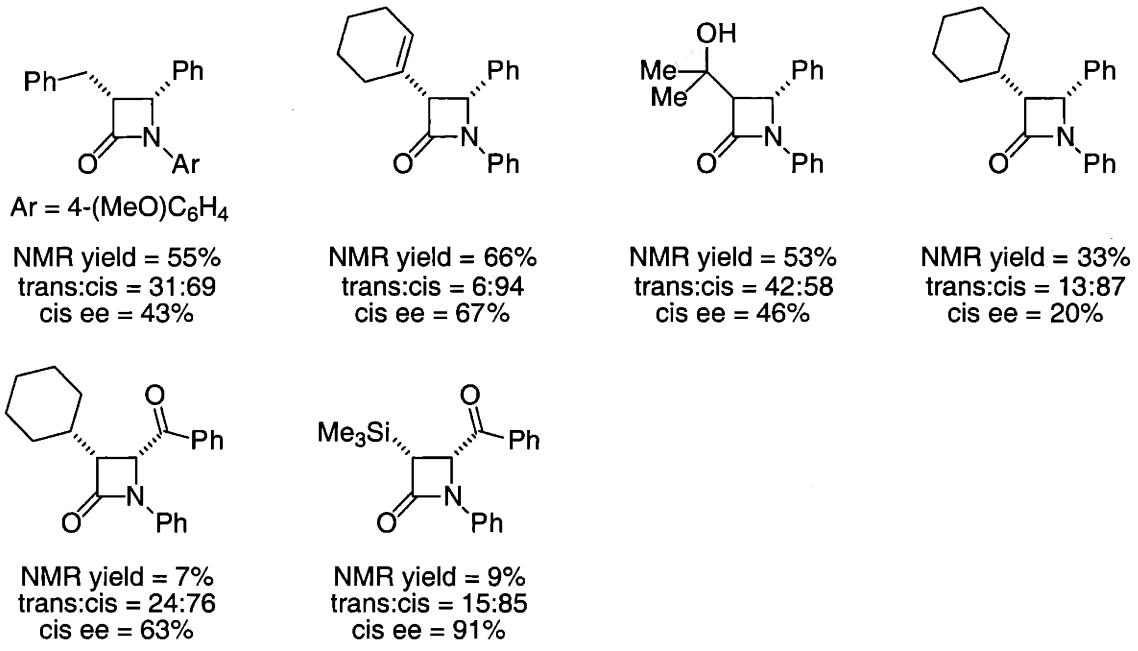
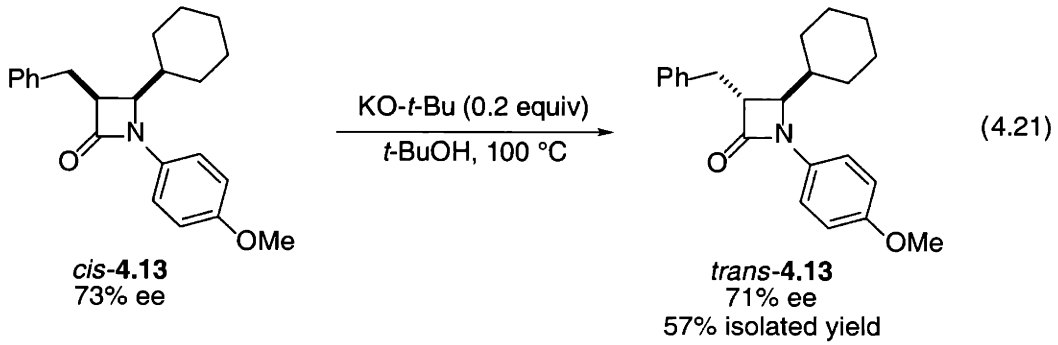


Figure 4.7. Less successful examples of the asymmetric Kinugasa reaction under the catalysis of Cu/**1.22**.

Under our reaction conditions, the cis 2-azetidinone is usually obtained with excellent stereoselectivity. Epimerization of this kinetic product should afford the trans diastereomer.[43] Miura has applied this strategy to obtain the trans diastereomer with 1,3,4-triphenyl-2-azetidinone.[28b] To show its generality for our cis 2-azetidinone products, we explored the epimerization of **4.13**, which has a relatively non-acidic proton at C3 (eq 4.21).

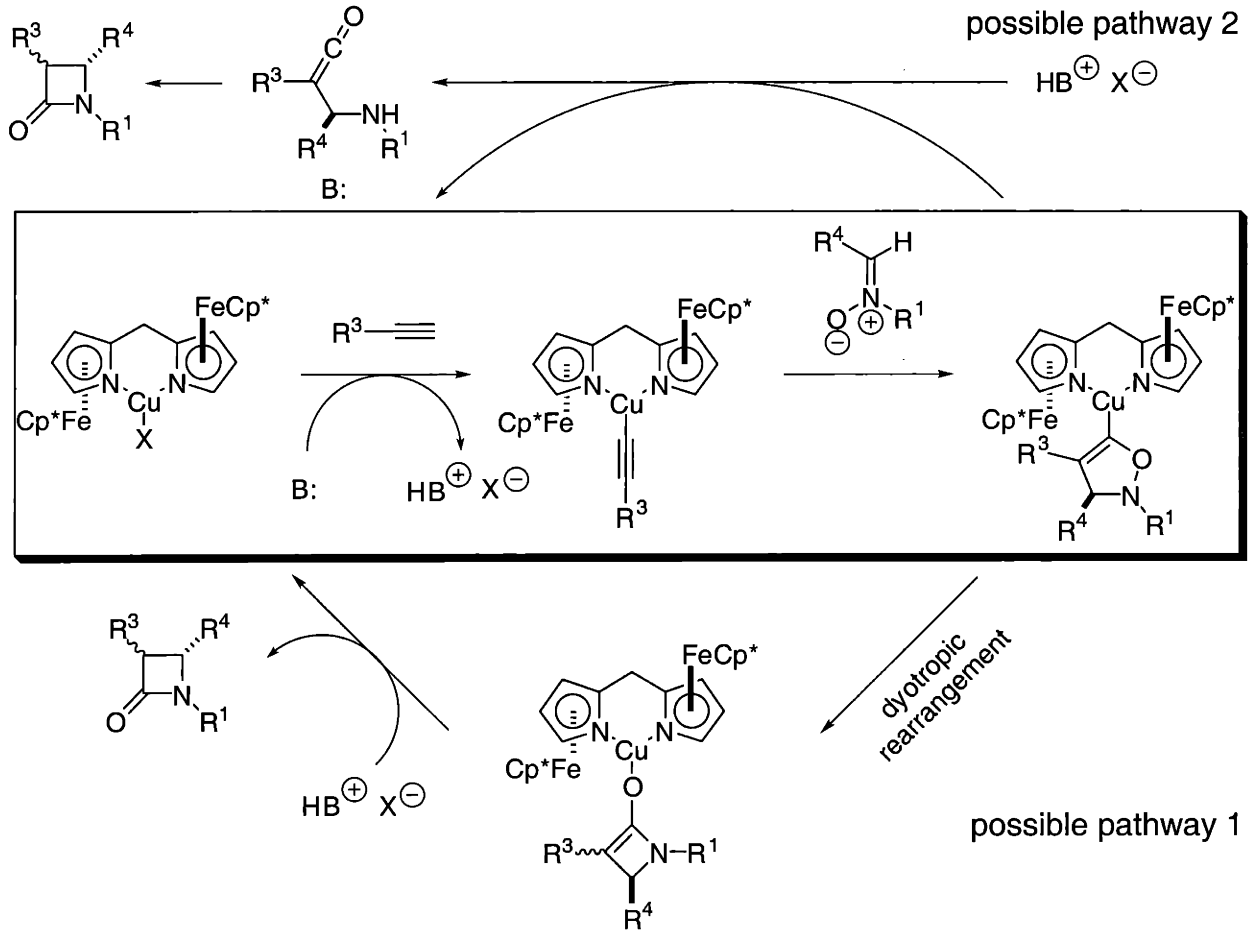


43 For examples involving 3,4-disubstituted 2-azetidinones, see: (a) TMSOTf–Et_3N: Chiba, T.; Nakai, T. *Tetrahedron Lett.* **1985**, *26*, 4647–4648. (b) KO-*t*-Bu: Fujisawa, T.; Ichikawa, M.; Ukaji, Y.; Shimizu, M. *Tetrahedron Lett.* **1993**, *34*, 1307–1310.

By heating *cis*-**4.13** in *t*-BuOH with a catalytic amount of KO-*t*-Bu, *trans*-**4.13** is obtained. Epimerization takes place exclusively at C3, and the isolated yield is fair. Further optimization would improve this route for enantiomerically enriched trans 2-azetidinones.

III. Proposed Mechanism and Stereochemical Model.

A possible catalytic cycle is proposed as follows:[44]



Scheme 4.2. Proposed catalytic cycle for the asymmetric Kinugasa reaction.

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44 The key step, 1,3-dipolar cycloaddition between a copper acetylide and a nitrone, was first proposed by Irwin (ref. 21).

1. The catalytic copper complex reacts with the terminal alkyne in the presence of a base (B:) to form a copper acetylide.
2. The copper acetylide undergoes 1,3-dipolar cycloaddition with the nitrone to give an isoxazole with copper at the 5-position. *This step is the stereodetermining step in which one prochiral face of the nitrone reacts preferentially over the other* (Figure 4.8).

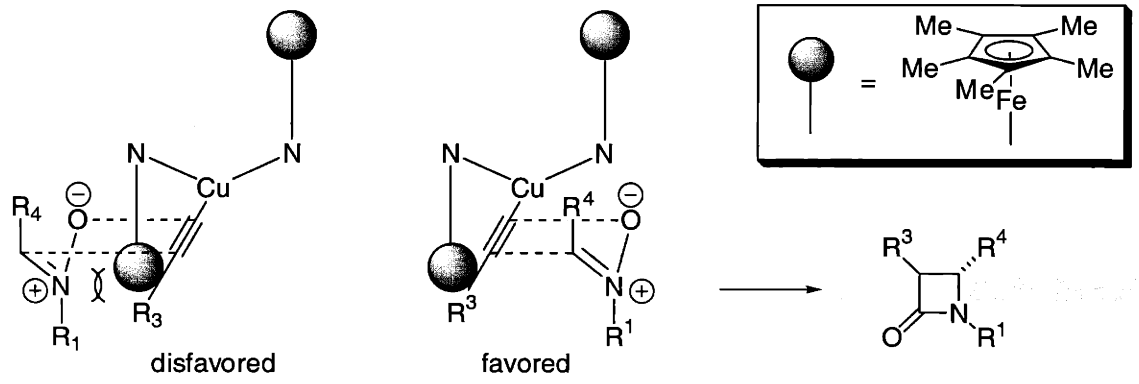

Figure 4.8. Stereochemical model for the prediction of the absolute stereochemistry of the product.

The origin of the stereodifferentiation arises from the repulsive interactions between the R^1 substituent of the nitrone and the methyl groups of the Cp* ring. The model predicts that the (*R*,*R*)-bis(azaferrocene) should favor the formation of the (4*R*)-enantiomer, which is consistent with the experimental result.[45]

After the formation of the isoxazole intermediate, there are two possible pathways to regenerate the copper catalyst:[46]

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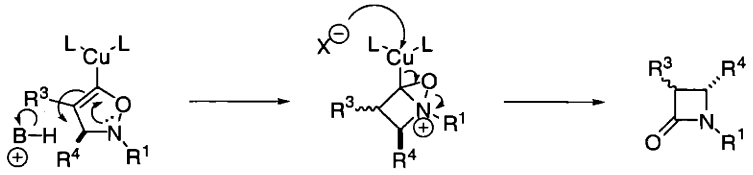
45 The absolute stereochemistry of (3*S*,4*S*)-1-(4-bromophenyl)-3,4-diphenyl-2-azetidinone was unambiguously determined by X-ray crystallography. Assignment of the absolute configuration of the other products is by analogy.

46 Irwin proposed in ref. 21 that after proton transfer, the isoxazole rearranges to give a strained bicyclo[2.1.0] species, which releases the 2-azetidinone upon nucleophilic attack of the counterion.



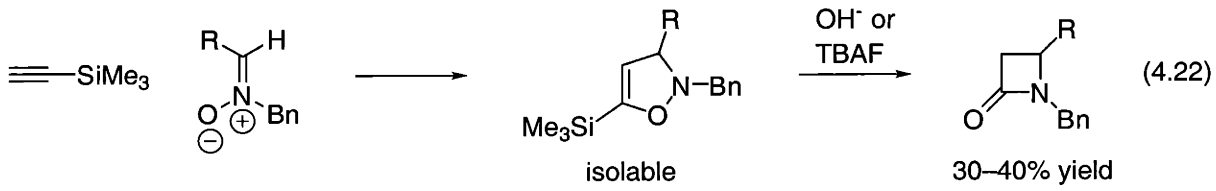
Pathway 1

3. The copper fragment and the nitrogen atom undergo a dyotropic rearrangement[47] across the C–O bond, generating a copper enolate of the 2-azetidinone.
4. Protonation of the enolate releases the 2-azetidinone product and regenerates the copper complex. *This step sets the relative stereochemistry of the 2-azetidinone ring.*

Pathway 2

3. The copper catalyst is regenerated by a nucleophilic attack of the counterion X^-, and the N–O bond in the isoxazole is cleaved to form a ketene intermediate.
4. The nitrogen atom attacks the electrophilic carbon of the ketene intramolecularly, closing the 2-azetidinone ring and *setting the relative stereochemistry.*

The unusual reactivity pattern between copper acetylides and nitrones to furnish 2-azetidinones bears some resemblance to that between silylacetylenes and nitrones. DeShong has reported that (trimethylsilyl)acetylene undergoes 1,3-dipolar cycloadditions with nitrones to give 5-(trimethylsilyl)isoxazoles with high regioselectivity. Treatment of these adducts with hydroxide or fluoride affords 2-azetidinones in modest yields (eq 4.22).[48]

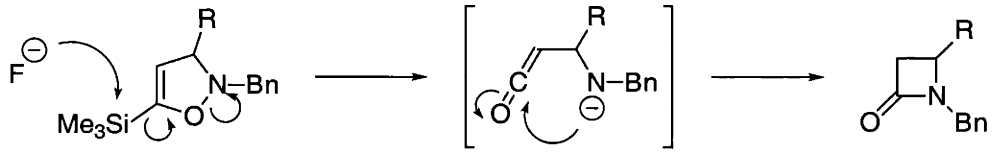


(4.22)

To account for the rearrangement, DeShong proposed that the fluoride attacks the trimethylsilyl group, cleaving the N–O bond and forming a ketene intermediate.

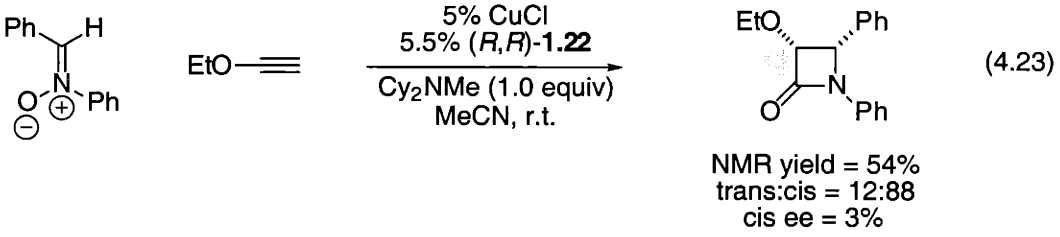
47 For a review, see: Reetz, M. T. *Adv. Organomet. Chem.* **1977**, *16*, 33–65.
48 Ahn, C.; Kennington, J. W., Jr.; DeShong, P. *J. Org. Chem.* **1994**, *59*, 6282–6286.

Intramolecular attack by the amide on the ketene furnishes the 2-azetidinone product. This proposal is similar to our second rearrangement pathway.



IV. Potential Applications.

Most biologically active 2-azetidinones contain a heteroatom at C3. The synthesis of these products through the Kinugasa reaction requires the use of a heteroatom-substituted alkyne. We have contemplated this possibility and examined the reaction between *N*,α-diphenylnitrone and ethoxyacetylene, both of which are commercially available (eq 4.23).



(4.23)

Though the product is essentially racemic, the experiment established that the reactivity of a heteroatom-substituted alkyne is similar to phenylacetylene, affording a moderate yield of the product in good cis diastereoselectivity. Given that alkynes bearing smaller substituents afford lower enantioselectivity in the reaction, further improvements to the enantioselection may come from alkynes bearing heteroatoms with sterically demanding groups, such as BHA.[49] Alternatively, alkynes containing

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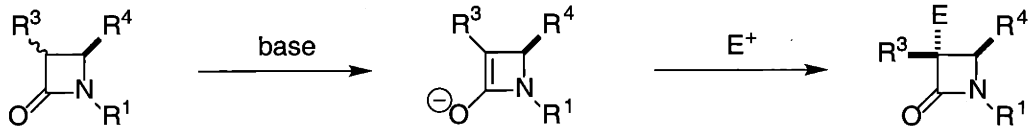
49 BHA = butylated hydroxyanisole, or 2,6-di-*t*-butyl-4-methoxyphenol.

silyl substituents that are masked hydroxy groups, e.g., $PhMe_2Si$ or $(EtO)_3Si$, could also be investigated.[50]

The absolute stereochemistry of the 2-azetidinone product at C4 is controlled by the ligand. We can take advantage of this feature in the synthesis of 2-azetidinones that inhibit cholesterol absorption, since SAR studies have established that the key for those compounds to have pharmacological activity is a (4*S*)-alkoxyaryl substituent.[51]

In a broader context, the substituent at C4 in our 2-azetidinone products can direct the subsequent installation of various substituents or fragments at C3 in the following stereoselective fashions:

1. Upon deprotonation, both diastereomers give the same enolate. Under kinetic conditions, the electrophile E^+ is delivered to the less hindered face of the enolate, thus forming a 3,3,4-trisubstituted 2-azetidinone stereoselectively with the initial 3,4-substituents cis to each other.

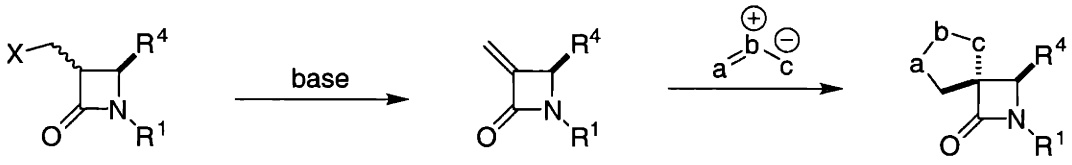


50 For a review of the oxidation of the carbon–silicon bond, see: Jones, G. R.; Landis, Y. *Tetrahedron* **1996**, *52*, 7599–7662.

51 For reports on the asymmetric syntheses of SCH 48461 and its analogs, which involve the use of chiral auxiliaries, see: (a) Burnett, D. A. *Tetrahedron Lett.* **1994**, *35*, 7339–7342. (b) Braun, M.; Galle, D. *Synthesis* **1996**, 819–820. (c) Shankar, B. B.; Kirkup, M. P.; McCombie, S. W.; Clader, J. W.; Ganguly, A. K. *Tetrahedron Lett.* **1996**, *37*, 4095–4098. (d) Vaccaro, W. D.; Sher, R.; Davis, H. R., Jr. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 319–322. (e) Wu, G. G. *Org. Process Res. Dev.* **2000**, *4*, 298–300.

This strategy has been validated with alkyl groups,[52] halogens,[53] nitrogen,[54] and sulfur[55] as electrophiles. It is possible to have the electrophile E^+ very similar to the substituent R^3; in those cases, alternative methods such as the Staudinger reaction are unlikely to provide effective control over the diastereoselectivity.[56]

2. If we incorporate a leaving group at the α-position in the C3-side chain, base elimination will generate 4-substituted 3-methylene-2-azetidinones. Since the C=C double bond is activated, these products now serve as good dienophiles or dipolarophiles for further reaction. Again, to minimize steric interactions with the C4-substituent, the diene or the dipole approaches from the less hindered face of the 2-azetidinone.[57] This method can be used to introduce heteroatoms stereospecifically to the 2-azetidinone core.



Alternatively, when the C4-substituent is a benzoyl group, we can make use of the stereochemistry installed at C3 for further stereoselective elaboration of the product.

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52 For some examples, see: (a) Firestone, R. A.; Schelechow, N.; Johnston, D. B. R.; Christensen, B. G. *Tetrahedron Lett.* **1972**, *5*, 375–378. (b) Brunwin, D. M.; Lowe, G. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1321–1328. (c) Finke, P. E.; Shah, S. K.; Flectcher, D. S.; Ashe, B. M.; Brause, K. A.; Chandler, G. O.; Dellea, P. S.; Hand, K. M.; Maycock, A. L.; Osinga, D. G.; Underwood, D. J.; Weston, H.; Davies, P.; Doherty, J. B. *J. Med. Chem.* **1995**, 38, 2449–2462.

53 (a) Fluroine: Genêt, J.-P.; Durand, J.-O.; Roland, S.; Savignac, M.; Jung, F. *Tetrahedron Lett.* **1997**, *38*, 69–72. (b) Chlorine: Moore, H.; Hughes, G. *Tetrahedron Lett.* **1982**, *23*, 4003–4006.

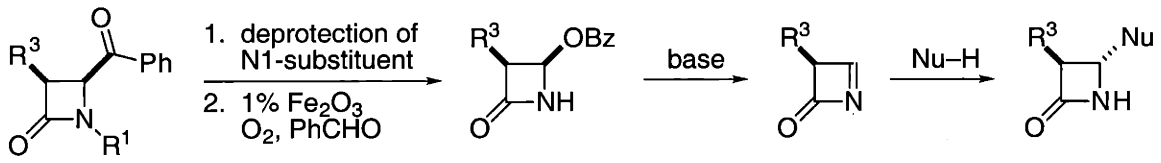
54 For some examples, see: (a) Pearson, M. J.; Tyler, J. W. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1927–1933. (b) Cossío, F. P.; Odriozola, J. M.; Oiarbide, M.; Palomo, C. *J. Chem. Soc., Chem. Commun.* **1989**, 74–76.

55 For some examples, see: (a) Bateson, J. H.; Quinn, A. M.; Southgate, R. *J. Chem. Soc., Chem. Commun.* **1986**, 1151–1152. (b) Nagao, Y.; Abe, T.; Shimizu, H.; Kumagai, T.; Inoue, Y. *Heterocycles* **1992**, *33*, 523–528.

56 This trans relationship between the electrophile and the R^4 substituent has been exploited to achieve diastereocontrol in the stereoselective synthesis of a 2-azaspiro[3.5]nonan-1-one. See: Chen, L.-Y.; Zaks, A.; Chackalamannil, S.; Dugar, S. *J. Org. Chem.* **1996**, *61*, 8341–8343.

57 For examples, see: (a) Basak, A.; Bdour, H. M. N.; Bhattacharya, G. *Tetrahedron Lett.* **1997**, *38*, 2535–2538. (b) Anklam, S.; Liebscher, J. *Tetrahedron* **1998**, *54*, 6369–6384.

Baeyer-Villiger oxidation of the benzoyl substituent provides 4-benzoyloxy-2-azetidinones.[58] Similar to 4-acetoxy-2-azetidinones, these intermediates can be readily functionalized at C4,[59] because they undergo displacement of the benzoyloxy group by a variety of carbon, oxygen, nitrogen, and sulfur nucleophiles.[60] The displacement occurs through a E1cB elimination–addition pathway, and, being shielded by the C3-substituent, the 1-azetin-4-one intermediate will undergo nucleophilic attack from the less hindered face to afford a trans product.



58 Murahashi, S.-I.; Oda, Y.; Naota, T. *Tetrahedron Lett.* **1992**, *33*, 7557–7560.

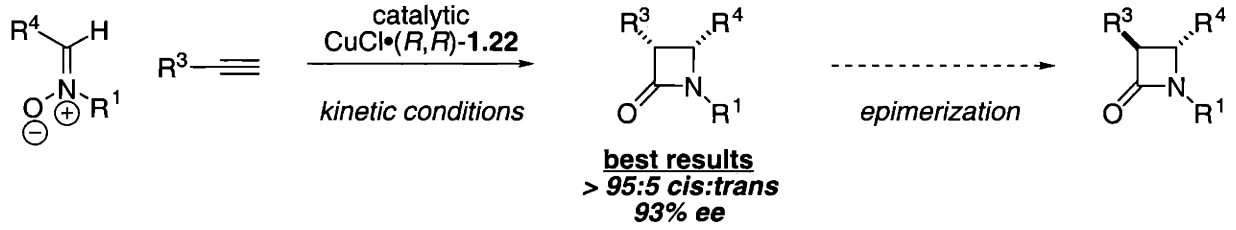
59 4-Benzoyloxy-2-azetidinones have been reported as synthetic intermediates in (a) penems: Hanessian, S.; Bedeschi, A.; Battistini, C.; Mongelli, N. *J. Am. Chem. Soc.* **1985**, *107*, 1438–1439. (b) thienamycin, carbapenems: Tschaen, D. M.; Fuentes, L. M.; Lynch, J. E.; Laswell, W. L.; Volante, R. P.; Shinkai, I. *Tetrahedron Lett.* **1988**, *29*, 2779–2782.

60 For a review of nucleophilic displacement reactions at C4, see ref. 1a. For specific examples, see: (a) Carbon: Ref. 59b. (b) Oxygen: Easton, C. J.; Love, S. G.; Wang, P. *J. Chem. Soc., Perkin Trans. 1* **1990**, 277–282. (c) Sulfur: Ref. 59a.

C. Conclusions.

We have achieved the three goals that we have set for improving the Kinugasa reaction: (a) the reaction is catalytic in copper (as low as 1%); (b) the reaction can give high cis diastereoselectivity (can be greater than 95:5) when a sterically demanding tertiary amine is employed as an added base; and, (c) high enantioselectivity is attained for a number of nitrones and alkynes bearing either aromatic or aliphatic substituents (up to 93%). The isolated yields for the cis 2-azetidinones range from moderate to excellent.

Our copper/**1.22** complex represents the most general catalyst for the stereoselective synthesis of 2-azetidinones based on the Kinugasa reaction. The configuration of the ligand controls the absolute stereochemistry at C4, while the reaction conditions determine the product configuration at C3.



A stereochemical model that can account for the observed asymmetric induction has been proposed. Finally, we have outlined some possible applications for the 3,4-disubstituted 2-azetidinones to enhance the utility of the reaction. We anticipate that the salient features of the reaction, which include the ready availability of the substrates and a tolerance to a wide range of functional groups, should make it an attractive route for the synthesis of biologically relevant 2-azetidinone derivatives.

D. Experimental.

I. General.

^{1}H and ^{13}C nuclear magnetic resonance spectra were recorded on a Varian VXR-500 NMR spectrometer at ambient temperature. ^{1}H data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane (δ scale), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broadened), integration, and coupling constant (Hz). ^{13}C chemical shifts are reported in parts per million downfield from tetramethylsilane (δ scale). All ^{13}C spectra were determined with broadband ^{1}H decoupling.

Infrared spectra were obtained on a Perkin-Elmer Series 1600 FT-IR spectrophotometer. High resolution mass spectra were recorded on a Finnegan MAT System 8200 spectrometer or a Bruker Daltonics Apex FT-ICR-MS (3 Tesla). Melting points were obtained on a Thomas Hoover Unimelt capillary melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter and are reported as follows: $[\alpha]^{Temp\ (^{\circ}C)}_{\lambda\ (nm)}$ (*c* solvent, enantiomeric purity).

Preparative achiral HPLC was performed on an Alltech Econosphere Silica 10U column (22 mm x 250 mm). Analytical chiral HPLC was performed on a Daicel Chiralcel OD column (4.6 mm x 25 cm). Analytical TLC was performed using EM Science 0.25 mm silica gel 60 plates and visualized with either UV light or ethanolic phosphomolybdic acid. Flash chromatography was performed on EM Science silica gel 60 (230–400 mesh).

THF, toluene, CH_2Cl_2 were purified by passing the solvent through two packed columns of neutral alumina and copper(II) oxide under argon. Anhydrous MeCN, PhCN, $CHCl_3$, HCO_2Me, EtOAc and DMF were purchased from Aldrich. $PhCF_3$ was distilled from calcium hydride.

Unless otherwise stated, all reagents were purchased from commercial suppliers and used as received. Alkynes, Cy_2NMe and Cy_2NEt were purified by distillation from calcium hydride under reduced pressure. *N*-Phenyl-α-benzoylnitrone[61] and 4-methoxynitrosobenzene[62] were synthesized according to literature procedures.

All reactions were carried out with magnetic stirring in oven-dried glassware under an atmosphere of argon (manifold) or under an atmosphere of nitrogen (Vaccum Atmospheres glove box), unless otherwise noted.

II. Synthesis of Nitrones.

The yields have not been optimized.

One-pot synthesis of nitrones from aldehydes and nitroarenes. General procedure A.[63] To a 500-mL round-bottom flask were added the nitroarene (50 mmol), the aldehyde (50 mmol), and NH_4Cl (65 mmol). The reaction mixture was suspended in a mixture of EtOH (100 mL) and water (100 mL), and cooled to 0 °C. Zinc (100 mmol) was added slowly to the reaction mixture over 4 h at 0 °C, which was then warmed up to r.t. and stirred for another 12 h. The reaction mixture was filtered through Celite. The filtrate was extracted by CH_2Cl_2, while the residue was washed with more CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo to afford

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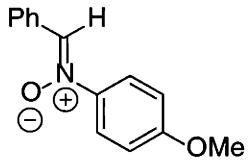
61 Huisgen, R.; Hauck, H.; Seidl, H.; Burger, M. *Chem.Ber.* **1969**, *102*, 1117–1128.

62 Mel'nikov, E. B.; Suboch, G. A.; Belyaev, E. Yu. *Russ. J. Org. Chem.* **1995**, *31*, 1640–1642.

63 After we have finished the synthesis of nitrones, Vallée reported a similar one-pot synthesis of functionalized nitrones from aldehydes and nitro compounds. See: Gautheron-Chapoulaud, V.; Pandya, S. U.; Cividino, P.; Masson, G.; Py, S.; Vallée, Y. *Synlett* **2001**, *8*, 1281–1283.

the crude product, which was then purified by flash chromatography or crystallized to afford the pure nitrone.

One-pot synthesis of nitrones from aldehydes and nitroarenes. General procedure B. The procedure was modified from the procedure of Davis[64] for the synthesis of *N*,α-diarylnitrones and the procedure of Tetsuo[65] for the synthesis of *N*-arylhydroxylamine. To a round-bottom flask were added the nitroarene (1.0 equiv), the aldehyde (1.0 equiv), 5% Pt/C (5 mg/mmol of nitroarene), $P(OEt)_3$ (0.005 equiv), and $MeSO_3H$ (0.015 equiv). H_2 was introduced through the septum-capped flask through a balloon. The progress of the reaction was monitored by TLC. When either all of the starting nitroarene had been consumed or the corresponding imine (from condensation of aldehyde with aniline/reduction of nitrone) started to form, the reaction mixture was filtered. The filtrate was concentrated in vacuo, and the crude product was purified by either flash chromatography or crystallization.



***N*-(4-Methoxyphenyl)-α-phenylnitrone.** General procedure A was followed. The product was recrystallized from CH_2Cl_2/hexanes (63% yield).

The ^1H NMR spectrum of the product matched the literature data.[66] ^{13}C NMR (126 MHz, $CDCl_3$): δ 55.8, 114.2, 123.1, 128.7, 129.1, 130.8, 131.0, 133.8, 142.5, 160.7.

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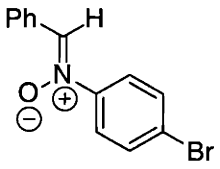
64 West, P. R.; Davis, G. C. *J. Org. Chem.* **1989**, *54*, 5176–5180.

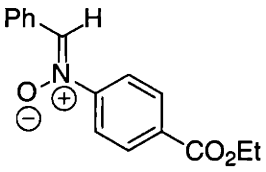
65 Tetsuo, T. (Showa Denko K. K., Japan). Selective Hydrogenation of Aromatic Nitro Compounds. Japan Kokai Tokkyo Koho 54-24837, 1979.

66 Arumugam, N.; Manisankar, P.; Sivasubramanian, S.; Wilson, D. A. *Org. Magn. Reson.* **1984**, *22*, 592–596.



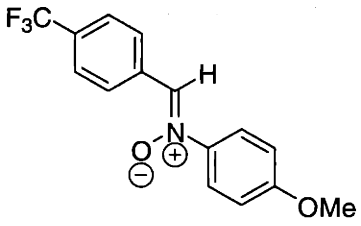
***N*-(4-Bromophenyl)-α-phenylnitrone.** General procedure B was followed. The product was recrystallized from THF/CH_2Cl_2/hexanes (34% yield).

The ^1H NMR spectrum of the product matched the literature data.[66] ^{13}C NMR (126 MHz, $CDCl_3$): δ 123.5, 124.0, 128.9, 129.3, 130.6, 131.4, 132.5, 134.8, 148.1. IR (KBr): 3055 (w), 1547 (m), 1481 (m), 1445 (s), 1416 (s), 1384 (m), 1191 (s), 1068 (s), 1009 (m), 886 (m), 844 (m), 816 (s), 751 (s), 688 (s) cm^{-1}.



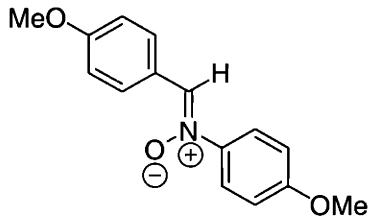
***N*-(4-Carboethoxyphenyl)-α-phenylnitrone.** General procedure A was followed. The product was recrystallized from CH_2Cl_2/hexanes (37% yield).

The ^1H NMR spectrum of the product matched the literature data.[64] ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.5, 61.7, 122.0, 129.0, 129.5, 130.5, 130.9, 131.7, 132.1, 135.6, 152.0, 165.5.



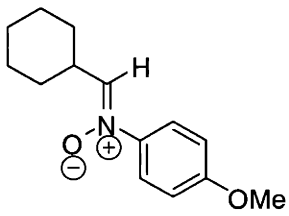
***N*-(4-Methoxyphenyl)-α-(4-trifluoromethylphenyl)nitrone.** General procedure A was followed. The product was recrystallized from CH_2Cl_2/hexanes (32% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.88 (s, 3H), 6.98 (d, 2H, J = 9.2), 7.71 (d, 2H, J = 8.2), 7.74 (d, 2H, J = 8.9), 7.96 (s, 1H), 8.49 (d, 2H, J = 8.5). ^{13}C NMR (126 MHz, $CDCl_3$): δ 56.9, 114.4, 123.2, 124.0 (q, $^1J_{C-F}$ = 272), 125.7 (q, $^3J_{C-F}$ = 3.9), 129.0, 131.8 (q, $^2J_{C-F}$ = 32.6), 132.3, 134.1, 142.4, 161.2. IR (KBr): 3100 (w), 3060 (w), 2970 (w), 2845 (w), 1606 (m), 1597 (m), 1548 (m), 1505 (s), 1409 (m), 1328 (s), 1260 (m), 1200 (m), 1162 (s), 1124 (s), 1080 (s), 851 (s), 831 (s) cm^{-1}. mp 183 °C. HRMS–EI (*m/z*): M^+ calcd for $C_{15}H_{12}F_3NO_2$, 295.0815; found, 295.0825.



***N*,α-Bis(4-methoxyphenyl)nitrone.** General procedure B was followed. The crude product was purified by flash chromatography (25/75 EtOAc/$CHCl_3$) to afford a white, cotton-like solid (12% yield).

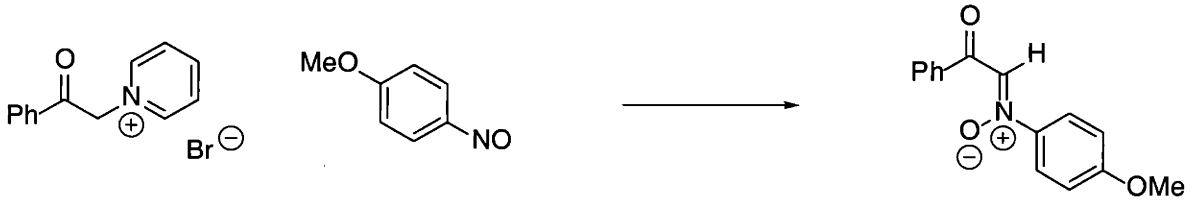
^{1}H NMR (500 MHz, $CDCl_3$): δ 3.86 (s, 3H), 3.88 (s, 3H), 6.95 (d, 2H, J = 8.9), 6.99 (d, 2H, J = 9.2), 7.72 (d, 2H, J = 9.2), 7.80 (s, 1H), 8.39 (d, 2H, J = 8.9). ^{13}C NMR (126 MHz, $CDCl_3$): δ 55.6, 55.8, 114.2, 123.0, 124.1, 131.2, 133.5, 142.5, 160.5, 161.5. IR (KBr): 3042 (w), 2935 (w), 2838 (w), 1605 (s), 1507 (s), 1304 (m), 1250 (s), 1179 (s), 1070 (s), 1026 (s), 849 (m), 829 (m), 754 (w) cm^{-1}. mp 147–149 °C. HRMS–EI (*m/z*): M^+ calcd for $C_{15}H_{15}NO_3$, 257.1046; found, 257.1051.



***N*-(4-Methoxyphenyl)-α-cyclohexylnitrone.** General procedure A was followed. The crude product was purified by flash chromatography (50/50 EtOAc/hexanes → 75/25 → 100% EtOAc) to afford a white crystalline solid (10% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.28 (dq, 3H, *J* = 3.1, 12.0), 1.44 (tq, 2H, *J* = 3.1, 12.2), 1.68–1.80 (m, 3H), 1.96–2.04 (m, 2H), 3.18 (tdt, 1H, *J* = 3.7, 7.3 ,11.0), 3.83 (s, 3H), 6.90 (d, 2H, *J* = 9.2), 6.99 (d, 1H, *J* = 7.3), 7.60 (d, 2H, *J* = 9.2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 25.4, 26.1, 29.0, 35.8, 55.7, 114.0, 123.0, 141.3, 142.6, 160.5. IR (KBr): 3047 (m), 2929 (s), 2848 (m), 1607 (m), 1596 (m), 1505 (s), 1447 (m), 1250 (s), 1061 (s), 1028 (m), 845 (s), 808 (m) cm^{-1}. mp 120 °C. HRMS–EI (*m/z*): M^+ calcd for $C_{14}H_{19}NO_2$, 233.1410; found, 233.1410.

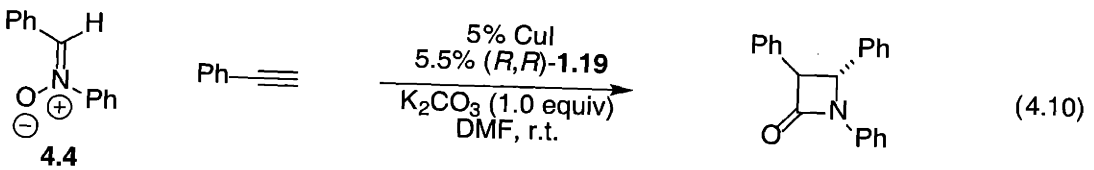
Alkylation of a nitrosoarene in the presence of base.



***N*-(4-Methoxyphenyl)-α-benzoylnitrone.** The procedure of Huisgen for the synthesis of *N*-phenyl-α-benzoylnitrone was modified.[61] 4-Methoxynitrosobenzene (1.39 g, 10.1 mmol) was dissolved in EtOH (45 mL) and cooled to -10 °C. A solution of 1-phenacylpyridinium bromide (2.85 g, 10.2 mmol) in water (10 mL) was added, followed by the slow addition of a solution of NaOH (0.405 g, 10.1 mmol) in water (10 mL) over 30 min, during which the green homogeneous reaction mixture slowly turned into a yellow slurry. After being stirred for another 30 min at -10 °C, the reaction mixture was filtered to afford a golden yellow solid (2.004 g, 78% yield). ^{1}H NMR indicated that the nitrone was an ~ 90:10 diastereomeric mixture. The diastereomeric ratio remained unchanged either after being heated in $CDCl_3$ to 60 °C or recrystallization.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.88 (s, 3H), 6.97 (d, 2H, J = 9.2), 7.46–7.52 (m, 2H), 7.58 (tt, 1H, J = 1.5, 7.4), 7.77 (d, 2H, J = 9.2), 7.91–7.95 (m, 2H), 8.30 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 56.0, 114.4, 123.4, 128.0, 128.3, 128.9, 133.5, 137.5, 142.3, 162.2, 184.3 (major diastereomer) 55.8, 114.1, 125.1, 128.4, 129.2, 131.6, 134.0, 137.0, 140.8, 161.4, 181.9 (minor diastereomer). IR (KBr): 3070 (w), 1651 (s), 1594 (m), 1500 (s), 1486 (s), 1261 (m), 1239 (m), 1209 (m), 1021 (m), 833 (m), 745 (m), 696 (m) cm^{-1}. mp 70 °C. dec. HRMS–ESI (m/z): $[M + Na]^+$ calcd for $C_{15}H_{13}NO_3$, 278.0788; found, 278.0784.

III. Kinugasa Reaction between *N*,α-Diphenylnitrone and Phenylacetylene under Miura Conditions (eq 4.10).



(4.10)

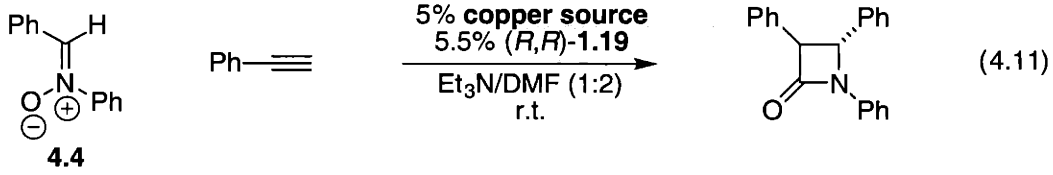
A solution of CuI (1.8 mg, 9.5 μmol) and (*R*,*R*)-**1.19** (5.8 mg, 11 μmol) was prepared in DMF (1 mL). After 45 min, the catalyst solution was added into a round-bottom flask containing **4.4** (38.4 mg, 0.195 mmol) and K_2CO_3 (26.4 mg, 0.191 mmol), and more DMF was added until the total volume is 3 mL. A solution of phenylacetylene (19.8 mg, 0.194 mmol) in DMF (0.5 mL) was added over 4 h to the reaction mixture using a syringe pump, during which the orange solution turned opaque. After 2.5 more h, the reaction mixture was filtered through a plug of silica with Et_2O as the eluant. The organic layer was washed with water, brine, dried ($MgSO_4$), and concentrated in vacuo to afford a brown liquid.

Anisole (27.3 mg) was added to the crude product, and the NMR yield thus determined for the trans and cis 2-azetidinones was 23%. The NMR analysis also showed that the product was a 32:68 trans:cis mixture. The crude product was purified by preparative TLC (20/80 EtOAc/hexanes) to afford a mixture of trans and cis 2-

azetidinones for HPLC analysis (trans ee: 57%, major enantiomer: 3*S*,4*R*; cis ee: 62%, major enantiomer: 3*R*,4*R*).

IV. Development of Reaction Conditions.

1. Copper Source (Table 4.2).

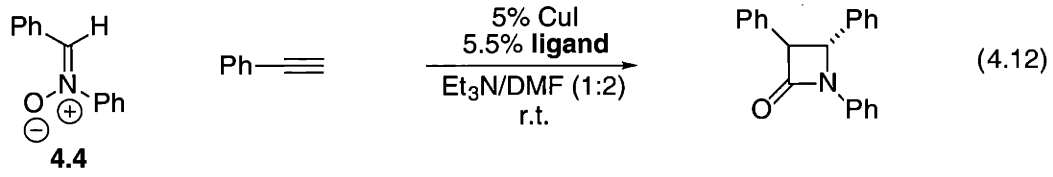


(4.11)

General procedure. A solution of the copper source (8 μmol) and (*R*,*R*)-**1.19** (4.6 mg, 8.7 μmol) was prepared in DMF (1 mL). After 30 min, a quarter of the catalyst solution was transferred to a DMF solution (0.25 mL) containing **4.4** (0.040 mmol), phenylacetylene (0.041 mmol), anthracene (3.1 mg), triptycene (3.8 mg), and Et_3N (0.25 mL). The progress of the reaction was monitored by GC at regular time intervals, with the yield determined using triptycene as the internal standard. After all nitrone was consumed, the reaction mixture was filtered through a plug of silica with Et_2O as the eluant. The organic layer was washed with water, dried ($MgSO_4$), and concentrated in vacuo for NMR analysis. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the product for HPLC analysis.

copper source	GC yield	trans : cis	%ee, cis
CuI	56% at 18.5 h	47 : 53	58
CuCN	45% at 230 h	80 : 20	57
CuOAc	32% at 4.5 h	46 : 54	52
CuCl	38% at 16 h	21 : 79	57
$Cu(MeCN)_4PF_6$	31% at 24 h	43 : 57	45

2. **Ligand (Table 4.3).**



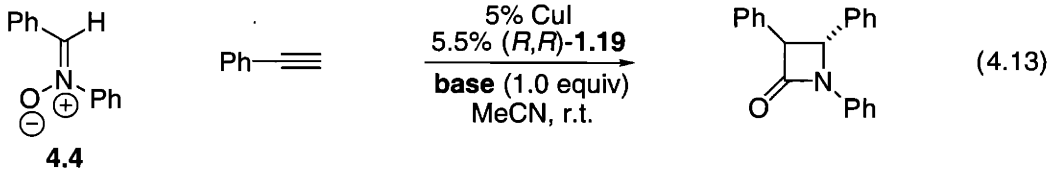
(4.12)

Entry 2. A solution of CuI (1.6 mg, 8.4 μmol) and (*R*,*R*)-**1.22** (6.2 mg, 11 μmol) was prepared in DMF (1 mL). After 30 min, a quarter of the catalyst solution was transferred to a DMF solution (0.25 mL) containing **4.4** (0.043 mmol), phenylacetylene (0.042 mmol), anthracene (2.6 mg), triptycene (3.6 mg), and Et_3N (0.2 mL). After 69 h, GC analysis showed that the yield was 62% (triptycene as internal standard). The reaction mixture was filtered through a plug of silica with Et_2O as the eluant. The organic layer was washed with water, dried ($MgSO_4$) and concentrated in vacuo. NMR analysis showed that the crude product was a 40:60 trans:cis mixture. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the product (trans ee: 69%, major enantiomer: 3*S*,4*R*; cis ee: 70%, major enantiomer: 3*R*,4*R*).

Entry 3. A solution of CuI (1.4 mg, 7.4 μmol) and (*S*,*S*)-**1.33** (13 mg, 7.8 μmol) was prepared in DMF (1 mL). After 30 min, a quarter of the catalyst solution was transferred to a DMF solution (0.2 mL) containing **4.4** (0.038 mmol), phenylacetylene (0.038 mmol), anthracene (3.2 mg), triptycene (4.8 mg), and Et_3N (0.15 mL). After 450 h, GC analysis showed that the yield was 40% (triptycene as internal standard). The reaction mixture was filtered through a plug of silica with Et_2O as the eluant. The organic layer was washed with water, dried ($MgSO_4$), and concentrated in vacuo. NMR analysis showed that the crude product was a 75:25 trans:cis mixture. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the product (trans ee: 2%, major enantiomer: 3*S*,4*R*; cis ee: 2%, major enantiomer: 3*S*,4*S*).

Entry 4. A solution of CuI (2.3 mg, 12 μmol) and (*S,S*)-**2.11** (8.1 mg, 13 μmol) was prepared in DMF (1 mL). After 30 min, a quarter of the catalyst solution was transferred to a DMF solution (0.25 mL) containing **4.4** (0.061 mmol), phenylacetylene (0.062 mmol), anthracene (3.1 mg), triptycene (3.6 mg), and Et_3N (0.2 mL). After 25 h, GC analysis showed that the yield was 59% (triptycene as internal standard). The reaction mixture was filtered through a plug of silica with Et_2O as the eluant. The organic layer was washed with water, dried ($MgSO_4$) and concentrated in vacuo. NMR analysis showed that the crude product was a 23:77 trans:cis mixture. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the product (trans ee: 41%, major enantiomer: 3*R*,4*S*; cis ee: 44%, major enantiomer: 3*S*,4*S*).

3. Base (Table 4.4).

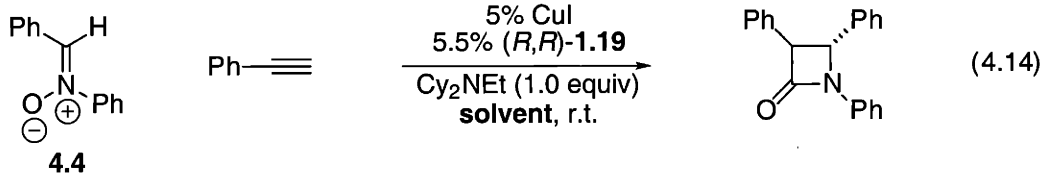


(4.13)

General procedure. A solution of CuI (1.6 mg, 8.4 μmol) and (*R,R*)-**1.19** (4.8 mg, 9.1 μmol) was prepared in MeCN (1 mL). After 1 h, a quarter of the catalyst solution was transferred to a MeCN solution (0.2 mL) containing **4.4** (0.044 mmol), phenylacetylene (0.047 mmol), triptycene (3.7 mg), and the base (1.0 equiv). The progress of the reaction was monitored by GC at regular time intervals, with the yield determined using triptycene as the internal standard. After all nitrone was consumed, the reaction mixture was filtered through a plug of silica with Et_2O as the eluant to afford the crude product for NMR analysis. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the product for HPLC analysis.

base	GC yield (%)	trans : cis	%ee, cis
$PhNMe_2$	23	very slow reaction	
BTPP	0	no reaction	
DMAN	62	26 : 74	57
DABCO	77	17 : 83	55
Et_3N	74	11 : 89	58
(*i*-Pr)$_2$N(*i*-Bu)	68	8 : 92	57
Cy_2NMe	71	7 : 93	58
Cy_2NEt	71	3 : 97	57
(*t*-Bu)(*i*-Pr)NMe	72	3 : 97	56
PMP	72	2 : 98	56

4. **Solvent (Table 4.5).**



(4.14)

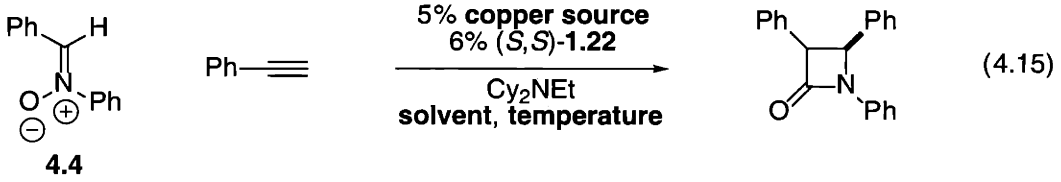
General procedure. A solution of CuI (1.8 mg, 9.5 μmol) and (*R*,*R*)-**1.19** (5.4 mg, 10.3 μmol) was prepared in CH_2Cl_2. After 1 h, the catalyst solution was divided into 4 equal parts and concentrated in vacuo to afford the catalyst. The catalyst was then redissolved in the solvent (0.5 mL), and the resultant catalyst solution was transferred to a vial containing **4.4** (0.050 mmol), phenylacetylene (0.054 mmol), triptycene (5.9 mg), and Cy_2NEt (0.048 mmol). The progress of the reaction was monitored by GC at regular time intervals, with the yield determined using triptycene as the internal standard. After all nitrone was consumed, the reaction mixture was filtered through a plug of silica with Et_2O as the eluant to afford the crude product for NMR analysis.

Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the product for HPLC analysis.

solvent	GC yield (%)	trans : cis	%ee, cis
PhCN	57	9 : 91	52
MeCN	71	3 : 97	57
acetone	30	9 : 91	64
THF	18	7 : 93	67
$PhCF_3$	19	9 : 91	67
$CHCl_3$	26	16 : 84	68
HCO_2Me	20	11 : 89	69
CH_2Cl_2[a]	42	8 : 92	69
EtOAc	16	7 : 93	72
toluene	14	11 : 89	74

[a] Cy_2NMe is used instead of Cy_2NEt.

5. Optimization of reaction parameters using 1.22 as the ligand (Table 4.6).



4.4 (4.15)

Entry 1. A solution of CuI (1.8 mg, 9.5 μmol) and (*R*,*R*)-**1.22** (4.1 mg, 10 μmol) was prepared in CH_2Cl_2. After 1 h, a quarter of the catalyst solution was transferred to a CH_2Cl_2 solution containing **4.4** (0.047 mmol), phenylacetylene (0.053 mmol), triptycene (3.4 mg) and Cy_2NEt (0.047 mmol). After 432 h, GC analysis showed that the yield was 32% (triptycene as internal standard). The reaction mixture was filtered through a plug of silica with Et_2O as the eluant. NMR analysis showed that the crude product was a

11:89 trans:cis mixture. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the cis product in 83% ee (major enantiomer: 3*R*,4*R*).

Entry 2. A solution of CuCl (0.7 mg, 7.1 μmol) and (*R*,*R*)-**1.22** (4.1 mg, 7.4 μmol) was prepared in CH_2Cl_2. After 2 h, the catalyst solution was divided into 4 equal parts and concentrated in vacuo to afford the catalyst. A CH_2Cl_2 solution containing **4.4** (0.036 mmol), phenylacetylene (0.070 mmol), triptycene (4.7 mg), and Cy_2NEt (0.035 mmol) was added to the catalyst. After 17 h, the reaction mixture was filtered through a plug of silica with Et_2O/CH_2Cl_2 as the eluant. NMR analysis showed that the crude product was a 9:91 trans:cis mixture, and the yield was 29%. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the cis product in 82% ee (major enantiomer: 3*R*,4*R*).

Entry 3. A solution of $Cu(MeCN)_4PF_6$ (3.8 mg, 10 μmol) and (*S*,*S*)-**1.22** (6.2 mg, 11 μmol) was prepared in MeCN. After 45 min, a quarter of the catalyst solution was transferred to a MeCN solution containing **4.4** (0.051 mmol), phenylacetylene (0.11 mmol), and Cy_2NEt (0.054 mmol). After 27 h, the reaction mixture was filtered through a plug of silica with Et_2O/CH_2Cl_2 as the eluant. Triptycene (10.0 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined was 57%. NMR analysis also showed that the crude product was a 4:96 trans:cis mixture. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the cis product in 75% ee (major enantiomer: 3*S*,4*S*).

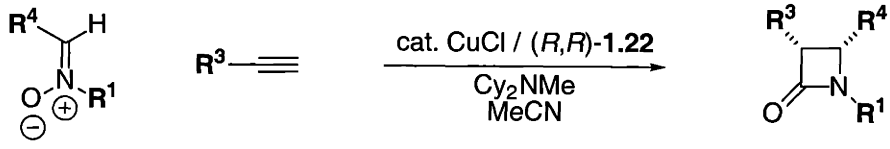
Entry 4. A solution of CuCl (0.7 mg, 7.1 μmol) and (*R*,*R*)-**1.22** (4.1 mg, 7.4 μmol) was prepared in CH_2Cl_2. After 2 h, the catalyst solution was divided into 4 equal parts and concentrated in vacuo to afford the catalyst. A MeCN solution containing **4.4** (0.037 mmol), phenylacetylene (0.072 mmol), triptycene (7.0 mg), and Cy_2NEt (0.036 mmol)

was added to the catalyst. After 17 h, the reaction mixture was filtered through a plug of silica with Et_2O/CH_2Cl_2 as the eluant. NMR analysis showed that the crude product was a 5:95 trans:cis mixture, and the yield was 70%. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the cis product in 72% ee (major enantiomer: 3*R*,4*R*).

Entry 5. A solution of CuCl (0.8 mg, 8.1 μmol) and (*S*,*S*)-**1.22** (5.2 mg, 9.4 μmol) was prepared in MeCN. After 1 h, a quarter of the catalyst solution was transferred to a MeCN solution containing **4.4** (0.043 mmol) and Cy_2NMe (0.045 mmol). The vial was cooled to 0 °C, and under Ar, a solution of phenylacetylene (0.082 mmol) was added dropwise. After 4 days, the reaction mixture was filtered through a plug of silica with Et_2O/CH_2Cl_2 as the eluant. Triptycene (9.6 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined was 71%. NMR analysis also showed that the crude product was a 5:95 trans:cis mixture. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the cis product in 75% ee (major enantiomer: 3*S*,4*S*).

Entry 6. A solution of CuCl (0.9 mg, 9.1 μmol) and (*S*,*S*)-**1.22** (5.9 mg, 11 μmol) was prepared in MeCN. After 1 h, a quarter of the catalyst solution was transferred to a MeCN solution containing **4.4** (0.047 mmol) and Cy_2NEt (0.047 mmol). The vial was cooled to -20 °C, and under Ar, a solution of phenylacetylene (0.092 mmol) was added dropwise. After 4 days, the reaction mixture was filtered through a plug of silica with Et_2O/CH_2Cl_2 as the eluant. Triptycene (12.9 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined was 58%. NMR analysis also showed that the crude product was a 2:98 trans:cis mixture. Purification by flash chromatography (25/75 $CHCl_3$/hexanes → 75/25) afforded the cis product in 77% ee (major enantiomer: 3*S*,4*S*).

V. Catalytic Asymmetric Kinugasa Reaction (Tables 4.7–4.9).



(4.16–4.18)

General procedure. The catalyst solution was prepared by adding a solution of (*S*,*S*)-**1.22** (10% excess relative to CuCl) in MeCN to CuCl and stirring it for 1 hour. It was added to Cy_2NMe (20-fold excess relative to CuCl), which was then transferred into a Schlenk tube containing the nitrone (0.4 mmol).[67] The reaction mixture was cooled to the indicated temperature, and a MeCN solution of the alkyne (1.5 equiv) was added dropwise under an atmosphere of Ar. In many cases, the reaction mixture is heterogeneous, but often turns homogeneous as reaction proceeds.[68] After TLC showed that the starting nitrone was all consumed, the reaction mixture was filtered through a plug of silica (MTBE/CH_2Cl_2 as the eluant).

All diastereoselectivities, enantioselectivities, and isolated yields that are reported in Table 4.7 through 4.9 are the average of two runs, one with each enantiomer of bisazaferrocene **1.22**.

Table 4.7, entry 1, R^1 = Ph. Run 1 was carried out using **4.4** (79.3 mg, 0.402 mmol), Cy_2NMe (16.0 mg, 0.0819 mmol), and phenylacetylene (61.2 mg, 0.599 mmol) in a total volume of 1.2 mL MeCN. The reaction temperature was 0 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 5 days. After workup, triptycene (37.6 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis product was 72%. NMR analysis also

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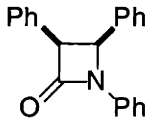
67 The nitrone is first transferred into the Schlenk tube as a solution in CH_2Cl_2, and later solvent is removed in vacuo.

68 The catalyst solution is orange if the system is completely free from air. If the reaction mixture turns brown, it suggests that air has been inadvertently let into the reaction system and has deactivated the catalyst.

showed that the product was a 5:95 trans:cis mixture. The crude product was purified by flash chromatography (80/20 benzene/pentane), which afforded the cis 2-azetidinone as a white solid (79.4 mg, 66% yield; 77% ee, major enantiomer: 3*S*,4*S*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 5:95 trans:cis mixture, and that the yield of the cis product was 73%. Purification afforded a 71% yield of the cis 2-azetidinone (77% ee, major enantiomer: 3*R*,4*R*).



(3*S*,4*S*)-1,3,4-Triphenyl-2-azetidinone. The ^{1}H NMR spectrum of the product matched the literature data.[69] $[\alpha]^{20}_D$ -8.6° ± 0.4° (*c* 0.88, $CHCl_3$; 77% ee).

Table 4.7, entry 2, R^1 = 4-(MeO)C$_6$H$_4$. Run 1 was carried out using **4.5** (93.4 mg, 0.411 mmol), Cy_2NMe (39.4 mg, 0.202 mmol), and phenylacetylene (62.4 mg, 0.611 mmol) in a total volume of 2.0 mL MeCN. The reaction temperature was 0 °C, the catalyst loading was 2.5%, and no residual nitrone was detected by TLC after 140 h. After workup, 1,3-diisopropylbenzene (59.3 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis product was 56%. NMR analysis also showed that the product was a 5:95 trans:cis mixture. The crude product was purified by flash chromatography (100% benzene), which afforded the cis 2-azetidinone as a pale yellow solid (74.1 mg, 55% yield; 85% ee, major enantiomer: 3*S*,4*S*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 4:96 trans:cis mixture, and that the yield of the cis product was

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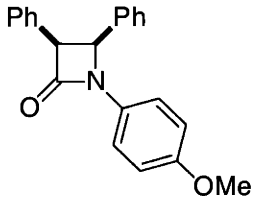
69 Cho, C. S..; Jiang, L. H.; Shim, S. C. *Synth. Commun.* **1999**, *29*, 2695–2703.

60%. Purification afforded a 51% yield of the cis 2-azetidinone (85% ee, major enantiomer: 3*R*,4*R*).



(3*S*,4*S*)-1-(4-Methoxyphenyl)-3,4-diphenyl-2-azetidinone. The ^{1}H NMR spectrum of the product matched the literature data.[70] $[\alpha]^{20}_D$ -9.3° ± 0.2° (*c* 1.0, $CHCl_3$).

Table 4.7, entry 3, R^1 = 4-BrC_6H_4. Run 1 was carried out using **4.6** (95.4 mg, 0.345 mmol), Cy_2NMe (34.7 mg, 0.178 mmol), and phenylacetylene (53.0 mg, 0.519 mmol) in a total volume of 1.3 mL MeCN. The reaction temperature was 0 °C, the catalyst loading was 2.5%, and no residual nitrone was detected by TLC after 5.5 days. After workup, 1,3-diisopropylbenzene (66.6 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis product was 78%. NMR analysis also showed that the product was a 5:95 trans:cis mixture. The crude product was purified by flash chromatography (75/25 benzene/pentane), which afforded the cis 2-azetidinone as a white solid (93.2 mg, 71% yield; 70% ee, major enantiomer: 3*S*,4*S*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 6:94 trans:cis mixture, and that the yield of the cis product was 84%. Purification afforded a 77% yield of the cis 2-azetidinone (73% ee, major enantiomer: 3*R*,4*R*).

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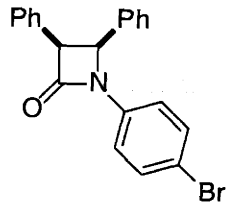
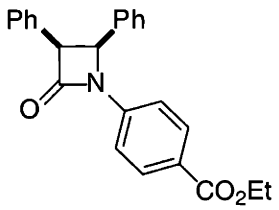
70 Hinz, W.; Just, G.; Sacripante, G. *Magn. Reson. Chem.* **1987**, *25*, 274–276.



(3*S*,4*S*)-1-(4-Bromophenyl)-3,4-diphenyl-2-azetidinone. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.04 (d, 1H, *J* = 6.1), 5.45 (d, 1H, *J* = 5.8), 7.02–7.15 (m, 10H), 7.31 (d, 2H, *J* = 8.9), 7.40 (d, 2H, *J* = 8.9). ^{13}C NMR (126 MHz, $CDCl_3$): δ 60.6, 60.8, 116.9, 119.0, 127.3, 127.5, 128.3, 128.3, 128.5, 129.0, 132.0, 132.3, 134.0, 136.8, 165.8. IR (KBr): 3064 (w), 3043 (w), 3031 (w), 2927 (w), 1747 (s), 1735 (s), 1592 (m), 1491 (s), 1454 (m), 1380 (s), 1168 (m), 1073 (m), 825 (m), 701 (s) cm^{-1}. $[\alpha]^{20}_D$ -15° (*c* 2.36, $CHCl_3$; 94% ee). HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{21}H_{16}BrNO$, 400.0307; found, 400.0297.

Table 4.7, entry 4, R^1 = 4-(EtO$_2$C)C$_6$H$_4$. Run 1 was carried out using **4.7** (93.6 mg, 0.348 mmol), Cy_2NMe (13.5 mg, 0.069 mmol), and phenylacetylene (53.0 mg, 0.519 mmol) in a total volume of 1.7 mL MeCN. The reaction temperature was 0 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 62 h. After workup, 1,3-diisopropylbenzene (78.8 mg) was added as an internal NMR standard, and the NMR yield thus determined for the cis product was 89%. NMR analysis also showed that the product was a 6:94 trans:cis mixture. The crude product was purified by flash chromatography (90/10 benzene/hexanes → 100% benzene), which afforded the cis 2-azetidinone as a white solid (106.8 mg, 83% yield; 65% ee, major enantiomer: 3*S*,4*S*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 7:93 trans:cis mixture, and that the yield of the cis product was 89%. Purification afforded a 75% yield of the cis 2-azetidinone (70% ee, major enantiomer: 3*R*,4*R*).



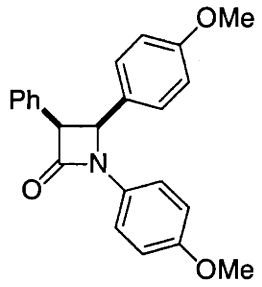
(3*S*,4*S*)-1-(4-Carboethoxyphenyl)-3,4-diphenyl-2-azetidinone. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.36 (t, 3H, *J* = 7.0), 4.34 (q, 2H, *J* = 7.0), 5.06 (d, 1H, *J* = 6.1), 5.51 (d, 1H, *J* = 6.1), 7.02–7.14 (m, 10H), 7.44 (d, 2H, *J* = 8.9), 7.98 (d, 2H, *J* = 8.5). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.5, 60.7, 60.8, 61.1, 116.9, 126.0, 127.2, 127.5, 128.3, 128.4, 128.5, 129.0, 131.1, 131.9, 134.0, 141.3, 166.2, 166.2. IR (KBr): 3064 (w), 3034 (w), 2982 (w), 2925 (w), 1749 (s), 1717 (s), 1605 (s), 1513 (m), 1455 (m), 1375 (s), 1275 (s), 1176 (m), 1103 (m), 769 (m), 701 (m) cm^{-1}. $[\alpha]^{20}_D$ -15° (*c* 0.99, $CHCl_3$; 81% ee). HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{21}NO_3$, 372.1594; found, 372.1578.

Table 4.7, entry 5, R^1 = 4-(EtO_2C)C_6H_4. Run 1 was carried out using **4.7** (97.2 mg, 0.361 mmol), Cy_2NMe (14.6 mg, 0.0747 mmol), and phenylacetylene (57.4 mg, 0.562 mmol) in a total volume of 1.2 mL MeCN. The reaction temperature was -20 °C, the catalyst loading was 2.5%, and no residual nitrone was detected by TLC after 8 days. After workup, 1,3-diisopropylbenzene (48.9 mg) was added as an internal NMR standard, and the NMR yield thus determined for the cis product was 96%. NMR analysis also showed that the product was a 4:96 trans:cis mixture. The crude product was purified by flash chromatography (90/10 benzene/hexanes → 100% benzene), which afforded the cis 2-azetidinone as a white solid (121.6 mg, 91% yield; 70% ee, major enantiomer: 3*S*,4*S*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 7:93 trans:cis mixture, and that the yield of the cis product was 90%. Purification afforded a 92% yield of the cis 2-azetidinone (71% ee, major enantiomer: 3*R*,4*R*).

Table 4.8, entry 2, R^4 = 4-(MeO)C_6H_4. Run 1 was carried out using **4.8** (104 mg, 0.402 mmol), Cy_2NMe (40.0 mg, 0.205 mmol), and phenylacetylene (62.6 mg, 0.613 mmol) in a total volume of 2.0 mL MeCN. The reaction temperature was r.t., the catalyst loading was 2.5%, and no residual nitrone was detected by TLC after 184 h. After workup, 1,3-diisopropylbenzene (52.8 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis product was 50%. NMR analysis also showed that the product was a 7:93 trans:cis mixture. The crude product was purified by flash chromatography (100% benzene → 1/99 MTBE/benzene; 20/80 MTBE/hexanes), which afforded the cis 2-azetidinone as a white solid (66.1 mg, 46% yield; 83% ee, major enantiomer: 3*S*,4*S*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 7:93 trans:cis mixture, and that the yield of the cis product was 48%. Purification afforded a 46% yield of the cis 2-azetidinone (84% ee, major enantiomer: 3*R*,4*R*).

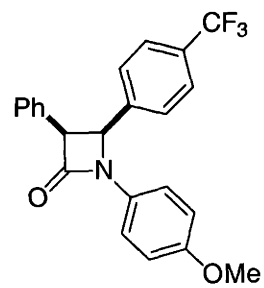


(3*S*,4*S*)-1,4-Bis-(4-methoxyphenyl)-3-phenyl-2-azetidinone. ^1H NMR (500 MHz, $CDCl_3$): δ 3.67 (s, 3H), 3.76 (s, 3H), 4.96 (d, 1H, *J* = 6.1), 5.38 (d, 1H, *J* = 6.1), 6.63 (d, 2H, *J* = 8.9), 6.81 (d, 2H, *J* = 9.2), 6.97 (d, 2H, *J* = 8.5), 7.06–7.12 (m, 5H), 7.34 (d, 2H, *J* = 9.2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 55.3, 55.6, 60.2, 60.4, 113.8, 114.5, 118.7, 126.6, 127.3, 128.3, 128.6, 129.0, 131.5, 132.6, 156.2, 159.3, 165.4. IR (KBr): 3064 (w), 3032 (w), 3006 (w), 2957 (w), 2836 (w), 1735 (s), 1614 (w), 1584 (w), 1512 (s), 1388 (m), 1242 (s), 1171 (m), 1028 (m), 852 (m), 830 (m), 815 (m), 804 (m), 728 (w), 692 (w) cm^{-1}. $[\alpha]^{20}_D$ -13.6° ± 0.4°

(*c* 1.50, $CHCl_3$; 83% ee). HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{23}H_{21}NO_3$, 360.1594; found, 360.1579.

Table 4.8, entry 3, R^4 = 4-$(F_3C)C_6H_4$. Run 1 was carried out using **4.9** (102 mg, 0.347 mmol), Cy_2NMe (33.5 mg, 0.171 mmol), and phenylacetylene (52.6 mg, 0.515 mmol) in a total volume of 1.7 mL MeCN. The reaction temperature was 0 °C, the catalyst loading was 2.5%, and no residual nitrone was detected by TLC after 10 days. NMR analysis showed that the product was a 7:93 trans:cis mixture. The crude product was purified by flash chromatography (80/20 benzene/pentane → 85/15), which afforded the cis 2-azetidinone as a white solid (72.6 mg, 53% yield; 89% ee, major enantiomer: 3*S*,4*S*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 7:93 trans:cis mixture, and that the yield of the cis product was 47%. Purification afforded a 48% yield of the cis 2-azetidinone (90% ee, major enantiomer: 3*R*,4*R*).

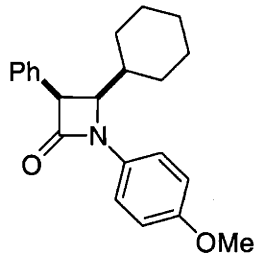


(3*S*,4*S*)-1-(4-Methoxyphenyl)-3-phenyl-4-(4-trifluoromethylphenyl)-2-azetidinone. ^1H NMR (500 MHz, $CDCl_3$): δ 3.76 (s, 3H), 5.04 (d, 1H, *J* = 6.1), 5.47 (d, 1H, *J* = 6.1), 6.83 (d, 2H, *J* = 9.2), 7.01–7.11 (m, 5H), 7.17 (d, 2H, *J* = 8.2), 7.32 (d, 2H, *J* = 8.9), 7.36 (d, 2H, *J* = 8.2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 55.7, 60.0, 60.7, 114.6, 118.6, 124.0 (q, $^1J_{C-F}$ = 272), 125.4 (q, $^3J_{C-F}$ = 3.9), 127.7, 127.7, 128.5, 128.9, 130.2 (q, $^2J_{C-F}$ = 33), 131.1, 131.8, 139.0, 156.5, 164.8. IR (KBr): 3064 (w), 2937 (w), 2838 (w), 1749 (s), 1513 (s), 1387 (m), 1326 (s),

1248 (m), 1169 (m), 1124 (m), 1110 (m), 1066 (m), 829 (m), 728 (m), 699 (m) cm^{-1}. $[\alpha]^{20}_D$ -4.3° (*c* 2.80, $CHCl_3$; 89% ee). HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{23}H_{18}F_3NO_2$, 398.1362; found, 398.1377.

Table 4.8, entry 4, R^4 = Cy. Run 1 was carried out using **4.10** (91.8 mg, 0.393 mmol), Cy_2NMe (16.3 mg, 0.0834 mmol), and phenylacetylene (63.1 mg, 0.618 mmol) in a total volume of 1.2 mL MeCN. The reaction temperature was 0 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 17 h. After workup, triptycene (39.1 mg) was added as an internal NMR standard, and the NMR yield thus determined for the cis product was 57%. NMR analysis also showed that the product was a 6:94 trans:cis mixture. The crude product was purified by flash chromatography (15/85 MTBE/hexanes), which afforded the cis 2-azetidinone as an off-white solid (78.7 mg, 60% yield; 88% ee, major enantiomer: 3*S*,4*R*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 7:93 trans:cis mixture, and that the yield of the cis product was 59%. Purification afforded a 54% yield of the cis 2-azetidinone (90% ee, major enantiomer: 3*R*,4*S*).

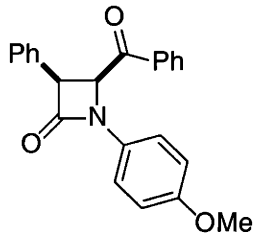


(3*S*,4*R*)-4-Cyclohexyl-1-(4-methoxyphenyl)-3-phenyl-2-azetidinone. ^1H NMR (500 MHz, C_6D_6): δ 0.6–0.7 (m, 2H), 0.7–0.9 (m, 3H), 1.1–1.2 (m, 1H), 1.3–1.5 (m, 4H), 1.6–1.7 (m, 1H), 3.30 (s, 3H), 3.59 (dd, 1H, *J* = 6.1, 8.5), 4.21 (d, 1H, *J* = 6.1), 6.81 (d, 2H, *J* = 8.9), 7.03–7.16 (m, 3H), 7.2–7.3 (m, 2H), 7.52 (d, 2H, *J* = 8.9). ^{13}C NMR (126 MHz, $CDCl_3$): δ

25.6, 26.0, 26.2, 29.7, 31.2, 39.6, 55.7, 57.7, 61.9, 114.3, 121.0, 127.9, 128.5, 130.2, 131.8, 133.3, 156.7, 167.3. IR (KBr): 3034 (w), 2930 (m), 2853 (m), 1728 (s), 1513 (s), 1389 (m), 1297 (m), 1248 (m), 1033 (m), 836 (m), 730 (m), 701 (m) cm^{-1}. $[\alpha]^{20}_D$ +78.1° (*c* 1.26, $CHCl_3$; 99% ee). HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{22}H_{25}NO_2$, 358.1778; found, 358.1760.

Table 4.8, entry 5, R^4 = PhCO. Run 1 was carried out using **4.11** (88.3 mg, 0.346 mmol), Cy_2NMe (13.3 mg, 0.0681 mmol), and phenylacetylene (53.3 mg, 0.522 mmol) in a total volume of 1.0 mL MeCN. The reaction temperature was 0 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 12 h. After workup, triptycene (34.5 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis product was 45%. NMR analysis also showed that the product was a 9:91 trans:cis mixture. The crude product was purified by flash chromatography (100% benzene → 1/99 MTBE/benzene), which afforded the cis 2-azetidinone as a white solid (49.8 mg, 40% yield; 71% ee, major enantiomer: 3*S*,4*S*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 9:91 trans:cis mixture, and that the yield of the cis product was 48%. Purification afforded a 43% yield of the cis 2-azetidinone (73% ee, major enantiomer: 3*R*,4*R*).



(3*S*,4*S*)-4-Benzoyl-1-(4-methoxyphenyl)-3-phenyl-2-azetidinone. The ^{1}H NMR spectrum of the product matched the literature data.[71] ^{13}C NMR (126 MHz, $CDCl_3$): δ 55.7, 59.6, 61.7, 114.5, 118.8, 128.1, 128.3, 128.6, 128.7, 129.4, 131.0, 131.4, 133.9, 135.2, 156.6, 163.8, 193.4. $[\alpha]^{20}_D$ -95° (*c* 1.01, $CHCl_3$; 81% ee).

Table 4.9, entry 1, R^3 = Ph. Run 1 was carried out using **4.10** (94.1 mg, 0.403 mmol), Cy_2NMe (16.3 mg, 0.0834 mmol), and phenylacetylene (62.4 mg, 0.611 mmol) in a total volume of 1.3 mL MeCN. The reaction temperature was -20 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 24 h. After workup, triptycene (49.7 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis product was 61%. NMR analysis also showed that the product was a 4:96 trans:cis mixture. The crude product was purified by flash chromatography (2.5/97.5 MTBE/benzene), which afforded the cis 2-azetidinone as a yellow solid (88.2 mg, 65% yield; 91% ee, major enantiomer: 3*S*,4*R*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 4:96 trans:cis mixture, and that the yield of the cis product was 57%. Purification afforded a 64% yield of the cis 2-azetidinone (92% ee, major enantiomer: 3*R*,4*S*).

Table 4.9, entry 2, R^3 = 4-(MeO)C_6H_4. Run 1 was carried out using **4.10** (93.8 mg, 0.402 mmol), Cy_2NMe (16.0 mg, 0.0819 mmol), and 1-ethynyl-4-methoxybenzene (80.9 mg, 0.612 mmol) in a total volume of 1.3 mL MeCN. The reaction temperature was -20 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 69 h. After workup, triptycene (52.9 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis product was 61%. NMR

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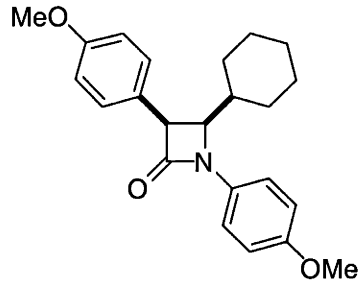
71 Alcaide, B.; Domínguez, G.; Escobar, G.; Parreño, U.; Plumet, J. *Heterocycles* **1986**, *24*, 1579–1583.

analysis also showed that the product was a 6:94 trans:cis mixture. The crude product was purified by flash chromatography (100% benzene → 1/99 MTBE/benzene), which afforded the cis 2-azetidinone as an off-white solid (88.8 mg, 60% yield; 90% ee, major enantiomer: 3*S*,4*R*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 9:91 trans:cis mixture, and that the yield of the cis product was 60%. Purification afforded a 60% yield of the cis 2-azetidinone (91% ee, major enantiomer: 3*R*,4*S*).

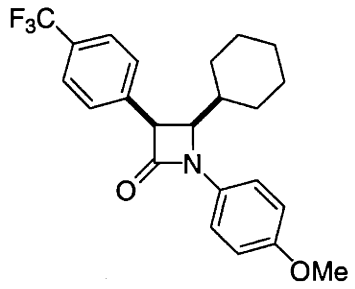


(3*S*,4*R*)-4-Cyclohexyl-1,3-bis-(4-methoxyphenyl)-2-azetidinone. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.70–1.05 (m, 5H), 1.22–1.28 (m, 1H), 1.4–1.6 (m, 5H), 3.80 (s, 3H), 3.82 (s, 3H), 4.09 (dd, 1H, *J* =5.8, 8.9), 4.59 (d, 1H, *J* = 5.8), 6.88 (d, 2H, *J* = 9.2), 6.89 (d, 2H, *J* = 8.9), 7.25 (d, 2H, *J* = 8.9), 7.35 (d, 2H, *J* = 9.2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 25.7, 26.1, 26.2, 29.6, 31.3, 39.7, 55.5, 55.7, 57.1, 62.1, 114.0, 114.3, 120.9, 125.3, 131.3, 131.9, 156.6, 159.2, 167.7. IR (KBr): 3059 (w), 3033 (w), 3005 (w), 2927 (m), 2851 (m), 1748 (s), 1611 (m), 1510 (s), 1460 (m), 1445 (m), 1366 (m), 1297 (m), 1250 (s), 1177 (m), 1029 (m), 833 (m) cm^{-1}. $[\alpha]^{20}_D$ +61° (*c* 1.89, $CHCl_3$; 90% ee). HRMS–ESI (*m*/*z*): $[M + Na]^+$ calcd for $C_{23}H_{27}NO_3$, 388.1883; found, 388.1867.

Table 4.9, entry 3, R^3 = 4-(F$_3$C)C$_6$H$_4$. Run 1 was carried out using **4.10** (94.6 mg, 0.405 mmol), Cy_2NMe (16.3 mg, 0.0834 mmol), and 4-ethynyl-α,α,α-trifluorotoluene (104.3 mg, 0.613 mmol) in a total volume of 1.3 mL MeCN. The reaction temperature

was -20 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 24 h. After workup, triptycene (52.1 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis product was 57%. NMR analysis also showed that the product was a 2:98 trans:cis mixture. The crude product was purified by flash chromatography (90/10 benzene/pentane → 100% benzene), which afforded the cis 2-azetidinone as an off-white solid (91.3 mg, 56% yield; 93% ee, major enantiomer: 3*S*,4*R*).

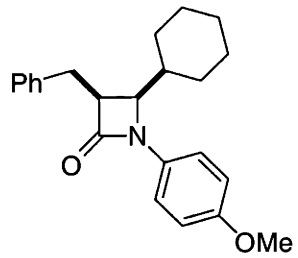
Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 2:98 trans:cis mixture, and that the yield of the cis product was 58%. Purification afforded a 58% yield of the cis 2-azetidinone (93% ee, major enantiomer: 3*R*,4*S*).



(3*S*,4*R*)-4-Cyclohexyl-1-(4-methoxyphenyl)-3-(4-trifluoromethylphenyl)-2-azetidinone. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.71 (tq, 1H, *J* = 3.4, 12.6), 0.84 (dq, 1H, *J* = 3.5, 12.3), 0.92–1.04 (m, 3H), 1.17–1.24 (m, 1H), 1.40–1.58 (m, 5H), 3.81 (s, 3H), 4.20 (dd, 1H, *J* = 5.8, 8.9), 4.69 (d, 1H, *J* = 6.1), 6.90 (d, 2H, *J* = 8.9), 7.36 (d, 2H, *J* = 8.9), 7.49 (d, 2H, *J* = 7.9), 7.64 (d, 2H, *J* = 8.2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 25.6, 25.9, 26.1, 29.8, 31.0, 39.7, 55.7, 57.2, 61.8, 114.4, 121.1, 124.2 (q, $^1J_{C-F}$ = 272), 125.5 (q, $^3J_{C-F}$ = 3.8), 130.1 (q, $^2J_{C-F}$ = 32), 130.5, 131.5, 137.6, 156.9, 166.2. IR (KBr): 3072 (w), 3003 (w), 2940 (m), 2924 (m), 2856 (m), 1752 (s), 1618 (w), 1511 (s), 1327 (s), 1249 (s), 1163 (s), 1125 (s), 1110 (s), 1068 (s), 835 (m), 809 (m) cm^{-1}. $[\alpha]^{20}_D$ +60° (*c* 1.67, $CHCl_3$; 93% ee). HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{23}H_{24}F_3NO_2$, 426.1651; found, 426.1647.

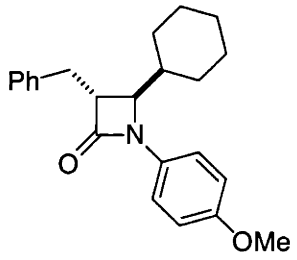
Table 4.9, entry 4, R^3 = $PhCH_2$. Run 1 was carried out using **4.10** (85.9 mg, 0.368 mmol), Cy_2NMe (14.0 mg, 0.0717 mmol), and 3-phenyl-1-propyne (63.5 mg, 0.547 mmol) in a total volume of 1.2 mL MeCN. The reaction temperature was -20 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 9 days. After workup, triptycene (40.6 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the trans and cis products was 67%. NMR analysis also showed that the product was a 27:73 trans:cis mixture. The crude product was purified first by flash chromatography (30/70 $CHCl_3$/hexanes → 1/30/69 MTBE/$CHCl_3$/hexanes; 10/90 MTBE/hexanes), and then by preparative achiral HPLC (1/4/95 *i*-PrOH/$CHCl_3$/hexanes), which afforded the trans 2-azetidinone as a white solid (21.0 mg, 16% yield; 70% ee, major enantiomer: 3*R*,4*R*) and the cis 2-azetidinone as a yellow liquid (52.9 mg, 41% yield; 73% ee, major enantiomer: 3*S*,4*R*).

Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 31:69 trans:cis mixture, and that the yield of the trans and cis products was 71%. Purification afforded the trans 2-azetidinone (24.1 mg, 18% yield; 70% ee, major enantiomer: 3*S*,4*S*) and the cis 2-azetidinone (58.5 mg, 45% yield; 73% ee, major enantiomer: 3*R*,4*S*).



(3*S*,4*R*)-3-Benzyl-4-cyclohexyl-1-(4-methoxyphenyl)-2-azetidinone. ^1H NMR (500 MHz, C_6D_6): δ 0.76–1.03 (m, 5H), 1.26–1.34 (m, 1H), 1.44–1.56 (m, 4H), 1.58–1.66 (m, 1H), 2.73 (dd, 1H, *J* = 7.0, 15.0), 3.18 (dd, 1H, *J* = 7.6, 15.0), 3.28 (s, 3H), 3.31 (dt, 1H, *J* = 6.0, 7.4), 3.47 (dd, 1H, *J* = 6.0, 6.9), 6.76 (d, 2H, *J* = 9.2), 7.08 (t, 1H, *J* = 7.3), 7.20 (t, 2H, *J* =

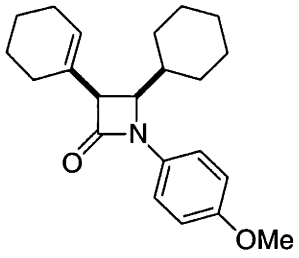
7.8), 7.28 (d, 2H, J = 7.3), 7.41 (d, 2H, J = 8.9). ^{13}C NMR (126 MHz, C_6D_6): δ 26.7, 26.8, 31.5, 31.7, 32.2, 39.9, 53.2, 55.3, 60.1, 114.7, 120.6, 127.0, 129.1, 129.4, 133.2, 140.3, 156.9, 168.1. IR (neat): 3027 (w), 2928 (m), 2852 (m), 1743 (s), 1511 (s), 1453 (m), 1386 (m), 1295 (m), 1245 (s), 1151 (m), 1031 (m), 828 (m), 744 (w), 697 (w) cm^{-1}. $[\alpha]^{20}_D$ -45° (*c* 2.47, $CHCl_3$; 73% ee). HRMS–ESI (*m/z*): [M + Na]$^+$ calcd for $C_{23}H_{27}NO_2$, 372.1934; found, 372.1937.



(3*R*,4*R*)-3-Benzyl-4-cyclohexyl-1-(4-methoxyphenyl)-2-azetidinone. ^{1}H NMR (500 MHz, C_6D_6): δ 0.40 (dq, 1H, J = 3.4, 12.5), 0.6–1.0 (m, 4H), 1.10–1.17 (m, 1H), 1.36–1.48 (m, 4H), 1.58–1.68 (m, 1H), 2.63 (dd, 1H, J = 8.5, 13.7), 2.99 (dd, 1H, J = 5.8, 13.7), 3.06 (ddd, 1H, J = 2.3, 5.8, 8.4), 3.25 (s, 3H), 3.43 (dd, 1H, J = 2.3, 5.0), 6.74 (d, 2H, J = 9.2), 7.00–7.06 (m, 1H), 7.08–7.14 (m, 4H), 7.44 (d, 2H, J = 8.9). ^{13}C NMR (126 MHz, C_6D_6): δ 26.3, 26.3, 26.7, 26.8, 29.9, 35.8, 38.9, 53.5, 55.3, 62.0, 115.1, 119.3, 127.1, 129.1, 129.9, 132.9, 139.6, 156.7, 166.6. IR (KBr): 3057 (w), 3026 (w), 2924 (m), 2851 (m), 1731 (s), 1513 (s), 1447 (m), 1394 (m), 1296 (m), 1246 (m), 1149 (m), 1029 (m), 834 (m), 749 (m), 698 (m) cm^{-1}. $[\alpha]^{20}_D$ -82° (*c* 1.97, $CHCl_3$; 70% ee). HRMS–ESI (*m/z*): [M + Na]$^+$ calcd for $C_{23}H_{27}NO_2$, 372.1934; found, 372.1939.

Table 4.9, entry 5, R^3 = 1-cyclohexenyl. Run 1 was carried out using **4.10** (94.6 mg, 0.405 mmol), Cy_2NMe (16.5 mg, 0.0845 mmol), and 1-ethynylcyclohexene (64.4 mg, 0.607 mmol) in a total volume of 1.3 mL MeCN. The reaction temperature was -20 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 10 days.

After workup, triptycene (36.8 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis product was 64%. NMR analysis also showed that the product was a 4:96 trans:cis mixture. The crude product was purified by flash chromatography (90/10 benzene/pentane → 100% benzene → 1/99 MTBE/benzene), which afforded the cis 2-azetidinone as an off-white solid (86.0 mg, 62% yield; 84% ee, major enantiomer: 3*S*,4*R*).

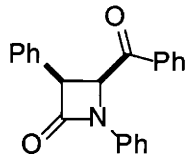


(3*S*,4*R*)-3-(Cyclohex-1-enyl)-4-cyclohexyl-1-(4-methoxyphenyl)-2-azetidinone. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.95–1.23 (m, 5H), 1.57–1.76 (m, 10H), 2.0–2.2 (m, 4H), 3.79 (s, 3H), 3.86 (d, 1H, *J* = 5.8), 3.98 (dd, 1H, *J* = 5.8, 8.2), 5.83 (s, 1H), 6.86 (d, 2H, *J* = 9.2), 7.28 (d, 2H, *J* = 8.9). ^{13}C NMR (126 MHz, $CDCl_3$): δ 22.2, 23.0, 25.6, 26.3, 26.4, 30.0, 30.9, 31.4, 40.0, 55.7, 59.0, 61.7, 114.2, 120.8, 129.4, 130.0, 132.0, 156.5, 167.7. IR (KBr): 3042 (w), 3013 (w), 2927 (m), 2847 (w), 1740 (s), 1728 (s), 1512 (s), 1246 (m), 1164 (m), 1031 (m), 835 (m) cm^{-1}. $[\alpha]^{20}_D$ +18° (*c* 1.28, $CHCl_3$; 84% ee). HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{22}H_{29}NO_2$, 362.2091; found, 362.2085.

Table 4.9, entry 6, R^3 = Ph. Run 1 was carried out using **4.12** (80.6 mg, 0.358 mmol), Cy_2NMe (14.4 mg, 0.0737 mmol), and phenylacetylene (55.8 mg, 0.546 mmol) in a total volume of 1.2 mL MeCN. The reaction temperature was -40 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 39 h. After workup, NMR analysis showed that the product was a 10:90 trans:cis mixture. The crude product was

purified twice by flash chromatography (80/20 benzene/hexanes), which afforded the cis 2-azetidinone as a white solid (65.7 mg, 56% yield; 90% ee, major enantiomer: 3*S*,4*S*).

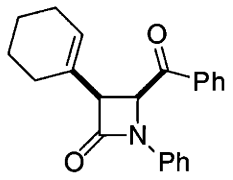
Run 2 was carried out similarly with (*R*,*R*)-**1.22**. NMR analysis revealed that the crude product was a 11:89 trans:cis mixture. Purification afforded a 56% yield of the cis 2-azetidinone (90% ee, major enantiomer: 3*R*,4*R*).



(3*S*,4*S*)-4-Benzoyl-1,3-diphenyl-2-azetidinone. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.00 (d, 1H, *J* = 6.7), 5.84 (d, 1H, *J* = 6.7), 7.08 (s, 5H), 7.13 (tt, 1H, *J* = 1.2, 7.5), 7.31–7.36 (m, 4H), 7.39–7.42 (m, 2H), 7.49 (tt, 1H, *J* = 1.2, 7.5), 7.65–7.69 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 59.6, 61.4, 117.3, 124.7, 128.1, 128.4, 128.6, 128.8, 129.3, 129.5, 130.9, 134.0, 135.2, 137.7, 164.3, 193.2. IR (KBr): 3064 (w), 3042 (w), 2947 (w), 1757 (s), 1678 (m), 1597 (m), 1502 (m), 1385 (m), 754 (m), 741 (m), 696 (m) cm^{-1}. $[\alpha]^{20}_D$ -120° (*c* 1.01, $CHCl_3$; 86% ee). HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{22}H_{17}NO_2$, 328.1332; found, 328.1321.

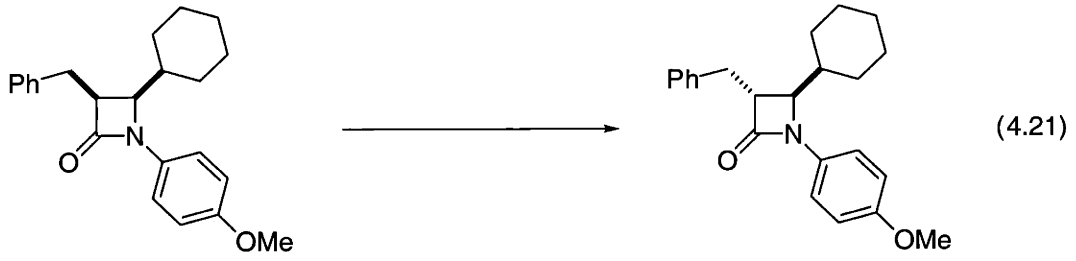
Table 4.9, entry 7, R^3 = 1-cyclohexenyl. Run 1 was carried out using **4.12** (81.1 mg, 0.360 mmol), Cy_2NMe (13.9 mg, 0.0712 mmol), and 1-ethynylcyclohexene (57.4 mg, 0.541 mmol) in a total volume of 1.2 mL MeCN. The reaction temperature was -40 °C, the catalyst loading was 1%, and no residual nitrone was detected by TLC after 39 h. After workup, triptycene (47.8 mg) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the cis product was 48%. NMR analysis also showed that the product was a 9:91 trans:cis mixture. The crude product was purified twice by flash chromatography (80/20 benzene/hexanes; 5/20/75 MTBE/$CHCl_3$/hexanes), which afforded the cis 2-azetidinone as a white solid (49.2 mg, 41% yield; 91% ee, major enantiomer: 3*S*,4*S*).

Run 2 was carried out similarly with (*R,R*)-**1.22**. NMR analysis revealed that the crude product was a 10:90 trans:cis mixture, and that the yield of the cis product was 46%. Purification afforded a 48% yield of the cis 2-azetidinone (92% ee, major enantiomer: 3*R*,4*R*).



(3*S*,4*S*)-4-Benzoyl-3-(cyclohex-1-enyl)-1-phenyl-2-azetidinone. ^{1}H NMR (500 MHz, C_6D_6): δ 0.96–1.10 (m, 4H), 1.44–1.55 (m, 1H), 1.58–1.74 (m, 3H), 3.78 (d, 1H, *J* = 6.7), 4.84 (d, 1H, *J* = 6.4), 5.59 (s br, 1H), 6.87 (t, 1H, *J* = 7.3), 7.00 (t, 2H, *J* = 7.6), 7.09 (t, 3H, *J* = 7.9), 7.52 (dd, 2H, *J* = 0.9, 8.5), 7.67 (dd, 2H, *J* = 1.4, 8.4). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.6, 22.3, 25.4, 28.0, 60.6, 61.4, 117.2, 124.4, 128.5, 128.5, 129.0, 129.2, 131.3, 134.2, 135.4, 137.8, 164.7, 193.7. IR (KBr): 3062 (w), 2927 (w), 2857 (w), 1752 (s), 1685 (m), 1597 (m), 1500 (m), 1389 (m), 758 (m), 689 (m) cm^{-1}. $[\alpha]^{20}_D$ -121° (*c* 0.59, $CHCl_3$; 97% ee). HRMS–EI (*m/z*): M^+ calcd for $C_{22}H_{21}NO_2$, 331.1572; found, 331.1566.

VI. Epimerization of cis-2-Azetidinones.



(4.21)

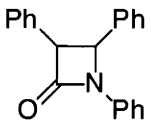
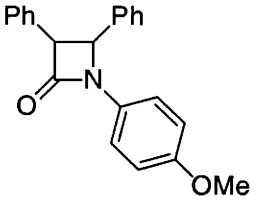
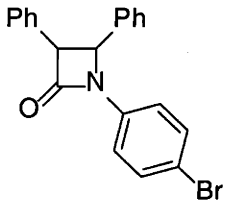
To a vial containing (3*S*,4*R*)-3-benzyl-4-cyclohexyl-1-(4-methoxyphenyl)-2-azetidinone (27.6 mg, 0.0790 mmol; cis ee: 73%) was charged a *t*-BuOH solution of KO-*t*-Bu (0.2 equiv) and heated overnight at 100 °C. It was then poured into 1 M HCl and extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$) and concentrated in

vacuo to afford the crude product, which by ^{1}H NMR analysis contained no residual cis 2-azetidinone. Purification by preparative TLC (20/80 EtOAc/hexanes) afforded (3*S*,4*R*)-3-benzyl-4-cyclohexyl-1-(4-methoxyphenyl)-2-azetidinone as a white solid (15.6 mg, 57% yield; trans ee: 71%).

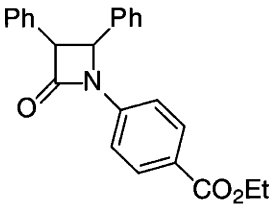
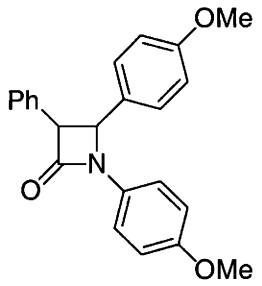
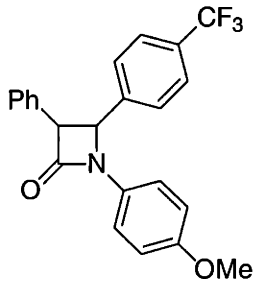
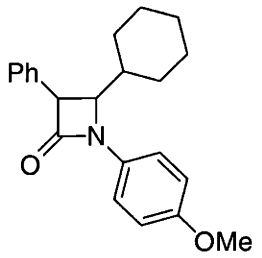
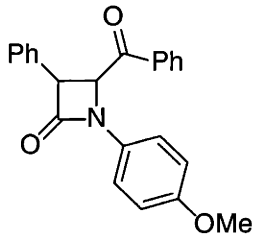
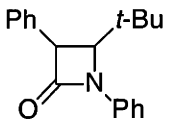
VII. Assay of Diastereoselectivity.

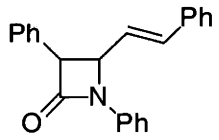
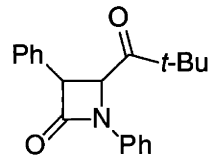
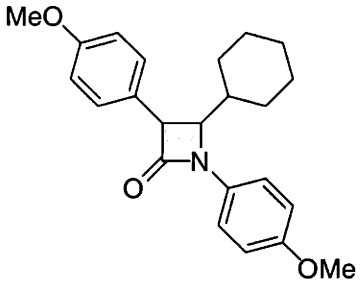
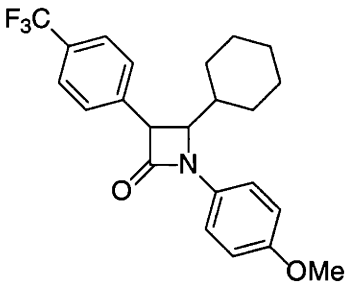
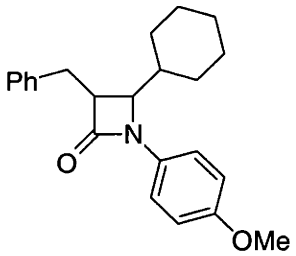
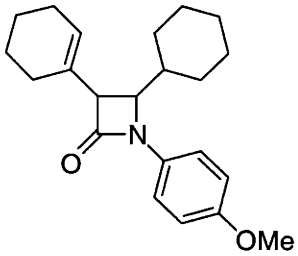
The diastereomeric ratios of the 2-azetidinones were all determined by integration of the ^{1}H NMR spectrum (delay time = 30 seconds). Table 4.10 lists the peaks used for integration. As noticed before,[72] the coupling constant for vicinal protons at C3 and C4 is 4.5–6 Hz for cis derivatives, and 2–2.5 Hz for trans derivatives. All the listed values are consistent with this observation. In addition, shielding from an aromatic system in the trans 2-azetidinones causes an upfield shift of the proton.

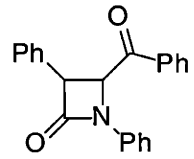
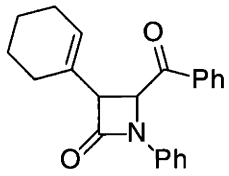
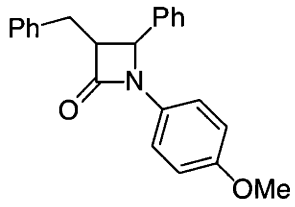
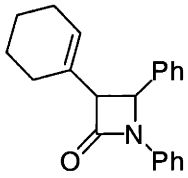
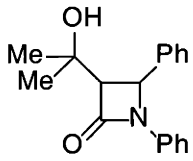
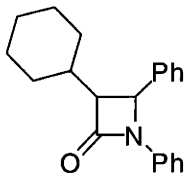
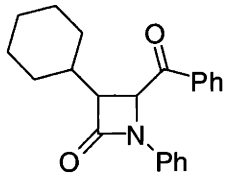
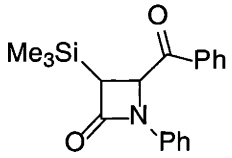
Table 4.10. NMR data for diastereomeric 2-azetidinones.

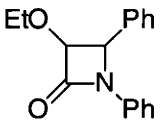
compound	solvent	δ (trans)	$^3J_{3,4}$ (trans)	δ (cis)	$^3J_{3,4}$ (cis)
	C_6D_6	4.02	2.8	4.46	6.1
	$CDCl_3$	4.26	2.4	4.99	6.1
	$CDCl_3$	4.30	2.4	5.03	6.1

72 De Kimpe, N. In *Comprehensive Heterocyclic Chemistry II*; Katritsky, A. R., Rees, C. W., Scriven, E. F. V., Padwa, A., Eds.; Pergamon: Oxford, 1996; Vol. 1B, p 537.

	C_6D_6	4.52	2.8	4.62	6.1
	$CDCl_3$	4.24	2.4	4.95	6.1
	C_6D_6	3.91	2.4	4.53	6.1
	$CDCl_3$	4.22	2.1	4.64	5.8
	$CDCl_3$	4.30	2.8	4.98	6.71
	$CDCl_3$	4.15	2.1	4.80	6.1

	$CDCl_3$	4.30	2.4	4.86	6.1
	$CDCl_3$	4.06	2.8	4.78	6.4
	$CDCl_3$	4.16	2.4	4.58	5.8
	$CDCl_3$	4.27	2.1	4.67	5.8
	C_6D_6	2.63[a]	2.3	2.73[a]	6.0
	C_6D_6	5.75[b]	2.6	5.84[b]	6.1

	$CDCl_3$	5.40	3.1	5.84	6.7
	$CDCl_3$	3.78	3.1	4.30	6.7
	$CDCl_3$	4.66	2.4	5.13	5.8
	$CDCl_3$	4.81	2.4	5.20	6.1
	$CDCl_3$	3.13	2.4	3.71	6.1
	$CDCl_3$	4.76	2.4	5.12	5.8
	$CDCl_3$	3.12	2.4[c]	3.51	6.1[d]
	$CDCl_3$	5.18	2.8	5.57	6.7

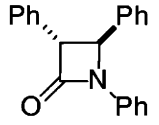
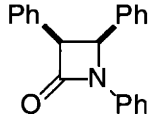
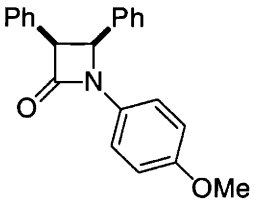
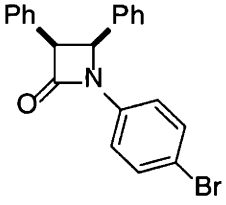
	$CDCl_3$	4.47	1.8	5.18	4.9

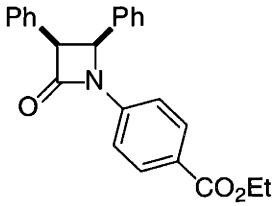
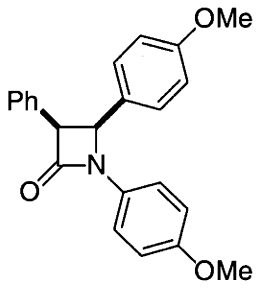
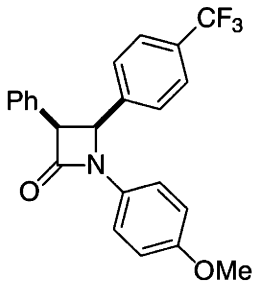
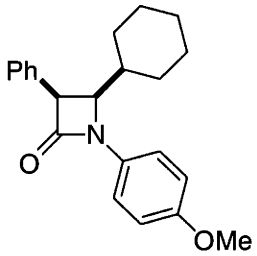
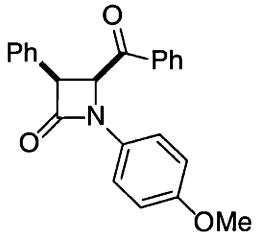
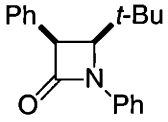
[a] Benzylic proton. [b] Vinylic proton. [c] Actual coupling pattern: dd, J = 2.4, 6.4. [d] Actual coupling pattern: dd, J = 6.1, 9.2.

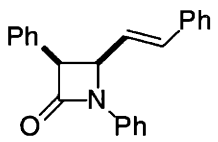
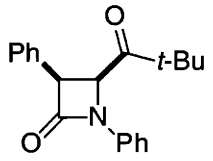
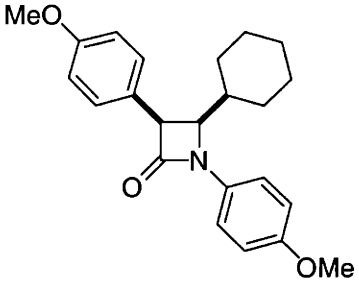
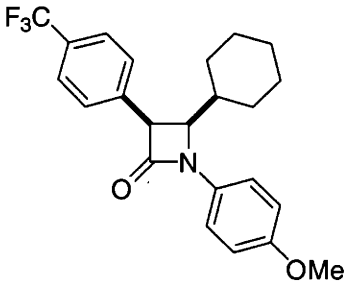
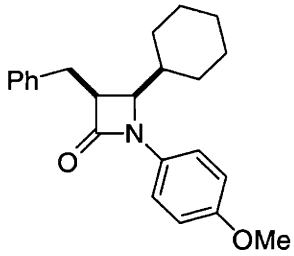
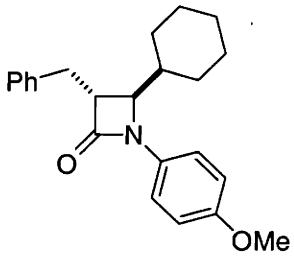
VIII. Assay of Enantioselectivity.

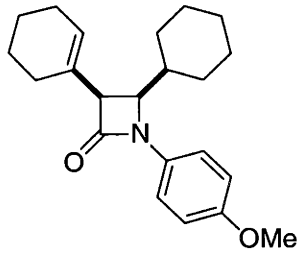
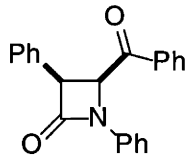
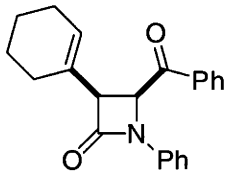
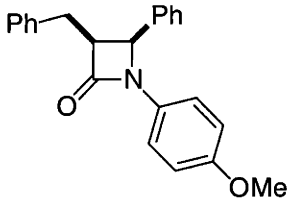
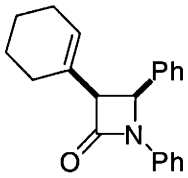
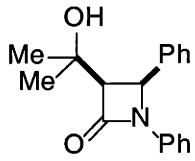
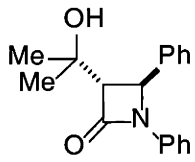
The enantiomeric excess of all 2-azetidinones were assayed directly by chiral HPLC with Daicel Chiralcel OD column at eluant flow 1.0 mL/min. Table 4.11 summarizes the assay conditions.

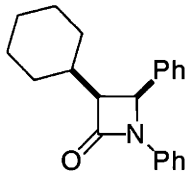
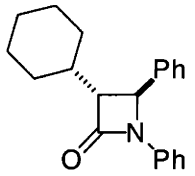
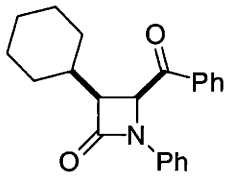
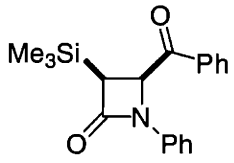
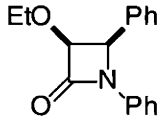
Table 4.11. Assay conditions for enantiomeric 2-azetidinones.

compound	solvent	illustrated config. t_R (min)	opposite config. t_R (min)
	2% *i*-PrOH/hexanes	11.5	10.4
	2% *i*-PrOH/hexanes	16.3	50.1
	10% *i*-PrOH/hexanes	11.5	27.2
	5% *i*-PrOH/hexanes	11.9	34.3

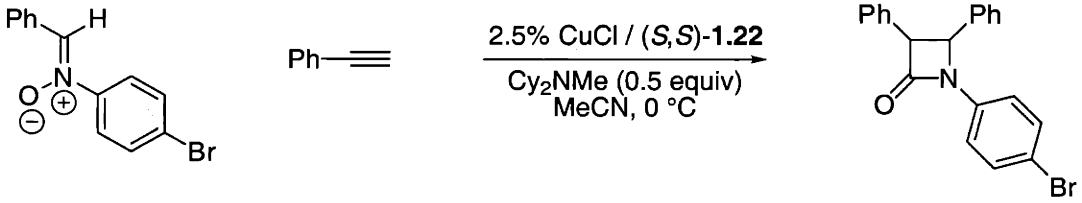
	5% *i*-PrOH/hexanes	19.8	38.6
	10% *i*-PrOH/hexanes	13.9	30.6
	10% *i*-PrOH/hexanes	14.2	48.1
	10% *i*-PrOH/hexanes	9.9	43.3
	20% *i*-PrOH/hexanes	15.1	30.4
	5% *i*-PrOH/hexanes	10.0	25.2

	5% *i*-PrOH/hexanes	10.6	25.7
	5% *i*-PrOH/hexanes	15.1	42.4
	20% *i*-PrOH/hexanes	10.7	27.8
	20% *i*-PrOH/hexanes	8.7	30.4
	10% *i*-PrOH/hexanes	11.9	43.7
	10% *i*-PrOH/hexanes	7.5	10.2

	5% *i*-PrOH/hexanes	9.1	35.8
	10% *i*-PrOH/hexanes	15.8	31.1
	5% *i*-PrOH/hexanes	20.7	39.2
	5% *i*-PrOH/hexanes	15.0	21.5
	5% *i*-PrOH/hexanes	6.4	15.0
	5% *i*-PrOH/hexanes	11.1	18.3
	5% *i*-PrOH/hexanes	10.1	13.1

	1% *i*-PrOH/hexanes	8.3	23.0
	1% *i*-PrOH/hexanes	8.1	10.1
	5% *i*-PrOH/hexanes	12.2	27.4
	5% *i*-PrOH/hexanes	11.1	26.0
	2% *i*-PrOH/hexanes	11.8	29.0

Assignment of absolute stereochemistry. The cis 2-azetidinone from the following reaction was structurally characterized by X-ray crystallography.



The absolute stereochemistry was determined unambiguously to be (3*S*,4*S*) (Figure 4.8). Based on this result, the absolute configurations of the products illustrated in Table 4.20 were assigned by analogy.

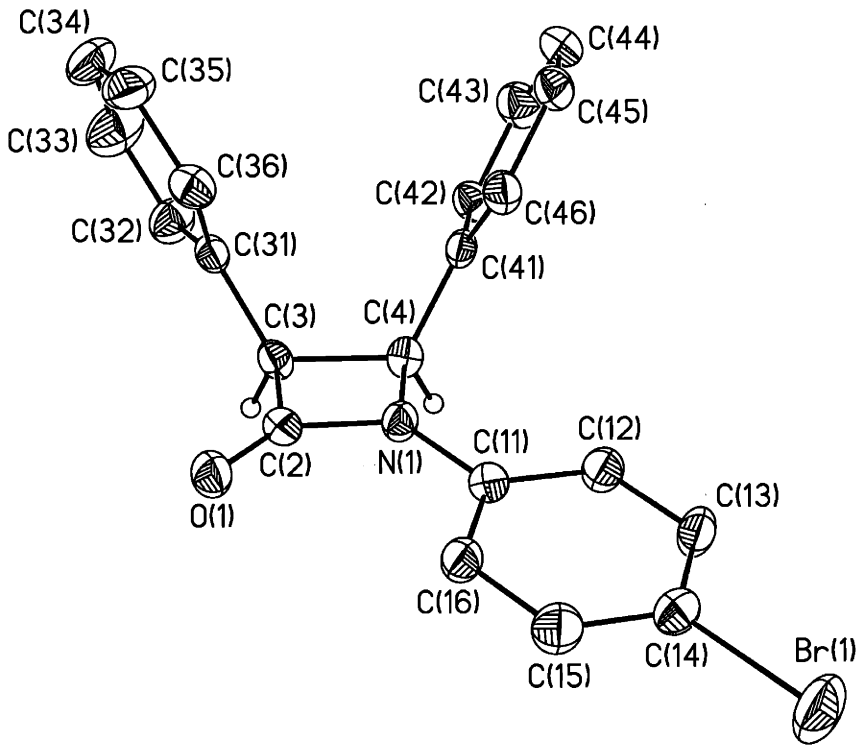


Figure 4.8. ORTEP plot of (3*S*,4*S*)-1-(4-bromophenyl)-3,4-diphenyl-2-azetidinone, with thermal ellipsoids drawn at the 35% probability level.

Curriculum Vitae

Education and Qualifications

1996–2001	Massachusetts Institute of Technology Doctor of Philosophy (Chemistry)
Thesis Supervisor	Prof. Gregory C. Fu
Thesis Title	Applications of C_2-Symmetric Bis(azaferrocenes) in Asymmetric Copper-Catalyzed Reactions
1993–1996	Hong Kong University of Science and Technology Master of Philosophy (Chemistry)
Thesis Supervisor	Prof. Paul R. Carlier
Thesis Title	Synthesis of γ-Aminoalcohol Derivatives and Study of the Mechanism of Cp-Ti Protonolysis
1990–1993	University of Hong Kong Bachelor of Engineering (Mechanical) Graduated with First Class Honor
Design Project	Design of a SNG (Substitute Natural Gas) Plant
Final Year Project	Study of Gas Flow Profiles above "Wet" Sieve Trays

Scholarships and Awards

1999–2000	Boehringer Ingelheim Predoctoral Fellowship
1998–1999	Pharmacia and Upjohn Predoctoral Fellowship

Publications

1. Bellemin-Laponnaz, S.; Lo, M. M.-C.; Peterson, T. H.; Allen, J. M.; Fu, G. C. *Organometallics* **2001**, *20*, 3453–3458.
2. Lo, M. M.-C.; Fu, G. C. *Tetrahedron* **2001**, *57*, 2621–2634.
3. Tao, B.; Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 353–354.
4. Shintani, R.; Lo, M. M.-C.; Fu, G. C. *Org. Lett.* **2000**, *2*, 3695–3697.
5. Tanaka, K.; Qiao, S.; Tobisu, M.; Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 9870–9871.
6. Carlier, P. R.; Lo, C. W.-S.; Lo, M. M.-C.; Wan, N. C.; Williams, I. D. *Org. Lett.* **2000**, *2*, 2443–2445.
7. Rios, R.; Liang, J.; Lo, M. M.-C.; Fu, G. C. *Chem. Commun.* **2000**, 377–378.
8. Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 10270–10271.
9. Garrett, C. E.; Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 7479–7483.
10. Carlier, P. R.; Lo, M. M.-C.; Lo, P. C.-K.; Richelson, E.; Tatsumi, M.; Reynolds, I. J.; Sharma, T. A. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 487–492.
11. Carlier, P. R.; Lo, K. M.; Lo, M. M.-C.; Lo, P. C.-K.; Lo, C. W.-S. *J. Org. Chem.* **1997**, *62*, 6316–6321.
12. Carlier, P. R.; Lo, K. M.; Lo, M. M.-C.; Williams, I. D. *J. Org. Chem.* **1995**, *60*, 7511–7517.

Patent

1. Carlier, P. R.; Lo, M. M.-C.; Lo, P. C.-K.; Richelson, E. 3-Hydroxypropanamine Derived Neuronal Reuptake Inhibitors. U. S. Patent 6,069,177, 2000.

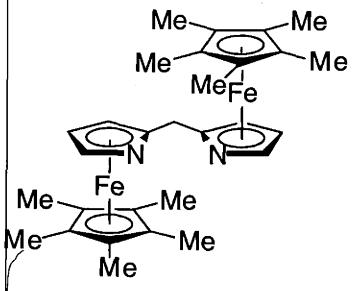
Appendix A

^{1}H NMR Spectra for Selected Compounds

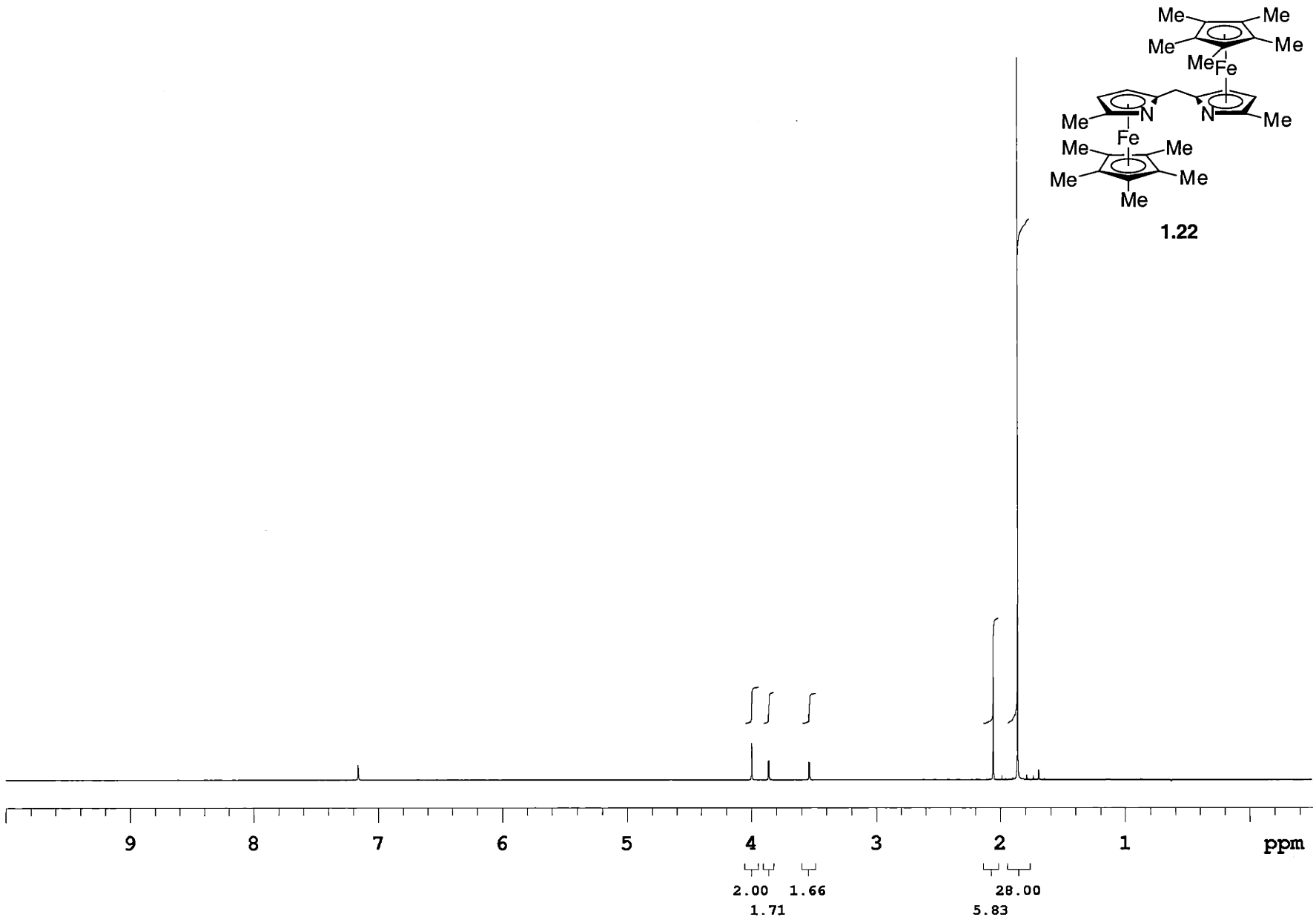
MML-IV-218a

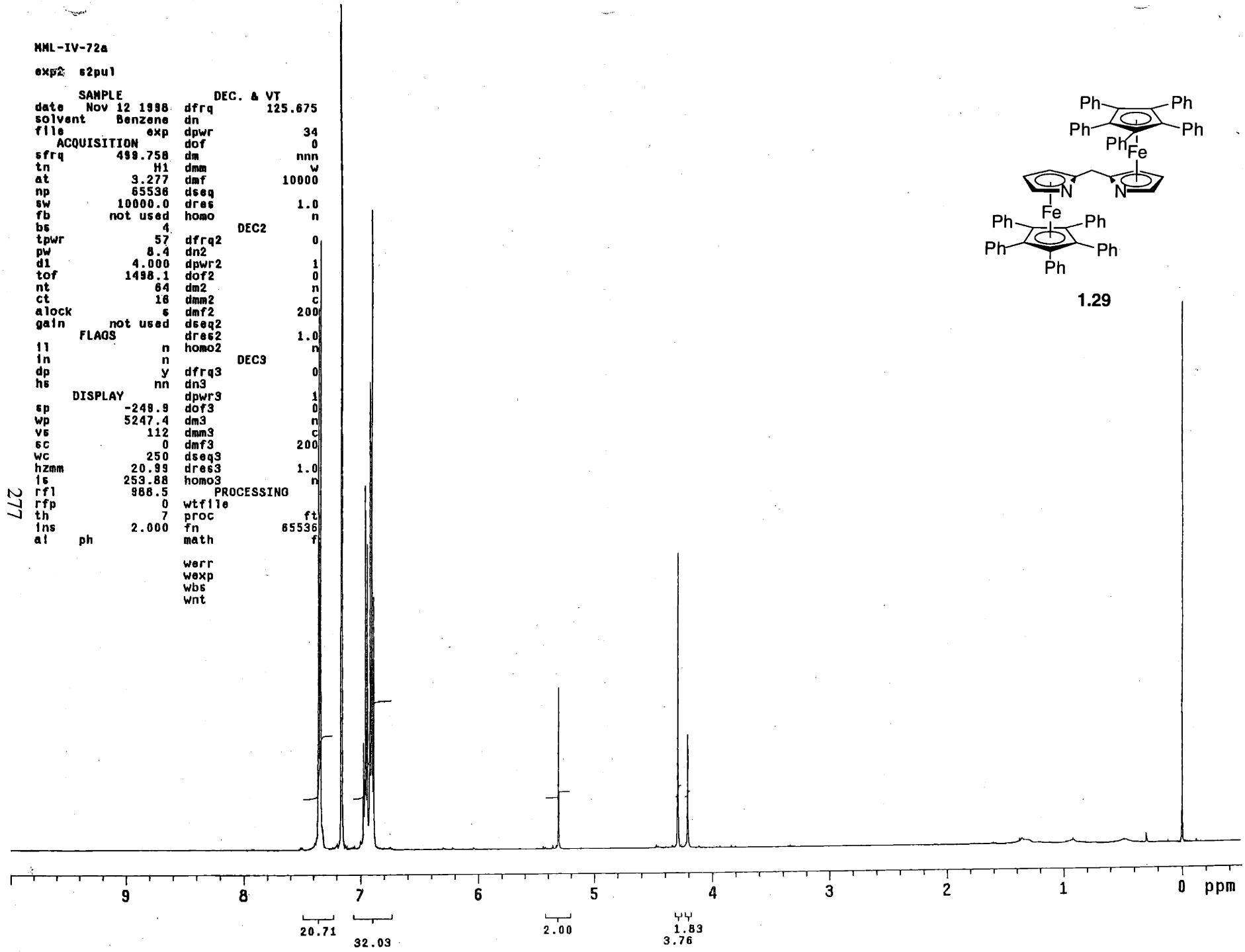
exp1 std1h

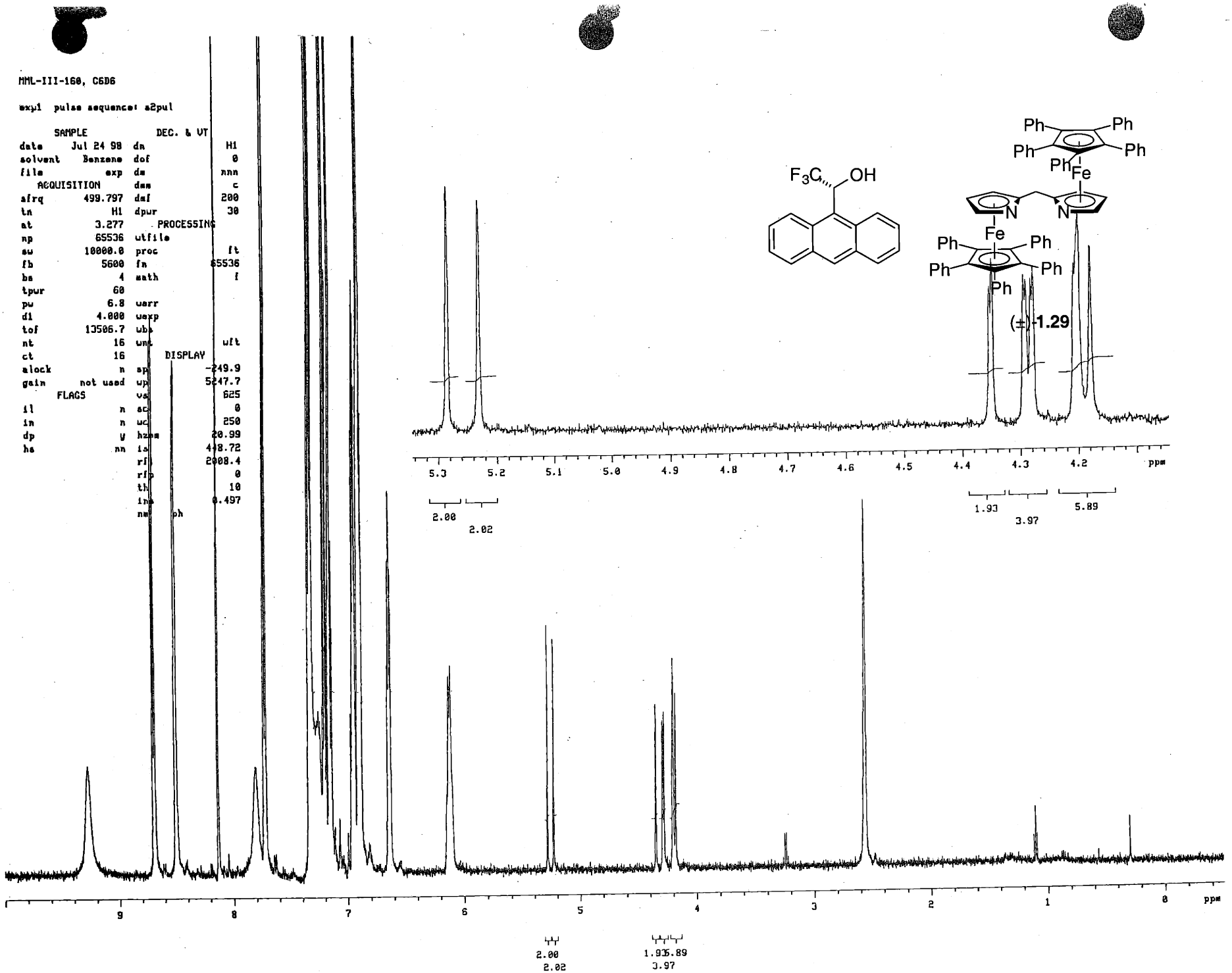
SAMPLE		DEC. & VT	
date	Jan 12 1999	dn	H1
solvent	Benzene	dof	0
file	exp	dm	nnn
ACQUISITION		dmm	c
sfrq	299.871	dmf	9900
tn	H1	dpwr	49
at	3.500	PROCESSING	
np	37376	wtfile	
sw	5339.7	proc	ft
fb	3000	fn	not used
bs	4	math	f
tpwr	60		
pw	12.0	werr	
d1	4.000	wexp	
tof	995.5	wbs	
nt	16	wnt	
ct	16	DISPLAY	
alock	n	sp	-150.0
gain	not used	wp	3148.6
FLAGS		vs	648
il	n	sc	0
in	n	wc	250
dp	y	hzmm	12.59
hs	nn	is	6352.91
		rfl	2732.0
		rfp	2147.1
		th	20
		ins	30.000
		nm	ph



1.19


Me
Me
Me
Me
Me
Fe
N
N
Me
Me
Fe
Me
Me
Me
Me
Me
1.22
9
8
7
6
5
4
3
2
1
ppm
2.00
1.71
1.66
28.00
5.83


MNL-IV-72a
exp2 s2pul
SAMPLE
date Nov 12 1998
solvent Benzene
file exp
ACQUISITION
sfrq 499.758
tn H1
at 3.277
np 65536
sw 10000.0
fb not used
bs 4
tpwr 57
pw 8.4
d1 4.000
tof 1498.1
nt 64
ct 16
alock s
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -248.9
wp 5247.4
vs 112
sc 0
wc 250
hzmm 20.99
is 253.88
rfl 988.5
rfp 0
th 7
ins 2.000
ai ph
DEC. & VT
dfrq 125.675
dn
dpwr 34
dof 0
dm nnn
dmm w
dmf 10000
dseq
dres 1.0
homo n
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 200
dseq2
dres2 1.0
homo2 n
DEC3
dfrq3 0
dn3
dpwr3 1
dof3 0
dm3 n
dmm3 c
dmf3 200
dseq3
dres3 1.0
homo3 n
PROCESSING
wtfile
proc ft
fn 65536
math f
werr
wexp
wbs
wnt
277
9
8
7
6
5
4
3
2
1
0 ppm
20.71
32.03
2.00
1.83
3.76
Ph
Fe
N
1.29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exp1 pulse sequence: s2pul
SAMPLE
date Jul 24 98
solvent Benzene
file exp
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tn H1
at 3.277
np 65536
sw 10000.0
fb 5600
bs 4
tpur 60
pw 6.8
d1 4.000
tof 13506.7
nt 16
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm nnn
dmm c
dmf 200
dpur 30
PROCESSING
utfile
proc ft
fn 65536
math f
uerr
uexp
ubs
umc ufl
DISPLAY
sp -249.9
wp 5247.7
vs 625
sc 0
wc 250
hzcm 20.99
is 478.72
rf1 2008.4
rf2 0
th 10
ins 0.497
nm ph
F3C
OH
Ph
Fe
N
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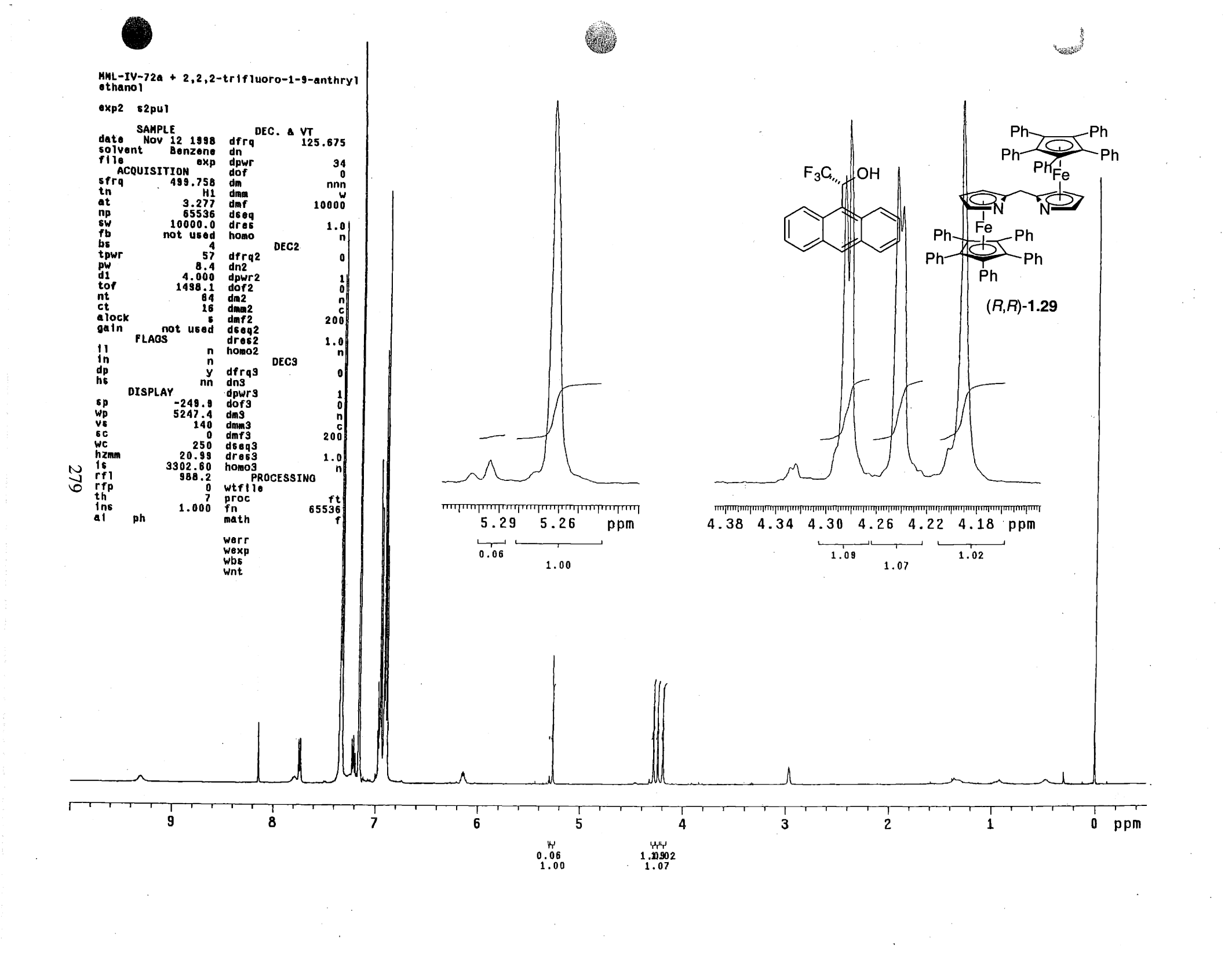
2.00
2.02
1.93
3.97
5.89
ppm


MML-IV-72a + 2,2,2-trifluoro-1-9-anthryl ethanol
exp2 s2pul
SAMPLE
date Nov 12 1998
solvent Benzene
file exp
ACQUISITION
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tn H1
at 3.277
np 65536
sw 10000.0
fb not used
bs 4
tpwr 57
pw 8.4
d1 4.000
tof 1498.1
nt 64
ct 16
alock s
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -249.9
wp 5247.4
vs 140
sc 0
wc 250
hzmm 20.99
is 3302.60
rfl 988.2
rfp 0
th 7
ins 1.000
ai ph
DEC. & VT
dfrq 125.675
dn
dpwr 34
dof 0
dm nnn
dmm w
dmf 10000
dseq
dres 1.0
homo n
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 200
dseq2
dres2 1.0
homo2 n
DEC3
dfrq3 0
dn3
dpwr3 1
dof3 0
dm3 n
dmm3 c
dmf3 200
dseq3
dres3 1.0
homo3 n
PROCESSING
wtfile
proc ft
fn 65536
math f
werr
wexp
wbs
wnt
F3C
OH
Ph
Fe
N
(R,R)-1.29
5.29 5.26 ppm
0.06
1.00
4.38 4.34 4.30 4.26 4.22 4.18 ppm
1.09
1.07
1.02
9 8 7 6 5 4 3 2 1 0 ppm
0.06
1.00
1.07
279

MML-IV-102a

exp1 s2pul

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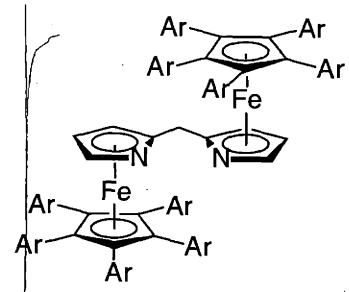
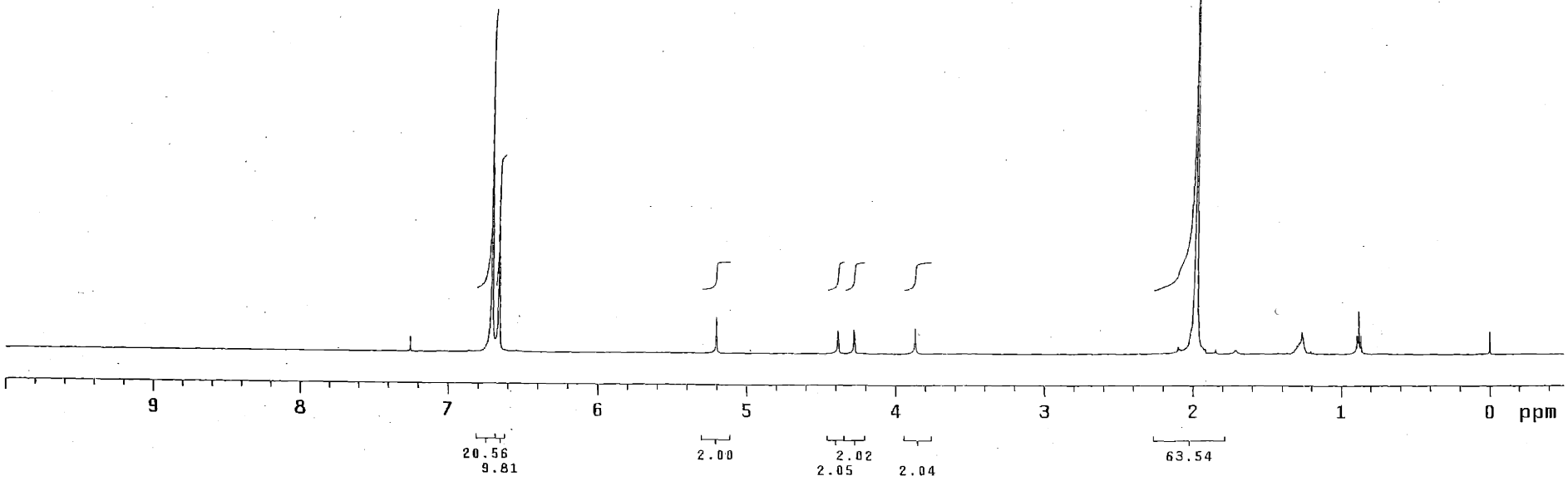
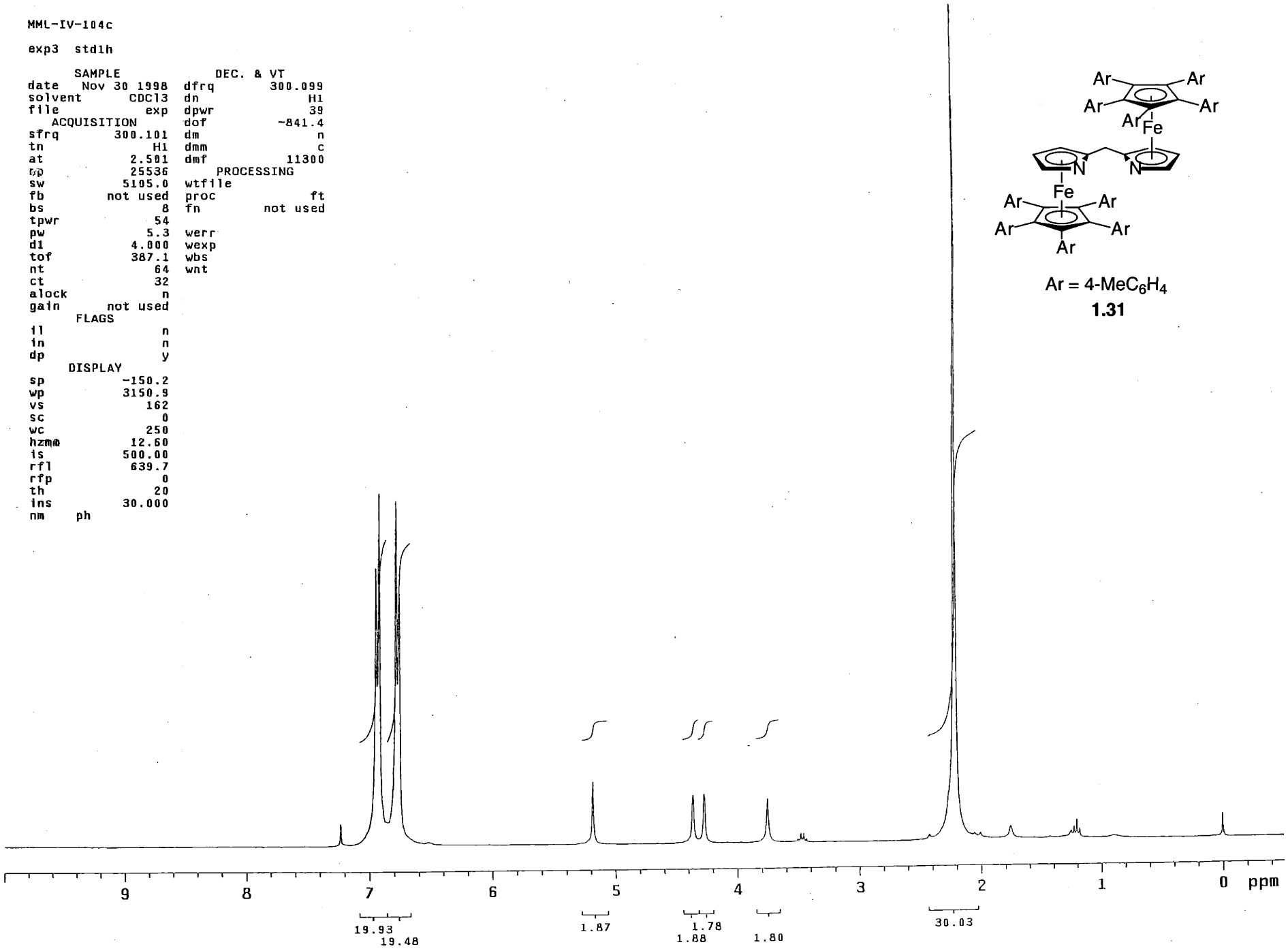
date	Nov 27 1998	dfrq	500.247
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	500.248	dm	nnn
tn	H1	dmm	c
at	3.277	dmf	10000
np	65536	dseq	
sw	10000.0	dres	1.0
fb	not used	homo	y
bs	4	PROCESSING	
tpwr	60	wtfile	
pw	8.1	proc	lp
d1	4.000	fn	not used
tof	1498.2	math	f
nt	16		
ct	16	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.3		
wp	5252.5		
vs	151		
sc	0		
wc	250		
hzmm	21.01		
is	659.29		
rfl	1007.4		
rfp	0		
th	7		
ins	2.000		
nm	ph		



Ar = 3,5-$Me_2C_6H_3$

1.30

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SAMPLE
date Nov 30 1998
solvent CDCl3
file exp
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sfrq 300.101
tn H1
at 2.501
np 25536
sw 5105.0
fb not used
bs 8
tpwr 54
pw 5.3
d1 4.000
tof 387.1
nt 64
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -150.2
wp 3150.9
vs 162
sc 0
wc 250
hzmm 12.60
is 500.00
rfl 639.7
rfp 0
th 20
ins 30.000
nm ph
DEC. & VT
dfrq 300.099
dn H1
dpwr 39
dof -841.4
dm n
dmm c
dmf 11300
PROCESSING
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
Ar
Fe
N
Ar = 4-MeC6H4
1.31
9
8
7
6
5
4
3
2
1
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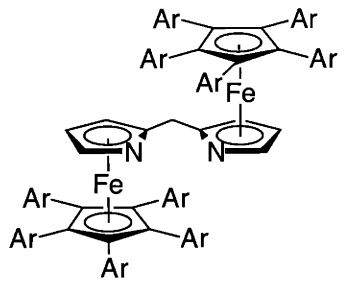
19.48
1.87
1.78
1.88
1.80
30.03



Ar = 4-(MeO)C_6H_4

1.32

MML-IV-106a

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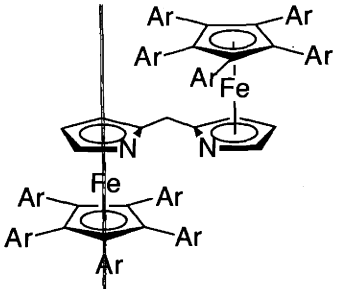
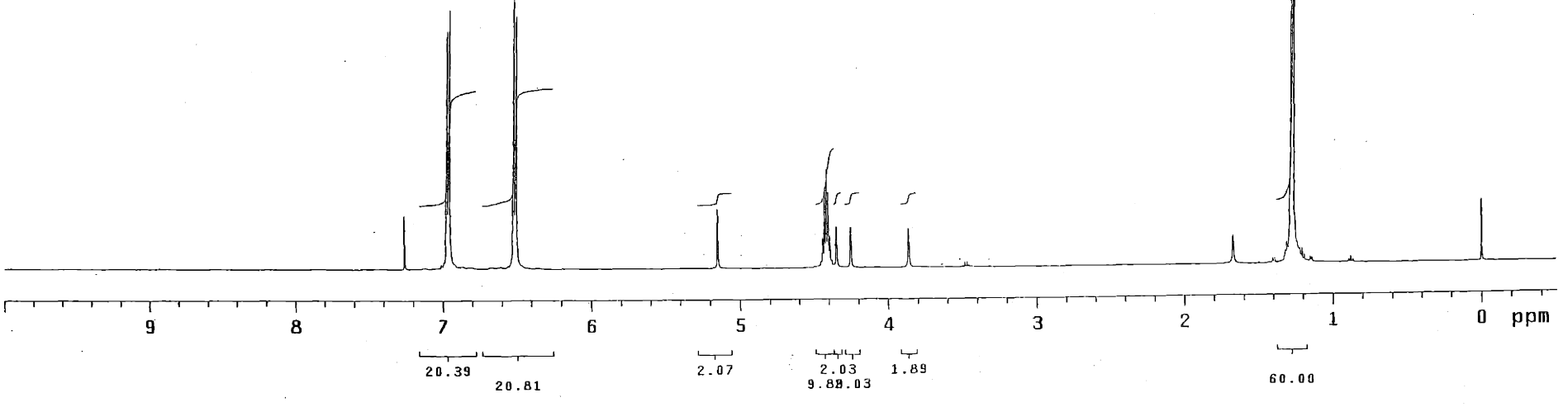
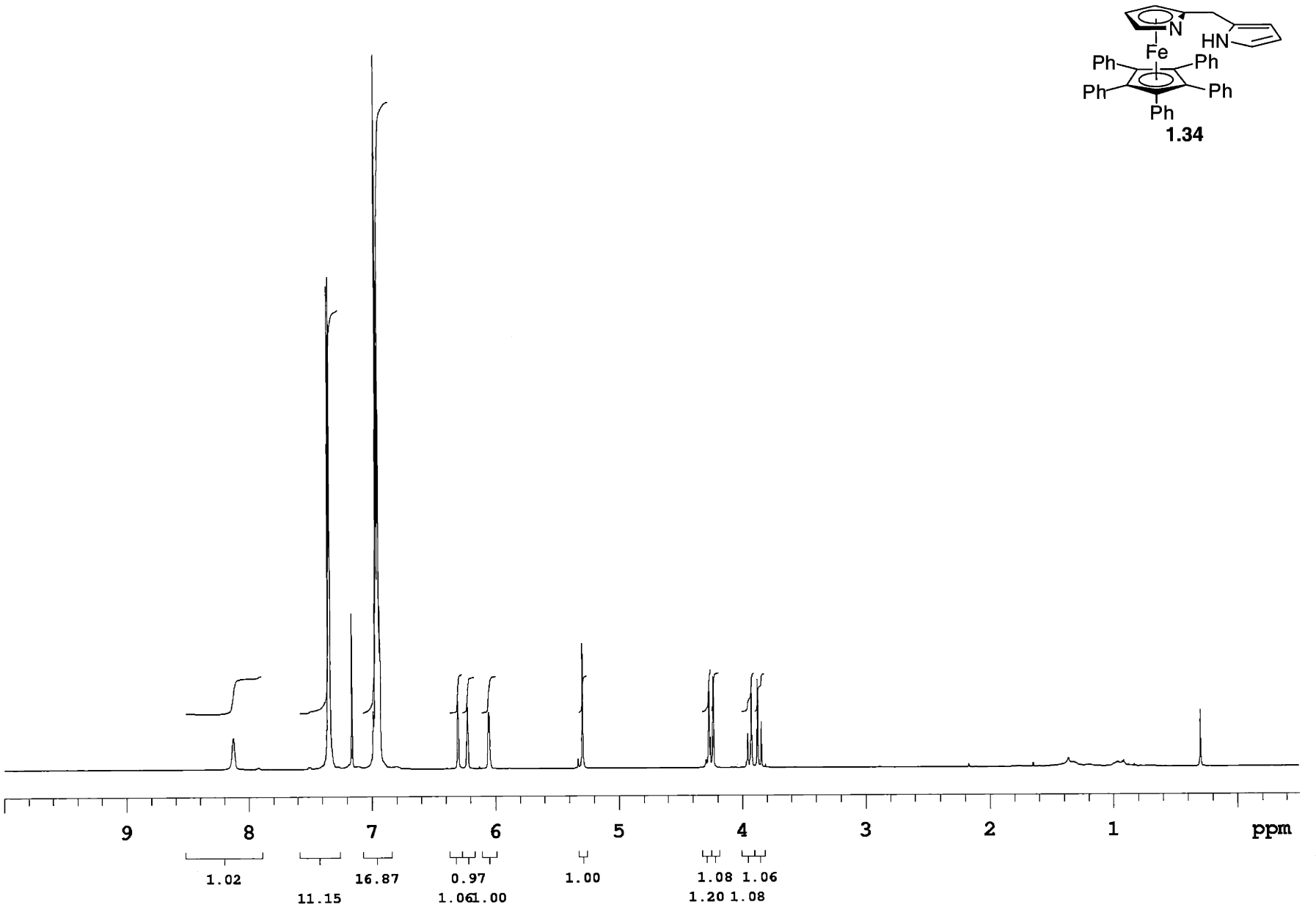
ACQUISITION		dof	0
sfrq	500.248	dm	nnn
tn	H1	dmm	c
at	3.277	dmf	10000
np	65536	dseq	
sw	10000.0	dres	1.0
fb	not used	homo	y
bs	8	PROCESSING	
tpwr	60	wtfile	
pw	8.1	proc	ft
d1	4.000	fn	not used
tof	1498.2	math	f
nt	64		
ct	32	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.3		
wp	5252.5		
vs	151		
sc	0		
wc	250		
hzmm	21.01		
is	465.54		
rfl	1003.4		
rfp	0		
th	7		
ins	60.000		
nm	ph		

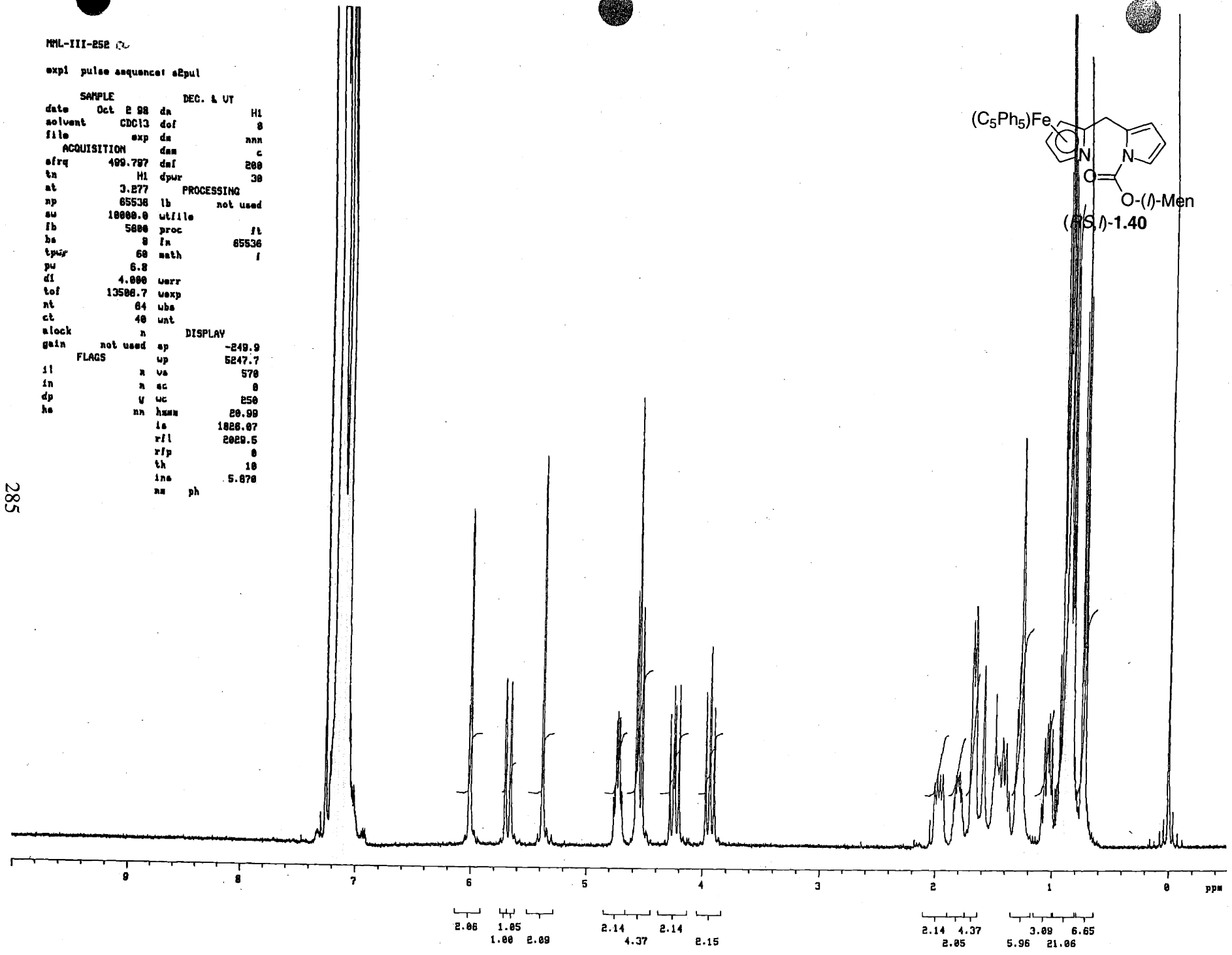


Ar = 4-(*i*-PrO)C_6H_4

1.33



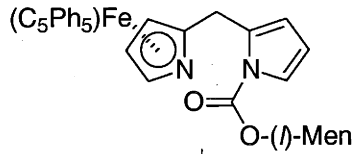

N
HN
Fe
Ph
Ph
Ph
Ph
Ph
1.34
9
8
7
6
5
4
3
2
1
ppm
1.02
11.15
16.87
0.97
1.06
1.00
1.00
1.08
1.20
1.06
1.08


MML-III-252
expl pulse sequence: s2pul
SAMPLE
date Oct 2 98
solvent CDCl3
file exp
ACQUISITION
sfrq 499.797
tn H1
at 3.277
np 65536
sw 10000.0
fb 5000
bs 8
tpwr 60
pw 6.8
dl 4.000
tof 13508.7
nt 64
ct 48
alock n
gain not used
FLAGS
il n
in n
dp y
he nn
DEC. & VT
dn H1
dof 0
dm nnn
dmm c
dmf 200
dpwr 38
PROCESSING
lb not used
wtfile
proc ft
fn 65536
math f
werr
wexp
wbs
wnt
DISPLAY
sp -249.9
wp 5247.7
vs 570
sc 0
wc 250
hzmm 20.99
is 1826.07
rfl 2029.5
rfp 0
th 10
ins 5.870
ns ph
(C5Ph5)Fe
N
N
O
O-(l)-Men
(RS,l)-1.40
9
8
7
6
5
4
3
2
1
0
ppm
2.06
1.05
1.00
2.09
2.14
4.37
2.14
2.15
2.14
4.37
2.05
3.09
6.65
5.96
21.06

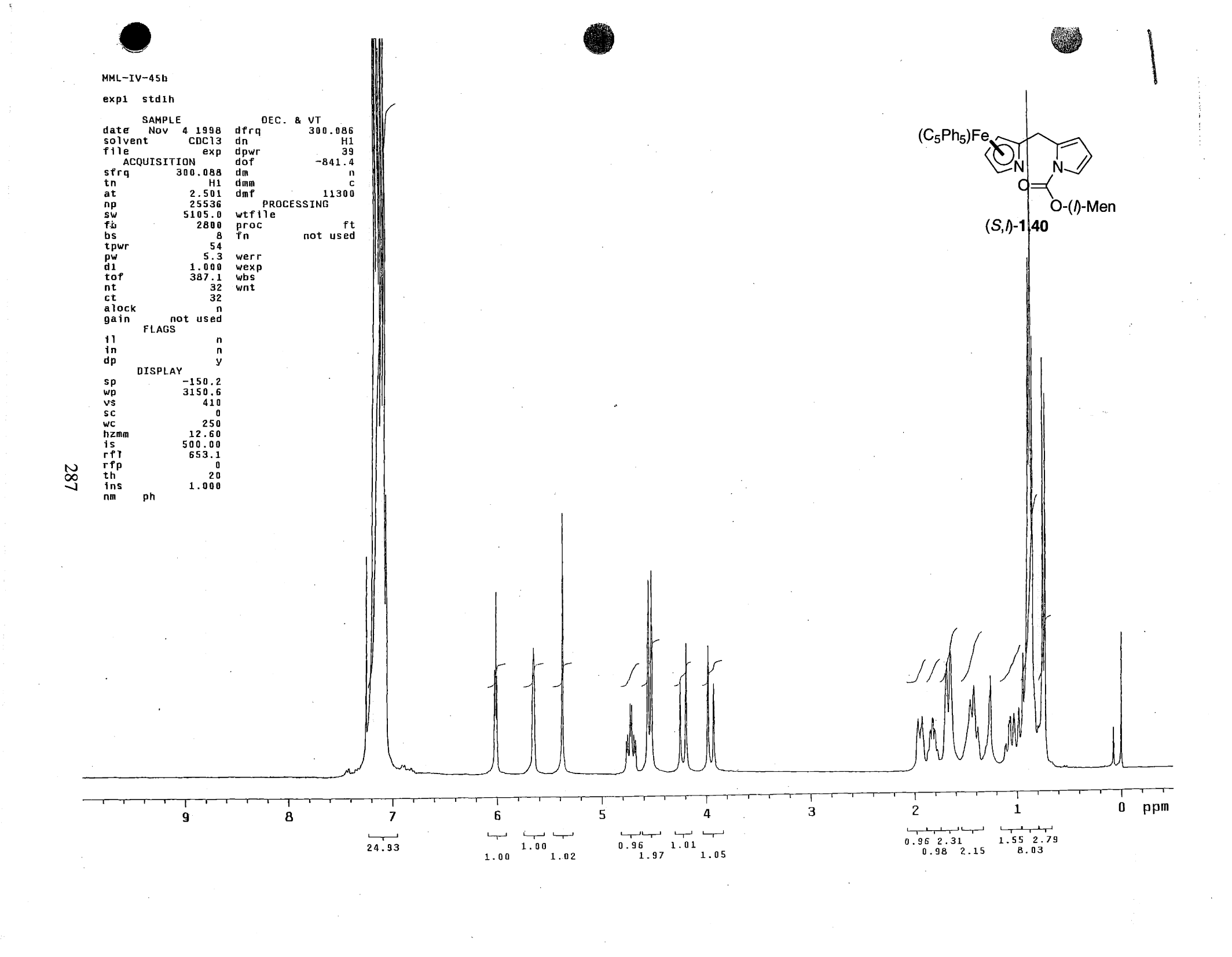
MML-IV-45a

exp1 pulse sequence: stdih

SAMPLE		DEC. & VT	
date	Nov 4 98	dn	H1
solvent	CDCl3	dof	0
file	exp	dm	nnn
ACQUISITION		dmm	c
sfrq	299.871	dmf	200
tn	H1	dpwr	15
at	3.500	PROCESSING	
np	37376	wtfile	
su	5339.7	proc	ft
fb	3000	fn	not used
bs	8	math	f
tpwr	60		
pw	23.0	werr	
d1	4.000	wexp	wft
tof	995.5	wbs	
nt	32	wnt	
ct	32	DISPLAY	
alock	n	sp	-150.1
gain	not used	wp	3148.6
FLAGS		vs	400
il	n	sc	0
in	n	wc	250
dp	y	hzmm	12.59
hs	nn	is	7991.23
		rfl	600.0
		rfp	0
		th	20
		ins	2.738
		nm ph	



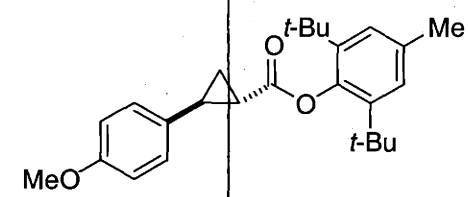
(*R*,*l*)-**1.40**


MML-IV-45b
exp1 stdih
SAMPLE
date Nov 4 1998
solvent CDCl3
file exp
ACQUISITION
sfrq 300.088
tn H1
at 2.501
np 25536
sw 5105.0
fb 2800
bs 8
tpwr 54
pw 5.3
d1 1.000
tof 387.1
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -150.2
wp 3150.6
vs 410
sc 0
wc 250
hzmm 12.60
is 500.00
rf1 653.1
rfp 0
th 20
ins 1.000
nm ph
DEC. & VT
dfrq 300.086
dn H1
dpwr 39
dof -841.4
dm n
dmm c
dmf 11300
PROCESSING
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
(C5Ph5)Fe
N
N
O
O-(l)-Men
(S,l)-140
9
8
7
6
5
4
3
2
1
0 ppm
24.93
1.00
1.00
1.02
0.96
1.97
1.01
1.05
0.96 2.31
0.98 2.15
1.55 2.79
8.03

MML-II-168b

expl pulse sequence: s2pul

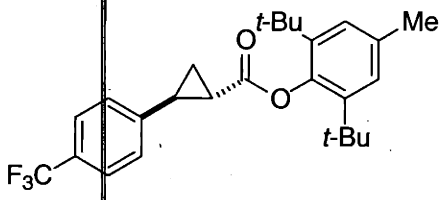
SAMPLE		DEC. & UT	
date	Feb 11 98	dn	H1
solvent	CDCl3	dof	0
file	exp	dm	nnn
ACQUISITION		dmm	c
sfrq	499.797	dmf	200
tn	H1	dpwr	30
at	1.638	PROCESSING	
np	32768	wtfile	
sw	10000.0	proc	ft
fb	5600	fn	65536
bs	16	math	f
tpwr	60		
pw	6.8	werr	
d1	2.000	wexp	
tof	13586.7	wbs	
ns	256	wnt	wft
ct	98	DISPLAY	
alock	n	sp	-249.9
gain	not used	wp	5247.7
FLAGS		vs	250
il	n	sc	0
in	n	wc	250
dp	y	hzmm	20.99
hs	nn	is	492.92
		rfl	2029.8
		rfp	0
		th	21
		ins	5.347
		nm ph	



MML-II-188 @

expl pulse sequence: s2pul

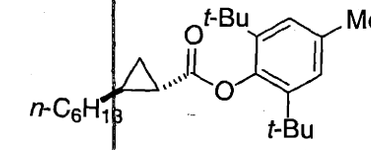
SAMPLE		DEC. & VT	
date	Feb 25 98	dn	H1
solvent	CDCl3	dof	0
file	exp	dm	nnn
ACQUISITION		dmm	c
sfrq	499.797	dmf	200
tn	H1	dpwr	30
at	1.638	PROCESSING	
np	32768	wtfile	
sw	10000.0	proc	ft
fb	5600	fn	65536
bs	4	math	f
tpwr	60		
pw	6.8	werr	
d1	4.000	wexp	
tof	13506.7	wbs	
nt	16	wnt	wft
ct	16	DISPLAY	
alock	n	sp	-249.9
gain	14	wp	5247.7
FLAGS		vs	400
il	n	sc	0
in	n	wc	250
dp	y	hzmm	20.99
hs	nn	is	603.53
		rfl	2028.9
		rfp	0
		th	10
		ins	1.000
		nm	ph



MML-II-176b

expl pulse sequence: s2pul

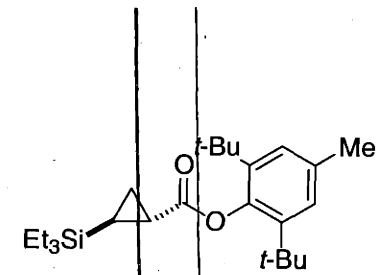
SAMPLE		DEC. & VT	
date	Mar 10 98	dn	H1
solvent	CDCl3	dof	0
file	exp	dm	nnn
ACQUISITION		dmm	c
sfrq	499.797	dmf	200
tn	H1	dpwr	38
at	1.638	PROCESSING	
np	32768	wtfile	
sw	10000.0	proc	ft
fb	5600	fn	65536
bs	4	math	f
tpwr	60		
pw	6.8	werr	
d1	4.000	wexp	
tof	13506.7	wbs	
nt	16	wnt	wft
ct	16	DISPLAY	
alock	n	sp	-249.9
gain	not used	wp	5247.7
FLAGS		vs	267
il	n	sc	0
in	n	wc	250
dp	y	hzmm	20.99
hs	nn	is	1250.00
		rfl	2028.9
		rfp	0
		th	4
		ins	5.469
		nm ph	

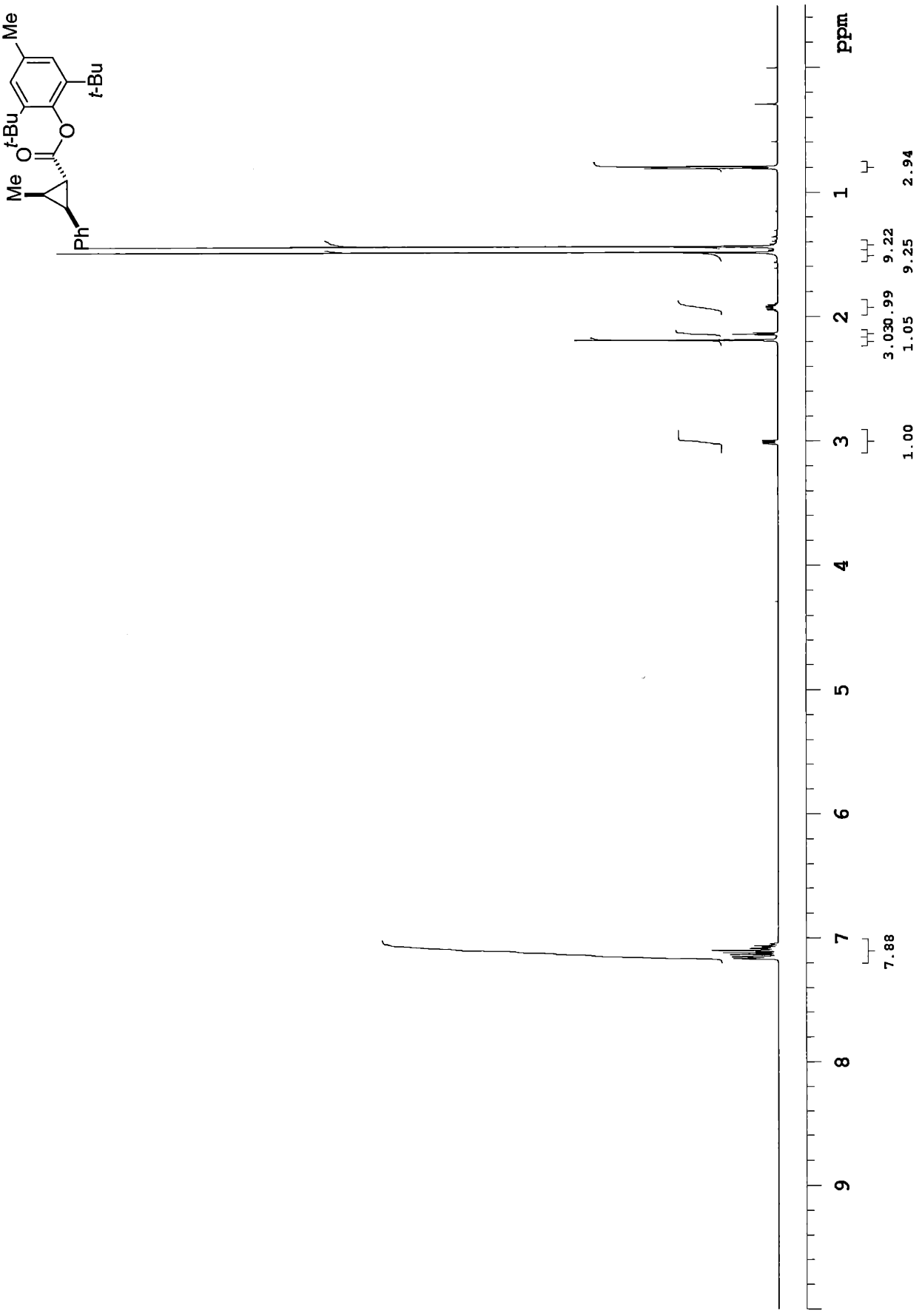


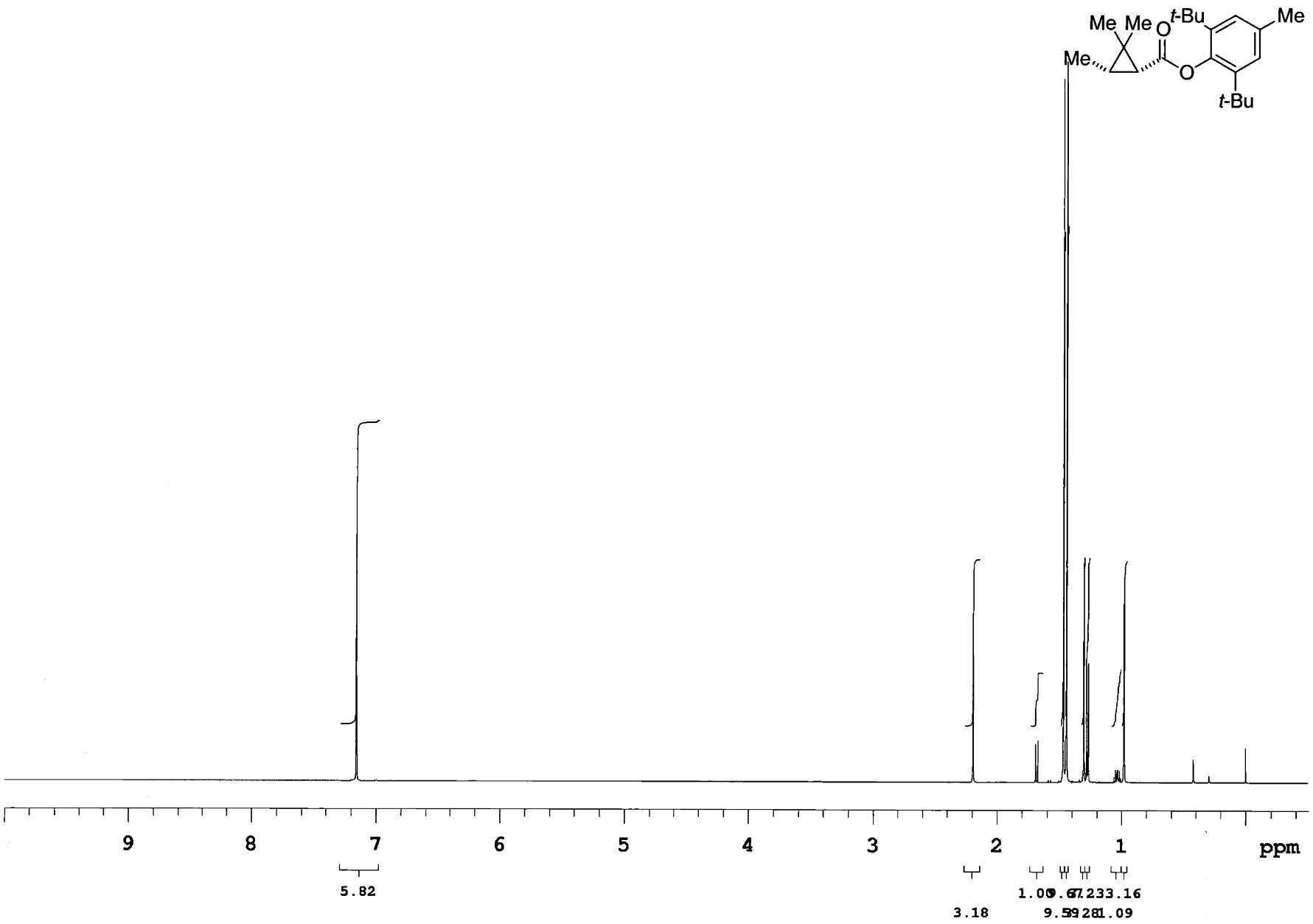
MML-II-178d

expl pulse sequence: s2pul

SAMPLE		DEC. & VT	
date	Mar 18 98	dn	H1
solvent	CDCl3	dof	0
file	exp	dm	nnn
ACQUISITION		dmm	c
sfrq	499.797	dmf	200
tn	H1	dpwr	38
at	1.638	PROCESSING	
np	32768	wtfile	
sw	10000.0	proc	lt
fb	5000	fn	65536
bs	4	wnth	f
tpwr	60		
pw	6.8	werr	
d1	4.000	wexp	
tof	13508.7	wbs	
nt	16	wnt	wlt
ct	16	DISPLAY	
alock	n	sp	-249.9
gain	not used	wp	5247.7
FLAGS		vs	400
il	n	sc	0
in	n	wc	250
dp	y	hzmm	28.99
hs	nn	is	1000.00
		rfl	2029.2
		rfp	0
		th	10
		ins	7.184
		ns	ph



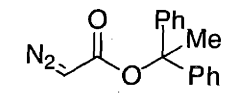

Me
t-Bu
t-Bu
O
O
Me
Ph
ppm
1
2
3
4
5
6
7
8
9
2.94
9.22
9.25
3.03
0.99
1.05
1.00
7.88


Me
Me
Me
O
t-Bu
Me
O
t-Bu
9
8
7
6
5
4
3
2
1
ppm
5.82
3.18
1.00
9.59
6.67
9.28
7.23
1.09
3.16

MML-VII-150c

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jul 8 2000	dfrq	125.675
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	2	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	40.000	dpwr2	1
tof	1498.1	dof2	0
mt	8	dm2	n
ct	8	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	328.96	homo3	n
rfl	1035.1	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	3.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	

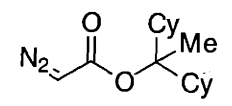


3.3

MML-VI-252a

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jul 6 2000	dfrq	125.675
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	2	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	40.000	dpwr2	1
tof	1498.1	dof2	0
nt	8	dm2	n
ct	8	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	774.89	homo3	n
rfl	999.1	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	3.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	

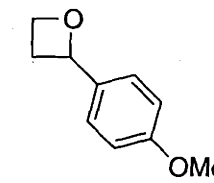


3.4

MML-VIII-92b

exp2 s2pul

SAMPLE		DEC. & VT	
date	Apr 29 2000	dfrq	125.675
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	414.29	homo3	n
rfl	986.8	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	

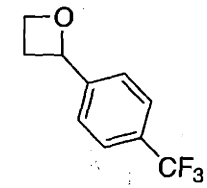


3.13

MNL-VII-292a

exp1 s2pul

SAMPLE		DEC. & VT	
date	Mar 16 2000	dfrq	125.675
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10400
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	55	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	3
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	3
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	819.12	homo3	n
rfl	987.2	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm ph		math	
		werr	
		wexp	
		wbs	
		wnt	

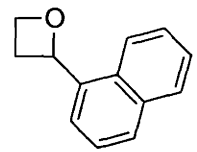


3.14

MML-VIII-18b

expl s2pul

SAMPLE		DEC. & VT	
date	Apr 8 2000	dfrq	500.247
solvent	Benzene	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	500.248	dm	nnn
tn	H1	dmm	c
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	y
bs	4	PROCESSING	
tpwr	58	wtfile	
pw	8.1	proc	ft
d1	4.000	fn	not used
tof	1498.2	math	f
nt	16		
ct	16	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.2		
wp	5252.5		
vs	151		
sc	0		
wc	250		
hzmm	21.01		
is	517.68		
rfl	983.2		
rfp	0		
th	7		
ins	1.000		
nm	ph		



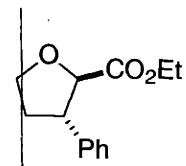
3.15

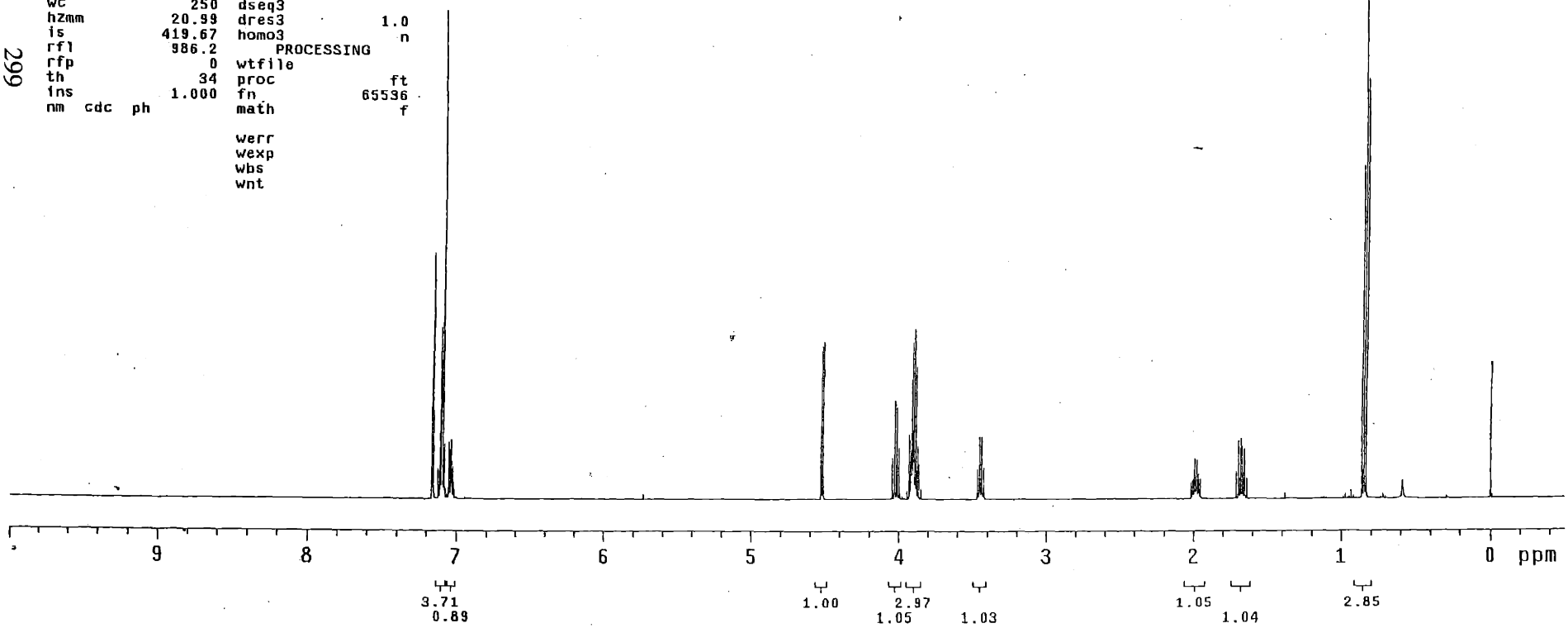
MML-VI-158b

exp1 s2pul

SAMPLE	
date	Jul 28 1999
solvent	Benzene
file	exp
ACQUISITION	
sfrq	499.758
tn	H1
at	3.277
np	65536
sw	9998.8
fb	not used
bs	4
tpwr	55
pw	8.5
d1	4.000
tof	1498.1
nt	16
ct	16
alock	n
gain	not used
FLAGS	
il	n
in	n
dp	y
hs	nn
DISPLAY	
sp	-249.9
wp	5247.3
vs	151
sc	0
wc	250
hzmm	20.99
is	419.67
rfl	986.2
rfp	0
th	34
ins	1.000
nm cdc ph	

DEC. & VT	
dfrq	125.675
dn	C13
dpwr	34
dof	0
dm	nnn
dmm	w
dmf	10400
dseq	
dres	1.0
homo	n
DEC2	
dfrq2	0
dn2	
dpwr2	1
dof2	0
dm2	n
dmm2	c
dmf2	200
dseq2	
dres2	1.0
homo2	n
DEC3	
dfrq3	0
dn3	
dpwr3	1
dof3	0
dm3	n
dmm3	c
dmf3	200
dseq3	
dres3	1.0
homo3	n
PROCESSING	
wtfile	
proc	ft
fn	65536
math	f
werr	
wexp	
wbs	
wnt	

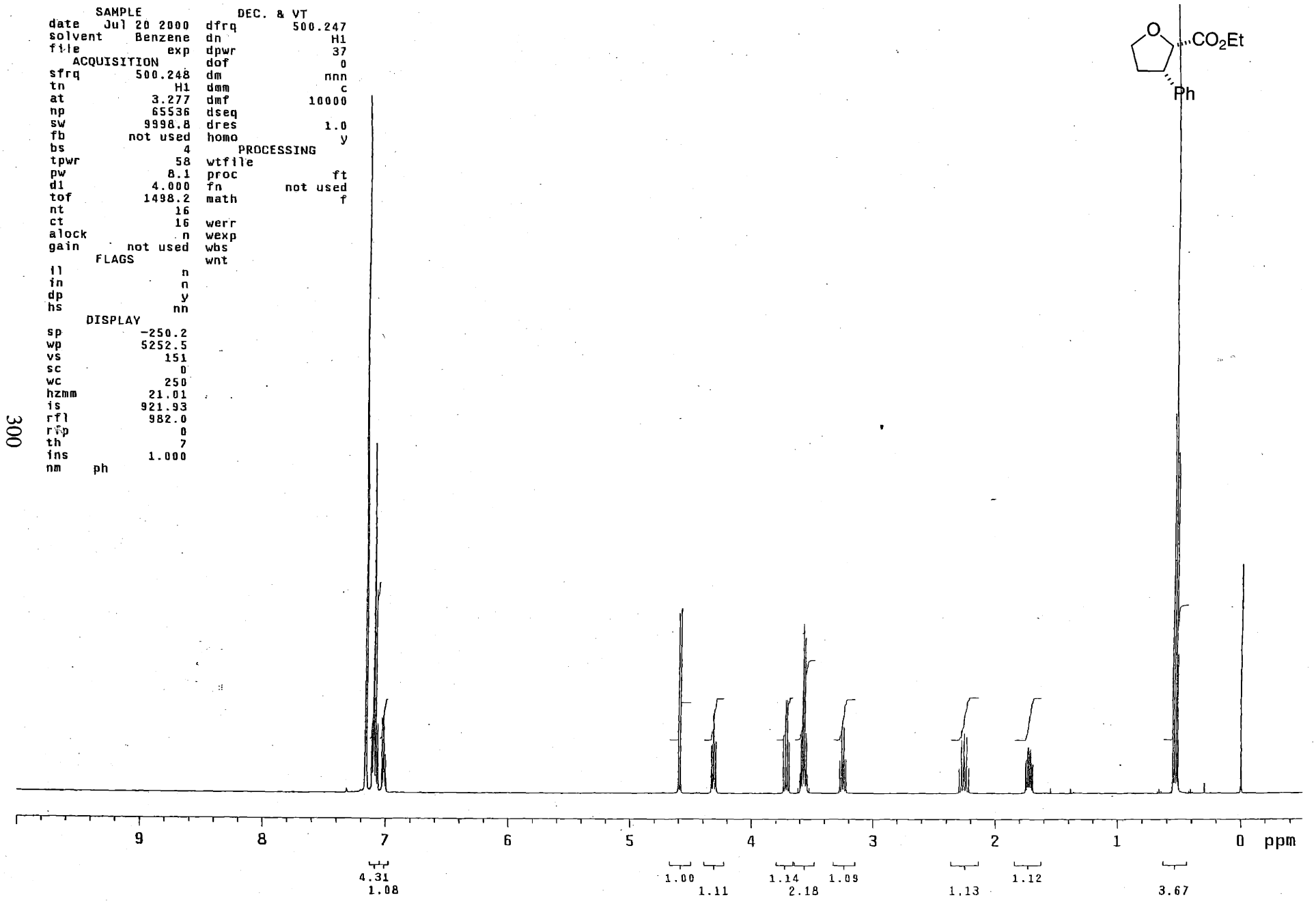




MML-VIII-196c

expl s2pul

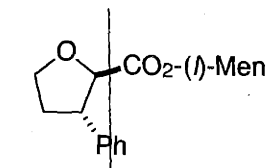
SAMPLE		DEC. & VT	
date	Jul 20 2000	dfrq	500.247
solvent	Benzene	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	500.248	dm	nnn
tn	H1	dmm	c
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	y
bs	4	PROCESSING	
tpwr	58	wtfile	
pw	8.1	proc	ft
d1	4.000	fn	not used
tof	1498.2	math	f
nt	16		
ct	16	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.2		
wp	5252.5		
vs	151		
sc	0		
wc	250		
hzmm	21.01		
is	921.93		
rfl	982.0		
rfp	0		
th	7		
ins	1.000		
nm	ph		

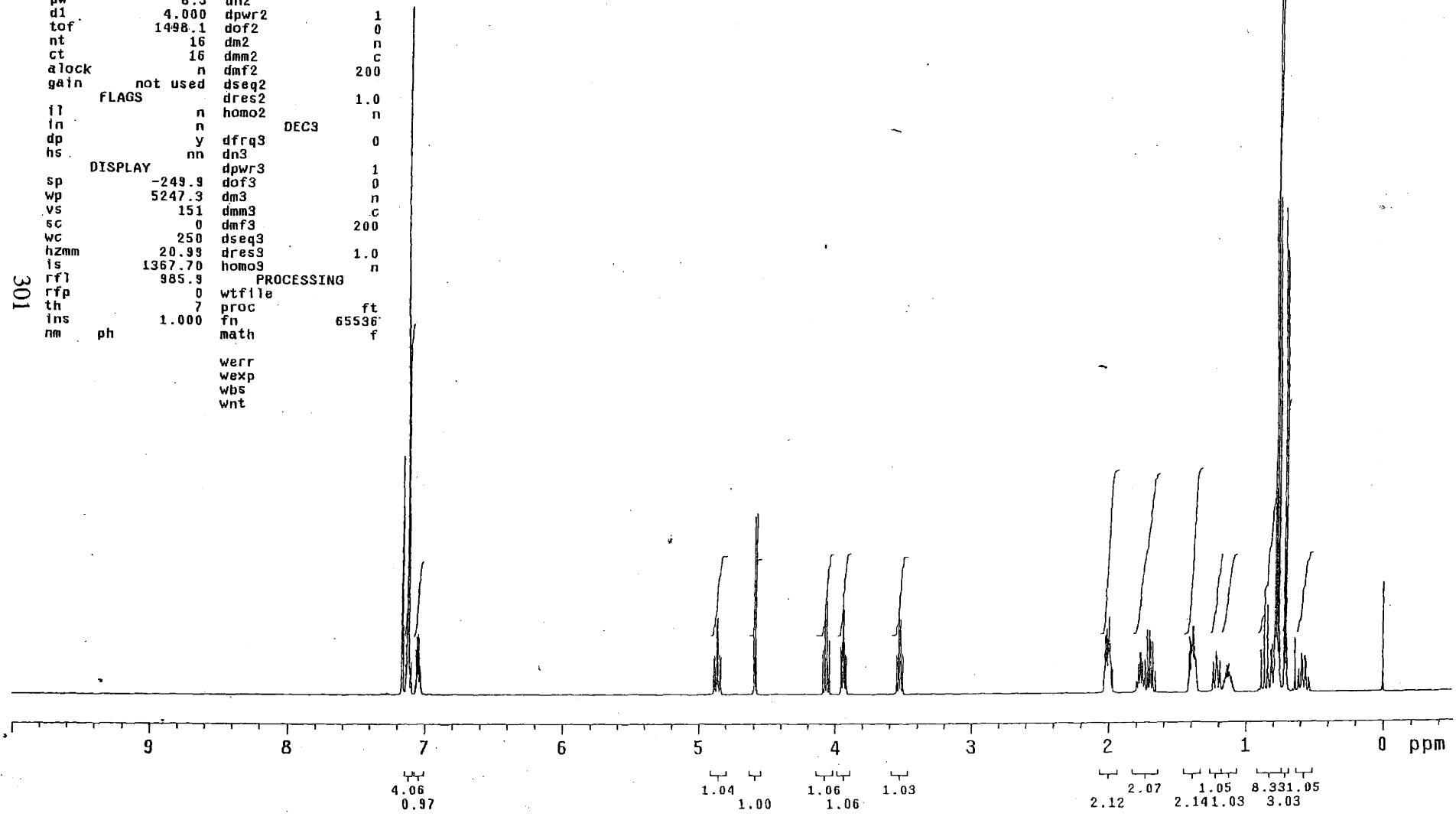


MML-VI-166c

exp1 s2pul

SAMPLE		DEC. & VT	
date	Aug 4 1999	dfrq	125.675
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10400
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	55	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.98	dres3	1.0
is	1367.70	homo3	n
rfl	985.9	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	

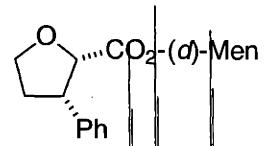


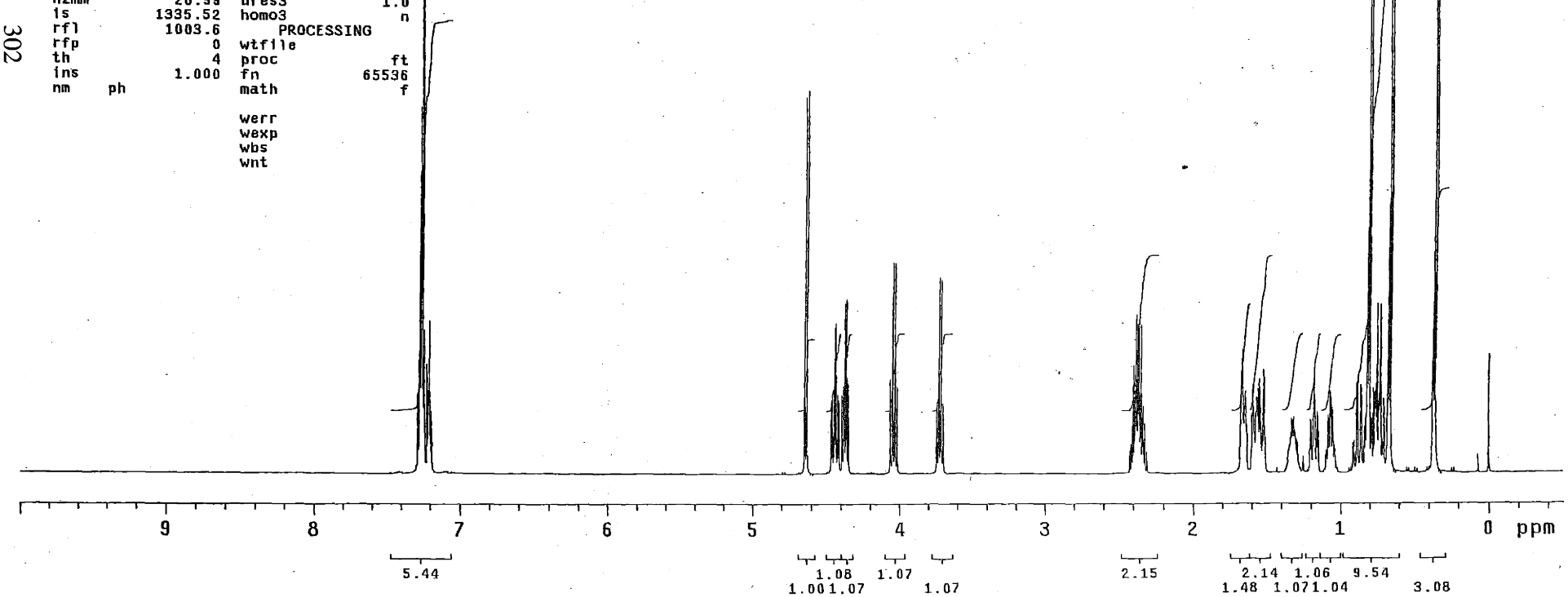


MML-VIII-206b

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jul 26 2000	dfrq	125.675
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	1335.52	homo3	n
rfl	1003.6	PROCESSING	
rfp	0	wtfile	
th	4	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	

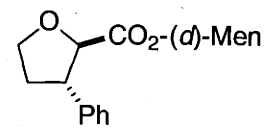




MML-VI-164b

exp1 s2pul

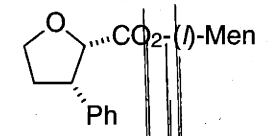
SAMPLE		DEC. & VT	
date	Jul 11 2000	dfrq	125.675
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	1305.84	homo3	n
rfl	4564.1	PROCESSING	
rfp	3578.2	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm	ph	math	f
		werr	
		wexp	
		wbs	
		wnt	

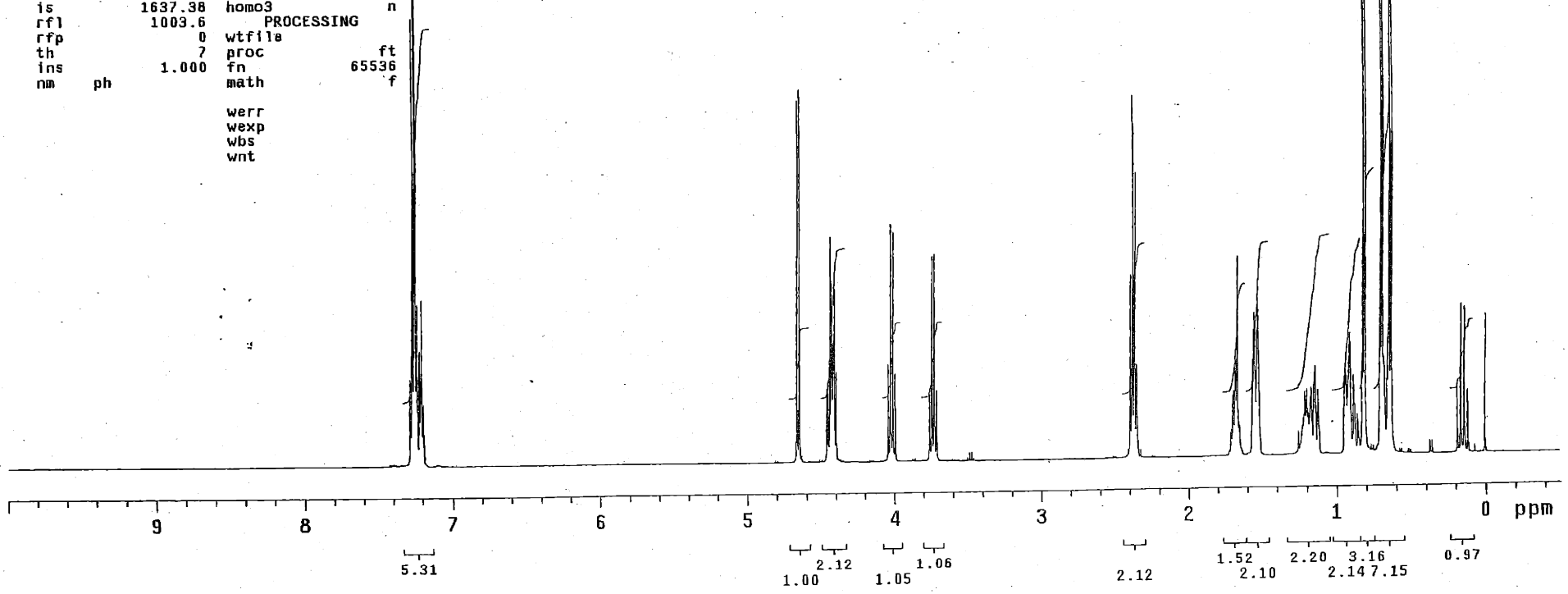


MML-VIII-208b

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jul 25 2000	dfrq	125.675
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	148	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	1637.38	homo3	n
rfl	1003.6	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	

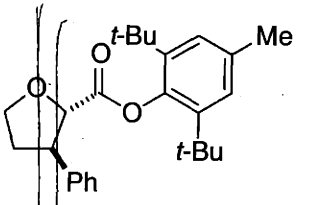


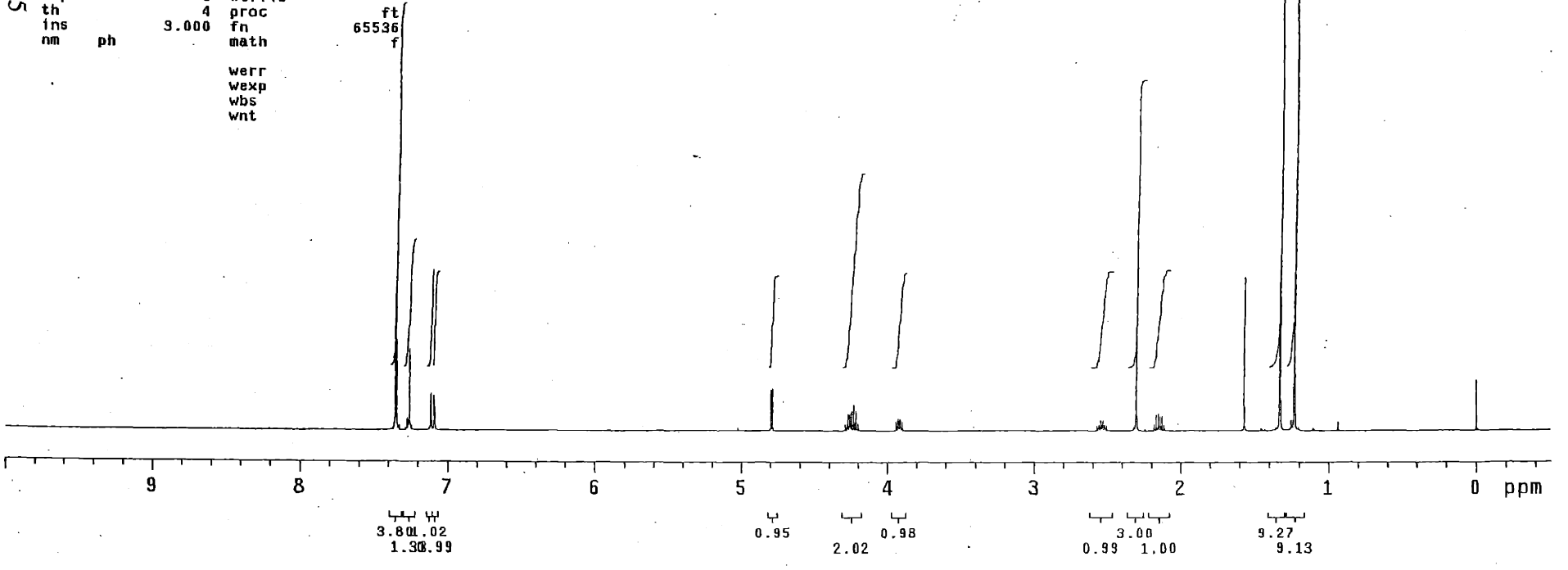


MML-VIII-220h

exp1 s2pul

SAMPLE		DEC. & VT	
date	Aug 3 2000	dfrq	125.675
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	1610.24	homo3	n
rfl	1008.2	PROCESSING	
rfp	0	wtfile	
th	4	proc	ft
ins	3.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	

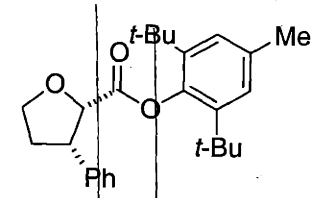


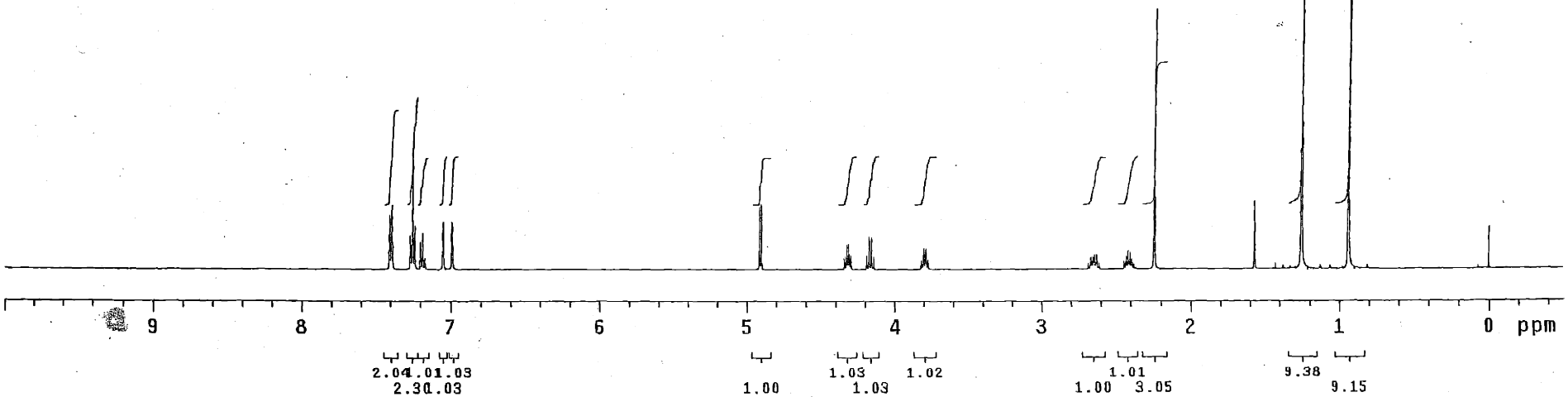


MML-VIII-220c

exp1 s2pul

SAMPLE		DEC. & VT	
date	Aug 16 2000	dfrq	125.675
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	918.63	homo3	n
rfl	1010.6	PROCESSING	
rfp	0	wtfile	
th	3	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	

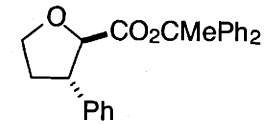




MML-VIII-193a

exp1 s2pul

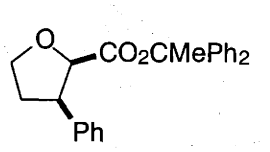
SAMPLE		DEC. & VT	
date	Jul 17 2000	dfrq	125.675
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	236.71	homo3	n
rfl	1013.4	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



MML-VII-158g

exp1 s2pul

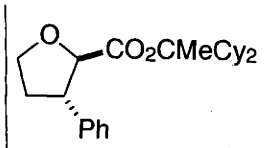
SAMPLE		DEC. & VT	
date	Jan 17 2000	dfrq	125.675
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	525.20	homo3	n
rfl	1015.5	PROCESSING	
rfp	0	wtfile	
th	5	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



MML-VI-154d

exp1 s2pul

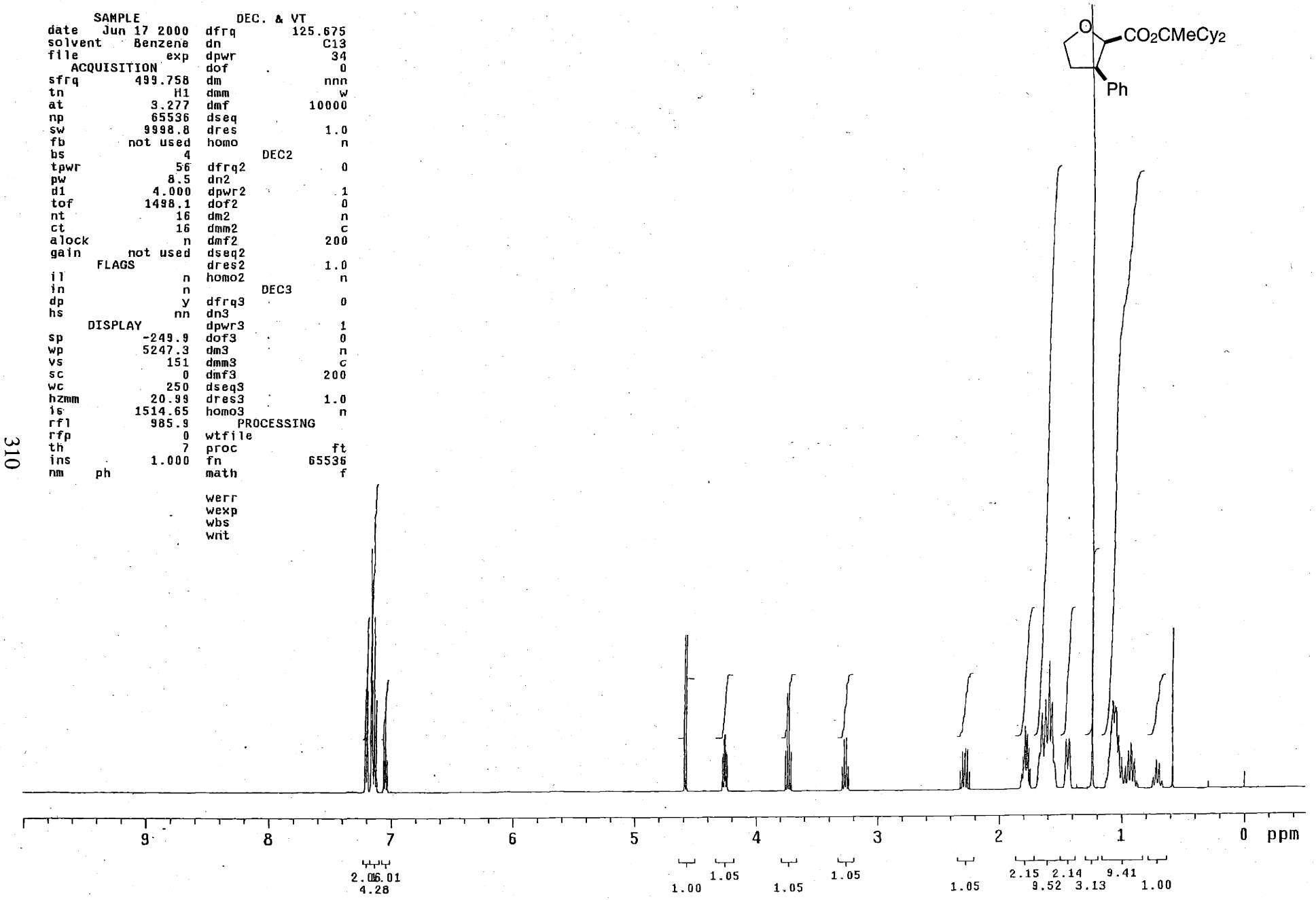
SAMPLE		DEC. & VT	
date	Jun 17 2000	dfrq	125.675
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	849.54	homo3	n
rfl	984.4	PROCESSING	
rfp	0	wtfile	
th	4	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



MML-VI-156b

exp1 s2pul

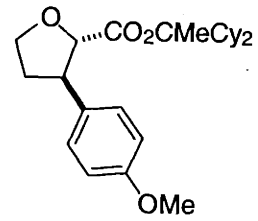
SAMPLE		DEC. & VT	
date	Jun 17 2000	dfrq	125.675
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	1514.65	homo3	n
rfl	985.9	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



MML-VIII-118b

exp1 s2pul

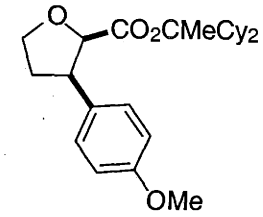
SAMPLE		DEC. & VT	
date	May 10 2000	dfrq	125.675
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	1485.00	homo3	n
rfl	986.5	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



MML-VIII-162c

exp1 s2pul

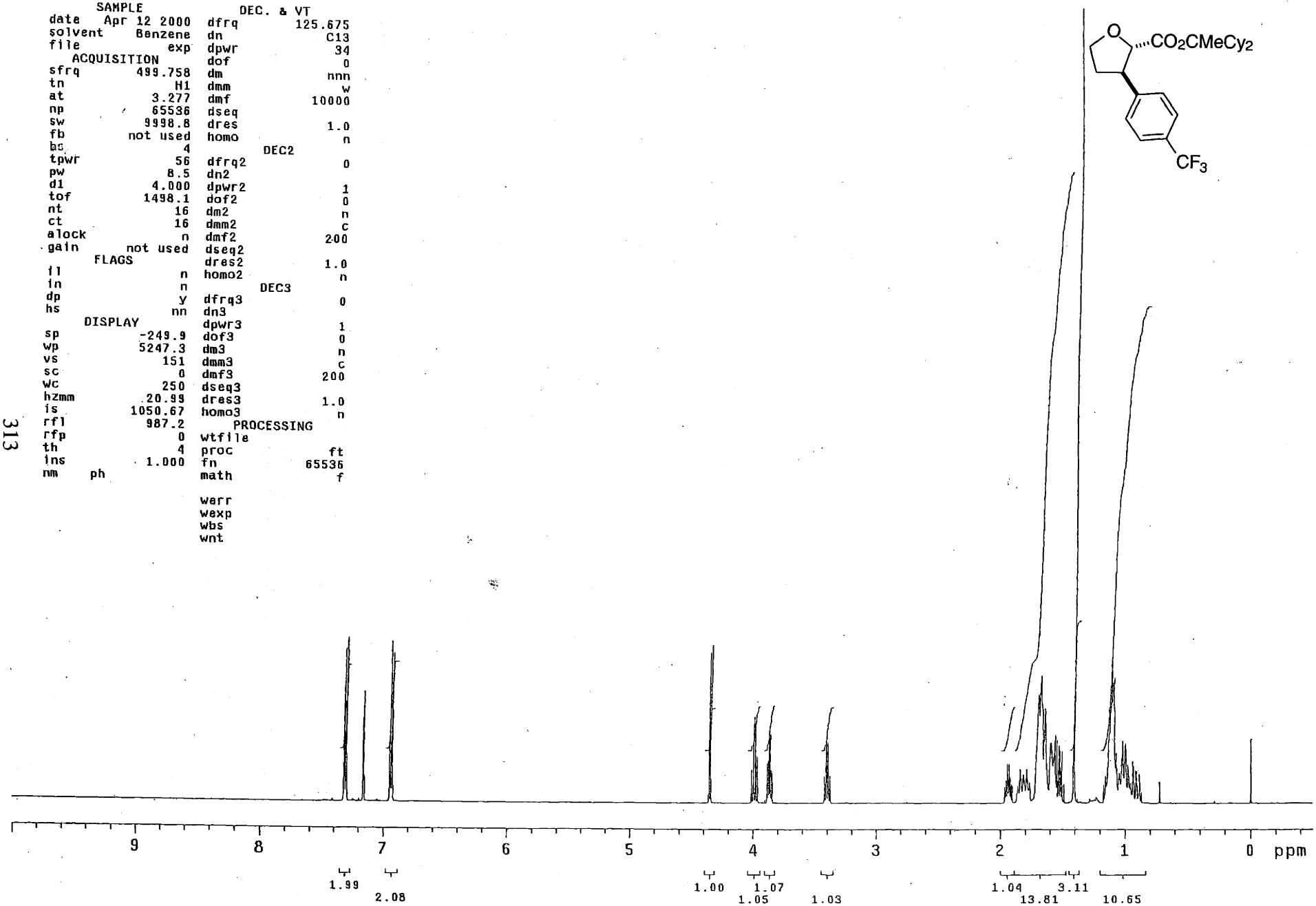
SAMPLE		DEC. & VT	
date	Jun 8 2000	dfrq	125.675
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	1751.64	homo3	n
rfl	986.2	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm	ph	math	f
		werr	
		wexp	
		wbs	
		wnt	

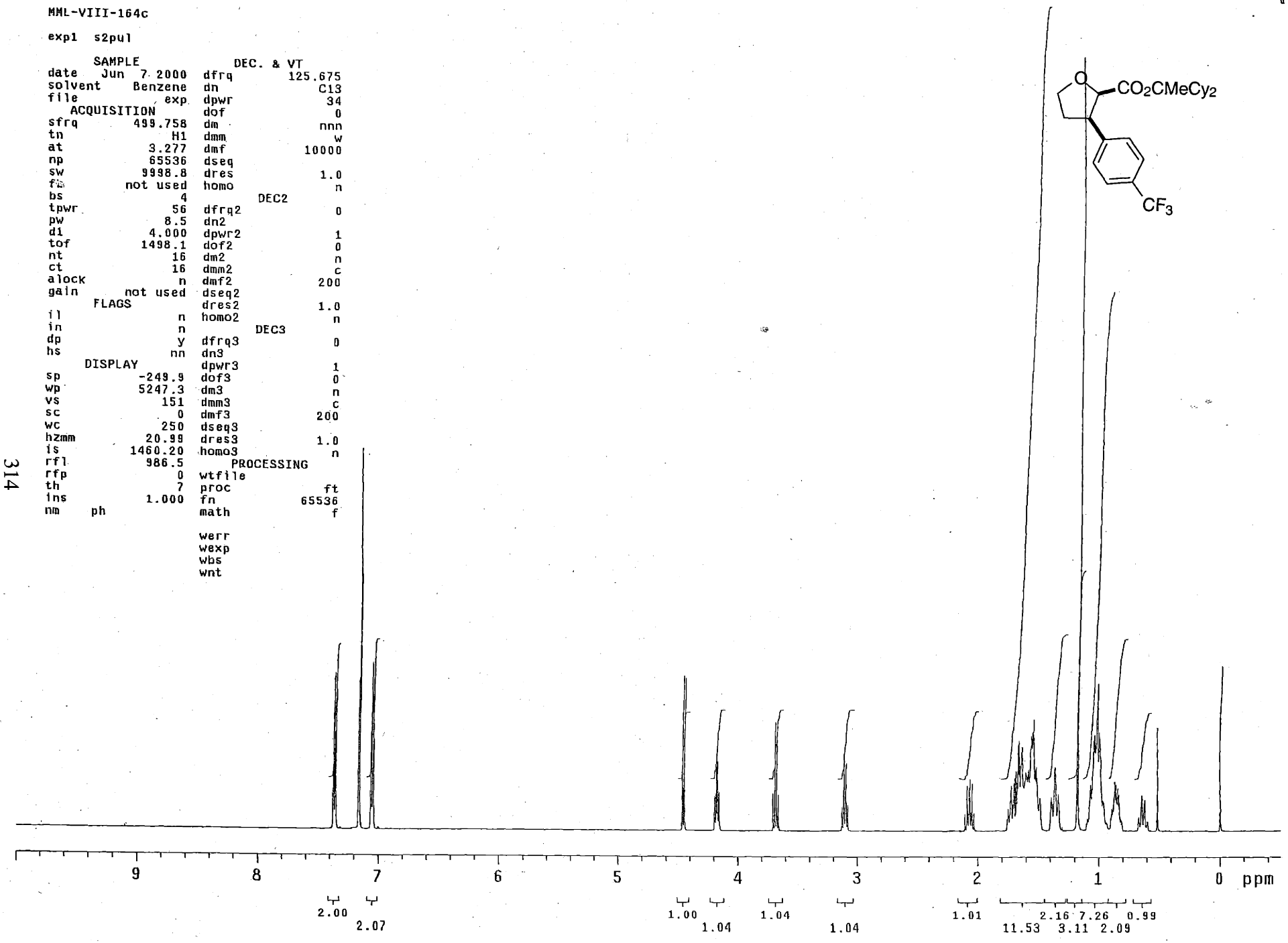


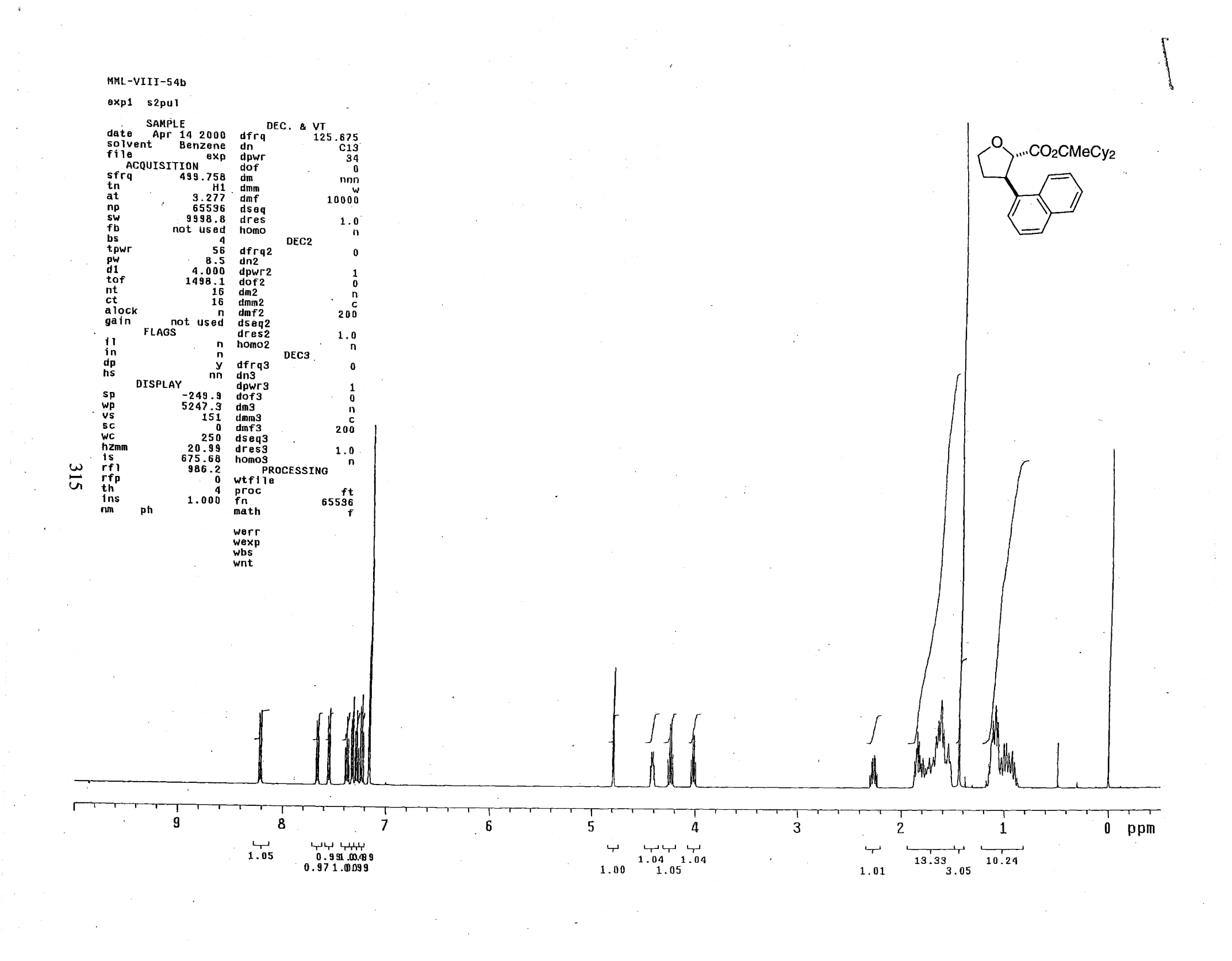
MML-VIII-52b

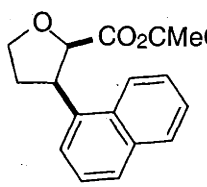
exp1 s2pul

SAMPLE		DEC. & VT	
date	Apr 12 2000	dfrq	125.675
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	1050.67	homo3	n
rfl	987.2	PROCESSING	
rfp	0	wtfile	
th	4	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	




MML-VIII-164c
exp1 s2pul
SAMPLE
date Jun 7 2000
solvent Benzene
file exp
ACQUISITION
sfrq 499.758
tn H1
at 3.277
np 65536
sw 9998.8
fb not used
bs 4
tpwr 56
pw 8.5
d1 4.000
tof 1498.1
nt 16
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -249.9
wp 5247.3
vs 151
sc 0
wc 250
hzmm 20.99
is 1460.20
rfl 986.5
rfp 0
th 7
ins 1.000
nm ph
DEC. & VT
dfrq 125.675
dn C13
dpwr 34
dof 0
dm nnn
dmm w
dmf 10000
dseq
dres 1.0
homo n
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 200
dseq2
dres2 1.0
homo2 n
DEC3
dfrq3 0
dn3
dpwr3 1
dof3 0
dm3 n
dmm3 c
dmf3 200
dseq3
dres3 1.0
homo3 n
PROCESSING
wtfile
proc ft
fn 65536
math f
werr
wexp
wbs
wnt
O
CO2CMeCy2
CF3
9
8
7
6
5
4
3
2
1
0
ppm
2.00
2.07
1.00
1.04
1.04
1.04
1.01
2.16
7.26
0.99
11.53
3.11
2.09


MML-VIII-54b
exp1 s2pul
SAMPLE
date Apr 14 2000
solvent Benzene
file exp
ACQUISITION
sfrq 499.758
tn H1
at 3.277
np 65536
sw 9998.8
fb not used
bs 4
tpwr 56
pw 8.5
d1 4.000
tof 1498.1
nt 16
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -249.9
wp 5247.3
vs 151
sc 0
wc 250
hzmm 20.99
is 675.68
rfl 986.2
rfp 0
th 4
ins 1.000
nm ph
DEC. & VT
dfrq 125.675
dn C13
dpwr 34
dof 0
dm nnn
dmm w
dmf 10000
dseq
dres 1.0
homo n
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 200
dseq2
dres2 1.0
homo2 n
DEC3
dfrq3 0
dn3
dpwr3 1
dof3 0
dm3 n
dmm3 c
dmf3 200
dseq3
dres3 1.0
homo3 n
PROCESSING
wtfile
proc ft
fn 65536
math f
werr
wexp
wbs
wnt
O
CO2CMeCy2
9
8
7
6
5
4
3
2
1
0 ppm
1.05
0.97
1.00
1.00
1.04
1.05
1.04
1.01
13.33
3.05
10.24



MML-VIII-166c

Current Data Parameters

NAME	Jun10-2000
EXPNO	10
PROCNO	1

F2 - Acquisition Parameters

Date_	20000610
Time	18.19
INSTRUM	spect
PROBHD	5mm BBO BB-1
PULPROG	zg30
TD	65536
SOLVENT	C6D6
NS	16
DS	2
SWH	8278.146 Hz
FIDRES	0.126314 Hz
AQ	3.9584243 sec
RG	228.1
DW	60.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

========== CHANNEL f1 ========

NUC1	1H
P1	7.90 usec
PL1	0.00 dB
SFO1	400.1324710 MHz

F2 - Processing parameters

SI	32768
SF	400.1300455 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

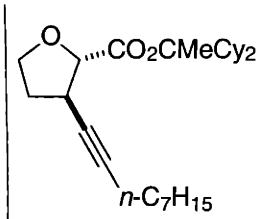
1D NMR plot parameters

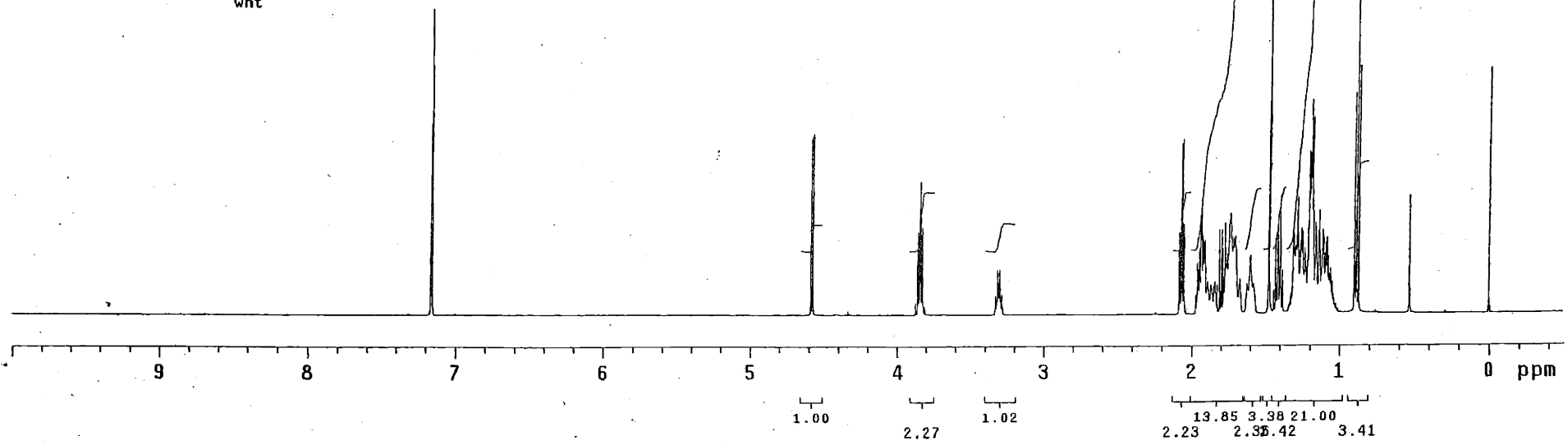
CX	20.00 cm
F1P	10.000 ppm
F1	4001.30 Hz
F2P	-0.500 ppm
F2	-200.07 Hz
PPMCM	0.52500 ppm/cm
HZCM	210.06827 Hz/cm

MML-VIII-116a

exp1 s2pul

SAMPLE		DEC. & VT	
date	May 9 2000	dfrq	125.675
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	0
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9898.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.5	dn2	
d1	4.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	5247.3	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	20.99	dres3	1.0
is	883.57	homo3	n
rfl	985.9	PROCESSING	
rfp	0	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm ph		math	f
		werr	
		wexp	
		wbs	
		wnt	

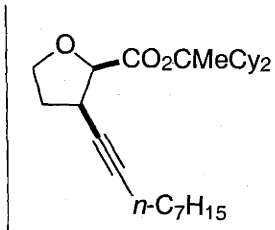


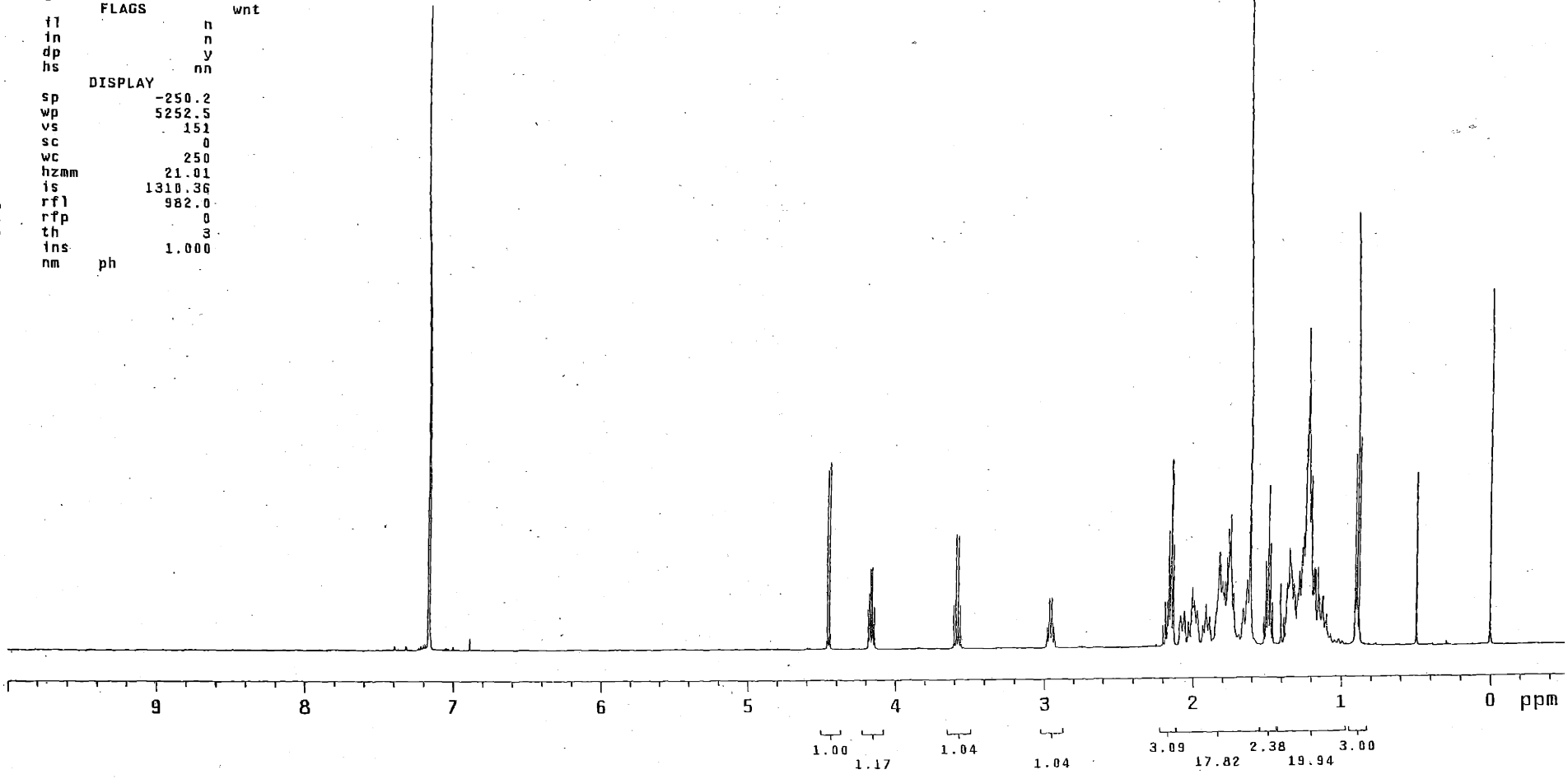


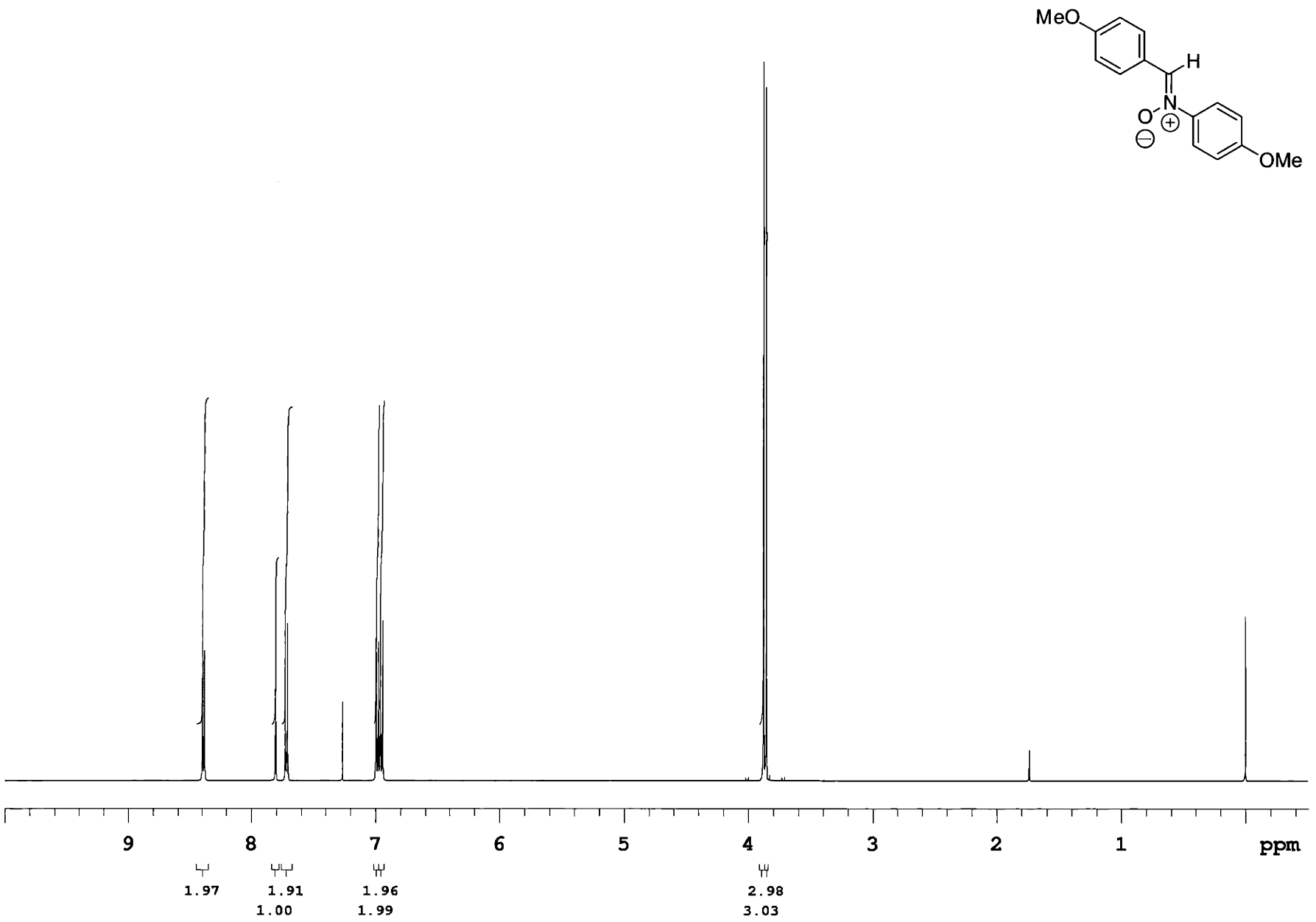
MML-VIII-160b

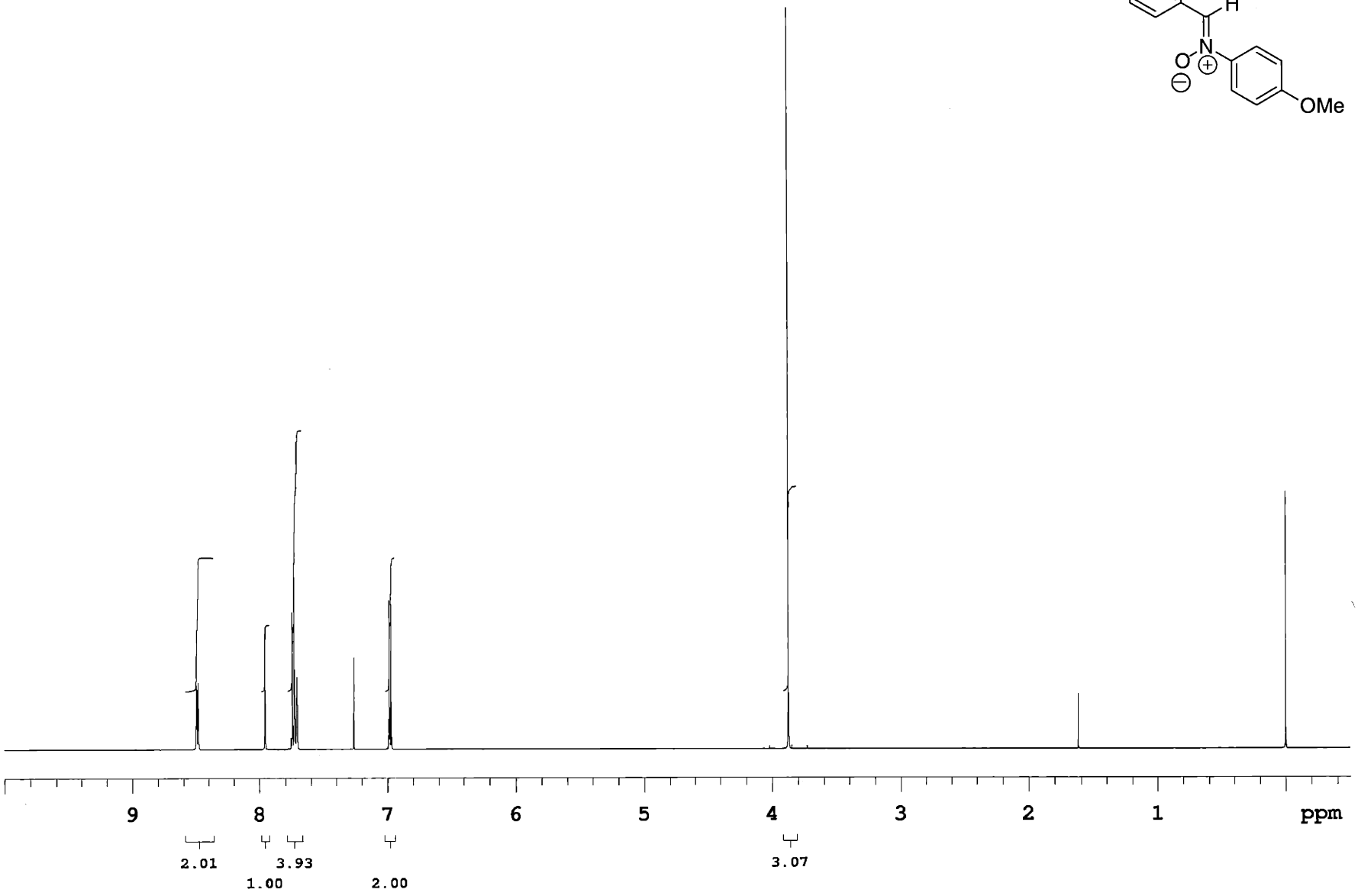
exp4 s2pul

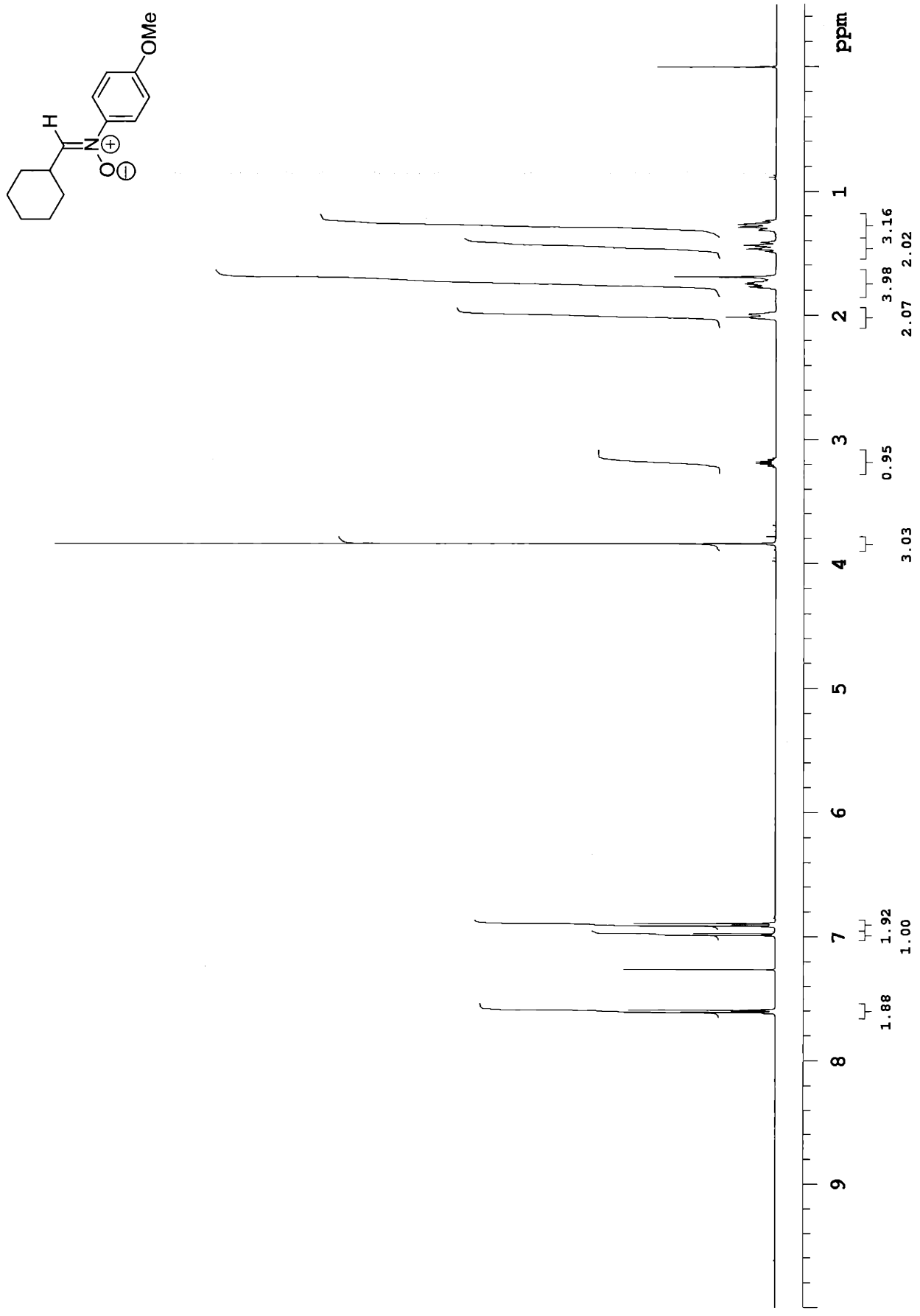
SAMPLE		DEC. & VT	
date	Jun 1 2000	dfrq	500.247
solvent	Benzene	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	500.248	dm	nnn
tn	H1	dmm	c
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	y
bs	4	PROCESSING	
tpwr	58	wtfile	
pw	8.1	proc	ft
d1	4.000	fn	not used
tof	1498.2	math	f
nt	16		
ct	16	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
fl	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.2		
wp	5252.5		
vs	151		
sc	0		
wc	250		
hzmm	21.01		
is	1310.36		
rfl	982.0		
rfp	0		
th	3		
ins	1.000		
nm	ph		

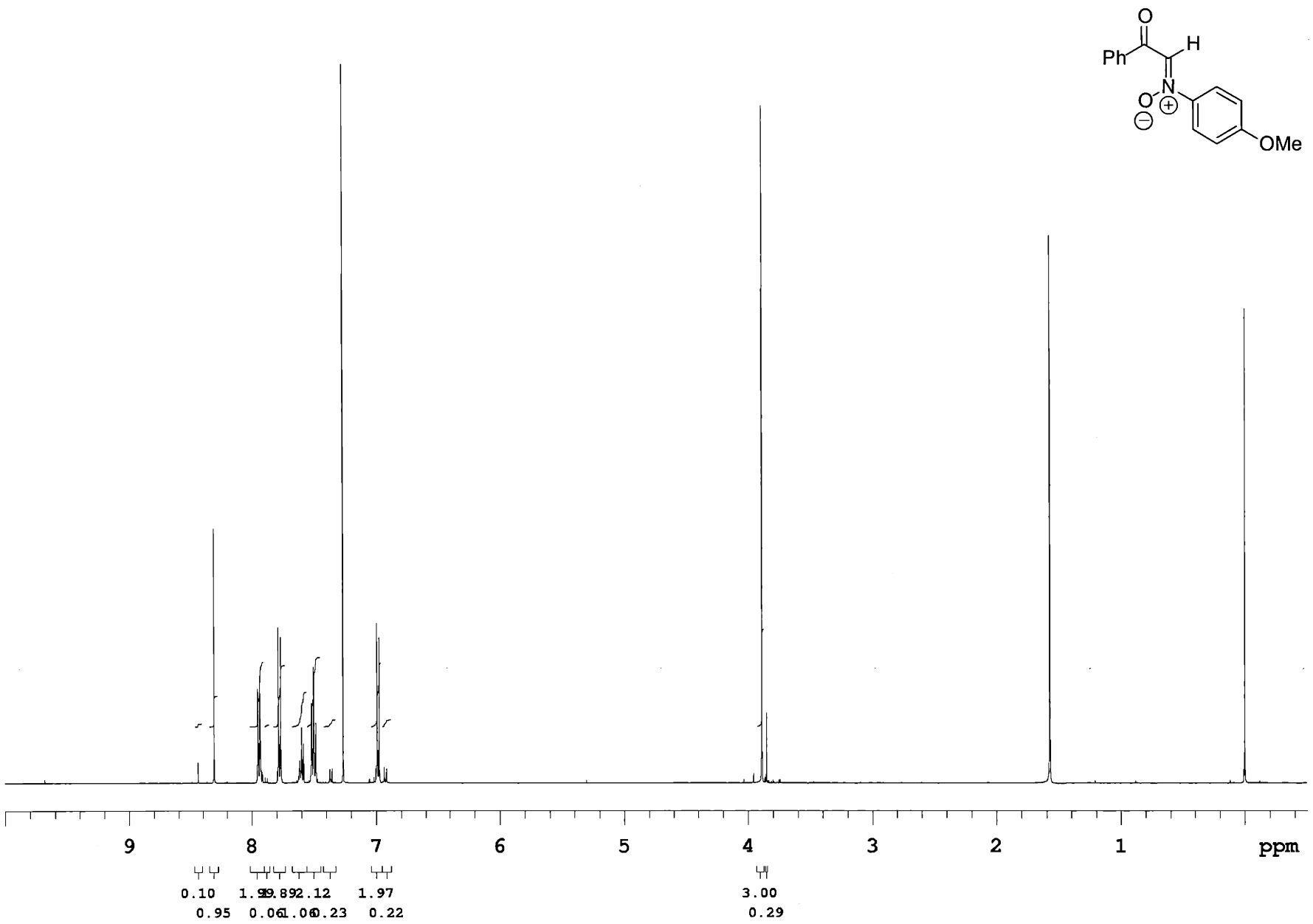


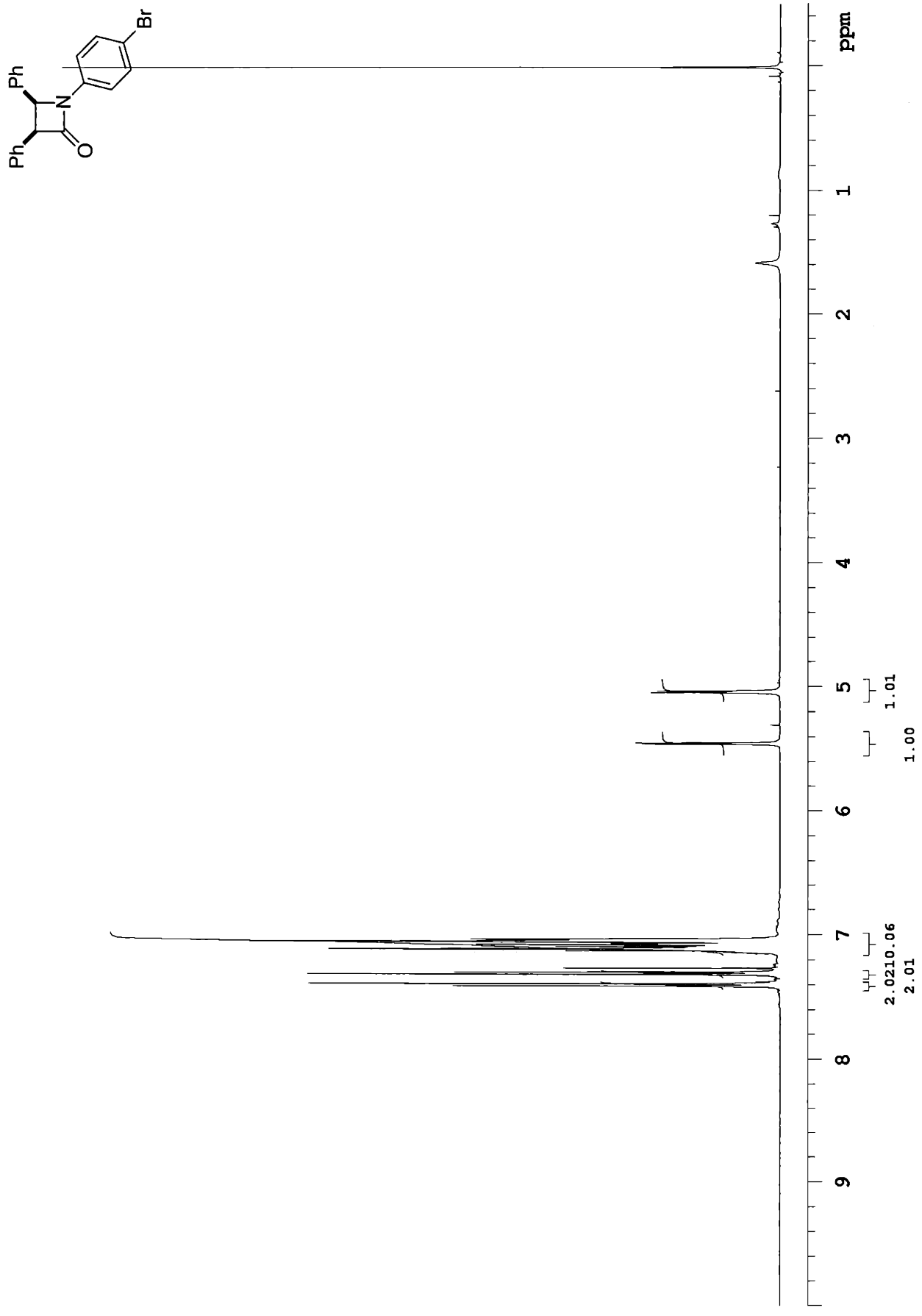


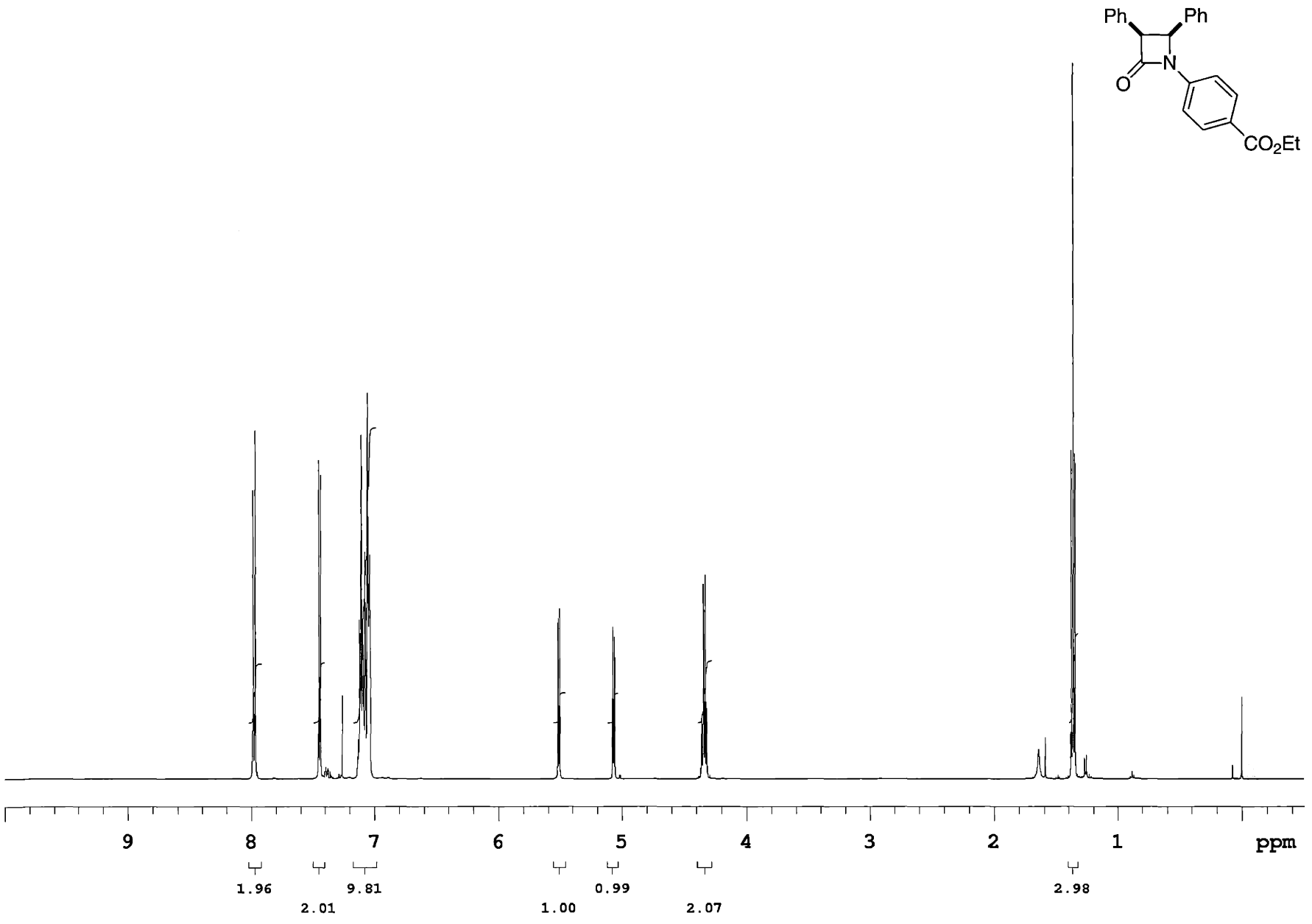

MeO
H
N
O
OMe
9
8
7
6
5
4
3
2
1
ppm
1.97
1.91
1.00
1.96
1.99
2.98
3.03

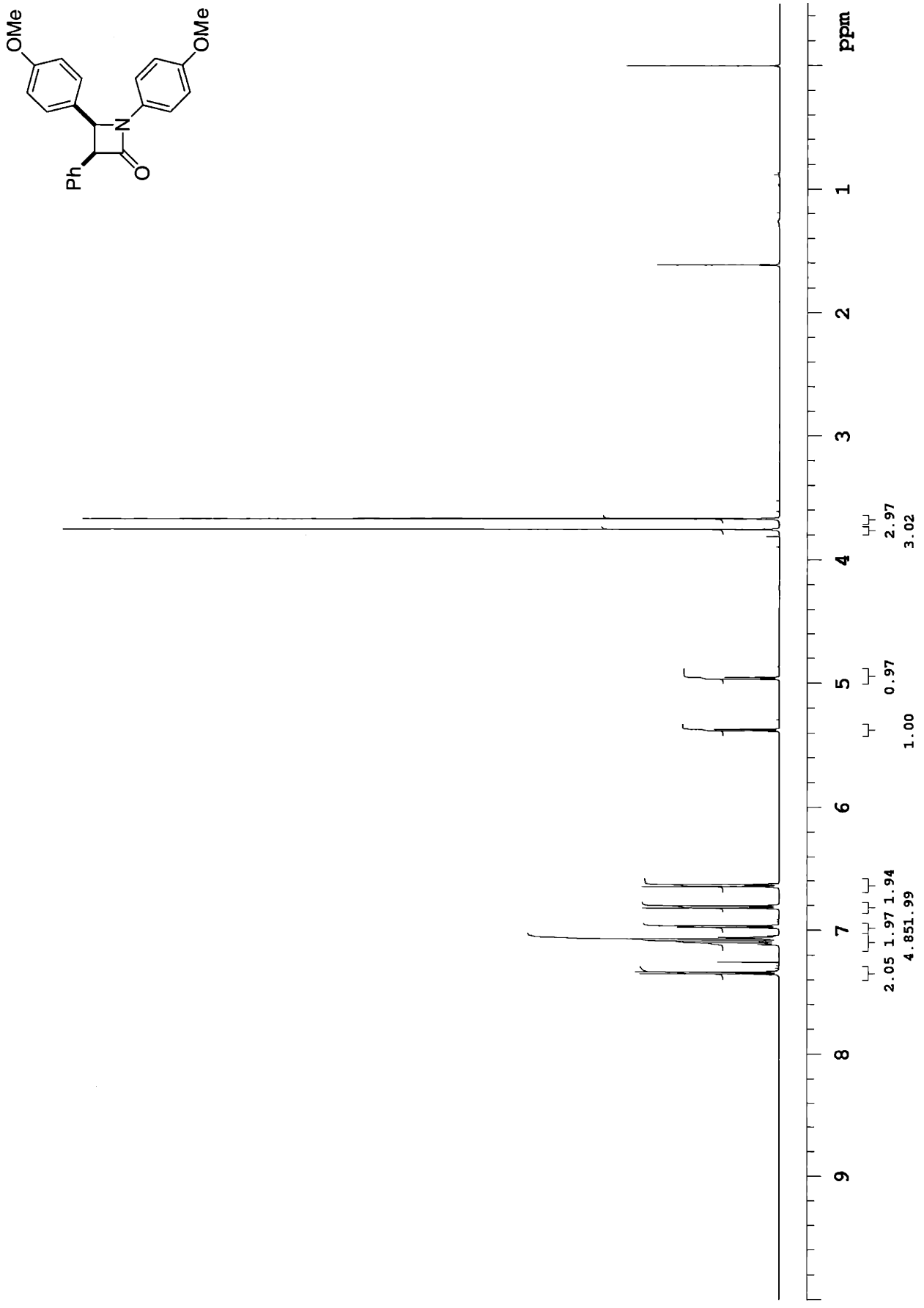

F3C
H
N
O
OMe
9
8
7
6
5
4
3
2
1
ppm
2.01
1.00
3.93
2.00
3.07

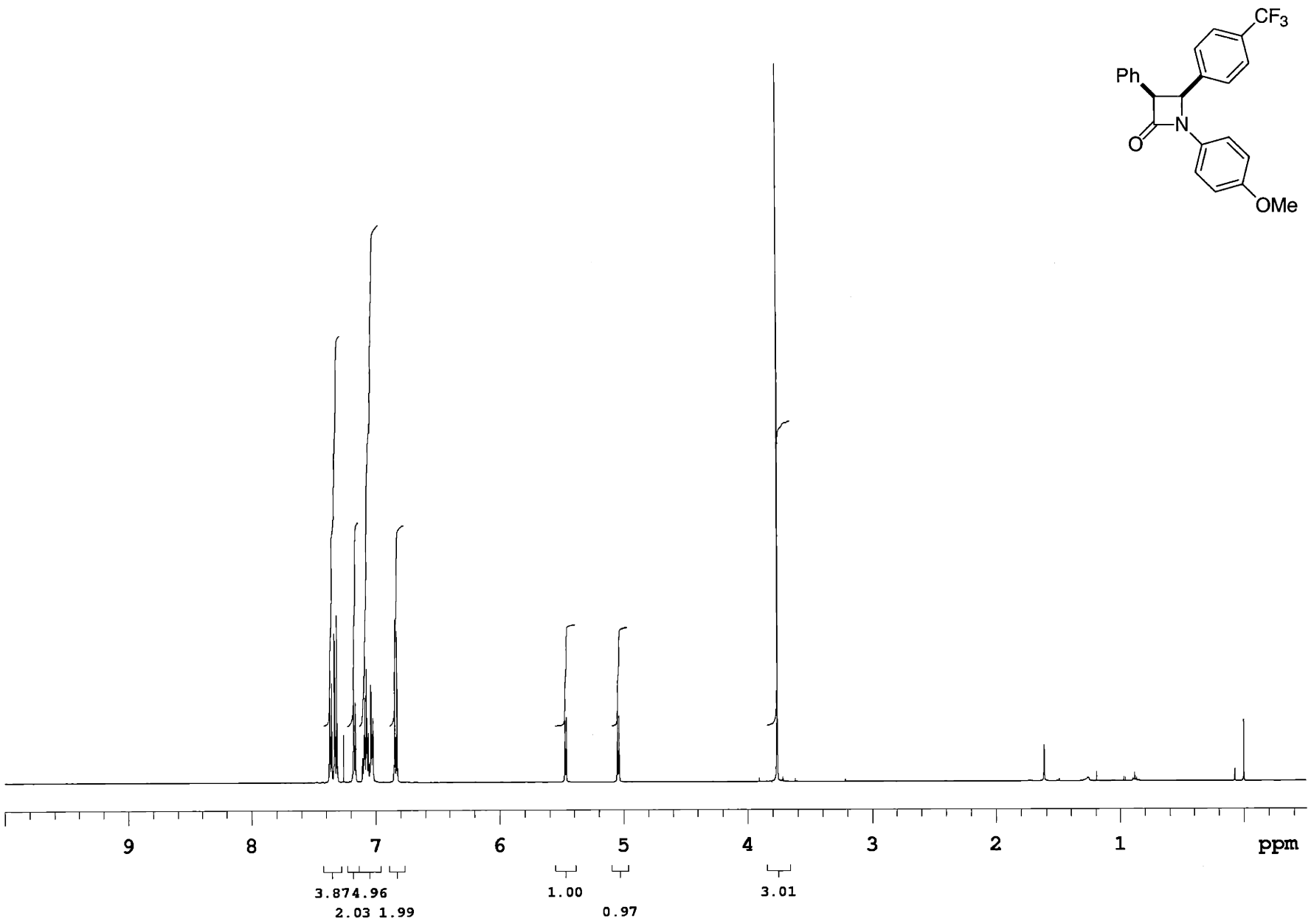

OMe
H
N
O
ppm
1
2
3
4
5
6
7
8
9
3.16
3.98
2.02
2.07
0.95
3.03
1.92
1.00
1.88

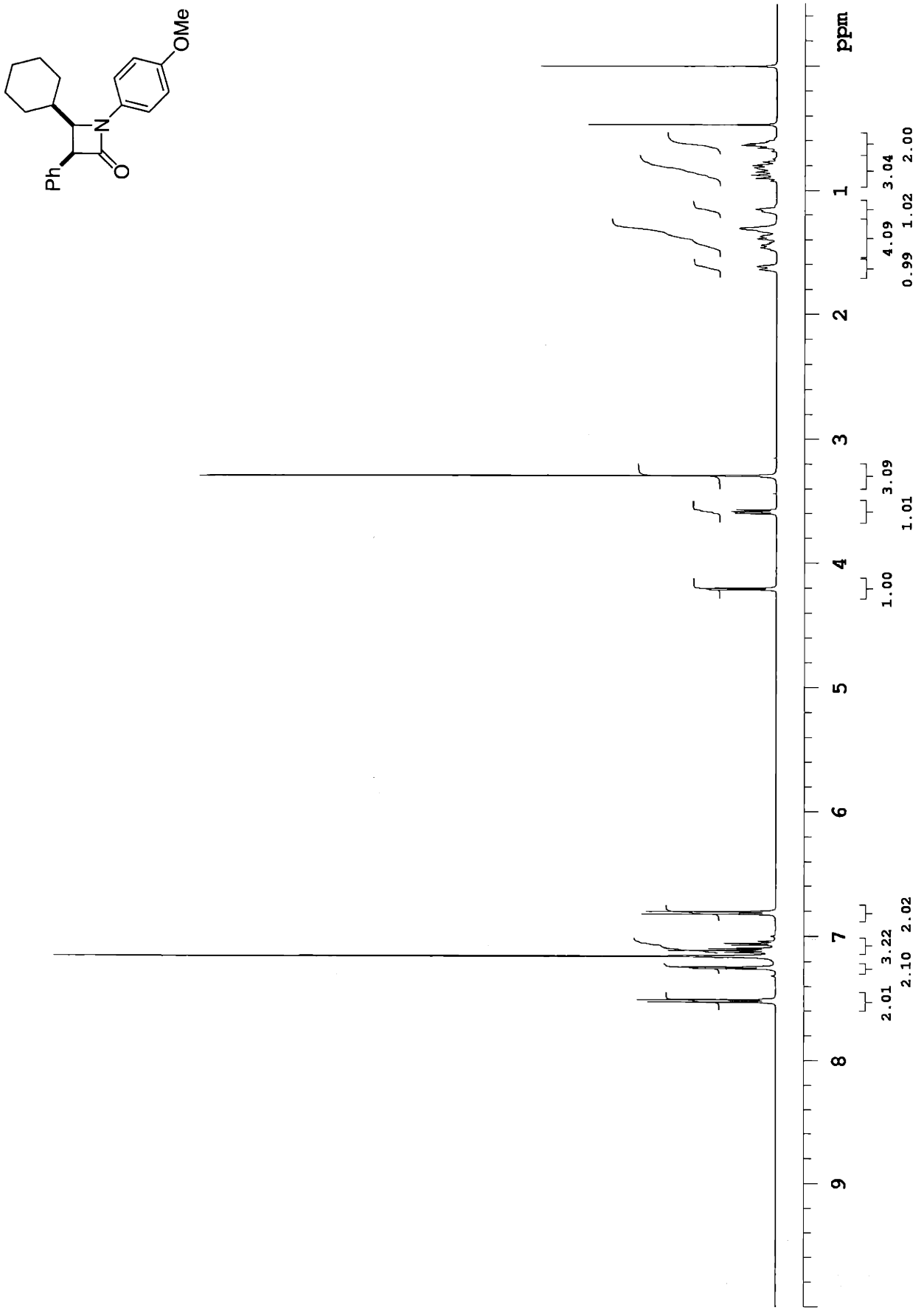

O
Ph
H
N
O
OMe
9
8
7
6
5
4
3
2
1
ppm
0.10
1.95
9.89
2.12
1.97
3.00
0.95
0.06
1.06
0.23
0.22
0.29

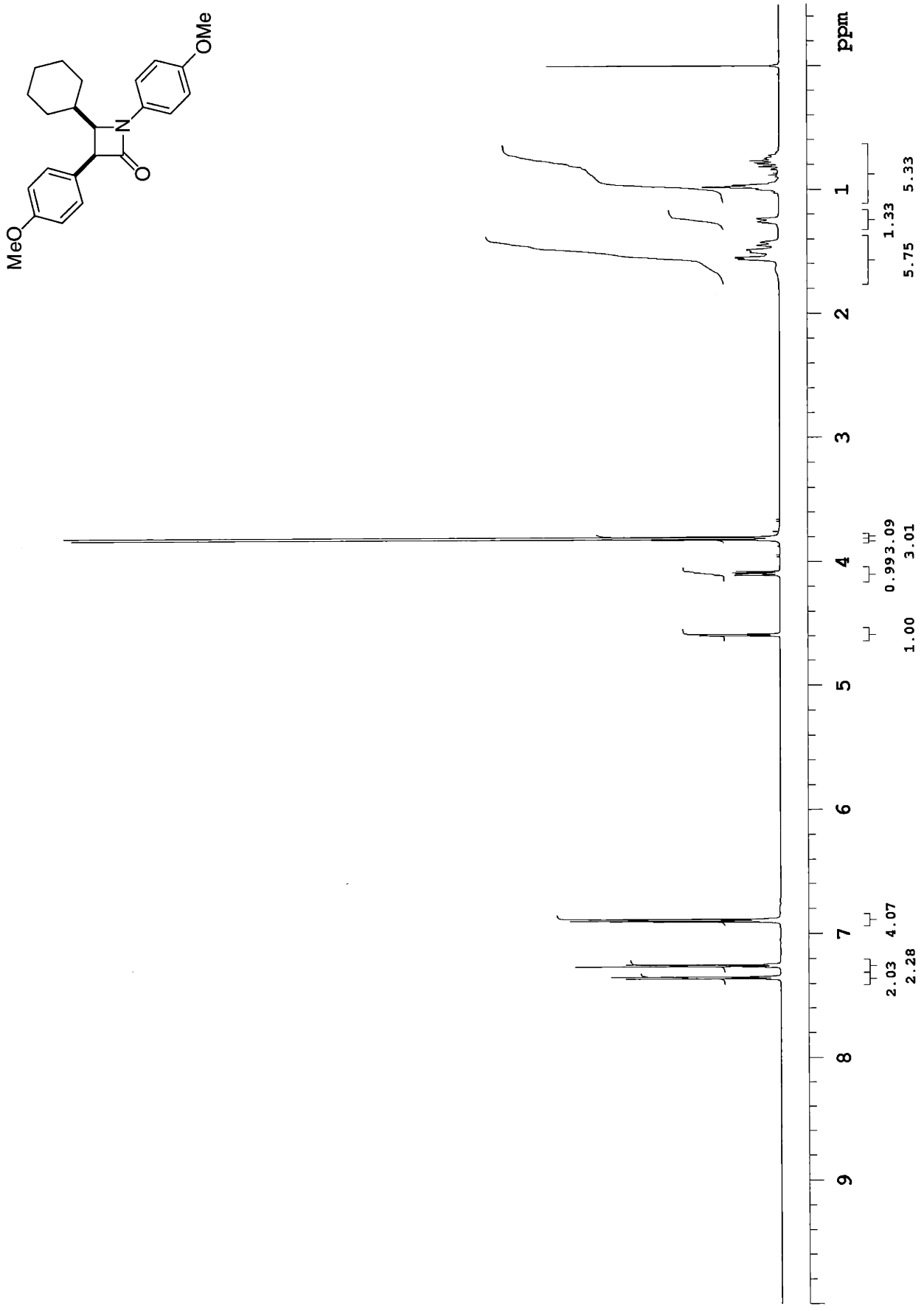

Br
Ph
N
Ph
O
ppm
1
2
3
4
5
6
7
8
9
1.01
1.00
2.0210.06
2.01

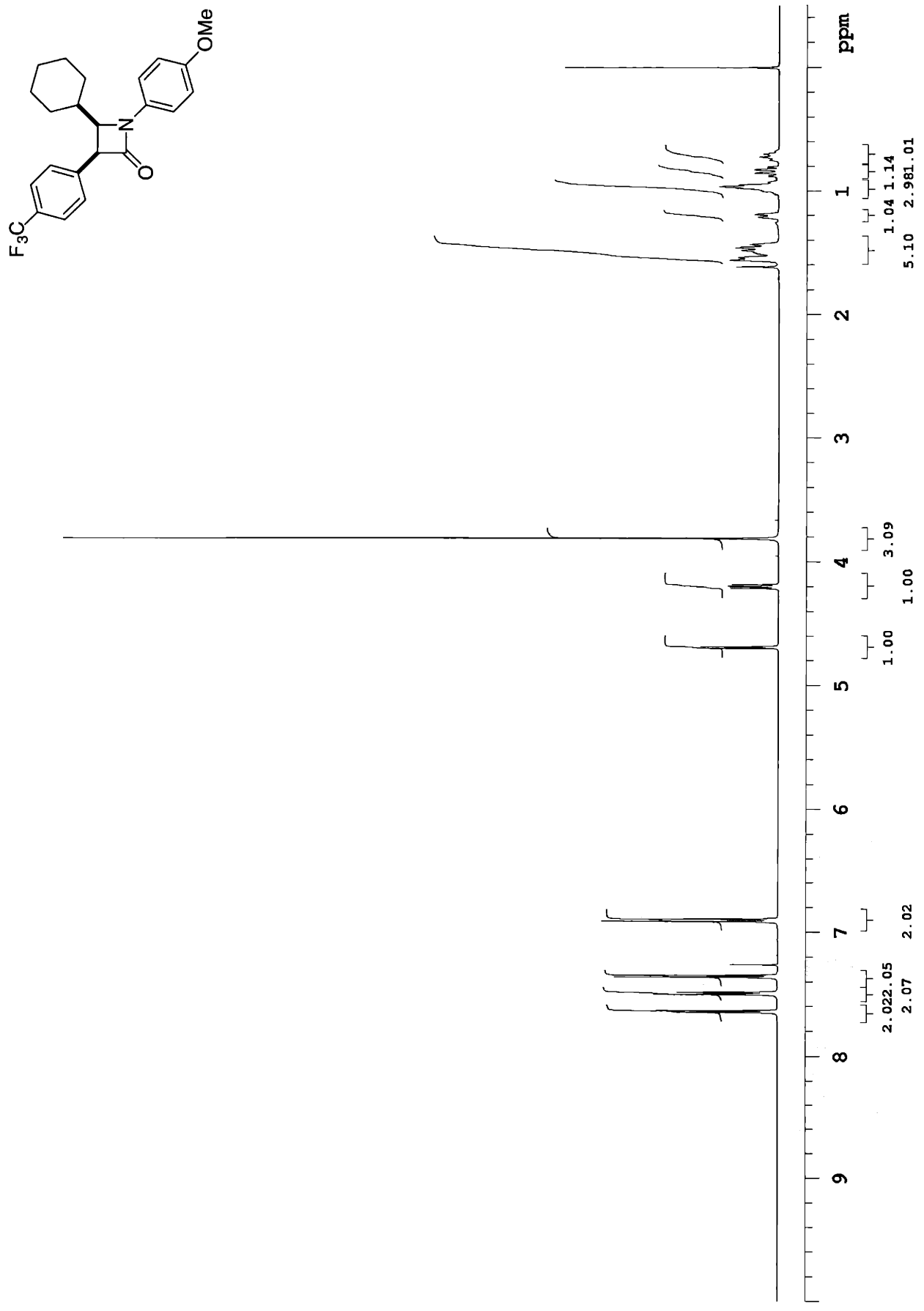

Ph
Ph
O
N
CO2Et
9
8
7
6
5
4
3
2
1
ppm
1.96
2.01
9.81
1.00
0.99
2.07
2.98


OMe
OMe
Ph
N
O
ppm
1
2
3
4
5
6
7
8
9
2.97
3.02
0.97
1.00
2.05 1.97 1.94
4.85 1.99


CF3
Ph
N
O
OMe
9
8
7
6
5
4
3
2
1
ppm
3.87
4.96
2.03
1.99
1.00
0.97
3.01


OMe
N
O
Ph
ppm
1
2
3
4
5
6
7
8
9
4.09
1.02
3.04
2.00
0.99
3.09
1.01
1.00
2.01
3.22
2.10
2.02


OMe
MeO
N
O
ppm
1
2
3
4
5
6
7
8
9
1.33
5.75
5.33
0.993.09
3.01
1.00
2.03
4.07
2.28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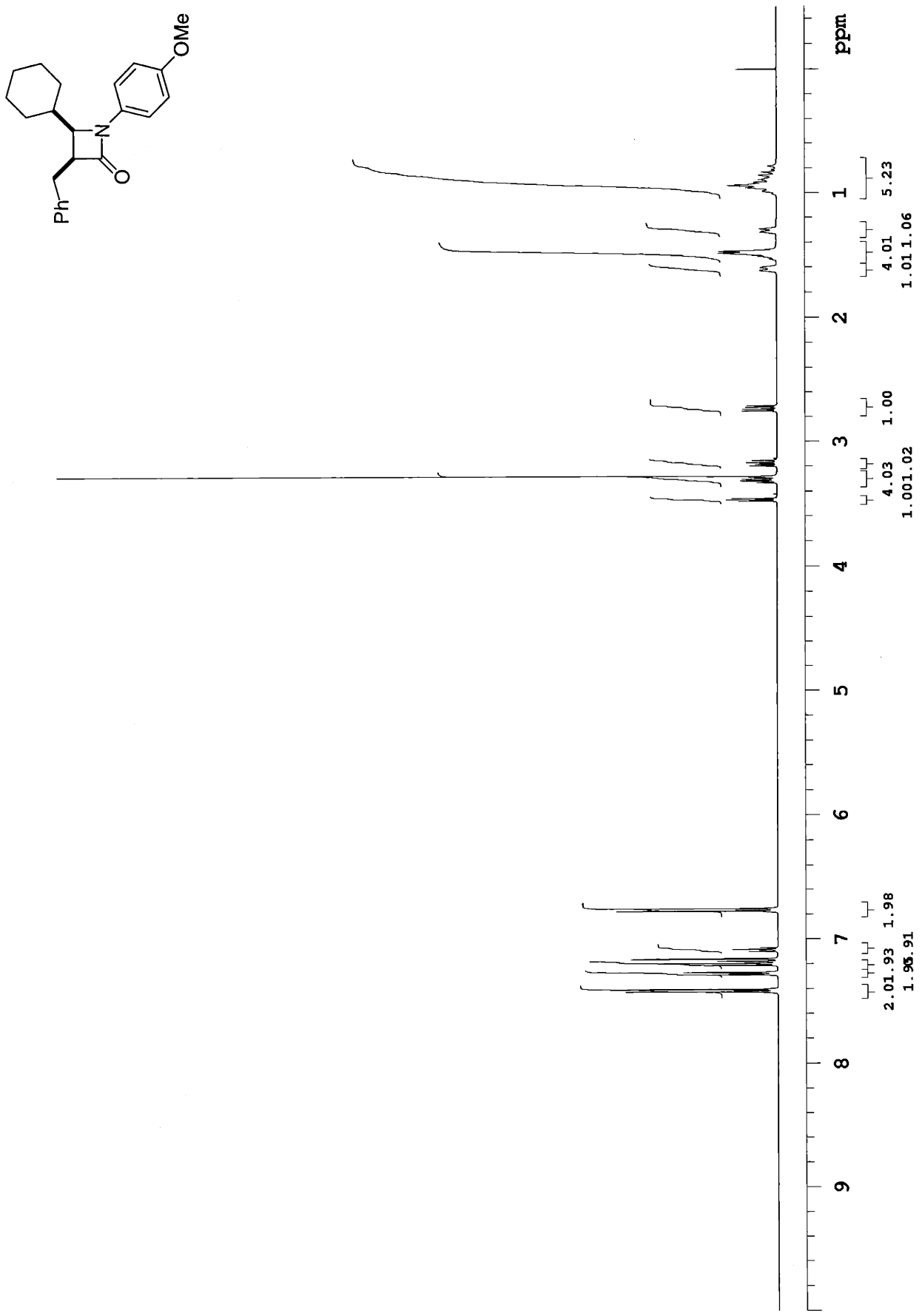
2.02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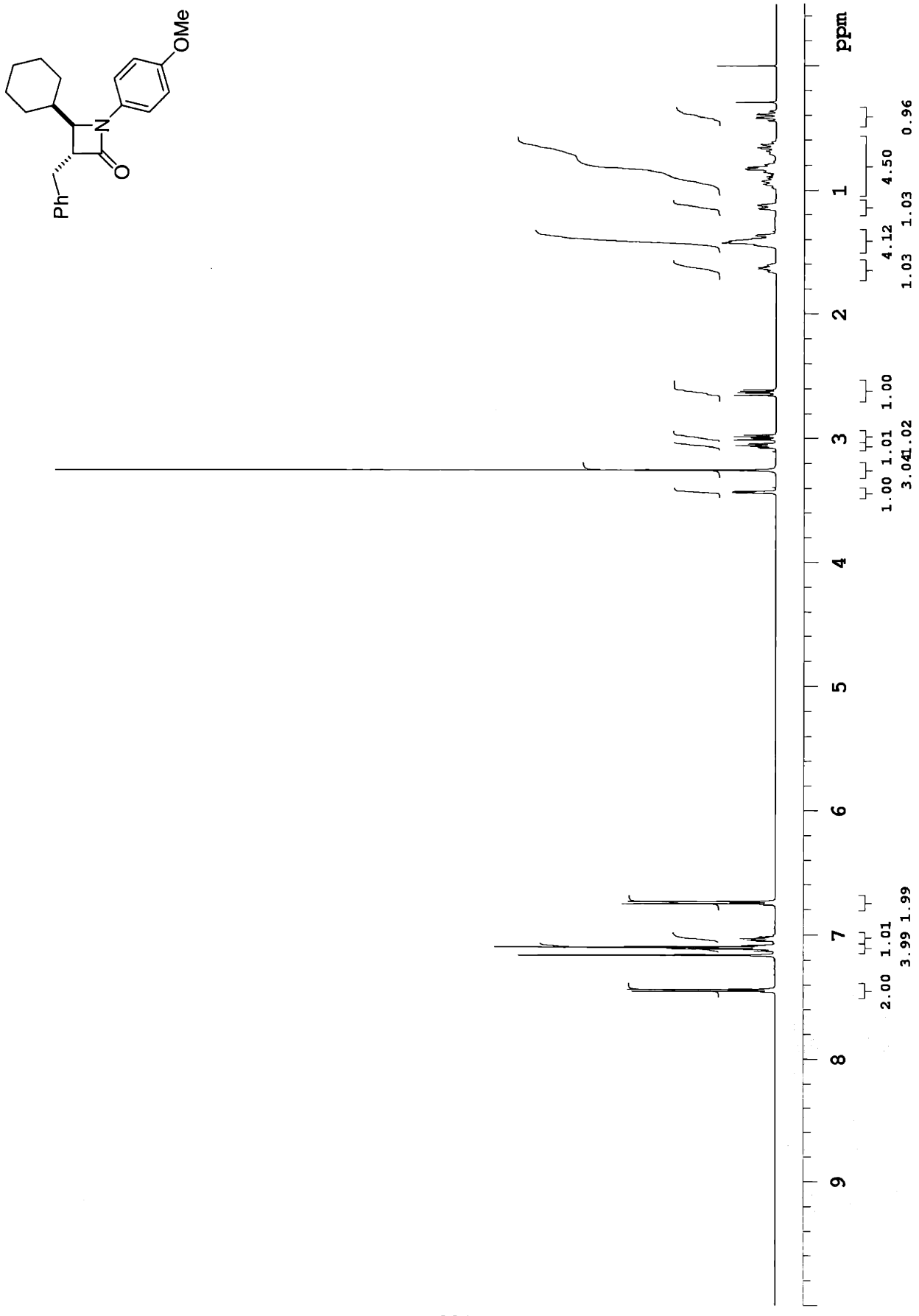
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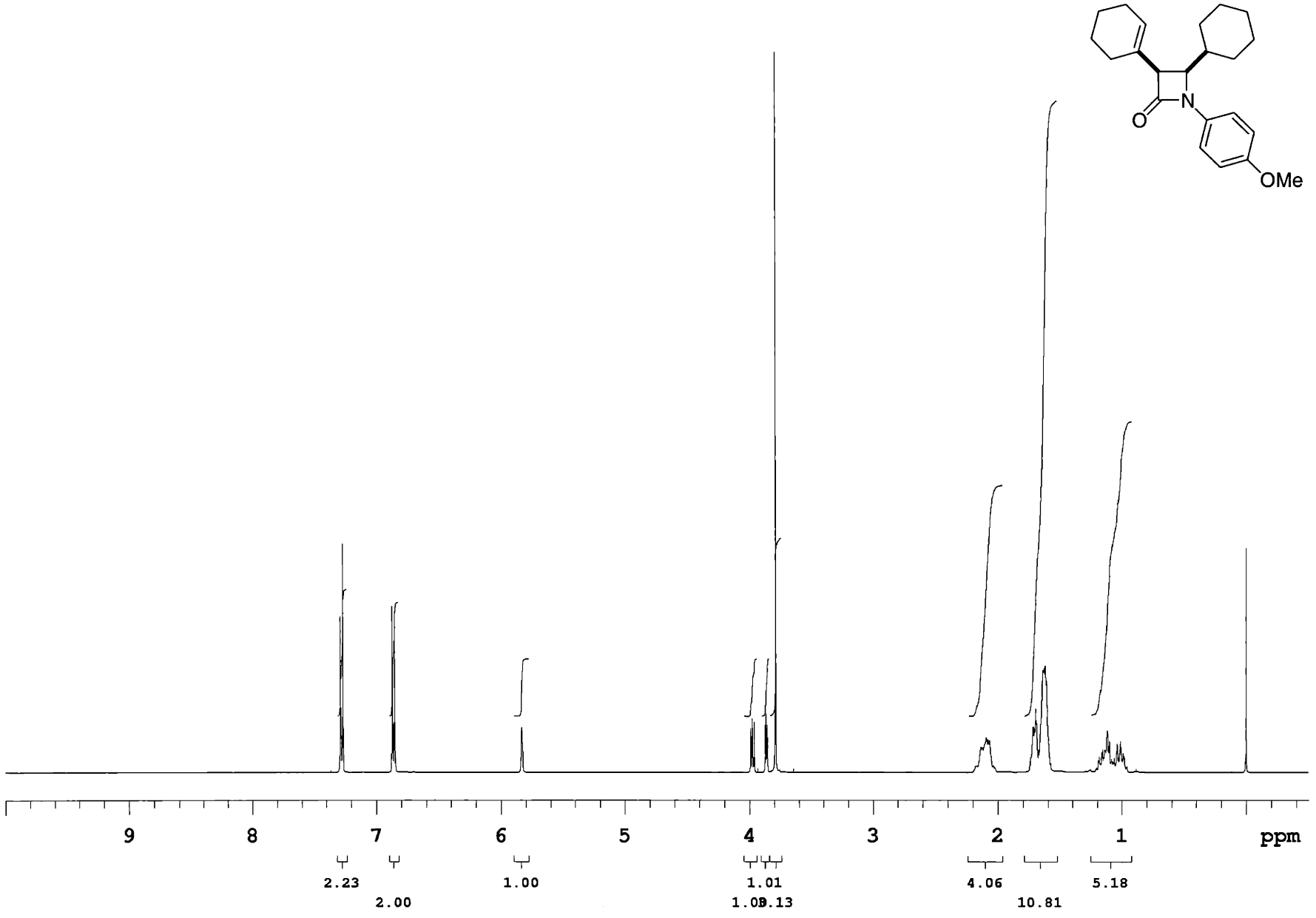
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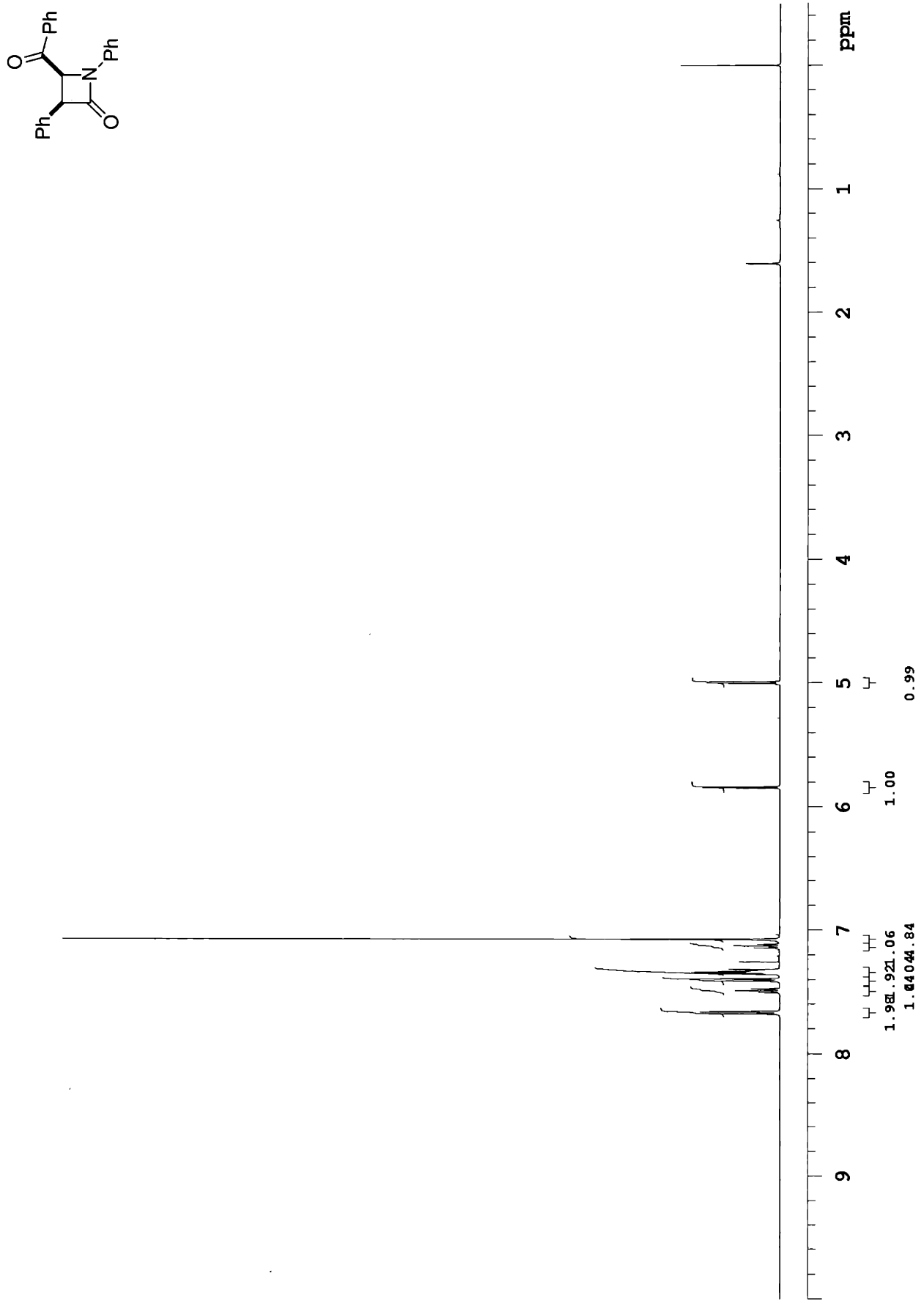
5.18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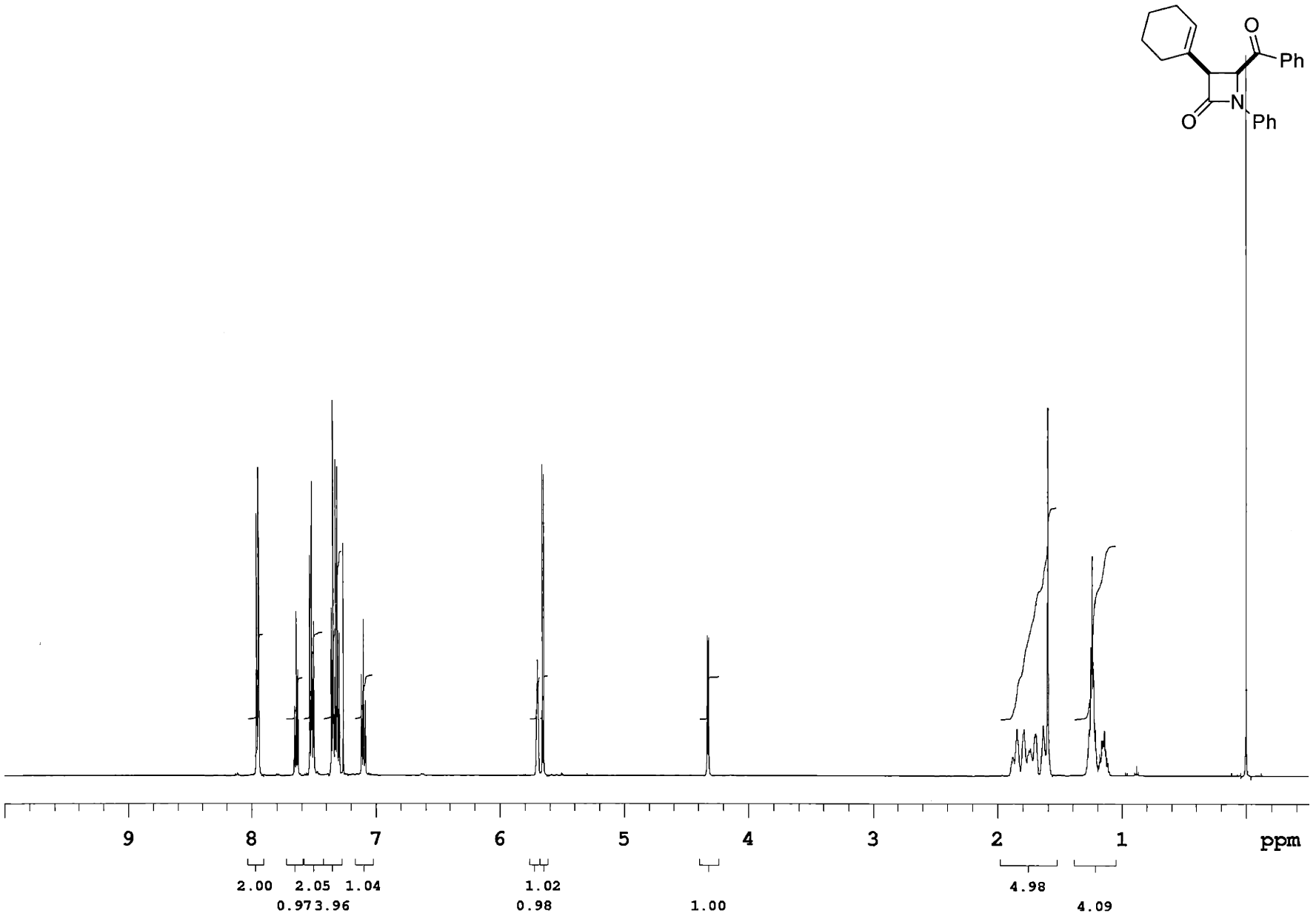
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3.96
1.02
0.98
1.00
4.98
4.09

Appendix B

X-ray Crystal Structure Data

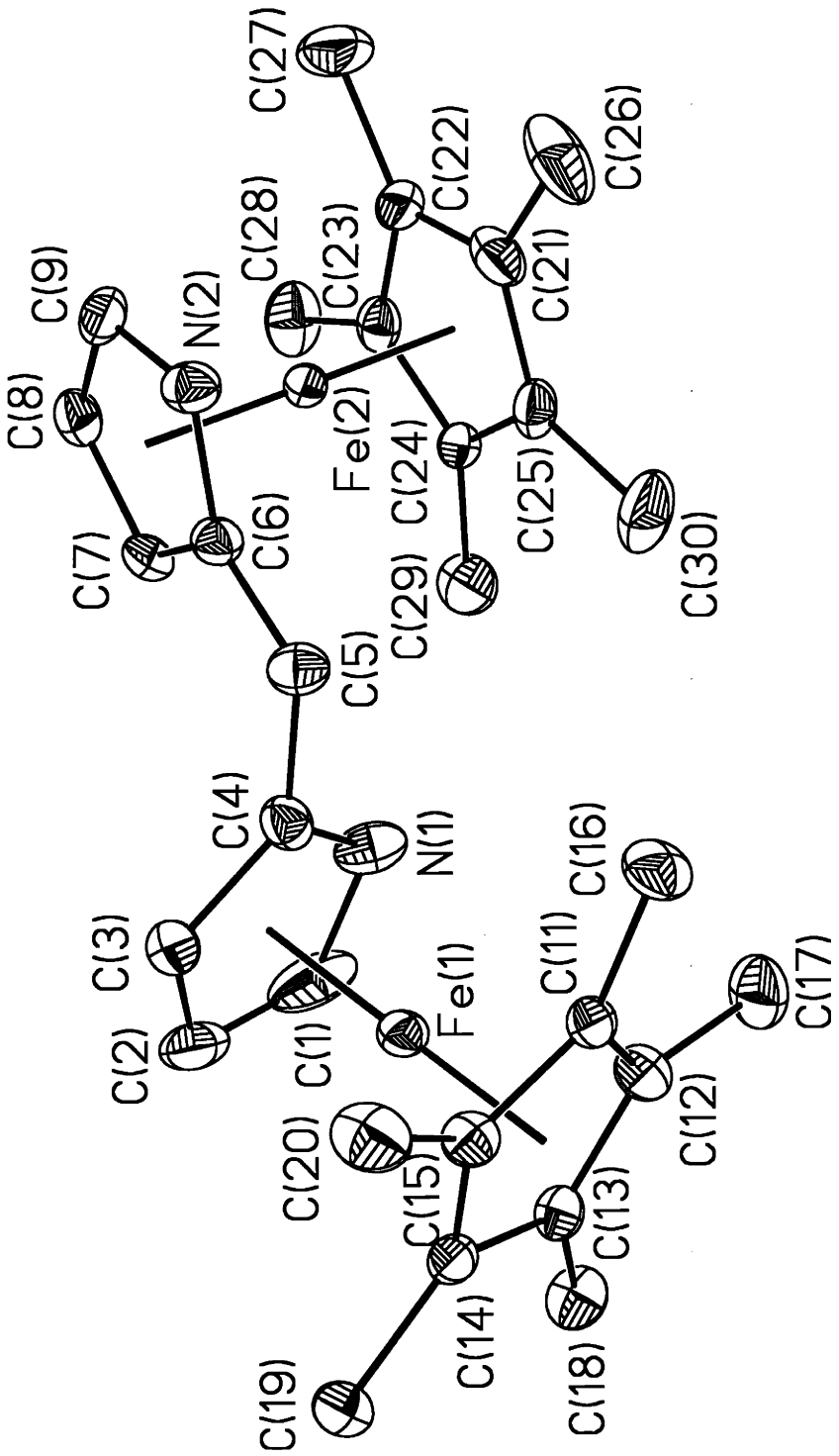

Figure 1. ORTEP plot of (*R*,*R*)-**1.19**, with thermal ellipsoids drawn at the 35% probability level.

Table 1.1. Crystal data and structure refinement for (*R*,*R*)-**1.19**.

Identification code	97070	
Empirical formula	C29 H38 Fe2 N2	
Formula weight	526.31	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 12.5015(3) Å	α = 90°.
	b = 8.26930(10) Å	β = 90.2310(10)°.
	c = 25.3384(5) Å	γ = 90°.
Volume	2619.43(9) Å^3	
Z	4	
Density (calculated)	1.335 Mg/m^3	
Absorption coefficient	1.126 mm^{-1}	
F(000)	1112	
Crystal size	0.06 x 0.08 x 0.18 mm^3	
Theta range for data collection	2.28 to 23.26°.	
Index ranges	-13<=h<=11, -9<=k<=9, -28<=l<=24	
Reflections collected	10135	
Independent reflections	3739 [R(int) = 0.0588]	
Completeness to theta = 23.26°	99.4 %	
Absorption correction	Empirical	
Max. and min. transmission	0.9057 and 0.5612	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3739 / 0 / 299	
Goodness-of-fit on F^2	1.193	
Final R indices [I>2sigma(I)]	R1 = 0.0649, wR2 = 0.1292	
R indices (all data)	R1 = 0.0833, wR2 = 0.1377	
Extinction coefficient	0.00058(14)	
Largest diff. peak and hole	0.394 and -0.390 e.Å^{-3}	

Table 1.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for 97070. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Fe(1)	2952(1)	8980(1)	3937(1)	28(1)
Fe(2)	7322(1)	6474(1)	3866(1)	25(1)
N(1)	4491(4)	8971(7)	3674(2)	40(1)
N(2)	6833(4)	5992(6)	4623(2)	33(1)
C(1)	4062(6)	10517(9)	3676(4)	61(2)
C(2)	3759(6)	11003(9)	4185(4)	65(3)
C(3)	4007(5)	9718(8)	4518(3)	49(2)
C(4)	4459(5)	8491(7)	4194(2)	32(2)
C(5)	4983(5)	6970(7)	4380(2)	33(2)
C(6)	6175(5)	7160(7)	4396(2)	28(1)
C(7)	6789(5)	8522(7)	4241(2)	31(1)
C(8)	7867(5)	8190(7)	4380(2)	34(2)
C(9)	7859(5)	6643(8)	4614(2)	35(2)
C(11)	2103(5)	6877(7)	3878(2)	28(1)
C(12)	2052(5)	7751(8)	3394(2)	33(2)
C(13)	1598(5)	9311(7)	3494(2)	29(1)
C(14)	1355(4)	9375(7)	4049(2)	27(1)
C(15)	1671(5)	7877(7)	4280(2)	29(1)
C(16)	2500(5)	5171(7)	3949(3)	41(2)
C(17)	2427(6)	7170(10)	2862(3)	54(2)
C(18)	1386(5)	10613(8)	3100(2)	39(2)
C(19)	831(5)	10774(7)	4323(3)	36(2)
C(20)	1560(6)	7432(9)	4855(2)	47(2)
C(21)	7414(6)	4347(8)	3461(3)	41(2)
C(22)	8411(5)	5167(8)	3448(2)	39(2)
C(23)	8230(5)	6698(8)	3208(2)	32(2)
C(24)	7128(5)	6811(7)	3071(2)	28(1)
C(25)	6620(5)	5349(8)	3229(2)	35(2)
C(26)	7217(8)	2675(8)	3683(3)	68(3)
C(27)	9479(6)	4539(11)	3640(3)	69(3)
C(28)	9064(6)	7978(9)	3106(3)	55(2)

C(29)	6606(6)	8214(9)	2800(3)	50(2)
C(30)	5467(5)	4945(11)	3134(3)	59(2)

Table 1.3. Bond lengths [Å] and angles [°] for 97070.

Fe(1)-C(1)	1.997(7)
Fe(1)-C(4)	2.031(6)
Fe(1)-N(1)	2.039(5)
Fe(1)-C(15)	2.039(6)
Fe(1)-C(11)	2.042(6)
Fe(1)-C(14)	2.044(6)
Fe(1)-C(12)	2.045(6)
Fe(1)-C(13)	2.046(6)
Fe(1)-C(2)	2.052(7)
Fe(1)-C(3)	2.065(7)
Fe(2)-C(9)	2.013(6)
Fe(2)-C(23)	2.030(6)
Fe(2)-C(22)	2.038(6)
Fe(2)-C(21)	2.039(6)
Fe(2)-C(8)	2.042(6)
Fe(2)-C(24)	2.046(6)
Fe(2)-C(6)	2.050(6)
Fe(2)-C(7)	2.054(6)
Fe(2)-N(2)	2.055(5)
Fe(2)-C(25)	2.055(6)
N(1)-C(4)	1.375(8)
N(1)-C(1)	1.386(9)
N(2)-C(6)	1.392(7)
N(2)-C(9)	1.392(8)
C(1)-C(2)	1.406(12)
C(2)-C(3)	1.391(11)
C(3)-C(4)	1.425(9)
C(4)-C(5)	1.494(8)
C(5)-C(6)	1.498(8)

C(6)-C(7)	1.419(8)
C(7)-C(8)	1.419(8)
C(8)-C(9)	1.410(9)
C(11)-C(15)	1.420(8)
C(11)-C(12)	1.426(8)
C(11)-C(16)	1.506(8)
C(12)-C(13)	1.433(8)
C(12)-C(17)	1.506(9)
C(13)-C(14)	1.442(8)
C(13)-C(18)	1.490(8)
C(14)-C(15)	1.425(8)
C(14)-C(19)	1.500(8)
C(15)-C(20)	1.511(8)
C(21)-C(25)	1.418(9)
C(21)-C(22)	1.419(9)
C(21)-C(26)	1.513(9)
C(22)-C(23)	1.423(9)
C(22)-C(27)	1.512(9)
C(23)-C(24)	1.421(8)
C(23)-C(28)	1.509(9)
C(24)-C(25)	1.424(8)
C(24)-C(29)	1.498(8)
C(25)-C(30)	1.499(9)

C(1)-Fe(1)-C(4)	65.6(3)
C(1)-Fe(1)-N(1)	40.1(3)
C(4)-Fe(1)-N(1)	39.5(2)
C(1)-Fe(1)-C(15)	166.8(3)
C(4)-Fe(1)-C(15)	120.3(2)
N(1)-Fe(1)-C(15)	151.8(2)
C(1)-Fe(1)-C(11)	151.5(3)
C(4)-Fe(1)-C(11)	109.6(2)
N(1)-Fe(1)-C(11)	117.6(2)
C(15)-Fe(1)-C(11)	40.7(2)
C(1)-Fe(1)-C(14)	128.7(3)
C(4)-Fe(1)-C(14)	153.2(2)

N(1)-Fe(1)-C(14)	165.8(2)
C(15)-Fe(1)-C(14)	40.9(2)
C(11)-Fe(1)-C(14)	68.9(2)
C(1)-Fe(1)-C(12)	118.3(3)
C(4)-Fe(1)-C(12)	128.6(2)
N(1)-Fe(1)-C(12)	107.2(2)
C(15)-Fe(1)-C(12)	68.5(2)
C(11)-Fe(1)-C(12)	40.8(2)
C(14)-Fe(1)-C(12)	68.8(2)
C(1)-Fe(1)-C(13)	107.9(3)
C(4)-Fe(1)-C(13)	165.1(2)
N(1)-Fe(1)-C(13)	126.9(2)
C(15)-Fe(1)-C(13)	69.2(2)
C(11)-Fe(1)-C(13)	69.3(2)
C(14)-Fe(1)-C(13)	41.3(2)
C(12)-Fe(1)-C(13)	41.0(2)
C(1)-Fe(1)-C(2)	40.6(3)
C(4)-Fe(1)-C(2)	67.0(3)
N(1)-Fe(1)-C(2)	68.8(3)
C(15)-Fe(1)-C(2)	128.4(3)
C(11)-Fe(1)-C(2)	166.4(3)
C(14)-Fe(1)-C(2)	107.9(3)
C(12)-Fe(1)-C(2)	151.7(3)
C(13)-Fe(1)-C(2)	117.6(3)
C(1)-Fe(1)-C(3)	66.8(3)
C(4)-Fe(1)-C(3)	40.7(2)
N(1)-Fe(1)-C(3)	68.5(3)
C(15)-Fe(1)-C(3)	109.2(3)
C(11)-Fe(1)-C(3)	129.4(3)
C(14)-Fe(1)-C(3)	118.4(3)
C(12)-Fe(1)-C(3)	167.2(3)
C(13)-Fe(1)-C(3)	151.2(3)
C(2)-Fe(1)-C(3)	39.5(3)
C(9)-Fe(2)-C(23)	125.6(2)
C(9)-Fe(2)-C(22)	107.7(2)
C(23)-Fe(2)-C(22)	41.0(3)

C(9)-Fe(2)-C(21)	120.9(3)
C(23)-Fe(2)-C(21)	68.5(3)
C(22)-Fe(2)-C(21)	40.7(3)
C(9)-Fe(2)-C(8)	40.7(2)
C(23)-Fe(2)-C(8)	105.9(2)
C(22)-Fe(2)-C(8)	118.6(3)
C(21)-Fe(2)-C(8)	154.3(3)
C(9)-Fe(2)-C(24)	162.7(2)
C(23)-Fe(2)-C(24)	40.8(2)
C(22)-Fe(2)-C(24)	68.8(2)
C(21)-Fe(2)-C(24)	68.2(3)
C(8)-Fe(2)-C(24)	124.8(2)
C(9)-Fe(2)-C(6)	66.1(2)
C(23)-Fe(2)-C(6)	155.3(2)
C(22)-Fe(2)-C(6)	163.3(3)
C(21)-Fe(2)-C(6)	127.6(3)
C(8)-Fe(2)-C(6)	67.8(2)
C(24)-Fe(2)-C(6)	121.8(2)
C(9)-Fe(2)-C(7)	67.3(2)
C(23)-Fe(2)-C(7)	119.2(3)
C(22)-Fe(2)-C(7)	153.6(3)
C(21)-Fe(2)-C(7)	164.3(3)
C(8)-Fe(2)-C(7)	40.5(2)
C(24)-Fe(2)-C(7)	107.8(2)
C(6)-Fe(2)-C(7)	40.5(2)
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C(23)-Fe(2)-N(2)	162.6(2)
C(22)-Fe(2)-N(2)	125.7(2)
C(21)-Fe(2)-N(2)	108.6(2)
C(8)-Fe(2)-N(2)	68.8(2)
C(24)-Fe(2)-N(2)	155.6(2)
C(6)-Fe(2)-N(2)	39.6(2)
C(7)-Fe(2)-N(2)	68.3(2)
C(9)-Fe(2)-C(25)	155.5(3)
C(23)-Fe(2)-C(25)	68.6(2)
C(22)-Fe(2)-C(25)	68.7(2)

C(21)-Fe(2)-C(25)	40.5(3)
C(8)-Fe(2)-C(25)	162.9(3)
C(24)-Fe(2)-C(25)	40.6(2)
C(6)-Fe(2)-C(25)	110.0(2)
C(7)-Fe(2)-C(25)	126.7(2)
N(2)-Fe(2)-C(25)	121.1(2)
C(4)-N(1)-C(1)	104.5(6)
C(4)-N(1)-Fe(1)	70.0(3)
C(1)-N(1)-Fe(1)	68.3(4)
C(6)-N(2)-C(9)	105.5(5)
C(6)-N(2)-Fe(2)	70.0(3)
C(9)-N(2)-Fe(2)	68.4(3)
N(1)-C(1)-C(2)	111.8(7)
N(1)-C(1)-Fe(1)	71.5(4)
C(2)-C(1)-Fe(1)	71.8(5)
C(3)-C(2)-C(1)	106.2(7)
C(3)-C(2)-Fe(1)	70.8(4)
C(1)-C(2)-Fe(1)	67.6(4)
C(2)-C(3)-C(4)	106.4(7)
C(2)-C(3)-Fe(1)	69.7(4)
C(4)-C(3)-Fe(1)	68.4(4)
N(1)-C(4)-C(3)	111.1(6)
N(1)-C(4)-C(5)	122.1(5)
C(3)-C(4)-C(5)	126.3(6)
N(1)-C(4)-Fe(1)	70.5(3)
C(3)-C(4)-Fe(1)	70.9(4)
C(5)-C(4)-Fe(1)	132.3(4)
C(4)-C(5)-C(6)	110.8(5)
N(2)-C(6)-C(7)	110.2(5)
N(2)-C(6)-C(5)	121.6(5)
C(7)-C(6)-C(5)	127.9(5)
N(2)-C(6)-Fe(2)	70.4(3)
C(7)-C(6)-Fe(2)	69.9(3)
C(5)-C(6)-Fe(2)	130.7(4)
C(8)-C(7)-C(6)	107.0(5)
C(8)-C(7)-Fe(2)	69.3(3)

C(6)-C(7)-Fe(2)	69.6(3)
C(9)-C(8)-C(7)	105.7(5)
C(9)-C(8)-Fe(2)	68.6(3)
C(7)-C(8)-Fe(2)	70.2(3)
N(2)-C(9)-C(8)	111.5(5)
N(2)-C(9)-Fe(2)	71.6(3)
C(8)-C(9)-Fe(2)	70.7(3)
C(15)-C(11)-C(12)	107.8(5)
C(15)-C(11)-C(16)	125.9(6)
C(12)-C(11)-C(16)	126.2(6)
C(15)-C(11)-Fe(1)	69.5(3)
C(12)-C(11)-Fe(1)	69.7(3)
C(16)-C(11)-Fe(1)	128.2(4)
C(11)-C(12)-C(13)	108.7(5)
C(11)-C(12)-C(17)	126.5(6)
C(13)-C(12)-C(17)	124.8(6)
C(11)-C(12)-Fe(1)	69.5(3)
C(13)-C(12)-Fe(1)	69.5(3)
C(17)-C(12)-Fe(1)	126.0(5)
C(12)-C(13)-C(14)	106.9(5)
C(12)-C(13)-C(18)	127.0(6)
C(14)-C(13)-C(18)	126.1(5)
C(12)-C(13)-Fe(1)	69.5(3)
C(14)-C(13)-Fe(1)	69.3(3)
C(18)-C(13)-Fe(1)	127.5(4)
C(15)-C(14)-C(13)	108.0(5)
C(15)-C(14)-C(19)	127.0(5)
C(13)-C(14)-C(19)	125.0(5)
C(15)-C(14)-Fe(1)	69.4(3)
C(13)-C(14)-Fe(1)	69.5(3)
C(19)-C(14)-Fe(1)	128.0(4)
C(11)-C(15)-C(14)	108.5(5)
C(11)-C(15)-C(20)	125.9(5)
C(14)-C(15)-C(20)	125.5(6)
C(11)-C(15)-Fe(1)	69.7(3)
C(14)-C(15)-Fe(1)	69.7(3)

C(20)-C(15)-Fe(1)	126.5(5)
C(25)-C(21)-C(22)	108.9(6)
C(25)-C(21)-C(26)	125.0(7)
C(22)-C(21)-C(26)	126.1(7)
C(25)-C(21)-Fe(2)	70.3(4)
C(22)-C(21)-Fe(2)	69.6(4)
C(26)-C(21)-Fe(2)	126.3(5)
C(21)-C(22)-C(23)	107.3(5)
C(21)-C(22)-C(27)	127.1(7)
C(23)-C(22)-C(27)	125.6(7)
C(21)-C(22)-Fe(2)	69.7(4)
C(23)-C(22)-Fe(2)	69.2(3)
C(27)-C(22)-Fe(2)	127.3(5)
C(24)-C(23)-C(22)	108.3(5)
C(24)-C(23)-C(28)	125.6(6)
C(22)-C(23)-C(28)	126.1(6)
C(24)-C(23)-Fe(2)	70.2(3)
C(22)-C(23)-Fe(2)	69.8(4)
C(28)-C(23)-Fe(2)	126.4(4)
C(23)-C(24)-C(25)	108.0(5)
C(23)-C(24)-C(29)	125.6(6)
C(25)-C(24)-C(29)	126.4(6)
C(23)-C(24)-Fe(2)	69.0(3)
C(25)-C(24)-Fe(2)	70.0(3)
C(29)-C(24)-Fe(2)	127.4(4)
C(21)-C(25)-C(24)	107.5(5)
C(21)-C(25)-C(30)	127.4(6)
C(24)-C(25)-C(30)	125.0(6)
C(21)-C(25)-Fe(2)	69.1(4)
C(24)-C(25)-Fe(2)	69.3(3)
C(30)-C(25)-Fe(2)	129.4(5)

Table 1.4. Anisotropic displacement parameters ($Å^2$ x 10^3) for 97070. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Fe(1)	26(1)	22(1)	36(1)	-1(1)	-2(1)	1(1)
Fe(2)	26(1)	22(1)	26(1)	-1(1)	-4(1)	1(1)
N(1)	25(3)	44(3)	51(4)	16(3)	6(2)	0(3)
N(2)	34(3)	35(3)	30(3)	3(2)	1(2)	6(2)
C(1)	36(4)	45(5)	102(7)	41(5)	-16(4)	-5(4)
C(2)	35(4)	33(4)	127(8)	-22(5)	-30(5)	9(3)
C(3)	40(4)	41(4)	66(5)	-23(4)	-16(4)	9(3)
C(4)	29(3)	30(3)	38(4)	-7(3)	4(3)	-3(3)
C(5)	33(3)	33(4)	34(4)	6(3)	1(3)	4(3)
C(6)	33(3)	26(3)	26(3)	1(3)	-1(3)	5(3)
C(7)	37(3)	21(3)	36(4)	-3(3)	-1(3)	6(3)
C(8)	36(4)	30(4)	36(4)	-7(3)	1(3)	-6(3)
C(9)	31(3)	43(4)	29(3)	-5(3)	-8(3)	-1(3)
C(11)	28(3)	21(3)	35(4)	-1(3)	-3(3)	-1(3)
C(12)	37(4)	31(4)	32(4)	-1(3)	5(3)	0(3)
C(13)	28(3)	29(3)	30(3)	0(3)	-2(3)	-4(3)
C(14)	23(3)	33(3)	25(3)	-1(3)	-2(3)	0(3)
C(15)	32(3)	21(3)	34(4)	5(3)	-2(3)	0(3)
C(16)	44(4)	21(3)	58(5)	2(3)	2(3)	2(3)
C(17)	66(5)	61(5)	34(4)	-12(4)	-7(4)	3(4)
C(18)	46(4)	40(4)	30(4)	13(3)	-5(3)	0(3)
C(19)	37(4)	34(4)	38(4)	-3(3)	2(3)	5(3)
C(20)	59(5)	46(4)	36(4)	9(3)	2(3)	14(4)
C(21)	59(5)	25(4)	39(4)	-4(3)	0(3)	4(3)
C(22)	37(4)	46(4)	32(4)	-10(3)	-10(3)	11(3)
C(23)	32(3)	41(4)	24(3)	-7(3)	3(3)	-5(3)
C(24)	30(3)	30(3)	24(3)	-3(3)	-3(3)	3(3)
C(25)	32(4)	36(4)	36(4)	-8(3)	-4(3)	-9(3)
C(26)	122(8)	26(4)	54(5)	-2(4)	4(5)	-9(5)
C(27)	54(5)	86(7)	65(5)	-12(5)	-8(4)	40(5)
C(28)	47(4)	68(5)	50(5)	-10(4)	10(4)	-20(4)

C(29)	67(5)	51(5)	32(4)	2(3)	-5(3)	12(4)
C(30)	42(4)	79(6)	57(5)	-16(5)	-6(4)	-22(4)

Table 1.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for 97070.

	x	y	z	U(eq)
H(1A)	3983	11169	3370	73
H(2A)	3448	12008	4283	78
H(3A)	3896	9668	4889	59
H(5A)	4792	6071	4140	40
H(5B)	4720	6698	4737	40
H(7A)	6528	9474	4075	38
H(8A)	8470	8869	4326	41
H(9A)	8477	6112	4748	42
H(16A)	2449	4865	4322	62
H(16B)	3248	5103	3836	62
H(16C)	2063	4435	3735	62
H(17A)	2297	8013	2598	80
H(17B)	2033	6189	2764	80
H(17C)	3194	6929	2879	80
H(18A)	1074	11551	3279	58
H(18B)	887	10214	2831	58
H(18C)	2059	10930	2932	58
H(19A)	705	11647	4068	54
H(19B)	1299	11166	4606	54
H(19C)	147	10424	4472	54
H(20A)	1238	8337	5048	70
H(20B)	2267	7195	5004	70
H(20C)	1102	6476	4888	70
H(26A)	7889	2232	3821	101
H(26B)	6941	1969	3404	101
H(26C)	6693	2742	3969	101
H(27A)	10030	5363	3582	103

H(27B)	9665	3555	3445	103
H(27C)	9436	4293	4018	103
H(28A)	9759	7605	3238	82
H(28B)	8863	8978	3287	82
H(28C)	9112	8181	2725	82
H(29A)	5842	7989	2751	75
H(29B)	6940	8384	2455	75
H(29C)	6693	9189	3016	75
H(30A)	5108	5868	2968	89
H(30B)	5121	4700	3471	89
H(30C)	5417	4002	2901	89

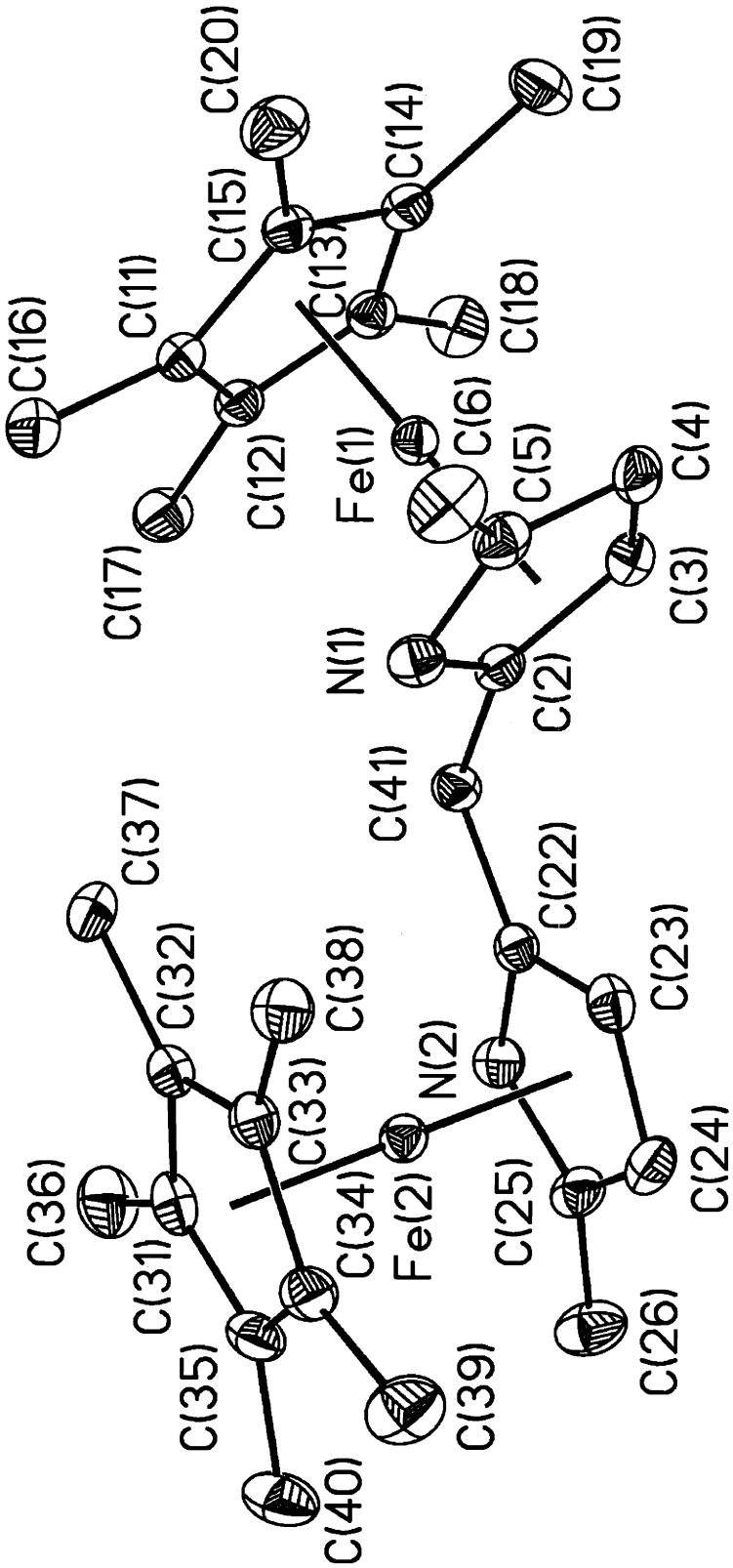

Figure 2. ORTEP plot of (*R*,*R*)-**1.22**, with thermal ellipsoids drawn at the 35% probability level.

Table 2.1. Crystal data and structure refinement for (*R*,*R*)-**1.22**.

Identification code	01146s	
Empirical formula	C31 H42 Fe2 N2	
Formula weight	554.37	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 8.4041(6) Å	α = 90°.
	b = 12.1348(8) Å	β = 90°.
	c = 26.9259(18) Å	γ = 90°.
Volume	2746.0(3) $Å^3$	
Z	4	
Density (calculated)	1.341 Mg/m^3	
Absorption coefficient	1.078 mm^{-1}	
F(000)	1176	
Crystal size	0.30 x 0.21 x 0.18 mm^3	
Theta range for data collection	2.26 to 23.27°.	
Index ranges	-7<=h<=9, -13<=k<=11, -29<=l<=29	
Reflections collected	11017	
Independent reflections	3939 [R(int) = 0.0194]	
Completeness to theta = 23.27°	99.7 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3939 / 0 / 316	
Goodness-of-fit on F^2	1.088	
Final R indices [I>2sigma(I)]	R1 = 0.0296, wR2 = 0.0792	
R indices (all data)	R1 = 0.0300, wR2 = 0.0795	
Absolute structure parameter	0.029(19)	
Largest diff. peak and hole	0.309 and -0.248 $e.Å^{-3}$	

Table 2.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for 01146s. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Fe(1)	4173(1)	1557(1)	1487(1)	23(1)
Fe(2)	1611(1)	5976(1)	1254(1)	23(1)
N(1)	4046(4)	3078(2)	1162(1)	28(1)
N(2)	1192(3)	5636(2)	1989(1)	28(1)
C(2)	3743(4)	3160(3)	1672(1)	25(1)
C(3)	5062(4)	2767(3)	1946(1)	30(1)
C(4)	6234(4)	2441(3)	1595(1)	32(1)
C(5)	5580(4)	2646(3)	1119(1)	29(1)
C(6)	6324(5)	2537(4)	616(2)	43(1)
C(11)	2848(4)	489(3)	1063(1)	27(1)
C(12)	2114(4)	647(3)	1537(1)	27(1)
C(13)	3208(4)	323(3)	1913(1)	27(1)
C(14)	4635(4)	-42(3)	1678(1)	26(1)
C(15)	4437(4)	54(3)	1147(1)	26(1)
C(16)	2148(5)	746(3)	562(1)	35(1)
C(17)	428(4)	1026(3)	1612(2)	39(1)
C(18)	2921(5)	359(3)	2466(1)	40(1)
C(19)	6096(4)	-465(3)	1929(2)	37(1)
C(20)	5627(5)	-262(3)	765(2)	39(1)
C(22)	2393(4)	4958(3)	1805(1)	24(1)
C(23)	3676(4)	5600(3)	1631(1)	29(1)
C(24)	3255(5)	6720(3)	1711(1)	31(1)
C(25)	1726(5)	6715(3)	1933(1)	31(1)
C(26)	789(6)	7673(3)	2121(2)	45(1)
C(31)	-514(4)	5851(3)	885(1)	32(1)
C(32)	581(4)	5039(3)	708(1)	28(1)
C(33)	1960(4)	5593(3)	518(1)	26(1)
C(34)	1700(5)	6765(3)	580(1)	31(1)
C(35)	183(5)	6910(3)	805(1)	32(1)
C(36)	-2115(5)	5634(4)	1110(2)	48(1)
C(37)	319(5)	3813(3)	703(1)	35(1)

C(38)	3400(5)	5065(3)	292(1)	33(1)
C(39)	2813(6)	7656(3)	419(2)	45(1)
C(40)	-580(6)	8017(3)	918(2)	47(1)
C(41)	2265(4)	3721(3)	1853(1)	26(1)

Table 2.3. Bond lengths [Å] and angles [°] for 01146s.

Fe(1)-C(5)	2.031(3)
Fe(1)-C(2)	2.040(3)
Fe(1)-C(14)	2.044(3)
Fe(1)-N(1)	2.045(3)
Fe(1)-C(13)	2.053(3)
Fe(1)-C(15)	2.053(3)
Fe(1)-C(11)	2.055(3)
Fe(1)-C(12)	2.057(3)
Fe(1)-C(4)	2.057(3)
Fe(1)-C(3)	2.059(3)
Fe(2)-C(25)	2.039(3)
Fe(2)-C(22)	2.040(3)
Fe(2)-C(35)	2.046(4)
Fe(2)-C(31)	2.049(3)
Fe(2)-C(32)	2.051(3)
Fe(2)-N(2)	2.053(3)
Fe(2)-C(34)	2.054(3)
Fe(2)-C(33)	2.056(3)
Fe(2)-C(24)	2.058(4)
Fe(2)-C(23)	2.061(3)
N(1)-C(5)	1.397(5)
N(1)-C(2)	1.400(4)
N(2)-C(25)	1.393(5)
N(2)-C(22)	1.394(5)
C(2)-C(3)	1.415(5)
C(2)-C(41)	1.498(5)
C(3)-C(4)	1.421(5)

C(4)-C(5)	1.414(5)
C(5)-C(6)	1.499(5)
C(11)-C(12)	1.432(5)
C(11)-C(15)	1.454(5)
C(11)-C(16)	1.504(5)
C(12)-C(13)	1.422(5)
C(12)-C(17)	1.503(5)
C(13)-C(14)	1.427(5)
C(13)-C(18)	1.510(5)
C(14)-C(15)	1.442(5)
C(14)-C(19)	1.492(5)
C(15)-C(20)	1.486(5)
C(22)-C(23)	1.411(5)
C(22)-C(41)	1.511(5)
C(23)-C(24)	1.420(5)
C(24)-C(25)	1.418(6)
C(25)-C(26)	1.492(5)
C(31)-C(35)	1.428(5)
C(31)-C(32)	1.430(5)
C(31)-C(36)	1.499(5)
C(32)-C(33)	1.435(5)
C(32)-C(37)	1.504(5)
C(33)-C(34)	1.447(5)
C(33)-C(38)	1.499(5)
C(34)-C(35)	1.422(6)
C(34)-C(39)	1.494(6)
C(35)-C(40)	1.519(5)

C(5)-Fe(1)-C(2)	66.55(14)
C(5)-Fe(1)-C(14)	128.98(14)
C(2)-Fe(1)-C(14)	151.32(14)
C(5)-Fe(1)-N(1)	40.07(13)
C(2)-Fe(1)-N(1)	40.08(12)
C(14)-Fe(1)-N(1)	166.84(13)
C(5)-Fe(1)-C(13)	167.63(15)
C(2)-Fe(1)-C(13)	119.29(14)

C(14)-Fe(1)-C(13)	40.75(14)
N(1)-Fe(1)-C(13)	151.24(13)
C(5)-Fe(1)-C(15)	107.36(14)
C(2)-Fe(1)-C(15)	167.23(13)
C(14)-Fe(1)-C(15)	41.20(14)
N(1)-Fe(1)-C(15)	128.11(12)
C(13)-Fe(1)-C(15)	69.07(14)
C(5)-Fe(1)-C(11)	117.06(14)
C(2)-Fe(1)-C(11)	129.85(14)
C(14)-Fe(1)-C(11)	69.14(14)
N(1)-Fe(1)-C(11)	107.64(13)
C(13)-Fe(1)-C(11)	68.67(13)
C(15)-Fe(1)-C(11)	41.45(14)
C(5)-Fe(1)-C(12)	150.61(14)
C(2)-Fe(1)-C(12)	110.28(13)
C(14)-Fe(1)-C(12)	68.51(13)
N(1)-Fe(1)-C(12)	117.96(13)
C(13)-Fe(1)-C(12)	40.47(14)
C(15)-Fe(1)-C(12)	69.08(14)
C(11)-Fe(1)-C(12)	40.75(14)
C(5)-Fe(1)-C(4)	40.47(15)
C(2)-Fe(1)-C(4)	67.55(14)
C(14)-Fe(1)-C(4)	107.42(14)
N(1)-Fe(1)-C(4)	68.52(14)
C(13)-Fe(1)-C(4)	129.36(15)
C(15)-Fe(1)-C(4)	115.79(14)
C(11)-Fe(1)-C(4)	149.64(14)
C(12)-Fe(1)-C(4)	168.11(15)
C(5)-Fe(1)-C(3)	67.49(14)
C(2)-Fe(1)-C(3)	40.38(14)
C(14)-Fe(1)-C(3)	117.20(14)
N(1)-Fe(1)-C(3)	68.42(13)
C(13)-Fe(1)-C(3)	109.19(14)
C(15)-Fe(1)-C(3)	149.50(14)
C(11)-Fe(1)-C(3)	168.43(14)
C(12)-Fe(1)-C(3)	130.44(14)

C(4)-Fe(1)-C(3)	40.39(14)
C(25)-Fe(2)-C(22)	66.35(14)
C(25)-Fe(2)-C(35)	108.33(14)
C(22)-Fe(2)-C(35)	162.65(15)
C(25)-Fe(2)-C(31)	120.58(15)
C(22)-Fe(2)-C(31)	126.06(15)
C(35)-Fe(2)-C(31)	40.82(16)
C(25)-Fe(2)-C(32)	155.07(15)
C(22)-Fe(2)-C(32)	108.73(14)
C(35)-Fe(2)-C(32)	68.64(14)
C(31)-Fe(2)-C(32)	40.83(15)
C(25)-Fe(2)-N(2)	39.81(13)
C(22)-Fe(2)-N(2)	39.82(13)
C(35)-Fe(2)-N(2)	125.52(13)
C(31)-Fe(2)-N(2)	107.64(13)
C(32)-Fe(2)-N(2)	120.45(13)
C(25)-Fe(2)-C(34)	125.91(13)
C(22)-Fe(2)-C(34)	156.00(15)
C(35)-Fe(2)-C(34)	40.60(16)
C(31)-Fe(2)-C(34)	68.74(15)
C(32)-Fe(2)-C(34)	68.91(14)
N(2)-Fe(2)-C(34)	162.31(13)
C(25)-Fe(2)-C(33)	163.12(15)
C(22)-Fe(2)-C(33)	121.19(13)
C(35)-Fe(2)-C(33)	68.85(14)
C(31)-Fe(2)-C(33)	68.92(14)
C(32)-Fe(2)-C(33)	40.91(14)
N(2)-Fe(2)-C(33)	155.26(12)
C(34)-Fe(2)-C(33)	41.24(14)
C(25)-Fe(2)-C(24)	40.50(15)
C(22)-Fe(2)-C(24)	67.33(14)
C(35)-Fe(2)-C(24)	120.30(15)
C(31)-Fe(2)-C(24)	155.15(15)
C(32)-Fe(2)-C(24)	162.76(15)
N(2)-Fe(2)-C(24)	68.12(13)
C(34)-Fe(2)-C(24)	107.44(15)

C(33)-Fe(2)-C(24)	125.38(14)
C(25)-Fe(2)-C(23)	67.44(15)
C(22)-Fe(2)-C(23)	40.25(15)
C(35)-Fe(2)-C(23)	155.12(15)
C(31)-Fe(2)-C(23)	162.92(15)
C(32)-Fe(2)-C(23)	125.82(14)
N(2)-Fe(2)-C(23)	68.02(13)
C(34)-Fe(2)-C(23)	120.49(15)
C(33)-Fe(2)-C(23)	107.68(14)
C(24)-Fe(2)-C(23)	40.33(15)
C(5)-N(1)-C(2)	106.0(3)
C(5)-N(1)-Fe(1)	69.42(18)
C(2)-N(1)-Fe(1)	69.75(17)
C(25)-N(2)-C(22)	106.4(3)
C(25)-N(2)-Fe(2)	69.56(18)
C(22)-N(2)-Fe(2)	69.60(18)
N(1)-C(2)-C(3)	110.1(3)
N(1)-C(2)-C(41)	120.1(3)
C(3)-C(2)-C(41)	129.4(3)
N(1)-C(2)-Fe(1)	70.16(17)
C(3)-C(2)-Fe(1)	70.54(19)
C(41)-C(2)-Fe(1)	131.3(2)
C(2)-C(3)-C(4)	106.9(3)
C(2)-C(3)-Fe(1)	69.08(19)
C(4)-C(3)-Fe(1)	69.75(19)
C(5)-C(4)-C(3)	106.5(3)
C(5)-C(4)-Fe(1)	68.75(19)
C(3)-C(4)-Fe(1)	69.9(2)
N(1)-C(5)-C(4)	110.5(3)
N(1)-C(5)-C(6)	119.5(3)
C(4)-C(5)-C(6)	129.9(3)
N(1)-C(5)-Fe(1)	70.51(18)
C(4)-C(5)-Fe(1)	70.8(2)
C(6)-C(5)-Fe(1)	128.8(3)
C(12)-C(11)-C(15)	107.7(3)
C(12)-C(11)-C(16)	127.1(3)

C(15)-C(11)-C(16)	125.1(3)
C(12)-C(11)-Fe(1)	69.71(19)
C(15)-C(11)-Fe(1)	69.19(19)
C(16)-C(11)-Fe(1)	125.4(2)
C(13)-C(12)-C(11)	108.6(3)
C(13)-C(12)-C(17)	126.8(3)
C(11)-C(12)-C(17)	124.5(3)
C(13)-C(12)-Fe(1)	69.59(19)
C(11)-C(12)-Fe(1)	69.54(19)
C(17)-C(12)-Fe(1)	129.6(2)
C(12)-C(13)-C(14)	108.3(3)
C(12)-C(13)-C(18)	126.2(3)
C(14)-C(13)-C(18)	125.5(3)
C(12)-C(13)-Fe(1)	69.94(19)
C(14)-C(13)-Fe(1)	69.3(2)
C(18)-C(13)-Fe(1)	126.4(3)
C(13)-C(14)-C(15)	108.5(3)
C(13)-C(14)-C(19)	126.7(3)
C(15)-C(14)-C(19)	124.8(3)
C(13)-C(14)-Fe(1)	69.95(19)
C(15)-C(14)-Fe(1)	69.72(19)
C(19)-C(14)-Fe(1)	126.6(3)
C(14)-C(15)-C(11)	106.9(3)
C(14)-C(15)-C(20)	126.0(3)
C(11)-C(15)-C(20)	127.1(3)
C(14)-C(15)-Fe(1)	69.07(19)
C(11)-C(15)-Fe(1)	69.36(19)
C(20)-C(15)-Fe(1)	127.6(3)
N(2)-C(22)-C(23)	110.2(3)
N(2)-C(22)-C(41)	120.3(3)
C(23)-C(22)-C(41)	129.2(3)
N(2)-C(22)-Fe(2)	70.58(18)
C(23)-C(22)-Fe(2)	70.68(19)
C(41)-C(22)-Fe(2)	129.9(2)
C(22)-C(23)-C(24)	106.7(3)
C(22)-C(23)-Fe(2)	69.1(2)

C(24)-C(23)-Fe(2)	69.7(2)
C(25)-C(24)-C(23)	106.6(3)
C(25)-C(24)-Fe(2)	69.0(2)
C(23)-C(24)-Fe(2)	70.0(2)
N(2)-C(25)-C(24)	110.0(3)
N(2)-C(25)-C(26)	121.7(3)
C(24)-C(25)-C(26)	128.2(3)
N(2)-C(25)-Fe(2)	70.64(18)
C(24)-C(25)-Fe(2)	70.47(19)
C(26)-C(25)-Fe(2)	128.4(3)
C(35)-C(31)-C(32)	107.8(3)
C(35)-C(31)-C(36)	126.0(4)
C(32)-C(31)-C(36)	126.2(4)
C(35)-C(31)-Fe(2)	69.5(2)
C(32)-C(31)-Fe(2)	69.63(19)
C(36)-C(31)-Fe(2)	126.8(3)
C(31)-C(32)-C(33)	108.3(3)
C(31)-C(32)-C(37)	126.2(3)
C(33)-C(32)-C(37)	125.4(3)
C(31)-C(32)-Fe(2)	69.5(2)
C(33)-C(32)-Fe(2)	69.75(19)
C(37)-C(32)-Fe(2)	128.2(3)
C(32)-C(33)-C(34)	107.3(3)
C(32)-C(33)-C(38)	126.6(3)
C(34)-C(33)-C(38)	126.0(3)
C(32)-C(33)-Fe(2)	69.34(19)
C(34)-C(33)-Fe(2)	69.29(19)
C(38)-C(33)-Fe(2)	127.2(2)
C(35)-C(34)-C(33)	107.8(3)
C(35)-C(34)-C(39)	126.5(3)
C(33)-C(34)-C(39)	125.7(4)
C(35)-C(34)-Fe(2)	69.4(2)
C(33)-C(34)-Fe(2)	69.46(19)
C(39)-C(34)-Fe(2)	128.0(3)
C(34)-C(35)-C(31)	108.7(3)
C(34)-C(35)-C(40)	125.0(4)

C(31)-C(35)-C(40)	126.3(3)
C(34)-C(35)-Fe(2)	70.0(2)
C(31)-C(35)-Fe(2)	69.7(2)
C(40)-C(35)-Fe(2)	128.2(3)
C(2)-C(41)-C(22)	111.4(3)

Table 2.4. Anisotropic displacement parameters ($Å^2$ x 10^3) for 01146s. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Fe(1)	23(1)	23(1)	22(1)	-1(1)	-1(1)	0(1)
Fe(2)	25(1)	23(1)	22(1)	-1(1)	0(1)	0(1)
N(1)	31(2)	25(1)	27(2)	3(1)	3(1)	0(1)
N(2)	33(2)	30(2)	22(2)	-2(1)	1(1)	1(1)
C(2)	31(2)	19(2)	24(2)	0(1)	0(1)	-2(1)
C(3)	31(2)	29(2)	29(2)	-5(2)	-4(2)	-1(2)
C(4)	21(2)	31(2)	44(2)	-8(2)	-3(2)	-3(2)
C(5)	27(2)	25(2)	36(2)	0(2)	3(2)	-6(2)
C(6)	46(3)	42(2)	40(2)	-2(2)	14(2)	-9(2)
C(11)	29(2)	21(2)	30(2)	-1(1)	-4(2)	-2(2)
C(12)	25(2)	22(2)	33(2)	-2(2)	0(2)	-1(1)
C(13)	28(2)	24(2)	30(2)	1(1)	1(2)	-2(2)
C(14)	30(2)	21(2)	28(2)	-1(1)	0(2)	-2(2)
C(15)	30(2)	21(2)	27(2)	0(1)	-2(2)	1(2)
C(16)	41(2)	31(2)	34(2)	-1(2)	-9(2)	0(2)
C(17)	26(2)	36(2)	54(2)	-6(2)	4(2)	1(2)
C(18)	45(2)	45(2)	30(2)	5(2)	6(2)	-3(2)
C(19)	32(2)	36(2)	44(2)	9(2)	-4(2)	5(2)
C(20)	41(2)	38(2)	38(2)	-8(2)	5(2)	2(2)
C(22)	27(2)	26(2)	18(2)	-1(1)	-2(1)	0(2)
C(23)	26(2)	36(2)	25(2)	-3(1)	-4(1)	1(2)
C(24)	37(2)	28(2)	29(2)	-2(1)	-2(2)	-10(2)
C(25)	45(2)	26(2)	22(2)	-5(1)	-1(2)	0(2)

C(26)	69(3)	33(2)	34(2)	-4(2)	7(2)	4(2)
C(31)	27(2)	45(2)	24(2)	-2(2)	-6(1)	1(2)
C(32)	31(2)	28(2)	26(2)	1(2)	-8(2)	0(2)
C(33)	29(2)	30(2)	19(2)	0(1)	-2(1)	0(2)
C(34)	40(2)	29(2)	22(2)	2(1)	-2(2)	1(2)
C(35)	37(2)	31(2)	29(2)	0(2)	-4(2)	13(2)
C(36)	30(2)	60(3)	53(3)	-3(2)	0(2)	-1(2)
C(37)	38(2)	31(2)	36(2)	-6(2)	-7(2)	-7(2)
C(38)	36(2)	34(2)	27(2)	-2(2)	2(2)	1(2)
C(39)	61(3)	39(2)	36(2)	6(2)	8(2)	-7(2)
C(40)	53(3)	39(2)	48(2)	3(2)	2(2)	21(2)
C(41)	29(2)	25(2)	25(2)	1(1)	-2(1)	2(1)

Table 2.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for 01146s.

	x	y	z	U(eq)
H(3)	5149	2728	2297	35
H(4)	7255	2144	1665	38
H(6A)	5548	2746	361	64
H(6B)	6656	1771	563	64
H(6C)	7254	3022	594	64
H(16A)	2911	546	302	53
H(16B)	1912	1536	541	53
H(16C)	1165	324	517	53
H(17A)	203	1080	1968	58
H(17B)	-303	495	1460	58
H(17C)	284	1750	1457	58
H(18A)	3866	86	2640	60
H(18B)	2004	-106	2549	60
H(18C)	2706	1119	2568	60
H(19A)	5944	-445	2289	56
H(19B)	7007	-3	1838	56
H(19C)	6295	-1225	1823	56

H(20A)	5189	-123	434	59
H(20B)	5881	-1047	799	59
H(20C)	6597	175	811	59
H(23)	4636	5336	1487	35
H(24)	3877	7349	1631	38
H(26A)	-234	7413	2251	68
H(26B)	600	8193	1849	68
H(26C)	1383	8041	2386	68
H(36A)	-2308	4838	1120	72
H(36B)	-2939	5989	908	72
H(36C)	-2146	5934	1447	72
H(37A)	1269	3446	571	52
H(37B)	-598	3639	492	52
H(37C)	115	3554	1042	52
H(38A)	3273	4263	295	49
H(38B)	4347	5268	483	49
H(38C)	3521	5320	-52	49
H(39A)	3770	7326	274	68
H(39B)	3110	8106	707	68
H(39C)	2288	8122	170	68
H(40A)	-1618	7899	1075	70
H(40B)	-721	8430	608	70
H(40C)	108	8435	1144	70
H(41A)	2081	3525	2205	32
H(41B)	1341	3458	1658	32

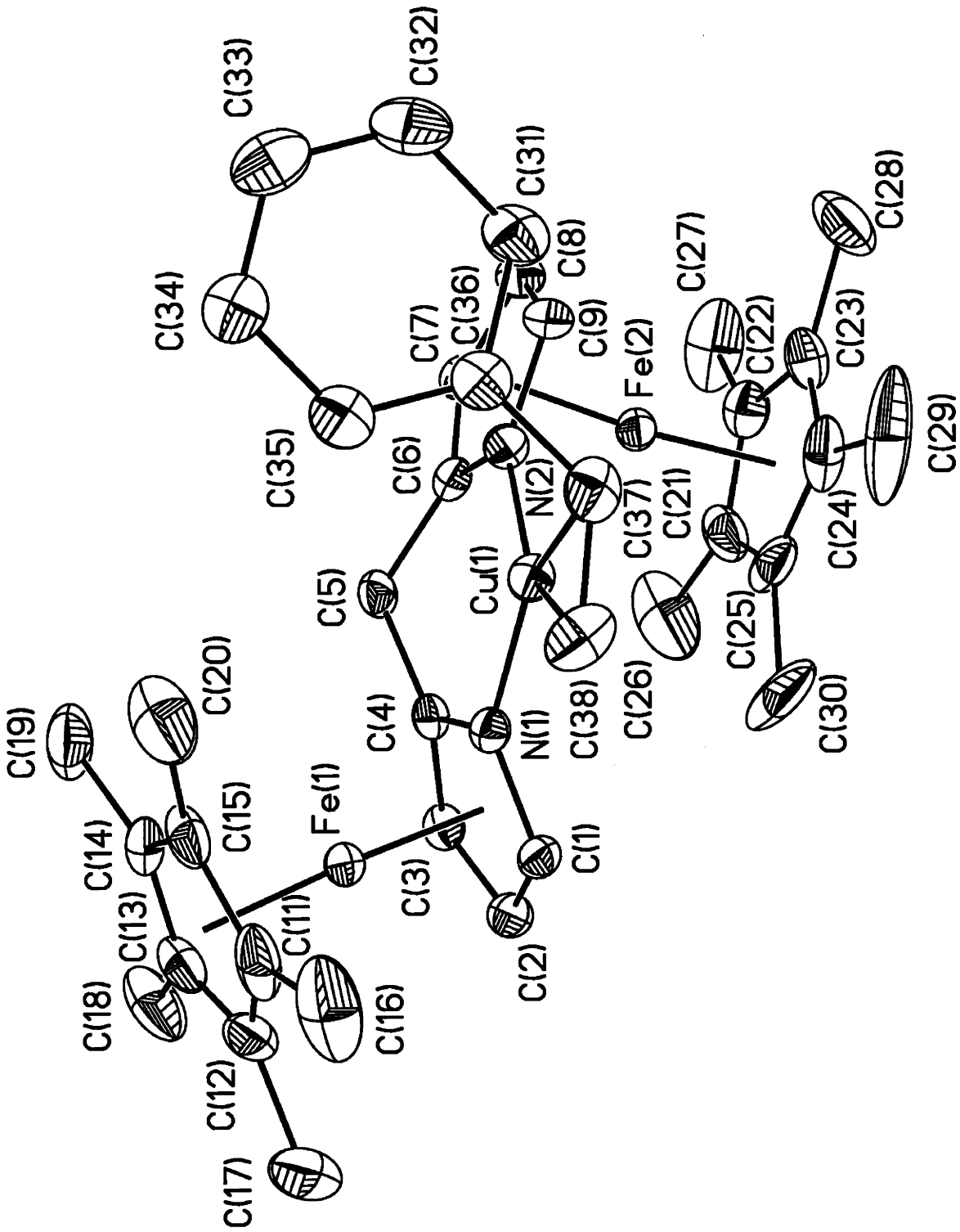

Figure 3. ORTEP plot of [CuOTf•(*S.S*)-**1.19**•styrene], with thermal ellipsoids drawn at the 35% probability level.

Table 3.1. Crystal data and structure refinement for [CuOTf•(*S.S*)-**1.19**•styrene].

Identification code	98085	
Empirical formula	C38 H46 Cu F3 Fe2 N2 O3 S	
Formula weight	843.07	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 9.25490(10) Å	α = 90°.
	b = 20.5570(3) Å	β = 93.65°.
	c = 9.8550(2) Å	γ = 90°.
Volume	1871.13(5) $Å^3$	
Z	2	
Density (calculated)	1.496 Mg/m^3	
Absorption coefficient	1.438 mm^{-1}	
F(000)	872	
Crystal size	0.15 x 0.36 x 0.42 mm^3	
Theta range for data collection	2.07 to 23.30°.	
Index ranges	-10<=h<=9, -22<=k<=22, -10<=l<=8	
Reflections collected	7746	
Independent reflections	5116 [R(int) = 0.0262]	
Completeness to theta = 23.30°	99.6 %	
Absorption correction	Empirical	
Max. and min. transmission	0.9745 and 0.7197	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5116 / 1 / 451	
Goodness-of-fit on F^2	1.074	
Final R indices [I>2sigma(I)]	R1 = 0.0334, wR2 = 0.0843	
R indices (all data)	R1 = 0.0351, wR2 = 0.0860	
Absolute structure parameter	0.004(15)	
Largest diff. peak and hole	0.369 and -0.336 $e.Å^{-3}$	

Table 3.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for 98085. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cu(1)	-7640(1)	-4899(1)	-6721(1)	32(1)
Fe(1)	-10368(1)	-4174(1)	-4573(1)	29(1)
Fe(2)	-9494(1)	-6046(1)	-8722(1)	32(1)
N(1)	-9282(3)	-4869(2)	-5571(3)	29(1)
N(2)	-8715(4)	-5124(2)	-8417(4)	35(1)
C(1)	-9323(5)	-5017(2)	-4194(4)	32(1)
C(2)	-10761(5)	-5091(2)	-3855(5)	35(1)
C(3)	-11636(5)	-4982(2)	-5054(4)	32(1)
C(4)	-10725(4)	-4846(2)	-6096(4)	29(1)
C(5)	-11106(5)	-4748(2)	-7599(4)	37(1)
C(6)	-10242(5)	-5112(2)	-8563(4)	30(1)
C(7)	-10704(5)	-5364(2)	-9845(4)	39(1)
C(8)	-9429(6)	-5538(3)	-10519(5)	46(1)
C(9)	-8256(5)	-5388(2)	-9624(5)	41(1)
C(11)	-9259(7)	-3462(2)	-3522(7)	59(2)
C(12)	-10618(7)	-3573(2)	-2972(5)	52(1)
C(13)	-11715(6)	-3454(2)	-3979(6)	48(1)
C(14)	-11087(5)	-3274(2)	-5169(5)	40(1)
C(15)	-9547(6)	-3267(2)	-4921(6)	46(1)
C(16)	-7804(8)	-3527(3)	-2767(9)	94(3)
C(17)	-10895(10)	-3774(4)	-1517(7)	89(2)
C(18)	-13342(7)	-3514(3)	-3839(8)	81(2)
C(19)	-11846(9)	-3083(3)	-6522(7)	79(2)
C(20)	-8466(8)	-3077(3)	-5885(9)	90(3)
C(21)	-10673(7)	-6735(3)	-7785(7)	64(2)
C(22)	-10374(6)	-6937(3)	-9120(6)	47(1)
C(23)	-8845(6)	-6962(2)	-9176(6)	47(1)
C(24)	-8208(7)	-6778(2)	-7902(7)	60(2)
C(25)	-9326(9)	-6644(2)	-7037(5)	68(2)
C(26)	-12160(10)	-6634(4)	-7270(12)	134(4)
C(27)	-11475(9)	-7099(3)	-10264(9)	96(3)

C(28)	-8054(9)	-7135(3)	-10415(8)	88(2)
C(29)	-6602(9)	-6729(4)	-7576(12)	135(5)
C(30)	-9109(16)	-6482(3)	-5538(7)	157(6)
C(31)	-4900(5)	-4553(3)	-9312(6)	49(1)
C(32)	-4739(6)	-4110(3)	-10368(6)	59(1)
C(33)	-4931(6)	-3455(3)	-10149(6)	58(2)
C(34)	-5276(5)	-3234(3)	-8899(6)	50(1)
C(35)	-5455(5)	-3668(3)	-7849(6)	46(1)
C(36)	-5290(4)	-4335(2)	-8050(5)	39(1)
C(37)	-5498(5)	-4826(3)	-6961(5)	46(1)
C(38)	-5812(5)	-4694(3)	-5630(5)	52(1)
S(1)	-4888(1)	-5816(1)	-12207(1)	48(1)
F(1)	-5180(8)	-6951(2)	-13381(6)	148(2)
F(2)	-3025(6)	-6608(3)	-13177(5)	124(2)
F(3)	-4474(4)	-6211(2)	-14678(3)	76(1)
O(1)	-3872(6)	-5312(3)	-12437(5)	96(2)
O(2)	-6313(5)	-5668(3)	-12648(5)	93(2)
O(3)	-4733(5)	-6131(3)	-10925(4)	87(2)
C(91)	-4376(7)	-6430(3)	-13405(6)	62(2)

Table 3.3. Bond lengths [Å] and angles [°] for 98085.

Cu(1)-N(2)	1.946(4)
Cu(1)-N(1)	1.954(3)
Cu(1)-C(38)	1.991(5)
Cu(1)-C(37)	2.017(4)
Fe(1)-C(1)	2.008(4)
Fe(1)-C(12)	2.029(5)
Fe(1)-C(11)	2.033(5)
Fe(1)-N(1)	2.036(3)
Fe(1)-C(14)	2.041(4)
Fe(1)-C(13)	2.045(5)
Fe(1)-C(15)	2.050(5)
Fe(1)-C(4)	2.051(4)

Fe(1)-C(2)	2.054(4)
Fe(1)-C(3)	2.072(4)
Fe(2)-C(9)	2.015(5)
Fe(2)-C(22)	2.032(5)
Fe(2)-C(23)	2.036(5)
Fe(2)-N(2)	2.042(4)
Fe(2)-C(21)	2.045(6)
Fe(2)-C(6)	2.049(4)
Fe(2)-C(24)	2.054(5)
Fe(2)-C(8)	2.059(5)
Fe(2)-C(25)	2.065(5)
Fe(2)-C(7)	2.070(4)
N(1)-C(1)	1.394(5)
N(1)-C(4)	1.402(5)
N(2)-C(9)	1.398(6)
N(2)-C(6)	1.412(6)
C(1)-C(2)	1.402(6)
C(2)-C(3)	1.406(6)
C(3)-C(4)	1.398(6)
C(4)-C(5)	1.514(6)
C(5)-C(6)	1.482(6)
C(6)-C(7)	1.406(6)
C(7)-C(8)	1.437(7)
C(8)-C(9)	1.389(7)
C(11)-C(12)	1.421(9)
C(11)-C(15)	1.444(8)
C(11)-C(16)	1.502(8)
C(12)-C(13)	1.395(8)
C(12)-C(17)	1.529(8)
C(13)-C(14)	1.392(8)
C(13)-C(18)	1.526(8)
C(14)-C(15)	1.431(7)
C(14)-C(19)	1.518(8)
C(15)-C(20)	1.475(8)
C(21)-C(25)	1.420(10)
C(21)-C(22)	1.423(8)

C(21)-C(26)	1.511(10)
C(22)-C(23)	1.420(7)
C(22)-C(27)	1.509(8)
C(23)-C(24)	1.404(8)
C(23)-C(28)	1.506(8)
C(24)-C(25)	1.409(10)
C(24)-C(29)	1.504(10)
C(25)-C(30)	1.516(8)
C(31)-C(36)	1.391(7)
C(31)-C(32)	1.397(8)
C(32)-C(33)	1.378(9)
C(33)-C(34)	1.370(8)
C(34)-C(35)	1.385(8)
C(35)-C(36)	1.395(7)
C(36)-C(37)	1.494(7)
C(37)-C(38)	1.388(8)
S(1)-O(2)	1.396(4)
S(1)-O(3)	1.419(4)
S(1)-O(1)	1.427(5)
S(1)-C(91)	1.812(6)
F(1)-C(91)	1.306(8)
F(2)-C(91)	1.308(8)
F(3)-C(91)	1.330(7)

N(2)-Cu(1)-N(1)	97.56(14)
N(2)-Cu(1)-C(38)	152.24(19)
N(1)-Cu(1)-C(38)	110.21(18)
N(2)-Cu(1)-C(37)	111.71(19)
N(1)-Cu(1)-C(37)	150.72(18)
C(38)-Cu(1)-C(37)	40.5(2)
C(1)-Fe(1)-C(12)	117.3(2)
C(1)-Fe(1)-C(11)	107.8(2)
C(12)-Fe(1)-C(11)	40.9(2)
C(1)-Fe(1)-N(1)	40.32(15)
C(12)-Fe(1)-N(1)	152.6(2)
C(11)-Fe(1)-N(1)	120.2(2)

C(1)-Fe(1)-C(14)	168.77(19)
C(12)-Fe(1)-C(14)	67.7(2)
C(11)-Fe(1)-C(14)	68.8(2)
N(1)-Fe(1)-C(14)	131.29(18)
C(1)-Fe(1)-C(13)	150.1(2)
C(12)-Fe(1)-C(13)	40.1(2)
C(11)-Fe(1)-C(13)	68.3(2)
N(1)-Fe(1)-C(13)	167.19(19)
C(14)-Fe(1)-C(13)	39.8(2)
C(1)-Fe(1)-C(15)	129.56(19)
C(12)-Fe(1)-C(15)	68.8(2)
C(11)-Fe(1)-C(15)	41.4(2)
N(1)-Fe(1)-C(15)	111.00(18)
C(14)-Fe(1)-C(15)	40.9(2)
C(13)-Fe(1)-C(15)	68.2(2)
C(1)-Fe(1)-C(4)	66.95(17)
C(12)-Fe(1)-C(4)	163.3(2)
C(11)-Fe(1)-C(4)	155.6(2)
N(1)-Fe(1)-C(4)	40.11(14)
C(14)-Fe(1)-C(4)	111.46(18)
C(13)-Fe(1)-C(4)	128.6(2)
C(15)-Fe(1)-C(4)	122.3(2)
C(1)-Fe(1)-C(2)	40.36(18)
C(12)-Fe(1)-C(2)	105.0(2)
C(11)-Fe(1)-C(2)	125.5(2)
N(1)-Fe(1)-C(2)	68.04(16)
C(14)-Fe(1)-C(2)	150.40(19)
C(13)-Fe(1)-C(2)	116.1(2)
C(15)-Fe(1)-C(2)	165.4(2)
C(4)-Fe(1)-C(2)	67.06(17)
C(1)-Fe(1)-C(3)	67.02(18)
C(12)-Fe(1)-C(3)	125.1(2)
C(11)-Fe(1)-C(3)	162.6(2)
N(1)-Fe(1)-C(3)	67.43(15)
C(14)-Fe(1)-C(3)	119.46(18)
C(13)-Fe(1)-C(3)	107.40(19)

C(15)-Fe(1)-C(3)	154.4(2)
C(4)-Fe(1)-C(3)	39.64(17)
C(2)-Fe(1)-C(3)	39.86(17)
C(9)-Fe(2)-C(22)	138.7(2)
C(9)-Fe(2)-C(23)	109.9(2)
C(22)-Fe(2)-C(23)	40.9(2)
C(9)-Fe(2)-N(2)	40.30(17)
C(22)-Fe(2)-N(2)	176.08(18)
C(23)-Fe(2)-N(2)	141.64(18)
C(9)-Fe(2)-C(21)	177.6(2)
C(22)-Fe(2)-C(21)	40.9(2)
C(23)-Fe(2)-C(21)	68.4(2)
N(2)-Fe(2)-C(21)	140.4(2)
C(9)-Fe(2)-C(6)	67.07(18)
C(22)-Fe(2)-C(6)	136.52(19)
C(23)-Fe(2)-C(6)	171.6(2)
N(2)-Fe(2)-C(6)	40.39(16)
C(21)-Fe(2)-C(6)	114.9(2)
C(9)-Fe(2)-C(24)	109.5(2)
C(22)-Fe(2)-C(24)	68.3(2)
C(23)-Fe(2)-C(24)	40.2(2)
N(2)-Fe(2)-C(24)	115.58(19)
C(21)-Fe(2)-C(24)	68.0(3)
C(6)-Fe(2)-C(24)	147.9(2)
C(9)-Fe(2)-C(8)	39.8(2)
C(22)-Fe(2)-C(8)	108.9(2)
C(23)-Fe(2)-C(8)	104.8(2)
N(2)-Fe(2)-C(8)	68.13(18)
C(21)-Fe(2)-C(8)	141.8(3)
C(6)-Fe(2)-C(8)	67.70(19)
C(24)-Fe(2)-C(8)	131.4(3)
C(9)-Fe(2)-C(25)	137.6(3)
C(22)-Fe(2)-C(25)	68.1(2)
C(23)-Fe(2)-C(25)	67.5(2)
N(2)-Fe(2)-C(25)	115.24(19)
C(21)-Fe(2)-C(25)	40.4(3)

C(6)-Fe(2)-C(25)	120.3(2)
C(24)-Fe(2)-C(25)	40.0(3)
C(8)-Fe(2)-C(25)	171.3(3)
C(9)-Fe(2)-C(7)	67.3(2)
C(22)-Fe(2)-C(7)	108.1(2)
C(23)-Fe(2)-C(7)	131.8(2)
N(2)-Fe(2)-C(7)	67.95(17)
C(21)-Fe(2)-C(7)	115.1(2)
C(6)-Fe(2)-C(7)	39.91(17)
C(24)-Fe(2)-C(7)	170.9(2)
C(8)-Fe(2)-C(7)	40.7(2)
C(25)-Fe(2)-C(7)	147.6(3)
C(1)-N(1)-C(4)	106.4(3)
C(1)-N(1)-Cu(1)	128.9(3)
C(4)-N(1)-Cu(1)	123.0(3)
C(1)-N(1)-Fe(1)	68.7(2)
C(4)-N(1)-Fe(1)	70.5(2)
Cu(1)-N(1)-Fe(1)	136.71(19)
C(9)-N(2)-C(6)	106.1(4)
C(9)-N(2)-Cu(1)	131.1(3)
C(6)-N(2)-Cu(1)	122.5(3)
C(9)-N(2)-Fe(2)	68.8(2)
C(6)-N(2)-Fe(2)	70.1(2)
Cu(1)-N(2)-Fe(2)	120.26(18)
N(1)-C(1)-C(2)	109.9(4)
N(1)-C(1)-Fe(1)	70.9(2)
C(2)-C(1)-Fe(1)	71.6(3)
C(1)-C(2)-C(3)	106.7(4)
C(1)-C(2)-Fe(1)	68.1(2)
C(3)-C(2)-Fe(1)	70.8(2)
C(4)-C(3)-C(2)	107.9(4)
C(4)-C(3)-Fe(1)	69.4(2)
C(2)-C(3)-Fe(1)	69.4(2)
C(3)-C(4)-N(1)	109.1(3)
C(3)-C(4)-C(5)	129.2(4)
N(1)-C(4)-C(5)	121.5(4)

C(3)-C(4)-Fe(1)	71.0(2)
N(1)-C(4)-Fe(1)	69.4(2)
C(5)-C(4)-Fe(1)	130.0(3)
C(6)-C(5)-C(4)	117.3(3)
C(7)-C(6)-N(2)	109.3(4)
C(7)-C(6)-C(5)	128.0(4)
N(2)-C(6)-C(5)	121.4(4)
C(7)-C(6)-Fe(2)	70.9(3)
N(2)-C(6)-Fe(2)	69.5(2)
C(5)-C(6)-Fe(2)	136.1(3)
C(6)-C(7)-C(8)	107.2(4)
C(6)-C(7)-Fe(2)	69.2(2)
C(8)-C(7)-Fe(2)	69.2(3)
C(9)-C(8)-C(7)	106.4(4)
C(9)-C(8)-Fe(2)	68.4(3)
C(7)-C(8)-Fe(2)	70.0(3)
C(8)-C(9)-N(2)	111.0(4)
C(8)-C(9)-Fe(2)	71.8(3)
N(2)-C(9)-Fe(2)	70.9(2)
C(12)-C(11)-C(15)	107.2(5)
C(12)-C(11)-C(16)	125.7(6)
C(15)-C(11)-C(16)	127.1(7)
C(12)-C(11)-Fe(1)	69.4(3)
C(15)-C(11)-Fe(1)	69.9(3)
C(16)-C(11)-Fe(1)	126.5(4)
C(13)-C(12)-C(11)	108.8(5)
C(13)-C(12)-C(17)	123.9(6)
C(11)-C(12)-C(17)	127.4(6)
C(13)-C(12)-Fe(1)	70.6(3)
C(11)-C(12)-Fe(1)	69.7(3)
C(17)-C(12)-Fe(1)	126.8(4)
C(14)-C(13)-C(12)	108.8(5)
C(14)-C(13)-C(18)	124.4(6)
C(12)-C(13)-C(18)	126.8(6)
C(14)-C(13)-Fe(1)	69.9(3)
C(12)-C(13)-Fe(1)	69.4(3)

C(18)-C(13)-Fe(1)	126.2(4)
C(13)-C(14)-C(15)	108.9(5)
C(13)-C(14)-C(19)	127.9(5)
C(15)-C(14)-C(19)	123.2(5)
C(13)-C(14)-Fe(1)	70.2(3)
C(15)-C(14)-Fe(1)	69.9(3)
C(19)-C(14)-Fe(1)	127.6(4)
C(14)-C(15)-C(11)	106.4(5)
C(14)-C(15)-C(20)	127.0(6)
C(11)-C(15)-C(20)	126.6(6)
C(14)-C(15)-Fe(1)	69.2(3)
C(11)-C(15)-Fe(1)	68.6(3)
C(20)-C(15)-Fe(1)	128.4(4)
C(25)-C(21)-C(22)	107.5(5)
C(25)-C(21)-C(26)	126.6(8)
C(22)-C(21)-C(26)	125.8(8)
C(25)-C(21)-Fe(2)	70.5(3)
C(22)-C(21)-Fe(2)	69.1(3)
C(26)-C(21)-Fe(2)	125.4(4)
C(23)-C(22)-C(21)	107.5(5)
C(23)-C(22)-C(27)	126.2(6)
C(21)-C(22)-C(27)	126.4(6)
C(23)-C(22)-Fe(2)	69.7(3)
C(21)-C(22)-Fe(2)	70.1(3)
C(27)-C(22)-Fe(2)	125.9(4)
C(24)-C(23)-C(22)	108.5(5)
C(24)-C(23)-C(28)	126.2(6)
C(22)-C(23)-C(28)	125.2(5)
C(24)-C(23)-Fe(2)	70.6(3)
C(22)-C(23)-Fe(2)	69.4(3)
C(28)-C(23)-Fe(2)	124.2(4)
C(23)-C(24)-C(25)	108.1(5)
C(23)-C(24)-C(29)	124.2(7)
C(25)-C(24)-C(29)	127.7(7)
C(23)-C(24)-Fe(2)	69.2(3)
C(25)-C(24)-Fe(2)	70.4(3)

C(29)-C(24)-Fe(2)	125.1(4)
C(24)-C(25)-C(21)	108.4(5)
C(24)-C(25)-C(30)	125.2(8)
C(21)-C(25)-C(30)	126.3(9)
C(24)-C(25)-Fe(2)	69.6(3)
C(21)-C(25)-Fe(2)	69.1(3)
C(30)-C(25)-Fe(2)	130.6(4)
C(36)-C(31)-C(32)	120.2(5)
C(33)-C(32)-C(31)	119.9(5)
C(34)-C(33)-C(32)	120.3(5)
C(33)-C(34)-C(35)	120.2(5)
C(34)-C(35)-C(36)	120.6(5)
C(31)-C(36)-C(35)	118.6(5)
C(31)-C(36)-C(37)	118.6(5)
C(35)-C(36)-C(37)	122.8(5)
C(38)-C(37)-C(36)	126.3(5)
C(38)-C(37)-Cu(1)	68.7(3)
C(36)-C(37)-Cu(1)	107.9(3)
C(37)-C(38)-Cu(1)	70.7(3)
O(2)-S(1)-O(3)	114.7(3)
O(2)-S(1)-O(1)	114.3(4)
O(3)-S(1)-O(1)	116.3(4)
O(2)-S(1)-C(91)	103.3(3)
O(3)-S(1)-C(91)	104.3(3)
O(1)-S(1)-C(91)	101.5(3)
F(1)-C(91)-F(2)	107.8(6)
F(1)-C(91)-F(3)	106.8(5)
F(2)-C(91)-F(3)	105.3(6)
F(1)-C(91)-S(1)	112.7(5)
F(2)-C(91)-S(1)	111.7(4)
F(3)-C(91)-S(1)	112.0(4)

Table 3.4. Anisotropic displacement parameters ($Å^2$ x 10^3) for 98085. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cu(1)	28(1)	33(1)	35(1)	4(1)	4(1)	0(1)
Fe(1)	34(1)	25(1)	30(1)	0(1)	2(1)	0(1)
Fe(2)	39(1)	29(1)	28(1)	-1(1)	-2(1)	4(1)
N(1)	28(2)	27(2)	30(2)	1(2)	-1(1)	1(2)
N(2)	39(2)	31(2)	35(2)	3(2)	9(2)	0(2)
C(1)	39(2)	29(2)	26(2)	1(2)	-2(2)	1(2)
C(2)	39(3)	31(2)	35(2)	0(2)	7(2)	-3(2)
C(3)	29(2)	27(2)	39(2)	0(2)	5(2)	-3(2)
C(4)	31(2)	21(2)	35(2)	-1(2)	1(2)	1(2)
C(5)	39(2)	35(3)	35(2)	-1(2)	-5(2)	14(2)
C(6)	33(2)	28(2)	29(2)	6(2)	-2(2)	2(2)
C(7)	45(3)	40(3)	30(2)	3(2)	-5(2)	9(2)
C(8)	61(3)	47(3)	29(2)	-2(2)	4(2)	11(2)
C(9)	47(3)	44(3)	32(2)	2(2)	14(2)	7(2)
C(11)	67(4)	26(3)	78(4)	-16(3)	-31(3)	7(2)
C(12)	79(4)	36(3)	42(3)	-9(2)	17(3)	-2(3)
C(13)	52(3)	31(3)	61(4)	-12(2)	13(3)	1(2)
C(14)	43(3)	25(2)	51(3)	3(2)	-4(2)	5(2)
C(15)	48(3)	22(2)	71(4)	-3(2)	23(3)	-1(2)
C(16)	79(5)	53(4)	142(7)	-29(4)	-55(5)	6(3)
C(17)	148(7)	71(5)	51(4)	-16(3)	17(4)	3(5)
C(18)	66(4)	59(4)	122(6)	-22(4)	42(4)	8(3)
C(19)	112(6)	43(3)	79(5)	2(3)	-26(4)	24(4)
C(20)	86(5)	48(4)	143(7)	1(4)	65(5)	-10(3)
C(21)	85(4)	29(3)	85(4)	9(3)	46(4)	9(3)
C(22)	46(3)	36(3)	56(3)	0(2)	-9(2)	-3(2)
C(23)	46(3)	29(3)	67(3)	-7(2)	-2(3)	2(2)
C(24)	71(4)	29(3)	75(4)	-2(3)	-33(3)	9(3)
C(25)	144(7)	23(3)	35(3)	5(2)	-13(4)	5(3)
C(26)	134(8)	55(4)	226(12)	25(6)	126(8)	-5(5)
C(27)	94(5)	54(4)	132(7)	-4(4)	-64(5)	-18(4)

C(28)	108(6)	52(4)	111(6)	-14(4)	56(5)	17(4)
C(29)	100(6)	52(4)	237(12)	20(6)	-112(8)	10(4)
C(30)	397(19)	29(3)	39(4)	9(3)	-30(7)	17(6)
C(31)	34(2)	55(3)	61(3)	-2(3)	16(2)	-5(2)
C(32)	51(3)	75(4)	54(3)	-10(3)	18(3)	-14(3)
C(33)	48(3)	72(4)	53(4)	12(3)	3(3)	-18(3)
C(34)	42(3)	50(3)	57(4)	4(3)	0(3)	-6(2)
C(35)	33(3)	53(3)	52(3)	-3(2)	2(2)	-2(2)
C(36)	17(2)	51(3)	50(3)	2(2)	4(2)	-3(2)
C(37)	24(2)	53(3)	60(3)	8(3)	2(2)	5(2)
C(38)	30(2)	73(4)	51(3)	16(3)	-8(2)	-11(2)
S(1)	40(1)	61(1)	45(1)	8(1)	10(1)	8(1)
F(1)	247(7)	67(3)	132(4)	-7(3)	37(5)	-63(4)
F(2)	127(4)	162(5)	82(3)	-13(3)	-4(3)	99(4)
F(3)	99(3)	84(3)	44(2)	-5(2)	0(2)	6(2)
O(1)	104(4)	90(3)	99(4)	-41(3)	54(3)	-43(3)
O(2)	56(3)	146(5)	78(3)	20(3)	9(2)	40(3)
O(3)	97(3)	114(4)	51(2)	25(3)	12(2)	37(3)
C(91)	85(5)	50(4)	51(4)	5(3)	-2(3)	2(3)

Table 3.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for 98085.

	x	y	z	U(eq)
H(1B)	-8497	-5061	-3576	38
H(2B)	-11084	-5194	-2985	42
H(3B)	-12663	-4999	-5140	38
H(5A)	-11867	-4465	-7912	44
H(5B)	-11009	-4279	-7799	44
H(7A)	-11678	-5409	-10199	47
H(8A)	-9394	-5721	-11402	55
H(9A)	-7272	-5456	-9809	49
H(16A)	-7042	-3421	-3378	141
H(16B)	-7675	-3975	-2441	141
H(16C)	-7745	-3228	-1992	141

H(17A)	-9967	-3832	-993	134
H(17B)	-11434	-4185	-1533	134
H(17C)	-11459	-3436	-1093	134
H(18A)	-13521	-3648	-2910	121
H(18B)	-13744	-3840	-4483	121
H(18C)	-13806	-3093	-4034	121
H(19A)	-11121	-2979	-7172	119
H(19B)	-12458	-2702	-6396	119
H(19C)	-12447	-3446	-6872	119
H(20A)	-7492	-3118	-5443	135
H(20B)	-8635	-2625	-6170	135
H(20C)	-8555	-3362	-6683	135
H(26A)	-12898	-6732	-7999	200
H(26B)	-12261	-6181	-6981	200
H(26C)	-12286	-6924	-6497	200
H(27A)	-10975	-7224	-11072	145
H(27B)	-12085	-6718	-10474	145
H(27C)	-12081	-7461	-9990	145
H(28A)	-8757	-7245	-11166	132
H(28B)	-7421	-7509	-10210	132
H(28C)	-7469	-6764	-10676	132
H(29A)	-6417	-6591	-6629	203
H(29B)	-6190	-6410	-8180	203
H(29C)	-6154	-7154	-7705	203
H(30A)	-8071	-6445	-5283	235
H(30B)	-9528	-6827	-5002	235
H(30C)	-9587	-6068	-5359	235
H(31A)	-4742	-5003	-9457	59
H(32A)	-4498	-4261	-11236	71
H(33A)	-4823	-3155	-10869	70
H(34A)	-5392	-2781	-8752	60
H(35A)	-5693	-3511	-6985	55
H(37A)	-4997	-5250	-7089	55
H(38A)	-5685	-4238	-5321	62
H(38B)	-5480	-5018	-4935	62

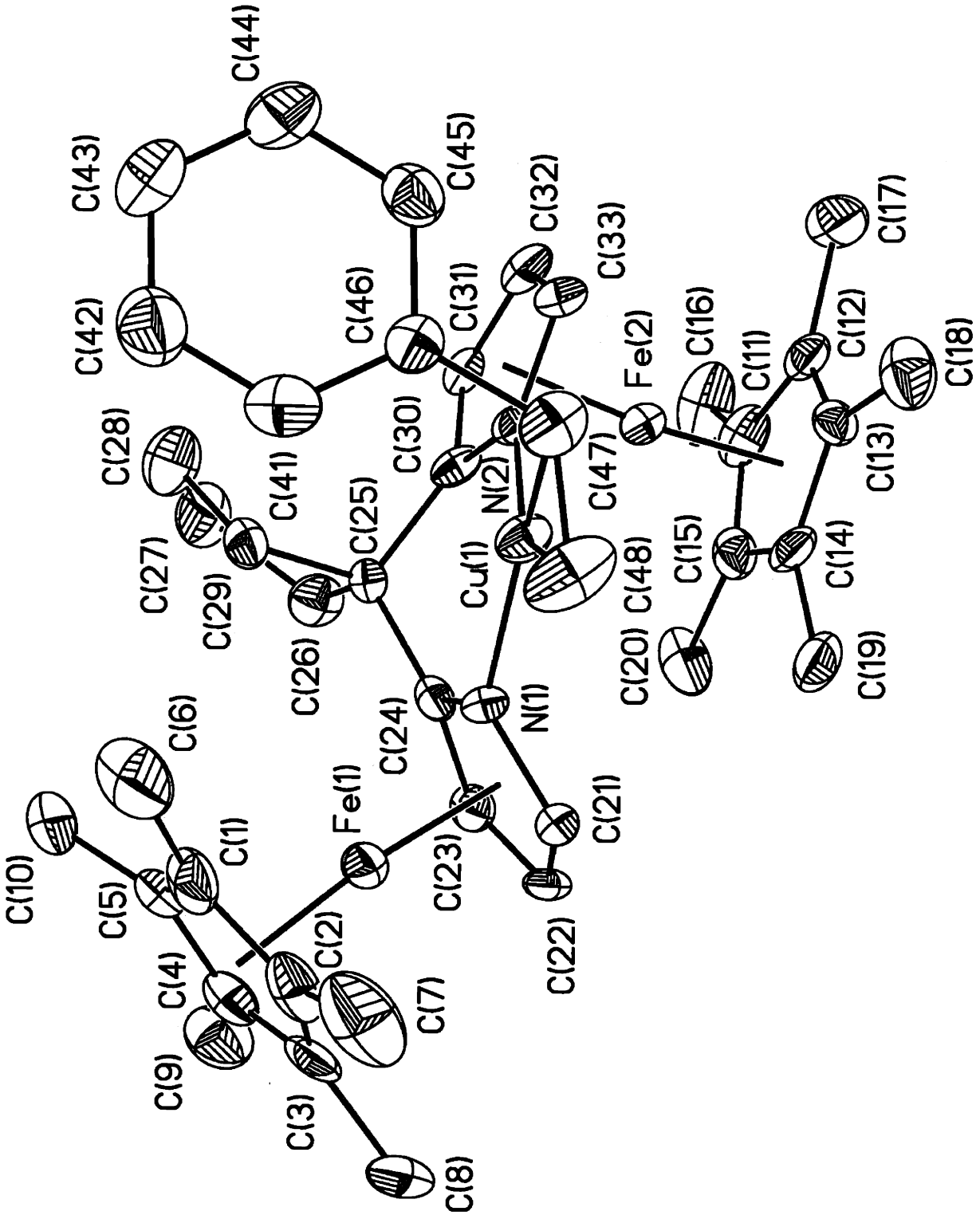

Figure 4. ORTEP plot of [CuOTf•(±)-**1.25**•styrene], with thermal ellipsoids drawn at the 35% probability level.

Table 4.1. Crystal data and structure refinement for [CuOTf•(±)-**1.25**•styrene].

Identification code	98198	
Empirical formula	C42 H52 Cu F3 Fe2 N2 O3 S	
Formula weight	897.16	
Temperature	184(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 11.2784(10) Å	α = 83.1420(10)°.
	b = 13.1948(11) Å	β = 84.2290(10)°.
	c = 14.0197(12) Å	γ = 86.360(2)°.
Volume	2058.1(3) $Å^3$	
Z	2	
Density (calculated)	1.448 Mg/m^3	
Absorption coefficient	1.312 mm^{-1}	
F(000)	932	
Crystal size	0.15 x 0.15 x 0.24 mm^3	
Theta range for data collection	1.47 to 23.29°.	
Index ranges	-12<=h<=7, -14<=k<=14, -15<=l<=15	
Reflections collected	8393	
Independent reflections	5727 [R(int) = 0.0556]	
Completeness to theta = 23.29°	96.5 %	
Absorption correction	Empirical	
Max. and min. transmission	0.8841 and 0.6355	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5727 / 0 / 551	
Goodness-of-fit on F^2	1.242	
Final R indices [I>2sigma(I)]	R1 = 0.0908, wR2 = 0.1710	
R indices (all data)	R1 = 0.1273, wR2 = 0.1940	
Largest diff. peak and hole	0.696 and -0.490 $e.Å^{-3}$	

Table 4.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for 98198. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cu(1)	-3111(1)	-1728(1)	11289(1)	38(1)
Fe(1)	-1955(1)	-1546(1)	13775(1)	37(1)
Fe(2)	-5257(1)	-3633(1)	11968(1)	33(1)
N(1)	-2991(7)	-1714(5)	12677(5)	31(2)
N(2)	-3633(7)	-3130(6)	11381(5)	32(2)
C(1)	-193(9)	-1255(10)	13280(9)	55(3)
C(2)	-857(9)	-362(8)	13615(9)	52(3)
C(3)	-1257(9)	-635(9)	14620(8)	51(3)
C(4)	-867(10)	-1671(9)	14880(8)	52(3)
C(5)	-217(9)	-2028(9)	14046(8)	48(3)
C(6)	414(11)	-1274(13)	12282(9)	90(5)
C(7)	-1011(13)	658(10)	13024(12)	95(5)
C(8)	-1933(11)	45(10)	15294(9)	72(4)
C(9)	-1062(12)	-2274(11)	15848(8)	72(4)
C(10)	489(11)	-3054(10)	14087(10)	78(4)
C(11)	-6769(9)	-4206(8)	12698(8)	50(3)
C(12)	-7002(9)	-3786(8)	11749(7)	41(2)
C(13)	-6735(8)	-2751(7)	11617(6)	35(2)
C(14)	-6400(9)	-2507(8)	12510(8)	43(3)
C(15)	-6394(9)	-3402(9)	13180(7)	44(3)
C(16)	-6971(11)	-5281(9)	13139(11)	82(5)
C(17)	-7425(10)	-4373(10)	10982(10)	72(4)
C(18)	-6842(10)	-2006(10)	10735(8)	63(3)
C(19)	-6165(10)	-1439(8)	12712(10)	65(4)
C(20)	-6136(10)	-3476(12)	14220(7)	74(4)
C(21)	-3466(8)	-930(7)	13227(7)	35(2)
C(22)	-3728(8)	-1341(7)	14173(7)	35(2)
C(23)	-3423(8)	-2391(8)	14245(7)	39(2)
C(24)	-2972(8)	-2614(7)	13306(6)	31(2)
C(25)	-2634(8)	-3641(7)	12925(6)	32(2)
C(26)	-2535(10)	-4511(8)	13714(8)	50(3)

C(27)	-1599(11)	-5308(9)	13305(9)	66(4)
C(28)	-1014(11)	-4778(9)	12358(9)	66(3)
C(29)	-1364(8)	-3648(7)	12366(8)	41(3)
C(30)	-3476(8)	-3839(6)	12185(6)	32(2)
C(31)	-3906(8)	-4785(7)	12037(7)	35(2)
C(32)	-4334(9)	-4653(7)	11126(8)	43(3)
C(33)	-4173(9)	-3645(7)	10727(7)	37(2)
C(41)	-632(11)	-1495(9)	9681(8)	59(3)
C(42)	330(12)	-2035(11)	9293(10)	71(4)
C(43)	179(12)	-2756(9)	8672(9)	65(3)
C(44)	-951(11)	-2887(8)	8448(9)	58(3)
C(45)	-1928(10)	-2334(8)	8836(8)	50(3)
C(46)	-1770(9)	-1620(8)	9479(7)	40(2)
C(47)	-2838(11)	-1069(8)	9896(7)	50(3)
C(48)	-2807(14)	-356(8)	10554(8)	72(4)
S(1A)	-4407(14)	2179(9)	11999(10)	100(7)
F(1A)	-5968(14)	2068(14)	13433(10)	65(5)
F(2A)	-4490(30)	2967(12)	13561(10)	67(6)
F(3A)	-4390(30)	1320(30)	13770(30)	66(8)
O(1A)	-3147(19)	2200(30)	11853(12)	124(14)
O(2A)	-4750(30)	1180(20)	11800(20)	97(11)
O(3A)	-5090(20)	2997(18)	11644(15)	41(4)
S(1B)	-4391(9)	2142(14)	11927(9)	31(6)
F(1B)	-6000(70)	1760(70)	13270(60)	280(50)
F(2B)	-4840(70)	3010(50)	13630(40)	170(30)
F(3B)	-3960(50)	1440(80)	13710(60)	74(16)
O(1B)	-3220(40)	2670(30)	12060(50)	170(30)
O(2B)	-4450(100)	1230(40)	11720(40)	210(60)
O(3B)	-5210(50)	2920(40)	11340(30)	44(9)
C(99)	-4816(15)	2121(10)	13225(8)	64(4)

Table 4.3. Bond lengths [Å] and angles [°] for 98198.

Cu(1)-N(2)	1.963(8)
Cu(1)-N(1)	1.966(7)
Cu(1)-C(48)	2.004(10)
Cu(1)-C(47)	2.043(10)
Fe(1)-C(21)	2.024(9)
Fe(1)-C(3)	2.028(10)
Fe(1)-C(22)	2.031(9)
Fe(1)-C(2)	2.032(10)
Fe(1)-C(4)	2.056(10)
Fe(1)-C(23)	2.063(10)
Fe(1)-N(1)	2.064(7)
Fe(1)-C(24)	2.077(9)
Fe(1)-C(5)	2.079(10)
Fe(1)-C(1)	2.082(10)
Fe(2)-C(33)	2.025(9)
Fe(2)-C(13)	2.038(9)
Fe(2)-C(11)	2.038(10)
Fe(2)-C(12)	2.048(10)
Fe(2)-N(2)	2.048(7)
Fe(2)-C(30)	2.058(10)
Fe(2)-C(32)	2.060(9)
Fe(2)-C(15)	2.064(10)
Fe(2)-C(14)	2.068(9)
Fe(2)-C(31)	2.084(9)
N(1)-C(24)	1.392(11)
N(1)-C(21)	1.411(11)
N(2)-C(30)	1.394(11)
N(2)-C(33)	1.410(12)
C(1)-C(5)	1.390(16)
C(1)-C(2)	1.455(16)
C(1)-C(6)	1.497(16)
C(2)-C(3)	1.445(15)
C(2)-C(7)	1.505(16)
C(3)-C(4)	1.425(16)

C(3)-C(8)	1.500(15)
C(4)-C(5)	1.429(15)
C(4)-C(9)	1.493(15)
C(5)-C(10)	1.524(16)
C(11)-C(12)	1.423(15)
C(11)-C(15)	1.430(15)
C(11)-C(16)	1.500(15)
C(12)-C(13)	1.403(13)
C(12)-C(17)	1.528(14)
C(13)-C(14)	1.421(13)
C(13)-C(18)	1.496(14)
C(14)-C(15)	1.418(14)
C(14)-C(19)	1.515(14)
C(15)-C(20)	1.506(14)
C(21)-C(22)	1.383(13)
C(22)-C(23)	1.401(13)
C(23)-C(24)	1.421(13)
C(24)-C(25)	1.528(13)
C(25)-C(26)	1.503(13)
C(25)-C(30)	1.530(13)
C(25)-C(29)	1.562(13)
C(26)-C(27)	1.559(15)
C(27)-C(28)	1.532(16)
C(28)-C(29)	1.519(14)
C(30)-C(31)	1.412(12)
C(31)-C(32)	1.399(14)
C(32)-C(33)	1.396(13)
C(41)-C(42)	1.363(17)
C(41)-C(46)	1.366(15)
C(42)-C(43)	1.393(17)
C(43)-C(44)	1.369(16)
C(44)-C(45)	1.384(15)
C(45)-C(46)	1.410(14)
C(46)-C(47)	1.472(14)
C(47)-C(48)	1.400(15)
S(1A)-O(3A)	1.36(3)

S(1A)-O(1A)	1.42(2)
S(1A)-O(2A)	1.46(3)
S(1A)-C(99)	1.728(17)
F(1A)-C(99)	1.31(2)
F(2A)-C(99)	1.35(2)
F(3A)-C(99)	1.32(4)
S(1B)-O(2B)	1.28(6)
S(1B)-O(3B)	1.56(6)
S(1B)-O(1B)	1.56(4)
S(1B)-C(99)	1.832(16)
F(1B)-C(99)	1.44(7)
F(2B)-C(99)	1.36(6)
F(3B)-C(99)	1.44(8)

N(2)-Cu(1)-N(1)	96.3(3)
N(2)-Cu(1)-C(48)	151.9(5)
N(1)-Cu(1)-C(48)	111.4(4)
N(2)-Cu(1)-C(47)	112.6(4)
N(1)-Cu(1)-C(47)	150.8(4)
C(48)-Cu(1)-C(47)	40.4(4)
C(21)-Fe(1)-C(3)	113.3(4)
C(21)-Fe(1)-C(22)	39.9(4)
C(3)-Fe(1)-C(22)	101.2(4)
C(21)-Fe(1)-C(2)	104.0(4)
C(3)-Fe(1)-C(2)	41.7(4)
C(22)-Fe(1)-C(2)	121.3(4)
C(21)-Fe(1)-C(4)	148.0(4)
C(3)-Fe(1)-C(4)	40.8(4)
C(22)-Fe(1)-C(4)	115.4(4)
C(2)-Fe(1)-C(4)	69.2(5)
C(21)-Fe(1)-C(23)	67.1(4)
C(3)-Fe(1)-C(23)	122.6(4)
C(22)-Fe(1)-C(23)	40.0(4)
C(2)-Fe(1)-C(23)	159.2(5)
C(4)-Fe(1)-C(23)	107.7(4)
C(21)-Fe(1)-N(1)	40.4(3)

C(3)-Fe(1)-N(1)	149.9(4)
C(22)-Fe(1)-N(1)	67.5(3)
C(2)-Fe(1)-N(1)	118.9(4)
C(4)-Fe(1)-N(1)	169.2(4)
C(23)-Fe(1)-N(1)	67.4(3)
C(21)-Fe(1)-C(24)	66.5(4)
C(3)-Fe(1)-C(24)	162.4(4)
C(22)-Fe(1)-C(24)	66.9(4)
C(2)-Fe(1)-C(24)	155.5(4)
C(4)-Fe(1)-C(24)	131.0(4)
C(23)-Fe(1)-C(24)	40.1(4)
N(1)-Fe(1)-C(24)	39.3(3)
C(21)-Fe(1)-C(5)	167.1(4)
C(3)-Fe(1)-C(5)	68.1(4)
C(22)-Fe(1)-C(5)	152.9(4)
C(2)-Fe(1)-C(5)	68.0(4)
C(4)-Fe(1)-C(5)	40.4(4)
C(23)-Fe(1)-C(5)	123.8(4)
N(1)-Fe(1)-C(5)	133.5(4)
C(24)-Fe(1)-C(5)	116.4(4)
C(21)-Fe(1)-C(1)	128.4(5)
C(3)-Fe(1)-C(1)	69.0(5)
C(22)-Fe(1)-C(1)	161.8(5)
C(2)-Fe(1)-C(1)	41.4(5)
C(4)-Fe(1)-C(1)	67.8(5)
C(23)-Fe(1)-C(1)	158.1(5)
N(1)-Fe(1)-C(1)	112.9(4)
C(24)-Fe(1)-C(1)	125.9(4)
C(5)-Fe(1)-C(1)	39.0(4)
C(33)-Fe(2)-C(13)	105.7(4)
C(33)-Fe(2)-C(11)	143.9(4)
C(13)-Fe(2)-C(11)	68.7(4)
C(33)-Fe(2)-C(12)	111.7(4)
C(13)-Fe(2)-C(12)	40.2(4)
C(11)-Fe(2)-C(12)	40.8(4)
C(33)-Fe(2)-N(2)	40.5(3)

C(13)-Fe(2)-N(2)	117.3(3)
C(11)-Fe(2)-N(2)	172.9(4)
C(12)-Fe(2)-N(2)	146.3(4)
C(33)-Fe(2)-C(30)	66.7(4)
C(13)-Fe(2)-C(30)	152.7(4)
C(11)-Fe(2)-C(30)	133.4(4)
C(12)-Fe(2)-C(30)	166.8(4)
N(2)-Fe(2)-C(30)	39.7(3)
C(33)-Fe(2)-C(32)	40.0(4)
C(13)-Fe(2)-C(32)	125.5(4)
C(11)-Fe(2)-C(32)	112.7(4)
C(12)-Fe(2)-C(32)	103.4(4)
N(2)-Fe(2)-C(32)	67.6(3)
C(30)-Fe(2)-C(32)	66.5(4)
C(33)-Fe(2)-C(15)	171.9(4)
C(13)-Fe(2)-C(15)	68.7(4)
C(11)-Fe(2)-C(15)	40.8(4)
C(12)-Fe(2)-C(15)	68.2(4)
N(2)-Fe(2)-C(15)	136.0(4)
C(30)-Fe(2)-C(15)	115.4(4)
C(32)-Fe(2)-C(15)	148.0(4)
C(33)-Fe(2)-C(14)	131.9(4)
C(13)-Fe(2)-C(14)	40.5(4)
C(11)-Fe(2)-C(14)	67.6(4)
C(12)-Fe(2)-C(14)	67.1(4)
N(2)-Fe(2)-C(14)	114.0(4)
C(30)-Fe(2)-C(14)	124.4(4)
C(32)-Fe(2)-C(14)	165.8(4)
C(15)-Fe(2)-C(14)	40.1(4)
C(33)-Fe(2)-C(31)	66.8(4)
C(13)-Fe(2)-C(31)	163.4(4)
C(11)-Fe(2)-C(31)	108.0(4)
C(12)-Fe(2)-C(31)	126.9(4)
N(2)-Fe(2)-C(31)	67.4(3)
C(30)-Fe(2)-C(31)	39.9(3)
C(32)-Fe(2)-C(31)	39.4(4)

C(15)-Fe(2)-C(31)	120.1(4)
C(14)-Fe(2)-C(31)	154.8(4)
C(24)-N(1)-C(21)	106.7(7)
C(24)-N(1)-Cu(1)	121.5(6)
C(21)-N(1)-Cu(1)	125.3(6)
C(24)-N(1)-Fe(1)	70.9(5)
C(21)-N(1)-Fe(1)	68.3(5)
Cu(1)-N(1)-Fe(1)	148.6(4)
C(30)-N(2)-C(33)	106.3(7)
C(30)-N(2)-Cu(1)	122.2(6)
C(33)-N(2)-Cu(1)	131.5(6)
C(30)-N(2)-Fe(2)	70.6(5)
C(33)-N(2)-Fe(2)	68.9(5)
Cu(1)-N(2)-Fe(2)	126.5(4)
C(5)-C(1)-C(2)	107.8(10)
C(5)-C(1)-C(6)	128.5(12)
C(2)-C(1)-C(6)	123.7(12)
C(5)-C(1)-Fe(1)	70.4(6)
C(2)-C(1)-Fe(1)	67.5(6)
C(6)-C(1)-Fe(1)	128.6(8)
C(3)-C(2)-C(1)	106.9(10)
C(3)-C(2)-C(7)	127.9(13)
C(1)-C(2)-C(7)	125.2(12)
C(3)-C(2)-Fe(1)	69.0(6)
C(1)-C(2)-Fe(1)	71.1(6)
C(7)-C(2)-Fe(1)	127.8(8)
C(4)-C(3)-C(2)	108.0(10)
C(4)-C(3)-C(8)	125.0(11)
C(2)-C(3)-C(8)	126.9(12)
C(4)-C(3)-Fe(1)	70.7(6)
C(2)-C(3)-Fe(1)	69.3(6)
C(8)-C(3)-Fe(1)	127.0(7)
C(3)-C(4)-C(5)	107.4(10)
C(3)-C(4)-C(9)	127.0(11)
C(5)-C(4)-C(9)	125.6(11)
C(3)-C(4)-Fe(1)	68.5(6)

C(5)-C(4)-Fe(1)	70.7(6)
C(9)-C(4)-Fe(1)	127.4(8)
C(1)-C(5)-C(4)	109.9(10)
C(1)-C(5)-C(10)	127.0(11)
C(4)-C(5)-C(10)	122.4(11)
C(1)-C(5)-Fe(1)	70.6(6)
C(4)-C(5)-Fe(1)	68.9(6)
C(10)-C(5)-Fe(1)	134.4(8)
C(12)-C(11)-C(15)	107.8(9)
C(12)-C(11)-C(16)	125.9(11)
C(15)-C(11)-C(16)	126.1(11)
C(12)-C(11)-Fe(2)	70.0(6)
C(15)-C(11)-Fe(2)	70.6(6)
C(16)-C(11)-Fe(2)	128.4(8)
C(13)-C(12)-C(11)	108.9(9)
C(13)-C(12)-C(17)	125.4(10)
C(11)-C(12)-C(17)	125.7(10)
C(13)-C(12)-Fe(2)	69.5(6)
C(11)-C(12)-Fe(2)	69.3(6)
C(17)-C(12)-Fe(2)	125.4(7)
C(12)-C(13)-C(14)	107.2(9)
C(12)-C(13)-C(18)	127.7(9)
C(14)-C(13)-C(18)	125.0(10)
C(12)-C(13)-Fe(2)	70.3(6)
C(14)-C(13)-Fe(2)	70.9(5)
C(18)-C(13)-Fe(2)	126.8(7)
C(15)-C(14)-C(13)	109.3(9)
C(15)-C(14)-C(19)	126.3(10)
C(13)-C(14)-C(19)	124.3(10)
C(15)-C(14)-Fe(2)	69.8(6)
C(13)-C(14)-Fe(2)	68.6(5)
C(19)-C(14)-Fe(2)	130.6(7)
C(14)-C(15)-C(11)	106.7(9)
C(14)-C(15)-C(20)	126.7(11)
C(11)-C(15)-C(20)	126.4(11)
C(14)-C(15)-Fe(2)	70.1(5)

C(11)-C(15)-Fe(2)	68.6(6)
C(20)-C(15)-Fe(2)	129.6(7)
C(22)-C(21)-N(1)	109.1(8)
C(22)-C(21)-Fe(1)	70.4(5)
N(1)-C(21)-Fe(1)	71.4(5)
C(21)-C(22)-C(23)	108.5(8)
C(21)-C(22)-Fe(1)	69.8(5)
C(23)-C(22)-Fe(1)	71.2(5)
C(22)-C(23)-C(24)	106.7(9)
C(22)-C(23)-Fe(1)	68.8(5)
C(24)-C(23)-Fe(1)	70.4(5)
N(1)-C(24)-C(23)	109.0(8)
N(1)-C(24)-C(25)	120.6(8)
C(23)-C(24)-C(25)	130.1(8)
N(1)-C(24)-Fe(1)	69.9(5)
C(23)-C(24)-Fe(1)	69.4(5)
C(25)-C(24)-Fe(1)	131.9(6)
C(26)-C(25)-C(24)	113.1(8)
C(26)-C(25)-C(30)	113.0(8)
C(24)-C(25)-C(30)	110.5(7)
C(26)-C(25)-C(29)	103.4(8)
C(24)-C(25)-C(29)	111.5(7)
C(30)-C(25)-C(29)	105.0(7)
C(25)-C(26)-C(27)	106.3(9)
C(28)-C(27)-C(26)	106.2(9)
C(29)-C(28)-C(27)	105.7(10)
C(28)-C(29)-C(25)	103.6(8)
N(2)-C(30)-C(31)	109.6(8)
N(2)-C(30)-C(25)	120.6(8)
C(31)-C(30)-C(25)	127.5(8)
N(2)-C(30)-Fe(2)	69.7(5)
C(31)-C(30)-Fe(2)	71.1(5)
C(25)-C(30)-Fe(2)	139.2(6)
C(32)-C(31)-C(30)	106.9(9)
C(32)-C(31)-Fe(2)	69.3(5)
C(30)-C(31)-Fe(2)	69.1(5)

C(33)-C(32)-C(31)	108.2(9)
C(33)-C(32)-Fe(2)	68.6(5)
C(31)-C(32)-Fe(2)	71.2(5)
C(32)-C(33)-N(2)	109.1(9)
C(32)-C(33)-Fe(2)	71.4(6)
N(2)-C(33)-Fe(2)	70.6(5)
C(42)-C(41)-C(46)	122.5(12)
C(41)-C(42)-C(43)	120.3(12)
C(44)-C(43)-C(42)	118.3(12)
C(43)-C(44)-C(45)	121.4(11)
C(44)-C(45)-C(46)	119.9(10)
C(41)-C(46)-C(45)	117.5(10)
C(41)-C(46)-C(47)	124.4(10)
C(45)-C(46)-C(47)	118.1(10)
C(48)-C(47)-C(46)	123.9(12)
C(48)-C(47)-Cu(1)	68.3(6)
C(46)-C(47)-Cu(1)	105.2(6)
C(47)-C(48)-Cu(1)	71.3(6)
O(3A)-S(1A)-O(1A)	119(2)
O(3A)-S(1A)-O(2A)	115.8(19)
O(1A)-S(1A)-O(2A)	108(2)
O(3A)-S(1A)-C(99)	102.1(12)
O(1A)-S(1A)-C(99)	107.9(14)
O(2A)-S(1A)-C(99)	101.2(15)
O(2B)-S(1B)-O(3B)	112(4)
O(2B)-S(1B)-O(1B)	126(5)
O(3B)-S(1B)-O(1B)	109(3)
O(2B)-S(1B)-C(99)	107(3)
O(3B)-S(1B)-C(99)	111.0(17)
O(1B)-S(1B)-C(99)	89(3)
F(1A)-C(99)-F(3A)	102.4(18)
F(1A)-C(99)-F(2A)	107.2(17)
F(3A)-C(99)-F(2A)	108(2)
F(2B)-C(99)-F(1B)	110(5)
F(2B)-C(99)-F(3B)	106(5)
F(1B)-C(99)-F(3B)	116(4)

F(1A)-C(99)-S(1A)	112.4(12)
F(3A)-C(99)-S(1A)	117(2)
F(2A)-C(99)-S(1A)	109.9(12)
F(2B)-C(99)-S(1B)	119(3)
F(1B)-C(99)-S(1B)	100(4)
F(3B)-C(99)-S(1B)	107(3)

Table 4.4. Anisotropic displacement parameters ($Å^2$ x 10^3) for 98198. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cu(1)	49(1)	29(1)	34(1)	-3(1)	1(1)	2(1)
Fe(1)	31(1)	44(1)	38(1)	-10(1)	-3(1)	-4(1)
Fe(2)	36(1)	31(1)	31(1)	-7(1)	0(1)	1(1)
N(1)	35(5)	27(4)	32(4)	-12(3)	-4(4)	0(3)
N(2)	33(4)	35(4)	29(4)	-11(4)	4(3)	1(4)
C(1)	25(6)	81(9)	61(8)	-10(7)	0(5)	-14(6)
C(2)	37(6)	45(7)	73(8)	11(6)	-17(6)	-19(5)
C(3)	33(6)	79(9)	50(7)	-27(6)	-10(5)	-22(6)
C(4)	48(7)	66(8)	45(7)	-6(6)	-24(6)	-5(6)
C(5)	38(6)	62(7)	52(7)	-20(6)	-20(5)	-2(5)
C(6)	47(8)	166(16)	59(9)	-21(9)	20(7)	-45(9)
C(7)	86(11)	73(10)	127(14)	24(9)	-40(10)	-40(9)
C(8)	62(8)	79(9)	87(10)	-52(8)	-17(7)	-12(7)
C(9)	72(9)	99(11)	45(7)	-6(7)	-6(6)	-17(8)
C(10)	50(8)	94(11)	100(11)	-38(9)	-34(8)	20(7)
C(11)	42(7)	41(6)	60(8)	5(6)	18(6)	-2(5)
C(12)	32(6)	41(6)	49(7)	-16(5)	6(5)	3(5)
C(13)	33(5)	44(6)	27(5)	-2(4)	-5(4)	0(5)
C(14)	30(6)	42(6)	59(7)	-26(5)	7(5)	3(5)
C(15)	29(6)	62(7)	40(6)	-5(5)	1(5)	2(5)
C(16)	56(8)	59(8)	118(12)	21(8)	23(8)	-5(7)
C(17)	37(7)	94(10)	98(10)	-56(8)	-1(7)	-18(7)

C(18)	48(7)	83(9)	53(7)	8(7)	0(6)	5(6)
C(19)	44(7)	48(7)	110(11)	-37(7)	-15(7)	14(6)
C(20)	39(7)	150(13)	27(6)	-1(7)	6(5)	5(8)
C(21)	34(6)	34(5)	41(6)	-14(5)	-10(5)	6(4)
C(22)	34(6)	44(6)	32(6)	-22(5)	-4(4)	-4(5)
C(23)	27(5)	53(7)	36(6)	-9(5)	3(4)	-6(5)
C(24)	25(5)	41(6)	29(5)	-2(4)	-7(4)	-2(4)
C(25)	27(5)	35(5)	34(5)	-5(4)	-7(4)	4(4)
C(26)	58(7)	37(6)	54(7)	-3(5)	-8(6)	-1(5)
C(27)	72(9)	38(7)	87(10)	0(6)	-26(7)	21(6)
C(28)	65(8)	51(7)	78(9)	0(7)	-5(7)	13(6)
C(29)	29(6)	45(6)	53(7)	-10(5)	-8(5)	-2(5)
C(30)	44(6)	20(5)	30(5)	-5(4)	7(4)	1(4)
C(31)	32(5)	32(5)	41(6)	-8(4)	3(5)	7(4)
C(32)	40(6)	31(6)	56(7)	-16(5)	11(5)	0(5)
C(33)	43(6)	39(6)	29(5)	-12(4)	3(4)	-1(5)
C(41)	68(9)	60(8)	52(7)	-14(6)	-4(6)	-10(7)
C(42)	56(8)	82(10)	74(9)	-8(8)	-7(7)	-5(7)
C(43)	59(9)	58(8)	75(9)	-13(7)	14(7)	5(7)
C(44)	70(9)	35(6)	70(8)	-14(6)	5(7)	-6(6)
C(45)	44(7)	60(7)	49(7)	-5(6)	-7(5)	-10(6)
C(46)	46(7)	43(6)	26(5)	5(5)	1(5)	3(5)
C(47)	71(8)	36(6)	36(6)	10(5)	-2(6)	9(6)
C(48)	119(12)	28(6)	58(8)	8(6)	19(8)	6(7)
S(1A)	173(17)	45(7)	87(9)	-22(5)	-36(8)	35(7)
F(1A)	51(9)	94(11)	44(8)	-14(7)	22(6)	-3(9)
F(2A)	146(17)	36(8)	22(7)	-8(6)	-24(8)	-11(8)
F(3A)	80(20)	69(13)	36(9)	8(7)	3(13)	29(17)
O(1A)	48(12)	270(40)	40(10)	-5(14)	-17(8)	58(17)
O(2A)	170(20)	50(17)	70(20)	-12(13)	-24(16)	-10(16)
O(3A)	90(10)	44(9)	0(10)	-15(8)	-44(9)	-4(7)
S(1B)	0(7)	85(15)	0(6)	8(6)	16(4)	11(5)
F(1B)	240(70)	320(80)	280(80)	70(60)	40(50)	-220(70)
F(2B)	150(40)	190(50)	150(40)	-80(40)	30(30)	40(30)
F(3B)	60(30)	80(30)	70(20)	-5(17)	20(20)	10(30)
O(1B)	50(20)	80(20)	380(90)	-100(40)	90(30)	-40(20)

O(2B)	530(140)	40(30)	30(20)	0(20)	90(50)	110(50)
O(3B)	80(20)	63(16)	0(19)	-34(16)	-33(16)	-14(13)
C(99)	106(13)	49(8)	32(7)	3(6)	-3(7)	11(8)

Table 4.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for 98198.

	x	y	z	U(eq)
H(6A)	264	-614	11901	135
H(6B)	101	-1818	11975	135
H(6C)	1275	-1404	12316	135
H(7A)	-647	614	12365	142
H(7B)	-623	1175	13313	142
H(7C)	-1863	850	13010	142
H(8A)	-2102	718	14942	108
H(8B)	-1453	120	15824	108
H(8C)	-2685	-258	15555	108
H(9A)	-692	-2964	15822	107
H(9B)	-1920	-2318	16033	107
H(9C)	-701	-1937	16326	107
H(10A)	302	-3446	14717	118
H(10B)	1345	-2939	13992	118
H(10C)	274	-3436	13577	118
H(16A)	-6743	-5371	13801	123
H(16B)	-6486	-5759	12758	123
H(16C)	-7816	-5416	13146	123
H(17A)	-7547	-5083	11253	108
H(17B)	-6822	-4361	10427	108
H(17C)	-8179	-4053	10774	108
H(18A)	-6594	-1338	10854	94
H(18B)	-7673	-1943	10578	94
H(18C)	-6330	-2249	10192	94
H(19A)	-6222	-964	12123	98
H(19B)	-5363	-1436	12924	98

H(19C)	-6757	-1226	13219	98
H(20A)	-6195	-4186	14514	111
H(20B)	-6717	-3035	14568	111
H(20C)	-5329	-3257	14255	111
H(21A)	-3587	-231	12986	43
H(22A)	-4059	-973	14688	42
H(23A)	-3502	-2863	14812	46
H(26A)	-3316	-4819	13892	60
H(26B)	-2267	-4268	14295	60
H(27A)	-994	-5516	13765	79
H(27B)	-1993	-5924	13186	79
H(28A)	-136	-4895	12322	79
H(28B)	-1309	-5041	11797	79
H(29A)	-1387	-3301	11702	50
H(29B)	-798	-3308	12704	50
H(31A)	-3904	-5394	12473	43
H(32A)	-4676	-5162	10830	51
H(33A)	-4393	-3353	10113	44
H(41A)	-507	-1014	10109	71
H(42A)	1108	-1918	9446	85
H(43A)	843	-3147	8410	78
H(44A)	-1067	-3369	8018	70
H(45A)	-2704	-2435	8668	60
H(47A)	-3547	-1004	9514	60
H(48A)	-3477	166	10577	86
H(48B)	-2022	-80	10601	86

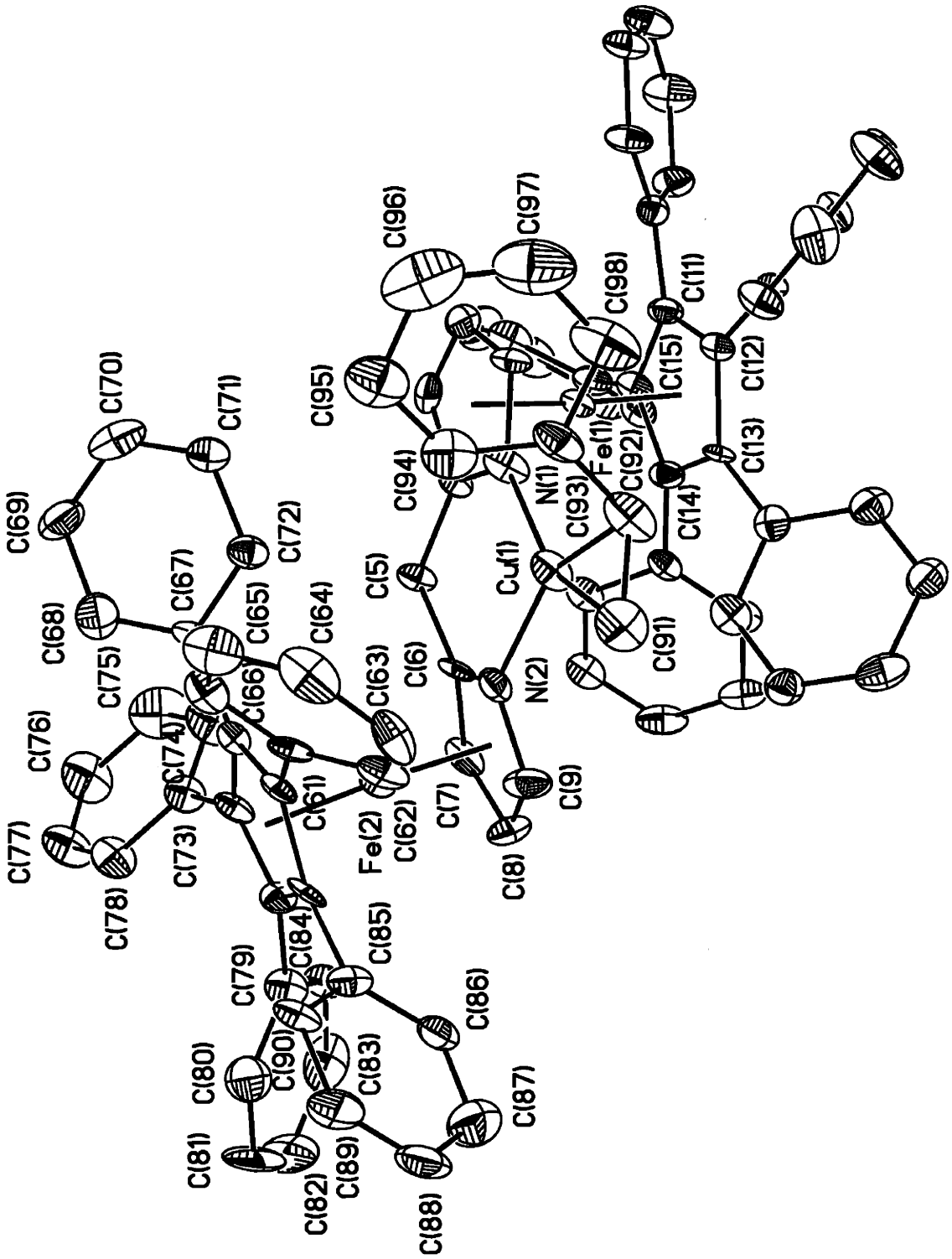

Figure 5. ORTEP plot of [CuOTf•(±)-**1.29**•styrene], with thermal ellipsoids drawn at the 35% probability level.

Table 5.1. Crystal data and structure refinement for [CuOTf•(±)-**1.29**•styrene].

Identification code	98153	
Empirical formula	C91 H72 Cl6 Cu F3 Fe2 N2 O3 S	
Formula weight	1718.51	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 13.1034(2) Å	α = 90°.
	b = 23.8323(4) Å	β = 98.8510(10)°.
	c = 25.9696(6) Å	γ = 90°.
Volume	8013.3(3) $Å^3$	
Z	4	
Density (calculated)	1.424 Mg/m^3	
Absorption coefficient	0.906 mm^{-1}	
F(000)	3528	
Crystal size	0.24 x 0.27 x 0.30 mm^3	
Theta range for data collection	1.17 to 23.26°.	
Index ranges	-11<=h<=14, -26<=k<=26, -23<=l<=28	
Reflections collected	31163	
Independent reflections	11433 [R(int) = 0.1202]	
Completeness to theta = 23.26°	99.3 %	
Absorption correction	Empirical	
Max. and min. transmission	0.9112 and 0.6688	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	11433 / 0 / 1020	
Goodness-of-fit on F^2	1.171	
Final R indices [I>2sigma(I)]	R1 = 0.1523, wR2 = 0.3708	
R indices (all data)	R1 = 0.1946, wR2 = 0.3991	
Largest diff. peak and hole	2.781 and -0.820 $e.Å^{-3}$	

Table 5.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for 98153. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cu(1)	7338(2)	8974(1)	2411(1)	35(1)
Fe(1)	5231(2)	9796(1)	1684(1)	27(1)
Fe(2)	9055(2)	10014(1)	3302(1)	29(1)
N(1)	6044(9)	9400(5)	2331(5)	35(3)
N(2)	8269(9)	9601(5)	2665(4)	32(3)
C(1)	5013(10)	9191(7)	2212(6)	33(3)
C(2)	4347(12)	9625(8)	2254(6)	44(4)
C(3)	4883(12)	10098(7)	2393(5)	36(4)
C(4)	5945(10)	9967(5)	2431(5)	25(3)
C(5)	6814(10)	10338(5)	2674(6)	28(3)
C(6)	7904(10)	10163(6)	2660(5)	26(3)
C(7)	8758(12)	10524(6)	2637(5)	35(4)
C(8)	9672(13)	10164(9)	2628(7)	59(5)
C(9)	9319(11)	9635(8)	2635(6)	47(4)
C(11)	4214(10)	9876(6)	995(5)	31(3)
C(12)	4876(10)	9416(6)	962(5)	24(3)
C(13)	5961(10)	9630(6)	1044(5)	28(3)
C(14)	5913(11)	10221(7)	1130(5)	34(3)
C(15)	4816(11)	10373(6)	1098(5)	29(3)
C(21)	3073(10)	9859(6)	897(5)	28(3)
C(22)	2513(11)	10254(7)	550(6)	40(4)
C(23)	1469(13)	10229(8)	422(7)	56(5)
C(24)	915(13)	9807(8)	607(7)	53(5)
C(25)	1439(11)	9417(6)	953(7)	42(4)
C(26)	2496(11)	9446(6)	1090(6)	38(4)
C(27)	4547(10)	8817(6)	823(6)	33(3)
C(28)	3816(12)	8742(7)	379(6)	42(4)
C(29)	3451(12)	8207(7)	261(6)	43(4)
C(30)	3818(15)	7751(7)	553(7)	57(5)
C(31)	4562(16)	7841(7)	972(7)	57(5)
C(32)	4930(12)	8362(6)	1120(6)	38(4)

C(33)	6892(11)	9297(6)	1012(5)	32(3)
C(34)	7803(12)	9390(6)	1356(6)	38(4)
C(35)	8691(12)	9115(6)	1301(6)	39(4)
C(36)	8731(12)	8737(7)	913(7)	49(4)
C(37)	7830(13)	8638(7)	555(7)	50(5)
C(38)	6931(12)	8914(6)	609(7)	42(4)
C(39)	6780(11)	10620(6)	1136(5)	29(3)
C(40)	6882(12)	11085(6)	1477(6)	36(4)
C(41)	7654(12)	11472(6)	1463(6)	38(4)
C(42)	8318(12)	11410(6)	1118(8)	47(5)
C(43)	8228(12)	10960(7)	768(7)	48(4)
C(44)	7451(11)	10574(6)	787(6)	33(3)
C(45)	4433(11)	10963(6)	1096(6)	35(4)
C(46)	4646(12)	11341(6)	718(6)	36(4)
C(47)	4221(16)	11861(7)	689(8)	62(5)
C(48)	3570(16)	12039(7)	1021(9)	64(6)
C(49)	3382(15)	11678(8)	1410(8)	64(5)
C(50)	3803(12)	11140(6)	1450(7)	43(4)
C(51)	9151(10)	9518(6)	3963(5)	27(3)
C(52)	8469(10)	9995(5)	3992(5)	26(3)
C(53)	9072(11)	10499(6)	3963(5)	31(3)
C(54)	10085(11)	10341(6)	3905(6)	31(3)
C(55)	10172(11)	9730(6)	3913(5)	32(3)
C(61)	8926(10)	8912(6)	4014(6)	30(3)
C(62)	9336(11)	8518(6)	3711(6)	38(4)
C(63)	9159(14)	7946(6)	3786(6)	43(4)
C(64)	8561(15)	7791(7)	4141(7)	54(5)
C(65)	8136(14)	8166(8)	4446(7)	54(5)
C(66)	8338(12)	8750(6)	4381(6)	38(4)
C(67)	7375(10)	9960(6)	4062(6)	32(3)
C(68)	6987(14)	10274(8)	4449(7)	53(5)
C(69)	5957(14)	10237(9)	4505(8)	61(5)
C(70)	5293(15)	9885(10)	4186(9)	71(6)
C(71)	5648(12)	9572(7)	3823(7)	46(4)
C(72)	6682(11)	9601(6)	3756(6)	34(3)
C(73)	8734(12)	11080(6)	4059(6)	38(4)

C(74)	7905(14)	11347(7)	3752(8)	55(5)
C(75)	7588(18)	11886(8)	3877(10)	78(7)
C(76)	8178(18)	12149(8)	4327(9)	70(6)
C(77)	8991(15)	11899(7)	4592(8)	59(5)
C(78)	9280(14)	11361(6)	4471(7)	46(4)
C(79)	10969(12)	10730(6)	3896(6)	40(4)
C(80)	11885(14)	10654(8)	4247(8)	59(5)
C(81)	12694(13)	11007(10)	4251(10)	74(7)
C(82)	12672(16)	11457(11)	3948(11)	85(8)
C(83)	11738(19)	11566(9)	3580(9)	79(7)
C(84)	10890(13)	11186(8)	3561(7)	49(4)
C(85)	11145(11)	9422(6)	3906(6)	34(4)
C(86)	11754(12)	9489(7)	3517(6)	42(4)
C(87)	12698(15)	9210(10)	3550(9)	75(6)
C(88)	13005(13)	8844(8)	3957(8)	59(5)
C(89)	12416(14)	8766(9)	4324(8)	63(6)
C(90)	11463(11)	9054(7)	4306(6)	40(4)
C(91)	8179(14)	8262(7)	2404(8)	53(5)
C(92)	7168(13)	8138(6)	2247(7)	45(4)
C(93)	6469(12)	7916(7)	2580(7)	45(4)
C(94)	6459(15)	8065(7)	3082(8)	54(5)
C(95)	5799(15)	7873(9)	3398(9)	66(6)
C(96)	5058(18)	7456(11)	3177(13)	90(8)
C(97)	5070(19)	7289(11)	2685(13)	94(8)
C(98)	5744(16)	7482(8)	2373(9)	71(6)
S(1)	3750(4)	3469(2)	2784(2)	68(2)
F(1)	1996(10)	3205(6)	3054(7)	104(5)
F(2)	1922(12)	3267(7)	2233(7)	126(6)
F(3)	2634(10)	2557(5)	2636(7)	104(5)
O(1)	4234(12)	3228(7)	3258(7)	101(6)
O(2)	4219(12)	3320(8)	2343(8)	105(6)
O(3)	3472(12)	4060(6)	2804(6)	79(4)
C(101)	2525(17)	3124(10)	2681(10)	77(7)
Cl(1A)	2305(10)	675(7)	2476(6)	33(9)
Cl(2A)	610(40)	930(20)	1660(30)	250(50)
Cl(1B)	2280(20)	728(17)	2449(12)	160(20)

Cl(2B)	591(10)	882(7)	1633(4)	68(8)
C(111)	1603(15)	444(9)	1871(8)	64(5)
Cl(3A)	4710(30)	1520(20)	3170(20)	210(18)
Cl(4A)	6073(12)	1888(4)	2503(4)	73(7)
Cl(3B)	4970(20)	1309(16)	3280(20)	108(14)
Cl(4B)	5970(80)	1940(30)	2490(30)	350(90)
C(112)	4940(30)	1998(14)	2729(15)	131(13)
Cl(5)	15190(30)	13008(10)	5233(12)	450(20)
Cl(6)	14960(20)	11865(13)	4950(16)	500(30)
C(113)	14740(70)	12520(30)	4650(40)	570(110)

Table 5.3. Bond lengths [Å] and angles [°] for 98153.

Cu(1)-N(1)	1.961(12)
Cu(1)-N(2)	1.978(12)
Cu(1)-C(91)	2.023(16)
Cu(1)-C(92)	2.042(15)
Fe(1)-C(1)	2.040(15)
Fe(1)-C(2)	2.055(15)
Fe(1)-C(4)	2.060(13)
Fe(1)-C(15)	2.061(13)
Fe(1)-C(11)	2.069(14)
Fe(1)-C(12)	2.070(13)
Fe(1)-N(1)	2.073(12)
Fe(1)-C(14)	2.073(14)
Fe(1)-C(13)	2.080(14)
Fe(1)-C(3)	2.090(14)
Fe(2)-C(9)	2.032(18)
Fe(2)-C(52)	2.054(14)
Fe(2)-C(54)	2.056(14)
Fe(2)-N(2)	2.060(11)
Fe(2)-C(53)	2.066(15)
Fe(2)-C(8)	2.069(17)
Fe(2)-C(51)	2.072(13)

Fe(2)-C(55)	2.098(14)
Fe(2)-C(7)	2.099(14)
Fe(2)-C(6)	2.100(12)
N(1)-C(4)	1.386(17)
N(1)-C(1)	1.429(18)
N(2)-C(9)	1.392(19)
N(2)-C(6)	1.421(18)
C(1)-C(2)	1.37(2)
C(2)-C(3)	1.35(2)
C(3)-C(4)	1.42(2)
C(4)-C(5)	1.501(18)
C(5)-C(6)	1.494(18)
C(6)-C(7)	1.419(19)
C(7)-C(8)	1.48(2)
C(8)-C(9)	1.34(3)
C(11)-C(12)	1.41(2)
C(11)-C(15)	1.43(2)
C(11)-C(21)	1.477(19)
C(12)-C(13)	1.495(18)
C(12)-C(27)	1.519(19)
C(13)-C(14)	1.43(2)
C(13)-C(33)	1.47(2)
C(14)-C(15)	1.47(2)
C(14)-C(39)	1.48(2)
C(15)-C(45)	1.49(2)
C(21)-C(26)	1.38(2)
C(21)-C(22)	1.43(2)
C(22)-C(23)	1.36(2)
C(23)-C(24)	1.37(3)
C(24)-C(25)	1.40(2)
C(25)-C(26)	1.38(2)
C(27)-C(32)	1.38(2)
C(27)-C(28)	1.39(2)
C(28)-C(29)	1.38(2)
C(29)-C(30)	1.37(2)
C(30)-C(31)	1.36(3)

C(31)-C(32)	1.37(2)
C(33)-C(34)	1.39(2)
C(33)-C(38)	1.40(2)
C(34)-C(35)	1.36(2)
C(35)-C(36)	1.36(2)
C(36)-C(37)	1.41(2)
C(37)-C(38)	1.38(2)
C(39)-C(44)	1.36(2)
C(39)-C(40)	1.41(2)
C(40)-C(41)	1.37(2)
C(41)-C(42)	1.35(2)
C(42)-C(43)	1.40(2)
C(43)-C(44)	1.38(2)
C(45)-C(50)	1.39(2)
C(45)-C(46)	1.39(2)
C(46)-C(47)	1.36(2)
C(47)-C(48)	1.37(3)
C(48)-C(49)	1.38(3)
C(49)-C(50)	1.39(2)
C(51)-C(55)	1.455(19)
C(51)-C(52)	1.456(19)
C(51)-C(61)	1.484(19)
C(52)-C(53)	1.445(19)
C(52)-C(67)	1.47(2)
C(53)-C(54)	1.41(2)
C(53)-C(73)	1.49(2)
C(54)-C(55)	1.46(2)
C(54)-C(79)	1.49(2)
C(55)-C(85)	1.47(2)
C(61)-C(66)	1.37(2)
C(61)-C(62)	1.38(2)
C(62)-C(63)	1.40(2)
C(63)-C(64)	1.35(2)
C(64)-C(65)	1.37(3)
C(65)-C(66)	1.43(2)
C(67)-C(72)	1.40(2)

C(67)-C(68)	1.41(2)
C(68)-C(69)	1.38(2)
C(69)-C(70)	1.39(3)
C(70)-C(71)	1.34(3)
C(71)-C(72)	1.39(2)
C(73)-C(78)	1.37(2)
C(73)-C(74)	1.40(2)
C(74)-C(75)	1.41(3)
C(75)-C(76)	1.44(3)
C(76)-C(77)	1.32(3)
C(77)-C(78)	1.39(2)
C(79)-C(84)	1.39(2)
C(79)-C(80)	1.40(2)
C(80)-C(81)	1.35(3)
C(81)-C(82)	1.33(3)
C(82)-C(83)	1.46(3)
C(83)-C(84)	1.43(2)
C(85)-C(90)	1.37(2)
C(85)-C(86)	1.39(2)
C(86)-C(87)	1.40(3)
C(87)-C(88)	1.38(3)
C(88)-C(89)	1.33(3)
C(89)-C(90)	1.42(2)
C(91)-C(92)	1.36(2)
C(92)-C(93)	1.45(2)
C(93)-C(94)	1.35(2)
C(93)-C(98)	1.45(3)
C(94)-C(95)	1.36(3)
C(95)-C(96)	1.44(3)
C(96)-C(97)	1.34(4)
C(97)-C(98)	1.37(3)
S(1)-O(1)	1.418(17)
S(1)-O(2)	1.424(16)
S(1)-O(3)	1.458(15)
S(1)-C(101)	1.79(2)
F(1)-C(101)	1.29(2)

F(2)-C(101)	1.35(3)
F(3)-C(101)	1.36(3)
Cl(1A)-C(111)	1.78(3)
Cl(2A)-C(111)	1.77(4)
Cl(1B)-C(111)	1.76(3)
Cl(2B)-C(111)	1.73(2)
Cl(3A)-C(112)	1.67(7)
Cl(4A)-C(112)	1.70(4)
Cl(3B)-C(112)	2.18(7)
Cl(4B)-C(112)	1.57(9)
Cl(5)-C(113)	1.93(10)
Cl(6)-C(113)	1.76(6)

N(1)-Cu(1)-N(2)	97.0(5)
N(1)-Cu(1)-C(91)	153.7(6)
N(2)-Cu(1)-C(91)	109.1(6)
N(1)-Cu(1)-C(92)	114.7(6)
N(2)-Cu(1)-C(92)	148.1(6)
C(91)-Cu(1)-C(92)	39.0(7)
C(1)-Fe(1)-C(2)	39.1(6)
C(1)-Fe(1)-C(4)	66.3(5)
C(2)-Fe(1)-C(4)	65.6(6)
C(1)-Fe(1)-C(15)	156.9(6)
C(2)-Fe(1)-C(15)	123.4(6)
C(4)-Fe(1)-C(15)	126.3(5)
C(1)-Fe(1)-C(11)	120.5(6)
C(2)-Fe(1)-C(11)	106.3(6)
C(4)-Fe(1)-C(11)	159.2(6)
C(15)-Fe(1)-C(11)	40.4(6)
C(1)-Fe(1)-C(12)	105.3(6)
C(2)-Fe(1)-C(12)	119.5(6)
C(4)-Fe(1)-C(12)	161.0(5)
C(15)-Fe(1)-C(12)	68.0(5)
C(11)-Fe(1)-C(12)	39.8(5)
C(1)-Fe(1)-N(1)	40.6(5)
C(2)-Fe(1)-N(1)	66.6(6)

C(4)-Fe(1)-N(1)	39.2(5)
C(15)-Fe(1)-N(1)	161.1(5)
C(11)-Fe(1)-N(1)	157.7(5)
C(12)-Fe(1)-N(1)	123.4(5)
C(1)-Fe(1)-C(14)	158.8(6)
C(2)-Fe(1)-C(14)	161.5(7)
C(4)-Fe(1)-C(14)	112.0(5)
C(15)-Fe(1)-C(14)	41.7(6)
C(11)-Fe(1)-C(14)	69.1(5)
C(12)-Fe(1)-C(14)	69.2(6)
N(1)-Fe(1)-C(14)	124.2(5)
C(1)-Fe(1)-C(13)	122.1(6)
C(2)-Fe(1)-C(13)	156.5(6)
C(4)-Fe(1)-C(13)	126.3(5)
C(15)-Fe(1)-C(13)	68.8(6)
C(11)-Fe(1)-C(13)	68.9(5)
C(12)-Fe(1)-C(13)	42.2(5)
N(1)-Fe(1)-C(13)	108.6(5)
C(14)-Fe(1)-C(13)	40.2(6)
C(1)-Fe(1)-C(3)	65.2(6)
C(2)-Fe(1)-C(3)	37.9(6)
C(4)-Fe(1)-C(3)	39.9(6)
C(15)-Fe(1)-C(3)	110.6(6)
C(11)-Fe(1)-C(3)	122.1(6)
C(12)-Fe(1)-C(3)	154.0(6)
N(1)-Fe(1)-C(3)	66.3(5)
C(14)-Fe(1)-C(3)	128.3(6)
C(13)-Fe(1)-C(3)	163.5(6)
C(9)-Fe(2)-C(52)	150.4(6)
C(9)-Fe(2)-C(54)	129.8(6)
C(52)-Fe(2)-C(54)	68.6(5)
C(9)-Fe(2)-N(2)	39.8(5)
C(52)-Fe(2)-N(2)	118.8(5)
C(54)-Fe(2)-N(2)	168.8(5)
C(9)-Fe(2)-C(53)	167.5(6)
C(52)-Fe(2)-C(53)	41.1(5)

C(54)-Fe(2)-C(53)	40.0(6)
N(2)-Fe(2)-C(53)	151.0(5)
C(9)-Fe(2)-C(8)	38.2(7)
C(52)-Fe(2)-C(8)	171.2(7)
C(54)-Fe(2)-C(8)	106.4(6)
N(2)-Fe(2)-C(8)	67.3(6)
C(53)-Fe(2)-C(8)	130.6(7)
C(9)-Fe(2)-C(51)	117.1(6)
C(52)-Fe(2)-C(51)	41.3(5)
C(54)-Fe(2)-C(51)	68.7(5)
N(2)-Fe(2)-C(51)	110.6(5)
C(53)-Fe(2)-C(51)	68.9(5)
C(8)-Fe(2)-C(51)	144.8(7)
C(9)-Fe(2)-C(55)	108.1(6)
C(52)-Fe(2)-C(55)	69.2(6)
C(54)-Fe(2)-C(55)	41.2(6)
N(2)-Fe(2)-C(55)	131.1(5)
C(53)-Fe(2)-C(55)	68.6(5)
C(8)-Fe(2)-C(55)	112.1(7)
C(51)-Fe(2)-C(55)	40.8(5)
C(9)-Fe(2)-C(7)	65.7(6)
C(52)-Fe(2)-C(7)	133.1(6)
C(54)-Fe(2)-C(7)	115.1(5)
N(2)-Fe(2)-C(7)	66.9(5)
C(53)-Fe(2)-C(7)	109.8(6)
C(8)-Fe(2)-C(7)	41.5(7)
C(51)-Fe(2)-C(7)	172.8(6)
C(55)-Fe(2)-C(7)	145.9(6)
C(9)-Fe(2)-C(6)	66.0(6)
C(52)-Fe(2)-C(6)	112.2(5)
C(54)-Fe(2)-C(6)	148.0(6)
N(2)-Fe(2)-C(6)	39.9(5)
C(53)-Fe(2)-C(6)	118.7(6)
C(8)-Fe(2)-C(6)	68.0(6)
C(51)-Fe(2)-C(6)	134.4(5)
C(55)-Fe(2)-C(6)	170.9(5)

C(7)-Fe(2)-C(6)	39.5(5)
C(4)-N(1)-C(1)	105.6(11)
C(4)-N(1)-Cu(1)	126.1(9)
C(1)-N(1)-Cu(1)	128.0(9)
C(4)-N(1)-Fe(1)	69.9(7)
C(1)-N(1)-Fe(1)	68.4(7)
Cu(1)-N(1)-Fe(1)	130.6(7)
C(9)-N(2)-C(6)	106.2(12)
C(9)-N(2)-Cu(1)	126.1(11)
C(6)-N(2)-Cu(1)	121.3(9)
C(9)-N(2)-Fe(2)	69.0(9)
C(6)-N(2)-Fe(2)	71.5(7)
Cu(1)-N(2)-Fe(2)	146.7(7)
C(2)-C(1)-N(1)	108.2(13)
C(2)-C(1)-Fe(1)	71.1(9)
N(1)-C(1)-Fe(1)	70.9(7)
C(3)-C(2)-C(1)	109.9(14)
C(3)-C(2)-Fe(1)	72.4(9)
C(1)-C(2)-Fe(1)	69.9(9)
C(2)-C(3)-C(4)	107.6(13)
C(2)-C(3)-Fe(1)	69.7(9)
C(4)-C(3)-Fe(1)	68.9(8)
N(1)-C(4)-C(3)	108.7(12)
N(1)-C(4)-C(5)	124.5(12)
C(3)-C(4)-C(5)	125.0(12)
N(1)-C(4)-Fe(1)	70.9(7)
C(3)-C(4)-Fe(1)	71.2(8)
C(5)-C(4)-Fe(1)	135.9(10)
C(6)-C(5)-C(4)	119.4(11)
C(7)-C(6)-N(2)	107.7(12)
C(7)-C(6)-C(5)	126.5(13)
N(2)-C(6)-C(5)	125.8(11)
C(7)-C(6)-Fe(2)	70.2(7)
N(2)-C(6)-Fe(2)	68.5(7)
C(5)-C(6)-Fe(2)	126.9(10)
C(6)-C(7)-C(8)	107.2(13)

C(6)-C(7)-Fe(2)	70.3(7)
C(8)-C(7)-Fe(2)	68.2(9)
C(9)-C(8)-C(7)	105.2(14)
C(9)-C(8)-Fe(2)	69.4(11)
C(7)-C(8)-Fe(2)	70.4(8)
C(8)-C(9)-N(2)	113.6(16)
C(8)-C(9)-Fe(2)	72.4(11)
N(2)-C(9)-Fe(2)	71.2(9)
C(12)-C(11)-C(15)	109.2(12)
C(12)-C(11)-C(21)	125.8(13)
C(15)-C(11)-C(21)	124.8(13)
C(12)-C(11)-Fe(1)	70.2(8)
C(15)-C(11)-Fe(1)	69.5(7)
C(21)-C(11)-Fe(1)	130.2(10)
C(11)-C(12)-C(13)	107.8(12)
C(11)-C(12)-C(27)	126.3(12)
C(13)-C(12)-C(27)	125.7(12)
C(11)-C(12)-Fe(1)	70.1(8)
C(13)-C(12)-Fe(1)	69.2(7)
C(27)-C(12)-Fe(1)	130.0(9)
C(14)-C(13)-C(33)	126.8(12)
C(14)-C(13)-C(12)	107.2(12)
C(33)-C(13)-C(12)	126.0(12)
C(14)-C(13)-Fe(1)	69.6(8)
C(33)-C(13)-Fe(1)	129.5(10)
C(12)-C(13)-Fe(1)	68.6(7)
C(13)-C(14)-C(15)	107.5(12)
C(13)-C(14)-C(39)	125.7(13)
C(15)-C(14)-C(39)	125.7(13)
C(13)-C(14)-Fe(1)	70.1(8)
C(15)-C(14)-Fe(1)	68.7(7)
C(39)-C(14)-Fe(1)	135.9(10)
C(11)-C(15)-C(14)	108.3(12)
C(11)-C(15)-C(45)	127.3(13)
C(14)-C(15)-C(45)	123.8(13)
C(11)-C(15)-Fe(1)	70.1(8)

C(14)-C(15)-Fe(1)	69.6(7)
C(45)-C(15)-Fe(1)	132.9(11)
C(26)-C(21)-C(22)	116.2(13)
C(26)-C(21)-C(11)	123.6(13)
C(22)-C(21)-C(11)	120.0(13)
C(23)-C(22)-C(21)	121.8(15)
C(22)-C(23)-C(24)	120.9(16)
C(23)-C(24)-C(25)	118.6(15)
C(26)-C(25)-C(24)	120.6(15)
C(25)-C(26)-C(21)	121.8(14)
C(32)-C(27)-C(28)	120.5(14)
C(32)-C(27)-C(12)	122.7(12)
C(28)-C(27)-C(12)	116.8(14)
C(29)-C(28)-C(27)	118.2(15)
C(30)-C(29)-C(28)	122.1(15)
C(31)-C(30)-C(29)	117.6(15)
C(30)-C(31)-C(32)	123.2(16)
C(31)-C(32)-C(27)	118.3(14)
C(34)-C(33)-C(38)	117.1(14)
C(34)-C(33)-C(13)	121.1(13)
C(38)-C(33)-C(13)	121.5(13)
C(35)-C(34)-C(33)	121.3(15)
C(36)-C(35)-C(34)	121.8(15)
C(35)-C(36)-C(37)	118.6(15)
C(38)-C(37)-C(36)	119.8(16)
C(37)-C(38)-C(33)	121.4(16)
C(44)-C(39)-C(40)	118.1(13)
C(44)-C(39)-C(14)	120.9(13)
C(40)-C(39)-C(14)	120.7(13)
C(41)-C(40)-C(39)	120.7(15)
C(42)-C(41)-C(40)	119.7(15)
C(41)-C(42)-C(43)	121.1(15)
C(44)-C(43)-C(42)	118.5(16)
C(39)-C(44)-C(43)	121.8(15)
C(50)-C(45)-C(46)	118.2(14)
C(50)-C(45)-C(15)	121.1(13)

C(46)-C(45)-C(15)	120.6(14)
C(47)-C(46)-C(45)	120.4(17)
C(46)-C(47)-C(48)	122.5(17)
C(47)-C(48)-C(49)	117.8(16)
C(48)-C(49)-C(50)	121.1(19)
C(45)-C(50)-C(49)	119.9(17)
C(55)-C(51)-C(52)	108.3(12)
C(55)-C(51)-C(61)	122.9(13)
C(52)-C(51)-C(61)	128.6(12)
C(55)-C(51)-Fe(2)	70.5(8)
C(52)-C(51)-Fe(2)	68.7(7)
C(61)-C(51)-Fe(2)	129.9(9)
C(53)-C(52)-C(51)	107.5(11)
C(53)-C(52)-C(67)	127.1(12)
C(51)-C(52)-C(67)	125.3(12)
C(53)-C(52)-Fe(2)	69.9(8)
C(51)-C(52)-Fe(2)	70.0(8)
C(67)-C(52)-Fe(2)	127.5(10)
C(54)-C(53)-C(52)	108.4(12)
C(54)-C(53)-C(73)	125.2(13)
C(52)-C(53)-C(73)	125.9(13)
C(54)-C(53)-Fe(2)	69.6(8)
C(52)-C(53)-Fe(2)	69.0(8)
C(73)-C(53)-Fe(2)	134.0(10)
C(53)-C(54)-C(55)	109.7(12)
C(53)-C(54)-C(79)	125.7(13)
C(55)-C(54)-C(79)	124.2(13)
C(53)-C(54)-Fe(2)	70.4(8)
C(55)-C(54)-Fe(2)	71.0(7)
C(79)-C(54)-Fe(2)	130.3(11)
C(51)-C(55)-C(54)	106.0(12)
C(51)-C(55)-C(85)	129.6(13)
C(54)-C(55)-C(85)	124.3(12)
C(51)-C(55)-Fe(2)	68.6(7)
C(54)-C(55)-Fe(2)	67.9(8)
C(85)-C(55)-Fe(2)	131.0(11)

C(66)-C(61)-C(62)	120.8(14)
C(66)-C(61)-C(51)	118.4(13)
C(62)-C(61)-C(51)	120.7(14)
C(61)-C(62)-C(63)	119.6(16)
C(64)-C(63)-C(62)	119.2(16)
C(63)-C(64)-C(65)	123.1(15)
C(64)-C(65)-C(66)	117.9(16)
C(61)-C(66)-C(65)	119.3(16)
C(72)-C(67)-C(68)	117.0(14)
C(72)-C(67)-C(52)	121.5(13)
C(68)-C(67)-C(52)	121.5(13)
C(69)-C(68)-C(67)	120.5(17)
C(68)-C(69)-C(70)	120.5(18)
C(71)-C(70)-C(69)	120.3(17)
C(70)-C(71)-C(72)	120.6(16)
C(71)-C(72)-C(67)	121.1(15)
C(78)-C(73)-C(74)	119.4(15)
C(78)-C(73)-C(53)	117.0(14)
C(74)-C(73)-C(53)	123.6(14)
C(73)-C(74)-C(75)	121.0(18)
C(74)-C(75)-C(76)	116.4(19)
C(77)-C(76)-C(75)	121.1(17)
C(76)-C(77)-C(78)	121.8(17)
C(73)-C(78)-C(77)	120.1(17)
C(84)-C(79)-C(80)	118.9(16)
C(84)-C(79)-C(54)	121.0(14)
C(80)-C(79)-C(54)	120.0(15)
C(81)-C(80)-C(79)	121(2)
C(82)-C(81)-C(80)	124(2)
C(81)-C(82)-C(83)	118.2(18)
C(84)-C(83)-C(82)	119(2)
C(79)-C(84)-C(83)	119.5(18)
C(90)-C(85)-C(86)	118.8(14)
C(90)-C(85)-C(55)	118.1(14)
C(86)-C(85)-C(55)	123.0(14)
C(85)-C(86)-C(87)	120.2(17)

C(88)-C(87)-C(86)	119.9(19)
C(89)-C(88)-C(87)	120.3(17)
C(88)-C(89)-C(90)	120.9(17)
C(85)-C(90)-C(89)	119.8(16)
C(92)-C(91)-Cu(1)	71.3(9)
C(91)-C(92)-C(93)	125.1(15)
C(91)-C(92)-Cu(1)	69.7(9)
C(93)-C(92)-Cu(1)	106.8(12)
C(94)-C(93)-C(98)	116.2(19)
C(94)-C(93)-C(92)	125.4(16)
C(98)-C(93)-C(92)	118.4(17)
C(93)-C(94)-C(95)	126.4(19)
C(94)-C(95)-C(96)	116(2)
C(97)-C(96)-C(95)	118(2)
C(96)-C(97)-C(98)	125(3)
C(97)-C(98)-C(93)	118(2)
O(1)-S(1)-O(2)	114.0(12)
O(1)-S(1)-O(3)	116.1(10)
O(2)-S(1)-O(3)	114.3(11)
O(1)-S(1)-C(101)	102.4(11)
O(2)-S(1)-C(101)	104.7(11)
O(3)-S(1)-C(101)	103.1(10)
F(1)-C(101)-F(2)	107.4(18)
F(1)-C(101)-F(3)	106.8(17)
F(2)-C(101)-F(3)	103(2)
F(1)-C(101)-S(1)	113(2)
F(2)-C(101)-S(1)	114.0(15)
F(3)-C(101)-S(1)	111.4(14)
Cl(2B)-C(111)-Cl(1B)	109.3(17)
Cl(2A)-C(111)-Cl(1A)	109(3)
Cl(3A)-C(112)-Cl(4A)	113(3)
Cl(4A)-C(112)-Cl(3B)	100.5(19)
Cl(6)-C(113)-Cl(5)	100(4)

Table 5.4. Anisotropic displacement parameters ($Å^2$ x 10^3) for 98153. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cu(1)	43(1)	17(1)	40(1)	-2(1)	-7(1)	6(1)
Fe(1)	24(1)	25(1)	28(1)	1(1)	-5(1)	-4(1)
Fe(2)	31(1)	22(1)	33(1)	2(1)	-3(1)	-2(1)
N(1)	36(7)	14(6)	49(8)	3(5)	-13(6)	5(5)
N(2)	34(7)	32(7)	29(6)	-8(5)	-2(5)	-4(5)
C(1)	19(7)	38(9)	39(8)	2(7)	-5(6)	-9(7)
C(2)	30(9)	73(13)	30(8)	-2(8)	5(7)	-5(9)
C(3)	43(9)	39(9)	27(8)	-4(7)	13(7)	9(7)
C(4)	30(8)	10(6)	32(7)	-3(6)	-2(6)	-4(6)
C(5)	21(7)	17(7)	43(8)	-3(6)	-8(6)	6(6)
C(6)	18(7)	31(8)	23(7)	8(6)	-14(6)	-7(6)
C(7)	50(10)	23(8)	29(8)	7(6)	-10(7)	-12(7)
C(8)	23(9)	99(16)	58(12)	-8(11)	16(8)	-14(10)
C(9)	23(8)	68(12)	47(10)	18(9)	-4(7)	-1(8)
C(11)	20(7)	41(9)	31(8)	2(7)	-2(6)	-4(6)
C(12)	19(7)	27(7)	22(7)	8(6)	-8(5)	6(6)
C(13)	14(7)	38(9)	29(7)	-8(6)	-2(6)	-13(6)
C(14)	24(8)	52(10)	24(7)	9(7)	-1(6)	-8(7)
C(15)	30(8)	28(8)	27(7)	11(6)	-8(6)	2(6)
C(21)	28(7)	27(8)	30(8)	0(6)	3(6)	0(6)
C(22)	25(8)	53(10)	40(9)	15(8)	-4(7)	3(7)
C(23)	37(10)	55(11)	69(12)	19(10)	-15(9)	15(9)
C(24)	29(9)	64(12)	58(11)	2(9)	-18(8)	1(9)
C(25)	30(8)	32(9)	60(11)	-4(8)	-3(8)	-10(7)
C(26)	23(8)	38(9)	48(9)	13(7)	-12(7)	-2(7)
C(27)	23(7)	42(9)	33(8)	-14(7)	7(6)	-15(7)
C(28)	48(10)	45(10)	29(8)	-6(7)	-3(7)	-6(8)
C(29)	45(10)	41(10)	38(9)	-25(8)	-8(7)	-9(8)
C(30)	75(13)	31(9)	59(12)	-9(8)	-14(10)	-14(9)
C(31)	86(14)	32(10)	53(11)	2(8)	8(10)	5(9)
C(32)	41(9)	34(9)	32(8)	11(7)	-13(7)	-3(7)

C(33)	36(8)	32(8)	29(8)	7(7)	5(7)	0(7)
C(34)	45(10)	27(8)	39(9)	6(7)	-3(7)	6(7)
C(35)	36(9)	37(9)	42(9)	-2(7)	5(7)	-1(7)
C(36)	31(9)	43(10)	74(13)	13(9)	9(9)	13(8)
C(37)	45(10)	38(10)	72(12)	-20(9)	25(9)	-13(8)
C(38)	39(9)	30(9)	59(11)	-3(8)	13(8)	-5(7)
C(39)	30(8)	21(7)	31(8)	0(6)	-7(6)	3(6)
C(40)	38(9)	25(8)	40(9)	0(7)	-7(7)	5(7)
C(41)	44(9)	24(8)	41(9)	6(7)	-5(8)	0(7)
C(42)	31(9)	26(9)	82(13)	15(9)	-3(9)	-5(7)
C(43)	29(9)	48(11)	66(12)	11(9)	3(8)	-5(8)
C(44)	36(8)	18(7)	43(9)	3(6)	2(7)	-3(6)
C(45)	28(8)	31(8)	41(9)	8(7)	-8(7)	2(6)
C(46)	45(9)	32(9)	29(8)	9(7)	-4(7)	-5(7)
C(47)	77(14)	30(10)	73(13)	17(9)	-8(11)	-4(9)
C(48)	70(13)	17(8)	93(15)	8(10)	-22(12)	10(9)
C(49)	58(12)	54(12)	81(14)	3(11)	17(11)	16(10)
C(50)	40(9)	22(8)	61(11)	-1(7)	-8(8)	10(7)
C(51)	28(7)	24(7)	24(7)	-3(6)	-8(6)	-12(6)
C(52)	30(7)	19(7)	25(7)	0(6)	-3(6)	1(6)
C(53)	29(8)	27(8)	32(8)	3(6)	-14(6)	0(6)
C(54)	29(8)	29(8)	34(8)	2(6)	4(6)	-13(6)
C(55)	27(8)	36(8)	27(8)	-7(6)	-15(6)	-13(7)
C(61)	16(7)	30(8)	40(8)	4(7)	-15(6)	4(6)
C(62)	25(8)	35(9)	48(10)	8(7)	-19(7)	11(7)
C(63)	70(12)	24(8)	30(8)	-1(7)	-10(8)	1(8)
C(64)	76(13)	20(9)	58(12)	15(8)	-13(10)	-13(9)
C(65)	56(11)	43(11)	58(11)	29(9)	-4(9)	-7(9)
C(66)	44(9)	30(8)	35(8)	8(7)	-8(7)	12(7)
C(67)	24(7)	30(8)	37(8)	3(7)	-10(6)	-4(6)
C(68)	53(11)	57(11)	49(10)	0(9)	5(9)	16(9)
C(69)	41(11)	76(14)	73(13)	-20(11)	29(10)	-8(10)
C(70)	38(11)	87(16)	94(16)	6(13)	27(11)	-1(11)
C(71)	37(9)	52(11)	48(10)	-6(8)	7(8)	-15(8)
C(72)	29(8)	27(8)	43(9)	-3(7)	1(7)	-1(6)
C(73)	42(9)	22(8)	47(9)	0(7)	4(8)	-6(7)

C(74)	64(12)	26(9)	69(12)	-17(8)	-7(10)	6(8)
C(75)	80(15)	38(11)	113(19)	19(12)	6(14)	16(11)
C(76)	90(16)	29(10)	87(15)	-23(10)	5(13)	-4(10)
C(77)	64(12)	33(10)	73(13)	-18(9)	-8(10)	-23(9)
C(78)	56(11)	25(9)	56(11)	-6(8)	3(9)	-16(8)
C(79)	42(9)	26(8)	50(10)	1(7)	2(8)	-4(7)
C(80)	57(12)	54(12)	65(12)	-15(10)	9(10)	-1(9)
C(81)	22(9)	87(17)	106(18)	-12(14)	-14(10)	-26(10)
C(82)	44(13)	98(19)	120(20)	-29(16)	18(13)	-48(13)
C(83)	102(18)	51(12)	95(17)	-36(12)	50(15)	-47(12)
C(84)	35(9)	61(12)	50(10)	-7(9)	-1(8)	-11(8)
C(85)	23(7)	18(7)	59(10)	-10(7)	1(7)	0(6)
C(86)	33(9)	52(10)	36(9)	-4(8)	-5(7)	-9(8)
C(87)	50(12)	103(18)	71(14)	2(13)	10(11)	15(12)
C(88)	29(9)	70(13)	69(13)	-15(11)	-18(9)	7(9)
C(89)	37(10)	89(15)	56(12)	15(11)	-15(9)	27(10)
C(90)	29(8)	43(9)	41(9)	2(7)	-15(7)	-2(7)
C(91)	61(12)	28(9)	66(12)	3(8)	-4(10)	21(8)
C(92)	56(11)	21(8)	49(10)	7(7)	-22(9)	14(8)
C(93)	38(9)	38(9)	50(11)	-4(8)	-18(8)	9(8)
C(94)	58(12)	33(10)	72(13)	4(9)	7(10)	1(8)
C(95)	53(12)	56(13)	85(15)	4(11)	-6(11)	16(10)
C(96)	67(16)	78(17)	130(20)	60(17)	19(16)	18(13)
C(97)	68(16)	87(19)	120(20)	36(18)	-9(16)	-9(14)
C(98)	73(14)	48(12)	83(15)	18(11)	-20(12)	-14(11)
S(1)	56(3)	59(3)	93(4)	-15(3)	20(3)	-13(3)
F(1)	77(9)	99(11)	148(14)	-2(10)	59(10)	-3(8)
F(2)	97(11)	116(13)	151(15)	43(11)	-28(10)	-39(10)
F(3)	74(9)	57(8)	180(15)	-16(9)	14(9)	-21(7)
O(1)	71(10)	86(12)	131(15)	16(11)	-35(10)	15(9)
O(2)	77(11)	109(13)	146(16)	-49(12)	70(11)	-27(10)
O(3)	106(12)	45(8)	90(10)	-17(7)	31(9)	-31(8)
C(101)	59(13)	68(15)	109(19)	38(13)	33(14)	17(11)
Cl(1A)	14(10)	59(13)	34(11)	-7(7)	31(6)	-6(6)
Cl(2A)	230(60)	150(40)	380(110)	110(40)	30(40)	110(40)
Cl(1B)	140(30)	190(30)	150(30)	-50(20)	7(18)	-50(20)

Cl(2B)	64(10)	100(11)	47(11)	20(6)	26(5)	38(7)
C(111)	61(12)	71(14)	62(12)	3(10)	11(10)	6(10)
Cl(3A)	200(30)	150(30)	330(40)	-80(30)	190(30)	-50(20)
Cl(4A)	127(12)	22(6)	77(9)	-11(4)	34(6)	-4(6)
Cl(3B)	67(16)	76(18)	190(30)	-93(19)	60(17)	-17(11)
Cl(4B)	550(170)	190(70)	290(80)	40(40)	40(70)	270(110)
C(112)	130(30)	90(20)	170(30)	-50(20)	-10(20)	10(20)
Cl(5)	690(50)	280(20)	530(40)	-100(30)	500(40)	-120(30)
Cl(6)	300(20)	340(30)	730(60)	-240(40)	-290(30)	90(20)
C(113)	510(130)	300(80)	730(180)	330(110)	-430(130)	-360(100)

Table 5.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for 98153.

	x	y	z	U(eq)
H(1)	4823	8815	2120	40
H(2)	3615	9597	2194	53
H(3)	4599	10454	2453	43
H(5A)	6714	10710	2504	34
H(5B)	6737	10392	3044	34
H(7)	8743	10922	2628	43
H(8)	10363	10281	2621	71
H(9)	9745	9315	2620	56
H(22A)	2880	10542	405	48
H(23A)	1118	10508	200	67
H(24A)	189	9780	503	63
H(25A)	1063	9130	1094	50
H(26A)	2837	9174	1324	46
H(28A)	3575	9051	163	50
H(29A)	2929	8153	-32	52
H(30A)	3562	7384	466	69
H(31A)	4839	7526	1170	69
H(32A)	5436	8410	1420	45
H(34A)	7805	9649	1633	46

H(35A)	9299	9190	1540	47
H(36A)	9354	8544	885	59
H(37A)	7842	8381	276	60
H(38A)	6325	8843	367	51
H(40A)	6412	11131	1718	43
H(41A)	7721	11782	1696	45
H(42A)	8855	11677	1112	57
H(43A)	8693	10921	523	58
H(44A)	7381	10269	549	39
H(46A)	5092	11234	479	43
H(47A)	4380	12111	428	74
H(48A)	3258	12400	985	76
H(49A)	2958	11797	1655	76
H(50A)	3661	10895	1719	51
H(62A)	9734	8634	3454	46
H(63A)	9458	7671	3590	52
H(64A)	8427	7402	4180	65
H(65A)	7721	8043	4694	64
H(66A)	8067	9023	4590	45
H(68A)	7436	10511	4674	64
H(69A)	5701	10455	4764	74
H(70A)	4585	9866	4224	85
H(71A)	5191	9327	3610	55
H(72A)	6921	9374	3499	41
H(74A)	7551	11160	3453	66
H(75A)	7015	12068	3677	94
H(76A)	7979	12509	4434	84
H(77A)	9388	12092	4874	70
H(78A)	9860	11188	4674	56
H(80A)	11938	10349	4485	71
H(81A)	13311	10929	4484	89
H(82A)	13250	11702	3971	102
H(83A)	11694	11884	3357	95
H(84A)	10277	11246	3320	59
H(86A)	11528	9727	3228	50
H(87A)	13129	9270	3293	90

H(88A)	13640	8648	3975	70
H(89A)	12635	8515	4603	76
H(90A)	11047	8993	4570	48
H(91A)	8638	8238	2136	63
H(91B)	8495	8113	2747	63
H(92A)	6981	8045	1868	55
H(94A)	6963	8329	3229	65
H(95A)	5823	8006	3744	80
H(96A)	4574	7303	3377	108
H(97A)	4575	7018	2543	113
H(98A)	5737	7337	2031	85
H(11A)	2072	414	1607	77
H(11B)	1302	69	1913	77
H(11C)	1421	62	1975	77
H(11D)	2078	410	1610	77
H(11E)	4956	2375	2891	158
H(11F)	4369	1993	2432	158
H(11G)	4309	1988	2466	158
H(11H)	4965	2361	2918	158
H(11I)	14000	12578	4505	684
H(11J)	15160	12575	4364	684

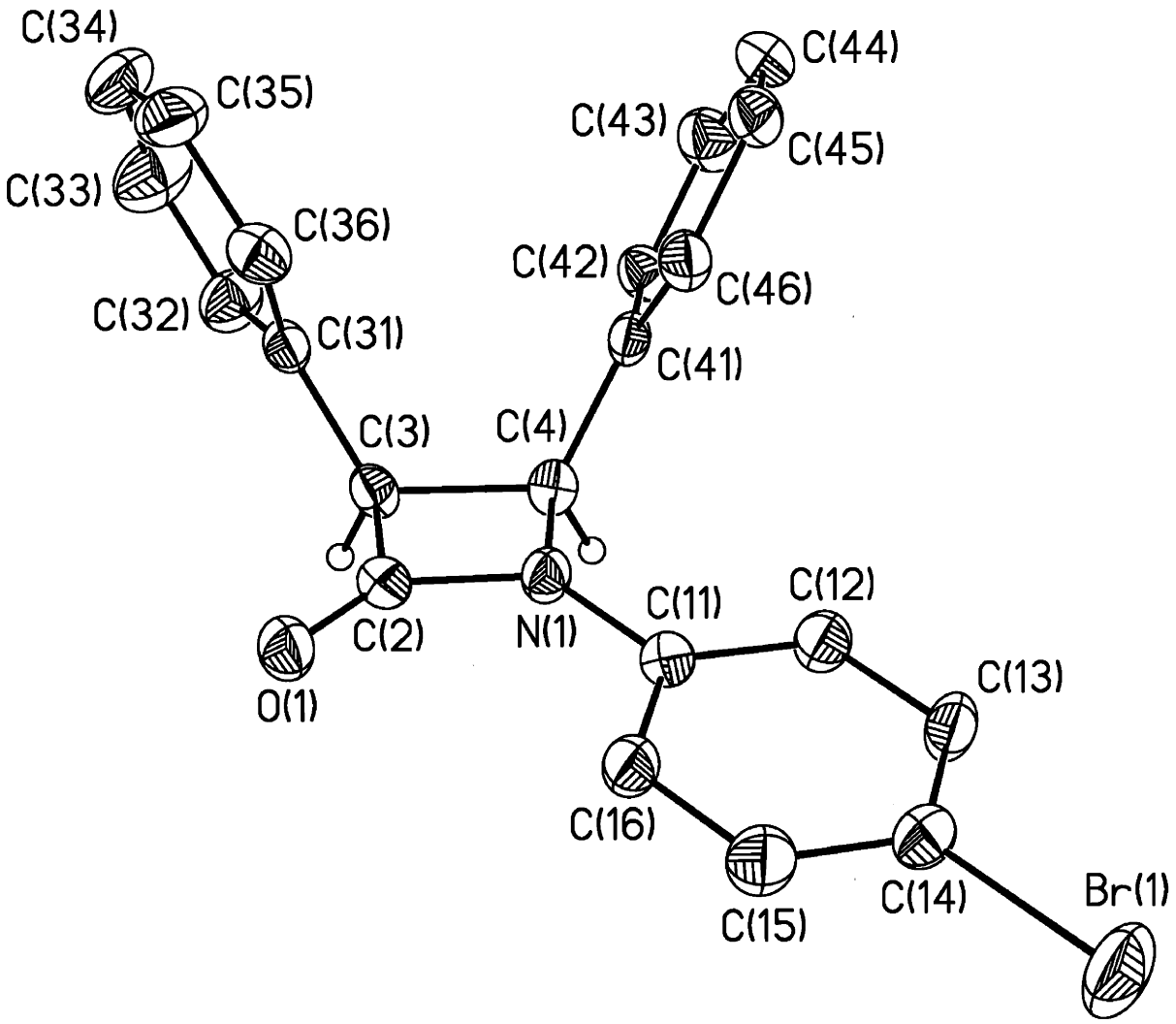

Figure 6. ORTEP plot of (3*S*,4*S*)-1-(4-bromophenyl)-3,4-diphenyl-2-azetidinone, with thermal ellipsoids drawn at the 35% probability level.

Table 6.1. Crystal data and structure refinement for (3*S*,4*S*)-1-(4-bromophenyl)-3,4-diphenyl-2-azetidinone.

Identification code	01157s	
Empirical formula	C21 H16 Br N O	
Formula weight	378.26	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Tetragonal	
Space group	P4(1)2(1)2	
Unit cell dimensions	a = 8.8016(5) Å	α = 90°.

	b = 8.8016(5) Å	β = 90°.
	c = 46.695(4) Å	γ = 90°.
Volume	3617.4(4) Å^3	
Z	8	
Density (calculated)	1.389 Mg/m^3	
Absorption coefficient	2.279 mm^{-1}	
F(000)	1536	
Crystal size	0.21 x 0.17 x 0.1 mm^3	
Theta range for data collection	2.35 to 23.27°.	
Index ranges	-9<=h<=8, -9<=k<=8, -41<=l<=51	
Reflections collected	14511	
Independent reflections	2597 [R(int) = 0.0448]	
Completeness to theta = 23.27°	99.8 %	
Absorption correction	Bruker SADABS	
Max. and min. transmission	0.8443 and 0.5414	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2597 / 0 / 218	
Goodness-of-fit on F^2	1.040	
Final R indices [I>2sigma(I)]	R1 = 0.0342, wR2 = 0.0718	
R indices (all data)	R1 = 0.0417, wR2 = 0.0744	
Absolute structure parameter	-0.008(13)	
Extinction coefficient	0.0012(3)	
Largest diff. peak and hole	0.194 and -0.206 e.Å^{-3}	

Table 6.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for 01157s. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	1326(1)	7512(1)	10207(1)	76(1)
O(1)	-2166(3)	2785(3)	9125(1)	45(1)
N(1)	-154(3)	4535(3)	9070(1)	32(1)
C(2)	-1138(4)	3396(4)	8994(1)	34(1)
C(3)	-424(4)	3211(4)	8700(1)	33(1)
C(4)	704(4)	4509(4)	8797(1)	30(1)

C(11)	187(4)	5227(4)	9335(1)	33(1)
C(12)	1393(4)	6225(4)	9355(1)	40(1)
C(13)	1736(5)	6899(4)	9615(1)	46(1)
C(14)	861(5)	6575(4)	9851(1)	46(1)
C(15)	-334(5)	5583(5)	9834(1)	51(1)
C(16)	-682(4)	4910(4)	9574(1)	41(1)
C(31)	-1408(4)	3432(4)	8440(1)	32(1)
C(32)	-1023(5)	2740(5)	8182(1)	49(1)
C(33)	-1921(6)	2926(6)	7946(1)	72(1)
C(34)	-3226(5)	3787(6)	7958(1)	64(1)
C(35)	-3617(5)	4477(5)	8210(1)	57(1)
C(36)	-2707(4)	4312(4)	8450(1)	43(1)
C(41)	731(4)	5945(4)	8627(1)	30(1)
C(42)	1638(4)	5982(4)	8383(1)	37(1)
C(43)	1698(5)	7265(5)	8213(1)	51(1)
C(44)	866(5)	8535(5)	8284(1)	48(1)
C(45)	-39(5)	8506(4)	8527(1)	43(1)
C(46)	-113(4)	7222(4)	8697(1)	37(1)

Table 6.3. Bond lengths [Å] and angles [°] for 01157s.

Br(1)-C(14)	1.899(3)
O(1)-C(2)	1.219(4)
N(1)-C(2)	1.371(4)
N(1)-C(11)	1.412(4)
N(1)-C(4)	1.482(4)
C(2)-C(3)	1.519(5)
C(3)-C(31)	1.504(5)
C(3)-C(4)	1.580(5)
C(4)-C(41)	1.491(5)
C(11)-C(12)	1.381(5)
C(11)-C(16)	1.382(5)
C(12)-C(13)	1.384(5)
C(13)-C(14)	1.376(5)

C(14)-C(15)	1.369(5)
C(15)-C(16)	1.386(5)
C(31)-C(36)	1.381(5)
C(31)-C(32)	1.391(5)
C(32)-C(33)	1.366(6)
C(33)-C(34)	1.377(6)
C(34)-C(35)	1.370(6)
C(35)-C(36)	1.384(5)
C(41)-C(46)	1.386(5)
C(41)-C(42)	1.392(5)
C(42)-C(43)	1.382(5)
C(43)-C(44)	1.377(6)
C(44)-C(45)	1.386(5)
C(45)-C(46)	1.383(5)

C(2)-N(1)-C(11)	132.5(3)
C(2)-N(1)-C(4)	95.1(3)
C(11)-N(1)-C(4)	130.8(3)
O(1)-C(2)-N(1)	131.4(3)
O(1)-C(2)-C(3)	135.6(3)
N(1)-C(2)-C(3)	92.9(3)
C(31)-C(3)-C(2)	118.6(3)
C(31)-C(3)-C(4)	119.9(3)
C(2)-C(3)-C(4)	85.6(2)
N(1)-C(4)-C(41)	116.9(3)
N(1)-C(4)-C(3)	86.4(2)
C(41)-C(4)-C(3)	118.1(3)
C(12)-C(11)-C(16)	119.9(3)
C(12)-C(11)-N(1)	119.8(3)
C(16)-C(11)-N(1)	120.3(3)
C(11)-C(12)-C(13)	120.0(3)
C(14)-C(13)-C(12)	119.5(3)
C(15)-C(14)-C(13)	121.0(3)
C(15)-C(14)-Br(1)	119.6(3)
C(13)-C(14)-Br(1)	119.4(3)
C(14)-C(15)-C(16)	119.6(4)

C(11)-C(16)-C(15)	120.0(3)
C(36)-C(31)-C(32)	118.4(3)
C(36)-C(31)-C(3)	121.5(3)
C(32)-C(31)-C(3)	120.1(3)
C(33)-C(32)-C(31)	120.3(4)
C(32)-C(33)-C(34)	121.1(4)
C(35)-C(34)-C(33)	119.1(4)
C(34)-C(35)-C(36)	120.3(4)
C(31)-C(36)-C(35)	120.7(4)
C(46)-C(41)-C(42)	118.8(3)
C(46)-C(41)-C(4)	123.6(3)
C(42)-C(41)-C(4)	117.6(3)
C(43)-C(42)-C(41)	120.7(3)
C(44)-C(43)-C(42)	120.4(4)
C(43)-C(44)-C(45)	119.2(4)
C(46)-C(45)-C(44)	120.8(4)
C(45)-C(46)-C(41)	120.1(3)

Table 6.4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for 01157s. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	94(1)	96(1)	39(1)	-20(1)	-4(1)	-37(1)
O(1)	49(2)	48(2)	36(1)	2(1)	0(1)	-18(1)
N(1)	36(2)	35(2)	26(2)	-3(1)	0(1)	-7(1)
C(2)	40(2)	29(2)	34(2)	3(2)	-4(2)	-3(2)
C(3)	40(2)	25(2)	33(2)	-1(2)	4(2)	-5(2)
C(4)	27(2)	32(2)	31(2)	-6(2)	3(2)	1(1)
C(11)	36(2)	31(2)	33(2)	0(2)	-2(2)	-1(2)
C(12)	40(2)	48(2)	32(2)	1(2)	2(2)	-12(2)
C(13)	48(3)	53(3)	36(2)	-4(2)	-6(2)	-21(2)
C(14)	60(3)	47(2)	30(2)	-3(2)	-5(2)	-9(2)
C(15)	60(3)	59(3)	32(2)	1(2)	4(2)	-16(2)

C(16)	45(2)	49(2)	30(2)	4(2)	-2(2)	-18(2)
C(31)	35(2)	28(2)	33(2)	2(2)	1(2)	-8(2)
C(32)	53(3)	50(3)	45(2)	-9(2)	-6(2)	4(2)
C(33)	88(4)	87(4)	42(3)	-19(2)	-14(2)	4(3)
C(34)	62(3)	85(4)	47(3)	9(3)	-23(2)	-14(3)
C(35)	44(3)	68(3)	60(3)	20(2)	-11(2)	-1(2)
C(36)	44(2)	40(2)	43(2)	5(2)	5(2)	-1(2)
C(41)	31(2)	29(2)	31(2)	-5(2)	-5(2)	-5(2)
C(42)	44(2)	31(2)	36(2)	-3(2)	4(2)	-1(2)
C(43)	61(3)	49(3)	44(2)	4(2)	7(2)	-9(2)
C(44)	58(3)	36(2)	50(2)	11(2)	-8(2)	-8(2)
C(45)	47(2)	28(2)	55(2)	-5(2)	-11(2)	1(2)
C(46)	35(2)	35(2)	41(2)	-1(2)	-2(2)	-5(2)

Table 6.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for 01157s.

	x	y	z	U(eq)
H(3)	124	2218	8688	39
H(4)	1753	4102	8825	36
H(12)	1987	6449	9190	48
H(13)	2570	7580	9630	55
H(15)	-921	5358	9999	61
H(16)	-1517	4230	9560	50
H(32)	-132	2135	8170	59
H(33)	-1641	2453	7771	87
H(34)	-3847	3902	7793	77
H(35)	-4517	5070	8221	69
H(36)	-2978	4809	8623	51
H(42)	2222	5114	8332	44
H(43)	2317	7272	8046	62
H(44)	911	9420	8168	58
H(45)	-615	9379	8577	52
H(46)	-743	7216	8862	45