Nickel-Catalyzed Asymmetric Cross-Couplings of Secondary Allylic Chlorides and Planar-Chiral Compounds in Asymmetric Synthesis

By

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B.S., Chemistry, Seoul National University, 2000

M.S., Chemistry, Seoul National University, 2002

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for the Degree of

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IN ORGANIC CHEMISTRY

at the

Massachusetts Institute of Technology

September 2008

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August 21, 2008

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ABSTRACT

In Part I, nickel-catalyzed asymmetric carbon-carbon bond-forming reactions are described. A nickel/Pybox system effectively catalyzes regio- and enantioselective cross-couplings between racemic secondary allylic chlorides and readily available alkylzinc halides. This method is applied to generate two stereo centers in a formal total synthesis of fluvirucinine A_1.

In Part II, the use of planar-chiral compounds as ligands or catalysts in organic synthesis is described. A C_2-symmetric planar-chiral bipyridine is an efficient ligand for copper-catalyzed asymmetric [4+1]-cycloadditions between enones and diazoacetates to form 2,3-dihydrofurans. The highly substituted dihydrofurans are not only obtained in good stereoselectivity but also readily converted to other useful molecules. This method is applied to the first catalytic enantioselective synthesis of a deoxy-C-nucleoside.

The synthesis of new C_2-symmetric planar-chiral catalysts is described. The diastereoslective functionalization of ferrocene using a chiral directing group enables the formation of a number of amines in enantiopure form. These catalysts are tested as several asymmetric catalysts.

Thesis Supervisor: Gregory C. Fu

Title: Professor of Chemistry

Preface

Portions of this thesis have appeared in the following publications:

"Copper-Catalyzed Asymmetric [4+1] Cycloadditions of Enones with Diazo Compounds to Form Dihydrofurans" Son, S.; Fu, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 1046–1047.

"Nickel-Catalyzed Asymmetric Negishi Cross-Couplings of Secondary Allylic Chlorides with Alkylzincs" Son, S.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 2756-2757.

Acknowledgement

Looking back last five years in graduate school, they seem to have flown by. I still remember the nervous orientation day and the first organic tutorial class as if they happened just yesterday. However, I also remember that each and every day of those five years was full of excitement and disappointment, and I could not have made it to this point of my life without help from numerous people around me.

My deepest gratitude is to my parents who have endless love and tremendous confidence in me. Their support and encouragement helped me through tough moments during my graduate studies. I am eternally in debt to them for their love and sacrifices.

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Part I

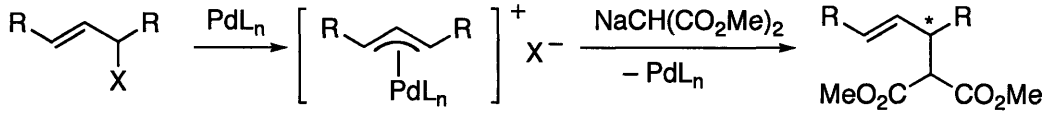
Nickel-Catalyzed Asymmetric Cross-Couplings

Chapter 1

Nickel-Catalyzed Regio- and Enantioselective Cross-Couplings of Secondary Allylic Chlorides with Alkylzinc Halides

A. Introduction

Metal-catalyzed asymmetric allylic alkylations (AAA) are one of the most investigated C-C bond-forming reactions.[1] A number of catalysts based on various transition metals have been developed, and the most successful results have been obtained with palladium, copper,[2] and nickel.[3] Among these, palladium-catalyzed allylations are not only the most well-studied but are also applied to syntheses of numerous complex molecules. The mechanism is believed to occur through a Pd-π-allyl complex, followed by direct attack of the nucleophile on the alkyl chain in the outer sphere of the complex to form a new C-C bond (eq 1). Although this transformation is highly efficient and stereoselective, the substrates are mainly limited to symmetrical allylic eletrophiles and soft nucleophiles (e.g., sodium malonate).



(1)

In contrast, asymmetric allylations catalyzed by copper and nickel incorporate hard nucleophiles, such as Grignard reagents or dialkylzincs. However, these highly reactive nucleophiles present certain limitations such as low functional-group compatibility. In addition, dialkylzinc reagents are not easily accessible but required in a large excess (e.g., 2–6 equiv) making the reaction inefficient.

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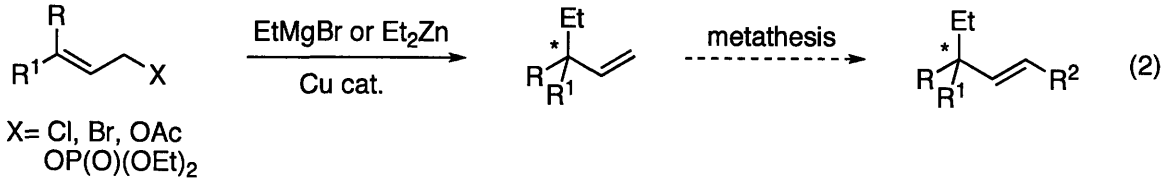
[1] For reviews, see: (a) Pfaltz, A.; Lautens, M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; Vol. 2, Chapter 24. (b) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395–422. See also: Kar, A.; Argade, N. P. *Synthesis* **2005**, 2995–3022.

[2] For reviews, see: (a) Alexakis, A.; Malan, C.; Lea, L.; Tissot-Croset, K.; Polet, D.; Falciola, C. *Chimia* **2006**, *60*, 124–130. (b) Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 4435–4439. For reactions with organozinc reagents, use of RZnX has been reported to be problematic (for examples, see: Dübner, F.; Knochel, P. *Angew. Chem., Int. Ed.* **1999**, *38*, 379–381 and Goldsmith, P. J.; Teat, S. J.; Woodward, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 2235–2237).

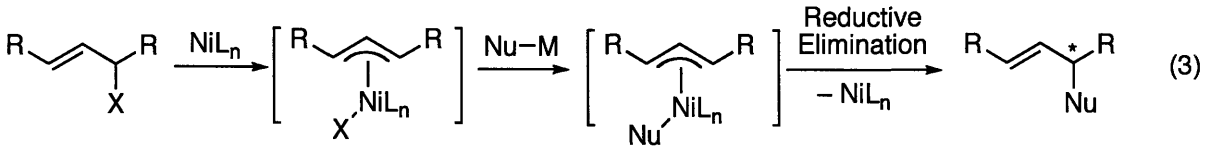
[3] For examples, see: (a) Consiglio, G.; Morandini, F.; Piccolo, O. *J. Chem. Soc., Chem. Commun.* **1983**, 112–114. (b) Gomez-Bengoa, E.; Heron, N. M.; Didiuk, M. T.; Luchaco, C. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 7649–7650.

In the case of copper-catalyzed reactions, primary allylic electrophiles are coupled with hard nucleophiles with S_N2' regioselectivity to form terminal olefins, which can be converted to disubstituted olefins by olefin metathesis (eq 2).



(2)

Nickel-catalyzed AAA is believed to form a π-allyl complex similar to the Pd cases. However, the nucleophile initially coordinates to the Ni center instead of to the alkyl chain, and the new C-C bond is formed after reductive elimination (eq 3). Since both reactants interact closely with the metal center when the new bond is formed, Ni-catalysis might be expected to have better control than palladium catalysis over the enantioselectivity. Nonetheless, only a few examples with good stereoselectivity have been reported, and these employed an excess of the Grignard reagent, with rather limited scope of electrophiles. There has been only moderate progress with more functional-group tolerant nucleophiles (e.g., alkylboron reagents).[4]

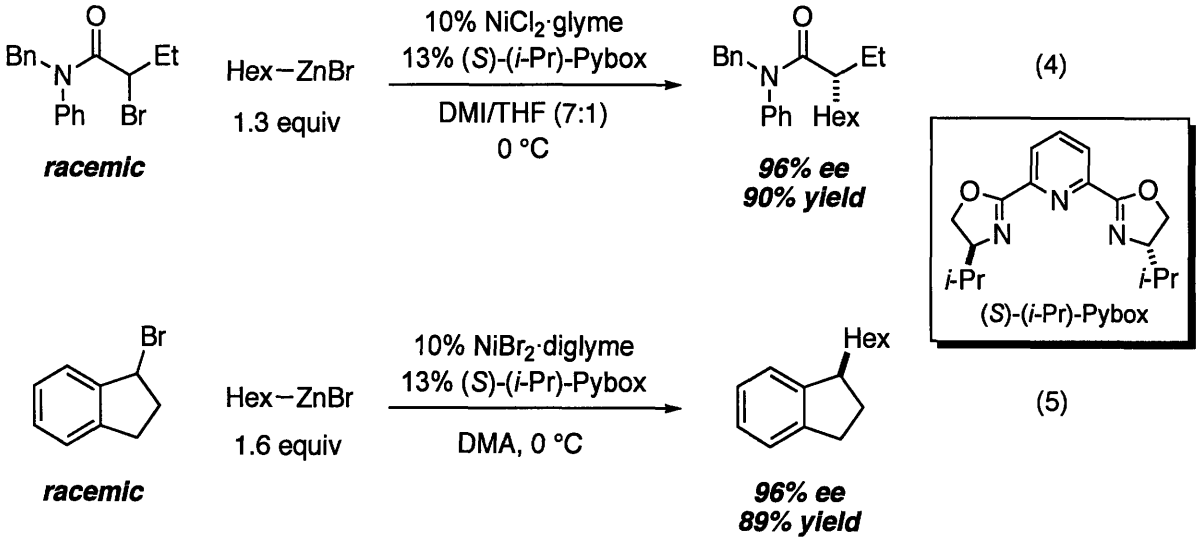


(3)

To complement these existing methods, development of an asymmetric allylic alkylation incorporating more functional-group tolerant hard nucleophiles with secondary electophiles in high regio- and stereoselectivity is needed.

[4] For examples, see: (a) Chung, K.-G.; Miyake, Y.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 15–18. (b) Chen, H.; Deng, M.-Z. *J. Organomet. Chem.* **2000**, *603*, 189–193. (c) Novak, A.; Fryatt, R.; Woodward, S. *Comptes Rendus Chimie* **2007**, *10*, 206–212.

Previously, our group has developed nickel-catalyzed enantioselective Negishi cross-couplings of secondary α-bromo amides and benzylic bromides (eq 4 and eq 5; DMI = 1,3-dimethyl-2-imidazolidinone).[5] In these reactions, racemic substrates reacted with primary alkylzinc halides (1.3–1.6 equiv),[6] which show good functional-group compatibility, to form the desired cross-coupling products in good yield and enantioselectivity. With these results as a starting point, we have developed a regio- and enantioselective allylic alkylation method complementary to existing methods.

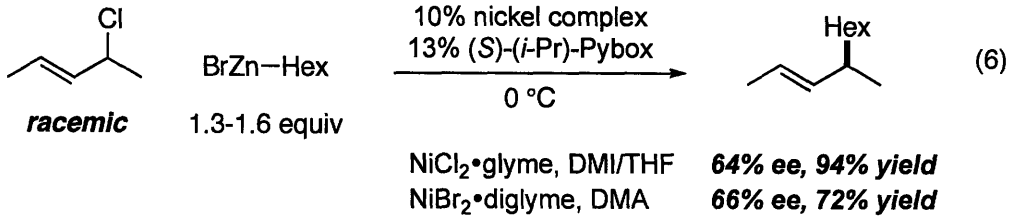


[5] (a) Fischer, C.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 4594–4595. (b) Arp, F. O.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 10482–10483.

[6] Huo, S. *Org. Lett.* **2003**, *5*, 423–425.

B. Results and Discussion

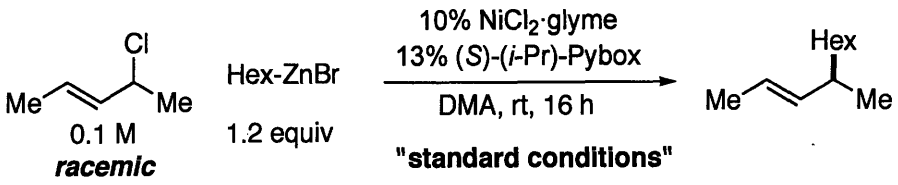
Unlike cross-couplings of α-bromoamides and benzylic bromides, allylic alkylation can have a regioselectivity issue. To simplify the initial investigation, we examined the reaction of "symmetrical" 4-chloropent-2-ene. Under the conditions that we had developed for α-bromoamides and benzylic bromides,[5] the allylic cross-coupling product was obtained in promising yield and enantioselectivity (eq 6).



(6)

Under the standard conditions in eq 7, we tested other allylic electrophiles (entries 2 and 3, Table 1). The allylic bromide produced the product with the same enantioselectivity as the allylic chloride but with slightly lower yield, probably due to its lower stability (entry 1 vs. 2). However, the allylic acetate, which is a typical substrate for Pd-catalyzed AAA, generated only a trace amount of product (entry 3). Investigation of other reaction parameters revealed that a DMF/DMA co-solvent system and lower temperature were slightly beneficial to enantioselectivity but detrimental to yield (entries 4 and 5). When these two conditions were combined, the ee increased to 78%, but the yield dropped to only 7% (entry 6).

Table 1. Evaluation of Reaction Parameters in Negishi Reactions of Secondary Allylic Electrophiles



entry	change from the standard conditions	yield (%)[a]	ee (%)[b]
1	none	85	66
2	Br instead of Cl	77	66
3	OAc instead of Cl	<2	—
4	0 °C instead of rt	46	72
5	DMA/DMF = 1 : 1	53	69
6	0 °C, DMA/DMF = 1 : 1	7	78

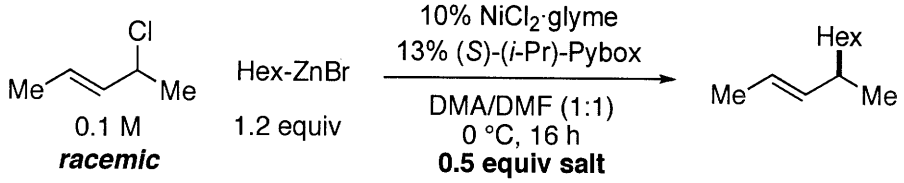
[a] Yield determined by GC versus an internal standard. [b] ee determined by chiral GC.

Thorough investigation of the reaction parameters, halide salts additives proved to be crucial to increase the reaction rate with little impact on ee (Table 2).[7] Almost identical results were obtained with various halide salts regardless of the identity of the cation or the anion, suggesting that simple ion exchange is not the origin of the increased reactivity. However, when a salt containing a non-coordinating anion was used, the yield increased only slightly, and the ee decreased to 66% (entry 8), indicating the importance of the coordinating ability of the anion. The yield could be further improved by increasing the amount of NaCl to two equiv (entry 3).[8] In terms of the role of halide salts, it is possible that halide salts enhance the reaction rate by increasing the ionic strength of the reaction medium or by activating the alkylzinc reagent.

[7] For a review of halide effects in transition-metal catalysis, see: Fagnou, K.; Lautens, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 26–47.

[8] Use of more than 2 equiv of NaCl was not beneficial to the reaction results, probably due to the limited solubility of NaCl under the reaction conditions.

Table 2. Effect of Halide Salt Additives on the Efficiency of a Negishi Reaction of a Secondary Allylic Chloride



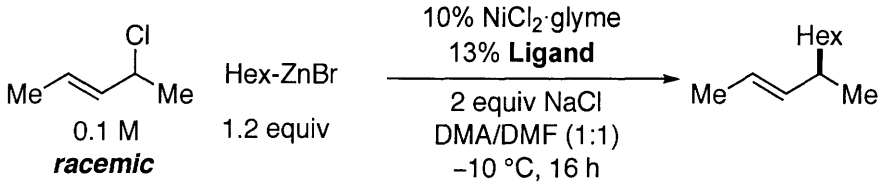
entry	additive	yield (%)[a]	ee (%)[b]
1	none	7	78
2	NaCl	34	77
3	NaCl (2.0 equiv)	93	76
4	NaBr	34	76
5	LiBr	27	76
6	KBr	35	76
7	CsBr	36	76
8	$NaBF_4$	15	66

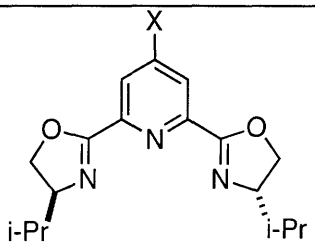
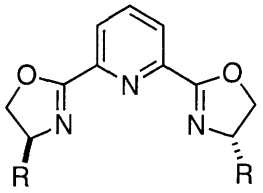
[a] Yield determined by GC versus an internal standard.
[b] ee determined by chiral GC.

Under these conditions, various Pybox ligands with different electronic and steric properties were examined (Table 3). When (*i*-Pr)-Pybox derivatives with different electronic properties[9] were tested, more electron-rich ligands generally exhibited lower reactivity (entries 1–4). When the steric environments around the coordination sites were modified by introducing other alkyl groups on the oxazoline rings, most of ligands gave enantioselectivity higher than 80% producing the best selectivity with $BnCH_2$-Pybox (entry 9), which was synthesized from commercially available compounds in two steps.[10] Even though the yield was slightly higher with a thioether containing ligand for this specific substrate (entry 8), $BnCH_2$-Pybox gave better results over a wide range of substrates.

[9] The para-substituted Pybox ligands were prepared according to a reported procedure: Nishiyama, H.; Yamaguchi, S.; Kondo, M.; Itoh, K. J. *J. Org. Chem.* **1992**, *57*, 4306–4309.
[10] The ligands in entries 5–9 of Table 3 were prepared from pyridine-2,6-dinitrile and aminoalcohols which were obtained by reduction of corresponding amino acids: Chelucci, G.; Deriu, S.; Pinna, G. A.; Saba, A.; Valenti, R. *Tetrahedron: Asymmetry* **1999**, *10*, 3803–3809.

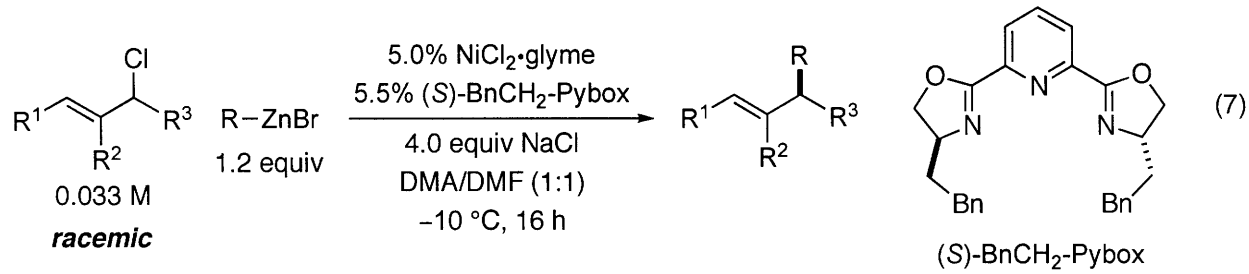
Table 3. Evaluation of Pybox Ligands with Different Electronic and Steric Properties on a Negishi Reaction of a Secondary Allylic Chloride



entry	Ligand		yield (%)[a]	ee (%)[b]
1		X = H	91	76
2		Cl	80	75
3		OMe	72	77
4		NMe_2	3	66
5		R = *i*-Bu	32	83
6		Bn	93	81
7		CH_2Cy	73	84
8		$CH_2CH_2SCH_3$	95	85
9		CH_2Bn	89	86

[a] Yield determined by GC versus an internal standard.
[b] ee determined by chiral GC.

After re-evaluation of the reaction parameters with $BnCH_2$-Pybox, the optimized conditions for enantioselective Negishi reactions of secondary allylic chlorides were obtained (eq 7). The diminished reactivity with lower catalyst loading could be recovered by adding more NaCl to the reaction mixture under more dilute conditions.

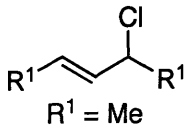
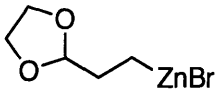
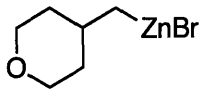
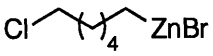
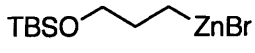
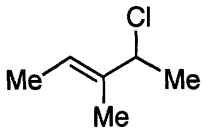
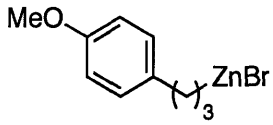


(7)

Under these standard conditions, various "symmetrical" allylic chlorides successfully react with a range of alkylzinc bromides (Table 4). Since racemic allylic electrophiles are used, we can postulate a mechanism involving a kinetic resolution of substrates to produce the highly enantio-enriched products. However, the combination of high yields and high ee's establishes that the two enantiomers of the substrate are transformed to the same enantiomer of the product with good enantioselectivity. With a sterically more demanding R^1 substituent, the stereoselectivity of the reaction decreases (entries 1–5). Therefore, unbranched alkyl-substituted allylic chlorides generally furnish good ee's (entries 1–4), but a diisopropyl-substituted substrate provides diminished stereoselectivity (entry 5). Increased steric demand on the nucleophile by β-branching also slows down the reaction rate, but in this case the reactivity can be recovered by employing a higher DMA/DMF ratio (entry 3; 9:1).[11] Excellent enantioselectivity can be obtained with the Ni/Pybox catalyst for a 1,2,3-trisubstituted allylic chloride (entry 6). Several functional groups, including an unactivated primary alkyl chloride (entry 4), can be incorporated without complication.

[11] Under the same conditions as in eq 7, 30% of the product was obtained. The reaction was complete after 72 h, furnishing 80% of the product.

Table 4. Enantioselective Negishi Reactions of "Symmetrical" Allylic Chlorides with Alkylzinc Reagents (eq 7)

entry	allylic chloride	R–ZnBr	yield (%)[a]	ee (%)
1	 R^1 = Me	*n*-Hex–ZnBr	95[b]	87
2	Me		93	90
3[c]	*n*-Pr		81	85
4	*n*-Pr		81	79
5	*i*-Pr		57	69
6			54	98

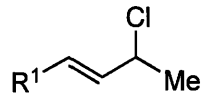
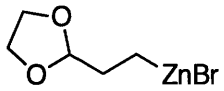
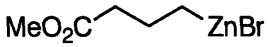
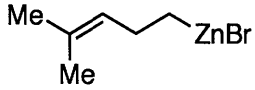
All data are the average of two experiments. [a] Isolated yield. [b] The product is volatile. The yield was determined by GC versus an internal standard. [c] Solvent: DMA/DMF (9:1).

Next, we examined enantioselective cross-couplings of unsymmetrical allylic chlorides, with which regioselectivity can be an issue (Table 5). Indeed, when two substituents are similar in size as in an *n*-butyl and a methyl group, regioselectivity is modest (1.9:1 selectivity in favor of reaction closer to the methyl group; entry 1); however, the combined yield is excellent, and the ee's are high for both regioisomers. For an array of other unsymmetrical allylic electrophiles, the reaction proceeds with outstanding regioselectivity (>20:1; entries 2-7). For an *i*-Pr/Me and a *t*-Bu/Me-substituted substrate, regioisomeric mixtures of the allylic chlorides[12] produce the cross-coupling products with excellent regioselectivity (entries 2 and 3). This contrasts with Cu-catalyzed allylic substitutions, which require regioisomerically pure allylic

[12] For *i*-Pr/Me and *t*-Bu/Me substrates, the ratios were respectively 1.4:1 and 2.4:1 in favor of chloride proximal to the methyl group.

electrophiles due to a strong preference to form regioisomers through S_N2' substitution.[2] Various electron-withdrawing groups can be incorporated on the allylic electrophile, and the cross-couplings of these conjugated allylic electrophiles proceed to form a new C-C bond predominantly at the γ position with high enantioselection (≥90% ee; entries 4–7).

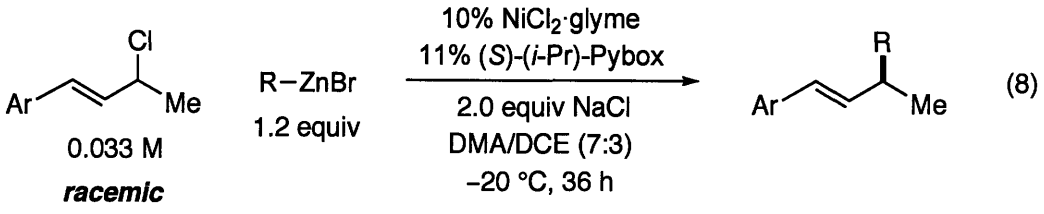
Table 5. Enantioselective Negishi Reactions of Unsymmetrical Allylic Chlorides with Alkylzinc Reagents (eq 7)

entry	allylic chloride	R–ZnBr	yield (%)[a]	ee (%)
1[b,c]	 R^1 = *n*-Bu		97	83
2[c]	*i*-Pr		95	84
3[c]	*t*-Bu		85	81
4	CO_2Et		86	96
5	$CONEt_2$	Et–ZnBr	57	91
6	CON(OMe)Me		91	93
7	$PO(OEt)_2$	*n*-Hex–ZnBr	63	90

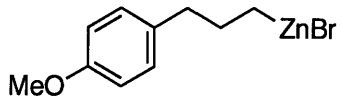
All data are the average of two experiments. Regioselectivity: >20:1, except for entry 1. [a] Isolated yield. [b] Regioselectivity: 1.9:1; ee of the minor regioisomer: 88%. [c] The allylic chloride is a mixture of regioisomers.

Negishi reactions of aryl-substituted allylic chlorides require slight modification of the standard conditions in eq 7 to obtain better reactivity (eq 8). With commercially available (*i*-Pr)-Pybox, the cross-couplings of aryl-substituted electrophiles proceed with excellent regioselectivity (>20:1) and ee (≥94%), albeit with modest yield. The regioselectivity of these reactions are complementary to Cu-catalyzed substitutions, which form a new C-C bond proximal to an aryl group.

Table 6. Enantioselective Negishi Reactions of Aryl-substituted Allylic Chlorides with Alkylzinc Reagents

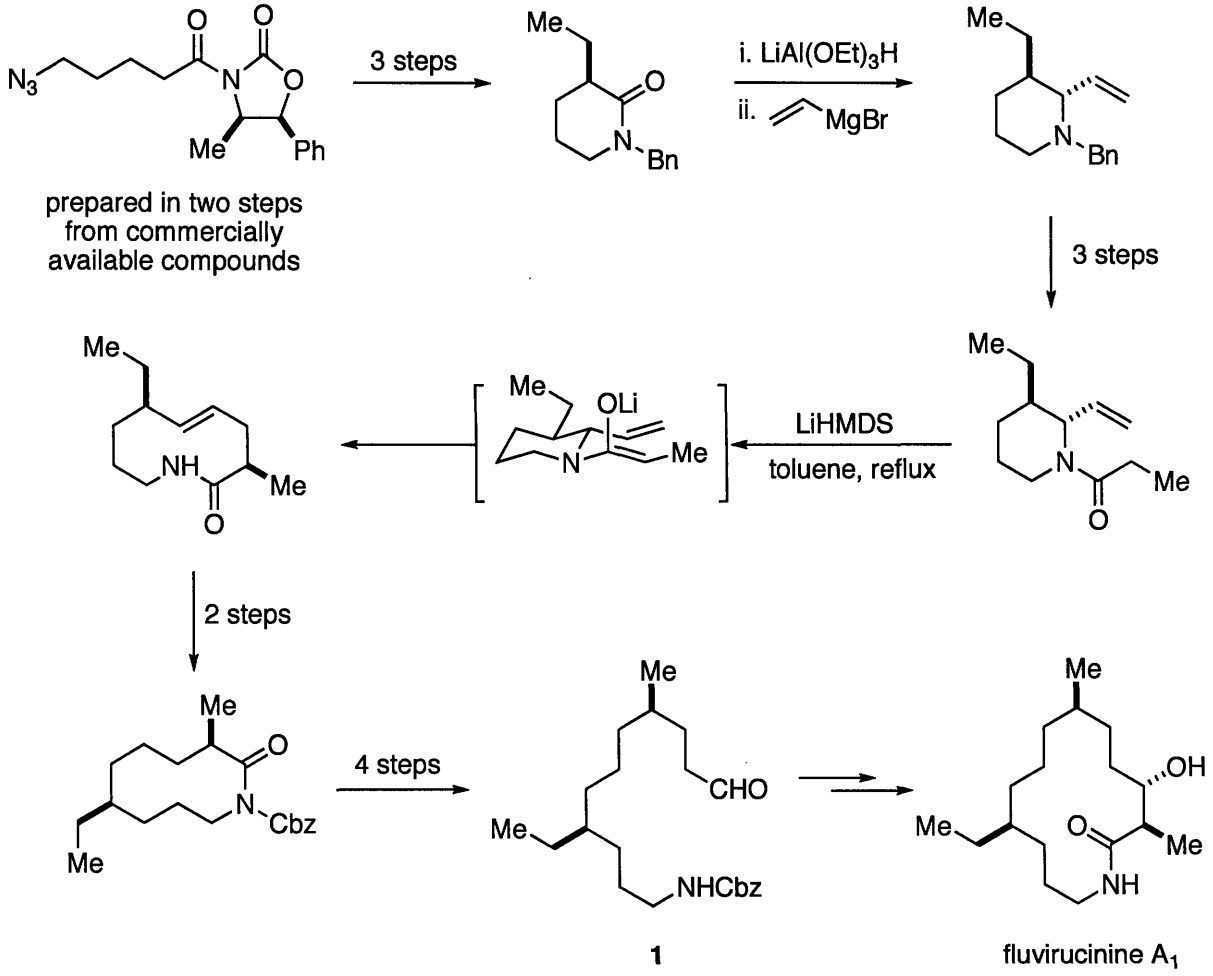


(8)

entry	Ar	R–ZnBr	yield (%)[a]	ee (%)
1	Ph	Hex–ZnBr	56	97
2	3-(CN)C_6H_4	Cl$(CH_2)_4$ZnBr	37	94
3	4-ClC_6H_4		55	97

All data are the average of two experiments. Regioselectivity: >20:1.
[a] Isolated yield.

We have applied this Ni/Pybox-catalyzed enantioselective cross-couplings to a formal synthesis of fluvirucinine A_1, which is a core unit of the antibiotic fluvirucin A_1 with inhibitory activity against influenza A virus.[13] Two total syntheses of fluvirucinine A_1 have been reported, including one by Suh in 1999.[14] In his report, Suh and his coworkers prepared fluvirucinine A_1, via aldehyde **1** as shown in Scheme 1. Using stoichiometric chiral-auxiliary chemistry, they installed one stereocenter and used this to introduce the second stereocenter through diastereoselective transformations.

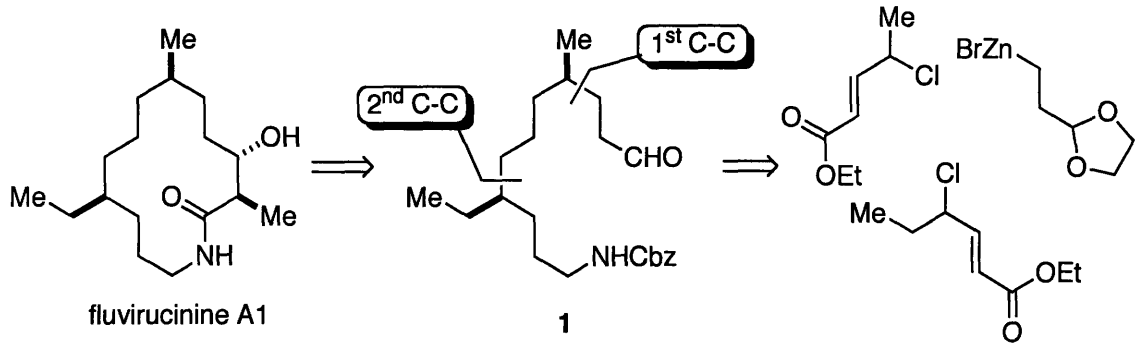


Scheme 1. Suh's Synthesis of Fluvirucinine A_1

[13] (a) Naruse, N.; Tenmyo, O.; Kawauo, K.; Tomita, K.; Ohgusa, N.; Miyaki, T.; Konishi, M.; Oki, T. *J. Antibiot.* **1991**, *44*, 733–740. (b) Naruse, N.; Tsuno, T.; Sawada, Y.; Konishi, M.; Oki, T. *J. Antibiot.* **1991**, *44*, 741–740. (c) Naruse, N.; Konishi, M.; Oki, T.; Inouye, Y.; Kakisawa, H. *J. Antibiot.* **1991**, *44*, 756–761. (d) Tomita, K.; Oda, N.; Hoshino, Y.; Ohgusa, N.; Chikazawa, H. *J. Antibiot.* **1991**, *44*, 940–948.

[14] (a) Suh, Y.-G.; Kim, S.-A.; Jung, J.-K.; Shin, D.-Y.; Min, K.-H.; Koo, B.-A.; Kim, H.-S. *Angew. Chem., Int. Ed.* **1999**, *38*, 3545–3547. (b) Liang, B.; Negishi, E. *Org. Lett.* **2008**, *10*, 193–195.

We envisioned that aldehyde **1** could be efficiently assembled using our Ni/Pybox-catalyzed Negishi reaction of allylic electrophiles (Scheme 2). Through two cross-coupling reactions of three components, two tertiary stereoenters can be installed from racemic allylic chlorides in a catalytic enantioselective fashion.



Scheme 2. Retrosynthesis of Intermediate **1**

The cross-coupling of racemic allylic chloride **2**, which can be prepared in two steps from commercially available ethyl (E)-4-oxo-2-butenoate, proceeds to form **3** in excellent yield, regioselectivity, and ee. Direct reduction of intermediate **3** to a saturated primary alcohol using various reagents, including copper hydride, was low yielding. But this problem can be solved by adding $LiAlH_4$ directly to the reaction mixture after hydrogenation is complete. Intermediate **4**, obtained after bromination, can be converted to the organozinc reagent and coupled with a secondary allylic chloride in good yield, regio- and stereoselectivity. Reduction of intermediate **5** produces the corresponding primary alcohol, and direct amination of the alcohol[15] followed by acidic workup to remove the acetal group furnishes aldehyde **1** in 8 steps overall.

[15] (a) Wood, M. R.; Kim, J. Y.; Books, K. M. *Tetrahedron Lett.* **2002**, *43*, 3887–3890. (b) Nicolaou, K. C.; Snyder, S. A.; Longbottom, D. A.; Nalbandian, A. Z.; Huang, X. *Chem. Eur. J.* **2004**, *10*, 5581–5606.

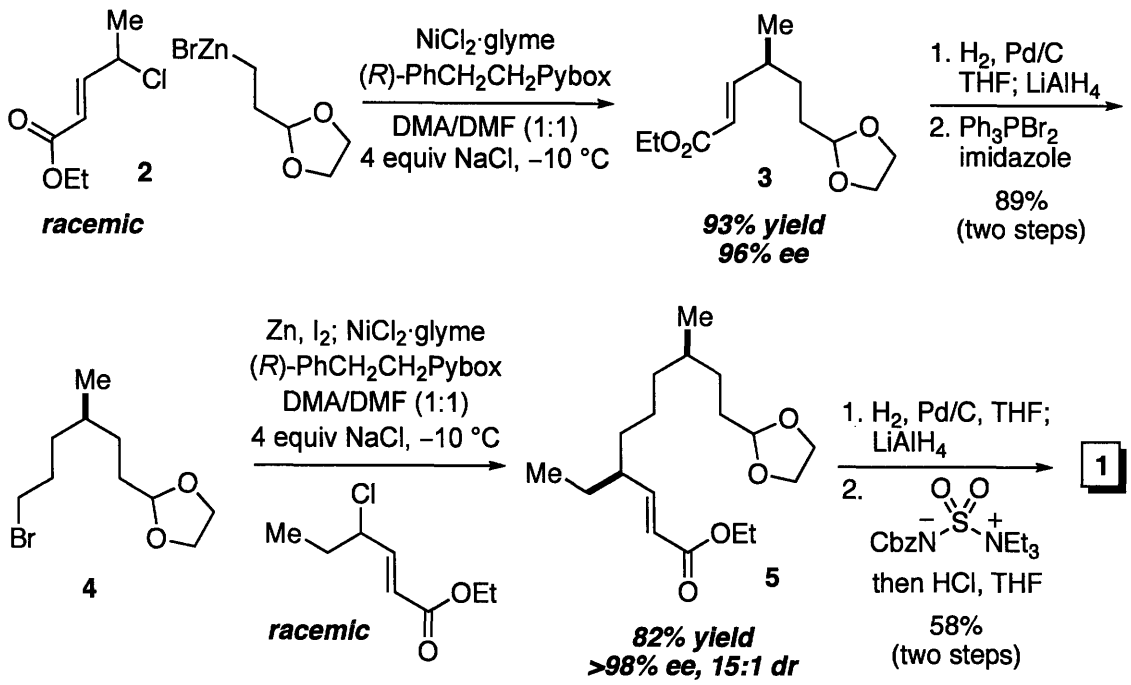


Figure 2. Synthesis of Intermediate **1**

C. Conclusions

In conclusion, we have developed an effective Ni/Pybox catalyst for regio- and enantioselective Negishi cross-couplings of racemic secondary allylic chlorides. This method complements previously developed asymmetric allylic alkylations catalyzed by other metals in several aspects. First, reactions with only a slight excess (1.2 equiv) of alkylzinc reagents as functional-group tolerant hard nucleophiles furnish the desired product in good yield and ee. Second, the regioselecivity of the reaction is independent of the regioisomeric ratio of the allylic chlorides. In addition, we have applied this method in two key steps of a formal synthesis of fluvirucinine A_1.

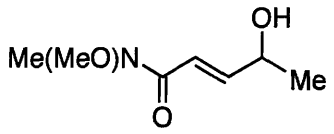
D. Experimental

1. General

HPLC analyses were carried out on an Agilent 1100 series system with Daicel Chiralpak® columns in hexane/isopropanol mixtures. GC analyses were performed on a Hewlett-Packard HP 6850 Series system with a Chrompack capillary column (CP Chirasil-Dex CB; 25m x 0.25 mm x 0.25 mm).

N,N-Dimethylacetamide (DMA; anhydrous in a Sure-Seal® bottle; Fluka), *N,N*-dimethylformamide (DMF; anhydrous in a Sure-Seal® bottle; Fluka), NaCl (anhydrous, Aldrich), Zn (Alfa-Aesar) and $NiCl_2$·glyme (Strem), were used as received. $BnCH_2$-Pybox was prepared according to a literature procedure.[10]

2. Preparation of Allylic Alcohols



(±)-(*E*)-4-Hydroxy-*N*-methoxy-*N*-methylpent-2-enamide. Activated 4Å molecular sieves (2.0 g) and $LiOH·H_2O$ (369 mg, 8.8 mmol) were added to a solution of diethyl (*N*-methoxy-*N*-methylcarbamoylmethyl)phosphonate (2.11 g, 8.8 mmol) in dry THF (6 mL), and the mixture was stirred under argon for 20 min at 40 °C. Then, the mixture was cooled to 0 °C, and 2-(*tert*-butyldimethylsilyloxy)propanal in THF (5 mL) was added. The mixture was stirred for 1 h at 0 °C and then overnight at room temperature. Next, water (30 mL) was added to the mixture, and the aqueous solution was extracted with Et_2O (30 mL x 3). The organic layer was dried over $MgSO_4$, filtered, and concentrated. The product was dissolved in *i*-PrOH (15 mL), and the solution was cooled to 0 °C. Concentrated HCl (0.8 mL) was added dropwise, and the resulting mixture was stirred overnight at room temperature. Next, solid $NaHCO_3$ was added until gas evolution ceased. Water (20 mL) and CH_2Cl_2 (20 mL) were added, and the aqueous layer was extracted with CH_2Cl_2 (20 mL x 2). The organic layer was dried over

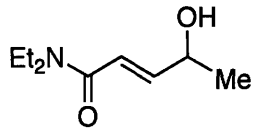
Na_2SO_4, filtered, and concentrated. The product was purified by flash chromatography with hexane/Et_2O (1:3) to give the title compound (622 mg, 3.9 mmol; 44%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.98 (dd, J = 15.4, 4.6 Hz, 1H), 6.60 (d, J = 15.5 Hz, 1H), 4.56-4.49 (m, 1H), 3.71 (s, 3H), 3.25 (s, 3H), 2.19 (d, J = 4.2 Hz, 1H), 1.34 (d, J = 6.6 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.9, 150.1, 117.0, 67.6, 62.0, 32.6, 23.1;

IR (film) 3406, 2973, 2937, 1662, 1622, 1424, 1386, 1151, 1002, 855, 802, 706 cm^{-1};

LCMS calcd for $C_7H_{14}NO_3$ ($M+H^+$) 160.1, found 160.0.



(±)-(*E*)-*N*-*N*-Diethyl-4-hyroxypent-2-enamide. The above procedure was followed.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.86 (dd, J = 15.0, 4.6 Hz, 1H), 6.38 (d, J = 15.0 Hz, 1H), 4.51-4.40 (m, 1H), 3.39 (q, J = 7.0 Hz, 2H), 3.35 (q, J = 7.0 Hz, 2H), 2.28 (br s, 1H), 1.29 (d, J = 6.6 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 148.6, 118.7, 67.7, 42.4, 41.0, 23.2, 15.0, 13.3;

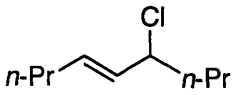
IR (film) 3383, 2975, 2934, 2875, 1662, 1603, 1485, 1449, 1363, 1278, 1138, 1074, 976, 852, 808, 717 cm^{-1};

LCMS calcd for $C_9H_{18}NO_2$ ($M+H^+$) 172.1, found 172.1.

3. Preparation of Allylic Chlorides

Representative Procedure A: A mixture of the allylic alcohol (17.1 mmol) and pyridine (0.14 mL, 1.7 mmol) was added dropwise to PCl_3 (0.55 mL, 6.3 mmol) at 0 °C. The reaction mixture was slowly warmed to room temperature, and then it was stirred for 2 h. The top (organic) layer was separated, and the product was isolated by fractional distillation.

Representative Procedure B: Cl_2PPh_3 (6.0 g, 18 mmol) was added dropwise to a solution of the allylic alcohol (15.0 mmol) and imidazole (1.22 g, 18.0 mmol) in CH_2Cl_2 (30 mL). The reaction mixture was stirred for 2 h at room temperature, and then the solvent was removed and the residue was purified by flash chromatography.



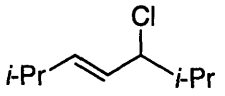
(±)-(*E*)-6-Chloronon-4-ene. This compound was prepared according to Representative Procedure A (distilled at ~31 °C at 0.5 mm Hg).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.68 (dt, *J* = 15.2, 6.7 Hz, 1H), 5.52 (ddt, *J* = 15.2, 8.7, 1.3 Hz, 1H), 4.36 (dt, *J* = 8.7, 7.0 Hz, 1H), 2.10-1.96 (m, 2H), 1.87-1.70 (m, 2H), 1.51-1.36 (m, 4H), 0.93 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 133.6, 131.4, 63.8, 41.1, 34.2, 22.3, 20.1, 13.8, 13.7;

IR (film) 2961, 2933, 2874, 1666, 1466, 1380, 965 cm^{-1};

GCMS calcd for $C_9H_{17}Cl$ (M^+) 160, found 160.



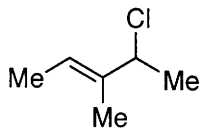
(±)-(*E*)-5-Chloro-2,6-dimethylhept-3-ene. This compound was prepared according to Representative Procedure A (distilled at ~26 °C at 0.5 mm Hg).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.65 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.52 (ddd, *J* = 15.3, 9.1, 1.2 Hz, 1H), 4.20 (dd, *J* = 9.1, 5.8 Hz, 1H), 2.32 (doublet of octets, *J* = 6.7, 1.2 Hz, 1H), 1.96 (doublet of octets, *J* = 6.7, 0.8 Hz, 1H), 1.01 (dd, *J* = 6.8, 0.8 Hz, 6H), 0.99 (dd, *J* = 9.2, 6.7 Hz, 6H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.2, 126.5, 70.7, 35.6, 30.8, 22.38, 22.35, 19.4, 19.1;

IR (film) 2963, 2934, 2873, 1665, 1468, 1386, 1368, 970, 713 cm^{-1};

GCMS calcd for $C_9H_{17}Cl$ (M^+) 160, found 160.



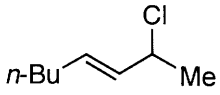
(±)-(*E*)-4-Chloro-3-methylpent-2-ene. This compound was prepared according to Representative Procedure A (distilled at ~32 °C at 20 mm Hg).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.59 (q, *J* = 6.8 Hz, 1H), 4.60 (q, *J* = 6.7 Hz, 1H), 1.72 (pentet, *J* = 1.1 Hz, 3H), 1.63 (dq, *J* = 6.8, 1.0 Hz, 3H), 1.59 (d, *J* = 6.8 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.9, 122.6, 65.1, 24.0, 13.5, 11.3;

IR (film) 2991, 2927, 2864, 1666, 1445, 1375, 1232, 1076, 830, 761, 655 cm^{-1};

GCMS calcd for $C_6H_{11}Cl$ (M^+) 118, found 118.



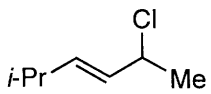
(±)-(*E*)-2-Chlorooct-3-ene. This compound was prepared according to Representative Procedure A as a 1.2:1 mixture of the title compound and (±)-(*E*)-4-chlorooct-2-ene (distilled at ~46 °C at 6 mm Hg).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.76-5.51 (m, 2H, mixture), 4.54 (pentet, *J* = 6.9 Hz, 0.55H, major), 4.34 (dt, *J* = 8.6, 7.0 Hz, 0.45H, minor), 2.04 (q, *J* = 6.8 Hz, 1.10H, major), 1.85-1.74 (m, 0.90H, minor), 1.72 (dd, *J* = 6.4, 1.5 Hz, 1.35H, minor), 1.59 (d, *J* = 6.6 Hz, 1.65H, major), 1.47-1.27 (m, 4H, mixture), 0.94-0.87 (m, 3H, mixture);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 132.8, 132.5, 132.3, 128.4, 63.5, 58.8, 38.8, 31.8, 31.2, 28.9, 25.7, 22.37, 22.36, 17.7, 14.2, 14.1;

IR (film) 3033, 2959, 2930, 2873, 2862, 1668, 1466, 1452, 1378, 1221, 1012, 964 cm^{-1};

GCMS calcd for $C_8H_{15}Cl$ (M^+) 146, found 146.



(±)-(*E*)-2-Chloro-5-methylhex-3-ene. This compound was prepared according to Representative Procedure A as a 1.4:1 mixture of the title compound and (±)-(*E*)-4-

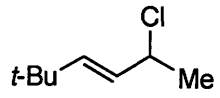
chloro-5-methylhex-2-ene (distilled at ~30 °C at 6 mm Hg).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.74-5.63 (m, 1H, mixture), 5.60-5.50 (m, 1H, mixture), 4.54 (pentet, J = 6.7 Hz, 0.6H, major), 4.21 (dd, J = 9.1, 5.7 Hz, 0.4H, minor), 2.30 (doublet of octets, J = 6.7, 1.0 Hz, 0.6H, major), 1.96 (octet, J = 6.7 Hz, 0.4H, minor), 1.73 (dd, J = 6.3, 1.4 Hz, 1.3H, minor), 1.59 (d, J = 6.6 Hz, 1.7H, major), 1.00-0.97 (m, 6H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.5, 130.6, 129.5, 129.1, 70.6, 58.9, 35.5, 30.6, 25.7, 22.22, 22.21, 19.4, 19.1, 17.8;

IR (film) 2966, 2931, 2873, 1665, 1467, 1386, 1212, 1013, 966 cm^{-1};

GCMS calcd for $C_7H_{13}Cl$ (M^+) 132, found 132.



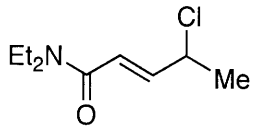
(±)-(*E*)-5-Chloro-2,2-dimethylhex-3-ene. This compound was prepared according to Representative Procedure A as a 2.4:1 mixture of the title compound and (±)-(*E*)-4-chloro-5,5-dimethylhex-2-ene (distilled at ~45 °C at 30 mm Hg).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.70 (dd, J = 15.5, 0.7 Hz, 0.7H, major), 5.69-5.56 (m, 0.6H, minor), 5.49 (dd J = 15.5, 8.1 Hz, 0.7H, major), 4.54 (dq, J = 6.7, 0.7 Hz, 0.7H, major), 4.15 (d, J = 9.2 Hz, 0.3H, minor), 1.73 (dd, J = 6.0, 1.0 Hz, 0.9H, minor), 1.59 (d, J = 6.6 Hz, 2.1H, major), 1.02 (s, 6.3H, major), 1.00 (s, 2.7H, minor);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.3, 129.6, 129.5, 127.4, 75.0, 59.2, 36.1, 33.0, 29.5, 26.9, 25.9, 17.8;

IR (film) 3035, 2963, 2868, 1660, 1477, 1464, 1446, 1365, 1266, 1222, 1195, 1010, 967, 646 cm^{-1};

GCMS calcd for $C_8H_{15}Cl$ (M^+) 146, found 146.



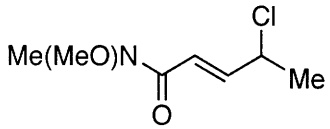
(±)-(*E*)-4-Chloro-*N*,*N*-diethylpent-2-enamide. The compound was prepared according to Representative Procedure B (eluant for chromatography: pentane/Et_2O 1:1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.91 (dd, J = 14.8, 6.9 Hz, 1H), 6.44 (dd J = 14.8, 1.1 Hz, 1H), 4.68 (doublet of pentets, J = 6.8, 1.1 Hz, 1H), 3.50-3.38 (m, 4H), 1.67 (d, J = 6.8 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.0, 144.5, 121.4, 56.1, 42.5, 41.1, 25.0, 15.1, 13.3;

IR (film) 2977, 2933, 1663, 1617, 1432, 1276, 909, 733 cm^{-1};

GCMS calcd for $C_9H_{16}ClNO$ (M^+) 189, found 189.



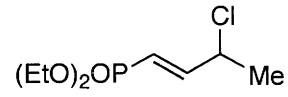
(±)-(*E*)-4-Chloro-*N*-methoxy-*N*-methylpent-2-enamide. The compound was prepared according to Representative Procedure B (eluant for chromatography: pentane/Et_2O 1:1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.97 (dd, J = 15.2, 7.1 Hz, 1H), 6.62 (d J = 15.2 Hz, 1H), 4.68 (doublet of pentets, J = 6.9, 1.0 Hz, 1H), 3.73 (s, 3H), 3.26 (s, 3H), 1.66 (d, J = 6.8 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.0, 146.0, 119.4, 62.1, 55.7, 32.6, 24.8;

IR (film) 2975, 2938, 1667, 1638, 1444, 1420, 1385, 1180, 1000, 978, 707 cm^{-1};

GCMS calcd for $C_7H_{12}ClNO_2$ (M^+) 177, found 177.



(±)-(*E*)-Diethyl 3-chlorobut-1-enylphosphonate. The compound was prepared according to Representative Procedure B (eluant for chromatography: Et_2O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.78 (ddd, J = 21.1, 16.8, 10.6 Hz, 1H), 5.93 (ddd, J = 18.2, 16.9, 1.3 Hz, 1H), 4.60 (triplet of pentets, J = 6.6, 1.7 Hz, 1H), 4.12 (pentet, J = 7.1 Hz, 4H), 1.65 (d, J = 6.8 Hz, 3H), 1.36 (dt, J = 7.0, 0.5 Hz, 6H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.3 (d, J_{CP} = 6.4 Hz), 118.1 (d, J_{CP} = 186.3 Hz), 62.21 (d, J_{CP} = 6.4 Hz), 62.17 (d, J_{CP} = 6.3 Hz), 56.1 (d, J_{CP} = 5.1 Hz), 24.3, 16.6, 16.5;

IR (film) 2984, 2933, 2908, 1633, 1445, 1393, 1246, 1025, 968, 847 cm^{-1};

GCMS calcd for $C_8H_{16}ClO_3P$ (M^+) 226, found 226.

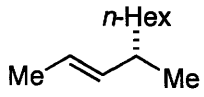
4. Negishi Cross-Coupling Reactions

Preparation of the organozinc reagents:[5] A 25-mL Schlenk tube was charged with zinc powder (1.47 g, 22.5 mmol) and heated to 70 °C under high vacuum for 30 min. After back-filling with argon, iodine (95 mg, 0.38 mmol) and DMA (to give a total volume of 15 mL) were added, and the resulting mixture was stirred until the red color of iodine had faded. Then, the allylic chloride (15 mmol; freshly distilled) was added. The colorless reaction mixture was allowed to stir for 12 h at 70 °C, and then the mixture was cooled to room temperature. The gray solution was passed through an Acrodisc® and stored under nitrogen in a dry container.

These solutions of organozinc halides can be stored at room temperature for several weeks without deterioration.

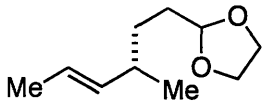
General Procedure: In the air, a 40-mL glass vial was charged with $NiCl_2$·glyme (11.0 mg, 0.050 mmol), (*R*)-BnCH_2-Pybox (23.4 mg, 0.055 mmol), and NaCl (234 mg, 4.0 mmol) and fitted with a septum cap. The vial was evacuated and then back-filled with Ar (three cycles). DMA (13.8 mL) and DMF (15.0 mL) were added, followed by the allylic chloride (1.0 mmol). The resulting mixture was cooled to –10 °C. Next, the organozinc solution (~1.0 M in DMA; 1.2 mL, 1.2 mmol) was added in a single portion to the mixture, which was stirred for 24 h at –10 °C. The reaction mixture was then diluted with water (30 mL) and extracted with Et_2O (30 mL x 3). The organic layer was dried over $MgSO_4$ and concentrated, and the residue was purified by flash chromatography.

A second run was conducted with (*S*)-BnCH_2-Pybox.



(*S,E*)-4-Methyldec-2-ene (Table 4, entry 1). The compound was prepared according to the General Procedure with (±)-(*E*)-4-chloropent-2-ene (105 mg, 1.0 mmol) and the organozinc reagent (~1.2 M in DMA; 1.00 mL, 1.2 mmol). The yield was determined by GC versus *n*-hexadecane as an internal standard: run 1, 94% yield, 87% ee; run 2, 96% yield, 87% ee.

The ee was determined by chiral GC: CP Chirasil-Dex CB, t_r (major) 5.4 min, t_r (minor) 5.3 min; temperature: 90 °C; 1.0 mL/min.



(+)-(*S,E*)-2-(3-Methylhex-4-enyl)-1,3-dioxolane (Table 4, entry 2). The compound was prepared according to the General Procedure with (±)-(*E*)-4-chloropent-2-ene (105 mg, 1.0 mmol) and the organozinc reagent (~1.4 M in DMA; 0.86 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O 10:1), the title compound was isolated as a colorless oil: run 1, 155 mg (91%; 89% ee); run 2, 160 mg (94%; 91% ee).

$[\alpha]^{22}_D$ = +12.6 (c = 2.34, $CHCl_3$);

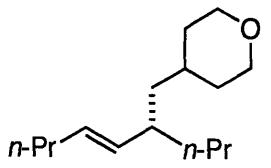
^1H NMR ($CDCl_3$, 400 MHz) δ 5.39 (ddq, *J* = 15.2, 6.2, 0.5 Hz, 1H), 5.26 (ddq, *J* = 15.2, 7.7, 1.3 Hz, 1H), 4.83 (t, *J* = 4.8 Hz, 1H), 4.01-3.92 (m, 2H), 3.89-3.81 (m, 2H), 2.07 (septet, *J* = 7.0 Hz, 1H), 1.73-1.57 (m, 5H), 1.43-1.28 (m, 2H), 0.97 (d, *J* = 6.7 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.1, 123.7, 105.0, 65.04, 65.03, 36.9, 32.0, 31.4, 21.1, 18.1;

IR (film) 2955, 2927, 2878, 1453, 1410, 1377, 1142, 1044, 967 cm^{-1};

GCMS calcd for $C_{10}H_{18}O_2$ (M^+) 170, found 170.

The ee was determined by chiral GC: CP Chirasil-Dex CB, t_r (major) 50.7 min, t_r (minor) 51.2 min; temperature: 80 °C; 1.0 mL/min.



(+)-(*S,E*)-4-(2-Propylhept-3-enyl)tetrahydro-2*H*-pyran (Table 4, entry 3). The compound was prepared according to the General Procedure with (±)-(*E*)-6-chloronon-4-ene (161 mg, 1.0 mmol) and the organozinc reagent (~1.8 M in DMA; 0.66 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O 30:1), the title compound was isolated as a colorless oil: run 1, 180 mg (80%; 86% ee); run 2, 182 mg (81%; 84% ee).

$[\alpha]^{22}_D$ = +23 (c = 2.1, $CHCl_3$);

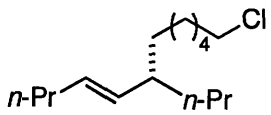
^1H NMR ($CDCl_3$, 400 MHz) δ 5.31 (dt, *J* = 15.2, 6.8 Hz, 1H), 5.05 (ddt, *J* = 15.2, 9.1, 1.1 Hz, 1H), 3.96-3.91 (m, 2H), 3.34 (ddt, *J* = 14.9, 12.1, 2.2 Hz, 2H), 2.08-1.97 (m, 1H), 1.98 (dq, *J* = 6.8, 1.1 Hz, 2H), 1.65-1.60 (m, 1H), 1.52-1.48 (m, 2H), 1.41-1.11 (m, 10H), 0.89 (t, *J* = 7.3 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.0, 130.4, 68.40, 68.36, 43.1, 39.4, 38.4, 34.9, 34.2, 32.8, 32.5, 23.0, 20.5, 14.4, 13.8;

IR (film) 2958, 2872, 2840, 2757, 2712, 1465, 1445, 1386, 1378, 1236, 1153, 1108, 1014, 970, 849 cm^{-1};

GCMS calcd for $C_{15}H_{28}O$ (M^+) 224, found 224.

The ee was determined by chiral GC: CP Chirasil-Dex CB, t_r (major) 38.3 min, t_r (minor) 37.6 min; temperature: 108 °C; 1.0 mL/min.



(+)-(*S,E*)-12-Chloro-6-propyldodec-4-ene (Table 4, entry 4). The compound was prepared according to the General Procedure with (±)-(*E*)-6-chloronon-4-ene (161 mg, 1.0 mmol) and the organozinc reagent (~0.9 M in DMA; 1.3 mL, 1.2 mmol). After purification by flash chromatography (hexanes), the title compound was isolated as a colorless oil: run 1, 196 mg (80%; 78% ee); run 2, 200 mg (81%; 79% ee).

$[\alpha]^{22}_D$ = +1.1 (c = 3.0, $CHCl_3$);

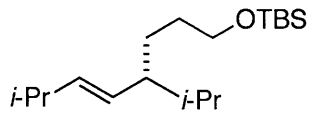
^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.31 (dt, J = 15.2, 6.7 Hz, 1H), 5.26 (ddt, J = 15.2, 8.8, 1.3 Hz, 1H), 3.53 (t, J = 6.8 Hz, 2H), 1.97 (dq, J = 7.0, 1.2 Hz, 2H), 1.90-1.80 (m, 1H), 1.77 (pentet, J = 7.1 Hz, 2H), 1.43-1.36 (m, 4H), 1.35-1.13 (m, 10H), 0.89 (t, J = 7.3 Hz, 3H), 0.87 (t, J = 6.9 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.3, 130.2, 45.4, 42.8, 38.1, 35.7, 34.9, 32.9, 29.2, 27.3, 27.1, 23.1, 20.6, 14.4, 13.9;

IR (film) 2957, 2928, 2859, 1465, 1378, 969, 727 cm^{-1};

GCMS calcd for $C_{15}H_{29}Cl$ (M^+) 244, found 244.

The ee was determined of 8-chloro-2-propyloctyl 4-nitrobenzoate [obtained by ozonolysis, reduction, and then benzoylation] by HPLC on an IA column (hexanes/isopropanol 99:1, 0.5 mL/min) with t_r (major) 19.9 min, t_r (minor) 20.8 min.



(+)-(*R*,*E*)-*tert*-Butyl(4-isopropyl-7-methyloct-5-enyloxy)dimethylsilane (Table 4, entry 5). The compound was prepared according to the General Procedure with (±)-(*E*)-5-chloro-2,6-dimethylhept-3-ene (161 mg, 1.0 mmol) and the organozinc reagent (~1.0 M in DMA; 1.2 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O 20:1), the title compound was isolated as a colorless oil: run 1, 172 mg (58%; 69% ee); run 2, 167 mg (56%; 69% ee).

$[\alpha]^{22}_D$ = +0.6 (c = 3.9, $CHCl_3$);

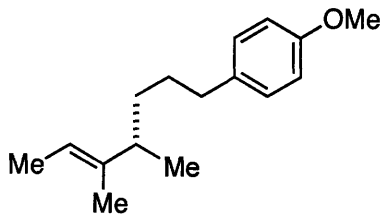
^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.30 (dd, J = 15.3, 6.7 Hz, 1H), 5.26 (ddd, J = 15.3, 9.2, 1.1 Hz, 1H), 3.59 (t, J = 6.6 Hz, 2H), 2.26 (doublet of octets, J = 6.6, 1.2 Hz, 1H), 1.70-1.63 (m, 1H), 1.58-1.52 (m, 2H), 1.51-1.34 (m, 2H), 1.24-1.15 (m, 1H), 0.98 (dd, J = 6.7, 1.1 Hz, 6H), 0.90 (s, 9H), 0.95 (d, J = 6.7 Hz, 3H), 0.80 (d, J = 6.8 Hz, 3H), 0.05 (s, 6H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.0, 129.1, 63.7, 49.1, 32.2, 31.5, 31.2, 28.8, 26.2, 23.1, 21.0, 19.2, 18.6, –5.0;

IR (film) 2957, 2930, 2860, 1472, 1464, 1385, 1361, 1255, 1102, 973, 836, 775 cm^{-1};

GCMS calcd for $C_{18}H_{38}OSi$ (M^+) 298, found 298.

The ee was determined by chiral GC: CP Chirasil-Dex CB, t_r (major) 17.6 min, t_r (minor) 18.0 min; temperature: 120 °C; 1.0 mL/min.



(+)-(*S,E*)-1-(4,5-Dimethylhept-5-enyl)-4-methoxybenzene (Table 4, entry 6). The compound was prepared according to the General Procedure with (±)-(*E*)-4-chloro-3-methylpent-2-ene (118 mg, 1.0 mmol) and the organozinc reagent (~1.1 M in DMA; 1.1 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O 30:1), the title compound was isolated as a colorless oil: run 1, 128 mg (55%; 97% ee); run 2, 123 mg (53%; 99% ee).

$[\alpha]^{22}_D$ = +5.7 (c = 2.3, $CHCl_3$);

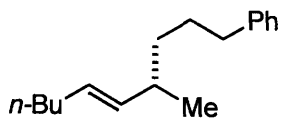
^1H NMR ($CDCl_3$, 400 MHz) δ 7.14-7.10 (m, 2H), 6.88-6.84 (m, 2H), 5.25 (q, *J* = 6.5 Hz, 1H), 3.82 (s, 3H), 2.62-2.49 (m, 2H), 2.14 (sextet, *J* = 7.0 Hz, 1H), 1.60 (dd, *J* = 6.6, 0.9 Hz, 3H), 1.52 (s, 3H), 1.53-1.45 (m, 2H), 1.44-1.36 (m, 1H), 1.34-1.25 (m, 1H), 0.99 (d, *J* = 6.9 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.8, 140.0, 135.2, 129.4, 117.9, 113.8, 55.4, 42.9, 35.3, 34.7, 30.1, 20.0, 13.4, 12.0;

IR (film) 2995, 2956, 2930, 2958**, 1613, 1584, 1513, 1463, 1442, 1300, 1246, 1177, 1040, 828 cm^{-1};

GCMS calcd for $C_{16}H_{24}O$ (M^+) 232, found 232.

The ee was determined by chiral GC: CP Chirasil-Dex CB, t_r (major) 113.9 min, t_r (minor) 118.3 min; temperature: 110 °C; 1.0 mL/min.



(+)-(*S,E*)-(4-Methyldec-5-enyl)benzene (Table 5, entry 1). The compound was prepared according to the General Procedure with a 1.2:1 mixture of (±)-(*E*)-2-chlorooct-

3-ene and (±)-(*E*)-4-chlorooct-2-ene (147 mg, 1.0 mmol) and the organozinc reagent (~1.2 M in DMA; 1.0 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O 30:1), the title compound and (*R*)-(*E*)-(4-(prop-1-enyl)octyl)benzene were obtained as a 1.9:1 mixture: run 1, 220 mg (95%; major, 84% ee; minor, 89% ee); run 2, 227 mg (99%; major, 82% ee; minor, 89% ee).

The characterization data of the mixture is reported.

$[\alpha]^{22}_D$ = +11.8 (c = 1.43, $CHCl_3$);

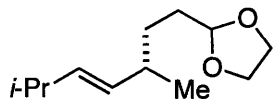
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.32-7.28 (m, 2H, mixture), 7.20-7.18 (m, 3H, mixture), 5.41-5.35 (m, 1H, mixture), 5.25 (dd, *J* = 15.3, 7.6 Hz, 0.7H, major), 5.14 (ddq, *J* = 15.2, 8.8, 1.6 Hz, 0.3H, minor), 2.64-2.56 (m, 2H, mixture), 2.10 (septet, *J* = 6.9 Hz, 0.7H, major), 2.12-1.94 (m, 1H, mixture), 1.93-1.88 (m, 0.3 H, minor), 1.72-1.59 (m, 3H, mixture), 1.37-1.16 (m, 7H, mixture), 0.99-0.88 (m, 5H, mixture);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.2, 143.1, 136.32, 136.26, 128.9, 128.6, 128.4, 125.8, 124.6, 43.0, 37.0, 36.9, 36.34, 36.28, 35.5, 35.4, 32.5, 32.1, 29.7, 29.5, 23.1, 22.4, 21.2, 18.2, 14.4, 14.2;

IR (film) 3063, 3027, 2957, 2927, 1605, 1496, 1454, 1377, 968, 747, 698 cm^{-1};

GCMS calcd for $C_{17}H_{26}$ (M^+) 230, found 230.

The ee was determined of 2-methyl-5-phenylpentyl benzoate (from the major regioisomer) and of 2-(3-phenylpropyl)hexyl benzoate (from the minor regioisomer) [obtained by ozonolysis, reduction, then benzoylation] by HPLC on an OD-H column (hexanes/isopropanol 95:5, 1.0 mL/min) with t_r (major enantiomer of the major regioisomer) 5.4 min, t_r (minor enantiomer of the major regioisomer) 7.5 min; t_r (major enantiomer of the minor regioisomer) 4.8 min, t_r (minor enantiomer of the minor regioisomer) 6.2 min.



(+)-(*S*,*E*)-2-(3,6-Dimethylhept-4-enyl)-1,3-dioxolane (Table 5, entry 2). The compound was prepared according to the General Procedure with a 1.4:1 mixture of (±)-(*E*)-2-chloro-5-methylhex-3-ene and (±)-(*E*)-4-chloro-5-methylhex-2-ene (133 mg, 1.0 mmol) and the organozinc reagent (~1.4 M in DMA; 0.86 mL, 1.2 mmol). After

purification by flash chromatography (hexanes/Et_2O 20:1), the title compound was isolated as a colorless oil: run 1, 188 mg (95%, 86% ee); run 2, 189 mg (95%, 82% ee).

$[\alpha]^{22}_D$ = +12.4 (c = 1.23, $CHCl_3$);

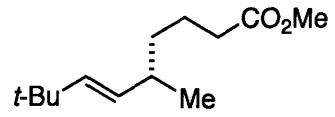
^1H NMR ($CDCl_3$, 400 MHz) δ 5.34 (dd, *J* = 15.4, 6.6 Hz, 1H), 5.18 (ddd, *J* = 15.4, 6.8, 1.0 Hz, 1H), 4.84 (t, *J* = 4.8 Hz, 1H), 3.99-3.93 (m, 2H), 3.89-3.83 (m, 2H), 2.28-2.16 (m, 1H), 2.06 (septet, *J* = 6.9 Hz, 1H), 1.71-1.56 (m, 2H), 1.46-1.31 (m, 2H), 0.98-0.95 (m, 9H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.6, 132.7, 105.0, 65.0, 36.8, 32.0, 31.5, 31.2, 23.0, 22.9, 21.2;

IR (film) 2957, 2927, 2870, 1458, 1409, 1142, 1046, 972, 882 cm^{-1};

GCMS calcd for $C_{12}H_{22}O_2$ (M^+) 198, found 198.

The ee was determined of 4-(1,3-dioxolan-2-yl)-2-methylbutyl benzoate [obtained by ozonolysis, reduction, then benzoylation] by HPLC on an OD-H column (hexanes/isopropanol 99:1, 1.0 mL/min) with t_r (major) 7.8 min, t_r (minor) 8.9 min.



(+)-(*S*,*E*)-Methyl 5,8,8-trimethylnon-6-enoate (Table 5, entry 3). The compound was prepared according to the General Procedure with a 2.4:1 mixture of (±)-(*E*)-5-chloro-2,2-dimethylhex-3-ene and (±)-(*E*)-4-chloro-5,5-dimethylhex-2-ene (147 mg, 1.0 mmol) and the organozinc reagent (~0.9 M in DMA; 1.3 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O 20:1), the title compound was isolated as a colorless oil: run 1, 182 mg (86%, 81% ee); run 2, 177 mg (83%, 80% ee).

$[\alpha]^{22}_D$ = +17.1 (c = 2.06, $CHCl_3$);

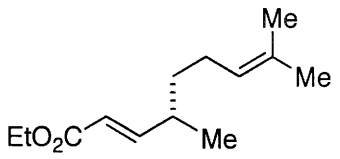
^1H NMR ($CDCl_3$, 400 MHz) δ 5.34 (dd, *J* = 15.6, 0.8 Hz, 1H), 5.08 (dd, *J* = 15.6, 7.9 Hz, 1H), 3.63 (s, 3H), 2.25 (t, *J* = 7.5 Hz, 2H), 2.00 (septet, *J* = 7.0 Hz, 1H), 1.63-1.47 (m, 2H), 1.30-1.16 (m, 2H), 0.94 (s, 9H), 0.91 (d, *J* = 6.7 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.5, 140.4, 130.3, 51.6, 36.8, 36.7, 34.3, 32.8, 30.0, 23.0, 21.2;

IR (film) 2957, 2907, 2868, 1744, 1462, 1363, 1197, 1170, 974 cm^{-1};

GCMS calcd for $C_{13}H_{24}O_2$ (M^+) 212, found 212.

The ee was determined of 6-methoxy-2-methyl-6-oxohexyl benzoate [obtained by ozonolysis, reduction, and then benzoylation] by HPLC on an OD-H column (hexanes/isopropanol 99:1, 1.0 mL/min) with t_r (major) 8.1 min, t_r (minor) 9.0 min.



(+)-(*S*,*E*)-Ethyl 4,8-dimethylnona-2,7-dienoate (Table 5, entry 4). The compound was prepared according to the General Procedure with (±)-(*E*)-ethyl 4-chloropent-2-enoate (163 mg, 1.0 mmol) and the organozinc reagent (~1.4 M in DMA; 0.86 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O 20:1), the title compound was isolated as a colorless oil: run 1, 180 mg (86%, 97% ee); run 2, 181 mg (86%, 94% ee).

$[\alpha]^{22}_D$ = +55 (c = 2.2, $CHCl_3$);

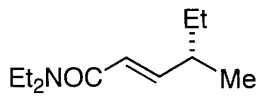
^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.87 (dd, *J* = 15.7, 8.0 Hz, 1H), 5.78 (dd, *J* = 15.7, 1.2 Hz, 1H), 5.07 (triplet of septets, *J* = 7.1, 1.4 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.31 (septet, *J* = 5.9 Hz, 1H), 1.96 (q, *J* = 7.5 Hz, 2H), 1.68 (d, *J* = 1.0 Hz, 3H), 1.59 (s, 3H), 1.47-1.35 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.05 (d, *J* = 6.7 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.1, 154.7, 132.1, 124.1, 119.9, 60.3, 36.2, 25.9, 25.8, 19.5, 17.9, 14.5;

IR (film) 2967, 2917, 2873, 2855, 1722, 1652, 1452, 1368, 1301, 1268, 1178, 1039, 985 cm^{-1};

GCMS calcd for $C_{13}H_{22}O_2$ (M^+) 210, found 210.

The ee was determined by HPLC on an AS-H column (hexanes, 1.0 mL/min) with t_r (major) 9.7 min, t_r (minor) 12.1 min.



(+)-(*S*,*E*)-*N*,*N*-Diethyl-4-methylhex-2-enamide (Table 5, entry 5). The compound was prepared according to the General Procedure with (±)-(*E*)-4-chloro-*N*,*N*-

diethylpent-2-enamide (190 mg, 1.0 mmol) and the organozinc reagent (~0.9 M in DMA; 1.3 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O 1:1), the title compound was isolated as a colorless oil: run 1, 102 mg (56%, 89% ee); run 2, 105 mg (57%, 92% ee).

$[\alpha]^{22}_D$ = +27 (c = 1.3, $CHCl_3$);

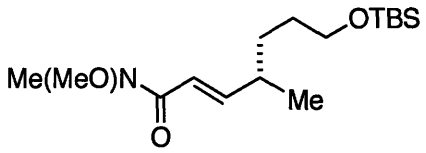
^1H NMR ($CDCl_3$, 400 MHz) δ 6.87 (dd, *J* = 15.0, 8.0 Hz, 1H), 6.13 (dd, *J* = 15.1, 1.0 Hz, 1H), 3.45-3.34 (m, 4H), 2.20 (septet, *J* = 6.8 Hz, 1H), 1.44-1.33 (m, 2H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.2, 151.5, 119.0, 42.3, 41.0, 38.6, 29.2, 19.6, 15.5, 13.4, 11.9;

IR (film) 2966, 2932, 2875, 1660, 1619, 1447, 1430, 1379, 1361, 1279, 1261, 983 cm^{-1};

GCMS calcd for $C_{11}H_{21}NO$ (M^+) 183, found 183.

The ee was determined by HPLC on an AD-H column (hexanes/isopropanol 99:1, 0.5 mL/min) with t_r (major) 40.3 min, t_r (minor) 38.2 min.



(+)-(*S*,*E*)-7-(*tert*-Butyldimethylsilyoxy)-*N*-methoxy-*N*,4-dimethylhept-2-enamide (Table 5, entry 6). The compound was prepared according to the General Procedure with (±)-(*E*)-4-chloro-*N*-methoxy-*N*-methylpent-2-enamide (178 mg, 1.0 mmol) and the organozinc reagent (~1.0 M in DMA; 1.2 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O 1:1), the title compound was isolated as a colorless oil: run 1, 285 mg (90%, 93% ee); run 2, 289 mg (92%, 92% ee).

$[\alpha]^{22}_D$ = +12.2 (c = 1.38, $CHCl_3$);

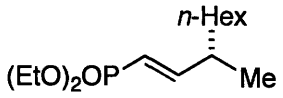
^1H NMR ($CDCl_3$, 400 MHz) δ 6.87 (dd, *J* = 15.4, 8.1 Hz, 1H), 6.35 (d, *J* = 15.4 Hz, 1H), 3.70 (s, 3H), 3.59 (t, *J* = 6.3 Hz, 2H), 3.24 (s, 3H), 2.35 (septet, *J* = 6.8 Hz, 1H), 1.55-1.48 (m, 2H), 1.45-1.39 (m, 2H), 1.07 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.3, 153.3, 117.2, 63.3, 61.8, 36.8, 32.6, 30.7, 26.2, 19.9, 18.6, 15.5, –5.1;

IR (film) 2956, 2931, 2857, 1666, 1635, 1471, 1463, 1412, 1381, 1256, 1099, 1006, 940, 836, 776 cm^{-1};

LCMS calcd for $C_{16}H_{34}NO_3Si$ ($M+H^+$) 316.2, found 316.2.

The ee was determined of 5-(*tert*-butyldimethylsilyloxy)-2-methylpentyl benzoate [obtained by ozonolysis, reduction, then benzoylation] by HPLC on an OD-H column (hexanes, 1.0 mL/min) with t_r (major) 15.4 min, t_r (minor) 19.6 min.



(+)-(*S,E*)-Diethyl 3-methylnon-1-enylphosphonate (Table 5, entry 7). The compound was prepared according to the General Procedure with (±)-(*E*)-diethyl 3-chlorobut-1-enylphosphonate (227 mg, 1.0 mmol) and the organozinc reagent (~0.9 M in DMA; 1.3 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O 1:1), the title compound was isolated as a colorless oil: run 1, 175 mg (63%, 90% ee); run 2, 170 mg (62%, 90% ee).

$[\alpha]^{22}_D$ = +20 (c = 1.9, $CHCl_3$);

^1H NMR ($CDCl_3$, 400 MHz) δ 6.70 (ddd, *J* = 22.2, 17.2, 7.5 Hz, 1H), 5.60 (ddd, *J* = 21.0, 17.2, 1.1 Hz, 1H), 4.13-4.04 (m, 4H), 2.30 (septet, *J* = 6.7 Hz, 1H), 1.34 (t, *J* = 7.1 Hz, 6H), 1.36-1.23 (m, 10H), 1.05 (d, *J* = 6.6 Hz, 3H), 0.89 (t, *J* = 6.8 Hz, 3H);

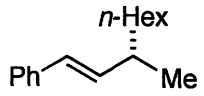
^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.5, 114.9 (d, J_{CP} = 186.3 Hz), 61.7 (d, J_{CP} = 6.4 Hz), 38.6, 38.4, 35.9, 31.9, 29.5, 27.3, 22.8, 19.3, 16.6, 16.5, 14.3;

IR (film) 2959, 2928, 2857, 1630, 1461, 1250, 1056, 1029, 963 cm^{-1};

LCMS calcd for $C_{14}H_{30}O_3P$ ($M+H^+$) 277.2, found 277.2.

The ee was determined of 2-methyloctyl 3,4,5-trimethoxybenzoate [obtained by ozonolysis, reduction, then benzoylation] by HPLC on an AD-H column (hexanes/isopropanol 99:1, 0.5 mL/min) with t_r (major) 23.1 min, t_r (minor) 21.8 min.

Procedure A for aryl-substituted olefins (eq 8): In the air, a 40-mL glass vial was charged with $NiCl_2$·glyme (22.0 mg, 0.10 mmol), (*R*)-(*i*-Pr)-Pybox (33.2 mg, 0.11 mmol), and NaCl (117 mg, 4.0 mmol) and fitted with a septum cap. The vial was evacuated and then back-filled with Ar (three cycles). DMA (19.8 mL) and DCE (9.0 mL) were added, followed by the allylic chloride (1.0 mmol). The resulting mixture was cooled to –10 °C. Next, the organozinc solution (~1.0 M in DMA; 1.2 mL, 1.2 mmol) was added in a single portion to the mixture, which was stirred for 36 h at –20 °C. The reaction mixture was then diluted with water (30 mL) and extracted with Et_2O (30 mL x 3). The organic layer was dried over $MgSO_4$ and concentrated, and the residue was purified by flash chromatography.



(+)-(*S*,*E*)-(3-methyldec-1-enyl)benzene (Table 6, entry 1). The compound was prepared according to the Procedure A with (±)-(*E*)-(3-chlorobut-1-enyl)benzene (167 mg, 1.0 mmol) and the organozinc reagent (~0.9 M in DMA; 1.3 mL, 1.2 mmol). After purification by flash chromatography (hexanes), the title compound was isolated as a colorless oil: run 1, 122 mg (56%, 96% ee); run 2, 119 mg (55%, 95% ee).

$[\alpha]^{22}_D = 107.91$ (c = 2.06, $CHCl_3$);

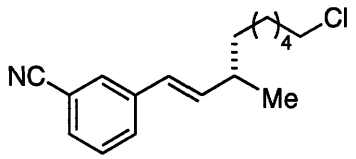
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38-7.36 (m, 2H), 7.33-7.29 (m, 2H), 7.23-7.18 (m, 1H), 6.35 (d, *J* = 15.9 Hz, 1H), 6.11 (dd, *J* = 15.9, 8.0 Hz, 1H), 2.30 (septet, *J* = 6.8 Hz, 1H), 1.42-1.35 (m, 2H), 1.34-1.24 (m, 8H), 1.09 (d, *J* = 6.7 Hz, 3H), 0.90 (t, *J* = 6.7 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.2, 137.3, 128.7, 128.1, 126.9, 126.2, 37.5, 37.4, 32.1, 29.7, 27.6, 22.9, 20.9, 14.3;

IR (film) 3082, 3060, 3025, 2957, 2926, 2855, 1649, 1598, 1494, 1455, 965, 746, 692 cm^{-1};

GCMS calcd for $C_{16}H_{24}$ (M^+) 216, found 216.

The ee was determined on 2-methyloctyl 3,4,5-trimethoxybenzoate obtained by ozonolysis of the title compound followed by benzoylation. The ee was determined by HPLC on an AD-H column (hexanes/*iso*-propanol 99:1, flow 0.5 mL/min.) with t_r(major) 24.6 min., t_r(minor) 23.4 min.



(+)-(*S*,*E*)-3-(9-chloro-3-methylnon-1-enyl)benzonitrile (Table 6, entry 2). The compound was prepared according to the Procedure A with (±)-(*E*)-3-(3-chlorobut-1-enyl)benzonitrile (192 mg, 1.0 mmol) and the organozinc reagent (~0.9 M in DMA; 1.3 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O = 20:1), the title compound was isolated as a colorless oil: run 1, 107 mg (39%, 94% ee); run 2, 96 mg (35%, 94% ee).

$[\alpha]^{22}_D$ = 50.76 (c = 1.77, $CHCl_3$);

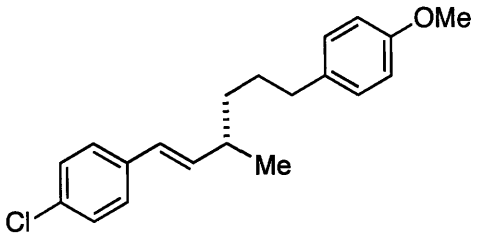
^1H NMR ($CDCl_3$, 400 MHz) δ 7.64 (d, *J* = 1.6 Hz, 1H), 7.57 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.49 (dt, *J* = 7.1, 1.4 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 6.33 (d, *J* = 15.9 Hz, 1H), 6.18 (dd, *J* = 15.9, 7.9 Hz, 1H), 3.55 (t, *J* = 6.7 Hz, 2H), 2.33 (septet, *J* = 6.7 Hz, 1H), 1.82-1.75 (m, 2H), 1.47-1.34 (m, 8H), 1.10 (d, *J* = 6.7 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.0, 139.3, 130.4, 130.3, 129.6, 129.4, 126.3, 119.2, 112.8, 45.4, 37.5, 36.9, 32.8, 29.2, 27.4, 27.0, 20.7;

IR (film) 2956, 2929, 2856, 2230, 1650, 1598, 1577, 1457, 967, 790, 686 cm^{-1};

GCMS calcd for $C_{17}H_{22}ClN$ (M^+) 275, found 275.

The ee was determined by HPLC on an OJ-H column (hexanes/*iso*-propanol 99:1, flow 0.8 mL/min.) with t_r(major) 18.7 min., t_r(minor) 19.9 min.



(+)-(*S*,*E*)-1-chloro-4-(6-(4-methoxyphenyl)-3-methylhex-1-enyl)benzene (Table 6, entry 3). The compound was prepared according to the Procedure A with (±)-(*E*)-1-chloro-4-(3-chlorobut-1-enyl)benzene (201 mg, 1.0 mmol) and the organozinc reagent (~1.1 M in DMA; 1.1 mL, 1.2 mmol). After purification by flash chromatography (hexanes/Et_2O = 20:1), the title compound was isolated as a colorless oil: run 1, 169 mg (54%, 97% ee); run 2, 176 mg (56%, 97% ee).

$[\alpha]^{22}_D = 56.30$ (c = 2.20, $CHCl_3$);

^1H NMR ($CDCl_3$, 400 MHz) δ 7.28 (s, 4H), 7.12-7.10 (m, 2H), 6.87-6.84 (m, 2H), 6.30 (d, *J* = 15.9 Hz, 1H), 6.08 (dd, *J* = 15.9, 8.0 Hz, 1H), 3.81 (s, 3H), 2.64-2.52 (m, 2H), 2.33 (septet, *J* = 6.9 Hz, 1H), 1.68-1.57 (m, 2H), 1.48-1.38 (m, 2H), 1.09 (d, *J* = 6.7 Hz, 3H);

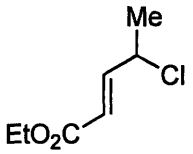
^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.8, 137.6, 136.5, 134.9, 132.5, 129.5, 128.8, 127.4, 127.2, 113.9, 55.4, 37.5, 36.7, 35.3, 29.8, 20.8;

IR (film) 3028, 2994, 2954, 2931, 2855, 1612, 1512, 1491, 1246, 1177, 1091, 1038, 968, 807 cm^{-1};

GCMS calcd for $C_{20}H_{23}ClO$ (M^+) 314, found 314.

The ee was determined by HPLC on an OJ-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 22.0 min., t_r(minor) 26.8 min.

5. Formal Total Synthesis of Fluvirucinine A_1 (Scheme 3)



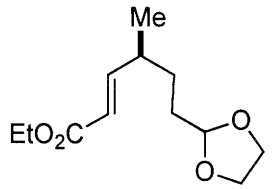
(±)-(*E*)-Ethyl 4-chloropent-2-enoate (2). MeMgBr (3.0 M in Et_2O; 14 mL, 42 mmol) was added dropwise over 30 min to a solution of ethyl (*E*)-4-oxo-2-butenoate (5.13 g, 40.0 mmol) in Et_2O (120 mL) at –85 °C. The reaction mixture was stirred for 2 h at –85 °C, and then the bath was removed. A saturated solution of NH_4Cl (100 mL) was added, and the aqueous layer was extracted with Et_2O (100 mL x 3). The organic layer was dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (hexanes/Et_2O 3:1) provided the allylic alcohol (4.21 g, 73%), which was converted to the allylic chloride by Representative Procedure A (Section III; 5.28 g, 81%).

^1H NMR ($CDCl_3$, 400 MHz) δ 6.95 (dd, *J* = 15.4, 7.0 Hz, 1H), 6.03 (dd, *J* = 15.4, 1.2 Hz, 1H), 4.63 (doublet of pentets, *J* = 6.8, 1.2 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 1.66 (d, *J* = 6.7 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.1, 147.2, 121.9, 60.9, 55.0, 24.4, 14.4;

IR (film) 2983, 1722, 1660, 1446, 1368, 1271, 1181, 1034, 975 cm^{-1};

GCMS calcd for $C_7H_{11}ClO_2$ (M^+) 162, found 162.



(+)-(*S,E*)-Ethyl 6-(1,3-dioxolan-2-yl)-4-methylhex-2-enoate (3). The compound was prepared according to the General Procedure (Section IV) with (*R*)-$BnCH_2$-Pybox, (±)-(*E*)-ethyl 4-chloropent-2-enoate (488 mg, 3.0 mmol), and the alkylzinc reagent (~1.2 M in DMA; 3.0 mL, 3.6 mmol). After purification by flash chromatography (hexanes/Et_2O 10:1), the title compound was obtained as a colorless oil: run 1, 620 mg (91%, 96% ee); run 2, 646 mg (94%, 95% ee).

$[\alpha]^{22}_D$ = +23 (c = 1.7, $CHCl_3$);

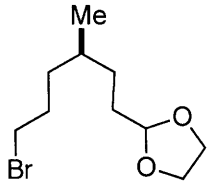
^1H NMR ($CDCl_3$, 400 MHz) δ 6.85 (dd, *J* = 15.7, 8.0 Hz, 1H), 5.79 (d, *J* = 15.7 Hz, 1H), 4.84 (t, *J* = 4.6 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.00-3.92 (m, 2H), 3.89-3.81 (m, 2H), 2.34 (septet, *J* = 7.0 Hz, 1H), 1.68-1.61 (m, 2H), 1.54-1.48 (m, 2H), 1.29 (dt, *J* = 7.1, 0.5 Hz, 3H), 1.07 (d, *J* = 6.7 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.0, 154.0, 120.3, 104.5, 65.09, 65.08, 60.4, 36.6, 31.7, 30.2, 19.6, 14.5;

IR (film) 2958, 2926, 1718, 1653, 1458, 1368, 1267, 1178, 1144, 1037, 987 cm^{-1};

GCMS calcd for $C_{12}H_{20}O_4$ (M^+) 228, found 228.

The ee was determined by HPLC on an IA column (hexanes/isopropanol 99:1, 1.0 mL/min) with t_r (major) 10.3 min, t_r (minor) 9.6 min.



(+)-(*S*)-2-(6-Bromo-3-methylhexyl)-1,3-dioxolane (4). A mixture of (+)-(*S,E*)-Ethyl 6-(1,3-dioxolan-2-yl)-4-methylhex-2-enoate (228 mg, 1.0 mmol) and palladium on

activated carbon (10 mg) in THF (3 mL) was stirred overnight under an atmosphere of H_2. Then, $LiAlH_4$ (1.0 M in Et_2O; 1.2 mL, 1.2 mmol) was added, and the reaction mixture was stirred for 10 min. Next, a saturated solution of Na_2SO_4 (0.2 mL) was added, and the mixture was stirred until a white precipitate formed. Then, the mixture was filtered through a short plug of silica gel (EtOAc as the eluant) and concentrated. The unpurified alcohol and imidazole (116 mg, 1.7 mmol) were dissolved in CH_2Cl_2 (10 mL), and Ph_3PBr_2 (633 mg, 1.5 mmol) was added to the solution in small portions. After 3 h, the solvent was removed, and the residue was purified by flash chromatography (hexanes/Et_2O 10:1), which furnished the title compound as a colorless oil: run 1, 221 mg (88%); run 2, 224 mg (89%).

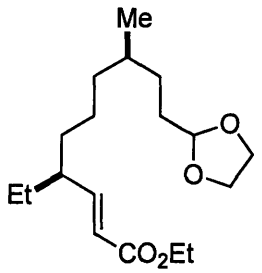
$[\alpha]^{22}_D$ = +1.5 (c = 1.6, $CHCl_3$);

^1H NMR ($CDCl_3$, 400 MHz) δ 4.84 (t, *J* = 4.7 Hz, 1H), 4.00-3.94 (m, 2H), 3.90-3.84 (m, 2H), 3.40 (dt, *J* = 6.9, 0.8 Hz, 2H), 1.96-1.80 (m, 2H), 1.75-1.60 (m, 2H), 1.53-1.39 (m, 3H), 1.32-1.20 (m, 2H), 0.91 (d, *J* = 6.4 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 105.0, 65.1, 35.5, 34.4, 32.3, 31.6, 31.0, 30.6, 19.6;

IR (film) 2955, 2925, 2854, 1462, 1128, 1034 cm^{-1};

GCMS calcd for $C_{10}H_{19}BrO_2$ (M^+) 250, found 250.



(+)-(4*S*,8*R*,*E*)-Ethyl 10-(1,3-dioxolan-2-yl)-4-ethyl-8-methyldec-2-enoate (5). The organozinc reagent derived from (+)-(*S*)-2-(6-bromo-3-methylhexyl)-1,3-dioxolane was prepared according to the procedure described above (Section IV). The title compound was prepared according to the General Procedure (Section IV) with (*R*)-$BnCH_2$-Pybox, this organozinc reagent (~0.9 M in DMA; 0.67 mL, 0.60 mmol), and (±)-(*E*)-ethyl 4-chlorohex-2-enoate (88 mg, 0.5 mmol). After purification by flash chromatography (hexanes/Et_2O 5:1), the title compound was obtained as a colorless oil: run 1, 127 mg (81%, 16:1 dr, >99% ee); run 2, 130 mg (83%, 14:1 dr, 98% ee).

$[\alpha]^{22}_D$ = +13.3 (c = 1.29, $CHCl_3$);

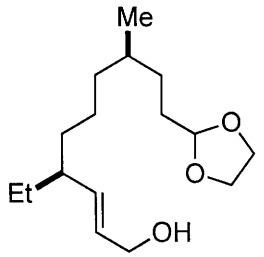
^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.72 (dd, *J* = 15.6, 9.3 Hz, 1H), 5.77 (d, *J* = 15.6 Hz, 1H), 4.83 (t, *J* = 4.8 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.01-3.93 (m, 2H), 3.90-3.83 (m, 2H), 2.11-2.00 (m, 1H), 1.73-1.59 (m, 2H), 1.52-1.35 (m, 4H), 1.33-1.07 (m, 7H), 1.30 (t, *J* = 7.1 Hz, 3H), 0.85 (d, *J* = 6.2 Hz, 3H), 0.85 (t, *J* = 7.3 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.0, 153.8, 121.3, 105.1, 65.03, 65.02, 60.3, 44.5, 37.1, 34.5, 32.8, 31.7, 31.3, 27.4, 24.8, 19.6, 14.5, 11.9;

IR (film) 2929, 2874, 1721, 1652, 1462, 1369, 1308, 1266, 1143, 1039, 987, 867 cm^{-1};

LCMS calcd for $C_{18}H_{33}O_4$ ($M+H^+$) 313.2, found 313.2.

The ee was determined by HPLC on an IA column (hexanes/isopropanol 99:1, 0.5 mL/min) with t_r (major) 19.8 min, t_r (minor) 18.1 min.



(+)-(4*S*,8*R*)-10-(1,3-Dioxolan-2-yl)-4-ethyl-8-methyldec-2-en-1-ol (Figure 2). A mixture of (+)-(4*S*,8*R*,*E*)-ethyl 10-(1,3-dioxolan-2-yl)-4-ethyl-8-methyldec-2-enoate (112 mg, 0.34 mmol) and palladium on activated carbon (3 mg) in THF (1 mL) was stirred overnight under an atmosphere of H_2. Then, $LiAlH_4$ (1.0 M in Et_2O; 0.41 mL, 0.41 mmol) was added, and the reaction mixture was stirred for 10 min. Next, a saturated solution of Na_2SO_4 (0.2 mL) was added, and the mixture was stirred until a white precipitate formed. Then, the mixture was filtered through a short plug of silica gel (EtOAc as the eluant) and concentrated. After purification by flash chromatography (hexanes/Et_2O 1:1), the title compound was obtained as a colorless oil: run 1, 91 mg (94%); run 2, 94 mg (96%).

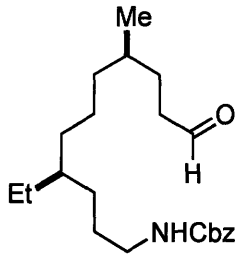
$[\alpha]^{22}_D$ = +0.5 (c = 1.5, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.84 (t, J = 4.8 Hz, 1H), 4.02-3.94 (m, 2H), 3.90-3.82 (m, 2H), 3.64 (t, J = 6.6 Hz, 2H), 1.74-1.59 (m, 2H), 1.58-1.51 (m, 2H), 1.48-1.40 (m, 2H), 1.32-1.19 (m, 12H), 1.16-1.04 (m, 1H), 0.88 (d, J = 6.5 Hz, 3H), 0.85 (t, J = 7.1 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 105.2, 65.04, 65.02, 63.8, 38.8, 37.5, 33.5, 32.8, 31.7, 31.2, 30.2, 29.2, 26.0, 24.1, 19.8, 11.1;

IR (film) 3423, 2929, 2861, 1461, 1409, 1379, 1143, 1125, 1054 cm^{-1};

LCMS calcd for $C_{16}H_{33}O_3$ ($M+H^+$) 273.2, found 273.2.



(+)-Benzyl (4*S*,8*R*)-4-ethyl-8-methyl-11-oxoundecylcarbamate (1). Under nitrogen, a mixture of (+)-(4*S*,8*R*)-10-(1,3-dioxolan-2-yl)-4-ethyl-8-methyldec-2-en-1-ol (81 mg, 0.30 mmol) and the Burgess-type reagent[15] (123 mg, 0.39 mmol) were mixed and heated at 100 °C for 1 h. The mixture was cooled to room temperature, and then HCl (1 N; 0.6 mL) and THF (1.8 mL) were added, and the mixture was stirred overnight at 60 °C. Next, a saturated solution of $NaHCO_3$ (5 mL) was added, and the aqueous layer was extracted with Et_2O (10 mL x 3). The organic layer was dried over $MgSO_4$, filtered, and concentrated. After purification by flash chromatography (hexanes/Et_2O 3:1), the title compound was obtained as a colorless oil: run 1, 67 mg (62%); run 2, 65 mg (60%). This compound was identical by ^{1}H NMR with the material reported by Suh.[14a]

$[\alpha]^{22}_D$ = +1.0 (c = 2.3, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.77 (t, J = 1.8 Hz, 1H), 7.42-7.30 (m, 5H), 5.10 (s, 2H), 4.81 (s, 1H), 3.18 (q, J = 6.7 Hz, 2H), 2.45-2.39 (m, 2H), 1.71-1.61 (m, 1H), 1.47-1.39 (m, 4H), 1.31-1.18 (m, 10H), 1.15-1.03 (m, 1H), 0.88 (d, J = 6.3 Hz, 3H), 0.83 (t, J = 7.1 Hz, 3H);

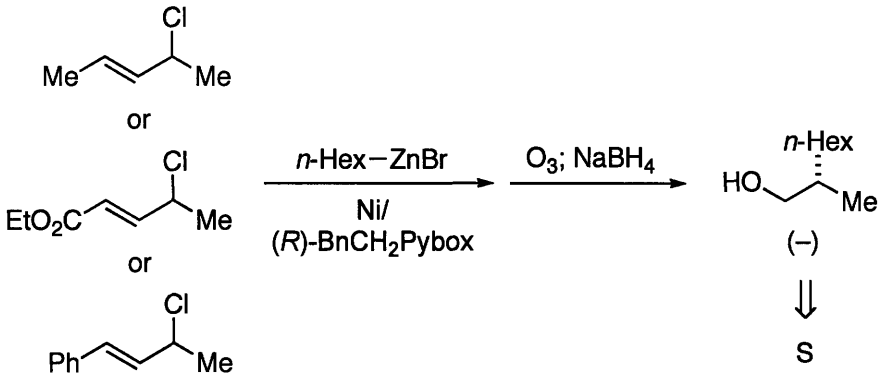
^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.3, 156.6, 136.8, 128.7, 128.3, 127.1, 77.4, 66.7, 41.9, 41.7, 38.7, 37.3, 33.4, 32.5, 30.3, 29.9, 29.1, 27.4, 25.9, 24.2, 19.5, 11.0;

IR (film) 3341, 2926, 2857, 1723, 1533, 1456, 1250, 1135, 697 cm^{-1};

LCMS calcd for $C_{22}H_{36}NO_3$ ($M+H^+$) 362.3, found 362.3.

6. Determination of Absolute Stereochemistry

The stereochemistry of the cross coupling products was assigned by correlation with (–)-(*S*)-2-methyloctan-1-ol.[1]



[1] Shirai, Y.; Seki, M.; Mori, K. *Eur. J. Org. Chem.* **1999**, 3139–3145.

7. ^{1}H NMR for Selected Compounds

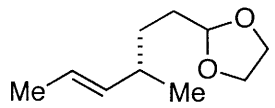


Table 4, entry 2

BRUKER

```
Current Data Parameters
NAME                  SS6-287
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070223
Time                    21 20
INSTRUM                 spect
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                 CDCl3
NS                         16
DS                          0
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    161.3
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      15.07 usec
PL1                      0.00 dB
SFO1              400.1324710 MHz

F2 - Processing parameters
SI                       131072
SF                400.1300057 MHz
WDW                         EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

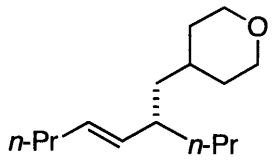


Table 4, entry 3


```
Current Data Parameters
NAME                  ss7-143
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070427
Time                  18.10
INSTRUM               spect
PROBHD   5 mm QNP 1H/13
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    203.2
DW                   60.400 usec
DE                    6.00 usec
TE                   291.2 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   13.88 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF            400.1300055 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

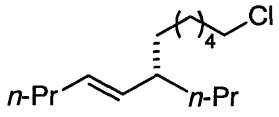


Table 4, entry 4


```
Current Data Parameters
NAME                  SS7-097
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070405
Time                   12.37
INSTRUM                spect
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                       181
DW                    60.400 usec
DE                     6.00 usec
TE                    293.2 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                      131072
SF             400.1300058 MHz
WDW                        EM
SSB                         0
LB                      0.30 Hz
GB                          0
PC                      1.00
```

ss7-37

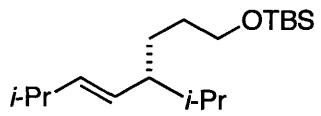


Table 4, entry 5

BRUKER

```
Current Data Parameters
NAME                  SS7-37
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20070313
Time                  17.01
INSTRUM                spect
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      114
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                    15.07 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                      131072
SF                400.1300057 MHz
WDW                       EM
SSB                        0
LB                     0.30 Hz
GB                         0
PC                      1.00
```

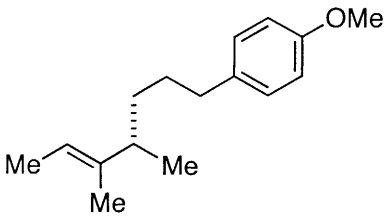


Table 4, entry 6


```
Current Data Parameters
NAME                  ss7-171
EXPNO                       5
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070508
Time                  22.44
INSTRUM               spect
PROBHD    5 mm QNP 1H/13
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                     114
DW                  60.400 usec
DE                   6.00 usec
TE                  293.2 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   13.88 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF            400.1300000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

ss7-41

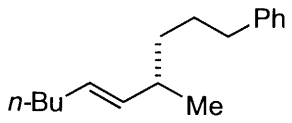


Table 5, entry 1

BRUKER

```
Current Data Parameters
NAME                  SS7-41
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20070313
Time                  17.15
INSTRUM               spect
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      114
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                    131072
SF             400.1300057 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

ss7-29

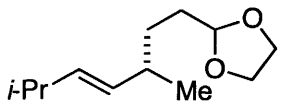


Table 5, entry 2

BRUKER

```
Current Data Parameters
NAME                  SS7-29
EXPNO                      3
PROCNO                     1

F2 - Acquisition Parameters
Date_              20070313
Time                  16.55
INSTRUM               spect
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      114
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1             1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    15.07 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                   131072
SF            400.1300057 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

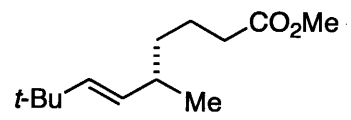


Table 5, entry 3


```
Current Data Parameters
NAME                  SS7-013
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070305
Time                   11.50
INSTRUN                spect
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      71.8
DW                    60.400 usec
DE                     6.00 usec
TE                    293.2 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    15.07 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300212 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

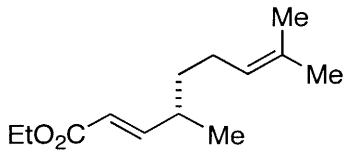


Table 5, entry 4


```
Current Data Parameters
NAME                  ss7-147
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070501
Time                   18.43
INSTRUM                spect
PROBHD    5 mm QNP 1H/13
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9586243 sec
RG                       90.5
DW                     60.400 usec
DE                      6.00 usec
TE                     293.2 K
D1                 1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      13.88 usec
PL1                      0.00 dB
SFO1              400.1324710 MHz

F2 - Processing parameters
SI                      32768
SF                400.1300000 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

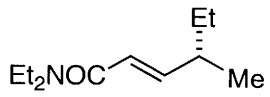


Table 5, entry 5


```
Current Data Parameters
NAME                  SS8-035
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070627
Time                  23.59
INSTRUM                spect
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                      114
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    15.07 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                     131072
SF            400.1300057 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

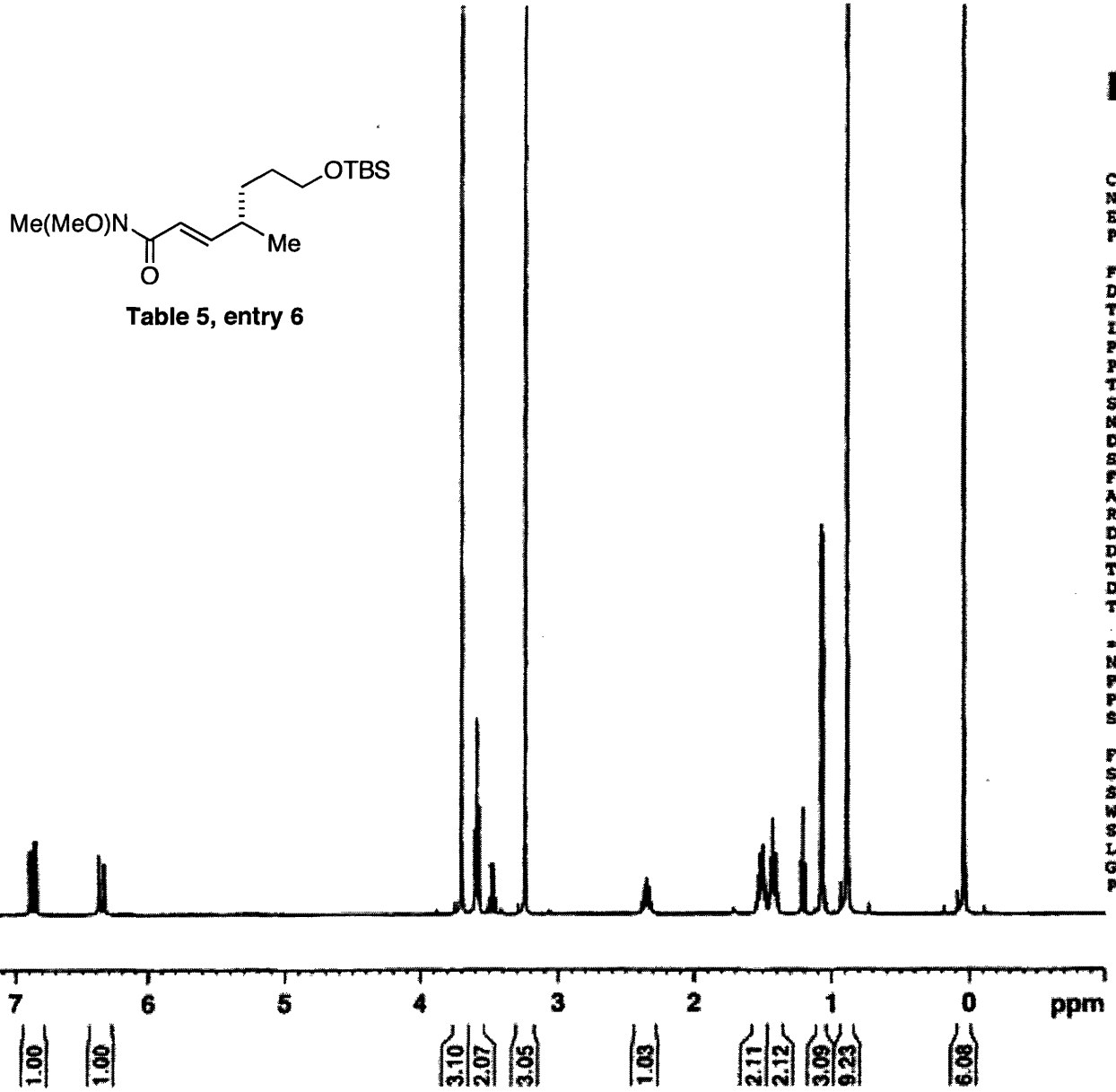


Table 5, entry 6

```
Current Data Parameters
NAME                  SS8-037
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070628
Time                   0.13
INSTRUM               spect
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                      114
DW                 60.400 usec
DE                  6.00 usec
TE                 293.2 K
D1            1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    1H
P1                 15.07 usec
PL1                 0.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                   131072
SF           400.1300057 MHz
WDW                      EM
SSB                       0
LB                  0.30 Hz
GB                        0
PC                     1.00
```

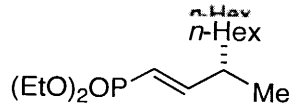


Table 5, entry 7

BRUKER

```
Current Data Parameters
NAME                  ss8-091
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070913
Time                  13.09
INSTRUM               spect
PROBHD    5 mm QNP 1H/13
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                        8
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                      256
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    1H
P1                   13.88 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF          400.1300000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

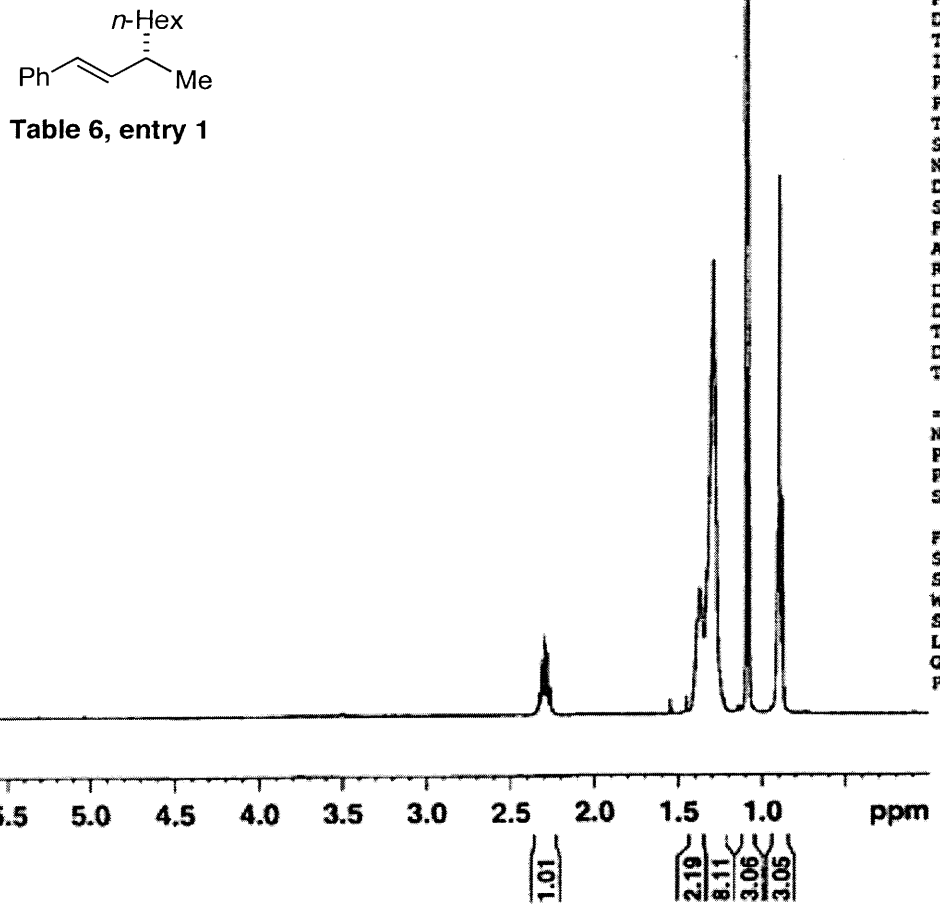


Table 6, entry 1

BRUKER

```
Current Data Parameters
NAME                  SS7-015
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070305
Time                 23.41
INSTRUM              spect
PROBHD   5 mm BBO BB-1H
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    114
DW                 60.400 usec
DE                  6.00 usec
TE                 293.2 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  15.07 usec
PL1                  0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                  65536
SF            400.1300058 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

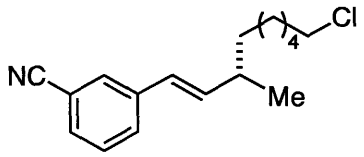


Table 6, entry 2

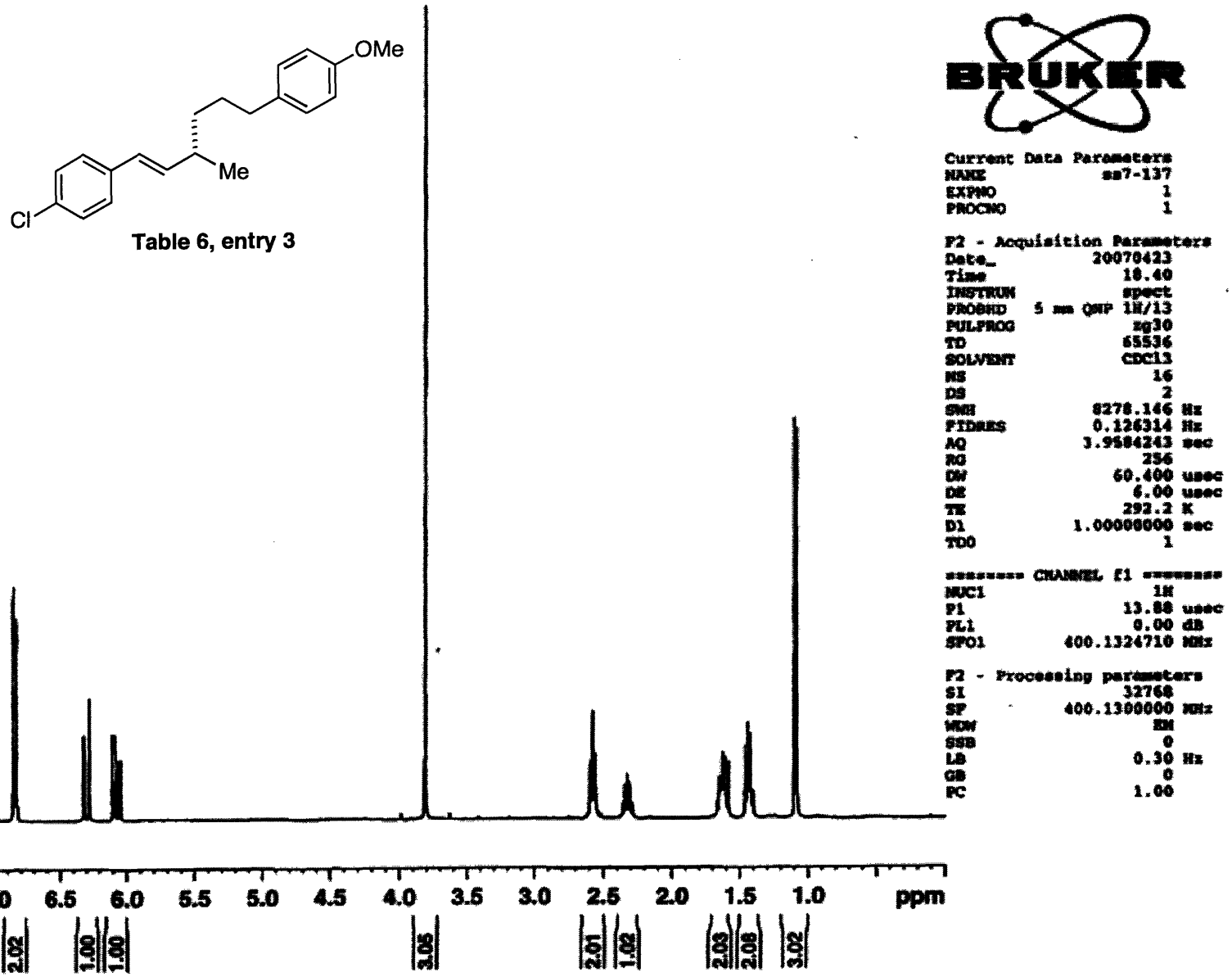
BRUKER

```
Current Data Parameters
NAME                  ss7-153
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070427
Time                  18.39
INSTRUM               spect
PROBHD   5 mm QNP 1H/13
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
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                    292.2 K
D1                 1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   13.88 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF            400.1300000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```



BRUKER

```
Current Data Parameters
NAME                 sm7-137
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20070423
Time                   18.40
INSTRUM                spect
PROBHD   5 mm QNP 1H/13
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      256
DW                   60.400 usec
DE                    6.00 usec
TE                   292.2 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     13.88 usec
PL1                     0.00 dB
SFO1           400.1324710 MHz

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SSB                        0
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PC                      1.00
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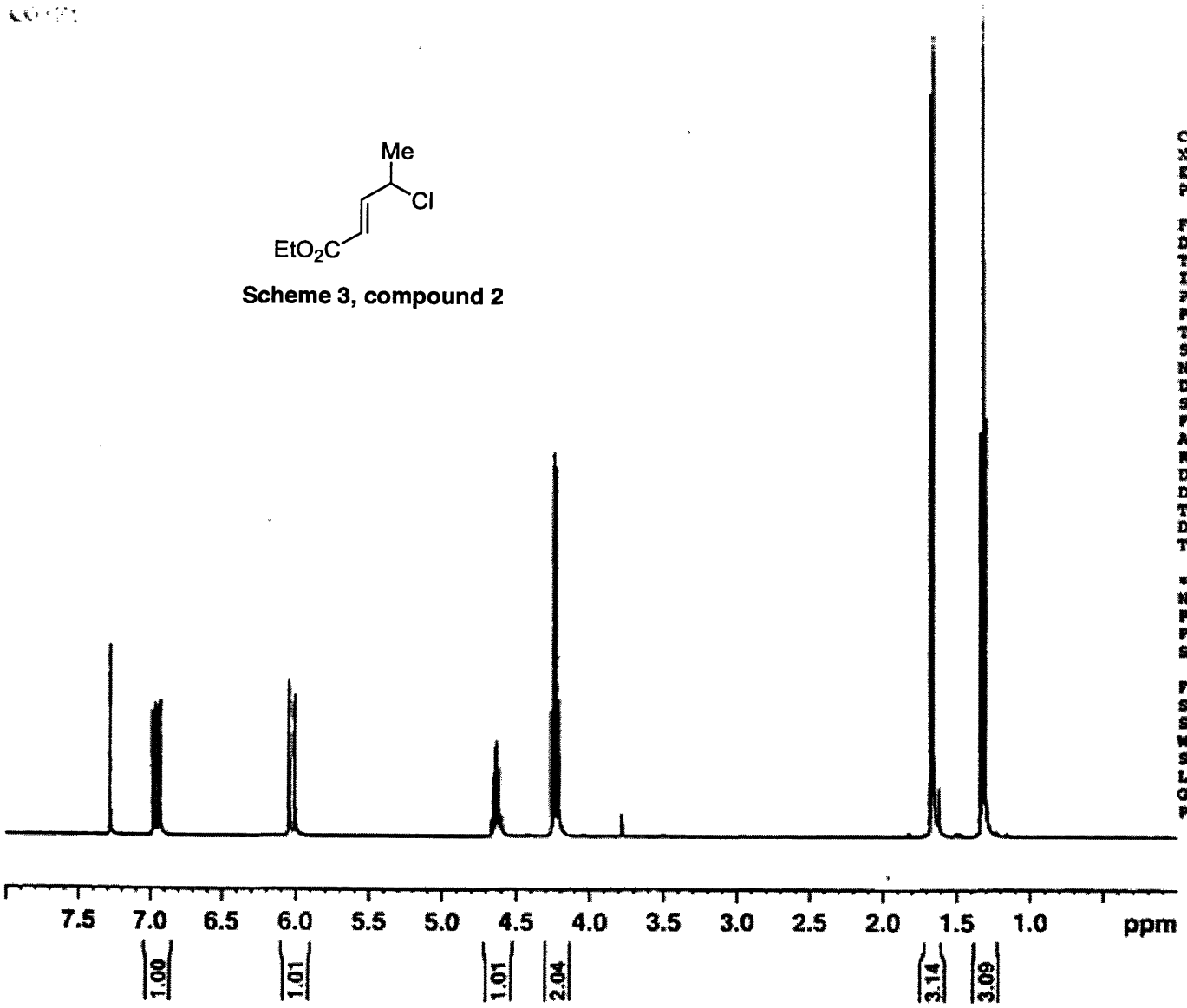

Scheme 3, compound 2

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PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
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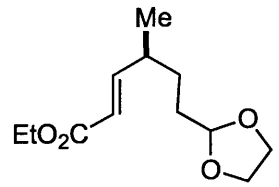
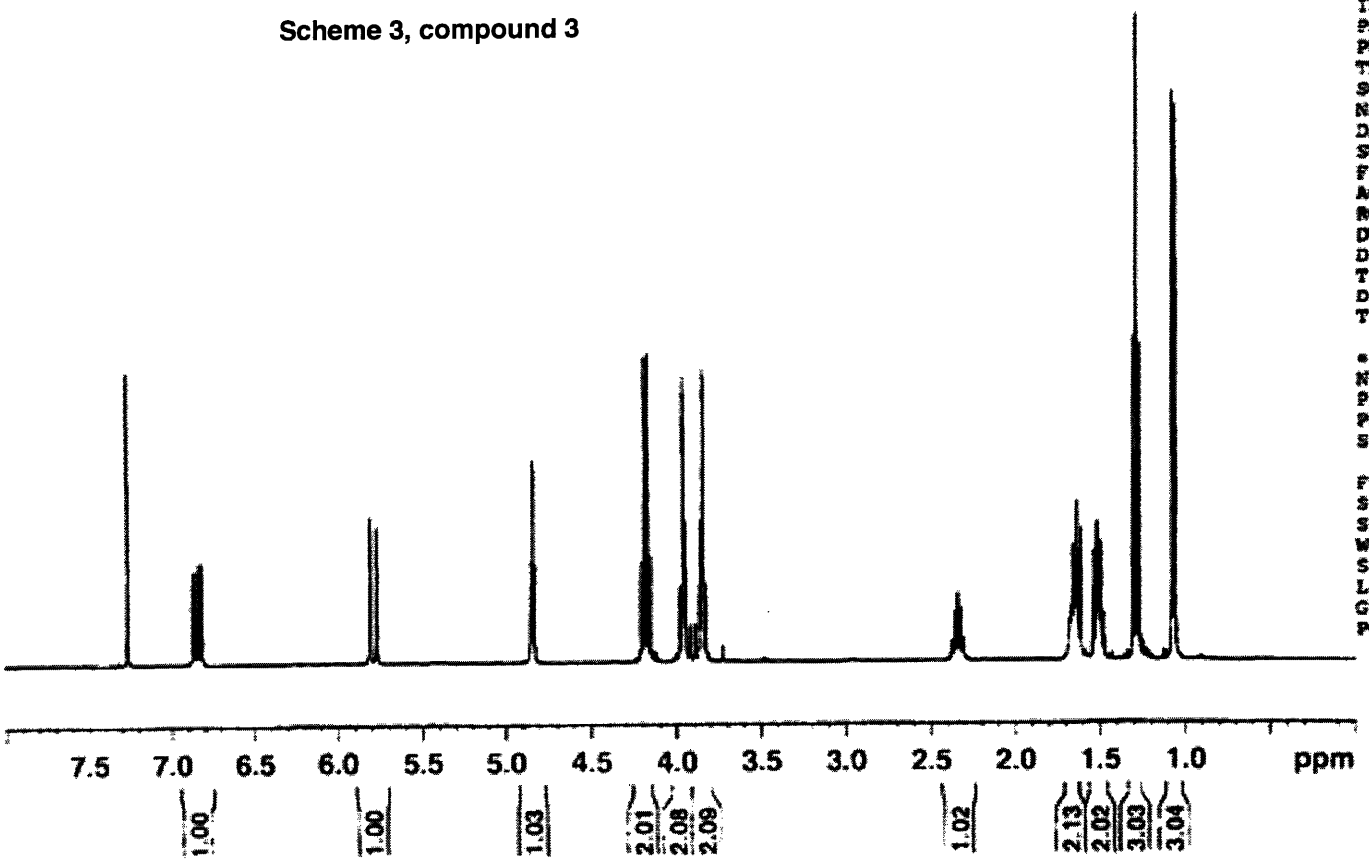


Scheme 3, compound 3



BRUKER

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PROCNO                     1

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NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      128
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
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SFO1          400.1326710 MHz

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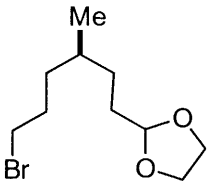
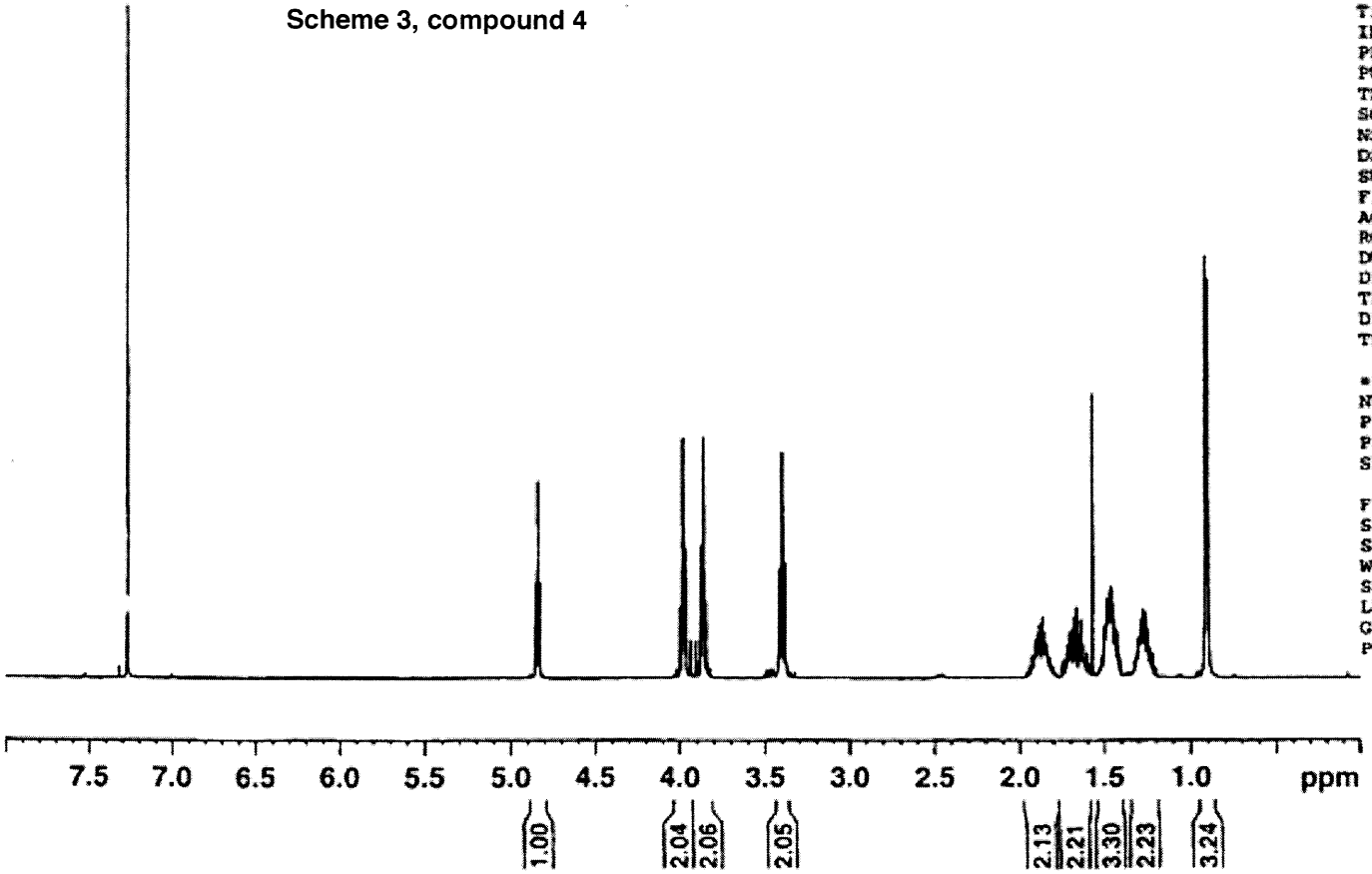


Scheme 3, compound 4

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PROCNO                     1

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PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    203.2
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1              1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
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PL1                     0.00 dB
SFO1           400.1324710 MHz

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SSB                        0
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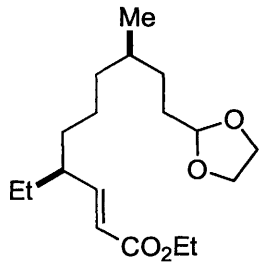
GB                         0
PC                      1.00
```

205-2



Scheme 3, compound 5

BRUKER

```
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PROCNO                     1

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INSTRUM                spect
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PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     101.6
DW                    60.400 usec
DE                     6.00 usec
TE                    293.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
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WDW                        EM
SSB                         0
LB                      0.30 Hz
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PC                      1.00
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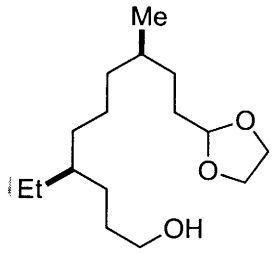
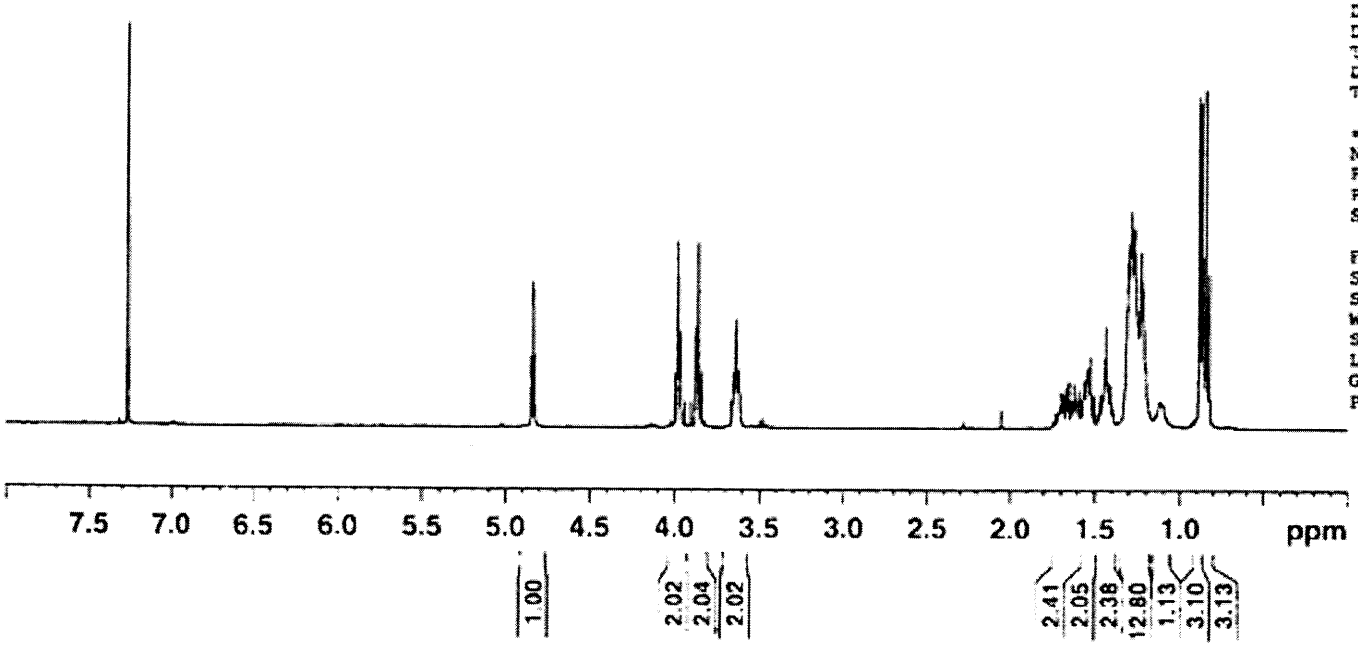


Scheme 3

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PROCNO                     1

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PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                      181
DW                   60.400 usec
DE                    6.00 usec
TE                  293.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    15.07 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
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WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
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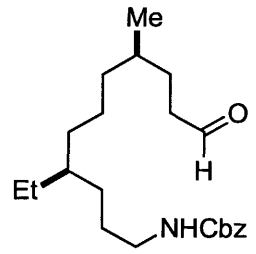
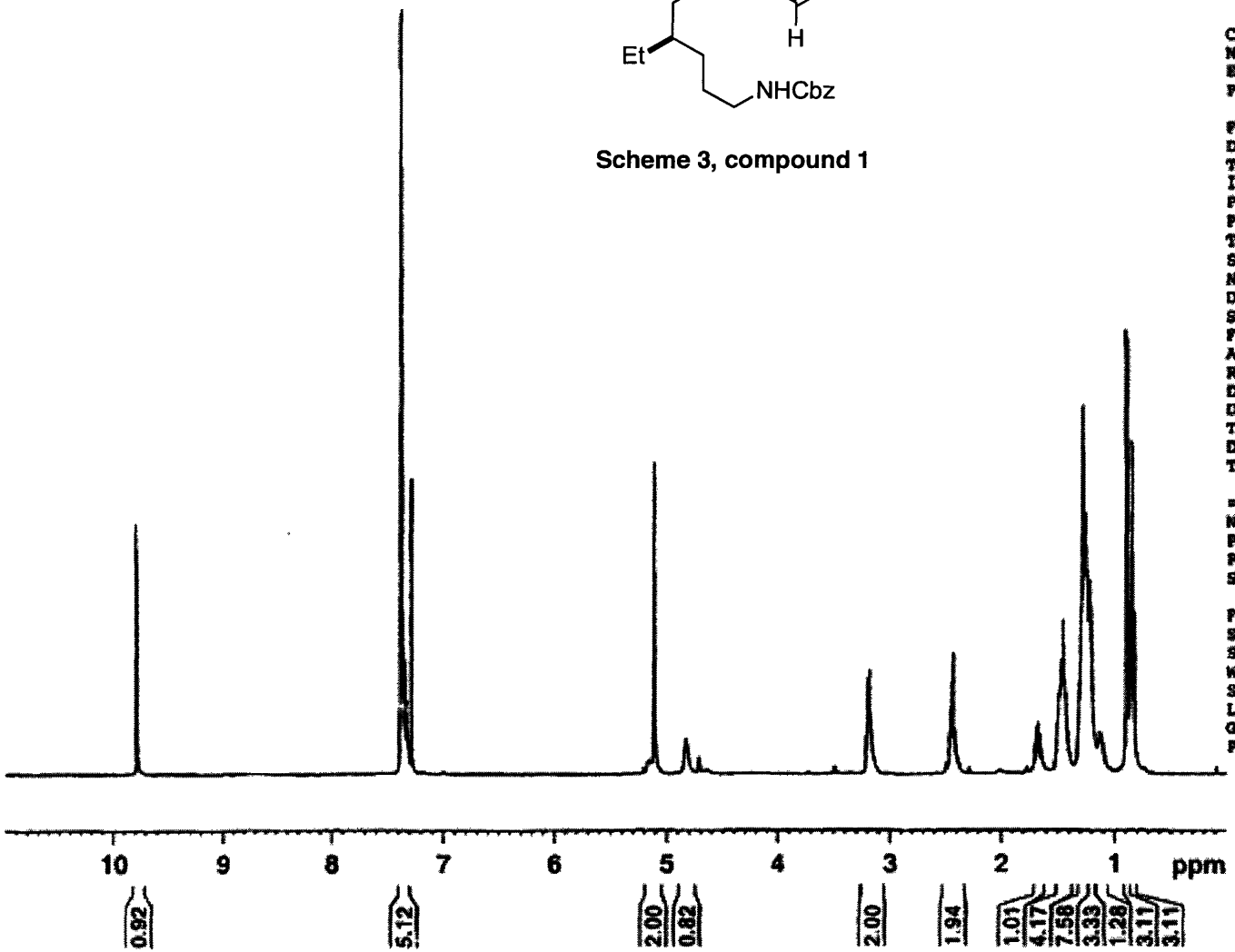


Scheme 3, compound 1

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EXPNO                       3
PROCNO                      1

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PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       128
DW                    60.400 usec
DE                     6.00 usec
TE                    293.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
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PL1                    0.00 dB
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F2 - Processing parameters
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LB                     0.30 Hz
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PC                     1.00
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Part II

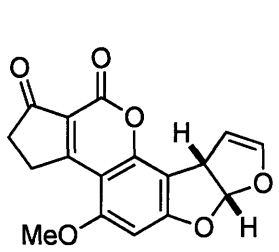
Planar-Chiral Compounds in Asymmetric Organic Synthesis

Chapter 2

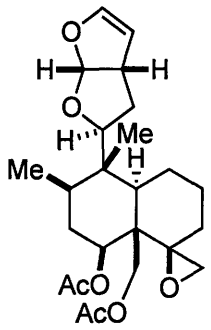
Copper-Catalyzed Asymmetric [4+1] Cycloadditions of Enones with Diazoacetates to form Dihydrofuran

A. Introduction

2,3-Dihydrofurans are very important molecules that can be found in an array of bioactive compounds, such as aflatoxin B_1 and clerodin (Figure 1).[1]



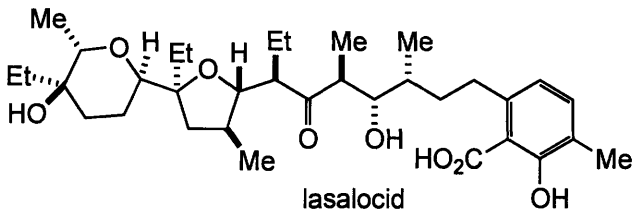
aflatoxin B_1



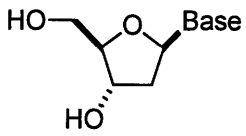
clerodin

Figure 1. Examples of Bioactive Natural Molecules Containing a 2,3-Dihydrofuran.

They also serve as extremely important synthetic intermediates, since they can be stereoselectively converted to a range of highly functionalized compounds. Highly substituted tetrahydrofurans[2] are of special interest since they can be found in numerous bioactive molecules, including lasalocid and deoxy nucleosides (Figure 2).



lasalocid



deoxy nucleoside:
DNA building block

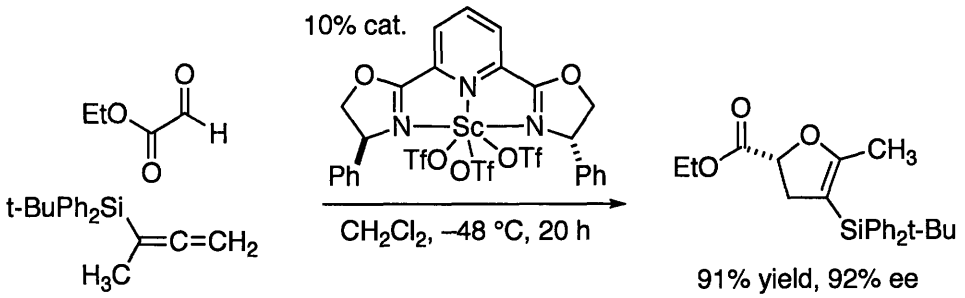
Figure 2. Representative Bioactive Natural Molecules Containing a Tetrahydrofuran.

---

[1] For a review and leading references, see: Kilroy, T. G.; O'Sullivan, T. P.; Guiry, P. J. *Eur. J. Org. Chem.* **2005**, 4929–4949.

[2] For leading references to the asymmetric synthesis of tetrahydrofurans, see: (a) Hou, X.-L.; Yang, Z.; Yeung, K.-S.; Wong, H. N. C. *Prog. Heterocycl. Chem.* **2005**, *17*, 142–171. (b) Elliott, M. C. *J. Chem. Soc., Perkin Trans. 1*, **2002**, 2301–2323. (c) Faul, M. M.; Huff, B. E. *Chem. Rev.* **2000**, *100*, 2407–2473.

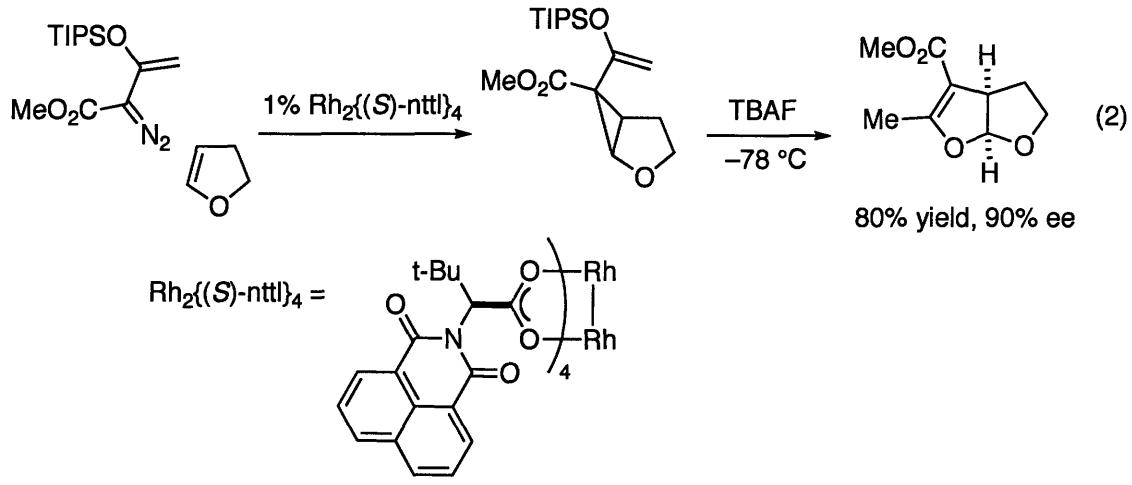
Although many methods have been developed for the synthesis of 2,3-dihydrofurans, only a few catalytic asymmetric strategies have been described.[3] Evans has reported a scandium/Pybox catalyst for [3+2] annulation of allenylsilanes (eq 1).[3a] Several allenylsilanes substituted with an unbranched alkyl group undergo the cyclization with good yield and enantioselectivity. However, the efficiency is lower for substrates with a branched alkyl group or an aryl group. They could substitute the silyl group with an acyl group via a Friedel-Crafts reaction, but the removal of the silyl group was not successful.



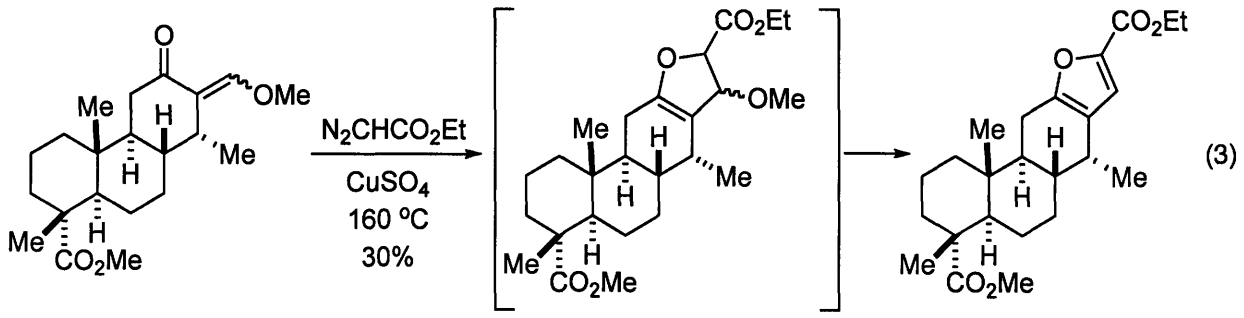
(1)

Mueller has reported a two-step procedure to generate 2,3-dihydrofurans (eq 2).[3b] After cyclopropanation of dihydrofuran or dihydropyran with 1-(silyloxy)vinyl diazoacetates, desilylation affords fused dihydrofurans with good stereoselectivity. Although this two-step strategy presents improved results from a previously reported one-step procedure by Ishitani,[3c] only two examples are described, one each from dihydrofuran and dihydropyran.

[3] For other catalytic asymmetric methods for the synthesis of 2,3-dihydrofurans from achiral precursors that proceed with good enantioselectivity, see: (a) Evans, D. A.; Sweeney, Z. K.; Rovis, T.; Tedrow, J. S. *J. Am. Chem. Soc.* **2001**, *123*, 12095–12096. (b) Mueller, P.; Bernardinelli, G.; Allenbach, Y. F.; Ferri, M.; Grass, S. *Synlett* **2005**, 1397–1400 (two examples, which differ in a silyl group). (c) Ishitani, H.; Achiwa, K. *Heterocycles* **1997**, *46*, 153–156 (one example).



In 1967, Spencer reported a $CuSO_4$-catalyzed [4+1] cycloaddition of β-methoxy-α,β-unsaturated ketones with ethyl diazoacetates to form furans and applied this method to a total synthesis of methyl vinhaticoate (eq 3).[4]



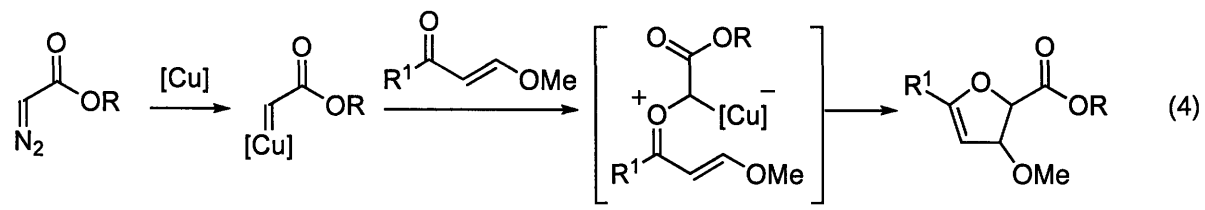
The reaction mechanism is believed to involve cyclization of a carbonyl ylide[5,6] to form a 2,3-dihydrofuran intermediate, which loses methanol under the reaction conditions leading to the furan (eq 4).

---

[4] (a) Storm, D. L.; Spencer, T. A. *Tetrahedron Lett.* **1967**, *8*, 1865–1867. (b) Spencer, T. A.; Villarica, R. M.; Storm, D. L.; Weaver, T. D.; Friary, R. J.; Posler, J.; Shafer, P. R. *J. Am. Chem. Soc.* **1967**, *89*, 5497–5499. (c) See also: Murayama, S. T.; Spencer, T. A. *Tetrahedron Lett.* **1969**, *10*, 4479–4482.

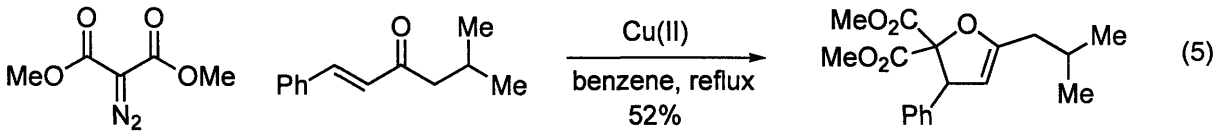
[5] For leading references to the chemistry of carbonyl ylides, see: (a) *Nitrogen, Oxygen and Sulfur Ylide Chemistry*; Clark, J. S., Ed.; Oxford: New York, 2002. (b) McMills, M. C.; Wright, D. *Chem. Heterocycl. Compd.* **2002**, *59*, 253–314. (c) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley: New York, 1998. (d) Padwa, A. *Helv. Chim. Acta* **2005**, *88*, 1357–1374.

[6] For leading references to catalytic asymmetric reactions of ylides formed from diazo compounds, see: Davies, H. M. L. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 2004; pp 83–94. (b) Hodgson, D. M.; Pierard, F. Y. T. M.; Stupple, P. A. *Chem. Soc. Rev.* **2001**, *30*, 50–61.



(4)

Since this study, there have been a few reports of copper-catalyzed cycloadditions of enones with diazo compounds (eq 5). However, none of these investigations have explored stereoselective transformations.[7]

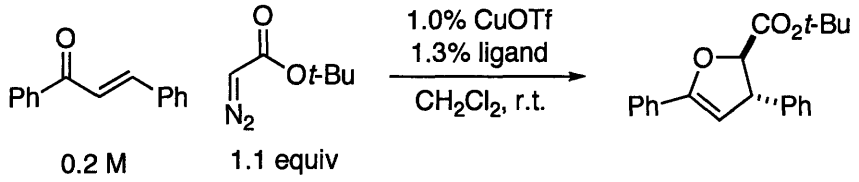


(5)

[7] (a) Anac, O.; Daut, A. *Liebigs Ann. Recueil.* **1997**, 1249–1254. (b) Anac, O.; Ozdemir, A. D.; Sezer, O. *Helv. Chim. Acta* **2003**, *86*, 290–298. (c) Anac, O.; Guengor, F. S.; Kahveci, C.; Cansever, M. S. *Helv. Chim. Acta* **2004**, *87*, 408–415. (d) See also: Paulissen, R.; Hayez, E.; Hubert, A. J.; Teyssie, P. *Tetrahedron Lett.* **1974**, *15*, 607–608.

B. Results and Discussion

To develop an efficient catalytic system for stereoselective synthesis of highly substituted 2,3-dihydrofurans, we chose chalcone and *t*-butyl diazoacetate as model substrates. The basic reaction conditions for more thorough optimization screening were determined after examination of several reaction parameters, including metal sources, solvents, temperature, and concentration (eq 6). To minimize carbene dimerization, the diazo compound was added over 4–6 hours using a syringe pump.



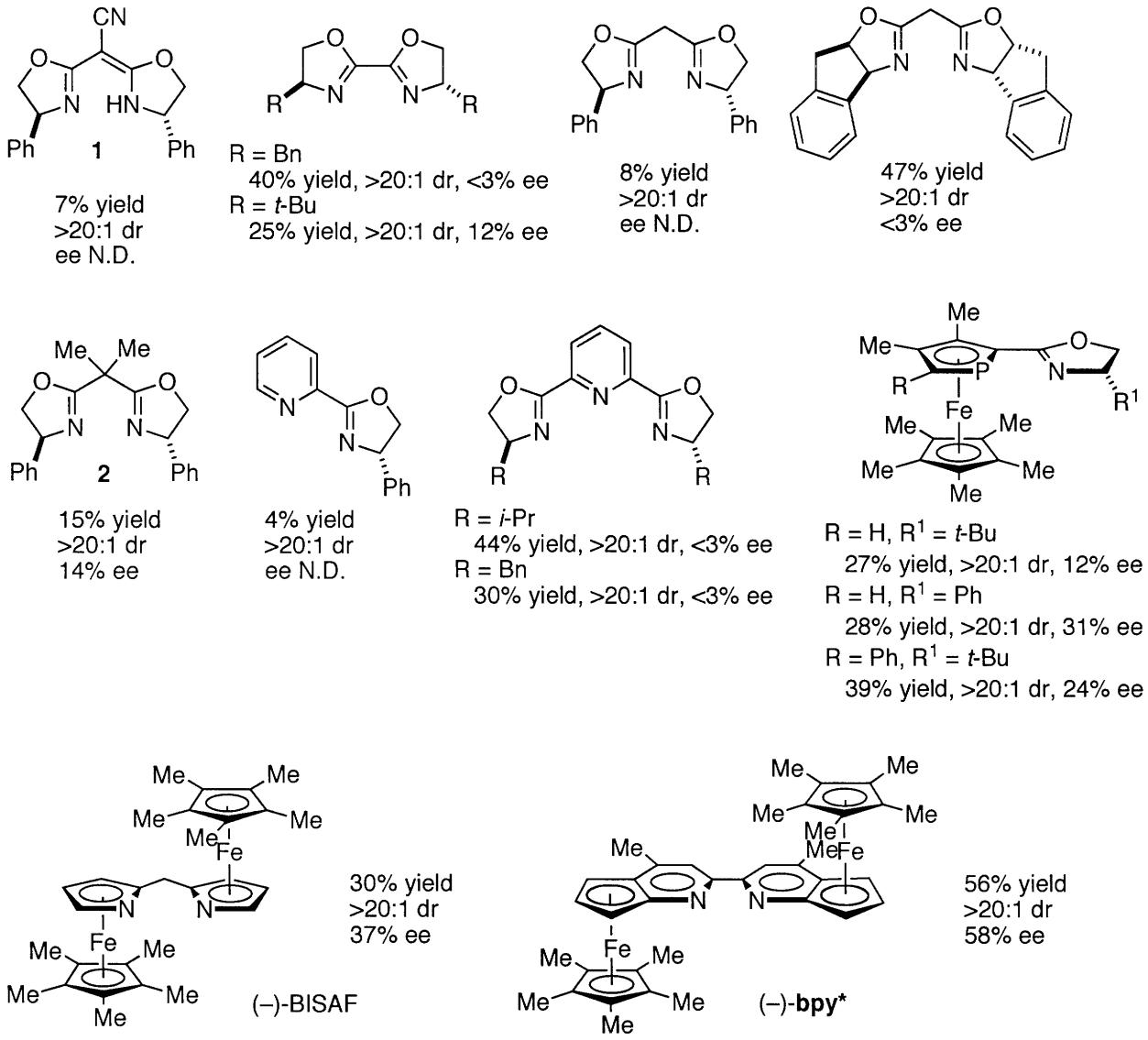
(6)

Under these conditions, we tested a variety of chiral ligands for the copper-catalyzed cycloaddition of enones with diazoacetates (Figure 3). Although some of the commercially available chiral ligands provided the desired 2,3-dihydrofuran product in moderate yield and good diastereoselectivity, the enantioselectivity was low in most of cases. Fortunately, a bis(azaferrocene) (**BISAF**)[8] and a planar-chiral 2,2′-bipyridine (**bpy***),[9,10] which have been developed in our group and successfully applied to other copper-catalyzed reactions, showed promising enantioselectivity.

[8] For leading references to previous applications, see: Maier, T. C.; Fu, G. C. *J. Am. Chem. Soc.* **2006**, *128*, 4594–4595.

[9] For the initial report of the synthesis of this ligand, see: Rios, R.; Liang, J.; Lo, M. M.-C.; Fu, G. C. *Chem. Commun.* **2000**, 377–378.

[10] For reviews of chiral 2,2′-bipyridine ligands, see: (a) Malkov, A. V.; Kocovsky, P. *Curr. Org. Chem.* **2003**, *7*, 1737–1757. (b) Fletcher, N. C. *J. Chem. Soc., Perkin Trans. 1*, **2002**, 1831–1842.



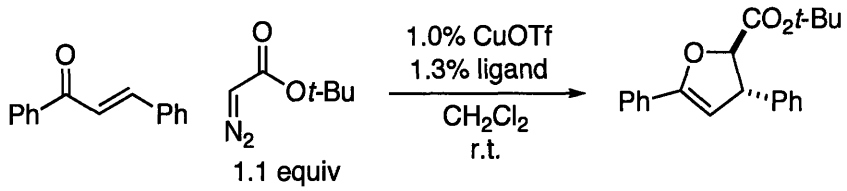
* N.D. = not determined

Figure 3. Copper-catalyzed Asymmetric [4+1] Cycloadditions: Survey of Ligands with Slow Addition of the Diazoacetate.

Even though slow addition of the diazo compound helps to minimize carbene dimerization, we decided to pursue a one-portion addition to make the reaction procedure more convenient. Results when the diazo compound was added in one portion in the presence of a few representative chiral ligands are shown in Table 1. As expected, with most of the ligands we obtained a lower yield without the slow addition

of the diazo compound. However, **bpy*** exhibited promising reactivity, and the stereoselectivity remained almost the same (entry 4).

Table 1. Copper-catalyzed Asymmetric [4+1] Cycloadditions: Survey of Ligands with One-Portion Addition of the Diazoacetate.

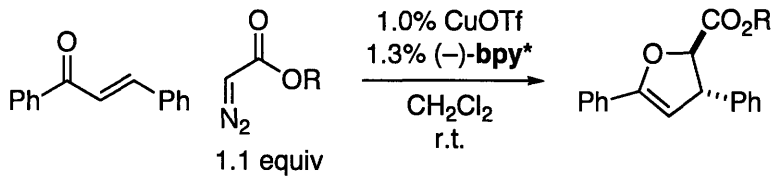


entry	ligand	yield (%)[a]	dr	ee (%)
1	bis(oxazoline) **2**	12	>20:1	–20[b]
2	semicorrin **1**	<2	–	–
3	**BISAF**	6	>20:1	34
4	(–)-**bpy***	45	>20:1	60
5	no ligand	10	>20:1	–
6	no CuOTf, no ligand	<2	–	–

All data are the average of two runs. [a]Isolated yield of the trans diastereomer. [b]The opposite enantiomer is produced.

To improve our initial lead and keep the convenient reaction setup, we examined the effect of steric demand of the diazoester on these Cu/**bpy***-catalyzed asymmetric [4+1] cycloadditions (Table 2). Diazo compounds containing a small alkyl or aryl group provided lower ee (entries 2 and 3 versus entry 1). When the steric hindrance of aryl groups increased, enantioselectivities improved (entries 4–6), and the best combination of yield, dr, and ee was obtained with the 2,6-diisopropylphenyl ester (entry 5).

Table 2. Impact of the Steric Demand of the Diazoacetate.

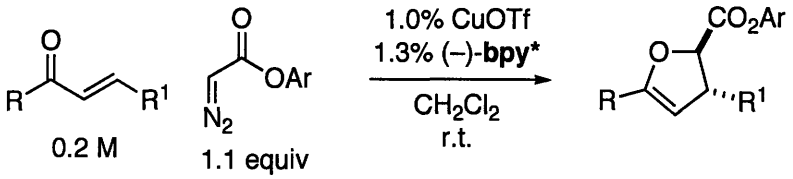


entry	R	yield (%)[a]	dr	ee (%)
1	*t*-Bu	45	>20:1	60
2	Et	43	>20:1	37
3	Ph	44	>20:1	37
4	2,6-dimethylphenyl	63	7:1	83
5	2,6-diisopropylphenyl	79	13:1	85
6	2,6-di-*t*-butyl-4-methylphenyl	47	16:1	85

All data are the average of two runs. [a]Isolated yield of the trans diastereomer.

We have examined the scope of this copper-catalyzed asymmetric [4+1] cycloaddition of enones with 2,6-diisopropylphenyl diazoacetate (Table 3). When both substituents of the enone are unsaturated, the enantioselectivity is the highest. Hence, enones with phenyl substituents of different electronic properties furnish good ee (entries 2–6), although an electron-poor substrate shows slightly diminished reactivity and enantioselectivity (entry 2). With substrates containing a heteroaromatic substituent, the reactions proceed with good enantioselectivities (entries 7 and 8). Furthermore, no competing cyclopropanation is observable when an alkenyl substituent is present (entry 9). Enones with an alkyl group at the β-position exhibit lower enantioselectivity than those with an unsaturated group. Nonetheless, the desired dihydrofurans are generally produced in good yield and with excellent diastereoselectivity (entries 10 and 11).

Table 3. Copper-Catalyzed Asymmetric [4+1] Cycloadditions: Enones with Unsaturated Substituents.



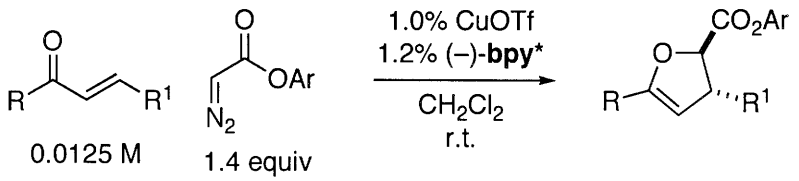
Ar = 2,6-diisopropylphenyl

entry	R	R^1	yield (%)[a]	dr	ee (%)
1	Ph	Ph	79	13:1	85
2	4-$(F_3C)C_6H_4$	Ph	59	19:1	76
3	4-ClC_6H_4	Ph	77	19:1	88
4[b]	4-$(MeO)C_6H_4$	Ph	84	19:1	92
5	Ph	4-ClC_6H_4	81	>20:1	88
6	Ph	4-$(MeO)C_6H_4$	84	9:1	93
7	*N*-Boc-2-pyrrolyl	Ph	68	>20:1	93
8	Ph	3-furyl	63	6:1	87
9	Ph	CH=CHPh	76	7:1	93
10	Ph	*n*-Bu	92	>20:1	78
11	Ph	*i*-Pr	85	>20:1	50

All data are the average of two runs. [a]Isolated yield of the trans diastereomer. [b]The product was hydrolyzed and then acetylated, prior to isolation.

This Cu/bpy*-catalyzed cycloaddition may also be applied when R is an alkyl group, albeit under slightly modified conditions (Table 4). In general, these enones undergo the cyclization in good yield and with good diastereoselectivity. However, enantiomeric excesses are around 70% regardless of the R group.

Table 4. Copper-Catalyzed Asymmetric [4+1] Cycloadditions: Enones with Alkyl Substituents.

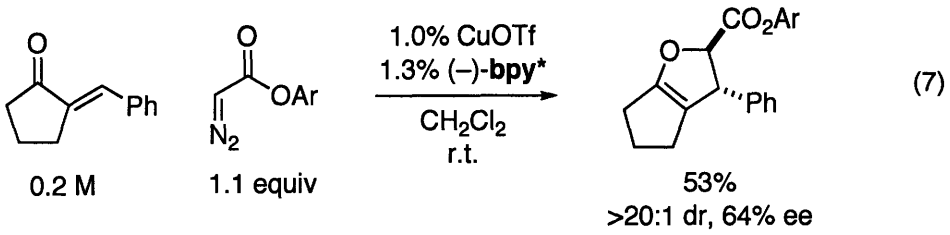


Ar = 2,6-diisopropylphenyl

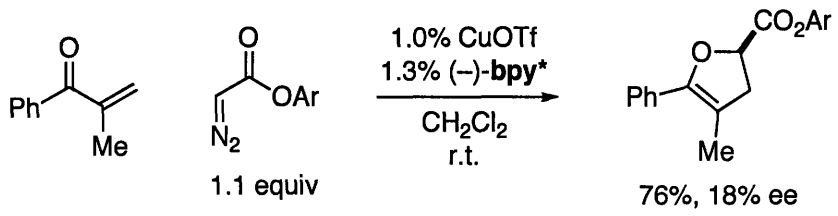
entry	R	R^1	yield (%)[a]	dr	ee (%)
1	*n*-Hex	Ph	69	13:1	75
2	*i*-Pr	Ph	87	16:1	66
3	*t*-Bu	Ph	82	>20:1	69
4	*n*-Hex	Me	80	>20:1	71
5[b]	$PhCH_2CH_2$	H	50	N/A	69

All data are the average of two runs. [a]Isolated yield of the trans diastereomer. [b]The product was hydrolyzed and then acetylated, prior to isolation.

Although various enones produce the desired 2,3-dihydrofurans with good efficiency as discussed above, some substrates prove to be more challenging for this cycloaddition under the current reaction conditions. For example, a cyclicketone with an external double bond produces the desired product in rather modest yield and ee (eq 7). The reaction of an enone with a substituent in the α-position proceeds in good yield but with poor enantioselectivity (eq 8). In addition, α,β-unsaturated esters are not suitable substrates under our standard conditions.

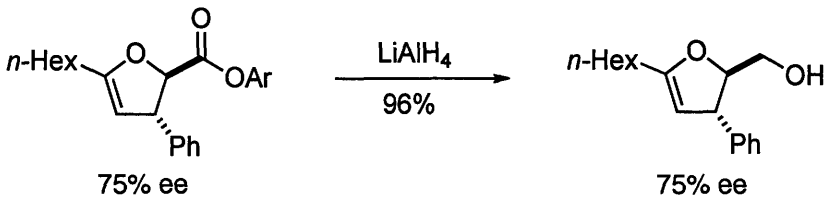


(7)



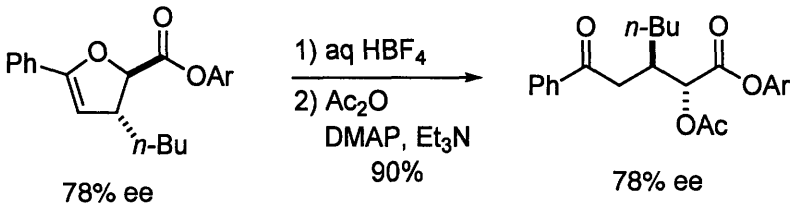
(8)

As mentioned earlier, the 2,3-dihydrofuran products can be converted to a variety of other useful compounds without any erosion in stereochemical purity. Therefore, treatment of the trans isomer of the cycloaddition product with $LiAlH_4$ furnishes a primary alcohol in good yield (eq 9). Hydrolysis followed by acetylation produces an acyclic ester with an α and a β stereocenter (eq 10).



(9)

Ar = 2,6-diisopropylphenyl



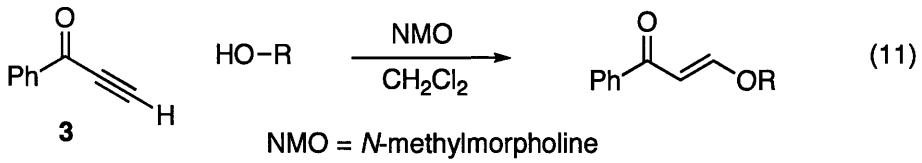
(10)

To further demonstrate the utility of our Cu/**bpy***-catalyzed [4+1] cycloaddition, we decided to apply this method to the catalytic asymmetric synthesis of useful molecules such as a deoxy-C-nucleoside.[11] Deoxy-C-nucleosides are mimics of natural building

[11] For some leading references, see: (a) Kool, E. T. *Acc. Chem. Res.* **2002**, *35*, 936–943. (b) Loakes, D. *Nucleic Acids Res.* **2001**, *29*, 2437–2447. (c) Watanabe, K. A. In *Chemistry of Nucleosides and Nucleotides*; Townsend, L. B., Ed.; Plenum: New York, 1994; Vol. 3, pp 421–535.

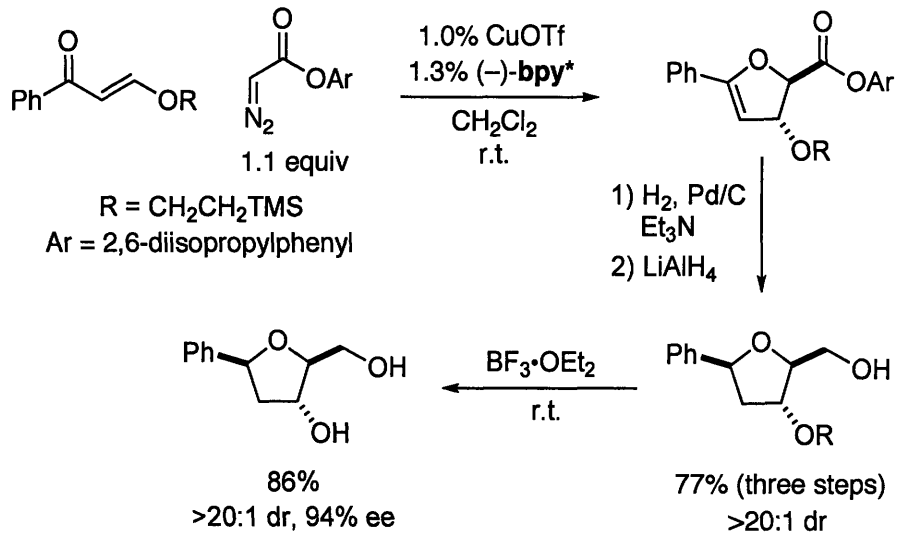
blocks of DNA and attract great interest in medicinal chemistry. Thus, a catalytic asymmetric method for the synthesis of these molecules is highly desirable, especially from easily accessible substrates.

The 3-hydroxytetrahydrofuran structure of deoxy-C-nucleosides can be easily constructed via cycloaddition of a β-alkoxy-α,β-unsaturated ketone. However, as shown in Spencer's report on the formation of furans from 4-methoxy-2,3-dihydrofurans (eq 3), the resulting dihydrofuran is prone to elimination of alcohol. For minimal elimination after cycloaddition and facile deprotection at the final step, we have tested several β-alkoxy-α,β-unsaturated ketones, which can be easily prepared by addition of alcohols to alkynylketone **3** (eq 11). The trimethylsilylethyl protecting group proved very efficient in not only the cycloaddition but also in the following step since the group is deprotected under orthogonal reaction conditions to other functionalization processes.



Cycloaddition of an α-diazoacetate to the vinylogous ester furnishes the desired 4-alkoxy-2,3-dihydrofuran, which is used for next transformations without isolation due to its sensitivity (Scheme 1). Catalytic hydrogenation in the presence of Et_3N produces the corresponding tetrahydrofuran without cleavage of the C2–O bond. After reduction of the ester, the desired primary alcohol was obtained in 77% yield for three steps with excellent diastereoselectivity (>20:1). Finally, deprotection of trimethylsilylethyl group provides the deoxy-C-nucleoside (94% ee).[12]

[12] For studies of this deoxy-C-nucleoside, see: (a) Initial work: Millican, T. A.; Mock, G. A.; Chauncey, M. A.; Patel, T. P.; Eaton, M. A. W.; Gunning, J.; Cutbush, S. D.; Neidle, S.; Mann, J. *Nucleic Acids Res.* **1984**, *12*, 7435–7453. (b) Matsuda, S.; Romesberg, F. E. *J. Am. Chem. Soc.* **2004**, *126*, 14419–14427. (c) Mathis, G.; Hunziker, J. *Angew. Chem. Int. Ed.* **2002**, *41*, 3203–3205. (d) Guckian, K. M.; Schweitzer, B. A.; Ren, R. X.-F.; Sheils, C. J.; Tahmassebi, D. C.; Kool, E. T. *J. Am. Chem. Soc.* **2000**, *122*, 2213–2222.



Scheme 1. Catalytic Enantioselective Synthesis of Deoxy-C-nucleoside.

C. Conclusions

In conclusion, we have reported the first example of diastereo- and enantioselective copper-catalyzed [4+1] cycloaddition of enones with diazo compounds. Use of sterically demanding aryl diazoacetates improves the efficiency and stereoselectivity of the reaction and also enables one-portion addition of the diazo compound. This method furnishes synthetically useful, highly substituted 2,3-dihydrofuranans from a variety of enones. The cycloaddition products can be converted to other useful molecules in high yield without an erosion of stereochemical purity. In addition, we have applied this method to the first catalytic enantioselective synthesis of a deoxy-C-nucleoside.

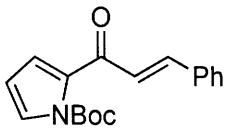
D. Experimental

1. General

All reactions were carried out in oven-dried glassware under an atmosphere of nitrogen. CH_2Cl_2 was purified by passage through a neutral alumina column under argon. $CuOTf{\cdot}0.5C_6H_5CH_3$ was purchased from Aldrich, and the diazo esters[13] and bpy*[14] were prepared according to literature procedures. All other chemicals were purchased from commercial suppliers and used as received, unless noted otherwise.

HPLC analyses were carried out on an Agilent 1100 series system with Daicel Chiralpak® columns in hexane/isopropanol mixtures. Melting points were measured on a Hoover melting point apparatus and are uncorrected.

2. Preparation of Starting Material



***tert*-Butyl 2-((*E*)-3-phenylacryloyl)-1*H*-pyrrole-1-carboxylate.** A 100-mL flask was charged with 2-acetylpyrrole (3.27 g, 30.0 mmol), 4-(dimethylamino)pyridine (73 mg, 0.6 mmol), triethylamine (4.2 mL, 30.0 mmol) and THF (30 mL). To this reaction mixture was added a solution of Boc anhydride (dropwise; 30 mL, 1.0M in THF, 30.0 mmol). The reaction mixture was stirred overnight, and then a saturated $NaHCO_3$ solution (30 mL) was added. The resulting mixture was extracted with Et_2O (30 mL x 3), and the combined extracts were dried over $MgSO_4$ and concentrated. The product was purified by column chromatography (hexanes/EtOAc 5:1), which furnished 5.64 g (90%) of *N*-Boc-2-acetylpyrrole.

N-Boc-2-acetylpyrrole (5.64 g, 27.0 mmol) was added to a stirred solution of LiHMDS solution (1.0 M in THF; 28 mL, 28 mmol) at –78 °C under argon, and the

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[13] (a) Nicewicz, D. A.; Johnson, J. S. *J. Am. Chem. Soc.* **2005**, *127*, 6170–6171. (b) Doyle, M. P.; Austin, R. E.; Bailey, A. S.; Dwyer, M. P.; Dyatkin, A. B.; Kalinin, A. V.; Kwan, M. M. Y.; Liras, S.; Oalmann, C. J.; Pieters, R. J.; Protopopova, M. N.; Raab, C. E.; Roos, G. H. P.; Zhou, Q.-L.; Martin, S. F. *J. Am. Chem. Soc.* **1995**, *117*, 5763–5775.

[14] Rios, R.; Liang, J.; Lo, M. M.-C.; Fu, G. C. *Chem. Commun.* **2000**, 377–378.

resulting mixture was stirred for 2 h. Then, benzaldehyde (2.8 mL, 27.0 mmol) was added, and the reaction mixture was stirred for an additional 2 h. The reaction was then quenched by the addition of saturated aq NH_4Cl (40 mL), and the mixture was extracted with Et_2O (30 mL x 3). The combined extracts were dried over $MgSO_4$, concentrated, and purified by column chromatography (hexanes/EtOAc 5:1), which furnished *N*-Boc-2-(3-hydroxy-1-oxo-3-phenylpropyl)pyrrole (6.82 g, 80%).

NEt_3 (9.0 mL, 65 mmol) and MsCl (1.65 mL, 21.7 mmol) were added to a solution of *N*-Boc-2-(3-hydroxy-1-oxo-3-phenylpropyl)pyrrole (6.82 g, 21.7 mmol) in THF (20 mL). This reaction mixture was stirred overnight, and then it was quenched by the addition of saturated aq NH_4Cl (40 mL). The mixture was extracted with Et_2O (30 mL x 3), and the combined extracts were dried over $MgSO_4$, concentrated, and purified by column chromatography (hexanes/EtOAc 5:1), which furnished *tert*-butyl 2-((*E*)-3-phenylacryloyl)-1*H*-pyrrole-1-carboxylate (5.89 g, 91%).

mp: 75-76 °C;

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.60-7.57 (m, 2H), 7.43-7.40 (m, 4H), 7.12 (d, *J* = 16.0 Hz, 1H), 6.86 (dd, *J* = 3.5, 1.6 Hz, 1H), 6.25 (t, *J* = 3.3 Hz, 1H), 1.56 (s, 9H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.8, 149.0, 143.7, 135.0, 134.3, 130.6, 129.1, 128.5, 127.4, 125.7, 120.8, 110.5, 85.2, 27.0;

IR (film) 2981, 1748, 1661, 1639, 1606, 1440, 1415, 1315, 1150 cm^{-1};

HRMS (ESI) calcd for $C_{18}H_{19}NO_3Na$ ($M + Na^+$) 320.1257, found 320.1266.

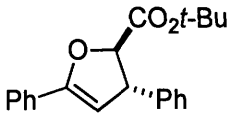
All other materials have been reported previously.

3. Copper-Catalyzed Asymmetric [4+1] Cycloadditions

All yields, dr's, and ee's are the average of two runs, one with (–)-bpy* and one with (+)-bpy*. All dr's were determined through analysis of the ^{1}H NMR spectra of the unpurified reaction mixtures.

General Procedure A. The catalyst was prepared by adding a solution of (–)-bpy* (8.4 mg ,0.013 mmol) in CH_2Cl_2 (4 mL) to CuOTf·$0.5C_6H_5CH_3$ (2.6 mg, 0.01 mmol) and stirring the resulting mixture for 20 min. This solution was then added to the enone (1.0 mmol), and the misture was tirred for 5 min. Then, a solution of the diazoacetate (1.1 mmol) in CH_2Cl_2 (1.0 mL) was added. After 1 h of stirring at room temperature, the reaction mixture was filtered through a plug of silica gel (50% Et_2O/hexane as the eluant).

General Procedure B. The catalyst was prepared by adding a solution of (–)-bpy* (7.7 mg, 0.012 mmol) in CH_2Cl_2 (10 mL) to CuOTf·$0.5C_6H_5CH_3$ (2.6 mg, 0.010 mmol) and stirring the resulting mixture for 20 min. This solution was then added to the enone (1.0 mmol) in CH_2Cl_2 (60 mL), and the mixture was stirred for 5 min. Then, a solution of the diazoacetate (1.4 mmol) in CH_2Cl_2 (10 ml) was added dropwise. After 1 h of stirring at room temperature, the reaction mixture was filtered through a plug of silica gel (50% Et_2O/hexane as the eluant).



(2*R*,3*S*)-*tert*-Butyl 2,3-dihydro-3,5-diphenylfuran-2-carboxylate (Table 2, entry 1).

General Procedure A was followed, with (–)-bpy*, *trans*-chalcone (208 mg, 1.0 mmol), and *tert*-butyldiazoacetate (156 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a cloudy oil: run 1, 145 mg (45%, >90% de, 59% ee); run 2, 145 mg (45%, >90% de, 61% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 6.5 min., t_r(minor) 7.6 min.

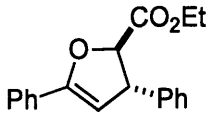
$[\alpha]^{22}_D = -26.3$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.86-7.83 (m, 2H), 7.37-7.35 (m, 2H), 7.26-7.15 (m, 6H), 5.34 (d, *J* = 2.8 Hz, 1H), 4.98 (d, *J* = 5.8 Hz, 1H), 4.59 (dd, *J* = 5.8, 2.8 Hz, 1H), 1.42 (s, 9H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.5, 157.6, 144.1, 131.2, 129.40, 129.36, 128.9, 127.8, 126.4, 99.0, 87.0, 81.6, 54.8, 28.3;

IR (film) 3062, 3029, 2978, 2933, 1751, 1728, 1648, 1602, 1494, 1369, 1156 cm^{-1};

HRMS (ESI) calcd for $C_{21}H_{22}O_3Na$ ($M + Na^+$) 345.1461, found 345.1463.



(2*R*,3*S*)-Ethyl 2,3-dihydro-3,5-diphenylfuran-2-carboxylate (Table 2, entry 2).

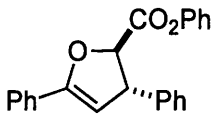
General Procedure A was followed, with (–)-bpy*, *trans*-chalcone (208 mg, 1.0 mmol), and ethyldiazoacetate (126 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), a 1:1 mixture of the title compound and chalcone was isolated as a colorless oil: run 1, 216 mg (43%, >95% de, 37% ee); run 2, 210 mg (42%, >95% de, 37% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 9.9 min., t_r(minor) 8.9 min.

^1H NMR (C_6D_6, 400 MHz) δ 7.74-7.71 (m, 2H), 7.25-7.22 (m, 2H), 7.20-7.03 (m, 6H), 5.24 (d, J = 2.9 Hz, 1H), 4.92 (d, J = 5.7 Hz, 1H), 4.49 (dd, J = 5.7, 2.9 Hz, 1H), 4.00-3.85 (m, 2H), 0.89 (t, J = 7.1 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 171.3, 157.3, 143.9, 131.0, 129.4, 129.0, 128.2, 126.4, 99.2, 99.5, 86.6, 61.5, 54.5, 14.4;

IR (film) 3028, 2981, 1756, 1734, 1665, 1648, 1494, 1449, 1069, 1029 cm^{-1};

HRMS (ESI) calcd for $C_{19}H_{19}O_3$ ($M + H^+$) 295.1329, found 295.1327.



(2*R*,3*S*)-Phenyl 2,3-dihydro-3,5-diphenylfuran-2-carboxylate (Table 2, entry 3).

General Procedure A was followed, with (–)-bpy*, *trans*-chalcone (208 mg, 1.0 mmol), and phenyldiazoacetate (178 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a white solid: run 1, 147 mg (43%, 94% de, 37% ee); run 2, 154 mg (45%, 94% de, 38% ee). The ee was determined

on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 16.1 min., t_r(minor) 18.6 min.

mp: 94-96 °C;

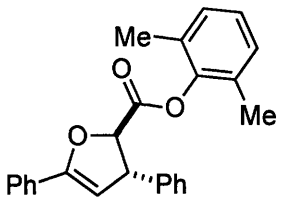
$[\alpha]^{22}_D = -50.1$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.87-7.84 (m, 2H), 7.36-7.34 (m, 2H), 7.26-7.15 (m, 6H), 7.13-7.09 (m, 4H), 7.00-6.96 (m, 1H), 5.36 (d, *J* = 2.9 Hz, 1H), 5.17 (d, *J* = 5.6 Hz, 1H), 4.69 (dd, *J* = 5.6, 2.8 Hz, 1H);

^{13}C NMR (C_6D_6, 100 MHz) δ 169.8, 157.5, 151.5, 143.5, 130.8, 130.0, 129.5, 129.0, 128.2, 128.0, 126.5, 126.4, 122.0, 99.2, 86.4, 54.7;

IR (film) 3062, 3029, 2920, 1778, 1649, 1592, 1493, 1194 cm^{-1};

HRMS (ESI) calcd for $C_{23}H_{18}O_3Na$ (M + Na^+) 365.1148, found 365.1161.



(2*R*,3*S*)-2,6-Dimethylphenyl 2,3-dihydro-3,5-diphenylfuran-2-carboxylate (Table 2, entry 4).

General Procedure A was followed, with (–)-bpy*, *trans*-chalcone (208 mg, 1.0 mmol), and 2,6-dimethylphenyldiazoacetate (209 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a cloudy oil: run 1, 233 mg (63%, 74% de, 83% ee); run 2, 230 mg (62%, 73% de, 82% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 11.6 min., t_r(minor) 14.5 min.

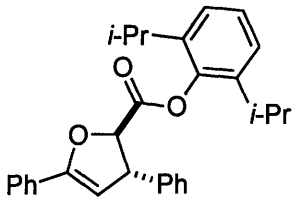
$[\alpha]^{22}_D = 108$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.88-7.85 (m, 2H), 7.42-7.40 (m, 2H), 7.29-7.18 (m, 6H), 7.00-6.94 (m, 3H), 5.42 (d, *J* = 2.9 Hz, 1H), 5.33 (d, *J* = 5.1 Hz, 1H), 4.86 (dd, *J* = 5.0, 3.0 Hz, 1H), 2.17 (s, 6H);

^{13}C NMR (C_6D_6, 100 MHz) δ 169.4, 157.5, 148.9, 143.4, 130.80, 130.78, 129.6, 129.3, 129.0, 128.3, 128.1, 126.6, 126.4, 99.3, 86.4, 54.6, 16.8;

IR (film) 3061, 3028, 2924, 1774, 1754, 1649, 1601, 1493, 1162 cm^{-1};

HRMS (ESI) calcd for $C_{25}H_{22}O_3Na$ (M + Na^+) 393.1461, found 393.1473.



(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-3,5-diphenylfuran-2-carboxylate (Table 2, entry 5).

General Procedure A was followed, with (–)-bpy*, *trans*-chalcone (208 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 341 mg (80%, 86% de, 84% ee); run 2, 328 mg (77%, 86% de, 86% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 0.7 mL/min.) with t_r(major) 13.9 min., t_r(minor) 15.0 min.

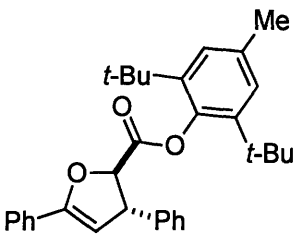
$[\alpha]^{22}_D$ = –106 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.75-7.73 (m, 2H), 7.33-7.31 (m, 2H), 7.18-7.04 (m, 9H), 5.35 (d, *J* = 2.9 Hz, 1H), 5.26 (d, *J* = 4.9 Hz, 1H), 4.83 (dd, *J* = 4.8, 1.8 Hz, 1H), 3.14 (septet, *J* = 6.8 Hz, 2H), 1.16 (d, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.6, 157.4, 146.5, 143.3, 141.1, 130.7, 129.6, 129.0, 127.5, 126.4, 124.7, 99.5, 86.6, 54.4, 28.3, 23.6;

IR (film) 3064, 3029, 2965, 2931, 2870, 1774, 1753, 1649, 1602, 1494, 1449, 1213 cm^{-1};

HRMS (ESI) calcd for $C_{29}H_{30}O_3Na$ (M + Na^+) 449.2087, found 449.2102.



(2*R*,3*S*)-2.6-Di-*tert*-butyl-4-methylphenyl 2,3-dihydro-3,5-diphenylfuran-2-carboxylate (Table 2, entry 6).

General Procedure A was followed, with (–)-bpy*, *trans*-chalcone (208 mg, 1.0 mmol), and BHT-diazoacetate (317 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a white solid: run 1, 220 mg (47%, 88% de, 85% ee); run 2, 216 mg (46%, 88% de, 84% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 6.5 min., t_r(minor) 4.9 min.

mp: 116-118 °C;

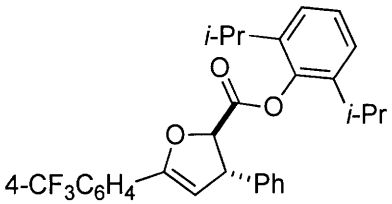
$[\alpha]^{22}_D = -112$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.90-7.88 (m, 2H), 7.44-7.42 (m, 2H), 7.27-7.15 (m, 8H), 5.47 (d, *J* = 2.9 Hz, 1H), 5.45 (d, *J* = 4.9 Hz, 1H), 5.07 (dd, *J* = 4.8, 2.9 Hz, 1H), 2.24 (s, 3H), 1.48 (s, 9H), 1.46 (s, 9H);

^{13}C NMR (C_6D_6, 100 MHz) δ 172.5, 157.0, 147.3, 143.8, 143.0, 142.7, 135.2, 134.9, 130.8, 129.6, 129.5, 129.0, 128.2, 128.0, 127.8, 127.6, 126.4, 99.8, 88.0, 53.6, 35.8, 35.7, 32.1, 32.0, 21.8;

IR (film) 3062, 3028, 2964, 2916, 1751, 1649, 1600, 1494, 1449, 1210, 1185 cm^{-1};

HRMS (ESI) calcd for $C_{32}H_{36}O_3Na$ (M + Na^+) 491.2556, found 491.2541.



(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-3-phenyl-5-(4-trifluoromethylphenyl) furan-2-carboxylate (Table 3, entry 2).

General Procedure A was followed, with (–)-bpy*, *trans*-4'-(trifluoromethyl)chalcone (276 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 282 mg (57%, 90% de, 76% ee); run 2, 297 mg (60%, 90%

de, 76% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 7.8 min., t_r(minor) 10.0 min.

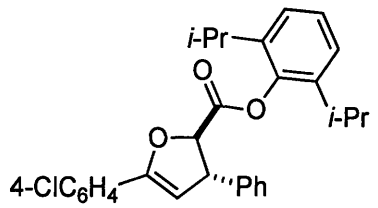
$[\alpha]^{22}_D = -90.1$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.54-7.52 (m, 2H), 7.33-7.27 (m, 4H), 7.18-7.04 (m, 6H), 5.29 (d, *J* = 2.9 Hz, 1H), 5.23 (d, *J* = 4.9 Hz, 1H), 4.79 (dd, *J* = 4.5, 3.1 Hz, 1H), 3.20-3.00 (m, 2H), 1.17 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.3, 156.0, 146.3, 142.8, 140.9, 129.7, 128.3, 128.0, 127.6, 126.6, 126.4, 126.0, 125.9, 124.8, 123.7, 101.9, 86.5, 54.4, 28.3, 23.6;

IR (film) 3066, 3030, 2966, 2932, 2872, 1773, 1755, 1647, 1619, 1493, 1457, 1326, 1165, 1070 cm^{-1};

HRMS (ESI) calcd for $C_{30}H_{29}F_3O_3Na$ (M + Na^+) 517.1961, found 517.1977.



(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-3-phenyl-5-(4-chlorophenyl)furan-2-carboxylate (Table 3, entry 3).

General Procedure A was followed, with (–)-bpy*, *trans*-4'-chlorochalcone (243 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 360 mg (78%, 92% de, 88% ee); run 2, 350 mg (76%, 88% de, 87% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 6.5 min., t_r(minor) 8.3 min.

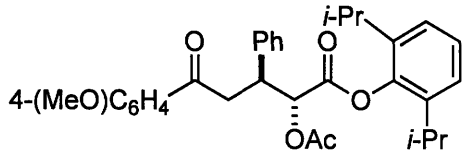
$[\alpha]^{22}_D = -108$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.46-7.43 (m, 2H), 7.30-7.28 (m, 2H), 7.18-7.04 (m, 8H), 5.23 (d, *J* = 3.3 Hz, 1H), 5.22 (d, *J* = 5.1 Hz, 1H), 4.79 (dd, *J* = 4.8, 3.0 Hz, 1H), 3.10 (septet, *J* = 6.4 Hz, 2H), 1.16 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.4, 156.3, 146.4, 143.1, 141.0, 135.4, 129.6, 129.2, 129.1, 128.5, 128.1, 127.7, 127.5, 124.8, 100.1, 86.5, 54.4, 28.3, 23.7;

IR (film) 3065, 3030, 2965, 2931, 2871, 1773, 1755, 1648, 1598, 1490, 1456, 1163 cm^{-1};

HRMS (ESI) calcd for $C_{29}H_{29}ClO_3Na$ ($M + Na^+$) 483.1697, found 483.1720.



(2*R*,3*S*)-2,6-Diisopropylphenyl 2-acetoxy-5-(4-methoxyphenyl)-5-oxo-3-phenyl pentanoate (Table 3, entry 4).

General Procedure A was followed, with (–)-bpy*, *trans*-4'-methoxychalcone (238 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). To the unpurified reaction mixture were added CH_3CN (2 mL) and 10% aq HBF_4 (2 mL). The mixture was stirred for 10 min, and then it was diluted with water and extracted with Et_2O (20 mL x 3). The combined organic layers were washed with water, dried over Na_2SO_4, and concentrated. The resulting hydroxyketone was dissolved in CH_2Cl_2 (10 mL), and NEt_3 (0.84 mL, 6.0 mmol), DMAP (24.4 mg, 0.2 mmol), and Ac_2O (0.47 mL, 5.0 mmol) were added to the stirring solution. After 15 min, the reaction mixture was diluted with water and extracted with CH_2Cl_2 (20 mL x 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. After chromatography on silica gel (hexanes/ethyl ether 20:1), the title compound was isolated as a white solid: run 1, 360 mg (85%, 90% de, 92% ee); run 2, 350 mg (83%, 90% de, 91% ee). The ee was determined on an OD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 17.8 min., t_r(minor) 26.0 min.

mp: 158-161 °C;

$[\alpha]^{22}_D = -58.8$ (c = 1.00, CH_2Cl_2);

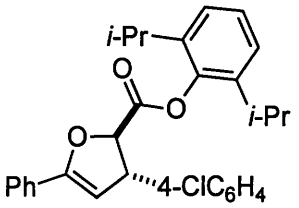
^1H NMR ($CDCl_3$, 400 MHz) δ 7.97-7.94 (m, 2H), 7.48-7.46 (m, 2H), 7.35-7.31 (m, 2H), 7.27-7.20 (m, 2H), 7.14-7.13 (m, 2H), 6.95-6.91 (m, 2H), 5.64 (d, *J* = 3.8 Hz, 1H), 4.39 (dt, *J* = 10.2, 3.5 Hz, 1H), 3.87 (s, 3H), 3.82 (dd, *J* = 18.0, 10.4 Hz, 1H), 3.40 (dd, *J* = 17.8, 3.1 Hz,

1H), 3.10-2.80 (m, 1H), 2.80-2.50 (m, 1H), 2.21 (s, 3H), 1.14 (d, J = 6.8 Hz, 6H), 1.30-0.80 (m, 6H);

^{13}C NMR (C_6D_6, 100 MHz) δ 195.4, 170.3, 168.2, 163.8, 145.1, 140.2, 130.5, 130.0, 128.8, 128.5, 127.6, 127.0, 124.1, 113.9, 76.0, 55.7, 41.8, 38.9, 27.3, 24.0, 22.8, 20.8;

IR (film) 2964, 2929, 2872, 1765, 1749, 1677, 1597, 1510, 1456, 1257 cm^{-1};

HRMS (ESI) calcd for $C_{32}H_{36}O_6Na$ (M + Na$^+$) 539.2404, found 539.2396.



(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-3-(4-chlorophenyl)-5-phenyl-furan-2-carboxylate (Table 3, entry 5).

General Procedure A was followed, with (–)-bpy*, *trans*-4-chlorochalcone (243 mg, 1.0 mmol) and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 360 mg (78%, 90% de, 86% ee); run 2, 383 mg (83%, 94% de, 89% ee). The ee was determined on an OD-H column (hexanes/*iso*-propanol 99:1, flow 0.7 mL/min.) with t_r(major) 8.1 min., t_r(minor) 5.9 min.

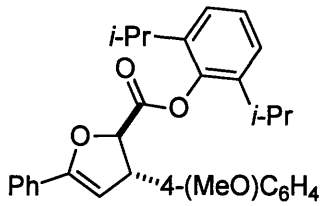
$[\alpha]^{22}_D$ = –126 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.74-7.71 (m, 2H), 7.16-7.00 (m, 10H), 5.23 (d, J = 2.9 Hz, 1H), 5.11 (d, J = 4.9 Hz, 1H), 4.69 (dd, J = 4.7, 3.0 Hz, 1H), 3.12 (septet, 2H), 1.16 (d, J = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.4, 157.7, 146.4, 141.7, 141.0, 133.9, 130.5, 129.8, 129.7, 129.5, 129.0, 127.5, 126.4, 124.8, 99.0, 86.3, 53.6, 28.3, 23.6;

IR (film) 3065, 3029, 2965, 2931, 2871, 1775, 1752, 1648, 1601, 1577, 1492, 1163 cm^{-1};

HRMS (ESI) calcd for $C_{29}H_{29}ClO_3Na$ (M + Na$^+$) 483.1697, found 483.1716.



(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-3-(4-methoxyphenyl)-5-phenyl-furan-2-carboxylate (Table 3, entry 6).

General Procedure A was followed, with (–)-bpy*, *trans*-4-methoxychalcone (238 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 384 mg (84%, 80% de, 93% ee); run 2, 379 mg (83%, 80% de, 93% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 7.4 min., t_r(minor) 9.6 min.

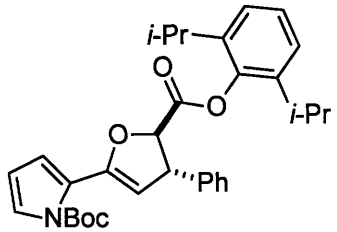
$[\alpha]^{22}_D = -130$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.77-7.75 (m, 2H), 7.26-7.24 (m, 2H), 7.16-7.04 (m, 6H), 6.81-6.79 (m, 2H), 5.39 (d, *J* = 2.9 Hz, 1H), 5.29 (d, *J* = 5.0 Hz, 1H), 4.84 (dd, *J* = 5.0, 2.9 Hz, 1H), 3.33 (s, 3H), 3.16 (septet, *J* = 6.7 Hz, 2H), 1.18 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.7, 160.0, 157.2, 146.5, 141.1, 135.3, 130.8, 129.6, 129.2, 129.0, 127.5, 126.4, 124.7, 115.0, 99.8, 86.8, 55.2, 53.8, 28.3, 23.7;

IR (film) 3065, 3029, 2965, 2932, 2870, 1773, 1752, 1648, 1610, 1584, 1512, 1462, 1448, 1251, 1145, 1033 cm^{-1};

HRMS (ESI) calcd for $C_{30}H_{32}O_4Na$ (M + Na^+) 479.2193, found 479.2216.



***tert*-Butyl 2-((4*S*,5*R*)-5-((2,6-diisopropylphenoxy)carbonyl)-4,5-dihydro-4-phenyl furan-2-yl)-1*H*-pyrrole-1-carboxylate (Table 3, entry 7).**

General Procedure A was followed, with (–)-bpy*, *tert*-butyl 2-((*E*)-3-phenylacryloyl)-1*H*-pyrrole-1-carboxylate (297 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate

(271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 347 mg (66%, >90% de, 94% ee); run 2, 368 mg (70%, >90% de, 92% ee). The ee was determined on an OD-H column (hexanes/*iso*-propanol 99:1, flow 0.9 mL/min.) with t_r(major) 5.2 min., t_r(minor) 4.8 min.

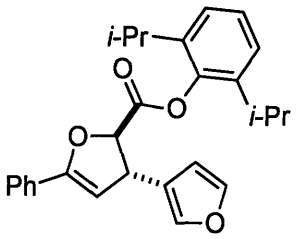
$[\alpha]^{22}_D = -129$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.54-7.52 (m, 2H), 7.26 (dd, *J* = 3.2, 1.8 Hz, 1H), 7.21-7.17 (m, 2H), 7.11-7.03 (m, 4H), 6.82 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.03 (t, *J* = 3.4 Hz 1H), 5.77 (d, *J* = 2.8 Hz, 1H), 5.31 (d, *J* = 5.8 Hz, 1H), 4.90 (dd, *J* = 5.8, 2.7 Hz, 1H), 3.13 (septet, 2H), 1.25 (s, 9H), 1.15 (d, *J* = 6.8 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.6, 150.3, 149.0, 146.5, 143.5, 141.1, 129.5, 128.5, 128.0, 127.4, 125.6, 124.8, 124.7, 117.9, 111.3, 103.4, 86.3, 84.0, 55.0, 28.2, 28.0, 23.7;

IR (film) 2966, 2932, 2871, 1754, 1652, 1456, 1306, 1144 cm^{-1};

HRMS (ESI) calcd for $C_{32}H_{37}NO_5Na$ (M + Na^+) 538.2564, found 538.2554.



(2R,3S)-2,6-Diisopropylphenyl 3-(furan-3-yl)-2,3-dihydro-5-phenylfuran-2-carboxylate (Table 3, entry 8).

General Procedure A was followed, with (–)-bpy*, (*E*)-1-(3-furyl)-3-phenyl-2-propen-1-one (198 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 258 mg (62%, 68% de, 85% ee); run 2, 262 mg (63%, 70% de, 88% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 0.7 mL/min.) with t_r(major) 12.5 min., t_r(minor) 13.1 min.

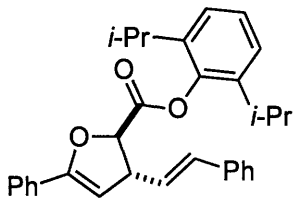
$[\alpha]^{22}_D = -97.1$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.72-7.70 (m, 2H), 7.14-7.00 (m, 8H), 6.23 (s, 1H), 5.27 (d, *J* = 2.9 Hz, 1H), 5.21 (d, *J* = 5.3 Hz, 1H), 4.73 (dd, *J* = 5.3, 2.8 Hz, 1H), 3.12 (septet, 2H), 1.16 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.4, 157.2, 146.4, 144.4, 141.0, 139.9, 130.7, 129.6, 129.0, 127.5, 127.3, 126.3, 124.8, 110.1, 98.5, 85.6, 45.0, 28.3, 23.7;

IR (film) 3065, 2965, 2871, 1774, 1753, 1650, 1578, 1448, 1162 cm^{-1};

HRMS (ESI) calcd for $C_{27}H_{28}O_4Na$ (M + Na$^+$) 439.1880, found 439.1870.



(2*R*,3*R*)-2,6-Diisopropylphenyl 2,3-dihydro-5-phenyl-3-(*E*)-styrylfuran-2-carboxylate (Table 3, entry 9).

General Procedure A was followed, with (–)-bpy*, *trans,trans*-1,5-diphenylpenta-2,4-dien-1-one (234 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 344 mg (76%, 76% de, 93% ee); run 2, 344 mg (76%, 74% de, 92% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 0.7 mL/min.) with t_r(major) 16.8 min., t_r(minor) 22.4 min.

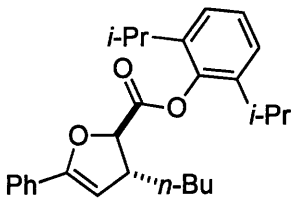
$[\alpha]^{22}_D$ = –176 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.76-7.73 (m, 2H), 7.22-7.20 (m, 2H), 7.16-7.04 (m, 9H), 6.52 (d, *J* = 15.7 Hz, 1H), 6.19 (dd, *J* = 15.7, 8.3 Hz, 1H), 5.25 (d, *J* = 2.8 Hz, 1H), 5.15 (d, *J* = 5.5 Hz, 1H), 4.43 (ddd, *J* = 8.0, 5.4, 2.6 Hz, 1H), 3.18 (septet, *J* = 6.7 Hz, 2H), 1.18 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.4, 157.2, 146.4, 141.0, 137.4, 132.3, 130.8, 130.2, 129.6, 129.2, 129.0, 128.3, 127.5, 127.2, 126.3, 124.7, 98.4, 84.4, 52.4, 28.3, 23.8;

IR (film) 3061, 3027, 2965, 2930, 2870, 1774, 1752, 1645, 1448, 1163, 1061 cm^{-1};

HRMS (ESI) calcd for $C_{31}H_{32}O_3Na$ (M + Na$^+$) 475.2243, found 475.2258.



(2*R*,3*R*)-2,6-Diisopropylphenyl 3-butyl-2,3-dihydro-5-phenylfuran-2-carboxylate (Table 3, entry 10).

General Procedure A was followed, with (–)-bpy*, (*E*)-1-phenyl-2-hepten-1-one (188 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 370 mg (91%, 96% de, 79% ee); run 2, 378 mg (93%, 97% de, 76% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 4.1 min., t_r(minor) 4.9 min.

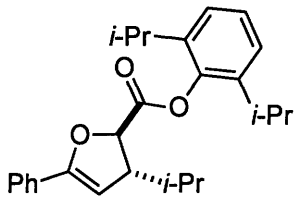
$[\alpha]^{22}_D = -53.6$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.74-7.72 (m, 2H), 7.14-7.03 (m, 6H), 5.27 (d, *J* = 2.8 Hz, 1H), 5.29 (d, *J* = 5.3 Hz, 1H), 3.61-3.52 (m, 1H), 3.23-3.06 (m, 2H), 1.58-1.38 (m, 2H), 1.34-1.10 (m, 16H), 0.85 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.9, 156.4, 146.5, 141.1, 131.2, 129.3, 128.9, 127.7, 127.4, 126.2, 124.7, 99.4, 84.2, 49.3, 36.1, 29.8, 28.3, 23.8, 23.3, 14.6;

IR (film) 3066, 3029, 2963, 2930, 2871, 1776, 1751, 1650, 1602, 1578, 1466, 1448 cm^{-1};

HRMS (ESI) calcd for $C_{27}H_{34}O_3Na$ (M + Na^+) 429.2400, found 429.2390.



(2*R*,3*R*)-2,6-Diisopropylphenyl 2,3-dihydro-3-isopropyl-5-phenylfuran-2-carboxylate (Table 3, entry 11).

General Procedure A was followed, with (–)-bpy*, (*E*)-4-methyl-1-phenyl-2-penten-1-one (188 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol).

After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 330 mg (84%, 96% de, 52% ee); run 2, 338 mg (86%, >90% de, 49% ee). The ee was determined on an OD-H column (hexanes/*iso*-propanol 99:1, flow 0.9 mL/min.) with t_r(major) 6.4 min., t_r(minor) 5.9 min.

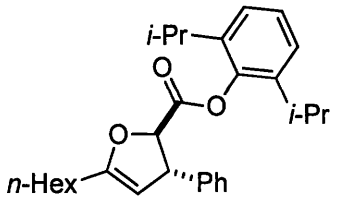
$[\alpha]^{22}_D = -38.0$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.73-7.70 (m, 2H), 7.13-7.02 (m, 6H), 5.24 (d, *J* = 2.9 Hz, 1H), 5.12 (d, *J* = 4.8 Hz, 1H), 3.45 (ddd, *J* = 6.4, 4.8, 3.0 Hz, 1H), 3.19 (br, 2H), 1.64 (octet, *J* = 6.7 Hz, 1H), 1.28-1.06 (m, 12H), 0.90 (dd, *J* = 6.7, 2.2 Hz, 6H);

^{13}C NMR (C_6D_6, 100 MHz) δ 171.2, 156.9, 146.5, 141.1, 131.1, 129.3, 128.9, 127.4, 126.2, 124.7, 97.3, 82.1, 56.1, 33.1, 28.3, 23.9, 23.3, 20.1, 19.8;

IR (film) 3065, 3029, 2963, 2931, 2871, 1776, 1751, 1650, 1602, 1578, 1465, 1448 cm^{-1};

HRMS (ESI) calcd for $C_{26}H_{32}O_3Na$ (M + Na^+) 415.2243, found 415.2235.



(2*R*,3*R*)-2,6-Diisopropylphenyl 5-hexyl-2,3-dihydro-3-phenylfuran-2-carboxylate (Table 4, entry 1).

General Procedure B was followed, with (–)-bpy*, (*E*)-1-phenyl-1-nonen-3-one (216 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (345 mg, 1.4 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 300 mg (69%, 84% de, 77% ee); run 2, 300 mg (69%, 88% de, 73% ee). The ee was determined after reduction by LAH on an OD-H column (hexanes/*iso*-propanol 98:2, flow 1.0 mL/min.) with t_r(major) 17.1 min., t_r(minor) 12.3 min.

$[\alpha]^{22}_D = -174$ (c = 1.00, CH_2Cl_2);

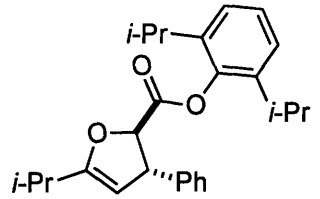
^{1}H NMR (C_6D_6, 400 MHz) δ 7.38-7.36 (m, 2H), 7.21-7.18 (m, 2H), 7.13-7.04 (m, 4H), 5.16 (d, *J* = 4.9 Hz, 1H), 4.71 (d, *J* = 2.3 Hz, 1H), 4.68 (dd, *J* = 4.6, 2.4 Hz, 1H), 3.13 (septet,

J = 6.7 Hz, 2H), 2.25 (t, J = 7.5 Hz 2H), 1.60 (quintet, J = 7.5 Hz 2H), 1.33-1.10 (m, 18H), 0.86 (t, J = 6.9 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.8, 161.1, 146.4, 144.2, 141.1, 129.5, 128.0, 127.4, 124.7, 98.6, 86.6, 54.3, 32.3, 29.6, 28.6, 28.3, 27.3, 23.9, 23.3, 14.7;

IR (film) 3065, 3029, 2962, 2930, 2871, 1776, 1754, 1673, 1602, 1493, 1456, 1248, 1144, 1096 cm^{-1};

HRMS (ESI) calcd for $C_{29}H_{38}O_3Na$ (M + Na$^+$) 457.2713, found 457.2733.



(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-5-isopropyl-3-phenylfuran-2-carboxylate (Table 4, entry 2).

General Procedure B was followed, with (–)-bpy*, (*E*)-4-methyl-1-phenyl-1-penten-3-one (174 mg, 1.0 mmol), and 2,6-diisopropylphenyl-diazoacetate (345 mg, 1.4 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 300 mg (86%, 86% de, 66% ee); run 2, 300 mg (88%, 90% de, 65% ee). The ee was determined after reduction by LAH on an OD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 11.5 min., t_r(minor) 14.0 min.

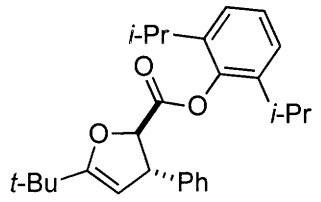
$[\alpha]^{22}_D$ = –152 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.36-7.34 (m, 2H), 7.20-7.16 (m, 2H), 7.13-7.04 (m, 4H), 5.15 (d, J = 4.5 Hz, 1H), 4.67-4.65 (m, 2H), 3.13 (septet, J = 6.8 Hz, 2H), 2.52 (septet, J = 6.9 Hz, 1H), 1.18 (d, J = 6.9 Hz, 6H), 1.15 (d, J = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.9, 166.3, 146.4, 144.1, 141.1, 129.5, 129.0, 127.9, 127.4, 124.8, 124.7, 96.6, 86.5, 54.1, 28.3, 28.2, 23.7, 20.7;

IR (film) 3065, 3029, 2965, 2932, 2872, 1776, 1752, 1667, 1603, 1493, 1468, 1456, 1384, 1248, 1164 cm^{-1};

HRMS (ESI) calcd for $C_{26}H_{32}O_3Na$ (M + Na$^+$) 415.2243, found 415.2254.



(2*R*,3*S*)-2,6-Diisopropylphenyl 5-*tert*-butyl-2,3-dihydro-3-phenylfuran-2-carboxylate (Table 4, entry 3).

General Procedure A was followed, with (–)-bpy*, (E)-4-methyl-1-phenyl-1-penten-3-one (174 mg, 1.0 mmol), and 2,6-diisopropylphenyl-diazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 321 mg (79%, 94% de, 69% ee); run 2, 337 mg (83%, >90% de, 71% ee). The ee was determined after reduction by LAH on an OD-H column (hexanes/*iso*-propanol 97:3, flow 1.0 mL/min.) with t_r(major) 8.6 min., t_r(minor) 9.2 min.

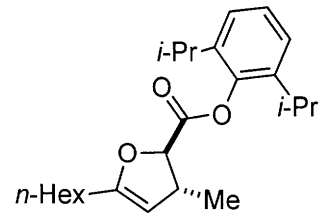
$[\alpha]^{22}_D = -147$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.35-7.33 (m, 2H), 7.20-7.16 (m, 2H), 7.12-7.04 (m, 4H), 5.14 (d, *J* = 4.5 Hz, 1H), 4.69 (d, *J* = 2.6 Hz, 1H), 4.62 (dd, *J* = 4.5, 2.6 Hz, 1H), 3.13 (septet, *J* = 6.9 Hz, 2H), 1.25 (s, 9H), 1.18 (d, *J* = 6.9 Hz, 6H), 1.15 (d, *J* = 6.9 Hz, 6H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.9, 168.7, 146.4, 144.2, 141.1, 129.6, 128.0, 127.9, 127.4, 124.7, 96.0, 86.6, 54.1, 32.7, 28.5, 28.2, 23.8;

IR (film) 3065, 3029, 2965, 2871, 1776, 1752, 1660, 1603, 1493, 1457, 1385, 1164 cm^{-1};

HRMS (ESI) calcd for $C_{26}H_{32}O_3Na$ (M + Na^+) 429.2400, found 429.2419.



(2*R*,3*S*)-2,6-Diisopropylphenyl 5-hexyl-2,3-dihydro-3-methylfuran-2-carboxylate (Taable 4, entry 4).

General Procedure A was followed, with (–)-bpy*, (*E*)-2-decen-4-one (154 mg, 1.0 mmol) and 2,6-diisopropylphenyldiazoacetate (345 mg, 1.4 mmol). After

chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 291 mg (78%, >90% de, 72% ee); run 2, 305 mg (82%, >90% de, 69% ee). The ee was determined after reduction by LAH on an OD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 7.4 min., t_r(minor) 8.8 min.

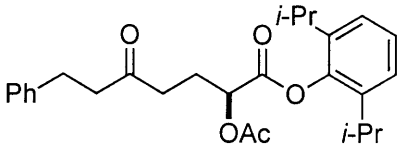
$[\alpha]^{22}_D = 70.8$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.11-7.04 (m, 3H), 4.77 (d, *J* = 5.7 Hz, 1H), 4.52-4.50 (m, 1H), 3.48-3.45 (m, 1H), 3.13 (septet, *J* = 6.8 Hz, 2H), 2.17 (t, *J* = 7.4 Hz 2H), 1.55 (quintet, *J* = 7.4 Hz 2H), 1.33-1.14 (m, 18H), 1.13-1.10 (d, *J* = 6.8 Hz, 3H), 0.84 (t, *J* = 6.7 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 171.0, 159.5, 146.4, 141.1, 127.3, 124.7, 100.1, 85.6, 43.8, 32.3, 29.5, 28.6, 28.3, 27.2, 23.9, 23.6, 23.3, 22.0, 14.6;

IR (film) 3067, 2963, 2930, 2871, 1778, 1751, 1674, 1459, 1245, 1161, 1095 cm^{-1};

HRMS (ESI) calcd for $C_{24}H_{36}O_3Na$ (M + Na^+) 395.2557, found 395.2562.



(*S*)-2,6-Diisopropylphenyl 2-acetoxy-5-oxo-7-phenylheptanoate (Table 4, entry 5)

General Procedure B was followed, with (–)-bpy*, 5-phenylpent-1-en-3-one (160 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (345 mg, 1.4 mmol). The crude product was hydrolyzed and then acetylated. After chromatography on silica gel (hexanes/ethyl ether 10:1), the title compound was isolated as a colorless oil: run 1, 220 mg (50%, 69% ee); run 2, 224 mg (51%, 69% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 11.3 min., t_r(minor) 9.1 min.

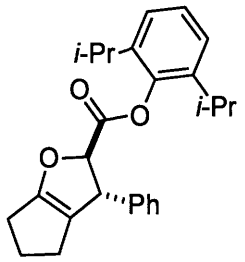
$[\alpha]^{22}_D = 19.1$ (c = 1.02, CH_2Cl_2);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33-7.30 (m, 2H), 7.25-7.18 (m, 6H), 5.35 (dd, *J* = 8.4, 4.4 Hz, 1H), 3.01 (br, 1H), 2.96 (t, *J* = 7.5 Hz, 2H), 2.86 (br, 1H), 2.81 (t, *J* = 7.7 Hz, 2H), 2.75-2.60 (m, 2H), 2.52-2.44 (m, 1H), 2.34-2.24 (m, 1H), 2.16 (s, 3H), 1.20 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 208.0, 170.4, 168.8, 145.1, 141.0, 140.6, 128.7, 128.5, 127.0, 126.4, 124.1, 71.3, 44.5, 38.3, 29.9, 27.4, 25.0, 23.9, 23.0, 20.7;

IR (film) 3064, 3028, 2966, 2932, 2871, 1771, 1750, 1717, 1604, 1442, 1374, 1241, 1164 cm^{-1};

LCMS (ES+APCI) calcd for $C_{27}H_{34}O_5Na$ ($M + Na^+$) 461.3, found 461.3.



(2*R*,3*R*)-2,6-Diisopropylphenyl 3,4,5,6-tetrahydro-3-phenyl-2*H*-cyclopenta[*b*]furan-2-carboxylate (eq 7).

General Procedure A was followed, with (–)-bpy*, (E)-2-(phenylmethylene) cyclopentanone (172 mg, 1.0 mmol), and 2,6-diisopropylphenyl-diazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 211 mg (54%, >90%, 64% ee); run 2, 203 mg (52%, >90%, 63% ee). The ee was determined after reduction by LAH on an OD-H column (hexanes/*iso*-propanol 95:5, flow 1.0 mL/min.) with t_r(major) 11.7 min., t_r(minor) 8.9 min.

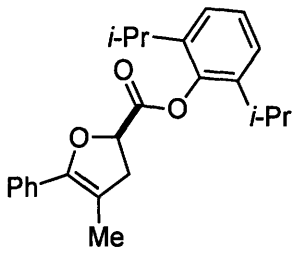
$[\alpha]^{22}_D = 103$ (c = 1.00, CH_2Cl_2);

^1H NMR (C_6D_6, 400 MHz) δ 7.32-7.31 (m, 2H), 7.20-7.16 (m, 2H), 7.12-7.04 (m, 4H), 5.53 (d, *J* = 5.2 Hz, 1H), 4.61 (dt, *J* = 4.9, 2.4 Hz, 1H), 3.15 (septet, *J* = 6.8 Hz, 2H), 2.28-2.27 (m, 2H), 2.03-2.01 (m, 4H), 1.17 (d, *J* = 6.8 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.6, 164.8, 146.4, 142.5, 141.1, 129.6, 128.1, 128.0, 127.4, 124.7, 117.5, 94.7, 53.3, 28.3, 27.6, 25.3, 24.2, 23.7;

IR (film) 3064, 3029, 2964, 2932, 2868, 1776, 1753, 1712, 1602, 1494, 1455, 1217, 1162 cm^{-1};

HRMS (ESI) calcd for $C_{26}H_{30}O_3Na$ ($M + Na^+$) 413.2087, found 413.2091.



(*R*)-2,6-Diisopropylphenyl 2,3-dihydro-4-methyl-5-phenylfuran-2-carboxylate (entry 8).

General Procedure A was followed, with (–)-bpy*, 2-methyl-1-phenyl-2-propen-1-one (146 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 284 mg (78%, 16% ee); run 2, 270 mg (74%, 21% ee). The ee was determined on an OD-H column (hexanes/*iso*-propanol 97:3, flow 1.0 mL/min.) with t_r(major) 18.6 min., t_r(minor) 16.3 min.

$[\alpha]^{22}_D = 3.33$ (c = 1.00, CH_2Cl_2);

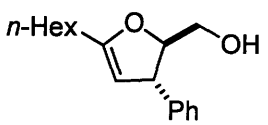
^{1}H NMR (C_6D_6, 400 MHz) δ 7.73-7.70 (m, 2H), 7.18-7.14 (m, 2H), 7.12-7.04 (m, 4H), 5.05 (dd, *J* = 10.9, 5.7 Hz, 1H), 3.13 (septet, *J* = 6.8 Hz, 2H), 3.06 (ddq, *J* = 15.8, 5.6, 1.0 Hz, 1H), 2.84 (ddq, *J* = 15.6, 10.9, 1.3 Hz, 1H), 1.67 (t, *J* = 1.3 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 171.4, 149.2, 146.5, 141.1, 132.1, 128.8, 127.9, 127.3, 124.7, 105.2, 76.5, 41.7, 28.2, 23.8, 12.7;

IR (film) 3064, 3027, 2965, 2930, 2870, 1774, 1756, 1682, 1602, 1496, 1460, 1249, 1165, 1065 cm^{-1};

HRMS (ESI) calcd for $C_{24}H_{28}O_3Na$ (M + Na$^+$) 387.1930, found 387.1919.

4. Derivatization of Dihydrofurans (eq 9 and eq 3)



((2*R*,3*S*)-2,3-Dihydro-5-hexyl-3-phenylfuran-2-yl)methanol (eq 9).

A solution of $LiAlH_4$ (1.0 M in Et_2O; 0.23 mL, 0.23 mmol) was added dropwise to a stirred solution of the ester (run 1, >90% de and 77% ee; run 2, >90% de and 73% ee; 100 mg, 0.23 mmol) in Et_2O (5.0 mL). The reaction mixture was stirred for 10 min, and then the reaction was quenched with 1.0 N NaOH (0.2 mL). The mixture was stirred for 5 min, and then it was filtered and concentrated. After chromatography on silica gel (hexanes/ethyl ether 15:1), the title compound was isolated as a colorless oil: run 1, 57 mg (95%, 77% ee); run 2, 58 mg (97%, 73% ee). The ee was determined on an OD-H column (hexanes/*iso*-propanol 98:2, flow 1.0 mL/min.) with t_r(major) 17.1 min., t_r(minor) 12.3 min.

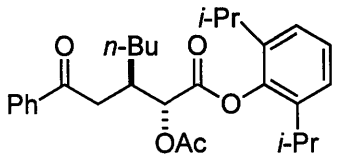
$[\alpha]^{22}_D = -74.9$ (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.18-7.12 (m, 4H), 7.07-7.04 (m, 1H), 4.56 (dt, *J* = 2.2, 1.1 Hz, 1H), 4.34 (dt, *J* = 6.7, 5.0 Hz, 1H), 3.83 (dq, *J* = 6.7, 1.9 Hz, 1H), 3.53 (t, *J* = 5.0 Hz, 2H), 2.12 (t, *J* = 7.8 Hz, 2H), 1.71 (t, *J* = 5.6 Hz, 1H), 1.51 (quintet, *J* = 7.5 Hz, 2H), 1.31-1.17 (m, 6H), 0.86 (t, *J* = 6.8 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 159.9, 145.4, 129.2, 128.2, 127.3, 99.4, 90.8, 64.9, 51.6, 32.3, 29.7, 28.7, 27.4, 23.3, 14.6;

IR (film) 3424, 3062, 3028, 2954, 2929, 2859, 1669, 1602, 1493, 1455, 1159 cm^{-1};

HRMS (ESI) calcd for $C_{17}H_{24}O_2Na$ (M + Na^+) 283.1669, found 283.1676.



(2*R*,3*R*)-2,6-Diisopropylphenyl 2-acetoxy-3-butyl-5-oxo-5-phenylpentanoate (eq 10)

The procedure for entry 4 of Table 3 was followed, with the ester (run 1, >90% de and 79% ee; run 2, >90% de and 76% ee; 50 mg, 0.12 mmol), 10% aq HBF_4 (1.0 mL), NEt_3 (0.10 mL, 0.74 mmol), DMAP (3.0 mg, 0.025 mmol), and Ac_2O (0.060 mL, 0.64 mmol) After chromatography on silica gel (hexanes/ethyl ether 20:1), the title compound was isolated as a colorless oil: run 1, 50 mg (87%; >90% de, 78% ee); run 2, 53 mg (92%; >90% de, 76% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min.) with t_r(major) 5.0 min., t_r(minor) 6.3 min.

$[\alpha]^{22}_{D}$ = -11.4 (c = 1.00, CH_2Cl_2);

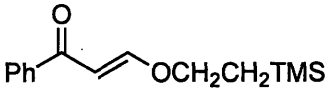
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03-8.00 (m, 2H), 7.60-7.57 (m, 1H), 7.50-7.47 (m, 2H), 7.23-7.13(m, 3H), 5.54 (d, *J* = 2.3 Hz, 1H), 3.24-3.22(m, 2H), 3.17-3.08(m, 1H), 3.08-2.90 (m, 1H), 2.90-2.60 (m, 1H), 2.22 (s, 3H), 1.62-1.52 (m, 2H), 1.50-1.33 (m, 4H), 1.17 (d, *J* = 6.3 Hz, 12H), 0.94 (t, *J* = 6.9 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 198.0, 170.6, 169.1, 145.1, 140.6, 137.2, 133.4, 128.9, 128.2, 127.0, 124.1, 73.5, 39.3, 35.4, 31.8, 29.5, 27.4, 23.7, 22.8, 20.8, 14.1;

IR (film) 3065, 2965, 2932, 2871, 1769, 1751, 1689, 1598, 1449, 1366, 1229, 1174 cm^{-1};

HRMS (ESI) calcd for $C_{29}H_{38}O_5Na$ (M + Na^+) 489.2611, found 489.2636.

5. Application to Deoxy-C-nucleoside Synthesis (Shceme 1)



(*E*)-3-(2-(Trimethylsilyl)ethoxy)-1-phenylprop-2-en-1-one.

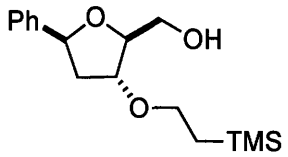
1-Phenylprop-2-yn-1-one (650 mg, 5.0 mmol) was added dropwise to a solution of trimethylsilylethanol (650 mg, 5.5 mmol) and *N*-methylmorpoline (657 mg, 6.5 mmol) in CH_2Cl_2 (5 mL) at r.t. The reaction mixture was stirred for 2 days, and then a saturated solution of NH_4Cl (10 mL) was added. The mixture was extracted with CH_2Cl_2 (10 mL x 3), and the combined organic layers were dried over $MgSO_4$ and concentrated. The resulting dark brown oil was purified by column chromatography (hexanes/Et_2O 8:1), which furnished the title product (820 mg, 66%). The reaction was not optimized.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91-7.89 (m, 2H), 7.77 (d, *J* = 12.2 Hz, 1H), 7.54-7.52 (m, 1H), 7.50-7.44 (m, 2H), 6.35 (d, *J* = 12.2 Hz, 1H), 4.13-4.09 (m, 2H), 1.15-1.11 (m, 2H), 0.09 (s, 9H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 218.2, 191.0, 164.4, 132.4, 128.6, 128.2, 102.3, 70.5, 18.1, –1.2;

IR (film) 3064, 2953, 2896, 1664, 1601, 1586, 1575, 1447, 1381, 1250, 1192, 1172, 858, 838 cm^{-1};

LCMS (ES+APCI) calcd for $C_{14}H_{20}O_2SiNa$ ($M + Na^+$) 271.1125, found 271.2.



((2S,3R,5S)-3-(2-(Trimethylsilyl)ethoxy)-tetrahydro-5-phenylfuran-2-yl)methanol.

General Procedure A was followed, with (–)-bpy*, (*E*)-3-(2-(trimethylsilyl)ethoxy)-1-phenylprop-2-en-1-one (248 mg, 1.0 mmol), and 2,6-diisopropylphenyl-diazoacetate (271 mg, 1.1 mmol). ^{1}H NMR analysis of the unpurified dihydrofuran product revealed only one diastereomer.

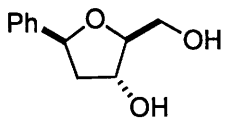
The unpurified product was subjected to hydrogenation (1 atm) with Pd on activated carbon (10% w/w; 5 mg) and NEt_3 (70 μL, 0.5 mmol) in MeOH (3.0 mL) for 1 h. The reaction mixture was filtered through a silica gel (Et_2O as the eluant) and concentrated. A solution of LAH (1.0 M in Et_2O; 1.0 mL, 1.0 mmol) was added to a solution of the tetrahydrofuran in Et_2O (4.0 mL). The reactio mixture was stirred for 5 minutes, and then the reaction was quenched by adding water (0.1 mL) and stirring for 10 minutes. The reaction mixture was dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography (hexanes/Et_2O 5:1), which furnishes the title compound as a colorless oil: run 1, 216 mg (73%); run 2, 236 mg (80%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.28 (m, 5H), 5.12 (dd, J = 10.5, 5.4 Hz, 1H), 4.09 (dt, J = 4.8, 3.4 Hz, 1H), 4.02 (ddd, J = 6.3, 2.8, 1.4 Hz, 1H), 3.88 (dd, J = 11.7, 3.6 Hz, 1H), 3.72 (dd, J = 11.7, 4.9 Hz, 1H), 3.60-3.53 (m, 2H), 2.35 (ddd, J = 13.3, 5.4, 1.5 Hz, 1H), 1.97 (br s, 1H), 1.91 (ddd, J = 13.3, 10.5, 6.4 Hz, 1H), 1.00-0.96 (m, 2H), 0.05 (s, 9H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.6, 128.9, 128.2, 126.4, 85.6, 81.1, 80.8, 67.0, 64.2, 41.7, 18.8, –0.9;

IR (film) 3414, 2952, 2893, 1715, 1362, 1222, 1098, 1057 cm^{-1};

LCMS (ES+APCI) calcd for $C_{16}H_{26}O_3SiNa$ ($M + Na^+$) 317.1543, found 317.2.



(2*S*,3*R*,5*S*)-Tetrahydro-2-(hydroxymethyl)-5-phenylfuran-3-ol.

To a solution of ((2*S*,3*R*,5*S*)-3-(2-(trimethylsilyl)ethoxy)-tetrahydro-5-phenylfuran-2-yl)methanol (50.0 mg, 0.17 mmol) in toluene (2.5 mL) was added $BF_3 \cdot OEt_2$ (23.5 μL, 0.19 mmol). The reaction mixture was stirred for 1 hour, and then the reaction was quenched by the addition of a saturated solution of $NaHCO_3$ (2.0 mL). The mixture was extracted with Et_2O (5 mL x 3), dried over $MgSO_4$, and concentrated. Purification by column chromatography (CH_2Cl_2/MeOH 50:1) furnished the title compound as a white solid: run 1, 30 mg (87%, 93% ee); run 2, 28 mg (85%, 94% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 95:5, flow 1.0 mL/min.) with t_r(major) 28.4 min., t_r(minor) 32.0 min.

The spectral data matched with the values reported previously.[15]

$[\alpha]^{22}_D = -44.9$ (c = 1.00, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.28 (m, 5H), 5.18 (dd, *J* = 10.2, 5.6 Hz, 1H), 4.41 (dt, *J* = 6.0, 2.4 Hz, 1H), 4.03-3.99 (m, 1H), 3.81 (dd, *J* = 11.6, 4.3 Hz, 1H), 3.73 (dd, *J* = 11.6, 5.0 Hz, 1H), 2.37 (br s, 2H), 2.25 (ddd, *J* = 13.3, 5.7, 1.9 Hz, 1H), 2.25 (ddd, *J* = 13.3, 10.2, 6.3 Hz, 1H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.2, 128.7, 128.1, 126.3, 87.5, 80.4, 73.9, 63.6, 44.0;

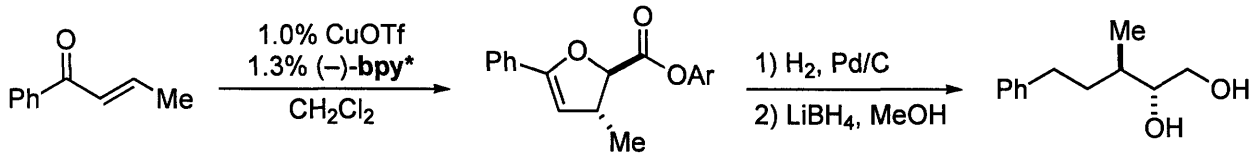
IR (film) 3274, 2940, 2832, 1490, 1452, 1358, 1102, 1054, 1028 cm^{-1};

LCMS (ES+APCI) calcd for $C_{11}H_{14}O_3Na$ ($M + Na^+$) 217.0835, found 217.1.

[15] (a) Calter, M. A.; Zhu, C. *J. Org. Chem.* **1999**, *64*, 1415–1419. (b) Sas, B.; Van Hemel, J; Vandenkerckhove, J; Peys, E; Van Der Eycken, J; Van Hoof, S. U.S. Patent 007245, 2004.

6. Absolute Stereochemistry Determination

The stereochemistry of the dihydrofurans was assigned on the basis of the synthesis described in Section 5 and by correlation with (2*R*,3*R*)-3-methyl-5-phenylpentane-1,2-diol.[16]



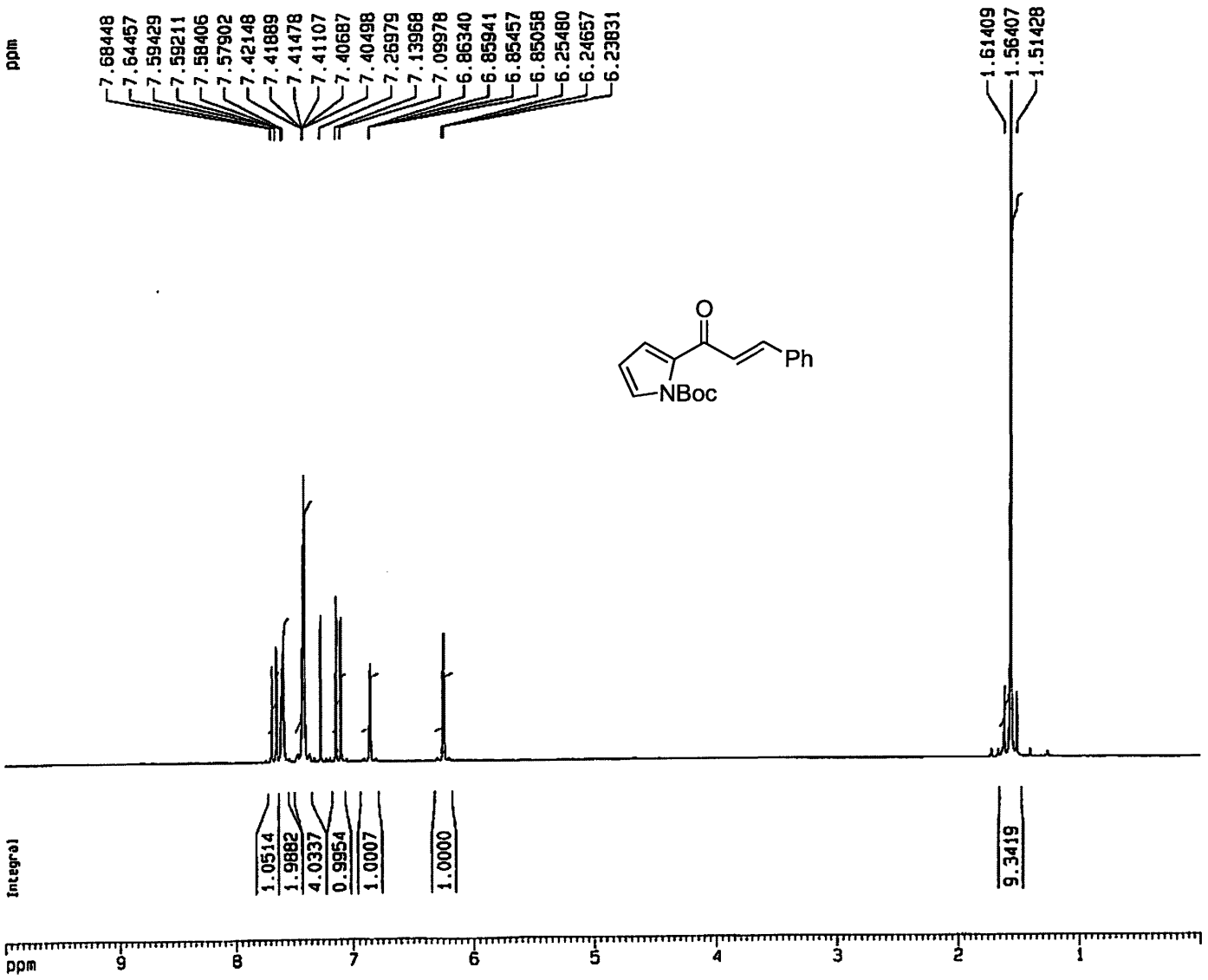
Scheme 1

The spectral data matched with the values reported previously.[2]

$[\alpha]^{22}_{D} = 17.3$ (c = 0.83, $CHCl_3$).

[16] Barrow, R. A.; Hemscheidt, T.; Liang, J.; Paik, S.; Moore, R. E.; Tius, M. A. *J. Am. Chem. Soc.* **1995**, *117*, 2479-2490.

7. ^{1}H NMR for Selected Compounds



Current Data Parameters

NAME	ss2-163
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20060124
Time	13.15
INSTRUM	spect
PROBHD	5mm BBO BB-1
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8278.146 Hz
FIDRES	0.126314 Hz
AQ	3.9584243 sec
RG	181
DW	60.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

========== CHANNEL f1 =========

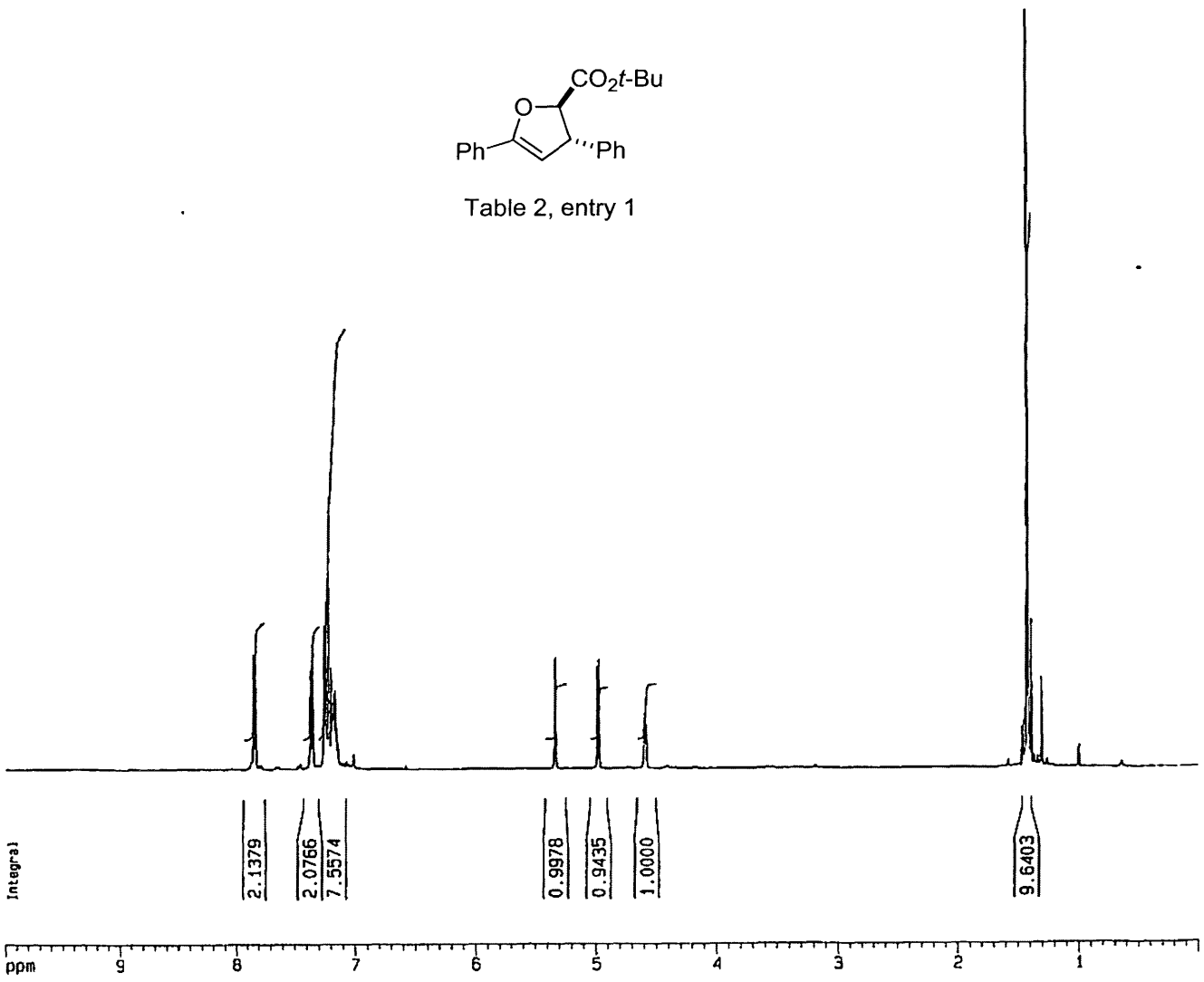
NUC1	1H
P1	7.90 usec
PL1	0.00 dB
SFO1	400.1324710 MHz

F2 - Processing parameters

SI	32768
SF	400.1300056 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	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	200.06500 Hz/cm



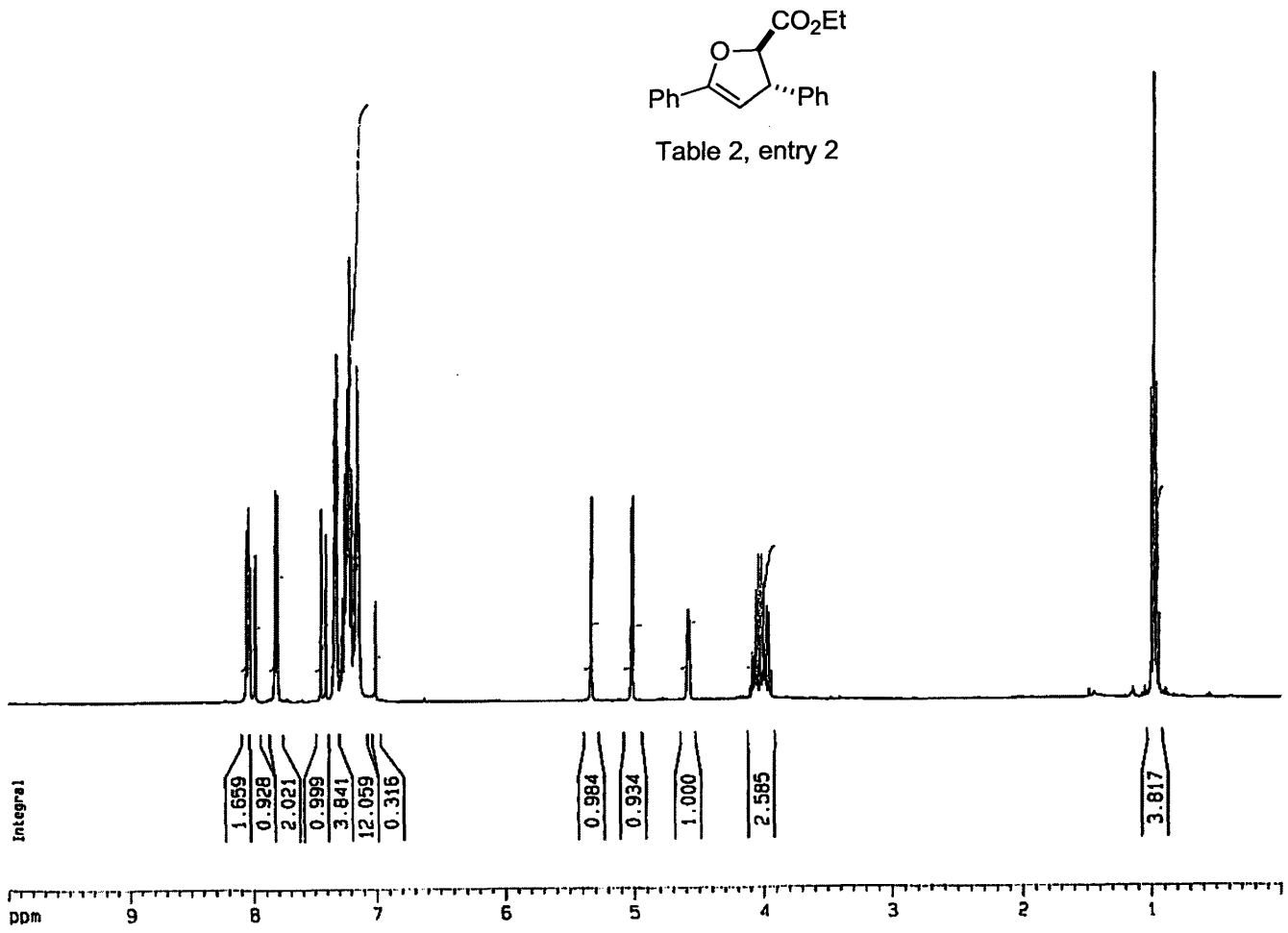

```
Current Data Parameters
NAME                  ss3-27-2
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20050630
Time                   19.04
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                       114
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                400.1300059 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                    0.000 ppm
F2                     0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06500 Hz/cm
```




```
Current Data Parameters
NAME                  ss3-27-1
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20050630
Time                    19.00
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                        64
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                 400.1300059 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                   0.000 ppm
F2                     0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06500 Hz/cm
```

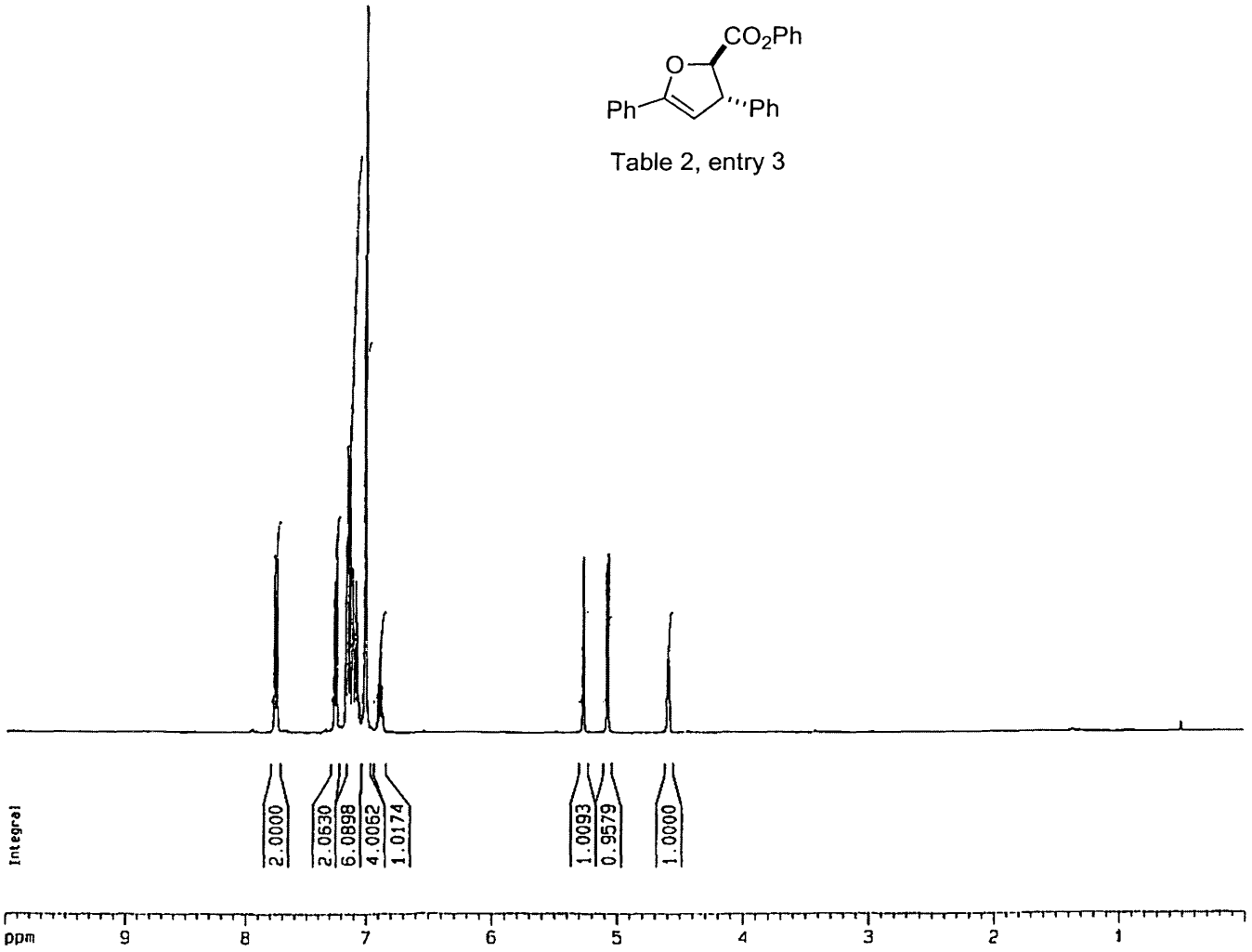


Table 2, entry 3

```
Current Data Parameters
NAME                  ss3-27-3
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20050630
Time                   19.18
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                       114
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                400.1300451 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                   0.000 ppm
F2                    0.00 Hz
PPMCM              0.50000 ppm/cm
HZCM              200.06502 Hz/cm
```

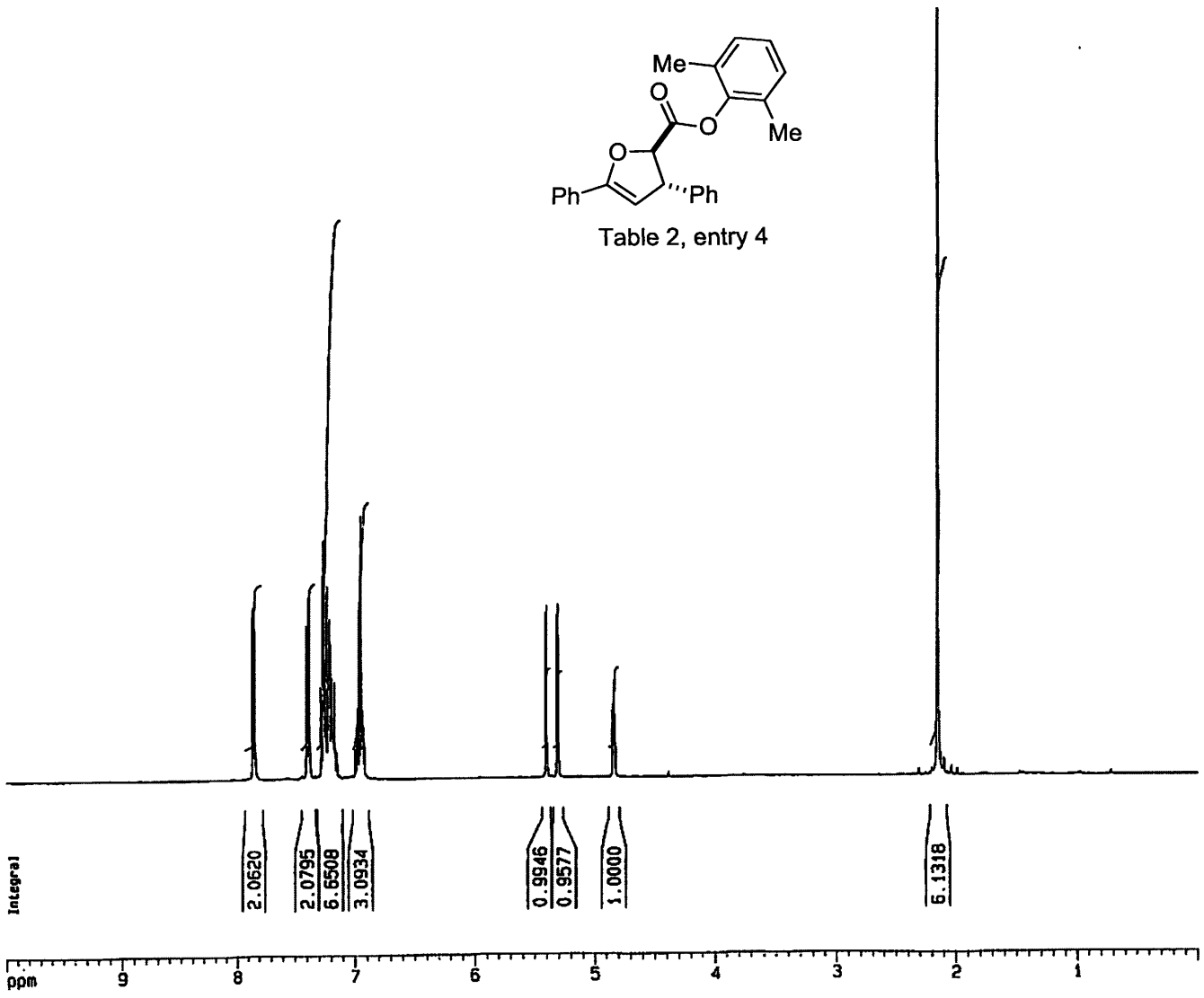


Table 2, entry 4

```
Current Data Parameters
NAME                  ss3-27-4
EXPNO                        3
PROCNO                       1

F2 - Acquisition Parameters
Date_              20050704
Time                  16.45
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                       57
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              400.1300059 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                   0.000 ppm
F2                    0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06500 Hz/cm
```

major pdt from chalcone

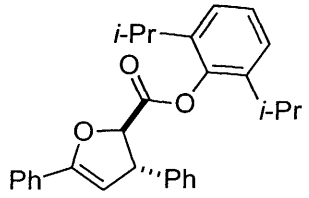


Table 2, entry 5


```
Current Data Parameters
NAME                  ss2-95
EXPNO                     10
PROCNO                     1

F2 - Acquisition Parameters
Date_               20050224
Time                   14.11
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                      25.4
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                 400.1300443 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                    0.000 ppm
F2                     0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06502 Hz/cm
```

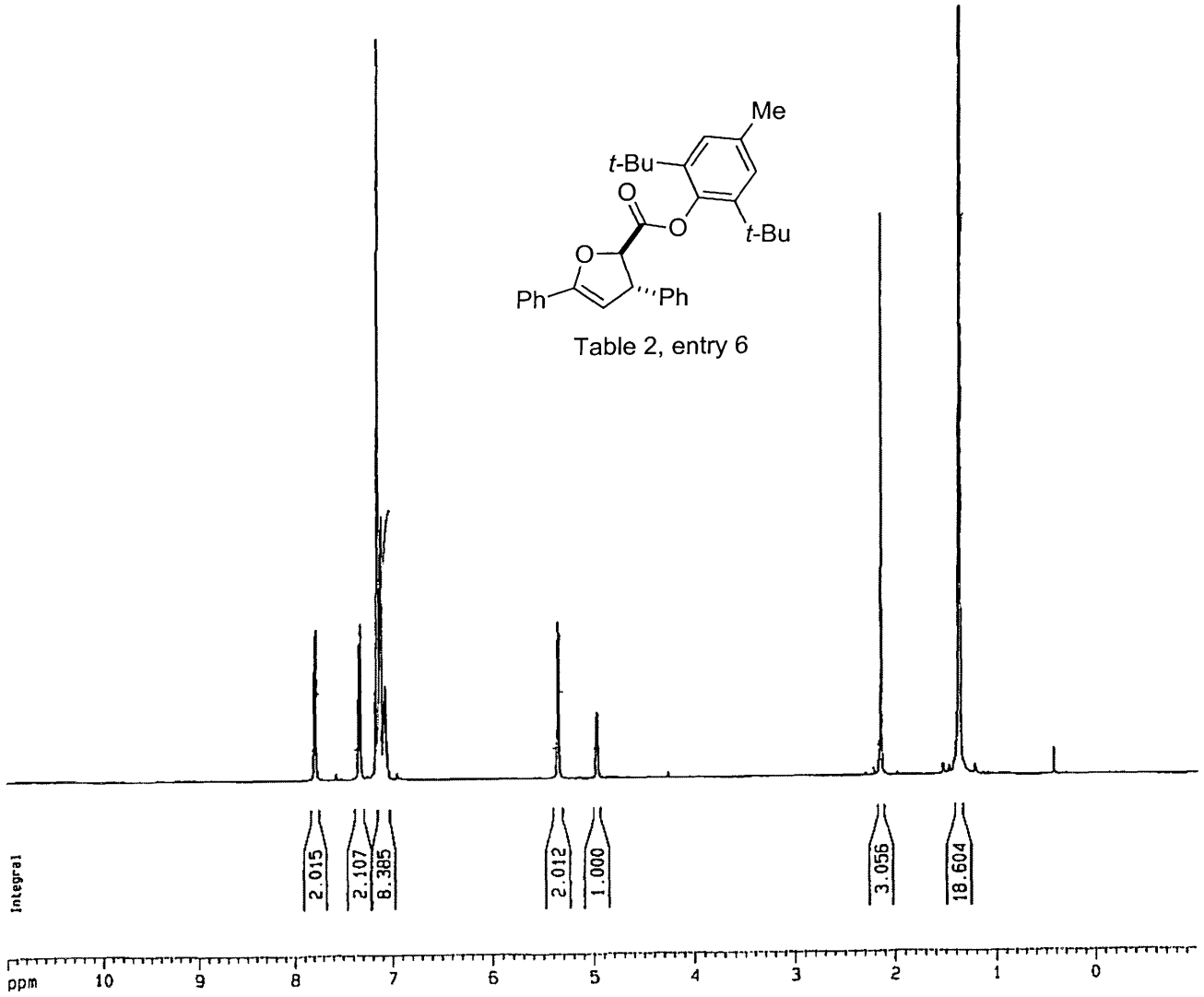


Table 2, entry 6

```
Current Data Parameters
NAME                  ss3-15-3
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20050618
Time                    23.34
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                     101.6
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                400.1300446 MHz
WDW                       EM
SSB                        0
LB                     0.30 Hz
GB                         0
PC                      1.00

1D NMR plot parameters
CX                    20.00 cm
F1P                   11.000 ppm
F1                  4401.43 Hz
F2P                   -1.000 ppm
F2                  -400.13 Hz
PPMCM                 0.60000 ppm/cm
HZCM                240.07803 Hz/cm
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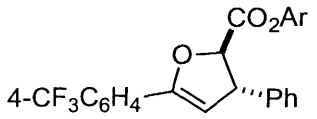
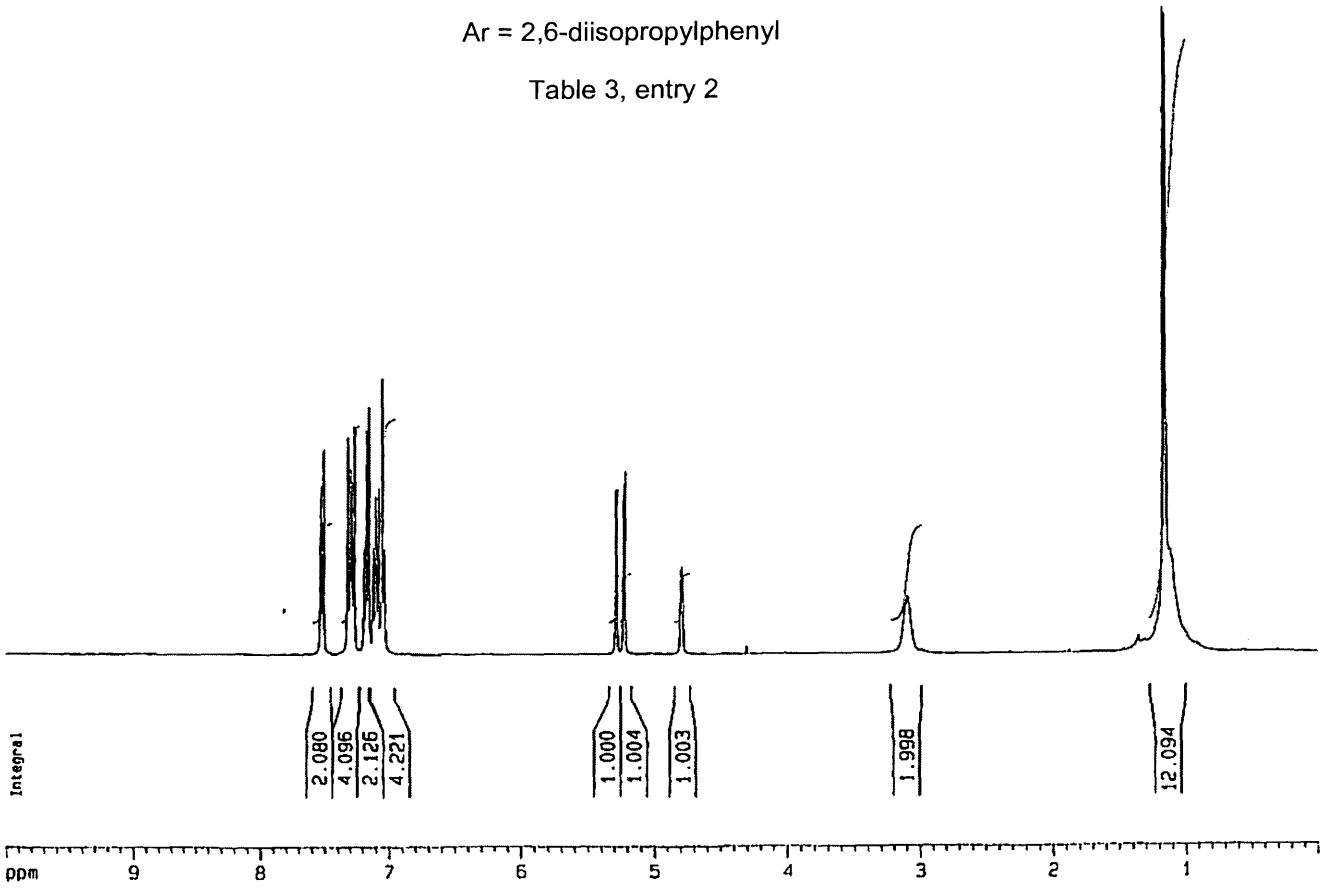
CF3-chalcone pdt



Ar = 2,6-diisopropylphenyl

Table 3, entry 2



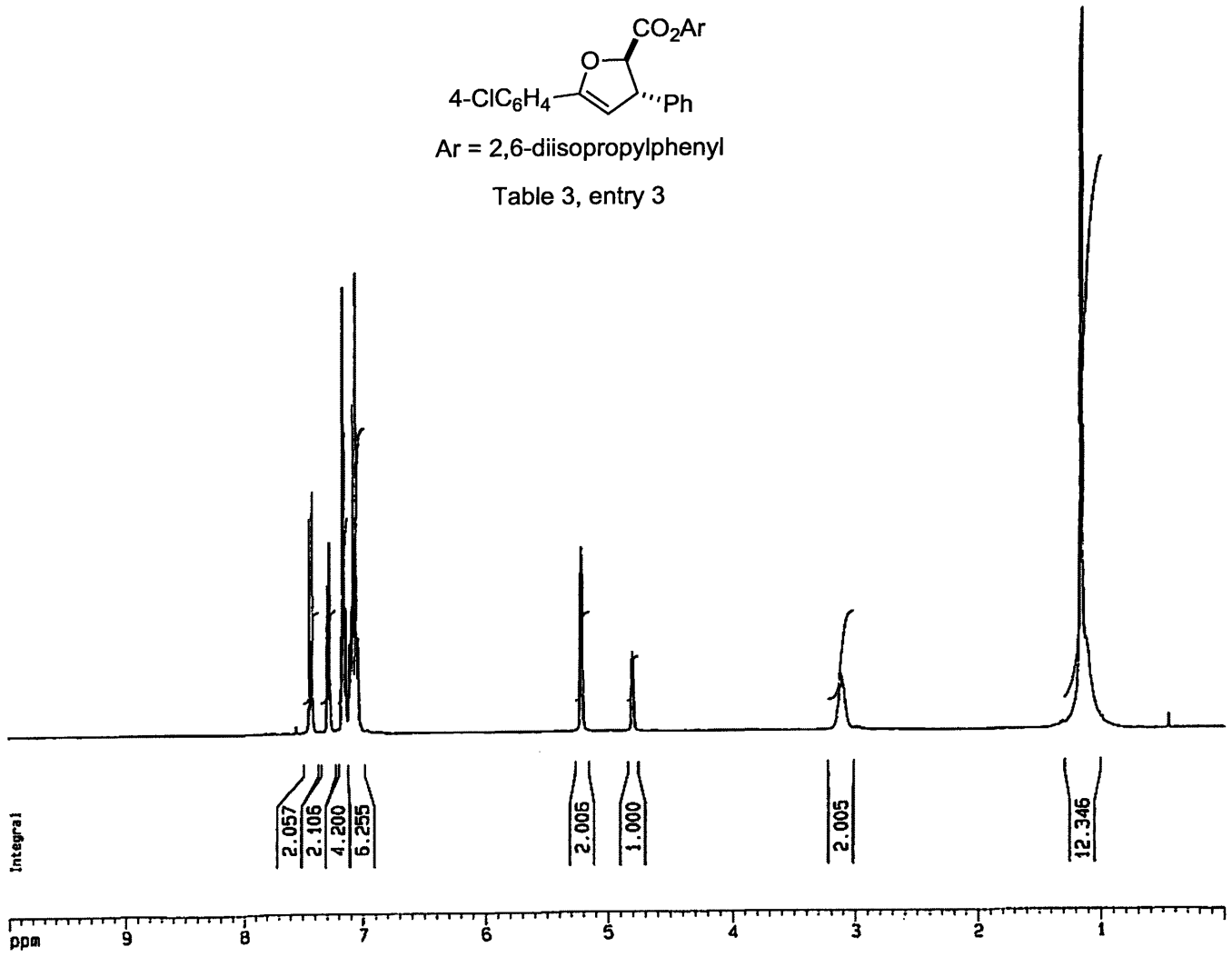

```
Current Data Parameters
NAME                  ss2-103
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20050316
Time                    17.35
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                        32
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                400.1300443 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                    0.000 ppm
F2                     0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06502 Hz/cm
```



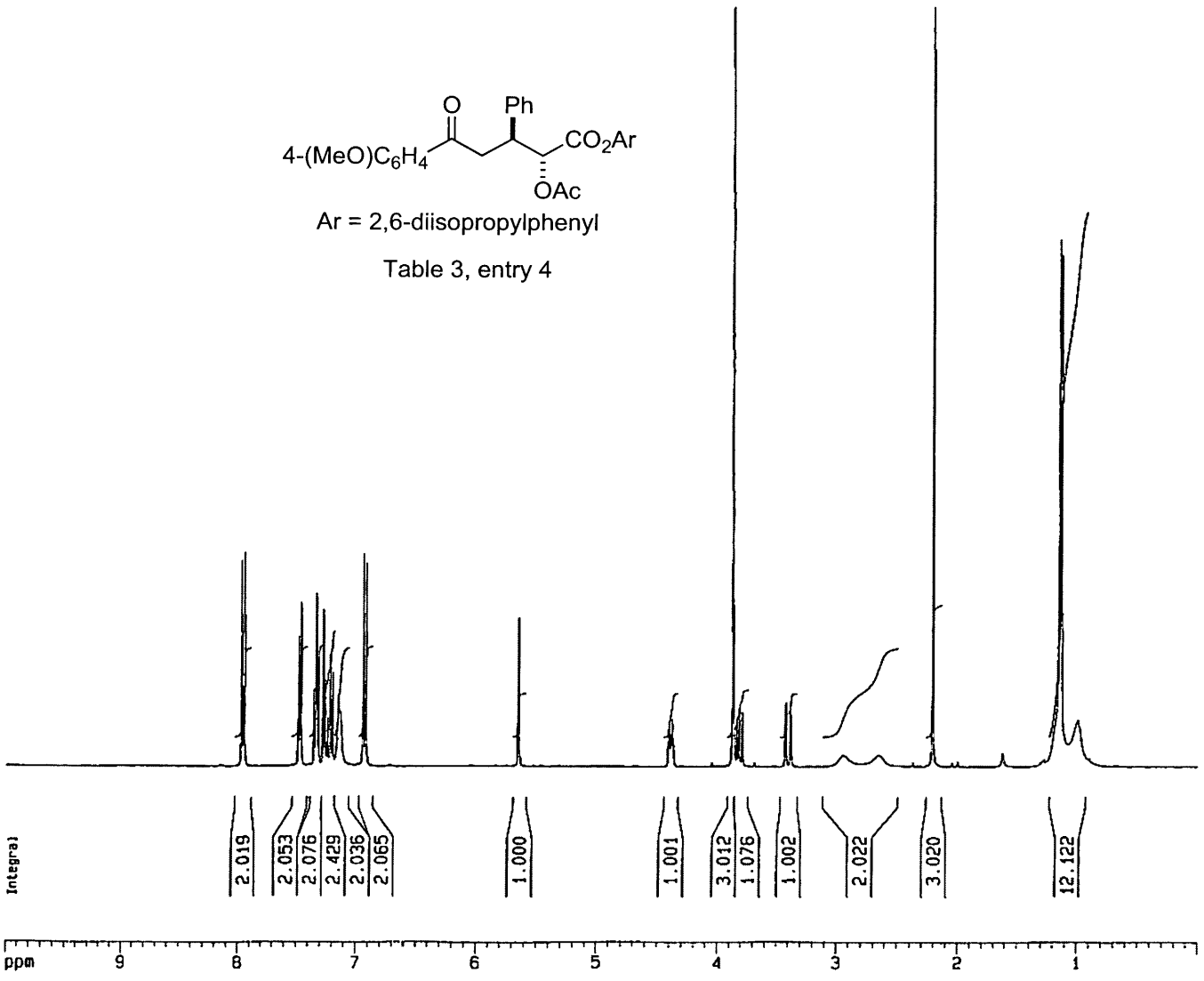

```
Current Data Parameters
NAME                  ss2-225
EXPNO                       6
PROCNO                      1

F2 - Acquisition Parameters
Date_              20050503
Time                  21.06
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                      64
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                400.1300443 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                   0.000 ppm
F2                    0.00 Hz
PPMCM             0.50000 ppm/cm
HZCM            200.06502 Hz/cm
```




```
Current Data Parameters
NAME                  ss3-80
EXPNO                      5
PROCNO                     1

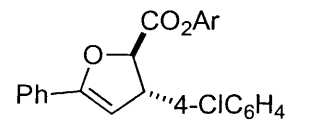
F2 - Acquisition Parameters
Date_              20050926
Time                  15.11
INSTRUM               spect
PROBHD     5mm BBO BB-1
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                     90.5
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                400.1300059 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                  0.000 ppm
F2                   0.00 Hz
PPMCM              0.50000 ppm/cm
HZCM             200.06500 Hz/cm
```

4'-Cl-chalcone major pdt



Ar = 2,6-diisopropylphenyl

Table 3, entry 5


```
Current Data Parameters
NAME                  ss2-97
EXPNO                     10
PROCNO                     1

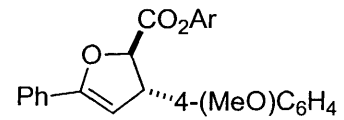
F2 - Acquisition Parameters
Date_               20050224
Time                   14.25
INSTRUM                spect
PROBHD     5mm BBO BB-1
PULPROG                zg30
TD                    65536
SOLVENT                C6D6
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       25.4
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                 400.1300443 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                    0.000 ppm
F2                     0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06502 Hz/cm
```

4'-OMe chalcone-major pdt



Ar = 2,6-diisopropylphenyl

Table 3, entry 6

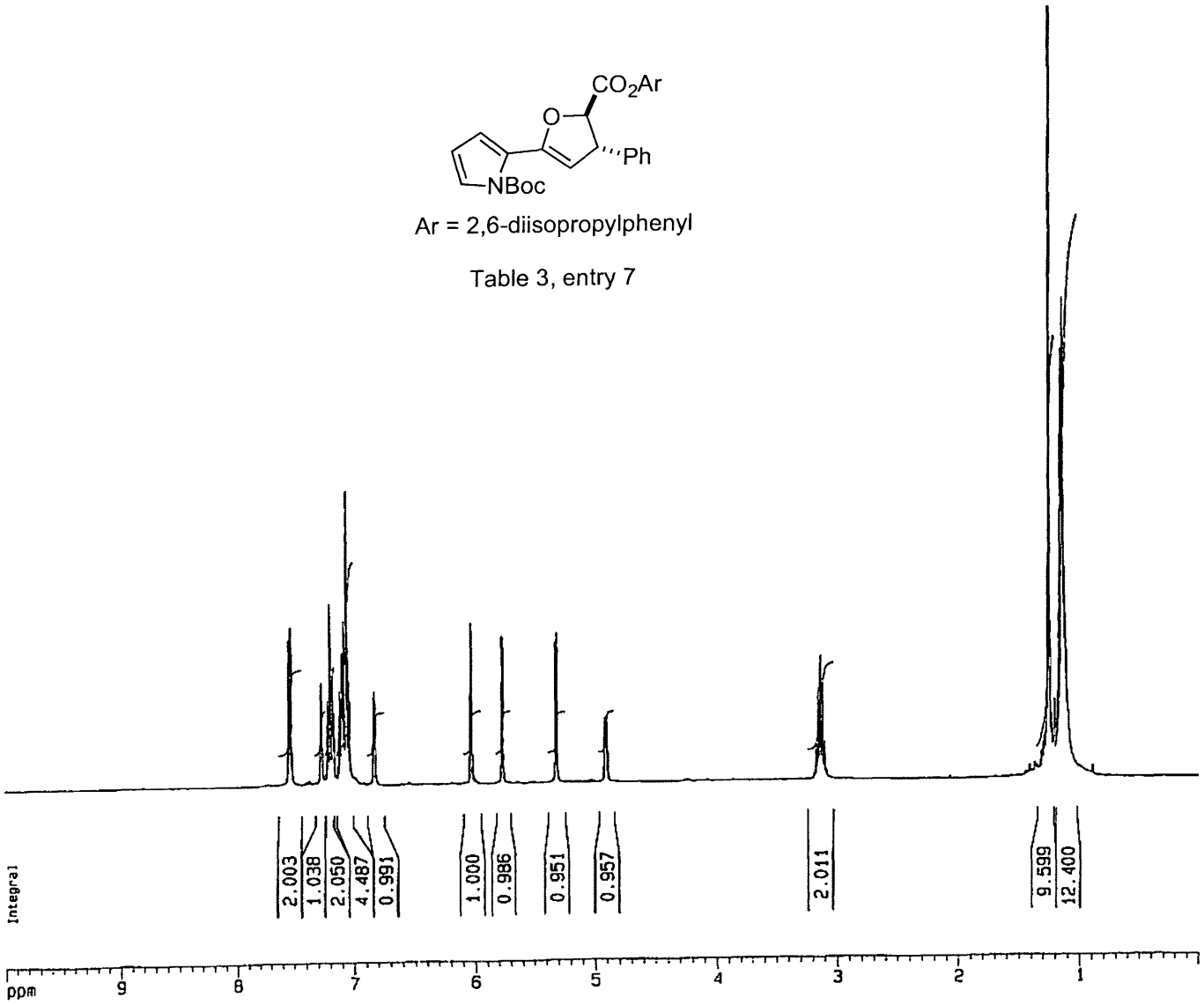
Current Data Parameters
NAME ss2-101
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20050224
Time 14.54
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 25.4
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 400.1300443 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 0.000 ppm
F2 0.00 Hz
PPMCM 0.50000 ppm/cm
HZCM 200.06502 Hz/cm



Ar = 2,6-diisopropylphenyl

Table 3, entry 7

```
Current Data Parameters
NAME                  ss2-235
EXPNO                       4
PROCNO                      1

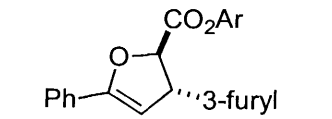
F2 - Acquisition Parameters
Date_              20050509
Time                   18.31
INSTRUM                spect
PROBHD     5mm BBO BB-1
PULPROG                 zg30
TD                     65536
SOLVENT                C6D6
NS                        16
DS                         2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                        16
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                400.1300443 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                   0.000 ppm
F2                    0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06502 Hz/cm
```

3-furyl enone (away)



Ar = 2,6-diisopropylphenyl

Table 3, entry 8


```
Current Data Parameters
NAME                ss2-105
EXPNO                     5
PROCNO                    1

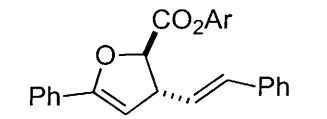
F2 - Acquisition Parameters
Date_              20050304
Time                 15.56
INSTRUM              spect
PROBHD     5mm BBO BB-1
PULPROG              zg30
TD                  65536
SOLVENT              C6D6
NS                     16
DS                      2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                     64
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            400.1300492 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                 0.000 ppm
F2                  0.00 Hz
PPMCM            0.50000 ppm/cm
HZCM           200.06502 Hz/cm
```

vinyl Ph enone-major pdt



Ar = 2,6-diisopropylphenyl

Table 3, entry 9


```
Current Data Parameters
NAME                  ss2-99
EXPNO                     10
PROCNO                     1

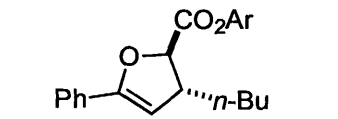
F2 - Acquisition Parameters
Date_              20050224
Time                  14.39
INSTRUM               spect
PROBHD      5mm BBO BB-1
PULPROG               zg30
TD                    65536
SOLVENT               C6D6
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                     25.4
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              400.1300443 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                  0.000 ppm
F2                    0.00 Hz
PPMCM              0.50000 ppm/cm
HZCM             200.06502 Hz/cm
```

nBu (away) - major pdt



Ar = 2,6-diisopropylphenyl

Table 3, entry 10


```
Current Data Parameters
NAME                  ss2-115
EXPNO                       5
PROCNO                      1

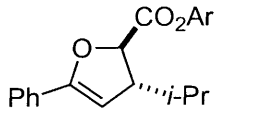
F2 - Acquisition Parameters
Date_                20050303
Time                    15.53
INSTRUM                 spect
PROBHD       5mm BBO BB-1
PULPROG                 zg30
TD                     65536
SOLVENT                 C6D6
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                         32
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                 400.1300518 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                   0.000 ppm
F2                    0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06503 Hz/cm
```

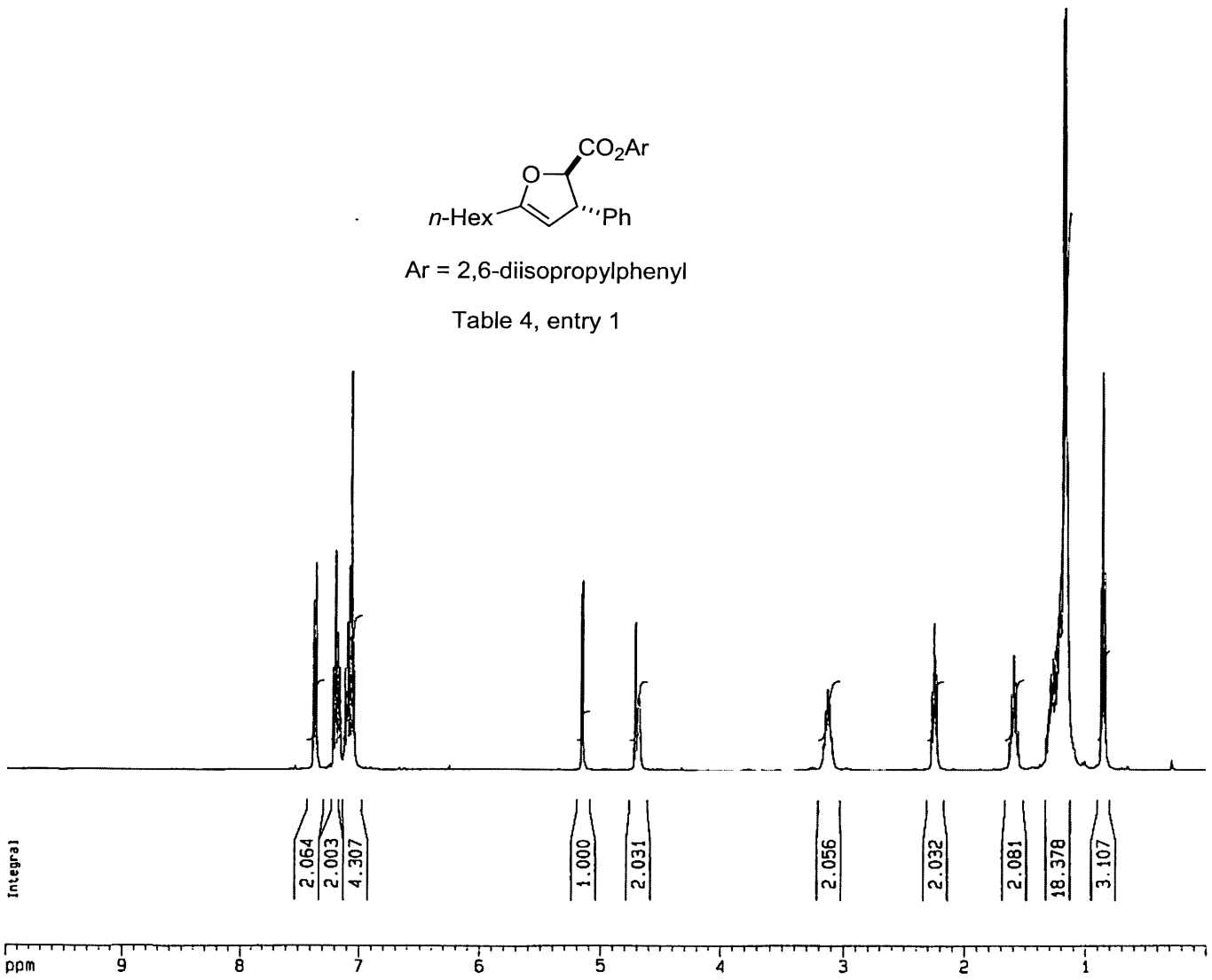
i-Pr (away)



Ar = 2,6-diisopropylphenyl

Table 3, entry 11

Current Data Parameters	
NAME	ss2-119
EXPNO	2
PROCNO	1
F2 - Acquisition Parameters	
Date_	20050308
Time	18.56
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	80.6
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	400.1300446 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	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	200.06502 Hz/cm




```
Current Data Parameters
NAME                  ss2-257
EXPNO                       2
PROCNO                      1

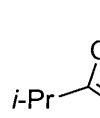
F2 - Acquisition Parameters
Date_              20050527
Time                   19.18
INSTRUM                spect
PROBHD     5mm BBO BB-1
PULPROG                 zg30
TD                     65536
SOLVENT                C6D6
NS                        16
DS                         2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                        18
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                400.1300446 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                    0.000 ppm
F2                     0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06502 Hz/cm
```

i-Pr enone pdt



Ar = 2,6-diisopropylphenyl

Table 4, entry 2


```
Current Data Parameters
NAME                  ss2-133
EXPNO                      10
PROCNO                      1

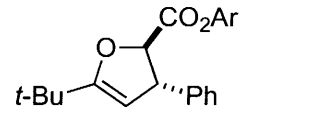
F2 - Acquisition Parameters
Date_               20050316
Time                   17.59
INSTRUM                spect
PROBHD     5mm BBO BB-1
PULPROG                zg30
TD                     65536
SOLVENT                C606
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                        32
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                400.1300443 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                    0.000 ppm
F2                     0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06502 Hz/cm
```

tBu (ketone side)



Ar = 2,6-diisopropylphenyl

Table 4, entry 3

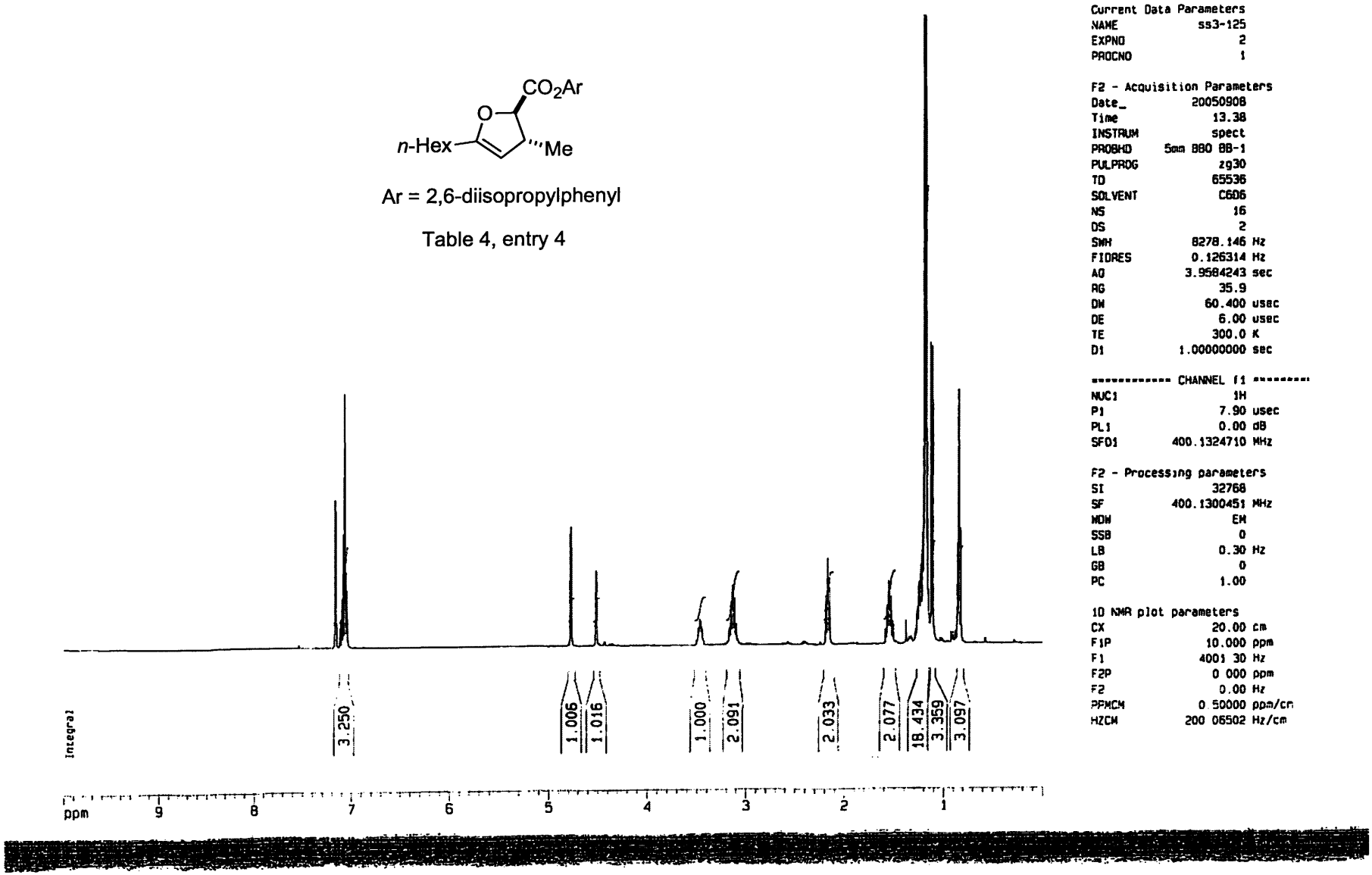

```
Current Data Parameters
NAME                  ss2-117
EXPNO                       1
PROCNO                      1

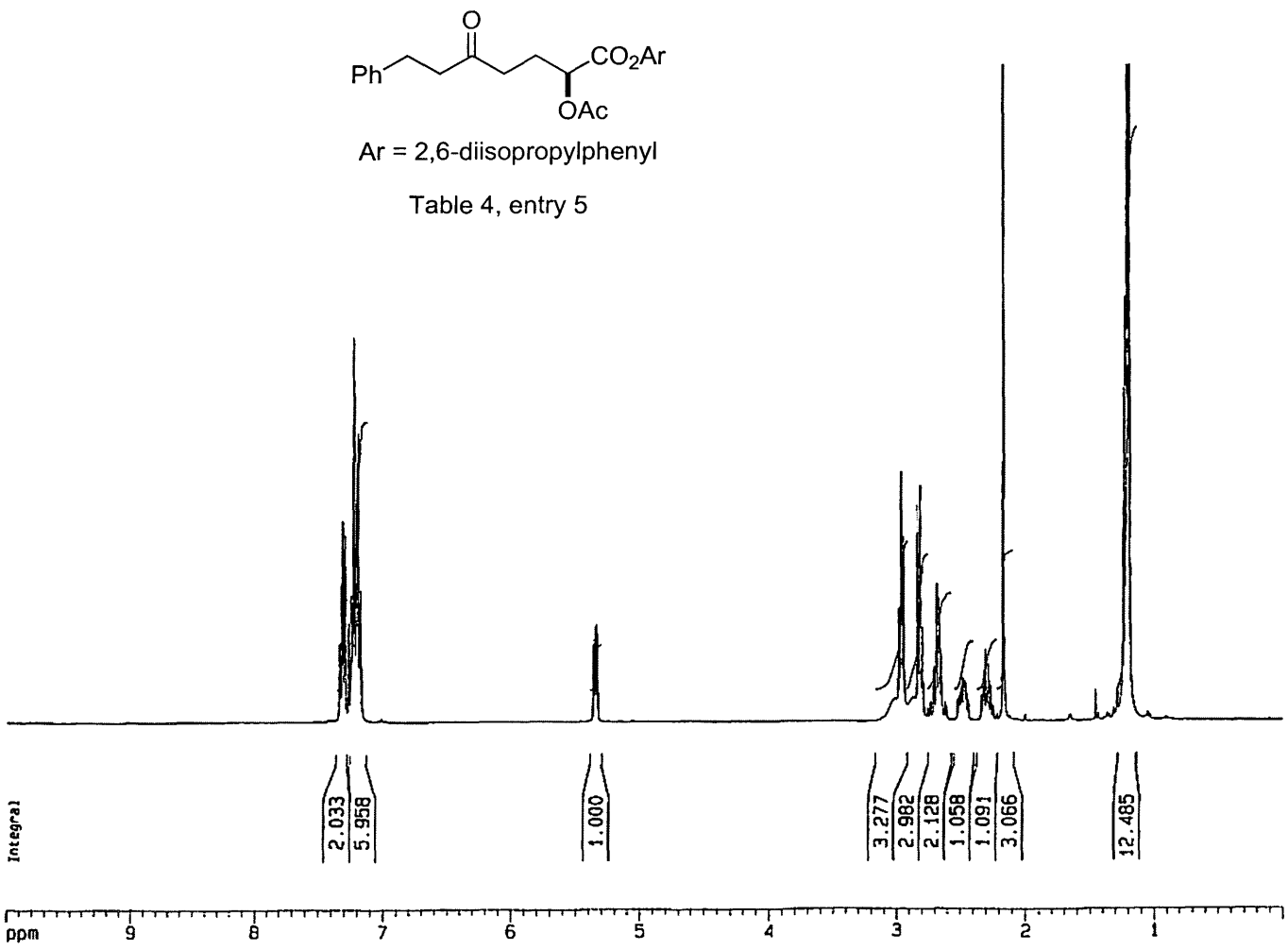
F2 - Acquisition Parameters
Date_              20050312
Time                  20.41
INSTRUM               spect
PROBHD     5mm BBO BB-1
PULPROG               zg30
TD                   65536
SOLVENT               C6D6
NS                      16
DS                       2
SWH                4789.272 Hz
FIDRES             0.073078 Hz
AQ                 6.8420086 sec
RG                      16
DW                   104.400 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           400.1320007 MHz

F2 - Processing parameters
SI                     32768
SF               400.1300632 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                   0.000 ppm
F2                    0.00 Hz
PPMCM              0.50000 ppm/cm
HZCM             200.06503 Hz/cm
```


CO2Ar
O
n-Hex
Me
Ar = 2,6-diisopropylphenyl
Table 4, entry 4
Current Data Parameters
NAME ss3-125
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20050908
Time 13.38
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 35.9
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 400.1300451 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 0.000 ppm
F2 0.00 Hz
PPMCM 0.50000 ppm/cm
HZCM 200.06502 Hz/cm
Integral
3.250
1.006
1.016
1.000
2.091
2.033
2.077
18.434
3.359
3.097
ppm
9
8
7
6
5
4
3
2
1



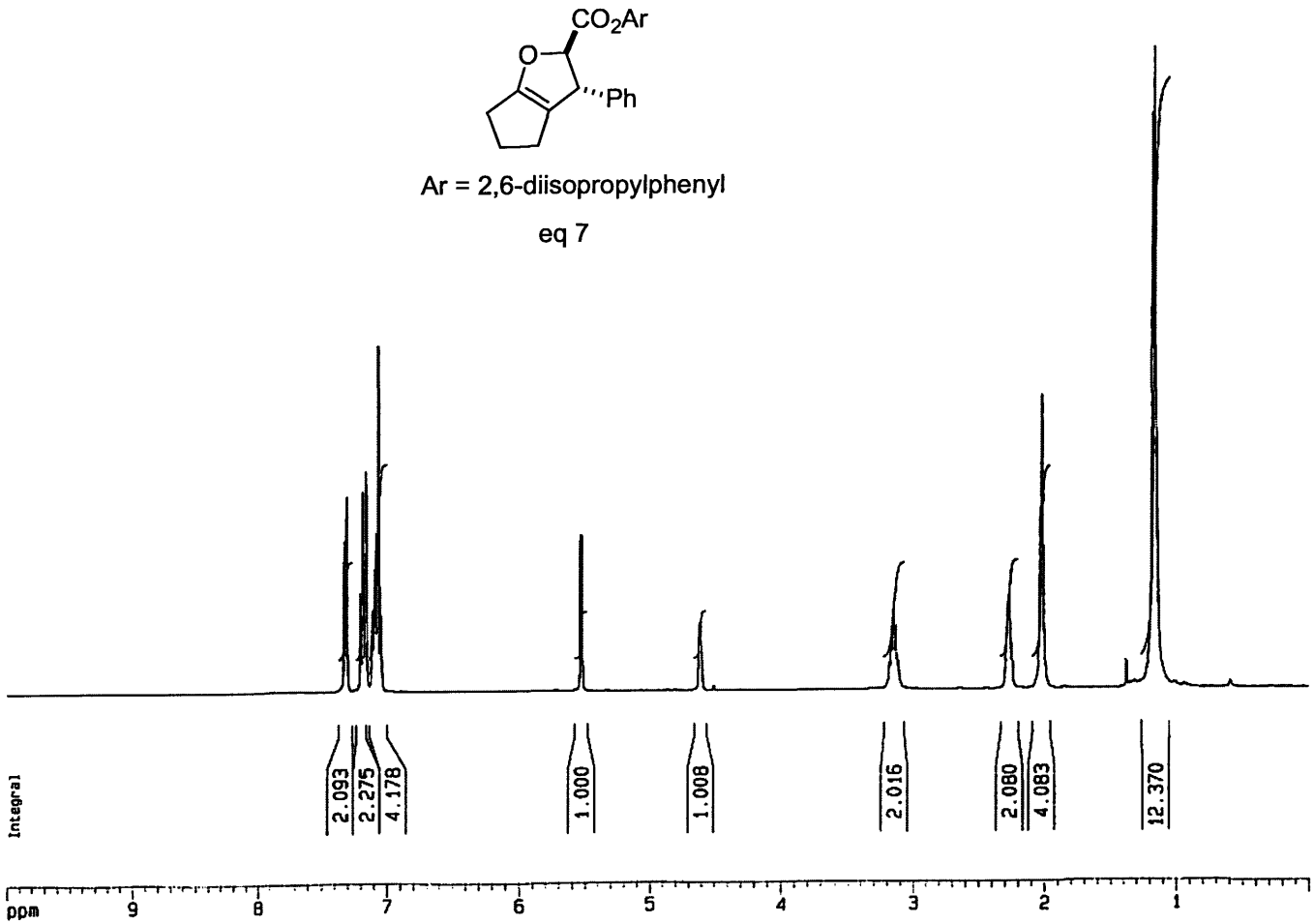

```
Current Data Parameters
NAME                  ss3-197
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20051109
Time                  16.26
INSTRUM               spect
PROBHD     5mm BBO BB-1
PULPROG               zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                       57
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                400.1300054 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                  0.000 ppm
F2                   0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06500 Hz/cm
```



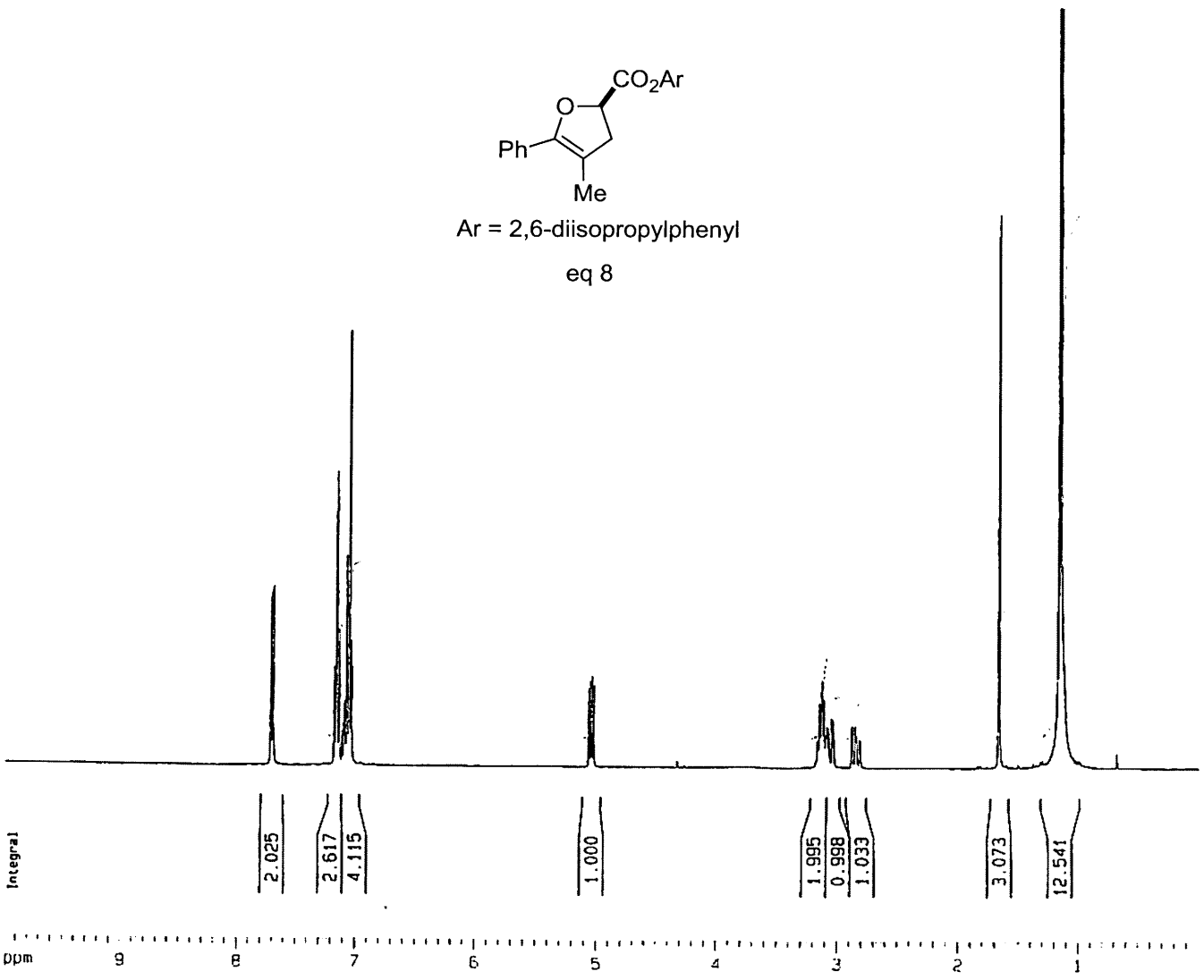

```
Current Data Parameters
NAME                  ss3-121
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20050830
Time                  16.36
INSTRUM               spect
PROBHD     5mm BBO BB-1
PULPROG               zg30
TD                   65536
SOLVENT               C606
NS                      16
DS                       2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      40.3
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                 400.1300451 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                   0.000 ppm
F2                    0.00 Hz
PPMCM                 0.50000 ppm/cm
HZCM                200.06502 Hz/cm
```



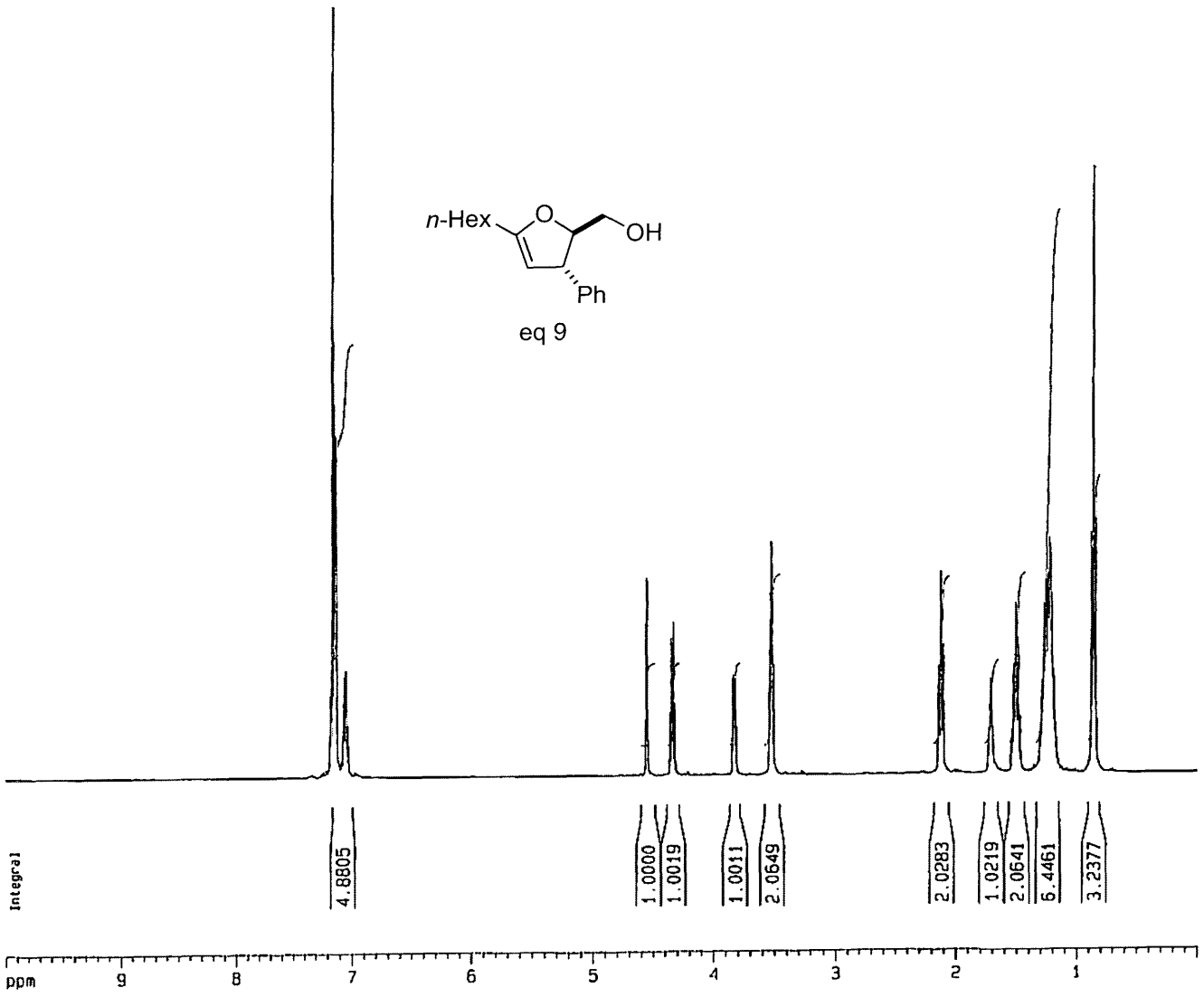

```
Current Data Parameters
NAME                  ss2-267
EXPNO                       4
PROCNO                      1

F2 - Acquisition Parameters
Date_              20050606
Time                  16.37
INSTRUM               spect
PROBHD     5 mm QNP  1H
PULPROG               zg30
TD                    65536
SOLVENT               C6D6
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                     35.9
DW                   60.400 usec
DE                    6.00 usec
TE                   300.0 K
D1                1.00000000 sec

============ CHANNEL f1 =============
NUC1                      1H
P1                     9.50 usec
PL1                    2.00 dB
SFO1            400.1324710 MHz

F2 - Processing parameters
SI                     32768
SF              400.1300446 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                    0.000 ppm
F2                     0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06502 Hz/cm
```



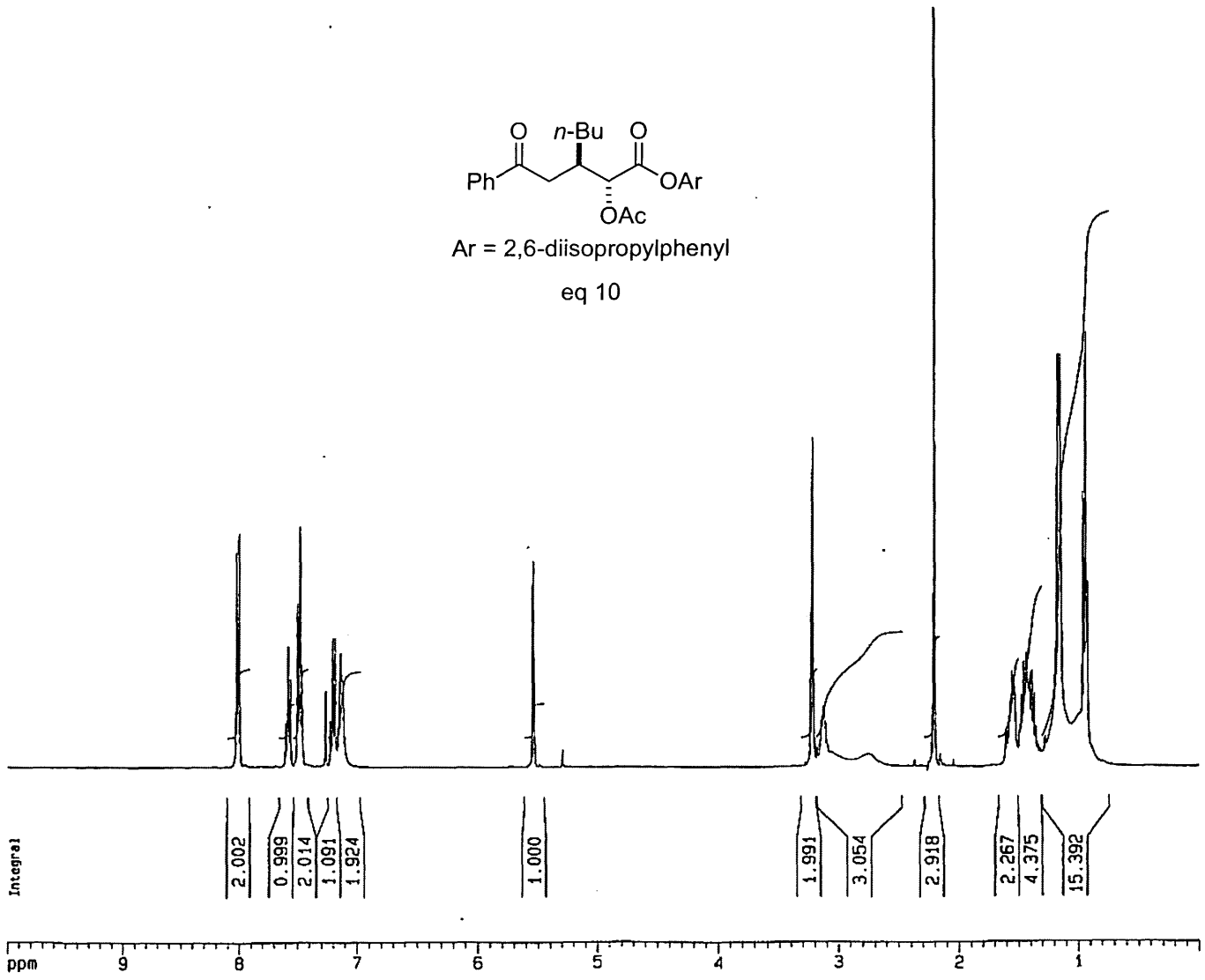

```
Current Data Parameters
NAME                  ss3-65
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20050718
Time                   22.56
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                      35.9
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                 400.1300547 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                    0.000 ppm
F2                     0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               200.06503 Hz/cm
```



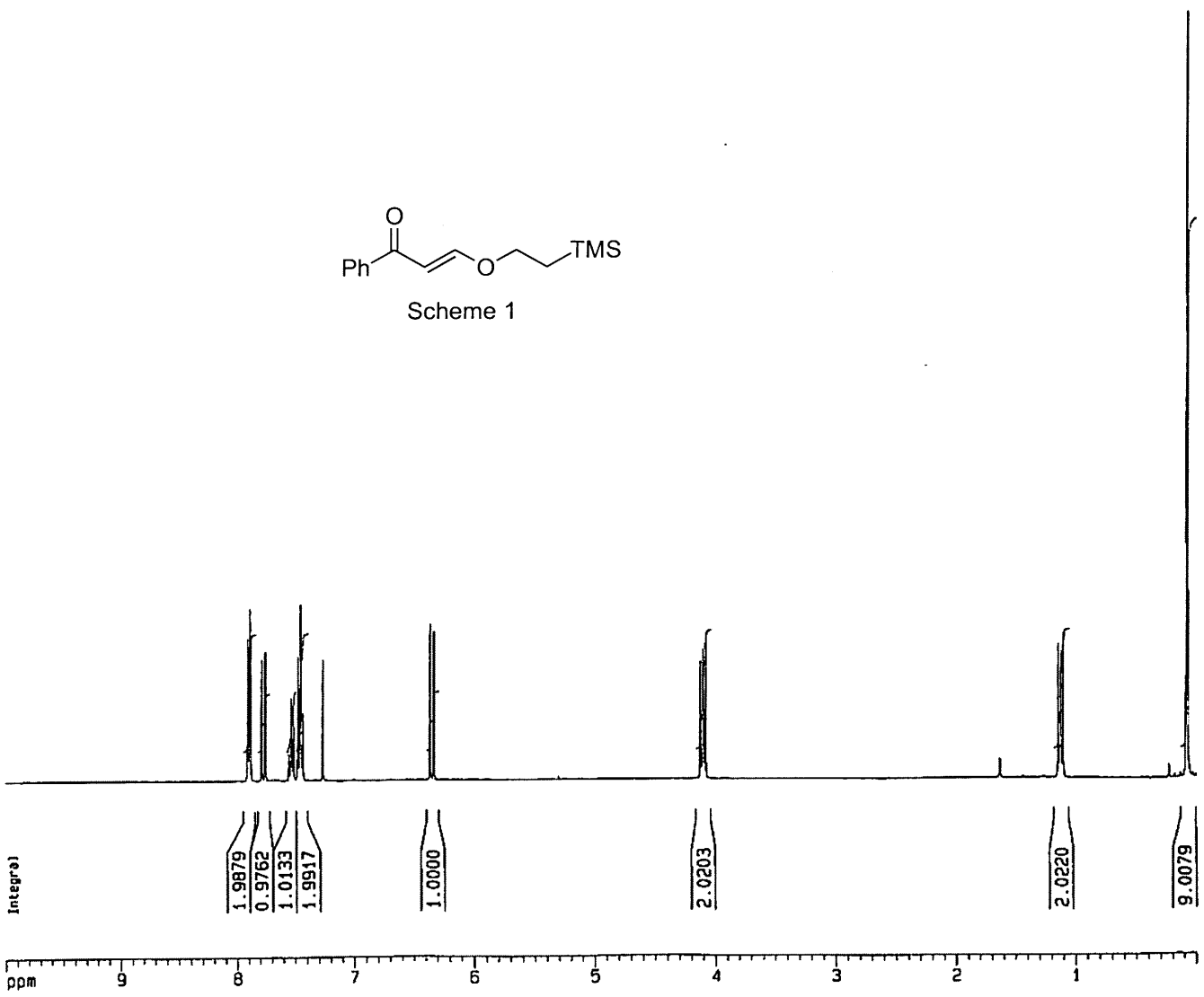

```
Current Data Parameters
NAME                  ss3-61
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20050718
Time                  10.32
INSTRUM               spect
PROBHD     5mm BBO BB-1
PULPROG               zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                     71.8
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                400.1300056 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                  0.000 ppm
F2                   0.00 Hz
PPMCM              0.50000 ppm/cm
HZCM             200.06500 Hz/cm
```



Scheme 1

```
Current Data Parameters
NAME              ss2-271
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20060125
Time                14.59
INSTRUM             spect
PROBHD   5 mm QNP  1H/1
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
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FIDRES           0.126314 Hz
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RG                    362
DW                 60.400 usec
DE                  6.00 usec
TE                 295.8 K
D1              1.00000000 sec
MCREST          0.00000000 sec
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PL1                 3.00 dB
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F2 - Processing parameters
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CY                   3.00 cm
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F2                   0.00 Hz
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HZCM            200.06500 Hz/cm
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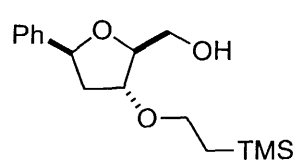
4-61-B from (+)-bipyFc*



Scheme 1

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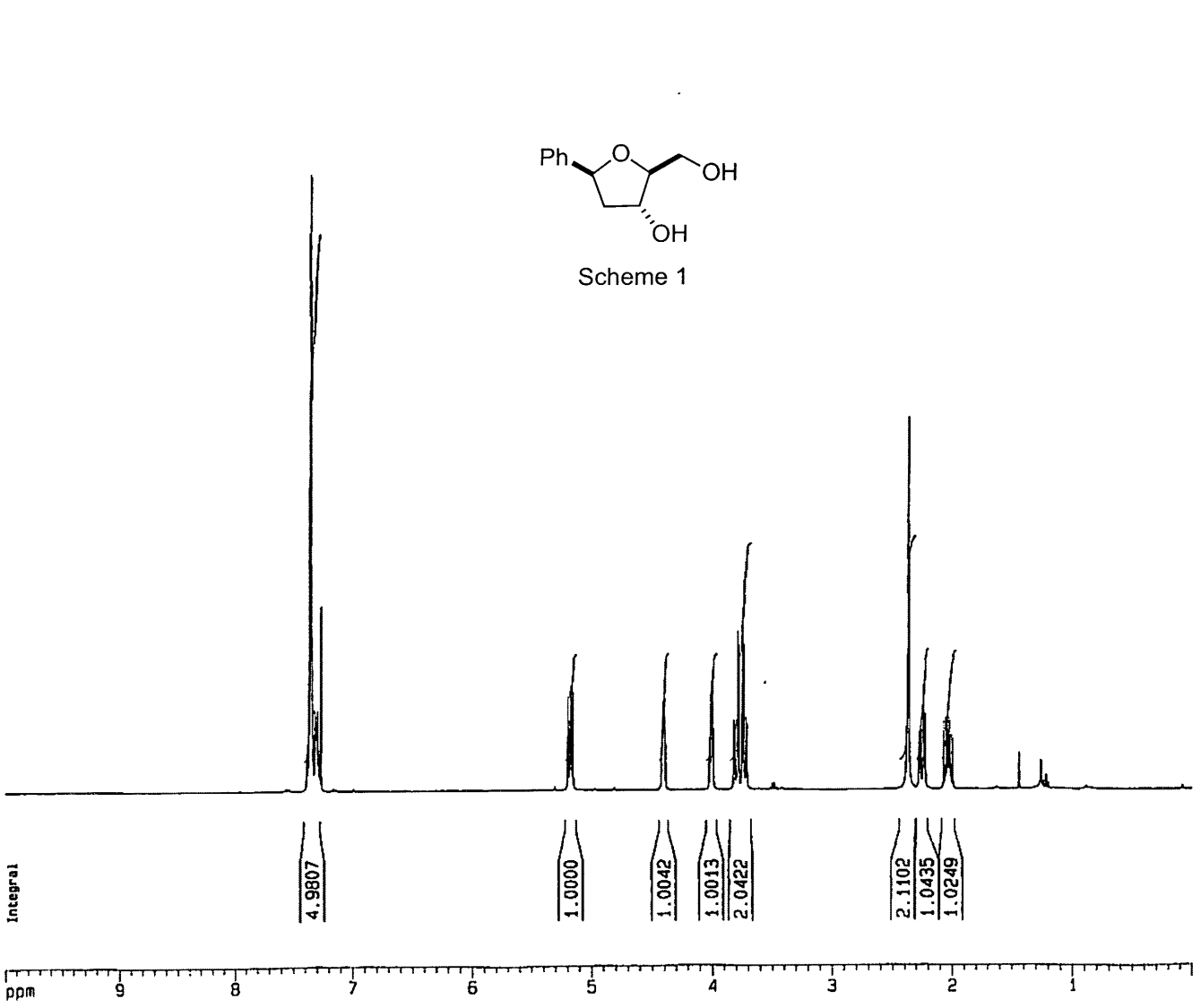

Scheme 1

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D1                 1.00000000 sec

============ CHANNEL f1 =========
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1D NMR plot parameters
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```

Chapter 3

Design, Synthesis, and Applications of C_2-Symmetric Planar-Chiral Catalysts

A. Introduction

Chiral ferrocene ligands have become extremely important in asymmetric organic synthesis, especially in processes catalyzed by metal complexes.[1] In recent years, numerous new chiral ferrocene ligands have been developed and successfully applied to various processes. In fact, one of the largest-scale enantioselective catalytic process in industry is the synthesis of a precursor of the herbicide (*S*)-metolachlor by an Ir/Xyliphos-catalyzed asymmetric hydrogenation reaction.[2]

Besides their excellent utility, chiral ferrocene ligands have several other advantages over other ligands. First, ferrocene compounds have a rigid scaffold and high stability, and they can be prepared from an inexpensive starting material. Moreover, there are well-established methods for functionalization at specific positions of ferrocene and its derivatives.

Due to these advantages of chiral ferrocene compounds, a large number of reports have been published on various asymmetric transition metal-catalyzed processes using chiral ferrocenes as ligands. However, the use of these planar-chiral ferrocenes as simple asymmetric catalysts has been mainly limited to planar-chiral DMAP derivatives (Figure 1), developed in our group.[3] Therefore, the development of other ferrocene-based catalysts is highly desirable.

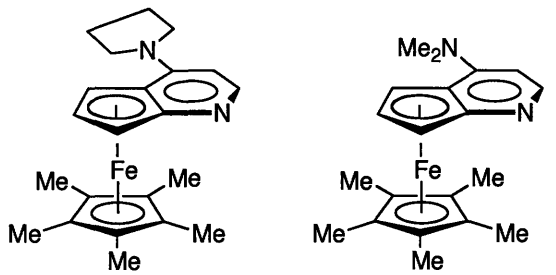

Figure 1. Planar-Chiral DMAP Derivatives.

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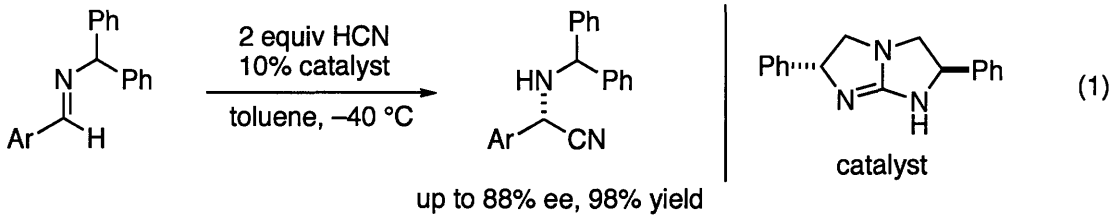
[1] For recent reviews, see: (a) Arrayas, R. G.; Adriio, J.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 7674–7715. (b) Atkinson, R. C. J.; Gibson, V. C.; Long, N. J. *Chem. Soc. Rev.* **2004**, *33*, 313–328. (c) Sutcliffe, O. B.; Bryce, M. R. *Tetrahedron: Asymmetry* **2003**, *14*, 2297–2325. (d) Colacot, T. J. *Chem. Rev.* **2003**, *103*, 3101–3118.

[2] (a) Blaser, H.-U. *Adv. Synth. Catal.* **2002**, *344*, 17–31. (b) Blaser, H.-U.; Brieden, W.; Pugin, B.; Spindler, F.; Studer, M.; Togni, A. *Top. Catal.* **2002**, *19*, 3–16.

[3] For reviews, see: (a) Kizirian, J.-C. *Chem. Rev.* **2008**, *108*, 140–205. (b) Wurz, R. P. *Chem. Rev.* **2007**, *107*, 5570–5595.

In the last decade, studies on asymmetric reactions catalyzed by small organic molecules have undergone an explosive expansion.[4] A wide range of chiral organic catalysts have been successfully applied to numerous reactions. We decided to develop ferrocene-based chiral guanidines, phosphines, and tertiary amines since they can be easily incorporated into the ferrocene structure.

There have been several reports of enantioselective organocatalysis by chiral guanidines.[5] In 1999, Corey reported an asymmetric Strecker reaction catalyzed by a C_2-symmetric bicyclic guanidine (eq 1).[5b] Various aryl imines and a *t*-butyl imine undergo the reaction in high yield with good enantioselectivity.



(1)

More recently, Terada has reported highly enantioselective reactions catalyzed by axially chiral guanidines (eq 2 and eq 3).[5h,5i] As shown from these results, chiral guanidines have great potential as catalysts due to their high basicity and substrate recognition ability through H-bonding. However, manipulation of the guanidine structure is challenging because of its basicity and the lack of a simple and general method for their synthesis.

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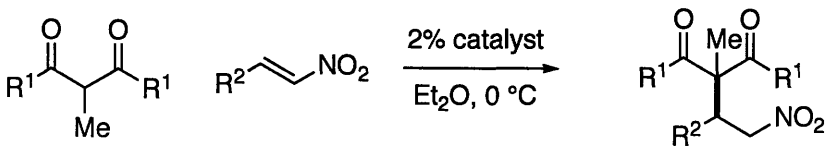
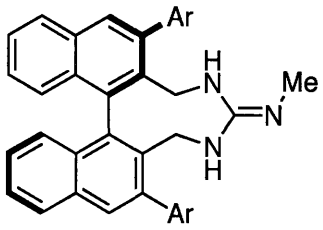
[4] For reviews, see: (a) Berkessel, A.; Groeger, H. *Asymmetric Organocatalysis-From Biomimetic Concepts to Powerful Methods for Asymmetric Synthesis*; Wiley-VCH: Weinheim, 2005. (b) Seayad, J.; List, B. *Org. Biomol. Chem.* **2005**, *3*, 719–724. (c) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520–1543. (d) *Enantioselective Organocatalysis*; Dalko, P. I., Ed.; Wiley-VCH: Weinheim, 2007.

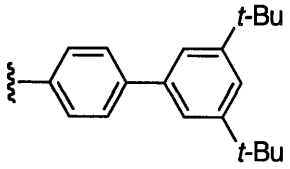
[5] For some leading references, see: (a) Iyer, M. S.; Gigstad, K. M.; Namdev, N. D.; Lipton, M. *J. Am. Chem. Soc.* **1996**, *118*, 4910–4911. (b) Corey, E. J.; Grogan, M. J. *Org. Lett.* **1999**, *1*, 157–160. (c) Ishikawa, T.; Araki, Y.; Kumamoto, T.; Seki, H.; Fukuda, K.; Isobe, T. *Chem. Commun.* **2001**, 245–246. (d) Kita, T.; Georgieva, A.; Hashimoto, Y.; Nakata, T.; Nagasawa, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 2832–2834. (e) Allingham, M. T.; Howard-Jones, A.; Murphy, P. J.; Thomas, D. A.; Caulkett, P. W. R. *Tetrahedron Lett.* **2003**, *44*, 8677–8680. (f) Sohtome, Y.; Hashimoto, Y.; Nagasawa, K. *Eur. J. Org. Chem.* **2006**, 2894–2897. (g) Shen, J.; Nguyen, T. T.; Goh, Y.-P.; Ye, W.; Fu, X.; Xu, J.; Tan, C.-H. *J. Am. Chem. Soc.* **2006**, *128*, 13692–13693. (h) Terada, M.; Ube, H.; Yaguchi, Y. *J. Am. Chem. Soc.* **2006**, *128*, 1454–1455. (i) Terada, M.; Nakano, M.; Ube, H. *J. Am. Chem. Soc.* **2006**, *128*, 16044–16045.

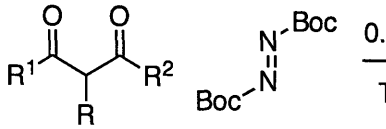


(2)

up to 98% ee, 99% yield

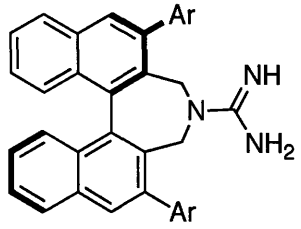


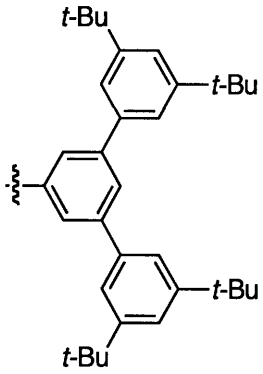
Ar = 



(3)

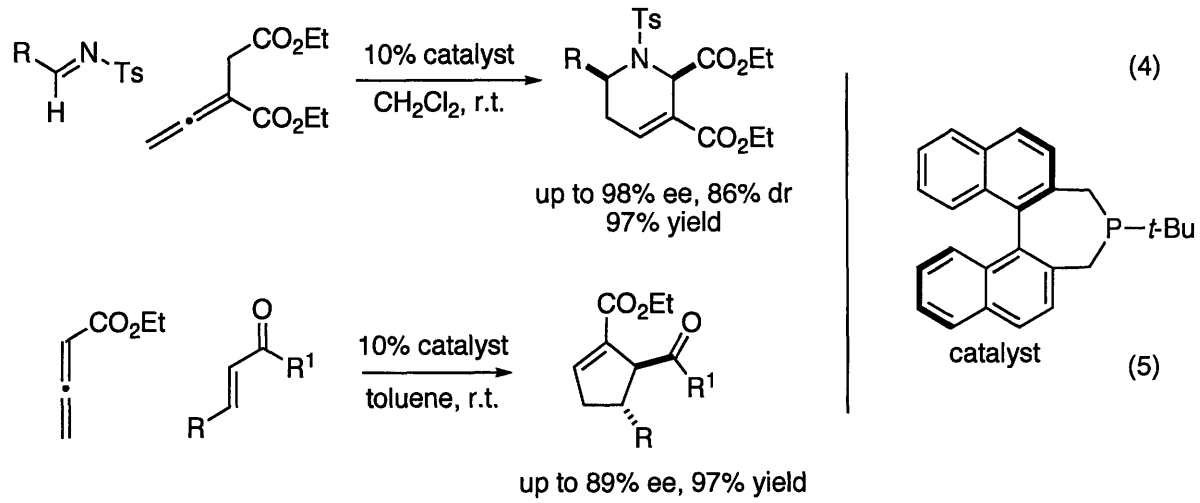
up to 98% ee, 99% yield



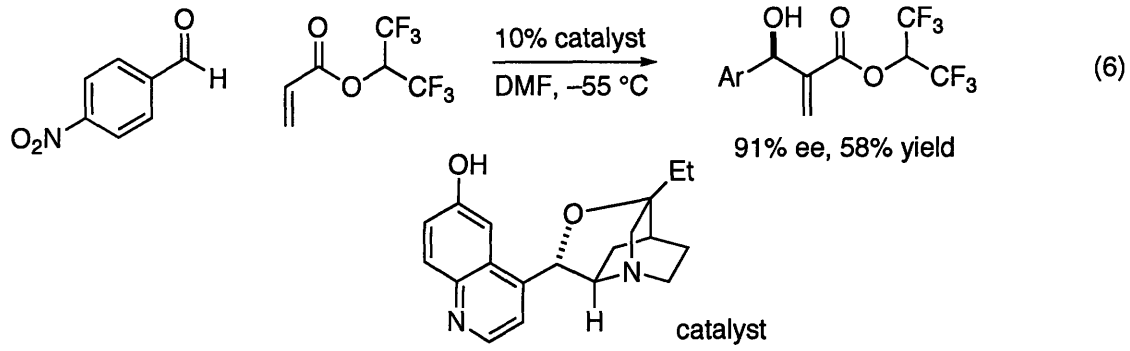
Ar = 

Although chiral phosphines have been mostly used as ligands for transition metal-catalyzed reactions, the number of studies using a phosphine as a chiral catalyst is increasing. Axially chiral phosphines have been successfully applied to reactions of α,β-unsaturated carbonyl compounds. We have also reported two phosphine-catalyzed asymmetric cycloadditions (eq 4 and eq 5),[6] and studies of phosphine-catalyzed intramolecular cyclization of alcohols and amines are currently undergoing in our group.

[6] (a) Wurz, R. P.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 12234–12235. (b) Wilson, J. E.; Fu, G. C. *Angew. Chem. Int. Ed.* **2006**, *45*, 1426–1429.



The first chiral amines employed as asymmetric catalysts were the cinchona alkaloids, which can be isolated by extracting the bark of the cinchona tree. Cinchona alkaloids and their tertiary amine derivatives have successfully catalyzed an array of transformations, including Morita-Baylis-Hillman reactions (eq 6).[7]



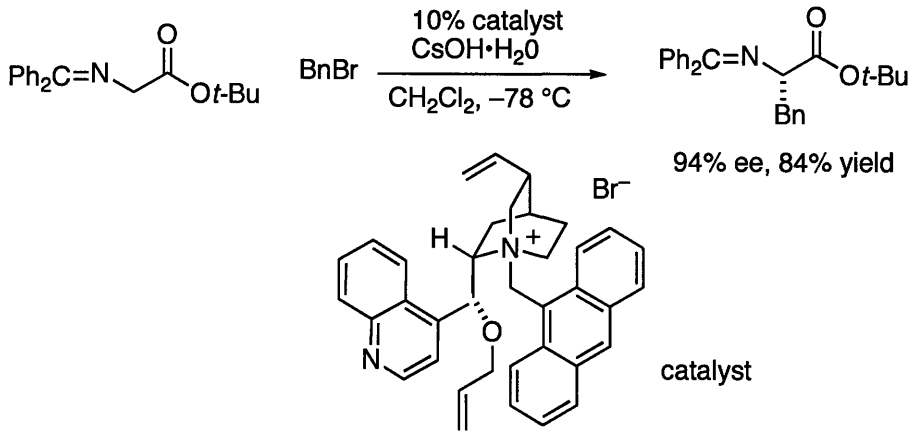
Tertiary ammonium salts of cinchona alkaloids can act as chiral phase transfer catalysts for reactions in biphasic medium.[8] Such catalysts have been used for the asymmetric alkylation of glycine imines, which provides an efficient synthesis of unnatural amino acids with high enantioselectiviry (eq 7).[9] Although most chiral phase

[7] (a) Wabuchi, Y.; Nakatani, M.; Yokoyama, S.; Hatakeyama, S. *J. Am. Chem. Soc.* **1999**, *121*, 10219–10220. (b) Nakano, A.; Kawahara, S.; Morokuma, K.; Nakatami, M.; Iwabuchi, Y.; Takahashi, K.; Ishihara, J.; Hatakeyama, S. *Tetrahedron* **2006**, *62*, 381–389.

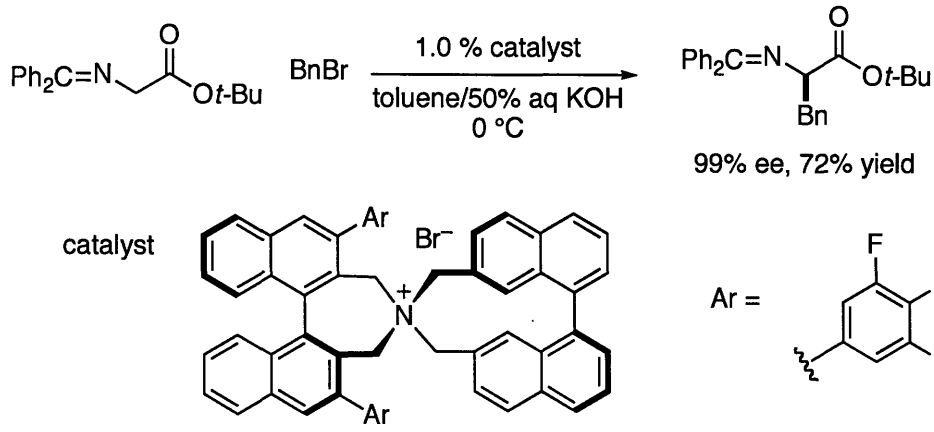
[8] For reviews, see: (a) Ooi, T.; Maruoka, K. *Angew. Chem. Int. Ed.* **2007**, *46*, 4222–4266. (b) Hashimoto, T.; Maruoka, K. *Chem. Rev.* **2007**, *37*, 506–517. (c) O'Donnell, *Acc. Chem. Res.* **2004**, *37*, 526–533.

[9] Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414–12415.

transfer catalysts have been derivatives of cinchona alkaloids, Maruoka has introduced highly efficient and tunable spiroammonium salts (eq 8).[10]



(7)



(8)

Inspired by these precedent results, we chose the molecules illustrated in Figure 2 as our target compounds. By employing C_2-symmetry, we expect to simplify the synthesis, reduce the number of possible transition states of the catalyzed reaction, and in turn make the structural modification of catalysts more straightforward.

[10] Ooi, T.; Maruoka, K. *J. Am. Chem. Soc.* **1999**, *121*, 6519–6520.

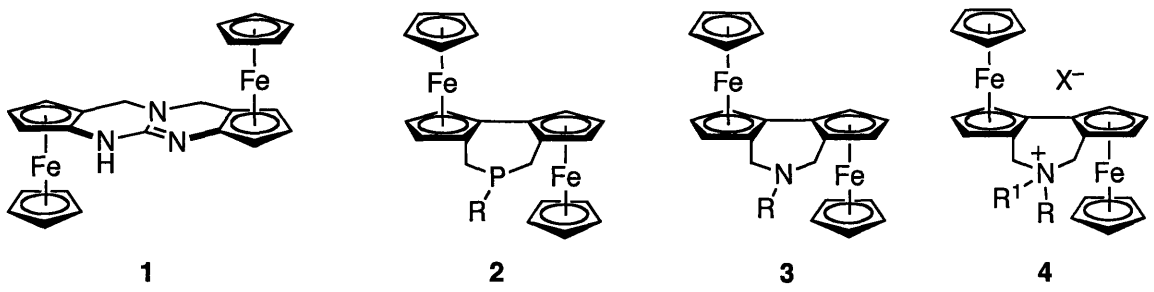
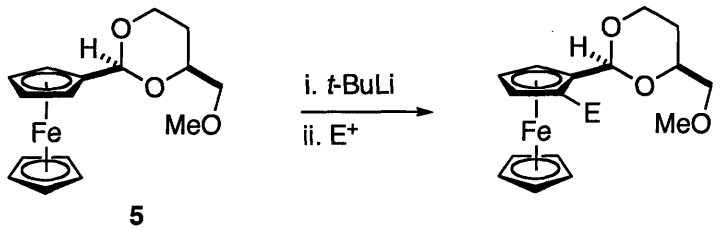


Figure 2. New C_2-Symmetric Planar-Chiral Catalysts: Target Molecules.

Our synthetic strategy involves the use of a chiral directing group for diastereoselective substitution at the ferrocene ring. Therefore, enantiomerically pure catalysts can be obtained without resolution. Among the various directing groups previously used in ferrocene chemistry, a chiral acetal is the most appropriate group since it can be easily converted to an aldehyde, which is necessary for further transformation (eq 9).[11] The combination of two monomers with proper functional groups will furnish precursors for target compounds.



(9)

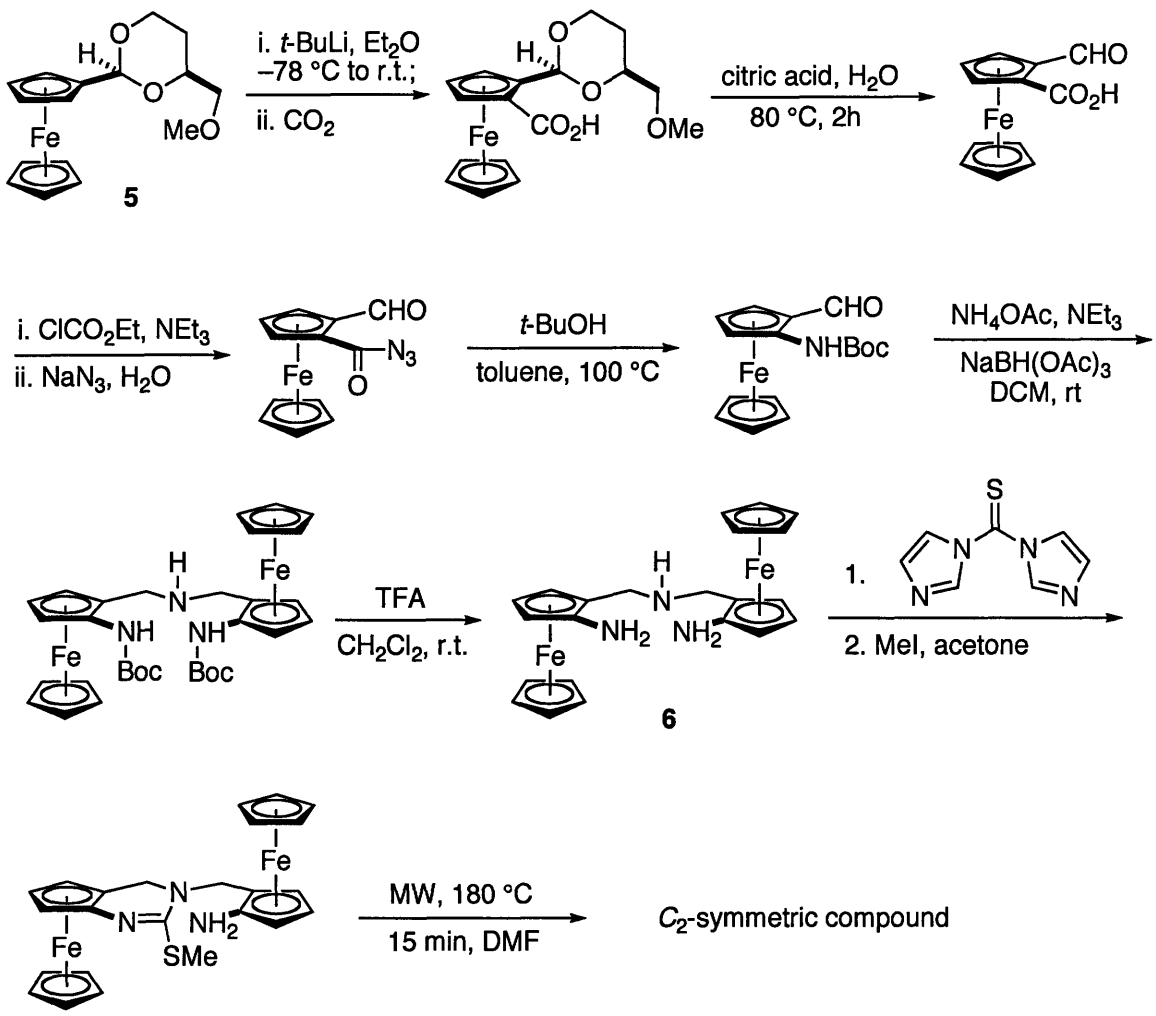
[11] (a) Riant, O.; Samuel, O.; Flessner, T.; Taudien, S.; Kagan, H. B. *J. Org. Chem.* **1997**, *62*, 6733–6745. (b) Riant, O.; Samuel, O.; Kagan, H. B. *J. Am. Chem. Soc.* **1993**, *115*, 5835–5836.

B. Results and Discussion

1. Synthesis of Planar-Chiral Guanidines

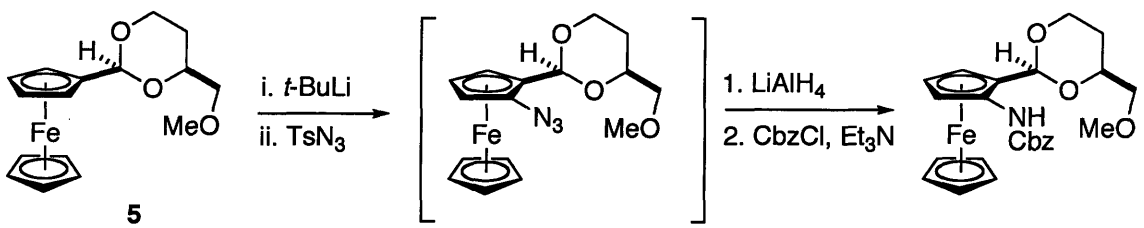
Previously, Jan Paradies in our group had devised a synthesis of planar-chiral guanidine **1** (Scheme 1).[12] Starting from acetal **5**, he could introduce a carboxylic acid diastereoselectively. After deprotection of the acetal group, a Boc-protected amino group was introduced by a two-step procedure. Reductive amination of the aldehyde furnished the triamine, which was treated with TFA for the deprotection of the Boc groups. However, the cyclization of free triamine **6** to form a guanidine proved to be the most challenging step. Several strategies were tested for the formation of a guanidine, but they failed to provide the desired product. When an isothiourea derived from triamine **6** was heated in a microwave reactor, a C_2-symmetric compound with a similar structure to **1** but with two extra methyl groups was generated. This compound proved to be unreactive for reactions that are catalyzed by other modified guanidines.

[12] Unpublished results.



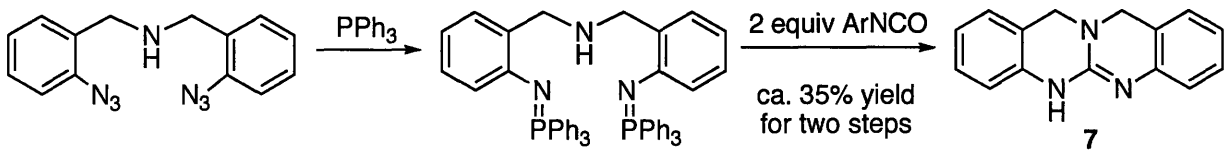
Scheme 1. Previous Synthetic Route for Guanidine **1.**

Starting from these results, we could make a slight improvement by introducing an amino group directly (eq 10). Due to the high lability of the azide-substituted ferrocene, it had to be reduced in situ. We explored several different strategies using aminoferrocenes with different protecting groups, however, the final cyclization steps remained problematic.



(10)

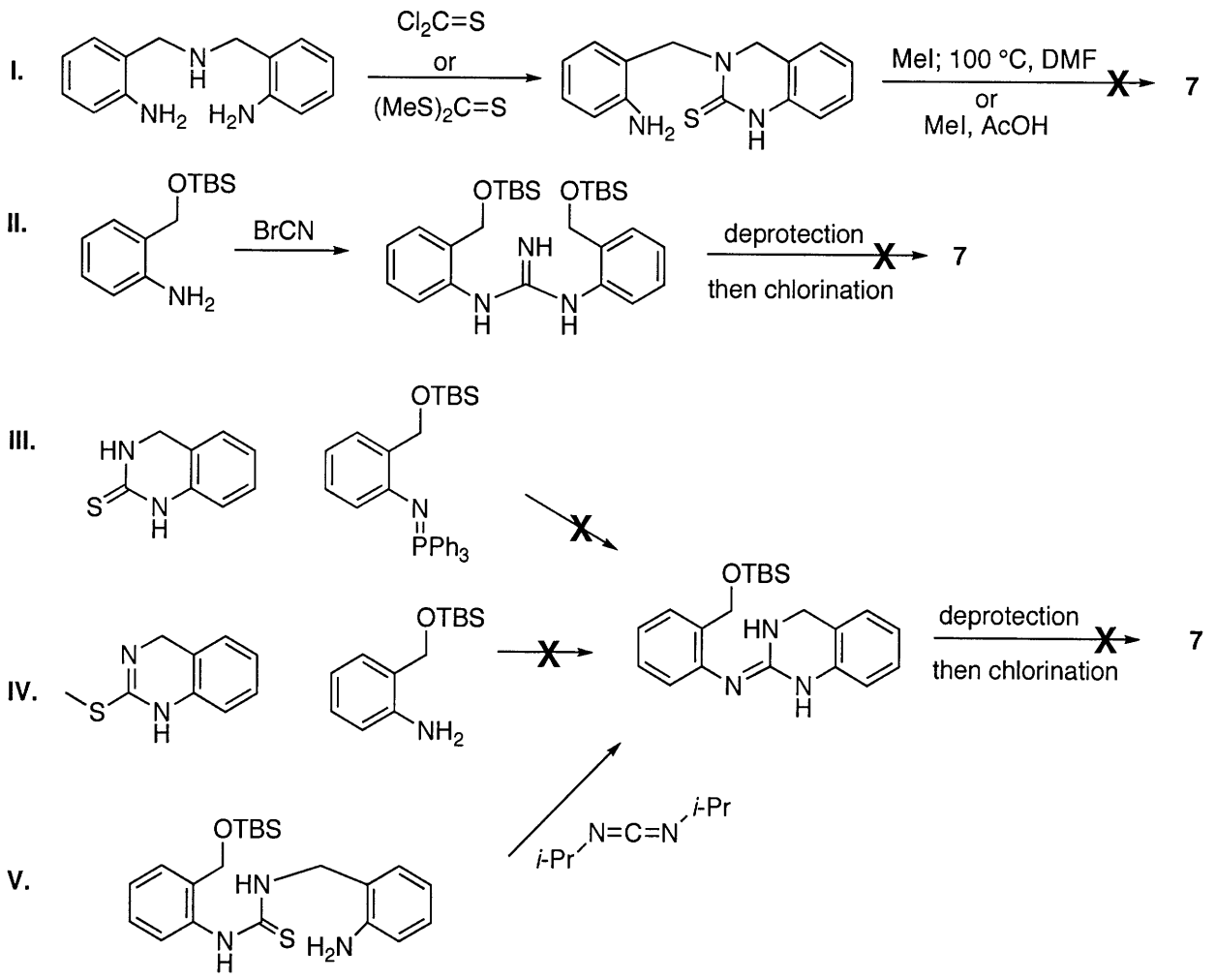
To investigate the cyclization reaction more thoroughly, we decided to prepare benzene-fused guanidine **7** as a model system. A synthesis of **7** has been reported in the literature following the procedure shown in Scheme 2.[13] However, due to the lability of the azide-substituted ferrocene, this route was not applicable to our original target.



Scheme 2. Reported Synthesis of Guanidine **7**.

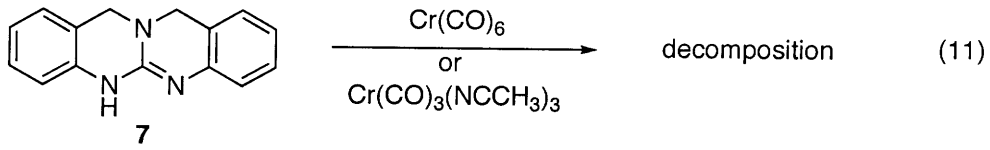
We have tested several different strategies that had been used for the synthesis of guanidines with different structures (Scheme 3). Unfortunately, all of these methods failed to produce the desired product.

[13] (a) Molina, P.; Alajarin, M.; Vidal, A. *J. Org. Chem.* **1993**, *58*, 1687–1695. (b) Molina, P.; Alajarin, M.; Vidal. A. *Tetrahedron* **1995**, *51*, 5351–5360.



Scheme 3. Alternative Synthetic Strategies for Guanidine **7**.

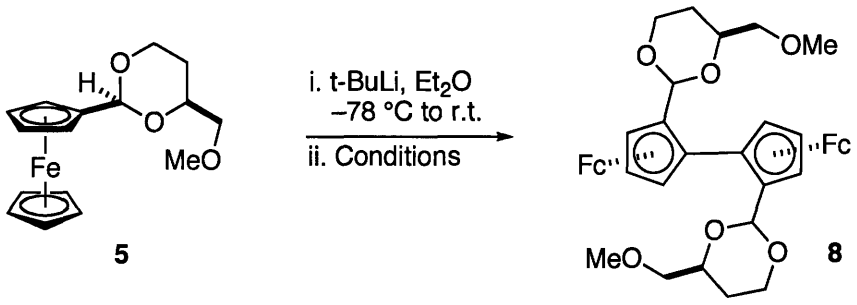
Although we could not find a method applicable to the synthesis of a ferrocene-based guanidine, we could prepare benzene-fused guanidine **7** via the literature procedure with the same efficiency (Scheme 2) and decided to prepare a chromium-complexed planar-chiral guanidine (eq 11). To our disappointment, direct complexation of guanidine **7** with chromium compounds only produced very unstable complexes, and the complexation of chromium to intermediates in Scheme 3 was not beneficial either.



2. Synthesis of Planar-Chiral Phosphines and Amines

The synthesis of C_2-symmetric phosphines and amines can be achieved by manipulation on the ferrocenyl dimer **8**. Gagne has reported a dimerization of acetal **4** by diastereoselective lithiation followed by oxidative coupling mediated by $Cu(OPiv)_2$.[14,15] When we tried this reaction, the yield ranged from 30 to 65%, and the conversion was often incomplete even after optimization of the reaction conditions. To address this irreproducibility, we tested several other dimerization conditions (Table 1). Other oxidative coupling methods furnished unsatisfactory results, however, a two-step reductive coupling of ferrocenyliodide with Cu powder provided the desired dimer in consistently good yield.

Table 1. Reaction Optimization for the Dimerization Reaction of **5**.

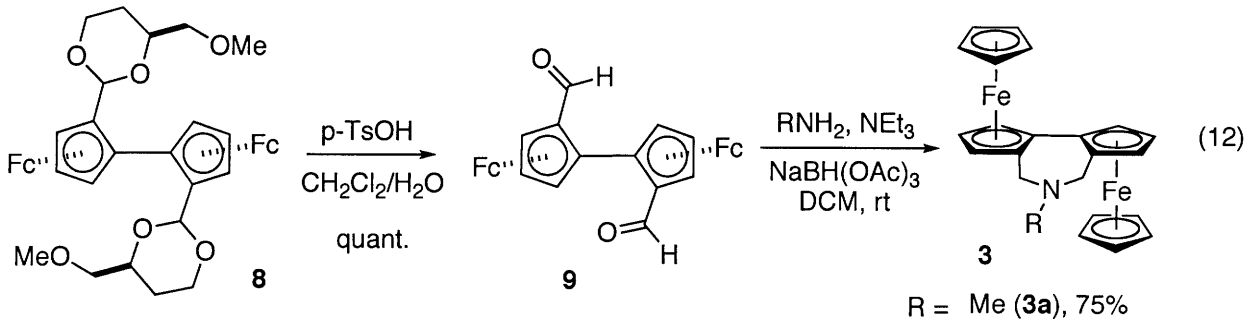


5 **8**

entry	Conditions	Results
1	$Cu(OPiv)_2$, –20 °C	30–65% yield, >20:1 dr
2	$Fe(OAc)_2$, 0 °C	<10%
3	a) 1,2-diiodoethane, THF, –78 °C b) $NiBr_2(PPh_3)_2$, Zn, Et_4NI, THF	Reduction to **5**
4	a) 1,2-diiodoethane, THF, –78 °C b) Cu(0) powder, neat, 60 °C	82%, >20:1 dr

[14] Larsen, A. O.; Taylor, R. A.; White, P. S.; Gagne, M. S. *Organometallics* **1999**, *18*, 5157–5162.
[15] $Cu(OPiv)_2$ is not commercially available.

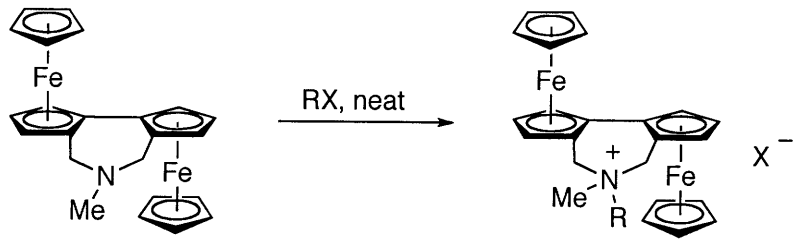
Deprotection of the acetal group produced dialdehyde **9** in excellent yield with high purity (eq 12). Simple reductive amination of **9** with a variety of primary amines furnished the desired planar-chiral tertiary amines. In the case of secondary amine **3i**, the direct reductive amination using ammonium acetate proceeded in low yield. Alternatively, Pd-catalyzed removal of the allyl group from **3d** produced the desired product in good yield.



(12)

R = Me (**3a**), 75%
Bn (**3b**), 65%
i-Pr (**3c**), 50%
allyl (**3d**), 82%
CH_2CH_2OH (**3e**), 64%
OMe (**3f**), 35%
OBn (**3g**), 30%
OH (**3h**), 60%
H (**3i**), 10%

Treatment of tertiary amine **3a** with alkylating reagents provided quaternary ammonium salts **4a** and **4b** (eq 13).

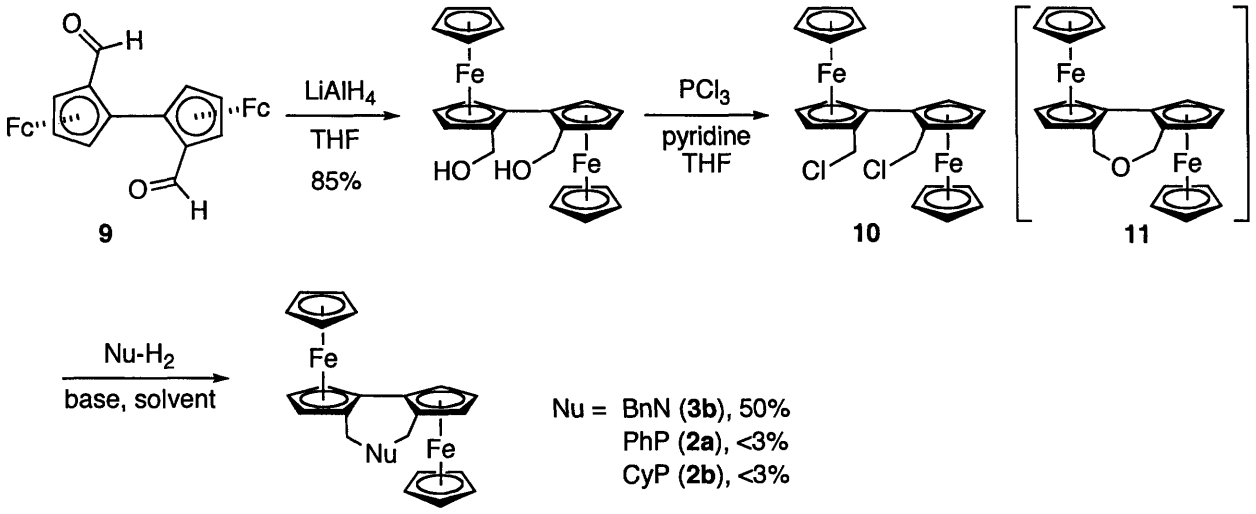


(13)

RX = MeI (**4a**), 50%
BnBr (**4b**), 55%

Some of the planar-chiral amines are unstable under air; however, they can be stored as tetrafluoroborate ammonium salts under air for months without decomposition and then converted back to the free amines after treatment with base.

Although tertiary amines are easily accessible through reductive amination reactions, planar-chiral phosphines require different synthetic strategies. We anticipated that the substitution of bisbenzylic chloride **10** with a phosphine would generate target molecule **2** (Scheme 4). Reduction of dialdehyde **9** provided the corresponding diol in good yield, but halogenation of the diol proved to be challenging. Under various reaction and isolation conditions, we could only isolate cyclic ether **11**. Therefore, we decided to use the unpurified dichloride without isolation. After chlorination, the reaction mixture was diluted with Et_2O and then filtered to remove precipitates. The filtrate was concentrated, and the residue was used for the next substitution reaction without further purification. The test reaction with benzylamine provided **3b** and demonstrated that the formation of dichloride **10** was successful. However, reactions with phenyl or cyclohexyl phosphine in the presence of a range of bases and solvents produced no desired product.



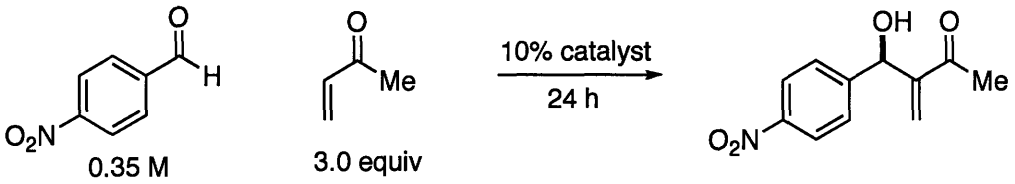
Scheme 4. Synthetic Route via Substitution of Bisbenzylic Chloride.

3. Applications of Planar-Chiral Amine Catalysts in Asymmetric Organic Synthesis

We have tested the newly prepared planar-chiral amines in various asymmetric organic reactions. The first reaction chosen for tertiary amine catalysis was the Morita-Baylis-Hillman (MBH) reaction. With 4-nitrobenzaldehyde and methylvinylketone as

model substrates, we screened several reaction parameters (Table 2). As observed in other studies,[16] addition of water was beneficial to both reactivity and selectivity (entry 1 versus entry 2). Unfortunately, most of the amines were unreactive under these conditions (entries 3–7), except for catalysts containing a hydroxy group, **3e** and **3h**. Lower temperature was beneficial for both yield and ee with a CH_3CN/H_2O solvent system (entry 8 versus entry 2).[17] However, decreasing the reaction temperature did not increase the yield when the solvent system was a mixture of a bulky alcohol and water (entries 9 and 10). In the presence of phenolic additives, the reactivity increased dramatically, albeit at the cost of enantioselectivity (entries 11 and 12).

Table 2. Morita-Baylis-Hillman Reaction Catalyzed by C_2-Symmetric Planar-Chiral Tertiary Amines.



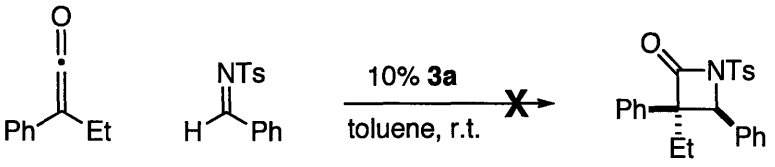
entry	catalyst	solvent	temp.	additive	conv. (%)[a]	y (%)[b]	ee (%)[c]
1	**3a**	CH_3CN	r.t.	none	4	3	6
2	**3a**	CH_3CN/H_2O (9:1)	r.t	none	50	12	45
3	**3b**	CH_3CN/H_2O (9:1)	r.t.	none	–	–	–
4	**3e**	CH_3CN/H_2O (9:1)	r.t.	none	49	43	8
5	**3f**	CH_3CN/H_2O (9:1)	r.t.	none	–	–	–
6	**3g**	CH_3CN/H_2O (9:1)	r.t.	none	–	–	–
7	**3h**	CH_3CN/H_2O (9:1)	r.t.	none	26	19	14
8	**3a**	CH_3CN/H_2O (9:1)	0 °C	none	79	33	50
9	**3a**	*i*-PrOH/H_2O (9:1)	r.t.	none	80	38	47
10	**3a**	*i*-PrOH/H_2O (9:1)	0 °C	none	27	11	55
11	**3a**	*t*-AmylOH/H_2O (9:1)	r.t.	(*R*)-2,2'-binaphthol	98	90	13
12	**3a**	*t*-AmylOH/H_2O (9:1)	r.t.	(*S*)-2,2'-binaphthol	98	90	14

[a] Conversion determined by ^1H NMR versus an internal standard. [b] Yield determined by ^1H NMR versus an internal standard. [c] ee determined by chiral HPLC.

[16] (a) Yu, C.; Liu, B.; Hu, L. *J. Org. Chem.* **2001**, *66*, 5413–5418. (b) Cai, J.; Zhou, Z.; Zhao, G.; Tang, C. *Org. Lett.* **2002**, *4*, 4723–4725.

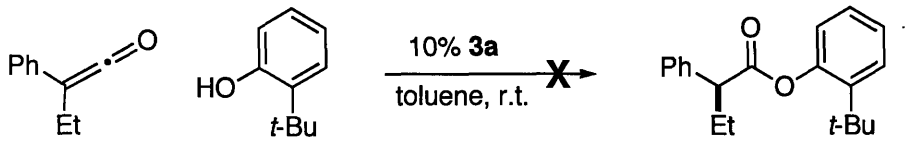
[17] This effect has been observed before. Krishna, P. R.; Kannan, V.; Reddy, P. V. N. *Adv. Synth. Catal.* **2004**, *346*, 603–606.

We also examined the use of these planar-chiral tertiary amines to the formation of β-lactams from ketenes (eq 14), which we have previously reported using **PPY*** as a nucleophilic catalyst.[18] Unfortunately, ferrocene-based tertiary amines were unreactive for these reactions. This result suggested that these azepines are weak nucleophiles.

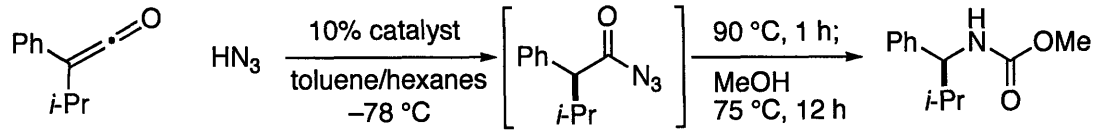


(14)

We have reported enantioselective additions of 2-*t*-butylphenol[19] and hydrazoic acid[20] to ketenes, and these reactions are believed to occur through enantioselective protonation of enolate intermediates by the conjugate acid of **PPY***. In case of addition of 2-*t*-butylphenol, catalyst **3a** did not produce the desired product (eq 15). However, the addition of hydrazoic acid to a ketene catalyzed by **3a** proceeded in excellent yield with modest enantioselectivity (eq 16). The stereoselectivity slightly improved with a more sterically demanding catalyst (**3c**).



(15)



(16)

catalyst = **3a** 90% yield, 25% ee
3c 85% yield, 33% ee

Secondary amine catalyst **3i** was also applied to a few reactions that have been successfully catalyzed by proline derivatives, but it showed no reactivity for these reactions under the reported conditions.

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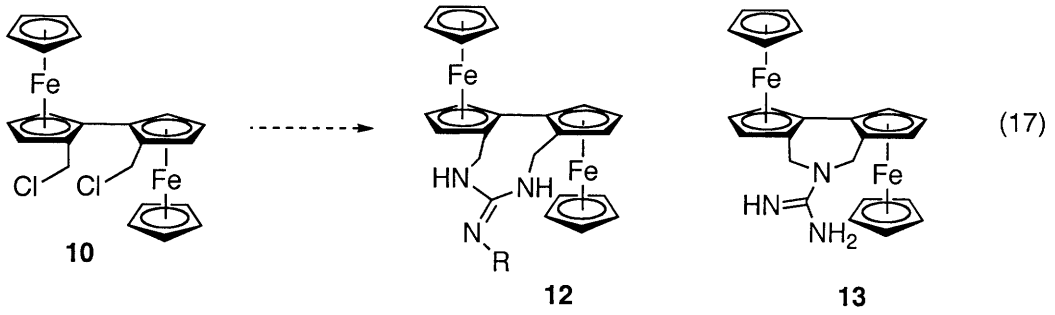
[18] Hodous, B. L.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 1578–1579.
[19] Wiskur, S. L.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 6176–6177.
[20] Dai, X.; Nakai, T.; Romero, J. A. C.; Fu, G. C. *Angew. Chem., Int. Ed.* **2007**, *46*, 4367–4369.

C. Conclusions and Outlook

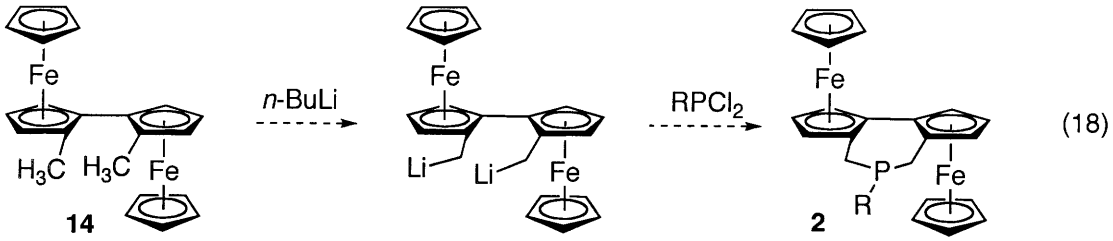
In conclusion, we have studied the synthesis of new ferrocene-based C_2-symmetric planar-chiral catalysts, such as guanidines, phosphines, and amines. Although the synthesis of planar-chiral guanidines and phosphines has been unsuccessful to date, we have prepared several planar-chiral azepines along with their quaternary ammonium salts. These planar-chiral amine catalysts were tested for a few asymmetric reactions and showed promising preliminary results. Due to their highly modular structure, we expect to be able to develop more effective planar-chiral amine catalysts.

In the future, we plan to devise other synthetic strategies for previously unsuccessful targets and to prepare new catalysts with different structures. For example, we expect to access guanidine **12** and **13** through modification of the procedures reported by Terada (eq 17).[5h,5i]



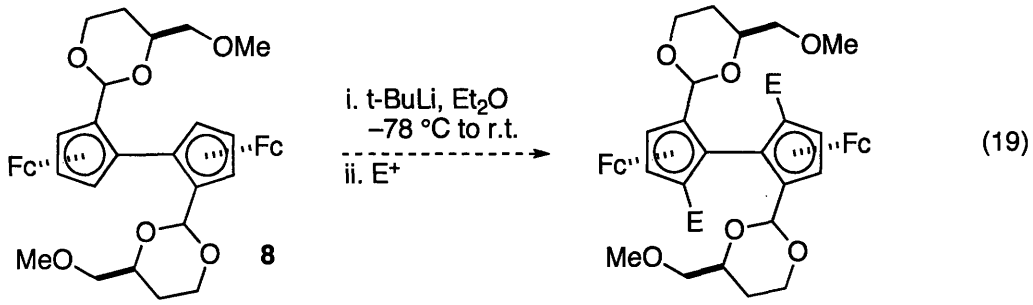
(17)

Another route to phosphine **2** will be explored using dimethyl-substituted ferrocene dimer **14**, similarly to the synthesis of axially chiral phosphines (eq 18).



(18)

We also hope to introduce additional substituents on the ferrocene rings to modify the chiral environment (eq 19).



(19)

In addition, the effect of an additional chiral center near the active catalytic sites will be studied (Figure 3).

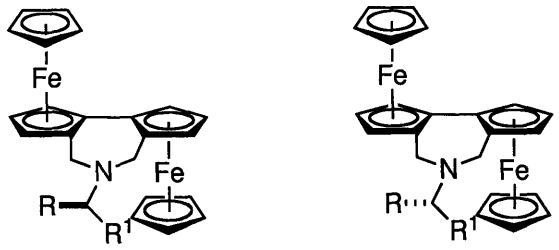


Figure 3. Planar-Chiral Amines with an Additional Chiral Center.

D. Experimental

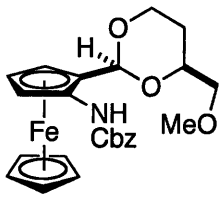
1. General

THF, CH_2Cl_2, and Et_2O were purified by passage through a neutral alumina column. Unless otherwise noted, all chemicals were used as received.

Melting points were measured on a Hoover melting point apparatus and are uncorrected.

Intermediate **5** was prepared by literature methods.[1]

2. Synthesis of Planar-Chiral Catalysts



(*S*)-1-[(2*S*,4*S*)-4-(Methoxymethyl)-1,3-dioxan-2-yl]-2-{[(Phenylmethoxy)carbonyl]amino}-ferrocene (eq 10).

An oven-dried flask was charged with the acetal **5** (200 mg, 0.63 mmol) under Ar and dissolved in dry ether (2.0 mL). The solution was cooled to –78 °C, and *t*-BuLi (1.7 M in pentane; 0.41 mL, 0.69 mmol) was added dropwise, yielding after a few min a bright yellow precipitate. After 10 min stirring, the cooling bath was removed and the mixture was allowed to stir at r.t. for 1h. The mixture was cooled to 0 °C, and a solution of TsN_3 (136 mg, 0.69 mmol) in dry ether (1.0 mL) was added dropwise. Once the addition was complete, the solution was warmed to r.t. and stirred overnight. The reaction mixture was quenched with water (3.0 mL) and extracted with ether (3 mL x 3). The combined organic layers were dried over $MgSO_4$ and concentrated. The product was purified by column chromatography (hexanes/ether 2:1) to give 187 mg (*S*)-1-Azido-2-[(2*S*,4*S*)-4-(methoxymethyl)-1,3-dioxan-2-yl]-ferrocene (83%).

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[1] Riant, O; Samuel, O.; Flessner, T.; Taudien, S.; Kagan, H. B. *J. Org. Chem.* **1997**, *62*, 6733–6745.

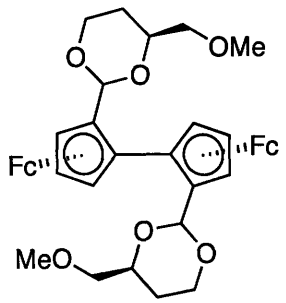
This azido ferrocene was dissolved in THF (5.0 mL), and the solution was cooled to 0 °C. A $LiAlH_4$ solution (1.0 M in ether; 0.5 mL, 0.5 mmol) was added to this solution dropwise, and the reaction mixture was stirred for 10 min. The reaction was quenched with a saturated Na_2SO_4 solution (0.2 mL), and precipitates were filtered. The filtrate was concentrated and dissolved in THF (5.0 mL). CbzCl (0.11 mL, 0.75 mmol) and Et_3N (0.21 mL, 1.5 mmol) were added to the solution, and the resulting mixture was stirred for 2 h. Volatiles were evaporated, and the residue was purified by column chromatography (hexanes/ether 2:1) to give the title compound (152 mg, 63%).

$[\alpha]^{22}_D = -449$ (c = 0.24, $CHCl_3$);

^1H NMR ($CDCl_3$, 400 MHz) δ 7.43-7.29 (m, 6H), 5.56 (s, 1H), 5.18 (s, 2H), 5.08 (s, 1H), 4.23 (dd, J = 11.4, 4.2 Hz, 1H), 4.16 (s, 5H), 4.09-4.01 (m, 2H), 3.96 (s, br, 1H), 3.91 (dt, J = 12.1, 2.5 Hz, 1H), 3.52 (d, J = 4.7 Hz, 2H), 3.37 (s, 3H), 1.81 (dq, J = 12.5, 5.1 Hz, 1H), 1.54 (d, J = 12.9 Hz, 1H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.6, 136.6, 128.5, 128.4, 128.1, 100.7, 94.9, 76.0, 75.4, 73.9, 70.0, 66.6, 63.7, 63.1, 61.1, 59.5, 27.6;

IR (film) 3384, 3092, 3033, 2926, 2875, 1731, 1547, 1485, 1455, 1384, 1360, 1275, 1218, 1147, 1100, 1057, 990, 951, 912, 819, 738, 698, 495 cm^{-1};



(*R*,*R*)-2,2″-Bis[(2S,4S)-4-(methoxymethyl)-1,3-dioxan-2-yl]-1,1″-biferrocene (8).

An oven-dried flask was charged with the acetal **5** (3.16 g, 10.0 mmol) under Ar and dissolved in dry ether (30 mL). The solution was cooled to –78 °C, and *t*-BuLi (1.7 M in pentane; 6.50 mL, 11.0 mmol) was added dropwise, yielding after a few min a bright yellow precipitate. After 10 min stirring, the cooling bath was removed and the mixture was allowed to stir at r.t. for 1h. The mixture was cooled to –78 °C, and a solution of 1,2-diiodoethane in dry THF (15 mL) was added dropwise. Once the addition was complete, the solution was warmed to r.t. in 30 min and quenched with water (5 mL). After

dilution with ether, the organic phase was washed with a solution of sodium thiosulfate (10% w/w; 30 mL), dried over $MgSO_4$, and concentrated. The unpurified product was purified by column chromatography (hexanes/EtOAc 5:1) to give 4.06 g (2*S*,4*S*,S_{FC})-4-(methoxymethyl)-2-(α-iodoferrocenyl)-1,3-dioxane (92%).

The ferrocenyl iodide was dissolved in CH_2Cl_2 (20 mL) and freshly activated Cu powder (31.8g, 500 mmol) was added. Immediately, the mixture was evaporated in vacuo and refilled with Ar. The resulting mixture was heated at 60 °C for 24 h and cooled to r.t. The mixture was diluted with CH_2Cl_2, filtered through celite, and concentrated. The residue was purified by column chromatography (hexanes/EtOAc 3:1) to give 2.50 g of the title compound (86%).

The spectral data matched with the values reported previously.[14]

$[\alpha]^{22}_D = 265$ (c = 0.18, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.77 (s, 2H), 4.54 (dd, *J* = 2.4, 1.5 Hz, 2H), 4.41 (dd, *J* = 2.4, 1.6 Hz, 2H), 4.37-4.29 (m, 2H), 4.31 (s, 10H), 4.17 (d, *J* = 2.5 Hz, 2H), 4.03-3.94 (m, 4H), 3.47 (dd, *J* = 10.2, 5.8 Hz, 2H), 3.36 (dd, *J* = 10.2, 5.1 Hz, 2H), 3.33 (s, 6H), 1.81 (dq, *J* = 12.7, 5.7 Hz, 2H), 1.54 (dq, *J* = 13.2, 1.1 Hz, 2H);

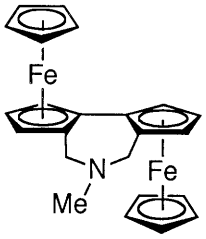
^{13}C NMR ($CDCl_3$, 100 MHz) δ 99.3, 84.9, 83.7, 76.1, 75.5, 71.4, 69.9, 67.1, 66.6, 59.4;

IR (film) 3099, 2923, 2848, 1474, 1372, 1290, 1241, 1147, 1106, 1003, 913, 819, 732, 495 cm^{-1};

Representative Procedure for the Synthesis of planar-chiral amine catalysts: p-TsOH·H_2O (0.050 equiv) was added to a solution of bis(acetal) **8** (1.0 equiv) in CH_2Cl_2/water (2:1, 0.50 M) at r.t., and the resulting mixture was vigorously stirred overnight. The reaction mixture was extracted with CH_2Cl_2 (10 mL x 3), and the combined organic layers were washed with a saturated solution of $NaHCO_3$ (10 mL) and dried over K_2CO_3. After filtration and concentration, the (*R*,*R*)-2,2″-diformyl-1,1″-biferrocene (**9**) was obtained with high purity and used without further purification.

RNH_2·HCl (1.1 equiv) and Et_3N (1.1 equiv) were added to a stirred solution of dialdehyde **9** (1.0 equiv) in CH_2Cl_2 (0.15 M), and then $NaBH(OAc)_3$ (5.0 equiv) was added in small portions. The reaction mixture was stirred overnight at r.t., poured onto ice, and basified with 1.0 N NaOH to pH 12. The mixture was extracted with Et_2O (20

mL x 3), and the combined extracts were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography.



(*R,R*)-2,2″-[(*N*-Methylamino)bis(methylene)]-1,1″-biferrocene (3a).

Representative Procedure was followed, with **9** (500 mg, 1.2 mmol), $MeNH_2$·HCl (87 mg, 1.3 mmol), Et_3N (180 μL, 1.3 mmol), and $NaBH(OAc)_3$ (1.20 g, 5.9 mmol). After purification by flash chromatography (hexanes/EtOAc 2:1), the title compound was isolated as an orange solid (373 mg, 75%). The reaction was not optimized.

m.p. 166–169 °C;

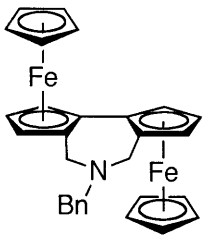
$[\alpha]^{22}_D$ = –877 (c = 0.12, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.36-4.35 (m, 2H), 4.10 (t, J = 2.4 Hz, 2H), 4.07-4.05 (m, 2H), 3.96 (s, 10H), 3.84 (d, J_{AB} = 15.0 Hz, 2H), 3.66 (d, J_{AB} = 15.0 Hz, 2H), 2.55 (s, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 85.6, 82.5, 69.9, 67.5, 66.3, 65.8, 58.7, 44.7;

IR (film) 3085, 2961, 2931, 2786, 2761, 1714, 1441, 1363, 1223, 1104, 813, 736 cm^{-1};

GCMS calcd for $C_{23}H_{23}Fe_2N$ (M^+) 425, found 425.



(*R,R*)-2,2″-[(*N*-Benzylamino)bis(methylene)]-1,1″-biferrocene (3b).

Representative Procedure was followed, with **9** (140 mg, 0.33 mmol), $BnNH_2$·HCl (52 mg, 0.36 mmol), Et_3N (50 μL, 0.36 mmol), and $NaBH(OAc)_3$ (347 mg, 1.7 mmol). After purification by flash chromatography (hexanes/EtOAc 3:1), the title compound was isolated as an orange solid (107 mg, 65%). The reaction was not optimized.

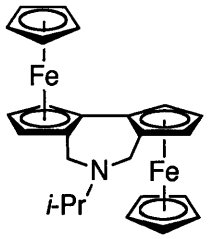
$[\alpha]^{22}_D$ = –675 (c = 0.23, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41-7.26 (m, 5H), 4.38 (dd, J = 2.2, 1.5 Hz, 2H), 4.11 (t, J = 2.4 Hz, 2H), 4.00-3.96 (m, 2H), 3.95 (s, 10H), 3.88 (d, J_{AB} = 14.9 Hz, 2H), 3.87 (s, 2H), 3.71 (d, J_{AB} = 15.0 Hz, 2H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.6, 129.0, 128.3, 127.0, 84.5, 82.5, 69.9, 67.7, 66.3, 65.8, 60.5, 56.6;

IR (film) 3090, 3027, 2917, 2800, 1494, 1454, 1410, 1358, 1133, 1105, 1029, 1000, 911, 818, 733 cm^{-1};

GCMS calcd for $C_{29}H_{27}Fe_2N$ (M^+) 501, found 501.



(*R,R*)-2,2″-[(*N*-Isopropylamino)bis(methylene)]-1,1″-biferrocene (3c).

Representative Procedure was followed, with **9** (219 mg, 0.51 mmol), *i*-PrNH$_2$ (48 μL, 0.56 mmol), and NaBH(OAc)$_3$ (540 mg, 2.6 mmol). After purification by flash chromatography (hexanes/EtOAc 2:1), the title compound was isolated as an orange solid (116 mg, 50%). The reaction was not optimized.

m.p. 169–171 °C;

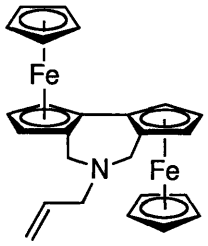
$[\alpha]^{22}_D$ = –631 (c = 0.12, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.33-4.31 (m, 2H), 4.09-4.05 (m, 4H), 3.96 (s, 10H), 3.80 (d, J_{AB} = 14.7 Hz, 2H), 3.66 (d, J_{AB} = 14.7 Hz, 2H), 3.15 (septet, J = 6.5 Hz, 1H), 1.18 (d, J = 6.5 Hz, 3H), 1.11 (d, J = 6.5 Hz, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 86.4, 82.5, 70.1, 67.8, 66.2, 65.6, 54.9, 54.0, 19.6, 19.3;

IR (film) 3092, 2962, 1461, 1409, 1383, 1361, 1169, 1105, 1001, 911, 815, 732 cm^{-1};

GCMS calcd for $C_{25}H_{27}Fe_2N$ (M^+) 453, found 453.



(*R,R*)-2,2″-[(*N*-Allylamino)bis(methylene)]-1,1″-biferrocene (3d).

Representative Procedure was followed, with **9** (450 mg, 1.1 mmol), allylamine (87 μL, 1.2 mmol), and $NaBH(OAc)_3$ (1.11 g, 5.3 mmol). After purification by flash chromatography (hexanes/EtOAc 2:1), the title compound was isolated as an orange solid (370 mg, 82%). The reaction was not optimized.

m.p. 112–114 °C;

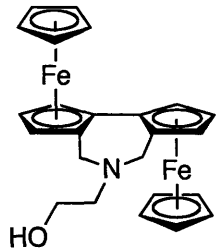
$[\alpha]^{22}_D = -764$ (c = 0.12, $CHCl_3$);

^1H NMR ($CDCl_3$, 400 MHz) δ 6.01-5.89 (m, 1H), 5.24-5.19 (m, 1H), 5.19-5.16 (m, 1H), 4.35 (dd, J = 2.3, 1.4 Hz, 2H), 4.10 (t, J = 2.4 Hz, 2H), 4.04 (dd, J = 2.3, 1.4 Hz, 2H), 3.96 (s, 10H), 3.84 (d, J_{AB} = 14.9 Hz, 2H), 3.71 (d, J_{AB} = 14.9 Hz, 2H), 3.39-3.27 (m, 2H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.4, 117.4, 84.8, 82.5, 69.9, 67.6, 66.2, 65.7, 59.5, 56.5;

IR (film) 3091, 2918, 2796, 1641, 1455, 1410, 1133, 1105, 999, 920, 817 cm^{-1};

GCMS calcd for $C_{25}H_{25}Fe_2N$ (M^+) 451, found 451.



(*R,R*)-2,2″-{[*N*-(2-Hydroxyethyl)amino]bis(methylene)}-1,1″-biferrocene (3e).

Representative Procedure was followed, with **9** (140 mg, 0.33 mmol), 2-hydroxyethylamine (22 μL, 0.36 mmol), and $NaBH(OAc)_3$ (347 mg, 1.7 mmol). After purification by flash chromatography (hexanes/EtOAc 2:1), the title compound was isolated as an orange solid (96 mg, 64%). The reaction was not optimized.

m.p. 197–198 °C;

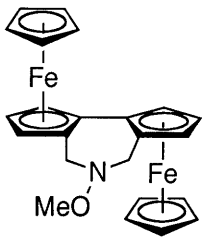
$[\alpha]^{22}_D = -974$ (c = 0.18, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.38 (dd, J = 2.4, 1.4 Hz, 2H), 4.12 (t, J = 2.4 Hz, 2H), 4.04 (dd, J = 2.2, 1.4 Hz, 2H), 3.95 (s, 10H), 3.92 (d, J_{AB} = 15.2 Hz, 2H), 3.83 (d, J_{AB} = 15.2 Hz, 2H), 3.64 (t, J = 5.2 Hz, 2H), 3.03 (s, 1H), 2.96-2.86 (m, 2H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 84.7, 82.5, 70.1, 67.5, 66.7, 66.3, 58.4, 56.1, 55.8;

IR (film) 3406, 3092, 2933, 1442, 1410, 1350, 1132, 1105, 1056, 1000, 911, 818, 730 cm^{-1};

GCMS calcd for $C_{24}H_{25}Fe_2NO$ (M^+) 455, found 409 [(M–EtOH)$^+$].



(*R,R*)-2,2″-[(*N*-Methoxyamino)bis(methylene)]-1,1″-biferrocene (3f).

Representative Procedure was followed, with **9** (140 mg, 0.33 mmol), $MeONH_2$·HCl (30 mg, 0.36 mmol), Et_3N (50 μL, 0.36 mmol), and $NaBH(OAc)_3$ (347 mg, 1.7 mmol). After purification by flash chromatography (hexanes/EtOAc 3:1), the title compound was isolated as an orange solid (51 mg, 35%). The reaction was not optimized.

m.p. 214–215 °C;

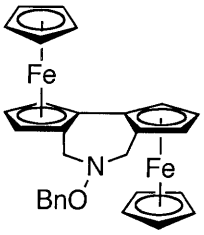
$[\alpha]^{22}_D$ = –389 (c = 0.13, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.34-4.30 (m, 2H), 4.18-4.10 (m, 6H), 3.98 (bs, 12H), 3.66 (s, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 81.0, 70.3, 68.4, 66.8, 65.6, 60.9, 59.9;

IR (film) 3090, 3079, 2975, 2937, 2805, 1454, 1410, 1356, 1218, 1103, 1052, 1030, 1000, 912, 820, 811, 733 cm^{-1};

GCMS calcd for $C_{23}H_{23}Fe_2NO$ (M^+) 441, found 441.



(*R,R*)-2,2″-[(*N*-Benzyloxyamino)bis(methylene)]-1,1″-biferrocene (3g).

Representative Procedure was followed, with **9** (140 mg, 0.33 mmol), $BnONH_2 \cdot HCl$ (58 mg, 0.36 mmol), Et_3N (50 μL, 0.36 mmol), and $NaBH(OAc)_3$ (347 mg, 1.7 mmol). After purification by flash chromatography (hexanes/EtOAc 5:1), the title compound was isolated as an orange solid (51 mg, 30%). The reaction was not optimized.

m.p. 116–117 °C;

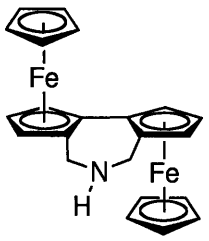
$[\alpha]^{22}_D = -274$ (c = 0.13, $CHCl_3$);

^1H NMR ($CDCl_3$, 400 MHz) δ 7.45-7.32 (m, 5H), 4.87 (d, J_{AB} = 11.4 Hz, 1H), 4.83 (d, J_{AB} = 11.4 Hz, 1H), 4.32-4.31 (m, 2H), 4.20 (d, J = 13.2 Hz, 2H), 4.11-4.09 (m, 4H), 4.08-3.94 (m, 2H), 3.93 (s, 10H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.1, 128.9, 128.6, 128.1, 80.9, 74.7, 70.3, 68.4, 66.8, 65.6, 61.7;

IR (film) 3091, 3030, 2909, 2828, 1455, 1364, 1289, 1220, 1105, 1032, 1000, 910, 818, 733, 697 cm^{-1};

GCMS calcd for $C_{29}H_{27}Fe_2NO$ (M^+) 517, found 409 [$(M–BnOH)^+$].



(*R*,*R*)-2,2″-[Aminobis(methylene)]-1,1″-biferrocene (3i).

To a solution of **3d** (225 mg, 0.5 mmol) in CH_2Cl_2 (2.5 mL) were added $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), PPh_3 (22 mg, 0.09 mmol), and *N*,*N*-dimethylbarbituric acid (234 mg, 1.5 mmol). The reaction mixture was stirred overnight at 35 °C, poured into a saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2 (5 mL x 3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. After purification by column chromatography (hexanes/EtOAc/Et_3N 5:1:0.1), the title compound was isolated as an orange solid (201 mg, 98%).

m.p. 215–216 °C;

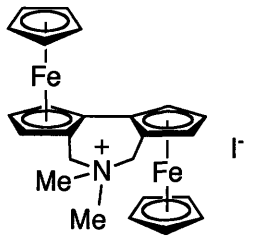
$[\alpha]^{22}_D = -427$ (c = 0.11, $CHCl_3$);

^1H NMR ($CDCl_3$, 400 MHz) δ 4.33 (t, J = 2.0 Hz, 2H), 4.13-4.10 (m, 4H), 4.05 (d, J_{AB} = 16.1 Hz, 2H), 3.96 (s, 10H), 3.91 (d, J_{AB} = 16.1 Hz, 2H), 1.65 (s, 1H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 88.3, 82.2, 69.9, 67.9, 66.6, 65.6, 51.8;

IR (film) 3451, 3091, 2913, 1642, 1444, 1409, 1217, 1104, 999, 819, 808, 780, 734, 673 cm^{-1};

GCMS calcd for $C_{22}H_{21}Fe_2N$ (M^+) 411, found 411.



(*R,R*)-2,2″-[(*N,N*-Dimethylammonium)bis(methylene)]-1,1″-biferrocene iodide (4a).

N-Methyl azepine **3a** (70 mg, 0.16 mmol) was mixed with MeI (0.2 mL), and the resulting mixture was stirred overnight at room temperature. The mixture was purified directly by column chromatography (CH_2Cl_2/EtOAc/MeOH 10:10:1) to give the title compound (47 mg, 50%). The reaction was not optimized.

m.p. 241–243 °C;

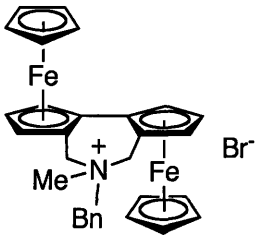
$[\alpha]^{22}_D$ = –695 (c = 0.11, $CHCl_3$);

^1H NMR ($CDCl_3$, 400 MHz) δ 4.66-4.61 (m, 4H), 4.59 (dd, *J* = 2.5, 1.0 Hz, 2H), 4.33 (t, *J* = 2.5 Hz, 2H), 4.14 (s, 10H), 4.05 (d, J_{AB} = 13.7 Hz, 2H), 3.45 (s, 6H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 86.0, 74.2, 70.9, 70.7, 69.2, 68.9, 64.5, 51.7;

IR (film) 3091, 3004, 2947, 1714, 1462, 1412, 1361, 1223, 1105, 1001, 911, 930, 733 cm^{-1};

GCMS calcd for $C_{24}H_{26}Fe_2IN$ (M^+) 566, found 425 [$(M–MeI)^+$].



(*R,R*)-2,2″-[(*N*-Benzyl-*N*-methylammonium)bis(methylene)]-1,1″-biferrocene bromide (4b).

N-Methyl azepine **3a** (70 mg, 0.16 mmol) was mixed with BnBr (0.4 mL), and the resulting mixture was stirred overnight at room temperature. The mixture was purified

directly by column chromatography (CH_2Cl_2/EtOAc/MeOH 10:10:1) to give the title compound (54 mg, 55%). The reaction was not optimized.

m.p. 195–196 °C;

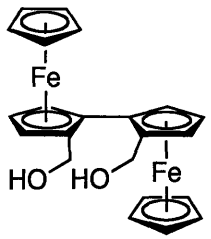
$[\alpha]^{22}_D$ = –517 (c = 0.11, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78-7.76 (m, 2H), 7.53-7.51 (m, 3H), 5.07 (d, *J* = 12.7 Hz, 1H), 4.81 (d, *J* = 12.6 Hz, 1H), 4.67 (d, *J* = 2.2 Hz, 2H), 4.62-4.49 (m, 4H), 4.40 (t, *J* = 2.5 Hz, 1H), 4.33 (t, *J* = 2.5 Hz, 1H), 4.13 (d, *J* = 6.5 Hz, 11H), 3.82 (d, *J* = 13.8 Hz, 1H), 3.26 (s, 3H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 133.6, 130.9, 129.6, 127.8, 86.3, 86.0, 74.5, 74.2, 71.2, 70.8, 70.7, 69.3, 69.2, 69.0, 64.5, 62.7, 60.8, 47.0;

IR (film) 3091, 2954, 1625, 1466, 1348, 1106, 1001, 923, 827, 775, 729 cm^{-1};

GCMS calcd for $C_{30}H_{30}BrFe_2N$ (M^+) 595, found 425 [(M–BnBr)$^+$].



(*R*,*R*)-2,2″-Bis(hydroxymethyl)-1,1″-biferrocene.

To a solution of dialdehyde **9** (224 mg, 0.5 mmol) in THF (5.0 mL) was added a $LiAlH_4$ solution (1.0 M in ether; 0.5 mL, 0.5 mmol) dropwise at 0 8C. The reaction mixture was stirred for 10 min then quenched with a saturated Na_2SO_4 solution (0.2 mL). The precipitates were filtered, and the filtrate was concentrated and purified by column chromatography (hexanes/EtOAc 2:1) to give the title compound (190 mg, 85%). The reaction was not optimized.

m.p. 114–116 °C;

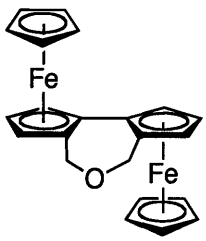
$[\alpha]^{22}_D$ = –814 (c = 0.13, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.48 (dd, *J* = 2.3, 1.5 Hz, 2H), 4.32 (dd, *J* = 2.4, 1.4 Hz, 2H), 4.25-4.19 (m, 16H), 3.98 (s, 2H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 87.7, 84.0, 73.2, 69.5, 69.4, 67.3, 59.4;

IR (film) 3327, 3095, 2935, 2876, 1642, 1454, 1412, 1295, 1198, 1106, 1032, 1000, 911, 817, 731 cm^{-1};

GCMS calcd for $C_{22}H_{22}Fe_2O_2$ (M^+) 430, found 412 [$(M-H_2O)^+$].



2,2′-[Oxybis(methylene)]-1,1′-biferrocene (11).

To a solution of (*R,R*)-2,2″-bis(hydroxymethyl)-1,1″-biferrocene (410 mg, 0.95 mmol) and imidazole (340 mg, 5.0 mmol) in CH_2Cl_2 (10 mL) was added dichlorotriphenylphosphorane (1.33 g, 4.0 mmol). The reaction mixture was stirred overnight at room temperature and concentrated. After purification by column chromatography (hexane/Et_2O 5:1), the title compound was isolated as an orange solid (163 mg, 42%). The reaction was not optimized.

m.p. 191–192 °C;

$[\alpha]^{22}_D$ = –443 (c = 0.11, $CHCl_3$);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.83 (d, J_{AB} = 14.2 Hz, 2H), 4.71 (d, J_{AB} = 14.2 Hz, 2H), 4.35 (dd, J = 2.3, 1.5 Hz, 2H), 4.14-4.12 (m, 4H), 3.98 (s, 10H);

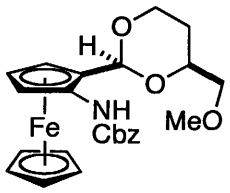
^{13}C NMR ($CDCl_3$, 100 MHz) δ 86.3, 82.3, 73.3, 70.2, 66.9, 66.8, 65.5;

IR (film) 3091, 2941, 2848, 1642, 1452, 1369, 1303, 1241, 1226, 1103, 1003, 918, 826, 809, 734 cm^{-1};

GCMS calcd for $C_{22}H_{20}Fe_2O$ (M^+) 412, found 412.

3. ^{1}H NMR for Selected Compounds

NHCbz acetal



eq 10

BRUKER

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D1                    1.00000000 sec
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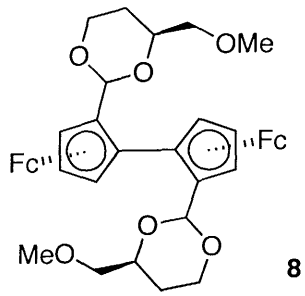
dimer



8

BRUKER

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PROCNO 1

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FIDRES 0.126314 Hz
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TE 292.2 K
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TD0 1

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PL1 0.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
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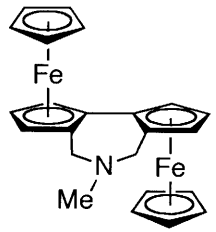
3a Me



3a

BRUKER

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Current Data Parameters
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PROCNO                       1

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TD                      65536
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NS                         16
DS                          2
SWH                  8278.146 Hz
FIDRES               0.126314 Hz
AQ                   3.9584243 sec
RG                        362
DW                     60.400 usec
DE                      6.00 usec
TE                     291.2 K
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TD0                         1

======== CHANNEL f1 ========
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PL1                      0.00 dB
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F2 - Processing parameters
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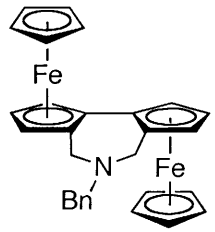
3b Bn



3b

BRUKER

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PROCNO 1

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RG 362
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DE 6.00 usec
TE 292.2 K
D1 1.00000000 sec
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PL1 0.00 dB
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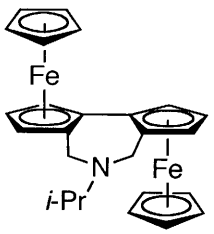
3c iPr



3c

BRUKER

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Current Data Parameters
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PROCNO                       1

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TD                      65536
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SWH                  8278.146 Hz
FIDRES               0.126314 Hz
AQ                   3.9584243 sec
RG                        362
DW                     60.400 usec
DE                      6.00 usec
TE                     292.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      13.88 usec
PL1                      0.00 dB
SFO1             400.1324710 MHz

F2 - Processing parameters
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SF               400.1300053 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
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PC                       1.00
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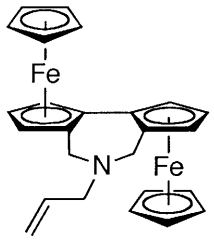
3d allyl



3d

BRUKER

Current Data Parameters
NAME Ch3-cat3
EXPNO 7
PROCNO 1

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Time 18.27
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PULPROG zg30
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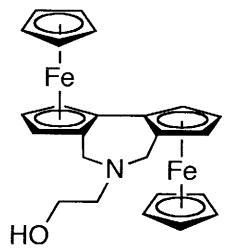
SOLVENT CDC13
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 362
DW 60.400 usec
DE 6.00 usec
TE 292.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 13.88 usec
PL1 0.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 65536
SF 400.1300053 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

3e ethanol



3e

BRUKER

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Current Data Parameters
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PROCNO                       1

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FIDRES               0.126314 Hz
AQ                   3.9584243 sec
RG                        362
DW                     60.400 usec
DE                      6.00 usec
TE                     292.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      13.88 usec
PL1                      0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                      65536
SF             400.1300053 MHz
WDW                        EM
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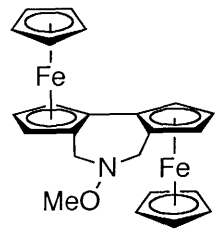
GB                          0
PC                       1.00
```

3f OMe



3f

BRUKER

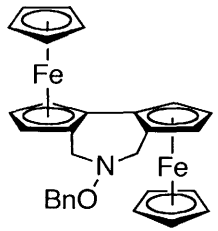
```
Current Data Parameters
NAME                  Ch3-cat3
EXPNO                       11
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20080809
Time                     19.04
INSTRUM                  spect
PROBHD     5 mm QNP 1H/13
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8278.146 Hz
FIDRES               0.126314 Hz
AQ                   3.9584243 sec
RG                        362
DW                     60.400 usec
DE                      6.00 usec
TE                     292.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                     13.88 usec
PL1                     0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                      65536
SF             400.1300053 MHz
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                       1.00
```

3f OBn



3g

BRUKER

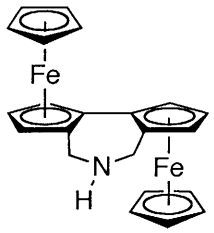
```
Current Data Parameters
NAME                  Ch3-cat3
EXPNO                       13
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20080809
Time                     19.28
INSTRUM                  spect
PROBHD     5 mm QNP 1H/13
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8278.146 Hz
FIDRES               0.126314 Hz
AQ                   3.9584243 sec
RG                        362
DW                     60.400 usec
DE                      6.00 usec
TE                      292.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      13.88 usec
PL1                      0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                      65536
SF             400.1300053 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

3i H



3i

BRUKER

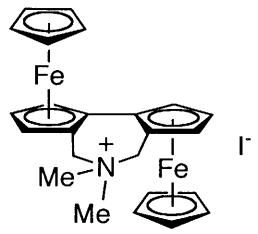
Current Data Parameters
NAME Ch3-cat3
EXPNO 17
PROCNO 1

F2 - Acquisition Parameters
Date_ 20080809
Time 19.59
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 362
DW 60.400 usec
DE 6.00 usec
TE 292.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 13.88 usec
PL1 0.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 65536
SF 400.1300053 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

4a Me2I



4a

BRUKER

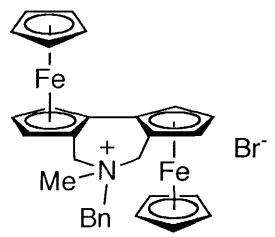
```
Current Data Parameters
NAME                  Ch3-cat3
EXPNO                       19
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20080810
Time                      0.04
INSTRUM                  spect
PROBHD     5 mm QNP 1H/13
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                   8278.146 Hz
FIDRES                0.126314 Hz
AQ                    3.9584243 sec
RG                         362
DW                      60.400 usec
DE                       6.00 usec
TE                      291.2 K
D1                    1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       13.88 usec
PL1                       0.00 dB
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                       65536
SF                400.1300053 MHz
WDW                         EM
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        1.00
```

4b Me Bn Br



4b

BRUKER

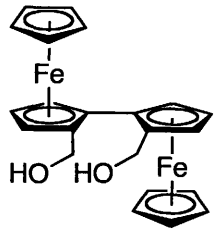
```
Current Data Parameters
NAME                  Ch3-cat3
EXPNO                       21
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20080810
Time                      0.19
INSTRUM                  spect
PROBHD     5 mm QNP 1H/13
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                   8278.146 Hz
FIDRES                0.126314 Hz
AQ                    3.9584243 sec
RG                         362
DW                      60.400 usec
DE                       6.00 usec
TE                      300.0 K
D1                    1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       13.88 usec
PL1                       0.00 dB
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                       65536
SF                400.1300053 MHz
WDW                         EM
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        1.00
```

diol



Scheme 4

BRUKER

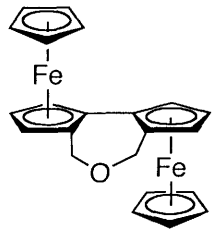
```
Current Data Parameters
NAME                  Ch3-cat3
EXPNO                       23
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20080810
Time                      0.33
INSTRUM                  spect
PROBHD    5 mm QNP 1H/13
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                   8278.146 Hz
FIDRES                0.126314 Hz
AQ                    3.9584243 sec
RG                         362
DW                       60.400 usec
DE                        6.00 usec
TE                       292.2 K
D1                    1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       13.88 usec
PL1                       0.00 dB
SFO1                400.1324710 MHz

F2 - Processing parameters
SI                       65536
SF                  400.1300053 MHz
WDW                         EM
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        1.00
```

11-ether



11

BRUKER

Current Data Parameters
NAME Ch3-cat3
EXPNO 25
PROCNO 1

F2 - Acquisition Parameters
Date_ 20080810
Time 0.48
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 362
DW 60.400 usec
DE 6.00 usec
TE 292.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 13.88 usec
PL1 0.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 65536
SF 400.1300053 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Curriculum Vitae

Education

Ph.D., Organic Chemistry, Massachusetts Institute of Technology, 2008
M.S., Organic Chemistry, Seoul National University, 2002
B.S., Chemistry, Seoul National University, 2000

Research Experience

Massachusetts Institute of Technology 2003–2008
Graduate Research Associate under Professor Gregory C. Fu.
- Currently developing new planar-chiral catalysts
- Developed regio- and enantioselective nickel-catalyzed allylic cross-couplings and applied this method for a formal synthesis of fluvirucinine A_1
- Developed copper-catalyzed stereoselective [4+1] cycloadditions to form dihydrofurans and applied this method for the synthesis of deoxy-C-nucleosides

Seoul National University 1998–2002
Graduate and Undergraduate Research Associate under Professor Eun Lee.
- Synthesized ambruticin using diastereoselective radical cyclizations
- Studied total synthesis of hippodamine
- Assisted in total syntheses of guaianolides.

Publications

(1) Son, S.; Fu, G. C. "Nickel-Catalyzed Asymmetric Cross-Couplings of Secondary Allylic Chlorides and Alkylzinc Reagents" *J. Am. Chem. Soc.* **2008**, *130*, 2756.
(2) Son, S.; Fu, G. C. "Copper-Catalyzed Asymmetric [4+1] Cycloadditions of Enones with Diazo Compounds to Form Dihydrofurans" *J. Am. Chem. Soc.* **2007**, *129*, 1046.
(3) Lee, E.; Choi, S. J.; Kim, H.; Han, H. O.; Kim, Y. K.; Min, S. J.; Son, S. H.; Lim, S. M.; Jang, W. S. "Total Synthesis of Ambruticin" *Angew. Chem. Int. Ed.* **2002**, *41*, 176.

Presentations

(1) Son, S.; Fu, G. C. "Copper-Catalyzed Asymmetric Cycloadditions to Form Dihydrofurans" Poster Presentation at the ACS National Meeting, Boston, August 2007.
(2) Son, S.; Fu, G. C. "Nickel-Catalyzed Asymmetric Cross-Couplings of Secondary Allylic Chlorides and Alkylzinc Reagents" Oral Presentation at the ACS National Meeting, Boston, August 2007.
(3) Son, S.; Fu, G. C. "Nickel-Catalyzed Asymmetric Negishi Cross-Couplings of Secondary Allylic Chlorides" Oral Presentation at the ACS National Meeting, San Francisco, September 2006.

Awards

Morse Travel Grant, 2006
Synlett Star Award, 2003
Seoul National University Fellowship, 1997–2002