METAL-CATALYZED REACTIONS: I. HYDROBORATION
II. NUCLEOPHILIC CATALYSIS WITH PI-BOUND HETEROCYCLES

by

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ABSTRACT

A variety of organotransition metal complexes (M=Rh, Fe, and Ru) were synthesized and their use in catalysis investigated. Our two principal areas of interest were in the directed, catalytic hydroboration of olefins and in nucleophile-catalyzed reactions. Indenylrhodium(olefin)$_2$ (and other Cp-derived rhodium complexes) were utilized in the directed hydroboration reactions. Both iron and ruthenium complexes with π-bound heterocyclic ligands were utilized in the study of nucleophilic catalysis.

The directed hydroborations utilized a variety of $Cp^XRh(olefin)_2$ catalysts. We were interested in exploring ring slippage of the Cp^X ligand to access the coordinative unsaturation necessary to accomplish a directed reaction. Generally, a 12 e$^-$ transition metal fragment is required for a directed process to occur. In the hydroboration reaction, the olefin ligands of $Cp^XRh(olefin)_2$ are rapidly hydroborated, leaving "η^5-Cp^XRh" as the active catalyst (14 e$^-$). For a directed process to occur, the Cp^X ligand must ring slip to η^3, therefore providing access to the necessary 12 e$^-$ metal center.

Tertiary amides were first investigated as directing groups for these reactions. The isomer expected for a directed reaction was formed under the reaction conditions. Upon further investigation, it was discovered that a facile background reaction was occurring in which the amide was reacting with the catecholborane resulting in hydroboration occurring *without* added metal catalysts. Furthermore, catalytic amounts of simple amides, such as dimethylacetamide, could be added to catecholborane to form an active hydroboration reagent. A range of alkyl-substituted olefins could be efficiently hydroborated under these reaction conditions. A study of the hydroboration system indicated that a BH_3-amide complex is formed under the reaction conditions and that this may be the active hydroborating agent.

Further study of a variety of directing groups showed that ethers might be suitable as directing groups, without causing the disproportionation of the catecholborane. Benzyl ether-directable reactions were feasible and occurred without disproportionation of the catecholborane. The reaction occurred via a metal-catalyzed pathway, and ring slippage was an important step in the directed reaction. This is the first example of a directed reaction in which ring slippage of the ligand is allowing for a coordination site to be generated and, therefore, allowing the directed reaction to occur.

Our second area of interest was in investigating the use of π-bound heterocycles as nucleophilic catalysts. Some preliminary results in our group had demonstrated the effectiveness of complexes of this type as nucleophilic catalysts. Some suitably substituted complexes were also shown to be effective asymmetric catalysts, but many other target complexes had yet to be investigated.

A series of complexes utilizing *N*-heterocycles bound to iron fragments were prepared and investigated. The effect of electronic and steric changes on the bottom Cp ring was investigated with respect to the reactivity of the complexes. It was found that tuning the nucleophilicity of the catalyst was possible by modifying the electronics of the bottom cyclopentadienyl ring of the complex.

In an effort to develop more reactive π-bound heterocycles as nucleophilic catalysts, ruthenium-derived systems were prepared and investigated. The preparation of these complexes proved to be challenging, as they were not accessible by the methodology used to prepared the ferrocene-based catalysts. Both pyrindinylruthenium and azaruthenocene complexes were prepared and found to be active nucleophilic catalysts for a variety of reactions. The pyrindinylruthenium complexes were at least as active, and in come cases more reactive, than their iron analogs. The stereoselectivity of processes utilizing these complexes was similar to that seen with the analogous iron complexes, with the exception of the kinetic resolution of secondary alcohols with acetic anhydride, which was less selective. X-ray crystal structure analyses of the (DMAP*)Ru(C_5R_5) complexes provided some insight into why this loss in selectivity was observed.

π-Bound phospholes were also investigated. A phosphaferrocene complex was prepared and utilized as a catalyst in the ring-opening of epoxides in the presence of TMSCl. This reaction was found to be quite facile and appears to occur by a mechanism other than simple Cl^- ion catalysis. Some efforts towards understanding the mechanism for this reaction (i.e., nucleophilic activation of TMSCl), as well as developing chiral versions of these phosphaferrocenes, were also investigated.

Thesis Supervisor: Gregory C. Fu

Title: Assistant Professor of Chemistry

Portions of this thesis have been published in the following papers:

Garrett, C. E. ; Fu, G. C. "Hydroboration of Olefins with Catecholborane at Room Temperature in the Presence of *N,N* - Dimethylacetamide", *J. Org. Chem.* **1996**, *61*, 3224-3225.

Garrett, C. E.; Fu, G. C. "π-Bound Phosphorus Heterocycles as Catalysts: Ring-Opening of Epoxides with TMSCl in the Presence of a Phosphaferrocene", *J. Org. Chem.* **1997**, *62*, 4534-4535.

Garrett, C. E.; Fu, G. C. "Exploiting η^5- to η^3-Indenyl Ring Slippage to Access a Directed Reaction: Ether-Directed, Rhodium-Catalyzed Olefin Hydroboration", *J. Org. Chem.* **1998**, *63*, 1370-1371.

Garrett, C. E.; Fu, G. C. "Nucleophilic Catalysis with π-Bound Nitrogen Heterocycles: Comparison of the Reactivity and Enantioselectivity of Iron and Ruthenium Complexes", *submitted for publication.*

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ABBREVIATIONS

acac = acetylacetonate

ACp = aminocyclopentadienyl

9-BBN = 9-borabicyclononane

Bn = benzyl

cat = catecholate

CB = catecholborane

Cp = cyclopentadienyl

Cp^X = any Cp-based ligand (e.g., Cp, Cp*, Ind, or Fluorenyl)

Dabco = 1,4-diazabicyclo[2.2.2]octane

DMAP = 4-dimethylaminopyridine

DMAP* = 4-dimethylaminopyrindinyl

DMS = dimethylsulfide

EDC = 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride

ee = enantiomeric excess

GC = gas chromatography

HPLC = high performance liquid chromatography

Ind = indenyl

NMR = nuclear magnetic resonance

PMA = phosphomolybdic acid

RBcat = alkyl catecholboronate ester

RBpin = alkyl pinacolboronate ester

TBAF = tetra-*n*-butyl ammonium fluoride

TBS = *tert*-butyldimethylsilyl

THF = tetrahydrofuran

TLC = thin layer chromatography

TMS = trimethylsilyl

Chapter One:

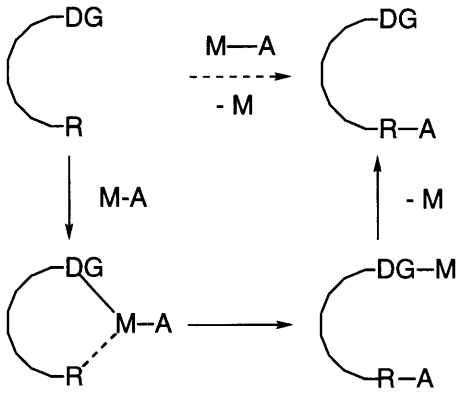
Directed, Catalyzed Hydroboration Reactions via Ring Slippage

INTRODUCTION

Directed reactions are fairly common in organic synthesis. A directed reaction may be defined as one in which a functional group of a substrate (DG) binds a metal-bound reagent (A) and then delivers that reagent intramolecularly to a second functional group (R) within the substrate (Scheme 1.1).[1] Directed processes serve as powerful tools for organic synthesis, since they are generally characterized by high levels of regio- and stereocontrol, due to their highly organized transition structures.

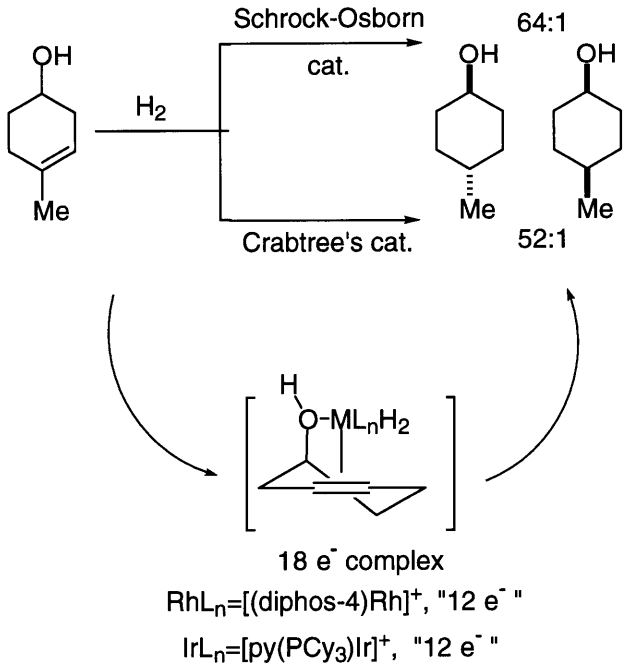
Scheme 1.1

DG = Lewis-Basic Moiety
R = Reactive Moiety
A = Addend



A well-known example of this type of process is the hydroxyl-directed hydrogenation of olefins.[2-6] This reaction occurs in a directed fashion in the presence of Rh(I) and Ir(I) catalysts, such that cis addition of dihydrogen is seen with respect to the hydroxyl-directing group (Scheme 1.2).[7,8] The selectivity for the trans-1,4 stereochemistry occurs due to the highly organized intermediate in which the directing group (OH), the olefin, and the addend (H_2) are all bound to the metal center.

Scheme 1.2



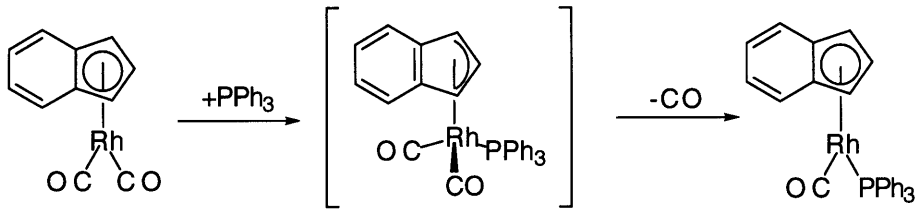
Although directed reactions are fairly common, late-transition metal complexes are rarely the catalyst of choice. As Crabtree has noted in the context of hydrogenation reactions,[9] access to a twelve-electron (or less) transition metal fragment is typically required for a directed olefin addition reaction. The lack of ready access to the necessary level of coordinative unsaturation accounts for the relative lack of directed reactions catalyzed by late transition metals. As shown in the intermediate (Scheme 1.2), when the directing group (OH, 2 e^-), addend (H_2, 2 e^-) and reactive moiety (olefin, 2 e^-) are all bound to the metal center, the metal must have an electron count of 12 e^- (or less) associated with it in order to accommodate the 18 e^- rule.

Coordinative unsaturation in organometallic complexes is most commonly generated by ligand dissociation,[10] such as in the directed hydrogenations with the Schrock-Osborn ($[(diphos\text{-}4)Rh(nbd)]^+BF_4^-$) and Crabtree ($[Ir(cod)py(PCy_3)]^+PF_6^-$) catalysts (Scheme 1.2). Wilkinson's complex ($RhCl(PPh_3)_3$) also catalyzes olefin hydrogenation reactions, but due to the lack of ready access to a 12 e^- intermediate,

Wilkinson's complex is not a useful catalyst for directed reactions.[9]

Another useful mechanism for generating coordinative unsaturation at a metal center relies upon the capacity of certain groups, including nitrosyl and Cp, to serve as variable electron donors through ligand isomerization (e.g., linear to bent geometry for nitrosyl,[11] η^5- to η^3- complexation for Cp[12-14]). These processes have been the subject of extensive investigation, mainly from the viewpoint of reaction mechanism. As Cp-metal complexes are known to be catalysts for a variety of olefin-addition reactions,[15] we chose to utilize these types of complexes in our studies.

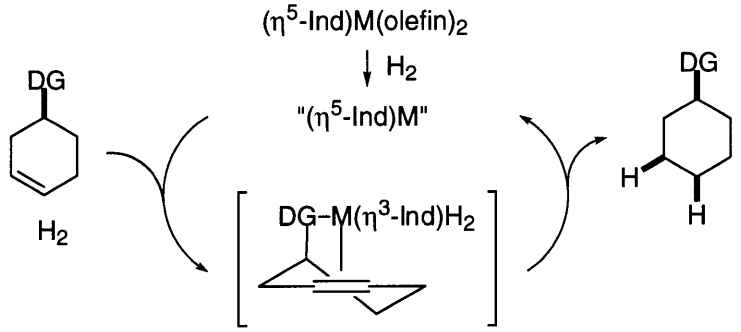
The propensity of Cp-type ligands (such as indenyl, cyclopentadienyl, and fluorenyl) to ring slip has been extensively investigated with respect to PPh_3 substitution reactions of coordinatively saturated η^5-$Cp^XRh(CO)_2$ complexes (Eq 1.1). It was found by Hart-Davis and Mawby in the late 1960's that indenyl ligands will ring slip more readily under these reaction conditions than will cyclopentadienyl ligands.[16-18] This has been attributed to the fact that in the η^3-indenyl isomer there is benzene stabilization, which is not present in the corresponding η^3-Cp. This added stability allows for a more readily accessed η^3-ligand, which accounts for the increased rate of substitution of indenyl versus cyclopentadienyl complexes. We hoped to utilize this rate difference between Cp and Ind ligands to provide evidence that ring slippage was in fact providing a coordinatively unsaturated intermediate by which a directed process could occur. It was expected that the rate difference between ligands would result in a selectivity difference for the directed reactions.



η^5-Ind 18 e⁻ η^3-Ind 18 e⁻ η^5-Ind 18 e⁻ (1.1)

By utilizing an indenyl complex of a Group IX metal, such as Co, Rh, or Ir, one way a directed reaction could occur would be through the intermediacy of the η^3-indenyl metal complex (Scheme 1.3). The presence of a metal-catalyzed, directed process, as evidenced by regio- and/or stereochemistry of the addition, would therefore provide evidence for the intermediacy of an η^3-Ind-metal complex as a low-energy pathway for accessing the coordination sites necessary for the directed reaction.[19] To the best of our knowledge, ligand isomerization has never been exploited as a means of generating the coordinative unsaturation necessary for effecting a directed reaction.

Scheme 1.3



with transient $\eta^5 \rightarrow \eta^3$ ring slippage: an accessible 18 e⁻ complex

Group IX-metal complexes bearing cyclopentadienyl-derived ligands are well known,[15] and are, in fact, catalysts for several olefin-addition reactions, such as hydrogenation and hydrosilation. Directed hydroboration reactions with non-Cp^X-Rh(I) and Ir(I) complexes have also been observed.[20] We first began investigating $IndRh(C_2H_4)_2$-catalyzed, directed hydroboration reactions with catecholborane. If a directed reaction was observed, we could then conclude that the anticipated ring slippage had also occurred. Prior to this study, the activity of $IndRh(C_2H_4)_2$ as a catalyst for olefin hydroboration reactions had not been explored.

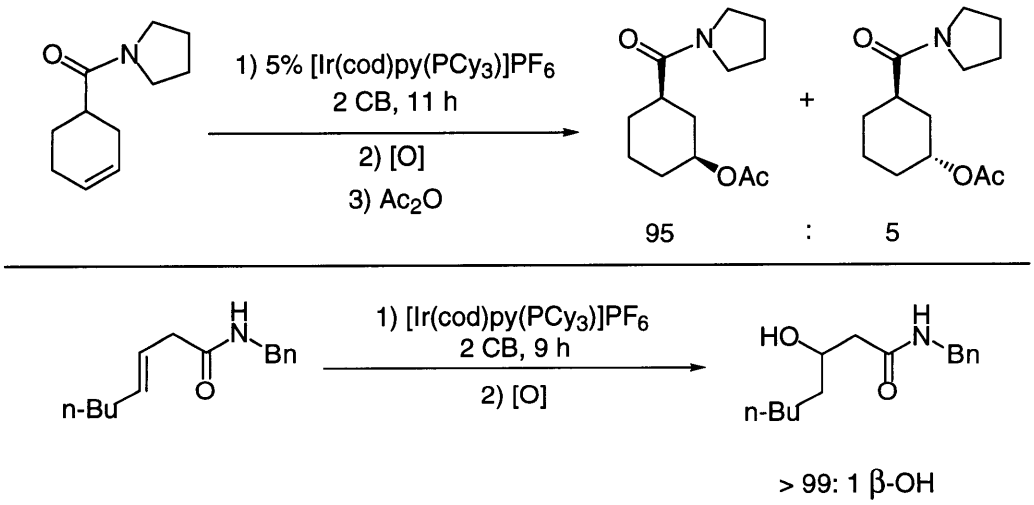
Chapter One, Part A:

Amides as Directing Groups

INTRODUCTION

Literature reports of attempts to promote directed hydroboration reactions utilizing catecholborane and late-transition metal catalysts date back to the late 1980s. Phosphinites[21] have been shown to direct hydroboration reactions in the presence of stoichiometric transition-metal complexes, while sulfones[22] have served as directing groups for transition-metal catalyzed hydroboration reactions. The directed hydroboration reaction utilizing the Crabtree and Schrock-Osborn catalysts was found to occur with the best selectivity when tertiary or secondary amides were used as the Lewis-basic moiety (Scheme 1A.1).[23,24]

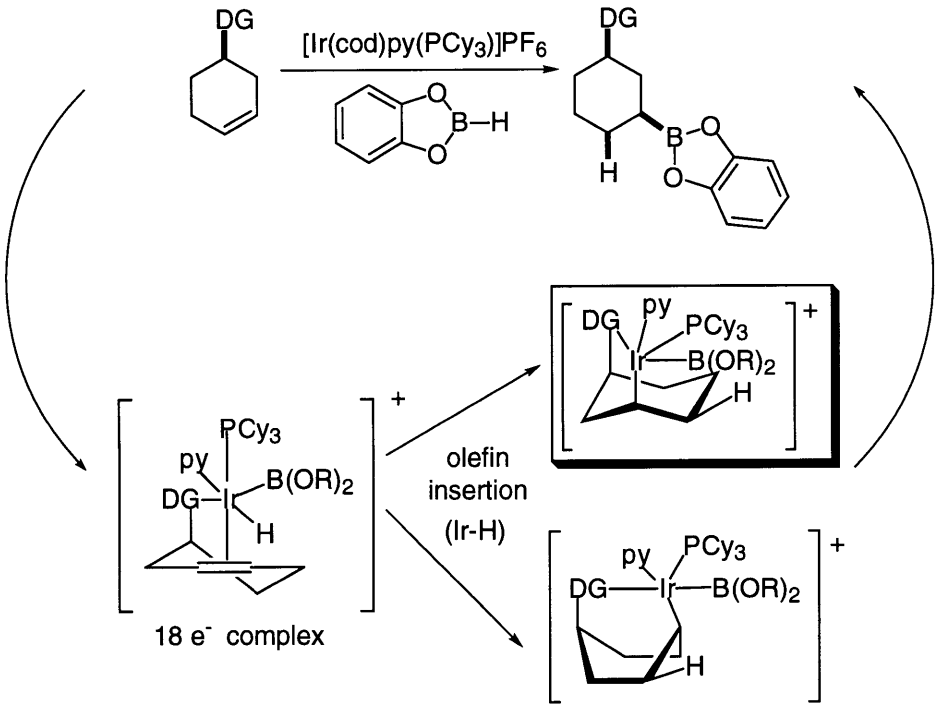
Scheme 1A.1



Cyclic substrates result in the *cis*-hydroxyamide products as the predicted isomer of a directed reaction. Both cyclic and acyclic substrates show proximal addition of the boron atom with respect to the directing group. These products are predicted based on the assumption that the smaller possible metallacycle, formed by insertion of the olefin into a Ir-H bond, will be formed in the stereo- and regiochemistry-determining step of the catalytic cycle.[25,26] This metallacycle reductively eliminates

to form the predicted products (Scheme 1A.2).

Scheme 1A.2



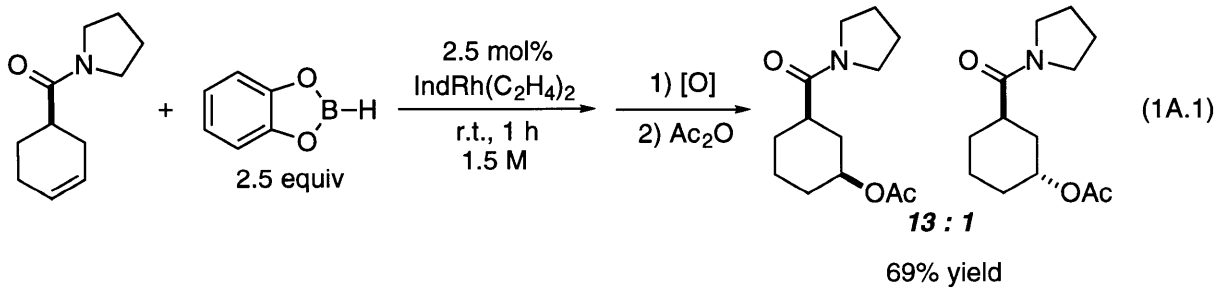
Although good yields of the desired directed product were seen with the secondary amide substrates, Evans noted competitive reduction of the tertiary amide during the catalytic hydroboration. For this reason, the secondary amides were the focus of his work.

RESULTS AND DISCUSSION

$IndRh(C_2H_4)_2$ Catalyzed Hydroborations

Although several reactions were initially investigated with the $IndRh(C_2H_4)_2$ complex (e.g., hydrogenation and hydrosilation), the hydroboration reaction (with catecholborane) showed the most promise. Catecholborane is a common hydroborating agent and has been shown to have little to no activity at room temperature in the absence of transition-metal catalysts. Generally, uncatalyzed hydroborations of olefins require temperatures ≥ 100 °C.

Following the lead of Evans,[20] we therefore began a study of olefinic amides as substrates for hydroborations in the presence of an $IndRh(C_2H_4)_2$ complex. We hoped that amide reduction would not be a problem with our catalytic system and therefore attempted the use of tertiary amides as directing groups. By utilizing conditions similar to those developed by Evans, we noted complete conversion of the olefin after only one hour (Eq 1A.1). Following oxidation and acetylation, evidence was seen for a directed process.

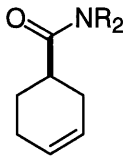
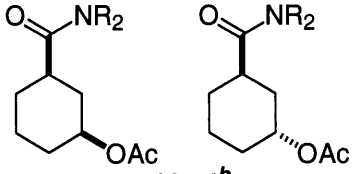
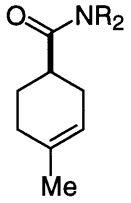
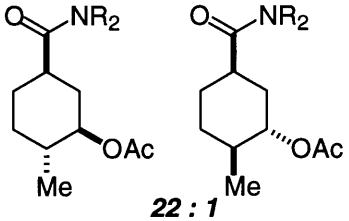
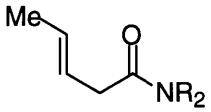
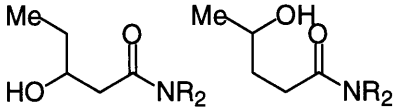
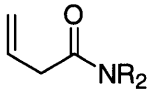
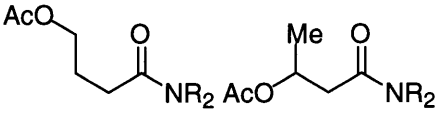
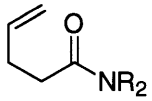
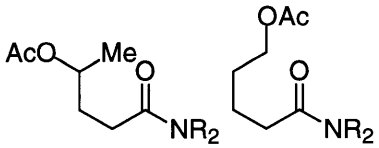


(1A.1)

Treatment of a series of olefinic amides with 2.5 mol% $IndRh(C_2H_4)_2$ and 2.5 equivalents of catecholborane (CB) in CH_2Cl_2 for one hour at room temperature, followed by an oxidative workup, provides the products anticipated for a directed reaction with moderate to high levels of regio- and diastereoselectivity (Table 1A.1). Little to no amide reduction is observed under these conditions. When the reaction

is run in the presence of mercury, similar results are seen both with respect to conversion and selectivity, suggesting that heterogeneous catalysis is not responsible for the observed reactivity.[27,28]

Table 1A.1. Amide-Directed, Indenylrhodium-Catalyzed Hydroboration of Olefins. (as in Eq 1A.1)

Entry	Substrate[a]	Products[b]	Yield (%)
1		 13 : 1[b]	69[c]
2		 22 : 1	61
3		 23 : 1	73
4		 1 : 1	54
5		 1 : 3	78

[a] All amides are pyrrolidine-derived amides.
[b] Entry 1: The 1,4-isomers are each produced in ~4% yield. Entries 2-5: Less than 2% of any other isomer is observed.
[c] Yield determined by GC versus a calibrated internal standard.

When the substrate is a cyclic, disubstituted olefin, the stereo- and regiochemistry of the addition are both indicative of a directed process (Table 1A.1, entry 1). The

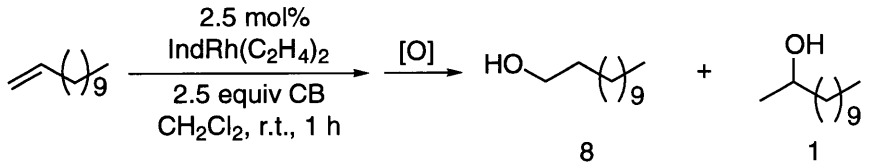
hydroboration of 1-(4-methylcyclohex-3-enylcarbonyl) pyrrolidine (Table 1A.1, entry 2) also results predominantly in the cis-1,3-hydroxyamide product, thus providing further evidence that a directed process is occurring.

The regioselectivity observed in the reaction of acyclic olefinic amides provides further support for the occurrence of a directed process and, therefore, for the intervention of a ring-slipped intermediate in indenylrhodium-catalyzed hydroborations. The hydroboration of a 1,2-disubstituted olefin typically affords a roughly equal mixture of the two possible regioisomeric alcohols. In contrast, $IndRh(C_2H_4)_2$-catalyzed hydroboration of the β,γ-unsaturated amide illustrated in entry 3 (Table 1A.1) produces the β-hydroxyamide with a high level of selectivity, a result consistent with direction by the amide.[24-26]

The presence of a suitably disposed amide directing group can overcome the strong bias for generation of primary alcohols in the indenylrhodium-catalyzed hydroboration of terminal olefins. Hydroboration of the 3-butenamide illustrated in entry 4 (Table 1A.1) affords a 1:1 mixture of primary and secondary alcohols. As expected, the strength of the directing effect diminishes with increased distance between the amide and the olefin (entry 4 versus entry 5, Table 1A.1).

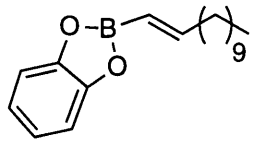
For comparison, we examined the hydroboration of non-directed terminal olefinic substrates. Surprisingly, the $IndRh(C_2H_4)_2$ catalyzed hydroboration of dodecene results in low yields (26%) of alcohols in an 8:1 ratio of primary to secondary (Eq 1A.2). The major products of the hydroboration are dodecanal (45%) and dodecane (29%). The dodecanal could result from oxidation of a vinyl boronate ester (**1A.1**) or bis(boronate ester) (**1A.2**). The pinacol boronate ester analogs of these materials have been shown to result from the catalyzed hydroboration of terminal olefins with Wilkinson's catalyst followed by ligand-exchange with pinacol.[29] Although oxidation of Wilkinson's catalyst can give results inconsistent with other mechanistic studies of the catalyzed hydroboration reaction,[30] the intermediacy of a

Rh-containing species is necessary for these products (**1A.1**, **1A.2**) to be formed.

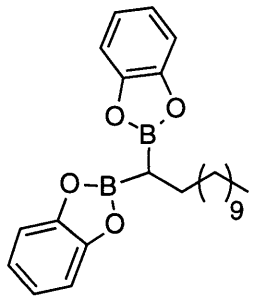


8 1

26% yield (1A.2)

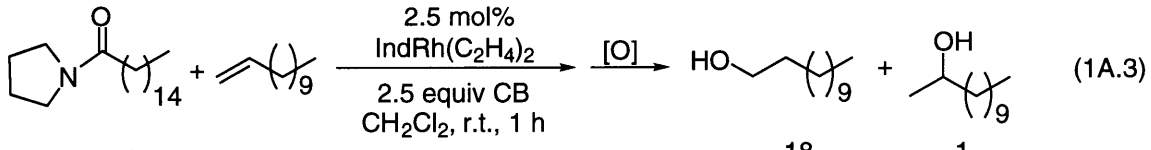


1A.1



1A.2

Only when an amide (the pyrrolidine-derived amide of palmitoyl chloride) is present does the $IndRh(C_2H_4)_2$-catalyzed hydroboration result in usable yields (>90%) of alcohols (Eq 1A.3). An in-depth discussion of this result is presented in a later section (Chapter One, Part A, "Non-Transition Metal Catalyzed Hydroborations").



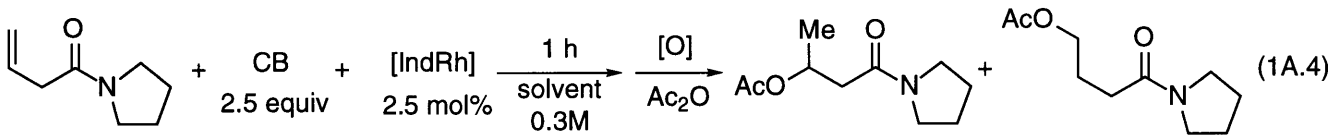
1.1 equiv 18 1

93% yield (1A.3)

Further Evidence for a Directed Process

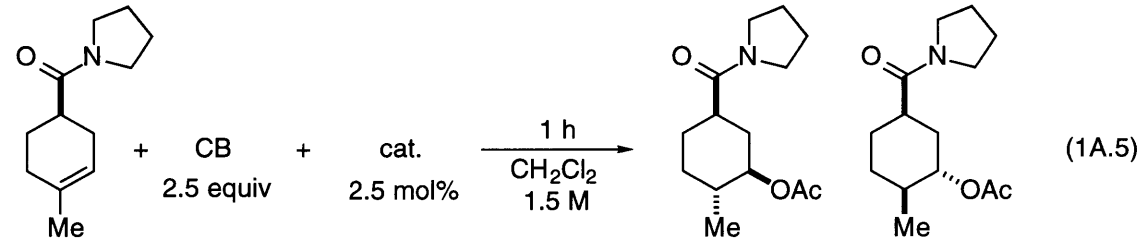
When the directed reaction is run in the presence of Lewis-basic solvents, a

significant decrease in the selectivity is seen, as would be expected from competition of the solvent with the directing-group (Eq 1A.4). This provides additional evidence that a directed reaction is occurring.[24]



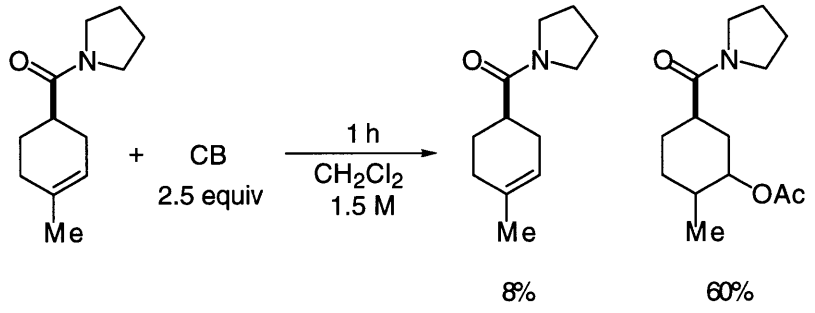
CD_2Cl_2	2.5 : 1.0
C_6D_6	2.6 : 1.0
THF-d_8	1.4 : 1.0

In order to further substantiate that ring slippage was in fact a crucial step in the catalytic cycle of the directed reaction, we compared the results of a catalyzed process utilizing $IndRh(C_2H_4)_2$ with the results of reactions catalyzed by systems which would access a 12 e$^-$ rhodium center less-readily[16] (e.g., $CpRh(C_2H_4)_2$) or not-at-all[9] (e.g., $ClRh(PPh_3)_3$). The results were disappointing (Eq 1A.5), as there was little difference in the selectivity observed with the Ind- and $CpRh(C_2H_4)_2$ catalysts. Furthermore, Wilkinson's catalyst, which should not be able to access a 12 e$^-$ metal center, showed an apparent directed reaction. We chose to investigate the uncatalyzed hydroboration of these olefinic amide substrates in an effort to understand how this unexpected directed hydroboration was occurring.



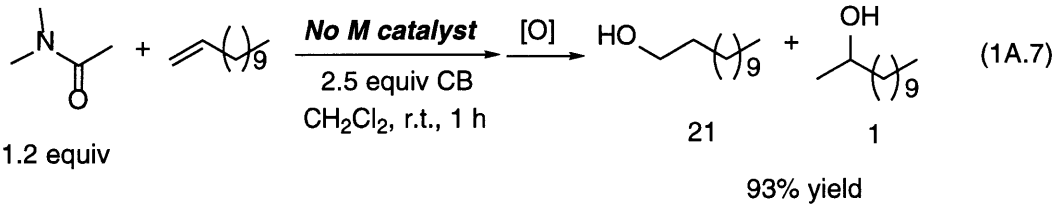
[IndRh]	22:1
[CpRh]	22:1
$[ClRh(PPh_3)_2]$	10:1

The addition of 2.5 equivalents of catecholborane to a solution of olefinic amide in CH_2Cl_2 after one hour at room temperature showed almost complete consumption of the olefin by ^{1}H-NMR (Eq 1A.6). Following the standard oxidation and isolation, the major product of the reaction was found to be the product of a hydroboration reaction. This uncatalyzed hydroboration process was found to be general for the substrates shown in Table 1A.2. The relative rates of the catalyzed and uncatalyzed reactions appeared to be similar (1 hour, 90-100% conversion of olefin), so we attempted to quantitate the activity of our $IndRh(C_2H_4)_2$ catalyst.



(1A.6)

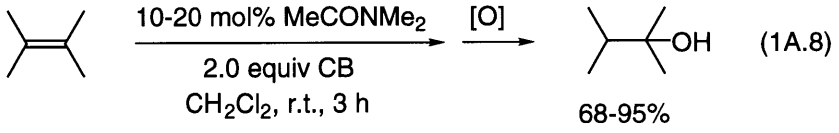
Since the hydroboration of dodecene with only catalyst present was known to result in low yields of alcohol (Eq 1A.2) and the hydroboration run in the presence of 1.1 equiv of an amide resulted in a high yield of alcohol (Eq 1A.3), it seemed that the catalyst was reacting with the amide and providing an effective hydroboration catalyst. We attempted to deduce the effect of the amide on the catalyst and soon found that even in the absence of catalyst, a simple amide (*N,N*-dimethylacetamide) will promote an efficient hydroboration reaction (Eq 1A.7). It now seemed that the amide was somehow reacting with the catecholborane to form an active hydroboration mixture.



(1A.7)

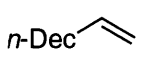
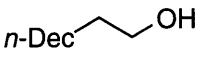
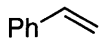
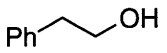
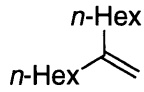
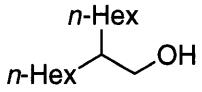
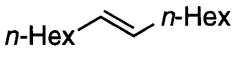
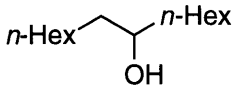
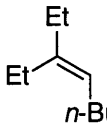
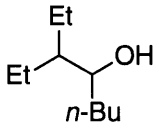
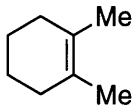
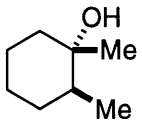
Non-Transition Metal Catalyzed Hydroborations

We discovered that even catalytic amounts of amide were very effective at inducing the hydroboration of unfunctionalized olefins. A wide range of olefins are efficiently hydroborated in the presence of 10-20 mol% *N,N*-dimethylacetamide and 2.5 equivalents of catecholborane (Eq 1A.8, Table 1A.2). A reaction time of three hours is sufficient to allow for complete hydroboration of even tetrasubstituted olefins, such as 1,2-dimethylcyclohexene (entry 6, Table 1A.2). The reactions were conducted under an inert atmosphere with purified reagents, although we have found that the hydroboration of 1-dodecene proceeds equally smoothly when the reaction is run open to the air with unpurified reagents. Following oxidation, moderate to good yields of alcohol are isolated in both cases. Control experiments establish that <10% conversion is noted in the absence of amide under otherwise identical conditions.



(1A.8)

Table 1A.2. Hydroboration of Olefins with Catecholborane in the Presence of N,N-Dimethylacetamide[a] (Eq 1A.8)

Entry	Substrate	Product[b]	Yield (%)[c]
1			95
2			88
3			78
4			79
5			71
6			68[d]

[a] Amount of *N,N*-dimethylacetamide used: entries 1-4: 10 mol%; entries 5-6: 20 mol%.

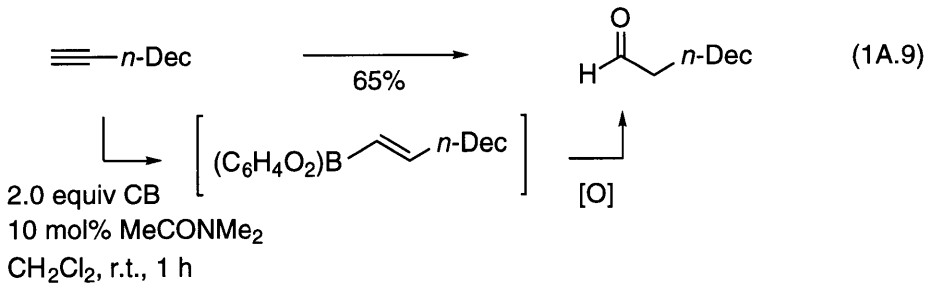
[b] Less than 3% of any other isomer is observed, except for entry 1 (94 : 6, primary : secondary) and entry 2 (85 : 15, primary : secondary).

[c] Average of two runs.

[d] The modest yield may be due in part to the volatility of the product alcohol.

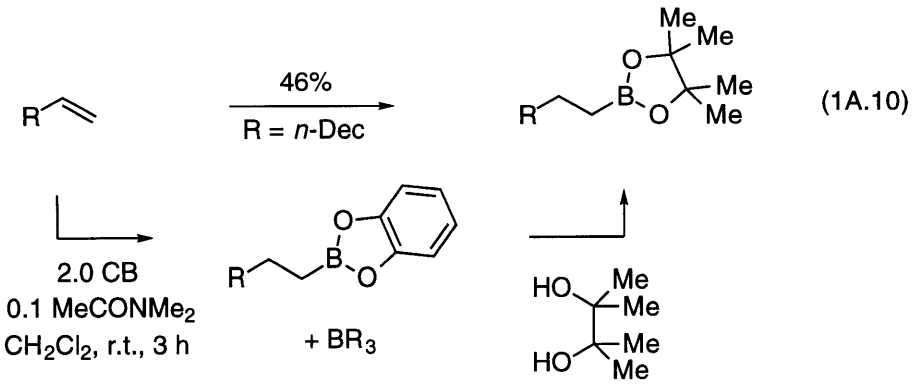
The hydroboration of monosubstituted olefins, both aliphatic and aromatic (entries 1 and 2, Table 1A.2), allows for the isolation of the alcohol in 88-95% yield. 1,1-Disubstituted and 1,2-disubstituted olefins (entries 3 and 4, Table 1A.2) result in slightly lower yields of alcohol (78-79%). Even tri- and tetrasubstituted olefins (entries 5 and 6, Table 1A.2) show complete conversion of the olefin after three hours. The low yield of the 1,2-dimethylcyclohexanol may be due to its difficulty in isolation (due to volatility). The stereochemistry of the product illustrated in entry 6 (Table 1A.2) establishes that the boron hydride adds in a cis fashion to the olefin, as

would be expected from previous studies of the hydroboration reaction. *N,N*-Dimethylacetamide (10 mol%) also facilitates the addition of catecholborane to alkynes (Eq 1A.9). The vinyl boronate ester formed was characterized by ^{11}B and ^{1}H NMR to verify the trans stereochemistry of the boron-containing intermediate.[31-33]

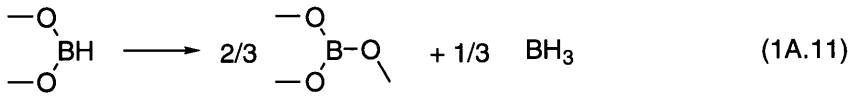


Analysis of the Hydroborating Agent

Tetrasubstituted olefins (see Table 1A.2, entry 6) are notoriously difficult to hydroborate with catecholborane, so we were very interested in determining whether catecholborane was really the hydroboration agent in this reaction. We began by looking at simple mono-substituted olefins. ^{11}B-NMR analysis of the hydroboration of dodecene in the presence of 10 mol% *N,N*-dimethylacetamide after three hours indicated the presence of both alkylboronate ester and trialkylborane (Eq 1A.10). The yield of alkylboronate ester (the expected product of a catecholborane hydroboration reaction) was quantitated by ligand exchange with pinacol and subsequent isolation of the material by column chromatography.[34] Only 46% of the theoretical yield of dodecyl pinacolboronate ester was obtained. We found that tridodecylborane does not transmetallate with pinacol, so all of the dodecylpinacol was due to dodecyl catecholboronate ester. The presence of trialkylborane in the boron-containing products was disturbing, though, as it suggested that BH_3 had been formed under the reaction conditions.



The formation of BH_3 via disproportionation reactions of dialkoxyboranes has been known for some time. It was reported in 1933 that dimethoxyborane will disproportionate to form a mixture of trimethoxyborane and BH_3 (Eq 1A.11).[35] No evidence for similar disproportionation reactions of catecholborane had been seen until the early 1990's. A series of reports at that time provided evidence for decomposition of catecholborane in the presence of certain metal complexes[36-40] (e.g., Wilkinson's catalyst[29] and bis(mesityl)niobium[41]) and phosphines[42] (i.e., PPh_3). These reports indicated the presence of BH_3 or BH_3-derived materials, resulting from the disproportionation of catecholborane.



Since these early reports, many different compounds have been shown to mediate the decomposition of catecholborane resulting in the formation of BH_3, which is capable of hydroborating compounds without the intervention of the transition metal catalyst. The presence of borane-derived products are noted as evidence of this.[42] Oxidation of these alkylboranes gives the product of a hydroboration reaction; therefore the isolation of an alcohol product does not give suitable information about the pre-oxidation mixture. Most reports prior to the mid-1990's did not analyze the *B*-containing intermediates for the presence of the expected boronate esters. Therefore, the identity of the pre-oxidation products has

not been unequivocally established for many of the published transition-metal catalyzed reactions.

We therefore attempted a simple mechanistic study of our amide-mediated hydroboration reaction utilizing ^{11}B NMR to determine the identity of the hydroborating agent. The reaction of *N,N*-dimethylacetamide (1.2 equiv) with catecholborane resulted in a very quick disproportionation reaction. After only 16 minutes at room temperature, the NMR spectrum indicated that all of the catecholborane had been consumed. One of the major resonances observed was a quartet (δ -11 ppm, J = 96 Hz). This indicated the presence of a BH_3 species. It was deduced that this was an amide-BH_3 complex, which was independently synthesized by the addition of *N,N*-dimethylacetamide to BH_3-THF. An immediate and almost quantitative substitution reaction took place to provide the amide-BH_3 complex (δ -11 ppm, J = 96 Hz)(Figure 1A.1). Attempts to isolate the complex were unsuccessful, as decomposition ensued, likely due to hydroboration of the carbonyl group of the acetamide.

Even in the presence of catalytic amounts of amide (0.05 equiv amide, 1 equiv catecholborane) BH_3-amide is formed in less than 3 minutes (Figure 1A.2). The major boron-containing material is still catecholborane (δ 28, d, J = 196), but the presence of even small amounts of an active BH_3 complex could account for the non transition-metal catalyzed hydroboration reaction that we observe.

In order to determine whether the BH_3-amide complex was the active hydroborating agent, we followed the hydroboration of dodecene under the amide-mediated reaction conditions (0.1 equiv *N,N*-dimethylacetamide, 2 equiv catecholborane, CH_2Cl_2). Previous results indicated that the hydroboration of dodecene is complete in less than 3 hours with 46% of the theoretical yield resulting from dodecyl catecholboronate ester. When the reaction was followed by NMR (^1H and ^{11}B), it was found that after two hours, 68% of the dodecene had been

Figure 1A.1. ^{11}B NMR of BH_3-THF and dimethylacetamide (1:1).

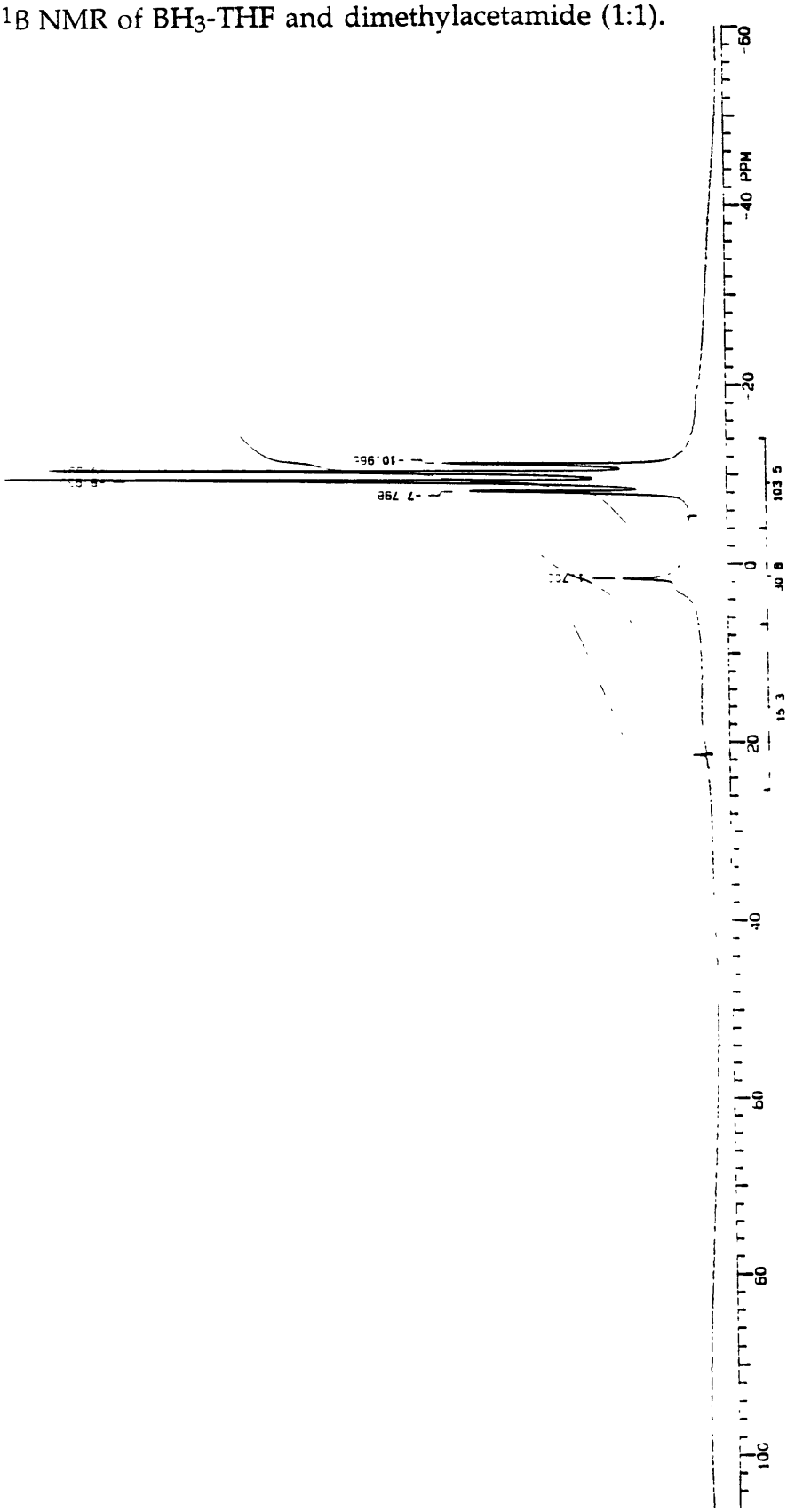
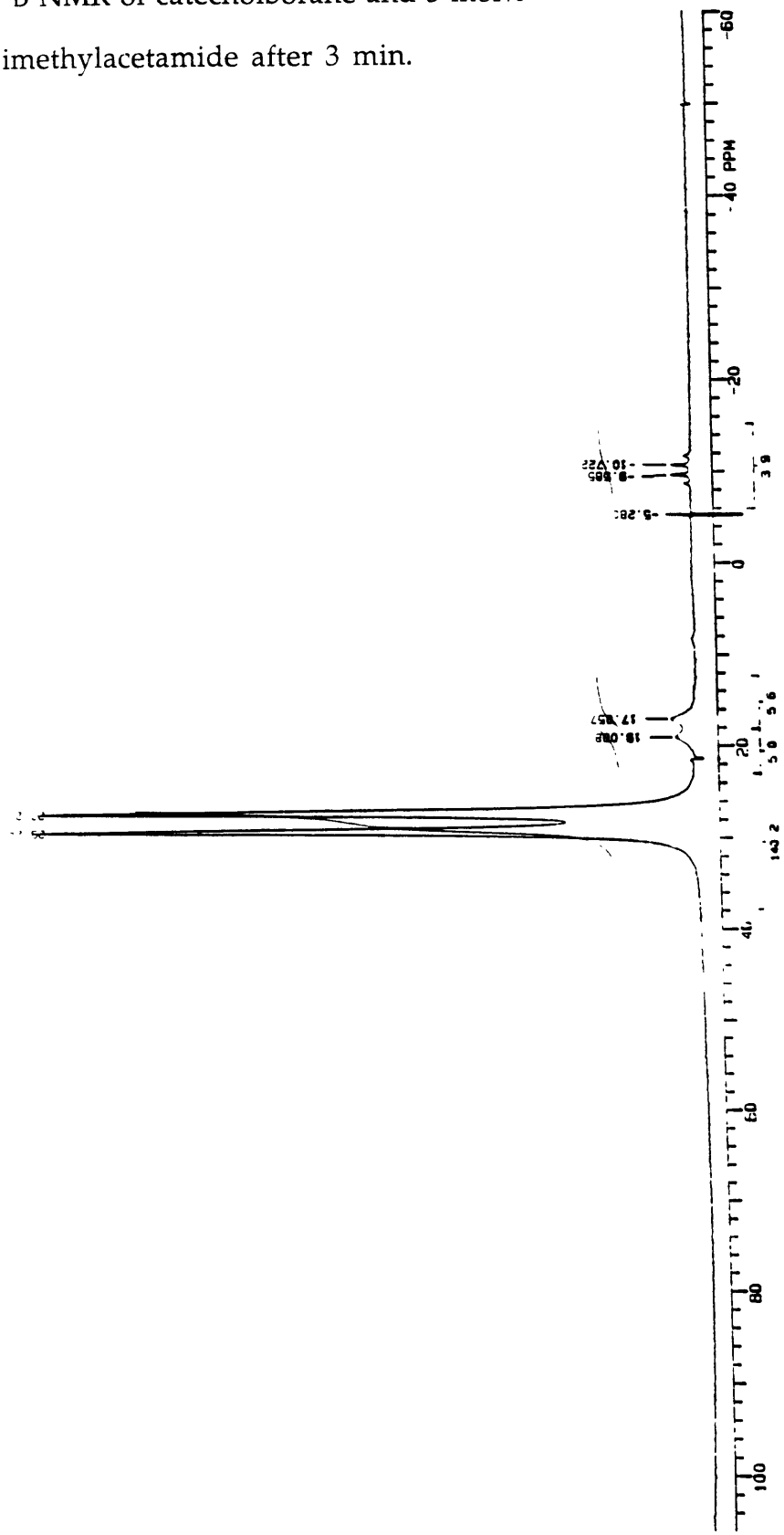
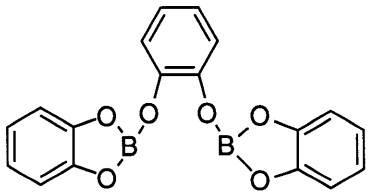


Figure 1A.2. ^{11}B NMR of catecholborane and 5 mol% *N,N*-dimethylacetamide after 3 min.

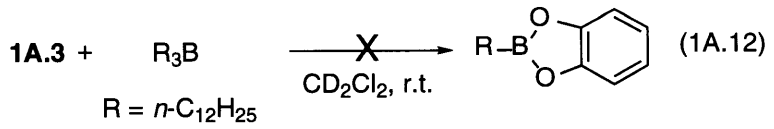


hydroborated. 25% of the conversion resulted in alkylboronate ester, while 43% of the conversion was accounted for by trialkylborane. After allowing the reaction to continue for 30 hours it was noted that all dodecene had been consumed and >65% of the yield was due to alkylboronate ester, while the remainder was now an unidentified boron-containing product, *not* tridodecylborane. The disappearance of trialkylborane and the concurrent formation of alkylboronate ester seemed to indicate that another disproportionation reaction may be responsible for the formation of some of the alkylboronate ester.

The disproportionation product of catecholborane, B_2cat_3 (**1A.3**), appeared to be a good candidate for this secondary disproportionation reaction with R_3B. We quickly determined that it was not responsible for the formation of alkylboronate ester, though, as no product was observed at room temperature (Eq 1A.12). Literature reports state that reactions of this type are not significant until the reaction temperature is 100 °C or higher.[43]



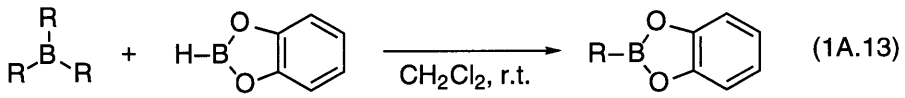
1A.3



(1A.12)

The reaction of trialkylborane with catecholborane, though, was found to be a slow but effective method for producing alkylboronate ester. We have found that treatment of tri-*n*-dodecylboron with catecholborane at room temperature does afford the *B*-alkyl catecholborane (Eq 1A.13), but at a rate that is too slow ($t_{1/2}$ ~ 1 day)

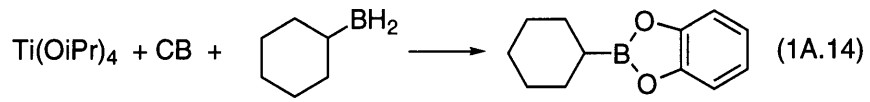
to account for all of the formation of *B*-alkyl catecholboronate ester in the hydroboration of 1-dodecene. The rate of the reaction illustrated in Eq 1A.13 (R=*n*-Dec) is not affected by the addition of *N,N*-dimethylacetamide, but less sterically hindered trialkylboranes, such as triethylborane, react more quickly with catecholborane (Eq 1A.13). This data suggests that smaller trialkylboranes, or possibly even di- or monoalkylboranes, could be very effective partners in this observed formation of alkylboronate ester. Since many BH_3-mediated hydroborations occur with incomplete utilization of all three active hydrides from the BH_3, the presence of dialkylboranes would not be surprising.



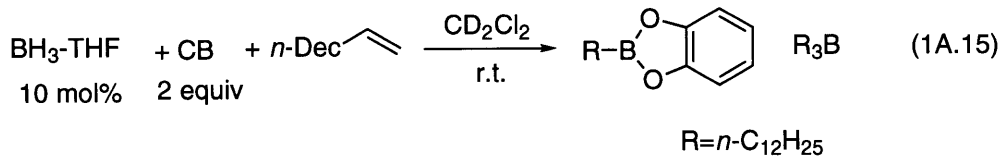
(1A.13)

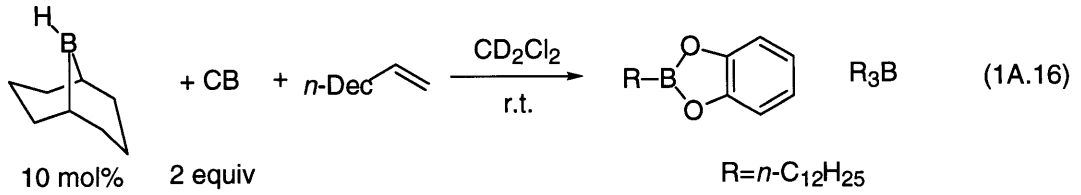
R = *n*-$C_{12}H_{25}$, $t_{1/2}$ ~ 1 day
R=Et, $t_{1/2}$ = 5 h

Burgess has reported a similar disproportionation process involving monoalkylboranes in the presence of catalytic $Ti(O\text{-}iPr)_4$ and catecholborane (Eq 1A.14).[39] We found that the hydroboration of dodecene in the presence of BH_3-THF and catecholborane resulted in the slow formation of dodecyl boronate ester, with very slight amounts of trialkylborane noted as well (Eq 1A.15). The monoalkylboranes were prepared *in situ* as these compounds tend to disproportionate rapidly upon isolation. The disproportionation of 9-BBN and catecholborane was also found to be a competent method for forming *B*-alkyl catechol boronate esters, although slow, probably due to the larger steric bulk of 9-BBN (Eq 1A.16). A slight amount of trialkylborane was again noted.



(1A.14)





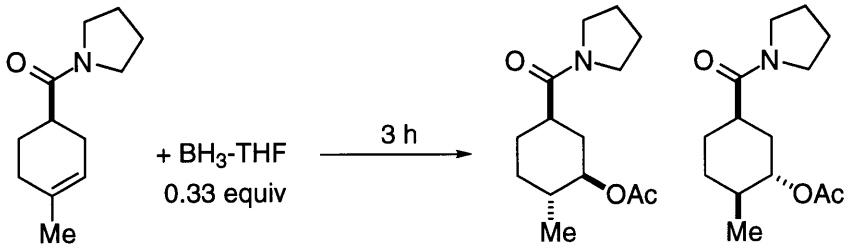
It appears that in the amide-mediated reactions, a BH_3-amide complex is initially formed via disproportionation of catecholborane. This BH_3 subsequently hydroborates the olefin resulting in a mono-, di-, or tri-alkylborane. These *B*-alkylboranes could further disproportionate with catecholborane to form alkylboronate esters. The resulting mixture, after oxidation, would result in a high yield of the desired alcohol product. As the majority of the mixture appears not to initially be alkylboronate ester, this would be problematic for any further reactions of the boron-containing product that require a boronate ester (e.g., Suzuki couplings). From this data we concluded that the predominant hydroborating agent in our amide-mediated hydroborations was in fact BH_3.[44-46]

Analysis of the hydroboration agent in directed, metal-catalyzed hydroborations

In light of these results, we attempted to show that our amide-directed reactions were in fact proceeding through a metal-catalyzed pathway. The most obvious route was to show that BH_3, or a BH_3-derived product, was *not* capable of providing a directed result for the hydroboration of an olefinic-amide substrate. The best results for the $IndRh(C_2H_4)_2$-catalyzed directed reaction were seen with the 1-(4-methylcyclohex-3-enyl carbonyl)pyrrolidine (Table 1A.1, entry 2), so this was chosen as a test substrate for the following reactions.

The hydroboration of this substrate with BH_3-THF gave results consistent with a

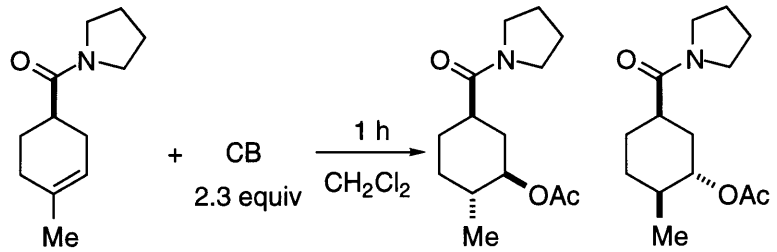
non-directed reaction (Eq 1A.17). Since amides displace THF almost instantaneously (see Figure 1A.1), the hydroboration should be occurring via a tethered amide-BH_3 complex. We had shown previously that the presence of a Lewis-basic solvent, such as THF, decreased the stereoselectivity seen in the directed reactions (Eq 1A.4), so it is possible that the presence of THF was responsible for the non-selectivity of this reaction. It was therefore attempted to produce borane gas in dichloromethane via the reaction of $NaBH_4$ with BF_3-OEt_2,[47] but the extent of reaction was not significant enough to draw any conclusions from the results.



(1A.17)

0.8 : 1.0

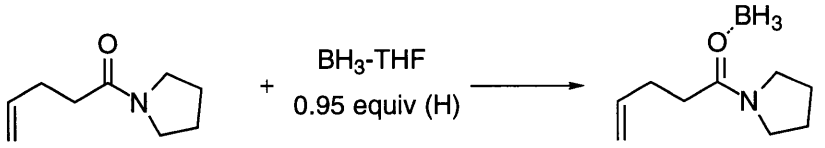
We then attempted the uncatalyzed hydroboration of this substrate with catecholborane. This reaction gave the most troubling results since, after oxidation of the boron-containing products, a significant selectivity was noted for the *directed product* (Eq 1A.18). This selectivity, though, was not completely reproducible. Using rigorously purified reagents and glassware, the reaction occurred with a selectivity of >8 : 1 in 4 out of 9 trials. The remaining runs produced a statistical mixture of the isomers. Therefore, we have not ruled out the possibility that a *non-metal catalyzed pathway* is resulting in a directed product.



(1A.18)

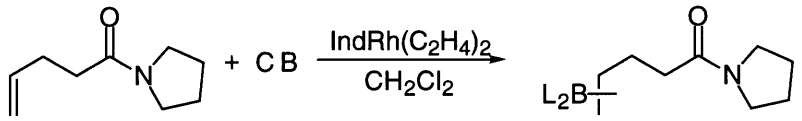
12 : 1

Preliminary ^{11}B NMR studies of the hydroboration of an olefinic amide also give some indication of the complexity of the system. The catalytic hydroboration of the 4-pentenoic acid derived amide is complete in 1 hour and shows some selectivity for the directed product, although diminished with respect to the butenoic amide substrate (Table 1A.1, compare entry 4 and entry 5) due to the increased distance between the directing group and the olefin. The hydroboration of the olefinic amide with 0.3 equivalents BH_3-THF, on the other hand, was not effective after even 14 hours (Eq 1A.19). Only BH_3-amide was seen in the ^{11}B NMR at this time, and none of the expected products of hydroboration with BH_3 were observed.



(1A.19)

The $IndRh(C_2H_4)_2$-catalyzed hydroboration also shows the formation of BH_3-amide after only 1.2 hours under the conditions shown in Eq 1A.20. After 14 hours the olefin has been completely consumed, but there is no evidence of alkyl catecholboronate ester (δ 35 ppm) from the ^{11}B NMR analysis of the mixture.[48] The major boron-containing peak is at 17.5 ppm. The major product of the thermal hydroboration of this substrate with catecholborane also displays a resonance at 17.5 ppm in the ^{11}B NMR. It appears that if this is the alkylboronate ester then some interaction of the amide with the boron atom must be occurring to shift the observed resonance upfield.



(1A.20)

We reasoned that this peak might be arising from complexation of the amide with the boron atom of the boronate ester, but treatment of dodecyl catecholboronate ester[49] with the pyrrolidine-derived amide of palmitoyl chloride

does not alter the ^{11}B NMR chemical shift of the alkyl boronate ester peak. This data does not rule out the possibility of an intramolecular complexation of the tethered amide to the boronate ester, resulting in the observed chemical shift (δ 17.5 ppm).

CONCLUSION

We have discovered that a tertiary amide (*N*,*N*-dimethylacetamide) efficiently promotes the hydroboration of olefins with catecholborane at room temperature. Disproportionation of the catecholborane occurs, and a borane-(Lewis-base) complex is formed as a result, which is an active hydroborating agent at room temperature. This work thus reveals unexpected reactivity for catecholborane in the presence of a common functional group. The use of catecholborane as a hydroborating agent on highly functionalized molecules is common in the literature, so this result may have marked implications for many hydroborations, both metal-catalyzed and non-metal-catalyzed.

Furthermore, a catalytic amount of amide in the presence of catecholborane results in an agent that is capable of hydroborating mono-, di-, tri-, and tetrasubstituted olefins very effectively. The boron-containing product of this reaction is a mixture of alkylboronate ester and alkylboranes. The alkylboronate ester appears to be the product of a disproportionation between an alkylborane and catecholborane.

Traditionally, most catalyzed hydroborations with catecholborane have not been analyzed prior to the oxidation step. The assumption has been that the alkylboronate ester was the pre-oxidation product, but we have shown that this may not be the case. Furthermore, the observation that a *B*-alkyl catecholboronate ester is formed has been put forward in earlier mechanistic and synthetic studies of metal-catalyzed hydroboration reactions as evidence that the product results from a metal-catalyzed reaction manifold, rather than from catecholborane degradation products such as BH_3. Our observation (Eq 1A.13) suggests that in certain instances such conclusions should be drawn cautiously. This point has been made previously by Burgess in the context of a $Ti(O\text{-}iPr)_4$-catalyzed disproportionation reaction (Eq 1A.14). We recommend that ^{11}B NMR analyses of the pre-oxidation products

should be performed to ensure that the boron-containing product is an alkylboronate ester. In addition, *in situ* analysis of the reaction is necessary to rule out BH_3 as the active hydroborating agent (as seen by the absence of BH_3 or BH_3-derived products). Although these analyses may help point out problems in a transition-metal catalyzed reaction, they are not a definitive proof of mechanism.

In light of these results, we have concluded that the predominance of a directed product in our $IndRh(C_2H_4)_2$-catalyzed hydroboration does not prove that this is a well-behaved transition-metal catalyzed reaction. The conclusion that only a transition-metal mediated hydroboration pathway is active is not valid in the absence of other mechanistic information. Preliminary ^{11}B NMR data indicates that the final product of our hydroborations of amide-containing substrates, with catecholborane, are *not* the desired alkylcatecholboronate esters. We have ruled out the possibility of a simple mechanistic study of this system due to the rapid disproportionation reactions that could occur among the products. Therefore, efforts towards establishing the metal-catalyzed pathway for the amide-directed substrates have been discontinued.

EXPERIMENTAL

General. ^{1}H and ^{13}C nuclear magnetic resonance spectra were recorded on a Varian XL-300 or VXR-500 NMR spectrometer at ambient temperature. ^{1}H data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane (δ scale), multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), integration, and coupling constant (Hz). For reaction products that are mixtures of isomers, no integration data are reported. ^{13}C chemical shifts are reported in ppm downfield from tetramethylsilane (δ scale). All ^{13}C spectra were determined with complete proton decoupling. ^{11}B chemical shifts are reported in ppm downfield from an external BF_3-etherate standard (δ scale).

Analytical thin layer chromatography was accomplished using EM Reagents 0.25 mm silica gel 60 plates. Flash chromatography was performed on EM Reagents silica gel 60 (230-400 mesh).

Gas chromatography analyses were performed on a Hewlett-Packard model 5890 Series 2 Plus gas chromatograph equipped with a flame ionization detector and a model 3392A integrator using a 50 m capillary column with DB1701 or DB1 as the stationary phase.

Infrared spectra were obtained on a Perkin-Elmer Series 1600 FT-IR spectrophotometer.

Microanalyses were performed by E + R Microanalytical Laboratory, Inc.

High resolution mass spectra were recorded on a Finnegan MAT System 8200 spectrometer.

All reactions, unless otherwise noted, were carried out under an atmosphere of nitrogen or argon using standard Schlenk and/or glove box techniques. All glassware was oven-dried, and magnetic stirring was utilized.

Pyrrolidine (Aldrich) was dried over sieves prior to use. Sodium hydride

(Aldrich, dry, 95%), pent-3-enoic acid (Fluka), vinyl acetic acid (Aldrich), and EDC (Aldrich) were used as received. *N,N*- Dimethyl acetamide was obtained from Aldrich and Anachemia and distilled before use. Dimethylcyclohexene (Wiley Organics), styrene (Aldrich), and dodecene (Fluka) were all distilled before use. 2-Hexyl-1-octene and 3-ethyl-3-octene were obtained from Wiley Organics. Dodecyne, and *trans*- 7-tetradecene were obtained from Aldrich. Column chromatography was used to purify these materials before use.

sec-Phenethyl alcohol, phenethyl alcohol, 1-dodecanol, 2-dodecanol, and dodecyl aldehyde were obtained from Aldrich. 2-Hexyl-1-octanol, 7-tetradecanol, and 3-ethyl-4-octanol were obtained from Wiley Organics. All materials were used as received. Methyl-3-cyclohexene carboxylate (Pfaltz & Bauer) was distilled before use.

2-Methyl cyclohexanone, 2,3-dihydroxy-2,3-dimethylbutane (pinacol), and methyl lithium (1.4 M in ether) were obtained from Aldrich and used as received. BH_3-THF (Fluka), $LiBH_4$ (Aldrich) and 9-BBN dimer (Aldrich) were stored under an inert atmosphere and used as received.

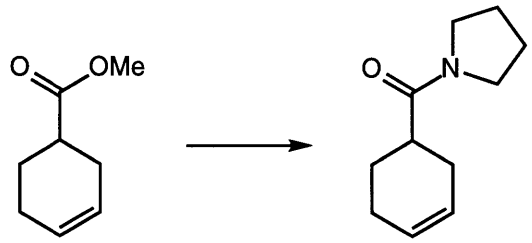
Pentane, tetrahydrofuran, ether, and benzene were dried and deoxygenated by refluxing and distilling from sodium/benzophenone under a nitrogen atmosphere. Toluene was dried and deoxygenated by refluxing and distilling from sodium. Dichloromethane was stored over and distilled from CaH_2. *N,N*-Dimethylformamide was dried over 4Å sieves. Deuterated solvents were obtained from Cambridge Isotope Laboratories. $CDCl_3$ was dried over Na_2CO_3 before use and d_8-THF was vacuum transferred; CD_2Cl_2 was used as received.

$IndRh(C_2H_4)_2$ was prepared by a method analogous to that reported by Green and Marder for $Ind^*Rh(C_2H_4)_2$ ($Ind^* = \eta^5$-1,2,3-$Me_3C_9H_4$).[50] Chlorobis-(ethylene)rhodium(I) dimer (Strem) was used as received. Indene (Aldrich) was purified by distillation. *n*-BuLi in hexanes (Aldrich) was titrated before each use. Although $IndRh(C_2H_4)_2$ does not appear to decompose after short periods (6 days) of

exposure to the atmosphere, we recommend that it be stored under vacuum, nitrogen, or argon.

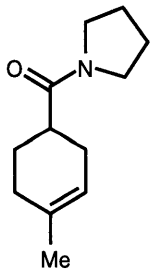
Catecholborane (CB) was obtained from Aldrich, Fluka, and Eastman Fine Chemicals and distilled at reduced pressure. We have found that commercial catecholborane is sometimes contaminated with dimethyl sulfide derived impurities (^{1}H NMR: δ 2.0-2.5 in $CDCl_3$) which are difficult to remove by distillation. The presence of these contaminants can have a deleterious effect on the stereoselectivity and/or activity of the catalyst. 2,2'-*o*-Phenylenedioxybis(1,3,2-benzodioxaborole) ($B_2(cat)_3$) was prepared via the method of Männig and Nöth.[45]

PREPARATION OF SUBSTRATES



Synthesis of Amides from Esters. Representative Procedure. Pyrrolidine (2.311 g, 32.50 mmol) was added to a flask containing methyl-3-cyclohexene carboxylate (1.495 g, 10.66 mmol; Pfaltz and Bauer). The resulting solution was refluxed for 65 h, then cooled to room temperature, diluted with EtOAc (15 mL), and washed with brine (20 mL), 2N HCl (2 x 20 mL), and then brine (2 x 20 mL). The solution was then dried (Na_2SO_4) and concentrated. Column chromatography (80% EtOAc/hexane) afforded 1.097 g (57%) of a white solid.[51]

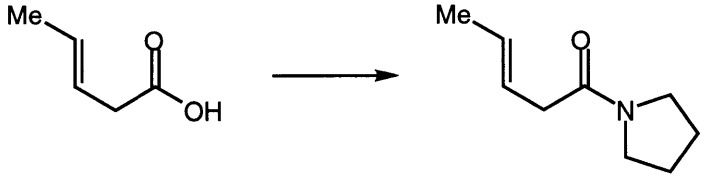
^{1}H NMR (300 MHz, $CDCl_3$) δ 1.7-2.1 (m, 9H), 2.33 (m, 1H), 2.66 (m, 1H), 3.45 (m, 4H), 5.87 (m, 2H).



1-[(4-methyl-3-cyclohexen-1-yl)carbonyl] pyrrolidine [99583-78-5]. Synthesized from the corresponding methyl ester, which was prepared by $AlCl_3$ (Aldrich)-catalyzed Diels-Alder reaction of isoprene (Aldrich) and methyl acrylate (Aldrich).

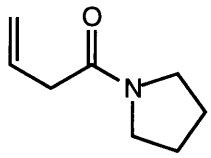
^{1}H NMR (300 MHz, $CDCl_3$) δ 1.65 (s, 3H), 1.7-2.1 (m, 9H), 2.28 (m, 1H), 2.51 (m,

1H) 3.46 (m, 4H), 5.40 (m, 1H); ^{13}C (125 MHz, $CDCl_3$) δ 22.8, 23.6, 25.0, 25.5, 27.0, 29.1, 38.0, 45.0, 45.7, 119.2, 132.6, 173.8; IR (neat) 3480, 2963, 2930, 2873, 1635, 1436, 1354, 1278, 1227, 1192, 1168, 915, 800, 533 cm^{-1}; HRMS *m/z* 193.1467 [M^+], calcd for $C_{12}H_{19}NO$: 193.1466.



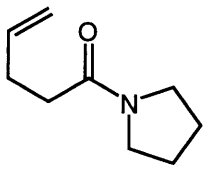
Synthesis of Amides from Acids. Representative Procedure. To a flask containing pent-3-enoic acid (510 μL, 5.01 mmol; Fluka), dichloromethane (22 mL), and pyrrolidine (460 μL, 5.51 mmol) was added EDC (1.09 g, 5.67 mmol; Aldrich). The resulting homogeneous solution was stirred for 24 h at room temperature. The solution was then diluted with EtOAc (20 mL) and extracted with brine (3 x 10 mL). The organic layer was dried (Na_2SO_4) and concentrated. Column chromatography (EtOAc) afforded 760 mg (99% yield) of a light yellow oil.

Pent-3-enoic acid, pyrrolidine amide. ^1H NMR (300 MHz, $CDCl_3$) δ 1.65 (d, J = 3.5, 3H), 1.81 (m, 2H), 1.89 (m, 2H), 2.96 (d, J = 5.3, 2H), 3.40 (q, J = 7.2, 4H), 5.53 (m, 2H); ^{13}C (125 MHz, $CDCl_3$) δ 17.0, 23.4, 25.2, 38.1, 44.7, 45.6, 123.1, 127.1, 168.8; IR (neat) 2970, 2874, 1639, 1436, 1340, 1254, 1227, 1192, 1189, 967 cm^{-1}; HRMS *m/z* 153.1153 [M^+], calcd for $C_9H_{15}NO$: 153.1154.



But-3-enoic acid, pyrrolidine amide [107364-68-1]. Prepared from the corresponding acid (Aldrich).

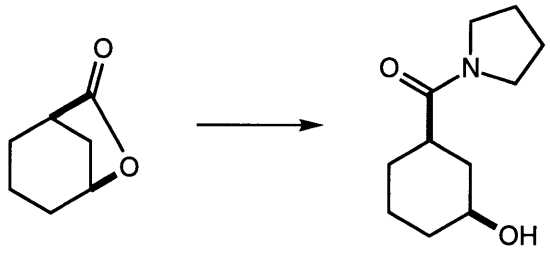
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.81 (m, 2H), 1.91 (m, 2H), 3.04 (d, J = 7.0, 2 H), 3.39 (m, 4H), 5.0 - 5.1 (m, 2H), 5.93 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.2, 24.9, 38.8, 44.4, 45.3, 116.0, 130.5, 167.7; IR (neat) 2973, 2874, 1647, 1439, 1341, 1297, 1227, 1192, 994, 913 cm^{-1}; HRMS *m/z* 139.0998 [M^+], calcd for $C_8H_{13}NO$: 139.0997.



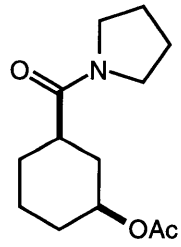
Pent-4-enoic acid, pyrrolidine amide [81911-99-1]. [52] Prepared from the corresponding acid (Aldrich).

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.81 (m, 4H), 2.35 (m, 4H), 3.38 (t, J = 6.6, 2H), 3.43 (t, J = 6.9, 2H), 4.94 (m, 2H), 5.83 (m, 1H).

PREPARATION OF AUTHENTIC PRODUCTS

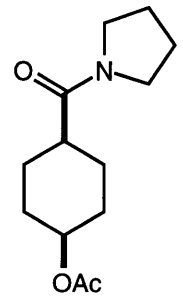


Hydroxyamides from Lactones. Representative Procedure. The lactone[53] (0.405 g, 0.321 mmol) and pyrrolidine (100 μL, 1.20 mmol) were added to a Schlenk flask. The sealed Schlenk was heated in a 75 °C oil bath for 3 days. The solution was cooled to r.t. and concentrated, providing a brown oil. Column chromatography (40% dichloromethane/EtOAc, then 100% EtOAc) afforded 28.8 mg (46%) of a light yellow oil.



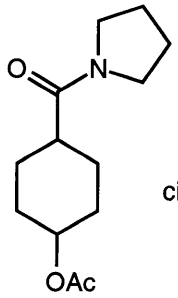
***cis* -1-[(3-hydroxycyclohexyl)carbonyl] pyrrolidine, acetate [133910-49-3].** Prepared by acetylation of the hydroxyamide.

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.3-2.0 (m, 15H), 2.43 (tt, J = 3.3, 11.7, 1H), 3.42 (m, 4H), 4.68 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1, 23.5, 24.1, 26.0, 27.6, 31.0, 33.8, 40.9, 45.6, 46.2, 72.2, 170.4, 172.6.



Prepared from the lactone[53] by reaction with pyrrolidine, followed by acetylation.

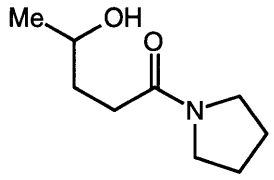
^{1}H NMR (300 MHz, $CDCl_3$) δ 1.5-2.1 (m, 15H), 2.36 (m, 1H), 3.43 (t, J = 6.9, 2H), 3.44 (t, J = 7.2, 2H), 4.98 (br t, J = 3.6, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1, 23.0, 24.0, 25.9, 28.9, 41.3, 45.6, 46.1, 68.4, 170.5, 173.8.



cis and trans isomers

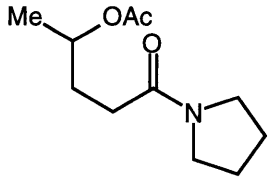
Prepared from a mixture of *cis*- and *trans*-hydroxyesters[53] by amide formation, followed by acetylation.

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.2-2.0 (m), 2.2-2.4 (m), 3.39 (m), 4.65 (m), 4.94 (br t, J = 3.0); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 21.4, 23.4, 24.2, 26.2, 27.0, 29.2, 31.0, 41.6, 45.8, 46.3, 68.7, 72.4, 170.7, 173.6, 174.0.



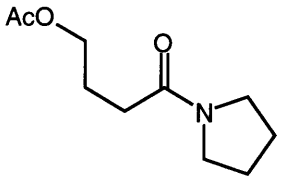
4-Hydroxypentanoic acid, pyrrolidine amide [116461-11-1]. Prepared from γ-valerolactone (Aldrich) by reaction with pyrrolidine.

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (d, J = 5.7, 3H), 1.7-1.9 (m, 6H), 2.42 (m, 2H), 3.41 (m, 4H), 3.7-3.8 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4, 24.2, 25.8, 31.3, 33.3, 45.6, 46.5, 67.1, 172.1.



4-Hydroxypentanoic acid, pyrrolidine amide, acetate. Prepared by acetylation of the alcohol (vide supra).

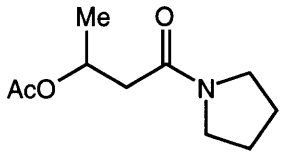
^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (d, J = 6.3, 3H), 1.7-2.0 (m, 9H), 2.20 (m, 2H), 3.30 (t, J = 6.9, 2H), 3.35 (t, J = 6.9, 2H), 4.83 (sextet, J = 6.0, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.0, 21.2, 24.3, 25.9, 30.5, 30.8, 45.5, 46.4, 70.5, 170.5, 170.6.



4-Butanoic acid, pyrrolidine amide, acetate. Prepared from γ-butyrolactone

(Aldrich) by reaction with pyrrolidine **[73200-24-5]**, followed by acetylation.

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.7-1.9 (m, 9H), 2.22 (t, J = 6.9, 2H), 3.31 (m, 4H), 4.00 (t, J = 6.3, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 23.8, 24.2, 25.9, 30.8, 45.6, 46.4, 63.8, 170.5, 170.9.

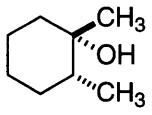


3-Hydroxybutanoic acid, pyrrolidine amide, acetate. Prepared from (±)-β-butyrolactone (Aldrich) by reaction with pyrrolidine, followed by acetylation.

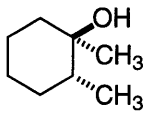
^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (d, J = 6.3, 3H), 1.8-2.0 (m, 7H), 2.36 (dd, J = 6.9, 15.3, 1H), 2.64 (dd, J = 6.9, 15.0, 1H), 3.40 (m, 4H), 5.27 (sextet, J = 6.6, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.0, 21.2, 24.2, 26.0, 40.9, 45.5, 46.7, 68.0, 168.1, 170.1.

1,2-Dimethylcyclohexanol (Table 1A.2, Entry 6). Methyl lithium in ether (9.5 mL, 1.4 M, 13 mmol) was added to a flask by syringe. The solution was cooled to -78 °C and 2-methylcyclohexanone (1.10 mL, 9.06 mmol) in ether (10 mL) was added dropwise over 30 minutes. The solution was warmed to r.t. for 1h, then cooled to 0 °C and an aqueous solution of saturated ammonium chloride (20 mL) was added slowly. The solution was stirred briefly and then diluted with ether. The ether solution was extracted with water (1X) and brine (1X). The organic layer was separated, dried over $MgSO_4$, filtered and the solvents removed. Column chromatography (silica gel, 20% ether/pentane) afforded samples of >95% purity (by GC) of both *cis-* and *trans-* 1,2-dimethylcyclohexanol. Proof of stereochemistry is based on comparison of the GC retention time of the product from a hydroboration

of 1,2-dimethyl cyclohexene.



***trans*- 1,2-dimethyl cyclohexanol [19879-11-9].** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (d, J = 6.2, 3H), 1.13 (s, 3H), 1.1-1.6 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.1, 22.1, 26.0, 28.6, 30.7, 40.0, 40.3, 70.9; TLC (20% ether/pentane, *p*-anisaldehyde-blue) R_f = 0.50.



***cis*- 1,2-dimethyl cyclohexanol [19879-12-0].** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (d, J = 6.7, 3H), 1.04 (s, 3H), 1.2-1.6 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.4, 20.9, 24.2, 25.4, 32.1, 41.4, 42.4, 73.2; TLC (20% ether/pentane, *p*-anisaldehyde-blue) R_f = 0.38.

****

In order to analyze by GC the isomer composition of the catalyzed/amide mediated hydroborations it was necessary to conduct regio *random* hydroboration reactions to obtain mixtures of all possible regioisomeric alcohols. This was accomplished through hydroboration with borane-THF. *Specific* isomers that were not available commercially were generated by the above procedures.

STANDARD PROCEDURES

Uncatalyzed hydroboration with BH_3. Into a flask was weighed the substrate (0.206 mmol). The flask was cooled to -45 °C for 3 minutes and BH_3-THF (1M in THF, 0.19 mL, 0.19 mmol) was then added by syringe and the resulting solution was stirred with slow warming to r.t. for 1.25 hours.

Oxidative workup.[20]

Basic. To the 0 °C hydroboration solution was added 1/1 THF/EtOH (2 mL per mmol of substrate) and then 2N NaOH (2 mL per mmol of substrate) followed by 30% H_2O_2 (2 mL per mmol of substrate). The solution was stirred (with slow warming to room temperature) for 2 h.

Neutral. To the 0 °C hydroboration solution was added 1/1 THF/EtOH (2 mL per mmol of substrate) and then pH 7 buffer (2 mL per mmol of substrate) followed by 30% H_2O_2 (2 mL per mmol of substrate). The solution was stirred (with slow warming to room temperature) for 12 hours.

$IndRh(olefin)_2$ CATALYZED HYDROBORATIONS

The yields and selectivities of the preparative scale $IndRh(C_2H_4)_2$-catalyzed hydroborations that are reported in the manuscript represent an average of two runs using two independently prepared batches of $IndRh(C_2H_4)_2$ and catecholborane.

Oxidative workup. Basic oxidative workups were performed.

Acetylation. As indicated in Table 1A.1, many of the reaction products were derivatized as the corresponding acetates. This conversion was necessitated by the difficulty encountered in purifying the highly polar hydroxyamides. Procedure: The oxidized reaction mixture was passed through a plug of silica gel with acetone as the eluent, concentrated, and then acetylated (cat. DMAP, excess Ac_2O, excess NEt_3, CH_2Cl_2, 0 °C → r.t.; 3 h). The CH_2Cl_2 was removed, and the residue was brought up in EtOAc and washed twice with sat $NaHCO_3$. The combined aqueous layers were extracted with EtOAc. The combined organic layers were dried ($MgSO_4$) and concentrated. Column chromatography (EtOAc) provided the acetylated product. In some cases, the product was contaminated by a residual NEt_3-derived impurity, which could be removed by extraction (EtOAc/sat $NaHCO_3$) followed by column chromatography.

Amide-directed hydroboration of olefins. Representative procedure (Eq 1A.1). Dichloromethane (0.54 mL) and the olefin (0.130 g, 0.846 mmol) were added to a flask containing $IndRh(C_2H_4)_2$ (6.0 mg, 0.022 mmol). The resulting homogenous, light yellow solution was stirred in a room temperature water bath while CB (0.220 mL, 2.06 mmol) was added by syringe over 0.5 min. The reaction was stirred at r.t. for one hour, then subjected to an oxidative workup. An aliquot was removed for GC analysis, and the remainder was purified by flash chromatography.

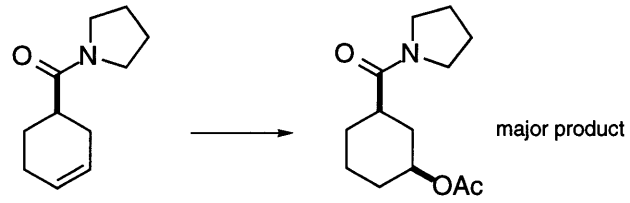


Table 1A.1, Entry 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.2-2.0 (m), 2.39 (br t), 3.30 (m), 4.64 (m), 4.9 (m), 5.1 (m); ^{13}C NMR (75 MHz, $CDCl_3$) (major isomer) δ 21.3, 23.6, 24.2, 26.1, 27.7, 31.2, 33.9, 41.1, 45.7, 46.3, 72.4, 170.6, 172.8; IR (neat) 2942, 2868, 1732, 1634, 1440, 1363, 1246, 1033 cm^{-1}; Anal. Calcd for $C_{13}H_{21}NO_3$: C, 65.25; H, 8.84. Found: C, 65.36; H, 8.87. GC analysis showed *cis*-1,3 : *trans*-1,3 : *cis*-1,4 : *trans*-1,4 = 80 : 7 : 6 : 6.

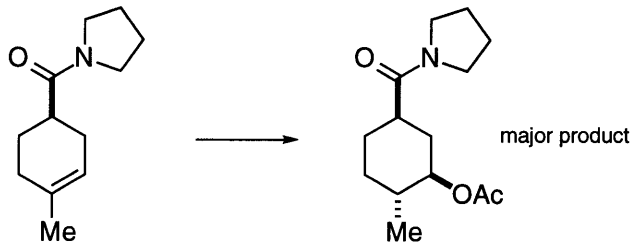


Table 1A.1, Entry 2. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (d, J = 6.3, 3H,), 1.0-1.2 (m, 1H), 1.5-2.1 (m, 13H), 2.45 (tt, J = 3.3, 11.4, 1H), 3.43 (m, 4H), 4.42 (dt, J = 4.8, 11.7, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.8, 20.8, 23.9, 25.8, 27.6, 32.3, 33.4, 36.2, 40.9, 45.5, 46.0, 76.5, 170.6, 172.5; IR (neat) 2955, 2932, 2873, 1731, 1634, 1441, 1362, 1245, 1034 cm^{-1}; Anal. Calcd for $C_{14}H_{23}NO_3$: C, 66.37; H, 9.15. Found: C, 66.30; H, 9.29. R_f = 0.38 (EtOAc). GC analysis showed 95 : 5 selectivity.

The stereochemical assignment is based on an analysis of ^{1}H NMR coupling constants. Hydroboration with borane-THF predominantly affords the opposite isomer (<2 : 1 selectivity).

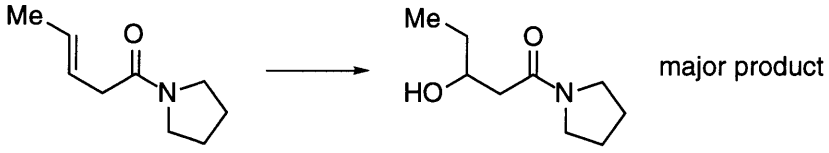


Table 1A.1, Entry 3. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J = 7.2, 3H), 1.3-1.6 (m, 2H), 1.8-2.0 (m, 4H), 2.23 (dd, J = 9.3, 16.2, 1H), 2.42 (dd, J = 2.1, 16.5, 1H), 3.3-3.5 (m, 4H), 3.93 (m, 1H), 4.45 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.9, 24.3, 25.9, 29.3, 40.1, 45.4, 46.5, 69.3, 171.4; IR (neat) 3417, 2965, 2876, 1616, 1455 cm^{-1}; Anal. Calcd for $C_9H_{17}NO_2$: C, 63.13; H, 10.01. Found: C, 63.14; H, 10.24. R_f = 0.15 (EtOAc). GC analysis showed 3-hydroxy : 4-hydroxy = 94 : 6.

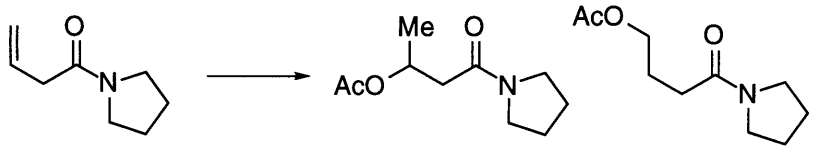
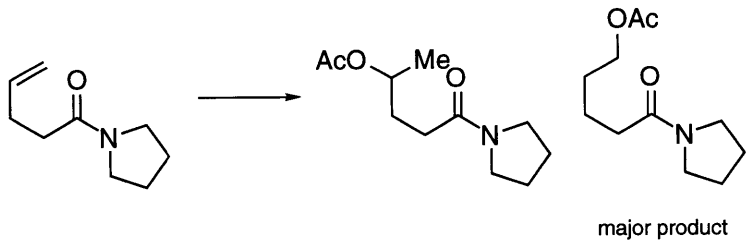


Table 1A.1, Entry 4. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (d, J = 6.3), 1.8-2.0 (m), 2.29 (t, J = 7.5), 2.35 (dd, J = 6.6, 14.7), 2.64 (dd, J = 6.6, 15.0), 3.3-3.5 (m), 4.08 (t, J = 6.3), 5.26 (sextet, J = 6.3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.0, 20.9, 21.2, 23.9, 24.2, 25.9, 30.8, 40.9, 45.5, 45.6, 46.4, 46.6, 63.8, 68.0, 168.0, 170.1, 170.3, 170.9; IR (neat) 2974, 2876, 1732, 1633, 1454, 1372, 1245, 1064, 1038 cm^{-1}; Anal. Calcd for $C_{10}H_{17}NO_3$: C, 60.28; H, 8.60. Found: C, 60.04; H, 8.83. R_f = 0.10-0.20 (EtOAc). GC analysis showed 3-acetoxy : 4-acetoxy = 1.05 : 1.00.



major product

Table 1A.1, Entry 5. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (d, J = 6.3), 1.6-2.0 (m), 2.22 (m), 3.35 (m), 4.01 (t, J = 3.9), 4.86 (sextet, J = 6.3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.0, 20.9, 21.2, 21.3, 24.3, 26.1, 28.3, 30.6, 30.9, 34.0, 45.6, 45.7, 46.5, 46.6, 64.1, 70.6, 170.7, 171.1; IR (neat) 2954, 2874, 1737, 1644, 1436, 1368, 1243, 1039 cm^{-1}; Anal. Calcd for $C_{11}H_{19}NO_3$: C, 61.95; H, 8.98. Found: C, 61.66; H, 8.81; R_f = 0.0-0.25 (streak; EtOAc). GC analysis showed 4-acetoxy : 5-acetoxy = 1 : 2.8.

Mercury test for homogeneity. $IndRh(C_2H_4)_2$ (0.9 mg, 0.003 mmol), CH_2Cl_2 (100 μL), and 1-(4-methylcyclohex-3-enylcarbonyl)pyrrolidine (29.9 mg, 0.155 mmol) were added to a flask containing a drop of mercury. The resulting light yellow solution was stirred for 5 min, and then CB (40 μL, 0.38 mmol) was added dropwise by syringe. The solution was stirred at r.t. for 1.75 h. After an oxidative workup, the reaction mixture was passed through a plug of silica gel with acetone as the eluent. The resulting solution was dried (Na_2SO_4), concentrated, and then acetylated. The acetylated reaction mixture was partitioned (EtOAc/sat $NaHCO_3$). The aqueous layer was extracted with EtOAc (6 X), and the combined organic layers were analyzed by GC, which showed complete conversion and a 45 : 1 (cis : trans) mixture of isomers.

Hydroboration of 1-dodecene (Eq 1A.2). In the glove box, $IndRh(C_2H_4)_2$ (1.1 mg, 0.004 mmol), 1-dodecene (32.5 μL, 0.146 mmol), and CD_2Cl_2 (100 μL) were added by syringe to a vial, and the resulting light yellow solution was stirred until homogeneous. The vial was placed in a room temperature solvent bath, and then

CB (40 μL, 0.38 mmol) was added dropwise by syringe. The solution bubbled gently upon addition of CB. The reaction mixture was stirred for 1 h and then subjected to an oxidative workup. After 2 h, the reaction mixture was partitioned (EtOAc/1N NaOH saturated with sodium chloride), and the aqueous layer was extracted three times with EtOAc. The combined organic layers were dried ($MgSO_4$) and concentrated to afford a light brown semi-solid. GC analysis of an aliquot of the reaction mixture showed 1-dodecanol : 2-dodecanol : dodecyl aldehyde : dodecane = 23 : 3 : 45 : 29; 1-dodecene was completely consumed.

Hydroboration of 1-dodecene in the presence of an amide (Eq 1A.3). $IndRh(C_2H_4)_2$ (1.1 mg, 0.004 mmol), the pyrrolidine-derived amide of palmitoyl chloride (50.7 mg, 0.164 mmol), 1-dodecene (33 μL, 0.15 mmol), and then CH_2Cl_2 (100 μL) were introduced into a flask. The reaction mixture was stirred until homogeneous, then cooled to -40 °C. CB (39 μL, 0.37 mmol) was then added dropwise by syringe. After the addition was complete, the solution was warmed to r.t. and stirred for 2.5 h, then subjected to an oxidative workup. After oxidation, the reaction mixture was passed through a plug of silica gel with acetone as the eluent. The resulting solution was concentrated, and the product, an oil, was analyzed by GC: 1-dodecanol : 2-dodecanol : dodecyl aldehyde : dodecane = 88 : 5 : 3 : 4; 1-dodecene completely consumed.

Effect of Lewis-basic solvents on the directed hydroboration (Eq 1A.4). Into a vial was weighed the catalyst (1.1 mg, 0.004 mmol). To this was added the butenoic acid, pyrrolidine amide (20.8 mg, 0.149 mmol), and the solvent (0.5 mL). The resulting light yellow solution was stirred and CB (38 μL, 0.36 mmol) was added dropwise. The solutions were then stirred for 2.5 h and oxidized. The solution was then extracted with EtOAc/NaOH and the aqueous layers dried over Na_2SO_4 and concentrated. The material was exhaustively acetylated to analyze for conversion and selectivity. The results are shown in Eq 1A.3.

Effect of catalyst changes on the directed hydroboration (Eq 1A.5). Into a vial was weighed the catalyst (0.003 mmol). To this was added 1-(4-methylcyclohex-3-enyl carbonyl) pyrrolidine (67.1 mg, 0.347 mmol) and CH_2Cl_2 (0.30 mL). The solutions were placed in a room temperature water bath and CB (69 μL, 0.65 mmol) was then added dropwise. The solutions were allowed stir at r.t. for 1 h. The solutions were then subjected to oxidative workup, followed by extraction, acetylation, and analysis by GC. The results are shown in Eq 1A.3.

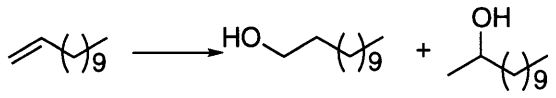
Background reaction (Eq 1A.6). Into a vial was weighed the 1-(4-methylcyclohex-3-enyl carbonyl) pyrrolidine (27.5 mg, 0.140 mmol). To this was added CH_2Cl_2 (100 μL) and the resulting solution was cooled to -30 °C. CB (40 μL, 0.38 mmol) was then added dropwise. The solution was kept cold for 5 minutes and then warmed to room temperature and stirred for 1 h. The solution was subjected to basic oxidative workup and the alcohol was filtered through a short plug of silica gel (acetone as eluent). The solution was concentrated and exhaustively acetylated. GC analysis showed 8% olefin remaining. The major products were confirmed to be the desired alcohol.

Uncatalyzed hydroboration of 1-dodecene in the presence of an amide (Eq 1A.7). 1-Dodecene (100.5 mg, 0.597 mmol), *N,N* -dimethylacetamide (60 μL, 0.69 mmol) and then CD_2Cl_2 (400 μL) were added to a vial. The reaction mixture was stirred until homogeneous, then cooled to -40 °C. CB (170 μL, 1.60 mmol) was then added dropwise by syringe. After the addition was complete, the solution was warmed to r.t. and stirred for 1 h, then subjected to an oxidative workup. After oxidation, the reaction mixture was passed through a plug of silica gel with acetone as the eluent. The resulting solution was concentrated, and the product, an oil, was analyzed by GC: 1-dodecanol : 2-dodecanol : dodecyl aldehyde : dodecane = 88 : 5 : 3 : 4; 1-dodecene completely consumed.

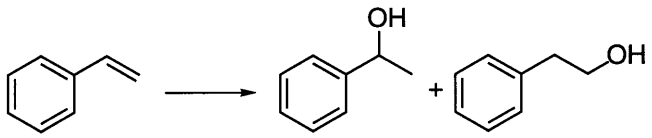
NON-TRANSITION METAL CATALYZED HYDROBORATIONS

The yields and selectivities of the preparative scale hydroborations that are reported in the manuscript represent an average of two runs using two independent batches of amide and catecholborane. Uncatalyzed reactions were performed on all substrates to determine the background activity of catecholborane. For all substrates, less than 10% hydroboration was seen during the time period utilized for the catalyzed reaction.

Catalyzed hydroboration with CB. Representative procedure (Eq 1A.8, Table 1A.2). Dodecene (228 μL, 1.03 mmol), *N,N*--dimethylacetamide (9.4 μL, 0.10 mmol) and CH_2Cl_2 (0.68 mL) were added by syringe to a flask. The resulting solution was cooled to 0 °C and CB (220 μL, 2.06 mmol) was added dropwise. Some bubbling of the solution was noted. The solution was stirred at 0 °C for 5 minutes and then at r.t. for 3 h.

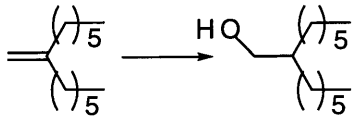


Dodecanol (Table 1A.2, Entry 2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, J = 6.9), 1.15 (d, J = 6.6), 1.23 (br s), 1.52 (q, J = 6.9), 3.61 (t, J = 6.9); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 23.3, 25.8, 26.0, 29.4, 29.5, 29.7, 32.0, 32.8, 62.7, 68.1; TLC (25% EtOAc/hexane, PMA - blue) 2-dodecanol R_f = 0.50, 1-dodecanol R_f = 0.42. GC analysis indicated 1°: 2° = 16 : 1.

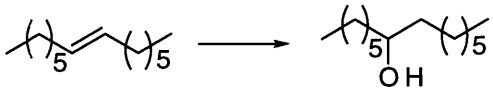


Phenethyl alcohol (Table 1A.2, Entry 1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.48 (d, J =

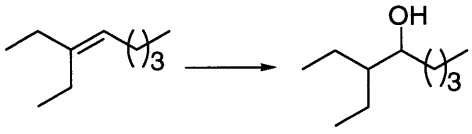
6.3), 1.77 (s), 2.85 (t, J = 6.0), 3.83 (t, J = 6.9), 4.86 (q, J = 6.3), 7.2-7.4 (m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.1, 39.1, 63.4, 70.1, 125.4, 126.3, 127.3, 128.3, 129.0, 138.6, 145.8. TLC (20% ether/pentane, PMA - blue) sec-Phenethyl alcohol R_f = 0.40, Phenethyl alcohol R_f = 0.24. GC analysis indicated 1°: 2° = 7 : 1.



2-Hexyl-1-octanol (Table 1A.2, Entry 3). ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, J = 7.0, 6H), 1.3-1.4 (br, 22H), 3.50 (d, J = 5.4, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1. 22.7. 26.9. 29.8. 31.0. 31.9. 40.6. 65.7; TLC (10% EtOAc/hexane, PMA - blue) R_f = 0.33. Major : Minor = >99 : 1.

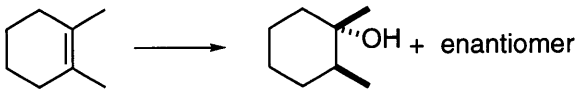


7-Tetradecanol (Table 1A.2, Entry 4). ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, J = 7.3, 1H), 1.3-1.4 (m, 24H), 3.56 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 25.7, 29.4, 29.5, 29.8, 31.9, 37.6, 72.0; TLC (10% EtOAc/hexane, PMA - blue) R_f = 0.41.



3-Ethyl-4-Octanol (Table 1A.2, Entry 5). ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, J = 7.4, 9H), 1.1-1.4 (m, 12H), 3.57 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.8, 11.9, 14.1,

21.2, 22.2, 22.8, 28.6, 33.8, 46.9, 73.2; TLC (10% ether/pentane, PMA - blue) R_f = 0.23. Major : Minor = 97 : 3.



1,2-dimethylcyclohexanol (Table 1A.2, Entry 6). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (d, J = 6.8, 3H), 1.04 (s, 4H), 1.3-1.6 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.4, 20.9, 24.2, 25.4, 32.1, 41.4, 42.3, 73.1; TLC (10% ether/pentane, PMA - blue) R_f = 0.15. 98% cis isomer.

Hydroboration of dodecene with no reagent purification. Dodecene (220 μL, 0.991 mmol) was added to a vial followed by *N,N*- dimethylacetamide (10.0 μL, 0.108 mmol) and CD_2Cl_2 (0.67 mL). The resulting solution was stirred and then cooled to 0 °C. CB (225 μL, 2.11 mmol) was then added and the solution was stirred open to air with slow warming to room temperature. The solution, which developed a light brown color, was stirred for 3 hours and then a basic oxidative workup was performed. GC analysis showed essentially complete conversion of alkene to alcohols. 1° : 2 ° = 15 : 1.

Uncatalyzed hydroboration with CB. Representative procedure. 1,2-Dimethyl-cyclohexene (66.2 mg, 0.60 mmol) was weighed into a flask. Dichloromethane (0.40 mL) was added and the resulting solution stirred, then cooled to 0 °C. CB (160 μL, 1.50 mmol) was then added by syringe and the solution was stirred with slow warming to room temperature for 3 h. GC analysis indicated <10% conversion of the olefin.

Hydroboration of dodecyne with CB and substoichiometric amide (Eq 1A.9). Dodecyne (210 μL, 0.982 mmol) was added to a vial followed by *N,N*- dimethyl acetamide (9.0 μL, 0.097 mmol) and CD_2Cl_2 (0.67 mL). The resulting solution was

stirred and then cooled to 0 °C. CB (220 μL, 2.06 mmol) was then added and the entire solution was transferred to an NMR tube.

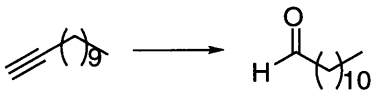
^{1}H NMR (CD_2Cl_2, 300 MHz) showed complete conversion of alkyne in one hour. ^{11}B NMR (CD_2Cl_2, 96.2 MHz) showed two peaks of equal intensity: δ 28 (d, J = 196, CB), 21.5 (s, vinyl boronate).

Neutral oxidative workup of the solution, followed by GC analysis confirmed the complete conversion of alkyne to dodecyl aldehyde (>85% of product mixture).

This reaction was repeated under identical conditions and analyzed by multinuclear NMR. The reaction progress is easily monitored by ^{1}H NMR. The acetylinic proton (δ 1.9, d of t, J = 2.0, 4.4, 1H) and α-CH_2 protons (δ 2.2, d of t, J = 2.0, 6.4, 2 H) disappear as the α-CH_2 (δ 2.4, q, J = 6.9, 2H) and internal olefinic H (δ 5.9, d of t, J = 1.5, 18.3) grow in. The large J_2 of the olefinic H indicates a *trans*- $J_{H\text{-}H}$ and therefore *cis*- addition of the B-H to the alkyne.

Upon complete consumption of dodecyne, the reaction mixture was analyzed by ^{13}C NMR. The presence of vinyl boronate ester was confirmed by comparison of spectral data with that of the authentic compound. The ^{11}B NMR shows a shoulder on the residual CB peak, indicating the presence of the vinyl boronate ester.

The authentic vinyl boronate ester was prepared via a thermal reaction of CB and dodecyne, and the spectral data compared for a confirmation of its presence in the above reaction.



Dodecyl aldehyde (Eq 1A.9). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (t, J = 6.8, 3H), 1.22 (s, 17H), 1.57 (quint, J = 7.3, 2H), 2.38 (d of t, J = 2.1, 7.2, 2H), 9.72 (t, J = 2.1, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.1, 22.7, 29.2, 29.3, 29.4, 29.5, 29.6, 32.0, 43.9, 202.9; TLC

(10% EtOAc in hexane, PMA - blue) R_f = 0.24. Major : Minor = 98 : 2.

Synthesis of dodecyl catechol boronate ester (RBcat) [BRN 7536183]. Dodecene (1.50 mL, 6.76 mmol) and CB (2.20 mL, 20.6 mmol) were added to a flask and stirred. The resulting solution was heated to 100 °C for 21 h, and then cooled to room temperature. The residual CB and dodecene were removed *in vacuo*. The resulting cloudy, white solution was diluted with pentane and filtered to remove solids. The solvents were removed from the resulting solution and the process repeated until no solids remained after dilution of the material with pentane. The resulting clear, colorless oil was stored until further use. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J = 6.7, 3H), 1.18 (t, J = 7.4, 2H), 1.3 (s, 19H), 1.59 (m, 3H), 6.82 (m, 2H), 7.07 (m, 1H). ^{11}B NMR (96.2 MHz, $CDCl_3$) δ 35.5 (s, RBcat), 22.6 (s, $B_2(cat)_3$). The peaks were seen in a 6 : 1 ratio. ^{13}C NMR (75 MHz, CD_2Cl_2) δ 14.7, 23.5, 24.5, 30.2, 30.4, 30.5, 32.7, 33.1, 112.8, 123.1, 149.1.

Stability of dodecyl catechol boronate ester. Dodecyl catechol boronate ester (209.7 mg) was weighed into a vial under inert atmosphere. The material was then chromatographed (silica gel, 2% ethyl acetate/hexane to 100% ethyl acetate) under ambient atmosphere yielding 212.8 mg (> 100% yield) dark brown oil. ^{11}B NMR (96.2 MHz, $CDCl_3$) δ 35.4 (s, RBcat, 2.3 B), 23.3 (s, 1B). ^{1}H NMR (300 MHz, $CDCl_3$) was not consistent with the desired product.

Synthesis of dodecyl pinacol boronate via amide catalyzed hydroboration (Eq 1A.10). Dodecene (90 μL, 0.41 mmol), *N,N*- dimethylacetamide (4 μL, 0.04 mmol), and CH_2Cl_2 (0.26 mL) were added to a flask and the resulting solution stirred, then cooled to -45 °C. CB (85 μL, 0.80 mmol) was then added to the solution. The solution was stirred with slow warming to room temperature for 3 h. The solvents were removed *in vacuo* and a solution of pinacol (145 mg, 1.23 mmol) in THF (1 mL) was added to the remaining oil. The resulting solution was stirred at room temperature for 19 h.

The solvents were removed from the solution *in vacuo* and the resulting material was chromatographed (silica gel, 2% ethyl acetate/hexane). Product fractions (analyzed by TLC, 10% ethyl acetate/hexane, PMA stain, R_f 0.33), were combined, filtered and solvents removed resulting in 0.058 g (48%) of a very pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.73 (t, J = 7.7, 2H), 0.85 (t, J = 7.1, 3H), 1.22 (s, 30H), 1.35 (m, 2H). ^{11}B NMR (96.2 MHz, $CDCl_3$) δ 33.8 (s, RBpin). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.8, 24.1, 24.9, 29.4, 29.5, 29.7, 29.8, 32.0, 32.5, 82.9.

Synthesis of dodecyl pinacol boronate [177035-82-4] via catechol boronate ester. Dodecyl catechol boronate ester (212 mg, 0.74 mmol) was weighed into a flask. To this was added a solution of pinacol (267 mg, 2.26 mmol) in THF (1.50 mL) and the resulting solution was stirred at room temperature for 18 h.[29]

The solvents were removed from the solution *in vacuo* and the resulting material was chromatographed (silica gel, 2% ethyl acetate in hexane). Product fractions were analyzed by TLC (10% ethyl acetate/hexane, PMA stain, R_f = 0.33), combined, filtered and solvents removed resulting in 0.20 g (93%) of a very pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.74 (t, J = 8, 2H), 0.85 (t, J = 7, 3H), 1.22 (br s, 30 H), 1.37 (m, 2H). ^{11}B NMR (96.2 MHz, $CDCl_3$) δ 34.0 (s, RBpin). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.8, 24.1, 24.9, 29.4, 29.5, 29.7, 29.8, 32.0, 32.5, 82.8.

Synthesis of tri(dodecyl)boron [14245-38-6]. Dodecene (1.0 mL, 4.5 mmol) was added to a Schlenk reaction flask followed by the BH_3-THF (1.5 mL, 1.5 mmol). Bubbling was observed with this addition. The flask was sealed under inert atmosphere and then stirred at room temperature for 12 h.

The solvents were removed *in vacuo* resulting in a thick oil. NMR analysis was consitent with published data. ^{11}B NMR (96.2 MHz, $CDCl_3$) δ 85.7 (br s, R_3B), ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, J = 7.0, 3H), 1.16 (q, J = 7.8, 2H), 1.24 (s, 17H), 1.35 (m, 3H), and ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 22.9, 24.7, 28.5, 29.6, 29.9, 32.2, 33.3, 33.4.

Synthesis of dodecyl pinacol boronate via tri(dodecyl) boron. Tridodecyl boron

(370 mg, 0.71 mmol) was weighed into a vial. A solution of pinacol (260 mg, 2.20 mmol) in THF (1.45 mL) was then added and the resulting solution was stirred for 17.5 h. The solvents were removed *in vacuo* and the resulting oil was analyzed by NMR. ^{11}B NMR (96.2 MHz, CH_2Cl_2) δ 82 (br s, R_3B).

Reaction of CB and *N,N*-Dimethylacetamide. *N,N*-Dimethylacetamide (55 μL, 0.59 mmol) was added to CD_2Cl_2 (0.40 mL) in an NMR tube. CB (45 μL, 0.42 mmol) was then added by syringe. Some bubbling was noted. ^{11}B NMR (96.2 MHz, CD_2Cl_2) δ 14.0 (s, $[B(cat)_2]^-$)[42] , 8.4 (s), -10 (q, J = 96, amide-BH_3). This reaction is complete in <16 minutes, showing no evidence of remaining CB (^{11}B NMR, 96.2 MHz, CD_2Cl_2; 28, d, J = 173, CB). The ratio of products is essentially the same at all times analyzed (between 0 and 3.5 h).

Reaction of BH_3-THF with *N,N*-dimethylacetamide (Figure 1A.1). *N,N*-Dimethylacetamide (100 μL, 1.08 mmol) was added to a vial via syringe. To this was added the BH_3-THF (1.1 mL, 1.1 mmol). Some effervescence was seen with the addition. The solution was quickly transferred to an NMR tube and analyzed by ^{11}B NMR. The spectrum showed almost complete conversion to the predicted 'BH_3-amide' species (δ -9.5, q, J = 86).

Reaction of CB with 5 mol% amide (Figure 1A.2). *N,N*- Dimethylacetamide (9.5 μL, 0.10 mmol) was added to a vial followed by CD_2Cl_2 (0.70 mL). The resulting solution was stirred, cooled to -45 °C, and CB (220 μL, 2.06 mmol) was then added. The clear, colorless solution was warmed to r.t. and transferred to an air-free NMR tube. ^{11}B NMR (96.2 MHz, CD_2Cl_2) t=30 min. δ -10.2 (q, J = 94, amide-BH_3), 18.9 (s), 21.0 (s, $B_2(cat)_3$), 28.3 (d, J = 195, CB). The identity of the peak at 21 ppm was confirmed by doping of the sample with independently prepared $B_2(cat)_3$.

The reaction was repeated under identical conditions which showed, by ^{11}B NMR (CD_2Cl_2, 96.2 MHz), the presence of BH_3-amide (2-3%) in as little as 3 minutes.

Hydroboration of dodecene with CB and substoichiometric amide. Dodecene

(220 μL, 0.991 mmol) was added to a vial followed by *N,N*- dimethyl acetamide (9.5 μL, 0.10 mmol) and CD_2Cl_2 (0.70 mL). The resulting solution was stirred and then cooled to 0 °C. CB (220 μL, 2.06 mmol) was then added and the entire solution was transferred to an NMR tube.

The reaction was followed by ^1H and ^{11}B NMR. ^1H NMR (CD_2Cl_2, 300 MHz) was used to analyze conversion by loss of olefinic resonances at δ 4.9 and 5.8 ppm. ^1H NMR at 2 h showed 68% conversion of the olefin. ^{11}B NMR (CD_2Cl_2, 96.2 MHz) at 2 h showed δ 88 (br s, R_3B), 35 (s, $RB(OR)_2$), 28 (d, J = 196, CB), 22 (s, $B_2(cat)_3$), and -11 (q, BH_3-amide, J = 106). After 30 hours no R_3B was seen and a new peak at 60 ppm was noted.

Disproportionation reaction of R_3B and B_2cat_3 (Eq 1A.12). Into a screw-cap NMR tube was weighed the B_2cat_3(**1A.1**) (173.3 mg, 0.501 mmol). To this was added CD_2Cl_2 (0.6 mL) and the R_3B (26.1 mg, 0.050 mmol). The NMR tube was sealed and analyzed by ^{11}B and ^{13}C NMR. No indication of RBcat was seen, even after 17 h.

Disproportionation reaction of tri(dodecyl) boron and CB (Eq 1A.13). Tri(dodecyl) boron (288 mg, 0.56 mmol) was weighed into an NMR tube and CH_2Cl_2 (0.65 mL) then added. CB (210 μL, 1.97 mmol) was added dropwise and solution shaken, then analyzed after 13 min. by ^{11}B NMR (96.2 MHz, CH_2Cl_2) δ 87 (br s, R_3B), 28 (d, J = 195, CB). After 3 h, 6% yield of dodecyl boronate ester was seen: δ 36 (s, RBcat), 28 (d, J = 195, CB). After four days, the yield of dodecyl catecholboronate ester was still increasing with respect to the residual CB. Some diborane (17.7, t of t, J = 44, 139) was also seen.

This reaction was repeated under identical conditions, and the presence of RBcat was confirmed by ^{13}C NMR.

Disproportionation reaction of tri(dodecyl) boron and CB in the presence of amide (Eq 1A.13). Tri(dodecyl) boron (252 mg, 0.49 mmol) was weighed into an NMR tube. *N,N*- Dimethylacetamide (9 μL, 0.1 mmol) and CH_2Cl_2 (0.63 mL) were

then added. CB (210 μL, 1.97 mmol) was added dropwise and the solution shaken, then analyzed after 20 min. by ^{11}B NMR (96.2 MHz, CH_2Cl_2) δ 86 (br s, R_3B), 28 (d, J = 195, CB), 21 (s, $B_2(cat)_3$), 20 (s), 8 (s), -10 (q, J = 102, BH_3-amide). After 3 h, 7% yield of dodecyl boronate ester was seen: δ 35 (s, RBcat), 28 (d, J = 194, CB), 21 (s, $B_2(cat)_3$), -10 (q, J = 98, BH_3-amide). After several days, the yield of dodecyl catecholboronate ester was still increasing with respect to the residual CB and the presence of diborane (17.7, tt, J = 44, 139) was also noted.

Disproportionation of triethylboron and CB (Eq 1A.13). Triethylboron (30 μL, 0.21 mmol), CD_2Cl_2 (0.5 mL), and CB (110 μL, 1.03 mmol) were added to a screw-cap NMR tube and the resulting homogeneous, clear solution was sealed under nitrogen and analyzed after 48 min by ^{11}B NMR (96.2 MHz, CD_2Cl_2) δ 86.3 (br s, R_3B), 35.5 (s, RBcat), 28.5 (d, J = 195, CB), 16 (dt, J = 44, 139, B_2H_6). After 5 h, 56% yield of ethyl boronate ester was seen: δ 35.5 (s, RBcat), 28.5 (d, J = 195, CB).

Disproportionation reaction of CB with BH_3-THF (Eq 1A.15). BH_3-THF (0.10 mL, 0.10 mmol) was added to a flask followed by CD_2Cl_2 (0.60 mL), CB (225 μL, 2.11 mmol) and dodecene (220 μL, 0.991 mmol). The resulting solution was then transferred to an air-free NMR tube and the reaction followed by ^1H and ^{11}B NMR.

After 5 h, ^{11}B NMR (96.2 MHz, CD_2Cl_2) showed RBcat (δ 35.3, s) increasing with respect to CB (δ 28.1, d, J = 190). R_3B (δ 88.1, br s) was also seen as a very minor component of the mixture. Over time, RBcat continued to increase with respect to CB. At 22 h, it appeared that the disproportionation reaction was still continuing: R_3B was still present and the amount of RBcat was still increasing. Between 22 h and 49 h the dodecene was completely consumed (^1H NMR).

Hydroboration of dodecene with CB in the presence of $LiBH_4$.[44] Lithium borohydride (2.7 mg, 0.12 mmol) was weighed into a vial followed by addition of d_8-THF (0.7 mL) and CB (110 μL, 1.03 mmol). The entire solution was transferred to an air-free NMR tube, and the reaction was observed by ^{11}B-NMR (THF, 96.2 MHz).

After 5 min. no $LiBH_4$ was seen (δ -41.7, quintet, J=94). BH_3-THF (δ -0.6, q, J = 102), $[Bcat_2]^-$ [29](δ 14.7, s), and CB (δ 23.7, d, J = 187) were seen.

Dodecene (230 μL, 1.04 mmol) was then added and the reaction observed by ^1H (d_8-THF, 300 MHz) and ^{11}B NMR (d_8-THF, 96.2 MHz). After 1 h no olefin was seen in the ^1H NMR. ^{11}B NMR (96.2 MHz) indicated the presence of an unidentified peak at δ16.8 (s) as well as CB (δ 24.6, d, J = 188), RBcat (δ 35, v small), and R_3B (δ 84.0, br s). ^{13}C NMR (75 MHz) indicated that R_3B is the major product of this reaction.

The reaction solution was then oxidized, extracted and analyzed by GC. Complete consumption of olefin was seen. The product mixture consisted of 7% olefin reduction and a ratio of 1-dodecanol : 2-dodecanol of 22 : 1.

Disproportionation reaction of CB and 9-BBN (Eq 1A.16). 9-BBN (12.8 mg, 0.052 mmol, 0.104 mmol B-H) was weighed into a flask. CD_2Cl_2 (0.65 mL) was added, followed by CB (220 μL, 2.06 mmol) and dodecene (230 μL, 1.04 mmol). The resulting homogeneous solution was transferred to an air-free NMR tube, and the reaction was followed by ^1H and ^{11}B NMR.

After 5 h, ^{11}B NMR (96.2 MHz, CD_2Cl_2) showed RBcat (δ 35.4, s) increasing with respect to CB (δ 28.5, d, J = 191). R_3B (δ 88.1, br s) was also seen as a minor component of the mixture. Over time, RBcat continued to increase with respect to CB. Between 8.3 h and 22 h the dodecene was completely consumed (^1H NMR). At 22 h, it appeared that the disproportionation reaction was still continuing: R_3B was still present, and the amount of RBcat was still increasing.

This reaction was repeated under identical conditions and the presence of RBcat confirmed by ^{13}C NMR.

ANALYSIS OF THE HYDROBORATION AGENT IN DIRECTED, METAL-CATALYZED HYDROBORATIONS

Reaction of 1-(4-methylcyclohex-3-enyl carbonyl) pyrrolidine with BH_3-THF (Eq 1A.17). Into a vial was weighed the olefinic amide (29.4 mg, 0.152 mmol). THF (50 μL) was added and the solution cooled to -30 °C. To this solution was added the BH_3-THF (1M, 50 μL, 0.050 mmol). The solution was kept cold for 5 minutes and then warmed to room temperature for 1 h. Following basic oxidation, the solution was filtered through a plug of silica gel with acetone as eluent. The resulting solution was concentrated and exhaustively acetylated. GC analysis showed 31% conversion and a ratio of 0.8 : 1.0 (cis-1,3 : trans-1,3).

Background reaction selectivity for 1-(4-methylcyclohex-3-enyl carbonyl) pyrrolidine (Eq 1A.18). Into a flask was weighed the alkene (31.3 mg, 0.162 mmol). To this was added CH_2Cl_2 (100 μL) and the resulting solution was cooled to 0 °C. CB (40 μL, 0.38 mmol) was then added via syringe and effervescence was noted. The solution was kept cold for 5 min, warmed to room temperature and stirred for 1 h. After a basic oxidative workup, the solution was filtered through a plug of silica gel with acetone as eluent. The resulting solution was concentrated and exhaustively acetylated. GC analysis showed complete conversion and a ratio of 12 : 1 (cis-1,3 : trans-1,3).

Hydroboration of 4-pentenoic acid, pyrrolidine amide with BH_3-THF (Eq 1A.19). Into a vial was weighed the olefin (48.6 mg, 0.317 mmol) and the vial was cooled to -30 °C. To this was added the BH_3-THF (0.1 mL, 0.1 mmol) via syringe. The resulting solution was kept cold for 5 min, and then stirred at room temperature for 1.2 h. The solution was aliquoted for analysis by ^{11}B NMR (96.2 MHz, THF) which indicated that BH_3-amide complex (δ -11.5 ppm, q, J=95) was the major boron containing material.

After 14 h, the solution was analyzed again, showing that BH_3-amide was still

the major component of the mixture. There was very little evidence for any of the expected hydroboration products.

Catalyzed hydroboration of 4-pentenoic acid, pyrrolidine amide with CB (Eq 1A.20). Into a vial was weighed the $IndRh(C_2H_4)_2$ (2.1 mg, 0.008 mmol) and then the olefinic amide (46.3 mg, 0.302 mmol). CH_2Cl_2 (0.2 mL) was added and the resulting light yellow solution was stirred briefly and then cooled to - 30 °C. To this solution was then added the CB (80 μL, 0.75 mmol), the solution was kept cold for 5 min, and then warmed to r.t. for 1.2 h. The solution was aliquoted for analysis by ^{11}B NMR (96.2 MHz, $CDCl_3$) which indicated that a small amount of BH_3-amide complex had been formed (δ 11.8, q, J=95, 2%). The major boron-containing material was still CB (δ 28.3, d, J=19, 42%), while 46% was δ 17.5, and 8% was RBcat (δ 35).

After 14 h, the solution was analyzed again showing a very similar spectrum. ^1H NMR (300 MHz, $CDCl_3$) showed that all of the olefin had been hydroborated.

Thermal hydroboration of 4-pentenoic acid, pyrrolidine amide with CB. Into a vials was weighed the olefin (86.0 mg, 0.561 mmol). To this was added the CB (110 μL, 1.03 mmol) and the resulting solution bubbled and became quite warm to the touch. The resulting viscous solution was transferred to a sealable NMR tube and heated to 80 °C for 9 h.

The material was dissolved in $CDCl_3$ under an inert atmosphere and analyzed by ^1H and ^{11}B NMR. ^1H NMR (300 MHz, $CDCl_3$) showed some olefin still remaining. ^{11}B NMR (96.2 MHz, $CDCl_3$) indicated the presence of 2 boron-containing products: δ 8.4 (s) and 17.6 (br s). No CB remained in the solution.

Thermal hydroboration of dodecene, followed by treatment with amide. Into a vial was weighed the olefin (101.5 mg, 0.603 mmol). To this was added CD_2Cl_2 (0.40 mL), and the resulting solution was cooled to -30 °C. To this was then added the CB (170 μL, 1.60 mmol), and the solution was warmed to r.t. after 5 min at -30 °C. The solution was transferred to a sealable NMR tube and analyzed by ^1H NMR (300

MHz, CD_2Cl_2). No conversion of the olefin was noted after 35 minutes and the solution was then heated to 80 °C for 20 h. Complete conversion of the olefin was then seen by ^1H NMR.

^{11}B NMR (96.2 MHz, CD_2Cl_2) indicated that CB (δ 28.5) and RBcat (δ 35.5) were the only 2 boron-containing materials present in about 1.5 : 1 ratio. Some of the CB was removed *in vacuo* such that the ratio of CB : RBcat was 0.80 : 1. To this solution was then added the pyrrolidine derived amide of palmitoyl chloride (80 mg, 0.918 mmol). Some bubbling occurred with the addition (reaction of CB with amide) and the solution was analyzed after 15 min by ^{11}B NMR. The RBcat was still at 35.5 ppm and the remaining peaks were from reaction of CB with amide (δ 14.0 br s, δ 8.4 s, δ -10 (BH_3-amide)). There was no change in the observed spectrum after 3 h at r.t.

Chapter One, Part B:

Ethers as Directing Groups

INTRODUCTION

Transition metal catalyzed additions of catecholborane to olefins have received considerable attention in the past 15 years. The relative inactivity of catecholborane at room temperature allows for almost no hydroboration of *unfunctionalized* olefins[54] other than that mediated by the catalyst.[55] Several reviews of the chemistry of catecholborane, including synthetic applications of *B*-alkylboronic esters, have been written,[56-59] as well as reviews of metal catalyzed hydroborations with catecholborane.[60,61] The potential for effecting enantioselective catalysis with transition metal and lanthanide metal-based systems has been duly noted (for literature reviews, see References 60 and 61) and to some extent achieved.[62,63]

Although recent studies have shown that many side reactions can make the analysis of a transition-metal catalyzed hydroboration with catecholborane more difficult (See Chapter 1A and references therein), the potential for stereoselective synthesis with such systems presents a compelling reason to continue research in this area. Evidence that the alternative pathways we had seen previously are not occurring *must* be shown before the assertion is made that a metal-catalyzed reaction manifold is responsible for that particular reaction.

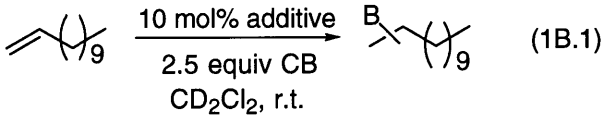
We therefore set out to investigate the use of our indenylrhodium catalyst with a series of directable substrates. The directing groups for this study would need to be chosen very carefully with respect to their Lewis basicity: groups that were too strong would probably cause the disproportionation of catecholborane, and groups that were too weak would not direct the reaction effectively. Once a suitable directing group had been found, the hydroboration could be run in the presence of $IndRh(C_2H_4)_2$. Any product of a directed reaction that was observed could indeed be

due to the intermediacy of the η^3-indenyl-metal complex as a low-energy pathway for accessing the coordination sites necessary for effecting a directed process.

RESULTS AND DISCUSSION

IndRh(C_2H_4)$_2$-Catalyzed Hydroborations

An initial screening of Lewis-basic functional groups indicated that catecholborane in the presence of a secondary amide (methylacetamide), a tertiary amine (triethylamine), or a triarylphosphine (triphenylphosphine) resulted in the formation of a borane-Lewis-base complex which promoted the hydroboration of dodecene (Eq 1B.1). We presumed that ethers would be suitable directing groups, though, since THF is Lewis basic enough to compete with strong directing groups, such as amides, for coordination sites on the metal catalyst in directed reactions (for an example, see Eq 1A.4 or Reference 24). Furthermore, catecholborane can be purchased as a solution in THF, which is stable for some time at room temperature, so we anticipated that the disproportionation of catecholborane would not be a problem with a suitable ether directing group.

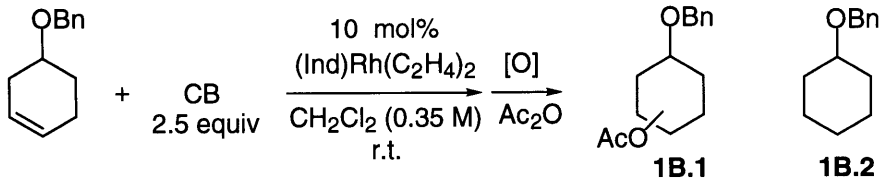


(1B.1)

N-methylacetamide, $t_{1/2}$ = <0.5 h
Triethylamine, $t_{1/2}$ = 0.5 h
PPh_3, $t_{1/2}$ = 17 h

We first chose to investigate the hydroboration of a benzyl-ether containing substrate. 4-Benzyloxycyclohexene was chosen, as the directed hydroboration would result in *cis*-1,3-benzyloxycyclohexanol (See Chapter 1A, Scheme 1A.2 for a discussion of the predicted regio- and stereoisomers of directed reactions). Treatment of this substrate in dichloromethane (0.35 M) with 10 mol% IndRh(C_2H_4)$_2$ and 2.5 equiv catecholborane for 15 hours at room temperature, followed by an oxidative workup, provided the products anticipated for a directed reaction with moderate levels of stereo- and regioselectivity (Eq 1B.2). Acylation was

necessary to allow for GC analysis of the stereo- and regiochemistry of the products.



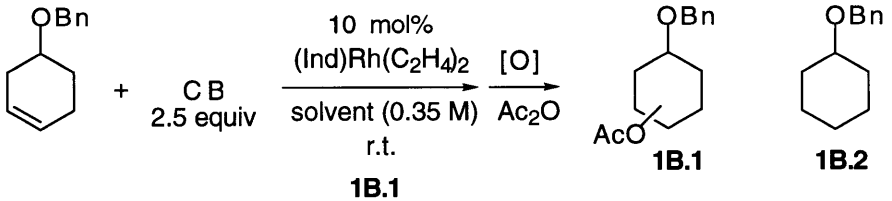
1B.1 1B.2 (1B.2)

1B.1					
cis-1,3 :	cis-1,4 :	trans-1,3 :	trans-1,4	% Conv.	1B.1 : 1B.2
73 :	7 :	10 :	10	100	1.5 : 1.0

We noted immediately that 40% of the material had been consumed by an olefin reduction reaction, instead of hydroboration. We set out to optimize the reaction conditions in an effort to increase selectivity, decrease reaction time, and decrease competitive olefin reduction.

A solvent study (Table 1B.1) indicated that most solvents (with the exception of Lewis-basic THF) gave similar selectivity for the cis-1,3 product. The conversion was quite good in dichloromethane and ether (Table 1B.1, entries 1 and 2), but only moderate conversion was seen in benzene and hexane (Table 1B.1, entries 4 and 5). Another major difference was in the ratio of alcohol to the olefin reduction product, benzyloxycyclohexane. Only dichloromethane and ether favored the formation of the desired alcohols (Table 1B.1, entries 1 and 2).

Table 1B.1. Solvent Effect on Directed Hydroboration.



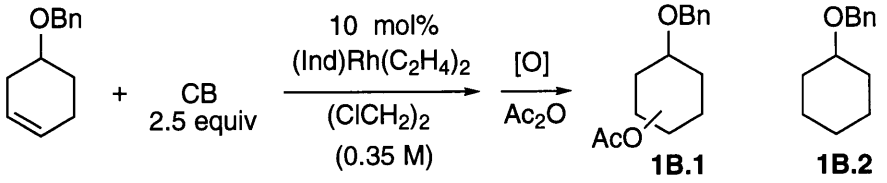
1B.1 1B.2

		1B.1					
Entry	Solvent	cis-1,3 :	cis-1,4 :	trans-1,3 :	trans-1,4	% Conv.	1B.1 : 1B.2
1	CH_2Cl_2	**73** :	7 :	10 :	10	100	1.5 : 1.0
2	Et_2O	**73** :	5 :	9 :	13	94	5.7 : 1.0
3	THF	**46** :	15 :	24 :	15	48	0.37 : 1.0
4	hexane	**74** :	7 :	7 :	11	59	0.11 : 1.0
5	benzene	**70** :	5 :	10 :	15	48	0.20 : 1.0

We postulated that a dihydride-Rh species was giving rise to the reduction

product, and that this could be formed from double addition of catecholborane to the metal complex. Furthermore, any H_2 in solution, formed by metal-mediated catecholborane decomposition,[29] could then bind to the complex and promote hydrogenation of the substrate. We reasoned that both of these processes could be affected by the temperature of the reaction and therefore analyzed the selectivity and amount of olefin reduction with respect to temperature (Table 1B.2). The use of dichloroethane allowed us to survey a broader temperature range than did the use of dichlormethane. Although it appears that dichloroethane is not as good of a solvent choice as is dichloromethane (compare Table 1B.2, entry 2 to Table 1B.1, entry 1), we noted no drastic selectivity differences between the three temperatures. The amount of olefin reduction was the lowest when the reaction was run at room temperature (Table 1B.2, entry 2).

Table 1B.2. Temperature Effect on Directed Hydroboration.



Entry	Temp. (°C)	1B.1 cis-1,3	cis-1,4	trans-1,3	trans-1,4	% Conv.	1B.1 : 1B.2
1	0	**59**	9	13	19	100	0.9 : 1.0
2	22	**54**	12	15	20	100	1.3 : 1.0
3	40	**44**	18	22	16	100	0.56 : 1.0

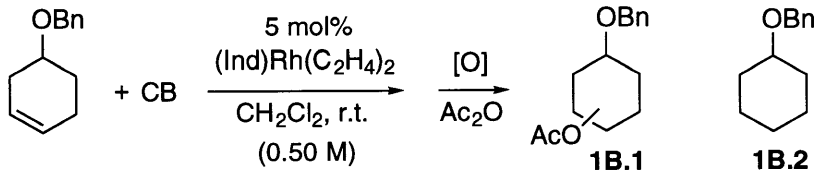
We then attempted slow addition of catecholborane (over 6 hours) at 0 °C in an attempt to decrease the amount of available hydride. This was no more effective at decreasing the saturated product (**1B.1 : 1B.2** = 0.9 : 1.0) than was running the reaction at 0 °C with a single addition of catecholborane. With slow addition of catecholborane, the conversion decreased to 68%. The use of only 1.5 equiv catecholborane at room temperature also resulted in a product ratio of 0.9 : 1.0 (**1B.1 : 1B.2**), but the conversion again suffered, showing only 74% conversion after the

same amount of time.

We next explored the effect of increasing the amount of catecholborane on the reaction. A reaction was run in which 4 equivalents of catecholborane were used with 5 mol% catalyst[64] in CH_2Cl_2, but a leak in the system allowed the solvent to evaporate over about 3 hours. Thinking the reaction was ruined, another was set up under the original conditions. Surprisingly, when both were analyzed the next day, the reaction from which the solvent had evaporated gave 73% of the *cis* -1,3-benzyloxycyclohexanol, as well as complete conversion, and a greatly decreased amount of reduced material (**1B.1 : 1B.2** = 5.6 : 1.0). The second reaction (run at a constant concentration) showed lower conversion (68%) and a poor ratio of alcohols : alkane (**1B.1 : 1B.2** = 0.2: 1.0).

Believing that the increased concentration of catecholborane had resulted in a decrease in the amount of reduction, we ran a set of experiments at 0.5 M with varying ratios of catecholborane : substrate (Table 1B.3). We found that while the selectivity seems relatively unaffected by the changes, the amount of olefin reduction is minimized when 9 equiv catecholborane are used (Table 1B.3, entry 3). The same reaction run with 2.5 mol% catalyst gave similar results.

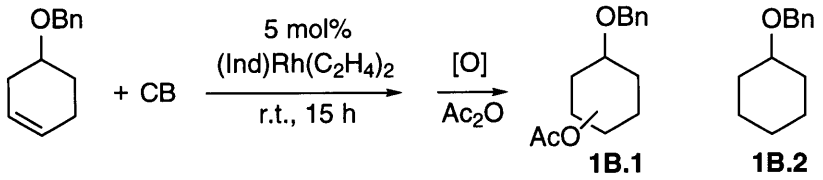
Table 1B.3. Effect of Varying CB equiv on Directed Hydroboration.



		1B.1							
Entry	Equiv CB	cis-1,3	:	cis-1,4	:	trans-1,3	:	trans-1,4	% Conv.	**1B.1 : 1B.2**
1	2.5	**75**	:	6	:	10	:	9	98	1.0 : 1.0
2	4	**69**	:	8	:	12	:	11	79	0.43 : 1.0
3	9	**75**	:	4	:	11	:	10	99	5.7 : 1.0
4	20	**82**	:	1	:	8	:	9	99	2.7 : 1.0

Since increasing the concentration of the reaction also seemed to improve matters greatly, we decided to run the reaction neat (Table 1B.4). Again, selectivities and conversions were very good under all three conditions (3, 10 and 20 equiv catecholborane) but the ratio of alcohol : alkane was best between 3 and 10 equiv of catecholborane (Table 1B.4, entries 1 and 2).

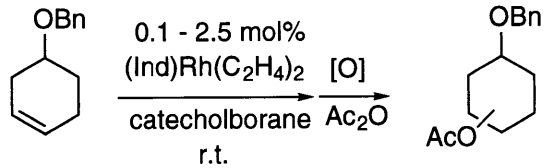
Table 1B.4. Effect of Varying CB equiv on Neat Directed Hydroboration.



1B.1 **1B.2**

Entry	Equiv CB	cis-1,3 : cis-1,4 : trans-1,3 : trans-1,4	% Conv.	**1B.1 : 1B.2**
1	3	**80** : 3 : 6 : 11	100	8.8 : 1.0
2	10	**80** : 3 : 6 : 11	99	12.6 : 1.0
3	20	**77** : 2 : 9 : 12	99	3.3 : 1.0

In an effort to minimize reagent waste, we decided to run the reaction neat, with six equivalents of catecholborane. Under these conditions, we found that the catalyst loading could be taken as low as 0.1 mol% (Eq 1B.3). Almost complete conversion (10% to alkane), good selectivity, and good isolated yield (78%) are seen under these conditions. The reaction run with 0.1 mol% cat required 15 hours to reach complete conversion, so in the interest of having a manageable reaction time, we decided to use 2.5 mol% catalyst in which case the reaction time was consistently 2.5 to 3 hours. The same results are seen at 0.1 and 2.5 mol% catalyst loading, including the isolated yield (79%).



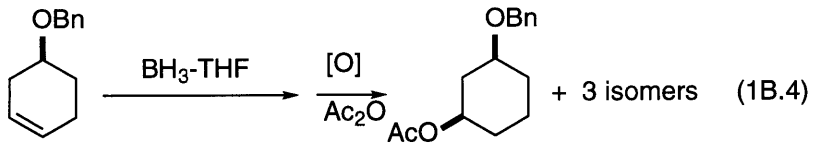
(1B.3)

	cis-1,3	:	cis-1,4	:	trans-1,3	:	trans-1,4	% Conv.
+ cat	**75**	:	4	:	6	:	15	99
no cat	**20**	:	20	:	20	:	40	11

The hydroboration of benzyloxycyclohexene run without $IndRh(C_2H_4)_2$ present, under otherwise identical conditions, showed only 11% conversion, suggesting that there is no ether-induced disproportionation of catecholborane and therefore no subsequent hydroboration of the substrate by BH_3 (See Eq 1B.3). The lack of selectivity for the cis-1,3 product also indicates that no inherent preference for the directed product exists.

Similar reaction rate and diastereoselectivity (as in Eq 1B.3, "+ cat.") are seen when the catalyzed hydroboration is run in the presence of mercury, suggesting that heterogeneous catalysis is not responsible for the observed reactivity.[27,28,65] Similar results, both for selectivity and conversion, are also noted when the reaction is run with catalyst that has been stored open to ambient atmosphere for 6 days.

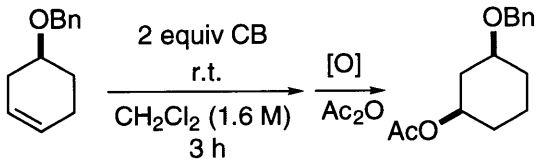
The hydroboration with BH_3-THF (Eq 1B.4) shows no overwhelming selectivity for the directed product. The amide-induced disproportionation of catecholborane in the presence of the benzyloxycyclohexene (Eq 1B.5) also shows no obvious preference for the directed product. Under identical conditions, the background reaction only proceeds in 5 % conversion.



(1B.4)

100 % conv.

cis-1,3	:	cis-1,4	:	trans-1,3	:	trans-1,4
32	:	10	:	38	:	20

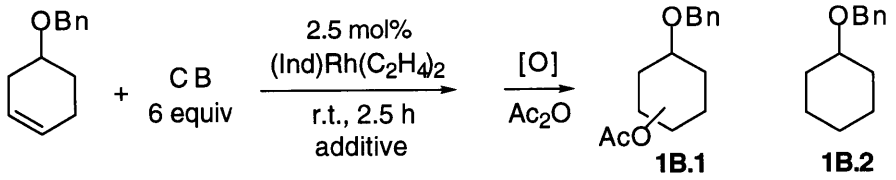


(1B.5)

	cis-1,3	:	cis-1,4	:	trans-1,3	:	trans-1,4	
+ 0 mol% amide	**33**	:	17	:	33	:	17	5% conv.
+ 10 mol% amide	**27**	:	25	:	34	:	17	96% conv.

In the course of this study we have found that commercially available catecholborane is sometimes contaminated with dimethyl sulfide derived impurities (^{1}H NMR: δ 2.0-2.5 ppm in $CDCl_3$) which are difficult to remove by distillation. The DMS impurity does not seem to have a noticeable affect on the amide-mediated chemistry or the amide-directed catalytic reactions. The presence of these contaminants does have a deleterious effect on the stereoselectivity and/or activity of the catalyst in the reactions directed by benzyl ethers (Table 1B.5). Although the percentage of DMS present in the catecholborane appears to be very small, the use of 6 equivalents of contaminated catecholborane introduces enough DMS to coordinate with the metal complex, making it unable to easily access the 12-electron metal center necessary to promote a directed reaction.[9] The addition of 6.9 mol% pure DMS to 'clean' catecholborane[66] has almost the same effect (compare Table 1B.5, entries 2 and 3 to entry 1). Although stirring a reaction using 'bad catecholborane'[67] with Hg appears to improve the results slightly (Table 1B.5, entry 4), we have not found a way to completely remove this harmful impurity (See Table 1B.5, entry 5). We have had to resort to preparing our own catecholborane from catechol and BH_3-THF[68] in order to complete some of our studies.

Table 1B.5. Effect of DMS Additives on Neat Directed Hydroboration.



Entry	Additive	1B.1 cis-1,3	:	cis-1,4	:	trans-1,3	:	trans-1,4	% Conv.	1B.1 : 1B.2
1	none	**75**	:	4	:	6	:	15	99	13.0 : 1.0
2	6.9 mol% DMS	**26**	:	26	:	32	:	16	29	3.2 : 1.0
3	'Bad' CB[a]	**29**	:	29	:	29	:	13	21	4.7 : 1.0
4	'Bad' CB + Hg[b]	**71**	:	7	:	7	:	16	76	3.9 : 1.0
5	'Bad' CB/Hg[c]	**22**	:	28	:	33	:	17	25	4.5 : 1.0

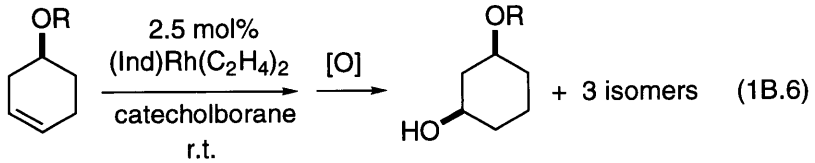
[a] 6 equiv CB contaminated with DMS, distilled before use.

[b] 6 equiv CB contaminated with DMS, distilled before use, stirred with a drop of Hg during reaction.

[c] 6 equiv CB contaminated with DMS, distilled, stirred over Hg,Hg removed and CB used for reaction.

Further Evidence of a Well-Behaved Directed Reaction

It seemed that our benzyl ether was acting in every way like a directing group,[70] and therefore that ring slippage was in fact a key process in our catalytic cycle. We felt it necessary, though, to run several control experiments in order to establish that we had a well-behaved reaction. There does not seem to be an inherent stereochemical preference for the cis-1,3 isomer, as the addition of catecholborane to cyclohexene derivatives which bear substituents that do not strongly coordinate to Lewis acidic metal centers[71] are relatively unselective (Eq. 1B.6). The statistical mixture of products observed in the background reaction indicates this as well (See Eq 1B.3, "no cat.").

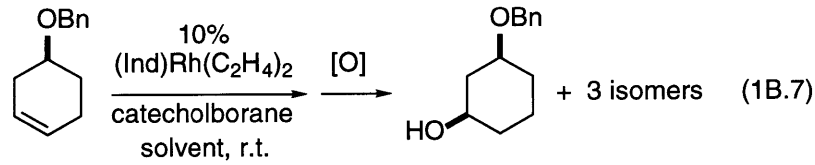


(1B.6)

	cis-1,3	:	trans-1,3	:	1,4 (cis + trans)
R = Bn	**75**	:	6	:	19
TBS	**46**	:	26	:	28

In situ ^{11}B NMR analysis of the catalytic hydroboration indicated that no BH_3 or BH_3-derived products were formed during the reaction. The only boron-containing product seen is the desired alkylboronate ester. This observation provides further evidence that a metal-catalyzed pathway is active for this reaction, and it is not simply a BH_3-mediated process.

Lewis-basic solvents, such as THF, have been shown to have a deleterious effect on the directed process (see Eq 1A.4 or Reference 24), presumably due to a competition between the THF and the directing group for sites on the metal center. We have found that this is the case in our ether-directed hydroboration as well (Eq 1B.7). When the reaction is run in either CH_2Cl_2 or hexane, ~75% of the alcohol mixture is *cis* -1,3-benzyloxycyclohexanol, in accord with our earlier results. When the solvent is THF, though, the selectivity decreases, such that only ~50% of the *cis* -1,3-benzyloxycyclohexanol is observed. This decrease in selectivity is consistent with the expectation for a directed reaction.

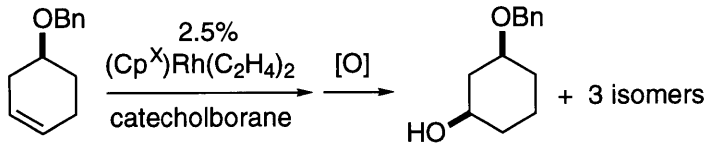


(1B.7)

	cis-1,3	:	cis-1,4	:	trans-1,3	:	trans-1,4
hexane	**75**	:	7	:	7	:	11
CH_2Cl_2	**74**	:	5	:	8	:	13
THF	**47**	:	15	:	23	:	15

Supporting evidence that ring-slippage could be a key step in the catalytic cycle is provided by the use of other Cp-derived rhodium catalysts. The hydroboration of the benzyloxycyclohexene substrate was run in the presence of 4 different catalysts: "[(η^5–Ind)Rh]", "[(η^5-TMInd)Rh]",[72] "[(η^5-Cp)Rh]", and "[(η^5-Cp*)Rh]" - all pseudo 14 e$^-$ species (Table 1B.6). The active catalysts were generated via the hydroboration of either the bis(ethylene) or (cod) complexes.[73]

Table 1B.6. Effect of Ring-Slippage on a Directed Hydroboration.



Entry	Cp^X	cis-1,3	:	cis-1,4	:	trans-1,3	:	trans-1,4
1	Ind	**75**	:	7	:	8	:	11
2	1,2,3-trimethylindenyl	**65**	:	10	:	12	:	13
3	Cp	**30**	:	28	:	30	:	12
4	Cp*	**26**	:	29	:	33	:	12

propensity to ring slip: Ind > 1,2,3-trimethylindenyl >> Cp > Cp*

The results shown in Table 1B.6 are consistent with the many studies that have been conducted on the ease of ring slippage for various Cp^X ligands. It is expected that ring slippage will decrease as the electron density of the ligand increases.[18] Therefore, the use of a permethylated indenyl ligand will result in slower ring-slippage than is seen with the parent indenyl ligand. The added steric bulk from the methyl substituents also decreases the rate of the reaction, but it has not been possible to quantify the electronic and steric factors separately. Indenyl ligands also ring slip more readily than Cp ligands due to the added electronic stabilization that the fused phenyl ring imparts on the η^3-indenyl.[16]

The anticipated increase in selectivity for the "directed" product is seen with the increasing ability of the ligand to ring-slip (see Table 1B.6). The selectivity seen with the Cp-based systems is consistent with the slow ring-slippage of these ligands with

respect to indenyl ligands noted in previous studies; the selectivity with the cyclopentadienyl complexes is similar to that seen in the background reaction. This indicates that essentially no ring slippage is occurring with the Cp-based ligands ($CpRh(C_2H_4)_2$ and $Cp^*Rh(C_2H_4)_2$).

CONCLUSION

Benzyl ethers appear to be capable of acting as a directing group for the $IndRh(C_2H_4)_2$-catalyzed hydroboration reaction.[70] Although this functional moiety is a strong enough Lewis base to coordinate to the rhodium, it is not so strong that it induces disproportionation of the catecholborane, as 2° and 3° amides, amines, and phosphines do. The moderate selectivity seen when utilizing the benzyl ether as a directing group implies that the binding event is not very strong.

The relative lack of a background reaction implies that there is no significant disproportionation of the catecholborane mediated by the ether. The background reaction that does occur (<10% conversion) gives rise to a statistical mixture of alcohols after oxidation, implying that there is no inherent substrate preference for formation of the "directed" *cis*-1,3-product. Also, the low selectivity seen when utilizing a functional group that is known not to bind well to Rh (-OTBS) indicates that the benzyl ether is in fact acting as a directing group for this reaction.

The ^{11}B NMR analysis of the reaction mixture shows no evidence of either BH_3 or BH_3-derived products. The only boron-containing product appears to be the alkylboronate ester. These two results imply that a metal-catalyzed addition of catecholborane is occurring. The lowered selectivity for this reaction when it is run in Lewis-basic THF also provides further evidence that the reaction is in fact a directed process. The use of Cp^XRh catalysts, with varying ability of the Cp^X ligand to ring slip, results in greater selectivity with ligands that ring-slip more readily. This also supports the suggestion that ring-slippage is a crucial part of the observed catalytic reaction.

Based on the above results of the benzyl ether directed reactions, it appears that the proposed ring-slippage strategy is viable. This report therefore signifies the first use of ring-slippage as a method for generating an open coordination site through which a directed process can proceed.

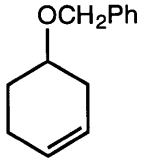
EXPERIMENTAL

General. Benzyl bromide (Aldrich), indene (Aldrich), and 1,2,3,4,5-pentamethylcyclopentadiene (Alfa) were purified by distillation. Sodium hydride (Aldrich, dry, 95%), *n*-BuLi in hexanes (Aldrich; titrated before each use), 1,3-cyclohexanediol (Aldrich; mixture of cis and trans), 1,4-cyclohexanediol (Aldrich; mixture of cis and trans), BH_3-THF (Aldrich), TBSCl (Aldrich), imidazole (Fluka), acetic anhydride (Mallinckrodt), triethylamine (EM Science), and Chlorobis(ethylene)rhodium(I) dimer (Strem) were used as received. Catechol (Acros) was purified by recrystallization. *N*- Methyl acetamide (Eastman) and triethylamine (Aldrich) were distilled before use. Triphenylphosphine was obtained from Riedel-deHaen, recrystallized (hexanes) and stored under an inert atmosphere until used.

Catecholborane (Aldrich, Fluka, or Eastman) was distilled at reduced pressure. Commercially available catecholborane is sometimes contaminated with SMe_2-derived impurities that affect catalyst activity and reaction diastereoselectivity. For this reason, we also prepared catecholborane by the method of Brown,[68] with purification by distillation at reduced pressure followed by vacuum transfer.

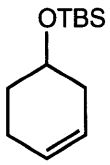
All catalysts were prepared according to the method reported by Green and Marder for $(\eta^5\text{-}1,2,3\text{-}Me_3C_9H_4)Rh(C_2H_4)_2$,[50] purified by crystallization and/or sublimation, and stored under nitrogen.[15] Solvents were distilled from the indicated drying agents: CH_2Cl_2 (CaH_2); benzene (Na/benzophenone); pentane (Na/benzophenone); hexane (Na/benzophenone); THF (Na/benzophenone); Et_2O (Na/benzophenone); toluene (Na). *N*,*N*-Dimethylformamide was dried over 4Å sieves.

PREPARATION OF SUBSTRATES



Benzyloxycyclohex-3-ene [100611-66-3]: 3-Cyclohexen-1-ol[74](0.745 g, 7.59 mmol) was added to a 0 °C suspension of sodium hydride (0.220 g, 9.18 mmol) in *N*,*N*-dimethylformamide (5 mL). Benzyl bromide (0.86 mL, 7.23 mmol) was added to the stirred, 0 °C suspension. The heterogeneous reaction mixture was allowed to warm to room temperature. After 9 h of stirring, the solution was diluted with pentane (20 mL) and washed with water (3 x 20 mL). The organic layer was dried (Na_2SO_4) and concentrated. Column chromatography (5% Et_2O/pentane) afforded 1.05 g (77%) of a very pale yellow oil.[75]

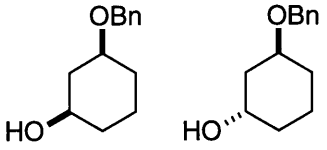
^{1}H NMR (300 MHz, $CDCl_3$) δ 1.6-2.4 (m, 6H), 3.64 (m, 1H), 4.57 (m, 2H), 5.52 (m, 2H), 7.29 (m, 5H).



(*tert*-Butyldimethylsilyloxy)cyclohex-3-ene [106810-75-7]: Prepared by silylation[76] of 3-cyclohexen-1-ol.[74]

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.91 (s, 9H), 1.60 (m, 1H), 1.81 (m, 1H), 1.9 - 2.3 (m, 4H), 3.89 (m, 1H), 5.60 (m, 2H); ^{13}C (125 MHz, $CDCl_3$) δ -4.6, 18.3, 24.5, 26.0, 31.9, 35.3, 68.1, 124.7, 126.6; IR (neat) 2954, 2928, 2895, 2857, 1472, 1462, 1256, 1106, 1092, 974, 887, 855, 836, 806, 774, 718, 666, 651 cm^{-1}.

PREPARATION OF AUTHENTIC PRODUCTS



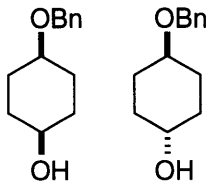
3-Benzyloxycyclohexanol. A solution of 1,3-cyclohexanediol (1.08 g, 9.27 mmol; mixture of cis and trans isomers) in DMF (6 mL) was added by syringe to a flask containing NaH (0.242 g, 10.1 mmol). The resulting solution was cooled to 0 °C, and benzyl bromide (1.00 mL, 8.41 mmol) was added by syringe. The mixture was stirred with slow warming to r.t. for 1.5 h. The reaction was then diluted with pentane (10 mL) and washed with 1N NaOH (2 x 20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and concentrated, yielding a light yellow oil. The two 3-benzyloxycyclohexanol isomers were separated by column chromatography (5% EtOAc/hexane).

Benzylation of one of the 3-benzyloxycyclohexanol isomers resulted in a 1,3-di(benzyloxy)cyclohexane in which the methylene hydrogens in the 2 position were inequivalent by ^1H NMR (⇒ cis isomer).

Cis isomer [(1R), 137331-23-8, (1S), 114737-99-4]. ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (m, 1H), 1.3-1.9 (m, 6H), 2.08 (br d, 1H, J = 13), 2.9 (br s, 1H), 3.55 (m, 1H), 3.73 (m, 1H), 4.55 (s, 2H), 7.34 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.4, 30.4, 34.2, 39.4, 68.3, 70.2, 75.4, 127.5, 128.4, 138.6; IR (neat) 3387 (br), 2935, 2859, 1453, 1358, 1056, 736, 698 cm^{-1}; HRMS *m/z* 206.1305 [M^+], calcd for $C_{13}H_{18}O_2$: 206.1307.

Trans isomer [(R,R) 114738-00-0]. ^1H NMR (300 MHz, $CDCl_3$) δ 1.2-1.8 (m, 8H), 1.94 (m, 1H), 3.81 (m, 1H), 4.10 (m, 1H), 4.53 (s, 2H), 7.34 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2, 30.3, 34.4, 39.4, 67.2, 70.1, 74.0, 127.4, 127.5, 128.4, 139.2; IR (neat) 3358 (br), 2932, 2850, 1452, 1126, 1066, 1028, 970, 735, 698 cm^{-1}; HRMS *m/z* 206.1307 [M^+],

calcd for $C_{13}H_{18}O_2$: 206.1307.



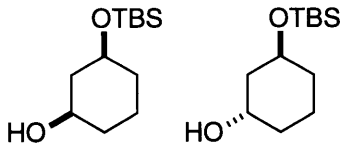
4-Benzyloxycyclohexanol. A mixture of cis and trans isomers was prepared by monobenzylation of a mixture of *cis*- and *trans*-1,4-cyclohexanediol.

[2976-80-9]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.2-2.1 (m, 9H), 3.3-3.6 (m, 1H), 3.6-3.8 (m, 1H), 4.4-4.5 (m, 2H), 7.1-7.3 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.5, 29.4, 30.5, 32.6, 68.3, 69.5, 69.6, 70.1, 73.5, 76.2, 127.4, 127.5, 128.4, 138.9, 139.1; IR (neat) 3386 (br), 2934, 2860, 1453, 1366, 1075, 1027, 969, 944, 736, 698 cm^{-1}; HRMS *m/z* 206.1307 [M^+], calcd for $C_{13}H_{18}O_2$: 206.1307.

Cis vs. trans stereochemistry was assigned through analysis of the ^{1}H NMR coupling constants of the methine protons of the two diastereomers. Some resonances of the isomers are also distinguishable by ^{13}C NMR, as shown by the analysis of the pure cis isomer as compared to the mixture of cis and trans.

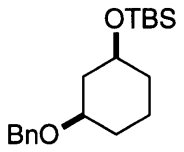
Cis isomer [127074-28-6]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.51 (tt, J = 3.0, 6.0, 1H), 3.74 (tt, J = 3.0, 8.0); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.6, 30.4, 30.6, 67.7, 68.6, 69.7, 73.6, 127.4, 127.5, 128.4, 128.5, 130.2, 133.5, 139.2; IR (neat) 3326 (br), 2933, 2849, 1717, 1452, 1367, 1065, 1028, 966, 737, 699 cm^{-1}; HRMS *m/z* 206.1305 [M^+], calcd for $C_{13}H_{18}O_2$: 206.1307.

Trans isomer [127074-29-7]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.39 (tt, J = 4.0, 9.5, 1H), 3.68 (tt, J = 4.5, 10.0, 1H).



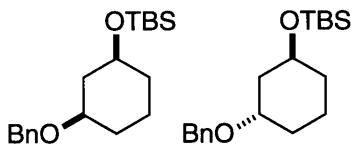
3-(*tert*-Butyldimethylsilyloxy)cyclohexanol. A mixture of cis and trans isomers was prepared by monosilylation of a mixture of *cis*- and *trans*-1,3-cyclohexanediol.

[*cis*-(1S,2R), 142798-56-9, *trans*- 155326-17-3]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.03-0.08 (m, 6H), 0.88-0.96 (m, 9H), 1.2-2.1 (m, 9H), 3.4-4.1 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -5.1, -4.9, 17.5, 17.9, 18.9, 25.7, 33.6, 33.8, 34.5, 41.4, 42.6, 66.5, 67.6, 68.0, 68.1, 69.4; IR (neat) 3343 (br), 2935, 2886, 2858, 1463, 1452, 1373, 1361, 1256, 1103, 1051, 863, 836, 775, 667 cm^{-1}; HRMS *m/z* 230.1701 [M^+], calcd for $C_{12}H_{26}SiO_2$: 230.1702.



The cis isomer was prepared by silylation of *cis*-3-benzyloxycyclohexanol.

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (s, 6H), 0.94 (s, 9H), 1.2-1.5 (m, 4H), 1.81 (m, 2H), 2.06 (m, 1H), 2.33 (br d, J = 11.0, 1H), 3.36 (m, 1H), 3.58 (m, 1H), 4.61 (s, 2H), 7.3-7.4 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.6, -4.5, 18.2, 20.9, 25.8, 26.0, 31.6, 35.5, 42.6, 70.0, 76.1, 127.5, 127.6, 128.4, 139.1; HRMS *m/z* 320.2173 [M^+], calcd for $C_{19}H_{32}SiO_2$: 320.2171.



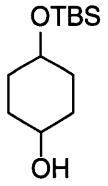
A mixture of cis and trans isomers was prepared by quantitative benzylation of the mixture of *cis*- and *trans*-3-(*t*-butyldimethylsilyloxy)cyclohexanol synthesized above. The resulting mixture of *cis*- and *trans*-1-benzyloxy-3-(*t*-butyldimethylsilyloxy)cyclohexane was determined to be predominantly cis by comparison with material prepared independently (see above). Therefore, the major isomer in the mixture of *cis*- and *trans*-3-(*t*-butyldimethylsilyloxy)cyclohexanol prepared above is also the cis isomer.

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.0-0.1 (m, 6H), 0.9-1.0 (m, 9H), 1.0-2.3 (m, 8H), 3.2-4.2 (m, 2H), 4.5-4.6 (m, 2H), 7.2-7.4 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.8, -4.7, -4.6, -4.5, 18.1, 18.2, 19.2, 20.9, 25.9, 26.0, 31.1, 31.5, 31.8, 34.3, 35.5, 38.9, 39.9, 42.6, 65.0, 67.7, 70.0, 72.1, 74.0, 75.9, 76.0, 126.0, 126.9, 127.3, 127.4, 127.5, 127.6, 127.8, 128.2, 128.3, 128.4, 128.8, 129.0, 139.0; HRMS *m/z* 320.2173 [M^+], calcd for $C_{19}H_{32}SiO_2$: 320.2171.

The methine protons of the cis and the trans isomers are distinguishable by ^{1}H NMR, and the resonances can be assigned for each isomer, since we have independently prepared *cis*-1-benzyloxy-3-(*t*-butyldimethylsilyloxy)cyclohexane (see above).

Cis isomer. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.33 (m, 1H), 3.54 (m, 1H).

Trans isomer. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77 (m, 1H), 4.11 (m, 1H).



4-(*tert*-Butyldimethylsilyloxy)cyclohexanol. A mixture of cis and trans isomers was prepared by monosilylation of a mixture of *cis*- and *trans*-1,4-cyclohexanediol.

[126931-29-1]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.0-0.1 (m, 6H), 0.8-0.9 (m, 9H), 1.2-2.0 (m, 9H), 3.6-3.9 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -4.9, -4.8, 18.0, 18.1, 25.8, 29.9, 31.4, 32.5, 32.9, 66.8, 68.6, 69.1, 70.1; IR (neat) 3341, 2934, 2885, 2857, 1472, 1462, 1374, 1360, 1253, 1098, 1051, 1018, 1006, 964, 879, 860, 836, 774, 677 cm^{-1}; HRMS *m/z* 230.1701 [M^+], calcd for $C_{12}H_{26}SiO_2$: 230.1701.

$IndRh(C_2H_4)_2$ CATALYZED HYDROBORATIONS

General procedure for oxidative workup of hydroboration reactions.[20] The hydroboration reaction mixture was cooled to 0 °C, and 1 : 1 THF : EtOH (2 mL per mmol of substrate), then 2N NaOH (2 mL per mmol of substrate), and then 30% H_2O_2 (2 mL per mmol of substrate) were added. The solution was stirred, with slow warming to room temperature, for 2 h.

Hydroboration of dodecene in the presence of CB and additives (Eq 1B.1). Into a vial was added, by syringe, the dodecene (220 μL, 0.991 mmol), CD_2Cl_2 (0.69 mL) and the additive (0.100 mmol). The solution was cooled to 0 °C and the CB (220 μL, 2.06 mmol) was added dropwise. The solution was kept cold for 5 min and then transferred to an NMR tube, and then followed by ^1H NMR.

N-methylacetamide: $t_{1/2}$ = <0.5h

Triethylamine: $t_{1/2}$ = 0.5h

Triphenylphosphine: $t_{1/2}$ = 17h

Hydroboration of 4-benzyloxycyclohexene with $IndRh(C_2H_4)_2$ (Eq 1B.2). Into a flask was weighed the catalyst (6.1 mg, 0.022 mmol). To this was added the CH_2Cl_2 (0.5 mL) and 4-benzyloxycyclohexene (31.2 mg, 0.166 mmol) via syringe. The resulting solution was cooled to 0 °C, and the CB (49 μL, 0.46 mmol) was then added via syringe. The resulting solution was stirred under inert atmosphere at room temperature for 15 h.

The solution was then subjected to basic oxidative workup conditions, followed by extraction of the product with ethyl acetate/1N NaOH. The organic layer was dried over Na_2SO_4 and the solution concentrated. The resulting residue was exhaustively acetylated and the selectivity (random), ratio of alcohol : benzyloxycyclohexane (**[16224-09-2]**) (1.5 : 1), and conversion (100%) analyzed by GC.

Solvent effect on directed hydroborations of 4-benzyloxycyclohexene (Table 1B.1). Into a flask was weighed the catalyst (6.1 mg, 0.022 mmol). To this was added the

solvent (0.5 mL) and 4-benzyloxycyclohexene (31.2 mg, 0.166 mmol) via syringe. The resulting solution was cooled to 0 °C and the CB (49 μL, 0.46 mmol) was then added via syringe. The resulting solution was stirred under inert atmosphere at room temperature for 15 h.

The solution was then subjected to basic oxidative workup conditions, followed by extraction of the product with ethyl acetate/1N NaOH. The organic layer was dried over Na_2SO_4 and the solution concentrated. The resulting residue was exhaustively acetylated and the selectivity, product ratio and conversion analyzed by GC.

The results are as shown in Table 1B.1 for: dichloromethane, diethylether, THF, hexane and benzene.

Temperature effect on directed hydroboration of 4-benzyloxycyclohexene (Table 1B.2). The reaction was run as in "Effect of solvent on directed hydroboration of 4-benzyloxycyclohexene" except that the solvent was dichloroethane and the reactions were run at temperatures of 0, 22, and 40 °C for 6 h. The results are as shown in Table 1B.2.

Effect of varying CB equiv on directed hydroborations of 4-benzyloxycyclohexene (Table 1B.3). Into a flask was weighed the catalyst (2.3 mg, 0.01 mmol). To this was added the solvent (0.35 mL) and 4-benzyloxycyclohexene (33.7 mg, 0.179 mmol) via syringe. The resulting solution was cooled to 0 °C and the CB (2.5, 4, 9, and 20 equiv) was then added via syringe. The resulting solution was stirred under inert atmosphere at room temperature for 15 h.

The solution was then subjected to basic oxidative workup conditions, followed by extraction of the product with ethyl acetate/1N NaOH. The organic layer was dried over Na_2SO_4 and the solution concentrated. The resulting residue was exhaustively acetylated and the selectivity, product ratio and conversion analyzed by GC.

The results are as shown in Table 1B.3.

Effect of varying CB equiv on neat directed hydroborations (Table 1B.4). Into a flask was weighed the catalyst (2.5 mg, 0.01 mmol). To this was added the 4-benzyloxycyclohexene (35.2 mg, 0.187 mmol) via syringe. The resulting solution was cooled to 0 °C and the CB (3, 10, and 20 equiv) was then added via syringe. The resulting solution was stirred under inert atmosphere at room temperature for 15 h.

The solution was then subjected to basic oxidative workup conditions, followed by extraction of the product with ethyl acetate/1N NaOH. The organic layer was dried over Na_2SO_4 and the solution concentrated. The resulting residue was exhaustively acetylated and the selectivity, product ratio and conversion analyzed by GC.

The results are as shown in Table 1B.4.

Catalyzed hydroboration of 4-benzyloxycyclohexene (Eq 1B.3). 4-Benzyloxycyclohexene (204 mg, 1.08 mmol) was added by syringe to a flask containing $IndRh(C_2H_4)_2$ (0.3 mg, 0.001 mmol). The resulting homogeneous, light-yellow solution was stirred for one minute, and then catecholborane (0.700 mL, 6.57 mmol) was added by syringe. A background reaction was run under the same conditions, except no catalyst was added to the solution.

The solutions were stirred for 15 h and then subjected to an oxidative workup. An aliquot was removed from each solution for GC analysis (acetylated), and the remainder was purified by flash chromatography (15 → 40% EtOAc/hexane). The catalyzed reaction provided 177 mg (78%) of a pale-yellow oil. GC analysis showed complete conversion, cis-1,4 : trans-1,4 : trans-1,3 : trans-1,4 = 80 : 3 : 6 : 11 and a product ratio of 13 : 1 (**1B.1 : 1B.2**). Identical results were obtained with 2.5% $IndRh(C_2H_4)_2$.

^1H NMR (300 MHz, $CDCl_3$) δ 1.2-2.2 (m, 8H), 2.8 (br s, 1H), 3.4-3.8 (m, 2H), 4.5-4.6 (m, 2H), 7.2-7.4 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.5, 27.5, 30.4, 34.2, 39.5, 68.2,

70.1, 75.4, 127.4, 127.5, 128.2, 128.3, 128.3, 138.5; IR (neat) 3385, 2936, 2859, 1453, 1358, 1096, 1059, 1029, 737, 698 cm^{-1}; Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.85; H, 8.89; HRMS: Calcd for $C_{13}H_{18}O_2$: 206.1307. Found: 206.1306; R_f = 0.34 (50% EtOAc/hexane).

The analysis of the background reaction indicated 11% conversion, cis-1,4 : trans-1,4 : trans-1,3 : trans-1,4 = 20 : 20 : 20 : 40 and a product ratio of 2.7 : 1 (**1B.1 : 1B.2**).

Mercury test for homogeneity. A drop of mercury was placed in a flask and degassed. Into this flask was weighed the $IndRh(C_2H_4)_2$ (1.7 mg, 0.01 mmol). The olefin (46.3 mg, 0.246 mmol) was added via syringe and the solution was cooled to -30 °C. CB (160 μL, 1.50 mmol) was added and the solution warmed to room temperature and stirred for 2.5 h. The solution was then subjected to basic oxidative workup, extracted and concentrated. The material was then exhaustively acetylated and analyzed by GC, which indicated 98% conversion and a ratio of 75 : 6 : 6 : 13 (cis-1,3 : cis-1,4 : trans-1,3 : trans-1,4).

Air-stability of $IndRh(C_2H_4)_2$. Into a vial was weighed the $IndRh(C_2H_4)_2$ (1.2 mg, 0.004 mmol). The flask was opened to air, sealed and stored in a dessicator for 6 days. The catalyst remained a bright, yellow powder during this time.

The flask was subsequently evacuated and filled with argon. To the flask was added the olefin (29.4 mg, 0.156 mmol) and the resulting solution was cooled to -30 °C. The CB (100 μL, 0.938 mmol) was then added and the solution warmed to room temperature and stirred for 2.5 h. The solution was then subjected to a basic oxidative workup, extraction and concentration. The material was then exhaustively acetylated and analyzed by GC, which indicated 98% conversion of the olefin and a ratio of 74 : 6 : 7 : 13 (cis-1,3 : cis-1,4 : trans-1,3 : trans-1,4).

BH_3-THF hydroboration of benzyloxycyclohexene (Eq 1B.4). Into a flask was added the BH_3-THF (1.1 mL, 1.1M) solution cooled to 0 °C and the olefin (98.9 mg, 0.525 mmol) was added via syringe. The solution was then warmed to room

temperature and stirred for 12 h.

A neutral oxidative workup was performed and the solution was then extracted with ether. The organics were dried over Na_2SO_4 and the solvents were removed. The material was then exhaustively acetylated and analyzed by GC, which indicated complete conversion and a ratio of 32 : 10 : 38 : 20 (cis-1,3 : cis-1,4 : trans-1,3 : trans-1,4).

Hydroboration of benzyloxycyclohexene in the presence of amide and catecholborane (Eq 1B.5). Into a vial was weighed the olefin (29.5 mg, 0.157 mmol). Dimethylacetamide (1.5 μL, 0.02 mmol) and CH_2Cl_2 (0.100 mL) were added via syringe and the solution was then cooled to -30 °C. CB (33 μL, 0.31 mmol) was then added by syringe and the solution warmed to room temperature and stirred for 3 h.

The solution was then subjected to basic oxidative workup, extracted with EtOAc and then concentrated. The material was then exhaustively acetylated and analyzed by GC, which indicated 96% conversion and a ratio of 27 : 25 : 34 : 17 (cis-1,3 : cis-1,4 : trans-1,3 : trans-1,4). In comparison the same reaction run without amide present, after three hours showed a 5% conversion and a ratio of 33 : 17 : 33 : 17 (cis-1,3 : cis-1,4 : trans-1,3 : trans-1,4).

Catalyzed hydroboration of 4-benzyloxycyclohexene with 6.9% DMS (Table 1B.5, entry 2). 4-Benzyloxycyclohexene (29.7 mg, 0.158 mmol) was added by syringe to a flask containing $IndRh(C_2H_4)_2$ (1.0 mg, 0.004 mmol). Dimethylsulfide (0.8 μL, 0.01 mmol) was then added via syringe and the resulting homogeneous, light-yellow solution was stirred for one minute, and then catecholborane (96 μL, 0.90 mmol) was added by syringe. The solution was stirred for 2.5 h and then subjected to an oxidative workup. An aliquot was removed from each solution for GC analysis (acetylated), and the remainder was purified by flash chromatography (15 → 40% EtOAc/hexane). GC analysis showed 29% conversion, cis-1,4 : trans-1,4 : trans-1,3 : trans-1,4 = 26 : 26 : 32 : 16 and a product ratio of 3.2 : 1 (**1B.1 : 1B.2**).

Effect of DMS on directed Hydroborations with $IndRh(C_2H_4)_2$ (Table 1B.5, entry 3). Into a vial was weighed the catalyst (0.8 mg, 0.003 mmol) and then the alkene (27.7 mg, 0.147 mmol). This solution was then cooled to -30 °C and 'Bad' CB[67] (96 μL, 0.90 mmol) was added slowly. The solution was slowly warmed to room temperature and stirred for 2.5 h. The solution was subjected to basic oxidative workup, filtered through a plug of silica gel with acetone as eluent and then concentrated. The resulting oil was exhaustively acetylated and analyzed by GC, which indicated 21% conversion and a ratio of 29 : 29 : 29 : 13 (cis-1,3 : cis-1,4 : trans-1,3 : trans-1,4).

Effect of mercury on CB with DMS impurity (Table 1B.5, entries 4 and 5). The reactions were run as in "Effect of DMS on directed hydroboration with $IndRh(C_2H_4)_2$" except:

Entry 4. The reaction was run with a drop of mercury present in the alkene solution. GC analysis indicated 76% conversion, a selectivity of 71 : 7 : 7 : 16 (cis-1,3 : cis-1,4 : trans-1,3 : trans-1,4), and **1B.1** : **1B.2** = 3.9 : 1.

Entry 5. The reaction was run with 'Bad' CB[67] that had been stored over Hg and then decanted under argon before use. GC analysis indicated 25% conversion, a selectivity of 22 : 28 : 33 : 17 (cis-1,3 : cis-1,4 : trans-1,3 : trans-1,4), and **1B.1** : **1B.2** = 4.5 : 1.

Catalyzed hydroboration of 4-(*t*-butyldimethylsilyloxy)cyclohexene (Eq 1B.6). 4-*t*-(Butyldimethylsilyloxy)cyclohexene (32.4 mg, 0.153 mmol) was added to a flask containing $IndRh(C_2H_4)_2$ (1.0 mg, 0.01 mmol). The resulting solution was stirred at -40 °C for 5 min, and then catecholborane (96 μL, 0.90 mmol) was added dropwise by syringe. The resulting light-yellow solution was stirred at r.t. for 2.5 h and then subjected to an oxidative workup. Following oxidation, the reaction mixture was passed through a plug of silica gel with acetone as the eluent. The solution was concentrated, and the resulting oil was diluted with EtOAc for analysis by GC

(acetylated), which showed complete conversion and cis-1,3 : trans-1,3 : 1,4 (cis + trans) = 46 : 26 : 28.

^{11}B NMR analysis of catalyzed hydroboration of 4-benzyloxycyclohexene. Into a vial was weighed the catalyst (2.2 mg, 0.01 mmol). To this was added the olefin (58.6 mg, 0.311 mmol) and the resulting light yellow solution was cooled to -45 °C and then CB (48 μL, 0.45 mmol). The solution was stirred with slow warming to r.t. and aliquots were taken to analyze by ^{11}B and ^{1}H NMR.

^{11}B NMR (96.2 MHz, $CDCl_3$) - 10 min- CB (δ 28, d) and RBcat (δ 33, br s) seen.

^{1}H NMR (300 MHz, $CDCl_3$) - 10 min- 33% conversion of olefin seen.

^{11}B NMR (96.2 MHz, $CDCl_3$) - 1 h- CB (δ 28, d) and RBcat (δ 33, br s) seen.

^{1}H NMR (300 MHz, $CDCl_3$) - 1 h- 56% conversion of olefin seen.

^{11}B NMR (96.2 MHz, $CDCl_3$) - 18.5 h- CB (δ 28, d) and RBcat (δ 33, br s) seen.

^{1}H NMR (300 MHz, $CDCl_3$) - 18.5 h- 100% conversion of olefin seen.

At no time during the analysis were BH_3 or any products derived from BH_3 seen by ^{11}B NMR.

Solvent study (Eq 1B.7). 4-Benzyloxycyclohexene (31.2 mg, 0.166 mmol) was added by syringe to a solution of $IndRh(C_2H_4)_2$ (4.8 mg, 0.02 mmol) in solvent (0.5 mL). The resulting homogeneous, light-yellow solution was cooled to 0 °C, and catecholborane (0.047 mL, 0.441 mmol) was added. The reaction mixture was stirred for 15 h at r.t., and then it was subjected to an oxidative workup and analyzed by GC (acetylated).

Catalyst study (Table 1B.6). The procedure described above ["Catalyzed hydroboration of 4-benzyloxycyclohexene (Eq 1B.3)"] was followed.

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45 We have found that the treatment of 0.1 equiv of $LiBH_4$ with catecholborane (THF, room temperature, 5 min) results in the complete consumption of $LiBH_4$ and in the clean formation of BH_3-THF and $Li(B(C_6H_4O_2)_2)$ (Männig, D.; Nöth, H. *J. Chem. Soc., Dalton Trans.* **1985,** 1689-1692) in a 2 : 1 ratio. Subsequent addition of 1-dodecene results in the generation of tri(*n*-dodecyl)borane.
46 Since it seems that an amide is intimately involved in our hydroboration complex we reasoned that the use of a chiral amide might induce enantioselectivity in the reaction. Our one attempt to do so resulted in a racemic mixture of the desired hydroboration products of β-methyl styrene.
47 Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*; Academic Press: New York, 1988.
48 Dodecyl catechol boronate ester displays a resonance at 35 ppm, consistent with the published reports of similar compounds.
49 Formed independently via the thermal addition of catecholborane to dodecene.
50 Franckom, T. M.; Green, J. C.; Nagy, A.; Kakkar, A. K.; Marder, T. B. *Organometallics* **1993**, *12*, 3688-3697.

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64 We found that we could decrease the catalyst loading to 5 mol% without a deleterious effect on the reaction.
65 For a general approach to distinguishing homogeneous from heterogeneous catalysis, see: Lin, Y.; Finke, R. G. *Inorg. Chem.* **1994**, *33*, 4891-4910.
66 'Clean' catecholborane is that purchased which does not contain any DMS impurities.
67 'Bad' catecholborane is catecholborane which was obtained with DMS impurity, and then distilled.
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70 Preliminary results suggest that esters may also be effective as directing groups for hydroboration reactions catalyzed by indenylrhodium$(C_2H_4)_2$ complexes.
71 For a discussion of the low Lewis basicity of silyl ethers, see: Shambayati, S.; Blake, J. F.; Wierschke, S. G.; Jorgensen, W. L.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 697-703.
72 TMInd = 1,2,3-trimethylindenyl.
73 The assumption that the olefin ligands are hydroborated and then displaced from the metal center resulting in a 14 e$^-$ complex ([η^5-Cp^{X}Rh]) seems justified, as both bis(ethylene) and (cod) complexes of the trimethylindenyl and pentamethylcyclopentadienyl rhodium catalysts give similar results.
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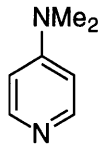
Chapter Two:

Ferrocene- and Ruthenocene-Derived Nucleophilic Catalysts

INTRODUCTION

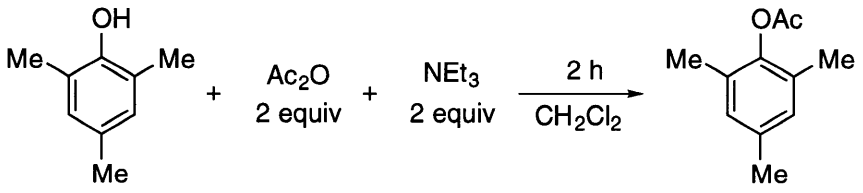
Nucleophilic catalysis is quite common in organic synthesis. One of the most common examples of a nucleophilic catalyst is 4-dimethylaminopyridine, or DMAP (**2.1**).



2.1

DMAP has been shown to be an effective accelerant for a variety of nucleophile-catalyzed reactions, such as the acylation of alcohols with acetic anhydride (Scheme 2.1). With no nucleophilic catalyst present, the reaction shows very little conversion after 2 hours reaction time. When only 1 mol% of DMAP is added to the reaction, almost complete conversion is seen after the same period of time.[1]

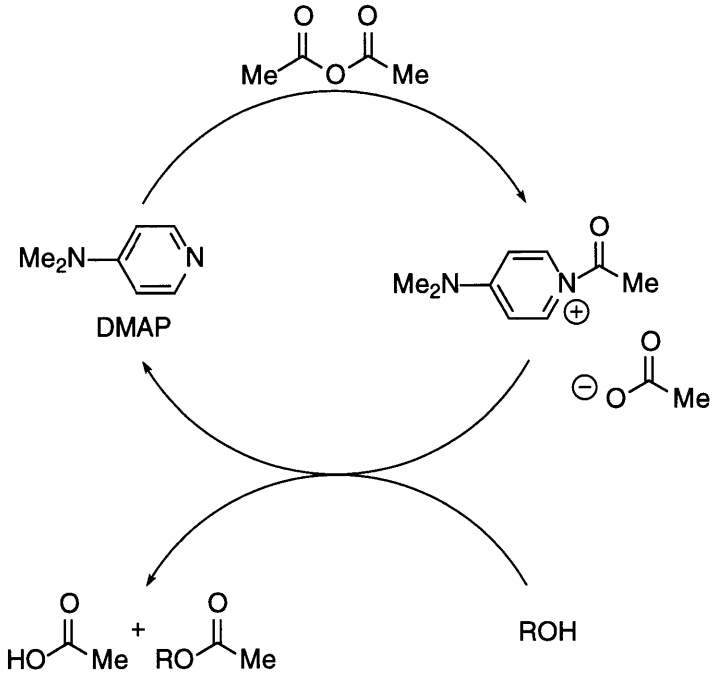
Scheme 2.1



no catalyst	0 %
2.1 (1 mol%)	94%

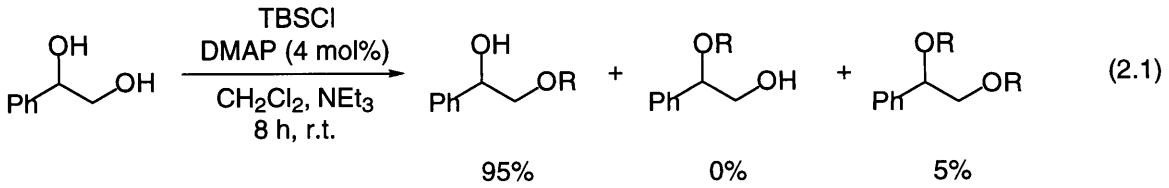
The mechanism of action of DMAP has been studied intensively, and the following catalytic cycle has been shown for the acylation of alcohols in the presence of acetic anhydride (with an equimolar amount of a base) and catalytic DMAP (Scheme 2.2).

Scheme 2.2

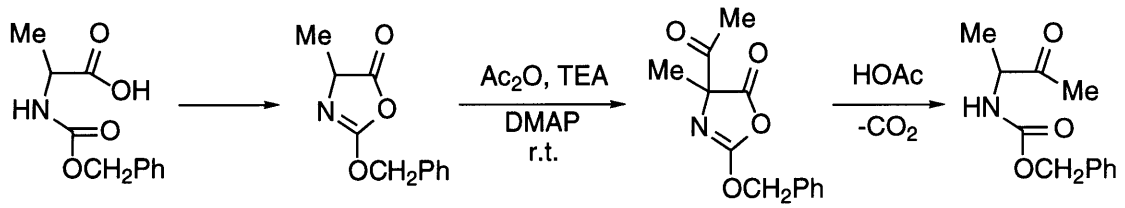


DMAP acts as a stronger nucleophile than the alcohol, and therefore reacts more rapidly with the acetic anhydride. The *N*-acyl iminium salt that is formed is more electrophilic than the acetic anhydride and reacts more quickly with the alcohol to form the desired product. The DMAP is released by the attack of the alcohol, and therefore the catalytic cycle can continue. The presence of a base is necessary for acylation reactions of this type, as an equivalent of acetic acid is formed upon acylation of the alcohol. If this acid remains in the solution it will protonate the DMAP, making it unreactive as a nucleophile. Addition of a non-nucleophilic base (so as not to compete with the DMAP) will neutralize the acetic acid and allow the DMAP to remain an active nucleophilic catalyst.

Many other reactions are prone to nucleophilic catalysis by DMAP, such as silylation (equation 2.1) and the Dakin-West reaction (equation 2.2).[2] A variety of compounds other than DMAP serve as nucleophilic catalysts, such as pyridine derivatives,[2] tertiary amines,[3] and phosphines.[4,5]



(2.1)



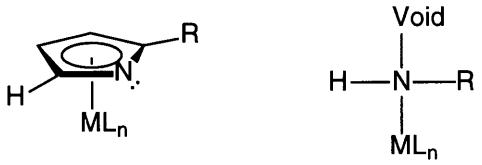
(2.2)

A great effort has recently been put forth to try and develop enantioselective versions of these nucleophile-catalyzed reactions. Attempts to develop chiral DMAP analogs have focused mostly on installing chiral groups α to the ring nitrogen atom.[6] The installation of a chiral group at this position, in order to provide an asymmetric environment close to the nucleophile, necessarily means the addition of some bulk at the α position. This added steric demand at the nucleophile generally results in lower reactivities for the chiral DMAP derivatives. The use of chiral phosphines as nucleophilic catalysts has also seen some development recently.[6]

BACKGROUND

Our group began exploring another route to chiral nucleophilic catalysts in 1995. It seemed that π-complexation of a substituted heterocycle to a transition metal fragment might provide the asymmetry needed at the nucleophilic atom. Although a substituent is still necessary α to the ring nitrogen, a small, non-bulky substituent should be sufficient. The asymmetry at nitrogen of these π-bound heterocycles is illustrated in Figure 2.1. The substituents on the heterocycle allow for differentiation between the top and bottom face (ML_n vs. a void) as well as between the right and left (R vs. H). These substituents desymmetrize both the vertical and the horizontal planes of the heterocycle, therefore providing a nucleophilic atom in an asymmetric environment.

Figure 2.1. A Chiral (π-Heterocycle) Metal Complex

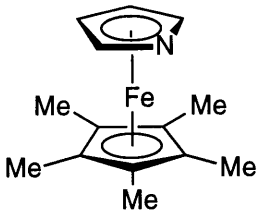


A A view along the (lone pair)-(nitrogen atom) axis of **A**

The initial development of achiral complexes of this type as nucleophilic catalysts was achieved by J. Craig Ruble. He synthesized (π-heterocycle)FeCp* complexes as the initial group of potential catalysts. Pyrrole-bound complexes of this type are known as azaferrocenes, and many had been synthesized up to this point in time, although none had been used as nucleophilic catalysts. It was known that the nitrogen atom in complexes of this type was indeed nucleophilic, but their first use as catalysts was described by our group in 1996.[7]

The achiral azaferrocene complex (**2.2**) was found to accelerate a variety of known nucleophile-catalyzed reactions, such as acylation of secondary alcohols with

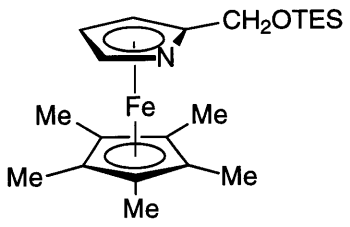
acetic anhydride, ketene solvolysis with secondary alcohols, and cyanosilylation of aldehydes.



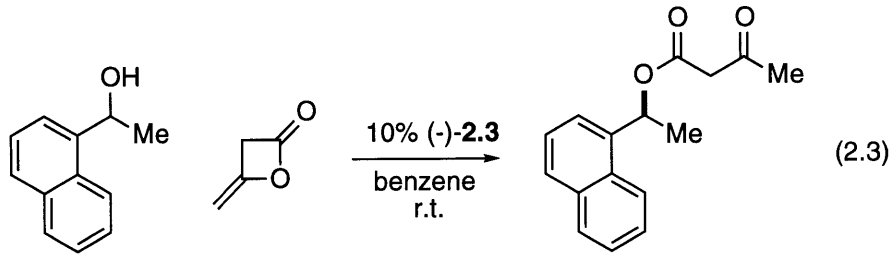
2.2

It was further shown that a *chiral* azaferrocene (**2.3**) could be prepared, resolved, and used to catalyze the kinetic resolution of secondary alcohols with diketene (Eq 2.3). At the time, a selectivity of 6.5 was the best known resolution of this substrate. This result further demonstrated the feasibility of using π-bound pyrroles as chiral nucleophilic catalysts.

We have chosen to use selectivity factors, or s factors, to describe our results in kinetic resolutions. A selectivity factor is simply a comparison of the rates of the fast-reacting substrate enantiomer to the rate of the slow-reacting enantiomer. A large relative rate allows for an effective kinetic resolution of the racemic starting material. Generally a relative rate of 10 or greater will allow for a >37% yield (out of 50%) of unreacted substrate which is between 90-100% enantiomeric purity.[8] It is important to note that a substrate which exhibits a low selectivity (i.e., s=2) can afford enantiomerically pure unreacted substrate, albeit in very low yield. Since the enantiomeric excess observed in kinetic resolutions is dependent on the conversion, s factors are useful for determining the relative effectiveness of various catalyst systems for a given reaction.



2.3

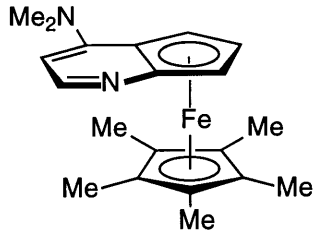


(2.3)

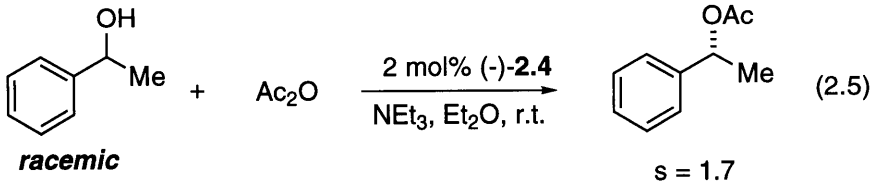
$\frac{k(R)}{k(S)} = s = 6.5$

87% ee at 67% conversion

We then developed a second class of complexes in which a π-bound pyrindine ((DMAP*)FeCp*, **2.4**) was used as a nucleophilic catalyst. The racemic complex was an accelerant for the same reactions as the chiral azaferrocene (**2.3**). When enantiopure (DMAP*)FeCp* (**2.4**) was used as a catalyst for a kinetic resolution, the selectivity (s = 1.7) was disappointingly low (Eq 2.5).

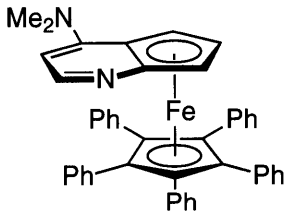


2.4

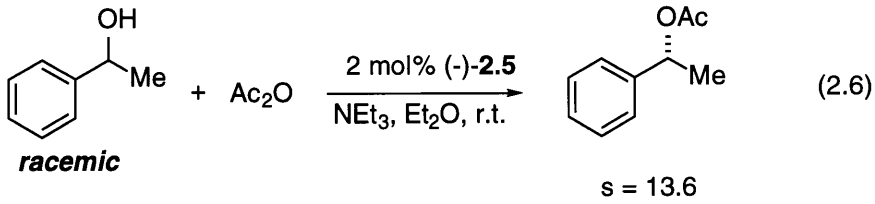


(2.5)

Although the pentamethylcyclopentadienyl ring is considered a very bulky ligand, we reasoned that a bulkier bottom ring might allow for better differentiation between the top and bottom faces of the complex, and therefore better selectivity for the kinetic resolutions. Dr. Hallie Latham first investigated this proposal by installing a pentaphenylcyclopentadienyl ring as the bottom ligand of the complex. Although the electron-withdrawing properties of the phenyl rings could diminish the activity of the nucleophile, it was hoped that the more asymmetric environment about the nucleophilic atom would more than make up for the loss in activity with a greatly enhanced selectivity. This new catalyst, (DMAP*)Fe(C_5Ph_5) (**2.5**), was found to dramatically increase the selectivity of the kinetic resolution of secondary alcohols with acetic anhydride (Eq 2.6).[9]

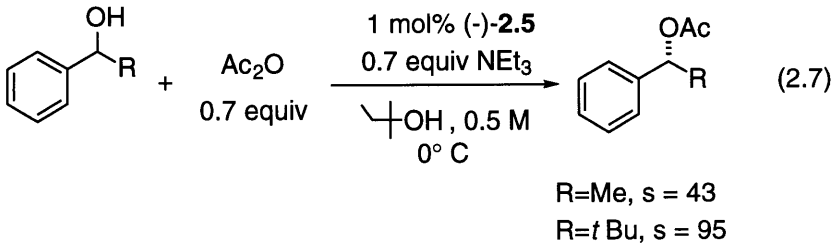


2.5



(2.6)

Subsequent improvements in the conditions for this reaction have allowed for still greater selectivities. The optimal conditions for the kinetic resolution of racemic secondary alcohols were found to use *tert*- amyl alcohol (0.5 M) as the solvent at 0 °C. Utilizing these conditions, the (DMAP*)Fe(C_5Ph_5) (**2.5**) catalyst allowed us to achieve selectivities of 32-95 for a variety of secondary aryl-alkyl alcohols (Equation 2.7).[10]



(2.7)

R=Me, s = 43
R=*t* Bu, s = 95

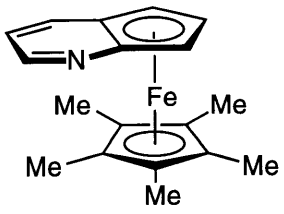
Chapter Two, Part A:

Ferrocene-Derived Complexes with *N*-Heterocyclic Ligands

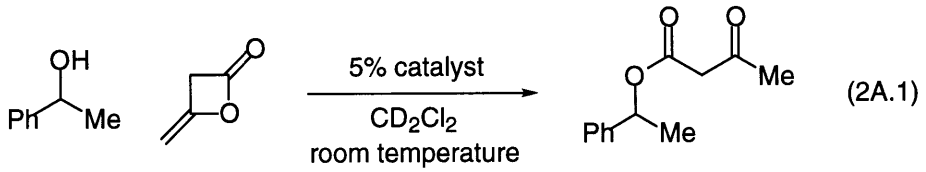
INTRODUCTION

The complexes that our group had previously utilized as nucleophilic catalysts used "standard" Cp^X ligands as the bottom ligand. Since we were developing a nucleophilic catalyst, having very electron-rich complexes was important. We reasoned that more electron-rich Cp^X rings would impart more nucleophilicity to our complex as a whole. Also, since the bottom ligand was important for imparting chirality on the heteroaromatic nitrogen, having a bulky ligand was also desired. Although the (C_5Ph_5) ligand appeared to be capable of completely blocking the bottom face of the catalyst (see use of (DMAP*)Fe(C_5Ph_5) in acylation, Eqs 2.6 and 2.7) it seemed that the electron withdrawing-nature of the phenyl groups might be decreasing the overall electron density of the complex.

We also knew, with respect to the pyrindinyl ferrocenes, that the dimethylamino moiety on the pyrindine boosted the nucleophilicity of the catalyst system. The analogous result has been seen with respect to the activities of DMAP and pyridine as nucleophilic catalysts.[2] The parent pyrindinyl complex (**2A.1**) shows greatly reduced activity (Eqs 2A.1 and 2A.2) as compared to the dimethylamino-substituted pyrindine complex ((DMAP*)FeCp*, **2.4**).[7] Since the synthesis of this dimethylaminopyrindine ligand (DMAP*H) is long and low-yielding (6 steps, 8% overall yield),[7] we hoped to find an electron-rich bottom ligand which could counter the loss of the dimethylamino group on the top ligand. In this way we could develop catalysts which utilized the easily prepared (3 steps, 44% yield) parent pyrindine ligand.

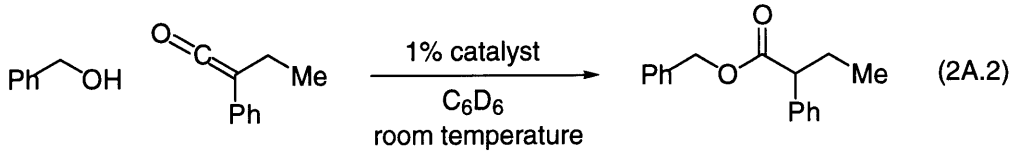


2A.1



(2A.1)

complex	half-life (min)
2A.1	~ 50,000
2.4	< 3
none	no reaction (3500 min)

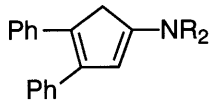


(2A.2)

complex	half-life (min)
2A.1	20
2.4	2
none	600

We therefore set out to develop both aza- and pyrindinylferrocene complexes that utilized less traditional Cp^X ligands which are both electron-rich and bulky. The aminocyclopentadienyl moiety (**2A.2**)[11] seemed a perfect candidate for this. The use of aminoCp ligands in organometallic complexes has become fairly common, most often to form complexes of the general formula "$(aminoCp)_2M$". Studies of the redox potentials of these complexes showed that the aminoCp ligands did increase the overall electron-richness of the metal center.[12] In all cases, crystal structure analyses of these complexes show that the Cp(C)-N bond is significantly shortened (as compared to normal C-N single bonds), indicating the donation of the

lone pair on nitrogen into the Cp ring.[12]



2A.2

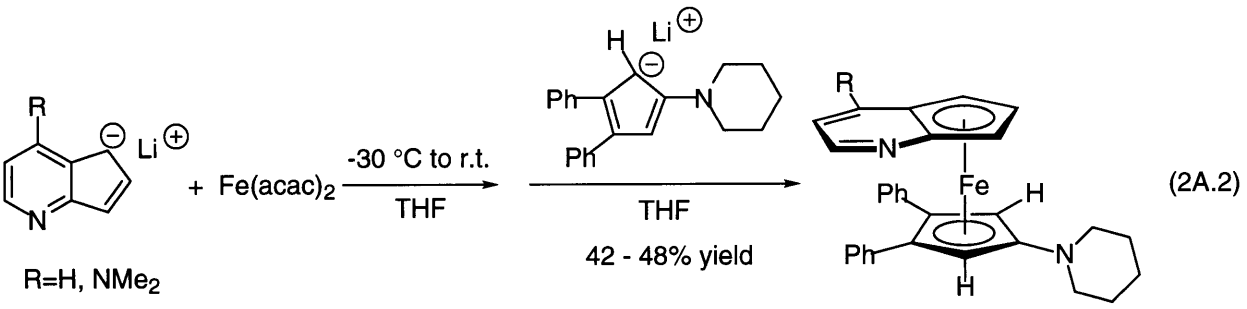
Although mixed sandwich complexes in which only one ligand was an aminoCp were unprecedented, it seemed the synthetic method commonly used to access the dimers could be modified such that the desired pyrrolyl- and pyrindinyl-aminocyclopentadienyl iron complexes could be prepared. We therefore set out to synthesize a series of these complexes and test their reactivity as nucleophilic catalysts. We hoped to be able to deduce whether the aminocyclopentadienyl ligand significantly affected the electron-richness of the top heterocyclic ligand and provided us with a more nucleophilic catalyst.

RESULTS AND DISCUSSION

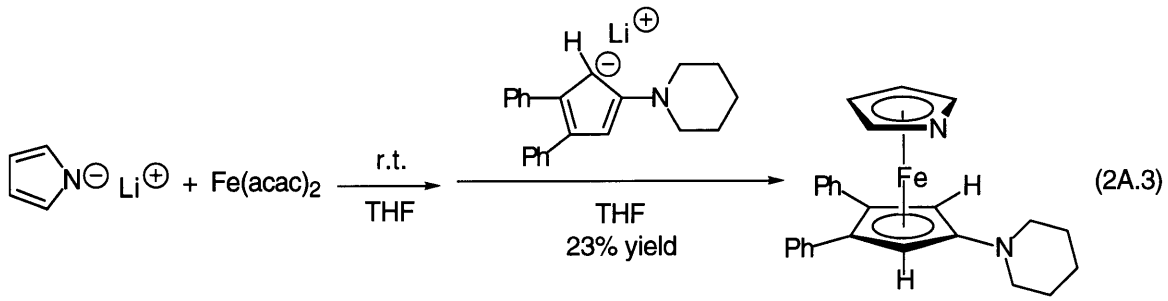
Preparation of Catalysts

The synthesis of the desired complexes required slightly different conditions than those used to prepare the complexes with "traditional" Cp^X ligands (Cp, Cp*, (C_5Ph_5)). Treatment of $FeCl_2$ with one equivalent of aminocyclopentadienyl lithium ($(ACp)^-Li^+$) and one equivalent of a pyrindinyl (or pyrrolyl) ligand resulted, in all cases, in the $(ACp)_2Fe$ complex. The use of $Fe(acac)_2$[13] as an Fe(II) source has been reported to be a much more effective way to prepare mixed sandwich complexes of iron. While addition of one equivalent of Cp*Li to $FeCl_2 \bullet 2THF$ usually results in Cp^*_2Fe, the same addition to $Fe(acac)_2$ results in only single addition of the Cp* anion. Subsequent reaction with a second equivalent of Cp^XLi results in the desired mixed-sandwich ferrocenes.[14]

In our hands, the use of $Fe(acac)_2$ in preparing pyrindinylferrocenes was initially ineffective. Addition of the $aminoCp^-Li^+$ to the $Fe(acac)_2$ resulted in only $(aminoCp)_2Fe$ being isolated. By reversing the order of addition, though, and adding the pyrindinyl anion to the $Fe(acac)_2$, followed by addition of the $aminoCp^-Li^+$, reasonable yields of the desired product were obtained. This appeared to be a general method of preparation for both pyrindinyl- (Eq 2A.2) and (η^5-pyrrolyl)-iron complexes (Eq 2A.3).

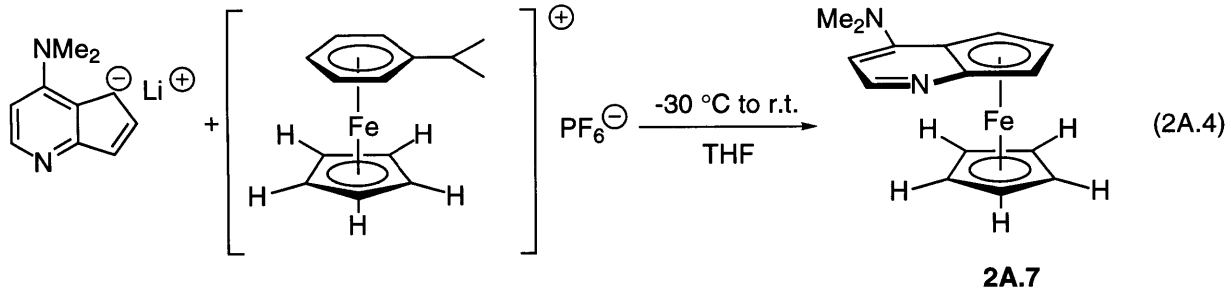


R=H, **2A.3**
R=NMe_2, **2A.4**



2A.5

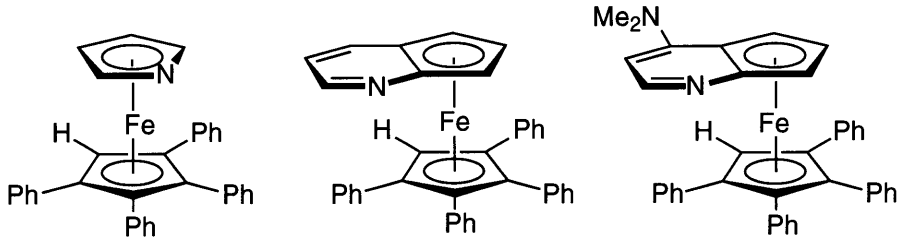
In order to fully investigate the effects of electron-donating and electron-withdrawing groups on the bottom ligand of the azaferrocene and pyrindinyliron complexes, we synthesized a variety of other complexes. Preparation of the parent Cp complexes had always proved troublesome due to the propensity of the Cp^-Li^+ to form Cp_2Fe instead of the desired mixed sandwich compounds. We found a literature precedent for synthesizing mixed sandwich cyclopentadienyl iron complexes which utilized the commercially available $[(cumene)CpFe]^+PF_6^-$ salt.[15] This salt, which is very soluble in THF, reacts rapidly with a second Cp^X anion to generate the desired mixed ligand cyclopentadienyliron complexes. The (DMAP*) ligand was successfully reacted with this salt to form the desired (DMAP*)FeCp complex, **2A.7** (Eq 2A.4).



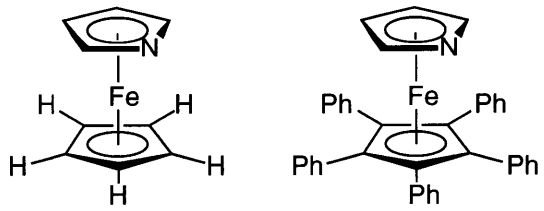
(2A.4)

2A.7

The tetraphenylCp ligand was also used as a bottom ligand for these complexes. The deprotonation of tetraphenylCpH is easily achieved using *n*-BuLi in THF at room temperature. The use of $FeCl_2$ as an iron source results in a large amount of octaphenylferrocene, while the use of $Fe(acac)_2$ allows for a much higher yield of the desired complex. Both (η^5-pyrrolyl) (**2A.8**) and pyrindinyl (**2A.9, 2A.10**) iron complexes were synthesized and isolated. The remaining complexes needed for these studies (**2A.11** and **2A.12**) had been prepared previously by members of our group.



2A.8 **2A.9** **2A.10**



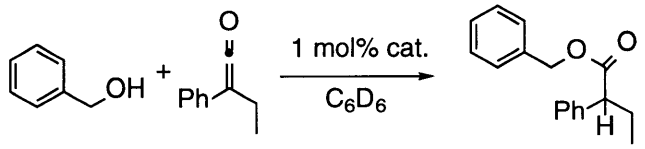
2A.11 **2A.12**

In order to compare the reactivity of these complexes, we chose the ketene solvolysis reaction for the azaferrocenes[7] and the Baylis-Hillman reaction for the pyrindinyl ferrocenes. We set out to investigate the relative effects of the Cp*, aminoCp (ACp), Cp, (C_5Ph_4H), and (C_5Ph_5) ligands on the reactivity of these

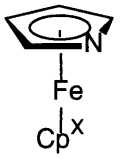
complexes.

Reactivity of (η^5-pyrrolyl)Fe(Cp^X) Complexes

Using the standard conditions (1.1 equiv benzyl alcohol, 1 equiv phenyl ethyl ketene, 1 mol% cat in C_6D_6 – 0.1 M),[7] we assessed the conversion in the presence of each catalyst by ^1H NMR (Eq 2A.5). The order of activity for these catalysts appears to be Cp* > (ACp) > Cp >>(C_5Ph_4H)> (C_5Ph_5) = no cat (**2.2** > **2A.5** > **2A.11** >> **2A.8** > **2A.12** = no cat.). From these data we can conclude that the aminoCp group adds some electron density to the catalyst in that (η^5-pyrrolyl)Fe(ACp) (**2A.5**) is a more active catalyst than (η^5-pyrrolyl)Fe(Cp) (**2A.11**), which has a non-sterically hindered, but also non-electron donating, Cp ligand. The catalysts with ligands bearing 4 or 5 phenyl groups ((η^5-pyrrolyl)Fe(C_5Ph_4H) (**2A.8**) and (η^5-pyrrolyl)Fe(C_5Ph_5) (**2A.12**) respectively) show greatly decreased activity for this reaction. This could be due to a combination of steric and electronic factors. Although the aminoCp ligand did not provide for a catalyst that was more active than the Cp* derivative, it seemed plausible that we could modulate the electronics of the catalyst using the aminoCp ligand.



(2A.5)



Cp^X	half-life (min)
Cp*, **2.2**	8
(ACp), **2A.5**	15
Cp, **2A.11**	23
(C_5Ph_4H), **2A.8**	230
(C_5Ph_5), **2A.12**	600
none	600

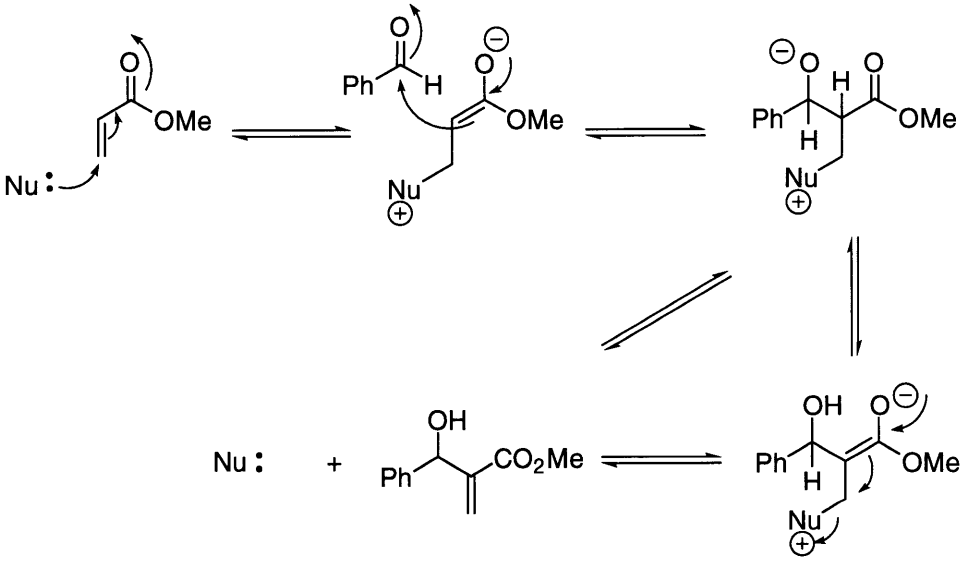
Reactivity of (DMAP*)Fe(Cp^X) Complexes

The Baylis-Hillman Reaction

The reaction that we chose to investigate with respect to the pyrindinyliron complexes was the Baylis-Hillman reaction. The first literature precedent for this reaction was a patent by Baylis and Hillman in 1972.[16,17]

The general reaction scheme involves carbon-carbon bond formation between an activated olefin and an aldehyde (or an imine). The reaction is known to be subject to nucleophilic catalysis, generally by tertiary amines, the most common of which is 1,4-diaza-bicyclo[2.2.2]octane, or Dabco. The mechanism has been shown to follow the scheme outlined in Scheme 2A.1.

Scheme 2A.1



Several versions of this reaction have been described in the literature. Many synthetically important products have the β-hydroxy-α-methylene-ketone (-nitrile, -ester) substructure, so improvements in this reaction are of considerable interest to the organic community. The main drawback to using this reaction is the very long reaction time. Even with the most active catalysts, the reaction can take anywhere from hours to weeks.

Reactivity of (DMAP*)FeCp* as a Catalyst for the Baylis-Hillman Reaction

We first set out to demonstrate the activity of the pyrindinyliron complexes for this reaction. We chose to focus on (DMAP*)FeCp* (**2.4**), as this would likely be the most active of our complexes. Many different activated olefins are commonly used for the Baylis-Hillman reaction, and a screening of those, with benzaldehyde as the aldehydic component, showed that methyl acrylate gave the best results with (DMAP*)FeCp* (**2.4**); acrylonitrile showed no reaction at all and methyl vinyl ketone polymerized rapidly under the reaction conditions. The desired product (5 mol% (DMAP*)FeCp* (**2.4**), 1 equiv benzaldehyde, 5 equivalents methyl acrylate) was formed in about 70% yield after 70 hours, at which point it appeared that the reaction had ceased. Decreasing the catalyst loading to 1 mol% results in a significant rate decrease, but the desired product is still produced.

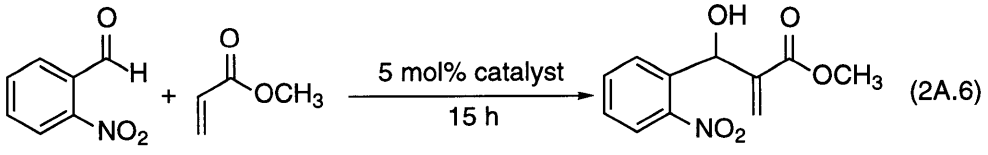
As expected, the presence of electron-rich substituents on the benzaldehyde slows down the reaction considerably, while the presence of electron-withdrawing substituents increases the rate of the reaction. Under the above conditions, 4-*t*-butyl benzaldehyde provides a 50% yield of product after 483 hours; reaction of 2-nitro benzaldehyde leads to complete consumption of the aldehyde after only 17 hours.

Although these reactions were much cleaner and faster when they were run neat, some literature reports have cited the use of solvents that stabilize the reactive zwitterionic intermediate (THF, Et_2O, MeOH) as an effective way to increase the rate of the reaction, sometimes even making this more effective than running the reaction neat.[17] For instance, using water, formamide or ethylene glycol as the solvent was found to increase the rate of the Dabco-catalyzed reaction between benzaldehyde and acrylonitrile. This was postulated to be an effect of the solubility of both benzaldehyde and acrylonitrile in these solvents.[18] Sonication[19] and increased pressure[20] have also been shown to increase the rate of the reaction.

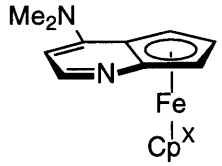
Unfortunately, the reaction catalyzed by (DMAP*)FeCp* (**2.4**) showed no conversion when run in THF or acrylonitrile, but in MeOH the rate was qualitatively the same as when the reaction was run neat. The use of water as a solvent resulted in a biphasic solution and apparent catalyst decomposition. Likewise, no added benefits were seen when using either sonication or slightly increased pressure (1600 psi).

Relative Reactivity of (DMAP*)FeCp^X complexes in the Baylis-Hillman Reaction

We next attempted to determine the effect of changing the bottom ring of the (DMAP*)FeCp^X complexes with respect to the rate of the reaction. Using 2-nitro benzaldehyde as the aldehydic partner and methyl acrylate (5 equiv) as the activated olefin, we ran the reaction with a variety of catalysts (5 mol%) at room temperature (Eq 2A.6). From this qualitative rate comparison it appears that (DMAP*)FeCp* (**2.4**) is the fastest catalyst, with (DMAP*)Fe(ACp) (**2A.4**) being a close second. The (DMAP*)FeCp complex (**2A.7**) is a competent catalyst, as is the tetraphenyl derivative ((DMAP*)Fe(C_5Ph_4H), **2A.10**). The (DMAP*)Fe(C_5Ph_5) (**2.5**) complex, as well as *all* parent pyrindinyl-based complexes (**2A.1** and **2A.3**), is inactive under the reaction conditions.



5 equiv



Cp^X	conv. (%)
Cp*, **2.4**	100
(ACp), **2A.4**	76
Cp, **2A.7**	46
(C_5Ph_4H), **2A.10**	62
(C_5Ph_5), **2.5**	0
2A.1, 2A.3	0
none	0

Some important conclusions were drawn from the relative rates: 1) The Cp

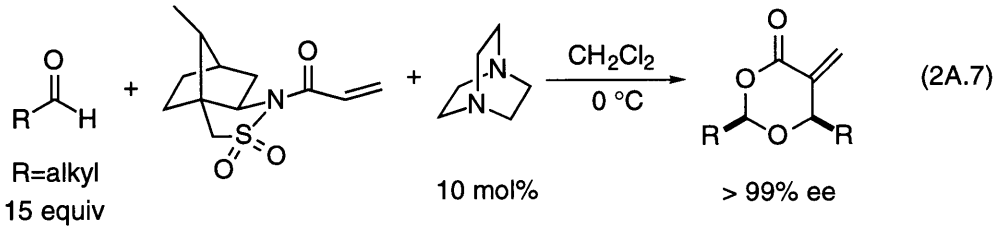
complex (**2A.7**) is an effective catalyst, but is slower than the Cp* (**2.4**). Therefore it appears that the added electron density of the Cp* ring boosts the nucleophilicity enough to counteract the steric effect of this moderately bulky ligand. 2) The parent pyrindinyl system, even with the nucleophilicity boost provided by the Cp* or (ACp) ligand (**2A.1, 2A.3**), is not an effective nucleophilic catalyst even with the fast-reacting 2-nitrobenzaldehyde. Therefore it seems that the added electron donation from the dimethylamino group on the pyrindine is necessary, unless another bottom ligand can be found that is more electron-donating than Cp*. The aminoCp ligand does not appear to be a stronger electron-donating ligand than Cp* in this case either.

It was reasoned that an aminoindene ligand[11,21] might add enough electron-density to the complex to counteract the loss of the dimethylamino group on the indenyl ligand, as well as add some steric bulk to the complex to allow for an enantioselective reaction. Unfortunately we were unable to synthesize an appropriate ligand. We ultimately had problems synthesizing and isolating even the parent indenyl(pyrindinyl)ferrocene.

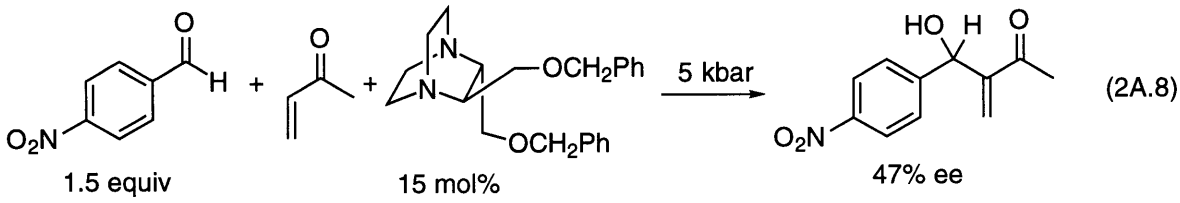
Enantioselective Baylis-Hillman Reactions with (DMAP*)Fe(Cp^X) Complexes

The development of an enantioselective version of this reaction would also greatly improve the usefulness of this reaction. With the rising use of enantiopure pharmaceuticals, more methods are needed that allow the efficient preparation of single enantiomers of a drug substance. A few examples of enantioselective Baylis-Hillman reactions have been presented in the literature. The most commonly used technique for achieving enantioselectivity is with the use of a chiral auxiliary on the olefinic substrate (Eq 2A.7).[22] The chiral auxiliary is removed after the reaction is complete to provide the desired product. Although the enantioselectivities are often good using this technique, the recovery of the chiral auxiliary can be time-

consuming and therefore costly on a production scale. The development of a highly active catalyst for an asymmetric Baylis-Hillman reaction might therefore be more desirable than using stoichiometric chiral auxiliary. Some efforts towards this end have produced promising results (Eq 2A.8).[20]



(2A.7)

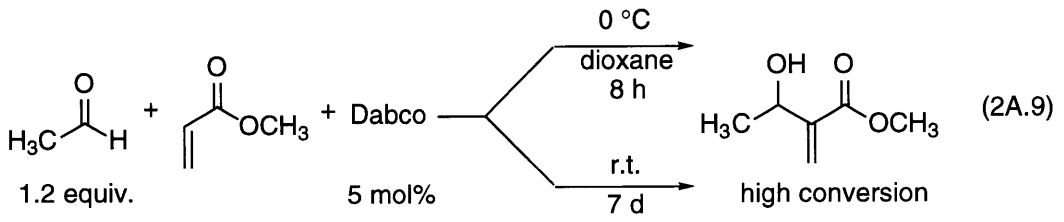


(2A.8)

Therefore, we set out to analyze the enantioselectivity of the reaction in the presence of the enantiopure (DMAP*)FeCp^{X}catalysts. Using the standard conditions (neat, 5 mol% cat, 5 equiv methyl acrylate), a series of aldehydes were screened resulting in a maximum ee of only 10% with benzaldehyde as an aldehydic partner. Alcoholic solvents showed no increase in ee and no apparent differences were seen between the (DMAP*)FeCp* (**2.4**) and (DMAP*)Fe(ACp) (**2A.4**) complexes.

During the course of this investigation, a report was published by Leahy that described a set of very effective conditions for the Baylis-Hillman reaction.[23] The use of dioxane as a solvent at 0 °C with Dabco as a catalyst resulted in increased rates of reaction as compared to reactions run at room temperature (Eq 2A.9). We reasoned that an enantioselective reaction might be more likely when run in a solvent, and the increased rate observed under these conditions could allow for a synthetically useful reaction. We therefore attempted to use these conditions for our enantioselective version of the Baylis-Hillman reaction. Although the selectivities were no higher than under our previous conditions, it did seem that

there was a slight rate increase, making the reaction run in solvent at least feasible as a synthetic method. We therefore set out to screen reaction conditions in an attempt to develop a more enantioselective reaction.



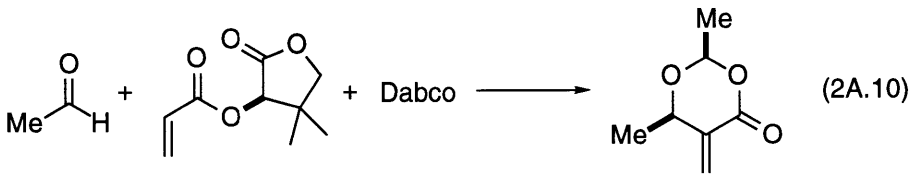
(2A.9)

A screening of solvents showed that many could be used with some success: dichloromethane, benzene, toluene, ether, ethanol, THF, trifluorotoluene, nitrobenzene, and *tert*- butyl methylether. The solvents that allowed for the highest conversion over a set period of time also had the lowest selectivities.[24] When the reaction was run with only a slight excess of *o*-chlorobenzaldehyde, methyl acrylate (1 equiv), and (DMAP*)Fe(ACp) (**2A.4**) (5 mol%) at 4 °C, the use of benzene as a solvent was the most effective, resulting in a 32% ee for the isolated product. Ether, THF and *tert*-butylmethylether also showed >26% ee under the same conditions. We therefore adopted the use of benzene (2.7 M) as a solvent for these reactions.

We found that the selectivity of the reaction was enhanced by decreasing the temperature from room temperature to 4 °C. Further decreases in the temperature had no significant impact on the selectivity. Changes in the concentration and catalyst loading do not appear to affect the enantiomeric excess. The rate of the reactions can be increased by using excess (5 equiv) aldehyde or acrylate, but the selectivity decreased dramatically with the use of excess acrylate. No change in the ee was seen with an excess of aldehyde. In an effort to drive the reaction to high conversion at a fairly rapid rate, while still achieving enantioselectivity, we adopted the standard conditions of aldehyde (5 equiv), acrylate (1 equiv), catalyst (5 mol%) and benzene (2.4 M).

Under these conditions, it was again noted that (DMAP*)FeCp* (**2.4**) was the most active complex; (DMAP*)Fe(ACp) (**2A.4**) was the only other active complex with both the (DMAP*)Fe(C_5Ph_4H) (**2A.10**) and (DMAP*)Fe(C_5Ph_5) (**2.5**) complexes showing no conversion after 23 hours. We therefore set out to compare the enantioselectivities of (DMAP*)FeCp* (**2.4**) and (DMAP*)Fe(ACp) (**2A.4**) for a variety of substrate pairs for the Baylis-Hillman reaction.

To our knowledge, no one has investigated the effect of the acrylate component on the enantioselectivity of the reaction. The acrylate component has been shown to have a large effect on the rate of the reaction, with arylacrylates showing substantial rate increases over simple alkylacrylates.[25] We therefore studied a series of acrylates as coupling partners with *o*-chloro benzaldehyde using both (DMAP*)Fe(ACp) (**2A.4**) and (DMAP*)FeCp* (**2.4**) under the standard conditions. We noted in certain cases that the final product did not appear to be the desired Baylis-Hillman product, but was the double addition product, which was noted by Drewes and Emslie in their attempts to use pantolactone acrylate as a coupling partner (Eq 2A.10).[26]



87% de, 10% ee

We found that this double addition product predominated with phenyl acrylate, trifluoroethylacrylate, pantolactone acrylate, and hexafluoroisopropyl acrylate. In order to assess the enantiomeric excess of these products we had to resort to transesterification with MeOH (procedure of Leahy, Eq 2A.11).[22] The final products in these cases were analyzed by GC as the methyl ester (chiral stationary phase) (Table 2A.1), but none were formed in good enantiomeric excess (≤ 10% ee)..

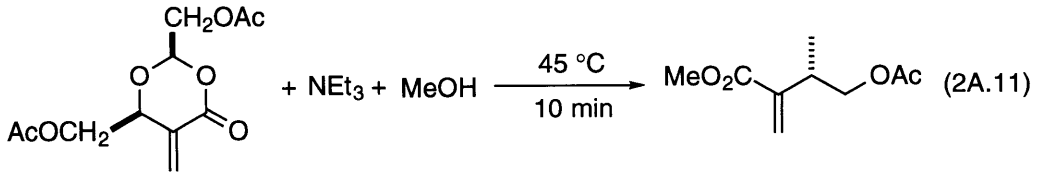
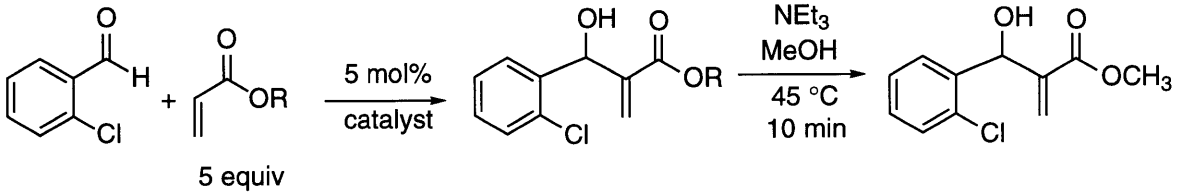


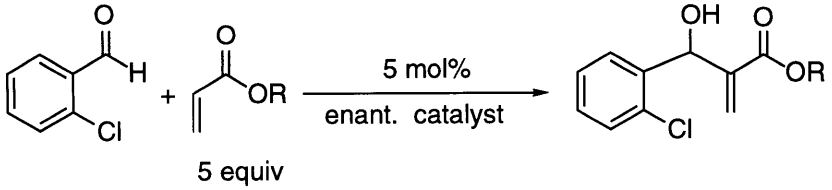
Table 2A.1. %ee of Baylis-Hillman Reaction with Varyious Acrylates.



Entry	Acrylate	catalyst	ee
1	R=Ph	**(-)-2A.4**	8%
2	R=CH_2CF_3	**(-)-2A.4**	10%
3	R=CH_2CF_3	**(+)-2.4**	2%
4	R=$CH_2CH(CF_3)_2$	**(-)-2A.4**	6%
5	R=$CH_2CH(CF_3)_2$	**(+)-2.4**	4%

Several other alkylacrylates were used as coupling partners and found to give the desired Baylis-Hillman adduct. The final products of the reaction of methyl, ethyl, *tert*-butyl, and *iso*-butyl acrylates with *o*-chloro benzaldehyde were analyzed as isolated (Table 2A.2). We found that the highest ee was achieved in the *iso*-butylacrylate coupling with *o*-chloro benzaldehyde in the presence of (DMAP*)Fe(ACp) (**2A.4**) (30% ee). In most cases, the products of reactions catalyzed by (DMAP*)Fe(ACp) (**2A.4**) had a higher ee than those produced by reactions catalyzed by (DMAP*)FeCp* (**2.4**).

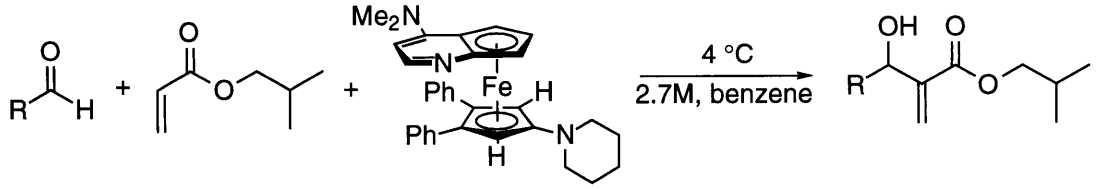
Table 2A.2. %ee of Baylis-Hillman Reaction with Various Alkyl Acrylates.

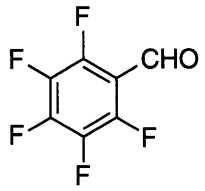
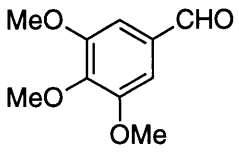
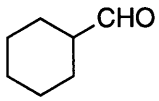
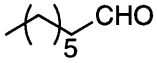
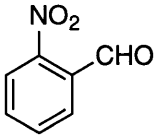
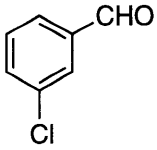
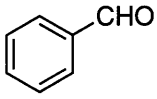


Entry	Acrylate	catalyst	ee
1	R=CH_3	**(+)-2A.4**	17%
2	R=CH_2CH_3	**(-)-2A.4**	12%
3	R=CH_2CH_3	**(+)-2.4**	16%
4	R=$C(CH_3)_3$	**(-)-2A.4**	NR
5	R=$C(CH_3)_3$	**(+)-2.4**	21%
6	R=$CH_2CH(CH_3)_2$	**(-)-2A.4**	30%
7	R=$CH_2CH(CH_3)_2$	**(+)-2.4**	21%

We then set out to investigate what effect changing the aldehyde would have on the observed enantioselectivity. Since *iso*-butylacrylate seemed to be the best olefinic coupling partner with *o*-chlorobenzaldehyde, we investigated the reaction of a series of aldehydes with *iso*-butylacrylate catalyzed by (DMAP*)Fe(ACp) (**2A.4**). The standard conditions were used except when the aldehydes were solids. In those cases (as with trimethoxybenzaldehyde and *o*-nitrobenzaldehyde), 10 equivalents of acrylate were used to solubilize the catalyst and aldehyde (1 equiv). In none of these cases was the coupling highly enantioselective (Table 2A.3).[27]

Table 2A.3. DMAP*FeACpF Catalyzed Baylis-Hillman - Aldehyde Variation.

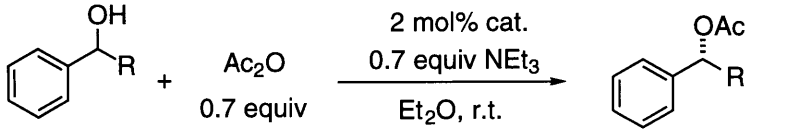


Entry	Aldehyde	ee
1		NR (144 h)
2		NR (145 h)
3		NR (145 h)
4		13%
5		0%
6		0%
7		0%

Kinetic resolution of 1-phenylethanol with (DMAP*)Fe(Cp^X)

In an attempt to determine the effect of the phenyl substituents of Cp^X on the enantioselectivity of the reaction, we ran the acylation of 1-phenylethanol with both

(DMAP*)Fe(ACp) (**2A.4**) and (DMAP*)Fe(C_5Ph_4H) (**2A.10**). Under the standard conditions at that time (see Eq 2A.12), both catalysts were much less selective than (DMAP*)Fe(C_5Ph_5) (**2.5**). We attribute this to the fact that both (DMAP*)Fe(ACp) (**2A.4**) and (DMAP*)Fe(C_5Ph_4H) (**2A.10**) have an unsubstituted carbon on the bottom cyclopentadienyl ligand which can orient itself underneath the reactive site, decreasing the chirality seen at the nucleophilic atom, and resulting in a relatively unselective reaction.

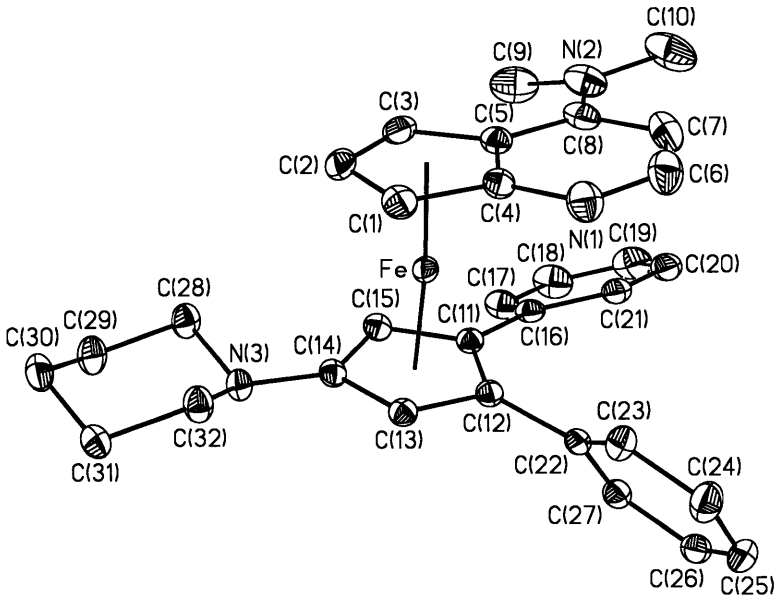


(2A.12)

(-)-2.5, s = 13.6
(-)-2A.4, s = 1.6
(-)-2A.10, s = 4.0

The crystal structure of (DMAP*)Fe(ACp) (**2A.4**) (Figure 2A.1) shows that the bulk of the bottom ligand is fairly small in comparison to a (C_5Ph_5) ligand. The piperidine is in a chair conformation and the phenyl rings are not very far out of planarity with the cyclopentadienyl ring. The ability of the (C_5Ph_5) ligand to act as a "perfect" blocking group is attributed to the fact that the phenyls are in a propeller-type conformation and completely occupying the space underneath the (DMAP*) ring.

Figure 2A.1. ORTEP illustration of rac-(DMAP*)Fe(ACp) (**2A.4**).



The C(14)-N(3) bond is also fairly short (1.387 Å as compared to 1.400 Å for a standard C-N single bond[12]) for (DMAP*)Fe(ACp) (**2A.4**), suggesting that the piperidinyl nitrogen is fully involved in the electronics of the Cp ring, as we expected from previous literature reports of these types of compounds.[12]

CONCLUSION

It appears that the use of an aminoCp ligand can slightly affect the electronics of these metallocene complexes. The use of a diphenylaminoCp ligand slightly decreases the nucleophilicity of (η^5-pyrrolyl)Fe(ACp) (**2A.5**) with respect to its activity in the ketene solvolysis reaction versus (η^5-pyrrolyl)Fe(Cp*) (**2.2**).

The use of the (ACp) ligand on the (DMAP*) complexes likewise has the effect of a slight decrease in the activity of the catalyst with respect to the pentamethylcyclopentadienyl complex. Again this may be due to the electron-withdrawing nature of the phenyl substituents or their steric bulk. (DMAP*)Fe(ACp) (**2A.4**) turns out to be more reactive than the less-bulky and less electron-rich Cp complex ((DMAP*)FeCp (**2A.7**)), therefore supplying further evidence that the (ACp) ligand does add some electron-richness to the complex versus the parent Cp. The tetraphenylCp derivative ((DMAP*)Fe(C_5Ph_4H) (**2A.10**)) of the catalyst is relatively inactive compared to the other catalysts mentioned, and the pentaphenylCp derivative ((DMAP*)Fe(C_5Ph_5) (**2.5**)) is completely inactive for these reactions.

The use of the (ACp) ligand also adds some of the bulk that seems to be necessary for enantioselectivity in this reaction. In most cases, Baylis-Hillman reactions run with enantiopure complex are more selective when (DMAP*)Fe(ACp) (**2A.4**) is used vs (DMAP*)FeCp* (**2.4**). The enantiomeric excess observed with (DMAP*)Fe(ACp) (**2A.4**) is, at the highest, 30%. The most successful enantioselective versions of the Baylis-Hillman reaction that have been published report enantioselectivities of 47%, under conditions that would be rather difficult to achieve on a benchtop (7 kbar). This moderate ee observed with (DMAP*)Fe(ACp) (**2A.4**) as a catalyst does *not* appear to be general, as most substrates give much lower selectivities in the coupling reaction.

The acylation of 1-phenylethanol is not very selective with either the aminoCp complex ((DMAP*)Fe(ACp) (**2A.4**)) or the tetraphenyl complex ((DMAP*)Fe(C_5Ph_4H)

(**2A.10**)). This seems to imply that for a very selective acylation reaction there must be complete blocking of the bottom face of the complex, as is seen in ((DMAP*)Fe(C_5Ph_5) (**2.5**)).

Although the aminocyclopentadienyl ligand that was used in this case did not impart greater electron-density on the metal than did Cp*, it is possible that an aminoCp that has only electron-donating substituents (such as alkyl groups) could be more electron-donating. Better synthetic methodology will be required to prepare ligands of this type.

EXPERIMENTAL

General. Pyrrole (Aldrich, from CaH_2) and *iso*- butylacrylate (Aldrich) were distilled and stored at -34 °C under an atmosphere of nitrogen. Benzyl alcohol (Aldrich), methanol, *i* -PrOH, triethylamine (from CaH_2), dioxane, ethanol, trifluorotoluene, nitrobenzene, tertbutlymethylether and acetic anhydride (from quinoline) were distilled prior to use.

C_6D_6 (CIL) and toluene-d_8 (CIL) were dried over alumina before use. Iron(II)dichloride (Strem) was ground before use.

Methyl acrylate, trifluoroethylacrylate, *tert*-butylacrylate, ethyl acrylate, 4-hydroxybutylacrylate, hexafluoroisopropyl acrylate, isobutylacrylate, pentafluorobenzaldehyde, cyclohexylaldehyde, octylaldehyde, *o*-chloro-benzaldehyde, *m*-chlorobenzaldehyde, and benzaldehyde were purchased from Aldrich and distilled before use.

n-BuLi (1.6 M in hexane, Strem), acetic acid (glacial, Mallinckrodt), tetraphenylcyclopentadiene (Aldrich), sulfuric acid (Mallinckrodt), dimethylamine (40% in H_2O, Fluka), acetyl chloride (Fluka), ethanol (Pharmco), NO_2PF_6 (Elf-Atochem), hydrogen peroxide (30%, Mallinckrodt), pyrindane (Acros), phenol (Aldrich), (R)-Pantolactone (Aldrich), acryloyl chloride (Aldrich), tosic acid (Fluka), benzil (Aldrich), 2,4-pentanedione (Aldrich), red phosphorus (Aldrich), CpFe(cumene)$^+PF_6^-$ (Aldrich), and Dabco (Aldrich) were used as received.

Trimethyoxybenzaldehyde and o-nitrobenzaldehyde were received from Aldrich and crystallized before use.

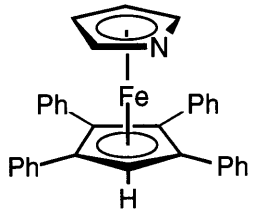
Piperidine (Aldrich) was dried over 4 Å sieves before use.

Phenyl ethyl ketene was prepared according to the method of Tidwell,[28] and 1-benzoyl-1-phenyl-propane **[62047-56-7]** was prepared as in previous references.[7]

Solvents were distilled from the indicated drying agents: CH_2Cl_2 (CaH_2);

benzene (Na/benzophenone); pentane (Na/benzophenone); hexane (Na/benzophenone); THF (Na/benzophenone); Et_2O (Na/benzophenone); toluene (Na); nitromethane (CaH_2).

PREPARATION OF CATALYSTS



(η^5-Pyrrolyl)Fe(C_5Ph_4H) (2A.8). Into a flask containing tetraphenylcyclopentadiene (185.4 mg, 0.500 mmol) and a stirbar was added THF (7 mL) by syringe. The resulting light yellow solution was stirred at room temperature and then *n*-BuLi (0.315 mL, 1.6 M in hexane, 0.504 mmol) was added via syringe. The solution immediately became a bright yellow color with a bluish phosphorescence. This was stirred at room temperature for 25 min.

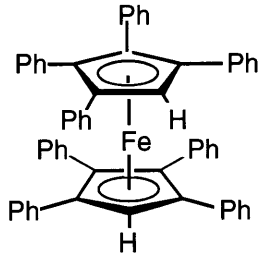
Into a second flask was added the pyrrole (35 μL, 0.51 mmol), a stirbar and THF (2 mL). To this clear, colorless solution was added *n*-BuLi (0.315 mL, 1.6 M in hexane, 0.504 mmol) by syringe. The resulting very light yellow solution was stirred at room temperature for 45 min.

Into a third flask was weighed the $FeCl_2$ (63.5 mg, 0.501 mmol). To this was added a stirbar and THF (3 mL). The resulting tan slurry was cooled to ~ -30 °C and then the tetraphenylcyclopentadienyl anion solution was added dropwise. Solution immediately became orange. After approximately 5 minutes at -30 °C the solution was allowed to warm to room temperature.

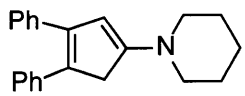
Once the solution began to warm, the color became reddish (indicating the formation of octaphenylferrocene) and the pyrrolyl anion solution was immediately added and the resulting solution was stirred at room temperature for 4 h, TLC (50 % EtOAc: hexane) showed desired tetraphenylazaferrocene (R_f = 0.83, vis-orange) and octaphenylferrocene (R_f = 0.90, vis-pink). Solution was stirred at room temperature for another 10 h.

The solution was filtered through a plug of celite and the solvents removed from the resulting orangish solution. The resulting reddish-orange solid was then chromatographed (silica gel, hexane, then 5-10% EtOAc/hexane). The tetraphenylazaferrocene was collected, filtered and the solution was concentrated down to an orange solid. Column chromatography was utilized a second time to remove trace octaphenyferrocene impurities. Orange solid (18.7 mg, 8% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.54 (s, 2H), 5.11 (s, 1H), 5.32 (s, 2H), 7.1-7.4 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 69.4, 76.8, 86.9, 89.2, 94.4, 126.8, 127.6, 128.0, 129.8, 132.3, 135.0, 136.6; IR (neat) 3058, 2923, 2851, 1600, 1502, 1441, 1264, 1113, 1073, 1027.6, 1010, 823, 792, 765, 737, 697, 632, 569, 553, 532 cm^{-1}; Anal. Calcd for $C_{33}H_{25}NFe$: C, 80.66; H, 5.13; N, 2.85. Found: C, 80.25; H, 5.21; N, 2.80; m.p. (N_2) 183-185 °C; TLC (50% EtOAc/hexane, vis-orange, PMA) R_f = 0.83.



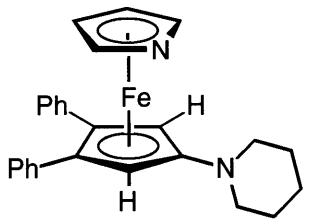
Octaphenylferrocene [12151-36-9]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70 (s, 2H), 6.8-7.1 (m, 19H), 7.2-7.4 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 67.9, 86.5, 91.9, 126.2, 126.3, 126.9, 127.6, 129.3, 132.2, 135.1, 135.3; IR (neat) 3057, 1600, 1499, 1440, 762, 730, 696, 556 cm^{-1}; HRMS*m/z* 794.2633 [M$^+$], calcd for $C_{58}H_{42}Fe$ 794.2636; m.p. > 250 °C; TLC (50% EtOAc/hexane, vis-pink, PMA) R_f = 0.90.



ACpH

3,4-diphenyl piperidinyl cyclopentadiene (ACpH). Material was prepared via a method analogous to that of Plenio and Burth.[11] A flask was charged with 3,4-diphenylcyclopent-2,3-enone (2.99 g, 12.8 mmol), *p*-toluenesulfonic acid (0.037g, 0.20 mmol), benzene (40 mL) and piperidine (1.9 mL, 19 mmol). A stirbar was added, and the solution was stirred for 5 min. A brown-yellow homogeneous solution resulted. A reflux condenser was fitted to the flask, and the solution was refluxed with removal of water. The solution became orange with heating and then darkened slightly, resulting in a brown solution. The solution was refluxed, with periodic removal of water, for 48 h.

The solution was cooled to room temperature and the solvents removed resulting in an orange oil with yellow solids. This was kept under an inert atmosphere and hexane (50 mL) was added. A yellow solid resulted, and this was filtered, and washed with pentane. After complete removal of solvents, a yellow solid resulted (2.761 g, 72% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.5-1.8 (m, 6H), 3.12 (m, 4H), 3.56 (s, 2H), 5.35 (s, 1H), 7.0-7.4 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 25.3, 42.7, 48.9, 104.6, 124.6, 124.7, 126.8, 126.9, 128.0, 128.3, 128.4, 138.6, 143.1, 157.6.



(η^5-Pyrrolyl)Fe(ACp) (2A.5). A solution of pyrrole (52 μL, 0.75 mmol) in THF (2

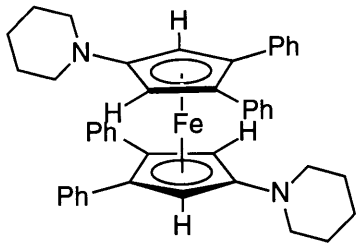
mL) was stirred at room temperature. To this clear, colorless solution was added *n*-BuLi (0.470 mL, 0.752 mmol) via syringe. The solution became very light yellow, but remained homogeneous. This was stirred at room temperature for 1 h.

A solution of **ACpH** (226.1 mg, 0.750 mmol) in THF (2 mL) was stirred at room temperature. The resulting brown-yellow solution was cooled to -30 °C and *n*-BuLi (0.470 mL, 0.752 mmol) was added via syringe. The resulting orange-brown solution was kept cold for 1 h.

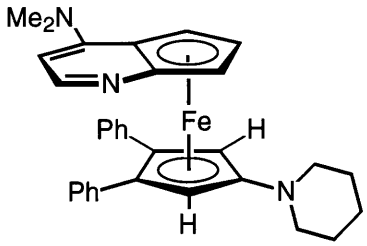
Into a third flask was weighed the $Fe(acac)_2$[14] (192.5 mg, 0.752 mmol). A stirbar and THF (4 mL) were added to the flask and the resulting brown-green solution was stirred at room temperature for 1 h. To this solution was then added the pyrrolyl anion solution. The resulting bright red solution was stirred at r.t. for one hour and the cyclopentadienyl anion solution was then added dropwise. The solution immediately became very deep red. This homogeneous solution was stirred at room temperature for 15 h.

The solution was then filtered through a plug of silica gel and material eluted with EtOAc. The solvents were removed resulting in a red-orange solid. TLC (50% EtOAc/hexane, Prod: vis-orange, R_f = 0.57; $(ACp)_2Fe$: vis-orange, R_f = 0.89). Material chromatographed on silica gel with 10%-50% EtoAc/hexane. Product fractions combined and solvents removed resulting in a bright orange solid (73.9 mg, 23% yield).

^1H NMR (300 MHz, $CDCl_3$) δ 1.69 (s, 2H), 1.81 (s, 4H), 3.05 (s, 4H), 4.43 (s, 2H), 4.58 (s, 2H), 5.57 (s, 2H), 7.28 (s, 6H), 7.50 (s, 4H) ; ^{13}C NMR (75 MHz, CDCl3) δ 24.1, 25.7, 50.4, 56.4, 74.9 (br), 82.0, 90.8 (br), 114.3, 126.3, 127.7, 129.8, 137.6; IR (neat) 2934, 2852, 1600, 1517, 1501, 1449, 1385, 1212, 1131, 1110, 818, 766, 735, 699, 590, 532 cm^{-1}; Anal. Calcd for $C_{26}H_{26}N_2Fe$: C, 73.94; H, 6.20; N, 6.63. Found: C, 73.51; H, 5.91; N, 6.48; m.p. (N_2) 127-128 °C; TLC (50% EtOAc/hexane, vis-orange, PMA-blue) R_f = 0.57.



Bis(aminocyclopentadienyl)ferrocene. Isolated as a red-orange solid. ^{1}H NMR (300 MHz, C_6D_6) δ 1.3 (br s, 4H), 1.4 (br s, 8H), 2.6 (br s, 8H), 4.2 (br s, 4H), 7.0 (br s, 12H), 7.5 (br s, 8H); ^{13}C NMR (75 MHz, C_6D_6) δ 25.0, 26.4, 51.6, 61.4, 82.8, 103.0, 116.3, 126.2, 128.1, 139.2; IR (neat) 2931, 2850, 1599, 1500, 1448, 970, 762, 697 cm^{-1}; HRMS*m/z* 656.2852 [M^+], calcd for $C_{44}H_{44}N_2Fe$ 656.2854; m.p. 214-215 °C; TLC (50% EtOAc/hexane, Prod: vis-orange, R_f = 0.89).



(DMAP*)Fe(ACp) (2A.4). ACpH (0.85 g, 2.8 mmol) was weighed into a flask and THF (16 mL) added. The resulting yellow solution was cooled to -30 °C and *n*-BuLi (1.87 mL, 2.99 mmol) was added dropwise. Resulting bright yellow solution was left cold for 1.5 h.

4-Dimethylaminopyrindine[7] (0.4831 g, 3.015 mmol) was weighed into a second flask and THF (12 mL) was added. The resulting light green solution was stirred while *n*-BuLi (1.87 mL, 2.99 mmol) was added dropwise. The resulting bright red solution was stirred at room temperature for 30 min.

A solution of $Fe(acac)_2$ (0.7250 g, 2.831 mmol) was prepared in THF (5 mL) and the resulting brown solution was cooled to -30 °C for 30 min. To this solution was

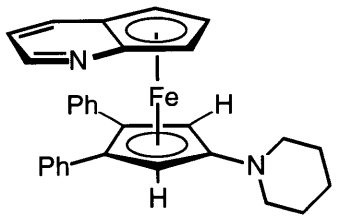
added the (DMAP*)Li anion solution. The resulting solution became reddish-brown. This was warmed to room temperature and stirred for 1 h. At this time, the enamine anion solution was added to the iron containing solution. The solution darkened and was then stirred at room temperature for 13.5 h.

The solution was filtered through a plug of silica gel with EtOAc and solvents removed from the resulting purple solution. The purple residue was then chromatographed on silica gel. Some $(ACp)_2Fe$ was noted as an orange band that eluted with hexane. The desired product was collected and condensed resulting in a plum-colored solid (0.6051 g, 42% yield).

^1H NMR (300 MHz, $CDCl_3$) δ 1.5-1.7 (m, 6H), 2.89 (s, 10H), 4.03 (d, J = 2.1, 1H), 4.22 (t, J = 2.9, 1H), 4.29 (d, J = 1.8, 1H), 4.56 (d, J = 1.5, 1H), 5.34 (d, J = 1.5, 1H), 5.58 (d, J = 5.4, 1H), 7.1-7.4 (m, 10H), 8.06 (d, J = 5.4, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.1, 25.7, 29.8, 41.1, 49.4, 54.9, 57.0, 63.3, 63.9, 71.3, 74.9, 79.1, 80.1, 96.4, 113.7, 125.9, 127.6, 129.4, 129.8, 137.4, 137.9 ; IR (neat) 2933, 1540, 14991, 1448, 1383, 1350, 1257, 1211.9, 1130, 1064, 1020, 908, 765, 698 cm^{-1}; Anal. Calcd for $C_{32}H_{33}N_3Fe$: C, 74.56; H, 6.45; N, 8.15. Found: C, 74.54; H, 6.47; N, 8.40; HRMS*m/z* 515.2024 [M^+], calcd for $C_{32}H_{33}N_3Fe$ 515.2024; m.p. 180-181 °C; TLC (10% NEt_3/EtOAc, vis- plum, blue-PMA) R_f = 0.57.

A suitable crystal for X-Ray crystal structure analysis was grown by slow diffusion of hexane into a dichloromethane solution of product at -11 °C.

The enantiomers of the product were separated using semi-preparative HPLC (Daicel CHIRALCEL OD, 1 cm X 25 cm, isopropanol/hexane/diethylamine = 22/78/0.2, 3 mL/min). Enantiomer 1 was collected from 11.50 to 14.5 min, and enantiomer 2 was collected from 16.0 to 22.5 min. Enantiomer 2: $[\alpha]^{20}_D$ = +2067° (c = 0.05, $CHCl_3$)



(P*)Fe(ACp) (2A.3). Pyrindine[29] (117.6 mg, 1.004 mmol) was weighed into a flask, followed by addition of THF (5 mL). The resulting clear, colorless solution was then cooled to -30 °C and *n*-BuLi (0.625 mL, 1.00 mmol) was then added dropwise to the solution. The resulting bright yellow solution was left cold for 5 min and then stirred at room temperature for 10 min.

The enamine (0.302 g, 1.00 mmol) was dissolved in THF (5 mL) and the resulting yellow solution was cooled to -30 °C and *n*-BuLi (0.625 mL, 1.00 mmol) added dropwise. The solution became dark yellow-orange and was kept cold for 15 min.

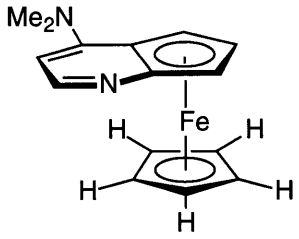
A solution of $Fe(acac)_2$ (256.9 mg, 1.003 mmol) was prepared in THF (5 mL) resulting in a brown solution. This solution was cooled to -30 °C and then the pyrindinyl anion solution was then added. The resulting red-orange solution was kept cold for 10 min and then stirred at room temperature for 20 min. The solution was yellow-green and homogeneous. To this was then added the enamine anion solution. The resulting solution was deep green and was stirred at room temperature for 5 h.

The solvent was removed from the solution and the resulting green residue was extracted with ether and filtered through an acrodisc. The solvents were removed from the resulting green solution and the green solid was then chromatographed on silica gel with EtOAc as an eluent. Product fractions were combined and solvents removed resulting in a very dark grey-purple solid (225.9 mg, 48% yield)

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.68 (m, 6H), 2.93 (s, 4H), 3.81 (s, 1H), 4.05 (s, 1H), 4.23 (m, 1H), 4.68 (s, 1H), 5.40 (s, 1H), 6.62 (m, 1H), 7.2-7.4 (m, 10H), 7.73 (d, J = 8.1, 1H), 8.42 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 25.6, 49.7, 55.1, 55.2, 62.2, 64.1, 74.2, 79.7, 80.0,

82.7, 110.1, 114.2, 118.5, 126.1, 126.2, 127.7, 127.8, 129.6, 137.5, 137.7, 139.6, 153.0; IR (neat) 3055, 2933, 2851, 1600, 1500, 1463, 1448, 1384, 1311, 1212, 1130, 765, 738, 698 cm^{-1}; Anal. calcd for $C_{30}H_{28}N_2Fe$: C, 76.27; H, 5.97; N, 5.93. Found: C, 76.22; H, 6.06; N, 5.55; m.p. (N_2) 131-132 °C; TLC (10% NEt_3/EtOAc, vis: grey-purple, PMA) R_f = 0.84.

The enantiomers of the product were separated using semi-preparative HPLC (Daicel CHIRALCEL OD, 1 cm X 25 cm, isopropanol/hexane/diethylamine = 12/88/0.2, 3 mL/min). Enantiomer 1 was collected from 13.00 to 17.00 min, and enantiomer 2 was collected from 18.25 to 22.00 min.

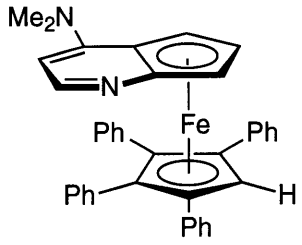


(DMAP*)FeCp (2A.7). Prepared by a method similar to that used by Roberts to prepare monophosphaferrocenes.[15] Into a vial was weighed the DMAP*H (115.1 mg, 0.718 mmol). To this was added THF (2 mL) and then *n*-BuLi (1.6 M, 0.45 mL, 0.72 mmol). The resulting reddish-brown solution was stirred at ~30° C for 1 h.

Into a second vial was weighed the [(cumene)CpFe]$^+PF6^-$ (275.4 mg, 0.713 mmol). To this was added THF (2 mL). The resulting yellow solution was cooled to -30 °C and the pyrindinyl anion solution was then added. The solution darkened considerably with the addition to a greenish-brown color. The solution was then warmed to ~30 °C and stirred for 1 h. The solution was now a reddish color. TLC (10% NEt_3/EtOAc) showed a reddish spot ~0.4 R_f. The solution was stirred for 17 h at 30 °C.

The solution was then concentrated and chromatographed (silica gel, 10% NEt_3/EtOAc). The product fractions were combined and then solvents removed resulting in a dark red, oily solid (90.8 mg, 46% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.35 (s, 6H), 3.90 (s, 5H), 4.13 (dd, J = 2.5, 3.0, 1H), 4.85 (dd, J = 1.0, 3.0, 1H), 5.23 (dd, J = 1.0, 2.5, 1H), 5.73 (d, J = 5.5, 1H), 8.20 (d, J = 5.0, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 41.5, 60.6, 62.3, 68.9, 69.0, 72.5, 95.3, 111.8, 154.1, 161.0; IR (neat) 2919, 1539, 1436, 1397, 1376, 1346, 1258, 1231, 1191, 1104, 1061, 1020, 1000, 908, 818, 643, 611, 531, 459 cm^{-1}; Anal. calcd for $C_{15}H_{16}N_2Fe$: C, 64.31; H, 5.76; N, 10.00. Found: C, 64.03; H,5.56; N, 9.80; TLC (10% NEt_3/EtOAc, vis: reddish-purple, PMA-blue) R_f = 0.38.



(DMAP*)Fe(C_5Ph_4H) (2A.10). The 4-dimethylaminopyrindine (0.1123 g, 0.763 mmol) was weighed into a flask followed by the addition of THF (4 mL) and then *n*-BuLi (0.50 mL, 0.80 mmol). The resulting red solution was then stirred at room temperature for 30 min.

Into a second flask was weighed the tetraphenylcyclopentadiene (303.0 mg, 0.818 mmol), This was dissolved in THF (8 mL) and the resulting light yellow solution was stirred at room temperature while *n*-BuLi (0.50 mL, 0.800 mmol) was added dropwise to the solution. The resulting bright yellow solution with a blue phosphorescence was stirred at room temperature for 1.5 h.

Into a third flask was weighed the $Fe(acac)_2$ (211.7 mg, 0.827 mmol). This was dissolved in THF (5 mL) and the resulting brown solution cooled to -30 °C. To this was added the (DMAP*)Li anion solution resulting in a red-brown solution which was warmed to room temperature and stirred for 1 h. After this time, the

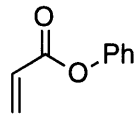
tetraphenylcyclopentadienyl anion solution was added and the solution immediately darkened. This was stirred at room temperature for 17 h.

The solvents were removed and the resulting purple oil was chromatographed (silica gel, 10% NEt_3/EtOAc). Very little octaphenylferrocene was eluted from the column. The desired product was concentrated resulting in a purple solid (0.2341 g, 53% yield).

^1H NMR (300 MHz, $CDCl_3$) δ 2.79 (s, 6H), 3.91 (t, J = 2.7, 1H), 4.70 (d, J = 4.0, 1H), 4.73 (s, 1H), 5.13 (d, J = 2.6, 1H), 5.53 (d, J = 5.3, 1H), 6.9-7.4 (m, 20H), 8.15 (d, J = 5.3, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.2, 65.1, 68.1, 68.7, 74.9, 77.8, 83.4, 85.8, 88.6, 88.7, 97.1, 113.6, 126.3, 126.5, 126.6, 126.8, 127.2, 127.5, 127.6, 127.7, 127.9, 129.2, 129.5, 132.6, 132.7, 135.3, 135.7, 136.1, 137.2, 154.4, 158.3; IR (neat) 3056, 1600, 1560, 1541, 1500, 1438, 1400, 1338, 1074, 1024, 908, 765, 736, 698 cm^{-1}; HRMS*m/z* 584.1916 [M^+], calcd for $C_{39}H_{32}N_2Fe$ 584.1915; m. p. 108-109 °C; TLC (10% NEt_3/EtOAc, vis-purple, PMA-blue) R_f = 0.56.

The enantiomers of the product were separated using semi-preparative HPLC (Daicel CHIRALCEL OD, 1 cm X 25 cm, chloroform/hexane/diethylamine 25/75/0.4, 3 mL/min). Enantiomer 1 was collected from 17.50 to 22.00 min, and enantiomer 2 was collected from 23.50 to 34.00 min. Enantiomer 2: $[\alpha]^{20}_D$ = +1563° (c = 0.05, $CHCl_3$)

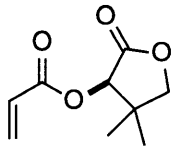
PREPARATION OF SUBSTRATES



Phenylacrylate [937-41-7]. Material was prepared by a method similar to that of Poll.[30] Phenol (3.62 g, 38.5 mmol) was weighed into a flask under an argon stream, followed by the addition of dichloromethane (50 mL) and triethylamine (8.0 mL, 57 mmol). The resulting clear, colorless solution was cooled to 0 °C and acryloyl chloride (3.8 mL, 47 mmol) was added dropwise to the solution over 20 min. The solution became yellow with the addition and salts began to form almost immediately. The solution was stirred at 0 °C for 1 h, and then extracted with 1N HCl (1 X 50 mL) and saturated $NaHCO_3$ (4 X 50 mL). The organics were dried over $MgSO_4$ and concentrated.

The product (a yellow oil) was then distilled at reduced pressure, resulting in a very light yellow liquid. This was redistilled and the resulting clear, colorless liquid (3.1018 g, 81% yield) was then taken into the glove box and stored at -34 °C until further use.

^1H NMR (300 MHz, $CDCl_3$) δ 5.43 (d, J = 9.9, 1H), 5.76 (dd, J = 10.6, 17.1, 1H), 6.03 (d, J = 17.0, 1H), 6.57 (d, J = 7.5, 2H), 6.67 (t, J = 7.3, 1H), 6.82 (t, J = 7.9, 2H)



(R)-Pantolactone Acrylate [102096-60-6]. Material was prepared by a method similar to that of Poll.[30] (R)-Pantolactone (5.01 g, 38.5 mmol) was weighed into a flask. Under an atmosphere of argon, dichloromethane (48 mL) and triethylamine (8.0 mL, 57 mmol) were added. The resulting clear, colorless solution was cooled to -29 °C (CH_3NO_2/N_2) and acryloyl chloride (3.75 mL, 46.2 mmol) was added dropwise

over 20 min. The resulting yellow solution began to form solids almost immediately. This solution was left cold for 4 h and then extracted with 1N HCl (1X 50 mL) and saturated $NaHCO_3$ (4 X 50 mL). The organics were dried over $MgSO_4$ and concentrated.

The product (a yellow oil) was then distilled at reduced pressure, resulting in a very light yellow liquid. This was redistilled at full vacuum and the resulting clear, colorless liquid (2.8365 g, 40% yield) was then taken into the glove box and stored at -34 °C until further use.

^1H NMR (300 MHz, $CDCl_3$) δ 1.10 (s, 3H), 1.19 (s, 3H), 4.03 (s, 2H), 5.41 (s, 1H), 5.94 (dd, J = 1.5, 11.0, 1H), 6.19 (dd, J = 10.2, 17.4, 1H), 6.49 (dd, J = 1.0, 17.0, 1H)

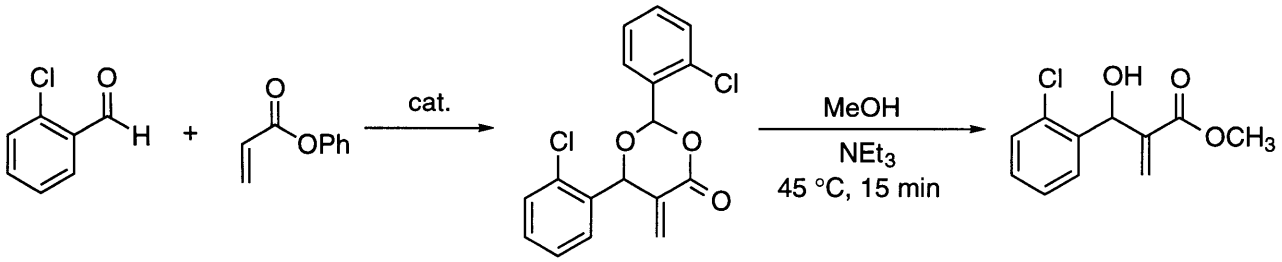
PREPARATION OF AUTHENTIC PRODUCTS

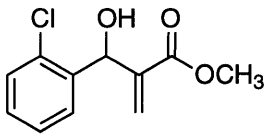
All racemic Baylis-Hillman adducts were prepared by a reaction of the two components in the presence of Dabco. The products were isolated and analyzed by GC, HPLC (chiral stationary phase) or ^{1}H NMR (with chiral shift reagents) for separation of the enantiomers. Derivation was necessary in some cases to anhance the separation of the enantiomers. Hydrogenation and/or transesterification were usually employed.

General procedure for Dabco catalyzed Baylis-Hillman reaction. To *o*-chlorobenzaldehyde (113 μL, 1.00 mmol) was added ethylacrylate (110 μL, 1.02 mmol) and diazabicyclooctane (1.8 mg, 0.015 mmol). The resulting homogeneous yellow solution was stirred at room temperature for 44.5 h. The solution was then diluted with ether (10 mL) and extracted with water (1 X 10 mL), 1N HCl (1 X 10 mL) and then water (1 X 10 mL). The organic layer was separated, dried over $MgSO_4$ and the solvent was removed resulting in a clear, very light yellow colored oil. Material was determined to be a mixture of product and starting materials by ^{1}H NMR. Material was pumped down and analyzed by GC (BPH chiral phase) for separation of enantiomers. Product was isolated by column chromatography (silica gel) and characterized by ^{1}H NMR, ^{13}C NMR, FTIR, and HRMS.

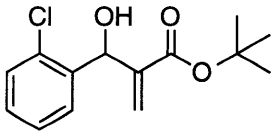
Hydrogenation of Baylis-Hillman adducts. The Baylis-Hillman reaction of octylaldehyde (360 μL, 0.384 mmol), *iso*-butylacrylate (60 μL, 0.42 mmol) and Dabco (5.0 mg, 0.041 mmol) was run as above. After isolation, the product was found to be unresolvable on GC or HPLC. Hydrogenation of the product with catalytic Pd/C under an atmosphere of hydrogen resulted in the desired product. This material was separable on chiral phase GC (BPH, 120 °C isothermal).

Transesterification of Baylis-Hillman adducts. Using the method of Leahy,[22] the Baylis-Hillman products were transesterfied, resulting in the methyl ester. We had already achieved the separation of this material by GC (chiral stationary phase, BPH).



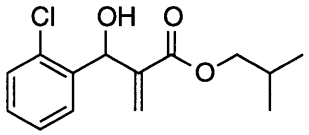


^{1}H NMR (300 MHz, $CDCl_3$) δ 3.40 (s, 1H), 3.81 (s, 3H), 5.62 (s, 1H), 6.01 (s, 1H), 6.37 (s, 1H), 7.2-7.4 (m, 3H), 7.59 (d, J = 7.2, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.8, 68.5, 126.5, 126.7, 127.9, 128.7, 129.1, 132.6, 138.3, 140.7, 166.5; IR (neat) 3432(br), 2952, 1723, 1631, 1473, 1440, 1396, 1337, 1269, 1195, 1149, 1056, 1029, 962, 937, 835, 818, 758, 741, 698 cm^{-1}; HRMS *m/z* 226.0397 [M^+], calcd for $C_{11}H_{11}O_3Cl$ 226.0397. TLC (10% EtOAc/hexane) R_f = 0.38 (UV-purple, PMA-blue). Clear, colorless liquid. Resolution of enantiomers by GC (chiral phase, BPH) 150 °C isothermal, 26.4 and 27.1 minutes.

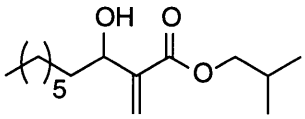


^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (s, 9H), 3.34 (d, J = 4.8, 1H), 5.56 (s, 1H), 5.95 (d, J = 4.5, 1H), 6.28 (s, 1H), 7.28 (m, 2H), 7.37 (d, J = 9.6, 1H), 7.53 (d, J = 6.9, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.9, 69.3, 81.7, 125.6, 127.0, 128.1, 128.9, 129.4, 133.0, 138.8, 142.3, 165.7; IR (neat) 3426(br), 2978, 2933, 1716, 1632, 1475, 1442, 1393, 1368, 1340, 1291, 1256, 1152, 1056, 1030, 960, 850, 756 cm^{-1}; HRMS *m/z* 268.0866 [M^+], calcd for $C_{14}H_{17}O_3Cl$ 268.0866. TLC (10% EtOAc/hexane) R_f = 0.20 (UV-purple, PMA-blue). Light yellow, thick oil. Resolution of enantiomers by GC (chiral phase, BPH) 150 °C isothermal,

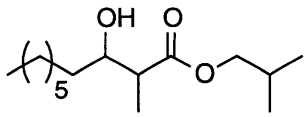
32.5 and 33.7 minutes.



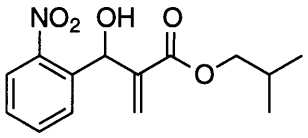
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (d, J = 5.7, 6H), 1.99 (m, 1H), 3.29 (d, J = 4.8, 1H), 3.97 (m, 2H), 5.66 (s, 1H), 6.03 (d, J = 4.8, 1H), 6.41 (s, 1H), 7.3-7.4 (m, 3H), 7.59 (d, J = 6.9, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 27.8, 69.3, 71.2, 126.7, 127.1, 128.2, 129.1, 129.5, 129.6, 133.0, 138.5, 140.9, 166.6; IR (neat) 3465(br), 2962, 1719 1632 1470 1441, 1380, 1270, 1149, 1056, 1029, 993, 960, 835, 757, 696 cm^{-1}; HRMS *m/z* 268.0866 [M^+], calcd for $C_{14}H_{17}O_3Cl$ 268.0866. TLC (10% EtOAc/hexane) R_f = 0.29 (UV-purple, PMA-blue). Very light yellow oil. Resolution of enantiomers by GC (chiral phase, BPH) 150 °C isothermal, 56.4 and 59.8 minutes.



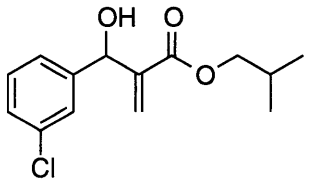
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, J = 6.6, 3H), 0.98 (d, J = 6.3, 6H), 1.28 (br s, 10H), 1.45 (m, 1H), 1.65 (m, 2H), 2.00 (m, 1H), 3.98 (d, J = 6.3, 2H), 4.40 (t, J = 6.3, 1H), 5.79 (s, 1H), 6.24 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 19.1, 22.7, 25.9, 27.8, 29.3, 29.4, 31.8, 36.4, 70.8, 71.5, 124.5, 142.9, 166.6; IR (neat) 3450(br), 2958, 2927, 2873, 2856, 1716, 1628, 1468, 1400, 1379, 1283, 1156, 1115, 1069, 995, 952, 819 cm^{-1}; TLC (10% EtOAc/hexane) R_f = 0.23 (UV-purple, PMA-blue). Very light yellow oil. Material was hydrogenated to afford an acceptable resolution.



^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9, 3H), 0.94 (d, J = 6.9, 6H), 1.2-1.5 (m, 15H), 1.95 (m, 1H), 2.5-2.7 (m, 2H), 3.66 (m, 1H), 3.90 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.9, 14.1, 14.3, 19.1, 22.7, 25.6, 26.0, 27.7, 29.3, 29.6, 31.8, 34.0, 34.7, 44.5, 45.3, 70.6, 70.6, 71.8, 73.3, 176.1; IR (neat) 3468(br), 2958, 2929, 2873, 2856, 1734, 1466, 1396, 1380, 1252, 1176, 1124, 1041, 991 cm^{-1}; HRMS *m/z* 258.2195 [M$^+$], calcd for $C_{15}H_{30}O_3$ 258.2195. TLC (10% EtOAc/hexane) R_f = 0.54 (UV-purple, PMA-blue). Very light yellow oil. Resolution of enantiomers by GC (chiral phase, BPH) 150 °C isothermal, 59.1 and 60.5 minutes.

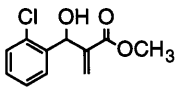
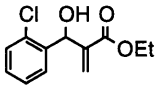
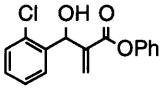
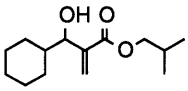
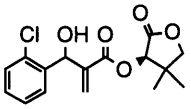
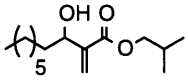
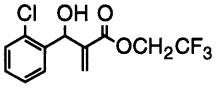
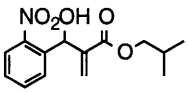
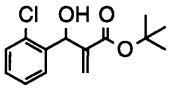
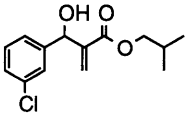
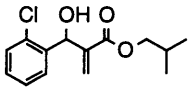
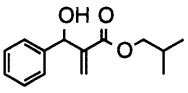
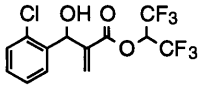
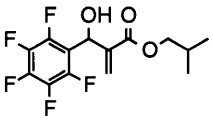


^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (d, J = 8.4, 6H), 1.87 (m, 1H), 3.88 (m, 3H), 5.74 (s, 1H), 6.18 (s, 1H), 6.37 (s, 1H), 7.44 (t, J = 7.2, 1H), 7.62 (t, J = 7.5, 1H), 7.72 (d, J = 8.1, 1H), 7.92 (d, J = 8.4, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.7, 27.4, 67.0, 70.9, 124.3, 126.0, 128.4, 128.7, 133.2, 136.3, 141.1, 148.0, 165.7; IR (neat) 3467(br), 2963, 2875, 1713, 1632, 1610, 1528, 1470, 1446, 1403, 1350, 1285, 1146, 1050, 992, 963, 944, 856, 833, 788, 752, 730, 707 cm^{-1}; HRMS *m/z* 279.1106 [M$^+$], calcd for $C_{14}H_{17}NO_5$ 279.1107. TLC (10% EtOAc/hexane) R_f = 0.13 (UV-purple, PMA-blue). Light yellow oil. Resolution of enantiomers by HPLC (chiral phase, OD, 20% iPA/hexane, 1mL/min.) 5.5 and 7.9 minutes.



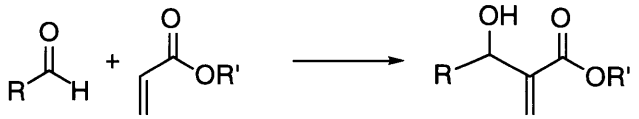
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (d, J = 6.6, 6H), 1.96 (m, 1H), 3.31 (d, J = 5.4, 1H), 3.94 (d, J = 6.3, 2H), 5.54 (d, J = 5.7, 1H), 5.88 (s, 1H), 6.41 (s, 1H), 7.30 (s, 3H), 7.41 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.0, 27.7, 71.0, 72.3, 124.7, 126.0, 126.7, 127.7, 129.5, 134.1, 141.6, 143.5, 165.8; IR (neat) 3452(br), 2963, 2875, 1713, 1630, 1597, 1575, 1470, 1431, 1380, 1285, 1151, 1096, 1079, 1043, 992, 960, 882, 818, 787, 739, 699 cm^{-1}; HRMS *m/z* 268.0868 [M^+], calcd for $C_{14}H_{17}O_3Cl$ 268.0866. TLC (10% EtOAc/hexane) R_f = 0.39 (UV-purple, PMA-blue). Clear, colorless oil. Resolution of enantiomers by GC (chiral phase, BPH) 150 °C isothermal, 79.1 and 83.2 minutes.

Table 2A.4. Resolution Conditions for Baylis-Hillman Adducts.

product	resolution	conditions	product	resolution	conditions
	as same	150 iso. BPH 26.4, 27.1		as same	150 iso. BPH 30.0, 31.1
	OMe			as same	150 iso. BPH 16.5, 17.3
	OMe			H_2	120 iso. BPH 59.1, 60.5
	OMe			as same	OD 20%iPA/H 1 mL/min 5.5, 7.9
	as same	150 iso. BPH 32.5, 33.7		as same	150 iso. BPH 79.1, 83.2
	OMe			as same	150 iso. BPH 28.3, 29.8
	as same	150 iso. BPH 56.4, 59.8		as same	150 iso BPH 20.1, 21.0

Phenylethylketene solvolysis with benzylalcohol (Eq 2A.5). A stock solution of catalyst (0.00392 mmol) in benzene-d_6 (0.58 mL) was prepared. A second stock solution of benzylalcohol (31 μL, 0.30 mmol) and phenyl ethyl ketene (40 μL, 0.26 mmol) in C_6D_6 (2.8 mL) was prepared. Reaction solutions were prepared in screw-cap NMR tubes consisting of 0.7 mL alcohol stock and 0.1 mL catalyst stock (or 0.1 mL benzene-d_6 for a background reaction). The reactions were then followed by ^1H NMR.

REACTIVITY OF (DMAP*)FeCp^X COMPLEXES



Comparison of catalytic activity for Baylis-Hillman reaction (Eq 2A.6). Into separate vials were weighed the catalysts (0.006 mmol). To these were added *o*-nitrobenzaldehyde (16.1 mg, 0.107 mmol) and then methyl acrylate (52 μL, 0.52 mmol). The solutions were then stirred at room temperature for 15-17 h and then aliquoted for analysis of conversion by ^{1}H NMR (300 MHz, $CDCl_3$).

The remaining solution was chromatographed (silica gel, ether) to separate the product and catalyst. The catalyst was then eluted with 10% NEt_3/EtOAc. The product fractions were concentrated and analyzed by GC (BPH chiral stationary phase) for %ee.

General procedure for metallocene-catalyzed Baylis-Hillman reactions (Table 2A.1, 2A.2, and 2A.3).

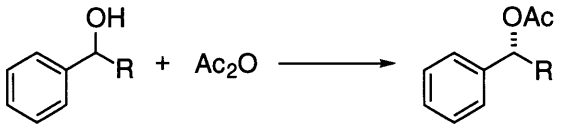
Liquid aldehydes. Into a vial was weighed the catalyst (0.0035 mmol). A stock solution of reactants consisting of aldehyde (1.07 mmol), acrylate (0.222 mmol) and benzene (105 μL) was prepared. Both the stock and the catalyst were cooled to ~ -30 °C and an aliquot (83 μL) of a stock solution was then added to the catalyst. The solution was sealed under nitrogen and then left at 4 °C for several days.

Product/starting material mixture was isolated by chromatography (silica gel, 10% EtOAc/hexane -> 70 % EtOAc/hexane). Catalyst was then eluted with 10% NEt_3/EtOAc. Mixture of product and starting material was concentrated and analyzed for enantiomeric excess as indicated.

Solid aldehydes. Into a vial was weighed the catalyst (0.002 mmol) and then the aldehyde (0.042 mmol). A solution of acrylate (0.42 mmol) in benzene (16 μL) was cooled, as was the solid mixture, to ~ -30 °C. The solution was added to the solids

and the resulting solution was sealed under nitrogen and left at 4 °C for several days.

Product/starting material mixture was isolated by chromatography (silica gel, 10% EtOAc/hexane -> 70 % EtOAc/hexane). Catalyst was then eluted with 10% NEt_3/EtOAc. Mixture of product and starting material was concentrated and analyzed for ee as indicated.



Kinetic resolution of 1-phenylethanol with (DMAP*)Fe(ACp) and (DMAP*)Fe(C_5Ph_4H) (Eq 2A.12). A stock solution was prepared of 1-phenylethanol (186.9 mg, 1.53 mmol), triethylamine (160 μL, 1.15 mmol) and Et_2O (3.0 mL). Into each of two vials was weighed the catalysts (0.008 mmol) and an aliquot (1.15 mL) of stock solution was added to each. The homogeneous solutions were stirred while Ac_2O (36 μL, 0.38 mmol) was added. The solutions were stirred at room temperature and aliquoted periodically to assess the conversion and selectivity.

The aliquots were run through a plug of silica gel with 50-75% EtOAc/hexane as eluent. The catalyst was then eluted with 10% NEt_3/EtOAc. The fractions containing alcohol and acetate were concentrated and analyzed by GC (BPH chiral stationary phase):

(-)-2A.4: 1 h, 24% conv., s = 1.6 (19% ee of (*R*) acetate, 9% ee of (*S*) alcohol)

6.5 h, 52% conv., s = 1.5 (14% ee of (*R*) acetate, 14% ee of (*S*) alcohol)

(-)-2A.10:

1 h, 13% conv., s = 4.1 (58% ee of (*R*) acetate, 12% ee of (*S*) alcohol)

6.5 h, 38% conv., s = 3.8 (48% ee of (*R*) acetate, 31% ee of (*S*) alcohol)

Chapter Two, Part B:

Ruthenocene-Derived Complexes with *N*-Heterocyclic Ligands

INTRODUCTION

Although the previously developed ferrocene-based catalysts (See Chapter Two, Background and Part A) proved to be useful for a variety of nucleophile-catalyzed reactions,[7,9,10,31,32] we were interested in trying to develop more reactive catalysts based on this model. We reasoned that analogs containing a more electron-rich metal center than iron might provide a more reactive catalyst.

Based on first principles, we believed that using one of the other Group VIII metals could in fact provide for a more reactive and more nucleophilic complex. Since both ruthenium and osmium have a larger covalent radius (1.25-1.26 Å) than iron (1.17 Å) we would expect there to be a longer ring-to-ring distance in these metallocene-type complexes.[33-35] This would allow for a less encumbered environment around the nucleophilic atom of the pyrindine ring. Also, ruthenium and osmium are more electron-rich and more polarizable than iron. This might affect the electron-richness of the attached ligand systems and allow for a more nucleophilic pyrindine ring. An initial survey showed that there are relatively few examples of the other Group VIII metal (Ru and Os) complexes of this type, likely due to a lack of efficient synthetic routes to these structures. The few reported examples show comparable oxidation potentials for the analogous metal complexes of the Group VIII triad.[35-37]

From this data, we were not able to conclude whether ruthenium and osmium analogs of the original ferrocene-based catalysts would in fact be more active catalysts. Since the starting materials of the ruthenium complexes would likely be much less toxic than the osmium complexes, we set out to investigate ruthenocene-based analogs of our original ferrocene catalysts. Although the preparation of the

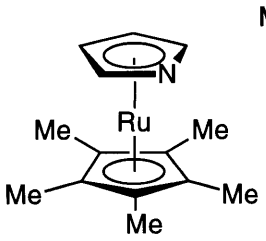
ruthenium and osmium analogs has not been as intensely developed as the iron complexes, several literature reports have described the synthesis of complexes related to those we desired.[35,38-40]

Therefore, we set out to synthesize the ruthenium analogs of our pyrindinyliron catalysts and to compare their relative performance as nucleophilic catalysts. Especially interesting would be the comparison of the structural and conformational aspects of these analogues with respect to the observed enantioselectivities of the asymmetric reactions.

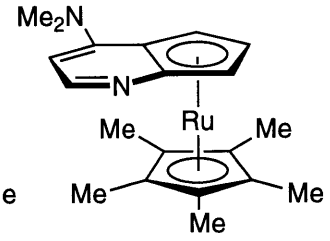
RESULTS AND DISCUSSION

Preparation of Catalysts

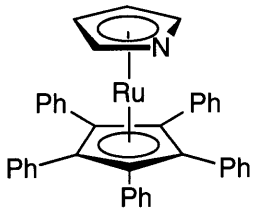
We first needed to synthesize the ruthenium analogs of the (η^5-pyrrolyl)- and pyrindinylferrocenes (**2B.1, 2B.2, 2B.3, 2B.4**).



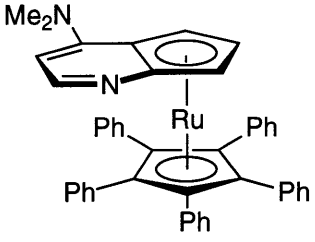
2B.1



2B.2
(DMAP*)RuCp*



2B.3



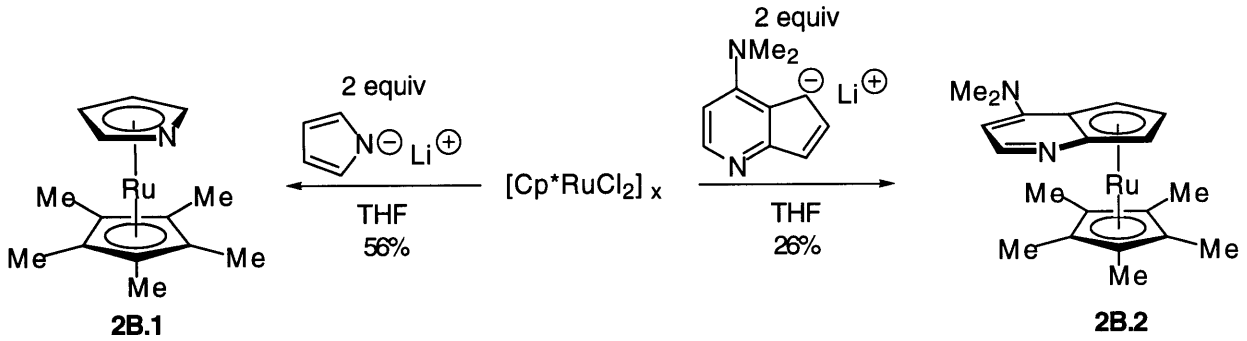
2B.4
(DMAP)*Ru(C_5Ph_5)

We quickly determined that the method by which the ferrocene complexes were prepared[7] was not applicable to the ruthenium analogs. Simple ruthenium dihalide starting materials are not commercially available, so step-wise reaction of 2 different cyclopentadienyl anions with a ruthenium(II) source is not a viable route to prepare these complexes.

The syntheses of unsymmetrical ruthenium complexes are generally low-yielding and several steps. A report from 1988 demonstrated the first general route to mixed-sandwich ruthenocenes, with one ligand being a Cp*.[35] This method calls for treatment of a $[Cp^*RuCl_2]_x$ oligomer with two equivalents of a cyclopentadienyl anion,[41] which results in the desired neutral ruthenocenes. The method was further elaborated by Kelly in 1992 who demonstrated the first synthesis of an azaruthenocene.[38] The method used was analogous to that originally put forth by Gassman (i.e., treatment of $[Cp^*RuCl_2]_x$ with 2 equiv of tetramethylpyrrolyl anion.) The yields observed by Kelly using this method to prepare azaruthenocenes were quite high (81% isolated yield), although a small amount of the (η^5-$C_4Me_4N)_2Ru$ was also isolated.

We were encouraged by the success of Kelly and set out to prepare the desired Cp*Ru(η^5-heterocycle) complexes. Both (η^5-pyrrolyl)RuCp* (**2B.1**) and (DMAP*)RuCp* (**2B.2**) were prepared using this method (Scheme 2B.1). Both complexes were isolated by column chromatography and the enantiomers of the chiral pyrindine complex (**2B.2**) were resolved via chiral semi-preparative HPLC (Chiralcel OD stationary phase).

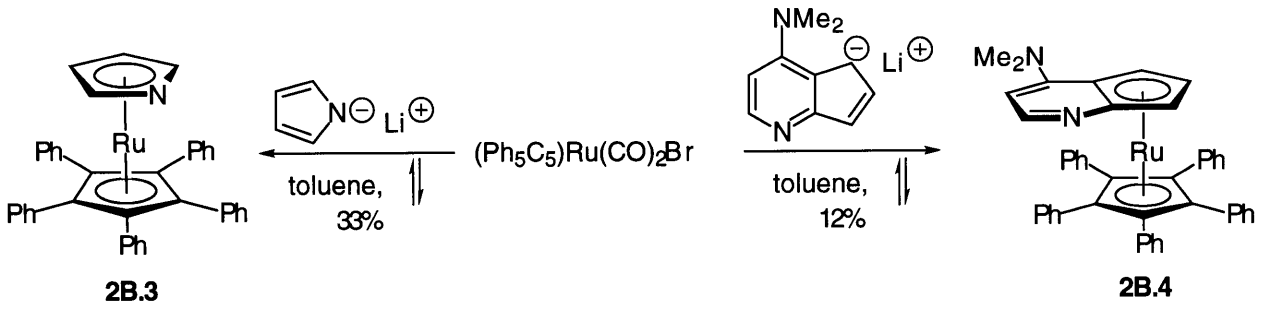
Scheme 2B.1



The ruthenocene complexes bearing the pentaphenylCp group (C_5Ph_5) were also of great interest to us. Again, we found that the synthesis of these compounds was not entirely straightforward. A literature search showed only a few precedents for ruthenium complexes bearing a (C_5Ph_5) group as one of the ligands. Only one report was found of a mixed-sandwich complex of ruthenium with at least one of the ligands being a (C_5Ph_5) ligand. This reference cited the use of a (C_5R_5)Ru(CO)$_2$X (R = H, CH_3, Ph; X = I, Br) complex which was reacted with a cyclopentadienyl anion.[40] Although no reports of heterocyclic ligands being complexed by this method were found, we attempted to synthesize the desired compounds by this route.

The preparation of the desired starting material, (C_5Ph_5)Ru(CO)$_2$Br, was achieved using the method of Slocum.[39] Treatment of this Ru(II) source with either pyrrolyl anion or pyrindinyl anion in refluxing toluene resulted in the desired complexes (**2B.3, 2B.4,** Scheme 2B.2)

Scheme 2B.2

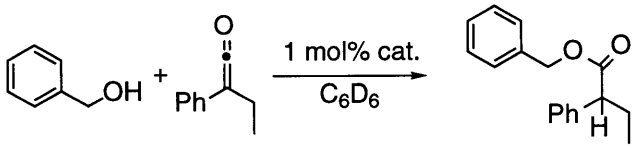


Both complexes were purified by column chromatography and (DMAP*)Ru(C_5Ph_5) (**2B.4**) was resolved using a Chiralcel AD stationary phase for semi-preparative HPLC.

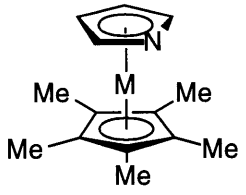
With all four desired ruthenocene analogues in hand, we set out to compare the reactivities and stereoselectivities of these complexes with respect to our previously reported complexes.

(η^5-pyrrolyl)RuCp^X as Nucleophilic Catalysts

We opted to investigate the catalyzed solvolysis of phenyl ethyl ketene with benzyl alcohol to analyze the performance of the azaruthenocene complexes (Eq 2B.1), since the reaction using the iron analogs had already been investigated. The reactions are easily analyzed by ^{1}H-NMR to determine the extent of conversion vs. time.[7] The pentamethyl ruthenium complex ((η^5-pyrrolyl)RuCp*, **2B.1**) exhibits slightly enhanced reactivity ($t_{1/2}$ = 3.8 min) as compared to the azaferrocene ($t_{1/2}$ = 9.6 min). Neither (η^5-pyrrolyl)M(C_5Ph_5) complex (M=Fe (**2.12**), M=Ru (**2B.3**)) showed significant activity as catalysts for this reaction, and they were not investigated further.

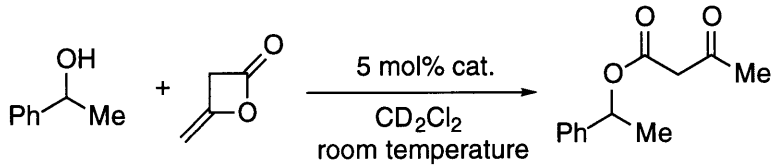


(2B.1)

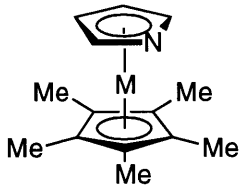


M	$t_{1/2}$ (min)
Fe (**2.2**)	9.6
Ru (**2B.1**)	3.8

We also investigated the use of (η^5-pyrrolyl)RuCp* (**2B.1**) as a catalyst for the solvolysis of diketene (Eq 2B.2), another reaction which had been investigated by our group. In this case the iron catalyst ((η^5-pyrrolyl)FeCp*, **2.2**) is slightly more reactive ($t_{1/2}$ = 21.0 min) as compared to ruthenium ($t_{1/2}$ = 27.5 min). We attempted to synthesize a chiral version of the (η^5-pyrrolyl)RuCp* which would allow us to determine what effect the change in metal had on the enantioselectivity of the catalyst (as in Eq 2.3), but our attempts to do this met with little success, so we moved on to the analysis of the pyrindinylruthenocenes as catalysts.



(2B.2)



M	$t_{1/2}$ (min)
Fe (**2.2**)	21.0
Ru (**2B.1**)	27.5

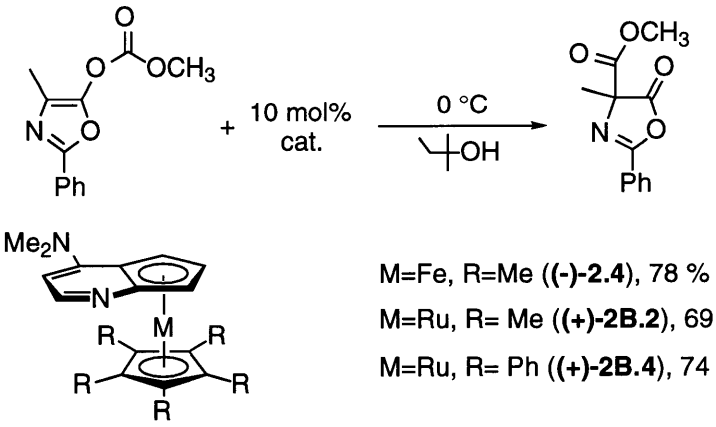
Pyrindinylruthenocenes as Nucleophilic Catalysts

The pyrindinylferrocene complexes ((DMAP*)FeCp* (**2.4**) and (DMAP*)Fe(C_5Ph_5) **2.5**) had been shown to catalyze a variety of nucleophile-catalyzed reactions. Some of the reactions investigated with these iron complexes were acylation with acetic

anhydride,[7,9,10] enol carbonate rearrangement,[32] ring-opening of azlactones with alcohols,[31] ketene solvolysis, and cyanosilylation of aldehydes.[7] These reactions had shown significant enantioselectivity when run in the presence of our pyrindinylferrocene complexes. We therefore set out to investigate the reactivity and stereoselectivity of the reactions using the chiral pyrindinylruthenium complexes.

Enol Carbonate Rearrangement

This rearrangement was initially investigated by J. C. Ruble and Dr. Y. S. Park in our group. It was found that the optimal conditions used *tert-* amyl alcohol as a solvent, 0.1 M substrate, 10 mol% catalyst loading, and a reaction temperature of 0 °C. Using (DMAP*)FeCp* (**2.4**) it was demonstrated that the product was formed with considerable enantioselectivity, generally taking 12-16 h to go to completion.[32] The ruthenium analogues turned out to be quite active for this reaction as well. Both (DMAP*)RuCp* (**(+)-2B.2**) and (DMAP*)Ru(C_5Ph_5) (**(+)-2B.4**) catalyzed the stereoselective formation of the acylated azlactone product (Equation 2B.3). The sense of stereoselection with **(+)-2B.2** and **(+)-2B.4** is opposite that seen with **(-)-2.4**.



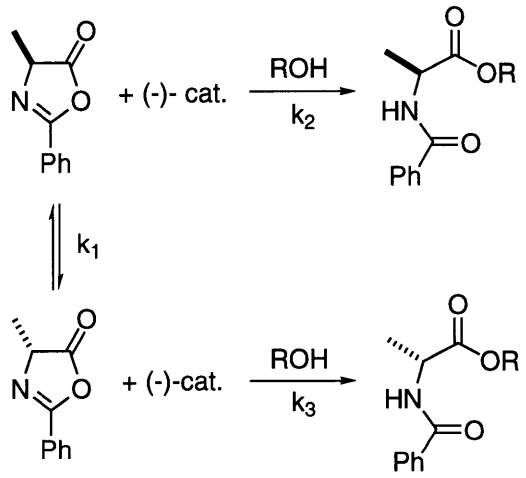
The slight decrease in enantioselectivity observed when utilizing the ruthenium analogues is not surprising considering that the reaction conditions are not

optimized for these catalysts. Optimization of conditions for the ruthenium catalysts could result in improvements in enantioselectivity. Regardless, all of the catalysts appear to behave similarly for this reaction, with respect to stereoselectivity.

Ring-Opening of Azlactones

Another reaction we had investigated using the ferrocene-based catalysts was a ring-opening of azlactones with alcohols and a nucleophilic catalyst.[31] This reaction has the potential to be a dynamic kinetic resolution (Scheme 2B.3). The azlactone starting material racemizes very quickly under the reaction conditions, so reaction in the presence of a very selective enantiopure catalyst could result in an amino acid derivative with a maximum yield of 100% and an ee of 100%.

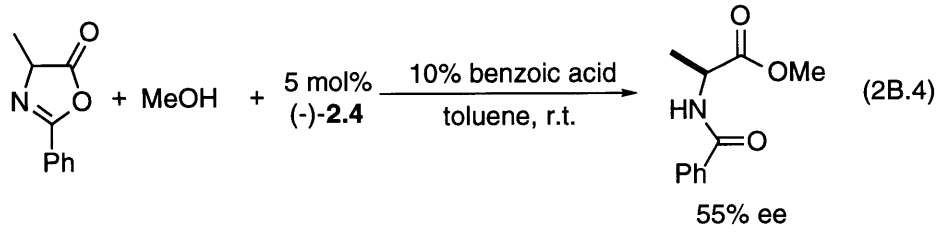
Scheme 2B.3



Dynamic Kinetic Resolution (k_1>>k_3; k_2>>k_3)

In investigating the effect of our enantiopure ferrocene-based catalysts on this reaction, we found that a catalytic amount of benzoic acid (or other protic acid) was necessary for the reaction to occur with stereoselectivity. The optimal conditions for this reaction were found to be: 0.1 M substrate in toluene, 5 mol% catalyst, 10 mol% benzoic acid, 1.5 equiv alcohol, at room temperature (Eq 2B.4). Although the selectivity of the reaction appears to be greatly dependent on the presence of benzoic

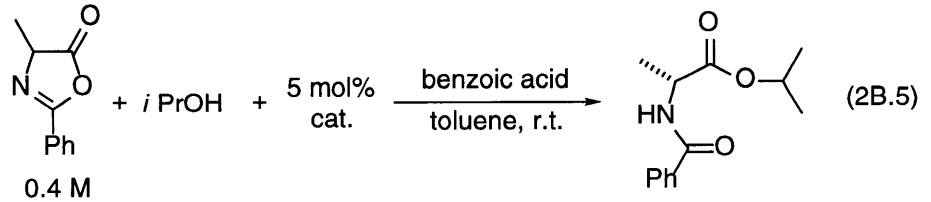
acid, a range of acid loadings (5-10 mol%) appear to give reasonably good results.[31]



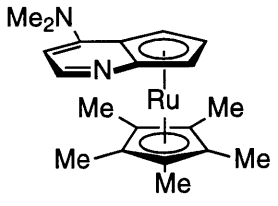
(2B.4)

The use of the ruthenium analogs in this reaction gave some interesting results. The selectivity and rate are only very slightly better with (DMAP*)RuCp* (**(-)-2B.2**, 57% ee, (L)- derived product, $t_{1/2}$ ~ 3.5 hours). The iron complex ((DMAP*)FeCp*, **(-)-2.4**) exhibits a 55% ee and $t_{1/2}$ ~ 4.75 hours under the same conditions. Benzoic acid is still necessary for the reaction to proceed with enantioselectivity, but it decreases the rate of the reaction with (DMAP*)RuCp* (**2B.2**) (Figure 2B.1). The presence of benzoic acid increases the rate of reaction with (DMAP*)FeCp* (**2.4**).

The use of *i*-PrOH as a reagent gave analogous results to those observed with methanol as a reagent. The presence of benzoic acid is still necessary for an efficient asymmetric reaction to occur, and the rate of the reaction is much slower than when there is no benzoic acid present. The overall reaction rate is also quite slow with *i*-PrOH (Equation 2B.5).



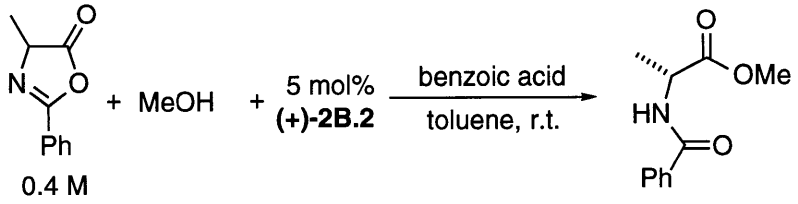
(2B.5)

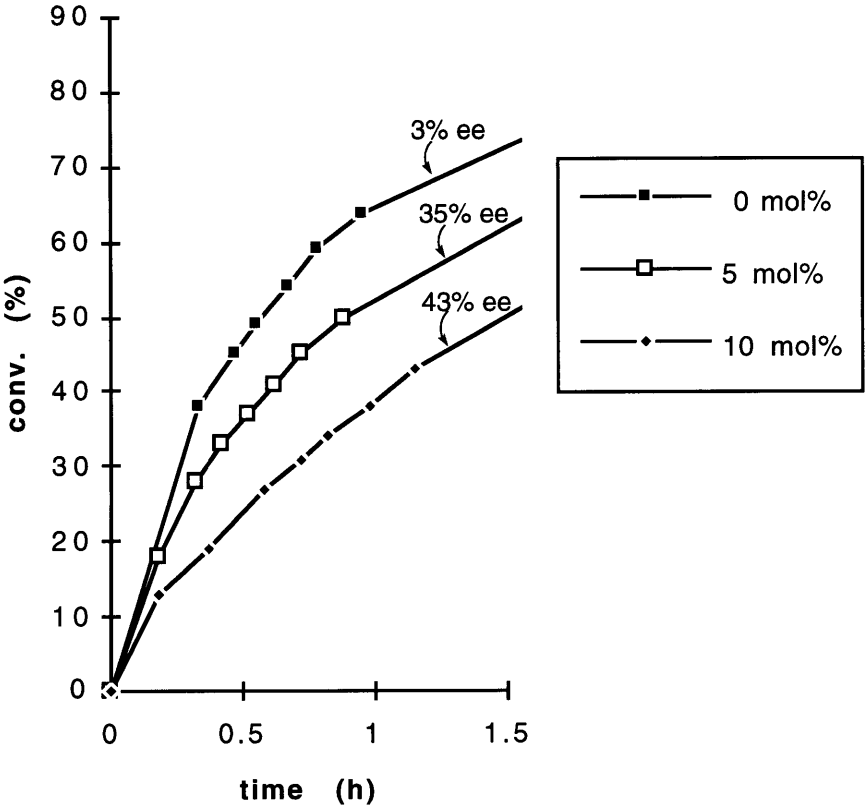


(+)-2B.2

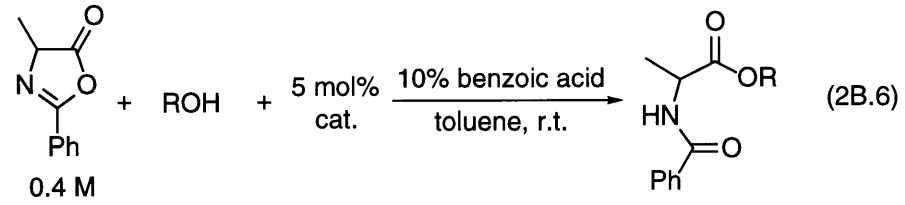
0% acid, 17% ee, $t_{1/2}$ = 47 h
10% acid, 63% ee, $t_{1/2}$ = 78 h

Figure 2B.1. DMAP*RuCp* Catalyzed Ring-Opening: Rate vs. Acid Loading

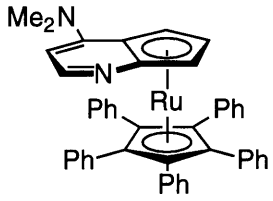




Although (DMAP*)Ru(C_5Ph_5) (**2B.4**) catalyzes these reactions, the selectivities are significantly decreased as compared to the Cp* derivatives (Eq 2B.6).



(2B.6)

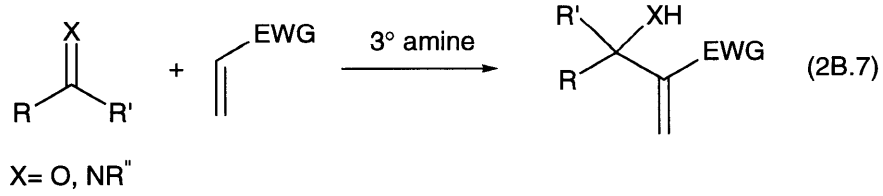


2B.4

(-)-2B.4, R=Me, 21% ee, (L)-derived
(+)-2B.4, R=*i* Pr, 36% ee, (D)-derived

Asymmetric Baylis-Hillman Reactions

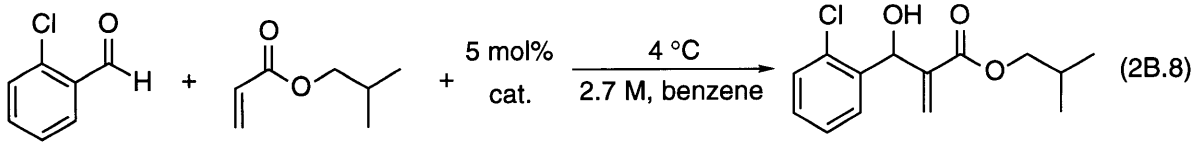
In the early 1970s, Baylis and Hillman discovered that a carbon-carbon bond-forming reaction between an activated olefin and an aldehyde (or imine) was catalyzed by the presence of tertiary amines (Eq 2B.7).[16] For a discussion of the Baylis-Hillman reaction and reports of asymmetric Baylis-Hillman reactions, see Chapter Two, Part A.



(2B.7)

We have previously shown that some of the pyrindinyliron complexes (**2.4, 2A.4, 2A.7, 2A.10**) were catalysts for the Baylis-Hillman reaction. The optimal conditions for these iron catalysts were utilized for the reaction catalyzed by (DMAP*)RuCp* (**2B.2**) (Eq 2B.8). The ruthenium complex appears slightly less

efficient than its iron analogue with respect to asymmetric induction. Neither (DMAP*)FeCp* (**2.4**) nor (DMAP*)RuCp* (**2B.2**) give as high a level of enantioselectivity as does (DMAP*)Fe(ACp) (**(-)-2A.4**, 30% ee). The sense of stereoselection is reversed when using catalysts with opposite optical rotation. See Chapter Two, Part A for a discussion of the preparation and uses of **2A.4**.



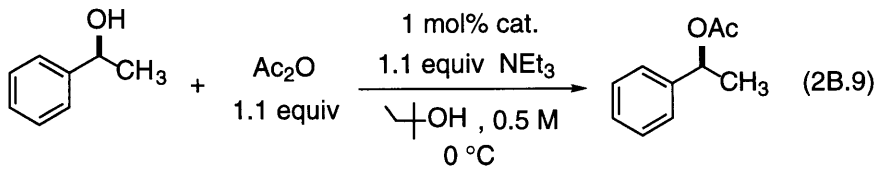
(2B.8)

5 equiv

Cat.	ee
(DMAP*)RuCp* **(+)-2B.2**	18%
(DMAP*)FeCp* **(+)-2.4**	21%
(DMAP*)Fe(ACp) **(-)-2A.4**	30%

Acylation with Acetic Anhydride

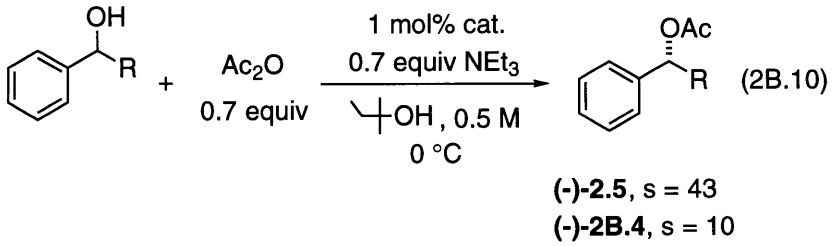
Another reaction, initially investigated by J. Craig Ruble, Dr. Hallie A. Latham, and Jennifer Tweddell, was the kinetic resolution of secondary alcohols with acetic anhydride.[7,9,10] In order to effectively compare the rates of the iron and ruthenium catalysts, the acylation reaction of an enantiopure alcohol was run using the matching enantiopure catalysts. It was observed that the rate with (DMAP*)Ru(C_5Ph_5) (**(+)-2B.4**) was more than twice as fast as the analogous rate with (DMAP*)Fe(C_5Ph_5) (**(+)-2.5**) with (S)-1-phenylethanol as the substrate (Eq 2B.9).



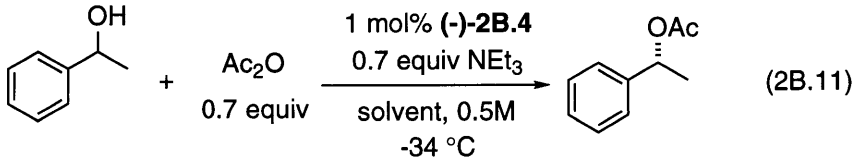
(2B.9)

(+)-2.5, $t_{1/2}$ = 212 min
(+)-2B.4, $t_{1/2}$ = 80 min

The enantioselectivity of the reaction was investigated next. Under the standard conditions, the selectivity for acylation of racemic 1-phenylethanol with (DMAP*)Ru(C_5Ph_5) (**(-)-2B.4**) was decreased dramatically (s = 10, $t_{1/2}$ = 4 hours) as compared to the reaction run with (DMAP*)Fe(C_5Ph_5) (**(-)-2.5**) (Eq 2B.10).

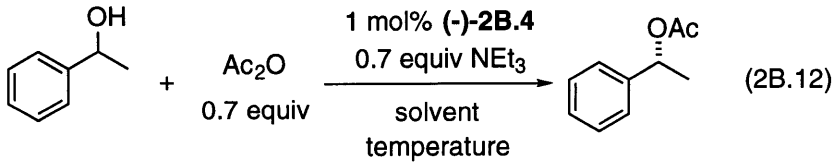


Since lowering the temperature was known to increase the selectivity of these reactions, a solvent study at -34 °C was run. The results indicated a slight increase in selectivity with diethylether as a solvent (Eq 2B.11), but the selectivities were still relatively low with (DMAP*)Ru(C_5Ph_5) (**2B.4**). The rates of the reactions decreased dramatically as well, due to the decrease in reaction temperature.



Solvent	s	$t_{1/2}$ (h)
THF	7	54
Et_2O	13	55
CH_2Cl_2	6	34

Furthermore, it was found that decreasing the concentration (0.34 M) and decreasing the temperature, with necessary solvent changes, resulted in further increases in the enantioselectivity (Equation 2B.12). To this date, though, we have not been able to achieve the very high selectivities (s = 43) previously seen with (DMAP*)Fe(C_5Ph_5) (**2.5**).



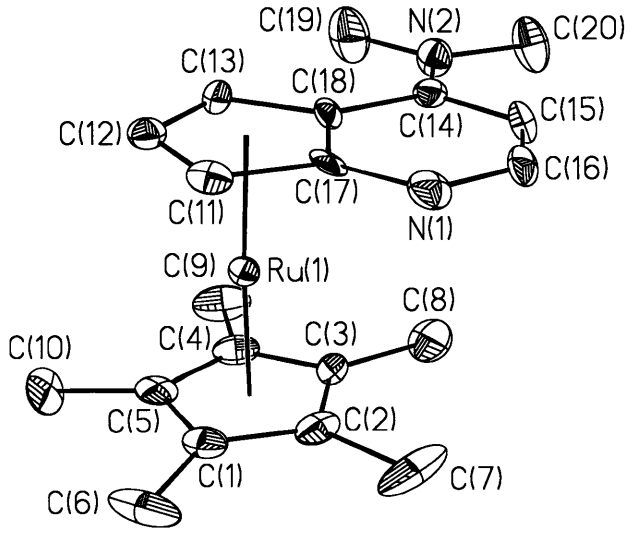
(2B.12)

Solvent	Temp.	s	$t_{1/2}$ (h)
t- amyl alcohol	-11 °C	11	11
2:1 Et_2O/*t*-amyl alcohol	-34 °C	18	77

Structural Analysis of the Pyrindinyl Complexes

In an effort to better understand the sense of stereoselection for the above reactions, we set out to get structural data for the pyrindinylruthenium complexes. Suitable crystals for X-ray crystallographic analysis were grown of (+)-(DMAP*)RuCp*(**2B.2**) (Figure 2B.2), and (+)-DMAP*Ru(C_5Ph_5) (**2B.4**) complexes.

Figure 2B.2. ORTEP illustration of (DMAP*)RuCp* (**(+)-2B.2**).



The (+)-(DMAP*)RuCp* structure indicates no distortion of the relative positions of the Cp rings and a total distance of 3.64 Å between the centroids of the five-membered rings. This distance between rings is slightly longer than the corresponding iron complex (3.41 Å), as would be expected.

The enantiomers of the DMAP*FeCp* (**2.4**) and DMAP*RuCp* (**2B.2**) have been

analyzed by X-ray crystal structure analyses. The sense of stereoselection using the (+)-enantiomer of both complexes is the same for all reactions investigated. The enantiomers of both complexes are eluted in the same relative order from the HPLC (Chiralcel OD chiral stationary phase) as well.

The racemic (DMAP*)Ru(C_5Ph_5) complex (**2B.4**) shows a significant dihedral angle between the five-membered rings (~8°) as compared to the structures of both (DMAP*)RuCp* (**2B.2**) and (DMAP*)FeCp* (**2.4**), which show no distortion of the planes of the Cp rings. This is presumably due to the steric demand of the propeller conformation of the (C_5Ph_5) ligand. Both the conformation of the (C_5Ph_5) ring and the size of the dihedral angle (with respect to the position of the five-membered rings) in the ruthenium complex ((DMAP*)Ru(C_5Ph_5) (**2B.4**)) are mimicked in the iron analog (DMAP*)Fe(C_5Ph_5) (**2.5**).

The distance between the Cp rings is the only noticeable difference between the ruthenium ((DMAP*)Ru(C_5Ph_5), **2B.4**) and iron ((DMAP*)Fe(C_5Ph_5), **2.5**) analogs of this complex. The ruthenium atom is located 1.852 Å from the centroid of the (DMAP*) ligand and 1.803 Å from the centroid of the (C_5Ph_5) ligand. The distance between the five-membered rings is equivalent to about 0.2 - 0.3 Å longer for the ruthenium complex than for its iron analog.

X-ray crystal structure analysis of the enantiomerically pure (DMAP*)Ru(C_5Ph_5) complex (**2B.4**) confirmed the structure of the complex, but the quality of the data was not good enough to unequivocally establish the absolute configuration. Since the sense of stereoselection and the optical rotation are the same for the 1st eluted enantiomer (Chiralcel OD stationary phase) of (DMAP*)Ru(C_5Ph_5) (**2B.4**) and (DMAP*)Fe(C_5Ph_5) (**2.5**) we are assuming that they have the same absolute stereochemistry.

CONCLUSION

A series of ruthenium complexes with π-bound heterocycles was prepared. These complexes are analogs of a series of iron catalysts that we had previously investigated. The synthesis of the ruthenocenes was significantly different than that reported for the ferrocene analogs. The use of $[Cp^*RuCl_2]_x$ and $[(C_5Ph_5)Ru(CO)_2Br]$ as ruthenium sources was necessitated. The isolated yields of the desired compounds were lower than the corresponding iron complexes in all cases.

In order to compare the reactivity and stereoselectivity of these ruthenocenes with the corresponding ferrocenes, we investigated a series of nucleophile-catalyzed reactions. All reactions had been optimized for catalysis with the ferrocene-based compounds. These conditions were used with the ruthenocenes in order to provide a direct comparison of the rates and enantioselectivities of the iron and ruthenium catalysts.

The azaruthenocenes appeared to be slightly more active than their iron analogs for the solvolysis of phenyl ethyl ketene with benzyl alcohol. Conversely, the azaruthenocene complex was slightly less reactive for the solvolysis of diketene with 1-phenylethanol, as compared to the iron analog. The derivatization of the azaruthenocene cannot be accomplished in the same way as for the iron complexes. Therefore, we were not able to compare stereoselectivities for the kinetic resolution of secondary alcohols with diketene and the chiral azametallocene complexes.

The pyrindinyl ruthenocenes can be prepared and resolved using chiral semi-preparative HPLC. These ruthenocene complexes are active catalysts for a variety of nucleophile-catalyzed reactions. The extent of enantioselectivity seen with these complexes compares favorably (vs. the iron complexes) for the enol carbonate rearrangement reaction and the azlactone ring-opening reaction. The selectivity with ruthenium is lower than for the iron for the acylation of secondary alcohols with acetic anhydride, although the rate of the reaction is twice as fast as with iron.

We believe the extra distance between the Cp rings of the ruthenocene catalysts may result in a less hindered nucleophile, thereby increasing its reactivity and decreasing its selectivity.

As with iron, the (DMAP*)Ru(C_5R_5) complexes are very robust and are generally recovered in almost quantitative yield after the reactions have been quenched. The optical purity of the complexes are similarly unaffected by the reaction conditions, as no loss of stereoselectivity is seen when recycled catalysts are used.

In all cases the sense of stereoselection is the same with matching enantiomers of ruthenium and iron complex. This implies a similar reaction mechanism for the action of these catalysts. We hope to be able to screen a variety of other nucleophile-catalyzed reactions to see if this statement holds true in all cases.

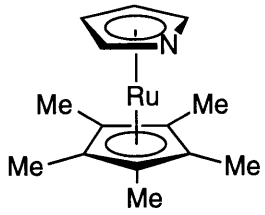
EXPERIMENTAL

General. Pyrrole (Aldrich, from CaH_2) and *iso*butylacrylate (Aldrich) were distilled and stored at -34 °C under an atmosphere of nitrogen. Benzyl alcohol (Aldrich), methanol, *i*-PrOH, *o*-chlorobenzaldehyde (Aldrich), triethylamine (from CaH_2), acetic anhydride (from quinoline), and *t*-amyl alcohol were distilled prior to use. C_6D_6 (CIL) and toluene-d_8 (CIL) were dried over alumina before use. nBuLi (1.6 M in hexane, Strem), $[Cp^*RuCl_2]_x$ (Strem), $Ru_3(CO)_{12}$ (Strem), acetic acid (glacial, Mallinckrodt), HBr (30% in acetic acid, Aldrich), phenylmagnesium bromide (3 M in ether, Aldrich), tetraphenylcyclopentadienone (Aldrich), sulfuric acid (Mallinckrodt), dimethylamine (40% in H_2O, Fluka), acetyl chloride (Fluka), ethanol (Pharmco), NO_2PF_6 (Elf-Atochem), hydrogen peroxide (30%, Mallinckrodt), pyrindane (Acros), and Dabco (Aldrich) were used as received. Benzoic acid was recrystallized prior to use.

Phenyl ethyl ketene was prepared according to the method of Tidwell.[28] 2,2-Dimethyl-1-phenyl-1-propanol was made by the reaction of *t*-butylmagnesium chloride with benzaldehyde and was purified by distillation followed by flash chromatography. 2-Phenyl-4-methyl-oxazalone **[13302-43-7]**, *N*-benzoylalanine, methyl ester ((DL) **[38767-73-6]**, (L) **[7244-67-9]**, (D) **[7260-27-7]**), *N*-benzoylalanine, isopropyl ester ((DL) **[126771-32-2]**, (L) **[126771-33-3]**, (D) **[126771-36-6]**), "enol carbonate" **[17153-01-4]**, 2-phenyl-4-methyl-4-acyl-oxazalone **[17136-91-3]**, 1-phenylethyl acetoacetate (rac **[40552-84-9]**, *(R)* **[123261-65-4]**, *(S)* **[132679-10-8]**), and 1-benzoyl-1-phenyl-propane **[62047-56-7]** were prepared as in earlier reports.[7,31,32]

Solvents were distilled from the indicated drying agents: CH_2Cl_2 (CaH_2); benzene (Na/benzophenone); pentane (Na/benzophenone); hexane (Na/benzophenone); THF (Na/benzophenone); Et_2O (Na/benzophenone); toluene (Na); nitromethane (CaH_2).

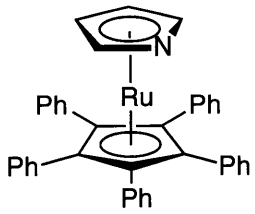
PREPARATION OF CATALYSTS



(η^5-pyrrolyl)RuCp* (2B.1). Material prepared by a method similar to that developed by Gassman.[35,38] To a solution of pyrrole (273.7 μL, 4.080 mmol) in THF (10 mL) was added *n*-BuLi (2.56 mL, 4.10 mmol) by syringe. The resulting light yellow solution was stirred at room temperature for 1 h. To this was then added the $[Cp^*RuCl_2]_x$ (504.2 mg, 1.641 mmol). The solution became reddish-brown in color. After stirring at room temperature for 3 h, the solution was bluish in color. After 24 h, the solution was filtered through a short plug of alumina, and a yellow band was eluted with EtOAc. This solution was condensed, resulting in a brown crystalline solid.

This material was rechromatographed (silica gel, hexane -> EtOAc) TLC (EtOAc, prod vis-yellow, PMA-blue, R_f = 0.59) and the product fractions were condensed, resulting in a golden-yellow solid (254.8 mg, 51% yield).

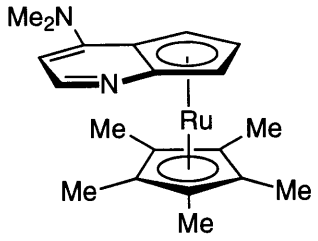
^1H NMR (500 MHz, C_6D_6) δ 1.84 (s, 15H), 4.39 (s, 2H), 5.45 (s, 2H); ^{13}C NMR (125 MHz, CDCl3) δ 12.5, 76.5, 85.5, 94.9; IR (neat) 2969, 2901, 2854, 1472, 1378, 1348, 1269, 1191, 1105, 1067, 1034, 1004, 855, 844, 804, 740, 703, 637, 457 cm^{-1}; HRMS *m/z* 303.0561 [M^+], calcd for $C_{14}H_{19}NRu$: 303.0561. Anal. calcd for $C_{14}H_{19}NRu$: C, 55.61; H, 6.33; N, 4.63. Found: C, 55.89; H, 6.42; N, 4.56; m.p. (N_2) 150-152 °C.



(η^5-pyrrolyl)Ru(C_5Ph_5) (2B.3). Material prepared by a method similar to that developed by Slocum.[40] To a 50-mL 2-neck flask was added pyrrole (52 μL, 0.75 mL). Toluene (3 mL) was added followed by a stirbar and then dropwise addition of *n*-BuLi (0.469 mL, 0.750 mmol). The resulting white slurry was stirred at room temperature for 1 h. To this slurry was added, with stirring, a light yellow solution of $(C_5Ph_5)Ru(CO)_2Br$[39] (516.3 mg, 0.7560 mmol) in toluene (10 mL). The solution became dark brown with the addition. An aliquot of toluene (5 mL) was used to rinse in any remaining ruthenium(II) solution. The flask was sealed under nitrogen.

Under a flow of argon, a reflux condenser was fitted to the flask and the solution was refluxed for 29 h. The solution was cooled to room temperature and then filtered through a plug of silica gel with EtOAc as eluent. Solvent was removed from the resulting brown solution. Material was chromatographed (silica gel, 10% EtOAc/hexane -> 50% EtOAc/hexane). Product fractions were combined and condensed resulting in a brown solid (152.5 mg, 33% yield). IR analysis showed that there was still a slight impurity of the carbonyl complex remaining in the material.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.16 (s, 2H), 5.88 (s, 2H), 7.03 (m, 10H), 7.09 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 80.3, 94.0, 97.6, 126.6, 127.2, 132.5, 134.5; IR (neat) 3057, 2039, 1970, 1601, 1502, 1444, 1072, 1028, 1008, 738, 697, 577, 555 cm^{-1}; HRMS *m/z* 613.1346 [M^+], calcd for $C_{39}H_{29}NRu$ 613.1344; m.p. (N_2) >240 °C; TLC (25 % EtOAc/hexane, UV-purple) R_f = 0.54.



(DMAP*)RuCp* (2B.2). This material was prepared by a method similar to that of Gassman.[35,38] Into a flask was weighed the 4-dimethylaminopyrindine[7] (119.5 mg, 0.746 mmol). THF (5 mL) was added and the resulting solution stirred while *n*-BuLi (0.5 mL, 0.8 mmol) was added dropwise. The resulting reddish solution was stirred at room temperature for 1 h and then $[Cp^*RuCl_2]_x$ (14.4 mg, 0.340 mmol) was added as a solid to the solution. A dark brown solution resulted and this was stirred at room temperature for 18 h.

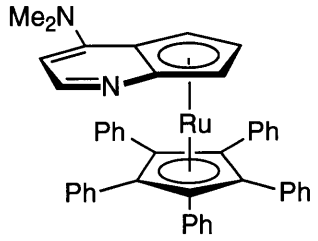
The solution was filtered through a plug of silica gel with 10% NEt_3:EtOAc as the eluent. A yellow-brown eluent was collected and removal of solvents resulted in a brown-green solid. This material was chromatographed several times with hexane -> EtOAc->10% NEt_3/EtOAc as eluents. A green-yellow solid resulted (32.2 mg, 24% yield).

^1H NMR (500 MHz, C_6D_6) δ 1.66 (s, 15H), 2.60 (s, 6H), 4.34 (t, J = 2.5, 1H), 4.59 (dd, J = 1.3, 2.8, 1H), 5.28 (dd, J = 1.3, 2.8, 1H), 5.43 (d, J = 5.0, 1H), 8.42 (d, J = 5.5, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.7, 41.4, 67.1, 69.9, 75.8, 77.3, 83.2, 93.7, 113.8, 151.0, 157.3; IR (neat) 2901, 1559, 1538, 1442, 1380, 1350, 1334, 1033, 1020, 903, 815, 787 cm^{-1}; Anal. calcd for $C_{20}H_{26}N_2Ru$: C, 60.74; H, 6.63; N, 7.08. Found: C, 60.94; H, 6.90; N, 6.89. TLC (10% NEt_3/EtOAc, vis-yellow) R_f = 0.53. Yellow solid. HRMS *m/z* 396.1142 [M^+], calcd for $C_{20}H_{26}N_2Ru$ 396.1140; m.p. (N_2) 140-142 °C.

The enantiomers of the product were separated using semi-preparative HPLC (Daicel CHIRALCEL OD, 1 cm X 25 cm, isopropanol/hexane/diethylamine 22/78/0.2, 3 mL/min). Enantiomer 1 was collected from 8.25 to 11.00 min, and enantiomer 2

was collected from 15.25 to 20.00 min.

A suitable crystal for X-Ray analysis was grown of the "fast" enantiomer of this complex (evaporation of ether/pentane solution at 4 °C). $[\alpha]^{20}_D$ = +969.5° (c = 0.13, $CHCl_3$) This enantiomer corresponds to the (+)-"fast" enantiomer of the DMAP*FeCp*.



(DMAP*)Ru(C_5Ph_5) (2B.4). Material prepared by a method similar to that developed by Slocum.[40] The 4-dimethylaminopyrindine[7] (64.1 mg, 0.400 mmol) was dissolved in toluene (2 mL) and *n*-BuLi (0.250 mL, 0.400 mmol) was added dropwise resulting in a tan, cloudy solution. This was stirred at room temperature for 1 h.

To this was added a purple solution of (C_5Ph_5)Ru(CO_2)Br[39] (275.4 mg, 0.404 mmol) in toluene (3 mL). The resulting brown solution was transferred to a 2-neck flask and sealed under nitrogen.

Under a flow of argon, a reflux condenser was fitted to the flask and the solution refluxed for 22 h. The solution was cooled to room temperature and the solvents removed. The brown residue was extracted with THF and the resulting brown solution was filtered through a plug of alumina. Material chromatographed (silica gel, 50% EtOAc/hexane -> 10% NEt_3/EtOAc) and product fractions were collected and concentrated resulting in a yellow solid (46.8 mg, 17% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.02 (s, 6H), 4.73 (t, J = 2.8, 1H), 5.27 (dd, J = 1.0, 1.5,

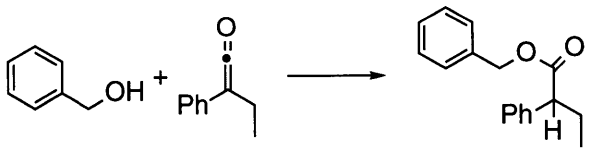
1H), 5.40 (d, J = 2.0, 1H), 5.74 (d, J = 5.0, 1H), 6.85 (d, J = 7.5, 10H), 7.00 (t, J = 8.0, 10H), 7.07 (m, 5H), 8.11 (d, J = 5.0 , 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 41.7, 69.5, 72.9, 79.1, 81.5, 91.8, 97.3, 116.8, 126.2, 127.0, 132.3, 134.9, 153.0, 156.9; IR (neat) 3055, 2925, 1600, 1564, 1540, 1502, 1443, 1397, 1349, 1028, 784, 740, 699, 572, 556 cm^{-1}; Anal. calcd for $C_{45}H_{36}N_2Ru$: C, 76.57; H, 5.14; N, 3.97. Found: C, 76.36; H, 4.99; N, 4.13; TLC (10% NEt_3/ EtOAc, vis-yellow) R_f = 0.61. Yellow solid. HRMS *m/z* 706.1921 [M^+] calcd for $C_{45}H_{36}N_2Ru$ 706.1922; m.p. > 250 °C.

A suitable crystal for crystal structure analysis was grown by slow diffusion of hexane into an ether solution of product at room temperature, followed by cooling to -11 °C.

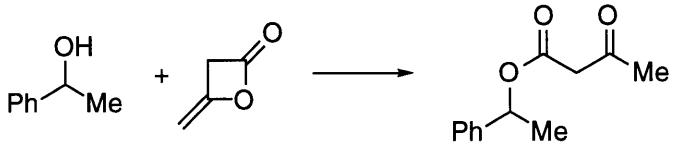
The enantiomers of the product were separated using preparative HPLC (Daicel CHIRALCEL AD, 5 cm X 50 cm, ethanol/hexane/diethylamine 5/95/0.3, 50 mL/min). Enantiomer 1 was collected starting at 62.00 minutes, and enantiomer 2 was collected starting at 103 minutes. Analytical chiral HPLC (same solvent, analytical AD column) showed enantiomer 1 eluting from 11 to 15 minutes and enantiomer 2 eluting from 18 to 24 minutes.

A crystal for X-Ray analysis was grown of the "slow" enantiomer of this complex (evaporation of benzene/hexane solution at 20 °C). The structure was not refinable to unequivocally establish the absolute stereochemistry of this enantiomer. The best approximation is that this enantiomer does correspond to the (+)-"slow" enantiomer of the DMAP*FeC_5Ph_5. $[\alpha]^{20}_D$ = +552.9° (c = 0.14, $CHCl_3$).

(η^5-pyrrolyl)RuCp^X AS NUCLEOPHILIC CATALYSTS

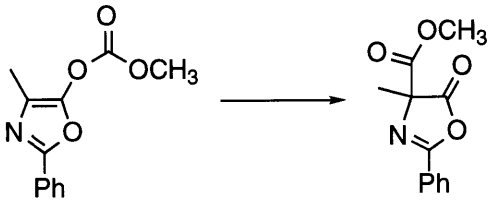


Ketene Solvolysis Reaction (Eq 2B.1). A stock solution of benzyl alcohol (31 μL, 0.30 mmol), phenyl ethyl ketene (40 μL, 0.27 mmol) and C_6D_6 (2.8 mL) was prepared. An aliquot (0.7 mL) of this solution was added to each of three sealable NMR tubes. Stock solutions of catalysts were prepared: catalyst (0.007 mmol) in C_6D_6 (1 mL). Aliquots of catalyst stock solution (0.1 mL) or C_6D_6 (0.1 mL) were added to each of the NMR tubes, which were then sealed under nitrogen. The reactions were observed by ^{1}H NMR to assess the half-lives of the reactions. Catalyst (DMAP*)FeCp* (**2.2**): $t_{1/2}$=9.6 min, Catalyst (DMAP*)RuCp* (**2B.1**): $t_{1/2}$=3.8 min.



Diketene Solvolysis Reaction (Eq 2B.2). A stock solution of 1-phenyl ethanol (32 μL, 0.27 mmol), diketene (24 μL, 0.31 mmol) and CD_2Cl_2 (4.0 mL) was prepared. Into each of two vials was weighed a catalyst (0.005 mmol) and an aliquot (1.6 mL) of the stock solution was added to each vial. Each reaction solution was transferred to a screw-cap NMR tube and the remaining stock solution was transferred to a third. Each tube was sealed under nitrogen. The reactions were observed by ^{1}H NMR to assess the half-lives of the reactions. Catalyst (DMAP*)FeCp* (**2.2**): $t_{1/2}$=21.0 min, Catalyst (DMAP*)RuCp* (**2B.1**): $t_{1/2}$=27.5 min.

(DMAP*)RuCp^X AS NUCLEOPHILIC CATALYSTS



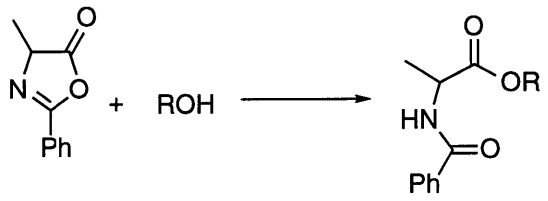
Enol carbonate rearrangement (Eq 2B.3). Into a vial was weighed the enol carbonate (24.3 mg, 0.104 mmol) to which was added *tert* - amyl alcohol (0.5 mL). Into a second vial was weighed the catalyst (0.01 mmol) to which was added *tert* - amyl alcohol (0.5 mL). The catalyst solution was loaded into a syringe under a nitrogen atmosphere and the substrate solution was sealed with a septum, also under nitrogen.

The substrate solution was cooled to 4 °C and the catalyst solution was then added via syringe. The solution became a dark yellow color with the addition. After 19 h the color of the solution was bright yellow again, and the solution was removed from the refrigerator and chromatographed (10%-25% EtOAc/hexane) to separate the catalyst from the products. Once the products had been removed, the catalyst was eluted with 10% NEt_3/EtOAc.

The product solution was concentrated and GC analysis (GTA chiral stationary phase) was used to assess the enantiopurity of the compound.

(DMAP*)RuCp*, (+)-2B.2: 69% ee

(DMAP*)Ru(C_5Ph_5), (+)-2B.4: 74% ee



Ring-Opening of Azlactones.

Side-by-side comparison: 10% acid, methanol (as in Eq 2B.4). A stock substrate solution was prepared consisting of azlactone (52.6 mg, 0.300 mmol), benzoic acid (3.8 mg, 0.031 mmol), methanol (18 μL, 0.44 mmol) and toluene-d_8 (3.0 mL). Into separate vials were weighed the catalysts (0.005 mmol), To each catalyst was added an aliquot (1.0 mL) of the stock solution. Each solution was transferred to a sealable NMR tube and the reaction was monitored by ^{1}H NMR for conversion.

NMR analysis showed both reactions having similar rates. After the reactions had reached completion, the product was isolated by column chromatography (silica gel, 25% EtOAc/hexane). Elution of the catalysts was performed with 10% NEt_3/EtOAc.

GC analysis (GTA chiral stationary phase) was used to assess the enantiopurity of the products.

(DMAP*)FeCp*, (-)-2.4: 55% ee, $t_{1/2}$ = 4.8 h, favoring the (L)-derived enantiomer

(DMAP*)RuCp*, (-)-2B.2: 57% ee, $t_{1/2}$ = 3.5 h, 75% yield, favoring the (L)-derived enantiomer

Rate analysis with variable acid loading, methanol (Figure 2B.1). For each reaction: azlactone (57.4 mg, 0.328 mmol), methanol (20 μL, 0.49 mmol), (DMAP*)RuCp* (**(+)-2B.2**, 6.0 mg, 0.015 mmol), and toluene-d_8 (0.8 mL) were added to a vial. This solution was immediately added to a second vial with benzoic acid (0 mol%, 5 mol%, or 10 mol%). Each solution was then transferred to a sealable NMR tube under nitrogen and the reactions were monitored by ^{1}H NMR for conversion.

0 mol% benzoic acid, $t_{1/2}$ = 0.55 h

5 mol% benzoic acid, $t_{1/2}$ = 0.90 h

10 mol% benzoic acid, $t_{1/2}$ = 1.5 h

After reaching >90% conversion, each solution was chromatographed to separate the products from the catalyst (silica gel, 10% - 50% EtOAc/hexane). Catalyst was then eluted with 10% NEt_3/EtOAc. The product fractions were concentrated and analyzed by GC (GTA chiral stationary phase) for enantiopurity.

0 mol% benzoic acid, 3% ee, favoring the (D)-derived enantiomer

5 mol% benzoic acid, 35% ee, favoring the (D)-derived enantiomer

10 mol% benzoic acid, 43% ee, favoring the (D)-derived enantiomer

Ring-opening with *i* PrOH (Eq 2B.5). The reactions were run as in "Rate analysis with variable acid loading, methanol" except the methanol was replaced with *i* -PrOH (38 μL, 0.50 mmol) and benzoic acid loadings were 0 mol% and 10 mol%.

0 mol% benzoic acid, $t_{1/2}$ = ~47 h, 17% ee, favoring the (D)-derived enantiomer

10 mol% benzoic acid, $t_{1/2}$ = ~78 h, 63% ee, favoring the (D)-derived enantiomer

Catalysis with (DMAP*)Ru(C_5Ph_5) and methanol (Eq 2B.6). A stock solution of azlactone (86.6 mg, 0.494 mmol), methanol (30 μL, 0.74 mmol) and toluene (1.2 mL) was prepared. (DMAP*)Ru(C_5Ph_5) (**(-)-2B.4**, 5.0 mg, 0.0071 mmol) was weighed into each of two vials and then benzoic acid was added (2 mol% or 12 mol%). An aliquot (0.44 mL) of the stock solution was added to each of the two vials. The vials were sealed under nitrogen and stirred at room temperature.

The solutions were chromatographed (silica gel, 10% - 50% EtOAc/hexane) after a day to separate the product and starting materials. The catalyst was eluted with 10% NEt_3/EtOAc. The product fractions were concentrated and analyzed by GC (GTA chiral stationary phase) for enantiopurity.

2 mol% benzoic acid, 10% ee, favoring the (L)-derived enantiomer

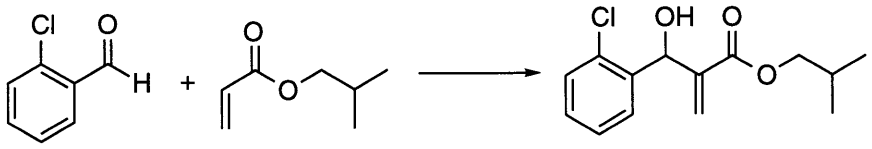
12 mol% benzoic acid, 21% ee, favoring the (L)-derived enantiomer

Catalysis with (DMAP*)Ru(C_5Ph_5) and*i*- PrOH (Eq 2B.6). The reactions were run

as in "Catalysis with (DMAP*)Ru(C_5Ph_5) and methanol" except the methanol was replaced with *i* -PrOH (58 μL, 0.758 mmol) and (DMAP*)Ru(C_5Ph_5) (**(+)-2B.4**) as the catalyst.

2 mol% benzoic acid, 17% ee, favoring the (D)-derived enantiomer

12 mol% benzoic acid, 36% ee, favoring the (D)-derived enantiomer

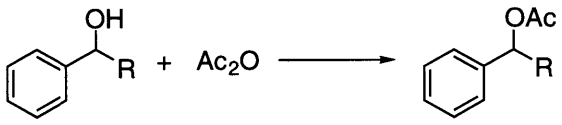


Asymmetric Baylis-Hillman Reaction (Eq 2B.8). A stock solution of *o*-chlorobenzaldehyde (120 μL, 1.07 mmol), *iso*-butylacrylate (32 μL, 0.22 mmol) and benzene (105 μL) was prepared. Into vials were weighed the catalysts (0.0035 mmol). To each vial was added an aliquot (86 μL) of stock solution. Each solution was sealed under nitrogen and allowed to react at 4 °C for 66 h.

The products were separated from the catalyst by column chromatography (silica gel, 10% EtOAc/hexane - 100% EtOAc). The catalyst was then recovered by elution with 10% NEt_3/EtOAc. The product fractions were concentrated and analyzed by GC (BPH chiral stationary phase).

(DMAP*)RuCp*, (+)-2B.2: 18% ee

(DMAP*)Ru(C_5Ph_5), (+)-2B.4: NR



Acylation with acetic anhydride.

Rate study using racemic catalysts, acylation of (S)-1-phenylethanol (Eq 2B.9). A stock solution of (S)-1-phenylethanol (108.9 mg, 0.903 mmol), triethylamine (141 μL, 1.01 mmol) and *tert*-amyl alcohol (1.5 mL) was prepared. Each catalyst (0.0028

mmol) was weighed into a vial and an aliquot (580 μL) of stock solution added to each. The solutions were sealed under nitrogen and then heated slightly to allow for complete dissolution of catalyst. The solutions were then cooled to 4 °C and acetic anhydride (32 μL, 0.34 mmol) was added to each vial.

The reactions were aliquoted periodically to assess the conversion: the simple organics were separated from the catalyst by column chromatography (silica gel, 25% EtOAc/hexane - 75% EtOAc/hexane). The catalyst was then recovered by elution with 10% NEt_3/EtOAc. The organic materials were concentrated and conversion was assessed by GC analysis (chiral stationary phase).

(DMAP*)Fe(C_5Ph_5), (+)-2.5:

24% conv. @ 75 min

43% conv. @ 165 min

60% conv. @ 280 min

(DMAP*)Ru(C_5Ph_5), (+)-2B.4:

44% conv. @ 60 min

79% conv. @ 170 min

Acylation of 1-phenylethanol with (DMAP*)Ru(C_5Ph_5) (Eq 2B.10). A stock solution of 1-phenylethanol (90 μL, 0.75 mmol), triethylamine (78μL, 0.56 mmol) and *tert*-amyl alcohol (1.5 mL) was prepared. Catalyst (0.0028 mmol) was weighed into a vial and an aliquot (0.56 mL) of stock solution was added to it. The vial was sealed under nitrogen with a septum and then heated slightly to dissolve the catalyst. Once the solution was homogeneous, it was cooled slowly to room temperature and then cooled to 4 °C. Acetic anhydride (18μL, 0.19 mmol) was then added and the solution allowed to react at 4 °C.

The reactions were aliquoted periodically, and the catalyst was separated from the organics by column chromatography (silica gel, 25% EtOAc/hexane to 75% EtOAc, then 10% NEt_3/EtOAc to elute catalyst). The product/SM fractions were

concentrated and analyzed by GC (chiral stationary phase).

(DMAP*)Ru(C_5Ph_5), (-)-2B.4:

19% conv. @ 1 h, s=9.1, (77% ee of (*R*) acetate, 18% ee of (*S*) alcohol)

43% conv. @ 4.5 h, s=10.0, (71% ee of (*R*) acetate, 54% ee of (*S*) alcohol)

(DMAP*)Ru(C_5Ph_5), (+)-2B.4:

24% conv. @ 1.5 h, s=7.6, (72% ee of (*S*) acetate, 23% ee of (*R*) alcohol)

40% conv. @ 3 h, s=8.2, (68% ee of (*S*) acetate, 46% ee of (*R*) alcohol)

Solvent study at -34 °C (Eq 2B.11). (DMAP*)Ru(C_5Ph_5), (**(-)-2B.4**, 1.8 mg, 0.0026 mmol) was weighed into each of 3 vials. To each vial was added 1-phenylethanol (30 μL, 0.25 mmol), triethylamine (26 μL, 0.19 mmol) and solvent (0.50 mL). Each solution sealed under nitrogen with a septum and heated gently until solution was homogeneous. Solutions then cooled to -34 °C and acetic anhydride (also cooled to -34 °C, 18 μL, 0.19 mmol) was then added.

Aliquots of the solution were taken periodically. They were diluted immediately with a copious amount of hexane (-34 °C) and immediately chromatographed to separate the catalyst from the simple organics (silica gel, 25% EtOAc/hexane - 75% EtOAc:hexane, followed by elution of catalyst with 10% NEt_3/EtOAc). The organic fractions were concentrated and analyzed by GC (chiral stationary phase) for conversion and %ee.

THF: 29% conv. @ 19 h, s = 7.4, (70% ee of (*R*) acetate, 29% ee of (*S*) alcohol)

43% conv. @ 43 h, s = 7.4, (64% ee of (*R*) acetate, 49% ee of (*S*) alcohol)

CH_2Cl_2: 41% conv. @ 19.5 h, s = 6.1, (60% ee of (*R*) acetate, 42% ee of (*S*) alcohol)

56% conv. @ 43 h, s = 6.1, (52% ee of (*R*) acetate, 66% ee of (*S*) alcohol)

Et_2O: 27% conv. @ 19.5 h, s = 13.1, (82%ee of (*R*) acetate, 30% ee of (*S*) alcohol)

41% conv. @ 43 h, s = 12.6, (76% ee of (*R*) acetate, 53% ee of (*S*) alcohol)

Acylation of 1-phenylethanol @ 0.34M (Eq 2B.12). A stock solution of 1-phenylethanol (67.3 mg, 0.551 mmol) in *t*-amyl alcohol (0.55 mL) was prepared. Into

each of 2 vials was weighed the (DMAP*)Ru(C_5Ph_5) (**(-)-2B.4**, 2.0 mg, 0.0028 mmol). To each vial was added a solvent (0.5 mL, *t*-amyl alcohol or ether) and then an aliquot (0.29 mL) of the stock solution. To each vial was then added triethylamine (27 μL, 0.19 mmol). The vials were sealed under nitrogen with a septum and heated gently to dissolve the catalyst. Once the solutions were homogeneous, they were cooled: ether/*t*-amyl alcohol (-34 °C), *t*-amyl alcohol (-11 °C). The acetic anhydride (cooled to -34 °C, 18 μL, 0.19 mmol) was then added to each vial and the reactions left cold to react.

The solutions were aliquoted periodically to assess conversion. The aliquots were diluted in a copious amount of cold hexane and chromatographed immediately to separate the catalyst from the simple organics (silica gel, 25% EtOAc/hexane - 75% EtOAc/hexane, followed by 10% NEt_3/EtOAc to elute the catalyst). The organic fractions were concentrated and analyzed by GC (chiral stationary phase) to assess conversion and %ee.

t-amyl alcohol (-11 °C):

24% conv. @ 2.5 h, s = 10.3, (78% ee of (*R*) acetate, 24% ee of (*S*) alcohol)

59% conv. @ 15.5 h, s = 11.2, (61% ee of (*R*) acetate, 87% ee of (*S*) alcohol)

2:1 Ether : *t*-amyl alcohol (-34 °C):

12% conv. @ 14 h, s = 17.5, (88% ee of (*R*) acetate, 12% ee of (*S*) alcohol)

28% conv. @ 42 h, s = 18.1, (86% ee of (*R*) acetate, 33% ee of (*S*) alcohol)

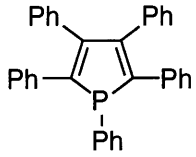
40% conv. @ 62 h, s = 17.9, (82% ee of (*R*) acetate, 55% ee of (*S*) alcohol)

Chapter Two, Part C:

Ferrocene-Derived Complexes with *P*-Heterocyclic Ligands

INTRODUCTION

The use of nitrogen heterocycles as ligands for iron has been studied since the late 1950s. The analogous use of *phosphorus* heterocycles has received relatively little interest, with most of the published work coming out of the research group of Mathey.[42] Beginning in 1959 with the first syntheses of phospholes (**2C.1**),[42-44] the precursors to phosphaferrocenes, interest was sparked in non-nitrogen heterocyclic ferrocene complexes. It has since been shown that phosphaferrocenes can be synthesized by a variety of methods and show very different reactivities as compared to their azaferrocene analogues. Although Mathey has shown that phosphaferrocenes can act as sigma donors to a metal center,[45] no one has demonstrated the use of a phosphaferrocene as a catalyst.

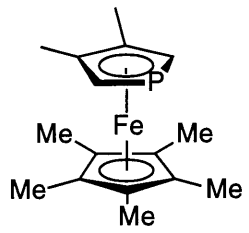


2C.1

Since azaferrocenes had recently been shown by our group to act as nucleophilic catalysts for a variety of reactions,[7] we were interested in extending this chemistry to phosphaferrocenes. We therefore began studying the synthesis and utilization of phosphaferrocene complexes. The synthesis of phosphaferrocenes is more complicated than the synthesis of the analogous nitrogen containing complexes. While many pyrroles are commercially available, no phosphole, to this date, is sold. The synthesis of simple phospholes is straightforward, but requires the cycloaddition of a diene to an equivalent of $PhPCl_2$ over several days to a week. A subsequent base-mediated elimination provides the desired phosphorous

heterocycle.[46] Phospholes show very little aromatic character as compared to pyrroles, furans, and thiophenes. Similarly, they show very different chemical reactivity as compared to their N, O, and S analogues.[42]

The phenyl-phosphorus bond of these compounds can be easily reduced with alkali metals, resulting in the phospholyl anion.[42] This anion will react with an iron(II) source to form phospholyliron complexes. The desired neutral phosphaferrocenes can be prepared by a variety of methods, the most common of which requires transmetallation of the Na salt of the phospholyl anion with $MgBr_2$, followed by complexation to a metal source. The use of $[Cp^*FeCl_2]_x$ as the metal source results in the pentamethyl phosphaferrocene complex (**2C.2**).[47]



2C.2

Derivatization of phosphaferrocenes has proven difficult, as strong bases (such as butyllithium) tend to attack the phosphorus atom instead of deprotonating at the α–position. Alpha-substituted phosphaferrocenes may be produced by several methods. Reaction of phosphaferrocene with the Vilsmeyer reagent affords the α-formyl product, and acetyl derivatives may be formed by refluxing the phosphaferrocene in a dichloromethane solution of acetyl chloride-$AlCl_3$.[47]

Alternately, substitution of the phenyl phosphole before complexation is possible.[42] A route of phosphorus protection, lithiation at the 2-position, trapping of an electrophile, and deprotection of the phosphorous has also been demonstrated.[48]

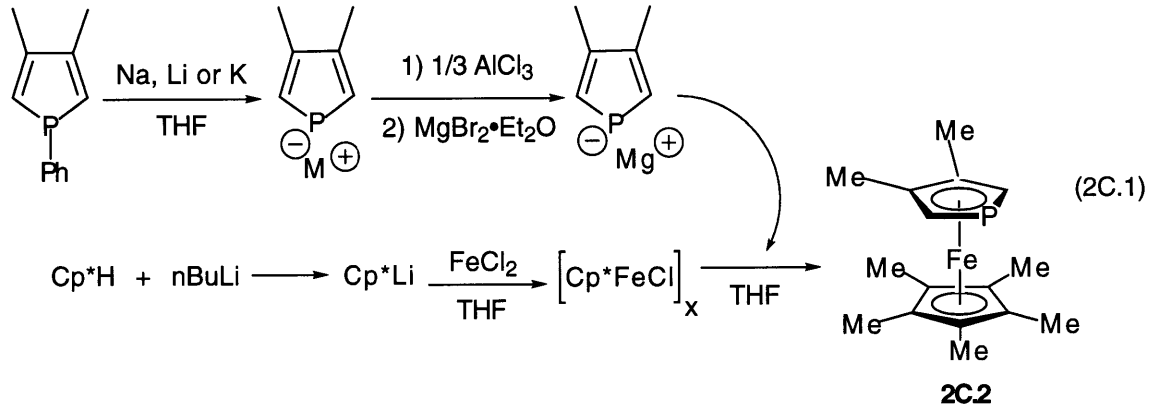
Phosphaferrocenes have never, to our knowledge, been investigated as catalysts

in organic reactions. Most of the complexes made were studied in terms of their electrochemistry[49] and the aromatic character (or lack thereof)[50] of the bound phosphole. As compared to the azaferrocenes, phosphaferrocenes have shown very different reactivity under most circumstances. Although there is still significant discussion in the literature as to whether the phosphorus of a phosphaferrocene will act as a nucleophile or whether a phosphole is an aromatic species, we were interested in studying the catalytic activity of phosphaferrocenes in organic reactions known to be nucleophile catalyzed. We were, of course, interested in extending any observed nucleophilic catalysis to asymmetric reactions, which would entail the preparation of a chiral phosphaferrocene, as we had previously achieved with the azaferrocene analogs.

RESULTS AND DISCUSSION

Synthesis and Reactivity of Phosphaferrocene Complexes

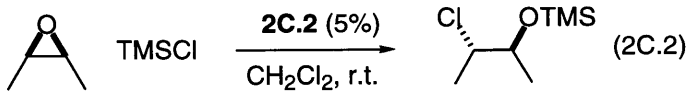
The initial synthesis of a simple pentamethyl 3,4-dimethylphosphaferrocene complex was achieved as shown below, using a combination of the methods published by Mathey (Eq 2C.1).[47,51] Upon synthesis and purification of **2C.2**,[49] we set out to analyze the reactivity profile of this complex (**2C.2**) as a nucleophilic catalyst.



2C.2

We attempted a variety of reactions with very little success: acylation with acetic anhydride, acylation with diketene, cyanosilylation of aldehydes, phenyl ethyl ketene solvolysis, the Baylis-Hillman reaction, silylation of alcohols, allylation of aldehydes, and the addition of trimethylsilylacetonitrile to aldehydes. None of these reactions showed much promise of being catalyzed by the phosphaferrocene; either there was no observed reaction or the catalyzed rate was only slightly faster than the background reaction. This was quite disappointing since other phosphines are known to catalyze a number of these reactions, or variants thereof.[4,5] A number of these reactions had also shown significant acceleration in the presence of our azaferrocene complexes.[7]

The phosphaferrocene (**2C.2**) was, however, found to catalyze the addition of TMSCl to an epoxide (Eq 2C.2). This reaction was first shown to be subject to catalysis by triphenylphosphine in 1981.[52]

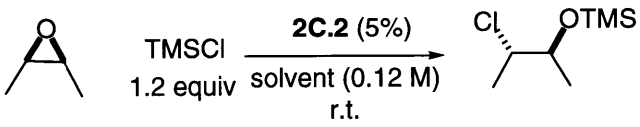


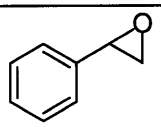
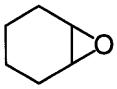
(2C.2)

The catalyzed ring opening of an epoxide in the presence of a phosphaferrocene complex was shown to be a very facile reaction when the substrate was styrene oxide. The reaction was shown to be competent in a variety of solvents (benzene, chloroform, and dichloromethane), but due to the possibility of HCl formation in chloroform (which can promote the acid-mediated ring opening of the epoxides), we chose to focus on dichloromethane or benzene as the solvent.

We found that while benzene was a reliable solvent to use for this reaction, the rate was dramatically decreased in comparison to the reaction run in dichloromethane (Table 2C.1). We therefore chose to focus on dichloromethane as the solvent for our optimization of the reaction conditions. We found that the rate of the reaction in CD_2Cl_2 was also affected drastically by the molarity of the reaction solution. Although some substrates (e.g., styrene oxide and cyclohexene oxide) show reasonable conversion at 0.12 M, the slower reacting substrates (e.g., *cis*-stilbene oxide) show little conversion (<5%) after 26 h at this concentration. For this reason we opted to run all reactions at a concentration of 0.33 M (substrate in CD_2Cl_2).

Table 2C.1. Rate Comparison with Solvent Change.



Solvent	Substrate	half-life (min)
CD_2Cl_2		<16
C_6D_6		376
CD_2Cl_2		82
C_6D_6		>1700

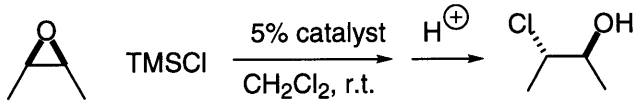
In monitoring the rate of ring opening for several substrates, we found that the reaction also appears to be very temperature sensitive. When the temperature is not carefully monitored, large rate differences can result. For this reason, all semi-preparative scale reactions were run at 23-24 °C and monitored by ^1H NMR for conversion.

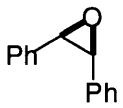
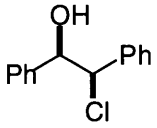
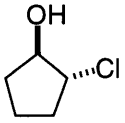
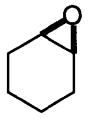
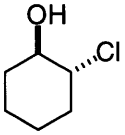
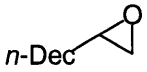
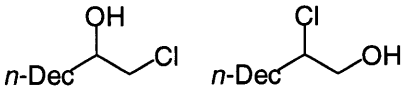
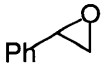
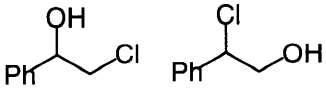
The product formed from the ring opening of epoxides in the presence of TMSCl is not completely stable to standard workup conditions (column chromatography), so a method by which the TMS group was efficiently cleaved (with retention of stereochemistry) was desired. We initially tried deprotection with TBAF, but we found that it was only effective on some of the chlorohydrins prepared. The same was found to be true with an alcoholic (MeOH) deprotection of the TMS ether. We finally found that deprotection with anhydrous HCl was a general and efficient method for deprotection of these products.

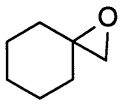
Thus, the treatment of an epoxide with 1.2 equivalents of TMSCl and 5 mol% of **2C.2** in CH_2Cl_2 (or CD_2Cl_2) at room temperature, followed by deprotection of the trimethylsilyl ether with anhydrous HCl, results in the desired chlorohydrin

products in moderate to good isolated yields (Table 2C.2). For each substrate indicated in Table 2C.2, no ring opening is observed in the absence of catalyst under otherwise identical conditions. We also attempted the ring opening of a 1,1-disubstituted epoxide (**2C.4**), but the reaction was not catalyzed by either PPh_3 or complex **2C.2**.

Table 2C.2. Ring Opening of Epoxides with TMSCl in the Presence of Catalyst 2C.2.



Entry	Substrate	Product(s)	Yield (%)
1			96
2			80
3			94
4		 9.3 : 1	100
5		 1 : 2.7	88

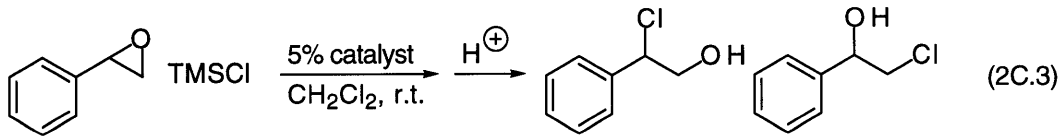


2C.4

The ring opening of *cis*-stilbene oxide (Table 2C.2, entry 1) and cyclopentene- and cyclohexene oxide (Table 2C.2, entries 2 and 3) was shown to occur with inversion of configuration at the carbon undergoing substitution. This was proven by subjecting

the deprotected products of the reaction to basic conditions (KOH/MeOH or d_8-THF) and monitoring the reaction for the formation of epoxide. For the cyclic chlorohydrins, complete conversion to the epoxide was seen, verifying the original trans configuration of the chlorohydrin. In the case of the *cis*-stilbene oxide, the methines of *cis*- and *trans*-stilbene oxide have characteristic resonances in the ^{1}H NMR (*cis*-stilbene oxide: δ 4.36, *trans*-stilbene oxide δ 3.89). By analysis of these regions, it is possible to tell if the product, upon ring closing, has the same relative stereochemistry as the original epoxide. The formation of a 95 : 5 mixture of *cis*- : *trans*-stilbene oxide was noted for the product depicted in Table 2C.2, entry 1.

The ring opening of unsymmetrical epoxides shows preferential displacement at the less hindered carbon (Table 2C.2, entry 4), barring an overriding electronic effect (Table 2C.2, entry 5). This regiochemical preference was compared with the results seen during ring opening of epoxides with PPh_3 and *n*-Bu_4NCl, in the hopes that we might gain some insight into the mechanism of ring opening. The ring opening of styrene oxide with phosphaferrocene **2C.2**, appears to be governed by an electronic effect, with preference shown for formation of the primary alcohol. The ring opening with both PPh_3 and *n*-Bu_4NCl show a similar preference (Eq 2C.3).

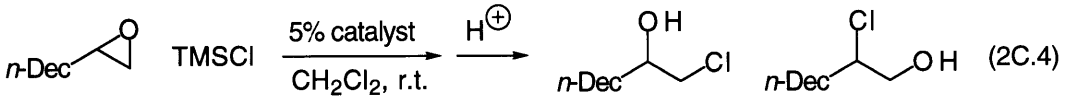


(2C.3)

2C.2	2.7 : 1
n-Bu_4NCl	2.8 : 1
PPh_3	3.2 : 1

The ring opening of dodecene oxide, though, shows marked differences in regiochemical preference. The ring opening with phosphaferrocene, **2C.2**, occurs with >9 : 1 preference for attack at the less hindered carbon (Eq 2C.4). With both PPh_3 and *n*-Bu_4NCl, this preference is diminished about 2-fold. Based on these data, it seems that the ring opening of styrene oxide is governed predominantly by electronics, with changes in the catalytic system having little effect on the

regiochemistry of addition. In the ring opening of dodecene, though, differences between the catalysts are evident. Tetrabutylammonium chloride, which should be operating by simple Cl^- ion catalysis, shows a similar regiochemical preference to the reaction catalyzed by PPh_3. Although presumed to be occurring by nucleophilic catalysis, mechanistic proof of triphenylphosphine acting as a nucleophilic catalyst was not provided in the original paper by Andrews.[52] From our data it seems that simple Cl^- ion catalysis could be the mode of action with triphenylphosphine. For our system, the high regiochemical preference for attack at the less hindered carbon suggests that sterics play a major role in the mode of attack.

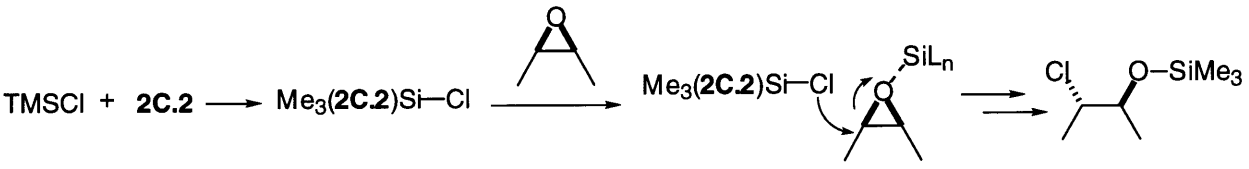


(2C.4)

2C.2	9.3 : 1
n-Bu_4NCl	4.9 : 1
PPh_3	3.6 : 1

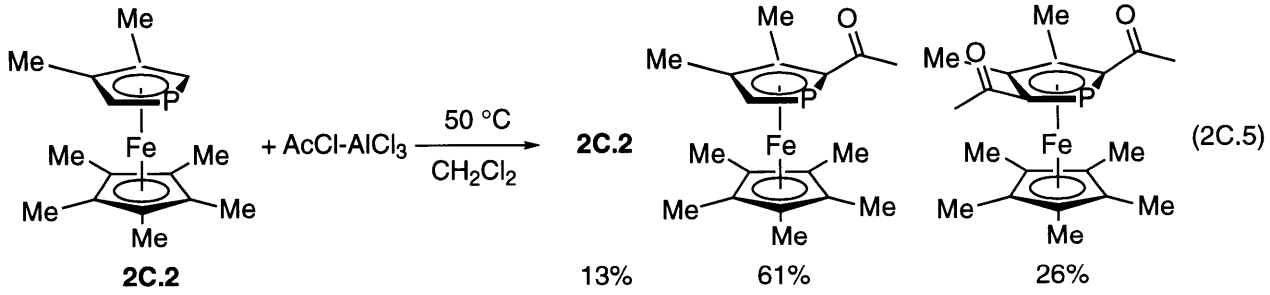
We postulate that a pentacoordinate **2C.2**-TMSCl[45] adduct might be a reactive intermediate in the ring-opening process catalyzed by the phosphaferrocene (Figure 2C.1). Nucleophile-activated organosilicon compounds are well precedented.[53,54] We reasoned that if our postulated intermediate is correct, the use of a chiral phosphaferrocene catalyst may impart enantioselectivity to the ring opening of suitably substituted epoxides. Several enantioselective versions of the ring opening of epoxides have been reported.[55-57]

Figure 2C.1. A possible mechanism for the ring opening of epoxides in the presence of **2C.2**-TMSCl.



Attempted Synthesis of Chiral Phosphaferrocenes

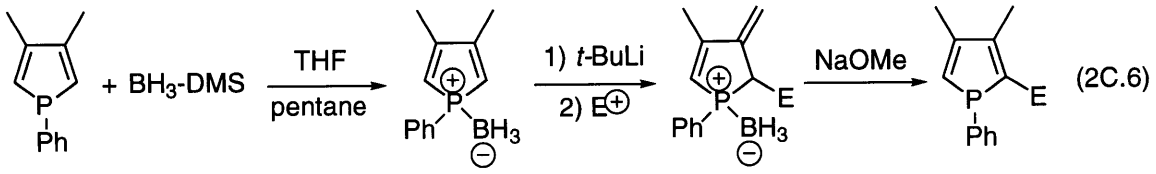
We set out to derivatize **2C.2** in the 2-position, knowing that a small group here might provide enough differentiation to have an efficient display of chirality at the phosphorus atom. We first attempted to acetylate **2C.2** and then reduce this moiety to the secondary alcohol. This complex could subsequently be resolved and derivatized, as had been done with the azaferrocene complexes. The Friedel-Crafts acetylation reaction[47] went smoothly (Eq 2C.5), providing a mixture of the unsubstituted (13%), monosubstituted (61%), and disubstituted (26%) materials. These were easily separated by column chromatography and isolated as red solids. Reductions of these complexes were attempted with a variety of reagents: lithium aluminum hydride, BH_3-THF, and catecholborane. Although several of the reactions showed complete conversion of the acetyl group, in no case was the desired reduced product isolated. The Corey-Bakshi-Shibata reduction protocol also failed to result in isolable product.



(2C.5)

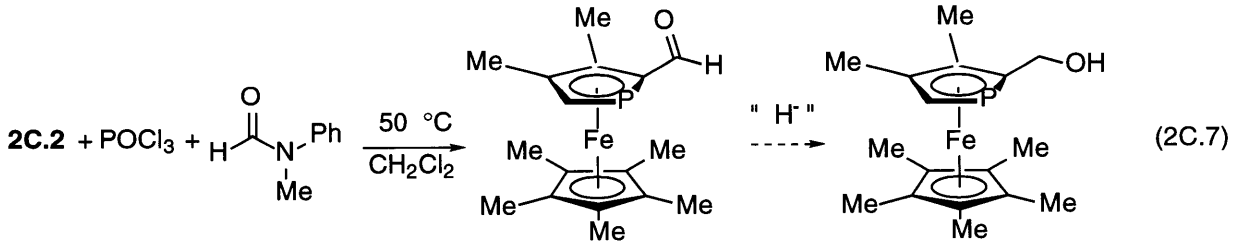
Next we set out to prepare a trisubstituted phosphole, which could be subsequently complexed to form a chiral phosphaferrocene. The preparation of trisubstituted phospholes had been demonstrated (Eq 2C.6),[48] but we found the synthesis difficult to reproduce. Although we were finally able to obtain a small amount of 2,3,4-trimethylphenylphosphole (Eq 2C.6, E = Me), complexation of this ligand (by the method used to prepare **2C.2**) proved difficult, and none of the desired

complex was isolated.



(2C.6)

Our last attempt to prepare a chiral phosphole was by formylation of the 2-position of a phosphaferrocene, followed by reduction (Eq 2C.7). The formylation procedure of Mathey (using the Vilsmeyer reagent as in Reference 47) was used for a small-scale reaction, and the desired product was formed. The reduction of this molecule should be trivial with simple reducing agents, but due to the small amount of complex we had prepared, our reduction with LAH failed to result in isolable product. This method was subsequently found by a member of our group (Shuang Qiao) to provide rapid access to the desired chiral phosphaferrocene complex. Another method has been published recently which allows the preparation of phosphaferrocenes with various substituents at the alpha position.[58] The preparation and the use of the chiral phosphaferrocenes as catalysts and ligands is currently being investigated in our group.



(2C.7)

CONCLUSION

We have shown that a phosphaferrocene (**2C.2**) is in fact capable of serving as a catalyst for the ring opening of epoxides in the presence of TMSCl, presumably through nucleophilic activation of the silicon compound. This allows for the catalytic ring opening of a variety of epoxides in the presence of 5 mol% of the catalyst, **2C.2**, with reaction times ranging from <10 minutes (styrene oxide) to almost 4 days for very slow-reacting substrates (e.g., *cis*-stilbene oxide). The isolated yields, after deprotection with anhydrous HCl, are good, and no competitive background reaction is seen for any of the substrates.

The ring opening occurs with inversion of configuration at the carbon undergoing substitution. In the ring opening of unsymmetrical epoxides, the electronic and steric nature of the substrate plays a large part in determining the regiochemistry of attack. Dodecene oxide undergoes substitution at the less hindered carbon, while styrene oxide undergoes preferential substitution at the more hindered carbon, with an overriding electronic effect driving the regiochemistry of the reaction. This electronic effect appears to control the ring opening regardless of the catalyst, while the ring opening of dodecene oxide appears more subject to regiochemical control by the catalyst. The phosphaferrocene **2C.2** shows an overwhelming preference for attack at the less hindered carbon of dodecene oxide (9 : 1), while simple Cl^- ion catalysis (*n*-Bu_4NCl) shows only a 5 : 1 preference for attack at the terminal carbon. Catalysis by PPh_3 leads to a ratio of 4 : 1 for attack at the terminal carbon. We postulate that the catalysis by phosphaferrocene **2C.2** is occurring through a nucleophile-activated TMSCl adduct (**2C.2**-TMSCl) which, due to size, might prefer attack at the less hindered carbon.

In conclusion, we have demonstrated the first use of a phosphaferrocene as a catalyst. Although the mechanism of action, i.e., nucleophilic activation of the TMSCl, has not been unequivocally proven, we hope that the development of chiral

phosphaferrocenes and their use in this reaction will provide the necessary data to show that a phosphaferrocene-TMSCl complex is in fact formed and responsible for the observed reaction.

EXPERIMENTAL

General. $FeCl_2$ (Aldrich) was ground to a fine powder prior to use. *n*-BuLi (1.6 M in hexanes; Strem), 2-chloroacetophenone (Aldrich), $MgBr_2 \bullet Et_2O$ (Aldrich), $NaBH_4$ (Aldrich), naphthalene (Aldrich), 1,2,3,4,5-pentamethylcyclopentadiene (Strem), PPh_3 (Aldrich), HCl (1 M in ether, Aldrich) KOH (Mallinckrodt) and *n*-Bu_4NCl (Aldrich), and sodium (Aldrich) were used without further purification.

Chlorotrimethylsilane (Aldrich), cyclohexene oxide (Aldrich), cyclopentene oxide (Aldrich), 1-dodecene oxide (Aldrich), and styrene oxide (Aldrich) were distilled prior to use. *cis*- Stilbene oxide (Aldrich) was purified by flash chromatography. THF was distilled from sodium/benzophenone, CH_2Cl_2 was distilled from CaH_2, d_8-THF was vac transferred, and CD_2Cl_2 was dried over alumina.

All reactions were carried out in oven-dried glassware with magnetic stirring under an atmosphere of nitrogen or argon using standard Schlenk or glove box techniques.

Preparation of Catalyst 2C.2. This procedure is nearly identical to that of Mathey.[47,51] A solution of naphthalene (4.12 g, 32.1 mmol) in THF (15 mL) was added to a flask containing sodium (0.781 g, 34.0 mmol) and 3,4-dimethyl-1-phenylphosphole[46] (3.00 g, 16.0 mmol), resulting in a dark-red solution, which was stirred at ~30 °C for 3 h. The excess sodium was then removed, and $MgBr_2 \bullet Et_2O$ (4.15 g, 16.1 mmol) was added. The resulting yellow-brown slurry was stirred at ~30 °C for 2 h.

Cp*Li was prepared by treating a solution of 1,2,3,4,5-pentamethylcyclopentadiene (2.5 mL, 16 mmol) in THF (20 mL) with *n*-BuLi (1.6 M in hexanes; 10 mL, 16 mmol), resulting in a yellow solution and a large quantity of precipitate. This mixture was added to a stirred slurry of $FeCl_2$ (2.02 g, 16.0 mmol) in

THF (5 mL). After completion of the addition, the reaction was stirred for 1 h at ~30 °C, resulting in a forest-green solution containing a very fine precipitate. The 3,4-dimethylphospholyl anion slurry (previous paragraph) was then added, immediately providing a dark-brown mixture. The reaction was stirred at ~30 °C for 13.5 h, then refluxed for 1.5 h. After cooling to room temperature, the solvents were removed in vacuo, and the resulting brown residue was extracted repeatedly with hexane. The washings were filtered, and the solvent was removed in vacuo. The resulting orange solid was sublimed (40 °C, 100 mtorr) and then chromatographed (adsorption alumina), affording an orange-yellow solid that was identical by ^{1}H, ^{13}C, and ^{31}P NMR with literature data for complex **2C.2**.[49]

PREPARATION OF AUTHENTIC PRODUCTS

All authentic products were prepared by the PPh_3-catalyzed ring opening of epoxides with TMSCl.[52] The resulting TMS ethers were cleaved by treatment with HCl (1 M in Et_2O), and the product alcohols were purified by flash chromatography and characterized by ^1H and ^{13}C NMR.

***trans*-2-Chloro cyclopentanol [1561-86-0].** ^1H NMR (300 MHz, $CDCl_3$) δ 1.60 (m, 1H), 1.85 (m, 3H), 2.14 (m, 1H), 2.26 (m, 1H), 2.46 (s, 1H), 4.02 (m, 1H), 4.24 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 31.3, 33.3, 65.6, 80.2; IR (neat) 3344(br), 2974, 1436, 1338, 1075, 990, 846, 708 cm^{-1}; HRMS *m/z* 120.0342 [M^+], calcd for C_5H_9OCl 120.0342. TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.21.

***trans*-2-Chloro cyclohexanol [1561-86-0].** ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (m, 3H), 1.64 (m, 3H), 2.04 (m, 1H), 2.16 (m, 1H), 3.00 (br s, 1H), 3.46 (m, 1H), 3.67 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.8, 25.4, 33.1, 35.0, 67.1, 75.0; IR (neat) 3390(br), 2939, 2861, 1450, 1363, 1260, 1215, 1126, 1075, 1037, 1010, 959, 866, 843, 798, 735, 542 cm^{-1}; HRMS *m/z* 134.0499 [M^+], calcd for $C_6H_{11}OCl$ 134.0498. TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.30.

2-Chloro dodecanol [31331-47-2]. ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J = 6.5, 2H), 1.2-1.6 (m, 16H), 1.72 (m, 2H), 2.3 (br s, 1H), 3.68 (m, 1H), 3.80 (m, 1H), 4.00 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 26.4, 29.1, 29.3, 29.5, 29.6, 31.9, 34.3, 65.4, 67.1; IR (neat) 3361(br), 2924, 2854, 1466, 1378, 1049, 722, 682, 616 cm^{-1}; HRMS *m/z* 220.1595 [M^+], calcd for $C_{12}H_{25}OCl$ 220.1594. TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.24.

1-Chloro dodecan-2-ol [2984-56-7]. ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J = 7.0, 2H), 1.25 - 1.51 (m, 16 H), 2.42 (br s, 1H), 3.47 (m, 1H), 3.61 (dd, J = 3.3, 11.0, 1H), 3.78 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1, 22.7, 25.6, 29.4, 29.5, 29.6, 31.9, 34.3, 50.5, 71.5; IR (neat) 3378(br), 2924, 2854, 1466, 1378, 1051, 741, 603 cm^{-1}; HRMS *m/z* 220.1595 [M^+], calcd for $C_{12}H_{25}OCl$ 220.1594. TLC (20% Et_2O/pentane;

phosphomolybdic acid) R_f = 0.33.

2-Chloro-1-phenyl ethanol [1674-30-2]. ^1H NMR (300 MHz, $CDCl_3$) δ 2.74 (br s, 1H), 3.69 (m, 2H), 4.91 (dd, J = 3.5, 8.6, 1H), 7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.0, 74.2, 126.2, 128.6, 128.8, 140.0; IR (neat) 3389(br), 3063, 3031, 2955, 1494, 1454, 1426, 1248, 1200, 1085, 1064, 1012, 917, 870, 769, 723, 698, 614, 545, 522 cm^{-1}; HRMS *m/z* 156.0342 [M^+], calcd for C_8H_9OCl 156.0342. TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.41.

2-Chloro-2-phenyl ethanol [1004-99-5]. ^1H NMR (300 MHz, $CDCl_3$) δ 2.34 (br s, 1H), 3.93 (m, 2H), 4.99 (7, J = 6.6, 1H), 7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 64.8, 67.9, 127.5, 128.8, 128.9, 137.9; IR (neat) 3376(br), 3062, 3031, 2924, 1493, 1453, 1067, 1026, 760, 697 cm^{-1}; HRMS *m/z* 156.0342 [M^+], calcd for C_8H_9OCl 156.0342. TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.31.

CATALYZED RING-OPENING REACTIONS

Rate of ring opening in CD_2Cl_2 versus C_6D_6, styrene oxide (Table 2C.1). Into a vial was weighed **2C.2** (1.1 mg, 0.0040 mmol). To this was added solvent (0.58 mL), TMSCl (11 μL, 0.083 mmol) and styrene oxide (7.9 μL, 0.069 mmol). The resulting solution was then transferred to a screw-cap NMR tube and analyzed by ^1H NMR for conversion.

in CD_2Cl_2: 74% conv. @ 16 min.

in C_6D_6: 51% conv. @ 376 min.

Rate of ring opening in CD_2Cl_2 versus C_6D_6, cyclohexene oxide (Table 2C.1). Into a vial was weighed **2C.2** (1.1 mg, 0.004 mmol). To this was added solvent (0.58 mL), TMSCl (10.5 μL, 0.083 mmol) and cyclohexene oxide (7.0 μL, 0.069 mmol). The resulting solution was then transferred to a screw-cap NMR tube and analyzed by ^1H NMR for conversion.

in CD_2Cl_2: 56% conv. @ 71 min.

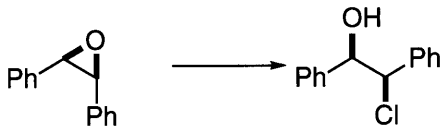
in C_6D_6: 23% conv. @ 1700 min.

Representative procedure for Table 2C.2, including monitoring the background reaction: ring opening of 1-dodecene oxide. A solution was prepared of 1-dodecene oxide (0.273 g, 1.48 mmol) and TMSCl (0.230 mL, 1.81 mmol) in CD_2Cl_2 (4.52 mL). A portion of this stock solution was transferred to a sealable NMR tube (background reaction), and 1.69 mL of the stock solution (0.49 mmol of epoxide, 0.60 mmol of TMSCl) was transferred to a flask containing catalyst **2C.2** (7.5 mg, 0.025 mmol). The resulting homogeneous orange solution was then transferred to a sealable NMR tube. The two reactions were followed by ^1H NMR.

After six hours, ^1H NMR showed that the catalyzed reaction was complete and that the background reaction had not proceeded (<5% conversion). For the catalyzed reaction, the solvent was removed *in vacuo*, and the TMS ether was treated with HCl (1 M in Et_2O) for 1 h at r.t. The resulting chlorohydrins were purified by flash

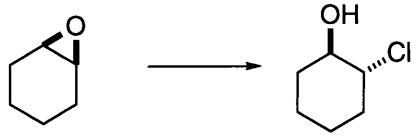
chromatography (20% Et_2O/pentane), yielding 110 mg (101%) of a 9.3 : 1 mixture of secondary : primary alcohols.

Note: A control experiment (no catalyst **2C.2**) was conducted for each substrate illustrated in Table 2C.2.



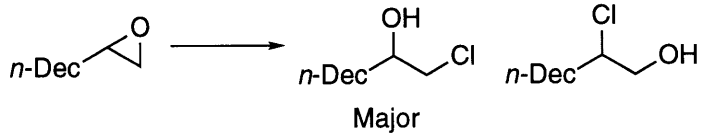
Ring opening of *cis*-stilbene oxide (Table 2C.2, entry 1). Run on 99 mg (0.50 mmol) of substrate; isolated 112 mg (96%) of product. Reaction time: 100 h. **(R*, R*)-2-Chloro-1,2-diphenylethan-1-ol[59][70332-51-3]:** ^1H NMR (300 MHz, $CDCl_3$) δ 3.28 (br s, 1H), 4.98 (d, J = 8.4, 1H), 5.06 (d, J = 8.1, 1H), 7.10-7.40 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 70.5, 78.7, 127.0, 127.1, 128.0, 128.1, 128.3, 128.5, 128.6, 137.8, 138.9; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.52. Treatment of the chlorohydrin with KOH regenerated *cis*-stilbene oxide (95% isomeric purity).

Ring opening of cyclopentene oxide (Table 2C.2, entry 2). Run on 44 mg (0.52 mmol) of substrate; isolated 50 mg (80%) of product. Reaction time: 2 h. ***trans*-2-Chlorocyclopentanol:** ^1H NMR (300 MHz, $CDCl_3$) δ 1.60 (m, 1H), 1.85 (m, 3H), 2.14 (m, 1H), 2.26 (m, 1H), 2.37 (s, 1H), 4.03 (m, 1H), 4.23 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.5, 31.2, 33.2, 65.6, 80.2; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.21. Treatment of the chlorohydrin with KOH regenerated cyclopentene oxide.

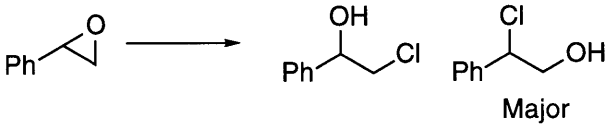


Ring opening of cyclohexene oxide (Table 2C.2, entry 3). Run on 48 mg (0.50 mmol) of substrate; isolated 63 mg (94%) of product. Reaction time: 2 h. ***trans*-2-**

Chlorocyclohexanol: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (m, 3H), 1.65 (m, 3H), 2.09 (m, 1H), 2.19 (m, 1H), 2.77 (br s, 1H), 3.50 (m, 1H), 3.71 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.0, 25.6, 33.2, 35.2, 67.4, 75.3; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.30. Treatment of the chlorohydrin with KOH regenerated cyclohexene oxide.



Ring opening of 1-dodecene oxide (Table 2C.2, entry 4). Run on 91 mg (0.49 mmol) of substrate; isolated 110 mg (101%) of product. Reaction time: 6 h. ^{1}H NMR revealed a 9.3 : 1.0 mixture of secondary : primary alcohols. **1-Chlorododecan-2-ol and 2-Chlorododecan-1-ol.** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J = 7.0, 3H), 1.20-1.70 (m, 18H), 2.48 (br s, 1H), 3.46 (dd, J = 7.0, 11.0, 1H-2° ROH), 3.61 (dd, J = 3.0, 11.0, 1H), 3.78 (br m, 1H), 4.00 (br m, 1H - 1° ROH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 25.6, 26.4, 29.2, 29.4, 29.6, 31.9, 34.3, 50.5, 65.3, 67.0, 71.5; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.24, 0.33.



Ring opening of styrene oxide (Table 2C.2, entry 5). Run on 60 mg (0.50 mmol) of substrate; isolated 69 mg (88%) of product. Reaction time: 0.1 h. ^{1}H NMR revealed a 1.0 : 2.7 mixture of secondary : primary alcohols. The identity of the secondary alcohol was confirmed by comparison with 2-chloro-1-phenylethan-1-ol prepared by reduction of 2-chloroacetophenone with $NaBH_4$. **2-Chloro-1-phenylethanol and 2-Chloro-2-phenylethanol.** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.48 (br s, 1H - 1° ROH), 3.00 (br s, 1H - 2° ROH), 3.70 (m, 2H - 2° ROH), 3.92 (br s, 2H - 1° ROH), 4.90 (br d, 1H - 2° ROH), 4.99 (t, J= 6.5 Hz, 2H - 1° ROH), 7.30-7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ

50.8, 64.8, 67.9, 74.1, 126.1, 127.5, 128.5, 128.7, 128.8, 128.9, 138.0, 140.1; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.31, 0.41.

Verification of relative stereochemistry of ring opening. All of the products obtained from ring opening of cyclic and stereochemically pure epoxides were subjected to ring closing conditions (KOH/ether) for 3 h. After this time the solution was filtered, solvents removed and the resulting product analyzed by ^1H NMR for chlorohydrins/epoxides.

cis-Stilbene oxide: 95% cis epoxide (δ 4.36, s), 5% trans-epoxide (δ 3.89, s).

Cyclohexene oxide: 100% epoxide noted.

Cyclopentene oxide : No epoxide or chlorohydrin seen (epoxide too volatile to allow removal of solvents in vacuo).

Due to the volatility of the cyclohexene oxide, the ring closing of this chlorohydrin was performed with KOH/d_8-THF. After 3 h, the KOH was filtered out of the solution and ^1H NMR analysis showed only the desired epoxide remaining; no chlorohydrin was observed.

Regiochemistry of ring opening with other catalysts, styrene oxide (Eq 2C.3). A stock solution of CD_2Cl_2 (1.1 mL), styrene oxide (85 μL, 0.75 mmol) and TMSCl (115 μL, 0.906 mmol) was prepared. Catalysts (0.110 mmol) were weighed into vials and an aliquot (0.8 mL) of stock solution was added to each. The resulting solutions were transferred to screw-cap NMR tubes and allowed to go to complete conversion. Each was then treated with anhydrous HCl for 3 h. The solutions were concentrated and analyzed by ^1H NMR for the ratio of 1° : 2° alcohol.

2C.2 : 2.7 : 1

n-Bu_4NCl : 2.8 : 1

PPh_3 : 3.2 : 1

Regiochemistry of ring opening with other catalysts, dodecene oxide (Eq 2C.4). A stock solution of CD_2Cl_2 (1.1 mL), dodecene oxide (162 μL, 0.742 mmol) and TMSCl

(115 μL, 0.906 mmol) was prepared. Catalysts (0.110 mmol) were weighed into vials and an aliquot (0.8 mL) of stock solution was added to each. The resulting solutions were transferred to screw-cap NMR tubes and allowed to go to complete conversion. Each was then treated with anhydrous HCl for 3 h. The solutions were concentrated and analyzed by ^{1}H NMR for the ratio of 2° : 1° alcohol.

2C.2 : 9.3 : 1

n-Bu_4NCl : 4.9 : 1

PPh_3 : 3.6 : 1

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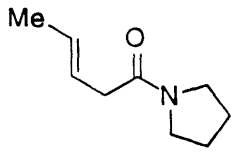
APPENDIX I: NMR DATA FOR SELECTED PRODUCTS

Page



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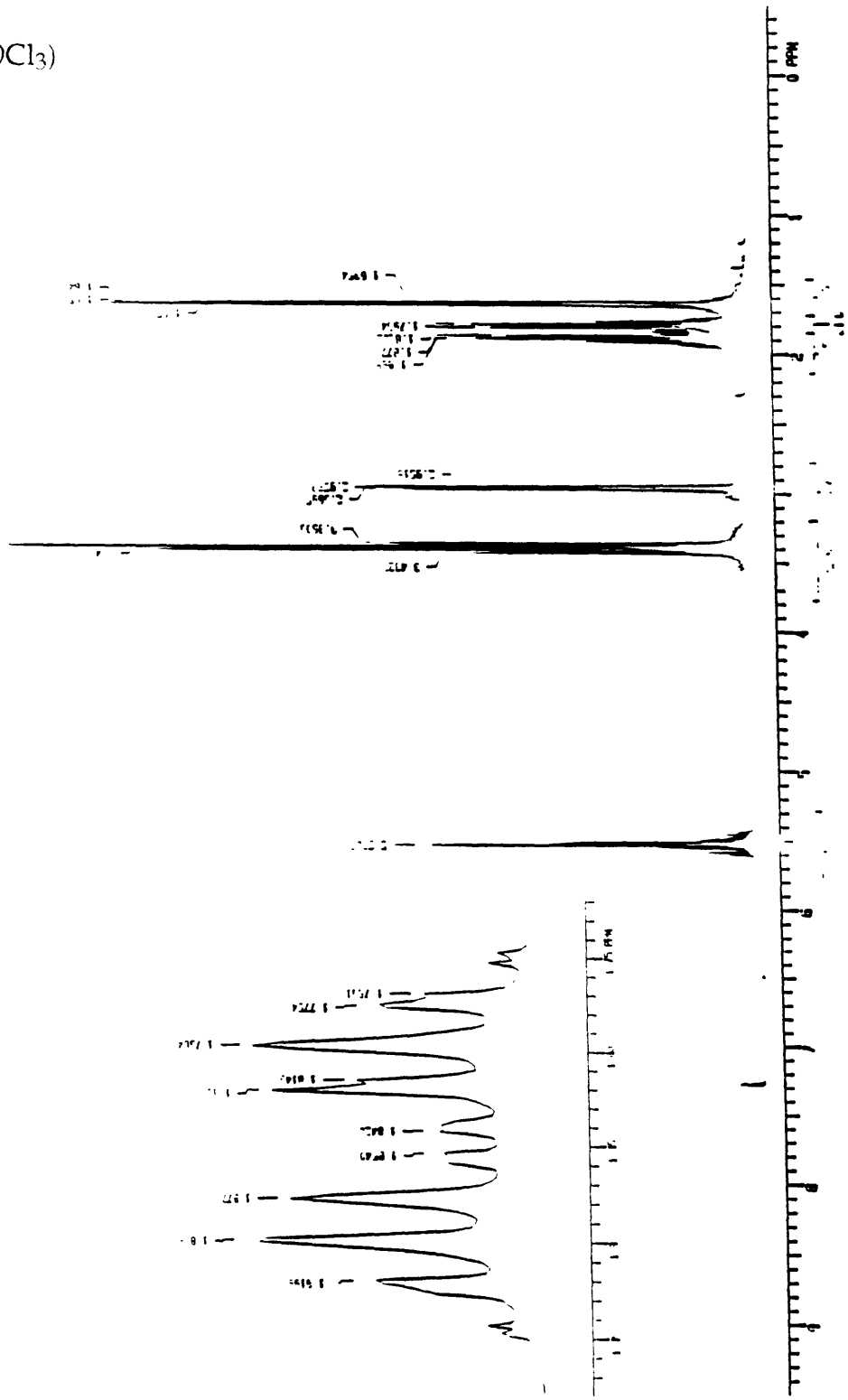

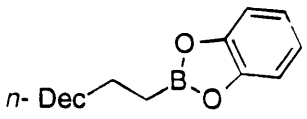

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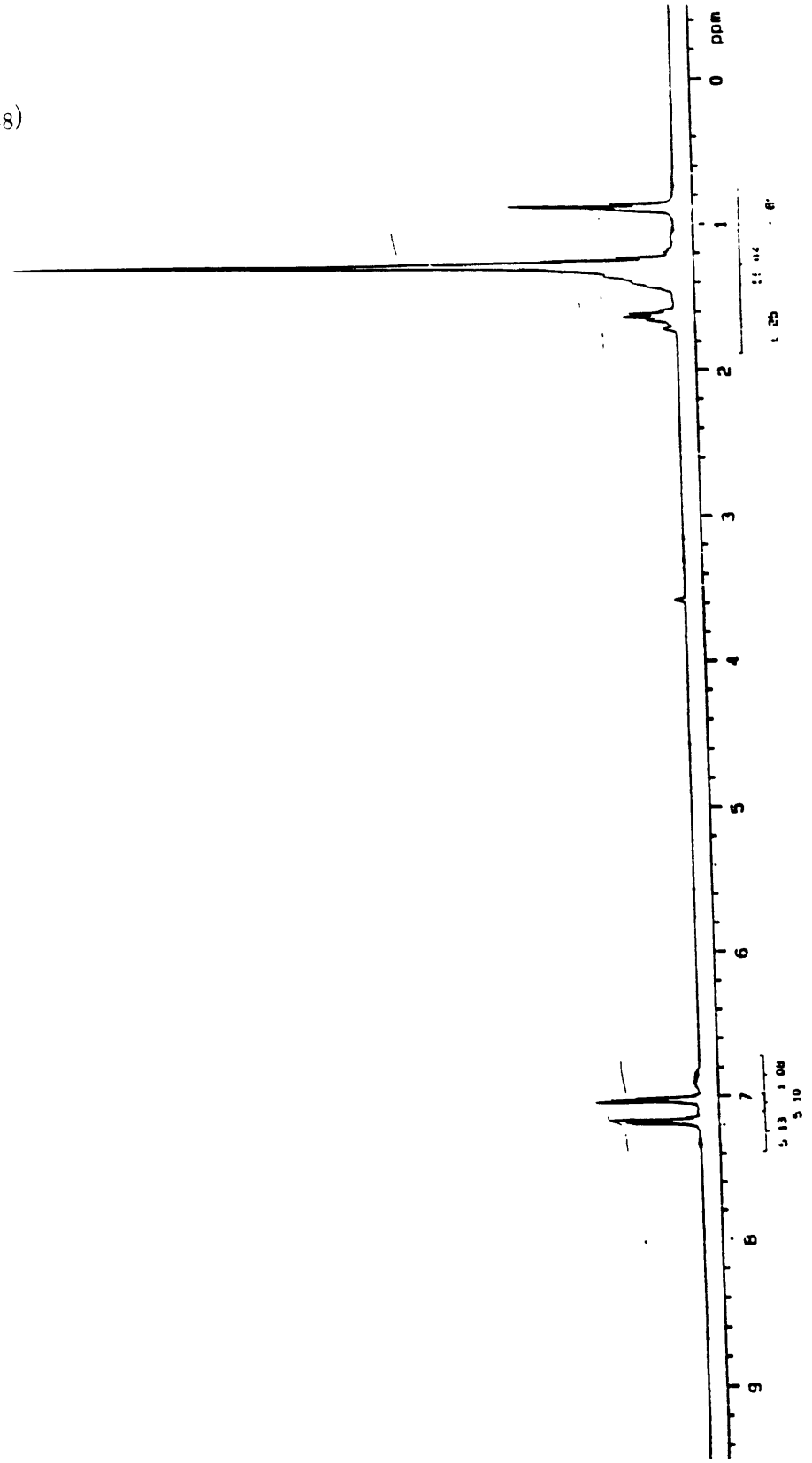

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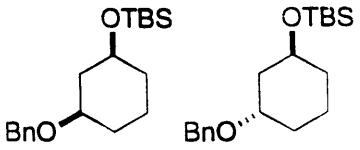

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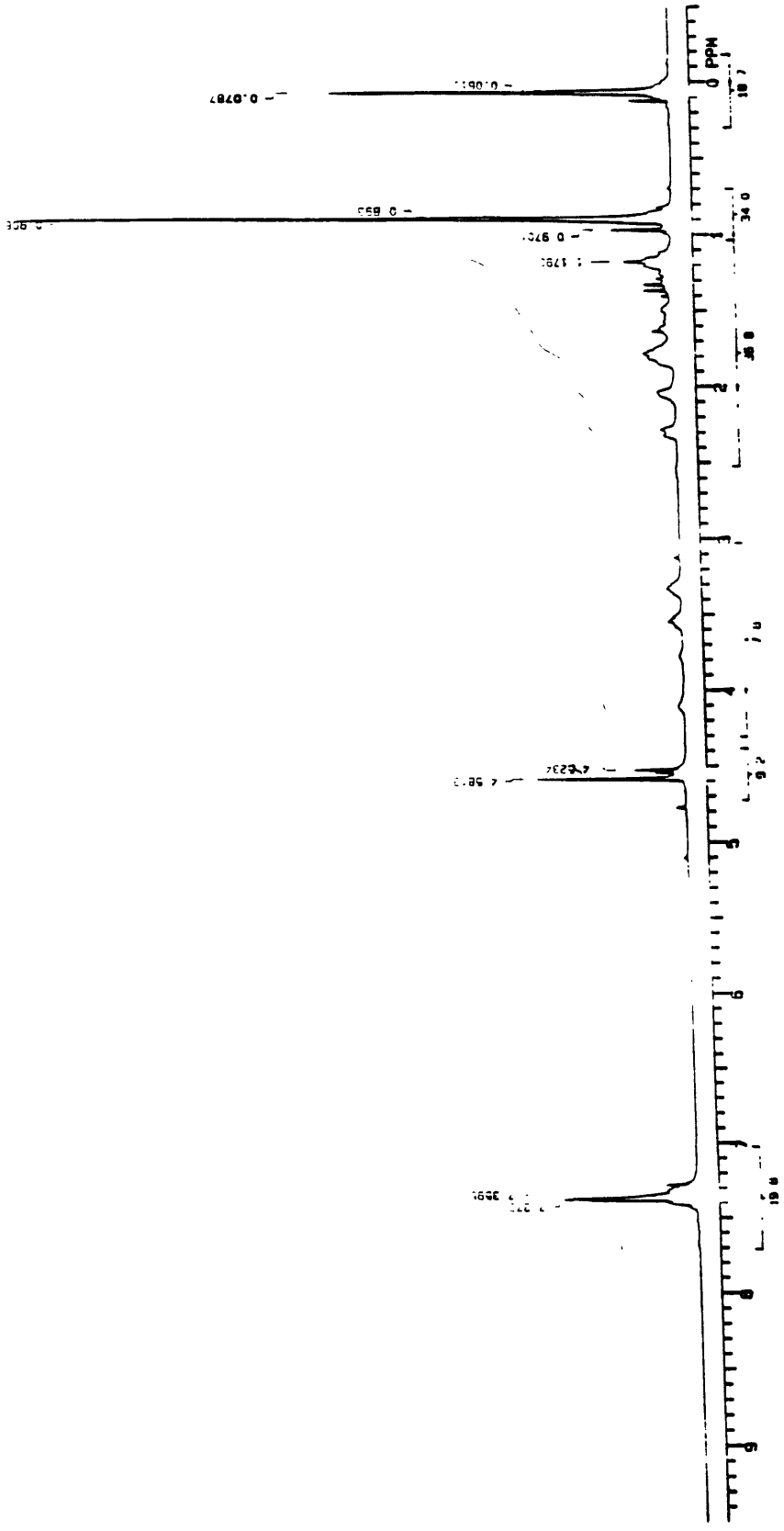

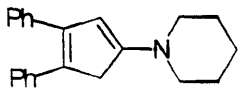

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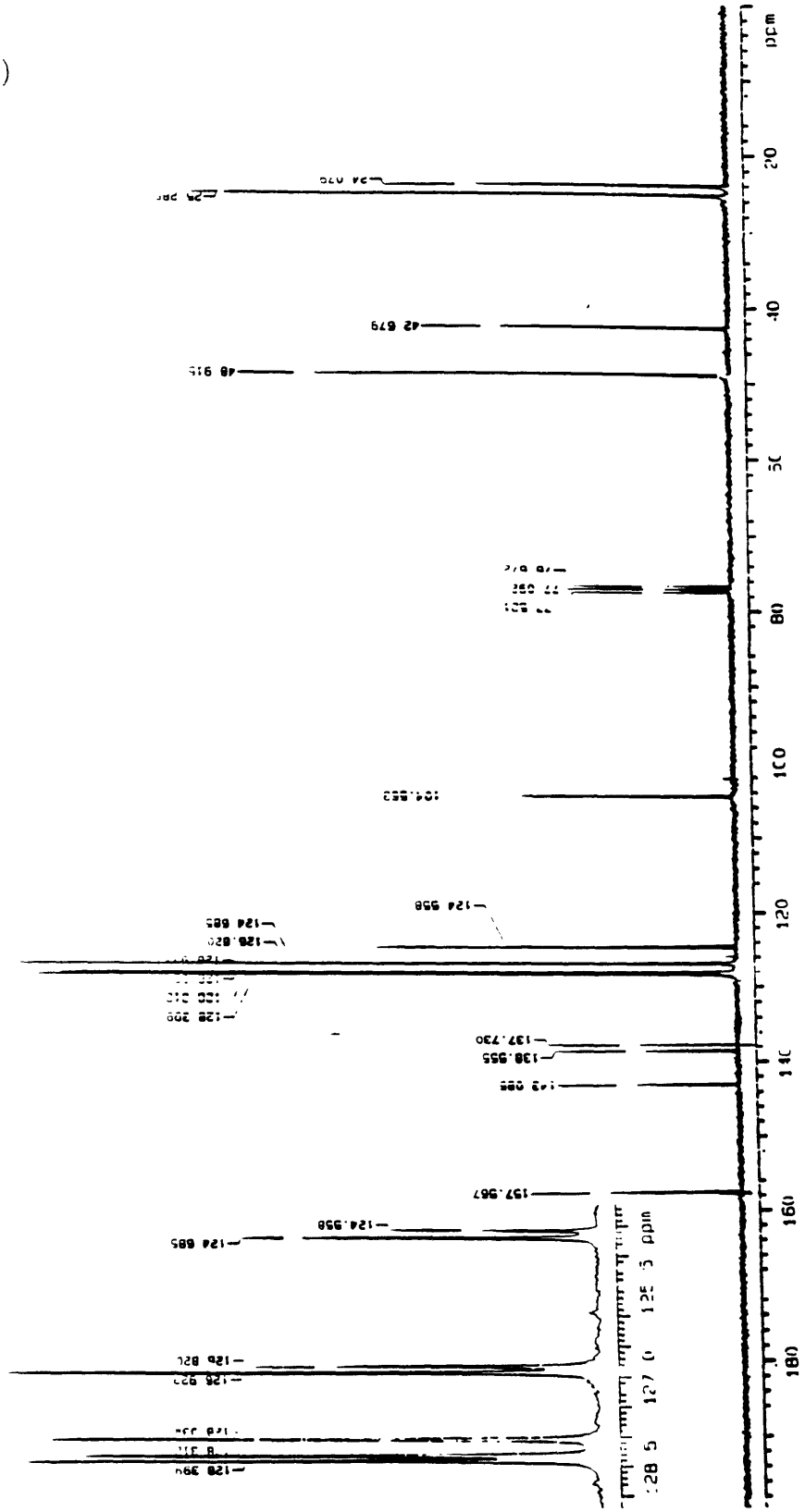

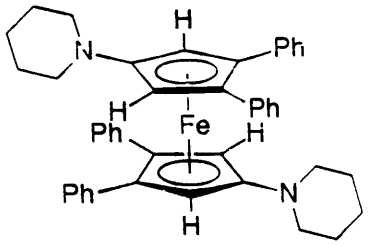

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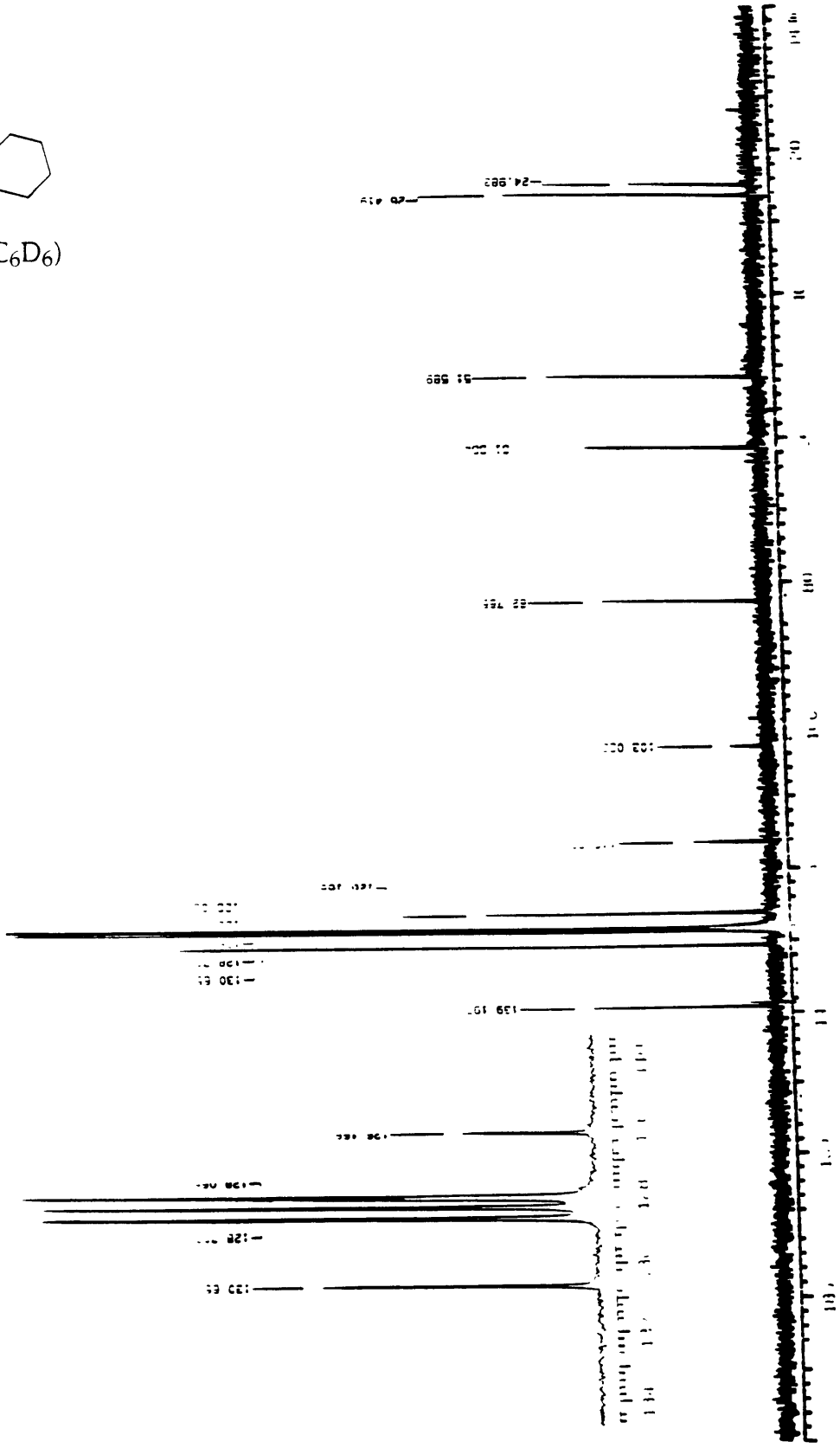

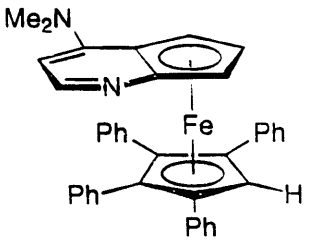

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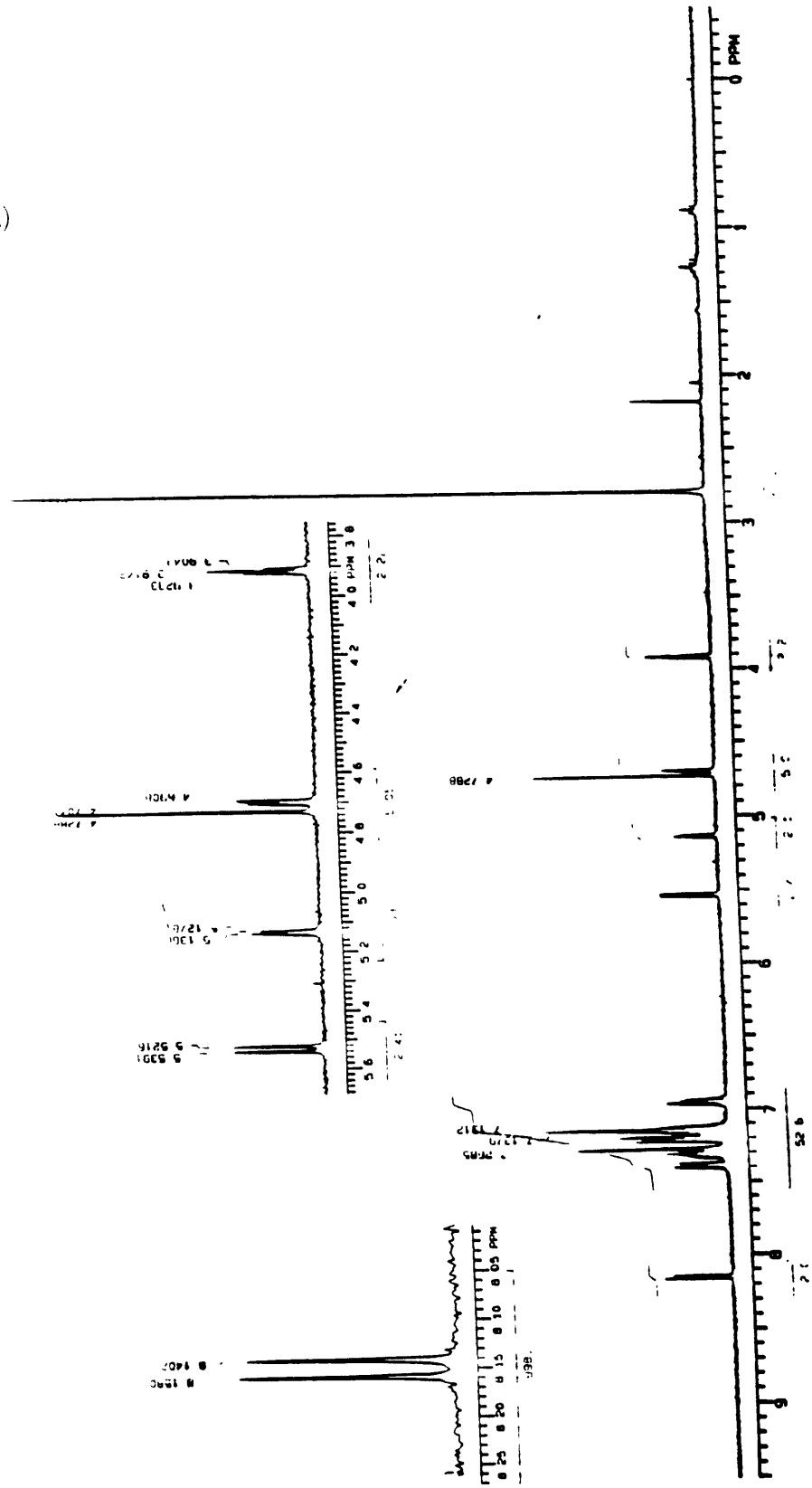

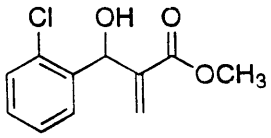

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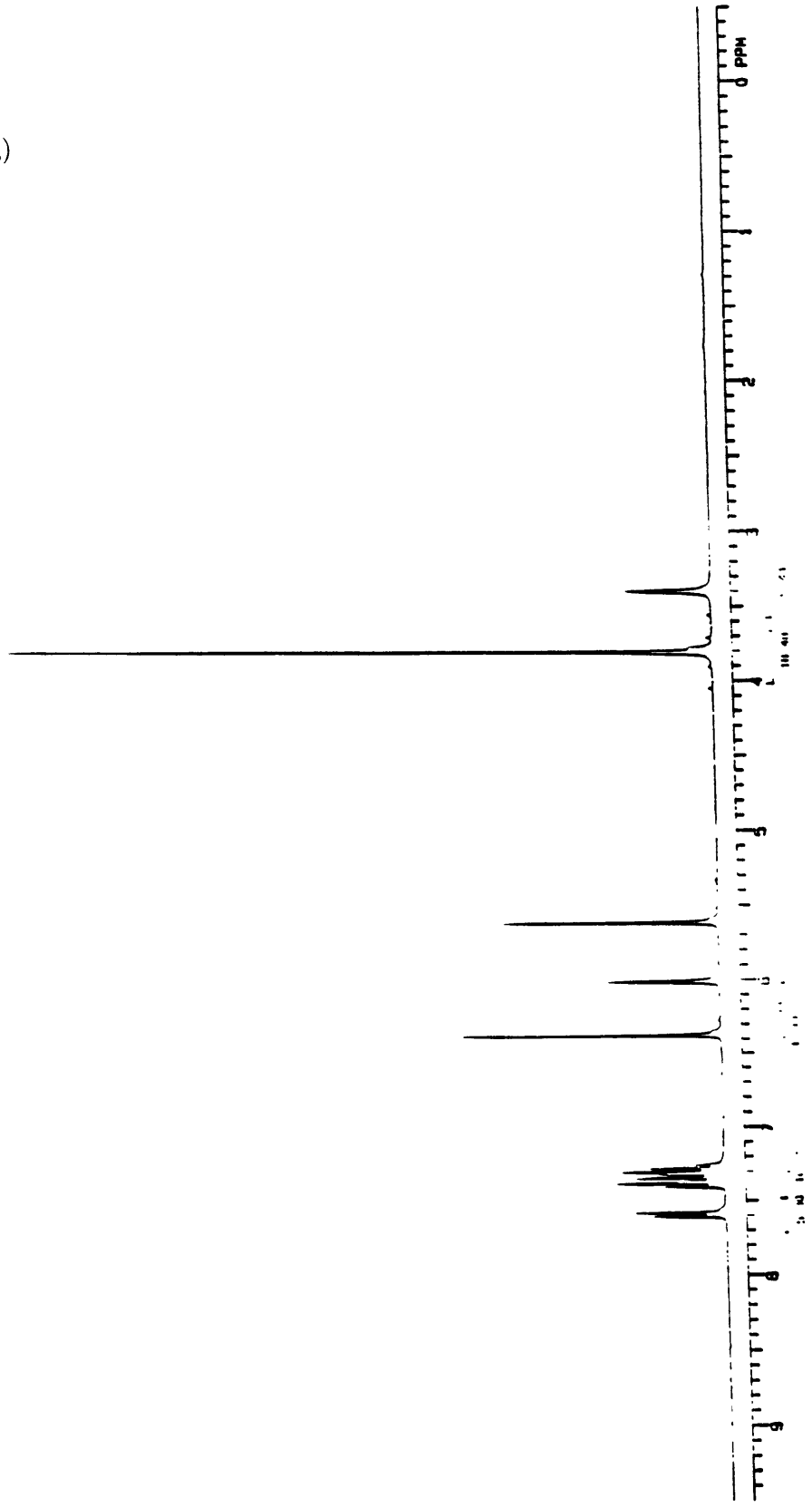

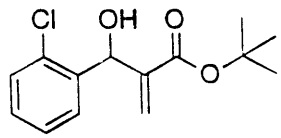

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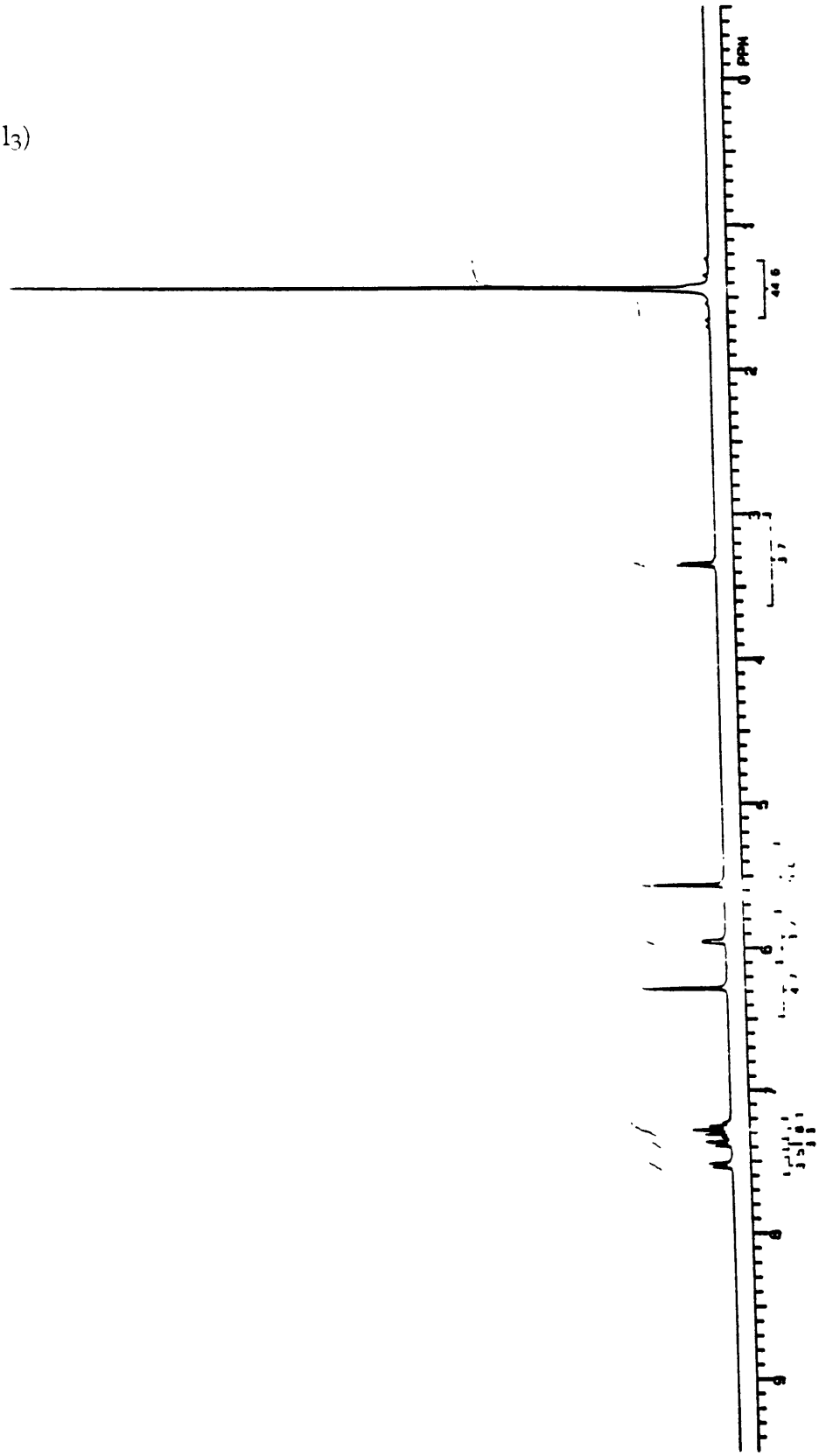

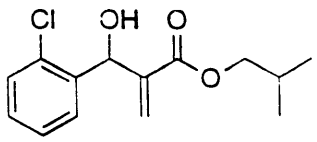

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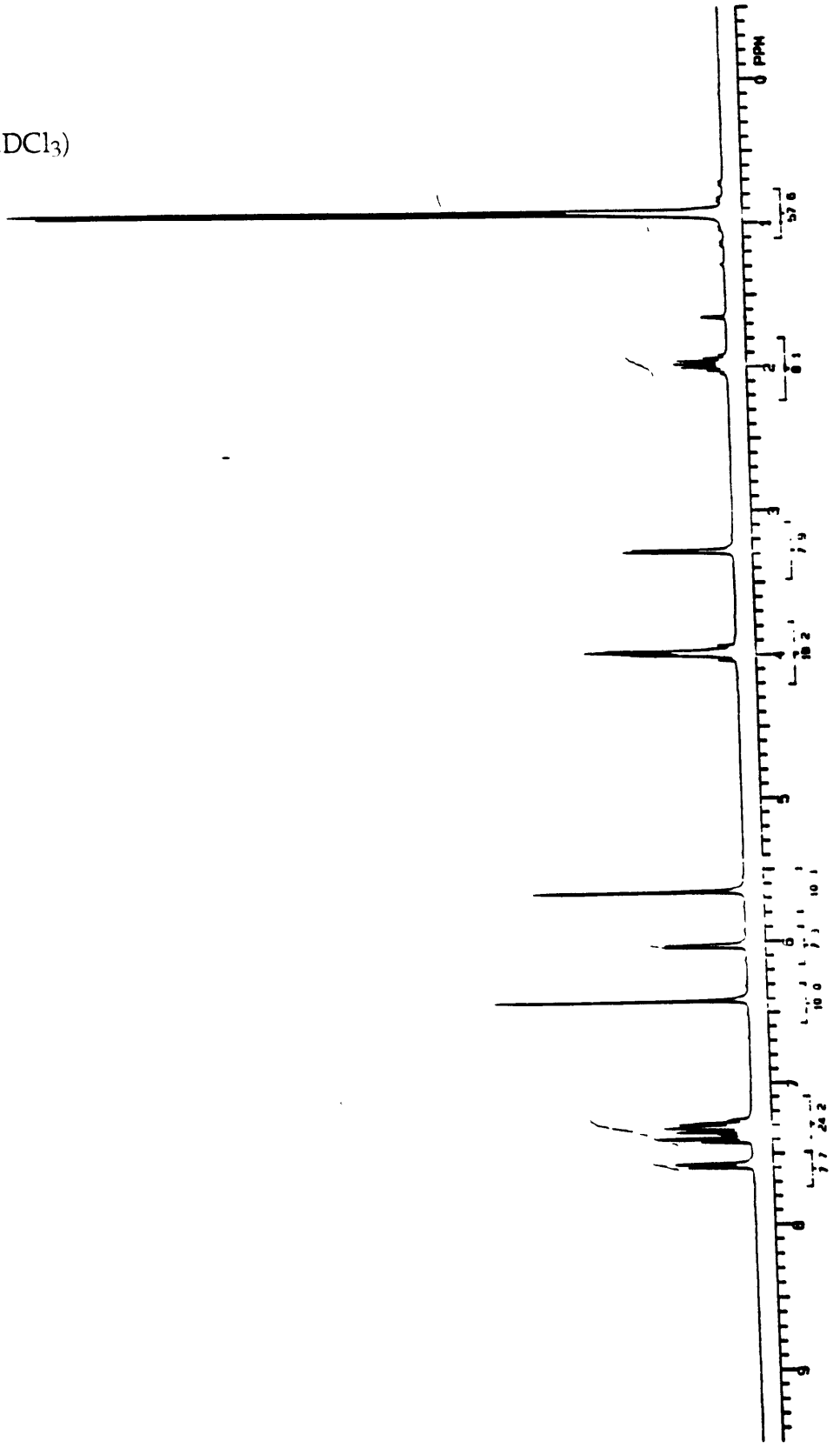

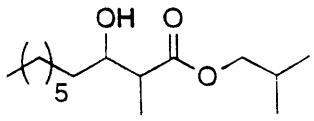

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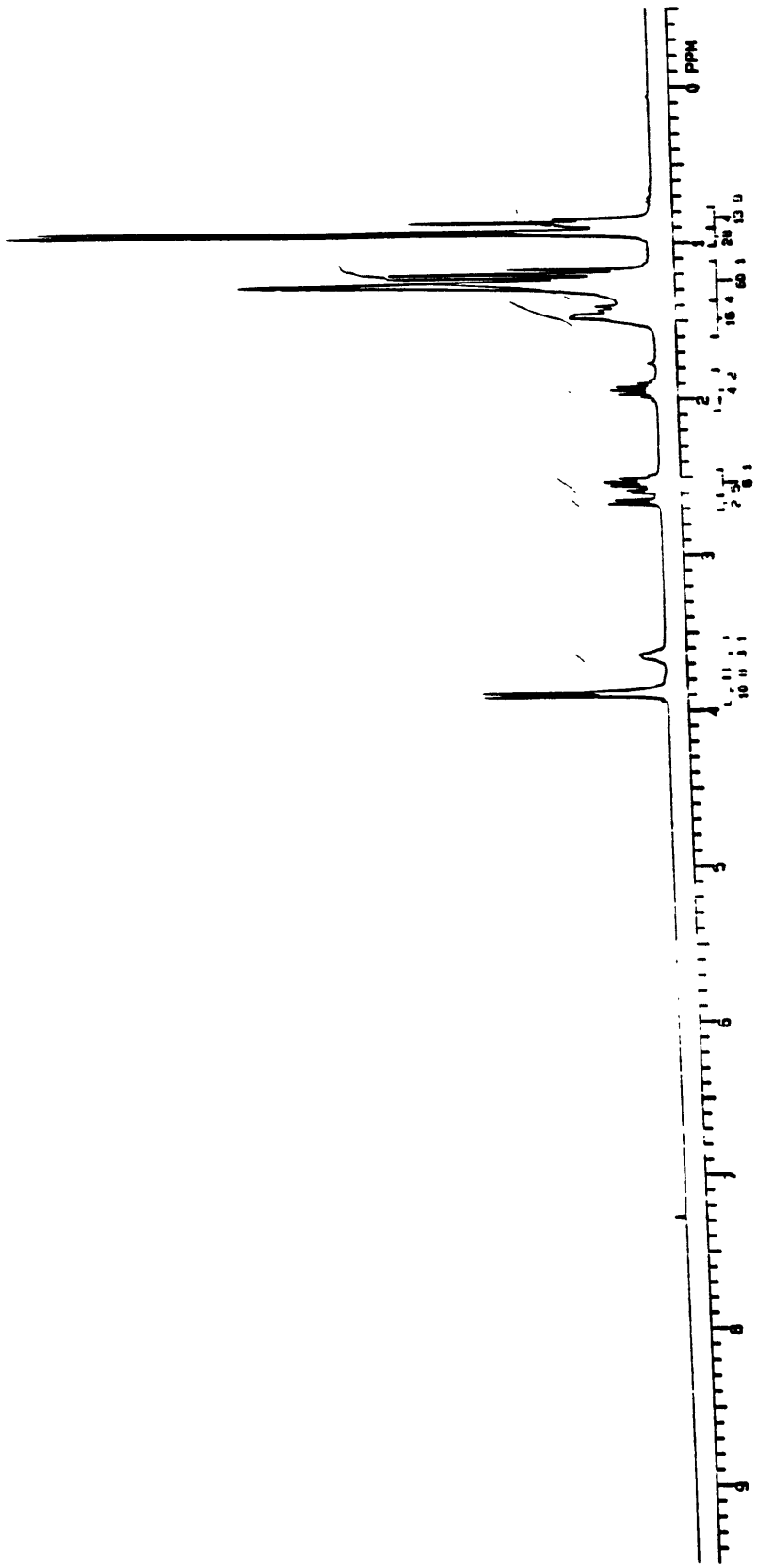

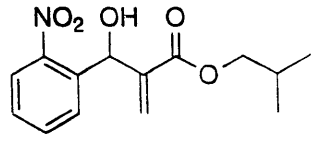

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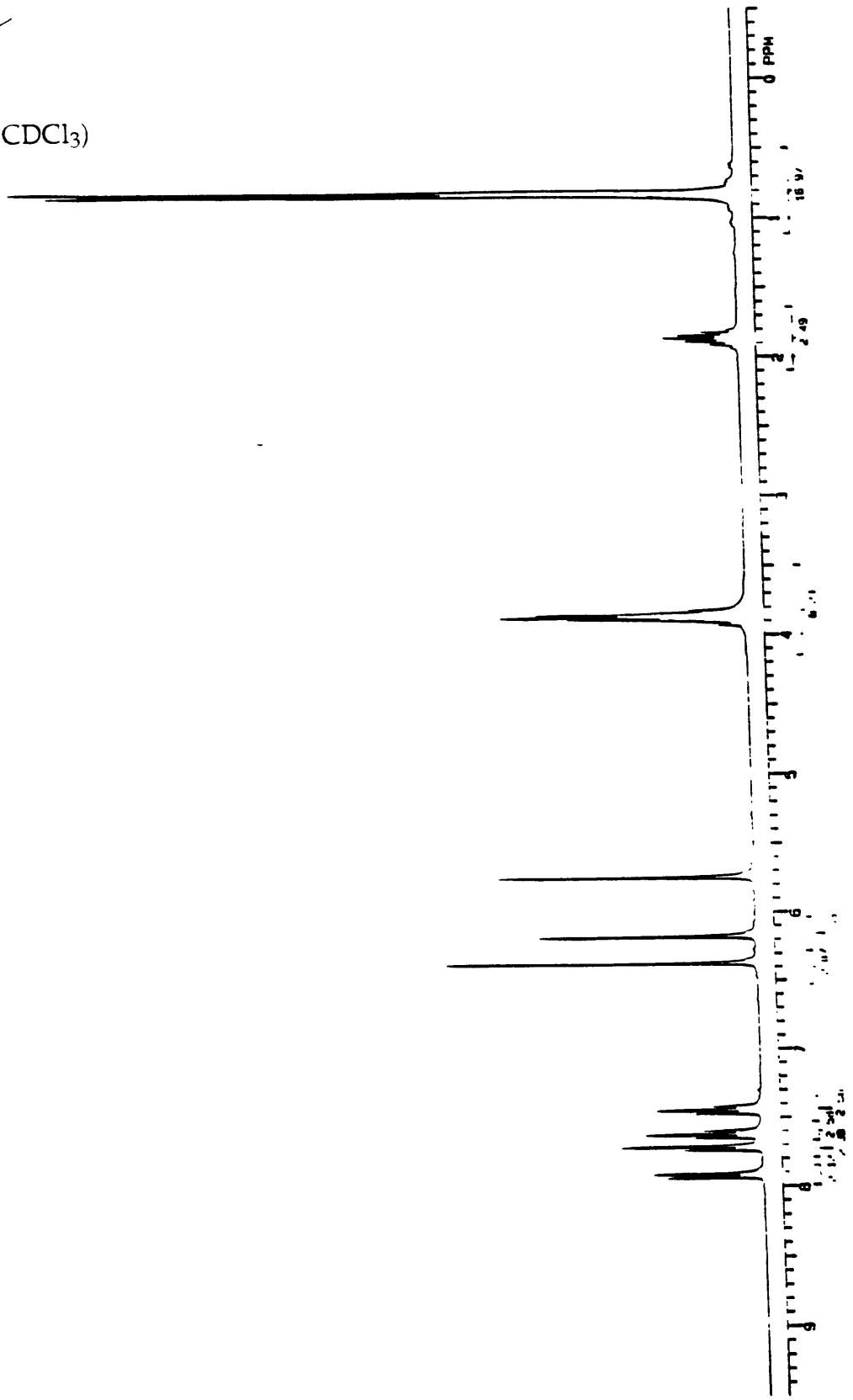

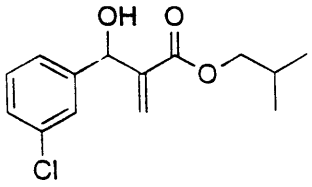

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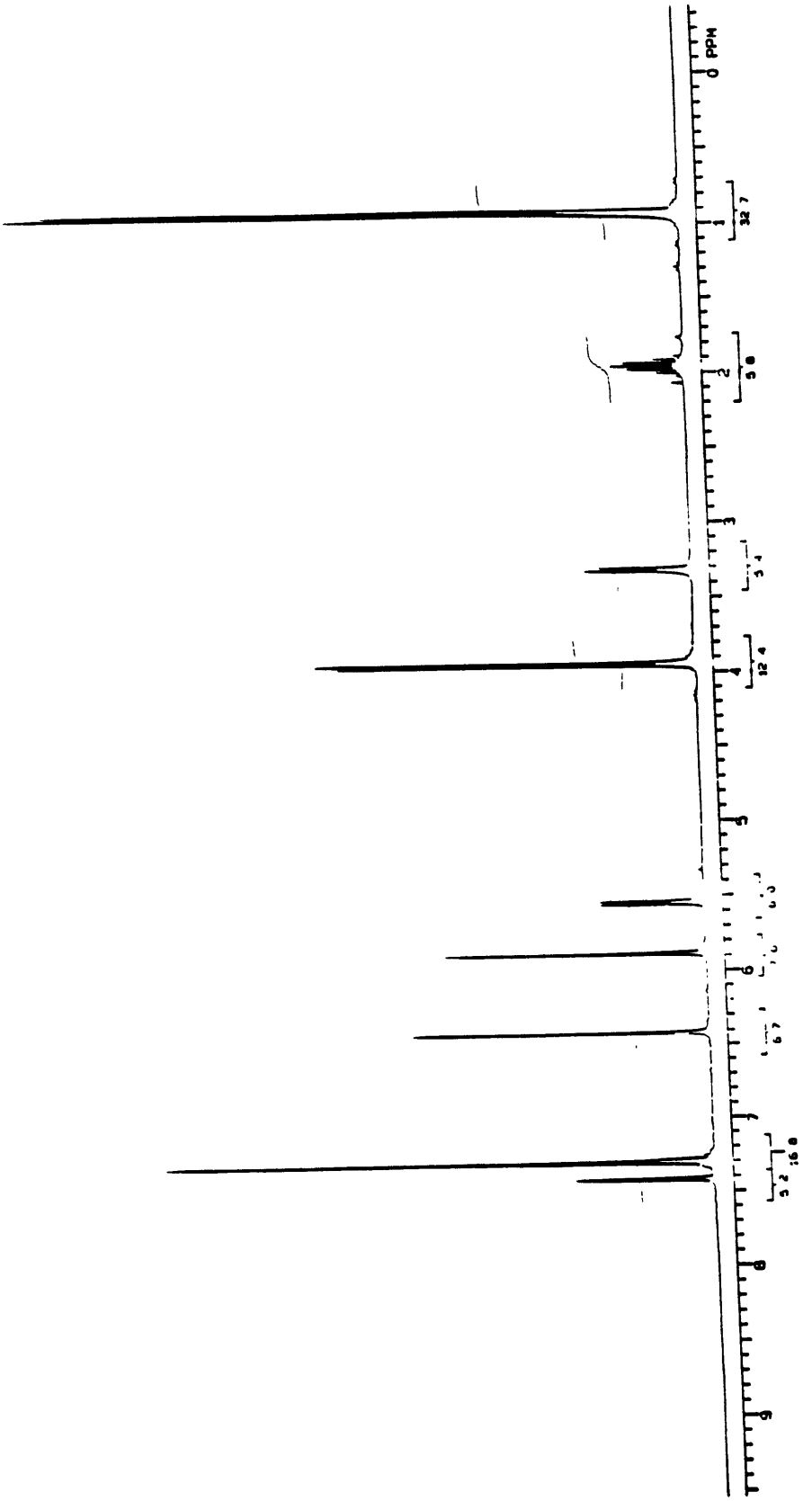

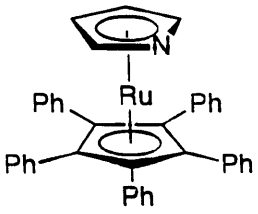

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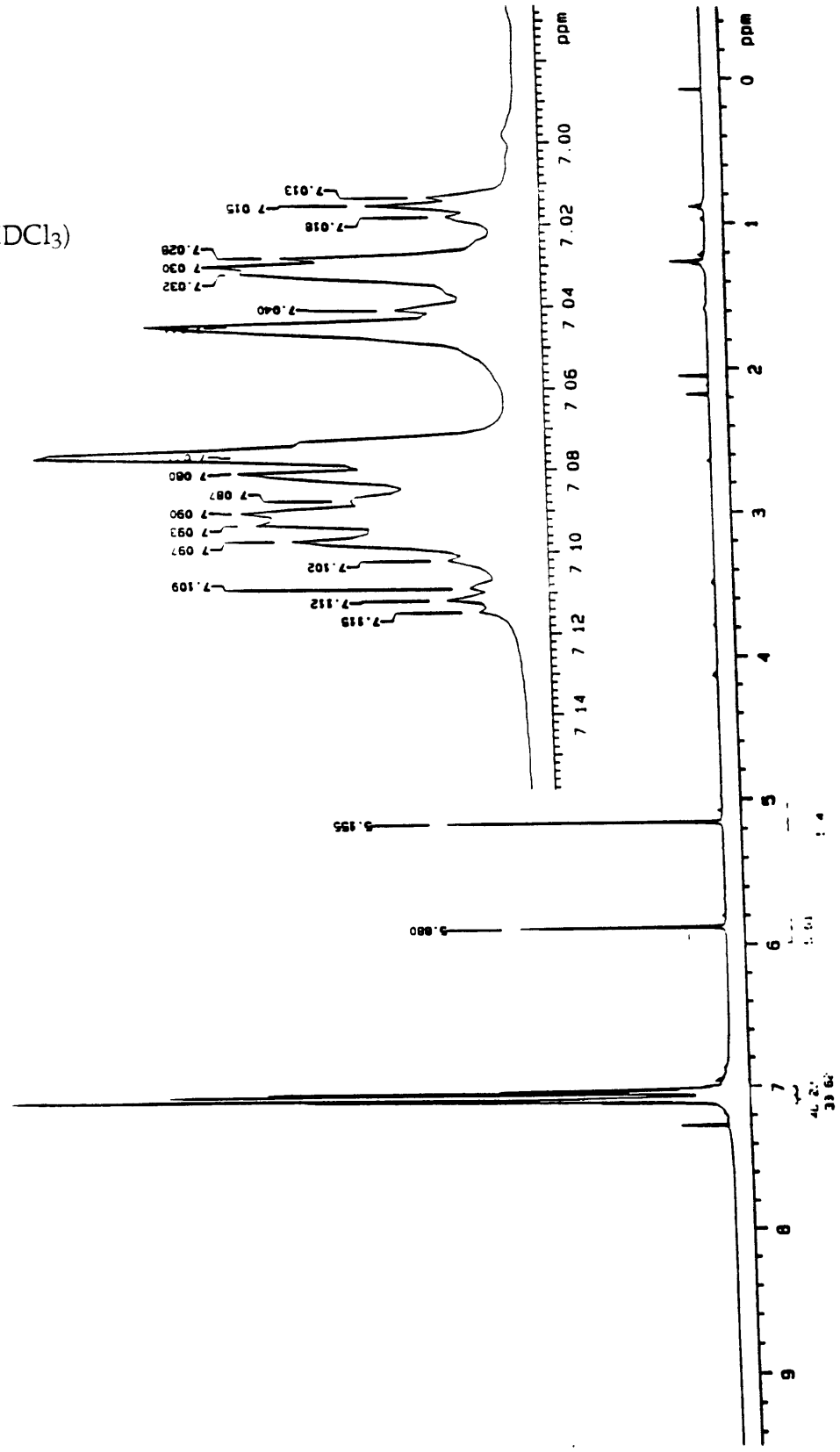
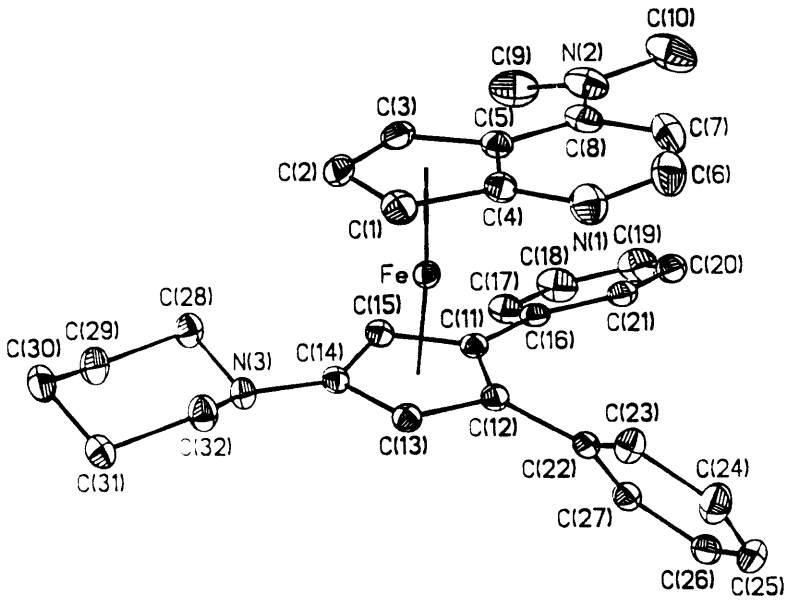


APPENDIX II: X-ray Crystal Structure Data for Catalyst 2A.4



Structure solved by: Diego A. Hoic

Table 1. Crystal data and structure refinement for 1.

A. Crystal Data

Identification code	97157
Empirical formula	$C_{32}H_{33}FeN_3$
Formula weight	515.46
Temperature	172(2) K
Wavelength	0.71073 Å
Crystal morphology	plate
Crystal size	.15 x .45 x .45 mm
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 16.9565(2) Å alpha = 90°
	b = 11.3365(2) Å beta = 94.4790(10)°
	c = 13.2193(2) Å gamma = 90°
Volume, Z	2533.35(7) $Å^3$, 4
Density (calculated)	1.351 Mg/m^3
Absorption coefficient	0.622 mm^{-1}
F(000)	1088

B. Data Collection and Reduction

Diffractometer	Siemens SMART/CCD
Scan Type	ω Scans
Scan angle	0.30°
θ range for data collection	1.20 to 23.25°
Limiting indices	$-18 \le h \le 18$, $-12 \le k \le 12$, $-14 \le l \le 7$

Reflections collected	10068
Independent reflections	3637 (R_{int} = 0.0305)
Absorption correction	Semi-empirical from psi-scans
Max. and min. transmission	0.6341 and 0.5126

C. Solution and Refinement

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3636 / 0 / 326
Goodness-of-fit on F^2	1.130
Final R indices [I>2σ(I)]	R1 = 0.0369, wR2 = 0.0826
R indices (all data)	R1 = 0.0404, wR2 = 0.0853
Extinction coefficient	0.0005(4)
Largest diff. peak and hole	0.338 and -0.261 eÅ^{-3}

Table 2. Atomic coordinates [x 10^4] and equivalent isotropic displacement parameters [$Å^2$ x 10^3] for 1. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Fe	2564(1)	295(1)	6354(1)	22(1)
N(1)	3166(1)	1757(2)	8334(2)	37(1)
N(2)	4661(1)	-1045(2)	7464(2)	45(1)
N(3)	1257(1)	357(2)	4447(2)	26(1)
C(1)	2852(2)	2065(2)	6481(2)	32(1)
C(2)	3137(2)	1577(2)	5593(2)	35(1)
C(3)	3659(2)	635(2)	5873(2)	33(1)
C(4)	3230(2)	1467(2)	7334(2)	27(1)
C(5)	3729(1)	547(2)	6969(2)	28(1)
C(6)	3611(2)	1092(3)	8963(2)	43(1)
C(7)	4105(2)	162(3)	8720(2)	42(1)
C(8)	4182(2)	-164(2)	7703(2)	34(1)
C(9)	4626(2)	-1592(3)	6480(3)	60(1)
C(10)	5164(2)	-1630(3)	8277(3)	65(1)
C(11)	2205(1)	-1425(2)	6527(2)	23(1)
C(12)	1728(1)	-633(2)	7068(2)	24(1)
C(13)	1357(1)	176(2)	6350(2)	24(1)
C(14)	1567(1)	-129(2)	5355(2)	24(1)
C(15)	2120(1)	-1082(2)	5480(2)	25(1)
C(16)	2681(1)	-2434(2)	6932(2)	27(1)
C(17)	2790(2)	-3413(2)	6316(2)	37(1)
C(18)	3221(2)	-4376(3)	6690(3)	49(1)
C(19)	3557(2)	-4385(3)	7672(3)	51(1)
C(20)	3456(2)	-3423(3)	8290(2)	42(1)
C(21)	3023(2)	-2454(2)	7929(2)	32(1)
C(22)	1497(1)	-743(2)	8125(2)	25(1)
C(23)	1504(2)	213(2)	8782(2)	31(1)
C(24)	1205(2)	104(3)	9726(2)	39(1)
C(25)	903(2)	-962(3)	10027(2)	39(1)
C(26)	904(2)	-1922(3)	9386(2)	36(1)
C(27)	1196(1)	-1815(2)	8438(2)	29(1)
C(28)	1707(2)	150(2)	3560(2)	32(1)
C(29)	1208(2)	427(3)	2585(2)	38(1)
C(30)	903(2)	1683(3)	2590(2)	37(1)
C(31)	454(2)	1890(3)	3528(2)	36(1)
C(32)	963(2)	1571(2)	4492(2)	32(1)

Table 3. Bond lengths [Å] and angles [°] for 1.

Fe-C(3)	2.046(3)	Fe-C(15)	2.050(2)
Fe-C(13)	2.051(2)	Fe-C(12)	2.053(2)
Fe-C(2)	2.055(3)	Fe-C(11)	2.061(2)
Fe-C(1)	2.069(3)	Fe-C(5)	2.096(2)
Fe-C(14)	2.117(2)	Fe-C(4)	2.120(2)
N(1)-C(6)	1.316(4)	N(1)-C(4)	1.374(3)
N(2)-C(8)	1.341(4)	N(2)-C(9)	1.439(4)
N(2)-C(10)	1.475(4)	N(3)-C(14)	1.387(3)
N(3)-C(28)	1.467(3)	N(3)-C(32)	1.467(3)
C(1)-C(2)	1.417(4)	C(1)-C(4)	1.424(4)
C(2)-C(3)	1.417(4)	C(3)-C(5)	1.449(4)
C(4)-C(5)	1.450(4)	C(5)-C(8)	1.436(4)
C(6)-C(7)	1.399(4)	C(7)-C(8)	1.411(4)
C(11)-C(15)	1.434(3)	C(11)-C(12)	1.436(3)
C(11)-C(16)	1.476(3)	C(12)-C(13)	1.430(3)
C(12)-C(22)	1.486(3)	C(13)-C(14)	1.432(3)
C(14)-C(15)	1.431(3)	C(16)-C(17)	1.397(4)
C(16)-C(21)	1.398(4)	C(17)-C(18)	1.383(4)
C(18)-C(19)	1.376(5)	C(19)-C(20)	1.381(5)
C(20)-C(21)	1.385(4)	C(22)-C(23)	1.388(4)
C(22)-C(27)	1.393(4)	C(23)-C(24)	1.388(4)
C(24)-C(25)	1.383(4)	C(25)-C(26)	1.379(4)
C(26)-C(27)	1.388(4)	C(28)-C(29)	1.518(4)
C(29)-C(30)	1.515(4)	C(30)-C(31)	1.522(4)
C(31)-C(32)	1.525(4)		

C(3)-Fe-C(15)	105.71(10)	C(3)-Fe-C(13)	160.29(10)
C(15)-Fe-C(13)	68.05(10)	C(3)-Fe-C(12)	156.27(11)
C(15)-Fe-C(12)	68.45(10)	C(13)-Fe-C(12)	40.80(10)
C(3)-Fe-C(2)	40.43(11)	C(15)-Fe-C(2)	115.42(10)
C(13)-Fe-C(2)	123.72(11)	C(12)-Fe-C(2)	163.23(11)
C(3)-Fe-C(11)	119.74(11)	C(15)-Fe-C(11)	40.85(10)
C(13)-Fe-C(11)	68.60(10)	C(12)-Fe-C(11)	40.86(10)
C(2)-Fe-C(11)	151.48(11)	C(3)-Fe-C(1)	68.17(11)
C(15)-Fe-C(1)	149.10(10)	C(13)-Fe-C(1)	107.02(10)
C(12)-Fe-C(1)	128.81(10)	C(2)-Fe-C(1)	40.19(11)
C(11)-Fe-C(1)	168.13(10)	C(3)-Fe-C(5)	40.92(10)
C(15)-Fe-C(5)	128.04(10)	C(13)-Fe-C(5)	156.91(10)
C(12)-Fe-C(5)	123.70(10)	C(2)-Fe-C(5)	68.05(10)
C(11)-Fe-C(5)	111.31(10)	C(1)-Fe-C(5)	68.10(10)
C(3)-Fe-C(14)	123.28(10)	C(15)-Fe-C(14)	40.12(10)
C(13)-Fe-C(14)	40.14(9)	C(12)-Fe-C(14)	67.93(9)
C(2)-Fe-C(14)	103.90(10)	C(11)-Fe-C(14)	68.04(9)
C(1)-Fe-C(14)	116.27(10)	C(5)-Fe-C(14)	162.77(10)
C(3)-Fe-C(4)	67.58(10)	C(15)-Fe-C(4)	167.64(10)
C(13)-Fe-C(4)	121.77(10)	C(12)-Fe-C(4)	113.23(10)
C(2)-Fe-C(4)	66.79(10)	C(11)-Fe-C(4)	132.34(10)
C(1)-Fe-C(4)	39.73(10)	C(5)-Fe-C(4)	40.21(10)
C(14)-Fe-C(4)	152.23(10)	C(6)-N(1)-C(4)	112.7(2)
C(8)-N(2)-C(9)	123.4(3)	C(8)-N(2)-C(10)	119.4(3)
C(9)-N(2)-C(10)	116.4(3)	C(14)-N(3)-C(28)	116.3(2)
C(14)-N(3)-C(32)	116.4(2)	C(28)-N(3)-C(32)	112.4(2)
C(2)-C(1)-C(4)	108.0(2)	C(2)-C(1)-Fe	69.4(2)
C(4)-C(1)-Fe	72.07(14)	C(1)-C(2)-C(3)	108.9(2)
C(1)-C(2)-Fe	70.4(2)	C(3)-C(2)-Fe	69.4(2)

C(2)-C(3)-C(5)	108.3(2)	C(2)-C(3)-Fe	70.1(2)
C(5)-C(3)-Fe	71.39(14)	N(1)-C(4)-C(1)	125.7(2)
N(1)-C(4)-C(5)	125.7(2)	C(1)-C(4)-C(5)	108.5(2)
N(1)-C(4)-Fe	131.2(2)	C(1)-C(4)-Fe	68.20(14)
C(5)-C(4)-Fe	69.03(14)	C(8)-C(5)-C(3)	135.4(2)
C(8)-C(5)-C(4)	118.3(2)	C(3)-C(5)-C(4)	106.2(2)
C(8)-C(5)-Fe	128.6(2)	C(3)-C(5)-Fe	67.68(14)
C(4)-C(5)-Fe	70.76(14)	N(1)-C(6)-C(7)	127.6(3)
C(6)-C(7)-C(8)	121.2(3)	N(2)-C(8)-C(7)	121.5(3)
N(2)-C(8)-C(5)	124.2(3)	C(7)-C(8)-C(5)	114.3(2)
C(15)-C(11)-C(12)	107.0(2)	C(15)-C(11)-C(16)	124.8(2)
C(12)-C(11)-C(16)	128.1(2)	C(15)-C(11)-Fe	69.17(13)
C(12)-C(11)-Fe	69.27(13)	C(16)-C(11)-Fe	128.0(2)
C(13)-C(12)-C(11)	107.9(2)	C(13)-C(12)-C(22)	122.8(2)
C(11)-C(12)-C(22)	128.1(2)	C(13)-C(12)-Fe	69.54(13)
C(11)-C(12)-Fe	69.87(13)	C(22)-C(12)-Fe	135.9(2)
C(12)-C(13)-C(14)	109.0(2)	C(12)-C(13)-Fe	69.66(14)
C(14)-C(13)-Fe	72.43(14)	N(3)-C(14)-C(15)	126.9(2)
N(3)-C(14)-C(13)	126.5(2)	C(15)-C(14)-C(13)	106.5(2)
N(3)-C(14)-Fe	132.8(2)	C(15)-C(14)-Fe	67.39(13)
C(13)-C(14)-Fe	67.43(13)	C(14)-C(15)-C(11)	109.4(2)
C(14)-C(15)-Fe	72.49(14)	C(11)-C(15)-Fe	69.98(14)
C(17)-C(16)-C(21)	118.2(2)	C(17)-C(16)-C(11)	119.8(2)
C(21)-C(16)-C(11)	121.9(2)	C(18)-C(17)-C(16)	120.6(3)
C(19)-C(18)-C(17)	120.7(3)	C(18)-C(19)-C(20)	119.4(3)
C(19)-C(20)-C(21)	120.6(3)	C(20)-C(21)-C(16)	120.5(3)
C(23)-C(22)-C(27)	118.7(2)	C(23)-C(22)-C(12)	122.2(2)
C(27)-C(22)-C(12)	118.8(2)	C(22)-C(23)-C(24)	120.4(3)
C(25)-C(24)-C(23)	120.4(3)	C(26)-C(25)-C(24)	119.6(3)
C(25)-C(26)-C(27)	120.2(3)	C(26)-C(27)-C(22)	120.6(3)
N(3)-C(28)-C(29)	110.8(2)	C(30)-C(29)-C(28)	110.9(2)
C(29)-C(30)-C(31)	110.0(2)	C(30)-C(31)-C(32)	111.0(2)
N(3)-C(32)-C(31)	111.1(2)		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for 1.

The anisotropic displacement factor exponent takes the form:

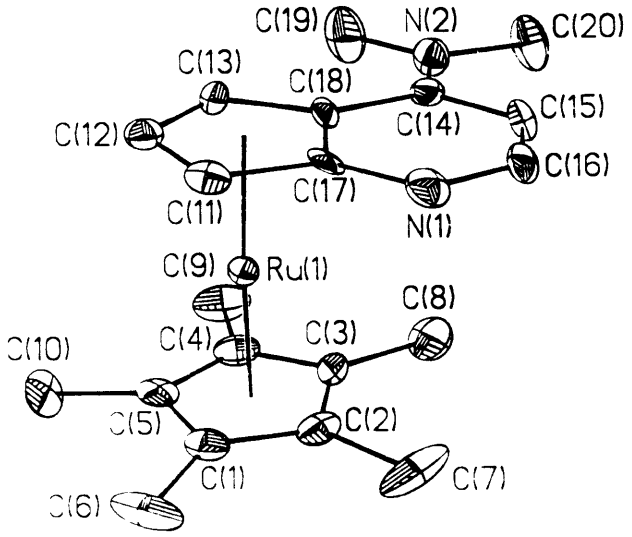
$-2\pi^2 [(ha^*)^2 U_{11} + \ldots + 2hka^*b^*U_{12}]$

	U11	U22	U33	U23	U13	U12
Fe	23(1)	23(1)	21(1)	1(1)	1(1)	-4(1)
N(1)	42(1)	35(1)	34(1)	-5(1)	0(1)	-1(1)
N(2)	30(1)	39(1)	65(2)	-5(1)	0(1)	2(1)
N(3)	30(1)	27(1)	21(1)	0(1)	0(1)	3(1)
C(1)	33(2)	23(1)	38(2)	2(1)	-3(1)	-8(1)
C(2)	37(2)	37(2)	31(2)	8(1)	-1(1)	-16(1)
C(3)	31(1)	40(2)	29(1)	-4(1)	8(1)	-12(1)
C(4)	28(1)	25(1)	28(1)	-2(1)	-1(1)	-7(1)
C(5)	24(1)	29(1)	30(1)	-2(1)	1(1)	-7(1)
C(6)	34(2)	44(2)	31(2)	-5(1)	-1(1)	-2(2)
C(7)	42(2)	43(2)	39(2)	2(1)	-12(1)	0(1)
C(8)	24(1)	31(2)	46(2)	0(1)	-3(1)	-5(1)
C(9)	43(2)	54(2)	83(3)	-13(2)	17(2)	7(2)
C(10)	37(2)	51(2)	105(3)	8(2)	-15(2)	12(2)
C(11)	22(1)	22(1)	27(1)	1(1)	1(1)	-3(1)
C(12)	23(1)	24(1)	26(1)	2(1)	0(1)	-4(1)
C(13)	24(1)	22(1)	26(1)	0(1)	2(1)	-2(1)
C(14)	24(1)	23(1)	24(1)	-2(1)	-1(1)	-4(1)
C(15)	25(1)	23(1)	26(1)	-4(1)	1(1)	-2(1)
C(16)	29(1)	25(1)	37(2)	5(1)	4(1)	-3(1)
C(17)	41(2)	2(2)	49(2)	0(1)	2(1)	1(1)
C(18)	42(2)	3(2)	71(2)	0(2)	4(2)	11(1)
C(19)	3(2)	41(2)	74(2)	20(2)	8(2)	16(2)
C(20)	37(2)	53(2)	46(2)	23(2)	1(1)	3(1)
C(21)	24(1)	36(2)	36(2)	8(1)	4(1)	-4(1)
C(22)	30(1)	30(1)	25(1)	7(1)	-1(1)	3(1)
C(23)	36(2)	31(2)	27(1)	4(1)	5(1)	1(1)
C(24)	46(2)	44(2)	28(2)	0(1)	7(1)	5(1)
C(25)	34(2)	56(2)	28(2)	12(1)	7(1)	2(1)
C(26)	26(1)	45(2)	37(2)	19(1)	-1(1)	-2(1)
C(27)	25(1)	32(2)	31(1)	6(1)	-1(1)	0(1)
C(28)	38(2)	35(2)	23(1)	-4(1)	2(1)	5(1)
C(29)	47(2)	45(2)	23(1)	-2(1)	-2(1)	1(1)
C(30)	38(2)	45(2)	27(1)	7(1)	-4(1)	5(1)
C(31)	30(1)	42(2)	34(2)	8(1)	-1(1)	8(1)
C(32)	36(2)	33(2)	27(1)	1(1)	2(1)	10(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for 1.

	x	y	z	U(eq)
H(1B)	2469(2)	2733(2)	6506(2)	38
H(2A)	2389(2)	1846(2)	4883(2)	42
H(3A)	1945(2)	136(2)	5396(2)	39
H(6A)	1596(2)	1264(3)	9665(2)	52
H(7A)	1394(2)	-257(3)	9250(2)	51
H(9A)	5028(2)	-2212(3)	6477(3)	89
H(9B)	4723(2)	-998(3)	5966(3)	89
H(9C)	4101(2)	-1940(3)	6327(3)	89
H(10A)	5477(2)	-2250(3)	7982(3)	98
H(10B)	4829(2)	-1981(3)	8768(3)	98
H(10C)	5519(2)	-1049(3)	8620(3)	98
H(13A)	994(1)	834(2)	6514(2)	29
H(15A)	2391(1)	-1465(2)	4921(2)	30
H(17A)	2565(2)	-3418(2)	5635(2)	44
H(18A)	3286(2)	-5038(3)	6264(3)	59
H(19A)	3855(2)	-5047(3)	7922(3)	61
H(20A)	3686(2)	-3427(3)	8969(2)	51
H(21A)	2958(2)	-1798(2)	8362(2)	38
H(23A)	1715(2)	947(2)	8585(2)	38
H(24A)	1207(2)	766(3)	10167(2)	47
H(25A)	995(2)	-1033(3)	10671(2)	47
H(26A)	706(2)	-2659(3)	9595(2)	43
H(27A)	1189(1)	-2478(2)	7998(2)	35
H(28A)	1879(2)	-684(2)	3552(2)	39
H(28B)	2186(2)	654(2)	3606(2)	39
H(29A)	1530(2)	315(3)	1999(2)	46
H(29B)	755(2)	-125(3)	2508(2)	46
H(30A)	549(2)	1827(3)	1972(2)	45
H(30B)	1353(2)	2240(3)	2590(2)	45
H(31A)	-32(2)	1405(3)	3482(2)	43
H(31B)	297(2)	2730(3)	3556(2)	43
H(32A)	1416(2)	2121(2)	4580(2)	38
H(32B)	646(2)	1657(2)	5085(2)	38

APPENDIX III: X-ray Crystal Structure Data for Catalyst (+)-2B.2



Structure solved by: Michael M. Lo

Table 1. Crystal data and structure refinement for 98008.

A. Crystal Data

Identification code	98008
Empirical formula	$C_{20}H_{26}N_2Ru$
Formula weight	395.50
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal morphology	block
Crystal size	.12 x .12 x .12 mm
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 8.3276(2) Å alpha = 90° b = 25.3953(4) Å beta = 91.6460(10)° c = 8.54210(10) Å gamma = 90°
Volume, Z	1805.75(6) $Å^3$, 4
Density (calculated)	1.455 Mg/m^3
Absorption coefficient	0.870 mm^{-1}
F(000)	816

B. Data Collection and Reduction

Diffractometer	Siemens SMART/CCD
Scan Type	ω Scans
Scan angle	0.30°
θ range for data collection	1.60 to 23.28°
Limiting indices	$-9 \le h \le 6$, $-28 \le k \le 28$, $-9 \le l \le 9$

Reflections collected	7470
Independent reflections	4864 (R_{int} = 0.0388)
Absorption correction	Semi-empirical from psi-scans
Max. and min. transmission	0.9475 and 0.6868

C. Solution and Refinement

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4864 / 1 / 416
Goodness-of-fit on F^2	1.168
Final R indices [$I>2\sigma(I)$]	R1 = 0.0455, wR2 = 0.1080
R indices (all data)	R1 = 0.0500, wR2 = 0.1156
Absolute structure parameter	-0.13(8)
Extinction coefficient	0.0000(3)
Largest diff. peak and hole	1.197 and -0.677 $eÅ^{-3}$

Table 2. Atomic coordinates [x 10^4] and equivalent isotropic displacement parameters [$Å^2$ x 10^3] for 98008. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Ru(1)	9092(1)	3613(1)	7163(1)	23(1)
Ru(2)	4139(1)	519(1)	7926(1)	22(1)
N(1)	8859(11)	2468(4)	5470(11)	35(2)
N(2)	9078(10)	2473(4)	10493(11)	35(2)
N(3)	3913(11)	1664(4)	9563(11)	32(2)
N(4)	3977(10)	1647(4)	4549(10)	32(2)
C(1)	10548(13)	4163(5)	5860(14)	36(3)
C(2)	11468(12)	3712(4)	6248(13)	36(3)
C(3)	11570(11)	3672(6)	7948(13)	34(3)
C(4)	10712(13)	4110(5)	8574(14)	38(3)
C(5)	10054(13)	4412(4)	7291(14)	36(3)
C(6)	10170(17)	4351(6)	4229(16)	68(4)
C(7)	12241(14)	3322(6)	5141(16)	71(5)
C(8)	12451(13)	3259(6)	8861(17)	59(4)
C(9)	10588(17)	4240(6)	10274(14)	58(4)
C(10)	9126(15)	4918(5)	7407(19)	62(5)
C(11)	7114(11)	3272(4)	5719(11)	27(2)
C(12)	6473(11)	3538(5)	6986(11)	30(3)
C(13)	7025(11)	3314(4)	8416(13)	27(2)
C(14)	8956(11)	2478(4)	8894(12)	26(2)
C(15)	9755(14)	2123(4)	7966(13)	31(2)
C(16)	9641(12)	2130(4)	6335(12)	29(2)
C(17)	8076(11)	2848(3)	6321(12)	25(2)
C(18)	8043(11)	2870(4)	7998(12)	23(2)
C(19)	8313(18)	2852(5)	11510(15)	62(4)
C(20)	10062(16)	2069(5)	11302(14)	54(3)
C(21)	5706(16)	29(5)	9375(14)	44(3)
C(22)	6645(11)	468(5)	8767(12)	36(3)
C(23)	6565(12)	418(5)	7092(13)	34(3)
C(24)	5636(14)	-34(4)	6696(13)	34(3)
C(25)	5114(11)	-262(4)	8108(12)	28(2)
C(26)	5564(18)	-73(7)	11088(15)	77(5)
C(27)	7458(16)	889(6)	9663(18)	70(4)
C(28)	7371(15)	789(4)	5966(16)	54(4)
C(29)	5322(17)	-249(6)	5067(15)	61(4)
C(30)	4206(18)	-783(6)	8247(21)	73(5)
C(31)	2193(11)	862(4)	9281(12)	28(2)
C(32)	1520(11)	583(5)	8032(12)	30(2)
C(33)	2021(11)	806(4)	6600(12)	27(2)
C(34)	3931(11)	1640(4)	6135(12)	25(2)
C(35)	4712(13)	2023(4)	7065(14)	33(3)
C(36)	4650(12)	2016(4)	8672(13)	31(2)
C(37)	3108(10)	1293(4)	8700(11)	21(2)
C(38)	3045(11)	1252(4)	7003(12)	24(2)
C(39)	3284(16)	1244(5)	3539(12)	50(3)
C(40)	4879(16)	2067(5)	3768(14)	55(3)

Table 3. Bond lengths [Å] and angles [°] for 98008.

Ru(1)-C(3)	2.157(10)	Ru(1)-C(2)	2.162(10)
Ru(1)-C(1)	2.176(11)	Ru(1)-C(4)	2.185(11)
Ru(1)-C(5)	2.185(10)	Ru(1)-C(13)	2.188(10)
Ru(1)-C(12)	2.190(9)	Ru(1)-C(18)	2.205(10)
Ru(1)-C(11)	2.205(9)	Ru(1)-C(17)	2.228(9)
Ru(2)-C(25)	2.147(9)	Ru(2)-C(21)	2.166(11)
Ru(2)-C(24)	2.169(11)	Ru(2)-C(23)	2.176(10)
Ru(2)-C(32)	2.192(9)	Ru(2)-C(22)	2.191(9)
Ru(2)-C(33)	2.193(9)	Ru(2)-C(31)	2.199(9)
Ru(2)-C(38)	2.207(10)	Ru(2)-C(37)	2.251(9)
N(1)-C(16)	1.296(14)	N(1)-C(17)	1.382(14)
N(2)-C(14)	1.367(12)	N(2)-C(19)	1.46(2)
N(2)-C(20)	1.471(13)	N(3)-C(36)	1.334(14)
N(3)-C(37)	1.362(13)	N(4)-C(34)	1.356(12)
N(4)-C(39)	1.447(14)	N(4)-C(40)	1.475(14)
C(1)-C(2)	1.41(2)	C(1)-C(5)	1.45(2)
C(1)-C(6)	1.50(2)	C(2)-C(3)	1.46(2)
C(2)-C(7)	1.52(2)	C(3)-C(4)	1.43(2)
C(3)-C(8)	1.49(2)	C(4)-C(5)	1.43(2)
C(4)-C(9)	1.50(2)	C(5)-C(10)	1.50(2)
C(11)-C(12)	1.39(2)	C(11)-C(17)	1.429(14)
C(12)-C(13)	1.411(14)	C(13)-C(18)	1.460(14)
C(14)-C(15)	1.38(2)	C(14)-C(18)	1.458(14)
C(15)-C(16)	1.394(14)	C(17)-C(18)	1.435(13)
C(21)-C(25)	1.39(2)	C(21)-C(22)	1.47(2)
C(21)-C(26)	1.49(2)	C(22)-C(23)	1.436(14)
C(22)-C(27)	1.47(2)	C(23)-C(24)	1.42(2)
C(23)-C(28)	1.52(2)	C(24)-C(25)	1.42(2)
C(24)-C(29)	1.51(2)	C(25)-C(30)	1.53(2)
C(31)-C(32)	1.39(2)	C(31)-C(37)	1.430(13)
C(32)-C(33)	1.42(2)	C(33)-C(38)	1.452(14)
C(34)-C(35)	1.40(2)	C(34)-C(38)	1.449(14)
C(35)-C(36)	1.38(2)	C(37)-C(38)	1.453(13)

C(3)-Ru(1)-C(2)	39.4(4)	C(3)-Ru(1)-C(1)	64.6(5)
C(2)-Ru(1)-C(1)	38.0(4)	C(3)-Ru(1)-C(4)	38.5(5)
C(2)-Ru(1)-C(4)	64.9(4)	C(1)-Ru(1)-C(4)	64.3(5)
C(3)-Ru(1)-C(5)	64.7(5)	C(2)-Ru(1)-C(5)	64.7(4)
C(1)-Ru(1)-C(5)	38.8(4)	C(4)-Ru(1)-C(5)	38.3(4)
C(3)-Ru(1)-C(13)	129.1(4)	C(2)-Ru(1)-C(13)	163.3(4)
C(1)-Ru(1)-C(13)	158.4(4)	C(4)-Ru(1)-C(13)	114.3(4)
C(5)-Ru(1)-C(13)	126.1(4)	C(3)-Ru(1)-C(12)	165.8(4)
C(2)-Ru(1)-C(12)	154.8(4)	C(1)-Ru(1)-C(12)	126.1(4)
C(4)-Ru(1)-C(12)	133.3(4)	C(5)-Ru(1)-C(12)	116.6(4)
C(13)-Ru(1)-C(12)	37.6(4)	C(3)-Ru(1)-C(18)	110.1(4)
C(2)-Ru(1)-C(18)	126.3(4)	C(1)-Ru(1)-C(18)	161.1(4)
C(4)-Ru(1)-C(18)	124.0(4)	C(5)-Ru(1)-C(18)	157.9(4)
C(13)-Ru(1)-C(18)	38.8(4)	C(12)-Ru(1)-C(18)	62.9(4)
C(3)-Ru(1)-C(11)	153.4(4)	C(2)-Ru(1)-C(11)	121.4(4)
C(1)-Ru(1)-C(11)	112.6(4)	C(4)-Ru(1)-C(11)	166.9(4)
C(5)-Ru(1)-C(11)	131.2(4)	C(13)-Ru(1)-C(11)	63.4(4)
C(12)-Ru(1)-C(11)	37.0(4)	C(18)-Ru(1)-C(11)	63.2(4)
C(3)-Ru(1)-C(17)	120.9(5)	C(2)-Ru(1)-C(17)	109.1(4)
C(1)-Ru(1)-C(17)	127.3(4)	C(4)-Ru(1)-C(17)	154.7(4)
C(5)-Ru(1)-C(17)	164.0(4)	C(13)-Ru(1)-C(17)	63.9(4)

C(12)-Ru(1)-C(17)	62.2(4)	C(18)-Ru(1)-C(17)	37.8(3)
C(11)-Ru(1)-C(17)	37.6(4)	C(25)-Ru(2)-C(21)	37.6(4)
C(25)-Ru(2)-C(24)	38.3(4)	C(21)-Ru(2)-C(24)	63.9(5)
C(25)-Ru(2)-C(23)	64.0(4)	C(21)-Ru(2)-C(23)	64.5(5)
C(24)-Ru(2)-C(23)	38.2(5)	C(25)-Ru(2)-C(32)	116.1(4)
C(21)-Ru(2)-C(32)	127.1(5)	C(24)-Ru(2)-C(32)	130.9(4)
C(23)-Ru(2)-C(32)	163.0(4)	C(25)-Ru(2)-C(22)	64.3(5)
C(21)-Ru(2)-C(22)	39.3(5)	C(24)-Ru(2)-C(22)	64.2(4)
C(23)-Ru(2)-C(22)	38.4(4)	C(32)-Ru(2)-C(22)	158.5(4)
C(25)-Ru(2)-C(33)	129.9(4)	C(21)-Ru(2)-C(33)	161.5(5)
C(24)-Ru(2)-C(33)	115.5(4)	C(23)-Ru(2)-C(33)	127.6(4)
C(32)-Ru(2)-C(33)	37.8(4)	C(22)-Ru(2)-C(33)	159.0(4)
C(25)-Ru(2)-C(31)	127.6(4)	C(21)-Ru(2)-C(31)	111.6(4)
C(24)-Ru(2)-C(31)	162.5(4)	C(23)-Ru(2)-C(31)	157.6(4)
C(32)-Ru(2)-C(31)	36.8(4)	C(22)-Ru(2)-C(31)	124.1(4)
C(33)-Ru(2)-C(31)	63.0(4)	C(25)-Ru(2)-C(38)	162.9(4)
C(21)-Ru(2)-C(38)	157.6(5)	C(24)-Ru(2)-C(38)	127.6(4)
C(23)-Ru(2)-C(38)	111.1(4)	C(32)-Ru(2)-C(38)	63.3(4)
C(22)-Ru(2)-C(38)	123.1(4)	C(33)-Ru(2)-C(38)	38.5(4)
C(31)-Ru(2)-C(38)	63.3(4)	C(25)-Ru(2)-C(37)	158.7(4)
C(21)-Ru(2)-C(37)	124.2(4)	C(24)-Ru(2)-C(37)	159.6(4)
C(23)-Ru(2)-C(37)	124.4(4)	C(32)-Ru(2)-C(37)	62.2(4)
C(22)-Ru(2)-C(37)	108.9(4)	C(33)-Ru(2)-C(37)	63.5(4)
C(31)-Ru(2)-C(37)	37.5(3)	C(38)-Ru(2)-C(37)	38.0(4)
C(16)-N(1)-C(17)	113.6(9)	C(14)-N(2)-C(19)	124.6(9)
C(14)-N(2)-C(20)	120.0(9)	C(19)-N(2)-C(20)	115.3(9)
C(36)-N(3)-C(37)	112.5(9)	C(34)-N(4)-C(39)	124.3(8)
C(34)-N(4)-C(40)	119.4(8)	C(39)-N(4)-C(40)	116.1(9)
C(2)-C(1)-C(5)	108.8(10)	C(2)-C(1)-C(6)	125.1(12)
C(5)-C(1)-C(6)	126.0(13)	C(2)-C(1)-Ru(1)	70.5(6)
C(5)-C(1)-Ru(1)	71.0(6)	C(6)-C(1)-Ru(1)	125.1(8)
C(1)-C(2)-C(3)	107.8(9)	C(1)-C(2)-C(7)	128.1(12)
C(3)-C(2)-C(7)	124.1(11)	C(1)-C(2)-Ru(1)	71.6(6)
C(3)-C(2)-Ru(1)	70.1(5)	C(7)-C(2)-Ru(1)	123.8(7)
C(4)-C(3)-C(2)	107.7(10)	C(4)-C(3)-C(8)	126.6(11)
C(2)-C(3)-C(8)	125.8(11)	C(4)-C(3)-Ru(1)	71.8(6)
C(2)-C(3)-Ru(1)	70.5(5)	C(8)-C(3)-Ru(1)	124.5(9)
C(3)-C(4)-C(5)	108.3(10)	C(3)-C(4)-C(9)	125.6(12)
C(5)-C(4)-C(9)	126.0(12)	C(3)-C(4)-Ru(1)	69.7(6)
C(5)-C(4)-Ru(1)	70.8(6)	C(9)-C(4)-Ru(1)	127.2(7)
C(4)-C(5)-C(1)	107.4(11)	C(4)-C(5)-C(10)	126.4(12)
C(1)-C(5)-C(10)	126.1(12)	C(4)-C(5)-Ru(1)	70.8(6)
C(1)-C(5)-Ru(1)	70.3(6)	C(10)-C(5)-Ru(1)	127.5(8)
C(12)-C(11)-C(17)	107.9(9)	C(12)-C(11)-Ru(1)	70.9(5)
C(17)-C(11)-Ru(1)	72.0(5)	C(11)-C(12)-C(13)	110.8(11)
C(11)-C(12)-Ru(1)	72.1(6)	C(13)-C(12)-Ru(1)	71.1(5)
C(12)-C(13)-C(18)	106.0(10)	C(12)-C(13)-Ru(1)	71.3(6)
C(18)-C(13)-Ru(1)	71.2(6)	N(2)-C(14)-C(15)	122.9(9)
N(2)-C(14)-C(18)	123.6(9)	C(15)-C(14)-C(18)	113.4(9)
C(14)-C(15)-C(16)	123.0(9)	N(1)-C(16)-C(15)	126.6(9)
N(1)-C(17)-C(11)	127.2(9)	N(1)-C(17)-C(18)	125.1(9)
C(11)-C(17)-C(18)	107.6(8)	N(1)-C(17)-Ru(1)	126.7(7)
C(11)-C(17)-Ru(1)	70.3(5)	C(18)-C(17)-Ru(1)	70.2(5)
C(17)-C(18)-C(13)	107.6(8)	C(17)-C(18)-C(14)	118.2(8)
C(13)-C(18)-C(14)	134.2(10)	C(17)-C(18)-Ru(1)	72.0(5)
C(13)-C(18)-Ru(1)	70.0(5)	C(14)-C(18)-Ru(1)	123.3(7)
C(25)-C(21)-C(22)	108.0(10)	C(25)-C(21)-C(26)	129.4(14)
C(22)-C(21)-C(26)	122.4(13)	C(25)-C(21)-Ru(2)	70.5(6)
C(22)-C(21)-Ru(2)	71.3(6)	C(26)-C(21)-Ru(2)	126.6(8)

C(23)-C(22)-C(21)	106.0(10)	C(23)-C(22)-C(27)	126.2(12)
C(21)-C(22)-C(27)	127.7(11)	C(23)-C(22)-Ru(2)	70.3(5)
C(21)-C(22)-Ru(2)	69.4(6)	C(27)-C(22)-Ru(2)	123.2(8)
C(24)-C(23)-C(22)	108.5(10)	C(24)-C(23)-C(28)	126.8(11)
C(22)-C(23)-C(28)	124.7(11)	C(24)-C(23)-Ru(2)	70.6(6)
C(22)-C(23)-Ru(2)	71.4(5)	C(28)-C(23)-Ru(2)	124.5(8)
C(25)-C(24)-C(23)	107.8(10)	C(25)-C(24)-C(29)	126.0(12)
C(23)-C(24)-C(29)	126.1(12)	C(25)-C(24)-Ru(2)	70.0(6)
C(23)-C(24)-Ru(2)	71.2(6)	C(29)-C(24)-Ru(2)	126.4(8)
C(21)-C(25)-C(24)	109.6(12)	C(21)-C(25)-C(30)	124.3(12)
C(24)-C(25)-C(30)	125.7(11)	C(21)-C(25)-Ru(2)	72.0(6)
C(24)-C(25)-Ru(2)	71.7(6)	C(30)-C(25)-Ru(2)	128.2(8)
C(32)-C(31)-C(37)	109.4(9)	C(32)-C(31)-Ru(2)	71.4(5)
C(37)-C(31)-Ru(2)	73.2(5)	C(31)-C(32)-C(33)	109.7(11)
C(31)-C(32)-Ru(2)	71.9(6)	C(33)-C(32)-Ru(2)	71.1(5)
C(32)-C(33)-C(38)	106.9(9)	C(32)-C(33)-Ru(2)	71.1(6)
C(38)-C(33)-Ru(2)	71.2(5)	N(4)-C(34)-C(35)	122.1(9)
N(4)-C(34)-C(38)	123.3(9)	C(35)-C(34)-C(38)	114.6(10)
C(36)-C(35)-C(34)	121.7(9)	N(3)-C(36)-C(35)	127.6(9)
N(3)-C(37)-C(31)	127.0(9)	N(3)-C(37)-C(38)	126.3(8)
C(31)-C(37)-C(38)	106.7(8)	N(3)-C(37)-Ru(2)	125.3(6)
C(31)-C(37)-Ru(2)	69.3(5)	C(38)-C(37)-Ru(2)	69.3(5)
C(34)-C(38)-C(37)	117.3(8)	C(34)-C(38)-C(33)	135.5(10)
C(37)-C(38)-C(33)	107.2(8)	C(34)-C(38)-Ru(2)	123.1(7)
C(37)-C(38)-Ru(2)	72.6(5)	C(33)-C(38)-Ru(2)	70.2(5)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for 98008.

The anisotropic displacement factor exponent takes the form:

$-2\pi^2 [(ha^*)^2 U_{11} + ... + 2hka^*b^* U_{12}]$

	U11	U22	U33	U23	U13	U12
Ru(1)	22(1)	19(1)	27(1)	0(1)	2(1)	-3(1)
Ru(2)	22(1)	18(1)	27(1)	1(1)	2(1)	3(1)
N(1)	43(6)	24(5)	38(6)	-7(4)	9(4)	-8(4)
N(2)	38(5)	36(6)	30(5)	5(4)	1(4)	4(4)
N(3)	41(5)	27(5)	28(5)	-4(4)	-2(4)	1(4)
N(4)	43(5)	29(5)	25(5)	2(4)	-5(4)	-12(4)
C(1)	31(6)	39(7)	38(7)	5(5)	2(5)	-13(5)
C(2)	28(5)	32(7)	48(7)	-21(5)	12(5)	-15(5)
C(3)	21(5)	30(7)	53(7)	7(7)	5(4)	2(6)
C(4)	30(6)	48(8)	36(7)	-4(6)	2(5)	-19(5)
C(5)	32(6)	22(6)	56(8)	-6(5)	10(5)	-19(5)
C(6)	69(9)	84(11)	51(9)	32(8)	-7(7)	-42(8)
C(7)	27(6)	117(13)	70(10)	-42(9)	17(6)	-16(7)
C(8)	25(6)	68(9)	84(11)	20(8)	-8(6)	3(6)
C(9)	59(9)	82(10)	34(8)	-13(7)	9(6)	-28(8)
C(10)	48(9)	11(7)	126(15)	-2(6)	2(8)	-7(5)
C(11)	27(5)	34(6)	21(5)	1(4)	-8(4)	-13(4)
C(12)	23(5)	32(7)	35(6)	6(5)	-1(4)	-6(5)
C(13)	23(5)	23(5)	35(6)	-1(5)	5(4)	4(4)
C(14)	23(5)	29(6)	28(6)	9(5)	3(4)	-1(4)
C(15)	40(7)	16(5)	36(7)	3(5)	-1(5)	6(5)
C(16)	38(6)	15(5)	34(6)	-6(4)	4(5)	3(4)
C(17)	28(5)	11(5)	36(7)	2(4)	1(4)	-13(4)
C(18)	22(5)	11(5)	35(7)	-1(4)	-3(4)	-3(4)
C(19)	87(10)	57(8)	42(8)	12(6)	-2(7)	21(7)
C(20)	76(9)	42(7)	42(7)	12(6)	-18(6)	19(6)
C(21)	51(8)	51(8)	30(7)	6(6)	-3(5)	40(6)
C(22)	31(5)	36(7)	39(6)	-6(6)	-6(4)	20(6)
C(23)	21(5)	38(8)	42(7)	2(5)	9(4)	14(5)
C(24)	47(7)	26(6)	28(7)	-6(5)	-7(5)	13(5)
C(25)	24(5)	23(5)	38(7)	7(5)	0(4)	11(4)
C(26)	73(10)	123(14)	37(8)	27(8)	23(7)	65(10)
C(27)	47(8)	79(10)	82(11)	-36(8)	-19(7)	16(7)
C(28)	54(8)	24(6)	86(11)	20(6)	31(7)	12(5)
C(29)	65(9)	83(11)	34(8)	-20(7)	-7(6)	27(8)
C(30)	56(11)	45(10)	109(15)	12(9)	11(9)	6(7)
C(31)	28(5)	26(5)	32(6)	6(4)	4(4)	8(4)
C(32)	21(5)	20(6)	50(6)	7(6)	11(4)	4(5)
C(33)	31(6)	22(5)	26(6)	-3(4)	-7(4)	5(4)
C(34)	23(5)	23(6)	30(6)	7(4)	-1(4)	0(4)
C(35)	28(6)	24(6)	48(8)	5(5)	5(5)	-11(5)
C(36)	27(5)	24(6)	41(7)	-2(5)	4(5)	-9(4)
C(37)	17(5)	19(5)	26(6)	0(4)	4(4)	5(4)
C(38)	21(5)	26(6)	35(7)	9(4)	-1(4)	3(4)
C(39)	82(9)	51(7)	15(5)	3(5)	-8(5)	-16(6)
C(40)	30(9)	55(8)	30(6)	12(6)	2(6)	-18(6)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for 98008.

	x	y	z	U(eq)
H(6A)	9527(17)	4664(6)	4269(16)	102
H(6B)	9590(17)	4083(6)	3659(16)	102
H(6C)	11152(17)	4428(6)	3712(16)	102
H(7A)	12796(14)	3055(6)	5740(16)	106
H(7B)	12991(14)	3504(6)	4502(16)	106
H(7C)	11425(14)	3162(6)	4484(16)	106
H(8A)	12924(13)	3013(6)	8153(17)	89
H(8B)	11718(13)	3076(6)	9516(17)	89
H(8C)	13281(13)	3420(6)	9500(17)	89
H(9A)	9943(17)	4551(6)	10387(14)	87
H(9B)	11642(17)	4302(6)	10720(14)	87
H(9C)	10098(17)	3952(6)	10807(14)	87
H(10A)	8825(15)	5039(5)	6375(19)	93
H(10B)	9783(15)	5179(5)	7927(19)	93
H(10C)	8176(15)	4859(5)	7995(19)	93
H(11A)	6882(11)	3348(4)	4611(11)	33
H(12A)	5726(11)	3835(5)	6896(11)	36
H(13A)	6703(11)	3414(4)	9470(13)	33
H(15A)	10398(14)	1868(4)	8452(13)	37
H(16A)	10181(12)	1865(4)	5813(12)	35
H(19A)	8571(18)	2768(5)	12584(15)	93
H(19B)	7170(18)	2838(5)	11337(15)	93
H(19C)	8693(18)	3200(5)	11280(15)	93
H(20A)	10019(16)	2121(5)	12413(14)	81
H(20B)	11154(16)	2098(5)	10983(14)	81
H(20C)	9654(16)	1726(5)	11037(14)	81
H(26A)	6099(18)	202(7)	11671(15)	116
H(26B)	6052(18)	-405(7)	11348(15)	116
H(26C)	4450(18)	-81(7)	11347(15)	116
H(27A)	7335(16)	829(6)	10762(18)	104
H(27B)	6991(16)	1223(6)	9379(18)	104
H(27C)	8580(16)	891(6)	9432(18)	104
H(28A)	7921(15)	1061(4)	6547(16)	81
H(28B)	6573(15)	944(4)	5276(16)	81
H(28C)	8129(15)	596(4)	5364(16)	81
H(29A)	5803(17)	-21(6)	4316(15)	91
H(29B)	4185(17)	-267(6)	4857(15)	91
H(29C)	5779(17)	-594(6)	4992(15)	91
H(30A)	3920(18)	-912(6)	7220(21)	110
H(30B)	3250(18)	-729(6)	8828(21)	110
H(30C)	4880(18)	-1037(6)	8782(21)	110
H(31A)	2004(11)	791(4)	10388(12)	34
H(32A)	778(11)	286(5)	8121(12)	36
H(33A)	1673(11)	698(4)	5543(12)	32
H(35A)	5286(13)	2288(4)	6582(14)	40
H(36A)	5184(12)	2287(4)	9199(13)	37
H(39A)	3462(16)	1333(5)	2466(12)	75
H(39B)	2150(16)	1221(5)	3703(12)	75
H(39C)	3779(16)	912(5)	3779(12)	75

H(40A)	4796(16)	2018(5)	2654(14)	82
H(40B)	5988(16)	2051(5)	4105(14)	82
H(40C)	4441(16)	2403(5)	4037(14)	82