nonchiral MECAM, measuring the Cotton effects in the presence and absence of MECAM. The ternary system was prepared by mixing equivalent amounts of the methanolic solution of the chiral ligand and of the methanolic solution of MECAM, followed by addition of 1 equiv of Fe^{3+}. The Tris buffer was then added, and the UV and CD spectra were measured after several hours of equilibration at room temperature and compared to the pure chiral complex solution containing 10% MeOH. Identical results were obtained after 24 h. The binary system was prepared in the same way without MECAM. The distribution of Fe^{3+} between the chiral ligand and MECAM was obtained from the difference between the intensities of the Cotton effect in the ternary and binary systems as follows: Let the intensities of the Cotton effects in the binary and ternary systems be I_{bin} and I_{ter}, respectively. The ratio between the concentrations of the chiral and achiral complexes in the ternary system is then $I_{tern}/(I_{bin} - I_{tern})$. The accuracy in estimating the binding ratio depends mainly on the accuracy in reading the difference $I_{bin} - I_{tern}$. The smaller the difference, the larger the error. We found our readings reproducible to within 2% and therefore could attribute to ligand **8a** only a lower limit (see Table II).

On the basis of these measurements, the ratio K_L/K_M is obtained as follows: Let $c = c_L = c_M = c_{Fe}$ be the equimolar initial concentration of the corresponding species, let xc and yc be the concentrations of the chiral ligand and MECAM metal complexes, respectively, and $(1 - x)c$, $(1 - y)c$, and $(1 - x - y)c$ be the concentrations of the free species, respectively. Then by the mass action law

$$K_L c = \frac{x}{(1 - x)(1 - x - y)} \quad (1)$$

$$K_M c = \frac{y}{(1 - y)(1 - x - y)} \quad (2)$$

The ratio K_L/K_M is seen to depend on x and y only

$$\frac{K_L}{K_M} = \frac{x}{1 - x} \cdot \frac{1 - y}{y} \quad (3)$$

From eq 1 y is obtained as a function of x

$$y = 1 - x - \frac{x}{(1 - x)K_L c} = (1 - x)\left[1 - \frac{x}{(1 - x)^2 K_L c}\right] \quad (4)$$

In all our ligands $K_L c$ is very large, so $x/(1 - x)^2 K_L c$ is negligibly small, and eq 4 is reduced to

$$y = 1 - x \quad (5)$$

Therefore

$$K_L/K_M = \frac{x^2}{(1 - x)^2} - \frac{(1 - d)^2}{d^2} \quad (6)$$

where $d = 1 - x$ is proportional to the measured difference between the intensities of ternary (I_{tern}) and binary (I_{bin}) systems.

When the ratio K_L/K_M is very large, d is too small to be measurable. In such cases one may add more MECAM to the ternary system. Letting $m = c_L/c_M$, it is easy to show that

$$K_L/K_M = (1 - d)(m - d)/d^2 \quad (7)$$

It follows that d_{min}, the smallest measurable d, is proportional to $\sqrt{m}$.

Acknowledgment. The authors gratefully acknowledge support by the U.S.–Israel Binational Science Foundation with Grant No. 8700401. Abraham Shanzer is holder of the Siegfried and Irma Ullmann Professorial Chair.

Registry No. 2, 69146-59-4; **2** (protected), 90734-96-6; **2** (Fe^{3+} complex), 141979-30-8; **2** (Ga^{3+} complex), 141902-59-2; **3**, 110374-76-0; **4a**, 110374-73-7; **4b**, 141849-39-0; **5a**, 110374-74-8; **5a** (Fe^{3+} complex), 141879-31-4; **5a** (Ga^{3+} complex), 141879-36-9; L,L,L-**5b**, 141849-41-4; L,L,L-**5b** (Fe^{3+} complex), 141879-32-5; D,D,D-**5b**, 141901-29-3; D,D,D-**5b** (Fe^{3+} complex), 141977-94-8; **6**, 141849-35-6; **6** (Fe^{3+} complex), 141879-33-6; **7a**, 141879-30-3; **7b**, 141849-40-3; **8a**, 141849-42-5; **8a** (Fe^{3+} complex), 141879-34-7; **8b**, 141849-43-6; **8b** (Fe^{3+} complex), 141879-35-8; TRAM, 77372-56-6; TREN, 4097-89-6; H-Leu-OH, 61-90-5; H-Ala-OH, 56-41-7; H-D-Ala-OH, 338-69-2; H-MeLeu-OH, 3060-46-6; 2,3-$(BnO)_2C_6H_3CO$-Leu-OH, 141849-36-7; 2,3-$(BnO)_2C_6H_3CO$-Ala-OH, 123198-04-9; 2,3-$(BnO)_2C_6H_3CO$-D-Ala-OH, 141849-37-8; 2,3-$(BnO)_2C_6H_3CO$-MeLeu-OH, 141849-38-9; 2,3-$(BnO)_2C_6H_3COCl$, 69146-58-3; $BnNH_2$, 100-46-9.

Rhodium(I)- and Iridium(I)-Catalyzed Hydroboration Reactions: Scope and Synthetic Applications

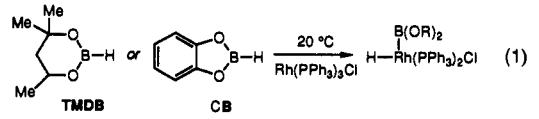
David A. Evans,* Gregory C. Fu,[1a] and Amir H. Hoveyda[1b]

Contribution from the Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138. *Received December 13, 1991*

Abstract: A study of the rhodium(I)- and iridium(I)-catalyzed hydroboration of olefins with catecholborane is described. Applications to organic synthesis were one focus of this investigation. The scope of the reaction was defined, and issues of stereoselection were addressed. The rhodium-catalyzed hydroboration of several classes of allylic alcohols was found to be highly diastereoselective, preferentially affording the isomer complementary to that furnished by the uncatalyzed variant of the reaction (9-BBN). The first two general approaches to effecting a directed olefin hydroboration were developed. Both phosphinites and amides proved capable of delivering the transition metal reagent.

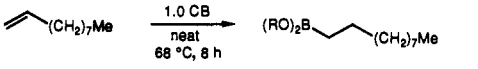
Introduction

The foundation for the present investigation was laid in 1975 by the observation that $Rh(PPh_3)_3Cl$ (Wilkinson's catalyst) undergoes oxidative addition when treated with either 4,4,6-trimethyl-1,3,2-dioxaborinane (TMDB) or catecholborane (1,3,2-benzodioxaborole, CB) (eq 1).[2] The structure of the TMDB–Wilkinson's catalyst adduct was characterized by Kono and Ito.



(1)

At the time of this report, the capacity of catecholborane[3,4] and TMDB[5] to hydroborate olefins had been demonstrated, and it had been established that the reactions required elevated temperatures (eq 2). Furthermore, Wilkinson's catalyst[6] was known to catalyze



(2)

(1) (a) NSF Predoctoral Fellow. (b) American Cancer Society Postdoctoral Fellow.

(2) Kono, H.; Ito, K. *Chem. Lett.* **1975**, 1095–1096.

(3) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1971**, *93*, 1816–1818.

(4) For a review of the chemistry of catecholborane, see: Kabalka, G. W. *Org. Prep. Proced. Int.* **1977**, *9*, 131–147.

(5) Woods, W. G.; Strong, P. L. *J. Am. Chem. Soc.* **1966**, *88*, 4667–4671.

(6) For a comprehensive review, see: Jardine, F. H. *Prog. Inorg. Chem.* **1981**, *28*, 63–202.

0002-7863/92/1514-6671$03.00/0

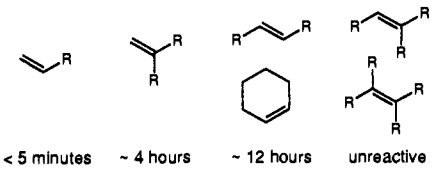
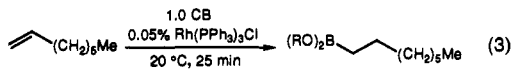


Figure 1. Approximate reaction times for complete hydroboration (2% $Rh(PPh_3)_3Cl$, 2.0 equiv of catecholborane, 20 °C, THF).

the hydrogenation and the hydrosilylation of alkenes.[7] The juxtaposition of these facts immediately suggests the development of a rhodium-catalyzed olefin hydroboration process. Yet, a decade elapsed before this idea was brought to fruition. In 1985, Männig and Nöth reported the first examples of rhodium-catalyzed olefin hydroboration.[8] These workers discovered that, under the influence of Wilkinson's catalyst, the hydroboration of certain alkenes by catecholborane can be effected at room temperature (eq 3).



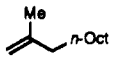
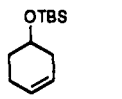
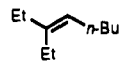
(3)

Although the overall transformations accomplished by the catalyzed and the uncatalyzed hydroboration processes are identical, the pathways by which these reactions arrive at their common product bear little resemblance to one another.[9] Because of this mechanistic dichotomy, the discovery of a catalyzed variant added another dimension to the hydroboration reaction.[10] In the following sections, we report an investigation into some aspects of this new process.[11-14]

Reaction Scope[15,16]

Overview. The present investigation verifies that the original system,[8] $Rh(PPh_3)_3Cl$/catecholborane, is generally the recipe of choice for effecting a catalyzed olefin hydroboration. For terminal alkenes, the reaction is complete within minutes at room temperature with as little as 0.05% catalyst and 1 equiv of catecholborane (CB). More highly substituted olefins are less reactive (Figure 1), and in these cases 2–5% $Rh(PPh_3)_3Cl$ and 2–4 equiv of CB are typically used to ensure that the reactions proceed to completion at a convenient rate. Rearranged alcohols are occasionally observed in the catalyzed hydroboration of acyclic 1,2-disubstituted olefins, an occurrence which limits the utility of the reaction for this particular class of substrates.

Table I. Effect of Olefin Substitution on the Rate of Hydroboration:[a] Percent Conversion after 1.0 h[b]

olefin	$Rh(PPh_3)_3Cl$	[Rh(nbd)-(diphos-4)]BF_4	[Ir(cod)-(PCy_3)(py)]PF_6
	46	59	2
7-tetradecene	15	29	2
	8	16	<2
	<2	<2	<2

[a] Conditions: 2% catalyst, 2.0 equiv of CB, THF, 20 °C. [b] Determined by GC versus an internal standard.

As a note of caution to those interested in carrying out rhodium-catalyzed hydroborations, care should be exercised by using freshly prepared catalyst, as well as distilled solvents and olefin substrates. The effects of catalyst oxidation on the overall course of the reaction can be dramatic. A detailed study of the effects of catalyst oxidation appears in the accompanying mechanistic study.[9]

Catalysts. In their original communication,[8] Männig and Nöth note that $RhCl(CO)(PPh_3)_2$, $RhCl(CO)(AsPh_3)_2$, and $[RhCl(cod)]_2$ catalyze the hydroboration of olefins by CB, although with a lower level of activity than does Wilkinson's catalyst, and that $RuHCl(CO)(PPh_3)_3$ is even less active. Complexes of platinum, palladium, iridium, and cobalt were reported to effect little, if any, catalysis. During the course of this study, we have screened a number of other transition metal complexes for catalytic activity in the hydroboration of 1-decene with CB[17] and have confirmed the observation that rhodium complexes appear to be the most suitable catalysts; Crabtree's iridium complex, [Ir(cod)(PCy_3)(py)]PF_6,[18] is a noteworthy exception to this generalization. In the hydroboration studies discussed in the following sections, we chose to focus on the use of $Rh(PPh_3)_3Cl$, [Rh(nbd)(diphos-4)]BF_4, and [Ir(cod)(PCy_3)(py)]PF_6 as catalysts, due to their demonstrated utility in homogeneous hydrogenation,[19] probably the most well understood transition metal catalyzed olefin addition reaction.[20]

Boron Hydrides. Männig and Nöth screened several boron hydrides during the course of their study of $Rh(PPh_3)_3Cl$-catalyzed olefin hydroboration.[8] They reported that the addition of both catecholborane and 4,4,6-trimethyl-1,3,2-dioxaborinane (TMDB)

(7) (a) Hydrogenation: Young, J. F.; Osborn, J. A.; Jardine, F. H.; Wilkinson, G. *J. Chem. Soc., Chem. Commun.* **1965**, 131–132. (b) Hydrosilation: Haszeldine, R. N.; Parish, R. V.; Parry, D. J. *J. Organomet. Chem.* **1967**, *9*, P13–P14.

(8) Männig, D.; Nöth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878–879.

(9) For the companion study of the mechanism of the catalyzed hydroboration reaction, see: Evans, D. A.; Fu, G. C.; Anderson, B. A. *J. Am. Chem. Soc.*, following article in this issue.

(10) Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*; Academic Press: New York, 1988.

(11) For a recent review of the transition metal catalyzed hydroboration reaction, see: Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179–1191.

(12) For preliminary accounts of this work, see: (a) Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1988**, *110*, 6917–6918. (b) Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 2280–2282. (c) Evans, D. A.; Fu, G. C. *J. Am. Chem. Soc.* **1991**, *113*, 4042–4043.

(13) For contributions of other workers to the development of synthetic applications of the catalyzed olefin hydroboration reaction, see: (a) Burgess, K.; Ohlmeyer, M. J. *J. Org. Chem.* **1988**, *53*, 5178–5179. (b) Burgess, K.; Ohlmeyer, M. J. *Tetrahedron Lett.* **1989**, *30*, 395–398. (c) Hayashi, T.; Matsumoto, Y.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 3426–3428. (d) Satoh, M.; Nomoto, Y.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1989**, *30*, 3789–3792. (e) Burgess, K.; Ohlmeyer, M. J. *Tetrahedron Lett.* **1989**, *30*, 5857–5860. (f) Sato, M.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1990**, *31*, 231–234. (g) Brown, J. M.; Lloyd-Jones, G. C. *Tetrahedron: Asymmetry* **1990**, *1*, 869–872. (h) Burgess, K.; Ohlmeyer, M. J. *J. Org. Chem.* **1991**, *56*, 1027–1036. (i) Zhang, J.; Lou, B.; Guo, G.; Dai, L. *J. Org. Chem.* **1991**, *56*, 1670–1672. (j) Hayashi, T.; Matsumoto, Y.; Ito, Y. *Tetrahedron: Asymmetry* **1991**, *2*, 601–612. (k) Burgess, K.; Donk, W. A.; Ohlmeyer, M. J. *Tetrahedron: Asymmetry* **1991**, *2*, 613–621. (l) Matsumoto, Y.; Hayashi, T. *Tetrahedron Lett.* **1991**, *32*, 3387–3390. (m) Burgess, K.; van der Donk, W.; Jarstfer, M. B.; Ohlmeyer, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 6139–6144.

(14) For leading references to related work, see the following. (a) Rhodacarborane catalysts: Belmont, J. A.; Soto, J.; King, R. E., III; Donaldson, A. J.; Hewes, J. D.; Hawthorne, M. F. *J. Am. Chem. Soc.* **1989**, *111*, 7475–7486. (b) Rhodium- and iridium-catalyzed addition of borazine to alkynes: Lynch, A. T.; Sneddon, L. G. *J. Am. Chem. Soc.* **1987**, *109*, 5867–5868. Lynch, A. T.; Sneddon, L. G. *J. Am. Chem. Soc.* **1989**, *111*, 6201–6209. (c) Rhodium(III) porphyrin catalyzed olefin hydration with $NaBH_4$ and O_2: Aoyama, Y.; Tanaka, Y.; Fujisawa, T.; Watanabe, T.; Toi, H.; Ogoshi, H. *J. Org. Chem.* **1987**, *52*, 2555–2559.

(15) Abbreviations: 9-BBN = 9-borabicyclo[3.3.1]nonane; binap = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl; Bn = benzyl; CB = catecholborane; cod = 1,5-cyclooctadiene; Cp* = pentamethylcyclopentadienylide anion; Cy = cyclohexyl; diphos-2 = 1,2-bis(diphenylphosphino)ethane; diphos-4 = 1,4-bis(diphenylphosphino)butane; nbd = norbornadiene; PMB = *p*-methoxybenzyl; py = pyridine; TBDPS = *tert*-butyldiphenylsilyl; TBS = *tert*-butyldimethylsilyl; TES = triethylsilyl; TMDB = 4,4,6-trimethyl-1,3,2-dioxaborinane.

(16) Unless otherwise specified, all hydroboration reactions described herein include a subsequent oxidative workup.

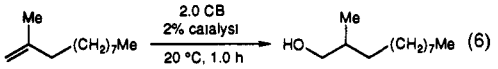
(17) Surveyed catalysts include the following: $CeCl_3$, $Fe_3(CO)_{12}$, $[FeCp(CO)_2]_2$, $Ni(PPh_3)_2(CO)_2$, $TiCp_2Cl_2$, $ZrCp_2Cl_2$, $Ni(PPh_3)_2Cl_2$, Pd/C, $Pd(acac)_2$, $PdCl_2(PhCN)_2$, $PdCl_2(PBu_3)_2$, $Pd(PPh_3)_2Cl(CH_2Ph)$, Pt/C, $Rh(CO)_2(acac)$, $RhCl_3{\cdot}nH_2O$, $[Rh(CO)_2Cl]_2$, Rh/C, Ru/C, $[RhCl(nbd)]_2$ + diphos-(2 and 4), [Rh(ndb)((−)-binap)]ClO_4, $RhCp^*Cl_2(PPh_3)$, $RhH(CO)(PPh_3)_3$, and $RhF(CO)(PPh_3)_2$.

(18) Crabtree, R. H.; Davis, M. W. *J. Org. Chem.* **1986**, *51*, 2655–2661.

(19) For leading references, see: Brown, J. M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 190–203.

(20) For leading references, see: Landis, C. R.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 1746–1754.

Table II. Effect of Solvent on the Rate of Hydroboration (eq 6): Percent Conversion after 1.0 h[a]



(6)

solvent	$[Rh(nbd)(diphos\text{-}4)]BF_4$	$Rh(PPh_3)_3Cl$	$[Ir(cod)(PCy_3)(py)]PF_6$
THF	59	46	2
ether[b]	44	5	2
toluene[b]	46	15	10
CH_2Cl_2	61	6	3
$ClCH_2CH_2Cl$	59	9	4

[a] Determined by GC versus an internal standard. [b] The catalysts were only partially soluble in this solvent.

is subject to catalysis, whereas that of dialkylboranes or 1,3-dimethyl-1,3,2-diazaborolidine is not. We have explored the participation of a number of other boron hydrides, focusing on the use of $Rh(PPh_3)_3Cl$ and $[Rh(nbd)(diphos\text{-}4)]BF_4$ as catalysts. On the basis of the successful activation of CB and TMDB, our efforts have emphasized boron hydrides bearing oxygen ligands. However, attempts to catalyze the hydroboration of 1-decene with a host of boron hydrides including bis(benzoyloxy)borane,[21] bis(trifluoroacetoxy)borane,[22] tetramethylammonium triacetoxyborohydride,[23] and thexylborane were unsuccessful.

Substrates. The rate of the catalyzed hydroboration reaction is very sensitive to the olefin substitution pattern (Table I). Any one of the three complexes catalyzes the quantitative hydroboration of terminal alkenes by CB within minutes at room temperature. 1,1-Disubstituted olefins require several hours for complete reaction with either $Rh(PPh_3)_3Cl$ or $[Rh(nbd)(diphos\text{-}4)]BF_4$ as the catalyst, whereas $[Ir(cod)(PCy_3)(py)]PF_6$ is ineffective for this class of substrates. 1,2-Disubstituted alkenes undergo hydroboration still more slowly, and trisubstituted olefins are essentially unreactive under the standard catalyzed hydroboration reaction conditions.[24] It is worth noting that the relative activity of these three complexes as catalysts for hydroboration is not the same as that observed for hydrogenation: in the case of hydroboration, the order $[Rh(nbd)(diphos\text{-}4)]BF_4 > Rh(PPh_3)_3Cl > [Ir(cod)(PCy_3)(py)]PF_6$ holds, whereas for hydrogenation the sequence is $[Ir(cod)(PCy_3)(py)]PF_6 > [Rh(nbd)(diphos\text{-}4)]BF_4 > Rh(PPh_3)_3Cl$.[19]

The sensitivity of the catalyzed reaction to steric effects provides the opportunity for selective hydroboration of the less hindered of two olefins within a substrate.[25] For example, limonene is preferentially hydroborated at the less hindered olefinic site (eq 4).[26] Furthermore, catalyzed hydroboration of the diene illustrated in eq 5 affords exclusively the alcohol derived from hydroboration of the terminal olefin.[27] All attempts to effect other electrophilic addition reactions selectively (e.g., epoxidation or uncatalyzed hydroboration) were unsuccessful with this substrate.

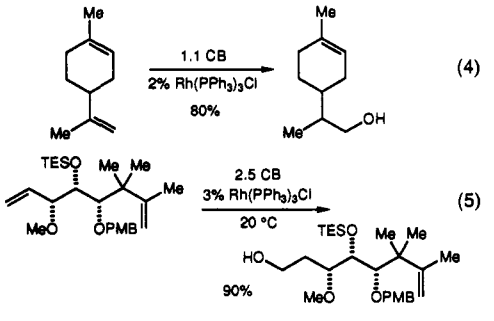
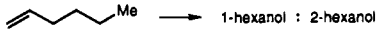


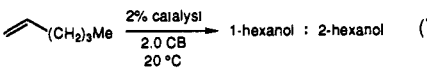
Table III. Hydroboration Regioselectivity



hydroborating agent	1-ol:2-ol[a]
9-BBN	>99:1
$Rh(PPh_3)_3Cl$, CB	99:1
$[Ir(cod)(PCy_3)(py)]PF_6$, CB	98:2
catecholborane[b]	98:2
$[Rh(nbd)(diphos\text{-}4)]BF_4$, CB, −40 °C	97:3
thexylborane	94:6
BH_3	94:6
$[Rh(nbd)(diphos\text{-}4)]BF_4$, CB	90:10

[a] Ratios were determined by GC. [b] 1-Decene was employed as the substrate.

Table IV. Effect of Solvent on the Regioselectivity of the Catalyzed Hydroboration (eq 7)[a]



(7)

catalyst	THF	Et_2O	$ClCH_2CH_2Cl$
$Rh(PPh_3)_3Cl$	99:1	99:1	99:1
$[Rh(nbd)(diphos\text{-}4)]BF_4$	90:10	94:6	96:4
$[Ir(cod)(PCy_3)(py)]PF_6$	98:2	98:2	98:2

[a] Ratios were determined by GC.

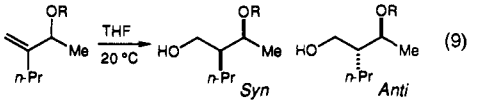
Solvents. The rate of the catalyzed hydroboration of 2-methyl-1-undecene was studied as a function of solvent (Table II). While solvent variations in the $[Rh(nbd)(diphos\text{-}4)]BF_4$-catalyzed reactions have little effect, the rate of $Rh(PPh_3)_3Cl$-mediated hydroboration shows a significant dependence, with THF clearly being the reaction medium of choice.[28]

Regioselectivity. The regioselectivities of the catalyzed hydroborations of 1-hexene compare favorably with those of uncatalyzed variants (Table III).[29] Although the reaction mediated by the cationic rhodium complex, $[Rh(nbd)(diphos\text{-}4)]BF_4$, is relatively nonselective in THF at 20 °C, appropriate manipulation of temperature (Table III) or solvent (Table IV) significantly improves the regioselectivity.

An understanding of the reaction parameters responsible for the high levels of regioselectivity is now in hand, and the relevant studies are described in the accompanying mechanistic investigation.[9] In brief, the regioselection in the hydride migration step of the catalytic cycle is rather low for terminal olefins. On the other hand, reductive elimination of the secondary alkylrhodium

(21) Pelter, A.; Hutchings, M. G.; Levitt, T. E.; Smith, K. *J. Chem. Soc., Chem. Commun.* **1970**, 347–348.
(22) Maryanoff, B. E.; McComsey, D. F. *J. Org. Chem.* **1978**, *43*, 2733–2735.
(23) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560–3578.
(24) During the reaction of less reactive substrates, olefin hydrogenation and isomerization can become significant reaction pathways. Analogous behavior has been observed in the Rh(I)-catalyzed hydrosilation reaction; for example, see: Onopchenko, A.; Sabourin, E. T.; Beach, D. L. *J. Org. Chem.* **1983**, *48*, 5101–5105.
(25) Männig and Nöth have reported the selective hydroboration of the terminal olefin of 3-vinylcyclohexene (ref 8).
(26) In contrast, the regioselective, uncatalyzed hydroboration of a 1,1-disubstituted olefin in the presence of a trisubstituted olefin could not be achieved in a recent synthesis of 5-*O*-methyllicoricidin (Shih, T. L.; Wyvratt, M. J.; Mrozik, H. *J. Org. Chem.* **1987**, *52*, 2029–2033.
(27) Evans, D. A.; Gage, J. R. *J. Org. Chem.* **1992**, *57*, 1958–1961.
(28) We have occasionally experienced difficulties reproducing the results of reactions run in CH_2Cl_2 (see also ref 13b). Use of $ClCH_2CH_2Cl$ circumvents this problem.
(29) (a) 9-BBN (THF, 25 °C): Brown, H. C.; Knights, E. F.; Scouten, C. G. *J. Am. Chem. Soc.* **1974**, *96*, 7765–7770. (b) Catecholborane (neat, 100 °C): Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 5249–5255. (c) Thexylborane (diglyme, 0 °C): Zweifel, G.; Brown, H. C. *J. Am. Chem. Soc.* **1963**, *85*, 2066–2072. (d) BH_3 (diglyme, 20 °C): Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1960**, *82*, 4708–4712.

Table V. Diastereoselective Hydroboration of Acyclic Allylic Alcohols (eq 9)



(9)

R	entry	conditions[a]	syn:anti[b]	yield (%)
H	1	A	17:83	91
	2	B	81:19	79
	3	C	50:50	60
CH_2Ph	4	A	25:75	82
	5	B	80:20	63
	6	C	50:50	81
$Si(t\text{-}Bu)Me_2$	7	A	13:87	85
	8	B	93:7	79
	9	C	60:40	54
$Si(t\text{-}Bu)Ph_2$	10	A	15:85	84
	11	B	93:7	82
	12	C	79:21	63

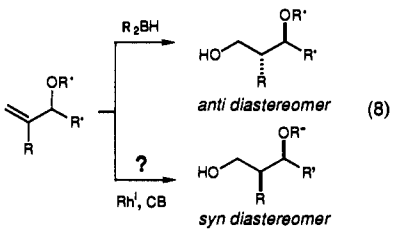
[a] A, 3 equiv of 9-BBN; B, 3 equiv of CB and 3% $Rh(PPh_3)_3Cl$; C, 3 equiv of CB and 3% [Rh(nbd)(diphos-4)]BF_4. [b] Ratios were determined by GC.

is exceptionally slow relative to the analogous reaction of the primary alkylrhodium species.

Diastereoselective Rhodium-Catalyzed Hydroboration

A number of studies have addressed the diastereoselective hydroboration of olefins by BH_3 and by alkylboranes.[30] A variety of models, most of which rely upon a combination of steric and electronic influences, have been advanced to rationalize the stereochemical outcome of these reactions.[31] The mechanism of the metal-catalyzed reaction[9] clearly is quite different from that of the uncatalyzed variant, and a priori there was no reason to believe that the two processes would share the same response to steric and electronic effects. Recognizing this, we decided to investigate the facial selectivity of the rhodium-catalyzed hydroboration of a series of chiral olefins.

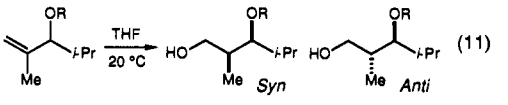
Acyclic Systems. Our initial investigation focused on 1,2-asymmetric induction in the reaction of 1,1-disubstituted olefins. The uncatalyzed diastereoselective hydroboration of this class of substrates has been documented by Still and Barrish,[30a] who found that reactions of allylic alcohol derivatives generally afford the anti isomer, with 9-BBN furnishing the highest selectivities (eq 8).



(8)

We discovered that the rhodium-catalyzed hydroboration of 1,1-disubstituted olefins provides a stereochemical outcome complementary to that observed with 9-BBN (Table V). Examination of the data in Table V reveals the following trends: (1) reactions catalyzed by $Rh(PPh_3)_3Cl$ are more diastereoselective and higher yielding than those of [Rh(nbd)(diphos-4)]BF_4 (entries 2, 5, 8, and 11 versus entries 3, 6, 9, and 12), and (2) as the size of R increases, the syn selectivity of the catalyzed hydroboration increases (entries 2, 5, 8, and 11; entries 3, 6, 9, and 12). In contrast, the uncatalyzed variant is less sensitive to changes in the second parameter (entries 1, 4, 7 and 10). Equation 10 and Table VI furnish additional data which support the generality of the stereochemical complementarity between the catalyzed and the uncatalyzed hydroboration processes.[32]

Table VI. Diastereoselective Hydroboration of Acyclic Allylic Alcohols (eq 11)

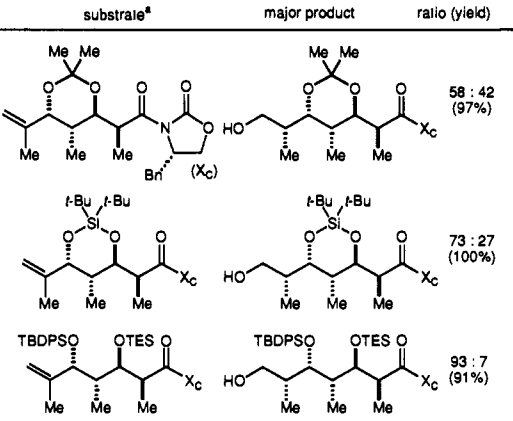


(11)

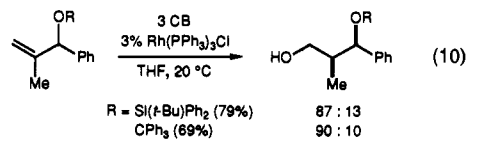
R	conditions[a]	syn:anti[b]	yield (%)
H	A	4:96	67
	B	50:50	68
$Si(t\text{-}Bu)Me_2$	A	5:95	72
	B	85:15	65
$Si(t\text{-}Bu)Ph_2$	A	5:95	75
	B	97:3	77

[a] A, 3 equiv of 9-BBN; B, 3 equiv of CB and 3% $Rh(PPh_3)_3Cl$; C, 3 equiv of CB and 3% [Rh(nbd)(diphos-4)]BF_4. [b] Ratios were determined by GC.

Table VII. Lonomycin A Model Studies

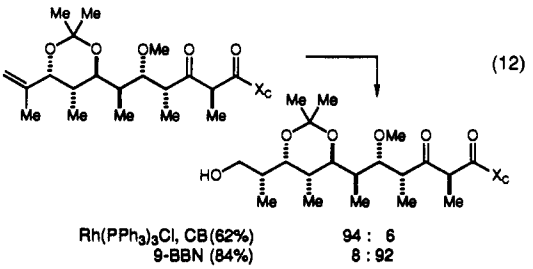


[a] TBDPS = *tert*-butyldiphenylsilyl; TES = triethylsilyl.



(10)

The utility of diastereoselective rhodium-catalyzed olefin hydroboration in complex substrates has recently been demonstrated in a synthesis of the C_1–C_{11} polypropionate portion of the polyether antibiotic lonomycin A.[33] Model studies, illustrated in Table VII, are consistent with the generalization that increasing the steric bulk of the allylic oxygen substituent enhances the diastereoselectivity of the hydroboration. However, the result from hydroboration of the actual system (eq 12) indicates that the factors governing reaction stereoselection can be rather subtle (cf. Table VII).



(12)

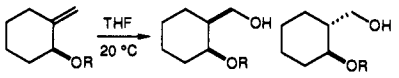
(30) For leading references, see: (a) Still, W. C.; Barrish, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 2487–2489. (b) Heathcock, C. H.; Jarvi, E. T.; Rosen, T. *Tetrahedron Lett.* **1984**, *25*, 243–246. (c) McGarvey, G. J.; Bajwa, J. S. *Tetrahedron Lett.* **1985**, *26*, 6297–6300.

(31) For leading references, see: (a) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 666–671. (b) Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G.; Wu, Y.-D.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science* **1986**, *231*, 1108–1117.

(32) For additional examples, see: (a) Reference 12a. (b) Fu, G. C. Ph.D. Thesis, Harvard University, Cambridge, MA, 1991.

(33) Evans, D. A.; Sheppard, G. *J. Org. Chem.* **1990**, *55*, 5192–5194.

Table VIII. Hydroboration of 2-Methylenecyclohexanol Derivatives (eq 13)

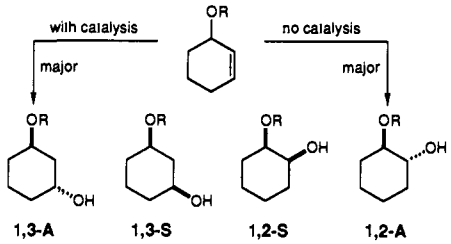


(13)

R	conditions[a]	syn:anti[b]	yield (%)
H	A	54:46	83
	B	91:9	93
	C	48:52	80
Si(*t*-Bu)Me_2	A	39:61	81
	B	93:7	87
	C	93:7	92

[a] A, 3 equiv of 9-BBN; B, 3 equiv of CB and 3% $Rh(PPh_3)_3Cl$; C, 3 equiv of CB and 3% $[Rh(nbd)(diphos\text{-}4)]BF_4$. [b] Ratios were determined by GC.

Table IX. Hydroboration of 2-Cyclohexen-1-ol Derivatives[a]



R	conditions[b]	1,3-A	1,3-S	1,2-S	1,2-A	yield (%)
H	A	72	9	1	18	84
	B	5	10	2	83	86
CH_2Ph	A	72	13	8	7	87
	B	13	19	0	68	73
Si(*t*-Bu)Me_2	A	86	11	1	2	79
	B	10	15	0	75	70

[a] Ratios were determined by GC. [b] A, 3 equiv of CB, 3% $Rh(PPh_3)_3Cl$, THF, 20 °C; B, 3 equiv of 9-BBN.

From deuterium labeling studies, we have concluded that olefin binding to the metal is irreversible for 1,1-disubstituted allylic alcohol derivatives.[9,12b] This information provides the data necessary to identify olefin–catalyst complexation as the stereochemistry-determining step of the hydroboration process. Subsequent to our work, Burgess and co-workers studied these and closely related substrates[13b,e,h] and proposed a model to rationalize the observed reaction diastereoselectivity.[13m]

Cyclic Systems. The diastereoselective hydroboration of exocyclic 1,1-disubstituted olefins was briefly explored. Whereas reaction with 9-BBN exhibits poor stereoselection, the rhodium-catalyzed hydroboration process displays a strong preference for addition to the alkene face opposite to the allylic substituent (eq 13, Table VIII) through a possible combination of reinforcing steric and stereoelectronic effects.

Hydroboration of derivatives of 2-cyclohexen-1-ol provides an additional example in which the catalyzed and uncatalyzed reaction variants afford stereochemically complementary products (Table IX). Whereas 9-BBN predominantly furnishes the 1,2-anti compound, the $Rh(PPh_3)_3Cl$-catalyzed process preferentially generates the 1,3-anti isomer.[34] The 1,2-regiochemistry of the uncatalyzed reaction is presumably due to the dominant influence of electronic effects, and the anti stereochemistry to steric effects. The preference of the catalyzed reaction for formation of the 1,3-anti isomer may reflect a sensitivity to steric effects.

In summary, the stereoselective hydroboration of chiral allylic alcohols represents a useful synthetic route to 1,3-diols, a substructure common to a variety of natural products. Conventional hydroboration typically affords a path to only one of the possible diols. The rhodium-catalyzed hydroboration of several classes of cyclic and acyclic allylic alcohols furnishes convenient access to the complementary isomer with high diastereoselectivity.

Directed Hydroboration

Although a fairly wide range of reactions have been demonstrated to be susceptible to a directed variant,[35] to date no general methods exist for effecting a directed, uncatalyzed olefin hydroboration.[36] Because of the ubiquity of hydroxyl groups in natural products, our initial goal was to develop a hydroxyl-delivered hydroboration reaction.[37] A hydroxyl-directed, catalyzed hydroboration process is precluded, however, by the fact that alcohols react rapidly with CB to form borate esters, which are poor ligands for rhodium. We therefore sought to develop a *net* hydroxyl-directed reaction by employing an auxiliary ligand. Diphenylphosphinites[38,39] were first examined as directing groups. These ligands are readily synthesized through alcohol derivatization with commercially available $ClPPh_2$. It is also known that they bind strongly, as well as reversibly, to rhodium.

2-Cyclohexenol was selected as the test substrate because the diastereofacial preferences of a directed and an undirected reaction are readily predictable (and different from one another) for this substrate: the directed process should preferentially afford the syn diol while the undirected variant should provide the anti diastereomer set (Table IX). In the event, the relevant experiments demonstrated that a phosphinite ligand positioned in the vicinity of an olefinic center can indeed deliver the metal-mediated addition of CB to an olefin to afford the syn 1,2-diol (eq 14) with good diastereoselectivity.[40] In contrast, when the hydroxyl group is converted to the nonligating silyl ether, the anti 1,3-diol is produced preferentially (eq 15; see Table IX).

Two additional examples demonstrate the generality of phosphinite directivity. The analogous $Rh(PPh_3)_3Cl$-mediated hydroboration of the phosphinite derived from 3-cyclohexenol preferentially furnishes the product of addition to the syn face of the olefin (eq 16), a result which requires directivity by the phosphorus ligand from the bishomoallylic position. Phosphinite-directed hydroboration can also be effected in acyclic systems. The high regioselectivity typically observed in the catalyzed hydroboration of a terminal olefin (99:1; see Table IV) may be overridden by the influence of a homoallylic phosphinite (eq 17). These directed reactions, however, could not be accomplished effectively in a catalytic manner. For example, the use of substoichiometric quantities of the rhodium complex (eq 14) leads to the formation of the syn 1,2-diol product in lower yield and with diminished stereoselectivity. It was ultimately demonstrated that phosphinites are unstable toward catecholborane, decomposing within minutes to diphenylphosphine and a borate ester. With a stoichiometric, rhodium-mediated, directed hydroboration reaction in hand, attention was directed to the development of a catalytic version of the process. Because the failure of the phosphinite/CB system to operate effectively in a catalytic fashion appeared to be attributable to the instability of the phosphorus directing group to the boron hydride, each of these components was varied separately in an attempt to surmount this problem. Although compatible (boron hydride)–(directing group) combi-

(34) The $Rh(PPh_3)_3Cl$-catalyzed hydroboration reactions also afford small quantities of the 1,4-isomer.

(35) For two recent examples of the directed hydride reduction of β-hydroxy ketones, see: (a) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560–3578. (b) Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447–6449.

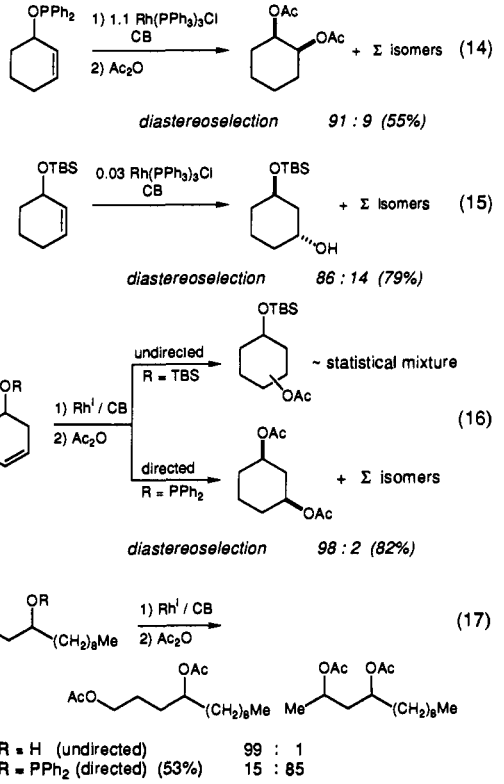
(36) Several workers have proposed reaction pathways involving delivery of boron hydride in order to explain anomalous regio- and stereoselectivities observed in uncatalyzed hydroboration reactions: (a) Zweifel, G.; Najafi, M. R.; Rajagopalan, S. *Tetrahedron Lett.* **1988**, *29*, 1895–1898. (b) Suzuki, K.; Miyazawa, M.; Shimazaki, M.; Tsuchihashi, G.-i. *Tetrahedron* **1988**, *44*, 4061–4072. (c) Welch, M. C.; Bryson, T. A. *Tetrahedron Lett.* **1989**, *30*, 523–526.

(37) Unsuccessful attempts to achieve a hydroxyl-directed hydroboration have been reported. See: Smith, A. B., III; Yokoyama, Y.; Huryn, D. M.; Dunlap, N. K. *Tetrahedron Lett.* **1987**, *28*, 3659–3662.

(38) When we began our work, two examples of phosphorus-directed organometallic reactions were known. Both were *phosphine*-directed hydroformylation reactions: (a) Burke, S. D.; Cobb, J. E. *Tetrahedron Lett.* **1986**, *27*, 4237–4240. (b) Jackson, W. R.; Perlmutter, P.; Suh, G.-H. *J. Chem. Soc., Chem. Commun.* **1987**, 724–725.

(39) Collum, D. B.; Depue, R. T.; Klang, J. A. *Organometallics* **1986**, *5*, 1015–1018. See also references cited therein.

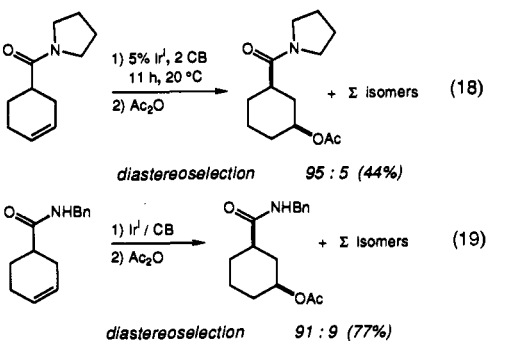
(40) $[Rh(nbd)(diphos\text{-}4)]BF_4$ may also be used in this reaction.



nations were found (for example, TMDB–phosphinite, CB-phosphite, and catecholborane–acylphosphine), not one was an effective participant in a directed $Rh(PPh_3)_3Cl$- or [Rh(nbd)-(diphos-4)]BF_4-catalyzed hydroboration reaction.

Several non-phosphorus directing groups, including cyclohexene-derived potassium alkoxides, esters, urethanes, and benzyl ethers, were also surveyed. The selection of functionality and catalyst ($Rh(PPh_3)_3Cl$, [Rh(nbd)(diphos-4)]BF_4, and [Ir(cod)-(PCy_3)(py)]PF_6) was based on precedent established in studies of the directed hydrogenation reaction.[19] Unfortunately, none of these catalyst–directing group combinations proved capable of effecting a delivered hydroboration.

We have found that a tertiary amide efficiently directs the hydroboration reaction[41] and, in the case of the cyclohexene-derived olefins, affords the syn 1,3-hydroxyamide as the major product with good selectivity (eq 18). This reaction represents the first example of a *catalytic*, directed hydroboration process. Unfortunately, the yield is a modest 44%, due to competitive reduction of the amide. As is the case for the phosphinites, the tertiary amide directing group is not inert to the hydroboration conditions. Use of a secondary, rather than a tertiary, amide effectively eliminates the carbonyl reduction pathway without having a serious impact on stereoselection. Thus, treatment of the illustrated olefin with [Ir(cod)(PCy_3)(py)]PF_6 and CB selectively affords the syn 1,3-hydroxyamide in good yield (eq 19).

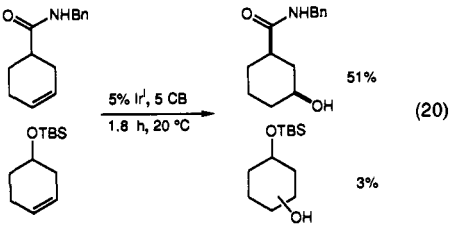


(41) Tertiary amides direct Ir-catalyzed hydrogenation. See: Schultz, A. G.; McCloskey, P. J. *J. Org. Chem.* **1985**, *50*, 5905–5907.

A number of observations support the assertion that these reactions are amide-delivered:

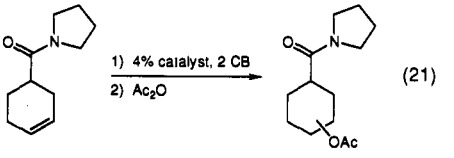
(1) Regio- and Stereoselectivity. The catalyzed hydroborations of a wide variety of other 4-substituted cyclohexenes furnish an essentially statistical mixture of the isomeric reaction products (vide supra). Predominant formation of the syn 1,3-hydroxyamide is congruent with the expectations for a delivered reaction.

(2) Enhanced Reactivity. In a competition experiment, 4-[*N*-(phenylmethyl)carbamoyl]cyclohexene is over 1 order of magnitude more reactive toward iridium-catalyzed hydroboration than is 4-[(*tert*-butyldimethylsilyl)oxy]cyclohexene (eq 20). Given the remoteness of the substituent from the olefin, a steric or an electronic effect is unlikely to be the origin of this disparity in relative rates of reaction.



(3) Solvent Effect on Stereoselectivity. The data in Table X reveal an inverse relationship between the Lewis basicity of the reaction solvent and the level of diastereoselectivity observed. This trend may be readily rationalized if the amide is delivering the metal; when the solvent is better able to compete with the amide moiety for metal complexation, the directed pathway becomes less favorable, and an erosion in stereoselectivity results. It is noteworthy that the cationic iridium catalyst is generally a more effective participant in the delivered reaction than is the cationic rhodium complex.

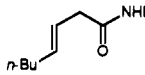
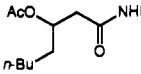
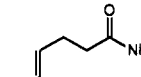
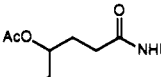
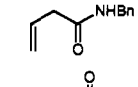
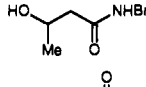
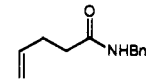
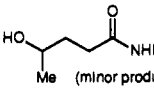
Table X. Solvent Effect on the Stereoselectivity of the Amide-Directed Hydroboration (eq 21)[a]



	1,3-syn:Σisomers	
solvent	[Ir(cod)(PCy_3)(py)]PF_6	[Rh(nbd)(diphos-4)]BF_4
THF	45:55	35:65
ether	52:48	61:39
$ClCH_2CH_2Cl$	95:5	74:26

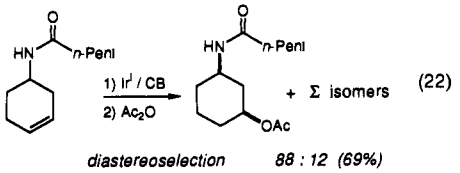
[a] Ratios were determined by GC.

Table XI. Amide-Directed, Metal-Catalyzed Hydroboration: Acyclic Systems

entry	substrate	product	catalyst[a]	selectivity[b] (yield)
1			Ir^I	>99 : 1 (73%)
2			Rh^+	20 : 1 (74%)
3			Ir^I	99 : 1 (78%)
4			Rh^+	70 : 20 : 10[c]
5			Ir^I	1 : 1 (78%)
6			Ir^I	1 : 3 (78%)

[a] Rh^+ = [Rh(nbd)(diphos-4)]BF_4, Ir^I = [Ir(cod)(PCy_3)(py)]PF_6. [b] Ratio of oxygenation proximal:distal, as determined by GC. [c] Ratio of oxygenation for γ:δ:ϵ.

Secondary amides derived from cyclic homoallylic amines are also effective in directing the iridium-catalyzed hydroboration process (eq 22).[42] In contrast, the corresponding reactions with $Rh(PPh_3)_3Cl$ or $[Rh(nbd)(diphos\text{-}4)]BF_4$ as catalyst afford a nearly statistical mixture of the four possible isomers.



(22)

diastereoselection *88 : 12 (69%)*

The amide-directed hydroboration reaction may also be applied to acyclic systems. For example, iridium-catalyzed hydroboration of the β,γ-unsaturated amide illustrated in Table XI (entry 1) affords the β-hydroxy amide with >99:1 selectivity. Reaction of a homologous substrate (entry 3) is only slightly less regioselective (99:1). On the other hand, the drop in selectivity between the corresponding $[Rh(nbd)(diphos\text{-}4)]BF_4$-catalyzed hydroborations is precipitous (entries 2 and 4).

The amide directing group is capable of turning over the normal regioselectivity of the iridium-catalyzed reaction of a terminal olefin. Whereas 1-hexene is hydroborated with 98:2 selectivity favoring formation of the primary alcohol (Table IV), reaction of the 3-butenamide affords the secondary alcohol as the major product (Table XI, entry 5; 1.2:1). As in the case of a disubstituted olefin (entry 1 versus 3), the directing influence of the amide diminishes with increasing distance (entry 5 versus 6).

In conclusion, the first two general approaches for effecting a delivered hydroboration reaction have been developed. One strategy employs a phosphinite as the directing group, thereby affording access to a net hydroxyl-directed hydroboration process. Examples of phosphinite delivery in cyclic and acyclic systems have been provided; however, the need for stoichiometric quantities of the rhodium complex limits the utility of this reaction. In the second approach, secondary amides have been shown to deliver the $[Ir(cod)(PCy_3)(py)]PF_6$-catalyzed hydroboration reaction. In contrast to the phosphinite-directed variant, this process is catalytic in the metal complex. A number of examples of diastereo- and regioselective amide-directed hydroboration reactions have been documented.

Conclusions

The net transformations effected by the uncatalyzed and the catalyzed hydroboration processes are identical, but the mechanisms by which these reactions arrive at their common product are profoundly different. It was this mechanistic dichotomy that provided the impetus for our investigation of the transition metal catalyzed hydroboration reaction. The scope of this new process has been defined, and two synthetic applications of the reaction have been explored in depth. A highly diastereoselective catalyzed hydroboration of allylic alcohols has been developed which affords the isomer complementary to that observed under uncatalyzed hydroboration conditions. Furthermore, two general strategies for accomplishing a directed olefin hydroboration have been demonstrated.

Experimental Section

General. Capillary gas chromatography was performed with a flame ionization detector, split mode capillary injection system, and 30 m × 0.25 μm fused silica DB-1 column (J & W Scientific) with helium as the carrier gas. Optical rotations were determined at λ = 589 nm (sodium lamp, D line) at 20 °C. 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). Solvents were distilled under N_2 prior to use (1,2-dichloroethane and dihloromethane from calcium hydride; ether, THF, and toluene from sodium/benzophenone). Wilkinson's catalyst ($Rh(PPh_3)_3Cl$) was prepared according to the method of Wilkinson.[43] $[Rh(nbd)(diphos\text{-}4)]BF_4$[44] and $[Ir(cod)(PCy_3)(py)]PF_6$[45] were synthesized according to literature procedures and stored in a vacuum desiccator prior to use. Reagent grade 30% H_2O_2 was purchased from Mallinckrodt. Catecholborane (Aldrich) was distilled under reduced pressure. TMDB was synthesized by the method of Smith and Brotherton.[46] All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring. One of two oxidative workup procedures was followed subsequent to each hydroboration. Substrates bearing a functionality potentially labile to basic conditions were oxidized using the neutral method. Otherwise, the choice between the two procedures was arbitrary.

Basic Oxidative Workup. To the reaction solution were added 2.0 mL of EtOH/THF (1:1), 2.0 mL of 2 N NaOH, and then 2.0 mL of 30% H_2O_2 (per millimole of starting olefin). The resulting mixture was stirred at 20 °C for at least 2 h.

Neutral Oxidative Workup. To the reaction solution were added 2.0 mL of EtOH/THF (1:1), 2.0 mL of pH 7.00 buffer (Fisher; 0.05 M potassium phosphate monobasic/sodium hydroxide), and then 2.0 mL of 30% H_2O_2 (per millimole of starting olefin). The resulting mixture was stirred at 20 °C for at least 12 h. Oxidation products prepared by both methods were isolated by extraction (EtOAc/saturated NaCl), dried over $MgSO_4$ or Na_2SO_4, filtered, and concentrated.

Catalyst Screening, General Procedure. CB (240 mg, 2.00 mmol) was added to a mixture of 1-decene (140 mg, 1.00 mmol) and the catalyst (0.05 mmol) in 3.0 mL of THF. The resulting solution was stirred at 20 °C for 6.0 h and then subjected to a basic oxidative workup. Dodecane (170 mg, 1.00 mmol) was added to the product as a GLC standard, and an aliquot was analyzed by GLC.

TMDB Hydroboration of 7-Tetradecene. TMDB (46 mg, 0.36 mmol) and 7-tetradecene (58.8 mg, 0.30 mmol) were added to an orange-red solution of $[Rh(nbd)(diphos\text{-}4)]BF_4$ (4.2 mg, 0.006 mmol) in 2.0 mL of THF. The reaction was stirred at 20 °C for 25 h and then subjected to a basic oxidative workup. Flash chromatography (10% EtOAc/hexane) afforded 38.0 mg (59%) of 1-tetradecanol as a white solid (identical with commercially available 1-tetradecanol by GLC, TLC, NMR, and IR).

Olefin Reactivity, General Procedure (Tables I and II). CB (120 mg, 1.00 mmol) was added to a mixture of the olefin (0.50 mmol) and the catalyst (0.01 mmol) in 2.0 mL of solvent. The resulting solution was stirred at 20 °C for 1.0 h and then subjected to a neutral oxidative workup. Pentadecane (212 mg, 0.50 mmol) was added as a GLC standard. The mixture was extracted (EtOAc/saturated NaCl), and an aliquot was analyzed by GLC.

***p*-Menth-1-en-9-ol.** CB (635 mg, 5.30 mmol) was added to a solution of $Rh(PPh_3)_3Cl$ (92.5 mg, 0.10 mmol) and limonene (681 mg, 5.00 mmol) in 15 mL of THF. The resulting yellow solution was stirred at 20 °C for 12 h and then subjected to a basic oxidative workup. Flash chromatography (15% EtOAc/hexane) afforded 620 mg (80%) of *p*-menth-1-en-9-ol as a colorless liquid (identical with commerically available *p*-menth-1-en-9-ol by ^1H NMR, ^{13}C NMR, TLC, and IR). ^{13}C NMR analysis indicated a 1–2:1 mixture of diastereomers. The corresponding reaction with $[Rh(nbd)(diphos\text{-}4)]BF_4$ (70.8 mg, 0.10 mmol) as catalyst afforded 657 mg (85%) of *p*-menth-1-en-9-ol as a 1–2:1 mixture of diastereomers (^{13}C NMR).

Regioselectivity, General Procedure (Tables III and IV). A mixture of 1-hexene (84 mg, 1.00 mmol) and catalyst (0.02 mmol) in 3.0 mL of solvent was immersed in a water bath (20 °C). CB (240 mg, 2.00 mmol) was added dropwise, so as to maintain a constant temperature (20 ± 2 °C). The resulting solution was stirred at 20 °C for 1.0 h and then subjected to a neutral oxidative workup, and an aliquot was analyzed by GLC.

Diastereoselective Hydroboration, General Procedure. CB (106 mg, 0.89 mmol) was added to a 0 °C mixture of olefin (67.5 mg, 0.30 mmol) and $Rh(PPh_3)_3Cl$ (8.2 mg, 0.0089 mmol) in 1.0 mL of THF. The resulting solution was warmed to 20 °C and stirred at that temperature. After 8 h, the reaction was subjected to a neutral oxidative workup. Flash chromatography afforded the desired alcohols.

(2*S,3*S**)-2-[(*tert*-Butyldimethylsilyl)oxy]-3-(hydroxymethyl)hexane:** R_f = 0.65 (50% ether/hexane); IR (neat) 3440, 2960, 2940, 2900, 2860, 1465, 1255, 1115, 1105, 1070, 1045, 1005 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.04 (m, 1 H, C*H*OTBS), 3.73 (t, 1 H, J = 10.3 Hz, C*H*HOH), 3.55 (m, 1 H, CH*H*OH), 3.47 (dd, 1 H, J = 8.1, 1.8 Hz, CH_2OH), 1.87 (m, 1 H, $CHCH_2OH$), 1.31 (m, 2 H, $CH_2CH_2CH_3$), 1.13 (d, 3 H, J = 6.4 Hz, $CHCH_3$), 1.02 (m, 2 H, CH_2CH_3), 0.89 (t, J = 7.4 Hz, CH_2CH_3), 0.87 (s, 9 H, OSi-*t*-Bu(CH_3)$_2$), 0.08 (s, 3 H, OSi-*t*-Bu($CH3$)$_2$), 0.06 (s, 3 H, OSi-*t*-Bu(CH_3)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 72.3, 63.9, 45.3, 30.2, 25.7, 20.8, 17.9, 17.5, 14.3, 6.6, 6.2; HRMS *m/z*

(42) Yield based on recovered starting material.
(43) Osborn, J. A.; Wilkinson, G. *Inorg. Synth.* **1967**, *10*, 67–71.
(44) Evans, D. A.; Morrissey, M. M. *J. Am. Chem. Soc.* **1984**, *106*, 3866–3868.
(45) Crabtree, R. H.; Morehouse, S. M. *Inorg. Synth.* **1986**, *24*, 172–176.
(46) Smith, H. D., Jr.; Brotherton, R. J. *Inorg. Chem.* **1970**, *9*, 2443–2446.

calcd for $C_{13}H_{31}O_2Si$ (M + H)$^+$ 247.2093, found 247.2084.

(2S*,3S*)-3-(Hydroxymethyl)-2-[(phenylmethyl)oxy]hexane: R_f = 0.70 (50% ether/hexane); IR (neat) 3440, 2960, 2940, 2880, 1455, 1100, 1070, 1030 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.35 (m, 5 H, aromatic H), 4.66 (d, 1 H, J = 11.8 Hz, C*H*HPh), 4.54 (d, 1 H, J = 11.8 Hz, CH*H*Ph), 3.60–3.80 (m, 3 H, C*H*OCHCH_2OH), 3.07 (dd, 1 H, J = 7.3, 3.4 Hz, O*H*), 2.00 (m, 1 H, C*H*CH_2OH), 1.25 (d, 3 H, J = 6.4 Hz, CH_3CH), 1.10–1.40 (m, 4 H, CH_2CH_2CH$_3$), 0.95 (t, 3 H, J = 7.2 Hz, CH_3CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) (mixture of isomers) δ 138.30, 128.37, 128.35, 127.66, 127.62, 127.55, 127.49, 78.93, 78.09, 70.97, 70.65, 63.63, 63.51, 45.76, 43.47, 30.72, 29.32, 20.74, 20.35, 17.44, 14.42, 14.21. Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.51; H, 10.04.

(2S*,3S)-2-[(*tert*-Butyldiphenylsilyl)oxy]-3-(hydroxymethyl)hexane: R_f = 0.60 (50% ether/hexane); IR (neat) 3450, 2970, 2940, 2900, 2870, 1475, 1470, 1115, 1070, 1050, 1010, 1005 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65–7.75 (m, 4 H, aromatic H), 7.35–7.45 (m, 6 H, aromatic H), 4.04 (m, 1 H, C*H*OTBDPS), 3.81 (t, 1 H, J = 10.3 Hz, C*H*HOH), 3.61 (m, 1 H, CH*H*OH), 3.39 (br s, 1 H, O*H*), 1.94 (m, 1 H, C*H*CH$_2$OH), 1.15 (m, 2 H, CH_2CH$_2$CH$_3$), 1.08 (s, 9 H, OSi-*t*-*Bu*Ph$_2$), 1.04 (d, 3 H, J = 6.3 Hz, CHCH_3), 0.90–1.00 (m, 2 H, CH$_2$CH_2CH$_3$), 0.79 (t, 3 H, J = 7.3 Hz, CH$_2$CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.9, 133.8, 133.3, 129.8, 129.7, 127.7, 127.5, 72.9, 63.8, 45.2, 30.2, 27.0, 20.6, 19.0, 17.3, 14.1. Anal. Calcd for $C_{23}H_{34}O_2Si$: C, 74.54; H, 9.25. Found: C, 74.63; H, 9.31.

(2S*,3S)-3-[(*tert*-Butyldimethylsilyl)oxy]-2,4-dimethylpentan-1-ol: R_f = 0.65 (50% ether/hexane); IR (CCl_4) 3650, 3530, 2970, 2940, 2890, 2860, 1475, 1465, 1255, 1095, 1045, 1030, 1010 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.59 (m, 1 H, C*H*HOH), 3.50 (dd, 1 H, J = 5.5, 2.8 Hz, C*H*OTBS), 3.46 (m, 1 H, CH*H*OH), 1.91 (m, 1 H, C*H*(CH$_3$)-CH$_2$OH), 1.85 (m, 1 H, CH$_2$O*H*), 1.79 (m, 1 H, C*H*(CH$_3$)$_2$), 0.91 (d, 3 H, J = 6.4 Hz, CH(CH_3)$_2$), 0.89 (s, 9 H, OSi-*t*-*BU*(CH$_3$)$_2$), 0.88 (d, 3 H, CH(C*H*3)$_2$), 0.84 (d, 3 H, J = 7.0 Hz, CH(CH_3)CH$_2$OH), 0.06 (s, 3 H, OSi-*t*-Bu(CH_3)$_2$), 0.04 (s, 3 H, OSi-*t*-Bu(CH_3)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 78.19, 66.33, 39.20, 31.49, 26.04, 20.28, 19.11, 18.31, 11.90, 5.60, 5.40. Anal. Calcd for $C_{13}H_{30}O_2Si$: C, 63.35; H, 12.27. Found: C, 63.46; H, 12.40.

(2S*,3S*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-2,4-dimethylpentan-1-ol: R_f = 0.55 (50% ether/hexane); IR (CCl_4) 3640, 3080, 2970, 2940, 2860, 1475, 1390, 1365, 1110, 1030, 910 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65–7.75 (m, 4 H, aromatic H), 7.35–7.45 (m, 6 H, aromatic H), 3.60 (dd, 1 H, J = 4.7, 2.2 Hz, C*H*OTBDPS), 3.43 (m, 1 H, C*H*HOH), 3.29 (m, 1 H, CH*H*OH), 1.83 (m, 2 H, C*H*(CH$_3$)$_2$ + C*H*(CH$_3$)CH$_2$OH), 1.12 (t, 1 H, J = 5.7 Hz, O*H*), 1.06 (s, 9 H, OSi-*t*-*Bu*Ph$_2$), 0.86 (d, 3 H, J = 6.7 Hz, CH(CH_3)$_2$), 0.83 (d, 3 H, J = 6.9 Hz, CH(CH_3)$_2$), 0.77 (d, 3 H, J = 6.8 Hz, CH(CH_3)CH$_2$OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.15, 136.12, 134.48, 134.08, 129.65, 129.50, 127.55, 127.35, 78.18, 66.00, 38.48, 32.30, 27.26, 19.76, 19.51, 19.29, 12.01. Anal. Calcd for $C_{23}H_{34}O_2Si$: C, 74.54; H, 9.25. Found: C, 74.54; H, 9.33.

(2S*,3R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-2-methyl-3-phenylpropan-1-ol: R_f = 0.65 (50% ether/hexane); IR (CCl_4) 3610, 3530, 3080, 2970, 2940, 2870, 1475, 1465, 1455, 1430, 1265, 1115, 1045, 1030 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15–7.70 (m, 15 H, aromatic H), 4.82 (d, 1 H, J = 3.9 Hz, C*H*OTBDPS), 3.43 (ddd, 1 H, J = 11.1, 8.9, 4.0 Hz, C*H*HOH), 3.26 (ddd, 1 H, J = 11.1, 7.3, 4.8 Hz, CH*H*OH), 2.00–2.10 (m, 2 H, CH$_3$C*H* + O*H*), 1.03 (s, 9 H, OSi-*t*-*Bu*Ph$_2$), 0.64 (d, 3 H, J = 7.0 Hz, CH_3CHCH$_2$OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.50, 136.02, 135.91, 133.75, 133.04, 129.83, 129.65, 127.73, 127.68, 127.39, 127.09, 78.15, 64.96, 42.60, 27.07, 19.40, 12.06. Anal. Calcd for $C_{26}H_{32}O_2Si$: C, 77.18; H, 7.97. Found: C, 77.08; H, 8.08.

(1S*,2S*)-2-(Hydroxymethyl)cyclohexanol: R_f = 0.15 (67% ether/hexane); IR (neat) 3360, 2940, 2860, 1450, 1095, 1065, 1040, 1020, 980 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.12 (br s, 1 H, C*H*OH), 3.75 (br s, 2 H, CH_2OH), 2.18 (br s, 1 H, O*H*), 2.09 (br s, 1 H, O*H*), 1.20–1.80 (m, 9 H, C*H*CH$_2$OH + 4CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 69.28, 65.64, 42.35, 32.68, 24.82, 23.48, 20.43. Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.22; H, 10.83.

(1S*,2S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-(hydroxymethyl)cyclohexane: R_f = 0.90 (50% ether/hexane); IR (neat) 3380, 2940, 2900, 2870, 1470, 1385, 1370, 1260, 1195, 1130, 1085, 1045, 1025, 915 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.03 (dt, 1 H, J = 5.7, 2.8 Hz, C*H*OTBS), 3.74 (m, 1 H, C*H*HOH), 3.50 (dt, 1 H, J = 10.2, 5.1 Hz, CH*H*OH), 2.19 (br s, 1 H, O*H*), 1.25–1.75 (m, 9 H, C*H*CH$_2$OH + 4 ring CH_2), 0.88 (s, 9 H, OSi-*t*-*Bu*(CH$_3$)$_2$), 0.05 (s, 6 H, OSi-*t*-Bu-(CH_3)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 70.21, 65.28, 43.68, 32.82, 25.77, 24.40, 24.30, 21.23, 17.99, −4.44, −5.16. Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 63.88; H, 11.55. Found: C, 63.94; H, 11.68.

(1R*,2R*)-3-[(Phenylmethyl)oxy]cyclohexanol: R_f = 0.25 (50% ether/hexane); IR (CCl_4) 3630, 2950, 2870, 1455, 1090, 1070, 1030, 975, 910 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.35 (m, 5 H, aromatic H), 4.52 (d, 1 H, J = 11.9 Hz, OCH_2Ph), 4.48 (d, 1 H, J = 11.9 Hz, OCH_2Ph), 4.07 (m, 1 H, C*H*O), 3.79 (m, 1 H, C*H*O), 1.30–2.00 (m, 9 H, O*H* + 4 ring CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 128.2, 127.3, 127.3, 73.9, 69.9, 66.9, 39.2, 34.2, 30.1, 19.0. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.61; H, 8.89.

(1R*,2R*)-3-[(*tert*-Butyldimethylsilyl)oxy]cyclohexanol: R_f = 0.60 (50% ether/hexane); IR (CCl_4) 3630, 3360, 2940, 2900, 2860, 1475, 1465, 1450, 1365, 1350, 1260, 1125, 1095, 1060, 1040, 975, 915 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.95–4.10 (m, 2 H, 2C*H*O), 1.25–1.80 (m, 9 H, O*H* + 4CH_2), 0.85 (s, 9 H, OSi-*t*-*Bu*(CH$_3$)$_2$), 0.04 (s, 3 H, OSi-*t*-Bu(CH_3)$_2$), 0.02 (s, 3 H, OSi-*t*-Bu(CH_3)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 67.59, 67.00, 42.79, 34.58, 33.68, 25.76, 18.88, 18.02. Anal. Calcd for $C_{12}H_{26}O_2Si$: C, 62.55; H, 11.37. Found: C, 62.70; H, 11.35.

(1R*,2S*)-1,2-Cyclohexanediol Diacetate. The phosphinite (198 mg, 0.70 mmol) was added as a 0.7-mL THF solution to a 20 °C mixture of Rh(PPh$_3$)$_3$Cl (712 mg, 0.77 mmol) and CB (504 mg, 4.20 mmol) in 20 mL of THF. The resulting red solution was stirred at 20 °C for 13 h and then subjected to a basic oxidative workup. The diol products were isolated by continuous extraction (CH$_2$Cl$_2$/H$_2$O). The less polar impurities present were removed by crude flash chromatography (50% EtOAc/hexane, then *i*-PrOH). The still impure diols were acetylated, and the resulting diacetates were flash chromatographed, yielding 78 mg (55%) of product. The ratio of isomers was determined by GLC analysis of the unpurified diacetates. For purpose of comparison, all six possible diacetylated cyclohexanediol isomers were prepared from the readily available diols. The major product of the reaction was identical (^{1}H and ^{13}C NMR spectra, GLC retention time, TLC) with (1*R**,2*S**)-1,2-cyclohexanediol diacetate: R_f = 0.40 (20% EtOAc/hexane); IR (neat) 2950, 1745, 1370, 1255, 1230, 1210, 1055 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.01 (dd, 2 H, J = 2.4, 5.9 Hz, C*H*OC*H*O), 2.06 (s, 6 H, COCH_3), 1.40–1.90 (m, 8 H, CH_2CH$_2$CH$_2$CH$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.41, 70.95, 27.58, 21.65, 21.14. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.99; H, 8.05. Found: C, 60.06; H, 8.01.

(1R*,3S*)-1,3-Cyclohexanediol Diacetate. CB (1.42 g, 11.9 mmol) was added dropwise over 3 min to a 20 °C mixture of the phosphinite (335 mg, 1.19 mmol) and Rh(PPh$_3$)$_3$Cl (1.21 g, 1.30 mmol) in 22 mL of THF (the temperature of the exothermic reaction was maintained at 20–25 °C during the addition). The resulting red solution was stirred at 20 °C for 20 h and then subjected to a basic oxidative workup. The diol products were isolated and acetylated as in the preceding experiment to yield 195 mg (82%) of product. The ratio of isomers was determined by GLC analysis of the unpurified diacetates. For purposes of comparison, all six possible diacetylated cyclohexanediol isomers were prepared from the readily available diols. The major product of the reaction was identical (^{1}H and ^{13}C NMR spectra, GLC retention time, TLC, IR spectrum) with (1*R**,3*S**)-1,3-cyclohexanediol diacetate: R_f = 0.35 (20% EtOAc/hexane); IR (neat) 2950, 2870, 1740, 1370, 1240, 1210, 1055, 1025, 980 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.74 (m, 2 H, 2C*H*O), 2.25 (m, 1 H, CHOC*H*HCHO), 1.80–2.10 (m, 9 H, 2COCH_3, 3 ring H), 1.20–1.50 (m, 4 H, ring H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.92, 70.30, 36.95, 30.59, 21.00, 19.91. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.99; H, 8.05. Found: C, 59.88; H, 7.94.

2,4-Tridecanediol Diacetate. CB (187 mg, 1.56 mmol) was added to a °C mixture of the phosphinite (59.8 mg, 0.16 mmol) and Rh(PPh$_3$)$_3$Cl (144 mg, 0.16 mmol) in 3.0 of mL THF. The resulting solution was stirred at 20 °C for 2 h and then subjected to a basic oxidative workup. The diol was isolated by extraction, and then it was acetylated. Flash chromatography afforded 25 mg (53%) of the diacetates. The regioselectivity (6:1) was determined from the integration of the protons α to the acetates in the ^{1}H NMR spectrum.

Stability of Phosphinites to Catecholborane. Cyclohexyl diphenylphosphinite (101 mg, 0.36 mmol) was added to 3 mL of THF/C_6D_6 (2:1) in an NMR tube (10-mm diameter). The ^{31}P NMR spectrum showed a singlet at δ 102. CB (70 mg, 0.58 mmol) was added to the solution, and a ^{31}P NMR spectrum was obtained immediately (acquisition occurred over a period 3–7 min after the addition of CB). The δ 102 resonance disappeared completely; it was cleanly replaced by a doublet at δ −44 (J = 215 Hz; collapsed to a singlet upon broadband decoupling; literature value for HPPh$_2$: δ −41, J = 214 Hz).[47] The ^{11}B NMR spectrum displayed a resonance for CB (δ 25.5, J = 190 Hz) and a singlet at δ 22.7 for the borate (literature value for (C$_6$H$_4$O$_2$)B(OEt) δ 23.0).[48]

Competition Experiment: Amide vs Silyl Ether (eq 20). CB (120 mg, 1.00 mmol) was added to a mixture of 4-[(*tert*-butyldimethylsilyl)oxy]-

(47) For a compilation of ^{31}P NMR chemical shifts, see: Crutchfield, M. M.; Dungan, C. H.; Letcher, J. H.; Mark, V.; Van Wazer, J. R. *P^{31} Nuclear Magnetic Resonance*; Wiley Interscience: New York, 1967.

(48) For a compilation of ^{11}B NMR chemical shifts, see: Noth, H.; Wrackmeyer, B. *Nuclear Magnetic Resonance Spectroscopy of Boron Compounds*; Springer-Verlag: New York, 1978.

cyclohexene (42.5 mg, 0.20 mmol), 4-[*N*-(phenylmethyl)carbamoyl]-cyclohexene (43.1 mg, 0.20 mmol), pentadecane (42.5 mg, 0.20 mmol), and $[Ir(cod)(PCy_3)(py)]PF_6$ (8.0 mg, 0.01 mmol) in 1.0 mL of $ClCH_2CH_2Cl$. The resulting homogeneous, pale yellow solution was stirred at 20 °C for 1.8 h and then subjected to a neutral oxidative workup. An aliquot was analyzed by GLC, which showed 93% recovered 4-[(*tert*-butyldimethylsilyl)oxy]cyclohexene and 3% of the derived alcohols and 36% recovered 4-[*N*-(phenylmethyl)carbamoyl]cyclohexene and 51% of the derived alcohol.

Solvent Effect on Stereoselectivity (Table X). CB (120 mg, 1.00 mmol) was added to a mixture of 1-(3-cyclohexenylcarbonyl)pyrrolidine (90 mg, 0.50 mmol) and catalyst (0.02 mmol) in 2.0 mL of solvent. The resulting homogeneous, pale yellow solution was stirred at 20 °C for 15 h and then subjected to a neutral oxidative workup. The unpurified reaction product was acetylated, and an aliquot was analyzed by GLC.

Hydroboration of *N*-(Phenylmethyl)-4-pentenamide. CB (192 mg, 1.60 mmol) was added to a solution of *N*-(phenylmethyl)-4-pentenamide (76 mg, 0.40 mmol) in 2.0 mL of $ClCH_2CH_2Cl$. The resulting mixture was stirred at 20 °C for 30 min and then cooled to 0 °C and stirred under vacuum for 25 min.[49] The reaction was then warmed to 20 °C, and $[Ir(cod)(PCy_3)(py)]PF_6$ (16.0 mg, 0.02 mmol) was added. The mixture immediately turned homogeneous, almost colorless. The solution was stirred at 20 °C for 40 min and then subjected to a neutral oxidative workup. The oxidized mixture was extracted (EtOAc/1 N NaOH), dried over $MgSO_4$, filtered, and concentrated. An aliquot was analyzed by GLC, which showed a 3:1 (primary:secondary) mixture of alcohols (compared with authentic products prepared independently by opening the relevant lactones with benzylamine). The alcohol products were isolated by flash chromatography, affording 17.2 mg (21%) of the secondary alcohol and 47.2 mg (57%) of the primary alcohol.

4-Hydroxy-*N*-(phenylmethyl)pentanamide: R_f = 0.20 (EtOAc); IR (neat) 3300, 2970, 2930, 1650, 1550, 1455, 1430, 1130, 1080 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25–7.40 (m, 5 H, aromatic H), 6.09 (br s, 1 H, N*H*), 4.42 (d, 2 H, *J* = 5.7 Hz, CH_2Ph), 3.84 (m, 1 H, C*H*OH), 2.38 (dt, 2 H, *J* = 2.3, 7.0 Hz, CH_2CO), 1.84 (m, 1 H, C*H*HCHOH), 1.71 (m, 1 H, CH*H*CHOH), 1.20 (d, 3 H, *J* = 6.2 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.34, 138.20, 128.72, 127.79, 127.52, 67.52, 43.76, 34.30, 33.18, 23.66; HRMS *m/z* calcd for $C_{12}H_{18}N_1O_2$ $(M + H)^+$ 208.1338, found 208.1346.

5-Hydroxy-*N*-(phenylmethyl)pentanamide: R_f = 0.15 (EtOAc); IR ($CHCl_3$) 3450, 3340, 3010, 2940, 1665, 1515, 1455, 1235 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25–7.40 (m, 5 H, aromatic H), 5.77 (br s, 1 H, N*H*), 4.46 (d, 2 H, *J* = 5.7 Hz, CH_2Ph), 3.66 (q, 2 H, *J* = 5.8 Hz, CH_2OH), 2.28 (t, 2 H, *J* = 7.1 Hz, CH_2CO), 1.55–1.85 (m, 5 H, $CH_2CH_2CH_2OH$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.12, 138.35, 128.61, 127.69, 127.39, 61.89, 43.54, 35.97, 31.95, 21.79. Anal. Calcd for $C_{12}H_{17}N_1O_2$: C, 69.54; H, 8.27. Found: C, 69.40; H, 8.25.

Acknowledgment. Support has been provided by the National Institutes of Health and the National Science Foundation. The NIH BRS Shared Instrumentation Grant Program (1 S10 RR01748-01A1) is acknowledged for providing NMR facilities. The authors wish to express their gratitude to Dr. Benjamin A. Anderson for his editorial efforts.

Supplementary Material Available: Details of selected experimental procedures and stereochemical proofs of the products derived from reactions illustrated in eq 9 and Table IX (4 pages). Ordering information is given on any current masthead page.

(49) It is necessary to remove H_2 from the reaction system prior to addition of the catalyst in order to minimize substrate hydrogenation.

Mechanistic Study of the Rhodium(I)-Catalyzed Hydroboration Reaction

David A. Evans,* Gregory C. Fu,[1a] and Benjamin A. Anderson[1b]

Contribution from the Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138. *Received December 13, 1991*

Abstract: The objective of this study has been to elucidate the mechanism of the rhodium(I)-catalyzed hydroboration process. Evidence that the reaction proceeds through a multistep pathway analogous to that of transition metal catalyzed olefin hydrogenation is presented. Deuterium labeling experiments reveal reversible elementary steps in the catalytic cycle; the level of reversibility is found to be substrate-dependent. Catalyst contamination through contact with adventitious oxidants has a pronounced effect on the reaction and appears to be the source of reported disparities involving product regioselection and deuterium labeling experiments.

In the preceding study,[2] the scope and synthetic applications of the transition metal catalyzed hydroboration reaction were presented. The objective of this companion investigation is to reveal some of the important mechanistic details of this process.

Fundamental mechanistic differences between the catalyzed hydroboration reaction and its uncatalyzed counterpart are manifested in the complementary chemo- and stereoselectivity of the two processes.[3] In their original report, Männig and Nöth suggested a mechanism for $Rh(PPh_3)_3Cl$-catalyzed hydroboration (Figure 1)[4] which is analogous to that proposed for other, more thoroughly investigated rhodium-catalyzed olefin addition reactions such as hydrogenation, hydrosilylation, and hydroformylation.[5] Support for this pathway was provided by their observation that adduct **1**, first isolated by Kono and Ito,[6] reacts stoichiometrically with olefins to afford hydroboration products.[4]

While significant effort has been focused on the catalyzed hydroboration reaction as a synthetic method,[2,3] few investigations have probed the mechanistic details of this process.[3,7-9] As a result, efforts to rationalize the unique behavior of the catalyzed process have been framed in the absence of a fundamental understanding of the elementary steps in the catalytic cycle. For

(1) (a) National Science Foundation Predoctoral Fellow. (b) National Institutes of Health Postdoctoral Fellow.

(2) Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.*, preceeding paper in this issue.

(3) For a recent review of the transition metal catalyzed hydroboration reaction, see: Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179–1191.

(4) Männig, D.; Nöth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878–879.

(5) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987.

(6) Kono, H.; Ito, K. *Chem. Lett.* **1975**, 1095–1096.

(7) For a preliminary account of this work, see: Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 2280–2282.

(8) Burgess, K.; Donk, W. A.; Kook, A. M. *J. Org. Chem.* **1991**, *56*, 2949–2951.

(9) For studies of related systems, see: (a) Oxidative addition of alkylboranes to Ir(I): Baker, R. T.; Ovenall, D. W.; Calabrese, J. C.; Westcott, S. A.; Taylor, N. J.; Williams, I. D.; Marder, T. B. *J. Am. Chem. Soc.* **1990**, *112*, 9399–9400. (b) Ir(I) model system for catalyzed hydroboration: Knorr, J. R.; Merola, J. S. *Organometallics* **1990**, *9*, 3008–3010. (c) Reactions of catecholborane with rhodium complexes: Westcott, S. A.; Taylor, N. J.; Marder, T. B.; Baker, R. T.; Jones, N. J.; Calabrese, J. C. *J. Chem. Soc., Chem. Commun.* **1991**, 304–305.

0002-7863/92/1514-6679$03.00/0