Transition-Metal-Promoted Hydroboration of Alkenes: A Unique Reversal of Regioselectivity

Terence C. Morrill,* Christopher A. D'Souza, Lu Yang, and Anthony J. Sampognaro

Department of Chemistry, Rochester Institute of Technology, Rochester, New York 14623

tcmsch@ritvax.isc.rit.edu

When hydroboration of 1-octene is carried out in the presence of catalytic amounts of rhodium trichloride followed by the usual oxidation (hydrogen peroxide in aqueous alkali), only minor proportions of 1-octanol (2.4%) are formed accompanied by very significant amounts of 2- (17.4%), 3- (36.9%), and 4-octanol (43.3%). These product compositions are obtained in good overall yield when the borane−THF complex is slowly added to a stirred solution of 1-octene in THF solvent containing the rhodium trichloride. Isomerization of 1-octene to 2-, 3-, and 4-octene in the presence of rhodium trichloride alone is far too slow to account for the foregoing results. The mechanism likely involves multiple and reversible addition/elimination of a Rh-activated B−H species across the double bonds.

Introduction

Transition-metal-catalyzed hydroborations have been studied extensively because of their synthetic utility.[1] While metals such as Li, Ni, La, Ru, Ir, and Ti[2] have been used with varying degrees of success, Rh(I) has remained the metal of choice for catalyzed hydroborations. In 1975, Kono and Ito[3] showed that $RhCl(PPh_3)_3$ (Wilkinson's catalyst), which was known to catalyze hydrogenation[4] and the hydrosilylation[5] of alkenes, undergoes oxidative addition when treated with catecholborane (CBH). However, the real impetus to the use of rhodium compounds to catalyze hydroborations was given by a very novel experiment by Männig and Nöth[6] in 1985. While, $RhCl(PPh_3)_3$-catalyzed addition of CBH to styrene has been shown to proceed with novel regio- and stereoselectivities,[7] aliphatic alkenes, under similar conditions,[8] yield products that are very similar to those obtained for the uncatalyzed reaction.[9]

The mechanism proposed for these reactions involves the oxidative addition of a B−H bond to the Rh(I) species, followed by alkene insertion into the Rh−H bond and subsequent C−B bond coupling.[6] The mechanism for the homogeneous hydrogenation has certainly been a model for Rh(I)-promoted hydroborations. Deuterium labeling experiments using 0.1 equiv of catecholborane-*d* revealed the presence of the label in the recovered starting material, indicating the reversibility of the migratory insertion of alkenes into Rh−H(D) bonds.[10] These labeling experiments also revealed the dramatic effect on the outcome of the reaction, as a consequence of catalyst oxidation.

Evans et al.[10a] obtained small quantities of isomeric octanols during the [Rh(nbd)(diphos-4)]BF₄-catalyzed hydroboration of *trans*-4-octene using CBH and only 4-octanol when $RhCl(PPh_3)_3$ was employed. In stark contrast, Srebnik and Pereira[11] obtained 100% terminal octyl pinacolboronate during the $RhCl(PPh_3)_3$-catalyzed hydroboration of *trans*-4-octene using pinacolborane (PBH), a result analogous to the hydrozirconation[12] of alkenes. Westcott et al.[13a] observed similar reversals of regioselectivity during the rhodium-catalyzed hydroboration of allylbenzene. These results clearly reveal the sensitivity of the elementary steps of the hydroboration catalytic cycle to the substrate, hydroborating agent, and catalyst.

(1) For reviews, see: (a) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179. (b) Evans, D. A.; Fu, G. C.; Muci, A. R. In *Advances in Catalytic Processes*; Doyle, M. P., Ed.; JAI: Greenwich, CT, 1995; Vol. 1, pp 95−121. (c) Pelter, A.; Beletskaya, I. *Tetrahedron* **1997**, *53*, 4957.

(2) For transition-metal-catalyzed hydroborations other than rhodium, see the following: (a) Ni: Kabalka, G. W.; Narayana, C.; Reddy, N. K. *Synth. Commun.* **1994**, 24, 1019. (b) Ru: Burgess, K.; Jaspars, M. *Organometallics* **1993**, *12*, 4197. (c) La: Harrison, K. N.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 9220. (d) Li: Arase, A.; Nunokawa, Y.; Masuda, Y.; Hoshi, M. *J. Chem. Soc., Chem. Commun.* **1991**, 205. (e) Ti: Hartwig, J. F.; He, X. *J. Am. Chem. Soc.* **1996**, *118*, 1696. (f) Ir: Sowa, J. R.; Brinkman, J. A.; Nguyen, T. T. *Org. Lett.* **2000**, *2*, 981.

(3) Kono, H.; Ito, K.; Nagai, Y. *Chem. Lett.* **1975**, 1095.

(4) Wilkinson, G.; Young, J. F.; Jardine, F. H.; Osborn, J. A. *J. Chem. Soc. (A)* **1966**, 1711.

(5) Haszeldine, R. N.; Parish, R. V.; Parry, D. J. *J. Organomet. Chem.* **1967**, *9*, 13.

(6) Männig, D.; Nöth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878; U. S. Patent No. 4 731 463, 1988.

(7) For a study of the selectivity of hydroborartion of vinylarenes with rhodium catalysts, see: (a) Hayashi, T.; Matsumoto, Y.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 3426. (b) Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 2280. (c) Suzuki, A.; Satoh, M.; Miyaura, N. *Tetrahedron Lett.* **1990**, *31*, 231. (d) Dai, L.; Zhang, J.; Lou, B.; Guo, G. *J. Org. Chem.* **1991**, *56*, 1670. (e) Hayashi, T.; Matsumoto, Y.; Ito, Y. *Tetrahedron: Asymmetry* **1991**, *2*, 601. (f) Burgess, K.; van der Donk, W. A.; Jarstfer, M. B.; Ohlmeyer, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 6139.

(8) (a) Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1988**, *110*, 6917. (b) Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1992**, *114*, 6671.

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

(10) (a) Evans, D. A.; Fu, G. C.; Anderson, B. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679. (b) Burgess, K.; van der Donk, W. A.; Marder, T. B.; Westcott, S. A.; Baker, T. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 9350. (c) Burgess, K.; Donk, W. A.; Kook, A. M. *J. Org. Chem.* **1991**, *56*, 2949, 7360.

(11) (a) Srebnik, M.; Pereira, S. *J. Am. Chem. Soc.* **1996**, *118*, 909. (b) Srebnik, M.; Pereira, S. *Tetrahedron Lett.* **1996**, *37*, 3283.

(12) Hart, D. W.; Schwartz, J. *J. Am. Chem. Soc.* **1974**, *96*, 8115.

(13) (a) Westcott, S. A.; Blom, H. P.; Marder, T. B.; Baker, R. T. *J. Am. Chem. Soc.* **1992**, *114*, 8863. (b) Westcott, S. A.; Blom, H. P.; Marder, T. B.; Baker, R. T.; Calabrese, J. C. *Inorg. Chem.* **1993**, *32*, 2175.

Although most of the rhodium-catalyzed hydroborations have used Rh(I) compounds, Rh(II)-catalyzed hydroborations have been investigated and shown to bring about a reversal of regioselectivity.[14] A combination of $NaBH_4$, O_2, and rhodium(III) porphyrin has also been used to bring about hydroboration−oxidation of alkenes.[15]

With this background, we decided to undertake a systematic study of the Rh(III)-catalyzed hydroboration of alkenes. In early studies with 1-octene, we used the Blum[16] conditions (RhCl₃−Aliquat 336, CH_2Cl_2 as the solvent, CBH) except that water could not be used due to the significant hydrolytic reactivity of the hydroborating agent. Later, we substituted BH_3−THF for CBH (since it afforded a much cleaner workup), and we usually found Aliquat 336 to be unnecessary. Surprisingly, analysis of the product mixture using a HP 6890-5873 GC-MS system, 60 m capillary column, revealed that it was indeed a mixture of 1-, 2-, 3-, and 4-octanol, with octane and octanones as side products (eq 1).

$$(1)$$
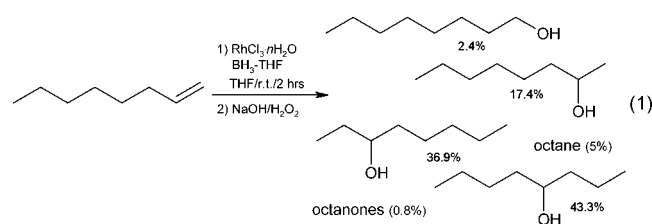
Results and Discussion

Transition-Metal-Promoted Hydroboration of Alkenes. Hydroboration of 1-octene proceeds with a unique regioselectivity, 1-octanol being the minor product and traces of 2-, 3-, and 4-octanones being produced. In most cases, alkene hydrogenation was about 2−7%. Yields of the isolated octanols were in the range of 65−75%. Solubilization of the $RhCl_3 \cdot nH_2O$ in the solvent seemed to be of considerable importance. A faster reaction and a higher percentage of 4-octanol always accompanied increased solubility. $RhCl_3 \cdot nH_2O$ was most soluble in THF, followed by diethyl ether, methylene chloride, and dioxane. The data (Table 1) suggest that regioselectivity is dependent on the solubility of the catalyst. Aliquat 336 worked very well as a phase transfer catalyst, except that 1-chloro octane (5.3%) was an undesired side product.

A similar reversal of regioselectivity was observed during the hydroboration of 1-octene in the presence of catalytic amounts of $RhBr_3 \cdot nH_2O$, $RhCl(PPh_3)_3$, [RhCl-(COD)]₂, $RuCl_3 \cdot nH_2O$, and $IrCl_3 \cdot nH_2O$ (Table 2). There is a clear indication that the reversed regioselectivity is dependent on the transition metal, its oxidation state, and the ligands surrounding it.

What impressed us most was the fact that, no matter which isomeric octene one starts with, the product ratio of the isomeric octanols follows a definite trend (Table

(14) (a) Doyle, M. P.; Brandes, B. D.; Kazala, A. P.; Pieters, R. J.; Jarsfter, M. B.; Watkins, L. M.; Eagle, C. T. *Tetrahedron Lett.* **1990**, *31*, 6613. (b) Doyle, M. P.; Devora, G. A.; Nefedov, A. O.; High, K. G. *Organometallics* **1992**, *11*, 549. (c) Doyle, M. P.; Westrum, L. J.; Protopopova, M. N.; Eismont, M. Y.; Jarstfer, M. B. *Mendeleev Commun.* **1993**, *3*, 81.

(15) Aoyama, Y.; Tanaka, Y.; Fujisawa, T.; Watanabe, T.; Toi, H.; Ogoshi, H. *J. Org. Chem.* **1987**, *52*, 2555.

(16) RhCl₃−Aliquat 336 was used under phase transfer conditions for the room-temperature reduction of olefins, acetylenes, and arenes. (a) Blum, J.; Amer, I.; Zoran, A.; Sasson, Y. *Tetrahedron Lett.* **1983**, *24*, 4139. (b) Blum, J.; Amer, I.; Bravdo, T. *Tetrahedron Lett.* **1987**, *28*, 1321.

Table 1. Effect of Solvent on the Regioselectivity of the $RhCl_3 \cdot nH_2O$-Promoted Hydroboration of 1-Octene with BH_3−THF[a]

solvent	1-ol	2-ol	3-ol	4-ol
THF	2.4	17.4	36.9	43.3
ether	1.5	21.7	39.1	37.7
CH_2Cl_2	11.2	36.2	49.4	3.2
CH_2Cl_2 + A336	2.7	18.7	38.0	40.6
dioxane	38.0	27.6	32.0	2.4

[a] 10 mL of the solvent was used. 1-Octene/$RhCl_3 \cdot nH_2O$/BH_3−THF = 3.19/0.048/3 mmol.

Table 2. Effect of Catalyst on the Hydroboration of 1-Octene with BH_3−THF in THF[a]

catalyst	1-ol	2-ol	3-ol	4-ol
$RhCl_3 \cdot nH_2O$	2.4	17.4	36.9	43.3
$RhBr_3 \cdot nH_2O$	7.4	24.2	41.7	26.7
$RhCl(PPh_3)_3$	16.9	27.3	39.4	16.4
[RhCl(COD)]₂	45.2	21.3	28.1	5.4
$RuCl_3 \cdot nH_2O$	42.6	20.2	27.8	9.4
$IrCl_3 \cdot nH_2O$	75.5	10.7	9.8	4.0

[a] 1-Octene/catalyst/BH_3−THF = 0.5 mL/10 mg/3 mL.

Table 3. $RhCl_3 \cdot nH_2O$-Promoted Hydroboration of Isomeric Octenes with BH_3−THF in THF[a]

olefin	1-ol	2-ol	3-ol	4-ol
1-octene	2.4	17.4	36.9	43.3
trans-2-octene	1.8	18.8	37.1	42.3
trans-4-octene	2.4	16.3	35.2	46.2
trans-4-octene + 1-octene	2.3	16.6	35.6	45.5

[a] Isomeric octene/$RhCl_3 \cdot nH_2O$/BH_3−THF = 3.19/0.048/3 mmol.

3). It appears as if all the reactions proceed through a common set of processes, thus yielding essentially the same product ratio.

The order in which the reactants are mixed and the rate of addition of BH_3−THF have a considerable effect on the product ratios. Reversing the order in which the reactants are normally mixed, that is, adding 1-octene into the rhodium compound−borohydride reagent mixture, gave us product ratios that were comparable with classical (uncatalyzed) hydroboration. Fast addition of BH_3−THF decreased the yields of 4-, 3-, and 2-octanols considerably (Table 4).

It was also observed that, trace amounts of water in the reaction mixture increased the percentage of octane considerably (>15%). The $RhCl_3 \cdot nH_2O$-promoted hydroboration of 1-heptene (Table 5) and allylbenzene (Table 6) showed a similar reversal of regioselectivity. However, the reaction with 3,3-dimethyl-1-butene (Table 7) and styrene (Table 8) apparently yielded the same product ratio as the uncatalyzed reaction.

Role and Fate of the Catalyst. The role, efficiency, and fate of the catalyst were investigated by modifying

Table 4. Effect of Varying Reaction Conditions on the Regioselectivity of the RhCl₃·nH₂O-Promoted Hydroboration of 1-Octene with BH₃−THF

conditions	1-ol	2-ol	3-ol	4-ol
uncatalyzed[a]	92.8	7.1	0.1	
reverse-1[b,f]	93.8	6.2		
reverse-2[c,f]	93.1	6.9		
fast[d,f]	83.2	9.7	6.4	0.7
slow[e,f]	2.4	17.4	36.9	43.3

[a] 1-Octene/BH₃−THF = 3.19/2 mmol. [b] BH₃−THF was added to a solution of RhCl₃·nH₂O in THF, and the resultant solution was treated with 1-octene. [c] BH₃−THF was added to 1-octene in THF followed by the addition of RhCl₃·nH₂O to the resultant solution. [d] BH₃−THF was added very fast within 10 min. [e] BH₃−THF was added very slowly into a solution of 1-octene and RhCl₃·nH₂O in THF. [f] 1-Octene/RhCl₃·nH₂O/BH₃−THF = 3.19/0.048/3 mmol.

Table 5. Hydroboration of 1-Heptene with BH₃−THF in THF

	1-ol	2-ol	3-ol	4-ol
uncatalyzed[a]	91.8	7.9	0.3	
catalyzed[b]	2.2	32.0	52.1	13.7

[a] 1-Heptene/BH₃−THF = 3.55/2 mmol. [b] 1-Heptene/RhCl₃·nH₂O/BH₃−THF = 3.55/0.048/3 mmol.

Table 6. Hydroboration of Allylbenzene with BH₃−THF in THF

	1	2	3
uncatalyzed[a]	90.0	10.0	
catalyzed[b]	1.8	15.3	82.9

[a] Allylbenzene/BH₃−THF = 3.77/2 mmol. [b] Allylbenzene/RhCl₃·nH₂O/BH₃−THF = 3.77/0.048/3 mmol.

Table 7. Hydroboration of 3,3-Dimethyl-1-butene with BH₃−THF in THF[a]

	1	2
uncatalyzed[b]	87.4	12.6
catalyzed[c]	87.8	12.2

[a] Starting material contained about 95% of 3,3-dimethyl-1-butene. [b] 3,3-Dimethyl-1-butene/BH₃−THF = 3.88/2 mmol. [c] 3,3-Dimethyl-1-butene/RhCl₃·nH₂O/BH₃−THF = 3.88/0.048/3 mmol.

the experimental procedure. Generally, the alkene (0.5 mL) and catalyst (10 mg) in THF were stirred in an atmosphere of dry nitrogen for 15 min. This was followed by a very slow dropwise (about 0.3 mL) addition of BH₃−THF during the first 30 min. The remainder BH₃−THF (2.7 mL) was added over the next 30 min, and the hydroboration was allowed to proceed for an additional 1 h, followed by basic oxidative workup. However, if the

Table 8. Hydroboration of Styrene with BH₃−THF in THF

	1	2
uncatalyzed[a]	82	18
catalyzed[b]	83	17

[a] Styrene/BH₃−THF = 4.36/2 mmol. [b] Styrene/RhCl₃·nH₂O/BH₃−THF = 4.36/0.048/3 mmol.

order in which the reactants were added was reversed, the reaction proceeded with the regioselectivity of an uncatalyzed reaction. Even the fast adddition of BH₃−THF changed the product ratio considerably. Elemental rhodium was obtained as a black residue at the end of each reaction.[13b,17]

Although RhCl₃·nH₂O has been extensively used as an effective catalyst for the isomerization of alkenes,[18,19] it failed to bring about sufficiently extensive isomerization of 1-octene in THF at room temperature, to account for the unusual internal alcohol formation reported herein.

An understanding of the reaction parameters responsible for this unique reversal of regioselectivity is now at hand. We believe that the role of the catalyst is to bring about the isomerization of an alkene, and its efficiency depended upon its generation and ultimate destruction. This was confirmed when the analysis of the reaction mixture carried out using a small amount of BH₃−THF [1-octene/RhCl₃·nH₂O/BH₃−THF = 3.19/0.048/0.3 mmol] revealed the presence of 1-octene (0.6%), isomeric internal octenes (87.0%), octane (6.6%), and isomeric octanols (5.8%). The catalyst generated in situ by the reaction of RhCl₃·nH₂O with catalytic amounts of BH₃−THF produces a rhodium hydride (Rh−H) or dihydride species, which is capable of isomerizing double bonds.[20] Consequently, excess BH₃−THF hydroborates these isomeric alkenes in the usual fashion to yield varying ratios of isomeric organoboranes. The dihydride, which is a catalyst precursor for the hydrogenation reaction, may be responsible for the reduction of the alkenes.[4]

We accept the mechanism that was proposed by Männig and Nöth,[6] which has been supported by Evans[10a] and Burgess.[10b] However, we believe that in our experiments alkene isomerization, caused by olefin insertion (into the Rh−H bond) followed by β-hydride elimination,

(17) (a) Brown, H. C.; Brown, C. A. *J. Am. Chem. Soc.* **1962**, *84*, 1493. (b) Glavee, G. N.; Klabunde, K. J.; Sorensen, C. M.; Hadjipanayis, G. C. *Inorg. Chem.* **1993**, *32*, 474. (c) Fehlner, T. P. *Contemporary Boron Chemistry*; Davidson, M. G., Hughes, A. K., Marder, T. B., Ed.; The Royal Society of Chemistry: 2000, Vol. 1, pp 254−262.

(18) (a) Grieco, P. A.; Mugio, N.; Marinovic, N.; Ehmann, W. J. *J. Am. Chem. Soc.* **1976**, *98*, 7102. (b) Barton, D. H. R.; Patin, H.; Andrieux, J. *J. Chem. Soc., Perkin Trans. I* **1977**, 359. (c) Paquette, L. A.; Fristad, W. E.; Dime, D. S.; Bailey, T. R. *J. Org. Chem.* **1980**, *45*, 3017. (d) Blum, J.; Zoran, A.; Sasson, Y. *J. Mol. Catal.* **1981**, *11*, 293. (e) Mehta, G.; Murthy, A. N. *J. Org. Chem.* **1987**, *52*, 2875. (f) Paquette, L. A.; Romine, J. L.; Lin, H.-S.; Wright, J. *J. Am. Chem. Soc.* **1990**, *25*, 9284. (g) Blum, J.; Sasson, Y.; Setty-Fichman, M.; Eisen, M. *Tetrahedron Lett.* **1994**, *35*, 781.

(19) (a) Cramer, R. *J. Am. Chem. Soc.* **1966**, *88*, 2272. (b) Harrod, J. F.; Chalk, A. J. *J. Am. Chem. Soc.* **1966**, *88*, 3491. (c) Cramer, R. *J. Am. Chem. Soc.* **1967**, *89*, 1633.

(20) (a) Abley, P.; McQuillin, F. J. *Discuss. Faraday Soc.* **1966**, *46*, 31. (b) Hudson, B.; Taylor, P. C.; Webster, D. E.; Wells, P. B. *Discuss. Faraday Soc.* **1966**, *46*, 37. (c) Schrock, R. R.; Osborn, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 2134.

occurs at a much more rapid rate compared to reductive elimination to give the C−B bond. The ratio of the alkenes formed depends on their relative stabilities. It is these isomeric alkenes that subsequently get hydroborated in the classical fashion.

Thus, the mechanism involves both a rhodium hydride species as well as double bond rearrangement controlled by thermodynamic stability. The latter was supported by the fact that styrene and 3,3-dimethyl-1-butene cannot undergo double-bond rearrangement, thus giving mainly primary (anti-Markovnikov addition) organoboranes arising from terminal alkenes.

In situ catalyst generation via slow addition of BH_3-THF allows for the fine-tuning of the isomerization aptitude of the catalyst, resulting in a high degree of reversal of regioselectivity in the overall reaction. The formation of the ketones may be due to the rhodium-catalyzed formation of vinylboranes, which presumably arise via alkene insertion into the Rh−B bond, followed by β-hydride elimination.[21]

Conclusions

Unlike all the previously reported rhodium-catalyzed hydroborations of alkenes, the results reported herein reveal a unique reversal of regioselectivity. The combination of $RhCl_3\cdot nH_2O$ and BH_3-THF offers an excellent route for the one-pot synthesis of isomeric internal organoboranes, starting with a terminal alkene. Proper control of in situ catalyst generation and choice of solvent can be used with some success to enhance the yield of the desired isomeric organoborane. The rapid reversibility of alkene insertion/β-hydride elimination in the mechanism thus has a greater control on the regioselectivity than was previously thought. We believe that these results will lead to the synthesis of numerous new organic molecules via established organoborane chemistry.

The nearly identical product ratios of the isomeric alcohols, irrespective of the isomeric octene starting material, suggest that the reactions in all these cases proceed through common equilibria or transition states.

BH_3-THF is the preferred hydroborating agent since it affords a much cleaner workup when compared to catecholborane.

Investigations using deuterium-labeled reagents and isomerization studies are in progress.

(21) (a) Brown, J. M.; Lloyd-Jones, G. C. *J. Chem. Soc., Chem. Commun.* **1992**, 710. (b) Westcott, S. A.; Marder, T. B.; Baker, R. T. *Organometallics* **1993**, *12*, 975. (c) Westcott, S. A.; Marder, T. B.; Nguygen, P.; Baker, R. T.; Calabrese, J. C. *J. Am. Chem. Soc.* **1993**, *115*, 4367.