The Rhodium-Catalyzed Hydroboration of Olefins: A Mechanistic Investigation

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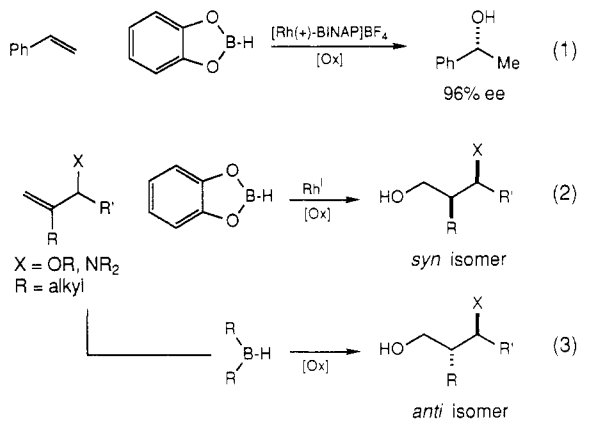
Summary: Labeling studies carried out on the rhodium-catalyzed olefin hydroboration reaction reveal that the degree of reversibility of the elementary steps in the catalytic cycle is highly substrate dependent. The implications of these observations are discussed.

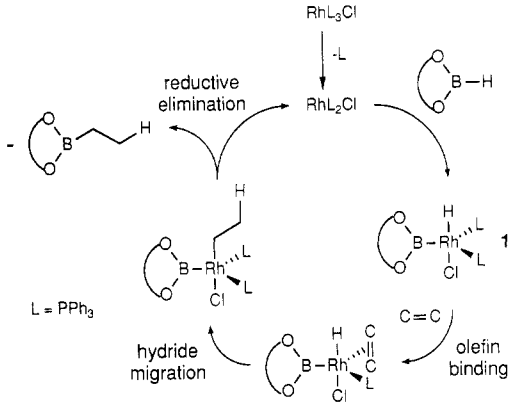
Significant interest has recently been generated by the potential applications of transition-metal-catalyzed alkene hydroboration to organic synthesis.[1-4] The stereochemical aspects of this process dealing with both reaction enantioselection (eq 1)[3] and diastereoselection (eq 2)[2] have received particular attention from a number of research groups. From the results reported to date, the catalyzed and uncatalyzed processes are quite complementary. Important differences between the two reactions include instances of inverted reaction regioselection, as exemplified in the uncatalyzed hydroboration of styrene which affords the terminal alcohol, and inverted diastereoselection in the hydroboration of 1,1-disubstituted allylic alcohol derivatives (eq 2 vs eq 3).[2,5]



Burgess and Ohlmeyer[2c] have recently proposed a model to explain the stereoselection observed in the hydroboration of chiral allylic alcohol and amine derivatives wherein they assume that binding of the diastereotopic faces of the alkene to rhodium is the stereochemistry-determining step of this multistep transformation. In this paper, we report labeling studies which demonstrate that this reaction is in fact kinetically complex and that the analysis of the stereochemical course of these reactions will prove to be highly substrate dependent.

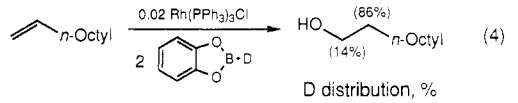
Mannig and Noth have suggested a mechanism for olefin hydroboration (Scheme I),[1,6] which is analogous to that

Scheme I



proposed for more thoroughly investigated rhodium-catalyzed hydrometalation reactions such as hydrogenation, hydrosilation, and hydroformylation.[7] We have examined the $Rh(PPh_3)_3Cl$[8]-catalyzed hydroboration of alkenes with deuteriocatecholborane in order to gain insight into the degree of reversibility of the olefin binding and hydride migration steps.[9-12]

Case 1: 1-Decene. Catalyzed hydroboration of 1-decene with deuteriocatecholborane (2% catalyst, THF, 20 °C), followed by oxidation, provides the terminal alcohol with 99:1 regioselectivity (eq 4). *However, regiospecific incorporation of deuterium at C_2 of the isolated 1-decanol is not observed.* Instead, a significant proportion of the deuterium in the product alcohol is found at the hydroxyl-bearing carbon, a result that clearly indicates that the reaction is not as straightforward as Scheme I suggests.



Nonregiospecific incorporation of deuterium can be accommodated within the Mannig–Noth mechanism if one assumes that the hydride migration step is *reversible*. To obtain a clearer picture of the degree of reversibility of the elementary steps in the catalytic cycle, the hydroboration of 1-decene under conditions simulating a reaction run to partial conversion was examined (0.1 equiv borane, 0.2% catalyst, THF, 20 °C, eq 5).[13] *It was found that deuterium is incorporated not only in the product alcohol,*

(1) Mannig, D.; Noth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878–879.

(2) (a) Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1988**, *110*, 6917–6918. (b) Burgess, K.; Ohlmeyer, M. J. *Tetrahedron Lett.* **1989**, *30*, 395–398. (c) Burgess, K.; Ohlmeyer, M. J. *Tetrahedron Lett.* **1989**, *30*, 5857–5860, 5861–5864.

(3) (a) Burgess, K.; Ohlmeyer, M. J. *J. Org. Chem.* **1988**, *53*, 5178–5179. (b) Satoh, M.; Nomoto, Y.; Miyaura, N.; Suzuki, A. 35th Symposium on Organometallic Chemistry, Osaka, Japan; November 5–6, 1988; p 202. (c) Hayashi, T.; Matsumoto, Y.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 3426–3428. (d) Sato, M.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1990**, *31*, 231–234.

(4) (a) Sato, M.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1989**, 1405–1408. (b) Satoh, M.; Nomoto, Y.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1989**, *30*, 3789–3792.

(5) Still, W. C.; Barrish, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 2487–2489.

(6) Complex 1, formed upon treatment of Wilkinson's catalyst with excess catecholborane, has been characterized: Kono, H.; Ito, K. *Chem. Lett.* **1975**, 1095–1096. We, as well as Mannig and Noth (ref 1), have independently confirmed this observation.

(7) 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.

(8) Use of $[Rh(nbd)(diphos\text{-}4)]BF_4$ as catalyst provides qualitatively similar results. For the sake of brevity, only the data for Wilkinson's catalyst are discussed.

(9) We have demonstrated that reductive elimination of the alkylborane is irreversible.

(10) The deuterium distribution of the reaction mixture was analyzed by 46-MHz ^2H NMR spectroscopy.

(11) We have not addressed the issue of the reversibility of oxidative addition of catecholborane to rhodium under the reaction conditions.

(12) Olefin hydrogenation is also observed in some of these reactions.

(13) Cases 2–4 were run under the same conditions. Only the deuterium-containing products are depicted.

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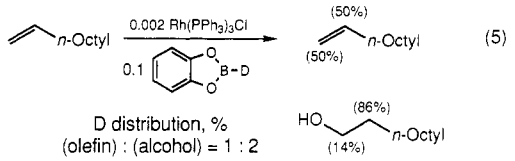
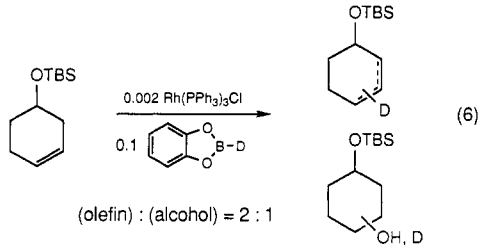


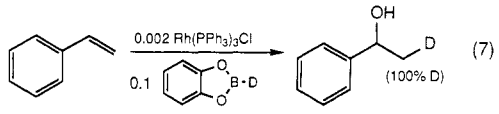
but in the recovered alkene as well. The presence of deuterium in the recovered 1-decene[14] demonstrates that migration (to form either the primary or the secondary rhodium alkyl) *and* olefin binding are reversible (Scheme II), although the level of incorporation (about one-third of all deuterium) indicates that these two steps are not both proceeding rapidly relative to reductive elimination.

The incorporation of deuterium at C_1 in both 1-decene and 1-decanol sheds light on the origin of the high primary to secondary alcohol selectivity (99:1) that is observed in this reaction. The presence of significant quantities of deuterium at C_1 establishes that migration of deuteride to the rhodium-bound alkene is only moderately regioselective, and in fact it is the reversibility of this step (*not* its regioselectivity), coupled with a high preference for reductive elimination of [boron–primary alkyl] rather than [boron–secondary alkyl],[15] that permits the nearly exclusive generation of the terminal alkylborane.

Case 2: 4-((*tert*-Butyldimethylsilyl)oxy)cyclohexene. *Reversible hydride migration and reversible olefin binding to catalyst are also evident in the hydroboration of the TBS ether of 4-hydroxycyclohexene (eq 6).* The deuterium-bearing allylic *tert*-butyldimethylsilyl ether is a significant byproduct of the reaction.

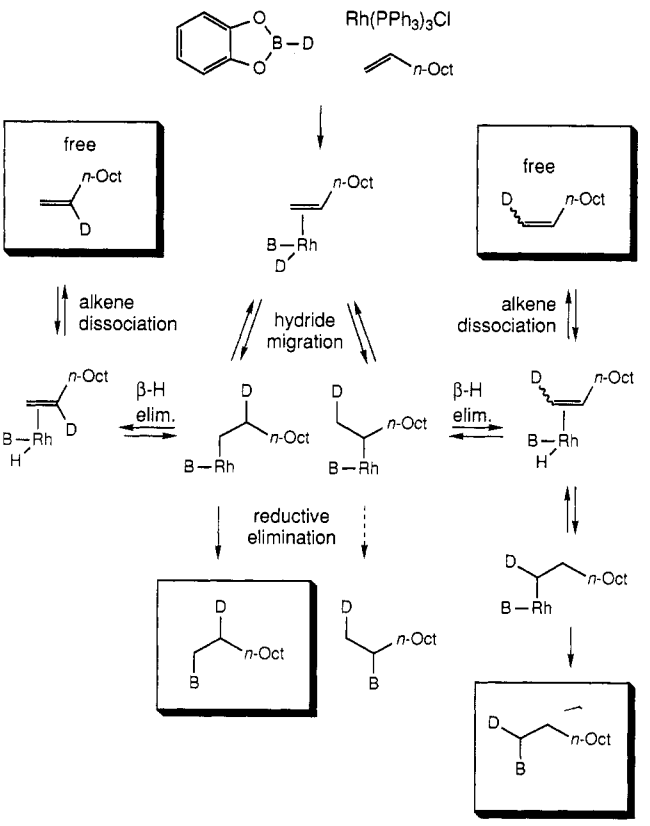


Case 3: Styrene. Hayashi and Ito have reported that styrene derivatives undergo highly enantioselective catalyzed hydroboration to generate nonracemic secondary alcohols (eq 3).[16] In contrast to cases 1 and 2, *labeling studies of the hydroboration of styrene provide no evidence for reversible olefin binding and hydride migration; reaction of excess olefin with deuteriocatecholborane under the standard conditions affords only one deuterium-containing product, 1-phenyl-2-deuterioethanol (eq 7).* This observation is inconsistent with olefin binding and hydride migration both being reversible for this substrate. The lack of deuterium incorporation in the benzylic position requires that the alcohol regioselectivity be determined exclusively in the migration step, not in the reductive elimination, in sharp contrast to 1-decene.

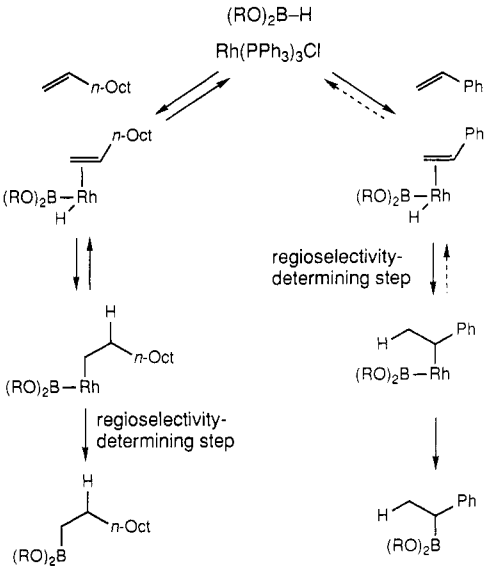


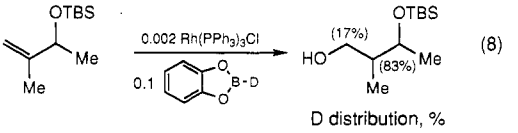
Case 4: 2-Methyl-3-((*tert*-butyldimethylsilyl)oxy)but-1-ene. Hydroboration of this 1,1-disubstituted olefin with deuteriocatecholborane provides yet another qualitatively distinct result (eq 8). *The incorporation of deuterium α to the hydroxyl group of the product alcohol indicates that hydride migration to form the tertiary rhodium alkyl occurs reversibly under the reaction conditions.* When coupled with the lack of deuterium in the recovered starting material, this observation also implies that binding to the catalyst is not highly reversible for this olefin. Preferential β-hydride elimination from one of the

Scheme II



Scheme III





(14) A small quantity of deuterated internal alkene is also produced.
(15) These data are consistent with our observation that metal-catalyzed hydroboration of an internal alkene can afford significant quantities of primary alcohol.
(16) For references to an analogous turnover in regioselectivity in the rhodium-catalyzed hydroformylation of styrenes, see: Doyle, M. M.; Jackson, W. R.; Perlmutter, P. *Tetrahedron Lett.* **1989**, *30*, 5357–5360.

two diastereotopic methyl groups of the tertiary rhodium alkyl intermediate is suggested by the absence of deuterium incorporation in the methyl group β to the hydroxyl.

Caution is unquestionably warranted when extrapolating to a much broader range of compounds those conclusions drawn from careful study of one particular substrate for a given reaction. We have found that the relative rates of the elementary steps in the hydroboration catalytic cycle are highly substrate dependent.[17] Thus, the alcohol regioselectivity-determining step is different for 1-decene and styrene (Scheme III).

An important prologue to the development of meaningful rationales for observed selectivity is the elucidation of the selectivity-determining step for the specific reaction of interest. Relevant in this regard are the many models proposed in order to rationalize diastereoselective addition reactions to chiral olefins. Frequently, the tacit assumption is made that the product stereochemistry is defined by irreversible complexation of the alkene to the reagent, as in the recent case of Burgess and Ohlmeyer in their analysis of the rhodium-catalyzed hydroboration reaction.[2c] Clearly, this need not be the case for multistep processes (e.g., oxymercuration[18] or hydrogenation[19]). Our observation that olefin binding to the rhodium catalyst, as well as subsequent hydride migration, is indeed reversible for certain substrates undergoing catalyzed hydroboration serves to underscore this caveat. Further studies probing the mechanism of the rhodium-catalyzed olefin hydroboration reaction are in progress.

Acknowledgment. Support has been provided by the National Institutes of Health and Merck. The NIH BRS Shared Instrumentation Program 1 S10 RR01748-01A1 is acknowledged for providing NMR facilities.

(17) For labeling studies of other rhodium-catalyzed olefin hydrometalation reactions, see: (a) Hydroformylation (leading references): Lazzaroni, R.; Uccello-Barretta, G.; Benetti, M. *Organometallics* **1989**, *8*, 2323-2327. (b) Hydrosilation: Ryan, J. W.; Speier, J. L. *J. Am. Chem. Soc.* **1964**, *86*, 895-898. Selin, T. G.; West, R. *J. Am. Chem. Soc.* **1962**, *84*, 1863-1868.

(18) For leading references, see: Chamberlin, A. R.; Mulholland, R. L., Jr.; Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 672-677.

(19) For example, see: Halpern, J. *Science* **1982**, *217*, 401-407.

Preparation of the 5,6-Arene Oxide of 3,3',4,4'-Tetrachlorobiphenyl. Decarboxylative Elimination as an Effective Last Step

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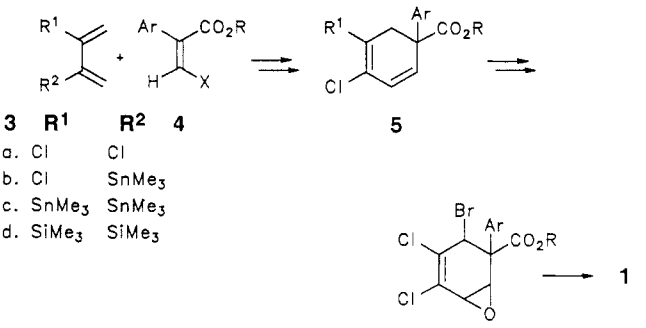
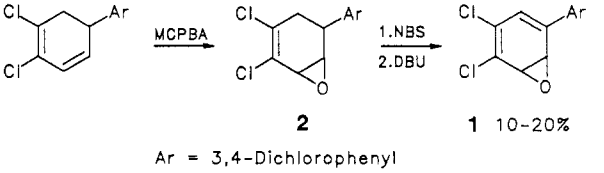
Summary: The 5,6-arene oxide of 3,3',4,4'-tetrachlorobiphenyl was prepared by a sequence in which two of the double bonds were introduced by decarboxylations. The first involved a Barton decarboxylative selenation and selenoxide elimination, the second a decarboxylative elimination.

The principal challenge in the synthesis of arene oxides is the introduction and manipulation of functionality in molecules that are on the verge of irreversible aromatization. This problem is exacerbated with halogenated biphenyl oxides, of interest as potential metabolites of polychlorinated biphenyls,[1] since highly halogenated intermediates have unusual reactivities and additional opportunities for aromatization compared to hydrocarbon analogues. Traditionally the synthesis of arene oxides, including halogenated ones,[2] has proceeded from a diene by epoxidation and bromination, with dehydrobromination as the final double bond forming step.[3] This method when applied to the 5,6-epoxide of 3,3',4,4'-tetrachlorobiphenyl

Scheme I



(1) gave only low and irreproducible yields due to extensive epoxide opening and aromatization during the bromination of **2**.[4]



Ar = 3,4-Dichlorophenyl

We report here a much more effective synthetic procedure for the preparation of arene oxide 1 using a bromodecarboxylative elimination as the final double bond forming step. The strategy is similar to that employed by Ganem[5] in a synthesis of senepoxide, in which thermal

(1) Kimbrough, R.; Buckley, J.; Fishbein, L.; Flamm, G.; Kasza, L.; Marcus, W.; Shibko, S.; Teske, R. *Environ. Health Perspect.* **1978**, *24*, 173. Forgue, S. T.; Preson, B. D.; Hargraves, W. A.; Reich, I. L.; Allen, J. R. *Biochem. Biophys. Res. Commun.* **1979**, *91*, 475. Stadnicki, S. S.; Lin, F. S. D.; Allen, J. R. *Res. Commun. Chem. Pathol. Pharmacol.* **1979**, *24*, 313. Stadnicki, S. S.; Allen, J. R. *Bull. Environ. Contam. Toxicol.* **1979**, *23*, 788. Preston, B. D.; Miller, E. C.; Miller, J. A. *Carcinogenesis* **1985**, *6*, 451. Yoshimura, H.; Yonemoto, Y.; Yamada, H.; Koga, N.; Oguri, K.; Saeki, S. *Xenobiotica* **1987**, *17*, 897.

(2) Reich, I. L.; Reich, H. J. *J. Org. Chem.* **1981**, *46*, 3721. Selander, H. G.; Jerina, D. M.; Piccolo, D. E.; Berchtold, G. A. *J. Am. Chem. Soc.* **1975**, *43*, 2711.

(3) Vogel, E.; Schubart, R.; Boll, W. A. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 510. Vogel, E.; Gunther, H. *Ibid.* **1967**, *6*, 385. Rastetter, W. H.; Nummy, L. J. *J. Org. Chem.* **1980**, *45*, 3149. Watabe, T.; Hiratsuka, A.; Aizawa, T.; Sawahata, T. *Tetrahedron Lett.* **1982**, *23*, 1185. McManus, M. J.; Berchtold, G. A.; Boyd, D. R.; Kennedy, D. A.; Malone, J. F. *J. Org. Chem.* **1986**, *51*, 2784.

(4) Use of several other allylic halogenating agents and the addition of oxiranes did not improve the results. Wiberg, N.; Raschig, F. *J. Organomet. Chem.* **1967**, *10*, 15.

(5) Ganem, B.; Holbert, G. W.; Weiss, L. B.; Ishizumi, K. *J. Am. Chem. Soc.* **1978**, *100*, 6483.

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