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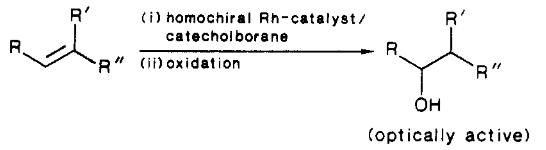
Communications

Enantioselective Hydroboration Mediated by Homochiral Rhodium Catalysts

Summary: Homochiral rhodium–phosphine complexes facilitate enantioselective hydroboration of alkenes by catecholborane; oxidation of the products affords optically active alcohols.

Sir: Existing methods for reagent-controlled asymmetric hydroboration are diastereoselective in that they involve interactions of homochiral boranes with prochiral alkenes.[1-5] Here we introduce *enantioselective* hydroboration of prochiral alkenes with an achiral reagent. Chiral induction in this process arises from diastereoselective transformations of rhodium complexes within a catalytic cycle, an asymmetric hydroboration technique that is fundamentally different from any that has been reported previously.



This work began with a series of simple NMR experiments that confirmed previous reports[6,7] that hydroboration of alkenes by catecholborane is accelerated by catalytic amounts of Wilkinson's catalyst [$RhCl(PPh_3)_3$]. We showed a number of structurally diverse alkenes reacted with catecholborane in hexadeuteriobenzene in the presence of catalytic $RhCl(PPh_3)_3$ whereas no reaction occurred in control samples (i.e. without catalyst). These NMR experiments also provided rough indications of reaction rates. For instance, norbornene was consumed within 1 h at 25 °C and even hindered alkenes like (*E*)-1,2-diphenylethene, and methylbut-2-ene reacted completely within 48 h. Norbornene was chosen for our preliminary work on enantioselective hydroborations since this substrate reacted rapidly and cleanly in the catalyzed process.

Treatment of norbornene (**1**) with catecholborane in the presence of rhodium-DIOP[8] or rhodium-BINAP[9] catalysts consistently gave, after oxidation, *exo*-norborneol in near quantitative yield (by ^{1}H NMR analysis of the crude material). This alcohol was isolated in yields of more than 90%. The optical purity of the norborneol produced was inversely related to the reaction temperature. At 40 °C material of 23% ee was produced (Table I, entry 1) but at −25 °C the enantiomeric excess increased to 57% (entry 5). Further decrease of the reaction temperature had no effect on the optical yield, but it is interesting that high chemical yields were obtained from reactions conducted at temperatures as low as −40 °C (entry 7). Entries 3 and 6 indicate that Rh-BINAP catalysts are slightly more enantioselective than Rh-DIOP systems in these reactions.

Enantioselective hydroboration/oxidation of norbornadiene (**2**) gave diol **7** of higher optical purity than norborneol formed under similar conditions (entries 4 and 8). A chemically separable meso diol constitutes a significant proportion of the stereoisomeric impurities formed in the hydroboration of norbornadiene (**2**);[10] the enantiomeric purity of diol **7** is enhanced as a consequence.[15] Our experiments with 1,2-diphenylethene indicate that both *E* and *Z* isomers can be hydroborated to give the corresponding alcohol in quantitative yield. However, optical yields are low for the cis isomer (entries 11 and 12) and insignificant for the trans isomer (entries 9 and 10).

Perhaps the most interesting of the results obtained were with 1,1′-disubstituted alkenes for which there is no satisfactory method of asymmetric hydroboration. Rhodium-catalyzed hydroboration/oxidation of 2-phenylpropene (**4**) and 2,3,3-trimethylprop-1-ene (**5**) gave the corresponding alcohols **9** and **10** in 27% and 69% ee (entry 13 and 14), respectively. These inductions are greater than any reported for diastereoselective hydroborations of 1,1-disubstituted alkenes.

The mechanism of rhodium-catalyzed hydroboration reactions has not been established, but circumstantial evidence suggests that rhodium–hydride complexes are involved. For instance, in other studies we have found catalytic hydroboration of (*Z*)-1,4-bis(benzyloxy)but-2-ene with catecholborane in the presence of catalytic [Rh(COD)(DIOP)]BF_4 at −25 °C affords the isomeric enol ether in 25% yield; presumably this is formed via rhodium-catalyzed double bond migration.[11] Furthermore, others

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(1) Brown, H. C.; Jodhavin, P. K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1985; Vol. 2, p 1.

(2) Midland, M. M. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1985; Vol. 2, p 45.

(3) Matteson, D. S. *Synthesis* **1986**, 973.

(4) Brown, H. C.; Singaram, B. *Pure Appl. Chem.* **1987**, 879.

(5) Masamune, S.; Kim, B. M.; Petersen, J. S.; Sato, T.; Veenstra, S. J.; Imai, T. *J. Am. Chem. Soc.* **1985**, *107*, 4549.

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

(7) Mannig, D.; Noth, H. *Fed. Rep. Ger. PI Ger. Offen.* DE 3528320 A1; *Chem. Abstr.* **1987**, *106*, 176654*n*.

(8) DIOP is 2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane.

(9) BINAP is 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl.

(10) Similar effects have been noted in asymmetric epoxidations of bifunctional substrates with mirror plane symmetry: Hoye, T. R.; Suhadolnik, J. C. *Tetrahedron* **1986**, *42*, 2855.

(11) Ohlmeyer, M. J., unpublished results. For references on Rh-mediated double bond migrations, see: Otsuka, S.; Tani, K. in *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1985; Vol. 5, p 171.

(12) Kono, H.; Ito, K. *Chem. Lett.* **1975**, 1095.

(13) Typical experimental procedure: A Schlenk tube charged with chloro(1,5-cyclooctadiene)rhodium(1) dimer (4.9 mg, 0.01 mmol), DIOP (10.5 mg, 0.021 mmol), and norbornene (94 mg, 1 mmol) was evacuated/flushed three times with argon. Two milliliters of THF was added, and the resulting golden-yellow solution stirred at 20 °C for 15 min. The solution was cooled to −78 °C, and catecholborane (144 mg, 1.2 mmol) was added. A white precipiate formed on stirring at −78 °C for 5 min. On warming to −40 °C, the precipitate dissolved and the solution becomes lime-green but returned to golden-yellow within an hour. The solution was allowed to stand at −40 °C for 72 h; no further color change occurred. It was cooled to −78 °C, and 1 mL of ethanol, 1.7 mL of 3 M NaOH, and 0.7 mL of 30% H_2O_2 was added. The mixture was warmed to 25 °C over ca. 1 h and stirred for 12 h. NaOH (1 M, 10 mL) was added, and the organic material was extracted with Et_2O (4 × 25 mL). The combined ether extracts were washed with 1 M NaOH and saturated aqueous NaCl and dried over $MgSO_4$. Removal of the solvents in vacuo gave 111 mg (99%) of crystalline *exo*-norborneol.

(14) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

(15) The chemical yield of diol **7** is reduced for the same reason. After aqueous workup, 59% combined yield of **7** and its meso isomer was isolated but only 10% of pure diol **7** was obtained after a (difficult) chromatographic separation.

(16) These results were presented at the Gordon Conference on Stereochemistry, Rhode Island, July 1988.

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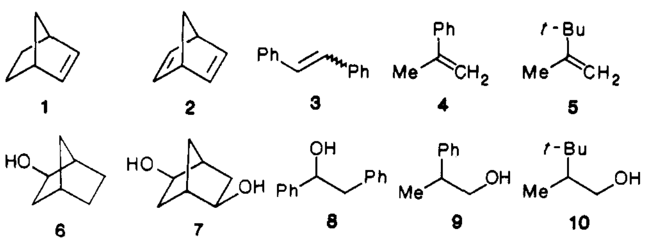
Table I. Enantioselective Hydroboration Experiments[a]



entry (substrate)	T, °C	catalyst[b]/ solvent	product	ee,[c] %	absolute configuration
1 (**1**)	40	A/C_6H_6	**6**[d]	23	1*R*,2*R*
2 (**1**)	5	A/C_6H_6	**6**	31	1*R*,2*R*
3 (**1**)	5	B/C_6H_6	**6**	43	1*R*,2*R*
4 (**1**)	−5	A/THF	**6**	46	1*R*,2*R*
5 (**1**)	−25	A/THF	**6**	57	1*R*,2*R*
6 (**1**)	−25	B/THF	**6**	64	1*R*,2*R*
7 (**1**)	−40	A/THF	**6**	55	1*R*,2*R*
8 (**2**)	−25	A/THF	**7**	76	1*S*,2*R*[d]
9 (*E*-(**3**))	20	A/C_6H_6	**8**	7	*S*
10 (*E*-(**3**))	5	A/C_6H_6	**8**	~0	
11 (*Z*-(**3**))	5	A/C_6H_6	**8**	17	*S*
12 (*Z*-(**3**))	−25	A/THF	**8**	19	*S*
13 (**4**)	−5	A/THF	**9**	27	*R*
14 (**5**)	−5	A/THF	**10**	69	*R*

[a] See note 13 for a typical experimental procedure. [b] A, in situ $[Rh(COD)Cl]_2\cdot 2DIOP$; B, in situ $[Rh(COD)Cl]\cdot 2BINAP$. [c] Determined by ^1H NMR analysis of Mosher's ester derivatives[14] and ^1H NMR experiments with $Eu(hfc)_3$, to within ±5%. [d] By inference from entries 1–7 only.

have shown[6] that stoichiometric amounts of catecholborane and Wilkinson's catalyst react to give a hydride complex $[RhClH(BO_2C_6H_4)(PPh_3)_2]$;[12] this reacts with alkenes to give hydroboration products. Thus the catalyzed reaction may proceed via oxidative addition of catecholborane to the rhodium(I) center, insertion of the alkene into the rhodium–hydride bond so formed, and reductive elimination of alkyl and boronate ligands.

Existing methods for asymmetric hydroboration are excellent for many applications[1-5] but are not generally applicable to all alkenes[3] and are sometimes limited by the cost/availability of the borane reagents.[5] Clearly the evolution of methods for chiral induction in hydroboration methodology is not complete. The results presented here provide an interesting perspective in the development of new asymmetric hydroboration techniques.[16]

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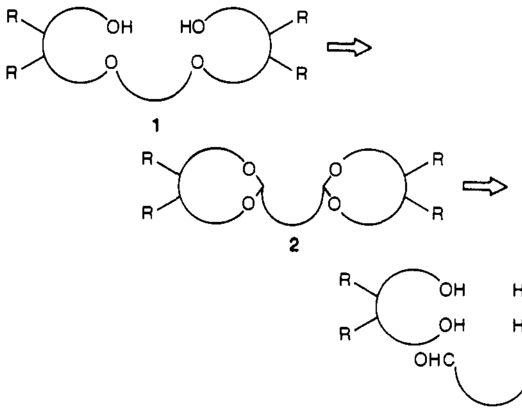
A Convenient Synthesis of Substituted Polyether Diols

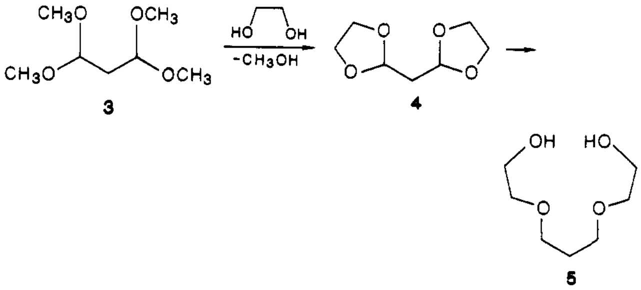
Summary: Alkyl-substituted polyether diols (or polythioether diols), which are potential precursors to substituted crown ethers, are produced in high yield by the selective reductive cleavage of C–O bonds in bis(cyclic acetals) [or bis(cyclic hemithioacetals)] by borane or monochloroborane.

Sir: Crown ethers bearing alkyl, aryl, and functional group substituents have been used in a variety of applications including enzyme mimics, receptor site models, and selective ionophores.[1-3] Our interest in the synthesis of highly substituted crown ethers prompted the development of methodology for the preparation of alkyl-substituted polyether diols **1** useful as acyclic precursors to these.

Our approach is conceptually simple: substituted polyether diols **1** would result from the reductive cleavage of one C–O bond in each 1,3-dioxolane (or 1,3-dioxane) ring in bis(acetals) **2**. These could, in turn, be prepared from a dialdehyde (or its synthetic equivalent) and 2 equiv of an appropriately substituted 1,2- or 1,3-diol. This is the first report of the generation of diether diols by such an approach.



To test the feasibility of this approach, we first attempted to selectively reduce **4**[4] to 3,7-dioxa-1,9-nonanediol (**5**) with $LiAlH_4/AlCl_3$ mixtures in diethyl ether solvent.[5a] However, only an 8–11% yield of diether diol **5** was obtained and no starting material was recovered. Manipulation of reaction conditions and isolation procedures failed to significantly increase yields.



This procedure, which required an aqueous workup to remove the aluminum salts, was unacceptable since most of the product was not recovered, possibly due to its great

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(1) Gokel, G. W.; Korzenniowski, S. H. *Macrocyclic Polyether Synthesis*; Springer Verlag: New York, 1982.

(2) Voegtle, F.; Weber, E. *Host–Guest Chemistry/Macrocycles*; Springer Verlag: New York, 1985.

(3) Izatt, R. M.; Christiansen, J. J., Eds. *Synthesis of Macrocycles: The Design of Selective Complexing Agents*; Wiley-Interscience: New York, 1987.

(4) Bis(acetals) **4**, **7**, **14a**, and **16a** have been previously prepared: Chastrette, F.; Hassambay, M.; Chastrette, M. *Bull. Soc. Chim. Fr.* **1976**, 601. We synthesized malonaldehyde bis(acetals) **4–9** by the toluenesulfonic acid catalyzed reaction of malonaldehyde bis(dimethyl acetal) and the appropriate diol in toluene solution. The reaction was driven to completion by distillation of the methanol–toluene azeotrope to give products in considerably higher yields than by procedures previously reported.

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