3-$CH_3OC_6H_4CH_2Cl$, 824-98-6; 4-$FC_6H_4CH_2Cl$, 352-11-4; 4-$ClC_6H_4CH_2Cl$, 104-83-6; 2-$BrC_6H_4CH_2Br$, 3433-80-5; 4-$BrC_6H_4CH_2Br$, 589-15-1; 2-$NCC_6H_4CH_2Br$, 22115-41-9; 4-$NCC_6H_4CH_2Br$, 17201-43-3; $C_6H_5CH(CH_3)Cl$, 672-65-1; 4-$CH_3C_6H_4CH_2Cl$, 104-82-5; 4-$CH_3OCOC_6H_4CH_2Cl$, 34040-64-7; 4-$HOCOC_6H_4CH_2Br$, 6232-88-8; 3-$BrCH_2C_6H_4CH_2Br$, 626-15-3; 4-ClC_6H_4COCl, 122-01-0; CH_3COCl, 75-36-5; $CH_3(CH_2)_6COCl$, 111-64-8; *trans*-$C_6H_5CH{=}CHCOCl$, 17082-09-6; $(CH_3)_2C{=}CHCOCl$, 3350-78-5; $CH_3OCOCH_2CH_2COCl$, 1490-25-1; $CH_3OCOCH_2CH_2CH_2COCl$, 1501-26-4; $ClCOCH_2CH_2COCl$, 543-20-4; CH_3OCH_2COCl, 38870-89-2; $C_6H_5COCOCl$, 25726-04-9; $(CH_3)_2NCOCl$, 79-44-7; C_6F_5COCl, 2251-50-5; $ClCOCOCl$, 79-37-8; $C_6H_5CH_2CH_2C_6H_5$, 103-29-7; $NCCH{=}CH_2$, 107-13-1; $CH_3COCH{=}CH_2$, 78-94-4; $H_2C{=}CHCH_2Br$, 106-95-6; $H_2C{=}C(CH_3)CH_2Cl$, 563-47-3; *trans*-$C_6H_5CH{=}CHCH_2Br$, 26146-77-0; *trans*-$CH_3CH{=}CHBr$, 590-15-8; *cis*-$CH_3CH{=}CHBr$, 590-13-6; *trans*-$C_6H_5CH{=}CHBr$, 588-72-7; C_6F_5I, 827-15-6; (1-naphthyl)chloromethane, 86-52-2; (2-naphthyl)bromomethane, 939-26-4; cyclohexylcarbonyl chloride, 2719-27-9; 2-furylcarbonyl chloride, 527-69-5.

Stereochemistry of the Hydride Reduction of 7-Oxabicyclo[2.2.1]heptanes

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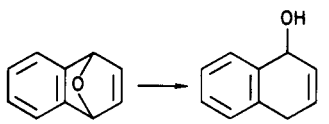
The reductive cleavage, by $LiAlD(O\text{-}t\text{-}Bu)_3/Et_3B$, of two 7-oxabicyclo[2.2.1]heptanes is found to occur with high inversion stereospecificity (≥96% and ≥98%, respectively). The substrates were chosen to present potential complicating factors, but the reactions occur cleanly by hydride (deuteride) attack at the cleaved center, suggesting that this stereochemical result will prove to be general for reduction of 1,4-epoxides. The conditions are mild enough to allow isolation of the "arene hydrate" 1-hydroxy-1,4-dihydronaphthalene from the reduction of 1,4-epoxy-1,4-dihydronaphthalene. The reaction provides a useful way to introduce deuterium stereospecifically, by reduction of isobenzofuran cycloadducts and related materials.

Brown and co-workers have shown that the potent reducing agent obtained by mixing lithium tri-*tert*-butoxyaluminohydride (LTBAH) and triethylborane efficiently cleaves certain types of ethers, e.g., THF and methoxyaliphatics.[1] The reagent is thought to consist of lithium triethylborohydride (Super-Hydride) and aluminum tri-*tert*-butoxide, with the latter species providing the electrophilic activation of the ether needed for facile cleavage. In keeping with this view, a mixture of LTBAH and catalytic triethylborane (10%) also effects such reductions.[1] Although electrophilic assistance is critical for reaction, product analyses from unsymmetrical ethers suggest an overall S_N2-like mechanism; i.e., hydride attack occurs preferentially at the less substituted carbon. The reduction of 1-methylcyclohexene oxide is informative; the tertiary alcohol is the major product (90%), while the minor product (10%, indicative of a strong electrophilic component) is *cis*-2-methylcyclohexanol, with the stereochemistry required of an S_N2 displacement.

We were intrigued by the observation[1] that 7-oxabicyclo[2.2.1]heptane is rapidly reduced to cyclohexanol by the mixed reagent. If this proved to be a general reaction of this ring system, it offered a potentially useful way to convert cycloadducts of isobenzofurans and related materials to the corresponding alcohols. Further, if such reductions were stereospecific, a novel method for hydrogen isotope incorporation at the remote site would be available.

Results and Discussion

The readily available cycloadduct of benzyne and furan, **1**, is an interesting substrate for testing the generality of the reduction. Since the ethereal bonds are both benzylic and allylic, **1** is expected to be especially susceptible to electrophile-induced cation formation and possible rearrangement. Also, Caple et al. have reported that **1** reacts with alkyllithium reagents at the double bond, leading, via oxa-ring opening, to *cis*-1,2-dihydro-2-alkylnaphthalenols,[2] and analogous attack by hydride represents another possible complication. However, we find that **1** reacts smoothly with LTBAH/20% triethylborane in tetrahydropyran (THP) solvent to give alcohol **2**, the anticipated product of direct reduction of the ether linkage.



1 **2** (1)

This deceptively simple-appearing product has been reported only once previously, formed by sulfite reduction of the hydroperoxide generated by autoxidation of 1,4-dihydronaphthalene.[3] Later workers[4] were unable to reproduce this finding, leaving some doubt about the earlier claim (the melting point of our **2**, however, coincides with that in the literature[3]). Compound **2** is a member of the so-called "arene hydrates"[5] and, as expected, exotherms on treatment with acid to form water and naphthalene. It can be recrystallized from hydrocarbon solvent (mp 46–47 °C) and has been successfully stored for several weeks at −10 °C. NMR spectra have been obtained in $CDCl_3$, although dehydration, presumably trace acid catalyzed, has been observed with some samples kept in this solvent.

In connection with ongoing studies of 1,4-elimination, we were particularly interested in converting **2** to the methyl ether derivative **3**. Attempts to do so with

(1) Brown, H. C.; Krishnamurthy, S.; Coleman, R. A. *J. Am. Chem. Soc.* **1972**, *94*, 1750. Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1979**, *44*, 3678.

(2) Caple, R.; Chen, G. M. S.; Nelson, J. D. *J. Org. Chem.* **1971**, *36*, 2874. See also: Jeffrey, A. M.; Yeh, H. J. C.; Jerina, D. M.; DeMarinis, R. M.; Foster, C. H.; Piccolo, D. E.; Berchtold, G. A. *J. Am. Chem. Soc.* **1974**, *96*, 6929. Brion, F. *Tetrahedron Lett.* **1982**, 5299.

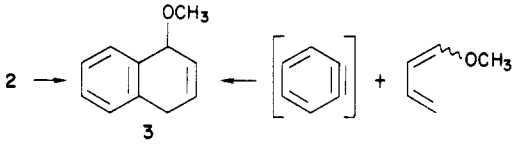
(3) Hock, H.; Depke, F. *Chem. Ber.* **1950**, *83*, 327.

(4) Jeffrey, A. M.; Jerina, D. M. *J. Am. Chem. Soc.* **1972**, *94*, 4048.

(5) Staroscik, J.; Rickborn, B. *J. Am. Chem. Soc.* **1971**, *93*, 3046.

0022-3263/85/1950-1381$01.50/0

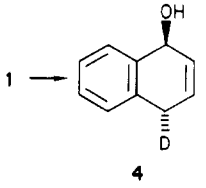
NaH/THF/CH_3I, or in HMPA solvent by addition of *n*-butyllithium followed by CH_3I, were unsuccessful. In both cases naphthalene was formed. The use of moist silver oxide/CH_3I, however, effects the desired conversion (eq 2). The ether **3** prepared in this way had ^1H NMR



(2)

features indentical with those of material obtained (in low yield) by trapping benzyne with 1-methoxy-1,3-butadiene, thus confirming the structure shown.

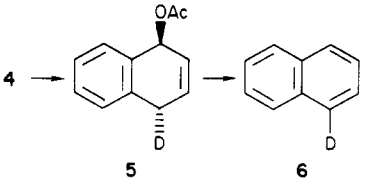
Lithium tri-*tert*-butoxyaluminodeuteride (LTBAD) was prepared from $LiAlD_4$ and *tert*-butylalcohol, and the reduction of **1** was carried out as described above with this material. Both ^1H NMR and MS analyses indicated the incorporation of approximately one D/mole in the product **4**. The methylene protons of **2** have very similar chemical



(3)

shifts, complicating the determination of the stereochemistry of the deuterated material **4**. The shift resolution was not improved in the ether **3**, and we therefore turned to the acetate derivative as a possible solution to this problem. In their elegant work on the stereochemistry of some 1,4-elimination processes, Hill and Bock[6] found that the acetate of **4** (formed as a transient intermediate in the cycloaddition of benzyne and 1-acetoxy-1,3-butadiene) spontaneously (60 °C) loses acetic acid to give naphthalene in a stereospecific (98 ± 2%) syn elimination process. This finding offered an additional unique method for establishing the stereochemistry of **4**.

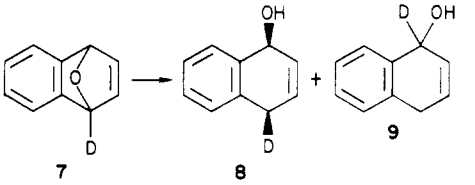
Although treatment of **2** in ether at 0 °C with a slight excess of *n*-butyllithium followed by quenching with water led to dehydration to naphthalene, the same sequence at −78 °C allowed clean recovery of **2**, showing that the lithium alkoxide is at least moderately stable at the lower temperature. It was hoped that low-temperature quenching of the alkoxide with acetyl chloride would allow formation and possible isolation of the acetate, but when the alkoxide was treated with acetyl chloride (15 min) followed by aqueous bicarbonate (all at −78 °C) and then warmed to room temperature, the crude product consisted of essentially pure naphthalene (NMR). Somewhat surprisingly, however, when the alcohol **2** in ether containing triethylamine was treated (25 °C) with acetyl chloride, it proved possible to isolate the acetate. This procedure was applied to the deuterated alcohol **4** to form the derivative **5**; a portion of this material was heated to effect elimina-



(4)

tion, and the deuterated naphthalene **6** was isolated for analysis. By ^1H NMR, **6** contained one D/mole in the position indicated. MS indicated 94% D/mol. Although our conditions do not exactly reproduce those of Hill and Bock, if it is assumed that the same syn elimination mechanism prevails, this establishes a lower limit for the extent of inversion in the reduction of **1**, i.e., 94%. The $LiAlD_4$ used to prepare the LTBAD was obtained from Aldrich Chemical Co. as 98 atom % deuterated material. The isotopic purity of the LTBAD was not determined. Since an excess of this reagent was employed in the reductions, any kinetic preference for transfer of hydride over deuteride would result in diminished deuterium content in the product, even for a completely stereospecific process.

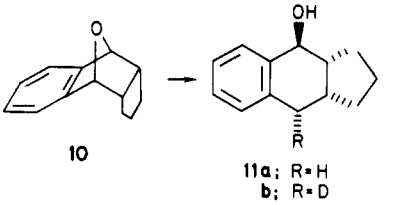
The proton-decoupled ^2H NMR spectrum of the acetate **5** consists of a singlet (δ 3.18; CCl_4 solvent with C_6D_6 internal standard) in the methylene region, as expected. In order to establish whether the alternative stereoisomer would be distinguishable by this method, a sample of bridgehead monodeuterated substrate (**7**) was prepared and subjected to LTBAH/Et_3B reduction, affording a mixture of **8** and **9** as shown in eq 5. Since deuterated



(5)

9 does not absorb in the region of concern in ^2H NMR, its presence does not complicate analysis. The mixture of acetates prepared from **8** and **9** displayed a singlet in the methylene region at δ 3.30. Further, when **5** was added to the sample containing **8**-OAc, two peaks were clearly discernible, although base-line separation was not achieved. It was thus possible to estimate, from the absence of any measurable absorption due to **8**-OAc in the spectrum of **5**, that the reduction of **1** must occur with at least 96% inversion, and it is likely a totally stereospecific process.

The second system chosen for stereochemical examination is the cycloadduct of isobenzofuran and cyclopentene, compound **10**. We have recently used this ma-

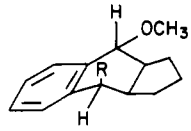


(6)

terial to determine the structure of the cycloadduct of α-methoxy-*o*-xylene and cyclopentene,[7] employing the LTBAH/Et_3B reduction procedure to form **11a**. The stereochemistry of this reduction is of particular interest since inversion processes are at least nominally hindered by the propano bridge. Indeed, although the reduction of **10** does occur, it is decidedly sluggish and it was necessary to use a fourfold excess of reducing agent to obtain satisfactory yields in convenient times. Thus **10** is much less reactive than **1** toward the complex reducing agent. To the extent that reduction with inversion is blocked or impeded, mixed stereochemistry or even retention might have resulted. However, the reaction of **10** with LTBAD/Et_3B is found to occur with complete inversion (>98%) to give **11b**. Analysis of this system was relatively straightforward, since the benzylic methylene protons of **11a** have quite different chemical shifts, and in the methyl ether derivative (**12**) these are sufficiently separated from other absorptions

(6) Hill, R. K.; Bock, M. G. *J. Am. Chem. Soc.* **1978**, *100*, 637.

(7) Moss, R. J.; Rickborn, B. *J. Org. Chem.* **1984**, *49*, 3694.



12a, R = H
b, R = D

to allow complete analysis. Difference NOE spectra were obtained, which established that the upfield benzylic methylene proton of **12a** is trans to the methoxy group; this is in keeping with the aromatic ring current effects anticipated for the extended conformation shown below. Deuterated **12b** had negligible absorption at this upfield position by ^1H NMR, while the ^2H NMR spectrum exhibited a strong peak at this position, and no measurable absorption at the lower field position. We estimate that >2% of the other stereoisomer would have been detected if present, and thus within the limits of measurement, the deuterium is introduced with complete inversion of the carbon center.

Conclusion

Although inversion was anticipated from Brown's earlier product analyses with unsymmetrical ethers, our results establish this unequivocally with two systems chosen as likely candidates for alternative processes to intervene, and consequently it is probable that inversion is a general result. It should be noted that other hydride reductions which are widely regarded as simple S_N2 displacements may in fact involve complications which can compromise analyses and conclusions; a good illustration is provided by the $LiAlH_4$ reduction of epoxides, in which a fraction of the product may be formed with inversion of both centers.[8]

Experimental Section

Melting points were obtained on a Mel-Temp apparatus in open capillary tubes and are uncorrected. High-field ^1H and proton-decoupled ^2H NMR spectra were obtained on a Nicolet NT-300. MS data were obtained on a VG Micromass ZAB-2F instrument. THP (distilled from Na and then from $LiAlH_4$), $LiAlD_4$ (98% isotopic purity), and Et_3B (1 M in THP) were purchased from Aldrich Chemical Co.

Reduction of 1. (a) By LTBAH. To a slurry of 7.6 g of LTBAH in 30 mL of THP was added 2.16 g of **1** dissolved in 5 mL of THP. After the mixture was cooled in an ice bath, 3.0 mL of 1 M Et_3B in THP was added dropwise over 5 min. The bath was removed, and the mixture was stirred for 0.5 h, then cooled again, and quenched with 8.0 mL of 3 M aqueous NaOH followed by 4.0 mL of 30% H_2O_2. The mixture was filtered to remove solids, taken up in either, and washed with water. Drying (K_2CO_3) and evaporation gave a colorless solid which was recrystallized from high-boiling petroleum ether to give pure **2**: 1.22 g (56%), mp 47.5–48 °C (lit.[3] mp 47–48 °C); NMR ($CDCl_3$) δ 1.80 (d, OH, J = 9.3 Hz), 3.41 (AB q, 2 H, CH_2), 5.16 (br s, 1 H), 6.10 (m, 2 H, vinyl), 7.25 (m, 3 H), 7.57 (d, 1 H, J = 6.9 Hz); MS; 146 (P, 100), 145 (49.0).

(b) By LTBAD. The same procedure was followed with a mixture of 3.6 g of **1**, 1.6 equiv of LTBAD (prepared in the same flask from 1.7 g of $LiAlD_4$ and 3.0 equiv of *tert*-butyl alcohol), and 0.4 equiv of Et_3B, in 50 mL of THP. Recrystallized **4** was obtained: 86% yield (3.14 g), mp 47–49 °C; NMR ($CDCl_3$) δ 1.94 (br s, OH), 3.41 (br s, 1 H, CHD), 5.13 (br s, CHOH), 6.08 (m, 2 H, vinyl), 7.25 (m, 3 H), 7.54 (m, 1 H); MS, 147 (P, 100), 146 (48.6).

1-Methoxy-1,4-dihydronaphthalene (3). A mixture of 146 mg of **2**, 243 mg of Ag_2O, and 3.5 equiv of CH_3I in 6.0 mL of $CHCl_3$ was stirred for 18 h at room temperature. After filtration and concentration, 109 mg of an iodine-discolored liquid was obtained.[9] This material has an NMR spectrum identical with that of the product from Diels–Alder reaction of benzyne (generated from anthranilic acid, ethyl nitrite, and trifluoroacetic acid catalyst) and 1-methoxy-1,3-butadiene:[10] 19% yield; NMR ($CDCl_3$) δ 3.1 (s, 3 H, methoxy), 3.35 (m, 2 H, CH_2), 5.05 (dd, 1 H, J = 7, 4 Hz), 6.1 (m, 2 H, vinyl), 7.05–7.6 (m, 4 H).

***trans*-1-Acetoxy-4-deuterio-1,4-dihydronaphthalene (5).** A mixture of 51 mg of **4**, 1.3 equiv of acetyl chloride (distilled prior to use), and 3.0 equiv of Et_3N in 1 mL of Et_2O was stirred for 48 h at ambient temperature. After addition of water, extraction with ether, and drying over K_2CO_3, vacuum evaporation of the solvent gave 65 mg of acetate **5** (contaminated with a trace of naphthalene) as a pale yellow liquid: ^1H NMR (CCl_4) δ 2.01 (s, 3 H, acetoxy), 3.44 (br s, 1 H, CHD),[11] 5.98 and 6.17 (AB q, 2 H, vinyl), 6.30 (m, 1 H, CHOAc), 7.0–7.3 (3 m, 4 H); ^2H NMR δ 3.18 (s).

Thermolysis of 5. Acetate **5** was prepared in a similar way (83%), from 50 mg of **4**, 1.0 equiv of acetyl chloride, and 1.1 equiv of Et_3N in 1.0 mL of ether but with quenching after 2 h; no naphthalene was detectable by NMR. The sample was sealed in an NMR tube with 0.6 mL of C_6D_6 and heated for 2 h at 80 ± 5 °C, at which time the elimination was judged complete. The naphthalene was isolated by preparative TLC followed by sublimation: 19 mg, mp 80–81 °C; MS, 129 (P, 100), 128 (17.0). Comparison with commercial naphthalene indicated that the sample contained 94.5 atom % D/mol. This conclusion was borne out by ^1H NMR, which also showed that the deuterium was in the 1-position.

1-Deuterio-1,4-epoxy-1,4-dihydronaphthalene (7). The procedure of Fieser and Haddadin[12] was used to prepare **7** from 5.5 g of anthranilic acid, 5.0 g of ethyl nitrite, and excess 2-deuteriofuran.[13] Recrystallization from high-boiling petroleum ether afforded 2.4 g of **7**, mp 55.5–57 °C (lit.[12] mp of protio analogue, 56 °C). ^1H NMR integration indicated that the material contained one D/mole.

Reduction of 7, with LTBAH. The procedure used for reduction of **1** was followed with 2.18 g of **7**, 2 equiv of LTBAH, and 0.4 equiv of Et_3B in 25 mL of THP. The mixture of alcohols **8** and **9** was obtained in 56% yield after recrystallization, mp 48–49 °C. ^1H NMR showed that equal amounts of **8** and **9** were present.

Acetylation of 8/9. A portion (51 mg) of this **8/9** mixture was treated with 1.3 equiv of acetyl chloride and 3.0 equiv of Et_3N in 1.0 mL of ether for 48 h. After the usual workup, 51 mg of product acetate was obtained. The ^1H NMR spectrum contained an AB quartet centered at δ 3.39 (benzylic methylene protons for the acetate of **9**), under a broad singlet at δ 3.30 due to the acetate of **8** (CHD): ^2H NMR (CCl_4) δ 3.30 (s, 1 D), 6.16 (s, CDOAc of **9**-OAc, 1 D).

Reduction of 10 with LTBAD. A sample of **10**[7] (167 mg) in 2.0 mL of THP was added to a slurry of 4.4 equiv of LTBAD (prepared by addition of 1.1 mL of *tert*-butyl alcohol in 1.0 mL of THP to 166 mg of $LiAlD_4$ in 2.0 mL of THP, with stirring for 1 h). After the mixture was cooled to 0 °C, 4.0 equiv of Et_3B solution was added; the ice bath was removed, and the mixture was stirred at room temperature for 42 h. Upon cooling and quenching with base and peroxide, the usual workup gave a residue which was chromatographed on silia gel (15% EtOAc in Skellysolv). Unreacted **10** was recovered (25 mg), and 101 mg (59%)

(8) Rickborn, B.; Quartucci, J. *J. Org. Chem.* **1964**, *29*, 3185. See also: Schwab, J. M. *J. Org. Chem.* **1983**, *48*, 2105.

(9) In another preparation of **3** from **2**, the iodine-colored residue decomposed with heat evolution after standing at room temperature a short time; the naphthalene formed was examined by NMR and found to contain 68 ± 10 atom % D/mol. Removal of the iodine (which presumably initiates the elimination) by washing the solution with a reducing agent was not explored.

(10) Everhardus, R. H.; Peterse, A.; Vermeer, P.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1974**, *93*, 90. Doric, J. P.; Martin, M. L.; Odiot, S.; Tonnard, F. *Org. Magn. Reson.* **1973**, *5*, 265.

(11) The fully protonated acetate of **2** was prepared in the same manner; the benzylic protons appear as an AB quartet centered at δ 3.39.

(12) Fieser, L. F.; Haddadin, M. J. *Can. J. Chem.* **1965**, *43*, 1599.

(13) The 2-deuteriofuran was prepared by formation of 2-lithiofuran[14] and quenching with slightly more than 1 molar equiv of D_2O. Spinning band distillation gave material which contained small amounts of butane, THF, and hexane but was satisfactory for direct use in the preparation of **7**.

(14) Crump, S. L.; Rickborn, B. *J. Org. Chem.* **1984**, *49*, 304.

of the alcohol **11b** was isolated. Recrystallization from hexane gave pure **11b** (45%), mp 159–159.5 °C. The proton NMR spectrum was identical with that of **11a**,[7] except for the changes associated with incorporation of deuterium. MS analysis: 171 (P - 18, 100); 170 (P - 19, 16.6), indicating 94 atom % D/mol.

Methyl Ether 12b. To an ice-cooled mixture of 30.5 mg of **11b** in 5.0 mL of HMPA was added sufficient *n*-butyllithium/hexane to reach an orange end point. Excess methyl iodide was then added and the cooling bath was removed. After 0.5 h water was added and the mixture was extracted with Skelly-solv, followed by drying and evaporation. The residue was subjected to preparative TLC (20% EtOAc in Skelly-solv) to yield 26.4 mg (81%) of **12b**. The ^{1}H NMR spectrum was identical with that of **12a**, except for the cis benzylic proton appearing as a broadened singlet (deuterium coupling; this proton is a dd in **12a**) and the absence of absorption at δ 2.4 (where the trans proton of **12a** appears): ^{2}H NMR (CCl_4) δ 2.165 (s) (no other absorptions detectable, indicating that all of the deuterium incorporated is found in the trans position); MS, 171 (P - CH_3OH, 100), 170 (11.87), indicating 93 atom % D/mol.

Acknowledgment. Financial support by the University of California Cancer Research Coordinating Committee is gratefully acknowledged. The NSF partially funded the NMR instrument used in this study. We especially thank Dr. Hugh Webb and Curt Breneman for their expert assistance in obtaining MS and NMR data, respectively.

Selective Reductions. 37. Asymmetric Reduction of Prochiral Ketones with *B*-(3-Pinanyl)-9-borabicyclo[3.3.1]nonane

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The chiral trialkylborane *B*-(3-pinanyl)-9-borabicyclo[3.3.1]nonane, either with the neat reagents or concentrated solutions, ≳2 M, reduces a wide range of prochiral carbonyl compounds with good to excellent asymmetric induction. Reduction of simple dialkyl ketones, 2-butanone, 2-octanone, 3-methyl-2-butanone, and 3,3-dimethyl-2-butanone, yields the corresponding alcohols with 43%, 48%, 62%, and 0.7% asymmetric induction. Acetophenone is reduced to 1-phenylethanol in 85% ee. The α,β-unsaturated ketones 3-buten-2-one, 1-acetyl-1-cyclohexene, 3-methyl-2-cyclohexenone, and *trans*-4-phenyl-3-buten-2-one are reduced to the corresponding allylic alcohols with 57%, 64%, 11%, and 97% asymmetric induction, respectively. The α,β-conjugated acetylenic ketones 3-butyn-2-one, 4-methyl-1-pentyn-3-one, and 4-phenyl-3-butyn-2-one underwent a rapid reduction to afford the corresponding propargylic alcohols with 79%, 99%, and 91% enantiomeric purities. The α-haloalkyl aromatic ketones α-chloroacetophenone, α-bromoacetophenone, α-iodoacetophenone, α,p-dibromoacetophenone, α-bromo-*p*-cyanoacetophenone, α-bromo-2′-acetonaphthone, and α,α,α-trifluoroacetophenone afforded the corresponding halohydrins with 96%, 93%, 93%, 96%, 96%, 90%, and 35% enantiomeric purities, respectively. The corresponding aliphatic analogue 1-bromo-3-methyl-2-butanone gave the halohydrin in 66% ee. The other isomer of this ketone, 3-bromo-3-methyl-2-butanone, failed to undergo reduction. Both the aliphatic and aromatic α-keto esters underwent rapid reduction to give the corresponding α-hydroxy esters with excellent enantiomeric excesses. Thus, methyl, ethyl, isopropyl, and *tert*-butyl pyruvates afforded the corresponding lactates with 86%, 83%, 78%, and 92% ee at 25 °C, respectively. Lowering the reaction temperature to 0 °C gave the *tert*-butyl lactate in 100% ee. Other aliphatic α-keto esters such as methyl and ethyl 2-oxopentanoates, methyl 3-methyl-2-oxobutanoate, and ethyl 4-methyl-2-oxopentanoate were reduced to the corresponding α-hydroxy esters with 96%, 96%, 11%, and 82% ee. The methyl, isopropyl, and *tert*-butyl benzoylformates were reduced to the corresponding mandelic esters with 90%, 96% and 100% ee, respectively. The reduction of the β-keto esters, however, proceeded slowly and ethyl acetoacetate gave the corresponding alcohol with 55% ee.

Over the past several decades, the asymmetric reduction or carbonyl compounds has been actively investigated by organic chemists.[2] Most of the early experiments in this direction, however, gave disappointingly low optical yield. The real breakthrough came with the advent of the lithium aluminum hydride/Darvon alcohol complex by Mosher and Yamaguchi in 1973,[3] who reduced acetophenone in 100% chemical yield and 75% ee. More recently, reagents prepared by the partial decomposition of lithium aluminum hydride with chiral amine and phenols (*N*-ethylephedrine + 3,5-dimethylphenol; Vigneron),[4] chiral diamines (xylylidinomethylpyrrolidine; Mukaiyama),[5] chiral binaphthols and simple alcohols (2,2′-dihydroxy-1,1′-binaphthyl + methanol; Noyori),[6] and chiral amine and simple amine (*N*-methylephedrine + *N*-ethylaniline; Terashima)[7] have been applied to the asymmetric reduction of carbonyl compounds with considerable success.

Boranes and borohydrides represent another family of reagents that has proved useful for asymmetric reductions. Even though monoisopinocampheylborane[8] and diisopinocampheylborane[9] are extremely selective chiral hydroborating agents, the chiral reduction of simple ketones with these reagents proceeded with only low asymmetric induction.[10] Similarly, the highly stereoselective chiral

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