Reductions of Conjugated Carbonyl Compounds with Cyanoborohydride in Acidic Media

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The reductions of a variety of conjugated aldehydes and ketones with $NaBH_3CN$ in acidic methanol and hexamethylphosphortriamide (HMPT) have been investigated. Alicyclic carbonyl compounds afforded principally the corresponding allylic alcohols in both solvents with methyl ethers as side products in methanol. The introduction of additional conjugation often resulted in reduction to allylic hydrocarbons, presumably via acid-induced ionization and hydride trapping. Formation of saturated alcohols was not observed in any alicyclic cases studied. Cyclic enones, on the other hand, gave mixtures of allylic and saturated alcohols resulting from competing 1,2 and 1,4 addition of cyanoborohydride.

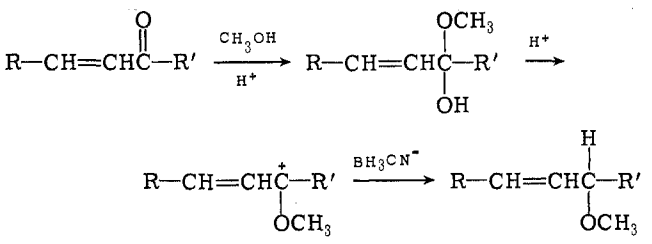
The problems often encountered in the reduction of α,β-unsaturated carbonyl systems with hydride reagents are legion.[1] In addition to affording the corresponding allylic alcohols, the reductions are often accompanied by such side reactions as concomitant reduction of the double bonds leading to saturated alcohols or, less commonly, reduction to enols which eventually give the saturated ketones. Such divergence in reduction products has been attributed to competing 1,2 vs. 1,4 attack by hydride, but predictions concerning the mode of attack for a particular substrate are difficult. In general, 1,4 addition competes favorably when the double bond is further conjugated with an aromatic ring,[2] contained in a five- or six-membered ring,[1b,3] or, at least with $NaBH_4$, conjugated with an additional carboxyl, cyano, or ester group.[4]

Our interest in the reducing capabilities of cyanoborohydride anion coupled with the unique (among metal hydrides) acid stability of the reagent prompted an exploration of its synthetic utility for effecting reductions of conjugated carbonyl systems. This article presents the results of such reductions with a variety of structurally different examples in two media, the polar protic solvent methanol and the polar aprotic solvent hexamethylphosphortriamide (HMPT).

Reductions in Acidic Methanol. As previously noted,[5] the carbonyl reducing capabilities of cyanoborohydride vary greatly with pH. Thus, in basic or neutral media, aldehydes and ketones are practically inert toward the reagent and adequate reduction rates are only obtained under acidic conditions where the carbonyl carbon is rendered more electrophilic by protonation. This was conveniently accomplished using Methyl Orange indicator and 2 N HCl to maintain the pH at about 3. Under these conditions most aldehydes and ketones are readily reduced at room temperature in 1–3 hr. Table I presents the reduction results for a selection of compounds chosen to determine the synthetic effectiveness and scope available in methanol. Both sodium and tetrabutylammonium[5b] cyanoborohydride were employed, but the latter displayed no advantage (entries 4, 7, 8).

Several features of the reductive results are noteworthy. First, the reduction of both alicyclic and β-aryl α,β-unsaturated carbonyls (entries 1–4, 6–9) gave products resulting only from 1,2 attack with no production of saturated alcohol observed. This qualitatively resembles previous investigations with $NaBH_4$ in methanol,[3b] although cyanoborohydride appears more discriminate toward carbonyl attack.[6]

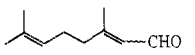
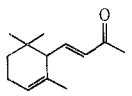
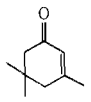
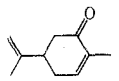
Unlike analogous reductions with borohydride, reductions in acidic methanol often afforded the corresponding methyl ethers in addition to the allylic alcohols. Ostensibly, these side products arise from protonation and ionization of the initially produced alcohol followed by solvent capture. The increase in the yields of such products with increasing conjugation is consistent with this interpretation. Thus, chalcone (entry 5) afforded only the corresponding methyl ether and the allylic hydrocarbon 1,3-diphenylpropene, this latter product apparently produced by hydride capture of the intermediate carbonium ion or displacement of the protonated alcohol. Indeed, treatment of the allylic alcohol chalcol with $NaBH_3CN$ in acidic methanol afforded the same two products. However, the formation of small amounts of methyl ethers from compounds containing less conjugation (entries 1, 6–8, 10) appears more complex than simple ionization of the intermediate allylic alcohols and subsequent solvent capture, since the alcohols were recovered unchanged when subjected to the reaction conditions. We envisioned that one possibility might involve an acid-induced reduction of initially generated acetals to methyl ethers in a similar fashion obtained in the reduction of acetals by mixed hydrides.[8] However, attempts to reduce 3-nitrobenzaldehyde dimethyl acetal with $NaBH_3CN$ in acidic methanol afforded only starting material. Other possibilities include the direct reduction of some allylic species (not the alcohol) or hydride trapping of an ion generated from an intermediate hemiacetal as shown below. This latter interpretation would also explain the absence of allylic hydrocarbon formation.



The reductions of cyclic ketones with $NaBH_3CN$ are considerably more prone to conjugate attack than the alicyclic analogs (entries 10 and 11), affording substantial or major amounts of the saturated alcohols. This parallels the situation in general for metal hydrides which provide hydride anion[3a,9] and is in agreement with previous reports of reductions of cyclic enones with $NaBH_3CN$ in acidic THF.[10]

Reductions in Acidic Hexamethylphosphortriamide (HMPT). The reductions of a variety of conjugated carbonyl compounds in acidic HMPT are presented in Table II. In general, the products paralleled those obtained in methanol with the exception that the nonnucleophilic HMPT precluded the formation of products stemming from solvent involvement. Thus, with alicyclic carbonyls (entries 23–27) and α,β-unsaturated β-aryl systems (entries

Table I
Reduction of Conjugated Carbonyl Compounds with Cyanoborohydride in Acidic Methanol

Entry	Compd	Registry no.	Reagent[a] (ratio hydride/compd)	Time, hr	Products, % yield[b] Allylic alcohol	Allylic hydrocarbon	Allylic ether	Saturated alcohol	Starting material
1	$C_6H_5CH{=}CHCOCH_3$	122-57-6	$NaBH_3CN$ (2)	1.5	77		11		
2	$C_6H_5C{\equiv}CCOCH_3$	1817-57-8	$NaBH_3CN$ (1)	1.25	70				15
3	$C_6H_5C{\equiv}CCOCH_3$		$NaBH_3CN$ (2)	1.5	89				
4	$C_6H_5C{\equiv}CCOCH_3$		TBAC (2)	1.5	80				
5	$C_6H_5CH{=}CHCOC_6H_5$	94-41-7	$NaBH_3CN$ (3)	2.5		48	26		12
6	$C_6H_5CH{=}CHCHO$	104-55-2	$NaBH_3CN$ (2)	1.5	80		8		
7	$C_6H_5CH{=}CHCHO$		TBAC (2)	1.5	58		10		
8		5392-40-5	TBAC (2)	2.0	69[c]		12		
9		127-41-3	$NaBH_3CN$ (2)	2.0	88				
10		78-59-1	$NaBH_3CN$ (2)	1.5	15		9	34	
11		99-49-0	$NaBH_3CN$ (2)	1.5	64			31	

[a] Solutions were acidified with 2 *N* HCl until the color change of Methyl Orange to red (ca. pH 3). [b] Overall yields were determined by isolation; relative percentages of mixture components were determined by GLC. [c] Composed of a mixture of geraniol and nerol.

12–15) exclusive 1,2 attack was observed and respectable yields of allylic alcohols obtained.[11] Likewise, the incorporation of further conjugation resulted in lower amounts (or absence) of allylic alcohols with a concurrent increase in the yields of allylic hydrocarbons (entries 16–22). As in methanol solvent, the allylic products from these highly conjugated systems most probably arise from hydride trapping of carbonium ions produced by protonation of initially formed alcohols. Thus, the relative yields of allylic alcohols and hydrocarbons were acid strength dependent with $NaBH_3CN$ (entries 19 and 20) and 1-(*p*-methoxyphenyl)-1-buten-3-one afforded both rearranged and unrearranged alkenes (entries 19–24). Unlike alicyclic systems, cyclic enones afforded substantial (entries 30–32) or exclusive (entries 28, 29) yields of the corresponding saturated alcohols resulting from 1,4 attack, again in analogy to the situation in methanol and THF.[10]

In summary, cyanoborohydride in acidic media provides a synthetically useful reagent system for the reduction of α,β-unsaturated carbonyls to the allylic alcohols provided that further conjugation is not present or the system is not a cyclic enone. In view of the general functional group selectivity possible with cyanoborohydride,[5] applications should be particularly attractive when other, normally sensitive, groups are present. Thus, although both aluminum hydride[12] and diisobutylaluminum hydride (DBAH)[13] are effective for reductions of conjugated systems to allylic alcohols, both are relatively powerful reducing reagents which would not tolerate the presence of many other functional groups in the molecule. For instance, DBAH readily reduces most common moieties[13b] including acids, esters, amides, epoxides, acetals, nitriles, and alkynes while cyanoborohydride leaves all of the above unmolested.[5] Aluminum hydride also shows poor discrimination among functional groups.[14]

Experimental Section

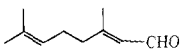
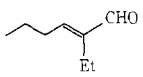
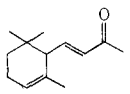
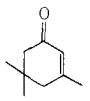
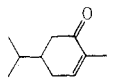
All melting points and boiling points are uncorrected. Infrared spectra were taken on a Perkin-Elmer Model 457 spectrometer. Proton nuclear magnetic resonance spectra were obtained on Varian A-60 spectrometer typically as 10–20% solutions using tetramethylsilane (Me_4Si) as an internal reference. Microanalyses were performed by Chemanalytics Inc., Tempe, Ariz. Gas chromatographic (GLC) analyses of product mixtures and purified samples were performed on a Hewlett-Packard Model 5250B instrument coupled to an L & N Model W recorder equipped with a disk integrator. All analyses were carried out on either a 6 ft × 0.125 in. or 10 ft × 0.125 in. stainless steel column packed with 10% OV-1 or 20% Carbowax 20M on 80/100 mesh Chromosorb W (DMCS). Organic solvents were dried over anhydrous magnesium sulfate. Sodium cyanoborohydride, obtained from ALFA Inorganics, was purified by decolorizing with alkaline Norit-A in hot tetrahydrofuran (THF) followed by solvent removal at reduced pressure. All the other chemicals used were either commercially available or prepared by standard procedures. Hexamethylphosphortriamide (HMPT), obtained from Fisher Scientific Co., was distilled over CaH_2 and stored over 13 A molecular sieves. Authentic samples of products were either obtained commercially or prepared by standard procedures and compared with literature preparations: 4-phenyl-3-buten-2-ol and the methyl ether;[15a] 1-phenyl-1-butyn-3-ol;[15b] cinnamyl alcohol methyl ether;[15c] 3,7-dimethyl-2,6-octadien-1-ol methyl ether;[15d] 1,3-diphenyl-1-propen-3-ol[15e] and the methyl ether;[15f] isophorol;[15g] dihydrocarveol.[15h]

Tetrabutylammonium Cyanoborohydride (TBAC). The reagent was prepared in a similar manner as described for the corresponding borohydride.[16] Thus 33.95 g (0.10 mol) tetrabutylammonium hydrogen sulfate suspended in 50 ml of water was treated at room temperature with 35 ml of 5 *N* NaOH and a solution of 6.93 g (0.11 mol) of $NaBH_3CN$ in 40 ml of water. After 15 min, the mixture was extracted three times with methylene chloride, and the organic solution was washed with water and dried (K_2CO_3). The methylene chloride layer was then decolorized with carbon and concentrated at reduced pressure to afford 22.2 g (78%) of white, crystalline product. This material was pure enough for use in a reduction; the analytical sample was obtained by recrystallization from ethyl acetate, mp 144–145°.

Anal. Calcd for $C_{17}H_{39}N_2B$: C, 72.32; H, 13.92; Found: C, 72.18; H, 13.94.

General Reduction Procedure for α,β-Unsaturated Carbonyl Compounds with $NaBH_3CN$ or TBAC. Methanol Solvent. The procedure was similar to that described by Borch and coworkers for THF.[10a] All reductions were carried out at pH 3. Five millimoles of the carbonyl compound and 10 mmol of the reducing agent were dissolved in 10 ml of solvent containing a trace

Table II
Reduction of Conjugated Carbonyl Compounds with Cyanoborohydride in Acidic HMPT

Entry	Compd		Reagent (ratio hydride/compd)	Acidity, *M*	Time, hr	Products, % yield[a] Allylic alcohol	Allylic hydrocarbon	Saturated alcohol	Starting material
12	$C_6H_5CH{=}CHCOCH_3$		$NaBH_3CN$ (4)	1.9	1.0	58			
13	$C_6H_5CH{=}CHCOCH_3$		TBAC (4)	1.9	1.0	65			
14	$C_6H_5C{\equiv}CCOCH_3$		$NaBH_3CN$ (4)	1.9	1.0	71			
15	$C_6H_5C{\equiv}CCOCH_3$		TBAC (4)	1.9	1.0	64			
16	$C_6H_5CH{=}CHCOC_6H_5$		$NaBH_3CN$ (4)	0.75	1.0		53[b]		16[b]
17					10.0		61[b]		
18	$C_6H_5CH{=}CHCOC_6H_5$		TBAC (4)	0.75	1.0		46[b]		12[b]
19	p-$CH_3OC_6H_4CH{=}CHCOCH_3$	943-88-4	$NaBH_3CN$ (4)	0.25	1.25	20	59[c]		2
20				0.84	1.25		82[d]		
21			TBAC (4)	0.25	1.25	41	34[e]		4
22			TBAC (4)	0.84	1.25	41	36[f]		2
23			$NaBH_3CN$ (4)	1.9	1.5	79			
24			TBAC (4)	1.9	1.5	76			
25		645-62-5	$NaBH_3CN$ (4)	0.5	1.5	82			
26			$NaBH_3CN$ (4)	1.9	1.5	60			
27			TBAC (4)	1.9	1.5	63			
28			$NaBH_3CN$ (4)	1.9	1.0			57	
29			TBAC (4)	1.9	1.0			56	
30		43205-82-9	$NaBH_3CN$ (4)	1.9	1.0	18		48	
31	Cholest-4-en-3-one	601-57-0	$NaBH_3CN$ (4)	1.1	1.0	16		77	
32			TBAC (4)	0.75	1.0	14		80	

[a] Overall yields were determined by isolation; unless specified otherwise relative percentages of mixture components were determined by GLC. [b] Yields determined by GLC using internal standards. [c] Mixture of 1-(*p*-methoxyphenyl)butene (27%) and 1-(*p*-methoxyphenyl)-2-butene (32%). [d] Mixture of 1-(*p*-methoxyphenyl)butene (44%) and 1-(*p*-methoxyphenyl)-2-butene (38%). [e] Mixture of 1-(*p*-methoxyphenyl)butene (15%) and 1-(*p*-methoxyphenyl)-2-butene (19%). [f] Mixture of 1-(*p*-methoxyphenyl)butene (18%) and 1-(*p*-methoxyphenyl)-2-butene (18%).

amount of Methyl Orange indicator. A solution of 2 *N* HCl–solvent was added dropwise in order to maintain the red color. After stirring for the appropriate length of time (no more change in red color) the solvent was evaporated in vacuo. The residue was taken up in water (8 ml) and extracted with ether (3 × 25 ml) and the ether layer was dried and concentrated to obtain the product.

HMPT Solvent. To cold (0°) HMPT (10–15 ml) was added sufficient sulfuric acid to bring the acidity to the appropriate value listed in Table II for ketones or for aldehydes, followed by the addition of 5 mmol of the carbonyl compound and 20 mmol of the reducing agent ($NaBH_3CN$ or TBAC). The reaction mixture was stirred at 25° for the appropriate length of time (Table II). Water was added and stirring was continued for an additional 1 hr. The reaction mixture was extracted with ether, which was washed with water, dried, and concentrated on a rotary evaporator. The residue was analyzed by GLC on a 20% Carbowax 20M column and the products were identified by ir, NMR, or by comparison with authentic samples. In some cases the residue was further purified by using a short alumina column. The procedures are presented as representative examples below.

Reduction of Benzalacetone with TBAC. The reduction of 0.92 g (6.3 mmol) of the ketone with 25 mmol (7.05 g) of TBAC in 25 ml of HMPT containing 15 equiv of sulfuric acid for 1.25 hr at room temperature gave, after the usual work-up, 0.91 g of residue. The residue on distillation from a Kugelrohr apparatus gave 0.8 g (86%) of liquid which by GLC and NMR was identified as 4-phenyl-3-buten-2-ol by comparison with an authentic sample.

Reduction of Benzalacetophenone with $NaBH_3CN$ in Methanol (2.5 hr). Following the general procedure, the reduction of 1.03 g (5 mmol) of the ketone with 0.95 g (15 mmol) of $NaBH_3CN$ in 10 ml of methanol at pH 3 for 2.5 hr gave, after the usual work-up, 0.88 g (86%) of residue. Analysis by GLC (6 ft 10% OV-1 column) indicated the presence of 48% 1,3-diphenyl-1-propene, 26% 1,3-diphenylallyl methyl ether, and 12% starting material. No alcohol was detected in the product mixture.

Isophorol Methyl Ether. To a cold (0°), stirred solution of 2.8 g (20 mmol) of isophorol in 20 ml of HMPT was added 0.96 g (40 mmol) of NaH. After 30 min, 5.7 g(40 mmol) of methyl iodide was added slowly and the stirring was continued for an additional 2 hr. Water was then added, the mixture was extracted with ether (3 × 25 ml), and the ether solution was washed with water, dried, and concentrated. Distillation of the residue afforded 1.8 g (59%) of product: bp 46° (0.9 mm); $n^{25}D$ 1.4568; ir (neat) 2900 (s), 1670 (m), 1450 (s), 1380, 1370 (s), 1360 (vs), 1265 (w), 1200 (m), 1160, 1140 (w), 1125 (s), 1090 (vs), 1000 (w), 960, 940 (s), 810 cm^{-1} (m); NMR ($CDCl_3$) δ 0.95 (d, 6 H, *gem*-dimethyl), 1.1–1.85 (m, 4 H, $-CH_2-$), 1.65 (s, 3 H, vinylic methyl), 3.32 (s, 3 H, $-OCH_3$), 3.73 (m, 1 H, $-CHOCH_3$), 5.48 (broad, 1 H, vinylic).

Anal. Calcd $C_{10}H_{18}O$: C, 77.87, H, 11.76. Found: C, 78.36; H, 11.95.

Registry No.—$NaBH_3CN$, 25895-60-7; TBAC, 43064-96-6; tetrabutylammonium hydrogen sulfate, 32503-27-8; methanol, 67-56-1; HMPT, 680-31-9; isophorol methyl ether, 50987-46-7; isophorol, 470-99-5; methyl iodide, 74-88-4.

References and Notes

(1) (a) For a discussion and leading references, see H. O. House, "Modern Synthetic Reactions", W. A. Benjamin, New York, N.Y., 1972, pp 89–96. (b) As an illustration of the divergence of product distributions from cyclic enones which may be obtained with different hydride reagents, see H. C. Brown and H. M. Hess, *J. Org. Chem.*, **34**, 2206 (1969). (c) Recently, exclusive 1,4 reduction of α,β-unsaturated systems to saturated ketones has been achieved using copper(I) hydride complexes; see R. K. Boeckman, Jr., and R. Michalak, *J. Am. Chem. Soc.*, **96**, 1623 (1974).

(2) R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, **70**, 3738 (1948).

(3) (a) W. R. Jackson and A. Zurqiyah, *J. Chem. Soc.*, 5280 (1965); (b) K. Iqbal and W. R. Jackson, *J. Chem. Soc. C*, 616 (1968).

(4) (a) J. A. Meschino and C. H. Bond, *J. Org. Chem.*, **28**, 3129 (1963); (b) G. Luciani and F. Montanari, *Boll. Sci. Fac. Chim. Ind. Bologna*, **18**, 47 (1960).

(5) (a) R. F. Borch, M. D. Bernstein, and H. D. Durst, *J. Am. Chem. Soc.*, **93**, 2897 (1971); (b) R. O. Hutchins and D. Kandasamy, *ibid.*, **95**, 6131 (1973).

(6) The increase in 1,2 addition by borohydride with increasing solvent polarity has been attributed to the ability of polar solvents (such as methanol) to more effectively stabilize the more charge-localized transition state of 1,2 addition.[3b] However, the rapid reaction of $NaBH_4$ with methanol[7] and the demonstrated preponderance of carbonyl attack by trialkoxyborohydride[3a] may account for much of the selectivity shown by borohydride. In addition, 1,4 attack of β-aryl conjugated systems involves loss of conjugation with the phenyl ring while no such loss occurs upon 1,2 addition.

(7) See H. C. Brown, "Boranes in Organic Chemistry", Cornell University Press, Ithaca, N.Y., 1972, p 214, and references cited therein.

(8) (a) P. T. Lansbury and R. E. Macleay, *J. Org. Chem.*, **28**, 1940 (1963); (b) E. L. Eliel, V. G. Badding, and M. N. Rerick, *J. Am. Chem. Soc.*, **84**, 2371 (1962).

(9) See H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, pp 89–97, and references cited therein.

(10) (a) Borch and coworkers obtained only cyclopentanol upon reduction of 2-cyclopentenone: R. F. Borch, M. D. Bernstein, and H. D. Durst, *J. Am. Chem. Soc.*, **93**, 2897 (1971). (b) Steroidal α,β-unsaturated ketones also give substantial 1,4-addition products with $NaBH_3CN$ in acidic THF: M.-H. Boutique, R. Jacquesy, and Y. Petit, *Bull. Soc. Chim. Fr.*, **11**, 3062 (1973).

(11) The absence of allylic hydrocarbons in the reductions of alicyclic carbonyl compounds reinforces the previous suggestion that the allylic ethers formed from these systems in acidic methanol did not arise from acid-catalyzed reactions of the allylic alcohols; otherwise the corresponding reductions in HMPT should have produced some allylic hydrocarbons (compare entries 1 and 8 with entries 12, 13, 23, and 24).

(12) C. G. Scouten and H. C. Brown, *J. Org. Chem.*, **38**, 4092 (1973); H. C. Brown, E. F. Knights, and C. G. Scouten, *J. Am. Chem. Soc.*, **96**, 7765 (1974).

(13) (a) K. E. Wilson, R. T. Seidner, and S. Masamune, *Chem. Commun.*, 213 (1970); (b) "The Use of Aluminum Alkyls in Organic Synthesis", Ethyl Corp., 1970 and 1973.

(14) Recently, Brown and Krisnamurthy have utilized 9-BBN to cleanly reduce conjugated systems to allylic alcohols. This reagent appears to offer good selectivity with respect to other functional groups: S. Krishnamurthy and H. C. Brown, presented at the 169th National Meeting of the American Chemical Society, Philadelphia, Pa., April 1975; S. Krishnamurthy and H. C. Brown, *J. Org. Chem.*, **40**, 1864 (1975).

(15) (a) J. Kenyon, S. M. Partridge, and H. Phillips, *J. Chem. Soc.*, 207 (1937); (b) G. A. Olah and C. U. Pittman, *J. Am. Chem. Soc.*, **87**, 5632 (1965); (c) B. Gredy, *Bull. Soc. Chim. Fr.*, 1093 (1936); (d) A. V. Semenovskii, V. A. Smit, T. N. Chernova, and V. F. Kucherov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **6**, 1068 (1965); (e) T. Sato and I. Homma, *Bull. Chem. Soc. Jpn.*, **44**, 1885 (1971); (f) E. Bergmann and T. Ukai, *Ber.*, **66**, 54 (1933); (g) H. Rubinstein, *J. Org. Chem.*, **27**, 3886 (1962); (h) C. V. Pigulevskii and I. S. Kozhima, *Zh. Obshch. Khim.*, **25**, 416 (1955); *Chem. Abstr.*, **50**, 2500*b* (1956).

(16) A. Brandstrom, U. Junggren, and B. Lamm, *Tetrahedron Lett.*, 3173 (1972).

Notes

Evidence of Significant Participation of the Less Stable Conformation in the Reduction of 2-Methylcyclohexanone by Sodium Borohydride

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The reduction of conformationally mobile 2-alkylcyclohexanones by complex metal hydrides can, in principle, occur through two conformations: one with the alkyl group equatorial and the other with the alkyl group axial. Thus it is possible that both cis and trans alcohols may arise via two different routes, i.e., axial or equatorial attack on a given conformation (Scheme I).

From the point of view of investigating the origin of the stereoselectivity in reductions of cyclohexanones by complex metal hydrides, the question of just how each alcohol is formed is a vital one, and in a previous study[1] we demonstrated, by analysis of the relative magnitudes of activation enthalpies, that the trans alcohol **2** is derived almost exclusively from conformation **1e**. However, we were unable to determine whether the cis alcohol was derived from conformation **1a**, **1e**, or both, owing to experimentally indistinguishable values of $\Delta H^{\ddagger}$ for the two possible processes. Since we know, however, that conformation **1a** does not

Scheme I
Reduction of 2-Methylcyclohexanone