Table I
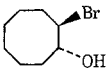### Reduction of Bromohydrins to Olefins with TiCl₃–LiAlH₄

	Yield, %
→ Cyclooctene	96
→ Indene	93
→ Cholesterol	79
2-Bromo-1-decanol → 1-Decene	74
2-Bromo-1-dodecanol → 1-Dodecene	91
erythro-5-Bromo-6-decanol → 5-Decene (4:1 trans/cis)	91
threo-5-Bromo-6-decanol → 5-Decene (2.3:1 trans/cis)	82

It had been our hope in initiating this study that titanium(II) might function as a two-electron reducing agent in the manner shown (path A). Should this occur, one would expect preferential trans elimination leading to specific olefin geometry (threo → cis; erythro → trans). Since this desired retention of geometry is not observed, however, we favor a mechanistic pathway involving one-electron transfer and the intermediacy of radicals, similar to that proposed for chromous ion[2] (path B).
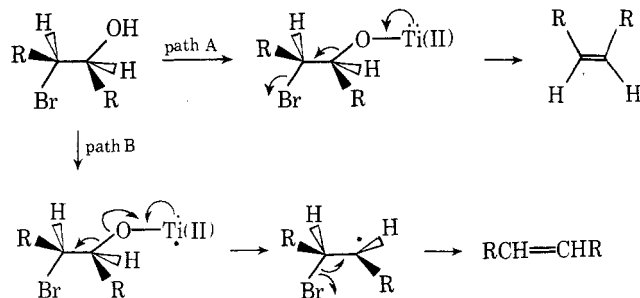
Experimental Section

General Reaction Procedure. The reactive titanium(II) species was made in either of two ways.

Method A. LiAlH₄ (0.142 g, 3.75 mmol) was added to a stirred slurry of TiCl₃ (2.3 g, 15 mmol) in 70 ml of dry tetrahydrofuran (THF) under a nitrogen atmosphere. Hydrogen evolution was immediate, and the resulting black titanium(II) suspension was stirred for 10 min at room temperature before use.

Method B. Alternatively, a 4:1 premix of TiCl₃ and LiAlH₄[6] (effective mol wt 164, 2.46 g, 15.0 mmol) was added cautiously with stirring to 70 ml of dry THF at room temperature under a nitrogen atmosphere. The black titanium(II) suspension was stirred for 10 min before use.

The substrate bromohydrin (5.0 mmol) in 5 ml of THF was added to the Ti(II) suspension, and the reaction mixture was refluxed for 16 hr. After cooling, the reaction was quenched by addition of 60 ml of water, and then diluted with pentane. The organic layer was drawn off, washed with brine, dried (MgSO₄), and concentrated by distillation. Product yields were then determined by GLC using appropriate internal standards. Product identities were determined in all cases by comparison with authentic samples. In this manner, the following reactions were run.

trans-2-Bromocyclooctanol gave **cyclooctene**, 96% as determined by GLC using indene as internal standard.

trans-1-Bromo-2-hydroxyindan gave **indene**, 93% as determined by GLC using cyclooctene as internal standard.

6β-Bromo-3β,5α-dihydroxycholestane gave **cholesterol**, 79% isolated yield, mp 148° (lit. 148.5°).

2-Bromo-1-decanol gave 1-decene, 74% as determined by GLC using 1-dodecene as internal standard.

2-Bromo-1-dodecanol gave 1-dodecene, 91% as determined by GLC using 1-decene as internal standard.

erythro-5-Bromo-6-decanol gave 5-decene, 91% as determined by GLC using 1-decene as internal standard. The product 5-decene was analyzed for cis/trans composition by the following method (the cis and trans 5-decenes were inseparable by GLC under all conditions tried). Epoxidation of the olefin mixture with *m*-chloroperbenzoic acid (CHCl₃, room temperature) gave a mixture of isomeric epoxides which could be analyzed either by NMR integration [*cis*-5-decene epoxide, NMR (CCl₄) δ 2.91 (–CHO–, broad singlet); *trans*-5-decene epoxide, NMR (CCl₄) δ 2.67 (–CHO–, broad singlet)] or by GLC (12 ft × 0.25 in. 5% Carbowax 20M on Chromosorb P). A control experiment on a known cis/trans mixture established the validity of the analysis.

The 5-decene thus analyzed contained 80% trans olefin and 20% cis olefin.

threo-5-Bromo-6-decanol gave 5-decene, 82% as determined by GLC using 1-decene as internal standard. The product was 70 trans, 30% cis.

Registry No.—*trans*-2-Bromocyclooctanol, 1502-14-3; *trans*-1-bromo-2-hydroxyindan, 56804-70-7; 6β-bromo-3β,5α-dihydroxycholestane, 1857-83-6; 2-bromo-1-decanol, 39579-74-3; 2-bromo-1-dodecanol, 56804-71-8; *erythro*-5-bromo-6-decanol, 56804-72-9; *threo*-5-bromo-6-decanol, 56804-73-0; cyclooctene, 931-88-4; indene, 95-13-6; cholesterol, 57-88-5; 1-decene, 872-05-9; 1-dodecene, 112-41-4; *trans*-5-decene, 7433-56-9; *cis*-5-decene, 7433-78-5.

References and Notes

(1) See D. R. James, R. W. Rees, and C. W. Shoppee, *J. Chem. Soc.,* 1370 (1955), for a study of the reaction.
(2) J. K. Kochi and D. M. Singleton, *J. Am. Chem. Soc.,* **90,** 1582 (1968).
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(5) For a careful study of the stereochemistry of the reaction, see J. W. Cornforth, R. H. Cornforth, and K. K. Mathew, *J. Chem. Soc.,* 112 (1959).
(6) This premix is sold commercially by Alfa Inorganics, Beverly, Mass.

## Stereochemistry of Hydride Reductions. Participation by Heteroatoms

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The reduction of alkyl halides with hydride ion is generally believed to occur by an SN2 mechanism leading to inversion of configuration. Studies using LiAlD₄, NaBD₄ in HMPA, and LiEt₃BD have shown exclusive inversion in the absence of any secondary factors.[1,2] However, a recent example of nitrogen participation through complexing with the hydride reagent has resulted in retention of configuration.[3]

We have studied the LiAlD₄ reduction of the isomeric *endo,endo*- and *exo,exo*-2,6-diiodo-9-oxabicyclo[3.3.1]nonanes[4,5] (structures 1 and 3). In each case reduction led to an identical product identified as *exo,exo*-2,6-dideuterio-9-oxabicyclo[3.3.1]nonane (2) by NMR, ir, and mass spectroscopy. In particular, the infrared spectrum showed C–D absorptions at 2140 and 2160 cm⁻¹ which correspond to values reported for axial C–D stretch in 1,3-dioxanes.[6] The NMR was studied in detail by use of Eu(thd)₃. The 9-oxabicyclononanes have been found to form strong shift com-

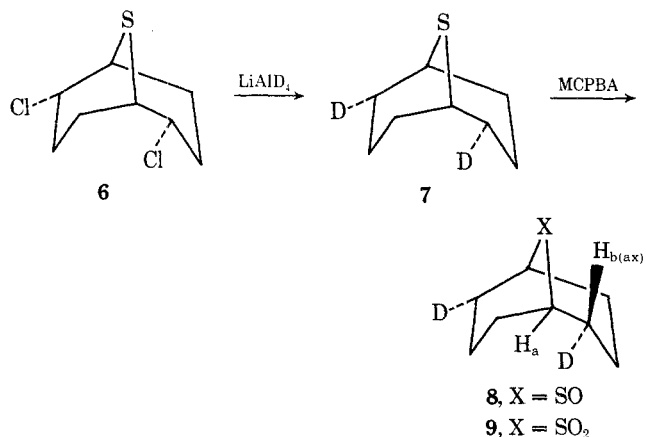Figure 1. Europium-shifted spectrum of exo,exo-2,6-dideuterio-9-oxabicyclo[3.3.1]nonane.
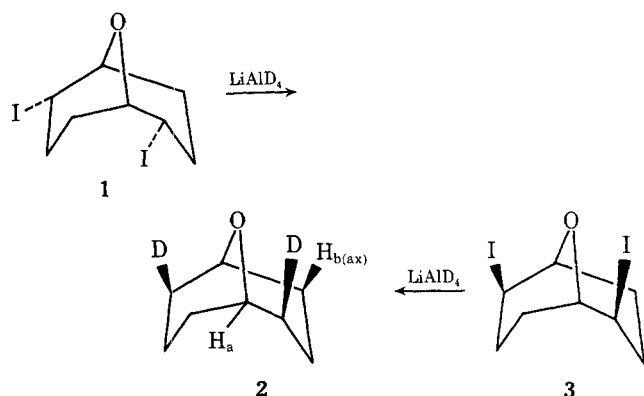
plexes (ΔEu = 37)[4] and it was possible to obtain individual peaks for all the protons of 2. Thus integration of the shifted spectrum $H_a/H_{b(axial)}$ (2:2) provided clear evidence that the deuteriums were in the axial (exo) positions (Figure 1).

Reduction of the exo,exo diiodide 3 with NaBH₄ (1:1) in HMPA at 45° gives the monoiodide 4 while reduction with excess hydride gives 9-oxabicyclo[3.3.1]nonane. Use of NaBD₄ gives 2,6-dideuterio-9-oxabicyclo[3.3.1]nonane (5)
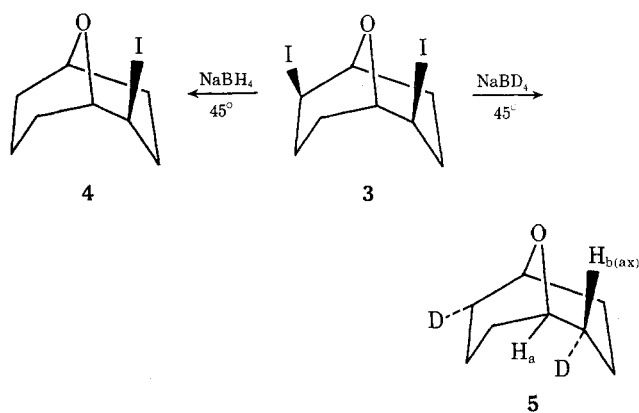
(mass spectrum and NMR). Analysis of the NMR with Eu(thd)₃ showed an $H_a/H_{b(axial)}$ ratio of 2:4 indicating that the deuteriums are in the equatorial (endo) positions. The results of the analysis for the location of the deuteriums become readily apparent when the shifted NMR spectra of the endo,endo diiodide 1, endo,endo-dideuterio-5, and exo,exo-dideuterio-2 are directly compared.

A similar reduction of endo,endo-2,6-dichloro-9-thiabicyclo[3.3.1]nonane (6) with LiAlD₄ was found to give exclusively endo,endo-2,6-dideuterio-9-thiabicyclo[3.3.1]nonane (7). For analysis 7 was converted into both the sulfoxide (8)

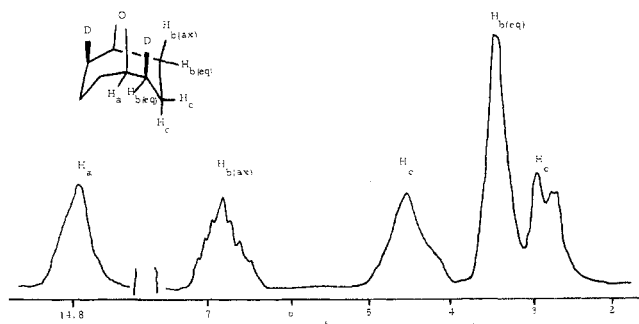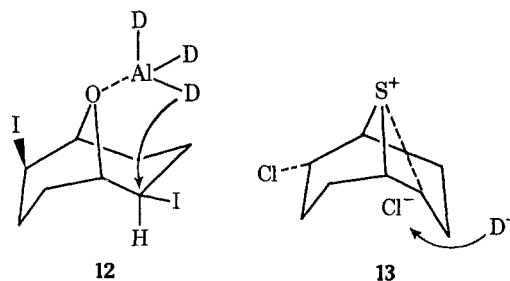and the sulfone (9). Mass spectral data of the parent peak and major cleavage peaks (sulfone, P − SO₂; sulfoxide, P −

O, P − SO) indicated the presence of two deuteriums while analysis of the NMR spectrum with Eu(thd)₃ showed the deuteriums to be in the equatorial (endo) positions. The sulfone 9 showed no change in the integrated ratio of the H_a to $H_{b(axial)}$ protons. The sulfoxide 8 spectrum was more complex because of the unsymmetrical nature of the structure and of its europium complex 10.[8] Thus, the protons H_b
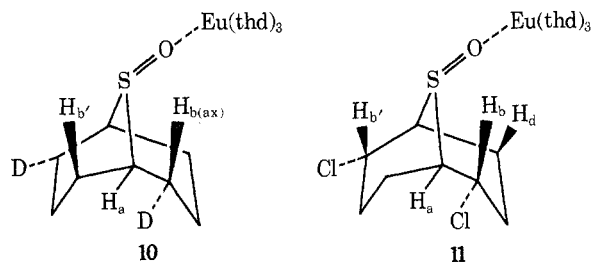
axial are different from $H_{b'(ax)}$ and have a higher ΔEu value (8.0) than the H_a proton (ΔEu = 5.0). Integration of these protons showed an H_a/H_b ratio of 2:2 indicating that the deuteriums are not in the axial (exo) position (no change in this integration between deuterated and nondeuterated 10). To further check these assignments, the europium-shifted spectrum of endo,endo-2,6-dichloro-9-thiabicyclo[3.3.1]nonane 9-oxide (11) was studied.[7] The ΔEu values obtained follow: H_a = 6.7, H_b = 11.7, H_d = 10.0, $H_{b'}$ = 1.4. Interestingly, proton H_d moves through both H_a and H_b with added amounts of Eu(thd)₃ and gives the correct proton ratios of H_d/H_b (1:1) and H_d/H_a (1:2). This behavior parallels that for the deuterated product (10) and supports the analysis.

The above results indicate that, in the presence of heteroatoms, hydride reduction can proceed with retention of configuration. The reduction of 3 requires a complex, whose exact nature is unclear, between the reagent and the bridging oxygen. A possible change in conformation of the ring to a pseudoboat conformation 12 with donation of deu-

teride from this intermediate, in which iodine is equatorial, could result in formation of 2. Evidence for oxygen participation in hydride reactions has been found in the reduction of bonds in 7-tert-butoxynorbornadiene and similar compounds,[9] in 2-methoxy-1,3-dioxanes,[6] and in allylic ace-

tals.[10] The reduction of the endo,endo isomer 1 proceeds with inversion as expected, but it could also involve a prior oxygen complex. The NaBD$_4$ reduction in HMPA also proceeds with inversion with the exo,exo diiodide (3) and would not involve any complexation. These contrasting stereochemical results between NaBD$_4$ and LiAlD$_4$ thus support an oxygen–aluminum complex as an intermediate in the LiAlD$_4$ reductions.

All reported S$_N$2 reactions of 6 proceed with retention of configuration through an episulfonium ion as an intermediate.[7] Thus a similar intermediate 13 could account for the observed retention in the hydride reduction of 6. The lack of rearrangement to the 9-thiabicyclo[4.2.1]nonane could be due to the stability of the episulfonium ion as well as the known thermodynamic stability of the bicyclo[3.3.1]nonane over the bicyclo[4.2.1]nonane.[4,11] In contrast to the oxa and thia cases, the aza analog, *endo,endo*-2,6-dichloro-*N*-methyl-9-azabicyclo[3.3.1]nonane, suffers 30% rearrangement to the [4.2.1] system.[12] The stereochemistry of this reduction is presently being investigated.

Experimental Section

Materials and Reactions. Ether was distilled from LiAlH$_4$ before use. The diiodides, 1 and 3, and the dichloride 6 were prepared from 1,5-cyclooctadiene as previously described and purified by recrystallization to the reported melting points.[4,5,7] The sulfone was prepared using acetic acid and hydrogen peroxide as reported[7] while the sulfoxide was prepared using *m*-chloroperbenzoic acid. The recrystallized products had the reported melting points.[7] The LiAlD$_4$ was purchased from Research Organic/Inorganic Corp., and the NaBD$_4$ from Ventron Corp. The analyses were done on a Varian EM-600 mass spectrometer, a Varian T-60 NMR spectrometer, and a Varian 1200 gas chromatograph. The reduction reactions were carried out on a 1-g scale with excess deuteride and worked up by standard procedures to give exclusively the products indicated. The 9-oxabicyclo[3.3.1]nonane was shown to be pure by GLC analysis at 105° on 10% CW-20M column.

Spectral Analysis. *exo,exo*-2,6-dideuterio-9-oxabicyclo-[3.3.1]nonane (2): NMR δ 4.0 (2), 1–2.0 (10); MS *m/e* 128 (P); infrared 2140, 2160, 1490, 1030 cm^{-1}. *endo,endo*-2,6-Dideuterio-9-oxabicyclo[3.3.1]nonane (5): NMR δ 4.0 (2), 1–2.0 (10); MS *m/e* 128 (P). *exo*-2-Iodo-9-oxabicyclo[3.3.1]nonane (4): NMR δ 4.4 (1) ($W_{1/2}$ = 8, endo $W_{1/2}$ = 16 Hz), 4.0 (2), 2.8–1.0 (10); infrared 1490, 1028 cm^{-1}. *endo,endo*-2,6-Dideuterio-9-thiabicyclo[3.3.1]nonane 9-dioxide (9): NMR δ 1.4–3.05; MS *m/e* 176 (P), 112 (P – SO$_2$); infrared 2920 w, 1280, 1120 (sulfone), 1090 cm^{-1}. Sulfoxide 8: NMR δ 1.4–3.2; MS *m/e* 160 (P), 144 (P – O), 112 (P – SO); infrared 2160, 2130, 1050 cm^{-1}.

References and Notes

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An Attempt to Observe Neighboring-Group Participation in Hydrogen Abstraction from β-(Substituted Phenyl)-Ethyl Bromides[1]

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Some recent applications of the Hammett equations have been concerned with nonlinearity. Streitwieser and his co-workers, for example, have shown that the data for acetolysis of substituted benzyl tosylates define two intersecting straight lines. This has been interpreted in terms of a change in the expected S$_N$1 mechanism to an S$_N$2 pathway when carbonium ion destabilizing groups are present.[2] Similarly Gassman and Fentiman have determined that a nonlinear behavior for the Hammett correlation of the data for dissociations of *syn*-7-aryl-*anti*-7-norbornenyl *p*-nitrobenzoates is indicative of variable nonclassical participation by the olefinic double bond.[3]

It was felt that a similar approach might be fruitfully applied to a problem in radical chemistry. Participation by neighboring bromine atoms in the course of hydrogen abstraction was first observed by Thaler in the bromination of 1-bromobutane.[4] Although there have been several attempts at refutation, this type of participation has been observed in many related systems. A vast body of evidence may be cited in support of the original findings.[5,6] One system which has not been investigated, however, is the formation of 1-aryl-2-bromoethyl radical (1) from β-(substituted phenyl)-ethyl bromides (2) via hydrogen abstraction.
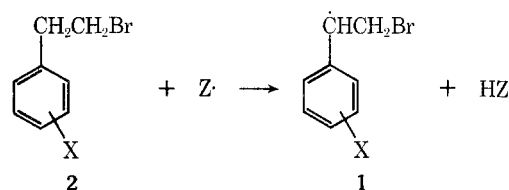
Normally a radical such as 1 would attain extensive stabilization by benzylic delocalization. Bromine participation would be unnecessary in such an event. As electron-withdrawing groups are introduced into the system, however, the destabilized radical might now make use of any additional mode of stabilization available. This should not only be true of 1, but also of the transition state leading to 1 in an endothermic reaction.[7]

As an additional point of reference, it was felt that a ρ value for hydrogen abstraction from 2 by the trichloromethyl radical could be theoretically evaluated in advance. Several series of α-substituted toluenes (3) have undergone
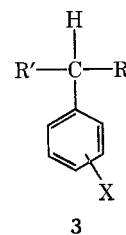
hydrogen abstraction with the radical generated from bromotrichloromethane. The corresponding ρ values are functions of the electronic and steric parameters of the groups directly attached to the reaction site. An empirical relationship has been developed which successfully correlated the available data (eq 1).[8]