J. Org. Chem. 1983, 48, 3091-3096

stirred vigorously and monitored by GLC for the disappearance of the alkyl bromide, maintaining the injector temperature at 100 °C. (It was established independently that at 100 °C injection temperature, the tertiary bromide passes through the column without any decomposition.) In 24 h, 93% of the bromide had disappeared.

Another run of this reaction was conducted exactly as above on a 5-mmol scale and allowed to stir for 24 h at 25 °C. Then excess hydride was destroyed, ether was added, and the ethereal layer was subjected to gas chromatographic examination on a 5% SE-30 column, 18 ft × 0.125 in. This revealed a <2% yield of 2-methylpentane, 17% of 2-methyl-1-pentene, 67% of 2-methyl-2-pentene, and 8% of unreacted 2-bromo-2-methylpentane.

Reduction of Cyclooctyl Bromide by Lithium Hydride in the Presence of a Catalytic Quantity of Triethylborane. The apparatus was the same as in the previous experiments. In the flask was placed 0.24 g of finely divided lithium hydride (30 mmol) and 12.4 mL of THF. The mixture was heated under reflux under nitrogen for 30 min. Then 0.56 mL of triethylborane (4 mmol) (as catalyst), 3.9 mL of *n*-decane (20 mmol) (internal standard), and 3.12 mL of cyclooctyl bromide (20 mmol) were introduced. The reaction mixture was stirred vigorously. As the reaction proceeds, the reaction mixture approaches clarity, due to conversion of the suspended lithium hydride to soluble lithium bromide and soluble lithium triethylborohydride. After 0.5 h, 0.5 mL of the reaction mixture was withdrawn by a syringe, quenched with water, extracted with ether, and analyzed by GLC on a 5% SE-30 column, 12 ft × 0.125 in. This revealed the presence of 77% cyclooctane and 23% of unreacted cyclooctyl bromide. After 1 h, GLC analysis revealed the presence of 98% cyclooctane and traces of cyclooctyl bromide. No cyclooctene was detected.

Reduction of 2-Bromooctane with Lithium Triethylborodeuteride. A typical reaction setup was assembled. Into the reaction flask maintained at 25 °C 10 mL of a 1.0 M solution of lithium triethylborodeuteride (10 mmol) was injected into the reaction flask, followed by 5 mL of a 1.0 M solution in THF of *n*-nonane (5 mmol) to serve as the internal standard. The reaction was monitored by GLC on a 5% SE-30 column, 12 ft × 0.125 in.; 92% of the reduction was over in 4 h. This reveals that the rate of reaction is slightly slower than the corresponding reaction involving LiEt$_3$BH. A small quantity of octane-2-*d* was separated from the reaction mixture by preparative GLC on a 10% SE-30 column, 12 ft × 0.5 in., and subjected to mass spectral analysis. Six individual scans were made. The percentage of deuterium incorporation was computed as follows: let M be the intensity of the peak at m/e 114 (due to unlabeled *n*-octane) and $M + 1$ be the intensity of the peak at m/e 115. Correcting for the contributions of the unlabeled species to the peak at m/e 115, the intensity of this peak due to octane-2-*d* alone is given by $(M + 1)_{\text{cor}} = (M + 1) - M \times 0.067$. The percentage of deuterium incorporated is given by

$$\frac{(M + 1)_{\text{cor}} \times 100}{(M + 1)_{\text{cor}} + M}$$

This was found to be 94 ± 1%; after correction for the isotopic purity of the starting lithium deuteride used (98.2%), the actual deuterium incorporation is 96 ± 1%.

Acknowledgment. Financial support of this study by the U.S. Army Research Office through grant DA 31-124-(AROCD)453 is gratefully acknowledged.

Registry No. LiEt$_3$BH, 22560-16-3; LiAlH$_4$, 16853-85-3; LiBH$_4$, 16949-15-8; *n*-octyl chloride, 111-85-3; cyclohexyl bromide, 108-85-0; benzyl bromide, 100-39-0; allyl bromide, 106-95-6; *n*-octyl iodide, 629-27-6; *n*-octyl bromide, 111-83-1; *n*-octyl tosylate, 3386-35-4; 1-bromo-2-methylpentane, 25346-33-2; neopentyl bromide, 630-17-1; 2-bromooctane, 557-35-7; 2-bromo-2-methylpentane, 4283-80-1; cyclohexyl iodide, 626-62-0; cyclohexyl chloride, 542-18-7; cyclopentyl bromide, 137-43-9; cycloheptyl bromide, 2404-35-5; cyclooctyl bromide, 1556-09-8; *exo*-norbornyl bromide, 2534-77-2; 1-bromonaphthalene, 90-11-9; lithium triethylborodeuteride, 74540-86-6; *n*-butyl mercaptide, 20733-16-8; thiophenoxide, 13133-62-5; borohydride, 16971-29-2; nitrate, 14797-55-8.

Selective Reductions. 32. Structural Effects on the Reduction of Epoxides by Lithium Triethylborohydride. A Kinetic Study

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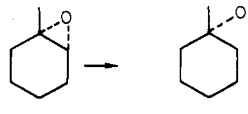
Received December 14, 1982

An analytical procedure for the estimation of lithium triethylborohydride utilizing iodimetry has been developed. The rates of reduction of a number of epoxides are studied. The reaction exhibits second-order kinetics, first order with respect to each reactant. Methyl substitution decreases the reactivity of the epoxide by a factor of 8–10. In the case of aliphatic derivatives, the cis epoxide reacts 12 times faster than the trans. On the other hand, *cis*- and *trans*-β-methylstyrene oxides exhibit the opposite trend. A remarkable change in the regioselectivity of reduction of these two epoxides was observed. A possible explanation is presented. The kinetic isotope effect has been established both by rate studies and by determination, by mass spectrometry, of the deuterium incorporation in a competitive reaction between LiEt$_3$BH, LiEt$_3$BD, and the epoxide. A value of $k_{\text{H}}/k_{\text{D}} \approx 1.4$–$1.5$ is obtained by both methods. A mechanism is proposed to account for these results.



(1)

(100% tertiary)

Reduction of epoxides by lithium triethylborohydride (Super-Hydride, Aldrich) is quite facile and highly regiospecific, yielding exclusively the Markovnikov alcohol.[1] Thus, 1,2-epoxybutane gives 2-butanol and 1-methylcyclohexene oxide gives 1-methylcyclohexanol exclusively (eq 1). Even the reduction of styrene oxide produces 97% of 1-phenylethanol. This remarkable regioselectivity prompted us to use this reaction as a model for a projected study of the asymmetric reduction of epoxides using optically active trialkylborohydrides, such as lithium *B*-iso-

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(1) Brown, H. C.; Kim, S. C.; Krishnamurthy, S. *J. Org. Chem.* **1980**, *45*, 1.

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Table I. Estimation of Lithium Triethylborohydride by Iodimetry[a]

$LiEt_3BH$ added y, mL	thiosulfate consumed z, mL	thiosulfate equiv to hydride $x - z$, mL	hydride, M
0.25	18.2	2.4	0.00974
0.50	15.8	4.8	0.00974
0.75	13.4	7.2	0.00974
1.00	11.1	9.5	0.00964

[a] 2 mL iodine = 20.6 mL of 0.00203 M thiosulfate.

pinocampheyl-9-borabicyclo[3.3.1]nonyl hydride.[2] Consequently, we undertook to study structural effects on the rate of reduction of epoxides by lithium triethylborohydride. However, a number of epoxides were reduced exceedingly rapidly, within 5 min at 0 °C, thus prohibiting any conclusion on structure–reactivity relationships.[1] Hence, to achieve a reasonable rate of reaction, it is necessary to decrease both the concentrations of the reactants and the temperature. Unfortunately, estimation of hydride by the hydrolysis method under these conditions is not practical. However, we then developed an analytical method using iodimetry that permits quantitative estimation of lithium triethylborohydride. Utilizing this procedure, we studied the kinetics of reduction of a variety of epoxides. The results of this investigation are presented in this paper.

Results and Discussion

Procedure for the Estimation of Lithium Triethylborohydride. The procedure involves two titrations: (a) titration of the iodine solution with thiosulfate and (b) the addition of a deficient amount of lithium triethylborohydride to the same volume of iodine solution as in (a) and titrating the residual iodine with thiosulfate. From the difference between the two titer values, the concentration of the hydride solution could be established. This method is based on reaction 2. However, a competitive

$$LiEt_3BH + I_2 \rightarrow LiI + Et_3B + HI \qquad (2)$$

reaction is also possible[3] (eq 3). If this reaction competes,

$$LiEt_3BH + HI \rightarrow LiI + Et_3B + H_2 \qquad (3)$$

it would decrease the equivalence between iodine and lithium triethylborohydride. Indeed, we found that a significant excess of iodine (2-fold) is necessary to get a quantitative estimation of hydride according to eq 2 in agreement with the hydrolysis method, within the limits of experimental error (±2%). However, in the presence of added substrate, such as epoxide, the reaction product, $LiEt_3BOR$, also reacts with iodine to produce alkyl iodide.[4] This problem could be solved by adding boron trifluoride etherate to the reaction mixture before reacting it with iodine. Thus, a 1-mL standard solution of lithium triethylborohydride (0.97 M, estimated by the hydrolysis method) was diluted with tetrahydrofuran (THF)[5] to 100 mL. Boron trifluoride etherate (1 mmol, 0.12 mL) was added to this solution. Different aliquots of this solution were estimated as indicated above. The data are presented in Table I. The results demonstrate the reliability of the proposed procedure.

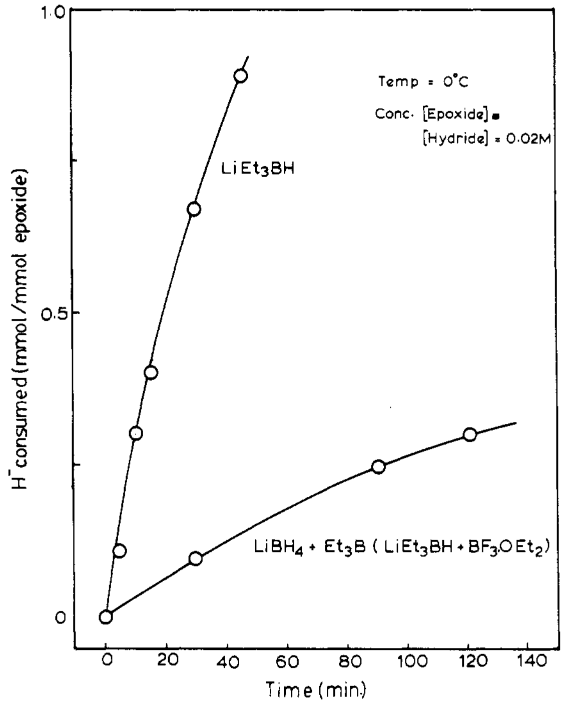

Figure 1. Comparison of rates of reduction of cyclohexene oxide by $LiEt_3BH$ with and without $BF_3{\cdot}OEt_2$.

Procedure for Kinetic Study. In a typical run, 1.0 mL of $LiEt_3BH$ solution in THF (0.1 M) was transferred to various 10-mL standard flasks and diluted with 3.0 mL of THF. The flasks were thermostated for 1 h at 0 °C. Simultaneously, a 1.0 M solution of the epoxide in THF was made and thermostated. The reaction was initiated by adding 1.0 mL of the epoxide solution to the $LiEt_3BH$ solution. Thus, the total volume becomes 5.0 mL, 0.02 M in each reactant. At regular intervals, the reaction was quenched by the addition of 0.012 mL (0.0142 g, 0.1 mmol) of boron trifluoride etherate (measured with a microsyringe) and diluted to 10 mL with cold (0 °C) THF. Aliquots of this solution were estimated as before to get concordant values. These data were used for the determination of rate constants using appropriate rate expressions.

Order and Stoichiometry of the Reduction of Epoxides by $LiEt_3BH$. Cyclohexene oxide was representative. It has been reported that the reduction of epoxides by lithium borohydride is catalyzed by triethylborane.[6] Since the addition of boron trifluoride etherate to quench the reaction would form lithium borohydride and triethylborane, it was necessary to study the rate of reduction of cyclohexene oxide by lithium borohydride under identical conditions (eq 4 and 5). Accordingly, boron tri-

$$LiEt_3BH + BF_3 \rightarrow LiBF_3H + Et_3B \qquad (4)$$

$$LiBF_3H \rightarrow {}^1/_4LiBH_4 + {}^3/_4LiBF_4 \qquad (5)$$

fluoride etherate was added to the hydride solution before initiating the reaction and the rate was followed by estimating the residual hydride. This rate is compared with the rate of reduction of cyclohexene oxide by lithium triethylborohydride in Figure 1. It is evident that the reduction by lithium borohydride is far too slow to affect the estimation of the concentration of hydride.

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(2) Krishnamurthy, S.; Vogel, F.; Brown, H. C. *J. Org. Chem.* **1977**, *42*, 2534.

(3) Wigfield, D. C.; Bowland, F. W. *Can. J. Chem.* **1977**, *55*, 3616.

(4) Brown, H. C.; Rathke, M. W.; Rogić, M. M. *J. Am. Chem. Soc.* **1968**, *90*, 5038.

(5) The purity of THF is critical, as otherwise the $LiEt_3BH$ will be destroyed by the large excess of solvent.

(6) Yoon, N. M., personal communication.

Table II. Determination of the Order of the Reaction of Cyclohexene Oxide and Lithium Triethylborohydride

[epoxide], M	[LiEt$_3$BH], M	10^3k_1 s^{-1}	10^2k_2, L mol^{-1} s^{-1}
0.02	0.02		1.31
0.05	0.01	0.692	1.32
0.10	0.01	1.26	1.26
0.15	0.01	1.94	1.30

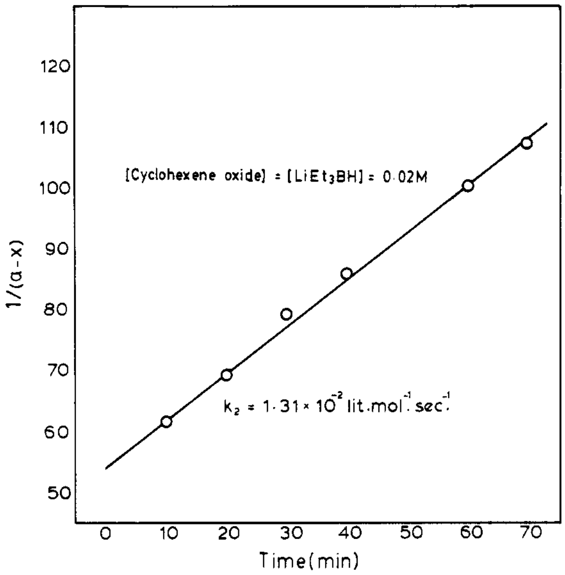
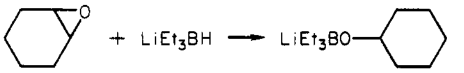


Figure 2. A typical second-order rate plot for the reduction of cyclohexene oxide.

The reaction of cyclohexene oxide with lithium triethylborohydride exhibited second-order kinetics over a wide range of substrate concentration (Table II). A typical second-order plot is presented in Figure 2. Thus, the reduction follows the rate law (eq 6):

$$\text{rate} = k_2[\text{epoxide}][\text{LiEt}_3\text{BH}] \tag{6}$$

Curiously, the reduction of alkyl halides by the same reagent showed inhibition by the product, triethylborane. This phenomenon is not observed in the present study (Figures 1 and 2).[7] A possible explanation is the absence of free triethylborane in the reduction of epoxides, in contrast to its presence in the reduction of alkyl halides (eq 7). Since the lithium alkoxide is a strong base, triethylborane would be present only as the ate complex. This is confirmed by the ^{11}B NMR spectra, which showed a peak around δ 2. On the other hand, reduction of alkyl halides forms free triethylborane (eq 8 and 9).



(7)

The species

$$\text{RX} + \text{LiEt}_3\text{BH} \rightarrow \text{LiX} + \text{Et}_3\text{B} + \text{RH} \tag{8}$$

$$\text{Et}_3\text{B} + \text{LiEt}_3\text{BH} \rightarrow \text{LiEt}_3\text{BH}\cdot\text{BEt}_3 \tag{9}$$

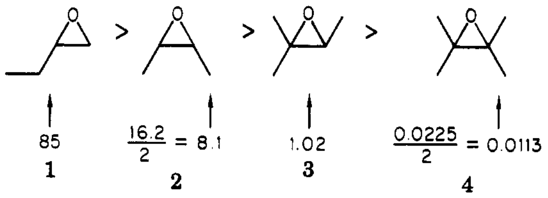
$\text{LiEt}_3\text{BH}\cdot\text{BEt}_3$ is less reactive.[7]

Having established the order and stoichiometry, we studied the rate of reduction of other epoxides under second-order conditions. The results are presented in Table III.

Table III. Second-Order Rate Constants for the Reduction of Epoxides with Lithium Triethylborohydride

epoxide	[epoxide] = [LiEt$_3$BH] M	10^2k_2, L mol^{-1} s^{-1}
1-butene oxide	0.02	85.00
cis-2-butene oxide	0.02	16.20
trans-2-butene oxide	0.02	1.40
2-methyl-2-butene oxide	0.02	1.02
2,3-dimethyl-2-butene oxide	0.2	0.023
3,3-dimethyl-1-butene oxide	0.02	1.24
cyclopentene oxide	0.02	2.39
cyclohexene oxide	0.02	1.31
1-methylcyclohexene oxide	0.02	0.25
cycloheptene oxide	0.02	2.43
exo-norbornene oxide	0.2	0.036
styrene oxide	0.02	34.30
cis-β-methylstyrene oxide	0.02	0.704
trans-β-methylstyrene oxide	0.02	4.13

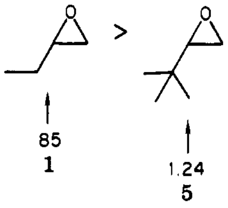
Effect of Structure on the Reactivity of Epoxides. From Table III, it is evident that terminal epoxides, such as 1,2-epoxybutane, react very fast. However, successive methyl substitution on the epoxide ring carbons decreases the rate of the reaction. The rate constants for hydride attack (10^2k, L mol^{-1}) at the positions indicated provide an approximate measure of this effect.



$k_1/k_2 \approx 10.5$; $k_2/k_3 \approx 8$

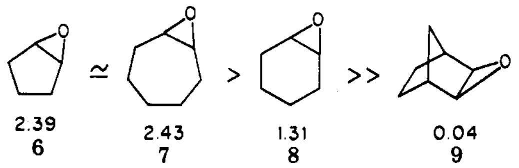
Thus, with the exception of tetramethylethylene oxide, each methyl substitution decreases the rate by a factor of 8–10.

Substitution at the γ-position also affects the rate to more or less the same extent.

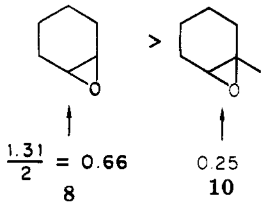


k_1/k_5 = 68.6 (~8.3 per methyl group)

Reduction of cyclic epoxides follows the usual trend:



However, methyl substitution in cyclic epoxides has a less prominent effect than in the case of aliphatic epoxides.



k_8/k_{10} = 2.6

Styrene oxide reacts slower than aliphatic terminal ep-

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[7] Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 849.

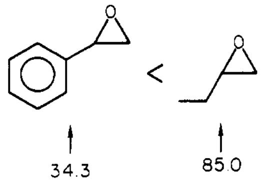
Table IV. Comparison of the Products from the Reduction of β-Methylstyrene Oxides with Various Reducing Agents

β-methylstyrene oxide	reagent	product(s)
cis	lithium triethylborohydride	1-phenyl-1-propanol
trans	lithium triethylborohydride	1-phenyl-2-propanol
cis	sodium cyanoborohydride	1-phenyl-1-propanol + 1-phenyl-2-propanol (~1:1)
trans	sodium cyanoborohydride	1-phenyl-2-propanol
cis	lithium aluminum hydride	1-phenyl-1-propanol + 1-phenyl-2-propanol
trans	lithium aluminum hydride	1-phenyl-1-propanol + 1-phenyl-2-propanol (13:87)

Table V. Kinetic Isotope Effect

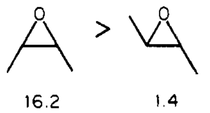
epoxide	10^2k_H, L mol^{-1} s^{-1}	10^2k_D, L mol^{-1} s^{-1}	k_H/k_D	mass spectral value
cis-β-methylstyrene oxide	0.704	0.508	1.39	1.36
trans-β-methylstyrene oxide	4.13	2.91	1.42	1.45
cyclohexene oxide	1.31	0.88	1.50	

oxide. The attack in styrene oxide is entirely on the β position.



11 1

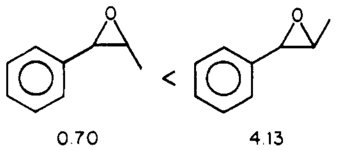
Aliphatic cis epoxides react faster than the corresponding trans isomers.



2 12

$k_2/k_{12} \approx 12$

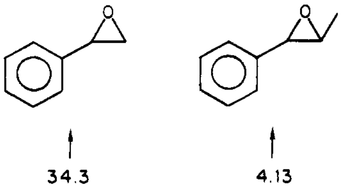
Thus, trans epoxides could be easily separated from a mixture of cis and trans epoxides by utilizing this difference in reactivity. However, in the case of β-methylstyrene oxides, the trend is reversed:



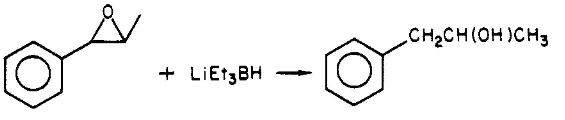
13 14

$k_{14}/k_{13} = 6$

This puzzling result could be explained as follows: In the aliphatic epoxides, the position of attack by the hydride is symmetrical. However, in the case of substituted styrene oxides, there are two possible points of attack—the α and β carbon atoms. Interestingly, the point of attack could be deduced by analogy with the earlier finding that the substitution of a methyl group on the epoxide ring carbon decreases the rate of hydride attack on the other ring carbon by a factor of 8–10. Thus, a rate ratio of 8.3 is observed for *trans*-β-methylstyrene oxide relative to styrene oxide itself. This indicates that the attack must be at the benzylic carbon position.

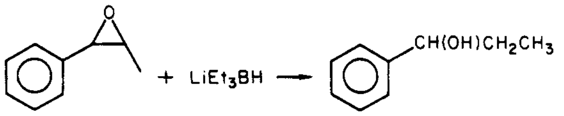


Indeed, study of the product indicated the exclusive formation of 1-phenyl-2-propanol (eq 10).



(10)

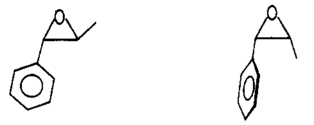
On the other hand, the corresponding cis epoxide produced only 1-phenyl-1-propanol (eq 11).



(11)

A comparison of the reduction of these two epoxides by other reducing agents is presented in Table IV.

A possible explanation for this is the steric effect of the phenyl group in the two epoxides. The phenyl group can be coplanar with the methyl substituent in the trans isomer, but not in the cis. Consequently, in the trans isomer attack of the reagent can occur at the more reactive benzyl secondary center, with the coplanar phenyl group hindering attack at the β position. In the cis isomer, rotation of the phenyl group hinders attack at the α benzylic position, but permits attack at the β position.



15 16

A similar interpretation was utilized to account for the directive effects observed in the hydroboration of *cis*- and *trans*-β-methylstyrene with 9-BBN.[8]

Kinetic Isotope Effect. To throw light on the mechanism of reduction, the isotope effect on the reduction was studied by using lithium triethylborodeuteride ($LiEt_3BD$). The second-order rate constant for the reduction of cyclohexene oxide with $LiEt_3BD$ was found to be 8.75×10^{-3} L mol^{-1} s^{-1}, thus showing an isotope effect of 1.50. Similarly, the kinetic isotope effect for *cis*- and *trans*-β-methylstyrene oxides was found to be 1.39 and 1.42, respectively.

In the case of styrene oxides, however, the isotope effect was also determined by product analysis in competitive reactions. Thus, the mass spectral analysis of the products from the reaction of deficient quantities of *cis*- and *trans*-β-methylstyrene oxides with an equimolecular mix-

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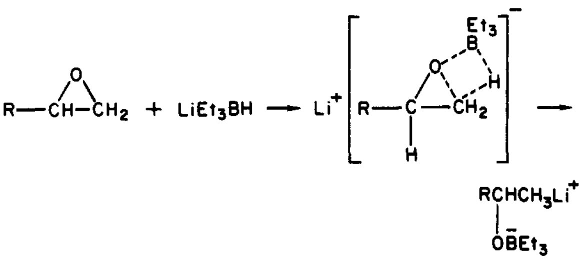
[8] Brown, H. C.; Nelson, D. J.; Scouten, C. G. *J. Org. Chem.* **1983**, *48*, 641.

ture of Super Hydride and Super Deuteride showed 44.6% and 43.5% deuterium incorporation, respectively. When the Ingold–Shaw expression was applied,[9] values of the kinetic isotope effect of 1.36 and 1.45 were obtained—in close agreement with the iodimetric values (Table V).

Mechanism. The kinetic study indicates that the reduction of epoxides is a bimolecular process. The kinetic isotope effect, although low, does not evidently correspond to a single electron transfer process. It has also been reported that lithium triethylborohydride reduces substrates by hydride transfer rather than by electron transfer reaction.[10] On the other hand, this low value itself could be the primary effect for a hydride transfer reaction, as demonstrated earlier.[11] This could mean either an early transition state or a very late transition state. Alternatively, the transition state for hydride reductions has frequently been considered to be four centered, which suggests a B—H—C angle in the neighborhood of 90°.[12] It has been calculated that isotope effects where such an angle deviates significantly from 180° can drastically diminish from 6–8 to 1–2.[13] Thus, the results could be explained by eq 12.



(12)

According to this mechanism, no free triethylborane is formed in the reaction.

Conclusion

The present study demonstrates a remarkable steric effect on the rate and product formation in the reduction of epoxides. Although the paucity of data does not permit a quantitative measure of the effect of methyl substitution, we believe that the results should be helpful in selecting reaction conditions for examining the asymmetric reduction of epoxides. The kinetic behavior exhibited by $LiEt_3BH$ suggests the possibility of certain functional groups without product inhibition by utilizing a base, such as lithium alkoxide, in the reaction mixture. The development of a suitable procedure for the estimation of $LiEt_3BH$ should facilitate further kinetic studies with this reagent.

Experimental Section

Materials and Methods. Most of the epoxides used were commercial products of very high purity. However, they were further purified by distillation when necessary. *cis*- and *trans*-β-methylstyrene oxides were synthesized by the epoxidation of the corresponding olefins using the general procedure.[14] The physical constants agreed well with literature values. Lithium triethylborohydride and lithium triethylborodeuteride were prepared from triethylborane and lithium hydride/deuteride according to literature procedures.[1] Tetrahydrofuran was distilled over $LiAlH_4$ just before use.

All glassware was dried in an oven (120 °C) and cooled under a stream of dry nitrogen. All 10-mL volumetric flasks used in the kinetic run were closed with rubber septa. Hypodermic syringes were used to transfer solutions. Boron trifluoride etherate was measured with a 50-μL syringe.

Estimation of Lithium Triethylborohydride. An approximately 0.002 N solution of sodium thiosulfate was standardized with a freshly prepared standard solution of potassium iodate. A solution of iodine in toluene (~0.01 M) was standardized with this thiosulfate solution.[15]

Lithium triethylborohydride solution was initially analyzed by hydrolysis method (0.97 M). One milliliter of this solution along with 0.12 mL (0.142 g, 1 mmol) of boron trifluoride etherate was diluted to 100 mL. Various known amounts of this dilute $LiEt_3BH$ solution were added to a known excess (2.0 mL) of iodine solution. The excess of iodine was titrated against thiosulfate solution and the amount of iodine consumed by the hydride was determined. The stoichiometry of the reaction of thiosulfate with iodine is given by

$$2S_2O_3^- + I_2 \rightarrow S_4O_6^{2-} + 2I^-$$

This equation, in combination with the reaction of iodine with the reagent,

$$LiEt_3BH + I_2 \rightarrow LiI + Et_3B + HI \qquad (2)$$

gives a 1:2 equivalence between $LiEt_3BH$ and thiosulfate. If the original titer of x mL of thiosulfate to reduce the iodine solution is reduced to z mL by the prior addition of y mL of $LiEt_3BH$ solution, the molarity of $LiEt_3BH$ (M_{SH}) is given by

$$M_{SH} = M_{Na_2S_2O_3}(x - z)/2y$$

The results, which were in excellent agreement with the hydrolysis value, are presented in Table I.

Kinetic Procedure. The following kinetic procedure was followed for all of the epoxides except *exo*-norbornene oxide and 2,3-dimethyl-2-butene oxide.

A stock solution of 0.1 M lithium triethylborohydride in freshly distilled THF was made. One milliliter of this solution was syringed out into various 10-mL volumetric flasks, followed by 3.0 mL of THF. Concomitantly, a 0.1 M solution of the epoxide in THF was prepared and all solutions were thermostated at 0 °C for about an hour. The reaction was initiated by the addition of 1.0 mL of the epoxide solution to each of the reaction flasks. Thus the concentration of both the $LiEt_3BH$ and epoxide was 0.02 M. At regular intervals, the reaction was quenched by the addition of 0.012 mL (0.0142 g, 0.1 mmol) of boron trifluoride etherate. The contents of the flask was increased to 10 mL with THF (kept at 0 °C) and 1.0 mL of the solution was added to 2.0 mL of iodine solution. The excess iodine was extracted into the aqueous layer by the addition of iodate-free potassium iodide (~2 mL, 10%) solution and titrated against thiosulfate solution. A typical second-order plot for the reduction of cyclohexene oxide is shown in Figure 2.

$$k_2 = \frac{1}{t}\,\frac{x}{a(a - x)}$$

Procedure for Less Reactive Epoxides. The above procedure was simplified as follows for *exo*-norbornene oxide and tetramethyl-2-butene oxide. Lithium triethylborohydride solution (2.06 mL, 0.97 M) was transferred into a 10-mL volumetric flask, followed by 6.0 mL of THF. This and a 1 M solution of the epoxide in THF were theromstated for about an hour. The reaction was started by adding 2.0 mL of epoxide solution to the $LiEt_3BH$ solution. At regular intervals, 0.5 mL of the reaction mixture was transferred into 10-mL volumetric flasks containing 0.012 mL of boron trifluoride etherate. The solutions were increased to 10 mL and estimated as in the above procedure.

Product Study. Products of reduction of *cis*- and *trans*-β-methylstyrene oxides were analyzed. The epoxide (660 mg, 5

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mmol) was dissolved in THF (10 mL) and $LiEt_3BH$ (5.7 mL of 0.97 M solution, 5.5 mmol) was added to it. The mixture was stirred for 1 h and water (1-2 mL) was added dropwise to hydrolyze the mixture. Oxidation of the mixture with alkaline hydrogen peroxide and extraction with ether gave the alcohols: *cis*-β-methylstyrene oxide gave 615 mg (92%) of 1-phenyl-1-propanol, ^1H NMR ($CDCl_3$, 60 MHz) δ 7.25 (s, 5 H), 4.47 (t, 1 H), 2.67 (s, 1 H), 1.66 (q, 2 H), 0.87 (t, 3 H); *trans*-β-methylstyrene oxide gave 620 mg (93%) of 1-phenyl-2-propanol, ^1H NMR ($CDCl_3$, 60 MHz) δ 7.25 (s, 5 H), 3.95 (q, 1 H), 2.73 (d, 2 H), 2.1 (s, 1 H), 1.2 (d, 3 H). Both products were confirmed by coinjection with authentic samples in GC and also by mass spectra.

Kinetic Isotope Effect. The procedure for the kinetic experiments with lithium triethylborodeuteride was exactly as described earlier for the corresponding hydrogen reagent.

Competitive Experiments and Mass Spectral Analysis. *cis*-β-Methylene oxide (660 mg, 5 mmol) was reduced with a mixture of 5 mmol each of $LiEt_3BH$ and $LiEt_3BD$. The product was worked up as described above. The mixture of normal and deuterated alcohols was found to contain 44.6% of deuterated compound by mass spectral analysis. A similar experiment with trans epoxide showed a 43.5% incorporation of deuterium (the peaks at m/e values of 119 and 120 were compared, EI 70 eV). Application of the Ingold-Shaw equation,[9]

$$\frac{k_H}{k_D} = \frac{\log [H_0] - \log [H]}{\log [D_0] - \log [D]}$$

where k_H and k_D are the rate constants for hydride and deuteride, respectively, and $[H_0]$ and $[D_0]$ are the initial concentrations and [H] and [D] are the final concentrations of $LiEt_3BH$ and $LiEt_3BD$, respectively, gives the k_H/k_D value of 1.36 and 1.45 for the *cis*- and *trans*-epoxides, respectively.

Acknowledgment. We thank the U.S. Army Research Office for support of this research (Grant ARO DAAG-29-79-C-0027).

Registry No. **1**, 106-88-7; **2**, 1758-33-4; **3**, 5076-19-7; **4**, 5076-20-0; **5**, 2245-30-9; **6**, 285-67-6; **7**, 286-45-3; **8**, 286-20-4; **9**, 3146-39-2; **10**, 1713-33-3; **11**, 96-09-3; **12**, 21490-63-1; **13**, 4541-87-1; **14**, 23355-97-7; $LiEt_3BH$, 22560-16-3; $LiBH_4$, 16949-15-8; Et_3B, 97-94-9; D_2, 7782-39-0.

Diels–Alder Syntheses with 1,4-Di-*tert*-butoxy-1,3-butadiene[1]

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Received August 9, 1982

The title compound (DTBU) enters into [4 + 2] cycloadditions with fumaronitrile, tetracyanoethene, maleic anhydride, diethyl azodicarboxylate, 1,2-dibenzoylethene, dimethyl acetylenedicarboxylate, *p*-benzoquinone, 2-carbomethoxybenzoquinone, 2-methylbenzoquinone, 1,4-naphthoquinone, 2-methyl-1,4-naphthoquinone, and 5-hydroxy-1,4-naphthoquinone. When prepared the DTBU isomers are present in the ratio *E,Z*:*Z,Z*:*E,E* = 45:45:10. Of these, *Z,Z*-DTBU appears to be unreactive. In several cases where multiple Diels–Alder products were possible, two related to *E,Z*- or *E,E*-DTBU were obtained. A connection between ^1H NMR data (δ and J) and stereochemical configuration and conformation was elaborated for adducts of DTBU with *p*-benzoquinones or maleic anhydride.

Our report on 1,4-dimethoxy-1,3-butadiene (DMBU)[2] prompted the suggestion that replacement of methyl by *tert*-butyl might lead to useful changes in reaction selectivity.[3] After preparing the title diene (DTBU) and exploring its [4 + 2] cycloadditions, we can report that no unusual selectivity was found. What was possible, however, was the identification of several isomeric pairs of bicyclic products and the association of ^1H NMR data with structure. Indeed the adducts of DTBU with 1,4-quinones or maleic anhydride provide useful models of the stereochemical possibilities inherent in (partly) reduced bicyclic systems.[4a] However, the regioselectivity of further reactions of these adducts, e.g., naphthoquinones on their way to anthracyclinones,[4b] is often influenced or even controlled by the substituents. It is also in these and more complex structures that stereochemical or leaving group preferences deriving from DTBU as the precursor should be in evidence.

Table I. Analysis of the DTBU Isomers[a]

	Z,Z	*E,Z*	*E,E*
NMR (alkene protons)[b,c]	41	48	11
NMR (*t*-Bu protons)[b,d]	46	46	8
GC[d]	45	45	10

[a] Given as percent of total. [b] At 300 MHz. [c] Less reliable. [d] More reliable (± 2).

Interest in the construction of new dienes[4] and adaptation of old ones for particular purposes, e.g., mechanistic, synthetic, etc., remain high.[5,6] In large measure this must be ascribed to the search for dienes whose reactivities are often inadequately foreseen on the basis of past experience, intuition, or theory. It will be useful, therefore, to outline some of the properties of DTBU so that its virtues and deficiences will be apparent.

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