The Mechanism of Mixed Hydride Reductions. Effects of Reagent Composition, Nature of Halogen, and Solvating Ligand on the Mechanism of Epoxide Reduction[1]

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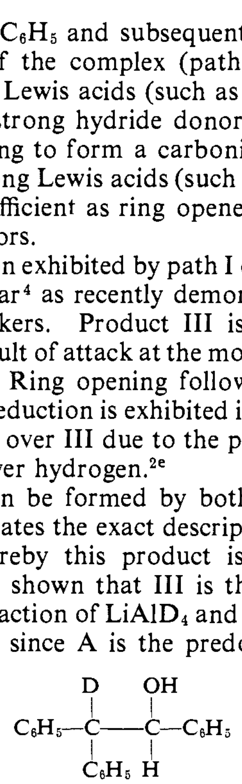
Abstract: Reductions of β-diisobutylene oxide by mixed hydride reagents have been studied. The reagents studied combined lithium aluminum hydride ($LiAlH_4$) and aluminum halide in ratios of 3:1, 1:1, 1:3, and 1:4. The influence of halogen in the aluminum halide (AlX_3) was observed for X = Cl, Br, and I. The influence of solvating ligand was studied using diethyl ether, tetrahydrofuran, and triethylamine. The role of LiCl and excess $AlCl_3$ in the mixed hydride reagent was also studied. The results of these studies are entirely consistent with the mechanistic paths previously proposed to explain the products formed in mixed hydride reductions of epoxides.

When $LiAlH_4$ is allowed to react with certain strongly acidic compounds, such as aluminum chloride, a reducing agent is obtained which exhibits a significantly different type of reactivity than that of $LiAlH_4$ or its alkoxy derivatives. The reagents produced on reaction of $LiAlH_4$ and $AlCl_3$ in 3:1, 1:1, 1:3, and 1:4 ratio are referred to as "mixed hydride" reagents. Foremost in the development of mixed hydride reagents as a tool in synthetic organic chemistry has been E. L. Eliel and coworkers.[2] These workers have shown that the nature of the products formed on reduction of triphenylethylene oxide with mixed hydride reagents is a function of the $LiAlH_4$:$AlCl_3$ ratio. In order to understand the mechanism whereby these different products are formed, it is necessary to know with some certainty the nature of the reactive species produced when $LiAlH_4$ and $AlCl_3$ are allowed to interact prior to their use as a mixed hydride reagent. Recently a study concerning the nature of mixed hydride reagents was reported.[3] Reaction of $LiAlH_4$ and $AlCl_3$ in 3:1, 1:1, 1:3, and 1:4 ratio was reported to produce AlH_3, H_2AlCl, $HAlCl_2$, and $HAlCl_2 + AlCl_3$, respectively, as the active hydride component in solution. The hydride species (AlH_nCl_{3-n}) was thought to be weakly complexed to the LiCl by-product since LiCl did not precipitate from the reaction mixtures immediately after reaction although LiCl is very insoluble in the reaction solvent (diethyl ether).

On the basis of the mixed hydride composition studies and the prior elegant work of Eliel and coworkers,[2] mechanisms were suggested[3] to explain the different products formed in mixed hydride reductions of epoxides when the ratio of $LiAlH_4$:$AlCl_3$ is varied (Figure 1). After complexation two competing reactions take place: one reaction represented by path I involves direct reduction, the other reaction is represented by path II and involves ring opening of the epoxide to form predominantly the more stable carbonium ion followed by migration of H, R, or C_6H_5 and subsequent reduction. Direct reduction of the complex (path I) appears to be favored by weak Lewis acids (such as AlH_3) which will also tend to be strong hydride donors. On the other hand, ring opening to form a carbonium ion (path II) is favored by strong Lewis acids (such as $HAlCl_2$) which would be more efficient as ring openers and less effective hydride donors.

Direct reduction exhibited by path I can be both intra- and intermolecular[4] as recently demonstrated by Lansbury and coworkers. Product III is favored over II since III is the result of attack at the more stable incipient carbonium ion. Ring opening followed by migration and subsequent reduction is exhibited in path II. Product IV is favored over III due to the preferential migration of phenyl over hydrogen.[2e]

Product III can be formed by both paths I and II. This fact complicates the exact description of the mechanistic path whereby this product is formed. However, it has been shown that III is the major product from path I by reaction of $LiAlD_4$ and $AlCl_3$ in 3:1 ratio (AlD_3 produced) since A is the predominant product.



$$C_6H_5-\overset{D}{\underset{C_6H_5}{C}}-\overset{OH}{\underset{H}{C}}-C_6H_5$$

A

Thus it is also established that III is not formed *via* reduction of $(C_6H_5)_2CHC(=O)C_6H_5$, a possible intermediate in these reactions. On the other hand III is presumed to be a minor product *via* path II since treatment of I with strong Lewis acids such as BF_3 or $AlCl_3$ results in predominant phenyl migration rather than hydrogen migration. In order to distinguish the amount of III produced by the two different mechanisms represented by paths I and II, it would be necessary to use $LiAlD_4$ in all reductions, $(C_6H_5)_2CD-C(OH)H-C_6H_5$ being produced by path I and $(C_6H_5)_2CH-C(OH)DC_6H_5$ being produced by path II. This problem has been dealt within the present study.

This study is concerned with a better understanding of the mechanism of mixed hydride reductions. By de-

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[1] (a) Supported in part by the National Aeronautics and Space Administration. (b) Presented in part at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 10–14, 1967.

[2] (a) E. L. Eliel and D. W. Delmonte, *J. Am. Chem. Soc.*, **80**, 1744 (1958); (b) E. L. Eliel and M. N. Rerick, *ibid.*, **82**, 1362 (1960); (c) E. L. Eliel, *Record Chem. Progr.*, **23**, 129 (1961); (d) E. L. Eliel, J. A. Pilato, and V. G. Badding, *J. Am. Chem. Soc.*, **84**, 2377 (1962); (e) M. Rerick and E. L. Eliel, *ibid.*, **84**, 2356 (1962).

[3] E. C. Ashby and J. Prather, *ibid.*, **88**, 729 (1966).

[4] P. T. Lansbury, D. J. Scharf, and V. A. Pattison, *J. Org. Chem.*, **32**, 1748 (1967).

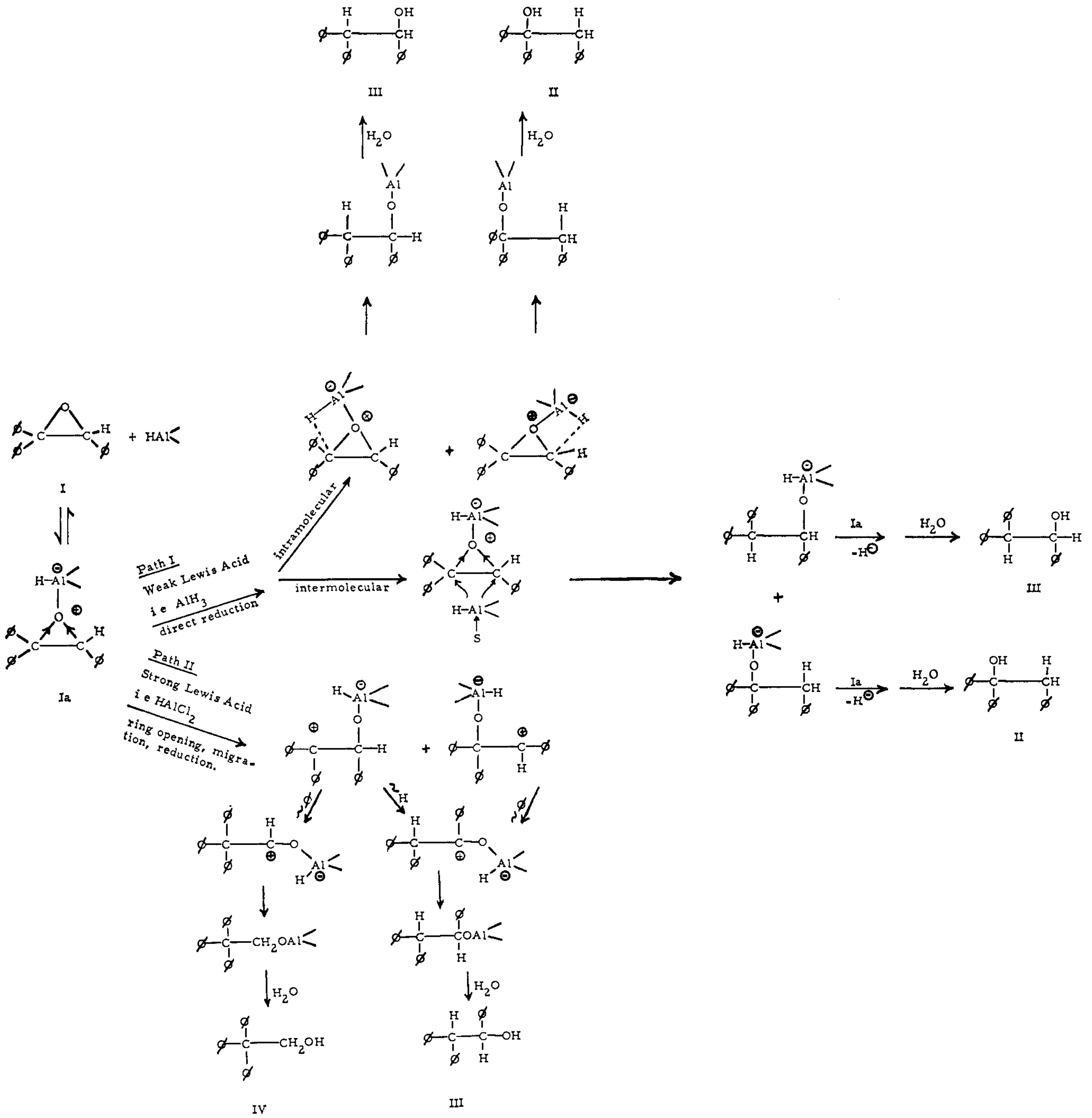
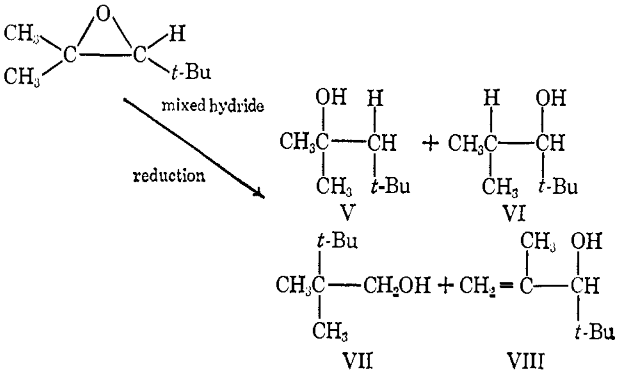


Figure 1. Mechanism of mixed hydride reduction of triphenylethylene oxide (ϕ = C_6H_5).

termining the effect of mixed hydride stoichiometry, the nature of the halogen in mixed hydride reagents (AlH_nX_{3-n}, where X = Cl, Br, I) and the solvating ligand (Et_2O, THF, Et_3N) on product ratios *in* epoxide reduction, a more consistent picture of the mechanism of mixed hydride reductions has evolved. The epoxide chosen for this study is one whose mixed hydride reduction products are separable by vpc and are such that it is clear whether they arise from direct reduction, or from migration and subsequent reduction without making extensive use of deuterium-labeling experiments. β-Diisobutylene oxide meets these requirements.

Results and Discussion

The mixed hydride reduction of β-diisobutylene oxide results in the formation of four products, V–VIII. According to the mechanistic scheme shown in Figure 1, compound V is the predominant product formed by



reduction with $LiAlH_4$ as a result of bimolecular backside attack at the least hindered carbon. Compound VI is the predominant product formed by mixed hydride reduction ($LiAlH_4:AlCl_3$ ratio 3:1) with a weak Lewis acid (AlH_3) and VII is the predominant product formed by mixed hydride reduction ($LiAlH_4:AlCl_3$ ratio 1:3) with a strong Lewis acid ($HAlCl_2$). Compound VIII becomes significant when a weak Lewis acid such as AlH_3 is used to reduce a sterically hindered epoxide (such as β-diisobutylene oxide) especially under forcing conditions.

The effect of adding excess $AlCl_3$ in mixed hydride reductions was studied by examining the product ratios of the reduction of both styrene oxide and β-diisobutylene oxide using $LiAlH_4:AlCl_3$ ratios of 1:3 and 1:4. The data from Tables I and II indicate that the mechanism of epoxide reduction is the same for the 1:3 and 1:4 mixed hydride reagent, thus excess $AlCl_3$ has little influence on the course of the reaction. Since the amount of VII would be particularly sensitive to the Lewis acidity of the complexing agent, it is reasonable to assume that $HAlCl_2$ is the complexing agent, in both cases. However, it is possible that $AlCl_3$ does take part in the complexation of the epoxide, without affecting the formation of VII if one considers that from a combined electronic and steric standpoint, $AlCl_3$ and $HAlCl_2$ should possess similar Lewis acidities.

Table I. Effect of Excess $AlCl_3$ in the Mixed Hydride Reduction of Styrene Oxide[a]

$LiAlH_4:AlCl_3$	$C_6H_5CH(OH)CH_3$	$C_6H_5CH_2CH_2OH$	Yield, %	Recovered epoxide
1:3	1	99	69	10
1:4	2	98	68	14
1:4[b]	2–5	95–98	71	..

[a] Three equivalents of hydride used per mole of epoxide in diethyl ether at room temperature. [b] Reference 2a.

Table II. Effect of Excess $AlCl_3$ in the Mixed Hydride Reduction of β-Diisobutylene Oxide[a]

$LiAlH_4:AlCl_3$	V	VI	VII	VIII	Yield, %
1:3	<1	16	74	9	84
1:4	<1	16	75	8	85

[a] Three equivalents of hydride used per mole of epoxide in diethyl ether at room temperature.

It has been suggested that LiCl may play a role as complexing agent prior to reduction.[5] This question as well as the question of the exact nature of the 1:3 mixed hydride reagent (that is, $4HAlCl_2 + LiCl$ or $3HAlCl_2 + LiAlHCl_3$) was studied by comparison of the product ratios on reduction of β-diisobutylene oxide with pure $HAlCl_2$ and with the 1:3 reagent (Table III). Reduction by $LiAlCl_3H$ would be expected to result in an increase in VI, the product of direct reduction, over VII, the product of migration, since $LiAlCl_3H$ should be a considerably better hydride donor than $HAlCl_2$. The data from Table III shows that 5% more of VI is produced at the expense of VII when the 1:3 reagent is used as compared to pure $HAlCl_2$. The differences in the formation of VI and VII look larger if one considers the differences in the product ratios of VI and VII in the two cases. In the case of the 1:3 $LiAlH_4:AlCl_3$ reagent the product ratio of VII:VI is 4.7 and in the case of $HAlCl_2$ it is 7.2. Since the above data were consistently reproducible (within 1% absolute) the conclusion is that it is possible that the complexed hydride ($LiAlCl_3H$) participates to some extent in the reaction. Since the ratio of $LiAlCl_3H$ to $HAlCl_2$ is only 1 to 3 in the 1:3 $LiAlH_4:AlCl_3$ reagent and since both reagents are reacting competitively, the differences observed in the product ratios of VII:VI are probably reasonable for such participation. These data do seem to exclude the possibility suggested earlier by Zakharkin[5] that LiCl takes part in the reaction by complexation with the epoxide. It would appear that much greater deviations than those reported above would have been observed if that was the case.

Table III. Comparison of $HAlCl_2$ and the 1:3 Mixed Hydride Reagent in the Reduction of β-Diisobutylene Oxide[a]

Reagent	V	VI	VII	VIII	Yield, %
$LiAlH_4 + 3AlCl_3$[b]	...	15	77	8	83
$LiAlH_4 + 3AlCl_3$	<1	16	75	8	85
$HAlCl_2$	<1	11	80	8	89

[a] Three equivalents of hydride used per mole of epoxide in diethyl ether at room temperature. [b] Reference 2e.

The nature of the halogen in the mixed hydride reagent was varied (Cl, Br, I) in an attempt to determine the sensitivity of the mechanisms involved to changes in the electronic and steric nature of the mixed hydride reagent. The results are shown in Table IV.

Table IV. Effect of Halogen in Mixed Hydride Reductions of β-Diisobutylene Oxide[a]

$LiAlH_4:AlX_3$	Reactive species	V	VI	VII	VIII	Yield, %
1:0	$LiAlH_4$	0	0	0	0	0
1:0[b]	$LiAlH_4$	100	0	0	0	21
3:1	AlH_3	12	34	9	45	90–93
1:1 (Cl)	H_2AlCl	2	24	65	8	91–93
1:1 (Br)	H_2AlBr	5	44	44	7	89
1:1 (I)	H_2AlI	0	33	35	32	88–90
1:3 (Cl)	$HAlCl_2$	1	16	75	8	85
1:3 (Br)	$HAlBr_2$	1	19	65	15	83–86
1:3 (I)	$HAlI_2$	3	23	54	20	85–88

[a] Three equivalents of hydride per mole epoxide used, room temperature, 2-hr reaction time. [b] Forcing conditions: reflux 24 hr, also ref 2b.

The fact that prior complexation is involved in mixed hydride reductions is shown by the fact that reactions of β-diisobutylene oxide with the mixed hydride reagents are complete within a few minutes at room temperature whereas this epoxide is inert to $LiAlH_4$ under the same conditions. It is only under forcing conditions (24 hr reflux) that limited reaction can be affected using $LiAlH_4$ alone. $LiAlH_4$ should be a better hydride donor than any of the mixed hydride reagents, indicating that prior complexation resulting in polarization of the carbon–oxygen bonds in the oxirane ring is important.

Aluminum hydride produces mainly direct reduction product V and VI as compared to migration product

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(5) L. I. Zakharkin and I. M. Khorline, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 5, 862 (1965).

VII with a relatively large amount of product VIII. One notes that product VIII increases from 8 to 32% in proceeding from H_2AlCl to the weaker Lewis acid H_2AlI and also from 8 to 20% in proceeding from $HAlCl_2$ to the weaker Lewis acid $HAlI_2$. Thus a 45% yield of VIII from AlH_3, a still weaker acid, appears to be consistent with the trend.

The extent of migration product VII is also clearly related to the Lewis acidity of the hydride reagent as was previously presumed.[3] The amount of VII decreases from 65 to 35% as the Lewis acidity of the reagent decreases from H_2AlCl to H_2AlI and from 75 to 54% as the Lewis acidity of the reagent decreases from $HAlCl_2$ to $HAlI_2$. In each case the $HAlX_2$ reagent produces a higher yield of migration product VII than the less acidic H_2AlX reagents. The yield of VII is lowest with AlH_3 which is the weakest Lewis acid of the mixed hydride reagents studied.

The amount of product V formed as a result of direct reduction with or without prior complexation is small. This is probably due to the fact that uncomplexed epoxide would be expected to react very slowly with poor hydride donors such as the mixed hydride reagents. If the epoxide is complexed by relatively strong Lewis acids such as the mixed hydride reagents, the carbon–oxygen bonds of the oxirane are sufficiently polarized that preferential reaction will take place at the more stable incipient carbonium ion thus producing VI in preference to V.

The fact that AlH_3 produces more of the direct reduction product V as compared to the more acidic mixed-hydride reagents is probably due to the fact that AlH_3 is a better hydride donor than the other mixed hydride reagents from an electronic and steric standpoint resulting in more direct reduction at the least hindered carbon of the complexed epoxide.

The amount of VI formed is also related to the Lewis acidity of the mixed hydride reagent. As the Lewis acidity of the mixed hydride reagent decreases from $HAlCl_2$ to $HAlI_2$ the hydride donor characteristics increase and thus an increase in the amount of VI is observed.

Thus in summary, it is concluded that a weak Lewis acid favors the formation of product VIII and direct reduction product VI at the expense of VII, and strong Lewis acids favor the migration product VII at the expense of VI and VIII. Using a sliding scale one should be able to roughly predict product ratios for other systems.

The data reported here are not in complete agreement with results reported earlier by Zakharkin and coworkers; however, an explanation for this difference is available. In comparing runs 1 and 2 of Table V, it can be seen that the product ratios are quite different. Unfortunately Zakharkin and coworkers gave few experimental details of their work. Run 3 shows that if the 3:1 reagent (AlH_3) is used in large excess (3 mol of AlH_3/mol of epoxide) the product ratios are more comparable to those obtained by Zakharkin, however the disagreement is still appreciable. On the other hand if the $LiAlH_4$:$AlCl_3$ ratio is 3.2:1 (run 4) the data approximate the results obtained by Zakharkin. Our explanation of the discrepancies between our results and those of Zakharkin is the following. The $AlCl_3$ in the present study was purified by sublimation. It has been our experience that reagent grade $AlCl_3$ contains considerable moisture and nonsublimable impurities. Previous workers in the field have not sublimed the $AlCl_3$ used in their experiments and thus the $LiAlH_4$:$AlCl_3$ ratios would actually be higher than calculated. This would result in a mixture of $LiAlH_4$ and AlH_3 (in the cases involving a calculated 3:1 ratio) that is actually higher in $LiAlH_4$ content than calculated. This would result in complexation of the epoxide by AlH_3 and subsequent reduction by $LiAlH_4$ which would be expected to produce predominantly V. This explanation would correlate the Zakharkin data with the data obtained at the 3.2:1 ratio. Likewise the results of Zakharkin at 1:1 ratio (run 5) appear somewhat intermediate between our results at the 1:1 ratio (run 6) and our results at 3:1 ratio (run 2) in keeping with the same explanation as above. Runs 6–8 simply show the consistency of the results with a variation in reaction temperature whereas run 9 shows that using a large excess of reagent tends to push the data in the direction of the Zakharkin results.

Table V. Discrepancies in the Data Reported for Mixed Hydride Reductions of β-Diisobutylene Oxide

Run	$LiAlH_4$: $AlCl_3$	V	VI	VII	VIII	Yield, %	Ref
1	3:1	36	50	4	10	96	5
2	3:1[a]	12	34	9	45	95–98	*b*
3	3:1[c]	19	55	5	21	84	*b*
4	3.2:1[a]	28	59	3	10	85	*b*
5	1:1	14	32	45	9	95	5
6	1:1	2	24	65	8	91–93	*b*
7	1:1[a,d]	2	26	62	10	93	*b*
8	1:1[a,e]	2	24	64	10	85	*b*
9	1:1[f]	3	31	60	6	92	*b*
10	3:1	..	83	5	12	99	2[e]
11	1:1	..	52	42	6	99	2[e]
12	1:4	..	15	77	8	83	2[e]

[a] Three equivalents of hydride per mole of epoxide in diethyl ether at room temperature. [b] This work. [c] Three moles of AlH_3 per mole of epoxide. [d] 0°. [e] Reflux. [f] Three moles of H_2AlCl used per mole of epoxide.

The results of this study are also not entirely consistent with the results previously reported by Eliel and coworkers[2e] (runs 10–12) for mixed hydride reduction of β-diisobutylene oxide. At the $LiAlH_4$:$AlCl_3$ ratio of 1:4, product ratios are quite similar, however at the 3:1 and 1:1 ratios, product ratios are quite different. Part of the problem as pointed out by Zakharkin lies in the fact that Eliel and coworkers did not report the formation of V and that actually the amount of V and VI reported by Zakharkin approximates the amount of VI reported by Eliel. Thus it appears that with the vpc column used by Eliel and coworkers V was not separable from VI.[6] In spite of this, the yield reported by Eliel for VI in the 3:1 case is still considerably higher (83%) than the yield of V and VI (46%) reported in the present study. However, this discrepancy is explained in the same way as was previously used to explain the difference between the present results and the Zakharkin data, namely, a higher ratio of $LiAlH_4$ than calculated is actually present, resulting in a higher yield of V and VI than reported in the present study.

The effect of solvated ligand attached to the mixed hydride reagent on product ratios was studied for the

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(6) The alcohol VI provided to us by Eliel prepared from $LiAlH_4$:$AlCl_3$ in 3:1 ratio did show an appreciable amount of V when subject to vpc analysis using a Carbowax 20M column.

ligands diethyl ether, tetrahydrofuran, and triethylamine. The results are shown in Table VI. The trends found in the product ratios when tetrahydrofuran and triethylamine are used as the solvating ligands for the mixed hydride reagent are similar to the trends observed with diethyl ether. Product VIII increases with a decrease in Lewis acidity; the migration product VII increases with an increase in Lewis acidity. The direct reduction product at the most stable incipient carbonium ion VI follows the same pattern for all solvents for reasons discussed earlier for diethyl ether, and the direct reduction product at the least hindered carbon atom V is relatively small except for the 3:1 reagent (AlH_3) for the same reasons discussed earlier for diethyl ether.

Table VI. Effect of Solvated Ligand on Reduction of β-Diisobutylene Oxide by Mixed Hydride Reagents[a]

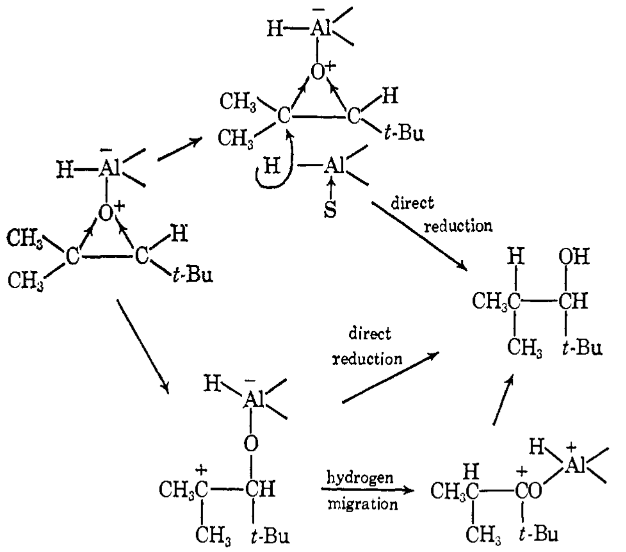
$LiAlH_4$: $AlCl_3$	Ligand	V	VI	VII	VIII	Yield, %
3:1	Et_2O	12	34	9	45	90–93
1:1	Et_2O	2	24	65	8	91–93
1:3	Et_2O	1	16	75	8	85
3:1	THF[b]	30	58	1	11	100
1:1	THF[b]	11	50	31	7	97–100
1:3	THF[b]	2	27	61	9	61–75
3:1	Et_3N[c]	21	44	3	32	70
1:1	Et_3N[c]	1	20	65	17	100
1:3	Et_3N[c]	0	12	71	17	100
1:3	Et_3N[d]	0	8	52	40	56

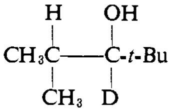
[a] Solvent in all cases was diethyl ether. Three equivalents of hydride used per mole of epoxide. [b] Two moles of THF used per mole of mixed hydride reagent. [c] One mole of Et_3N used per mole of mixed hydride reagent. [d] Two moles Et_3N used per mole of mixed hydride reagent.

Although the trends are similar for the different ligands, certain differences appear to be informative. When the mixed hydride reagents are solvated by tetrahydrofuran as compared to diethyl ether, the resulting mixed hydride should be a stronger hydride donor due to the greater basicity of tetrahydrofuran. This is reflected in the lower yields of the migration product VII and the higher yields of the direct reduction products V and VI. The results obtained with triethylamine as the ligand are very similar to the results obtained in the diethyl ether case. This is to be expected since triethylamine should be more comparable to diethyl ether than to tetrahydrofuran in basicity toward Lewis acids, such as the mixed hydride reagents, due to F-strain considerations. The higher product ratio of V in tetrahydrofuran (30) as compared to triethylamine (21) also reflects this relationship.

An interesting experiment using 2 mol of triethylamine/mol of mixed hydride reagent was also very informative. In this experiment the formation of VII is reduced from 71 to 52% and VIII increased from 17 to 40% as compared to the results using only 1 mol of triethylamine/mol of mixed hydride reagent. Since AlH_3 is known to form a stable bistrimethylamine solvate,[7] it is reasonable to presume that a bistriethylamine solvate also has some stability in solution. Thus an increase in the hydride donor properties as well as the steric requirement of the attacking hydride species would be expected to increase the formation of VIII at the expense of the other products.

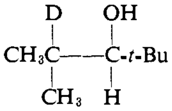
As was implied earlier, product VI can be formed by two different paths. One path involves direct reduction whereas the other path involves hydrogen migration after carbonium ion formation. It was previously shown that the product ratios from $AlCl_3$- and $AlBr_3$ catalyzed rearrangements of triphenylethylene oxide are identical.[2e] It is therefore probable that the ratios of VI arising from a hydride migration and VII arising from a *t*-Bu migration should be reasonably constant in reductions involving mixed hydride reagents of varying Lewis acidity. Previous work by Eliel and coworkers[2b] involving the reaction of β-diisobutylene oxide with $AlCl_3$ showed that 93% of the product was the result of *t*-butyl migration and 7% was the result of hydride migration. A check on this observation was made by allowing β-diisobutylene oxide to react with 1:3 $LiAlD_4$:$AlCl_3$. The products were separated by preparative vpc, and nmr was used to determine the amount of deuteration produced at the two sites representing hydrogen migration and direct reduction. Hydrogen migration produces C and direct reduction produces D.





$\mathrm{CH_3C(H)(CH_3)\text{—}C(OH)(D)\text{-}}t\text{-Bu}$

C



$\mathrm{CH_3C(D)(CH_3)\text{—}C(OH)(H)\text{-}}t\text{-Bu}$

D

Nmr interpretation indicates that C and D are produced in approximately equal amounts. The product ratio of VI:VII was 11:80 for this reaction. Therefore the amount of VI produced by hydrogen migration is 11/2 or 5.5, thus the H migration:*t*-Bu migration is 5.5/80 or approximately 7%. These results are in agreement with those previously reported by Eliel and indicate that the *t*-Bu group migrates preferentially to hydrogen. Also, when the mixed hydride reagent is a strong Lewis acid, a significant amount of VI is produced as a result of H migration, whereas when the mixed hydride reagent is a weak Lewis acid, only a small amount of VI would be a result of hydrogen migration. If one now compares the amount of VI produced only by direct reduction to the total migration products as determined from the above studies for $LiAlH_4$:$AlCl_3$ in 1:3 and 1:4 ratio and pure $HAlCl_2$, further evidence for the participation of $LiAlCl_3H$ in mixed hydride reductions is provided (see Table VII).

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(7) G. W. Schaeffer and E. R. Anderson, *J. Am. Chem. Soc.*, 71, 2143 (1949).

Table VII. Further Evidence for $LiAlCl_3H$ Participation in Mixed Hydride Reductions

$LiAlH_4:AlCl_3$	VI direct reduction only / Total migration products
1:3	0.13
1:4	0.13
$HAlCl_2$	0.06

Table VIII. Vpc Data for Reaction Mixture Analysis

Compound	Retention time, min	*Z*
β-Diisobutylene oxide	2.2	1.01
V	5.6	1.02
VI	6.8	1.01
VII	9.0	1.08
VIII	12.8	1.01
1-Octanol (standard)	18.0	...

Experimental Section

Materials. All manipulations were performed in a nitrogen atmosphere using a Kewaunee drybox equipped with a recirculating system to remove oxygen and moisture. Diethyl ether, tetrahydrofuran, and triethylamine were obtained from Fisher and distilled over $LiAlH_4$ (Et_2O) or $NaAlH_4$ (THF and Et_3N) just prior to use. $LiAlH_4$ was obtained from Alpha Inorganics. Solutions of $LiAlH_4$ were prepared by allowing $LiAlH_4$ in diethyl ether to stir overnight followed by filtration. The resulting clear $LiAlH_4$ solutions were analyzed by EDTA for aluminum. Anhydrous aluminum chloride bromide and iodide (certified Reagent Grade) were obtained from Fisher and purified by vacuum sublimation. Aluminum halide ether solutions were prepared at −20° and standardized by EDTA analysis for aluminum. The resulting solutions were used immediately after preparation although the solutions were stable for at least 33 hr after preparation. The stability was followed by halogen analysis since ether cleavage produces unhydrolyzable halogen (RCl). β-Diisobutylene oxide, 2,4,4-trimethylpentanol-2, and 2,2,4,4-tetramethylbutanol were furnished by Professor E. L. Eliel. The β-diisobutylene oxide was dried over anhydrous K_2CO_3 and distilled twice in a dry nitrogen atmosphere through a spinning-band column, bp 123–124° uncor (lit.[8] 130–131°). Results from nmr analysis were consistent with the structure of β-diisobutylene oxide and vpc showed the product to be 97% pure. 2,2,4,4-Tetramethylbutanol was also isolated by preparative vpc from the reaction mixture of β-diisobutylene oxide and 1:3 $LiAlH_4:AlCl_3$ and found to be identical with the sample furnished by Professor Eliel. 2,4,4-Trimethylpentanol-3 was prepared from *t*-butylmagnesium chloride and isobutyraldehyde in diethyl ether, bp 148–151° (lit.[9] value 155°). Further purification was effected by preparative vpc. 2,4,4-Trimethylpenten-1-ol-3 was prepared according to the procedure of Rerick and Eliel.[2e] The product was purified by preparative vpc and shown by nmr analysis to be the desired compound (see Table VIII).

Analysis of Reduction Products. Analysis of reaction mixtures were made by vpc using a 6-ft column packed with Carbowax 20M on Diataport S; separation conditions: column temperature, 135, injection port temperature, 250°, detector temperature, 350°; He flow rate, 40 cc/min.

General Procedure for Mixed Hydride Reductions. The mixed hydride reagents were prepared in the drybox by slowly adding measured amounts of standardized $LiAlH_4$–diethyl ether solution to a flask containing a magnetic stirrer, a measured amount of freshly prepared and standardized ethereal aluminum halide–diethyl ether solution, and an amount of diethyl ether sufficient to bring the resulting reaction mixture up to a certain approximate volume. The reaction mixture was allowed to stand for 30 min and in the case of those experiments in which the effect of ligand was studied, exact molar amounts of THF or Et_3N were added at this point followed by an additional standing period of 10 min. To this solution containing a small amount of white precipitate was added a measured amount of a standard solution of β-diisobutylene oxide in diethyl ether such that the ratio of the hydride equivalent of the mixed hydride reagent to the epoxide was 3:1. The resulting mixture was allowed to stand for 2 hr and then carefully hydrolyzed with 10 ml of water and enough dilute mineral acid to dissolve the basic aluminum salts. The ethereal and aqueous layers were separated, and the aqueous layer was extracted with three 5-ml portions of ether. The ether layers were combined and dried over anhydrous K_2CO_3, and a measured amount of 1-octanol was added. The resulting solution was then analyzed by vpc. All reactions were carried out in duplicate runs in approximately the same manner.

Typical Mixed Hydride Reduction. 1:4 $LiAlH_4:AlCl_3$ Reduction of β-Diisobutylene Oxide. To 14.76 ml (11.68 mol) of 0.789 *M* $AlCl_3$ solution in diethyl ether was added 4.18 ml (2.92 mol) of 0.698 *M* $LiAlH_4$ solution in diethyl ether at room temperature. To this solution was added 2.95 ml (0.500 g, 3.8 mmol) of a diethyl ether solution containing 0.1694 g/ml of β-diisobutylene oxide. The reaction work-up was carried out as described above. To the gross product was added 0.462 g of 1-octanol and the resulting solution analyzed by vpc.

Mixed Hydride Generation Temperature Dependence. Generation of the mixed hydride reagent from 1:1 $LiAlH_4:AlCl_3$ at 0°, room temperature, and reflux temperature produced reaction mixtures with identical infrared spectra (strong band at 5.40 μ characteristic of Al–H stretching vibration). Reaction of the mixed hydride reagents prepared at the three different temperatures with β-diisobutylene oxide produced the same product ratios within experimental error (Table V).

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