

Selective Reductions. 25. Remarkably Facile Reductive Opening of Cyclic Ethers by the Lithium Tri-*tert*-butoxyaluminumhydride-Triethylborane Combination

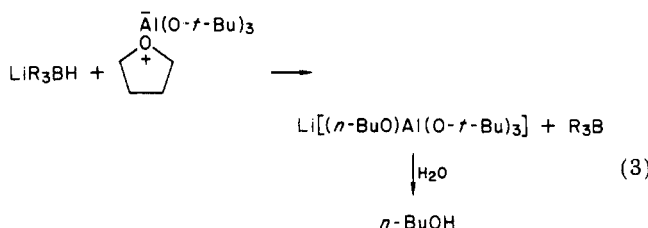
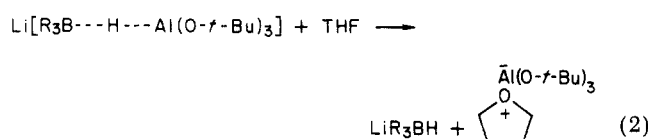
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Solutions of lithium tri-*tert*-butoxyaluminumhydride, stable indefinitely in tetrahydrofuran, undergo rapid reaction in the presence of triethylborane to lose hydride and form 1-butanol (92% in 3 h at 25 °C) through reductive cleavage of the tetrahydrofuran molecule. The reaction is attributed to the rapid formation of a lithium triethylborohydride-aluminum *tert*-butoxide complex. The development led to an exploration of a method for generalizing this reductive cleavage of ethers. In tetrahydropyran, this type of reductive cleavage is much slower (24 h, 17%). Consequently, this was utilized as the solvent to explore the reductive cleavage of a variety of more reactive cyclic and acyclic ethers. The reaction is quite sensitive to the steric and electronic environment of the ether linkage. Epoxides, such as cyclohexene oxide, 1-methylcyclohexene oxide, etc., are instantly and quantitatively cleaved to their corresponding carbinols. Oxetane and tetrahydrofuran are readily cleaved, whereas the reductive cleavage of oxepane is quite sluggish. The utility of the lithium tri-*tert*-butoxyaluminumhydride-triethylborane system is emphasized by the facile reductive cleavage of 2,5-dihydrofuran to *cis*-crotyl alcohol and 7-oxabicyclo[2.2.1]heptane to cyclohexanol. Dimethyl ether and methyl alkyl ethers are cleaved rapidly. The reductive cleavage of ethers bearing higher alkyl substituents is very slow. Thio analogues, such as dimethyl sulfide and tetrahydrothiophene, undergo very little reductive cleavage.

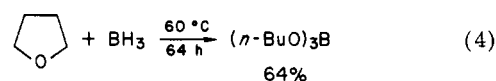
Solutions of lithium tri-*tert*-butoxyaluminumhydride (LTBA) in tetrahydrofuran (THF) are stable indefinitely.^{1,2} We recently discovered and reported that the addition of triethylborane to a THF solution of LTBA results in a vigorous and exothermic reaction. We observed rapid loss of the active hydride and the concurrent formation of 1-butanol³ (after hydrolysis). The rate of reductive cleavage of THF is exceptionally rapid (5 min, 72%), represented graphically in Figure 1. Further, chemical and spectral investigations of this reaction suggest the intermediacy of lithium triethylborohydride and aluminum *tert*-butoxide^{4,5} (eq 1-3). Even a small catalytic quantity



of triethylborane is effective (Figure 1). The reaction is general and can be initiated by other trialkylboranes, such as tri-*sec*-butylborane, tricyclohexylborane, trisiamylborane, etc.⁵ However, the rate of reductive cleavage decreases drastically with increasing steric requirements of the trialkylborane.

Tetrahydrofuran is the most frequently utilized solvent for reductions involving metal hydrides and complex metal

hydrides.⁶ Tetrahydrofuran solutions of alkali metal complex aluminumhydrides, alkali metal complex borohydrides, and their alkyl- or alkoxy-substituted derivatives are indefinitely stable, exhibiting no evidence for the reductive cleavage of THF. However, THF solutions of metal hydrides which are Lewis acids are known to cleave THF. Thus, solutions of aluminum hydride open the ring of tetrahydrofuran very slowly at room temperature (3-5% in 72 h) and faster at higher temperatures.⁷ Diborane, which is also a Lewis acid, also cleaves THF reductively under refluxing conditions.⁸ However, the reaction requires prolonged periods of time.



So far, we know of no such metal hydride or complex metal hydride that reductively opens the THF so rapidly and efficiently as that of the LTBA-triethylborane combination. Accordingly, we undertook to explore the effectiveness of the LTBA-triethylborane system for the reductive cleavage of a variety of ethers.

Results and Discussion

Reaction of LTBA with Triethylborane in Representative Ether Solvents. A known quantity of commercial LTBA (white powder) was placed in a typical reaction flask maintained at room temperature under an inert atmosphere. The calculated quantity of the desired ethereal solvent was introduced so as to make the final concentration of the reaction mixture 0.5 M in LTBA and in triethylborane. LTBA either dissolves to give a clear solution (THF, monoglyme, diglyme, and tetrahydropyran) or remains as an insoluble solid (ether and dioxane). Alternatively, a standard solution of LTBA in ethereal solvents can also be used. An equivalent quantity of triethylborane was introduced and the resulting mixture stirred well for a period of 1 h. Then the mixture was hydrolyzed with water, and the hydrogen evolved was

(1) H. C. Brown and R. F. McFarlin, *J. Am. Chem. Soc.*, **80**, 5372 (1958).
 (2) H. C. Brown and P. M. Weissman, *Isr. J. Chem.*, **1**, 430 (1963).
 (3) H. C. Brown, S. Krishnamurthy, and R. A. Coleman, *J. Am. Chem. Soc.*, **94**, 1750 (1972).
 (4) H. C. Brown and S. Krishnamurthy, *J. Chem. Soc., Chem. Commun.*, 868 (1972).
 (5) H. C. Brown, S. Krishnamurthy, J. L. Hubbard, and R. A. Coleman, *J. Organomet. Chem.*, **166**, 281 (1979).

(6) (a) H. C. Brown and S. Krishnamurthy, *Tetrahedron*, **35**, 567 (1979);
 (b) H. C. Brown and S. Krishnamurthy, *Aldrichimica Acta*, **12**, 3 (1979);
 (c) S. Krishnamurthy, *ibid.*, **7**, 55 (1974).
 (7) N. M. Yoon and H. C. Brown, *J. Am. Chem. Soc.*, **90**, 2927 (1968).
 (8) J. Kollonitsch, *J. Am. Chem. Soc.*, **87**, 5614 (1965).

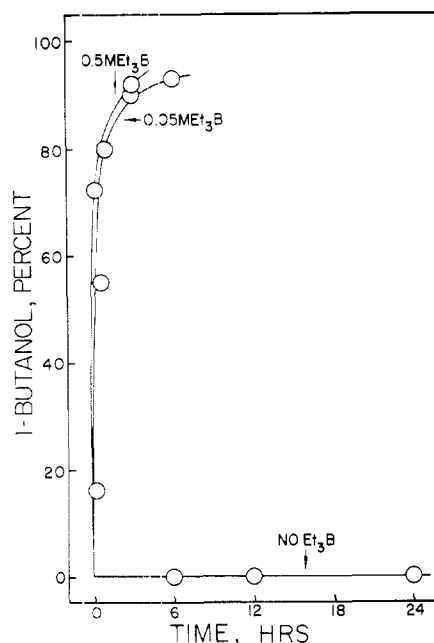


Figure 1. Reductive cleavage of tetrahydrofuran at 25 °C by lithium tri-*tert*-butoxyaluminumhydride (0.5 M) in the absence and presence of triethylborane.

measured with a gas meter. From this, the residual hydride concentration could be calculated. Alternatively, the reaction could be monitored by GLC by analyzing the alcohol produced after reductive cleavage, utilizing an internal standard or by measuring the amount of methane evolved with time (in the case of methyl ethers).

In diethyl ether, LTBA is essentially insoluble. After the addition of triethylborane, no visible change was observed. Hydrolysis of the reaction mixture at the end of 1 h indicated the presence of 95% of the original active hydride introduced.

The behavior was similar in dioxane. At the end of 1 h, a loss of only 5–10% of the available hydride was realized.

Addition of triethylborane to a diglyme solution of LTBA resulted in vigorous evolution of a gas, presumably methane. In 1 h, the gas evolved corresponded to 60% reaction. Hydrolysis of the reaction mixture indicated the presence of 40% residual hydride. Further reaction over longer periods of time was quite slow. Similarly, a clear solution of LTBA in monoglyme reacts with triethylborane vigorously with the evolution of a gas (presumably methane). The reaction was monitored by GLC for the production of 2-methoxyethanol with time (1 h 47%, 12 h 58%).

Clear solutions of LTBA in tetrahydrofuran react vigorously with triethylborane. The reaction mixture turned milky after 30 min due to the formation of lithium tetraalkoxyaluminumate, sparingly soluble in the solvent. In 3 h, 95% of the active hydride disappeared, and there was present 92% of 1-butanol (after hydrolysis).

In tetrahydropyran (THP), LTBA dissolves completely to give a clear solution. Addition of triethylborane to this solution does result in a vigorous and exothermic reaction. However, the reductive cleavage of THP as monitored by GLC analysis was relatively slow compared with that of THF; only 17% cleavage was realized in 24 h. Indeed, ^{11}B NMR and chemical examination of the mixture of LTBA and triethylborane in tetrahydropyran immediately after mixing revealed a rapid hydride transfer, forming a complex of lithium triethylborohydride and aluminum *tert*-butoxide.⁵ But further reaction, the cleavage of THP,

Table I. Reaction of Lithium Tri-*tert*-butoxyaluminumhydride with Triethylborane in Representative Ethers at 25 °C^a

ether	time, h	% of residual hydride	% of alcohol formed ^b
ethyl ether ^c	1	97	
dioxane ^c	1	95	
monoglyme	1		47 ^d
	24		65 ^d
diglyme	1	40	60 ^e
tetrahydrofuran	1	5	
	24	3	92
tetrahydropyran	24		17

^a In all cases, the solutions were 0.5 M in LTBA and Et_3B . ^b Analyzed by GLC, using a suitable internal standard. ^c LTBA and also the resulting mixture formed after the addition of Et_3B are insoluble. ^d The alcohol formed is 2-methoxyethanol. ^e Not determined directly; based on the volume of methane evolved.

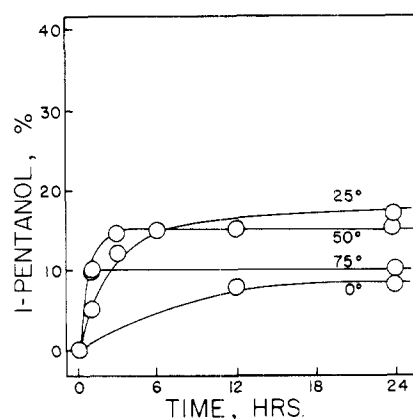
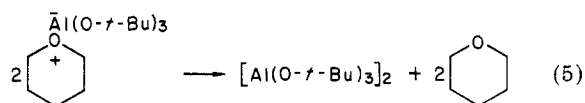


Figure 2. Reaction of lithium tri-*tert*-butoxyaluminumhydride with triethylborane in tetrahydropyran (both reagents 0.5 M).

is very sluggish. The results are summarized in Table I. Temperature has an unusual and interesting influence on the rate of reductive cleavage of ethers. We examined the reductive cleavage of THP by LTBA–triethylborane at 0, 25, 50, and 75 °C. The results are represented graphically in Figure 2. At 0 °C, the rate of reductive cleavage is quite slow; in a 12-h period, 8% reductive cleavage was realized, a value which did not change with time. At 25 °C, 17% of reductive cleavage was observed in 24 h. At 50 °C, there was observed 15% of reductive cleavage in less than 3 h, exhibiting no increase even after 24 h. At 75 °C, 10% of reductive cleavage occurred in 1 h, exhibiting no increase in 24 h. These results are clearly in line with our previous observations that the freshly generated aluminum *tert*-butoxide in the absence of a good trapping agent is converted to the inactive dimer⁵ (eq 5). An increase in



the temperature of the reaction appears to facilitate the dissociation of the aluminum *tert*-butoxide–THP complex, with consequent formation of the inactive dimer. The incomplete reaction observed for some systems is attributed to this phenomenon.

Reaction of Representative Ethers with the LTBA–Triethylborane System in THP. Among the six representative ethers examined toward the LTBA–triethylborane system, the behavior of this mixture in THP is quite interesting. The mixture is soluble in this solvent, yielding a clear solution. The spectral and chemical ev-

Table II. Reaction of a Lithium Tri-*tert*-butoxyaluminumhydride-Triethylborane Mixture with Representative Ethers in Tetrahydropyran at 25 °C^a

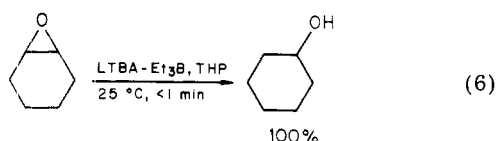
ether	time, h	molar ratio			products	yield, % ^b
		LTBA	Et ₃ B	R ₂ O		
cyclohexene oxide	0.25	2	0	1	cyclohexanol	4
	<0.01	2	2	1	cyclohexanol	100
	<0.01	2	0.2	1	cyclohexanol	100
styrene oxide ^c	0.01 ^c	1	1	1	cyclohexanol	97
	0.16	1	1	1	1-phenylethanol 2-phenylethanol	89.5 10.5
1-methylcyclohexene oxide ^c	0.16	1	1	1	1-methylcyclohexanol <i>cis</i> -2-methylcyclohexanol	90 10
oxetane	0.08	2	2	1	1-propanol	98
tetrahydrofuran	24.0	2	0.2	1	1-butanol	100
	0.5	2	2	1	1-butanol	98
2-methyltetrahydrofuran	6.0	4	4	1	2-pentanol	95
2,2-dimethyltetrahydrofuran	24.0	4	4	1	2-methyl-2-pentanol	5
2,5-dihydrofuran	24.0	2	0.2	1	<i>cis</i> -crotyl alcohol	91
	2.0	2	2	1	<i>cis</i> -crotyl alcohol	95
7-oxabicyclo[2.2.1]heptane	3.0	4	4	1	cyclohexanol	97
4,5-dihydro-2-methylfuran	24.0	2	2	1	2-pentanone	0
oxepane	24.0	2	2	1	1-hexanol	3
dimethyl ether	6.0	2	2	1	methanol ^d	>90
diethyl ether	24.0	2	2	1	ethanol ^d	<5
methyl <i>n</i> -butyl ether	6.0	2	2	1	1-butanol	68
anisole	6.0	2	2	1	phenol ^d	0
dimethyl sulfide	6.0	2	2	1	methanethiol ^d	0
tetrahydrothiophene	6.0	2	2	1	butanethiol ^d	0

^a In all cases, reaction mixtures were 0.5–1.0 M in ether. ^b All the yields reported were determined by GLC, utilizing a suitable internal standard. ^c In THF. ^d Not determined directly; by the analysis of the alkane formed or by residual hydride analysis.

idence indicated the instant occurrence of the first step of the reaction—the hydride transfer (eq 1). However, the second step, the reductive cleavage of THP, is relatively slow. Consequently, it should be possible to take advantage of this situation by utilizing THP as the solvent to explore the reductive cleavage of more reactive ethers. Accordingly, we undertook to examine the effectiveness of this new reagent system, LTBA-triethylborane in THP, for the reductive cleavage of representative ethers.

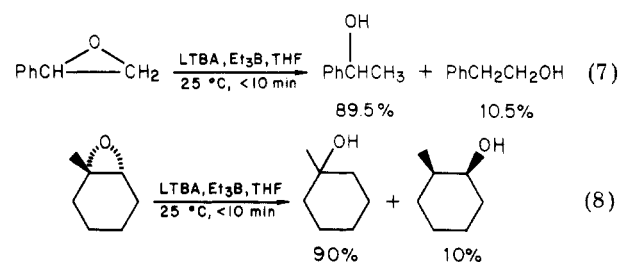
The general procedure adopted was to place a known quantity of commercial LTBA in a reaction flask under an inert atmosphere. To this, a known amount of THP was added. Depending upon the amount of THP added, the LTBA dissolved either completely or partially. Alternatively, a standard solution of LTBA in THP was utilized. The ether under investigation was added either as a neat liquid or as a standard solution in THP. This was followed by the addition either of a catalytic or a stoichiometric quantity of triethylborane. The resulting mixture was stirred well, and the course of the reaction was monitored by GLC analysis for reductive cleavage product (alcohol), using an internal standard, by residual hydride analysis or by measuring the methane gas evolved (in the case of methyl ethers). The results are summarized in Table II.

The reaction of LTBA with epoxides, such as cyclohexene oxide, is very slow.² The addition of molar quantities of triethylborane leads to a vigorous and exothermic reaction resulting in instantaneous opening of the epoxide ring⁹ (eq 6). Even small catalytic quantities of



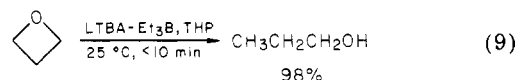
(9) The reductive opening of many reactive epoxides by this system is so rapid that the reaction can be carried out even in THF without significant attack of THF.

triethylborane are effective. Similarly, styrene oxide and 1-methylcyclohexene oxide are cleaved instantly to the corresponding carbinols (eq 7 and 8). It should be pointed

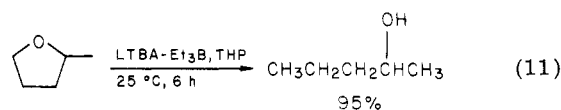
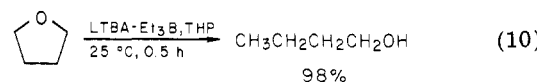


out that the reductive cleavage of epoxides by this system is less regioselective than those observed with lithium triethylborohydride alone.¹⁰ The lower regioselectivity is attributed to prior coordination of aluminum *tert*-butoxide with the epoxide oxygen causing electron shifts which make it possible for hydride to attack at both positions of the epoxide ring.

Trimethylene oxide, oxetane, is also cleaved quite rapidly.

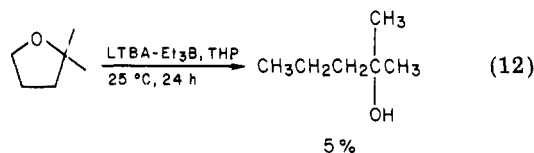


This reductive cleavage in THP could be readily applied to THF and 2-methyltetrahydrofuran (eq 10 and 11). The



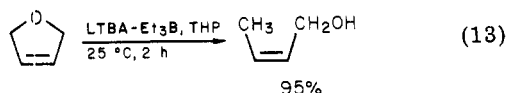
(10) S. Krishnamurthy, R. M. Schubert, and H. C. Brown, *J. Am. Chem. Soc.*, **95**, 8486 (1973).

reductive cleavage of 2,2-dimethyltetrahydrofuran is both slow and incomplete (eq 12). Presumably, the presence

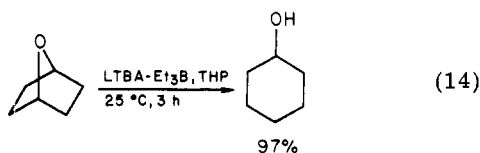


of the *gem*-dimethyl substituents interferes with the coordination of the aluminum *tert*-butoxide.

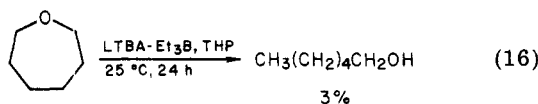
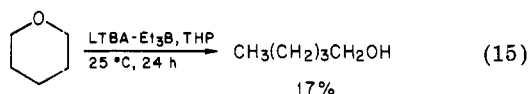
2,5-Dihydrofuran is readily converted to *cis*-crotyl alcohol in 95% yield (eq 13). Even the bicyclic ether, 7-



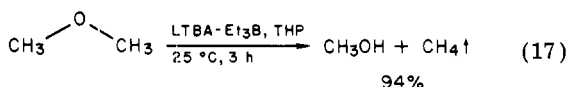
oxabicyclo[2.2.1]heptane, undergoes smooth ring cleavage to cyclohexanol (eq 14).



The reductive cleavage of both THP and oxepane is very sluggish and incomplete.



On the other hand, dimethyl ether undergoes a facile reductive cleavage evolving methane.



Theoretical Considerations. The effectiveness of the LTBA-triethylborane system to achieve the reductive cleavage of ethers appears to depend upon two major factors. One is the ability of the ether to complex with the monomeric aluminum *tert*-butoxide initially formed in the reaction. The second is the relative ease with which the triethylborohydride can attack the activated α position of the complexed ether.

Thus the results discussed above clearly reveal that both electronic and steric changes which decrease the coordinating ability of the ether decrease the rate of this reductive cleavage. Thus, the very slow cleavage of 2,2-dimethyltetrahydrofuran relative to tetrahydrofuran, or of diethyl ether relative to dimethyl ether, can be attributed to the greater steric requirements of the two slower ethers. For example, a study of the coordination of BF_3 with dialkyl ethers reveals the steric order: $\text{Me}_2\text{O} > \text{Et}_2\text{O} > i\text{-Pr}_2\text{O}$.¹¹

Similarly, the very slow rates of anisole and 4,5-dihydro-2-methylfuran toward the hydride cleavage reaction can be attributed to the effect of conjugation in dimin-

ishing the ability of the oxygen atom in these derivatives to coordinate with aluminum *tert*-butoxide.

The dramatic difference between ethers and thio ethers may be attributed to the lower donor properties of thio ethers toward aluminum *tert*-butoxide.

The inertness of diethyl ether as compared to dimethyl ether may arise not only from the lower coordinating ability of the former but also from the fact that $\text{S}_{\text{N}}2$ displacements on ethyl derivatives are considerably slower than such displacements on methyl derivatives. In the same way, the much lower reactivity of THP as compared to THF may arise both from a lower coordinating ability of the more flexible six-ring ether as compared to the five-ring ether and from a much lower sensitivity of six-ring systems to $\text{S}_{\text{N}}2$ displacements.

With cyclic ethers, the ring size has a significant effect on their donor abilities.¹² Complexation ability of representative cyclic ethers toward dimethylzinc has been reported to be¹³ ethylene oxide > oxetane > tetrahydrofuran > tetrahydropyran. Indeed, we observed an identical order of reactivity in our present reductive cleavage reaction: epoxide > oxetane > tetrahydrofuran > tetrahydropyran > oxepane.

Conclusions

Reaction of lithium tri-*tert*-butoxyaluminumhydride with triethylborane in tetrahydropyran gives the lithium triethylborohydride-aluminum *tert*-butoxide complex. At room temperature, the reaction is very rapid. The resulting mixture reductively cleaves a variety of ethers rapidly and quantitatively. The reductive cleavage of ethers by this reagent combination is highly sensitive to the steric and electronic environments of the ether linkage. The ability of this system to function as an efficient cleaving agent for ethers largely depends upon two factors: (i) the complexing ability of ethers toward aluminum *tert*-butoxide; and (ii) the ease with which the activated complex can undergo $\text{S}_{\text{N}}2$ displacement with lithium triethylborohydride. The reagent combination provides a clean and facile procedure for the reductive cleavage of epoxides, oxetane, tetrahydrofuran, and related derivatives. However, the system is less effective for acyclic ethers. The system should be useful for selective cleavage of the methoxy substituent in the presence of higher alkoxy or thioalkoxy substituents. The present study has led to a better understanding of the scope as well as the limitation of this reagent for the reductive cleavage of ethers.

Experimental Section

General Comments. All glassware was dried at least 4 h at 140 °C, assembled hot, and cooled under a stream of prepurified nitrogen. All reactions were carried out under a dry nitrogen atmosphere. Additions of solvents and liquid reagents were carried out with oven-dried, nitrogen-purged, hypodermic syringes fitted with stainless-steel needles.

Materials. Tetrahydrofuran, tetrahydropyran, monoglyme, and diglyme were distilled from excess lithium aluminum hydride and stored under nitrogen. Reagent grade diethyl ether and dioxane were utilized, after they were dried over molecular sieves. 1-Methylcyclohexene oxide was synthesized from 1-methylcyclohexene and *m*-chloroperbenzoic acid. All other ethers and thioethers utilized in this study are commercial products of the highest purity. They were freshly distilled before use. LTBA utilized in this study was either commercial¹⁴ or synthesized from

(11) H. C. Brown and R. M. Adams, *J. Am. Chem. Soc.*, **64**, 2557 (1942).

(12) For a thorough discussion on this subject, see S. Patai, Ed., "The Chemistry of Ether Linkage", Interscience, New York, 1967, pp 243-308.

(13) F. H. Thiele, *Z. Anorg. Allg. Chem.*, **319**, 183 (1962).

lithium aluminum hydride and 3 mol of *tert*-butyl alcohol.¹

GLC Analyses. GLC analyses were carried out by using a Varian Model 1200 FID Chromatograph fitted with stainless-steel columns.

Reaction of LTBA with Triethylborane in Tetrahydrofuran. A 100-mL flask with a septum inlet, thermometer well, and a magnetic stirring bar was connected to a mercury bubbler, and the apparatus was purged with nitrogen. The flask was immersed in a water bath (ca. 25 °C) and LTBA (33.2 mL, 20 mmol of a 0.6 M solution in THF) was placed in the reaction flask followed by 4 mL (8 mmol) of a 2 M solution of *n*-dodecane in THF (internal standard). To this well-stirred mixture, triethylborane, 2.84 mL (20 mmol), was added. A vigorous and exothermic reaction (~45 °C) was observed. After 5 min, 4 mL of the reaction mixture was withdrawn and hydrolyzed with water and the hydrogen evolved measured. There was present only 28% of the residual hydride (based on the original hydride concentration). Simultaneously, another minute sample was withdrawn, hydrolyzed, and analyzed for the 1-butanol formed by GLC on a Carbowax 20M 6 ft × 1/8 in. column. There was present 73% of 1-butanol. The reductive cleavage was essentially complete in 3 h.

Another reaction was carried out by utilizing only a catalytic quantity of triethylborane (10 mol %). The results are summarized in Figure 1.

Reaction of LTBA with Triethylborane in Diethyl Ether. A typical reaction setup was assembled. Commercial LTBA, 2.54 g (10 mmol), was introduced into the reaction flask. Diethyl ether, 18.6 mL, was introduced into the reaction flask and the mixture stirred well. LTBA remains insoluble in ether. To this well-stirred solution, 1.42 mL (10 mmol) of triethylborane was introduced. No visible change was observed. Another identical reaction (blank) was conducted in which instead of triethylborane 1.42 mL of diethyl ether was added. After 1 h, both mixtures were hydrolyzed with water, and the hydrogen evolved was measured with a gas buret, connected to the system through a dry-ice trap. There was present 95% of the originally introduced active hydride in the reaction mixture.

Reaction of LTBA-Triethylborane with 7-Oxabicyclo[2.2.1]heptane in THP. A typical reaction setup was assembled. In the flask was placed 2.54 g (10 mmol) of LTBA and 2.6 mL

of THP. The flask was immersed in a water bath (ca. 25 °C). Then 0.5 mL of a 5.0 M solution in THP of 7-oxabicyclo[2.2.1]heptane (2.5 mmol) was injected into the reaction flask, followed by 0.5 mL of a 2.0 M solution in THP of *n*-tridecane (1 mmol) to serve as an internal standard, followed by 1.42 mL of triethylborane (10 mmol). The mixture was stirred vigorously. After 1 h, 0.5 mL of the reaction mixture was withdrawn with a syringe and quenched with a mixture of water and ether. The aqueous phase was saturated with anhydrous potassium carbonate. GLC analysis of the dry ethereal layer revealed the presence of 91% of cyclohexanol. In 3 h, a 97% yield of cyclohexanol was realized.

Reaction of LTBA-Triethylborane with 2,5-Dihydrofuran. A typical reaction setup was assembled. LTBA (2.8 g, 11 mmol), was placed in the reaction flask followed by 6.6 mL of THP. 2,5-Dihydrofuran (1 mL of a 5 M solution in THP, 5 mmol) was introduced into the reaction flask followed by 1 mL of a 2 M solution of *n*-tridecane in THP (2 mmol) to serve as an internal standard. To this well-stirred mixture, triethylborane, 1.42 mL (10 mmol), was added. The reaction was monitored periodically by GLC. In 2 h, there was realized a 95% yield of pure *cis*-crotyl alcohol.

Another reaction carried out by using a catalytic quantity of triethylborane (10 mol %) yielded *cis*-crotyl alcohol in 91% yield in a 24-h period.

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Registry No. LTBA, 17476-04-9; Et₃B, 97-94-9; cyclohexene oxide, 286-20-4; styrene oxide, 96-09-3; 1-methylcyclohexene oxide, 1713-33-3; oxetane, 503-30-0; tetrahydrofuran, 109-99-9; 2-methyltetrahydrofuran, 96-47-9; 2,2-dimethyltetrahydrofuran, 1003-17-4; 2,5-dihydrofuran, 1708-29-8; 7-oxabicyclo[2.2.1]heptane, 279-49-2; 4,5-dihydro-2-methylfuran, 1487-15-6; oxepane, 592-90-5; dimethyl ether, 115-10-6; diethyl ether, 60-29-7; methyl butyl ether, 628-28-4; anisole, 100-66-3; dimethyl sulfide, 75-18-3; tetrahydrothiophene, 110-01-0; dioxane, 123-91-1; monoglyme, 110-71-4; diglyme, 111-96-6; tetrahydropyran, 142-68-7; 2-methoxyethanol, 109-86-4; cyclohexanol, 108-93-0; 1-phenylethanol, 98-85-1; 1-methylcyclohexanol, 590-67-0; *cis*-2-methylcyclohexanol, 7443-70-1; 1-propanol, 71-23-8; 1-butanol, 71-36-3; 2-pentanol, 6032-29-7; 2-methyl-2-pentanol, 590-36-3; *cis*-crotyl alcohol, 4088-60-2; 1-hexanol, 111-27-3; methanol, 67-56-1; ethanol, 64-17-5.

(14) Available from Aldrich Chemical Co., Inc., Milwaukee, Wis. 53233.

Carbon Isotopic Fractionation in the Schmidt Decarboxylation: Evidence for Two Pathways to Products

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The evolution of CO₂ at 5 ± 2 °C from the H₂SO₄-catalyzed reaction of *n*-octanoic acid with HN₃ in CHCl₃ (the Schmidt decarboxylation) takes place in two kinetic phases with different carbon kinetic isotope effects. Experiments were carried out under high-efficiency stirring conditions at HN₃ concentrations ranging from 1.47 to 0.24 M. At an initial HN₃ concentration of 1.47 M, the pseudo-first-order rate constant for the first kinetic phase was 0.07 ± 0.03 h⁻¹, with ¹²k/¹³k = 1.0589 ± 0.0003. After a lag time of 48 min the rate of CO₂ evolution changed, with the pseudo-first-order rate constant (1.47 M HN₃) increasing to 0.45 ± 0.02 h⁻¹; ¹²k/¹³k ≈ 1.03. Results obtained at lower HN₃ concentrations showed that the first, slower reaction phase displayed overall first-order kinetics, its rate being independent of HN₃ concentration. The first reaction phase could be suppressed by addition of KHSO₄ to the H₂SO₄. Preequilibration of the HN₃/CHCl₃ with H₂SO₄ markedly affected the isotopic composition of the initial CO₂ product, apparently effecting the initial transient utilization of the second-phase reaction pathway through the action of the H₂SO₄ on the HN₃. Although the kinetic phases could not be resolved at 22 °C, the isotopic composition of the evolved CO₂ indicated that both pathways to the product were being utilized.

The reaction between hydrazoic acid and carbonyl compounds is known as the Schmidt reaction. When the carbonyl compound is a carboxylic acid, attack of HN₃ is followed by rearrangement and decarboxylation as indi-

cated in eq 1.^{1,2} Despite the fact that this reaction is a well-known example of a rearrangement involving mi-

