Selective Reductions. X. Reaction of Aluminum Hydride with Selected Organic Compounds Containing Representative Functional Groups. Comparison of the Reducing Characteristics of Lithium Aluminum Hydride and Its Derivatives

Herbert C. Brown and Nung Min Yoon[1]

Contribution from the Richard B. Wetherill Laboratory of Purdue University, Lafayette, Indiana. *Received November 3, 1965*

Abstract: The addition of the calculated quantity of 100% sulfuric acid to solutions of lithium aluminum hydride in tetrahydrofuran precipitates lithium sulfate and provides clear, relatively stable solutions of aluminum hydride. This convenient preparation of aluminum hydride was utilized in a systematic survey of the rates and stoichiometry of the reaction of the reagent in tetrahydrofuran at 0° with selected organic compounds containing representative functional groups in order to establish the utility of the reagent as a selective reducing agent and to compare its characteristics with those of lithium aluminum hydride, trimethoxyaluminohydride, and tri-*t*-butoxyaluminohydride previously examined. Aldehydes and ketones were rapidly reduced, with no complications involved by the presence of a conjugated double bond as in cinnamaldehyde. Norcamphor was reduced with good stereoselectivity, yielding 7% *exo*- and 93% *endo*-norborneol. Anthraquinone utilized 2 equiv of hydride, without hydrogen evolution, indicating clean reduction to the 9,10-dihydro-9,10-anthracenediol stage. Acids, acid anhydrides, acid chlorides, esters, and lactones were rapidly reduced to the alcohol stage. Epoxides were also reduced rapidly, with 1,2-butylene oxide and 1-methyl-1,2-cyclohexene oxide, yielding 2-butanol and 1-methylcyclohexanol exclusively. However, styrene oxide exhibited more opening at the secondary center than is observed with lithium aluminum hydride, yielding 76% secondary and 24% primary alcohol. Tertiary amides were rapidly reduced, whereas primary amides were reduced more slowly. Nitriles, oximes, phenyl isocyanate, and pyridine N-oxide were reduced rapidly. On the other hand, both aliphatic and aromatic nitro compounds, azobenzene, and azoxybenzene proved to be relatively stable to the reagent. Pyridine reacted at a moderate rate with the uptake of one hydride per mole in 12 hr. Di-*n*-butyl disulfide was reduced only slowly, but diphenyl disulfide and dimethyl sulfoxide were rapidly reduced. Finally, sulfones, sulfonic acids, and cyclohexyl tosylate were stable to the reagent under these conditions. A detailed comparison is made of the relative characteristics and special advantages for the reduction of specific groups by lithium aluminum hydride, lithium trimethoxyaluminohydride, lithium tri-*t*-butoxyaluminohydride, and aluminum hydride.

Lithium aluminum hydride, a very powerful reducing agent, is widely used for the reduction of functional groups.[2] The introduction of alkoxy groups into lithium aluminum hydride[3,4] modifies its reducing characteristics[5-8] and has made possible a number of selective reductions of considerable utility in synthetic work.[9-13]

In the boron hydride area, it was observed that diborane as a reducing agent[14] exhibits major differences in its characteristics from sodium borohydride.[2a] This was attributed to the fact that diborane is a Lewis acid and possesses an affinity for reaction centers of high electron density, whereas sodium borohydride is a nucleophilic agent and attacks preferentially at centers of low electron density.[14] Consequently, it appeared of interest to explore the reducing properties of aluminum hydride.

Aluminum hydride may be prepared by treating lithium aluminum hydride with aluminum chloride.[15]

$$3LiAlH_4 + AlCl_3 \longrightarrow 4AlH_3 + 3LiCl\downarrow$$

The lithium chloride precipitates and an ether solution of the reagent is obtained. Unfortunately, such solutions are metastable and, on standing, the aluminum hydride associates and precipitates from solution.[15,16]

$$xAlH_3 \longrightarrow (AlH_3)'\downarrow$$

This behavior has discouraged any significant study of its reducing characteristics.[17,18] The tendency has been to utilize solutions stabilized by the presence of additional aluminum chloride.[19-22] Such

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[2] For comprehensive reviews, see (a) N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, Inc., New York, N. Y., 1956; (b) W. G. Brown, *Org. Reactions*, **6**, 469 (1951); (c) V. M. Mićović and M. L. Mihailović, "Lithium Aluminum Hydride in Organic Chemistry," Naukna Knjiga, Belgrade, Yugoslavia, 1955.

[3] H. C. Brown and R. F. McFarlin, *J. Am. Chem. Soc.*, **78**, 252 (1956); **80**, 5374 (1958).

[4] H. C. Brown and C. J. Shoaf, *ibid.*, **86**, 1079 (1964).

[5] H. C. Brown, P. M. Weissman, and N. M. Yoon, *ibid.*, **88**, 1458 (1966).

[6] H. C. Brown and P. M. Weissman, *ibid.*, **87**, 5614 (1965).

[7] H. C. Brown and P. M. Weissman, *Israel J. Chem.*, **1**, 430 (1963).

[8] G. Hesse and R. Schrödel, *Ann.*, **607**, 24 (1957).

[9] H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **80**, 5377 (1958).

[10] H. C. Brown and C. P. Garg, *ibid.*, **86**, 1086 (1964).

[11] H. C. Brown and A. Tsukamoto, *ibid.*, **86**, 1089 (1964).

[12] P. M. Weissman and H. C. Brown, *J. Org. Chem.*, **31**, 283 (1966).

[13] H. C. Brown and H. M. Deck, *J. Am. Chem. Soc.*, **87**, 5620 (1965).

[14] H. C. Brown and B. C. Subba Rao, *ibid.*, **82**, 681 (1960).

[15] A. E. Finholt, A. C. Bond, and H. I. Schlesinger, *ibid.*, **69**, 1999 (1947).

[16] E. Wiberg, H. Graf, M. Schmidt, and R. Uson, *Z. Naturforsch.*, **7b**, 578 (1952).

[17] E. Wiberg and A. Jahn, *ibid.*, **7b**, 581 (1952).

[18] One highly important exception is the discovery of the reduction of ethyl cinnamate and cinnamaldehyde to cinnamyl alcohol, without attack of the double bond: M. J. Jorgenson, *Tetrahedron Letters*, No. **13**, 559 (1962).

[19] E. Wiberg, *Angew. Chem.*, **65**, 16 (1953).

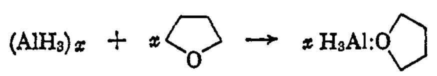
[20] R. F. Nystrom, *J. Am. Chem. Soc.*, 77, 2544 (1955), and subsequent papers.

solutions doubtless contain such intermediates as AlH_2Cl, $AlHCl_2$,[19-22] and their addition compounds with lithium chloride.[22] (Lithium chloride does not precipitate from these solutions containing aluminum chloride in excess over the amount required to form aluminum hydride.) Consequently, the results, although interesting and valuable, cannot be used to define the reducing characteristics of aluminum hydride itself.

In view of this background, we decided to undertake the development of a simple, convenient procedure for the preparation of solutions of aluminum hydride in tetrahydrofuran and to examine its behavior toward the standard list of compounds previously examined with lithium aluminum hydride,[5] lithium trimethoxyaluminum hydride,[8] and lithium tri-*t*-butoxyaluminohydride.[7] In order to facilitate comparison of the results with the earlier data, we maintained the solvent, concentrations, and temperatures as near as possible to the conditions utilized in the earlier explorations.[5-7]

Results and Discussion

Preparation of Aluminum Hydride Solutions. As was pointed out earlier, aluminum hydride is commonly prepared by mixing the calculated quantity of aluminum chloride with lithium aluminum hydride in ether solution. The lithium chloride precipitates and is readily separated from the ether solution. On standing overnight or longer, the aluminum hydride associates, forming a white, insoluble precipitate. This precipitate will dissolve in tetrahydrofuran, presumably depolymerizing to form a 1:1 addition compound.[23]



While this provided a reasonably useful means of obtaining the desired solutions of the reagent, we undertook to explore other methods. The procedure finally adopted involved the addition of 0.5 mole of 100% sulfuric acid to 1 mole of lithium aluminum hydride in tetrahydrofuran solution. Hydrogen is evolved and lithium sulfate precipitates quantitatively.

$$2LiAlH_4 + H_2SO_4 \xrightarrow{THF} Li_2SO_4\downarrow + 2AlH_3 + 2H_2$$

The lithium sulfate separates easily to give a clear supernatant solution. Analysis revealed the presence of aluminum and hydride in the molar ratio of 1:3 and the absence of sulfate.

It has been reported that aluminum hydride is unstable in refluxing tetrahydrofuran and opens the ring to produce *n*-butyl alcohol.[24] However, the solutions prepared by the above procedure proved to be adequately stable at room temperature for our needs. Such a solution (0.50 *M*) showed no significant change in the hydride concentration in 24 to 48 hr at room temperature. Only after 3 days was there observed a decrease in the hydride concentration to 0.49 *M*, with the formation of the corresponding quantity of *n*-butyl alcohol indicated by gas chromatographic examination of the hydrolyzed reaction mixture.

Procedure for Rate and Stoichiometry Studies. The procedure adopted was to add 10 mmoles of the organic compound to 13.3 mmoles of aluminum hydride in sufficient tetrahydrofuran to give 40 ml of solution. This makes the reaction mixture 0.33 *M* in aluminum hydride (*i.e.*, 1.00 *M* in hydride) and 0.25 *M* in the compound under examination. In those cases where the compound consumes more than 3 equiv of hydride, the hydride concentration was maintained constant, but the concentration of the compound was reduced to 0.166 *M*, giving a hydride to compound ratio of 6:1. The solution was maintained at 0° and aliquots were removed at appropriate intervals and analyzed for residual hydride. In this manner it was possible both to establish the rate at which reduction proceeds and the stoichiometry of the reaction, *i.e.*, the number of hyrides utilized per mole of compound when the reaction comes to an effective halt.

Alcohols, Phenols, Amines, and Thiols. The alcohols, phenols, and thiols examined all liberated hydrogen instantly and quantitatively. On the other hand, *n*-hexylamine liberated only 1 equiv of hydrogen rapidly, with the second being evolved only slowly and not yet complete after 24 hr. The results are summarized in Table I.

Table I. Reaction of Aluminum Hydride with Representative "Active Hydrogen" Compounds in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b,c]	Hydride used[b,c]	Hydride used for reduction[b]
1-Hexanol	0.25	1.01	1.01	0
Benzyl alcohol	0.25	1.04	1.04	0
3-Hexanol	0.25	1.02	1.02	0
3-Ethyl-3-pentanol	0.25	1.03	1.03	0
Phenol	0.25	1.03	1.03	0
n-Hexylamine	0.25	1.10	1.10	0
	1.0	1.30	1.30	0
	24.0	1.87	1.87	0
1-Hexanethiol	0.25	1.00	1.00	0
Benzenethiol	0.25	1.04	1.04	0

[a] 10.0 mmoles of compound, except where otherwise indicated, to 13.3 mmoles of aluminum hydride (40 mmoles of hydride). [b] Millimoles/millimole of compound. [c] Hydrogen evolved from blank minus the hydrogen evolved on hydrolysis of the reaction mixture after the indicated reaction period.

Aldehydes and Ketones. Aldehydes and ketones of diverse structure, such as caproaldehyde, benzaldehyde, 2-heptanone, norcamphor, acetophenone, and benzophenone were rapidly reduced to the corresponding alcohols, the reactions apparently being complete within 1 hr at 0°. The reduction of norcamphor appears to be appreciably more stereoselective than lithium aluminum hydride, yielding 7% *exo*- and 93% *endo*-norborneol, as compared to the 10:90 distribution realized with the latter reagent.[13] Cinnamaldehyde reacted immediately with 1 equiv of hydride;[18] a 92% yield of cinnamyl alcohol with no trace of hydrocinnamyl alcohol was indicated by the gas chromato-

$$R_2CO + AlH_3 \longrightarrow [R_2CHOAlH_2] \xrightarrow{H_2O} R_2CHOH$$

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(21) J. H. Brewster and H. O. Bayer, *J. Org. Chem.*, **29**, 105 (1964), and following papers.

(22) E. E. Eliel, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **22**, 129 (1961).

(23) E. Wiberg and W. Gösel, *Z. Naturforsch.*, **116**, 485 (1956).

(24) W. J. Bailey and F. Marktscheffel, *J. Org. Chem.*, **25**, 1797 (1960).

Table II. Reaction of Aluminum Hydride with Representative Aldehydes and Ketones in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
Caproaldehyde	0.25	0.15	1.02	0.87
	0.5		1.03	0.88
	1.0		1.06	0.91
	3.0		1.18	1.03
Benzaldehyde	0.25	0.13	1.03	0.90
	0.5		1.03	0.90
	1.0		1.07	0.94
	3.0		1.09	0.96
2-Heptanone	0.25	0.09	0.86	0.77
	0.5		1.07	0.98
	1.0		1.07	0.98
	3.0		1.09	1.00
Norcamphor	0.25	0.07	1.10	1.03
	0.5		1.07	1.00
	1.0		1.09	1.02
Acetophenone	0.25	0.10	0.98	0.88
	0.5		1.05	0.95
	1.0		1.08	0.98
	3.0		1.09	0.99
Benzophenone	0.25	0.02	0.85	0.83
	0.5		1.01	0.99
	1.0		1.07	1.05
	3.0		1.05	1.03
Cinnamaldehyde[d]	0.25	0.04	1.02	0.98
	0.5		1.04	1.00
	1.0		1.04	1.00

[a-c] See corresponding footnotes in Table I. [d] White precipitate.

graphic examination of the product. These results are summarized in Table II.

Quinones. As was pointed out earlier,[5] the reduction of a quinone to a hydroquinone should utilize 2 equiv of hydride, 1 for reduction and 1 for hydrogen evolution. On the other hand, the reduction of the quinone to the 1,4-dihydroxycyclohexadiene stage should require 2 equiv of hydride for reduction, without hydrogen evolution. On this basis, the reduction of *p*-benzoquinone proceeded to give a 50:50 distribution between the two paths, whereas anthraquinone appeared to reduce cleanly to 9,10-dihydro-9,10-anthracenediol. The results are summarized in Table III.

Table III. Reaction of Aluminum Hydride with Representative Quinones in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
p-Benzoquinone[d]	0.25	0.49	2.00	1.51
	0.5	0.53	2.00	1.47
	3.0	0.51	1.98	1.47
Anthraquinone[e]	0.5	0.05	2.05	2.00
	1.0	0.05	2.00	1.95

[a-c] See corresponding footnotes in Table I. [d] Dark precipitate. [e] Reverse addition (solution of reagent added to suspension of anthraquinone).

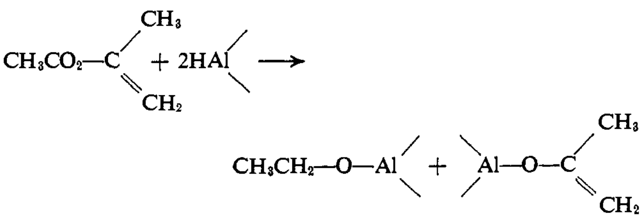
Carboxylic Acids and Derivatives. Carboxylic acids were reduced rapidly after immediate hydrogen evolution corresponding to the active hydrogen on the carboxylic acid group. Acid anhydrides also underwent quantitative reduction in 1 to 3 hr. Acid chlorides underwent reduction with remarkable ease, the reactions appearing to be complete in less than 15 min. This was unexpected, since diborane reacted only slowly with acid chlorides although it reduced carboxylic acids with great ease.[14] The results are summarized in Table IV.

Table IV. Reaction of Aluminum Hydride with Representative Carboxylic Acids and Acyl Derivatives in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
Caproic acid	0.25	1.06	2.86	1.80
	0.5		2.94	1.88
	1.0		2.96	1.90
	3.0		3.03	1.97
Benzoic acid	0.25	1.06	2.76	1.70
	0.5		2.82	1.76
	1.0		2.82	1.76
	3.0		2.88	1.82
Acetic anhydride[d]	0.25	0.1	3.57	3.47
	0.5		3.71	3.61
	1.0		4.09	3.99
	3.0		4.18	4.08
Succinic anhydride[d,e]	0.25	0.04	3.56	3.52
	0.5		3.65	3.61
	1.0		3.71	3.67
	3.0		3.90	3.86
Phthalic anhydride[d,f]	0.25	0.12	3.86	3.74
	0.5		3.91	3.79
	1.0		3.95	3.83
	3.0		4.15	4.03
Caproyl chloride	0.25	0.06	2.06	2.00
	0.5		2.07	2.01
	1.0		2.07	2.01
Benzoyl chloride	0.25	0	2.03	2.03
	0.5		2.04	2.04
	1.0		2.00	2.00

[a-c] See corresponding footnotes in Table I. [d] 6.66 mmoles of compound (hydride/compound = 6). [e] White precipitate. [f] Light yellowish precipitate.

Esters and Lactones. The esters and lactones examined were all completely reduced within the first examination period, 15 to 30 min. In contrast to its behavior with lithium aluminum hydride, isopropenyl acetate utilized only 2 moles of hydride rapidly, with only a very slow incomplete reaction being evident thereafter. This suggests that the reduction proceeds to give an aluminum derivative of the enol form of acetone and that this is relatively stable to conversion to



$$CH_3CO_2{-}C(CH_3){=}CH_2 + 2HAl\lt \longrightarrow CH_3CH_2{-}O{-}Al\lt + \gt Al{-}O{-}C(CH_3){=}CH_2$$

acetone, which would be rapidly reduced. The experimental results are summarized in Table V.

In order to test the possibility that aluminum hydride might be capable of bringing about a partial reduction of these acid derivatives to aldehydes,[25] we added

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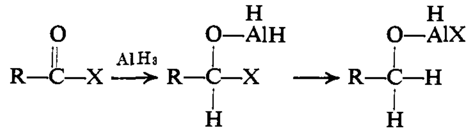
[25] The successful reduction of esters to aldehydes by diisobutylaluminum hydride and by sodium aluminum hydride has recently been described: L. I. Zakharkin and I. M. Khorlina, *Tetrahedron Letters*, No. 14, 619 (1962); L. I. Zakharkin, V. V. Gavrilenko, D. N. Maslin, and I. M. Khorlina, *ibid.*, No. 29, 2087 (1963).

Table V. Reaction of Aluminum Hydride with Representative Esters and Lactones in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydrogen used[b,c]	Hydride used for reduction[b]
Ethyl caproate	0.25	0.09	2.10	2.01
	0.5		2.10	2.01
	1.0		2.12	2.03
Ethyl benzoate[d]	0.25	0.1	2.10	2.00
	0.5		2.13	2.03
	1.0		2.13	2.03
Phenyl acetate	0.25	0.05	2.10	2.05
	0.5		2.10	2.05
	1.0		2.10	2.05
γ-Butyrolactone[d]	0.5	0.07	2.07	2.00
	1.0	0.07	2.04	1.97
Phthalide[d]	0.5	0.02	2.07	2.05
	1.0	0.02	2.07	2.05
Isopropenyl acetate	0.25	0.1	2.08	1.98
	0.5		2.12	2.02
	1.0		2.21	2.11
	3.0		2.30	2.20
	6.0		2.40	2.30
	24.0		2.42	2.32

[a–c] See corresponding footnotes in Table I. [d] Gelatinous white precipitate.

aluminum hydride to caproic acid, benzoic acid, caproyl chloride, benzoyl chloride, ethyl caproate, and ethyl benzoate, all in tetrahydrofuran solution at 0°, in the stoichiometric ratio for reduction to aldehyde. After 1 hr at 0°, gas chromatographic analysis indicated the formation of 6% caproaldehyde from caproic acid, but only traces of aldehyde from the other derivatives. This suggests that the initial reaction product, presumably the result of addition to the carbonyl group, must be very unstable and undergo rapid reduction further in preference to reacting with another molecule.



$$\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}X \xrightarrow{AlH_3} R{-}\underset{\underset{H}{|}}{\overset{O-\overset{H}{Al}H}{\overset{|}{C}}}{-}X \longrightarrow R{-}\underset{\underset{H}{|}}{\overset{O-\overset{H}{Al}X}{\overset{|}{C}}}{-}H}$$

Epoxides. The epoxides examined all reacted exceeding rapidly, the uptake of one hydride per mole of epoxide being essentially complete within 30 min at 0°. This is true even for an epoxide which might be considered to be somewhat hindered, such as 1-methyl-1,2-cyclohexene oxide. The reduction of 1,2-butylene oxide gives 2-butanol and the reduction of 1-methyl-1,2-cyclohexene oxide gives 1-methylcyclohexanol, both free of the other possible isomer and both in quantitative yield, as indicated by gas chromatographic examination.

In the case of styrene oxide, however, some tendency to open at the more substituted position was noted, the product consisting of a mixture of 26% 2- and 74% 1-phenylethanol. In this case lithium aluminum hydride gives a cleaner product, 4% 2-, 96% 1-,[5] with the trimethoxy derivative being more selective still, 1% 2-, 99% 1-.[6]

We are currently exploring the reduction of epoxides by aluminum hydride to ascertain whether it may not have advantages in sterically hindered cases where the reduction with lithium aluminum hydride has been reported to be difficult. The experimental results are summarized in Table VI.

Table VI. Reaction of Aluminum Hydride with Representative Epoxides in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction
1,2-Butylene[d] oxide	0.25	0.04	0.94	0.90
	0.5		1.16	1.12
	1.0		1.13	1.09
Styrene oxide[e]	0.25	0.03	0.75	0.72
	0.5		1.03	1.00
	1.0		1.03	1.00
Cyclohexene oxide	0.25	0.02	0.95	0.93
	0.5		0.97	0.95
	1.0		1.04	1.02
	3.0		1.05	1.03
1-Methyl-1,2-cyclohexene oxide[f]	0.25	0.03	1.10	1.07
	0.5		1.10	1.07

[a–c] See corresponding footnotes in Table I. [d] Product, 100% 2-butanol. [e] Product, 76% 1-phenylethanol, 24% 2-phenylethanol. [f] Product, 100% 1-methylcyclohexanol.

Amides and Nitriles. Primary amides liberated 1 equiv of hydrogen rapidly, but the second equivalent is quite slow, being incomplete in 24 hr. Hydride utilization for reduction is also relatively slow, requiring approximately 24 hr for the uptake of 2 molar equiv of hydride corresponding to reduction to the amine. On the other hand, the reductions of tertiary amides were extraordinarily rapid, the uptake of 2 molar equiv of hydride being complete in less than 15 to 30 min.

Both capronitrile and benzonitrile utilized 2 molar equiv of hydride rapidly. Somewhat unexpectedly, the reduction of benzonitrile appeared to proceed considerably more rapidly than the aliphatic derivative. In the case of the latter, no hydrogen evolution was noted. Such hydrogen evolution, representing attack of the reagent on the active hydrogen of the α position, is believed to be responsible for the decreased yields encountered in the reduction of aliphatic nitriles by lithium aluminum hydride.[20,26] Consequently, the use of aluminum hydride for such reductions may provide a convenient alternative to the use of lithium aluminum hydride–aluminum chloride mixtures.[20] We are exploring this possibility. The results are summarized in Table VII.

Here also, to explore the possibility of achieving a partial reduction to the aldehyde stage, 1 equiv of aluminum hydride was added to solutions of N,N-dimethylcaproamide, N,N-dimethylbenzamide, capronitrile, and benzonitrile in tetrahydrofuran at 0°. After 1 hr, the reaction products were hydrolyzed. Gas chromatographic examination revealed the absence of either aldehydes or alcohols. Titration revealed the presence of nearly the theoretical quantity of amine (~100% yield based on the hydride utilized). Consequently, here also the reduction rapidly goes by the intervening stage to form the amine derivative.

Nitro Compounds and Their Derivatives. Nitro compounds, both aliphatic and aromatic, proved to be relatively inert to the reagent. Similarly, azobenzene and azoxybenzene reacted only very slowly. This is in marked contrast to the behavior of lithium alu-

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(26) L. M. Soffer and E. W. Parrotta, *J. Am. Chem. Soc.*, **76**, 3580 (1954); L. M. Soffer and M. Katz, *ibid.*, **78**, 1705 (1956).

Table VII. Reaction of Aluminum Hydride with Representative Amides and Nitriles in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
Caproamide[d]	0.25	1.13	1.51	0.38
	1.0	1.22	2.13	0.91
	2.0	1.41	2.62	1.21
	6.0	1.41	2.88	1.47
	24.0	1.41	3.42	2.01
Benzamide[d]	0.25	1.32	1.50	0.18
	1.0	1.42	2.06	0.64
	3.0	1.45	2.44	0.99
	6.0	1.45	2.88	1.43
	24.0	1.45	3.42	1.97
N,N-Dimethylcaproamide[e]	0.25	0.18	2.20	2.02
	0.5		2.22	2.04
	1.0		2.20	2.20
N,N-Dimethylbenzamide[e]	0.5	0.06	2.10	2.04
	1.0	0.06	2.08	2.02
Capronitrile	0.25	0.05	1.72	1.67
	0.5		1.84	1.79
	1.0		2.00	1.96
	3.0		2.11	2.06
Benzonitrile[f]	0.25	0.03	2.04	2.01
	0.5		2.15	2.12
	1.0		2.08	2.05
	3.0		2.08	2.05

[a–c] See corresponding footnotes in Table I. [d] 6.66 mmoles of compound (hydride/compound = 6). [e] White precipitate. [f] Solution changed from colorless to yellow.

minum hydride and opens up the possibility of many selective reductions in the presence of these groups. The results are summarized in Table VIII.

Table VIII. Reaction of Aluminum Hydride with Nitro Compounds and Their Derivatives in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
1-Nitropropane	1.0	0.02	0.02	0
	3.0	0.02	0.04	0.02
	6.0	0.04	0.08	0.04
Nitrobenzene	1.0	0	0	0
	3.0	0.06	0.07	0.01
	6.0	0.19	0.28	0.09
Azobenzene	1.0		0.02	0.02[d]
	3.0		0.05	0.05[d]
	6.0		0.09	0.09[d]
	12.0		0.14	0.14[d]
Azoxybenzene	1.0		0	0
	3.0		0.06	0.06[d]
	6.0		0.09	0.09[d]
	12.0		0.27	0.27[d]

[a–c] See corresponding footnotes in Table I. [d] Hydrogen evolution was included.

Other Nitrogen Compounds. Cyclohexanone oxime rapidly liberated hydrogen and utilized two hydrides for reduction, corresponding to the formation of cyclohexylamine. However, the rate and stoichiometry of the hydrogen evolution are not in accord with this possible reaction. Consequently, decision as to the course of the reaction is best deferred until it is possible to explore this reaction in greater detail.

Phenyl isocyanate utilizes 3 equiv of hydride rapidly, corresponding to reduction to N-methylaniline.

Pyridine underwent reaction at a moderate rate, utilizing 1 equiv of hydride in 12 hr. Pyridine N-oxide underwent relatively rapid reduction. However, it is best to defer for the present consideration of the nature of these reaction products. The experimental results are summarized in Table IX.

Table IX. Reaction of Aluminum Hydride with Other Nitrogen Compounds in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
Cyclohexanone oxime[d]	0.5	1.50	2.86	1.36
	1.0	1.50	2.91	1.41
	3.0	1.50	3.43	1.93
	6.0	1.50	3.59	2.09
Phenyl isocyanate	0.25	0.04	2.81	2.77
	0.5		2.84	2.80
	1.0		2.89	2.85
	3.0		2.90	2.86
Pyridine[e]	0.5	0.09	0.25	0.16
	3.0		0.55	0.46
	6.0		0.68	0.59
	12.0		1.10	1.01
Pyridine N-oxide[d,f]	1.0	0.53	2.62	2.09
	3.0		2.79	2.26
	6.0		2.91	2.38
	24.0		3.84	3.31

[a–c] See corresponding footnotes in Table I. [d] 6.66 mmoles of compound (hydride/compound = 6). [e] Solution changed from colorless to yellow. [f] Turbid yellow solution.

Sulfur Compounds. Diphenyl disulfide was rapidly reduced in 15 min, with evolution of 1 molar equiv of hydrogen. On the other hand, di-*n*-butyl disulfide was reduced quite slowly, requiring approximately 24 hr for complete reaction. Dimethyl sulfoxide was rapidly reduced, although both the sulfide and the sulfone examined were inert. The sulfonic acids liberated the theoretical quantity of hydrogen, but were not reduced. Finally, cyclohexyl tosylate exhibited only traces of reaction in 24 hr. Consequently, the results indicate the possibility of achieving the selective reduction of many functional groups in the presence of these relatively inert sulfur substituents. The results are summarized in Table X.

Comparison of the Reducing Characteristics of Aluminum Hydride, Lithium Aluminum Hydride, Lithium Trimethoxyaluminohydride and Lithium Tri-*t*-butoxyaluminohydride. Since their discovery and application to organic reductions some 20 years ago, the complex hydrides have been widely adopted and utilized. There are thousands of references to individual applications.[2] With the introduction of the alkoxy derivatives,[3,4,8] aluminum hydride,[17] "mixed hydrides,"[20,22] as well as diborane[14] and its alkyl derivatives,[27] the organic chemist may well be overwhelmed by the remarkable versatility of these reagents and fail to utilize the reagent and conditions which would be most promising for the reduction he wishes to perform.

In the hope of systematizing our knowledge of the reducing characteristics of these reagents and ultimately arriving at simple generalizations governing their behavior, we initiated some time ago a program to

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(27) H. C. Brown and D. B. Bigley, *J. Am. Chem. Soc.*, 83, 486, 3166 (1961).

Table X. Reaction of Aluminum Hydride with Representative Sulfur Derivatives in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
Di-*n*-butyl disulfide	0.25	0.13		
	0.5	0.18		
	1.0	0.22	0.55	0.33
	3.0	0.32	0.74	0.42
	6.0	0.44	1.10	0.66
	24.0	0.60	1.91	1.31
Diphenyl disulfide	0.25	0.92	2.01	1.09
	0.5		2.15	1.23
	1.0		2.11	
Methyl *p*-tolyl sulfide	0.25	0	0	0
	0.5		0.02	0.02
	1.0		0.02	0.02
Dimethyl sulfoxide	0.25	1.13	1.88	0.75
	0.5		2.06	0.93
	1.0		2.06	0.93
Diphenyl sulfone	0.25	0.02	0.02	0
	0.5		0.02	0
	1.0		0.02	0
Methanesulfonic acid	0.25	1.06	1.06	0
	0.5		1.06	0
	1.0		1.06	0
p-Toluenesulfonic acid monohydrate[d]	0.25	3.15	3.15	0
	0.5		3.15	0
	1.0		3.18	0.03
	3.0		3.17	0.02
Cyclohexyl tosylate	0.25	0.02	0.04	0.02
	0.5		0.04	0.02
	1.0		0.02	0
	3.0		0.04	0.02
	6.0		0.05	0.03
	24.0		0.07	0.05

[a-c] See corresponding footnotes in Table I. [d] 6.66 mmoles of compound (hydride/compound = 6).

examine the rate and stoichiometry of the reaction of these reagents with a representative list of derivatives. Data are now available for aluminum hydride (AlH_3), lithium aluminum hydride[5] (LAH), lithium trimethoxyaluminohydride[6] (LTMA), and lithium tri-*t*-butoxyaluminohydride[7] (LTBA).[28] It appears appropriate for the objectives of this program to summarize our findings and point out the relative advantages of each of the reagents for specific reductions.[29]

I. **Active Hydrogen Compounds.** AlH_3, LAH, and LTMA quantiatively liberate 1 mole of hydrogen from alcohols, phenols, thiols, and primary amines. In the case of the latter there is a slower evolution of a second mole which, in some cases, requires more than 24 hr for completion. On the other hand, lithium tri-*t*-butoxyaluminohydride does not react with tertiary alcohols or with primary amines, and the hydrogen evolution with alcohols and phenols is not quantitative.

II. **Aldehydes and Ketones.** All four reagents quickly and quantitatively reduce aldehydes and ketones to the corresponding alcohols. Although LAH and LTMA reduce the double bond in cinnamaldehyde, neither LTBA nor AlH_3[18] affect the double bond, so that both reagents can be used for such derivatives. AlH_3 appears to be appreciably more stereoselective in reducing norcamphor (7.5% *exo*) than LAH (10% *exo*). However, LTMA (2% *exo*) is much more stereoselective than LAH in this case and in other bicyclic systems examined.[13]

III. **Quinones.** The reduction of *p*-benzoquinone by LTMA appears to proceed rapidly in a simple manner to the hydroquinone, as judged by the stoichiometry. On the other hand, aluminum hydride appears to be the preferred reagent for anthraquinone. The reduction of both quinones by LTBA appears to proceed in a simple manner, without hydrogen evolution. However, these derivatives require a more intensive study with identification of products before definite conclusions can be reached.

IV. **Carboxylic Acids and Acyl Derivatives.** Carboxylic acids are reduced to the corresponding alcohols by AlH_3, LAH, and LTMA. On the other hand, the acids show no signs of reduction by LTBA. Consequently, the latter reagent should be useful for selective reductions of a reducible group in the presence of a free carboxylic acid substituent. The ease of reduction appears to decrease from AlH_3 to LAH to LTMA. However, the difference is not great, so that LAH would appear to be preferable, except in cases where it is desired to reduce the carboxylic acid group selectively in the presence of other groups. AlH_3 is a more selective reducing agent. Together with its greater reactivity toward carboxylic acids, it would appear to offer major advantages over LAH for such reductions. (Attention is called to the observation that the carboxylic acid group is reduced with really remarkable speed by diborane in tetrahydrofuran.[14,28] Its application permits the selective reduction of the carboxylic acid group in the presence of almost any other substituent.)

The complete reduction of cyclic anhydrides by LAH requires either long reaction times or elevated temperatures. This may be the result of relatively complex cross-linking which appear possible in the interaction of such multifunctional compounds. Both AlH_3 and LTMA give more rapid reactions which are complete in 3 hr at 0°. LTBA exhibits an interesting behavior toward these anhydrides which should find useful application. It reacts to reduce only one of the two carboxyl groups, thus converting a cyclic anhydride into the corresponding lactone.

Acid chlorides are rapidly reduced by all four reagents. Consequently, LAH would appear to be the reagent of choice except where the presence of other reducible substituents makes preferable the use of a more selective reagent. (Again, attention is called to a unique characteristic of diborane. Although carboxylic acid groups are reduced very rapidly by this reagent, the acid chloride group is relatively stable to it.[14,28]) Finally, attention is called to the convenient reduction of acid chlorides to aldehydes by the use of 1 equiv of LTBA.[9]

V. **Esters and Lactones.** Esters and lactones are rapidly and quantitatively reduced by AlH_3, LAH, and LTMA. Again LAH would appear to be the recommended reagent in the absence of interfering substit-

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(28) A similar systematic survey for diborane, thexylborane, and disiamylborane (with Drs. P. Heim and D. B. Bigley) has been completed and will be reported shortly.

(29) Unless specific mention of other conditions is made, it should be understood that the conclusion is for tetrahydrofuran solution at 0°. We shall attempt to generalize on the basis of the data obtained with the standard list, as well as such other data that may be available in the literature. While the conclusions should be valid for the average derivative, it should be recognized that the rich variations possible in organic chemistry will doubtless result in exceptions to the generalizations.

uents. Isopropenyl acetate utilizes three hydrides from LAH and LTMA, corresponding to reduction of both the acetate group and the acetone intermediate. On the other hand, AlH_3 transfers only two hydrides, suggesting that the aluminum derivative of the enolate is stable under the reaction conditions.

LTBA reacts only very slowly with aliphatic and not noticeably with aromatic esters. There is a rapid transfer of one hydride to phenyl acetate, with a slow utilization of a second. The initial reaction provides the basis for the conversion of aliphatic acids, *via* their phenyl esters, into the corresponding aldehydes.[12] The data suggest that there is a similar rapid transfer of one hydride to isopropenyl acetate, as well as to the lactones. This would provide a means of reducing such lactones to the corresponding hydroxyaldehydes, a reduction which can be achieved with disiamylborane.[27]

VI. **Epoxides.** Both AlH_3 and LAH reduce epoxides with remarkable rapidity, the reactions being complete in less than 1 hr at 0°. The reduction with LTMA is much slower and with LTBA is slower still. Consequently, these latter reagents may be utilized in selective reductions of other groups in the presence of epoxide linkages. Even though the reactions with these reagents are slow, they are apparently more stereoselective. Thus the amount of primary isomer obtained in the reduction of styrene oxide is: LTBA, 0%; LTMA, 1%; LAH, 4%; AlH_3, 24%. Therefore, LTMA and LTBA may find useful applications for the reduction of epoxides where a highly selective opening of the three-membered ring is required. Finally, attention is called to the interesting observation that it is possible to achieve an inversion by reduction with "mixed hydride" to yield 95–98% of the primary isomer.[30]

VII. **Amides and Nitriles.** Primary amides are reduced to amines by AlH_3, LAH, and LTMA, with evolution of hydrogen, in 24 hr at 0° or 3 to 6 hr at 25°. Tertiary amides are likewise reduced to amines, but the reactions are surprisingly fast, being complete in 30 min at 0° for AlH_3 and LTMA, and in 3 hr for LAH. Finally, nitriles are reduced to the amines with remarkable ease by AlH_3, and at slower, but quite satisfactory rates with LAH and LTMA. LTBA does not react with these derivatives.

The use of LAH for the reduction of these compounds to amines appears quite satisfactory, except in the case of aliphatic nitriles containing relatively acidic hydrogen in the α position. The "mixed hydrides" have been recommended for such reductions.[20] AlH_3 and LTMA also appear promising for such reductions.

Diborane also serves to convert amides to amines.[31] It has proven especially helpful in reducing N-substituted fluoroacetamide derivatives to the fluoroethylamines in cases where both LAH and mixed reagent caused hydrogenolysis of the fluorine–carbon bond.[32]

Finally, attention is called to the observation that lithium triethoxyaluminohydride in ether converts both nitriles[10] and dimethylamides[11] into the corresponding aldehydes in highly satisfactory yields.

VIII. **Nitro Compounds and Derivatives.** LAH and LTMA reduce both 1-nitropropane and nitrobenzene in a relatively slow reaction either to the amine or the hydrazine stage. Azobenzene and azoxybenzene utilize hydride corresponding to reduction to the hydrazobenzene stage. AlH_3 and LTBA do not reduce these compounds at any significant rate.

IX. **Other Nitrogen Compounds.** Oximes appear to be reduced rapidly to the amine stage both by AlH_3 and LAH. Both LTMA and LTBA evolve hydrogen but do not reduce the oxime. (Diborane reduces the oxime to the corresponding hydroxylamine.[33])

Isocyanates are rapidly reduced to the N-methylaniline stage by AlH_3, LAH, and LTMA, with an uptake of three hydrides per mole. On the other hand, the reaction with LTBA halts effectively after the uptake of one hydride, corresponding to the formanilide stage.

Pyridine is essentially inert under these conditions toward LAH, LTMA, and LTBA, but reacts at a moderate rate with AlH_3, with the uptake of one hydride, presumably forming dihydropyridine.

Pyridine N-oxide is inert toward LTBA, but utilizes two hydrides from the other three reagents. This would correspond to reduction to the pyridine stage, but the hydrogen evolution varies with each reagent and does not correspond to a simple reduction of this kind. Definition of the precise nature of the product requires further investigation.

X. **Sulfur Compounds.** Aromatic disulfides are reduced to mercaptans by all four reagents, although LTBA requires 6 hr at 0° compared to 1 hr or less for the others. Alkyl disulfides are reduced rapidly by LAH and LTMA, but slowly by AlH_3 and negligibly by LTBA. Sulfoxides are rapidly reduced by AlH_3, LAH, and LTMA, but not by LTBA. Sulfides, sulfones, and sulfonic acids are not readily reduced by the four reagents, although a slow reaction of diphenyl sulfone and LAH is indicated. Finally, only LAH appears to react at a significant rate with cyclohexyl tosylate.

The experimental data supporting these conclusions and generalizations are summarized in Table XI.

In this table are reported the moles of hydrogen evolved and the hydride utilization observed per mole of compound under the standard conditions. In cases where no significant reduction was observed, in spite of the evident possibility for such reduction, the values reported are for the longest period for which the observation was made. Where reaction occurred, the data are for the shortest period where essentially constant values of hydrogen evolution and hydride uptake were realized. Thus the values do not necessarily give the maximum evolution of hydrogen nor the maximum possible utilization of hydride. They merely define the point where further reduction either does not occur, or proceeds so slowly as to provide a convenient stopping place for the reaction.

Experimental Section

Materials. The compounds used were from the same collection used in the earlier studies.[5–7] The standard solutions of lithium aluminum hydride were prepared, filtered, and stored as de-

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[30] E. L. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, **82**, 1362 (1960).

[31] H. C. Brown and P. Heim, *ibid.*, **86**, 3566 (1964).

[32] Z. B. Papanastassiou and R. J. Bruni, *J. Org. Chem.*, **29**, 2870 (1964).

[33] H. Feuer and B. F. Vincent, Jr., *J. Am. Chem. Soc.*, **84**, 3771 (1962).

Table XI. Reaction of Representative Organic Derivatives with Excess Aluminum Hydride, Lithium Aluminum Hydride, Lithium Trimethoxyaluminohydride, and Lithium Tri-*t*-butoxyaluminohydride in Tetrahydrofuran at 0°

	AlH_3[e]			$LiAlH_4$[f]			$LiAlH(OMe)_3$[g]			$LiAlH(O\text{-}t\text{-}Bu)_3$[h]		
	Hydride used		Time,	Hydride used		Time,	Hydride used		Time,	Hydride used		Time,
Compound[a]	Evol	Redn	hr	Evol	Redn	hr	Evol	Redn	hr	Evol	Redn	hr
I. Active Hydrogen												
1-Hexanol	1.01	0	0.25	1.01	0	0.5	1.03	0	0.5	0.34	0	1.0
Benzyl alcohol	1.04	0	0.25	1.07	0	0.5	0.96	0	0.5	0.51	0	4.0
3-Hexanol	1.02	0	0.25	1.02	0	0.5	1.09	0	0.5	0.15	0	6.0
3-Ethyl-3-pentanol	1.03	0	0.25	1.11	0	0.5	1.08	0	0.5	0.0	0	6.0
Phenol	1.03	0	0.25	1.02	0	0.5	0.99	0	0.5	0.53	0	24
n-Hexylamine	1.1	0	0.25	2.02	0	0.5	2.00	0	0.5	0.0	0	24
1-Hexanethiol	1.00	0	0.25	0.99	0	0.5	1.00	0	0.5	0.14	0	2.0
Benzenethiol	1.04	0	0.25	1.0	0	0.5	1.00	0	3.0	0.95	0	72
II. Aldehydes and Ketones												
Caproaldehyde	0	1.03	3.0	0	1.02	0.5	0	1.0	0.5	0	0.98	0.5
Benzaldehyde	0	0.96	3.0	0	0.96	0.5	0	1.0	3.0	0	0.86	0.5
2-Heptanone	0	1.00	3.0	0	1.01	0.5	0	1.0	0.5	0	1.00	0.5
Norcamphor	0	1.03	0.25	0	1.07	0.5	0	0.95	0.5	0	0.98	0.5
Acetophenone	0	0.98	1.0	0	1.04	0.5	0	1.00	0.5	0	0.96	0.5
Benzophenone	0	0.99	0.5	0	1.01	0.5	0	0.93	1.0	0	0.89	1.0
Cinnamaldehyde	0	1.00	0.5	0	2.08	0.5	0	2.0	0.5	0	1.00	0.5
III. Quinones												
p-Benzoquinone	0.49	1.51	0.25	0.58	1.20	0.5	0.96	1.03	0.5	0	1.0	0
Anthraquinone	0	2.00	0.5	0.23	1.67	3.0	0.48	1.56	0.5	0	1.78	2.0
IV. Carboxylic Acids and Acyl Derivatives												
Caproic acid	1.06	1.97	3.0	1.05	1.95	6.0[b]	1.0	2.06	3.0	0.98	0	6.0
Benzoic acid	1.06	1.82	3.0	1.01	1.99	6.0[b]	1.0	2.11	3.0[i]	0.49	0	6.0
Acetic anhydride	0	3.99	1.0[b]	0	4.01	3.0[b]	0	4.22	3.0[i,c]	0	1.87	2.0
Succinic anhydride	0	3.86	3.0[b]	0	3.76	24[b]	0	3.86	3.0[c]	0	1.98	0.5
Phthalic anhydride	0	4.03	3.0[b]	0	3.74	12[b]	0	4.03	3.0[c]	0	1.99	1.0
Caproyl chloride	0	2.01	0.25	0	1.97	0.5	0	2.02	0.5	0	1.99	0.5
Benzoyl chloride	0	2.03	0.25	0	1.97	0.5	0	2.00	1.0	0	2.01	1.0
V. Esters and Lactones												
Ethyl caproate	0	2.01	0.25	0	2.03	0.5	0	2.17	0.5	0	0.91	24.0
Ethyl benzoate	0	2.00	0.25	0	1.97	0.5	0	2.12	0.5	0	0	6.0
Phenyl acetate	0	2.05	0.25	0	1.99	0.5	0	2.03	0.5	0	1.00	0.5
γ-Butyrolactone	0	2.00	0.5	0	2.13	0.5	0	1.93	0.5	0	2.00	24
Phthalide	0	2.05	0.5	0	1.99	0.5	0	2.02	0.5	0	2.01	192
Isopropenyl acetate	0	1.98	0.25	0	2.95	24.0	0	2.88	0.5[c]	0	1.16	6.0
VI. Epoxides												
1,2-Butylene oxide	0	1.12	0.5	0	1.02	1.0	0	1.21	3.0[i]	0	1.0	24
Styrene oxide	0	1.00	0.5	0	1.00	0.5	0	0.86	12.0[i]	0	1.07	24
Cyclohexene oxide	0	1.02	1.0	0	0.96	1.0	0	0.97	3.0[i]	0	0.96	144
1-Methyl-1,2-cyclohexene oxide	0	1.07	0.25	0	0.96	1.0	0	1.02	96.0	0	0.66	96
VII. Amides and Nitriles												
Caproamide	1.41	2.01	24[b]	2.01	2.03	6.0[i,b]	1.94	2.21	24[c]	0	0	24
Benzamide	1.45	1.97	24[b]	2.2	2.07	3.0[i,b]	2.04	1.79	3.0[i,c]	0	0	24
Dimethylcaproamide	0	2.02	0.25	0	1.98	3.0	0	2.09	0.5	0	0	24
Dimethylbenzamide	0	2.06	0.5	0	2.02	3.0	0	1.98	0.5	0	0	24
Capronitrile	0	1.96	1.0	0.24	1.79	3.0	0	1.99	3.0	0	0	24
Benzonitrile	0	2.01	0.25	0	1.94	3.0	0	1.85	6.0	0	0	24
VIII. Nitro Compounds and Derivatives												
1-Nitropropane	0.04	0.04	6.0	2.92	3.05	48[i,d]	2.99	3.04	3.0[i,c]	0.97	0	2.0
Nitrobenzene	0.09	0.09	6.0	2.53	2.53	3[i,d]	2.13	2.14	48[i,c]	0	0	24
Azobenzene	0	0.09	6.0	0.99	1.06	3[i,b]	0.8	0.79	48[i]	0	0	24
Azoxybenzene	0	0.09	6.0	1.99	2.05	3[c]	1.93	2.07	48[i,b]	0	0.14	6.0
IX. Other Nitrogen Compounds												
Cyclohexanone oxime	1.5	2.09	6.0[b]	1.82	1.84	6[i,b]	1.03	0	3.0	0.74	0	1.0
Phenyl isocyanate	0	2.80	1.0	0	2.99	24	0	3.08	3.0[i,c]	0	0.98	0.5
Pyridine	0	1.01	12	0	0.12	6[i]	0	0	3.0	0	0	24
Pyridine oxide	0.53	2.2	0.25[b]	0.34	1.93	1.0	0.1	2.05	3.0[i]	0	0.1	24
X. Sulfur Compounds												
Di-*n*-butyl disulfide	0.6	1.3	24	0.98	1.01	1.0	1.02	0.98	0.5	0.13	0.04	24
Diphenyl disulfide	0.92	1.09	0.25	1.02	1.00	0.5	1.05	1.16	0.5	1.03	0.96	6.0
Methyl *p*-tolyl sulfide	0	0.02	3.0	0	0.2	24[i]	0	0	24[i]	0	0	1.0
Dimethyl sulfoxide	1.13	0.93	0.5	1.12	0.94	6.0	0.86	1.32	3.0[i]	0	0	1.0
Diphenyl sulfone	0	0	1.0	0	0.43	3.0[i]	0	0.32	4.0[i]	0	0.04	24
Methanesulfonic acid	1.06	0	1.0	1.14	0.01	3.0[i]	1.15	0.17	3.0	1.0	0	1.0
Toluenesulfonic acid[j]	3.15	0	3.0	3.10	0.10	24[i,b]	2.98	0	3.0	2.33	0	6.0
Cyclohexyl tosylate	0	0.05	24.0	0.28	0.51	24[i]	0.20	0.24	24	0	0.32	24

[a] Hydride to compound ratio 4:1, except where otherwise indicated. [b] Hydride to compound ratio 6:1. [c] Hydride to compound ratio 8:1. [d] Hydride to compound ratio 10:1. [e] 0.33 *M* AlH_3 (1.00 *M* hydride). [f] 0.25 *M* $LiAlH_4$ (1.00 *M* hydride). [g] 0.40 *M* $LiAlH(OMe)_3$ (0.40 *M* hydride). [h] 1.00 *M* $LiAlH(O\text{-}t\text{-}Bu)_3$ (1.00 *M* hydride). [i] At 25°. [j] Monohydrate.

scribed earlier.[6] Analysis at regular intervals revealed no measurable change in the hydride content over several weeks at room temperature.

Preparation of Aluminum Hydride Solutions. By means of a hypodermic syringe, 100 ml of 1.2 *M* lithium aluminum hydride and 100 ml of tetrahydrofuran were introduced into a 300-ml flask, fitted with an inlet port, rubber syringe cap, and magnetic stirring bar and connected to a gas meter *via* the reflux condenser. To this solution 5.88 g of 100% sulfuric acid (60 mmoles) was added slowly by means of a syringe, while stirring the solution vigorously. There was evolved 121 to 122 mmoles of hydrogen. The solution was permitted to stir for 1 hr, and then allowed to stand at room temperature to permit the lithium sulfate precipitate to settle. The clear, supernatent solution was removed by a syringe and analyzed for hydride (volumetrically), aluminum (as the 8-hydroxyquinolate[34]), and sulfate (barium chloride–potassium chromate titration[35]). The hydride/aluminum ratio was 3.00:1.00, and no sulfate was present.

A solution 0.50 *M* in aluminum hydride was stored under nitrogen for 3 days and aliquots were removed for analysis. Only after 3 days was there observed a change from 0.50 to 0.49 *M*. Gas chromatographic examination showed an amount of 1-butanol corresponding to the loss of hydride.

Procedure. All reduction experiments were carried out under a dry nitrogen atmosphere, using hypodermic syringes to transfer solutions.

The reduction of styrene oxide is described as an example of the experimental procedure. The aluminum hydride solution, 23.5 ml of 0.57 *M* (40 mmoles hydride), and 6.5 ml of tetrahydrofuran were introduced into a dried, 100-ml flask fitted with rubber syringe cap on an inlet port, a magnetic stirring bar, and a nitrogen inlet, and connected to a gas buret through a Dry Ice vapor trap. The flask was immersed in an ice bath, the stirred solution was brought to 0°, and 1.20 g of styrene oxide (10.0 mmoles) in 10 ml of tetrahydrofuran solution was injected rapidly.

After 15 min, a 4.0-ml aliquot of the reaction mixture was removed and injected into a 50–50 mixture of glycerine and water to hydrolyze residual hydride. The hydrogen evolved amounted to 3.26 mmoles, as compared to 3.98 mmoles for a blank reaction (in which 10 ml of tetrahydrofuran was substituted for the 10 ml of the solution of the compound). The difference (0.72) represents the number of mmoles of hydride used per mmole of compound added. Aliquots were also removed and hydrolyzed after 0.5 and 1.0 hr of reaction time. Both produced 2.98 mmoles of hydrogen, indicating 1.00 equiv of hydride had been consumed. Obviously the reaction had been incomplete at 0.25 hr, but was complete in 0.5 hr.

To determine the reaction product, 20 ml of the reaction mixture was removed and treated with methanol to destroy residual hydride and precipitate aluminum methoxide. Benzyl alcohol (0.54 g, 5.0 mmoles) was added as an internal standard. The gas chromatographic analysis showed 75% 1-phenylethanol, 23% 2-phenylethanol, and 2% residual styrene oxide.

Treatment of Ethyl Benzoate with Limited Quantity of Aluminum Hydride. The solution of aluminum hydride (3.0 ml) containing 1.67 mmoles (5.0 mmoles of hydride) was added to ethyl benzoate (0.75 g, 5.0 mmoles) in 7.0 ml of tetrahydrofuran at 0°. After 1 hr 0.62 mmole of hydride per mole of ester had been consumed. Gas chromatographic analysis showed 0.26 mmole of benzyl alcohol and 0.65 mmole of unreacted ethyl benzoate per mole of ester used. No benzaldehyde was found.

Treatment of N,N-Dimethylbenzamide with Limited Quantity of Aluminum Hydride. The experiment was carried out precisely as above, but substituting 0.746 g (5.0 mmoles) of N,N-dimethylbenzamide for the ester. After 1 hr, 0.85 mmole of hydride had been consumed per mmole of amide. Gas chromatographic analysis showed neither benzyl alcohol nor benzaldehyde. In a duplicate experiment, the reaction mixture was hydrolyzed with water and the amine was titrated with standard hydrochloric acid. (Blank tests showed that the precipitated aluminum salts did not interfere. The analysis showed the presence of 0.47 mmole of base, presumably benzyldimethylamine, per mmole of amide.)

Reaction of Cyclohexyl Tosylate with Aluminum Hydride and Lithium Aluminum Hydride. Two identical reaction mixtures were set up containing cyclohexyl tosylate (0.25 *M*) and (a) aluminum hydride (0.33 *M*) and (b) lithium aluminum hydride (0.25 *M*). (Both solutions were therefore 1.0 *M* in hydride.) The reaction mixtures were maintained for 24 hr at 25°. Hydrolysis of (a) showed no hydride utilization and gas chromatographic examination revealed less than 1% of cyclohexane, cyclohexene, and cyclohexanol. Hydrolysis of the second flask (b) yielded 17.5% cyclohexane, 8.9% cyclohexene, and 3.5% cyclohexanol.

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[34] I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," 3rd ed, The Macmillan Co., New York, N. Y., 1956, p 321.

[35] "Scott's Standard Methods of Chemical Analysis," Vol. I, N. H. Furman, Ed., 6th ed, D. Van Nostrand Co., Inc., Princeton, N. J., 1962, p 1011.