of mercuric trifluoroacetate were carried out as reported previously.[6]

Procedures. The procedures for the kinetic runs and the isomer distribution determinations were carried out as previously described for the toluene[7] and the monoalkylbenzenes.[8] The gas chromatographic analysis of the isomeric mixtures of the bromohalobenzenes was carried out, utilizing a 2-m tricresyl phosphate on a Celite column, at 100° for the bromofluorobenzenes, 125° for the bromochlorobenzenes, and 130° for the dibromobenzenes. Excellent resolution of the three isomers was realized.

Selective Reductions. IX. Reaction of Lithium Aluminum Hydride with Selected Organic Compounds Containing Representative Functional Groups[1]

Herbert C. Brown, Paul M. Weissman,[2] and Nung Min Yoon[2]

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

Abstract: The stoichiometry of the reaction of excess lithium aluminum hydride with 56 selected organic compounds containing representative functional groups under standardized conditions (tetrahydrofuran solution, 0°) was examined in order to compare the behavior of the parent compound with its derivatives, lithium trimethoxy- and tri-*t*-butoxyaluminohydride, previously explored. In general the data confirm the results already available in the literature, but provide data in a single solvent with controlled concentration and temperature. Although the behavior of lithium trimethoxyaluminohydride resembles that of lithium aluminum hydride closely, there are significant differences. The latter reagent reduces epoxides, cyclohexanone oxime, azobenzene, and cyclohexyl tosylate, whereas the reduction of these compounds by lithium trimethoxyaluminohydride is either much slower or does not occur under these conditions. Consequently, a number of selective reductions appear practical with the latter reagent which would offer difficulties with lithium aluminum hydride. Lithium trimethoxyaluminohydride also appears more selective in opening up unsymmetrical epoxides and it was previously shown to be more stereoselective in reducing cyclic and bicyclic ketones. Finally, considerable hydrogen evolution is observed in reducing aliphatic nitriles with lithium aluminum hydride, whereas this undesirable side reaction appears to be absent in the corresponding reduction with lithium trimethoxyaluminohydride. It was previously reported that lithium tri-*t*-butoxyaluminohydride is a far more selective reducing agent than the other two under discussion. Consequently, the availability of detailed surveys of the reducing characteristics of these three reagents should prove helpful in selecting the most favorable reagent for a specific reduction.

The reducing action of lithium aluminum hydride has been extensively studied.[3] However, most of the data available are for reactions carried out in ether for preparative purposes, with the concentrations of the reactants, the temperature of the reaction, and the time not specified.

We had recently carried through a systematic study of the approximate rates and the stoichiometry of the reaction of lithium tri-*t*-butoxyaluminohydride[4] and of lithium trimethoxyaluminohydride[5] in tetrahydrofuran solution at 0° with a standard list of compounds representative of the more common functional groups. In attempting to compare the behavior of these new reagents with the characteristics of lithium aluminum hydride, we were frustrated by the wide variation in the experimental conditions used as well as by the frequent failure to report the experimental conditions. As a consequence we decided to undertake a systematic examination of the reaction of lithium aluminum hydride with the standard list under the standard conditions.

Results and Discussion

The general procedure involved preparing a reaction mixture of lithium aluminum hydride (0.25 *M*, 1.00 *M* in hydride[6]) and compound (0.25 *M*) in tetrahydrofuran at 0°. The hydrogen evolved on adding the compound to the reagent was noted. After the desired reaction time, the solution was hydrolyzed and the hydrogen evolved was noted. A blank reaction was performed under identical conditions, but without addition of the compound. From the difference in yields of hydrogen in the two cases, the hydride utilized by the compound for reduction was calculated. In this way it was possible to arrive at a value for the number of moles of hydride utilized by the compound to evolve hydrogen and the number of moles of hydride utilized for reduction.

In some cases the hydride/compound ratio of 4:1 was inadequate to achieve complete reduction. In such cases the hydride concentration was maintained constant, but the concentration of compound was re-

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(1) Based in part upon a thesis submitted by P. M. Weissman in August 1964, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Graduate research assistant on a research grant (DA-ARO(D)-31-124-117) supported by the U. S. Army Research Office (Durham).

(3) 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*, 469 (1951); (c) V. M. Mićović and M. L. Mihailović, "Lithium Aluminum Hydride in Organic Chemistry," Naukna Knjiga, Belgrade, Yugoslavia, 1955.

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

(5) H. C. Brown and P. M. Weissman, *J. Am. Chem. Soc.*, 87, 5614 (1965).

(6) It is convenient to discuss the utilization of the reagent in terms of moles of hydride taken up per mole of compound. Thus a ketone utilizes 1 mole of hydride and an ester 2 moles in being reduced to the alcohol stage.

duced to give a higher ratio. In some cases where the reaction proceeded so slowly at 0° that it was difficult to establish the stoichiometric relationship, the reaction was repeated at 25°.

Alcohols, Phenols, Amines, and Thiols. All of the active hydrogen compounds examined evolved 1 molar equiv of hydrogen immediately on adding the compounds. The results are summarized in Table I.

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

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
1-Hexanol	0.5	1.01	1.03	0.02
Benzyl alcohol	0.5	1.07	1.14	0.07
	1.0	1.01	1.02	0.01
3-Hexanol	0.5	1.02	1.11	0.09
	1.0	0.97	1.03	0.06
3-Ethyl-3-pentanol	0.5	1.11	1.13	0.01
Phenol	0.5	1.02	1.03	0.01
n-Hexylamine	0.25	2.02	2.01	0
1-Hexanethiol	0.5	0.98	1.06	0.08
	1.0	1.02	1.02	0
Benzenethiol	0.5	1.01	1.10	0.09
	1.0	1.10	1.13	0.03

[a] 5.00 mmoles of compound, except where otherwise indicated, to 5.00 mmoles of lithium aluminum hydride (20 mmoles of hydride). [b] Millimoles/millimole mmole 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. All of the saturated aldehydes and ketones examined took up 1 equiv of hydride rapidly, without evolution of any significant quantity of hydrogen. Consequently, in these cases the reduction goes cleanly to the alcohol stage. As previously noted,[7] cinnamaldehyde utilized two hydrides, indicating rapid involvement of the double bond. The same behavior was previously noted with lithium trimethoxyaluminohydride,[5] although the *t*-butoxy reagent reduces the aldehyde group cleanly without affecting the double bond.[4]

The reduction of norcamphor under these conditions yields 90% *endo*-, 10% *exo*-norborneol.[8] Lithium trimethoxyaluminohydride is more stereoselective, yielding 98% *endo*- and 2% *exo*-.[8] The data are summarized in Table II.

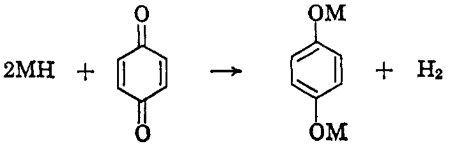
Quinones. The data for the two quinones examined are quite interesting. In ether, hydroquinone has been isolated from the reduction of benzoquinone by lithium aluminum hydride in a yield of 70%.[9] On the other hand, the same procedure produced only 13% 9,10-dihydro-9,10-anthracenediol, with much starting material being recovered.[10] This yield was raised to 45% by using tetrahydrofuran as the solvent.[10]

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

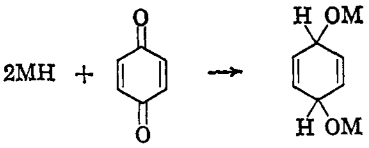
Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
Caproaldehyde	0.5	0.04	1.06	1.02
	1.0	0.04	1.02	0.98
Benzaldehyde	0.5	0.11	1.07	0.96
	1.0	0.12	1.07	0.95
2-Heptanone	0.5	0.09	1.10	1.01
	1.0	0.09	1.08	0.99
Norcamphor	0.5	0.02	1.09	1.07
	1.0	0.03	0.99	0.96
Acetophenone	0.5	0.04	1.08	1.04
	1.0	0.02	1.05	1.03
Benzophenone	0.5	0	1.01	1.01
	1.0	0	0.99	0.99
Cinnamaldehyde[d]	0.5	0.06	2.14	2.08
	1.0	0.06	2.00	1.94

[a-c] See corresponding footnotes in Table I. [d] White precipitate after 10 min.

Reduction of a quinone to the hydroquinone stage should result in an uptake of 2 equiv of hydride per mole of quinone, 1 mole being utilized for reduction and the second for hydrogen evolution (MH represents 1 equiv of $LiAlH_4$). On the other hand, reduction of a



quinone to the 1,4-dihydroxycyclohexadiene stage should require 2 moles of hydride for reduction and none for hydrogen evolution.



It is evident that the data (Table III) do not indicate that the reaction takes either of these possible courses exclusively. The total uptake of hydride is almost exactly 2, within the limits of the experimental pro-

Table III. Reaction of Lithium 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[f]	1.0	0.58	1.78	1.20
	3.0	0.59	1.81	1.22
	6.0	0.55	1.89	1.34
	3.0[d]	0.62	1.93	1.31
	6.0[d]	0.83	2.10	1.27
	12.0[d]	0.70	2.04	1.34
Anthraquinone[e,g]	1.0	0.23	1.68	1.45
	3.0	0.23	1.90	1.67
	6.0	0.24	2.05	1.81
	3.0[d]	0.24	2.17	1.93
	6.0[d]	0.30	2.09	1.79
	12.0[d]	0.39	2.23	1.84

[a-c] See corresponding footnotes in Table I. [d] At 25°. [e] Reverse addition (solution of reagent added to suspension of anthraquinone). [f] Instant green precipitate, changing to greenish white as hydrogen is evolved. [g] Orange paste.

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(7) F. A. Hochstein and W. G. Brown, *J. Am. Chem. Soc.*, 70, 3484 (1948).

(8) H. C. Brown and H. M. Deck, *ibid.*, 87, 5620 (1965).

(9) R. F. Nystrom and W. G. Brown, *ibid.*, 70, 3738 (1948).

(10) E. Boyland and D. Manson, *J. Chem. Soc.*, 1837 (1951).

cedure, but at 0° there is approximately 50% of 1 mole of hydrogen evolution in the case of *p*-benzoquinone and 20% in the case of anthraquinone. This suggests that at 0° approximately 50% of the *p*-benzoquinone is undergoing reaction to hydroquinone and 50% to 1,4-dihydroxycyclohexadiene, with a related 20:80 distribution for anthraquinone. At 25° considerably more hydrogen is evolved. Consequently, the results suggest that the clean reduction of quinones to the dihydroxydihydroquinone stage may be quite feasible at lower temperatures.

In the case of lithium trimethoxyaluminohydride, the stoichiometry indicated a simple reduction of *p*-benzoquinone to hydroquinone, but a 50:50 distribution at 25° for anthraquinone.[5] On the other hand, no hydrogen evolution was observed during the reduction of the two quinones by lithium tri-*t*-butoxyaluminohydride. These results suggest this group of reagents possess interesting possibilities for the selective reductions of quinones. We plan to explore this area in greater detail. The results are summarized in Table III.

Carboxylic Acids and Acyl Derivatives. Carboxylic acids instantly evolve 1 equiv of hydrogen and then react at a moderate rate, taking up 2 equiv of hydride for reduction to the alcohol stage in 6 hr. A slight precipitate was observed in the caproic acid mixture, while the benzoic acid solution remained clear throughout the reaction. In view of some of the difficulties which have been noted for reductions of carboxylic acids in ether,[3b] the use of tetrahydrofuran for such reductions would appear to offer real advantages. Acid chlorides and acid anhydrides rapidly reacted with the utilization of the calculated quantity of hydride to achieve reduction to the alcohol or diol stage. The results are summarized in Table IV.

The results with lithium trimethoxyaluminohydride were similar.[5] On the other hand, lithium tri-*t*-butoxyaluminohydride gave no reduction of carboxylic acids, half reduction of anhydrides (to form the hydroxy acid in the case of cyclic derivatives), and complete reduction of acid chlorides.[4]

Esters and Lactones. Esters and lactones reacted exceedingly rapidly with the uptake of 2 equiv of hydride per mole. In a slower reaction isopropenyl acetate utilized a total of 3. The experimental data are summarized in Table V.

Lithium trimethoxyaluminohydride likewise reduced these derivatives rapidly.[5] On the other hand, lithium tri-*t*-butoxyaluminohydride failed to reduce ethyl benzoate and reacted only sluggishly with ethyl caproate.[4] Finally, with this reagent there was a relatively rapid partial reduction of phenyl acetate to form the aldehyde, and this reaction provides a new general procedure for the conversion of aliphatic carboxylic acids into the corresponding aldehydes.[11]

Epoxides. The reaction with the epoxides examined (Table VI) proved very fast, an uptake of 1 equiv of hydride per mole of epoxide being realized in 1 hr or less. The reaction also proved to be quite selective, with the hydride undergoing transfer to the less substituted of the two carbon atoms of the epoxide ring.[12] For example, styrene oxide yielded 96% of the secondary alcohol, 1-phenylethanol, and 4% of the primary, 2-phenylethanol, and 1-methyl-1,2-cyclohexene oxide yielded the tertiary alcohol with no detectable quantity of the secondary.

The reaction of the alkoxy-substituted reagents with epoxides was much slower, but the opening of the epoxide ring appears to be even more selective. Thus in the case of styrene oxide, the 4% primary alcohol observed with the parent hydride was decreased to 1%

Table IV. Reaction of Lithium 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[d,f]	0.5	1.05	2.37	1.32
	1.0	1.05	2.38	1.33
	3.0	1.06	2.43	1.37
	6.0	1.05	3.00	1.95
Benzoic acid[d]	0.5	1.04	2.03	0.99
	1.0	1.01	2.06	1.05
	3.0	1.01	2.31	1.30
	6.0	1.01	3.00	1.99
Acetic anhydride[d,g]	0.5	0.11	2.85	2.74
	1.0	0.04	2.78	2.74
	3.0	0.17	4.18	4.01
	6.0	0.05	4.05	4.00
Succinic anhydride[d,h]	0.5	0.06	2.72	2.66
	3.0	0.06	2.97	2.91
	12.0	0.16	3.76	3.60
	24.0	0.06	3.82	3.76
	3.0[e]	0.03	3.87	3.84
Phthalic anhydride[d,i]	0.5	0.11	3.00	2.89
	3.0	0.23	3.27	3.04
	6.0	0	3.64	3.64
	12.0	0	3.74	3.74
	3.0[e]	0	4.28	4.28
Caproyl chloride[f]	0.5	0	1.97	1.97
	1.0	0	2.00	2.00
Benzoyl chloride	0.5	0	1.97	1.97
	1.0	0	2.00	2.00

[a-c] See corresponding footnotes in Table I. [d] 3.33 mmoles of compound (hydride/compound = 6). [e] At 25°. [f] White precipitate. [g] Solution milky immediately following addition, but became clear. [h] Milky solution. [i] Instant white precipitate, but became clear.

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

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
Ethyl caproate	0.5	0.04	2.07	2.03
	1.0	0	1.98	1.98
Ethyl benzoate	0.5	0.08	2.05	1.97
	1.0	0.08	2.05	1.97
Phenyl acetate	0.5	0.05	2.04	1.99
	1.0	0.04	2.02	1.98
γ-Butyrolactone	0.5	0.04	2.17	2.13
	1.0	0.04	2.18	2.14
Phthalide	0.5	0.04	2.03	1.99
	1.0	0	1.96	1.96
Isopropenyl acetate	1.0	0.07	2.71	2.64
	12.0	0.07	2.84	2.77
	24.0	0.10	3.05	2.95

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

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

(12) E. L. Eliel and D. W. Delmonte, *J. Am. Chem. Soc.*, 80, 1744 (1958).

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

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b,c]	Hydride used for reduction[b]
1,2-Butylene oxide	0.5	0	0.97	0.97
	1.0	0	1.02	1.02
Styrene oxide[d]	0.5	0.02	1.02	1.00
	1.0	0.02	1.01	0.99
Cyclohexene oxide	0.5	0.04	0.82	0.78
	1.0	0.04	1.00	0.96
1-Methyl-1,2-cyclohexene oxide[e]	0.5	0.04	0.94	0.90
	1.0	0.04	1.00	0.96
	3.0	0.04	1.04	1.00

[a–c] See corresponding footnotes in Table I. [d] Product: 96% 1-phenylethanol, 4% 2-phenylethanol. [e] Product, 100% 1-methylcyclohexanol.

Table VII. Reaction of Lithium 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	3.0	2.00[f]	3.02	1.02
	24.0	2.00	3.45	1.45
	12.0[d]	2.00	3.60	1.60
	24.0[d]	2.00	4.18	2.18
	6.0[d,e]	2.01	4.04	2.01
Benzamide[d]	3.0	2.02[g]	2.43	0.41
	6.0	1.96	2.61	0.65
	12.0	1.97	2.93	0.96
	24.0	1.97	3.35	1.38
	3.0[e,h]	2.20	4.27	2.07
	24.0[e]	2.01	4.20	2.19
N,N-Dimethylcaproamide	0.5	0	1.83	1.83
	1.0	0	1.86	1.86
	3.0	0.03	2.01	1.98
	6.0	0	1.99	1.99
N,N-Dimethylbenzamide	0.5	0.03	1.89	1.86
	3.0	0	2.02	2.02
Capronitrile[i]	0.5	0.24	1.90	1.66
	3.0	0.24	2.03	1.79
	24.0	0.24	2.16	1.92
Benzonitrile	0.5	0.03	1.25	1.22
	3.0	0	1.94	1.94

[a–c] See corresponding footnotes in Table I. [d] 3.33 mmoles of compound (hydride/compound = 6). [e] At 25°. [f] One equivalent of hydrogen evolved instantly, the second over 50 min. [g] Solution changed from colorless to yellow after 2 equiv of hydrogen had been evolved. [h] White precipitate after 2 hr. [i] Solution was slightly turbid during the reaction.

with lithium trimethoxyaluminohydride[5] and to 0% with lithium tri-*t*-butoxyaluminohydride.

Amides and Nitriles. Caproamide evolved 1 equiv of hydrogen instantly and the second only slowly, over some 50 min. In the case of benzamide, there was observed a change from colorless to yellow when the hydrogen evolution had been completed. In both cases precipitates were observed and uptake of 2 equiv of hydride for reduction was a relatively slow process, requiring 24 hr or more at 0°, or 3 to 6 hr at 25°. (An 80% yield of *n*-hexylamine was demonstrated in a 6-hr reaction time at room temperature.[13]) On the other hand, tertiary amides take up 2 equiv of hydride rapidly at 0°. Finally, the nitriles rapidly utilize approximately two hydrides for reduction.

In the case of capronitrile there was evolved 0.24 equiv of hydrogen, presumably by reaction of the reagent with the active α hydrogen of the nitrile, and the hydride utilization was somewhat less than 2 by approximately this amount. In ether solution even larger evolutions of hydrogen have been noted and condensation of the nitrile is a serious side reaction.[14,15] Consequently, it appears that this undesirable side reaction can be diminished by carrying out the reaction in tetrahydrofuran instead of in ether, by using lithium trimethoxyaluminohydride where the hydrogen evolution was insignificant,[5] or by using mixtures of aluminum chloride and lithium aluminum hydride.[15]

Lithium trimethoxyaluminohydride also reduces these derivatives, but there would appear to be no advantages to its use, except for the reduction of aliphatic nitriles just discussed.[16] Lithium tri-*t*-butoxyaluminohydride does not reduce these compounds under the standard conditions. The results are summarized in Table VII.

Nitro Compounds and Their Derivatives. 1-Nitropropane consumes a total of 6 equiv of hydride, with 3 equiv of hydride being utilized for reduction and 3 for hydrogen evolution, corresponding to the stoichiometry expected for reduction to the amine.[9] However, an examination of the rate data (Table VIII) reveals that 5 of the 6 equiv of hydride are utilized relatively rapidly, with the final equivalent of hydride being consumed at a much slower pace. This corresponds to a rapid reduction to the hydrazo stage, with a slower rupture of the nitrogen–nitrogen bond to form the amine derivative.

In the case of nitrobenzene, the reaction proceeds quite rapidly to the uptake of 5 equiv of hydride, corresponding to the formation of a derivative of hydrazobenzene (Table VIII). However, in this case the reaction fails to proceed further under the conditions examined. Thus, no further utilization of hydride was observed at 25° with an increase in the reaction time from 3 to 48 hr.

The reduction in ether solution appears to be more sluggish, with a greater tendency to halt at the azobenzene stage. Thus, in ether solution it was noted that the reduction utilized only 4 equiv of hydride and produced an 84% yield of azobenzene.[6] Under these conditions, azobenzene is not reduced further, and the reduction to azobenzene is often used as a quantitative analysis for aromatic nitro compounds. However, the preparation of hydrazobenzene from azobenzene in 90% yield after a 3-day reaction time has been reported.[17] Consequently, the precise end product realized may well be a function of the concentration of the reactants and the reaction time.

Under the standard conditions of the present study, azobenzene utilized 2 equiv of hydride in 3 hr at 25°, 1 equiv for reduction and 1 for hydrogen evolution. This corresponds to reduction to hydrazobenzene. Azoxybenzene also reacts rapidly with the uptake of 4

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(13) The conversion of stearamide to octadecylamine in 88% yield has been reported: F. Wessely and W. Swoboda, *Monatsh.*, **82**, 621 (1951).

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

(15) R. F. Nystrom, *ibid.*, **77**, 2544 (1955).

(16) The reactions of lithium triethoxyaluminohydride in ethyl ether with nitriles and with dimethylamides provide useful synthetic routes to aldehydes: H. C. Brown and C. P. Garg, *ibid.*, **86**, 1085 (1964); H. C. Brown and A. Tsukamoto, *ibid.*, **86**, 1089 (1964).

(17) F. Bohlmann, *Ber.*, **85**, 390 (1952).

Table VIII. Reaction of Lithium 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^{f}	0.5	2.01	4.14	2.13
	6.0	2.31	4.81	2.50
	12.0	2.55	5.21	2.66
	24.0	2.67	5.43	2.76
	3.0^{g}	2.61	5.33	2.72
	6.0^{g}	2.75	5.42	2.67
	12.0^{g}	2.66	5.36	2.70
	24.0^{g}	2.75	5.70	2.95
	48.0^{g}	2.92	5.97	3.05
Nitrobenzene^{f,h}	0.5	1.84	3.78	1.94
	3.0	2.29	4.84	2.55
	6.0	2.50	5.06	2.56
	3.0^{g}	2.53	5.06	2.53
	6.0^{g}	2.40	5.03	2.63
	12.0^{g}	2.48	5.00	2.52
	48.0^{g}	2.54	5.06	2.52
Azobenzene^{i}	24.0	0.61	1.26	0.65
	48.0	0.9	1.93	1.03
	3.0^{d,g}	0.99	2.05	1.06
	12.0^{d,g}	1.00	1.98	0.98
	24.0^{d,g}	0.99	2.00	1.01
Azoxybenzene^{j}	1.0	1.02	2.67	1.65
	3.0^{e}	1.99	4.04	2.05
	6.0^{e}	2.00	3.96	1.96
	24.0^{e}	1.99	4.21	2.22
	1.0^{e,g}	2.06	4.05	1.99
	24.0^{e,g}	2.08	4.26	2.18

$^{a-c}$ See corresponding footnotes in Table I. ^{d} 3.33 mmoles of compound (hydride/compound = 6). ^{e} 2.50 mmoles of compound (hydride/compound = 8). ^{f} 1.67 mmoles of compound (hydride/compound = 10). ^{g} At 25°. ^{h} Solution dark green in initial stages, becoming pale yellow after 24 hr. ^{i} Solution dark green in 10 min, the faded away gradually. ^{j} Solution changed from orange to dark green after 1 equiv of hydrogen had been evolved.

equiv of hydride, again corresponding to reduction to hydrazobenzene.

These results indicate that reduction of nitro aromatics and their derivatives by lithium aluminum hydride in tetrahydrofuran should provide a convenient route to the corresponding hydrazo derivatives.

Interesting color changes are observed in these reductions. In the initial stages of the reduction of nitrobenzene the solution became dark green, changing to a light yellow in the later stages. Similarly, within 10 minutes the azobenzene solution became dark green and the color then gradually faded away. In the case of azoxybenzene, when 1 equiv of hydrogen had been evolved, the original orange solution became dark green, and this green color gradually disappeared as the reduction proceeded.

Lithium tri-*t*-butoxyaluminohydride does not react with nitrobenzene, azobenzene, or azoxybenzene.[4] Therefore, it is useful for selective reductions in the presence of these groups. Lithium trimethoxyaluminohydride reduces 1-nitropropane readily to the amine stage,[5] but the reactions with nitrobenzene, azobenzene, and azoxybenzene are considerably more sluggish and further investigation will be required to establish whether it possesses any utility to achieve partial reduction in this area. These results are summarized in Table VIII.

Other Nitrogen Compounds. The reduction of cyclohexanone oxime to cyclohexylamine should require 4 equiv of hydride, 2 for reaction and 2 for hydrogen evolution. The reaction reveals a rapid evolution of 1 equiv of hydrogen, followed by a slow utilization of 2 equiv of hydride for reduction and the slow liberation of a second mole of hydrogen.[18] This contrasts with the alkoxy reagents, where hydrogen evolution, but no reduction, was observed.

Phenyl isocyanate utilizes 3 equiv of hydride for reduction, corresponding to the formation of N-methylaniline.

Pyridine reacts only very slowly with the reagent.[19] 4-Picoline N-oxide utilizes 2 equiv of hydride, but the hydrogen evolution is low for the formation of the parent base and the nature of the reaction product remains to be established. The experimental data for these nitrogen derivatives are presented in Table IX.

Table IX. Reaction of Lithium 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	0.5	1.09	1.59	0.5
	6.0	1.27	2.08	0.81
	12.0	1.04	2.06	1.02
	24.0	1.04	2.88	1.84
	3.0^{d,e}	1.86	3.41	1.55
	6.0^{d,e}	1.87	3.69	1.82
	12.0^{d,e}	1.60	3.74	2.14
	24.0^{d,e}	1.70	3.96	2.26
Phenyl isocyanate	0.5	0.04	2.12	2.08
	6.0	0.07	2.52	2.45
	24.0	0.04	3.03	2.99
Pyridine^{f}	0.5	0.05	0.08	0.03
	1.0	0.03	0.08	0.05
	3.0^{e}	0.06	0.18	0.12
4-Picoline N-oxide^{g}	0.5	0.25	1.98	1.73
	1.0	0.34	2.27	1.93
	3.0^{e}	0.29	2.21	1.92

$^{a-c}$ See corresponding footnotes in Table I. ^{d} 3.33 mmoles of compound (hydride/compound = 6). ^{e} At 25°. ^{f} Faint green color. ^{g} Reverse addition. Turbid yellow solution.

Sulfur Compounds. Disulfides react rapidly with the utilization of 2 moles of hydride, 1 mole for reduction, and the second for hydrogen evolution.

$$R_2S_2 + 2MH \longrightarrow 2RSM + H_2$$

Phenyl *n*-propyl sulfide proved stable to the reagent under the standard conditions,[20] although a slight uptake of hydride was indicated over long periods of time. Dimethyl sulfoxide utilized 2 equiv of hydride corresponding to reduction to the sulfide. Diphenyl sulfone was stable at 0°, but partial reduction was observed in 24 hr at 25°.[21] Methanesulfonic acid and *p*-toluene-

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[18] A 71% yield of cyclohexylamine has been realized for this reduction in tetrahydrofuran: D. R. Smith, M. Maienthal, and J. Tipton, *J. Org. Chem.*, 17, 294 (1952).

[19] Lithium aluminum hydride dissolves in pyridine with addition to the heterocyclic ring system and the product reduces aromatic ketones, such as benzophenone, more rapidly than alicyclic ketones, such as 2-methylcyclopentanone: P. T. Lansbury and J. O. Peterson, *J. Am. Chem. Soc.*, **85**, 2236 (1963).

[20] J. Strating and H. J. Backer, *Rec. Trav. Chim.*, **69**, 638 (1950); E. Kniisli, *Experientia*, **8**, 262 (1952).

[21] C. S. Marvel and P. D. Caesar, *J. Am. Chem. Soc.*, **72**, 1033 (1950), observed no reduction in ether, but apparently realized a 31% yield of *p*-toluenesulfinic acid in tetrahydrofuran, as quoted in ref 3a, p 846.

Table X. Reaction of Lithium 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	0.5	0.93	1.88	0.95
	1.0	0.98	1.99	1.01
Diphenyl disulfide	0.5	1.01	2.01	1.00
	1.0	1.02	2.08	1.06
	3.0	1.02	2.05	1.03
Phenyl *n*-propyl sulfide	0.5	0	0.08	0.08
	24.0	0	0.20	0.20
Dimethyl sulfoxide[f]	3.0	1.03	1.63	0.60
	6.0	1.12	2.06	0.94
	12.0	1.10	2.04	0.94
	24.0	1.07	2.15	1.08
Diphenyl sulfone[g]	0.5	0.03	0.03	0
	1.0	0.03	0.06	0.03
	24.0[e]	0.02	0.31	0.29
Methanesulfonic acid	0.5	1.05	1.08	0.03
	1.0	1.05	1.08	0.03
	3.0[e]	1.14	1.15	0.01
p-Toluenesulfonic acid monohydrate[d,h]	0.5	2.96	3.00	0.04
	1.0	3.01	3.02	0.01
	6.0[e]	3.10	3.13	0.03
	24.0[e]	3.10	3.20	0.10
Cyclohexyltosylate	3.0	0	0.04	0.04
	6.0	0	0.10	0.10
	12.0	0	0.10	0.10
	24.0	0	0.12	0.12
	12.0[e]	0.12	0.51	0.39
	24.0[e]	0.28	0.79	0.51

[a–c] See corresponding footnotes in Table I. [d] 3.33 mmoles of compound (hydride/compound = 6). [e] At 25°. [f] Solution milky after 24 hr. [g] Light yellow color. [h] White precipitate.

sulfonic acid hydrate liberated hydrogen quantitatively, but no reduction was observed. Finally, cyclohexyl tosylate underwent a slow reaction at 25°. After 24 hr, gas chromatographic examination of the solution revealed 17% cyclohexane, 9% cyclohexene, and 4% cyclohexanol. In a second experiment 10 mmoles of cyclohexyl tosylate was treated with 20 mmoles of lithium aluminum hydride for 48 hr at 25°. There was found 54.1% cyclohexane, 25.4% cyclohexene, and 19.5% cyclohexanol.

In comparison, lithium tri-*t*-butoxyaluminohydride reduces diphenyl disulfide at a reasonable rate, but the corresponding reaction with di-*n*-butyl disulfide is very slow. Otherwise no reductions of the remaining compounds under standard conditions were observed,[4] so this reagent can be utilized for selective reductions in the presence of these groups. Lithium trimethoxyaluminohydride appears to be quite similar to the parent compound in its behavior toward this group of derivatives. The results are summarized in Table X.

Conclusions

This study has largely served to confirm previous conclusions as to the reactions of lithium aluminum hydride with various functional groups.[3] However, the earlier conclusions were based largely on ether solutions with the temperature and concentrations frequently undefined. Consequently, the present study provides a consistent set of results for the behavior of the reagent in tetrahydrofuran under standard conditions of temperature and concentrations. The data permit ready comparison of the rates and stoichiometry of the reactions of lithium aluminum hydride, lithium trimethoxyaluminohydride,[5] and lithium tri-*t*-butoxyaluminohydride[4] under standardized conditions so that definite conclusions can be drawn as to the particular reagent which would be most advantageous to apply for a specific reduction.

Experimental Section

Materials. The standard list of compounds examined was essentially the same as that utilized in our earlier studies.[4,5] The preparation of standard solutions of lithium aluminum hydride was described previously.[5]

Procedure. All reactions and solutions were maintained under a dry nitrogen atmosphere. Hypodermic syringes were used at all times to transfer materials. All glass apparatus was dried in an oven, assembled, and then conditioned in a stream of dry nitrogen. A static nitrogen atmosphere was then maintained.

The reduction of caproic acid is illustrative of the procedure utilized. In a dry, 100-ml flask, fitted with a rubber syringe cap, magnetic stirring bar, nitrogen inlet, and connection to an inverted gas buret *via* a spiral reflux condenser and a Dry Ice vapor trap, 5.0 mmoles of lithium aluminum hydride in tetrahydrofuran and enough extra solvent to make a total volume of 15 ml was added. The solution was cooled to 0° in an ice bath and 3.33 mmoles of caproic acid in 5.0 ml of tetrahydrofuran solution was added. The hydrogen evolved was collected in the buret and measured (3.54 mmoles). After 6 hr at 0°, the solution was hydrolyzed by injecting a small quantity of very dilute sulfuric acid and 9.73 mmoles of hydrogen was collected. In a blank run, performed with the addition of 5.0 ml of pure tetrahydrofuran in place of the solution of compound, there was obtained 3.28 mmoles of hydrogen on treatment with the dilute sulfuric acid. Therefore, 10.55 mmoles of hydride (20.28 − 9.73) was consumed by the caproic acid, corresponding to a utilization of 3.18 mmoles of hydride per mmole of compound, 1.06 being used by the acidic hydrogen of the carboxyl group to form hydrogen and 2.12 being utilized for reduction to the alcohol stage.

Product Identification. In cases where it was desirable to identify the product, or to analyze for several products, it proved convenient to destroy the residual hydride with ethylene glycol. This material simultaneously precipitated the inorganic components of the reaction mixture, yielding a dry tetrahydrofuran solution which, in most cases, could be injected directly into the gas chromatograph.

The following reduction of styrene oxide and analysis of the reaction product is representative. Utilizing the general procedure described above, 5.0 mmoles of lithium aluminum hydride and 5.0 mmoles of styrene oxide in 20 ml of tetrahydrofuran solution were permitted to react for 30 min at 0°. The reaction mixture was then treated with ethylene glycol. The tetrahydrofuran solution was separated and the solids were extracted with ether. The combined extracts were brought to a definite volume, with addition of an internal standard, and subjected to gas chromatographic examination (150 ft Carbowax 20M capillary column). The analysis indicated the formation of 88% 1-phenylethanol and 4% 2-phenylethanol, normalized to 96:4 ratio of secondary/primary.