

0°, oxidation yielded 6.9 mmoles of α -pinene (6.9%) and 38.5 mmoles of 2-phenyl-1-propanol, a yield of 77%. 2-Phenyl-1-propanol was first separated from the isopinocampheol by liquid phase chromatography on alumina, eluting the isopinocampheol

with ether and the 2-phenyl-1-propanol with a mixture of ether-methanol. The solvents were removed and the product was further purified by gas chromatography: n_D^{20} 1.5250, $[\alpha]_D^{25}$ + 0.80°.

[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY, LAFAYETTE, IND.]

Selective Reductions. III. Further Studies of the Reaction of Alcohols with Lithium Aluminum Hydride as a Route to the Lithium Alkoxyaluminumhydrides¹

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The reactions of methyl, ethyl, isopropyl, and *t*-butyl alcohols with lithium aluminum hydride in ethyl ether, tetrahydrofuran, and diglyme were studied in order to establish whether these reactions provide convenient synthetic routes to lithium di- and trialkoxyaluminumhydrides. As reported earlier, the reaction of *t*-butyl alcohol can be controlled to yield lithium di- and tri-*t*-butoxyaluminumhydride without difficulty. Similarly, the reaction of methanol with lithium aluminum hydride appears to lead, without complications, to the formation of lithium di- and trimethoxyaluminumhydride, insoluble in ethyl ether, but highly soluble in tetrahydrofuran and diglyme. Lithium trimethoxyaluminumhydride can also be prepared by the reaction of lithium aluminum hydride with lithium tetramethoxyaluminumhydride. The reaction of ethyl alcohol with lithium aluminum hydride appears to lead to products which are predominantly lithium di- and triethoxy derivatives, but the reaction is less simple than the previous cases. Finally, both isopropyl and *sec*-butyl alcohol react to yield complex mixtures, involving the formation and precipitation of major amounts of the tetraalkoxy derivative. Utilization of acetone in place of isopropyl alcohol yields similar results. Lithium di-*t*-butoxyaluminumhydride reacts with 1 mole of methanol to give a mixed alkoxy derivative, lithium monomethoxydi-*t*-butoxyaluminumhydride. Lithium trimethoxyaluminumhydride is a far more powerful reducing agent than the tri-*t*-butoxy derivative, but not as active as the parent compound. Preliminary experiments revealed that the product obtained by reaction of 3 moles of ethyl alcohol per mole of lithium aluminum hydride is a promising reagent for the reduction of both aromatic and aliphatic nitriles to aldehydes in good yield.

The alkali metal borohydrides⁴ and the corresponding alkali metal aluminum hydrides⁵ constitute two families of reducing agents of vastly different characteristics. Thus sodium borohydride, at one extreme, reduces only aldehyde, ketone, and acid chloride groups at a convenient rate,⁶ whereas lithium aluminum hydride, at the other extreme, rapidly reduces practically all functional groups.⁷

For organic syntheses there would be obvious advantages in having available not merely these two extremes but rather an entire series of reagents of graduated activities. In line with this objective, we have been investigating means of increasing the activity of the borohydride reagents, and of decreasing the activity of the aluminum hydride compounds. Thus it was observed that the activity of sodium borohydride could be increased by the addition of certain metal salts⁸ and by the introduction of alkoxy substituents.⁹ On the other hand, the introduction of three ethoxy¹⁰ or *t*-butoxy¹¹ substituents considerably diminishes the reducing power of the alkali metal aluminum hydride.¹²

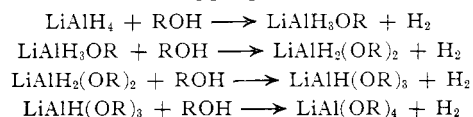
Lithium tri-*t*-butoxyaluminumhydride, conveniently synthesized *in situ* by the reaction of 3 moles of *t*-butyl alcohol with lithium aluminum hydride in an appropriate solvent,¹¹ has proved to be an excellent

reagent for the reduction of acid chlorides to aldehydes,^{11,13} for the stereospecific reduction of steroids,¹⁴ as well as for other selective reductions.^{15,16} On the other hand, sodium triethoxyaluminumhydride has found relatively little application in organic synthesis. It is probable that the synthesis, *i.e.*, the reaction of sodium hydride with freshly prepared, monomeric aluminum ethoxide in tetrahydrofuran at 70 to 90° in an autoclave,^{10,17} is too inconvenient for the preparation of small quantities of the reagent required for an individual reaction.

Our success in synthesizing lithium tri-*t*-butoxyaluminumhydride by the reaction of *t*-butyl alcohol with the parent compound encouraged us to make a detailed examination of the reaction of methyl, ethyl, and isopropyl alcohols with lithium aluminum hydride with the primary objective of ascertaining whether the reactions could be controlled to provide a convenient synthetic route to the corresponding di- and trialkoxyaluminumhydrides.

Results and Discussion

Lithium aluminum hydride and its alkoxy derivatives are highly reactive materials, exceedingly sensitive to traces of water, oxygen, carbon dioxide, etc. In view of the special objectives of this investigation, it was decided that major emphasis should be placed on a determination of the nature of the species formed by treating lithium aluminum hydride in solution with 1, 2, and 3 moles of the appropriate alcohol.



Ethyl ether, tetrahydrofuran, and diglyme were selected as representative solvents. Standardized solu-

(1) Addition Compounds of the Alkali Metal Hydrides. XIII.
 (2) Based upon a thesis submitted by Charles J. Shoaf, in 1957, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.
 (3) Research assistant on Contract DA-33-008-ORD-992 supported by the Office of Ordnance Research, U. S. Army.
 (4) H. I. Schlesinger and H. C. Brown, *J. Am. Chem. Soc.*, **63**, 3429 (1940); H. I. Schlesinger, H. C. Brown, H. R. Hoekstra, and L. R. Rapp, *ibid.*, **75**, 199 (1953).
 (5) A. E. Finholt, A. C. Bond, Jr., and H. I. Schlesinger, *ibid.*, **69**, 1199 (1947).
 (6) S. W. Chaikin and W. G. Brown, *ibid.*, **71**, 122 (1949).
 (7) R. F. Nystrom and W. G. Brown, *ibid.*, **69**, 1197, 2548 (1947); **70**, 3738 (1948).
 (8) H. C. Brown and B. C. Subba Rao, *ibid.*, **78**, 2582 (1956).
 (9) H. C. Brown, E. J. Mead, and C. J. Shoaf, *ibid.*, **78**, 3613 (1956).
 (10) G. Hesse and R. Schrödel, *Ann.*, **507**, 24 (1957).
 (11) H. C. Brown and R. F. McFarlin, *J. Am. Chem. Soc.*, **78**, 252 (1956); **80**, 5372 (1958).
 (12) For a summary of the developments in this area, see H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962, Chapter 17.

(13) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **80**, 5377 (1958).
 (14) O. H. Wheeler and J. L. Mateos, *Can. J. Chem.*, **36**, 14 (1958).
 (15) C. Tamm, *Helv. Chim. Acta*, **43**, 338 (1960).
 (16) Lithium tri-*t*-butoxyaluminumhydride is now available commercially from Metal Hydrides Incorporated, Beverly, Mass.
 (17) O. Schmitz-Dumont and V. Habernickel, *Ber.*, **90**, 1054 (1957).

tions of lithium aluminum hydride in these solvents were treated with 1, 2, and 3 molar equivalents of the alcohol. The hydrogen evolved was measured. Interpretation of the results is facilitated by the fact that all of the tetraalkoxyaluminumhydrides are insoluble in the three solvents. If a precipitate formed, an aliquot of the clear solution was removed and analyzed for hydride and aluminum content. The composition of the precipitate was then calculated by difference. It is apparent that a simple reaction, leading to one and only one product, will require that the hydride/aluminum ratio be a simple integer, with the same value for the precipitate and the solution.

***t*-Butyl Alcohol.**—The reaction of *t*-butyl alcohol with lithium aluminum hydride was explored primarily to test the experimental methods in the light of information available from the earlier results.¹¹

In ethyl ether, addition of 2 moles of *t*-butyl alcohol evolved 2 moles of hydrogen and the solution remained clear. Addition of a third mole of *t*-butyl alcohol caused the deposition of a white precipitate and analysis showed the ether to be free of all soluble aluminum and active hydrogen. The white solid was completely soluble in diglyme and hydrolysis evolved the fourth mole of hydrogen.

If *t*-butyl alcohol was added in slight excess of 2 molar equivalents to lithium aluminum hydride in ether, the slight amount of lithium tri-*t*-butoxyaluminumhydride formed from the excess alcohol slowly precipitated. Analysis of the remaining clear solution showed a return to 1.00/2.00 for the ratio of soluble aluminum/hydride. This solution was stable and no further precipitation was observed.

Addition of *t*-butyl alcohol to lithium aluminum hydride in ether, tetrahydrofuran, or diglyme at 25° liberates a maximum of 3 moles of hydrogen and the solutions remain clear. Under reflux in tetrahydrofuran (64°), or at 80° in diglyme, the fourth mole of hydrogen is slowly evolved and the tetra-*t*-butoxy derivative precipitates.

The experimental results are summarized in Table I.

TABLE I
THE REACTION OF *t*-BUTYL ALCOHOL WITH LITHIUM ALUMINUM HYDRIDE AT 25°

Lithium aluminum hydride, mmoles	Alcohol added, mmoles	Hydrogen evolved, mmoles	—Analysis of solution—			Composition of ppt.	
			Hydride, M	Aluminum, M	H ⁻ /Al	Al pptd., %	H ⁻ /Al
A. Ethyl ether ^a							
110	110	114	1.56	0.53	2.94	0	1.00
	220	227	0.93	.51	1.82	0	
	330	327	0.0	.0		100	
B. Tetrahydrofuran ^b							
24	24	24	1.40	0.46	3.04	0	
	48	47	0.87	.44	1.98	0	
	72	71	0.42	.44	0.96	0	
C. Diglyme ^c							
23	23	23	1.40	0.46	3.04	0	
	46	46	0.91	.45	2.02	0	
	69	70	0.45	.45	1.00	0	

^a 200 ml. of 0.55 M lithium aluminum hydride. ^b 50 ml. of 0.48 M lithium aluminum hydride. ^c 50 ml. of 0.46 M lithium aluminum hydride.

Isopropyl Alcohol.—The results were much less simple with isopropyl alcohol. Here, the addition of 1 molar equivalent of isopropyl alcohol to the reagent in ethyl ether results in the precipitation of 22% of the available aluminum and the H⁻/Al ratio in solution corresponds closely to the 4.0 value required by LiAlH₄.

The results are not changed significantly by the second and third molar equivalents of the alcohol. Evidently, lithium tetraisopropoxyaluminumhydride is the preferred reaction product and precipitates from solution.

The use of tetrahydrofuran and diglyme as the reaction media decreased somewhat the amount of precipitated material, but it was evident that the preparation of simple products was not being achieved. Here also the addition of 3 moles of isopropyl alcohol results in the formation of a considerable quantity of precipitated material. This precipitate contains only trace amounts of hydride and must therefore be the insoluble lithium tetraisopropoxyaluminumhydride.

The experimental data are summarized in Table II.

TABLE II
THE REACTION OF ISOPROPYL ALCOHOL WITH LITHIUM ALUMINUM HYDRIDE AT 25°

Lithium aluminum hydride, mmoles	Alcohol added, mmoles	Hydrogen evolved, mmoles	—Analysis of solution—			Composition of ppt.	
			Hydride, M	Aluminum, M	H ⁻ /Al	Al pptd., %	H ⁻ /Al
A. Ethyl ether ^a							
112	112	113	1.60	0.41	3.90	22	0.11
	224	225	0.83	.20	4.15	60	.55
	336	336	0.30	.10	3.00	76	.33
B. Tetrahydrofuran ^b							
24.5	24.5	25	1.44	0.49	2.94	0	0.0
	49	50	0.89	.37	2.38	19	
	73.5	75	0.39	.21	1.86	52	
C. Diglyme ^c							
120	120	120	1.16	0.34	3.42	13	0.0
	240	240	0.72	.22	3.27	41	.18
	360	359	0.29	.11	2.64 ^d	68	.12

^a 200 ml. of 0.56 M lithium aluminum hydride. ^b 50 ml. of 0.49 M lithium aluminum hydride. ^c 300 ml. of 0.40 M lithium aluminum hydride. ^d This value was essentially unchanged after 12 hr. at 59°.

Various reaction temperatures from -80 to 65° were explored, but did not serve to give the desired trialkoxy compound from isopropyl alcohol. Substitution of acetone for isopropyl alcohol gave essentially the same results in diglyme and tetrahydrofuran as those obtained with isopropyl alcohol. For example, the addition of 3 moles of acetone to lithium aluminum hydride in diglyme at 25° gave an aluminum/hydride ratio in solution of 1.00/2.53; and in tetrahydrofuran, 1.00/1.51 at 0°. In both cases, considerable quantities of precipitate were formed.

sec-Butyl alcohol reacted with lithium aluminum hydride in a manner very similar to that of isopropyl alcohol. For example, the addition of 3 moles of the alcohol to the reagent in ethyl ether at 25° resulted in a large quantity of precipitate, and the solution revealed an aluminum/hydride ratio of 1.00/2.50 instead of the value of unity required by the Li(*sec*-BuO)₃AlH composition.

Ethyl Alcohol.—Addition of 2 moles of ethyl alcohol to lithium aluminum hydride in ethyl ether results in a small quantity of precipitated material, and the material in solution exhibits an aluminum/hydride ratio of 1.00/2.06. It therefore appears that lithium diethoxyaluminumhydride is a major product of the reaction. Addition of a third mole of ethanol results in considerable precipitation, presumably lithium tetraethoxyaluminumhydride, and the material in solution exhibits an aluminum/hydride ratio of 1.48. Evidently we are dealing here with the formation of a mixture of the di- and triethoxyaluminumhydride.

Replacement of the 3 moles of ethyl alcohol by 1.5 moles of ethyl acetate yields a product that is indistinguishable from that produced with the alcohol.

The results in tetrahydrofuran are similar. In diglyme the amount of precipitated material is even larger.

The data are summarized in Table III.

TABLE III
THE REACTION OF ETHYL ALCOHOL WITH LITHIUM HYDRIDE AT 25°

Lithium aluminum hydride, mmoles	Alcohol added, mmoles	Hydrogen evolved, mmoles	—Analysis of solution—			Composition of ppt.	
			Hydride, M	Aluminum, M	H ⁻ /Al	Al pptd., %	H ⁻ /Al
A. Ethyl ether ^a							
104	104	107	1.44	0.49	2.94	3	
	208	214	0.91	.44	2.06	10	0.40
	312	313	0.46	.31	1.48	33	0.20
B. Tetrahydrofuran ^b							
24.5	24.5	25	1.41	0.49	2.89	0	
	49	51	0.94	.50	1.87	0	
	73.5	76	0.44	.33	1.33	29	0.0
C. Diglyme ^c							
26.5	26.5	27	1.41	0.49	2.88	0	
	53	55	0.85	.34	2.47	30	0.75
	79.5	84	0.31	.19	1.62	60	0.31

^a 200 ml. of 0.52 M lithium aluminum hydride. ^b 50 ml. of 0.49 M lithium aluminum hydride. ^c 50 ml. of 0.53 M lithium aluminum hydride.

Methyl Alcohol.—Fortunately, the results with methanol proved to be considerably simpler, leading to the direct synthesis of lithium trimethoxyaluminumhydride.

The addition of 3 molar equivalents of methyl alcohol to a solution of lithium aluminum hydride in tetrahydrofuran or diglyme resulted in a vigorous reaction with the evolution of the theoretical amount of hydrogen. The resulting solutions were clear, and analysis yielded the aluminum/hydrogen ratio of 1.00/1.00 to be expected for the formation of lithium trimethoxyaluminumhydride. Addition of a fourth mole of methyl alcohol resulted in the liberation of the fourth mole of hydrogen and the precipitation of lithium tetramethoxyaluminumhydride.

It was noted that as the drops of the methyl alcohol solution reached the solution of lithium aluminum hydride, a white precipitate immediately formed, which then readily dissolved into the stirred solution. The precipitate became more and more evident and the rate of redissolving decreased as the amount of methyl alcohol added approached 3 molar equivalents. These observations suggest that some insoluble tetramethoxy derivative is formed initially, but is converted by reaction with the lithium aluminum hydride (and its methoxy derivatives in solution) into soluble methoxy derivatives. Ultimately, all of the material is converted into the trimethoxy derivative, provided that a maximum of 3 moles of the alcohol per mole of lithium aluminum hydride is added.

The solutions of lithium trimethoxyaluminumhydride are clear and show no tendency to precipitate the insoluble lithium tetramethoxyaluminumhydride over long periods of time. Consequently, the trimethoxyaluminumhydride differs in this respect from the analogous sodium trimethoxyborohydride.⁹ Solutions of lithium trimethoxyaluminumhydride in diglyme in concentrations as high as 2 M have been prepared.

In the case of ethyl ether, the addition of 1 mole of methyl alcohol causes the precipitation of 42% of the

available aluminum, and the precipitate contains an aluminum/hydride ratio of 1.00/1.66. Moreover, the solution contains lithium aluminum hydride. This suggests the formation of an insoluble lithium dimethoxyaluminumhydride. The addition of 2 moles of methyl alcohol causes the complete precipitation of all of the available aluminum. These results are consistent with the formation of lithium dimethoxyaluminumhydride, but do not eliminate the possibility that the precipitate is a mixture of insoluble mono-, di-, and trimethoxy derivatives.

Addition of a third molar equivalent of methyl alcohol to the mixture resulted in the evolution of a third molar equivalent of hydrogen. However, there was no obvious physical change in the precipitate, and the solution was still free of any soluble aluminum or hydride derivative. The white precipitate dissolved rapidly and completely in diglyme and liberated a fourth molar equivalent of hydrogen with methyl alcohol. Thus lithium trimethoxyaluminumhydride must be essentially insoluble in ether.

The experimental data are summarized in Table IV.

TABLE IV
THE REACTION OF METHYL ALCOHOL WITH LITHIUM ALUMINUM HYDRIDE AT 25°

Lithium aluminum hydride, mmoles	Alcohol added, mmoles	Hydrogen evolved, mmoles	—Analysis of solution—			Composition of ppt.	
			Hydride, M	Aluminum, M	H ⁻ /Al	Al pptd., %	H ⁻ /Al
A. Ethyl ether ^a							
104	104	102	1.20	0.30	4.00	42	1.66
	208	208	0.0	.0		100	2.02
	312	315	0.0	.0		100	0.97
B. Tetrahydrofuran ^b							
24.5	24.7	25	1.44	0.50	2.88	0	
	49.0	48	0.99	.50	1.95	0	
	74.1	74.4	0.50	.50	1.00	0	
C. Diglyme ^c							
21.5	21.5	21.5	1.25	0.42	2.98	0	
	43.0	43	0.83	.41	2.02	0	
	64.5	64	0.41	.40	1.02	0	

^a 200 ml. of 0.52 M lithium aluminum hydride. ^b 50 ml. of 0.49 M lithium aluminum hydride. ^c 50 ml. of 0.43 M lithium aluminum hydride.

Reaction of Lithium Aluminum Hydride with Lithium Tetraalkoxyaluminumhydrides.—The observation that the initial precipitate formed in the reaction of methyl alcohol with lithium aluminum hydride in tetrahydrofuran and diglyme slowly redissolved suggested the possibility that the desired trialkoxy derivatives might be realized through a redistribution reaction of lithium aluminum hydride with the corresponding lithium tetraalkoxyaluminumhydride. Accordingly, solutions of lithium aluminum hydride in diglyme were treated with the calculated quantities of the tetramethoxy-, -ethoxy-, -isopropoxy, and -*t*-butoxy derivatives.¹¹ Since these compounds are insoluble in diglyme, a change in the aluminum concentration in solution provided evidence for reaction.

At 25°, lithium tetramethoxyaluminumhydride readily dissolved in the solution of lithium aluminum hydride, forming a solution of lithium trimethoxyaluminumhydride indistinguishable from the product formed in the reaction with methyl alcohol.

The tetraethoxy and tetraisopropoxy derivatives did not react as readily, giving aluminum/hydride ratios of 1.00/2.36 and 1.00/2.49, respectively, after standing for 3 days with occasional shaking. These

values correspond closely to those realized from the addition of 3 moles of alcohol to 1 mole of lithium aluminum hydride in diglyme (Tables II and III).

No reaction was observed between lithium aluminum hydride in ether and lithium tetra-*t*-butoxyaluminumohydride after refluxing for 1 hr. The same reactants in diglyme showed only slight reaction after heating for 2 hr. at 100°.

Consequently, it appears that only in the case of lithium trimethoxyaluminumohydride does this reaction provide a good approach to its synthesis.

Reaction of Alcohols with Lithium Di-*t*-butoxyaluminumohydride.—As was pointed out earlier, the addition of 2 molar equivalents of *t*-butyl alcohol to a solution of lithium aluminum hydride in ether results in the formation of the soluble product, lithium di-*t*-butoxyaluminumohydride. It was of interest to explore the possibility of synthesizing mixed alkoxy derivatives by adding a third mole of a different alcohol to the initial product.

Addition of 1 molar equivalent of methyl alcohol to the ether solution of lithium di-*t*-butoxyaluminumohydride provided a stable, clear solution with an aluminum/hydride ratio of 1.00/0.99. Further addition of methyl alcohol resulted in the formation of a very gelatinous white precipitate. These experiments clearly support the formation of a soluble lithium monomethoxydi-*t*-butoxyaluminumohydride.

In the case of ethyl alcohol, the formation of a white solid was observed. This readily settled. Analysis of the clear supernatant liquid yielded an aluminum/hydride ratio of 1.00/1.47. Consequently, the reaction is not simple in this case.

Finally, the addition of isopropyl alcohol to the ether solution of lithium di-*t*-butoxyaluminumohydride caused the precipitation of 75% of the available aluminum. (From an original molarity of 0.28, the solution dropped to 0.08 *M* in aluminum.) The resulting solution exhibited an aluminum/hydride ratio of 1.00/0.98. Consequently, it appears that in this case the reaction proceeds predominantly to the formation of a slightly soluble lithium monoisopropoxydi-*t*-butoxyaluminumohydride.

Reducing Properties of Lithium Trimethoxyaluminumohydride.—Lithium trimethoxyaluminumohydride resembles lithium aluminum hydride in its reducing power more than it does lithium tri-*t*-butoxyaluminumohydride.¹¹ Thus, the latter reagent in tetrahydrofuran or diglyme solution fails to react with ethyl benzoate or benzonitrile at 0° over long periods of time. However, under the same conditions lithium trimethoxyaluminumohydride (in excess) shows the loss of two hydrides per mole of ethyl benzoate or benzonitrile. When lithium trimethoxyaluminumohydride was added to ethyl benzoate at 0° in a 1:1 molar ratio, the hydride content of the reagent was completely utilized, but no trace of aldehyde was found.

At -80° the reagent failed to react with ethyl benzoate after 2 hr., whereas lithium aluminum hydride rapidly reacts.

Similarly, *n*-butyronitrile was treated with lithium aluminum hydride and lithium trimethoxyaluminumohydride at 0° in diglyme. After 5 min., the reaction mixtures were quenched and the residual hydride content established. The results indicated that the lithium aluminum hydride was reacting at a rate approximately twice that of the trimethoxy derivative.

A detailed study of the utility of lithium trimethoxyaluminumohydride as a selective reducing agent is under way.^{18,19}

(18) H. C. Brown and H. R. Deck, manuscript in preparation.

(19) Research in progress with P. Weissman.

It is of considerable theoretical interest that alkoxy substituents increase the reducing activity of the borohydride ion, but decrease that of the aluminumohydride ion.¹¹

Reduction of Nitriles to Aldehydes.—It was reported by Hesse and Schrödel that sodium triethoxyaluminumohydride was an excellent reagent for the conversion of aromatic nitriles to aldehydes, but was unsatisfactory for aliphatic.¹⁰ Prior to the appearance of their publication, we had also explored the applicability of these alkoxy derivatives for this purpose. We discovered that lithium triethoxyaluminumohydride²⁰ is capable of reducing both aromatic and aliphatic nitriles to the corresponding aldehydes in good yield.²¹ In the following paper²² we suggest a possible explanation for the different results realized with the sodium and the lithium derivatives.

Preliminary experiments revealed that lithium aluminum hydride reacts with benzonitrile at 0° in an equimolar ratio to give a 92% yield of benzaldehyde. On the other hand, under the same conditions *n*-butyronitrile was not converted to the aldehyde. On this basis, it appeared that the conversion of aromatic nitriles to aldehydes offers no problem, and the emphasis of the investigation was placed on the development of a practical reduction of aliphatic nitriles into the corresponding aldehydes.

It was pointed out previously that lithium tri-*t*-butoxyaluminumohydride fails to react with nitriles. It therefore appeared that a less hindered reagent was necessary. However, lithium trimethoxyaluminumohydride was apparently too active—yields of only 15 to 30% were realized with this reagent. Consequently, we explored the intermediate reagents. The use of lithium triethoxyaluminumohydride in ether resulted in a 59% yield of *n*-butyraldehyde.

These results are summarized in Table V.

TABLE V
YIELDS OF *n*-BUTYRALDEHYDE REALIZED IN THE CONTROLLED REDUCTION OF *n*-BUTYRONITRILE AT 25° BY THE ALKOXY DERIVATIVES OF LITHIUM ALUMINUM HYDRIDE

Reagent	Ethyl ether	Tetrahydrofuran	Diglyme
LiAlH ₄	22	23	21
Li(MeO) ₃ AlH ^a	31 ^b	15	19
Li(EtO) ₃ AlH ^a	59	25	15
Li(<i>i</i> -PrO) ₃ AlH ^a	30 ^c	25	15
Li(<i>t</i> -BuO) ₃ AlH ^a	0 ^d	0 ^d	0 ^d

^a Prepared by the addition of 3 moles of alcohol per mole of lithium aluminum hydride in the appropriate solvent. ^b Hydride insoluble, 51% recovered unreacted. A 50:50 mixture of ether and diglyme gave a 25% yield. ^c 25% of hydride recovered unreacted. ^d No reaction.

We explored briefly other reagents. The use of lithium di-*t*-butoxyaluminumohydride resulted in a 45% yield of *n*-butyraldehyde, whereas lithium monomethoxydi-*t*-butoxyaluminumohydride gave a lower yield, 22%. The use of crude lithium triethoxyaluminumohydride at 0°, without attempting to filter the insoluble by-products, gave a 68% yield of *n*-butyraldehyde. The reaction did not appear to be very sensitive to the mode of addition or the reaction temperature. Benzonitrile provided benzaldehyde in a 98% yield. Capronitrile was converted into its aldehyde in 60%

(20) It is convenient to refer to the product from the reaction of 3 moles of ethanol, or 1.5 moles of ethyl acetate, with 1 mole of lithium aluminum hydride, as "lithium triethoxyaluminumohydride" even though the evidence is that this is merely the major component, with significant quantities of the diethoxy derivative also present.

(21) A preliminary communication reporting this discovery was published previously: H. C. Brown, C. J. Shoaf, and C. P. Garg, *Tetrahedron Letters*, No. 3, 9 (1959).

(22) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, **86**, 1085 (1964).

TABLE VI
 THE REDUCTION OF NITRILES TO ALDEHYDES WITH LITHIUM ALKOXYALUMINOHYDRIDES

Reagent ^a	Nitrile	H ⁻ /RCN ^b	Solvent	Temp., °C.	Time, ^c min.	Aldehyde yield, ^d %
LiAlH ₄	Benzonitrile	4.0	Diglyme	0	60	92
LiAlH ₄	<i>n</i> -Butyronitrile	4.0	Ether	-80	90	10 ^e
LiAlH ₄	<i>n</i> -Butyronitrile	1.00	Diglyme	0	15	18
Li(MeO) ₃ AlH	<i>n</i> -Butyronitrile	1.22	Diglyme	0	90	17
Li(EtO) ₃ AlH	<i>n</i> -Butyronitrile	1.00	Ether	0	60	60
Li(EtO) ₃ AlH ^f	<i>n</i> -Butyronitrile	1.00	Ether	0	90	68
Li(EtO) ₃ AlH	<i>n</i> -Butyronitrile	0.98	Ether	(-80) ^h	30	53
Li(EtO) ₃ AlH	<i>n</i> -Butyronitrile	.98	Ether	25	15	58
Li(EtO) ₃ AlH	<i>n</i> -Butyronitrile	.97	Ether	25	15	52 ^g
Li(EtO) ₃ AlH	<i>n</i> -Butyronitrile	.99	Ether	-80	90	No reacn.
Li(<i>t</i> -BuO) ₂ AlH ₂	<i>n</i> -Butyronitrile	.97	Ether	0	60	45
Li(<i>t</i> -BuO) ₂ AlH ₂	<i>n</i> -Butyronitrile	.50	Ether	0	60	30
Li(<i>t</i> -BuO) ₂ (MeO)AlH	<i>n</i> -Butyronitrile	.96	Ether	0	60	22
Li(EtO) ₃ AlH	Benzonitrile	.99	Ether	25	15	98
Li(EtO) ₃ AlH	Capronitrile	1.01	Ether	25	15	60
Li(EtO) ₃ AlH	Benzyl cyanide	0.98	Ether	25	15	0 ⁱ
Li(EtO) ₃ AlH	Adiponitrile	2.05	Ether	25	15	42 ^j

^a Footnote 20. Clear filtered solutions of the reagents were added to the nitriles unless otherwise indicated. ^b Lithium aluminum hydride contains four "hydrides" per molecule. ^c Unless otherwise noted, all of the available hydride was utilized in the time indicated. ^d By analysis with 2,4-dinitrophenylhydrazine. ^e Hydride loss/nitrile was 1.49. ^f Addition of the crude reaction product from the addition of 3 moles of ethanol to lithium aluminum hydride, without filtration, to the nitrile. ^g Nitrile added to hydride. ^h Reactants mixed at -80° and allowed to warm slowly to room temperature. ⁱ 73% hydrogen evolved. ^j Analysis low because of some solubility of the 2,4-dinitrophenylhydrazine in water.

yield, and adiponitrile was converted into the dialdehyde in a 42% yield.²³

The results of this initial exploration of the new aldehyde synthesis are summarized in Table VI.

Conclusions.—The reaction of alcohols with lithium aluminum hydride provides a convenient route to lithium di- and trimethoxyaluminumhydride and to lithium di- and tri-*t*-butoxyaluminumhydride. Lithium trimethoxyaluminumhydride has proved valuable for the stereoselective reduction of bicyclic ketones,¹⁸ and lithium tri-*t*-butoxyaluminumhydride has provided convenient aldehyde syntheses from acid chlorides^{11,13} and phenyl esters²⁴ and as a selective reducing agent.^{14,15} Although the reaction of ethanol with lithium aluminum hydride is not as simple as the above reactions, the products "lithium di- and triethoxyaluminumhydride" have provided convenient selective reductions of nitriles^{21,22} and dimethylamides²⁵ to aldehydes. The results already realized suggest a promising future for these reagents as reducing agents of modified activity.

Experimental

Materials.—The lithium aluminum hydride was the commercial material obtained from Metal Hydrides Inc. Tetrahydrofuran and diglyme were purified as previously described.²⁶ Mallinckrodt (Analytical Reagent) anhydrous ethyl ether was used without further treatment.

Solutions of lithium aluminum hydride were prepared simply by addition of lithium aluminum hydride, in a 10 to 15% excess over that required for the desired concentration, to the solvent and stirring vigorously with a magnetic stirrer. This method proved to be much simpler and faster than the procedure originally used of refluxing solvent over the hydride. In this manner, a saturated solution in diglyme, 1.03 *M*, was obtained after 1 hr. at room temperature (the heat of solution results in an initial temperature rise). In the same manner, a 1.61 *M* solution in ethyl ether was obtained after 0.5 hr.

All operations were carried out under a nitrogen atmosphere.

The alcohols used were the best available commercial materials and were dried over and distilled from calcium hydride. The

(23) A more detailed study of this reaction was subsequently carried out by C. P. Garg. He was able to improve the procedure and the yields, as described in the accompanying publication, ref. 22.

(24) H. C. Brown and P. M. Weissman, manuscript in preparation.

(25) H. C. Brown and A. Tsukamoto, *J. Am. Chem. Soc.*, **81**, 502 (1959); **86**, 1089 (1964).

(26) H. C. Brown, E. J. Mead, and B. C. Subba Rao, *ibid.*, **77**, 6209 (1955).

nitriles were all commercial products which exhibited boiling points and refractive indices in agreement with literature values.

Analyses.—The lithium aluminum hydride solutions in ethyl ether and tetrahydrofuran were analyzed by removing the volatile solvent under vacuum, adding dry diglyme to the solid, and hydrolyzing with water. With the alkoxy substituted aluminumhydrides, addition of the diglyme was not necessary. The evolved hydrogen was measured in an inverted buret or a flowmeter. Diglyme solutions of the hydrides were hydrolyzed directly. The precipitated aluminum hydroxide was dissolved in dilute hydrochloric acid, then precipitated, dried, and weighed as the 8-hydroxyquinolate.

Reaction of Ethyl Alcohol with Lithium Aluminum Hydride in Tetrahydrofuran.—The following procedure is typical of those used to study the reaction of alcohols with lithium aluminum hydride in various solvents. The apparatus consisted of a 100-ml. round-bottom, three-neck flask, fitted by means of standard taper joints with a rubber syringe cap, mechanical stirrer, and a Dry Ice condenser leading to a wet-test meter through a -80° vapor trap. The apparatus was flamed out under a stream of dry nitrogen. The lithium aluminum hydride solution was transferred to the flask using a dried pipet. The alcohol was introduced through the syringe cap using a conventional hypodermic syringe.

To 50 ml. of a 0.49 *M* solution of lithium aluminum hydride (24.5 mmoles) in tetrahydrofuran was added 1.43 ml. of ethyl alcohol (24.5 mmoles) over a period of 10 min. with rapid stirring. Hydrogen evolution amounted to 25.4 mmoles. The solution remained clear and the reaction was rapid. Analysis of a 5-ml. sample showed the remaining solution to be 1.41 *M* in hydride and the aluminum/hydride ratio to be 1.00/2.89.

A second reaction was run, adding twice as much ethyl alcohol as previously (2.86 ml., 49.0 mmoles) over a period of 13 min. Hydrogen evolution amounted to 50.9 mmoles. Some initial precipitate became evident toward the end of the addition, but rapidly disappeared. Analysis of a 5-ml. sample showed the solution to be 0.94 *M* in hydride and the aluminum/hydride ratio to be 1.00/1.87.

A third reaction was run, using three times the initial amount of ethyl alcohol, or a 3:1 molar ratio of alcohol to lithium aluminum hydride. Here 4.29 ml. of ethyl alcohol (73.5 mmoles) was added to 50 ml. of 0.49 *M* lithium aluminum hydride (24.5 mmoles) in tetrahydrofuran over a period of 18 min. Hydrogen evolution was found to be 76.2 mmoles. The solution became permanently cloudy after the addition of about 2.5 moles of the alcohol. Analysis of a clear 10-ml. sample showed the solution to be 0.44 *M* in hydride and the ratio of aluminum/hydride to be 1.00/1.33.

Reaction of Acetone with Lithium Aluminum Hydride in Tetrahydrofuran at 0°.—The apparatus was identical with that used for reaction with the alcohols with the addition of an ice bath around the flask. Acetone (5.26 ml., 72 mmoles) was added to 50 ml. of a 0.48 *M* solution of lithium aluminum hydride (24.0 mmoles) over a period of 25 min. No hydrogen was evolved. Analysis of a clear 10-ml. sample showed the solution to be 0.25

M in hydride and the ratio of soluble aluminum/hydride to be 1.00/1.51.

Reaction of Lithium Di-*t*-butoxyaluminumhydride in Ether with Methyl, Ethyl, and Isopropyl Alcohols.—In the apparatus described above, ethyl alcohol (14.0 mmoles) was added over a period of 3 min. to 50 ml. of 0.28 *M* lithium di-*t*-butoxyaluminumhydride (14.0 mmoles) in ether. A precipitate formed which readily settled out. Hydrogen evolution amounted to 0.324 l. at standard conditions, or 14.4 mmoles. Analysis of a 10-ml. sample of the clear solution showed it to be 0.22 *M* in hydride and gave an aluminum/hydride ratio of 1.00/1.47. Using isopropyl alcohol (14.0 mmoles), considerable precipitate was obtained; the resulting clear solution was 0.07 *M* and the aluminum/hydride ratio was 1.00/0.98. An analysis of the solid gave 1.00/1.16 for the aluminum/hydride ratio. Using methyl alcohol (14.0 mmoles), a clear solution was obtained which was 0.30 *M* in hydride and exhibited an aluminum/hydride ratio of 1.00/0.99.

Reaction of Lithium Aluminum Hydride with Lithium Aluminum Tetraalkoxides in Diglyme.—Lithium aluminum hydride, 10 ml. of an 0.80 *M* solution (8.0 mmoles), in diglyme was added to each of three flasks containing 21.5 mmoles of lithium aluminum tetramethoxide, -ethoxide, and -isopropoxide, respectively, suspended in 50 ml. of diglyme. The mixtures were allowed to stand several days. The mixture containing the tetramethoxide became clear and additional tetramethoxide was added. The -ethoxide and -isopropoxide mixtures showed only a slight decrease in the amount of insoluble matter present. Analyses of the clear solutions after several days standing gave for the soluble aluminum/hydride ratios, 1.00/0.82, 1.00/2.36, and 1.00/2.49 for the tetramethoxide, -ethoxide, and -isopropoxide, respectively.

A similar reaction in ether showed a marked decrease in lithium aluminum hydride concentration in the presence of lithium aluminum tetraethoxide after 10 days, with the aluminum/hydride ratio in solution remaining 1.00/4.00. Since a large excess of the tetraethoxide was present, no analysis was made of the solid, although it was shown to contain some insoluble hydride. With the tetraisopropoxide, little reaction was evident after 10 days and the soluble aluminum/hydride ratio was 1.00/3.80.

An Attempt to Obtain Lithium Triethoxyaluminumhydride in Diglyme at 135–140°.—A 50-ml. solution, 0.49 *M* in lithium aluminum hydride (24.5 mmoles), to which had been added 73.5 mmoles of ethyl alcohol at room temperature, was heated at 130–140° under a dry nitrogen atmosphere for 15 hr. with rapid stirring. No decrease was noticed in the white precipitate present. Upon cooling, the solution became extremely gelatinous which made analysis extremely difficult. A sample extracted with ether gave an aluminum/hydride ratio of 1.00/1.23.

Preparation and Purification of Lithium Triethoxyaluminumhydride in Ether.—In the usual apparatus, ethyl alcohol (294 mmoles) was added to lithium aluminum hydride (98.0 mmoles) in 200 ml. of ethyl ether. The precipitate was allowed to settle and the clear solution was removed under nitrogen pressure through a sintered glass filter. The precipitate was washed three times with ether but still retained some active hydrogen. Analysis of the main solution plus the first wash fraction gave a ratio of 1.00/1.26 for aluminum/hydride. All attempts to precipitate the soluble hydride from the ether with hexane (b.p. 60–70°) were unsuccessful. Evaporation of the solution to a sirup, followed by addition of hexane, resulted in the formation of a small amount of precipitate. Analysis of the resulting hexane solution gave an aluminum/hydride ratio of 1.00/1.13. Analysis after standing for several days gave 1.00/0.97 for aluminum/hydride. It was found that the ether could be removed under vacuum until only a white solid remained. The solid was almost completely soluble in hexane (60–70°).

An identical experiment conducted in tetrahydrofuran showed no change in the aluminum/hydride ratio in the hexane-soluble fraction from the original value: 1.00/1.40 in tetrahydrofuran and 1.00/1.41 in hexane.

Reaction of Lithium Triethoxyaluminumhydride with Ethyl Benzoate.—The following procedure is representative of that used in determining the reactivities of the alkoxyaluminumhydrides toward various organic compounds.

To 100 ml. of a 0.29 *M* lithium aluminum hydride (29.0 mmoles) solution in diglyme was added 5.1 ml. of ethyl alcohol (87 mmoles). Hydrogen evolution amounted to 90 mmoles. Next, 10 ml. of a 1.04 *M* solution of ethyl benzoate (10.4 mmoles) in diglyme was added to the above mixture which had been cooled to 0°. Hydrolysis after 1 hr. at 0° yielded 6.3 mmoles of hydrogen. Therefore, hydride loss from solution by reduction amounted to 19.7 mmoles corresponding closely to the 2 moles of hydride required for total reduction to the alcohol.

Solubility of Lithium Aluminum Hydride in Diglyme.—The apparatus consisted of an ethylene glycol temperature bath in which was placed a flask equipped with an air stirrer and maintained under a positive pressure of dry nitrogen. Samples were removed for analysis by means of a glass-wool tipped pipet. Sufficient time was allowed to obtain equilibrium as shown by no

TABLE VII
SOLUBILITY OF LITHIUM ALUMINUM HYDRIDE IN DIGLYME

Temp., °C.	Molar concn.
90	2.98
77	2.34
54	1.93
28	1.02
0	0.27

change in concentration with time. Results are shown in Table VII.

No reaction was noted between the solvent and the hydride even after several days at 90°. No gas evolution was evident and the aluminum/hydride ratio in solution remained at 1.00/4.00.

Removal of the solvent from a lithium aluminum hydride solution in diglyme under vacuum at 60° for 24 hr. resulted in the deposition of a white solid corresponding in analysis to a disolvate. *Anal.* Calcd. for $\text{LiAlH}_4 \cdot 2$ diglyme: Al, 8.82; H⁻, 1.31. Found: Al, 8.65; H⁻, 1.2. The solid melted at 82–84°.

Analysis of a saturated ether solution of lithium aluminum hydride obtained by removal of ether under vacuum showed it to be 4.0 *M*, corresponding to the results reported by Finholt, Bond, and Schlesinger.⁵

Reduction of *n*-Butyronitrile with Lithium Aluminum Hydride and Lithium Trimethoxyaluminumhydride.—In the apparatus previously described, with the syringe replaced with a pressure-equalized dropping funnel and the flask placed in an ice bath at 0°, 10 ml. of a 1.00 *M* butyronitrile solution (10.0 mmoles) was added in 4 sec. to 25 ml. of 0.47 *M* lithium trimethoxyaluminumhydride (11.7 mmoles) in diglyme with rapid stirring. The reaction was quenched after 5 min. with methyl alcohol. Hydrogen evolution was 238 ml. at 26° (749 mm.) or 9.2 mmoles. Hydride loss was 11.7 – 9.2 = 2.5 mmoles. Therefore hydride loss/nitrile was 0.25.

In an identical experiment, 10 ml. of a 1.00 *M* butyronitrile (10.0 mmoles) solution in diglyme was added in 4 sec. to 25 ml. of a 0.44 *M* lithium aluminum hydride solution (11.0 mmoles) at 0°. After 5 min. the reaction was quenched with methyl alcohol giving 1.010 l. of hydrogen at 25° (744 mm.) or 39.2 mmoles. Hydride loss was 44.0 – 39.2 = 4.8 mmoles, or hydride loss/nitrile was 0.48, almost twice that with lithium trimethoxyaluminumhydride.

At 0°, the lithium aluminum hydride solution was cloudy due to a solubility of only 0.27 *M* at 0°; however, it cleared immediately upon the addition of the nitrile solution and the reaction then proceeded homogeneously. The temperature rise initially in both reactions upon addition of the nitrile solution was 5°.

Reaction of Benzonitrile with Lithium Aluminum Hydride in Diglyme.—The following reaction shows the high aldehyde yield which is obtained with benzonitrile when lithium aluminum hydride is present in a 1:1 molar ratio, or a fourfold excess of hydride.

In the usual apparatus, 25 ml. of 0.49 *M* lithium aluminum hydride (12.2 mmoles) solution in diglyme was added to 1.291 g. of benzonitrile (12.5 mmoles) in 10 ml. of diglyme cooled to 0°. Addition time was 6 min. The solution assumed a bright yellow color during the reaction. After 1 hr., hydrolysis liberated 33.6 mmoles of hydrogen. Therefore, hydride loss/nitrile was 1.21/1.00. Analysis showed the presence of 11.5 mmoles of benzaldehyde corresponding to a 92% yield based upon nitrile used.

Effect of Solvent upon the Reduction of *n*-Butyronitrile with Lithium Ethoxy Substituted Aluminumhydride.—The following experiment is typical of the series which was run to study the aldehyde yields obtained by reducing benzonitrile and *n*-butyronitrile in ether, tetrahydrofuran, and diglyme with lithium aluminum hydride, and solutions of the latter to which had been added 3 moles of various alcohols.

Three reactions were run simultaneously in which 3 moles of ethyl alcohol was added to solutions of lithium aluminum hydride in ether, tetrahydrofuran, and diglyme. The resulting solutions or mixtures were then added to the nitrile solutions. After hydrolysis, the usual aldehyde analyses were performed. The reactants are given in Table VIII. The melting point of the 2,4-dinitrophenylhydrazones was 123–124°. In all three cases complete hydride utilization occurred.

Reduction of *n*-Butyronitrile with Lithium Triethoxyaluminumhydride in Ether.—The following reduction was run by adding the entire triethoxy mixture, including the white precipitate formed, to the nitrile solution. The ethoxy mixture was prepared by slowly adding 1.80 ml. of ethyl alcohol (31 mmoles) to 25 ml. of 0.44 *M* lithium aluminum hydride (11.0 mmoles) in ether cooled to –80° to reduce alcohol loss during the vigorous reaction. The resulting solution and precipitate were allowed to warm to 0°, and then added to 10 ml. of 1.00 *M* *n*-butyronitrile (10.0 mmoles) in ether also at 0°. After 1 hr. at 0°, the mixture was hydrolyzed with 20 ml. of 2 *N* hydrochloric acid and the ether carefully removed under vacuum. No active hydrogen was evident during the hydrolysis. Analysis with 2,4-dinitrophenyl-

TABLE VIII
REACTION OF *n*-BUTYRONITRILE WITH LITHIUM
TRIETHOXYALUMINOHYDRIDE AT 25°

		Diglyme, 25 ml.	THF, 25 ml.	Ether, 25 ml.
LiAlH ₄ solution	molarity	0.46	0.41	0.41
	mmoles	11.5	10.2	10.2
Ethyl alcohol added	ml.	2.00	1.75	1.75
	mmoles	33	30	30
Butyronitrile solution	ml.	10.0	10.0	10.0
	molarity	1.00	1.00	1.00
	mmoles	10.0	10.0	10.0
Reaction time	min.	15.0	15.0	15.0
Aldehyde yield	%	15	25	59

hydrazine gave a derivative corresponding to a 68% yield of *n*-butyraldehyde, melting at 123–124°

Preparation of Lithium Di-*t*-butoxyomomethoxyaluminumohydride in Ether and Reduction of Butyronitrile.—Methyl alcohol (0.80 ml., 20 mmoles) was added by means of a hypodermic syringe to 50 ml. of 0.40 *M* lithium di-*t*-butoxyaluminumohydride in ether over a 7-min. period. Hydrogen evolution was measured as 0.58 l. at 25° (737 mm.), or 22.0 mmoles. The solution remained crystal clear. Analysis showed it to be 0.40 *M* in hydride and gave a hydride/aluminum ratio of 1.04/1.00.

From this solution, 20 ml. (8.0 mmoles) was added in 3 min. to 0.576 g. of *n*-butyronitrile (8.3 mmoles) in 10 ml. of anhydrous ether at 0°. After 1 hr., no physical changes were evident in the reaction mixture and no hydrogen evolution had occurred. Upon

hydrolysis, 20 ml. of hydrogen was collected at 25° (738 mm.), 0.8 mmole at STP. *n*-Butyraldehyde, isolated with 2,4-dinitrophenylhydrazine, amounted to 1.56 mmoles, corresponding to a 21.6% yield based upon hydride utilization.

Preparation of Lithium Triethoxyaluminumohydride in Ether.—In the apparatus described previously, 32.1 ml. of ethyl alcohol (0.549 mole) was added to 300 ml. of 0.61 *M* lithium aluminum hydride (0.183 mole) in ether over a 45-min. period at room temperature. Hydrogen evolution was measured as 14.68 l. at 25° (739 mm.) or 0.565 mole at STP. Considerable white precipitate formed which was allowed to settle overnight. The clear solution was transferred under dry nitrogen pressure through a sintered glass disk into a clean dry flask. An analysis of a 5-ml. sample of the clear solution gave 77.8 ml. of hydrogen at 26° (740 mm.) or 2.98 mmoles, and 0.9345 g. of aluminum 8-hydroxyquinolate or 2.03 mmoles. The solution was therefore 0.60 *M* in hydride and had a hydride/aluminum ratio of 1.47/1.00.

Reduction of Capronitrile with Lithium Triethoxyaluminumohydride in Ether.—This reaction is typical of other nitrile reductions. In the previously described apparatus 10 ml. of 0.65 *M* lithium triethoxyaluminumohydride (6.5 mmoles) solution in ether giving a hydride/aluminum ratio of 1.47/1.00 was added to 0.624 g. of capronitrile (6.4 mmoles) in 5 ml. of ether. The nitrile was weighed out using a hypodermic syringe. The addition time for the hydride solution was 6 min. The reaction mixture immediately took on an orange color and became cloudy and viscous, becoming more viscous as the reaction proceeded. No hydrogen evolution was evident during the reaction. Hydrolysis after 15 min. showed no unreacted hydride. Following the usual aldehyde analysis, 1.0655 g. of 2,4-dinitrophenylhydrazone was obtained, melting at 104–106°, corresponding to 3.81 mmoles of caproaldehyde, a 59.5% yield.

[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY, LAFAYETTE, IND.]

Selective Reductions. IV. The Partial Reduction of Nitriles with Lithium Triethoxyaluminumohydride—A Convenient Aldehyde Synthesis^{1,2}

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The reaction of nitriles with "lithium triethoxyaluminumohydride" (from the treatment of 1 mole of lithium aluminum hydride in ether with 3 moles of ethanol or 1.5 moles of ethyl acetate) produces an addition product which is readily hydrolyzed to the corresponding aldehyde. A simple study of the variables has led to conditions which provide the basis for a relatively simple, but broadly general, synthetic procedure. Aliphatic and aromatic nitriles of widely varying structural types have been transformed into the aldehydes, generally in yields of 70 to 90%. The factors influencing the selective reduction of nitriles by hydride reagents are discussed.

In the past the Stephen reaction has been the recommended procedure for converting a nitrile into the corresponding aldehyde.⁵ However, while it is usually satisfactory for aromatic nitriles, it has proved less than satisfactory for aliphatic derivatives.^{6,7}

It was suggested that the controlled reduction of aliphatic nitriles at low temperatures by lithium aluminum hydride provides a convenient synthetic route.⁸ Unfortunately, the experimental details have not appeared and numerous workers have experienced difficulty with this synthesis.⁹

(1) Previous studies in this general area of research have appeared in connection with other series. For a survey of the results of these investigations, see H. C. Brown, *J. Chem. Educ.*, **38**, 173 (1961), and H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., Chapter 17.

(2) Based upon a thesis submitted by C. P. Garg in January, 1962, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) Research assistant on a grant provided by the Parke, Davis and Co., 1957–1958.

(4) Research assistant on Contract DA-33-008-ORD-992 supported by the Office of Ordnance Research, U. S. Army.

(5) H. Stephen, *J. Chem. Soc.*, 1874 (1925).

(6) E. Mossetig, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 218–257.

(7) C. J. Claus and J. L. Morgenthau, Jr., *J. Am. Chem. Soc.*, **73**, 5005 (1951); J. W. Williams, *ibid.*, **61**, 2248 (1939); E. Lieber, *ibid.*, **71**, 2862 (1949); J. A. Knight and H. D. Zook, *ibid.*, **74**, 4560 (1952); S. Peitra and C. Trincherà, *Gazz. chim. ital.*, **85**, 1705 (1955); C. F. H. Allen, M. R. Gilbert, and D. M. Young, *J. Org. Chem.*, **2**, 231 (1937).

(8) L. Friedman, Abstracts of Papers, 116th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept., 1949, p. 5-M.

(9) N. C. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, Inc., New York, N. Y., 1956.

Recently, sodium triethoxyaluminumohydride has been applied successfully for the conversion of various aromatic nitriles to the corresponding aldehydes, but it was reported that this procedure is not applicable to the selective reduction of aliphatic nitriles.¹⁰

We have had considerable success in utilizing alkoxy substituted lithium aluminumohydrides, conveniently synthesized by treating lithium aluminum hydride with the appropriate alcohol,^{11,12} for selective reductions. Thus, lithium tri-*t*-butoxyaluminumohydride reduces both acid chlorides¹³ and phenyl esters¹⁴ into the corresponding aldehydes. Lithium trimethoxyaluminumohydride has proved valuable for the stereoselective reduction of bicyclic ketones.¹⁵ Finally, lithium di- and triethoxyaluminumohydrides have provided a convenient synthetic route from the dimethylamides to the corresponding aldehydes.¹⁶

It was recently observed that lithium triethoxyaluminumohydride¹⁷ reacts with *n*-butyronitrile and capro-

(10) G. Hesse and R. Schrödel, *Angew. Chem.*, **68**, 438 (1956); *Ann.*, **607**, 24 (1957).

(11) H. C. Brown and R. F. McFarlin, *J. Am. Chem. Soc.*, **80**, 5372 (1958).

(12) H. C. Brown and C. J. Shoaf, *ibid.*, **86**, 1079 (1964).

(13) H. C. Brown and B. C. Subba Rao, *ibid.*, **80**, 5377 (1958).

(14) H. C. Brown and P. M. Weissman, manuscript in preparation.

(15) H. C. Brown and H. R. Deck, manuscript in preparation.

(16) H. C. Brown and A. Tsukamoto, *J. Am. Chem. Soc.*, **81**, 502 (1959); **86**, 1089 (1964).

(17) It is convenient to refer to the product from the reaction of 3 moles of ethanol, or 1.5 moles of ethyl acetate, with 1 mole of lithium aluminum