TABLE I

Concn. g./100 ml.	$\tau \times 10^2$ (cm.$^{-1}$)	I_1/I_2	Turbidity correction factor	$\tau \times 10^2$ (cor.)	$H\frac{c}{\tau} \times 10^8$
0.0290	2.26	1.67	1.59	3.60	2.54
.0145	1.035	1.78	1.74	1.80	2.54
.0097	0.68	1.83	1.81	1.23	2.49

weight-average molecular weight of $M = 40 \times 10^6$ with a probable error of 5%. In this determination of the molecular weights from light scattering no assumptions need be made about the percentage of hydration of the particles. If the length and molecular weight of the particles as determined by the light scattering measurements are used with a value of 0.73 for the partial specific volume of the virus, the diameter of the cylindrically shaped virus particles can be calculated to be 15.2 mμ. This value is in agreement with that obtained in X-ray[22] and electron microscope[16] studies.

Summary

Light scattering measurements were made on a freshly prepared sample of purified tobacco mosaic virus. The length of the particles determined from dissymmetry of light scattered by the solutions were found to be 270 mμ. Application of the dissymmetry to turbidity measurements gave a weight average molecular weight of 40 millions for the particles. These values are in complete agreement with sizes determined from electron microscope and viscosity studies made on the same sample. This agreement indicates the validity of the light scattering method.

For dilute solutions of tobacco mosaic in water the dissymmetry decreases with increasing virus concentration thus indicating that strong interaction with a consequent increase in order of the scattering particles is occurring. However, the dissymmetry is independent of concentration for dilute solutions of the virus in 0.1 M sodium phosphate buffer at pH 7.

PRINCETON, N. J.
CAMBRIDGE, ENGLAND
BERKELEY, CALIFORNIA RECEIVED NOVEMBER 18, 1946

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

Reduction of Organic Compounds by Lithium Aluminum Hydride. I. Aldehydes, Ketones, Esters, Acid Chlorides and Acid Anhydrides

BY ROBERT F. NYSTROM[1] AND WELDON G. BROWN

Following the discovery of lithium aluminum hydride by Finholt, Bond and Schlesinger[2] some preliminary experiments were carried out on a vacuum-line scale by Finholt, Schlesinger and Wilzbach[3] to ascertain its behavior toward some common types of organic compounds. These experiments indicated that this hydride is capable of reducing carbonyl, carbalkoxy, acyl chloride and nitro groups, but is without action on the double bond of simple olefins. It was thus evident that the reagent offered some promise as a synthetic tool and, with the consent and coöperation of these authors, we have undertaken a more extensive survey of such applications.

The attractive features of lithium aluminum hydride as a reagent which, combined, place it in a unique position are (1) that it is easily prepared on either a large or a small scale from commercially available lithium hydride, (2) that it is indefinitely stable at room temperature, (3) that it is ether-soluble, (4) that as compared with other reducing agents, excepting hydrogen, it has a favorable ratio of reducing capacity to mass, (5) that the reductions occur at room temperature, and (6) that no unusual equipment is needed. The present high cost of lithium hydride is partially offset by the consideration stated under (4) above. As the technique stands at present, compounds which are insoluble in ether do not react satisfactorily, and there is a further limitation connected with the fact that some substances containing active hydrogen decompose the reagent with the liberation of hydrogen.

This paper summarizes the results achieved in the reduction of representative aldehydes, ketones, acid chlorides and acid anhydrides. These functional groups, in the cases thus far examined, are reduced to the alcohol stage with extreme rapidity and with virtually no side-reactions. The yields appear to be limited principally by the efficiency of the procedures employed subsequently in isolating the products. As determined by the hydride consumed, the reductions proceed quantitatively inac cordance with the following general equations

Aldehydes and ketones

$$4R_2CO + LiAlH_4 \longrightarrow LiAl(OCHR_2)_4$$

Esters

$$2RCOOR' + LiAlH_4 \longrightarrow LiAl(OR')_2(OCH_2R)_2$$

Acid chlorides

$$2RCOCl + LiAlH_4 \longrightarrow LiAlCl_2(OCH_2R)_2$$

Acid anhydrides

$$(RCO)_2O + LiAlH_4 \longrightarrow LiAlO(OCH_2R)_2$$

The unsaturated compounds for which data are included in this summary are crotonaldehyde, methyl oleate and sorbyl chloride, the product in

(1) Naval Research Laboratory Fellow.

(2) Finholt, Bond and Schlesinger, THIS JOURNAL, **69**, 1199 (1947).

(3) Finholt, Schlesinger and Wilzbach, unpublished work.

each case being the corresponding unsaturated alcohol. However, as will be shown in forthcoming papers, the carbon-to-carbon double bonds in certain unsaturated ketones, acids, nitro compounds and heterocyclic nitrogen compounds are hydrogenated by the reagent. The data accumulated thus far point to a general similarity, but not a one-to-one correspondence, in the specificity and mode of action of lithium aluminum hydride and of sodium metal in hydroxylic media (alcohol or moist ether).

Experimental

In general, the experimental procedures for effecting reduction by lithium aluminum hydride are substantially identical to those commonly employed in Grignard syntheses. Starting with a prepared solution of lithium aluminum hydride in ether, the same precautions against the access of moisture are taken, and following the usual Grignard technique the substance to be reduced, generally diluted with ether, is added with stirring at a rate determined by the vigor of the reaction as indicated by the refluxing ether. The reaction results in precipitation of a complex alcoholate which may cause the mixture to thicken and may necessitate the addition of further quantities of ether. As in Grignard syntheses, the metal alcoholate is decomposed by acid hydrolysis and the product is isolated from the ether extract.

For convenience, solutions of lithium aluminum hydride in diethyl ether were prepared in bulk, following the procedure of Finholt, Schlesinger and Bond.[2] These stock solutions were assayed by the method given by these authors and were stored in closed containers until needed. It has been our practice to use an excess of the reagent, and consequently in the hydrolytic decomposition of the reaction mixture quantities of hydrogen gas are formed. On this account the use of spark-proof stirring motors is recommended.

A variation of this general procedure is employed for the special case in which the substance to be reduced is of limited solubility in ether. It consists of placing the material in the porous cup of an extractor so that it is carried into the reaction flask by the refluxing ether. We have actually used a Soxhlet extractor for this purpose, but one providing continuous solvent return would be preferable.

The two modes of operation are illustrated by the description of the preparation of *n*-heptyl alcohol from *n*-heptaldehyde and of phthalyl alcohol from phthalic anhydride.

Reduction of an Ether-soluble Compound, *n*-Heptaldehyde to *n*-Heptyl Alcohol.—A solution of 19 g. (0.5 mole) of lithium aluminum hydride in 600 ml. of ether was placed in a two-liter three-necked flask equipped with reflux condenser, dropping funnel and mechanical stirrer, and protected from moisture until completion of the reaction by calcium chloride tubes attached to the openings. Through the dropping funnel, 200 g. (1.75 moles) of *n*-heptaldehyde (b. p. 152–152.5° (748 mm.), $n^{20}D$ 1.4133) was introduced at a rate such as to produce gentle reflux. Ten minutes after the last addition and with continued stirring, water was added dropwise and cautiously, cooling the flask if during the exothermic decomposition of excess hydride the refluxing becomes too vigorous. The mixture was then poured into 200 ml. of ice water, and to this was then added 1 liter of 10% sulfuric acid. After separation of the ether layer, the aqueous layer was extracted with two further 100-ml. portions of ether. The product obtained after evaporation of the ether from the dried ether extracts was fractionally distilled, using a 15-inch wire-spiral column, whereupon an 86% yield of *n*-heptyl alcohol (b. p. 175–175.5° (750 mm.)) was secured.

Reduction of a Compound Slightly Soluble in Ether, Phthalic Anhydride to Phthalyl Alcohol.—The apparatus differed from that described above in that a Soxhlet extractor was inserted between the flask and the reflux condenser. A solution containing 4.5 g. (0.12 mole) of lithium aluminum hydride in 500 ml. of ether was placed in the flask, and 16.8 g. (0.113 mole) of phthalic anhydride (m. p. 130°) was placed in the extractor thimble. The solution was then warmed until all of the anhydride had been transferred to the reaction flask. When this was complete, the extractor was replaced by a reflux condenser, the stirrer was started and water was added dropwise to decompose the excess hydride. The mixture was poured into 200 ml. of ice water and then acidified by the addition of 300 ml. of 10% sulfuric acid. The mixture was transferred to a continuous ether extractor containing an additional 500 ml. of ether and the extraction was continued for one day. Upon evaporation of the ether from the dried extract, a solid residue having a light yellow color remained. Washing with two 100-ml. portions of hot petroleum ether furnished colorless crystals of phthalyl alcohol, m. p. 64°, in 87% yield. The diacetate derivative melted at 35°.

Experimental Results

Following procedures similar to those outlined above, modified only to the extent necessitated by the individual problems of isolating and purifying the products, a number of aldehydes, ketones, esters, acid anhydrides and acid chlorides have been reduced with the results summarized in Table I. The stated yields pertain to products having physical constants identical with the best literature values within acceptable limits. The alcohols were further identified by derivatives—in most instances the N-phenylcarbamates.

TABLE I

REDUCTIONS BY LITHIUM ALUMINUM HYDRIDE

Compound reduced	Product	Yield, %
	Aldehydes	
n-Heptaldehyde	*n*-Heptyl alcohol	86
Crotonaldehyde	Crotyl alcohol	70
Benzaldehyde	Benzyl alcohol	85
	Ketones	
Butanone-2	*s*-Butyl alcohol	80
Cyclopentanone	Cyclopentanol	62
Acetomesitylene	Mesitylmethylcarbinol	[a]
	Esters	
Ethyl palmitate	Hexadecanol-1	98
Methyl laurate	Dodecanol-1	94
Ethyl adipate	Hexandiol-1,6	83
Methyl oleate	Oleyl alcohol	86
Ethyl benzoate	Benzyl alcohol	90
	Acid Chlorides	
Benzoyl chloride	Benzyl alcohol	72
Palmityl chloride	Hexadecanol-1	99
i-Caproyl chloride	Isohexyl alcohol	95
Trimethylacetyl chloride	Neopentyl alcohol	86
sym-o-Phthalyl chloride	Phthalyl alcohol	95
Sorbyl chloride	Sorbyl alcohol	98
	Anhydrides	
Benzoic anhydride	Benzyl alcohol	87
Phthalic anhydride	Phthalyl alcohol	87

[a] Crude mesitylmethylcarbinol, melting 68–69°, was obtained in quantitative yield. After two recrystallizations from methanol it melted sharply at 69°. The literature melting point is 71° (Klages and Allendorff, *Ber.*, 31, 1008 (1898)).

Acknowledgment.—The support afforded us by the Naval Research Laboratory in the conduct of this work is gratefully acknowledged. We are especially indebted to Dr. H. I. Schlesinger, Dr. A. E. Finholt and Dr. K. E. Wilzbach for their generous assistance and for making available to us the experience gained in their pioneering work in this field.

Summary

The reduction of aldehydes, ketones, esters, acid chlorides and acid anhydrides to the corresponding alcohols by lithium aluminum hydride in ether solution is described. Because of the ease and convenience with which these reductions may be carried out, the technique being similar to that employed in Grignard syntheses, and because of the uniformly good yields, it is believed to be a useful synthetic process. It will be particularly valuable for the preparation of unsaturated alcohols, since double bonds are not reduced.

CHICAGO, ILLINOIS RECEIVED NOVEMBER 27, 1946

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

Lithium Aluminum Hydride, Aluminum Hydride and Lithium Gallium Hydride, and Some of their Applications in Organic and Inorganic Chemistry[1]

BY A. E. FINHOLT, A. C. BOND, JR.,[2] AND H. I. SCHLESINGER

When lithium hydride is treated with an ether solution of aluminum chloride under the conditions described in the experimental part of this paper, the new ether soluble compound, lithium aluminum hydride, $LiAlH_4$, is formed according to the equation

$$4LiH + AlCl_3 \xrightarrow{\text{ether}} LiAlH_4 + 3LiCl$$

Addition of further quantities of aluminum chloride yields an ethereal solution of aluminum hydride

$$3LiAlH_4 + AlCl_3 \xrightarrow{\text{ether}} 4AlH_3 + 3LiCl$$

The latter solution is not stable; it soon deposits a white solid in which the atomic ratio of aluminum to hydrogen still is 3:1, but from which the ether cannot be completely removed without loss of hydrogen.[3] Lithium aluminum hydride, on the other hand, may be freed from the solvent completely by evaporation of the latter under suitable conditions. Lithium gallium hydride, $LiGaH_4$, has been prepared by the method used for the corresponding aluminum compound, but has not yet been studied in detail.[4]

Although we have obtained indirect evidence of the existence of sodium and of calcium aluminum hydrides, lithium aluminum hydride and lithium gallium hydride are the only compounds containing the AlH_4 and GaH_4 groups as yet isolated.[5a] Nevertheless, the existence of these two compounds, as well as of aluminum hydride and of digallane,[5] demonstrates that the questions raised and widely discussed in connection with the nature of the chemical bonds in the hydrides of boron and in the borohydrides, are not problems unique to boron chemistry. These new developments have, therefore, emphasized the importance of these questions and will, we hope, aid in their solution. But the new compounds, especially lithium aluminum hydride, possess not only theoretical interest; their discovery has already led to significant applications in both inorganic and organic chemistry.

Through the use of lithium aluminum hydride, new methods, far simpler than any hitherto available, have been developed for the preparation of hydrides such as silane and stannane and of their partially alkylated derivatives. In addition, its use has led to the preparation of previously unknown hydrides such as those of zinc and of beryllium. The types of reaction by which these results have been achieved are illustrated by the equations

$$LiAlH_4 + SiCl_4 \xrightarrow{\text{ether}} LiCl + AlCl_3 + SiH_4$$

$$LiAlH_4 + 2(CH_3)_2SnCl_2 \xrightarrow{\text{ether}} LiCl + AlCl_3 + 2(CH_3)_2SnH_2$$

$$LiAlH_4 + (CH_3)_2Zn \xrightarrow{\text{ether}} LiAl(CH_3)_2H_2 + ZnH_2$$

Reactions such as these usually proceed smoothly at room temperature, and in general give excellent yields of products of high purity.[6]

(1) Presented in abbreviated form before the Symposium on Hydrides and Related Compounds at the Chicago meeting of the American Chemical Society, September 10, 1946.

(2) Present address: University of Michigan, Ann Arbor, Michigan.

(3) O. Stecher and E. Wiberg, *Ber.*, **75**, 2003 (1942), have described the preparation of solid aluminum hydride by a method which does not involve the use of ether, but which is far more cumbersome than the procedure herein described. Their product was also not entirely pure.

(4) The terminology, lithium aluminum hydride and lithium gallium hydride, is not entirely consistent with the name "borohydride" used by Schlesinger and his collaborators for the corresponding boron compounds. Since the latter term is also not entirely satisfactory, and the terminology would not be very euphonious for the aluminum and gallium compounds, we have tentatively decided on the nomenclature herein employed.

(5a) Since this paper was submitted, sodium and calcium aluminum hydrides have been prepared by us.

(5) E. Wiberg and Th. Johannsen, *Die Chemie*, **55**, 38 (1924).

(6) In some, though by no means in all such reactions, lithium hydride may be used in place of lithium aluminum hydride. Even in those cases in which lithium hydride gives the desired product, the reactions are slower and the yields less satisfactory. For some purposes aluminum hydride may be advantageously employed in place of the lithium salt (see page 1202).