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Reduction of Organic Compounds by Mixed Hydrides. I. Nitriles

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The reducing properties of lithium aluminum hydride have been modified by the addition of aluminum chloride. By use of this acidic reagent improvements have been made in the conversion of nitriles to amines as well as in the selective reduction of aromatic nitroaldehydes and bromoacid chlorides.

The action of lithium aluminum hydride on organic compounds can be modified by the addition of a Lewis acid, aluminum chloride. When molar quantities of hydride and aluminum chloride are mixed, the first reaction is the formation of aluminum hydride and lithium chloride.[1] Next, further reaction might take place to form aluminum chlorohydride, AlH_2Cl.[2] The first recorded use of the *lithium aluminum hydride–aluminum* chloride reagent for the reduction of organic compounds in the ratio one and one-half moles of halide per mole of hydride has been announced by Brown.[3] In the same year Wiberg and Jahn[4] reduced some common types of organic compounds, including nitriles and nitro compounds, mainly with a mixture of AlH_2Cl and $AlHCl_2$. In this Laboratory, using one hour reaction times and a reducing solution containing equimolar amounts of aluminum chloride and lithium aluminum hydride, aromatic nitro compounds are not reduced to amines, as reported by Wiberg.[4] Therefore, a study is now underway to determine the constitution of the reduction mixture described in this paper.

The selective reduction of organic compounds by this new reagent is particularly attractive. Some nitriles, which contain active hydrogen with respect to lithium aluminum hydride, are reduced completely without liberation of hydrogen by use of lithium aluminum hydride–aluminum chloride. Also, it has been found that the reduction of other nitriles is facilitated and improved by use of the acidic hydride. Another example of the usefulness of this new reagent is the reduction of certain aromatic nitroaldehydes to nitroalcohols. Still another example of its selectivity is the conversion of bromoacid chlorides and bromoketones to the bromohydrin in high yields. Finally, an explanation for the virtual cessation of the reduction of certain alkyl halides after one of the four hydrogens of the original lithium aluminum hydride has reacted might be provided by this new reagent.

Experimental

The experimental results are summarized in Table I. The stated yields pertain to products having physical constants identical with the best literature values within acceptable limits. The amines were further identified in most cases by either the acetyl or benzoyl derivatives.

TABLE I

REDUCTIONS BY LITHIUM ALUMINUM HYDRIDE AND LITHIUM ALUMINUM HYDRIDE–ALUMINUM CHLORIDE MIXTURE

Compd. reduced	Product	Yield, %	Hydride employed (reducing ratio)[a]	Active hydrogen,[b] %
Diphenylacetonitrile	2,2-Diphenylethylamine	61	$LiAlH_4$ (1:1)[5,6]	48
Diphenylacetonitrile	2,2-Diphenylethylamine	46[c]	$LiAlH_4$ (1:1)	48
Diphenylacetonitrile	2,2-Diphenylethylamine	91	$LiAlH_4$–$AlCl_3$ (1:1)	3
Phenylacetonitrile	Phenethylamine	46	$LiAlH_4$ (1:1)	59
Phenylacetonitrile	Phenethylamine	83	$LiAlH_4$–$AlCl_3$ (1:1)	4
Phenylacetonitrile	Phenethylamine	58	$LiAlH_4$–$AlCl_3$ (2:1)	4
Phenylacetonitrile	Phenethylamine	83	$LiAlH_4$–$AlCl_3$ (1.33:1)	4
Sebaconitrile	1,10-Decanediamine	58	$LiAlH_4$ ($^1/_2$:1)	0
Sebaconitrile	1,10-Decanediamine	86	$LiAlH_4$–$AlCl_3$ ($^1/_2$:1)	5
n-Valeronitrile	Pentylamine	63[d]	$LiAlH_4$ (1:1)	8
n-Valeronitrile	Pentylamine	75[d]	$LiAlH_4$–$AlCl_3$ (1:1)	8
p-Nitrotoluene[e]	No reaction		$LiAlH_4$–$AlCl_3$ (1:1)	0
Nitrobenzene[e]	No reaction		$LiAlH_4$–$AlCl_3$ (1:1)	0
p-Nitrobenzaldehyde[e]	*p*-Nitrobenzyl alcohol	75	$LiAlH_4$–$AlCl_3$ (1:1)	0
3-Bromopropionyl chloride	3-Bromo-1-propanol	46	$LiAlH_4$ (1.5:1)	
3-Bromopropionyl chloride	3-Bromo-1-propanol	77	$LiAlH_4$–$AlCl_3$ (1.5:1)	

[a] The reducing ratio () gives the moles of nitrile or organic compound employed per mole of hydride. [b] The active hydrogen values are accurate to about ± 6%. [c] Ethyl acetate was used to destroy the excess hydride. When water is employed for this purpose the possibility exists that the salt of the nitrile (formed *via* active hydrogen) is hydrolyzed to the nitrile which is in turn partially reduced to the amine by some hydride. [d] Appreciable mechanical losses were encountered because of the volatility of the product. [e] The reaction mixture was hydrolyzed five minutes after the last addition of nitro compound.

The reductions have been carried out by adding a known quantity of organic substance to a known quantity of hydride. In some reductions hydrogen is liberated during the addition of organic compound. If this occurs, the volume of gas is measured by means of a wet-test meter which is at-

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(1) A. E. Finholt, A. C. Bond, Jr., and H. I. Schlesinger, THIS JOURNAL, **69**, 1199 (1947).

(2) E. Wiberg and M. Schmidt, *Z. Naturforsch.*, **6b**, 460 (1951).

(3) B. R. Brown, *J. Chem. Soc.*, 2756 (1952).

(4) E. Wiberg and A. Jahn, *Z. Naturforsch.*, **7b**, 580 (1952).

(5) L. H. Amundsen and L. S. Nelson, THIS JOURNAL, **73**, 242 (1951).

(6) R. F. Nystrom and W. G. Brown, *ibid.*, **70**, 3740 (1948).

tached to the system. After the reaction is complete, water is added dropwise to decompose the excess hydride, and the volume of hydrogen is measured.

Filtered solutions of lithium aluminum hydride in diethyl ether are prepared in bulk, following the procedure of Finholt, Bond and Schlesinger.[1] These stock solutions are assayed by the method given by these authors and stored in closed containers until needed. The solid hydride obtained from Metal Hydrides assayed 84% lithium aluminum hydride. However, after dissolving the material in ether and filtering through a sintered glass funnel using helium pressure the product assayed 94% lithium aluminum hydride.

Following procedures similar to those outlined below, modified only to the extent necessitated by the individual problems of isolating and purifying the products, a number of nitriles were reduced using the same concentration of organic material and hydride.

Reduction of Diphenylacetonitrile to 2,2-Diphenylethylamine by $LiAlH_4$.—A one-liter, three-necked flask was equipped with a reflux condenser, a mechanical mercury-sealed stirrer and a dropping funnel. The gas outlet tube on the condenser was attached to two traps cooled at −80° and then to a wet-test meter. A solution of 0.1 mole of lithium aluminum hydride in 250 ml. of ether was placed in the flask. Through the dropping funnel, a solution of 19.3 g. (0.1 mole) of diphenylacetonitrile in 200 ml. of ether was added dropwise to the well-stirred mixture. During the addition of nitrile, hydrogen was liberated and by calculation the standard volume was 1.03 liters. One hour after the last addition of organic compound, water was added dropwise to decompose the excess hydride and the volume of gas evolved was measured. By calculation the standard volume was found to be 5.13 liters. Then 140 ml. of 6 *N* sulfuric acid and 100 ml. of water were added. The clear mixture was transferred to a separatory funnel and, after separating the ether layer, the aqueous layer was extracted with four 100-ml. portions of ether. Next the aqueous layer was cooled by ice-water and potassium hydroxide pellets were cautiously added until the *p*H of the solution was 11. The basic mixture was diluted with 600 ml. of water and then extracted with four 100-ml. portions of ether. From the combined ether extracts there was obtained, after drying over drierite and removal of ether, 6.5 g. of crude material in the acid extract and 14 g. of crude material in the basic extract. The latter was purified by fractional distillation through a 12-inch column under reduced pressure and there was obtained a 61% yield of 2,2-diphenylethylamine, b.p. 182° (14 mm.), m.p. 44–44.5°. The acetyl derivative melted at 88–89°.

Reduction of Diphenylacetonitrile to 2,2-Diphenylethylamine by $LiAlH_4$–$AlCl_3$.—The apparatus described above was employed. A solution of 0.1 mole of lithium aluminum hydride in 100 ml. of ether was placed in the three-necked flask. Through the dropping funnel, a solution of 13.3 g. (0.1 mole) of aluminum chloride in 150 ml. of ether was added rapidly to the hydride solution. Five minutes after the last addition of halide, a solution of 19.3 g. (0.1 mole) of diphenylacetonitrile in 200 ml. of ether was added dropwise to the well-stirred mixture. An evolution of 0.075 liter of hydrogen was noted during the addition of nitrile. One hour after the last addition of organic compound, water was added dropwise to decompose the excess hydride and the volume of gas evolved was measured. By calculation the standard volume of hydrogen was found to be 4.14 liters. The reaction mixture was treated as described in the previous example. From the combined ether extracts there was obtained, after drying over drierite and removal of ether, 0.5 g. of crude material from the acid extract and 21 g. of crude material from the basic extract. The latter was purified by fractional distillation through a 12-inch column under reduced pressure and there was obtained a 91% yield of 2,2-diphenylethylamine, b.p. 184° (17 mm.), m.p. 44–45°. The acetyl derivative melted at 88.5–89°.

Attempted Reduction of *p*-Nitrotoluene by $LiAlH_4$–$AlCl_3$.—The apparatus and techniques described above were employed. During the addition of *p*-nitrotoluene to the hydride solution, no evolution of hydrogen was noted. Five minutes after the last addition of nitro compound, 50 ml. of water was added dropwise to decompose the excess hydride. The organic material was isolated in the usual manner and the starting material was recovered.

By employing longer reaction times before hydrolysis in other experiments, a liberation of hydrogen and production of basic material was noted. The results of these experiments will be reported in a forthcoming paper.

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NOTES

The Relative Rates of Reaction of Hexamethylbenzene and Hexaethylbenzene with Perbenzoic Acid

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The equilibrium constant for the interaction of hexaethylbenzene with iodine to form a 1:1 complex in carbon tetrachloride solution is much less than that for hexamethylbenzene.[1,2] Presumably the alkyl groups of hexaethylbenzene are collectively sufficiently bulky to prevent the close approach of the iodine acceptor to the π-electrons of the aromatic nucleus.[3]

In the absence of such steric problems the equilibrium to form aromatic donor–acceptor complexes is electronically favored by an increase in the number of alkyl substituents in the donor molecule; similarly an increase in the number of alkyl substituents in general enhances the rate at which the aromatic nucleus is attacked by electrophilic reagents.[4] Therefore the possibility has been considered that the steric barrier which leads to repression of formation of the hexaethylbenzene complex might also have an unfavorable effect on the kinetic course of the reaction of hexaethylbenzene with an electrophilic reagent. This point has been tested in the present study by determining the relative rates of reaction of hexamethylbenzene and hexaethylbenzene with perbenzoic acid in chloroform solution at 25°.[5] To evaluate the relative contributions of electronic influences of methyl and ethyl ring substituents to the over-all kinetic picture, the rates of reaction of mesitylene and *sym*-

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(1) L. J. Andrews and R. M. Keefer, THIS JOURNAL, **74**, 4500 (1952).

(2) M. Tamres, D. R. Virzi and S. Searles, *ibid.*, **75**, 4358 (1953).

(3) R. M. Keefer and L. J. Andrews, *ibid.*, **77**, 2164 (1955).

(4) L. J. Andrews, *Chem. Revs.*, **54**, 713 (1954).

(5) It has been established previously that perbenzoic acid functions as an electrophilic reagent in initiating the oxidation of aromatic substances to form ring cleavage products or quinoid derivatives: *cf.* I. M. Roitt and W. A. Waters, *J. Chem. Soc.*, 3060 (1949); S. L. Friess and A. Miller, THIS JOURNAL, **72**, 2611 (1950); S. L. Friess, A. H. Soloway, B. K. Morse and W. C. Ingersoll, *ibid.*, **74**, 1305 (1952).