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

Quantitative Studies on Lithium Aluminum Hydride Reactions[1]

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The reactions of lithium aluminum hydride closely resemble those of Grignard reagents.[3,4,5,6,7] These agents appear to differ principally in the more aggressive behavior of the hydride, resulting in a lessening of side-reactions and of steric influences. An analytical procedure employing lithium aluminum hydride may, therefore, be more generally useful than the Zerewitinoff procedure which was so elegantly refined on a macro scale by Kohler and co-workers.[8,9]

Results obtained in the determination of active hydrogen in alcohols, glycols, phenols and amines are satisfactory. Benzyl alcohol, *n*-amyl alcohol,

TABLE I

COMPARISON OF HYDRIDE METHOD AND ZEREWITINOFF METHOD FOR ENOLIZABLE COMPOUNDS

Compound	Solvent	Active hydrogen, found By $LiAlH_4$	Active hydrogen, found By CH_3MgI
Acetophenone	None	0.03–0.05	0.12^{a}
	Dibutyl ether	.02– .03	
	Diamyl ether		.15,^{b} 0.12^{a} .13–0.23^{c}
	Dioxane	.38– .42	.78^{e}
Acetomesitylene	None	.02– .03	
	Dibutyl ether	.01– .03	
	Diamyl ether		.73^{d}–0.99^{b}
	Dioxane	.10– .13	
	Xylene		1.03^{e}
Ethyl acetoacetate	None	.67– .73	
	Dibutyl ether	.57– .74	1.00^{f}
	Diamyl ether		0.92,^{g} 0.95^{h}
	Dioxane	.74– .78	
	Pyridine		.87^{h}
Ethyl malonate	None	.45– .46	
	Dibutyl ether	.52	1.00^{f}
	Pyridine		1.70^{k}
Indanedione	Dioxane	.23– .30	
	Ethyl morpholine	1.17–1.18	

[a] Lieff, Wright and Hibbert, THIS JOURNAL, **61**, 865 (1939). [b] Kohler, Stone and Fuson, *ibid.*, 49, 3181 (1927). [c] Hollyday and Cottle, *Ind. Eng. Chem.*, *Anal. Ed.*, 14, 774 (1942). [d] R. G. Kadesch, Ph.D. Thesis, University of Chicago, 1941. [e] Smith and Guss, THIS JOURNAL, 59, 804 (1937). [f] Fuchs, Ishler and Sandoff, *Ind. Eng. Chem.*, *Anal. Ed.*, **12**, 507 (1940). [g] Hibbert and Sudborough, *J. Chem. Soc.*, **85**, 933 (1904). [h] Zerewitinoff, *Ber.*, 41, 2223 (1908). [k] Fischer and Walter, *ibid.*, **60**, 1987 (1927).

TABLE II

DETERMINATION OF VARIOUS REDUCIBLE GROUPS[n]

Compound	Active H_2 found	Moles $LiAlH_4$ consumed	Temp., °C.	Solvent[v]
I Carbonyl group (theor.: No active hydrogen; 0.25 mole $LiAlH_4$)				
Cyclopentanone	0	0.227–0.238	75–90	A
	0	.245	24	B
Xanthone	0	.248– .255	26	B
	0	.278	100	B
Benzoin	1.02^{a}	.480^{b}	25	B
Benzil	0	.512– .514^{b}	25	B
II Esters (theor.: no active hydrogen; 0.5 mole $LiAlH_4$)				
Ethyl benzoate	0	0.491–0.500	28	A
Butyl carbitol acetate	0	.492– .495	25	A
Stearin	0	1.495^{c}	26	B
		1.520^{c}	90	B
Palmitin	0	1.483^{c}	27	B
		1.515^{c}	75	B
β-Propiolactone	0	0.520	95	B
γ-Valerolactone	0	.475– .490	28	A
α-Angelica lactone	0.10	.497– .510	90	B
	0.10	.388	27	B
β-Angelica lactone	0	.478– .519	90	B
Di-*n*-butylcarbonate	0	.685– .751^{d}	25	A
		.735^{d}	80	A
Protocatechualdehyde carbonate	0	.875^{a}	27	B
	0	1.015^{a}	80	B
1-Tyrosine ethyl ester	2.0–2.4^{m}	0.95–1.10^{e}	90	B
Coumarin	0	.640	100	B
III Acids (theor.: 1.0 active hydrogen; 0.75 mole $LiAlH_4$)				
Benzoic	0.99–1.02	0.503–0.517	25	A
	1.02	.595	25	B
	1.02–1.03	.753–0.758	75–90	B
Stearic	1.00–1.01	.613–0.615	25	A
	1.02	.765	75	B
	1.00	.809–0.838	75–85	A
Salicylic	2.01^{f}	....	28	A
Triphenylacetic	1.04–1.05	.81–0.84^{k}	100	B
Phthalic anhydride	0^{g}	.96–0.99^{c}	85–90	A
IV Amides (theor.: 1.0 active hydrogen; 0.75 mole $LiAlH_4$)				
Benzamide	1.96^{f}	....	34	B
Ethyl benzamide	0.985–1.01	0.715–0.81	90	B
	.985–0.995	....	29	A
	1.005	.334	24	B
Methyl formanilide	0.03^{g}	.517^{b}	90	B
	......	.453	27	B
Phthalimide	.96–1.00	.48–0.42^{h}	25	B
	1.96–2.03	1.17–1.19^{h}	95	B
N-Phenyl glutarimide	0.0^{g}	1.01	100	B
N-Phenyl succinimide	.0^{g}	1.01	90	B
Urea	4.4^{j}	....	100	B
V Oximes (theor.: 1.0 active hydrogen)				
Acetaldoxime	1.04	0.49	25	B
Benzophenone oxime	1.04	.275	25	B
	1.04	.505	80	B
VI Miscellaneous Compounds				
Benzoyl peroxide	0.93–1.025^{a}	1.725–1.50^{c}	100	A
Triphenylacetonitrile^{k}	0^{g}	0.20–0.28^{b}	80–100	B
Nitrobenzene	2.25–2.55^{f}	....	70–75	A, B
2-Nitrobutane	2.5–2.7^{m}	....	75	A, B
	3.2^{m}	1.65^{c}	70	B

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[2] U. S. Rubber Company Fellow, 1947–1948.

[3] Nystrom and Brown, THIS JOURNAL, **69**, 1197 (1947).

[4] Nystrom and Brown, *ibid.*, **69**, 2548 (1947).

[5] Krynitsky, Johnson and Carhart, *ibid.*, **70**, 486 (1947).

[6] Nystrom and Brown, *ibid.*, **70**, 3738 (1948).

[7] Hochstein and Brown, *ibid.*, **70**, 3484 (1948).

[8] Kohler, Stone and Fuson, *ibid.*, **49**, 3181 (1927).

[9] Kohler and Richtmyer, *ibid.*, **52**, 3736 (1930).

TABLE II (*Continued*)

Compound	Active H_2 found	Moles $LiAlH_4$ consumed	Temp., °C.	Solvent
o-Nitroaniline	3.3[i]	....	29	A
	4.5[i]	....	75	A
	5.1[i]	....	30	B
Azoxybenzene	1.04[a]	0.58[b]	75	B
Fluorene	< 0.03	....	75	A
Triphenylmethane	< 0.06	....	75	A
Naphthalene	...	< 0.05	100	B

[a] 1.0 active hydrogen calcd. [b] 0.5 mole $LiAlH_4$ calcd. [c] 1.5 mole $LiAlH_4$ calcd. [d] 0.75 mole $LiAlH_4$ calcd. [e] 1.25 mole $LiAlH_4$ calcd. [f] 2.0 active hydrogen calcd. [g] No active hydrogen calcd. [h] Nature of reaction not known. [i] 4.0 active hydrogen calcd. Very small sample used, so percentage error was large. [k] Red color at end of reaction, which disappears on hydrolysis. [m] 3.0 active hydrogen calcd. [n] Reaction time ten to twenty minutes. [y] A = dibutyl ethers; B = N-ethylmorpholine.

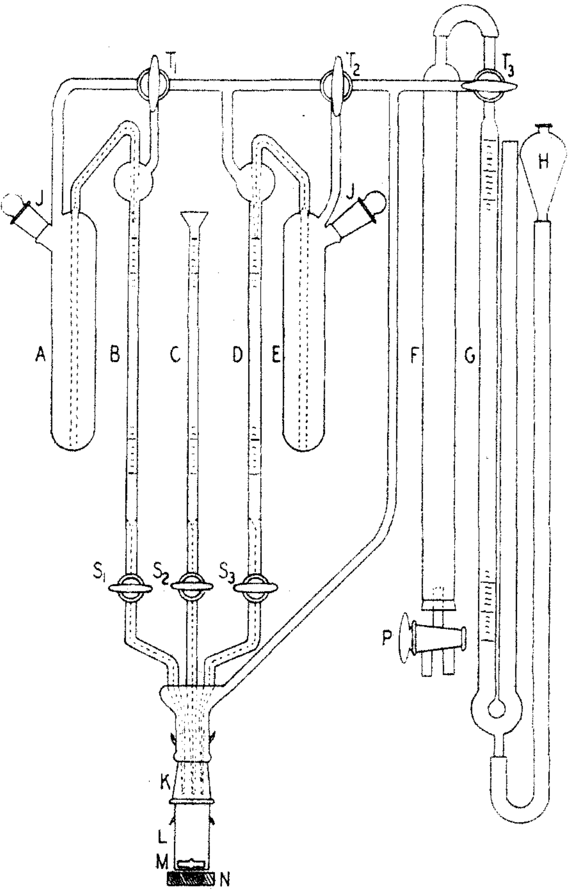

Fig. 1.—Apparatus for measurement of active hydrogen and of $LiAlH_4$ consumption: A, E, 125 ml. reservoirs; B, 2 ml. reagent buret; C, 2 ml. hydrolyzing agent buret; D, 5 ml. solvent buret; F, nitrogen drying tube, packed with phosphorus pentoxide on pumice; G, 25 ml. gas measuring buret; H, mercury reservoir; J, 14/30 ₮ filling ports; K, 24/40 ₮ female joint; L, 12 ml. reaction flash, with 24/40 ₮ male joint; M, glass covered iron stirrer; N, rotating magnet; P, three-way stopcock, for nitrogen; S_1, S_2, S_3, 1 mm. capillary bore stopcocks; T_1, T_2, T_3, three-way 6 mm. stopcocks.

β-naphthol, thio-β-naphthol, 2,4,6-tribenzylphenol, benzylaniline, diphenylamine and dibenzylamine gave values indicating 1.00 active hydrogen, with an average deviation of ±0.015. Phenylethylene glycol, 1,6-hexanediol, hydroquinone, aniline and *n*-butylamine gave values indicating 2.00 active hydrogen, with an average deviation of ±0.010. Water, in N-ethylmorpholine solution, gave values indicating 1.7 to 1.9 active hydrogen.

TABLE III

REACTIONS OF $LiAlH_4$ WITH UNSATURATED COMPOUNDS[a]

Compound	Active hydrogen found	Moles $LiAlH_4$ consumed Found	Moles $LiAlH_4$ consumed Calcd.[b]	Temp. °C.
Allyl alcohol[c]	1.01	0.41	0.25	95
Cinnamyl alcohol	1.01	.365	.25	25
	1.01	.496–0.521	.25	95
Cinnamic acid[c]	1.03	.794	.75	28
	0.97–1.03	.92–1.02	.75	80
Phenylpropiolic acid	1.03	.89	.75	27
	1.03–1.06	1.09–1.11	.75	100
Maleic anhydride	0	0.90–0.91	1.00	100
Benzalacetophenone	0	.266	0.25	25
	0	.494	.25	90
p-Benzoquinone[d,e]	0.50–0.52	.46–0.49	.50	27
	.74–0.84	.49	.50	25
	.86	.485	.50	75
Phenanthraquinone[e]	.85	.481	.50	25
	.76	.52	.50	70
Acenaphthenequinone	.13–0.25	.45–0.48	.50	80
Perinaphthenone	0	.28–0.39	.25	27
	0	.31	.25	80
Benzanthrone	0.26[e]	.35	.25	26
	0.50–0.68	.41–0.42	.25	90

[a] Reactions carried out in N-ethylmorpholine. Reaction time ten to fifteen minutes. [b] Assuming no reduction of carbon–carbon double bonds. [c] Reaction time sixty minutes. [d] Dibutyl ether solvent. [e] 1.0 mole active hydrogen calcd.

TABLE IV

REDUCING OF VARIOUS COMPOUNDS BY $LiAlH_4$[a]

Compound	Reaction time, hr.	Yield, %	Product
Fluorenone	1/4	99	9-Fluorenol
Perinaphthenone	1/4	23	Perinaphthene
Benzalacetophenone	1/4	65	Phenylstyrylcarbinol
α-Angelica lactone	24	65	γ-Acetylpropanol
β-Angelica lactone[b]	4	10	2,4-Pentanediol[c]
Coumarin	24	50	3-(*o*-Hydroxyphenyl)-propanol
		10	*o*-Hydroxycinnamyl alcohol[d]
1-Tyrosine ethyl ester[b]	2	60	2-Amino-3-(*p*-hydroxyphenyl)-propanol[e]
Benzophenone oxime[b]	7	60	Benzhydrylamine[f]

[a] Reductions carried out in ether at 35° unless otherwise specified. [b] Reductions carried out in tetrahydrofuran at 65°. [c] Isolated as diacetate, d^{20}_{20} 1.028, n^{20}_{D} 1.4294. [d] New compound. Colorless needles from benzene, m. p. 110.5–111.5°. *Anal.* Calcd. for $C_9H_{10}O_2$: C, 72.0; H, 6.71; act. H_2 1.33%; Br. No., 108. Found: C, 72.0; H, 6.52; act. H_2, 1.37%; Br. No., 118. Dibenzoate (act. H_2 0.0%), rectangular plates from methanol, m. p. 92.5–93.5°. [e] New compound: isolated as triacetyl derivative; white needles from alcohol m. p. 118–119°. *Anal.* Calcd. for $C_{15}H_{19}O_5N$: N, 4.78. Found: N, 4.76, 4.89. $[\alpha]^{25}_{D}$, + 1.95° (in ethanol). 2-Amino-3-(*p*-hydroxyphenyl) propanol sulfate, m. p. 272–7° (decomp.). *Anal.* Calc. for $(C_9H_{13}NO_2)_2H_2SO_4$: SO_4, 22.2. Found: SO_4, 22.3. [f] 20% of oxime recovered unchanged.

Further data, with reference to types of compounds which undergo reduction as well as replacement of active hydrogen, are presented in Tables I-III. The agreement with the theory is in general within the limits of experimental error.

It was occasionally desirable to run larger scale reactions in order that reaction products might be investigated. Some of these are described in Table IV, the procedures having been described previously.[4]

Experimental

Early experiments were carried out with the usual type of micro-scale Grignard machine,[10] the reactions being performed in air. Erratic results, due to a slow reaction of the hydride with oxygen and the consequent liberation of hydrogen, were remedied by carrying out the operations in an atmosphere of nitrogen. Difficulties encountered because of the leaking and fouling of the three-way stopcock were overcome by a modification of the apparatus. Dioxane, anethole and N-methylmorpholine are less satisfactory than dibutyl ether as a solvent, while N-ethylmorpholine is the most satisfactory solvent used to date. Pyridine cannot be used since it is reduced by the reagent.

The design of the apparatus is shown in Fig. 1. It may be noted that if an accuracy of better than one per cent. is desired, the design should be altered to minimize the free space in the head of the reaction vessel and in the connections to the gas buret, and also that the latter should be maintained at constant temperature.

The operation of the apparatus is similar in principle to that described by Soltys.[10] A weighed sample is placed in the reaction vessel, L, the apparatus is flushed with dry nitrogen, and the desired quantity of solvent is added from the buret, D. The gas buret is levelled at zero, and with stirring by the magnetic bar, M, the desired quantity of lithium aluminum hydride solution (taken in 20–30% excess) is added from buret, B. The evolution of hydrogen from compounds containing active hydrogen is usually complete in one to ten minutes at room temperature; reduction reactions may require a longer time, or may require heating. After measurement of the hydrogen gas volume, the excess hydride is decomposed by the addition, from buret, C, of 1.0 ml. of a mixture of amyl alcohol in two volumes of dibutyl ether. Complete decomposition of the reagent may require some time; usually fifteen minutes at room temperature is adequate.

Reagents.—Stock solutions of lithium aluminum hydride were prepared by shaking 2 g. of the compound[11] with 200 ml. of dibutyl ether for fifteen minutes or longer, allowing the mixture to settle and filtering the supernatant liquid through sintered glass, all operations being conducted under nitrogen. This yields a clear solution, 0.20–0.25 molar in $LiAlH_4$, which slowly deposits a white precipitate and deteriorates at a rate of less than 1% per month when stored under dry nitrogen.

The solvents, N-ethylmorpholine and dibutyl ether, were first dried over calcium hydride, then treated with lithium aluminum hydride (2 g. per l.) at 90–100° for two hours, and were then distilled at 20 mm. pressure. After placing the solvent in the reservoir, control runs were made on the basis of which the calculated quantity of lithium aluminum hydride solution was added to the solvent contained in the reservoir and the mixture heated to 70° for one hour. With this procedure the quantity of hydrogen liberated from 1 ml. of solvent by the addition of hydride solution could be made smaller than 0.05 ml.

Cylinder nitrogen was used without purification, other than drying over phosphorus pentoxide.

The test compounds were purified by conventional procedures but with special care to exclude moisture. In the recrystallization of solids it was necessary to avoid the use of hydroxylic solvents. Liquids were dried over calcium hydride where possible, otherwise over Drierite.

Acknowledgments.—Dr. Weldon G. Brown offered much helpful advice in the development of this method; he supplied many of the compounds tested in the apparatus.

Summary

The quantitative aspect of the reaction of lithium aluminum hydride with several types of organic compounds has been investigated. It is shown that lithium aluminum hydride may be used as a reagent for the determination of active hydrogen, and reducible groups.

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[10] Soltys, *Mikrochemie*, **20**, 107 (1937). See also Niederl and Niederl, "Micromethods of Quantitative Organic Elementary Analysis," J. Wiley and Sons, Inc., New York, N. Y., 1938, p. 206.

[11] Lithium aluminium hydride was prepared in this Laboratory by the method of Finholt, Bond and Schlesinger, THIS JOURNAL, **69**, 1199 (1947).

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An Empirical Expression for the Melting Points of the Straight-Chain Dicarboxylic Acids

BY JOHN G. ERICKSON

It was pointed out by Baeyer[1] in 1877 that the melting points of the unsubstituted aliphatic dibasic acids are of an oscillatory nature, that is, the melting points of successive members of the series are alternately high and low. The melting points converge to an asymptotic value, the melting points of the acids with an even number of carbon atoms decreasing and the melting points of the acids with an odd number of carbon atoms increasing with the length of the carbon chain. The convergence value for the dibasic acids is 123°. This oscillation is not peculiar to the melting points of the dicarboxylic acids; other homologous series, including aliphatic monobasic acids and their α-hydroxy derivatives, α,α'-dibromodicarboxylic acids, dinitriles, glycols, diamines, dialdehydes, alcohols and paraffins, show similar oscillatory effects and other physical properties, including solubilities, molecular volumes, optical rotatory powers and dissociation constants are affected. However, the oscillatory or "alternating" effect is much the most pronounced with the dicarboxylic acids and has attracted the most atten-

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[1] Baeyer, *Ber.*, **10**, 1286 (1877).