The product was reoxidized with sodium dichromate[18] to menthone ($[\alpha]^{25}\text{D}$ −23.7°) showing no change in the configuration of the starting material had occurred.

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[18] *Organic Syntheses*, Coll. Vol. I, John Wiley and Sons, Inc., New York 16, N. Y., 1944, p. 340.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

A New Powerful Reducing Agent—Sodium Borohydride in the Presence of Aluminum Chloride and Other Polyvalent Metal Halides[1,2]

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The addition of aluminum chloride to sodium borohydride in the dimethyl ether of diethylene glycol (diglyme) gives a clear solution with enormously more powerful reducing properties than those of sodium borohydride itself. Esters, lactones and carboxylic acids are readily reduced to the corresponding alcohols. Sodium salts of the carboxylic acids are not reduced, so that the reagent permits the selective reduction of an ester group in the presence of the carboxylate group. Nitro groups are not attacked by the reagent, permitting the ready reduction of nitro esters to the corresponding nitro alcohols. Nitriles are reduced to primary amines in good yield. A survey was made of the reactivity of various functional groups toward the reagent by examining the hydrogen utilization by various representative compounds under standard reaction conditions. The results lead to the following conclusions. Simple acid amides form only salts (by reaction with one of the active hydrogen atoms of the amide group) which do not undergo reduction, whereas reduction does occur with the disubstituted amides. Aldehydes, ketones, epoxides and anhydrides utilize hydride corresponding to reduction to the alcohol. Disulfides and sulfonyl chlorides are reduced, whereas a simple sulfone was not. Pyridine-N-oxide is reduced at 25°, whereas pyridine itself does not react at this temperature. Benzyl chloride was not affected at 25°, but appeared to undergo reaction at 75°. Other polyvalent metal halides, such as gallium trichloride and titanium tetrachloride, also appear capable of greatly increasing the reducing potentialities of sodium borohydride.

In the past decade sodium borohydride[4,5] and lithium aluminum hydride[6,7] have revolutionized the reduction of functional groups in organic chemistry. Of these two reagents, sodium borohydride is a relatively mild reducing agent which is practically specific for the carbonyl group in aldehydes and ketones. On the other hand, lithium aluminum hydride is an exceedingly powerful reagent which attacks almost all reducible groups.

There would be advantages in possessing reagents with reducing capacities somewhere between these two extremes. One possible means of achieving this end would be to increase the reducing properties of the borohydride; another, to diminish the reducing properties of the aluminohydride. Both procedures are under active investigation in our laboratories.

It is quite clear that the reducing capacity of the borohydride is markedly affected by the metal ion present in the salt. Thus sodium borohydride reduces typical esters, such as ethyl acetate and ethyl benzoate, only very slowly, whereas lithium borohydride[8,9] reduces such esters quite easily.[10]

Kollonitsch, Fuchs and Gabor achieved the successful reduction of simple esters by sodium borohydride in tetrahydrofuran in the presence of lithium and magnesium iodides,[11] as well as by the application of calcium, strontium and barium borohydrides.[12]

The dimethyl ether of diethylene glycol (diglyme) is an excellent solvent for sodium borohydride. The addition of lithium bromide or magnesium chloride to such solutions provides a reagent which permits the ready reduction of esters.[13] In continuing this line of investigation, we have discovered that the addition of anhydrous aluminum chloride or other polyvalent metal halides, such as gallium chloride or titanium tetrachloride, provides solutions of tremendously enhanced reducing capacities.[14] We, therefore, turned our attention to a detailed examination of the potentialities of these new reducing systems.

Results

Mixture of freshly prepared solutions of aluminum chloride (2 *M*) and sodium borohydride (1.0 *M*), in diglyme in a molar ratio $\text{AlCl}_3\text{:}3\text{NaBH}_4$ gives a clear solution which exhibits very powerful reducing properties. Preliminary experiments revealed that esters, such as ethyl benzoate, ethyl stearate and ethyl *p*-nitrobenzoate, were essentially completely reduced by the reagent in one hour at room temperature.

The precise order of mixing the reagents does not appear to be important. At least no significant difference in results was observed in (1) adding the aluminum chloride solution to a mixture of sodium borohydride and ester in the solvent, (2) adding the sodium borohydride solution to a mixture of the ester and aluminum chloride in the solvent or (3) adding the ester to a mixture of aluminum chloride and sodium borohydride in diglyme. We fi-

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[1] Addition Compounds of the Alkali Metal Halides. IV.

[2] Based upon a thesis submitted by B. C. Subba Rao in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[3] Parke, Davis and Co. Fellow at Purdue University, 1952–1955.

[4] H. I. Schlesinger, H. C. Brown, H. R. Hoekstra and L. R. Rapp, THIS JOURNAL, **75**, 199 (1953).

[5] S. W. Chaikin and W. G. Brown, *ibid.*, **71**, 122 (1949).

[6] A. F. Finholt, A. C. Bond, Jr., and H. I. Schlesinger, *ibid.*, **69**, 1199 (1947).

[7] R. F. Nystrom and W. G. Brown, *ibid.*, **69**, 1197, 2548 (1947); **70**, 3738 (1948).

[8] H. I. Schlesinger and H. C. Brown, *ibid.*, **62**, 3429 (1940).

[9] R. F. Nystrom, S. W. Chaikin and W. G. Brown, *ibid.*, **71**, 3245 (1949).

[10] The ester groups in certain sugar lactones are readily reduced even by sodium borohydride: M. L. Wolfrom and H. B. Wood, THIS JOURNAL, **73**, 2933 (1951).

[11] J. Kollonitsch, P. Fuchs and V. Gabor, *Nature*, **173**, 125 (1954).

[12] J. Kollonitsch, P. Fuchs and V. Gabor, *ibid.*, **175**, 346 (1955).

[13] H. C. Brown, E. J. Mead and B. C. Subba Rao, THIS JOURNAL, **77**, 6209 (1955).

[14] H. C. Brown and B. C. Subba Rao, *ibid.*, **77**, 3164 (1955).

nally adopted the first of these procedures for our examination of the scope of the reaction.[15]

The preparation and formation of the reagent appeared to be free of any special hazard. Thus a solution, 1.0 *M* in diglyme, was stable in dry air. It could be poured in open air and no violent reaction was observed in pouring the solution into water.

The reduction of typical esters was examined at 25 and 75° utilizing various ratios of hydride[16] to ester. The results indicated that essentially quantitative reduction of esters could be achieved by the use of 25% excess hydride in 1 hour reaction time at 75°, or in 3 hours at 25° with 100% excess hydride.

No significant difference was observed in the ease of reduction of aliphatic and aromatic esters. Ethyl *p*-chlorobenzoate was reduced without attack of the halogen. The results indicated attack of the double bond in the reduction of ethyl cinnamate and ethyl oleate.

Typical results are summarized in Table I.

TABLE I

REACTION OF ESTERS WITH SODIUM BOROHYDRIDE—ALUMINUM CHLORIDE IN DIGLYME

Ethyl ester	Compd., mmoles	Hydride, mmoles	Temp., °C.	Time, hr.	Hydride used, mmoles	Hydride/compd.	
						Calcd.	Expt.
Benzoate	5.00	18.9	25	1.0	9.8	2.0	2.0
	8.00	18.6	25	1.0	13.4	2.0	1.7
	8.00	18.4	25	2.0	14.2	2.0	1.8
	8.00	18.4	25	3.0	15.4	2.0	1.9
p-Chlorobenzoate	7.15	19.8	25	0.5	14.4	2.0	2.0
	6.53	19.8	25	3.0	13.8	2.0	2.1
	7.59	18.8	75	1.0	14.4	2.0	1.9
Acetate	6.33	19.8	25	0.5	12.7	2.0	2.0
	6.69	19.8	25	3.0	13.3	2.0	2.0
	6.96	18.8	75	1.0	13.4	2.0	1.9
Stearate	7.38	19.8	25	0.5	16.0	2.0	2.2
	7.25	19.8	25	3.0	15.9	2.0	2.2
	6.23	18.8	75	1.0	13.3	2.0	2.1
Cinnamate	6.30	19.8	25	0.5	16.3	3.0[a]	2.5
	6.00	19.8	25	3.0	17.7	3.0[a]	2.9
	4.93	18.8	75	1.0	15.5	3.0[a]	3.1
Oleate	5.20	19.8	25	0.5	12.5	3.0[a]	2.4
	5.50	19.8	25	3.0	13.1	3.0[a]	2.4
	5.04	18.8	75	1.0	12.9	3.0[a]	2.5

[a] On basis of reaction with double bond as well as with ester group.

Carboxylic acids react with the reagent to liberate one mole of hydrogen (with loss of one mole of hydride), followed by reduction to the alcohol (with utilization of two additional moles of hydride). Again no significant difference in the reactivity of aliphatic and aromatic carboxylic acids was observed.

Sodium salts of carboxylic acids do not appear to react with the reagent. The data therefore point to a remarkable difference in the reactivity toward the reagent of carboxylic acids and their sodium salts.

The results are summarized in Table II.

The action of the reagent on various other types of oxygen functional groups was examined. Benzyl alcohol reacted to liberate one mole of hydrogen, but was not otherwise affected. Typical aldehydes and ketones utilized one hydride per mole. Mesityl oxide utilized two hydrides per mole, indicating reaction with both the double bond and the carbonyl group. Epoxides also utilized one hydride per mole, corresponding to reduction to the alcohol. Acid chlorides and lactones appear to react readily, utilizing two hydrides per mole, corresponding to reduction to the alcohol and glycol, respectively. Cyclic acid anhydrides reacted somewhat more sluggishly. However, complete reduction could be achieved at 75° using 100% excess of hydride. Reverse addition appeared to favor this reaction. Here also the unsaturated derivative utilized more hydride than would be required by the anhydride group. Consequently, it appears that here also the double bond must react.

The experimental results are summarized in Table III.

The behavior of typical nitrogen derivatives was also examined. Both aliphatic and aromatic nitriles utilized approximately two hydrides per mole, corresponding to complete reduction to the primary amine. N,N-Diethylbenzamide reacted readily, utilizing somewhat more than the theoretical two moles of hydride. However, benzamide itself reacted with the reagent liberating only one mole of gas and utilizing no additional hydride. Consequently, it appears that simple amides are not reduced under mild conditions, in contrast to the fully substituted amides.

Both nitrobenzene and 1-nitropropane appeared to be unaffected by the reagent at both 25 and 75°. Consequently, it would appear that the reagent should be particularly valuable in selectively reducing other functional groups in the presence of nitro substituents. Azobenzene appeared to take up one hydride per mole at 25°, corresponding to reduction to the hydrazo derivative. There was some indication that the reduction proceeds further at 75°.

Finally, pyridine-N-oxide appeared to be reduced cleanly to pyridine at 25°. Pyridine itself appears to be stable to the reagent at 25°, but at 75° hydride is utilized, suggesting that there may be a reaction to form a dihydropyridine derivative.

The data are summarized in Table IV.

The action of the reagent on several representative sulfur derivatives was examined. Diphenyl disulfide utilized approximately two hydrides per mole. Benzenesulfonyl chloride appeared to utilize nearly three hydrides per mole. No reaction was observed with *p*-bromophenylmethyl sulfone. Cyclohexyl tosylate reacted at 25°. However, the stoichiometry of the reaction is not definite.

It was also observed that an active organic halide, such as benzyl chloride, is apparently stable to the reagent at 25°, but does undergo reaction at 75°. No reaction was observed with naphthalene. Finally, a reaction was observed at 75° with sim-

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(15) Occasionally the reaction was carried out by adding the sodium borohydride in diglyme to the organic compound and aluminum chloride in the same solvent. This procedure is designated as "reverse addition."

(16) It is frequently convenient to discuss the reducing agent in terms of the available "hydride" content of the solution. Each borohydride ion contains four active "hydrides."

Table II

Reaction of Carboxylic Acids and Sodium Carboxylates with Sodium Borohydride—Aluminum Chloride in Diglyme

Compound	Compd., mmoles	Hydride, mmoles	Temp., °C.	Time, hr.	Gas evolved[a]	Hydride used, mmoles	Hydride/compd. Calcd.[b]	Hydride/compd. Expt.
Benzoic acid	3.77	19.2	25	0.5	4.3	10.7	3.0	2.8[c]
	5.57	19.5	25	3.0		13.9	3.0	2.5
	2.76	19.2	75	1.0		8.9	3.0	3.2
Sodium benzoate	6.12	19.3	25	3.0		0.6	2.0	0.1
	5.60	18.6	75	1.0		1.2	2.0	.2
	6.20	18.0	75	3.0		1.3	2.0	.2
	7.8	16.7	75	6.0		2.5	2.0	.3
p-Chlorobenzoic acid	3.19	20.3	25	0.5	4.0	7.3	3.0	2.3[c]
	4.84	19.3	75	1.0		13.8	3.0	2.8
Sodium *p*-chlorobenzoate	5.87	19.3	75	1.0		1.1	2.0	0.2
Acetic acid	4.62	19.9	25	0.5	5.3	10.9	3.0	2.4[c]
	4.68	19.9	25	3.0		12.7	3.0	2.7
	5.18	18.9	75	1.0		14.9	3.0	2.9
Sodium acetate	10.6	18.5	75	3.0		6.9	2.0	0.7
Sodium propionate	9.6	16.7	75	6.0		3.3	2.0	.3
Isobutyric acid	4.49	18.7	75	1.0		12.6	3.0	2.8
	3.96	19.9	25	0.5	4.2			[c]

[a] Assumed to be hydrogen formed by reaction of the reagent with the acidic hydrogen of the carboxyl group. [b] Includes one hydride for the reaction with the active hydrogen of the carboxyl group. [c] In these experiments reverse addition (footnote 15) was used.

Table III

Reaction of Various Oxygen Derivatives with Sodium Borohydride—Aluminum Chloride in Diglyme

Compound	Compd., mmoles	Hydride, mmoles	Temp., °C.	Time, hr.	Hydride used, mmoles	Hydride/compd. Calcd.	Hydride/compd. Expt.
Benzyl alcohol	8.81	19.4	25	3.0	8.9	1.0	1.0
	8.17	18.3	75	1.0	8.6	1.0	1.0
Benzaldehyde	6.22	19.9	25	0.5	6.0	1.0	1.0[a]
	7.59	19.2	75	1.0	7.9	1.0	1.0
Benzophenone	5.43	19.9	25	0.5	5.7	1.0	1.0[a]
	7.88	19.2	75	1.0	7.8	1.0	1.0
Mesityl oxide	5.14	19.9	25	0.5	10.5	2.0[b]	2.0[a]
Styrene oxide[c]	4.86	20.3	25	1.0	5.0	1.0	1.0
	8.00	19.3	75	1.0	8.7	1.0	1.1
Propylene oxide	4.2	20.3	25	0.5	3.6	1.0	0.9
	7.9	19.3	75	1.0	6.3	1.0	.8
γ-Butyrolactone	7.8	20.3	25	0.5	15.5	2.0	2.0
	6.90	19.2	75	1.0	13.0	2.0	2.0
Benzoyl chloride	6.77	19.9	25	0.5	14.7	2.0	2.2[a,d]
	7.74	19.8	75	3.0	15.7	2.0	2.0
p-Chlorobenzoyl chloride	5.54	20.3	25	0.5	14.3	2.0	2.5
Lauroyl chloride	4.94	20.3	25	0.5	12.6	2.0	2.5
Phthalic anhydride	2.17	21.9	25	3.0	8.0	4.0	3.6
	2.93	21.5	75	1.0	11.0	4.0	3.8
	2.60	21.5	75	1.0	10.8	4.0	4.1[a]
Succinic anhydride	3.75	21.9	25	3.0	4.2	4.0	1.1
	2.39	21.5	75	1.0	7.6	4.0	3.2
	2.44	21.5	75	1.0	9.7	4.0	4.0[a]
Maleic anhydride	3.10	21.9	25	3.0	3.9	5.0[c]	1.3
	2.24	21.5	75	1.0	9.1	5.0[c]	4.1
	2.93	21.5	75	1.0	14.0	5.0[c]	4.8[a]

[a] Reverse addition (footnote 15). [b] Calculated on basis of reaction with double bond. [c] Reaction quite vigorous and should be carried out with caution. [d] 1.25 mmoles of gas evolved.

ple olefins, such as 1-hexene and cyclohexene, utilizing one hydride per mole of olefin.

These experiments are summarized in Table V.

It was important to establish the behavior of the reagent toward bifunctional molecules. The results indicate that this behavior can be predicted with considerable certainty from the behavior of the monosubstituted derivative toward the reagent, except where physical difficulties, such as low solubility, intervene.

For example, both ester groups of dimethyl terephthalate underwent simple reduction to the alcohol stage. On the other hand, dicarboxylic acids such as adipic and succinic were not very soluble in the reaction mixture, and did not utilize the theoretical quantity of hydride under standard conditions.

TABLE IV

REACTION OF VARIOUS NITROGEN DERIVATIVES WITH SODIUM BOROHYDRIDE—ALUMINUM CHLORIDE IN DIGLYME

Compound	Compd., mmoles	Hydride, mmoles	Temp., °C.	Time, hr.	Hydride used, mmoles	Hydride/compd. Calcd.	Hydride/compd. Expt.
Benzonitrile	7.16	19.4	25	3.0	14.8	2.0	2.1
	7.66	18.4	75	1.0	14.6	2.0	1.9
p-Tolunitrile	4.88	20.4	25	0.5	10.1	2.0	2.0
	5.75	19.2	75	1.0	11.0	2.0	1.9
Acetonitrile	5.63	19.4	25	3.0	10.3	2.0	1.9
	6.11	19.2	75	1.0	12.5	2.0	2.0
Capronitrile	5.38	20.4	25	0.5	10.1	2.0	1.9
	6.03	20.4	25	3.0	12.0	2.0	2.0
Benzamide	5.31	19.9	25	0.5	6.16	3.0[c]	1.2[a,b]
	8.00	19.9	25	3.0	8.14	3.0[c]	1.0
	9.48	19.0	75	1.0	14.8	3.0[c]	1.6
N,N-Diethylbenzamide	4.50	20.3	25	1.0	10.9	2.0	2.4
	6.02	19.5	75	1.0	15.3	2.0	2.6
Nitrobenzene	6.87	19.8	25	3.0	0.1	6.0	0.0
	7.83	18.7	75	1.0	.5	6.0	.0
1-Nitropropane	7.24	19.8	25	3.0	.0	6.0	.0
	9.19	18.7	75	1.0	.0	6.0	.0
Pyridine-N-oxide	8.51	19.9	25	0.5	5.2	1.0	0.6[a]
	8.90	19.9	25	3.0	9.9	1.0	1.1
	9.72	18.9	75	1.0	9.7	1.0	1.0
Pyridine	5.34	19.9	25	3.0	1.8	1.0[d]	0.3
	5.32	18.7	75	1.0	7.4	1.0[d]	1.4
Azobenzene	3.26	19.9	25	0.5	5.5	1.0[e]	1.3[a]
	4.55	18.9	75	1.0	8.3	1.0[e]	1.8

[a] Reverse addition (footnote 15). [b] 5.8 mmoles of gas evolved. [c] Calculated for reduction to amine with one hydride being utilized to form hydrogen. [d] Calculated for reduction to a dihydro derivative. [e] Calculated for reduction to hydrazobenzene.

TABLE V

REACTION OF MISCELLANEOUS COMPOUNDS WITH SODIUM BOROHYDRIDE—ALUMINUM CHLORIDE IN DIGLYME

Compound	Compd., mmoles	Hydride, mmoles	Temp., °C.	Time, hr.	Hydride used, mmoles	Hydride/compd. Calcd.	Hydride/compd. Expt.
Diphenyl disulfide	4.01	19.9	25	0.5	6.8	2.0	1.7
	4.17	18.9	75	1.0	7.6	2.0	1.8
Benzenesulfonyl chloride	5.62	20.3	25	0.5	13.5	3.0	2.4
	5.98	20.3	25	0.5			[a,b]
	4.50	20.3	25	3.0	12.9	3.0	2.8
Cyclohexyl tosylate	5.60	20.9	25	3.0	6.8	1.0[d]	1.2
	2.22	20.9	25	1.0			[a,c]
	6.00	19.2	75	1.0	10.9	1.0[d]	1.8
p-Bromophenylmethylsulfone	5.24	20.3	25	3.0	0.3	2.0	0.0
	4.77	19.3	75	1.0	0.4		.0
Benzyl chloride	6.74	19.4	25	3.0	1.8	1.0	.2
	8.07	18.4	75	1.0	5.8		.7
Naphthalene	8.14	19.2	75	1.0	0.0		.0
1-Hexene	6.40	19.9	25	3.0	4.8	1.0	.8
	7.48	18.9	75	1.0	7.1	1.0	1.0
Cyclohexene	8.21	18.9	75	1.0	8.2	1.0	1.0

[a] Reverse addition. [b] 5.0 mmoles of gas evolved. [c] 3.2 mmoles of gas evolved. [d] Calculated on basis of a simple reduction to cyclohexane and tosylate ion.

Ethyl *p*-nitrobenzoate readily reacted to utilize two hydrides per mole, corresponding to reduction of the ester group without attack of the nitro group. Similarly, *p*-nitrobenzoic acid reacted smoothly without attack of the nitro group. Partial reaction was observed with sodium *p*-nitrobenzoate at 75°. Finally, sodium ethyl phthalate utilized slightly more than two hydrides per mole, corresponding to reduction of the ester group without significant attack of the carboxylate group.

The results are summarized in Table VI.

In making this broad survey of the possible utility of the new reagent for organic reductions, the conclusions were based upon the utilization of hydride ion by the organic compound. It appeared desirable to confirm these conclusions by the actual isolation and identification of the products. Accordingly, a number of derivatives were reduced on a preparative scale (0.2–0.4 mole) and the products isolated and identified. The results are summarized in Table VII.

The products obtained in the corresponding reduction of ethyl cinnamate, ethyl oleate and cinnamic acid could not be isolated in pure form. It appears that the reaction of the reagent with the double bond involves the formation of boron–car-

TABLE VI

REACTION OF BIFUNCTIONAL DERIVATIVES WITH SODIUM BOROHYDRIDE—ALUMINUM CHLORIDE IN DIGLYME

Compound	Compd., mmoles	Hydride, mmoles	Temp., °C.	Time, hr.	Hydride used, mmoles	Hydride/compd. Calcd.[a]	Hydride/compd. Expt.
Dimethyl terephthalate	2.44	20.3	25	0.5	7.8	4.0	3.2
	2.91	20.3	25	3.0	11.0	4.0	3.8
	3.80	19.3	75	1.0	13.2	4.0	3.5
Succinic acid	1.80	19.9	25	0.5	7.0	6.0	3.9[b,c]
Adipic acid	1.86	18.9	75	1.0	4.5	6.0	2.4
Ethyl *p*-nitrobenzoate	4.81	19.8	25	0.5	9.8	2.0	2.1
	8.22	18.8	75	1.0	16.6	2.0	2.0
p-Nitrobenzoic acid	3.18	20.3	25	0.5	7.5	3.0	2.4[b,d]
	3.87	20.3	25	3.0	10.3	3.0	2.6
	4.53	19.3	75	1.0	13.9	3.0	3.1
Sodium *p*-nitrobenzoate	7.84	19.2	75	1.0	8.2	0.0	1.0
Sodium ethyl phthalate	7.90	18.6	75	1.0	11.7	2.0	1.5
	5.50	18.0	75	3.0	12.2	2.0	2.2

[a] Calculated assuming reduction will proceed as observed in the monofunctional derivatives. [b] Reverse addition (footnote 15). [c] 3.5 mmoles of gas evolved. [d] 4.0 mmoles of gas evolved.

TABLE VII

YIELDS AND PRODUCTS REALIZED IN THE REDUCTION OF REPRESENTATIVE COMPOUNDS BY SODIUM BOROHYDRIDE—ALUMINUM CHLORIDE IN DIGLYME

Compound	Product	Yield, %
Ethyl stearate	1-Octadecanol	91
Ethyl *p*-chlorobenzoate	*p*-Chlorobenzyl alcohol	84
Ethyl *p*-nitrobenzoate	*p*-Nitrobenzyl alcohol	77
Dimethyl terephthalate	*p*-Xylylene glycol	70
p-Chlorobenzoic acid	*p*-Chlorobenzyl alcohol	64
p-Nitrobenzoic acid	*p*-Nitrobenzyl alcohol	82
p-Tolunitrile	*p*-Methylbenzylamine	85
Capronitrile	*n*-Hexylamine	65

bon bonds which are not easily hydrolyzed. Consequently the reagent would not appear to be useful for the reduction of unsaturated derivatives.

The ready formation of organoboron derivatives from the reagent and olefins or unsaturated derivatives is, of course, highly interesting in its own right. The reaction may provide a new simple route to the synthesis of such derivatives. We plan to investigate this aspect of the reaction further.[17]

In this study diglyme was utilized as the solvent because of the high solubilities of sodium borohydride in this medium. The applicability of other solvents for the reduction of ethyl benzoate was examined briefly. Refluxing tetrahydrofuran proved quite satisfactory, while ethyl ether was poorer and dioxane was unsatisfactory. The presence of as little as 20% diglyme resulted in rapid reductions in either tetrahydrofuran or ethyl ether.

We also examined the applicability of other polyvalent metal halides in this reaction. Both gallium trichloride and titanium tetrachloride proved capable of bringing about the reduction of ethyl benzoate by sodium borohydride whereas zinc chloride was unsuitable. Since aluminum chloride was so satisfactory for the great majority of reductions which were attempted, the utility of these other metal halides was given only a cursory examination.

Discussion

A mixture of sodium borohydride and aluminum chloride in diglyme gives a clear solution with reducing properties far greater than those of sodium borohydride itself. Insofar as the reducing properties of the reagent can be defined by the results of the present study, they are summarized in Table VIII.

TABLE VIII

REDUCING PROPERTIES OF SODIUM BOROHYDRIDE–ALUMINUM CHLORIDE IN DIGLYME

Functional group	Hydride used per mole	Product	Remarks
Alcohol	1	Alcohol	1 mole H_2 evolved
Aldehyde	1	Alcohol	Very fast at 25°
Ketone	1	Alcohol	Very fast at 25°
Ester	2	Alcohol	Fast at 25°, 75°
Acid	3	Alcohol	1 mole H_2 evolved
Acid salt	0		No reaction 25°, 75°
Acid chloride	2	Alcohol	Fast at 25°
Cyclic acid anhyd.	4	Glycol	75°
Epoxide	1	Alcohol	Fast at 25°
Lactone	2	Glycol	Fast at 25°
Amide, unsubstd.	1–2		1 mole H_2 evolved, 25° 2 moles, 75°
Amide, disubstd.	2	*t*-Amine	75°
Nitrile	2	Amine	Fast at 25°
Nitro	0		No reaction 25°, 75°
Pyridine-N-oxide	1	Pyridine	Fast, 25°
Pyridine	1	Dihydropyridine	Slow, 75°
Disulfide	2	Thiol	
Sulfonyl chloride	3	Thiol	
Sulfone	0		No reaction 25°, 75°
Benzyl chloride	1	Toluene	Slow, 75°
Olefin	1	Organoboron	Slow, 75°

It is now apparent that the reducing properties of sodium borohydride can be varied markedly by the simple expedient of adding various metal salts to the reaction mixture. This simple technique should greatly facilitate the task of devising suitable synthetic procedures based upon selective reductions of polyfunctional molecules.

In the present paper it was demonstrated that sodium borohydride and aluminum chloride permits

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(17) With this one exception we plan no further investigations on the applicability of this reagent. We hope that other workers will feel free to apply the reaction to synthetic problems and to explore its full utility.

the selective reduction of carboxylic acid and ester groups in the presence of the nitro group. The results also suggest the possibility of reducing the ester group in the presence of the carboxylate group. A careful study of the reducing properties of reagents prepared from sodium borohydride and other metal salts will doubtless reveal the practicality of many other selective reductions.

The question naturally arises as to the function of the aluminum chloride. One possibility to consider is that aluminum borohydride is formed in the reaction mixture and is responsible for the reducing characteristics of the solution.

$$AlCl_3 + 3NaBH_4 = Al(BH_4)_3 + 3NaCl$$

Sodium chloride is insoluble in the solvent. Consequently, the failure to observe a precipitate in preparing the reagent means that this simple explanation cannot hold. It follows that either aluminum borohydride is not formed in the reaction mixture, or it is formed only in trace amounts. If the former, the reducing properties of the solution must be ascribed to the catalytic activity of the metal halide. If the latter explanation holds, it must follow that the reaction proceeds through the minute amounts of aluminum borohydride present, continually formed from the reagents as that present is removed by reaction with the organic reactant.

We are continuing our studies on this question in the hope of arriving at an understanding of the nature of the reagent and the function of the aluminum chloride.

Experimental Part

Materials.—Commercial diglyme (Ansul ether No. 141) was distilled over calcium hydride and then redistilled under reduced pressure from a small quantity of lithium aluminum hydride. Other solvents, such as tetrahydrofuran, ethyl ether and dioxane, were purified by standard methods followed by a distillation from lithium aluminum hydride.

Commercial sodium borohydride (Metal Hydrides, Inc., and Callery Chemical Co.) was purified by recrystallization from diglyme.[13]

Commercial aluminum chloride was purified by sublimation and stored out of contact with air. Gallium trichloride was synthesized from the pure metal by reaction with dry hydrogen chloride at 300°. Other metal halides (stannic chloride, zinc chloride and titanium tetrachloride) were the purest commercial products available and were utilized without further purification.

The organic reactants were standard organic chemicals which were purified by standard procedures where such purification appeared desirable.

Aluminum chloride is highly soluble in diglyme (>2.5 *M*). Because of the high heat of solution, the aluminum chloride was mixed with the solvent in small portions at 0°. The resulting solutions were colorless when freshly prepared, but darkened after 24 hours, depositing a sediment. Consequently, we utilized freshly prepared solutions in the study.

The aluminum chloride was utilized in the form of a 2.0 *M* solution in diglyme; sodium borohydride, in the form of a 1.0 *M* solution.

General Procedure for Reduction Studies.—Two 50-ml. round-bottom flasks were carefully dried and 5.0 mmoles of sodium borohydride (5.00 ml. of 1.0 *M* solution in diglyme) introduced into each. To one was added a weighed quantity of the organic compound; the other was maintained as a control. To both sets was added 1.7 mmoles of aluminum chloride (0.85 ml. of 2.0 *M* solution in diglyme). The rate of addition was controlled to prevent a significant rise in the reaction temperatures, usually 25 or 75°. In some cases reverse addition was followed. In these experiments the aluminum chloride solution was added to the weighed compound in the flask, followed by the slow addition of sodium borohydride in diglyme. The reverse addition procedure was followed in these cases where it was desired to measure the quantity of gas formed in the reaction. In these cases a side arm to the flask was connected to a gas buret and the gas was collected and measured over mercury.

After the appropriate reaction time, the flask was brought to room temperature, and 10 ml. of 2 *M* hydrochloric acid was added through a pressure equalized dropping funnel to hydrolyze the remaining borohydride. The hydrogen evolved was collected in a gas buret over water. The unreacted borohydride was estimated from the volume of hydrogen corrected to normal temperature and pressure.

Reduction of Ethyl Stearate.—Sodium borohydride (8.5 g., 0.25 mole) was placed in a 1-l. 3-neck flask together with 250 ml. of diglyme. After stirring for a few minutes to facilitate the solution of the borohydride, 0.4 mole of ethyl stearate (b.p. 198–199° at 10 mm.) was added. Vigorous stirring was initiated and 0.084 mole of aluminum chloride (42 ml. of a 2.0 *M* solution in diglyme) was added through he dropping funnel at such a rate that the temperature inside the flask did not rise above 50°. After all of the aluminum chloride had been added, the reaction mixture was stirred for an hour at room temperature, followed by heating on a steam-cone for 0.5–1.0 hour.

The reaction mixture was cooled to room temperature and poured into a beaker containing 500 g. of crushed ice and 50 ml. of concentrated hydrochloric acid. The precipitate was collected on a filter, washed with ice-water, pressed and dried *in vacuo*. The crude product was crystallized fron aqueous alcohol. There was obtained 98.2 g. of 1-octadecanol, m.p. 58–59°, a yield of 91%.

Reduction of Ethyl *p*-Chlorobenzoate.—By the same procedure described above, 0.4 mole of ethyl *p*-chlorobenzoate (b.p. 235–236° at 740 mm., n^{20}_{D} 1.5240) was reduced to *p*-chlorobenzyl alcohol (m.p. 74–75°) in a yield of 48.0 g., 84%.

Reduction of Ethyl *p*-Nitrobenzoate.—In the same way, 0.4 mole of ethyl *p*-nitrobenzoate (m.p. 56–57°) was reduced, taking special care that the initial reaction occurred below 50°. The final heating was not permitted to go above 75° in order to minimize the possibility for further reduction. After hydrolysis, the crude precipitate was collected and the filtrate was partially evaporated under reduced pressure to remove diglyme. The residue was then repeatedly extracted with boiling water, the extracts concentrated, and allowed to crystallize. The combined product was then recrystallized from hot water. There was obtained 47.0 g. of *p*-nitrobenzyl alcohol (m.p. 92–93°), a yield of 77%.

Reduction of Dimethyl Terephthalate.—Dimethyl terephthalate (m.p. 140°) was reduced on a 0.2-mole scale using 75% excess hydride (0.35 mole of sodium borohydride and 0.12 mole of aluminum chloride in 420 ml. of diglyme). The reaction temperature was maintained at 50° with a reaction time of 4–6 hours. After hydrolysis, the reaction mixture was neutralized with sodium carbonate and evaporated dry under reduced pressure. The solid residue was extracted repeatedly with absolute ethanol to obtain the crude product. On recrystallization from hot water there was obtained 20.0 g. of *p*-xylylene glycol (m.p. 113–115°), a yield of 70%.

Reduction of *p*-Chlorobenzoic Acid.—*p*-Chlorobenzoic acid (m.p. 237–239°) was reduced on a 0.2-mole scale using 25% excess hydride (0.18 mole of sodium borohydride and 0.06 mole of aluminum chloride in 210 ml. of diglyme). The isolation procedure was similar to that used for the ester. There was obtained 18.1 g. of *p*-chlorobenzyl alcohol (m.p. 74–75°), a yield of 64%.

Reduction of *p*-Nitrobenzoic Acid.—The reduction of *p*-nitrobenzoic acid (m.p. 240–242°) produced 25.1 g. of *p*-nitrobenzyl alcohol (m.p. 92–93°), a yield of 82%.

Reduction of *p*-Tolunitrile.—Using the procedure previously described for ethyl stearate, 0.2 mole of *p*-tolunitrile (b.p. 215°) was reduced using 25% excess hydride (0.125 mole of sodium borohydride, 0.042 mole of aluminum chloride in 125 ml. of diglyme.) The product was hydrolyzed with crushed ice and hydrochloric acid. The filtrate was concentrated and allowed to crystallize. After recrystallization from hot ethanol, there was obtained 24.8 g. of *p*-methylbenzylamine hydrochloride (m.p. 233–234°), a yield of 78%.

A yield of 85% was realized when the reduction was repeated using 50% excess hydride.

Reduction of Capronitrile.—Using 25% excess hydride, 0.2 mole of capronitrile produced 18.0 g. of *n*-hexylamine hydrochloride (m.p. 218–219°), a yield of 65.5%.

TABLE IX

REDUCTIONS OF ETHYL BENZOATE IN VARIOUS SOLVENTS

Solvent	Reactants, mmoles Ester	NaBH$_4$	AlCl$_3$	Temp.,[a] °C.	Time, hr.	Hydride used, mmoles	Reduction, %
Tetrahydrofuran	5.00	5.50	1.80	80	3.0	8.5	85
Diethyl ether	5.00	7.50	2.50	40	3.0	3.4	34
Dioxane	5.00	4.00	1.40	100	3.0	Small	Small
Tetrahydrofuran–diglyme (4:1)	5.00	5.00	1.70	80	3.0	9.7	97
Ethyl ether–diglyme (4:1)	5.00	5.00	1.70	40	3.0	10.9	100

[a] Bath temperature.

Other Solvents for Reduction.—The utility of other ether solvents for these reductions was examined by treating ethyl benzoate with sodium borohydride and aluminum chloride in tetrahydrofuran, ethyl ether, dioxane, and in tetrahydrofuran and ethyl ether each containing 20% diglyme. The results are summarized in Table IX.

Other Metal Halides in Reductions.—On mixing titanium tetrachloride with equivalent amounts of sodium borohydride in diglyme, no precipitation or gas evolution was observed immediately. However, the solution changed color and eventually a gray precipitate separated.

In the case of gallium chloride and zinc chloride mixing, the reagents resulted in the formation of a white precipitate. Stannic chloride produced a vigorous evolution of gas and a gray precipitate separated out. In this process nearly 50% of the initial hydride was utilized.

The precise nature of these reactions is under investigation. In the present study these reaction mixtures were mixed with ethyl benzoate under a set of standard reaction conditions and the extent of reduction estimated from the utilization of hydride by the ester.

The results are summarized in Table X.

The results indicate that both gallium chloride and titanium tetrachloride are effective in bringing about the reduction of ethyl benzoate by sodium borohydride. The reagents formed by these two metal halides appear to be considerably less active than that formed by aluminum chloride. The cost of gallium chloride precludes its application in organic synthesis. Consequently, titanium tetrachloride appears to be particularly promising in producing a reagent with an intermediate activity.

TABLE X

REACTION OF ETHYL BENZOATE WITH SODIUM BOROHYDRIDE—METAL HALIDE MIXTURES IN DIGLYME

Reactants, mmoles Ester	NaBH$_4$[a]	Halide	Temp., °C.	Time, hr.	Hydride used, mmoles	Reduction, %
5.0	5.0	1.7 GaCl$_3$	25	1.0	0.6	6
5.0	5.0	1.7 GaCl$_3$	75	1.0	8.8	88
5.0	5.0	1.7 GaCl$_3$	75	1.0	9.2	92
8.0	5.0	1.7 GaCl$_3$	75	1.0	12.8	80
8.0	5.0	1.7 GaCl$_3$	75	1.0	14.5	90
5.0	5.0	1.25 TiCl$_4$	25	3.0	2.3	23
5.0	5 0	1.25 TiCl$_4$	75	1.0	8.2	82
5.0	5.0	1.25 TiCl$_4$	75	2 0	9.9	99
5.0	5.0[b]	1.25 SnCl$_4$	25	1.0	2.9	29
5.0	5.0[b]	1 25 SnCl$_4$	75	1.0	5.0	50
5.0	5.0	2.5 ZnCl$_2$	25	1.0	0.3	
5.0	5.0	2.5 ZnCl$_2$	75	1.0	0.1	

[a] Solution 1.0 *M* in sodium borohydride. [b] Initial concentration of sodium borohydride. Blanks indicate loss of over 50% of available hydride due to reaction with stannic chloride.

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE B. F. GOODRICH RESEARCH CENTER]

Vinylidene Cyanide. VIII. Reaction with Enolized 1,3-Dicarbonyl Compounds

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When vinylidene cyanide and enolized 1,3-dicarbonyl compounds of the type ACOCH$_2$COB, where A is alkyl or aryl and B is alkyl, aryl or alkoxy, are heated, compounds of the type ACOCH(CH$_2$CH(CN)$_2$)COB are formed. The preparation, properties and the results of structural studies of some of these compounds are given.

As a continuation of the study of the reactions of vinylidene cyanide (I),[1] the reaction of I with 1,3-dicarbonyl compounds was studied. This paper reports the preparation and properties of several monosubstituted malononitriles of the type ACOCH(CH$_2$CH(CN)$_2$)COB, where A is alkyl or aryl and B is alkyl, aryl or alkoxy.

Contrary to the behavior of I with enolized ketones reported by Ardis, *et al.*,[2] it was found that polymer-free I and an equivalent amount of ethyl acetoacetate could be mixed at room temperature without immediate polymerization. No polymer was evident after five hours, but after 21 hours the reaction mixture was a clear, firm gel. A small amount of CH$_3$COCH(CH$_2$CH(CN)$_2$)COOC$_2$H$_5$ (II) was isolated from the polymer gel. It was found that using an excess of ethyl acetoacetate and heating the solution caused the rate of addition of ethyl acetoacetate to I to increase faster than the rate of polymerization of I. The compounds in Table I were prepared in this manner.

The structures of the products were shown to be ACOCH(CH$_2$CH(CN)$_2$)COB by hydrolysis with aqueous hydrochloric acid and isolation of the acids formed as shown in Chart I. With dibenzoylmethane and I a mixture of products was obtained. In addition to the product in Table I, a product derived from one molecule of dibenzoylmethane and two molecules of I was also formed. The structure of the bis-compound is not the expected open chain compound, (C$_6$H$_5$CO)$_2$C(CH$_2$CH(CN)$_2$)$_2$. The structure of the bis-compound will be reported later.

No products were isolated when the reaction of I with ethyl cyanoacetate and with nitromethane was

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[1] For paper VII in this series, THIS JOURNAL, **78**, 1669 (1956).

[2] A. E. Ardis, *et al.*, *ibid.*, **72**, 1306 (1950).