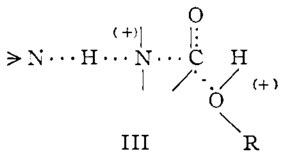

III

The rates of the general base catalyzed reactions of phenyl acetate with glycine and with ammonia are 1.1 and 1.5 times faster in water than in deuterium oxide (Table II). Rate differences of this magnitude may be expected simply from the solvent properties of deuterium oxide.[31] The absence of a significant deuterium isotope effect in these reactions is unexpected, since they must almost certainly involve a proton transfer in the rate-limiting step.[32] One possible explanation is that "bond-making" of hydrogen or deuterium to the catalyzing amine molecule is as important as "bond-breaking" from the positively charged nitrogen atom in the activated complex; a similar explanation has been proposed by Wiberg[33] to explain the absence of a deuterium isotope effect in the transfer of a proton from –OH to C^-. Similarly, there is no significant difference between the rates of proton transfer from H_3O^+ and from D_3O^+ in the ketonization of methylacetylacetone enol[31] and in the general acid catalyzed mutarotation of glucose,[34] for which there is evidence that proton transfer occurs in the rate-limiting step. This may be the result of an anomalously small difference in the zero point vibrational energies of H_3O^+ and D_3O^+, which is reflected in the greater tendency of D_3O^+ to donate a deuteron to bases of both greater and lesser basicity than water.[15,17,35] This does not seem to be the explanation for the lack of an isotope effect with $H_2N^+<$ and $D_2N^+<$, however, since anilinium ion and glycine were found to have approximately the same K'_{HA}/K'_{DA} ratios as acetic acid and phenol (see Experimental and ref. 17). In any case, the results serve to emphasize the necessity of interpreting the absence of a deuterium isotope effect in a proton transfer reaction with caution.

Acknowledgment.—The authors wish to express their appreciation to the National Science Foundation, the National Cancer Institute of the National Institutes of Health (Grant #C-3975) and to the Lilly Research Laboratories, for financial support.

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(31) F. A. Long and D. Watson, *J. Chem. Soc.*, 2019 (1958).

(32) If the reaction were specific base and general acid-catalyzed it would involve, in addition to breaking a N^+–H bond, the equilibria for formation of amide ion and of ammonium ion; from the known effects of deuterium oxide on acid–base equilibria[15,17] the isotope effect for such a reaction should be larger than for a general base catalyzed reaction.

(33) K. B. Wiberg, THIS JOURNAL, **77**, 5987 (1955).

(34) E. L. Purlee, *ibid.*, **81**, 263 (1959).

(35) J. G. Pritchard and F. A. Long, *ibid.*, **80**, 4162 (1958).

WALTHAM 54, MASS.

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

Hydroboration. III. The Reduction of Organic Compounds by Diborane, an Acid-type Reducing Agent

BY HERBERT C. BROWN AND B. C. SUBBA RAO[1]

RECEIVED JUNE 8, 1959

Diborane is a powerful reducing agent for organic compounds, rapidly reducing at room temperatures aldehydes, ketones, epoxides, lactones, carboxylic acids, nitriles, azo compounds and *t*-amides. Esters are reduced more slowly, and acid chlorides, nitro compounds and sulfones do not react under these conditions. These reductions can be carried out either by passing diborane, generated externally, into a solution of the organic compound in a suitable solvent, such as diglyme or tetrahydrofuran, or by adding boron trifluoride etherate to a solution of sodium borohydride and the compound in diglyme. These procedures make possible a number of selective reductions, such as the reduction of a carboxylic acid group or a nitrile group in the presence of the nitro group. The marked difference in the relative sensitivity of various groups to reduction by sodium borohydride and by diborane is attributed to the acid–base characteristics of these reducing agents. Sodium borohydride is essentially a base, reaction occurring through nucleophilic attack of the borohydride ion on an electron deficient center of the reacting groups. On the other hand, diborane is a Lewis acid, and preferentially attacks the group at a position of high electron density. By a judicious use of diborane and alkali metal borohydrides, it becomes possible to reduce many groups in the presence of other groups, and to reverse the process at will.

Some time ago it was demonstrated that diborane reacts rapidly with simple aldehydes and ketones, such as acetaldehyde and acetone, to produce the corresponding dialkoxyboranes.[2] Since these substances are readily hydrolyzed to form boric acid and the corresponding alcohol, it was evident that the procedure offered a promising route for the reduction of carbonyl groups.

However, at the time diborane was a rarity, prepared only with difficulty in relatively minor amounts.[3] Consequently, this synthetic route appeared to be of theoretical interest only, and it was not examined further.

The discovery of the alkali metal borohydrides[4] and aluminohydrides[5] made possible an alternate route for such reductions.[6] Although a number of simple, practical synthetic routes to diborane are now available,[7,8] there appeared, at first, little

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(1) Post-doctorate research assistant, 1955–1957, on grants provided by the Upjohn Co., Parke, Davis and Co., and Merck and Co.

(2) H. C. Brown, H. I. Schlesinger and A. B. Burg, THIS JOURNAL, **61**, 673 (1939).

(3) H. I. Schlesinger and A. B. Burg, *ibid.*, **53**, 4311 (1931).

(4) H. I. Schlesinger and H. C. Brown, *ibid.*, **62**, 3429 (1940); H. I. Schlesinger, H. C. Brown, H. R. Hockstra and L. R. Rapp, *ibid.*, **75**, 199 (1953).

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

(6) R. F. Nystrom and W. G. Brown, *ibid.*, **69**, 1197, 2548 (1947); **70**, 3738 (1948); S. W. Chaikin and W. G. Brown, *ibid.*, **71**, 122 (1949).

(7) H. I. Schlesinger, H. C. Brown, J. R. Gilbreath and J. J. Katz, *ibid.*, **75**, 195 (1953).

(8) H. C. Brown and P. A. Tierney, *ibid.*, **80**, 1552 (1958).

incentive to study reductions with diborane in view of the simple procedures made possible by the alkali metal borohydrides and aluminohydrides.

Careful scrutiny of the available data, however, revealed interesting differences in reductions by sodium borohydride and by diborane. For example, diborane does not reduce chloral,[2] whereas sodium borohydride reduces this aldehyde with great ease.[9] Moreover, acetyl chloride does not react with diborane under the usual conditions,[2] whereas it is rapidly reduced by sodium borohydride.[6,10]

In view of these interesting differences in the reducing activities of diborane and sodium borohydride, it appeared appropriate to undertake an extensive study of the reduction by diborane of organic compounds containing representative functional groups.[11]

Results

The procedure was similar to that utilized previously for the hydroboration of olefins.[12] In this procedure, 6.0 mmoles of diborane, generated from sodium borohydride and boron trifluoride etherate in diglyme,[8] was passed over a period of 30 minutes into the reaction vessel containing 9 to 15 mmoles of the compound under examination in 15.0 ml. of either diglyme or tetrahydrofuran. The exit to the reaction vessel led to a wash bottle containing acetone, an effective trap for diborane (in the form of diisopropoxyborane). The reaction mixture was permitted to remain at room temperature for a further 30 minutes, and ethylene glycol was then added to convert residual hydride in the reaction mixture to hydrogen. Diborane not absorbed in the reaction vessel was estimated by analyzing the acetone wash solution for boric acid. From these two analyses, the hydride not utilized for addition was obtained. Subtraction of this quantity from the blank value gave the hydride utilized for reduction.

Because of the much greater solubility of diborane in tetrahydrofuran than in diglyme, the former solvent offers some advantage in this procedure. However, other than this convenience, no significant difference was observed using either solvent. Consequently, the results observed with both solvents are combined and summarized in Table I.

These results indicated the possibility of reducing selectively one of several groups in a polyfunctional molecule. To test this possibility, several bifunctional molecules were treated with diborane in the identical procedure utilized for the monofunctional molecules. The results are summarized in Table II.

These experiments indicated that diborane should be particularly effective for the reduction of carboxylic acid and nitrile groups, and should be capable of reducing such groups in the presence of ester, acid chloride and nitro groups. This conclusion was tested by carrying out several representative reductions. The results are summarized in Table III.

Table I

Reaction of Representative Organic Compounds with Excess Diborane at 25°

Compound	Compd., mmoles	Solvent[a]	Hydride used, mmoles	Hydride used / compound
Benzaldehyde	15.0	THF	16.2	1.08
n-Butyraldehyde	12.1	THF	13.4	1.10
Benzophenone	15.0	DG	13.9	0.93
Cyclohexanone	14.3	THF	13.5	0.95
Styrene oxide	15.0	DG	16.9	1.12
Propylene oxide	11.4	THF	12.0	1.05
γ-Butyrolactone	12.4	THF	20.0	1.61
Ethyl benzoate	12.0	DG	3.7	0.31
Ethyl caproate	12.4	THF	17.2	1.39
Ethyl acetate	12.0	DG	21.7	1.81
Benzoic acid[b]	12.0	DG	33.3	2.78
n-Caproic acid[b]	9.3	THF	27.6	2.97
Sodium *p*-chlorobenzoate	10.9	THF	2.0	0.18
Sodium propionate	11.5	THF	0.9	.08
Benzoyl chloride	12.0	DG	3.6	.30
Isobutyryl chloride	12.0	DG	3.9	.33
Benzonitrile	12.0	DG	24.3	2.02
n-Butyronitrile	12.0	THF	26.1	2.18
Nitrobenzene	12.0	DG	0.7	0.06
1-Nitropropane	12.5	THF	0.4	0.03
Azobenzene	12.0	DG	21.6	1.80
Dimethyl sulfoxide	16.2	THF	10.4	0.64
p-Tolyl phenyl sulfone	10.6	THF	3.1	.29
Bromobenzene	12.2	THF	0.4	.03
Naphthalene	12.0	DG	.1	.01
Phenanthrene	13.0	THF	.8	.06
Benzamide[c]	13.7	THF	28.0	2.04
N,N-Dimethylbenzamide	12.0	DG	30.1	2.51

[a] 15.0 ml. of solvent: THF, tetrahydrofuran; DG, diglyme (dimethyl ether of diethylene glycol). [b] Hydride used includes one mole of hydrogen evolved per mole of acid. [c] Gas (presumably hydrogen) evolved with deposition of solid on walls of the reaction vessel.

Table II

Reaction of Representative Bifunctional Molecules with Diborane at 25°

Compound	Compd., mmoles	Solvent	Hydride used	Hydride used / compound
m-Nitrobenzoic acid	8.6	THF	22.4	2.60
p-Nitrobenzoic acid[a]	12.0	DG	29.3	2.44
Ethyl *p*-nitrobenzoate	11.0	THF	1.8	0.16
p-Nitrobenzoyl chloride	10.3	THF	8.6	0.83
m-Nitrobenzonitrile	11.1	THF	22.0	1.98
Ethyl *p*-cyanobenzoate	12.4	THF	21.6	1.74
p-Carboethoxybenzoic acid	8.8	THF	26.6	3.02

[a] Not completely soluble.

The very fast reduction of carboxylic acids by diborane was particularly unexpected and this reaction was explored further. Treatment of benzoic acid in tetrahydrofuran with the calculated quantity of diborane (6 $C_6H_5CO_2H/B_2H_6$) liberated one mole of hydrogen per mole of acid. On hydrolysis, the benzoic acid was recovered unchanged. Consequently, the reaction must involve the formation of triacylborane, $(C_6H_5CO_2)_3B$. This

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[9] E. H. Jensen, "A Study on Sodium Borohydride," Nyt Nordisk Forlag Arnold Busck, Copenhagen, 1954, p. 98.

[10] Unpublished observations with Dr. K. Ichikawa.

[11] A preliminary Communication reporting our observations has been published: H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, **22**, 1135 (1957).

[12] H. C. Brown and B. C. Subba Rao, This Journal, **81**, 6428 (1959).

TABLE III

REDUCTIONS BY DIBORANE ON A PREPARATIVE SCALE

Compound reduced[a]	Product	Yield, %	Physical constants, m.p., °C.
p-Nitrobenzoic acid	*p*-Nitrobenzyl alcohol	79	91–93
p-Chlorobenzoic acid	*p*-Chlorobenzyl alcohol	88	74–75
m-Nitrobenzonitrile	*m*-Nitrobenzylamine hydrochloride	88	225–227
Adiponitrile	1,6-Hexamethylene diamine dihydrochloride	85	246–248

[a] 0.2 mole.

product proved to be quite susceptible to reduction, being readily reduced either by diborane or by sodium borohydride.

On the other hand, treatment of one mole of sodium borohydride in diglyme with one mole of propionic acid resulted in the formation of one mole of hydrogen, but no reduction occurred, in spite of the excess of "hydride." Similarly, treatment of sodium propionate with diborane led to absorption of the gas, but not to significant reduction. In these experiments it would appear that the reaction product, $[C_2H_5CO_2BH_3]^- Na^+$, is formed but that, unlike the triacylborane, it is not susceptible to further reaction. An interpretation of the high reactivity of triacylboranes will be presented in the Discussion.

In the hydroboration of olefins similar results were realized in treating the olefin in ether solution with diborane generated externally, or in treating a solution of the olefin and sodium borohydride with boron trifluoride etherate. For large scale preparations the latter procedure is especially convenient. Accordingly, we examined the possibility that a similar procedure could be utilized for the reduction of representative organic substances.

In these experiments 7.15 mmoles of sodium borohydride and 4 to 10 mmoles of the compound under examination in diglyme solution was treated with 4.0 mmoles of boron trifluoride etherate. The use of an excess of sodium borohydride (only 3.0 mmoles are required to react with 4.0 mmoles of boron trifluoride) ensured that the initial reaction product would be the addition compound, $NaBH_4 \cdot BH_3$,[8] and that no diborane would be lost from the reaction mixture.

The boron trifluoride etherate was added relatively rapidly over 2 to 3 minutes. A control experiment, with identical solutions and operations, but without the compound under examination, was carried out simultaneously. After reaction times of 0.5 and 1.0 hour, ethylene glycol was added to the reaction flasks and the hydrogen evolved was measured. The difference between the hydrogen evolved by the blank and the reaction mixture gave the mmoles of hydride utilized by the compound for reduction.

The results of these experiments are summarized in Table IV. Although diborane does not reduce acid chlorides under the conditions of this study (Table I), these compounds react rapidly with sodium borohydride. Consequently, it was not possible to include acid chlorides in this modification of the reduction procedure.

TABLE IV

REACTION OF REPRESENTATIVE ORGANIC COMPOUNDS WITH SODIUM BOROHYDRIDE–BORON TRIFLUORIDE ETHERATE IN DIGLYME SOLUTION AT 25°

Compound	Compd., mmoles	Time, hr.	Hydride used, mmoles	Hydride used / compound
Benzaldehyde[a]	8.6	0.5	9.4	1.09
n-Butyraldehyde[a]	7.4	.5	7.8	1.05
Benzophenone[a]	5.24	.5	6.3	1.19
Cyclohexanone[a]	7.67	.5	7.1	0.93
Styrene oxide	4.86	.5	4.8	.99
Propylene oxide	8.55	.5	8.0	.94
γ-Butyrolactone	3.97	.5	7.3	1.84
	4.35	1.0	9.1	2.09
Ethyl benzoate	4.80	0.5	1.1	0.23
	5.57	1.0	2.1	.38
Ethyl caproate	5.15	0.5	4.2	.82
	4.23	1.0	6.0	1.42
Ethyl acetate	5.44	0.5	7.0	1.29
	5.23	1.0	8.7	1.66
Benzoic acid	3.70	0.5	10.9	2.95[b]
	3.91	1.0	11.3	2.89[b]
Caproic acid	4.01	0.5	12.5	3.12[b]
	4.19	1.0	13.2	3.15[b]
Sodium *p*-chlorobenzoate	5.46	0.5	2.5	0.46
	5.29	1.0	4.7	.89
Sodium propionate	6.17	0.5	1.8	.29
	5.67	1.0	1.7	.30
Benzonitrile	4.86	0.5	9.7	2.00
	4.95	1.0	9.8	1.98
n-Butyronitrile	5.41	0.5	10.1	1.86
	4.55	1.0	9.2	2.02
Nitrobenzene	5.02	0.5	0.2	0.04
	4.63	1.0	.4	.09
1-Nitropropane	4.83	0.5	.2	.04
	6.23	1.0	.4	.06
Azobenzene	5.08	0.5	11.4	2.24
	6.23	1.0	12.0	1.93
N,N-Dimethylbenzamide	5.50	1.0	12.0	2.18
Dimethyl sulfoxide	6.31	1.0	2.9	0.46
p-Tolyl phenyl sulfone	4.80	1.0	0.6	.13
Bromobenzene	6.10	1.0	.4	.07
Naphthalene	6.33	1.0	.4	.06

[a] Compound in diglyme solution added to a solution of sodium borohydride–boron trifluoride etherate in diglyme under nitrogen. [b] Includes one equivalent of hydrogen evolved through the action of the acid on the borohydride.

A similar series of experiments were carried out using bifunctional molecules in which rapid reduction of only one of the two functions was anticipated on the basis of the results in Table IV. The procedure was identical, except that the compounds were utilized in such amounts that the hydride analysis would indicate whether one or both substituents was undergoing reduction. The results are summarized in Table V.

The utility of this procedure for organic synthesis was tested by applying it on a preparative scale (0.2 to 0.4 mole) for the reduction of a number of representative organic compounds. The results are summarized in Table VI.

Discussion

The addition of the boron–hydrogen bond of diborane to multiple linkages appears to be a reaction

TABLE V

REACTION OF REPRESENTATIVE BIFUNCTIONAL MOLECULES WITH SODIUM BOROHYDRIDE–BORON TRIFLUORIDE ETHERATE AT 25°

Compound	Compd., mmoles	Time, hr.	Hydride used, mmoles	Hydride used / compound
m-Nitrobenzoic acid	3.98	0.5	12.5	3.14
	4.06	1.0	13.2	3.25
Ethyl *p*-nitrobenzoate	4.46	0.5	1.8	0.40
	5.04	1.0	2.5	0.50
p-Carboethoxybenzoic acid	4.38	0.5	12.4	2.83
	5.13	1.0	14.6	2.85
Ethyl *p*-cyanobenzoate	4.45	0.5	9.4	2.11
	4.10	1.0	9.5	2.32

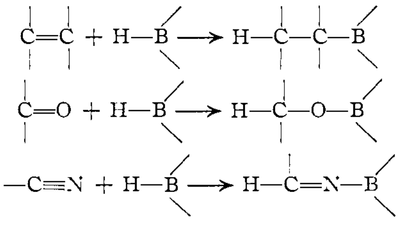
TABLE VI

REDUCTIONS BY SODIUM BOROHYDRIDE–BORON TRIFLUORIDE ETHERATE ON A PREPARATIVE SCALE

Compound reduced	Product	Yield, %	M.p. or b.p. (mm.)
p-Nitrobenzoic acid[a]	*p*-Nitrobenzyl alcohol	79	91–93
p-Chlorobenzoic acid[a]	*p*-Chlorobenzyl alcohol	92	73–75
Benzonitrile[b]	Benzylamine	83	181–183 (734)
Phenylacetonitrile[a]	2-Phenylethylamine	84	196–198 (746)
Styrene oxide[b]	2-Phenylethanol	52	103–105 (14)
	1-Phenylethanol	19	91–92 (14)

[a] 0.2 mole. [b] 0.4 mole.

of wide generality. Thus, the addition to carbon–carbon double[12] and triple bonds[13] at room temperature occurs with remarkable ease. The addition to the carbon–oxygen double bond of aldehydes and ketones had long been known.[2] In the present study, the rapid addition of such bonds to the carbon–nitrogen triple bond of nitriles has been demonstrated.



$$\begin{gathered} >C=C< + H-B< \longrightarrow H-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-B< \\ >C=O + H-B< \longrightarrow H-\overset{|}{\underset{|}{C}}-O-B< \\ -C\equiv N + H-B< \longrightarrow H-\overset{|}{C}=N-B< \end{gathered}$$

Consequently, it appears that the addition of the hydrogen–boron bond of diborane to multiple linkages is as general a reaction as the addition of hydrogen to such bonds. It differs from the latter reaction notably in the great ease with which diborane adds to such multiple linkages without the metal catalysts required by hydrogen. The general term, hydroboration, was suggested for this important general addition reaction.[14]

In the present study, the reaction of diborane with a number of organic compounds was examined. Insofar as it may be valid to generalize these observations, the reducing action of diborane toward representative functional groups has been summarized in Table VII.

Diborane exhibits a number of remarkable differences in its reducing power from those exhibited by the alkali metal borohydrides. Thus nitriles are not reduced under these conditions by borohydrides, yet they are rapidly converted to amines by diborane at room temperature. Similarly, carboxylic acids are generally considered to be relatively resistant to reducing agents. Yet diborane converts these compounds into the corresponding alcohols with remarkable rapidity.[15]

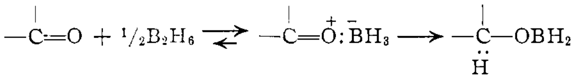
TABLE VII

REDUCING PROPERTIES OF DIBORANE IN ETHER SOLVENTS AT 25°

Functional group	Hydride used per mole	Product[a]	Remarks
Alcohol	1	Alcohol	1 mole of hydrogen evolved
Aldehyde[b]	1	Alcohol	Very fast
Ketone	1	Alcohol	Very fast
Acid chloride	0		Very slow reacn.
Ester	2	Alcohol	Slow reaction
Lactone	2	Glycol	Moderate reaction
Carboxylic acid	3	Alcohol	1 mole of hydrogen evolved; fast redn.
Carboxylic salt	0		No reaction
Epoxide	1	Alcohol	Fast reaction
Amide	2		2 moles hydrogen evolved
t-Amide	2		
Nitrile	2	Amine	Fast reaction
Nitro compounds	0		No reaction
Azo compounds	2	Amine	Fast reaction
Sulfoxide			Slow reaction
Sulfone	0		No reaction
Aryl halides	0		No reaction
Aromatic hydrocarbons	0		No reaction

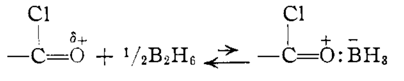
[a] After hydrolysis of the hydroboration intermediate. [b] Chloral is not reduced (ref. 2).

It was previously noted that the carbonyl groups of simple aldehydes and ketones react rapidly with diborane, whereas the carbonyl groups of chloral and acid chlorides are relatively inert to the hydride.[2] It was considered significant that those aldehydes and ketones which react readily with diborane also form stable addition compounds with boron trifluoride, whereas chloral and acetyl chloride add this Lewis acid only with difficulty at low temperatures.[2] It was suggested that the initial stage of the reaction of diborane with the carbonyl group involves an acid–base interaction, with borane adding to the oxygen atom, followed by a transfer of a hydride unit from boron to carbon.



$$-\overset{|}{C}=O + {}^1/_2B_2H_6 \rightleftarrows -\overset{|}{C}=\overset{+}{O}:\overset{-}{B}H_3 \longrightarrow -\overset{|}{\underset{\ddot{H}}{C}}-OBH_2$$

On this basis, the inertness of acetyl chloride and of chloral toward diborane was attributed to the decreased basic properties of the oxygen atom of the carbonyl group, resulting from the powerful inductive effects of the halogen substituents.



$$-\overset{Cl}{\overset{|}{C}}=\overset{\delta+}{O} + {}^1/_2B_2H_6 \rightleftarrows -\overset{Cl}{\overset{|}{C}}=\overset{+}{O}:\overset{-}{B}H_3$$

It is noteworthy that both acetyl chloride and chloral are highly reactive toward sodium borohydride. It is not unreasonable that the electron deficiency, induced by the chlorine substituents,

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(13) H. C. Brown and G. Zweifel, THIS JOURNAL, **81**, 1512 (1959).

(14) H. C. Brown and B. C. Subba Rao, *ibid.*, **81**, 6423 (1959).

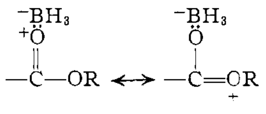
(15) Unpublished observations of Dr. W. Korytnyk have established that carboxylic acids are reduced in this procedure even more rapidly than the carbonyl group of ketones.

which serves to inhibit attack by the Lewis acid, diborane, should facilitate attack by the nucleophilic borohydride ion.

In other words, diborane is a Lewis acid which functions best as a reducing agent in attacking groups at positions of high electron density, whereas borohydride is a Lewis base which prefers to attack a group at positions of low electron density.

This interpretation can be extended to account for the behavior of nitriles. The nitrile group is relatively insensitive to attack by nucleophilic reagents. Consequently, its relative inertness toward attack by borohydride ion is not unexpected. However, the nitrogen atom of the nitrile group is relatively basic. It adds boron trifluoride to form addition compounds of moderate stability.[16] Presumably, the rapid reduction of nitriles by diborane involves an initial attack of the reagent at this relatively basic position.[17]

Two factors presumably account for the relatively slow rate of reduction of carboxylic esters. First, addition of the borane particle to the oxygen atom of the carbonyl group must compete with addition to the oxygen atom of the alkoxy group. Secondly, transfer of hydride from boron to oxygen will presumably be hindered by the stabilization provided the carbonyl group by resonance with the oxygen atom of the alkoxy group,



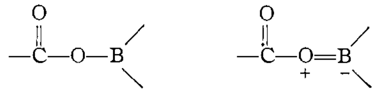
$$-\overset{\overset{\overset{{}^{-}BH_3}{\overset{+}{O}}}{\|}}{C}-OR \longleftrightarrow -\overset{\overset{\overset{{}^{-}BH_3}{O}}{|}}{C}=\underset{+}{O}R$$

The fast rate of reaction of diborane with carboxylic acids remains to be considered. It was observed that treatment of three moles of *p*-chlorobenzoic acid with one-half mole of diborane resulted in the evolution of three moles of hydrogen. Hydrolysis of the reaction product yielded unchanged *p*-chlorobenzoic acid. Consequently, the first stage in the reaction must be the formation of a triacylborane.[18]

$$3RCO_2H + {}^1/_2B_2H_6 \longrightarrow (RCO_2)_3B + 3H_2$$

This initial reaction product is readily reduced by further treatment with diborane. Indeed, the carboxylic acid group in this intermediate is so active that reduction by sodium borohydride is also observed.

The following interpretation of this interesting phenomenon is proposed. The electron deficiency of the boron atom in the triacylborane should exert a powerful demand on the electron pairs of the acyl oxygen. Such resonance as occurs will involve interaction of this oxygen atom with the boron atom, rather than the usual resonance with the carbonyl group.



According to this interpretation, the carbonyl groups in the triacylboranes should resemble those in aldehydes and ketones far more than the less active carbonyl groups of esters. We are examining this proposal.

This study was originally undertaken to examine the utility of diborane for selective reductions. Consequently, the emphasis was primarily exploratory and practical in nature. It now appears that diborane provides a valuable adjunct to the complex hydrides as a reducing agent. Moreover, in the course of this study a number of new and interesting theoretical problems have been uncovered. We are examining the reaction of diborane with nitriles and with carboxylic acids in considerable detail in order to test the above tentative interpretations of the unusual reactivity exhibited by these compounds toward diborane.

Experimental Part

Materials.—The solvents, sodium borohydride and boron trifluoride etherate, were purified by procedures described earlier.[12] Diborane was prepared from sodium borohydride and boron trifluoride etherate using the procedure described previously.[12] The various compounds examined were standard research chemicals which were purified by distillation or crystallization prior to use.

Small Scale Reduction Studies.—The procedures utilized for examining the reduction of various types of compounds by either diborane or sodium borohydride–boron trifluoride etherate were essentially identical with those previously utilized for studying the hydroboration of olefins.[12] Consequently, they need not be described here.

Reaction of Diborane with Carboxylic Acids.—The following experiments are typical of the experiments exploring the reaction of diborane with carboxylic acids. *p*-Chlorobenzoic acid, 1.88 g., 12.0 mmoles, was dissolved in diglyme and treated with 2.0 mmoles of diborane (from 3.3 mmoles of sodium borohydride and 12.0 mmoles of boron trifluoride etherate in diglyme solution). Hydrogen was evolved, 12.5 mmoles. The clear solution was hydrolyzed, the precipitate collected on the filter, washed and dried. There was obtained 1.75 g. of *p*-chlorobenzoic acid, m.p. 236–238°, a recovery of 93%.

Similarly, treatment of 1.88 g., 12.1 mmoles, of *p*-chlorobenzoic acid with 8.0 mmoles of diborane resulted in the evolution of 12.1 mmoles of hydrogen. At the end of 1.0 hour, the reaction product was hydrolyzed and the hydrogen evolved was collected. In this way, it was estimated that 21.8 mmoles of hydride had been utilized for reduction. Hydrolysis of the reaction product yielded 1.38 g. of *p*-chlorobenzyl alcohol, m.p. 73–75°, a yield of 81%.

Reductions on a Preparative Scale.—The following procedures are representative of the large scale reductions with either diborane or with sodium borohydride–boron trifluoride.

In a 500-ml. round-bottom three-neck flask fitted with a thermometer, an inlet tube for diborane, and a reflux condenser, the top of which was connected to an outlet tube leading to an acetone wash bottle, was placed a solution of 29.6 g. (0.20 mole) of *m*-nitrobenzonitrile, m.p. 116–117°, in 150 ml. of tetrahydrofuran. The system was flushed with nitrogen. Diborane, 0.080 mole, generated in an adjacent flask by the addition of 5.1 g. (0.135 mole) of sodium borohydride in 125 ml. of diglyme in a dropping funnel to 28.5 g. (0.20 mole) of boron trifluoride etherate in 50 ml. of diglyme, was passed into the reaction flask over a period of 1 hour. The reaction mixture was allowed to stand at room temperature for a second hour. Ethanol was then added cautiously to destroy excess diborane (hydrogen evolved). Dry hydrogen chloride was passed in. After removal of the solvent, the reaction mixture was allowed to cool, the solid hydrochloride was collected on a filter, washed with a small amount of ethanol, and dried. There was obtained 33.2 g., 88%, of the crude amine hydrochloride, m.p. 223–225°.

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(16) H. C. Brown and R. B. Johannesen, THIS JOURNAL, **72**, 2934 (1950), and literature cited therein.

(17) The precise nature of the reaction product is under investigation.

(18) Considerable discussion has appeared on whether the "boron acetate" obtained from the action of acetic anhydride on boric oxide [A. Pictet and A. Geliznoff, *Ber.*, **36**, 2219 (1903)] is really triacetylborane, $(CH_3CO_2)_3B$, or is a product derived from this by the loss of acetic anhydride $(CH_3CO_2)_2BOB(O_2CCH_3)_2$; T. Ahmad and M. J. Khundkar, *Chemistry & Industry*, 248 (1954); W. Gerrard and E. F. Mooney, *ibid.*, 227 (1958).

Recrystallization from absolute ethanol yielded pure *p*-nitrobenzylamine hydrochloride, m.p. 225–227°, a yield of 79%.

Similarly, 0.20 mole of adiponitrile, b.p. 154–156° at 8 mm., was treated with 0.16 mole of diborane. After 4 hours, the product was treated with hydrogen chloride and isolated as in the above procedure in the form of the dihydrochloride: 32.2 g., m.p. 245–247°, 85% yield. Recrystallization from absolute ethanol–benzene gave 28.0 g., 74% yield, of 1,6-hexamethylenediamine dihydrochloride, m.p. 246–248°.

p-Chlorobenzoic acid, m.p. 237–239°, 31.3 g., 0.20 mole, was cautiously added to 0.18 mole of sodium borohydride (180 ml. of 1.0 *M* solution in diglyme) in a 500-ml. round-bottom flask, fitted with a magnetic stirrer and a separatory funnel. When the acid had gone into solution, evolving hydrogen, 0.24 mole of boron trifluoride etherate, in 50 ml. of diglyme, was added over a period of 1 hour through the separatory funnel to the stirred solution. After 3 additional hours at room temperature, the reaction mixture was poured onto crushed ice, the precipitated solid collected on a filter, washed with ice-water and dried. The crude product, 27.7 g., m.p. 73–75°, 92% yield, was recrystallized from hot aqueous ethanol to give *p*-chlorobenzyl alcohol, m.p. 74–75°, in 81% yield.

In a similar manner, 0.20 mole of *p*-nitrobenzoic acid, 33.4 g., m.p. 240–242°, was reduced with sodium borohydride–boron trifluoride etherate, and the product poured onto crushed ice and dilute hydrochloric acid. The precipitated alcohol was separated, and the aqueous filtrate extracted with ethyl ether. The ether extract was washed with small quantities of ice-water to remove diglyme. There was obtained a total of 24.1 g. of product, m.p. 91–93°, a yield of 79%. After treatment with active carbon and recrystallization from hot water, pure *p*-nitrobenzyl alcohol, white crystals, m.p. 92–93°, was obtained in a yield of 72%.

Using essentially the same procedure, 41.3 g., 0.4 mole, of benzonitrile, b.p. 189° at 743 mm., was treated with 0.27 mole of sodium borohydride (30% excess) and 0.36 mole of boron trifluoride etherate. After a reaction time of 2 hours (1 hour addition of the boron trifluoride etherate, followed by 1 hour standing at room temperature), the excess hydride in the reaction mixture was destroyed by adding concentrated hydrochloric acid. The solvent and excess acid was removed under reduced pressure, leaving a residue of inorganic salts and benzylamine hydrochloride. Strong aqueous alkali was added, the amine extracted with ether, dried and distilled. There was obtained 35.7 g. of benzylamine, b.p. 181–183° at 734 mm., a yield of 83%.

Similarly, 0.20 mole of phenylacetonitrile, b.p. 107–108° at 10 mm., yielded 20.3 g. of β-phenylethylamine, b.p. 196–198° at 748 mm., a yield of 84%.

Styrene oxide, 0.40 mole, 48.0 g., b.p. 190–191° at 749 mm., was treated with 0.11 mole of sodium borohydride and 0.13 mole of boron trifluoride etherate. After a reaction time of 1 hour, the product was hydrolyzed and the alcohol recovered with ether. There was obtained 36.6 g. of mixed alcohols, a yield of 75%. On distillation there was obtained 25.1 g. of 2-phenylethanol, b.p. 103–105° at 14 mm., and 9.3 g. of 1-phenylethanol, b.p. 91–92° at 14 mm.

LAFAYETTE, IND.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CINCINNATI]

The Rates of Reaction of Some Substituted Diarylmercury Compounds with Hydrogen Chloride

BY RAYMOND E. DESSY AND JIN-YOUNG KIM[1]

RECEIVED JUNE 15, 1959

The rates of reaction of a series of substituted aromatic organomercury compounds with HCl in DMSO–dioxane have been investigated (eq. 2). It is found that the series Z = *p*-CH_3O, Cl, F, C_6H_5 and *m*-NO_2 obeys the Hammett plot log $k = (\sigma + \sigma^+/2)\,\rho$, with $\rho = -2.8$. E^* is a linear function of ΔS^* and the isokinetic temperature is 500°K. It is suggested that the linear relationship between E^* and ΔS^* is the result of changes in the ground state solvation of the organomercury and consequent changes in the C–Hg–C angle.

In a previous paper in this series[2] the rates of reaction of some dialkymercury compounds with hydrogen chloride in dimethyl sulfoxide–dioxane solution were reported, and a mechanism for the reaction proposed.

$$R_2Hg + HCl \xrightarrow[10:1]{\text{DMSO–dioxane}} RHgCl + RH \quad (1)$$

In light of the increased interest in the reactions of organomercury compounds, it was felt that an investigation of the reaction rates of a series of substituted aromatic mercury compounds would prove valuable

$$(Z\text{-}C_6H_4)_2Hg + HCl \xrightarrow[10:1]{\text{DMSO–dioxane}} Z\text{-}C_6H_4HgCl + Z\text{-}C_6H_5 \quad (2)$$

Although considerable experimental evidence has accumulated concerning electrophilic substitution at an aromatic carbon involving proton expulsion, and nucleophilic substitution at a saturated carbon center, little work has been done on electrophilic substitution at such centers which involve the expulsion of a group other than hydrogen.

Experimental

Organomercury Compounds.—The organomercury compounds were prepared by standard techniques.[3]

Diphenylmercury was prepared by treating phenylmagnesium bromide with mercuric chloride in ether-benzene.[3] The product was recrystallized from chloroform, m.p. 122–124°.

Bis-*p*-chlorophenylmercury.—*p*-Chlorobromobenzene was converted to the Grignard reagent, and treated with $HgCl_2$ in ether. The product crystallized from chloroform, m.p. 249–252° (lit.[4] 242–243°).

Anal. Calcd. for $C_{12}H_8Cl_2Hg$: C, 34.01; H, 1.90. Found: C, 34.31; H, 2.05.

Bis-*p*-fluorophenylmercury.—*p*-Fluorobromobenzene was converted to the Grignard reagent and treated with $HgCl_2$ in ether. The product was recrystallized from ligroin–benzene, m.p. 151–154° (lit.[5] 151–155°).

Anal. Calcd. for $C_{12}H_8F_2Hg$: C, 36.87; H, 2.06. Found: C, 36.30; H, 2.61.

Bis-*p*-diphenylmercury.—4-Bromodiphenyl was converted to the Grignard reagent, and treated with $HgCl_2$ in ether,

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[1] National Science Foundation Research Fellow.

[2] Raymond E. Dessy, G. F. Reynolds and Jin-Young Kim, THIS JOURNAL, **81**, 2683 (1959).

[3] F. C. Whitmore, "Organic Compounds of Mercury," Chemical Catalogue Co., Inc. (Reinhold Publ. Corp.), New York, N. Y., 1921.

[4] Fr. Hein and K. Wagler, *Ber.*, **58**, 1499 (1925).

[5] G. C. Hampson, *Trans. Faraday Soc.*, **30**, 877 (1934).