[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

Addition Compounds of Alkali Metal Hydrides. II. Sodium Trimethoxyborohydride as a Reducing Agent for Organic Compounds[1,2]

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Sodium trimethoxyborohydride is readily prepared by the reaction of sodium hydride and methyl borate in the presence of tetrahydrofuran as solvent: $Na^+H^- + B(OCH_3)_3 = Na^+BH(OCH_3)_3^-$. The product readily reduces aldehyde, ketone, acid chloride and acid anhydride groups. Ester and nitrile groups are only slowly reduced at elevated temperatures, whereas the carboxylate group does not appear to react. The nitro group is not reduced at lower temperatures, but undergoes reaction at 140°. Double bonds appear stable, even when conjugated with a carbonyl group. At low temperatures (0 to −80°) sodium trimethoxyborohydride in stoichiometric amounts appears to react with acid chlorides to form aldehydes in accordance with the equation: $RCOCl + NaBH(OCH_3)_3 = RCHO + NaCl + B(OCH_3)_3$.

The reagent sodium trimethoxyborohydride, $NaBH(OCH_3)_3$, has been observed to be a powerful reducing agent toward various inorganic substances; and accordingly we have examined its utility for similar action upon organic compounds.

The parent compound, sodium borohydride, has been shown to be an excellent reducing agent for aldehyde and ketone groups.[3,4] It has been extensively utilized for selective reductions, particularly in the steroid field.[5] Sodium triphenylborohydride has been studied by Wittig.[6] The easy preparation of the trialkoxyborohydrides together with the numerous possible variations in structure, suggest that these compounds should possess interesting possibilities for selective reductions.

Sodium trimethoxyborohydride was originally prepared by refluxing the sodium hydride with an excess of methyl borate for several hours. The sodium hydride was an active material which is no longer available. The commercial product now available reacts much more sluggishly and complete reaction could not be obtained in reaction periods of less than 15–20 hours.

Sodium trimethoxyborohydride is highly soluble in tetrahydrofuran. By use of this material as the medium, the reaction with the sodium hydride was greatly accelerated and could be completed in a matter of minutes, with heat transfer as the limiting factor.

For an initial survey of its reducing characteristics, the organic compound in the inert medium (ethyl ether or butyl ether) was heated under reflux with an excess of trimethoxyborohydride suspended in the reaction mixture. After 4 hours, the unreacted trimethoxyborohydride was decomposed with acid and the hydrogen collected and measured.

The results are summarized in Table I.

TABLE I

REACTION OF ORGANIC COMPOUNDS WITH EXCESS SODIUM TRIMETHOXYBOROHYDRIDE

Compound	Moles $NaBH(OCH_3)_3$/mole compound Ethyl ether	 *n*-Butyl ether
Benzaldehyde	0.97	0.90
n-Heptaldehyde	.93	.93
Chloral	1.00	..
Cinnamaldehyde	.93	.91
Crotonaldehyde	.71	.85
Acetophenone	.82	.92
n-Amyl methyl ketone	.83	.74
Pinacolone	.60	..
Acetomesitylene	.30	1.2[a]
Benzoyl chloride	1.70	2.00
Acetyl chloride	.71	..
Ethyl benzoate	.02	.88
Ethyl butyrate	.58	.76
Benzonitrile	.11	.54
Acetic anhydride	1.68	1.68
Phthalic anhydride	.56	1.49
Benzoic acid	.82	.93
Sodium benzoate	.01	.02
Nitrobenzene	.00	2.00

[a] The reaction mixture turned dark indicating that some decomposition had taken place.

The validity of these results was confirmed in several instances by repeating the experiments on a preparative scale (0.2 mole) with isolation and identification of the product. The results are summarized in Table II.

TABLE II

YIELDS OBTAINED IN REDUCTIONS WITH SODIUM TRIMETHOXYBOROHYDRIDE

Compound	Yield, %	Product	B.p., °C.	Mm.	$n^{20}D$
Benzaldehyde	78	Benzyl alcohol	93–95	13	1.5406
Acetophenone	82	1-Phenylethanol	93–95	13	1.5244
Cinnamaldehyde	79	Cinnamyl alcohol	134–135	13	1.5824
Benzoyl chloride	66	Benzyl alcohol	90–93	10	1.5386
Ethyl benzoate	33	Benzyl alcohol	93–95	13	1.5405

These and other experiments indicate that aldehyde, ketone, acid chloride and acid anhydride groups are readily reduced at moderate temperatures (35°), ester and nitrile groups are more slowly reduced even at somewhat higher temperatures (100–140°), while the carboxylate group is not altered under these conditions. Carbon to carbon double bonds appear stable, even when conjugated with a carbonyl group. The nitro group is not reduced at the lower temperature but does undergo reaction at 140°. The nature of the product formed in this reaction was not investigated.

It is probable that in a suitable solvent sodium

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(1) Paper I in this series: H. C. Brown, H. I. Schlesinger, I. Sheft and D. M. Ritter, THIS JOURNAL, **75**, 192 (1953).

(2) Based upon a thesis submitted by Edward J. Mead in partial fulfillment of the requirements for the M.S. degree, Jan., 1952.

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

(4) S. W. Chaikin and W. G. Brown, *ibid.*, **71**, 122 (1949).

(5) L. Fieser, *et al.*, *ibid.*, **73**, 5252 (1951); *ibid.*, **75**, 116, 1700, 1704 (1953); C. Djerassi, *et al.*, *ibid.*, **75**, 1286, 1745 (1953); R. B. Woodward, *et al.*, *ibid.*, **73**, 3547, 3548, 4057 (1951); W. G. Dauben, *et al.*, *ibid.*, **73**, 4463, 4496 (1951); *ibid.*, **74**, 3852 (1952); E. G. Hershberg, *et al.*, *ibid.*, **75**, 269, 486, 488 (1953).

(6) G. Wittig, G. Keicher, A. Ruckert and P. Raff, *Ann.*, **563**, 110 (1949).

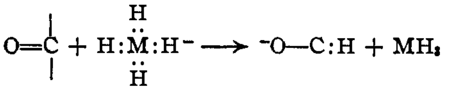
trimethoxyborohydride would exhibit more powerful reducing properties so that it could be used for the convenient reduction of esters and nitriles. We are currently examining the properties of such solutions.

We also investigated the reaction of sodium trimethoxyborohydride in tetrahydrofuran solution with acid chlorides at low temperatures (0 to −80°). We had hoped that the reaction would proceed in accordance with the equation

$$\mathrm{RCOCl + NaBH(OCH_3)_3 \longrightarrow RCHO + NaCl + B(OCH_3)_3}$$

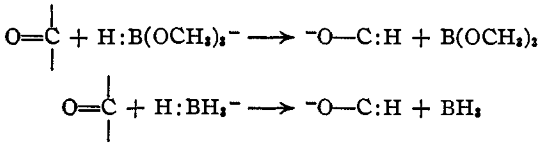
We established that aldehydes react relatively slowly with the reducing agent at 0° with negligible reduction occurring at lower temperatures (−30 to −80°). On the other hand, the acid chloride reacts practically instantly, even at −80°. Although these relative reactivities strongly favor the desired reaction path, we have obtained only relatively poor yields of aldehyde, 25–40%. Considerable quantities of both the alcohol, $\mathrm{RCH_2OH}$, and the methyl ester, $\mathrm{RCO_2CH_3}$, are concurrently formed. We are continuing our study of this reaction in the hope of circumventing the side reactions which are responsible for the poor yield.

The mechanism of reduction with the complex hydrides is believed to involve transfer of a hydride ion.[7]



$$\mathrm{O{=}\overset{|}{\underset{|}{C}} + H{:}\overset{\overset{H}{\cdot\cdot}}{\underset{\underset{H}{\cdot\cdot}}{M}}{:}H^- \longrightarrow {}^-O{-}C{:}H + MH_3}$$

If so, it would be expected that transfer of the strong base, hydride ion, would proceed more readily from the weak acid, methyl borate, than from the much stronger acid, borine.



$$\mathrm{O{=}\overset{|}{\underset{|}{C}} + H{:}B(OCH_3)_3^- \longrightarrow {}^-O{-}C{:}H + B(OCH_3)_3}$$

$$\mathrm{O{=}\overset{|}{\underset{|}{C}} + H{:}BH_3^- \longrightarrow {}^-O{-}C{:}H + BH_3}$$

Although the experiments reported in the present paper give some support for this view, we are undertaking a study of the kinetics of the reaction of the two reagents in the hope of obtaining quantitative data to decide this question.

Experimental Part

Materials.—The sodium hydride and methyl borate were obtained from Metal Hydrides, Inc., Beverly, Massachusetts. Tetrahydrofuran (du Pont) was purified by standing for several hours over potassium hydroxide pellets, followed by distillation from lithium aluminum hydride under a nitrogen atmosphere. The remaining chemicals were commercial products which were distilled where further purification appeared desirable.

Preparations of Sodium Trimethoxyborohydride.—In a typical preparation, 85.6 g. (3.56 moles) of sodium hydride was heated under reflux with 857 g. (8.24 moles) of methyl borate in a nitrogen atmosphere. After 15 hr., the solid material had expanded approximately 5 times its original volume. The excess methyl borate was removed by distillation. There was obtained 441 g. (3.45 moles) of product. In contrast to the earlier preparations using a more reactive sodium hydride,[1] the product was caked and was therefore powdered and then bottled with minimum exposure to the atmosphere.

Sodium trimethoxyborohydride is insoluble in the simple ethers (ethyl and *n*-butyl), but is moderately soluble in dioxane and highly soluble in tetrahydrofuran. This observation led to an improved synthetic procedure.

The sodium hydride (5.4 g., 0.225 mole) was placed in a 500-ml., 3-neck flask fitted with a reflux condenser, dropping funnel and inlet for nitrogen. The air was displaced with nitrogen and 370 ml. of tetrahydrofuran added. After the material had been brought to reflux, methyl borate (17.2 g., 0.167 mole) was added through the dropping funnel. The rate of addition was controlled to maintain a gentle reflux and avoid a violent reaction. (Warning! It is important not to add the methyl borate to the cold reaction mixture. A large concentration of the borate might be built up and lead to a sudden, violent exothermic reaction.) After 0.5 to 1 hr., the flask was allowed to cool to room temperature and the solution was forced, by means of a slight pressure of nitrogen, through a sintered glass filter into the reaction flask (for reductions) or glass vessels (for storage). In most cases it has proven convenient to synthesize and to utilize the reagent in solution without isolation.

Reduction Procedure without Isolation of Product.—Solid sodium trimethoxyborohydride (0.0443 mole) was placed in the 200-ml., 3-neck flask and a solution of the compound to be examined (0.015 mole) in 25 ml. of anhydrous ethyl ether was added through the dropping funnel. The mixture was refluxed for 4 hr. The top of the reflux condenser was then connected through a −80° trap and a soda lime tube to a wet-test meter. Dilute sulfuric acid was added through the dropping funnel to hydrolyze unreacted trimethoxyborohydride. The hydrogen liberated was measured on the wet-test meter.

In a typical experiment 1.746 g. (0.0153 mole) of *n*-heptaldehyde was treated in this way. There was obtained 676 ml. (0.0301 mole) of hydrogen (STP), corresponding to 92.8% of theory for utilization of the reducing agent.

Reduction of Cinnamaldehyde.—The following preparation will illustrate the procedure used for reductions in which the products were isolated. Sodium trimethoxyborohydride, 40 g., together with 100 ml. of ether, was placed in a 500-ml. flask which was fitted with a mercury-sealed stirrer, condenser and dropping funnel. Upon addition of 21.7 g. (0.165 mole) of freshly distilled cinnamaldehyde, the reaction mixture began refluxing. This was continued for 4 hr. with external heating. The flask was cooled and dilute sulfuric acid was run in until hydrogen was no longer evolved. The ether layer was dried over sodium sulfate and the solvent removed. Distillation of the product through a short Vigreux column yielded 17.5 g. (0.133 mole) of cinnamyl alcohol, b.p. 134–135° at 13 mm., $n^{20}\mathrm{D}$ 1.5824.

Reduction of Benzaldehyde at 0°.—The following procedure was used to determine the rate of aldehyde reduction at 0°. A 200-ml. flask was fitted with a mercury-sealed

TABLE III

ANALYSES FOR ALDEHYDE AND HYDRIDE IN BENZALDEHYDE REDUCTION AT 0°

Time, min.	Aldehyde mmole/ml. soln.	Time, min.	Hydride, mmole/ml. soln.
0	0.113[a]	0	0.102[a]
15	.091	22	.060
30	.084	52	.045
45	.080	90	.039
60	.074		

[a] Calcd. from initial concentrations before mixing.

TABLE IV

ANALYSES FOR ALDEHYDE AND HYDRIDE IN BENZOYL CHLORIDE REDUCTION AT 0°

Time, min.	Aldehyde, mmole/ml. soln.	Time, min.	Hydride, mmole/ml. soln.
0	0.000[a]	0	0.101[a]
15	.034	3	.005
30	.034	22	.000
45	.041	77	.000
60	.038		

[a] Calcd. from concentration of stock solution.

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(7) L. W. Trevoy and W. G. Brown, THIS JOURNAL, 71, 1675 (1949).

stirrer, a reflux condenser and dropping funnel. The flask was flamed to remove water and the air displaced by nitrogen. The benzaldehyde (0.777 g., 7.33 mmoles) in 50.0 ml. of tetrahydrofuran was introduced into the flask and maintained at 0°. A solution of sodium trimethoxyborohydride (15.0 ml. containing 0.440 mmole/ml.) was added through the dropping funnel over a period of 2 min. Aliquot samples were removed at suitable intervals and analyzed for residual aldehyde using 2,4-dinitrophenylhydrazine[8] and for active hydride, using the procedure of Lyttle, Jensen and Struck.[9] The results are summarized in Table III.

Reduction of Benzoyl Chloride at 0°.—The experiment was carried out precisely as in the case of benzaldehyde described above, except that 1.00 g. (7.11 mmoles) of benzoyl chloride was used. The results of the aldehyde and hydride determinations are summarized in Table IV.

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[8] H. A. Iddles, A. W. Low, B. D. Rosen and R. T. Hart, *Anal. Ed.*, **11**, 103 (1939).

[9] D. A. Lyttle, E. H. Jensen and W. A. Struck, *ibid.*, **24**, 1843 (1952).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

Complexes of Aromatic Hydrocarbons with Aluminum Bromide[1,2]

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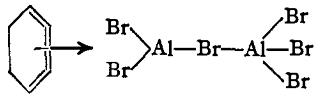
Aluminum bromide possesses the dimeric formula, Al_2Br_6, in benzene solution. Vapor pressure–composition phase studies at 17.7° show the existence of solid compounds $Al_2Br_6 \cdot ArH$ with benzene and toluene. Similar studies of the corresponding *m*-xylene and mesitylene systems did not indicate the formation of similar solid complexes. However, the color of the solutions as well as molecular weight determinations of solutions of mesitylene and aluminum bromide in cyclopentane support the existence of similar complexes in the case of the latter two hydrocarbons. It is proposed that these aromatic aluminum bromide compounds are π-complexes with the structure



Introduction

Aluminum bromide is readily soluble in aromatic hydrocarbons, apparently with the formation of complexes. Unfortunately a number of serious conflicts exists in the observations and data recorded in the literature and unequivocable formulation of the complexes is not now possible.

For example, two groups of workers[4,5] agree that aluminum bromide possesses a high dipole moment in dilute benzene solutions. However, one group claims that the dipole moment drops to zero at higher concentrations[5] and differs, thereby, from the first group.[4] The change in dipole moment with concentration is attributed to the existence of aluminum bromide in dilute solutions in the monomeric form, $AlBr_3$, complexed with the aromatic hydrocarbon, and in the dimeric uncomplexed form in the more concentrated solutions. Parachor measurements[6] and molecular weight determinations by freezing point[4,7] and vapor pressure lowering[7] indicate a dimeric formula for aluminum bromide in benzene solution. Moreover, the dimeric formula is also supported by the observation that the molar refractivities of solutions of aluminum bromide in benzene and toluene exhibit strict additivity.[8] The parachor measurements[6] were made in dilute solution, comparable to those used in the dipole moment determinations.[5] A serious conflict exists between the respective conclusions of the two groups of authors.[5,6]

As a result of his study of the systems of aluminum bromide with benzene, toluene and *p*-xylene, Menshutkin[9] decided that complex formation did not occur. However, as a result of a similar study, Plotnikov and Gratsianskii[10,11] concluded that aluminum bromide does form complexes with benzene, *p*-xylene and *m*-xylene (m.p. 37, 31.2, 4.5°, respectively). The complexes melt incongruently. The arrests in the phase diagrams occurred on the hydrocarbon-rich side of equimolar proportions of aluminum bromide and hydrocarbon so that the complexes were assigned the empirical formula $AlBr_3 \cdot ArH$. Moreover, a recent study of the benzene–aluminum bromide system has been considered to confirm Plotnikov's conclusion.[12] The authors also formulate the complex as $AlBr_3 \cdot C_6H_6$ with an incongruent m.p. of 37°. However, Van Dyke concluded that the solid compound which separates from these solutions should be formulated as $Al_2Br_6 \cdot 2C_6H_6$, since aluminum bromide exhibits the dimeric molecular weight in benzene solution.[7]

A different formulation for these complexes is indicated by data reported by Norris and Ingraham.[13] They prepared ternary complexes of aluminum bromide and hydrogen bromide with benzene, toluene, mesitylene and 1,3,5-triethylbenzene. At reduced pressures the ternary complexes lost both hydrogen bromide and hydrocarbon. The benzene

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[1] The Catalytic Halides. V.

[2] Abstracted from a thesis submitted by William J. Wallace in partial fulfillment of the requirements for the Ph.D. degree.

[3] Standard Oil Company (Indiana) Fellow, 1950–1952.

[4] H. Ulich and W. Nespital, *Z. Elektrochem.*, **37**, 559 (1933); H. Ulich, *Z. physik. Chem.*, *A* (*Bodenstein Festband*), 423 (1931); W. Nespital, *Z. physik. Chem.*, **B 16**, 153 (1932).

[5] V. A. Plotnikov, I. A. Sheka and Z. A. Yankelewich, *Mem. Inst. Chem., Akad. Sci. Ukrain. S.S.R.*, **4**, 382 (1939).

[6] L. Poppick and A. Lehrman, THIS JOURNAL, **61**, 3237 (1939).

[7] R. E. Van Dyke, *ibid.*, **72**, 3619 (1950).

[8] V. V. Korshak, N. N. Lebedeev and S. D. Fedoseev, *J. Gen. Chem.* (*U.S.S.R*), **17**, 575 (1947).

[9] B. N. Menshutkin, *J. Russ. Phys. Chem. Soc.*, **41**, 1089 (1908).

[10] V. A. Plotnikov and N. N. Gratsianskii, *Mem. Inst. Chem., Akad. Sci., Ukrain S.S.R.*, **5**, 213 (1939).

[11] V. A. Plotnikov and N. N. Gratsianskii, *Bull. Acad. Sci. U.S. S.R., Classe sci. chim.*, 101 (1947).

[12] D. D. Eley and P. J. King, *Trans. Faraday Soc.*, **47**, 1287 (1951).

[13] J. F. Norris and J. N. Ingraham, THIS JOURNAL, **62**, 1298 (1940).