Reduction of Carbonyl Compounds by Sodium Borohydride (Tetrahydridoborate) in Water, Dimethyl Sulphoxide, and their Mixtures as Solvents: Products and Kinetics

By **Chitra Adams, Victor Gold,*** and **David M. E. Reuben,** Department of Chemistry, King's College, Strand, London WC2R 2LS

Rate measurements are reported for the reduction of acetone pivalaldehyde, and benzaldehyde by sodium and tetramethylammonium tetrahydridoborates in dimethyl–sulphoxide–water systems, some containing a low concentration of sodium hydroxide to impede the hydrolysis of tetrahydridoborate. The reactions obey second-order kinetics. The rate constants decrease as the water content of the solvent is reduced but, with the most reactive substrate (benzaldehyde), the reduction is still detectable even in a solvent not containing any added water. Evidence has been obtained that the reduction product of benzaldehyde in dimethyl sulphoxide solution is sodium tetrakisbenzyloxyborate, which is readily hydrolysed to benzyl alcohol. A condensation product of benzaldehyde and dimethyl sulphoxide (2-methylsulphinyl-1-phenylethanol) has been isolated as a by-product. Attempts to trap borane during the reduction gave negative results.

THE selective reduction of aldehydes and ketones by alkali-metal tetrahydridoborates (borohydrides) is thought to involve in the first step a hydride transfer to the carbonyl compound and at some stage a proton transfer from the solvent to an anionic intermediate.[1] The conclusion that the reduction consists of at least two distinct (though conceivably synchronous) processes led us to examine the kinetics of the reaction under conditions of low proton availability, in parallel with a study of aldehydic hydrogen exchange [2] (reported in the following paper).

One mole of borohydride can effect the reduction of four moles of carbonyl group; nevertheless the reduction of ketones by sodium tetrahydridoborate in hydroxylic solvents is found to be of the first order in

---

[1] H. O. House, 'Modern Synthetic Reactions,' 2nd edn., Benjamin, Menlo Park, 1972, p. 52.

[2] C. Adams, V. Gold, and D. M. E. Reuben, following paper.

each reactant,[3-5] with the implication that the transfer of the first hydride from boron is slower than the second, third, and fourth hydride transfers.[6,7] However, it has also been found that the product composition in the reduction of an alkylcyclohexanone to *cis*- and *trans*-alkylcyclohexanols varies over the course of the reaction.[8] The result could be quantitatively explained by assuming that the fourth hydride transfer is slower than the preceding two, so that the monohydride species builds up to a significant concentration during the reaction, but that this build-up does not noticeably disturb the the kinetic order.

The overall result of each of the four hydride transfers has been represented by H. C. Brown and his co-workers [4,5] by the processes (1)—(4) for the reduction of the ketone R_2CO, with subsequent solvolysis of the

$$R_2CO + BH_4^- \longrightarrow (R_2CH{\cdot}O)BH_3^- \quad (1)$$

$$R_2CO + (R_2CH{\cdot}O)BH_3^- \longrightarrow (R_2CH{\cdot}O)_2BH_2^- \quad (2)$$

$$R_2CO + (R_2CH{\cdot}O)_2BH_2^- \longrightarrow (R_2CH{\cdot}O)_3BH^- \quad (3)$$

$$R_2CO + (R_2CH{\cdot}O)_3BH^- \longrightarrow (R_2CH{\cdot}O)_4B^- \quad (4)$$

$$(R_2CH{\cdot}O)_4B^- + 4H_2O \longrightarrow 4R_2CH{\cdot}OH + B(OH)_4^- \quad (5)$$

tetra-alkoxyborate anion, as in (5). It had alternatively been suggested [3] that the product of reaction (1) itself undergoes hydrolysis [reaction (6)], and that the second proton transfer (7) takes place from the hydroxy-species formed. The subsequent steps in this scheme likewise consist of successive hydrolysis and hydride-transfer processes.

$$(R_2CH{\cdot}O)BH_3^- + H_2O \longrightarrow R_2CH{\cdot}OH + BH_3(OH)^- \quad (6)$$

$$R_2CO + BH_3(OH)^- \longrightarrow (R_3CH{\cdot}O)BH_2(OH)^- \quad (7)$$

Since the reaction steps after (1) have so far escaped direct observation, it is not possible to distinguish between these alternative schemes in partially aqueous media. Reactions (6) and (7) and their analogues could, however, not occur in aprotic media. For this reason, the observation [5] that sodium hydridotri-isopropoxyborate is a very reactive reducing agent *in diglyme* [*bis*-(2-*methoxyethyl*) *ether*] *solution* [9] does not provide a differentiating test of mechanism. Jones and Wise [10] have instead proposed that, in such a solvent (diglyme), borane (BH_3) is set free in the slow first reduction step (8), and that this species reduces a second molecule of substrate (9) to yield an alkoxyborane. It is this alkoxyborane and the consecutively generated dialkoxyborane which are then held to be the hydride donors in the subsequent steps. However, the stereochemistry of the alcohols isolated from reductions by complexed borane or by diborane is not consistent with the suggestion that boranes are involved in the reduction steps after the first. On the other hand, the course of the reaction in diglyme solution was affected by the addition of triethylamine,[10] a reagent known to trap boranes [4] (10), which suggests that reaction (8) represents a first stage of reaction (1).

$$R_2CO + BH_4^- \longrightarrow R_2CH{\cdot}O^- + BH_3 \quad (8)$$

$$R_2CO + BH_3 \longrightarrow R_2CH{\cdot}OBH_2 \quad (9)$$

$$Et_3N + BH_3 \longrightarrow Et_3\overset{+}{N}\text{-}\overset{-}{B}H_3 \quad (10)$$

Apart from such kinetic investigations of the reduction, the dependence of its stereochemical course on various parameters has been the basis for detailed discussion of transition state structure in the rate-limiting step (steric-approach control *versus* product-development control).[7,11-13]

The present work attempts to clarify some of these mechanistic ambiguities of an important reaction of preparative organic chemistry. Dimethyl sulphoxide (by itself and in its mixtures with water) was selected for this study because relatively stable solutions of sodium tetrahydridoborate can be prepared in it so that the hydrolysis of this reactant was invariably negligible. It emerged that the solvent gave rise to other complications, which are of some practical relevance.

Following H. C. Brown, the product of the reduction of aldehydes and ketones in non-aqueous media, before the hydrolysis during work-up, is usually represented as a tetra-alkoxyborate salt [see equation (7)]. This hypothesis appears to have defied confirmation so far, and has even been disputed.[13] Various tetra-alkoxyborate salts have been known for many years,[14] and sodium tetrakisbenzyloxyborate itself was isolated by Meerwein and Bersin.[15] Alternative procedures for the

---

[3] E. R. Garrett and D. A. Lyttle, *J. Amer. Chem. Soc.*, 1953, **75**, 6051.

[4] H. C. Brown, E. J. Mead, and B. C. Subba Rao, *J. Amer. Chem. Soc.*, 1955, **77**, 6209.

[5] H. C. Brown, O. H. Wheeler, and K. Ichikawa, *Tetrahedron*, 1957, **1**, 214; H. C. Brown and K. Ichikawa, *J. Amer. Chem. Soc.*, 1961, **83**, 4372.

[6] H. C. Brown and J. Muzzio, *J. Amer. Chem. Soc.*, 1966, **88**, 2811.

[7] B. Rickborn and M. T. Wuesthoff, *J. Amer. Chem. Soc.*, 1970, **92**, 6894.

[8] M. T. Wuesthoff, *Tetrahedron*, 1973, **29**, 791.

[9] H. C. Brown, E. J. Mead, and C. J. Shoaf, *J. Amer. Chem. Soc.*, 1956, **78**, 3616.

[10] W. M. Jones and H. E. Wise, *J. Amer. Chem. Soc.*, 1962, **84**, 997.

[11] W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Amer. Chem. Soc.*, 1956, **78**, 2579; H. C. Brown and K. Ichikawa, *Tetrahedron*, 1957, **1**, 221; D. M. S. Wheeler and M. M. Wheeler, *J. Org. Chem.*, 1962, **27**, 2796; H. C. Brown and H. R. Deck, *J. Amer. Chem. Soc.*, 1965, **87**, 5620; E. L. Eliel and Y. Senda, *Tetrahedron*, 1970, **26**, 2411; P. Geneste and G. Lamaty, *Bull. Soc. chim. France*, 1968, 669; P. Laszlo and Z. Welvart, *ibid.*, 1966, 2412; P. Geneste, G. Lamaty, and J. P. Roque, *Tetrahedron Letters*, 1970, 5007.

[12] J. C. Richer, *J. Org. Chem.*, 1965, **30**, 324; A. V. Kamernitzky and A. A. Akhrem, *Tetrahedron*, 1962, **18**, 705; M. Cherest and H. Felkin, *Tetrahedron Letters*, 1968, 2205; D. C. Wigfield and D. J. Phelps, *Chem. Comm.*, 1970, 1152; *Canad. J. Chem.*, 1972, **50**, 388; *J. Amer. Chem. Soc.*, 1974, **96**, 543.

[13] D. J. Pasto and B. Lepeska, *J. Amer. Chem. Soc.*, 1976, **98**, 1091.

[14] H. Copaux, *Compt. rend.*, 1898, **127**, 719; L. Cambi, *Atti. Accad. naz. Lincei, Rend. Classe sci. fis. mat. nat.*, 1914 [v], 23, i, 244 [*Chem. Soc. Abs.*, 1914, 106(i), 478].

[15] H. Meerwein and T. Bersin, *Annalen*, 1929, **476**, 113.

preparation of tetra-alkoxyborate salts have since appeared.[16] However, there is only one recent report of the isolation of such a product from a reduction with tetrahydridoborate (the 1,4-reduction of methyl α-phenyl-*trans*-cinnamate in dimethyl sulphoxide).[17] The present work provides evidence that sodium tetrakisbenzyloxyborate is formed in this solvent from benzaldehyde, and the reduction may possibly offer a more convenient general route for the preparation of simple tetra-alkoxyborate salts.

EXPERIMENTAL

Materials.—Purified acetone (B.D.H. AnalaR), was found to be 99.8% pure by analytical g.l.c. Benzaldehyde (Fison's AnalaR) was distilled and the fraction of b.p. 62° at 10 mmHg was collected and stored under nitrogen. Benzyl alcohol (B.D.H. laboratory reagent) was redistilled under nitrogen (b.p. range 89—91° at 7 mmHg). Diglyme (B.D.H. laboratory reagent) was distilled (b.p. 186°) from lithium aluminium hydride and stored under nitrogen in the dark. Dimethyl sulphoxide (AnalaR) was dried (CaH_2; 12 h) and distilled (18 mmHg) then stored over molecular sieves and under nitrogen. $[^2H_6]$Dimethyl sulphoxide (Prochem) was dried over molecular sieves. Pivalaldehyde (Fluorochem) was redistilled (b.p. 77—78°) and stored in the dark under nitrogen. Sodium tetrahydridoborate (B.D.H.; *ca.* 85%) was recrystallised from diglyme [4,*] and assayed by iodine titration.[18] Tetramethylammonium tetrahydridoborate (Alfa Inorganics) was recrystallised from 95% ethanol. All other commercial reagents were used without further purification. Trimethylamine and 2-methylsulphinyl-1-phenylethanol [19] were prepared by established methods.

Mixed solvents were prepared by volume. The mixture produced by dilution of x cm^3 with water (containing the requisite amount of base to give the desired final molar concentration of base) to a total volume of 100 cm^3 at 25 °C is in the following referred to as x% Me_2SO.

Instruments.—U.v. spectra were recorded on a Unicam SP 800 spectrophotometer. For kinetic spectrophotometry a Gilford 222 photometer, combined with the monochromator of a Unicam SP 500 instrument, with a thermostatted cell compartment, was used. 90 MHz N.m.r. spectra were obtained with an HFX 90 Bruker spectrometer by using the Fourier transform technique. 60 MHz Spectra were obtained with a Perkin-Elmer R 12B spectrometer. I.r. spectra were recorded with a Perkin-Elmer 257 grating spectrometer. M.p.s were taken on a Kofler hot-stage apparatus.

Reaction Products.—(A) *Water-rich media.* On the basis of earlier work it was assumed that, for protic solvent systems, such as water or its mixtures with Me_2SO up to 90% Me_2SO, the products of the reaction were the alcohol (and its sodium salt) and sodium borate. No attempt was made to isolate these products. In the case of benzaldehyde, n.m.r. spectra (see below) indicate formation of benzyl alcohol. However, a water-soluble white precipitate, thought to be sodium borate, began to appear in the later stages of kinetic runs in solvent systems containing at least 60% Me_2SO.

(B) *Water-poor media.* In 98% Me_2SO the rate of reduction of pivalaldehyde with tetrahydridoborate increased with time, an indication that pivalaldehyde was also being lost by a process other than reduction. This process could not be an inter-aldehyde condensation reaction since pivalaldehyde has no α-hydrogen atoms.

In a similar manner, when benzaldehyde (*ca.* 0.5M) was reduced with tetrahydridoborate (*ca.* 0.1M) in $(CD_3)_2SO$, it was found from n.m.r. observations that benzaldehyde disappeared faster than tetrahydridoborate. In the course of reduction the peaks of the aldehyde proton (δ 10.05) and of the aromatic protons (δ 7.60—8.05) disappear, and new peaks appear at δ 7.39 and 4.51. By comparison benzyl alcohol in $(CD_3)_2SO$ has a doublet at δ 4.50 (2 H, CH_2) and a singlet at δ 7.31 (5 ArH).

During the course of the reduction in $(CD_3)_2SO$ the intensity ratio of the peaks at δ 7.34 and 4.51 increases with time from an initial value of 5 : 2. This is consistent with the formation of an additional product (besides sodium benzyl oxide) in which the aromatic protons are in a similar chemical environment to those of benzyl alcohol, but in which the CH_2 group is in a slightly different environment. This product was suspected to be the benzaldehyde–Me_2SO condensation product 2-methylsulphinyl-1-phenylethanol.[19] From an experiment in which sodium tetrahydridoborate (0.01 mol) was added to 50 cm^3 of a 0.51M-solution of benzaldehyde in Me_2SO a small sample of this product (the only product with an R_F value greater than that of Me_2SO) was isolated by t.l.c. (Merck GF_{254} silica gel; ethanol as eluant) after a reaction time of 24 h under nitrogen. Its n.m.r. spectrum was identical with that of an authentic sample [19] of 2-methylsulphinyl-1-phenylethanol.

The reduction product of the reaction, expected to be sodium tetrakisbenzyloxyborate, was isolated as a voluminous white precipitate when the reduction was carried out at higher concentrations (benzylaldehyde 2.0M; sodium borohydride 0.5M) in Me_2SO (50 cm^3). The precipitate formed after 2 h was filtered off quickly, washed with diethyl ether, pumped dry for 5 min, and stored in a desiccator. The compound was very unstable to moisture. It was soluble in water, acetone, acid, and cyclohexane. It was identified as follows. (1) The n.m.r. spectrum in $(CD_3)_2SO$ shows singlet peaks at δ 7.3 and 4.5 in the ratio 5 : 2, corresponding to the peaks observed in the reduction runs. (2) The m.p. was greater than 300°, suggesting an inorganic compound, possibly a borate. (3) Preliminary flame and silver nitrate tests for borates [20] gave positive results. (4) The mass spectrum (A.E.I. MS30 instrument) showed m/e 79 (100%), 77(63), 91(74), 107(64), 108(79), 240(1.3), and 241(5.2). The ratio of intensities of peaks at m/e 241 and 240 was 4 : 1, respectively. This is consistent with a fragment containing boron, since the natural $^{11}B : ^{10}B$ ratio is 4 : 1. The fragment at m/e 241 is consistent with $[C_{14}H_{14}O_3\text{-}{}^{11}B]^+$ and the formula $(PhCH_2O)_2B^+O$, and indicates that the parent compound is the tetrakisbenzyloxyborate salt $(PhCH_2\cdot O)_4B^-Na^+$. The only alternative possibility, that

---

[*] We thank Professor H. C. Brown for advice concerning this crystallisation.

[16] H. I. Schlesinger, H. C. Brown, H. R. Hoekstra, and L. R. Rapp, *J. Amer. Chem. Soc.*, 1953, **75**, 199; E. Wiberg and W. Sturm, *Z. Naturforsch.*, 1955, **10B**, 108; H. C. Brown and E. J. Mead, *J. Amer. Chem. Soc.*, 1956, **78**, 3614.

[17] J. H. Schauble, G. L. Walter, and J. G. Morin, *J. Org. Chem.*, 1974, **39**, 775.

[18] D. A. Lyttle, E. J. Jensen, and W. A. Struck, *Analyt. Chem.*, 1962, **24**, 1843.

[19] E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 1965, **87**, 1345.

[20] A. I. Vogel, ' Qualitative Chemical Analysis,' 3rd edn., Longmans, London, 1945, p. 283.

the compound is tribenzyl borate, was eliminated since this tri-ester is known to be a liquid.

Addition of 1,4-diazabicyclo[2.2.2]octane or of trimethylamine to reaction mixtures did not lead to the appearance of n.m.r. signals characteristic of BH_3–amine adducts.

Kinetic Procedure.—Solutions of the tetrahydridoborate salt and of the carbonyl compound were separately made up in solvent which had been deoxygenated by passage of nitrogen (1 h). Acetone stock solutions were kept in a storage syringe to avoid evaporation loss. Kinetic runs with acetone and with pivalaldehyde were started by mixing equal volumes of the two thermostatted solutions in a quartz spectrophotometer cell. The carbonyl absorbance was used to monitor the progress of the reaction. Samples transferred to and sealed into 5 cm³ ampoules were kept for 10 half-lives and were used to check infinity readings. The procedure was modified for the reduction of benzaldehyde. Because of the high extinction coefficient of its carbonyl absorbance, a 0.02 cm³ sample was taken from the reaction mixture and diluted with 2 cm³ of solvent, which effectively stopped the reaction, and the absorbance was then measured manually. For every system studied the validity of Beer's law was checked. All rate measurements relate to a temperature of 25 °C.

The stoicheiometry of the reduction is given by equation (11). If a is the initial concentration of the carbonyl compound, b the initial tetrahydridoborate concentration and x the amount of tetrahydridoborate which has reacted at time t, then the second-order rate expression for disappearance of tetrahydridoborate can be written as equation (12) or, in integrated form, as equation (13), provided the rate-limiting step is a second-order reaction between carbonyl compound and tetrahydridoborate. Since the reductions were followed by monitoring the carbonyl absorption, x is given by equation (14) in terms of absorbances D_t and D_0 of the carbonyl compound after times t and zero, respectively. The second-order rate constants k_2 were evaluated by computed linear regression of y in equation (13) upon t.

$$4R_2CO + BH_4^- + 4H_2O \longrightarrow 4R_2CH{\cdot}OH + B(OH)_4^- \qquad (11)$$

$$dx/dt = k_2(a - 4x)(b - x) \qquad (12)$$

$$k_2t = \frac{1}{a - 4b}\ln\frac{b(a - 4x)}{a(b - x)} \text{ or } k_2\,t = y \qquad (13)$$

$$x = 0.25a\,(1 - D_t/D_0) \qquad (14)$$

RESULTS

Experiments with Acetone.—Rate constants for the reduction of acetone (*ca.* 0.1M) by sodium tetrahydridoborate in water and in various Me_2SO–H_2O mixtures are given in Table 1. Iodate titration of solutions of tetrahydridoborate[18] itself showed that in mixtures containing not more than 50% Me_2SO by volume, 0.5M-sodium hydroxide was required to prevent the hydrolysis of $NaBH_4$, and this concentration was present in all such runs given in Table 1.

In media of higher Me_2SO content it was possible to reduce the concentration of NaOH to 0.01M. The unwanted base-catalysed condensation of acetone as well as salting out effects were thus kept down. The NaOH concentration has only a small effect on the reduction rate constants (Table 2).

As sodium borate is one of the products, the effect of added sodium borate (0.0284M) on the rate was measured in 60% Me_2SO solvent, for initial concentrations $[Me_2CO]$ = 0.0909M; $[NaBH_4]$ = 0.0284M and [NaOH] = 0.01M. The observed value of k_2 (4.7×10^{-4} dm³ mol⁻¹ s⁻¹), is to be compared with a rate constant of 4.8×10^{-4} dm³ mol⁻¹ s⁻¹ for a run under the same conditions in the absence of added sodium borate. In solvent mixtures containing more than 60% Me_2SO, slight precipitation of sodium borate was noticeable towards the end of runs. However, all experiments could be followed to more than 60% of total reaction and showed strict adherence to the second-order rate law (13).

TABLE 1

Kinetic experiments with acetone

Run no.	Vol. % Me_2SO	$[NaBH_4]$/M	$[Me_2CO]/[NaBH_4]$	10^4k_2/dm³ mol⁻¹ s⁻¹
1	0	0.100 6	0.99	263
2	0	0.080 5	1.23	251
3	0	0.060 4	1.65	253
4	0	0.030 2	3.29	228
5	0	0.020 1	4.95	222
6	0	0.010 1	9.84	216
11	10	0.099 5	1.00	198
12	10	0.079 6	1.25	191
13	10	0.059 7	1.67	193
14	10	0.059 7	1.67	188
15	10	0.029 9	3.33	189
16	10	0.029 9	3.33	188
17	10	0.019 9	5.01	192
21	20	0.100 1	0.99	116
22	20	0.080 1	1.24	110
23	20	0.060 1	1.65	118
24	20	0.040 0	2.49	121
25	20	0.030 0	3.31	119
26	20	0.010 0	9.94	118
31	30	0.101 4	0.99	56
32	30	0.081 1	1.23	55
33	30	0.060 8	1.64	56
34	30	0.040 6	2.46	58
35	30	0.030 4	3.29	57
36	30	0.020 3	4.92	57
41	40	0.101 3	0.98	29
42	40	0.081 0	1.23	28
43	40	0.060 8	1.63	28
44	40	0.040 5	2.45	25
45	40	0.030 4	3.27	25
51	50	0.100 5	1.00	11.3
52	50	0.080 4	1.25	11.1
53	50	0.060 3	1.66	10.9
54	50	0.040 2	2.50	10.1
55	50	0.030 2	3.32	10.1
61	60	0.030 0	3.33	4.8
62	60	0.030 8	3.25	4.9
71	70	0.095 4	1.03	1.18
72	70	0.038 2	2.58	1.10
81	80	0.100 8	0.98	0.18
82	80	0.060 5	1.63	0.16
83	80	0.030 2	3.27	0.14

TABLE 2

Dependence of acetone reduction on NaOH concentration in 50% Me_2SO–H_2O

$[Me_2CO]$ = 0.099M; $[NaBH_4]$ = 0.0314M

[NaOH]/M	10^3k_2/dm³ mol⁻¹ s⁻¹
0.10	1.33
0.50	1.33
1.00	1.07

In one experiment tetramethylammonium hydroxide (0.01M) and tetrahydridoborate (0.0217M) were used in place of the sodium compounds in 70% Me_2SO. A second-order rate constant of 0.83×10^{-4} l mol^{-1} s^{-1} was obtained.

Experiments with Pivalaldehyde (*Table* 3).—0.01M-Tetramethylammonium hydroxide was added for experiments in 80% Me_2SO, 0.001M for those in 90% Me_2SO, and none for those in 98% Me_2SO. (In every case this adequately inhibited hydrolysis of tetrahydridoborate.)

In the 98% Me_2SO runs the plots of y against t [equation(13)] were linear over the first part of the reaction and then became steeper, suggesting that pivalaldehyde was being lost at a greater rate than tetrahydridoborate. At higher water concentrations plots of y against t were strictly linear. The rate constant for run 10 in Table 3 was calculated from the initial linear part of the curve which corresponded to 67% reaction.

TABLE 3

Reduction of pivalaldehyde in Me_2SO–H_2O

Run	% Me_2SO	$[CMe_3{\cdot}CHO]$/M	$[Me_4NBH_4]$/M	$[CMe_3{\cdot}CHO]$/ $[Me_4NBH_4]$	10^5k_2/ dm^3 mol^{-1} s^{-1}
1	80	0.096 6	0.052 7	1.83	3 140
2	80	0.096 6	0.042 1	2.29	2 890; 2 840
3	80	0.096 6	0.031 6	3.06	2 990; 3 030
4	80	0.096 6	0.026 4	3.66	2 940
5	80	0.096 6	0.021 1	4.58	3 600
6	90	0.083 7	0.089 1	0.94	187
7	90	0.083 7	0.044 6	1.88	219
8	90	0.083 7	0.029 7	2.82	209
9	90	0.083 7	0.022 3	3.75	250
10	98	0.122 6	0.096 1	1.28	392
11	98	0.122 6	0.048 1	2.55	
12	98	0.122 6	0.032 0	3.83	

TABLE 4

Reduction of benzaldehyde in Me_2SO–H_2O

Run	% Me_2SO	M in $M^+BH_4^-$	[PhCHO]/M	$[BH_4^-]$/M	[PhCHO]/ $[BH_4^-]$	$[Me_4NOH]$/M	10^5k_2/ dm^3 mol^{-1} s^{-1}
1	80	Me_4N	0.104 2	0.027 5	3.79	0.01	1 160
2	80		0.104 2	0.025 4	4.10	0.01	1 030
3	80		0.104 2	0.017 8	5.85	0.01	1 170
4	85		0.099 6	0.046 5	2.14	0.001	340
5	85		0.099 6	0.028 0	3.56	0.001	320
6	85		0.099 6	0.018 0	5.53	0.001	320
7	90		0.100 6	0.078 3	1.28	0.001	78
8	90		0.100 6	0.053 8	1.87	0.001	81
9	90		0.100 6	0.027 8	3.62	0.001	85
10	98		0.098 7	0.037 3	2.65		2.05
11	98		0.098 7	0.011 6	8.51		1.75
12	98		0.098 7	0.007 8	12.65		1.54
13	100	Na	0.099 6	0.034 9	2.85		1.27
14	100		0.099 6	0.028 5	3.49		1.30
15	100		0.099 6	0.016 1	6.19		0.90

Kinetic Experiments with Benzaldehyde.—The rates of reduction of benzaldehyde in Me_2SO–H_2O are given in Table 4. In 100% Me_2SO the slopes of the kinetic plots decreased over the course of the reaction and the rate constants are based on the first 35% of reaction for which y was proportional to t.

TABLE 5

Effects of added benzyl alcohol and water on the reduction of benzaldehyde in 100% Me_2SO

Run	[PhCHO]/ M	$[NaBH_4]$/ M	$[H_2O]$/ M	$[PhCH_2{\cdot}OH]$/ M	10^5k_2/ dm^3 mol^{-1} s^{-1}
1	0.099 8	0.025 2			1.28
2	0.099 8	0.025 2	0.098 9		1.52
3	0.099 8	0.025 2		0.048 7	2.55
4	0.099 8	0.025 2		0.107 9	3.61
5	0.099 8	0.025 2		0.202 0	6.36

The effect of added benzyl alcohol on the reduction rate of benzaldehyde in 100% Me_2SO is shown in Table 5.

DISCUSSION

The kinetic runs at low concentration, in which disappearance of the carbonyl function is being monitored, and the n.m.r. observations on reaction mixtures at higher concentrations establish that reduction of carbonyl compounds occurs in all the solvent mixtures examined. The reaction is very slow at low water concentrations, especially for acetone, which is a much less reactive substrate than benzaldehyde and pivalaldehyde. We have identified sodium tetrakisbenzyloxyborate as a product in Me_2SO, and this observation lends support to H. C. Brown's reaction scheme [equations (1)—(4)]. However, pure Me_2SO is not a convenient solvent for these reductions because the highly basic medium produced by the reduction of the carbonyl compound induces the condensation of benzaldehyde and Me_2SO [formation of 2-methylsulphinyl-1-phenylethanol, $PhCH(OH){\cdot}CH_2{\cdot}SOMe$]. Presumably the reaction is initiated by the generation of dimsyl ion under these conditions.

Attempts to trap BH_3 as a transient reaction intermediate by the addition of amines gave negative results, although similar experiments had been successful in diglyme as solvent.[10] From our hydrogen exchange study [2] it seems probable that BH_3 *is* formed as the result of hydride transfer from tetrahydridoborate ions, and the implications of the negative trapping result will be further considered in that context. It seems possible that BH_3 is less stable in Me_2SO than in an ether solvent; an adduct between tetrahydrofuran and BH_3 is known to exist.

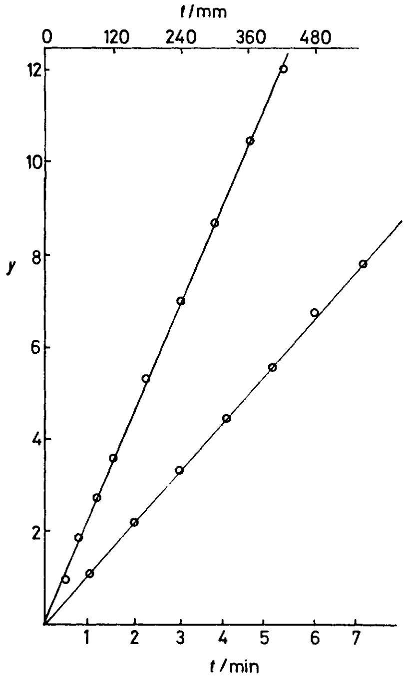


FIGURE 1 Specimen kinetic runs for reduction of acetone (upper curve corresponds to upper time axis, 60% Me_2SO; lower curve and lower time axis, 20% Me_2SO)

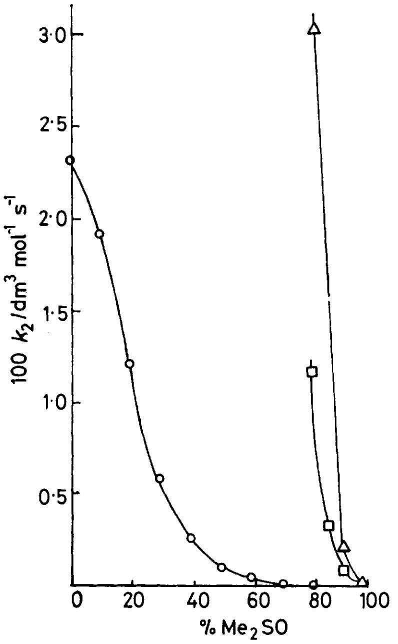
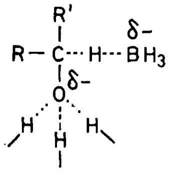


FIGURE 2 Solvent dependence of rate constants (circles, acetone; squares, benzaldehyde; triangles, pivalaldehyde)

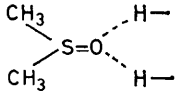
In water-rich media, individual reduction runs accurately follow second-order kinetics (Figure 1) [equation (13)], as established in earlier studies. However, values of the second-order rate constant for the reduction of acetone increase slightly with concentration of sodium tetrahydridoborate (Table 1), suggesting that a more complete rate law (in water) should be written as equation (15), with $k_2^0 \gg k_3$ $[BH_4^-]$·$(k_2^0/k_3 \simeq 0.44$ mol dm^{-3}). These effects are absent or masked in the Me_2SO-rich media.

$$\mathrm{d}x/\mathrm{d}t = [\mathrm{Me_2CO}]\,[\mathrm{BH_4^-}](k_2^0 + k_3[\mathrm{BH_4^-}]) \qquad (15)$$

Perhaps the most striking feature of the kinetic results is the strong rate reduction caused by the addition of Me_2SO (Figure 2). We interpret this as indicating extensive charge stabilisation by hydrogen bonding which a hydroxylic solvent can supply in the transition state (1), but not to the reactant molecules. Such stabilisation is not provided by Me_2SO, which furthermore itself competes for hydrogen bonds [see (2)]. Alcohols behave in a similar manner to water, and this accounts for the small difference between reduction rates in water and in alcohol solvents as well as for the accelerating effect of benzyl alcohol on the reduction in Me_2SO.

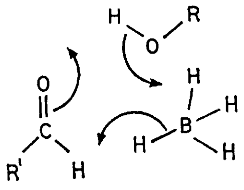


(1)



(2)

It has recently been suggested that the reduction mechanism can be formulated in terms of a six-membered cyclic transition state (3), written here for an aldehyde,



(3)

in which ROH is a molecule of hydroxylic solvent. Such a scheme would clearly not apply in a non-hydroxylic solvent such as diglyme or Me_2SO, but it would explain the acceleration of the reduction observed when an alcohol is added to diglyme solvent [4] or, in our experiments, when either water or benzyl alcohol is added to Me_2SO. However, at least as it stands, this mechanism is not compatible with our observation [2] that hydrogen isotope exchange between tetrahydridoborate and aldehydic hydrogen occurs alongside the reduction of benzaldehyde in Me_2SO–H_2O mixtures. The transition state (3) implies production of R'CH_2·OH and RO·BH_3 in the first reaction step, and this is unlikely to be a reversible process from which R′CTO would be recoverable if tritiated borohydride were employed.

As evidence in support of the transition state (3) it has briefly been reported[21] that during the reduction of a ketone in alcoholic solution it is the tetra-alkoxyborate derived from the aliphatic solvent alcohols that is formed and not the tetra-alkoxyborate derived from the secondary alcohol related to the ketone. It has also been found that there is no exchange between alkoxyborate ions and certain alcohols. However, the reported evidence does not include a demonstration that tetra-alkoxyborates related to the ketones actually used (typically cyclohexanone) are not converted into solvent-derived tetra-alkoxyborates by solvolysis. In view of the known occurrence of some such substitution reactions[22] it would be necessary to demonstrate their absence *for the actual ketone and solvent* for which the solvent-derived tetra-alkoxyborates have been isolated, before one can validly conclude that these experiments[21] have the significance placed upon them.

[6/2323 *Received, 21st December*, 1976]

---

[21] D. C. Wigfield and F. W. Gowland, *Tetrahedron Letters*, 1976, 3373.

[22] G. L. Cunningham and F. Pretka, Canad. Pat. 631,509/1961.