Hydrogen Isotope Exchange in the Aldehyde Group during the Reduction of Benzaldehyde by Tritiated Sodium Borohydride (Tetrahydridoborate)

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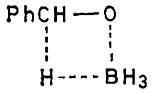
The reduction of benzaldehyde by tritiated sodium tetrahydridoborate in dimethyl sulphoxide and dimethyl sulphoxide–water mixtures as solvents is accompanied by the incorporation of tritium into the aldehyde group of unchanged benzaldehyde. The occurrence of the exchange implies that the hydride-transfer step of the reduction is reversible. As it is improbable that there is reversibility *after* the formation of a stable boron–oxygen bond, it is concluded that the hydride-transfer step precedes the step in which the boron–oxygen bond is formed. However, attempts to detect the implied intermediate borane in dimethyl sulphoxide solution by trapping with amines had proved negative. It follows that borane is destroyed by reaction with the other product of the first reaction step (the benzyl oxide ion) more effectively than it can react with an amine. Since the reaction of borane with a tertiary alkylamine is likely to be very rapid, the reactions between borane and benzyl oxide ion (leading either back to the starting materials with hydrogen exchange or, predominantly, to an alkoxyhydridoborate species) are considered to occur competitively as cage reactions before the primary reaction products have diffused apart.

The exchange reaction exhibits kinetic complications which are attributed to a more rapid hydrogen exchange between benzaldehyde and the reaction product sodium tetrakisbenzyloxyborate (which is shown to take place) and to the instability of this product in the media employed. It is suggested that the high basicity of the reaction solutions is due to the presence of some sodium benzyl oxide in equilibrium with sodium tetrakisbenzyloxyborate, leading to the formation of dimsyl ions.

THE reduction of aldehydes by sodium tetrahydridoborate in the polar aprotic solvent dimethyl sulphoxide leads to sodium tetrakisbenzyloxyborate, from which the ultimate product, benzyl alcohol, can be generated by hydrolysis.[1] This reduction therefore consists of hydride transfers from boron to carbon and the formation of oxygen–boron bonds. The present work is concerned with the question as to whether these two mechanistic events are synchronous (and energetically concerted) or whether they take place in discrete steps. For the first and rate-limiting hydride transfer (1) a synchronous

$$BH_4^- + PhCHO \longrightarrow PhCH_2{\cdot}OBH_3 \qquad (1)$$

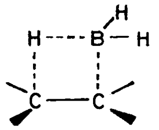
mechanism appears to imply a transition state containing a four-membered ring[2] [structure (1)], whereas a step-wise process initiated by hydride transfer would require a transient liberation of borane (BH_3). A step-wise process in which the co-ordination of a tetrahydridoborate anion to the aldehyde precedes the hydride transfer seems improbable, since it would involve the formation of a stable penta-co-ordinated boron anion (2). To the extent that similar (though partial) formation of a penta-valent boron anion is implied by the transition state (1), the concerted process seems less plausible than a two-step mechanism. Nevertheless, the four-centre transition state (1) has in the past received serious attention.[1] In the reaction of borane with an unsaturated compound



(1)

$PhCH{\cdot}OBH_4^-$

(2)



(3)

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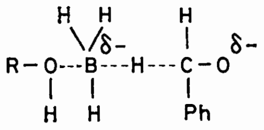
[1] C. Adams, V. Gold, and D. M. E. Reuben, preceding paper, where further references to reduction kinetics are cited.

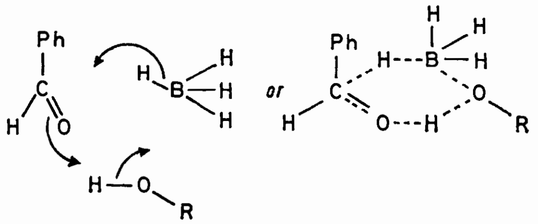
[2] O. R. Vail and D. M. S. Wheeler, *J. Org. Chem.*, 1962, **27**, 3803.

the electron-deficiency of BH_3 could make a cyclic transition state (3) energetically favourable and allowed,[3] but the case is not analogous to (1).

In hydroxylic solvents a synchronous mechanism can also be formulated with participation of one (or more) solvent molecules, as in equation (2) and transition state (4) [4] or (5).[5,6] Such possibilities must be considered for the mixed $Me_2SO–H_2O$ solvents to which some of the present work refers. It is, however, inapplicable to reductions in pure Me_2SO.



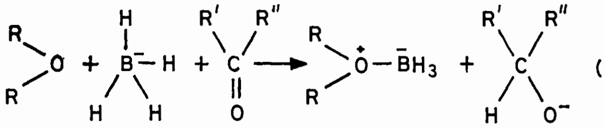
(4)



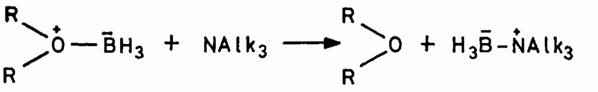
(5)

$$PhCHO + BH_4^- + ROH \longrightarrow PhCH_2{\cdot}OH + ROBH_3^- \quad (2)$$

It is known that BH_3 can be trapped (as the amine–borane adduct) by adding trialkylamine to the medium for the reduction of a ketone (4-t-butylcyclohexanone) by sodium tetrahydridoborate in diglyme [bis-(2-methoxyethyl)ether] solution.[4,7] A process other than that involving the transition state (1) is therefore indicated under these conditions. In view of the known affinity of ethers for borane, the result may not be directly applicable to different solvents. It is conceivable that displacements on boron could be involved in ether solvents, as in reactions (3) and (4).



$$R_2O + H\overset{-}{B}H_3 + R'R''C{=}O \longrightarrow R_2\overset{+}{O}{-}\overset{-}{B}H_3 + R'R''C(H){-}O^- \quad (3)$$



$$R_2\overset{+}{O}{-}\overset{-}{B}H_3 + NAlk_3 \longrightarrow R_2O + H_3\overset{-}{B}{-}\overset{+}{N}Alk_3 \quad (4)$$

Analogous attempts to trap BH_3 during reductions in Me_2SO solution gave entirely negative results.[1] Accordingly, no experimental evidence in support of a two-step mechanisms was available at the outset of the present work.

Our investigation started with the objective of discovering whether the first step in the reduction of carbonyl compounds by tetrahydridoborate could be identified with an uncomplicated hydride transfer. It was anticipated that in an aprotic non-basic medium, in which the products of this reaction are not immediately removed by subsequent rapid processes, a non-concerted hydride transfer should be somewhat reversible. By the use of tritium-labelled borohydride this reversibility should become detectable, since it would lead to labelled aldehyde *via* reactions (5) and (6). There is a precedent for an exchange reaction involving tetrahydridoborate ion in the labelling of nitrobenzene by tritiated borohydride in Me_2SO solution.[8]

$$ArCHO + BH_3T^- \longrightarrow ArCHTO^- + BH_3 \quad (5)$$

$$ArCHTO^- + BH_3 \longrightarrow ArCTO + BH_4^- \quad (6)$$

As the title of the paper indicates, the sought-for tritium exchange in benzaldehyde was, in fact, observed, although the concurrently obtained negative results for borane-trapping experiments indicate that equations (5) and (6) are an inadequate representation of the exchange process.

The detailed results and their interpretation will be discussed below.

Of course, the observation of hydrogen isotope exchange is compatible with several reaction mechanisms. The only requirement is that there should be chemical equilibrium between the reactants and *any* stage of the reaction (including the final products) subsequent to the hydride transfer. However, the strong exothermicity expected [9] for reaction (1) or (2) seems to rule out the occurrence of isotope exchange *via* the reversal of these reactions. For this reason we infer that the occurrence of the exchange does not involve a species produced after formation of the boron–oxygen bond. Exchange will therefore be considered only in terms of reversion to reactants from the products of reaction (5) or from intermediates during the course of reaction (5).

EXPERIMENTAL

Materials and Preparations.—[α-^{14}C]Benzyl alcohol (4.4×10^{12} disint. min^{-1} mol^{-1}) from the Radiochemical Centre, Amersham, was diluted with inactive benzyl alcohol to between 7.4×10^9 and 7.34×10^{10} disint. min^{-1} mol^{-1}. Sodium benzyl oxide was prepared by the addition of sodium (2.3 g) to benzyl alcohol (10 g) in hexane (200 cm^3). After hydrogen evolution had ceased, the solution was filtered and the excess of sodium was removed. The hexane was evaporated off in a stream of nitrogen (24 h). The solid was dried at 60 °C under reduced pressure.

[3] G. Klopman, 'Chemical Reactivity and Reaction Paths,' Wiley, New York, 1974, p. 133.

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

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

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

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

[8] V. Gold and V. Nowlan, *J.C.S. Chem. Comm.*, 1974, 482.

[9] A. Hajòs, 'Komplexe Hydride,' VEB Deutscher Verlag der Wissenschaften, Berlin, 1966, ch. 4.

Sodium [^{3}H]tetrahydridoborate (*ca.* 490 Ci mol^{-1}; Radiochemical Centre, Amersham) was diluted to the required activity (*ca.* 0.4 Ci mol^{-1}) by addition of pure inactive sodium tetrahydridoborate. The mixture was then recrystallised from diglyme (B.D.H. laboratory reagent; purified [10]). According to information supplied by Dr. E. A. Evans of the Radiochemical Centre, the active material had been prepared by equilibration of sodium tetrahydridoborate with tritiated hydrogen gas. The tritium label is therefore present mostly in the form of BH_3T^-, with only a trivial admixture of salt containing more than one tritium atom per tetrahydridoborate ion.

The gross radioactivity of the sample was obtained by dissolving an accurately weighed amount (*ca.* 10 mg) of the active salt in 1 : 5 acetone–ethanol (10 cm^3). A weighed sample (*ca.* 0.1 g) of the solution was counted. This method does not distinguish between tritium incorporated in an active reducing form and tritium contained in any non-reducing impurities. To determine the activity due to the former, a weighed quantity of sodium [^{3}H]tetrahydridoborate was added to butanal in 0.5M-sodium hydroxide to effect reduction. Carrier butan-1-ol was added. The organic layer was then extracted with cyclohexane and washed four times with saturated sodium chloride solution. A representative sample of pure butan-1-ol was isolated by preparative g.l.c. and counted. The two methods of tritium analysis agreed within experimental error. The analyses were repeated periodically throughout the investigation.

AnalaR Me_2SO was dried (CaH_2; 12 h) and distilled at 18 mmHg. It was stored under nitrogen and over molecular sieves, and further deoxygenated by passage of nitrogen for 1 h immediately prior to use.

Sodium tetrakis[α-^{3}H]benzyloxyborate was prepared by reduction of benzaldehyde with sodium [^{3}H]tetrahydridoborate in Me_2SO solution at room temperature (2 h).[1] The white precipitate was filtered off, washed with diethyl ether, and pumped dry. The tritium content (per mole) of the preparation was the same (0.4 Ci mol^{-1}) as that of the labelled sodium tetrahydridoborate.

Preparation and purification procedures for other materials have been described.[1]

Measurements and Instrumentation.—A Beckman CPM 200 liquid scintillation counter was used for radioactivity measurements. Measured counting rates were converted into disintegrations min^{-1} by application of the external standard ratios method. The requisite calibration curve was determined with standard [^{3}H]hexadecane (Radiochemical Centre).

Kinetic Procedure.—Stock solutions of benzaldehyde and sodium [^{3}H]tetrahydridoborate in Me_2SO at 25 °C were mixed in the proportions required to give the desired final concentrations in the reaction mixture. Samples were removed at timed intervals and analysed for tritium incorporation.

In the initial runs, a 25 cm^3 portion was withdrawn for each point from the reaction solution and extracted with 10 cm^3 of cyclohexane, and the extract was washed with sodium chloride solution. It was then dried over molecular sieves (48 h) and the benzaldehyde was isolated by preparative g.l.c. and counted for tritium activity.

In later runs a 10 cm^3 portion was withdrawn and quenched in hydrochloric acid (20 cm^3). The solution was then neutralised with M-sodium hydroxide (20 cm^3). Semicarbazide solution [semicarbazide hydrochloride (0.4 g) and sodium acetate (0.4 g) in water (4 cm^3)] was added. The semicarbazone was filtered off, recrystallised, and counted.

The same method was used to follow the formation of [^{14}C]benzaldehyde from solutions of inactive benzaldehyde and labelled sodium benzyl oxide.

The corresponding kinetic and work-up procedure (semicarbazone formation) was used for the exchange of benzaldehyde with sodium tetrakis[α-^{3}H]benzyloxyborate.

It was established separately that there is no tritium exchange between sodium tetrahydridoborate and Me_2SO. The absence of such exchange after long reaction times was further demonstrated by the stability of sodium tetrahydridoborate in $(CD_3)_2SO$. The residual proton n.m.r. signal of Me_2SO was shown not to increase with time.

Position of Tritium Incorporation.—A sample of benzaldehyde was recovered (preparative g.l.c.) from the reaction of benzaldehyde (3M) with sodium [^{3}H]tetrahydridoborate (0.03M) in Me_2SO after 2 weeks. The specimen was assayed for tritium before and after being re-chromatographed. One portion of it was then converted into the semicarbazone and another into benzoic acid (by oxidation with saturated potassium permanganate solution, followed by addition of sodium sulphite to dissolve the precipitated manganese dioxide and subsequent acidification with concentrated hydrochloric acid to precipitate benzoic acid). The tritium assays of the various fractions are given in Table 1.

TABLE 1

Results relating to position of tritium incorporation in benzaldehyde

Compound	10^{-6} × Molar activity (disint. min^{-1} mol^{-1})
Benzaldehyde (after first g.l.c.)	1.30
Benzaldehyde (after second g.l.c.)	1.24
Semicarbazone	1.12 to 1.8
Benzoic acid	0.001

Evaluation of Rate Constants.—The initial rate of tritium uptake by an aldehyde is expressed in terms of a rate constant k_{ex}, defined in equation (7), where F and ϕ, are the

$$(\mathrm{d}\phi/\mathrm{d}t)_{t\to 0} = k_{ex}\, F_0[BH_4^-] \qquad (7)$$

fractional abundances of exchangeable tritium in tetrahydridoborate and aldehyde, respectively, and the subscript zero denotes a zero-time value. As tritium is initially present only as BH_3T^-, F and ϕ can be expressed by equations (8) and (9). The occurrence of exchange implies

$$F = [BH_3T^-]/4[BH_4^-] \qquad (8)$$

$$\phi = [RCTO]/[RCHO] \qquad (9)$$

equation (10) during the early stages and rate equation (11), or its equivalent form (12). During the initial stage the

$$RCHO + BH_3T^- \underset{4k_{-1}}{\overset{k_1}{\rightleftharpoons}} RCTO + BH_4^- \qquad (10)$$

$$(\mathrm{d}[RCTO]/\mathrm{d}t)_{t\to 0} = k_1\,[RCHO][BH_3T^-] \qquad (11)$$

reversal of reaction (10) is negligible and the concentration of BH_3T^- is the initial one.

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[10] L. F. Fieser and M. Fieser, 'Reagents for Organic Synthesis,' vol. 1, p. 1967, p. 255.

The initial exchange rate is therefore given by (11) or (12) from which it follows that the observed constant k_{ex} is equal

$$(\mathrm{d}\phi/\mathrm{d}t)_{t\to0} = 4\,k_1F_0[\mathrm{BH_4^-}] \qquad (12)$$

to $4k_1$. (The numerical factor four is introduced for the sake of statistical consistency.)

The formal representation of the initial rate of exchange between an aldehyde and tritiated tetra-alkoxyborate ion depends on the nature of the labelling. If, as seems most probable in the light of the later discussion, the use of $\mathrm{NaBH_3T}$ leads to the singly-labelled product $\mathrm{NaB(OCHTR)(OCH_2R)_3}$, the initial rate is written as equation (13), in which F_0' is given by equation (14).

$$\mathrm{d}\phi/\mathrm{d}t = 8\,k_1'\,F_0'\,[\mathrm{B(O{\cdot}CH_2R)_4^-}] \qquad (13)$$

$$F_0' = ([\mathrm{B(O{\cdot}CHTR)(O{\cdot}CH_2R)_3^-}]/8[\mathrm{B(O{\cdot}CH_2R)_4^-}])_{t\to0} \qquad (14)$$

Values of $(\mathrm{d}\phi/\mathrm{d})_{t\to0}$ were obtained from the initial slopes of graphs of the molar activity of the isolated semicarbazone of the aldehyde.

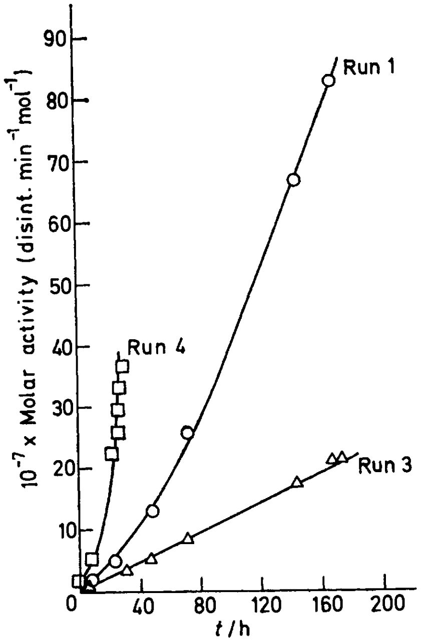


Figure 1 Exchange runs with benzaldehyde and sodium [^{3}H]tetrahydridoborate in $\mathrm{Me_2SO}$

For the formation of [^{14}C]benzaldehyde by exchange of benzaldehyde with labelled sodium benzyl oxide [equation-(15)] the initial rate of exchange is given by equation (16),

$$\mathrm{PhCHO} + \mathrm{Ph\overset{*}{C}H_2{\cdot}O^-Na^+} \underset{k}{\overset{k}{\rightleftharpoons}} \mathrm{Ph\overset{*}{C}HO} + \mathrm{PhCH_2{\cdot}O^-Na^+} \qquad (15)$$

where F_0'' and ϕ'' now refer to ^{14}C activities in sodium benzyl oxide and benzaldehyde, respectively.

$$(\mathrm{d}\phi''/\mathrm{d}t)_{t\to0} = kF_0''\ [\mathrm{NaO{\cdot}CH_2Ph}] \qquad (16)$$

Results of Rate Measurements.—Results with sodium [^{3}H]-tetrahydridoborate for pure $\mathrm{Me_2SO}$ as solvent are given in Figures 1 and 2. The rate constants in Table 2 were deduced from the gradients of the initial portions of the exchange curves, shown in detail in Figure 2. (The effect of added benzyl alcohol is further illustrated in Figure 3.)

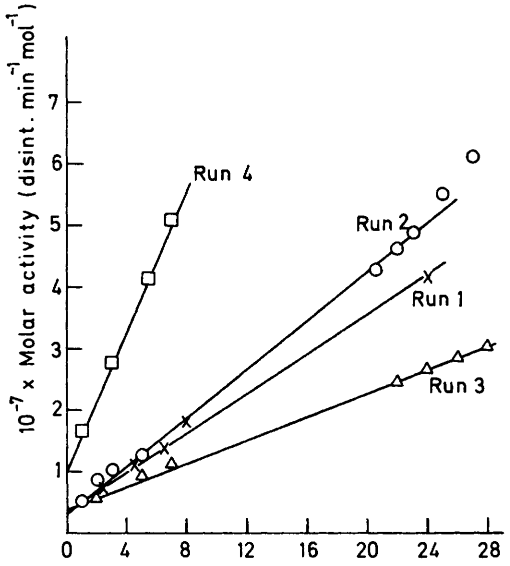


Figure 2 Initial parts of exchange runs with benzaldehyde and sodium [^{3}H]tetrahydridoborate in $\mathrm{Me_2SO}$

The corresponding exchange experiments in $\mathrm{Me_2SO{-}H_2O}$ mixtures are summarised in Table 3 and Figure 4 and the results for the exchange of benzaldehyde with sodium tetrakis[α-^{3}H]benzyloxyborate in Table 4.

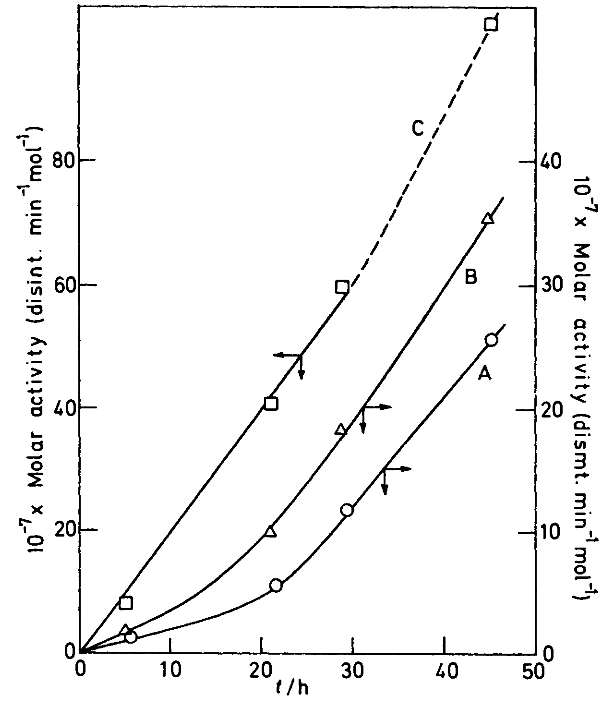


Figure 3 Effect of benzyl alcohol addition on exchange between benzaldehyde and sodium [^{3}H]tetrahydridoborate ([$\mathrm{PhCH_2{\cdot}OH}$] A, 0; B, 0.013M; C, 0.157M; for all three runs zero points are at the origin

When a solution of benzaldehyde (0.1M) in Me_2SO containing sodium benzyl oxide (0.01M), [α-^{14}C]benzyl alcohol (0.0097M; activity 7.34 × 10^{10} disint. min^{-1} mol^{-1}) and inactive benzyl alcohol was left for 3 days, the recovered benzaldehyde (after conversion into the hydrazone) was found to have acquired some ^{14}C activity. The increase with time was not linear (24 h, 3.5 × 10^7; 48 h, 5.36; 64 h, 5.80; 72 h, 5.57 × 10^7 disint. min^{-1} mol^{-1}). The molar activity appeared to pass through a broad maximum or to level off after *ca.* 64 h at an activity of 5.8 × 10^7 disint. min^{-1} mol^{-1}. (The value corresponding to random distribution of ^{14}C amongst all α-carbon atoms in benzyl-containing species and benzaldehyde is 8.4 × 10^8 disint. min^{-1} mol^{-1}). In calculating the molar activities of benzaldehyde in this experiment, the activity observed from a sample immediately after mixing was in each case subtracted. This zero-time activity was observed even in the absence of sodium benzyl oxide and is almost certainly due to a small concentration (*ca.* 10%) of ^{14}C-labelled benzaldehyde in the [α-^{14}C]benzyl alcohol. In a similar experiment with omission of additional inactive benzyl alcohol the increase in activity beyond the zero-time activity was not observed.

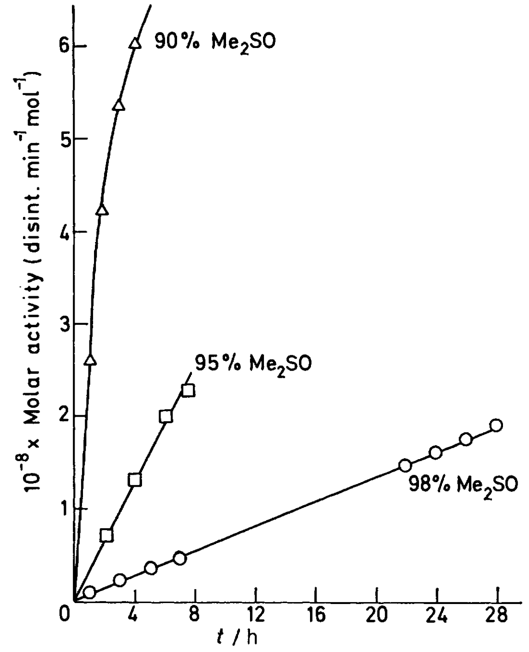


FIGURE 4 Effect of water concentration on exchange between benzaldehyde and sodium [^{3}H]tetrahydridoborate

TABLE 2

Exchange between benzaldehyde and sodium [^{3}H]tetrahydridoborate in Me_2SO

Run no.	[PhCHO]/ M	[NaBH$_4$]/ M [a]	10^7k_{ex}/ dm^3 mol^{-1} s^{-1}	% Reaction followed
3	0.156	0.014 2	0.82	0.36
1	0.156	0.028 5	0.75	0.88
2	0.156	0.030 9	0.81	0.06
4	0.150	0.058 7	1.26	0.27
5 [b]	0.157	0.040 3	6.2	0.89

[a] Tritium activity 0.4 Ci mol^{-1}. [b] In presence of 0.157M-benzyl alcohol.

TABLE 3

Exchange between benzaldehyde and sodium [^{3}H]tetrahydridoborate in Me_2SO–H_2O

% MeSO [a]	[PhCHO]/ M	[NaBH$_4$]/ M [b]	10^7k_{ex}/dm^3 mol^{-1} s^{-1}	% Reaction followed
98	0.154	0.024 7	2.6	0.23
95	0.145	0.020 3	20	0.28
90	0.142	0.020 3	141	0.75

[a] See preceding paper for definition of solvent composition. [b] Tritium activity 0.4 Ci mol^{-1}.

TABLE 4

Exchange between benzaldehyde and sodium tetrakis[α-^{3}H]benzyloxyborate in Me_2SO

[PhCHO]/ M	[Na(O·CH$_2$Ph)$_4$B]/ M [a]	10^7k_{ex}/dm^3 mol^{-1} s^{-1}	% Reaction followed
0.100 4	0.029 4	170	4.0
0.100 5	0.029 7	151	3.2

[a] Tritium activity 0.4 Ci mol^{-1}.

TABLE 5

Stability of sodium tetrakisbenzyloxyborate (0.01M)

Expt. no.	[H_2O]/M	*t*/h	Decomposition
1	None added	0	0
		24.0	27
		72.0	28
2	1.0	1.0	33
		1.5	40
3	0.46	0.0	4.8
4	0.93	0.0	9.0

The decomposition of sodium tetrakisbenzyloxyborate in Me_2SO was followed by measurements of optical absorbance at 272 nm as a function of time (Table 5).

DISCUSSION

The results (Tables 2—4 and Figures 1—4) show that representative samples of benzaldehyde isolated from reaction media (containing initially tritiated tetrahydridoborate and inactive benzaldehyde) at successive times become progressively more radioactive. The incorporation of tritium is confined to the α-position (see Table 1). The exchange is slow compared to the accompanying reduction. In consequence, only the very early stages of tritium uptake by benzaldehyde are observable. For reactions in slightly aqueous Me_2SO (95—98% Me_2SO) the activity of samples increased linearly with time during this initial period, as expected for a first-order isotope exchange process up to 1—2% of reaction. The initial exchange rate increased with the water content of the medium, as for the rate of reduction. A comparison of this solvent effect on the two reactions is given in Table 6. In 90% Me_2SO the linear portion of the reaction is followed by less rapid tritium uptake (see Figure 4), whereas

TABLE 6

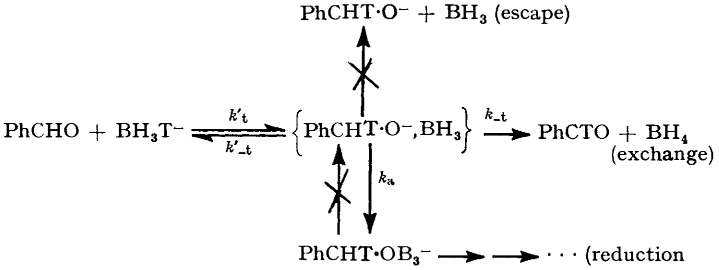
Comparison of rate constants for hydrogen exchange and reduction

Solvent (vol. % Me_2SO)	[NaBH$_4$]	$\frac{10^7k_{ex}}{\text{dm}^3\ \text{mol}^{-1}\ \text{s}^{-1}}$	$\frac{10^5k_2}{\text{dm}^3\ \text{mol}^{-1}\ \text{s}^{-1}}$	k_2/k_{ex}
100	0.014 2	0.82		
	0.028 5	0.75	1.30	174
	0.030 9	0.81		
98	0.024 7	2.64	2.05	78
95	0.020 3	20.0	12.5	63
90	0.020 3	141	81	57

in 100% Me_2SO the rate of the reaction appears to increase with time (Figure 1).

The occurrence of isotope exchange, coupled with the failure to detect any reaction of BH_3 with added amine during the reduction, implies that BH_3 is formed but that it is not ' free ' in the sense of being scavengeable by amine. BH_3 is the first intermediate formed in reaction (1) after the hydride transfer. The lack of its ' free-ness ' can therefore only mean that its destruction, either by the reversal of the hydride transfer or by bond formation between boron and oxygen, occurs before reaction of amine with the newly formed borane entity can compete. Since the trapping of BH_3 by an amine is expected to have only a very small activation energy, and hence to have a rate limited essentially by diffusion, the destruction of BH_3 by the other processes must be more rapid than a diffusion-controlled reaction. This is possible if the further reaction between benzyl oxide ion and borane takes place within the solvent cage in which these species were formed, before they have diffused apart.

According to this model of the reaction, the caged pair, indicated in Scheme 1 by braces, is the product of tritide transfer (with a corresponding rate constant k'_t). The pair is destroyed by four possible processes: (i) the reversal of this tritide transfer (characterised by k'_{-t}), (ii) the corresponding hydride transfer (characterised by k_{-t}) by which the exchange reaction is carried to completion, (iii) the attachment of BH_3 to the oxygen atom (k_a), and (iv) diffusion apart (escape) of the partners of the pair. Reversion to the reactant is assumed not to occur once the boron–oxygen bond is formed. Steps subsequent to the formation of $PhCHT{\cdot}OBH_3^-$ are rapid and lead to the reduction product, tetrakisbenzyloxyborate. Since we were unable to detect BH_3 by trapping experiments, we conclude that diffusion apart of the cage pair is an insignificant process.



Scheme 1

The concentration of the caged pair is evidently very small, and the stationary-state treatment may therefore be applied to the system of reactions in Scheme 1. Accordingly we have equation (17) or, using the definitions of equations (7)—(9), equation (18). Comparison

$$\frac{d[PhCTO]}{dt} = \frac{k_t'k_{-t}}{k_{-t}' + k_{-t} + k_a}[PhCHO][BH_3T^-] \quad (17)$$

$$\left(\frac{d\phi}{dt}\right)_{t \to 0} = \left(\frac{k'_t k_{-t}}{k'_{-t} + k_{-t} + k_a}\right) 4\,F_0\,[BH_4^-] \quad (18)$$

of equations (7) and (18) allows us to write equation (19).

$$k_{ex} = 4k'_t k_{-t}/(k'_{-t} + k_{-t} + k_a) \quad (19)$$

The rate of reduction is similarly expressed in terms of the rate coefficients of Scheme 1 [equation (20)]. It must be remembered that formation of one $PhCH_2{\cdot}OBH_3^-$ ion represents the rate-limiting step for the destruction of one tetrahydridoborate ion (or four benzaldehyde molecules). In this equation $4k_t$ is the rate constant for

$$-\frac{d[BH_4^-]}{dt} = \left(\frac{4k_tk_a}{k_{-t} + k_a}\right)[PhCHO][BH_4^-] \quad (20)$$

hydride (protide) transfer from tetrahydridoborate to benzaldehyde. The numerical factor is statistical and introduced so that k_t and k'_t may each correspond to the rate constant per hydrogen nucleus (protium or tritium). The rate constant k_2 for reduction is defined in terms of equation (21) [*cf.* equation (12) of the preceding paper]. Combination of equations (20) and (21) then gives (22).

$$-\,d[BH_4^-]/dt = k_2[PhCHO][BH_4^-] \quad (21)$$

$$k_2 = 4k_tk_a/\,(k_{-t} + k_a) \quad (22)$$

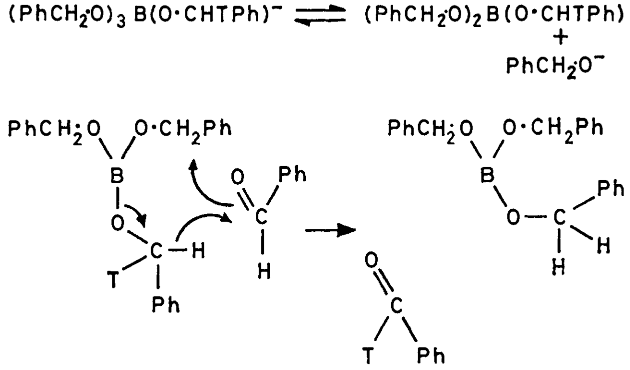
Because of a kinetic isotope effect, $k_{-t} \gg k'_{-t}$, so that equation (23) relates k_2 and k_{ex}. Values for k_2/k_{ex} deduced from the present work and the parallel investigation of the reduction of benzaldehyde are given in Table

$$k_2/k_{ex} = k_tk_a/k'_tk_{-t} \quad (23)$$

6. Allowing for a primary kinetic tritium isotope effect k_t/k'_t in the hydride-transfer step of between 8 and 20, we deduce that the rate constant k_a for the association step is larger than k_{-t}, the rate constant for hydride transfer to BH_3, by a small factor of between 8 and 20 for Me_2SO solutions. Such a relatively small rate difference is reasonable for two competing reactions within a cage, both of which, according to our model, would be faster than the diffusion apart of the reactive species.

Whilst the above analysis explains the initial exchange rates, it does not account for some of the observed complications. The most important of these is the increase in exchange rate in Me_2SO solution as the reaction proceeds (Figure 1). Qualitatively, the effect would be consistent with progressive slow absorption of water by the solution (since deliberate addition of water increases the exchange rate, as shown in Table 3). However, the rate increase during the course of the reaction is too marked to be explained in this way. It could, however, be due to the formation of a tritiated reduction product which itself undergoes tritium exchange with benzaldehyde. As sodium tetrakisbenzyloxyborate is thought to be the only reduction product whose concentration builds up to a significant value during reaction, we briefly examined the exchange between a tritiated sample of this substance with benzaldehyde under the same experimental conditions as the other exchange experiments in Me_2SO. It was found that benzaldehyde takes up tritium from sodium tetrakisbenzyloxyborate at a greater rate than it does from tritiated sodium tetrahydridoborate (Table 4). However, we also found that sodium tetrakisbenzyloxyborate is very unstable in Me_2SO solution (Table 5) and disappears either by hydrolysis by traces of water in the solvent or by some unidentified reaction with Me_2SO itself. For this reason we do not believe that these exchange observations have more than qualitative significance.

The mechanism of the exchange between benzaldehyde and tetrakisbenzyloxyborate can be represented speculatively by Scheme 2, on the basis of strict analogy with the mechanism[11] of the Meerwein–Ponndorf–Verley and Oppenauer reactions. Scheme 2 implies the partial dissociation of tetrakisbenzyloxyborate into tribenzyl borate and a benzyl oxide ion, which is supported by titration studies.[12] In this way it is possible to avoid the postulation of penta-co-ordinated boron [which would arise if the tetrakisbenzyloxyborate ion itself, rather than tribenzyl borate, were the species from which hydride (tritide) is transferred]. There are other reasons why a small amount of such dissociation seems probable. The fact that an addition product of Me_2SO to benzaldehyde can be isolated[1] as a by-product of the reduction in Me_2SO implies the formation of dimsyl ions and a very high basicity of the reaction system. The high basicity of reaction media was also indicated by the troublesome incursion of base-catalysed reactions with carbonyl compounds containing β-hydrogen atoms (which explains why the present studies were restricted to the particular substrate used). The formation of dimsyl ions by reaction of alkoxide ions with Me_2SO is well established.[13] Sodium tetrahydridoborate itself can hardly be credited with such high basicity, since its reaction with Me_2SO would then lead to evolution of hydrogen, which is inconsistent with the known high stability of sodium tetrahydridoborate in Me_2SO. It is more reasonable to suppose that the high basicity is due to the reduction product—or rather, to benzyl oxide ions, formed in an equilibrium such as that in the first step of Scheme 2.



Scheme 2

The question then arises as to whether tritiated benzyl oxide ions themselves are responsible for the enhancement of tritium uptake by benzaldehyde after the initial stage of the reaction. To test this possibility, we examined the occurrence of exchange between sodium benzyl oxide and benzaldehyde, using ^{14}C labelling, initially of the α-position in the benzyl compound. An exchange reaction was observed but its rate was less than that for tritium exchange between benzaldehyde and sodium tetrakisbenzyloxyborate. Accordingly, the latter process is more likely to be the cause of the progressive increase in the rate of exchange between benzaldehyde and sodium tetrahydridoborate. There are, however, some complications in the kinetics of the benzyl oxide–benzaldehyde exchange. First, the exchange reaction slows down long before equilibrium is reached and, second, it only takes place when an appreciable concentration of benzyl alcohol is present. One possible explanation of these observations is that the equilibrium (24) is established—rapidly in the absence of benzyl alcohol and more slowly when it is present—but in each case so as to lower the benzyl oxide concentration to a small value.

$$PhCH_2{\cdot}O^- + Me_2SO \rightleftharpoons PhCH_2{\cdot}OH + CH_2{\cdot}SOMe \quad (24)$$

The occurrence of at least two routes by which tritium incorporation into benzaldehyde occurs (one by reaction with tetrahydridoborate ion and the other by reaction with tetrakisbenzyloxyborate ion) complicates medium effects on the reaction rate at a stage when both reactions contribute. For example, added water or benzyl alcohol may accelerate reaction (1) by stabilising the incipient negative charge in the transition state on oxygen by hydrogen bonding, thereby increasing the initial exchange rate. On the other hand, the exchange route of Scheme 2 may not be affected in the same manner, and the stability of the tetrakisbenzyloxyborate ion in different media may also have to be considered. A discussion of such details of reaction mechanism does not seem warranted at this stage.

We thank the S.R.C. for partial support of the work reported in the present and the preceding paper, and King's College, London, for a Tutorial Studentship (to C. A.).

[6/2322 *Received*, 21*st December*, 1976]

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