The Stokes' law friction coefficient $f = 6\pi\eta r$, where r is the radius of the diffusing particle, is of course in error when applied to an estimate of D_0's for which the calculated values are some 40% below the ones obtained from extrapolation of experimental values.

The self-consistency of the diffusion data for this system, particularly at 25°, suggests that they should be of value for calibration purposes in diffusion techniques for which benzene may be used as the solvent.

Acknowledgments.—The authors have enjoyed and profited from discussions of this problem with various members of the Yale Department of Chemistry. We are also indebted to L. G. Longsworth for some very fruitful advice.

The work was supported by the Atomic Energy Commission under Contract AT (30-1)-1375. Purchase of equipment was made possible by several grants from the George Sheffield Scientific fund.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE CHEMISTRY DIVISION, ARGONNE NATIONAL LABORATORY]

Hydrogen Isotope Effect in the Bromine Oxidation of Ethanol

BY LOUIS KAPLAN

RECEIVED APRIL 23, 1954

At 37.5° the rate of oxidation of ethanol-1-*t* by bromine is 0.57 times that of ethanol, corresponding to a ratio of about 0.15 for the rates of removal of tritium and hydrogen atoms from the methylene carbon. This result, taken together with the reaction kinetics, rules out the formation of ethyl hypobromite as the precursor of acetaldehyde in the oxidation, and lends support to a mechanism involving the transfer of a hydride ion from the methylene carbon to bromine.

The oxidation of ethanol by bromine has been investigated by Bugarszky[1] and more recently by Farkas, Perlmutter and Schächter.[2] In aqueous solutions of ethanol ranging from 1 to 76% by weight, the reaction is first order in *free* bromine, tribromide ion being unreactive. In 1 to 4% solutions, the reaction is also first order in ethanol. Below *p*H 3, the rate is independent of hydrogen ion concentration. In 76% solution, the only products are ethyl acetate and hydrogen bromide; in 41% solution acetic acid is also formed; while in 1–4% solutions very little ester is formed. In no case is there produced a significant amount of organically bound bromine. The reaction takes place in two stages

$$CH_3CH_2OH + Br_2 \xrightarrow{k_I} CH_3CHO + 2HBr \quad (I)$$

$$CH_3CHO + Br_2 + H_2O \xrightarrow{k_{II}} CH_3COOH + 2HBr \quad (II)$$

in dilute solution at 25° the value of k_{II}/k_I is about 200.

Farkas, Perlmutter and Schächter[2] have suggested the following three alternative mechanisms for reaction I, all of which are consistent with the reaction kinetics

(a) $CH_3CH_2OH + Br_2 \longrightarrow CH_3CH_2OBr + HBr$ (III)

$CH_3CH_2OBr \longrightarrow CH_3CHO + HBr$ (IV)

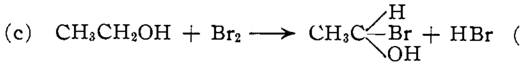
with reaction III the rate-determining step.

(b) $CH_3CH_2OH + Br_2 \longrightarrow [CH_3CHOH]^+ + Br_2H^-$ (V)

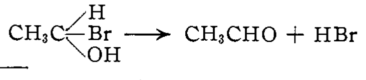
$[CH_3CHOH]^+ \longrightarrow CH_3CHO + H^+$ (VI)

$Br_2H^- \longrightarrow H^+ + 2Br^-$ (VII)

with V rate-determining.



(c) $CH_3CH_2OH + Br_2 \longrightarrow CH_3C\begin{matrix}H\\Br\\OH\end{matrix} + HBr$ (VIII)



$CH_3C\begin{matrix}H\\Br\\OH\end{matrix} \longrightarrow CH_3CHO + HBr$ (IX)

with VIII rate-determining. They appear to favor mechanism (a), largely on the grounds that alkyl hypochlorites are known[3] to break up into aldehyde and hydrochloric acid.

Although all three mechanisms give the same rate law, there is an essential difference between (a) on the one hand and (b) and (c) on the other. In mechanisms (b) and (c), a carbon–hydrogen bond is ruptured in the rate-determining step; in mechanism (a), this bond is ruptured in a subsequent fast reaction. The two cases can be distinguished by comparing the rate of reaction of the normal compound with that of one which has been isotopically substituted at the position of bond rupture. There is experimental evidence,[4] as well as theoretical justification,[5] that if a bond involving the isotope is broken in the rate-determining step of the reaction, the molecule containing the heavy isotope will, in general, react more slowly than that containing the light isotope.[6] This paper presents the results of a study of the effect of the substitution of tritium for protium in the methylene position of ethanol on the rate of oxidation by bromine.

Calculations

Ethanol containing tracer amounts of ethanol-1-*t* was subjected to incomplete oxidation by bromine. In principle, the isotopic rate ratio for a reaction

$$AH + B \longrightarrow XH + Y$$

can be determined[7] by measuring the isotopic content of either the reaction product XH or the unreacted AH. Since, in the reaction studied,

---

[1] (a) S. Bugarszky, *Z. physik. Chem.*, **38**, 561 (1901); (b) *ibid.*, **42**, 545 (1903); (c) *ibid.*, **71**, 705 (1910).

[2] L. Farkas, B. Perlmutter and O. Schächter, THIS JOURNAL, **71**, 2829 (1949).

[3] F. D. Chattaway and O. G. Backeberg, *J. Chem. Soc.*, **123**, 2999 (1923).

[4] (a) C. Reitz, *Z. physik. Chem.*, **A179**, 119 (1937); (b) F. H. Westheimer and N. Nicolaides, THIS JOURNAL, **71**, 25 (1949).

[5] (a) J. Bigeleisen, *J. Chem. Phys.*, **17**, 675 (1949); (b) L. Melander, *Arkiv Kemi*, **2**, 211 (1950); (c) H. Eyring and F. W. Cagle, Jr., *J. Phys. Chem.*, **56**, 889 (1952).

[6] For examples of isotope effects without bond rupture see (a) V. J. Shiner, Jr., THIS JOURNAL, **75**, 2925 (1953); (b) E. S. Lewis and C. E. Boozer, *ibid.*, **76**, 791 (1954).

[7] J. Bigeleisen, *Science*, **110**, 14 (1949).

the product is hydrogen bromide, which undergoes rapid exchange with the aqueous medium, the rate ratio was calculated from the change in specific activity of the unreacted alcohol. The isotopic reactions can be formulated as

$$\mathrm{CH_3CH_2OH + Br_2} \xrightarrow{2k_1} \mathrm{CH_3CHO + 2HBr}$$

$$\mathrm{CH_3CHTOH + Br_2} \begin{cases} \xrightarrow{k_2} \mathrm{CH_3CHO + HBr + TBr} \\ \xrightarrow{k_3} \mathrm{CH_3CTO + 2HBr} \end{cases}$$

By an analysis similar to that given by Bigeleisen,[7] it can be shown that, for incomplete consumption of the alcohol

$$\frac{\log\ (\mathrm{A}')/(\mathrm{A}')_0}{\log\ (\mathrm{A})/(\mathrm{A})_0} = \frac{k_2 + k_3}{2k_1} \qquad (1)$$

where (A′) and (A) refer to the final concentrations of CH_3CHTOH and CH_3CH_2OH, respectively, and $(A')_0$ and $(A)_0$ to the corresponding initial concentrations This expression can be rewritten in terms of specific activities

$$\frac{k_2 + k_3}{2k_1} = 1 + \frac{\log N_\mathrm{A}/N_\mathrm{A}{}^\circ}{\log (\mathrm{A})/(\mathrm{A}_0)} \qquad (2)$$

in which $N_A{}^0$ and N_A are, respectively, the specific activities of the initial alcohol and of the fraction $(A)/(A)_0$ which remains unreacted.

Isotopic analysis of the acetaldehyde formed at the very start of the reaction would permit the experimental evaluation[7] of the ratio k_1/k_3. Since, however, the oxidation of the aldehyde is so much faster than that of the alcohol, the large correction required for the isotope effect in the aldehyde oxidation precludes the determination of the ratio in this way. To a first approximation, this ratio can be taken equal to unity, since the two rates, k_1 and k_3, involve the rupture of a carbon–protium bond, and differ only in the isotopic nature of the bond which remains intact. Using this approximation, the isotopic rate ratio can be calculated from the expression

$$\frac{k_\mathrm{T}}{k_\mathrm{H}} = \frac{k_2}{k_1} = 2\,\frac{k_2 + k_3}{2k_1} - 1 \qquad (3)$$

Results

In Table I are summarized the results of oxidations in which the consumption of ethanol varied between 45 and 85%. The data from run 1 indicate that the specific activity of the alcohol is not significantly changed by contact with the hydrobromic acid produced in the reaction, nor by the procedure used in isolating the alcohol and forming its derivative. Run 5 shows that the measured rate ratio is not appreciably affected by the acid concentration of the reaction mixture. The values of the rate ratio $(k_2 + k_3)/2k_1$, calculated by equation 2, agree within the experimental error of measuring the concentration and specific activity of the alcohol. The mean value, 0.575, is probably accurate to about 1%. Assuming that $k_1 = k_3$, the value of k_T/k_H calculated by equation 3 is 0.15 ± 0.02.

TABLE I

PARTIAL OXIDATION OF ETHANOL-1-*t* BY BROMINE AT 37.5°

Run	EtOH initial, mmoles $(A)_0$	Br_2, mmoles	EtOH final, mmoles (A)	Specific activity, μc./mmole, N_A	$(k_2 + k_3)/2k_1{}^d$
1	9.52	0[a]	9.52[b]	12.34[c]	
2	9.52	9.1	5.10	16.15	0.569 ± 0.023
3	9.52	14.5	2.47	22.00	.571 ± .010
4	19.04	33.3	2.95	26.85	.583 ± .007
5	9.52	9[a]	5.28	15.95	.565 ± .024
			Weighted mean		.575

[a] Solution contained also 40 mmoles of HBr. [b] Actually recovered 9.25 mmoles. All values in this column have been multiplied by 9.52/9.25. [c] The *p*-nitrobenzoate prepared directly from the initial EtOH-1-*t* contained 12.23 ± 0.10 μc./mmole. [d] The estimated error is the maximum which could be produced by 1% errors in $(A)/(A)_0$ and $N_A/N_A{}^\circ$.

Discussion

The relative rate of consumption of isotopic molecules in a *competitive* system is not necessarily the ratio of the rates which would be observed if the isotopic molecules were permitted to react independently[8] The rather large isotope effect found for the oxidation of ethanol by bromine does not, therefore, establish that the rupture of the carbon–hydrogen bond occurs in the rate-determining step of the reaction; it does, however, require that this bond rupture occur in the slowest step which involves the ethanol molecule being oxidized. In mechanism (a) the slow step does not involve such a bond rupture, and this reaction path appears, therefore, to be ruled out as the mechanism of the oxidation. Since the formation of ethyl hypobromite in a rapid equilibrium step is inconsistent with the lack of dependence of the reaction rate on hydrobromic acid concentration,[2] it must be concluded that the hypobromite is not a precursor of acetaldehyde.

Of the other two mechanisms outlined above, mechanism (c) seems rather implausible[2] since it requires that hydrogen be replaced by bromine in a second order reaction occurring at room temperature. Mechanism (b), which involves the transfer of a hydride ion from carbon to bromine, is much more attractive. The removal of hydrogen with a pair of electrons would explain the inactivity of the tribromide ion. Hydride transfers have been postulated for a number of reactions of alcohols.[9] Of particular interest is the reduction of aryl diazonium salts by alcohols, for which Dewar[10] has proposed that the alcohol supplies hydride ions. Isotope effects in the reactions of ethanol and methanol with *o*- and *m*-nitrobenzenediazonium salts have been studied by Melander[11] who obtained values of k_T/k_H very close to those found in the present investigation.

It is, of course, possible to write other mechanisms consistent with the experimental findings. For example, the sequence

$$\mathrm{CH_3CH_2OH + Br_2} \overset{\text{fast}}{\rightleftarrows} \mathrm{CH_3CH_2OH \cdot Br_2}$$

---

[8] The situation is analogous to that in the nitration of homologous aromatic compounds; under certain conditions a number of such compounds nitrate at identical rates when measured separately but at quite different rates when measured competitively. C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 245, 275.

[9] For some examples, see G. Baddeley and W. Pickles, *J. Chem Soc.*, 3726 (1953).

[10] M. J. S. Dewar, *Research*, **3**, 154 (1950).

[11] L. Melander, *Arkiv Kemi*, **3**, 525 (1952).

$$CH_3CH_2OH\cdot Br_2 \xrightarrow{\text{slow}} [CH_3CHOH]^+ + Br_2H^-$$

would, if the equilibrium concentration of the addition complex in aqueous solution were small, be quite indistinguishable from mechanism (b).

Still other mechanisms consistent with the experimental results involve the reaction of a molecule of bromine with a molecule of ethanol in a rate-determining step to give either an ethanol–bromine complex or ethyl hypobromite which then rapidly oxidized a second molecule of ethanol to acetaldehyde. In these mechanisms, unlike mechanism (a), the ethyl hypobromite (or the complex) is not the precursor of the acetaldehyde but serves only as a carrier for bromine. Such mechanisms can be distinguished from those previously discussed in that they predict little or no difference in the separately measured reaction rate constants between ordinary ethanol and ethanol-1-d_2.

The kinetic studies in aqueous solution provide little information regarding the form in which bromine reacts. The participation of a solvated species, formed in a rapid equilibrium, is suggested by the kinetics of the oxidation in carbon tetrachloride and carbon disulfide solutions. In these solvents, the dependence of the rate on alcohol concentration[1c] is very similar to that found by Andrews and Keefer[12] for the reaction of bromine with *t*-amyl alcohol, which they attribute to the reaction of a 1:1 bromine–alcohol complex with a second molecule of alcohol. In dilute aqueous solution, where the ethanol–bromine reaction is first order in ethanol, it is possible that a molecule of water substitutes for one of the alcohol molecules.

Experimental

Ethanol-1-*t*.—Onto 0.302 g. (7.9 mmoles, 92 mc. T) of lithium aluminum hydride-*t*[13] in an evacuated flask at −195° was distilled 15 cc. of dry ether and 1.845 g. (21.0 mmoles) of ethyl acetate. The flask was warmed to −22° and, after the reaction had subsided, was allowed to stand at room temperature for two hours with occasional shaking. The ether and excess ethyl acetate were removed in a high vacuum and 2 g. of water was distilled onto the residue. After standing for two hours at room temperature, the volatile material was distilled *in vacuo* successively onto two 15-g. portions of Drierite, and then fractionated through a series of traps on the vacuum line. The product, which had a vapor pressure of 12.5 mm. at 0° and 43.5 mm. at 20°, weighed 1.138 g. (78% of theory, based on $LiAlH_4$) and contained 55.3 mc. of T. (The unreacted ethyl acetate was found to contain a considerable amount of tritium.) For use in the oxidation experiments, a portion of the product was diluted about 200-fold with absolute ethanol.

To determine the fraction of tritium which might have been incorporated in the methyl group of the ethanol, a 200-mg. sample containing 126 μc. T per mmole was oxidized at room temperature with 900 mg. $KMnO_4$ in 10 cc. of water to which 240 mg. $Mg(NO_3)_2\cdot 6H_2O$ had been added to remove hydroxide ion. The resultant acetic acid was isolated as the silver salt and found to contain only 0.032 μc. per mmole. That methyl tritium was not lost by exchange during the permanganate oxidation was demonstrated in a parallel experiment using ordinary ethanol and tritiated water; the silver acetate from this reaction contained only 0.4% of the tritium which would have been present had the tritium been distributed statistically between water and methyl hydrogen.

Oxidation by Bromine.—An aliquot of a stock aqueous solution of ethanol-1-*t* was added to a weighed amount of bromine in a glass-stoppered flask containing sufficient water to make the alcohol concentration about 0.2 *M*. (In some cases, aqueous hydrobromic acid was added instead of, or in addition to, the bromine.) The stopper was sealed with a little silicone lubricant, and the flask was placed in a constant temperature bath at 37.5° for two weeks; at the end of this time all reaction mixtures were completely colorless. The reaction mixture was treated with silver oxide and heated at 60° to remove acetaldehyde[14] and HBr. The mixture was subjected to distillation through a small Vigreux column, the volume of distillate collected being about one-third of the total. After titration of aliquots for ethanol, as described below, the remainder of the distillate was saturated with potassium carbonate and extracted with two 10-cc. portions of benzene. The benzene solution was treated with 5 cc. of pyridine and excess of *p*-nitrobenzoyl chloride and heated at 60–70° for 15 min. The benzene was evaporated in a stream of nitrogen and the residue was taken up in dilute aqueous pyridine, filtered and washed with dilute NaOH and with water. The ethyl *p*-nitrobenzoate was recrystallized repeatedly from *n*-pentane and dried *in vacuo*. The samples used for tritium assay melted at 55.5–60°.

Analytical Procedures.—Tritium was determined[15] in the form of hydrogen gas in an ion chamber filled to atmospheric pressure with tank hydrogen. Organic tritium compounds were combusted[16] over copper oxide, any oxides of nitrogen were reduced by passage over hot copper, the combustion water was condensed *in vacuo* at −95°, and was converted to hydrogen by passage over heated zinc. After the combustion train had been conditioned by burning a sample, duplicate analyses of the same material agreed within 1%.

Ethanol was determined, after removal of acetaldehyde, by oxidation to acetic acid with excess dichromate in sulfuric acid solution. A sample containing 0.1–0.4 mmole of alcohol was treated with an excess of standard potassium dichromate solution and 15 cc. 18 *N* sulfuric acid and made up to 25 cc. with water. The mixture was heated in a stoppered flask for 10 min. at 90°, cooled, diluted with 25 cc. of water, and titrated with standard ferrous ammonium sulfate solution to a Ferroin end-point. Samples of pure ethanol gave results of 100 ± 1% by this procedure. Samples treated with silver oxide and distilled as in the oxidation runs gave over-all recoveries of 97–98%.

LEMONT, ILLINOIS

---

[12] L. J. Andrews and R. M. Keefer, THIS JOURNAL, **75**, 3557 (1953).

[13] K. E. Wilzbach and L. Kaplan, *ibid.*, **72**, 5795 (1950).

[14] J. Mitchell, Jr., and D. M. Smith, *Anal. Chem.*, **22**, 746 (1950).

[15] K. E. Wilzbach, A. R. Van Dyken and L. Kaplan, *ibid.*, **26**, 880 (1954).

[16] These experiments were performed before the development of the more convenient zinc fusion technique: K. E. Wilzbach, L. Kaplan and W. G. Brown, *Science*, **118**, 522 (1953).