676. *Tracer Studies on Alcohols. Part II.* The Exchange of Oxygen-18 between* sec.*-Butyl Alcohol and Water.*

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The observation that, for a given perchloric acidity, the rate of racemisation of optically active *sec.*-butyl alcohol in water is twice the rate of oxygen exchange, has been extended to sulphuric acid solutions, and to higher acid concentrations than those used earlier. Plots of the logarithms of the first-order rate coefficients for racemisation and oxygen exchange against $-H_0$ (the Hammett acidity function) have slopes near to unity, indicating that the rate-determining step in both processes is the heterolysis of the oxonium ion, ROH_2^+. In the more concentrated acid solutions the rate of racemisation is less than twice the rate of oxygen exchange. This is because olefin elimination, which is negligible at low acid concentrations (Part I), increases with increasing acidity, and by subsequent hydration of the olefin provides an alternative route for oxygen exchange, with complete racemisation.

The stereochemistry of S_N1 reactions is discussed.

In Part I * it was shown that over a range of perchloric acid concentrations (up to *ca.* M), the rate of oxygen exchange of *sec.*-butyl alcohol, followed isotopically, was, within experimental error, half the rate of racemisation of the optically active material, and that the oxygen exchange did not go by way of elimination and subsequent hydration of olefin. This result showed that every oxygen exchange between the alcohol and water gives complete inversion of configuration. The rates of exchange and racemisation were measured in aqueous acid, where the simpler mechanistic tests cannot be applied, but where a distinction between acid-catalysed uni- and bi-molecular processes can be made from the dependence of rate on acid concentration. Within the limited acidity range studied the rates of both racemisation and oxygen exchange followed the Hammett acidity function, and not the concentration of hydroxonium ions, $[H_3O^+]$. This distinction is diagnostic of mechanism because it can be shown that if the transition state of an acid-catalysed solvolytic reaction does not contain a water molecule from the solvent its rate should be proportional to h_0, but that the rate of a bimolecular reaction, where the transition state contains this water molecule, should be proportional, at least approximately, to the hydroxonium ion concentration, $[H_3O^+]$. These hypotheses have been tested in numerous examples where there is independent evidence.[1]

The kinetics of oxygen exchange at 99·8° were followed by the methods described in Part I. In some experiments isotopically enriched *sec.*-butyl alcohol was allowed to exchange its oxygen with isotopically normal water, and the increasing isotopic abundance of the water followed with time; in others the increase in the isotopic abundance of intially isotopically normal *sec.*-butyl alcohol in isotopically enriched water was followed by isolation of the alcohol. The racemisation was followed at 82·0° and 99·8°. The results

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* The paper, *J.*, 1955, 604, is regarded as Part I.

[1] Hammett, " Physical Organic Chemistry," McGraw-Hill, New York, 1940, pp. 273—277; Long and his co-workers, *J. Amer. Chem. Soc.*, 1950, **72**, 3267; *J. Phys. Chem.*, 1951, **55**, 829.

are shown in Fig. 1 and are tabulated. The Arrhenius activation energy for racemisation is *ca.* 36 kcal. mole^{-1}. This leads to a value of +12·3 cal. mole^{-1} deg.$^{-1}$ for the entropy of activation. A positive value for this term seems to be a characteristic of unimolecular acid-catalysed reactions.[2]

The slope of the logarithm of the rate coefficient for oxygen exchange against $-H_0$ is 1·02, and for racemisation is 0·97 (at both temperatures). At acid concentrations less than *ca.* 1·5 molal the rate of racemisation is almost exactly twice the rate of exchange, indicating that each exchange of oxygen atoms between alcohol and water gives complete inversion of configuration of the asymmetric carbon atom. The dependence of both exchange and racemisation on the Hammett function shows that water molecules from the solvent do not enter into the common slow stage of these processes (except by solvation of the ions concerned). This slow stage therefore is the formation of a carbonium ion intermediate whose life is not sufficiently long for the carbon atom to lose its asymmetry. This complete inversion for a unimolecular reaction is very similar to that observed in the acid hydrolysis of epoxides.[3]

FIG. 1. *Plots of the logarithms of the first-order rate coefficients* ($\times 10^5$) *for racemisation (upper line) and oxygen exchange (lower line) against* $-H_0$.

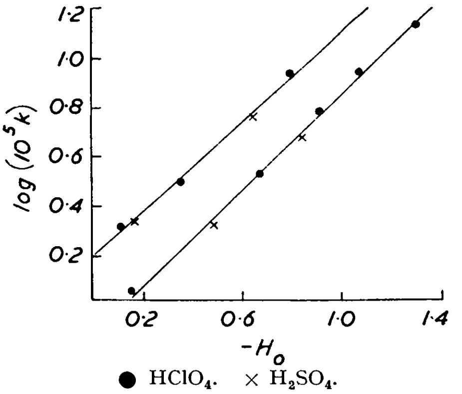
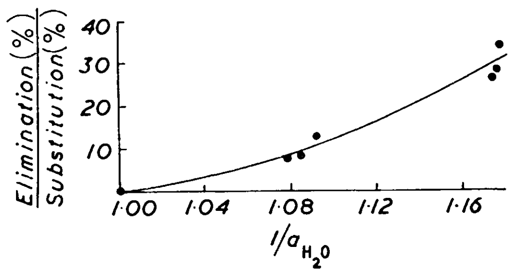


FIG. 2. *Dependence of elimination upon activity of water in perchloric acid.*



As the acidity is increased, and the water activity decreased, the elimination of olefin, which was insignificant at low acid concentrations (Part I), increases (see p. 3406). Elimination and subsequent hydration of the olefin will give a racemic alcohol (with no rearrangement [4]), and provided that allowance is made for the amount of oxygen exchange and racemisation by this route we find that oxygen exchange through substitution is giving complete inversion of configuration at each individual replacement, at all acidities up to 4m (see p. 3406).

This dependence of elimination upon acidity provides further evidence for the hypothesis that the processes studied are unimolecular in the rate-determining step. The stereochemical fate of a given carbonium ion is determined by competition between two reactions, one the capture of this ion to regenerate the alcohol with oxygen exchange, the other the loss of a proton to give an olefin, which will hydrate to regenerate the alcohol or can be aspirated out of solution. Thus the rate of oxygen exchange (in a closed system) will not depend on the fate of the carbonium ion. The formation of an olefin by loss of a proton from a carbonium ion does not require the immediate intervention of a water molecule. This follows from several independent pieces of evidence. The rate of hydration of an olefin follows the Hammett acidity function,[4, 5] and therefore does not require

[2] Long, personal communication.
[3] Long and Pritchard, *J. Amer. Chem. Soc.*, 1956, **78**, 2663, 2667.
[4] Taft, *J. Amer. Chem. Soc.*, 1952, **74**, 5372; Levy, Taft, and Hammett, *ibid.*, 1953, **75**, 1253.
[5] Taft, Purdie, Riesz, and De Fazio, *ibid.*, 1955, **77**, 1584.

a water molecule in the slow step of reaction. This step is either the rearrangement of a π (or other) complex of the proton and olefin to a carbonium ion, or the addition to the olefin of a proton not closely bound to a water molecule.[6] Elimination of a proton from a carbonium ion should follow the same reaction path as the hydration and be independent of the concentration or activity of water. It is known that the rate of proton loss from the carbonium ion formed by *tert.*-butyl bromide in nitromethane, by the $E1$ mechanism, is not dependent on the presence of nucleophilic reagents such as halide ions.[6] In agreement with this is the observation that there is no deuterium isotope effect in the $E1$ elimination from a tertiary alkyl carbonium ion.[7]

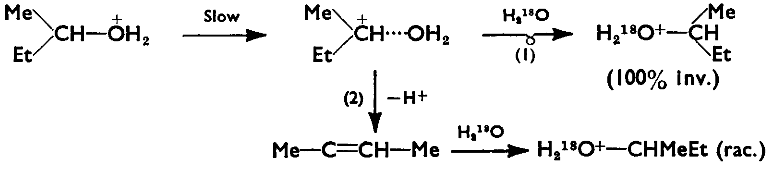
The ratio of elimination to substitution (with oxygen exchange) is given by the expression :

$$\frac{\text{Elimination (\%)}}{\text{Substitution (\%)}} \propto \frac{1}{a_{H_2O}} \cdot \frac{f_S^*}{f_E^*}$$

where f_S^* and f_E^* are the activity coefficients of S* and E*, the transition states for attack of a water molecule on, and elimination of a proton from, the carbonium ion. The transition state for substitution will contain a water molecule from the solvent, that for elimination will not. The ratio of elimination to substitution plotted against the reciprocal of the water activity, a_{H_2O}, does not give a straight line (Fig. 2), the ratio f_S^*/f_E^* increasing with increasing acidity (decreasing water activity of the medium [8]). Deno *et al.*[9] have shown that f_{R^+}/f_{HB^+}, where R^+ is the carbonium ion of a tertiary alcohol and HB^+ the cation of a typical Hammett base, increases rapidly with increasing sulphuric acidity. This ratio should approximate to f_S^*/f_E^* because S* is akin to a protonated alcohol, and therefore to HB^+, and E* is akin to a carbonium ion. Our results, although obtained with an alcohol structurally somewhat different from those investigated by Deno *et al.*, show qualitatively the dependence of the ratio of elimination to oxygen exchange predicted by their measurements. In making this comparison we assume that the variation of a_{H_2O} with temperature does not depend upon acidity.

These considerations will not apply to bimolecular elimination and substitution, which should both be affected by changes in the concentration or activity of water, and in fact proton loss from the β-carbon atom of the conjugate acid of a ketone (a reaction analogous to $E2$ elimination) requires a water molecule, and its rate, followed by measuring the rate of enolisation, is proportional to $[H_3O^+]$.[1]

Oxygen exchange and racemisation *via* substitution and elimination, with subsequent hydration, can therefore be represented as :



In this scheme the slow formation of the carbonium ion is the rate of oxygen exchange, and at low acidities (where elimination can be neglected) this is the rate of inversion of configuration of the carbonium ion, steps 1 and 2 being fast.

The solvent water molecule attacks the carbonium-ion centre sufficiently soon after the energy maximum is reached for the expelled water molecule to exert a marked " shielding " effect, giving complete inversion of configuration, but the kinetic form shows that making and breaking of these bonds are not synchronous. This means that the

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[6] de la Mare, Hughes, Ingold, and Pocker, *J.*, 1954, 2930.

[7] Shiner, *J. Amer. Chem. Soc.*, 1953, **75**, 2925.

[8] Robinson and Baker, *Trans. Roy. Soc. New Zealand*, 1946, **76**, 250.

[9] Deno and his co-workers, *J. Amer. Chem. Soc.*, 1955, **77**, 3044; data reported at Sixth Reaction Mechanism Conference, Swarthmore College, 1956.

lifetime of the carbonium-ion intermediate, which is determined by the rates of water attack (1) and the proton loss (2), is not long enough for the expelled water molecule to move sufficiently far away to make the carbon atom, at the reaction centre, susceptible to attack from all directions. This will no longer be true when the carbonium ion is stabilised by aryl groups, and the acid-catalysed oxygen exchange of 4-methoxydiphenylmethanol gives complete loss of optical activity at every step of substitution.[10]

The Steric Course of S_N1 Reactions.—In 1937 it was shown that, in the absence of configuration-retaining groups, the product of an S_N1 reaction was usually partially racemic, with some inversion of configuration.[11] In some cases, particularly where kinetic distinctions are not clear-cut, it has been assumed that absence of complete racemisation is proof of a bimolecular component of mechanism. Much recent work has shown that this is not necessarily correct, although the converse, that observation of racemisation is evidence for a unimolecular mechanism, does hold.

Oxygen exchange between *sec.*-butyl alcohol and water is one of several reactions in which kinetic, or other, evidence shows that the transition state does not contain a solvent or reagent molecule, but in which the carbon centre is completely inverted.

The acid hydrolysis of epoxides is a unimolecular process,[3] but formation of the *trans*-diol shows that the carbon atom at the reaction centre is completely inverted. Similarly there are a large number of substitutions at the $C_{(1)}$ atom of a hexose ring, which are carried out under conditions in which an S_N1 reaction is expected, and which give complete inversion of the configuration of this atom.[12] Interpretation of the stereochemistry of many of these reactions is complicated by the presence of acetoxy-groups, which may interact with the carbonium-ion centre. However, recently it has been shown that the methanolysis of 2 : 3 : 4 : 6-tetra-*O*-methyl-α-D-glucopyranosyl chloride gives a completely inverted product.[13] This is a system in which there are no interfering groups.

In an intensive series of investigations on the hydrolysis of alkyl hydrogen sulphates, Burwell *et al.*[14] find almost complete inversion of configuration for the base-hydrolysis of optically active *sec.*-alkyl hydrogen sulphates. The rate of these reactions is little affected by hydroxide ion, is faster than those of the primary alkyl compounds, and is unaffected by steric hindrance. This evidence, and that from olefin formation, suggests that the mechanism is S_N1, although these reactions give little racemisation or rearrangement of the carbon skeleton for the simple *sec.*-alkyl compounds.

Methanolysis of 1-methylheptyl toluene-*p*-sulphonate gives a completely inverted product, at a rate little affected by added methoxide ion, and faster than that of the primary alkyl compounds.[15] This substitution is therefore similar to those of the alkyl hydrogen sulphates.

The only cases of S_N1 solvolyses giving complete racemisation are those in which the carbonium ion is stabilised by strongly electron-releasing groups, or in which the solvent molecules are such poor nucleophilic agents that the life of the carbonium ion is long compared with the rate of attack upon it. This conclusion does not seem to be particularly dependent on the nature of the leaving group.

EXPERIMENTAL

Experimental methods are in general those described in Part I. *sec.*-Butyl alcohol was resolved through the brucine salt of its hydrogen phthalate;[16] a specimen had b. p. 98—99°, $[\alpha]_D^{25}$ +6·86°.

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[10] I. Wilson, unpublished results.

[11] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell & Sons, Ltd., London, 1953.

[12] Lemieux, *Adv. Carbohydrate Chem.*, 1954, **9**, 1; Haynes and Newth, *ibid.*, 1955, **10**, 207.

[13] Rhind-Tutt and Vernon, personal communication.

[14] Burwell *et al.*, *J. Amer. Chem. Soc.*, 1952, **74**, 1462; 1955, **77**, 6441.

[15] Bunton and Deschamps, unpublished results.

[16] Pickard and Kenyon, *J.*, 1911, **99**, 45; Kanter and Hauser, *J. Amer. Chem. Soc.*, 1953, **75**, 1744.

Isotopically enriched *sec.*-butyl alcohol was that used as described in Part I. Its isotopic abundance in oxygen was 9·73 atom % excess.

Kinetics of racemisation were followed in aqueous perchloric and sulphuric acid at 82·0° and 99·8°. At appropriate times the optical activity of the solution was measured at 25°. Oxygen exchange was followed under conditions similar to those of racemisation but at 99·8° only. The first-order rate coefficients for oxygen exchange and racemisation were calculated as described in Part I. Some of the results shown in the Fig. 1 were calculated from data in Part I and the activation energy determined here.

Values of the acidity function were interpolated from published values, the effect of temperature differences and of the *sec.*-butyl alcohol being neglected.[17] The latter effect should not affect our general conclusions, although it may alter the slope of the plots of log k against $-H_0$.

Examples of kinetic runs are given below, k being obtained graphically.

Exchange of isotopically enriched sec.*-butyl alcohol with isotopically normal water at* 99·8°. HClO$_4$] = 4·10 molal. N is the abundance of ^{18}O in atom % excess.

Time (min.)	36	111	174	270	∞
N (water)	0·090	0·208	0·238	0·257	0·291 (calc.)

10^5k = 13·4 (sec.$^{-1}$)

Exchange of isotopically normal sec.*-butyl alcohol with isotopically enriched water* (*abundance* = 0·641 *atom % excess*), *at* 99·8°. [H$_2$SO$_4$] = 1·82 molal.

Time (min.)	100	190	250	305	∞
N (Bu^{s}OH)	0·071	0·126	0·147	0·190	0·619 (calc.)

10^5k = 2·07 (sec.$^{-1}$)

Racemisation of optically active sec.*-butyl alcohol at* 82·0°. [HClO$_4$] = 2·34 molal.

Time (hr.)	0	5·2	13·2	21·1	27·0	36·4	44·2	51·9
$[\alpha]_D^{25}$	1·100°	1·007°	0·815°	0·686°	0·603°	0·470°	0·393°	0·340°

10^6k = 6·30 (sec.$^{-1}$)

Rates of exchange and racemisation in aqueous acid.

Exchange runs.

At 99·8°	HClO$_4$ (m)					H$_2$SO$_4$ (m)	
[Acid]	1·152[a]	2·35[b]	2·94	3·40[b]	4·10[b]	1·82	2·52
10^5k (sec.$^{-1}$)	1·09	3·36	5·74	8·57	13·4	2·07	4·90

[a] From results in Part I. [b] *sec.*-Butyl alcohol initially enriched in ^{18}O.

Racemization runs.

At 99·8°	HClO$_4$ (m)			H$_2$SO$_4$ (m)		HClO$_4$ (m) at 82·0°	
[Acid]	1·096	1·484	2·57	1·085	2·10	1·45	2·34
10^6k (sec.$^{-1}$)	1·93	3·03	8·20	2·15	5·95	0·258	0·630

Formation of Olefin.—The olefin was swept out of solution in a stream of nitrogen, as fast as it was formed, and trapped at −80°. Its amount was determined by addition of a known excess of bromine in carbon tetrachloride and estimation of the residual bromine iodometrically.

The results of these experiments in aqueous perchloric acid at 99·8° are tabulated :

[HClO$_4$] (m)	1·79	1·86	2·04	3·12	3·15	
Time (hr.)	6	7	5·5	4·5	4·5	7
Olefin (%)	3·2	3·8	5·2	13·6	15	23
$\frac{\text{Elimination}}{\text{Exchange}}$ (%)	8·1	8·3	12	21	22	26

(The rates of exchange were interpolated.)

On the assumption that at all acidities exchange *via* substitution gives complete inversion of configuration and exchange *via* elimination and hydration gives a racemic alcohol we calculate, from the known amount of elimination, that for 3m-perchloric acid the ratio k_R/k_E should be

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[17] Bartlett and McCollum, *ibid.*, 1956, **78**, 1441.

1·8 and the actual value is 1·85. With 2m-perchloric acid the observed and calculated ratios are 1·9.

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