957. *Tracer Studies on Alcohols. Part IV.* The Oxygen Exchange and Racemisation of 4-Methoxydiphenylmethanol.*

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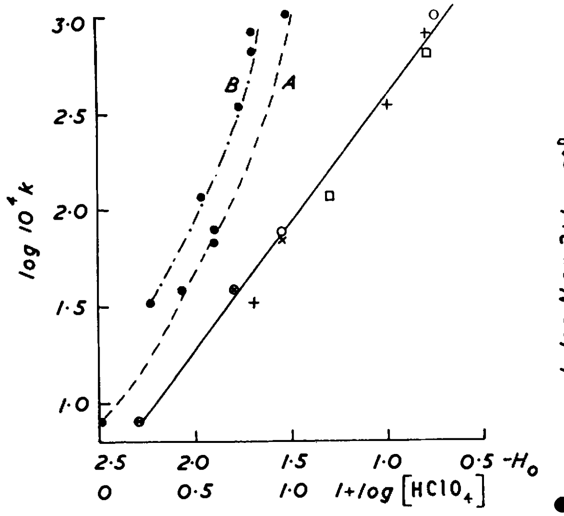
The rates of oxygen exchange and racemisation of 4-methoxydiphenylmethanol in aqueous dioxan containing perchloric acid are very similar. The logarithms of the first-order rate constants are proportional to $-H_0$, with a slope of 1·3. The common slow step of these processes is therefore the heterolysis of the conjugate acid, ROH_2^+, of the alcohol. Because each single step of oxygen exchange gives complete racemisation, the life of the carbonium ion must be sufficiently long for it to become planar before it is captured by a water molecule.

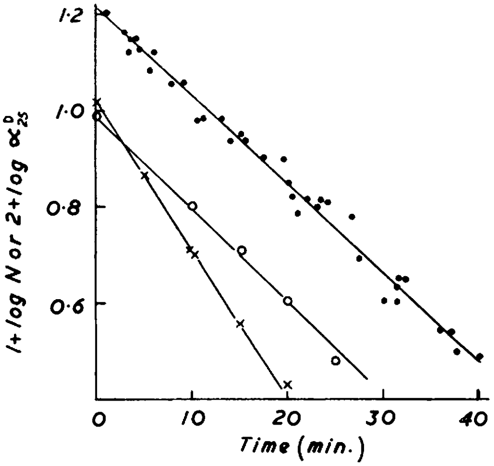
The stereochemical course of oxygen exchange between alcohols and water has been examined for two compounds, *viz.*, *sec.*-butyl alcohol[1] and 1-phenylethanol.[2] The asymmetric carbon atom of *sec.*-butyl alcohol is completely inverted at every exchange of oxygen atoms, but for 1-phenylethanol this inversion is accompanied by considerable racemisation. This increase in racemisation, due to attachment of electron-releasing groups to the reaction centre, in a unimolecular substitution is well known.[3]

Fig. 1. *Relation between rates and acidity.*



Dioxan–water (60 : 40 v/v): ○ Exchange, × racemisation.
Dioxan–water (40 : 60 v/v): + Exchange, □ racemisation.
● log k as a function of log $[HClO_4]$ in dioxan–water: *A* 60 : 40 v/v, *B* 40 : 60 v/v.

Fig. 2. *Racemisation and oxygen exchange.*



● Racemisation in dioxan–water (60 : 40 v/v); $[HClO_4] = 0·394$.
○ Exchange in dioxan–water (60 : 40 v/v); $[HClO_4] = 0·394$.
× Exchange in dioxan–water (40 : 60 v/v); $[HClO_4] = 0·350$.

We have now investigated the acid-catalysed oxygen exchange between water and 4-methoxydiphenylmethanol, and the concurrent racemisation of the alcohol. The kinetics of exchange and racemisation were followed in aqueous dioxan containing perchloric acid, because the alcohol is only slightly soluble in water. The acidity function,

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* Part III, *J.*, 1958, 403.

[1] Bunton, Konasiewicz, and Llewellyn, *J.*, 1955, 604; Bunton and Llewellyn, *J.*, 1957, 3402.

[2] Grunwald, Heller, and Klein, *J.*, 1957, 2604.

[3] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons, Ltd., London, 1953, p. 387.

H_0, had been measured for perchloric acid in aqueous dioxan.[4] For a given composition of the medium the rates of exchange and racemisation agreed within experimental error (Fig. 1, Table 1), and the rate dependence was upon Hammett rather than stoicheiometric acidity, suggesting that the transition state does not contain a water molecule from the solvent.[5a, b]

TABLE 1. *Rates of oxygen exchange and racemisation in aqueous dioxan.*

Temp. 25°. *R* indicates racemisation.

	Dioxan–water (60 : 40 v/v)				Dioxan–water (40 : 60 v/v)			
$[HClO_4]$M	0·101	0·265	0·394	0·936	0·182	0·350	0·530	0·630
H_0	*ca.* 2·3	1·8	1·55	0·75	*ca.* 1·7	1·3	1·0	0·80
10^4k (sec.$^{-1}$)...	0·8 $0·82^R$	3·8 $3·8^R$	7·5 $7·0^R$	104	$3·2^R$	12	35^R	67 83^R

DISCUSSION

Steric Course of Oxygen Exchange.—Complete racemisation with every substitution is the result expected for an S_N1 reaction which generates a long-lived carbonium ion.[3] The incoming reagent does not begin to form a covalent bond with the carbonium ion until the expelled group is sufficiently far away to exert no " shielding " effect. Nucleophilic attacks upon the carbonium ion from either the " front " or the " back " are then equally probable. In many of the systems studied, complete racemisation with substitution is not found for reactions with water or alcohols, although hydrolyses of carboxylic esters [6, 7a, b] provide examples of carbonium-ion intermediates which give racemic products.

The steric course of the oxygen exchange between 1-phenylethanol and water is very similar to that for the hydrolysis or alcoholysis of the optically active chloride.[2] It has been suggested that all these unimolecular substitutions have a common reaction path, in which the first step is formation of an " intimate " ion-pair of finite life, which may react with the solvent or reagent, or dissociate further to give a " solvent-separated " ion-pair. This in turn may react with the solvent, or reagent, or may dissociate further to give a free carbonium ion. Attack upon this will give a completely racemic product.

The original theory to explain the steric course of S_N1 reactions [3] envisaged a gradual extension of the breaking bond, with the reagent intervening from the " back " in the course of bond extension, rather than postulating a series of stable, or metastable, intermediates of structures between the initial reactant R^-X and the carbonium ion R^+. Our observations on the steric course of the oxygen exchange of 4-methoxydiphenylmethanol do not differentiate between these possibilities; it is sufficient to suppose that the carbonium ion is completely free before the solvent molecule attacks. However, experiments on reactions of carboxylic esters of 4-methoxydiphenylmethanol [7a, b] and 2 : 4-dimethylhexan-4-ol [8] suggest that ion-pair intermediates are playing no essential part in the kinetics, or the steric course, of hydrolyses of these particular compounds in water or mixed aqueous–organic solvents.

Kinetic Form of Acid Catalysis.—A useful mechanistic test for acid-catalysed reactions is provided by the Zucker–Hammett hypothesis,[5a, 6] which suggested that the rate of acid-catalysed unimolecular hydrolysis, *A*-1, should be proportional to the acidity function $h_0(= a_{H^+} . f_B/f_{HB^+}$, where B is a neutral base).

It is almost certain that oxygen exchange and racemisation of 4-methoxydiphenylmethanol is unimolecular. This system should give a correlation between rate constant and h_0. The logarithms of the rate constants for exchange and racemisation, in both solvents, are plotted against both the logarithm of $[HClO_4]$ and $-H_0$. The plots against concentration are curved and different for the two solvents, but against $-H_0$ they give

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[4] Bunton, Ley, Rhind-Tutt, and Vernon, *J.*, 1957, 2327.

[5] (*a*) Zucker and Hammett, *J. Amer. Chem. Soc.*, 1939, **61**, 2791; (*b*) Long and Paul, *Chem. Rev.*, 1957, **57**, 1, 935.

[6] Davies and Kenyon, *Quart. Rev.*, 1955, **9**, 203.

[7] (*a*) Bourns, Bunton, and Llewellyn, *Proc.*, 1957, 120; (*b*) Bunton and Hadwick, *J.*, 1957, 3043.

[8] Experiments quoted by Streitweiser, *Chem. Rev.*, 1956, **56**, 571.

the same straight line for both solvents. There is another acidity function, J_0 or C_0,[5b] which applies to equilibrium formation of carbonium ions from neutral molecules, but for unimolecular acid-catalysed reactions in which a carbonium ion is formed slowly, and converted rapidly into products, the correlation between rate and acidity is usually with the Hammett function h_0 (cf. ref. 9). In some cases this may be because, in the acidity ranges studied, H_0 and J_0 do not diverge sufficiently, but it seems that in many cases the energy maximum in the reaction path is reached for rather small bond extensions,[10] and that therefore the appropriate acidity function is that applying to protonation of a neutral base. Where the carbonium ion is in equilibrium with the reactants the rate correlates with $-\text{antilog}\ J_0$.[11]

The H_0 scale gives the relative protonating powers of various acidic solutions, and from the Zucker–Hammett hypothesis, the rate of an *A*-1 reaction should depend only upon H_0, and not upon the particular acid or solvent.[5a, b] In fact the correlation between rate and Hammett acidity for *A*-1 reactions in different solvents is sometimes bad, even though the correlation for a particular solvent may be good, *e.g.*, the rate of hydrolysis of sucrose correlates well with h_0 for changes of acidity in a given solvent, but badly if comparison is made between different solvents.[4] The relation between Hammett acidity and the first-order rate constant, *k*, for an *A*-1 reaction of a neutral compound S, is:

$$k \propto a_{\mathrm{H}^+} \,.\, f_{\mathrm{S}}/f_{\mathrm{H^+S}} \propto h_0 \ (\text{when } f_{\mathrm{S}}/f_{\mathrm{H^+S}} = f_{\mathrm{B}}/f_{\mathrm{H^+B}})$$

This equality of the ratios of activity coefficients may hold for aqueous solutions of varying concentration, but it is more likely to fail with drastic changes in the medium, by addition of a neutral salt, or an organic solvent. A breakdown of this relationship is most likely when the structures of the indicator base, B, and the reactant, S, are very different,[12] as for aromatic amines and sucrose. It should be less likely to fail for reactions of 4-methoxydiphenylmethanol, because the geometry of this compound is not very different from those of aromatic amines, and here the correlation between rate constant and h_0 is good, for changes in medium as well as acid concentration. This is shown in Fig. 1. The slope is greater than unity, but this is quite common for reactants with molecular sizes similar to that of 4-methoxydiphenylmethanol. It is very similar to that observed for the hydrolysis of 4-methoxydiphenylmethyl acetate in aqueous dioxan by mechanism $\mathrm{A_{AL}1}$.[7b]

It is, however, possible that this high slope comes about because the appropriate acidity function for kinetic comparison is J_0. This possibility has been considered for the racemisation and oxygen exchange of 1-phenylethanol.[2] Unfortunately we have no values for J_0 in acid aqueous dioxan, although this acidity scale should increase more rapidly with increasing acid concentration than does H_0, and the values of H_0 and J_0 would not be expected to coincide in the different aqueous dioxan solvents, with their different water contents. The points of Fig. 1 show some divergence from a straight line, but this is probably because of experimental uncertainties in H_0, which are largest at low acidities, and in the rate constants at high acidities where the half-life is *ca.* 1 min. This is particularly serious for experiments in the more aqueous solvent where low solubility restricts the precision of the kinetic measurements.

EXPERIMENTAL

Materials.—The solvent for most of the experiments was aqueous dioxan made up by mixing appropriate volumes of purified dioxan and water.

Acid solutions were made up by mixing 72% " AnalaR " perchloric acid with the aqueous

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[9] Deno and Perizollo, *J. Org. Chem.*, 1957, **22**, 836.
[10] Bateman, Church, Hughes, Ingold, and Taher, *J.*, 1940, 979.
[11] Bethell and Gold, *J.*, 1958, 1905.
[12] Deno and Perizollo, *J. Amer. Chem. Soc.*, 1957, **79**, 1345.

dioxan solvent, and adding purified dioxan sufficient to restore the ratio of dioxan to water.[4] The acid concentration was checked by acid–base titration at the beginning or end of the run.

4-Methoxydiphenylmethanol, prepared and resolved by the original procedures,[13] was supplied by Professor A. N. Bourns; it had $[\alpha]_D^{25} = -7{\cdot}8°$ (in CS_2). Isotopically labelled alcohol enriched in the hydroxylic oxygen atom, and prepared by hydrolysis of the chloride in ^{18}O-containing water, was similarly obtained. It contained 0·98 atom % excess of ^{18}O.

The isotopic abundance of the hydroxylic oxygen atom was determined by a method devised with Professor A. N. Bourns. A known amount of the alcohol was heated in a sealed tube with a known amount of carbon dioxide for 24 hr. at 250°. One mol. is eliminated from 2 mol. of the alcohol, and this water is allowed to equilibriate its oxygen atom with those of the carbon dioxide. The total isotopic abundance, N_t, of the carbon dioxide is given by $N_t = 100/(2KR + 1)$ atom % (where R is the ratio of masses 44 : 46, and $K = 1{\cdot}038$). The excess abundance is then calculated by subtracting the abundance of isotopically normal carbon dioxide. The excess of isotopic abundance of the water (and therefore of the alcohol) is then calculated from the excess abundance of the carbon dioxide and the known amounts of alcohol and carbon dioxide present initially. This neglects any isotopic fractionation in the thermal dehydration of the alcohol.

Kinetics of Oxygen Exchange.—In dioxan–water (60 : 40 v/v) samples of the isotopically enriched alcohol (*ca.* 0·1 g.) were dissolved by shaking them in 5 c.c. of the acid solvent, which was at the temperature of the thermostat. After the appropriate reaction time sufficient 5% sodium hydroxide was added to neutralise the acid and so stop the exchange. The alcohol was extracted with ether, the ether evaporated under reduced pressure, and the alcohol dried in a desiccator. The alcohol was finally purified by vacuum sublimation at 75—80°, and its purity checked by m. p. The recovery of alcohol was between 80 and 95%. The isolation procedure does not change the isotopic enrichment, or the rotation of the alcohol.

The time of dissolution was sufficiently short for this procedure to be used for most of the exchange experiments in this solvent. However, the exchange in 0·936M-perchloric acid is too fast for this procedure to be used, and here samples of the alcohol (0·1 g.) were first dissolved in the purified dioxan. This solution and the aqueous acid were brought to thermostat temperature and then mixed. The reaction was stopped by addition of alkali and the alcohol isolated as described.

Oxygen Exchange in Dioxan–Water (40 : 60 *v/v*).—The procedure was that described above for the run in dioxan–water (60 : 40 v/v) and 0·936M-perchloric acid, except that samples of *ca.* 0·1 g. in 20 c.c. of solvent were used.

This procedure could not be used for the fastest run in this solvent (with 0·63N-perchloric acid) because here the time of mixing the solutions was becoming appreciable relative to the half-life, and this time of mixing could differ for the various points of the run. Therefore the isotopically enriched 4-methoxydiphenylmethanol was dissolved in 40·0 c.c. of purified dioxan and this and 63·0 c.c. of 1·04M-aqueous perchloric acid were brought to thermostat temperature. The two solutions were mixed rapidly, giving a solution of 0·63M-perchloric acid (checked by titration). At appropriate times aliquot portions were removed, and the acid was neutralised and the alcohol extracted and purified as already described.

Miscellaneous Exchange Experiments in Water.—Optically active 4-methoxydiphenylmethanol is racemised in boiling water, in which it is slightly soluble.[13] This racemisation may be a spontaneous transformation of the neutral alcohol molecule, or it may be catalysed by the protons generated by autoprotolysis of water, or by the small amounts of carbon dioxide present. The oxygen exchange under these conditions was therefore studied.

Isotopically labelled alcohol (0·25 g.) was added to boiled and thoroughly degassed distilled water (500 c.c.), in a flask with its ground-glass stopper sealed with a high-vacuum Silicone grease. The flask was heated to 100°, and most, but not all, of the alcohol dissolved with thorough shaking. On cooling, the alcohol separated and was extracted with ether and purified as above. After being heated for 42 hr. the alcohol had exchanged 57% of its hydroxylic oxygen atoms with the water; in a second experiment under similar conditions there was 19% of exchange after 10 hours' heating.

Similar experiments were carried out with sodium hydroxide added to the solution. With 0·1M-sodium hydroxide, and the solution not degassed, there was <2% of exchange after heating for 48 hr. at 100°. In a second experiment with M-sodium hydroxide, 10 hours' heating

[13] Balfe, Doughty, Kenyon, and Poplett, *J.*, 1942, 605.

at 100° gave <4% of exchange. It seems that the addition of hydroxide suppresses an acid-catalysed oxygen exchange, and it is therefore possible that the racemisation observed by Kenyon and his co-workers was also acid-catalysed.

Kinetics of Racemisation.—In dioxan-water (60 : 40 *v*/*v*). The solubility of the alcohol in this solvent is sufficient for the run to be followed directly in a 2 dm. jacketed polarimeter tube kept at 25·0° by circulating water. The solutions were made up as for the exchange runs. For the run with 0·101M-perchloric acid it was possible for 8—12 readings of the rotation to be taken for each point.

The rate of racemisation with [$HClO_4$] > 0·1M was such that it was difficult to take a large number of points at any given time. Therefore a large number of individual readings of the rotation were taken; the logarithms of these observed rotations are plotted against time for one run in Fig. 2.

In dioxan-water (40 : 60 *v*/*v*). The low solubility of the alcohol in this solvent made it necessary to isolate and purify the alcohol, for each individual point of the run, by the procedure described for the exchange experiments in this solvent. The rotations of these isolated samples were then determined in carbon disulphide, using a 2 dm. micropolarimeter tube holding about 3 c.c. of solution.

The first-order rate constants were calculated graphically, for exchange by plotting the logarithm of the excess isotopic abundance, *N*, against time, and for racemisation by plotting the logarithm of the rotation (or the specific rotation where appropriate) against time.

Examples of the results obtained are shown in the Table 2 and in Fig. 2.

TABLE 2. *Racemisation in dioxan-water* (40 : 60 *v*/*v*) *at* 25°.

[$HClO_4$] = 0·530M. 0·04—0·09 g. of material was isolated for each point of run. Specific rotation measured in CS_2.

Time (min.)	0	1·0	2·0	3·0 *		6·0
$[\alpha]_D^{25}$	−7·3	−5·8	$-4{\cdot}8_5$	$-4{\cdot}7_5$	−4·3	−2·2

* Separate samples.

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