

*Oxygen Exchange and the Walden Inversion in sec.-Butyl Alcohol.*

By C. A. BUNTON, (MRS.) ALICJA KONASIEWICZ, and D. R. LLEWELLYN.

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The rates of oxygen exchange and racemization of an optically active alcohol have been measured for *sec.*-butyl alcohol in aqueous perchloric acid, of up to 1M-concentration. In the range of acid studied the rates of both oxygen exchange and racemization follow the Hammett acidity function,  $h_0$ , rather than the stoichiometric acid concentration. Within the experimental error the overall rate of racemization, at any given acidity, is twice that of oxygen exchange, indicating that every oxygen exchange gives complete inversion of configuration. These results are interpreted in terms of a rate-determining heterolysis of the oxonium ion ( $\text{ROH}_2^+$ ), in which the incoming water molecule is prevented from entering on the same side as the expelled group and which therefore gives inversion of configuration.

A COMPARISON of the rates of isotopic halide-ion exchange and racemization of some secondary alkyl halides (Hughes, *Trans. Faraday Soc.*, 1938, **34**, 202) proved to be a very powerful tool in the study of the Walden inversion and led to an understanding of this phenomenon in terms of current theories of nucleophilic substitution. In this system the molecularity of the exchange and racemization processes was directly determined from the kinetic form. However, the racemization described in the present work was followed under solvolytic conditions, where the simpler kinetic tests of mechanism are not available.

It has been pointed out by Hammett ("Physical Organic Chemistry," McGraw-Hill, 1940, p. 273—277) that, if the transition state of an acid-catalyzed solvolytic reaction contains the water molecule, the overall rate of that reaction should be proportional to the hydrogen-ion concentration  $\text{H}_3\text{O}^+$ , but that where the water molecule does not intervene in the rate-determining step of the reaction the rate should be proportional to the acidity function  $h_0$ , defined as  $h_0 = a_{\text{H}^+}f_{\text{B}}/f_{\text{BH}^+}$ , where B is a neutral base. This test of mechanism gives reasonable results in cases in which it has been applied, *viz.*, in the hydrolyses of sucrose and cyanamide and the enolization of *m*-nitroacetophenone (Hammett, *op. cit.*), and in the acid-catalyzed hydrolyses of  $\beta$ - and  $\gamma$ -lactones which have been studied by Long and his co-workers (*J. Amer. Chem. Soc.*, 1950, **72**, 3267; *J. Phys. Chem.*, 1951, **55**, 829).

In the present work the rates of racemization were followed in aqueous perchloric acid up to *ca.* 1M at 100.8°. Typical examples of the kinetic form for individual runs, together with those of oxygen exchange, are tabulated, and the dependence of racemization rate on perchloric acid concentration is shown in Fig. 1, which also gives the corresponding rates for oxygen exchange.

The kinetics of oxygen exchange were followed by two general methods. In the first, *sec.*-butyl alcohol enriched in  $^{18}\text{O}$  was prepared by exchange of ethyl methyl ketone with  $\text{H}_2^{18}\text{O}$ , and reduction of the ketone with lithium aluminium hydride. In any given exchange run the increase in the  $^{18}\text{O}$  content of the water was followed with time. In the second method the increase of the isotopic abundance of initially isotopically normal *sec.*-butyl alcohol in enriched water was followed. The alcohol was isolated as an azeotrope with toluene, and its  $^{18}\text{O}$  content determined by pyrolysis to carbon monoxide, and mass-spectrometric analysis of this gas. Results of typical runs are shown in tabulated form in the Experimental section, and the dependence of exchange rate on perchloric acid concentration is shown in Fig. 1.

Two salient points emerge from these results. First, neither racemization nor exchange rates follow the hydrogen-ion concentration above the range where it diverges from the acidity function, but both follow the acidity function (Fig. 2). Secondly, the rate of racemization is always twice the rate of oxygen exchange, within the experimental error of the measurement. This latter result implies that every act of substitution gives complete inversion of configuration:  $(+)\text{-ROH} + \text{H}_2^{18}\text{O} \longrightarrow (-)\text{-R}^{18}\text{OH} + \text{H}_2\text{O}$ .

The form of the acid catalysis indicates an  $S_N1$  reaction [see equation (2)] and not an  $S_N2$  reaction because the dependence of reaction rate on the acidity function proves that a water molecule does not enter stoichiometrically into the kinetic expression for the velocity of the substitution reaction. In other words, the bimolecular sequence



can be excluded. In the  $S_N1$  reaction the rate-determining step is the heterolysis of the oxonium ion, in which the energy maximum is reached for such a short extension of C-O

FIG. 1.

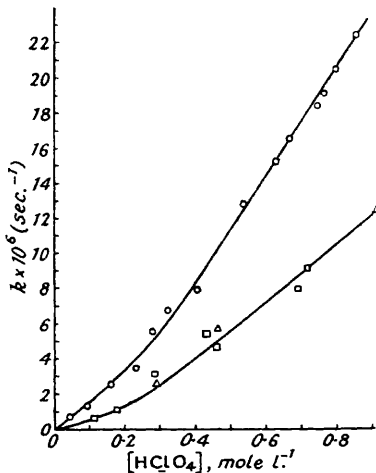
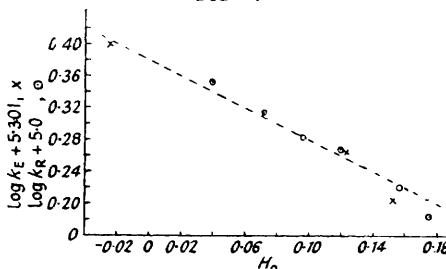
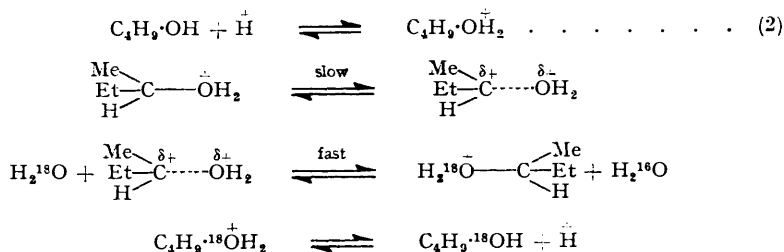


FIG. 2.



bond that the incipiently formed carbonium ion never becomes completely free from the influence of the expelled water molecule, which exerts a shielding effect such that the incoming water molecule always enters from the opposite side.



Similar cases of reactions which are of the  $S_N1$  type, since the addition of a reagent ( $OH^-$  or  $OR^-$ ) of a greater nucleophilic power than that of the solvent molecules does not affect the rate, but which give almost complete inversion of configuration are (i) the hydrolysis of *sec.*-butyl hydrogen sulphate, which is independent of pH (Burwell and Holmquist, *J. Amer. Chem. Soc.*, 1948, **70**, 878) and (ii) the methanolysis of 1-methyl-*n*-heptyl toluene-*p*-sulphonate, where the rate is not highly dependent on methoxide-ion concentration (unpublished results, Bunton and Deschamps). The general phenomenon of steric shielding has recently been discussed by Waters and de la Mare (*Ann. Reports*, 1953, **50**, 135). In the particular case now discussed there will be a contributing effect in that the proton co-ordinated to the oxygen atom will decrease the local activity of the water molecules in its vicinity and hence impose a restraint on attack of the substituting agent from the direction giving retention of configuration.

## EXPERIMENTAL

*Resolution.*—*sec.*-Butyl alcohol was resolved *via* the brucine salt of its hydrogen phthalate by the general method of Pickard and Kenyon (*J.*, 1911, 99, 45). The alcohol obtained from the hydrolysis of the resolved hydrogen phthalate had, after fractional distillation, b. p. 98–99°,  $n_D^{25}$  1.3943,  $[\alpha]_D^{18} + 8.33^\circ$ .

*Kinetics of Racemization.*—All runs were carried out in aqueous perchloric acid at 100.8°. At appropriate times the optical activity of portions of the solution was determined at room temperature. The racemization at room temperature was sufficiently slow to allow this procedure to be used.

The acid concentrations quoted are corrected for expansion of the solvent.

*Oxygen Exchange.*—*Preparation of enriched sec.-butyl alcohol.* Ethyl methyl ketone (20 g.) was refluxed with *ca.* 30 c.c. of *ca.* 12%  $H_2^{18}O$  containing 1 drop of concentrated sulphuric acid. The enriched ketone was fractionally distilled from the solution and was reduced with lithium aluminium hydride in dry ether. The enriched alcohol was fractionally distilled; the first fraction (*ca.* 5 g.) had b. p. 98–98.5°, the second (*ca.* 10 g.) had b. p. 99° and an isotope abundance of oxygen = 9.73 atoms % excess. The latter sample was used for the exchange runs.

In the exchange runs, portions of *ca.* 200 mg. of the reacting solution were sealed in separate tubes. After appropriate heating, the solvent was distilled off *in vacuo*, and the isotopic abundance determined by equilibration with carbon dioxide and mass-spectrometric analysis of that gas.

*Exchange with sec.-butyl alcohol not originally enriched in  $^{18}O$ .* The alcohol was dissolved in aqueous perchloric acid in enriched water (*ca.* 1% excess  $H_2^{18}O$ ). Portions of *ca.* 20 c.c. were heated in the thermostat, and the alcohol was extracted with toluene from the solution saturated with sodium sulphate. After being dried over several portions of sodium sulphate the *sec.*-butyl alcohol-toluene azeotrope was fractionally distilled, and the  $^{18}O$  abundance of its alcohol determined by pyrolysis to carbon monoxide over hot gauze, or over heated carbon *in vacuo*. The mass-spectrometric analysis was carried out on the carbon monoxide gas, samples being checked for the presence of argon to preclude possibility of atmospheric contamination.

All the rate coefficients quoted were determined from the equations

$$\begin{aligned} \text{for racemization} & \quad \log \alpha_0 - \log \alpha = kt/2.3 \\ \text{for oxygen exchange} & \quad \log [\beta_\infty / (\beta_\infty - \beta)] = kt/2.3 \end{aligned}$$

where  $\beta_\infty$  and  $\beta$  are the isotopic abundances at times  $\infty$  and  $t$ , respectively, and  $t$  is in sec.

The acidity functions used were interpolated from the values quoted by Hammett *et al.* (*J. Amer. Chem. Soc.*, 1934, 56, 827). No allowance is made for any variation with temperature, and in the use of this function as a criterion of mechanism we assume the activity of water to be constant in the acidity range considered.

Examples of specimen runs, and the rate constants, are tabulated below, with the concentrations of perchloric acid, and the interpolated values of  $H_0$ , where  $H_0 = -\log_{10} h_0$ . In the racemization runs 1 c.c. of the alcohol was added to 10 c.c. of the perchloric acid in each case. For the exchange runs the concentration of alcohol was varied, and it is therefore tabulated below:

*Typical Runs.—Polarimetric run; 100.8°.*

Run No. 2R.  $[HClO_4] = 0.0815M$ ,  $NaClO_4 = 0.217M$ .

Time (hr.)	0	21.25	43.1	65.75	112.6	138.2	158	181.4
$[\alpha]_D^{18}$	0.294°	0.267°	0.247°	0.220°	0.181°	0.158°	0.143°	0.125°

$$10^4 k_1 = 1.28 \text{ sec.}^{-1} \text{ (obtained graphically).}$$

*Exchange runs; 100.8°.*

Run No. 19E.  $[HClO_4] = 0.286M$ . Isotopically normal *sec.*-butyl alcohol exchanged with  $H_2^{18}O$  (0.931 atom % excess). Isotopic abundance of alcohol for complete exchange ( $\beta_\infty$ ) = 0.916 atom % excess.

Time (hr.)	7.9	10.25	15.2	22.33	41.2
$\beta$ (atom % excess)	0.077	0.105	0.117	0.183	0.267

$$10^4 k_1 = 2.62 \text{ sec.}^{-1} \text{ (obtained graphically).}$$

Run No. 10E.  $[\text{HClO}_4] = 0.690\text{M}$ . Enriched *sec.*-butyl alcohol ( $\beta = 9.73$  atom % excess) exchanged with normal water. Isotopic abundance of water for complete exchange ( $\beta_\infty$ ): Calc., 0.251 atom % excess; found, 0.253, 0.241, 0.256 atom % excess.

Time (hr.)	4.5	6.5	8.5	10.5	16.5	23.5	33
$\beta$ (atom %) excess	0.0026	0.039	0.053	0.074	0.094	0.122	0.150

$10^6 k_1 = 8.00 \text{ sec.}^{-1}$  (obtained graphically).

*Polarimetric runs:*

Run No.	1R	2R *	3R	4R	5R	6R	7R
$[\text{HClO}_4]$	0.0408	0.0815	0.164	0.229	0.276	0.319	0.405
$H_0$	—	—	—	—	—	—	—
$10^6 k_1$ (sec. <sup>-1</sup> )	0.78	1.28	2.53	3.50	5.60	6.80	7.97
Run No.	8R	9R	10R	11R	12R	13R	14R
$[\text{HClO}_4]$	0.536	0.628	0.668	0.747	0.769	0.801	0.860
$H_0$	—	0.175	0.157	0.120	0.107	0.072	0.040
$10^6 k_1$ (sec. <sup>-1</sup> )	12.8	15.3	16.6	18.5	19.2	20.6	22.5

\* 0.217M- $\text{NaClO}_4$  was added to this solution.

*Exchange runs:*

Run No.	4E	5E	8E	19E *	17E	16E	18E *	10E	11E	12E *
$[\text{HClO}_4]$	0.111	0.176	0.284	0.286	0.432	0.458	0.461	0.690	0.717	0.910
$H_0$	—	—	—	—	—	—	—	0.152	0.123	-0.025
$10^6 k_1$ (sec. <sup>-1</sup> )	0.67	1.08	3.18	2.62	5.41	4.78	5.94	8.00	9.15	12.5
$[\text{Bu}^o\text{OH}]$	1.43	1.40	1.59	1.20	1.06	1.20	2.09	1.16	0.79	0.80

\* Runs 12E, 18E, and 19E were carried out with alcohol not originally enriched in  $^{18}\text{O}$ .

*Formation of Olefin.*—Experiments were carried out to decide whether the elimination and subsequent hydration of a butene played any part in the racemizations and exchanges observed. Solutions were aspirated with nitrogen to remove any olefin as fast as it might be formed. The aspirated gases passed through a reflux condenser to a trap at  $-80^\circ$ . After a period of time any olefin collected was determined by the addition of excess of bromine, and the estimation of bromine used by iodometry. Two experiments were carried out; in the first the alcohol was heated at  $100.8^\circ$  in 0.4M-aqueous perchloric acid for 6 hr., and in the second with 0.617M-perchloric acid for 6 hr. In both cases the amount of olefin elimination was less than 0.5%.

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WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,  
UNIVERSITY COLLEGE, LONDON.

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