672. *Tracer Studies in Ester Hydrolysis. Part VIII.* The Oxygen Exchange between Water and Carboxylic Acids.*

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The rate of exchange of oxygen atoms between water and benzoic acid, in aqueous sulphuric and perchloric acid, is proportional to the concentration of hydrogen ions. The entropy of activation is *ca.* -30 e.u. The rate of exchange between mesitoic acid and water, in aqueous dioxan and catalysed by perchloric acid, is proportional to Hammett's acidity function, h_0, and the entropy of activation is *ca.* $+9$ e.u. The results suggest that the mechanism of exchange of benzoic acid is bimolecular, and that of mesitoic acid unimolecular.

THE acid-catalysed oxygen exchange between water and benzoic acid is analogous to carboxyl esterification and hydrolysis.[1] Recently it was shown that the rates of oxygen exchange of substituted benzoic acids were little affected by substituents in the *ortho*- and *para*-positions, but that di-*ortho*-substituents decreased the rate.[2] This suggested a bimolecular mechanism for oxygen exchange. The rates of hydrolyses of several alkyl benzoates [3] were proportional to the acid concentration. In contrast, the rate of hydrolysis of methyl mesitoate was dependent upon the Hammett acidity function, h_0.[3] These results suggest that the first group of reactions have the bimolecular, *A*-2, mechanism, whereas the hydrolysis of methyl mesitoate has the unimolecular, *A*-1, mechanism.[4] This is in agreement with other evidence.[5,6]

We have extended the experiments on the oxygen exchange of carboxylic acids to concentrations of mineral acids sufficiently high for application of the Zucker–Hammett hypothesis.[4] We have also measured the entropies of activation, because it has been shown that these are usually negative for bimolecular, *A*-2, reactions, and near to zero or positive, for unimolecular *A*-1 reactions.[7] The oxygen exchange of benzoic acid was followed with sulphuric and perchloric acid in water. Mesitoic acid is only slightly soluble in water, so dioxan–water (60 : 40 v/v) was chosen as solvent. The values of the Hammett acidity function for perchloric acid in this solvent are known.[8]

The first-order rate coefficients for oxygen exchange (k_1) are given in the Table, which also illustrates the variation of exchange rates with the concentrations of catalysing acids.

Benzoic Acid.—The rate of oxygen exchange in water is directly proportional to the

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* Part VII, *J.*, 1958, 3718.

[1] Herbert and Lauder, *Trans. Faraday Soc.*, 1938, **34**, 1219; Roberts and Urey, *J. Amer. Chem. Soc.*, 1939, **61**, 2580.

[2] Bender, Stone, and Dewey, *J. Amer. Chem. Soc.*, 1956, **78**, 319.

[3] Chmiel and Long, *J. Amer. Chem. Soc.*, 1956, **78**, 3326.

[4] Zucker and Hammett, *J. Amer. Chem. Soc.*, 1939, **61**, 2791; Long and Paul, *Chem. Reviews*, 1957, **57**, 935.

[5] Treffers and Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 1708.

[6] Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686; Newman, *J. Amer. Chem. Soc.*, 1941, **63**, 2431.

[7] Taft, *J. Amer. Chem. Soc.*, 1952, **74**, 5372; Long, Pritchard, and Stafford, *ibid.*, 1957, **79**, 2362.

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

concentration of sulphuric acid. The rate is slightly less for the same molar concentration of perchloric acid [Table, section (i)]. The sum of log $k_1 + H_0$ is not constant, but decreases steadily with increasing concentration of acid. This good correlation between rate coefficient and concentration of acid is interesting because the rates of *A*-2 reactions are not usually exactly proportional to concentration of acid.[4] The rates of hydrolyses of primary alkyl benzoates do, however, show this proportionality.[3] This evidence for a bimolecular, A-2, mechanism is supported by the value of the entropy of activation, $\Delta S^* = -30$ e.u., which is in the range usually observed for *A*-2 reactions. The activation energy, 16 kcal. mole^{-1}, is much lower than that for the oxygen exchange of mesitoic acid, but is in the range typical of ester hydrolysis by mechanism $A_{\text{Ac}}2$.

The oxygen exchange between carboxylic acids and water can be regarded as an esterification by water, and the rate of exchange of benzoic acid is similar to its rate of esterification, and to the rates of acid hydrolyses of primary alkyl benzoates (cf. ref. 1). Our results confirm this; the second-order rate constant for the hydrolysis of methyl benzoate in aqueous perchloric acid at 90° is $1·9 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$, and at the same temperature and acidity the estimated value for the oxygen exchange is 9×10^{-4} l. mole^{-1} sec.$^{-1}$.

Mesitoic Acid.—The rate of oxygen exchange of mesitoic acid in aqueous dioxan is not proportional to the concentration of perchloric acid [Table, section (ii)]. The sum of log $k_1 + H_0$ is nearly constant, showing that the rate is proportional to Hammett's acidity function, h_0, and a plot of log k_1 against $-H_0$ has a slope of 0·97. This is the result expected for an *A*-1 mechanism. The value of the entropy of activation, $\Delta S^* = +9$ e.u., supports this conclusion, and the value of the energy of activation, 33 kcal. mole^{-1}, is much larger than that for the bimolecular oxygen exchange between benzoic acid and water (see above).

Oxygen exchange between carboxylic acids and water.

(i) Benzoic acid. In water at 73·0° with sulphuric acid unless otherwise specified.

[Acid] (M)	0·41	1·10	1·55 [c]	1·96	3·00 [c]	0·99 [a]	1·38 [a]
$10^4 k_1$ (sec.$^{-1}$)	1·36	3·64	4·0	6·66	10	2·74	4·23
$10^4 k_1/[\text{H}^+]$	3·0	3·3	2·6	3·4	3·3	2·8	3·1
log $k + H_0 + 3$	0·45	0·40	0·22	0·19	−0·07	0·39	0·33
[Acid] (M)	0·05 [b]	0·145 [b]					
$10^4 k_1$ (sec.$^{-1}$)	0·92	2·68					
$10^4 k_1/[\text{H}^+]$	18·4	18·5					

(ii) Mesitoic acid. In dioxan–water (60 : 40 v/v) with perchloric acid at 100° unless otherwise specified.

[HClO_4] (M)	0·43	1·20	2·09	2·93	3·78	3·00 [d]
$10^7 k_1$ (sec.$^{-1}$)	5·94	14·7	104	584	3800	27·4
$10^6 k_1/[\text{H}^+]$	1·38	1·22	5·00	19·9	101	
log $k_1 + H_0 + 7$	2·1	1·7	1·6	1·7	1·8	

[a] Perchloric acid. [b] At 101°. [c] Two point-runs. [d] At 73°.

The acid hydrolysis of methyl mesitoate is an *A*-1 reaction,[3] almost certainly with acyl–oxygen fission. Direct comparison between its rate and that of the oxygen exchange of mesitoic acid cannot be made, because the solvents are different. Comparison can be made between rates at the same values of Hammett acidity, H_0. For the oxygen exchange of mesitoic acid at $H_0 = -1·78$, at 90°, the estimated value of k_1 is 12×10^{-5} sec.$^{-1}$, and is very similar to the value of $3·1 \times 10^{-5}$ sec.$^{-1}$, for the hydrolysis of methyl mesitoate, catalysed by perchloric acid, at that temperature and Hammett acidity, but in water the agreement is even better if comparison is made between the rates of exchange in aqueous dioxan containing perchloric acid, and those of ester hydrolysis in aqueous sulphuric acid. It is known that the rates of *A*-1 reactions often differ for the same values of $-H_0$ in different solvents,[8,9] so this close agreement between oxygen exchange and ester hydrolysis

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[9] Pritchard and Long, *J. Amer. Chem. Soc.*, 1958, **80**, 4162; Satchell, *J.*, 1957, 3524.

may be partly fortuitous. The analogy between esterification and oxygen exchange can therefore be extended to the unimolecular mechanism with acyl–oxygen fission.

The two mechanisms of oxygen exchange can be written as:

$$R\cdot CO_2H + H^+ \rightleftharpoons R\cdot CO_2{}^+H, \quad \text{(fast)}$$

A-2, *e.g.*, benzoic acid:

$$R\cdot CO_2{}^+H + H_2{}^{18}O \rightleftharpoons R\cdot C^{18}O\cdot O^+H_2 + H_2O$$

A-1, *e.g.*, mesitoic acid:

$$R\cdot CO_2{}^+H \rightleftharpoons R\cdot\overset{+}{C}O\cdot + H_2O$$

The bimolecular exchange can be formulated either as a nucleophilic addition [2] or as a synchronous displacement; our results do not differentiate between these possibilities.

We cannot make a direct comparison between the rates of the bimolecular exchange of benzoic acid and the unimolecular exchange of mesitoic acid, because solvents are different. However, the results of Bender, Stone, and Dewey [2] show that in dioxan–water (33 : 67 v/v) containing 0·07M-hydrochloric acid, the oxygen exchange of benzoic acid is 1000 times faster than that of mesitoic acid. The relative rates of the hydrolyses of a primary alkyl benzoate by mechanism $A_{Ac}2$ and methyl mesitoate by mechanism $A_{Ac}1$ are similar.[3]

EXPERIMENTAL

Materials.—Mesitoic acid, prepared from mesitylene,[10] had m. p. 154°. Benzoic acid had m. p. 122°.

Dioxan was purified by the usual method.[11] The aqueous dioxan contained 60 vol. of dioxan and 40 vol. of water at room temperature; solutions of perchloric acid in aqueous dioxan were made up from 72% perchloric acid so that the dioxan–water ratio was kept constant.

Kinetics.—In all experiments the isotopic tracer was in the water.

Benzoic Acid.—Benzoic acid (*ca.* 0·05 g.) was put into an ampoule and 10 c.c. of $H_2{}^{18}O$ containing either sulphuric or perchloric acid were added. The sealed ampoules were shaken vigorously in a thermostat. The solubility of benzoic acid is lower in acid than in water, and it was necessary to use finely powdered benzoic acid for the runs with the higher concentrations of mineral acid. At definite times the ampoules were cooled to 0°, and the precipitated benzoic acid was removed by filtration. It was washed with small amounts of ice–water and then converted into silver benzoate by adding silver nitrate in aqueous ethanol to a solution of benzoic acid at pH 4. The silver benzoate was washed successively by water, ethanol, and ether, and dried in a vacuum desiccator. It was decomposed to carbon dioxide by heating *in vacuo*, and the oxygen-18 content of this gas was determined mass spectrometrically.

Mesitoic Acid.—All the exchanges were in dioxan–water (60 : 40 v/v) containing perchloric acid. The procedure was similar to that described for the exchange of benzoic acid, except that *ca.* 0·4 g. of mesitoic acid was dissolved in 10 c.c. of the solvent. At definite times the contents of the cooled ampoules were poured into *ca.* 400 c.c. of distilled water. The mesitoic acid was removed by filtration, washed by water, and dried in a vacuum desiccator. It was decomposed to carbon monoxide by passing it over red hot carbon *in vacuo.* The isotope analysis was made mass spectrometrically.

Mesitoic acid is slowly decarboxylated in strong acids; [12] this would not affect the kinetics of oxygen exchange. The amount of decarboxylation was small in our experiments, because little gas was released when the ampoules were opened.

In both sets of experiments the water was in large excess over the carboxylic acid, and the first-order rate coefficient of oxygen exchange, with respect to the carboxylic acid, is

$$k_1 = 2 \times 2{\cdot}3 \text{ d} \log (N_{H_2O} - N_{R\cdot CO_2H})/\text{d}t$$

where N_{H_2O} is the isotopic abundance of the water and $N_{R\cdot CO_2H}$ that of the carboxylic acid at time *t*. The isotopic abundances are in atom % above normal. Examples of the experimental

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[10] *Org. Synth.*, 1941, **21**, 78.

[11] Vogel, " Practical Organic Chemistry," Longmans Green, London, 1948, p. 175.

[12] Schubert, *J. Amer. Chem. Soc.*, 1949, **71**, 2639.

results are given below. The entropy and energy of activation were calculated by using the formula

$$k_2 = (e\boldsymbol{k}T/\boldsymbol{h}) \exp (\Delta S^*/\boldsymbol{R}) \exp (-E/\boldsymbol{R}T)$$

Benzoic acid: $[H_2SO_4]$ = 1·10M. Water. Temp. 73·0°. N_{H_2O} = 0·980 atom % excess.

Time (min.)	39	54	90	123
$N_{R\cdot CO_2H}$	0·335	0·443	0·623	0·716

10^4k_1 = 3·64 sec.$^{-1}$.

Mesitoic acid: $[HClO_4]$ = 3·0M. Dioxan–water (60: 40 v/v). Temp. 73·0°. N_{H_2O} = 0·880 atom % excess.

Time (hr.)	48	96	192	314	360
$N_{R\cdot CO_2H}$	0·160	0·355	0·521	0·680	0·790

10^6k_1 = 2·74 sec.$^{-1}$.

The values were calculated from the interpolated rates of exchange at 1M-sulphuric acid for benzoic acid and 3M-perchloric acid for mesitoic acid.

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