

110. Tracer Studies of Carboxylic Acids. Part I. Acetic and Pivalic Acid.

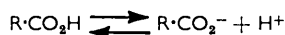
By D. R. LLEWELLYN and CHARMIAN O'CONNOR (*née* BISHOP).

The rate of oxygen exchange of acetic and pivalic acid with water varies with hydrogen-ion concentration. Three paths are postulated for this exchange, of which two are major contributors. The activation energies, frequency factors, and entropies of activation have been calculated. Further information on the mechanism of the acid-catalysed path has been found by studying the deuterium isotope effect.

MANY investigations have been carried out to determine the mechanism for the esterification of acids and the hydrolysis of esters.¹ It is known that carboxylic acids undergo acid-promoted oxygen exchange, which may be classed as a specialisation of acid-catalysed hydrolysis and esterification.² It is evident that, in this special case of the oxygen exchange of acids, acyl-oxygen fission must be involved. No systematic study has been made of the exchange of the oxygen atoms of carboxylic acids with water as solvent. The only information available for acetic acid indicates that, of the species present when the acid is dissolved in water, the acetate ion undergoes no exchange in up to 118 hours at 25°,³ and that acetic acid undergoes exchange slowly.⁴

This paper describes the exchange of the oxygen atoms of acetic and pivalic (trimethylacetic) acid with water over the hydrogen-ion concentrations $4M-10^{-11}M$ and between the temperature range 25—123°.

Mechanism of Oxygen Exchange—In an aqueous solution of a monocarboxylic acid the following equilibrium occurs:



It can be assumed that there are three paths for the species in this equilibrium to exchange oxygen atoms with water:

- (1) $R\cdot CO_2H + H^+ + H_2O$
- (2) $R\cdot CO_2H + H_2O$ or $R\cdot CO_2^- + H^+ + H_2O$
- (3) $R\cdot CO_2H + OH^-$ or $R\cdot CO_2^- + H_2O$

Reactions (2) and (3) are mechanistically different but cannot be distinguished chemically.

This treatment neglects exchange due to attack on a carboxylate by a hydroxyl ion because it is inherently improbable, and also any second-order terms in $R\cdot CO_2H$ [*i.e.*, catalysis of reaction (1) by $R\cdot CO_2H$ instead of by H^+] because the rate is found to be independent of the stoichiometric concentration, C , of total carboxylic acid added.

If f is the fraction of the stoichiometric concentration present as $R\cdot CO_2H$, then the rate of exchange is:

$$R = fC(k_1[H^+][H_2O] + k_2[H_2O] + k_3[OH^-]).$$

Let $R/[H_2O]C = R^*$.

Then $R^*/f = k_1[H^+] + k_2 + k_3[OH^-]/[H_2O]$

¹ Bunton, *Ann. Reports*, 1959, **56**, 179.

² Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, New York, 1953, p. 752.

³ Herbert and Lauder, *Trans. Faraday Soc.*, 1938, **34**, 1219.

⁴ Bentley, *J. Amer. Chem. Soc.*, 1949, **71**, 2675.

Allowance has been made for variation of the acid dissociation constant, K_a , of acetic acid with temperature, by using the empirical relation:⁵

$$\log K = \log K_m - [5.0 \times 10^{-5}(t - \theta)^2]$$

where θ is the temperature at which K_a is a maximum, *i.e.*, equal to K_m . For acetic acid,⁶ $\theta = 22.6^\circ$ and $\log K_m = -4.754$. The variation of K_a of pivalic acid with temperature was calculated from the relation, $\log K = -A_1/T + A_2 - A_3T$, where⁷ $A_1 = 1045$, $A_2 = 2.49$, $A_3 = 0.0135$. At 25° , $K_a = 8.91 \times 10^{-6}$.

The pH of all solutions was measured at room temperature and no allowance has been made for its variation with temperature.

The McKay plots⁸ for exchange were found to be linear over the range studied, which was up to 93% of complete exchange.

The experimental values of R^* are shown in Tables 1 and 2. The fact that the run

TABLE 1.
Exchange for 0.3M-acetic acid- $H_2^{18}O$.

At $I = 1$.														
Temp.	53.3°	53.3°	53.3°	53.3°	53.3°	53.3°	78.0°	78.0°	78.0°	101.0°	101.0°	101.0°	†101.0°	101.0°
pH	1.47	2.03	2.51	2.95	3.49	3.86	2.51	2.92	3.43	2.46	2.92	3.40	3.46	4.12
$10^6 R^*$	27.8	7.95	2.55	1.04	0.298	0.122	13.2	6.42	2.21	600	258	80.6	60.0	14.3
At $I = 4$.														
Temp.	101.0°	101.0°	101.0°	101.0°	123.0°	123.0°	123.0°	123.0°	123.0°	123.0°	123.0°	123.0°	123.0°	123.0°
pH	4.71	5.87	10.18	11.35	2.46	2.96	3.55	4.12	4.45	4.92	5.87	10.12	11.35	
$10^6 R^*$	3.20	0.720	0.710	0.720	199	62.2	16.3	4.03	1.93	1.12	0.620	0.627	0.636	

At $I = 4$.				No salt added.						
Temp.	25.0°	25.0°	25.0°	Temp.	55.0°	55.0°	55.0°	78.0°	78.0°	78.0°
[H ⁺]	3.70	2.77	1.85	pH	1.42	2.13	2.80	1.42	2.13	2.80
$10^6 R^*$	3.56	2.50	1.84	$10^6 R^*$	6.25	1.18	0.262	31.1	3.78	1.24

R^* in l. mole⁻¹ sec.⁻¹. † [HOAc] = 0.1M.

TABLE 2.
Exchange for 0.3M-pivalic acid- $H_2^{18}O$.

At $I = 1$.												
Temp.	55.0°	55.0°	55.0°	55.0°	78.0°	78.0°	78.0°	78.0°	101.0°	101.0°	101.0°	101.0°
pH	1.48	1.90	2.63	3.10	1.48	1.90	2.63	3.10	1.48	1.90	2.63	3.10
$10^6 R^*$	42.2	16.1	2.55	0.872	190	69.5	11.9	3.89	670	275	48.9	16.9
At $I = 4$.												
Temp.	101.0°	101.0°	101.0°	101.0°	101.0°	123.0°	123.0°	123.0°	123.0°	123.0°	123.0°	123.0°
pH	3.52	4.22	5.76	9.89	10.89	2.63	3.10	3.52	4.22	5.76	9.89	10.89
$10^6 R^*$	5.70	1.96	0.185	0.185	0.185	132	47.2	20.2	5.14	1.83	1.90	1.84

At $I = 4$.				
Temp.	45.3°	45.3°	45.3°	45.3°
[H ⁺]	3.70	2.77	1.85	0.92
$10^6 R^*$	3.25	2.29	1.61	0.853

at 101.0°, where [HOAc] = 0.1M, fits into the series for which [HOAc] = 0.3M shows that the rate of ^{18}O exchange depends solely on the difference in isotopic abundance of the two species, acetic acid and water, and is independent of their concentration. Thus the possibility of catalysis of exchange by molecular carboxylic acid can be discounted.

Typical pH profiles of the rate of exchange (*i.e.*, $-\log R^*$ plotted against pH) are shown in the Figure. At pH < 3 the slopes of the curves are equal to 1.0, *i.e.*, the contribution of k_2 is negligible and $R^*/f = k_1[H^+]$. Also at pH < 3, $f = 1$; therefore k_1 can be determined from the straight line through the experimental values.

The values of k_1 , k_2 , and k_3 are shown in Tables 3 and 4.

⁵ Harned and Embree, *J. Amer. Chem. Soc.*, 1934, **56**, 1050.

⁶ Harned and Ehlers, *J. Amer. Chem. Soc.*, 1932, **54**, 1350.

⁷ Everett, Landsman, and Pinsett, *Proc. Roy. Soc.*, 1952, *A*, **215**, 403.

⁸ McKay, *Nature*, 1938, **142**, 997.

TABLE 3.

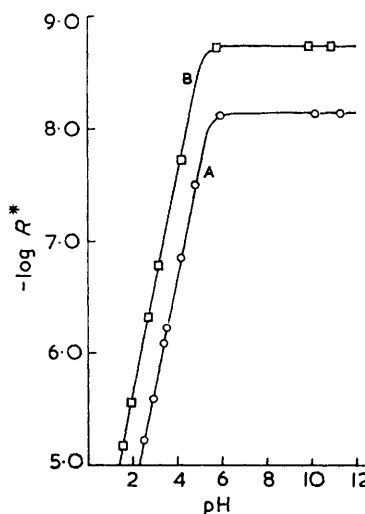
Temp.	Rate constants for ^{18}O exchange of acetic acid.			Conditions
	$10^3 k_1$ (l. ² mole ⁻² sec. ⁻¹)	$10^6 k_2$ (l. mole ⁻¹ sec. ⁻¹)	$10^{-2} k_3$ (l. mole ⁻¹ sec. ⁻¹)	
25.0°	1.00			$I = 4$
53.3	8.70	<0.2		$I = 1$
78.0	53.6			"
101.0	215	<1	3.45	"
123.0	582	<7	19.6	"
55.0	15.3			No salt added
78.0	78.7			" "

TABLE 4.

Temp.	Rate constants for ^{18}O exchange of pivalic acid.			Conditions
	$10^6 k_1$ (l. ² mole ⁻² sec. ⁻¹)	$10^6 k_2$ (l. mole ⁻¹ sec. ⁻¹)	$10^{-2} k_3$ (l. mole ⁻¹ sec. ⁻¹)	
45.3°	8.72			$I = 4$
55.0	13.5			$I = 1$
78.0	52.5			"
101.0	220	<1	0.46	"
123.0	564	<4	3.36	"

There is uncertainty in the value of k_2 because its evaluation depends upon small differences between large quantities. It is difficult to be certain that there is exchange by path (2), because the evidence depends upon the evaluation of the rates of the other two

Dependence of rate of exchange on pH.
 (A) Acetic acid- H_2^{18}O ; $I = 4$; 101.0°.
 (B) Pivalic acid- H_2^{18}O ; $I = 1$; 101.0°.



paths, and therefore upon the uncertainties of pH at high temperatures. Better information about the possible importance of k_2 would be obtained by working in the region between pH 6 and pH 9 where both k_1 and k_3 should make least contribution. However, this is the region of the equivalence point and there are considerable experimental difficulties in adjusting the pH within these limits.

The rate constant k_1 , calculated from results of experiments with no added salt, is larger than the corresponding k_1 at the ionic strength 1. This result, which indicates that the exchange is subject to a negative salt effect, is surprising, because the primary salt effect on the dissociation of acetic acid should result in a positive salt effect. However, this could arise if the effect of the salt on the glass electrode were greater than the effect of the salt on the rate.

Arrhenius plots of $\log k_1$ against $1/T$ were linear. Hence the frequency factors A , the activation energies E , and the entropies of activation ΔS^* could be evaluated.

For convenience the rate constant k_1 (Tables 3 and 4) was calculated so that it did not include $[\text{H}_2\text{O}]$, but the Arrhenius parameters (see Table 5) are calculated on the conventional rate constant k_1' , where $k_1' = k_1[\text{H}_2\text{O}] = 55.5k_1$. These entropies of activation are similar to those obtained in acid-catalysed hydrolysis of esters by mechanism $A_{Ac} 2.9$

TABLE 5.
Arrhenius parameters for rate constant k_1' .

Acid	Conditions	E (kcal. mole ⁻¹)	$\log A$	ΔS^* (cal. deg. ⁻¹ mole ⁻¹)
Acetic	No salt added	15	8	-23
Acetic	$I = 1$	15	8	-21
Pivalic	$I = 1$	15	7	-28

The Arrhenius parameters for path (3) depend on whether the rate constant is calculated as k_3 or k_3' , where

$$R_3 = k_3[\text{R}\cdot\text{CO}_2\text{H}][\text{OH}^-] = k_3'[\text{R}\cdot\text{CO}_2^-][\text{H}_2\text{O}],$$

or conventionally $= k_3''[\text{R}\cdot\text{CO}_2^-]$.

The values of k_3 are listed in Tables 3 and 4, those of k_3'' in Table 6.

TABLE 6.
 $k_3'' = k_3K_w/K_a$.

Acid	Acetic		Pivalic	
Temp.	101.0°	123.0°	101.0°	123.0°
$10^7k_3''$ (sec. ⁻¹)	3.98	35.2	1.02	10.2

It is not possible to say whether path (3) is governed by k_3 or k_3'' ; the Arrhenius parameters for both rate constants are given in Table 7.

TABLE 7.

Acid	Rate constant	Conditions	E (kcal. mole ⁻¹)	$\log A$	ΔS^* (cal. deg. ⁻¹ mole ⁻¹)
Acetic	k_3	$I = 1$	23	16	+18
Acetic	k_3''	$I = 1$	29	11	-11
Pivalic	k_3	$I = 1$	27	17	+19
Pivalic	k_3''	$I = 1$	31	11	-9

The Deuterium Isotope Effect.—The observed rate of oxygen exchange of acetic acid in H_2^{18}O was greater at 74° than in D_2^{18}O . The ratio (K_H/K_D) for the ionisation of acetic acid in H_2O and in 92% D_2O is equal to 3 at 25°. ¹⁰

Also (K_H'/K_D') , the ratio at 74°, may be evaluated from the expression: ¹¹

$$\log (K_H/K_D)/\log (K_H'/K_D') = T'/T.$$

Hence at 74° $K_H' = 1.30 \times 10^{-5}$, $K_D' = 0.50 \times 10^{-5}$, and so it is possible to calculate $[\text{H}^+]$ and $[\text{D}^+]$ for the exchange solutions. At these acidities, $f = 1$ and

$$R^* = k_{1(\text{H}_2\text{O})}[\text{H}^+] \text{ or } = k_{1(\text{D}_2\text{O})}[\text{D}^+]$$

Hence

$$k_{1(\text{H}_2\text{O})}k_{1(\text{D}_2\text{O})} = 0.70.$$

The results of these calculations are given in Table 8.

TABLE 8.

Temp.	$[\text{HOAc}]$	$10^8[\text{H}^+]$	$10^8[\text{D}^+]$	10^8R^*	$10^4k_{1(\text{H}_2\text{O})}$	$10^4k_{1(\text{D}_2\text{O})}$
74.0°	0.325	2.06		1.01	4.90	
74.0°	0.325		1.28	0.890		6.97

⁹ Moelwyn-Hughes, "Kinetics of Reactions in Solutions," Oxford Univ. Press, 1947, p. 321.

¹⁰ Korman and La Mer, *J. Amer. Chem. Soc.*, 1936, **58**, 1396.

¹¹ Wiberg, *Chem. Rev.*, 1955, **55**, 713.

This result for the acid-catalysed exchange of acetic acid is in accordance with a fast proton pre-equilibrium, followed by slow nucleophilic attack of water on the conjugate acid. The secondary solvent isotope effect is comparable in magnitude with those for other acid-catalysed reactions.¹²

EXPERIMENTAL

Materials.—The solvent for most of the experiments was water containing ~ 1 atom % abundance ^{18}O . The solvent used to study the deuterium isotope effect was ^{18}O -enriched deuterium oxide, made by adding 1 ml. of 10 atom % abundance H_2^{18}O to 10 ml. of 99.9 atom % abundance D_2O .

"AnalaR" glacial acetic acid was redistilled (b. p. 118°). Pivalic acid (B.D.H.) was recrystallised from water (m. p. 35.5°).

Recrystallised sodium perchlorate and lithium perchlorate were used to adjust the ionic strength in the reactions of acetic and pivalic acid, respectively.

Acid solutions with $[\text{H}^+] > 0.1\text{M}$ were made up by mixing 60% "AnalaR" perchloric acid with water. The acid concentration was checked by acid-base titration.

The pH of other solutions was adjusted by adding a few drops of 60% "AnalaR" perchloric acid or of a solution of "AnalaR" sodium hydroxide or lithium hydroxide, and measured on a Doran pH-meter.

Kinetics of Oxygen Exchange.—(a) *Solutions of pH > 1.* Weighed samples of carboxylic acid were dissolved by shaking them in solvent (sometimes containing perchlorate salt). After adjustment of the pH, aliquot parts (0.5 ml.), sealed in ampoules, were placed in a constant-temperature bath.

(b) *Solutions of $[\text{H}^+] > 0.1\text{M}$.* Weighed samples of carboxylic acid were dissolved by shaking them in solvent containing perchloric acid and perchlorate salt, which was at the temperature of the thermostat-bath.

Samples were removed at intervals, cooled rapidly in liquid air, and brought to pH ~ 7 (colourless to phenolphthalein) by addition of dilute perchloric acid to basic solutions and dilute sodium or lithium hydroxide to acidic solutions. A few drops of silver nitrate were added, and the precipitate of silver acetate or pivalate was filtered off, washed with alcohol, and dried under a vacuum. The silver salts were pyrolysed by gentle heating *in vacuo*, to give carbon dioxide which was analysed on a A.E.I. M.S.3 mass spectrometer. The carbon dioxide from the thermal decomposition of silver pivalate was contaminated with a substance (possibly dimethyl ether) of mass 46, which interfered with the mass-spectrometric analysis. This impurity was removed by mixing the volatile decomposition products with bromine, passing then through a carbon tube heated by a radio-frequency induction furnace, then through a trap cooled in solid carbon dioxide and alcohol, and finally the carbon dioxide was collected in a gas bulb surrounded by liquid air.

The initial abundance of ^{18}O in the carboxylic acid was measured on an unlabelled sample of silver salt, and excess abundances were calculated relative to this value. For the fast reactions the infinite-time value for complete exchange was measured after ~ 8 – 10 half-lives. If $t_{1/2}$ was greater than 4 days, the infinite-time abundance was measured on a sample of carbon dioxide which had been in equilibrium with a portion of the exchange solution for 36 hr. at 100° .

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CHEMISTRY DEPARTMENT, UNIVERSITY OF AUCKLAND,
AUCKLAND, NEW ZEALAND.

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¹² Bunton and Shiner, *J. Amer. Chem. Soc.*, 1961, **83**, 3207.