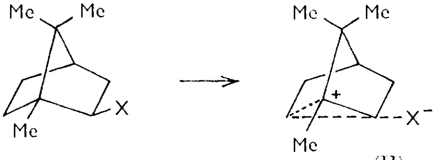
598. *Tracer Studies in Ester Hydrolysis. Part XIV.* The Hydrolysis of Bornyl and Isobornyl Acetates*

By C. A. Bunton, K. Khaleeluddin, and D. Whittaker

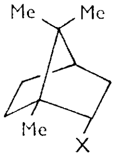
Hydrolysis of bornyl and isobornyl acetate follows mechanism $B_{\mathrm{Ac}}2$ in alkaline and $A_{\mathrm{Ac}}2$ in dilute acidic solution. Hydrolysis of both esters is accompanied by extensive exchange between the carbonyl oxygen atom and the water of the solvent. It is suggested that the decomposition of the tetrahedral addition intermediate to products is unusually slow during hydrolysis of these esters.

The kinetic form of the acid hydrolysis of isobornyl acetate suggests that there is a mechanistic change towards mechanism $A_{\mathrm{Al}}1$ in more concentrated acid. Experiments with the model compounds isopropyl and t-butyl acetate support this conclusion.

Isobornyl chloride (I; X = Cl) is unusually reactive in $S_{\mathrm{N}}1$ solvolyses, because the forming carbonium-ion centre in the transition state (II) is stabilised by delocalisation of sigma electrons.[1a,b,2] This speeding of ionisation has been called "synartesis," or "anchimerism." The reactivity of the *endo*-isomer, bornyl chloride (III; X = Cl) is similar to that of other secondary alkyl chlorides,[1a] because the transition state for its solvolysis is not stabilised by electronic delocalisation, and factors such as angle strain and non-bonding interactions are relatively small and self-cancelling.[1b]



(I) (II)



(III)

Therefore, it seemed likely that the acid hydrolysis of isobornyl acetate (I; X = OAc) would follow mechanism $A_{\mathrm{Al}}1$, with accelerated formation of a carbonium ion from the conjugate acid (I; X = $\mathrm{O{\cdot}MeC^{+}{\cdot}OH}$), that the acid hydrolysis of bornyl acetate (III; X = OAc) would follow the more usual mechanism $A_{\mathrm{Ac}}2$, and that in alkali both esters would be hydrolysed by mechanism $B_{\mathrm{Ac}}2$. We were unable to use oxygen-18 to determine the position of bond fission in the acid hydrolysis of isobornyl acetate, because there is a

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* Part XIII, C. A. Bunton and B. N. Hendy, *J.*, 1963, 3137.

[1] (*a*) S. Winstein and D. S. Trifan, *J. Amer. Chem. Soc.*, 1949, **71**, 2953; S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan, and H. Marshall, *ibid.*, 1952, **74**, 1127; J. D. Roberts and C. C. Lee, *ibid.*, 1951, **73**, 5009; F. Brown, E. D. Hughes, C. K. Ingold, and J. F. Smith, *Nature*, 1951, **168**, 65; (*b*) P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1964, **86**, 1854.

[2] P. Beltramé, C. A. Bunton, A. Dunlop, and D. Whittaker, *J.*, 1964, 658.

relatively rapid acid-catalysed oxygen exchange between isoborneol and water, involving a carbonium-ion rearrangement to camphene hydrate, which then itself rearranges back to the thermodynamically more stable isoborneol.[3] The rate of this reaction is similar to that of the acid hydrolysis of isobornyl acetate, and the hydrolysis products are therefore thermodynamically, rather than kinetically, controlled.

Carboxylic esters of borneol are hydrolysed in alkali more rapidly than those of isoborneol, by factors of 5—25, because the *gem*-dimethyl groups sterically hinder attack of a nucleophile upon the carbonyl carbon atom of the isobornyl esters, which have the *exo*-configuration.[4] For hydrolysis in dilute acid, and in alkali, bornyl actate was more reactive than isobornyl acetate in our experiments (Tables 1—3 and Figures 1 and 2). In more concentrated acid, however, isobornyl acetate is the more reactive ester, suggesting different

TABLE 1

Acid hydrolysis of bornyl acetate

Solvent dioxan–water (3 : 2 v/v), at 44·6°

$[HClO_4]$ (M)	0·261	0·465	0·599	0·930	1·51	2·06	2·10	3·40
10^6k_1 (sec.$^{-1}$)	18·6	38·1	61·9	162	359	508	489	1410

Effect of added lithium perchlorate; $[HClO_4]$ = 0·930M

$[LiClO_4]$ (M)	—	0·88	1·57	2·30
10^6k_1 (sec.$^{-1}$)	162	173	180	198

Effects of variations of temperature and acid concentration

	10^6k_1 (sec.$^{-1}$) at								
$[HClO_4]$ (M)	25·0°		35·1°		44·6°	60·0°	75·0°	100·9°	E (kcal. mole^{-1})
0·122	1·21	1·23	2·60	2·78	5·72	16·6	—	225	15
0·222	—		8·4		17·8	—	129	567	14·5
1·01	31·1		70·4		155 *	—	—	—	15

Effects of variations of temperature and salt concentration. $[HClO_4]$ = 0·222M

	10^6k_1 (sec.$^{-1}$) at				
$[LiClO_4]$ (M)	35·1°	44·6°	75·0°	100·9°	E (kcal. mole^{-1})
1·04	11·8	23·3	170	672	14
2·09	19·5	41·7	297	1131	13·5

* Extrapolated value.

TABLE 2

Acid hydrolysis of isobornyl acetate in dioxan–water (3 : 2; v/v) at 44·6° except where specified

$[HClO_4]$ (M) ...	—		0·121	0·134	0·165		0·258			0·289	
10^6k_1 (sec.$^{-1}$)...	1·2^{a}	6·3^{b}	0·903	0·947	98·1^{b}	96·8^{b,d}	1·92	7·26^{c}	164^{b}	8·17^{e}	188^{b}

$[HClO_4]$ (M) ...	0·326		0·344	0·80	1·06	1·73		2·38	2·60		3·63	4·34
10^6k_1 (sec.$^{-1}$)...	11·4^{c}	219^{b}	2·72	14·6	20·3	55·6	58·3^{e}	153	203	195^{e}	1390	2470

^{a} 72·9°. ^{b} 100·9°. ^{c} 60·0°. ^{d} Toluene *p*-sulphonic acid. ^{e} Analysis by g.l.c.

Effects of variations of temperature and salt concentration

$[HClO_4]$ (M)	$[LiClO_4]$ (M)	25·0°	35·1°	44·6°	60·0°	75·0°	100·9°	E (kcal. mole^{-1})	ΔS * (e.u.)
0·121	—	0·160, 0·147	0·378, 0·380	0·903	3·12	—	68·8	17·5	−29
0·344	—	—	1·48	2·72	—	34·3	212	17·5	−27
0·344	1·05	—	2·65	5·89	—	103	1360	19·5	−19
0·344	1·54	—	3·92	9·11	—	223	2220	22	−10
0·344	2·27	—	10·2	27·6	—	803	—	23·5	−4

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[3] C. A. Bunton, K. Khaleeluddin, and D. Whittaker, *Tetrahedron Letters*, 1963, 1825.

[4] G. Vavon and P. Peignier, *Compt. rend.*, 1925, **181**, 184; *Bull. Soc. chim. France*, 1926, **39**, 924; M. Lipp and E. Bund, *Ber.*, 1935, **68***B*, 255.

TABLE 3

Alkaline hydrolysis of bornyl and isobornyl acetates in dioxan–water (3 : 2; v/v) at 44·9°

$[\overline{\text{OH}}] = [\text{Ester}] = 0{\cdot}020\text{M}$
Bornyl acetate: $10^3k_2 = 7{\cdot}5$ l. mole^{-1} sec.$^{-1}$
Isobornyl acetate $10^3k_2 = 1{\cdot}48$ l. mole^{-1} sec.$^{-1}$

mechanisms of hydrolysis at high and at low acid concentration. The experiments in dilute and concentrated acid will be discussed separately.

In dilute perchloric acid in dioxan–water (3 : 2; v/v) the higher reactivity of bornyl acetate suggests that both esters are reacting by mechanism $A_{\text{Ac}}2$. The energies and entropies of activation are in the range associated with bimolecular A-2 reactions:[5]

Bornyl acetate, $\Delta S^* = -31$ e.u., $E = 15$ kcal. mole^{-1};
Isobornyl acetate, $\Delta S^* = -28$ e.u., $E = 17{\cdot}5$ kcal. mole^{-1}
(from rate constants in 0·1—0·3 M-HClO_4; Tables 1 and 2).

Borneol, recovered from acid hydrolysis in dioxan–[^{18}O]water, was isotopically normal Table 7 and Experimental section). The oxygen exchange of borneol is much slower than

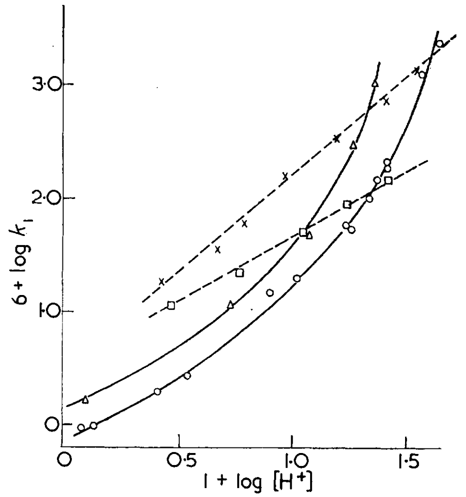

FIGURE 1. Acid hydrolysis in dioxan–water (3 : 2 v/v). Plot of log k_1 against log H$^+$

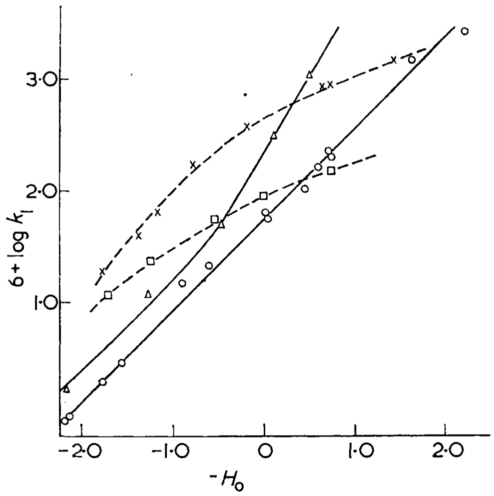

FIGURE 2. Acid hydrolysis in dioxan–water (3 : 2 v/v). Plot of log k_1 against Hammett's acidity function, $-H_0$

Hydrolysis of bornyl acetate × – – – × } at 44·6°
Hydrolysis of isobornyl acetate ○——○ } at 44·6°
Hydrolysis of isopropyl acetate □ – – – □ } at 25·0°
Hydrolysis of t-butyl acetate △——△ } at 25·0°

the acid hydrolysis of its acetate (Tables 1 and 7, pp. 3291, 3299 and ref. 3). Bornyl acetate, recovered after partial hydrolysis, is, however, extensively enriched, and all the tracer is upon the carbonyl oxygen atom (Experimental section). Isoborneol similarly recovered from hydrolysis of the ester is isotopically enriched, but control experiments show that its enrichment could arise by its subsequent acid-catalysed oxygen exchange (Experimental section and ref. 3). However, the unchanged isobornyl acetate is very extensively enriched isotopically, and again all the tracer is upon the carbonyl oxygen atom (Experimental section). Therefore, the acid hydrolysis of bornyl acetate follows mechanism

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[5] F. A. Long, J. G. Pritchard, and F. E. Stafford, *J. Amer. Chem. Soc.*, 1957, **79**, 2362; L. L. Schaleger and F. A. Long, *Adv. Phys. Org. Chem.*, 1963, **1**, 1.

$A_{Ac}2$, and this mechanism is important in the hydrolysis of isobornyl acetate, at least in dilute acid.

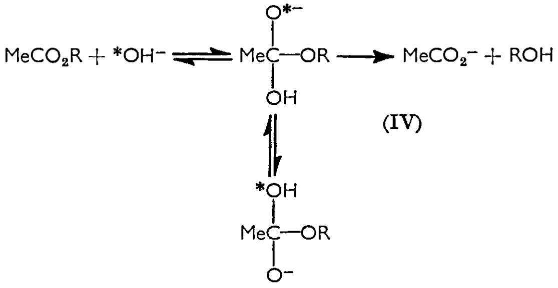
TABLE 4

Oxygen exchange of bornyl and isobornyl acetate in dioxan–water (3 : 2; v/v), at 45·0°

	Bornyl acetate			Isobornyl acetate		
	1M-$HClO_4$	1·51M-$HClO_4$	0·02M-NaOH	0·55M-$HClO_4$	1M-$HClO_4$	0·02M-NaOH
k_h/k_e	1·5	1·7	1·8	0·48	0·42	0·48

The ratio of the rate constants for acid hydrolysis and oxygen exchange, k_h/k_e, (Table 4), is much smaller for these than for other esters,[6,7] *e.g.*, for acid hydrolysis and alkaline hydrolysis of alkyl benzoates $k_h/k_e = 3$—10, and for some esters it is so large that no exchange is observed during hydrolysis.[7] Only in the alkaline hydrolysis of amides has oxygen exchange been found to be as fast as hydrolysis.[8] We therefore examined the alkaline hydrolysis of bornyl and isobornyl acetate, and found that it too is accompanied by extensive oxygen exchange between ester and water (Table 4). In agreement with earlier work,[4] bornylacetate is more reactive than isobornyl acetate (Table 3).

The differences between the behaviour of these and other carboxylic esters suggests that the bicyclic alkyl group is having a large effect upon the partitioning of the tetrahedral intermediate, *e.g.*, (IV), formed by nucleophilic addition to the ester.



(IV)

(A similar multistage reaction can be written for the acid hydrolysis)

Observation of oxygen exchange during ester hydrolysis requires that, (*a*) the intermediate (IV) must revert to reactants as well as decompose to products and, (*b*) that two of the oxygen atoms in the intermediate (IV) must become equivalent by proton transfer. The differences between these and other esters, in respect to their ready oxygen exchange, depends on the way in which these bulky bicyclic alkyl groups may affect these two requirements. Bulky groups might hinder proton transfer from one oxygen atom to another in the intermediate (IV), or in the corresponding intermediate in the acid hydrolysis, but such an effect should reduce the amount of oxygen exchange during hydrolysis. They might also sterically accelerate the breakdown of the intermediate (IV) to products, but again this effect should reduce the amount of oxygen exchange relative to hydrolysis.

Decomposition of the tetrahedral intermediate to products probably requires complete or partial transfer of a proton to the alkyl oxygen atom, *i.e.*, there is electrophilic assistance to loss of the alkoxy group.* The bulky bicyclic group may hinder approach of a

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* There is kinetic and isotopic evidence which suggests that two water molecules are involved in *A*-2 hydrolysis of simple carboxylic esters, and that the second water molecule is donating a proton to the alkoxy-group.[9]

[6] M. L. Bender, *J. Amer. Chem. Soc.*, 1951, **73**, 1626; *Chem. Rev.*, 1960, **69**, 53.

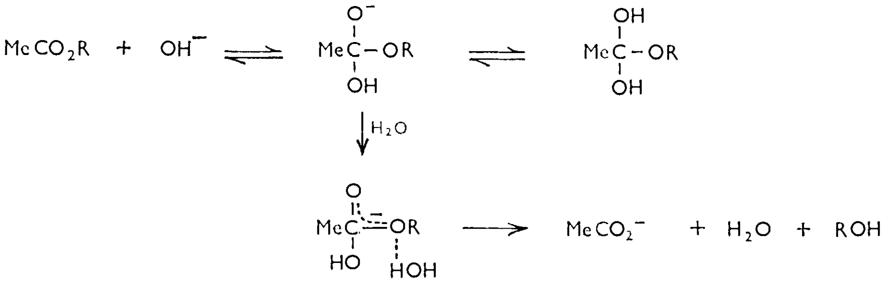
[7] C. A. Bunton and D. N. Spatcher, *J.*, 1956, 1079; M. L. Bender, H. Matsui, R. J. Thomas, and S. W. Tobery, *J. Amer. Chem. Soc.*, 1961, **83**, 4193.

[8] M. L. Bender, R. D. Ginger, and K. C. Kemp, *J. Amer. Chem. Soc.*, 1954, **76**, 3350; M. L. Bender, and R. D. Ginger, *ibid.*, 1955, **77**, 348; M. L. Bender and R. J. Thomas, *ibid.*, 1961, **83**, 4183; C. A. Bunton, T. A. Lewis, and D. R. Llewellyn, *Chem. and Ind.*, 1954, 1154.

[9] P. Salomaa, L. L. Schaleger, and F. A. Long, *J. Amer. Chem. Soc.*, 1964, **86**, 1; C. A. Lane, *ibid.*, p. 2521.

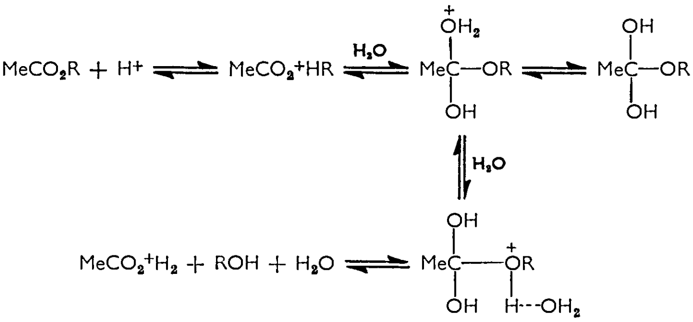
water molecule or hydronium ion, or of any acid, towards this alkyl oxygen atom, and loss of a water molecule, or of a solvated hydroxide ion, could therefore be easier than loss of borneol or isoborneol. The intermediate would then return to reactants rather than go forward to products. This hypothesis suggests that general acids should catalyse hydrolysis of these esters, by assisting breaking of the acyl oxygen bond, and evidence for this is being sought. Possible modes of electrophilic assistance of loss of the alkoxy-group are shown below; other schemes can be written in which the charge distributions differ from those shown. The smaller value of k_h/k_e for isobornyl acetate suggests that one of the *gem*-dimethyl groups is particularly effective in hindering donation of a proton, or formation of a hydrogen bond, to the alkyl oxygen atom of the tetrahedral intermediate.

Alkaline hydrolysis:



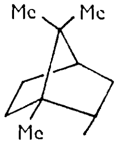
Note: The dots represent partial bonds, and indicate that the negative charge will be transferred from one oxygen to another.

Acid hydrolysis:



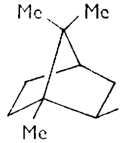
bornyl acetate

R =



isobornyl acetate

R =



Our evidence suggests that steric effects are affecting the relative reactivity of bornyl and isobornyl acetate in two different ways, because nucleophilic attack upon isobornyl acetate is hindered by one of the *gem*-dimethyl groups, which also retards decomposition of the tetrahedral intermediate to products. For alkaline hydrolysis in dioxan–water (3 : 2; v/v), bornyl acetate is *ca.* five times more reactive than its epimer (Table 3), and for 1M-perchloric acid the rates of hydrolysis differ ten-fold. (Tables 1 and 2 and Figures 1 and 2.) In these reactions, about half the rate-differences are caused by hindrance to nucleophilic attack upon the ester, and the rest by the preferential partitioning of the intermediate to reactants in the hydrolysis of isobornyl acetate (Table 4).

There is permissive evidence for a slow proton-transfer during the rate-limiting step of *A*-2 ester hydrolysis;[9] also, the transition state for aminolysis of esters contains a second amine molecule, which acts as a general base.[10] To this extent our isotopic experiments agree with conclusions based on rate measurement.

Although bornyl acetate is more reactive than isobornyl acetate in dilute perchloric acid, the rate of its hydrolysis increases much less sharply with increasing acid concentration. The obvious explanation is that the hydrolysis of bornyl acetate follows mechanism $A_{Ac}2$ over the whole range of acidity studied, but that, although the hydrolysis of isobornyl acetate follows mechanism $A_{Ac}2$ in dilute acid, a new mechanism appears at higher acid concentrations. If this mechanism were unimolecular, *e.g.*, mechanism $A_{Al}1$, it would be much more sensitive than mechanism $A_{Ac}2$ to increasing acid concentration, because the rates of most A-1 reactions are approximately proportional to Hammett's acidity function, h_0, and therefore increase much more rapidly than the hydrogen-ion concentration, whereas the rates of A-2 reactions are more closely proportional to hydrogen-ion concentration.[11,12] Most of the existing evidence relates to reactions in aqueous acid, but similar situations should hold in aqueous organic solvents, at least in those of high water content, as has been demonstrated for a number of hydrolyses.[13]

The plot of log k_1 against log[$HClO_4$] for the acid hydrolysis of bornyl acetate (Figure 1) is linear with a slope of 1·7, the corresponding plot against $-H_0$ is a curve of steadily decreasing slope (Figure 2). For isobornyl acetate, a plot of log k_1 against log[$HClO_4$] (Figure 1) is a curve of steadily increasing slope, and the corresponding plot against $-H_0$ is nearly linear, with a slope of *ca.* 0·75 (Figure 2).

Salt effects support the suggested mechanistic change in the acid hydrolysis of isobornyl acetate. Many salts increase the protonating power of acids, as measured by Hammett's acidity function, and lithium perchlorate is particularly effective in this respect.[14] Therefore an A-1 reaction, whose rate should follow the protonating power of the acid rather than its concentration, should be especially sensitive to added salts. An A-2 reaction, on the other hand, should be relatively insensitive to salts with non-nucleophilic anions. Lithium perchlorate speeds up the acid hydrolysis of isobornyl acetate very markedly, but that of bornyl acetate only slightly (Tables 1 and 2), suggesting that it is preferentially assisting an A-1 hydrolysis of isobornyl acetate.

The value of the entropy of activation, ΔS^*, is often used as a mechanistic test, and generally ΔS^* is zero, or slightly positive, for A-1 reactions, and negative for A-2 reactions,[5] although this test is not universally applicable.[15] At low acidities, the entropy and energy of activation for the hydrolysis of both esters in dioxan–water are in the range usually associated with A-2 reactions (p. 3292 and Tables 1 and 2), and this situation holds over a wide range of acid and salt concentration for the acid hydrolysis of bornyl acetate. But, for the acid hydrolysis of isobornyl acetate in 0·344 M-perchloric acid, there is a steady increase in the activation energy, and the entropy of activation becomes less negative, with addition of lithium perchlorate (Table 2).

This evidence suggests that a second mechanism of hydrolysis appears in the hydrolysis of isobornyl acetate in more concentrated acid, but it is possible that perchloric acid, or lithium perchlorate, has a specific effect upon the $A_{Ac}2$ hydrolysis of isobornyl acetate, but not on that of bornyl acetate. Tracer evidence for the incursion of mechanism $A_{Al}1$ could not be obtained (Experimental section), and therefore we examined the acid

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[10] J. F. Bunnett and G. T. Davies, *J. Amer. Chem. Soc.*, 1960, **82**, 665; W. P. Jencks and J. Carriuolo, *ibid.*, p. 675; T. C. Bruice and S. J. Benkovic, *ibid.*, 1964, **86**, 418.

[11] F. A. Long and M. A. Paul, *Chem. Rev.*, 1957, **57**, 935; J. F. Bunnett, *J. Amer. Chem. Soc.*, 1961, **83**, 4956.

[12] R. P. Bell, A. L. Dowding, and J. A. Noble, *J.*, 1955, 3106; C. T. Chmiel and F. A. Long, *J. Amer. Chem. Soc.*, 1956, **78**, 3326.

[13] C. A. Bunton, J. B. Ley, A. J. Rhind-Tutt, and C. A. Vernon, *J.*, 1957, 2327; C. A. Bunton and T. Hadwick, *J.*, 1957, 3043; C. A. Bunton and S. G. Perry, *J.*, 1960, 3070.

[14] G. Harbottle, *J. Amer. Chem. Soc.*, 1951, **73**, 4024; M. A. Paul, *ibid.*, 1954, **76**, 3236; F. A. Long and D. McIntyre, *ibid.*, p. 3243.

[15] E. Whalley, *Trans. Faraday Soc.*, 1959, **55**, 798.

hydrolysis of two simple alkyl acetates in acidic aqueous dioxan, and in water. The hydrolysis of t-butyl acetate follows mechanism $A_{Al}1$ in aqueous hydrochloric acid,[16] and mechanisms $A_{Al}1$ and $A_{Ac}2$ run concurrently in acidic aqueous dioxan, but the hydrolysis of isopropyl acetate follows mechanism $A_{Ac}2$ in aqueous hydrochloric acid,[17] and should do so in acidic aqueous dioxan. Therefore these esters should be good models for the acid hydrolysis of isobornyl and bornyl acetates.

TABLE 5

Acid hydrolysis of isopropyl acetate

In water

At 25·0°.

$[HClO_4]$ (M)	0·507	0·990	2·15	3·54
10^6k_1 (sec.$^{-1}$)	29·5	57·7	111	172
$5 + \log k_1 - \log [HClO_4]$	0·765	0·757	0·713	0·687

Effect of temperature

	10^6k_1 (sec.$^{-1}$) at			
$[HClO_4]$ (M)	0·0°	25·0°	35·1°	44·6°
0·507	2·17	29·5	71·4	175
3·54	12·7	172	464	

$E = 17$ kcal. mole^{-1}; $\Delta S^* = -22$ e.u.

In dioxan–water (3 : 2 v/v)

At 25·0°.

$[HClO_4]$ (M)	0·288	0·574	1·12	1·70	2·60
10^6k_1 (sec.$^{-1}$)	11·5	22·4	50·9	92·7	155

Effect of temperature

$[HClO_4]$ (M)	0·0°	25·0°	35·1°	44·6°	60·0°
0·574	1·93	22·4	55·6	124	376
2·60	12·4	155	403	833	—

$E = 16·5$ kcal. mole^{-1}: $\Delta S = -25$ e.u. (mean value for two acid concentrations).

Salt effect at $[HClO_4] = 0·288$M

	10^6k_1 (sec.$^{-1}$)				E
$[LiClO_4]$ (M)	0·0°	25·3°	35·1°	44·6°	(kcal. mole^{-1})
—	0·925	11·5	26·3	60·8	16·5
1·62	1·25	16·2	37·5	80·9	16
2·26	1·27	17·8	38·6	85·5	16

The acid hydrolysis of isopropyl acetate will be considered first. In agreement with Salomaa's results for hydrolysis in aqueous hydrochloric acid,[17] we find that the first-order rate constant, k_1, is approximately proportional to the concentration of perchloric acid, as shown by the approximate constancy of the values of $\log k_1 - \log[HClO_4]$ in Table 5. Therefore, this reaction has the kinetic form predicted for an A-2 hydrolysis by the Zucker–Hammett hypothesis, or by Bunnett's more recent treatment.[11] (Many other esters behave similarly.[12]) In dioxan-water (3 : 2; v/v), a plot of $\log k_1$ against $\log[HClO_4]$ is linear, of slope 1·2, but the corresponding plot against $-H_0$ is a curve of steadily decreasing slope; isopropyl and bornyl acetates therefore behave similarly in acidic aqueous dioxan (Figures 1 and 2). Lithium perchlorate mildly speeds up the acid hydrolysis of isopropyl acetate in aqueous dioxan (Table 5), again bornyl acetate behaves similarly (Table 1). In both water and dioxan-water (3 : 2; v/v) the energies of activation are in the range generally observed for ester hydrolysis by mechanism $A_{Ac}2$. Under our conditions, isopropyl acetate is slightly more reactive than bornyl acetate, but this is the result of a cancellation of the Arrhenius parameters, because the energy of activation is slightly higher, and the entropy more positive, for the hydrolysis of isopropyl

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[16] C. A. Bunton and J. L. Wood, *J.*, 1955, 1522.

[17] P. Salomaa, *Suomen Kem.*, 1959, *B*32, 145.

acetate in aqueous dioxan. Added lithium perchlorate has little effect upon the activation energy, as for the hydrolysis of bornyl acetate.

The dependence of the rate of hydrolysis of t-butyl acetate upon Hammett's acidity function, h_0, confirms that mechanism $A_{\mathrm{Al}}1$ is followed in aqueous hydrochloric acid.[16,17] The entropy of activation, +12·5 e.u., for hydrolysis of t-butyl acetate in aqueous perchloric acid is similar to those found for other A-1 hydrolyses of carboxylic esters,[5] and is considerably more positive than those found for the hydrolyses of isopropyl and bornyl acetates; conversely, the energy of activation is larger. The solvent deuterium-isotope-effect, $k_{\mathrm{D_2O}}/k_{\mathrm{H_2O}} = 2{\cdot}1$, for hydrolysis in 0·107M-perchloric acid in water (Table 6) further confirms the $A_{\mathrm{Al}}1$ mechanism.[18]

For acid hydrolysis in dioxan–water (3 : 2; v/v), the kinetic, as well as the isotopic,[16] evidence suggests that mechanisms $A_{\mathrm{Ac}}2$ and $A_{1}1$ run concurrently in dilute acid, but that increasing the acid concentration favours mechanism $A_{\mathrm{Al}}1$. (In the less aqueous dioxan–water (7 : 3; v/v), containing 0·24M-hydrochloric acid, there is approximately 40% of alkyl–oxygen fission.[16]) A plot of log k_1 against Hammett's acidity function, $-H_0$, in dioxan–water (3 : 2; v/v) is a curve at low acidities (Figure 2), but becomes a straight line of slope 1·3 at higher acidities where mechanism $A_{\mathrm{Al}}1$ should predominate: with 1M-perchloric acid in dioxan–water (3 : 2; v/v) the entropy of activation is −1 e.u., and the energy of activation 25·5 kcal. mole^{-1}, suggesting that mechanism $A_{\mathrm{Al}}1$ predominates.[5] The activation energy is, as expected, low in more dilute acid, *e.g.*, in 0·1M-perchloric acid it is 24 kcal. mole^{-1} (Table 6).

TABLE 6

Acid hydrolysis of t-butyl acetate

In water

[HClO$_4$] (M)	10^6k_1 (sec.$^{-1}$) at 25·0°	35·1°	44·6°	60·0°
0·083	15·3	54·2	222	1900
0·098	17·7	—	258	—
0·107	—	—	281, 599 †	

E = 27 kcal. mole^{-1}; ΔS^* = +12·5 e.u.

In dioxan–water (3 : 2 v/v)

At 25·0°.

[HClO$_4$] (M)	0·125	0·529	1·185	1·823	2·289
10^6k_1 (sec.$^{-1}$)	1·64	11·9	49·2	309	1100

Effect of temperature

[HClO$_4$] (M)	10^6k_1 (sec.$^{-1}$) at 0·00°	25·0°	35·1°	44·6°	60·0°	E (kcal. mole^{-1})
0·125	—	1·64	5·76	16·9	117	24
1·82	6·13	309	—	—	—	25·5
2·29	20·6	1100	—	—	—	25·5

E = 25·5 kcal. mole^{-1}; ΔS^* = −1 e.u., at 1M-[HClO$_4$].

† D$_2$O.

These experiments show that there is the expected variation in kinetic form as the mechanism changes from $A_{\mathrm{Ac}}2$ towards $A_{\mathrm{Al}}1$ with increasing acidity. However, t-butyl acetate is not a completely satisfactory model for isobornyl acetate because, even in dilute acidic aqueous dioxan, mechanism $A_{\mathrm{Al}}1$ is important, and becomes all-important as the acidity increases, whereas, with isobornyl acetate, mechanism $A_{\mathrm{Ac}}2$ is all-important in

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[18] J. G. Pritchard and F. A. Long, *J. Amer. Chem. Soc.*, 1956, **78**, 6008; 1958, **80**, 4162; C. A. Bunton and V. J. Shiner, *ibid.*, 1961, **83**, 3207.

dilute acidic aqueous dioxan, and mechanism $A_{\mathrm{Al}}1$ probably makes little contribution except at higher acidities. It is therefore difficult to assess the relative importance of mechanisms $A_{\mathrm{Ac}}2$ and $A_{\mathrm{Al}}1$ in the acid hydrolysis of isobornyl acetate at moderate acid concentrations, although comparison with model compounds provides kinetic evidence for incursion of a second mechanism of acid hydrolysis at high concentrations of perchloric acid or lithium perchlorate.

EXPERIMENTAL

Materials.—Borneol, purified as its hydrogen phthalate,[19a] had m. p. 205·5—206° (lit.,[19] 208·5°), which suggests that any contaminating isoborneol had been removed (borneol and isoborneol form mixed crystals [20]). Its purity was confirmed by gas–liquid chromatography (g.l.c.). The sodium derivative of borneol was treated with freshly distilled acetic anhydride in refluxing light petroleum (b. p. 60—80°). Bornyl acetate was purified by vacuum distillation [Found: *M* (by hydrolysis), 194. Calc.: *M*, 196].

Crude isoborneol, either commercial or prepared by reduction of camphor with lithium aluminium hydride, was purified by chromatography over alumina [21] by using light petroleum as the eluting solvent. Borneol is much more strongly adsorbed by alumina than is isoborneol. The purified isoborneol had m. p. 213—214° (lit.,[19,20] 214°), and its purity was confirmed by g.l.c. It was acetylated with acetic anhydride by the methods given above.

Isopropyl acetate was a commercial sample, and t-butyl acetate was prepared in the usual way.[22] G.l.c. of both esters on Tween-Celite or silicone E301–Celite columns gave single peaks.

The solvent was made up from water and purified dioxan,[23] so that its composition was dioxan : water 3 : 2 (v/v), for both acid and alkaline solutions.

Tracer Experiments.—The water of the solvent was enriched in oxygen-18. Because bornyl and isobornyl acetates are sparingly soluble in dioxan–water (3 : 2 v/v), the ester concentration was <M/50. After partial or complete hydrolysis, the organic compounds were extracted into pentane, and the pentane solution was washed with water to remove dioxan, then with dilute sodium carbonate, and finally dried over potassium carbonate. The alcohols and esters were separated by g.l.c. on a Tween–Celite column. (This procedure was also used for some rate measurements.) The isotopic abundance was determined by the method of Dahn, Moll, and Menassé,[24] or by heating the organic compound *in vacuo* with a mixture of phenylenediamine hydrochloride and guanidine hydrochloride. The evolved carbon dioxide was analysed mass-spectrometrically.

In the experiments on the oxygen exchange of the esters, the isolated esters were also cleaved by lithium aluminium hydride to the alcohol, which was found to be isotopically normal (Table 7). Therefore, the tracer in the ester was located on the carbonyl oxygen atom. As additional evidence that isotopic exchange did not occur by rearrangement of the esters, we used optically-active esters in Expts. 1, 2, and 6, and found no racemisation of the unchanged esters. The rotations were measured with a Bendix–Ericson electronic polarimeter on an approximately 1% solution in benzene.

Bornyl acetate $[\alpha]_{\mathrm{Hg}} = -30{\cdot}2°$; from Expt. 1, $[\alpha]_{\mathrm{Hg}} = 29{\cdot}9°$, from Expt. 2, $[\alpha]_{\mathrm{Hg}} = -29{\cdot}5°$.

Isobornyl acetate $[\alpha]_{\mathrm{Hg}} = -9{\cdot}1°$; from Expt. 6, $[\alpha]_{\mathrm{Hg}} = -9{\cdot}0°$.

The detailed results of the tracer experiments are shown in Table 7. The method of calculation of the relative rates of hydrolysis and exchange $k_{\mathrm{h}}/k_{\mathrm{e}}$ has been described.[6] Calculation of the amount of alkyl–oxygen fission in the acid hydrolysis of isobornyl acetate, by methods already described,[25] is not reliable, because the oxygen exchange of isoborneol is as fast as the

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[19] (*a*) T. Ikeda and Y. Fujita, *Bull Inst. Phys. Chem. Res., Tokyo*, 1928, **7**, 257; (*b*) R. H. Pickard and W. O. Littlebury, *J.*, 1907, **91**, 1978; J. Kenyon and R. H. Pickard, *J.*, 1915, **107**, 35; J. L. Simonsen and L. N. Owen, " The Terpenes," vol. II, Cambridge Univ. Press, London, 1957, p. 349.

[20] A. McKenzie and A. G. Mitchell, *Biochem. Z.*, 1929, **208**, 474.

[21] G. Vavon and B. Gastambide, *Compt. rend.*, 1948, **226**, 1201.

[22] B. Ambrovitch, J. C. Shivers, B. E. Hudson, and C. R. Hauser, *J. Amer. Chem. Soc.*, 1943, **65**, 986.

[23] A. I. Vogel, " Practical Organic Chemistry," Longmans, London, 1951, p. 175.

[24] H. Dahn, H. Moll, and R. Menassé, *Helv. Chim. Acta*, 1959, **42**, 1225.

[25] C. A. Bunton, D. R. Llewellyn, K. G. Oldham, and C. A. Vernon, *J.*, 1958, 3574.

ester hydrolysis. In Expt. 7, correction for the exchange of isoborneol gives 4% alkyl–oxygen fission, but the uncertainty in this figure is large.

Kinetics.—Hydrolysis was generally followed by acid-base titration, except for two experiments with isobornyl acetate, where the reaction was followed by g.l.c. (Table 2). For the runs where the concentration of perchloric acid was greater than 0·5M, the bulk of the acid was neutralised by the addition of a fixed amount of relatively concentrated sodium hydroxide, and the residue was titrated with dilute sodium hydroxide, with phenolphthalein as indicator, under nitrogen. Sealed tubes were used at high temperatures. The procedure for analysis by g.l.c. was similar to that used for separation of the products (p. 3298). In all the experiments, the integrated first- and second-order rate constants, k_1 and k_2, were calculated by graphical methods, by plotting log $(a - x)$ against time for the first-order reactions, and $x/(a - x)$ against time for the second-order reactions, which were carried out with equal concentrations of reactants. Toluene-*p*-sulphonic acid, in dilute solution, is as effective a catalyst as perchloric acid (Table 2).

TABLE 7

Exchange and bond fission in dioxan–water (3 : 2 v/v), at 45·0°
Isotopic abundance in atom-% excess: [Ester] *ca.* 0·02M

			Isotopic abundance					
					Alcohol			
Expt.	Reagent	Time (hr.)	H_2O	Ester	Hydrolysis	Cleavage	Control †	k_h/k_e
			Bornyl acetate					
1	1M-$HClO_4$	1·25	0·822	0·158	0·001	0·001	—	1·5
2	1·51M-$HClO_4$	0·56	0·774	0·106	—	—	—	1·7
3	1M-$HClO_4$	18 *	0·781	—	0·092	—	0·052	
4	2·8M-$HClO_4$	4 *	0·610	—	0·042	—	0·052	
5	0·02M-NaOH	2	0·894	0·15	0·00	—	—	1·8
			Isobornyl acetate					
6	0·55M-$HClO_4$	20·5	0·872	0·331	0·133	0·00		0·48
7	1M-$HClO_4$	10	0·822	0·340	0·219	0·00	0·493	0·42
8	0·13M-$HClO_4$	120 *	1·35	—	0·33	—	0·33	
9	0·02M-NaOH	12·4	0·894	0·346	0·004	—		0·48

* Complete hydrolysis. † Under conditions used for hydrolysis.

The values of the Arrhenius parameter, *E*, are given to the nearest 0·5 kcal. mole^{-1}, and those of ΔS^* to the nearest 0·5 e.u.

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WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES, UNIVERSITY COLLEGE,
GOWER STREET, LONDON W.C.1. [*Received, July* 28*th*, 1964.]