Tracer Studies on Ester Hydrolysis. Part II. The Acid Hydrolysis of* tert.*-Butyl Acetate.*

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Isotopic tracer studies on the acid-catalysed hydrolysis of *tert.*-butyl acetate, in water and in aqueous dioxan, show that although the fission in water is predominantly of the alkyl–oxygen bond ($A_{\mathrm{Al}}1$), yet in aqueous dioxan it is largely of the acyl–oxygen bond. Kinetic studies show a marked increase in hydrolysis rate in going from aqueous dioxan to pure water, and this increase in rate can be correlated with the change of position of bond fission.

CARBOXYLIC esters of tertiary aliphatic alcohols provide a favourable system for the observation of alkyl–oxygen fission in hydrolysis. The observation of racemisation with accompanying inversion of the alcohol obtained in the acid hydrolysis of optically active ethylmethyl*iso*hexylcarbinyl (1-ethyl-1 : 5-dimethylhexyl) acetate (Bunton, Hughes, Ingold, and Meigh, *Nature*, 1950, **166**, 679) demonstrates the existence of this bond fission. Similarly, the products isolated show that methanolysis of some *tert.*-butyl esters involves alkyl–oxygen bond fission (Cohen and Schneider, *J. Amer. Chem. Soc.*, 1941, **63**, 3382). In these systems hydrolysis or methanolysis in the presence of alkali gives acyl–oxygen bond fission.

The comparable system of the acid hydrolysis of *tert.*-butyl acetate has been studied by the use of ^{18}O as an isotopic tracer. In this system the aqueous hydrolysis was shown to involve fission of the alkyl–oxygen bond (Bunton, Comyns, and Wood, *Research*, 1951, **4**, 383). However, owing to the low solubility of the ester in water the hydrolysis was carried out under heterogeneous conditions, and it is convenient therefore to supplement the evidence obtained in hydrolysis by water with that of homogeneous acid hydrolysis in aqueous dioxan.

The observation of minima in the value of the acid catalysis constant throughout a series of esters (acetates and succinates), in which the alkyl group is varied from methyl to ethyl, *iso*propyl, and *tert.*-butyl (Olsson, *Z. phys. Chem.*, 1928, **133**, 233; Skrabal and Hugetz, *Monatsh.*, 1926, **47**, 17; Meyer, *Z. phys. Chem.*, 1909, **66**, 96; Homan, *Rec. Trav. chim.*, 1944, **63**, 181), can be interpreted as a possible change of mechanism from $A_{\mathrm{Ac}}2$ to $A_{\mathrm{Al}}1$. However, the existence of a pre-equilibrium between the neutral ester molecule and its conjugate acid precludes the use of this evidence as an unambiguous test for a change of mechanism, particularly as an increase in the inductive electron release from the alkyl group will favour the conjugate acid.

Position of Bond Fission.—The position of bond fission in ester hydrolysis can be determined unambiguously by the use of ^{18}O as an isotopic tracer, provided always that the possibility of extraneous isotopic exchange is eliminated by blank tests. In the experiments described here the *tert.*-butyl alcohol was isolated from the reaction mixture by direct distillation or by azeotropic distillation with benzene. The oxygen isotopic content of the *tert.*-butyl alcohol was determined by various methods; in certain experiments the alcohol–benzene azeotrope was pyrolysed over platinised quartz, and the oxides of carbon so produced were reduced by hydrogen to water with a thoriated nickel catalyst, the general

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method devised for elementary analysis of oxygen (Russell and Fulton, *Ind. Eng. Chem. Anal.*, 1933, **5**, 384). The water produced was then equilibrated with carbon dioxide. This general method has certain disadvantages : the large surfaces increase adsorption, and dilution and memory effects are large; therefore considerable time has to elapse between samples, and large samples (*ca.* 2 g.) of the alcohol are desirable.

In later experiments the sample was pyrolysed *in vacuo* over Monel gauze at 850°, or in a carbon tube heated *in vacuo* to *ca.* 1200° in an induction furnace. The latter methods give carbon monoxide directly, and the isotopic analyses were carried out directly on this gas.

The isotopic results and the methods used are listed in Table 1. This shows that acid hydrolysis in water gives almost complete alkyl-oxygen bond fission; in aqueous dioxan this proportion is reduced to *ca.* 36%. In neither solvent does the exchange of the alcohol complicate the result. The significance of these results can only be considered with the dependence of acid hydrolysis rate on the water content of the solvent.

TABLE 1. *Hydrolyses in isotopically enriched solvents at 25°.*

Expt. no.	Solvent	$[H^+]$	Time (hr.)	^{18}O abundance (atoms % excess) H_2O	^{18}O abundance (atoms % excess) Bu^tOH	Alkyl–oxygen fission (%)
1	Water	0·24	48	0·522	0·506	97
2	,,	0·175	26	0·438	0·428 *	98
3	Aq. 70% dioxan	0·175	144	0·438	0·153 *	35
4	,, ,,	0·240	70	0·438	0·165 *	38
Blank tests :						
	Water	0·27	48	0·327	0·026	
	Aq. 70% dioxan	0·17	98	0·692	0·011	
	,, ,,	0·167	98	0·692	0·010	

* Isotopic analyses by direct pyrolysis to CO.

Kinetics of Acid Hydrolysis.—The kinetics of acid hydrolysis of *tert.*-butyl acetate were followed by acid–alkali titration (Table 2). The effect of an increase in the water content is to increase the overall rate of hydrolysis and to modify the mechanism. If we assume that the isotopic evidence for alkyl–oxygen bond fission, obtained under non-kinetic conditions in water, can be applied to the more dilute solutions used in the rate measurements, the rates of acyl and alkyl oxygen bond fission can be calculated for the two solvents used (Table 3).

TABLE 2. *Kinetics of acid hydrolysis of* tert.*-butyl acetate at 25°.*

$[H^+]$ (mole l.$^{-1}$)	$[CNS^-]$ (mole l.$^{-1}$)	10^7k_1 (sec.$^{-1}$)	10^6k_A (sec.$^{-1}$ mole^{-1} l.)	$[H^+]$ (mole l.$^{-1}$)	$[CNS^-]$ (mole l.$^{-1}$)	10^7k_1 (sec.$^{-1}$)	10^6k_A (sec.$^{-1}$ mole^{-1} l.)
Solvent : H_2O				*Solvent* : Aq. 70% dioxan			
0·0996	0·109	141	142 *	0·0984	—	6·72	6·82
0·0996	0·170	148	149 *	0·0984	—	6·60	6·70

* These values are comparable with those obtained by Skrabal (*loc. cit.*), *viz.*, 1·26 × 10^{-4} sec.$^{-1}$ mole^{-1} l.; the difference is presumably due to the greater ionic strength of the solutions used in this work. Extrapolation to the ionic strength of Skrabal's work gives k_A = 1·28 × 10^{-4} sec.$^{-1}$ mole^{-1} l.

TABLE 3. *Rates of acid-catalysed alkyl- and acyl-oxygen fissions at 25°.**

Solvent	10^6k_A (overall)	10^6k_A (alkyl)	10^6k_A (acyl)
H_2O	128	*ca.* 124	*ca.* 4
Aq. 70% dioxan	6·76	2·4	4·3

* The percentages of alkyl–oxygen fission are taken as 97 and 36 in water and aqueous dioxan, respectively : the enrichment due to exchange between the alcohol and water is ignored.

This analysis shows that, whereas the rate of acid-catalysed acyl–oxygen fission ($A_{Ac}2$) is almost independent of the water content of the solvent (cf. hydrolysis of ethyl acetate by the $A_{Ac}2$ mechanism; Lapworth, *J.*, 1908, **93**, 100; Burrows, *J.*, 1919, **115**, 1230), the corresponding alkyl–oxygen fission is accelerated by an increase in the water content of the solvent. This solvent effect on the $A_{Al}1$ mechanism in *tert.*-butyl acetate is qualitatively similar to that observed in the acid hydrolysis of triphenylmethyl acetate (Part I), and in the acid hydrolysis of di-*tert.*-butyl succinate (Homan, *loc. cit.*), where we assume the positions of bond fission to be qualitatively similar to those observed in this work.

The overall mechanism of acid hydrolysis of *tert.*-butyl acetate in water by $A_{\text{Al}}1$ can be formulated as

$$CH_3{\cdot}CO_2{\cdot}CMe_3 + H^+ \xrightleftharpoons{\text{Fast}} [CH_3{\cdot}CO_2H{\cdot}CMe_3]^+$$

$$[CH_3{\cdot}CO_2H{-}\vdots CMe_3]^+ \xrightleftharpoons{\text{Slow}} CH_3{\cdot}CO_2H + {}^+CMe_3$$

$${}^+CMe_3 + H_2O \xrightleftharpoons{\text{Fast}} CMe_3{\cdot}OH + H^+$$

The mechanism $A_{\text{Al}}1$ involves a carbon–oxygen heterolysis as the rate-determining step of the reaction. Such heterolyses frequently generate a carbonium ion of sufficiently long life for it to be captured by a reagent other than the water molecule. Such intervention experiments have frequently been made with sodium azide as the reagent (*e.g.*, Bateman, Hughes, and Ingold, *J.*, **1940**, 974). It was thought possible that, in the acidic solutions used in these ester hydrolyses, the thiocyanate ion would be a more useful intervening agent. The hydrolysis of diphenylmethyl chloride in aqueous dioxan was in fact subject to marked intervention by this reagent. However, in water both the acid hydrolysis of *tert.*-butyl acetate and the hydrolysis of *tert.*-butyl chloride show no such intervention by thiocyanate, and this test therefore gives no evidence on the precise nature of the alkyl–oxygen fission examined.

EXPERIMENTAL

Preparation of Materials.—*tert.*-Butyl acetate was prepared from the alcohol by treatment with acetyl chloride in the presence of pyridine (Abramovitch, Shivers, Hudson, and Hauser, *J. Amer. Chem. Soc.*, **1943**, **65**, 986). A typical specimen had b. p. 97—98°, n_D^{25} 1·3480 (Found : C, 62·7; H, 10·5. Calc. for $C_6H_{12}O_2$: C, 62·2; H, 10·4%). Dioxan was purified by decomposition of the acetals with hydrochloric acid in a stream of nitrogen, followed by washing, drying, and finally distillation over sodium. The aqueous 70% dioxan solvent was made up by volume at room temperature.

Kinetic Measurements.—The kinetic runs were made in stoppered flasks. Samples were withdrawn at suitable intervals, the reaction stopped by addition of acetone, and the acid titrated with standard barium hydroxide. The rate coefficients were calculated from the equation $k_1 = [2{\cdot}3/(t_2 - t_1)]\log_{10} (a - x_1)/(a - x_2)$, where $(a - x_1)$ and $(a - x_2)$ are the concentrations of ester at times t_1 and t_2, respectively, and t is in seconds.

The possibility of intervention by thiocyanate ion in the hydrolyses of both *tert.*-butyl acetate and *tert.*-butyl chloride was tested by estimation of inorganic thiocyanate, in the course of the kinetic run, with silver nitrate. No intervention was observed in any of these hydrolyses. A typical experiment illustrating the kinetic form of hydrolyses and the non-intervention of thiocyanate ions is quoted below :

Run 33. Temp. 25·00° ± 0·05°. [HCl] = 0·0996M, [Bu^tOAc] = 0·0539M, [KCNS] = 0·170M. Solvent, water.

Acid estimation : 2·90-c.c. samples were titrated with 0·0599N-barium hydroxide. Thiocyanate estimation : 2·90-c.c. samples were back-titrated with 0·0452M-thiocyanate after addition of 10 c.c. of 0·1013N-silver nitrate.

Time (min.)	Acid titre (c.c.)	10^5k_1 (sec.$^{-1}$)	CNS^- titre (c.c.)	Time (min.)	Acid titre (c.c.)	10^5k_1 (sec.$^{-1}$)	CNS^- titre (c.c.)
0	5·00	—	—	1197	6·54	1·35	4·57
46	—	—	4·50	1585	6·77	1·40	—
136	5·36	1·48	4·65	7 days	7·35, 7·37	—	—
261	5·59	1·62	4·65	α (calc.)	7·42	—	—
396	5·80	1·54	4·60				

Mean value of $k_1 = 1{\cdot}48 \times 10^{-5}$ sec.$^{-1}$; $k_A = 1{\cdot}49 \times 10^{-4}$ sec.$^{-1}$ mole^{-1} l.

Position of bond fission. To minimise extraneous exchange between the *tert.*-butyl alcohol and water the hydrolyses were stopped after *ca.* 40% reaction.

The alcohol was isolated from the aqueous dioxan solvent by the following procedure. The solution was saturated with sodium sulphate and extracted with ether, and, after drying (K_2CO_3), the ether was evaporated. It was found that the alcohol could be separated as its azeotrope with benzene (Young, *J.*, **1902**, **81**, 746), with no contamination by dioxan or *tert.*-butyl acetate.

This isolation in the benzene azeotrope was used in one of the hydrolyses in water (Expt. 1). In the other (Expt. 2), the unhydrolysed ester was extracted with chloroform, the acid first neutralised, and the alcohol isolated by fractional distillation. Blank tests were carried out under the general conditions of the hydrolyses.

Expt. 2. Hydrolysis in water. The ester (5 c.c.) was shaken in 100 c.c. of enriched water ($[HClO_4] = 0{\cdot}175$M) for 26 hr. at 25°. The unchanged ester was extracted with chloroform, and the *tert.*-butyl alcohol distilled from a low-hold-up, metal spiral-packed column (b. p. 82·5—82·8°, n_D^{25} 1·3850).

Expt. 3. Hydrolysis in aqueous dioxan. The ester (10 c.c.) was hydrolysed in 100 c.c. of solvent for 144 hr. at 25°. The crude ether extract was dried, the ether evaporated, dry benzene added, and the azeotrope (b. p. 73·0—73·4°, n_D^{25} 1·4495) obtained by fractionation.

Two general methods were used for the isotopic assays. In the first (used for the product of Expt. 1), the alcohol was pyrolysed over hot platinised quartz, and the carbon oxides reduced with hydrogen over a thoriated nickel catalyst by the general method of Russell and Fulton (*loc. cit.*). The water produced was equilibriated with carbon dioxide, and this gas analyzed mass-spectrometically.

This method required comparatively large samples and was subject to large dilution and memory effects, and direct pyrolysis to carbon monoxide was used for most of the experiments. The samples of carbon monoxide were analyzed mass-spectrometrically; the absence of atmospheric nitrogen (giving mass 28) was demonstrated by the absence of argon.

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