

*The Kinetics of Alkyl-Oxygen Fission in Ester Hydrolysis.  
tert.-Butyl 2 : 4 : 6-Trimethylbenzoate in Aqueous Ethanol.*

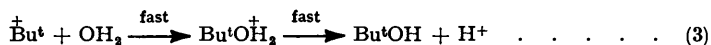
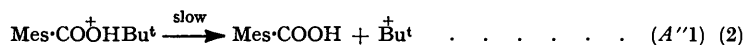
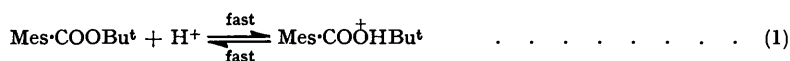
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The kinetics of the acid-catalysed hydrolysis of *tert.*-butyl 2 : 4 : 6-trimethylbenzoate have been studied in various water-ethanol mixtures, at various acid concentrations and at three temperatures. The Arrhenius equation is accurately followed but the values of  $E$  and  $A$  are significantly different from those found in the "normal" hydrolysis of esters. The variation of rate with solvent composition usually found in acid-catalysed reactions in this solvent is observed.

FOUR possible mechanisms for the acid-catalysed hydrolysis of esters, together with their steric and electronic requirements, have been described by Day and Ingold (*Trans. Faraday Soc.*, 1941, **37**, 686). Esters of primary alcohols are most commonly hydrolysed in acid conditions *via* mechanism  $A'2$  which involves attack by a water molecule on the carbonyl-carbon atom of the esterium ion and is thus highly sensitive to steric effects at this position.

Mechanism  $A'1$  involves as key intermediate a stable acylium ion,  $\text{RCO}^+$ . In general, esters of the sterically hindered 2 : 4 : 6-trimethylbenzoic acid resist hydrolysis in aqueous or alcoholic solvents, *i.e.*, by mechanism  $A'2$ , and form the acylium ion only in such solvents as pure sulphuric acid. Mechanisms  $A'1$  and  $A'2$  involve alkyl-oxygen fission,  $A'1$  being insensitive to steric hindrance but demanding strong electron release from the alkyl group. Cohen and Schneider (*J. Amer. Chem. Soc.*, 1941, **63**, 3382) have shown that *tert.*-butyl 2 : 4 : 6-trimethylbenzoate is readily hydrolysed in acidic aqueous and alcoholic media, and further, have proved that alkyl-oxygen fission is involved in alcoholysis, *tert.*-butyl methyl ether being obtained in neutral methanol, and a quantitative yield of 2 : 4 : 6-trimethylbenzoic acid, not the methyl ester, in methanolic hydrogen chloride, and we have assumed that alkyl-oxygen fission also occurs in aqueous ethanol. To distinguish kinetically between mechanisms  $A'1$  and  $A'2$  it is necessary to measure the variation of rate with water concentration. Mechanism  $A'1$  seems more likely by analogy with the well-known unimolecular hydrolysis of the *tert.*-butyl halides; further the *tert.*-butyl group is electron releasing and hence meets the requirement of this mechanism. The mechanism may be formulated thus :



where Mes denotes 2 : 4 : 6-trimethylphenyl.

Step (1) is the fast reversible addition of a proton to form the esterium ion, which slowly undergoes alkyl-oxygen fission in the rate-controlling step (2). The kinetic consequence is that  $dx/dt \propto [\text{H}^+][\text{ester}]$ ; *i.e.* in a medium of constant hydrogen-ion concentration, the rate, is of first order in ester, and the first-order rate constants ( $k_1$ ) so obtained are proportional to the catalyst concentration.

#### EXPERIMENTAL

*Preparation of Materials.*—*tert.*-Butyl 2 : 4 : 6-trimethylbenzoate, prepared as described by Cohen and Schneider (*loc. cit.*), who report b. p. 114–115°/3 mm.,  $d_4^{23}$  0.9654,  $n_D^{23}$  1.4920, was fractionated twice and then had b. p. 96°/0.6 mm.,  $d_4^{15}$  0.970,  $n_D^{18}$  1.4932.

Ethanol (2 l.) was successively distilled from concentrated sulphuric acid (25 c.c.) and sodium

hydroxide (10 g.), then refluxed with magnesium ethoxide (from 10 g. of magnesium in 200 c.c. of dry ethanol) for 4 hr., and distilled. The first 100 c.c. were rejected in each distillation.

*Solvents.*—The various solvent mixtures were made from measured volumes of ethanol and distilled water, and the compositions checked by density measurements. Stock aqueous ethanolic solutions of hydrogen chloride were made by bubbling the gas from "AnalaR" sodium chloride and concentrated sulphuric acid into each solvent mixture.

*Kinetic Measurements.*—At 77° and 85° the thermostat was constant to better than 0.1° but at 97°, where a boiling-water bath was used, the temperature varied between runs over several tenths of a degree owing to changes in the barometric pressure. As no consequent systematic variation in  $k_1$  was observed a mean temperature was taken.

Measured portions (5 c.c.) of solutions of the ester of known concentration, from which  $a$  was calculated, were pipetted into Pyrex-glass bulbs which were sealed and placed in the thermostat. After a measured time the total acid content was determined by titration with 0.01N-baryta, the increase in titre above that at zero time giving  $x$ . The rate constant  $k_1$  was then calculated from the formula  $k_1 = (1/t) \log_e a/(a - x)$ , 10–20 values being obtained from each run. Because 2 : 4 : 6-trimethylbenzoic acid is not esterified by ethanol in the presence of hydrogen chloride, the hydrolysis was not reversible and the straightforward first-order equation was adequate.

*Titration.*—Constant-boiling hydrochloric acid consistent with "assay" silver was used as standard. The end-point to phenolphthalein in 0.01N-solution was sharp in freshly boiled distilled water in an atmosphere of nitrogen. Volumetric glassware was standardised. No correction for the expansion of the solvent was made to the concentration terms as calculation showed that the resulting correction to  $E$  did not exceed the experimental error.

*Corrections due to the Reaction of the Catalyst with the Solvent.*—Bird, Hughes, and Ingold (*J.*, 1943, 258), using 0.1N-solutions in 88% ethanol at 75°, found a considerable decrease in rate constant after about 50% reaction, due to the liberated hydrogen bromide reacting with the solvent. To obviate this difficulty Timm and Hinshelwood (*J.*, 1938, 863), working at temperatures up to 150° with the more slowly hydrolysed ethyl benzoate, used benzenesulphonic acid; however with 0.01N-acid, only in 100% ethanol at 97° was the removal of acid so large that a simple correction did not yield a consistent value of  $k_1$ . Experiments with the acidified solvent alone were run in parallel with the hydrolysis and the decrease of titre was observed. A corresponding correction was then made, amounting to 2 and 6% of  $x$  in 80 and 90% ethanol at 97°, respectively. In 100% ethanol at 97° the rate constant for the removal of acid by ethanol was determined ( $k_1 = 5.3 \times 10^{-3} \text{ min.}^{-1}$ , when  $[\text{HCl}]_{t=0} = 0.0127$ ) and found to be *ca.* 1/3 of the rate of the hydrolysis. In these circumstances the correction was about 30%, and a hydrolysis rate constant accurate to only *ca.* 1/5 was obtained. In the remaining runs no correction was necessary.

The following are typical runs, with and without corrections.

a in mole/bulb. Temp. 97.3°. Baryta 0.01160N.						
Solvent : 60% EtOH; $a = 7.40 \times 10^{-5}$ ; [HCl] = 0.0101; [ester] = 0.0148.			Solvent : 90% EtOH; $a = 7.80 \times 10^{-5}$ ; [HCl] = 0.0093; [ester] = 0.0156.			
No correction			Correction = + $6 \times 10^{-4}$ c.c./min.			
Time (min.)	Titre (c.c.)	$10^3 k_1$ (min. <sup>-1</sup> )	Time (min.)	Titre (c.c.)	Titre (corr.) (c.c.)	$10^3 k_1$ (min. <sup>-1</sup> )
0	4.36	—	0	4.00	4.00	—
35	5.57	5.9	90	5.18	5.23	2.25
50	6.00	5.9	150	5.82	5.90	2.24
61	6.33	6.0	210	6.41	6.53	2.25
75	6.71	6.1	281	7.02	7.18	2.27
100	7.24	5.9	339	7.34	7.53	2.20
139	7.92	5.9	409	7.74	7.98	2.19
160	8.28	5.9	433	7.91	8.16	2.24
192	8.74	6.0	474	8.09	8.35	2.20
220	9.03	6.0				
254	9.27	5.8				Mean 2.23
		Mean 5.9				

## RESULTS AND DISCUSSION

The rate of hydrolysis of *tert.*-butyl 2 : 4 : 6-trimethylbenzoate is directly proportional to the concentration of the acid catalyst and of the ester (cf. Table 1): this is consistent with, but not conclusive for, mechanism A'1. No uncatalysed solvolytic reaction was

detected (cf. Fig. 1). The Arrhenius equation  $k_1/c_A = A_{\text{Arr.}}e^{-E_{\text{Arr.}}/RT}$  is accurately followed and  $E_{\text{Arr.}}$  is independent of solvent composition (cf. Table 2). The variation of rate with solvent composition is not great, e.g., the factor for change from 60% to 80% aqueous ethanol is 2.0.

TABLE 1. First-order rate constants ( $k_1$ ) for the hydrolysis of *tert.*-butyl 2 : 4 : 6-trimethylbenzoate.

( $C_A$  and  $C_E$  are the concentrations of hydrochloric acid and ester.)

Ethanol (% by vol.)	Temp.	$10^2 C_A$ (mole/l.)	$10^2 C_E$ (mole/l.)	$10^3 k_1$ (min. <sup>-1</sup> )	$10 k_1 / C_A$ (min. <sup>-1</sup> ) l. mole <sup>-1</sup>	$10^2 C_A$ (mole/l.)	$10^2 C_E$ (mole/l.)	$10^3 k_1$ (min. <sup>-1</sup> )	$10 k_1 / C_A$ (min. <sup>-1</sup> ) l. mole <sup>-1</sup>
60	97.3°	2.73	1.45	15.6	5.7	0.413	0.96	2.4	5.8
		1.71	2.43	9.8	5.7	0.406	1.38	2.5	6.1
		1.52	1.53	8.8	5.8	0.356	0.56	2.2	6.2
		1.01	1.48	5.9	5.8				
70	97.3	1.94	1.30	7.4	3.8	0.99	1.46	3.8	3.8
80	97.3	1.90	0.78	5.0	2.6	1.09	1.18	2.9	2.7
		1.61	1.54	4.6	2.8	0.76	0.95	2.1	2.8
		1.63	0.86	4.2	2.6	0.58	1.00	1.7	2.9
		1.45	0.83	4.1	2.8	0.160	1.69	0.46	2.9
		1.15	1.07	3.3	2.9				
91	97.3	1.88	1.24	4.5	2.4	0.93	1.56	2.2	2.4
100	97.3	1.27	1.68	17	13				
60	85.4	1.09	1.60	1.69	1.55	0.51	1.51	0.77	1.52
80	85.4	2.34	1.43	1.69	0.72	1.14	1.46	0.89	0.78
91	85.1	1.93	1.33	1.19	0.60				
60	77.7	2.08	1.51	1.30	0.63	1.10	1.43	0.72	0.65
70	76.8	0.88	1.27	0.31	0.35				

TABLE 2.

Ethanol (% by vol.)	$E_{\text{Arr.}}$ (kcal./mole)	$\log_{10} A_{\text{Arr.}}$ ( $A$ in sec. <sup>-1</sup> )	$\Delta S_{97.3}^\ddagger$ (cal. mole <sup>-1</sup> deg. <sup>-1</sup> )	Ethanol (% by vol.)	$E_{\text{Arr.}}$ (kcal./mole)	$\log_{10} A_{\text{Arr.}}$ ( $A$ in sec. <sup>-1</sup> )	$\Delta S_{97.3}^\ddagger$ (cal. mole <sup>-1</sup> deg. <sup>-1</sup> )
60	29.4	15.5	9.9	80	29.1	15.2	8.5
70	29.8	15.3	8.9	90	29.8	15.1	8.1
Mean	29.5						

$\log_{10} A$  was calculated by using the average value of  $E$ .

*The Rate of the Reaction.*—The value of  $\log_{10}(10^3 k_1 / c_A)$  (sec.<sup>-1</sup>) is 4.1 in 60% ethanol at 100°. Timm and Hinshelwood (*loc. cit.*) list 13 values ranging from 4.0 to 0.7 for the ethyl esters of substituted aromatic and aliphatic acids. For benzoic and *p*-toluic esters the values are 1.95 and 1.89. The acid hydrolysis of *tert.*-butyl 2 : 4 : 6-trimethylbenzoate is thus as fast as that of ethyl acetate and over a hundred times as fast as those of ethyl benzoate and *p*-toluate at 100°.

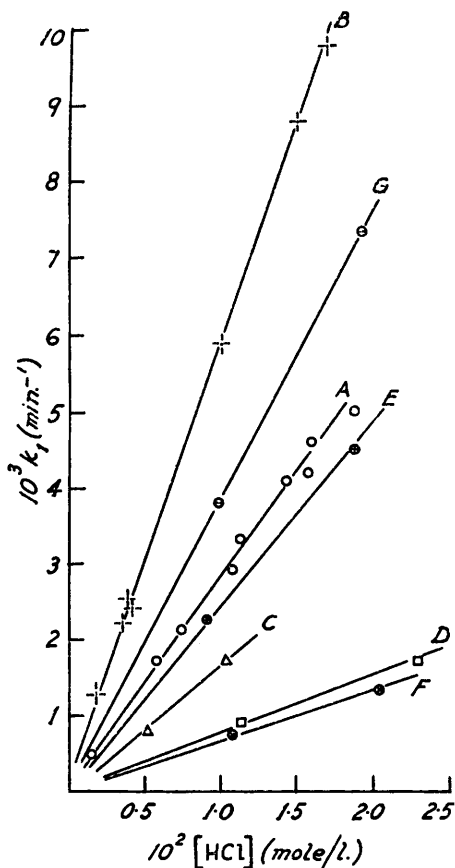
*The Value of  $E_{\text{Arr.}}$* —The magnitude of  $E$  is significantly different from those found in the normal acid hydrolysis of esters involving acyl-oxygen fission. Timm and Hinshelwood (*loc. cit.*) and Newling and Hinshelwood (*J.*, 1936, 1357) found values of 17–21 kcal./mole for the methyl and ethyl esters of various benzoic acids in 60% ethanol and 60% acetone; Davies and Evans (*J.*, 1940, 339) and Smith and Steele (*J. Amer. Chem. Soc.*, 1941, 63, 3466) found 15–17 kcal./mole for ethyl esters of aliphatic acids in 70% acetone; and Tommila and Hinshelwood (*J.*, 1938, 1806) and Newling and Hinshelwood (*loc. cit.*) found 14–17 kcal./mole for various benzyl and phenyl acetates in 60% acetone. Timm and Hinshelwood (*loc. cit.*) have shown that electron-releasing groups (e.g. methyl) attached to the benzoic acid raised the activation energy for the ethyl benzoates. The increase is of the order of 0.1 kcal./mole for one methyl group, and it is not likely therefore that the present value of 29 kcal./mole can be explained in this way.

A well-known reaction that involves the rupture of an alkyl-oxygen bond is the formation of an alkyl halide from an alcohol. Hinshelwood (*J.*, 1935, 599) has studied the reaction of methanol and *tert.*-butanol with hydrogen chloride, and Bennett and Reynolds (*J.*, 1935, 131) that of methanol with hydrogen bromide. The reactions have activation

energies of 26–27 kcal./mole. For the reaction of ten higher aliphatic alcohols of both straight and branched chains Bennett and Reynolds (*loc. cit.*) find activation energies of 29–31 kcal./mole. These values are in contrast to those found in the reaction of an alcohol with a carboxylic acid, which involves acyl-oxygen fission, viz. 10–15 kcal./mole, but are comparable with the present value.

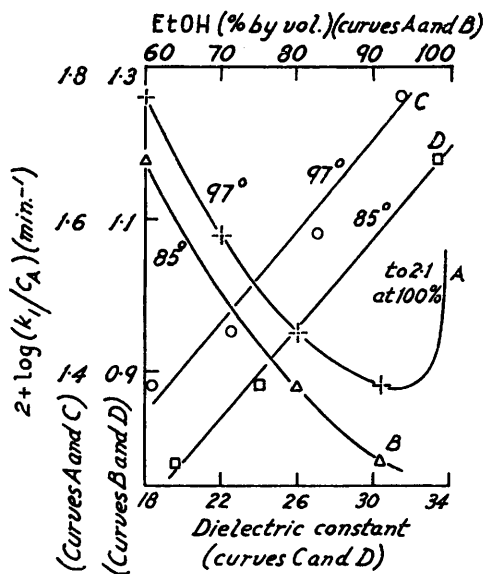
An interesting contrast between alkyl-oxygen and acyl-oxygen fission is shown in the rearrangement and hydrolysis of 1-ethynylbut-2-enyl acetate (Braude, *J.*, 1948, 795) in

FIG. 1.



A, 80% EtOH, 97° C.	E, 91% EtOH, 97° C.
B, 60% " 97° C.	F, 60% " 77° C.
C, 60% " 85° C.	G, 70% " 97° C.
D, 80% " 85° C.	

FIG. 2.



aqueous dioxan. As far as the positions of the ruptured and newly formed alkyl-oxygen bonds are concerned this rearrangement bears the same relation to Day and Ingold's mechanism  $A''2$  (*loc. cit.*) as does  $S_N2'$  to  $S_N2$  (de la Mare, Hughes, and Vernon, *Nature*, 1952, 169, 672) but because of the strongly electron-attracting ethynyl group the hydrolysis is normal. For the hydrolysis  $E_{Arr.} = 19-20$  kcal./mole whereas for the rearrangement  $E_{Arr.} = 27-28$  kcal./mole.

*The Value of  $A_{Arr.}$ .*— $\log_{10} A_{Arr.}$ , shown in Table 2, has the value 15–16. This is of a different order from that found in the normal acid hydrolysis of esters. Tommila and Hinshelwood, Timm and Hinshelwood, and Davies and Evans (*loc. cit.*) find values for  $\log_{10} PZ$  of 7–8, 5–8, and 6–8, respectively. For anionotropic rearrangements Braude

and Jones (*J.*, 1946, 122, 128) and Braude and Stern (*J.*, 1947, 1096) find  $\log_{10} A = 13-18$  (32 cases with 2 exceptions).  $A$  is related to the entropy of activation by the expression  $A = e kT / h e^{\Delta S^\ddagger / R}$  (Glasstone, Laidler, and Eyring, "The Theory of Rate Processes," McGraw-Hill, 1941, p. 417). The values of  $\Delta S^\ddagger$ , tabulated in Table 2, are substantially constant with varying solvent composition. The positive value of 8-10 cal. mole<sup>-1</sup> deg.<sup>-1</sup> contrasts with the negative value of 14-16 cal. mole<sup>-1</sup> deg.<sup>-1</sup> found by Braude (*loc. cit.*) in the hydrolysis of 1-ethynylbut-2-enyl acetate, which involves acyl-oxygen fission, but is comparable with the value found for the rearrangement which involves alkyl-oxygen fission. The positive value is also consistent with the proposed unimolecular mechanism.

*Variation of Rate with the Dielectric Constant of the Solvent.*—Over the limited range of solvent composition, 60-90% ethanol, the variation in rate follows approximately the relation,  $\log_{10} (k_1/C_A) = mD + n$ , where  $D$  is the dielectric constant of the alcohol-water mixture at the temperature concerned, and  $m$  and  $n$  are constants (cf. Fig. 2). The dielectric constants were obtained by interpolation and extrapolation from Akerlöf's data (*J. Amer. Chem. Soc.*, 1932, 54, 4130). At 85°  $m = 0.029$  and at 97°  $m = 0.030$ . For the anionotropic rearrangement of alcohols, Braude (*J.*, 1944, 444) finds values of  $m = 0.04-0.06$ , showing a larger variation of rate with dielectric constant; the value of  $m$  is also independent of temperature. In the hydrolysis of 1-ethynylbut-2-enyl acetate, involving acyl-oxygen fission, however, the values of  $m$  are temperature-dependent. In the present case the range of measurement is not sufficiently extensive to permit any conclusion to be drawn; however the constancy of  $m$  is in accord with the mechanism.

*The Isodielectric Energy of Activation.*—The isodielectric energy of activation is given by  $E_D = E_{\text{exp.}} + \Delta E_D$  (Braude, *loc. cit.*), where  $E_D = 2.3RT_1T_2mb$ ,  $b$  being the magnitude of the temperature gradient of dielectric constant for the solvent. The values of  $\Delta E_D$  for 60 and 80% ethanol are 3.0 and 2.5 kcal./mole, the difference, 0.5 kcal./mole, being of the same order as the probable error in  $E_{\text{exp.}}$ . Thus the experimental and isodielectric energies of activation are both substantially independent of solvent composition.

*The Variation of Rate with Solvent Composition.*—The plot of the catalytic constant  $k_1/c_A$  against solvent composition (Fig. 2) shows a steady fall from 60 to 90% ethanol, a minimum occurs at about 95% ethanol and thereafter the curve rises steeply to a value at 100% considerably in excess of that at 60% ethanol. This is in accordance with the well-known behaviour of acid-catalysed reactions in aqueous ethanol (for leading references see Braude, *J.*, 1944, 443) and has been quantitatively explained in the case of anionotropic rearrangements (Braude and Stern, *J.*, 1948, 1982) in terms of the varying acidity function of the medium.

*The Variation of Rate with Acid Concentration.*—Although a strict linear proportionality holds between  $k_1$  and  $C_A$  (Fig. 1) the relations between  $k_1$  and  $C_A$  and  $k_1$  and  $H$  (acidity function), derived by Braude (*loc. cit.*) for the determination of the rate-controlling step in an analogous system, are not diagnostic in the present low acid concentrations where it is likely that  $H = n \log C_A + m$  and  $n \approx 1.00$  in aqueous ethanol (cf. Braude, *J.*, 1948, 1973).

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