

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

By V. R. STIMSON.

[Reprint Order No. 5937.]

The kinetics of the acid-catalysed hydrolysis of *tert.*-butyl 2 : 4 : 6-trimethylbenzoate have been studied in acetone-water mixtures at various acid concentrations and at three temperatures, and in acetone-ethanol mixtures at 97°. The Arrhenius equation is accurately followed, and the values of E and A are significantly different from those found in ester hydrolysis with acyl-oxygen fission. The variation of rate with solvent composition is discussed in terms of proton-availability.

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 have proved that alkyl-oxygen fission is involved in alcoholysis. Stimson and Watson (Part I *) have shown that the kinetics of the acid-catalysed hydrolysis in aqueous ethanol display features not usually found in ester hydrolysis with acyl-oxygen fission. The hydrolysis has now been studied in aqueous acetone.

EXPERIMENTAL

Acetone (2 l.) was refluxed with potassium permanganate until the pink colour remained, distilled, dried (K_2CO_3), and distilled, the first 100 c.c. being rejected; the fraction used had b. p. 53.3°/680 mm., n_D^{20} 1.3598. The experimental procedure has been described (Part I, *loc. cit.*). All runs (except *a*, *b*, *c*, and *d*) gave integrated first-order rate constants (\bar{k}_1) (Bateman, Hughes, and Ingold, *J.*, 1940, 963) that agreed to *ca.* 1 part in 50 parts.

As previously noted by Church and Hughes (*J.*, 1940, 920), the acid titre decreased when hydrochloric acid was heated in acetone containing only small quantities of water. The decrease per hour was found to be *ca.* 1% of the titre in 98% acetone at 97° for 0.01*N*-solutions. With benzenesulphonic acid, however, the titre after 15 hr. under the same conditions agreed to 1 part in 200 parts with the initial titre.

RESULTS AND DISCUSSION

The hydrolysis of *tert.*-butyl 2 : 4 : 6-trimethylbenzoate in aqueous acetone accurately follows first-order kinetics (except in cases *a*, *b*, *c*, and *d*) (see Table 1) and the rate constants (\bar{k}_1) are independent of the ester concentration and proportional to the acid-catalyst concentration, which is in accordance with the kinetic requirements of the proposed mechanism $A''1$ (Part I, *loc. cit.*).

The Arrhenius equation $k_1/c_A = A_{Arr.} \exp(-E_{Arr.}/RT)$ is obeyed in 60% acetone where $E_{Arr.} = 30.5 \pm 0.5$ kcal./mole, $\log_{10} A_{Arr.}$ (sec.⁻¹) = 16.1, and ΔS_{97}^\ddagger (cf. Part I) = 12 cal. mole⁻¹ deg.⁻¹. In 80% acetone these values are 31.0 kcal./mole, 16.2, and 13 cal. mole⁻¹ deg.⁻¹, respectively. The value of $\log_{10}(10^6 k_1/c_A)$ (k_1 in sec.⁻¹) is 4.1 (calc.) at 100°

* Part I, *J.*, 1954, 2848.

in 60% aqueous acetone, this rate being more than 100 times that of the hydrolysis of ethyl esters of nine substituted benzoic acids in the same solvent (Timm and Hinshelwood, *J.*, 1938, 862).

It is clear from its high rate that this reaction is not sterically hindered. In general, the rate of hydrolysis is not very different from that in aqueous ethanol of comparable composition. The activation energy is again of the order of 30 kcal./mole, which is quite different from that for acid-catalysed hydrolysis involving acyl-oxygen fission in this

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, in moles/l., of acid catalyst and ester, respectively.)

Solvent : Acetone-water.						Solvent : Acetone-ethanol.*					
COMe ₂ (% by vol.)	Temp.	10 ² c_A	10 ² c_E	10 ³ k_1 (min. ⁻¹)	10 k_1/c_A *	COMe ₂ (% by vol.)	10 ² c_A	10 ² c_E	Temp. 97.2° 10 ³ k_1 (min. ⁻¹)	10 k_1/c_A *	
60	97.2°	2.00	1.73	11.9	5.9	0	0.56	1.47	9.7	17.1	
"	"	1.52	1.27	8.6	5.6	10	0.51	1.45	8.2	16.1	
"	"	1.10	1.13	6.4	5.8	20	0.55	1.27	7.6	13.8	
"	"	0.72	1.35	4.2	5.8	40	0.54	1.85	7.2	13.3	
"	84.3	1.06	1.41	1.36	1.28	60	0.52	1.70	6.5	12.4	
"	72.3	2.39	2.30	0.68	0.285	80	0.54	1.51	5.8	10.7	
80	97.2	1.09	1.46	4.4	4.0	90	0.55	1.78	5.6 ^b	10.2	
"	84.3	1.11	1.71	0.96	0.86						
90	97.1	1.13	1.31	3.9	3.5						
95	97.2	1.15	1.33	2.9 ^a	2.5						
96	97.2	1.62	1.60	3.4 ^c	2.1						
98	97.2	1.89	1.75	2.2 ^d	1.2						

(a), (b), (c), (d). In solvent mixtures less aqueous than 90% acetone and with hydrochloric acid as catalyst the reaction did not follow the simple first-order equation, the rate falling as the reaction proceeded. For (a) and (b) $\bar{k}_1^{(0.5)}/k_1^{(0)} = 0.9$, and for (c) and (d) 0.7 and 0.6. The value of $k_1^{(0)}$ was obtained by extrapolation to zero time. The cause of the fall in rate in (a), (c), and (d) is largely the loss of hydrochloric acid by reaction with acetone. (e) Benzenesulphonic acid was used as catalyst (cf. Part I). The reaction in this solvent is $C_6H_5Me_3CO_2Bu^t + HOEt \longrightarrow C_6H_5Me_3CO_2H + Bu^tOEt$.

* In units min.⁻¹ l. mole⁻¹.

solvent (Timm and Hinshelwood, *loc. cit.*; Davies and Evans, *J.*, 1940, 339; Smith and Steele, *J. Amer. Chem. Soc.*, 1941, 63, 3466). The values of A_{Arr} and ΔS_{97}^\ddagger are comparable with those found in aqueous ethanol (Part I).

As in aqueous ethanol (Part I) $\log_{10} k_1/c_A = mD + n$ for 60–90% acetone (cf. Fig. 1). The value of m (0.016) is independent of temperature. In 60 and 80% acetone, $\Delta E_D = 1.7$ and 1.4 kcal./mole, respectively.

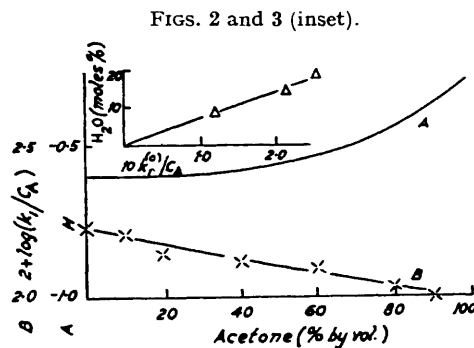
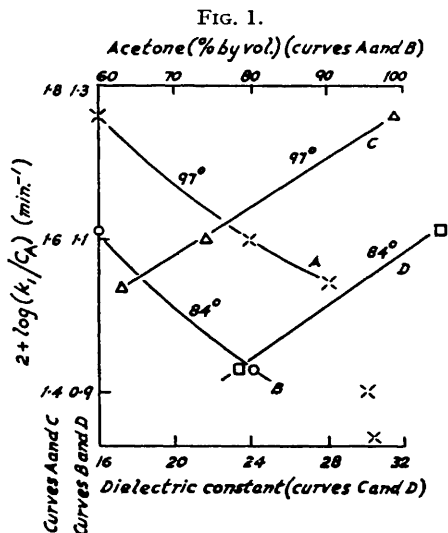
The mechanism $A''1$ proposed in Part I is consistent with the demonstration that racemisation occurs in the acid-catalysed hydrolysis of the acetate of the tertiary alcohol isohexylethylmethylcarbinol (3 : 7-dimethyloctan-3-ol) in 70% aqueous acetone at 76° (Bunton, Hughes, Ingold, and Meigh, *Nature*, 1950, 166, 680). They found k_1/c_A to be 6.2×10^{-1} min.⁻¹ l. mole⁻¹, which is 20 times the rate for *tert.*-butyl 2 : 4 : 6-trimethylbenzoate interpolated from the present results. The relation between these two rates is of the expected kind and order of magnitude.

TABLE 2. *First-order rate constants for the hydrolysis at 97° and the H function for the solvent.^a*

Aqueous ethanol. ^{b,c}				Aqueous acetone.			
EtOH (%)	$\log_{10} k' - H$	EtOH (%)	$\log_{10} k' - H$	COMe ₂ (%)	$\log_{10} k' - H$	COMe ₂ (%)	$\log_{10} k' - H$
60	0.8	90	0.6	60	0.9	90	0.9
70	0.7	100	1.8	80	1.0	95	0.5
80	0.7						

^a The H function is that of Braude (*J.*, 1948, 1971) and is the negative of the Hammett acidity function. An increase in H corresponds to an increase in the protonating power of the solvent. No values of H for 0.01M-hydrogen chloride in the mixed solvents are available but from the relation between H and c_A it seems likely that the H -solvent composition curves for 0.01M- and 0.1M-hydrogen chloride will be parallel; the values of H were taken as one unit less than those of 0.1M-hydrogen chloride (Braude and Stern, *J.*, 1948, 1976). ^b From Part I. ^c k' is the rate constant interpolated for 0.0100M-hydrogen chloride.

Since primary alkyl esters of 2 : 4 : 6-trimethylbenzoic acid are hydrolysed only with difficulty in aqueous or alcoholic solvents it appears unlikely that hydrolysis with acyl-oxygen fission, *i.e.*, by mechanism $A_{Ac}2$, occurs at an appreciable rate in any esters of this acid, this mechanism being influenced more strongly by the acid than the alcohol portion of the ester. In non-aqueous solvents acyl-oxygen fission would lead to trans-esterification, in the present case by the reaction $C_6H_2Me_3 \cdot CO_2Bu^t + HOEt \rightarrow C_6H_2Me_3 \cdot CO_2Et + Bu^tOH$, no acid being produced. Cohen and Schneider (*loc. cit.*) found that 100% of 2 : 4 : 6-trimethylbenzoic acid was produced in methanolysis, and in the present case, where the initial quantity of ester was measured by weighing and the reaction followed by titrating the acid produced; good first-order constants were obtained throughout the reaction in ethanol and ethanol-acetone, so that the reaction must occur almost entirely by alkyl-oxygen fission in these solvents. The rate shows that hydrolysis by this mechanism is not unusually difficult; the mechanism should be available in aqueous solvents and the similar rate supports this contention.



Variation of Rate with Solvent Composition.—For the proposed mechanism (Part I) variations of rate with solvent composition may occur in the protonating (step 1) and the bond-breaking (step 2) process. The effect in the former may be considered by the method that Braude and Stern (*J.*, 1948, 1982) have used in the case of anionotropic rearrangement. The values of $(\log_{10} k' - H)$ (Table 2) are reasonably constant for solvent mixtures containing up to 90% of the organic component. Protonation of esters is not likely to vary in exactly the same way as that of the nitroanilines with which H was measured, so that $\log_{10} k' - H$ cannot be expected to be strictly constant, and it is noteworthy that the same kind of small variation in $\log_{10} k' - H$ found by Braude and Stern (*loc. cit.*) for the alcohols is found in the present case. They showed that a constant difference between $\log_{10} k'$ and H is evidence that the protonation step is fast.

In the limited range of solvents used (those containing 60–90% of ethanol or acetone) variations in rate may be accounted for by a consideration of step 1, so that the effect due to step 2 is probably small. In less aqueous solvents other considerations become necessary as is shown by a number of features.

(i) Although in 100% ethanol the rate is 5 times that in 90% ethanol (Part I), yet it is only *ca.* 1/10 of that expected from a consideration of H alone (*cf.* Table 2). No such discrepancy is observed in anionotropic rearrangements in which the slow second step is internal (Braude and Stern, *loc. cit.*; Braude, *J.*, 1948, 794). In the present case the solvent, especially when of low water content, is likely to have a significant effect on the second step, the production of a molecule and an ion.

(ii) In aqueous acetone containing more than 90% of acetone the rate decreases (cf. Fig. 1) although the H function rises steeply; in fact for more than 95% of acetone the rate is roughly proportional to the amount of water present (Fig. 3), which is like the behaviour of S_N1 reactions (Bateman, Cooper, and Hughes, *J.*, 1940, 913).

It is suggested that as long as the solvating power of the solvent remains high owing to considerable water content, the variation of rate with solvent composition is determined largely by the protonating power of the medium, but when this is not so the power of the solvent to assist the second step becomes the determining factor.

Some confirmation of this is afforded by the rate in ethanol-acetone mixtures where the H function shows no minimum but rises steadily with increasing acetone content (Braude and Stern, *loc. cit.*); the rate falls, however, approximately linearly with the ethanol content (Fig. 2).

The author thanks Dr. N. V. Riggs for discussion.

NEW ENGLAND UNIVERSITY,
ARMIDALE, N.S.W., AUSTRALIA.

[Received, December 3rd, 1954.]
