

The Brønsted Acid-catalysed Hydrolysis of Acyl Fluorides in Aqueous Media

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In dioxane–water mixtures rich in dioxane, the hydrolysis of benzoyl fluoride is catalysed by hydrogen ions by two mechanisms, one dominant at low, and the other at high, values of $[H_3O^+]$. In purely aqueous solutions, and in water-rich dioxane–water mixtures, the only catalysis observed is that at high acid concentrations. The effect of temperature, and of *p*-substituents suggests this later catalysis involves an A1 mechanism. We tentatively assign an AB_{AC}3 mechanism to the catalysis found at low acid concentrations in dioxane-rich media. The hydrolysis of phenylacetyl fluoride in dioxane–water exhibits a behaviour pattern similar to that found for benzoyl fluoride.

Of acyl halides only the fluorides have as yet been found to exhibit a Brønsted acid-catalysed hydrolysis [eqn. (1)] in aqueous



media. This has been attributed to the greater affinity of F, than of Cl, Br or I for protons.¹ Previous work shows that the hydrolyses of acetyl, butyryl, and benzoyl fluorides in a 60% (v/v) dioxane–water solvent are detectably catalysed by hydrogen ions² when $[H_3O^+] > 0.05 \text{ mol dm}^{-3}$. The ratio k_{H^+}/k_0 [where k_{H^+} and k_0 are the (second-order) catalytic rate constant and the spontaneous rate constant, respectively] is *ca.* 5 for all three fluorides. The rate of the catalysed reaction follows $[H_3O^+]$ rather than H_0 over the acidity range covered (0–1.4 mol dm⁻³), and an A2 mechanism was suggested. For benzoyl fluoride studies³ with acetone–water mixtures using a limited range of $[H_3O^+]$ values, also reveal catalysis, show that it is not due to a positive salt effect, and suggest that the ratio k_{H^+}/k_0 falls as the water content of the solvent rises (k_0 increases more rapidly than does k_{H^+}). Recent work⁴ with benzoyl fluoride in a purely aqueous solvent is compatible with this result, and shows that the catalysed reaction is not detectable even at $[H_3O^+] = 1.0 \text{ mol dm}^{-3}$. However, a study⁵ of the reaction of acetyl fluoride in a purely aqueous solvent indicates that k_{H^+}/k_0 has increased to *ca.* 200, and that the catalysis is readily detectable when $[H_3O^+] \approx 10^{-3} \text{ mol dm}^{-3}$. This contrasting behaviour led us to examine such systems in more detail over a wider range of acidity. We report here on the susceptibility to catalysis of three *p*-substituted benzoyl fluorides in water, and on the behaviour of benzoyl and phenylacetyl fluorides in various dioxane–water mixtures.

Experimental

Materials.—Benzoyl fluoride was the Aldrich product. The other fluorides were prepared by slow distillation of the corresponding chloride with an excess of dry potassium hydrogen difluoride. *p*-Methyl and *p*-fluoro-benzoyl fluorides⁶ had b.p. 174 and 110 °C, respectively, and phenylacetyl fluoride⁷ had b.p. 85 °C/15 mmHg. All hydrolysed to give an effectively quantitative yield of the parent carboxylic acid. Perchloric acid was of AnalaR grade and dioxane the Aldrich HPLC grade.

Kinetics.—The hydrolyses were followed spectroscopically by observing the loss of acyl fluoride. The fluorides absorb strongly at *ca.* 225 nm and weakly at *ca.* 260 nm. The product acids

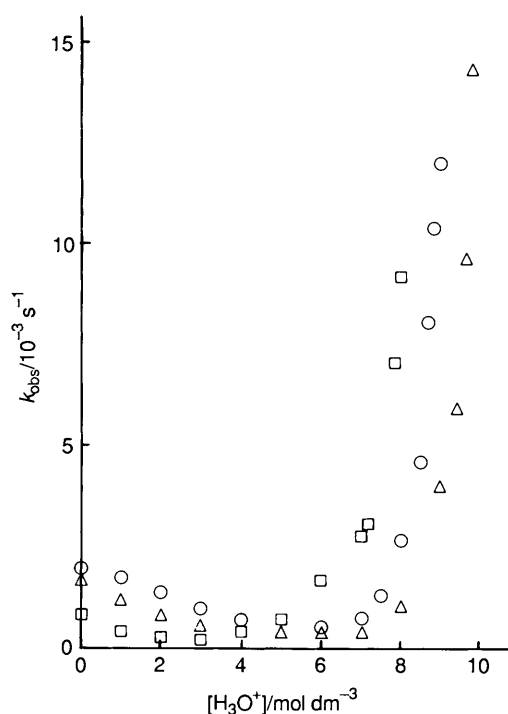


Fig. 1 Dependence of k_{obs} on $[H_3O^+]$ in water at 25 °C: $[p\text{-RC}_6\text{H}_4\text{COF}]_{initial} \approx 10^{-4} \text{ mol dm}^{-3}$; H_3O^+ from $HClO_4$; \square , R = Me; \circ , R = H; \triangle , R = F

absorb less strongly and at slightly shorter wavelengths. Good isosbestic points were obtained, and the reactions were accurately first-order over several half-lives. The observed first-order rate constant, k_{obs} , was reproducible to within $\pm 6\%$. For each solvent k_{obs} was measured for a wide range of $[H_3O^+]$ values, and some effects of temperature and of added sodium perchlorate were also studied. The acyl fluoride was added to a reaction mixture as a stock solution in dioxane and an otherwise purely aqueous solvent then contained *ca.* 1% (v/v) dioxane. In making solutions of perchloric acid in the mixed solvents allowance was made for the water content of the stock perchloric acid. Our rate constants are in Table 1 and Figs. 1–4, together with the concentration and other conditions.

Results and Discussion

Our results for the three benzoyl fluorides in aqueous solution are in Fig. 1. The values for benzoyl fluoride itself (Fig. 1) are in good numerical agreement with the (few) values given⁴ by

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Table 1 Rate constants for hydrolysis of acyl fluorides

(1) <i>p</i> -RC ₆ H ₄ COF ^a in water at 25 °C					
R	$k_0/10^{-3} \text{ s}^{-1}$	$k'_{\text{H}^+}/10^{-8} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	m^*m^\ddagger		
Me	0.79	380	0.70 ± 0.04		
H	2.0	3.1	1.1 ± 0.03		
F	1.7	7.1	0.87 ± 0.03		
(2) PhCOF in dioxane–water mixtures ^b					
(i) Spontaneous hydrolysis and catalysis at low [H ₃ O ⁺] at 25 °C					
Dioxane (% v/v)	$k_0/10^{-4} \text{ s}^{-1}$	$k'_{\text{H}^+}/10^{-4} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$			
0	20				
20	4.0				
40	1.3	≈ 3.9			
50	0.90	3.3			
60	0.39 (0.65) ^c	2.5			
60	0.39 ^d				
60	0.36 ^e				
(ii) Effect of temperature					
[HClO ₄]/mol dm ⁻³	Dioxane (%)	T/°C	$k_{\text{obs}}/10^{-4} \text{ s}^{-1}$	$\Delta H^\ddagger/\text{kJ mol}^{-1}$	$\Delta S^\ddagger/\text{J K}^{-1} \text{ mol}^{-1}$
0.60	60	25.0	1.6	83 ± 6^f	-55 ± 7
		30.0	3.1		
		34.5	4.9		
		40.0	7.3		
6.8	40	25.0	22	103 ± 8	-20 ± 10^g
		30.0	46		
		34.5	97		
		40.0	167		
(3) PhCH ₂ COF in dioxane–water mixtures ^h					
(i) Spontaneous hydrolysis and catalysis at low [H ₃ O ⁺] at 25 °C					
Dioxane (% v/v)	$k_0/10^{-4} \text{ s}^{-1}$	$k'_{\text{H}^+}/10^{-4} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$			
5	21				
20	9.3				
60	0.41	2.3			
60	0.40 ⁱ				
60	0.38 ^j				
(ii) Effect of temperature for 60% (v/v) dioxane mixtures					
[HClO ₄]/mol dm ⁻³	T/°C	$k_{\text{obs}}/10^{-4} \text{ s}^{-1}$	$\Delta H^\ddagger/\text{kJ mol}^{-1}$	$\Delta S^\ddagger/\text{J K}^{-1} \text{ mol}^{-1}$	
0	18.0	0.30	30 ± 3	-196 ± 10	
	25.0	0.41			
	32.0	0.55			
0.60	18.0	0.95	67 ± 6^k	-90 ± 15	
	25.0	1.5			
	32.0	3.3			
5.89	18.0	4.1	100 ± 10^l	-24 ± 10^m	
	25.0	9.1			
	32.0	27			

^a [ArCOF]_{initial} $\approx 10^{-4} \text{ mol dm}^{-3}$. For k_0 and k'_{H^+} see text (error in $k'_{\text{H}^+} \pm 30\%$). ^b [PhCOF]_{initial} $\approx 10^{-4} \text{ mol dm}^{-3}$. ^c 34.5 °C. ^{d,e} [NaClO₄] = 0.10 and 0.50 mol dm⁻³, respectively; k'_{H^+} = second-order (catalytic) rate constant at low [H₃O⁺] from slopes of plots in Fig. 3. ^f Calculated after correction for spontaneous rate. ^g Calculated (approximately) assuming value for k'_{H^+} is half that in water. ^h [PhCH₂COF]_{initial} $\approx 10^{-3} \text{ mol dm}^{-3}$. ^{i,j} [NaClO₄] = 0.10 and 0.50 mol dm⁻³, respectively. ^k Calculated after correction for spontaneous rate. ^l Calculated after (approximate) correction for catalysis at low [H₃O⁺]. ^m Calculated (approximately) assuming k'_{H^+} is one third value in 5% dioxane mixture (see the text).

Jencks and Song; catalysis is not detected when [H₃O⁺] $\approx 6.0 \text{ mol dm}^{-3}$, and k_{obs} even falls slightly in this region owing to a negative salt effect. This slow decrease in k_{obs} as [H₃O⁺] rises can be seen for all the fluorides in Fig. 1. Eventually, however, we find that catalysis does appear. It becomes detectable at a somewhat different [H₃O⁺] value for each fluoride, but relatively high concentrations are required. The k_{obs} values at [H₃O⁺] = 0 (k_0 , Table 1) are in good agreement with Jencks

and Song's for both the *p*-Me and *p*-H compounds. (These authors did not study the *p*-F derivative). The results at high acid concentrations are plotted⁸ against the excess acidity⁹ in Fig. 2. Approximate values of the second-order (catalytic) rate constants (k'_{H^+}) for the acid catalysis can be obtained⁸ from the intercepts at $X = 0$ of the plots in Fig. 2. The values (Table 1) show that electron-release assists the catalytic path, and a Hammett plot against σ^+ has a slope $\rho^+ > 6$. The slopes of the

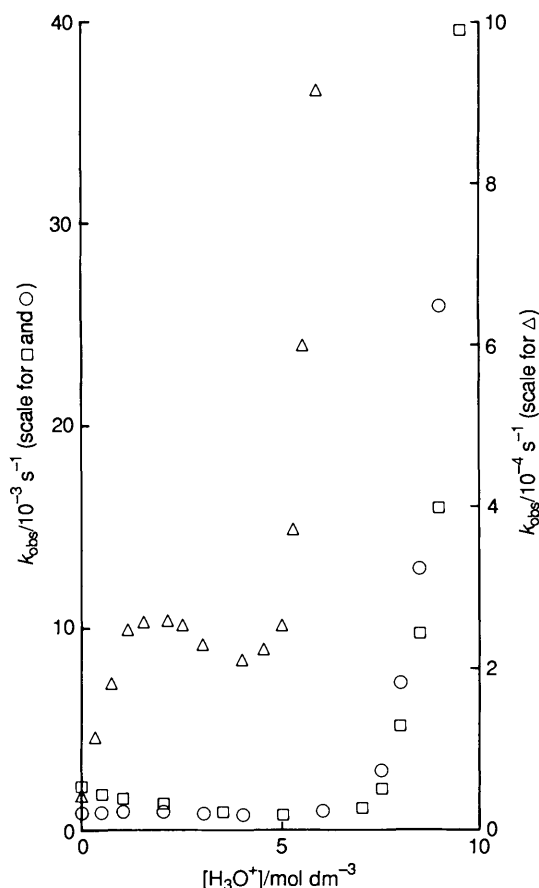


Fig. 4 Effect of solvent composition on the variation of k_{obs} with $[\text{H}_3\text{O}^+]$ at 25 °C for phenylacetyl fluoride: Δ , 60:40; \circ , 20:80; \square , 5:95 (v/v) dioxane–water

(Table 1). If a negative salt effect is operating as $[\text{HClO}_4]$ increases, the $\text{AB}_{\text{AC}3}$ mechanism could be the explanation of our results. It implies that the spontaneous hydrolysis proceeds *via* a tetrahedral intermediate.

$$k_{\text{obs}} = (k_0 + k_c[\text{H}_3\text{O}^+]) / (1 + k_b[\text{H}_3\text{O}^+]) \quad (6)$$

The effects of temperature on the two regions of acid catalysis

* We used at least 5% dioxane to maintain solubility in strongly acidic solutions.

in dioxane–water are given in Table 1. The derived activation parameters, although only approximate, are significantly different, and are compatible with a change in mechanism, perhaps from $\text{AB}_{\text{AC}3}$ to A1. No acyl fluoride has previously been shown to exhibit two mechanisms of catalysis in different acidity regions. The parallelism with carboxylic ester, amide and acid hydrolysis is interesting.¹ Carboxylic anhydrides have also recently been shown to display two mechanisms of acid catalysis.¹³

The foregoing results are all consistent with the earlier findings for benzoyl fluoride;^{2–4} they simply extend them to higher acidities and to other dioxane–water mixtures. There remains the marked acid catalysis in water reported⁵ for acetyl fluoride at low values of $[\text{H}_3\text{O}^+]$. As an example of an aliphatic acyl fluoride we chose phenylacetyl fluoride whose boiling point is more convenient than that of acetyl fluoride (20 °C). Our results (Fig. 4, Table 1) for three dioxane–water mixtures reveal a behaviour pattern similar to that shown by benzoyl fluoride (Fig. 3, Table 1). The X -plot for the 5% dioxane mixture (for which X values are available¹⁴) has a slope 0.90, and gives $k'_{\text{H}^+} = 3 \times 10^{-7} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ at 25 °C. It is clear (i) that negligible acid catalysis would be found in a purely aqueous solvent* at low values of $[\text{H}_3\text{O}^+]$, and (ii) in dioxane-rich media the same type of change in acid-catalysed mechanism probably obtains for phenylacetyl fluoride as for benzoyl fluoride.

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