

The Effect of Pressure and Competing *A1* and *A2* Mechanisms in the Acid-catalysed Hydrolysis of Substituted Benzoic Anhydrides in Dioxan-Water Mixtures

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Negative values of the activation volume indicating an *A2* mechanism were obtained for the perchloric acid-catalysed hydrolysis of benzoic, 4-chlorobenzoic, and 4-nitrobenzoic anhydrides in dioxan-water mixtures containing more than about 1 mol of water per litre. When the amount of water in the reaction mixture was decreased, the values of the activation volume became positive. A change in mechanism from *A2* to *A1* is indicated also by simultaneous large changes in substituent and solvent effects, in activation entropies and enthalpies when the solvent composition is altered.

In a previous study¹ of the perchloric acid-catalysed hydrolysis of benzoic anhydride and some 4-substituted benzoic anhydrides in dioxan-water mixtures, a change of mechanism from *A2* in water-rich solvent mixtures to *A1* in water-poor mixtures was assumed to occur in order to account for the changes in reaction rates due to substituent and solvent effects. Changing the solvent composition of dioxan-water mixtures caused only relatively small changes in the rates of typical *A2* hydrolyses such as the perchloric acid-catalysed hydrolysis of ethyl acetate.² On the other hand, large solvent effects were observed in typical *A1* hydrolysis reactions such as, for example, the hydrolysis of acetal³ in dioxan-water mixtures of low water content. It is therefore possible that in some cases a change of mechanism may occur when the solvent composition is altered. In order to get more information about such changes of mechanism we measured the effect of pressure on acid hydrolysis of benzoic and three substituted benzoic anhydrides in dioxan-water mixtures.

EXPERIMENTAL

Materials. Benzoic anhydride, m.p. 41–42°C, 4-methoxybenzoic anhydride, m.p. 96–98°C, 4-chlorobenzoic anhydride, m.p. 193–195°C, and 4-nitrobenzoic anhydride, m.p. 192–194°C, were prepared and dioxan (Fluka AG, *purum*) was purified as described earlier.¹ Perchloric acid, 70 % (E. Merck AG, guaranteed reagent), was used as received.

Rate measurements. Kinetic experiments were carried out as previously¹ using the pressure equipment described earlier.⁴

Acid hydrolyses of benzoic and 4-substituted benzoic anhydrides were found to be of third order, first order in anhydride, water and perchloric acid in dioxan-water mixtures about 0.02 M in both water and anhydride. Second-order rate constants were approximately constant over the range from about 10 % to about 80 % change in each experiment. The first-order rate equation was used to calculate the rate constants in mixtures containing water in large excess relative to anhydride. The third-order rate constants in Table 1 were obtained by dividing the difference between the first-order rate constants

Table 1. Values of $\log 10^4 k$ (M^2s^{-1}) and activation volumes ΔV^* of perchloric acid-catalysed hydrolyses of 4-substituted benzoic anhydrides in dioxane-water mixtures at 60°C.

Substi- tuent	H ₂ O	$\log 10^4 k$ M^2s^{-1} at					ΔV^* cm ³ mol ⁻¹
	M	1 atm	500 atm	1000 atm	1500 atm	2000 atm	
4-MeO	0.023	6.238	6.182	6.130	6.082	5.992	7.5
	0.100	5.158	5.099	5.046	4.976	4.942	7.5
	1.00	2.164	2.100	2.064	2.032	2.013	4.8
	10.0	-0.316	-0.328	-0.325	-0.320	-0.325	0.6
H	0.017	4.973	4.952	4.931	4.834	4.787	6.7
	0.107	3.464	3.395	3.362	3.318	3.312	5.0
	1.07	0.815	0.878	0.918	1.008	1.110	-5.6
	10.0	-0.770	-0.678	-0.585	-0.488	-0.207	-17.8
4-Cl	27.6	-0.717	-0.588	-0.327	-0.174	0.099	-25.4
	0.020	4.480	4.449	4.400	4.340	4.316	6.0
	0.100	2.795	2.731	2.673	2.648	2.640	5.3
	1.00	0.559	0.659	0.733	0.801	0.850	-9.5
4-NO ₂	5.00	-0.501	-0.303	-0.096	0.031	0.183	-22.6
	0.0242	2.976	2.850	2.784	2.773	2.745	6.8
	0.100	2.045	2.090	2.136	2.170	2.221	-5.6
	1.00	0.759	1.059	1.059	1.122	1.189	-9.0

in the presence and absence of catalyst acid by the product of the water and perchloric acid concentrations. The hydrolysis of 4-nitrobenzoic anhydride was autocatalytic in dioxan containing 0.0247 mol of water per l. The rate constants of hydrolysis of the different anhydrides at the same water concentration in dioxan obtained by interpolation are shown in Table 2.

Table 2. Values of $\log 10^4 k$ (M^2s^{-1}) for perchloric acid-catalysed hydrolysis reactions of benzoic and 4-substituted benzoic anhydrides in dioxane-water mixtures at 60°C and 1 atm obtained by interpolation.

Substi- tuent	H ₂ O M					
	0.020	0.10	1.0	5.0	10.0	27.6
4-MeO	6.390	5.158	2.164		-0.316	
H	4.800	3.620	0.880		-0.670	-0.716
4-Cl	4.480	2.795	0.559	-0.501		
4-NO ₂	2.980	2.045	0.759			

The activation volumes were calculated using the equation

$$\Delta V^* = -2.303 RT \frac{d \log k}{dp} \quad (1)$$

In most cases, the plot of $\log k$ against p was linear. The curvilinear plots were assumed to be due mainly to experimental errors. The most accurate values of the slope and activation volume can be obtained at 1000 atm, *i.e.* at the midpoint of the pressure range from 1 to 2000 atmospheres. Usually, however, values of activation volume at 1 atm pressure are reported. When the plot is linear, the activation volume is independent of pressure and only for curved plots do activation volumes at 1 atm differ from those at 1000 atm. The activation volumes shown in Table 1 are estimated to be accurate to $\pm 1.5 \text{ cm}^3 \text{ mol}^{-1}$.

DISCUSSION

Activation volume. When the concentration of water in dioxan decreases the activation volumes of the perchloric acid-catalysed hydrolyses of benzoic anhydride, 4-methoxybenzoic, 4-chlorobenzoic, and 4-nitrobenzoic anhydrides tended to become approximately constant and equal to about $6.8 \text{ cm}^3 \text{ mol}^{-1}$ (Table 1). Positive values of the activation volume are usually obtained ⁴ for reactions between a neutral molecule and an ion occurring by the *A1* mechanism.

Because of the low solubilities of the 4-substituted benzoic anhydrides, their hydrolysis reactions could be studied only in a limited range of dioxan-water mixtures. Negative values of the activation volume were obtained for the reactions in solvent mixtures containing relatively large amounts of water (Table 1). The mean value of the activation volume ΔV^* is $-22.6 \text{ cm}^3 \text{ mol}^{-1}$ in the dioxan-water mixture 5 M in water and $-11.3 \text{ cm}^3 \text{ mol}^{-1}$ in the mixture 1 M in water. These values are of the order of magnitude usually obtained for *A2* reactions. Large changes in activation volume indicate a change in mechanism from *A2* to *A1* when the water concentration decreases in dioxan-water mixtures.

If the hydrolysis is assumed to occur simultaneously by two mechanisms, one an *A1* and the other an *A2* mechanism, the experimentally obtained activation volume is

$$\Delta V_{\text{exp}}^* = \frac{k_1}{k_1 + k_2} \Delta V_1^* + \frac{k_2}{k_1 + k_2} \Delta V_2^* \quad (2)$$

where k_1 and k_2 are the rate constants and ΔV_1^* and ΔV_2^* the activation volumes of the reactions occurring by the *A1* and *A2* mechanisms, respectively. Using the values $\Delta V_1^* = 6.8 \text{ cm}^3 \text{ mol}^{-1}$ and $\Delta V_2^* = -11.3 \text{ cm}^3 \text{ mol}^{-1}$, the relative contributions of the *A1* reactions were estimated (Table 4). A change of reaction mechanism occurs at different solvent compositions for different anhydrides. Approximately equal contributions of the *A1* and *A2* mechanisms are observed in a dioxan-water mixture about 0.1 M in water for 4-nitrobenzoic anhydride, in a mixture about 0.5 M in water for 4-chlorobenzoic anhydride, in a mixture about 1 M in water for benzoic anhydride and in a mixture about 20 M in water for 4-methoxybenzoic anhydride. Instead of two different mechanisms these results can also be interpreted by assuming the reactions to occur by a borderline *A1*–*A2* mechanism.

Solvent effect. The changes in reaction rate when the composition of the reaction medium is altered can be used as a criterion when deciding the mechanism of a reaction. As already mentioned, different solvent effects have been observed for acid-catalysed hydrolysis reactions in dioxan-water mixtures of low water content that occur either by the *A1* or by the *A2* mechanism.

Rates of acid hydrolysis of 4-nitrobenzoic and 4-chlorobenzoic anhydrides were measured in dioxan-water mixtures of low water content in which the molar ratio of perchloric acid to water was about 1 : 3 (Table 1). It has been shown previously⁵ that water and perchloric acid form a 2-1 complex in dioxan. Water in the complex is likely to be less reactive than "free" water in dioxan. When the third-order rate constants were recalculated to correspond the free water concentration and logarithms of the *k* values were plotted against water concentration, lines of slope about -2.3 were obtained for all the anhydrides studied in dioxan-water mixtures from 0.02 M to 0.1 M in water (Fig. 1). The similar solvent effects for all the anhydrides indicate a similar mechanism in this range of solvent mixtures. In a previous study⁵ on protonation equilibria of 2,4-dichloroaniline in dioxan-water mixtures containing perchloric acid, the plot of $-\log K_a$ against water concentration was approximately linear and had a slope of about -2 at low water concentrations. The similar solvent effects observed in the acid hydrolysis of anhydrides and the protonation of 2,4-dichloroaniline indicate that the solvent effects observed in the hydrolysis are mainly due to changes in the protonation pre-equilibria.

For the reactions in water-rich solvent mixtures, relatively small solvent effects were observed in agreement with a change of the mechanism to *A2*. For reactions occurring by either a borderline *A1-A2* mechanism or by simultaneous *A1* and *A2* mechanisms, the contribution of the *A1* reaction can be estimated from the observed solvent effects (Table 4). The calculations involve assumptions that the rates of reactions occurring by the *A2* mechanism are independent of solvent composition² and the reactions occurring by the *A1* mechanism show a similar solvent effect as the hydrolysis of 4-methoxybenzoic anhydride which takes place largely by the *A1* mechanism in the range of dioxan-water mixtures used in this work.

Substituent effect. Electron-withdrawing substituents in 4-substituted benzoic anhydrides accelerate and electron-repelling substituents retard their acid hydrolysis in dioxan-water mixtures of low water content (Table 2 and Fig. 2). The slopes ρ of the linear parts of curves plotting $\log k$ against values of substituent constants σ^+ are about -2.25 for reactions in solvent mixtures 0.02 M and 0.1 M in water. The *A1* mechanism proposed above for these reactions is associated with a large negative substituent effect. Opposite substituent effects are evident in dioxan-water mixtures of high water content. 4-Nitrobenzoic anhydride, for example, reacts faster than 4-chlorobenzoic anhydride in dioxan containing 1 M water (Fig. 1) indicating a change in mechanism from *A1* to *A2*. When values of $\log k$ estimated for *A2* reactions (Table 4) were plotted against the substituent constant σ^+ , a slope of about 0.5 was obtained. Hydrolysis reactions of anhydrides occurring by the *A2* mechanism are thus associated with a small positive substituent effect.

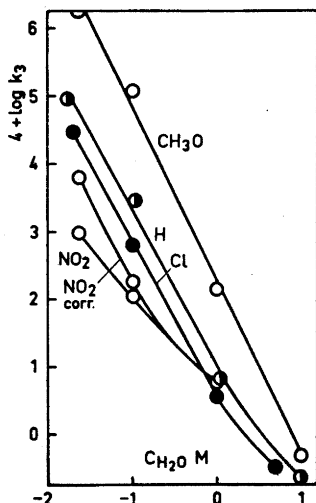


Fig. 1. Logarithm of third-order rate constant ($\log k$) at 60°C plotted against the logarithm of water concentration in dioxan-water mixtures. Rate constants of hydrolysis of 4-nitrobenzoic anhydride corrected for the extent of complex formation of water and perchloric acid.

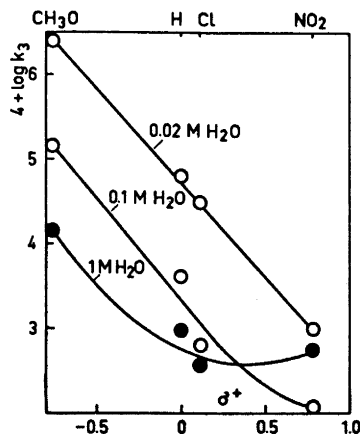


Fig. 2. Logarithm of third-order rate constant ($\log k$) plotted against the value of the substituent constant σ^+ in dioxan-water mixtures at 60°C containing water 0.02 M, 0.1 M and 1.0 M.

If the substituent effects are assumed independent of solvent composition in the range of dioxan-water mixtures used in this work, estimates can be obtained for contributions of the A1 mechanism (Table 4). An electron-repelling substituent increases the basicity and promotes protonation of an anhydride. Electron-repelling substituents also assist heterolysis of the carbon oxygen bond and thus a strong negative substituent effect can be expected

Table 3. Values of $\log 10^7 k$ (s^{-1}) and activation volumes for uncatalysed hydrolyses of benzoic and 4-substituted benzoic anhydrides in dioxan-water mixtures at 60°C.

Substi- tuent	H_2O M	$\log 10^7 k$ M^2s^{-1} at					ΔV^\ddagger $cm^3 mol^{-1}$
		1 atm	500 atm	1000 atm	1500 atm	2000 atm	
4-MeO	10.0	0.48					
	1.07	0.716				1.114	-13.3
	10.1	1.670	1.810	2.020	2.146	2.261	-21.1
4-Cl	27.8	2.713	2.907	3.133	3.308	3.518	-26.6
	1.0	1.375				1.709	-11.1
	5.0	1.811	1.965	2.097	2.210	2.350	-17.6
4-NO ₂	0.1	0.62					
	1.0	2.030	2.072	2.110	2.206	2.389	-9.3

Table 4. Contributions in per cent of the *A1* mechanism to the hydrolysis of benzoic and 4-substituted benzoic anhydrides in dioxane-water mixtures of varying water concentration as estimated from activation volumes (v), substituent effects (s) and solvent effects (w).

Substituent	Method	H ₂ O M			
		0.02	0.10	1.0	10.0
4-MeO	v	100	100	89	65
	s	100	100	99	85
	w	100	99.9		
H	v	100	100	32	0
	s	100	100	70	0
	w	99.9	99	55	9
4-Cl	v	100	91	10	
	s	100		17	
	w	99.9	94	22	
4-NO ₂	v	100	32	0	
	s			0	
	w	92		0.7	

for *A1* reactions. The weak substituent effect observed for *A2* reactions is due to a partial cancellation of opposite effects in the two consecutive steps of hydrolysis reaction. Protonation is favoured by electron-repelling substituents which increase the electron density and reduce the reactivity of the carbonyl carbon atom towards nucleophiles and the net substituent effect is approximately zero.

Activation entropy and enthalpy. Values of the activation entropy and enthalpy of acid hydrolyses of substituted benzoic anhydrides occurring in dioxane-water mixtures by either the *A1* or the *A2* mechanism¹ are approximately independent of the substituent (Table 5). The difference in the activation entropies of *A1* and *A2* reactions is about 42 cal K⁻¹ mol⁻¹ (Table 5). The activation enthalpy for unimolecular heterolysis of a bond is usually large compared with that for bond heterolysis accompanied by simultaneous bond formation. In the present cases, this difference is about 12 kcal mol⁻¹ (Table 5).

Uncatalysed hydrolysis. The activation volumes of the uncatalysed hydrolyses of benzoic, 4-chlorobenzoic, and 4-nitrobenzoic anhydrides are all negative and of the order of magnitude expected for *S_N2* reactions (Table 3). The

Table 5. Mean values of activation enthalpy ΔH^* , entropy ΔS^* and volume ΔV^* and the constant ρ of the Hammett equation for the hydrolysis of benzoic anhydride and substituted benzoic anhydrides in dioxane-water mixtures occurring by the *A1* and the *A2* mechanism.

	ΔH^* kcal mol ⁻¹	ΔS^* cal K ⁻¹ mol ⁻¹	ΔV^* cm ³ mol ⁻¹	ρ
<i>A1</i>	28 ± 2	16 ± 2	6.8 ± 1	-2.2
<i>A2</i>	16 ± 1	-26 ± 3	-21 ± 2	0.5

activation volumes of these reactions increase as the proportion of water in the solvent mixtures decreases. Electron-withdrawing substituents increase the activation volume in dioxan 1 M in water.

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