Evidence for a First Order Mechanism in Amide Hydrolysis

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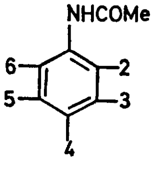
Summary Hydrolysis of acetanilide derivatives in concentrated acids is confirmed as an A-1 mechanism by use of *w* and ϕ parameters.

AMIDES generally exhibit a maximum in their hydrolysis rate profiles at moderate acidity,[1] and in the case of some nitro-derivatives of acetanilide this is followed by a local minimum at *ca.* 70—75% *w/w* sulphuric acid.[2,3] We recently reported[4] this phenomenon in the hydrolysis of *N*-acetylsulphanilic acid in sulphuric acid. On the basis of increasing values of activation energy over this region of increasing rate, the mechanism of hydrolysis was interpreted[2,3,4] as having changed from bimolecular to unimolecular. Vinnik *et al.*[3] considered specifically that the activated complex incorporated the protonated substrate and a sulphuric acid molecule.

We now report that the phenomenon of increasing rate in concentrated acid media occurs for a large number of substituted acetanilides (I) undergoing hydrolysis in sulphuric acid, and in an extreme case in perchloric acid also. For those substrates where the rate increases were sufficiently large over an adequate range of acidity, to justify mathematical analysis, we have tested the data using the Bunnett w[5] and Bunnett–Olsen linear free energy[6] relationships (see Table). In all cases correlation coefficients were good (generally better than 0·99). The values of w all lie in the range —2·5 to 0·0 and the values of ϕ are all negative (although some are $<-0{\cdot}34$, the original limit of values found by Bunnett and Olsen[6]) and thus they are characteristic of reactions in which water is not involved in the rate determining step. These results record the first application of w and ϕ values to an A-1 mechanism for amide hydrolysis.



(I)

TABLE

Typical rate data for hydrolysis of substituted acetanilides in concentrated acid media and analysis of the data by use of Bunnett w *and Bunnett–Olsen linear free energy relationships.*

Temp. (°C)	Position of substituent[a]					$10^5k_\psi(s^{-1})$		w	ϕ
	2	3	4	5	6	% w/w H_2SO_4			
						80·0	96·6		
100·0			SO_3H			14·2	99·6	—0·48	—0·39
95·3			SO_3H			7·36	52·0	—0·52	—0·41
90·0			SO_3H			5·03	30·9	—0·43	—0·38
80·3			SO_3H			2·09	15·5	—0·49	—0·40
80·0			SO_3H			1·78	6·43	—0·34	—0·26
100·0			Cl			0·499	1·12		
105·0			Cl			0·930	2·47		
100·0			Br			0·574	1·44		
105·0			Br			1·55	4·09		
100·0			I			2·29	11·9	—0·51	—0·45
100·0		OH	SO_3H			44·5	297	—0·44	—0·37
100·0	SO_3H		CH_3			0·905	4·31		
100·0	Br		Br		Br	258	578	—0·21	—0·15
55·0			NO_2			0·233[b]	13·9[b]		
65·0		NO_2		NO_2		1·50[b]	16·7[b]	—0·48	—0·47
						% w/w $HClO_4$			
						50·0	70·0		
100·0	Br		Br		Br	128	551	—0·52	—0·16
25·0	NO_2		NO_2			30·6	<0·1		

[a] Substituent is H unless stated otherwise; [b] interpolated from ref. 2; [c] interpolated from ref. 3(b).

(*Received, 28th February* 1972; *Com.* 333.)

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