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KINETIC MODEL FOR ACID-CATALYSED HYDROLYSIS OF BENZOHYDROXAMIC ACID*

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The kinetics of the hydrolysis of benzohydroxamic acid have been investigated in hydrochloric, sulphuric and perchloric acids in 10% (v/v) dimethyl sulphoxide–water at 55 °C. Activation parameters were also determined. Rate correlation by the Cox–Yates excess acidity method shows an A-2 mechanism involving rapid pre-equilibrium protonation of the substrate followed by rate-limiting attack of water at the carbonyl carbon atom to form a tetrahedral intermediate which collapses, in a fast step, to the products.

INTRODUCTION

Recently, much attention has been focused on biological[1,2] and analytical studies[3,4] of hydroxamic acids. Surprisingly very little work has been carried out on the hydrolysis of hydroxamic acids under non-dilute acidic conditions.[5–10] The acid-catalysed hydrolysis of hydroxamic acids affords carboxylic acids and hydroxylamine. We have previously shown that *N*-benzylbenzohydroxamic acid[6] (BBHA) hydrolyses by an A-2 mechanism in mineral acids at all concentrations, whereas *N*-phenylbenzohydroxamic acid[9] (PBHA) hydrolyses by an A-2 mechanism but switches to an A-1 mechanism at high acidity. As an extension of our work on the mechanistic aspects of its hydrolysis reactions, we report here the hydrolysis of benzohydroxamic acid ($C_6H_5CONHOH$) (BHA) catalysed by mineral acids in 10% (v/v) dimethyl sulphoxide (DMSO) medium. The excess acidity method[11] has been applied to hydrolysis rate data. Buglass *et al.*[12] also examined the acid-catalysed hydrolysis of BHA and five *para*-substituted derivatives. Their study covered the low-acidity range, where the information gained about detailed mechanisms is limited.

RESULTS AND DISCUSSION

The kinetics of the hydrolysis of BHA were followed spectrophotometrically by following the decrease in the characteristic absorption of the iron(III)–BHA complex. The reaction followed pseudo-first-order kinetics:

$$-\frac{d}{dt}[BHA] = k[BHA][H^+] = k_\psi[BHA]$$

Benzoic acid and hydroxylamine were the products of the hydrolysis.

Recently, the excess acidity method[11] has proved to be of considerable value in determining the details of the mechanisms of reactions in strongly acidic media and several examples of the use of the method are available.[13–15] This method, applied to reaction kinetics, consists in deriving a rate equation based on a reasonable reaction mechanism. Kinetic data, together with other relevant information, are given in Table 1. Rate maxima were observed for all three acids used and these maxima are similar to those observed in the acid-catalysed hydrolysis of PBHA[9] and BBHA.[6] At low acidity, an increased acid concentration causes an increased hydrolysis rate by increasing the concentration of protonated substrate. However, as the acidity becomes sufficient to convert a large fraction of the substrate into its protonated form, further increases in acid concentration have little additional effect. A new factor now becomes important, namely the decrease in the activity of water with increasing acid concentration. As water becomes progressively less available, the hydrolysis rate diminishes steadily. In a recent analysis of the rate maxima which exist in the acid-catalysed

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Table 1. Pseudo-first-order rate constants for the hydrolysis of BHA

Concentration (M)	$k_\psi \times 10^3$ (min^{-1})								
	HCl			H_2SO_4			$HClO_4$		
	45 °C	55 °C	65 °C	45 °C	55 °C	65 °C	45 °C	55 °C	65 °C
0·75	0·51	1·40	3·51	—	2·12	5·20		1·20	
1·75	1·44	3·33	7·40	1·20	3·10	7·76	0·634	2·74	6·18
2·9	2·35	5·85	14·4	2·16	5·30	12·3	0·979	3·88	8·73
3·5	—	6·60	—	—	—	—	—	—	—
4·2	3·0	7·40	18·3	2·40	6·80	18·9		4·25	
5·0	—	8·03	—	2·34	7·10	19·6	1·17	4·30	10·8
5·8	—	8·30	—	—	6·40	—		3·40	
6·5	3·46	8·72	22·5	1·87	4·70	14·0	0·820	2·47	5·58
7·5	—	8·37	—	—	3·10	—		1·12	
8·5	2·73	7·65	21·0	0·509	1·50	4·40		[a]	
9·5	—	5·14	—	—	0·40	—			
10·4	—	4·44	—	—	—	—			

[a] Higher perchloric acid concentrations bring about uncontrollable reactions (destruction).

hydrolysis of benzamides, Lemetais and Carpentier[16] proposed that the rate maxima occur because the acid–base pre-equilibrium step and the transition-state formation step are governed by different acidity functions. In particular, the acidity function controlling the transition-state formation increases less rapidly than the acidity function governing the acid–base equilibrium with increasing acid concentration. The catalytic effect of acids is characteristic of a bimolecular mechanism[17] decreasing in the order HCl > H_2SO_4 > $HClO_4$.

Activation parameters were also determined for some of the acid solutions (Table 2). These values are not substantially different from those obtained for an ester and amide hydrolysis according to an A-2 mechanism. Therefore, we conclude that the hydrolysis of BHA proceeds via a rate-determining attack of water on the protonated substrate, with formation of a tetrahedral intermediate that rapidly breaks down to products. No evidence for a unimolecular pathway, such as changes in activation entropies, was seen for the hydrolysis of BHA in the acidity range studied.

Rate–acidity correlations

Several methods for the correlation of rates wih acidity functions have been reported. These include Bunnett–Olsen LFER,[18] Yates–McClelland r hydration treatment,[19] Modena–Scorrano treatment,[20] the M_c function of Marziano *et al.*[21] and the Cox–Yates excess acidity method.[11] The excess acidity method is capable of revealing mechanistic features which other methods of analysing kinetic data in strong acids cannot. We employed this method to test for an A-2 mechanism. The r plots of the Yates–McClelland hydration treatment (using H_A values) lie close to a straight line (Figure 1) with slopes $r = 1{\cdot}90$ in HCl, $2{\cdot}13$ in H_2SO_4 and $2{\cdot}30$ in $HClO_4$. The r value gives a measure of the change in hydration on going from the protonated species to the rate-determining transition state. For typical A-2 ester hydrolysis, $r \approx 2$. Treatment of the data according to Bunnett–Olsen LFER (Figure 1) gave linear plots with slope values ϕ. (Table 3). The experimental curves in Figure 1 indicate an A-2

Table 2. Activation parameters for the hydrolysis of BHA[a]

Concentration (M)	HCl				H_2SO_4				$HClO_4$			
	E_a	$\Delta G^{\neq}$	$\Delta H^{\neq}$	$\Delta S^{\neq}$	E_a	$\Delta G^{\neq}$	$\Delta H^{\neq}$	$\Delta S^{\neq}$	E_a	$\Delta G^{\neq}$	$\Delta H^{\neq}$	$\Delta S^{\neq}$
0·75	20·6	25·5	19·9	−17·2	19·7	25·3	19·0	−19·2	—	—	—	—
1·75	17·5	24·9	16·8	−24·7	19·3	24·9	18·6	−19·5	23·1	25·3	22·4	−8·5
2·9	19·4	24·3	18·7	−17·8	18·5	24·8	17·8	−20·7	23·7	24·6	22·4	−7·8
4·2	19·3	24·4	18·6	−17·7	22·5	24·4	21·9	−8·0	—	—	—	—
6·5	19·9	24·2	19·2	−15·6	21·6	24·6	20·9	−11·5	20·4	25·2	19·7	−16·8
8·5	21·7	24·6	21·1	−10·2	23·7	25·4	23·0	−7·5	—	—	—	—

[a] E_a, $\Delta H^{\neq}$ and $\Delta G^{\neq}$ in kcal mol^{-1} and $\Delta S^{\neq}$ in e.u.

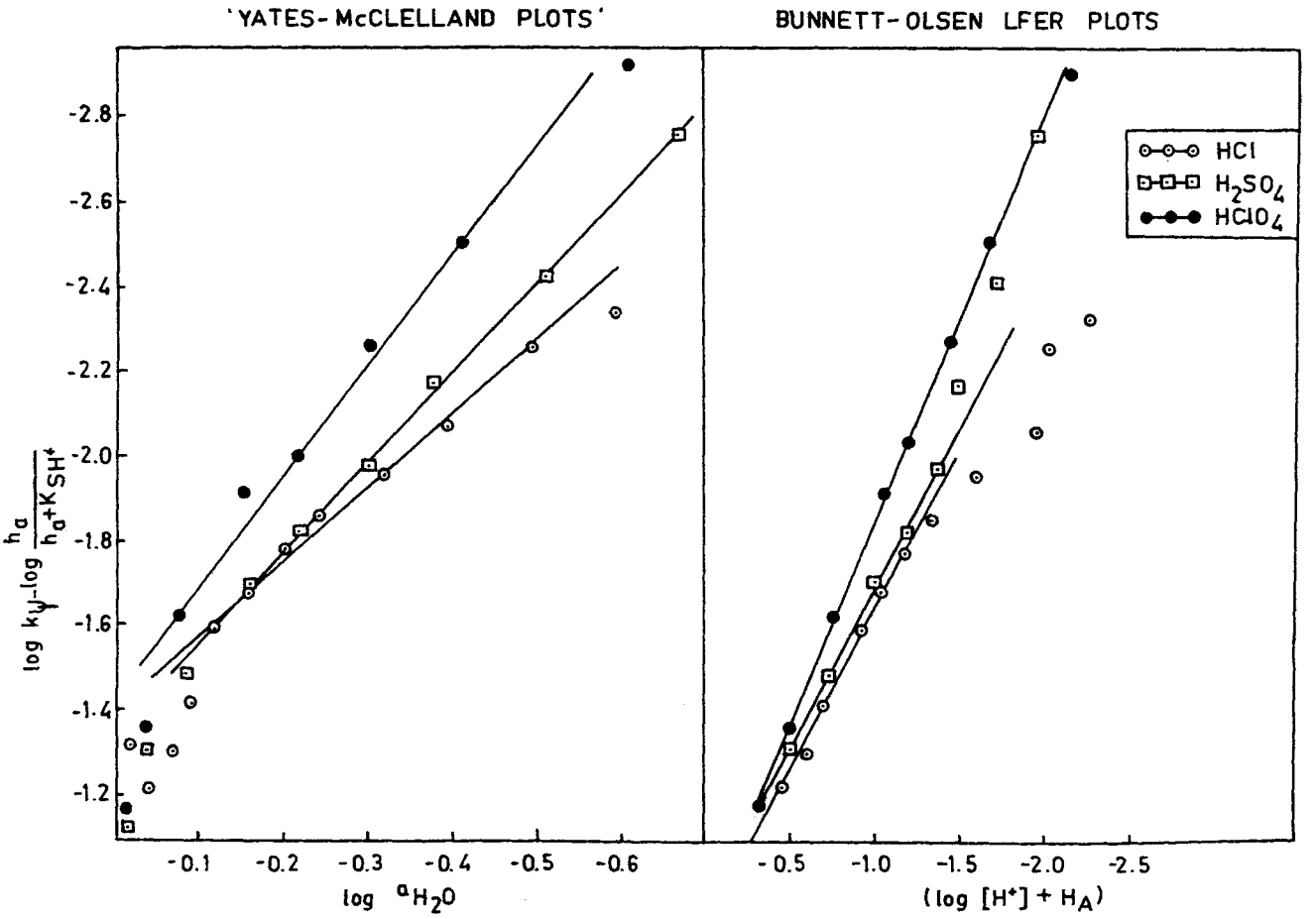


Figure 1. (Left) Yates–McClelland and (right) Bunnett–Olsen LFER plots for the hydrolysis of BHA at 55 °C. ○, HCl; □, H_2SO_4; • $HClO_4$

Table 3. Rate correlations for the hydrolysis of BHA

Acid	Yates–McClelland (r)	Bunnett–Olsen (ϕ)	Excess acidity ($m_2^{\neq} m^*$)
HCl	1·90	0·74	0·26
H_2SO_4	2·13	0·83	0·37
$HClO_4$	2·30	0·98	0·12

mechanism. Similar treatment of data had been employed earlier by Edward *et al.*[22] concerning the A-2 hydrolysis of 4-nitrothioacetanilide. The pK_{SH^+} value of BHA is −1·93 (using the H_A scale) taken from earlier studies of Buglass *et al.*[12]

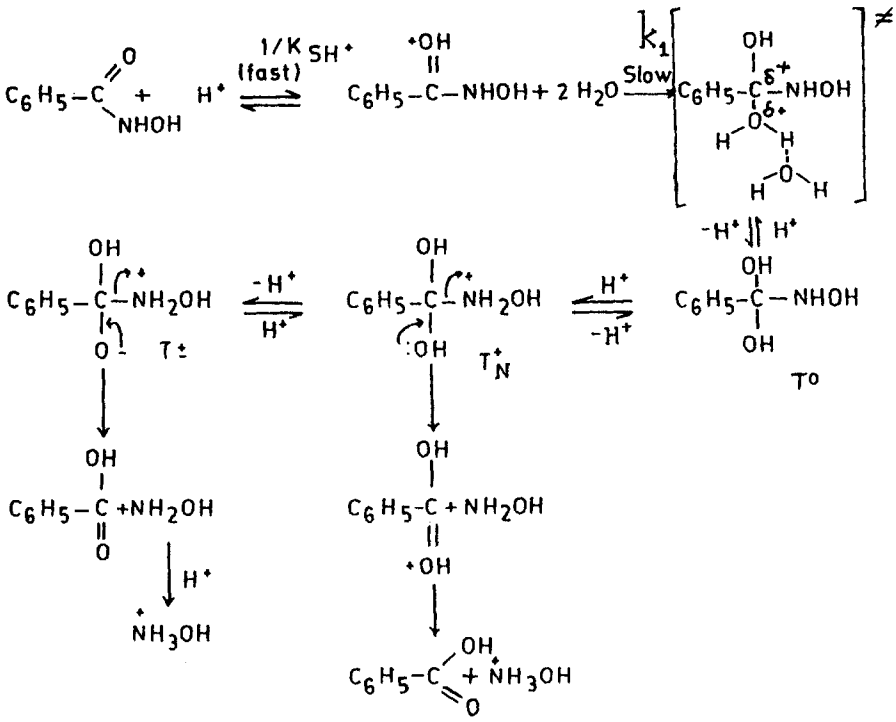
To apply the Cox–Yates excess acidity treatment, equation (1) is derived for A-2 mechanism in Scheme 1:

$$\log k_\psi - \log C_{H^+} - \log a_{H_2O} = (\log k_1/K_{SH^+}) + m_2^{\neq} m^* X \quad (1)$$

As two water molecules are involved in the rate-determining step equation (1) is modified to

$$\log k_\psi - \log C_{H^+} - 2 \log a_{H_2O} = (\log k_1/K_{SH^+}) + m_2^{\neq} m^* X \quad (2)$$

A plot of the left-hand side of equation (2) against X should be linear with slope = $m_2^{\neq} m^*$. For A-2 reactions $m_2^{\neq} \simeq 1$ and m^* for carbonyl oxygen protonation is 0·6 or less. Hence an overall slope[13,23] against X of 0·6 or less should result for equation (2). The plots obtained are shown in Figure 2, and it is seen that linearity is achieved. The slope values for all three acids are given in Table 3. The $m_2^{\neq} m^*$ values indicate that BHA reacts by an A-2 mechanism over the entire range of acidity. X values for HCl, H_2SO_4 and $HClO_4$ were obtained from $-(H_A + \log C_{H^+})$. We used H_A because the protonation behaviour of hydroxamic acids correlates better with H_A than H_0. In fact, H_A has been



Scheme 1

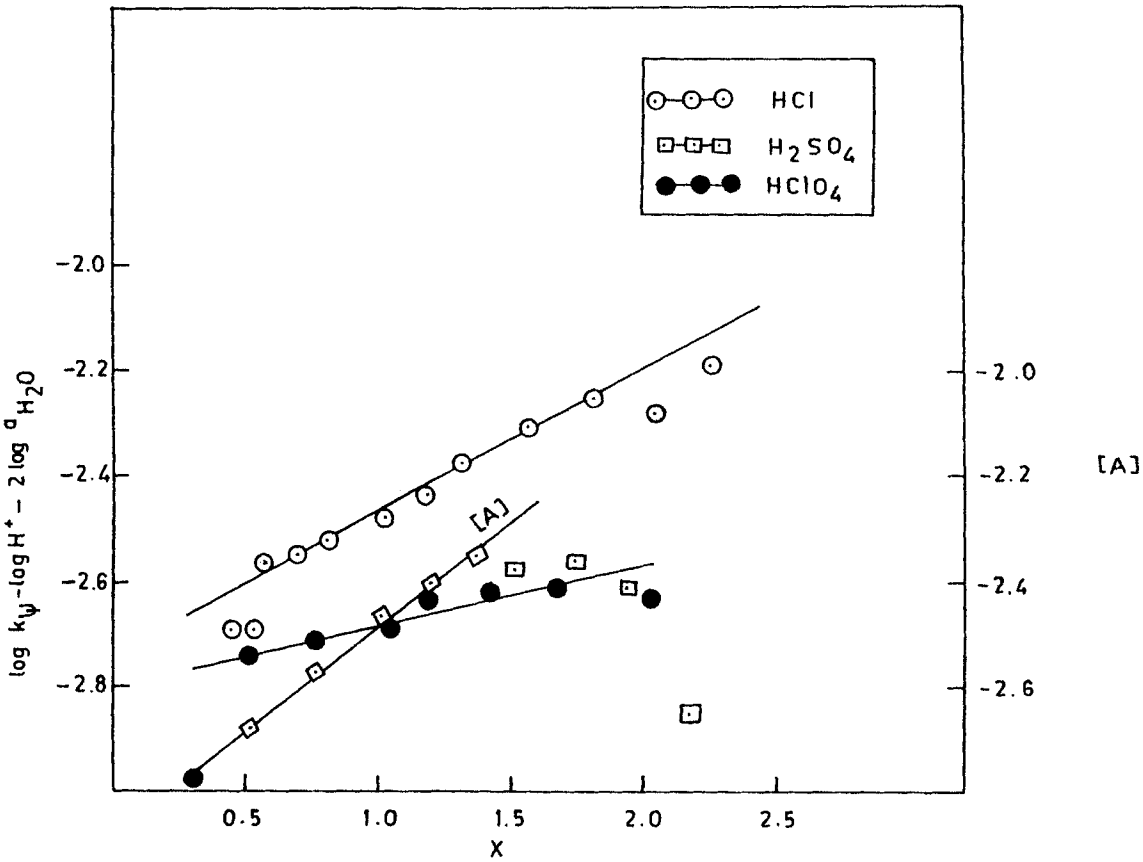


Figure 2. Cox–Yates plots for the A-2 mechanism of hydrolysis of BHA at 55 °C. ○, HCl; □, H_2SO_4; •, $HClO_4$

shown to be applicable when ionization or protonation on oxygen was occurring. We favour protonation on oxygen for BHA (see Scheme 1). Recently, Novak *et al.*[7] suggested that for acid-catalysed hydrolysis of *N*-hydroxyacetanilides, the protonation of the carbonyl oxygen is favoured over the hydroxyl oxygen by about seven orders of magnitude.

The detailed mechanism for an A-2 reaction as set out in Scheme 1 would involve two molecules of water in the rate-determining step, as indicated by the Cox–Yates excess acidity method demonstrated above. The requirement for two water molecules stems from the need for one to act as a nucleophile and the other to assist in dispersing the positive charge developed on oxygen in the transition state as progress is made toward the tetrahedral intermediate T^0. The second water molecule is then in a position to accept a proton in the formation of neutral species T^0; further proton transfers result in the intermediates T_N^+ and $T^{\pm}$. Protonation of T^0 at nitrogen gives T_N^+ and this is the major fate of T^0. In acidic media strong enough to support the formation of a protonated ester, T_N^+ can lose NH_2OH directly, as shown. More probable at moderate and low acid concentrations is the loss of an OH proton to give the zwitterion $T^{\pm}$, which then readily loses NH_2OH to give the acid.

In summary, it may be concluded that rate and product studies, combined with activation parameters and three quantitative analytical treatments, have produced an extensive description of the mechanistic framework of hydroxamic acid hydrolysis.

EXPERIMENTAL

The benzohydroxamic acid was prepared by a standard method.[24] The acids used were of analytical-reagent grade. Their concentrations were determined by titration with standard alkali. DMSO (Sarabhai M Chemicals (India) Laboratory Reagent) was used without further purification. The iron(III) chloride solution used in the colorimetric procedure was prepared by dissolution of 44·0 g of anhydrous iron(III) chloride (SM, LR) in 1 l of distilled water containing 10 ml of concentrated hydrochloric acid. Kinetic measurements were made by use of the spectrophotometric method reported previously[9] using a Specol instrument (Carl Zeiss, Jena, Germany) set at 520 nm.

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