Kinetic and mechanistic study of acid-catalysed hydrolysis of 3-chlorobenzohydroxamic acid

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The rate of hydrolysis of 3-chlorobenzohydroxamic acid [3-Cl-C_6H_4.CO.NHOH] has been measured over a wide range of acidities in hydrochloric, sulfuric and perchloric acids in 10% (v/v) DMSO-Water at 55°C. The kinetics have been analysed by Bunnett, Bunnett-Olsen and Cox-Yates excess acidity treatments. Kinetic solvent isotope, salt and temperature effects have also been probed. The mechanism of the acid catalysed hydrolysis is postulated as involving two steps: a rapid protonation and a rate-determining A-2 nucleophilic attack by water.

The chemistry of hydroxamic acids continues to attract the attention of chemists due to their versatile applications in the analytical[1,2], biological[3-5] and industrial fields[6]. There is scant information about the complete mechanistic investigations[7-9]. Continuing our study on hydrolysis of unsubstituted[10] and N-substituted hydroxamic acids[11,12] under non-dilute acidic conditions, we report herein hydrolysis of 3-chlorobenzohydroxamic acid [3-Cl.C_6H_4.CO.NHOH] in mineral acids. No kinetic data of this compound have previously been reported. Recently, the excess acidity method[13], developed as a tool for the elucidation of reaction mechanisms in strong acid media, was applied to rate data.

Materials and Methods

The compound was prepared by standard method[14]. The acids used were of analytical reagent quality and their concentrations were determined by titration with standard alkali. DMSO (Merck AR) was used without further purification. Deuterium oxide, D_2O (isotopic purity 99.8%) and D_2SO_4 in D_2O (isotopic purity > 95%) were procured from BARC, Bombay.

Kinetic measurements were made by the spectrophotometric method reported previously[11] employing an EC digital spectrophotometer set at 520 nm. Values of pseudo-first order rate constants were calculated for each run from the standard equation.

Least square analyses were carried out on a Wipro SX-386 personal computer under MS-DOS.

Results and Discussion

Rate profiles

The data in Table 1 for the catalytic effects of hydrochloric, sulfuric and perchloric acids show that the log (observed first order rate constant) versus

Table 1—Observed pseudo-first order rate constants for the hydrolysis of 3-Cl-benzohydroxamic acid

Temp. = 55°C, Solvent: Aq. DMSO 10% (v/v)

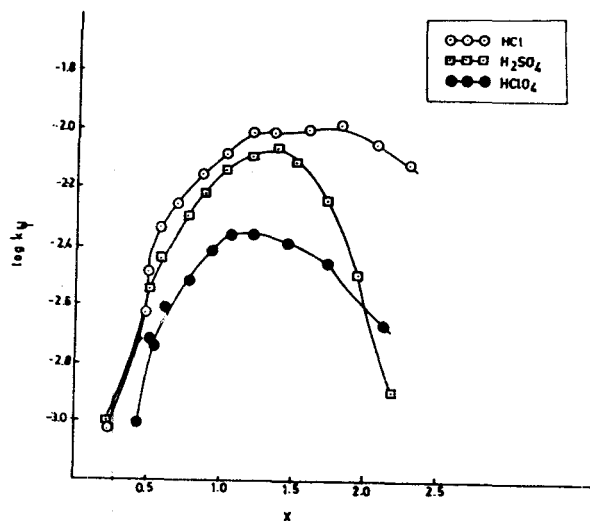| Acid (mol dm^{-3})	$k\psi$ .10^3 (min^{-1})		
	HCl	H_2SO_4	$HClO_4$
0.75	0.937	0.989	1.02
1.45	—	—	1.82
1.75	2.37	2.80	1.90
2.20	3.21	3.65	2.47
2.90	4.55	4.97	3.03
2.90a	—	8.36	—
3.50	5.53	6.22	3.91
3.50a	—	9.95	—
4.20	6.96	7.21	4.34
4.20a	—	10.89	—
5.00	8.16	7.99	4.33
5.80	9.73	8.60	4.09
5.80a	—	10.99	—
6.50	9.77	7.75	3.51
6.50a	—	8.53	—
7.50	9.95	5.68	2.15
7.50a	—	5.81	—
8.50	10.40	3.18	—
9.50	8.84	1.29	—
10.40	7.55	—	—

(a) D_2SO_4 in D_2O

Fig. 1—Observed first order hydrolysis rate constants for 3-Cl-BHA at 55°C as a function of excess acidity
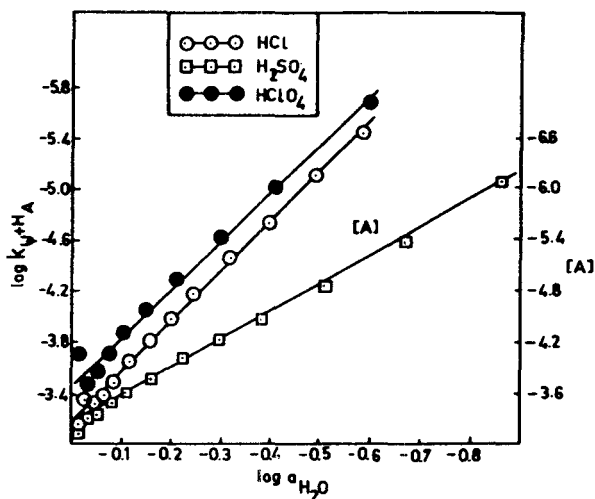

Fig. 2—Bunnett.ω plots for hydrolysis of 3-Cl-BHA

Table 2—Activation parameters for the hydrolysis of 3-Cl-BHA

Acid [mol dm⁻³]	HCl				H₂SO₄				HClO₄			
	Ea	$\triangle H^{\neq}$	$\triangle S^{\neq}$	$\triangle G^{\neq}$	Ea	$\triangle H^{\neq}$	$\triangle S^{\neq}$	$\triangle G^{\neq}$	Ea	$\triangle H^{\neq}$	$\triangle S^{\neq}$	$\triangle G^{\neq}$
2.90	88.4	85.6	-54.7	103.6	82.5	79.8	-71.7	103.3	90.7	87.9	-49.9	104.3
5.00	88.8	85.9	-49.2	102.1	80.6	77.9	-73.7	102.0	92.5	89.8	-42.2	103.7
6.50	86.5	84.0	-53.5	102.0	85.3	84.0	-60.2	103.7	91.9	89.4	-45.1	104.1
8.50	84.8	82.1	-58.5	101.3	91.6	88.9	-47.6	104.5	—	—	—	—
10.40	90.0	87.3	-45.6	102.2	—	—	—	—	—	—	—	—

Ea, $\triangle H^{\neq}$, $\triangle G^{\neq}$ in kJ mol⁻¹ and $\triangle S^{\neq}$ in J mol⁻¹K⁻¹.

excess acidity (X) profiles go through maximum (Fig.1). This non-linearity arises in parts because the equilibrium between the reactants and the protonated species of the rate-determining step does not correspond to a simple protonation, but also to addition of a water molecule. Such rate profiles are characteristic of the A-2 hydrolysis of amides, esters and other carboxylic acid derivatives. The position of the maximum depends on the catalysing acid and on the basicity of the hydroxamic acid. An expected and interesting feature of the maxima in the hydrolysis of 3-Cl-BHA is that their positions occur at higher acidities than in the rate acid profiles for benzohydroxamic[10] and 4-methoxy benzohydroxamic acids[15]. The less basic substrates become appreciably protonated at higher acid concentrations.

Temperature effects

Table 2 gives the values of the Arrhenius parameters Ea, $\triangle H^{\ddagger}$, $\triangle S^{\ddagger}$ and $\triangle G^{\ddagger}$ as a function of molarity of acid. These values are fairly typical for A-2 reactions[16]. $\triangle S^{\neq}$ changing from a larger negative value

in the dilute acid region, to less negative values in more concentrated acid region. This implies that a change from a more to less restricted transition state is occurring as the acidity is increased (or as a_{H_2O} is decreased). The other activation parameters do not vary greatly at different acid concentrations.

Rate correlations

Bunnett ω[17], Bunnett-Olsen LFER 'φ'[18] and Cox-Yates excess acidity plots[13] were carried out on the data in Table 1. The results of analysis of the kinetic data in terms of various criteria are shown in Table 3. Bunnett ω plots (Fig.2) of log k_ψ + H$_A$ versus log a_{H_2O} were linear with slopes (ω values) in the range 3.2 to 4.0 for all three acids used. Such values of ω fall into the range normally associated with water acting as a nucleophile. Similar values of ω in this ranges were obtained for the hydrolysis of BBHA[15] in mineral acids for which a bimolecular mechanism was proposed. The plots (Figure not shown) of log k_ψ + H$_A$ versus (log[H⁺] + H$_A$) for Bunnett-Olsen treatment gave φ values in the range 1.0-1.2. Such φ

Table 3—Summary of rate correlations

Correlation	Acid	Acid range mol. dm^{-3}	Slope	Correlation coefficient
Bunnett ω	HCl	0.75-9.5	4.02	0.997
	H$_2$SO$_4$	2.2 -9.5	3.22	0.999
	HClO$_4$	2.2 -7.5	3.75	0.998
Bunnett-Olsen (ϕ)	HCl	2.2 -9.5	1.06	0.997
	H$_2$SO$_4$	2.2 -6.5	1.13	0.995
	HClO$_4$	1.45-6.5	1.29	0.997
Cox-Yates excess acidity m$_2^{\neq}$ m*	HCl	2.2 -9.5	0.42	0.997
	H$_2$SO$_4$	0.75-7.5	0.52	0.997
	HClO$_4$	1.75-7.5	0.35	0.998

values lie in the range said to be characteristic of water acting as a proton transfer agent. It is interesting to note that the values of both ω and ϕ were consistently high and consistent with water playing an additional role beyond that of a nucleophile. O'Connor *et al.*[19] suggested that the limits for the Bunnett-Olsen ϕ for the hydrolysis of amides should be extended to $0.47 \leqslant \phi \leqslant 0.98$. Actually the value of ϕ obtained is a composite value, being the sum of ϕ_e and ϕ_r, the values of equilibrium protonation and the rate limiting step, respectively.

The Cox-Yates method for correlating rates using the concept of "excess acidity" (X-functions) has been employed to establish the mechanisms of the acid catalysed hydrolysis of diverse substrates[20-22]. Recently[10] we have applied this method for hydrolysis of benzohydroxamic acid to check its validity. The excess acidity method is capable of revealing mechanistic features which other methods of analyzing kinetic data in strong acids cannot. Equation 1 have been derived for A-2 reactions.

$$\log k_\psi - \log C_H - 2 \log a_{H_2O} = (\log k_1/K_{SH^-}) + m_2^{\neq} m^* X \quad \ldots (1)$$

where m* is obtained from protonation studies, m$_2^{\neq}$ is characteristic of the type of reaction, and log a_{H_2O} for the A-2 reaction represents nucleophilic activity and is commonly equivalent to 2 log a_{H_2O}, where two water molecules are involved in forming the transition state. The m* for carbonyl oxygen protonation is 0.6 or less and m$_2^{\neq}$ for A-2 reactions is $\simeq 1$, thus an overall slope against X of 0.6 or less should result[23] for Eq.(1). Good linear plots were obtained (Fig.3) with slopes in the range 0.35-0.52 characteristic of an A-2 process. Similar behaviour has been observed for the hydrolysis of benzohydroxamic acid[10] and 4-methoxy benzohydroxamic acid[15]. The X values for HCl, H$_2$SO$_4$ and HClO$_4$ were obtained from $-(H_A + \log C_{H^+})$. For these correlations values of H_A and a_{H_2O}
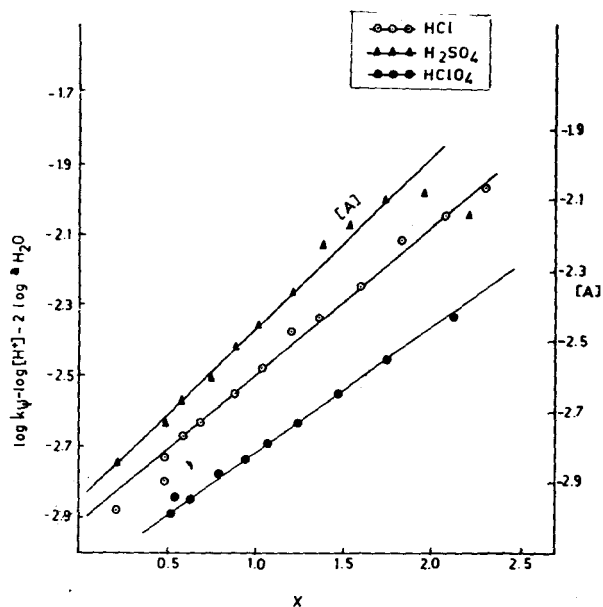

Fig. 3—Cox-Yates plots for the A-2 mechanism of hydrolysis of 3-Cl-BHA at 55°C

determined at 25°C and in aqueous medium were used whilst the reaction were carried out at 55°C and this might affect the magnitudes of the slopes.

Salt effects

Many added salts increase the protonating power of the medium, as measured by acidity function, and therefore, generally assist acid hydrolyses. Bunton *et al.*[24] have shown that the salt effect of perchlorates is negligible or slightly negative in A-2 acid catalysed hydrolysis of esters, whereas chlorides assist the hydrolysis slightly. The rate of hydrolysis of 3-Cl-BHA was studied in perchloric acid (1.45 mol dm^{-3}) using NaCl, NaBr and NaClO$_4$. Added chloride and perchlorate produces slight acceleration in rates whereas added bromide has retarding effect.
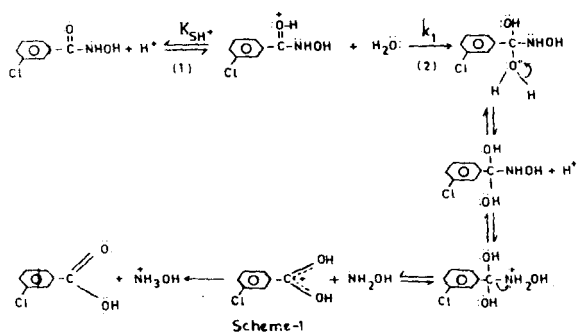
Kinetic solvent isotope effect

From the data in Table 1 kinetic solvent isotope effect (k_D/k_H) can be calculated for the 3-Cl-BHA at 55°C. The k_D/k_H values for the hydrolysis in various concentrations of sulphuric acid lie in the range 1.68-1.02. These values are consistent with a fast pre-equilibrium protonation of the substrate with a higher concentration of the conjugate acid in D$_2$SO$_4$ than H$_2$SO$_4$. The kinetic solvent isotope effect thus comprises a contribution for the pre-equilibrium protonation and one for the attack of water on the protonated substrate. Similar isotope effects have been observed in our earlier studies[25].

Conclusion

Having applied several mechanistic criteria in relation to the present study, we can now evaluate the results of these treatments. The Bunnett and Bunnett-Olsen plots, the excess acidity treatment, the salt effect and the solvent isotope effects support an A-2 type mechanism (see Scheme 1). In this mechanism, electron-donating substituents accelerate the protonation (step 1), and electron-withdrawing substituents facilitate the attack of water molecules on the protonated species (step 2). If the hydrolysis rate of the 3-Cl-BHA is compared at the same low concentration of acid catalyst, the effect of substituents will influence both the protonation equilibrium and the rate-limiting reaction step. When the [H$^+$] is low, the rate of hydrolysis of 3-Cl-BHA is slower than BHA. On the other hand, when [H$^+$] is high, the reaction rate of 3-Cl-BHA is greater than BHA.

Therefore, it is concluded that the hydrolysis of 3-Cl-BHA proceeds via rate determining attack of water on the protonated substrate, with formation of a tetrahedral intermediate that rapidly collapses to products: 3-chlorobenzoic acid and hydroxylamine (Scheme 1). There is no direct evidence available to indicate the site of protonation of this substrate. The conjugate acid is formulated with protonated oxygen atom, but the tautomer with the protonated nitrogen atom must be considered too. We have three choices, the carbonyl oxygen, the nitrogen atom and the OH group. Modena et al.[8] showed that the hydrolysis of hydroxamic acids occurs via nucleophilic attack of water on the N-protonated conjugate acid. They concluded, that these cations are minor components in the tautomeric equilibrium. Novak et al.[7] advocated for O-protonation. The most telling evidence comes from NMR and UV studies[25,26] and there is virtually universal agreement that the O-protonated form is favoured in concentrated acid solutions. As solutions of hydroxamic acid cations are made still more acidic, the UV spectra of most hydroxamic acids continue to undergo changes, although these are almost always quite small. The O-protonated ions possess considerable charge delocalization, and it is argued that they will be less affected by removal of water from the medium than the N-protonated ions. Accordingly, the equilibrium will be tipped from the N- to the O-protonated form as the concentration of acid becomes high.

Acknowledgement

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Scheme-1