

Kinetic Study of Acid-Catalysed Hydrolysis of p-Methyl Benzyl-2-Furo Hydroxamic Acid

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Abstract

The kinetics of the hydrolysis of the title compound has been investigated in hydrochloric, sulphuric, and perchloric acids at 55°C in 20% Dioxane-water medium. Rate maxima are observed for hydrolysis of each acid. Activation parameters have also been determined. Based on Bunnett, Bunnett-Olsen, and Cox-Yate's excess acidity treatments, the mechanism is seen as involving a pre-equilibrium protonation followed by a rate-limiting A-2 type nucleophilic attack by water.

Keywords - Hydroxamic acid, activation parameters, kinetics, Bunnett, Bunnett Olsen, Cox Yates.

INTRODUCTION

The chemistry of hydroxamic acids and their derivatives seems neverending, each time of its investigation opens a new area of research in biological¹⁻⁶ and analytical⁷⁻¹⁰ fields continuing our research^{11,12} in the field of the mechanism of hydrolysis of unsubstituted and N-substituted heterocyclic hydroxamic acids^{14,15} in acidic medium, we report herein the acid-catalyzed hydrolysis of p-Methyl Benzyl-2-Furo Hydroxamic acid [4-CH₃-C₆H₄N(O.H.)-C(O)-C₄H₃O] at 55°C in 20% (v/v) Dioxane-water medium. The excess acidity method¹⁶ has been applied to the hydrolysis rate data for the elucidation of the reaction mechanism in acid medium.

EXPERIMENTAL

p-Methyl Benzyl-2-Furo Hydroxamic acid was prepared by standard method¹⁷. The acids used were of analytical reagent quality, and titrations determined their concentrations with standard alkali. Dioxane (B.D.H., AR) was used without further purification. The ferric chloride solution used in the colorimetric procedure was prepared by dissolution of 44.0g of anhydrous ferric chloride (Qualigen, AR) in 1 litre distilled water containing 10ml of concentrated hydrochloric acid. The use made kinetic measurements of the spectrophotometric method reported previously¹⁸ employing a UV-VIS 106 systronics spectrophotometer set at 540 nm.

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RESULTS AND DISCUSSION

The reaction followed pseudo-first-order kinetics.

$$-\frac{d}{dt}[\text{HA}] = K_2[\text{HA}][\text{H}^+] \\ = k_v[\text{HA}]$$

The observed pseudo-first-order rate constants for the catalytic effect of hydrochloric, sulphuric, and perchloric acid are given in Table-1. The rate of hydrolysis passes through a maximum, followed by a rate decrease with further increasing acid concentration. This non-linearity is because the equilibrium between the reactants and the protonated species of the rate-determining step does not correspond only to a simple protonation but also to the addition of water molecules. On the one hand, increased acidity raises the concentration of the substrate's reactive conjugate acid form. Still, at the same time, it reduces the activity of water needed to complete the hydrolysis. This is true only for A-2 hydrolysis since, in A-1 reactions, water does not intervene during the rate-limiting step. As water becomes progressively less available, the hydrolysis rate diminishes steadily. The order of the relative rate of hydrolysis of p-TFHA in moderately concentrated acids is HClO₄ > H₂SO₄ > HCl.

Table 1: Observed Pseudo first-order rate constants the hydrolysis of p-CH₃BFHA.



Temp = 55°C, Solvent : 20% (v/v) 1-4 Dioxane

[Concentration] [M]	$K_{\psi} \times 10^4$ (min ⁻¹)		
	HCl	H ₂ SO ₄	HClO ₄
0.75	4.02	3.85	16.22
1.45	6.74	5.2	25.19
2.9	10.66	15.6	46.03
3.5	13.13	18.19	52.61
4.5	27.69	45.4	157.04
5	28.38	61.65	340.69
5.8	37.88	158.82	721.72
6.5	51.68	179.72	1175.33
7.54	70.76	594.48	a
8.5	108.44	–	–

Higher perchloric acid concentrations bring about uncontrolled reactions (destruction).

ACTIVATION PARAMETERS

Activation parameters were also determined for some acidities are recorded in Table - 2. These values are fairly typical for A-2 reaction²². ΔS^{\ddagger} changing from a larger negative value in the dilute acid region to less negative values in a more concentrated acid region. This implies that a

change from a more to less restricted transition state occurs as the acidity is increased (or as $a_{\text{H}_2\text{O}}$ is decreased). The other activation parameters do not vary significantly at different acid concentrations.

Table 2: Activation parameters for the hydrolysis of p-CH₃BFHA.

Conc. [M]	HCl				H ₂ SO ₄				HClO ₄			
	Ea	ΔH^{\ddagger}	ΔG^{\ddagger}	ΔS^{\ddagger}	Ea	ΔH^{\ddagger}	ΔG^{\ddagger}	ΔS^{\ddagger}	Ea	ΔH^{\ddagger}	ΔG^{\ddagger}	ΔS^{\ddagger}
0.75	69.88	67.15	110.37	-131.76	68.76	66.04	110.49	-135.52	78.24	75.52	106.57	-94.67
2.9	76.42	73.69	107.71	-103.72	63.46	60.73	106.67	-140.06	74.43	71.71	103.72	-97.61
5.8	64.69	61.97	104.25	-128.91	74.65	71.93	100.34	-86.64	83.61	80.61	96.21	-46.73

Ea, ΔH^{\ddagger} , ΔG^{\ddagger} in KJ mol⁻¹ and ΔS^{\ddagger} in J mol⁻¹ K⁻¹.

RATE-ACIDITY CORRELATIONS

Bunnett (ω)¹⁹, Bunnett-Olsen (ϕ)²⁰, and Cox-Yates excess acidity plots¹⁶ were carried out on the data in Table-1. The results of the analysis of the kinetic data in terms of various criteria are shown in Table-3. Bunnett (ω) plots (Fig. I) of $\log k_{\psi} + H_0$ versus $\log a_w$ were linear with slopes (ω values) in the range 1.5 to 3.1 for all three acids used. Such values of (ω) fall into the range normally associated with water acting

as a nucleophile. The plots (Fig. II) of $\log k_{\psi} + H_0$ versus $\log [H^+] + H_0$ for Bunnett-Olsen treatment gave (ϕ) values in range 0.27 to 0.49. Such (ϕ) values lie in the range said to be characterized by water acting as a proton transfer agent. It is interesting to note that both (ω) and (ϕ) values were consistent with water playing an additional role beyond that of a nucleophile.

Table 3: Rate correlations for the hydrolysis of p-CH₃BFHA.

Correlation	Acid	Slope	Correlation Coefficient
Bunnett (ω)	HCl	3.09	0.862
	H ₂ SO ₄	1.49	0.936
	HClO ₄	1.49	0.928
Bunnett- Olsen (ϕ)	HCl	0.27	0.949
	H ₂ SO ₄	0.49	0.946
	HClO ₄	0.47	0.913
Cox-Yates excess acidity ($m_2^*m^*$)	HCl	0.6	0.967
	H ₂ SO ₄	0.11	0.893
	HClO ₄	0.65	0.977

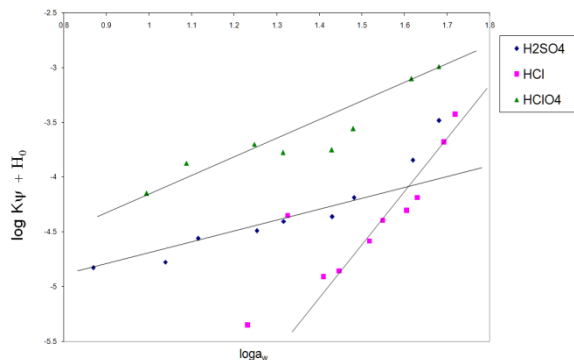


Fig. 1: Bunnett ‘ ω ’ Plots for the hydrolysis of p-CH₃BFHA in 20% (v/v) Dioxane-water at 55°C

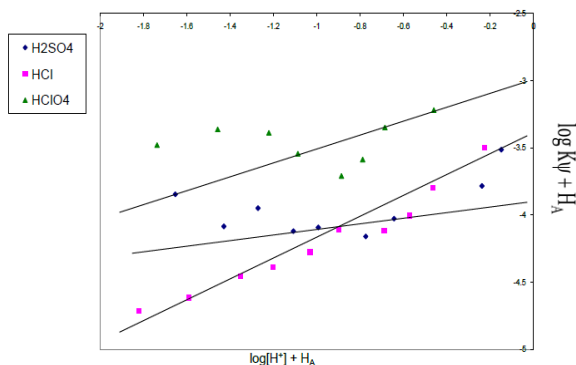


Fig.2: Bunnett – Olsen ‘ ϕ ’ Plots for the hydrolysis of p-CH₃BFHA in 20% (v/v) Dioxane-water at 55°C

The Cox-Yates method can reveal mechanistic features that other methods of analyzing kinetic data in strong acid cannot. We employed this method to test for an A-2 mechanism. Equation 1 has been derived for A-2 reactions.

$$\log K_{\psi} - \log C_{H^+} - 2 \log a_w = (\log K_1 / K_{SH^+}) + m_2^* m^* x \quad \dots(1)$$

Where m^* is obtained from protonation studies, m_2^* is characteristic of the type of reaction. The $\log a_w$ for the A-2 response represents nucleophilic activity and is commonly equivalent to $2 \log a_w$, 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^* for A-2 reactions is $\cong 1$. Thus an overall slope against X of 0.6 or less should result¹⁶ for Eq. (1). Linear plots were obtained (Fig. III) with slopes in the range of 0.11 to 0.65 characteristic of an A-2 process. For these correlations, H.A. values and a_w determined at 25°C and in the aqueous medium were used while the reaction was carried out at 55°C, which might affect the magnitudes of the slopes.

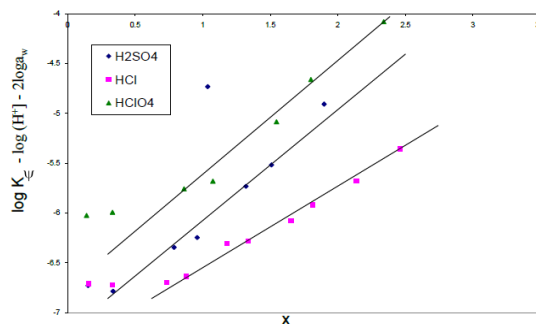


Fig.3: COX- Yates Excess Acidity Plots for the hydrolysis of p-CH₃BFHA in 20% (v/v) Dioxane- water at 55°C

SALT EFFECT

In addition, many salts increase the protonating power of the medium, as measured by acidity function and, therefore, generally assist acid hydrolysis. Bunton et al²¹. Have shown that the salt effect of perchlorates is negligible or slightly negative in A-2 acid catalyzed hydrolysis of esters, whereas chlorides assist the hydrolysis slightly.

The hydrolysis rate of p-TFHA was studied in hydrochloric acid (1.45 M) using NaCl, KCl, and LiCl. Added Cl⁻ produce a slight acceleration in rates. Thus, the data in Table-4 suggest that the substrate is undergoing reaction by an A-2 pathway.

Table 4: Effect of salt on the hydrolysis of p-CH₃BFHA in 20% (v/v) Dioxane-water at 55°C.

$K_{\psi} \times 10^4 \text{ (min}^{-1}\text{)}$			
HCl (1.45 M)			
Salt [M]	LiCl	NaCl	KCl
NIL	6.7	6.7	6.7
0.5	8.8	17.9	12.3
1	8.9	19	10.4
1.5	9.6	10.5	9.3
2	10	8.7	8

SOLVENT EFFECT

The hydrolysis of p-CH₃BFHA was measured by varying percentage of co-solvents from 10%-70% (v/v) in 2.9 M HCl at 55°C. The results listed in Table-5 shows that the rate constant of hydrolysis reaction is sensitive to solvent composition. In DMSO, the constant rate increases and then decreases with increasing solvent composition. In dioxane, acetonitrile, acetone, and ethanol, rate constants decrease with increasing solvent composition.

The interpretation of the kinetic solvent effect on reaction rates is difficult and is, in general, dominated more by exceptions than rules. How a particular solvent will affect each step in a reaction is hard to predict since, experimentally, is the net effect. No simple theory appears adequate to explain the effects observed.

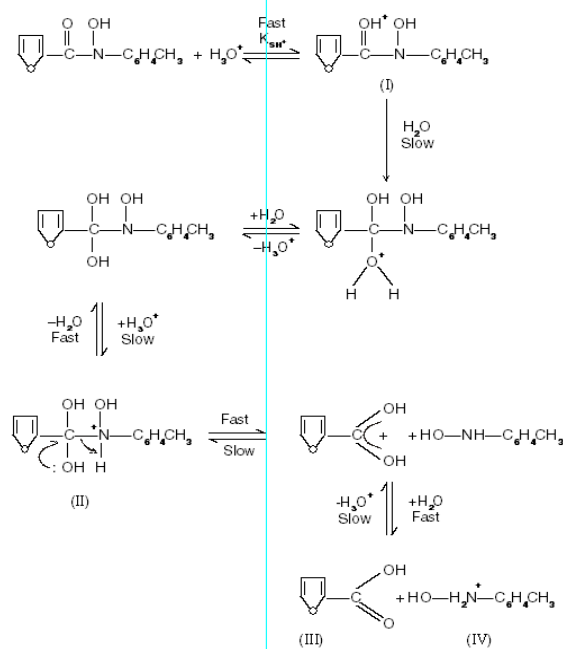
Table 5: Effect of different solvents on the hydrolysis of p-CH₃BFHA at 55°C.

$K_{\psi} \times 10^4 \text{ (min}^{-1}\text{)}$					
Solvent % (v/v)	Dioxane	DMSO	Acetonitrile	Acetone	Ethanol
10	20.3	18.8	10.2	11.8	11.8
20	17.3	19.1	7.9	9.6	8.4
40	15.5	20.5	5.4	7.8	6.3
60	11.8	13.6	5.1	2.2	4.4
70	9.9	8.9	8.1	–	2.9

MECHANISM

Based on the above discussion and results obtained from Bunnett, Bunnett-Olsen, and excess acidity analysis, the most plausible mechanism (Scheme-I) appears to involve a rapid protonation of p-Methyl Benzyl-2-Furo Hydroxamic acid, followed by a slow reaction of water with O-protonated form, (I), leading to the transition complex, (II), and subsequent hydrolysis resulting in the fission of N-acyl bond giving corresponding carboxylic acid, (III), and protonated

hydroxylamine, (IV), as the products.



Scheme-I

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