RESEARCH ARTICLE

Mechanistic Investigation for the Acidic Hydrolysis of p-Methyl Benzyl-2-Theno Hydroxamic Acid

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Mechanistic Investigation for the Acidic Hydrolysis of p-Methyl Benzyl-2-Theno Hydroxamic Acid

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Abstract
The rates of hydrolysis of p-Methyl Benzyl-2-Theno Hydroxamic Acid have been studied over a wide range of acidities in hydrochloric, sulphuric, and perchloric acids in 20% (v/v) dioxane-water at 55ºC. Plots of the first order rate constant, K_{obs} against H^+ show maxima, which are caused by protonation of the substrate. The kinetics of the hydrolysis has been analyzed by Bunnett, Bunnett Olsen and Cox-Yates excess acidity methods. The variation of reaction rate with acid concentration can be described by a two parameter equation. The mechanism of the reactions was found to be A-2, which involves two steps. A rapid protonation is followed by rate determining step in which nucleophilic attack of water at the carbonyl carbon takes place giving a tetrahedral intermediate, which rapidly changes to the hydrolytic products. Arrhenius activation parameters were also determined.

Keywords: Hydroxamic acid; protonation; Bunnett; Bunnett Olsen; Cox Yates; kinetics; nucleophilic.

1. Introduction

In recent years we have been studying the synthesis, structure and nucleophilicities of hydroxamic acids and the work continues because of their versatile applications in different fields. Extensive works have been carried out on their synthesis [1, 2] complexation with metal ions [3-5], biological [6-8], kinetics [9-13], and medicinal applications [14-17]. Since very little work has been done on the kinetics and mechanistic studies of heterocyclic hydroxamic acids containing thiophene ring i.e. theno hydroxamic acids. This paper reports a kinetic study of acid catalyzed hydrolysis of p-methyl benzyl-2-theno hydroxamic acid in aqueous mineral acids (HCl, $HClO_4$ and H_2SO_4) using 20 % (v/v) dioxane-water at 55°C. The order of the reaction and the mechanistic information's obtained directly from the rate acidity profile has been described. A variety of rate acidity correlations have been applied in the deduction of mechanism of hydrolysis.

2. Methods

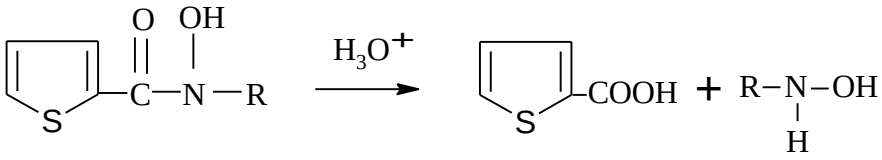
All the thenohydroxamic acids used were prepared by standard method given by Priyadarshini and Tandon [1]. All the chemicals used were AR grade. The concentrations of mineral acids were determined by titration with standard alkali. The standard ferric chloride solution used for colorimetric method was prepared by dissolving 44.0 gm anhydrous ferric chloride in 1dm^3 of distilled water containing 10 cm^3 of concentrated hydrochloric acid during spectrophotometric determination 2 cm^3 aliquot of reaction mixture containing 20 % dioxane was periodically removed and added to 2 cm^3 of ferric chloride solution which was further diluted to 10 cm^3 of distilled water and absorbance was measured with a UV-Vis. 118 spectrophotometer at 540 nm. The reaction rates were measured by using different ranges of acidities of hydrochloric, sulphuric and perchloric acids.

3. Results and Discussion

A characteristic decrease in absorption of the iron (III) p-CH_3BTHA complex was observed while studying the kinetics of acid hydrolysis of N-Methyl benzyl-2-theno hydroxamic acid (p-CH_3BTHA) spectrophotometrically. As the hydrolysis was carried out in excess of hydronium ion hence it was concluded that the reaction followed pseudo first order kinetics.

$$-\frac{d[HA]}{dt} = K[HA][H_3O^+]$$

$$= K[HA] \quad \text{(HA stands for hydroxamic acid)}$$



The data in Table 1 represents the catalytic effect of different concentrations of hydrochloric, sulphuric and perchloric acid on the pseudo first order rate constant. It is clear from the data that the catalytic effect is in the order $HClO_4 > H_2SO_4 > HCl$ in moderate concentrations for p-CH_3BTHA.

Table 1: Observed pseudo-first order rate constants for hydrolysis of p-CH_3BTHA at 55 °C.

Acid (mol dm^{-1})	$k_\psi \times 10^4$ min^{-1}		
	HCl	H_2SO_4	$HClO_4$
0.75	5.027	4.389	19.897
1.45	7.942	6.198	27.235
1.75	8.186	12.363	36.178
2.90	10.265	16.672	56.823
3.50	16.297	19.219	82.49
4.50	23.106	35.787	160.92
5.00	29.389	55.265	256.17
5.80	39.012	77.892	348.94
6.50	56.418	122.37	692.72
7.50	80.932	151.56	-
8.50	110.24	391.81	-

The rates of acid catalyzed hydrolysis of hydroxamic acids were measured at 45°C, 55°C and 65°C using HCl, H_2SO_4 and $HClO_4$.Higher perchloric acid concentration brings about uncontrolled reaction, hence studies at higher molarities were not possible. The various activation parameters viz. energy of activation (E_a), free energy of activation ($\Delta G^{\neq}$), enthalpy of activation ($\Delta H^{\neq}$), and entropy of activation $\Delta S^{\neq}$) were calculated. Table 2 shows the Arrhenius parameters at different molarities for p-CH_3BTHA.

Table 2: Activation parameters for the hydrolysis of p-CH_3BTHA.

Acid mol dm^{-3}	HCl				H_2SO_4				$HClO_4$			
	Ea	$\Delta H^{\neq}$	$\Delta S^{\neq}$	$\Delta G^{\neq}$	Ea	$\Delta H^{\neq}$	$\Delta S^{\neq}$	$\Delta G^{\neq}$	Ea	$\Delta H^{\neq}$	$\Delta S^{\neq}$	$\Delta G^{\neq}$
1.45	17.7	17.0	-19.3	23.3	16.0	15.4	-24.9	23.5	16.2	15.5	-22.6	22.9
2.90	19.7	19.1	-12.4	23.2	17.2	16.5	-19.4	22.9	15.9	15.2	-20.8	22.0
5.80	20.1	19.6	-08.5	22.4	18.9	18.2	-10.7	21.8	19.5	18.8	-18.9	25.1

Acid catalyzed hydroxamic acid hydrolysis reaction can be discussed in terms of a two-step mechanism i.e. an equilibrium state in which the substrate is protonated and a rate limiting step. Acid catalyzed hydrolysis reactions in which the rate limiting step does not involve water are characterized A-1 while those which involve water in the rate limiting step have been designated as A-2. The value of $\Delta S^{\neq}$ is

positive or small negative for many A-1 reactions. Here the $\Delta S^{\neq}$ shows large negative values at lower concentration and at higher concentration it shows less negative values. The other activation parameters do not vary much at different concentrations of the mineral acids.

Rate correlation: According to Bunnett correlation [18] following Equation-1, if log $k_\psi + H_o$ are plotted against log a_{H2O} (log of activity of water) straight lines are obtained.

$$\log k_\psi + H_0 = \omega \log a_{H2O} + \text{constant} \qquad (1)$$

Figure 1 shows Bunnett 'ω' plots for p-CH_3BTHA. In the present investigation, linear free energy relationship developed by Bunnett-Olsen [19] 'φ' are obtained for acid catalyzed hydrolysis of p-CH_3BTHA following the Equation-2, if log $k_\psi + H_o$ are plotted against log $[H^+] + H_o$ (Figure 2).

$$\log k_\psi + H_X = \varphi[H_X + \log [H^+]] \qquad (2)$$

where $H_X = H_o$ or H_A

The correlation values of 'ω' and 'φ' are summarized in Table 3. The values of 'ω' are > 3.6 such values of 'ω' falls in the range where water is acting as a proton transfer agent in rate determining step and a bimolecular mechanism is favoured. The values of 'φ' obtained ranges from 0.26-1.5 indicative of water acting as nucleophile and proton transfer agent.

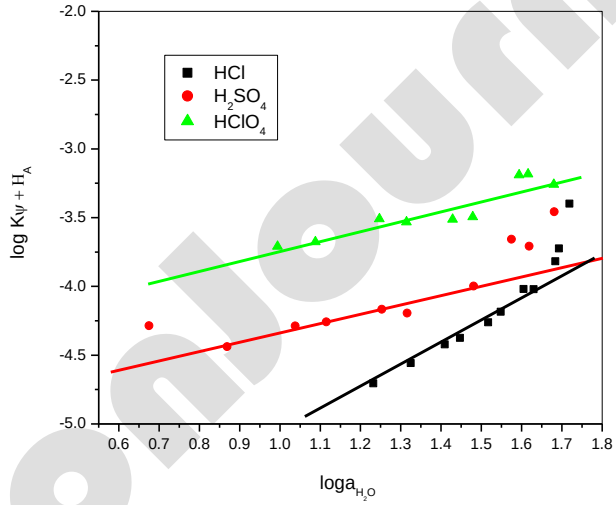


Figure 1: Bunnett 'ω' plots for the acidic hydrolysis of p-CH_3BTHA in 20 % (V/V) dioxane at 55 °C.

Recently, Cox-Yates excess acidity method [20, 21] was applied for investigation of reaction mechanism in strong mineral acids and Equation-3 has been derived for A-2 reaction.

$$\log k_\psi - \log [H^+] - 2 \log a_{H2O} = (\log k_1 / K_{SH^+}) + m_2^{\neq} m^* X \qquad (3)$$

Table 3: Rate correlation data for p-CH_3BTHA.

Hydroxamic acid	Mineral acid	Acid range [M]	Bunnett 'ω'	Bunnett Olsen 'φ'	Cox-Yates Excess Acidity $m_2^{\neq} m^*$
p-CH_3BTHA	HCl	0.75-8.50	2.3	0.74	0.58
	H_2SO_4	0.75-8.50	0.82	0.49	1.0
	$HClO_4$	0.75-8.50	0.76	0.42	0.38

The resulting plot is shown in Figure 3 for p-CH_3BTHA. The slope values giving m_2 m* for both theno and hydroxamic acid are shown in Table 3.

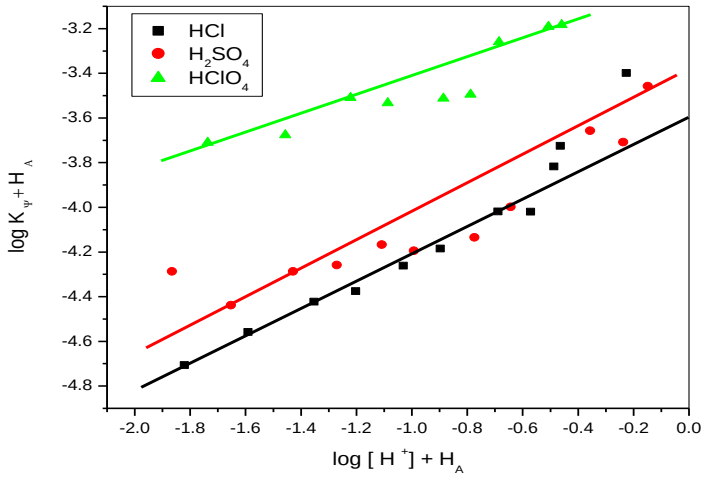


Figure 2: Bunnett 'φ' plots for the acidic hydrolysis of p-CH_3BTHA in 20 % (V/V) dioxane at 55 °C.

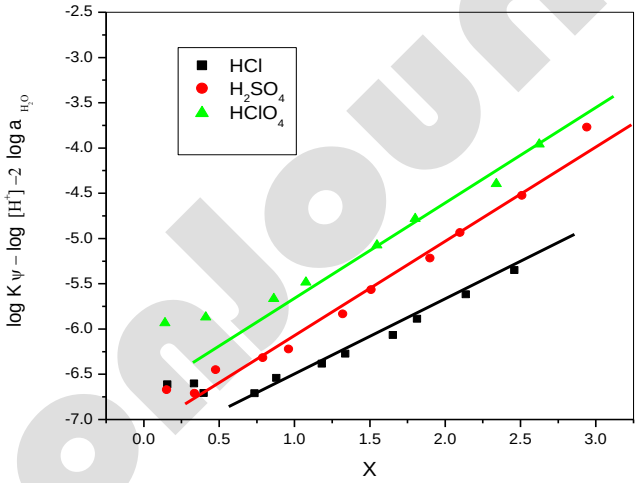


Figure 3: Cox-Yates excess acidity plots for the acidic hydrolysis of p-CH_3BTHA in 20 % (V/V) dioxane at 55 °C.

4. Conclusion

The acid catalyzed hydrolysis of p-CH_3BTHA takes place through A-2 mechanism. The carbonyl oxygen is rapidly protonated followed by slow reaction of water with the o-protonated form and after proton transfer the transition complex is obtained which on subsequent hydrolysis, due to N-aryl bond fission leads to formation of hydrolytic products. for these correlations, values of H_o and log a_{H2O} determined at 25°C in aqueous medium, were used while the reaction were carried out at 55°C and this might affect the magnitudes of the slopes.

Competing Interests

Authors do not have any competing interests with the publication of this work.

Authors' Contributions

Both authors contributed more or less equally to this work.

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