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An Investigation into the Mechanism of Acid-Catalyzed Hydrolysis of *N*-Benzylbenzohydroxamic Acid[†]

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(Received July 27, 1988)

The catalytic effects of hydrochloric, perchloric, and sulfuric acids on the hydrolysis of *N*-benzylbenzohydroxamic acid (BBHA) have been examined in 10% (v/v) dioxane-water at 55 °C. Plots of the pseudo-first-order rate constants k_ψ against $[H^+]$ show maxima which arise from extensive protonation of the substrate. Analyses of the kinetic data by Bunnett and Bunnett-Olsen criteria, solvent deuterium isotope effects, salt effects and entropies of activation are consistent with a bimolecular mechanism.

As a part of a broad program on the hydrolysis reaction of hydroxamic acids in concentrated mineral acids,[1–6] we have presently undertaken the study of the acid catalyzed hydrolysis of *N*-benzylbenzohydroxamic acid (BBHA). No kinetic study of the hydrolysis of BBHA have previously been reported. BBHA has been found to be a highly selective reagent for the spectrophotometric determination of vanadium(V).[7] However, due to hydrolysis of hydroxamic acids into the parent carboxylic acids and hydroxylamines in concentrated mineral acids severe problems are faced in achieving the desired objectives. Hence, reaction mechanisms and hydrolytic stabilities have been investigated.

In investigating the mechanism we have examined our kinetic data in 10% (v/v) dioxane-water medium, with reference to four different diagnostic criteria; the effect of mineral acid and of added salt, the solvent isotope effect, and the effect of temperature.

Experimental

BBHA was provided by Prof. Usha Tandon of this laboratory and characterized by mp, elemental analysis, UV, IR, NMR, and mass spectral data. The acids used were of analytical reagent quality. Their concentrations were determined by titration with standard alkali. Sodium perchlorate was a recrystallized commercial sample. It was dehydrated at 150 °C. Anhydrous sodium chloride was dried similarly. Dioxane (BDH, AR) was used after purification. Deuterium oxide, D_2O (isotopic purity>99.8%), DCl (isotopic purity>95%), and D_2SO_4 (isotopic purity>95%) were procured from BARC, Bombay. Iron(III)-chloride solution used in colorimetric procedure was prepared by the standard method.

Kinetic measurements were made by use of the spectrophotometric method reported previously[1] using a SPEKOL set at 520 nm.

Results

Rate Profiles. The observed pseudo-first-order rate constants for the catalytic effect of hydrochloric, perchloric and sulfuric acids are given in Table 1. In order to emphasise the difference in the catalytic efficiencies of the different acids and to illustrate that the rate acidity profiles go through maxima, these data have been plotted in Fig. 1. In sulfuric and hydrochloric acid the dependance of BBHA is characterized by an initial rate increase with the acid concentration, passing through a maximum, followed by a rate decrease with further increasing acid concentration. In the case of perchloric acid, the same trend is observed with a maximum except that the final increase occurs at higher acid concentration. We have previously observed,[1] and commented on, similar maxima in the hydrolysis of *N*-phenylbenzohydroxamic acid (PBHA). Such maxima are attributed to two opposing effects of increasing the acid concentration. On the one hand increased acidity raises the concentration of the reactive conjugate acid form of the substrate, but at the same time reduces the available water needed to complete the hydrolysis. The rate maxima that we observe are superficially similar to those found in acid hydro-

Table 1. Observed Pseudo-First-Order Rate Constants for Hydrolysis of *N*-Benzylbenzohydroxamic Acid (BBHA) (Temp=50 °C, Solvent: Dioxane 10% (v/v))

Acid	$k_\psi \cdot 10^3/\text{min}^{-1}$		
M	HCl	H_2SO_4	$HClO_4$
0.72	—	2.71	—
1.16	4.23	—	2.52
1.45	5.06	5.08	4.36
2.02	—	7.00	—
2.32	8.29	—	6.74
2.90	10.5	10.1	8.05
3.50	11.9	12.0	8.80
4.00	13.6	14.2	9.30
4.50	15.4	14.8	8.97
5.00	—	14.2	8.19
5.22	17.1	—	—
5.80	18.5	—	6.23
6.00	—	12.0	—
6.50	19.0	8.67	4.24
7.00	18.5	7.44	—
7.50	17.6	—	1.81
8.00	16.3	3.56	1.06
8.50	14.6	—	1.00
9.00	13.1	1.24	0.257
9.50	11.1	—	—
10.0	—	0.597	—
10.1	—	—	0.745
10.4	9.06	—	—

[†] Presented in part at the 7th IUPAC Conference on Physical Organic Chemistry, Auckland, New Zealand, August 1984.

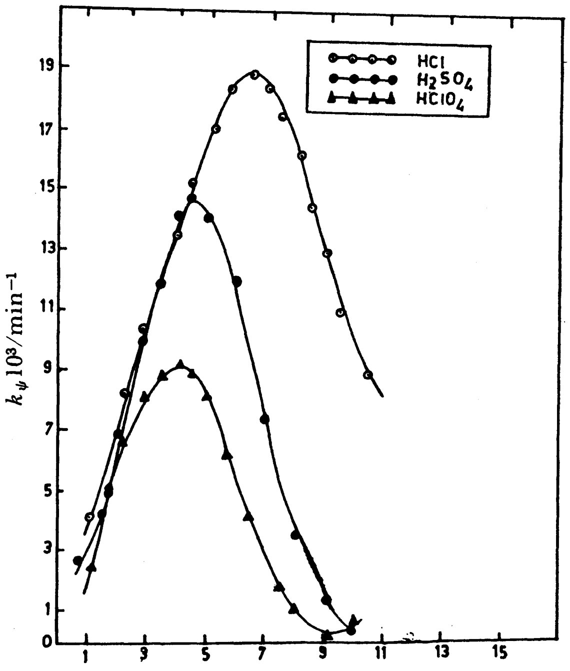


Fig. 1. Rate acidity profiles of pseudo-first-order rate constants for the hydrolysis of BBHA at 55 °C.

lyses of esters,[8] amides,[9] lactams,[10] and hydrazines.[11]

At acid concentrations in the range 0.72 to 4.5 M the catalytic effect (1M=1 mol dm^{-3}) of acids decreases in the order $HCl \approx H_2SO_4 > HClO_4$. At acid concentration above 5.0 M, the catalytic effectiveness of the acids decreases in the sequence $HCl > H_2SO_4 > HClO_4$. Bunton[12] and his co-workers have suggested that such an order is associated with an A-2 mechanism. They attributed this behavior in part to a propensity of perchlorate ion, a large ion of low charge density, to associate preferentially with carbenium ions, actual or partially formed in a transition state. They also consider that transition states with little or no carbenium ion character but with good sites for hydrogen bonding with the medium will be favored in mineral acids having anions of higher charge density (e.g., HSO_4^- or Cl^-). Studies at higher molarities are not possible because of the strong oxidizing and dehydrating properties of H_2SO_4.

The rate of hydrolysis of BBHA is fast as compared to PBHA[1] upto particular acidity region (0.72 to 7.0 M H_2SO_4 and 1.16 to 6.5 M $HClO_4$). It may be due to electron donating nature of $-CH_2$ group attached between C_6H_5 and the nitrogen of the functional group. This may facilitate the protonation of substrate.

Treatment of Rate Data. For all the sets of data in Table 1, we have correlated the data in terms of the acidity function H_0[13] and H_A,[14] activity of water a_{H_2O} and total concentration of hydrogen ion $[H^+]$.

One of the difficulties in the present study in using criteria which utilize acidity function (H_0 and H_A) or activity of water (a_{H_2O}) values is the difference between the temperature and medium at which the hydrolysis of BBHA was studied (55 °C and 10% (v/v) dioxane) and that for which the vast majority of such data is available (25 °C and aqueous medium), and the lack of precise information on the protonation behavior of BBHA. Very few detailed studies of the variation of acidity function with temperature and medium have been reported. We have therefore in the present study used acidity function and water activity at 25 °C for all the acids used. Bunnett and Olsen[15] adopted a similar approach in a study of the acid-catalyzed hydrolysis of *o*-tolunitrile at 133 °C.

The results of Bunnett and Bunnett-Olsen analysis are summarized in Table 3. Most of the correlations

Table 3. Kinetic Solvent Isotope Effect at 55 °C

Solvent	Catalyst	$k_\psi \cdot 10^3$ / min^{-1}	k_D/k_H
H_2O	1.45 M HCl	5.06	2.1
D_2O	1.45 M DCl	11.0	
H_2O	2.90 M HCl	10.5	1.58
D_2O	2.90 M DCl	16.6	
H_2O	5.80 M HCl	18.5	1.37
D_2O	5.80 M DCl	25.4	
H_2O	10.4 M HCl	9.06	1.16
D_2O	10.4 M DCl	10.6	
H_2O	0.72 M H_2SO_4	2.71	1.62
D_2O	0.72 M D_2SO_4	4.40	
H_2O	4.0 M H_2SO_4	14.2	1.52
D_2O	4.0 M D_2SO_4	21.6	
H_2O	5.0 M H_2SO_4	14.2	1.19
D_2O	5.0 M D_2SO_4	17.0	
H_2O	8.50 M H_2SO_4	1.90	0.63
D_2O	8.50 M D_2SO_4	1.20	

Table 2. Analysis of Rate Data[a] for the Hydrolysis of BBHA at 55 °C by Use of Bunnett and Bunnett-Olsen Lfer

Acid	Bunnett			Bunnett-Olsen lfer ϕ	
	w		w^*		
	H_0	H_A		H_0	H_A
HCl	5.6 (1.45—9.00)	4.4 (2.32—10.4)	1.7 (4.5—10.4)	1.26 (2.9—10.4)	1.14 (1.16—8.12)
H_2SO_4	4.2 (2.02—9.00)	3.9 (2.02—10.0)	0.93 (2.02—6.0)	1.08 (0.72—6.0)	1.24 (2.02—6.00)
$HClO_4$	6.4 (1.16—8.00)	4.1 (2.9—9.00)	1.12 (1.16—8.00)	1.32 (1.45—6.00)	1.56 (1.45—6.00)

a) The acid concentration range in which the parameters are calculated is inserted in the parentheses.

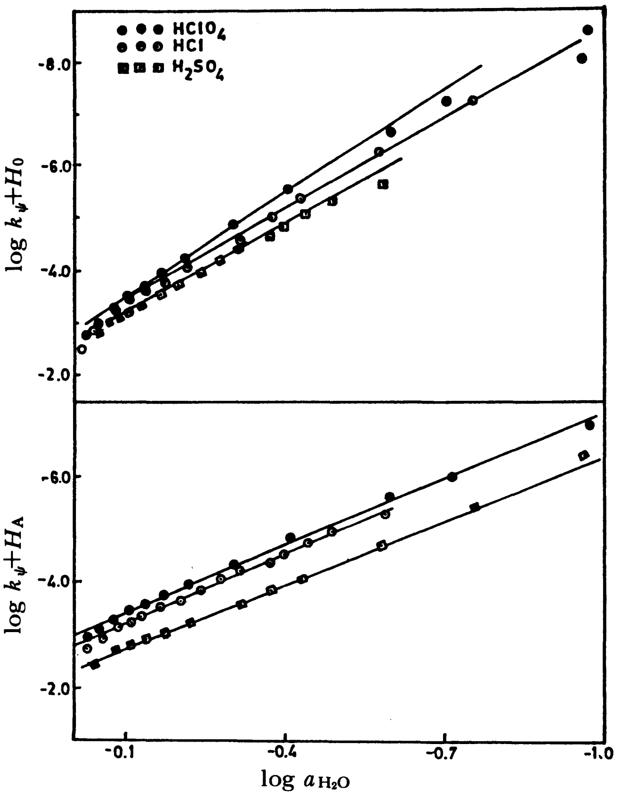


Fig. 2. Bunnett '*w*' plots for the hydrolysis of BBHA at 55 °C.

are good rather than superb, because of scatter of experimental points. Bunnett[16] plots for the hydrolysis of BBHA (using H_0 and H_A values) are shown in Fig. 2. A good linear correlation is obtained with slopes (*w* values) in the range 3.9 to 6.4 for all three acids used. Such values of '*w*' fall into the range normally associated with water acting as a proton-transfer agent. Plots of (log k_ψ −log [H$^+$]) versus log a_{H_2O} gave Bunnett 'w^*' values of 1.70, 0.92, and 1.12 for hydrochloric, sulfuric, and perchloric acids respectively. Such values are consistent with the mechanistic classification indicated by the Bunnett '*w*' values.

Treatment of the data according to Bunnett-Olsen,[17] which does not involve any water-activity data, gave linear plots with slope values ϕ (Table 2). The Bunnett-Olsen plots were far less satisfactory and showed a scattering of points at higher acidities, which could only be resolved into straight lines by omitting certain points and considering limited acid concentration ranges. The 'ϕ' values implies that water plays some additional role in the rate-determining step besides behaving as a nucleophile.

Solvent Isotope Effect. The values obtained for the deuterium kinetic solvent effect, k_D/k_H, for the hydrolysis of BBHA are shown in Table 3. The values for hydrolysis in various concentrations of hydrochloric acid lie in the range 2.1—1.16 which is consistent with specific hydrogen ion catalysis.[18] The values in sulfuric acid are all greater than unity and lie in the range 1.62 to 1.19 approaching less than unity at high concentrations of acid. Thus, the magnitude of the solvent isotope effect at a given acid strength reflects the relative importance of the protonation and the hydrolytic *N*-acyl bond cleavage steps at that acid strength. These values are also consistent with a reaction involving a preequilibrium at lower acidities followed by a rate-determining nucleophilic attack of D$_2$O or H$_2$O.

Salt Effects. Table 4 shows the effect of added sodium chloride and perchlorate on the rate of hydrolysis of BBHA. It is seen that both salts assist the rate of hydrolysis, chlorides doing so more than perchlorates. Bunton et al.[12] have shown that the salt effect of anions of low charge density such as ClO_4^- is slightly negative in A-2 acid-catalyzed ester hydrolysis and anions of high charge density such as Cl$^-$ hinder only slightly or assist the hydrolysis. Thus the data in Table 4 suggest that the substrate is undergoing reaction by an A-2 pathway.

Activation Parameters. The various activation parameters are given in Table 5. The entropy ($\Delta S^{\neq}$) and enthalpy ($\Delta H^{\neq}$) of activation were calculated from the equation $k=(kT/h)\exp(\Delta S^{\neq}/R)\exp(-\Delta H^{\neq}/RT)$ by a least-square procedure. These values are fairly typical for A-2 reactions.[19]

Mechanism. On the basis of the above results the plausible mechanism (Scheme 1) appears to involve a rapid protonation equilibrium of BBHA followed by a slow reaction of water with the protonated form, leading to the transition complex and subsequent hydrolysis resulting in the fission of *N*-acyl bond giving benzoic acid and *N*-benzylhydroxylamine as the products. At the present time there is no direct evidence as to

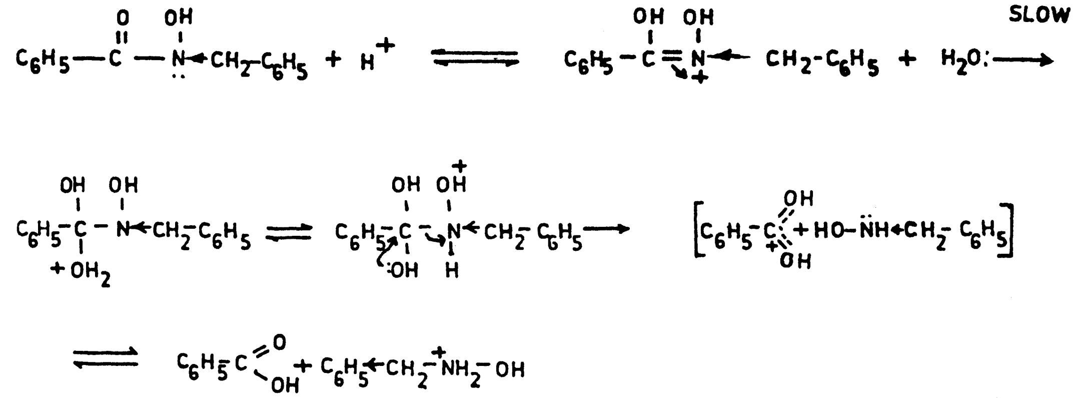
Table 4. Salt Effects on the Hydrolysis of BBHA in HClO$_4$ at 55 °C

HClO$_4$	Added salt	$k_\psi \cdot 10^3$/min^{-1}		
M	M	Nil	Added NaCl	Added NaClO$_4$
1.45	1.00	4.36	5.47	4.51
1.45	2.00	4.36	5.50	4.45
1.45	3.00	4.36	5.86	4.52
2.90	1.00	8.05	8.92	8.20

Table 5. Activation Parameters for Hydrolysis of BBHA

Acid	ΔE	$\Delta H^{\neq}$	$\Delta S^{\neq}$
	kJ mol^{-1}	kJ mol^{-1}	J K^{-1}mol^{-1}
1.45 M H$_2$SO$_4$	75.4(45—55)	72.7	−93.8
2.9 M H$_2$SO$_4$	74.4(45—65)	71.6	−91.3
6.0 M H$_2$SO$_4$	73.7(45—65)	71.0	−91.7
8.0 M H$_2$SO$_4$	78.5(45—65)	76.2	−87.3
2.9 M HClO$_4$	78.4(45—55)	76.2	−78.9
2.9 M HCl	77.4(45—65)	74.6	−81.7
6.5 M HCl	77.6(45—65)	74.8	−75.9
9.0 M HCl	78.8(45—65)	76.1	−75.4

Temperature range is indicated in the parentheses.



Scheme 1.

whether initial protonation of hydroxamic acid occurs on nitrogen or on oxygen. Protonation studies[20] on *N*-methylhydroxamic acid in concentrated sulfuric acid reveal the presence of both the species. Below 60% (w/w) H_2SO_4 *N*-protonation is preferred and above 60% (w/w) *O*-protonation. Recently, Novak et al.[21] have suggested that for the acid-catalyzed hydrolysis of *N*-hydroxyacetanilides, the protonation of the carbonyl oxygen is favored over the hydroxyl oxygen by ca. 7 orders of magnitude.

One of the authors (KKG) is grateful to CSIR, New Delhi for financial support. We are grateful to Dr. Robin A. Cox, Dr. A. Bagno, and Prof. G. Modena for stimulating correspondence.

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