

Substituent effects in the micellar hydrolysis of N-phenylbenzohydroxamic acid under acidic conditions

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The rates of hydrolysis of some *para*-substituted N-phenylbenzohydroxamic acids ($X.C_6H_4.(C=O).N(OH)C_6H_5$; $X=H, CH_3, OCH_3, F, NO_2$) under acidic conditions with cationic, anionic and nonionic surfactants have been measured. Substituent effects upon first order rate constants in water and at the micellar surface fitted Hammett equation, based on $\sigma, \sigma^+, \sigma^-$ parameters. Values of ' ρ ' increase with increasing surfactant concentration. The substituent effects indicate specific micellar influences on the rates and a difference in mechanism between the bulk aqueous phase and the micellar phase. The lipophilicity and polar effects of the substituents have also been evaluated.

Micelle catalysed reactions become an area of rapidly increasing interest in the last decade. There are a number of extremely important thermodynamics and kinetics studies of organic reactions in micellar solutions¹⁻⁸. Nevertheless, we are still far off from a quantitative understanding of micellar kinetic effects of the hydrolysis of hydroxamic acids^{9,10}. The growing interest in hydroxamic acids results from their tremendous medicinal and biological research applications. This paper describes the application of the Hammett equation of the acid catalysed hydrolysis of some *para*-substituted N-phenylbenzohydroxamic (PBHA) acids ($X.C_6H_4.C(=O).N(OH)C_6H_5$) in cationic, anionic and nonionic surfactants.

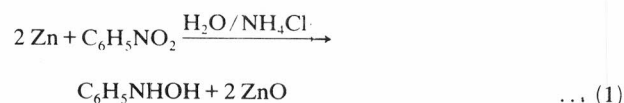
A systematic study of the effect of cationic micelles of cetyltrimethylammonium chloride and bromide [$(C_{16}H_{33}N^+(CH_3)_3 X$; $X=Br, Cl$; CTACl and CTAB respectively), dodecyltrimethylammonium bromide ($C_{12}H_{25}N^+(CH_3)_3Br$, DTAB), tetradecyltrimethylammonium bromide ($C_{14}H_{29}N^+(CH_3)_3Br$, TTAB), cetylpyridinium chloride and bromide ($C_{16}H_{33}N^+C_5H_5^+X^-$, $X=Cl^-, Br^-$, CPC and CPB), cetyldimethylethyl ammonium bromide ($C_{16}H_{33}N^+(CH_3)_2C_2H_5Br^-$; CDEAB), benzalkonium chloride ($C_{12}H_{25}N^+(CH_3)_2C_7H_7Cl$; BC), anionic micelles of lithium dodecyl sulphate ($C_{12}H_{25}OSO_3^-Li^+$, LDS) and nonionic micelles of Brij-35 ($C_{12}H_{25}(OCH_2CH_2)_{35}OH$) on this reaction have been measured in 10% (v/v) dioxane medium at 55°C.

Since many reports^{11,12} of Hammett correlations in micellar environments are not available we have made an attempt to contribute to this field.

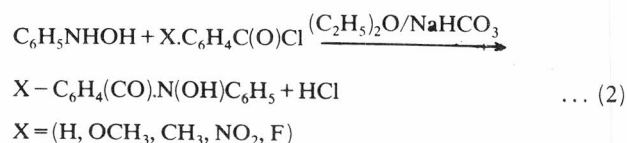
Recently Bunton *et al.*¹³ studied Hammett equation and micellar effects upon deacylation reaction. The results presented herein provide the pathways for the micellar hydrolysis of hydroxamic acid and also allow the study of substituent effects.

Materials and Methods

Hydroxamic acids were prepared by benzoylating freshly prepared and purified N-phenylhydroxylamine which in turn, was prepared by adding a 2:1 molar ratio of Zn dust to the appropriate nitrobenzene as shown in Eqn (1).



The substituted benzoyl chlorides were reacted with N-phenylhydroxylamine according to Eqn (2) in as close to a 1:1 ratio as possible.



Elemental analysis and melting points were used as criteria of purity.

CTAB, CPC, (LOBA CHEMIE), CTACl (FLUKA), DTAB, TTAB, CDEAB, CPB, BC, LDS, Brij-35 (SIGMA) were used as such. HCl was of analytical reagent grade. Dioxane (BDH, GR) was used without further purification.

Kinetics were followed spectrophotometrically by measuring the concentration of the hydroxamic acids

by the colour reaction with Fe^{3+} ions. An aliquot (2 mL) of the reaction mixture was periodically removed and added to ferric chloride (2 mL) and the resulting solution was diluted to 10 mL and its absorbance determined with Systronics 108 UV-VIS spectrophotometer. Beer's law was obeyed by the system.

All solutions were made in twice-distilled water. The CMC's of anionic and cationic surfactants were determined by conductivity method from the interaction of two lines on the plots of specific conductance vs concentration.

Results and Discussion

The observed first order rate constants for the acidic hydrolysis of a series of *para*-substituted PBHA

at 55°C over a range of surfactants concentrations are given in Table I. For each compound, as the concentration of surfactant is increased, the observed rate constant decreased. Catalysis by micelles involves at least three main steps: (i) binding of the substrate(s) to the micelle, (ii) the actual chemical transformation in the micelle (usually at the micellar surface) and (iii) release of products. The actual micellar rate effect is caused by a composite of noncovalent interactions between the micelle on one hand and the reaction and activated complex on the other hand. This is an extremely complicated problem because a number of different interactions are involved including those associated with the headgroup of the surfactant, different segments of the alkyl chain and the counter ions.

Table I—Pseudo first order rate constant for *p*-substituted *N*-phenylbenzo-hydroxamic acids in micelles at 55°C and in 10% (v/v) dioxane

[Surfactant] $10^3 M$ <i>p</i> -XC ₆ H ₄ C(O) N(OH)C ₆ H ₅	$k_{\psi} \cdot 10^5 (s^{-1})$					[Surfactant] $10^3 M$ <i>p</i> -XC ₆ H ₄ C(O)- N(OH)C ₆ H ₅	$k_{\psi} \cdot 10^5 (s^{-1})$				
	0.823	1.17	4.11	6.44	18.3		0.823	1.17	4.11	6.44	18.3
DTAB						CPC					
-H	1.72	1.63	1.56	1.51	1.47	-H	1.96	1.81	1.71	1.63	1.31
-NO ₂	1.60	1.59	1.48	1.32	1.11	-NO ₂	1.53	1.49	1.31	1.11	1.05
-OCH ₃	1.69	1.52	1.41	1.36	1.25	-CH ₃	2.20	2.19	1.91	1.73	1.42
-CH ₃	2.21	1.80	1.71	1.53	1.45	-OCH ₃	1.69	1.61	1.42	1.31	1.06
-F	1.90	1.62	1.52	1.31	1.15	-F	1.80	1.72	1.63	1.39	1.19
TTAB						CPB					
-H	1.73	1.52	1.44	1.27	1.19	-H	1.79	1.72	1.69	1.52	1.44
-NO ₂	1.53	1.32	1.29	1.00	0.73	-NO ₂	1.59	1.50	1.43	1.29	1.23
-OCH ₃	1.35	1.21	1.01	0.99	0.92	-CH ₃	1.63	1.52	1.43	1.30	1.09
-CH ₃	2.20	1.83	1.73	1.53	1.23	-OCH ₃	2.03	1.98	1.88	1.78	1.57
-F	1.82	1.40	1.35	1.10	0.82	-F	1.91	1.81	1.75	1.43	1.22
CTAB						BC					
-H	1.90	1.66	1.53	1.43	1.20	-H	1.53	1.14	0.99	0.82	0.74
-NO ₂	1.65	1.39	1.01	0.775	0.695	-NO ₂	1.49	1.21	1.18	0.95	0.63
-CH ₃	2.16	1.38	1.23	1.14	1.03	-CH ₃	1.25	1.03	0.99	0.72	0.70
-OCH ₃	1.50	1.48	1.23	1.02	0.925	-OCH ₃	1.73	1.50	1.46	1.31	1.00
-F	1.75	1.49	1.41	1.36	1.29	-F	1.24	1.09	1.03	0.91	0.78
CTACI						LDS					
-H	1.89	1.78	1.61	1.42	1.27	-H	1.88	1.76	1.60	1.59	1.44
-NO ₂	1.65	1.43	1.31	1.12	1.02	-NO ₂	1.66	1.54	1.25	1.19	1.01
-CH ₃	2.00	1.91	1.82	1.56	1.32	-CH ₃	1.59	1.51	1.41	1.38	1.19
-OCH ₃	1.62	1.51	1.43	1.21	1.02	-OCH ₃	1.50	1.42	1.51	1.43	1.20
-F	1.73	1.61	1.52	1.23	1.14	-F	1.67	1.60	1.51	1.43	1.20
CDEAB						Brij-36					
-H	1.92	1.88	1.56	1.75	1.11	-H	1.94	1.82	1.75	1.70	1.67
-NO ₂	1.61	1.53	1.41	1.11	0.92	-NO ₂	1.55	1.24	1.23	1.15	1.10
-CH ₃	1.93	1.74	1.43	1.23	1.14	-CH ₃	1.77	1.47	1.40	1.39	1.37
-OCH ₃	1.68	1.41	1.29	1.12	0.96	-OCH ₃	1.67	1.49	1.51	1.38	1.34
-F	1.75	1.42	1.35	1.21	1.02	-F	1.64	1.52	1.47	1.42	1.31

Rate constant in the absence of surfactant i.e. $k_w \cdot 10^5 (s^{-1}) = \text{H} = 2.00$; $\text{NO}_2 = 1.71$; $\text{CH}_3 = 2.25$; $\text{OCH}_3 = 1.76$; $\text{F} = 1.95$.

Table II – Correlations of the rate data by Eqn (3) in C_D range 0.00082M-0.0183M

p -X.C ₆ H ₄ - C(O)N(CH)C ₆ H ₅	k_w 10 ⁵ (s ⁻¹)	K_s	k_M 10 ⁵ (s ⁻¹)	k_M/k_w	r	p -X.C ₆ H ₄ - C(O)N(CH)C ₆ H ₅	k_w 10 ⁵ (s ⁻¹)	K_s	k_M 10 ⁵ (s ⁻¹)	k_M/k_w	r
DTAB						CPC					
-H	2.00	5640.0	1.47	0.73	0.993	-H	2.00	157.4	1.12	0.56	0.884
-NO ₂	1.71	688.2	1.26	0.73	0.994	-NO ₂	1.71	781.0	0.987	0.57	0.985
-OCH ₃	1.76	2854.4	1.42	0.80	0.912	-OCH ₃	1.76	194.8	0.881	0.50	0.999
-CH ₃	2.25	2312.3	1.10	0.49	0.999	-CH ₃	2.25	126.8	1.00	0.44	0.998
-F	1.95	1251.9	1.12	0.57	0.998	-F	1.95	125.7	0.893	0.45	0.982
TTAB						CPB					
-H	2.00	605.60	1.08	0.540	0.988	-H	2.00	234.0	1.22	0.610	0.991
-NO ₂	1.71	153.1	0.912	0.53	0.983	-NO ₂	1.71	328.0	0.913	0.533	0.972
-OCH ₃	1.76	2625.7	0.993	0.560	0.940	-OCH ₃	1.76	227.6	1.41	0.801	0.999
-CH ₃	2.25	262.3	0.233	0.100	0.990	-CH ₃	2.25	305.3	1.11	0.493	0.996
-F	1.95	282.6	0.549	0.29	0.997	-F	1.95	192.5	1.53	0.784	0.950
CTAB						BC					
-H	2.00	378.0	1.14	0.57	0.943	-H	2.00	2128.0	0.695	0.347	0.997
-NO ₂	1.71	534.0	0.753	0.44	0.954	-NO ₂	1.71	492.1	0.592	0.346	0.998
-OCH ₃	1.76	138.3	0.982	0.55	0.999	-OCH ₃	1.76	1260.8	0.989	0.561	0.956
-CH ₃	2.25	401.0	0.533	0.236	0.964	-CH ₃	2.25	981.1	0.968	0.430	0.968
-F	1.95	1219.0	1.26	0.64	0.997	-F	1.95	2053.4	0.760	0.389	0.991
CTACI						LDS					
-H	2.00	249.5	1.04	0.52	0.992	-H	2.00	576.99	0.374	0.1857	0.998
-NO ₂	1.71	307.7	0.639	0.37	0.967	-NO ₂	1.71	531.00	0.808	0.472	0.939
-OCH ₃	1.76	105.4	0.906	0.51	0.978	-OCH ₃	1.76	1236.02	0.518	0.294	0.942
-CH ₃	2.25	168.9	0.836	0.371	0.962	-CH ₃	2.25	412.39	1.21	0.537	0.998
-F	1.95	227.7	0.817	0.41	0.940	-F	1.95	897.27	1.10	0.564	0.999
CDEAB						Brij-35					
-H	2.00	71.0	0.898	0.449	0.982	-H	2.00	47.10	1.93	0.965	0.99
-NO ₂	1.71	86.0	0.794	0.46	0.952	-NO ₂	1.71	342.63	1.48	0.865	0.919
-OCH ₃	1.76	335.0	1.14	0.64	0.992	-OCH ₃	1.76	1004.21	1.59	0.903	0.999
-CH ₃	2.25	732.0	1.41	0.62	0.978	-CH ₃	2.25	92.93	1.72	0.764	0.999
-F	1.95	446.9	0.886	0.45	0.998	-F	1.95	346.16	1.72	0.882	0.999

r = correlation coefficient.

The rate surfactant profiles can be treated in terms of the pseudophase model¹³ in which water and micelle are regarded as distinct reaction media. This model yields Eqn (3).

$$\frac{1}{k_w - k_\psi} = \frac{1}{k_w - k_M} + \left(\frac{1}{k_w - k_M} \right) \left(\frac{1}{K_s(C_D - \text{CMC})} \right) \dots (3)$$

k_ψ , k_w and k_M are the observed pseudo first order, aq. phase and micellar phase rate constants, respectively and K_s is the binding constant for binding of the substrate to the micelle.

The data for all compounds yield a good fit to Eqn (3) values for K_s and k_M were obtained by least squares analysis of the linear relationship between $1/(k_w - k_\psi)$ and $(1/C_D - \text{CMC})$ from Eqn (3). The results are given in Table II. The results show that sub-

strate binds strongly to micelles. Under these conditions k_M is very small relative to k_w .

The effects of substitution has been assessed by the use of Hammett equation for uncatalysed and micellar catalysed hydrolysis. Rate constants were correlated with firstly σ and then with σ^+ and σ^- . The values of the reaction constant ' ρ ' are shown in Table III. The Hammett plots (Figure not shown) were less satisfactory and showed a scattering of points, which could be resolved into straight lines by omitting p -NO₂ substituent. For all the cases, the slopes of the Hammett plots (using σ values¹⁴) (ρ) for the catalysed hydrolysis (in micellar pseudophase) were greater than for the uncatalysed hydrolysis (aq. pseudophase). This is typical for micellar catalysed reactions and has previously been observed for the acidic hydrolysis of p -substituted orthobenzoates¹⁵ and p -substituted benzaldehyde diethyl acetals¹⁶. The introduction of an electron withdrawing or donating

Table III – Hammett reaction constant (ρ) for the acidic hydrolysis of *p*-substituted PBHA in micelle

10^3M	0.823			1.17			4.11			6.44			18.3		
	ρ	s	r	ρ	s	r	ρ	s	r	ρ	s	r	ρ	s	r
DTAB	0.178	0.023	0.987	–	–	–	0.184	0.017	0.936	0.936	–	–	–	–	–
TTAB	0.587	0.013	0.991	0.341	0.041	0.813	0.829	0.013	0.996	0.829	0.013	0.995	–	–	–
CTAB	0.256	0.036	0.869	0.212	0.038	0.719	–	–	–	0.600	0.009	0.996	–	–	–
CTACI	0.446	0.054	0.952	0.215	0.061	0.562	0.331	0.032	0.862	0.402	0.027	0.926	0.325	0.034	0.775
CDEAB	0.0142	0.034	0.952	–	–	–	0.281	0.030	0.990	0.538	0.006	0.998	–	–	–
CPC	0.243	0.007	0.983	0.129	0.861	0.996	0.217	0.024	0.991	0.303	0.027	0.918	0.163	0.140	0.983
CPB	0.199	0.032	0.780	0.230	0.009	0.990	–	–	–	–	–	–	2.14	0.112	0.980
BC	–	–	–	0.044	0.015	0.868	0.085	0.010	0.986	0.115	0.026	0.949	0.0816	0.001	0.999
LLS	0.256	0.036	0.890	0.312	0.0211	0.991	–	–	–	–	–	–	–	–	–
Brij-35	0.239	0.001	0.999	0.325	0.028	0.910	–	–	–	–	–	–	–	–	–

s = standard deviation, r = correlation coefficient.

substituent in *para*-position causes a decrease in rate of hydrolysis. Differences in ' ρ ' for reactions in water and at the micellar surfaces are more informative than raw data in analysing medium effects of micelles on reactivity. The linear plot for the micelle-catalysed reaction suggests a single mechanism is operational throughout the series. The kinetics of micellar solutions is governed by electrostatic and hydrophobic interactions between micelles and reactants. In all the cases rate retards with increasing surfactant concentration. Mechanism of acidic hydrolysis of PBHA involves participation of water as a nucleophile in the rate-determining step would be expected to be much slower in a micellar environment than in water, because of the relative scarcity of water in the micelle compared with bulk solvent. It is reasonable to relate this effect to the lower polarity of micellar surfaces, as compared to water, based on analogies with solvent effect upon values of ρ . In order to learn the effects of substituent 'hydrophobicity' (lipophilicity) on K_s and k_M the rate data have been empirically evaluated by the substituents parameter, π , σ^+ . The Stern layer is less polar than water and the interior of an aq. micelle in hydrophobic. Eqn (4) assumes that lipophilicity and polar effects as represented by the π and σ^+ parameters are separable. α is a susceptibility constant and k_M^H is the rate constant for hydrogen as substituent¹⁶.

$$\log k_M = \rho_\sigma^+ + \alpha\pi + \log k_M^H \quad \dots (4)$$

Multiple regression analysis yields ρ , α and $\log k_M$ (Table IV). The lipophilicity parameters reflect various solvation factors of substituent effect in micellar environment. The data have also been analysed by Eqn (5).

$$\log (K/N) = \rho_\sigma^+ + \alpha\pi + \log (K^H/N) \quad \dots (5)$$

Since the experimental conditions were identical for the compounds, the value of N will be the same for

Table IV – Correlation of $\log k_M$ by Eqn (4)

Surfactants	ρ	α	$\log k_M^H$	$\log k_M^H$	R
DTAB	-0.048	0.046	-4.908	-4.832	0.891
TTAB	-0.399	0.057	-5.219	-4.966	0.880
CTAB	-0.112	0.030	-5.062	-4.942	0.990
CTACI	-0.047	0.120	-5.089	-4.982	0.964
CDEAB	0.258	-0.713	-4.655	-4.046	0.890
CPC	0.293	0.004	-5.010	-4.950	0.910
CPB	0.004	0.238	-4.953	-4.913	0.881
BC	-0.906	1.343	-4.859	-5.1307	0.890
LDS	-0.020	0.016	-4.7726	-4.714	0.990
Brij-35	-0.014	0.709	-5.273	-5.427	0.807

Table V – Correlation of $\log K_s/N$ by Eqn (5)

Surfactants	ρ	α	$\log (K_s^H/N)$	$\log (K^H/N)$ (actual)	R
DTAB	-0.351	-0.379	3.338	3.751	0.970
TTAB	-0.574	-1.936	2.806	2.781	0.960
CTAB	-0.242	0.895	2.653	2.758	0.810
CTACI	-0.224	-0.160	2.372	2.396	0.760
CDEAB	-0.740	-0.226	1.710	0.822	0.780
CPC	0.474	-0.234	2.382	2.197	0.998
CPB	-0.059	0.252	2.358	2.350	0.820
BC	-0.199	-0.431	3.145	3.328	0.960
LDS	-0.902	0.509	2.537	2.761	0.970
Brij-35	-0.014	0.216	1.965	1.673	0.921

these compounds. Therefore, the micellar binding constant K_s is proportional to the KN . The result of multiple regression analysis are given in Table V. The correlation of $\log (K_s/N)$ with the lipophilicity parameter is consistent with the lower polarity of the micellar phase compared to that of the aq. phase.

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References

- Rodenas E, Dolcet C, Valiente M & Valeron E C, *Langmuir*, 10, 1994, 2088.

- 2 Bunton C A, Wright S, Holland P M & Nome F, *Langmuir*, 9, **1993** 117; Rubio D A R, Zanetti D, Nome F & Bunton C A, *Langmuir*, 10, **1994**, 1155.
- 3 Bravo C, Herves P, Leis J R & Pena M E, *J Colloid Interface Sci*, 153, **1992**, 529.
- 4 Moroi Y; *Micelles, theoretical and applied aspect* (Plenum Press, New York), Ch 4, 1992.
- 5 Bunton C A, in *surfactants in solution*, edited by K L Mittal & D O Shah (Plenum Press, New York), 11, **1991**, 17.
- 6 Blasko A, Bunton C A, Armstrong C, Gotham W, He Z M, Nikles J L & Romsted L S, *J Phys Chem*, 95, **1991**, 6747.
- 7 Bunton C A, Savelli G, in *Advances in physical organic chemistry*, edited by V Gold & D Bethell (Academic Press, New York), **1986**, 213.
- 8 Iglesias E & Montenegro L, *J chem Soc, Faraday Trans*, 91, **1995**, 1349.
- 9 Berndt D C, He Z Ayoub M E, *Int J Chem Kinet*, 24, **1992**, 695; Berndt D C, Utrapiromsuk N & Conran D E, *J Org chem*, 49, **1984**, 106.
- 10 Berndt D C, Rossman C A, Hach C L & Fillar D J, *Int J chem Kinet*, 22, **1990**, 483.
- 11 Bartoletti A, Bartolini S, Germani R, Savelli G & Bunton C A, *J Chem Soc, Perkin Trans II*, **1994**, 723.
- 12 Marin M A B, Nome F, Zanette D, Zucco C & Romsted L S, *J Phys Chem*, 99, **1995**, 10879.
- 13 Bunton C A, Nome F, Quina F H & Romsted L S, *Acc Chem Res*, 24, **1991**, 357; Menger F M, *Pure Appl Chem*, 51, **1979**, 999.
- 14 Carpenter B K, *Determination of organic reaction mechanism* (John Wiley, New York), **1980**, 145; Hansch C, Leo A, Unger S H, Kim K H, Nikaitani D & Lien E J, *J Med Chem*, 16, **1973**, 1207.
- 15 Dunlop R B & Cordes E H, *J Phys Chem*, 73, **1969**, 361.
- 16 Dunlop R B, Ghanim G A & Cordes E H, *J Phys Chem*, 73, **1969**, 1898.