*Polish J. Chem.*, **77**, 1185–1190 (2003)

# Activity Coefficient Behaviour of Nonelectrolytes in Sulfuric Acid Solutions

**by H. Vanjari and R. Pande***

*School of Studies in Chemistry, Pt. Ravishankar Shukla University, Raipur (C.G.), 492 010, India*

*(Received February 26th, 2003; revised manuscript May 30th, 2003)*

Activity coefficient behaviour of ten nonelectrolytes in sulfuric acid solutions have been investigated by evaluating their distribution ratios as a function of electrolyte concentrations. Their salting-in parameters and values of Setschenow constant are also reported to understand the structure-activity relationship.

**Key words:** activity coefficient, Setschenow constant, nonelectrolytes

Hydroxamic acids (of general formula, $R_1$ NOH·$R_2$C═O, where $R_1$ and $R_2$ are phenyl or substituted phenyl groups) have exhibited many interesting facets of chemistry, since they were first reported by H. Lossen in 1869 [1]. Their presence in nature was reported in 1967 [2]. These are mentioned to be present in microorganism also. At present, a number of hydroxamic acids and their derivatives are reported as effective anti-inflammatory [3], antitumor [4], antibiotics [5] and antimalarial [6] agents. They also serve as collagenase inhibitors [7], antiinfectives [8] and influenza virus polymerase inhibitors. Commercially available 'Desferal' is used for the removal of iron from the body [9] in iron-chelating therapy with thalassemia patients [10], and in pharmacokinetic studies in beagle dogs [11]. Their use as agonists [12], antagonists [13] and pesticides [14] is also reported.

The study involving influence of electrolyte on the activity coefficient behaviour of hydroxamic acids, the nonelectrolytes are important, due to its relation to biochemical processes [15,16] and to know more about ion-solvent interaction as a function of medium. These parameters are also useful in various studies, like reaction kinetics, hydrolysis, complexation reactions, electrode potential and extractions. In view of this the present investigation is undertaken.

## EXPERIMENTAL

Electronic corporation of India, Hyderabad, Model GS 5700 a Digital Spectrophotometer with 10 mm matched, silica cells was used for measurement of absorbance. Hydroxamic acids were prepared in this laboratory following the procedure reported in [17]. These were purified by recrystallization thrice with benzene before use. Saturated solution of ammonium metavanadate was prepared in glass distilled

* Corresponding author, e-mail: rama_pande10@yahoo.com

water. Chloroform used was shaken. Six times with equal volume of water and distilled. It was stored in dark coloured bottle in a cool place.

Partition data of the hydroxamic acids investigated are measured as a function of sulfuric acid concentration (10–55%) using carbon tetrachloride as organic phase at 303.65 K. The phases were analysed following the vanadium(V) method [18].

## RESULTS AND DISCUSSION

**Activity coefficient, $f_{HA}$:** The values of medium effect, which is equal to the ratio of the solubilities of the substances in two media, can be determined exactly for nonelectrolytes, if the solubility of a solute is limited both in water and in an other solvent. In those cases, where the solubility increases with increasing acid concentration and it becomes very high, then the measurement of partition data between the aqueous acid mixture and an inert solvent are used to obtain the activity coefficients [19], following the equation,

$$f_{HA} = \frac{\gamma}{\gamma_0}\left(\frac{K_{BH^+}}{K_{BH^+} + h_0}\right) \quad (1)$$

where, $f_{HA}$ is the activity coefficient of hydroxamic acid, $\gamma$ is partition coefficient of nonelectrolyte between carbon tetrachloride and aqueous acid mixture. $\gamma_0$ is partition coefficient between pure water and carbon tetrachloride. $h_0$ is the Hammett activity coefficient postulate, obtained following the equation, $H_0 = -\log [h_0]$. $H_0$ values for sulfuric acid solutions were taken from [20]. $K_{BH^+}$ values are derived from $pK_{BH^+}$ values of hydroxamic acids, $pK_{BH^+} = -\log K_{BH^+}$.

**Measurement of $pK_{BH^+}$ of hydroxamic acids:** Hydroxamic acids HA are protonated in presence of sulfuric acid solution.

$$HA + H^+ \underset{pK_{BH^+}}{\rightleftharpoons} H_2A^+ \quad (2)$$

Values of their protonation constants, $pK_{BH^+}$, were calculated for the reverse of (2), following the excess acidity method [21,22]:

$$\log I = pK_{BH^+} + \log C_{H^+} + m^*X \quad (3)$$

where, ionization ratio, $I = C_{H_2A^+}/C_{HA}$. It is the ratio of the concentration of protonated and unprotonated species and can be measured by the equation, that describes the variation of distribution ratio, D, with changing acidity. Thus, $I = (K_D - D)/D$. $K_D$ is the thermodynamic distribution constant between the carbon tetrachloride and aqueous acid in the region, where appreciable protonation is occurring and is estimated by least square method, and D is $\gamma$ in (1). $C_{H^+}$ is the proton concentration,

$m^*$ is the slope obtained by plotting log I *vs* X, where X is the excess acidity, which is the difference between the observed acidity and that which the system would have, if it were ideal. X values are available for the aqueous sulfuric acid solution [23].

The values of $\gamma_0$, $-H_0$, X and $D/\gamma$ as a function of sulfuric acid concentration, along with experimental error are presented in Table 1 and values of $pK_{BH^+}$ along with $K_D$, $m^*$, r, $K_{BH^+}$, $\sigma$ are presented in Table 2. Thereafter, the values of $f_{HA}$ calculated as a function of sulfuric acid concentration in the range from 30–55% are presented in Table 3.

**Setschenow constant, $k_S$:** The activity coefficient of a nonelectrolyte dissolved in aqueous electrolyte solution is empirically found to be a function of the molar concentration of electrolyte, s, and of nonelectrolyte, S, as proposed [24] in the following equation,

$$\log f_{HA} = k_S \cdot s + K \cdot S \tag{4}$$

where, $k_S$ is the Setschenow constant or salting constant. The first term of RHS concerns the solute–solvent interaction and the second term denotes the solute–solute interaction, among the nonelectrolyte molecules. For very dilute solution of organic solute, the solute–solute interactions are very small, thus are negligible. Therefore, (4) becomes,

$$\log f_{HA} = k_S \cdot s \tag{5}$$

The empirical Setschenow equation was only formulated to describe the effect of molar electrolyte concentration on the activity coefficient behaviour of nonelectrolyte solutes. Values of $k_S$ for ten hydroxamic acids are presented in Table 3.

## CONCLUSIONS

In the present system, the activity coefficients are considered in connection with acidity function are actually "medium effects activity coefficient" because, on transferring one mole of the species from its infinitely dilute solution in water to that in the acid solution, is the departure of the solute from ideal behaviour to that with the solvent. The data presented in tables show that with increasing acid concentrations, distribution ratios decrease, due to salting-in behaviour of solute. This is further confirmed by the negative values of activity coefficients. Hydroxamic acids act as weak organic bases and thus are H-bond acceptors in the presence of strong acidic solutions also provide a support for their salting-in behaviour. Setschenow constants represent the contribution to the salting-coefficient from cavity formation or interaction. The negative values of $k_S$ explain, that once a cavity is formed in the electrolyte solution, it is easier to introduce a nonelectrolyte molecule than it is in pure water.

**Table 1.** Distribution ratios of hydroxamic acids as a function of sulfuric acid concentration.

| Solute No. | Hydroxamic acid | $\gamma_0$ | % $H_2SO_4$ | 30 | 35 | 40 | 45 | 50 | 55 |
|---|---|---|---|---|---|---|---|---|---|
| | | | $-H_0$ | 1.72 | 2.06 | 2.41 | 2.85 | 3.38 | 3.91 |
| | | | X | 1.03 | 1.31 | 1.62 | 1.96 | 2.34 | 2.76 |
| | | | | | | D/$\gamma$ | | | |
| 1 | N-phenylbenzo- | 20.33 | 14.87 (±0.03) | | 9.09 (±0.02) | 4.80 (±0.07) | 2.01 (±0.13) | 0.63 (±0.12) | 0.21 (±0.11) |
| 2 | N-phenylcinnamo- | 145.63 | 84.41 (±0.01) | | 52.35 (±0.07) | 28.08 (±0.03) | 11.38 (±0.10) | 3.52 (±0.11) | 1.05 (±0.13) |
| 3 | N-phenyl-p-chlorobenzo- | 85.45 | 55.14 (±0.04) | | 34.79 (±0.12) | 19.23 (±0.06) | 7.95 (±0.08) | 2.48 (±0.11) | 0.74 (±0.07) |
| 4 | N-phenyl-p-nitrobenzo- | 11.96 | 13.32 (±0.03) | | 9.78 (±0.10) | 6.23 (±0.13) | 2.90 (±0.06) | 0.96 (±0.06) | 0.29 (±0.03) |
| 5 | N-phenyl-p-methoxybenzo- | 26.25 | 21.82 (±0.06) | | 12.59 (±0.09) | 6.40 (±0.17) | 2.50 (±0.02) | 0.76 (±0.03) | 0.22 (±0.04) |
| 6 | N-o-tolylbenzo- | 17.38 | 13.69 (±0.02) | | 8.37 (±0.03) | 4.45 (±0.10) | 1.79 (±0.01) | 0.55 (±0.01) | 0.16 (±0.06) |
| 7 | N-p-tolylbenzo- | 76.03 | 50.67 (±0.01) | | 30.59 (±0.06) | 16.23 (±0.06) | 6.50 (±0.02) | 2.05 (±0.14) | 0.62 (±0.08) |
| 8 | N-p-tolyl-2-furo- | 3.28 | 4.76 (±0.09) | | 3.08 (±0.05) | 1.75 (±0.08) | 0.78 (±0.04) | 0.30 (±0.03) | 0.09 (±0.02) |
| 9 | N-m-chlorophenylbenzo- | 22.97 | 22.20 (±0.11) | | 15.07 (±0.03) | 8.70 (±0.12) | 3.72 (±0.06) | 1.18 (±0.04) | 0.35 (±0.07) |
| 10 | N-p-chlorophenylbenzo- | 60.76 | 77.02 (±0.13) | | 53.51 (±0.01) | 31.55 (±0.10) | 13.75 (±0.11) | 4.42 (±0.09) | 1.37 (±0.03) |

**Table 2.** Protonation parameters of N-arylhydroxamic acids in sulfuric acid solutions.

| Solute No. | $K_D$ | $pK_{BH^+}$ | m* | r | $K_{BH^+}$ | $\sigma$ |
|---|---|---|---|---|---|---|
| 1 | 32.87 | –2.077 | 1.238 | 0.9996 | 119.53 | 0.881 |
| 2 | 182.35 | –2.148 | 1.260 | 0.9995 | 140.86 | 0.889 |
| 3 | 110.16 | –2.190 | 1.262 | 0.9995 | 154.95 | 0.999 |
| 4 | 19.67 | –2.499 | 1.246 | 0.9993 | 316.15 | 1.003 |
| 5 | 58.28 | –2.015 | 1.295 | 0.9993 | 103.56 | 0.935 |
| 6 | 30.29 | –2.128 | 1.269 | 0.9995 | 134.33 | 0.887 |
| 7 | 115.37 | –2.082 | 1.261 | 0.9996 | 120.94 | 0.879 |
| 8 | 9.16 | –2.132 | 1.174 | 0.9996 | 135.67 | 0.903 |
| 9 | 39.89 | –2.329 | 1.251 | 0.9990 | 213.55 | 0.863 |
| 10 | 130.75 | –2.376 | 1.246 | 0.9991 | 238.12 | 0.881 |

**Table 3.** Log $f_{HA}$ and $k_S$ of hydroxamic acids in sulfuric acid solutions.

| Solute No. / % Acid | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | log $f_{HA}$ | $K_S$ | log $f_{HA}$ | $K_S$ | log $f_{HA}$ | $K_S$ | log $f_{HA}$ | $K_S$ | log $f_{HA}$ | $K_S$ | log $f_{HA}$ | $K_S$ | log $f_{HA}$ | $K_S$ | log $f_{HA}$ | $K_S$ | log $f_{HA}$ | $K_S$ | log $f_{HA}$ | $K_S$ |
| 30 | –0.293 | –0.078 | –0.374 | –0.100 | –0.316 | –0.084 | –0.019 | –0.005 | –0.258 | –0.069 | –0.246 | –0.066 | –0.332 | –0.089 | – | – | –0.110 | –0.029 | – | – |
| 35 | –0.642 | –0.142 | –0.703 | –0.156 | –0.631 | –0.140 | –0.221 | –0.049 | –0.643 | –0.142 | –0.585 | –0.129 | –0.685 | –0.152 | –0.294 | –0.065 | –0.370 | –0.082 | –0.226 | –0.050 |
| 40 | –1.124 | –0.211 | –1.166 | –0.219 | –1.072 | –0.201 | –0.541 | –0.101 | –1.154 | –0.216 | –1.056 | –0.198 | –1.165 | –0.218 | –0.734 | –0.137 | –0.764 | –0.143 | –0.602 | –0.113 |
| 45 | –1.844 | –0.297 | –1.889 | –0.304 | –1.777 | –0.286 | –1.125 | –0.181 | –1.917 | –0.309 | –1.785 | –0.288 | –1.906 | –0.307 | –1.414 | –0.066 | –1.425 | –0.230 | –1.244 | –0.200 |
| 50 | –2.832 | –0.397 | –2.872 | –0.403 | –2.754 | –0.386 | –2.026 | –0.284 | –2.920 | –0.409 | –2.772 | –0.389 | –2.889 | –0.405 | –2.299 | –0.322 | –2.376 | –0.333 | –2.182 | –0.306 |
| 55 | –3.818 | –0.470 | –3.910 | –0.481 | –3.787 | –0.466 | –3.032 | –0.373 | –3.966 | –0.488 | –3.809 | –0.469 | –3.920 | –0.482 | –3.328 | –0.409 | –3.400 | –0.418 | –3.193 | –0.393 |

## REFERENCES


1. Lossen H., *Ann. Chem.,* **50,** 314 (1869).
2. Neilands J.B., *Science,* **156,** 1443 (1967).
3. Leoni F., Zaliani A., Bertolini G., Porro G., Pagani P., Pozzi P., Dona G., Fossati G., Sozzani S., Azam T., Bufler P., Fantuzzi G., Goncharov I., Kim S. H., Pomerantz B.J., Reznikov L.L., Siegmund B., Diharello C.A. and Mascagni P., *Proc. Natl. Acad. Sci. USA,* **99,** 2995 (2002).
4. Komatsu Y., Tomlzaki K.Y., Tsukamoto M., Koto J., Nishino N., Sato S., Yamori T., Tsuruo T., Furumai R., Yoshida M., Horinouchi S. and Hayashi H., *Cancer. Res.,* **61,** 4459 (2001).
5. Clements J.M., Beckett R.P., Brown A., Catlin G., Labell M., Palan S., Thomas W., Whittaker M., Wood S., Salama S., Baker P. J., Rodgers H. F., Barynin V., Rice D.W. and Hunter M.G., *Antimicrob. Agents Chemother.,* **45,** 563 (2001).
6. Holland K.P., Elford H.L., Bracchi V., Annis C.G., Schuster S.M. and Chakrabarti D., *Antimicrob. Agents Chemother.,* **42,** 2456 (1998).
7. Clare B.W., Scozzafava A. and Supuran C.T., *J. Med. Chem.,* **44,** 2253 (2001).
8. Onishi H.R., Pelak B.A., Gerckens L.S., Silver L.L., Kahan F.M., Chen M.H., Patchett A.A., Galloway S.M., Hyland S.A., Anderson M.S. and Ruetz C.R.H., *Science,* **274,** 980 (1996).
9. Tabuchi K., Okubo H., Fujihira K., Tsuji S., Hara A. and Kusakari J., *Neurosci. Lett.,* **307,** 29 (2001).
10. Taher A., Sheikh–Taha M., Koussa S., Inati A., Neeman R. and Mourad F., *Eur. J. Haematol.,* **67,** 30 (2001).
11. Xue C.B., Voss M.E., Nelson D.J., Duan J.J., Cherney R.J., Jacobson I.C., He X., Roderick J., Chen L., Corbett R.L., Wang L., Meyer D.T., Kennedy K., DeGradodagger W.F., Hardman K.D., Teleha C.A., Jaffee B.D., Liu R.Q., Copeland R.A., Covington M.B., Christ D.D., Trzaskos J.M., Newton R.C., Magoldo R.L., Wexler R.R. and Decicco C.P., *J. Med. Chem.,* **44,** 2636 (2001).
12. Montuschi P., Tringali G., Mirtella A., Parente L., Preziosi P. and Novarra P., *Eur. J. Pharmacol.,* **275,** 31 (1995).
13. Lee E., Robertson T., Smith J. and Kilfeather S., *Am. J. Respir. Crit. Care. Med.,* **161,** 1881 (2000).
14. Nicol D. and Wratten S.D., *Ann. Appl. Biol.,* **130,** 387 (1997).
15. Diamond R.M. and Tuck D.G., Progress in Inorganic Chemistry, Wiley, Interscience, NY 1960, vol. 2, p. 109.
16. Katzin L.I., The Chemistry of Non-aqueous Solvents, Academic Press, NY 1966, vol. 2, p. 173.
17. Pande R. and Tandon S.G., *J. Chem. Eng. Data,* **24,** 72 (1979).
18. Pande R. and Tandon S.G., *Z. Anal. Chem.,* **296,** 407 (1979).
19. Liler M., Reaction Mechanism in Sulfuric Acid and Other Strong Acids Solutions, Academic Press, London and NY 1971, p. 26.
20. Paul M.A. and Long F.A., *Chem Rev.,* **57,** 1 (1957).
21. Cox R.A. and Yates K., *J. Am. Chem. Soc.,* **100,** 3861 (1978).
22. Cox R.A. and Yates K., *Can. J. Chem.,* **59,** 2116 (1981).
23. Rochester C.H., Acidity Function, Academic Press, London and NY 1970.
24. Coetzee J.F. and Calvin D.R., Solute–Solvent Interactions, NY 1969, p. 329.