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Thermodynamics of the Second Ionisation of Piperazine-N,N′-Bis(2-Ethanesulfonic Acid) in Water and in Aqueous Methanol

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Apparent values for the free energy, enthalpy, entropy, and heat capacity for the second ionisation of the biological buffer piperazine-N,N′-bis(2-ethanesulfonic acid) (pipes) were obtained in water and in solutions containing 10, 20 and 30% (w/w) methanol. The free energy values were obtained from potentiometric measurements. The other thermodynamic parameters were obtained spectrophotometrically, making use of the pronounced thermochromacy of the system neutral red-pipes. Thermodynamic values for the transfer of pipes from water to the methanolic solvents were calculated. The medium effect term, $\log({}_m\gamma_{A^-}/{}_m\gamma_{HA^-})$, was estimated as a function of the acid and base forms of the pipes species, for each solvent medium. Conclusions were drawn regarding the charge disposition on the acid and base forms in pipes as well as the nature of interactions between the two pipes species and the solvent.

INTRODUCTION

Over the past few years, several papers from this laboratory[1-4] dealt with the application of the novel thermochromic method to the determination of thermodynamic properties associated with the proton ionisation of buffers and indicators. The fundamental aspects of this method were presented in the first article, and the subsequent ones, in addition to dealing with specific cases discussed, provided elaborations, expansions and some useful generalities. Briefly, this method utilizes the temperature dependence of the absorbance of solutions containing system comprised of a buffer (B) and an indicator (I). The selection of these compounds must comply with a few requirements[1,2] *viz.* the close proximity of the pK's of buffer and indicator, the presence of well-defined isosbestic points and a significant sensitivity of absorbance to temperature. The observable quantity is R, the ratio of the base to the acid forms of the indicator. For many buffers and indicators, this quantity varies with temperature[2-4] according to the equation

$$\log R = a/T - b + cT \qquad (1)$$

where a, b and c are constants whose values were determined from computer regression analysis. The thermodynamic parameters of several systems were obtained[2,3] from these constants by the use of the following set of equations

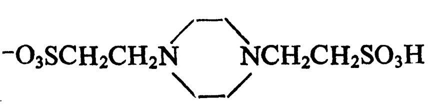
$$\delta\Delta H' = \Delta H'_B - \Delta H_I = 2.303R(a - cT^2) \qquad (2)$$

$$\delta\Delta C'_p = \Delta C'_{p,B} - \Delta C'_{p,I} = -4.606RcT \qquad (3)$$

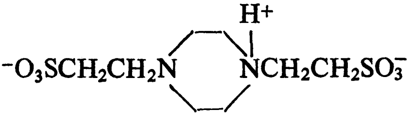
$$\delta\Delta G' = \Delta G'_B - \Delta G'_I = 2.303R(a - bT + cT^2) \qquad (4)$$

$$\delta\Delta S' = \Delta S_B - \Delta S'_I = 2.303R(b - 2cT) \qquad (5)$$

In this work, attention is focused on the second proton ionisation of piperazine N,N'-bis(2 ethanesulfonic acid) with the trivial name 'pipes'. This compound belongs to the class of biological buffers, synthesised by Good *et al.*,[5] so called because they do not interact with enzymes and their buffering action spans the pH range 6–8, of interest for biological systems. The ionisation under consideration may proceed from either of the two species depicted below, (I) being a mononegative ion and (II) a zwitter ion.



(I)



(II)

There are numerous examples and compilations in the literature of thermodymanic studies on the proton ionisation of amines and amino acids[6–9]. Most of these studies, however, have been carried out in water only and on fully protonated amines. In any case, little attention was paid to the ionisation of a second proton from amphoteric dibasic amines. This is unfortunate in view of the likelihood that significant information may be derived from such studies since, with amines, it is possible to introduce substituents in the immediate vicinity of the site at which proton loss occurs. Thus, one may anticipate higher sensitivity of thermodynamic ionisation parameters to such substituents than, for example, in the case of carboxylic acids. Secondly, the possible ambiguity in the charge type introduces an additional problem to be resolved by the experimental results. Furthermore, it is of interest to determine the degree to which the free energy for the ionisation process is entropic in origin, as this might serve to shed light on the extent of loss of vibrational and rotational freedom, due to the presence of charge in the dissociating species. Finally, when this type of dissociation is studied in different solvent media, insight is gained into the effect of the solvent on ion-solvent interactions and the protolysis process as a whole.

The indicator neutral red was selected as a probe for determining the thermodynamic parameters of pipes. This selection meets the requirement[1,2] of close proximity of the two pK's (at 20°C, these are 6.96 for pipes[5] and 6.77 for neutral red[10]). In addition, the large dependence of absorbance on temperature, particularly for the acid band of the indicator serves to enhance the sensitivity and hence the reliability of the calculated thermodynamic properties. Methanol was chosen as a cosolvent because thermodynamic parameters for neutral red are available only in aqueous solutions of this alcohol[3], and these are required for calculation of those for the buffer from equations[2–5]. Secondly, estimates of the medium effect of the hydrogen ion are most extensively found in aqueous methanol[11] and these are required for calculation of the medium effect for the pipes species.

EXPERIMENTAL

A commercial preparation of pipes was recrystallized twice from 50% aqueous ethanol and dried for *ca.* 48 hrs in vacuo. Solutions were prepared after conversion of the slightly soluble compound to the very soluble monosodium salt. All other chemicals were of reagent grade and were used without further purification. Spectral and pH measurements were performed in the manner described earlier[2,3]. Temperatures were monitored to within 0.02° using an RS 151–192 thermocouple. Potentiometric titrations were performed under a nitrogen atmosphere using *ca.* 0.1 mol dm^{-3} carbonate-free sodium hydroxide. The indicator concentration was maintained near 10^{-6} mol dm^{-3} and that of the buffer at 0.05 mol dm^{-3}. The R values were calculated, in all cases, at the acid peak of 528 nm, at which the thermochromic effect was most pronounced. For each solvent composition, at least three independent sets of spectral scans were obtained, each comprised of about 12 spectra spanning the temperature range 2–55°C.

RESULTS AND DISCUSSION

As in the earlier papers[2–4], the log R and Kelvin temperature values were fitted to equation (1) and computer assisted regression analysis performed. In addition to equation (1), the fit for the following two equations was investigated

$$\log R = \log R_m + b\,(T-T_m)^2 \tag{6}$$

$$\log R = a/T - bT + c\,\log T \tag{7}$$

The above equations may be readily derived, in the manner shown earlier (2) for the derivation of equation (1), by assuming that the pK's of buffer and indicator follow the Harned and Embree[12] equation

$$pK = pK_m + b'\,(T-T_m)^2 \tag{8}$$

or the Everett and Wynne-Jones[13] equation

$$pK = \frac{a'}{T} - b' + c' \log T \tag{9}$$

where R_m, T_m and pK_m are constants. The computer program has been modified so as to give the log R values predicted by equations (1), (6) and (7), for all the four solvent media, equation (1) gave the least variance in the calculated values and was accordingly adopted for computation of the thermodynamic parameters. Equation (6) gave good fits of the data at high and intermediate temperatures only and equation (7), which suffers from the limitation of assuming the heat capacity to be independent of temperature, was less adequate than equation (1) in describing the behaviour throughout the temperature range employed.

Fig. 1 gives plots of log R vs 1/T for the four solvent media investigated. The points represent the experimental results and the solid lines are plots of equation (1). These plots are displaced with respect to the log R axis, in the manner indicated, in order to afford better clarity.

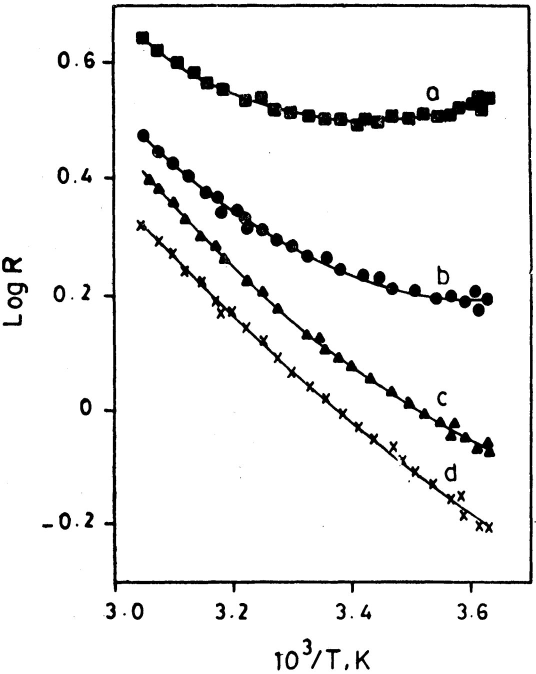


Fig. 1 Dependence of log R on 1/T for the system pipes—neutral red in water and in 10, 20 and 30% (w/w) methanol (a, b, c and d respectively). The solid curves are best fits to equation (1) and the points represent experimental values. For clarity, curves (a) and (d) are moved up and down 0.1 units, respectively, along the log R axis

Table 1 summarises the results, it is noteworthy that the values of the three constants progressively decrease upon enrichment of the solvent with methanol. The effects of these changes are reflected in the apparent thermodynamic difference parameters, calculated at 298.15 K with the aid of equations (2–5). On going from water to 30% methanol, the values of $\delta\Delta G'$ drop from 2.86 to –0.01 kJ mol^{-1} whereas those for $\delta\Delta H'$) exhibit a much larger dependence, decreasing from –2.53 to –15.35 kJ mol^{-1}. With $\delta\Delta S'$, a shallow minimum of –57.5 JK^{-1} mol^{-1} at 20% methanol follows a large drop from –18.1 JK^{-1} mol^{-1} in water. The heat capacity changes are highly pronounced with the value of $\delta(\Delta C_p')$ varying from –424 J K^{-1} mol^{-1} in water to –121 J K^{-1} mol^{-1} in 30% methanol. This effect is translated into the clearly apparent decrease in the curvature of the plots of Fig. 1 with methanol addition. Furthermore, values for T_{max} (or $1/T_{min}$), the temperature at which the log R vs 1/T plot has its minimum value, given by $(a/c)^{1/2}$, are seen to decline from 292.1 K in water to 107.9 K in 30% methanol.

Table 1 also lists the apparent thermodynamic parameters for the buffer. The tabulated free energy values were obtained directly from potentiometric measurements, whereas in principle they could be obtained by applying equation (5) to the thermochromic results. However, the closeness of the pK values of buffer and indicator would result in relatively high uncertainty in $\Delta G_B'$ when calculated from equation (5), since in this case the term $\delta\Delta G'$ necessarily represents a small difference between two large numbers. At 298.15 K, pK_B' values were found to be 6.862, 6.791, 6.800 and 6.881 in 0, 10, 20 and 30% methanol, respectively. The observation of a minimum at 10% methanol leads to the supposition that a significant portion of the dissociation is isoelectric rather than ionogenic, *i.e.*, originating from structure (II) as opposed to (I). Such minima arise from the complex dependence of the nonelectrostatic component of the free energy, ΔG_{nonel}, on the basicity of the medium. This basicity at first increases, then begins to decrease as methanol is added to water[14]. When no new ions are created, the contribution of ΔG_{el} to the total free energy is small and may be overlooked. In the case of pipes, however, caution must be exercised, for two reasons. First, the minimum is relatively shallow, amounting to a decrease in pK_B of only 0.071 units, whereas minima for the dissociation of protonated amines lie typically in the range 0.2–0.7 units. Secondly, these minima are usually located at higher methanol compositions[14]. Thus, from the behaviour of the dissociation constant alone, it appears that both structures coexist and that the electrostatic factor plays a significant role in the protolysis process.

Notwithstanding the large variation in $\delta\Delta H'$ values, $\Delta H_B'$ for pipes displays little change, remaining essentially constant in the 0, 10

TABLE 1

CONSTANTS FOR EQUATION (1), APPARENT THERMODYNAMIC DIFFERENCE VALUES BETWEEN PIPES BUFFER (B) AND NEUTRAL RED INDICATOR (I) AND APPARENT THERMODYNAMIC IONISATION VALUES FOR PIPES, AS A FUNCTION OF SOLVENT COMPOSITION AT 298.15 K. T_{max} VALUES ARE ALSO TABULATED

	% Methanol (w/w)			
	0	10	20	30
a	3166	2171	1074	123.4
b	21.18	15.79	9.58	3.59
c	0.037	0.029	0.021	0.011
$\delta\Delta G' \pm$ (−0.10, kJ mol^{-1})	2.86	1.47	1.79	−0.10
$\delta\Delta H' \pm$ (−0.08, kJ mol^{-1})	−2.53	−8.47	−15.35	−15.68
$\delta\Delta S' \pm$ (−2, J K^{-1} mol^{-1})	−18.1	−33.3	−57.5	−52.3
$\delta C_P' \pm$ (−8, J K^{-1} mol^{-1})	−424	−336	−241	−121
T_{max}, K	292.1	271.7	225.6	107.9
$\Delta H_I'$*, kJ mol^{-1}	17.70	24.08	30.72	30.40
$\Delta S_I'$*, J K^{-1} mol^{-1}	−79.4	−57.9	−40.1	−32.1
$\Delta C_{p,I}'$ J K^{-1} mol^{-1}	345	246	175	−103
pK′B	6.862	6.791	6.800	6.881
$\Delta G_B' \pm$ (−0.03, kJ mol^{-1})	39.17	38.77	38.82	39.28
$\Delta H_B'$ (−0.14 kJ mol^{-1})	15.17	15.61	15.37	18.72
$\Delta S_B'$ (−3, J K^{-1} mol^{-1})	−97.5	−91.2	−97.6	−84.4
$\Delta C_{p,B}'$ (−14, J K^{-1} mol^{-1})	−79	−90	−66	−224

*Ref. 3

and 20% solvents (15.17, 15.61 and 15.37 kJ mol^{-1}, respectively) before going up to 18.72 kJ mol^{-1} in the 30% solvent. The value in water is in agreement with the approximate one of 14.5 kJ mol^{-1}, calculated from the data of Good *et al.*[5] from measurements at three temperatures. These results lead to the conclusion that the minimum in $\Delta G_B'$ in 10% methanol occurs in spite of, and not due to, the slightly higher $\Delta H_B'$ value at this composition. This is not surprising in view of the belief that the enthalpy term may be much more complex than the free energy term. For whereas the latter is influenced predominantly by electrostatic and nonelectrostatic factors, the former involves structural and steric factors of unknown magnitude[11]. The relatively high value of $\Delta H'_B$ in 30% methanol may be attributed to decreased solvation of the dissociated species in this medium and to a reduction in the extent of H-bonding with the solvent. It is instructive to compare the enthalpy results with those obtained for other amines of the same acidic strength. The comparison will be made for data in water only since more are available in aqueous methanol. Lumme *et al.*[6] prepared a graph for the enthalpy of ionisation of various amines as a function of their pK values. Two classes were distinct, protonated amines and neutral amines, with the former having nearly double the values of $\Delta H'_B$ for a given pK. This has been explained on the basis that the ionogenic dissociation of the neutral species is less endothermic, due to the liberation of heat when the newly formed ions are solvated. When the observed $\Delta H'_B$ for pipes were compared with values on this chart for the same pK, it was found to be close to the value expected from a neutral species. This confirms the conclusion, based on the pK values, that the dissociation process is partly ionogenic. Put differently, the electrostatic component of the enthalpy of ionisation is probably quite substantial.

Table 1 reveals that the $\Delta S'_B$ values are all negative but do not vary considerably with solvent composition. These values are, however, *ca.* 30–42 J K^{-1} mol^{-1} less negative than would be expected from the dissociation of a mononegative ion, being nearer the range observed for neutral species[15]. This adds credence to the supposition made above that the zwitter ion is a significant species in water as well as the methanolic solutions. This is because the dissociation of a mononegative ion would create two additional charges which would be expected to exert a considerable influence in ordering the solvent molecules around them, whereas no new charges are created from the dissociation of a zwitter ion. The relatively low value for $\Delta S'_B$ in 30% methanol may be due to a reduction in the ability of the dissociated pipes ion to orient solvent molecules.

The values of $C'_{p,B}$ are -79, -90, -66 and -224 J K^{-1} mol^{-1} for the 0, 10, 20 and 30% solutions, respectively. The first three quantities lie within the normal or expected range for such dissociations. In 30% methanol, however, the heat capacity term is fairly large. A similar result[4] has been recently obtained with another biological buffer, 'ada', for which $\Delta C'_p$ for this solvent composition was -232 J K^{-1} mol^{-1}. This apparent anomaly was explained on the basis that, in 30% methanol, the structure of water is more liable to breaking down with increasing temperature, thereby releasing more water molecules for solvation of the proton. In this connection, it ought to be mentioned that the 10 and 20% solvents lie within the region of structure enhancement of water by methanol. In the 30% solvent, however, as evidenced by volumetric studies on amino acids[16], methanol begins to act as a structure breaker.

Table 2 lists the apparent transfer parameters of the buffer species from water to the methanolic solvents, as obtained by subtracting the buffer parameters in water from those in each medium. The apparent free energy of transfer is related to the medium effect, ${}_m\gamma_i$, of each species by the equation

$$\Delta G_t' = 2.303 \log ({}_m\gamma_{H^+} \cdot {}_m\gamma_{A} = {}_m\gamma_{HA^-}) \qquad (10)$$

Feakins, from extrathermodynamic considerations, estimated the free energies of transfer of hydrogen ions from water to aqueous methanol[11]. These values, also listed in Table 2, when combined with those for G_t'

TABLE 2

APPARENT THERMODYNAMIC VALUES, AT 298.15 K, FOR THE TRANSFER OF PIPES FROM WATER TO AQUEOUS METHANOL

	% Methanol (w/w)		
	10	20	30
$\Delta H_t'$, K J mol^{-1}	0.44	0.20	3.55
$\Delta S_t'$, J K mol^{-1}	6.3	−0.1	13.1
$\Delta C_{p,t}'$, J K^{-1} mol^{-1}	−11	13	−145
$\Delta G_t'$, k J mol^{-1}	−0.40	−0.35	0.11
$\Delta G_t(H^+)$, k J mol^{-1}*	−2.09	−3.81	−6.80†
$\log ({}_m\gamma_{A^=}/{}_m\gamma_{HA^\pm})$	0.30	0.61	0.02

*Ref. 9. †Interpolated value.

lead to an evaluation of the expression $\log ({}_m\gamma_{A^=}/{}_m\gamma_{HA^\pm})$ for each medium. This expression bears a special significance since it includes pipes terms only. In addition, being equivalent to the term $[\Delta G_t'(A'') - \Delta G_t'(HA^-)]/2.303\ RT$, it constitutes a measure of the difference in free energies involved in the transfer of one mole each of the base and acid forms of pipes from water to the methanolic medium. At 298.15 K, values for this term are 0.30, 0.61 and 0.02 for the transfer to 10, 20 and 30 per cent methanol, respectively. It is noteworthy, however, that $\Delta G_t'$ is dominated by the free energy of transfer of the hydrogen ion rather than that of the pipes species (Table 2). This is especially the case in 30% methanol, for which $\Delta G_t(H^+)$ is −6.80 kJ mol^{-1} as compared to only 0.11 kJ mol^{-1} for the total transfer free energy, $\Delta G_t'$.

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REFERENCES

1. F. H. Jumean, M. I. Khamis and G. N. Salaita, *J. Indian Chem. Soc.*, **57**, 995 (1980).
2. F. H. Jumean, *J. Indian Chem. Soc.*, **63**, 967 (1986).
3. F. H. Jumean and M. I. Qaderi, *J. Indian Chem. Soc.*, **65**, 141 (1988).
4. F. H. Jumean, *J. Indian Chem. Soc.* (in press).
5. N. E. Good, G. D. Winget, W. Winter, T. N. Connolly, S. Izawa and R. M. M. Singh, *Biochemistry*, **5**, 467 (1966).
6. P. Lumme, P. Lahermo and J. Tummavuori, *Acta, Chem. Scand.*, **19**, 2175 (1965).
7. J. J. Christensen, R. M. Izzat, D. P. Wrathall and L. E. Hansen, *J. Chem. Soc. (A)*, 1212 (1969).
8. Handbook of Biochemistry and Molecular Biology, 3rd ed., (ed.) G. D. Fasman, CRC Press, Cleveland, vol. 1, pp. 153–262 (1976).
9. A. Albert and E. Serjeant, The Determination of Ionisation Constants, Chapman and Hall, London, pp. 150–156 (1984).
10. F. H. Jumean, unpublished results.
11. D. Feakins in Physiochemical Chemical Processes in Mixed Aqueous Solvents (ed.), F. Frank, Elsevier, New York, pp. 71–90 (1967).
12. H. S. Harned and N. D. Embree, *J. Am. Chem. Soc.*, **56**, 1050 (1934).
13. D. H. Everett and W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, **35**, 1380 (1939).
14. R. G. Bates and R. A. Robinson, in Chemical Physics of Ionic Solutions, (eds.) B. E. Conway and R. G. Barradas, Wiley, New York, pp. 211–235 (1966).
15. J. J. Christensen and R. W. Izzat, *J. Phys. Chem.*, **66**, 1030 (1962).
16. J. S. Sandhu, P. Kaur and U. Kashyap, *J. Indian Chem. Soc.*, **58**, 729 (1986).

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