Medium Effects on Protonation Equilibria in Ethylene Glycol for Some t-Butyl-substituted Phenols and Nitro-substituted Amines

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The free energies of transfer at 25 °C from water to ethylene glycol (EG) for some neutral indicator acids (HA), *viz.* some t-butyl-substituted phenols and nitro-substituted amines have been determined by use of solubility and partition measurements. Utilizing these data and the known values of the acid dissociation constants, $(K_a)_{HA}$, of these acids in water and EG and also the free energy of transfer of a proton, $\Delta G_t^\circ(H^+)$, from water to EG at 25 °C estimated previously, the corresponding free energies of transfer for the anions of these acids, $\Delta G_t^\circ(A^-)$, have been determined. An attempt has been made to explain the relative magnitudes of these transfer quantities in terms of the relative structure and charge distribution of these acids and their anions and their possible interaction with water and EG.

IN our recent papers [1,2] on acidity functions $(H_-)^{EG}$ of alkali-metal 2-hydroxyethoxides in ethylene glycol (EG) we reported the dissociation constants $(K_a)_{HA}$ of some nitro-substituted amines (HA) and of some t-butyl-substituted phenols (HA) in EG. In this paper we deal with the medium effects on the protonation equilibria of these acids.

It is becoming clear [3,4] that the effect of solvent on the dissociation constant of an acid (HA) in any solvent other than water becomes relatively easier to explain if one takes into account the free-energy change accompanying the protonation equilibria of the acid–base system, $(HA - A^-)_{sys.}$, in a particular solvent (SH) and in water, *i.e.*, the free-energy change $\Delta G_t^\circ(HA - A^-)_{sys.}$ accompanying the process (1) where (s) and (w) indicate that the species concerned is in the standard state in the

$$HA(s) + A^-(w) + SH(s) + H_3O^+(w) \longrightarrow$$
$$HA(w) + A^-(s) + H_2O(w) + SH_2^+(s) \quad (1)$$
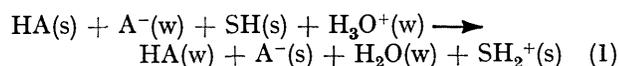
solvent SH and water respectively. Consequently, $\Delta G_t^\circ(HA - A^-)_{sys.}$ is related to the dissociation constants in water $(_wK_a)_{HA}$ and in the solvent $(_sK_a)_{HA}$ by equation (2). It is also related to the free energies of

$$\Delta G_t^\circ(HA - A^-)_{sys.} = \\ 2 \cdot 303 \, RT \, [p(_sK_a)_{HA} - p(_wK_a)_{HA}] \quad (2)$$

transfer ΔG_t° of H^+, A^-, and HA from water to the solvent [equation (3)].

$$\Delta G_t^\circ(HA - A^-)_{sys.} = \\ \Delta G_t^\circ(H^+) + \Delta G_t^\circ(A^-) - \Delta G_t^\circ(HA) \quad (3)$$

Equation (3) suggests that the estimates of individual transfer quantities are an aid to better understanding of solvent effects on the protonation equilibria. Now, $\Delta G_t^\circ(H^+)$, which stands for a measure of the basicity of the solvent relative to that of water,[4-6] though not directly accessible from experimental measurements, has been evaluated for EG by reasonable extra-thermodynamic assumptions described in the footnote of Table 2. It is therefore possible to compute the values of $\Delta G_t^\circ(A^-)$ for the anions (A^-) from equation (3), provided that $\Delta G_t^\circ(HA)$ for the neutral acid (HA) is experimentally determined. As the resultant effect of these transfer quantities constitutes the medium effects for an individual acid–base system, an insight into these medium effects, besides providing an estimate of the relative basicity of the solvents, will necessarily entail an increase of the understanding of these transfer quantities in terms of the relative solvent interactions on the acids and their anions guided by their respective structure and charge distribution.

The free energy of transfer $\Delta G_t^\circ(HA)$ of an acid (HA) from water to glycol has been obtained from solubility

[1] K. K. Kundu and L. Aiyar, *J. Chem. Soc. (B),* 1971, 40.
[2] L. Aiyar, A. N. Dutta, and K. K. Kundu, *J.C.S. Perkin II,* 1972, 1046.
[3] P. Schindler, R. A. Robinson, and R. G. Bates, *J. Res. Nat. Bur. Stand., Sect. A,* 1968, *A,* 72, 141.
[4] K. K. Kundu, A. L. De, and M. N. Das, *J.C.S. Dalton,* 1972, 381.

[5] R. G. Bates, 'Hydrogen-Bonded Solvent System,' eds. A. K. Covington and P. Jones, Taylor and Francis, London, 1968, pp. 49—86.
[6] D. Feakins, 'Physico-Chemical Processes and Mixed Aqueous Solvents,' ed. F. Franks, Heinemann, London, 1967, pp. 71—91.

or partition coefficient data [equations (4) and (5), respectively].

$$\Delta G_t^\circ(HA) = 2.303 \, RT \log w^S/g^S \quad (4)$$

$$\Delta G_t^\circ(HA) = 2.303 \, RT \log g^\gamma/w^\gamma \quad (5)$$

where w^S and g^S are the solubilities (mol fraction) of the acid HA in water and in glycol respectively and w^γ and g^γ are the corresponding partition coefficients for a common inert solvent like xylene, defined by $w^\gamma = C_{xy}/C_w$ and $g^\gamma = C_{xy}/C_g$, where C denotes the concentration (mol fraction) of HA. A positive value of $\Delta G_t^\circ(HA)$ indicates that HA is more solvated by water than by glycol.

EXPERIMENTAL

The amines and phenols were purified as earlier.[1,2] The $\Delta G_t^\circ(HA)$ values of all the amines and 2,4,6-tri-t-butyl-phenol were determined by solubility measurements in water and EG, whereas those of the rest of the phenols were determined by partition between water and xylene and between EG and xylene. EG was purified as earlier.[7]

Solubility Measurements.—A sufficient quantity of acid was added to water or glycol (*ca*. 10—20 ml) in a well-stoppered bottle and shaken mechanically for several h. The solution was then left at 25 ± 0.1 °C for several h. The clear solution was carefully pipetted out and the concentration of the acid was determined spectrophotometrically after dilution. Shaking at 25 °C was repeated until constant readings were obtained.

Partition Measurements.—Xylene was the same sample as used before.[2] A dilute solution (10^{-2}—10^{-3}M) of the phenol in glycol or water (*ca*. 25 ml) was made in a weighed bottle. A portion of the solution (*ca*. 1 ml) was taken separately for measurement of the initial phenol concentration. The weight of the solution and thereby the volume was estimated. Then 5, 10, or 25 ml of xylene, as suitable, was added to the solution which was shaken mechanically for several h and then stood at 25 ± 0.1 °C for several h. The glycol layer was pipetted out carefully and the concentration of phenol was determined spectrophotometrically after dilution. The concentration of phenol in xylene was calculated from the initial phenol concentration, the concentration of phenol in glycol and the known volumes of glycol and xylene. Three different solutions with slightly different initial phenol concentration were studied for each particular distribution and the average was taken. As xylene absorbs in the range 250—290 nm, due correction was made in the observed optical density values for the concentration of phenol after partition. Correction for the solubility of xylene in glycol was made as earlier.[2]

RESULTS AND DISCUSSION

Table 1 gives the $p(K_a)_{HA}$ values of the acids in water, $p({}_wK_a)_{HA}$ and in EG, $p({}_gK_a)_{HA}$. The values in methanol,[8] $p({}_mK_a)_{HA}$ are also given for the phenols for comparison. pK_r In Table 1 is the difference of the $p(K_a)_{HA}$ values for a substituted phenol and for phenol in a particular solvent. Table 2 gives the experimental solubility and distribution data for the acids and the

calculated $\Delta G_t^\circ(HA)$, $\Delta G_t^\circ(HA - A^-)_{sys.} = 2.303 \, RT[p({}_gK_a)_{HA} - p({}_wK_a)_{HA}]$ and $\Delta G_t^\circ(A^-)$ values.

According to Rochester,[8] if steric inhibition to solvation of the phenoxide anions is a contributing factor to the large increase in the $p(K_a)_{HA}$ value on introducing an *o*-t-butyl group into phenol, this effect would be smaller the smaller the solvent molecules. He claims that support for this contention is given by the deviation between the pK_r values of *o*-t-butyl-substituted phenols in methanol and water observed by him. If this is true, the p_gK_r values in EG should be larger than the corresponding p_mK_r values compared to p_wK_r values, which is not the fact, except in the case of 2,4,6-tri-t-butyl-phenol. Hence, we may conclude that steric inhibition is not the guiding factor in dictating the $p(K_a)_{HA}$ values of the *o*-t-butyl-substituted phenols, but other factors such as the hydrophobism and solvophilism of the t-butyl groups perhaps play quite significant roles.

Table 2 shows that the $\Delta G_t^\circ(HA)$ values for all the phenols and amines are negative, *i.e.* they are more stabilized in glycol than in water. This is reasonable, for organic molecules prefer organic solvents. As resonance in phenol is hindered by the electron-repelling t-butyl substituents the partial protonic character of the phenolic hydrogen atom decreases with an increasing number of t-butyl substituents. We also know [9,10] that the negative charge density on an oxygen atom of glycol, $g_\delta-$, is greater than that of water, $w_\delta-$, and that any solvation involving the negative charge centre of the solvent dipole with the partial positive charge centre of a solute molecule will be more favoured in glycol than in water. Hence $\Delta G_t^\circ(HA)$ is expected to be most negative for phenol and become less negative for increasing number of t-butyl substituents. Again, as steric inhibition to solvation is expected to be greater in glycol than in water, the $\Delta G_t^\circ(HA)$ values are expected to become decreasingly negative for an increasing number of *o*-t-butyl groups. But the $\Delta G_t^\circ(HA)$ value for phenol is least negative (Table 2) and the values become more and more negative for an increasing number of t-butyl groups. This suggests that the solvophilism and hydrophobism of the t-butyl groups play a predominant role in the relative solvation of these compounds in water and glycol. This is also borne out by the large difference between the $\Delta G_t^\circ(HA)$ values of phenol and *p*-t-butylphenol and a small difference in the corresponding values of 2- and 4-t-butylphenols.

The $\Delta G_t^\circ(A^-)$ values are all positive (Table 2). This is expected, for it is known [9,10] that anions are more solvated in water than in glycol. Of the $\Delta G_t^\circ(A^-)$ values for phenols, phenol itself has the largest value. Here again the absence of highly hydrophobic t-butyl groups, and at the same time the possibility of its existence in the quinonoid form to some extent due to resonance, presumably bring about greater solvation in water compared

[7] K. K. Kundu and M. N. Das, *J. Chem. and Eng. Data*, 1964, **87**, 9.

[8] C. H. Rochester, *J. Chem. Soc.*, 1965, 855, 4603.

[9] K. K. Kundu, A. K. Rakshit, and M. N. Das, *J. Electrochimica Acta*, in the press.

[10] K. K. Kundu, D. Jana, and M. N. Das, *J. Phys. Chem.*, 1970, **74**, 2625.

with other phenols. The lowest value of $\Delta G_t°(A^-)$, for 4-t-butylphenol (containing no sterically hindering *ortho*-substituent), again shows that the hydrophobism and at the same time the solvophilism of the t-butyl group play an important part by decreasing solvation in water and increasing solvation in glycol. In the case of

of electrons should be greater in (I) than in (II). But the nitro-group in ring B of (I) and (II) pulls electrons in the opposite direction owing to its inductive effect and so reduces the effective delocalization to a considerable extent [more in (II) than in (I)]. Thus resultant delocalization should be greatest in (III) and least in (II).

TABLE 1

$p(K_a)_{HA}$ And pK_r values for phenols in water, glycol, and methanol and $p(K_a)_{HA}$ values for amines in water and glycol at 25 °C

Compound	$p(_gK_a)_{HA}$	p_gK_r	$p(_wK_a)_{HA}$	p_wK_r	$p(_mK_a)_{HA}$	p_mK_r
(1) Phenol	13·33 [a]	0	9·97 [b]	0	14·10 [b]	0
(2) 4-t-Butylphenol	13·55 [a]	0·22	10·23 [b]	0·26	14·43 [b]	0·33
(3) 2-t-Butylphenol	15·15 [a]	1·82	11·33 [b]	1·36	16·25 [b]	2·15
(4) 2,4-Di-t-butylphenol	15·43 [a]	2·10	11·56 [b]	1·59	16·53 [b]	2·43
(5) 2,6-Di-t-butylphenol	16·18 [a]	2·85	11·70 [b]	1·73	17·08 [b]	2·98
(6) 2,4,6-Tri-t-butylphenol	16·73 [a]	3·40	12·19 [b]	2·22	17·40 [b]	3·30
(7) 2,4,4'-Trinitrodiphenylamine	14·35 [c]		12·35 [d]			
(8) 2,3',4-Trinitrodiphenylamine	14·95 [c]		12·65 [d]			
(9) 6-Bromo-2,4-dinitroaniline	16·185 [c]		13·63 [d]			
(10) 2,4-Dinitrodiphenylamine	16·445 [c]		13·84 [d]			

[a] Ref. 2.   [b] Ref. 9.   [c] Ref. 1.   [d] R. Stewart and J. P. O'Donnell, *Canad. J. Chem.*, 1964, **42**, 1681.

TABLE 2

Distribution and solubility data for the phenols and amines at 25 °C and the relevant $\Delta G_t°$ values for HA, A$^-$, and $(HA - A^-)_{sys}$. $\Delta G_t°(H^+) = -4·37$ kcal mol^{-1} [a]

Compound [b]	w^γ or w^s [c]	g^γ or g^s [c]	$\Delta G_t°(HA)$/kcal mol^{-1}	$\Delta G_t°(HA - A^-)_{sys}$/kcal mol^{-1}	$\Delta G_t°(A^-)$/kcal mol^{-1}
1	8·64	1·20	$-1·20$	3·92	7·09
2	$4·49 \times 10^2$	1·32	$-3·45$	3·86	4·78
3	$9·16 \times 10^2$	2·87	$-3·42$	4·54	5·49
4	$1·71 \times 10^3$	4·75	$-3·49$	4·68	5·56
5	$2·87 \times 10^4$	$6·53 \times 10$	$-3·60$	5·44	6·21
6	$2·29 \times 10^{-7}$	$1·21 \times 10^{-4}$	$-3·72$	5·32	6·18
7	$4·62 \times 10^{-8}$	$4·69 \times 10^{-5}$	$-4·10$	2·06	2·33
8	$9·73 \times 10^{-8}$	$2·12 \times 10^{-5}$	$-3·19$	2·47	3·65
9	$2·14 \times 10^{-6}$	$1·14 \times 10^{-3}$	$-3·72$	2·82	3·47
10	$5·81 \times 10^{-8}$	$1·12 \times 10^{-4}$	$-4·48$	2·88	2·77

[a] The $\Delta G_t°(H^+)$ value has been evaluated by the method of 'simultaneous extrapolation' [9] which is essentially similar to those of Izmailov *et al.* (V. V. Aleksandrov and N. A. Izmailov, *Zhur. fiz. Khim.*, 1958, **32**, 404; N. A. Izmailov, *Doklady Akad. Nauk*, 1960, **127**, 104; *Zhur. fiz. Khim.*, 1960, **24**, 2414) and Feakins *et al.* (D. Feakins and P. Watson, *Chem. and Ind.*, 1965, 2008; *J. Chem. Soc.*, 1963, 4734; and A. L. Andrews, H. P. Bennetto, D. Feakins, K. G. Lawrence, and R. P. T. Tomkins, *J. Chem. Soc. (A)*, 1968, 1486, and also ref. 6). The basic assumption involved in these procedures is that the electrostatic part of the solvation energy of an ion will approach zero as the radius (r) of the ion becomes very large. The simultaneous extrapolation [9] to $(r_X-)^{-1} = 0$ of the plots of $\Delta G_t°(HX)$ and $\Delta G_t°(HCl - HX)$, *i.e.* $\Delta G_t°(Cl^- - X^-)$ against $(r_X-)^{-1}$ suitably aimed at having the least discrepancies in the sum of the extrapolated values of $[\Delta G_t°(H^+) - 2·303\ RT \log M_s/M_w]$ and $[\Delta G_t°(Cl^-) + 2·303\ RT \log M_s/M_w]$ with respect to experimental values of $\Delta G_t°(HCl)$, lent an extra confidence to the extrapolation. It may be noted that even if the value of $\Delta G_t°(H^+)$ varies depending on the particular assumption employed, the relative values in Table 2 are unchanged, and the general arguments of the discussion are not affected by the choice of $\Delta G_t°(H^+)$ value.   [b] Numbers refer to compounds in Table 1.   [c] w^γ or g^γ refer to compounds 1—5 and w^s or g^s refer to compounds 6—10.

other phenols, though hydrophobism and solvophilism of the t-butyl groups play a part, steric hindrance due to bulky *ortho*-groups would have a greater effect in glycol than in water. Hence the expected order of $\Delta G_t°(A^-)$ values for phenols is 4-t-butyl- < 2-t-butyl- $\approx$ 2,4-di-t-butyl- < 2,6-di-t-butyl- $\approx$ 2,4,6-tri-t-butyl.

The less positive $\Delta G_t°(A^-)$ values of the amines compared to those of the phenols may be due to the greater polarity of the amines [11] and a stronger dispersive interaction with glycol than with water, resulting in their increased stability in glycol.

Among the amine indicators we can compare the diphenylamines (I)—(III). Delocalization of the lone pair of electrons of the amino-nitrogen atom and the resulting resonance stabilization of aniline is greatly enhanced by a *p*-NO₂ group. Hence, such delocalization

[11] D. Dolman and R. Stewart, *Canad. J. Chem.*, 1967, **45**, 911.

Due to such delocalization of electrons the protonic character of the amino-hydrogen atom is increased and such an effect is greatest in (III) and least in (II). As a
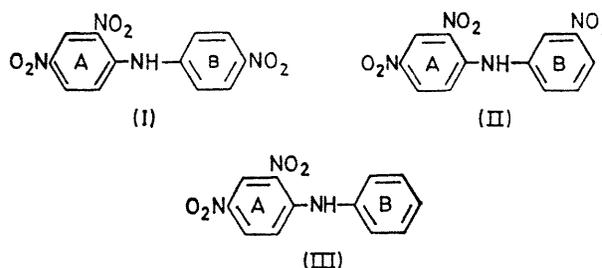
result, solvation through hydrogen-bond formation by the negatively charged oxygen centre of solvent dipoles will be greatest in (III) and least in (II). Since $g_{\delta-} >$

$w_{\delta-}$[9,10] the partial contribution of this effect to $\Delta G_t{}^\circ$(HA) will be most negative in the case of (III) and least in the case of (II), and this tallies with the observed values of $\Delta G_t{}^\circ$(HA).

Charge delocalization and resonance stabilization of an anilide anion are greatly helped by a p-NO$_2$ group. The anion of (I) with two p-NO$_2$ groups is likely to be most stabilized through charge delocalization due to the occurrence of the quinonoid form (IV).

(IV)
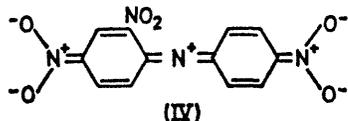
The m-NO$_2$ group in the anion of (II) probably decreases the stabilization brought about by the o- and p-NO$_2{}^-$ groups in the anion of (II) to a value less than that of (III). As a result of this relative charge delocaliz-ation in the anions, the negative charge density on the amino-nitrogen atom is least for the anion of (I) and greatest for the anion of (II). Consequently, solvation by hydrogen bonding with a positively charged hydrogen centre of the solvent dipoles will be least for the anion of (I) and greatest for the anion of (II). And since $w_{\delta+} >$ $g_{\delta+}$,[9,10] the partial contribution of this effect to $\Delta G_t{}^\circ$(A$^-$) will be most positive in the case of the anion of (II) and least in the anion of (I), as observed.

The observed negative and positive magnitudes of $\Delta G_t{}^\circ$(A$^-$) and $\Delta G_t{}^\circ$(HA) respectively for 6-bromo-2,4-dinitroaniline also appear to be in fair agreement with what is expected from the consideration of the relative solvation of the neutral acid and its anion in the two solvents.