BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 52 (2), 574—578 (1979)

Medium Effect on the Ionisation Constants of Some Hydroxy Derivatives of 1-Ethyl-2-styrylpyridinium and -quinolinium Iodides

M. R. Mahmoud,* R. Abd-El-Hamide, and K. A. Idriss

Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt

(Received February 13, 1978)

The pK_a values of 1-ethyl-2-(4 or 2-hydroxystyryl)pyridinium and -quinolinium iodides in different organic solvent–water mixtures were determined. The organic solvents used are methanol, ethanol, acetone, DMF and DMSO. The ionisation of the compounds under investigation depends largely on both the proportion and the nature of the organic co-solvent used. The ionisation constant decreases with increase in the proportion of the organic co-solvent in the medium. The major important effect responsible for this is the difference in the stabilization of base by donor hydrogen bond from solvent molecules. The free energy of solvation of both acid and proton by electrostatic interaction and that of the base by donor hydrogen bond from solvent molecules were calculated. The effect of the molecular structure of the compound on pK_a is also discussed.

So far only a few studies seem to have appeared on the ionisation of hydroxystyryl derivatives.[1] The pK_a values of some hydroxy derivatives of 1-ethyl-2-styrylpyridinium and -quinolinium iodides in pure aqueous medium were determined by Mahmoud *et al.*[2] However, it is known that the hydroxystyryl derivatives are quite interesting compounds because of their application as photosensitizers[3,4] and use as antiseptics, trypanocidal and anticarcinogenic agents.[5–8]

We have investigated the ionisation of some hydroxystyryls in aqueous solutions containing varying proportions of organic solvents (methanol, ethanol, acetone, *N*,*N*-dimethylformamide, dimethyl sulfoxide). The pK_a values have been determined and discussed in terms of solvent properties.

Experimental

Materials and Solutions. The hydroxystyryl dyes used are 1-ethyl-2-(4-hydroxystyryl)pyridinium iodide I, 1-ethyl-2-(2-hydroxystyryl)pyridinium iodide II, 1-ethyl-2-(4-hydroxystyryl)quinolinium iodide III and 1-ethyl-2-(2-hydroxystyryl)quinolinium iodide IV. These derivatives were synthesized by the reaction of the corresponding aldehyde with 1-ethyl-2-methylpyridinium iodide or 1-ethyl-2-methylquinolinium iodide using piperidine as a condensation reagent.[9,10] The products obtained were crystallized several times from ethanol. The compounds used for the preparation of the derivatives and the organic solvents were of high purity (A. R. or spectrograde). Stock solutions 10^{-3} M of the compounds were prepared by dissolving the solid in the solvent. pH control was achieved by using a modified universal buffer solution.[11]

To account for the difference in acidity, basicity, dielectric constant and ion activities in partially aqueous solutions relative to pure aqueous ones, the pH values of the former solutions were corrected making use of the attempts described by Douheret[12]

$$\mathrm{pH}^* = \mathrm{pH(R)} - \delta,$$

where pH* is the corrected reading and pH(R) is the meter reading obtained in a partially aqueous medium, where the pH-meter is standardized using aqueous buffer.

The values of δ of the aqueous buffer solutions containing varying proportions of each of the organic solvents under investigation were determined by Douheret.[12,13]

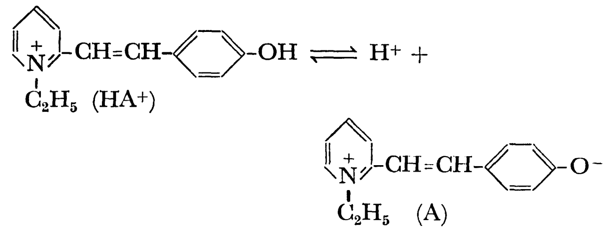
Apparatus. The absorption spectra were measured on a UNICAM S.P 8000 Spectrophotometer within the wavelength range 300—700 nm using 1 cm matched silica cells. The pH-measurements were carried out at 25 °C with a UNICAM MK_2 pH-meter, equipped with the usual glass and calomel electrodes, accurate to ±0.005 unit. The temperature was controlled by placing the solutions as well as the pH-meter in an air thermostat accurate to ±0.5 °C.

Results and Discussion

The visible absorption spectra of the compounds measured either in buffer solutions or in those containing different proportions of an organic solvent (methanol, ethanol, acetone, DMF, and DMSO) show mainly two bands (Fig. 1). The spectra of solutions with low pH are characterized by only one visible band mainly due to the absorption by species with non-ionised OH-group. This band was assigned to an intramolecular charge transfer transition.[2] Its intensity decreases with increase in pH in media of pH≥7. At the same time another band appears at longer wavelength, its intensity increasing with increase in pH. The behaviour can be explained as follows. With increase in the pH of the medium, the ionisation of the proton starts which in turn increases the proportion of the ionised form in solution, making the energy barrier of the intramolecular CT smaller.

The results (Tables 1 and 2) indicate that the $\lambda_{\max}$ of the band responsible for the absorption by the free base exhibits a clear red shift on increasing the proportion of the organic solvent in the medium, $\lambda_{\max}$ for the band of the acid shifting slightly.

The spectra of the compounds (I—IV) in all media investigated display clear isosbestic points, showing the existence of equilibrium of the form



The absorbance —pH curves obtained at selected wavelengthes (Fig. 2) are typical of dissociation and association types, revealing the existence of one acid-base equilibrium in each case.

Table 1. Mean values of pK_a for compounds I(1.50×10^{-5} M) and II(4×10^{-5} M) and the λ_{max} values of the non-ionised and ionised forms in different water–organic solvent mixtures at 25 °C

Organic co-solvent	% (w/w) of organic solvent	Mole fraction of organic solvent	Dielectric constant of the medium 25 °C	Compound I			Compound II		
					λ_{max}, nm			λ_{max}, nm	
				pK_a	non-ionic form	ionic form	pK_a	non-ionic from	ionic form
—	Zero	Zero	78.40	8.32	359	427	8.17	355	436
Methanol	7.92	0.046	76.24	8.46	359	430	8.20	358	438
	15.84	0.0957	73.81	8.58	360	435	8.26	359	444
	23.76	0.149	71.06	8.66	362	440	8.35	360	448
	31.68	0.2067	67.92	8.82	365	446	8.45	361	452
Ethanol	7.91	0.0325	76.60	8.58	360	430	8.20	348	425
	15.82	0.0685	74.50	8.68	362	436	8.30	350	435
	23.73	0.1085	72.07	8.82	365	446	8.40	356	440
	31.64	0.1533	69.15	9.06	367	453	8.58	357	452
Acetone	7.92	0.026	76.85	8.65	363	436	8.30	356	440
	15.84	0.0552	75.06	8.80	366	447	8.46	358	448
	23.78	0.0883	72.90	9.16	369	452	8.62	360	456
	31.68	0.1258	70.28	9.32	372	462	8.75	362	460
DMF	15.82	0.0443	76.52	8.60	366	448	8.25	360	444
	23.76	0.0714	75.35	8.71	367	451	8.36	362	452
	31.60	0.1022	74.47	8.84	368	456	8.50	363	458
	38.00	0.131	72.77	8.92	370	459	8.62	364	466
DMSO	15.82	0.04156	77.08	8.57	363	439	8.20	358	445
	23.76	0.0671	76.50	8.64	364	442	8.30	360	450
	31.60	0.0963	75.42	8.73	367	450	8.45	364	460
	44.04	0.1537	73.80	8.85	369	458	8.58	365	467

Table 2. Mean values of pK_a for III(1.07×10^{-5} M) and IV(4×10^{-5} M) and the λ_{max} values of the non-ionised and ionised forms in different water–organic solvent mixtures at 25 °C

Organic co-solvent	% (w/w) of organic solvent	Mole fraction of organic solvent	Dielectric constant of the medium 25 °C	Compound III			Compound IV		
					λ_{max}, nm			λ_{max}, nm	
				pK_a	non-ionic from	ionic form	pK_a	non-ionic form	ionic form
—	Zero	Zero	78.40	8.04	400	487	7.96	392	488
Methanol	7.92	0.046	76.24	8.12	402	492	7.98	393	492
	15.84	0.0957	73.81	8.20	408	499	8.10	397	498
	23.76	0.149	71.06	8.30	410	506	8.25	399	504
	31.68	0.2067	67.92	8.40	413	513	8.35	401	511
Ethanol	7.91	0.0325	76.60	8.12	408	496	8.08	392	494
	15.82	0.0685	74.50	8.25	409	505	8.19	398	502
	23.73	0.1085	72.07	8.35	412	515	8.30	400	511
	31.64	0.1533	69.15	8.55	417	527	8.40	402	520
Acetone	7.92	0.026	76.85	8.27	406	503	8.20	395	500
	15.84	0.0552	75.06	8.40	408	510	8.35	398	510
	23.78	0.0883	72.90	8.52	410	518	8.52	400	518
	31.68	0.1258	70.28	8.70	414	528	8.60	403	526
DMF	15.82	0.0443	76.25	8.15	409	512	8.10	394	504
	23.73	0.0714	75.35	8.23	412	520	8.22	396	516
	31.60	0.1022	74.47	8.30	413	526	8.35	398	522
	38.00	0.1310	72.77	8.40	413	532	8.48	401	530
DMSO	15.82	0.04156	77.08	8.20	406	500	8.10	395	500
	23.76	0.0671	76.50	8.26	407	507	8.25	397	508
	31.60	0.0963	75.42	8.35	411	517	8.36	400	516
	44.08	0.1537	73.80	8.45	413	528	8.45	402	526

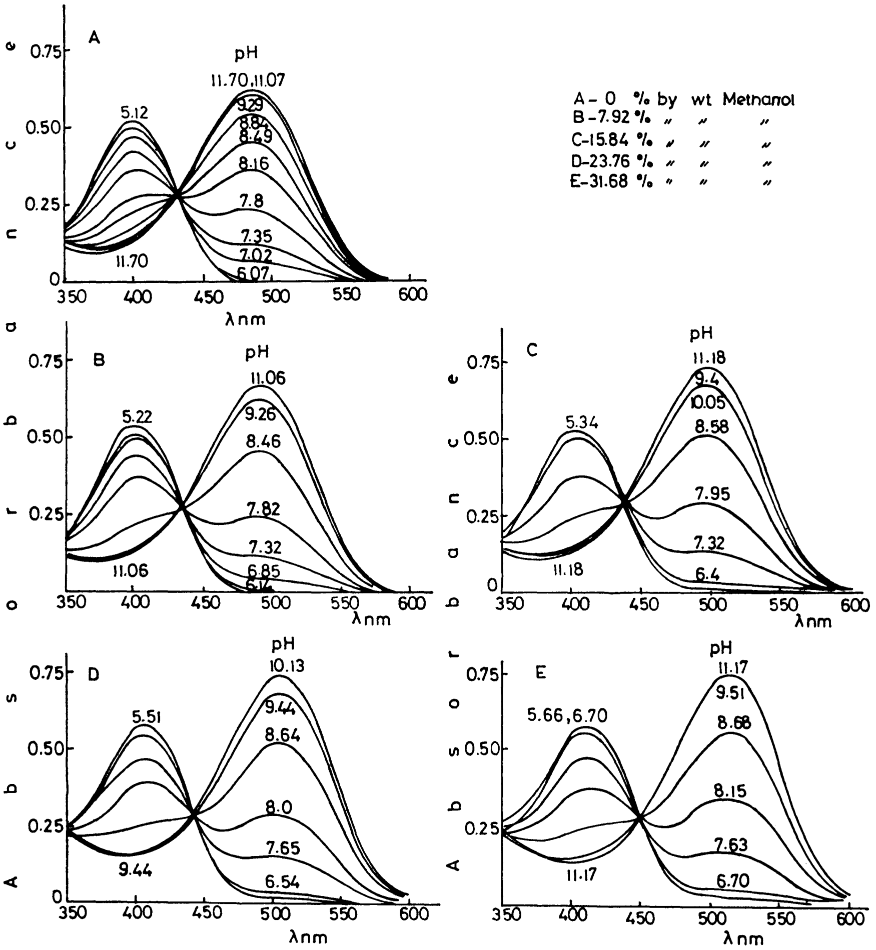


Fig. 1. Absorption spectra of 1.07×10^{-5} M 1-ethyl-2-(4-hydroxystyryl)quinolinium iodide III solution containing different percentages of methanol.

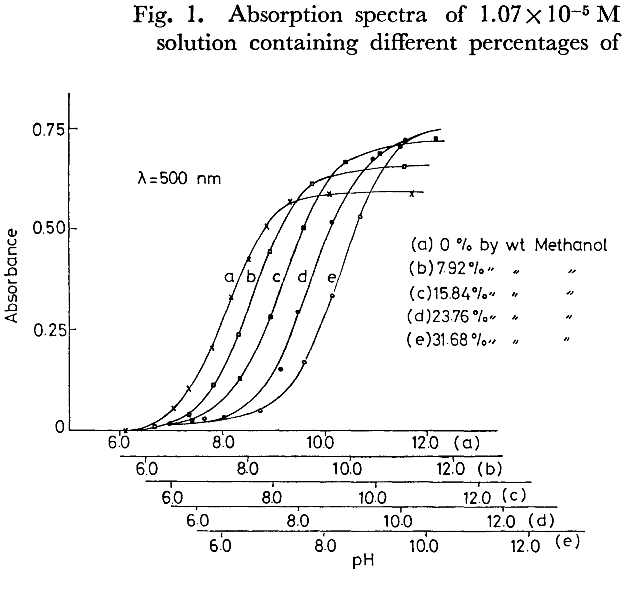


Fig. 2. Absorbance-pH curves for 1-ethyl-2-(4-hydroxystyryl)quinolinium iodide III in universal buffer solutions containing different percentages of methanol.

The acid dissociation constant, pK_a, of the compounds in different media was determined from the variation of absorbance with pH with use of three different spectrophotometric methods viz half-height, limiting absorbance and Colleter methods.[14,15] The results are given in Tables 1 and 2.

It is evident that the pK_a values depend largely on both the proportion and the nature of the organic solvent. The ionisation constant decreases with increase in the amount of solvent in the medium. This behaviour is the opposite of that observed with *p*-dimethylaminostyryl derivatives.[16]

According to Coetzee and Ritchie,[17] the acidity constant in aqueous medium $K_{a(1)}$ is related to that in partially aqueous medium $K_{a(2)}$ by means of

$$K_{a(1)} = K_{a(2)} \frac{\gamma_{H^+}\gamma_A}{\gamma_{HA^+}}, \qquad (1)$$

where the γ is the activity coefficient of the subscripted species in a partially aqueous medium relative to that in a pure one. It is known that the electrostatic effect resulting from the change in dielectric constant of the medium will operate on the activity coefficient of the charged species only, its magnitude being inversely proportional to the radius of the ionic species considered.[18] Consequently the magnitude of this effect on the proton exceeds that on the acid (HA^+). Thus, the ionisation constant of the compounds is expected to decrease with increase in the proportion of the organic solvent in the medium, which is in line with the results given in Tables 1 and 2.

However, in the light of the relation given by Charlot and Tremillon,[19] giving the variation of pK_a with

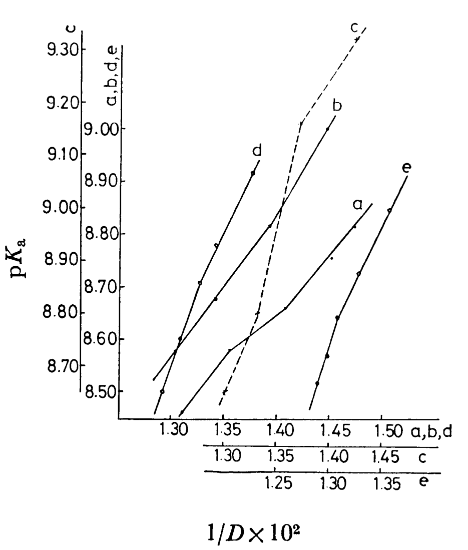


Fig. 3. Variation of pK_a of compound I in aqueous organic solvent mixture with $1/D$ of the medium at 25 °C.
a: Methanol, b: ethanol, c: acetone, d: DMF, e: DMSO.

dielectric constant (D), the plots of pK_a against $1/D$ are not strictly linear (Fig. 3). This indicates that the decrease in the ionisation constant of these compounds, though mainly governed by the dielectric constant effect, is strongly influenced also by other solvent effects. The behaviour can be interpreted by calculating the change in the ionisation constant produced by electrostatic effect (ΔpK_{el}) for compounds I and III in the presence of each organic solvent (31.60 % by wt). The calculation was made by means of the Bron equation,[18] valid for large radii,[20] and following the principles described by Tremillion.[21] The following equation is obtained for the calculation of ΔpK_{el} value:

$$\Delta pK_{el} = \frac{Ne^2}{4.6RT}\left[\frac{1}{r_{HA^+}} - \frac{1}{r_{H_3^+O}}\right]\left[\frac{1}{D_{mix}} - \frac{1}{D_{H_2O}}\right],$$

where N=Avogadro's number, e=electron charge, r=radius of ion expressed in Å, D=dielectric constant, $r_{H_3^+O}=r_{H_2O}=1.93$ Å. The radius of the monovalent cation (HA^+) was determined by assuming that its density is approximately equal to the one belonging to the corresponding non-quaternized derivative. The densities of the non-quaternized derivatives of compounds I and III were determined by means of the technique developed by Clark and White.[22]

$$d = \frac{m \times d_{Hg}}{m+w},$$

where d_{Hg}=density of mercury m=weight of the non-quaternized compound in the air, w=the weight to be added to the pan in order to level the fixed mark on the stem back to the surface of Hg. The density values obtained for the non-quaternized derivatives of compounds I and III are 1.1055 and 1.2685 gm/cm³, respectively; thus the calculated radii are 4.30 and 4.42 Å respectively. Hydrogen bonding, solvent basicity, despersion forces and proton-solvent interaction effects are commonly recognized as influencing factors in the ionisation constants of acids in the presence of organic solvent.

We can attribute the decrease in the ionisation constant of each compound due to increase in the proportion of organic solvent in the medium to the following effects besides the electrostatic effect.

(a) Decrease in the ionisation of the OH group of the compound (*i.e.* high pK_a) caused by the relatively low basicity of alcohols or acetone with respect to water.

(b) The high stabilization of the base (A) by donor hydrogen bond in pure aqueous medium relative to that in presence of organic solvent. This is presumably due to the greater tendency of water molecules to donate hydrogen bond as compared with other solvent molecules.[17] Increase in solvent proportion in the aqueous medium will result in an increase in the activity coefficient of the base, thereby causing decrease in the ionisation constant of the compound (*i.e.* high pK_a).

Since the organic co-solvent is characterized by high polarizability relative to water, the base would be more highly stabilized by dispersion forces in solvent–water mixtures than in water. On the other hand, the proton is expected to be highly stabilized in partially aqueous media relative to pure ones through proton-solvent interactions. Thus, the ionisation constant of the compound should increase with increase in the amount of the organic co-solvent in the medium. However, this is not the case (Tables 1 and 2). We see that the dispersion forces and proton-solvent interactions do not appear to be of much importance in the ionisation of the hydroxystyryl derivatives.

The results (Tables 1 and 2) indicate that the variation of pK_a values in solutions containing either the same percentage or more or less the same mole fraction (≈ 0.1) of alcohol or acetone appears to be in the order:

methanol < ethanol < acetone.

This is presumably due to the decrease in the tendency of the solvent molecules to donate hydrogen bond to the base on going from methanol to acetone. This was deduced from the fact that the tendency of alcohol to associate with solutes through H- bond decreases with increase in the molecular weight of alcohol.[23] Acetone is characterized by a very weak tendency to donate hydrogen bond.[17]

The decrease in ionisation with decrease in the donor hydrogen-bond character of the organic co-solvent is in line with the fact that the difference in the stabilization of the base by donor-hydrogen bond from solvent molecules is a major factor responsible for the increase in pK_a resulting from the increase in the amount of the solvent in the medium.

It is evident that the pK_a value in presence of the poorer donor-hydrogen bond DMF or DMSO is less than either the one obtained in the presence of the same amount or nearly the same mole faction (≈ 0.10) of acetone or ethanol (Tables 1 and 2). This can be attributed to the high basic character of the former solvents, reflecting itself in the construction of a strong acceptor hydrogen bond from the OH group of the non-ionised form and thus facilitating the ionisation process of the OH group (*i.e.* low pK_a).

Table 3. Values of ΔpK_{el}, ΔpK_{nonel}, ΔG_{el}, and ΔG_{nonel} obtained for compounds I and III

Solvent	$+\Delta pK_t$		$+\Delta pK_{el}$		$+\Delta pK_{nonel}$		$+\Delta G_{el}$ cal/mol 25 °C		ΔG_{nonel} kcal/mol 25 °C	
	I	III	I	III	I	III	I	III	I	III
31.68 wt % Methanol	0.50	0.36	0.065	0.067	0.435	0.293	89.1	91.8	0.60	0.40
31.64 wt % Ethanol	0.74	0.51	0.058	0.060	0.682	0.450	79.5	82.3	0.94	0.62
31.68 wt % Acetone	1.00	0.66	0.051	0.052	0.949	0.608	69.9	71.3	1.30	0.83
31.60 wt % DMF	0.52	0.26	0.023	0.024	0.497	0.236	31.5	32.9	0.68	0.32
31.60 wt % DMSO	0.41	0.31	0.017	0.018	0.393	0.292	23.3	24.7	0.54	0.40

The free energy of solvation of both the acid and proton by electrostatic interactions and that of the base, by donor hydrogen bond, which are equal to the free energy of transfer due to electrostatic (ΔG_{el}) and non-electrostatic (ΔG_{nonel}) interactions respectively were calculated for compounds I and III in the presence of each organic solvent (31.60% by wt) (Table 3). It is evident that the ΔG_{nonel} value of the same base becomes less positive on going from acetone→ethanol→methanol. This is in line with the increase in hydrogen bond donor character of the solvent in the same direction. On the other hand, the less positive value of ΔG_{nonel} obtained in the presence of DMF or DMSO with respect to the same percentage of the other solvents can be attributed to the high basicity of these solvents.

The observed red shift in λ_{max} belonging to the base and observed as the proportion of the organic solvent in the medium increases, can be interpreted as follows. Increase of the latter would cause an increase of the free negative charge on the oxygen atom of the base. This is due to the weak tendency of the molecules of the solvent in forming donor hydrogen bond with the oxygen atom relative to water moleucles. This in turn will reflect itself in the increase of the intramolecular charge transfer from oxygen atom to the delocalized molecular orbital of the pyridinium (I, II) and quinolinium (III, IV) cations (*i.e.* increase of the induced dipole moment of the molecule), and thus a lower excitation energy is required. This behaviour can be considered as further evidence for the fact that the donor hydrogen bond from solvent molecules to the base is important in the ionisation process of the hydroxystyryl derivatives.

Effect of Molecular Structure on pK_a. The results (Tables 1 and 2) show that the pK_a values of the 1-ethyl-2-(hydroxystyryl)quinolinium iodides (III, IV) are smaller than the corresponding ones belonging to the 1-ethyl-2-(hydroxystyryl)pyridinium iodides (I, II). This is presumably due to the high co-planarity of compounds III and IV resulting from the greater bulk of the heterocyclic moiety attached to the -CH=CH- centre. This leads to an increase in the intramolecular CT from the phenyl moiety, affording a lower negative charge density on the aromatic system resulting in weaker bonding of the proton (low pK_a value).

The pK_a values of the 4-hydroxy derivatives (I,III) are greater than the ones belonging to the 2-hydroxy derivatives (II, IV). This is probably due to the high inductive effect of the OH group on 2-position of styryl group which facilitates liberation of the proton from the compound (low pK_a value).

References

1) L. H. Feldman, A. M. Herz, and I. M. Regan, *J. Phys. Chem.* **72**, 2008 (1968).

2) M. R. Mahmoud, Z. H. Khalil, and R. M. Issa, *Acta Chim. Acad. Sci. Hung.*, **87**, 121 (1975).

3) J. M. Eder and L. Luppocramer "Ausfurliches Handbuch der Photographie," (1932), Band III, Teil 3.

4) T. Takahashi and K. Sato, *Yakugaku Zasshi*, 467 (1958).

5) M. Banno, *Kanko Shikiso*, **34**, 1 (1955).

6) L. K. Mushkalo, *Zh. Obshch. Khim.*, **29**, 1030, 1034 (1959).

7) C. Bahner, C. Cook, J. Dale, J. Fain, E. Franklin, J. Goan, W. Stump, J. Wilson, *J. Org. Chem.* **22**, 682 (1957).

8) C. Bahner, J. Dale, J. Fain, E. Franklin, J. Goan, W. Stump, M. West, and J. Wilson, *J. Org. Chem.*, **22**, 1110 (1957).

9) A. P. Phillips, *J. Org. Chem.*, **12**, 333 (1947).

10) G. T. Pilyugin, I. N. Chernyuk, *Zh. Obshch. Khim.*, **31**, 1585 (1961).

11) H. T. S. Britton, "Hydrogen Ions," Chapman & Hall, London (1952), p. 364.

12) G. Douheret, *Bull. Soc. Chim. Fr.*, **1967**, 1412.

13) G. Douheret, *Bull. Soc. Chim. Fr.*, **1968**, 3122.

14) R. M. Issa, H. Sadek, and I. I. Izzat, *Z. Phys. Chem. N. F.*, **74**, 17 (1971).

15) J. C. Colleter, *Ann. Chem. (Paris)*, **1960**, 415.

16) M. R. Mahmoud and R. Abd-El-Hamide, *Indian J. Chem.*, in press.

17) J. F. Coetzee and C. D. Ritchie, "Solute-Solvent Interactions," Marcel Dekker Ltd., New York, London (1969), p. 221.

18) M. Born, *Z. Phys.*, **1920**, 45.

19) G. Charlot and B. Tremillon, "Chemical Reactions In Solvents and Melts," Pergamon Press (1969), p. 55.

20) L. G. Hepler, *Aust. J. Chem.*, **17**, 587 (1964).

21) B. Tremillon, "Chemistry in Non-Aqueous Solvents," Publishing company, Dordrecht, Holland (1974), p. 232.

22) P. W. Clark and J. White, *Trans. Brit. Ceram. Soc.*, **49**, 305 (1950).

23) F. Frank and D. J. G. Ives, *Quart. Rev.*, **20**, 1 (1966).