Ionization Constants of Some Schiff's Bases in 80% (w/w) Dimethyl Sulphoxide–Water Solvent at 25 °C

Sau-Fun Tan, Kok-Peng Ang, and Harilakshmi Jayachandran
Department of Chemistry, National University of Singapore, Kent Ridge, Singapore 0511

p*K* Determination in 80% (w/w) dimethyl sulphoxide–water solvent at 25 °C has been used as a means of studying the tautomerism in a series of Schiff's bases derived from some *C*-acylhydroxypyrones. While their much lower acidities compared with the corresponding parent compounds indicate a predominance of ketoamine tautomers, their higher acidities compared with amides and other nitrogen acids suggest significant contributions from dipolar structures. Correlation of the wide range of p*K* values with the structures is discussed.

Aromatic hydroxy-aldehydes or -ketones are known to exist practically entirely in enolic forms. However, their Schiff's bases can have enolimine or ketoamine forms or equilibrium mixtures of these depending on structures, physical state, and solvents.[1,2] Tautomerism in Schiff's bases has been studied mainly by spectroscopic methods. As enolimines may be expected to be more acidic than the corresponding ketoamines, p*K* measurements should provide useful information. Thus, *N*-salicylideneamines, which exist predominantly in enolimine forms in the solid state or in non-polar solvents, as shown by *X*-ray analysis, n.m.r., i.r, and u.v. spectra, are believed to exist as ketoamines in polar solvents.[3] Their p*K* values, obtained indirectly,[4] support the latter deduction.

That p*K* measurement as a method of investigation has not been widely applied to Schiff's bases is probably because many of them are sparingly soluble and relatively unstable in aqueous solutions. The Schiff's bases of some *C*-acylhydroxypyrones have been shown by n.m.r. studies in $CDCl_3$ to exist primarily as ketoamines.[5] Their p*K* values in 80% (w/w) dimethyl sulphoxide–water solvent have now been determined by spectrophotometric method and compared with those of the parent compounds.[6] These p*K* values are summarised in Table 1; detailed results are given in Supplementary Publication No. SUP 23566 (41 pp).* This solvent system has been chosen as it possesses many desirable properties [7,8] and as the Schiff's bases are very sparingly soluble in water.

Results and Discussion

The Schiff's bases (IIA—H), (VA—G), (VI), and (VII), being vinylogous amides, are very much weaker acids than the parent enolic compounds (I), (III), (VIII), and (IX).[6] The difference in acidity is even more striking than that noted between the p*K* of some salicylideneamines [4] and that of salicylaldehyde. This huge difference suggests strongly that the difference in structure between the Schiff's bases and the parent compounds is not merely the replacement of a carbonyl oxygen by an imino nitrogen but provides evidence for the ionization of the hydrogen bonded to nitrogen of the ketoamine. Moreover, a substantial energy barrier probably exists between the enolimine and the ketoamine forms, otherwise, during measurements, equilibrium could shift from the ketoamine to the more acidic enolimine form. It is also noted that whereas compound (III) is much more acidic than compound (I), their Schiff's bases (V) and (II) have very similar p*K* values. These Schiff's bases, though weakly acidic, have lower p*K* values than amides. This could be due to important contribution to the resonance hybrids from dipolar structures *e.g.* structures (a) and (b) for compound (VI).

These dipolar structures are favoured because of resonance stabilisation of the pyrone rings, a postulate supported by i.r. spectra of (IV)—(VII) which clearly show the presence of α-pyrone absorptions but an absence of the anhydride absorptions expected for the ketoamine forms. The partial positive charge on the nitrogen atom contributes to the relatively higher acidity of these compounds than would be expected from the vinylogous amide structures. Further support for the dipolar forms also comes from the ^{15}N–H coupling constants found for those ^{15}N-enriched Schiff's bases (IIA,C), (VA,C), (VI), and (VII).[5] Substitution of these $J_{^{15}N-H}$ values into the formula [9] $s = 0.43J - 6$ gives the percentage *s* character of the nitrogen atom ranging from 29.7 to 32.3, close to that expected of sp^2 nitrogen. Some variation in *J* is likely to result from various degrees of electronic displacement on the nitrogen atoms.[10]

The mono-Schiff's bases (IVA—J) are much stronger acids than the Schiff's bases (IIA—H) and the bis-Schiff's bases (VA—G), their p*K* values being of similar order of magnitude to that of compound (I). This is consistent with the structures previously deduced from n.m.r. studies [5] that an ionizable OH group is present at C-4, a situation similar to compound (I). A second ionization involving the NH group corresponds to a p*K* value in the region of 14.5.

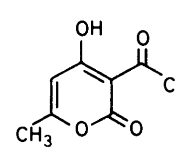
When compared with those of (IIC) and (VC), the p*K* values of Schiff's bases (VI) and (VII) are remarkably low for nitrogen acids. However, this becomes understandable in the light of the much higher acidities of the parent 6-hydroxy-2-pyrones (VIII) and (IX) than the 4-hydroxy-2-pyrones (I) and (III).[6] Here again, the higher acidities of (VI) and (VII) are likely to be the result of stabilisation of the anions by more extensive electron delocalisation. The differences between the p*K* values of the Schiff's bases (IIC), (VI), and (VII) and their respective parent hydroxypyrones are of similar order of magnitude, Δp*K* being in the range 4.5—6 units.

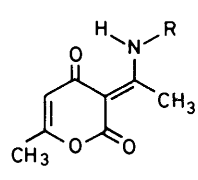
For comparison with Schiff's base (IIC), the acidities of compounds (X) and (XII), with an alicyclic and an aromatic ring respectively, are measured. Compound (IIC) is more strongly acidic than either (X) or (XII), as expected from the electron-withdrawing nature of the pyrone ring. For further comparison, an acyclic Schiff's base, 1-phenyl-3-anilinobut-2-enone (XIC), is found to be even more weakly acidic, as it exists practically entirely in the ketoamine form and electron delocalisation is less extensive in its anion.

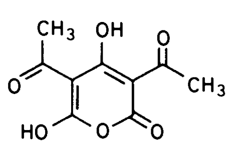
p*K* Values of the parent carbonyl compounds of the Schiff's bases (XI)—(XIII) were also determined in the same solvent for comparison. Whereas the difference in p*K* values of compound (XIC) and its parent compound, benzoylacetone (p*K* 9.84), is 5.2 which is in the expected range in view of its

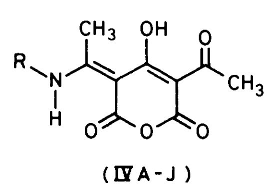
---

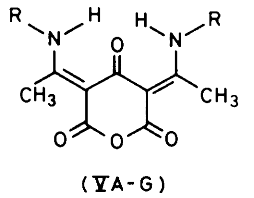
* For details of Supplementary Publications see Notice to Authors in *J. Chem. Soc., Perkin Trans. 2*, 1983, Index Issue.

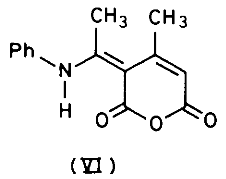

(I)

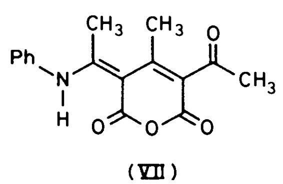

(IIA-H)

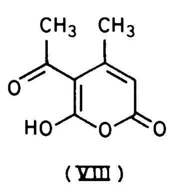

(III)

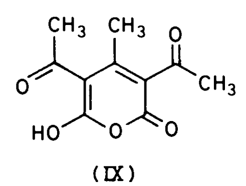

(IVA-J)

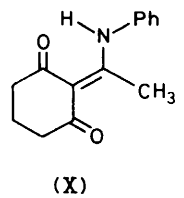

(VA-G)

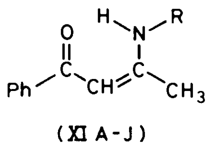

(VI)

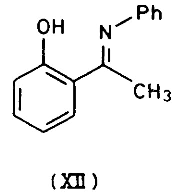

(VII)

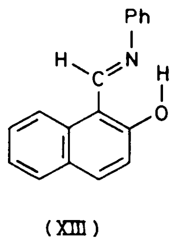

(VIII)


(IX)

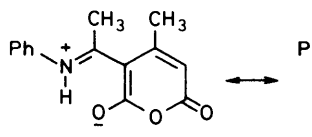

(X)


(XIA-J)


(XII)


(XIII)

A; R = CH_3
B; R = $C_6H_5CH_2$
C; R = C_6H_5
D; R = p-$MeOC_6H_4$
E; R = p-ClC_6H_4
F; R = p-$CH_3C_6H_4$
G; R = p-BrC_6H_4
H; R = p-$CH_3COC_6H_4$
J; R = p-$NO_2C_6H_4$


(a) (b)

(VI)

ketoamine structure, the p*K* differences between the aromatic Schiff's bases (XII) and (XIII) and their respective parent compounds (*o*-hydroxyacetophenone, p*K* 11.21; 2-hydroxy-1-naphthaldehyde, p*K* 7.97) are in the region 2.5—3.3, noticeably smaller than the corresponding differences between the p*K* values of the pyrone Schiff's bases (IIC), (VI), and (VII) and their respective parent compounds. This is consistent with the observation by Dudek[1] from studies of ^{15}N–H coupling constants that the aromatic Schiff's bases are mixtures of significant proportions of ketoamine and enolimine forms, the latter forms contributing to lowering the experimentally measured p*K* values. Similarly Green and Sleet,[4] who determined the p*K* of the Schiff's bases of hydroxybenzaldehydes, attributed the much higher p*K* values of the *ortho*- and *para*-isomers than the *meta*-isomer to contributions from dipolar structures to the former two but not the latter compound, which necessarily exists in the enolimine form.

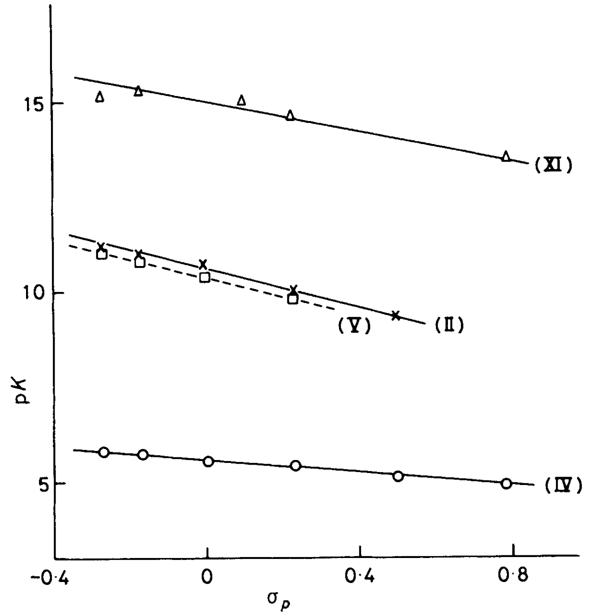
Correlation of p*K Values with Hammett's Substituent Constants.*—For each of the series of Schiff's bases (IIC—H) and (VC—G) which are derived from *p*-substituted anilines, their p*K* values are linearly correlated with Hammett's constants (Figure). The reaction constant ρ is comparable to those for anilines[11] (Table 2). This reinforces the view that the ionizable hydrogen is bonded to the nitrogen and that there is substantial contribution from the dipolar structures, so that electron donation from the *p*-substituents will partially disperse the positive charge and thereby increase the stability of the undissociated molecule relative to its anion. It is interesting to note that although the p*K* of (IV) is a measure of the ionization of the enolic OH group, the effect of variation of the *p*-substituent (R) is still observable and the p*K* of (IVC—J) plotted against the Hammett constants still gives a straight line. The slope, however is much smaller (0.85) than those of similar plots for the Schiff's bases (II) and (V). This is to be expected since the effect of substituent R on the acidities

Table 1. p*K* in 80% (w/w) dimethyl sulphoxide–water solvent at 25 °C

pK of Schiff's bases									pK of protonated precursor amines [a]	Hammett substituent constants [b]
(IIA–H)	(IVC–J)	(VA–G)	(VI)	(VII)	(X)	(XI C–J)	(XII)	(XIII)		σ_p
A *14.4	A	A *14.8							10.66	
B *13.7	B	B *14.1							9.33	
C	C 5.54 (pK_1) 14.59 (pK_2)	C 10.43	7.28	4.00	11.31	C 15.04	13.73	*11.3	4.6	0
D 11.22	D 5.81	D 11.08				D 15.16			5.31	−0.27
E 9.96	E 5.51	E 9.97				E 14.63			3.98	+0.23
F 11.01	F 5.76	F 10.86				F 15.23			5.10	−0.17
G 9.83	G 5.48	G 9.87							3.80	+0.23
H •9.4	H 5.15								2.75	+0.5
J	J *5.0					J 13.55			1.02	+0.78

[a] p*K* in water from D. D. Perrin, ' Dissociation Constants of Organic Bases in Aqueous Solution,' Butterworths, London, 1965. [b] J. Shorter, ' Correlation Analysis in Organic Chemistry,' Clarendon Press, Oxford, 1973.

* Approximate value.



Plot of p*K* values of Schiff's bases *versus* σ_p values of the precursor amines. Schiff's base series: ×, (IIA—H); ○, (IVA—J); □, (VA—G); and △, (XIC—J)

of (II) and (V) is direct whereas that of R on the acidity of (IV) is indirect and necessarily of smaller magnitude. A comparison may be made with the effect of substituents in the aryl group of styryl-substituted phenols, 3-hydroxypyrones, or tropolones, where similar Hammett slopes have been obtained.[12] The p*K* values of these Schiff's bases are also linearly correlated with those of the protonated precursor amines, aromatic as well as aliphatic (Table 2).

Martin *et al.*[13] had determined the p*K* of enaminones derived from β-diketones in dioxan–water mixtures and concluded that these compounds existed in the enolimine form since the p*K* values were insensitive to substituents on the nitrogen. However, in the present solvent system, a correlation is found to exist between p*K* of the Schiff's bases series (XIC—J) and σ_p, the slope of the linear plot being −1.64. This strongly suggests that the influence of the substituents is direct, consistent with the ketoamine structures.

Table 2. Correlations between p*K* values of Schiff's bases with p*K* values of the protonated precursor amines and with the Hammett constants

Schiff's base	Slope [a]	*b*
(IIA–H)	0.65	−2.51
(IVA–J)	0.20	−0.85
(VA–G)	0.74	−2.33
(XIC–J)	0.40	−1.64

[a] p*K* (Schiff's base) *versus* p*K* (protonated precursor amine). [b] p*K* (Schiff's base) *versus* σ_p (Hammett constant).

Materials.—Compound (I), benzoylacetone, *o*-hydroxyacetophenone, and 2-hydroxy-1-napthaldehyde were commercially available. The rest were prepared according to literature procedures [6,14] and characterized by i.r. and n.m.r. spectra. All compounds were purified by repeated recrystallization or distillation and their purity checked by microanalyses. Triply distilled water and spectrophotometric grade dimethyl sulphoxide were used for preparing the solvent mixture. Buffer solutions were prepared from carbonate-free sodium hydroxide solution. Indicators [7,15] were purified according to published methods.

Spectrophotometric Measurements.—Measurements were made on triplicate solutions at 25 °C using matched 1-cm silica cells. The temperature of the thermostatted cell compartment was maintained at 25 ± 0.2 °C and the temperature of the air-conditioned room was kept close to 25 °C. The experimental details and methods of calculation of the p*K* values are given in refs. 16 and 17.

The stability of all the compounds was checked by recording the u.v. spectra at regular intervals over a period of time. The compounds marked with an asterisk (Table 1) were found to be unstable to alkali and slow hydrolysis caused a decrease in absorbance reading with time. For these compounds, the absorbance at a fixed wavelength was measured immediately after mixing the solutions and over a period of time. It was plotted against time and extrapolated to give the absorbance at the time of mixing. The change in p*K* values over 30 min was *ca.* 0.2—0.3 unit for compounds (IIH), (IVJ), and (XIII). The alkyl Schiff's bases, which were hydrolysed faster, showed a change of 0.5—1.0 units over 30 min. Their estimated p*K* values are included in Table 1 for the purposes of discussion.

References

1 (*a*) G. O. Dudek and E. P. Dudek, *J. Am. Chem. Soc.*, 1964, **86**, 4283; (*b*) G. O. Dudek and R. H. Holm, *ibid.*, 1961, **83**, 3914.

2 N. M. D. Brown and D. C. Nonhebel, *Tetrahedron*, 1968, **24**, 5655.

3 P. W. Alexander and R. J. Sleet, *Aust. J. Chem.*, 1970, **23**, 1183.

4 (*a*) R. W. Green and P. W. Alexander, *Aust. J. Chem.*, 1965, **18**, 329; (*b*) R. W. Green and R. J. Sleet, *ibid.*, 1966, **19**, 233; 2101; 1969, **22**, 917.

5 S. F. Tan, K. P. Ang, H. L. Jayachandran, A. J. Jones, and W. R. Begg, *J. Chem. Soc., Perkin Trans. 2*, 1982, 513.

6 S. F. Tan, K. P. Ang, and H. L. Jayachandran, *J. Chem. Soc., Perkin Trans. 2*, 1983, 471.

7 E. H. Baughman and M. M. Kreevoy, *J. Phys. Chem.*, 1974, **78**, 421.

8 M. Georgieva, G. Velinov, and O. Berdevsky, *Anal. Chim. Acta*, 1977, **90**, 83.

9 G. Binsch, J. B. Lambert, B. W. Roberts, and J. D. Roberts, *J. Am. Chem. Soc.*, 1964, **86**, 5564.

10 G. O. Dudek and E. P. Dudek, *J. Chem. Soc. B*, 1971, 1356.

11 J. Shorter, 'Correlation Analysis in Organic Chemistry,' Clarendon Press, Oxford, 1973, p. 10.

12 H. Besso, K. Imafuku, and H. Matsumura, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 2161.

13 D. F. Martin, G. A. Janusonis, and B. B. Martin, *J. Am. Chem. Soc.*, 1961, **83**, 73.

14 A. K. Kiang, S. F. Tan, and W. S. Wong, *J. Chem. Soc. C*, 1971, 2721.

15 M. Georgieva, P. Zikolov, and O. Budevsky, *Anal. Chim. Acta*, 1980, **115**, 411.

16 K. P. Ang and T. W. S. Lee, *Aust. J. Chem.*, 1977, **30**, 521.

17 R. A. Robinson and A. K. Kiang, *Trans. Faraday Soc.*, 1955, **51**, 1398.

Received 14*th October* 1982; *Paper* 2/1766