Tetrahedron, 1963, Vol. 19, pp. 357 to 372. Pergamon Press Ltd. Printed in Northern Ireland

THE APPLICATION OF THE HAMMETT EQUATION TO THE THEORY OF TAUTOMERIC EQUILIBRIUM—II

TAUTOMERISM OF α-ARYLSULPHAMINOPYRIDINES*

T. A. MASTRUKOVA, YU. N. SHEINKER, I. K. KUZNETSOVA, E. M. PERESLENI, T. B. SAKHAROVA, M. I. KABACHNIK

Institute of Organo-Element Compounds, USSR Academy of Sciences; Institute of Chemistry of Natural Products, USSR Academy of Sciences, Moscow USSR

(*Received* 20 *July* 1962)

Abstract—In general principles the application of the Hammett equation to the study of tautomeric equilibrium has been investigated. It has been shown that the $pK_a - \sigma$ plot for the dissociation constants of tautomeric acids is characterized by the deviations from the linear Hammett dependence, no deviations being observed except under definite conditions.

The deviations from the linear dependence are related to the tautomeric equilibrium constant by the relationship $K_T = 10^a - 1 = 1/10^b - 1$ with "a" and "b" being the deviations of the curve $pK_a = f(\sigma)$ from the asymptotes.

These principles were applied to the investigation of the tautomeric equilibrium of α-arylsulphaminopyridines, substituted into the benzene ring.

Two independent methods—potentiometric and spectrophotometric—were used. The electron releasing substituents have been shown to shift the equilibrium toward the amino forms and the electron attracting ones toward the imino forms.

The comparison of the quantitative results obtained by the two methods showed them to be in a good agreement.

1. GENERAL CONSIDERATIONS

THE effect of structure on the strength of organic acids can be evaluated in terms of correlation equations such as the Hammett[1,2]

$$\log \frac{K}{K^0} = \rho\sigma \tag{1}$$

where K^0 and K are the dissociation constants for the non substituted and substituted acids, respectively, σ is the substituent constant, and ρ is the reaction constant.

In a previous article[3] the effective dissociation constants of tautomeric acids $HA_1 \rightleftarrows HA_2$ have been shown to follow the Hammet equation only when the tautomeric equilibrium is strongly shifted towards one of the forms. Otherwise, usual deviations from linear dependence are observed due to the equilibrium of two acids of different chemical type, characterized, respectively, by different constants, K^0 and ρ. Thus for the tautomeric form HA_1:

$$pK_1 = pK_1^0 - \rho_1\sigma \tag{2}$$

for the tautomeric form HA_2:

$$pK_2 = pK_2^0 - \rho_2\sigma \tag{3}$$

* Translated by A. L. Pumpiansky, Moscow.

[1] L. P. Hammett, *Physical Organic Chemistry*, New York (1940).

[2] H. H. Jáffe, *Chem. Rev.* **53**, 191 (1953).

[3] M. I. Kabachnik, T. A. Mastrukova, A. E. Shipov and T. A. Melentyeva, *Tetrahedron* **9**, 10 (1960).

In the coordinates of pK and σ this gives in a general case two intersecting straight lines A and B (Fig. 1). The ordinate intercept between the straight lines corresponding to the particular value of σ refers to the tautomeric equilibrium constant K_T:

$$pK_T = pK_1 - pK_2 \tag{4}$$

where $K_T = [HA_2]/[HA_1]$

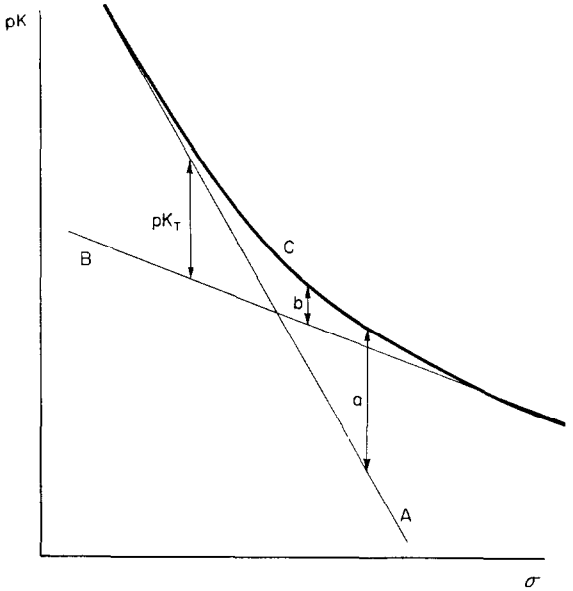


FIG. 1. Dependence of pK_a on σ for tautomeric acids $HA_1 \rightleftarrows HA_2$.

Determined experimentally are, however, not the dissociation constants of particular forms K_1 and K_2 but some effective dissociation constant of the equilibrium mixture K_a, that is related to the dissociation constants of particular forms by the relationship[4]:

$$K_a = \frac{K_1 K_2}{K_1 + K_2} \tag{5}$$

This effective dissociation constant is also a function of σ[3]:

$$pK_a = pK_1^0 + pK_2^0 - (\rho_1 + \rho_2)\sigma + \log (K_1^0 \cdot 10^{p_1\sigma} + K_2^0 \cdot 10^{p_2\sigma}) \tag{6}$$

Graphically the equation (6) in the coordinates of pK and σ is expressed by the curve (C), with straight lines A and B being its asymptotes (Fig. 1). With low values of σ, when the tautomeric equilibrium is shifted toward the form HA_1, the curve (C) practically coincides with the straight line A and the K_a value follows the equation (2). At medium values of σ a deviation from the linear dependence is observed, the greater, the more HA_2 form is found in the equilibrium. At higher values of σ the curve (C) coincides with the straight line B and the K_a value follows the linear dependence (3). The tautomeric equilibrium is shifted in this area toward the form HA_2.

Experience has shown that the above relationships do not always hold true. There may be cases when the change in σ over an experimentally available range does not markedly affect the tautomeric equilibrium (Fig. 2). In the left part of Fig. 2 is

[4] M. I. Kabachnik, *Dokl. Akad. Nauk. SSSR* **83**, 407 (1952).

given an instance when the tautomeric equilibrium is shifted toward the form HA_1 over the whole available range of changes in σ ($K_T \ll 1$). Here the curve C coincides with the straight line A (the point of intersection of straight lines A and B lying to the right at the bottom outside the plot). The right part of Fig. 2 shows the tautomeric equilibrium shifted toward the form HA_2 ($K_T \gg 1$) and the curve C coincides with the straight line B over the whole available range of changes in σ (the point of intersection of the straight lines lying to the left at the top outside the plot). Such relationships are observed, for example, with the tautomerism of salts of substituted dialkylaminoazobenzenes,[5] studied by Savitsky.[6] In such and similar cases the effective dissociation constants of tautomeric mixtures follow the Hammett linear dependence.

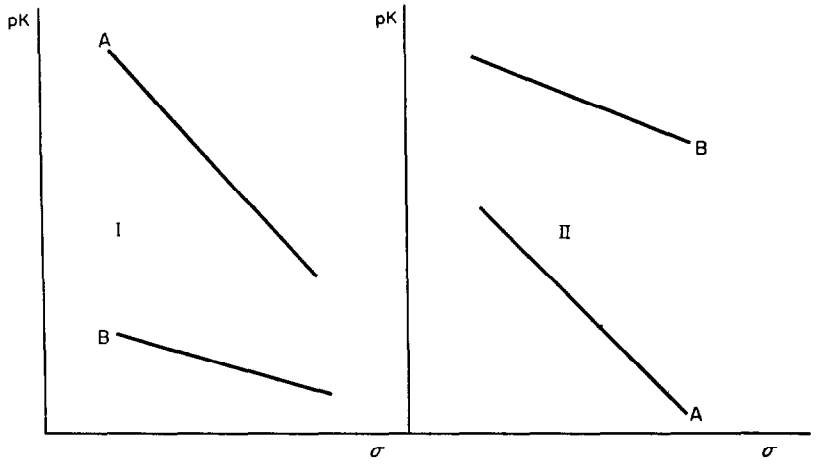


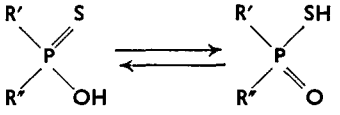
FIG. 2. Dependence of pK_a on σ for tautomeric acids with strongly shifted equilibrium. The straight line A: $pK_1 = pK_1^0 - \rho_1\sigma$; The straight line B: $pK_2 = pK_2^0 - \rho_2\sigma$.

No deviation from this dependence due to tautomerism may be observed also with A and B intersecting at a very acute angle. Then the points corresponding to the experimental values of pK_a are practically on a straight line, the equilibrium constant is near to unity and is little affected by the change in σ (cf. a rather similar case below—Fig. 4).

When, however, tautomerism leads to deviations from the linear Hammett dependence, the magnitude of these deviations allow the tautomeric equilibrium constants to be determined. In the work quoted[3] two of the authors and Shipov and Melentyeva have shown that the constant of tautomeric equilibrium K_T is related to the deviations from the linear dependence along the ordinate "a" (Fig. 1) by the relationship (7).

$$K_T = 10^a - 1 \tag{7}$$

Using this relationship we have investigated the effect of substituents R′ and R″ upon the tautomeric equilibrium of phosphorous thioacids:



[5] M. I. Kabatschnik, *Acta Chim. Acad. Sci. Hung.* **18,** 426 (1959).
[6] E. Sawicki, *J. Org. Chem.* **21,** 605 (1956); **22,** 621 (1957).

For these compounds the plot of pK_a vs σ had a long linear part corresponding to the predominance of the thione forms (HA_1), and a part of the deviations from the linear dependence due to the appearance in the equilibrium of thiol forms (HA_2).

It was also of interest to investigate such cases of tautomerism where the change in σ so markedly affects the tautomeric equilibrium that it proves possible to investigate the curve C all along its length. We have found such instances on studying the tautomerism of α-arylsulphaminopyridines substituted into the benzene ring.

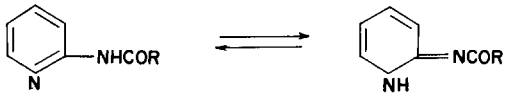
The tautomerism of α-aminopyridine (I) was first reported by Tchitchibabin[7] when studying the dual reactivity of this compound and some of its derivatives.

I

The crystalline α-aminopyridine proved, however, to be a pure amino form.[8] In solutions of α-aminopyridine the tautomeric equilibrium is so strongly shifted toward the amino form that the presence of the imino form cannot be detected either spectrally[9] or by means of highly sensitive "carbonate" procedure due to Goldfarb and Damyushevsky.[10] Angyal and Angyal[11] evaluated the tautomeric equilibrium constant of α-aminopyridine ($K_T = C_{Im}/C_{Am}$) as $5 \cdot 10^{-6}$.

Different relationships are observed on the introduction of electrophilic radicals into the amino group.[12]

As shown by one of the authors,[12–14] α-acylaminopyridines (II and III) are compounds with pronounced aminoimino tautomerism with the tautomeric equilibrium strongly depending on the electrophilicity of the acyl group and on the solvent. In particular, the alcoholic solution of α-phenylsulphaminopyridine (III, R = C_6H_5)



II

III

[7] A. E. Tchitchibabin, R. A. Konovalova and A. A. Konovalova. *Zh. Ruask. Fiz. Khim. Obshch.* **53,** 193 (1921).

[8] D. N. Shigorin, Ja. L. Danyushevsky and Ja. L. Goldfarb, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* **1956,** N 1, 120.

[9] L. C. Anderson and N. V. Seeger, *J. Amer. Chem. Soc.* **71,** 340 (1949).

[10] Ja. L. Goldfarb and Ja. L. Danyushevsky, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* 154 (1953).

[11] S. I. Angyal and C. L. Angyal, *J. Chem. Soc.* **1952,** 1461.

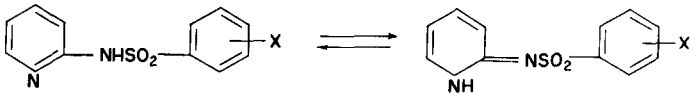
[12] Ju. N. Sheinker and I. K. Kuznetsova, *Zh. Fiz. Khim.* **31,** 2656 (1957).

[13] Yu. N. Sheinker, *Dokl. Akad. Nauk SSSR* **113,** 1080 (1957).

[14] Yu. N. Sheinker, E. M. Peresleni, N. P. Zosimova and Yu. J. Pomerantsev, *Zh. Fiz. Khim.* **33,** 2096 (1959).

contains 53% of the amino form which percentage increases up to 81 on the introduction of the amino group into the *para*-position of the benzene ring (III; R = $C_6H_4NH_2$ — p). In the aqueous solution this increase is 1 : 7.

On the basis of these data we undertook a systematic investigation of the tautomerism of substituted α-arylsulphaminopyridines. Using different substituents X in the benzene ring (IV)



IV

and varying the solvent we have investigated both the particular cases of the curve C and the whole curve. This investigation was carried out potentiometrically.

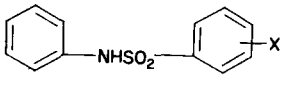
The choice of α-arylsulphaminopyridines for study proved also fortunate because these compounds could be investigated not only potentiometrically but also by an independent, spectrophotometric procedure. The coincidence of the results obtained by both methods confirmed the validity of the principles stated above and the method of the investigation of tautomeric systems based on these principles.

2. THE POTENTIOMETRIC INVESTIGATION

We have investigated the solutions of α-arylsulphaminopyridines, listed in Table 1, in 50 and 80%* aqueous ethanol and in 80% aqueous dioxan. The pK_a values were evaluated in terms of the pH values of partly neutralized solutions (Table 1). It will be seen from the data that the strength of the acids investigated increases by 1·2–1·7 pK units when passing from the electron releasing to electron attracting substituents.

The treatment of results obtained in terms of the Hammett equation necessitated the choice of σ constants for *para*-substituents. It is known that these constants are not strictly permanent values and vary to a certain degree depending on the availability and character of the conjugation of the substituent with the reaction centre.[25] Recently, Taft[26] has derived the σ^0 constants for *para*-substituents in the benzene ring for those cases when the conjugation chain between the substituent and the reaction centre is broken by the non-conductive atom grouping. In α-arylsulphaminopyridines the part of such an insulating group is played by the SO_2 group. Therefore, we came to the conclusion that it was the σ^0 constants that had to be utilized in this investigation.

This conclusion was substantiated by applying the Hammett equation to the dissociation constants of arylsulphanilides (V) involving corresponding *para*-substituents in the sulphated ring. These compounds differ from the tautomeric α-arylsulphaminopyridines having a benzene rather than a pyridine ring. Hence they fail to tautomerize but the effect of the substituent in the sulphated ring upon the amino group is of course similar. The acidic properties of arylsulphanilides in aqueous solution were



V

* wt %.

investigated by Willy[27] who showed that the pK's of these acids satisfy the Hammett equation with Hammett's σ constants. However, there are systematic deviations from linear dependence for the *p*-NH_2-group, where the difference between σ and σ^0 are greatest. Dauphin and Kergomard[28] reported on solutions in 23·4% alcohol but

TABLE 1. α-ARYLSULPHAMINOPYRIDINES (IV)

NN	X	m.p.°C	m.p.°C Lit.	pK_a 50% aq. alcohol	pK_a 80% aq. alcohol	pK_a 80% aq. dioxan
1	*p*-$N(CH_3)_2$	218–220	218–220[15]	—	10·33	11·25
2	*p*-NH_2	191–192	192[16]	9·54	10·34	11·23
3	*p*-CH_3	213–214	212[17]	9·16	9·89	10·60
4	*p*-CH_3O*	182–184	—	9·25	9·91	10·64
5	*p*-CH_3CONH	224–225	224–225[18]	9·25	—	10·54
6	H	172–173	171–172[16]	9·05	9·65	10·41
7	*p*-C_6H_5O†	163·5–165	—	—	9·68	10·37
8	*p*-F	151–152	151–152[19]	8·88	9·48	10·18
9	*p*-Br‡	199–201·5	—[20]	8·75	9·25	10·04
10	*p*-Cl	190–191·5	193–194[21]	8·74	9·34	10·05
11	*p*-CN	194–195·5	193–194[22]	8·37	8·83	9·59
12	*m*-NO_2	227–228	228–229[23]	—	—	9·58
13	*p*-NO_2	163–165	164–165[24]	—	—	9·52

* Found %: N, 10·5, 10·4. $C_{12}H_{12}O_3N_2S$. Calc.: N, 10·6%.
† Found %: N, 8·7, 8·8. $C_{17}H_{14}O_3N_2S$. Calc.: N, 8·6%.
‡ Found %: N, 8·8, 8·8. $C_{11}H_9O_2N_2SBr$. Calc.: N, 8·9%.

their data does not agree with that of Willy. In the recently published measurements Lushina and Berkman[29] do not, unfortunately, present data for amino- and dimethylamino groups and therefore, we deemed it necessary to determine the pK's of substituted arylsulphanilides in 50% and 80% aqueous ethanol and to compare the correlations obtained by using the σ of Hammett-MacDaniel-Brown[30] and σ^0 of Taft.[26] The results are summarized in Table 2. In Fig. 3 is presented the pK — σ plot for arylsulphanilides using the Taft σ^0 constants. The treatment of results following

[15] A. J. Ewins and M. A. Phillips, Brit. 512, 145 (1939); *Chem. Abstr.* **35,** 1068 (1941).
[16] Z. V. Pushkareva and Z. Yu Kokoshko, *Zh. Obshch. Khim.* **24,** 870 (1954).
[17] C. J. Cavallito and T. H. Haskell, *J. Amer. Chem. Soc.*, **66,** 1927 (1944).
[18] M. L. Crossley, E. H. Northey and M. E. Hultquist, *J. Amer. Chem. Soc.*, **62,** 372 (1946).
[19] A. Sveinbjornsson and C. A. Vander Werf, *J. Amer. Chem. Soc.*, **73,** 869 (1951).
[20] W. B. Wright and J. M. Smith, *USP* 2. 542.856 (1951); *Chem. Abstr.* **46,** 3078b (1952).
[21] M. Kulke, *Canad. J. Chem.* **32,** 604 (1954).
[22] C. Andrews and H. King, *Proc. Roy. Soc.* (*London*) **B33,** 20 (1946).
[23] K. Yu. Tsekhanovich, J. Ya. Postovsky and V. F. Degtyarev, *Zh. Obshch. Khim.* **25,** 1162 (1955).
[24] W. Lorenz, R. Behnisch and F. Mietzsch, *USP* 2, 443, 742; *Chem. Abstr.* **42,** 8822e (1948).
[25] H. Bekkum, P. E. Van Verkade and B. M. Wepster, *Rec. Trav. Chim. Pays-Bas* **78,** 815 (1959).
[26] R. W. Taft, Jr., S. Ehrenson, I. C. Lewis and R. E. Glick, *J. Amer. Chem. Soc.*, **81,** 5352 (1959).
[27] A. W. Willy, *Helv. Chem. Acta* **39,** 46 (1956).
[28] G. Dauphin and A. Kergomard, *Bull. soc. chim. Fr.* N3. 486, 1961.
[29] N. P. Lushina and Ya. P. Berkman, *Zh. Obshch. Khim.* **32,** 280 (1962).
[30] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23,** 420 (1958).

TABLE 2. ARYLSULPHANILIDES (V)

NN	X	m.p.°C	Lit.°C m.p.	pK 50% alcohol	pK 80% alcohol	σ^0
1	*p*-$N(CH_3)_2$	174–176	176[31]	—	11·60	−0·44
2	*p*-NH_2	198–199	200[32]	10·94	11·59	−0·38
3	*p*-CH_3	102	103[33]	10·42	11·12	−0·15
4	*p*-CH_3O	109–110	110[34]	10·47	11·05	−0·12
5	*p*-CH_3CONH	211–213	214[32]	10·26	10·93	−0·03
6	H	110	110[35]	10·18	10·86	0
7	*p*-C_6H_5O	86–88	86–88[36]	10·17	10·75	+0·05
8	*p*-F	109–111*	—	9·93	10·64	+0·17
9	*p*-Br	116–117	119[37]	9·78	10·32	+0·26
10	*p*-Cl	103–104	104[38]	9·77	10·43	+0·27
11	*m*-NO_2	125–126	126[39]	9·02	9·62	+0·71

* Found%: S, 13·0, 13·0; $C_{12}H_{10}O_2NSF$. Calc.: S, 12·8%.

Jaffe[2] gave for 50% alcohol $pK = 10{\cdot}23 - 1{\cdot}726\sigma^0$ for 80% alcohol it resulted in $pK = 10{\cdot}86 - 1{\cdot}757\sigma^0$* with the correlation coefficients being 0·998 and 0·997, respectively. The application of σ constants of Hammett-MacDaniel-Brown gives a poorer correlation (0·968 and 0·955). Consequently, the σ^0 constants used in this investigation were those due to Taft.

Figs. 4, 5, and 6 show the dependence of pK on σ^0 for the α-arylsulphamino-pyridines investigated. For the 50% alcohol (Fig. 4) the results indicate linear dependence. Thus, it may be concluded that the tautomeric equilibrium is either shifted to one side or is little affected by substituents. The dependence in 80% alcohol (Fig. 5) corresponds to a gentle curve. In 80% dioxan (Fig. 6) the deviations from linearity are seen to be the greatest thus indicating the presence of two tautomeric forms and a marked influence of the substituent X on equilibrium.

The treatment of data obtained was effected by successive approximations in terms of formula (6), (7), and (8).

$$K_T = \frac{1}{10^b - 1} \tag{8}$$

Formula (8) similar to formula (7) relates K_T to the deviations "b" of the experimental curve "C" from the straight line HA_2 (see Fig. 1). The treatment leads to the following data. For 80% alcohol:

The straight line HA_1: $pK_1 = 9{\cdot}34 - 1{\cdot}895\sigma^0$ $\quad (r_1 = 0{\cdot}997)$

* For groups C_6H_5O and CH_3CONH the values of σ^0 were estimated from the data obtained in the present investigation as $\sigma^0_{C_6H_5O} = 0{\cdot}05 \pm 0{\cdot}02$ and $\sigma^0_{CH_3CONH} = -0{\cdot}03 \pm 0{\cdot}01$.

[31] F. Fichter and W. Tamm, *Ber. Dtsch. Chem. Ges.* **43**, 3037 (1910).
[32] A. Gelmo, *J. Prakt. Chem.* (2) **77**, 373 (1908).
[33] F. Reverdin and P. Crépilux, *Ber. Dtsch. Chem. Ges.* **34**, 3000 (1901).
[34] L. Gattermann, *Ber. Dtsch. Chem. Ges.* **32**, 1154 (1899).
[35] O. Hinsberg, *Ber. Dtsch. Chem. Ges.* **36**, 2706 (1903).
[36] C. M. Suter, *J. Amer. Chem. Soc.* **53**, 1112 (1931).
[37] E. Noelting, *Ber. Dtsch. Chem. Ges.* **8**, 597 (1875).
[38] O. Wallach and Th. Huth, *Ber.* **9**, 426 (1876).
[39] F. D. Chattway, *J. Chem. Soc.* **85**, 1187 (1904).

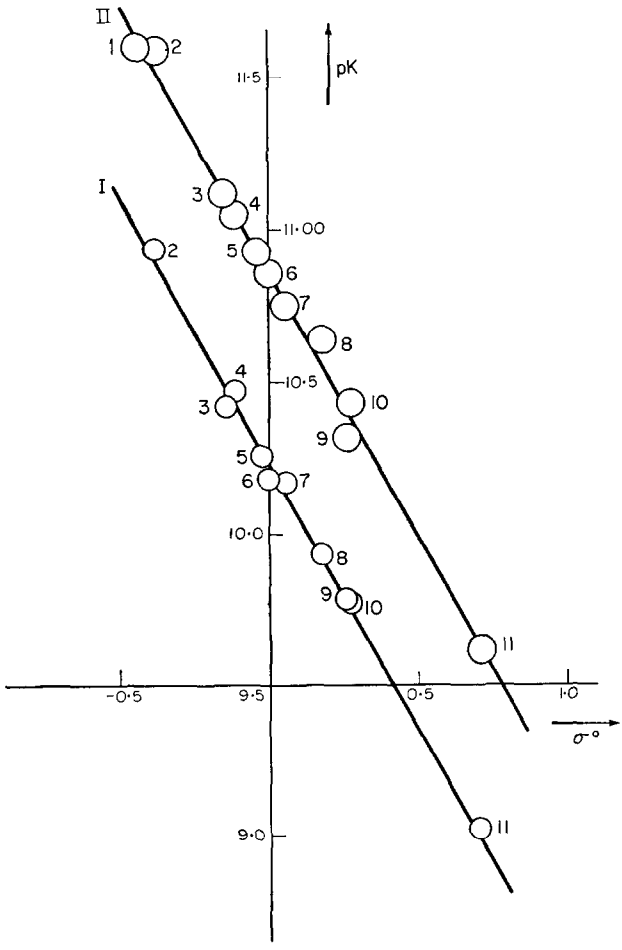


FIG. 3. Dependence of pK on σ° for arylsulphanilides. The numbering of points as in Table 2.

The straight line HA_2: $pK_2 = 9{\cdot}45 - 1{\cdot}114\sigma^0$ $(r_2 = 0{\cdot}991)$

The tautomeric equilibrium constants in 80% alcohol:

$$\log K_T = 0{\cdot}11 + 0{\cdot}781\sigma^0$$

For 80% dioxan

The straight line HA_1: $pK_1 = 10{\cdot}24 - 2{\cdot}235\sigma^0$ $(r_1 = 0{\cdot}999)$

The straight line HA_2: $pK_2 = 10{\cdot}02 - 0{\cdot}713\sigma^0$ $(r_2 = 0{\cdot}988)$

The tautomeric equilibrium constants in 80% dioxan:

$$\log K_T = -0{\cdot}22 + 1{\cdot}522\sigma^0$$

Comparing the constants ρ for 80% alcohol of α-arylsulphaminopyridines (−1·895) and arylsulphanilides (−1·757) it may be concluded that the straight line HA_1 corresponds to the amino form of the same acid type (in terms of Brønsted theory) as arylsulphanilides. The structurally different imino forms also give another

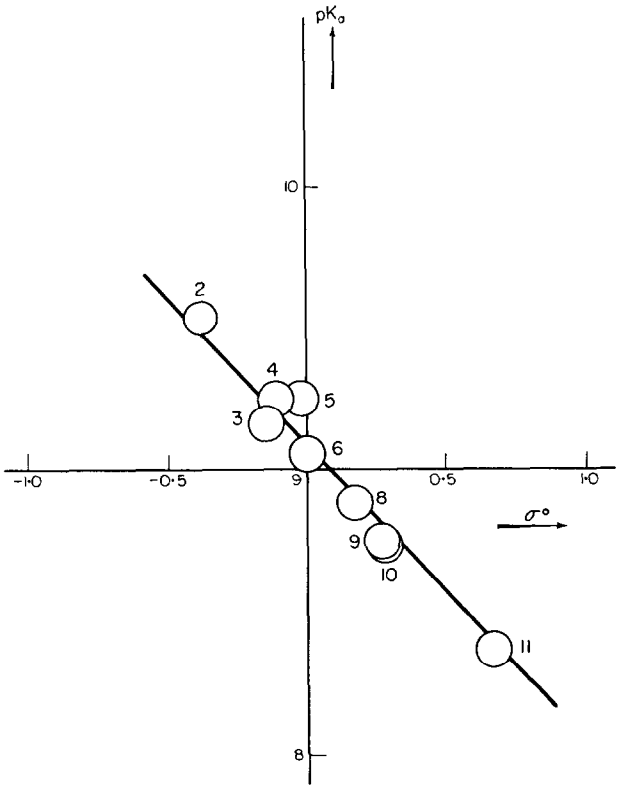
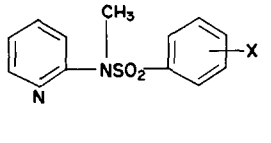


FIG. 4. Dependence of pK_a on σ° for α-arylsulphaminopyridines in 50% aqueous ethanol. The numbering of points as in Table 1.

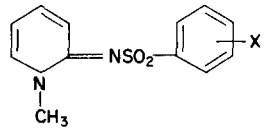
value of ρ (−1·114). Correspondingly, in 80% dioxan the steeper straight line HA_1 refers to the amino forms, and HA_2 to imino forms. In 50% alcohol solutions (pK_a = 9·08 − 1·137σ^0; r = 0·982), the slope of the straight line suggests a predominance at equilibrium of the imino forms over the total range of the change in σ^0. This has been confirmed spectrally (see below).

3. SPECTROPHOTOMETRIC INVESTIGATION

The spectral method used in this investigation to determine the tautomeric equilibrium constants is based on a comparison of absorption spectra in the ultra-violet of solutions of tautomeric α-arylsulphaminopyridines with those of corresponding reference compounds of like structure but not tautomeric such as the methylated derivatives (VI and VII) with the labile hydrogen atom of the aminopyridine system substituted by the methyl group. As shown previously[13,14] the ultra-violet spectra of amino and imino tautomeric forms of α-arylsulphaminopyridines (IV) are very different. The former, as well as those of the corresponding non-tautomeric methylated derivatives (VI), exhibit an absorption maximum at 260–270 mμ (log ε = 3·6–3·8); above 300 mμ the compounds practically show no absorption.[14] The latter, as well as those of the corresponding derivatives (VII) exhibit an absorption band at 240–250 mμ together with an intensive absorption at 310–325 mμ (log ε = 4·0).



VI



VII

Fig. 7 shows the absorption spectra of solutions in various solvents of *p*-cyanophenylsulphaminopyridine (IV, X = *p*-CN) and *p*-anisylsulphaminopyridine (IV, X = *p*-CH_3O) as well as their methylated derivatives. This type of spectra is characteristic of solutions of all α-arylsulphaminopyridines investigated.

From the spectra in Fig. 7 it will be seen that the rising electrophilicity of the group in the phenyl ring is accompanied by an increase in the percentage of the imino form: the absorption intensity at 320 mμ for the *p*-cyanoderivative being stronger than for the *p*-CH_3O derivative in each solvent. The increasing polarity of the solvents shifts the equilibrium to the same side. The spectra exhibit a sharp isobestic point thus pointing to the processes, that lead to spectral changes in going from one solvent to another, being in equilibrium.

As could be expected, the spectra of arylsulphanilides are similar in character to those of amino forms or their corresponding methylated derivatives (VI). Their appearance not being affected by the solvent (Fig. 8).

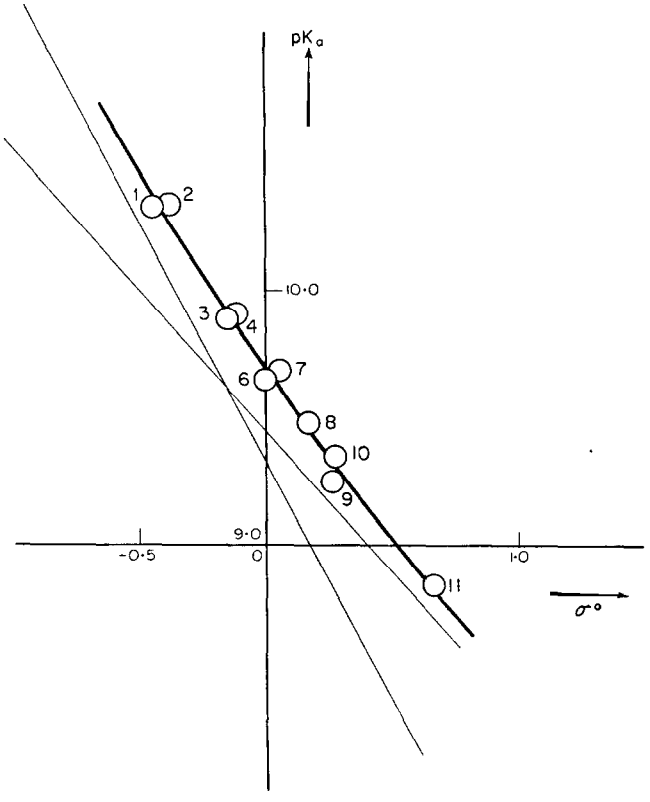


FIG. 5. Dependence of pK_a on σ° for α-arylsulphaminopyridines in 80% aqueous ethanol. The numbering of points as in Table 1.

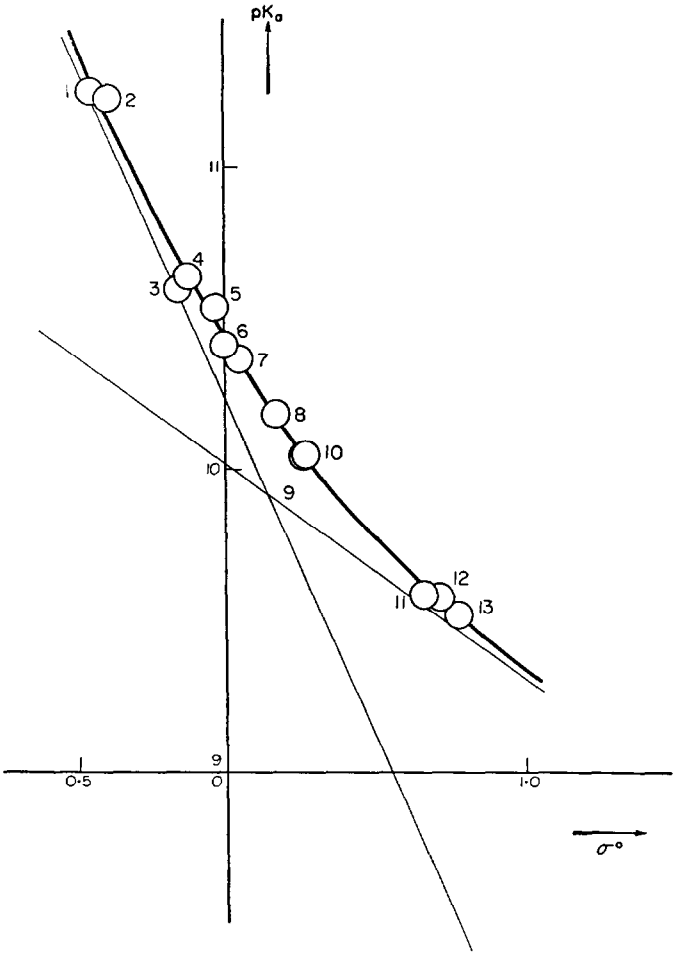


FIG. 6. Dependence of pK_a on σ° for α-arylsulphaminopyridines in 80% aqueous dioxan. The numbering of points as in Table 1.

In order to evaluate the tautomeric equilibrium constants the absorption band at 310–325 mμ, exhibited by the spectra of imino forms of α-arylsulphaminopyridines and their methylated derivatives (VII) and absent in the spectra of amino forms were used. An allowance being made since the intensity of this band does not change on passing from the tautomeric imino form to its methylated derivative. The validity of such an allowance was proved earlier.[14]

The percentage of the imino and amino tautomeric forms in the mixture was calculated in terms of formula (9) and (10).

$$C_{Im} = \frac{\varepsilon_X}{\varepsilon_{Me}} \cdot 100 \quad (9) \qquad C_{Am} = \left(1 - \frac{\varepsilon_X}{\varepsilon_{Me}}\right) \cdot 100 \quad (10)$$

The tautomeric equilibrium constants were calculated in terms of formula (11)

$$K_T = \frac{\varepsilon_x}{\varepsilon_{Me} - \varepsilon_x} \quad (11)$$

where ε_X is the molar extinction coefficient of the tautomeric compound in question

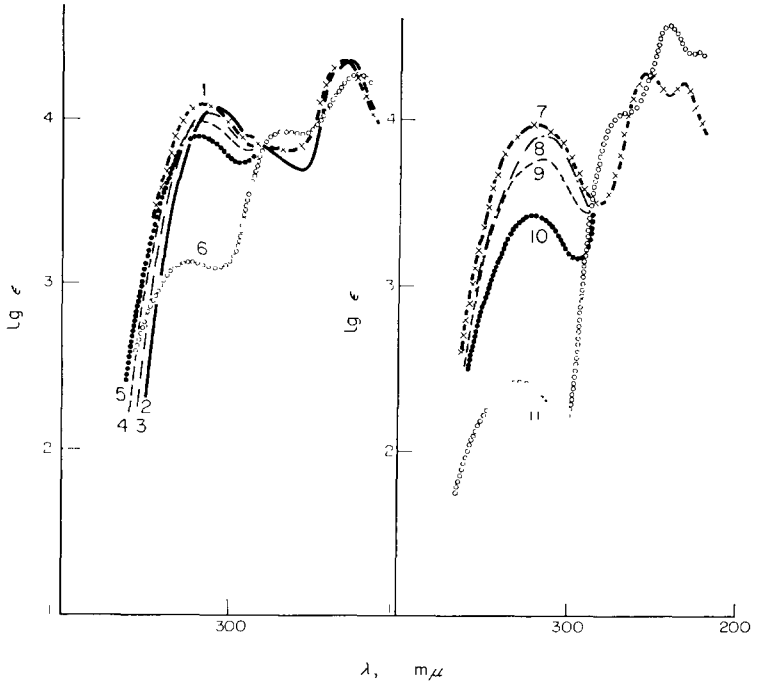


FIG. 7. Ultra-violet absorption spectra

1. (*p*-cyanophenylsulpho)-N-methyl-α-pyridonimine in 80% aqueous alcohol.
2. α-*p*-cyanophenylsulphaminopyridine in water.
3. Idem in 50% aqueous alcohol.
4. Idem in 80% aqueous alcohol.
5. Idem in 80% aqueous dioxan.
6. Idem in anhydrous dioxan.
7. (*p*-Anisylsulpho)-N-methyl-α-pyridonimine in 80% aqueous alcohol.
8. α-*p*-Anisylsulphaminopyridine in 50% aqueous alcohol.
9. Idem in 80% aqueous alcohol.
10. Idem in 80% aqueous dioxan.
11. Idem in anhydrous dioxan.

in a particular solvent and ε_{Me} is the molar extinction coefficient of the corresponding reference compound (VII) in the same solvent. The reference compounds are listed in Table 5. The error in spectrophotometric evaluations did not exceed $\pm 2\%$ (relative), the range of the relative concentrations of the imino tautomeric form studied was between 1 to 95%. Table 3 gives the tautomeric equilibrium constants determined spectrophotometrically.

4. DISCUSSION

Both methods used in this work to determine the tautomeric equilibrium constants are based on some allowances.

In the potentiometric study such allowances are, for example, due to the use of concentration constants, of the Hammett equation etc. In the spectrophotometric investigation the main allowance is the assumption of the equality of the molar extinction coefficients of tautomeric forms and their corresponding methylated derivatives. The estimation of the error due to these allowances seems to be rather involved. It may, however, be said that the sources of errors involved in both methods

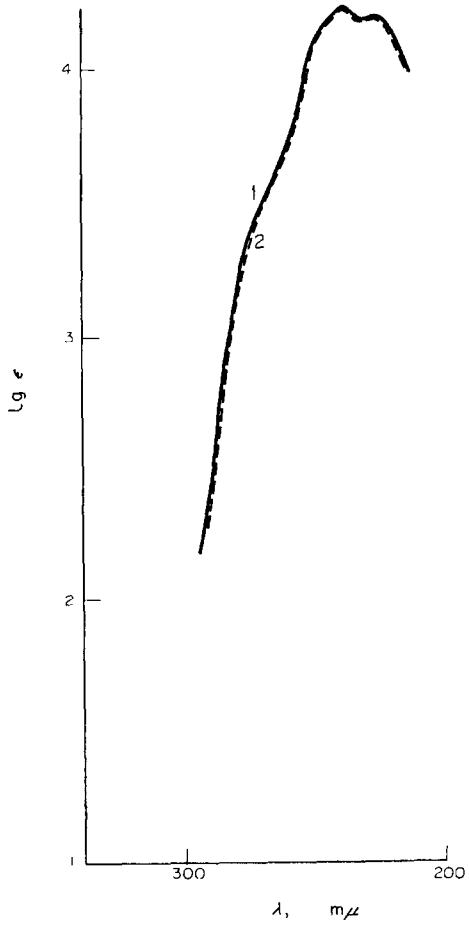


FIG. 8. Ultra-violet absorption spectrum of *p*-anisylsulphanilide.
1—in alcohol; 2—in dioxan.

are so different in their origin and essence that it is improbable that they could affect in the same way the end results.

In Table 4 the percentages of imino forms in solutions of α-arylsulphaminopyridines in 80% alcohol and 80% dioxan obtained by the two methods are compared. The potentiometric evidence shows a somewhat stronger influence of substituents on equilibrium than the spectral one, the spectrophotometric evidence reveals some deviations from the parallelism of changes in K_T and σ^0. On the whole, however, the coincidence of the data obtained by the two methods is more than satisfactory and this shows that essentially both methods give correct results.

The method based on deviations from the Hammett linear dependence has, as well as the spectral one, the advantage of being applicable to the study of the tautomerism of short lived forms inaccessible for purely chemical analytical methods. It can however be used only for the investigation of such tautomeric systems the competing forms of which belong to markedly different chemical types and hence have quite different ρ constants. An additional requirement must be met: the substituents

TABLE 3. THE TAUTOMERIC EQUILIBRIUM CONSTANTS OF α-ARYLSULPHAMINOPYRIDINES (IV) CALCULATED FROM SPECTROPHOTOMETRIC DATA

NN	X	K_T			
		50% aqueous alcohol	80% aqueous alcohol	80% aqueous dioxan	100% dioxan
1	*p*-$N(CH_3)_2$	1·82	0·76	0·18	0·01
2	*p*-NH_2	1·60	0·65	0·16	0·01
3	*p*-CH_3	3·55	1·62	0·54	0·03
4	*p*-CH_3O	3·18	1·46	0·41	0·03
5	*p*-CH_3CONH	4·61	1·71	0·53	—
6	H	4·72	2·06	0·69	0·04
7	*p*-C_6H_5O	4·28	1·76	0·57	—
8	*p*-F	6·06	2·13	0·80	0·05
9	*p*-Br	8·50	3·18	1·00	0·07
10	*p*-Cl	7·25	2·80	1·02	0·08
11	*p*-CN	15·80	6·08	2·58	0·16
12	*m*-NO_2	—	—	2·48	0·21
13	*p*-NO_2	23·83	5·9	2·86	0·26

TABLE 4. THE PERCENTAGE OF THE IMINOFORM IN SOLUTIONS OF α-ARYLSULPHAMINOPYRIDINES (IV)

NN	X	80% aqueous alcohol		80% aqueous dioxan	
		Potentiometrically	Spectrophotometrically	Potentiometrically	Spectrophotometrically
1	*p*-$N(CH_3)_2$	36·8	43·2	11·4	15·3
2	*p*-NH_2	39·4	39·4	13·7	13·8
3	*p*-CH_3	49·6	62·0	26·2	35·1
4	*p*-CH_3O	50·9	59·4	28·2	29·1
5	*p*-CH_3CONH	—	63·1	35·2	34·6
6	H	56·3	67·3	37·7	40·8
7	*p*-C_6H_5O	58·5	63·8	47·5	36·3
8	*p*-F	63·6	68·1	54·5	44·4
9	*p*-Br	67·3	76·1	60·0	50·0
10	*p*-Cl	67·7	73·7	60·9	50·5
11	*p*-CN	85·9	85·9	86·0	72·06
12	*m*-NO_2	—	—	88·0	71·26
13	*p*-NO_2	—	85·5	90·3	74·09

must strongly affect the equilibrium. The spectrophotometric method is free of these limitations but, in turn, must fulfil the requirement that the absorption of the competing forms be quite different and of a suitable character. Therefore, the methods are supplementary.

The tautomeric equilibrium constants of α-arylsulphaminopyridines must, of course, follow the Hammett equation. Fig. 9 shows the respective plots in terms of pK_T and σ^0 constructed on spectrophotometric data, the respective correlation coefficients r being I:0·993, II:0·977, III:0·982, IV:0·993.

It will be seen that the tautomeric equilibrium of α-arylsulphaminopyridines is strongly affected by the nature of the substituent X. The electron releasing substituents shift the equilibrium strongly toward the amino form whereas the electron

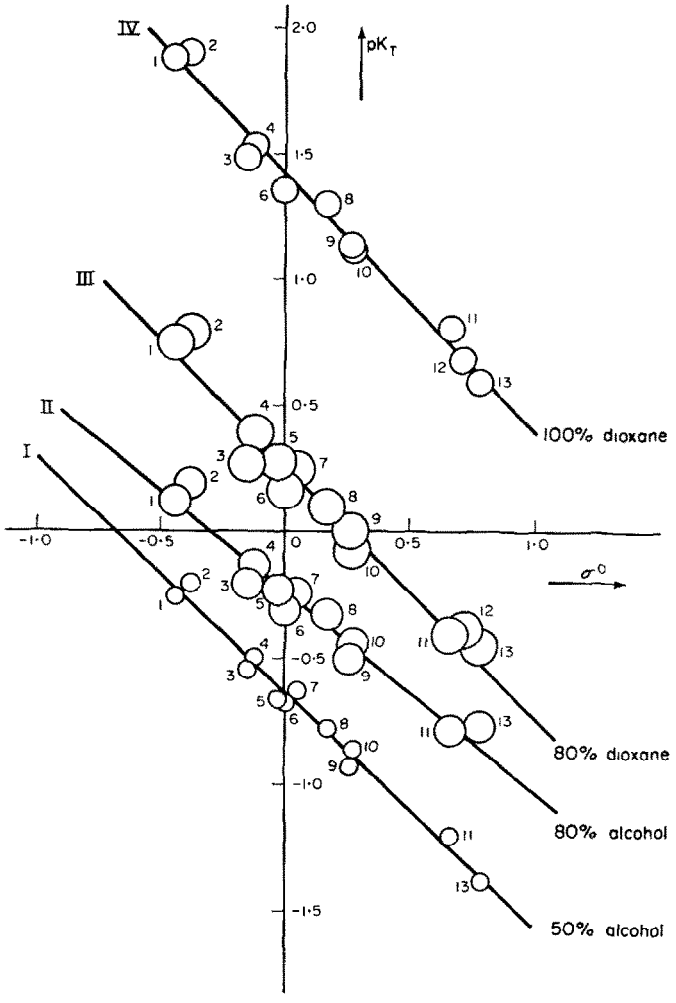


FIG. 9. Dependence of pK_T on σ° for α-arylsulphaminopyridines according to spectrophotometric data. The numbering of points as in Table 3.

attracting ones shift it towards the imino form. This is accounted for by the fact, that the transmitting chain of atoms between the substituent X and the acidic hydrogen atom is shorter in the amino than in the imino form. The electron attracting substituents enhance the acidic properties of the amino forms more than they do those of the imino forms thus leading to the equilibrium shift toward the latter. The electron releasing substituents weaken the acidic properties of the amino forms to a greater extent, than they do those of the imino forms, with the equilibrium shifting toward the amino forms. In all cases the equilibrium is shifted toward the weaker acids as predicted by the theory of the tautomeric equilibrium.[40]

The tautomeric equilibrium is also markedly affected by the nature of the solvent with the polar solvents shifting it toward more polar imino forms and *vice versa*.

[40] M. J. Kabachnik, *Dokl. Akad. Nauk SSSR* **83**, 407 (1952).

5. EXPERIMENTAL

Materials. α-Arylsulphaminopyridines were prepared following the general procedure due to Phillips[41] by treating α-aminopyridine in pyridine solution with arylsulphochlorides. The properties of the compounds used are listed in Table 1.

α-Arylsulphaminopyridines were methylated by the Shepherd *et al.*[42] procedure with dimethylsulphate in aqueous-alkaline solution. The m.ps. and analyses of methylated derivatives are given in Table 5.

TABLE 5. ARYLSULPHO-N-METHYL-α-PYRIDONIMINES (VII)

X	m.p. °C	Lit. m.p.	Analysis %C Found	%C Calc.	%H Found	%H Calc.	%N Found	%N Calc.
p-$N(CH_3)_2$	180–182	—	—	—	—	—	14·4	14·3
							14·3	—
p-NH_2	225	225[12]	—	—	—	—	—	—
p-CH_3	139–140·5	—	59·6	59·5	5·3	5·4	10·8	10·7
			59·6		5·4		10·9	
p-CH_3O	164–165	—	—	—	—	—	10·1	10·1
							10·2	
p-CH_3CONH	231	231[18]	—	—	—	—	—	—
p-C_6H_5O	118–119	—	63·4	63·5	4·8	4·7	8·2	8·2
			63·3		5·0		8·1	
p-F	141–142	—	—	—	—	—	10·7	10·5
							10·7	
p-Br	154–155	—	—	—	—	—	8·6	8·6
							8·5	
p-Cl	150–151	—	—	—	—	—	9·8	9·9
							10·0	
p-CN	191–192	—	57·2	57·1	4·1	4·1	—	—
			57·1		4·2			
m-NO_2	198–200	—	—	—	—	—	14·3	14·3
							14·3	
p-NO_2	202–204	—	—	—	—	—	14·3	14·3
							14·6	

Arylsulphamilides were obtained according to Shepherd,[43] and their properties are listed in Table 2.

p-Dimethylaminophenylsulphanilide was prepared following Bossard *et al.*[44], the same method being used to prepare α-*p*-dimethylaminophenylsulphaminopyridine.

pH was evaluated by means of a lamp potentiometer LP-5 with a glass electrode adjusted with an aqueous biphthalate buffer (pH = 4·00) and calibrated with a hydrogen electrode in the range of high pH values. The concentration of solutions measured was $3·5–5·0\ 10^{-3}$ mole/l; 20°. The accuracy of measurements ±0·05 pH units. pK was calculated from the pH data for solutions neutralized 30, 50, and 70%, the ionic strength was 0·001 to 0·0035. No corrections for the activity coefficients were made so that the constants obtained are concentration constants. As the measurements of these compounds were all carried out in each solvent under strictly constant conditions these corrections should not have affected the ultimate values of pK_T.*

Spectrophotometric evaluations were carried out on a spectrophotometer SF-4, the concentration of solutions being $10^{-4}–10^{-5}$ mole/l.

* The corrections calculated in terms of the limiting Debye equation average for 50% alcohol 0·05 pK units, for 80% alcohol 0·08 pK units and only for 80% dioxan do they attain up to 0·5 pK units.

[41] M. A. Phillips, *J. Chem. Soc.* 9 (1941).

[42] R. G. Shepherd, A. C. Bratton and K. C. Blanchard, *J. Amer. Chem. Soc.* **64**, 2532 (1942).

[43] R. G. Shepherd, *J. Org. Chem.* **12**, 275 (1947).

[44] H. H. Bosshard, R. Mory, M. Schmid and Hch. Zollinger, *Helv. Chim. Acta* **42**, 1653 (1959).