LITERATURE CITED

1. G. N. Dorofeenko, A. N. Tkachenko, and V. V. Mezheritskii, Khim. Geterotsikl. Soedin., No. 4, 465 (1975).
2. G. N. Dorofeenko and V. G. Korobkova, Khim. Geterotsikl. Soedin., No. 3, 342 (1974).
3. N. Barbulesku and J. Potmischil, Tetrahedron Lett., 27, 2309 (1969).
4. J. A. Van Allan and J. A. Reynold, J. Org. Chem., 33, 1102 (1968).
5. V. G. Kharchenko, A. P. Krivenko, O. V. Fedotova, and T. G. Nikolaeva, Khim. Geterotsikl. Soedin., No. 7, 944 (1982).
6. L. K. Kulikova, V. G. Kharchenko, O. V. Fedotova, and G. K. Kravtsova, Khim.-Farm. Zh., 16, 545 (1982).
7. G. V. Pavel', M. N. Tilichenko, and A. D. Chumak, Dep. in VINITI, No. 4253. Dep.; Ref. Zh. Khim., 15Zh245 (1977).

TAUTOMERISM OF 6- AND 2-(ARYLAZO)-3-HYDROXYPYRIDINES IN APROTIC POLAR SOLVENTS

K. M. Dyumaev, L. A. Osmolovskaya, and B. A. Korolev

UDC 547.556.3:547.823:541.62

On the basis of calculations of the basicities of possible protonation sites, electronic spectra, and potentiometric titration, it has been shown that 6- and 2-(arylazo)-3-hydroxypyridines exist in nitromethane and acetonitrile in the hydroxyazo-form, and are protonated at the pyridine nitrogen atom.

A number of dyes have recently been developed both for natural and synthetic fibers, derived from 3-hydroxypyridine [1, 2]. Dyeing of synthetic fibers presupposes working in nonaqueous solvents, and it is therefore of great importance to examine the tautomerism of arylazo-3-hydroxypyridines in such media. The scattered reports in the literature on this topic, especially for aprotic solvents, are contradictory. For instance, in acetonitrile and dimethylformamide azo-3-hydroxypyridines exist as tautomeric mixtures of the azo- and hydrazono-forms [3, 4], whereas in nitromethane (which is similar to acetonitrile in its properties), they exist in the hydroxyazo-form [5]. To resolve this contradiction, we have carried out further studies with 6- and 2-(arylazo)-3-hydroxypyridines in aprotic polar solvents (nitromethane and acetonitrile), by examination of the acid–base properties and UV spectra of the compounds.

The 6- and 2-(arylazo)-3-hydroxypyridines (Tables 1 and 2) were obtained by azo-coupling. Earlier workers [6] have shown that reaction of 3-hydroxypyridine with p-nitrophenyldiazonium chloride gives a mixture of the 6- and 2-isomers, coupling in the 4-position not occurring [7]. It is known that the chromatographic mobility of 2-(p-nitrophenylazo)-3-hydroxypyridine is much higher than that of the 6-substituted compound, and by analogy with [6] we have tentatively regarded the compounds with low R_f values as the 6-azo-compounds (IIa-f) (Table 1), and those with high R_f values as the 2-derivatives (IXa-f). The assignment of compounds with high R_f values to the 2-azo series is supported by the presence in their IR spectra of a broad absorption band in the region of stretching of the hydroxyl group involved in intramolecular hydrogen bonding (2700-3200 cm^{-1}), and by identification of the reduction product of one of them (IXb) as 2-amino-3-hydroxypyridine.

To confirm the structure of the second series of isomers (IIa-f), diazotized 2,4,6-trimethyl-3,5-dinitroaniline was coupled with 3-hydroxypyridine to give the isomer with a low R_f value (IIg), the structure of which was proved by PMR. Actually, the spectrum of the 2-substituted compound should contain signals of different multiplicity, and the 4-substituted compound, from

Research Institute for Organic Intermediates and Dyes, Moscow 103787. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1656-1661, December, 1984. Original article submitted January 3, 1983; revision submitted April 29, 1984.

 0009-3122/84/2012-1364$08.50

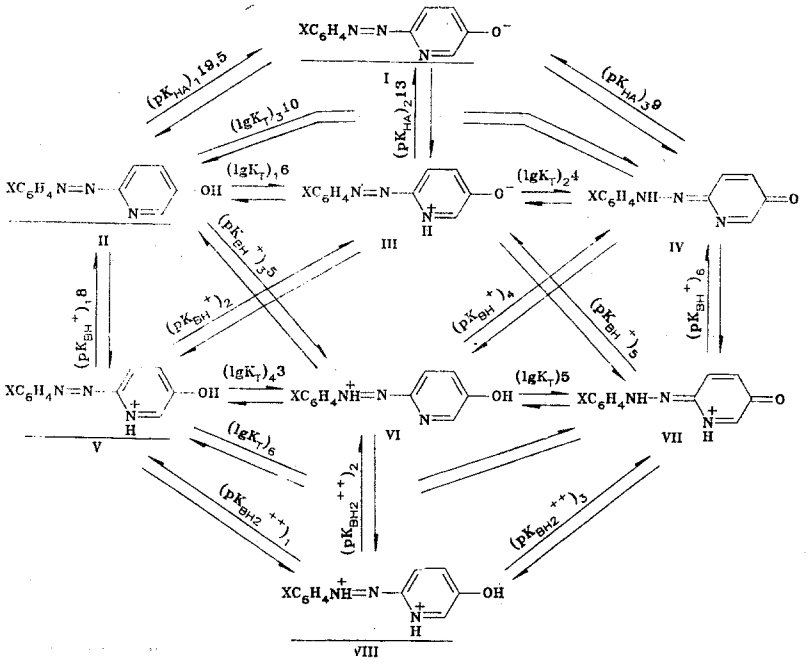


Fig. 1. Protolytic and tautomeric interconversions in substituted 6-arylazo-3-hydroxypyridines. The structures which predominate in nitromethane solution are underlined. The calculated values for pK_{HA}, pK_{BH^+}, and log K_T for (IIb) (X = H) are shown.

results for pyridines [8, 9], would be expected to possess much lower coupling constants ($^4J \approx {}^5J \approx 0$, $^3J \approx 5$ Hz).

Figure 1 shows the acid–base and tautomeric interconversions which are possible in solutions of substituted 6-arylazo-3-hydroxypyridines (II). The anion (I) has three possible centers of protonation, i.e., in the neutral azo-compound the proton may be present at the oxygen atom (the hydroxyazo-form (II)), at the nitrogen atom of the pyridine ring (zwitterionic form (III)), or at the nitrogen atom of the azo-group (hydrazonium form (IV)). Each of these tautomers can be protonated in two ways, to give the three monocations (V-VII), which add a second proton to give the dication (VIII). The spectral characteristics of the zwitterionic tautomer are unknown, and therefore in examining the tautomerism we gave priority to the evaluation of the basicity of the possible centers of protonation.

In order to determine which of the three tautomers (II, III, or IV) predominates in nitromethane solution, it is necessary to determine the basicities of the three centers in anion (I) mentioned above, a measure of which is provided by the pK_{HA} values of the conjugate OH-, $^+$NH-, and NH-acids: $(pK_{HA})_1$, $(pK_{HA})_2$, and $(pK_{HA})3$ respectively (Fig. 1).

For this purpose, we made use of data for 3-hydroxypyridine (Fig. 2), which is a model for protonation of tautomers (Ib-IIIb) at the oxygen atom and the pyridine nitrogen, and azobenzene, which is a model for addition of a proton at the azo-group in structures (Ib), (IIb), and (Vb). It has previously been found [10] that lg K_T = 4 for 3-hydroxypyridine in nitromethane, and $(pH_{BH^+})_1$ = 11.85 [5]. We have found that $(pK_{HA})_1$ = 21.0, thus enabling the values of $(pK_{HA})_2$ = 17.0 and $(pK_{BH^+})_2$ = 15.85 in this medium to be found (Fig. 2). We have also found that the value of (pK_{BH^+}) for azobenzene in nitromethane is ∿4.5.

From these results, the basicities of the possible protonation centers in anion (I) (X = H) can be calculated by means of Hammet's equation: $pK = pK_0 - \rho\sigma_X$.

The basicity of the oxygen center $(pK_{HA})_1$ was calculated by regarding (IIb) (Fig. 1) as 3-hydroxypyridine with the phenylazo-group as a p-substituent. In this case, pK_0 and pK are the ionization constants of unsubstituted and substituted 3-hydroxypyridine in nitromethane, $\sigma_X = \sigma_n(phN{=}N) = 0.33$ [11],* and the value of ρ in the equation must be close [13] to the value

*Bearing in mind that in pyridine there is no conjugation of electron-acceptor substituents with the π-electron system of the ring [12], in this instance it is more correct to use the set of σ-rather than σ⁻-constants.

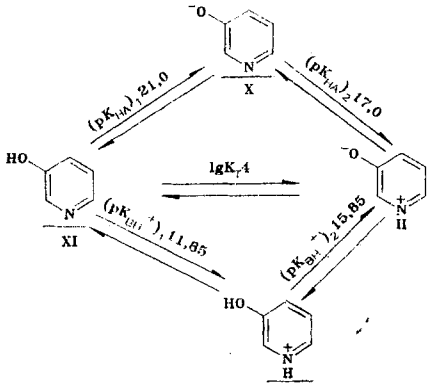


Fig. 2. Protolytic and tautomeric interconversions of 3-hydroxypyridine. The structures predominating in nitromethane solution are underlined.

of ρ for the correlation of the acidities of phenols (4.54 [14]). From these results, we obtain $(pK_{HA})_1 \approx 19.5$.

The basicity of the pyridine nitrogen $(pK_{HA})_2$ in anion (Ib) was calculated from the basicity of this center in the 3-hydroxypyridine anion (X) (Fig. 2), allowing for the influence of the ortho-phenylazo-group. The basicities of ortho-substituted pyridines in nitromethane correlate with the σ_m constants of substituents with a value ρ = 13.6 [15], and σ_m(PhN=N) = 0.29 [11]. Hence, we obtain $(pK_{HA})_2 \approx 13$.

The basicity of the azo-group $(pK_{HA})_3$ was calculated from the basicity of azobenzene, allowing for the influence of the substituents, namely, the para-oxide group ($\sigma^+ = -2.3$ [11]) and the ortho-oriented pyridine nitrogen ($\sigma^+ = \sigma = 0.71$ [16]). The value of ρ for this case was calculated from the angular correlation coefficient between pK_{BH^+} for tertiary amines in nitromethane and water (1.35 [17]) and the value of ρ for the correlation of the basicities of azobenzenes in 20% aqueous alcohol (2.19 [18]), bearing in mind that in water and 20% alcohol the value of ρ will differ only slightly. In nitromethane, therefore, we may take $\rho \approx 2.9$, and $(pK_{HA})_3 \approx 9$.

Comparison of the calculated pK_{HA} values for the different centers shows that in nitromethane protonation must occur at the oxygen atom (pK_{HA} 19.5), i.e., in this medium 6-phenylazo-3-hydroxyazo-form (II), and the concentrations of tautomers (III) and (IV) must be 6-10 orders of magnitude less. The experimentally determined value $(pK_{Ha})_{exp} = 20.3$ confirms the correctness of these calculations.

Similar calculations of the basicity of anion (I), containing a nitro-group, leads to the same results: $(pK_{HA})_1 = 18.6$, $(pK_{HA})_2 = 11.4$, and $(pK_{HA})_3 = 6.8$,* the experimental value $(pK_{HA})_{exp} = 19.08$ being close to $(pK_{HA})_1$.

Since, in the remaining compounds, the substituents are intermediate in their electronic character between the oxygen atom and the para-nitro group, or only differ slightly from them, we are justified in assuming that the compounds (IIa-f) all exist in azomethane in the hydroxyazo-form.

These findings were confirmed by the criterion of the calculated positions of the tautomeric equilibria of oxygen-containing tautomeric systems, based on the existence in nitromethane of associates of oxygen acids and bases, of types $AH\cdots A^-$ and $BH^+\cdots B$ [10, 14]. The titration curves of 6-arylazo-3-hydroxypyridines with tetrabutylammonium hydroxide in nitromethane show an enhanced slope, and an additional potential jump at the half-neutralization point, due to association of the $AH\cdots A^-$ type, indicating deprotonation of the oxygen center, i.e., in nitromethane the hydroxyazo-tautomer (II) predominates.

Turning now to the protonation of the hydroxyazo-compounds (II), we note that they can add a proton either at the pyridine nitrogen or at the azo-group. In unsubstituted 6-phenylazo-3-hydroxypyridine (II, X = H), the basicity of the ring nitrogen (pK_{BH^+}) was calculated by regarding (IIb) as 3-hydroxypyridine (XI) substituted in the ortho-position by the phenylazo-group. Then (see above), $(pK_{BH^+})_1 \approx 8$. Similarly, knowing the basicity of azobenzene in nitromethane, and allowing for the influence of the para-hydroxy group ($\sigma^+ = 0.92$ [11]) and the pyridine nitrogen in the ortho-position, the value of $(pK_{BH^+})_3$ for the azo-group was calcu-

*Use was made of the values $\sigma_m(p\text{-}O_2NC_6H_4N{=}N\text{-}) = 0.41$ [19] and $\sigma_n(p\text{-}O_2NC_6H_4N{=}N\text{-}) = 0.54$ (calculated from the transmission factor of the phenylazo-group $\pi' = 0.27$ [20], σ_n(PhN=N) = 0.33 [11] and $\sigma_n(NO_2) = 0.78$).

TABLE 1. UV Spectra of Aryl-Substituted 3-Hydroxypyridines (II) and (IX) (in acetonitrile)

Compound	X	λ_{max}, nm (lg ε)			
		anion	natural compound	monocation	dication (in nitromethane)
IIa	*p*-Me	461 (4,50)	342 (4,35)	375 (4,42)	—
IIb	H	470 (4,48)	339 (4,30)	363 (4,38)	485 (4,59)
IIc	*p*-Br	481 (4,58)	343 (4,39)	371 (4,47)	519 (4,63)
IId	*m*-Br	483 (4,45)	343 (4,20)	360 (4,26)	470 (4,34)
IIe	*m*-NO_2	492 (4,36)	343 (4,09)	357 (4,19)	448 (3,86)
IIf	*p*-NO_2	551 (4,52)	360 (4,27)	367 (4,37)	477 (4,29)
IXa	*p*-Me	510 (4,18)	379 (4,24)	403 (4,41)	496 (4,59) 523 (4,76)
IXb	H	508 (4,11)	373 (4,12)	387 (4,31)	473 (4,41) 496 (4,45)
IXc	*p*-Br	525 (4,34)	379 (4,32)	396 (4,51)	500 (4,54) 528 (4,63)
IXd	*m*-Br	523 (4,19)	377 (4,15)	386 (4,32)	477 (4,06)
IXe	*m*-NO_2	527 (4,25)	375 (4,14)	382 (4,35)	466 (4,35) 490 (4,38)
IXf	*p*-NO_2	587 (4,39)	391 (4,22)	391 (4,41)	469 (4,42) 492 (4,70)

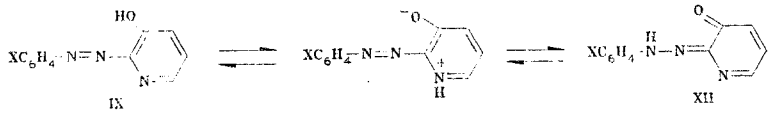
lated to be ≈ 5. Comparison of the calculated values for $(pK_{BH^+})_1$ and $(pK_{BH^+})_3$ shows that (IIb) must add a proton in nitromethane at the pyridine nitrogen. The value of $(pK_{BH^+})_{exp}$ = 8.88 confirms the correctness of this calculation.

Similarly calculated were the values $(pK_{BH^+})_1$ = 6.3 and $(pK_{BH^+})_3$ = 2.8 for the p-nitro compound (IIf), comparison of which indicates protonation at the heterocyclic nitrogen. The value of $(pK_{BH^+})_{exp}$ = 7.94 is in agreement with this conclusion.

The UV spectra in acetonitrile (Table 1), which is similar in its properties to nitromethane, but is transparent to UV, confirm our conclusions as to the tautomeric composition and sites of protonation of 6-arylazo-3-hydroxypyridines (II). For the neutral compounds, the absorption maxima occur at 340-370 nm, characteristic of azo-forms [21], but in the >470 nm region, where the long-wavelength absorption of the hydrazo-form is usually found [21], there is little absorption. The weak band (lg ε < 3) in 6-arylazo-3-hydroxypyridines in this region is not affected by the type of solvent (acetonitrile, dimethylformamide, dimethyl sulfoxide, dioxane, alcohol, 25-60% aqueous alcohol containing acetate buffer), and it is not, therefore, due to the hydrazone tautomer as previously suggested [4]. Addition of perchloric acid to 6-arylazo-3-hydroxypyridines causes a small shift to longer wavelengths (10-30 nm; Table 1), which is in complete agreement [22] with the initial protonation of the heterocyclic nitrogen. The second proton adds to the azo-group which, as would be expected, results in a strong bathochromic shift (90-150 nm; Table 1).

A careful examination of the dependence of the UV spectra on the solvent provides further evidence of the existence of neutral azo-compounds in the hydroxyazo-form (II). It was found that deprotonation of 6-arylazo-3-hydroxy-pyridines (lg K_{AHA^-} ∿ 4, this communication) at a concentration of $\sim 10^{-4}$ mole/liter results in the appearance of two isobestic points (Fig. 3a) corresponding to the transformation of HA into associates AH···A^- and of AH···A^- into A^-. When the solution is diluted to 10^{-6} mole/liter, the degree of association of the complex AH···A^- increases, and the two isobestic points merge into one (Fig. 3b).

In the case of ortho-hydroxyazo-compounds (2-arylazo-3-hydroxypyridines), it will be seen that the pK_{HA} values for the OH and NH groups in the tautomers (IX) and (XII) should be somewhat greater, and the pK_{BH^+} values somewhat less, than the corresponding values for the para-isomers (II) and (IV), as a result of OH···H and NH···O intramolecular hydrogen bonding. These conclusions assume that (IX) (and its para-isomer (II)) exist in the hydroxyazo form. This is in accordance with results for their structural analogs, the para- and ortho-azophenols, the tautomeric equilibria of which in a variety of solvents are strongly shifted towards the hydroxyazo-forms [21]. Furthermore, in the azonaphthols, the difference between the K_T values for the para- and ortho-hydroxyazo-forms is less than an order of magnitude (calculated for benzene, chloroform, and hexane from the results given in [23], and for alcohol, from the results in [24]). These findings show that the ortho-hydroxyazo-form (IX), like its para-isomer (II), exists in the hydroxyazo-form (IX), and adds the first proton at the pyridine nitrogen.



IX XII

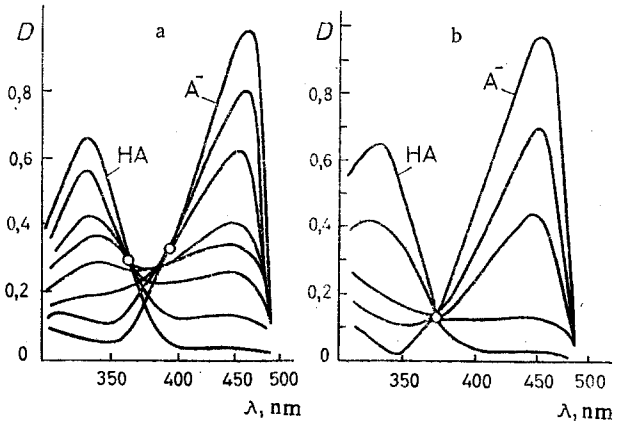


Fig. 3. Changes in the UV spectrum of 6-phenylazo-3-hydroxypyridine (IIb) as it is gradually deprotonated in acetonitrile by the addition of tetrabutylammonium hydroxide. a) c $3 \cdot 10^{-4}$ mole/liter, layer thickness 0.1 cm; b) c $3 \cdot 10^{-6}$ mole/liter, layer thickness 10 cm.

TABLE 2. Properties of Arylazo-3-hydroxypyridines (II) and (IX)

Compound	Mp, °C *	Found, %			Empirical formula	Calculated, %		
		C	H	N		C	H	N
IIa	207—207,5	67,2	5,0	19,5	$C_{12}H_{11}N_3O$	67,7	5,2	19,7
IIc	224—225	47,7	2,9	15,1	$C_{11}H_8BrN_3O$	47,5	2,9	15,1
IId	210	48,0	2,9	15,0	$C_{11}H_8BrN_3O$	47,5	2,9	15,1
IIe †	213—214	54,2	3,5	23,2	$C_{11}H_8N_4O_3$	54,1	3,3	23,0
IIg †	215—216	51,3	4,0	21,0	$C_{14}H_3N_5O_5$	50,8	3,9	21,2
IXa	104—105	67,4	5,1	19,6	$C_{12}H_{11}N_3O$	66,7	5,2	19,7
IXb	115	66,2	4,7	21,2	$C_{11}H_9N_3O$	66,3	4,5	21,1
IXc	154—155	47,3	3,0	15,0	$C_{11}H_8BrN_3O$	47,5	2,9	15,1
IXd	123—124	47,9	2,8	15,1	$C_{11}H_8BrN_3O$	47,5	2,9	15,1
IXe	174—175	54,0	3,3	23,0	$C_{11}H_8N_4O_3$	54,1	3,3	23,0

*(IIa) was recrystallized from CCl_4 and methanol, (IIc), (IIe), and (IXb) from 50% aqueous ethanol, (IId), (IIg), and (IXc) from ethanol, (IXa) and (IXe) from light petroleum, and (IXd) from methanol.

†PMR spectrum (DMSO): 11.0 (br. s, OH), 8.5 (d, J = 2 Hz, 2-H), 8.1 (d, J = 9 Hz, 5-H), and 7.7 ppm (d.d., J = 9 and 2 Hz, 4-H). The signals for the methyl protons were hidden by the DMSO signals.

The spectral data (Table 1) confirm this conclusion, since the neutral molecules of 2-arylazo-3-hydroxypyridines absorb at wavelengths typical of the hydroxyazo-form (IX), addition of the first proton resulting in only slight spectral changes, but addition of the second proton causing a considerable bathochromic shift.

Thus, in the aprotic polar solvents nitromethane and acetonitrile, 6- and 2-arylazo-3-hydroxypyridines exist in the hydroxyazo-form, and are protonated at the pyridine nitrogen atom. Since 6-arylazo-2-substituted-3-hydroxypyridines contain significant amounts of the hydroazone tautomer in a variety of solvents [3], this may be due to the influence of the substituent in the 2-position of the pyridine ring [25].

EXPERIMENTAL

IR spectra were obtained on a UR-20 spectrometer in CCl_4, and PMR spectra of (IIg) on a BS-467 instrument (60 MHz, external standard HMDS). UV spectra were recorded on a Specord UV-VIS. The values of pH_{BH^+} and pK_{HA} in nitromethane were determined potentiometrically as described in [14] and [26].

The 6- and 2-arylazo-3-hydroxypyridines (II) and (IX) were synthesized by the method given in [6], and purified by recrystallization. The properties of the novel compounds are given in Table 2.

The isomer of phenylazo-3-hydroxypyridine with a high R_f value was reduced by the method given in [27], and the reduction product identified by paper chromatography in the system light petroleum–butanol–water, 1:2:3.

LITERATURE CITED

1. G. Back and A. Fasciata, West German App. No. 2,201,030; C.A., 77, 166,154 (1972).
2. G. Back and A. Buehler, West German App. No. 2,450,884; C.A., 83, 99,179 (1975).
3. B. E. Zaitsev, G. V. Sheban, K. M. Dyumaev, and D. D. Smirnov, Khim. Geterotsikl. Soedin., No. 2, 224 (1973).
4. K. M. Dyumaev and R. E. Lokhov, Khim. Geterotsikl. Soedin., No. 6, 810 (1973).
5. K. M. Dyumaev, B. A. Korolev, and R. E. Lokhov, Zh. Obshch. Khim., 41, 2520 (1971).
6. J. A. Moore and F. G. Marascia, J. Amer. Chem. Soc., 81, 6049 (1959).
7. K. M. Dyumaev, R. E. Lokhov, N. E. Zaitsev, and L. D. Sairnov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 11, 2601 (1970).
8. A. Zhunke, Nuclear Magnetic Resonance in Organic Chemistry [Russian translation], Mir, Moscow (1974), pp. 59, 87.
9. U. Vögeli and W. Philipsborn, Org. Magnetic Resonance, 5, 551 (1973).
10. B. A. Korolev, L. A. Osmolovskaya, and K. M. Dyumaev, Zh. Obshch. Khim., 48, 2358 (1978).
11. N. B. Chapman and J. Shorter, Correlation Analysis in Chemistry, Plenum Press, New York (1978), p. 439.
12. A. Fisher, W. J. Galloway, and J. Vaughan, J. Chem. Soc., No. 10, 3591 (1964).
13. A. Gordon, A. R. Katritzky, and S. K. Roy, J. Chem. Soc., B, No. 5, 556 (1968).
14. B. A. Korolev and E. I. Kashkovskaya, Zh. Obshch. Khim., 49, 2360 (1979).
15. B. A. Korolev and M. A. Mal'tseva, Zh. Obshch. Khim., 43, 1556 (1973).
16. J. H. Blanch, J. Chem. Soc., B, No. 10, 937 (1966).
17. B. A. Korolev, Zh. Obshch. Khim., 50, 841 (1980).
18. H. H. Jaffe and R. W. Gardner, J. Amer. Chem. Soc., 80, 319 (1958).
19. W. J. B. Huysmans, Trans-azobenzeen- en trans-stilbenderivaten. Diss., Haaga (1964).
20. J. Socha, J. Horska, and M. Večeřa, Coll., 34, 2982 (1969).
21. I. Ya. Bernshtein and O. F. Ginzburg, Usp. Khim., 41, 177 (1972).
22. A. Albert, Angew. Chem., Intern. Ed., 6, 919 (1967).
23. A. Burawoy and A. R. Thompson, J. Chem. Soc., No. 5, 1443 (1953).
24. A. Burawoy, A. Salem, and A. R. Thompson, J. Chem. Soc., No. 12, 4793 (1952).
25. J. Elguero, C. Marzin, A. R. Katritzky, and P. Kinda, The Tautomerism of Heterocycles, Academic Press, New York (1976), p. 89.
26. B. A. Korolev and B. I. Stepanov, Izv. Vuzov., Khim. i Khim, Tekhnol., 11, 1193 (1968).
27. H. Bojarska-Dahlig and T. Urbanski, Prace Placowek Nauk-Badawcz. Ministerstwa Przemyslu Chem., 1, 1 (1952).