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THE TAUTOMERISM OF 6-HYDROXY-, 6-AMINO- AND 6-ACYLAMINO-7-AZAINDOLINES

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Abstract—The lactam–lactim tautomerism of 6-hydroxy-7-azaindolines and amino–imine tautomerism of 6-amino- and 6-acylamino-7-azaindolines has been studied by IR and UV spectroscopy. It is shown that the lactam–lactim tautomeric equilibrium of 6-hydroxy-7-azaindolines in contrast to the other analogous N-heteroaromatic compounds is not completely shifted for the lactam. The commensurable amounts of both tautomeric forms can be observed in the solutions of 6-hydroxy-7-azaindolines and it is possible to elucidate distinctly the influence of the solvent polarity upon the lactam–lactim tautomeric equilibrium. The tautomeric equilibrium of 6-amino- and 6-acylamino-7-azaindolines is practically completely shifted for the amino form, and even acylation with *p*-toluenesulfonic acid does not result in a noticeable shift of the tautomeric equilibrium for the amino form in contrast to the other N-heterocyclic amines.

INVESTIGATIONS on the lactam–lactim and amino–imine tautomerism of N-heterocyclic compounds having a potentially tautomeric α- (or γ-) hydroxy group have shown that the equilibrium shifted in favour of the lactam form.[1] The determining factor is the considerable difference in electronegative nitrogen and oxygen atoms and the gain in energy with the transference of the lactim to the lactam group is so considerable that the lactam form prevails in the solutions irrespective of the solvent polarity.[2]

A series of substituted 6-hydroxy-7-azaindolines have been synthesized and the lactam–lactim tautomerism of these compounds investigated.*

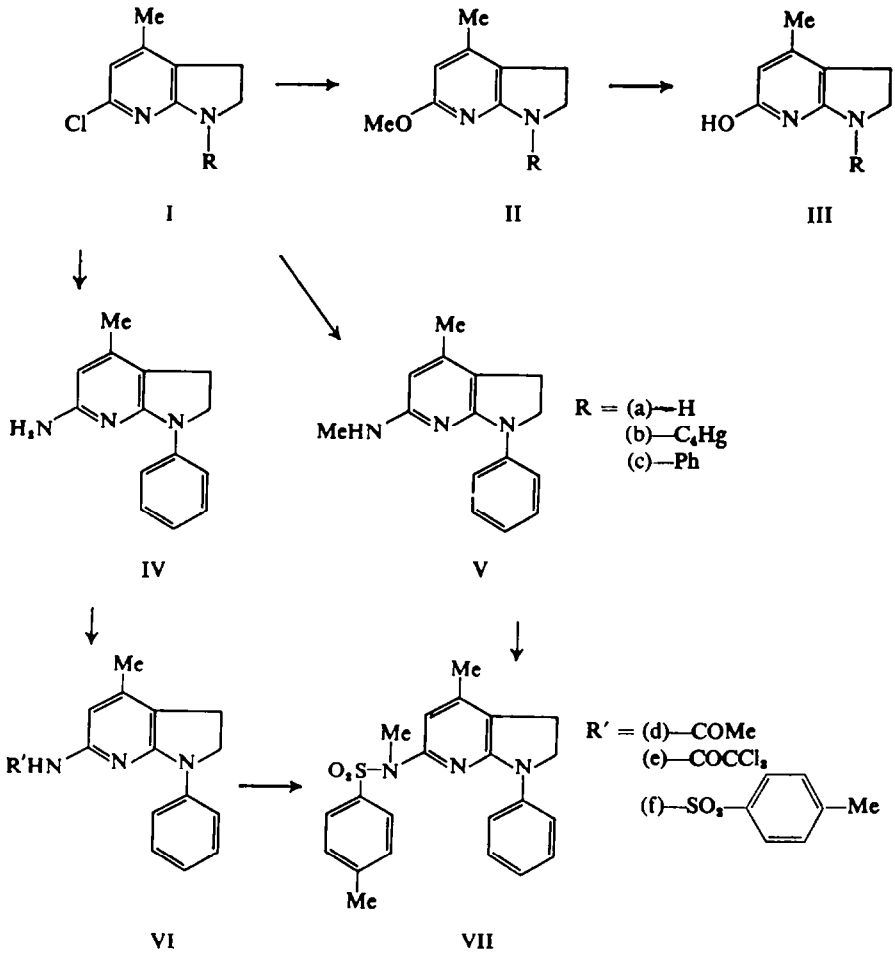
For the synthesis 4-methyl-6-chloro-7-azaindoline (Ia),[3] 1-butyl-4-methyl-6-chloro-7-azaindoline (Ib)[4] and 1-phenyl-4-methyl-6-chloro-7-azaindoline (Ic)[4] obtained previously were used.

As nucleophilic substitution of the halogen atom in the sixth position of the azaindoline molecule is difficult,[3,5] the transition from Ia at IIa is brought about by interaction with sodium methylate at 190°.[3] Hindrance by the butyl substituent in the first position resulted in 21% replacement of the chlorine in Ib by the methoxy group in Ib at 190°. Compound Ic does not react with potassium methylate at 190° but reaction at 250° resulted in a 72% yield of the 6-methoxy derivative (IIc).

It is interesting that IIc is formed in a high yield on interaction of Ic with potassium

* The present article is the 23rd report of the series "The derivatives of 7-azaindoles". The previous reports were published in *Zhur. Obshchei Khim.* and in the Russian journal *Chemistry of Heterocyclic Compounds.*

[1] For a review see: A. R. Katritzky and J. M. Lagowski, *Advances in Heterocyclic Chemistry* Vols 1 and 2. Academic Press, New York (1963).
[2] Ju N. Sheinker and E. M. Peresleni, *Zh. Fiz. Khim.* **36**, 1705 (1962).
[3] L. N. Jakhontov, M. Ja. Uritskaya and M. V. Rubstov, *Zh. Obshch Khim.* **34**, 1449 (1964).
[4] L. N. Jakhontov and M. V. Rubtsov, *Zh. Obshch Khim.* **30**, 3300 (1960).
[5] L. N. Jakhontov and M. V. Rubtsov, *Zh. Obshch Khim.* **34**, 493 (1964).



methylate or with methanolic or aqueous methanolic solution of the potassium hydroxide. In an acidic medium, however, the methoxy group IIc is easily saponified, this being already observed at room temperature in the course of extraction from a hydrochloric acid solution. When IIc is heated with hydrochloric acid 84% of the 6-hydroxy derivative (IIIc) is obtained. Similarly, the methoxy groups in IIa and IIb are easily saponified.

The lactam–lactim tautomerism of the 6-hydroxy-7-azaindolines (IIIa–c) was studied by UV and IR spectroscopy. Compounds IIa–c were used as models of fixed lactim structure and consideration of the UV spectra (Figs. 1, 2 and 3) shows that absorption maxima are respectively for IIa–250 mμ (log ε 3·84), 308 mμ (log ε 3·93); IIb–254 mμ (log ε 3·87), 314 mμ (log ε 3·94); IIc–276 mμ (log ε 4·20), 330 mμ (log ε 4·34). Just as it was in all cases the position and intensity of the maxima are practically unchanged in solvents of different polarity (dioxan, ethanol, water). On the other hand the UV spectra of 6-hydroxy-7-azaindolines (IIIa–c) depend on the polarity of the solvent used. In solvents such as dioxan or dioxan with an insignificant addition of ethanol, two main absorption maxima are observed in the regions 248–275 mμ and 308–332mμ

and in the long wave region an insignificant absorption at 346–374 mμ. Under these conditions, therefore, the spectra of IIIa–c are similar to the corresponding spectra of IIa–c (Figs. 1–3). The character of the UV spectra of IIIa–c changes with increasing solvent polarity—the intensity of the maxima at 308–332 mμ gradually diminishing and that in the long wave region (346–374 mμ) simultaneously increasing. This process is accomplished by the transition to the UV spectra having only two absorption maxima at 248–275 mμ and 346–374 mμ. The changes observed are reversible in that a decrease in solvent polarity (by changing the dioxan:ethanol ratio) lowers the intensity of long wave maxima and strengthens the absorption in the short wave region.

As it was noted in the UV spectra of N-methyl-2-pyridone and 2-ethoxypyridine[6] the transfer from lactim to the lactam form is accompanied by a bathochromic shift of the long wave maximum by 25–30 mμ. An analogous shift of the long wave maxima was observed in the lactam–lactim tautomerism and in the other N-heterocyclic hydroxy derivatives.[7] This suggests that the long wave absorption maxima 346–374 mμ in IIIa–c are due to the lactam tautomeric form. On the basis of UV spectroscopic data the tautomeric constants, K_t of IIIa–c were calculated.

$$K_t = \frac{\% \text{ of lactam}}{\% \text{ of lactim}}$$

The results obtained are listed in Table 1.

It was found that the position of the tautomeric lactam–lactim equilibrium for different 6-hydroxy-7-azaindolines depends upon the character of the substituent in the first position. In dioxan solution 88% of IIIa is present in the lactim form which changes to lactam on dilution with ethanol and in absolute ethanol only the lactam form is present. In IIIb this transition takes place in changing from a mixture of 90% dioxan–10% ethanol solution to 75% ethanol–25% water solution. 1-Phenyl-4-methyl-6-hydroxy-7-azaindoline contains 88% of the lactim form even in mixtures of equal amounts of ethanol and dioxan, a complete transition to the lactam form only being brought about in water containing 2% ethanol.

The influence of the substituents in the first position upon the lactam–lactim tautomeric equilibrium is correlated with the influence of these substituents upon the ease of nucleophilic substitution of the chlorine in the derivatives of Ia–c.

The 6-hydroxy-7-azaindolines studied differ from the other α-hydroxy-N-heteroaromatic compounds not only in the position of the lactam–lactim tautomeric equilibrium but also in chemical properties. Methylation of 2-pyridone with dimethyl sulphate in the water–alkaline medium yields N-methylpyridone in high yield,[8] similar to the N-alkylation described for other α-hydroxy-N-heteroaromatic compounds.[9,10]

In contrast the reaction of dimethyl sulphate with IIIc results in only O-methylation (63·7%) to IIc. As no N-methyl-7-azaindolines-6 were obtained on methylation of IIa–c, the latter were used as model lactam forms to calculate the tautomeric equilibrium constants when in strongly polar solvents a further increase in the solvent polarity did not change the character and intensity of their absorption.

[6] H. Specker and H. Gawrosch, *Ber. Dtsch. Chem. Ges.* **75**, 1338 (1942).
[7] S. F. Mason, *J. Chem. Soc.* 5010 (1957).
[8] C. Räth, *Liebig's Ann.* **489**, 108 (1931).
[9] D. Davidson and O. Baudisch, *J. Amer. Chem. Soc.* **48**, 2379 (1926).
[10] G. T. Newbold and F. S. Spring, *J. Chem. Soc.* 519 (1948).

TABLE 1

Substances	Solvents	98% water–2% EtOH	50% water–50% EtOH	25% water–75% EtOH	Abs EtOH	50% EtOH–50% dioxan	25% EtOH–75% dioxan	15% EtOH–85% dioxan	10% EtOH–90% dioxan	5% EtOH–95% dioxan	Dioxan
IIIa	% of the lactim form				<1	14·6	29·2	41·7	59·7	72·7	88·0
	K_t				>99·0	5·85	2·43	1·40	0·68	0·38	0·14
IIIb	% of the lactim form			<1	25·2	36·1	61·1	85·8	88·2		95·9
	K_t			>99·0	2·97	1·77	0·64	0·20	0·13		0·04
IIIc	% of the lactim form	<1	24·6	52·3	79·1	88·8	90·0				
	K_t	>99·0	3·07	0·91	0·26	0·13	0·11				

The IR spectra of 6-hydroxy-7-azaindolines (IIIa–c) and 6-methoxy-7-azaindolines (IIa–c) were taken as solid crystals and in the solutions of dioxan and CCl_4. The characteristic absorption bands are listed in Table 2.

TABLE 2

Substance		ν C=O in cm^{-1}	ν C=N and C=C cycles in cm^{-1}	ν OH, NH in cm^{-1}
IIa	crystals		1603, 1510	3310
	soln in dioxan		1601	3365
IIIa	crystals*	1638	1603, 1526	3306
IIb	without solvent		1620, 1589, 1505	
	soln in dioxan		1617, 1594, 1509	
IIIb	crystals	1635	1568, 1545	
	soln in CCl_4	1645	†	3582
	soln in dioxan	1632	1592, 1508	3305
IIc	crystals		1607, 1587, 1507	
	soln in dioxan		1605, 1586, 1506	
IIIc	crystals	1634	1603, 1585, 1500	
	soln in CCl_4	1630	†	3580
	soln in dioxan	1626	1605, 1586, 1506	3290

* Substance IIIa is poorly soluble in CCl_4 and dioxan, and IR spectra for these could not be obtained.

† This region of the spectrum is exceeded by the absorption of the solvent for 0·02% solvents in CCl_4.

In the region of double bond vibrations the spectra of the crystals of IIIa–c show intensive bands of the lactam carbonyl group at 1634–1638 cm^{-1} and the C=C and C=N stretching vibrations of the aromatic and heteroaromatic cycles at 1500–1603 cm^{-1}. In compounds with a fixed lactim structure (IIa–c) the carbonyl bonds, as expected, were absent and only bands 1505–1620 cm^{-1} due to the stretching vibrations of double bonds of the cycles were present.

This data supports the lactam structure in the crystalline form of all the 6-hydroxy-7-azaindolines (IIIa–c) studied. The absorption band at 3290–3310 cm^{-1} observed in the high frequency region cannot be used in studying the lactam–lactim tautomerism as these bands cannot be correlated to the stretching vibrations of only NH or OH groups participating in hydrogen bonds. The absorption bands at 1626–1632 cm^{-1} absent in the spectra of IIa–c are distinctly displayed in the IR spectra of dioxan solutions of IIIb–c, thus testifying to the presence of the lactam form in solution. The agreement between this data with that determined by UV spectra for dioxan solutions containing 88–95% of the lactim form is convincing evidence for the lactam–lactim tautomerism of IIIb–c.

The IR spectra of dilute CCl_4 solution of 6-hydroxy-7-azaindolines show the presence of both tautomeric forms simultaneously: the lactam form being displayed as a carbonyl band at 1630–1645 cm^{-1} and the lactim form having a characteristic absorption at 3580–3582 cm^{-1} due to the stretching vibrations of the hydroxy group.

The amino–imine tautomerism of N-heteroaromatic amines differs from that of the lactam–lactim in the position of the tautomeric equilibrium. On the basis of numerous investigations[1] it was shown that the amino–imine tautomeric equilibrium is practically completely shifted for the amino form. This is due to the energetic

advantage of the structure with the largest increase in π-electronic orbits, since the factor of different electronegatively of cyclic and exocyclic heteroatoms is of no practical value for the amino–imine tautomerism.[2,11]

If the shift in tautomeric equilibrium of the 6-hydroxy-7-azaindoline is greater for the lactim form than for other N-heteroaromatic hydroxy compounds, then in 6-amino derivatives the amino–imine tautomeric equilibrium should be more strongly shifted for the amino form. In view of the parallelism between the position of the amino–imine tautomeric equilibrium of amines and N-acyl derivatives[12] the tautomerism of

TABLE 3

Substance	λ_{max} in mμ	log ε
IV	280	4·15
	338	4·24
V	266	4·13
	334	4·03
VId	292	4·20
	334	4·20
VIe	302	4·17
	338	4·08
VIf	282	4·21
	336	4·19
VII	288	4·23
	332	4·05

TABLE 4

Substance		ν NH (NH_2) (in cm^{-1})	ν C=O (in cm^{-1})	ν C=C C=N δNH_2 (in cm^{-1})
IV	crystals	3323, 3472		1606, 1585, 1505
	soln in $CHCl_3$	3420, 3525		1618, 1596, 1512
	soln in dioxan	3373, 3483		1612, 1589, 1506
V	crystals	3427		1612, 1589, 1507
	soln in $CHCl_3$	3425		1608, 1508
VId	crystals	3338	1658	1623, 1602, 1588, 1531, 1505
	soln in $CHCl_3$	3433	1685	1625, 1605, 1590, 1523, 1503
	soln in dioxan	3332	1701	1624, 1606, 1591, 1547, 1504
VIe	crystals	3348	1710	1626, 1601, 1598, 1506
	soln in $CHCl_3$	3413	1721	1625, 1605, 1589, 1504
	soln in dioxan	3431	1730	1630, 1607, 1594, 1510
VIf	crystals	3283		1623, 1605, 1591, 1506
	soln in $CHCl_3$	3380		1625, 1605, 1593, 1507
VII	crystals			1625, 1600, 1586, 1507

[11] E. M. Peresleni, Ju. N. Sheinker, N. P. Zosimova and Ju. I. Pomerantsev, *Zh. Fiz. Khim.* **37**, 2713 (1963).

[12] Ju. N. Sheinker, E. M. Peresleni, N. P. Zosimova and Ju. I. Pomerantsev, *Zh. Fiz. Khim.* **33**, 2096 (1959).

1-phenyl-4-methyl-6-amino-7-azaindoline (IV) and its N-acetyl- (VId), N-trichloroacetyl- (VIe) and N-*p*-toluenesulfo (VIf) derivatives were investigated.

1-Phenyl-4-methyl-6-amino-7-azaindoline (IV) was prepared by the interaction of Ic with ammonia, but as ammonia is a weaker nucleophile than the ethoxy ion, only 37% conversion was obtained at 250° for 28 hr in the presence of the copper catalyst.

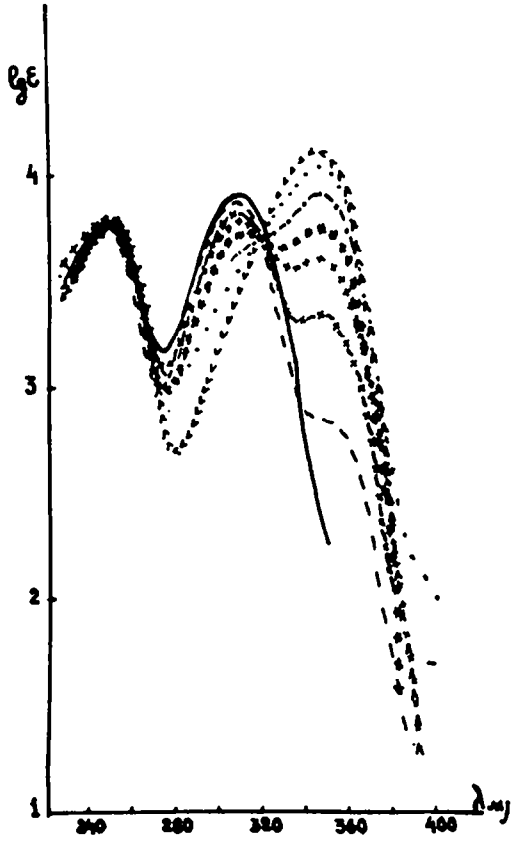


FIG. 1. UV spectra of 4-methyl-6-hydroxy-7-azaindoline (IIIa) (1) in absolute ethanol (< < <), (2) ethanol–dioxan 1:1 (· · · · ·), (3) dioxan with 25% ethanol (– · – ·), (4) dioxan with 15% ethanol (* * * *), (5) dioxan with 10% ethanol (× × ×), (6) dioxan with 5% ethanol (– × – ×), (7) dioxan (– – –) and UV spectra of 4-methyl-6-methoxy-7-azaindoline (IIa) in different solvents (—).

As *p*-toluenesulfamide is a still weaker nucleophile, it does not react with Ic even at 360° for 6 hr. Acylation of IV was carried out with acetic anhydride, trichloroacetyl chloride and *p*-toluenesulfochloride. It is of interest that methylation of VIf with dimethyl sulfate yielded only 1-phenyl-4-methyl-6-N-methyl-*p*-toluenesulfamino-7-azaindoline (VII) identical with that obtained from I, which reacts with methylamine to give 1-phenyl-4-methyl-6-methylamino-7-azaindoline (V) and then with *p*-toluenesulfochloride to give VII. The UV spectra of IV–VII, taken in solvents of different polarity have two absorption maxima: at 266–302 mμ (log ε 4·6–4·2) and 332–338 mμ (log ε 4·0–4·2) (Table 3).

In all cases the position and intensity of the maxima do not depend on the solvent.

Similarity of the UV spectral curves of 6-amino(or acylamino)-7-azaindolines (long wave maximum 330 mμ, log ε 4·32) and their difference from the spectra of 6-oxo-7-azaindolines (long wave maximum 374 mμ) confirms that in the 6-amino- and 6-acylamino-7-azaindolines studied the amino–imine tautomeric equilibrium is almost completely shifted for the amino form.

This conclusion is also supported by the IR spectra (Table 4).

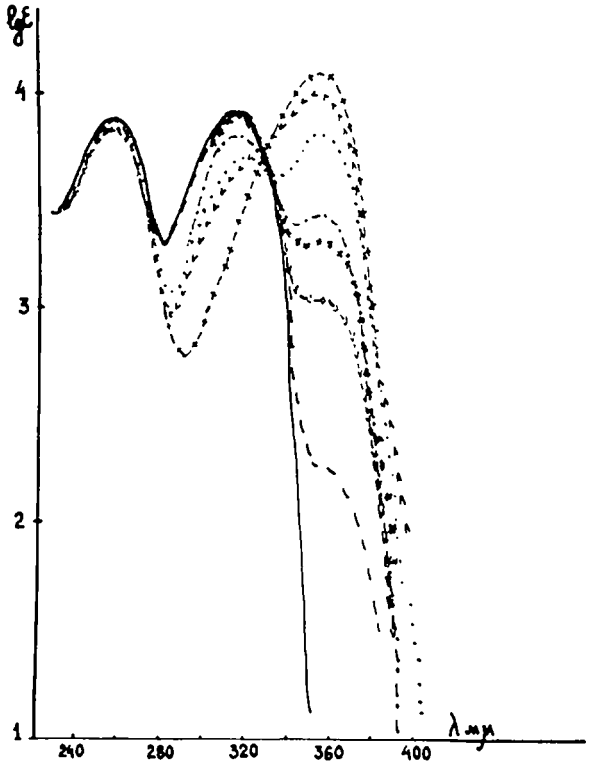


FIG. 2. UV spectra of 1-butyl-4-methyl-6-hydroxy-7-azaindoline (IIIb) (1) in ethanol with 25% water (— + — +), (2) absolute ethanol (< < < <), (3) ethanol-dioxan 1:1 (· · · · ·), (4) dioxan with 25% ethanol (— · — ·), (5) dioxan with 15% ethanol (+ + +), (6) dioxan with 10% ethanol (— > — >), (7) dioxan (— — —) and UV spectra of 1-butyl-4-methyl-6-methoxy-7-azaindoline (IIb) in different solvents (—).

1-Phenyl-4-methyl-6-amino-7-azaindoline in crystal form gives intensive absorption bands at 1606, 1585 and 1505 cm^{-1} analogous to the bands (1607, 1587, 1507 cm^{-1}) in the spectrum of 1-phenyl-4-methyl-6-methoxy-7-azaindoline and therefore, due to the C=C and C=N bonds of the heteroaromatic and aromatic rings. At the same time a closer consideration of the complex broad intensive band at 1606 cm^{-1} suggests that both stretching vibrations of the cyclic double bonds and deformation vibrations of the primary amino group are involved. The weakening of the high frequency region of this band on deuteration of IV supports this conclusion. In the high frequency region of the IR spectra of dilute solutions of IV in chloroform (and in CCl_4) two bands 3420 and 3525 cm^{-1} are observed characteristic for the symmetrical and unsymmetrical stretching vibrations of the primary amino groups.

In the IR spectra of 6-acetylamino- and 6-trichloroacetylamino-7-azaindoline

crystals (VId–f), absorption bands at 1658 and 1710 cm^{-1} respectively are observed (for solutions in chloroform 1685 and 1710 cm^{-1}, in dioxan 1701 and 1730 cm^{-1}) characteristic for the stretching vibrations of the amide carbonyl group. In the case of acylimine structure of these compounds the shift of the carbonyl bands for the low frequency region 1616–1640 cm^{-1} was to be expected.[12]

Thus the investigation carried out shows that the 7-azaindoline system has substantial peculiarities which are displayed in the tautomeric properties of 6-hydroxy- and

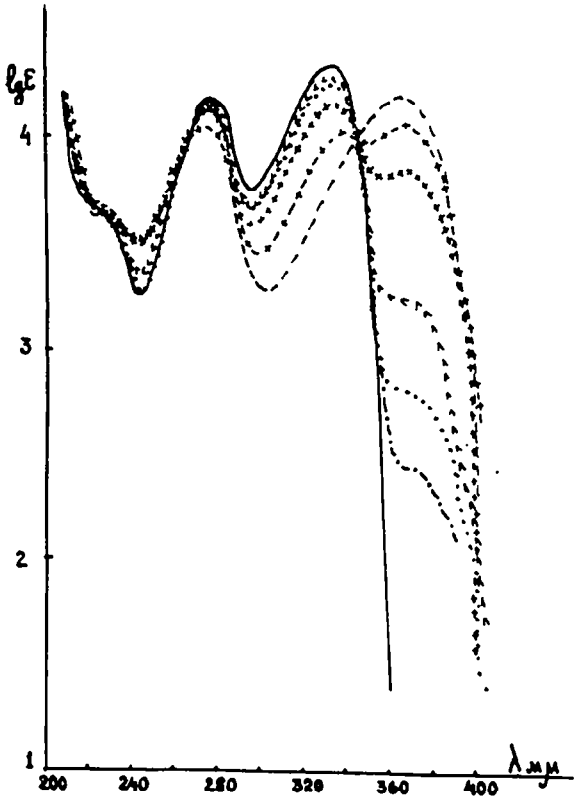


FIG. 3. UV spectra of 1-phenyl-4-methyl-6-hydroxy-7-azaindoline (IIIc) (1) in water with 2% ethanol (— — —), (2) water–ethanol 1:1 (+ — + —), (3) ethanol with 25% water (+ + +), (4) absolute ethanol (< < < <), (5) ethanol–dioxan 1:1 (· · · · ·), (6) dioxan with 25% ethanol (— · — ·) and UV spectra of 1-phenyl-4-methyl-6-methoxy-7-azaindoline (IIc) in different solvents (—).

6-amino(acylamino) derivatives. The tautomeric equilibrium of these compounds is noticeably shifted for the lactim and respective amino(acylamino) forms in comparison to that of the other N-heteroaromatic systems. We suggest that this is due to the change in the electron plane on the nitrogen atom of the pyridine on account of delocalization of electrons between nitrogen atoms of the pyridine and pyrrolidine rings.

EXPERIMENTAL*

1-Phenyl-4-methyl-6-methoxy-7-azaindoline (IIc). (a) Compound Ic (9·78 g) was heated at 250° for 10 hr in a sealed tube with MeOK (from 2·28 g K and 76 ml MeOH). The MeOH was then distilled

* Ju. I. Pomerantsev, N. P. Zosimova, L. Nosina and A. S. Paisova took part in the experimental work.

off, 8% HCl (20 ml) added and the soln extracted several times with benzene. The extracts were dried (K_2CO_3), evaporated *in vacuo*, and the residue IIc recrystallized from MeOH, yield 6·9 g (71·8%). The substance is readily soluble in acetone, benzene, $CHCl_3$ and AcOEt, less soluble in MeOH and insoluble in pet. ether, heptane and water. (Found: C, 74·36; H, 6·12; N, 12·58; OH, 6·81. Calc. for $C_{14}H_{14}N_2O$: C, 74·31; H, 6·24; N, 12·38; OH, 7·51%.)

(b) A mixture of Ic (4·89 g) with KOH (1·64 g) in water (10 ml) and MeOH (28 ml) was heated at 250° for 10 hr in a stainless steel autoclave (150 ml). The reaction mixture was evaporated to 8 ml and extracted with $CHCl_3$. The extract was dried (K_2CO_3) and evaporated and the residue distilled *in vacuo*. The fraction with b.p. 184–187°/1 mm was collected and yielded IIc (2·6 g; 54%), m.p. 81–82° (from MeOH). The substance was identified by the IR spectrum and mixed m.p. with IIc prepared by the procedure (a).

1-Butyl-4-methyl-6-methoxy-7-azaindolines (IIb). Compound Ib (4·49 g) was heated in a sealed tube at 250° for 10 hr with MeOK (from 1·14 g K and 38 ml MeOH). The reaction is accompanied by resinification. MeOH was distilled off *in vacuo*, water (15 ml) was added and the mixture extracted with benzene. The extract was dried (K_2CO_3) evaporated to *ca.* 10 ml and chromatographed (75 cm × 25 mm column) with aluminium oxide (200 g) washed with pet. ether and eluted first with 1 l. pet. ether and then with 0·5 l. benzene. The product was distilled at 142–144°/3 mm, yield 1·88 g (42·7%) of IIb as a colourless, mobile liquid, n_D^{20} 1·5310. It is miscible with the usual organic solvents, but only slightly miscible with water. (Found: C, 70·84; H, 8·86; N, 12·55. Calc. for $C_{15}H_{20}N_2O$: C, 70·87; H, 9·15; N, 12·72%.)

4-Methyl-6-hydroxy-7-azaindoline (IIIa). 4-Methyl-6-methoxy-7-indoline (1·47 g) was boiled with conc. HCl (15 ml) for 6 hr. The soln was evaporated *in vacuo*, the residue treated with water (15 ml), the soln filtered off with coal and made alkaline with 50% K_2CO_3 (phenolphtaleine) and the resulting IIIa was filtered off, washed with water and dried in a vacuum-desiccator, yield 1·07 g (79·8%), m.p. 264–265° (in a sealed capillary; from alcohol). The substance is soluble in hot EtOH, slightly soluble in $CHCl_3$, acetone, AcOEt, benzene, ether, dioxan and insoluble in water and pet. ether. (Found: C, 64·20; H, 7·00; N, 18·31. Calc. for $C_8H_{10}N_2O$: C, 63·98; H, 6·71; N, 18·65%.)

Compound IIIb was prepared similarly by boiling 0·5 g of IIb with 5 ml conc. HCl and recrystallizing the product from heptane, yield 0·33 g (70·4%), m.p. 164–165°. The substance is soluble in $CHCl_3$ and benzene, slightly soluble in AcOEt, acetone and ether and insoluble in water and pet. ether. (Found: C, 69·97; H, 8·54; N, 13·28. Calc. for $C_{12}H_{18}N_2O$: C, 69·87; H, 8·79; N, 13·58%.)

Compound IIIc was prepared similarly from 1 g IIc, yield 0·78 g (84%), m.p. 195–197°. The substance was identified by mixed m.p. with IIIc described above.

Methylation of 1-phenyl-4-methyl-6-hydroxy-7-azaindoline. To IIIc (2·26 g), dissolved in a mixture of acetone (80 ml) and 2N NaOH (5 ml), Me_2SO_4 (1·26 g) was added dropwise with stirring and cooling (ice-cold water). After standing 45 min the mixture was evaporated *in vacuo* and the residue distilled with benzene. A mixture of substances for separation was put as a suspension in 20 ml of hot benzene on a column (45 cm × 24 mm) of cellulose (~50 g), washed with pet. ether.

The product was first eluted with pet. ether (250 ml) and then with benzene. The process was controlled by descending paper chromatography, the mobile phase being pet. ether, and detection of a blue luminescence on UV radiation. For IIc R_f 0·87, for IIIc R_f 0·58. The first 350 ml of the eluate contained 1·98 g IIc with a little admixture of IIIc (according to paper chromatography). The subsequent 800 ml of the eluate contained 0·44 g pure IIIc, m.p. 195–197°.

For further purification of IIc from admixture of IIIc, the 1·98 g material was chromatographed on aluminium oxide (60 g) washed with pet. ether on a column (40 cm × 18 mm). The mixture in benzene solution was put on the column and eluted with 400 ml. pet. ether. 1·53 g IIc, m.p. 81–82° was obtained (yield 63·7% with reference to IIIc taken in the reaction). Subsequent elution with 300 ml benzene resulted in 0·02 g which was a mixture of IIc and IIIc (according to paper chromatography). Finally 0·12 g IIIc was eluted with 300 ml $CHCl_3$. The total yield of IIIc was 0·56 g (24·8%).

Similar methylation of IIIb (1·03 g) resulted in, after separation, 0·38 g (34·5%) of IIb.

1-Phenyl-4-methyl-6-amino-7-azaindoline (IV). Compound Ic (4·9 g) was heated at 250° in a sealed tube with 25% aq ammonia (20 ml) and cuprous sulfate (0·4 g) for 28 hr. The contents of the tube were acidified with 8% HCl and the nonbasic portion (1·3 g) extracted with benzene and not subjected to further investigation. The HCl solution was made alkaline with 50% K_2CO_3aq soln and the base extracted with benzene. The benzene soln was dried (K_2CO_3) and evaporated *in vacuo* and the residue

was distilled at 218–220° (2 mm) to yield 1·67 g (37·1%) of IV as colourless crystals, m.p.143–144° (from alcohol). The substance is readily soluble in $CHCl_3$, acetone, AcOEt and benzene, less soluble in ether and EtOH, slightly soluble in pet. ether and insoluble in water. (Found: C, 74·80; H, 6·80; N, 18·55. Calc. for $C_{14}H_{18}N_2$: C, 74·60; H, 6·76; N, 18·70%.)

Deuteration of IV was carried out three times by dissolving in deuterated alcohol C_2H_5OD (the contents of the main substance are 97–98%, amount of deuterium in atomic%—91%) and distillation of the solvent *in vacuo*. Deuteration was not complete since in the IR spectrum of the deuterated compound the NH_2 bands, 3323 and 3472 cm^{-1}, were just visible together with the intensive ND_2 bands (2443, 2591 cm^{-1}). This, however, did not interfere with the reliable data obtained on the absorption bands of the NH_2 group.

1-*Phenyl*-4-*methyl*-6-*acetylamino*-7-*azaindoline* (VId). To IV (0·49 g), Ac_2O (4 ml) was added at room temp. The mixture became warm and homogenous before precipitation of IVd began. After standing for 20 min VId (0·44 g, 93·5%) was filtered off and washed with benzene; and recrystallized from benzene, m.p. 179–180°. The substance is readily soluble in $CHCl_3$, less soluble in acetone, AcOEt and benzene, slightly soluble in ether and pet. ether. (Found: C, 72·03; H, 6·58; N, 15·96. Calc. for $C_{16}H_{17}N_3O$: C, 71·88; H, 6·41; N, 15·72%.)

1-*Phenyl*-4-*methyl*-6-*trichloroacetylamino*-7-*azaindoline* (VIe). Trichloroacetic chloride (0·23 ml) was added to IV (0·45 g) dissolved in dry pyridine (1·5 ml). After standing for 45 min at room temp, the solution was made alkaline with 25% K_2CO_3aq and extracted with benzene. The mixture was dried (K_2CO_3) and evaporated *in vacuo*. The residue was washed with ether and recrystallized from abs. EtOH yielding 0·22 g (29·8%) of VIe as colourless crystals, m.p. 146–148°. The substance is readily soluble in benzene, less soluble in acetone, $CHCl_3$ and AcOEt, slightly soluble in EtOH and insoluble in water. (Found: C, 52·23; H, 3·75; N, 11·67; Cl, 28·42. Calc. for $C_{16}H_{14}N_3Cl_3O$: C, 51·84; H, 3·81; N, 11·34; Cl, 28·70%.)

1-*Phenyl*-4-*methyl*-6-p-*toluene-sulfamino*-7-*azaindoline* (VIf). To the mixture of IV (0·5 g) in benzene (20 ml) and 10% NaOHaq (10 ml), *p*-toluenesulfochloride in benzene (15 ml) was added. The mixing was carried out at room temp for 10 hr. The benzene layer was then separated and the aqueous layer extracted 5 times with benzene. The combined benzene solutions were dried (K_2CO_3), evaporated *in vacuo* and the residue washed with ether and recrystallized from alcohol, yield of VIf 0·28 g (33·3%) as colourless crystals, m.p. 207–208°. The substance is readily soluble in $CHCl_3$ and acetone, less soluble in AcOEt, benzene, EtOH and ether, not soluble in pet. ether and water. (Found: C, 66·85; H, 5·52; N, 11·07; S, 8·47. Calc. for $C_{21}H_{21}N_3O_2S$: C, 66·46; H, 5·58; N, 11·07; S, 8·47%.)

After recrystallization of VIf the alcoholic mother liquor was evaporated to a small volume and the resulting crystals filtered off (0·22 g) and purified by column chromatography (column 22 cm × 9 mm) on aluminium oxide (30 g) washed with pet. ether. Elution with benzene (350 ml) and then with $CHCl_3$ (200 ml) yielded 0·14 g (28%) identical by mixed m.p. with IV.

Methylation of 1-*phenyl*-4-*methyl*-6-p-*toluenesulfamino*-7-*azaindoline*. 2N NaOH (0·33 ml) and Me_2SO_4 (0·06 ml) were added to IVb (0·25 g) dissolved in acetone (5 ml). After standing at room temp for 1 hr, the residue was filtered off, washed with water and acetone, yielding 0·2 g (77·8%) of 1-phenyl-4-methyl-6-N-methyl-*p*-toluenesulfamino-7-azaindoline as colourless crystals, m.p. 150–151° (from heptane). The substance is readily soluble in $CHCl_3$, less soluble in acetone and insoluble in water and ether. (Found: C, 67·40; H, 5·73; N, 10·52; S, 8·16. Calc. for $C_{22}H_{23}N_3O_2S$: C, 67·15; H, 5·89; N, 10·68; S, 8·15%.)

1-*Phenyl*-4-*methyl*-6-*methylamino*-7-*azaindoline* (V). Compound Ic (4·9 g) and methylamine (3·2 ml) were heated at 250° in a sealed tube for 6 hr. 10% HCl (15 ml) was added to the reaction mixture and the products of non-basic character extracted with benzene. The HCl solution was made alkaline with 50% K_2CO_3aq and extracted with benzene. The extract was dried (K_2CO_3) and evaporated *in vacuo*. The residue was distilled, the fraction with b.p. 207–208°/2 mm yielded V, 0·9 g (19%) which crystallized, m.p. 88–89° (from 80% EtOH). The substance is readily soluble in benzene, ether, acetone and AcOEt, less soluble in EtOH; poorly soluble in pet. ether and insoluble in water. (Found: C, 75·22; H, 6·90; N, 17·63. Calc. for $C_{15}H_{17}N_3$: C, 75·28; H, 7·16; N, 17·56%.)

1-*Phenyl*-4-*methyl*-6-N-*methyl*-p-*toluenesulfamino*-7-*azaindoline* (VII). *p*-Toluenesulfochloride (0·57 g) in benzene (10 ml) was added to a mixture of V (0·48 g) dissolved in benzene (10 ml) and 10% NaOHaq (10 ml). After mixing at room temp for 12 hr the benzene layer was separated. The aqueous layer was extracted with benzene and the combined benzene extracts were dried (K_2CO_3) and evaporated

in vacuo. The residue (0·48 g) was washed with heptane and recrystallized from EtOH yielding 0·11 g (14%) of VII, m.p. 150–151°. The substance was identified by IR spectrum and mixed m.p. with VII obtained by methylating VIf.

The UV spectra of the compounds II–VII were taken by spectrophotometer Cϕ4 in solutions of different polarity: dioxan, mixture of dioxan and EtOH (20:1 to 1:1 ratio), abs EtOH, EtOH (water 25–50%) and water containing 2% EtOH. The spectra of II–VII were taken by registering spectrophotometer UR-10 in saturated solns of dioxan or $CHCl_3$, in dilute solns of $CHCl_3$ and in 0·02% solns of CCl_4, in crystals as pastes on Vaseline oil.