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SYNTHESIS AND PMR SPECTRA OF 2-HETARYL-SUBSTITUTED IMIDAZO[4,5-b]-PYRIDINES AND IMIDAZO[4,5-c]PYRIDINES

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UDC 547.832.5'828'827.7'785.5:543.422.25

A simple method for the synthesis of 2-hetarylimidazopyridines based on the oxidation with sulfur of a mixture of p-diaminopyridine and heterocyclic compounds that contain an active methyl group is proposed. The reaction of diamines with N-oxides of of α- and γ-picolines and the intramolecular oxidative cyclization of 3-amino-4-(2-pyridylmethylamino)pyridine lead to the same result. The PMR spectra of the synthesized 2-pyridylimidazopyridines were studied.

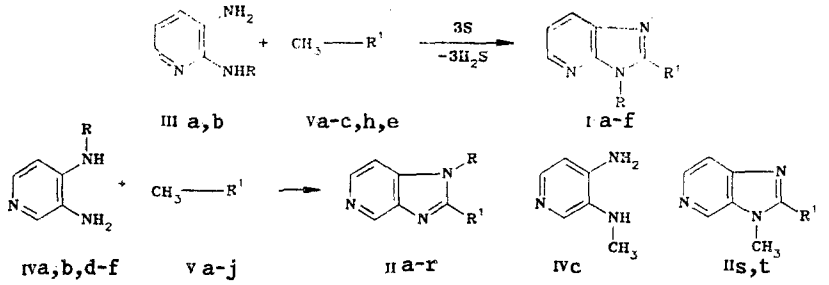
Despite certain experimental difficulties, the reaction of o-diaminopyridines and carboxylic acids of the heterocyclic series or their nitriles in polyphosphoric acid (PPA) is most often used to obtain 2-hetarylimidazopyridines [1-5]. The use of frequently difficult-to-obtain derivatives and precursors of carboxylic acids such as thioamides [6], hydrazides [7], an imino ester [8], and trichloromethylbenzimidazole [9] has lesser significance in the synthesis of 2-hetarylimidazopyridines.

The principle of the oxidative cyclization of o-diaminopyridines with compounds that contain a methylidyne or methylene group that is activated by a heteroatom (N or O) and an aryl (hetaryl) group was placed at the foundation of the new method for the synthesis of 2-hetarylimidazopyridines [10]. In conformity with this o-diaminopyridines should also be capable of reacting with methylheterocycles of the α- and γ-picoline type. A similar possibility was previously established in the case of the synthesis of 2-pyridyl and 2-quinolyl derivatives of benzimidazole from 2-picoline or quinaldine and o-phenylenediamine in the presence of sulfur [11].

We demonstrated for the first time [12] that 2-hetarylimidazo[4,5-b]- and -[4,5-c]-pyridines Ia-f and IIa-t (Table 1) can be readily obtained by this method in high yields.

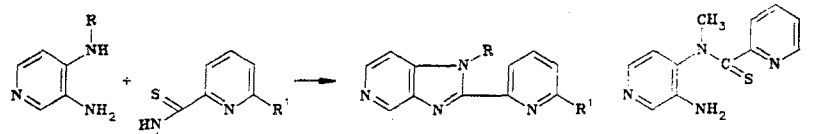
Institute of Physical Organic Chemistry and Coal Chemistry, Academy of Sciences of the Ukrainian SSR, Donetsk 340114. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 940-947, July, 1989. Original article submitted November 13, 1987.

For this a mixture of stoichiometric amounts of o-diaminopyridines IIIa,b or IVa-f, sulfur, and aromatic N-heterocycles Va-j is heated at the temperature at which hydrogen sulfur is evolved.



Ia-d, f R = H, e R = CH_3; a R^1 = 6-methyl-2-pyridyl, b R^1 = 5-ethyl-2-pyridyl, c R^1 = imidazo[4,5-c]-2-pyridyl, d,e R^1 = 2-quinolyl, f R^1 = 4-pyridyl; IIa-f R = H, g-o R = CH_3, p R = $CH(CH_3)_2$, R = CH_2CH_2OH, r R = $CH_2C_6H_5$, a R^1 = 2-pyridyl, b,h R^1 = 6-methyl-2-pyridyl, c,g,q,s R^1 = 4-pyridyl, d,i,r R^1 = 5-ethyl-2-pyridyl, e,j,p R^1 = 2-quinolyl, f,k R^1 = 2-benzothiazolyl, ℓ R^1 = 2-benzimidazolyl, m,t R^1 = imidazo[4,5-c]-2-pyridyl, n R^1 = 1-methylimidazo[4,5-c]-2-pyridyl, o R^1 = 3-methylimidazo[4,5-c]-2-pyridyl; IIIa R = H, b R = CH_3; IVa R = H, b R = CH_3, d R = $CH(CH_3)_2$, e R = CH_2CH_2OH, f R = $CH_2C_6H_5$; Va R^1 = 6-methyl-2-pyridyl, b R^1 = 5-ethyl-2-pyridyl, c R^1 = 4-pyridyl, d R^1 = 2-pyridyl, e R^1 = 2-quinolyl, f R^1 = 2-benzothiazolyl, g R^1 = 2-benzimidazolyl, h R^1 imidazo[4,5-c]-2-pyridyl, i R^1 = 1-methylimidazo[4,5-c]-2-pyridyl, j R^1 = 3-methylimidazo[4,5-c]-2-pyridyl.

Heterocycles IIℓ,t were obtained from different combinations of the starting compounds, viz., from diamines IVb,c and methyl-substituted heterocycles Vg, h, on the one hand, and o-phenylenediamine, 3,4-diaminopyridine IVa, and methylimidazopryridines Vi,j, on the other, respectively. The mechanism of the reaction under consideration includes, in all likelihood, a step involving the formation of an intermediate Willgerodt–Kindler thioamide (of the VI type, for example), which then undergoes cyclization to the final 2-hetarylimidazopyridine with splitting out of hydrogen sulfide. We were unable to isolate such intermediate thioamides; however, it was shown that 2-pyridylimidazo[4,5-c]pyridines IIa,b,h,u-w (Table 1) are readily formed in high yields when o-diaminopyridines IVa,b,f,g are fused with picoline-2-thiocarboxylic acid anilide (VIIa) and its 6-methyl derivative (VIIb) (aniline is formed as a side product).



II u R=CH_3, R^1=H; v R=$CH_2C_6H_5$, R^1=H; w R=C_6H_5, R^1=H; IV g R=C_6H_5

Compound IIn was also obtained by fusing diamine IVb with 1-methylimidazo[4,5-c]pyridine-2-thiocarboxylic acid amide.

Like the conversion of N-benzyl-substituted o-diaminopyridines to 2-phenylimidazopyridines [10], the intramolecular cyclization of 3-amino-4-(2-pyridylmethylamino)pyridine (IVh) on fusion with sulfur also leads to the formation of imidazo[4,5-c]pyridine IIa. The closeness in space of the amino group and the methylene group is apparently the deciding factor in this transformation, since the activity of the methylene group should be decreased to a significant degree because of the donor effect of the nitrogen atom bonded to it.

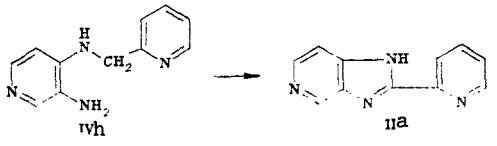


TABLE 1. 2-Hetarylimidazo[4,5-b]pyridines Ia-f and 3-Hetarylimidazo[4,5-c]pyridines IIa-y

Compound*	Empirical formula	Starting compounds**		Treact, °C	Reaction time, h	mp, °C*** (literature data)	Yield, %
Ia	$C_{12}H_{10}N_4$	IIIa [20]	Va	150...160	11	187...188	87
Ib	$C_{13}H_{12}N_4$	IIIa	Vb	155...165	10	220...221	90
Ic	$C_{12}H_8N_6$	IIIa	Vh	200...210	4	380	98
Id	$C_{15}H_{10}N_4$	IIIa	Ve	200...205	5	276...277	90
Ie	$C_{16}H_{12}N_4$	IIIb [21]	Ve	140...145	15	148...149	80
If		IIIa	Vc	160...170	24	303...304 (297 [3])	72
IIa		IVa [22]	VIIa	200...205	3	232...233 (234...235 [4])	85
		IVa	Vd	150...160	10	233...234	70
IIb	$C_{12}H_{10}N_4$	IVa	VIIb	210...220	1	153...154	92
IIc		IVa	Va	150...160	15	153...154	80
		IVa	Vc	150...160	15	284...285 (285...286 [3])	82
		IVa	Vℓ	155...165	20	285...286	66
IId	$C_{13}H_{12}N_4$	IVa	Vb	160...170	20	118...119	68
IIe		IVa	Ve	175...185	12	224...226 (227...230 [1])	82
IIf	$C_{13}H_8N_4S$	IVb	Vf	200...210	6	380	83
IIg	$C_{12}H_{10}N_4$	IVb [23]	Vc	150...160	15	174...175,5	78
		IVb	Vℓ	155...160	8	174...175	80
IIh	$C_{13}H_{12}N_4$	IVb	Va	180...200	4	144...145	85
		IVb	VIIb	190...200	2	144...145	90
IIi	$C_{14}H_{14}N_4$	IVb	Vb	150...160	15	111...112	70
IIj	$C_{16}H_{12}N_4$	IVb	Ve	170...180	15	178...179	85
IIk	$C_{14}H_{10}N_4S$	IVb	Vf	175...185	3	204...205	84
IIℓ	$C_{14}H_{11}N_5$	IVb	Vg	175...185	3	283	85
IIm	$C_{13}H_{10}N_6$	IVb	Vh	170...180	5	270...272	78
IIn	$C_{14}H_{12}N_6$	IVb	Vi	180...190	5	311...312	98
IIo	$C_{14}H_{12}N_6$	IVb	Vj	160...170	4	289...290	83
IIp	$C_{18}H_{16}N_4$	IVd	Ve	180...190	6	119...120	86
IIq	$C_{13}H_{12}N_4O$	IVe	Vc	150...160	30	95...96	77
IIr	$C_{20}H_{18}N_4$	IVf [24]	Vb	150...160	24	97,5	75
IIs	$C_{12}H_{10}N_4$	IVc [25]	Vc	160...170	10	142...143	65
IIt	$C_{13}H_{10}N_6$	IVc	Vh	170...180	6	341	70
IIu	$C_{12}H_{10}N_4$	IVb	Vk	155...165	11	139...140	88
		IVb	VIIa	205...210	15	140...141	80
IIv	$C_{18}H_{14}N_4$	IVf	Vk	155...166	10	126...128	85
		IVf	VIIa	190...200	4	127...128	82
IIw	$C_{17}H_{12}N_4$	IVg [26]	Vk	155...165	12	132...133	90
		IVg	VIIa	190...200	3	133	87
IIx	$C_{18}H_{14}N_4$	IVf	Vℓ	155...160	5	137	
IIy	$C_{17}H_{12}N_4$	IVg	Vℓ	155...160	3	162	65

*Base IIh had m/z 224, IIj had m/z 260, IIk had m/z 266, IIn had m/z 264, and IIw had m/z 272.

**Compounds IIIa,b and IVa-g are diamines, and Va-ℓ and VIIa,b are methyl-substituted heterocycles.

***The compounds were crystallized: imidazopyridines Ia and IIf, m,o from methanol, Ib,e and IIb,s from octane, Id and IIn,q from dioxane, IId from undecane, IIg,r,u,w,x from decane, IIh, i,v from heptane, IIj from hexane, IIk,ℓ,p from benzene, IIt from DMF, and IIy from nonane; Ic was reprecipitated from a solution in weak alkali by means of hydrochloric acid.

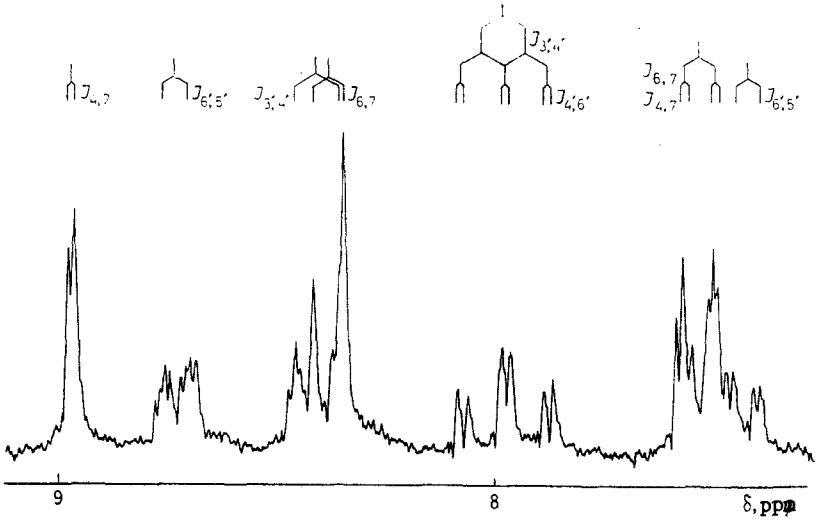


Fig. 1. PMR spectrum of IIu in $(CH_3)_2CO$-d_6 (80 MHz).

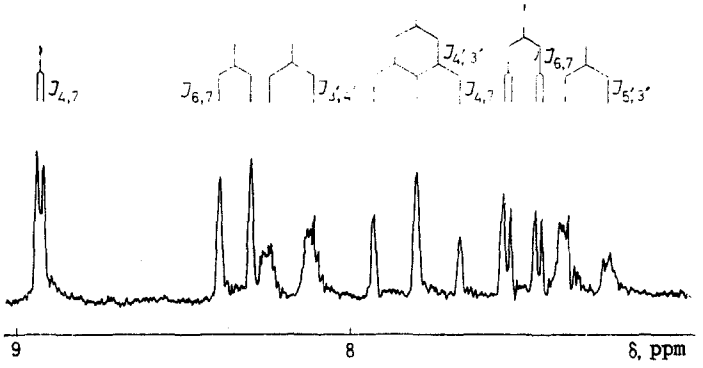
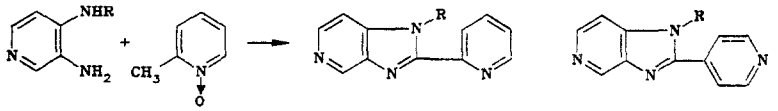


Fig. 2. PMR spectrum of IIh in $(CH_3)_2CO$-d_6 (60 MHz).

One of the possible modifications of the examined oxidative cyclization of o-diaminopyridines may involve the replacement of the α-methyl-substituted heterocycles by their N-oxides. The oxidation with sulfur of a mixture of o-diaminopyridines IVa,b,f,g and α- and γ-picoline N-oxides Vk,ℓ at 150-160°C leads to the formation of 2-pyridyl derivatives IIc, g,u-y of imidazopyridines (Table 1) but not their N-oxides, since the hydrogen sulfide liberated during the reaction probably also reduces the N → O group.



IV b,f,g V k II u-w II c,g,x,y

II x R=$CH_2C_6H_5$; y R=C_6H_5

In this variant the synthesis of 2-pyridylimidazopyridines is accelerated significantly, and the yields reach 60-90%, while according to the data in [3, 4] they do not exceed 30%. The described reaction proceeds more readily with N-oxides Vk,ℓ than with bases Vc,d and without resinification. However, N-unsubstituted diaminopyridines IIIa and IVa react ambiguously with 2-picoline N-oxide, and high-melting compounds with unestablished structures are also formed along with the expected compounds (IIa, for example).

The structures of the 2-hetarylimidazopyridines obtained were confirmed by, in addition to the chemical evidence presented above, the masses of the molecular ions for IIh,j,k,n,u (Table 1) obtained by mass spectrometry and data from the PMR spectra of IIg-i,n,u.

In connection with the presence of several nonequivalent coupling aromatic protons in the molecules of the investigated 2-hetarylimidazo[4,5-c]pyridines IIg-i,n,u the PMR spectra of these compounds are often rather complex, particularly if superimposition of the multiplets occurs (Fig. 1-3). The signals of the pyridine fragment of the imidazo[4,5-c]pyridine mole-

TABLE 2. PMR Spectra of 2-Hetarylimidazo[4,5-c]pyridines IIg-i,n,u

Compound	Chemical shift, δ, ppm (in $(CD_3)_2CO$)					SSCC, Hz	S_W, Hz
	4-H (1H)	6-H (d, 1H)	7-H (1H)	2-R'	1-R		
IIg*,**	9,74 s	9,25	8,33 d	8,75 (m, 4H, C_5H_4N)	4,24 (s, 3H, N—CH_3)	J_{67}=7,0	1000
IIg**	8,91 d	8,41	7,38 d.d	8,82 and 7,69 (two m 2H each, α_1- and β_1-C_5H_4N)	3,99 (s, 3H, N—CH_3)	J_{67}=5,5; J_{47}=1,0	250
IIh**	8,95 d	8,33	7,46 d.d	8,15 (d.d, 1H, 3'-H); 7,79 (t, 1H, 4'-H); 7,28 (d.d, 1H, 5'-H)	4,23 (s, 3H, N—CH_3); 2,53 (s, 3H, $C_{(6')}$—CH_3)	J_{67}=5,5; J_{47}=1,0; $J_{3'5'}$=1,5; $J_{3'4'}$=8,0	250
IIi*,**	9,45 s		8,25 d	8,86...8,51 (t, 3H, 6-H, 3'-H, 4'-H); 8,95 (s, 1H, 6'-H)	1,28 (s, 3H, N—CH_3); 1,43 (t, 3H, J=7,6, $C_{(5')}$—$CH_2\mathbf{CH_3}$); 3,06 (q, 2H, J=7,6, $C_{(5')}$—$\mathbf{CH_2}CH_3$)	J_{67}=7,0	1000
IIi**	8,95 d	8,37	7,50 d.d	8,30 (d, 1H, 3'-H); 7,78 (d.d, 1H, 4'-H); 8,57 (d, 1H, 6'-H)	4,2 (s, 3H, N—CH_3); 1,21 (t, 3H, $C_{(5')}$—$CH_2\mathbf{CH_3}$); 2,68 (q, 2H, $C_{(5')}$—$\mathbf{CH_2}CH_3$)	J_{67}=5,56; J_{47}=1,0; $J_{3'4'}$=8,0; $J_{6'4'}$=2,0	250
IIi***	8,93 d	8,37	7,50 d.d	8,31 (d, 1H, 3'-H); 7,79 (d.d, 1H, 4'-H); 8,56 (d, 1H, 6'-H)	1,25 (s, 3H, N—CH_3); 1,27 (t, 3H, J=6,8; $C_{(5')}$—$CH_2\mathbf{CH_3}$); 2,75 (q, 2H, J=6,8; $C_{(5')}$—$\mathbf{CH_2}CH_3$)	J_{67}=5,56; J_{47}=1,0; $J_{3'4'}$=8,0; $J_{6'4'}$=2,0	250
IIn*	9,56 s	8,76	8,27 d		4,56 (s, 3H, N—CH_3)	J_{67}=6,75	1000
IIu**	8,91 d	8,32	7,48 d	8,37 (d, 1H, 3'-H); 7,92 (t.d, 1H, 4'-H); 7,43 (d, 1H, 5'-H); 8,67 (d.d, 1H, 6'-H)	4,23 (s, 3H, N—CH_3)		1000
IIu***	8,97 d	8,40	7,55 d	8,41 (d.d, 1H, 3'-H); 7,97 (t.d, 1H, 4'-H); 7,47 (d.d, 1H, 5'-H); 8,73 (d.d, 1H, 6'-H)	4,30 (s, 3H, N—CH_3)	J_{67}=5,5; J_{47}=1,0; $J_{3'4'}$=7,75; $J_{6'4'}$=1,75; $J_{6'5'}$=4,6	250

*The spectra were recorded in CF_3COOH.
**The operating frequency was 60 MHz.
***The operating frequency was 80 MHz.

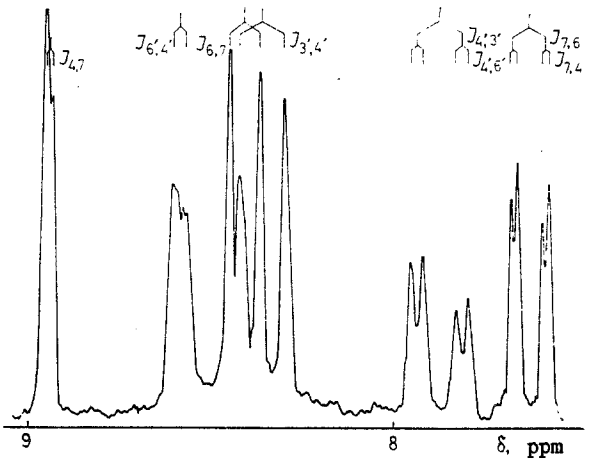


Fig. 3. PMR spectrum of IIi in $(CH_3)_2CO$-d_6 (60 MHz); S_w = 250 Hz.

cule usually show up in the lowest-field part of the spectrum and are not, as a rule, overlapped by the signals of the protons of the substituent in the 2 position. For example, the 4-H signal is observed at 8.91-9.74 ppm, while the centers of the 6-H and 7-H doublets are found at 8.32-9.25 ppm and 7.38-8.33 ppm, respectively (Table 2); the solvent (acetone or trifluoroacetic acid, for example) has the greatest effect on their positions, and the effect of the substituent in the 2 position is insignificant. The presence of doublets of vicinal protons in the 6 and 7 positions in the PMR spectra is characteristic for the examined compounds. The spin-spin coupling constants (SSCC) of these protons are virtually independent of the properties of the substituent in the 2 position but increase when the neutral solvent is replaced by a protic solvent (5.5 Hz in deuteroacetone and 7 Hz in CF_3COOH). Long-range spin-spin coupling (SSC) can be observed for the protons in the 4 and 7 positions in neutral solvents (1 Hz in deuteroacetone) but not in trifluoroacetic acid (IIg-i,u); it is interesting to note the absence of SSC between the protons in the meta positions (4-H and 6-H). The above-presented characteristics of the spectra of the examined compounds correspond to the known data for 2-substituted imidazo[4,5-c]pyridines [2, 13].

Compound IIn has a symmetrical structure relative to the 2–2' bond, and only a 4-H singlet at 9.56 ppm and two doublets of 6-H and 7-H signals with SSCC 6.75 Hz, as well as an N–CH_3 singlet at 4.56 ppm, are therefore observed in its spectrum (in CF_3COOH) (Table 2).

The PMR spectra of 2-pyridylimidazopyridines IIg-i,u are the most complex. In addition to the signals of the pyridine fragment of the two-ring system, two complex and remote multiplets of symmetrically oriented α and β protons of the γ-pyridyl substituent (8.82 and 7.69 ppm, respectively) (Table 2) can be observed in the spectrum of IIg in deuteroacetone.

The spectra of bases IIh,i,u were compared with one another and with the spectra of 2-substituted pyridines [14]. For the identification of the SSC of the protons of these compounds their spectra were recorded at different instrument operating frequencies. A comparison of the PMR spectra of 2-(2'-pyridyl)-1-methyl-1H-imidazo[4,5-c]pyridine (IIu) and 2-(6'-methyl-2'-pyridyl)-1-methyl-1H-imidazo[4,5-c]pyridine (IIh) showed that the doublet at 8.73 ppm with SSCC 4.6 Hz (6'-H, 5'-H) belongs to the 6'-H signal (Table 2). Spin-spin coupling with the remote protons (4'-H and 3'-H) leads to the development of a finer structure for this signal. The doublet at 8.56 ppm in the spectrum of 2-(5'-ethyl-2'-pyridyl)-1-methyl-1H-imidazo[4,5-c]pyridine (IIi) also belongs to the α proton of the substituent (6'-H), the constant of SSCC of which with the proton attached to the $C(_4')$ atom is 2.0 Hz. In turn, the proton attached to the $C(_4')$ atom gives, in the spectrum of IIi, a complex doublet (7.79 ppm) as a consequence of coupling with the ortho proton (3'-H) ($J_{3',4'}$ = 8.0 Hz) and the proton attached to the $C(_6')$ atom ($J_{4',6'}$ = 2.0 Hz). The 3'-H signals in the spectra of IIh,i,u are found at 8.15-8.41 ppm and have the form of doublets with an SSCC of ∿8 Hz, the hyperfine splitting of which, particularly in the case of bases IIh,u, is due to the long-range SSCC with the 5' and 6' protons. Partial superimposition of the 6-H doublet of the two-ring system (8.40 and 8.37 ppm) on the signals of the protons attached to the $C(_3')$ atom in IIi,u hinders their assignment. A comparison of the spectra of bases IIh,u,i makes it possible to identify the signals of the 5' proton of the first two compounds. These signals are situated in the strongest-field part of the spectrum of the aromatic protons and have a

complex form. In the simplest case, viz., for IIh, this is a doubled doublet (7.28 ppm) with SSCC $J_{4',5'}$ = 8 Hz and $J_{3',5'}$ = 1.5 Hz. It is difficult to determine the multiplicity and precise position of the signal of the proton attached to the $C(_{5'})$ atom in the spectrum of base IIu because of the superimposition on it of the 7-H doublet of the 7-H-imidazopyridine ring. The 4' proton in IIh, which is found in the field of two vicinal (with respect to it) β protons of the pyridine ring (3'-H and 5'-H) gives in the PMR spectrum a characteristic triplet centered at 7.79 ppm with an SSCC of 8.0 Hz. In the case of IIu this sort of triplet undergoes splitting (SSCC 1.75 Hz) to a multiplet as a result of long-range couping of 4'-H and 6'-H (Table 2).

EXPERIMENTAL

The PMR spectra of solutions of the compounds in deuteroacetone and trifluoroacetic acid were recorded with Tesla BS-467 (60 MHz) and Tesla BS-487-B (80 MHz) spectrometers with tetramethylsilane (TMS) as the internal standard. The molecular masses (m/z) were determined with an MS-902 mass spectrometer at 70 eV. The IR spectra of suspensions in mineral oil were recorded with an IR-20 spectrometer. Chromatography was carried out on Silufol UV-254 plates; the eluent was alcohol, and development was carried out with iodine vapors. Compounds IIa,g,h,ℓ,s,u-y were identified from the TLC data and from the absence of melting-point depressions of mixtures with samples obtained by different methods.

The reaction conditions and the characteristics of the synthesized compounds are presented in Tables 1 and 2. The results of elementary analysis for C, H, and N were in agreement with the calculated values.

2-Hetarylimidazopyridines Ia-f and IIa-y. A. A mixture of 10 mmoles of o-diamines IIIa,b or IVa-g, 11 mmole of a heterocycle with an active methyl group (Va-j) or an α- and γ-picoline N-oxide (Vk,l), and 30 mmole of sulfur was heated in a flask equipped with an air condenser. The resulting melt, after cooling, was purified by crystallization or reprecipitation.

B. A mixture consisting of equimolar amounts of o-diaminopyridine IVa,b,f,g and thioanilide VIIa,b [15, 16] was heated until hydrogen sulfide evolution ceased, after which the melt was mixed with hot ethanol, and the mixture was filtered. The solution was evaporated, and the residue was recrystallized to give 2-hetarylimidazopyridines IIa,b,h,s,u,w.

3-Amino-4-isopropylaminopyridine (IVd). A 25-g (440 mmole) sample of iron carbonyl and 4 ml of concentrated HCl were added in portions with stirring to a refluxing solution of 10 g (55 mmole) of 3-nitro-4-isopropylaminopyridine [17] in a mixture of 50 ml of alcohol and 25 ml of water, after which the mixture was refluxed for 2 h and filtered hot. The precipitate was washed thoroughly on the filter with hot alcohol and water, and the filtrate was evaporated to one fourth of its original volume and made alkaline to pH 9 with 20% aqueous NaOH solution. The resulting precipitate was removed by filtration and washed with a small amount of cold water to give 7.25 g (87%) of a product with mp 157-158°C (from dioxane) (mp 157-159°C [17]).

4-(2'-Pyridylmethylamino)-3-nitropyridine ($C_{11}H_{10}N_4O_2$). A solution of 7.60 g (45 mmole) of 3-nitro-4-ethoxypyridine [18] in 3 ml of ether was poured into 5.88 g (54 mmole) of 2-aminomethylpyridine, and the mixture was heated gradually to 120°C and maintained at this temperature for 15 min. The contents of the flask were cooled, 5 ml of water was added to the melt, and the precipitate was removed by filtration and dried to give 8.4 g (81%) of product. Crystallization from benzene gave yellow crystals with mp 145-146°C.

4-(2'-Pyridylmethylamino)-3-aminopyridine (IVh, $C_{11}H_{12}N_4$). This compound was obtained as in the preparation of diamine IVd by the reduction of 1.6 g (7 mmole) of 4-(2'-pyridylmethylamino)-3-nitropyridine with 5.77 g (103 mmole) of iron carbonyl in a mixture of 21 ml of alcohol, 13 ml of water, and 0.9 ml of concentrated HCl. Workup gave 0.55 g (39%) of a product with mp 103-104°C (from water).

4-(β-Hydroxyethylamino)-3-nitropyridine ($C_7H_9N_3O_3$). A mixture of 8.4 g (50 mmole) of 3-nitro-4-ethoxypyridine and 3.1 g (50 mmole) of monoethanolamine was heated at 140-150°C for 1.5 h until boiling ceased. Water (20 ml) was added to the solidified reaction mass, and the precipitate was removed by filtration, washed with water, and dried to give 7.8 g (85%) of a product with mp 141-142°C (from benzene).

4-(β-Hydroxyethylamino)-3-aminopyridine (IVe, $C_7H_{11}N_3O$). A 14.5-g (79 mmole) sample of 4-(β-hydroxyethylamino)-3-nitropyridine was added in portions at 75-80°C to a solution of 52 g (216 mmole) of $Na_2S \cdot 9H_2O$ in 240 ml of water, after which the mixture was evaporated to

one third of its original volume and cooled. The precipitate was removed by filtration to give 9.7 g (80%) of a product with mp 127-128°C (from dioxane).

1-Methyl-1H-imidazo[4,5-c]pyridine-2-thiocarboxylic Acid Amide ($C_8H_8N_4S$). A 0.16-g (1 mmole) sample of 2-cyano-1-methyl-1H-imidazo[4,5-c]pyridine [19] was dissolved in 5 ml of a 27% methanol solution of ammonia, and a stream of hydrogen sulfide was passed through the solution for 1 h. The reaction mixture was evaporated to dryness at room temperature, and the residue was extracted with hot methanol. The solvent was removed by distillation, and the precipitate was crystallized from benzene to give 0.12 g (62%) of a product with mp 176-178°C.

Bis(1-methylimidazo[4,5-c]-2-pyridyl) (IIn). A mixture of 0.18 g (0.9 mmole) of 1-methyl-1H-imidazo[4,5-c]pyridine-2-thiocarboxylic acid amide and 0.12 g (0.9 mmole) of 3-amino-4-methylaminopyridine IVb was heated at 170-190°C for 30 min until H_2S evolution ceased completely. The solidified mass was recrystallized from dioxane to give 0.18 g (75%) of a product with mp 311-312°C.

2-(2'-Pyridyl)imidazo[4,5-c]pyridine (IIa). A mixture of 0.20 g (1 mmole) of pyridine IVh and 0.064 g (2 mmole) of sulfur was heated at 170-180°C for 4 h in an argon atmosphere until hydrogen sulfide evolution ceased. The melt was pulverized and purified by reprecipitation from dilute hydrochloric acid solution (1:1) by means of ammonia to give 0.12 g (61%) of the base with mp 233-234°C (from benzene) (mp 234-235°C [5]).

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