640. *Formation of 2′-Hydroxyimidazo(4′,5′:2,3)pyridine from the Hydrazides and Hydroxamic Acids of 2-Aminonicotinic and 3-Aminopicolinic Acids.*

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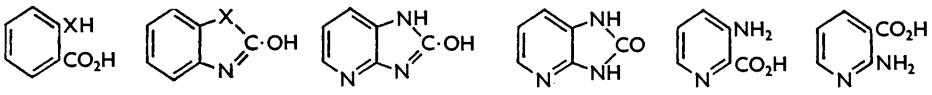
2′-Hydroxyimidazo(4′,5′:2,3)pyridine (III) is formed in the pyrolysis of either 2-aminonicotinhydroxamic acid or 3-aminopicolinhydroxamic acid. Better yields are obtained from the corresponding hydrazides by the Curtius reaction.

The attempted conversion of *ortho*-substituted carboxylic acids (I; X = –NH– or –O–) into the corresponding amine, *via* the acid amide, hydrazide, or hydroxamic acid, yields 2-hydroxy-benzimidazoles or -benzoxazoles (II).[1] We originally planned to investigate the application of this route to the synthesis of 2′-hydroxyimidazopyridines. However, Dornow and Hahmann[2] recently described the preparation of 2′-hydroxyimidazo-(4′,5′:2,3)pyridine (III) and certain alkyl and aryl derivatives from both hydrazides and amides of the corresponding 2-aminonicotinic acids. In consequence, we have studied only the hydroxamic acids and record here the results obtained on these compounds and on the isomeric hydrazide not studied by Dornow and Hahmann.



(I) (II) I) (IV). (V) (VI)

The azides from the acids (V) and (VI) decompose smoothly in hot toluene or xylene to give the heterocylic compounds (III). The same product is obtained, but in moderate yield only, by heating 3-aminopicolinhydroxamic acid above its m. p. for a short time. Similar treatment of the isomeric hydroxamic acid gave a difficultly separable mixture of the expected product (III) and 2-aminonicotinic acid.

From the infrared spectrum the amide structure (IV) appears more probable than (III), at least in the solid. Ultraviolet spectra of some of the compounds studied are summarized in the Table.

	In ethanol		In 0·1N-NaOH	
	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$
2-Hydroxybenzimidazole	225·5, 280	7,200, 7,500	242, 285	5,700, 7,800
2′-Hydroxyimidazo(4′,5′:2,3)pyridine	228, 292	3,400, 12,300	234 (inf.), 299·5	2,800, 11,400
Monoacetyl ,, ,,	251, 286	5,800, 10,400		
Diacetyl ,, ,,	238·5, 284	8,800, 9,700 [a]		
2-Aminonicotinic acid			243, 314	9,400, 5,200
Substance A			241, 300	(375), (655) [b]

[a] Approximate values only. Solution in ethanol unstable. [b] $E^{1\%}_{1\,cm.}$

By the action of acetic anhydride on the imidazopyridine (III) either the mono- or the di-acetyl derivative can be obtained. Work on the structure of these compounds and on the acylation of 2-hydroxybenzimidazole will be reported later.

Experimental

2-Aminonicotinic Acid.—Phillips's method[3] was modified by performing the Hofmann reaction on the crude ammonium quinolinamate instead of isolating the free acid.

Preparation and Decomposition of o-Amino-carboxyazides.—3-Aminopicolinhydrazide[5] (1 g.), m. p. 117—119°, in 4N-acetic acid (13 ml.) at 0—5° was treated with aqueous sodium nitrite

[1] (*a*) Stoermer, *Ber.*, 1909, **42**, 3133; (*b*) Scott and Mote, *J. Amer. Chem. Soc.*, 1927, **49**, 2545.
[2] Dornow and Hahmann, *Arch. Pharm.*, 1957, **290**, 20.
[3] Phillips, *Ber.*, 1894, **27**, 839.
[4] Kirpal, *Monatsh.*, 1900, **21**, 957.
[5] Oakes, Pascoe, and Rydon, *J.*, 1956, 1045.

(3·9 ml.) [from sodium nitrite (4·6 g.) and water (40 ml.)]. After 15 min., the product was collected, washed with water, and dried overnight ($CaCl_2$). The crude azide (0·61 g., 56%) had m. p. 116° (explosion). A portion (0·12 g.) in toluene (10 ml.) was heated (oil-bath), first at 90° for a few minutes, then to boiling for 10 min. The brown solid (0·05 g., 50% from azide), after crystallization from ethanol, afforded 2'-hydroxyimidazo(4',5' : 2,3)pyridine, m. p. 270—272° not depressed by an authentic sample [6] (lit., m. p. 265—266°; [2,7] 238—239°; [8] 274° [6]) (Found: C, 53·3; H, 3·7; N, 31·3. Calc. for $C_6H_5ON_3$: C, 53·3; H, 3·7; N, 31·1%); $\nu_{max.}$ 1695s (amide I), 1632, 1610, 1492, 1452s, 1047s, 867s, 768s, and 697s cm.$^{-1}$ (potassium bromide disc).

Similarly 2-aminonicotinhydrazide [2,5] was converted into an azide, m. p. 124° (explosion) (lit.,[2] 127°); decomposition in xylene gave the crude 2'-hydroxyimidazopyridine (96% from azide). Also, 2-aminobenzazide [9] was decomposed in toluene to give 2-hydroxybenzimidazole (45%), m. p. 313—316° (lit.,[10] 310—312°) not depressed by an authentic sample from *o*-phenylenediamine and urea; $\nu_{max.}$ 1750s (amide I), 1487s, 1368, 1273, 1200, 1030, 734s, and 704s cm.$^{-1}$ (potassium bromide disc).

Acetylation of 2'-Hydroxyimidazo(4',5':2,3)pyridine.—The imidazopyridine (0·15 g.) and acetic anhydride (1 ml.) were refluxed gently for 30 min. After a few minutes' boiling with water (3 ml.) and cooling a *monoacetyl derivative* (0·1 g.) separated. Crystallization from benzene gave needles, m. p. 212—213° (Found: C, 54·3; H, 4·2; N, 23·6. $C_8H_7O_2N_3$ requires C, 54·2; H, 3·9; N, 23·7%). When water was not added a *diacetyl derivative* was obtained, forming needles, m. p. 136—138°, from acetic anhydride (Found: C, 54·7; H, 4·4; N, 19·2. $C_{10}H_9O_3N_3$ requires C, 54·8; H, 4·1; N, 19·2%). The diacetyl compound was hydrolysed to monoacetyl by boiling water, and complete hydrolysis was rapid in hot 0·5N-sodium hydroxide.

2-Aminonicotinhydroxamic Acid.—Cold solutions of hydroxylammonium chloride (13·9 g.) in water (20 ml.) and 20% sodium hydroxide (80 ml.) were mixed. Methyl 2-aminonicotinate [4] (1·2 g.) in methanol (8 ml.) was added to the above solution (9 ml.) and the mixture set aside at room temperature for 7 days. Removal of methanol (reduced pressure) and addition of water (5 ml.) gave a yellow solution, to which acetic acid (1·5 ml.) was added cautiously, precipitating *2-aminonicotinhydroxamic acid* (1·1 g., 91%), m. p. 182—185°. After two recrystallizations from water the acid had m. p. 190°, but complete liquefaction was not observed (Found: C, 46·9; H, 4·8; N, 27·4. $C_6H_7O_2N_3$ requires C, 47·1; H, 4·6; N, 27·4%).

Similarly, ethyl 3-aminopicolinate [5] afforded a *hydroxamic acid* (49%), m. p. 143—145°, (from water) (Found: C, 46·6; H, 4·4; N, 26·9%).

Pyrolysis of o-Amino-hydroxamic Acids.—3-Aminopicolinhydroxamic acid (0·3 g.) was heated for 5 min. at 210—220° (bath-temp.). A solution of the brown residue in water on cooling gave crude 2'-hydroxyimidazopyridine (0·1 g.), m. p. 272—274° after crystallization from ethanol (charcoal). Similarly, 2-aminobenzhydroxamic acid [11] heated at 150—170° for 7 min. gave 2-hydroxybenzimidazole.

2-Aminonicotinhydroxamic acid (3·3 g.), however, when treated similarly gave a crude solid (*A*) (1·8 g.), m. p. 246—248° not raised by repeated crystallization from water, believed to be a mixture of the expected 2'-hydroxy-compound and 2-aminonicotinic acid. Quantitative separation and positive identification of the contaminant has not been achieved. By repeated crystallization from ethanol, least soluble fractions being rejected each time, a small amount of 2'-hydroxyimidazopyridine was obtained. An alternative separation was the isolation of the hydroxy-compound as its monoacetyl derivative. Ultraviolet spectroscopy [12] indicated that (*A*) contained 35—40% of 2-aminonicotinic acid.

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[9] Heller and Siller, *J. prakt. Chem.*, 1927, **116**, 9.
[10] Niementowski, *Ber.*, 1910, **43**, 3021.
[11] Scott and Wood, *J. Org. Chem.*, 1942, **7**, 508.
[12] Dewar and Urch, *J.*, 1957, 345.