

a brown solid which was recrystd ( $C_6H_6$ -hexane) to give 2.5 g (58%) of brown crystals, mp 110–115°. A small sample was sublimed at 120° (0.10 mm) to provide 1,2,4,6-tetrahydro-1-methyl-2-phenyl-3*H*-furo[3,4-*c*]pyrazol-3-one (9a) as white crystals, 127–128°. *Anal.* ( $C_{12}H_{12}N_2O_2$ ) C, H, N.

**C. With MeI-K<sub>2</sub>CO<sub>3</sub>.** A mixt of 2.0 g (0.01 mole) of 6a, 6 g of K<sub>2</sub>CO<sub>3</sub>, and 0.7 ml (0.011 mole) of MeI in 50 ml of Me<sub>2</sub>CO was stirred at room temp for 24 hr. The mixt was filtered, and the filtrate concd under reduced pressure to 2.6 g of a mixt of crystals and brown liquid. Chromatography on prep tlc plates provided three fractions. The least polar fraction gave 0.23 g of a tacky solid which was recrystd (hexane) to give 0.059 g (2.7%) of straw-colored crystals, mp 56–70°. An additional recrystn (pentane) provided 2,3a,4,6-tetrahydro-3a-methyl-2-phenyl-3*H*-furo[3,4-*c*]pyrazol-3-one (10a) as cream-colored crystals, mp 65–70°. *Anal.* ( $C_{12}H_{12}N_2O_2$ ) C, H, N. Pure compounds were not isolated from other fractions. The ir spectrum of the most polar chromatographic band showed it to be the *N*-Me deriv.

**D. With C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>Br.** A mixt of 2.0 g (0.01 mole) of 6a, 6 g of K<sub>2</sub>CO<sub>3</sub>, and 1.5 ml (0.013 mole) of C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>Br in 50 ml of Me<sub>2</sub>CO was stirred at room temp for 20 hr. The mixt was filtered, and the filtrate concd under reduced pressure to 3.1 g of a brown liquid which was chromatographed on prep tlc plates. The most polar fraction was recrystd ( $C_6H_6$ -hexane) to give 0.32 g (11%) of cream-colored crystals, mp 163–167°. An additional recrystn (cyclohexane) provided 1-benzyl-1,2,4,6-tetrahydro-2-phenyl-3*H*-furo[3,4-*c*]pyrazol-3-one (9c) as cream-colored crystals, mp 163–165°. *Anal.* ( $C_{18}H_{16}N_2O_2$ ) C, H, N.

The least polar chromatographic fraction yielded 0.41 g of a tacky solid which was recrystd (hexane) to give 0.17 g (6%) of 3a-benzyl-2,3a,4,6-tetrahydro-2-phenyl-3*H*-furo[3,4-*c*]pyrazol-3-one (10c) as off-white crystals, mp 98–100° dec. *Anal.* ( $C_{18}H_{16}N_2O_2$ ) C, H, N.

**E. With Allyl Bromide.** A mixt of 8.0 g (0.04 mole) of 6a, 24 g of K<sub>2</sub>CO<sub>3</sub>, and 4.8 g (0.04 mole) of allyl bromide in 300 ml of Me<sub>2</sub>CO was stirred at room temp for 20 hr. The mixt was filtered, and the filtrate was concd under reduced pressure to 14 g of a mobile, brown liquid which was chromatographed on a silica gel dry column. The more polar fraction provided 2.48 g of a tacky solid which was recrystd (hexane) to give 0.66 g (7%) of straw-colored crystals, mp 110–113°. An additional recrystn (cyclohexane) provided 1-allyl-1,2,4,6-tetrahydro-2-phenyl-3*H*-furo[3,4-*c*]pyrazol-3-one (9b) as straw-colored crystals, mp 110–113°. *Anal.* ( $C_{14}H_{14}N_2O_2$ ) C, H, N.

The less polar chromatographic fraction yielded 2.88 g of a mobile, brown liquid. Distn at 0.1 mm gave 1.6 g (16%) of 3a-allyl-2,3a,4,6-tetrahydro-2-phenyl-3*H*-furo[3,4-*c*]pyrazol-3-one (10b) as a viscous, brown liquid, bp 132–140°. *Anal.* ( $C_{14}H_{14}N_2O_2$ ) C, H, N; calcd, 11.6; found, 11.1.

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## Imidazo[1,2-*a*]pyridine Anthelmintic and Antifungal Agents

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A number of 2-substituted imidazo[1,2-*a*]pyridines have been prepared for anthelmintic and antifungal testing. High anthelmintic activity was found with acylated derivatives of 6-amino-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine. One of the

more potent compounds, 6-ethoxycarbonylamino-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine, was orally effective in sheep at a dose of 25 mg/kg against a wide range of helminths. Broad antifungal activity was demonstrated by a variety of compounds but did not correlate well with anthelmintic activity.

2-(4-Thiazolyl)benzimidazole, reported from these laboratories in 1961,<sup>1</sup> has gained wide acceptance as a safe, broad-spectrum anthelmintic agent. In an attempt to extend this activity to other heterocyclic systems, we have synthesized a number of imidazo[1,2-*a*]pyridines of related structure. Early results with simple 2-aryl- or 2-heteroaryl-substituted imidazo[1,2-*a*]pyridines were interesting in that while many compounds demonstrated high *in vitro* anthelmintic activity, little or no activity could be shown *in vivo*. 2-(4-Thiazolyl)imidazo[1,2-*a*]pyridine and 2-methoxycarbonylaminoimidazo[1,2-*a*]pyridine were broadly effective *in vivo* but of low potency. It was speculated that the general lack of activity *in vivo* was not intrinsic but was due to rapid metabolism and excretion. If true, modification of the anticipated sites of metabolism could be expected to lead to more active compounds.

2-Phenylimidazo[1,2-*a*]pyridine is known to undergo electrophilic attack at the 3 position<sup>2</sup> and, since it is common for enzymatic aromatic hydroxylation to occur at the site of electrophilic attack, this position was the first choice for the blockage of metabolism. Derivatives of 2-(4-thiazolyl)imidazo[1,2-*a*]pyridine were prepared in which the 3 position was substituted with nitro, amino, acetamido, diacetylamino, methoxycarbonylamino, chloro, and bromo. In all cases activity was destroyed. The failure of carbamate substitution in the 3 position was particularly disappointing because the carbamate group has been shown, in these laboratories, to be an effective inhibitor of aromatic hydroxylation.<sup>3</sup>

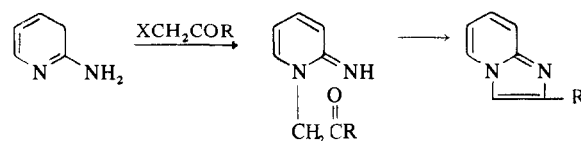
A second possible choice for the site of enzymatic hydroxylation was the 6 position and, in order to test this, derivatives of 2-(4-thiazolyl)imidazo[1,2-*a*]pyridine were prepared in which the 6 position was substituted with methyl, chloro, bromo, cyano, carbamoyl, carboxy, nitro, amino, and acylated amino. Success was attained with acylated 6-amino derivatives and in fact 6-ethoxycarbonylamino-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine was approximately twenty times as active *in vivo* as the parent compound.

Substitution in the 5, 7, and 8 positions reduced activity.

Oxidation of the 2-(4-thiazolyl)imidazo[1,2-*a*]pyridines with trifluoroperacetic acid gave the thiazole 3-oxide derivatives which were approximately as active as the parent compounds.

**Chemistry.** The chemistry of imidazo[1,2-*a*]pyridines has recently been reviewed by Mosby.<sup>4</sup> The new compounds prepared are listed in Tables I, II, III, and IV together with some previously described compounds. Synthetic procedures, generalized where possible, are described in the Experimental Section.

2-Substituted imidazo[1,2-*a*]pyridines were synthesized by reaction of 2-aminopyridines with the appropriate halo-ketones, *e.g.*,



Appropriately substituted 2-aminopyridines similarly yielded 5-, 6-, 7-, and 8-substituted imidazo[1,2-*a*]pyridines.

Table I

Compound No.	R	Syn method	Recrystn solvent	Mp, °C	Formula	Analyses	Anthelmintic activity		Antifungal activity					
							<i>in vitro</i>	<i>in vivo</i>	An	Pp	Pl	Cg	Tv	Rs
1	C <sub>6</sub> H <sub>5</sub>	<i>a</i>			C <sub>13</sub> H <sub>10</sub> N <sub>2</sub>		A	I	I	100	I	100	I	100
2		A	<i>i</i>	169-170	C <sub>10</sub> H <sub>7</sub> N <sub>3</sub> S	C, H, N, S	A	400	100	100	100	100	100	100
3		A	<i>j</i>	89-90	C <sub>11</sub> H <sub>8</sub> N <sub>2</sub> O	C, H, N	A	I	100	100	100	100	100	100
4		<i>b</i>			C <sub>11</sub> H <sub>8</sub> N <sub>2</sub> S		A	I	I	100	100	100	100	100
5	2-C <sub>10</sub> H <sub>7</sub>	<i>c</i>			C <sub>17</sub> H <sub>12</sub> N <sub>2</sub>		A	I	I	10	100	10	100	100
6	4-FC <sub>6</sub> H <sub>4</sub>	<i>d</i>			C <sub>13</sub> H <sub>9</sub> FN <sub>2</sub>			400	I	I	I	I	I	100
7		B	<i>k</i>	203.5-204.5	C <sub>10</sub> H <sub>7</sub> N <sub>3</sub> OS	C, H, N, S		200	I	I	I	100	I	I
8	4-ClC <sub>6</sub> H <sub>4</sub>	<i>e</i>			C <sub>13</sub> H <sub>9</sub> ClN <sub>2</sub>			I	I	I	I	I	I	100
9	4-C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>4</sub>	<i>f</i>	<i>k</i>	219-220	C <sub>19</sub> H <sub>14</sub> N <sub>2</sub>	C, H, N		400	I	I	I	I	I	I
10	CH <sub>3</sub> CONH	<i>g</i>			C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O		A	I	I	I	100	10	100	I
11	C <sub>2</sub> H <sub>5</sub> OCO	<i>h</i>			C <sub>10</sub> H <sub>10</sub> N <sub>2</sub> O <sub>2</sub>			I	I	I	I	I	I	I
12	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	<i>c</i>			C <sub>14</sub> H <sub>12</sub> N <sub>2</sub> O		A	I	I	I	I	I	I	100
13	NH <sub>2</sub> CO	C	<i>l</i>	222-223	C <sub>8</sub> H <sub>7</sub> N <sub>3</sub> O	C, H, N	I	I	I	I	I	I	I	I
14	NC	D	<i>m</i>	174-175	C <sub>8</sub> H <sub>5</sub> N <sub>3</sub>	C, H, N		I						
15	NH <sub>2</sub> CS		<i>m</i>	204-205	C <sub>8</sub> H <sub>7</sub> N <sub>3</sub> S	C, H, N, S	I	I	I	I	I	100	I	I
16	C <sub>6</sub> H <sub>5</sub> CONH	E	<i>i</i>	177-178	C <sub>14</sub> H <sub>11</sub> N <sub>3</sub> O	C, H, N		I	I	I	I	I	I	I
17	CH <sub>3</sub> OCONH	E	<i>n</i>	240-241	C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O <sub>2</sub>	C, H, N	A	400	100	100	100	100	100	100
18		A	<i>m</i>	168	C <sub>12</sub> H <sub>9</sub> N <sub>3</sub>	C, H, N		I	I	I	I	I	I	I
19	2-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	A	<i>o</i>	224-225 (HCl)	C <sub>14</sub> H <sub>12</sub> N <sub>2</sub> O	C, H, N	A	I	I	I	I			I

<sup>a</sup>See ref 7. <sup>b</sup>See ref 8. <sup>c</sup>See ref 9. <sup>d</sup>See ref 10. <sup>e</sup>See ref 11. <sup>f</sup>See ref 12. <sup>g</sup>See ref 13. <sup>h</sup>See ref 14. <sup>i</sup>Ethyl acetate. <sup>j</sup>Ethyl acetate-petroleum benzin. <sup>k</sup>Ethanol. <sup>l</sup>Water. <sup>m</sup>Methanol. <sup>n</sup>Methylene chloride. <sup>o</sup>Acetonitrile.

Table II

Compound No.	R	R <sub>1</sub>	Syn method	Recrystn solvent	Mp, °C	Formula	Analyses	Anthelmintic activity		Antifungal activity					
								<i>in vitro</i>	<i>in vivo</i>	An	Pp	Pl	Cg	Tv	Rs
20	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	A	<i>a</i>	158-160	C <sub>14</sub> H <sub>12</sub> N <sub>2</sub>	C, H, N		400	I	I	I	100	I	100
21		NO <sub>2</sub>		<i>b</i>	220-221	C <sub>10</sub> H <sub>8</sub> N <sub>4</sub> O <sub>2</sub> S	C, H, N		I	I	I	I	I	100	
22		NH <sub>2</sub>	F	<i>c</i>	231-233	C <sub>10</sub> H <sub>8</sub> N <sub>4</sub> S	C, H, N		400	I	I	I	I	I	
23		CH <sub>3</sub> CONH		E	<i>d</i>	154	C <sub>12</sub> H <sub>10</sub> N <sub>4</sub> OS	C, H, N		I					
24		CH <sub>3</sub> OCONH		E	<i>c</i>	179-180	C <sub>12</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S	C, H, N, S		I	I	I	I	I	I
25		Br			<i>e</i>	153-155	C <sub>10</sub> H <sub>6</sub> BrN <sub>3</sub> S	C, H, N, S	I	I	I	I	I	I	I
26		Cl			<i>e</i>	155-156	C <sub>10</sub> H <sub>6</sub> ClN <sub>3</sub> S	C, H, N	I	I	I	I	I	I	I
27		(CH <sub>3</sub> CO) <sub>2</sub> N		E	<i>f</i>	163-165	C <sub>14</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S	C, H, N, S	I	I					

<sup>a</sup>Acetone. <sup>b</sup>Methylene chloride. <sup>c</sup>Methanol. <sup>d</sup>Ethyl acetate-petroleum benzin. <sup>e</sup>Carbon tetrachloride. <sup>f</sup>Ether.

Functional groups in the 2, 6, and 8 positions underwent chemical manipulation in a completely normal manner.

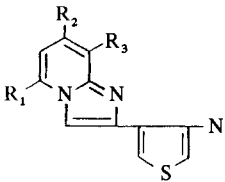
2-(4-Thiazolyl)imidazo[1,2-*a*]pyridine underwent substitution in the 3 position yielding 21, 25, and 26. Reduction of 21 to the amine followed by acylation gave 22, 23, 24, and 27.

The thiazole 3-oxides 7, 52, and 53 were prepared by oxidation with trifluoroacetic acid. It was of interest that no oxidation of the imidazo[1,2-*a*]pyridine ring occurred and that to achieve oxidation of the thiazole a peracid derived

from a strong acid (e.g., trifluoroacetic acid, dichloroacetic acid) was necessary. No oxidation took place with peracetic acid.

**Biological Activity.** Biological results are shown in Tables I, II, III, and IV. The compounds were tested for *in vitro* antifungal activity against six fungi, *Aspergillus niger*, *Pullularia pullulans*, *Penicillium luteum*, *Chaetomium globosum*, *Trichoderma viride*, and *Rhizoctonia solani*. The tabulated figures show either the lowest concentration in parts per million which demonstrated activity or inactivity

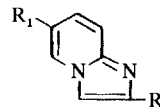
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
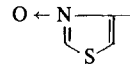


Compd No.	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	Syn method	Recrystn solvent	Mp, °C	Formula	Analyses	Anthelmintic activity		Antifungal activity					
									<i>in vitro</i>	<i>in vivo</i>	An	Pp	Pl	Cg	Tv	Rs
28	CH <sub>3</sub>	H	H	A	<i>a</i>	111-112	C <sub>11</sub> H <sub>9</sub> N <sub>3</sub> S	C, H, N	I							
29	H	CH <sub>3</sub>	H	A	<i>b</i>	193-195	C <sub>11</sub> H <sub>9</sub> N <sub>3</sub> S	C, H, N	A	I	I	I	I	I	I	I
30	H	H	CH <sub>3</sub>	A	<i>c</i>	152-154	C <sub>11</sub> H <sub>9</sub> N <sub>3</sub> S	C, H, N	A	400	I	I	I	I	I	I
31	H	H	NO <sub>2</sub>	A	<i>d</i>	210-211	C <sub>10</sub> H <sub>8</sub> N <sub>4</sub> O <sub>2</sub> S	C, H, N	A	I	I	I	I	I	I	I
32	H	H	NH <sub>2</sub>	F	<i>b</i>	156-158	C <sub>10</sub> H <sub>8</sub> N <sub>4</sub> S	C, H, N	I	I	I	I	I	I	I	I
33	H	H	CH <sub>3</sub> OCONH	E	<i>b</i>	220-222	C <sub>12</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S	C, H, N	I	I	I	I	I	I	I	I

<sup>a</sup>Ethyl acetate-petroleum benzin. <sup>b</sup>Ethyl acetate. <sup>c</sup>Acetone. <sup>d</sup>Ethanol.

Table IV



Compound No.	R	R <sub>1</sub>	Syn method	Recrystn solvent	Mp, °C	Formula	Analyses	Anthelmintic activity		Antifungal activity					
								<i>in vitro</i>	<i>in vivo</i>	An	Pp	Pl	Cg	Tv	Rs
34	C <sub>6</sub> H <sub>5</sub>	HOOC	<i>a</i>			C <sub>13</sub> H <sub>10</sub> N <sub>2</sub> O <sub>2</sub>		I	I	I	I	I	I	I	I
35	C <sub>6</sub> H <sub>5</sub>	NO <sub>2</sub>	A	<i>b</i>	255-260	C <sub>13</sub> H <sub>9</sub> N <sub>3</sub> O <sub>2</sub>	C, H, N	I	I						
36	C <sub>6</sub> H <sub>5</sub>	NH <sub>2</sub> CO	A	<i>c</i>	273-275	C <sub>14</sub> H <sub>11</sub> N <sub>3</sub> O	C, H, N	I	I						
37		CH <sub>3</sub>	A	<i>d</i>	172-172.5	C <sub>11</sub> H <sub>9</sub> N <sub>3</sub> S	C, H, N	A	I	100	100	100	100	100	100
38		NO <sub>2</sub>	A	<i>b</i>	279-280	C <sub>10</sub> H <sub>8</sub> N <sub>4</sub> O <sub>2</sub> S	C, H, N			400					
39		NH <sub>2</sub>	F	<i>e</i>	212-216	C <sub>10</sub> H <sub>8</sub> N <sub>4</sub> S	C, H, N	A	50	I	I	I			I
40		CH <sub>3</sub> OCONH	E	<i>d</i>	250-252	C <sub>12</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S	C, H, N	A	12.5	100	I	100			
41		Br	A	<i>f</i>	212	C <sub>10</sub> H <sub>8</sub> BrN <sub>3</sub> S	C, H, N	I	I	I	I	I			I
42		NH <sub>2</sub> CO	A	<i>g</i>	276.5-278	C <sub>11</sub> H <sub>8</sub> N <sub>4</sub> OS	C, H, N	I	I	I	I	I			I
43		Cl	A	<i>f</i>	206-208	C <sub>10</sub> H <sub>8</sub> ClN <sub>3</sub> S	C, H, N	A	I	I	I	I			I
44		NC	D	<i>g,h</i>	277-278	C <sub>11</sub> H <sub>8</sub> N <sub>4</sub> S	C, H, N	A	I	I	I	I			I
45		C <sub>6</sub> H <sub>5</sub> CONH	E	<i>d</i>	231-232	C <sub>17</sub> H <sub>12</sub> N <sub>4</sub> OS	C, H, N	A	50	I	I	I			I
46		(CH <sub>3</sub> ) <sub>2</sub> CHOCONH	E	<i>f</i>	215-216	C <sub>14</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S	C, H, N, S	A	25	10	10	10			100
47	C <sub>2</sub> H <sub>5</sub> OCONH	E	<i>d</i>	207-209	C <sub>13</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S	C, H, N	A	12.5	I	I	I			I	
48	HOOC	<i>g</i>		350-355	C <sub>11</sub> H <sub>7</sub> N <sub>3</sub> O <sub>2</sub> S	C, H, N	I	I	I	I	I			I	
49	C <sub>2</sub> H <sub>5</sub> OCO	NO <sub>2</sub>	A	<i>b</i>	202-203 (HBr)	C <sub>10</sub> H <sub>9</sub> N <sub>4</sub> O	C, H, N	I	I	I	I			I	
50	NH <sub>2</sub> CO	NO <sub>2</sub>	C	<i>c</i>	280-282	C <sub>8</sub> H <sub>6</sub> N <sub>4</sub> O <sub>3</sub>	C, H, N	I	I	I	I			I	
51	NC	NO <sub>2</sub>	D	<i>d</i>	175-177	C <sub>8</sub> H <sub>4</sub> N <sub>4</sub> O <sub>2</sub>	C, H, N	I	I	I	I			I	
52		CH <sub>3</sub> OCONH	B	<i>c</i>	340-345	C <sub>12</sub> H <sub>10</sub> N <sub>4</sub> O <sub>3</sub> S	C, H, N		25						
53		C <sub>2</sub> H <sub>5</sub> OCONH	B	<i>c</i>	247-250	C <sub>13</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S	C, H, N		6.25						

<sup>a</sup>Obtained from the Aldrich Chemical Co. <sup>b</sup>Ethanol. <sup>c</sup>Methanol. <sup>d</sup>Ethyl acetate. <sup>e</sup>Benzene. <sup>f</sup>Acetone. <sup>g</sup>DMSO. <sup>h</sup>Water.

(I) at 100 ppm. The *in vitro* anthelmintic results indicate A (active) or I (inactive) vs. trichostrongyles at 100 µg/ml. *In vivo* anthelmintic results show the lowest oral dose in mg/kg which demonstrated activity against trichostrongyles in a laboratory animal model assay<sup>5</sup> or inactivity (I) at 400 mg/kg. Compound 47 was active against a broad spectrum of parasites in sheep at an oral dose of 25 mg/kg.<sup>6</sup>

### Experimental Section†

**4-Acetylthiazole.** A solution of 190 g (1.73 moles) of 4-cyanothiazole in 1.3 l. of ether was added slowly to a stirred solution of 303 g (1.83 moles) of methylmagnesium iodide in 0.8 l. of ether, the rate being adjusted to maintain a moderate reflux. After completion of addition, the mixture was refluxed for 2.5 hr. The mixture was cooled to 0°, 750 ml of 6*N* hydrochloric acid was added, and the mixt was then stirred for 15 min, and neutralized with 50% sodium hydroxide to pH 7. The product was extracted with ether and purified by recrystallization from a mixture of ether and hexane, 155.8 g (71%), mp 59–60°.

**4-Bromoacetylthiazole.** Bromine (69.5 g, 0.43 mole) was slowly added to a refluxing solution of 55 g (0.43 mole) of 4-acetylthiazole in 300 ml of carbon tetrachloride. After the addition was completed the solvent was decanted from the precipitated solid. The solid was stirred with a mixture of ice and water and then the mixture was extracted with ether. Evaporation of the ether yielded the crude product, 77.6 g (87%), mp 41–44°, which was used without further purification.

**Method A. 2-(4-Thiazolyl)imidazo[1,2-*a*]pyridine (2).** A solution of 71 g (0.34 mole) of 4-bromoacetylthiazole in 200 ml of acetone was added to a solution of 31.5 g (0.34 mole) of 2-aminopyridine in 100 ml of acetone. After 1.5 hr, the precipitated solid was filtered off, dissolved in water, and basified with sodium hydroxide solution. The product was extracted with methylene chloride from which it was obtained by evaporation, 32.5 g (48.3%). Crystallization from ethyl acetate gave mp 169–170°. *Anal.* (C<sub>10</sub>H<sub>7</sub>N<sub>3</sub>S) C, H, N, S.

**Method B. 2-(3-Oxothiazol-4-yl)imidazo[1,2-*a*]pyridine (7).** A 32% solution (4 ml) of hydrogen peroxide in water (0.037 mole) was added to 20 ml of trifluoroacetic acid, with stirring. After 10 min, 5 g (0.025 mole) of 2-(4-thiazolyl)imidazo[1,2-*a*]pyridine was added, and the mixture heated on a steam bath for 2 hr. Ice water was added and the mixture made basic with ammonia. The product was extracted with methylene chloride and, after evaporation of the solvent, crystallized from ethanol, 4.3 g (79.7%), mp 203.5–204.5°. *Anal.* (C<sub>10</sub>H<sub>7</sub>N<sub>3</sub>OS) C, H, N, S.

**Method C. 2-Carbamoylimidazo[1,2-*a*]pyridine (13).** A solution of 15 g of 2-ethoxycarbonylimidazo[1,2-*a*]pyridine in 150 ml of methanol and 150 ml of liquid ammonia was heated at 100° for 8 hr. Evaporation of the solvent and recrystallization of the residue from water yielded the product, 8.1 g (72.2%), mp 222–223°. *Anal.* (C<sub>8</sub>H<sub>7</sub>N<sub>3</sub>O) C, H, N.

**Method D. 2-Cyanoimidazo[1,2-*a*]pyridine (14).** A solution of 6 g of 2-carbamoylimidazo[1,2-*a*]pyridine in 30 ml of phosphorus oxychloride was refluxed for 30 min. The excess of reagent was evaporated, and the residue treated with ice water and basified with ammonia. The precipitated product was collected and crystallized from methanol, 4 g (75.1%), mp 174–175°. *Anal.* (C<sub>8</sub>H<sub>5</sub>N<sub>3</sub>) C, H, N.

**2-Thiocarbamoylimidazo[1,2-*a*]pyridine (15).** A solution of 4 g of 2-cyanoimidazo[1,2-*a*]pyridine in a mixture of 25 ml of pyridine, 4 ml of triethylamine, and 10 ml of dimethylformamide was saturated with hydrogen sulfide and then allowed to stand for 2 hr at room temperature. Addition of water precipitated a yellow solid which was collected and crystallized from methanol, 4 g (80.8%), mp 204–205°. *Anal.* (C<sub>8</sub>H<sub>7</sub>N<sub>3</sub>S) C, H, N, S.

**Method E. 6-Ethoxycarbonylamino-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine (47).** To a stirred solution of 400 mg (0.0019 mole) of 6-amino-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine in 6 ml of pyridine was slowly added 225 mg (0.0021 mole) of ethylchloroformate. After 1.5 hr, the solution was diluted with ice water, and the product extracted with methylene chloride. Evaporation of the

solvent and recrystallization of the residue from ethyl acetate yielded the product, 210 mg (43%), mp 207–209°. *Anal.* (C<sub>13</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub>S) C, H, N.

**3-Nitro-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine (21).** To a stirred solution of 5 g (0.025 mole) of 2-(4-thiazolyl)imidazo[1,2-*a*]pyridine in 10 ml of concentrated sulfuric acid at 0° was added dropwise 3 ml (0.05 mole) of concentrated nitric acid. The mixture was allowed to come to room temperature and then stirred for a further 20 min. Ice was added and the solution adjusted to pH 6 with sodium hydroxide. The product was extracted with methylene chloride and after drying and evaporation was crystallized from a small volume of methylene chloride, 2 g (32.7%), mp 220–221°. *Anal.* (C<sub>10</sub>H<sub>8</sub>N<sub>4</sub>O<sub>2</sub>S) C, H, N.

**Method F. 3-Amino-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine (22).** A solution of 8.8 g of 3-nitro-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine in 300 ml of ethanol was reduced with hydrogen at 40 psi pressure using 1 g of 10% palladium on carbon as the catalyst. The catalyst was filtered off, the filtrate was evaporated, and the residue was crystallized from methanol, 7.7 g (99.7%), mp 231–233°. *Anal.* (C<sub>10</sub>H<sub>8</sub>N<sub>4</sub>S) C, H, N.

**3-Bromo-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine (25).** A solution of 2 g (0.01 mole) of 2-(4-thiazolyl)imidazo[1,2-*a*]pyridine, 4.4 g (0.025 mole) of *N*-bromosuccinimide, and 20 mg of benzoyl peroxide in 300 ml of carbon tetrachloride was allowed to stir at room temperature for 1.5 hr. The solution was charcoal treated and evaporated to yield an oil which was crystallized from a small volume of carbon tetrachloride, 1.4 g (50.2%), mp 153–154°. *Anal.* (C<sub>10</sub>H<sub>6</sub>BrN<sub>3</sub>S) C, H, N, S.

**3-Chloro-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine (26).** A solution of 2 g (0.01 mole) of 2-(4-thiazolyl)imidazo[1,2-*a*]pyridine, 1.6 g (0.012 mole) of *N*-chlorosuccinimide, and 10 mg of benzoyl peroxide was stirred for 4 hr at room temperature. Evaporation yielded an oily residue which crystallized from carbon tetrachloride, 0.75 g (32%), mp 155–156°. *Anal.* (C<sub>10</sub>H<sub>6</sub>ClN<sub>3</sub>S) C, H, N.

**2-(4-Thiazolyl)imidazo[1,2-*a*]pyridine-6-carboxylic Acid (48).** A mixture of 0.5 g of 6-carbamoyl-2-(4-thiazolyl)imidazo[1,2-*a*]pyridine and 20 ml of 40% aqueous sodium hydroxide was refluxed for 2 hr. The solution was diluted with ice and water and acidified with acetic acid to precipitate the product. Crystallization from dimethylformamide yielded 0.21 g (42%), mp 350–355°. *Anal.* (C<sub>11</sub>H<sub>7</sub>N<sub>3</sub>O<sub>2</sub>S) C, H, N.

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†Where analyses are indicated only by symbols of the elements analytical results obtained for those elements were within ±0.4% of the theoretical values. Melting points were taken on a Thomas-Hoover Uni-Melt apparatus and are uncorrected.