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The synthesis of novel imidazo[4,5-*c*]pyridines **11-13** and imidazo[4,5-*b*]pyridines **18-20** is described using **2** as the starting material. The synthesis is generally applicable for the introduction of a wide variety of substituents.

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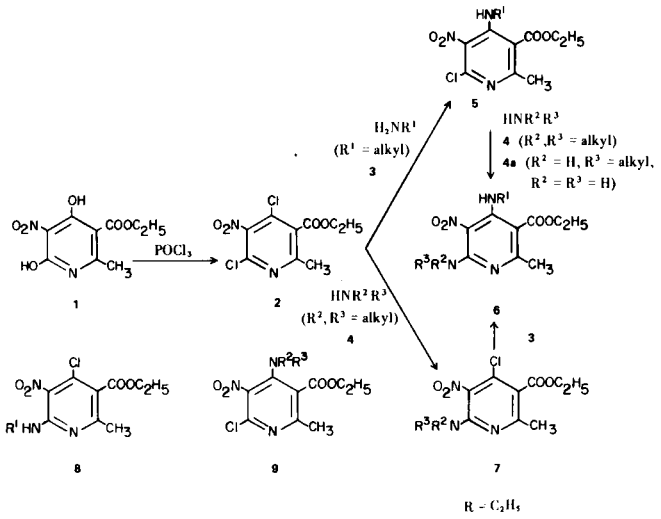
4,6-Dichloro-2-methyl-5-nitro-3-pyridine carboxylic acid, ethyl ester **2** is used as the starting material and is obtained by chlorination of the corresponding 4,6-dihydroxy compound **1** (1). The synthesis takes advantage of the graduated reactivity of the two chlorine atoms, caused by steric reasons. On treatment of **2** with primary amines **3** the more activated halogen in the 4-position is preferably substituted forming **5**. However, in the reaction with secondary amines **4**, the 4-position is sterically hindered and substitution of the 6-chlorine is favoured resulting in the formation of **7**. The isomers **8** and **9** are only formed in negligible yield (Scheme 1). The structure of **5** was established by its ir spectrum. The position of the amino substituent of **7** was assigned by treatment with **3**, leading to **6**, which can also be prepared by reaction of **5** with the corresponding amine **4**.

Scheme 1



Imidazo[4,5-*c*]pyridines.

Catalytic hydrogenation of the nitro group of **5** can be accomplished without attacking the halogen. The resulting **10** is subsequently treated with triethyl orthoformate or orthoacetate (2), forming the imidazole ring **11**. In these compounds the halogen is sufficiently activated to react with alkoxides or amines (3,4) and yield **12** and **13**, respectively. An alternate route for the preparation of **13** *via* **14** uses **6** wherein R^2, R^3 is alkyl or hydrogen; however, this procedure is rather unsatisfactory. When either R^2 or R^3 is hydrogen, ring closure results in the formation of both isomeric imidazopyridines **13** and **20**, which must be separated by repeated crystallisation; (Scheme 2).

Imidazo[4,5-*b*]pyridines.

Analogously to the reaction of **2** with secondary amines **4**, **2** also reacts with alkyl substituted hydrazines **15**. The greater steric hindrance of the 4-position and the steric requirements of the more nucleophilic alkyl substituted hydrazine-*N*-atom result in attack at the 6-position, thus affording **16** in high yield, whose structure is confirmed by reaction with *n*-butylamine. In this way, the same compound **21** arises as from reaction of **5d** (Table I) with **15**. The hydrazine N-N bond of **16** is cleaved and the nitro group is reduced simultaneously by catalytic hydrogenation in the presence of Raney-Nickel (5). Under the

Scheme 2

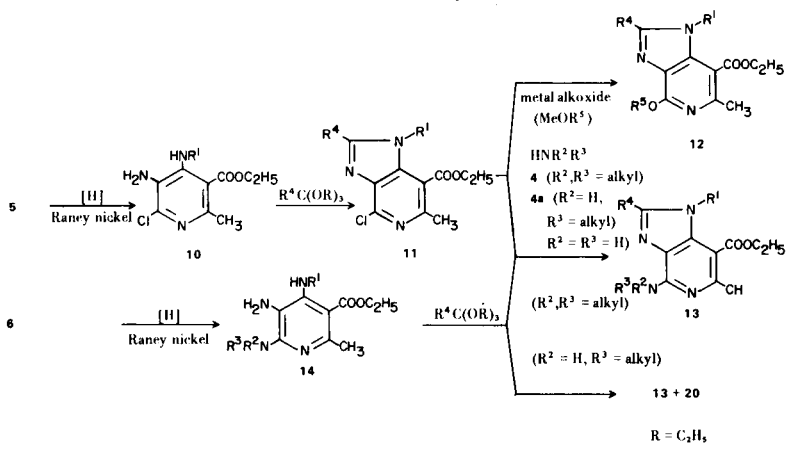
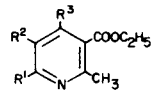


Table I

Pyridine Derivatives **5**, **6**, **7**, **10**, **14**, **16**, **17** and **21**



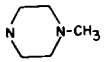
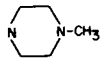
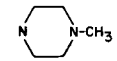
No.	R^1	R^2	R^3	M.p. °C Crystallization Solvent	B.p. °C (a) (torr)	Yield %	Formula	Analyses % Calculated/Found C	H	N	Ir (cm^{-1}) (b) ν CO
5a	Cl	NO_2	$NHCH(CH_3)_2$	55-57 A		81	$C_{12}H_{16}ClN_3O_4$	47.77 47.87	5.34 5.30	13.93 13.80	1690
5b	Cl	NO_2	NHC_2H_5	35-36 A		70	$C_{11}H_{14}ClN_3O_4$	45.92 45.90	4.91 4.83	14.61 14.77	1635, 1725
5c	Cl	NO_2	$NHCH_3$	44-46 A		63	$C_{10}H_{12}ClN_3O_4$	43.89 44.12	4.42 4.32	15.35 15.46	1685
5d	Cl	NO_2	NHC_4H_9	35-36 A		78	$C_{13}H_{18}ClN_3O_4$	49.44 49.56	5.75 5.97	13.31 13.43	1685, 1735
6a	$N(C_2H_5)_2$	NO_2	$NHCH(CH_3)_2$		185 (0.01)	83	$C_{16}H_{26}N_4O_4$	56.78 57.01	7.74 7.91	16.56 16.83	1722 (c)
6b		NO_2	NHC_2H_5		205 (0.004)	76	$C_{16}H_{25}N_5O_4$	54.69 54.53	7.17 7.31	19.93 20.05	1714 (c)
6c	NHC_2H_5	NO_2	NHC_4H_9	58-60 B		88	$C_{15}H_{24}N_4O_4$	55.53 55.63	7.45 7.37	17.27 17.35	1718
6d	NH_2	NO_2	NHC_4H_9	98-99 C		83	$C_{13}H_{20}N_4O_4$	52.69 52.58	6.80 6.89	18.91 19.12	1720
7a	$N(C_2H_5)_2$	NO_2	Cl	61-62 B		63	$C_{13}H_{18}ClN_3O_4$	49.44 49.30	5.75 5.63	13.31 13.40	1732
7b		NO_2	Cl	62-64 D		64	$C_{14}H_{19}ClN_4O_4$	49.05 49.24	5.59 5.57	16.35 16.50	1743
10a	Cl	NH_2	$NHCH(CH_3)_2$		180 (0.05)	76	$C_{12}H_{18}ClN_3O_2$	53.04 52.99	6.68 6.81	15.46 15.27	1721, 1705 (c)
10b	Cl	NH_2	NHC_2H_5		210 (0.05)	69	$C_{11}H_{16}ClN_3O_2$	51.26 51.17	6.26 6.35	16.31 16.68	1720 (c)
10c	Cl	NH_2	$NHCH_3$		185 (0.05)	72	$C_{10}H_{14}ClN_3O_2$	49.29 49.28	5.79 5.91	17.24 17.43	1715 (c)
10d	Cl	NH_2	NHC_4H_9		180 (0.05)	75	$C_{13}H_{20}ClN_3O_2$	54.64 54.51	7.05 6.99	14.70 14.83	1717 (c)
14a	$N(C_2H_5)_2$	NH_2	$NHCH(CH_3)_2$		180 (0.05)	93	$C_{16}H_{28}N_4O_2$	62.31 62.41	9.15 9.18	18.17 18.32	1685 (c)
14b		NH_2	NHC_2H_5		185 (0.006)	95	$C_{16}H_{27}N_5O_2$	59.79 60.01	8.47 8.19	21.79 21.91	1695, 1704 (c)
14c	NHC_2H_5	NH_2	NHC_4H_9		190 (0.1)	95	$C_{15}H_{26}N_4O_2$	61.20 61.18	8.90 9.04	19.03 19.27	1680 (c)

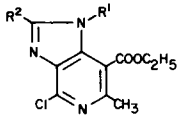
Table I (continued)

No.	R^1	R^2	R^3	M.p. °C; Crystallization Solvent	B.p. °C (a) (torr)	Yield %	Formula	Analyses % Calculated/Found C	H	N	Ir (cm^{-1}) (b) ν CO
14d	NH_2	NH_2	NHC_4H_9	82-83 C		87	$C_{13}H_{22}N_4O_2$	58.62 58.74	8.33 8.52	21.04 20.79	1690, 1725
16a	$N(CH_3)NH_2$	NO_2	Cl	64-65 A		74	$C_{18}H_{13}ClN_4O_4$	41.60 41.50	4.54 4.37	19.41 19.28	1715
16b	$N(C_2H_5)NH_2$	NO_2	Cl	117-119 A		72	$C_{11}H_{15}ClN_4O_4$	43.64 43.75	4.99 4.93	18.51 18.55	1724
16c	$N(C_4H_9)NH_2$	NO_2	Cl	50-52 A		68	$C_{13}H_{19}ClN_4O_4$	47.20 47.27	5.79 6.01	16.94 16.70	1721
17a	$NHCH_3$	NH_2	Cl	72.74 B		72	$C_{10}H_{14}ClN_3O_2$	49.29 49.36	5.79 5.83	17.24 17.19	1695
17b	NHC_2H_5	NH_2	Cl	63-65 B		70	$C_{11}H_{16}ClN_3O_2$	51.26 51.24	6.26 6.24	16.31 16.07	1715
17c	NHC_4H_9	NH_2	Cl		180 (0.05)	75	$C_{13}H_{20}ClN_3O_2$	54.64 54.48	7.05 7.02	14.70 14.78	1728 (c)
21	$N(CH_3)NH_2$	NO_2	NHC_4H_9	79-81 A		85	$C_{14}H_{23}N_5O_4$	56.68 56.89	7.13 7.01	21.53 21.75	1685

Crystallization solvent: A: methanol; B: diethyl ether; C: ethylalcohol; D: ligroin. (a) distillation with a rotating bulb column. (b) In potassium bromide. (c) film.

Table II

4-Chloroimidazo[4,5-c]pyridines **11**



No.	R^1	R^2	M.p. °C; (a)	B.p. °C (b) (torr)	Yield %	Formula	Analyses % Calculated/Found C	H	N	Ir (cm^{-1}) (Potassium Bromide) ν CO	Nmr (ppm) Imidazole-H (Deuteriochloroform)
11a	$CH(CH_3)_2$	H	54-56		62	$C_{13}H_{16}ClN_3O_2$	55.42 55.31	5.72 5.78	14.92 14.83	1728	8.1
11b	C_2H_5	H	40-42		71	$C_{12}H_{14}ClN_3O_2$	53.84 53.76	5.27 5.33	15.70 15.99	1720	8.0
11c	CH_3	H	120-122		76	$C_{11}H_{12}ClN_3O_2$	52.08 52.24	4.77 4.68	16.56 16.50	1725	7.85
11d	C_2H_5	CH_3		200 (0.05)	78	$C_{13}H_{16}ClN_3O_2$	55.42 55.36	5.72 5.96	14.92 15.08	1723 (c)	
11e	C_4H_9	H		195 (0.05)	73	$C_{14}H_{18}ClN_3O_2$	56.85 56.71	6.13 6.12	14.21 14.18	1725 (c)	7.90

(a) Crystallization solvent: diethyl ether. (b) Distillation with a rotating bulb column. (c) Film.

Table III

4-Alkoxyimidazo[4,5-c]pyridines **12**

No.	R^1	R^2	R^3	M.p. °C; (a)	B.p. °C (b) (torr)	Yield %	Formula	Analyses % Calculated/Found C	H	N	Ir (cm^{-1}) (Potassium Bromide) ν CO	Nmr (ppm) Imidazole-H (Deuteriochloroform)
12a	$CH(CH_3)_2$	H	$(CH_2)_3N(CH_3)_2$		215 (0.05)	58	$C_{18}H_{28}N_4O_3$	62.05 61.94	8.10 8.20	16.08 16.05	1728 (c)	7.9
12b	C_2H_5	H	$(CH_2)_2CH(CH_3)_2$		215 (0.05)	67	$C_{17}H_{25}N_3O_3$	63.93 64.04	7.89 7.68	13.16 13.12	1721 (c)	7.82
12c	C_2H_5	H	C_2H_5	45-46		83	$C_{14}H_{19}N_3O_3$	60.64 60.44	6.91 6.89	15.15 15.29	1714	7.9
12d	CH_3	H	C_2H_5	49-51		85	$C_{13}H_{17}N_3O_3$	59.30 59.20	6.51 6.42	15.96 15.87	1715	7.7
12e	$CH(CH_3)_2$	CH_3	CH_3		215 (0.05)	81	$C_{15}H_{21}N_3O_3$	61.84 61.56	7.27 7.31	14.42 14.29	1718 (c)	
12f	CH_3	CH_3	C_2H_5	92-94		78	$C_{14}H_{19}N_3O_3$	60.64 60.47	6.91 6.67	15.15 15.24	1725	

(a) Crystallization solvent: ligroin. (b) Distillation with a rotating bulb column. (c) Film.

Scheme 3

reaction conditions the halogen remains unaffected. After the ring closure of **17** with triethyl orthoformate or orthoacetate (2) **19**, respectively, **20** are formed by treating **18** with alkoxides or amines; (Scheme 3). In the case of **14c** the imidazole ring closure could be accomplished with acetylacetone to give **20a**. Neither the possible 7-ring **21** nor the isomer **13g** was formed.

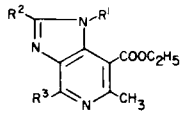
Ir and Nmr Spectra.

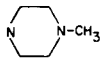
The structure of **5** is based upon the fact that the ester carbonyl band is shifted to lower wave lengths (1685-1695 cm^{-1}) due to the formation of a hydrogen bond with the neighbouring N-H proton (6,7,8). An additional weak C=O band at 1725-1735 cm^{-1} is present which is due to the unassociated ester group. If instead of **5** the isomer **8** was present, the carbonyl band would be apparent at higher wave lengths because of the inability to form an intramolecular hydrogen bond.

The isomeric 4-aminoimidazo[4,5-*c*]- and [4,5-*b*]-pyridines **13** and **20** can also be distinguished by the characteristic position of their C=O band. When a hydrogen bond can be formed as in **20**, the C=O band is at

Table IV

4-Aminoimidazo[4,5-*c*]pyridines **13**

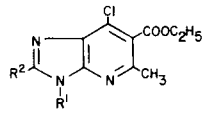


No.	R^1	R^2	R^3	M.p. °C (a)	Yield %	Formula	Analyses % Calculated/Found C	H	N	Ir (cm^{-1}) (Potassium Bromide) ν CO	Nmr (ppm) Imidazole-H (Deuteriochloroform)
13a	C_2H_5	H		53-55	78	$C_{17}H_{25}N_5O_2$	61.61 61.83	7.60 7.70	21.13 21.16	1705	7.6
13b	C_2H_5	CH_3	NHC_2H_5	36-38	81	$C_{15}H_{22}N_4O_2$	62.04 62.03	7.63 7.63	19.29 19.00	1710	
13c	C_2H_5	H	NHC_4H_9	34-36	69	$C_{16}H_{24}N_4O_2$	63.13 63.01	7.95 8.05	19.41 18.32	1705	7.6
13d	$CH(CH_3)_2$	H	$N(C_2H_5)_2$	36-38	75	$C_{17}H_{26}N_4O_2$	64.12 64.07	8.23 8.51	17.60 17.56	1775	7.7
13e	CH_3	H	NHC_4H_9	70-72	78	$C_{15}H_{22}N_4O_2$	62.04 62.18	7.63 7.46	19.29 19.19	1695	7.5
13f	C_4H_9	H	NHC_2H_5	42.45	83	$C_{16}H_{24}N_4O_2$	63.13 63.40	7.95 7.83	18.41 18.31	1700	7.6

(a) Crystallization solvent: diethyl ether.

Table V

4-Chloroimidazo[4,5-*b*]pyridines **18**

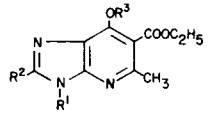


No.	R^1	R^2	M.p. °C; (a)	B.p. °C (torr)	Yield %	Formula	Analyses % Calculated/Found C	H	N	Ir (cm^{-1}) (Potassium Bromide) ν CO	Nmr (ppm) Imidazole-H (Deuteriochloroform)
18a	CH_3	CH_3	73-75		68	$C_{12}H_{14}ClN_3O_2$	53.84 54.04	5.27 5.21	15.70 15.66	1731	
18b	C_2H_5	H		195 (0.05)	73	$C_{12}H_{14}ClN_3O_2$	53.84 53.76	5.27 5.50	15.70 15.57	1736 (c)	8.1
18c	C_4H_9	H		190 (0.05)	71	$C_{14}H_{18}ClN_3O_2$	56.85 56.79	6.13 6.20	14.21 14.41	1729 (c)	8.1
18d	CH_3	H	80-82		75	$C_{11}H_{12}ClN_3O_2$	52.08 51.81	4.77 4.70	16.56 16.08	1735	8.05

(a) Crystallization solvent: ligroin. (b) Distillation by a rotating bulb column. (c) Film.

Table VI

4-Alkoxyimidazo[4,5-*b*]pyridines **19**

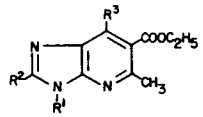


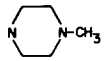
No.	R^1	R^2	R^3	M.p. °C; (b)	B.p. °C (a) (torr)	Yield %	Formula	Analyses % Calculated/Found C	H	N	Ir (cm^{-1}) (film) ν CO	Nmr (ppm) Imidazole-H (Deuteriochloroform)
19a	CH_3	CH_3	$(CH_2)_2CH(CH_3)_2$		195 (0.05)	76	$C_{17}H_{25}N_3O_3$	63.93 64.13	7.89 8.19	13.16 13.15	1725	
19b	C_2H_5	H	$CH(CH_3)_2$		180 (0.05)	81	$C_{15}H_{21}N_3O_3$	61.84 61.79	7.27 7.26	14.42 14.28	1730	7.9
19c	C_4H_9	H	*n*-C_4H_9		190 (0.05)	80	$C_{18}H_{27}N_3O_3$	64.84 64.54	8.16 8.10	12.60 12.30	1736	7.9
19d	CH_3	H	$(CH_2)_3N(CH_3)_2$		180 (0.05)	65	$C_{16}H_{24}N_4O_3$	59.98 60.27	7.55 7.13	17.49 17.71	1720	7.95
19e	C_2H_5	H	C_2H_5	63-65	(b)	85	$C_{14}H_{19}N_3O_3$	60.64 60.70	6.91 6.94	15.15 15.10	1723 (c)	7.95
19f	C_2H_5	CH_3	C_2H_5		195 (0.05)	83	$C_{15}H_{21}N_3O_3$	61.84 61.93	7.27 7.18	14.42 14.36	1735	

(a) Distillation by a rotating bulb column. (b) Crystalization solvent: ligroin. (c) Potassium Bromide.

Table VII

4-Aminoimidazo[4,5-*b*]pyridines **20**



No.	R^1	R^2	R^3	M.p. °C Crystallization Solvent	Yield %	Formula	Analyses % Calculated/Found C	H	N	Ir (cm^{-1}) (Potassium Bromide) ν CO	Nmr (ppm) Imidazole-H (Deuteriochloroform)
20a	C_2H_5	CH_3	NHC_4H_9	73-74 A	81	$C_{17}H_{26}N_4O_2$	64.12 63.98	8.23 8.03	17.60 17.68	1685	
20b	C_2H_5	H		70-72 A	79	$C_{17}H_{25}N_5O_2$	61.61 61.50	7.60 7.62	21.13 21.12	1715	7.7
20c	C_4H_9	CH_3	$NHCH(CH_3)_2$	60-62 A	77	$C_{18}H_{28}N_4O_2$	65.03 64.86	8.49 8.59	16.85 16.94	1670	
20d	C_2H_5	CH_3	$NH(CH_2)_3N(CH_3)_2$	68-70 A	63	$C_{18}H_{29}N_5O_2$	62.22 62.42	8.30 8.30	20.10 20.10	1674	
20e	C_2H_5	H		37-39 A	69	$C_{17}H_{24}N_4O_2$	64.53 64.48	7.65 7.74	17.71 17.69	1711	7.85
20f	H	CH_3	NHC_4H_9	148-149 B	56	$C_{15}H_{22}N_4O_2$	62.04 61.86	7.63 7.56	19.29 19.27	1665	
20g	CH_3	H	NHC_4H_9	54-55 B	76	$C_{15}H_{22}N_4O_2$	62.04 61.75	7.63 7.49	19.29 19.13	1660	7.65
20h	H	H	NHC_4H_9	122-124 B	53	$C_{14}H_{20}N_4O_2$	60.85 60.73	7.30 7.28	20.28 20.16	1665	7.8
20i	C_2H_5	H	NHC_4H_9	42-44 A	78	$C_{16}H_{24}N_4O_2$	63.13 63.15	7.95 7.89	18.41 18.27	1670	7.7

Crystallization solvent: A: diethyl ether; B: methanol.

1660-1685 cm^{-1}. However, in **13** it again appears in the normal aromatic ester range (1715-1735 cm^{-1}) (6,7,8). This is also the range for the carbonyl absorption of the imidazopyridines **11**, **12**, **18** and **19**.

Imidazole hydrogen signals appear at different field strengths in the nmr depending upon the substituents in the pyridine nucleus. The proton of **11** (R^4 = H) is located at δ 7.85-8.1 and of **18** (R^4 = H) at δ 8.05-8.1. When the pyridine nucleus is of the alkoxy substituted type, as in **12**, the protons are at δ 7.7-7.9 and in **19** at δ 7.9-7.95, respectively. When an amino substituent is present, as in **13** or **20**, hydrogen absorption occurs at δ 7.5-7.7 or at δ 7.65-7.8.

EXPERIMENTAL

Melting points were determined in a Lindstroem capillary melting point apparatus. Ir spectra were recorded on a Beckman Acculab IV. Nmr spectra were determined in a Varian T-60 instrument with TMS as internal standard.

4,6-Dichloro-2-methyl-5-nitropyridine-3-carboxylic Acid, Ethyl Ester (2).

4,6-Dihydroxy-2-methyl-5-nitropyridine-3-carboxylic acid, ethyl ester (24.2 g.) (**1**) (1) was heated in 50 ml. of phosphorus oxychloride for 60 hours at 80° with stirring. The solution was poured onto ice and precipitated **2** was removed by filtration, yield, 19.5 g. (70%), m.p. 45-46° (methanol); ir: 1740 cm^{-1}.

Anal. Calcd. for $C_9H_8Cl_2N_2O_4$: C, 38.73; H, 2.89; Cl, 25.41; N, 10.04. Found: C, 38.87; H, 3.01; Cl, 25.31; N, 10.00.

4-Amino-6-chloro-2-methyl-5-nitropyridine-3-carboxylic Acid, Ethyl Esters (**5a-5d**).

Compound **2** (0.1 mole) and 0.1 mole of triethylamine were dissolved in 100 ml. of alcohol. The solution was refluxed with stirring, while 0.1 mole of amine **3** was added dropwise. After the addition was completed, heating was continued for an additional hour. The solvent was removed under vacuum and the crystalline residue was extracted with 200 ml. of boiling ethyl acetate. After evaporation of the solvent **5a-5d** remained and was recrystallized (Table I).

6-Amino-4-chloro-2-methyl-5-nitropyridine-3-carboxylic Acid, Ethyl Esters (**7a**, **7b**).

The amine **4** (0.1 mole) was added dropwise with stirring to a solution consisting of 0.1 mole of **2** and 0.1 mole of triethylamine in 100 ml. of alcohol at reflux temperature. Refluxing was continued for 1 hour. The solvent was distilled off under vacuum and the residue treated with diluted aqueous sodium hydroxide solution. After extraction with ethyl acetate and evaporation of the solvent, **7a**, **7b** were obtained (Table I).

4,6-Diamino-2-methyl-5-nitropyridine-3-carboxylic Acid, Ethyl Esters (**6a-6d**) from (**5a-5d**) and (**6a**, **6b**) from (**7a**, **7b**).

Compounds **5a-5d** (0.1 mole) and 0.1 mole of triethylamine were refluxed with stirring in 100 ml. of alcohol together with 0.1 mole of amine **4**, or **4a** for 1 hour. (In the case of **6d** the reaction was accomplished with 100 ml. of 30% of aqueous ammonia in an autoclave at 100° for 12 hours. After cooling, **6d** crystallized and was filtered.) After removal of the solvent under reduced pressure, the residue was treated with 50 ml. of water made alkaline with sodium hydroxide solution and extracted three times with 100 ml. portions of ethyl acetate. The solvent was dried over sodium sulfate, filtered and evaporated. Compounds **6c** and **6d** were recrystallized while **6a** and **6b** were purified with a rotating bulb column (Table I).

Analogously, **6a** and **6b** were obtained by treatment of **7a** and **7b** with **3**. (Yield, **6a** = 80%; **6b** = 72%).

6-Chloro-4,5-diamino-2-methylpyridine-3-carboxylic Acid, Ethyl Esters (**10a-10d**).

Compounds **5a-5d** (0.1 mole) were dissolved in 100 ml. of alcohol and hydrogenated in the presence of 2-3 g. of Raney nickel at room temperature and at ordinary pressure. After the calculated amount of hydrogen had been absorbed, the hydrogenation was stopped, the catalyst filtered and the solution evaporated to dryness. The residue of **10a-10d** was purified with a rotating bulb column (Table I).

2-Methyl-4,5,6-triaminopyridine-3-carboxylic Acid, Ethyl Esters (**14a-14d**).

Compounds **6a-6d** (0.1 mole) were agitated with hydrogen in alcoholic solution with 10% palladium on charcoal at 70° and 3 atmospheres of hydrogen pressure. The catalyst was filtered, the solvent evaporated under vacuum and the remaining **14a-14c** were distilled by means of a rotating bulb column. Compound **14d** was recrystallized (Table I).

4-Chloro-6-hydrazino-2-methyl-5-nitropyridine-3-carboxylic Acid, Ethyl Esters (**16a-16c**).

Compound **2** (0.1 mole) was dissolved in 100 ml. of methanol. A mixture of 0.1 mole of alkylhydrazine **15** and 0.1 mole of triethylamine were dropped in with stirring at such a rate, that the temperature did not exceed 30°. Stirring was continued for further 30 minutes. The solution was cooled in an ice bath and **16a-16c** were filtered (Table I).

4-Butylamino-6-(1-methyl)hydrazino-2-methyl-5-nitropyridine-3-carboxylic Acid, Ethyl Ester (**21**) from **16a** or **5d**.

Compound **16a** (0.1 mole) was refluxed with 0.02 mole of butylamine for 30 minutes. Or 0.01 mole of **5d** and 0.02 mole of methylhydrazine **15** were allowed to react in the same way. After cooling **21** was obtained in either case. Melting points, ir and nmr spectra were identical (Table I).

4-Chloro-5,6-diamino-2-methylpyridine-3-carboxylic Acid, Ethyl Esters (**17a-17c**).

Compounds **16a-16c** (0.1 mole) were hydrogenated with Raney nickel at room temperature under atmospheric pressure until hydrogen absorption ceased. (Because of ammonia formation, it was advisable to flush the apparatus several times with hydrogen). The solvent was removed under vacuum. Compounds **17a** and **17b** were obtained as crystalline compounds; **17c** was distilled with a rotating bulb column (Table I).

4-Chloroimidazo[4,5-*c*]pyridines (**11a-11e**).

Compounds **10a-10d** (0.5 mole) were refluxed with stirring for 24 hours in 500 ml. of triethyl orthoformate in the case of **11a,b,c,e**, or 500 ml. of triethyl orthoacetate in the case of **11d**. Excess triethyl orthoester was removed under vacuum and the remaining **11a-11c** recrystallized. Compounds **11d** and **11e** were distilled with a rotating bulb column (Table II).

4-Alkoxyimidazo[4,5-*c*]pyridines (**12a-12f**).

A suspension of 0.025 mole of sodium hydride in 50 ml. of dry benzene was refluxed with the theoretical amount of the corresponding alcohol with stirring for 10 hours. Compounds **11a-11e**

(0.01 mole) were then added and heating continued for another 10 hours. The insoluble precipitate was filtered and the solvent removed under vacuum. Compounds **12c,d,f** were crystallized; **12b** and **12e** were distilled with a rotating bulb column.

In the case of **12a** it was advantageous to use the following procedure: The theoretical amount of a butyllithium solution in hexane was added to a solution of 0.02 mole of 3-dimethylamino-1-propanol and 50 ml. of dry benzene. The solution was stirred for 30 minutes at room temperature. Compound **11a** (0.015 mole) was added and the solution refluxed for 12 hours. After shaking the solution with 10 ml. of a 2*N* aqueous sodium hydroxide, the organic layer was dried over sodium sulfate, filtered and evaporated to dryness. The residue of **12a** was distilled with a rotating bulb column (Table III).

4-Aminoimidazo[4,5-*c*]pyridines (**13a-13f**).

Compounds **11a-11e** (0.01 mole) were refluxed with 10 ml. of the appropriately substituted amine **4** or **4a** for 5 hours. (For the reactions with ethylamine an autoclave was used, temperature 80°). Excess amine was distilled off and 20 ml. of water were added to the residue. Compounds **13a-13f** were extracted three times with 20 ml. portions of diethyl ether. The combined ether layers were dried over sodium sulfate, filtered, the solvent removed and **13a-13f** recrystallized (Table IV).

4-Chloroimidazo[4,5-*b*]pyridines (**18a-18d**).

Compounds **17a-17c** (0.1 mole) were refluxed with stirring for 24 hours in 100 ml. of triethyl orthoacetate in the case of **18a**, or triethyl orthoformate in the case of **18b-18d**, for 20 hours. Excess triethyl orthoester was distilled off under vacuum. Compounds **18a** and **18d** were crystallized, **18b** and **18c** were distilled with a rotating bulb column (Table V).

4-Alkoxyimidazo[4,5-*b*]pyridines (**19a-19f**).

The theoretical amount (0.025 mole) of the corresponding alcohol was added to a suspension of 0.03 mole of sodium hydride in 50 ml. of dry benzene and the mixture was refluxed with stirring for 10 hours. Then 0.01 mole of **18a-18d** was added and heating was continued for another 10 hours. The insoluble precipitate which formed was filtered and the solvent removed. Compound **19e** was crystallized, **10a-19c** and **19f** were distilled with a rotating bulb column (Table VI).

In the case of **19d** the following procedure was used: The theoretical amount of a butyllithium solution in benzene was added to a solution of 0.02 mole of 3-dimethylamino-1-propanol in 50 ml. of dry benzene. After stirring for 30 minutes at room temperature, 0.015 mole of **18d** was added and the solution was refluxed for 12 hours. The mixture was shaken with 10 ml. of 2*N* sodium hydroxide, dried over sodium sulfate, filtered and evaporated to dryness. The remaining **19d** was purified with a rotating bulb column.

4-Aminoimidazo[4,5-*b*]pyridines (**20a-20h**).

Compounds **18b-18h** (0.01 mole) were refluxed with 10 ml. of the appropriate amine **4** or **4a** for 5 hours. The excess amine was distilled off under vacuum, the residue treated with 20 ml. of water and extracted three times with 20 ml. portions of ether. The combined ether layers were dried over sodium sulfate, filtered, the solvent removed and the residue recrystallized (Table VII).

4-Butylamino-1-ethyl-2,6-dimethylimidazo[4,5-*b*]pyridine-5-carboxylic Acid, Ethyl Ester (**20a**) from **14c** with Acetylacetone.

Compound **14c** (29.4 g., 0.1 mole) was heated at reflux temperature with 11 g. of acetylacetone (0.11 mole) for 5 minutes. After cooling to room temperature the mixture was dissolved in about 50 ml. of ether. Five ml. of ligroin was added and the solution was kept in an ice-bath for 1 hour, during which time **20a** crystallized, yield, 27.2 g. (84%) (Table VII).

4-Aminoimidazo[4,5-*c*]pyridines (**13a, 13d**) from **14a, 14b**.

Compounds **14a** or **14b** (0.01 mole) were treated with 30 ml. of triethyl orthoformate for 24 hours at reflux temperature. The excess of orthoester was removed under vacuum and the oily residue was distilled with a rotating bulb column, yield, **13a** 75%; **13d** 70%.

1-Butyl-4-ethylamino-6-methylimidazo[4,5-*c*]pyridine-7-carboxylic Acid, Ethyl Ester (**13f**) and 4-Butylamino-1-ethyl-6-methylimidazo-[4,5-*b*]pyridine-5-carboxylic Acid, Ethyl Ester (**20i**) from **14c**.

Compound **14c** (5 g.) was refluxed for 5 hours together with 50 ml. of triethyl orthoformate. The excess of orthoester was removed under vacuum and the residue dissolved in 10 ml. of ether. The solution was cooled to -50°; **20i** crystallized and was filtered (1.3 g., m.p. 42-44°). The mother liquor was evaporated to dryness. By repeated crystallization with an ether/ligroin mixture, 0.6 g. of **13f** (m.p. 42-45°) was obtained (Tables IV, VII).

4-Butylamino-2,6-dimethylimidazo[4,5-*b*]pyridine-5-carboxylic Acid, Ethyl Ester (**20f**) and 4-Butylamino-6-methylimidazo[4,5-*b*]pyridine-5-carboxylic Acid, Ethyl Ester (**20h**) from **14d**.

Compound **14d** (0.01 mole) was refluxed with 50 ml. of triethyl orthoformate for 12 hours with stirring. The excess of orthoester was removed under vacuum and the residue **20f** was crystallized. For the preparation of **20h** triethyl orthoformate was replaced by triethyl orthoacetate (Table VII).

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