Contribution from the Department of Chemistry, Arizona State University
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The Synthesis of Various Chloroimidazo[4,5-c]pyridines and Related Derivatives(1)

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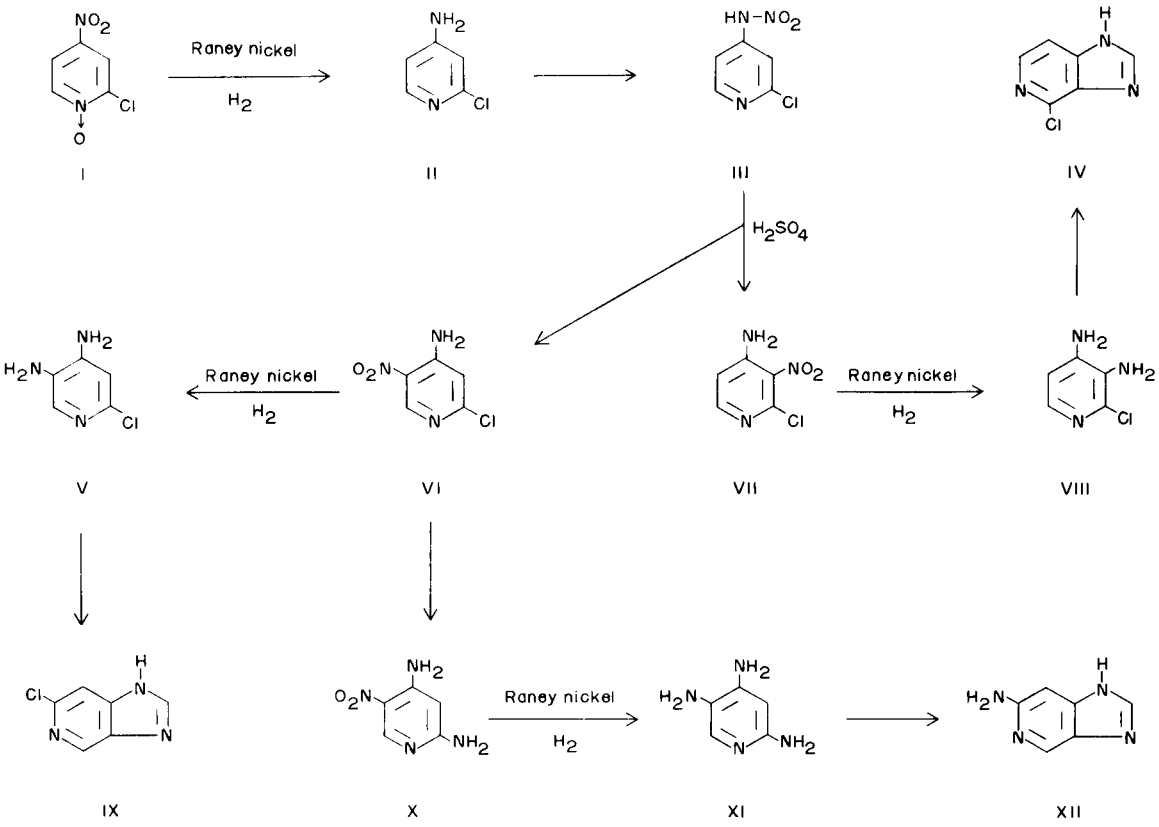
A new and convenient route to the synthesis of 4-chloroimidazo[4,5-c]pyridine (IV) has been devised. The preparation of 6-chloroimidazo[4,5-c]pyridine (IX) and 4,6-dichloroimidazo[4,5-c]pyridine (XX) has been accomplished for the first time by ring closure of the requisite chloro-3,4-diaminopyridines with ethyl orthoformate and acetic anhydride. Ring closure of 2,4,5-triaminopyridine (XI) with ethyl orthoformate and acetic anhydride gave 6-aminoimidazo[4,5-c]pyridine (XII). Imidazo[4,5-c]pyridine-4-thione (XXI) has been prepared from 4-chloroimidazo[4,5-c]pyridine.

The synthesis of a number of imidazo[4,5-c]-pyridines from imidazole intermediates was recently reported (3) from our laboratory. The present study deals with an extension of this work involving ring closure of the requisite 3,4-diaminopyridine to yield various 4 and 6-substituted imidazo[4,5-c]pyridines.

Salemink and van der Want (4, 5) have reported the synthesis of a number of 4-substituted imidazo[4,5-c]-pyridines including 4-chloroimidazo[4,5-c]pyridine (4). Because of the many steps involved and the low yields obtained we have sought new synthetic procedures for the preparation of the required 3,4-diaminopyridine intermediates needed for ring closure to the corresponding imidazo[4,5-c]pyridines. After the present work was completed a communication appeared (6) describing an improved synthesis of a number of 4-substituted imidazo[4,5-c]pyridines from pyridine intermediates, which compares favorably with some of the synthetic routes devised in our own laboratory. For our work we began with 2-chloro-pyridine (7) which was converted to 2-chloro-4-nitropyridine-1-oxide (I) by the procedure of Talik and Plazek (8). These authors (9) used powdered iron and zinc in acetic acid to change I to 4-amino-2-chloropyridine (II). In our hands a much superior procedure to remove the N-oxide function and at the same time reduce the nitro group was catalytic hydrogenation of I with Raney nickel. By this procedure yields of 4-amino-2-chloropyridine (II) in excess of 90% were obtained. Nitration of II followed by rearrangement of the product is reported (9) to give a mixture of 4-amino-2-chloro-3-nitropyridine (VII) and 4-amino-2-chloro-5-nitropyridine (VI), which were separated by fractional crystallization from benzene. The structural assignment of 4-amino-2-chloro-3-nitropyridine (VII) as the higher melting isomer (m.p. 205-207°) was shown to be correct by inspection of the p.m.r. spectrum of VII which showed two similar doublets, J = 2.5 c.p.s., characteristic of the AB splitting pattern due to the adjacent H_5 and H_6 protons. The H_5 doublet occurs at δ 7.2 and the H_6 doublet at δ 8.0 in trifluoroacetic acid. (TMS internal standard.) The lower melting isomer 4-amino-2-chloro-5-nitropyridine (VI) was purified and found to melt at 190-191° instead of 155-156° as previously recorded (9). The structure of VI was confirmed by p.m.r. spectra in trifluoro acetic acid which showed H_3 as a sharp singlet at δ 7.3 and H_6 as a sharp singlet at δ 9.2.

Treatment of 4-amino-2-chloro-3-nitropyridine (VII) with Raney nickel gave 2-chloro-3,4-diamino-pyridine (VIII) isolated as a hydrochloride salt. Ethyl orthoformate and acetic anhydride mixture and VIII gave over 90% yield of the desired 4-chloro-imidazo[4,5-c]pyridine (IV). This product proved to be identical to the compound prepared recently *via* another procedure by Mizuno and coworkers (6) as judged by ultraviolet and p.m.r. spectral data. Raney nickel and 4-amino-2-chloro-5-nitropyridine (VI) gave 2-chloro-4,5-diaminopyridine (V) in good yield. Ring closure of V was accomplished in good yield to give 6-chloroimidazo[4,5-c]pyridine (IX). The p.m.r. spectrum of IX in trifluoroacetic acid confirmed the structure and showed three singlets at δ 8.4, 9.5 and 9.6 corresponding to the three protons H_4, H_2 and H_7. It is interesting to note that a prior assignment of the structure 2-chloro-4,5-diaminopyridine (10) has been shown to be in error (6) and a previous attempt to prepare 6-chloro-imidazo[4,5-c]pyridine was therefore, unsuccessful (6). Amination of 4-amino-2-chloro-5-nitropyridine (VI) gave 2,4-diamino-5-nitropyridine (X) which was reduced catalytically to 2,4,5-triaminopyridine (XI). When XI was treated with ethyl orthoformate and acetic anhydride mixture 6-aminoimidazo[4,5-c]-pyridine (XII) was obtained in good yield. Another imidazo[4,5-c]pyridine derivative desired for future work was 4,6-dichloroimidazo[4,5-c]pyridine (XX). The success in the synthesis of 4-chloro- and 6-chloroimidazo[4,5-c]pyridine suggested a similar route for XX. The key intermediate pyridine de-

REACTION SCHEME I



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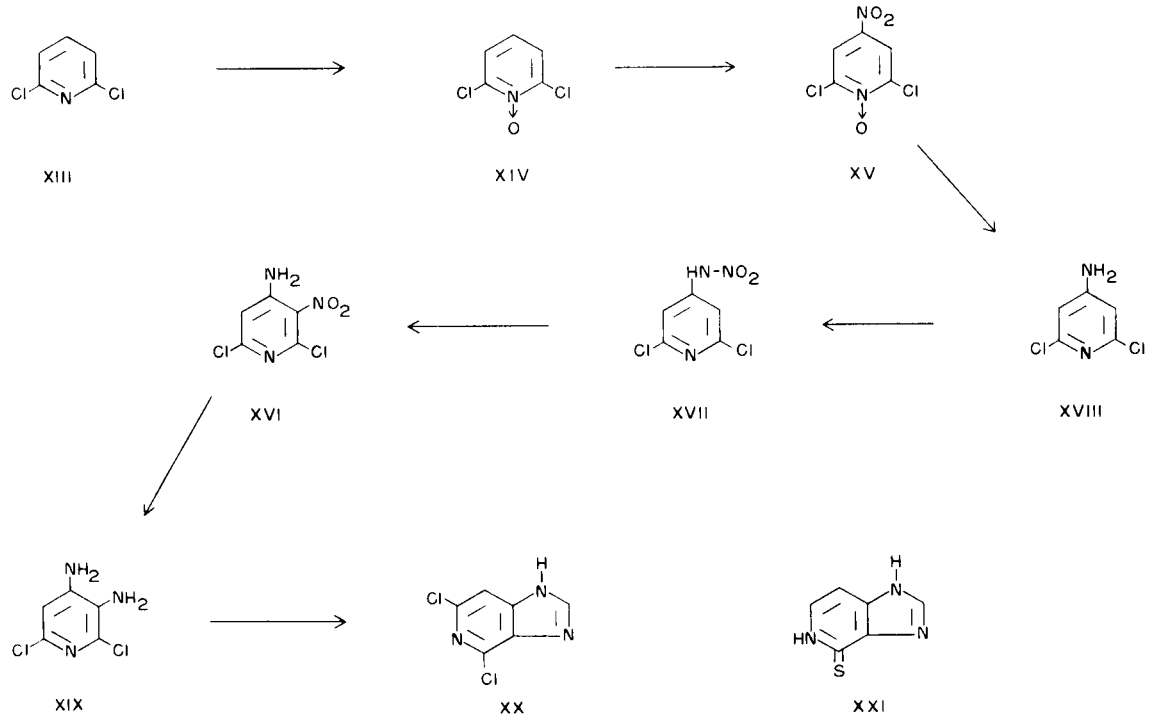

TABLE I

Ultraviolet Absorption Spectra of Some Substituted Pyridines

Compound	λ max mμ *p*H 1	ε max	λ max mμ *p*H 11	ε max
2-Chloro-4-nitro-pyridine-1-oxide (I)	237 312	10,950 12,300	237 312	11,500 13,150
4-Amino-2-chloro-pyridine (II).	264	8,580	244	6,940
2-Chloro-4-nitramino-pyridine (III).	276 331	13,500 3,100	299	12,000
4-Amino-2-chloro-3-nitro-pyridine (VII).	239 259-264s 341	16,250 6,900 2,320	239 280 350	16,600 3,170 2,660
4-Amino-2-chloro-5-nitro-pyridine (VI).	236 258-270s 341	26,500 6,900 3,710	236 271 354	24,100 5,900 4,380
2-Chloro-3,4-diamino-pyridine (VIII).	296	8,250	244 284	2,920 3,360
2-Chloro-4,5-diamino-pyridine (V).	290	6,990	295 238-244s	3,880 8,730
2,4-Diamino-5-nitro-pyridine (X).	242 268 313	17,100 32,400 6,640	233 263 349	13,700 8,790 15,900
2,4,5-Triamino-pyridine (XI).	267	6,730	296	3,460
2,6-Dichloropyridine-1-oxide (XIV).	260	13,800	260	13,100
2,6-Dichloro-4-nitropyridine-1-oxide (XV).	245 313	8,151 8,770	245 313	7,730 8,360
4-Amino-2,6-dichloro-pyridine (XVIII).	252 265	9,950 9,450	247	12,200
2,6-Dichloro-4-nitramino-pyridine (XVII).	270	12,100	229 302	10,600 11,200
4-Amino-2,6-Dichloro-3-nitropyridine (XVI).	243 281 351	12,100 2,080 1,660	243 281 251	12,100 2,080 1,660
3,4-Diamino-2,6-dichloro-pyridine (XIX).	295	4,730	256 292	5,580 4,510

rivative needed was 4-amino-2,6-dichloropyridine (XVIII). This compound has previously been reported by Meyer and Von Beck (11) by a rather lengthy route from 2,6-dihydroxypyridine-4-carboxylic acid. In the present work 2,6-dichloropyridine (7) served as the starting material. 2,6-Dichloropyridine-1-N-oxide (XIV) was prepared from 2,6-dichloropyridine (XIII) and hydrogen peroxide in the presence of trifluoroacetic acid. Nitration of XIV gave 2,6-dichloro-4-nitropyridine-1-oxide (XV) in good yield. Catalytic reduction of XV removed the N-oxide function as well as reduced the nitro group to give the desired 4-amino-2,6-dichloropyridine (XVIII) in good yield. 2,6-Dichloro-4-nitraminopyridine (XVII) was readily formed from XVIII. Rearrangement of XVII in concentrated sulfuric acid gave 4-amino-2,6-dichloro-3-nitropyridine (XVI) in good yield. Catalytic reduction of XVI gave 2,6-dichloro-3,4-diaminopyridine (XIX) in essentially quantitative yield isolated as a hydrochloride salt. Ring closure of

TABLE II

Ultraviolet Absorption Spectra of Some Substituted imidazo[4, 5-c]pyridines

Compound	λ max mμ *p*H 1	ε max	λ max mμ *p*H 11	ε max
4-Chloroimidazo[4, 5-c]-pyridine (IV).	268	6,140	275	5,530
6-Chloroimidazo[4, 5-c]-pyridine (IX).	234	4,480	250	3,360
	273	3,840	275	3,840
	280	3,200		
6-Aminoimidazo[4, 5-c]-pyridine (XII).	267	5,980	262	4,940
	295	3,640		
Imidazo[4, 5-c]pyridine-4-thione (XXI)	336	14,800	229	13,300
			246	11,800
			320	16,500
4,6-Dichloroimidazo[4, 5-c]-pyridine (XX)	240	4,150	255	3,400
	277	5,100	286	4,900

2,6-dichloro-3,4-diaminopyridine hydrochloride with a mixture of acetic anhydride and ethyl orthoformate gave the desired 4,6-dichloroimidazo[4, 5-c]pyridine (XX) in above 90% yield.

Although the reactions of the various chloroimidazo[4,5-c]pyridines prepared in the present study will be the subject of subsequent communication, it is of interest to report the synthesis of imidazo-[4, 5-c]pyridine-4-thione (XXI) (3-deaza-6-mercaptopurine). Sodium hydrosulfide in refluxing ethylene glycol converted 4-chloroimidazo[4,5-c]pyridine to imidazo[4, 5-c]pyridine-4-thione (XXI) in above 75% yield. The ultraviolet absorption spectral data for the substituted pyridine derivatives are recorded in Table I. Similar data for the imidazo[4, 5-c]pyridines are recorded in Table II.

EXPERIMENTAL

4-Amino-2-chloropyridine (9) (II).

2-Chloro-4-nitropyridine-1-oxide (8) (I) (20 g.) in methanol (200 ml.) was hydrogenated over Raney nickel catalyst (20 g. wet) for 3.5 hours at 45 p.s.i. in a Parr apparatus. After the addition of Celite the mixture was shaken vigorously and the solution was filtered into 100 ml. of methanol saturated at 0° with dry hydrogen chloride gas. This solution was evaporated to a colorless solid *in vacuo*, triturated with diethyl ether and the solid was separated by filtration to yield 16.5 g. (92%) of 4-amino-2-chloropyridine as the monohydrochloride salt. This product recrystallized from a mixture of methanol and ethyl ether to give colorless crystals m.p. 223-224°.

Anal. Calcd. for $C_5H_5ClN_2 \cdot HCl$: C, 36.4; H, 3.66; N, 17.0. Found: C, 36.8; H, 3.76; N, 17.1.

When this compound was dissolved in a small amount of water and the resulting solution was neutralized with base and cooled overnight, crystals were obtained which were identical to the product obtained by the procedure of Talik and Plazek (9).

4-Amino-2-chloro-3-nitropyridine (VII) and 4-amino-2-chloro-5-nitropyridine (VI).

The procedure of Talik and Plazek (9) was modified in the following manner: Finely ground 2-chloro-4-nitraminopyridine (III) (100 g.) was carefully dissolved in concentrated sulfuric acid (800 ml.) and heated on a steam bath for 30 minutes (internal temperature 88°). After the solution had cooled to room temperature it was poured onto crushed ice (2.14 kg.) and treated with concentrated ammonium hydroxide until *p*H 2.5 was reached. The temperature was kept below 20° with an acetone-dry ice bath. The yellow solid was separated by filtration and after washing it well with ice water it was dried; 90.5 g. of solid was obtained.

The finely ground, dried product was added to benzene (5 l.) and this mixture was heated to the boiling point and stirred continuously just below the boiling point of benzene. After the mixture had remained for 5 hours at room temperature the solid was removed by filtration and washed well with benzene. This solid (62.5 g., 62.5%) was recrystallized from ethanol to give yellow needles of 4-amino-2-chloro-3-nitropyridine (VI) which melted at 209-210° (lit. (9) 205-207°).

The benzene filtrate was evaporated to dryness *in vacuo* to give 26 grams of impure 4-amino-2-chloro-5-nitropyridine (contaminated with VII). This product was recrystallized several times from a 1:1 ethanol: water mixture, then several times from ethyl acetate to give light orange platelets of pure 4-amino-2-chloro-5-nitropyridine (VI) which melted at 190-191°.

Anal. Calcd. for $C_5H_4ClN_3O_2$: C, 34.6; H, 2.32; N, 24.2. Found: C, 35.0; H, 2.53; N, 24.3.

2-Chloro-3,4-diaminopyridine dihydrochloride (9) (VIII).

4-Amino-2-chloro-3-nitropyridine (VII) (10 g.) in ethanol (200 ml.) was hydrogenated over Raney nickel catalyst (10 g. wet) for 2 hours at 45 p.s.i. in a Parr hydrogenation apparatus. After removal from the shaker, Celite (2 g.) was added, the mixture was shaken vigorously and filtered into 100 ml. of ethanol saturated at 0° with dry hydrogen chloride gas. This solution was evaporated to dryness *in vacuo* to yield 11.0 g. (92.2%) of crystalline 2-chloro-3,4-diaminopyridine as the dihydrochloride, m.p. 175-177°. Infrared spectra and paper chromatography and mixed m.p. data showed this compound to be identical with the dihydrochloride isolated by Talik and Plazek (9) by the zinc and hydrochloric acid reduction of VIII.

4-Chloroimidazo[4, 5-c]pyridine (4, 6) (IV).

2-Chloro-3,4-diaminopyridine dihydrochloride (VIII) (28 g.) was refluxed in a 1:1 mixture of ethyl orthoformate:acetic anhydride (250 ml.) for 2.5 hours. The excess reagents were removed *in vacuo* using a steam bath as a source of heat. The light tan residue was treated with water (50 ml.), warmed on a steam bath and 10% sodium hydroxide was added until the *p*H of the solution remained at 9. The *p*H was then adjusted to 7 with glacial acetic acid and the mixture was cooled overnight. The solid 4-chloroimidazo[4,5-c]pyridine was removed by filtration, washed with ice water and dried to yield 15 g. The filtrate was extracted to yield additional product in a continuous extractor with diethyl ether. The ether phase was dried over anhydrous sodium sulfate and evaporated to dryness *in vacuo*. The combined yield was 18.5 g. (93.5%). The product was recrystallized from an ethanol-

heptane mixture to give a colorless flocculent precipitate of melting point 243°.

Anal. Calcd. for $C_6H_4ClN_3$: C, 46.9; H, 2.61; N, 27.3. Found: C, 46.8; H, 2.90; N, 27.3.

Imidazo[4,5-c]pyridine-4-thione (XXI).

4-Chloroimidazo[4,5-c]pyridine (IV) (1 g.), sodium hydrosulfide (2 g.) and ethylene glycol (20 ml.) were refluxed for 6 hours. The dark green solution was added to water (100 ml.). The aqueous solution was boiled with charcoal, filtered while hot, and acidified with glacial acetic acid to yield a tan precipitate. This product was filtered and reprecipitated from hot dilute aqueous ammonia with acetic acid to yield 0.8 g. (78.6%) of product. The light yellow material decomposed at 365°.

Anal. Calcd. for $C_6H_5N_3S$: C, 47.7; H, 3.33; N, 27.8. Found: C, 47.7; H, 3.66; N, 27.5.

2-Chloro-4,5-diaminopyridine (V).

4-Amino-2-chloro-5-nitropyridine (VI) (10 g.) in ethyl alcohol (200 ml.) was hydrogenated at 35 p.s.i. in a Parr apparatus. Raney nickel (5 g. wet) was used as catalyst. After 3 hours the hydrogenation bottle was removed, Celite (2 g.) was added, the solution was immediately filtered into 50 ml. of ethanol saturated with dry hydrogen chloride gas at 0°. After the mixture had cooled overnight at -20°, 10.5 g. (92.3%) of colorless crystalline 2-chloro-4,5-diaminopyridine hydrochloride was collected by filtration. This material was recrystallized from an ethyl alcohol and ethyl ether mixture to give colorless crystals m.p. 238-239°.

Anal. Calcd. for $C_5H_6ClN_3 \cdot 1^1/_2HCl$: C, 30.3; H, 3.81; N, 21.2. Found: C, 30.5; H, 3.74; N, 21.5.

6-Chloroimidazo[4,5-c]pyridine (IX).

2-Chloro-4,5-diaminopyridine (V) (7 g.) was added to a 1:1 mixture of ethyl orthoformate:acetic anhydride (100 ml.) and the solution refluxed for 2.5 hours. The excess reagents were removed *in vacuo* using a steam bath as a source of heat. The syrup was treated with 10% sodium hydroxide (15 ml.) and the solution stirred and heated on a steam bath for 10 minutes. This solution was neutralized to *p*H 7 with glacial acetic acid. The solid was separated by filtration, washed well with ice water and dried to yield 5.0 g. (92.5%) of 6-chloroimidazo[4,5-c]pyridine (IX). Several recrystallizations from an ethanol-*n*-heptane mixture gave a fine white powder which melted at 243.5-245°.

Anal. Calcd. for $C_6H_4ClN_3$: C, 46.9; H, 2.61; N, 27.3. Found: C, 46.7; H, 2.62; N, 27.2.

2,4-Diamino-5-nitropyridine (9) (X).

The procedure of Talik and Plazek (9) was modified as follows: Pure 4-amino-2-chloro-5-nitropyridine (VI) (3.0 g.) and concentrated ammonium hydroxide (150 ml.) were heated in a glass lined steel reaction vessel at 160° for 10 hours. After the reaction mixture had cooled, amber needles of 2,4-diamino-5-nitropyridine (2.0 g.) were removed by filtration. The filtrate was evaporated to a small volume *in vacuo* and an additional 0.5 g. of product was obtained by filtration for a total yield of 94%. The crude product was recrystallized from water, to yield light yellow needles, m.p. 197.5-198° (lit. (9) m.p. 166-168°).

Anal. Calcd. for $C_5H_6N_4O_2$: C, 39.0; H, 3.93; N, 36.3. Found: C, 39.3; H, 3.96; N, 36.6.

2,4,5-Triaminopyridine dihydrochloride (XI).

2,4-Diamino-5-nitropyridine (X) (2.0 g.) was hydrogenated in methanol (200 ml.) for 3 hours at 40 p.s.i. in a Parr hydrogenation apparatus. Raney nickel (2 g. wet) was used as catalyst. The solution was filtered into 50 ml. of methanol saturated at 0° with dry hydrogen chloride gas (care was taken to complete this process in a minimum amount of time since exposure to air, even for a few seconds, produced a red color in the neutral solution). After the filtrate had cooled overnight at -20°, 2.5 g. of the stable hydrochloride salt was obtained (97.5% yield). This product was recrystallized from a mixture of methanol and diethyl ether to give colorless crystals which darkened at 260° and melted at 298° dec.

Anal. Calcd. for $C_5H_8N_4 \cdot 2HCl$: C, 30.5; H, 5.11; N, 28.4. Found: C, 30.3; H, 5.09; N, 28.4.

6-Aminoimidazo[4,5-c]pyridine (XII).

2,4,5-Triaminopyridine (XI) (2.5 g.) was refluxed in a 1:1 mixture of ethyl orthoformate:acetic anhydride (75 ml.) for 3 hours. The excess reagents were removed *in vacuo*. The tan residue was heated in 20 ml. 10% sodium hydroxide solution for 5 minutes, neutralized to *p*H 7 with glacial acetic acid and the mixture was cooled for 14 hours at 10°. The solid was removed by filtration, and dried to yield 1.7 g. of 6-aminoimidazo[4,5-c]pyridine (yield nearly quantitative). This product was recrystallized from water to give colorless crystals which melted at 287° dec.

Anal. Calcd. for $C_6H_6N_4$: C, 53.8; H, 4.48; N, 41.8. Found: C, 53.7; H, 4.66; N, 42.0.

2,6-Dichloropyridine-1-oxide (XIV).

2,6-Dichloropyridine (XIII) (16.0 g.), trifluoroacetic acid (200 g.), and 30% hydrogen peroxide (22.5 ml.) were heated on a steam bath for 4 hours. After the solution had cooled to room temperature, 1,500 ml. of water was added. The precipitate which resulted (3 g.) was removed by filtration and was found to be unreacted 2,6-dichloropyridine. The yellow-orange filtrate was evaporated to a small volume at 30° *in vacuo* (20 mm. Hg.) and chloroform (500 ml.) was added to this residual material. This solution was treated with anhydrous potassium carbonate until carbon dioxide evolution had ceased. After removal of the drying agent the chloroform solution was evaporated to dryness *in vacuo* to afford 11.0 g. (62%) of colorless crystalline 2,6-dichloropyridine-1-oxide. After recrystallization from a mixture of benzene and heptane the product melted at 139.5-140.5°.

Anal. Calcd. for $C_5H_3Cl_2NO$: C, 36.6; H, 1.83; N, 8.54. Found: C, 36.8; H, 2.10; N, 8.70.

2,6-Dichloro-4-nitropyridine-1-oxide (XV).

2,6-Dichloropyridine-1-oxide (XIV) (0.9 g.) was added carefully to a mixture of concentrated sulfuric acid (20 ml.) and 90% fuming nitric acid (10 ml.) and the solution heated on a steam bath for 2 hours. The yellow-orange solution was cooled and poured onto 65 g. of crushed ice. The solution was neutralized with concentrated ammonium hydroxide while the temperature was maintained below 30°. The light yellow platelets (0.8 g., 79% yield) of 2,6-dichloro-4-nitropyridine-1-oxide (XV) which precipitated after the solution had cooled 14 hours at 10°, was recrystallized from water, m.p. 177-178.5°.

Anal. Calcd. for $C_5H_2Cl_2N_2O_3$: C, 28.7; H, 0.96; N, 13.4. Found: C, 28.8; H, 1.26; N, 13.5.

4-Amino-2,6-dichloropyridine (11) (XVIII).

2,6-Dichloro-4-nitropyridine-1-oxide (XV) (1.5 g.) was hydrogenated in methanol (100 ml.) at 35 p.s.i. for 2 hours using Raney nickel catalyst (1.5 g.). The catalyst was removed by filtration and the filtrate evaporated to dryness *in vacuo* to give 1.1 g. (99%) of colorless crystalline 4-amino-2,6-dichloropyridine. After recrystallization from hot water, the melting point was 172-173° (lit. (11) 176°).

Anal. Calcd. for $C_5H_4Cl_2N_2$: C, 36.8; H, 2.45; N, 17.2. Found: C, 36.7; H, 2.46; N, 17.0.

2,6-Dichloro-4-nitraminopyridine (XVII).

4-Amino-2,6-dichloropyridine (XVIII) (1.3 g.) was carefully added to 6.5 ml. of concentrated sulfuric acid. The mixture was cooled to 0° and 2.6 ml. of 90% nitric acid was added dropwise while the inside temperature was maintained below 10° with an acetone, dry ice bath. The solution was stirred for one hour at room temperature and then poured onto 26 g. of crushed ice and allowed to cool at 10° for 14 hours. The cream-colored precipitate which separated was removed by filtration, washed well with ice water, and dried to yield 1.4 g. (88%) of crystalline 2,6-dichloro-4-nitraminopyridine (XVII). A small sample was purified by recrystallization from hot water (charcoal added) to give a product, m.p. 114-115°.

Anal. Calcd. for $C_5H_3Cl_2N_3O_2$: C, 28.8; H, 1.44; N, 20.2. Found: C, 28.6; H, 1.69; N, 20.1.

4-Amino-2,6-dichloro-3-nitropyridine (XVI).

2,6-Dichloro-4-nitraminopyridine (XVII) (1.4 g.) was carefully added to 11 ml. of concentrated sulfuric acid and the solution heated on a steam bath for 20 minutes. The solution was then cooled to room temperature and poured onto 28 g. of ice at which time a creamy white precipitate was noted. The mixture was neutralized with concentrated ammonium hydroxide while the temperature was maintained below 20° with an acetone, dry ice bath. The mixture was cooled overnight at 10°, filtered and the product washed well with ice water to yield 1.0 g. (71%) of 4-amino-2,6-dichloro-3-nitropyridine (XVI). The product was recrystallized from a mixture of ethanol and water, m.p. of 142-143°. This compound exhibited strong lachrymatory properties.

Anal. Calcd. for $C_5H_3Cl_2N_3O_2$: C, 28.8; H, 1.44; N, 20.2. Found: C, 28.7; H, 1.62; N, 20.3.

3,4-Diamino-2,6-dichloropyridine (XIX).

4-Amino-2,6-dichloro-3-nitropyridine (XVI) (0.8 g.) was hydrogenated in methanol (100 ml.) at 35 p.s.i. for 2 hours using Raney nickel catalyst (1.0 g.). The solution was filtered into 20 ml. of methanol saturated at 0° with anhydrous hydrogen chloride gas and the solution evaporated to dryness *in vacuo* to give 0.8 g. of 3,4-diamino-2,6-dichloropyridine as the hydrochloride salt. After recrystallization

from a mixture of ethanol and ethyl acetate the melting point was 205-207°.

Anal. Calcd. for $C_5H_4Cl_2N_3 \cdot {}^1/_2HCl$: C, 30.5; H, 2.80; N, 21.4. Found: C, 30.2; H, 2.86; N, 21.4.

4,6-Dichloroimidazo[4,5-c]pyridine (XX).

3,4-Diamino-2,6-dichloropyridine (XIX) (0.7 g.) was added to a 1:1 mixture of ethyl orthoformate-acetate anhydride (7 ml.) and the solution refluxed for 30 minutes. The excess reagents were removed *in vacuo*. The residue was dissolved in 10 ml. of 10% sodium hydroxide and warmed on a steam bath for 5 minutes. The solution which resulted was cooled to room temperature, neutralized to *p*H of 6 with glacial acetic acid and the solution cooled for 14 hours at 10°. The precipitate which separated was removed by filtration to yield 0.6 g. of light tan material (90%). This residue was recrystallized from water containing a small amount of ethanol to yield white crystalline needles, m.p. 253-254°.

Anal. Calcd. for $C_6H_3Cl_2N_3$: C, 38.3; H, 1.61; N, 22.4. Found: C, 38.3; H, 1.94; N, 22.4.

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