

Pyrido[1,2-*b*]indazole and its Derivatives

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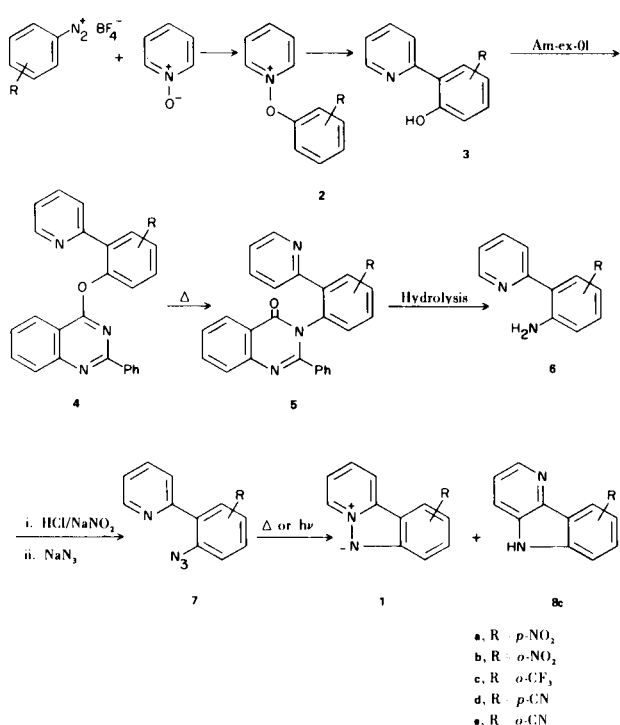
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Received April 29, 1974

A new route to pyrido[1,2-*b*]indazole and its derivatives is described and the nitration of the parent compound is reported. The formation of  $\delta$ -carbolines as byproducts is discussed.

Pyrido[1,2-*b*]indazole (**1**) was first prepared by heating 2-(2-nitrophenyl)pyridine with ferrous oxalate, or by the thermal or photochemical decomposition of 2-(2-azido-phenyl)pyridine (**1**). The corresponding nitro- and nitroso-derivatives have also been deoxygenated with triethylphosphite (**2**). Little is known about this ring system which is isomeric with the biologically interesting carboline ring system, and derivatives substituted at carbon have not been prepared until recently, probably because of the lack of readily available necessary precursors. Very recently, a number of derivatives of pyrido[1',2':2,3]pyrazolo[5,4-*c*]quinolin-6(5*H*)one have been prepared from the appropriate azide (**3**).

SCHEME 1

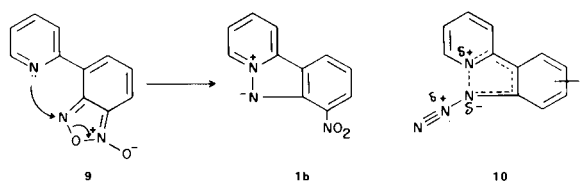


In 1971, we reported (4) a convenient synthesis of 2-(2-hydroxyphenyl)pyridines (**3**) by the base-catalyzed rearrangement of *N*-aryloxypyridinium salts (**2**), and this, coupled with the ready conversion of phenols to amines

(**5**) promised to lead to the desired 2-(2-aminophenyl)pyridines required for the synthesis of derivatives of **1**.

The approach is outlined in Scheme 1. Condensation of the sodium salts of the phenol **3** with 4-chloro-2-phenylquinazoline (**5**) (Am-ex-01) in dry *N,N*-dimethylacetamide gave **4** which, on heating, gave the O  $\rightarrow$  N migration products **5**. The course of the rearrangement could be followed conveniently by tlc. Hydrolysis of **5** was best carried out in two stages: alkaline hydrolysis to give the amidine followed by acidification to liberate **6**. The nitrile group in **5d** was stable to the hydrolytic conditions (50% aqueous ethanolic sodium hydroxide), but that in **5e** underwent hydrolysis and the desired **6e** was not obtained. Cyclization of **7** to **1** could be effected either by heating the azide alone or in toluene, or photochemically (3500 Å). A number of these cyclizations deserve comment.

When **7b** was decomposed it gave **1b** in high yield (81-94.5%), and no other product was isolated. The decomposition of *o*-nitrophenyl azide is known to proceed with intramolecular assistance at 65-80° (as compared with unassisted decompositions which proceed at 130-170°) to give benzofuroxan (**6**). No benzofuroxan derivative (**9**) was detected from **7b** and it is probable that it is formed initially but that it rearranges to give the more stable 8-nitropyrido[1,2-*b*]indazole (**1b**). Indeed, the fact that azides **7** give **1** in boiling toluene may suggest some degree of participation by the pyridine nitrogen lone pair in the decomposition of the azide (**10**) so that a free nitrene is not formed in most cases.

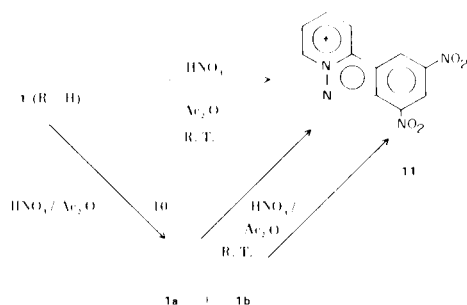


The situation in which a trifluoromethyl group is present *ortho* to the azide function, as in **7c**, is an interesting one, for while the CF<sub>3</sub> group cannot participate in the decomposition of the azide as does an *ortho* nitro-group, it is expected to sterically hinder the formation of a planar transition state as is postulated in **10**, so that assisted decomposition of the azide might no longer take

place. This indeed seems to be the case. The decomposition of **7c** in boiling toluene was very slow, requiring 72 hours. In the absence of solvent the thermolysis only took place at a convenient rate of 145°, as opposed to **7a**, **b**, and **d** which decomposed readily at 110°. Also significant was that in this case alone was some 6-trifluoromethyl- $\delta$ -carboline (**8c**) (28.8%) obtained. The latter is the product expected if a free nitrene were formed, consistent with an unassisted unimolecular decomposition of the azide. Ning, Madan, and Sternbach (3) reported the similar formation of some  $\delta$ -carboline derivatives, together with the expected pyrido[1,2-*b*]indazoles; the starting azide they used had a carbonyl group *ortho* to the azido function.  $\delta$ -Carboline formation had only been reported previously when the pyridine nitrogen atom was blocked by *N*-oxide formation, so that participation in the azide decomposition by the nitrogen lone pair was no longer possible (1). Earlier in the present work, being in need of the parent compound **1** (R = H) (*vide infra*), we repeated the cyclization of 2-(2-nitrophenyl)pyridine with ferrous oxalate. Previously, this had been shown to give consistently high yields of **1**, no primary amine 6 (R = H) or  $\delta$ -carboline (8; R = H) being isolated. We now obtained much lower yields of **1** (13-18%), together with appreciable quantities of **6** (21-25%) and **8** (4-6%). The only explanation we can think of which will account for this discrepancy is that the quality of the ferrous oxalate used in the two cases must have been different.

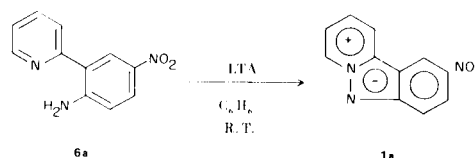
Electrophilic substitution of pyrido[1,2-*b*]indazole (**1**) has not been studied before. We have investigated its nitration. This proved to be remarkably facile. With an excess of nitric acid in either sulfuric acid or acetic anhydride at room temperature, it gave 6,8-dinitropyrido[1,2-*b*]indazole (**11**), whose structure followed from its spectroscopic properties and the transformations below. Mononitration was achieved by treating the ylide (**1**) with one equivalent of 41% nitric acid in acetic anhydride at -5 to -10°. A mixture of mono-nitro derivatives was obtained which could be resolved by preparative tlc into **1a** and **1b**, identical with the products obtained synthetically above. Further nitration of each one of these

SCHEME II



gave **11**, thus confirming the orientation of the substituents (Scheme II).

Attempts were made to bypass the preparation of **7** in the synthesis of **1**, with varying degrees of success. Oxidation of **6a** with lead tetraacetate in benzene at room temperature gave a fairly good yield of the desired **1a**. With the *ortho* nitro analog **6b**, however, prolonged boiling of the reaction mixture was necessary, which resulted in low yields of **1b**; starting material was recovered and much tar was formed. No oxidative cyclization was achieved when **6** (R = H) was treated with lead tetraacetate. The amine was decomposed by the reagent and much tar was formed. Manganic acetate, known to cause oxidative coupling of 1-aminobenzophenones to acridones (7), was not effective in causing the cyclization of **6** to **1**.



## EXPERIMENTAL

Melting points are uncorrected.

Compounds **3a-d** were prepared as described in the literature (4).

1-(2-Cyanophenoxy)-pyridinium Tetrafluoroborate (**2e**).

This was prepared (19.2%) from *o*-cyanobenzendiazonium tetrafluoroborate and pyridine-1-oxide, and had m.p. 160.5-162° dec., (methanol);  $\nu$  (potassium bromide): 2240 (C≡N), 1030-1150 cm<sup>-1</sup> (BF<sub>4</sub><sup>-</sup>); nmr (DMSO-d<sub>6</sub>):  $\delta$  9.08 (t, 2, H<sub>2</sub>, H<sub>6</sub>), 8.2 (m, 1, H<sub>4</sub>), 7.8 (m, 2, H<sub>3</sub>, H<sub>5</sub>), 7.46 (q, *J*<sub>3'4'</sub> = 4 Hz, *J*<sub>3'5'</sub> = 1 Hz, 1, H<sub>3</sub>), 7.2-6.8 (m, 2, H<sub>4</sub>, H<sub>5'</sub>), 6.4 (d, *J*<sub>5'6'</sub> = 4 Hz, 1, H<sub>6'</sub>).

Anal. Calcd. for C<sub>12</sub>H<sub>9</sub>N<sub>2</sub>OBF<sub>4</sub>: C, 50.74; H, 3.20. Found: C, 50.76; H, 3.20.

2-(3-Cyano-2-hydroxyphenyl)pyridine (**3e**).

It was obtained in 28.5% yield from **2e** and potassium phenoxide in acetonitrile and had m.p. 180-182° (ethanol);  $\nu$  (potassium bromide): 2240 cm<sup>-1</sup> (C≡N); nmr (trifluoroacetic acid):  $\delta$  8.79 (d, *J*<sub>5,6</sub> = 3 Hz, 1, H<sub>6</sub>), 8.64 (d, *J*<sub>3,4</sub> = 4 Hz, 1, H<sub>4</sub>), 8.36 (d, *J*<sub>3,4</sub> = 4 Hz, 1, H<sub>3</sub>), 8.14-7.76 (m, 3, H<sub>5</sub>, H<sub>4'</sub>, H<sub>6'</sub>), 7.36 (t, *J*<sub>4'5'</sub> = *J*<sub>5'6'</sub> = 4 Hz, 1, H<sub>5'</sub>).

Anal. Calcd. for C<sub>12</sub>H<sub>8</sub>N<sub>2</sub>O: C, 73.46; H, 4.12. Found: C, 73.23; H, 4.17.

4-[4-Nitro-2-(2-pyridyl)phenoxy]-2-phenylquinazoline (**4a**).

Compound **3a** (1.5 g., 0.007 mole) in a solution of sodium hydroxide (0.29 g., 0.007 mole) in water (20 ml.) and acetone (5 ml.) was evaporated to dryness. The orange solid was dried overnight in a vacuum desiccator over phosphorus pentoxide and then dissolved in dry (8) *N,N*-dimethylacetamide (80 ml.). Amex-01 (1.6 g.) was added and the solution was boiled under reflux for 10 hours, cooled, evaporated to one third of its volume under vacuum, and poured into water (200 ml.). The precipitate was filtered and recrystallized from ethanol to give **4a** (2 g., 69%); m.p. 188-190°;  $\nu$  (potassium bromide): 1620, 1515 (NO<sub>2</sub>); 1390, 1370, 1340 (NO<sub>2</sub>), and 1210 cm<sup>-1</sup>; nmr (trifluoroacetic

TABLE I

Compound	Reaction Time, Hours	Yield (%)	M.p.	Recryst. solvent	Ir (cm <sup>-1</sup> )
<b>4b</b>	10	70	172.5-174°	Ethanol	1618, 1528 (NO <sub>2</sub> ), 1372, 1348 (NO <sub>2</sub> ), 1218
<b>4c</b> (a)	5	72	138-139°	Methanol	1630, 1385, 1360, 1340 (CF <sub>3</sub> ), 1225, 940
<b>4d</b> (a)	5	75	181-183°	Ethanol	2245 (C≡N), 1630, 1385, 1360, 1225, 945
<b>4e</b> (a)	5	87	148-150°	Aqueous Ethanol	2240 (C≡N), 1625, 1375, 1345, 1205, 930

(a) The initial sodium salt was prepared using sodium ethoxide in ethanol.

TABLE II

Compound	Yield (%)	M.p.	Recryst. solvent	Ir (cm <sup>-1</sup> )
<b>5b</b>	70	166.5-168.5°	Acetone	1670, 1529 (NO <sub>2</sub> ), 1340 (NO <sub>2</sub> ), 1265
<b>5c</b>	79.5	157-158°	Ether-Hexane	1690, 1335 (CF <sub>3</sub> ), 1270
<b>5d</b>	72	217.5-218.5°	Ethanol	2190 (C≡N), 1670, 1265
<b>5e</b>	80	193-194.5°	Ethanol	2240 (C≡N), 1690, 1270

$\delta$  9.0-7.46; mass spectrum: *m/e* 420 (M<sup>+</sup>), 390 (M<sup>+</sup>-NO), 374 (M<sup>+</sup>-NO<sub>2</sub>).

*Anal.* Calcd. for C<sub>25</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub>: C, 71.41; H, 3.83. Found: C, 71.43; H, 3.94.

The following compounds in Table I were prepared similarly. 3-[4-Nitro-2-(2-pyridyl)phenyl]-2-phenyl-4(3H)quinazolinone (**5a**).

The quinazolinone **4a** (2.6 g., 0.0062 mole) was heated under nitrogen at 300-310° for 30 minutes. The indicated complete conversion of **4a** to **5a**. The solid was dissolved in hot acetone, treated with charcoal, filtered and concentrated to give **5a** (2 g., 77%), m.p. 222-224°; ir (potassium bromide): 1674, 1520 (NO<sub>2</sub>), 1340 (NO<sub>2</sub>), and 1270 cm<sup>-1</sup>; nmr (trifluoroacetic acid):  $\delta$  9.01 (d, *J* = 3 Hz, 1), 8.78-7.4 (m, 15); mass spectrum: *m/e* 420 (M<sup>+</sup>), 390 (M<sup>+</sup>-NO), 374 (M<sup>+</sup>-NO<sub>2</sub>).

*Anal.* Calcd. for C<sub>25</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub>: C, 71.41; H, 3.83. Found: C, 71.45; H, 3.95.

The following compounds in Table II were prepared similarly. 2-(2-Amino-5-nitrophenyl)pyridine (**6a**).

3-[4-Nitro-2-(2-pyridyl)phenyl]-2-phenyl-4(3H)quinazolinone (**5a**) (1 g.) was boiled under reflux for 1 hour in ethanol (40 ml.) containing a 50% aqueous solution (4 g.) of sodium hydroxide. The reaction mixture was cooled and acidified to pH 1 with 12*N* hydrochloric acid. It was then heated at 40-50° for 45 minutes, the alcohol was evaporated under reduced pressure, the residue diluted with water and brought to pH 8. The precipitate was filtered and recrystallized from dilute acetone to give **6a** (0.28 g., 53%), m.p. 141-143°; ir (potassium bromide): 3435, 3295 (NH<sub>2</sub>), 1605, 1580, 1470 (NO<sub>2</sub>), 1305 cm<sup>-1</sup> (NO<sub>2</sub>) (9); nmr (deuteriochloroform):  $\delta$  6.85 (br s, 2, exchanges with deuterium oxide, NH<sub>2</sub>); mass spectrum: *m/e* 215 (M<sup>+</sup>), 185 (M<sup>+</sup>-NO), 176 (M<sup>+</sup>-HCN-H<sub>2</sub>), 169 (M<sup>+</sup>-NO<sub>2</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>: C, 61.40; H, 4.21. Found: C, 61.37; H, 4.31.

The following amines were prepared similarly.

2-(2-Amino-3-nitrophenyl)pyridine (40%), m.p. 95-96° (ethanol (after purification by column chromatography on silica gel); nmr (deuteriochloroform):  $\delta$  8.54 (d, *J*<sub>5,6</sub> = 2.5 Hz, 1, H<sub>6</sub>), 8.5 (over-

lapping signal at  $\delta$  8.54) (br, 2, exchanges with deuterium oxide, NH<sub>2</sub>), 8.14 (d, *J*<sub>4',5'</sub> = 4 Hz, 1, H<sub>4'</sub>), 7.84-7.53 (m, 3, H<sub>3</sub>, H<sub>4</sub>, H<sub>6</sub>), 7.22 (t, *J*<sub>4,5</sub> = *J*<sub>5,6</sub> = 2.5 Hz, 1, H<sub>5</sub>), 6.62 (t, *J*<sub>4',5'</sub> = *J*<sub>5',6'</sub> = 4 Hz, 1, H<sub>5'</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>: C, 61.40; H, 4.21. Found: C, 61.41; H, 4.30.

2-(2-Amino-3-trifluoromethylphenyl)pyridine (71%), b.p. 112-115° /0.1 mm (after purification by column chromatography); ir (film): 3480, 3280 (NH<sub>2</sub>), 1340 cm<sup>-1</sup> (CF<sub>3</sub>); nmr (deuteriochloroform):  $\delta$  8.50 (d, *J*<sub>5,6</sub> = 2.5 Hz, 1, H<sub>6</sub>), 7.7-7.4 (m, 4, H<sub>3</sub>, H<sub>4</sub>, H<sub>4'</sub>, H<sub>6'</sub>), 7.07 (m, *J*<sub>5,6</sub> = *J*<sub>4,5</sub> = 2.5 Hz, *J*<sub>3,5</sub> = 1 Hz, 1, H<sub>5</sub>), 6.66 (t, *J*<sub>4',5'</sub> = *J*<sub>5',6'</sub> = 4 Hz, 1, H<sub>5'</sub>), 6.4 (br s, 2, exchanges with deuterium oxide, NH<sub>2</sub>).

*Anal.* Calcd. for C<sub>12</sub>H<sub>9</sub>F<sub>3</sub>N<sub>2</sub>: C, 60.49; H, 3.80. Found: C, 60.51; H, 4.01.

2-(2-Amino-5-cyanophenyl)pyridine (**6d**) (52%), colorless oil; ir: 3410, 3280 (NH<sub>2</sub>), 2200 cm<sup>-1</sup> (C≡N). The crude amine was converted directly to the azide **7d**.

2-(2-Azido-5-nitrophenyl)pyridine (**7a**).

A solution of sodium nitrite (0.145 g.) in water (5 ml.) was added dropwise with stirring at 0-5° to 2-(2-amino-5-nitrophenyl)pyridine (**6a**) (0.45 g.) in concentrated hydrochloric acid (3.5 ml.) and water (50 ml.). After stirring for an additional 35 minutes the solution was neutralized with a suspension of calcium carbonate in water and a solution of sodium azide (0.13 g.) in water (5 ml.) was added dropwise with cooling. The faint yellow precipitate was filtered and washed with water to give **7a** (0.38 g., 78%), m.p. 110° dec. It was dissolved in ether, the solution filtered, and added to an equal volume of hexane and concentrated *in vacuo* at room temperature to give the azide, m.p. 111-112° (dec.); ir (potassium bromide): 2120 (N<sub>3</sub>), 1520 and 1340 cm<sup>-1</sup> (NO<sub>2</sub>); nmr (deuteriochloroform):  $\delta$  8.61 (d, *J*<sub>4',5'</sub> = 1 Hz, 1, H<sub>6'</sub>), 8.8-8.52 (m, 1, H<sub>6</sub>), 8.25 (q, *J*<sub>3',4'</sub> = 4.5 Hz, *J*<sub>4',6'</sub> = 1 Hz, 1, H<sub>4'</sub>), 7.86-7.58 (m, 2, H<sub>3</sub>, H<sub>4</sub>), 7.33 (d, *J*<sub>3',4'</sub> = 4.5 Hz, 1, H<sub>3'</sub>), 7.44-7.1 (m, 1, H<sub>5</sub>); mass spectrum: *m/e* 213 (M<sup>+</sup>-N<sub>2</sub>), 183 (M<sup>+</sup>-N<sub>2</sub>-NO), 167 (M<sup>+</sup>-N<sub>2</sub>-NO<sub>2</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>7</sub>N<sub>5</sub>O<sub>2</sub>: C, 54.77; H, 2.93. Found: C, 54.58; H, 3.28.

The following azides were prepared similarly.

2-(2-Azido-3-nitrophenyl)pyridine (**7b**) (91.5%), m.p. 97-98° dec.; ir (potassium bromide): 2125 (N<sub>3</sub>), 1515 and 1340 cm<sup>-1</sup> (NO<sub>2</sub>); mass spectrum: m/e 213 (M<sup>+</sup>-N<sub>2</sub>), 183 (M<sup>+</sup>-N<sub>2</sub>-NO), 167 (M<sup>+</sup>-N<sub>2</sub>-NO<sub>2</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>7</sub>N<sub>5</sub>O<sub>2</sub>: C, 54.77; H, 2.93. Found: C, 54.76; H, 2.95.

2-(2-Azido-3-trifluoromethylphenyl)pyridine (**7c**) (76%), m.p. 49.5-51.5° (hexane); ir: 2120 (N<sub>3</sub>), 1330 cm<sup>-1</sup> (CF<sub>3</sub>).

*Anal.* Calcd. for C<sub>12</sub>H<sub>7</sub>N<sub>4</sub>F<sub>3</sub>: C, 54.55; H, 2.67. Found: C, 54.66; H, 2.75.

2-(2-Azido-5-cyanophenyl)pyridine (**7d**) (70%), m.p. 118-119° dec.; ir (potassium bromide): 2250 (C≡N), 2140 (N<sub>3</sub>); nmr (deuteriochloroform): δ 9.17 (d, J<sub>5,6</sub> = 2.5 Hz, 1, H<sub>6</sub>), 8.50 (s, 1, H<sub>6</sub>'), 8.30-8.06 (m, 3, H<sub>3</sub>, H<sub>4</sub>, H<sub>4</sub>'), 7.78 (d, J<sub>3',4'</sub> = 4 Hz, 1, H<sub>3</sub>') superimposed on (m, 1, H<sub>5</sub>).

*Anal.* Calcd. for C<sub>12</sub>H<sub>7</sub>N<sub>5</sub>: C, 65.15; H, 3.19. Found: C, 65.08; H, 3.2.

#### 6-Nitropyrido[1,2-*b*]indazole (**1a**).

##### (a) By Decomposition of **7a**.

2-(2-Azido-5-nitrophenyl)pyridine (**7a**) (0.154 g.) was heated alone under nitrogen at 110°. A vigorous exothermic reaction occurred. The yellow solid was recrystallized from ethanol to give **1a** (0.08 g., 59%), m.p. 256-258°; ir (potassium bromide): 1640 (Ar-N) (1), 1490 and 1308 cm<sup>-1</sup> (NO<sub>2</sub>); nmr (trifluoroacetic acid): δ 9.4 (d, J<sub>5,7</sub> = 1 Hz, 1, H<sub>5</sub>), 9.45-9.24 (m, 1, H<sub>1</sub>), 8.8 (q, J<sub>5,7</sub> = 1 Hz, J<sub>7,8</sub> = 4.5 Hz, 1, H<sub>7</sub>), 8.94-8.72 (m, 1, H<sub>3</sub>), 8.36 (t, J<sub>2,3</sub> = J<sub>1,2</sub> = 3.5 Hz, 1, H<sub>2</sub>), 8.0 (d, J<sub>7,8</sub> = 4.5 Hz, 1, H<sub>8</sub>), 8.12-7.94 (m, 1, H<sub>4</sub>); mass spectrum: m/e 213 (M<sup>+</sup>), 183 (M<sup>+</sup>-NO), 167 (M<sup>+</sup>-NO<sub>2</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>7</sub>N<sub>3</sub>O<sub>2</sub>: C, 61.97; H, 3.31. Found: C, 61.85; H, 3.41.

##### (b) By Oxidative Coupling of **6a**.

2-(2-Amino-5-nitrophenyl)pyridine (**6a**) (0.1 g.) in dry benzene (15 ml.) was added dropwise to lead tetraacetate (0.25 g.) in dry benzene (15 ml.) with stirring. When the addition was complete another portion of lead tetraacetate (0.25 g.) was added and the mixture was stirred at room temperature for 5 hours. Tlc indicated that some starting amine remained. The benzene solution was washed with 5% aqueous sodium carbonate, dried (magnesium sulfate) and evaporated to give a yellow solid. This, or recrystallization from ethyl acetate, gave **1a** (0.026 g.), m.p. 255-257°, undepressed on admixture with a sample obtained as under (a), and identical in ir to it. A further amount (8 mg.) could be resolved from unchanged amine (17 mg.) by preparative tlc (hexane-ethyl acetate 3:2 v/v). Overall yield based on recovered amine: 41.5%.

#### 8-Nitropyrido[1,2-*b*]indazole (**1b**).

##### (a) Thermolysis of the Azide.

Decomposition of **7b** followed by preparative tlc of the product (using hexane-ethyl acetate 1:1 v/v as the developer) gave traces of unreacted azide and of a compound with a light blue fluorescence, and **1b** (81%), m.p. 240-241° (ethanol); ir (potassium bromide): 1640 (Ar-N), 1495 and 1300 cm<sup>-1</sup> (NO<sub>2</sub>); nmr (trifluoroacetic acid): δ 9.36 (d, J<sub>1,2</sub> = 4 Hz, 1, H<sub>1</sub>), 8.88-8.72 (m, 3, H<sub>3</sub>, H<sub>5</sub>, H<sub>7</sub>), 8.38 (t, J<sub>1,2</sub> = J<sub>2,3</sub> = 4 Hz, 1, H<sub>2</sub>), 8.1-7.78 (m, 2, H<sub>4</sub>, H<sub>6</sub>); mass spectrum: m/e 213 (M<sup>+</sup>), 183 (M<sup>+</sup>-NO), 167 (M<sup>+</sup>-NO<sub>2</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>7</sub>N<sub>3</sub>O<sub>2</sub>: C, 61.97; H, 3.31. Found: C, 62.10; H, 3.36.

##### (b) Thermolysis in Toluene.

The azide (0.092 g.) in dry toluene (10 ml.) was boiled under reflux under nitrogen for 8 hours. The product (0.075 g., 94.5%) was thus isolated, identical with that obtained above.

##### (c) Photolysis.

The azide (0.09 g.) in methylene chloride (250 ml.) was irradiated using 3500 Å lamps for 3 hours to give **1b** (0.073 g., 92%).

##### (d) Oxidative Coupling of **6b**.

A mixture of **6b** (0.1 g.) and lead tetraacetate (0.52 g.) in dry benzene (25 ml.) was stirred at room temperature for 3 hours and then boiled under reflux for 36 hours. The cooled solution was washed with 5% aqueous potassium carbonate and then with water, dried (magnesium sulfate) and evaporated to dryness. Preparative tlc of the residue gave **1b** (0.008 g., 10%).

##### Thermolysis of **7c** in Toluene.

2-(2-Azido-3-trifluoromethylphenyl)pyridine (**7c**) (0.1 g.) in dry toluene (10 ml.) was boiled under reflux for 1 hour. Tlc analysis indicated that the azide was almost completely undecomposed. Boiling of the solution was continued for 72 hours by which time all the azide had decomposed. The products were resolved by preparative tlc on silica gel using hexane-ethyl acetate (4:1.5 v/v) as the developer to give: 8-trifluoromethylpyrido[1,2-*b*]indazole (**1c**) (43.6%), R<sub>f</sub> = 0.50, m.p. 142.5-143.5°; ir (potassium bromide): 1645 (Ar-N), 1330 cm<sup>-1</sup> (CF<sub>3</sub>); nmr (deuteriochloroform): δ 8.84 (d, J<sub>1,2</sub> = 2.5 Hz, 1, H<sub>1</sub>), 8.14-7.74 (m, 3), 7.4-7.06 (m, 3).

*Anal.* Calcd. for C<sub>12</sub>H<sub>7</sub>F<sub>3</sub>N<sub>2</sub>: C, 61.01; H, 2.98. Found: C, 61.09; H, 3.05.

6-Trifluoromethyl-8-carboline (**8c**) (28.8%), R<sub>f</sub> = 0.36, m.p. 198-199.5°; ir: 3200 (NH), 1320 cm<sup>-1</sup> (CF<sub>3</sub>); nmr (deuteriochloroform): δ 9.26 (br s, 1, exchangeable, NH), 8.7-8.4 (m, 2), 7.84-7.66 (m, 2), 7.46-7.20 (m, 2).

*Anal.* Calcd. for C<sub>12</sub>H<sub>7</sub>F<sub>3</sub>N<sub>2</sub>: C, 61.01; H, 2.98; N, 11.86. Found: C, 60.65; H, 3.04; N, 11.87.

#### 6-Cyanopyrido[1,2-*b*]indazole (**1d**).

The azide **7d** (0.07 g.) in dry toluene (10 ml.) was boiled under reflux under nitrogen for 6 hours to give **1d** (0.052 g., 85.5%), m.p. 223-224° (ethanol); ir: 2210 (C≡N), 1640 cm<sup>-1</sup> (Ar-N); nmr (trifluoroacetic acid): δ 9.23 (d, J<sub>1,2</sub> = 4 Hz, H<sub>1</sub>), 8.90 (s, 1, H<sub>5</sub>), 8.74 (d, J<sub>7,8</sub> = 4 Hz, 1, H<sub>7</sub>), 8.4-7.88 (m, 4, H<sub>2</sub>, H<sub>3</sub>, H<sub>4</sub>, H<sub>8</sub>).

*Anal.* Calcd. for C<sub>12</sub>H<sub>7</sub>N<sub>3</sub>: C, 74.60; H, 3.65. Found: C, 74.67; H, 3.62.

#### Action of Ferrous Oxalate Dihydrate on 2-(2-Nitrophenyl)pyridine.

2-(2-Nitrophenyl)pyridine was heated with ferrous oxalate dihydrate at 300° as described earlier (1). The crude reaction mixture was analyzed by preparative tlc on silica gel (hexane-ethyl acetate 3:1 v/v) to give: pyrido[1,2-*b*]indazole (**1**; R = H) (13-18%), R<sub>f</sub> = 0.35, identical with an authentic sample (1); 2-(2-aminophenyl)pyridine (**6**; R = H) (21-25%), R<sub>f</sub> = 0.53, identical with an authentic sample (10); and δ-carboline (**8**; R = H) (4-6%), R<sub>f</sub> = 0.21, identical with an authentic sample (11).

#### 6,8-Dinitropyrido[1,2-*b*]indazole (**11**).

A solution of 41% nitric acid (0.5 g.) in acetic anhydride (5 ml.) was added dropwise to a solution of pyrido[1,2-*b*]indazole (0.16 g.) in acetic anhydride (10 ml.) at 0°. The solution was stirred for 1 hour at room temperature then poured onto ice to

give the dinitro-compound (**11**), m.p.  $> 360^\circ$  (dichloromethane);  $\nu$ : 1640 (ArN), 1498 and 1303  $\text{cm}^{-1}$  ( $\text{NO}_2$ ); nmr (trifluoroacetic acid):  $\delta$  9.8-9.5 (m, 3, H<sub>1</sub>, H<sub>5</sub>, H<sub>7</sub>), 9.3-9.0 (m, 1, H<sub>3</sub>), 9.0-8.0 (m, 2, H<sub>2</sub>, H<sub>4</sub>); mass spectrum: m/e 258 ( $\text{M}^+$ ), 228 ( $\text{M}^+ - \text{NO}$ ), 212 ( $\text{M}^+ - \text{NO}_2$ ), 182 ( $\text{M}^+ - \text{NO} - \text{NO}_2$ ), 166 ( $\text{M}^+ - 2\text{NO}_2$ ).

Anal. Calcd. for  $\text{C}_{11}\text{H}_6\text{N}_4\text{O}_4$ : C, 51.17; H, 2.34; N, 21.70. Found: C, 51.63; H, 2.36; N, 21.70.

The same product was obtained by the nitration of **1** (R = H), **1a**, or **1b** in sulfuric acid at 20-50° using slightly more than a two-fold excess of 41% nitric acid. The yields were 90, 96, and 96%, respectively.

#### Mononitration of Pyrido[1,2-*b*]indazole.

To a solution of **1** (R = H) (0.12 g.) in acetic anhydride (5 ml.) was added 41% nitric acid (0.085 ml.) in acetic anhydride (2 ml.) dropwise at -10°. The solution was stirred at that temperature for 1.5 hours, it was then poured over ice and the precipitated 6-nitropyrido[1,2-*b*]indazole (0.085 g., 55%) was filtered and was found to be identical with authentic **1a**. The filtrate was extracted with methylene chloride, the extract was dried and evaporated, and the residue was purified by preparative tlc (hexane-ethyl acetate 1:1 v/v) to give 8-nitropyrido[1,2-*b*]indazole (0.008 g., 5.2%), identical with an authentic sample of **1b**.

#### Acknowledgements.

We wish to thank the Polish Academy of Sciences for a leave of absence to J. K. and the National Institutes of Health for financial support of this work (CA 15628).

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