

## Synthesis of Some Substituted Pyridylsydnones (1a)

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Synthesis of the 1-oxide (**2**) of the photochromic *N*-(3-pyridyl) sydnone (**1**), of *N*-(5-bromo-3-pyridyl) sydnone (**3**), and the 1-oxide (**4**) of **3** were undertaken in order to study the effect on photochromism exerted by substituents on the pyridine ring. Compounds **2** and **3** were prepared *via* the corresponding aminopyridines and *N*-pyridylglycines by the general procedure used earlier to prepare **1**. The required amines, 3-aminopyridine 1-oxide and 3-amino-5-bromopyridine, were obtained by Hofmann rearrangement of the corresponding amides. An excellent preparation of 5-bromonicotinamide was developed involving bromination in thionyl chloride followed by reaction of the bromoacid chloride with ammonia in chloroform. Proof of structure for **2** and **3** was accomplished by acid hydrolysis to the corresponding hydrazines, which were isolated, respectively, as acetophenone 3-pyridylhydrazone 1-oxide and as 5-bromo-3-pyridylhydrazine hydrochloride. These products were identical with samples prepared by reduction of the respective diazotized amines. Sydnone **4** eluded preparation by this general procedure. 3-Amino-5-bromopyridine 1-oxide was prepared conveniently from 5-bromonicotinamide but attempts to prepare the corresponding glycine by catalytic hydrogenation of a mixture of the amine and butyl glyoxylate afforded, in acid solution, *N*-(3-pyridyl)glycine and, in neutral or alkaline solution, the 1-oxide of *N*-(3-pyridyl)glycine. Both products resulted from the reductive cleavage of the bromine atom. Neither **2** nor **3** was photochromic.

In the course of the preparation of various monosubstituted hydrazines *via* sydnones (2a), the first *N*-heteroarylsydnone to be prepared, namely *N*-(3-pyridyl)sydnone (**1**) unexpectedly was found to be photochromic (2b).

The syntheses presented here of the 1-oxide of *N*-(3-pyridyl)sydnone (**2**), *N*-(5-bromo-3-pyridyl)sydnone (**3**), and the 1-oxide of *N*-(5-bromo-3-pyridyl)sydnone (**4**) were undertaken for the express purpose of studying the effect of substituted pyridines on pyridylsydnone photochromism.

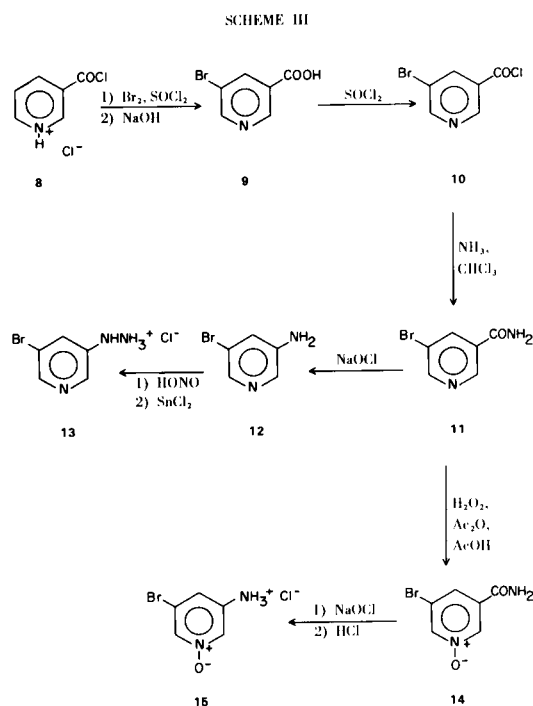
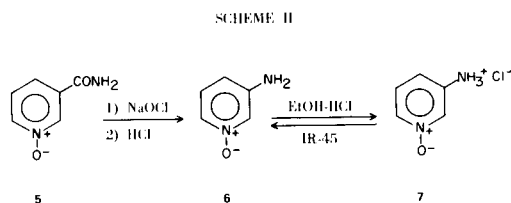
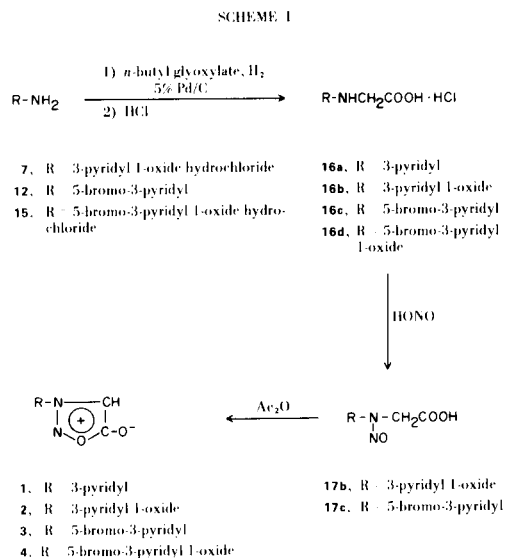
*N*-(3-Pyridyl)sydnone (**1**) was synthesized (2b) by the procedure shown in Scheme I, where R is 3-pyridyl. The compounds **2** and **3** (R = 3-pyridyl 1-oxide and 5-bromo-3-pyridyl, respectively) also were prepared by this general procedure.

3-Aminopyridine 1-oxide hydrochloride (**7**, Scheme II), required for the preparation of **2**, had been prepared by Leonard and Wajngurt (3) and also by Jaffe and Doak (4), both groups using essentially the same procedure, namely oxidation of the acetylated 3-aminopyridine with peracetic acid. The low yields obtained by these workers warranted investigation of an alternate procedure. The 3-aminopyridine 1-oxide used in this synthesis was prepared successfully and in high yield by application of a Hofmann rearrangement to nicotinamide 1-oxide (**5**). Application of Allen and Wolf's (5) procedure in the initial experiments

produced some nicotinic acid 1-oxide. This was not unexpected since hydrolysis of an amide may occur prior to its rearrangement (**6**). The report that the rearrangement has a higher temperature coefficient than the hydrolysis and that higher temperatures reduce interference from hydrolysis of the amide to negligible proportions (7) led us to raise the temperature of the rearrangement (85-90°) which gave high yields of **6**.

Murray and Hauser (8) prepared **6** by treatment of 3-bromopyridine 1-oxide with an ammonium hydroxide-cupric sulfate solution, crystals of the amine oxide hydrate being precipitated from chloroform-water-ethanol by cooling in dry ice. Brown (9) found the 2-amino isomer was stable to air but the 4-aminopyridine 1-oxide could only be isolated as its hydrochloride salt (10). Our crude amine oxide **6** could be stored several months in a vacuum desiccator without deterioration. However, a pure sample, conveniently obtained by treating **7** with Amberlite IR-45 ion exchange resin, and obtained as a white powder after sublimation, soon acquired a light green color. After several days the sample turned light brown. It has been reported the 4-amino isomer is oxidized in air to the azo compound.

3-Amino-5-bromopyridine (**12**, Scheme III) needed for the preparation of **3**, had been previously prepared in low yield from 3,5-dibromopyridine by sealed tube amination



(11) and in unspecified yield by application of the Curtius reaction to the hydrazide of 5-bromonicotinamide (12).

The 5-bromonicotinic acid (**9**) required in the latter procedure may be prepared in low yield by oxidation of 3-bromoquinoline followed by decarboxylation of the bromoquinolinic acid (**13**) or in unspecified yield by the Sandmeyer reaction on 5-aminonicotinic acid (**12**). The latter compound was prepared by a sealed tube amination of 5-chloronicotinic acid, which in turn resulted in low yield, along with 5,6-dichloronicotinic acid, from the sealed tube chlorination of nicotiny chloride with thionyl chloride (**14**).

It appeared desirable, in view of the low yields and the apparent inconvenience of these processes, to formulate a new synthesis of **12** by application of the Hofmann reaction to 5-bromonicotinamide (**11**). Although this amide had not been reported in the literature, the corresponding acid **9** had been prepared, as mentioned above, in a variety of ways. Hawkins and Roe (15) oxidized 3-bromoquinoline to 5-bromonicotinic acid (**9**) in 38% yield. Gilman and Spatz (16) prepared **9** in 41% yield by carbonation of the lithium derivative of 3,5-dibromopyridine, while Bachman and Micucci (17) prepared **9** in 87% yield by bromination of nicotiny chloride at 150-170° (apparently in a sealed tube) followed by hydrolysis. Although the experimental directions of the last-named authors (17) were not explicit, the procedure described herein represents a modification of their method.

It is known that thionyl chloride may be used as a solvent for brominating carboxylic acids (18). Thus, a gently refluxing solution of nicotiny chloride hydrochloride (**8**), prepared according to Mndzhoyan (19), was treated with 1.5 molar equivalents of bromine during some twelve hours which afforded **9** in yields of 43-66%. 5-Bromonicotinamide (**11**) was obtained from 5-bromonicotinyl chloride (**10**) in yields as high as 80% by addition to chloroform saturated with anhydrous ammonia.

Application of the Hofmann reaction to the amide **11** produced the bromoamine **12** in yields of 67%. Initial attempts at this rearrangement using excess sodium hypochlorite afforded 5,5'-dibromo-3,3'-azopyridine (**20**).

Although a completely rigorous proof of structure was not performed, certain factors support the bromination product as the 5-bromo isomer **9**. The melting point agrees with the literature values (12,16,17), the amide **11** was converted to the known amine **12** (11,12) which in turn was converted by reduction of its diazonium salt to the known (21) 5-bromo-3-pyridylhydrazine hydrochloride (**13**). Some indirect support for this assignment is the report (14) of a preparation of 3-chloroisonicotinic acid with thionyl chloride at elevated temperatures which was later shown (22) to actually be the 2-chloroisonicotinic acid. The chlorination occurred *meta* not *ortho* to the carboxyl group.

The reaction mechanism for this facile bromination has not been elucidated. The reaction temperature required (*ca.* 79°), compared with the extreme conditions for brominating pyridine itself (23), appear to reject any straightforward electrophilic process. Results obtained from an extension of this method of halogenation (24) appear to support a proposed mechanism (25).

5-Bromonicotinamide 1-oxide (14) was prepared in yields of 45-81% by heating the amide 11 in a solution of peracetic acid in glacial acetic acid (26) for nine hours on a steam bath. Treatment of 14 with sodium hypochlorite produced 3-amino-5-bromopyridine 1-oxide (15), isolated as the hydrochloride salt in yields of 31-85%. We found 11 more resistant to oxidation than nicotinamide (27). This is explicable on the basis of a cumulative effect by the bromine and the amide substituents in decreasing the electron density on the ring nitrogen atom (28).

Although it has been reported (29) that amine oxides are deoxygenated by catalytic (palladium) reduction in a hydrochloric acid medium, 3-aminopyridine 1-oxide hydrochloride (7) was converted in 60% yield to the 1-oxide of *N*-(3-pyridyl)glycine hydrochloride (16b, Scheme I) by reductive amination of *n*-butylglyoxylate (30) with 5% palladium on charcoal. Initial attempts to prepare *N*-(5-bromo-3-pyridyl)glycine hydrochloride (16c) by the same procedure (1c,2b,31) resulted in hydrogenolysis of the bromine substituent with formation of *N*-(3-pyridyl)glycine hydrochloride (16a) as determined by melting point, neutral equivalent and combustion analysis. Careful control of the pressure change during hydrogenation gave the desired bromoglycine hydrochloride 16c. The replacement of a 2- or 4-bromine substituent might be expected, but hydrogenolysis of the 3-bromine substituent certainly was unexpected. Likewise, attempts to prepare the 1-oxide of *N*-(5-bromo-3-pyridyl)glycine hydrochloride (16d) by the same procedure using 15 resulted in the production of 16a. The reduction of the *N*-oxide function was not totally unexpected (29) in acidic media and hydrogenolysis of the bromine substituent is less remarkable in the case of 16d than in 16c since the *N*-oxide function has the greater electron withdrawing effect. An attempt at hydrogenation in neutral or alkaline solution merely preserved the *N*-oxide function, 16b being isolated. Attempts to prepare 16d by oxidation of 16c with 40% peracetic acid were unsuccessful.

The glycines 16b and 16c were nitrosated to afford the nitrosoglycines 17b and 17c, respectively. Dehydrative cyclization with acetic anhydride converted these nitrosoglycines to the respective sydnones 2 and 3.

Proof of structure of sydnone 2 and the absence of *N*-oxide rearrangement during treatment of 16b with acetic anhydride was shown by (i) catalytic reduction of the *N*-oxide moiety using W-6 Raney nickel to produce

the phototropic sydnone 1 and (ii) by acidic hydrolysis of 2 to 3-pyridylhydrazine 1-oxide, isolated as acetophenone 3-pyridylhydrazine 1-oxide. Comparison of this hydrolysis product with a sample prepared by reduction (32) of diazotized 3-aminopyridine 1-oxide showed the required identity. The structure of 3 was proven by acidic hydrolysis to 13 which showed the required identity with an authentic sample prepared by the method of Zwart and Wibaut (21).

The light cream-colored sydnones 2 and 3 were irradiated with ultraviolet light ( $\lambda = 3660\text{\AA}$ ) and like many other sydnones, were found to be light sensitive but not visibly photochromic. They changed to a light orange color on 0.5 hour exposure, but the original cream color was not regenerated on standing four weeks in the dark or on heating to 60°

#### EXPERIMENTAL (33)

##### Starting Materials.

Nicotinamide 1-oxide (5), m.p. 291-293° dec., was prepared in yields of 46-49% according to the procedure of Taylor and Crovetti (27). Nicotinyl chloride hydrochloride (8), m.p. 158-160°, was obtained in quantitative yields essentially according to the procedure of Mndzhoyan (19).

##### 5-Bromonicotinic Acid (9).

To 53.2 g. (0.298 mole) of nicotinyl chloride hydrochloride was added sufficient thionyl chloride (202.3 g., 1.7 moles) to dissolve the acid chloride on refluxing. Bromine (47.6 g., 0.298 mole, 15.2 ml.) was added dropwise over a four hour period. An additional two hours boiling was followed by dropwise addition of 23.8 g. (0.149 mole) of bromine over a four hour period with gently refluxing. Heating was continued for 9.5 hours and the solution reduced to 1/3 its original volume *in vacuo*, poured on a minimum of crushed ice with vigorous manual stirring and filtered. The filtrate was adjusted to pH 3 with concentrated sodium hydroxide solution thereby depositing a bright yellow solid. The yield after drying the filtered product in an oven at 80° for one day was 35.6 g. (66%, based on nicotinic acid), m.p. 180-184°, lit. (12,16,17) m.p. 183°. Recrystallization from absolute ethanol produced a light cream colored powder, m.p. (Thiele apparatus) 183-184°.

##### 5-Bromonicotinamide (11).

To 35.95 g. (0.178 mole) of 9 was added sufficient thionyl chloride (*ca.* 200 g.) to cover the acid. The mixture was heated to gentle refluxing, and the additional thionyl chloride added if required to effect complete solution. After 0.5 hour the orange solution was cooled and evaporated to almost dryness at reduced pressure. The orange-brown oil was dissolved in a little chloroform and cautiously added with stirring to *ca.* 300 ml. of chloroform saturated with ammonia and cooled in an ice bath. The amide-chloroform mixture was heated on a steam bath to remove most of the excess ammonia (should not become acidic) and filtered. The residue was recrystallized from aqueous ethanol to yield 28.5 g. (80.1%) light cream colored crystalline powder, m.p. 219-219.5°;  $uv \lambda \text{ max (nm) } (\epsilon \times 10^{-4})$  277 (0.33);  $ir$  3550, 3200, 3025, 2925, 1725 (carbonyl), 1650, 1620, 1575  $\text{cm}^{-1}$ .

*Anal.* Calcd. for  $\text{C}_6\text{H}_5\text{BrN}_2\text{O}$ : C, 35.85; H, 2.51; N, 13.94. Found: C, 36.15; H, 2.65; N, 13.66.

5-Bromonicotinamide 1-Oxide (**14**).

To 48 ml. of glacial acetic acid (50.4 g., 0.838 mole) was added 9.6 ml. (13.8 g., 0.121 mole) of 30% hydrogen peroxide followed by 13 ml. (14.1 g., 0.138 mole) of acetic anhydride (care must be taken in mixing these reagents). The solution was heated for 10 minutes on a steam bath. To the hot solution was added 5.0 g. (0.024 mole) of 5-bromonicotinamide, which dissolved almost instantly with extreme effervescence. The solution was heated for nine hours and then poured into 200 ml. of water and cooled overnight in a refrigerator to yield 2.3 g. of a white crystalline powder. The filtrate was treated with manganese dioxide until decomposition of the peroxide ceased, filtered, and the filtrate evaporated to dryness. This residue was recrystallized once from aqueous ethanol to yield 1.95 g. of light tan powder, total yield of **14** was 4.25 g. (81.5%); m.p. (after two recrystallizations from aqueous ethanol) 285-288° dec. The rectangular needles began sweating at ca. 205°, partially melted at 209-210° with resolidification by 212° and final melting at 285-288°;  $\epsilon \times 10^{-4}$  max (nm) 231 (2.20), 266 (1.03).

*Anal.* Calcd. for  $C_6H_5BrN_2O_2$ : C, 33.17; H, 2.30; Br, 36.86; N, 12.90. Found: C, 33.46; H, 2.53; Br, 36.62; N, 12.71.

3-Aminopyridine 1-Oxide (**6**).

To a solution of 20.4 g. (0.10 mole) of granular HTH (Mathieson Chemical Co.) (**34**) in 200 ml. of water was added 24.0 g. (0.60 mole) of sodium hydroxide pellets. The mixture was stirred in an ice bath until solution was essentially complete (10-15 minutes) and the resulting milky solution was rapidly filtered with suction. The clear filtrate was cooled to 0° in an ice-salt bath, whereupon 14.4 g. (0.10 mole) of nicotinamide 1-oxide was added in one portion. The mixture was stirred in the ice-salt bath until almost all of the solid dissolved, the temperature being kept below 5°. After standing 15 minutes at room temperature, during which time complete solution was usually effected, the reaction solution was heated on a steam bath for 45-60 minutes (internal temperature 85-90°). The solution gradually turned from light green to orange and finally, with effervescence, to a deep burgundy. The solution was gradually cooled to room temperature and adjusted to a pH of 2 with concentrated hydrochloric acid. Addition of 70 ml. of acid to 280 ml. of solution gave approximately a 3 N solution which was evaporated to dryness at reduced pressure. The residue was boiled with 50 ml. portions of absolute ethanol until the final extract was colorless. The combined extracts were cooled, treated with four drops of concentrated hydrochloric acid, and any precipitated inorganic salts removed by filtration. The extract was boiled with a small amount of Norit, filtered, and the cooled filtrate diluted with ether beyond the cloud point and the resulting precipitate filtered. By repeated dilutions and filtrations, 11.4 g. (77.4%) of product was isolated, m.p. 117-119.5°, lit. (9) m.p. 124-125°. Yields ranged from 60-83% in ten preparations. The superiority of this synthesis for converting **5** to **6** is evidenced by the overall yield of only 14% for **7** reported by Leonard and Wajngurt (3) compared to the average overall yield (nine preparations) by our method of 43% (based on nicotinamide);  $\epsilon \times 10^{-4}$  max (nm) 234 (2.28) 252 (inflexion) 314 (0.27); hydrochloride salt, m.p. 149-150°, lit. (3,4) m.p. 149-150°.

3-Amino-5-bromopyridine (**12**).

This material was prepared by a procedure similar to that for **6**, using a solution of 2.6 g. (0.13 mole) of HTH, 60 ml. of water and 4.3 g. (0.11 mole) of sodium hydroxide pellets to which 5.4 g. (0.026 mole) of 5-bromonicotinamide was added in one portion.

Yields of 67% were reproducible, m.p. 69-69.5°, lit. m.p.'s: 65° (12) and 66-67° (11).

3-Amino-5-bromopyridine 1-Oxide Hydrochloride (**15**).

By a similar procedure to that for the preparation of **6** this compound was prepared in yields of 39-85%, m.p. 125-130°;  $\epsilon \times 10^{-4}$  max (nm) 220 (2.16), 241 (2.26), 325 (0.02).

*Anal.* Calcd. for  $C_5H_6BrClN_2O$ : C, 26.63; H, 2.68; Cl, 15.72. Found: C, 26.33; H, 3.00; Cl, 15.76.

The 1-Oxide of *N*-(3-Pyridyl)glycine Hydrochloride (**16B**).

3-Aminopyridine 1-oxide hydrochloride (10.0 g., 0.068 mole) (or 7.5 g. of free base **6**) in 40 ml. of water was mixed with 14.7 g. of *n*-butyl glyoxylate (60% purity), i.e., 0.068 mole of pure glyoxylate, and hydrogenated at once over 1.5 g. of 5% palladium-charcoal catalyst (**36**). After 20 hours at 23° the pressure changed from 28 to 23.9 lbs/in<sup>2</sup>. The filtered catalyst was washed with a little water and the combined filtrate and washings evaporated to dryness at reduced pressure over a boiling water bath. The orange oil was heated to boiling with 30 ml. of concentrated hydrochloric acid. Overnight refrigeration yielded 11.58 g. (83.3%) of a light cream crystalline powder, m.p. 196-198° dec.;  $\epsilon \times 10^{-4}$  max (nm) 244 (2.45), 330 (0.34).

*Anal.* Calcd. for  $C_7H_9ClN_2O_3$ : C, 41.09; H, 4.43; Cl, 17.33; N, 13.69; O, 23.46; neut. equiv. 102.3. Found: C, 41.32; H, 4.71; sCl, 17.62; N, 13.93; O, 23.53; neut. equiv. 105.6.

*N*-(5-Bromo-3-pyridyl)glycine Hydrochloride (**16c**).

By a similar procedure to that described for **16b** this compound was prepared in yields of 65%, m.p. 209-212°;  $\lambda$  max (nm) ( $\epsilon \times 10^{-4}$ ) 244 (1.61), 323 (0.28).

*Anal.* Calcd. for  $C_7H_8BrClN_2O_2$ : C, 31.42; H, 3.01; N, 10.47; neut. equiv. 133.7. Found: C, 31.61; H, 3.05; N, 10.52; neut. equiv. 133.0.

The 1-Oxide of *N*-Nitroso-*N*-(3-pyridyl)glycine (**17b**).

To a suspension of 11.58 g. (0.057 mole) of **16b** in 114 ml. of water a concentrated solution of sodium hydroxide was added dropwise until the glycine was completely dissolved at 0°. At this temperature, 5.86 g. (0.085 mole) of solid sodium nitrite was added portionwise with stirring. The solution was adjusted to pH 2 with concentrated hydrochloric acid. After 20 minutes in the ice-salt bath, almost all the nitrosoglycine was precipitated. After overnight refrigeration, 8.4 g. (74.6%) of a light orange powder was collected and air dried, m.p. 171.5-172° (bubbling);  $\epsilon \times 10^{-4}$  max (nm) 259 (2.28). Four recrystallizations from aqueous methanol gave the analytical sample, m.p. 174-175° dec. The product gave a positive Liebermann test.

*Anal.* Calcd. for  $C_7H_7N_3O_4$ : C, 42.64; H, 3.58; N, 21.32; neut. equiv. 197. Found: C, 42.82; H, 3.62; N, 21.02; neut. equiv. 199 and 195.

*N*-Nitroso-*N*-(5-bromo-3-pyridyl)glycine (**17c**).

By a similar procedure described for **17b**, this material was prepared in yields of 56-70%, m.p. 168-170° dec.;  $\epsilon \times 10^{-4}$  max (nm) 284 (1.04). The product gave a positive Liebermann test.

*Anal.* Calcd. for  $C_7H_6BrN_3O_3$ : C, 32.32; H, 2.32; N, 16.15; neut. equiv. 260. Found: C, 32.41; H, 2.32; N, 16.00; neut. equiv. 255.1.

The 1-Oxide of *N*-(3-Pyridyl)sydnone (**2**).

A suspension of 3.74 g. (0.019 mole) of **17b** in 90 ml. of acetic anhydride was heated at 95-100° until solution was complete

(ca. 0.5 hour). Evaporation of the acetic anhydride and trituration of the resulting brown oil with ethanol gave 1.20 g. (35.2% of a light tan crystalline powder which gave a negative Liebermann nitroso test. After two recrystallizations from hot ethanol diluted to the cloud point with petroleum ether (b.p. 90-100°) gave light cream-colored plates, m.p. 174-175.5° (bubbling);  $\nu \lambda$  max (nm) ( $\epsilon \times 10^{-4}$ ) 238 (1.97), 265 (1.34), 313 (0.51); ir (potassium bromide), 3125 (sydnone CH), 3080 (pyridine CH), 1744 (sydnone carbonyl), 1775 sh., 723 (CH deformation of sydnone ring)  $\text{cm}^{-1}$ .

*Anal.* Calcd. for  $\text{C}_7\text{H}_5\text{N}_3\text{O}_3$ : C, 46.93; H, 2.81; N, 23.46. Found: C, 46.98; H, 2.74; N, 23.55.

#### *N*-(5-Bromo-3-pyridyl)sydnone (3).

By a similar procedure described for **2**, this compound was obtained in 50-69% yield from the corresponding nitrosoglycine **17c**, m.p. 139.5-140.5°;  $\nu \lambda$  max (nm) ( $\epsilon \times 10^{-4}$ ) 288 (0.61), 240 inf. (1.14), 315 (0.49); ir (potassium bromide), 3175 (sydnone CH), 3040 (pyridine CH), 1775 (sydnone carbonyl) 1763 sh. and 1738 sh., 723 (sydnone CH deformation)  $\text{cm}^{-1}$ .

*Anal.* Calcd. for  $\text{C}_7\text{H}_4\text{BrN}_3\text{O}_2$ : C, 34.73; H, 1.66; Br, 33.01; N, 17.36. Found: C, 34.78; H, 1.81; Br, 32.77; N, 17.23.

#### Reduction of the 1-Oxide of *N*-(3-Pyridyl)sydnone (2).

The sydnone **2** (0.2 g., 0.001 mole) was heated in 40 ml. of absolute ethanol until it dissolved. To the cooled solution was added two microspatulas of Raney nickel (W-6) and the mixture hydrogenated for 22.5 hours during which time the pressure dropped from 35 to 33.4 lbs/in<sup>2</sup> and the temperature changed from 31° to 25.5°. The catalyst was filtered and washed with absolute ethanol and the combined filtrates evaporated at reduced pressure to a yellow oil which solidified in a few minutes at room temperature. Trituration with absolute ethanol afforded a light cream-colored product, m.p. 117-120° dec., lit. (2b) m.p. for **1**, 119-121° dec. On exposure to direct sunlight the reduction product almost instantly turned a deep blue color, ir (potassium bromide), 3120 (CH sydnone), 3050 (CH pyridine), 1725 (sydnone carbonyl), 729 (CH deformation, sydnone)  $\text{cm}^{-1}$ .

#### Acetophenone 3-Pyridylhydrazone 1-Oxide.

##### (a) From Sydnone 2.

To 3 ml. of concentrated hydrochloric acid, 0.5 g. (0.003 mole) of **2** was added cautiously. After effervescence ceased, the dark solution was heated on a hot plate for 10 minutes. The solution was evaporated to dryness at reduced pressure and the residue (theoretically ca. 0.436 g. of hydrazine hydrochloride) was then dissolved in 50 ml. of absolute ethanol. Acetophenone (0.49 g., 0.0041 mole) was added and the solution refluxed for eight hours. Evaporation of the ethanol *in vacuo* left only a dark oil which was redissolved in 5 ml. of ethanol, diluted (until cloudy) with water and warmed on a hot plate until a clear solution resulted. Upon cooling, oily crystals precipitated. Redissolving in ethanol and treatment of the solution as described above gave, after three performances of this purification procedure, 0.038 g. (6.2%) of a beige colored crystalline powder, m.p. 214-217°.

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{15}\text{N}_3\text{O}_2$  (hydrazine hydrate): C, 63.65; H, 6.16. Found: C, 63.43; H, 5.91.

##### (b) By Reduction of Diazotized 3-Aminopyridine 1-Oxide.

The amine **6** was diazotized and reduced essentially according to Rath (33). The resulting acidic solution was then treated with 50% potassium hydroxide (pH 10) and then acidified with concentrated hydrochloric acid to pH 4. The stannous hydroxide was filtered by suction and washed with 95% ethanol. The combined filtrates were evaporated to dryness on a steam bath and the dry

salts extracted with absolute ethanol. The extract was reduced to 1/8 its original volume and refluxed with acetophenone for 4.5 hours. The hydrazone was isolated essentially according to the procedure described in (a), m.p. 219.5-220°.

Mixture m.p.'s of the products from (a) and (b) were without depression and the infrared spectra of the two hydrazones were identical.

#### 5-Bromo-3-pyridylhydrazine Hydrochloride (13).

##### (a) By Acid Hydrolysis of Sydnone 3.

To 3 ml. of concentrated hydrochloric acid was added portionwise 0.3 g. (0.0012 mole) of sydnone **3** and after the violent effervescence ceased, the solution was heated to boiling on a hot plate. Upon cooling in an ice bath, a light yellow crystalline powder precipitated. Recrystallization from absolute methanol gave 0.1 g. (37%) of cream colored needles, m.p. 172-176° dec.

##### (b) By Reduction of Diazotized 3-Amino-5-bromopyridine.

Following the procedure of Zwart and Wibaut (21) the amine **12** was converted to the hydrazine in 29% yield and on treatment with ethanol-dry hydrogen chloride solution gave **13**, m.p. 178-180°.

Mixture melting points of both hydrochlorides showed no depression.

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