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3-Hydrazino-4-hydroxy- and 3-hydrazino-4-methoxypyridines, which could not be obtained by reduction of the corresponding diazonium salts, have been prepared by decomposition of *N*-(4-substituted-pyrid-3-yl)-sydnone.

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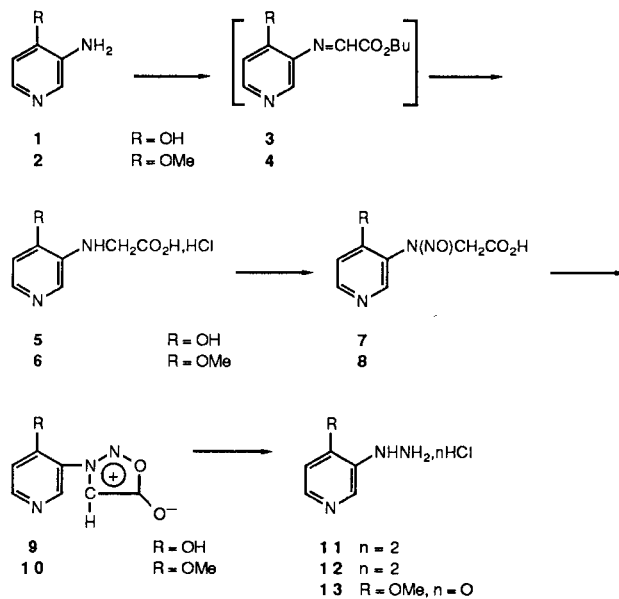
Hydrazinopyridines are a relatively poorly represented group of compounds in the chemical literature though the parent compounds and simple derivatives are useful starting materials in the synthesis of triazolopyridines [1], tetrazolopyridines [2] and pyrrolopyridines [3]. The 2- and 4-hydrazinopyridines are usually obtained by nucleophilic substitution of the corresponding chloropyridines while 3-hydrazinopyridines are generally derived readily from 3-aminopyridines by diazotisation and reduction of the diazonium salt. We have had reason to prepare some substituted 3-hydrazinopyridines and describe here the preparation of two such compounds which were unusually difficult to obtain.

3-Nitro-4-pyridone [4] readily gave 3-chloro-4-nitropyridine [5] which then yielded 4-methoxy-3-nitropyridine on treatment with sodium methoxide in a reaction similar to that used by Besley and Goldberg [6] for the preparation of 3-nitro-4-pyridone. Both 3-nitro-4-pyridone and 4-methoxy-3-nitropyridine upon catalytic hydrogenation in methanol at room temperature over palladium charcoal gave almost quantitative yields of the corresponding amines **1** and **2**, respectively.

Several attempts to isolate the hydrazines from the reduction of the diazonium salts from **1** or **2** by either stannous chloride [7] or sodium sulphite [8] were unsuccessful though other 3-hydrazinopyridines had been obtained readily by these procedures. Attention was turned to the use of sydnone [9] as intermediates in the preparation of the required hydrazines (Scheme). Condensation of the 3-amino-4-substituted pyridine hydrochlorides with *n*-butyl glyoxylate [10] and hydrogenation of the anils **3** and **4** without prior isolation over a palladium-charcoal catalyst at room temperature gave 4-substituted *N*-pyridylglycine hydrochlorides **5** and **6**, respectively. The presence of two carbonyl stretching frequency absorptions and an absorption due to NH in the infrared spectrum indicated that **5** exists in the pyridone form. Nitrosation of **5** and **6** proceeded smoothly and the *N*-nitroso compounds **7** and **8** were obtained, the latter as its dihydrochloride. Each of the nitroso compounds was converted to the corresponding sydnone upon treatment with acetic anhydride. The

methoxy compound **10** showed a strong absorption at 1720-1780 cm^{-1} , which is in good agreement with the reported values of 1723 to 1781 (maximum 1761) cm^{-1} for *N*-benzylsydnone [9]. Compound **10** showed a strong and broader band of absorption at 1700 to 1780 (maximum 1740) cm^{-1} which may indicate that the azine is in the pyridone form. The sydnone **9** and **10** showed absorptions at 3200 and 3150 cm^{-1} respectively, assigned to the CH stretching vibration of the sydnone ring [11]. Photochromism has been observed [9] in 2-pyridylsydnone and their *N*-oxides but this property was not seen in **9** or **10**. Acidification of a solution of the sydnone with hydrochloric acid caused rapid evolution of carbon dioxide and produced the required hydrazines **11** and **12** as their dihydrochlorides. Since only a weak band at 1640 cm^{-1} was observed in the 1600-1800 cm^{-1} region of the ir spectrum it appeared that the dihydrochloride **11** exists in the hydroxy form. The overall yield of **11** and **12** was 21 and 27%, respectively.

Scheme



EXPERIMENTAL

The ir and nmr spectra were recorded on Pye Unicam SP200 and Varian T-60 spectrometers, respectively, with TMS as internal standard in the latter case. The mass spectra were recorded on an A. E. I. MS-902 spectrometer. Melting points were determined in glass capillary tubes and are uncorrected.

General Methods.

Preparation of *N*-(4-Substituted-pyrid-3-yl)glycines **5** and **6**.

3-Amino-4-hydroxypyridine [12] and 3-amino-4-methoxypyridine [4] were converted into their hydrochlorides by passing dry hydrogen chloride through an ethereal solution of the amine to give **1.HCl**, mp 224-226° dec and **2.HCl**, mp 178-179° dec. The hydrochloride (0.027 mole) in water (20 ml) was added to *n*-butyl glyoxylate (5.4 g, 0.028 mole) and the mixture was immediately hydrogenated over palladium charcoal (0.4 g, 10%) at room temperature and on initial pressure of hydrogen of 30 lbs/square inch until absorption ceased. Removal of the catalyst, acidification with concentrated hydrochloric acid and evaporation of the solvent gave a gum which crystallised.

N-(Pyrid-4-on-3-yl)glycine Hydrochloride **5**.

This compound was obtained in 76% yield, mp 205-207° (ethanol and petroleum-ether mixture); ir (potassium bromide): 3450, 2700, 1740, 1620, 1585, 1510, 1330, 1195, 1110, 810 cm⁻¹; nmr (DMSO-d₆): δ 4.05 (s, 2H, CH₂), 7.3 (d, J = 6 Hz, 1H, 5-H), 7.8 (s, 1H, 2-H), 8.0 (d, J = 6 Hz, 1H, 1H, 6-H), 8.6 (v br s, exchanged with deuterium oxide, 1H, OH), 10.2 (br s, exchanged with deuterium oxide, 3H, NH and H₂N⁺).

Anal. Calcd. for C₇H₇ClN₂O₃: C, 41.07; H, 4.44; N, 13.69; Cl, 17.33. Found: C, 41.15; H, 4.85; N, 13.35, Cl, 17.13.

N-(4-Methoxypyrid-3-yl)glycine Hydrochloride **6**.

This compound was obtained in a yield of 71%, mp 174-176° (ethanol and diethyl ether mixture); ir (potassium bromide): 3400, 3100 to 2700, 2830, 2500 to 2300, 1725, 1570, 1310, 1220, 1015 cm⁻¹; nmr (DMSO-d₆): δ 4.05 (br s, 2H, CH₂), 4.2 (s, 3H, CH₃), 6.4 (br s, exchanged with deuterium oxide, 1H, OH), 7.45 (d, J = 6 Hz, 1H, 5-H), 7.9 (s, 1H, 2-H), 8.2 (d, J = 6 Hz, 1H, 6-H).

Anal. Calcd. for C₈H₁₁N₂O₃Cl: C, 43.95; H, 5.07; N, 12.81; Cl, 16.22. Found: C, 44.08; H, 5.04; N, 12.74; Cl, 16.05.

N-Nitroso-*N*-(4-substituted-pyrid-3-yl)glycines **7** and **8**.

The 3-pyridylglycine hydrochloride (0.006 mole) was dissolved in water (15 ml) and cooled to 0° and sufficient aqueous alcoholic sodium hydroxide solution was added to effect solution. Sodium nitrite (0.6 g) was added portionwise to the stirred cold solution followed by concentrated hydrochloric acid to bring the solution to pH 2. The yellow solid was filtered off in the case of **7** but **8** did not crystallise from the reaction mixture and the solvent was removed under reduced pressure and the residue extracted with ethanol.

N-Nitroso-*N*-(pyrid-4-on-3-yl)glycine (**7**).

This compound was obtained in a yield of 90%, mp 165-166°; ir (potassium bromide): 3500, 3600 to 2400, 1650, 1465, 1405, 1150, 970, 860, 700 cm⁻¹; nmr (DMSO-d₆): δ 4.5 (s, 2H, CH₂), 7.5 (d, J = 6 Hz, 1H, 5-H), 7.8 (d, J = 6 Hz, 1H, 6-H), 8.2 (s, 1H, 2-H).

Anal. Calcd. for C₇H₇N₃O₄: C, 42.63; H, 3.58; N, 21.32. Found: C, 42.38; H, 3.65; N, 21.35.

N-Nitroso-*N*-(4-methoxypyrid-3-yl)glycine Dihydrochloride (**8**).

This compound was obtained in a yield of 87%, mp 156-157° (ethanol and diethyl ether mixture); ir (potassium bromide): 3500, 2500, 1730, 1500, 1400, 1310, 1190, 1180, 940, 800 cm⁻¹; nmr (DMSO-d₆): δ 4.2 (s, 3H, CH₃), 4.7 (s, 2H, CH₂), 7.85 (d, J = 5 Hz, 1H, 5-H), 8.35 (br s, exchanged with deuterium oxide, 2H, OH and HN⁺), 8.9 (br s, 2H, 2-H and 6-H).

Anal. Calcd. for C₈H₁₁Cl₂N₃O₄: C, 33.82; H, 3.90; N, 14.8. Found: C, 34.25; H, 3.63; N, 15.1.

N-(4-Substituted-pyrid-3-yl)syndones **9** and **10**.

The *N*-nitroso compound **7** or the *N*-nitroso dihydrochloride **8** (0.008 mole) was added to freshly distilled acetic anhydride (40 ml) and heated on a boiling water-bath for 30 minutes. The solvent was removed under reduced pressure and the residue triturated with methanol to produce a deep yellow solid.

N-(Pyrid-4-on-3-yl)syndone (**9**).

This compound was obtained in a yield of 75%, mp 214-215° dec (methanol); ir (potassium bromide): 3200, 1740, 1650, 1560, 1200, 1150, 1040, 960, 845, 740 cm⁻¹; nmr (DMSO-d₆): δ 6.5 (d, J = 5 Hz, 1H, 5-H), 7.45 (s, 1H, 2-H), 7.9 (d, J = 5 Hz), 1H, 6-H), 8.5 (s, 1H, CH of syndone).

N-(4-Methoxypyrid-3-yl)syndone (**10**).

This compound was obtained in a yield of 92%, mp 170-171° dec (methanol); ir (potassium bromide): 3150, 1760, 1600, 1310, 1010, 860, 750 cm⁻¹; nmr (DMSO-d₆): δ 3.35 (s, 3H, CH₃), 7.5 (t, 2H), 5- and 6-H), 8.8 (d, 2H, 2-H and CH of syndone).

Anal. Calcd. for C₈H₇N₃O₃: C, 49.75; H, 3.65; N, 21.75. Found: C, 49.88; H, 3.66; N, 21.4.

3-Hydrazino-4-substituted-pyridine Dihydrochlorides **11** and **12**.

The syndone **9** or **10** (0.007 mole) was added to a mixture of concentrated hydrochloric acid (5 ml) in water (10 ml) and heated on a boiling water-bath until gas evolution ceased. The cooled solution gave a yellow precipitate of **11** but the reaction mixture from **10** was evaporated to dryness under reduced pressure to give **12**.

3-Hydrazino-4-hydroxypyridine dihydrochloride (**11**).

This compound was obtained in a yield of 41%, mp 204-205° dec (dilute hydrochloric acid); ir (potassium bromide): 3300, 3100, 2500 to 2200, 1575, 1520, 1340, 1145, 900, 820, cm⁻¹; nmr (DMSO-d₆): δ 8.0 (d, J = 6 Hz, 1H, 5-H), 8.9 (d, J = 6 Hz, 1H, 6-H), 8.8 (s, 1H, 2-H), 11.3 (br s, exchanged with deuterium oxide, 6H, OH, NH, HN⁺, H₂N⁺).

Anal. Calcd. for C₆H₇Cl₂N₃O: C, 30.32; H, 4.58; N, 21.22; Cl, 35.80. Found: C, 29.98; H, 4.59; N, 20.79; Cl, 37.92.

3-Hydrazino-4-methoxypyridine Dihydrochloride (**12**).

This compound was obtained in a yield of 48%, mp 146-147° dec (ethanol and diethyl ether mixture); ir (potassium bromide) 3150, 2700-2400, 1600, 1520, 1310, 1160, 1015, 810 cm⁻¹; nmr (DMSO-d₆): δ 4.15 (s, 3H, CH₃), 6.2 (br s, exchanged with deuterium oxide, 6H, OH, NH, HN⁺, H₂N⁺), 7.5 (d, J = 5 Hz, 1H, 5-H), 8.4 (d, J = 5 Hz, 2H, 6-H) 8.3 (s, 1H, 2-H).

Anal. Calcd. for C₆H₁₁Cl₂N₃O: C, 33.98; H, 5.23; N, 19.81. Found: C, 34.24; H, 5.12; N, 19.89.

3-Hydrazino-4-methoxypyridine (**13**).

Basification of the dihydrochloride **12** and extraction of the solution with ether yielded 3-hydrazino-4-methoxypyridine, mp 115-117° (benzene and petroleum-ether mixture); ir (potassium bromide): 3400, 3340, 3300, 1525, 1255, 1380, 830 cm⁻¹; nmr (deuteriochloroform): δ 3.85 (s, 3H, CH₃), 4.2 (br s, exchanged with deuterium oxide, 3H, NH and NH₂), 6.65 (d, J = 5 Hz, 1H, 5-H), 8.0 (d, J = 5 Hz, 1H, 6-H), 8.25 (s, 1H, 2-H).

Anal. Calcd. for C₆H₇N₃O: C, 51.79; H, 6.52; N, 30.2. Found: C, 51.56; H, 6.15, N, 29.8.

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