Synthesis and Unexpected Reactions of 2-Hydroxy-3-pyridinylacetic Hydrazides. Formation of 2*H*-Pyrrolo[2,3-*b*]pyridin-2-ones

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Treatment of 2-hydroxy-3-pyridinylacetic hydrazides under mild mesylation conditions provided 2*H*-pyrrolo[2,3-*b*]pyridin-2-ones as unexpected products. This rearrangement is believed to result from an intramolecular attack of the hydrazide on a reactive pyridinium species formed under the reaction conditions.

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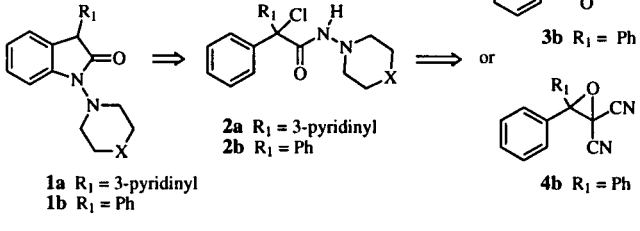
Our investigation into biological activity of novel neurotransmitter release enhancers required the synthesis of 3-pyridinyloxindoles **1a**. Previous investigation had shown that 3-phenyloxindoles **1b** had could be synthesized from phenyl acetic hydrazide **2b**; in turn, derived from either **3b** [1-3] or **4b** [4,5]. The lack of commercially available starting materials for **3** or **4** (R_1 = 3-pyridyl) necessiated an alternative route to **2a**, precursor for bicylic system **1a**.

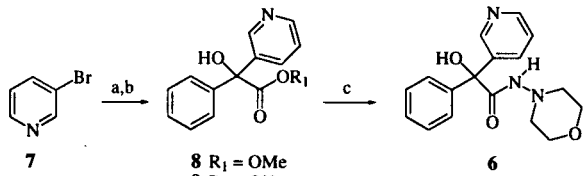
Scheme 1



2-Hydroxy-3-pyridinylacetic hydrazide **6** was synthesized as an alternative to **2a**, with the idea that the tertiary hydroxyl could be converted to a mesyloxy group, similar in reactivity to the chloride in **2b** (Scheme 2). Bromopyridine **7** was metallated with *n*-butyllithium at low temperature [6] and the pyridyllithium was treated with methyl benzoylformate to afford tertiary alcohol **8** in 61% yield. Hydrolysis using aqueous ethanolic potassium hyrdoxide gave acid **9** (77% yield), which was coupled with 4-aminomorpholine using dicyclohexylcarbodiimde, hydroxybenzotriazole to give hydrazide **6** (79% yield).

Reaction of the tertiary hydroxyl in **6** required 3-5 equivalents of methanesulfonyl chloride and triethylamine (at 0°) to cause complete disappearance (tlc) of starting material (Scheme 3). Heating with excess triethylamine did not alter the original product distribution [7]. Upon isolation and purification of the products, none of the expected oxindole **1a** was found. Surprisingly, C- and O-sulfonylated **11**, **12** were obtained in 8% and 46% yield. The ^{1}H nmr clearly showed the absence of one pyridine proton (*vs.* **1a**) and decoupling experiments confirmed the regioselective addition to the 2-position.

Scheme 2



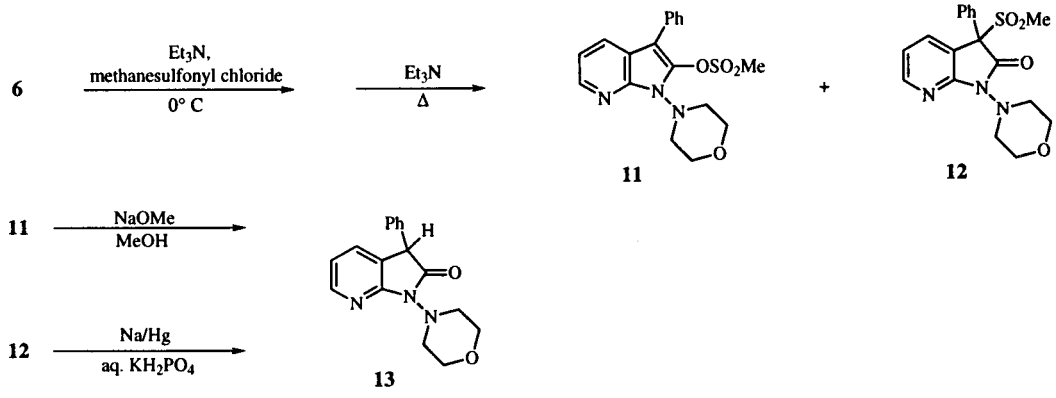
(a) *n*-BuLi, -78°, Et_2O; $PhC(=O)CO_2Me$, -78° → reflux; (b) KOH, H_2O, EtOH, dioxane; (c) hydroxybenzotriazole, dicyclohexylcarbodiimide, dioxane, tetrahydrofuran, H_2N-4-morpholine, $NaHCO_3$.

The labile enol mesylate **11** was easily hydrolyzed (catalytic sodium methoxide in methanol) to **13**, whereas C-sulfonylated **12** required reducing conditions (sodium-amalgam, methanolic potassium hydrogen phosphate) [8] to generate pyrrolopyridin-2-one **13**. Attempts to promote rearrangement of **6** using anhydrous hydrogen chloride (in dioxane or ether) or aqueous sulfuric acid failed to give appreciable amounts of **1a** or **13**.

This unexpected reaction was explored in further detail using the simpler pyridylacetic hydrazide **16** lacking the phenyl substitution in the hydrazide **6** (Scheme 4). Reaction of pyridine-3-carboxaldehyde **14** with aqueous potassium cyanide provided the known cyanohydrin [9] in 71% yield. Hydrolysis of the cyanide under esterification conditions gave the α-hydroxy ester (77% yield), which was converted to *t*-butyldimethylsilyl ether **15** using *t*-butyldimethylsilyl chloride under standard conditions. The ester was subsequently treated with trimethylaluminum [10] and either 4-aminomorpholine or 1-aminopiperidine, and provided hydrazides **16c** and **16d** in 89% and 75% yield from **15** after deprotection using tetrabutylammonium fluoride in tetrahydrofuran.

Applying the original procedure (triethylamine, methanesulfonyl chloride, 0°) afforded low, but isolable, amounts of the rearrangement products **17c** and **17d**. The conversion was improved to 45% for both **16c** and **16d** by

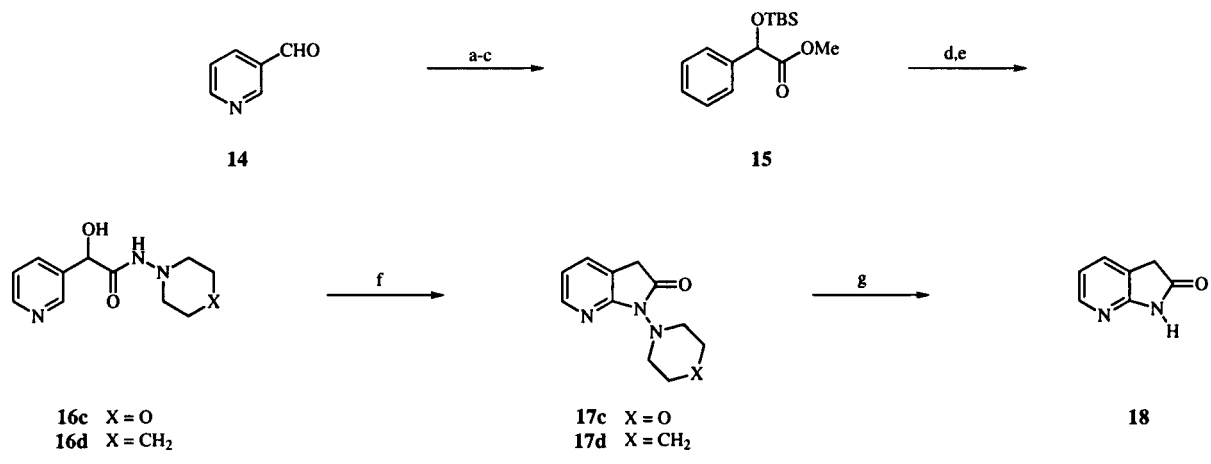
Scheme 3



substituting methanesulfonic anhydride for methanesulfonyl chloride. The regiochemistry of addition to the pyridine core of **16c,d** was identical to that seen in the phenyl substituted series **6**. Reaction products derived from C- or O-sulfonylation of the pyrrolopyridin-2-ones were not seen in **17**; however, the modest yields suggest other reaction processes were taking place with this series. The regiochemistry of the hydrazide addition at the 2-position of the pyridine ring was confirmed by conversion of **17c** to known 7-azaoxindole **18**. To our surprise, **17c** was unaffected by refluxing zinc in acetic acid, and required dissolving metal in ammonia to cleave the N-N bond. This provided **18** in 70% yield, identical in mp, ms, and nmr to that reported earlier by Marfat [11].

To gain some understanding of the mechanism of this rearrangement, mesylate **19** was formed from **16c** using 1.1 equivalents of methanesulfonyl chloride, triethylamine (Scheme 5). Acetic anhydride (1.1 equivalents) was then added, followed by additional triethylamine (1.1 equivalents). After 2 hours, the only material isolated from the reaction was **17c** in 33% yield. Acetic anhydride was chosen because of it's ability to activate pyridine ring nitrogens [12]; in the case of **20**, it must be serving in this same capacity. Activation of **20** to nucleophilic attack by hydrazide thus cyclizes to **21**, which upon rearomatization provides **17c**. Under the reaction conditions where methanesulfonic anhydride or methanesulfonyl chloride were used, the excess reagent must also be serving this same

Scheme 4

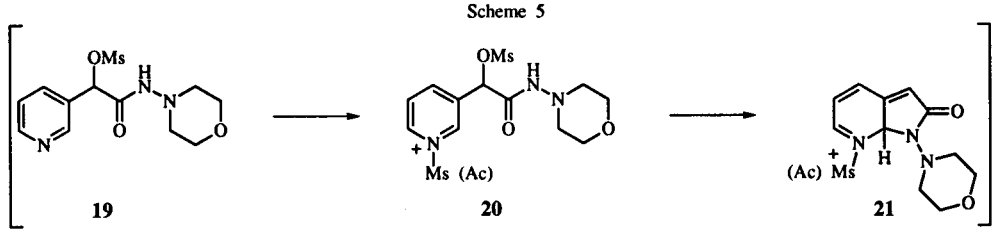


(a) KCN, aq. HCl; (b) MeOH, H_2SO_4; (c) *t*-butyldimethylsilyl chloride, imidazole, dimethylformamide; (d) $Al(Me)_3$, 4-aminomorpholine or 1-aminopiperidine, $CHCl_3$; (e) $(n\text{-}Bu)_4NF$, tetrahydrofuran; (f) methanesulfonyl chloride or methanesulfonic anhydride, Et_3N, CH_2Cl_2; (g) Li, NH_3.

function. The importance of the nature leaving group was determined based on the observation that treatment of **16c** with excess acetic anhydride, triethylamine did not give **17c**, suggesting that an acetoxy group is not a sufficient leaving group when compared to a mesyloxy group. Furthermore, the necessity for pyridine activation was demonstrated by the observation that **19** remained unchanged when treated with excess triethylamine. The formation of **1b** from **2b** was speculated to proceed by the elimination of hydrogen chloride to a form an α-lactam intermediate, which underwent a sigmatropic rearrangement and rearomatization give oxindole **1b** [1-5]. We do not favor this mechanism to explain our results based on the observation that heating **19** in the presence of triethylamine did not lead to appreciable amounts of **17c**.

The isolation of sulfonylation products **11** and **12** with no trace of **13**, contrasts with the absence of sulfonylation in the reaction of **16**. This dichotomy may be attributed to the presence (or absence) of the 3-phenyl group and it's effect on the stability and reactivity of the ionic intermediates in the pathway toward the product(s). It appears that these reactions are sensitive to the nature of the leaving group and activation of the pyridine nucleus in the form of a pyridinium salt, both of which are required for the rearrangement to occur.

Scheme 5



In conclusion, a new method for the formation of 2*H*-pyrrolo[2,3-*b*]pyridin-2-ones has been described. These products result from an unexpected reaction of 2-hydroxy-2-(3-pyridinyl)acetic hydrazides under mesylation conditions with excess reagents. The method has been shown to be applicable to both secondary and tertiary alcohols. Preliminary investigation into the mechanism of this novel rearrangement was studied using secondary alcohol **16c**. The rearrangement was shown to proceed by conversion of the alcohol to a leaving group (mesyloxy), activation of the pyridine ring with mesyl or acetyl, followed by intramolecular hydrazide attack on the pyridine ring and elimination of the leaving group. The regiochemistry of pyridine addition was consistent within the two series **6** and **16**, when compared to **18** reported earlier. The investigation into the generality of these findings is ongoing.

EXPERIMENTAL

Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. Unless otherwise noted, ^{1}H nmr spectra (300 MHz) were recorded in deuteriochloroform and referenced to tetramethylsilane unless noted otherwise. Mass spectra were obtained on either VG 70-VSE (High Res DCI) or Finnigan MAT 8230 (DCI) mass spectrometers.

2-Hydroxy-2-phenyl-2-(3-pyridinyl)acetic Acid (**9**).

To a -78° solution of **7** (2.9 ml, 30.0 mmoles) in ether (150 ml) was added *n*-butyllithium (2.5 *M* in hexane, 13.2 ml). After stirring for 45 minutes, the solution was transferred *via* cannula to a -78° solution of methyl benzoylformate (4.3 ml, 33.0 mmoles) in ether (1500 ml). After an additional 20 minutes at -78°, the reaction was allowed to slowly warm to room temperature followed by heating to reflux for 2 hours. The reaction was quenched with saturated ammonium chloride (200 ml), the layers were separated and the aqueous fraction extracted with ether. The combined extracts were washed with brine, dried over magnesium sulfate, filtered, concentrated *in vacuo* and the orange residue was heated to 75° at 1 mm for 4 hours. Further purification by chromagraphy (silica gel methanol in chloroform, 7:93, v/v) gave ethyl 2-hydroxy-2-phenyl-2-(3-pyridinyl)acetate **8** (4.45 g, 61%) as a yellow oil; ^{1}H nmr: δ 8.70 (br s, 1H), 8.57 (br d, 1H), 7.78 (m, 1H), 7.38 (m, 5H), 7.27 (m, 1H), 4.37 (br s, 1H deuterium oxide exchangable), 3.89 (s, 3H); ms: (NH_3-CI) m/z 244 ($M+H^+$, 100%).

The ester **8** (7.9 g, 0.33 mole) was hydrolyzed in a mixture of ethanol (34 ml), dioxane (67 ml) and water (13 ml) using potassium hydroxide (3.65 g, 0.065 mole) at reflux for 2 hours. The volatile materials were removed under vacuum at 40°. The resulting syrup was diluted with water (60 ml) and the neutral impurities extracted with dichloromethane. The *p*H was adjusted to 2.7 using concentrated hydrochloric acid and after brief heating, product **9** precipitated as a yellow solid (5.73 g, 77%), mp 185-187°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 8.55 (d, J = 1.8 Hz, 1H), 8.47 (dd, J = 4.4, 1.4 Hz, 1H), 7.73 (dt, J = 8.4, 1.8 Hz, 1H), 7.4-7.30 (m, 6H); ms: (NH_3-CI) m/z 184 ($M+H-CO_2^+$, 100%).

Anal. Calcd. for $C_{13}H_{11}NO_3 \cdot 1/4H_2O$: C, 66.80; H, 4.96; N, 5.99. Found: C, 66.85; H, 4.69; N, 5.89.

N-(4-Morpholinyl)-2-hydroxy-2-phenyl-2-(3-pyridinyl)acetamide (**6**).

A mixture of **9** (3.48 g, 0.015 mole), hydroxybenzotriazole hydrate (4.10 g, 0.03 mole), dicyclohexylcarbodiimide (3.09 g,

0.015 mole), 4-aminomorpholine (1.45 ml, 0.015 mole), sodium bicarbonate (1.26 g, 0.015 mole), *N,N*-dimethylformamide (36 ml) and dioxane (36 ml) were stirred at room temperature overnight. The volatile materials were removed *in vacuo*, dichloromethane (170 ml) was added, the solids were filtered and the organic layer was washed with saturated sodium bicarbonate and brine. After drying, filtration and concentration, the residue was purified by chromatography (silica gel, methanol in chloroform, 10:90 v/v) to give the product as a white foam (3.72 g, 79%); ^{1}H nmr: δ 8.68 (d, J = 2.2 Hz, 1H), 8.49 (dd, J = 4.7, 1.4 Hz, 1H), 7.82 (dt, J = 4.9, 1.9 Hz, 1H), 7.55 (br s, 1H deuterium oxide exchangable), 7.37 (m, 5H), 7.26 (m, 1H), 4.28 (br s, 1H deuterium oxide exchangable), 3.80 (t, J = 4.3 Hz, 4H), 2.84 (t, J = 2.2 Hz, 4H); ir (potassium bromide): 3272-292 (s), 1669 (s) cm^{-1}; hrms: Calcd. for $C_{17}H_{19}N_3O_3$: 314.1505 (M+H). Found: 314.1501.

Representative Procedure for Rearrangement. Preparation of 1-(4-Morpholinyl)-3-phenyl-2-oxosulfonylmethyl-2*H*-pyrrolo[2,3-*b*]-pyridin-2-one (**11**) and 1,3-Dihydro-1-(4-morpholinyl)-3-phenyl-3-sulfonylmethyl-2*H*-pyrrolo[2,3-*b*]pyridin-2-one (**12**).

To a 0° solution of **6** (75 mg, 0.24 mmoles) in toluene (3 ml) and dichloromethane (2 ml) was added triethylamine (37 µl, 0.26 mmole) and methanesulfonyl chloride (20 µl, 0.26 mmole). Equal amounts (1 equivalent) of triethylamine and methanesulfonyl chloride were continually added every 30 minutes (typically 5 were required) until all of **6** was consumed. The reaction was quenched with water and chloroform (10 ml each). The layers were separated and the aqueous extracted copiously with chloroform. After drying (magnesium sulfate) and concentration, the residue was purified by chromatography (silica gel, methanol in chloroform, 3:97 v/v). The first fraction collected was **11** (5.8 mg, 8%); ^{1}H nmr: δ 8.37 (dd, J = 4.8, 1.5 Hz, 1H), 8.03 (dd, J = 8.1, 1.5 Hz, 1H), 7.61 (dd, J = 7.7, 1.4 Hz, 1H), 7.49 (t, J = 7.7 Hz, 2H), 7.35 (t, J = 7.4 Hz, 1H), 7.15 (dd, J = 8.0, 4.7 Hz, 1H), 4.40 (br m, 2H), 4.00 (br m, 2H), 3.87 (br m, 2H), 3.17 (br m, 2H), 2.94 (s, 3H); ms: (DCI- NH_3) m/z 374 (M+H, 100%). The second fraction to be collected was **12** (44 mg, 46% yield); ^{1}H nmr: δ 8.38 (dd, J = 5.5, 1.8 Hz, 1H), 8.13 (dd, J = 7.7, 1.5 Hz, 1H), 7.97 (m, 2H), 7.46 (m, 3H), 7.12 (dd, J = 7.3, 1.5 Hz, 1H), 3.94 (t, J = 4.4 Hz, 4H), 3.58 (br t, 4H), 3.00 (s, 3H); ^{13}C nmr: ppm 168.3, 156.1, 149.4, 135.5, 130.4, 129.8, 129.4, 127.8, 119.4, 115.8, 74.3, 66.9, 51.3, 36.7; ms: m/z 374 (M+H, 100%).

1,3-Dihydro-1-(4-morpholinyl)-3-phenyl-2*H*-pyrrolo[2,3-*b*] pyridin-2-one (**13**).

A solution of **12** (44 mg, 0.12 mmole) in potassium hydrogen phosphate-buffered methanol (98 mg in 2 ml) was stirred with sodium-amalgam (300 mg) for 45 minutes. Isolation and purification by chromatography (silica gel, methanol in chloroform, 3:97, v/v) gave **13** as a yellow oil (21.4 mg, 64%); ms: m/z 296 (M+H, 100%); ^{1}H nmr: δ 8.32 (br d, 1H, C6-H), 7.39 (m, 1H, C5-H), 7.38-7.31 (m, 3H), 7.17 (dd, J = 5.9, 1.4 Hz, 2H), 7.00 (dd, J = 5.9, 1.4 Hz, 1H, C4-H), 4.58 (s, 1H), 3.92 (t, J = 5.1 Hz, 4H), 3.53 (br m, 4H). When the desulfurizations were conducted in the presence of air, 1,3-dihydro-1-(4-morpholinyl)-3-hydroxy-3-phenyl-2*H*-pyrrolo[2,3-*b*]pyridin-2-one was also isolated in 10% yield; ^{1}H nmr: δ 8.30 (dd, J = 5.5, 1.5 Hz, 1H), 7.54 (dd, J = 7.3, 1.4 Hz, 1H), 7.41-7.33 (m, 5H), 7.01 (dd, J = 7.3, 5.5 Hz, 1H), 3.93 (t, J = 4.7 Hz, 4H), 3.73 (br m, 5H); ir (potassium bromide): 3368, 1732 cm^{-1}; hrms: Calcd. for $C_{17}H_{17}N_3O_3$: 312.1348 (M+H). Found: 312.1350.

Methyl 2-(*t*-Butyldimethylsiloxy)-2-(3-pyridinyl)acetate (**15**).

To a stirred solution of 3-pyridinecarboxaldehyde (25.0 g, 230 mmoles) in aqueous 2 *N* hydrochloric acid (105 ml) was added 20% aqueous potassium cyanide solution (97 ml) at -5°. A white crystal sludge precipitated within 30 minutes and was subsequently removed by vacuum filtration. The collected solid was taken up in concentrated hydrochloric acid (110 ml) and refluxed for 16 hours. The reaction was concentrated by rotory evaporation to yield 2-hydroxy-2-(3-pyridinyl)acetic acid hydrochloride salt (31 g, 71%); ms: (NH_3-CI) m/z 167.9 (M + H)$^+$; ^{1}H nmr: δ 5.5 (s, 1H), 8.0 (m, 1H), 8.6 (m, 2H), 8.8 (s, 1H). This material was used without further purification.

A solution of 2-hydroxy-2-(3-pyridinyl)acetic acid, hydrochloride (31 g, 0.163 mole) in methanol (125 ml) and concentrated sulfuric acid (2 ml) was refluxed through a modified Dean-Stark trap for 16 hours. The reaction was cooled and the solvent removed *in vacuo*. The solid was taken up in water (100 ml), basified with aqueous potassium carbonate and extracted with chloroform. The organic layer was washed with brine, dried (magnesium sulfate) filtered and concentrated *in vacuo* to give the methyl ester (20.94 g, 77%) as a yellow oil, which was used in the next reaction as isolated.

The methyl ester (10 g, 5.98 mmoles), *t*-butyldimethylsilyl chloride (10.82 g, 7.18 mmoles), and imidazole (10.87 g, 15.96 mmoles) in *N,N*-dimethylformamide (22 ml) was stirred at 35° for 5 hours. The solution was taken up in chloroform (150 ml) and washed copiously with water, dried over magnesium sulfate, filtered and concentrated *in vacuo* to give the product (11.9, 92%); tlc: (ethyl acetate in hexane, 1:1, v/v, R_f = 0.5); ^{1}H nmr: δ 8.65 (d, J = 2.2 Hz, 1H), 8.51 (dd, J = 4.8, 1.5 Hz, 1H), 7.76 (d, J = 7.6 Hz, 1H), 7.24 (m, 1H), 5.22 (s, 1H), 3.66 (s, 3H), 0.86 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H); ms: (NH_3/CI) m/z 282.0 (M+H, 100%).

Anal. Calcd. for $C_{14}H_{23}NO_3Si$: C, 59.75; H, 8.24; N, 4.98. Found: C, 59.66; H, 8.22; N, 4.99.

N-(4-Morpholinyl)-2-hydroxy-2-(3-pyridinyl)acetamide (**16c**).

To a 0° solution of 4-aminomorpholine (5.14 ml, 53.3 mmoles) in chloroform (50 ml) under nitrogen was added trimethylaluminium (2 *M* in hexanes, 26.6 ml), followed by stirring at room temperature for 1 hour. A solution of **15** (6.0 g, 21.3 mmoles) in chloroform (12 ml) was added dropwise and the stirring continued at 45° for 4 hours. The reaction was quenched by adding to a saturated potassium sodium tartrate (150 ml) and stirred for 15 minutes. Extraction with chloroform, followed by drying (magnesium sulfate), filtering and concentration provided a crude yellow oil which was purified by chromatography (silica gel, methanol in chloroform, 7:93, v/v, R_f = 0.33) to yield the product (4.4 g, 57%). The product was carried on without further characterization.

The silyl ether was dissolved in tetrahydrofuran (45 ml) with 1 *M* tetrabutylammonium fluoride in tetrahydrofuran (21 ml) at room temperature for 4 hours. The solvent was removed and the crude reaction purified by chromatography (silica gel, methanol in chloroform, 10:90, v/v) to give the product (3.54 g, 52%), recrystallization from a mixture of ethanol and ether afforded white crystals, mp 129-132°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 8.6 (s, 1H), 8.4 (d, 1H), 7.8 (d, 1H), 7.2 (t, 1H), 5.0 (s, 1H), 3.6

(t, 4H), 2.8 (t, 4H); ms: (NH_3/CI) m/z 238.1 (M+H, 100%); ir (potassium bromide): 3200-2800, 1670, 1206, 1112 cm^{-1}.

Anal. Calcd. for $C_{11}H_{15}N_3O_3$: C, 55.69; H, 6.37; N, 17.71. Found: C, 55.60; H, 6.37; N, 17.63.

N-(1-Piperidinyl)-2-hydroxy-2-(3-pyridinyl)acetamide (**16d**).

This compound was synthesized in 75% overall yield using the procedure for **16c**, except substituting 1-aminopiperidine for 4-aminomorpholine. The product was recrystallized from ethyl acetate, mp 162-164°; ^1H nmr (rotomers A:B 4:1): δ 8.75 (m, 1.25H), 8.55 (m, 1.25H), 1.0-2.0 (m, 4H), 7.8 (m, 0.25H), 7.65 (m, 1H), 7.25 (m, 1.25H), 6.45 (s, 1H), 5.4 (s, 1H), 5.1 (s, 0.25H), 3.1 (m, 1H), 2.75 (m, 1H), 2.6 (m, 1H), 2.25 (m, 1H).

Anal. Calcd. for $C_{12}H_{17}N_3O_2$: C, 61.26; H, 7.28; N, 17.86. Found: C, 60.90; H, 7.23; N, 17.49.

1,3-Dihydro-1-(4-morpholinyl)-2*H*-pyrrolo[2,3-*b*]pyridin-2-one (**17c**).

To a solution of **16c** (0.2 g, 0.85 mmole), triethylamine (0.26 ml, 1.88 mmoles) in dichloromethane (20 ml) and dioxane (4 ml) at 0° was added a solution of methanesulfonic anhydride (0.33 g, 1.88 mmoles) in dichloromethane (4 ml). A faint pink color appeared after approximately 15 seconds and changed to yellow within minutes. The reaction was allowed to warm to room temperature after 15 minutes and more triethylamine (2.2 equivalents) was added. Following one hour of stirring at 25°, another 2.2 equivalents of triethylamine were added and the reaction allowed to proceed for 2 hours. The solvent was removed *in vacuo* and the remaining dark residue purified by chromatography (silica gel, methanol in chloroform, 7:93, v/v) to give the product (85 mg, 46%) as an oil; ^1H nmr: δ 8.25 (dd, J = 5.1, 0.7 Hz, 1H), 7.47 (dd, J = 7.0 Hz, 1.1 Hz, 1H), 6.97 (dd, J = 7.3, 5.1 Hz, 1H), 3.91 (t, J = 4.8 Hz, 4H), 3.53 (m, 6H); ms: (NH_3/CI-DDIP) m/z 220.1 $(M+H)^+$. Compound **17c** was converted to the hydrochloride salt using 1 *M* hydrogen chloride in ether for elemental analysis, mp 231-235°; ^1H nmr (dimethyl sulfoxide-d_6): δ 8.18 (d, 1H), 7.65 (m, 1H), 7.10 (m, 1H), 3.78 (m, 4H), 3.60 (s, 2H), 3.39 (m, 4H).

Anal. Calcd. for $C_{11}H_{13}N_3O_2$•HCl: C, 51.67; H, 5.52; N, 16.43; Cl, 13.86. Found: C, 51.66; H, 5.38; N, 16.23; Cl, 13.82.

1,3-Dihydro-1-(1-piperidinyl)-2*H*-pyrrolo[2,3-*b*]pyridin-2-one (**17d**).

Using **16d** and the method of **17c**, the product was obtained in 46% yield; ms: (NH_3/CI-DDIP) m/z 218.2 $(M+H)^+$; ^1H nmr: δ 8.25 (d, J = 5.5 Hz, 1H), 7.44 (d, J = 7.3 Hz, 1H), 6.93 (dd, J = 7.0, 5.3 Hz, 1H), 3.44 (m, 6H), 1.81 (m, 4H), 1.57 (m, 2H). The free base of **17d** was converted to the hydrochloride salt for elemental analysis, mp 202-204°.

Anal. Calcd. for $C_{12}H_{15}N_3O$•HCl: C, 56.80; H, 6.36; N, 16.56; Cl, 13.97. Found: C, 56.91; H, 6.11; N, 16.49; Cl, 13.83.

1,3-Dihydro-2*H*-pyrrolo[2,3-*b*]pyridin-2-one (7-Azaoxindole, **18**).

To a -78° solution of ammonia (4 ml), **17c** (70 mg, 0.32 mmoles) and tetrahydrofuran (3 ml) was added lithium wire (18 mg, 2.4 mmoles) and the solution allowed to warm. Warming was continued to -58°, whereupon the blue color disappeared. The reaction was quenched with ammonium chloride (solid, 535 mg) and the ammonia was allowed to evaporate. Water (20 ml) was added and the aqueous layer was extracted with chloroform (3 x 20 ml). The organic extracts were washed with brine, dried (sodium sulfate), filtered and concentrated. The product was obtained as a pink solid (30 mg, 70%), mp 173-174.5° (lit 178-179° [11]); ms: (NH_3/CI-DDIP) m/z 134.9 $(M+H)^+$; ^1H nmr: δ 8.13 (m, 1H), 7.48 (m, 1H), 6.96 (m, 1H), 3.59 (s, 2H).

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