

## Synthesis of new pyrrolo[3,4-*b*]indol-3-ones as latent substrates for pyrrolo[3,4-*b*]indoles

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This paper is in celebration of the retirement of Peter A. Jacobi: friend, colleague, outstanding researcher, and consummate educator

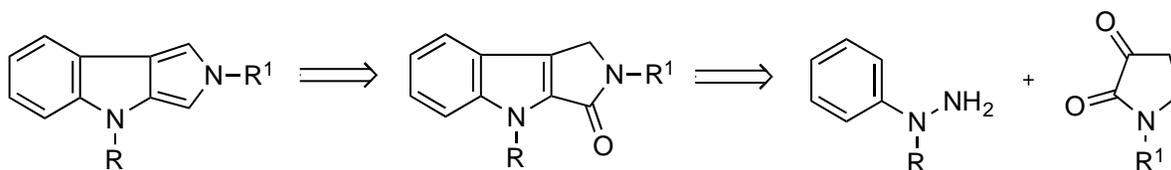
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### Abstract

We report the synthesis of new examples of the 1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-one ring system via Fischer indolization between the appropriate phenylhydrazines and pyrrolidine-2,3-diones. Lithiation at the C-1 position with lithium diisopropylamide following by quenching with iodomethane affords 1-methyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-ones in excellent yield.



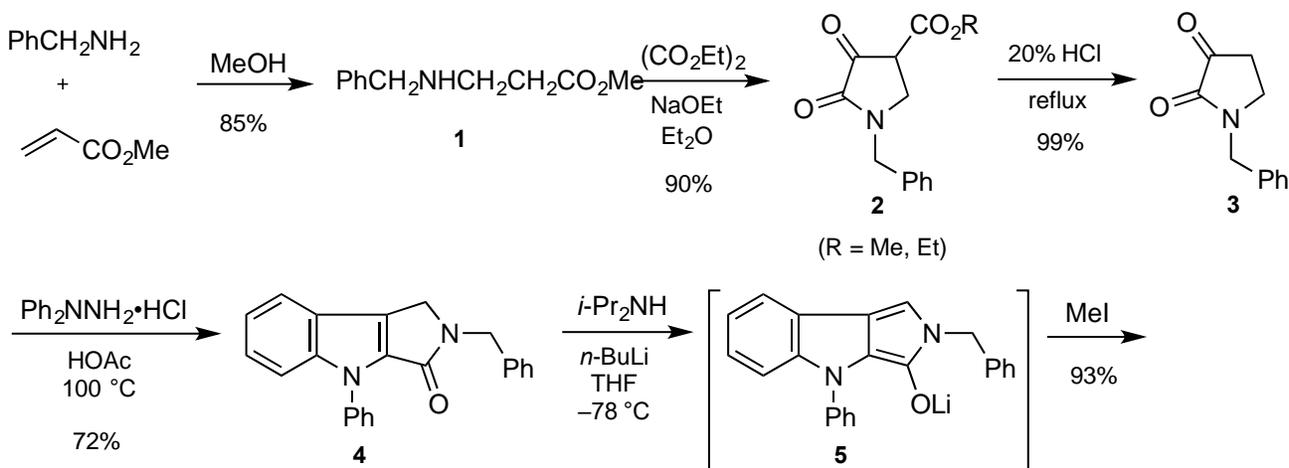
**Keywords:** Indole, pyrrolo[3,4-*b*]indole, pyrrolo[3,4-*b*]indolone, Fischer indolization, pyrrolidine-2,3-dione

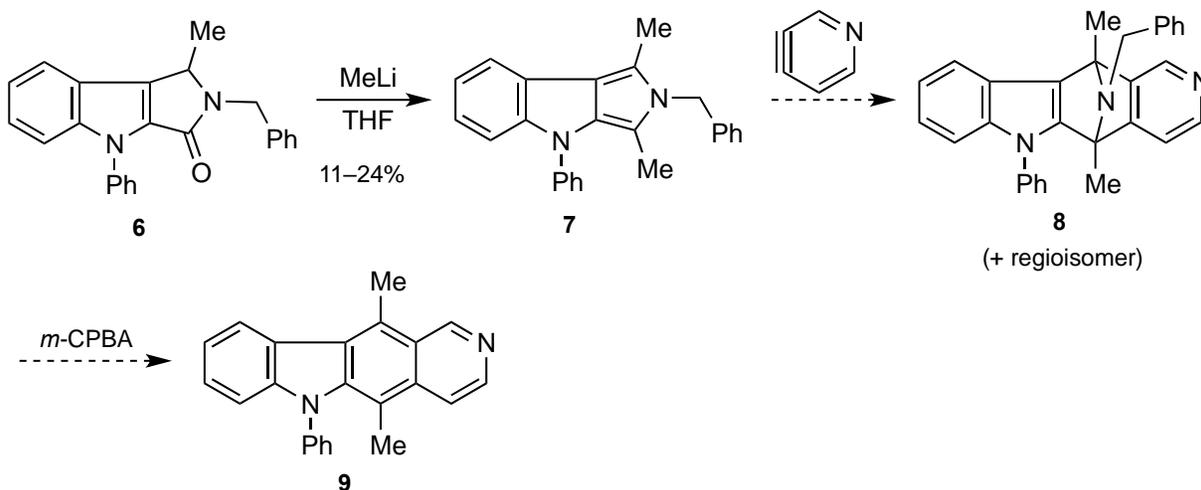
## Introduction

In continuation of our interest in the synthesis and chemistry of pyrrolo[3,4-*b*]indoles,<sup>1–6</sup> we desired a direct preparation of pyrrolo[3,4-*b*]indol-3-(2*H*)-ones having either removable nitrogen substituents or without nitrogen substitution. Guided by the seminal work both by Southwick on the synthesis of 2,3-dioxypyrrolidines<sup>7–9</sup> and the subsequent Fischer indolization to afford the first example of the pyrrolo[3,4-*b*]indole ring system (i.e., 1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-one),<sup>10</sup> and by Welch on the first generation of a 2,4-dihydropyrrolo[3,4-*b*]indole,<sup>11</sup> we now report our synthesis of new pyrrolo[3,4-*b*]indol-3(2*H*)-ones as prospective substrates for 2,4-dihydropyrrolo[3,4-*b*]indoles.

## Results and Discussion

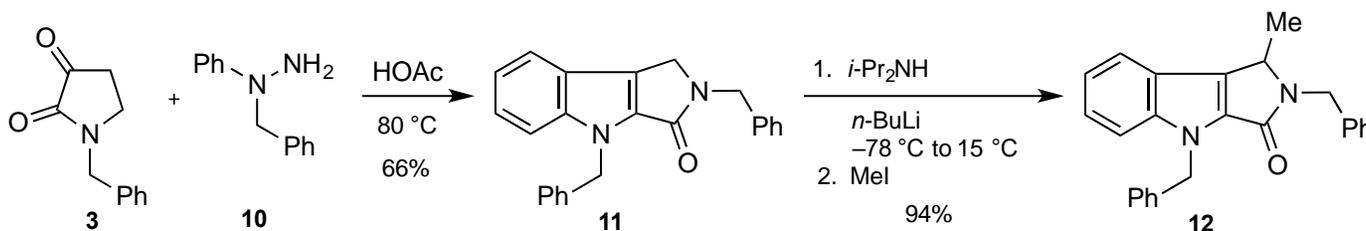
Our synthesis of 2-benzyl-1-methylpyrrolo[3,4-*b*]indol-3(2*H*)-one (**6**) is summarized in Scheme 1. Following the literature procedures,<sup>8,11</sup> we prepared the known **4** in good overall yield. Whereas the literature method employed sodium methoxide and dimethyl oxalate to give the methyl ester (**2**, R = Me) in 75% yield,<sup>8</sup> we obtained a 90% yield using sodium ethoxide and diethyl oxalate. Methylation of the C-1 position via lithiation with lithium diisopropylamide (LDA) to generate pyrrole oxide **5** and quenching with iodomethane afforded **6** in 93% yield. Treatment of indolone **6** with methyl lithium in diethyl ether or tetrahydrofuran at room temperature or reflux gave the labile pyrrolo[3,4-*b*]indole **7** in low yields (11–24%). However, efforts to trap this species with 3,4-pyridyne afforded a complex mixture of products, which, upon attempted deamination with *m*-chloroperbenzoic acid,<sup>12</sup> gave at best a trace of *N*-phenylellipticine (**9**) and/or the corresponding isoellipticine (not shown).





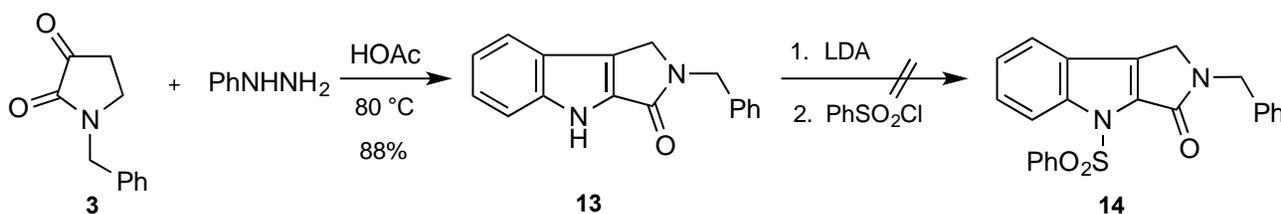
**Scheme 1.** Synthesis of 2-benzyl-1-methyl-4-phenyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-one (**6**).

In similar fashion, we prepared the new 2,4-dibenzyl-1-methylpyrrolo[3,4-*b*]indol-3-one **12** from 1-benzyl-1-phenylhydrazine (**10**)<sup>13</sup> and pyrrolidine-2,3-dione (**3**) (Scheme 2). As before, the C-1 lithiation/methylation sequence on indolone **11** proceeded in excellent yield to give **12**.



**Scheme 2.** Synthesis of 2,4-dibenzyl-1-methyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-one (**12**).

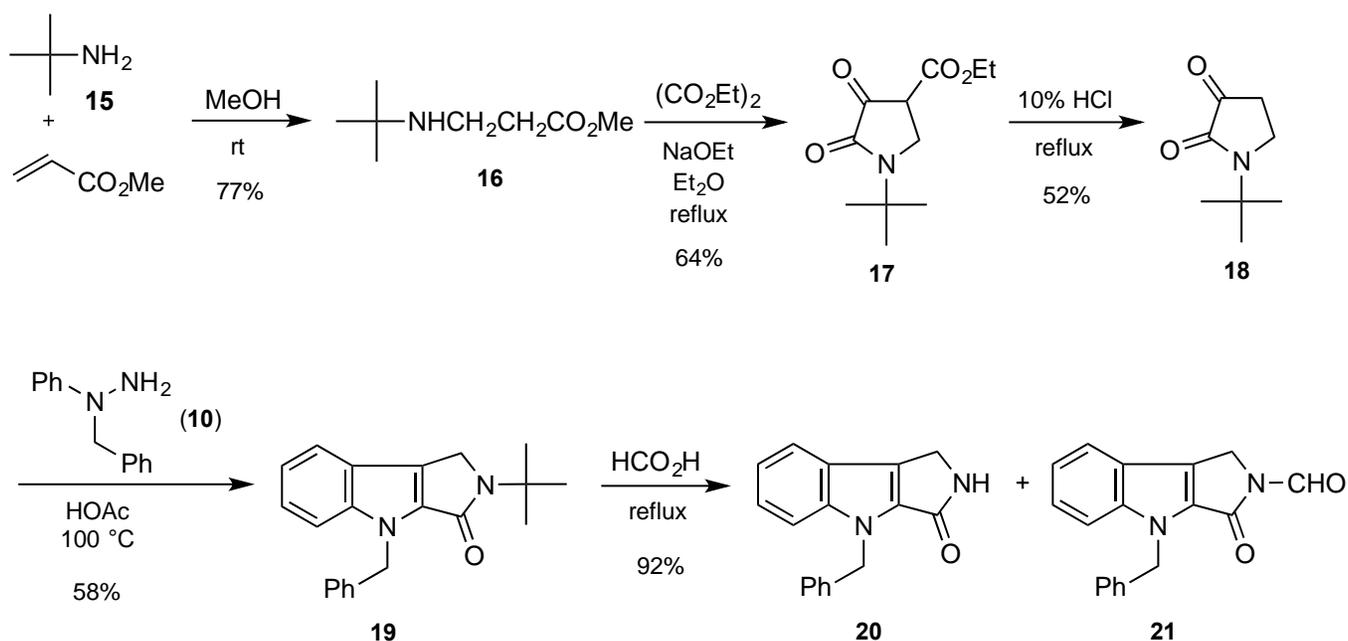
As shown in Scheme 3, we synthesized the first example of an unsubstituted indole nitrogen in the pyrrolo[3,4-*b*]indole series. Thus, 2-benzylpyrrolo[3,4-*b*]indole **13** was formed in 88% yield from dione **3** and phenylhydrazine. Attempts to prepare the *N*-phenylsulfonyl derivative **14** failed (KOH, DMSO, PhSO<sub>2</sub>Cl; *n*-Bu<sub>4</sub>NHSO<sub>4</sub>, NaOH, PhSO<sub>2</sub>Cl).



**Scheme 3.** Synthesis of 2-benzyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-one (**13**).

Our approach to an N(2) unsubstituted pyrrolo[3,4-*b*]indolone **20** is shown in Scheme 4. The known 1-(*tert*-butyl)pyrrolidine-2,3-dione (**18**) was subjected to Fischer indolization to give indolone **19** in 58% yield.

Removal of the *tert*-butyl group with refluxing formic acid afforded a mixture of the desired product **20** and the *N*-formyl **21**. As a result this approach was no longer pursued.



**Scheme 4.** Attempted synthesis of 4-benzyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2H)-one (**20**).

## Conclusion

As a designed route to pyridocarbazoles and other carbazoles via 2,4-dihydropyrrolo[3,4-*b*]indoles, we have synthesized the new pyrrolo[3,4-*b*]indolones **6**, **11**, **12**, and **13**, the latter of which is the first example of an *N*(4) unsubstituted pyrrolo[3,4-*b*]indolone. We have demonstrated a C-1 lithiation-alkylation sequence via the presumed pyrrole alkoxide **5**. And, we revealed the feasibility of generating the pyrrolo[3,4-*b*]indole **7** ring system from pyrrolo[3,4-*b*]indolone **6**, although under these conditions trapping of **7** with 3,4-pyridyne did not succeed. The chemistry of these new pyrrolo[3,4-*b*]indolones **6**, **11**, **12**, and **13** will be reported in due course.

## Experimental Section

**General.** Melting points were determined in open capillaries with a Mel-Temp Laboratory Devices or a Büchi 510 melting point apparatus and are uncorrected. Elemental analyses were performed by Atlantic Microlabs, Atlanta, GA. Infrared spectra were recorded on a Perkin-Elmer 599 instrument or a Perkin-Elmer 1600 Fourier transform spectrometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were routinely obtained with a JEOL-FX60Q Fourier transform NMR spectrometer or a Varian XL-300 multinuclear Fourier transform instrument. Chemical shifts are reported in parts per million downfield from tetramethylsilane as the internal reference. Low resolution mass spectra were determined on a Finnigan EI-Cl gas chromatograph-mass spectrometer or a Hewlett Packard 5890 Instrument. Ultraviolet (UV) spectra were recorded on a Unicam SF-800A spectrophotometer or a Hewlett Packard 5890 Diode-Array spectrophotometer. Thin layer chromatography (TLC) was performed on

precoated (0.2 mm) silica gel 60 F<sub>254</sub> plastic sheets (E. Merck). Spots were visualized under 254 nm UV light, an iodine chamber, and/or by spraying with a solution of 3% aqueous ceric ammonium sulfate in 10% H<sub>2</sub>SO<sub>4</sub> followed by brief heating. THF was distilled from Na/benzophenone and diisopropylamine was distilled from NaH. All reactions were performed in oven-dried (130 °C) or flame-dried glassware under prepurified Ar or N<sub>2</sub>.

**Methyl 3-Benzylaminopropionate (1).** To a solution of benzylamine (53.58 g, 0.500 mol) in absolute MeOH (400 mL) under N<sub>2</sub> was added freshly distilled methyl acrylate (43.05 g, 0.500 mol). The resulting colorless mixture was allowed to stand for 24 h and the solvent was removed under reduced pressure to give a colorless oil which was fractionally distilled. After benzylamine (53–55 °C/2 Torr) (8.05 g) was collected, there was obtained 69.98 g (85% based on recovered benzylamine) of **1** as a colorless liquid: bp 112–114 °C/1 Torr (lit.<sup>8</sup> bp 145–147 °C/7 Torr); IR (KBr) 3110, 2880, 2820, 1740, 1440, 1170, 740, and 690 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.28 (s, 5H), 3.79 (s, 2H), 3.65 (s, 3H), 2.90 (t, 2H), 2.48 (t, 2H), 1.60 (broad s, 1H).

**Ethyl (Methyl) 1-Benzyl-4,5-dioxopyrrolidine-3-carboxylate (2).** To a solution of freshly prepared solid NaOEt (23.31 g, 0.343 mol) in anhydrous Et<sub>2</sub>O (170 mL) under N<sub>2</sub> was added diethyl oxalate (50.10 g, 0.343 mol) followed by the dropwise addition of amino ester **1** (66.25 g, 0.343 mol) in dry Et<sub>2</sub>O (170 mL) over 2 min. The resulting solution was refluxed for 0.5 h with magnetic stirring and then allowed to stand overnight under N<sub>2</sub>. After rotary evaporation of the solvent, the resulting pale yellow solid was dissolved in warm H<sub>2</sub>O (1700 mL) and slowly acidified with 20% HCl until the aqueous portions became slightly acidic. The mixture was allowed to stand for 20 h and the colorless precipitate was collected, washed with cold H<sub>2</sub>O, and dried at 50–60 °C/20 Torr for 24 h to give 76.55 g (90%) of **2** as a mixture of methyl and ethyl esters: mp 139–150 °C (MeOH); Recrystallization of a small portion from MeOH gave a colorless crystalline solid mixture of the two esters (NMR) mp 136–143 °C: IR (KBr) 3100, 3020, 2920, 1670, 1420, 1230, 740, and 690 (cm<sup>-1</sup>); NMR (CDCl<sub>3</sub>) δ 1.30 (t, 3H, *J* 6 Hz), 3.80 (s, 2H), 3.90 (s, 3H), 4.30 (q, 2H, *J* 6 Hz), 4.65 (s, 2H), 7.38 (s, 5H), and 8.42 (s, 1H) ppm. The melting point of the pure methyl ester is mp 183–184 °C.<sup>8</sup>

**1-Benzylpyrrolidine-2,3-dione (3).** A mixture of the ester mixture **2** (6.05 g, 24.0 mmol) in 20% HCl (160 mL) was refluxed until CO<sub>2</sub> evolution has subsided and all the material has dissolved (2.5–3 h). The solution was cooled and extracted with CHCl<sub>3</sub> (4 x 125 mL). The combined extracts were washed with H<sub>2</sub>O (1 x 50 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated *in vacuo* to afford 4.50 g (99%) of **3** as an off-white solid: mp 95–97 °C (lit.<sup>8</sup> mp 99–100 °C); IR (KBr) 3290, 3020, 2920, 1750, 1700, 1490, 1435, 1300, 870, 740, 690 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.31 (s, 5H), 4.66 (s, 2H), 3.53 (t, 2H), 2.60 (t, 2H).

**2-Benzyl-4-phenyl-1,4-dihydropyrrolo[3,4-*b*]indol-3-(2H)-one (4).** To a suspension of 1,1-diphenylhydrazine hydrochloride (3.20 g, 14.5 mmol) in glacial HOAc (46 mL) was added a solution of dione **3** (2.77 g, 14.5 mmol) in glacial HOAc (46 mL) and the mixture was heated for 15 min on a steam bath. Concentrated HCl (23 mL) was then added to the warm solution and this mixture was heated for an additional 25 min. The reaction mixture was cooled, diluted with H<sub>2</sub>O (75 mL), and allowed to stand at 5 °C for 2–3 h. The product was collected by filtration, washed several times with H<sub>2</sub>O, and dried at 40–50 °C/20 Torr for 24 h to give 3.52 g (72%) of **4** as an off-white solid, mp 138–140 °C. Crystallization from EtOAc gave **4** as colorless crystals: mp 145–146 °C (lit.<sup>11</sup> mp 145.5–146.5 °C); IR (CHCl<sub>3</sub>) 3030, 1682, 1500, 1452, 1380, 1215, 690 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.70–7.10 (m, 9H), 7.30 (s, 5H), 4.76 (s, 2H), 4.31 (s, 2H); UV (MeO) λ<sub>max</sub> 246, 299 nm.

**2-Benzyl-1-methyl-4-phenyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2H)-one (6).** A magnetically stirred solution of lithium diisopropylamide (LDA) (3.7 mmol) was prepared from *i*-Pr<sub>2</sub>NH (0.38 g, 3.7 mmol) and *n*-BuLi (1.6 M in hexane; 2.32 mL, 3.7 mmol) in dry THF (10 mL) under N<sub>2</sub> at –78 °C. After 20 min at –78 °C, a solution of indolone **4** (1.00 g, 2.96 mmol) in dry THF (10 mL) was slowly added to the LDA. The resulting blue-green solution was warmed to 15 °C over 2 h, cooled to –78 °C, and quenched with a solution of iodomethane (0.28

mL, 4.5 mmol) in dry THF (8 mL) over 1 min. After warming to rt overnight, the reaction mixture was partially concentrated *in vacuo*, and then slowly added to a solution of concentrated HCl (1 mL) in H<sub>2</sub>O (50 mL). The resulting precipitate was dissolved in EtOAc (150 mL) and the aqueous layer was further extracted with EtOAc (2 x 100 mL). The combined organic portions were washed with H<sub>2</sub>O (2 x 100 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and rotary evaporated to give 0.97 g (93%) of **6** as a light tan solid. Recrystallization from EtOAc gave the analytical sample: mp 178–179 °C; IR (CHCl<sub>3</sub>) 3025, 1680, 1500, 1380, 1215, 690 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.75–7.15 (m, 9H), 7.30 (s, 5H), 5.40–4.20 (m, 3H), 1.60 (d, 3H, *J* 6 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 161.6, 141.9, 137.9, 136.2, 133.0, 132.7, 129.1, 128.6, 127.9, 127.3, 127.1, 125.8, 124.7, 121.7, 121.2, 119.7, 112.3, 51.3, 44.0, 18.2; UV (MeOH) λ<sub>max</sub> 245, 299 nm. *Anal.* Calcd for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O: C, 81.79; H, 5.72; N, 7.95. Found: C, 81.54; H, 5.75; N, 7.95.

**1-Benzyl-1-phenylhydrazine (10).** To a magnetically stirred solution of phenylhydrazine (10.8 g, 0.100 mol) in distilled H<sub>2</sub>O (30 mL) were added NaHCO<sub>3</sub> (20 g) and PhCH<sub>2</sub>Br (11.9 mL, 0.100 mol). The resultant mixture was refluxed for 3 h and then allowed to cool to 25 °C. The layers were separated and the yellow upper layer was diluted with Et<sub>2</sub>O (100 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated *in vacuo* to afford 19.6 g (99%) of **10** as a yellow oil. This material was identical by NMR with a sample prepared from the commercial hydrochloride salt, and was normally used without further purification. On standing for several weeks at 0 °C the oil darkened and was distilled, bp 125–130 °C/1.5 Torr (lit.<sup>13</sup> bp 157–159 °C/4 Torr); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 3.31 (br s, 2H), 4.49 (s, 2H), 6.57–7.52 (m, 5H), 7.24 (s, 5H).

**2-Dibenzyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-one (11).** To a suspension of 1-benzyl-1-phenylhydrazine hydrochloride (**10**-HCl) (8.74 g, 0.044 mol) in glacial HOAc (80 mL) was added a solution of **3** (7.5 g, 0.040 mol) in glacial HOAc (80 mL). The resulting suspension was stirred and warmed to 80 °C over a period of approximately 20 min to effect hydrazone formation. Then concentrated HCl (45 mL) was added to the warm solution with subsequent heating for an additional 2.5 h. After 10 min more of heating at 95–100 °C, the hot solution was diluted with distilled H<sub>2</sub>O (125 mL) to yield 8.63 g (66%) of greenish crystalline **11**. Recrystallization from EtOAc gave off-white crystals, mp 144–146 °C. Pertinent spectral data for **11** are as follows: IR (KBr) 3025, 2940, 1670, 1555, 1440, 1390, 740, 690 (cm<sup>-1</sup>); NMR (CDCl<sub>3</sub>) δ 4.30 (s, 2H), 4.76 (s, 2H), 5.65 (s, 2H), 7.05–7.65 (m, 4H), 7.30 (s, 10H) ppm; UV (95% EtOH) λ<sub>max</sub> 215, 232 (sh), 298, 307 (sh) nm; MS *m/e* 352 (M<sup>+</sup>), 261, 247, 156, 128, 91 (100%); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 45.4, 46.9, 47.4, 111.6, 120.0, 120.4, 121.8, 124.1, 124.5, 127.4, 127.9, 128.5, 128.6, 134.0, 137.3, 137.5, 141.6, 162.8. *Anal.* Calcd for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O: C, 81.79; H, 5.72; N, 7.95. Found: C, 81.90; H, 5.79; N, 7.96.

**2,4-Dibenzyl-1-methyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-one (12).** To a solution of *i*-Pr<sub>2</sub>NH (0.83 g, 0.0082 mol) in THF (20 mL) (freshly distilled) at –78 °C under N<sub>2</sub>, was added slowly, with stirring 1.70 M *n*-BuLi/hexane (4.60 mL, 0.0078 mol). After stirring for 30 min at –78 °C, a solution of pyrrole **11** (2.5 g, 0.0071 mol) in THF (20 mL) was added, resulting in the formation of a brightly brown-colored solution. The presumed enolate was allowed to gradually warm to 15 °C over a 2.0 h period, cooled again to –78 °C, and then iodomethane (2.0 g, 0.014 mol) was added dropwise over 1 min. After 1.0 h, the solution had become lighter brown and it was allowed to warm to rt over 15 h. After this period saturated NaHCO<sub>3</sub> solution (100 mL) was added slowly. The resulting oil was then dissolved in Et<sub>2</sub>O, the aqueous filtrate was twice extracted with EtOAc (2 x 100 mL), and the combined extracts were washed with H<sub>2</sub>O (1 x 100 mL), brine (1 x 100 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated *in vacuo* to give 2.43 g (94%) of **12** as a viscous oil that crystallized under N<sub>2</sub>. Recrystallization from EtOAc (3X) gave **12** as off-white crystals, mp 117.5–119 °C; IR (KBr) 3040, 2930, 1670, 1550, 1480, 1440, 1375, 1215, 735, 690 cm<sup>-1</sup>; NMR (CDCl<sub>3</sub>) δ 1.55 (d, 3H, *J* = 6Hz), 4.20–5.40 (m, 3H), 5.65 (s, 2H), 7.05–7.70 (m, 14H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 18.3, 43.9, 47.6, 51.7, 111.7, 119.7, 120.4, 121.5, 124.0, 127.3, 127.4, 127.8, 128.6, 130.4, 133.3, 137.3, 137.8, 141.7, 162.4; UV (95% EtOH) λ<sub>max</sub> 208, 222 (sh), 300,

310 (sh) nm; MS,  $m/e$  366 ( $M^+$ ), 351, 275, 260, 247, 170, 140, 91 (100%). *Anal.* Calcd for  $C_{25}H_{22}N_2O$ : C, 81.94; H, 6.05; N, 7.64. Found: C, 81.83; H, 5.85; N, 7.96.

**2-Benzyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-one (13).** To a suspension of phenylhydrazine (1.73 g, 0.0155 mol) in glacial HOAc (55 mL) was added a solution of **3** (2.80 g, 0.0148 mol) in glacial HOAc (55 mL), and the resulting solution was warmed to 80 °C over a period of about 10 min to effect hydrazone formation. Concentrated HCl (30 mL) was added to the warm solution, with subsequent heating for an additional 2.5 h. After 10 min more of heating at 90–100 °C, the hot solution was diluted with distilled  $H_2O$  (125 mL) to yield 3.44 g (88%) of an off-white solid (**13**). Crystallization from EtOAc gave an off-white fluffy powder, mp 282–286 °C, and recrystallization from EtOAc gave the analytical sample of **13** as very light, fluffy needles: mp 290–293 °C dec; IR (KBr) 3195, 1650, 1450, 1340, 750, 710  $cm^{-1}$ ; NMR ( $CDCl_3$ )  $\delta$  3.80 (broad, 1H), 4.45 (s, 2H), 4.80 (s, 2H), 7.0–7.4 (s, 9H) ppm;  $^{13}C$  NMR ( $d_6$ -DMSO)  $\delta$  45.6, 46.1, 113.3, 119.9, 121.5, 123.8, 125.0, 127.2, 128.6, 134.2, 138.1, 141.3, 162.1; UV (95% EtOH)  $\lambda_{max}^{EtOH}$  220, 235 (sh), 298, 307 (sh) nm; MS,  $m/e$  262 ( $M^+$ ), 171, 157, 129, 106, 91 (100%). *Anal.* Calcd for  $C_{17}H_{14}N_2O$ : C, 77.84; H, 5.38; N, 10.68. Found: C, 77.76; H, 5.41; N, 10.63.

**Methyl 3-(*tert*-Butylamino)propionate (16).** To a solution of *tert*-butyl amine (**15**) (34.8 g, 0.48 mol, 50 mL) in MeOH (380 mL) under  $N_2$  was added freshly distilled methyl acrylate (41.3 g, 0.48 mol, 43.2 mL). The resulting colorless solution was allowed to stand for 96 h under  $N_2$ . The solvent was removed under reduced pressure. The crude product was collected by vacuum distillation at 82 °C/10 Torr (lit.<sup>15</sup> bp 63 °C/10 Torr) to yield 58.5 g (77%) of (**16**) as a colorless liquid, which was used directly in the next step;  $^1H$  NMR  $\delta$  3.65 (s, 3H), 3.32 (s, 1H), 2.80 (m, 2H), 2.47 (m, 2H), 1.07 (s, 9H); IR 2950, 1749  $cm^{-1}$ .

**Ethyl 1-(*tert*-Butyl)-4,5-dioxopyrrolidine-3-carboxylate (17).** To a solution of freshly prepared solid NaOEt (19.6 g, 288 mmol) in anhydrous ether (125 mL) under  $N_2$  was added diethyl oxalate (42.2 g, 288 mmol) followed by dropwise addition of amino ester **16** (45.8 g, 288 mmol) in dry ether (125 mL) over a period of 5 min. The resulting solution was heated at reflux for 30 min and then let stand overnight. The solvent was removed and the resulting pale yellow solid was dissolved in  $H_2O$  (1500 mL) and then acidified slightly with 20% aqueous HCl. The mixture was placed in a separatory funnel and the organic layer separated. The aqueous layer was allowed to stand for 24 h, which yielded 31.9 g of **17** as white crystals. The organic layer was evaporated under reduced pressure to yield an additional 7.3 g of **17**, for a combined 39.2 g (64%) of **17**. Recrystallization from petroleum ether (60–120 °C) gave mp 120–122 °C (lit.<sup>9</sup> mp 126.5–127.5 °C). (Enolic form)  $^1H$  NMR  $\delta$  4.33 (q, 2H,  $J$  7.0 Hz), 4.04 (s, 2H), 3.85 (s, 1H), 1.49 (s, 9H), 1.34 (t, 3H,  $J$  7.0 Hz).

**1-(*tert*-Butyl)pyrrolidine-2,3-dione (18).** A solution of 10.0 g (0.044 mol) of amino ester (**17**) in 10% aqueous HCl (250 mL) was heated at reflux until  $CO_2$  evolution had ceased and all of the material had dissolved (2.5 h). The reaction mixture was cooled to rt and extracted with  $CH_2Cl_2$  (3 x 50 mL). The combined organic extracts were washed with  $H_2O$ , and then dried ( $Na_2SO_4$ ). The solvent was removed under reduced pressure to yield 3.8 g (52%) of (**18**) as a crystalline orange solid; mp 97–99 °C (lit.<sup>9</sup> mp 103.5–104 °C);  $^1H$  NMR  $\delta$  3.74 (m, 2H), 2.67 (m, 2H), 1.50 (s, 9H).

**4-Benzyl-2-(*tert*-butyl)-1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-one (19).** To a stirred suspension of 1-benzyl-1-phenylhydrazine (**10**) (1.98 g, 10.0 mmol) in glacial HOAc (30 mL) was added a solution of dione **18** (1.55 g, 10.0 mmol) in glacial HOAc (30 mL) and the mixture was heated for 15 min on a steam bath. Concentrated HCl (15 mL) was added to the warm solution and the resulting solution heated for an additional 35 min on the steam bath. The reaction mixture was cooled, diluted with  $H_2O$  (50 mL), and allowed to stand at 5 °C overnight. Filtration of the resulting product gave 0.37 g of **19**. The filtrate was extracted with  $CH_2Cl_2$  and the organic layer was washed with aqueous 10% NaOH,  $H_2O$ , and dried ( $Na_2SO_4$ ). Evaporation gave an additional 1.6 g of **19** as a tan solid. The solids were combined and recrystallized from EtOH to give 1.85 g (58%) of **19** as

an off-white solid, mp 196–198 °C, which was used directly in the next step;  $^1\text{H}$  NMR  $\delta$  7.16–8.17 (m, 9H), 5.59 (s, 2H), 4.46 (s, 2H), 1.59 (s, 9H);  $^{13}\text{C}$  NMR  $\delta$  163.7, 141.5, 137.5, 128.6, 128.5, 127.4, 127.3, 123.8, 123.3, 121.5, 120.3, 119.9, 111.7, 55.0, 47.1, 44.0, 28.2.

**4-Benzyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2H)-one (20)** and **4-Benzyl-2-formyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2H)-one (21)**. A solution of pyrroloindolone **19** (0.135 g, 0.42 mmol) in HCOOH (5 mL) was heated at reflux for 2 h. Water (10 mL) was added while the solution was hot and the reaction was allowed to cool to rt. The resulting product was filtered to give 0.101 g (92%) of a mixture of **20** and **21** as an off-white solid, mp 195 °C dec;  $^1\text{H}$  NMR  $\delta$  7.70–7.22 (m, 9H), 5.59 (s, 2H), 4.83 (s, 2H), 1.65 (br s, 1H);  $^{13}\text{C}$  NMR  $\delta$  159.6, 143.5, 136.6, 130.8, 129.6, 128.7, 127.9, 127.5, 124.4, 121.4, 121.3, 121.2, 111.8, 47.8, 41.8; IR 3290, 1672  $\text{cm}^{-1}$ ; MS *m/e* (relative intensity): 262 (24), 234 (13.5), 185 (9), 91 (100). This mixture was not further characterized.

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