Novel and Simple Syntheses of 5*H*-Pyrido[4,3-*b*]indole (γ-Carboline) Derivatives Having a Methoxycarbonyl Group at the 4-Position Based on 1-Hydroxyindole Chemistry[1)]

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A simple synthetic method for 5*H*-pyrido[4,3-*b*]indole (γ-carboline) derivatives having a methoxycarbonyl group at the 4-position was developed based on 1-hydroxyindole chemistry. By applying the method, various 3-substituted methyl 5*H*-pyrido[4,3-*b*]indole-4-carboxylates and 2-substituted methyl 2,3-dihydro-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylates were prepared.

Key words 1-hydroxyindole; 1-methoxyindole-3-carbaldehyde; 5*H*-pyrido[4,3-*b*]indole; dimethyl 2-(3-formylindol-2-yl)malonate; methyl 5*H*-pyrido[4,3-*b*]indole-4-carboxylate; methyl 2,3-dihydro-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate

The members of the 5*H*-pyrido[4,3-*b*]indole[2)] family (**1**, γ-carboline) include various biologically active substances, such as Tryp-P-2[3)] (**2**), omeril[4)] (**3**), stobadine[5)] (**4**), alosetron[6)] (**5**), and so on (Fig. 1).[7)] γ-Carbolines, however, have attracted less interest than the related 9*H*-pyrido[3,4-*b*]indoles[2)] (**6**, β-carboline).

In our continuing search[8)] for biologically active compounds using reactions developed by us,[8)] we have focused on novel γ-carboline derivatives having a substituent at the 4-position. We required methyl 2,3-dihydro-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylates (A) and methyl 5*H*-pyrido[4,3-*b*]indole-4-carboxylates (B) as key synthetic intermediates. Although many synthetic methods for γ-carbolines[9)] have been reported in the literatures,[9)] they are not suitable for the syntheses of A and B. In this report, we wish to describe a novel and simple synthetic method for A and B.

We have thus far established a convenient two-step synthesis of 1-methoxyindole-3-carbaldehyde[10)] (**9**) from 2,3-dihydroindole (**7**) through 1-methoxyindole (**8**) and also disclosed its characteristic reactivity[11)] to give the corresponding 2-substituted indoles (C) as shown in Chart 1. Based on these nucleophilic substitution reactions of 1-hydroxyindole, we have now succeeded in developing the desired simple synthetic method for γ-carbolines.

Compound **9** reacted with methyl malonate in the presence of sodium methoxide (NaOMe) as a base in refluxing methanol (MeOH), resulting in the formation of dimethyl 2-(3-formylindol-2-yl)malonate (**10a**) and methyl 2-(3-formylindol-2-yl)acetate (**11a**) in 53 and 7%

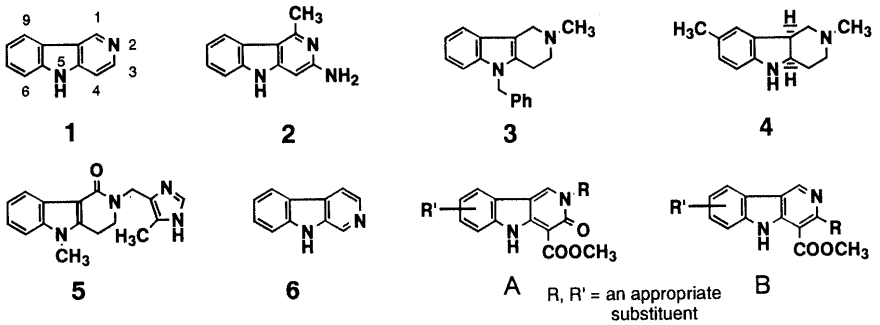

Fig. 1

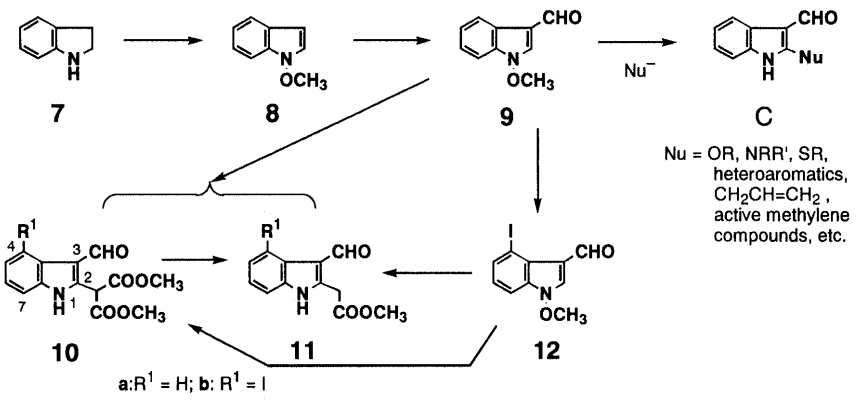

Chart 1

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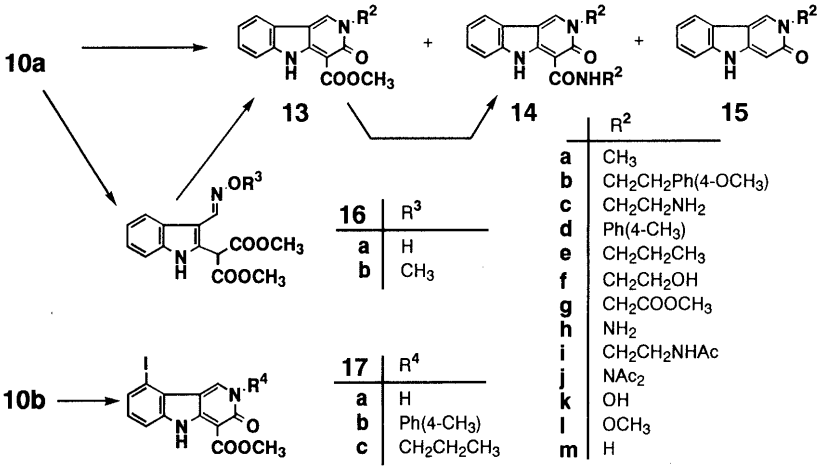


Chart 2

yields, respectively, together with 39% recovery of unreacted **9**. When the above reaction was carried out in *N*,*N*-dimethylformamide (DMF) with potassium tertiary butoxide (KO^{t}Bu) as a base at room temperature, **10a** was obtained in only 17% yield with 71% recovery of **9**. Compound **11a** was also obtained from **10a** in 56% yield together with 31% recovery of **10a** by treatment with NaOMe in refluxing MeOH.

It should be noted that the reaction of 4-iodo-1-methoxyindole-3-carbaldehyde (**12**), prepared from **9** according to our procedure,[10] with methyl malonate and NaOMe in refluxing MeOH resulted in the selective formation of methyl 2-(3-formyl-4-iodoindol-2-yl)acetate (**11b**) in 88% yield. When the same reaction was carried out in DMF with KO^{t}Bu as a base at room temperature, **10b** was selectively produced in 98% yield. These contrasting results can probably be explained as follows: smaller methoxide can undergo nucleophilic addition to the carbonyl carbon atom of the dimethyl malonate moiety in **10b** to remove one methoxycarbonyl group, but the bulky tertiary butoxide can not approach the ester carbonyl carbon atom, so that **10b** remains untouched.

As shown in Chart 2, **10a** and **10b** were found to be useful building blocks for our purpose. The reaction of **10a** with an excess amount of methylamine in refluxing MeOH for 30 min produced methyl 2,3-dihydro-2-methyl-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (**13a**), 2,3-dihydro-2,*N*-dimethyl-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxamide (**14a**), and 2-methyl-5*H*-pyrido[4,3-*b*]indol-3-one (**15a**) in 72, 22, and 5% yields, respectively. When the same reaction was carried out for a longer time (20 h), **14a** was obtained in 74% yield together with 14% recovery of **10a**. Similarly, the reaction of **10a** with 4-methoxyphenethylamine in refluxing MeOH for 1 h produced **13b** and **14b** in 73 and 17% yields, respectively. Ethylenediamine reacted with **10a** to give **13c** and **14c** in the respective yields of 75 and 22%. These compounds, **13b** and **13c**, were readily converted to **14b** and **14c** in 42 (together with 43% recovery) and 88% yields, by reaction with the corresponding amines for 24 and 23 h, respectively.

4-Methylaniline, propylamine, and ethanolamine reacted with **10a** to afford methyl 2,3-dihydro-3-oxo-2-(*p*-tolyl)- (**13d**), -2-propyl-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (**13e**), and methyl 2,3-dihydro-2-(2-hydroxyethyl)-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (**13f**) in 98, 96, and 98% yields, respectively. The reaction of **10a** with glycine methyl ester hydrochloride in refluxing MeOH in the presence of K_2CO_3 afforded the 2-methoxycarbonylmethyl derivative (**13g**) in 98% yield.

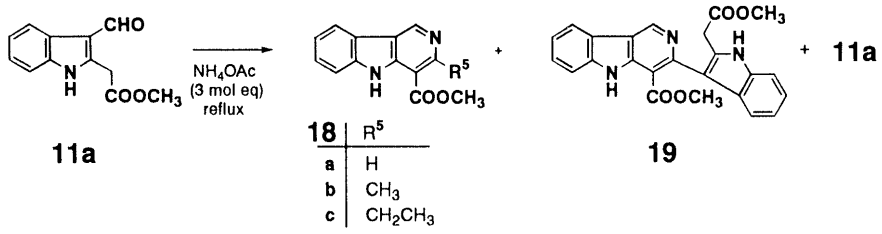
The reaction of **10a** with hydrazine in refluxing MeOH for 5 min afforded **13h** and unreacted **10a** in 41 and 50% yields, respectively. The structures of **13c** and **13h** were proved by reacting them with acetic anhydride to give the amide (**13i**) and diacetylamino (**13j**) derivatives in 99 and 62% yields, respectively. In the reactions of **10a** with hydroxylamine hydrochloride and *O*-methylhydroxylamine hydrochloride, formation of the oxime (**16a**) and oxime methyl ether (**16b**) was observed in the respective yields of 84 and 99%. In each case, the product was a single isomer, which was presumed to be the thermodynamically stable *anti*-isomer.

When **16a** was treated with K_2CO_3 in refluxing MeOH, ring closure was attained, giving 2-hydroxy-γ-carbolin-3-one (**13k**) in 89% yield. On the other hand, heating at reflux in DMF successfully converted **16b** into 2-methoxy-γ-carbolin-3-one (**13l**) in 72% yield. Although **13k** was stable, **13l** was a relatively unstable compound and gradually transformed to **13m** on standing. Heating of an MeOH solution of **13l** at reflux for 5 h also produced **13m** in 24% yield, in addition to 61% recovery of **13l**. Alternatively, **13l** was prepared from **13k** by methylation with dimethyl sulfate at room temperature.

The reaction of **10b** with ammonium acetate (NH_4OAc) in refluxing MeOH produced methyl 2,3-dihydro-9-iodo-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (**17a**) and **11b** in 66 and 12% yields, respectively. 4-Methylaniline and propylamine also reacted successfully with **10b** in refluxing MeOH, resulting in the formation of **17b** and **17c** in 91 and 91% yields, respectively. Since these compounds have iodide at the 9-position, derivatives having various side chains at this position can be produced.

To our surprise, an attempt to prepare **15m** by reacting **11a** with NH_4OAc in refluxing MeOH for 10 h resulted in the formation of **18a** and **19** in 28 and 59% yields, respectively (Table 1, entry 1). Even when pure MeOH was used immediately after distillation over sodium

Table 1



Entry	Reagent	Reaction conditions Solvent	Time (h)	Products and yield (%) 18	19	11a
1	—	CH_3OH	10	**18a** (28)	59	—
2	—	CH_3OH distilled over $NaBH_4$	10	**18a** (17)	53	—
3	—	CH_3OH distilled over $NaBH_4$, Ar gas	10	**18a** (5)	43	—
4	$(CH_2O)_n$ (1 mol eq)	CH_3OH	1	**18a** (42)	—	—
5	—	CH_3CH_2OH	10	**18b** (19)	69	—
6	CH_3CHO (1 mol eq)	CH_3CH_2OH	1	**18b** (45)	29	10
7	—	$CH_3CH_2CH_2OH$	2	**18c** (14)	39	20
8	C_2H_5CHO (3 mol eq)	$CH_3CH_2CH_2OH$	1	**18c** (55)	—	—

borohydride (entry 2), the formation of **18a** was observed, though the yield dropped to 17%. When the same reaction was carried out under an Ar atmosphere, the yield of **18a** further dropped to 5% (entry 3). An authentic sample of **18a** was obtained in 42% yield by reacting **11a** with paraformaldehyde (entry 4), and direct comparison with the above-mentioned **18a** confirmed its structure. The structure of **19** was determined by leading it to the quaternary salt with methyl iodide (quantitative) and by comparing the spectral data of both compounds.

The reaction of **11a** with NH_4OAc in refluxing EtOH for 10 h afforded **18b** and **19** in 19 and 69% yields, respectively (entry 5). Similarly, **11a** afforded **18c** and **19** in 14 and 39% yields, respectively, by reaction with NH_4OAc in refluxing PrOH for 2 h (entry 7). For the structural confirmation, authentic **18b** and **18c** were prepared in 45 and 55% yields, respectively, by reacting **11a** with either acetaldehyde in refluxing EtOH (entry 6) or propionaldehyde in refluxing propanol (entry 8).

The above results clearly show that **11a** functions to catalyze air oxidation of alcohol to aldehyde, though the mechanism is not known. We are now attempting to clarify the mechanism and reactivity of **11a**.

In conclusion, we have established a simple methodology for the synthesis of γ-carboline derivatives having a methoxycarbonyl group at the 4-position. Building blocks (**13**, **17**, **18**) obtained in the present paper should be useful for the syntheses of various novel γ-carboline derivatives.

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were determined with a Shimadzu IR-420 spectrophotometer, and proton nuclear magnetic resonance (^{1}H-NMR) spectra with a JEOL GSX-500 spectrometer, with tetramethylsilane as an internal standard. Mass spectra (MS) were recorded on a JEOL SX-102A spectrometer. Preparative thin-layer chromatography (p-TLC) was performed on Merck Kiesel-gel GF_{254} (Type 60) (SiO_2). Column chromatography was performed on silica gel (SiO_2, 100—200 mesh, from Kanto Chemical Co. Inc.).

Dimethyl 2-(3-Formylindol-2-yl)malonate (10a) and Methyl 2-(3-Formylindol-2-yl)acetate (11a) from 1-Methoxyindole-3-carbaldehyde (9) A solution of dimethyl malonate (754.3 mg, 5.713 mmol) in anhydrous MeOH (5.0 ml) was added to a solution of NaOMe [prepared with sodium (121.0 mg, 5.26 mmol) and anhydrous MeOH (3.0 ml)] and the mixture was stirred for 10 min at room temperature. To the resultant solution, a solution of **9** (500.0 mg, 2.86 mmol) in anhydrous MeOH (10.0 ml) was added and the mixture was refluxed for 15 min with stirring. After addition of ice and H_2O, the whole was made acidic by adding aqueous 2 N HCl and extracted with $CHCl_3$–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2 to give **9** (193.8 mg, 39%), **10a** (446.0 mg, 53%), and **11a** (44.5 mg, 7%) in the order of elution. **10a**: mp 162—163 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3170, 1757, 1734, 1626, 1449, 1384, 1325, 1238, 1147, 743 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.83 (6H, s, $2\times CH_3$), 5.84 (1H, s, C<u>H</u>$(COOCH_3)_2$), 7.30 (1H, dt, J=1.5, 7.1 Hz, C_5- or C_6-H), 7.33 (1H, dt, J=1.6, 7.1 Hz, C_5- or C_6-H), 7.44—7.48 (1H, m, C_7-H), 8.14—8.19 (1H, m, C_4-H), 9.85 (1H, br s, NH), 10.31 (1H, s, CHO). MS *m/z*: 275 (M^+). *Anal.* Calcd for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76; N, 5.09. Found: C, 61.25; H, 4.71; N, 5.04. **11a**: mp 116—118 °C (colorless leaves, recrystallized from MeOH–H_2O). IR (KBr): 3330, 1730, 1644, 1465, 1438, 1389, 1305, 1215, 1163, 1024, 756, 749 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.82 (3H, s, CH_3), 4.29 (2H, s, $ArCH_2CO$), 7.26—7.31 (2H, m, C_5-, C_6-H), 7.39—7.44 (1H, m, C_7-H), 8.14—8.19 (1H, m, C_4-H), 9.88 (1H, br s, NH), 10.24 (1H, s, CHO). MS *m/z*: 217 (M^+). *Anal.* Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.44; H, 5.06; N, 6.48.

Dimethyl 2-(3-Formylindol-2-yl)malonate (10a) from 9 KO^{t}Bu (63.8 mg, 0.569 mmol) was added to a solution of dimethyl malonate (78.4 mg, 0.594 mmol) in anhydrous DMF (1.0 ml) and the mixture was stirred for 10 min at room temperature. To the resultant solution, a solution of **9** (50.0 mg, 0.286 mmol) in anhydrous DMF (1.0 ml) was added and stirring was continued for 24 h at room temperature. After addition of ice and H_2O, the whole was made near neutral by adding saturated aqueous NH_4Cl and extracted with $CHCl_3$–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$ to give **9** (35.4 mg, 71%) and **10a** (13.5 mg, 17%) in the order of elution.

Dimethyl 2-(3-Formyl-4-iodoindol-2-yl)malonate (10b) from 12 KO^{t}Bu (74.2 mg, 0.661 mmol) was added to a solution of dimethyl malonate (88.0 mg, 0.667 mmol) in anhydrous DMF (2.0 ml) and the mixture was stirred for 10 min at room temperature. To the resultant solution, a solution of **12**[10] (100.0 mg, 0.332 mmol) in anhydrous DMF (2.0 ml) was added and stirring was continued for 2 h at room temperature. After addition of ice and H_2O, the whole was made near neutral by adding saturated aqueous NH_4Cl and extracted with AcOEt. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$ to give **10b** (130.0 mg, 98%). **10b**: mp 174—175 °C (colorless prisms, recrystallized from hexane–CH_2Cl_2). IR (KBr): 3284, 1752, 1724, 1649, 1524, 1398, 1325, 1195, 1154, 1138, 776, 740, 649 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.83 (6H, s, 2×CH_3), 6.29 (1H, s, C$\underline{H}$($COOCH_3$)$_2$), 7.00 (1H, dd, J=8.0, 7.6 Hz, C_6-H), 7.48 (1H, dd, J=8.0, 1.0 Hz, C_5- or C_7-H), 7.79 (1H, dd, J=7.6, 1.0 Hz, C_5- or C_7-H), 9.97 (1H, br s, NH), 11.35 (1H, s, CHO). MS m/z: 401 (M^+). *Anal.* Calcd for $C_{14}H_{12}INO_5$: C, 41.92; H, 3.02; N, 3.49. Found: C, 41.73; H, 2.93; N, 3.43.

Methyl 2-(3-Formylindol-2-yl)acetate (11a) from 10a A solution of **10a** (100.0 mg, 0.364 mmol) in anhydrous MeOH (4.0 ml) was added to a solution of NaOMe [prepared with sodium (20.2 mg, 0.878 mmol) and anhydrous MeOH (1.0 ml)] and the mixture was refluxed for 15 min with stirring. After addition of ice and H_2O, the whole was made acidic by adding aqueous 2 N HCl and extracted with CH_2Cl_2–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (49 : 1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.71—0.59 with CH_2Cl_2–MeOH (95 : 5, v/v) gave unreacted **10a** (30.8 mg, 31%). Extraction of the band having an *Rf* value of 0.59—0.46 with CH_2Cl_2–MeOH (95 : 5, v/v) gave **11a** (43.8 mg, 56%).

Methyl 2-(3-Formyl-4-iodoindol-2-yl)acetate (11b) from 12 A solution of dimethyl malonate (180.6 mg, 1.368 mmol) in anhydrous MeOH (2.0 ml) was added to a solution of NaOMe [prepared with sodium (31.5 mg, 1.370 mmol) and anhydrous MeOH (2.0 ml)] and the mixture was stirred for 50 min at room temperature. To the resultant solution, a solution of **12**[10] (200.0 mg, 0.662 mmol) in anhydrous MeOH (5.0 ml) was added and the mixture was refluxed for 20 min with stirring. After addition of ice and H_2O, the whole was made acidic by adding aqueous 2 N HCl and extracted with $CHCl_3$–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (99 : 1, v/v) to give **11b** (198.8 mg, 88%). **11b**: mp 161—162 °C (orange needles, recrystallized from hexane–CH_2Cl_2). IR (KBr): 3152, 1742, 1617, 1460, 1380, 1288, 1165, 1112, 820, 777, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.83 (3H, s, CH_3), 4.44 (2H, s, ArCH_2CO), 6.96 (1H, dd, J=8.0, 7.6 Hz, C_6-H), 7.45 (1H, dd, J=8.0, 0.7 Hz, C_5- or C_7-H), 7.78 (1H, dd, J=7.6, 0.7 Hz, C_5- or C_7-H), 10.31 (1H, br s, NH), 11.33 (1H, t, J=0.7 Hz, CHO). MS m/z: 343 (M^+). *Anal.* Calcd for $C_{12}H_{10}INO_3$: C, 42.01; H, 2.94; N, 4.08. Found: C, 41.81; H, 2.78; N, 4.02.

Methyl 2,3-Dihydro-2-methyl-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13a), 2,3-Dihydro-2,*N*-dimethyl-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxamide (14a), and 2-Methyl-5*H*-pyrido[4,3-*b*]indol-3-one (15a) from 10a $MeNH_2$ (40%, 1.0 ml, 12.8 mmol) was added to a solution of **10a** (39.6 mg, 0.144 mmol) in MeOH (4.0 ml) and the mixture was refluxed for 30 min with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 2 : 0.2, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (49 : 1, v/v) to give **14a** (7.9 mg, 22%), **13a** (26.4 mg, 72%), and **15a** (1.5 mg, 5%) in the order of elution. **13a**: mp 295—298 °C (pale brown prisms, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3340, 1663, 1558, 1465, 1355, 1307, 1212, 1083, 1070, 798 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.71 (3H, s, CH_3), 4.00 (3H, s, CH_3), 7.21 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.31 (1H, br d, J=7.5 Hz, C_6- or C_9-H), 7.36 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.71 (1H, d, J=7.5 Hz, C_6- or C_9-H), 8.22 (1H, s, C_1-H), 10.29 (1H, br s, NH). MS m/z: 256 (M^+). *Anal.* Calcd for $C_{14}H_{12}N_2O_3$: C, 65.62; H, 4.72; N, 10.93. Found: C, 65.41; H, 4.59; N, 10.86. **14a**: mp 286—288 °C (pale yellow prisms, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3315, 1666, 1576, 1465, 1415, 1355, 1236, 1055, 800, 765, 725, 685 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.02 (3H, d, J=5.0 Hz, collapsed to s on addition of D_2O, NHC$\underline{H}_3$), 3.76 (3H, s, CH_3), 7.20 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.32 (1H, dt, J=7.5, 0.8 Hz, C_6- or C_9-H), 7.37 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.73 (1H, br d, J=7.5 Hz, C_6- or C_9-H), 8.15 (1H, s, C_1-H), 9.85 (1H, br s, NH), 10.99 (1H, br s, NH). *Anal.* Calcd for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found: C, 65.57; H, 5.15; N, 16.39. **15a**: Yellow oil. IR (film): 3080, 1663, 1613, 1557, 1461, 1400, 1240, 1065, 875, 810, 725 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.69 (3H, s, CH_3), 6.28 (1H, s, C_4-H), 7.14 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.24 (1H, d, J=7.5 Hz, C_6- or C_9-H), 7.31 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.68 (1H, d, J=7.5 Hz, C_6- or C_9-H), 7.88 (1H, s, C_1-H), 9.48 (1H, br s, NH). High-resolution MS m/z: Calcd for $C_{12}H_{10}N_2O$: 198.0793. Found: 198.0794.

2,3-Dihydro-2,*N*-dimethyl-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxamide (14a) from 13a $MeNH_2$ (40%, 1.0 ml, 12.8 mmol) was added to a solution of **13a** (40.2 mg, 0.157 mmol) in MeOH (4.0 ml) and the mixture was refluxed for 20 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 2 : 0.2, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (49 : 1, v/v) to give **14a** (29.8 mg, 74%).

Methyl 2,3-Dihydro-2-(4-methoxyphenethyl)-3-oxo-5*H*-pyrido[4,3-*b*]-indole-4-carboxylate (13b) and 2,3-Dihydro-2,*N*-bis(4-methoxyphenethyl)-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxamide (14b) from 10a A solution of 4-methoxyphenethylamine (9.900 g, 65.4 mmol) in MeOH (10.0 ml) was added to a solution of **10a** (200.0 mg, 0.727 mmol) in MeOH (10 ml) and the mixture was refluxed for 1 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 1 : 0.1, v/v) to give **14b** (59.4 mg, 17%) and **13b** (199.2 mg, 73%) in the order of elution. **13b**: mp 103—105 °C (pale yellow prisms, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3680, 3430, 1708 (sh), 1664, 1618, 1565, 1513, 1468, 1361, 1240, 1030, 805 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.08 (2H, t, J=7.0 Hz, CH_2), 3.75 (3H, s, OCH_3), 4.03 (3H, s, OCH_3), 4.27 (2H, t, J=7.0 Hz, NCH_2), 6.81 (2H, m, A_2 part of A_2B_2, ArH), 7.11 (2H, m, B_2 part of A_2B_2, ArH), 7.18 (1H, ddd, J=8.0, 7.5, 1.5 Hz, C_7- or C_8-H), 7.30 (1H, br d, J=7.5 Hz, C_6- or C_9-H), 7.34 (1H, ddd, J=8.0, 7.5, 1.5 Hz, C_7- or C_8-H), 7.57 (1H, br d, J=7.5 Hz, C_6- or C_9-H), 7.79 (1H, s, C_1-H), 10.32 (1H, br s, NH). MS m/z: 376 (M^+). *Anal.* Calcd for $C_{22}H_{20}N_2O_4$: C, 69.78; H, 5.33; N, 7.40. Found: C, 69.79; H, 5.25; N, 7.4. **14b**: Brown oil. IR (film): 3380, 1670, 1616, 1514, 1468, 1359, 1250, 1032, 805, 672, 565 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.94 (2H, t, J=7.5 Hz, CH_2), 3.07 (2H, t, J=7.5 Hz, CH_2), 3.66—3.72 (2H, m, NCH_2), 3.75 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.31 (2H, t, J=7.5 Hz, NCH_2), 6.81 (2H, m, A_2 part of A_2B_2, ArH), 6.86 (2H, m, B_2 part of A_2B_2, ArH), 7.08 (2H, m, A_2 part of A_2B_2, ArH), 7.16 (1H, ddd, J=8.0, 7.5, 1.5 Hz, C_7- or C_8-H), 7.22 (2H, m, B_2 part of A_2B_2, ArH), 7.29 (1H, dt, J=8.0, 0.5 Hz, C_6- or C_9-H), 7.35 (1H, ddd, J=8.0, 7.5, 1.5 Hz, C_7- or C_8-H), 7.60 (1H, br d, J=8.0 Hz, C_6- or C_9-H), 7.72 (1H, s, C_1-H), 10.11 (1H, t, J=6.0 Hz, NH), 11.00 (1H, br s, NH). High-resolution MS m/z: Calcd for $C_{30}H_{29}N_3O_4$: 495.2158. Found: 495.2171.

2,3-Dihydro-2,*N*-bis(4-methoxyphenethyl)-3-oxo-5*H*-pyrido[4,3-*b*]-indole-4-carboxamide (14b) from 13b A solution of 4-methoxyphenethylamine (1.448 g, 9.577 mmol) in MeOH (2.0 ml) was added to a solution of **13b** (40.0 mg, 0.106 mmol) in MeOH (2.0 ml) and the mixture was refluxed for 24 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 2 : 0.2, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.96—0.81 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) gave **14b** (22.1 mg, 42%). Extraction of the band having an *Rf* value of 0.75—0.59 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) gave unreacted **13b** (17.2 mg, 43%).

Methyl 2-(2-Aminoethyl)-2,3-dihydro-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13c) and 2,*N*-Bis(2-aminoethyl)-2,3-dihydro-3-oxo-5*H*-pyrido-[4,3-*b*]indole-4-carboxamide (14c) from 10a A solution of ethylenediamine (786.3 mg, 13.08 mmol) in MeOH (2.0 ml) was added to a solution of **10a** (39.8 mg, 0.145 mmol) in MeOH (2.0 ml) and the mixture was refluxed for 15 min with stirring. After evaporation of the solvent,

brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.30—0.12 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) gave **14c** (9.9 mg, 22%). Extraction of the band having an *Rf* value of 0.12—0.03 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) gave **13c** (31.0 mg, 75%). **13c**: Pale yellow oil. IR (film): 3385, 1710, 1668, 1584, 1465, 1350, 1319, 1232, 1217, 1121, 800, 750 cm^{-1}. ^1H-NMR (5% CD_3OD in $CDCl_3$) δ: 3.15 (2H, t, J=6.0 Hz, CH_2), 4.00 (3H, s, OCH_3), 4.19 (2H, t, J=6.0 Hz, CH_2), 7.23 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.34 (1H, dt, J=8.0, 0.5 Hz, C_6- or C_9-H), 7.38 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.76 (1H, dt, J=8.0, 0.5 Hz, C_6- or C_9-H), 8.35 (1H, s, C_1-H), 10.39 (1H, br s, NH). High-resolution MS *m/z*: Calcd for $C_{15}H_{15}N_3O_3$: 285.1114. Found: 285.1114. **14c**: Yellow oil. IR (film): 3350, 1668, 1610, 1540, 1462, 1353, 1315, 1227, 795, 740, 662, 548 cm^{-1}. ^1H-NMR (5% CD_3OD in $CDCl_3$) δ: 2.94 (2H, t, J=6.0 Hz, CH_2), 3.15 (2H, t, J=6.0 Hz, CH_2), 3.55 (2H, t, J=6.0 Hz, CH_2), 4.23 (2H, t, J=6.0 Hz, CH_2), 7.23 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.37 (1H, br d, J=7.5 Hz, C_6- or C_9-H), 7.40 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.80 (1H, d, J=7.5 Hz, C_6- or C_9-H), 8.32 (1H, s, C_1-H), 10.14 (0.4H, br t, J=6.0 Hz, NH), 10.96 (0.3H, br s, NH). High-resolution MS *m/z*: Calcd for $C_{16}H_{19}N_5O_2$: 313.1540. Found: 313.1539.

2,*N*-Bis(2-aminoethyl)-2,3-dihydro-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxamide (14c) from 13c A solution of ethylenediamine (765.2 mg, 12.74 mmol) in MeOH (2.0 ml) was added to a solution of **13c** (39.8 mg, 0.145 mmol) in MeOH (2.0 ml) and the mixture was refluxed for 72 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.15—0.09 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) gave **14c** (38.9 mg, 88%).

Methyl 2,3-Dihydro-3-oxo-2-(*p*-tolyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13d) from 10a A solution of 4-methylaniline (1.400 g, 13.06 mmol) in MeOH (2.0 ml) was added to a solution of **10a** (39.9 mg, 0.145 mmol) in MeOH (2.0 ml) and the mixture was refluxed for 30 min with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (49 : 1, v/v) to give **13d** (47.1 mg, 98%). **13d**: Yellow oil. IR (film): 3380 (br), 1710, 1660, 1618, 1560, 1470, 1436, 1362, 1220, 1065, 802, 740 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.43 (3H, s, CH_3), 3.97 (3H, s, OCH_3), 7.21 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.30 (4H, s, Ar-H), 7.33 (1H, dt, J=8.0, 0.5 Hz, C_6- or C_9-H), 7.38 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H) , 7.68 (1H, dd, J=8.0, 0.5 Hz, C_6- or C_9-H), 8.24 (1H, d, J=0.5 Hz, C_1-H), 10.41 (1H, br s, NH). High-resolution MS *m/z*: Calcd for $C_{20}H_{16}N_2O_3$: 332.1161. Found: 332.1169.

Methyl 2,3-Dihydro-3-oxo-2-propyl-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13e) from 10a *n*-$PrNH_2$ (770.2 mg, 13.03 mmol) was added to a solution of **10a** (39.8 mg, 0.145 mmol) in MeOH (4.0 ml) and the mixture was refluxed for 30 min with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 2 : 0.2, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 1 : 0.1, v/v) to give **13e** (39.4 mg, 96%). **13e**: Pale yellow oil. IR (film): 3430, 1712, 1663, 1619, 1562, 1470, 1440, 1364, 1243, 1218, 1098, 806, 750 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.01 (3H, t, J=7.5 Hz, CH_3), 1.88 (2H, sext, J=7.5 Hz, $C\underline{H}_2CH_3$), 4.00 (3H, s, OCH_3), 4.08 (2H, t, J=7.5 Hz, NCH_2), 7.21 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.31 (1H, dd, J=7.5, 1.0 Hz, C_6- or C_9-H), 7.36 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.71 (1H, dd, J=7.5, 1.0 Hz, C_6- or C_9-H), 8.18 (1H, s, C_1-H), 10.32 (1H, br s, NH). High-resolution MS *m/z*: Calcd for $C_{16}H_{16}N_2O_3$: 284.1161. Found: 284.1171.

Methyl 2,3-Dihydro-2-(2-hydroxyethyl)-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13f) from 10a Ethanolamine (3.00 g , 41.12 mmol) was added to a solution of **10a** (150.0 mg, 0.546 mmol) in MeOH (15.0 ml) and the mixture was refluxed for 30 min with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) to give **13f** (153.2 mg, 98%). **13f**: mp 270—273 °C (pale yellow prisms, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3390, 1665, 1605, 1568, 1472, 1440, 1327, 1215, 1080, 805, 750, 720, 630 cm^{-1}. ^1H-NMR (DMSO-d_6) δ: 3.68 (2H, q, J=5.0 Hz, OCH_2), 3.82 (3H, s, OCH_3), 4.08 (2H, t, J=5.0 Hz, NCH_2), 4.87 (1H, t, J=5.0 Hz, OH), 7.15 (1H, dt, J=1.0, 7.5 Hz, C_7- or C_8-H), 7.29 (1H, dt, J=1.0, 7.5 Hz, C_7- or C_8-H), 7.53 (1H, d, J=7.5 Hz, C_6- or C_9-H), 7.85 (1H, d, J=7.5 Hz, C_6- or C_9-H), 8.78 (1H, s, C_1-H), 11.27 (1H, s, NH). *Anal.* Calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.79. Found: C, 62.76; H, 4.90; N, 9.90.

Methyl 2,3-Dihydro-2-methoxycarbonylmethyl-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13g) from 10a K_2CO_3 (1799.2 mg, 13.01 mmol) was added to a solution of **10a** (39.7 mg, 0.144 mmol) and glycine methyl ester hydrochloride (1631.9 mg, 12.97 mmol) in MeOH (3.0 ml) and the mixture was refluxed for 30 min with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) to give **13g** (31.7 mg, 98%). **13g**: mp 226—229 °C (pale yellow prisms, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3320 (br), 1750, 1710, 1655, 1616, 1559, 1440, 1180, 1038, 800, 740 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 3.80 (3H, s, OCH_3), 3.98 (3H, s, OCH_3), 4.78 (2H, s, NCH_2), 7.19 (1H, dt, J=1.0, 7.5 Hz, C_7- or C_8-H), 7.30 (1H, dt, J=7.5, 1.0 Hz, C_6- or C_9-H), 7.36 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.67 (1H, dd, J=8.0, 1.0 Hz, C_6- or C_9-H), 8.13 (1H, d, J=1.0 Hz, C_1-H), 10.36 (1H, br s, NH). *Anal.* Calcd for $C_{16}H_{14}N_2O_5$: C, 61.14; H, 4.49; N, 8.91. Found: C, 61.02; H, 4.35; N, 8.88.

Methyl 2-Amino-2,3-dihydro-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13h) from 10a A solution of hydrazine (10.3 mg, 0.206 mmol) in MeOH (2.0 ml) was added to a solution of **10a** (39.9 mg, 0.145 mmol) in MeOH (2.0 ml) and the mixture was refluxed for 5 min with stirring. Precipitates (**13h**, 25.1 mg) were collected by filtration and washed. The filtrate and washing were combined and the solvent was evaporated. The residue was taken up in brine and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (49 : 1, v/v) to give a further crop of **13h** (22.0 mg). The total yield of **13h** was 47.1 mg (98%). **13h**: mp > 310 °C [colorless fine needles, recrystallized from dimethyl sulfoxide (DMSO)–H_2O]. IR (KBr): 3300, 3205, 1660, 1610, 1560, 1468, 1435, 1360, 1325, 1278, 1240, 1210, 1147, 1100, 1050, 1031, 970, 900, 788, 735 cm^{-1}. ^1H-NMR (DMSO-d_6) δ: 3.84 (3H, s, OCH_3), 6.14 (2H, s, NH_2), 7.16 (1H, t, J= 8.0 Hz, C_7- or C_8-H), 7.31 (1H, t, J=8.0 Hz, C_7- or C_8-H), 7.56 (1H, d, J=8.0 Hz, C_6- or C_9-H), 7.96 (1H, d, J=8.0 Hz, C_6- or C_9-H), 9.05 (1H, s, C_1-H), 11.34 (1H, br s, NH). *Anal.* Calcd for $C_{13}H_{11}N_3O_3$: C, 60.69; H, 4.31; N, 16.34. Found: C, 60.48; H, 4.21; N, 16.20.

Methyl 2-(2-Acetylaminoethyl)-2,3-dihydro-3-oxo-5*H*-pyrido[4,3-*b*]-indole-4-carboxylate (13i) from 13c Acetic anhydride (1.0 ml) was added to a solution of **13c** (43.1 mg, 0.151 mmol) in pyridine (2.0 ml) and the mixture was stirred at room temperature for 22 h. The solvent was evaporated under reduced pressure to leave a crystalline solid, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH (95 : 5, v/v) to give **13i** (48.9 mg, 99%). **13i**: mp 266—267 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3300, 1672, 1653, 1603, 1355, 1211 cm^{-1}. ^1H-NMR (DMSO-d_6) δ: 1.76 (3H, s, $COCH_3$), 3.39 (2H, q, J=5.9 Hz, $NHC\underline{H}_2$), 3.82 (3H, s, OCH_3), 4.05 (2H, t, J=5.9 Hz, NCH_2), 7.16 (1H, dt, J=1.0, 7.6 Hz, C_7- or C_8-H), 7.31 (1H, ddd, J=8.1, 7.6, 1.0 Hz, C_7- or C_8-H), 7.54 (1H, d, J=8.1 Hz, C_6- or C_9-H), 7.88 (1H, d, J=7.6 Hz, C_6- or C_9-H), 7.95 (1H, t, J=5.6 Hz, CONH), 8.76 (1H, s, C_1-H), 11.31 (1H, br s, NH). *Anal.* Calcd for $C_{17}H_{17}N_3O_4$: C, 62.37; H, 5.24; N, 12.84. Found: C, 62.37; H, 5.25; N, 12.75.

Methyl 2-Diacetylamino-2,3-dihydro-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13j) from 13h Acetic anhydride (1.0 ml) was added to a solution of **13h** (15.3 mg, 0.060 mmol) in pyridine (2.0 ml) and the mixture was stirred at room temperature for 65 h. The solvent was evaporated under reduced pressure to leave a crystalline solid, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH (97 : 3, v/v) to give **13j** (12.6 mg, 62%). **13j**: mp 241—244 °C (dec.) (colorless needles, re-

crystallized from MeOH). IR (KBr): 3360, 1733, 1714, 1675, 1654, 1224 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.32 (6H, s, 2 × $COCH_3$), 3.83 (3H, s, OCH_3), 7.23 (1H, dt, J=1.0, 7.6 Hz, C_7- or C_8-H), 7.40 (1H, ddd, J=8.1, 7.6, 1.0 Hz, C_7- or C_8-H), 7.60 (1H, d, J=8.1 Hz, C_6- or C_9-H), 7.82 (1H, d, J=7.6 Hz, C_6- or C_9-H), 9.00 (1H, s, C_1-H), 11.67 (1H, br s, NH). *Anal.* Calcd for $C_{13}H_{11}N_3O_3 \cdot 1/3H_2O$: C, 58.79; H, 4.55; N, 12.10. Found: C, 58.79; H, 4.47; N, 11.81.

Methyl 2,3-Dihydro-2-hydroxy-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13k) from 16a K_2CO_3 (19.8 mg, 0.144 mmol) was added to a solution of **16a** (40.0 mg, 0.138 mmol) in MeOH (5.0 ml) and the mixture was refluxed for 15 min with stirring. After addition of brine, the whole was made acidic by adding 2 N HCl and extracted with $CHCl_3$–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a crystalline solid, which was recrystallized from AcOEt to give **13k** (34.4 mg, 89%). **13k**: mp 263—266 °C (pale yellow prisms). IR (KBr): 3200, 1695 (br), 1563, 1445, 1296, 1190, 1135, 1096, 1040, 1000, 908, 792, 729, 635 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.80 (3H, s, OCH_3), 7.01 (1H, t, J=8.0 Hz, C_7- or C_8-H), 7.11 (1H, t, J=8.0 Hz, C_7- or C_8-H), 7.47 (1H, d, J=8.0 Hz, C_6- or C_9-H), 7.73 (1H, d, J=8.0 Hz, C_6- or C_9-H), 8.79 (1H, s, C_1-H), 10.73 (1H, s, NH). *Anal.* Calcd for $C_{13}H_{10}N_2O_4 \cdot 1/2H_2O$: C, 58.42; H, 3.98; N, 9.75. Found: C, 58.86; H, 4.12; N, 10.09.

Methyl 2,3-Dihydro-2-methoxy-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13l) and Methyl 2,3-Dihydro-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13m) from 16a K_2CO_3 (20.0 mg, 0.145 mmol) was added to a solution of **16a** (40.0 mg, 0.138 mmol) in MeOH (5.0 ml) and the mixture was refluxed for 20 min with stirring. Dimethyl sulfate (4.0 ml) was added to the solution and the mixture was refluxed for an additional 2 h with stirring. After addition of brine, the whole was extracted with $CHCl_3$–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 2 : 0.2, v/v) to give **13l** (153.2 mg, 84%) and **13m** (4.6 mg, 14%) in the order of elution. **13l**: mp 248—251 °C (dec.) (pale yellow prisms, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3370, 1647, 1555, 1465, 1435, 1233, 1215, 1049, 976, 801, 756, 718 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.80 (3H, s, OCH_3), 4.21 (3H, s, OCH_3), 7.24 (1H, ddd, J=8.0, 7.0, 1.0 Hz, C_6- or C_9-H), 7.33 (1H, d, J=8.0 Hz, C_7- or C_8-H), 7.39 (1H, ddd, J=8.0, 7.0, 1.0 Hz, C_6- or C_9-H), 7.72 (1H, d, J=8.0 Hz, C_7- or C_8-H), 8.43 (1H, s, C_1-H), 10.41 (1H, br s, NH). MS m/z: 272 (M^+). *Anal.* Calcd for $C_{14}H_{12}N_2O_4 \cdot 1/8H_2O$: C, 61.25; H, 4.40; N, 10.21. Found: C, 61.31; H, 4.54; N, 10.05. **13m**: mp 260—263 °C (pale yellow prisms, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3240, 1665, 1565, 1470, 1435, 1370, 1323, 1260, 1198, 1065, 1022, 790, 741 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.81 (3H, s, OCH_3), 7.14 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.29 (1H, ddd, J=8.0, 7.0, 1.0 Hz, C_7- or C_8-H), 7.54 (1H, d, J=7.5 Hz, C_6- or C_9-H), 7.91 (1H, d, J=7.5 Hz, C_6- or C_9-H), 8.53 (1H, s, C_1-H), 11.32 (1H, br s, NH), 11.81 (1H, br s, NH). MS m/z: 242 (M^+). *Anal.* Calcd for $C_{13}H_{10}N_2O_3 \cdot 1/8H_2O$: C, 63.87; H, 4.12; N, 11.46. Found: C, 64.05; H, 4.00; N, 11.51.

Methyl 2,3-Dihydro-2-methoxy-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13l) from 16b A solution of **16b** (100.0 mg, 0.329 mmol) in DMF (7.0 ml) was refluxed for 2 h with stirring. After addition of brine, the whole was extracted with AcOEt. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 2 : 0.2, v/v) to give **13l** (64.1 mg, 72%).

Methyl 2,3-Dihydro-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (13m) from 13l A solution of **13l** (30.0 mg, 0.110 mmol) in MeOH (5.0 ml) was refluxed for 5 h with stirring. After addition of brine, the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH (95 : 5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.56—0.40 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) gave unreacted **13l** (18.4 mg, 61%). Extraction of the band having an *Rf* value of 0.23—0.13 with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v) gave **13m** (6.3 mg, 24%).

Dimethyl 2-[3-(*N*-Hydroxyiminomethyl)indol-2-yl]malonate (16a) from 10a A solution of hydroxylamine (2.280 g, 32.81 mmol) in MeOH (5.0 ml) was added to a solution of **10a** (100.2 mg, 0.364 mmol) in MeOH (4.0 ml) and the mixture was refluxed for 15 min with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH (49 : 1, v/v) to give **16a** (153.2 mg, 84%). **16a**: mp 163—165 °C (colorless prisms, recrystallized from $CHCl_3$–MeOH). IR (KBr): 3405, 1755, 1728, 1635, 1552, 1435, 1322, 1258, 1190, 1233, 1030, 932, 747 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.80 (6H, s, 2 × OCH_3), 5.39 (1H, s, C<u>H</u>($COOCH_3$)$_2$), 7.20 (1H, br t, J=7.5 Hz, C_7- or C_8-H), 7.27 (1H, br t, J=7.5 Hz, C_7- or C_8-H), 7.40 (1H, dd, J=7.5, 1.0 Hz, C_6- or C_9-H), 7.97 (1H, d, J=7.5 Hz, C_6- or C_9-H), 8.47 (1H, s, C_1-H), 9.35 (1H, br s, NH). *Anal.* Calcd for $C_{14}H_{14}N_2O_5 \cdot 1/4H_2O$: C, 57.04; H, 4.79; N, 9.50. Found: C, 56.92; H, 4.72; N, 9.39.

Dimethyl 2-[3-(*N*-Methoxyiminomethyl)indol-2-yl]malonate (16b) from 10a A solution of *O*-methylhydroxylamine (1.101 g, 13.18 mmol) in MeOH (2.0 ml) was added to a solution of **10a** (40.2 mg, 0.146 mmol) in MeOH (2.0 ml) and the mixture was refluxed for 5 min with stirring. After addition of brine, the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH (99 : 1, v/v) to give **16b** (153.2 mg, 84%). **16b**: Yellow oil. IR (KBr): 3406, 2966, 1750, 1728, 1450, 1290, 1155, 1047, 875, 770 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.80 (6H, s, 2 × OCH_3), 4.00 (3H, s, OCH_3), 5.36 (1H, s, C<u>H</u>($COOCH_3$)$_2$), 7.20 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.26 (1H, ddd, J=8.0, 7.5, 1.5 Hz, C_7- or C_8-H), 7.39 (1H, dm, J=8.0 Hz, C_6- or C_9-H), 8.03 (1H, dm, J=8.0 Hz, C_6- or C_9-H), 8.39 (1H, s, C_1-H), 9.32 (1H, br s, NH). High-resolution MS m/z: Calcd for $C_{15}H_{16}N_2O_5$: 304.1059. Found: 304.1058.

Methyl 2,3-Dihydro-9-iodo-3-oxo-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (17a) and Methyl 2-(3-Formyl-4-iodoindol-2-yl)acetate (11b) from 10b NH_4OAc (172.4 mg, 2.239 mmol) was added to a solution of **10b** (300.0 mg, 0.748 mmol) in MeOH (5.0 ml) and the mixture was refluxed for 12 h. Precipitates (**17a**, 168.2 mg) were collected by filtration and washed with MeOH. The combined filtrate and washing were evaporated under reduced pressure. After addition of brine to the residue, the whole was extracted with $CHCl_3$–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 2 : 0.2, v/v) to give unreacted **10b** (63.6 mg, 21%), **11b** (29.7 mg, 12%), and a further crop of **17a** (12.6 mg) in the order of elution. The total yield of **17a** was 180.8 mg (66%). **17a**: mp 282—285 °C (dec.) (pale yellow prisms, recrystallized from MeOH–AcOEt). IR (KBr): 3400, 1705, 1655, 1600, 1555, 1430, 1302, 1270, 1198, 1155, 795 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.82 (3H, s, OCH_3), 7.09 (1H, t, J=7.5 Hz, C_7-H), 7.60 (1H, d, J=7.5 Hz, C_6- or C_8-H), 7.63 (1H, d, J=7.5 Hz, C_6- or C_8-H), 8.82 (1H, s, C_1-H), 11.55 (1H, br s, NH), 11.96 (1H, br s, NH). MS m/z: 368 (M^+). *Anal.* Calcd for $C_{13}H_9IN_2O_3$: C, 42.42; H, 2.46; N, 7.61. Found: C, 42.32; H, 2.41; N, 7.35.

Methyl 2,3-Dihydro-9-iodo-3-oxo-2-(*p*-tolyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (17b) from 10b A solution of 4-methylaniline (895.2 mg, 8.354 mmol) in MeOH (2.0 ml) was added to a solution of **10b** (40.0 mg, 0.100 mmol) in MeOH (3.0 ml) and the mixture was refluxed for 1 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46 : 2 : 0.2, v/v) to give **17b** (41.4 mg, 91%). **17b**: mp 292—295 °C (dec.) (pale yellow prisms, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3380, 1667, 1585, 1443, 1433, 1353, 1293, 1225, 795 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.41 (3H, s, $ArCH_3$), 3.82 (3H, s, OCH_3), 7.12 (1H, t, J=8.0 Hz, C_7-H), 7.36 (2H, br d, J=8.0 Hz, Ar-H), 7.39 (2H, br d, J=8.0 Hz, Ar-H), 7.60 (1H, d, J=8.0 Hz, C_6- or C_8-H), 7.65 (1H, d, J=8.0 Hz, C_6- or C_8-H), 9.04 (1H, s, C_1-H), 11.62 (1H, br s, NH). MS m/z: 458 (M^+). *Anal.* Calcd for $C_{20}H_{15}IN_2O_3$: C, 52.42; H, 3.30; N, 6.11. Found: C, 52.12; H, 3.29; N, 5.93.

Methyl 2,3-Dihydro-9-iodo-3-oxo-2-propyl-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (17c) from 10b *n*-$PrNH_2$ (495.0 mg, 8.374 mmol) was added to a solution of **10b** (40.0 mg, 0.100 mmol) in MeOH (5.0 ml) and the mixture was refluxed for 15 min with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–

MeOH–28% NH_4OH (46 : 2 : 0.2, v/v) to give **17c** (337.1 mg, 91%). **17c**: Pale yellow oil. IR (KBr): 3280, 1707, 1645, 1603, 1557, 1430, 1298, 1203, 1155, 795 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.03 (3H, t, J=7.5 Hz, CH_3), 1.91 (2H, sext, J=7.5 Hz, CH_2CH_3), 4.00 (3H, s, OCH_3), 4.12 (2H, t, J=7.5 Hz, NCH_2), 7.06 (1H, t, J=8.0 Hz, C_7-H), 7.32 (1H, dd, J=8.0, 1.0 Hz, C_6- or C_8-H), 7.62 (1H, dd, J=8.0, 1.0 Hz, C_6- or C_8-H), 9.10 (1H, s, C_1-H), 10.45 (1H, br s, NH). High-resolution MS *m/z*: Calcd for $C_{16}H_{15}IN_2O_3$: 410.0127. Found: 410.0130.

Methyl 5*H*-Pyrido[4,3-*b*]indole-4-carboxylate (18a) and Methyl 3-(2-Methoxycarbonylmethylindol-3-yl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (19) from 11a. [Entry 1] NH_4OAc (44.4 mg, 0.55 mmol) was added to a solution of **11a** (40.0 mg, 0.183 mmol) in MeOH (3.0 ml, freshly distilled) and the mixture was refluxed for 10 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with CH_2Cl_2–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (49 : 1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.67—0.58 with CH_2Cl_2–MeOH (95 : 5, v/v) gave **18a** (11.7 mg, 28%). Extraction of the band having an *Rf* value of 0.56—0.50 with CH_2Cl_2–MeOH (95 : 5, v/v) gave **19** (22.6 mg, 59%).

18a: mp > 310 °C (pale yellow prisms, recrystallized from MeOH). IR (KBr): 3260, 1702, 1600, 1468, 1431, 1306, 1270, 1200, 1163 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 4.07 (3H, s, OCH_3), 7.39 (1H, dt, J=1.5, 7.8 Hz, C_7- or C_8-H), 7.56 (1H, dt, J=1.0, 7.8 Hz, C_7- or C_8-H), 7.59 (1H, br d, J=7.8 Hz, C_6- or C_9-H), 8.17 (1H, br d, J=7.8 Hz, C_6- or C_9-H), 9.13 (1H, s, C_1- or C_3-H), 9.40 (1H, s, C_1- or C_3-H), 10.01 (1H, br s, NH). MS *m/z*: 226 (M^+). *Anal.* Calcd for $C_{13}H_{10}N_2O_2 \cdot 1/8H_2O$: C, 68.33; H, 4.42; N, 12.26. Found: C, 68.53; H, 4.33; N, 12.24.

19: mp > 310 °C (yellow prisms, recrystallized from MeOH). IR (KBr): 3430, 1736, 1597, 1455, 1437, 1330, 1214, 1157, 736 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 3.48 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 4.07 (1H, br s, $HCHCOOCH_3$), 4.22 (1H, br s, $HCHCOOCH_3$), 7.08 (1H, ddd, J=8.0, 7.1, 1.0 Hz, Ar-H), 7.17 (1H, ddd, J=8.0, 7.1, 1.2 Hz, Ar-H), 7.37 (1H, ddd, J=8.0, 7.1, 1.2 Hz, Ar-H), 7.41 (2H, br d, J=8.0 Hz, Ar-H), 7.53 (1H, ddd, J=8.0, 7.1, 1.2 Hz, Ar-H), 7.70 (1H, br d, J=7.1 Hz, Ar-H), 8.16 (1H, br d, J=7.1 Hz, Ar-H), 9.15 (1H, br s, NH), 9.41 (1H, s, C_1-H), 10.00 (1H, br s, NH). MS *m/z*: 413 (M^+). *Anal.* Calcd for $C_{24}H_{19}N_3O_4 \cdot 1/8H_2O$: C, 69.34; H, 4.61; N, 10.10. Found: C, 69.24; H, 4.52; N, 9.97.

Quaternary Salt of **19** with MeI: mp 247—249 °C (dec.) (yellow prisms, recrystallized from MeOH–hexane–$CHCl_3$). IR (KBr): 3220, 1740, 1720, 1609, 1457, 1326, 1245, 1200, 1138, 1094, 758 cm^{-1}. ^1H-NMR (DMSO-d_6) δ: 3.56 (3H, s, OCH_3), 3.64 (3H, s, OCH_3), 3.77 (1H, d, J=17.5 Hz, A part of AB, CH_2COOCH_3), 3.82 (1H, d, J=17.5 Hz, B part of AB, CH_2COOCH_3), 4.00 (3H, s, NCH_3), 7.07 (1H, ddd, J=8.0, 7.0, 1.0 Hz, Ar-H), 7.21 (1H, ddd, J=8.0, 7.0, 1.0 Hz, Ar-H), 7.26 (1H, d, J=8.0 Hz, Ar-H), 7.51 (1H, dt, J=8.0, 1.0 Hz, Ar-H), 7.58 (1H, ddd, J=8.0, 7.0, 1.0 Hz, Ar-H), 7.77 (1H, ddd, J=8.0, 7.0, 1.0 Hz, Ar-H), 7.90 (1H, d, J=8.0 Hz, Ar-H), 8.42 (1H, dt, J=8.0, 1.0 Hz, Ar-H), 10.11 (1H, s, C_1-H), 11.72 (1H, br s, NH). *Anal.* Calcd for $C_{25}H_{22}IN_3O_4 \cdot 1/2H_2O$: C, 53.20; H, 4.11; N, 7.45. Found: C, 52.87; H, 3.93; N, 7.28.

[Entry 2] NH_4OAc (43.8 mg, 0.569 mmol) was added to a solution of **11a** (40.7 mg, 0.188 mmol) in MeOH (5.0 ml, used immediately after distillation from $NaBH_4$) and the mixture was refluxed for 10 h with stirring. After the same work-up and separation as described in entry 1, **18a** (7.1 mg, 17%) and **19** (20.3 mg, 53%) were obtained.

[Entry 3] NH_4OAc (47.7 mg, 0.619 mmol) was added to a solution of **11a** (40.6 mg, 0.187 mmol) in MeOH (5.0 ml, used immediately after distillation from $NaBH_4$) and the mixture was refluxed for 10 h with stirring under an Ar atmosphere. After the same work-up and separation as described in entry 1, **18a** (2.3 mg, 5%) and **19** (16.5 mg, 43%) were obtained.

[Entry 4] Paraformaldehyde (6.1 mg, 0.068 mmol) was added to a solution of **11a** (39.8 mg, 0.183 mmol) and NH_4OAc (42.1 mg, 0.547 mmol) in MeOH (5.0 ml) and the mixture was refluxed for 1 h with stirring. After the same work-up and separation as described in entry 1, **18a** (17.8 mg, 42%) was obtained.

Methyl 3-Methyl-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (18b) and 19 from 11a. [Entry 5] NH_4OAc (42.1 mg, 0.547 mmol) was added to a solution of **11a** (39.8 mg, 0.183 mmol) in EtOH (5.0 ml, freshly distilled) and the mixture was refluxed for 10 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with CH_2Cl_2–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (95 : 5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.93—0.81 with CH_2Cl_2–MeOH (95 : 5, v/v) gave **19** (26.4 mg, 69%). Extraction of the band having an *Rf* value of 0.75—0.56 with CH_2Cl_2–MeOH (95 : 5, v/v) gave **18b** (8.0 mg, 19%).

18b: mp > 310 °C (pale yellow prisms, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3300 (br), 1685, 1438, 1319, 1200, 740 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 3.00 (3H, s, CH_3), 4.08 (3H, s, OCH_3), 7.33 (1H, ddd, J=8.0, 7.5, 1.5 Hz, C_7- or C_8-H), 7.49 (1H, ddd, J=8.0, 7.5, 1.0 Hz, C_7- or C_8-H), 7.52 (1H, dm, J=8.0 Hz, C_6- or C_9-H), 8.11 (1H, dd, J=7.5, 1.0 Hz, C_6- or C_9-H), 9.21 (1H, s, C_1-H), 10.02 (1H, br s, NH). MS *m/z*: 240 (M^+). *Anal.* Calcd for $C_{14}H_{12}N_2O_2 \cdot 1/2H_2O$: C, 67.46; H, 4.85; N, 11.24. Found: C, 67.69; H, 4.73; N, 11.22.

[Entry 6] Acetaldehyde (9.0 mg, 0.068 mmol) was added to a solution of **11a** (39.3 mg, 0.181 mmol) and NH_4OAc (43.0 mg, 0.547 mmol) in EtOH (5.0 ml) and the mixture was refluxed for 1 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with EtOAc as a developing solvent to give **18b** (19.6 mg, 45%) and **19** (10.7 mg, 29%).

Methyl 3-Ethyl-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (18c) and 19 from 11a. [Entry 7] NH_4OAc (42.1 mg, 0.547 mmol) was added to a solution of **11a** (39.5 mg, 0.182 mmol) in *n*-PrOH (5.0 ml, freshly distilled) and the mixture was refluxed for 2 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with CH_2Cl_2–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (49 : 1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.69—0.66 with CH_2Cl_2–MeOH (95 : 5, v/v) gave **18c** (6.4 mg, 14%). Extraction of the band having an *Rf* value of 0.57—0.48 with CH_2Cl_2–MeOH (95 : 5, v/v) gave **19** (14.5 mg, 39%).

18c: mp 172—174 °C (colorless prisms, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3400, 1668, 1599, 1440, 1319, 1202, 1059, 818, 735 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.37 (3H, t, J=7.5 Hz, CH_3), 3.36 (2H, q, J=7.5 Hz, CH_2), 4.08 (3H, s, OCH_3), 7.32 (1H, ddd, J=7.5, 7.0, 1.5 Hz, C_7- or C_8-H), 7.48 (1H, ddd, J=7.5, 7.0, 1.0 Hz, C_7- or C_8-H), 7.51 (2H, br m, J=7.0 Hz, C_6- or C_9-H), 8.11 (1H, dd, J=7.5, 1.0 Hz, C_6- or C_9-H), 9.25 (1H, d, J=0.5 Hz, C_1-H), 9.99 (1H, br s, NH). *Anal.* Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.79; H, 5.44; N, 10.95.

[Entry 8] Propionaldehyde (32.7 mg, 0.563 mmol) was added to a solution of **11a** (39.3 mg, 0.181 mmol) and NH_4OAc (43.7 mg, 0.568 mmol) in *n*-PrOH (5.0 ml) and the mixture was refluxed for 1 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_4OH (46 : 5 : 0.5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (49 : 1, v/v) as a developing solvent to give **18c** (25.6 mg, 55%).

References and Notes

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