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The Chemistry of Indoles. XXXIII.[1] Substituent Effect in Regioselective Metalation of 3-Indolecarbaldehyde and Syntheses of Indoles Carrying a Carbon Side Chain at the 4-, 5-, 6-, or 7-Position

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The nature of a substituent on the pyrrole ring of 3-indolecarbaldehyde plays a significant role in governing the regioselectivity of metalation. To confirm the structures of the products, various indoles carrying a carbon side chain at the 4-, 5-, 6-, or 7-position were prepared by other methods. Synthesis of 5-substituted 1-hydroxyindoles is also described.

Keywords——thallation; mercuration; 4-substituted indole; 5-substituted indole; 6-substituted indole; 7-substituted indole; regioselective metalation; 3-indolecarbaldehyde; thallation–palladation; 1-hydroxyindole

In the previous paper,[2] we reported regioselective functionalization of 3-indolecarbaldehyde and methyl 3-indolecarboxylate at the 4-position by the one-pot thallation–palladation method, and succeeded in the synthesis of indoles carrying a carbon, an oxygen, or a halogen substituent at the 4-position.[3] These reactions rely on the regioselective electrophilic addition of thallium tris-trifluoroacetate (TTFA).[4] Now, we have found that when an extra substituent is introduced into the pyrrole ring of 3-indolecarbaldehyde, the regioselectivity is dramatically influenced. In order to examine these effects, methyl acrylate was used as a carbon side chain throughout the present study.

I. Regioselectivity in the Thallation–Palladation Method and Mercuration–Palladation Method

When 1-methoxy-3-indolecarbaldehyde[5] (**1**) was thallated with 1.5 molar eq of TTFA, followed by treatment with methyl acrylate in the presence of a catalytic amount of palladium acetate ($Pd(OAc)_2$), methyl 3-(3-formyl-1-methoxyindol-4-yl)acrylate (**2**) and a significant amount of the corresponding 5-substituted indole (**3**) were obtained in addition to recovery of the starting material. The results are summarized in Table I. When 1-methoxycarbonyl-3-indolecarbaldehyde (**4**) was subjected to the one-pot thallation–palladation method, the corresponding 4-, 7-, and 5-substituted indoles (**5**, **6**, and **7**) were formed in 32.5%, 6.9%, and 1.2% yields, respectively, together with recovery of the starting material in 45.1% yield (Chart 1).

It is interesting to note that when mercuric bis-trifluoroacetate[6] was used instead of TTFA in the presence of cupric chloride ($CuCl_2$) as a reoxidant of palladium, 3-indolecarbaldehyde (**8**) afforded the corresponding 4- and 5-substituted indoles (**9** and **10**) in 29.5% and 17.2% yields, respectively, together with 19.7% recovery of **8**. Under similar reaction conditions, 1-methoxy-3-indolecarbaldehyde (**1**) afforded 47.9% and 6.7% yields of 4- and 5-substituted indoles, respectively (**2** and **3**). These results suggest that the regioselectivity is governed by the balance of the electron density of the indole nucleus and substituents, which can function as coordinating groups to the metal, and the electrophilicity of metal reagents. From these points of view, we are carrying out extensive studies aimed at controlling

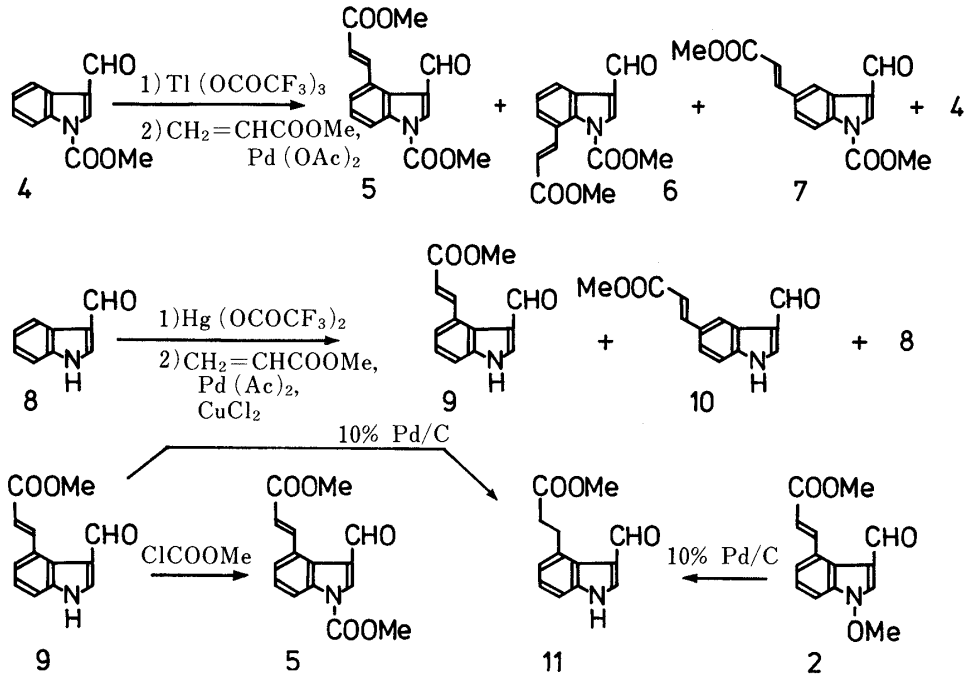
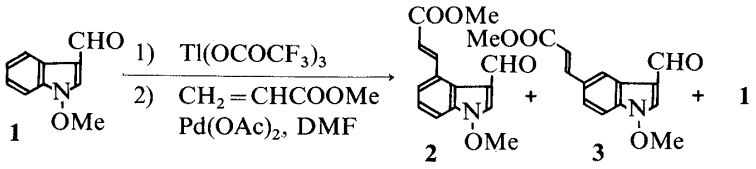


Chart 1

TABLE I. One-Pot Introduction of Methyl Acrylate onto the Indole Skeleton



Entry	Reaction time of thallation (h)	Yield (%) of 2	3	1
1	1	29.1	8.9	43.2
2	2	46.7	11.2	24.8
3	4	45.8	6.2	23.4

1 —(1) $Hg(OCOCF_3)_2$; (2) $CH_2=CHCOOMe$, $Pd(OAc)_2$, $CuCl_2$, DMF→ **2** (47.9%)+**3** (6.7%).

the position of functional group introduction by varying the metal reagent and the substituents on the pyrrole ring.

II. Syntheses of 4-Substituted Indoles for Structural Confirmation

The structures of the products described above were unequivocally determined by alternative synthesis as described below. Authentic methyl 3-(3-formylindol-4-yl)acrylate (**9**) was prepared from 3-indolecarbaldehyde (**8**) by the thallation—palladation method as described before.[2] Treatment of **9** with sodium hydride (NaH) in absolute *N*,*N*-dimethylformamide (DMF), and then with methyl chloroformate afforded **5** in 82.5% yield, proving the structure of **5** to be as shown in Chart 1. Catalytic hydrogenation of methyl 3-(3-

formyl-1-methoxyindol-4-yl)acrylate (**2**) over 10% palladium on carbon (Pd/C) at room temperature and atmospheric pressure caused reduction of the double bond and easy loss of the 1-methoxy group to produce methyl 3-(3-formylindol-4-yl)propionate (**11**) in 60.0% yield. The same compound (**11**) was alternatively derived from authentic **9** in 62.8% yield by catalytic hydrogenation over 10% Pd/C (Chart 1).

III. Syntheses of 5-Substituted Indoles for Structural Confirmation

The Leimgruber–Batcho method[7] with titanium(III) chloride ($TiCl_3$) as a reducing reagent was employed for confirming the structures of various 5-substituted indoles obtained by the above thallation–palladation reaction. Thus, treatment of methyl 3-methyl-4-nitrobenzoate (**12**) with dimethylformamide dimethyl acetal (DMFDMA), followed by reduction with aq. $TiCl_3$ afforded methyl 5-indolecarboxylate (**13**) and methyl 1-hydroxy-5-indolecarboxylate (**14**) in 49.0% and 25.9% yields, respectively (Chart 2).

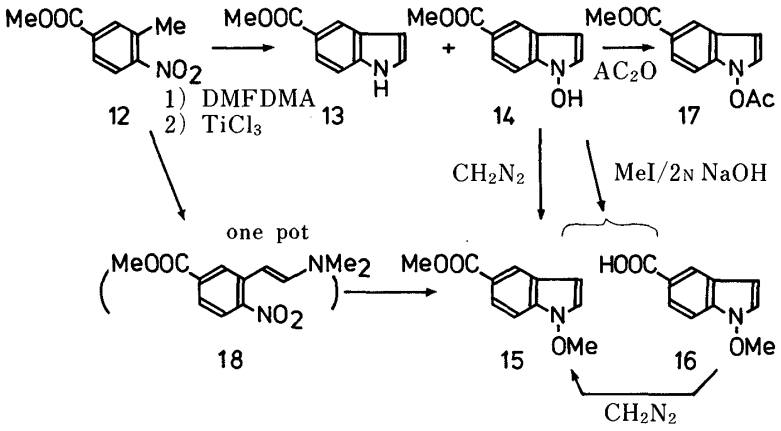


Chart 2

Although the structure of **14** was suggested by its spectral data, confirmation was carried out as described below. First, **14** was treated with ethereal diazomethane to give a 58.6% yield of methyl 1-methoxy-5-indolecarboxylate (**15**), whose proton nuclear magnetic resonance (^{1}H-NMR) spectrum clearly indicated the presence of two kinds of methoxy groups resonating at δ 3.87 and 4.06. In the high-resolution mass spectrum (MS) of **14** or **15**, loss of oxygen or methoxy group from the respective molecular ion was observed. These results clearly suggest the 1-hydroxy- or 1-methoxyindole structure. When **14** was reacted with methyl iodide in the presence of 2 N sodium hydroxide, under usual reaction conditions for methylating 1-hydroxyindoles, **15** and 1-methoxy-5-indolecarboxylic acid (**16**) were formed in 19.6% and 70.0% yields, respectively. Esterification of **16** with ethereal diazomethane again provided **15** in 72.4% yield. Further structural confirmation of **14** was attempted by the reaction with acetic anhydride and pyridine to give, in 75.1% yield, the unstable methyl 1-acetoxy-5-indolecarboxylate (**17**), whose infra-red (IR) spectrum showed a strong absorption band at 1814 cm^{-1} ascribable to the 1-acetoxy group. Based on these results, we can now produce **15** in 69.5% overall yield from **12** by means of the following sequence of reactions: DMFDMA treatment, reduction of the resultant enamine (**18**) with zinc and ammonium chloride, and treatment with ethereal diazomethane.

Although direct synthesis of **3** from **15** is in progress, the structure of **3** was determined as follows. Compound **3** was converted to methyl 3-(3-formylindol-5-yl)propionate (**22**) by catalytic hydrogenation over 10% Pd/C in 56.1% yield. On the other hand, authentic **22** was derived from **13** by means of the following sequence of reactions (Chart 3). Lithium aluminum hydride ($LiAlH_4$) reduction of **13** afforded 5-indolemethanol (**19**) in 82.0% yield. Oxidation of **19** with active manganese dioxide (MnO_2) in methylene chloride (CH_2Cl_2) produced 5-

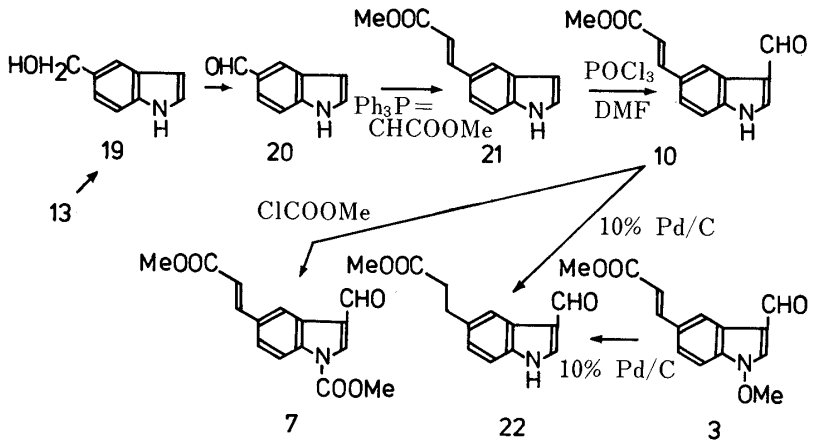


Chart 3

indolecarbaldehyde (**20**) in 91.7% yield. Treatment of **20** with methoxycarbonylmethylenetriphenylphosphorane in benzene gave methyl 3-(indol-5-yl)acrylate (**21**) in 95.2% yield. Subsequent Vilsmeier reaction with phosphorus oxychloride ($POCl_3$) and DMF converted **21** to methyl 3-(3-formylindol-5-yl)acrylate (**10**) in 71.6% yield. Finally, catalytic hydrogenation of **10** over 10% Pd/C gave (in 60.6% yield) **22**, which was identical with the sample derived from **3**.

On the other hand, treatment of **10** with NaH and then with methyl chloroformate afforded, in 70.3% yield, authentic methyl 3-(3-formyl-1-methoxycarbonylindol-5-yl) acrylate (**7**), which was identical with the sample derived from **4** by the thallation–palladation method.

IV. Syntheses of 7-Substituted Indoles for Structural Confirmation

Methyl 7-indolecarboxylate (**24**) was readily prepared in 56.5% yield from methyl 3-methyl-2-nitrobenzoate (**23**) by the Leimgruber–Batcho method[7] using $TiCl_3$ as a reducing reagent (Chart 4). Subsequent reduction of **24** with $LiAlH_4$ afforded 7-indolemethanol (**25**) in 90.9% yield. Conversion of **25** to 7-indolecarbaldehyde (**26**) was achieved in 63.6% yield by

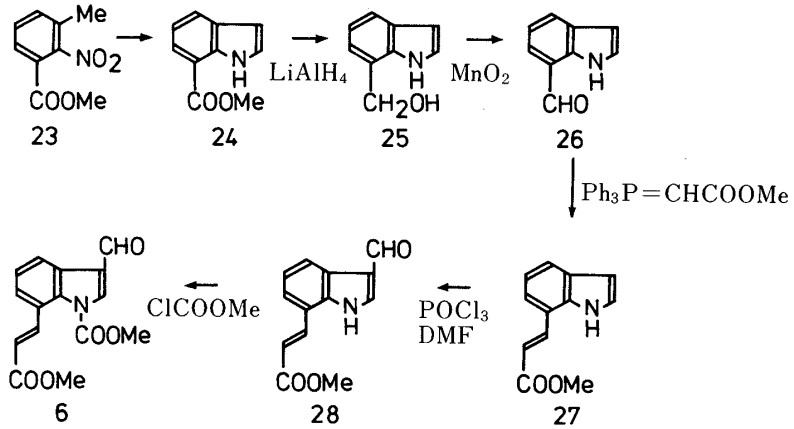


Chart 4

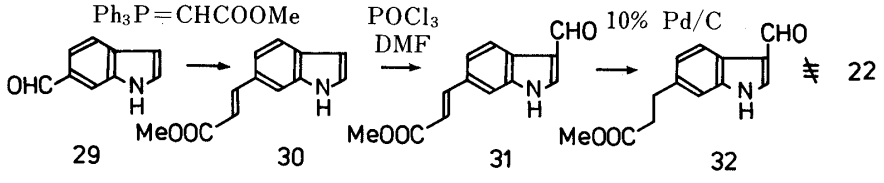


Chart 5

oxidation with active MnO_2 in CH_2Cl_2. Wittig reaction of **26** with methoxycarbonylmethylenetriphenylphosphorane proceeded readily to yield methyl 3-(indol-7-yl)acrylate (**27**) in 88.1% yield. Compound **27** readily underwent Vilsmeier reaction with $POCl_3$ and DMF to give methyl 3-(3-formylindol-7-yl)acrylate (**28**) in 96.6% yield. Subsequent methoxycarbonylation with NaH and methyl chloroformate produced methyl 3-(3-formyl-1-methoxycarbonylindol-7-yl)acrylate (**6**) in 54.5% yield. This product (**6**) was found to be identical with that obtained from **4** by the thallation–palladation method by direct comparison.

V. Syntheses of 6-Substituted Indoles for Structural Confirmation

Essentially the same reaction sequences as for 5-substituted indoles were employed, as shown in Chart 5. Thus, readily available 6-indolecarbaldehyde[1b] (**29**) was reacted with methoxycarbonylmethylenetriphenylphosphorane to yield methyl 3-(indol-6-yl)acrylate (**30**) in 93.9% yield. Subsequent Vilsmeier reaction of **30** afforded methyl 3-(3-formylindol-6-yl)acrylate (**31**) in 95.6% yield. Catalytic hydrogenation of **31** over 10% Pd/C produced methyl 3-(3-formylindol-6-yl)propionate (**32**) in 66.9% yield. Although these compounds, **31** and **32**, exhibited spectral data closely similar to those of **10** and **22**, respectively, they were proved not to be identical by direct comparisons.

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were determined with a Shimadzu IR-420 spectrophotometer, and ^{1}H-NMR spectra with a JEOL JNM-PMX60 spectrometer with tetramethylsilane as an internal standard. MS were recorded on a Hitachi M-80 spectrometer. Commercial aq. titanium(III) chloride ($TiCl_3$, 16%, d=1.5, from Kanto Chemical Co., Inc.) was used. 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.) throughout the present study.

Methyl 3-(3-Formyl-1-methoxyindol-4-yl)acrylate (2) and Methyl 3-(3-Formyl-1-methoxyindol-5-yl)acrylate (3) from 1-Methoxy-3-indolecarbaldehyde (1). General Procedure——A 0.88 M solution of TTFA (1.5 mol eq) was added to a solution of **1** in CF_3COOH (TFA, 0.5 ml) and stirring was continued at room temperature for an appropriate time. After removal of the solvent under reduced pressure, the residue was dissolved in DMF (2.0 ml). $Pd(OAc)_2$ (10.0 mg) and a solution of freshly distilled methyl acrylate (3 mol eq) in DMF (1.0 ml) were added, and the whole was heated at 120 °C with stirring for 1 h. After addition of CH_2Cl_2–MeOH (95 : 5, v/v) to the reaction mixture, solid material was removed by filtration through SiO_2. The filtrate was concentrated under reduced pressure to leave a crude product, which was subjected to column chromatography on SiO_2 with CH_2Cl_2–hexane (1 : 1, v/v) as an eluent. From the early fractions, starting material was recovered. From the next fractions, **3** was obtained. From the later fractions, **2** was obtained.

Run 1: In the general procedure, 87.0 mg of **1** was used and thallation was conducted for 1 h. After work-up and column chromatography as described above, 37.6 mg (43.2%) of **1**, 37.4 mg (29.1%) of **2**, and11.4 mg (8.9%) of **3** were obtained. **2**: mp 139.0—140.0 °C (colorless needles, recrystallized from MeOH). IR (KBr): 1708, 1648, 1627 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.76 (3H, s), 4.10 (3H, s), 6.29 (1H, d, J=16 Hz), 7.05—7.56 (3H, m), 7.83 (1H, s), 8.91 (1H, d, J=16 Hz), 9.72 (1H, s). MS m/z: 259 (M^+). *Anal.* Calcd for $C_{14}N_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.46; H, 5.04; N, 5.51. **3**: mp 148.0—149.0 °C (colorless needles, recrystallized from MeOH–H_2O). IR (KBr): 1710, 1658, 1628 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.76 (3H, s), 4.13 (3H, s), 6.36 (1H, d, J=16 Hz), 7.38 (2H, br s), 7.70 (1H, d, J=16 Hz), 7.73 (1H, s), 8.33 (1H, br s), 9.78 (1H, s). *Anal.* Calcd for $C_{14}H_{13}NO_4$: C, 64.86: H, 5.05; N, 5.40. Found: C, 64.79; H, 5.14; N, 5.66.

Run 2: In the general procedure, 88.9 mg of **1** was used and thallation was conducted for 2 h. After work-up and column chromatography as described above, 22.1 mg (24.8%) of **1**, 61.5 mg (46.7%) of **2**, and 14.7 mg (11.2%) of **3** were obtained.

Run 3: In the general procedure, 80.0 mg of **1** was used and thallation was conducted for 4 h. After work-up and column chromatography as described above, 18.7 mg (23.4%) of **1**, 54.2 mg (45.8%) of **2**, and7.3 mg (6.2%) of **3** were obtained.

Methyl 3-(3-Formyl-1-methoxycarbonylindol-4-yl)acrylate (5), Methyl 3-(3-Formyl-1-methoxycarbonylindol-7-yl)acrylate (6), and Methyl 3-(3-Formyl-1-methoxycarbonylindol-5-yl)acrylate (7) from 1-Methoxycarbonyl-3-indolecarbaldehyde (4)——A 0.88 M solution of TTFA in TFA (0.76 ml) was added to a solution of **4** (99.0 mg) in TFA (1.0 ml) and stirring was continued for 2 h at room temperature. After removal of the solvent under reduced pressure, the residue was dissolved in DMF (2.0 ml). $Pd(OAc)_2$ (11.0 mg) and a solution of freshly distilled methyl acrylate

(143.0 mg) in DMF (1.0 ml) were added and the whole was heated at 120 °C with stirring for 30 min. After addition of CH_2Cl_2–MeOH (95 : 5, v/v) to the reaction mixture, solid material was removed by filtration through SiO_2. The filtrate was concentrated under reduced pressure to leave a crystalline solid, which was subjected to column chromatography on SiO_2 with CH_2Cl_2 as an eluent. From the early fractions, **4** (41.0 mg, 45.1%) was recovered. From the next fractions, **6** (9.8 mg, 6.9%) was obtained as colorless needles. The subsequent fractions yielded **7** (1.7 mg, 1.2%) as colorless prisms. From the later fractions, **5** (46.7 mg, 32.5%) was obtained as colorless needles. **5**: mp 168.0—169.0 °C (colorless needles, recrystallized from MeOH). This compound was identical with the sample prepared from authentic **9**. **6**: mp 146.0—147.0 °C (pale yellow needles, recrystallized from MeOH). This compound was identical with the sample derived from authentic **28**. **7**: mp 186.0—187.5 °C (colorless needles, recrystallized from MeOH). This compound was found to be identical with the sample derived from authentic **10**.

Methyl 3-(3-Formylindol-4-yl)acrylate (9) and Methyl 3-(3-Formylindol-5-yl)acrylate (10) from 3-Indolecarbaldehyde (8)——1. Preparation of a Solution of Mercuric Bis-trifluoroacetate[6] in TFA: Mercuric oxide (2.1012 g) was added to a mixture of TFA (3.0 ml) and $(CF_3CO)_2O$ (2.104 g) and the whole was heated under reflux for 8 h with stirring. After removal of the solvent *in vacuo*, the residual crystals were dissolved in TFA (10.0 ml).

2. A TFA solution of $Hg(OCOCF_3)_2$ (0.89 ml 1.5 mol eq), prepared as described above, was added to a solution of **8** (83.6 mg) in TFA (0.5 ml) and stirring was continued for 4 h at room temperature. After removal of the solvent under reduced pressure, the residue was dissolved in DMF (3.0 ml). $Pd(OAc)_2$ (10.0 mg), dried $CuCl_2$ (163.5 mg), and freshly distilled methyl acrylate (148.5 mg, 3 mol eq.) were added to the solution and the whole was heated with stirring at 113 °C for 30 min. CH_2Cl_2–MeOH (95 : 5, v/v) was added to the reaction mixture and solid material was removed by filtration through SiO_2. The filtrate was concentrated to leave an oil, which was subjected to column chromatography on SiO_2 with CH_2Cl_2–MeOH (95 : 5, v/v) as an eluent. From the early fractions, **8** (16.5 mg, 19.7%) was recovered. The subsequent fractions yielded **10** (22.7 mg, 17.2%). From the later fractions, **9** (39.0 mg, 29.5%) was obtained. **9**: mp 187.0—188.0 °C (colorless prisms, recrystallized from MeOH). This compound was identical with the sample prepared from methyl 2-methyl-3-nitrobenzoic acid as reported previously.[2] **10**: mp 237.5—238.0 °C (colorless prisms, recrystallized from MeOH). This compound was identical with the sample derived from authentic **21**.

2 and 3 from 1——A TFA solution of $Hg(OCOCF_3)_2$ (0.89 ml, 1.5 mol eq), prepared by the procedure described in the reaction of **8**, was added to a solution of **1** (100.3 mg) in TFA (0.5 ml), and stirring was continued for 4 h at room temperature. After removal of the solvent under reduced pressure, the residue was dissolved in DMF (2.0 ml). $Pd(OAc)_2$ (10.0 mg), dried $CuCl_2$ (165.6 mg), and a solution of freshly distilled methyl acrylate (163.0 mg) in DMF (1.0 ml) were added to the solution and the whole was heated at 120 °C with stirring for 30 min. CH_2Cl_2–MeOH (95 : 5, v/v) was added to the reaction mixture and solid material was removed by filtration through SiO_2. The filtrate was concentrated under reduced pressure to leave a crystalline solid, which was subjected to column chromatography on SiO_2 with CH_2Cl_2–hexane (1 : 1, v/v) as an eluent. From the early fractions, **3** (10.0 mg, 6.7%) was obtained. From the later fractions, **2** (71.0 mg, 47.9%) was obtained.

Methyl 3-(3-Formylindol-4-yl)propionate (11) from 2——A solution of **2** (54.0 mg) in MeOH (10.0 ml) was hydrogenated over 10% Pd/C (25.0 mg) at room temperature and atmospheric pressure for 2 h. After removal of the catalyst by filtration through SiO_2, the filtrate was concentrated under reduced pressure to leave a crystalline solid, which was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (98 : 2, v/v) as a developing solvent to afford **11** (30.5 mg, 60.0%). This compound was identical with the sample prepared from authentic **9**.

11 from 9——A solution of **9** (45.0 mg) in MeOH (10.0 ml) was hydrogenated over 10% Pd/C (25.0 mg) at room temperature and atmospheric pressure for 2 h. After removal of the catalyst by filtration through SiO_2, the filtrate was concentrated under reduced pressure to leave a crystalline solid, which was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (98 : 2, v/v) as a developing solvent to afford **11** (28.5 mg, 62.8%). mp 119.0—120.0 °C (colorless needles, recrystallized from benzene). IR (KBr): 1735, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.69 (2H, t, J=8 Hz), 3.60 (2H, t, J=8 Hz), 3.60 (3H, s), 6.90—7.30 (3H, m), 7.72 (1H, d, J=3.2 Hz, C_2-H), 9.76 (1H, s), 10.11 (1H, br, NH). MS *m/z*: 231 (M^+). *Anal.* Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.66; N, 6.06. Found: C, 67.67; H, 5.61; N, 6.04.

5 from 9——A solution of **9** (79.0 mg) in abs. DMF (3.0 ml) was added to a stirred 50% NaH (22.0 mg, washed twice with benzene). The mixture was stirred for 10 min at room temperature, then a solution of methyl chloroformate (191.5 mg) in benzene (1.0 ml) was added and stirring was continued for 14 h at room temperature. Ice and H_2O were added and the whole was extracted with CH_2Cl_2. The extract was washed with H_2O, dried over Na_2SO_4, and evaporated to leave a crude product, which was purified by column chromatography on SiO_2 with CH_2Cl_2 as an eluent to afford **5** (81.6 mg, 82.5%). mp 168.0—169.0 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 1752, 1708, 1672, 1625 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.78 (3H, s), 4.03 (3H, s), 6.26 (1H, d, J=16 Hz), 7.21 (1H, t, J=8 Hz), 7.45 (1H, dd, J=8, 1.6 Hz), 8.05 (1H, dd, J=8, 1.6 Hz), 8.11 (1H, s), 8.85 (1H, d, J=16 Hz), 9.76 (1H, s). MS *m/z*: 287 (M^+). *Anal.* Calcd for $C_{15}H_{13}NO_5$: C, 62.71; H, 4.56; N, 4.88. Found: C, 62.78; H, 4.54; N, 4.88.

Methyl 5-Indolecarboxylate (13) and Methyl 1-Hydroxy-5-indolecarboxylate (14) from Methyl 3-Methyl-4-nitrobenzoate (12)——A solution of **12** (2.949 g) and DMFDMA (5.397 g, 3 mol eq) in abs. DMF (24 ml) was heated under reflux for 13 h with stirring. After evaporation of the solvent under reduced pressure, the residue was dissolved in MeOH (200 ml). Aq. $TiCl_3$ (68.0 ml) was added to the solution as a single portion and stirring was continued for

7 min at room temperature. The reaction mixture was extracted with CH_2Cl_2 (2 l). The extract was washed with sat. aq. $NaHCO_3$, then with sat. aq. NaCl, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to column chromatography on SiO_2 with CH_2Cl_2–MeOH (99 : 1, v/v) as an eluent. From the early fractions, **13** (1.295 g, 49.0%) was obtained. From the later fractions, **14** (746.5 mg, 25.9%) was obtained as unstable crystals. **13**: mp 127.0—128.0 °C (lit.[8] mp 124—126 °C, colorless prisms, recrystallized from MeOH). IR (KBr): 3300, 1692, 1610 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.87 (3H, s), 6.51 (1H, m), 7.13 (1H, dd, J=3.2, 2.4 Hz), 7.24 (1H, d, J=8 Hz), 7.80 (1H, dd, J=8, 1.6 Hz), 8.31 (1H, s), 8.66 (1H, br s). *Anal.* Calcd for $C_{10}H_9NO_2$: C, 68.60; H, 5.10; N, 8.00. Found: C, 68.81; H, 5.11; N, 7.93. **14**: mp 116.0—117.5 °C (dec., colorless prisms, recrystallized from MeOH–H_2O). IR (KBr): 3210, 1664 cm^{-1}. ^{1}H-NMR (10% CD_3OD in $CDCl_3$) δ: 3.83 (3H, s), 6.30 (1H, d, J= 3.2 Hz), 7.15 (1H, d, J=3.2 Hz), 7.30 (1H, d, J=8 Hz), 7.74 (1H, dd, J=8, 1.6 Hz), 8.17 (1H, br s). High-resolution MS m/z: Calcd for $C_{10}H_9NO_3$: 191.0581. Found: 191.0582.

Methyl 1-Methoxy-5-indolecarboxylate (15) from 14——An ethereal solution of diazomethane was added to a solution of **14** (88.5 mg) in MeOH (5.0 ml) until the yellow color persisted, and the mixture was allowed to stand for 30 min at room temperature. After evaporation of the solvent under reduced pressure, the crude product was purified by column chromatography on SiO_2 with CH_2Cl_2–MeOH (99 : 1, v/v) as an eluent to give **15** (55.7 mg, 58.6%) as a colorless oil. IR (film): 1708, 1613 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.87 (3H, s), 4.06 (3H, s), 6.38 (1H, br d, J=3.2 Hz), 7.20 (1H, br d, J=3.2 Hz), 7.30 (1H, dd, J=8, 0.8 Hz), 7.84 (1H, dd, J=8, 1.6 Hz), 8.22 (1H, br m). High-resolution MS m/z: Calcd for $C_{11}H_{11}NO_3$: 205.0738. Found: 205.0742.

Methyl 1-Acetoxy-5-indolecarboxylate (17) from 14——Acetic anhydride (0.5 ml) was added to a solution of **14** (48.9 mg) in pyridine (1.0 ml) and the mixture was allowed to stand for 5 h with stirring. After evaporation of the solvent under reduced pressure, sat. aq. $NaHCO_3$ was added to the residue and the mixture was extracted with CH_2Cl_2. The extract was washed with H_2O, dried over Na_2SO_4, and evaporated to leave a crystalline solid, which was purified by column chromatography on SiO_2 with CH_2Cl_2 as an eluent to give **17** (44.8 mg, 75.1%) as unstable crystals. On standing, the compound gradually changed to a violet tar. mp 102.0—104.0 °C (dec., colorless prisms, crystallized from CCl_4). IR (KBr): 1814, 1714, 1618 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.36 (3H, s), 3.85 (3H, s), 6.47 (1H, dd, J=3.2, 0.8 Hz), 7.05 (1H, d, J=3.2 Hz), 7.06 (1H, br d, J=8 Hz), 7.81 (1H, dd, J=8, 1.6 Hz), 8.22 (1H, br s). High-resolution MS m/z: Calcd for $C_{12}H_{11}NO_4$: 233.0686. Found: 233.0672.

15 and 1-Methoxy-5-indolecarboxylic Acid (16) from 14——Methyl iodide (1.0 ml) was added to a stirred solution of **14** (280.3 mg) in MeOH (10.0 ml) and 2 N NaOH (10.0 ml). The mixture was stirred for 15 h at room temperature, then the solvent was evaporated off under reduced pressure. H_2O was added and the whole (pH = 11) was extracted with CH_2Cl_2, washed with H_2O, dried over Na_2SO_4, and evaporated to leave a neutral crude product (**15**). On the other hand, the combined water layer was made acidic (pH = 2) by adding 2 N HCl and the whole was extracted with CH_2Cl_2–MeOH (95 : 5, v/v). The extract was washed with sat. aq. NaCl, dried over Na_2SO_4, and evaporated to leave a crystalline solid. Recrystallization from MeOH afforded **16** (130.9 mg) as colorless prisms. Purification of the mother liquor by p-TLC on SiO_2 with CH_2Cl_2–MeOH (95 : 5, v/v) as a developing solvent gave a further crop of **16** (65.4 mg). Total yield of **16** was 196.3 mg (70.0%). mp 200.0—204.0 °C (dec.). IR (KBr): 2920 (br), 1672, 1608 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.06 (3H, s), 6.40 (1H, d, J=3.2 Hz), 7.20 (1H, d, J=3.2 Hz), 7.35 (1H, br d, J=8 Hz), 7.93 (1H, dd, J=8, 1.6 Hz), 8.34 (1H, br s). High-resolution MS m/z: Calcd for $C_{10}H_9NO_3$: 191.0581. Found: 191.0578. A neutral crude product (**15**) was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (99 : 1, v/v) as a developing solvent to give pure **15** (15.6 mg, 19.6%) as a colorless oil. This compound was identical with the sample prepared from **14** by reaction with diazomethane.

15 from 16——An ethereal solution of diazomethane was added to a solution of **16** (86.0 mg) in MeOH (15.0 ml) until the yellow color persisted, and the mixture was allowed to stand for 1 h at room temperature with stirring. The solvent was evaporated off under reduced pressure to leave an oil, which was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (97 : 3, v/v) as a developing solvent to give **15** (66.8 mg, 72.4%) as a colorless oil. This compound was identical with the sample prepared from **14** by reaction with diazomethane.

15 from 12——A solution of **12** (1.003 g) in abs. DMF (8.0 ml) and DMFDMA (1.843 g, 3.0 mol eq) was heated under reflux for 14 h with stirring. The solvent was evaporated off under reduced pressure to leave an oil, which was dissolved in a mixture of MeOH (50.0 ml) and H_2O (10.0 ml). NH_4Cl (1.103 g, 4 mol eq) and zinc dust (6.421 g, 19 mol eq) were added, and rapid stirring was continued for 2 h at room temperature. The whole was filtered through filter paper to remove solid material, which was washed well with hot MeOH (300 ml). The washing was combined with the filtrate. The solvent was evaporated off under reduced pressure to leave an oil, which was dissolved in MeOH, and ethereal diazomethane was added until the yellow color persisted. After stirring of the mixture for 24 h at room temperature, the solvent was evaporated off under reduced pressure to give a crude product, which was purified by column chromatography on SiO_2 with CH_2Cl_2 as an eluent to give **15** (732.0 mg, 69.5%) as a colorless oil. This compound was identical with the sample prepared from **14** by reaction with diazomethane.

5-Indolemethanol (19) from 13——$LiAlH_4$ (442.8 mg) was added to a stirred solution of **13** (485.3 mg) in abs. THF (10.0 ml) and the mixture was heated under reflux for 3 h with stirring. Excess $LiAlH_4$ was destroyed by adding ethyl acetate and then H_2O. Aqueous Rochelle salt was added and the whole was extracted with CH_2Cl_2. The extract was washed with sat. aq. NaCl, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil,

which was purified by column chromatography on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v) as an eluent to give **19** (334.3 mg, 82.0%) as a colorless oil. IR (film): 3400, 1620, 996 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.75 (1H, s, OH), 4.66 (2H, s), 6.35—6.55 (1H, br m), 6.95—7.35 (3H, m), 7.48 (1H, br s), 8.15 (1H, br, NH). MS *m/z*: 147 (M^+).

5-Indolecarbaldehyde (20) from 19——Active MnO_2 (1.325 g) was added to a solution of **19** (269.1 mg) in CH_2Cl_2 (10.0 ml) and stirring was continued for 113 h at room temperature. After addition of CH_2Cl_2 (10.0 ml) and MeOH (20.0 ml) to the reaction mixture, the whole was filtered through SiO_2 to remove solid material. The filtrate was concentrated to afford a crude product, which was purified by column chromatography on SiO_2 with CH_2Cl_2 as an eluent to give **20** (243.6 mg, 91.7%). mp 99.5—100.5 °C (lit.[8] mp 99—101 °C, pale pink prisms, recrystallized from MeOH–H_2O). IR (KBr): 3255, 1658, 1612 cm^{-1}. ^{1}H-NMR (10% CD_3OD in $CDCl_3$) δ: 6.56 (1H, br d, J=3.2 Hz), 7.19 (1H, d, J=3.2 Hz), 7.35 (1H, d, J=8 Hz), 7.64 (1H, dd, J=8, 1.6 Hz), 8.02 (1H, br s), 9.81 (1H, s). *Anal.* Clacd for C_9H_7NO: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.39; H, 4.77; N, 9.67.

Methyl 3-(Indol-5-yl)acrylate (21) from 20——A solution of methoxycarbonylmethylenetriphenylphosphorane (404.0 mg) and **20** (82.5 mg) in benzene (10.0 ml) was heated under reflux for 6.5 h with stirring, then concentrated under reduced pressure to give a crystalline solid, which was purified by column chromatography on SiO_2 with CH_2Cl_2–MeOH (97:3, v/v) as an eluent to afford **21** (108.9 mg, 95.2%). mp 141.0—142.0 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3310, 1693, 1627, 1610 cm^{-1}. ^{1}H-NMR (1% CD_3OD in $CDCl_3$) δ: 3.73 (3H, s), 6.30 (1H, d, J=16 Hz), 6.46 (1H, br m), 7.09 (1H, m), 7.26 (2H, br s), 7.66 (1H, br s), 7.73 (1H, d, J=16 Hz), 8.46 (1H, br, NH). *Anal.* Calcd for $C_{12}H_{11}NO_2$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.43; H, 5.44; N, 6.94.

10 from 21——A solution of **21** (78.6 mg) in abs. DMF (1.5 ml) was added to stirred Vilsmeier reagent, prepared by mixing $POCl_3$ (197.7 mg) with ice-cooled abs. DMF (0.5 ml), and stirring was continued for 17 h at room temperature. The reaction mixture was cooled on an ice bath, H_2O was added, and the whole was made alkaline by adding 2 N NaOH then extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with sat. aq. NaCl, dried over Na_2SO_4 and evaporated to leave a crystalline solid. Recrystallization from MeOH afforded **10** (42.3 mg) as colorless prisms. The mother liquor was purified by column chromatography on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v) as an eluent to give a further crop of **10** (21.8 mg). Total yield of **10** was 64.1 mg (71.6%). mp 237.5—238.0 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3180, 1703, 1638, 1612 cm^{-1}. ^{1}H-NMR (10% CD_3OD in $CDCl_3$) δ: 3.76 (3H, s), 6.37 (1H, d, J=16 Hz), 7.34 (2H, br s), 7.73 (1H, d, J=16 Hz), 7.74 (1H, br m), 8.33 (1H, br s), 9.81 (1H, s). *Anal.* Calcd for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.85; N, 6.11. Found: C, 68.01; H, 4.76; N, 6.17.

Methyl 3-(3-Formylindol-5-yl)propionate (22) from 10——A solution of **10** (51.9 mg) in MeOH (20.0 ml) was hydrogenated over 10% Pd/C (54.4 mg) at room temperature and atmospheric pressure for 1 h. After removal of the catalyst by filtration through SiO_2, the filtrate was concentrated under reduced pressure to leave a crude product, which was purified by column chromatography on SiO_2 with CH_2Cl_2–MeOH (97:3, v/v) as an eluent to afford **22** (31.7 mg, 60.6%). mp 146.0—147.0 °C (colorless prisms, recrystallized from MeOH–H_2O). The compound was identical with the sample derived from **3** by catalytic hydrogenation.

7 from 10——A solution of **10** (176.8 mg) in abs. DMF (4.0 ml) was added to stirred 50% NaH (78.6 mg, washed twice with dry benzene). The mixture was stirred for 10 min at room temperature, then a solution of methyl chloroformate (160.6 mg) in benzene (1.0 ml) was added and the whole was stirred for 2 h at room temperature. Ice and H_2O were added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with H_2O, dried over Na_2SO_4, and evaporated to leave a crude product, which was purified by column chromatography on SiO_2 with CH_2Cl_2 as an eluent to afford **7** (155.7 mg, 70.3%). mp 186.0—187.5 °C (colorless needles, recrystallized from MeOH). IR (KBr): 1750, 1710, 1678, 1638 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.77 (3H, s), 4.07 (3H, s), 6.41 (1H, d, J=16 Hz), 7.47 (1H, dd, J=8, 1.6 Hz), 7.70 (1H, d, J=16 Hz), 8.05 (1H, d, J=8 Hz), 8.12 (1H, s), 8.33 (1H, br s), 9.94 (1H, s). MS *m/z*: 287 (M^+). *Anal.* Calcd for $C_{15}H_{13}NO_5$: C, 62.71; H, 4.56; N, 4.88. Found: C, 62.90; H, 4.50; N, 4.86.

22 from 3——A solution of **3** (20.0 mg) in MeOH (10.0 ml) was hydrogenated over 10% Pd/C (20.0 mg) at room temperature and atmospheric pressure for 2 h. After removal of the catalyst by filtration through SiO_2, the filtrate was concentrated under reduced pressure to leave a crystalline solid, which was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (96:4, v/v) as a developing solvent to afford **22** (10.1 mg, 56.1%). mp 146.0—147.0 °C (colorless prisms, recrystallized from MeOH–H_2O). IR (KBr): 3148, 1727, 1640—1617 (br) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.46—2.81 (2H, m, A_2 part of A_2B_2), 2.90—3.21 (2H, m, B_2 part of A_2B_2), 3.61 (3H, s), 7.01 (1H, dd, J=8, 1.6 Hz), 7.21 (1H, d, J=8 Hz), 7.65 (1H, d, J=3.2 Hz), 8.00 (1H, br s), 9.38 (1H, br s), 9.83 (1H, s). MS *m/z*: 231 (M^+). *Anal.* Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.70; H, 5.76; N, 6.02. This compound was identical with the sample derived from **10** by catalytic hydrogenation.

Methyl 7-Indolecarboxylate (24) from Methyl 3-Methyl-2-nitrobenzoate (23)——A solution of **23** (3.995 g) and DMFDMA (7.281 g) in abs. DMF (16.0 ml) was heated under reflux for 13.5 h with stirring. The solvent was evaporated off under reduced pressure and the residue was dissolved in MeOH (300 ml). Aqueous $TiCl_3$ (92.2 ml) was added to the stirred solution as a single portion. After rapid stirring for 7 min, the whole was extracted with CH_2Cl_2. The extract was washed with sat. aq. $NaHCO_3$, dried over Na_2SO_4, and concentrated to leave a crystalline solid, which was purified by column chromatography on SiO_2 with CH_2Cl_2–hexane (1:3, v/v) as an eluent to give **24** (2.026 g, 56.5%). mp 42.5—43.0 °C (colorless prisms, recrystallized from MeOH–H_2O). IR (KBr): 3380, 1688 cm^{-1}.

^{1}H-NMR ($CDCl_3$) δ: 3.91 (3H, s), 6.47 (1H, dd, J=3.2, 2.4 Hz), 7.01 (1H, dd, J=8, 7.2 Hz), 7.17 (1H, dd, J=3.4, 2.4 Hz), 7.63—7.89 (2H, m), 9.73 (1H, br s). MS m/z: 175 (M^+). *Anal.* Calcd for $C_{10}H_9NO_2$: C; 68.56; H, 5.18; N, 8.00. Found: C, 68.46; H, 5.08; N, 7.90.

7-Indolemethanol (25) from 24——$LiAlH_4$ (419.7 mg) was added to a stirred solution of **24** (494.2 mg) in abs. THF (10.0 ml) and the whole was heated under reflux for 2 h with stirring. Excess $LiAlH_4$ was destroyed by adding ethyl acetate and then H_2O. Aqueous Rochelle salt was added, and the whole was extracted with CH_2Cl_2. The extract was washed with H_2O, dried over Na_2SO_4, and concentrated under reduced pressure to leave a crystalline solid, which was purified by column chromatography on SiO_2 with CH_2Cl_2–MeOH (95 : 5, v/v) as an eluent to afford **25** (377.2 mg, 90.9%). mp 56.0—56.5 °C (lit.[8] mp 55—56 °C, colorless needles, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3390, 3220, 1608, 1435 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.93 (1H, br s, OH), 4.85 (2H, s), 6.43 (1H, dd, J=3.2, 2.4 Hz), 6.83—7.16 (3H, m), 7.48 (1H, dd, J=6, 3 Hz), 8.68 (1H, br s). MS m/z: 147 (M^+). *Anal.* Calcd for C_9H_9NO: C, 73.45; H, 6.16, N, 9.52. Found: C, 73.52; H, 6.00; N, 9.47.

7-Indolecarbaldehyde (26) from 25——Active MnO_2 (496.1 mg) was added to a solution of **25** (97.1 mg) in CH_2Cl_2 (10.0 ml) and stirring was continued for 110 h at room temperature. After addition of CH_2Cl_2 (10.0 ml) and MeOH (20.0 ml) to the reaction mixture, the whole was filtered through SiO_2 to remove solid material. The filtrate was concentrated to afford a crude product, which was purified by column chromatography on SiO_2 with CH_2Cl_2 as an eluent to give **26** (60.9 mg, 63.6%). mp 86.5—87.0 °C (lit.[8] mp 87—89 °C, colorless needles, recrystallized from hexane). IR (KBr): 3340, 1665 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 6.49 (1H, dd, J=3.2, 2 Hz), 7.09 (1H, t, J=7.5 Hz), 7.17 (1H, dd, J=3.2, 2 Hz), 7.46 (1H, dd, J=7.5, 1 Hz), 7.79 (1H, dd, J=7.5, 1 Hz), 9.91 (1H, s), 10.09 (1H, br s). MS m/z: 145 (M^+). *Anal.* Calcd for C_9H_7NO: C, 74.47; H, 4.86; N, 9.64. Found: C, 74.71; H, 4.75; N, 9.61.

Methyl 3-(Indol-7-yl)acrylate (27) from 26——A solution of **26** (280.1 mg) and methoxycarbonylmethylenetriphenylphosphorane (1.292 g) in benzene (12.0 ml) was heated under reflux for 2 h with stirring. Evaporation of the solvent under reduced pressure left a crystalline solid, which was purified by column chromatography on SiO_2 with CH_2Cl_2 as an eluent to give **27** (342.7 mg, 88.1%). mp 96.0—96.5 °C (pale yellow needles, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3315, 1683, 1633 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.76 (3H, s), 6.42 (1H, d, J=16 Hz), 6.46 (1H, dd, J=3.2, 2.0 Hz), 6.99 (1H, t, J=7.2 Hz), 7.06 (1H, br t, J=3.2 Hz), 7.30 (1H, d, J=7.2 Hz), 7.57 (1H, d, J=7.2 Hz), 7.99 (1H, d, J=16 Hz), 8.87 (1H, br s). MS m/z: 201 (M^+). *Anal.* Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.86; H, 5.46; N, 6.83.

Methyl 3-(3-Formylindol-7-yl)acrylate (28) from 27——A solution of **27** (175.0 mg) in abs. DMF (4.0 ml) was added to stirred Vilsmeier reagent, prepared by mixing $POCl_3$ (271.4 mg) with ice-cooled abs. DMF (2.0 ml), and stirring was continued for 3 h at room temperature. The mixture was cooled on an ice bath, H_2O was added, and the whole was made alkaline by adding 2 N NaOH, then extracted with CH_2Cl_2–MeOH (95 : 5, v/v). The extract was washed with sat. aq. NaCl, dried over Na_2SO_4, and evaporated to leave a crude product, which was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (94 : 6, v/v) as a developing solvent. Extraction with CH_2Cl_2–MeOH (95 : 5, v/v) from the band having Rf 0.41—0.53 afforded **28** (192.6 mg, 96.6%). mp 199.0—200.0 °C (pale yellow needles, recrystallized from CH_2Cl_2). IR (KBr): 3310, 3200, 1713, 1697, 1643 cm^{-1}. ^{1}H-NMR (10% CD_3OD in $CDCl_3$) δ: 3.79 (3H, s), 6.48 (1H, d, J=16 Hz), 7.18 (1H, t, J=7.2 Hz), 7.46 (1H, dd, J=7.2, 3.2 Hz), 7.82 (1H, s), 8.00 (1H, d, J=16 Hz), 8.21 (1H, dd, J=7.2, 3.2 Hz), 9.86 (1H, s). MS m/z: 229 (M^+). *Anal.* Calcd for $C_{13}H_{11}NO_3$: C, 68.12; H, 4.88; N, 6.11. Found: C, 68.17; H, 4.80; N, 5.99.

6 from 28——A solution of **28** (26.5 mg) in abs. DMF (1.0 ml) was added to a stirred 50% NaH (14.0 mg, washed twice with dry benzene). The mixture was stirred for 5 min, then a solution of methyl chloroformate (28.4 mg) in benzene (1.0 ml) was added and stirring was continued for 2 h at room temperature. H_2O was added to the reaction mixture and the whole was extracted with benzene. The extract was washed with H_2O, dried over Na_2SO_4, and evaporated to leave a crystalline solid, which was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (98 : 2, v/v) as a developing solvent. Extraction with CH_2Cl_2–MeOH (95 : 5, v/v) from the band having Rf 0.60—0.74 afforded **6** (18.1 mg, 54.5%). mp 146.0—147.0 °C (pale yellow needles, recrystallized from MeOH). IR (KBr): 1763, 1705, 1680 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.76 (3H, s), 4.01 (3H, s), 6.16 (1H, d, J=16 Hz), 7.09—7.49 (2H, m), 8.13 (1H, s), 8.16 (1H, d, J=16 Hz), 8.21 (1H, dd, J=7, 1.6 Hz), 9.91 (1H, s). MS m/z: 287 (M^+). *Anal.* Calcd for $C_{15}H_{13}NO_5$: C, 62.72; H, 4.56; N, 4.88. Found: C, 62.54; H, 4.50; N, 4.87.

Methyl 3-(Indol-6-yl)acrylate (30) from 6-Indolecarbaldehyde (29)——A solution of **29**[1b] (86.0 mg) and methoxycarbonylmethylenetriphenylphosphorane (304.5 mg) in benzene (10.0 ml) was heated under reflux for 5.5 h. After evaporation of the solvent, the residue was purified by column chromatography on SiO_2 with CH_2Cl_2–MeOH (98 : 2, v/v) as an eluent to give **30** (112.0 mg, 93.9%). mp 132.0—133.0 °C (pale yellow prisms, recrystallized from MeOH). IR (KBr): 3320, 1688, 1633, 1608 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.74 (3H, s), 6.30 (1H, d, J=16 Hz), 6.43 (1H, m), 7.03—7.46 (4H, m), 7.68 (1H, d, J=16 Hz), 8.36 (1H, br s). MS m/z: 201 (M^+). *Anal.* Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.59; H, 5.38; N, 7.02.

Methyl 3-(3-Formylindol-6-yl)acrylate (31) from 30——A solution of **30** (90.0 mg) in abs. DMF (1.0 ml) was added to stirred Vilsmeier reagent, prepared by mixing $POCl_3$ (120.0 mg) with an ice-cooled abs. DMF (0.5 ml), and stirring was continued for 12 h at room temperature. Ice and H_2O were added and the whole was made alkaline by adding 2 N NaOH, and then extracted with CH_2Cl_2–MeOH (97 : 3, v/v). The extract was washed with sat. aq. NaCl,

dried over Na_2SO_4, and evaporated to leave a crystalline solid, which was recrystallized from MeOH to afford **31** (45.8 mg) as pale yellow prisms. The mother liquor was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (97 : 3, v/v) as a developing solvent to give a further crop of **31** (52.2 mg). The total yield of **31** was 98.0 mg (95.6%). mp 243.0—245.0 °C (pale yellow prisms, recrystallized from MeOH). IR (KBr): 1713, 1636 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ : 3.70 (3H, s), 6.54 (1H, d, J = 16 Hz), 7.50 (1H, dd, J = 8, 0.8 Hz), 7.63 (1H, br s), 7.84 (1H, d, J = 16 Hz), 8.10 (1H, s), 8.46 (1H, d, J = 8 Hz), 10.05 (1H, s). High-resolution MS m/z: Calcd for $C_{13}H_{11}NO_3$: 229.0737. Found: 229.0736.

Methyl 3-(3-Formylindol-6-yl)propionate (32) from 31——A solution of **31** (75.5 mg) in MeOH (30.0 ml) was hydrogenated over 10% Pd/C (45.5 mg) at room temperature and atmospheric pressure for 2 h. After removal of the catalyst by filtration through SiO_2, the solvent was evaporated off under reduced pressure to leave a crystalline solid, which was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (97 : 3, v/v) as a developing solvent to afford **32** (51.0 mg, 66.9%). mp 160.0—161.0 °C (colorless prisms, recrystallized from MeOH–H_2O). IR (KBr): 3180, 1732, 1628 cm^{-1}. ^{1}H-NMR (10% CD_3OD in $CDCl_3$) δ : 2.46—2.86 (2H, m, A_2 part of A_2B_2), 2.86—3.19 (2H, m, B_2 part of A_2B_2), 3.62 (3H, s), 7.01 (1H, dd, J = 8, 0.8 Hz), 7.18 (1H, br s), 7.70 (1H, s), 8.04 (1H, d, J = 8 Hz), 9.76 (1H, s). MS m/z: 231 (M^+). *Anal.* Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67: N, 6.06. Found: C, 67.72; H, 5.75; N, 6.02.

References and Notes

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