

# Nucleophilic substitution reaction of 1-methoxyindole-3-carbaldehyde

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## NUCLEOPHILIC SUBSTITUTION REACTION OF 1-METHOXYINDOLE-3-CARBALDEHYDE<sup>1,#</sup>

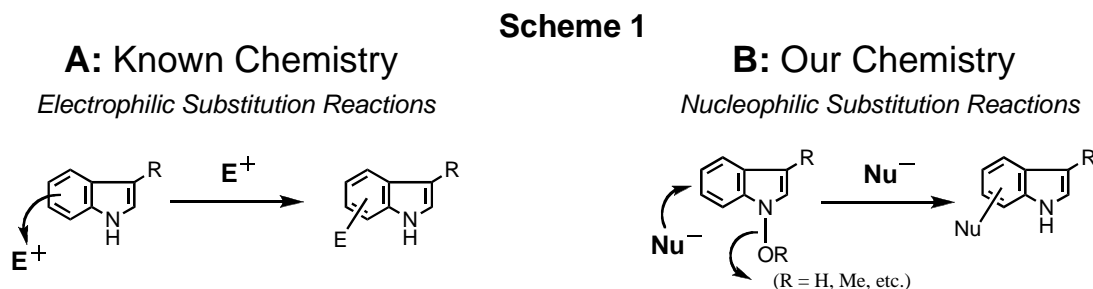
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**Abstract** – 1-Methoxyindole-3-carbaldehyde is proved to be a versatile electrophile and reacts regioselectively at the 2-position with various types of nucleophiles providing 2-substituted indole-3-carbaldehydes.

Indole is one of the electron rich hetero-aromatics. This is the reason why electrophilic substitution reactions have been well studied<sup>2</sup> in the indole chemistry (shown in general formula in Scheme 1, **A**). On the other hand, nucleophilic substitution reaction<sup>3</sup> was not familiar until we developed 1-hydroxyindole chemistry.<sup>4</sup> We demonstrated that a hydroxy or a methoxy group at the 1-position of indole skeleton functions as a good leaving group when at least one electron withdrawing group<sup>3b,4</sup> (ester, halogen)<sup>3c</sup> is present in the indole nucleus (Scheme 1, **B**). Since various types of 1-hydroxy- and 1-methoxyindoles are available,<sup>4</sup> they can now be utilized as substrates for nucleophilic substitution reactions.

1-Methoxyindole-3-carbaldehyde<sup>5</sup> (**1**, Scheme 2) is one of the simplest 1-methoxyindoles and a natural product, isolated from radish as a phytoalexin by Takasugi<sup>6</sup> and co-workers. They also isolated another phytoalexin, brassicanal A (**2**), from Chinese cabbage.<sup>7</sup> Taking these reports into consideration, we



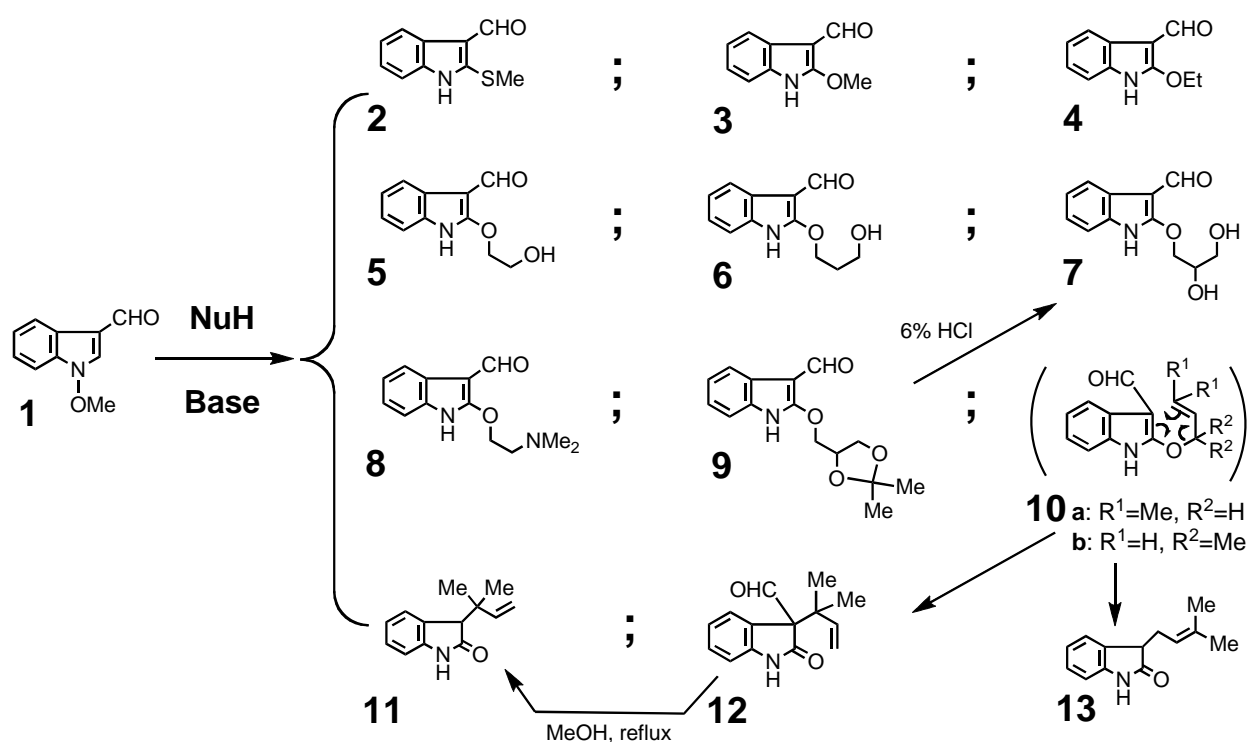
# Dedicated to the 77<sup>th</sup> birthday of Prof. Ei-ichi Negishi. ‡ Professor Emeritus of Kanazawa University. Present address: 56-7 Matsuhidai, Matsudo-shi, Chiba-ken, 270-2214, Japan.

came up with the idea that plant family *Brassicaceae* utilizes simple indole-3-carbaldehydes for not only protecting them from diseases and insects, but also promoting their growth.<sup>8</sup> To examine the idea we needed many kinds of 2-substituted indole-3-carbaldehydes. In this paper, we wish to report the preparation of them, which are rarely available by electrophilic substitution reactions. Since we have established a rapid and high yield synthetic method<sup>4</sup> for **1** employing our 1-hydroxyindole chemistry, we chose it as a starting material for nucleophilic substitution reactions.

### I. Reaction of **1** with Sulfur- and Oxygen-Centered Nucleophiles

First of all, we tried potent nucleophiles such as sulfur- and oxygen-centered species and the results are summarized in Scheme 2. As expected, NaSMe reacted with **1** in refluxing MeOH for 2 h to give brassicanal A (**2**) in 94% yield. With this simple and successful synthesis of phytoalexin in hand, we next tried the reaction of **1** with NaOMe and NaOEt in refluxing MeOH and EtOH, respectively. The expected 2-methoxy- (**3**) and 2-ethoxyindole-3-carbaldehyde (**4**) were obtained in 90 and 95% yields, respectively. In reactions of **1** with sodium salt of ethylene glycol, 1,3-propanediol, glycerol, and *N,N*-dimethylethanol, the yield of the desired product decreased even though longer reaction time was employed. Thus, **5**, **6**, **7**, and **8** were obtained in 50, 76, 30, and 36% yields, respectively. 2,2-Dimethyl-1,3-dioxolan-4-methanol also reacted with **1** in the presence of Na metal in *N,N*-dimethylformamide (DMF) to produce **9** in 57% yield. Hydrolysis of **9** with aqueous 6% HCl at room temperature (rt) afforded **7** in 63% yield.

**Scheme 2. Reaction of **1** with Sulfur- and Oxygen-Centered Nucleophiles**



When 3-methylbut-2-en-1-ol was reacted with **1** at rt for 24 h in the presence of NaH in DMF, the

expected **10a** was not obtained. Instead of **10a**, a 2:5 mixture of 2-oxindoles, **11** and **12**, was obtained. Heating a MeOH solution of the mixture at reflux for 24 h transformed **12** into **11**. By carrying out these reactions continually, **11** was prepared in 75% yield directly from **1**.

Since **12** is an unstable intermediate, its isolation as pure compound was not successful. However, <sup>1</sup>H-NMR inspection of the crude reaction residue clearly showed the presence of **12**. The mechanism of the formation of **11** is considered as follows. Initial production of **10a**, followed by Claisen rearrangement to give **12**, and subsequent liberation of formyl group of **12** result in the formation of **11**. Similarly, the reaction of **1** with potassium salt of 2-methylbut-3-en-2-ol in hexamethylphosphoric triamide (HMPA) produced 26% yield of **13** through unstable intermediate **10b**.

## II. Reaction of **1** with Nitrogen-Centered Nucleophiles

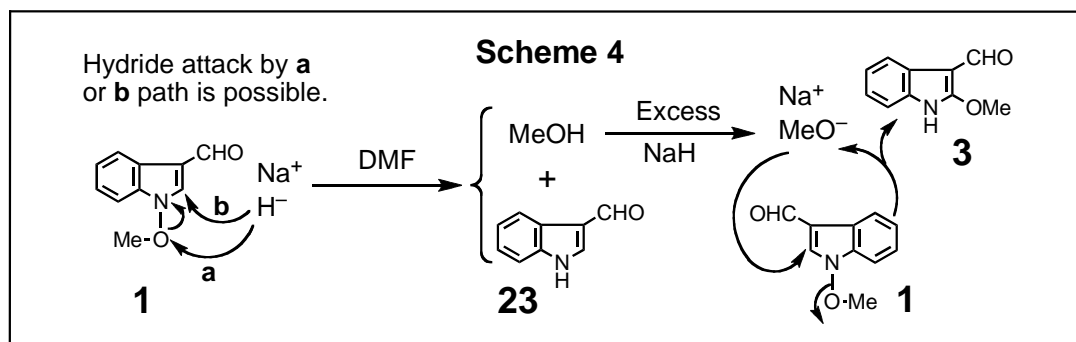
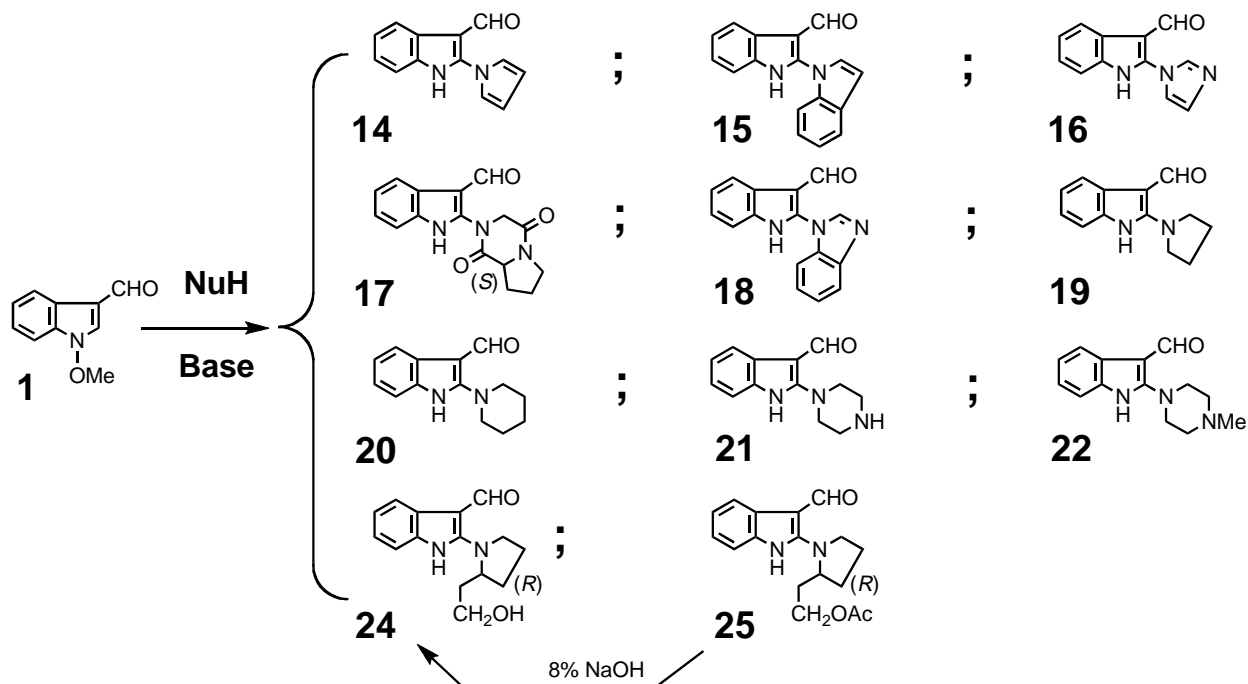
Reactions of **1** with nitrogen containing heterocycles were examined in the presence of NaH in DMF at rt and the results are summarized in Scheme 3. Nucleophiles, such as pyrrole, indole, imidazole, and (8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazine-1,4-dione, afforded the expected products, **14**, **15**, **16**, and **17** in 99, 95, 80, and 67% yields, respectively. In the reaction of **1** with benzimidazole, the reaction rate was slow and even after 5 days, the desired **18** was obtained in only 30% yield with starting material as the major product (62%).

The reactions of **1** with sodium salts of alicyclic amines are interesting to note. Although **19** and **20** were obtained in 71 and 26% yields in the respective reactions with pyrrolidine and piperidine, a significant amount of **3** was generated in both cases in 24 and 63% yields respectively. The reaction of **1** with piperazine provided **21** in 16% yield together with 48% yield of **3**. Similar reaction with *N*-methylpiperazine afforded **22** in 13% yields in addition to 36% yield of **3**.

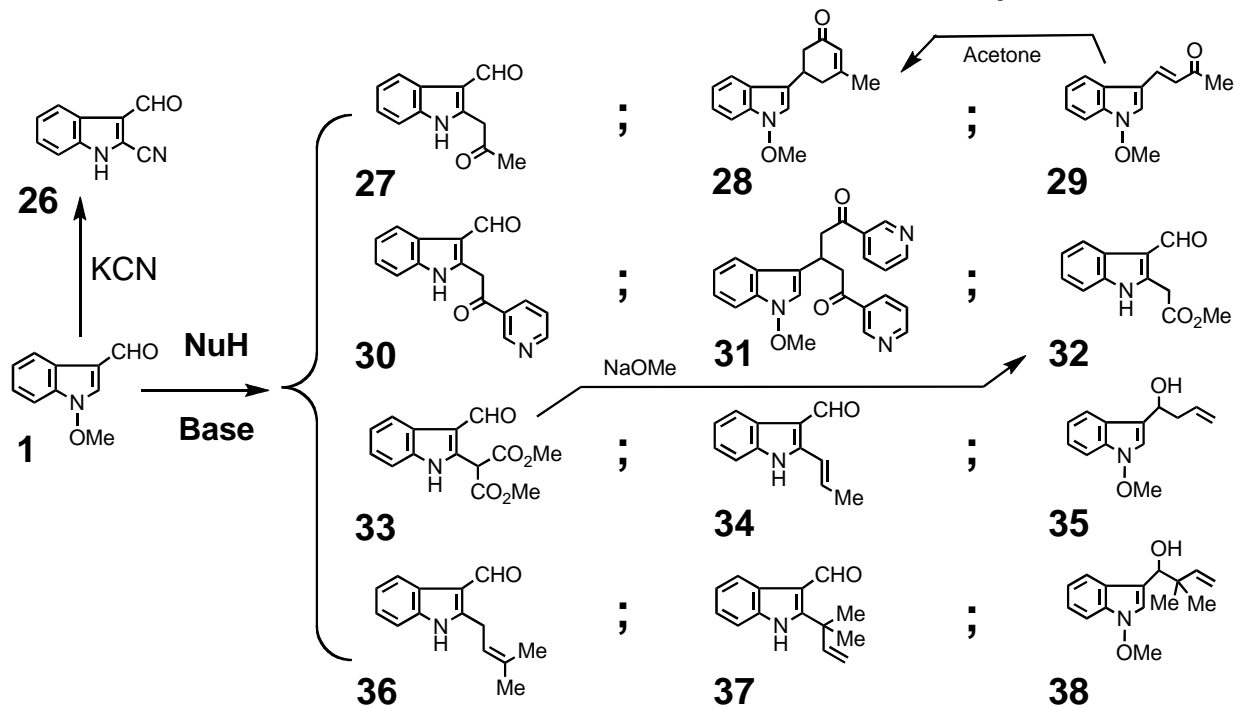
The formation of **3** observed in the reactions utilizing these weak nucleophiles and NaH in DMF may be explained as follows (Scheme 4). The initial reductive cleavage of *N*-OMe bond in **1** with NaH by **a** or **b** path liberates indole-3-carbaldehyde (**23**) and MeOH. Hydride reduction of 3-formyl group and the liberation of MeOH is another possible mechanism. Excess NaH instantly convert MeOH into NaOMe. Once NaOMe is generated, it attacks the second molecule of **1** giving **3** and NaOMe, which in turn attacks the third molecule of **1**, and infinite repetition of the processes leads to complete transformation of **1** to **3**. In order to examine this explanation, treatment of **1** with NaH in DMF at rt was attempted proving the formation of **3** as a sole isolable product in 78% yield, though the formation of **23** was not detected at all.

The reaction of **1** with (*R*)-(-)-2-pyrrolidinemethanol in the presence of NaH afforded 2-[(*R*)-2-hydroxymethylpyrrolidin-1-yl]indole-3-carbaldehyde (**24**) in 14% yield together with a significant amount (23%) of unknown compound (MS *m/z*: 226 (*M*<sup>+</sup>)). In the same reaction, treatment of the crude reaction residue with Ac<sub>2</sub>O provided 2-[(*R*)-2-acetoxymethylpyrrolidin-1-yl]indole-3-carbaldehyde (**25**)

### Scheme 3. Reaction of 1 with Nitrogen-Centered Nucleophiles



### Scheme 5. Reaction of 1 with Carbon-Centered Nucleophiles



in 43% yield, which was converted to **24** by treatment with aqueous 8% NaOH in a quantitative yield.

### III. Reaction of **1** with Carbon-Centered Nucleophiles

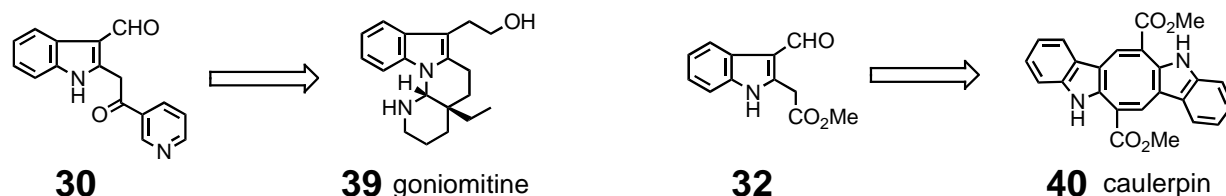
As for a carbon nucleophile, we chose KCN at first (Scheme 5). The reaction proceeded smoothly to give **26** in 98% yield. The reaction of **1** with acetone in the presence of KH in acetone–THF produced the expected **27** together with **28** in 51 and 29% yields, respectively. On the other hand, when aqueous 8% NaOH was used as base in acetone–MeOH, nucleophilic substitution reaction did not take place, instead the aldol reaction product (**29**) was obtained exclusively in 92% yield. The structure of **28** was proved through the conversion of **29** to **28** in 62% yield by the reaction with acetone in the presence of KH. Similar results were observed when 3-acetylpyridine was used as a nucleophile. Thus, the reaction of **1** in the presence of KH in THF produced **30** and **31** in 74 and 9% yields, respectively.

Dimethyl malonate reacted with **1** using NaOMe in refluxing MeOH to give **32** and **33** in 46 and 13% yields, respectively. Treatment of **33** with NaOMe in refluxing MeOH afforded **32** in 64% yield.

When **1** was reacted with allyltrimethylsilane in the presence of Bu<sub>4</sub>NF in THF, **34** and **35** were obtained in 23 and 28% yields, respectively. In the similar reaction using (3-methylbut-2-en-1-yl)trimethylsilane, **36**, **37**, and **38** were produced in 7, 12, and 14% yields, respectively.

In conclusion, we have demonstrated that **1** is a good electrophile and reacts regioselectively at the 2-position with sulfur-, oxygen-, nitrogen-, and carbon-centered nucleophiles. Consequently, various types of 2-substituted indole-3-carbaldehydes become readily available, which are not accessible by employing electrophilic reactions. With **30** and **32** in hand as useful building blocks for the respective synthesis of natural products, goniomitine<sup>9</sup> (**39**, Scheme 6) and caulerpin<sup>10</sup> (**40**), the attempts are now in progress. Biological evaluation of novel 2-substituted indole-3-carbaldehydes reported in this paper is also under investigation as sterilizer and plant growth regulator.<sup>8</sup>

Scheme 6



## EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were determined with a Shimadzu IR-420 or Horiba FT-720 spectrophotometer, and <sup>1</sup>H-NMR spectra with a JEOL EX-270 or GSX-500 spectrometer with tetramethylsilane as an internal standard. MS spectra were recorded on Hitachi M-80 or JEOL JMS-SX 102A spectrometer. Preparative thin-layer chromatography (p-TLC) was performed on Merck Kiesel-gel GF<sub>245</sub> (Type 60) (SiO<sub>2</sub>). Column

chromatography was performed on silica gel (SiO<sub>2</sub>, 100–200 mesh, from Kanto Chemical Co., Inc.) or activated alumina (Al<sub>2</sub>O<sub>3</sub>, 300 mesh, from Wako Pure Chemical Industries, Ltd.) throughout the present study.

**2-Methylthioindole-3-carbaldehyde (2) from 1-methoxyindole-3-carbaldehyde (1)** — An aq. 15% NaSMe (2.5 mL, 5.35 mmol) was added to a solution of **1** (43.7 mg, 0.25 mmol) in MeOH (4 mL) and heated at reflux for 2 h. After evaporation of solvent under reduced pressure, sat. aq. NH<sub>4</sub>Cl was added. The whole was extracted with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v). The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (99:1, v/v) to give **2** (44.6 mg, 94%). **2**: mp 233–234 °C (lit.,<sup>7</sup> mp 210–213 °C colorless prisms, recrystallized from MeOH). IR (KBr): 1626, 1581, 1447, 1371, 1347, 1225, 848, 755, 657 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CD<sub>3</sub>OD) δ: 2.68 (3H, s), 7.19 (1H, ddd, *J*=7.1, 7.0, and 1.3 Hz), 7.22 (1H, ddd, *J*=7.1, 7.0, and 1.5 Hz), 7.38–7.42 (1H, m), 8.04–8.08 (1H, m), 10.04 (1H, s). MS *m/z*: 191 (M<sup>+</sup>). *Anal.* Calcd for C<sub>10</sub>H<sub>9</sub>NOS: C, 62.74; H, 4.74; N, 7.32. Found: C, 62.61; H, 4.80; N, 7.25.

**2-Methoxyindole-3-carbaldehyde (3) from 1** — [**General Procedure**] (reaction with NaOMe): Na (136.5 mg, 5.93 mmol) was added to an ice-cooled anhydrous MeOH (2 mL) and stirred at rt for 5 min. To the resultant solution, a solution of **1** (40.1 mg, 0.23 mmol) in anhydrous MeOH (1 mL) was added. The mixture was refluxed for 2 h with stirring. After evaporation of solvent under reduced pressure, sat. aq. NH<sub>4</sub>Cl was added. The whole was extracted with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v). The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (97:3, v/v) to give **3** (35.9 mg, 90%). **3**: mp 251–252 °C (colorless plates, recrystallized from MeOH). IR (KBr): 1611, 1583, 1567, 1502, 1345, 1307, 1233, 1058, 745, 715 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CD<sub>3</sub>OD) δ: 4.19 (3H, s), 7.13 (1H, ddd, *J*=6.1, 6.0, and 1.5 Hz), 7.15 (1H, ddd, *J*=6.1, 6.0, and 1.5 Hz), 7.28 (1H, dd, *J*=6.1 and 1.5 Hz), 7.95 (1H, dd, *J*=6.1 and 1.5 Hz), 9.75 (1H, s). MS *m/z*: 175 (M<sup>+</sup>). *Anal.* Calcd for C<sub>10</sub>H<sub>9</sub>NO<sub>2</sub>: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.42; H, 5.22; N, 7.98. [**Second Procedure**] (reaction with NaH): A solution of **1** (32.9 mg, 0.19 mmol) in anhydrous DMF (3 mL) was added to 60% NaH (168.4 mg, 4.21 mmol) and stirred at rt for 17 h. After the same work-up as described in general procedure, **3** (25.8 mg, 78%) was obtained.

**2-Ethoxyindole-3-carbaldehyde (4) from 1** — In the general procedure for **3**, Na (180.3 mg, 7.84 mmol), anhydrous EtOH (2 mL), and **1** (46.1 mg, 0.26 mmol) in anhydrous EtOH (2 mL) were used. After the same work-up and column chromatography, **4** (47.2 mg, 95%) was obtained. **4**: mp 227–228 °C (decomp., colorless prisms, recrystallized from MeOH). IR (KBr): 1604, 1573, 1485, 1364, 1344, 1234, 1050, 743, 657 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CD<sub>3</sub>OD) δ: 1.52 (3H, t, *J*=7.1 Hz), 4.47 (2H, q, *J*=7.1 Hz), 7.12 (1H, ddd, *J*=7.3, 7.2, and 1.7 Hz), 7.15 (1H, ddd, *J*=7.3, 7.2, and 1.5 Hz), 7.24–7.29 (1H, m), 7.93–7.98 (1H, m), 9.75 (1H, s). MS *m/z*: 189 (M<sup>+</sup>). *Anal.* Calcd for C<sub>11</sub>H<sub>11</sub>NO<sub>2</sub>: C, 69.82; H, 5.68; N, 7.40. Found: C, 69.82;

H, 5.88; N, 7.31.

**2-(2-Hydroxyethoxy)indole-3-carbaldehyde (5) from 1** — [General procedure] Na (105.4 mg, 4.58 mmol) was added to an ice-cooled anhydrous ethylene glycol (3 mL) and stirred at rt for 2.5 h. To the resultant solution, a solution of **1** (76.4 mg, 0.44 mmol) in anhydrous ethylene glycol (3 mL) was added and the mixture was heated at 60 °C for 19 h with stirring. Sat. aq. NH<sub>4</sub>Cl was added and the whole was extracted with EtOAc. The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (99:1, v/v) to give **1** (3.7 mg, 5%) and **5** (44.9 mg, 50%). **5**: mp 188–190 °C (yellow prisms, recrystallized from MeOH). UV (MeOH) λ<sub>max</sub> nm (log ε): 304 (4.12), 267 (4.11), 244 (4.21). IR (KBr): 1608, 1545, 1345, 1258, 1233, 1070, 1052, 883, 750 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CD<sub>3</sub>OD) δ: 3.96 (2H, ddd, *J*=4.5, 3.7, and 1.4 Hz), 4.46 (2H, ddd, *J*=4.5, 3.7, and 1.4 Hz), 7.13 (1H, ddd, *J*=7.4, 7.3, and 1.7 Hz), 7.15 (1H, ddd, *J*=7.4, 7.3, and 1.4 Hz), 7.25–7.29 (1H, m), 7.94–7.98 (1H, m), 9.82 (1H, s). MS *m/z*: 205 (M<sup>+</sup>). *Anal.* Calcd for C<sub>11</sub>H<sub>11</sub>NO<sub>3</sub>: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.08; H, 5.50; N, 6.86.

**2-(3-Hydroxypropyloxy)indole-3-carbaldehyde (6) from 1** — Na (71.9 mg, 3.126 mmol) was added to an ice-cooled anhydrous 1,3-propanediol (1 mL) and stirred at rt for 5 min. To the resultant solution, a solution of **1** (105.9 mg, 0.60 mmol) in anhydrous 1,3-propanediol (2 mL) was added and the mixture was heated at 70 °C for 5 h with stirring. After the same work-up in the general procedure for **5** except for employing CHCl<sub>3</sub>–MeOH–28%NH<sub>3</sub> (46:5:0.5, v/v) as an eluent, **6** (100.3 mg, 76%) was obtained. **6**: mp 172–174 °C (yellow powder, recrystallized from CHCl<sub>3</sub>). UV (MeOH) λ<sub>max</sub> nm (log ε): 305 (4.13), 267 (4.06), 244 (4.17), 211 (4.26). IR (KBr): 1605, 1480, 1450, 1348, 1237, 1054, 1007, 908, 874, 738, 715, 645 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CD<sub>3</sub>OD) δ: 2.10 (2H, quint, *J*=6.1 Hz), 3.79 (2H, t, *J*=6.1 Hz), 4.53 (2H, t, *J*=6.1 Hz), 7.11–7.17 (2H, m), 7.28 (1H, dd, *J*=7.3 and 1.7 Hz), 7.95 (1H, dd, *J*=5.6 and 2.4 Hz), 9.77 (1H, s). MS *m/z*: 219 (M<sup>+</sup>). *Anal.* Calcd for C<sub>12</sub>H<sub>13</sub>NO<sub>3</sub>·1/8H<sub>2</sub>O: C, 65.07; H, 5.92; N, 6.32. Found: C, 65.25; H, 5.94; N, 6.31.

**2-(2,3-Dihydroxypropyloxy)indole-3-carbaldehyde (7) from 1** — Na (133.2 mg, 5.79 mmol) was added to a solution of glycerol (1 mL) in anhydrous DMF (1 mL) and the mixture was heated at 70 °C for 17 h. To the resultant solution, a solution of **1** (201.5 mg, 1.15 mmol) in anhydrous DMF (4 mL) was added and heated at 70 °C for additional 5 h. After the same work-up in the general procedure for **5** except for employing CHCl<sub>3</sub>–MeOH–28%NH<sub>3</sub> (46:2:0.2, v/v) as an eluent, **7** (80.6 mg, 30%) was obtained. **7**: mp 194.0–195.0 °C (yellow powder, recrystallized from MeOH–benzene). UV (MeOH) λ<sub>max</sub> nm (log ε): 304 (4.15), 267 (4.10), 244 (4.21), 210 (4.41). IR (KBr): 1608, 1560, 1486, 1460, 1360, 1239, 1124, 1062, 885, 748 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CD<sub>3</sub>OD) δ: 3.70 (2H, d, *J*=5.6 Hz), 4.06 (1H, dtd, *J*=6.1, 5.6 and 3.9 Hz), 4.41 (1H, dd, *J*=9.8 and 6.1 Hz), 4.50 (1H, dd, *J*=9.8 and 3.9 Hz), 7.11–7.17 (2H, m), 7.26–7.29 (1H, m), 7.94–7.97 (1H, m), 9.81 (1H, s). MS *m/z*: 235 (M<sup>+</sup>). *Anal.* Calcd for C<sub>13</sub>H<sub>13</sub>NO<sub>4</sub>: C,



61.27; H, 5.27; N, 5.95. Found: C, 60.97; H, 5.55; N, 6.00.

**2-(2-*N,N*-Dimethylaminoethoxy)indole-3-carbaldehyde (8) from 1** — Na (156.4 mg, 6.80 mmol) was added to an ice-cooled anhydrous *N,N*-dimethylaminoethanol (3 mL) and stirred at rt for 5 min. To the resultant solution, a solution of **1** (240.8 mg, 1.37 mmol) in anhydrous THF (7 mL) was added and the mixture was heated at 70 °C for 2 h with stirring. After the same work-up in the general procedure for **5** except for employing CHCl<sub>3</sub>–MeOH–28%NH<sub>3</sub> (46:2:0.2, v/v) as an eluent, **8** (114.1 mg, 36%) was obtained. **8**: mp 148–149 °C (yellow plates, recrystallized from MeOH–H<sub>2</sub>O). UV (MeOH) λ<sub>max</sub> nm (log ε): 304 (4.16), 267 (4.11), 244 (4.22), 210 (4.45). IR (KBr): 1601, 1580, 1485, 1348, 1238, 1238, 1045, 880, 734, 650 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.49 (6H, s), 2.85 (2H, t, *J*=4.2 Hz), 4.46 (2H, t, *J*=4.2 Hz), 7.15 (1H, dd, *J*=7.6 and 7.1 Hz), 7.19 (1H, d, *J*=7.6 Hz), 7.21 (1H, dd, *J*=7.8 and 7.1 Hz), 8.34 (1H, d, *J*=7.8 Hz), 9.96 (1H, s). MS *m/z*: 232 (M<sup>+</sup>). *Anal.* Calcd for C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.28; H, 6.93; N, 12.00.

**2-(2,2-Dimethyl-1,3-dioxolan-4-yl)methoxyindole-3-carbaldehyde (9) from 1** — Na (139.6 mg, 6.07 mmol) was added to (2,2-dimethyl-1,3-dioxolane-4-yl)methanol (2 mL) and the mixture was heated at 80 °C for 1.5 h. To the resultant solution, a solution of **1** (205.7 mg, 1.17 mmol) in anhydrous DMF (6 mL) was added and heated at 80 °C for additional 1 h. After addition of H<sub>2</sub>O, the whole was made acidic with 6% HCl and extracted with EtOAc. The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil (2.493 g), which was dissolved in pyridine (6 mL). To the resultant solution, Ac<sub>2</sub>O (3 mL) was added and the mixture was stirred at rt for 1 h. After evaporation of the solvent, sat. aq. NaHCO<sub>3</sub> was added to the residue and the whole was extracted with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v). The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CHCl<sub>3</sub>–MeOH–28%NH<sub>3</sub> (100:1:0.1, v/v) to give **9** (183.5 mg, 57%). **9**: mp 214–215 °C (red brown flakes, recrystallized from MeOH). UV (MeOH) λ<sub>max</sub> nm (log ε): 304 (4.16), 267 (4.11), 244 (4.23), 208 (4.43). IR (KBr): 1600, 1570, 1480, 1342, 1235, 1050, 835, 735, 655 cm<sup>-1</sup>. <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>) δ: 1.31 (3H, s), 1.35 (3H, s), 3.87 (1H, dd, *J*=8.6 and 5.5 Hz), 4.13 (1H, dd, *J*=8.6 and 6.5 Hz), 4.41–4.46 (1H, m), 4.47–4.54 (2H, m), 7.10–7.15 (2H, m), 7.28–7.32 (1H, m), 7.89–7.93 (1H, m), 9.86 (1H, s), 12.13 (1H, br s). MS *m/z*: 275 (M<sup>+</sup>). *Anal.* Calcd for C<sub>15</sub>H<sub>17</sub>NO<sub>4</sub>: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.43; H, 6.21; N, 5.11.

**7 from 9** — 6% HCl (2 mL) was added to a solution of **9** (19.2 mg, 0.070 mmol) in MeOH (2 mL) and the mixture was stirred at rt for 0.5 h. Sat. aq. NaHCO<sub>3</sub> was added and the whole was extracted with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v). The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CHCl<sub>3</sub>–MeOH–28%NH<sub>3</sub> (46:10:1, v/v) to give **7** (10.4 mg, 63%).

**3-(1,1-Dimethylallyl)-2-oxindole (11) through 3-(1,1-dimethylallyl)-3-formyl-2-oxindole (12) from 1** — 3-Methylbut-2-en-1-ol (350.3 mg, 4.0 mmol) in anhydrous DMF (1 mL) was added to 60% NaH (122.7 mg, 3.1 mmol) at rt and stirred for 10 min. To the resultant mixture, a solution of **1** (53.0 mg, 0.30 mmol) in anhydrous DMF (2 mL) was added and stirred at rt for 24 h. After addition of sat. aq. NH<sub>4</sub>Cl, the whole was extracted with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v). The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CH<sub>2</sub>Cl<sub>2</sub> to give a 2:5 mixture (50.7 mg) of **11** and **12**. The mixture was dissolved in MeOH (4 mL) and refluxed for 24 h. After evaporation of solvent, the resultant crude **11** was purified by column chromatography on SiO<sub>2</sub> with CH<sub>2</sub>Cl<sub>2</sub> to give pure **11** (12.1 mg, 75%). **11**: mp 149–150 °C (colorless leaves, recrystallized from MeOH–H<sub>2</sub>O). IR (KBr): 1706, 1661, 1617, 1470, 1332, 1233, 920, 735, 680 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.12 (3H, s), 1.34 (3H, s), 3.25 (1H, s), 4.98 (1H, dd, *J*=17.5 and 1.0 Hz), 5.06 (1H, dd, *J*=10.7 and 1.0 Hz), 5.98 (1H, dd, *J*=17.5 and 10.7 Hz), 6.82 (1H, d, *J*=7.5 Hz), 6.95 (1H, ddd, *J*=7.5, 7.4, and 1.1 Hz), 7.19 (1H, ddd, *J*=7.7, 7.4, and 1.1 Hz), 7.31 (1H, d, *J*=7.7 Hz), 7.83 (1H, br s, disappeared on addition of D<sub>2</sub>O). MS *m/z*: 201 (M<sup>+</sup>). *Anal.* Calcd for C<sub>13</sub>H<sub>15</sub>NO: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.68; H, 7.59; N, 6.92. **12**: Unstable intermediate. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.22 (3H, s), 1.29 (3H, s), 5.02 (1H, dd, *J*=17.4 and 0.7 Hz), 5.16 (1H, dd, *J*=10.8 and 0.7 Hz), 6.13 (1H, dd, *J*=17.4 and 10.8 Hz), 6.90 (1H, ddd, *J*=7.7, 1.1, and 0.6 Hz), 7.06 (1H, ddd, *J*=7.7, 7.6, and 1.1 Hz), 7.26 (1H, ddd, *J*=7.7, 7.6, and 1.1 Hz), 7.49 (1H, ddd, *J*=7.7, 1.1, and 0.6 Hz), 8.63 (1H, br s), 9.88 (1H, s).

**3-(3-Methylbut-2-en-1-yl)-2-oxindole (13) from 1** — 2-Methylbut-3-en-2-ol (0.60 mL, 5.66 mmol) was added to a suspension of 35% KH (288.0 mg, 2.51 mmol) in HMPA (0.5 mL), and the whole was stirred at rt for 10 min. To the resultant solution, a solution of **1** (100.8 mg, 0.57 mmol) in HMPA (2.0 mL) was added and stirred at rt for 1 h. After addition of H<sub>2</sub>O, the whole was made acidic by adding 6% HCl and extracted with EtOAc. The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with EtOAc–hexane (1:3, v/v) to give **13** (29.8 mg, 26%) and **3** (37.8 mg, 38%). **13**: mp 109–109.5 °C (pale yellow prisms, recrystallized from EtOAc–hexane). IR (KBr): 1699, 1652, 1608, 1453, 1385, 1324, 1229, 821, 742 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.58 (3H, s), 1.67 (3H, s), 2.58 (1H, ddd, *J*=14.5, 7.5, and 6.5 Hz), 2.69–2.76 (1H, m), 3.46 (1H, dd, *J*=7.5 and 5.0 Hz), 5.11–5.16 (1H, m), 6.87 (1H, d, *J*=7.6 Hz), 7.00 (1H, td, *J*=7.6 and 1.1 Hz), 7.20 (1H, td, *J*=7.6 and 1.1 Hz), 7.23 (1H, d, *J*=7.6 Hz), 8.19 (1H, br s, disappeared on addition of D<sub>2</sub>O). MS *m/z*: 201 (M<sup>+</sup>). *Anal.* Calcd for C<sub>13</sub>H<sub>15</sub>NO: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.51; H, 7.57; N, 6.83.

**2-(Pyrrol-1-yl)indole-3-carbaldehyde (14) from 1** — [General procedure] A solution of pyrrole (71.4 mg, 1.06 mmol) in anhydrous DMF (1 mL) was added to 60% NaH (35.3 mg, 0.88 mmol) at 0 °C with stirring. After 10 min, a solution of **1** (49.9 mg, 0.28 mmol) in anhydrous DMF (2 mL) was added at 0 °C.

After stirring at rt for 3 h, sat. aq.  $\text{NH}_4\text{Cl}$  was added. The whole was extracted with  $\text{CH}_2\text{Cl}_2$ -MeOH (95:5, v/v). The extract was washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , and evaporated under reduced pressure to leave solid, which was column chromatographed on  $\text{SiO}_2$  with  $\text{CH}_2\text{Cl}_2$ -MeOH (99:1, v/v) to give **14** (59.1 mg, 99%). **14**: mp 266–268 °C (decomp., colorless leaves, recrystallized from MeOH). IR (KBr): 1612, 1582, 1564, 1487, 1457, 1372, 1071, 726  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (5%  $\text{DMSO-}d_6$  in  $\text{CDCl}_3$ )  $\delta$ : 6.44 (2H, dd,  $J=2.2$  and 2.1 Hz), 7.22 (2H, dd,  $J=2.2$  and 2.1 Hz), 7.25–7.30 (2H, m), 7.39–7.44 (1H, m), 8.25–8.30 (1H, m), 10.07 (1H, s), 12.04 (1H, br s, disappeared on addition of  $\text{D}_2\text{O}$ ). MS  $m/z$ : 210 ( $\text{M}^+$ ). *Anal.* Calcd for  $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}$ : C, 74.27; H, 4.79; N, 13.33. Found: C, 74.54; H, 4.87; N, 13.04.

**2-(Indol-1-yl)indole-3-carbaldehyde (15) from 1** — In the general procedure for **14**, indole (51.4 mg, 0.44 mmol) instead of pyrrole, 60% NaH (14.2 mg, 0.35 mmol), **1** (47.0 mg, 0.27 mmol), and 24 h as for reaction time were employed. After the same work-up except for employing EtOAc as an extraction solvent and  $\text{CH}_2\text{Cl}_2$ -hexane (1:1, v/v) as an eluent, **15** (66.4 mg, 95%) was obtained. **15**: mp 259–260 °C (colorless leaves, recrystallized from MeOH). IR (KBr): 1615, 1578, 1555, 1486, 1449, 1381, 1355, 747, 736, 721  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (5%  $\text{DMSO-}d_6$  in  $\text{CDCl}_3$ )  $\delta$ : 6.80 (1H, dd,  $J=3.4$  and 0.9 Hz), 7.25 (1H, ddd,  $J=7.0$ , 6.8, and 1.1 Hz), 7.27–7.35 (3H, m), 7.46–7.51 (1H, m), 7.49 (1H, d,  $J=3.4$  Hz), 7.60 (1H, ddd,  $J=8.2$ , 0.9, and 0.8 Hz), 7.71 (1H, ddd,  $J=8.9$ , 0.9, and 0.8 Hz), 8.29–8.34 (1H, m), 9.92 (1H, s), 12.29 (1H, br s, disappeared on addition of  $\text{D}_2\text{O}$ ). MS  $m/z$ : 260 ( $\text{M}^+$ ). *Anal.* Calcd for  $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}$ : C, 78.44; H, 4.65; N, 10.76. Found: C, 78.66; H, 4.60; N, 10.76.

**2-(Imidazol-1-yl)indole-3-carbaldehyde (16) from 1** — In the general procedure for **14**, imidazole (33.7 mg, 0.49 mmol) instead of pyrrole, 60% NaH (19.8 mg, 0.49 mmol), **1** (52.7 mg, 0.30 mmol), and 48 h as for reaction time were employed. After the same work-up except for employing EtOAc-MeOH (99:5, v/v) as an extraction solvent,  $\text{Al}_2\text{O}_3$  as an adsorbent, and  $\text{CH}_2\text{Cl}_2$ -MeOH (97:3, v/v) as an eluent, **16** (51.3 mg, 80%) was obtained. **16**: mp 233–234 °C (colorless needles, recrystallized from MeOH). IR (KBr): 1638, 1567, 1531, 1486, 1465, 1398, 1066, 1021, 748  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (5%  $\text{DMSO-}d_6$  in  $\text{CDCl}_3$ )  $\delta$ : 7.28–7.36 (2H, m), 7.30 (1H, br d,  $J=1.2$  Hz), 7.43–7.48 (1H, m), 7.56 (1H, br s), 8.14 (1H, br s), 8.24–8.29 (1H, m), 10.04 (1H, s), 12.44 (1H, br s, disappeared on addition of  $\text{D}_2\text{O}$ ). MS  $m/z$ : 211 ( $\text{M}^+$ ). *Anal.* Calcd for  $\text{C}_{12}\text{H}_9\text{N}_3\text{O} \cdot 1/6\text{MeOH}$ : C, 67.48; H, 4.50; N, 19.40. Found: C, 67.45; H, 4.35; N, 19.21.

**(8a*S*)-2-(3-Formylindol-2-yl)hexahydropyrrolo[1,2-*a*]pyrazine-1,4-dione (17) from 1** — In the general procedure for **14**, (8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazine-1,4-dione (551.9 mg, 3.58 mmol) instead of pyrrole, 60% NaH (143.1 mg, 3.58 mmol), **1** (201.4 mg, 1.15 mmol), and 6 h as for reaction time were employed. After the same work-up except for employing  $\text{CH}_2\text{Cl}_2$ -MeOH (95:5, v/v) as an eluent, **17** (229.4 mg, 67%) was obtained. **17**: mp 231–233 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 1701, 1680, 1608, 1577, 1469, 1406, 1351, 1314, 1206, 769  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (5%  $\text{DMSO-}d_6$  in  $\text{CDCl}_3$ )  $\delta$ : 1.96–2.07 (1H, m), 2.07–2.15 (1H, m), 2.21–2.30 (1H, m), 2.42–2.49 (1H, m),

3.61–3.73 (2H, m), 4.19 (1H, d,  $J=16.1$  Hz), 4.42 (1H, t,  $J=8.1$  Hz), 4.86 (1H, d,  $J=16.1$  Hz), 7.24–7.31 (2H, m), 7.39–7.43 (1H, m), 8.41–8.46 (1H, m), 10.07 (1H, s), 11.80 (1H, br s, disappeared on addition of D<sub>2</sub>O). MS  $m/z$ : 297 (M<sup>+</sup>). *Anal.* Calcd for C<sub>16</sub>H<sub>15</sub>N<sub>3</sub>O<sub>3</sub>: C, 64.64; H, 5.08; N, 14.13. Found: C, 64.57; H, 5.06; N, 14.03.

**2-(Benzimidazol-1-yl)indole-3-carbaldehyde (18) from 1** — In the general procedure for **14**, benzimidazole (75.3 mg, 0.64 mmol) instead of pyrrole, 60% NaH (22.3 mg, 0.56 mmol), **1** (49.0 mg, 0.28 mmol), and 5 days as for reaction time were employed. After the same work-up except for employing EtOAc as an eluent, **18** (21.8 mg, 30%) was obtained together with **1** (30.3 mg, 62%). **18**: mp 278–280 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 1657, 1562, 1490, 1472, 1451, 1392, 1213, 741 cm<sup>-1</sup>. <sup>1</sup>H-NMR (5% DMSO-*d*<sub>6</sub> in CDCl<sub>3</sub>)  $\delta$ : 7.34–7.40 (2H, m), 7.41–7.46 (2H, m), 7.50–7.54 (1H, m), 7.58–7.63 (1H, m), 7.89–7.94 (1H, m), 8.31–8.36 (1H, m), 8.42 (1H, m), 9.95 (1H, s), 12.60 (1H, br s, disappeared on addition of D<sub>2</sub>O). MS  $m/z$ : 261 (M<sup>+</sup>). *Anal.* Calcd for C<sub>16</sub>H<sub>11</sub>N<sub>3</sub>O: C, 73.55; H, 4.24; N, 16.08. Found: C, 73.72; H, 4.16; N, 15.98.

**2-(Pyrrolidin-1-yl)indole-3-carbaldehyde (19) from 1** — In the general procedure for **14**, pyrrolidine (414.5 mg, 5.83 mmol) instead of pyrrole, 60% NaH (219.8 mg, 5.50 mmol), **1** (49.3 mg, 0.28 mmol), and 6 h as for reaction time were employed. After the same work-up except for employing CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v) as an eluent, **3** (11.8 mg, 24%) and **19** (42.7 mg, 71%) were obtained. **19**: mp 343 °C (decomp., colorless leaves, recrystallized from MeOH). IR (KBr): 1625, 1608, 1591, 1563, 1477, 1454, 1410, 1370, 1352, 1327, 742, 670 cm<sup>-1</sup>. <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>)  $\delta$ : 2.00–2.07 (4H, m), 3.45–3.61 (4H, m), 6.95–7.00 (2H, m), 7.11–7.16 (1H, m), 8.01–8.07 (1H, m), 9.79 (1H, s), 10.82 (1H, br s, disappeared on addition of D<sub>2</sub>O). MS  $m/z$ : 214 (M<sup>+</sup>). *Anal.* Calcd for C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O: C, 72.87; H, 6.59; N, 13.08. Found: C, 72.62; H, 6.58; N, 12.98.

**2-(Piperidin-1-yl)indole-3-carbaldehyde (20) from 1** — In the general procedure for **14**, piperidine (467.2 mg, 5.49 mmol) instead of pyrrole, 60% NaH (211.2 mg, 5.28 mmol), **1** (47.5 mg, 0.27 mmol), and 6 h as for reaction time were employed. After the same work-up except for employing CH<sub>2</sub>Cl<sub>2</sub>–MeOH (97:3, v/v) as an eluent, **20** (16.0 mg, 26%) and **3** (30.0 mg, 63%) were obtained. **20**: mp 262–263 °C (decomp., colorless leaves, recrystallized from MeOH). IR (KBr): 1597, 1563, 1444, 1382, 1241, 743 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CD<sub>3</sub>OD)  $\delta$ : 1.70–1.81 (6H, m), 3.58–3.63 (4H, m), 7.02–7.08 (2H, m), 7.13–7.17 (1H, m), 7.90 (1H, br s), 9.77 (1H, s). MS  $m/z$ : 228 (M<sup>+</sup>). *Anal.* Calcd for C<sub>14</sub>H<sub>16</sub>N<sub>2</sub>O: C, 73.66; H, 7.06; N, 12.27. Found: C, 73.57; H, 6.95; N, 12.04.

**2-(Piperazin-1-yl)indole-3-carbaldehyde (21) from 1** — A solution of piperazine (797.2 mg, 9.25 mmol) in anhydrous DMF (8 mL) was added to 60% NaH (369.7 mg, 9.24 mmol, washed with hexane) under ice cooling and stirring was continued at rt for 1 h. To the resultant solution, a solution of **1** (81.0 mg, 0.46 mmol) in anhydrous DMF (2 mL) was added and the mixture was heated at 60 °C for 3 h with

stirring. After addition of H<sub>2</sub>O, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CHCl<sub>3</sub>–MeOH–28%NH<sub>3</sub> (46:2:0.2, v/v) to give **3** (38.6 mg, 48%) and **21** (16.7 mg, 16%). **21**: mp 198–200 °C (yellow flakes, recrystallized from MeOH–benzene). UV (MeOH) λ<sub>max</sub> nm (log ε): 329 (4.02), 275 (4.16), 255 (4.33), 219 (4.38). IR (KBr): 1595, 1565, 1465, 1375, 1230, 995, 745, 657 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CD<sub>3</sub>OD) δ: 3.02 (4H, t, *J*=5.0 Hz), 3.59 (4H, t, *J*=5.0 Hz), 7.05–7.09 (2H, m), 7.18–7.20 (1H, m), 7.88 (1H, br s), 9.82 (1H, s). MS *m/z*: 229 (M<sup>+</sup>). *Anal.* Calcd for C<sub>13</sub>H<sub>15</sub>N<sub>3</sub>O: C, 68.10; H, 6.59; N, 18.33. Found: C, 67.96; H, 6.51; N, 17.95.

**2-(4-Methylpiperazin-1-yl)indole-3-carbaldehyde (22) from 1** — A solution of 1-methylpiperazine (4.630 g, 46.2 mmol) in anhydrous DMF (4 mL) was added to 60% NaH (1.836 g, 45.9 mmol, washed with hexane) under ice cooling and stirring was continued at rt for 1 h. To the resultant solution, a solution of **1** (201.5 mg, 1.15 mmol) in anhydrous DMF (4 mL) was added and the mixture was heated at 65 °C for 1 h with stirring. After addition of H<sub>2</sub>O, the whole was made acidic with 6% HCl and extracted with EtOAc. The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CHCl<sub>3</sub>–MeOH–28%NH<sub>3</sub> (46:5:0.5, v/v) to give **3** (72.8 mg, 36%) and **22** (36.2 mg, 13%). **22**: mp 229–230 °C (brown powder, recrystallized from MeOH–benzene). UV (MeOH) λ<sub>max</sub> nm (log ε): 329 (4.06), 274 (4.18), 255 (4.36), 219 (4.40). IR (KBr): 1570, 1380, 1365, 1249, 1228, 1147, 993, 903, 830, 748, 663 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.42 (3H, s), 2.71 (4H, t, *J*=4.6 Hz), 3.69 (4H, t, *J*=4.6 Hz), 7.11 (1H, ddd, *J*=8.1, 6.4, and 1.1 Hz), 7.18 (1H, ddd, *J*=7.1, 6.4, and 1.2 Hz), 7.22 (1H, dd, *J*=8.1 and 1.2 Hz), 7.96 (1H, dd, *J*=7.1 and 1.1 Hz), 8.88 (1H, br s), 10.06 (1H, s). MS *m/z*: 243 (M<sup>+</sup>). *Anal.* Calcd for C<sub>14</sub>H<sub>17</sub>N<sub>3</sub>O: C, 69.11; H, 7.04; N, 17.27. Found: C, 68.87; H, 6.95; N, 17.18.

**(R)-(-)-2-(2-Hydroxymethylpyrrolidin-1-yl)indole-3-carbaldehyde (24) and an unknown compound from 1** — A solution of (*R*)-(-)-2-pyrrolidinemethanol (597.6 mg, 5.92 mmol) in anhydrous DMF (3 mL) was added to 60% NaH (469.5 mg, 11.7 mmol, washed with hexane) under ice cooling and stirring was continued at rt for 1 h. To the resultant solution, a solution of **1** (206.6 mg, 1.18 mmol) in anhydrous DMF (4 mL) was added and the mixture was stirred at rt for 0.5 h. After addition of H<sub>2</sub>O, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CHCl<sub>3</sub>–MeOH–28%NH<sub>3</sub> (46:2:0.2, v/v) to give **24** (39.4 mg, 14%) and unknown compound (61.1 mg, 23%). **24**: mp 187.0–188.5 °C (purple prisms, recrystallized from MeOH). UV (MeOH) λ<sub>max</sub> nm (log ε): 322 (4.17), 269 (4.23), 258 (4.40), 217 (4.36). [α]<sub>D</sub><sup>24</sup>: –59 (c=0.5, MeOH). IR (KBr): 1560, 1368, 1238, 1040, 742, 662 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CD<sub>3</sub>OD) δ: 2.11–2.25 (4H, m), 3.55–3.63 (1H, m), 3.69 (1H, dd, *J*=11.5 and 5.6 Hz), 3.73 (1H, dd, *J*=11.5 and 5.6 Hz), 3.74–3.80 (1H, m), 4.21 (1H, br s), 7.02–7.04 (2H,

m), 7.11–7.13 (1H, m), 8.10 (1H, br s), 9.70 (1H, s). MS  $m/z$ : 244 ( $M^+$ ). *Anal.* Calcd for  $C_{14}H_{16}N_2O_2 \cdot 1/8H_2O$ : C, 68.20; H, 6.54; N, 11.36. Found: C, 68.34; H, 6.59; N, 11.40. Unknown compound: mp 221–223 °C (pale brown prisms, recrystallized from  $CH_2Cl_2$ –hexane). UV (MeOH)  $\lambda_{max}$  nm (log  $\epsilon$ ): 348 (4.30), 281 (4.18), 276 (4.26), 272 (4.17), 242 (3.81), 209 (4.57).  $[\alpha]_D^{30}$ : –702 ( $c=0.36$ , MeOH). IR (KBr): 1635, 1426, 1390, 1308, 1262, 1222, 1095, 1060, 1009, 922, 745  $cm^{-1}$ .  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 1.63–1.73 (1H, m), 1.94–2.04 (2H, m), 2.25–2.32 (1H, m), 3.58–3.76 (4H, m), 4.48 (1H, d,  $J=12.3$  Hz), 7.03 (1H, dd,  $J=7.5$  and 7.3 Hz), 7.12 (1H, dd,  $J=7.9$  and 7.3 Hz), 7.29 (1H, d,  $J=7.5$  Hz), 7.39 (1H, d,  $J=7.9$  Hz), 7.41 (1H, s). MS  $m/z$ : 226 ( $M^+$ ). *Anal.* Calcd for  $C_{14}H_{14}N_2O$ : C, 74.31; H, 6.24; N, 12.38. Found: C, 74.29; H, 6.16; N, 12.31.

**(R)-(-)-2-(2-Acetoxymethylpyrrolidin-1-yl)indole-3-carbaldehyde (25) from 1** — In the same procedure as described for **24**, (R)-(-)-2-pyrrolidinemethanol (586.5 mg, 5.80 mmol), 60% NaH (229.8 mg, 5.74 mmol, washed with hexane), **1** (202.4 mg, 1.15 mmol) were used. After the same work-up as for **24**, the resultant residue was dissolved into pyridine (4 mL). To the resultant solution,  $Ac_2O$  (2 mL) was added and the mixture was stirred at rt for 0.5 h. After evaporation of the solvent, sat. aq.  $NaHCO_3$  was added to the residue 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 column chromatographed on  $SiO_2$  with  $CH_2Cl_2$ –MeOH (98:2, v/v) to give **25** (143.3 mg, 43%). **25**: mp 156–157 °C (pale gray prisms, recrystallized from  $CH_2Cl_2$ –hexane). UV (MeOH)  $\lambda_{max}$  nm (log  $\epsilon$ ): 321(4.17), 268 (4.24), 257 (4.40), 217 (4.40).  $[\alpha]_D^{30}$ : –69 ( $c=0.18$ , MeOH). IR (KBr): 1742, 1600, 1562, 1375, 1224, 1045, 922, 748, 667  $cm^{-1}$ .  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 2.00–2.22 (4H, m), 2.19 (3H, s), 3.49–3.55 (1H, m), 3.74 (1H, dd,  $J=11.5$  and 9.2 Hz), 3.75–3.80 (1H, m), 4.06–4.13 (1H, m), 4.48 (1H, dd,  $J=11.5$  and 2.5 Hz), 7.11 (1H, td,  $J=7.6$  and 1.2 Hz), 7.15 (1H, td,  $J=7.6$  and 1.0 Hz), 7.22 (1H, dd,  $J=7.6$  and 1.2 Hz), 8.26 (1H, dd,  $J=7.6$  and 1.0 Hz), 9.82 (1H, br s), 9.88 (1H, s). MS  $m/z$ : 286 ( $M^+$ ). *Anal.* Calcd for  $C_{16}H_{18}N_2O_3$ : C, 67.12; H, 6.34; N, 9.78. Found: C, 67.33; H, 6.27; N, 9.79.

**24 from 25** — Aq. 8% NaOH (1 mL) was added to a solution of **25** (21.5 mg, 0.075 mmol) in DMF (1 mL) and the mixture was stirred at rt for 1 h. After addition of  $H_2O$ , the whole was extracted with EtOAc. The extract was washed with brine, dried over  $Na_2SO_4$ , and evaporated under reduced pressure to leave **24** (18.5 mg, 100%) as crystals.

**2-Cyanoindole-3-carbaldehyde (26) from 1** — A solution of KCN (76.5 mg, 1.17 mmol) in  $H_2O$  (1 mL) was added to a solution of **1** (37.3 mg, 0.21 mmol) in DMF (4 mL) and heated at 75–80 °C for 2 h with stirring. After evaporation of solvent under reduced pressure, sat. aq.  $NH_4Cl$  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 column chromatographed on  $SiO_2$  with  $CH_2Cl_2$ –MeOH (99.5:0.5, v/v) to give **26** (35.6 mg, 98%). **26**: mp 228–230 °C (decomp.,

colorless prisms, recrystallized from MeOH). IR (KBr): 2230, 1647, 1575, 1447, 1436, 1380, 654, 640  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CD}_3\text{OD}$ )  $\delta$ : 7.37 (1H, ddd,  $J=8.1, 7.1,$  and  $1.0$  Hz), 7.47 (1H, ddd,  $J=8.4, 7.1,$  and  $1.2$  Hz), 7.53 (1H, ddd,  $J=8.4, 1.0,$  and  $0.9$  Hz), 8.23 (1H, ddd,  $J=8.1, 1.2,$  and  $0.9$  Hz), 10.20 (1H, s). MS  $m/z$ : 170 ( $\text{M}^+$ ). *Anal.* Calcd for  $\text{C}_{10}\text{H}_6\text{N}_2\text{O}$ : C, 70.58; H, 3.55; N, 16.45. Found: C, 70.45; H, 3.84; N, 16.46.

**1-(3-Formylindol-2-yl)propan-2-one (27) and 5-(1-methoxyindol-3-yl)-3-methylcyclohex-2-enone (28) from 1** — Under Ar atmosphere, a solution of acetone (0.88 mL, 11.9 mmol) in anhydrous THF (1 mL) was added to a suspension of 35% KH (1.33 g, 11.6 mmol, washed with benzene) in anhydrous THF (5 mL) with stirring under ice cooling. After gas evolution ceased, a solution of **1** (102.9 mg, 0.59 mmol) in anhydrous THF (6 mL) was added to the resultant solution and the mixture was stirred at rt for 6 h. After addition of  $\text{H}_2\text{O}$ , the whole was made acidic with  $\text{NH}_4\text{Cl}$  and extracted with  $\text{CH}_2\text{Cl}_2$ -MeOH (9:1, v/v). The extract was washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , and evaporated under reduced pressure to leave an oil, which was column chromatographed on  $\text{SiO}_2$  with  $\text{CH}_2\text{Cl}_2$ -MeOH (98:2, v/v) to give **28** (42.9 mg, 29%) and **27** (61.3 mg, 51%) in the order of elution. **27**: mp 133–135 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 1712, 1628, 1469, 1394, 1188, 740  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 2.39 (3H, s), 4.43 (2H, s), 7.25–7.31 (2H, m), 7.40–7.45 (1H, m), 8.07–8.12 (1H, m), 9.99 1H, br s, disappeared on addition of  $\text{D}_2\text{O}$ , 10.28 (1H, s). MS  $m/z$ : 201 ( $\text{M}^+$ ). *Anal.* Calcd for  $\text{C}_{12}\text{H}_{11}\text{NO}_2$ : C, 71.63; H, 5.51; N, 6.96. Found: C, 71.48; H, 5.45; N, 7.13. **28**: mp 70–71 °C (pale brown prisms, recrystallized from hexane). UV (MeOH)  $\lambda_{\text{max}}$  nm (log  $\epsilon$ ): 290 (3.72), 277 (3.70), 224 (4.60). IR (KBr): 1645, 1440, 1368, 1239, 1205, 1021, 953, 880, 738  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 2.02 (3H, s), 2.57 (1H, dd,  $J=18.1$  and  $6.2$  Hz), 2.60 (1H, dd,  $J=16.3$  and  $12.1$  Hz), 2.71 (1H, dd,  $J=18.1$  and  $4.6$  Hz), 2.81 (1H, dd,  $J=16.3$  and  $4.2$  Hz), 3.60–3.68 (1H, m), 4.07 (3H, s), 6.00 (1H, s), 7.07 (1H, s), 7.12 (1H, ddd,  $J=7.9, 7.0,$  and  $0.9$  Hz), 7.26 (1H, ddd,  $J=8.2, 7.0,$  and  $0.7$  Hz), 7.43 (1H, dd,  $J=8.2$  and  $0.9$  Hz), 7.51 (1H, dd,  $J=7.9$  and  $0.7$  Hz). MS  $m/z$ : 255 ( $\text{M}^+$ ). *Anal.* Calcd for  $\text{C}_{16}\text{H}_{17}\text{NO}_2 \cdot 1/8\text{H}_2\text{O}$ : C, 74.61; H, 6.65; N, 5.44. Found: C, 74.76; H, 6.87; N, 5.32.

**(E)-4-(1-Methoxyindol-3-yl)but-3-en-2-one (29) from 1** — Aq. 8% NaOH (0.5 mL) was added to a solution of **1** (103.0 mg, 0.59 mmol) in MeOH-acetone (1:1, v/v, 2 mL) and the mixture was stirred at rt for 6 h. After evaporation of solvent under reduced pressure, brine was added. The whole was extracted with EtOAc. The extract was washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , and evaporated under reduced pressure to leave an oil, which was column chromatographed on  $\text{SiO}_2$  with  $\text{CH}_2\text{Cl}_2$ -MeOH (99:1, v/v) to give **29** (116.5 mg, 92%). **29**: pale yellow oil. IR (film): 1670, 1580  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 2.37 (3H, s), 4.16 (3H, s), 6.77 (1H, d,  $J=16.1$  Hz), 7.26 (1H, ddd,  $J=8.1, 7.1,$  and  $1.1$  Hz), 7.34 (1H, ddd,  $J=8.2, 7.1,$  and  $1.1$  Hz), 7.52 (1H, ddd,  $J=8.2, 1.1,$  and  $0.9$  Hz), 7.86 (1H, d,  $J=16.1$  Hz), 7.92 (1H, ddd,  $J=8.1, 1.1,$  and  $0.9$  Hz), 8.00 (1H, s). High resolution MS  $m/z$ : Calcd for  $\text{C}_{13}\text{H}_{13}\text{NO}_2$ : 215.0946. Found:

215.0941.

**28 from 29** — Under Ar atmosphere, a solution of acetone (0.7 mL, 9.53 mmol) in anhydrous THF (1 mL) was added to a suspension of 35% KH (1.026 g, 8.98 mmol, washed with benzene) in anhydrous THF (5 mL) with stirring under ice cooling. After gas evolution ceased, a solution of **29** (102.3 mg, 0.48 mmol) in anhydrous THF (6 mL) was added to the resultant solution and the mixture was stirred at rt for 1 h. After addition of H<sub>2</sub>O, the whole was made acidic with 6% HCl and extracted with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v). The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (98:2, v/v) to give **28** (75.2 mg, 62%).

**3-[2-(3-Formylindol-2-yl)acetyl]pyridine (30) and 1,5-di(pyrid-3-yl)-3-(1-methoxyindol-3-yl)pentane-1,5-dione (31) from 1** — Under Ar atmosphere, a solution of 3-acetylpyridine (88.1 mg, 0.72 mmol) in anhydrous THF (2 mL) was added to 35% KH (66.1 mg, 0.58 mmol, washed with hexane) with stirring under ice cooling. After gas evolution ceased, a solution of **1** (83.2 mg, 0.47 mmol) in anhydrous THF (2 mL) was added to the resultant solution and the mixture was stirred at rt for 40 min. After addition of H<sub>2</sub>O, the whole was made acidic with 6% HCl and extracted with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (9:1, v/v). The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CHCl<sub>3</sub>–MeOH–28%NH<sub>3</sub> (46:2:0.2, v/v) to give **1** (4.2 mg, 5%), **31** (16.5 mg, 9%), and **30** (93.1 mg, 74%) in the order of elution. **30**: mp 208–210 °C (orange needles, recrystallized from MeOH). UV (MeOH) λ<sub>max</sub> nm (log ε): 301 (4.08), 266 (4.15), 244 (4.31), 212 (4.57). IR (KBr): 1698, 1628, 1580, 1460, 1390, 1218, 1000, 977, 758 cm<sup>-1</sup>. <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>) δ: 5.09 (2H, s), 7.18–7.24 (2H, m), 7.48 (1H, dd, *J*=6.9 and 1.1 Hz), 7.65 (1H, ddd, *J*=8.0, 4.7, and 1.0 Hz), 8.10 (1H, d, *J*=7.2 Hz), 8.45 (1H, ddd, *J*=8.0, 2.2, and 1.9 Hz), 8.87 (1H, dd, *J*=4.7 and 2.2 Hz), 9.31 (1H, dd, *J*=1.9 and 1.0 Hz), 10.08 (1H, s), 12.04 (1H, br s). MS *m/z*: 264 (M<sup>+</sup>). *Anal.* Calcd for C<sub>16</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>: C, 72.72; H, 4.58; N, 10.60. Found: C, 72.51; H, 4.46; N, 10.40. **31**: yellow oil. IR (KBr): 1682, 1582, 1447, 1418, 1360, 1275, 1223, 739, 700 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 3.51 (2H, dd, *J*=16.6 and 6.6 Hz), 3.62 (2H, dd, *J*=16.6 and 7.1 Hz), 4.00 (3H, s), 4.37 (1H, tt, *J*=7.1 and 6.6 Hz), 7.12 (1H, dd, *J*=8.1 and 5.8 Hz), 7.18 (1H, s), 7.24 (1H, dd, *J*=8.1 and 5.8 Hz), 7.38 (1H, d, *J*=8.1 Hz), 7.42 (2H, dd, *J*=7.8 and 4.9 Hz), 7.61 (1H, d, *J*=8.1 Hz), 8.24 (2H, ddd, *J*=7.8, 1.6, and 1.5 Hz), 8.76 (2H, dd, *J*=4.9 and 1.5 Hz), 9.16 (2H, d, *J*=1.6 Hz). MS *m/z*: 399 (M<sup>+</sup>). High resolution MS *m/z*: Calcd for C<sub>24</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub>: 399.1581. Found: 399.1580.

**Methyl 2-(3-formylindol-2-yl)acetate (32) and dimethyl 2-(3-formylindol-2-yl)malonate (33) from 1** — A solution of dimethyl malonate (85.6 mg, 0.65 mmol) in anhydrous MeOH (1 mL) was added to a NaOMe solution in anhydrous MeOH (prepared by dissolving Na (12.0 mg, 0.52 mmol) in anhydrous MeOH (0.5 mL)) and stirred at rt for 1 h. To the resultant solution, a solution of **1** (49.8 mg,



0.28 mmol) in anhydrous MeOH (2 mL) was added and the mixture was refluxed for 30 min with stirring. After addition of H<sub>2</sub>O, the whole was made acidic with 6% HCl and extracted with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v). The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (99:1, v/v) to give **1** (13.3 mg, 27%), **33** (10.5 mg, 13%), and **32** (31.6 mg, 46%) in the order of elution. **32**: mp 116–118 °C (colorless leaves, recrystallized from MeOH–H<sub>2</sub>O). IR (KBr): 1730, 1644, 1465, 1451, 1438, 1389, 1305, 1215, 1163, 1024, 756, 749 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 3.82 (3H, s), 4.29 (2H, s), 7.26–7.31 (1H, m), 7.39–7.44 (1H, m), 8.14–8.19 (1H, m), 9.88 (1H, s), 10.24 (1H, s). MS *m/z*: 217 (M<sup>+</sup>), 185, 158. *Anal.* Calcd for C<sub>12</sub>H<sub>11</sub>NO<sub>3</sub>: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.44; H, 5.06; N, 6.48. **33**: mp 162–163 °C (colorless needles, recrystallized from MeOH). IR (KBr): 1757, 1734, 1626, 1449, 1384, 1325, 1238, 1147, 743 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 3.83 (6H, s), 5.84 (1H, s), 7.30 (1H, ddd, *J*=7.2, 7.1, and 1.5 Hz), 7.33 (1H, ddd, *J*=7.2, 7.1, and 1.6 Hz), 7.44–7.48 (1H, m), 8.14–8.19 (1H, m), 9.85 (1H, br s), 10.31 (1H, s). MS *m/z*: 275 (M<sup>+</sup>), 243. *Anal.* Calcd for C<sub>14</sub>H<sub>13</sub>NO<sub>5</sub>: C, 61.09; H, 4.76; N, 5.09. Found: C, 61.25; H, 4.71; N, 5.04.

**32 from 33** — A solution of **33** (56.1 mg, 0.19 mmol) in anhydrous MeOH (2 mL) was added to a NaOMe solution in anhydrous MeOH (prepared by dissolving Na (8.9 mg, 0.38 mmol) in anhydrous MeOH (0.5 mL)) and the mixture was refluxed for 2 h with stirring. After addition of H<sub>2</sub>O, the whole was made acidic with 6% HCl and extracted with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v). The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO<sub>2</sub> with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (98:2, v/v) as a developing solvent. Extraction of the band having an *R<sub>f</sub>* value of 0.63–0.52 with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v) afforded **33** (4.3 mg, 8%). Extraction of the band having an *R<sub>f</sub>* value of 0.47–0.27 with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v) afforded **32** (28.6 mg, 64%).

**2-[(*E*)-Propen-1-yl]indole-3-carbaldehyde (34) and 1-(1-methoxyindol-3-yl)but-3-en-1-ol (35) from 1** — Under an Ar atmosphere, a solution of **1** (54.1 mg, 0.31 mmol) in anhydrous THF (4 mL) was added to a mixture of Bu<sub>4</sub>NF•3H<sub>2</sub>O (106.8 mg, 0.34 mmol, dried for 2 h under reduced pressure) and molecular sieve (4 angstrom, 353.4 mg, flame dried, 1 h). To the mixture, allyltrimethylsilane (0.15 mL, 0.94 mmol) was added and stirred at rt for 6 h. After addition of sat. aq. NH<sub>4</sub>Cl, the whole was extracted with CH<sub>2</sub>Cl<sub>2</sub>–MeOH (95:5, v/v). The extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO<sub>2</sub> with CH<sub>2</sub>Cl<sub>2</sub>–hexane (7:3, v/v) to give **35** (18.9 mg, 28%), **34** (13.3 mg, 23%), and unknown product (8.8 mg) in the order of elution. **34**: mp 217–218 °C (yellow prisms, recrystallized from MeOH). IR (KBr): 1628, 1585, 1463, 1382, 1245, 948, 749, 740 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CD<sub>3</sub>OD) δ: 2.03 (3H, dd, *J*=6.8 and 1.7 Hz), 6.66 (1H, dq, *J*=15.9 and 6.8 Hz), 7.03 (1H, dq, *J*=15.9 and 1.7 Hz), 7.17 (1H, ddd, *J*=7.8, 7.1, and 0.9 Hz), 7.23 (1H,

ddd,  $J=8.1$ ,  $7.1$ , and  $1.3$  Hz),  $7.37$  (1H, ddd,  $J=8.1$ ,  $1.0$ , and  $0.9$  Hz),  $8.11$  (1H, ddd,  $J=7.8$ ,  $1.3$ , and  $0.9$  Hz),  $10.12$  (1H, s). MS  $m/z$ :  $185$  ( $M^+$ ),  $170$ . Anal. Calcd for  $C_{12}H_{11}NO$ : C,  $77.81$ ; H,  $5.99$ ; N,  $7.56$ . Found: C,  $77.77$ ; H,  $6.09$ ; N,  $7.51$ . **35**: colorless oil. IR (film):  $1638$ ,  $1450$ ,  $1438$ ,  $1350$ ,  $1319$ ,  $1226$ ,  $1092$ ,  $1046$ ,  $1031$ ,  $1010$ ,  $1000$ ,  $979$ ,  $954$ ,  $917$ ,  $758$ ,  $739$   $cm^{-1}$ .  $^1H$ -NMR ( $CD_3OD$ )  $\delta$ :  $2.62$ – $2.73$  (2H, m),  $4.05$  (3H, s),  $4.96$  (1H, t,  $J=6.7$  Hz),  $5.01$  (1H, ddt,  $J=10.2$ ,  $2.1$ , and  $1.1$  Hz),  $5.07$  (1H, ddt,  $J=17.1$ ,  $2.1$ , and  $1.5$  Hz),  $5.85$  (1H, ddt,  $J=17.1$ ,  $10.2$ , and  $7.0$  Hz),  $7.05$  (1H, ddd,  $J=7.9$ ,  $7.1$ , and  $0.9$  Hz),  $7.19$  (1H, ddd,  $J=8.2$ ,  $7.1$ , and  $1.1$  Hz),  $7.34$  (1H, s),  $7.38$  (1H, ddd,  $J=8.2$ ,  $0.9$ , and  $0.7$  Hz),  $7.67$  (1H, ddd,  $J=7.9$ ,  $1.1$ , and  $0.7$  Hz). High resolution MS  $m/z$ : Calcd for  $C_{13}H_{15}NO_2$ :  $217.1102$ . Found:  $217.1101$ .

**2-(3,3-Dimethylallyl)- (36), 2-(1,1-dimethylallyl)indole-3-carbaldehyde (37), and 2,2-dimethyl-1-(1-methoxyindol-3-yl)but-3-en-1-ol (38) from 1** — Under an Ar atmosphere, a solution of **1** ( $53.5$  mg,  $0.31$  mmol) in anhydrous THF ( $4$  mL) was added to a mixture of  $Bu_4NF \cdot 3H_2O$  ( $108.5$  mg,  $0.34$  mmol, dried for  $2$  h under reduced pressure) and molecular sieve ( $4$  angstrom,  $416.4$  mg, flame dried,  $1$  h). To the mixture, (3-methylbut-2-en-1-yl)trimethylsilane ( $0.20$  mL,  $1.1$  mmol) was added and stirred at rt for  $3$  h. After addition of sat. aq.  $NH_4Cl$ , 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  $CHCl_3$ –hexane ( $7:3$ , v/v) as a developing solvent. Extraction of the band having an  $R_f$  value of  $0.65$ – $0.58$ ,  $0.58$ – $0.50$ ,  $0.49$ – $0.43$ ,  $0.42$ – $0.37$  with  $CHCl_3$ –MeOH ( $95:5$ , v/v) afforded **38** ( $10.6$  mg,  $14\%$ ), unreacted **1** ( $20.5$  mg,  $38\%$ ), **37** ( $7.7$  mg,  $12\%$ ), and **36** ( $4.4$  mg,  $7\%$ ), respectively. **36**: mp  $149$ – $150$   $^{\circ}C$  (colorless needles, recrystallized from MeOH– $H_2O$ ). IR (KBr):  $1627$ ,  $1580$ ,  $1461$ ,  $1381$ ,  $1232$   $cm^{-1}$ .  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ :  $1.77$  (3H, s),  $1.84$  (3H, d,  $J=1.5$  Hz),  $3.88$  (2H, d,  $J=7,3$  Hz),  $5.40$  (1H, tq,  $J=7.3$  and  $1.5$  Hz),  $7.24$  (1H, ddd,  $J=8.5$ ,  $7.1$ , and  $1.3$  Hz),  $7.27$  (1H, ddd,  $J=8.5$ ,  $7.1$ , and  $1.3$  Hz),  $7.33$ – $7.36$  (1H, m),  $8.21$ – $8.26$  (1H, m),  $8.47$  (1H, br s, disappeared on addition of  $D_2O$ ),  $10.23$  (1H, s). MS  $m/z$ :  $213$  ( $M^+$ ). Anal. Calcd for  $C_{14}H_{15}NO$ : C,  $78.84$ ; H,  $7.09$ ; N,  $6.54$ . Found: C,  $78.97$ ; H,  $7.16$ ; N,  $6.52$ . **37**: mp  $194$ – $195$   $^{\circ}C$  (colorless needles, recrystallized from  $CH_2Cl_2$ –hexane). IR (KBr):  $3160$ ,  $1621$ ,  $1581$ ,  $1440$ ,  $1369$   $cm^{-1}$ .  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ :  $1.69$  (6H, s),  $5.292$  (1H, d,  $J=17.5$  Hz),  $5.294$  (1H, d,  $J=10.6$  Hz),  $6.23$  (1H, dd,  $J=17.5$  and  $10.6$  Hz),  $7.25$  (1H, ddd,  $J=8.8$ ,  $7.3$ , and  $1.5$  Hz),  $7.28$  (1H, ddd,  $J=8.8$ ,  $7.3$ , and  $1.5$  Hz),  $7.35$ – $7.38$  (1H, m),  $8.35$ – $8.39$  (1H, m),  $8.52$  (1H, br s, disappeared on addition of  $D_2O$ ),  $10.47$  (1H, s). MS  $m/z$ :  $213$  ( $M^+$ ). Anal. Calcd for  $C_{14}H_{15}NO$ : C,  $78.84$ ; H,  $7.09$ ; N,  $6.54$ . Found: C,  $78.63$ ; H,  $7.13$ ; N,  $6.49$ . **38**: colorless oil. IR (film):  $1634$ ,  $1449$ ,  $1355$ ,  $1093$ ,  $1043$ ,  $1034$ ,  $1009$ ,  $955$ ,  $912$ ,  $662$ ,  $639$   $cm^{-1}$ .  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ :  $1.07$  (3H, s),  $1.08$  (3H, s),  $1.57$  (1H, br s, disappeared on addition of  $D_2O$ ),  $4.08$  (3H, s),  $4.82$  (1H, s),  $5.14$  (1H, dd,  $J=17.4$  and  $1.3$  Hz),  $5.15$  (1H, dd,  $J=10.8$  and  $1.3$  Hz),  $6.04$  (1H, dd,  $J=17.4$  and  $10.8$  Hz),  $7.10$  (1H, ddd,  $J=8.1$ ,  $7.1$ , and  $0.9$  Hz),  $7.23$  (1H, ddd,  $J=8.2$ ,  $7.1$ , and  $0.9$  Hz),  $7.25$  (1H, s),  $7.41$  (1H, ddd,  $J=8.2$ ,  $0.9$ , and  $0.8$  Hz),  $7.66$  (1H, ddd,  $J=8.1$ ,  $0.9$  and  $0.8$  Hz). High resolution MS  $m/z$ : Calcd for  $C_{15}H_{19}NO_2$ :  $245.1416$ . Found:  $245.1415$ .

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