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The Chemistry of Indoles. XXXII.[1] A Facile Synthetic Method for 6-Indolecarbaldehyde, 6-Indolemethanol, and 6-Substituted 1-Hydroxyindoles and Its Application for the Synthesis of a Natural Alkaloid, (*E*)-6-(3-Methylbuta-1,3-dienyl)indole

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Trivalent titanium ion can reduce arylaldehydes, and the reaction is controllable by selecting the pH of the reaction medium. Utilizing this new finding, 6-indolecarbaldehyde and 6-indolemethanol were conveniently produced by the modified Leimgruber–Batcho method with titanium(III) chloride as the reducing agent. Syntheses of a natural alkaloid, (*E*)-6-(3-methylbuta-1,3-dienyl)indole, and some new 6-substituted 1-hydroxyindoles are also reported.

Keywords——titanium(III) chloride; 6-indolecarbaldehyde; 6-indolemethanol; (*E*)-6-(3-methylbuta-1,3-dienyl)indole; (*Z*)-6-(3-methylbuta-1,3-dienyl)indole; 1-hydroxy-6-indolecarbaldehyde; 1-methoxy-6-indolecarbaldehyde; 1-acetoxy-6-indolecarbaldehyde; Leimgruber–Batcho method; reduction

In nature, there are many interesting indole derivatives having a substituent at the 6-position.[2] In order to synthesize these compounds, 6-indolecarbaldehyde (**1**) and/or 6-indolemethanol (**2**) are needed as basic building blocks. Although the Leimgruber–Batcho method[3] seems to allow easy access to them, the requirement for catalytic hydrogenation results in hydrogenolysis of the benzylic C–O bond and therefore attempts to synthesize **1** and **2** have so far resulted in only poor yield.[3] In this paper, we describe a convenient synthesis of **1** and **2** and its application for the synthesis of a natural alkaloid, (*E*)-6-(3-methylbuta-1,3-dienyl)indole (**3**).[4]

We have already established that titanium(III) chloride ($TiCl_3$) is the reagent of choice for reducing the intermediate nitroenamine produced in the Leimgruber–Batcho indole synthesis.[5] In our continuing studies on the reducing ability of $TiCl_3$,[6] we have found that reduction of 4-methyl-3-nitrobenzylalcohol (**4**) in tetrahydrofuran (THF) with 8 molar eq of $TiCl_3$, which is sufficient to reduce both the nitro group and the benzylic C–O bond, afforded 3-amino-4-methylbenzylalcohol (**5**) in 85% yield without forming any detectable amount of 2,5-dimethylaniline (**6**). This result and our previous synthesis of 4-benzyloxyindole[7] clearly showed that trivalent titanium ion (Ti^{3+}) has no capability for reductive cleavage of the benzyloxygen sigma bond. Based on these results, we attempted to synthesize **1** and **2** by the Leimgruber–Batcho method with $TiCl_3$ as the reducing agent (Chart 1).

Oxidation of 4-methyl-3-nitrobenzylalcohol (**4**) with active manganese dioxide (MnO_2) readily afforded 4-methyl-3-nitrobenzaldehyde (**7**) in 75% yield. Subsequent treatment of **7** with 3 molar eq of dimethylformamide dimethylacetal (DMFDMA) provided the corresponding nitroenamine (**8**) in quantitative yield; the structure of **8** was supported by the proton nuclear magnetic resonance (^1H-NMR) spectrum. Without further purification, **8** was reduced with aq. $TiCl_3$ to produce a mixture of **1** and **2**. Their yields changed considerably

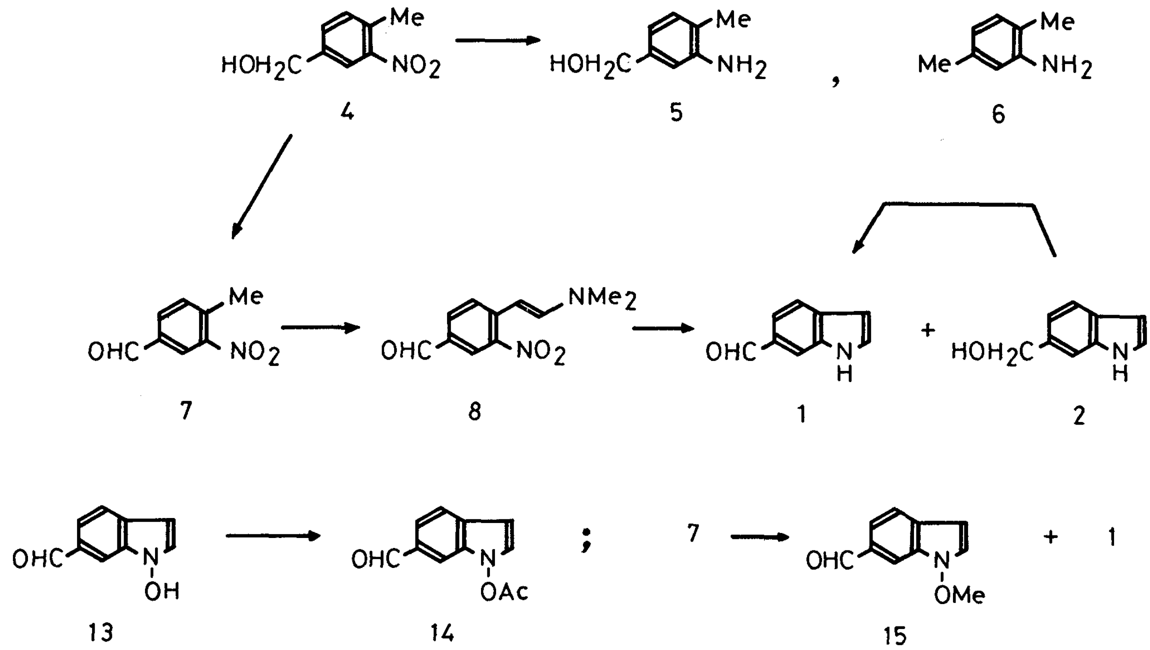
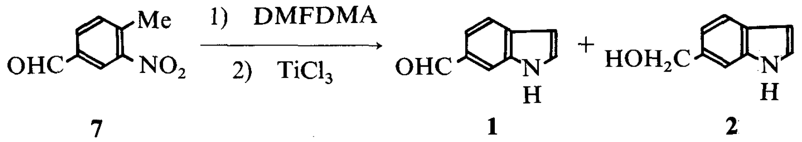


Chart 1

Table I. One-Pot Preparation of 6-Indolecarbaldehyde and 6-Indolemethanol



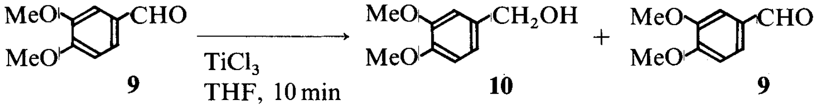
Entry	$TiCl_3$ (mol eq)	Solvent system	Reaction conditions		Yield (%) of	
			Time (min)	Temp. (°C)	**1**	**2**
1	8.0	THF	4	0	10.8	2.8
2	6.5	THF–AcONa (pH 2.0)	3	20	2.4	0.9
3	6.5	pyridine	4	20	5.9	26.1
4	6.5	THF–pyridine (pH 2.0)	7	18	22.3	20.4
5	8.0	THF–pyridine (pH 4.0)	7	17	10.2	42.9
6	13.0	THF–pyridine (pH 4.0)	12	11	5.9	56.3
7	19.5	THF–pyridine (pH 4.0)	20	7	2.8	59.3

Formation of the 1-hydroxyindole derivative was not observed.

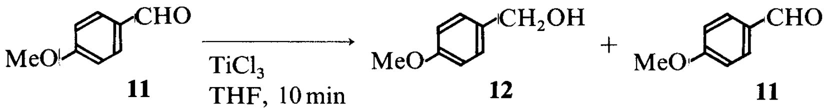
depending on the reaction conditions, and the results are summarized in Table I. With 8 molar eq of $TiCl_3$ in THF, **1** and **2** were produced only in poor yields due to the inherently unstable nature of 3-unsubstituted indoles under strongly acidic conditions (entry 1). Although addition of sodium acetate did not improve the yields (entry 2), pyridine was found to function as a good pH regulator and to give better results (entry 3). Based on these findings, reduction of the enamine (**8**) was carried out in THF–pyridine with the pH controlled at 2 to 4. The more $TiCl_3$ used, the better the yield of **2** (entries 4—6) and finally under the reaction conditions described in entry 7, 6-indolemethanol (**2**) was produced selectively in 59.3% yield.

Interestingly, this is the first observation that Ti^{3+} ion can reduce an aryl aldehyde to aryl

Table II. Reduction of Arylaldehyde with Titanium(III) Chloride

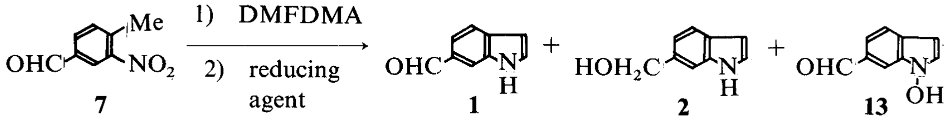


Entry	$TiCl_3$ (mod eq)	Additive (mol eq)	Yield (%) of 10	Yield (%) of 9
1	6	—	83.7	10.2
2	6	NH_4OAc (21)	21.0	73.1



Entry	$TiCl_3$ (mol eq)	Additive (mol eq)	Yield (%) of 12	Yield (%) of 11
3	6	—	84.3	1.8
4	6	NH_4OAc (21)	30.9	61.0

Table III. One-Pot Preparation of 6-Indolecarbaldehyde, 6-Indolemethanol, and 1-Hydroxy-6-indolecarbaldehyde



Entry	Reducing agent (mol eq)	Solvent	NH_4OAc (mol eq to $TiCl_3$)	Reaction conditions Time (min)	Reaction conditions Temp. (°C)	Yield (%) of 1	Yield (%) of 2	Yield (%) of 13
1	$TiCl_3$ (6.5)	THF	3	2	13	36.7	0	11.8
2	$TiCl_3$ (6.7)	THF	4.1	7	13	42.8	0	18.3
3	$TiCl_3$ (14.6)	THF	3.5	7	13	49.8	2.0	3.6
4	Zn–NH_4Cl (excess)	THF–H_2O	—	60	11.5	16.2	0	29.0

alcohol.[8] To confirm this new finding, reduction of both 3,4-dimethoxybenzaldehyde (**9**) and 4-methoxybenzaldehyde (**11**) was carried out with 6 molar eq of $TiCl_3$ in THF, and it was found that the corresponding benzyl alcohols, **10** and **12**, were prepared in 83.7% and 84.0% yeilds, respectively (Table II).

It is interesting to note that when ammonium acetate (NH_4OAc) was used as the pH controlling reagent, the reducing ability of Ti^{3+} ion was weakened. Thus, reduction of **9** with 6 molar eq of $TiCl_3$ in the presence of 21 molar eq of NH_4OAc gave only a 21.0% yield of the corresponding alcohol (**10**) and 73.1% of the starting material was recovered. Under similar reaction conditions, **11** afforded **12** and recovered **11** in 30.9% and 61.0% yields, respectively (Table II).

Based on these results, reduction of the nitroenamine (**8**) with $TiCl_3$ in the presence of NH_4OAc was carried out. The expected 6-indolecarbaldehyde (**1**) was produced together with unstable 1-hydroxy-6-indolecarbaldehyde (**13**). The results are summarized in Table III. Under the reaction conditions described in entry 3, the formation of by-products was minimized and **1** was produced in 49.8% yield. When zinc and ammonium chloride were used as the reducing agent instead of $TiCl_3$, **13** was produced as the major product (entry 4).

Thus, we can now prepare **1**[9] or **2**[9] selectively, simply by choosing a suitable pH controlling reagent in the Leimgruber–Batcho synthesis. Conversion of **2** to **1** was also attained in 70.3% yield by oxidation with active MnO_2 in methylene chloride.

Although 1-hydroxy-6-indolecarbaldehyde (**13**) was quite unstable even in the crystalline state, its structure was determined based on the spectral data. Further confirmation of its structure was obtained by the reaction with acetic anhydride and pyridine to afford, in 47.6% yield, the unstable 1-acetoxy-6-indolecarbaldehyde (**14**), whose infrared spectrum exhibited a characteristic absorption band at $1813\,cm^{-1}$, ascribable to the N-acetoxy group. In contrast, 1-methoxy-6-indolecarbaldehyde (**15**) was a stable compound and was readily produced from **7** in 36.2% overall yield by the following reaction sequence: i) reaction of **7** with DMFDMA, ii) reduction of the resulting enamine (**8**) with zinc and ammonium chloride, and iii) methylation of **13** with methyl iodide in the presence of potassium carbonate (Chart 1).

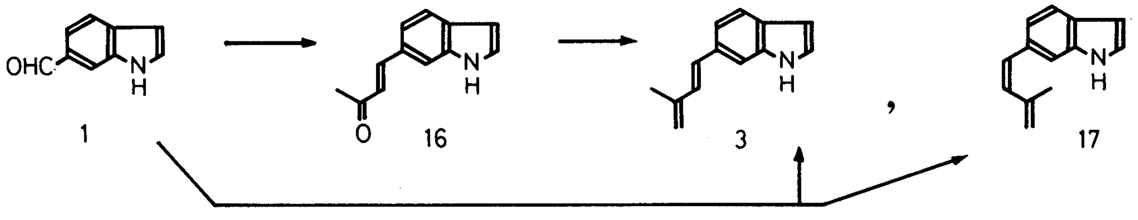


Chart 2

With 6-indolecarbaldehyde (**1**) in hand, we prepared the unstable natural product, (*E*)-6-(3-methylbuta-1,3-dienyl)indole (**3**),[4] in 35.3% yield together with (*Z*)-6-(3-methylbuta-1,3-dienyl)indole (**17**) as an oil in 25% yield by the Wittig reaction with 2-methylallylidene-triphenylphosphorane (Chart 2). The structure of **3** was confirmed by the conversion of **1** to **3** *via* 4-(indol-6-yl)-3-buten-2-one[10] (**16**) as follows. Thus, treatment of **1** with acetone in methanolic sodium hydroxide afforded **16** in 95.7% yield. According to Ishii *et al.*,[10] compound (**16**) was reacted with methylenetriphenylphosphorane to give an authentic sample of **3** in 36.5% yield. This was proved to be identical with the above product (**3**) by direct comparisons.

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were determined with a Shimadzu IR-420 spectrophotometer, and ^{1}H-NMR spectra with a JEOL JNM-PMX60 spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were recorded on a Hitachi M-80 spectrometer. Commercial aqueous 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.

3-Amino-4-methylbenzylalcohol (5) from 4-Methyl-3-nitrobenzylalcohol (4)——Aqueous $TiCl_3$ (3.07 ml, 8 mol eq) was added to a solution of **4** (99.8 mg) in THF (3.0 ml) with rapid stirring at room temperature. After being stirred for 7 min, the whole was made alkaline by adding 2 N NaOH and extracted with CH_2Cl_2–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave 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 give **5** (69.6 mg, 85.0%). **5**: mp 110.0—111.0 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3340, 3190, 1625 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.10 (3H, s), 4.45 (2H, s), 6.43—6.66 (2H, m), 6.88 (1H, d, J=8.0 Hz). *Anal.* Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.75; H, 8.09; N, 10.15.

4-Methyl-3-nitrobenzaldehyde (7) from 4——A mixture of **4** (4.527 g) and active MnO_2 (20.4 g) in CH_2Cl_2 (80.0 ml) was stirred at room temperature for two weeks. Methanol (8.0 ml) was added and the insoluble material was removed by filtration through SiO_2 gel. The filtrate was evaporated under reduced pressure to leave a crystalline solid, which was purified by column chromatography on SiO_2 with CH_2Cl_2 as an eluent to give **7** (3.5043 g, 78.3%). **7**: mp 45.0—46.0 °C (colorless needles, recrystallized from MeOH–H_2O). IR (KBr): 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.66 (3H, s), 7.43 (1H, d, J=8.0 Hz), 7.90 (1H, dd, J=8.0, 1.6 Hz), 8.30 (1H, d, J=1.6 Hz), 9.88 (1H, s). MS *m/z*: 165 (M^+).

6-Indolecarbaldehyde (1) and 6-Indolemethanol (2) from 7——Representative Experiment for Table I. Entry 6: A solution of **7** (94.5 mg) and DMFDMA (174.0 mg) in abs. dimethylformamide (DMF) (3.0 ml) was heated under reflux for 13.5 h with stirring. Removal of the solvent *in vacuo* afforded a red colored crystalline nitroenamine (**8**). Without further purification, **8** was dissolved in a mixed solvent composed of THF (20.0 ml) and pyridine (5.0 ml). With rapid stirring, aq. $TiCl_3$ (4.8 ml, 13.0 mol eq) was added to the solution in one portion and stirring was continued at room temperature for 12 min (the pH of the reaction mixture was 4.0). Brine (20.0 ml) was added to the reaction mixture and the whole was adjusted to pH 5.0 by adding 2 N NaOH. The organic layer was salted out and separated. The brine layer was further extracted with THF and the combined THF extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a crystalline solid, to which CH_2Cl_2–MeOH (95 : 5, v/v) was added. Insoluble material was separated by filtration. Evaporation of the filtrate afforded a crystalline solid, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (98 : 2, v/v) as a developing solvent. Under ultraviolet (UV) light, two bands were detected. Extraction from the upper fluorescent band with CH_2Cl_2–MeOH (95 : 5, v/v) afforded **1** (4.9 mg, 5.9%). Extraction from the lower band with the same solvent afforded **2** (47.4 mg, 56.3%). **8**: ^{1}H-NMR ($CDCl_3$) δ: 2.96 (6H, s), 5.89 (1H, d, J=13.0 Hz), 7.25 (1H, d, J=13.0 Hz), 7.38 (1H, d, J=8.0 Hz), 7.63 (1H, dd, J=8.0, 2.0 Hz), 8.11 (1H, d, J=2.0 Hz), 9.63 (1H, s), **1**: mp 130.0—131.0 °C (lit.[9] mp 127—129 °C, pale yellow prisms, recrystallized from CH_2Cl_2). IR (KBr): 3275, 2750, 1662 cm^{-1}. ^{1}H-NMR (10% CD_3OD in $CDCl_3$) δ: 6.47 (1H, br d, J=3.2 Hz), 7.32 (1H, br d, J=3.2 Hz), 7.52 (2H, br s), 7.82 (1H, br s), 9.79 (1H, s). MS *m/z*: 145 (M^+). *Anal.* Calcd for C_9H_7NO: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.66; H, 4.85; N, 9.43. **2**: mp 52.0—53.0 °C (lit.[9] mp 62—63 °C, colorless prisms, recrystallized from benzene). IR (film): 3400 (br) cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 4.57 (2H, s), 6.27 (1H, dd, J=3.2, 0.8 Hz), 6.85 (1H, dd, J=8.0, 1.4 Hz), 7.01 (1H, d, J=3.2 Hz), 7.21 (1H, br m), 7.35 (1H, d, J=8.0 Hz). MS *m/z*: 147 (M^+). *Anal.* Calcd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.43; H, 6.16; N, 9.34.

Entry 7: A solution of **7** (95.0 mg) and DMFDMA (186.0 mg) in abs. DMF (3.0 ml) was heated under reflux for 13.5 h with stirring. After removal of the solvent *in vacuo*, the residual nitroenamine (**8**) was dissolved in a mixed solvent composed of THF (30.0 ml) and pyridine (7.0 ml). With rapid stirring, aq. $TiCl_3$ (7.2 ml, 19.5 mol eq) was added to the solution in one portion and stirring was continued at room temperature for 20 min. After usual work-up and purification as described for entry 6, **1** (2.3 mg, 2.8%) and **2** (50.1 mg, 59.3%) were obtained.

1 from 2——A mixture of **2** (22.5 mg) and active MnO_2 (433.5 mg) in CH_2Cl_2 (7.0 ml) was stirred at 17 °C for 89 h. MeOH (1.0 ml) was added and insoluble material was removed by filtration through SiO_2 gel. The filtrate was evaporated 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 give **1** (15.6 mg, 70.3%) as pale yellow prisms.

1, 2, and 1-Hydroxy-6-indolecarbaldehyde (13) from 7——Representative Experiment for Table III. Entry 3: A solution of **7** (95.0 mg) and DMFDMA (183.9 mg) in abs. DMF (3.0 ml) was heated under reflux for 12.5 h. After removal of the solvent *in vacuo*, the residual nitroenamine (**8**) was dissolved in THF (20.0 ml). NH_4OAc (2.30 g, 3.5 mol eq to $TiCl_3$) was added to the solution, followed by addition of aq. $TiCl_3$ (5.42 ml, 14.6 mol eq to **7**) in one portion with rapid stirring. After being stirred at room temperature for 7 min, the whole was adjusted to pH 4 by adding 2 N NaOH and extracted with CH_2Cl_2 and then with CH_2Cl_2–MeOH (97 : 3, v/v). The combined organic layer was washed successively with brine, aq. $NaHCO_3$, and brine, and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure afforded a crystalline residue, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (97 : 3, v/v) as a developing solvent. Under UV light, three bands were detected. Extraction from the upper blue fluorescent band with CH_2Cl_2–MeOH (95 : 5, v/v) afforded **1** (41.6 mg, 49.8%). Extraction from the middle band with the same solvent afforded **13** (3.4 mg, 3.6%). Extraction of the lower band with the same solvent afforded **2** (1.7 mg, 2.0%).

Entry 4: A solution of **7** (94.0 mg) and DMFDMA (184.2 mg) in abs. DMF (3.0 ml) was heated under reflux for 12 h. After removal of the solvent *in vacuo*, the residual nitroenamine (**8**) was dissolved in THF (5.0 ml) and H_2O (1.5 ml). NH_4Cl (544.2 mg) and zinc dust (516.3 mg) were added to the solution and rapid stirring was continued at 11.5 °C for 1 h. CH_2Cl_2–MeOH mixture (97 : 3, v/v, 50 ml) was added and the insoluble material was removed by filtration through SiO_2 gel. The filtrate 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 at 7 °C with CH_2Cl_2–MeOH (96 : 4, v/v) as a developing solvent. Under UV light, two bands were detected. Extraction from the upper blue fluorescent band with CH_2Cl_2–MeOH (95 : 5, v/v) afforded **1** (13.4 mg, 16.2%). Extraction from the lower band with the same solvent afforded **13** (26.6 mg, 29.0%) as crystals. **13**: Unstable pale yellow prisms. Recrystallization caused partial decomposition and therefore the melting point could not be determined accurately. IR (KBr): 3074, 1652 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 6.26 (1H, dd, J=3.2, 0.8 Hz), 7.13——7.64 (3H, m), 7.81 (1H, br s), 9.76 (1H, s). High-resolution MS m/z: Calcd for $C_9H_7NO_2$: 161.0476. Found: 161.0463.

Reduction of Arylaldehyde with Titanium(III) Trichloride——I. 4-Methoxybenzylalcohol (**12**) from 4-Methoxybenzaldehyde (**11**). Entry 3: Aqueous $TiCl_3$ (2.90 ml, 6 mol eq) was added in one portion to a solution of **11** (100.4 mg) in THF (10.0 ml) with rapid stirring, and stirring was continued for 10 min. The whole was made neutral by adding 2 N NaOH and extracted with CH_2Cl_2–MeOH (97 : 3, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2 as a developing solvent. Under UV light, two bands were detected. Extraction from the upper band with CH_2Cl_2–MeOH (95 : 5, v/v) afforded unchanged **11** (1.8 mg, 1.8%). Extraction from the lower band with the same solvent afforded **12** (85.8 mg, 84.3%) as colorless prisms. mp 20 °C. All spectral data were identical with those of a commercial sample.

Entry 4: Aqueous $TiCl_3$ (2.80 ml, 6 mol eq) was added to a stirred mixture of **11** (99.4 mg) and NH_4OAc (1.181 g, 21 mol eq, 3.5 mol eq to $TiCl_3$) in THF (10.0 ml) in one portion, and stirring was continued for 10 min. After the same work-up and purification as described for entry 1, **11** (60.7 mg, 61.0%) and **12** (31.2 mg, 30.9%) were obtained.

II. 3,4-Dimethoxybenzylalcohol (**10**) from 3,4-Dimethoxybenzaldehyde (**9**). Entry 1: Aqueous $TiCl_3$ (2.4 ml, 6 mol eq) was added to a stirred solution of **9** (100.4 mg) in THF (10.0 ml) in one portion. Stirring was continued for 10 min and the whole was made neutral by adding 2 N NaOH then extracted with CH_2Cl_2–MeOH (97 : 3, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated to leave a crystalline solid, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (96 : 4, v/v) as a developing solvent. Under UV light, two bands were detected. Extraction from the upper band with CH_2Cl_2–MeOH (95 : 5, v/v) afforded unchanged **9** (10.3 mg, 10.2%). Extraction from the lower band with the same solvent afforded **10** (85.1 mg, 83.7%) as a colorless oil. All spectral data were identical with those of a commercial sample.

Entry 2: Aqueous $TiCl_3$ (2.4 ml, 6 mol eq) was added to a stirred suspension of **9** (102.1 mg) and NH_4OAc (1.0406 g, 21 mol eq 3.5 mol eq to $TiCl_3$) in THF (10.0 ml) in one portion and stirring was continued at 7 °C for 10 min. After the same work-up and purification as described for entry 3, **9** (74.7 mg, 73.1%) and **10** (21.7 mg, 21.0%) were obtained.

1-Acetoxy-6-indolecarbaldehyde (14) from 13——Acetic anhydride (0.5 ml) was added to a solution of **13** (25.0 mg) in pyridine (1.0 ml) and the whole was stirred at 6 °C for 11.5 h. Evaporation of the solvent *in vacuo* left an oil, which was purified by p-TLC on SiO_2 with CH_2Cl_2 as a developing solvent to afford **14** (15.0 mg, 47.6%). mp 88.5—90.0 °C (pale pink prisms, recrystallized from MeOH–H_2O). On standing at 5—10 °C, the compound gradually decomposed to a red tar. IR (KBr): 1813, 1680 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.37 (3H, s), 6.40 (1H, dd, J=3.2, 0.8 Hz), 7.31—7.57 (3H, m), 7.67 (1H, br s), 9.74 (1H, s). High-resolution MS m/z: Calcd for $C_{11}H_9NO_3$: 203.0582. Found: 203.0585.

1-Methoxy-6-indolecarbaldehyde (15) and 1 from 7——A solution of **7** (92.8 mg) and DMFDMA (183.4 mg) in abs. DMF (3.0 ml) was heated under reflux for 16.5 h. After removal of the solvent *in vacuo*, the residual enamine (**8**) was dissolved in THF (10.0 ml). A solution of NH_4Cl (527.1 mg) in H_2O (2.0 ml) and zinc dust (513.5 mg) were added to the solution and the whole was stirred at 13.5 °C for 30 min. The zinc dust and precipitate were removed by filtration through SiO_2 gel. A solution of methyl iodide (1.00 g) in THF (1.0 ml), a solution of tri-*n*-octylmethylammonium chloride (77.5 mg) in THF (1.0 ml), and 2 N NaOH (10.0 ml) were added to the filtrate and the whole was stirred at 11 °C for 2 h. After addition of brine, the whole was extracted with THF, washed with brine, dried over Na_2SO_4, and evaporated to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (97 : 3, v/v) as a developing solvent. Under UV light, two bands were detected. Extraction from the lower band with CH_2Cl_2–MeOH (95 : 5, v/v) afforded **1** (9.3 mg, 11.4%). Extracts from the upper band with the same solvent were further purified by p-TLC on SiO_2 with CH_2Cl_2–hexane (3 : 2, v/v) as a developing solvent. Under UV light, two bands were detected. Extraction from the upper band with CH_2Cl_2–MeOH (95 : 5, v/v) afforded **15** (35.6 mg, 36.2%). Extraction from the lower band with the same solvent afforded 1-methyl-6-indolecarbaldehyde (6.5 mg, 7.3%). ^{1}H-NMR (CD_3OD) δ: 3.80 (3H, s), 6.40 (1H, d, J=3.2 Hz), 7.26 (1H, d, J=3.2 Hz), 7.46 (2H, br s), 7.79 (1H, br s), 9.76 (1H, s). **15**: mp 68.5—69.5 °C (pale yellow prisms, recrystallized from MeOH–H_2O). IR (KBr): 1687 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 6.33 (1H, dd, J=3.2, 0.8 Hz), 7.40—7.66 (3H, m), 7.85 (1H, br s), 9.80 (1H, 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, 68.26; H, 5.02, N, 7.75.

4-(Indol-6-yl)-3-buten-2-one (16) from 1——A mixture of **1** (164.0 mg), acetone (7.5 ml), and 2 N NaOH (2.5 ml) was stirred at 7.5 °C for 14.5 h. After evaporation of the solvent under reduced pressure, brine was added and the whole was extracted with CH_2Cl_2–MeOH (95 : 5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated to leave a crystalline solid. Recrystallization from MeOH afforded **16** (132.0 mg) as yellow prisms. The mother liquor was purified by column chromatography on SiO_2 with CH_2Cl_2 as an eluent to give a further crop of **16** (68.1 mg). The total yield of **16** was 200.1 mg (95.7%). **16**: mp 138.0—139.0 °C (lit.[10] mp 135—137 °C, yellow prisms, recrystallized from MeOH–H_2O). IR (KBr): 1665, 1634, 1603 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.32 (3H, s), 6.43 (1H, br m), 6.60 (1H, d, J=16.0 Hz), 7.08—7.30 (2H, m), 7.41 (1H, br s), 7.48 (1H, d, J=8.0 Hz), 7.51 (1H, d, J=16.0 Hz), 8.52 (1H, br s). MS m/z: 185 (M^+). *Anal.* Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.52. Found: C, 77.60; H, 5.84; N, 7.48.

(*E*)-6-(3-Methylbuta-1,3-dienyl)indole (3) from 16——Under an argon atmosphere, a 1.6 M solution of *n*-BuLi in hexane (1.13 ml) was added to a suspension of methyltriphenylphosphonium bromide (569.2 mg) in abs. THF (7.0 ml) at 0 °C, and stirring was continued for 10 min. A solution of **16** (33.5 mg) in abs. THF (3.0 ml) was added to the resultant yellow ylide solution at 0 °C and the mixture was stirred at 11 °C for 40 min. Brine was added and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated to leave an oil, which was purified by column chromatography on SiO_2 with CH_2Cl_2–hexane (1 : 1, v/v) as an eluent to give **3** (12.1 mg, 36.5%) as unstable prisms. **3**: mp 126.0—129.0 °C (lit.[10] mp 124—127 °C, colorless leaflets, recrystallized from hexane). IR (KBr): 3366, 1604 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.94 (3H, br s), 4.93 (2H, br m), 6.21 (1H, d, J = 3.2 Hz), 6.45 (1H, d, J = 16.0 Hz), 6.78 (1H, d, J = 16.0 Hz), 7.00 (1H, d, J = 3.2 Hz), 7.02 (1H, d, J = 8.0 Hz), 7.25 (1H, s), 7.36 (1H, d, J = 8.0 Hz). MS m/z: 183 (M^+). These spectral data were identical with those provided by Dr. H. Ishii.

3 and (*Z*)-6-(3-Methylbuta-1,3-dienyl)indole (17) from 1——Under an argon atmosphere, a 1.6 M solution of *n*-BuLi in hexane (2.01 ml) was added to a suspension of 2-methylallyltriphenylphosphonium chloride (932.6 mg) in abs. THF (7.0 ml) with stirring at 0 °C. After stirring for 10 min, a solution of **1** (51.0 mg) in abs. THF (3.0 ml) was added to the resultant orange-red ylide solution at 0 °C and stirring was continued at 12 °C for 20 min. Brine was added to the reaction mixture and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated to leave an oil, which was subjected to column chromatography on SiO_2 with CH_2Cl_2–hexane (1 : 1, v/v) as an eluent. From the early part of the fractions, **17** (16.1 mg, 25.0%) was obtained. From the later part of the fractions, **3** (22.7 mg, 35.3%) was obtained. **17**: Unstable colorless oil. IR (film): 3420, 1623 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.70 (3H, br s), 4.90 (2H, br s), 5.98 (1H, d, J = 12.0 Hz), 6.27 (1H, dd, J = 3.2, 0.8 Hz), 6.43 (1H, d, J = 12.0 Hz), 6.86 (1H, dd, J = 8.0, 1.6 Hz), 7.05 (1H, d, J = 3.2 Hz), 7.08 (1H, br s), 7.30 (1H, d, J = 8.0 Hz). High-resolution MS m/z: Calcd for $C_{13}H_{13}N$: 183.1047. Found: 183.1053.

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