The first preparation of the unstable 1-hydroxy-2,3-dimethylindole, and structural determination of its air-oxidized product, 3-hydroxy-2,3-dimethyl-3*H*-indole *N*-oxide[1]

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Dedicated to Professor Keiichiro Fukumoto on his 70th birthday
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Abstract
1-Hydroxy-2,3-dimethylindole (**1**) has been prepared for the first time. Under atmospheric oxygen, **1** was converted rapidly into 3-hydroxy-2,3-dimethyl-3*H*-indole *N*-oxide (**2**). The structure was deduced, based on its products obtained by the reaction with Ac_2O in pyridine and confirmed by X-ray single crystallographic analysis.

Keywords: 2,3-Dimethylindole, 1-hydroxyindole, 1-hydroxy-2,3-dimethylindole, 3-hydroxy-2,3-dimethyl-3*H*-indole *N*-oxide, 5-acetoxy-2-acetoxymethyl-3-methylindole, 7-acetoxy-2-acetoxymethyl-3-methylindole

Introduction

In 1989,[2] we devised a simple and general synthetic method for 1-hydroxyindoles[3] consisting of the following two steps: (1) reduction of indoles to 2,3-dihydroindoles, (2) their oxidation with 30% H_2O_2 in the presence of a catalytic amount of sodium tungstate or phosphotungstate. Employing the 1-hydroxyindole synthetic method, we have succeeded in preparing novel 3-substituted 1-hydroxyindoles, including 1-hydroxytryptophans and 1-hydroxytryptamines.[4]

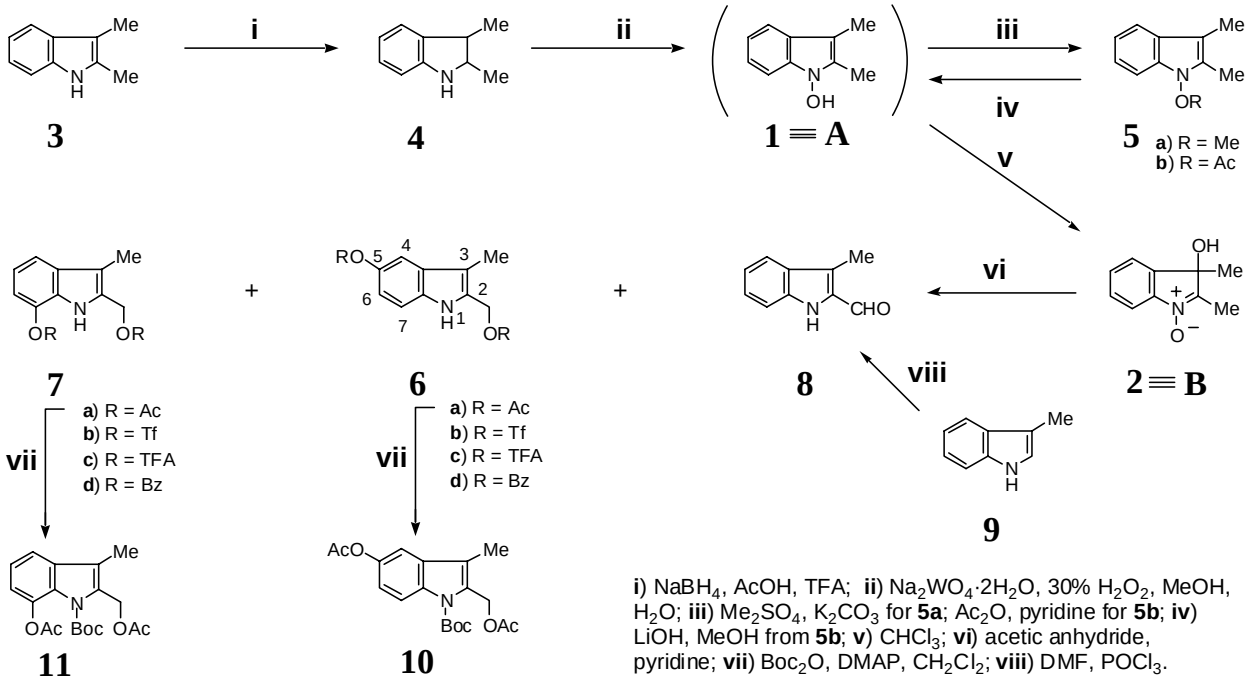
In this paper, we report the first preparation of 1-hydroxy-2,3-dimethylindole (**1**) as a representative of 1-hydroxyindoles having an alkyl substituent at both 2- and 3-positions. Compound (**1**) was quite sensitive to air and was converted into a novel 3-hydroxy-2,3-dimethyl-3*H*-indole *N*-oxide (**2**). Treatment of **2** with Ac_2O in pyridine afforded 5- and 7-acetoxy-2-acetoxymethyl-3-methylindoles together with 3-methylindole-2-carboxaldehyde. On the basis of these chemical results and X-ray analysis, the structure of **2** was determined unequivocally.

Results and Discussion

We attempted to synthesize the previously unknown 1-hydroxy-2,3-dimethylindole (**1**) (Scheme 1). 2,3-Dimethylindole (**3**) was converted into 2,3-dimethyl-2,3-dihydroindole (**4**) by reduction with $NaBH_3CN$ in AcOH/trifluoroacetic acid (TFA) (3/1, v/v) in 93% yield according to Gribble's procedure.[5] Compound (**4**) was obtained as a 3:1 mixture of stereoisomers, checked by ^1H NMR analysis, and used for the next oxidation step without separation.

Application of our 1-hydroxyindole synthetic reaction to **4** showed the major formation of an unknown product (**A**), monitored on TLC. Upon standing in the reaction mixture at room temperature, this product (**A**) changed rapidly into another new, stable product (**B**).

Attempts to isolate **A** in pure state were not successful because it polymerized during column-chromatography owing to its instability and sensitivity to air. Therefore, the *in situ* methylation with Me_2SO_4/K_2CO_3 of the **A** in the reaction mixture obtained immediately after the oxidation of **4** was examined. As a result, the stable 1-methoxy-2,3-dimethylindole (**5a**) was obtained in 22% overall yield from **4**. A similar acetylation of **A** with Ac_2O in pyridine afforded the stable 1-acetoxy-2,3-dimethylindole (**5b**) in 63% yield. These facts prove that the product (**A**) is 1-hydroxy-2,3-dimethylindole (**1**). Finally, we succeeded in the isolation of **1** in 67% yield by the alkaline hydrolysis of **5b**, and its spectroscopic data were taken. The half-life of **1** in the pure state is found to be about 24 h. A half-life of **1** in $CHCl_3$ at room temperature under atmospheric oxygen is shown to be about 4 h.



Scheme 1

On the basis of the above observations, the compound (**B**) was obtained in 64% overall yield from **4** by the sequence of reactions: (1) oxidation of **4** to **1** and work-up, and (2) allowing a $CHCl_3$ solution of crude **1** to stand at room temperature under atmospheric oxygen for 22 h, a sufficient time for transforming **1** completely into **B**.

In an attempt to determine the structure of **B** chemically, it was reacted with Ac_2O in pyridine at room temperature, providing a 56% yield of 3-methylindole-2-carboxaldehyde (**8**) together with 5- (**6a**) and 7-acetoxy-2-acetoxymethyl-3-methylindoles (**7a**) in 2 and 3% yields, respectively. The yields of these three products were not affected by reaction temperature or time as can be seen from Table 1.

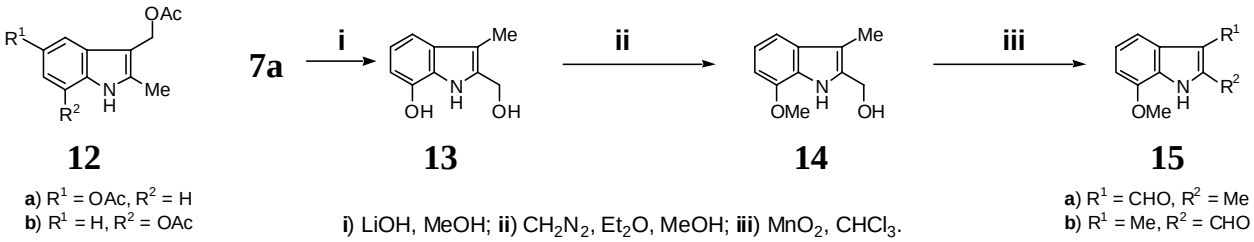
Table 1. The reaction of **2** with Ac_2O

Entry	Reaction Temp. (°C)	Time (h)	Yield (%) **6a**	**7a**	**8**
1	20	3	2	3	56
2	50	3	2	4	57
3	50	17	2	3	54
4	75	3	1	4	56

The reaction of **B** with trifluoromethanesulfonic anhydride did not produce **6b**, **7b**, and **8** at all, (in contrast to Ac_2O). With trifluoroacetic anhydride and benzoic anhydride, the expected formation of **6c**,**d** and **7c**,**d** was not observed, although the aldehyde (**8**) was obtained in 8–24% yield. The aldehyde (**8**) was identical with the authentic 3-methylindole-2-carboxaldehyde, prepared by Vilsmeier–Haack reaction of 3-methylindole (**9**) by the procedure of Chatterjee *et al*.[6] The structures of **6a** and **7a** were determined by the following observations. Compounds **6a** and **7a** were allowed to react with Boc_2O in CH_2Cl_2 in the presence of *N*,*N*-dimethylaminopyridine (DMAP)[7] to provide 5-acetoxy- (**10**) and 7-acetoxy-2-acetoxymethyl-1-*tert*-butoxycarbonyl-3-methylindole (**11**) in 96 and 82% yields, respectively. Comparison of the ^{1}H NMR spectra of **10** with **6a** demonstrates an anisotropy effect of the Boc group on the *ortho*-coupled C(7)-proton (δ 8.15, d, J = 9.0 Hz) by *ca*. 0.9 ppm, proving these are 5-substituted compounds. In the case of **11**, however, the protons did not shift toward lower magnetic field compared with those of **7a**. This fact confirms that **7a** and **11** are 7-substituted indoles.

There are still other possibilities that **6a** and **7a** are the 3-acetoxymethyl-2-methylindoles, **12a** and **12b**, respectively, as shown in Scheme 2. In order to eliminate these structures, we applied the following series of reactions to **7a**. First, **7a** was converted into 7-hydroxy-3-methylindole-2-methanol (**13**) in 73% yield by the hydrolysis with LiOH in MeOH. Then, selective methylation of the phenolic group of **13** with CH_2N_2 provided an 87% yield of 7-methoxy-3-methylindole-2-methanol [8] (**14**). Subsequent oxidation of **14** with active MnO_2 in $CHCl_3$ afforded a formyl compound (**15b**) in 44% yield. By these reactions, **12b** should have been transformed into **15a**. At this stage, comparison of the ^{1}H NMR spectrum of **14** with that of

15b was made, and no anisotropy effect of the formyl group on the C(4)-proton was observed. Consequently, the formyl group should not be present at the 3-position of the indole nucleus and **15b** is proved to be 7-methoxy-3-methylindole-2-carboxaldehyde.[8]



Scheme 2

The structure of **6a** was determined by comparing the differences between the ^{1}H NMR chemical shifts of the diacetoxy compounds (**6a**, **7a**) and the 1-acyl compounds (**10**, **11**). As shown in Table 2, the Δδs observed between protons of **10** and **6a** were almost the same with those observed between protons of **11** and **7a**. These findings confirm that **6a** has a structure similar to **7a**.

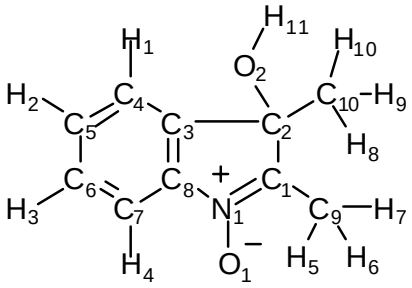
Table 2. ^{1}H NMR data of **6a**, **7a**, **10**, and **11**, and the differences between chemical shifts

Position	**6a** δ_{6a}	**10** δ_{10}	Δ δ δ_{10}- δ_{6a}	**7a** δ_{7a}	**11** δ_{11}	Δ δ δ_{11}- δ_{7a}
COC<u>H</u>$_3$	2.08 (3H, s)	2.06 (3H, s)	-0.02	2.09 (3H, s)	2.05 (3H, s)	-0.04
COC<u>H</u>$_3$	2.30 (3H, s)	2.28 (3H, s)	-0.02	2.33 (3H, s)	2.31 (3H, s)	-0.02
and 3-C<u>H</u>$_3$	2.31 (3H, s)	2.32 (3H, s)	-0.01	2.40 (3H, s)	2.34 (3H, s)	-0.06
2-C<u>H</u>$_2$	5.21 (2H, s)	5.45 (2H, s)	+0.24	5.22 (2H, s)	5.38 (2H, s)	+0.16
4	7.23	7.22	-0.01	7.41	7.40	-0.01
	(d, 2.2)	(d, 2.2)		(dd, 7.6, 0.9)	(dd, 7.8, 1.0)	
5				7.07 (t, 7.6)	7.23 (t, 7.8)	+0.17
6	6.91	7.04	+0.13	6.99	7.04	+0.05
	(dd, 8.6, 2.2)	(dd, 9.0, 2.2)		(dd, 7.6, 0.9)	(dd, 7.8, 1.0)	
7	7.27	8.15	+0.88			
	(d, 8.6)	(d, 9.0)				
1	8.40 (N<u>H</u>)	1.66 (9H, s)		8.30 (N<u>H</u>)	1.62 (9H, s)	

Although the structure (**B**) was deduced to be **2** on the basis of its spectroscopic data and chemical behavior upon reaction with Ac_2O as stated above, we still needed conclusive evidence. Finally, we luckily found a suitable recrystallizing solvent for **B**, providing prisms for X-ray

single crystallographic analysis. The results shown in Figure 1 clearly show a novel 3-hydroxy-2,3-dimethyl-3*H*-indole *N*-oxide (**2**) structure. The atomic parameters are listed in Table **3**.

The mechanism for the formation of **6a**, **7a**, and **8** may be explained as shown in Scheme 3. In the reaction of **2** with Ac_2O, the diacetate (**16**) is formed initially. The following [3,3]-sigmatropic rearrangement of either the 3- (route **a**) or 1-acetoxy groups (route **b**) to the methylene carbon at the 2-position affords **17** or **18**, respectively. In the intermediate (**17**), subsequent [3,5] or [3,3]-sigmatropic rearrangement of the 1-acetoxy group toward the benzene ring results in the formation of **6a** or **7a** (route **c**). On the other hand, **8** would be formed either through the vinylic acetate **19**, a tautomer of **18**, or through the vinylic acetate **20** originating from **17** (route **d**).



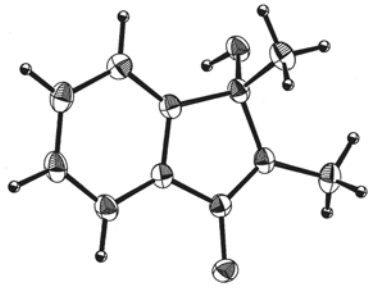
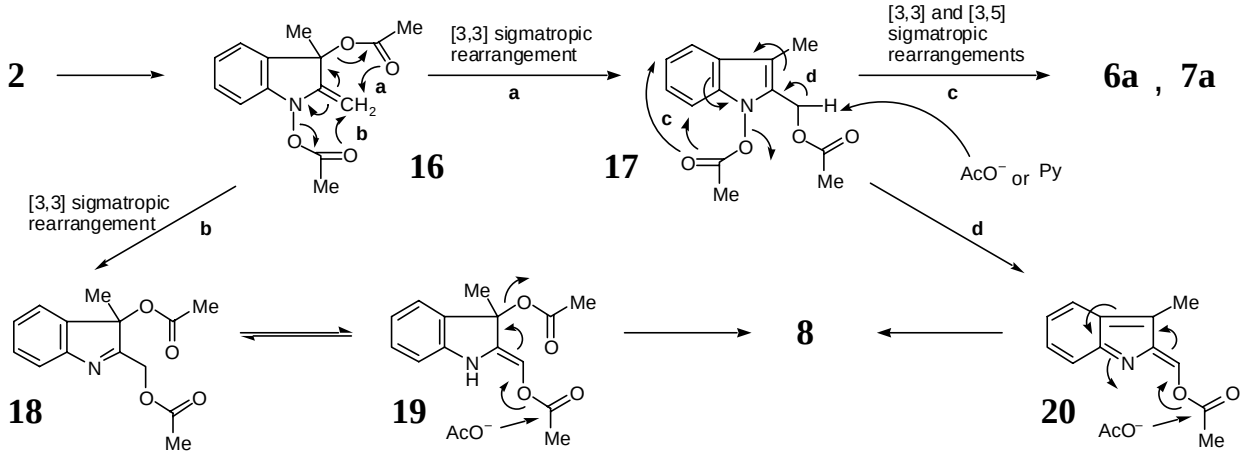


Figure 1 ORTEP Drawing of 2



Scheme 3

In conclusion, we have succeeded in the first preparation of 1-hydroxy-2,3-dimethylindole (**1**), which was an unstable compound and oxidized rapidly into a novel compound, 3-hydroxy-2,3-dimethyl-3*H*-indole *N*-oxide (**2**), on standing at room temperature under atmospheric oxygen. An interesting chemical behavior of **2** upon reaction with Ac_2O was also demonstrated.

Experimental Section

General Procedures. Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were determined with a HORIBA FT-720 spectrophotometer, and ^{1}H NMR spectra with a JEOL GSX-500 spectrometer, with tetramethylsilane as internal standard. MS spectra at 70 eV using electron impact mode were recorded on a JEOL SX-102A or JEOL JMS-GC mate mass spectrometer. Column chromatography was performed on silica gel 60N (SiO_2, 70–230 mesh, from Kanto Chemical Co. Inc.) throughout the present study.

2,3-Dimethylindoline (4). The procedure of Gribble *et al.*[5] was slightly modified. $NaBH_3CN$ (267.8 mg, 4.27 mmol) was added to a stirred solution of 2,3-dimethylindole (**3**) (305.4 mg, 2.11 mmol) in AcOH/TFA (3:1, 8 mL) at 0 °C and the mixture was stirred at room temperature for 1 h. After evaporation of the solvent under reduced pressure, the whole was made alkaline by adding 8% NaOH under ice cooling and extracted with $CHCl_3$. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$/hexane (1:1) to give **4** (287.4 mg, 93%) as a 3:1 mixture of stereoisomers. **4**: ^{1}H NMR ($CDCl_3$) δ: 1.13 (3/4H, d, *J* = 6.6 Hz), 1.18 (3/4H, d, *J* = 7.2 Hz), 1.30 (9/4H, d, *J* = 6.8 Hz), 1.32 (9/4H, d, *J* = 6.1 Hz), 2.82 (3/4H, dq, *J* = 9.2, 6.8 Hz), 3.26 (1/4H, dq, *J* = 8.1, 7.2 Hz), 3.46 (3/4H, dq, *J* = 9.2, 6.1 Hz), 3.94 (1/4H, dq, *J* = 8.1, 6.6 Hz), 6.61 (1H, d, *J* = 7.8 Hz), 6.72 (1H, t, *J* = 7.8 Hz), 6.98–7.08 (2H, m). Careful integration of the area between δ 1.5 and 4.0 disclosed the presence of 1H (NH proton), which disappeared on addition of D_2O. Compound (**4**) was used for the next step without separation of the isomers.

1-Methoxy-2,3-dimethylindole (5a). 30% H_2O_2 (0.75 mL, 7.28 mmol) was added to a solution of **4** (108.8 mg, 0.74 mmol) and $Na_2WO_4{\cdot}2H_2O$ (47.9 mg, 0.036 mmol) in MeOH/H_2O (10:1, 11 mL) at 0 °C, and the mixture was stirred at room temperature for 45 min. To this solution were added K_2CO_3 (511.1 mg, 3.70 mmol) and a solution of Me_2SO_4 (277.4 mg, 2.20 mmol) in MeOH (1 mL), and the whole was stirred at room temperature for 2 h. After addition of H_2O, the whole was extracted with AcOEt. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$/hexane (1:3) to give **5a** (28.2 mg, 22%), as a colorless oil. IR (film): 1458, 1234, 1171, 737 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 2.20 (3H, s), 2.36 (3H, s), 3.99 (3H, s), 7.07 (1H, ddd, *J* = 7.8, 7.1, 1.0 Hz), 7.16 (1H, ddd, *J* = 8.1, 7.1, 1.0 Hz), 7.34 (1H, dd, *J* = 8.1, 1.0 Hz), 7.45 (1H, br d, *J* = 7.8 Hz). High-Resolution EI-MS *m/z*: Calcd for $C_{11}H_{13}NO$: 175.0997. Found: 175.0997.

1-Acetoxy-2,3-dimethylindole (5b). 30% H_2O_2 (0.73 mL, 7.15 mmol) was added to a solution of **4** (105.2 mg, 0.72 mmol) and $Na_2WO_4{\cdot}2H_2O$ (53.0 mg, 0.16 mmol) in MeOH/H_2O (10:1, 11 mL) at 0 °C, and the mixture was stirred at room temperature for 1.5 h. After addition of H_2O, the whole was extracted with $CHCl_3$. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. To the residue, pyridine (2 mL) and Ac_2O (1 mL) were added, and the mixture was stirred at room temperature for 5 h. AcOEt was added and the whole

was washed with saturated NH_4Cl, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with AcOEt/hexane (1:3) to give **5b** (91.2 mg, 63%) as a colorless oil. IR (film): 1801 cm^{-1}. ^1H NMR (DMSO-d_6) δ: 2.17 (3H, s), 2.19 (3H, s), 2.43 (3H, s), 7.06 (1H, ddd, *J* = 7.6, 7.1, 1.0 Hz), 7.11 (1H, ddd, *J* = 8.1, 7.1, 1.0 Hz), 7.23 (1H, dd, *J* = 8.1, 1.0 Hz), 7.45 (1H, br d, *J* = 7.6 Hz). High-Resolution EI-MS *m/z*: Calcd for $C_{12}H_{13}NO_2$: 203.0947. Found: 203.0950.

1-Hydroxy-2,3-dimethylindole (1). LiOH (16.2 mg, 0.68 mmol) was added to a solution of **5b** (65.0 mg, 0.32 mmol) in MeOH (4 mL) and the mixture was stirred at room temperature for 20 min. After addition of AcOEt, the whole was washed with saturated NH_4Cl, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with AcOEt/hexane (1:4) to give **1** (38.4 mg, 67%) as a colorless oil. IR (film): 3159, 1574, 1456 cm^{-1}. ^1H NMR (CD_3OD) δ: 2.19 (3H, s), 2.33 (3H, s), 6.94 (1H, dd, *J* = 7.8, 7.3 Hz), 7.04 (1H, dd, *J* = 7.8, 7.3 Hz), 7.27 (1H, d, *J* = 7.8 Hz), 7.36 (1H, d, *J* = 7.8 Hz). High-Resolution EI-MS *m/z*: Calcd for $C_{10}H_{11}NO$: 161.0841. Found: 161.0843.

1-Hydroxy-2,3-dimethyl-3*H*-indole *N*-oxide (2). 30% H_2O_2 (4.85 mL, 47.1 mmol) was added to a solution of **4** (698.5 mg, 4.75 mmol) and $Na_2WO_4 \cdot 2H_2O$ (316.6 mg, 0.96 mmol) in MeOH/H_2O (10:1, 49.5 mL) at 0 °C and the mixture was stirred at room temperature for 45 min. After addition of H_2O, the whole was extracted with $CHCl_3$. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. To the residue, $CHCl_3$ (15 mL) was added and the resultant solution was stirred at room temperature under atmospheric oxygen for 22 h. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO_2 with $CHCl_3$/MeOH (97:3) to give **2** (538.2 mg, 64%). **2**: mp 164–166 °C (colorless prisms, recrystallized from AcOEt). IR (KBr): 3116, 1633, 1577, 1319 cm^{-1}. ^1H NMR (CD_3OD) δ: 1.60 (3H, s), 2.29 (3H, s), 7.52 (1H, dt, *J* = 1.5, 7.6 Hz), 7.54 (1H, dt, *J* = 1.7, 7.6 Hz), 7.59–7.65 (2H, m). EI-MS *m/z:* 177 (M^+). Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.91. Found: C, 67.69; H, 6.29; N, 7.91%.

X-Ray crystallographic analysis of 2. The reflection data were collected on a Rigaku AFC5R diffractometer over the range of $78.64° < 2\theta < 80.02°$ using Cu$K\alpha$ radiation (λ=1.54178 Å) and the ω–2θ scan method at a 2θ scan speed of 6°/min. The structure of **2** was solved by the direct method using MITHRIL[9] and refined by the full-matrix least-squares method with anisotropic thermal factors for non-hydrogen atoms and with isotropic ones for hydrogen atoms. The final *R*- and *R*w-factors were 0.038 and 0.054 for 1283 observed reflections [$I > 3.00\sigma(I)$], respectively. Crystal data for **2**: $C_{10}H_{11}NO_2$; *M*=177.20; monoclinic; space group, *C*2/c (#15); *a*=11.344 (1) Å, *b*=12.3639 (8) Å, *c*=13.785 (1) Å; β=105.391 (6)°; *V*=1864.1 (2) $Å^3$, *Z*=8, $D_{calc.}$=1.263 g/cm^3. Positional parameters and *B* (eq) for **2** are summarized in Table 3.

5-Acetoxy- (6a), 7-acetoxy-2-acetoxymethyl-3-methylindole (7a) and 3-methylindole-2-carboxaldehyde (8). Entry 1: Ac_2O (1 mL, 10.6 mmol) was added to a solution of **2** (102.3 mg, 0.58 mmol) in pyridine (2 mL) and the mixture was stirred at room temperature for 3 h. After evaporation of the solvent, brine was added and the whole was extracted with $CHCl_3$/MeOH (95:5). 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 AcOEt/hexane (1:3) to give **8** (51.1 mg, 56%) and a mixture of **6a** and **7a** in order of elution. The mixture was subjected to HPLC [column, CPS-223L-1 (i.d., 22 x 100 mm); solvent, AcOEt/hexane (1:5); flow rate, 5.0 mL/min; UV detection, 300 nm]. **6a** (2.5 mg, 2%) and **7a** (3.9 mg, 3%) were obtained in the order of elution. **6a**: mp 70–72 °C (colorless prisms, recrystallized from $CHCl_3$/hexane). IR (KBr): 3363, 1739 cm^{-1}. High-resolution EI-MS *m/z*: Calcd for $C_{14}H_{15}NO_4$: 261.1001. Found: 261.1001. The ^1H NMR data of **6a** are in Table 2. **7a**: mp 102–103 °C (colorless prisms, recrystallized from $CHCl_3$/hexane). IR (KBr): 3350, 1738, 1728 cm^{-1}. EI-MS *m/z*: 261 (M^+). Anal. Calcd for $C_{14}H_{15}NO_4 \cdot 0.5CHCl_3$: C, 54.26; H, 4.87; N, 4.36. Found: C, 53.87; H, 4.92; N, 4.38. The ^1H NMR data of **7a** are shown in Table 2. **8**: mp 137–140 °C (lit.[5] mp 138–140 °C) (colorless needles from hexane). IR (KBr): 3307, 1635 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.65 (3H, s), 7.13–7.19 (1H, m), 7.36–7.41 (2H, m), 7.70 (1H, br d, *J* = 8.1 Hz), 8.81 (1H, br s, disappeared on addition of D_2O), 10.04 (1H, s). EI-MS *m/z*: 159 (M^+).

Entry 2: Ac_2O (8 mL, 84.6 mmol) was added to a solution of **2** (389.7 mg, 2.20 mmol) in pyridine (16 mL) and the mixture was heated at 50 °C for 3 h with stirring. After the same work-up and purification as described in Entry 1, **8** (200.6 mg, 57%), **6a** (10.8 mg, 2%), and **7a** (22.9 mg, 4%) were obtained (in order of elution).

5-Acetoxy-2-acetoxymethyl-1-*tert*-butoxycarbonyl-3-methylindole (10). Boc_2O (0.01 mL, 0.04 mmol) was added to a solution of **6a** (5.8 mg, 0.02 mmol) and DMAP (3.2 mg, 0.03 mmol) in CH_2Cl_2 (1 mL), and the mixture stirred at room temperature for 3 h. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO_2 with $CHCl_3$ to give **10** (7.7 mg, 96%). **10**: mp 63–65 °C (colorless prisms, recrystallized from hexane). IR (film): 1757, 1738, 1718 cm^{-1}. High-Resolution EI-MS *m/z*: Calcd for $C_{19}H_{23}NO_6$: 361.1525. Found: 361.1528. The ^1H NMR data of **10** are shown in Table 2.

7-Acetoxy-2-acetoxymethyl-1-*tert*-butoxycarbonyl-3-methylindole (11). Boc_2O (0.01 mL, 0.04 mmol) was added to a solution of **7a** (4.9 mg, 0.02 mmol) and DMAP (2.6mg, 0.02 mmol) in CH_2Cl_2 (1 mL), and the mixture was stirred at room temperature for 3 h. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO_2 with $CHCl_3$ to give **11** (5.6 mg, 82%). **11**: mp 97–99 °C (colorless prisms, recrystallized from hexane). IR (film): 1753, 1736, 1724 cm^{-1}. High-Resolution EI-MS *m/z*: Calcd for $C_{19}H_{23}NO_6$: 361.1525. Found: 361.1526. The ^1H NMR data of **11** are shown in Table 2.

7-Hydroxy-3-methylindole-2-methanol (13). LiOH (23.4 mg, 0.98 mmol) was added to a solution of **7a** (28.6 mg, 0.11 mmol) in MeOH (3 mL) and the mixture was stirred at room temperature for 1 h under argon atmosphere. After addition of saturated NH_4Cl, the whole was extracted with $CHCl_3$/MeOH (95:5). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a solid, which was column-chromatographed on SiO_2 with $CHCl_3$/MeOH (95:5) to give **13** (14.1 mg, 73%). **13**: mp 158–160 °C (dec., colorless prisms, recrystallized from $CHCl_3$/hexane). IR (KBr): 3390, 3309, 3140, 1637, 1579, 1321, 1261, 972 cm^{-1}. ^1H NMR (CD_3OD) δ: 2.25 (3H, s), 4.71 (2H, s), 6.50 (1H, dd, *J* = 7.8, 0.7 Hz),

6.80 (1H, t, *J* = 7.8 Hz), 6.96 (1H, dd, *J* = 7.8, 0.7 Hz). High-Resolution EI-MS *m/z*: Calcd for $C_{10}H_{11}NO_2$: 177.0790. Found: 177.0788.

Table 3. Positional parameters and *B* (eq) of **2**

Atom	*x*	*y*	*z*	***B*** (eq)
O (1)	0.3989 (1)	-0.0311 (1)	0.12803 (8)	4.87 (5)
O (2)	0.7602 (1)	0.0210 (1)	0.05423 (9)	4.67 (5)
N (1)	0.5029 (1)	0.0144 (1)	0.12735 (8)	3.82 (5)
C (1)	0.6083 (1)	-0.0325 (1)	0.1399 (1)	4.00 (6)
C (2)	0.7047 (1)	0.0491 (1)	0.1316 (1)	4.15 (6)
C (3)	0.6301 (1)	0.1524 (1)	0.1111 (1)	3.94 (6)
C (4)	0.6603 (2)	0.2569 (1)	0.0933 (1)	4.80 (7)
C (5)	0.5690 (2)	0.3350 (1)	0.0776 (1)	5.42 (8)
C (6)	0.4516 (2)	0.3089 (2)	0.0809 (1)	5.58 (9)
C (7)	0.4201 (2)	0.2040 (2)	0.0983 (1)	4.86 (7)
C (8)	0.5117 (1)	0.1285 (1)	0.1115 (1)	3.89 (6)
C (9)	0.6257 (2)	-0.1485 (1)	0.1611 (2)	5.30 (8)
C (10)	0.8069 (2)	0.0554 (2)	0.2290 (1)	5.67 (9)
H (1)	0.744 (2)	0.276 (1)	0.089 (1)	5.90 (1)
H (2)	0.589 (2)	0.407 (2)	0.061 (2)	6.73 (1)
H (3)	0.390 (2)	0.367 (2)	0.070 (2)	7.10 (1)
H (4)	0.336 (2)	0.187 (1)	0.099 (1)	5.38 (1)
H (5)	0.636 (3)	-0.163 (2)	0.235 (2)	10.83 (3)
H (6)	0.704 (3)	-0.177 (2)	0.150 (2)	7.94 (2)
H (7)	0.561 (4)	-0.188 (2)	0.126 (2)	12.08 (4)
H (8)	0.773 (2)	0.069 (2)	0.288 (2)	5.55 (1)
H (9)	0.867 (2)	0.111 (2)	0.220 (1)	6.25 (1)
H (10)	0.852 (2)	-0.009 (2)	0.239 (2)	7.01 (1)
H (11)	0.702 (2)	0.026 (1)	-0.008 (2)	6.52 (2)

7-Methoxy-3-methylindole-2-methanol (14). An excess of ethereal CH_2N_2 was added to a solution of **13** (6.3 mg, 0.04 mmol) in MeOH (2 mL) and the mixture was stirred at room temperature for 1.5 h. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO_2 with $CHCl_3$/MeOH (97:3) to give **14** (5.9 mg, 87%). **14**: mp 176–178 °C (lit.[8] mp 169–170 °C) (colorless needles, recrystallized from $CHCl_3$/hexane). IR (KBr): 3479, 3284, 1628, 1572, 1244, 985 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.61 (1H, br s, disappeared on addition of D_2O), 2.27 (3H, s), 3.95 (3H, s), 4.81 (2H, s), 6.64 (1H, d, *J* = 7.8 Hz), 7.02 (1H, t, *J* = 7.8 Hz), 7.14 (1H, d, *J* = 7.8 Hz), 8.35 (1H, br s, disappeared on addition of D_2O). High-Resolution EI-MS *m/z*: Calcd for $C_{11}H_{13}NO_2$: 191.0946. Found: 191.0945.

7-Methoxy-3-methylindole-2-carboxaldehyde (15b). Active MnO_2 (56.8 mg, 0.65 mmol) was added to a solution of **14** (6.9 mg, 0.04 mmol) in $CHCl_3$ (2 mL) and the mixture was stirred at room temperature for 32 h. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO_2 with $CHCl_3$ to give **15b** (3.0 mg, 44%). **15b**: mp 132–134 °C (lit.[8] mp 130 °C) (colorless needles, recrystallized from Et_2O/hexane). IR (KBr): 3288, 1649, 1325, 1259 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.63 (3H, s), 3.96 (3H, s), 6.77 (1H, d, *J* = 7.6 Hz), 7.07 (1H, dd, *J* = 8.1, 7.6 Hz), 7.27 (1H, d, *J* = 8.1 Hz), 8.89 (1H, br s, disappeared on addition of D_2O), 10.02, (1H, s). High-Resolution EI-MS *m/z*: Calcd for $C_{11}H_{11}NO_2$: 189.0790. Found: 189.0790.

References and Notes

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