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Oxidation of 1-Acylindoles with Oxodiperoxomolybdenum (VI), $MoO_5 \cdot HMPA$. Preparation of 2,3-Dihydroxyindoline and Indoxyl Derivatives

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The oxidation of 1-acylindoles, **1**, **15**, **20**, and **22**, with (hexamethylphosphoramide)oxodiperoxomolybdenum (VI), $MoO_5 \cdot HMPA$, in dry methanol gives a variety of products depending on the indole substituents; *trans*- and *cis*-1-acyl-3-hydroxy-2-methoxyindolines **2** and **3** are obtained from 2,3-unsubstituted 1-acylindoles **1**, 1-acetyl-2-hydroxy-3-methoxy-3-methylindoline (**16**) from 1-acetyl-3-methylindole (**15**), 1-acetyl-2,3-dihydroxy-2,3-dimethylindoline (**21**) from 1-acetyl-2,3-dimethylindole (**20**), and 1-acetyl-2-hydroxy-2-methylindoxyl (**23**) from 1-acetyl-2-methylindole (**22**). Reaction of **2** and **3** with acids gives 1-acylindoxyl **10**, respectively, while reaction of **16** with the acid gives 3-methyloxindole (**19**). Treatment of 3-acetoxy-1-acetyl-2-methoxyindoline (**5**) with stannic chloride gives 1-acetylindoxyl (**10a**) and 1-acetyl-3-chloroindole (**14**).

Keywords——indole oxidation; *N*-acetylindole; peroxomolybdenum complex; 2,3-dihydroxyindoline derivative; indoxyl; oxindole; stereochemistry

We have briefly reported the oxidation of 1-acylindoles with (hexamethylphosphoramide)oxodiperoxomolybdenum (VI), $MoO_5 \cdot HMPA$, to give 1-acyl-2,3-dihydroxyindoline derivatives.[1] The present paper describes the experimental details of this work and some chemical properties of the novel oxidative products.

Treatment of 1-acetylindole (**1a**) with $MoO_5 \cdot HMPA$ in dry methanol under argon at room temperature for a week gave *trans*- and *cis*-1-acetyl-3-hydroxy-2-methoxyindolines, (**2a**) and (**3a**) in 56 and 15% yields, respectively. The structures were assigned on the basis of spectral (see Experimental) and chemical evidence. Oxidation of **2a** and **3a** with $CrO_3 \cdot$pyridine gave 1-acetyl-2-methoxyindoxyl (**4**) in 81 and 66% yields, respectively; the structure of **4** was confirmed by comparison of its infrared (IR) spectrum (1730 and 1685 cm^{-1}) with those of 1-acetylindoxyl (1710 and 1673 cm^{-1})[2] and 1-acetyloxindole (1755 and 1710 cm^{-1}).[2] The stereochemical relationship of hydroxy and methoxy groups in **2a** and **3a** was ascertained by an examination of the proton nuclear magnetic resonance (^{1}H-NMR) spectra of the acetates, **5** and **6**; **5** showed a coupling constant ($J_{2,3}$) of 0 Hz, while **6** showed a coupling constant ($J_{2,3}$) of 6 Hz. These coupling constants are in good agreement with the reported values for *trans*- and *cis*-vicinal coupling in 1-acetylindolines,[3] respectively.

In a similar manner, the oxidation of 1-benzoyl- (**1b**), 1-methoxycarbonyl- (**1c**), and 1-tosylindole (**1d**) with $MoO_5 \cdot HMPA$ afforded the corresponding indolines **2b—d** and **3b—d** in good yields, respectively; the structures were supported by the spectral data (see Experimental). The formation of **2** and **3** presumably proceeds *via* methanolysis of the initially formed epoxide **7**; direct methanolysis of **7** gives **2** (path a), while ring-opening of **7** into the carbonium ion **8** followed by methanolysis of **8** gives **2** and **3** (path b). The ratio of **2** and **3** was affected by the substituents of **1**; thus, the ratio of **2a—c** and **3a—c** was *ca.* 3.5 : 1, and that of

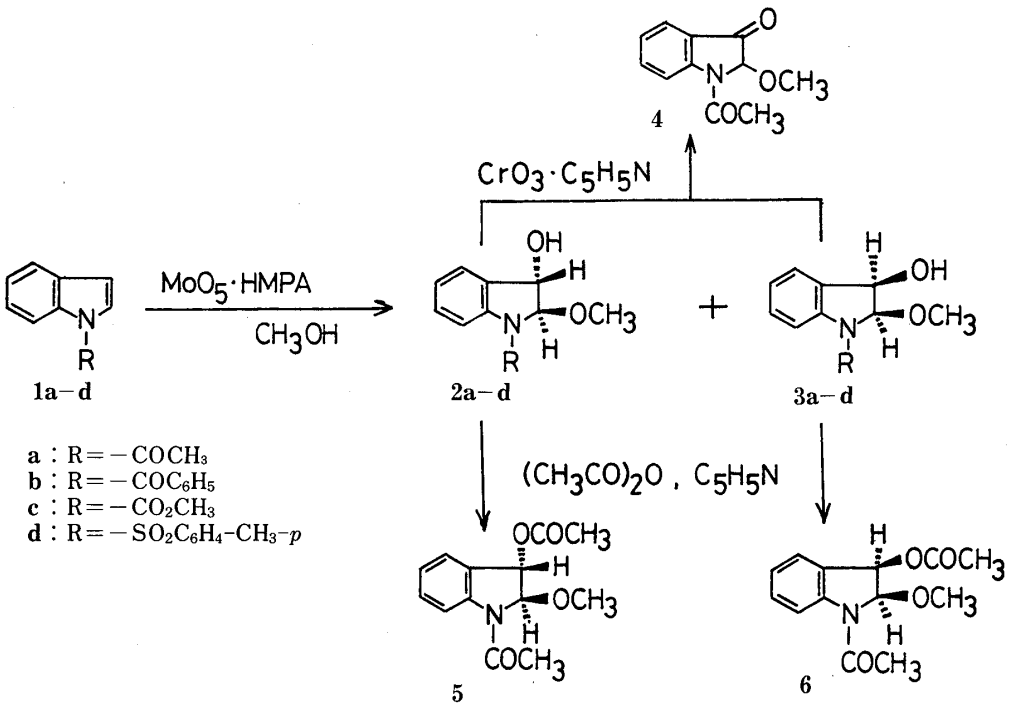


Chart 1

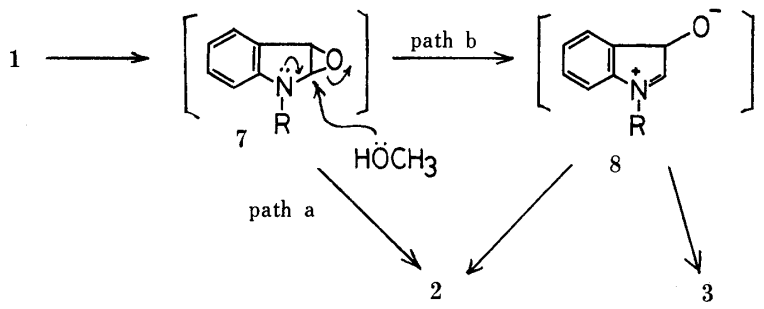
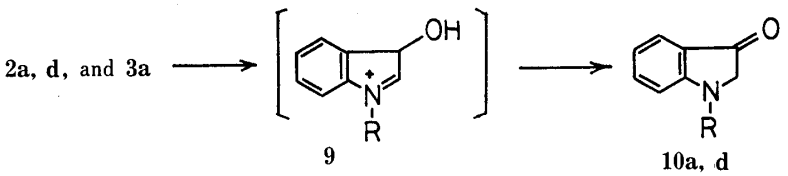
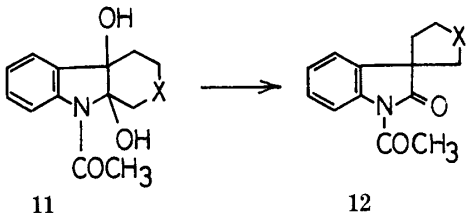
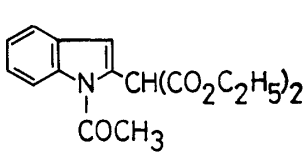


Chart 2







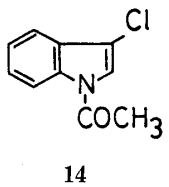


Chart 3

2d and **3d** was *ca.* 10:1. The difference can be explained as follows; in the case of **1d**, the solvolysis of **7d** mainly occurred *via* path a, since the contribution of the nitrogen lone pair to ring-opening of **7d** to **8d** is decreased by the greater electron-withdrawing effect of the tosyl group as compared to the others.

Treatment of **2a** or **3a** with stannic chloride gave 1-acetylindoxyl (**10a**) in quantitative yield; the structure of **10a** was assigned by comparison of the spectral data with those of an authentic sample.[2] Compound **10a** was also obtained by treatment of **2a** with sulfuric acid or tosyl chloride in 56 or 57% yield. A similar transformation of **2d** to **10d** took place spontaneously on standing at room temperature for several weeks. These findings are in contrast to the observation of Patrick's[4] and van Tamelen's groups[5] that the reaction of 2,3-dihydroxyindolines **11** with acetic anhydride produces exclusively oxindoles **12**. The formation of **10** may be understood in terms of a release of methanol from **2** and **3** *via* the indolenium ion **9**. Recently, Saito's group[6] has reported that the Lewis acid-promoted reaction of 3-substituted 2-alkoxy-3-hydroxyindolines with nucleophiles proceeds *via* an indolenium ion such as **9** to give 2-substituted indoles. In order to capture **9** derived from **2a**, we examined the reaction of **2a** with diethyl malonate in the presence of stannic chloride. However, the reaction did not give the desired product **13**, but gave **10a** in 65% yield. In a similar manner, reaction of the acetate **5** with diethyl malonate in the presence of stannic chloride gave **10a** and 1-acetyl-3-chloroindole (**14**) in 25 and 40% yields, and that of the indoxyl **4** did not occur.

We next examined the oxidation of 1-acetyl-3-methyl- (**15**), -2,3-dimethyl- (**20**), and -2-methyl-indoles (**22**) with $MoO_5 \cdot HMPA$. Treatment of **15** with $MoO_5 \cdot HMPA$ in dry methanol under the same conditions as mentioned above gave a 75% yield of 1-acetyl-2-hydroxy-3-methoxy-3-methylindoline (**16**), whose structure was confirmed by spectral data and chemical evidence. The product **16** is a mixture of *trans* and *cis* isomers, which could not be separated by chromatography or recrystallization due to the isomerization induced by the tautomerization between **16** and the corresponding oxo-compound **16'**.[7] Acetylation of **16** gave a single isomer of the acetate **17** in 92% yield; this product was hydrolyzed with aqueous ammonia to give a mixture of *trans* and *cis* isomers of **16** in 76% yield. The ^{1}H-NMR spectrum showed a signal due to H-2 shifted to lower field (from δ 5.42 to δ 6.68) on acetylation. Oxidation of **16** with $CrO_3 \cdot$pyridine afforded 1-acetyl-3-methoxy-3-methyloxindole (**18**) in 44% yield. Treatment of **16** with sulfuric acid gave 3-methyloxindole

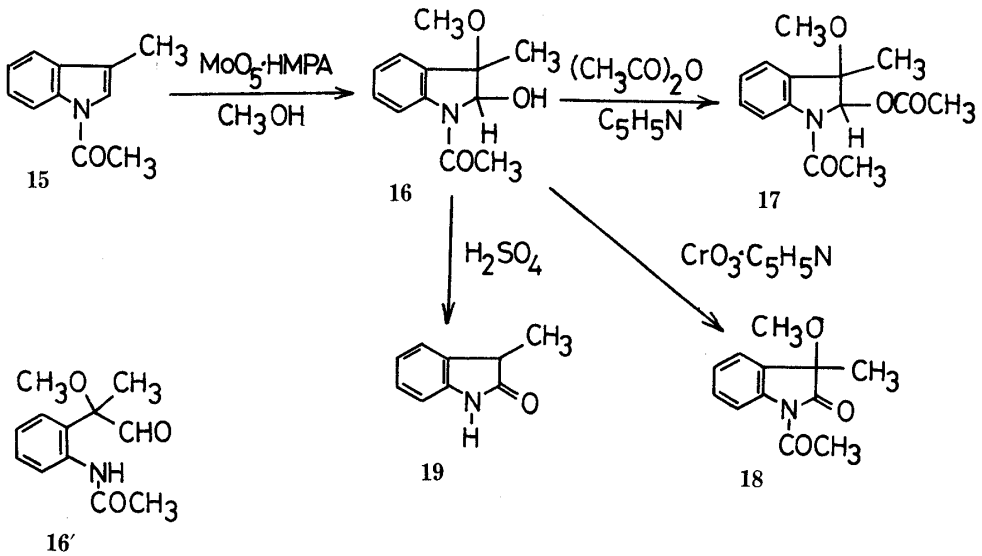


Chart 4

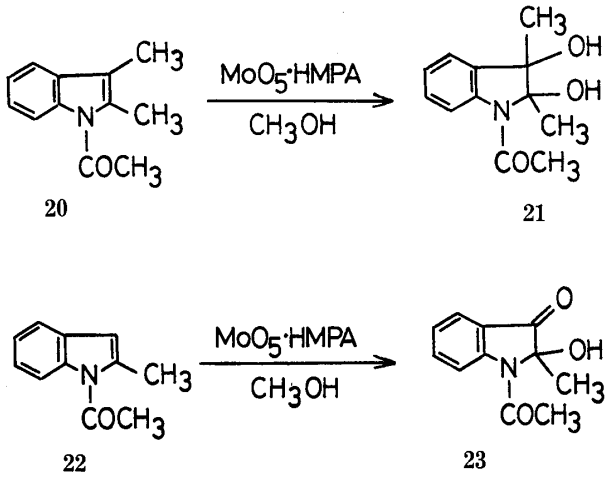


Chart 5

(**19**) in 56% yield.

Similarly, the oxidation of **20** with $MoO_5 \cdot HMPA$ gave a mixture of *trans* and *cis* isomers of 1-acetyl-2,3-dihydroxy-2,3-dimethylindoline (**21**) in 51% yield; the structure of **21** was confirmed by comparison of the spectral data with those of an authentic specimen.[8] The oxidation of **22** gave 1-acetyl-2-hydroxy-2-methylindoxyl (**23**) in 63% yield; again the structure was supported by the spectral data (see Experimental). The reaction of 3-formylindole with $MoO_5 \cdot HMPA$ did not occur under the same conditions.

These results indicate that MoO_5 oxidation of 1-acetylindoles gives a variety of products depending on the indole substituents, and that all of the products may be derived from the epoxide **7** as the initial intermediate.

Experimental

All melting points are uncorrected. IR spectra were recorded on a Hitachi 260-10 spectrophotometer. ^{1}H-NMR spectra were measured with JEOL JNM-PMX 60 and PS-100 spectrometers, with tetramethylsilane as an internal standard, and mass spectra (MS) were obtained on a JEOL D-300 spectrometer. Column chromatography was carried out on silica gel (80—100 mesh, Kanto Chemical Co., Inc.). Silica gel 60 PF_{254} (Merck) was used for preparative thin-layer chromatography (TLC).

Materials——(Hexamethylphosphoramide)oxodiperoxomolybdenum (VI), $MoO_5 \cdot HMPA$, was prepared by the method of Mimoun and co-workers.[9] 1-Acetyl- (**1a**), 1-benzoyl- (**1b**), 1-methoxycarbonyl (**1c**), 1-acetyl-3-methyl (**15**), 1-acetyl-2,3-dimethyl- (**20**), and 1-acetyl-2-methyl-indole (**22**) were prepared according to the procedure of Illi.[10] 1-Tosylindole (**1d**) was prepared by the method of Bowman and co-workers.[11]

***trans*- and *cis*-1-Acetyl-3-hydroxy-2-methoxyindolines (2a) and (3a)**——A solution of **1a** (1590 mg, 10 mmol) and $MoO_5 \cdot HMPA$ (3905 mg, 11 mmol) in dry CH_3OH (100 ml) was stirred at room temperature under argon for a week. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel with CH_2Cl_2–ethyl acetate (50 : 3) as an eluent to give **2a** (1170 mg, 56%) and **3a** (310 mg, 15%).

2a: mp 98—99 °C (from ether). *Anal.* Calcd for $C_{11}H_{13}NO_3$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.89; H, 6.35; N, 6.71. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300 (OH), 1660 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.78 (3H, s, $NCOCH_3$), 3.28 (3H, s, OCH_3), 4.26 (1H, br d, J=8 Hz, OH, exchangeable), 4.80 (1H, d, J=8 Hz, –CH–OH), 5.01 (1H, s, N–CH–OCH_3), 6.9—7.5 (3H, m, Ar–H), 8.05 (1H, d, J=8 Hz, Ar–H). MS *m/e*: 207 (M^+).

3a: mp 121—122 °C (from ether). *Anal.* Calcd for $C_{11}H_{13}NO_3$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.74; H, 6.33; N, 6.69. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300 (OH), 1660 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.33 (3H, s, $NCOCH_3$), 2.90 (1H, d, J= 11 Hz, OH, exchangeable), 3.54 (3H, s, OCH_3), 5.0—5.4 (2H, m, –CH–OH and N–CH–OCH_3), 6.9—7.5 (3H, m, Ar–H), 8.05 (1H, b, Ar–H). MS *m/e*: 207 (M^+).

1-Acetyl-2-methoxyindoxyl (4)——1) From **2a**: A cool solution of CrO_3 (321 mg, 3.3 mmol) in H_2O (0.2 ml) was added gradually to pyridine (3.2 ml) at 0—5 °C,[12] and then a solution of **2a** (220 mg, 1.1 mmol) in pyridine (0.6 ml) was added to the mixture at the same temperature. The reaction mixture was allowed to warm to room temperature, stirred for 2 d, and extracted with ether. The extract was washed with 10% HCl and H_2O, dried over Na_2SO_4, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography on silica gel with $CHCl_3$

as an eluent to give **4** (176 mg, 81%), mp 72—73 °C (from *n*-hexane). *Anal.* Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.47; H, 5.42; N, 6.77. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (C=O), 1685 (N–C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.36 (3H, s, N–$COCH_3$), 3.37 (3H, s, OCH_3), 5.10 (1H, s, N–C<u>H</u>–OCH_3), 7.12 (1H, t, J=8 Hz, Ar–H), 7.35—7.85 (2H, m, Ar–H), 8.41 (1H, d, J=8 Hz, Ar–H). MS *m/e*: 205 (M^+).

2) From **3a**: A similar treatment of **3a** (621 mg, 3 mmol) with CrO_3 (900 mg, 9 mmol) gave **4** (404 mg, 66%).

***trans*-3-Acetoxy-1-acetyl-2-methoxyindoline (5)**——A solution of **2a** (414 mg, 2 mmol) and acetic anhydride (511 mg, 5 mmol) in dry pyridine (5 ml) was allowed to stand at room temperature for 2 d. Concentration of the mixture under reduced pressure gave a residue, which was purified by column chromatography on silica gel with $CHCl_3$–CH_3OH (20:1) as an eluent to give **5** (490 mg, 98%), mp 108.5—109.5 °C (from ether). *Anal.* Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.02; N, 5.62. Found: C, 62.48; H, 6.12; N, 5.58. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (O–C=O), and 1670 (N–C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.06 (3H, s, $NCOCH_3$), 2.33 (3H, s, $OCOCH_3$), 3.40 (3H, s, OCH_3), 5.25 (1H, s, N–C<u>H</u>–OCH_3), 5.90 (1H, s, –CH–OCO–), 6.9—7.5 (3H, m, Ar–H), 8.05 (1H, br, Ar–H). MS *m/e*: 249 (M^+).

***cis*-3-Acetoxy-1-acetyl-2-methoxyindoline (6)**——Using a procedure similar to that described above for the preparation of **5**, the acetate **6** (49 mg, 98%) was obtained from **3a** (41 mg, 0.2 mmol), mp 78—80 °C (from ether). *Anal.* Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.02; N, 5.62. Found: C, 62.59; H, 6.04; N, 5.58. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 (O–C=O), 1670 (N–C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.23 (3H, s, $NCOCH_3$), 2.36 (3H, s, $OCOCH_3$), 3.23 (3H, s, OCH_3), 5.73 (1H, d, J=6 Hz, N–C<u>H</u>–OCH_3), 6.03 (1H, d, J=6 Hz, –CH–OCO–), 7.0—7.35 (3H, m, Ar–H), 7.93 (1H, br, Ar–H). MS *m/e*: 249 (M^+).

***trans*- and *cis*-1-Benzoyl-3-hydroxy-2-methoxyindolines (2b) and (3b)**——Using a procedure similar to that described above for the preparation of **2a** and **3a**, **1b** (663 mg, 3 mmol) was treated with MoO_5·HMPA (1172 mg, 3.3 mmol) in dry CH_3OH (25 ml). The reaction mixture was purified by column chromatography on silica gel with CH_2Cl_2 as an eluent to give **2b** (449 mg, 56%) and **3b** (147 mg, 18%).

2b: mp 178—180 °C (from ether–ligroin). *Anal.* Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.42; H, 5.56; N, 5.19. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3430 (OH), 1630 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.92 (1H, s, OH, exchangeable), 3.17 (3H, s, OCH_3), 4.82 (1H, s, –C<u>H</u>–OH), 5.13 (1H, s, N–C<u>H</u>–OCH_3), 7.0—7.9 (9H, m, Ar–H). MS *m/e*: 269 (M^+).

3b: mp 116—117 °C (from ether–ligroin). *Anal.* Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.26; H, 5.56; N, 5.28. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560 (OH), 1655 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 3.18 (1H, s, OH, exchangeable), 3.40 (3H, s, OCH_3), 5.23 (1H, br d, J=6 Hz, –C<u>H</u>–OH), 5.45 (1H, d, J=6 Hz, N–C<u>H</u>–OCH_3), 7.0—7.8 (9H, m, Ar–H). MS *m/e*: 269 (M^+).

***trans*- and *cis*-3-Hydroxy-2-methoxy-1-methoxycarbonylindolines (2c) and (3c)**——Using a procedure similar to that described above for the preparation of **2a** and **3a**, **1c** (700 mg, 4 mmol) was treated with MoO_5·HMPA (1558 mg, 4.4 mmol) in dry CH_3OH (40 ml). The reaction mixture was purified by column chromatography on silica gel with CH_2Cl_2 as an eluent to give **2c** (615 mg, 69%) and **3c** (170 mg, 19%).

2c: mp 98—100 °C (from C_6H_6). *Anal.* Calcd for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87; N, 6.28. Found: C, 58.93; H, 5.91; N, 6.22. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1710 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.42 (1H, d, J=7 Hz, OH, exchangeable), 3.43 (3H, s, OCH_3), 3.83 (3H, s, NCO_2CH_3), 4.78 (1H, d, J=7 Hz, –C<u>H</u>–OH), 5.35 (1H, s, N–C<u>H</u>–OCH_3), 6.9—7.8 (4H, m, Ar–H). MS *m/e*: 223 (M^+).

3c: mp 102—104 °C (from C_6H_6). *Anal.* Calcd for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87; N, 6.28. Found: C, 59.21; H, 5.89; N, 6.24. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1700 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.82 (1H, d, J=10 Hz, OH, exchangeable), 3.58 (3H, s, OCH_3), 3.87 (3H, s, NCO_2CH_3), 5.18 (1H, dd, J=10, 6 Hz, –C<u>H</u>–OH), 5.43 (1H, d, J=6 Hz, N–C<u>H</u>–OCH_3), 6.9—7.8 (4H, m, Ar–H). MS *m/e*: 223 (M^+).

***trans*- and *cis*-3-Hydroxy-2-methoxy-1-tosylindolines (2d) and (3d)**——Using a procedure similar to that described above for the preparation of **2a** and **3a**, **1d** (217 mg, 1 mmol) was treated with MoO_5·HMPA (391 mg, 1.1 mmol) in dry CH_3OH (15 ml). The reaction mixture was purified by column chromatography on silica gel with CH_2Cl_2 as an eluent to give **2d** (220 mg, 69%) and **3d** (23 mg, 7%).

2d: Oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 1360, 1170 (SO_2). ^{1}H-NMR ($CDCl_3$) δ: 1.57 (1H, br s, OH), 2.30 (3H, s, Ar–CH_3), 3.52 (3H, s, OCH_3), 4.60 (1H, s, –C<u>H</u>–OH), 5.23 (1H, s, N–C<u>H</u>–OCH_3), 7.0—7.8 (8H, m, Ar–H). MS *m/e*: 319 (M^+).

3d: Oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550 (OH), 1360, 1170 (SO_2). ^{1}H-NMR ($CDCl_3$) δ: 1.27 (1H, s, OH), 2.37 (3H, s, Ar–CH_3), 3.63 (3H, s, OCH_3), 4.70 (1H, br d, J=6 Hz, –C<u>H</u>–OH), 5.27 (1H, d, J=6 Hz, N–C<u>H</u>–OCH_3), 7.0—7.8 (8H, m, Ar–H). MS *m/e*: 319 (M^+).

1-Acetylindoxyl (10a)——1) Treatment of **2a** with $SnCl_4$: $SnCl_4$ (169 mg, 0.65 mmol) was added to a solution of **2a** (104 mg, 0.5 mmol) in dry CH_2Cl_2 (2 ml) at 0 °C. The mixture was allowed to warm to room temperature, then stirred for 30 min, diluted with CH_2Cl_2 (7 ml), and washed with saturated NaCl solution. The CH_2Cl_2 layer was dried over Na_2SO_4, and concentrated *in vacuo* to give a solid, which was recrystallized from C_6H_6 to give **10a** (87 mg, 99%), mp 134—137 °C [lit.[2] mp 135—140 °C]. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (C=O), 1678 (N–C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.30 (3H, s, $NCOCH_3$), 4.27 (2H, s, N–CH_2–CO), 7.0—7.75 (3H, m, Ar–H), 8.50 (1H, br, Ar–H). MS *m/e*: 175 (M^+).

2) Treatment of **3a** with $SnCl_4$: A similar treatment of **3a** (104 mg, 0.5 mmol) with $SnCl_4$ (169 mg, 0.65 mmol) in dry CH_2Cl_2 (2 ml) gave **10a** (87 mg, 99%).

3) Treatment of **2a** with H_2SO_4: Concentrated H_2SO_4 (0.5 ml) was added to a solution of **2a** (104 mg, 0.5 mmol) in CH_2Cl_2 (1 ml) at 0 °C with stirring. The mixture was stirred for 5 min, diluted with CH_2Cl_2 (7 ml), and washed with cooling H_2O. The CH_2Cl_2 layer was dried over Na_2SO_4 and concentrated *in vacuo* to give a residue. The residue was purified by preparative TLC with CH_2Cl_2 as a developing solvent to give **10a** (48 mg, 55%).

4) Treatment of **2a** with Tosyl Chloride: A solution of **2a** (104 mg, 0.5 mmol) and tosyl chloride (105 mg, 0.55 mmol) in dry pyridine (1 ml) was kept at 80 °C for 18 h, then diluted with ether, and washed with 10% HCl and H_2O. The ether solution was dried over Na_2SO_4 and concentrated to give a residue. The residue was purified by column chromatography on silica gel with CH_2Cl_2 as an eluent to give **10a** (50 mg, 57%).

5) Treatment of **2a** with Diethyl Malonate in the Presence of $SnCl_4$: $SnCl_4$ (390 mg, 1.5 mmol) was added to a solution of **2a** (207 mg, 1 mmol) and diethyl malonate (480 mg, 3 mmol) in dry CH_2Cl_2 (2 ml) at 0 °C. The mixture was allowed to warm to room temperature, stirred for 5 h, diluted with CH_2Cl_2 (7 ml), and washed with saturated NaCl solution. The CH_2Cl_2 solution was dried over Na_2SO_4, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography on silica gel with $CHCl_3$ as an eluent to give **10a** (114 mg, 65%).

6) Treatment of **5** with Diethyl Malonate in the Presence of $SnCl_4$: A similar treatment of **5** (97 mg, 0.4 mmol) and diethyl malonate (81 mg, 0.5 mmol) with $SnCl_4$ (132 mg, 0.5 mmol) gave **10a** (17 mg, 25%) and 1-acetyl-3-chloroindole (**14**) (30 mg, 40%), after chromatography of the crude products on a silica gel column with $CHCl_3$ as an eluent.

14: mp 102—104 °C (from CH_3OH). *Anal.* Calcd for $C_{10}H_8ClNO$: C, 62.03; H, 4.16; N, 7.23. Found: C, 62.09; H, 4.02; N, 7.22. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705 (C=O). ^{1}H-NMR ($CDCl_3$): δ: 2.57 (3H, s, $NCOCH_3$), 7.1—7.7 (4H, m, Ar–H), 8.43 (1H, m, Ar–H). MS *m/e*: 195 (M^++2), 193 (M^+).

1-Tosylindoxyl (10d)——The oily product **2d** (128 mg, 0.45 mmol) was allowed to stand at room temperature for several weeks. The dark oil was purified by preparative TLC with CH_2Cl_2 as a developing solvent to give **10d** (63 mg, 55%), mp 161—165 °C (dec.) (from ether). *Anal.* Calcd for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.87. Found: C, 62.63; H, 4.52; N, 4.90. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 (C=O), 1370, 1170 (SO_2). ^{1}H-NMR ($CDCl_3$) δ: 2.37 (3H, s, Ar–CH_3), 4.10 (2H, s, N–CH_2–CO), 6.95—8.2 (8H, m, Ar–H). MS *m/e*: 287 (M^+).

1-Acetyl-2-hydroxy-3-methoxy-3-methylindoline (16)——Using a procedure similar to that described above for the preparation of **2a** and **3a**, **15** (1730 mg, 10 mmol) was treated with MoO_5·HMPA (3905 mg, 11 mmol) in dry CH_3OH (100 ml). The reaction mixture was purified by column chromatography on silica gel with CH_2Cl_2–ethyl acetate (6 : 1) as an eluent to give **16** (1662 mg, 75%), mp 136—139 °C (from C_6H_6). *Anal.* Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.06; H, 6.84; N, 6.28. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560 (OH), 1650 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.59 (3H, s, CH_3), 2.34 (3H, s, $NCOCH_3$), 3.02 (3H, s, OCH_3), 3.75 (1H, br, OH, exchangeable), 5.42 (1H, br s, N–C<u>H</u>–OH), 7.0—7.45 (3H, m, Ar–H), 7.99 (1H, br, Ar–H). MS *m/e*: 221 (M^+).

2-Acetoxy-1-acetyl-3-methoxy-3-methylindoline (17)——A solution of **16** (221 mg, 1 mmol) and acetic anhydride (255 mg 2.5 mmol) in dry pyridine was allowed to stand at room temperature for 2 d. After concentration of the reaction mixture, the residue was purified by column chromatography on silica gel with CH_2Cl_2–ethyl acetate (10 : 1) as an eluent to give **17** (242 mg, 92%), mp 74—76 °C (from C_2H_5OH). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 63.88; H, 6.47; N, 5.32. Found: C, 63.93; H, 6.55; N, 5.27. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740 (O–C=O), 1680 (N–C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.53 (3H, s, CH_3), 2.12 (3H, s, $NCOCH_3$), 2.26 (3H, s, $OCOCH_3$), 3.10 (3H, s, OCH_3), 6.68 (1H, s, N–C<u>H</u>–OCO–), 7.05—7.55 (3H, m, Ar–H), 8.13 (1H, br d, Ar–H). MS *m/e*: 263 (M^+).

Hydrolysis of 17——A solution of **17** (375 mg, 1.4 mmol) and 28% ammonia water (0.6 ml) in CH_3OH (3 ml) was allowed to stand at 0—5 °C for 20 min. The reaction mixture was diluted with H_2O (10 ml), acidified with 10% HCl, and extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, and concentrated *in vacuo* to give a solid. The solid was recrystallized from C_6H_6 to give **16** (238 mg, 76%), mp 136—137 °C.

1-Acetyl-3-methoxy-3-methyloxindole (18)——Using a procedure similar to that described above for the preparation of **4**, treatment of **16** (221 mg, 1 mmol) with CrO_3 (310 mg, 3.1 mmol) gave **18** (96 mg, 44%), together with the starting **16** (31 mg, 14%).

18: mp 106—107 °C (from *n*-hexane). *Anal.* Calcd for $C_{12}H_{13}NO_3$: C, 65.75; H, 5.93; N, 6.39. Found: C, 66.03; H, 6.00; N, 6.42. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765, 1710 (–CO–N–CO–). ^{1}H-NMR ($CDCl_3$) δ: 1.60 (3H, s, CH_3), 2.70 (3H, s, $NCOCH_3$), 3.07 (3H, s, OCH_3), 7.15—7.65 (3H, m, Ar–H), 8.25 (1H, m, Ar–H). MS *m/e*: 219 (M^+).

3-Methyloxindole (19)——The indoline **16** (111 mg, 0.5 mmol) was dissolved in concentrated H_2SO_4 (0.5 ml) at 0 °C. The mixture was poured over ice, and extracted with ether. The extract was washed with H_2O, dried over Na_2SO_4, and concentrated to give a residue. The residue was purified by preparative TLC with CH_2Cl_2–ethyl acetate (15 : 2) as a developing solvent to give **19** (43 mg, 59%), mp 119—121 °C (from C_6H_6–pet. ether). [lit.[13] mp 121—122 °C]. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3430 (NH), 1710 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.50 (3H, d, J=8 Hz, CH_3), 3.45 (1H, q, J=8 Hz, –CH–CO–), 6.7—7.5 (4H, m, Ar–H), 8.93 (1H, br, NH). MS *m/e*: 147 (M^+).

1-Acetyl-2,3-dihydroxy-2,3-dimethylindoline (21)——Using a procedure similar to that described above for the preparation of **2a** and **3a**, **20** (748 mg, 4 mmol) was treated with MoO_5·HMPA (1570 mg, 4.4 mmol) in dry CH_3OH (32 ml). The reaction mixture was purified by column chromatography on silica gel with CH_2Cl_2–ethyl acetate (50 : 3) as an eluent to give **21** (447 mg, 51%), mp 137.5—138 °C (from CH_3OH) [lit.[8] mp 130—132 °C]. IR ν_{max}^{Nujol} cm^{-1}: 3410, 3290 (OH), 1630 (N–C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.45 and 1.73 (3H, s and s, CH_3 of *cis* and

trans), 1.55 and 1.92 (3H, s and s, CH_3 of *cis* and *trans*), 2.33 and 2.03 (3H, s and s, $NCOCH_3$ of *cis* and *trans*), 3.60 and 4.27 (2H, s and s, OH of *cis* and *trans*, exchangeable), 7.0—8.45 (4H, m, Ar–H). MS *m/e*: 221 (M^+). The NMR spectrum indicated the product to be a mixture of the *cis* and *trans* stereoisomers in a ratio of 1 : 2.

1-Acetyl-2-hydroxy-2-methylindoxyl (23)——Using a procedure similar to that described above for the preparation of **2a** and **3a**, **22** (346 mg, 2 mmol) was treated with $MoO_5 \cdot HMPA$ (779 mg, 2.1 mmol) in dry CH_3OH (20 ml). The reaction mixture was purified by column chromatography on silica gel with CH_2Cl_2–ethyl acetate (50 : 3) as an eluent to give **23** (260 mg, 63%), mp 133—134.5 °C (from C_6H_6). *Anal.* Calcd for $C_{11}H_{11}NO_3$: C, 64.39; H, 5.37; N, 6.83. Found: C, 64.20; H, 5.33; N, 6.70. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3250 (OH), 1725 (C=O), 1660 (N–C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.68 (3H, s, CH_3), 2.45 (3H, s, $NCOCH_3$), 4.62 (1H, s, OH, exchangeable), 7.06 (1H, d, J=7 Hz, Ar–H), 7.2—7.7 (2H, m, Ar–H), 8.01 (1H, d, J=8 Hz, ar–H). MS *m/e*: 205 (M^+).

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