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REARRANGEMENT REACTION OF 1-ETHOXY- AND 1-HYDROXY-2-PHENYLINDOLE[1†]

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Abstract – Photoirradiation of 1-ethoxy-2-phenylindole in methanol and the reaction of 1-hydroxy-2-phenylindole with tosyl chloride produced 6-ethoxy- and 6-tosyloxy-2-phenylindoles, respectively, as minor products. The latter was derived to 6-ethoxy-2-phenylindole. The structure is determined by direct comparison of the spectral data with those of the authentic 4-, 5-, 6-, and 7-ethoxy-2-phenylindoles whose syntheses are reported in detail.

We speculated that indole natural products having 3-, 4-, and/or 6-methoxy (or hydroxy) substituent could be produced in plant leaves by the sun light from the corresponding 1-alkoxy- or 1-hydroxyindoles.[2] In order to examine this 1-hydroxyindole hypotheses,[2] we attempted the photochemical reaction[3] of 1-ethoxy-2-phenylindole (**2**), derived from 1-hydroxy-2-phenylindole[4] (**1**).

Upon irradiation of **2** with Hannovia UV lamp in MeOH, we characterized 2-phenylindole (**3**) and 3-ethoxy-2-phenylindole (**4**) in 35 and 12% yields, respectively, from the closely overlapped eight products monitored on tlc (Scheme 1).[3] At the same time, we isolated a 3% yield of product X (**5**), which was a 2-phenylindole carrying an ethoxy group in the benzene ring.[3] On the other hand, upon reaction of **1** with tosyl chloride,[5] we isolated a 6% yield of product Y (**6**), which has a tosyloxy group on the benzene ring, in addition to 2-phenyl-3-tosyloxyindole (**7**), 2,2'-diphenyl-3,3'-bisindolyl (**8**), and **3** in 53, 2, and 5% yields, respectively.

† Dedicated to Prof. Dr. Albert Padwa.

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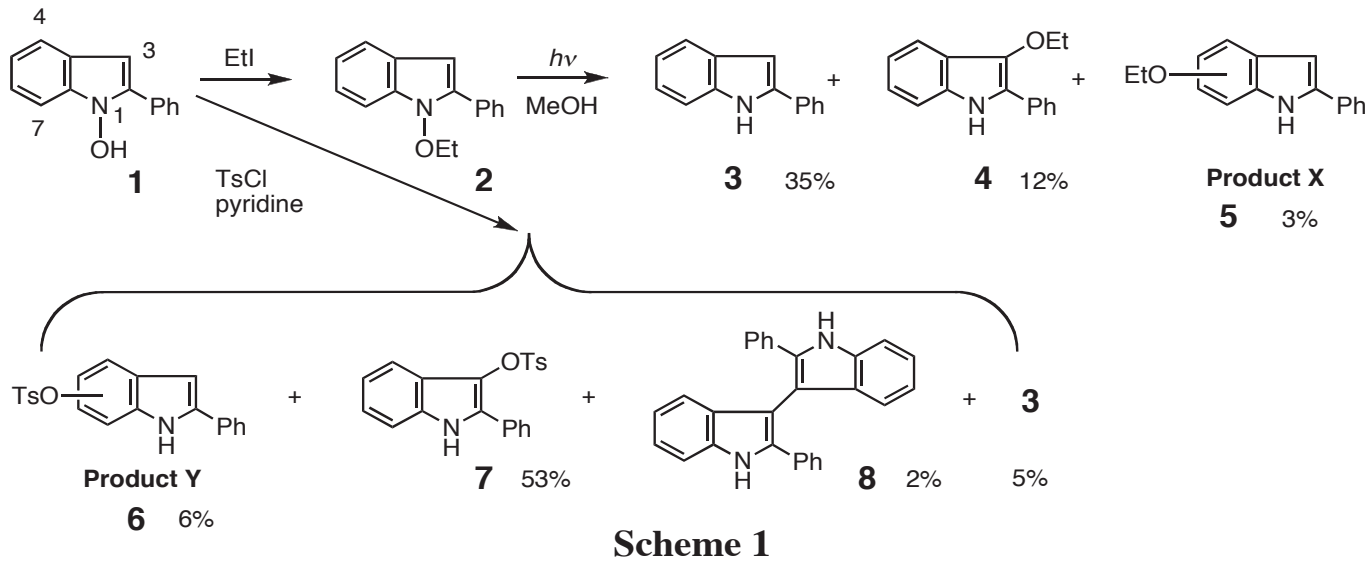
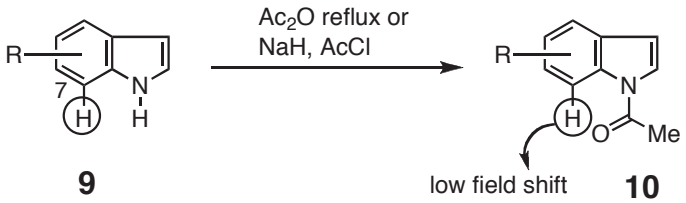


Scheme 1

At that time, we employed ^{1}H-NMR spectrum in order to determine the position of substituent on the indole ring utilizing the anisotropy effect of 1-acyl group (Scheme 2). Thus, the unknown indole having R-group (**9**) is led to the corresponding 1-acyl derivative (**10**), where the $C_{(7)}$-proton shifts to lower magnetic field and becomes clearly discernible from other aromatic protons. Based on its coupling pattern, we can determine the position of the R-group unequivocally.

In cases of product X (**5**) and product Y (**6**) the above structural determination method was impossible because the phenyl group at the 2-position blocked the introduction of an acyl group into the 1-position under various reaction conditions (Ac_2O reflux or NaH, AcCl).



Utilization of Anisotropy Effect of 1-Acyl Group

Scheme 2

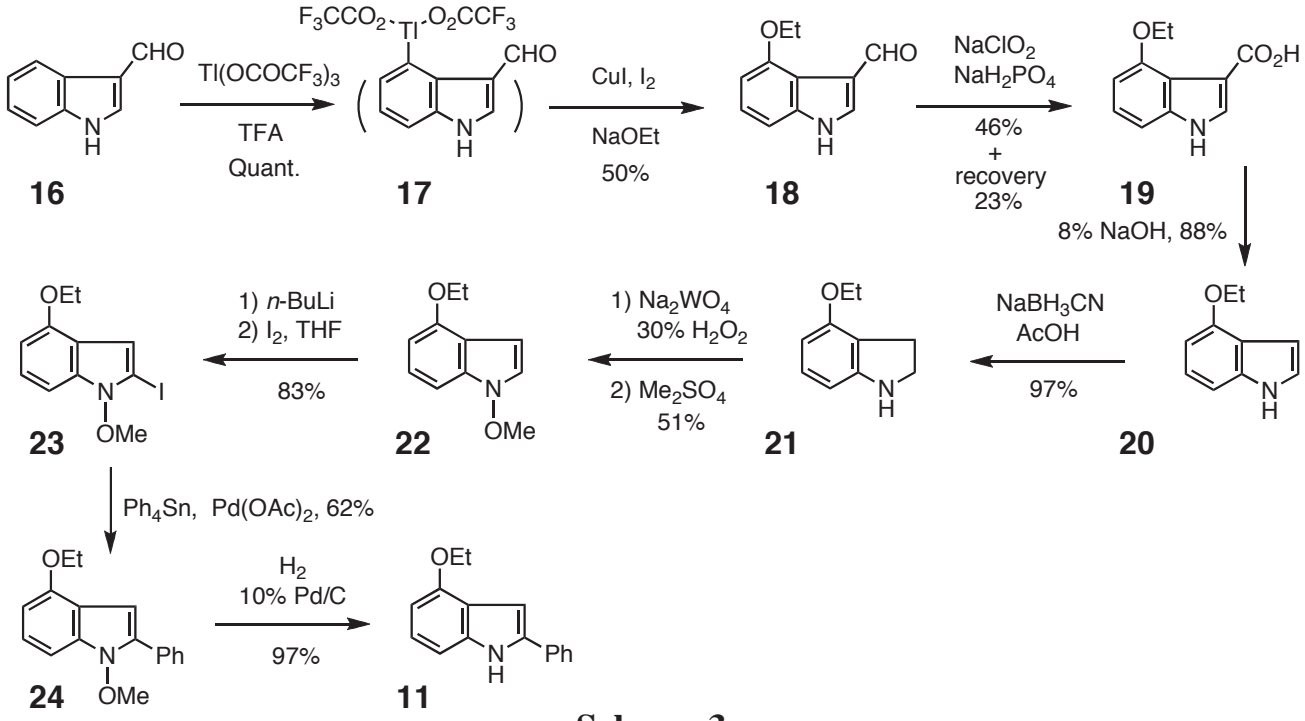
Moreover, the low resolving power of 60 MHz ^{1}H-NMR apparatus at that time was of no use for analyzing the coupling pattern of aromatic protons. Although we could later utilize a 270 and a 500 MHz ^{1}H-NMR instruments, they have still not enough resolving power to judge the coupling pattern of the indole benzenoid protons due to the overlapping protons of 2-phenyl group.

The left course for the structure determination of product X (**5**) and product Y (**6**) was the only one, direct comparison with the authentic 4- (**11**), 5- (**12**), 6- (**13**), and 7-ethoxy-2-phenylindoles (**14**). Their syntheses required new reactions such as regioselective thallation-palladation method for the preparation of 4-substituted,[6] and 7-substituted indoles,[7] general preparation method for 1-hydroxyindoles,[2,8] and selective 2-lithiation method[9] of 1-methoxyindoles. After discovering these essential new methods, we succeeded at last in the syntheses of authentic **11**, **12**, **13**, and **14** in 1998.[1] Consequently, structures of product X (**5**) and product Y (**6**) not clear for 25 years became clear and were proved unequivocally to be

6-ethoxy-2-phenylindole (**13**) and 6-tosyloxy-2-phenylindole (**15**), respectively. This paper reports the details of the structural determination of product X (**5**) and product Y (**6**).

1. Preparation of Authentic 4-Ethoxy-2-phenylindole (11)

4-Ethoxy-2-phenylindole (**11**) was produced as follows (Scheme 3). According to our synthetic method for 4-substituted indoles,[6,10] 4-ethoxyindole-3-carbaldehyde[10] (**18**) was prepared from indole-3-carbaldehyde (**16**) *via* (3-formylindol-4-yl)thallium bis(trifluoroacetate) (**17**) in 50% yield in one pot reaction. Treatment of **18** with sodium hypochlorite afforded a 46% yield of 4-ethoxyindole-3-carboxylic acid (**19**), which was then decarboxylated with 8% NaOH to provide 4-ethoxyindole (**20**) in 88% yield.[6]



Scheme 3

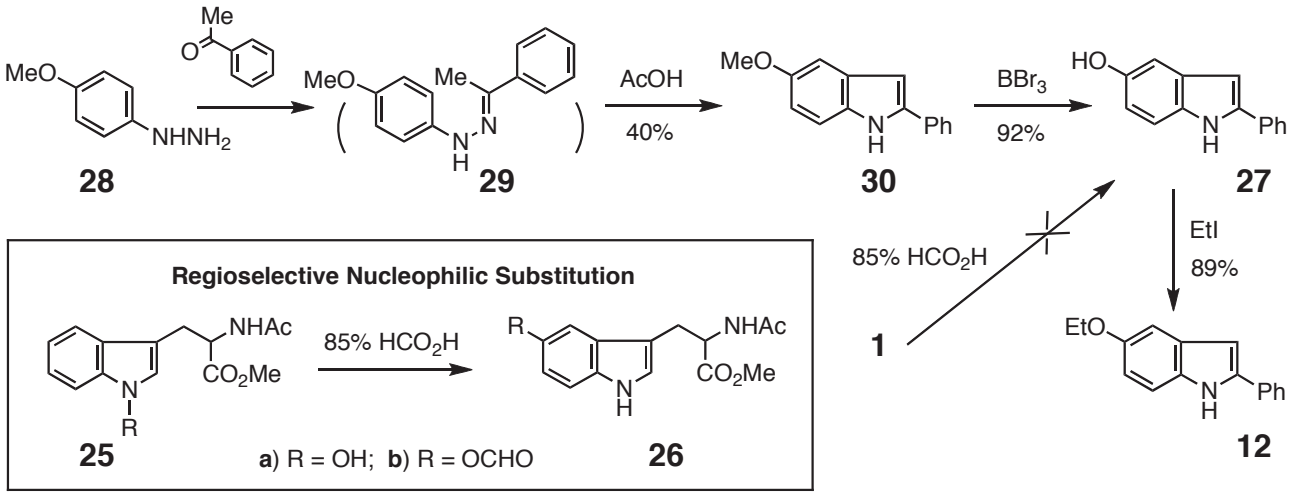
Reduction of **20** with $NaBH_3CN$ in AcOH[11] afforded 4-ethoxy-2,3-dihydroindole (**21**) in 97% yield. Application of our 1-methoxyindole synthetic method to **21**, thus oxidation with 30% aqueous H_2O_2 in the presence of a catalytic amount of $Na_2WO_4 \cdot 5H_2O$,[8] followed by methylation with dimethyl sulfate,[8] produced 4-ethoxy-1-methoxyindole (**22**) in 51% yield. Regioselective lithiation[12] of **22** with *n*-BuLi and quenching of the resultant 2-lithio species with I_2 afforded 4-ethoxy-2-iodo-1-methoxyindole (**23**) in 83% yield. The palladium catalyzed Stille coupling[13] of **23** with tetraphenyltin gave 62% yield of the desired 4-ethoxy-1-methoxy-2-phenylindole (**24**). Final conversion of **24** to the authentic 4-ethoxy-2-phenylindole (**11**) was carried out in 97% yield by catalytic hydrogenation with 10% Pd/C under atmospheric hydrogen.

2. Preparation of 5-Ethoxy-2-phenylindole (12)

We developed regioselective nucleophilic substitution reaction[2,14] for the introduction of a hydroxy group

into the 5-position of indole nucleus by the treatment of 1-hydroxyindoles with 85% formic acid as shown in the conversion of 1-hydroxytryptophan derivative (**25a**) into the corresponding 5-hydroxytryptophan product (**26a**, Scheme 4).[14] The mechanism is believed to proceed *via* initial formation of 1-formyloxy compound (**25b**) followed by its rearrangement to give 5-formyloxytryptophan derivative (**26b**). We observed **26b** spectroscopically as an unstable transient intermediate. We applied the reaction to 1-hydroxy-2-phenylindole (**1**) with an expectation to realize direct synthesis of 5-hydroxy-2-phenylindole (**27**). However, the attempt did not work probably because phenyl group at the 2-position blocked the initial formylation of 1-hydroxy group.

We next tried the Fischer indole synthesis.[15] Thus the reaction of 4-methoxyphenylhydrazine (**28**) and acetophenone upon heating in AcOH afforded 5-methoxy-2-phenylindole (**30**) in 40% yield without isolation of the intermediate hydrazone (**29**). Demethylation of **30** with BBr_3 afforded 5-hydroxy-2-phenylindole (**27**) in 92% yield. Subsequent ethylation of **27** with EtI and K_2CO_3 produced the authentic 5-ethoxy-2-phenylindole (**12**) in 89% yield.

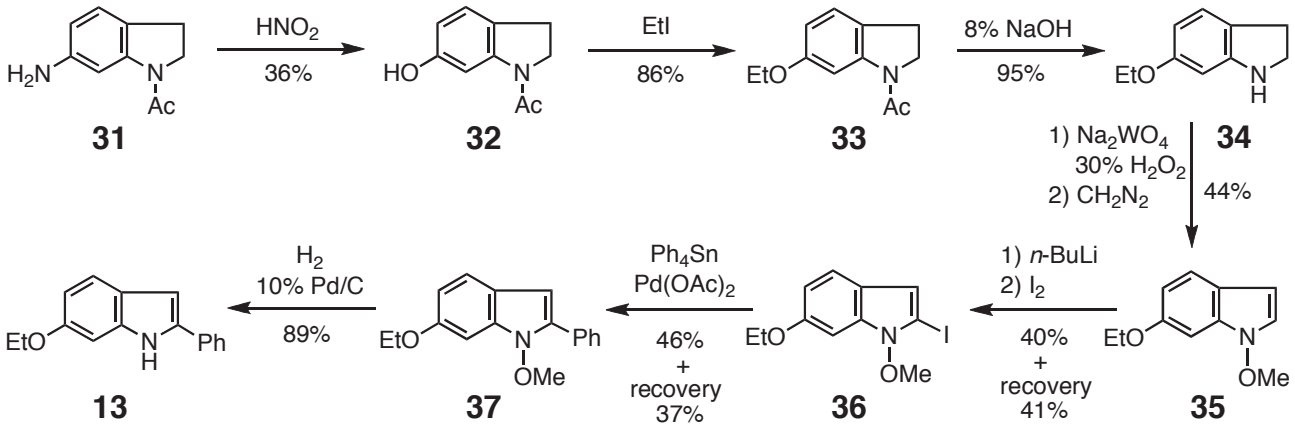


Scheme 4

3. Preparation of 6-Ethoxy-2-phenylindole (13)

1-Acetyl-6-amino-2,3-dihydroindole (**31**) was obtained from 2,3-dihydroindole in 72% overall yield according to a series of the established reactions: nitration, acetylation and subsequent catalytic hydrogenation. Diazotization of **31** with sodium nitrite and subsequent pyrolysis produced the desired 1-acetyl-2,3-dihydro-6-hydroxyindole (**32**) in 36% yield. Treatment of **32** with EtI and K_2CO_3 provided 1-acetyl-2,3-dihydro-6-ethoxyindole (**33**) in 86% yield. Subsequent alkaline hydrolysis of **33** afforded 2,3-dihydro-6-ethoxyindole (**34**) in 95% yield. Application of our 1-methoxyindole synthetic method[2] to **34** produced 6-ethoxy-1-methoxyindole (**35**) in 44% yield. Regioselective lithiation of **35** with *n*-BuLi, followed by the reaction with I_2, furnished 6-ethoxy-2-iodo-1-methoxyindole (**36**) in 40% yield. The Stille coupling of **36** with tetraphenyltin gave 46% yield of 6-ethoxy-1-methoxy-2-phenylindole (**37**). Removal of the 1-methoxy group of **37** was carried out by the catalytic hydrogenation with 10% Pd/C

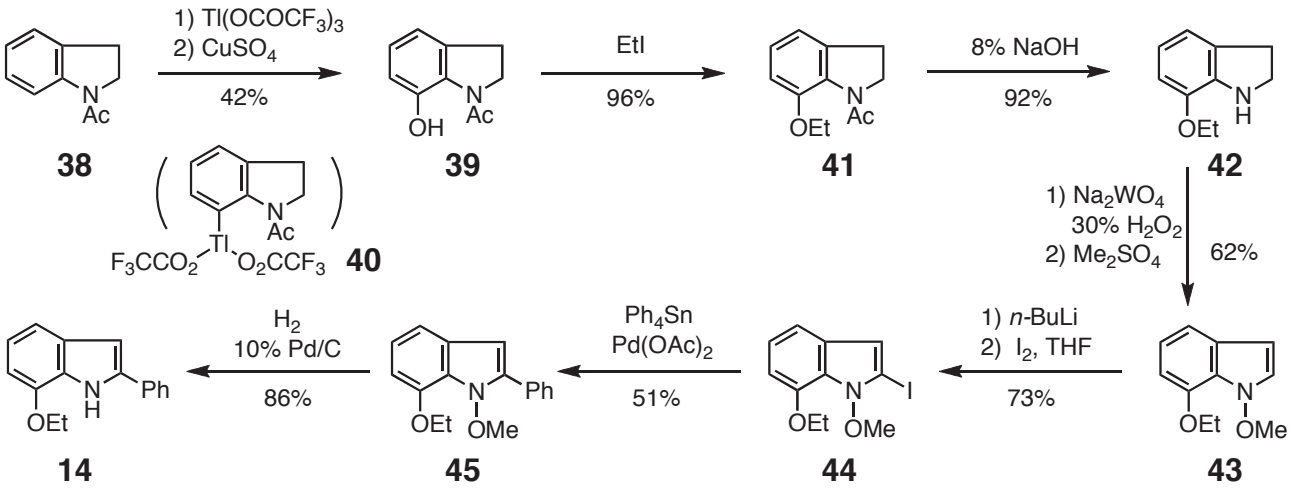
resulting in the formation of the authentic 6-ethoxy-2-phenylindole (**13**) in 89% yield (Scheme 5).



Scheme 5

4. Preparation of 7-Ethoxy-2-phenylindole (14)

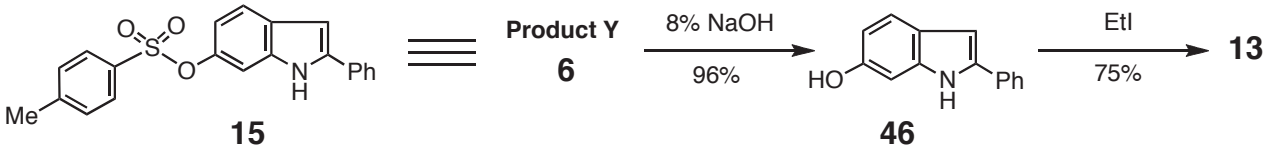
According to our synthetic method for 7-substituted indoles,[7] 1-acetyl-2,3-dihydroindole (**38**) was converted to 1-acetyl-2,3-dihydro-7-hydroxyindole (**39**) in 42% yield through (1-acetyl-2,3-dihydroindol-7-yl)thallium bis(trifluoroacetate) (**40**, Scheme 6). Ethylation of **39** with EtI and K_2CO_3 afforded 96% yield of 1-acetyl-2,3-dihydro-7-ethoxyindole (**41**), which was then hydrolyzed with aqueous 8% NaOH to give 2,3-dihydro-7-ethoxyindole (**42**) in 92% yield. Application of our 1-methoxyindole synthetic method[2] to **42** produced 7-ethoxy-1-methoxyindole (**43**) in 62% yield.



Scheme 6

Regioselective lithiation of **43** with *n*-BuLi, followed by the reaction with I_2, produced 7-ethoxy-2-iodo-1-methoxyindole (**44**) in 73% yield. The Stille coupling of **44** with tetraphenyltin in the presence of catalytic amount of $Pd(OAc)_2$ gave 51% yield of 7-ethoxy-1-methoxy-2-phenylindole (**45**), which was then converted to the authentic 7-ethoxy-2-phenylindole (**14**) in 86% yield by the catalytic hydrogenation with 10% Pd/C.

Comparing the spectral data (IR, UV, ^{1}H-NMR, and MS) and melting points of the four authentic samples with those of product X (**5**), we have at last determined unequivocally that it is 6-ethoxy-2-phenylindole (**13**). On the other hand, hydrolysis of product Y (**6**) with aqueous NaOH provided 6-hydroxy-2-phenylindole (**46**) in 96% yield (Scheme 7). Subsequent ethylation with EtI and K_2CO_3 gave a 75% yield of the ethoxy derivative, which was identical with 6-ethoxy-2-phenylindole (**13**). Therefore, the structure of product Y is determined to be 2-phenyl-6-tosyloxyindole (**15**).



Scheme 7

We have thus proved 1-alkoxy and 1-tosyloxy groups rearrange to the 3- and 6-position of the indole nucleus by photo and thermal reactions, respectively, in accord with our 1-hydroxyindole hypotheses.[2]

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded with a Shimadzu IR-420 and proton nuclear magnetic resonance (^{1}H-NMR) spectra with a JEOL GSX-500 spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were recorded on a JEOL JMS-SX102A instruments. Preparative thin-layer chromatography (p-TLC) was performed on Merck Kiesel-gel GF_{245} (Type 60) (SiO_2). Column chromatography was performed on silica gel (SiO_2, 100—200 mesh, from Kanto Chemical Co., Inc.) or on alumina (Al_2O_3, 300 mesh, from Wako Pure Chemical Industries, Ltd.) throughout the present study.

2-Phenyl-6-tosyloxyindole (6, Product Y) from 1-Hydroxy-2-phenylindole (1) — A solution of TsCl (1.15 g, 6.03 mmol) in pyridine (5 mL) was cooled to 0 °C and added to a cooled solution of **1** (251.2 mg, 1.20 mmol) in $CHCl_3$ (50 mL) and pyridine (5 mL). The resulting solution was stirred at 0 °C for 30 min and then at rt for 20 h. After evaporation of the solvent, the residue was column-chromatographed repeatedly on SiO_2 with EtOAc–hexane (1:5, v/v) and $CHCl_3$–hexane (1:5, v/v), and then column-chromatographed on Al_2O_3 with $CHCl_3$–hexane (1:1, v/v) to give 2-phenyl-3-tosyloxyindole (**7**) (231.1 mg, 53%), **6** (27.5 mg, 6%), 2,2'-diphenyl-3,3'-biindolyl (**8**) (4.9 mg, 2%), 2-phenylindole (**3**) (10.6 mg, 5%), and unreacted **1** (23.1 mg, 9%). **6**: mp 196.5—197.5 °C (colorless fine needles, recrystallized from $CHCl_3$–hexane). IR (KBr): 3390, 1594, 1491, 1448, 1373, 1353, 1310, 1191, 1174, 1127, 1114, 1089, 957, 868 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.44 (3H, s), 6.63 (1H, dd, *J*=8.7, 2.2 Hz), 6.77 (1H, dd, *J*=2.2, 1.0 Hz), 7.16 (1H, d, *J*=2.2 Hz), 7.29 (2H, d, *J*=8.3 Hz), 7.34 (1H, tt, *J*=7.4, 1.2 Hz), 7.43 (1H, d, *J*=8.7 Hz), 7.45 (2H, dd, *J*=8.3, 7.4 Hz), 7.63 (2H, dd, *J*=8.3, 1.2 Hz), 7.72 (2H, d, *J*=8.3 Hz), 8.40

(1H, brs, NH). MS *m/z*: 363 (M^+). High-resolution MS *m/z*: Calcd for $C_{21}H_{17}NO_3S$: 363.0930. Found: 363.0930. *Anal.* Calcd for $C_{21}H_{17}NO_3S$: C, 69.40; H, 4.72; N, 3.85. Found: C, 69.32; H, 4.72; N, 3.35.

4-Ethoxyindole-3-carboxylic Acid (19) from 4-Ethoxyindole-3-carbaldehyde (18) — The aldehyde (**18**, 50.3 mg, 0.27 mmol) was dissolved in a mixture of *tert*-butyl alcohol (3 mL) and 2-methyl-2-butene (3 mL). A solution of $NaClO_2$ (601.2 mg, 5.32 mmol) and $NaH_2PO_4 \cdot H_2O$ (623.2 mg, 4.00 mmol) in H_2O (3 mL) was added drop wise over a 2 min. The reaction mixture was stirred at rt for 24 h. The resultant mixture was extracted with $CHCl_3$–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a residue, which was column-chromatographed on SiO_2 successively with EtOAc–hexane (1:3 and then 1:2, v/v) to give the unreacted **18** (11.8 mg, 23%) and **19** (24.9 mg, 46%) in the order of elution. **19**: mp 204—206 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 3117, 1691, 1674, 1521, 1397, 1323, 1252, 1188, 1073 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.43 (3H, t, *J*=7.0 Hz), 4.26 (2H, q, *J*=7.0 Hz), 6.76 (1H, dd, *J*=2.0, 6.6 Hz), 7.11—7.16 (2H, m), 7.98 (1H, d, *J*=2.9 Hz), 11.67 (1H, brs, disappeared on addition of D_2O), 11.97 (1H, brs, disappeared on addition of D_2O). *Anal.* Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.23; H, 5.39; N, 6.72.

4-Ethoxyindole (20) from 19 — An aqueous 8% NaOH (3 mL) was added to a solution of **19** (24.9 mg) in MeOH (3 mL), and the mixture was refluxed for 1 h with stirring. The resultant solution was made acidic by adding aqueous 8% HCl under ice cooling, and extracted with $CHCl_3$–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a residue, which was column-chromatographed on SiO_2 with $CHCl_3$–hexane (1:1, v/v) to give **20** (17.2 mg, 88%). **20**: mp 77—77.5 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 3340, 1585, 1501, 1369, 1355, 1236, 1089, 1056, 740, 726 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.50 (3H, t, *J*=7.0 Hz), 4.20 (2H, q, *J*=7.0 Hz), 6.52 (1H, d, *J*=7.8 Hz), 6.67 (1H, t, *J*=2.7 Hz), 7.01 (1H, d, *J*=7.8 Hz), 7.09 (1H, t, *J*=7.8 Hz), 7.11 (1H, t, *J*=2.7 Hz), 8.13 (1H, brs, NH). *Anal.* Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.40; H, 6.90; N, 8.56.

4-Ethoxy-2,3-dihydroindole (21) from 20 — 95% $NaCNBH_3$ (44.3 mg, 0.67 mmol) was added to a solution of **20** (52.2 mg, 0.32 mmol) in AcOH (3 mL) and the mixture was stirred at rt for 30 min. After addition of H_2O, the whole was made alkaline by adding aqueous 40% NaOH, and then 8% NaOH under ice cooling, and extracted with EtOAc. 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, v/v) to give **21** (50.6 mg, 97%). **21**: mp 46—46.5 °C (colorless needles, recrystallized from petroleum ether). IR (KBr): 3270, 1608, 1598, 1466, 1249, 1110, 1079 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.29 (3H, t, *J*=7.1 Hz), 2.79 (2H, t, *J*=8.5 Hz), 3.38 (2H, t, *J*=8.5 Hz), 3.98 (2H, q, *J*=7.1 Hz), 5.38 (1H, brs, NH, disappeared on addition of D_2O), 6.13 (1H, d, *J*=8.0 Hz), 6.17 (1H, t, *J*=8.0 Hz),

6.84 (1H, t, *J*=8.0 Hz). *Anal.* Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.46; H, 8.06; N, 8.50.

4-Ethoxy-1-methoxyindole (22) from 21 — A solution of $Na_2WO_4 \cdot 2H_2O$ (24.7 mg, 0.075 mmol) in H_2O (0.5 mL) was added to a solution of **21** (70.9 mg, 0.37 mmol) in MeOH (4 mL), and then a solution of 30% H_2O_2 (421.1 mg, 3.71 mmol) in MeOH (1 mL) was added to the reaction mixture under ice cooling. After stirring at rt for 15 min, K_2CO_3 (258.6 mg, 1.87 mmol) and a solution of Me_2SO_4 (97.5 mg, 0.77 mmol) in MeOH (1 mL) were added. The mixture was stirred at rt for 1 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 leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–hexane (1:4, v/v) to give **22** (42.1 mg, 51%). **22**: colorless oil. IR (film): 2990, 2950, 1611, 1583, 1509, 1475, 1392, 1354, 1341, 1248, 1055, 1033 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.48 (3H, t, *J*=7.1 Hz), 4.07 (3H, s), 4.18 (2H, q, *J*=7.1 Hz), 6.47 (1H, d, *J*=3.4 Hz), 6.50 (1H, d, *J*=8.0 Hz), 7.04 (1H, d, *J*=8.0 Hz), 7.13 (1H, t, *J*=8.0 Hz), 7.16 (1H, d, *J*=3.4 Hz). High-resolution MS *m/z*: Calcd for $C_{11}H_{13}NO_2$: 191.0947. Found: 191.0943.

4-Ethoxy-2-iodo-1-methoxyindole (23) from 22 — A solution of 1.58 M BuLi in hexane (0.21 mL, 0.33 mmol) was added drop wise to a solution of **22** (53.2 mg, 0.28 mmol) in THF (3 mL) under nitrogen atmosphere at –16 °C. The solution was stirred at –16 °C for 30 min and then a solution of I_2 (69.9 mg, 0.28 mmol) in THF (3 mL) was added drop wise over a 5 min. The mixture was stirred at –16 °C for 10 min. After addition of H_2O and brine, the whole was extracted with EtOAc. The extract was washed with aqueous 10% $Na_2S_2O_3$ and 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 (1:10, v/v) to give **23** (73.0 mg, 83%) and unreacted **22** (5.7 mg, 11%) in the order of elution. **23**: colorless hard oil. IR (film): 2985, 2945, 1608, 1583, 1501, 1460, 1456, 1414, 1336, 1325, 1250, 1050 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.46 (3H, t, *J*=7.1 Hz), 4.05 (3H, s), 4.15 (2H, q, *J*=7.1 Hz), 6.47 (1H, d, *J*=8.0 Hz), 6.74 (1H, d, *J*=0.7 Hz), 7.02 (1H, d, *J*=8.0 Hz), 7.07 (1H, t, *J*=8.0 Hz). High-resolution MS *m/z*: Calcd for $C_{11}H_{12}NO_2I$: 316.9912. Found: 316.9912.

4-Ethoxy-1-methoxy-2-phenylindole (24) from 23 — A mixture of **23** (32.6 mg, 0.10 mmol), Ph_4Sn (87.8 mg, 0.21 mmol), NaOAc (16.9 mg, 0.21 mmol), and $Pd(OAc)_2$ (4.7 mg, 0.02 mmol) in DMF (10 mL) was heated at 100 °C for 30 min with stirring. After evaporation of the solvent, the residue was column-chromatographed on SiO_2 successively with hexane and then EtOAc–hexane (1:99, v/v) to give **24** (18.6 mg, 62%). **24**: colorless hard oil. IR (film): 2980, 1588, 1504, 1474, 1341, 1255, 1045, 754 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.51 (3H, t, *J*=7.0 Hz), 3.75 (3H, s), 4.21 (2H, q, *J*=7.0 Hz), 6.54 (1H, d, *J*=7.9 Hz), 6.74 (1H, s), 7.08 (1H, d, *J*=7.9 Hz), 7.16 (1H, t, *J*=7.9 Hz), 7.35 (1H, tt, *J*=1.2, 7.6 Hz), 7.45 (2H, dd, *J*=7.6, 8.0 Hz), 7.86 (2H, dd, *J*=1.2, 8.0 Hz). High-resolution MS *m/z*: Calcd for $C_{17}H_{17}NO_2$: 267.1259.

Found: 267.1261.

4-Ethoxy-2-phenylindole (11) from 24 — A suspension of **24** (38.5 mg, 0.14 mmol) and 10% Pd on charcoal (28.4 mg, 0.03 mmol) in MeOH (1.5 mL) was stirred at rt for 1 h under hydrogen atmosphere. After the catalyst was filtered off, the filtrate was evaporated under reduced pressure to leave a solid, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:20, v/v) to give **11** (33.0 mg, 97%). **11**: mp 111—112 °C (colorless fine needles, recrystallized from $CHCl_3$–hexane). IR (KBr): 3405, 1604, 1589, 1487, 1474, 1454, 1437, 1365, 1343, 1263, 1240, 1181, 1124, 1102, 773, 764 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.52 (3H, t, *J*=7.0 Hz), 4.22 (2H, q, *J*=7.0 Hz), 6.53 (1H, d, *J*=8.0 Hz), 6.96 (1H, d, *J*=2.0 Hz), 7.02 (1H, d, *J*=8.0 Hz), 7.09 (1H, t, *J*=8.0 Hz), 7.30 (1H, t, *J*=7.8 Hz), 7.43 (2H, t, *J*=7.8 Hz), 7.66 (2H, d, *J*=7.8 Hz), 8.32 (1H, brs, NH, disappeared on addition of D_2O). MS *m/z*: 237 (M^+). *Anal.* Calcd for $C_{16}H_{15}NO \cdot 1/4\ H_2O$: C, 79.47; H, 6.46; N, 5.79. Found: C, 79.77; H, 6.25; N, 5.82.

5-Methoxy-2-phenylindole (30) from 4-Methoxyphenylhydrazine Hydrochloride (28) — Acetophenone (0.14 mL, 1.18 mmol) was added to a solution of **28** (102.7 mg, 0.59 mmol) in AcOH (5 mL) and the mixture was refluxed for 4 h with stirring. After evaporation of the solvent, the residue was column-chromatographed on SiO_2 with EtOAc–hexane (1:10, v/v) to give **30** (52.7 mg, 40%). **30**: mp 172—174 °C (colorless fine needles, recrystallized from EtOAc–hexane). IR (KBr): 3425, 1618, 1586, 1532, 1472, 1443, 1400, 1350, 1298, 1273, 1214, 1146, 1113, 1075, 1024, 942, 843, 800, 793, 762, 752, 734, 689 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.87 (3H, s), 6.76 (1H, dd, *J*=1.0, 2.2 Hz), 6.86 (1H, dd, *J*=2.6, 8.8 Hz), 7.09 (1H, d, *J*=2.6 Hz), 7.29 (1H, d, *J*=8.8 Hz), 7.32 (1H, tt, *J*=1.2, 7.5 Hz), 7.44 (2H, dd, *J*=7.5, 8.6 Hz), 7.65 (2H, dd, *J*=1.2, 8.6 Hz), 8.23 (1H, brs, NH). *Anal.* Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.77; H, 5.87; N, 6.23.

5-Hydroxy-2-phenylindole (27) from 30 — A solution of 1 M BBr_3 in heptane (1.21 mL, 1.21 mmol) was added drop wise to a solution of **30** (26.9 mg, 0.12 mmol) in $CHCl_3$ (5 mL) under ice cooling. The solution was stirred at rt for 1 h. After addition of H_2O under ice cooling, the whole was extracted with $CHCl_3$–MeOH (95:5, v/v). 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 $CHCl_3$ to give unreacted **30** (1.6 mg, 6%) and **27** (23.3 mg, 92%) in the order of elution. **27**: mp 246—251 °C (colorless prisms, recrystallized from $CHCl_3$–MeOH). IR (KBr): 3420, 1620, 1585, 1531, 1453, 1443, 1403, 1372, 1334, 1277, 1233, 1205, 1138, 1069, 1024, 948, 904, 855, 800, 786, 758, 733, 685, 610 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 6.61 (1H, dd, *J*=2.4, 8.5 Hz), 6.70 (1H, d, *J*=1.5 Hz), 6.83 (1H, d, *J*=2.4 Hz), 7.18 (1H, d, *J*=8.5 Hz), 7.28 (1H, t, *J*=7.5 Hz), 7.43 (2H, dd, *J*=7.5, 8.5 Hz), 7.80 (2H, d, *J*=8.5 Hz), 8.66 (1H, brs, disappeared on addition of D_2O), 11.19 (1H, brs, disappeared on addition of D_2O). *Anal.* Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.29; H, 5.29; N, 6.68.

5-Ethoxy-2-phenylindole (12) from 27 — A mixture of **27** (17.4 mg, 0.08 mmol), K_2CO_3 (116.1 mg,

0.84 mmol) and EtI (0.1 mL, 1.25 mmol) in DMF (1.5 mL) was stirred at rt for 5 h. After addition of H_2O under ice cooling, the whole was extracted with $CHCl_3$–MeOH (95:5, v/v). 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 $CHCl_3$–hexane (1:1, v/v) to give **12** (17.6 mg, 89%). **12**: mp 145—145.5 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 3420, 2980, 1620, 1600, 1585, 1533, 1466, 1451, 1388, 1348, 1297, 1273, 1226, 1209, 1149, 1116, 1107, 1072, 1044, 938, 900, 846, 826, 805, 794, 764, 736, 693 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.44 (3H, t, *J*=7.1 Hz), 4.09 (2H, q, *J*=7.1 Hz), 6.74 (1H, dd, *J*=0.7, 2.2 Hz), 6.86 (1H, dd, *J*=2.4, 8.8 Hz), 7.08 (1H, d, *J*=2.4 Hz), 7.28 (1H, d, *J*=8.8 Hz), 7.31 (1H, tt, *J*=1.2, 7.4 Hz), 7.43 (2H, dd, *J*=7.4, 8.1 Hz), 7.64 (2H, dd, *J*=1.2, 8.1 Hz), 8.21 (1H, brs, NH). *Anal.* Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.99; H, 6.35; N, 5.87.

1-Acetyl-6-hydroxy-2,3-dihydroindole (32) from 1-Acetyl-6-amino-2,3-dihydroindole (31) — A solution of **31** (105.0 mg, 0.37 mmol) in H_2O (10 mL) and concentrated H_2SO_4 (5 mL) was cooled to 0—5 °C. A solution of $NaNO_2$ (164.5 mg, 2.38 mmol) in H_2O (10 mL) was added drop wise over 5 min. The mixture was stirred for 30 min, and poured into a cooled separatory funnel containing cooled $CHCl_3$ (10 mL) and cooled H_2O (10 mL). The organic layer was added to hot H_2O (300 mL), and the solution was heated to 80 °C for 5 min. The mixture was cooled to rt, and extracted with $CHCl_3$–MeOH (95:5, v/v). 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 (97:3, v/v) to give **32** (35.4 mg, 36%). **32**: mp 274—279 °C (colorless fine needles, recrystallized from $CHCl_3$–MeOH). IR (KBr): 3130, 1629, 1602, 1489, 1448, 1419, 1355, 1272, 1246, 874 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.12 (3H, s), 2.99 (2H, t, *J*=8.4 Hz), 4.05 (2H, t, *J*=8.4 Hz), 6.36 (1H, dd, *J*=2.4, 8.1 Hz), 6.96 (1H, d, *J*=8.1 Hz), 7.59 (1H, d, *J*=2.4 Hz), 11.97 (1H, brs, OH, disappeared on addition of D_2O). *Anal.* Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.91. Found: C, 67.60; H, 6.22; N, 7.85.

1-Acetyl-6-ethoxy-2,3-dihydroindole (33) from 32 — A mixture of **32** (61.0 mg, 0.35 mmol), K_2CO_3 (480.5 mg, 3.48 mmol) and EtI (0.41 mL, 5.13 mmol) in DMF (3 mL) was stirred at rt for 30 min. After addition of H_2O under ice cooling, the whole was extracted with $CHCl_3$–MeOH (95:5, v/v). 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 (99:1, v/v) to give **33** (60.6 mg, 86%). **33**: mp 151.5—152 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 1658, 1606, 1590, 1489, 1451, 1438, 1399, 1355, 1315, 1287, 1239, 1192, 1171, 1114 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.30 (3H, t, *J*=7.0 Hz), 2.12 (3H, s), 3.04 (2H, t, *J*=8.4 Hz), 3.95 (2H, q, *J*=7.0 Hz), 4.08 (2H, t, *J*=8.4 Hz), 6.53 (1H, dd, *J*=2.4, 8.3 Hz), 7.08 (1H, d, *J*=8.3 Hz), 7.68 (1H, d, *J*=2.4 Hz). *Anal.* Calcd for $C_{10}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 69.93; H, 7.34; N, 6.73.

6-Ethoxy-2,3-dihydroindole (34) from 33 — An aqueous 8% NaOH (5 mL) was added to a solution of

33 (45.3 mg, 0.22 mmol) in MeOH (5 mL) and the mixture was refluxed for 20 h with stirring. The resultant solution was cooled to rt, 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 EtOAc–hexane (1:2, v/v) to give **34** (34.3 mg, 95%). **34**: colorless oil. IR (film): 3380, 2985, 1619, 1595, 1502, 1474, 1459, 1396, 1336, 1113, 1286, 1257, 1173, 1155 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.38 (3H, t, *J*=7.0 Hz), 2.95 (2H, t, *J*=8.3 Hz), 3.55 (2H, t, *J*=8.3 Hz), 3.97 (2H, q, *J*=7.0 Hz), 6.24 (1H, d, *J*=2.2 Hz), 6.24 (1H, dd, *J*=2.2, 8.6 Hz), 6.97 (1H, d, *J*=8.6 Hz). High-resolution MS *m/z*: Calcd for $C_{10}H_{13}NO$: 163.0997. Found: 163.0996.

6-Ethoxy-1-methoxyindole (35) from 34 — A solution of $Na_2WO_4 \cdot 2H_2O$ (11.0 mg, 0.03 mmol) in H_2O (0.25 mL) was added to a solution of **34** (24.5 mg, 0.15 mmol) in MeOH (1.5 mL) and then a solution of 30% H_2O_2 (178.5 mg, 1.58 mmol) in MeOH (1 mL) was added to the reaction mixture under ice cooling. After stirring at rt for 20 min, excess CH_2N_2 in Et_2O was added. The mixture was stirred at rt for 10 min. After addition of H_2O, the whole was extracted with $CHCl_3$–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 $CHCl_3$–hexane (1:2, v/v) to give **35** (12.6 mg, 44%). **35**: colorless hard oil. IR (film): 2990, 1624, 1572, 1493, 1472, 1454, 1442, 1392, 1317, 1230, 1206 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.46 (3H, t, *J*=7.0 Hz), 4.06 (3H, s), 4.10 (2H, q, *J*=7.0 Hz), 6.27 (1H, d, *J*=3.4 Hz), 6.76 (1H, dd, *J*=2.2, 8.8 Hz), 6.89 (1H, d, *J*=2.2 Hz), 7.14 (1H, d, *J*=3.4 Hz), 7.44 (1H, d, *J*=8.8 Hz). High-resolution MS *m/z*: Calcd for $C_{11}H_{13}NO_2$: 191.0947. Found: 191.0945.

6-Ethoxy-2-iodo-1-methoxyindole (36) from 35 — A solution of 1.58 M BuLi in hexane (0.14 mL, 0.22 mmol) was added drop wise to a solution of **35** (13.8 mg, 0.07 mmol) in THF (2 mL) under argon atmosphere at –17 °C. The solution was stirred at –17 °C for 20 min and then a solution of I_2 (16.5 mg, 0.07 mmol) in THF (1 mL) was added drop wise over 5 min. The mixture was stirred at –17 °C for 30 min. 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 an oil, which was purified by p-TLC on SiO_2 developed twice with $CHCl_3$–hexane (1:5, v/v). Extraction of the band having an *Rf* value of 0.50—0.33 with $CHCl_3$ gave **36** (9.1 mg, 40%). Extraction of the band having an *Rf* value of 0.33—0.17 with $CHCl_3$ gave unreacted **35** (5.7 mg, 41%). **36**: colorless hard oil. IR (film): 2990, 2945, 1622, 1574, 1495, 1487, 1473, 1455, 1435, 1421, 1396, 1317, 1288, 1225, 1206, 1110, 1054, 1035, 962, 813 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.45 (3H, t, *J*=7.0 Hz), 4.04 (3H, s), 4.09 (2H, q, *J*=7.0 Hz), 6.52 (1H, d, *J*=0.7 Hz), 6.73 (1H, dd, *J*=2.2, 8.6 Hz), 6.88 (1H, d, *J*=2.2 Hz), 7.34 (1H, dd, *J*=0.7, 8.6 Hz). High-resolution MS *m/z*: Calcd for $C_{11}H_{12}NO_2I$: 316.9913. Found: 316.9915.

6-Ethoxy-1-methoxy-2-phenylindole (37) from 36 — A mixture of **36** (11.1 mg, 0.04 mmol), Ph_4Sn (30.6 mg, 0.07 mmol), NaOAc (5.6 mg, 0.07 mmol), and $Pd(OAc)_2$ (2.6 mg, 0.01 mmol) in DMF (3 mL)

was heated at 100 °C for 2 h with stirring. After evaporation of the solvent, the residue was column-chromatographed on SiO_2 with $CHCl_3$–hexane (1:5, v/v) to give unreacted **36** (4.1 mg, 37%) and **37** (4.3 mg, 46%) in the order of elution. **37**: mp 96—97 °C (colorless prisms, recrystallized from CCl_4-hexane). IR (KBr): 2975, 2940, 1615, 1599, 1572, 1529, 1487, 1480, 1470, 1439, 1344, 1326, 1233, 1206, 1189, 1106, 1050, 1033, 1022, 960, 810, 759, 733, 696 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.47 (3H, t, *J*=6.9 Hz), 3.73 (3H, s), 4.13 (2H, q, *J*=6.9 Hz), 6.51 (1H, d, *J*=0.7 Hz), 6.79 (1H, dd, *J*=2.2, 8.6 Hz), 6.94 (1H, d, *J*=2.2 Hz), 7.34 (1H, tt, *J*=1.2, 7.4 Hz), 7.44 (2H, dd, *J*=7.4, 8.5 Hz), 7.45 (1H, d, *J*=8.6 Hz), 7.81 (2H, dd, *J*=1.2, 8.5 Hz). *Anal.* Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.16; H, 6.28; N, 5.09.

6-Ethoxy-2-phenylindole (13) from 37 — A suspension of **37** (7.7 mg , 0.03 mmol) and 10% Pd on charcoal (9.2 mg, 0.009 mmol) in MeOH (2 mL) was stirred at rt for 1 h under hydrogen atmosphere. After evaporation of the solvent, the residue was column-chromatographed on SiO_2 with $CHCl_3$–hexane (1:1, v/v) to give **13** (6.1 mg, 89%). **13**: mp 126—127 °C (colorless prisms, recrystallized from CCl_4-hexane). IR (KBr): 3430, 1620, 1601, 1534, 1498, 1444, 1385, 1348, 1319, 1252, 1170, 1109, 1044, 820, 758, 734, 686 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.45 (3H, t, *J*=7.0 Hz), 4.09 (2H, q, *J*=7.0 Hz), 6.75 (1H, d, *J*=2.2 Hz), 6.79 (1H, dd, *J*=2.2, 8.6 Hz), 6.90 (1H, d, *J*=2.2 Hz), 7.29 (1H, tt, *J*=1.2, 7.3 Hz), 7.42 (2H, dd, *J*=7.3, 8.3 Hz), 7.48 (1H, d, *J*=8.6 Hz), 7.62 (2H, dd, *J*=1.2, 8.3 Hz), 8.20 (1H, brs, NH). *Anal.* Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.90; H, 6.33; N, 5.92.

1-Acetyl-7-ethoxy-2,3-dihydroindole (41) from 1-Acetyl-7-hydroxy-2,3-dihydroindole (39) — A mixture of **39** (103.9 mg, 0.59 mmol), K_2CO_3 (813.0 mg, 5.88 mmol), and EtI (0.70 mg, 8.75 mmol) was stirred at rt for 15 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 an oil, which was column-chromatographed on SiO_2 successively with $CHCl_3$–hexane (2:1, v/v) and $CHCl_3$ to give **41** (115.5 mg, 96%). **41**: colorless hard oil. IR (film): 2990, 1654, 1646, 1593, 1486, 1474, 1460, 1379, 1356, 1334, 1275, 1243, 1056 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.43 (3H, t, *J*=7.0 Hz), 2.22 (3H, s), 2.95 (2H, t, *J*=7.6 Hz), 4.09 (2H, q, *J*=7.0 Hz), 4.21 (2H, t, *J*=7.6 Hz), 6.80 (1H, d, *J*=8.3 Hz), 6.87 (1H, dd, *J*=1.0, 7.3 Hz), 7.04 (1H, dd, *J*=7.3, 8.3 Hz). High-resolution MS *m/z*: Calcd for $C_{12}H_{15}NO_2$: 205.1103. Found: 205.1101.

7-Ethoxy-2,3-dihydroindole (42) from 41 — An aqueous 8% NaOH (5 mL) was added to a solution of **41** (46.8 mg, 0.23 mmol) in MeOH (5 mL) and the mixture was refluxed for 2 h with stirring. The resultant solution was cooled to rt, and extracted with EtOAc. 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 EtOAc–hexane (1:10, v/v) to give **42** (34.3 mg, 92%). **42**: colorless oil. IR (film): 2985, 2935, 2850, 1612, 1592, 1490, 1472, 1391, 1292, 1270, 1250, 1204, 1115, 1071 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.40 (3H, t, *J*=7.0 Hz), 3.06 (2H, t, *J*=8.4 Hz), 3.57 (2H, t, *J*=8.4 Hz), 4.04 (2H, q, *J*=7.0 Hz), 6.63 (1H,

d, *J*=7.5 Hz), 6.67 (1H, dd, *J*=7.1, 7.5 Hz), 6.78 (1H, d, *J*=7.1 Hz). High-resolution MS *m/z*: Calcd for $C_{10}H_{13}NO$: 163.0997. Found: 163.0995.

7-Ethoxy-1-methoxyindole (43) from 42 — A solution of $Na_2WO_4 \cdot 2H_2O$ (24.9 mg, 0.07 mmol) in H_2O (0.3 mL) was added to a solution of **42** (59.9 mg, 0.37 mmol) in MeOH (2 mL) and then a solution of 30% aq. H_2O_2 (435.5 mg, 3.84 mmol) in MeOH (1 mL) was added to the reaction mixture under ice cooling. After stirring at rt for 30 min, K_2CO_3 (254.5 mg, 1.84 mmol) and a solution of Me_2SO_4 (97.8 mg, 0.75 mmol) in MeOH (1 mL) were added. The mixture was stirred at rt for 1 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 leave an oil, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:99, v/v) to give **43** (43.3 mg, 62%). **43**: colorless oil. IR (film): 2985, 2940, 1611, 1578, 1517, 1476, 1432, 1358, 1291, 1260, 1113, 1082, 1057, 1036, 967, 777, 710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.52 (3H, t, *J*=7.0 Hz), 4.11 (3H, s), 4.21 (2H, q, *J*=7.0 Hz), 6.28 (1H, d, *J*=3.4 Hz), 6.67 (1H, d, *J*=7.8 Hz), 6.99 (1H, t, *J*=7.8 Hz), 7.16 (1H, d, *J*=7.8 Hz), 7.18 (1H, d, *J*=3.4 Hz). High-resolution MS *m/z*: Calcd for $C_{11}H_{13}NO_2$: 191.0946. Found: 191.0945.

7-Ethoxy-2-iodo-1-methoxyindole (44) from 43 — A solution of 1.58 M BuLi in hexane (0.45 mL, 0.71 mmol) was added drop wise to a solution of **43** (89.5 mg, 0.47 mmol) in THF (4 mL) under nitrogen atmosphere at –18 °C. The solution was stirred at –18 °C for 30 min and then a solution of I_2 (116.8 mg, 0.46 mmol) in THF (2 mL) was added drop wise over 5 min. The mixture was stirred at –18 °C for further 30 min. After addition of H_2O, the whole was extracted with EtOAc. The extract was washed with aqueous 10% $Na_2S_2O_3$ and 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 (1:10, v/v) to give **44** (108.2 mg, 73%) and unreacted **43** (21.3 mg, 24%) in the order of elution. **44**: colorless hard oil. IR (film): 2990, 2945, 1607, 1571, 1508, 1458, 1404, 1387, 1331, 1294, 1253, 1112, 1081, 1055 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.52 (3H, t, *J*=7.0 Hz), 4.09 (3H, s), 4.20 (2H, q, *J*=7.0 Hz), 6.55 (1H, s), 6.62 (1H, d, *J*=7.8 Hz), 6.97 (1H, t, *J*=7.8 Hz), 7.06 (1H, d, *J*=7.8 Hz). High-resolution MS *m/z*: Calcd for $C_{11}H_{12}NO_2I$: 316.9913. Found: 316.9915.

7-Ethoxy-1-methoxy-2-phenylindole (45) from 44 — A mixture of **44** (55.5 mg, 0.18 mmol), Ph_4Sn (148.8 mg, 0.35 mmol), NaOAc (28.6 mg, 0.35 mmol), and $Pd(OAc)_2$ (8.0 mg, 0.036 mmol) in DMF (5 mL) was heated at 100 °C for 30 min with stirring. After evaporation of the solvent, the residue was column-chromatographed repeatedly on SiO_2 with $CHCl_3$ and EtOAc–hexane (1:99, v/v) to give **45** (23.8 mg, 51%). **45**: mp 107—108 °C (colorless prisms, recrystallized from hexane). IR (KBr): 2930, 2875, 1580, 1572, 1502, 1472, 1256, 1202, 1110, 1082, 967 769, 721, 699 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.51 (3H, t, *J*=7.0 Hz), 3.72 (3H, s), 4.22 (2H, q, *J*=7.0 Hz), 6.52 (1H, s), 6.74 (1H, d, *J*=7.9 Hz), 6.98 (1H, t, *J*=7.9 Hz), 7.11 (1H, d, *J*=7.9 Hz), 7.36 (1H, tt, *J*=1.2, 7.3 Hz), 7.45 (2H, dd, *J*=7.3, 8.3 Hz), 7.81 (2H, dd,

J=1.2, 8.3 Hz). *Anal.* Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.53; H, 6.43; N, 5.21.

7-Ethoxy-2-phenylindole (14) from 45 — A suspension of **45** (29.5 mg , 0.11 mmol) and 10% Pd on charcoal (18.5 mg, 0.017 mmol) in MeOH (5 mL) was stirred at rt for 1 h under hydrogen atmosphere. After the catalyst was filtered off, the solvent was evaporated under reduced pressure to leave a solid, which was column-chromatographed on SiO_2 with $CHCl_3$–hexane (1:2, v/v) to give **14** (22.4 mg, 86%). **14**: mp 133.5—134 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 3815, 1579, 1482, 1450, 1438, 1392, 1330, 1314, 1257, 1116, 1081, 772, 731 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.52 (3H, t, *J*=7.0 Hz), 4.24 (2H, q, *J*=7.0 Hz), 6.64 (1H, d, *J*=7.8 Hz), 6.80 (1H, d, *J*=2.2 Hz), 7.01 (1H, t, *J*=7.8 Hz), 7.22 (1H, d, *J*=7.8 Hz), 7.31 (1H, tt, *J*=1.2, 7.3 Hz), 7.44 (2H, dd, *J*=7.3, 8.3 Hz), 7.70 (2H, dd, *J*=1.2, 8.3 Hz), 8.56 (1H, brs, NH). MS *m/z*: 237 (M^+). *Anal.* Calcd for $C_{16}H_{15}NO \cdot 1/8H_2O$: C, 80.22; H, 6.42; N, 5.85. Found: C, 80.49; H, 6.39; N, 5.86.

6-Hydroxy-2-phenylindole (46) from 6 (Product Y) — An aqueous 8% NaOH (5 mL) was added to a solution of **6** (16.1 mg, 0.04 mmol) in MeOH (5 mL) and the mixture was refluxed for 3 h with stirring. After the resultant solution was made acidic by adding aqueous 6% HCl under ice cooling, the whole was extracted with $CHCl_3$–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an solid, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:3, v/v) to give **46** (8.9 mg, 96%). **46**: mp 222—227 °C (colorless amorphous, recrystallized from Et_2O). IR (KBr): 3395, 1624, 1594, 1580, 1541, 1512, 1485, 1455, 1450, 1416, 1367, 1121, 1288, 1270, 1158, 959, 906, 841, 817, 764 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 6.52 (1H, dd, *J*=8.3, 2.2 Hz), 6.74 (1H, d, *J*=2.2 Hz), 6.77 (1H, d, *J*=2.2 Hz), 7.25 (1H, t, *J*=7.4 Hz), 7.29 (1H, d, *J*=8.3 Hz), 7.41 (2H, dd, *J*=8.3, 7.4 Hz), 7.76 (2H, d, *J*=8.3 Hz), 8.99 (1H, s, OH, disappeared on addition of D_2O), 11.11 (1H, brs, NH). *Anal.* Calcd for $C_{14}H_{11}NO \cdot 1/4H_2O$: C, 78.67; H, 5.42; N, 6.55. Found: C, 78.52; H, 5.17; N, 6.51.

6-Ethoxy-2-phenylindole (13) from 46 — A mixture of **46** (8.3 mg, 0.04 mmol), K_2CO_3 (55.1 mg, 0.4 mmol), and EtI (0.05 mL, 0.625 mmol) was stirred at rt for 5 h. After addition of H_2O, the whole was extracted with $CHCl_3$–MeOH (95:5, v/v). 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 $CHCl_3$–hexane (1:1, v/v) to give **13** (7.1 mg, 75%).

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