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

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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. In order to examine this 1-hydroxyindole hypotheses, we attempted the photochemical reaction of 1-ethoxy-2-phenylindole (2), derived from 1-hydroxy-2-phenylindole (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). 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. On the other hand, upon reaction of 1 with tosyl chloride, 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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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$_2$O reflux or NaH, AcCl).

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

![Scheme 1](image-url)

![Scheme 2](image-url)
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-carbaldehyde10 (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

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Scheme 3
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Reduction of 20 with NaBH3CN in AcOH11 afforded 4-ethoxy-2,3-dihydroindole (21) in 97% yield. Application of our 1-methoxyindole synthetic method to 21, thus oxidation with 30% aqueous H2O2 in the presence of a catalytic amount of Na2WO4·5H2O,8 followed by methylation with dimethyl sulfate,8 produced 4-ethoxy-1-methoxyindole (22) in 51% yield. Regioselective lithiation12 of 22 with n-BuLi and quenching of the resultant 2-lithio species with I2 afforded 4-ethoxy-2-iodo-1-methoxyindole (23) in 83% yield. The palladium catalyzed Stille coupling13 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 reaction2,14 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). 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. 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 BBr3 afforded 5-hydroxy-2-phenylindole (27) in 92% yield. Subsequent ethylation of 27 with EtI and K2CO3 produced the authentic 5-ethoxy-2-phenylindole (12) in 89% yield.

![Scheme 4](image-url)

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 K2CO3 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 to 34 produced 6-ethoxy-1-methoxyindole (35) in 44% yield. Regioselective lithiation of 35 with n-BuLi, followed by the reaction with I2, furnished 6-ethoxy-2-ido-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).

\[
\begin{align*}
\text{H} & \quad \text{HNO}_2 & \quad 36\% & \quad \text{H}_2 & \quad 10\% \text{ Pd/C} & \quad 89\% \\
\text{Ac} & \quad \text{EtI} & \quad 86\% & \quad \text{Ph} & \quad \text{Pd(OAc)}_2 & \quad 89\% \\
\text{Ac} & \quad \text{8\% NaOH} & \quad 95\% & \quad \text{Ac} & \quad \text{Ph}_4\text{Sn} & \quad 44\%
\end{align*}
\]

\[\text{Scheme 5}\]

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\(_2\)CO\(_3\) 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.

\[
\begin{align*}
\text{Ac} & \quad 1) \text{Ti(OOCOCF}_3\text{)}_3 & \quad 42\% & \quad \text{Ac} & \quad \text{EtI} & \quad 96\% \\
\text{Ac} & \quad \text{8\% NaOH} & \quad 92\% & \quad \text{Ac} & \quad \text{Ph}_4\text{Sn} & \quad 62\% \\
\text{Ac} & \quad \text{1) n-BuLi} & \quad 73\% & \quad \text{Ac} & \quad \text{Ph}_4\text{Sn} & \quad 73\%
\end{align*}
\]

\[\text{Scheme 6}\]

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$_2$CO$_3$ 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](image)

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$_2$O$_3$, 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$_2$O$_3$ 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
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$_2$PO$_4$, H$_2$O (623.2 mg, 4.00 mmol) in H$_2$O (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$_2$SO$_4$, 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-$d_6$) $\delta$: 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$_2$O), 11.97 (1H, brs, disappeared on addition of D$_2$O). 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$_2$SO$_4$, 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$_3$) $\delta$: 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), 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$_2$O, 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$_2$SO$_4$, 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-$d_6$) $\delta$: 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$_2$O), 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_4·2H_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. ^1H-NMR (CDCl₃): 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 I₂ (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 H₂O and brine, the whole was extracted with EtOAc. The extract was washed with aqueous 10% Na₂S₂O₃ and brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO₂ with CHCl₃–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. ^1H-NMR (CDCl₃): 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), Ph₄Sn (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 SiO₂ 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. ^1H-NMR (CDCl₃): 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.
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 SiO₂ with EtOAc–hexane (1:20, v/v) to give 11 (33.0 mg, 97%).

11: mp 111—112 °C (colorless fine needles, recrystallized from CHCl₃–hexane). IR (KBr): 3405, 1604, 1589, 1487, 1474, 1454, 1437, 1365, 1343, 1263, 1240, 1181, 1124, 1102, 773, 764 cm⁻¹. ¹H-NMR (CDCl₃): 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 D₂O). MS m/z: 237 (M⁺). Anal. Calcd for C₁₆H₁₅NO ·1/₄ H₂O: 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 SiO₂ 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. ¹H-NMR (CDCl₃): 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 C₁₅H₁₃NO: 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 BBr₃ in heptane (1.21 mL, 1.21 mmol) was added drop wise to a solution of 30 (26.9 mg, 0.12 mmol) in CHCl₃ (5 mL) under ice cooling. The solution was stirred at rt for 1 h. After addition of H₂O under ice cooling, the whole was extracted with CHCl₃–MeOH (95:5, v/v). The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave a solid, which was column chromatographed on SiO₂ with CHCl₃ 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 CHCl₃–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. ¹H-NMR (DMSO-d₆): 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 D₂O), 11.19 (1H, brs, disappeared on addition of D₂O). Anal. Calcd for C₁₄H₁₁NO: 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), K₂CO₃ (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 H2O under ice cooling, the whole was extracted with CHCl3–MeOH (95:5, v/v). The extract was washed with brine, dried over Na2SO4, and evaporated under reduced pressure to leave a solid, which was column-chromatographed on SiO2 with CHCl3–hexane (1:1, v/v) to give 12 (17.6 mg, 89%). 12: mp 145—145.5 °C (colorless prisms, recrystallized from CHCl3–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. 1H-NMR (CDCl3): 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 C16H15NO: 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 H2O (10 mL) and concentrated H2SO4 (5 mL) was cooled to 0—5 °C. A solution of NaNO2 (164.5 mg, 2.38 mmol) in H2O (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 CHCl3 (10 mL) and cooled H2O (10 mL). The organic layer was added to hot H2O (300 mL), and the solution was heated to 80 °C for 5 min. The mixture was cooled to rt, and extracted with CHCl3–MeOH (95:5, v/v). The extract was washed with brine, dried over Na2SO4, and evaporated under reduced pressure to leave a solid, which was column-chromatographed on SiO2 with CHCl3–MeOH (97:3, v/v) to give 32 (35.4 mg, 36%). 32: mp 274—279 °C (colorless fine needles, recrystallized from CHCl3–MeOH). IR (KBr): 3130, 1629, 1602, 1489, 1448, 1419, 1355, 1272, 1246, 874 cm−1. 1H-NMR (DMSO-d6): 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 D2O). Anal. Calcd for C10H11NO2: 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), K2CO3 (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 H2O under ice cooling, the whole was extracted with CHCl3–MeOH (95:5, v/v). The extract was washed with brine, dried over Na2SO4, and evaporated under reduced pressure to leave a solid, which was column-chromatographed on SiO2 with CHCl3–MeOH (99:1, v/v) to give 33 (60.6 mg, 86%). 33: mp 151.5—152 °C (colorless prisms, recrystallized from CHCl3–hexane). IR (KBr): 1658, 1606, 1590, 1489, 1451, 1438, 1399, 1355, 1315, 1287, 1239, 1192, 1171, 1114 cm−1. 1H-NMR (DMSO-d6): 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 C10H15NO2: 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
(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 CHCl₃. The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO₂ 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. ¹H-NMR (CDCl₃): 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 C₁₀H₁₃NO: 163.0997. Found: 163.0996.

6-Ethoxy-1-methoxyindole (35) from 34 — A solution of Na₂WO₄·2H₂O (11.0 mg, 0.03 mmol) in H₂O (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% H₂O₂ (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 CH₂N₂ in Et₂O was added. The mixture was stirred at rt for 10 min. After addition of H₂O, the whole was extracted with CHCl₃–MeOH (95:5, v/v). The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO₂ with CHCl₃–hexane (1:2, v/v) to give 35 (12.6 mg, 44%). 35: colorless hard oil. IR (film): 2990, 1624, 1493, 1472, 1454, 1442, 1392, 1317, 1230, 1206 cm⁻¹. ¹H-NMR (CDCl₃): 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 C₁₁H₁₃NO₂: 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 I₂ (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 H₂O, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO₂ with CHCl₃–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. ¹H-NMR (CDCl₃): 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 C₁₁H₁₃NO₂: 191.0947. Found: 191.0945.

6-Ethoxy-1-methoxy-2-phenylindole (37) from 36 — A mixture of 36 (11.1 mg, 0.04 mmol), Ph₄Sn (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 SiO2 with CHCl3–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 CCl4-hexane). IR (KBr): 2975, 2940, 1615, 1599, 1572, 1487, 1480, 1470, 1439, 1344, 1326, 1233, 1206, 1189, 1106, 1050, 1022, 960, 810, 759, 733, 696 cm⁻¹. ¹H-NMR (CDCl₃): 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 C₁₇H₁₇NO₂: 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 SiO₂ with CHCl₃–hexane (1:1, v/v) to give 13 (6.1 mg, 89%). 13: mp 126—127 °C (colorless prisms, recrystallized from CCl₄-hexane). IR (KBr): 3430, 1620, 1601, 1534, 1498, 1444, 1385, 1348, 1319, 1252, 1170, 1109, 1044, 820, 758, 734, 686 cm⁻¹. ¹H-NMR (CDCl₃): 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 C₁₆H₁₅NO: 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), K₂CO₃ (813.0 mg, 5.88 mmol), and EtI (0.70 mg, 8.75 mmol) was stirred at rt for 15 h. After addition of H₂O, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO₂ successively with CHCl₃–hexane (2:1, v/v) and CHCl₃ 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. ¹H-NMR (CDCl₃): 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 C₁₂H₁₅NO₂: 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 Na₂SO₄, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO₂ 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. ¹H-NMR (CDCl₃): 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, \( J=7.5 \text{ Hz} \), 6.67 (1H, dd, \( J=7.1, 7.5 \text{ Hz} \)), 6.78 (1H, d, \( J=7.1 \text{ Hz} \)). 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_{2}WO_{4} \cdot 2H_{2}O (24.9 mg, 0.07 mmol) in H_{2}O (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_{2}O_{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_{2}CO_{3} (254.5 mg, 1.84 mmol) and a solution of Me_{2}SO_{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_{2}O, the whole was extracted with CHCl_{3}. The extract was washed with brine, dried over Na_{2}SO_{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\(_{3}\)): 1.52 (3H, t, \( J=7.0 \text{ Hz} \)), 4.11 (3H, s), 4.21 (2H, q, \( J=7.0 \text{ Hz} \)), 6.28 (1H, d, \( J=3.4 \text{ Hz} \)), 6.67 (1H, d, \( J=7.8 \text{ Hz} \)), 6.99 (1H, t, \( J=7.8 \text{ Hz} \)), 7.16 (1H, d, \( J=7.8 \text{ Hz} \)), 7.18 (1H, d, \( J=3.4 \text{ Hz} \)). 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 \(-18^\circ\text{C}\). The solution was stirred at \(-18^\circ\text{C}\) 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 \(-18^\circ\text{C}\) for further 30 min. After addition of H_{2}O, the whole was extracted with EtOAc. The extract was washed with aqueous 10% Na_{2}S_{2}O_{3} and brine, dried over Na_{2}SO_{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, \( J=7.0 \text{ Hz} \)), 4.11 (3H, s), 4.21 (2H, q, \( J=7.0 \text{ Hz} \)), 6.28 (1H, d, \( J=3.4 \text{ Hz} \)), 6.67 (1H, d, \( J=7.8 \text{ Hz} \)), 6.99 (1H, t, \( J=7.8 \text{ Hz} \)), 7.06 (1H, d, \( J=3.4 \text{ Hz} \)). High-resolution MS \( m/z \): Calcd for C_{11}H_{12}NO_{2}I: 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\(_{4}\)Sn (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\(_{3}\)OD): δ: 1.51 (3H, t, \( J=7.0 \text{ Hz} \)), 3.72 (3H, s), 4.22 (2H, q, \( J=7.0 \text{ Hz} \)), 6.52 (1H, s), 6.74 (1H, d, \( J=7.9 \text{ Hz} \)), 6.98 (1H, t, \( J=7.9 \text{ Hz} \)), 7.11 (1H, d, \( J=7.9 \text{ Hz} \)), 7.36 (1H, tt, \( J=1.2, 7.3 \text{ Hz} \)), 7.45 (2H, dd, \( J=7.3, 8.3 \text{ Hz} \)), 7.81 (2H, dd,
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 SiO2 with CHCl3–hexane (1:2, v/v) to give 14 (22.4 mg, 86%). 14: mp 133.5—134 °C (colorless prisms, recrystallized from CHCl3–hexane). IR (KBr): 3815, 1579, 1482, 1450, 1438, 1392, 1330, 1257, 1116, 1081, 772, 731 cm⁻¹. ¹H-NMR (CDCl3): 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 C₁₇H₁₇NO₂: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.53; H, 6.43; N, 5.21.

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 CHCl₃–MeOH (95:5, v/v). The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave an solid, which was column-chromatographed on SiO₂ with EtOAc–hexane (1:3, v/v) to give 46 (8.9 mg, 96%). 46: mp 222—227 °C (colorless amorphous, recrystallized from Et₂O). IR (KBr): 3395, 1624, 1594, 1580, 1541, 1512, 1485, 1455, 1450, 1416, 1367, 1121, 1288, 1270, 1158, 959, 906, 841, 817, 764 cm⁻¹. ¹H-NMR (CDCl₃): 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 D₂O), 11.11 (1H, brs, NH). Anal. Calcd for C₁₄H₁₁NO·1/4H₂O: C, 80.22; H, 6.42; N, 5.85. Found: C, 80.49; H, 6.39; N, 5.86.

6-Ethoxy-2-phenylindole (13) from 46 — A mixture of 46 (8.3 mg, 0.04 mmol), K₂CO₃ (55.1 mg, 0.4 mmol), and EtI (0.05 mL, 0.625 mmol) was stirred at rt for 5 h. After addition of H₂O, the whole was extracted with CHCl₃–MeOH (95:5, v/v). The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave a solid, which was column-chromatographed on SiO₂ with CHCl₃–hexane (1:1, v/v) to give 13 (7.1 mg, 75%).

REFERENCES AND NOTES


