Novel formations of 6-mesyloxytryptamines and 1-substituted 3a-(4-chlorobutoxy)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indoles in the reaction of nb-substituted 1-hydroxytryptamines with mesyl chloride

NOVEL FORMATIONS OF 6-MESYLOXYTRYPTAMINES AND 1-SUBSTITUTED 3a-(4-CHLOROBUTOXY)-1,2,3,3a,8,8a-HEXAHYDROPYRROLO-[2,3-*b*]INDOLES IN THE REACTION OF *N*b-SUBSTITUTED 1-HYDROXYTRYPTAMINES WITH MESYL CHLORIDE[1]

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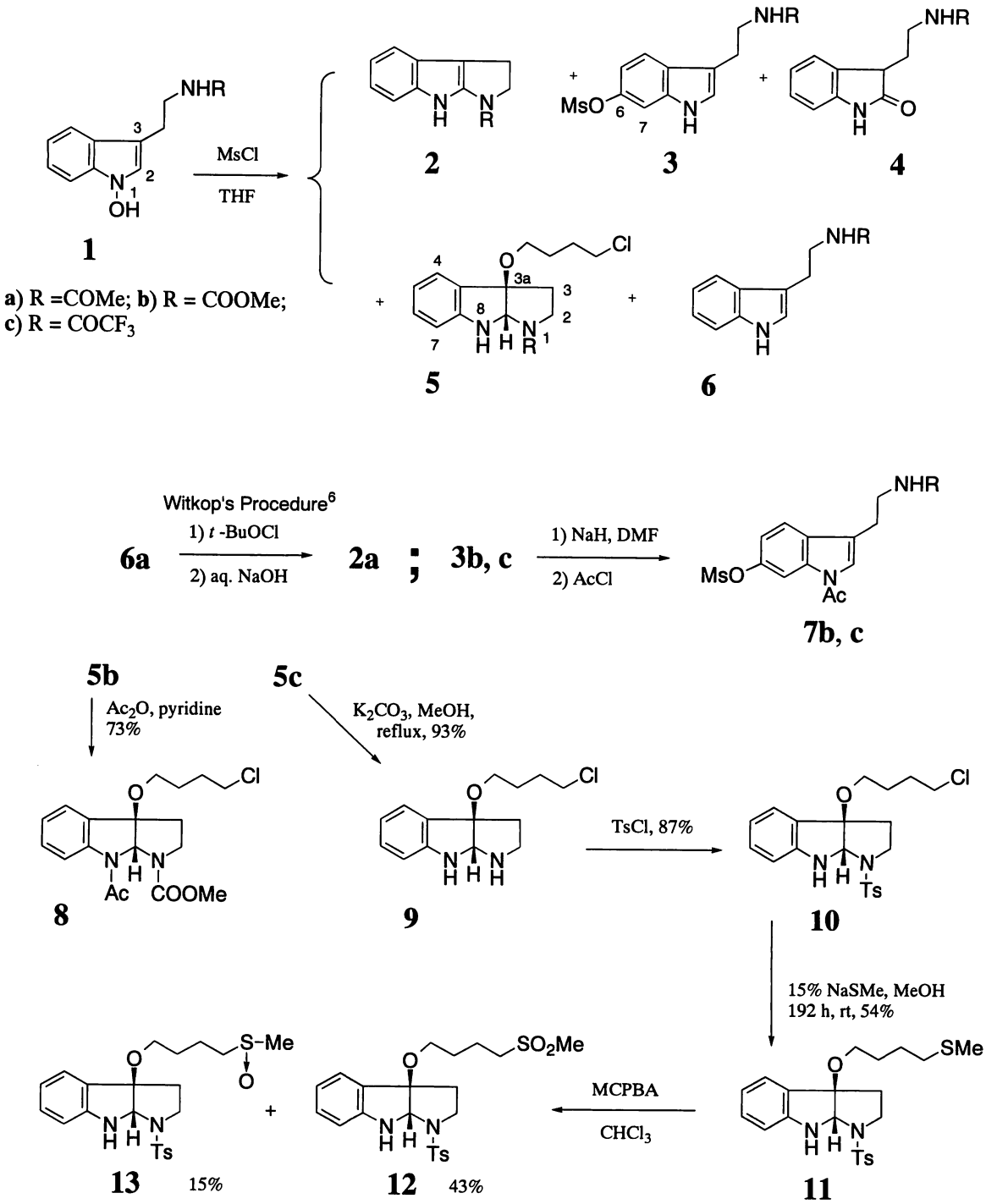
Abstract — Formations of 6-mesyloxytryptamines and 1-substituted 3a-(4-chlorobutoxy)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indoles were newly found in the reactions of *N*b-substituted 1-hydroxytryptamines with mesyl chloride in THF. The latter compounds suggest that the intermediate indol-3-yl cations can trap THF and cleave the ether bond.

We have thus far disclosed that 1-hydroxyindoles[2,3,4] undergo six types of reactions such as 1) regioselective nucleophilic substitution to give 5-substituted indoles,[4] 2) formation of pyrrolo[2,3-*b*]indoles,[4a] 3) formation of kabutanes,[4e] 4) dimerization to afford 2,2'-bisindole derivatives,[5] 5) dehydroxylation to give indoles,[4] and 6) formation of 3a,3a'-bispyrrolo[2,3-*b*]indoles[1b] depending on reaction conditions and structures of 1-hydroxyindoles. Now we wish to report additional novel findings observed in the reactions of *N*b-substituted 1-hydroxytryptamines with mesyl chloride (MsCl).

The reaction of *N*b-acetyl-1-hydroxytryptamine (**1a**) with MsCl in THF in the presence of triethylamine at 0 °C produced 1-acetyl-1,2,3,8-tetrahydropyrrolo[2,3-*b*]indole (**2a**), *N*b-acetyl-6-mesyloxytryptamine (**3a**), *N*b-acetyl-2,3-dihydro-2-oxotryptamine (**4a**), 1-acetyl-3a-(4-chlorobutoxy)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (**5a**), and *N*b-acetyltryptamine (**6a**) in 35, 4, 5, 7, and 2% yields, respectively. Under similar reaction conditions, 1-hydroxy-*N*b-methoxycarbonyltryptamine (**1b**) provided **3b**, **4b**, and **5b** in 7, 34, and 9% yields, respectively, but formation of **2b** was not observed. In the case of *N*b-trifluoroacetyl-1-hydroxytryptamine (**1c**), **2c**, **3c**, **4c**, and **5c** were isolated in 45, 8, 4, and 6% yields, respectively. It is interesting to note that the yield of **2** increases, while the yield of **4** decreases, in the order of electron withdrawing ability of *N*b-substituents (COOMe<COMe<$COCF_3$). These data seem to suggest that stability of **2** governs the quantity of **4**, which is probably formed by hydrolysis of **2**.

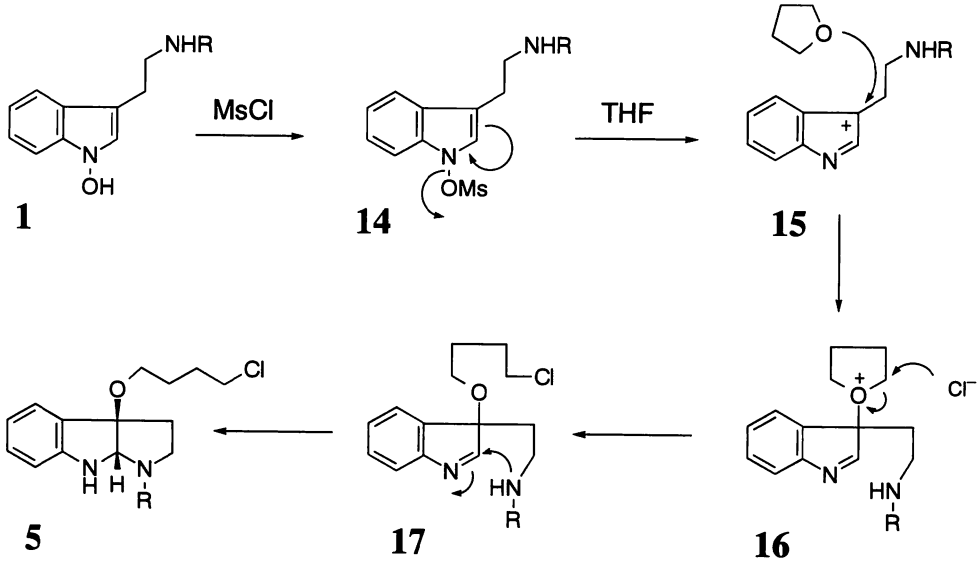
Structural determinations were carried out as follows. The compound (**2a**) was identical with the authentic sample prepared according to Witkop's procedure[6] by reacting **6a** with *t*-butyl hypochlorite, followed by treatment with aqueous NaOH. The structures of **2b** and **2c** were confirmed by comparing their spectral data with those of **2a**. On the other hand, compounds (**3b** and **3c**) were transformed to 1-acetyl compounds (**7b** and **7c**) in 71 and 71% yields, respectively, by treatment with NaH in DMF, followed by reaction with AcCl. In their ^{1}H-NMR spectra, *meta*-coupled C(7)-protons are deshielded by 1 ppm compared with those

Scheme 1


NHR
MsCl
THF
1
a) R =COMe; b) R = COOMe;
c) R = COCF3
2
3
4
5
6
Witkop's Procedure[6]
1) t -BuOCl
2) aq. NaOH
6a
2a ; 3b, c
1) NaH, DMF
2) AcCl
7b, c
5b
Ac2O, pyridine
73%
5c
K2CO3, MeOH,
reflux, 93%
8
9
TsCl, 87%
10
15% NaSMe, MeOH
192 h, rt, 54%
11
MCPBA
CHCl3
13 15%
12 43%

of **3b** and **3c**, proving that these compounds are 6-substituted indoles. The structures of compounds (**4a-c**) and **6a** were determined by their spectral data.

Scheme 2



Although structures of **5a-c** were deduced by spectral data, there remained a little worry because we failed to substitute the chlorine atom on the butoxy side chain for a hydroxy or acetoxy group under various reaction conditions with NaI-bases, NaOAc, and AgOAc. The presence of N(8)-H in **5b** was confirmed by obtaining acetyl derivative (**8**) in 73% yield by the reaction with Ac_2O-pyridine. Introduced acetyl group at the 8-position of **8** showed deshielding anisotropy effect on the C(7)-proton by 1 ppm.

In order to determine the presence of the chlorobutoxy side chain in **5c**, its trifluoroacetyl group was first removed off in 93% yield with K_2CO_3 in refluxing MeOH affording **9**, which was then derived to stable sulfonamide derivative (**10**) in 87% yield by treatment with TsCl. The reaction of **10** with 15% aqueous NaSMe in MeOH was a slow process and after 192 h at room temperature thioether compound (**11**) was isolated in 54% yield together with 32% yield of recovery. When the reaction was performed at elevated temperature, the yield of **11** dropped significantly. Oxidation of **11** with *m*-chloroperbenzoic acid in $CHCl_3$ produced sulfone (**12**) and sulfoxide (**13**) as a mixture of diastereoisomers in 43 and 15% yields, respectively. The series of reactions and comparisons of spectral data of **9** through **13** clearly proved the existence of four carbon unit in their structures.

Formations of **5a-c** are interesting to note and the reaction mechanism might be explained as shown in Scheme 2. Departure of the mesyloxy group from the initially formed 1-mesyloxytryptamine (**14**) would generate intermediate indol-3-yl cation (**15**), which then traps THF as an oxonium ion (**16**). Subsequent chloride attack on the carbon atom connected to the positive oxygen atom would cleave ether ring to build chlorobutoxy side chain on **17**. Final cyclization of *N*b-nitrogen to the imine carbon atom would result in

the formation of pyrrolo[2,3-*b*]indole structure. It is worthy to note as well that 6-substituted indoles (**3a-c**) were observed for the first time in the reaction of 1-hydroxyindoles. The mechanism of their formations would be explained by the [3,7] sigmatropic rearrangement of the intermediate (**14**).

In summary, we have discovered interesting reactions characteristic to 1-hydroxyindole structure.[3] Reactions of 1-hydroxyindoles with *p*-toluenesulfonic acid and *p*-toluenesulfonyl chloride have also exhibited another novel results and they will be reported in due course. Applications of the present results and improvement of the yields are in progress.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were determined with a Shimadzu IR-420 spectrophotometer, and ^{1}H-NMR spectra with a JEOL GSX-500 spectrometer, with tetramethylsilane as an internal standard. MS spectra were recorded on a JEOL SX-102A spectrometer. Column chromatography was performed on silica gel (SiO_2, 100-200 mesh, from Kanto Chemical Co. Inc.).

1-Acetyl-1,2,3,8-tetrahydropyrrolo[2,3-*b*]indole (2a), *N*b-acetyl-6-mesyloxytryptamine (3a), *N*b-acetyl-2,3-dihydro-2-oxotryptamine (4a), *cis*-1-acetyl-3a-(4-chlorobutoxy)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (5a), and *N*b-acetyltryptamine (6a) from *N*b-acetyl-1-hydroxytryptamine (1a) — A solution of MsCl (250.3 mg, 2.185 mmol) in dry THF (1.0 mL) was added to a solution of **1a** (299.5 mg, 1.374 mmol) in dry THF (10.0 mL) and dry Et_3N (1.0 mL) and stirring was continued for 6 h at 0 °C. 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 recrystallized twice from $CHCl_3$ – hexane to give **2a** (95.6 mg, 35%). The mother liquor was column-chromatographed repeatedly on SiO_2 successively with $CHCl_3$, $CHCl_3$–MeOH (99:1, v/v), and AcOEt to give **5a** (30.5 mg, 7%), **6a** (6.7 mg, 2%), **3a** (16.0 mg, 4%), and **4a** (15.0 mg, 5%) in the order of elution. **2a**: mp 221 °C (decomp, colorless powder recrystallized from MeOH–CH_2Cl_2) (lit.,[6] mp 243—244 °C; in our hand, authentic sample prepared according to Witkop's procedure[6] melted at 221 °C with decomp). IR (KBr): 3300, 1643, 1610, 1585, 1530, 1440, 1350, 1325, 1215, 970, 735, 710 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.13 (3H, s), 3.09 (2H, t, *J*=7.5 Hz), 4.48 (2H, t, *J*=7.5 Hz), 6.90 (1H, dt, *J*=2.0 and 7.5 Hz), 6.94 (1H, dt, *J*=2.0 and 7.5 Hz), 7.23 (1H, d, *J*=7.5 Hz), 7.33 (1H, d, *J*=7.5 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{12}N_2O$: 200.0950. Found: 200.0944 (M^+). *Anal.* Calcd for $C_{12}H_{12}N_2O \cdot 2/3H_2O$: C, 67.92; H, 5.66; N, 13.20. Found: C, 67.68; H, 5.85; N, 12.83. **3a**: mp 143—144 °C (colorless prisms recrystallized from AcOEt). IR (KBr): 3390, 3255, 1631, 1552, 1364, 1174, 974, 873, 815, 528 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.91 (3H, s), 2.93 (2H, dt, *J*=0.6 and 7.3 Hz), 3.12 (3H, s), 3.45 (2H, t, *J*=7.3 Hz), 6.98 (1H, dd, *J*=8.8 and 2.2 Hz), 7.16 (1H, s), 7.31 (1H, dd, *J*=2.2 and 0.5Hz), 7.59 (1H, dd, *J*=8.8 and 0.5 Hz). *Anal.* Calcd for $C_{13}H_{16}N_2O_4S$: C, 52.69; H, 5.44; N, 9.45. Found: C, 52.68; H, 5.46; N, 9.27. **4a**: mp 146—147 °C (colorless prisms recrystallized from MeOH–CH_2Cl_2). IR (KBr): 3300, 3060, 1693, 1618, 1543, 1225, 940, 740 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.88 (3H, s), 2.00—2.08 (1H, m), 2.10—2.18 (1H,m), 3.21—3.29 (1H, m), 3.32—3.40 (1H, m), 3.49 (1H, t, *J*=6.3 Hz), 6.89 (1H, d, *J*=7.5 Hz), 7.02 (1H, dt, *J*=1.3 and 7.5 Hz), 7.20 (1H, t, *J*=7.5

Hz), 7.32 (1H, d, *J*=7.5 Hz). MS *m/z*: 218 (M^+). *Anal.* Calcd for $C_{12}H_{14}N_2O_2$: C, 66.03; H, 6.47; N, 12.84. Found: C, 66.05; H, 6.53; N, 12.80. **5a**: mp 107—108 °C (colorless prisms recrystallized from AcOEt). IR (KBr): 3323, 2950, 2945, 2898, 1617, 1609, 1439, 1313, 1197, 1101, 1085, 1070, 750 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.55—1.65 (2H, m), 1.75—1.83 (2H, m), 2.03 (3H, s), 2.40—2.54 (2H, m), 3.14 (1H, dt, *J*=9.3 and 6.4 Hz), 3.25 (1H, dt, *J*=6.4 and 10.5 Hz), 3.31 (1H, dt, *J*=9.3 and 6.4 Hz), 3.48 (2H, t, *J*=7.0 Hz), 3.68 (1H, ddd, *J*=10.5, 7.8, and 2.4 Hz), 5.24 (1H, br s, disappeared on addition of D_2O), 5.41 (1H, s), 6.61 (1H, d, *J*=8.0 Hz), 6.81 (1H, ddd, *J*=8.0, 7.5, and 0.8 Hz), 7.18 (1H, ddd, *J*=8.0, 7.5, and 1.2 Hz), 7.21 (1H, br d, *J*=7.5 Hz). MS (EI^+) *m/z*: 311 (MH^+) and 309 (MH^+). *Anal.* Calcd for $C_{16}H_{21}N_2O_2Cl$: C, 62.23; H, 6.85; N, 9.07. Found: C, 62.04; H, 6.87; N, 9.09.

6-Mesyloxy-*N*b-methoxycarbonyltryptamine (3b), 2,3-dihydro-*N*b-methoxycarbonyl-2-oxotryptamine (4b) and *cis*-3a-(4-chlorobutoxy)-1,2,3,3a,8,8a-hexahydro-1-methoxycarbonylpyrrolo[2,3-*b*]indole (5b) from 1-hydroxy-*N*b-methoxycarbonyltryptamine (1b) — A solution of MsCl (427.5 mg, 3.732 mmol) in dry THF (5.0 mL) was added to a solution of **1b** (703.8 mg, 3.008 mmol) in dry THF (22.0 mL) and dry Et_3N (2.7 mL) at 0 °C and stirring was continued for 1 h at 0 °C. 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 an oil, which was column-chromatographed repeatedly on SiO_2 successively with $CHCl_3$, $CHCl_3$ – MeOH (99:1, v/v), and $CHCl_3$ – MeOH – 28% aqueous NH_3 (46:2:0.2, v/v) to give **5b** (87.0 mg, 9%), **3b** (61.3 mg, 7%), and **4b** (239.5 mg, 34%) in the order of elution. **3b**: Colorless oil. IR (film): 3400, 2950, 1703, 1623, 1523, 1458, 1353, 1250, 1175, 1118, 950, 860 cm^{-1}. ^{1}H-NMR (5% CD_3OD–$CDCl_3$) δ: 2.95 (2H, t, *J*=5.6 Hz), 3.14 (3H, s), 3.48 (2H, q, *J*=5.6 Hz), 3.66 (3H, s), 5.10 (1H, br s), 7.00 (1H, dd, *J*=2.5 and 8.8 Hz), 7.10 (1H, s), 7.35 (1H, d, *J*=2.5Hz), 7.58 (1H, d, *J*=8.8 Hz), 9.24 (1H, br s). High resolution MS *m/z*: Calcd for $C_{13}H_{16}N_2O_5S$: 312.0780. Found: 312.0781 (M^+). **4b**: mp 123.5 — 125.0 °C (colorless powder recrystallized from CH_2Cl_2-hexane). IR (KBr): 3390, 3190, 3090, 1695, 1620, 1538, 1466, 1282, 1264, 1232, 1181, 1142, 747 cm^{-1}. ^{1}H-NMR (pyridine-d_5+D_2O, 60°C) δ: 2.21—2.29 (1H, m), 2.29—2.37 (1H, m), 3.57—3.66 (4H, m), 3.67 (3H, s), 7.00 (1H, dd, *J*=7.8 and 7.4 Hz), 7.04 (1H, d, *J*=7.8 Hz), 7.20 (1H, dd, *J*=7.4 and 7.8 Hz), 7.36 (1H, d, *J*=7.4 Hz). MS *m/z*: 234 (M^+). *Anal.* Calcd for $C_{12}H_{14}N_2O_3 \cdot 1/4H_2O$: C, 60.36; H, 6.12; N, 11.73. Found: C, 60.48; H, 5.95; N, 11.61. **5b**: Colorless oil. IR (film): 3350, 2950, 1703 (br), 1613, 1458, 1383, 1305, 1200, 1100, 750 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 90 °C) δ: 1.51—1.59 (2H, m), 1.68—1.76 (2H, m), 2.24—2.37 (2H, m), 3.12 (1H, dt, *J*=8.8 and 5.6 Hz), 3.27 (1H, dt, *J*=8.8 and 5.6 Hz), 3.54 (2H, t, *J*=6.3 Hz), 3.56—3.65 (3H, m), 5.25 (1H, d, *J*=1.9 Hz), 6.24 (1H, br s), 6.60 (1H, d, *J*=6.3 Hz), 6.68 (1H, dt, *J*=1.3 and 6.3 Hz), 7.08 (1H, dt, *J*=1.3 and 6.3 Hz), 7.16 (1H, d, *J*=6.3 Hz). High resolution MS *m/z*: Calcd for $C_{16}H_{21}N_2O_3Cl$: 326.1211 and 324.1241. Found: 326.1225 (M^+) and 324.1243 (M^+).

1-Trifluoroacetyl-1,2,3,8-tetrahydropyrrolo[2,3-*b*]indole (2c), *N*b-trifluoroacetyl-6-mesyloxytryptamine (3c), *N*b-trifluoroacetyl-2,3-dihydro-2-oxotryptamine (4c), and *cis*-3a-(4-chlorobutoxy)-1-trifluoroacetyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (5c) from *N*b-trifluoroacetyl-1-hydroxytryptamine (1c) — A solution of MsCl (653.7 mg, 5.70 mmol) in dry THF (5.0 mL) was added to a solution of **1c** (1.2308 g, 4.53 mmol) in dry THF (35.0 mL) and dry Et_3N (4.0 mL) and stirring was continued for 1 h at 0°C. After

addition of H_2O under ice-cooling, the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a solid, which was recrystallized from CH_2Cl_2-hexane to give **2c** (435.3 mg). The mother liquor was column-chromatographed repeatedly on SiO_2 successively with CH_2Cl_2 and AcOEt–hexane (1:1, v/v) to give additional **2c** (77.5 mg, total 512.8 mg, 45%), **5c** (99.8 mg, 6%) and **3c** (121.1 mg, 8%) and **4c** (46.8 mg, 4%) in the order of elution. **2c**: mp 238—240 °C (decomp, colorless plates recrystallized from CH_2Cl_2–hexane). IR (KBr): 3370, 1670, 1619, 1446, 1351, 1278, 1233, 1203, 1139, 1069, 746 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 3.30 (2H, t, *J*=7.4 Hz), 4.71 (2H, t, *J*=7.4 Hz), 7.15 (1H, dt, *J*=1.6 and 6.9 Hz), 7.18 (1H, dt, *J*=1.6 and 6.9 Hz), 7.36 (1H, dd, *J*=6.9 and 1.6 Hz), 7.42 (1H, dd, *J*=6.9 and 1.6 Hz), 9.11 (1H, br s). High resolution MS *m/z*: Calcd for $C_{12}H_9N_2OF_3$: 254.0665. Found: 254.0662 (M^+). **3c**: mp 114.5—115.5 °C (colorless needles recrystallized from CH_2Cl_2-hexane). IR (KBr): 3430, 3340, 1700, 1563, 1355, 1172, 1119, 976, 952, 870 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 3.04 (2H, t, *J*=6.6 Hz), 3.15 (3H, s), 3.67 (2H, q, *J*=6.6 Hz), 6.37 (1H, br s), 7.05 (1H, d, *J*=8.8 Hz), 7.11 (1H, s), 7.37 (1H, br s), 7.58 (1H, d, *J*=8.8 Hz), 8.26 (1H, br s). High resolution MS *m/z*: Calcd for $C_{13}H_{13}N_2O_4F_3S$: 350.0546. Found: 350.0539 (M^+). **4c**: mp 182.0—182.5 °C (pale beige prisms recrystallized from benzene). IR (KBr): 3275, 1704, 1671, 1472, 1232, 1208, 1174, 752 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.99—2.07 (1H, m), 2.36—2.42 (1H, m), 3.50—3.56 (2H, m), 3.76—3.82 (1H, m), 6.91 (1H, d, *J*=7.5 Hz), 7.10 (1H, t, *J*=7.5 Hz), 7.25 (1H, d, *J*=7.5 Hz), 7.26 (1H, t, *J*=7.5 Hz), 8.18 (2H, br s). High resolution MS *m/z*: Calcd for $C_{12}H_{11}N_2O_2F_3$: 272.0771. Found: 272.0777 (M^+). **5c**: Colorless oil. IR (film): 3370, 2940, 1694, 1612, 1486, 1471, 1255, 1206, 1145, 1101, 1066, 750 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.60—1.69 (2H, m), 1.75—1.83 (2H, m), 2.34—2.41 (1/6H, m), 2.47—2.59 (5/6H, m), 3.15 (5/6H, dt, *J*=8.8 and 6.4 Hz), 3.20 (1/6H, dt, *J*=8.8 and 6.4 Hz), 3.25 (1/6H, dt, *J*=8.8 and 6.4 Hz), 3.30 (5/6H, dt, *J*=8.8 and 6.4 Hz), 3.36 (1H, dt, *J*=6.4 and 11.2 Hz), 3.49 (2H, t, *J*=7.8 Hz), 3.95—3.98 (5/6H, m), 4.14—4.18 (1/6H, m), 5.52 (5/6H, br s), 5.64 (1/6H, br s), 6.65 (1H, d, *J*=7.8 Hz), 6.85 (5/6H, t, *J*=7.8 Hz), 6.86 (1/6H, t, *J*=7.8 Hz), 7.22 (1H, t, *J*=7.8 Hz), 7.23 (1H, d, *J*=7.8 Hz). High resolution MS *m/z*: Calcd for $C_{16}H_{18}N_2O_2ClF_3$: 364.0978 and 362.1007. Found: 364.1003 (M^+) and 362.1022 (M^+).

***cis*-8-Acetyl-3a-(4-chlorobutoxy)-1,2,3,3a,8,8a-hexahydro-1-methoxycarbonylpyrrolo[2,3-*b*]indole (8) from 5b** — Ac_2O (3.5 mL) was added to a solution of **5b** (69.1 mg, 0.213 mmol) in pyridine (7.0 mL) and the mixture was stirred for 48 h at rt. After evaporation of the solvent, H_2O was added to the residue and 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 repeatedly on SiO_2 successively with $CHCl_3$–hexane (1:2, v/v) and $CHCl_3$ to give **8** (56.6 mg, 73%). **8**: Colorless oil. IR (film): 3500, 2970, 1713, 1673, 1453, 1398, 1377, 1105, 760 cm^{-1}. ^1H-NMR (DMSO-d_6, 90°C) δ: 1.50—1.58 (2H, m), 1.65—1.75 (2H, m), 2.32 (1H, dt, *J*=8.8 and 11.3 Hz), 2.42 (1H, m), 2.42 (3H, s), 2.73 (1H, dq, *J*=11.3 and 6.9 Hz), 3.16 (1H, dt, *J*=8.8 and 6.9 Hz), 3.32 (1H, dt, *J*=8.8 and 6.9 Hz), 3.53 (2H, t, *J*=6.9 Hz), 3.64 (3H, s), 3.77 (1H, dd, *J*=8.8 and 11.3 Hz), 5.96 (1H, s), 7.18 (1H, dt, *J*=1.9 and 7.5 Hz), 7.36 (1H, dt, *J*=1.9 and 7.5 Hz), 7.44 (1H, dd, *J*=1.9 and 7.5 Hz), 7.92 (1H, d, *J*=7.5 Hz). High resolution MS *m/z*: Calcd for $C_{18}H_{23}N_2O_4Cl$: 368.1317 and 366.1346. Found: 368.1319 (M^+) and 366.1331 (M^+).

1-Acetyl-6-mesyloxy-*Nb*-methoxycarbonyltryptamine (7b) from 3b— A solution of **3b** (58.8 mg, 0.188 mmol) in dry DMF (5.0 mL) was added to 60% NaH (30.5 mg, 0.763 mmol, washed with dry benzene) at 0 °C with stirring. A solution of AcCl (60.5 mg, 0.771 mmol) in dry DMF (0.5 mL) was added to the resultant solution and the mixture was stirred for 1 h at rt. After addition of H_2O under ice cooling, the whole was extracted with AcOEt. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed repeatedly on SiO_2 successively with $CHCl_3$ and AcOEt to give **7b** (47.0 mg, 71%). **7b**: mp 132.0 °C (colorless powder recrystallized from CH_2Cl_2–hexane). IR (KBr): 3400, 2970, 1695, 1613, 1520, 1360, 1180, 970, 960, 908, 884, 840, 808 cm^{-1}. ^1H-NMR (DMSO-d_6) δ: 2.63 (3H, s), 2.82 (2H, t, *J*=6.3 Hz), 3.32 (2H, q, *J*=6.3 Hz), 3.38 (3H, s), 3.53 (3H, s), 7.30 (1H, dd, *J*=7.5 and 3.1 Hz), 7.68 (1H, d, *J*=7.5 Hz), 7.77 (1H, s), 8.25 (1H, d, *J*=3.1 Hz). MS *m/z*: 354 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2O_6S \cdot 1/4\ H_2O$: C, 50.20; H, 5.20; N, 7.81. Found: C, 50.38; H, 4.97; N, 7.77.

1-Acetyl-6-mesyloxy-*Nb*-trifluoroacetyltryptamine (7c) from 3c — A solution of **3c** (109.6 mg, 0.313 mmol) in dry DMF (2.0 mL) was added to 60% NaH (20.7 mg, 0.518 mmol, washed with dry benzene) at 0 °C with stirring. A solution of AcCl (49.8 mg, 0.634 mmol) in dry DMF (2.0 mL) was added to the resultant solution and the mixture was stirred for 2 h at rt. After addition of H_2O under ice cooling, the whole was extracted with AcOEt. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed repeatedly on SiO_2 with AcOEt-hexane (1:1, v/v) to give unreacted **3c** (19.8 mg, 18%) and **7c** (47.0 mg, 71%) in the order of elution. **7c**: mp 133–134°C (colorless needles recrystallized from CH_2Cl_2–hexane). IR (KBr): 3260, 3100, 1728, 1691, 1568, 1442, 1341, 1326, 1192, 1175, 1154, 894, 807 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.51 (3H, br s), 3.01 (2H, t, *J*=6.3 Hz), 3.20 (3H, s), 3.72 (2H, q, *J*=6.3 Hz), 6.70 (1H, br s), 7.28 (1H, d, *J*=8.7 Hz), 7.31 (1H, s), 7.54 (1H, d, *J*=8.7 Hz), 8.37 (1H, s). High resolution MS *m/z*: Calcd for $C_{15}H_{15}N_2O_5F_3S$: 392.0653. Found: 392.0653 (M^+).

***cis*-3a-(4-Chlorobutoxy)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (9) from 5c** — 20% Aqueous K_2CO_3 (2.0 mL) was added to a solution of **5c** (35.2 mg, 0.097 mmol) in MeOH (2.0 mL) at 0 °C. The mixture was stirred for 15 min at rt. After addition of ice cooled H_2O, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% aqueous NH_3 (46:5:0.5, v/v) to give **9** (24.0 mg, 93%). **9**: Pale brown oil. IR (film): 3250, 2920, 1610, 1483, 1470, 1310, 1103, 1078, 743 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.62—1.68 (2H, m), 1.79—1.85 (2H, m), 2.22—2.28 (2H, m), 2.74—2.82 (1H, m), 3.08—3.12 (1H, m), 3.17 (1H, dt, *J*=9.3 and 6.4 Hz), 3.24 (1H, dt, *J*=9.3 and 6.4 Hz), 3.51 (2H, d, *J*=6.6 Hz), 4.77 (1H, s, disappeared on addition of D_2O), 5.05 (1H, s), 6.59 (1H, d, *J*=6.8 Hz), 6.78 (1H, t, *J*=6.8 Hz), 7.13 (1H, t, *J*=6.8 Hz), 7.17 (1H, t, *J*=6.8 Hz). High resolution MS *m/z*: Calcd for $C_{14}H_{19}N_2OCl$: 268.1156 and 266.1186. Found: 268.1181 (M^+) and 266.1184 (M^+).

***cis*-3a-(4-Chlorobutoxy)-1,2,3,3a,8,8a-hexahydro-1-tosylpyrrolo[2,3-*b*]indole (10) from 9** — *p*-Toluenesulfonyl chloride (10.4 mg, 0.055 mmol) was added to a solution of **9** (12.5 mg, 0.047 mmol) in pyridine (1.0 mL) at 0 °C. The mixture was stirred for 15 min at rt. Evaporation of the solvent under reduced

pressure afforded an oil, which was column-chromatographed on SiO_2 with $CHCl_3$ to give **10** (17.1mg, 87%). **10**: Colorless oil. IR (film): 3385, 2950, 1613, 1483, 1473, 1340, 1160, 820, 753, 665 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.50—1.56 (2H, m), 1.66—1.72 (2H, m), 2.17 (1H, ddd, *J*=8.1, 9.4 and 12.5 Hz), 2.27 (1H, ddd, *J*=3.8, 6.3 and 12.5 Hz), 2.45 (3H, s), 3.08 (1H, dt, *J*=9.4 and 6.3 Hz), 3.15 (1H, dt, *J*=9.4 and 6.3 Hz), 3.21 (1H, ddd, *J*=6.3, 9.4 and 10.0 Hz), 3.41 (1H, ddd, *J*=3.8, 8.1 and 10.0 Hz), 3.43 (2H, t, *J*=6.3 Hz), 4.90 (1H, br s), 5.19 (1H, s), 6.65 (1H, d, *J*=7.5 Hz), 6.80 (1H, dt, *J*=1.3 and 7.5 Hz), 7.13 (1H, d, *J*=7.5 Hz), 7.18 (1H, dd, *J*=1.3 and 7.5 Hz), 7.35 (2H, d, *J*=8.1 Hz), 7.76 (2H, d, *J*=8.1 Hz). High resolution MS *m/z*: Calcd for $C_{21}H_{25}N_2O_3ClS$: 422.1245 and 420.1275. Found: 422.1247 (M^+) and 420.1270 (M^+).

***cis*-3a-(4-Methylthiobutoxy)-1,2,3,3a,8,8a-hexahydro-1-tosylpyrrolo[2,3-*b*]indole (11) from 10** — 15% Aqueous NaSMe (9 mL, 19.3 mmol) was added to a solution of **10** (57.5 mg, 0.137 mmol) in MeOH (4.5 mL) and stirring was continued for 192 h at rt. 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 repeatedly on SiO_2 with CH_2Cl_2–hexane (10:1, v/v) to give unreacted **10** (18.6 mg, 32%) and **11** (31.7mg, 54%) in the order of elution. **11**: Colorless oil. IR (film): 3370, 2930, 1615, 1485, 1470, 1343, 1160, 815, 750, 665 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.47—1.53 (4H, m), 2.05 (3H, s), 2.18 (1H, dt, *J*=12.5 and 7.5 Hz), 2.28 (1H, ddd, *J*=3.8, 6.3 and 12.5 Hz), 2.39 (2H, t, *J*=7.3 Hz), 2.45 (3H, s), 3.03—3.10 (1H, m), 3.11—3.17 (1H, m), 3.20 (1H, dt, *J*=6.3 and 9.7 Hz), 3.41 (1H, ddd, *J*=3.8, 7.5 and 10.6 Hz), 4.89 (1H, br s), 5.20 (1H, s), 6.64 (1H, d, *J*=7.5 Hz), 6.80 (1H, t, *J*=7.5 Hz), 7.14 (1H, d, *J*=7.5 Hz), 7.18 (1H, t, *J*=7.5 Hz), 7.34 (2H, d, *J*=8.1 Hz), 7.76 (2H, d, *J*=8.1 Hz). High resolution MS *m/z*: Calcd for $C_{22}H_{28}N_2O_3S_2$: 432.1541. Found: 432.1540 (M^+).

***cis*-1,2,3,3a,8,8a-Hexahydro-3a-(4-mesylbutoxy)-1-tosylpyrrolo[2,3-*b*]indole (12) and *cis*-1,2,3,3a,8,8a-hexahydro-3a-(4-methylsulfinylbutoxy)-1-tosylpyrrolo[2,3-*b*]indole (13) from 11** — *m*-Chloroperoxybenzoic acid (80%, 23.0 mg, 107 mmol) was added to a solution of **11** (21.9 mg, 0.051 mmol) in $CHCl_3$ (2.0 mL) and the mixture was stirred for 15 min at rt. 10% Aqueous $Na_2S_2O_3$ was added to the reaction mixture under ice cooling and the whole was extracted with AcOEt. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed repeatedly on SiO_2 successively with AcOEt–hexane (3:1, v/v) and MeOH–CH_2Cl_2 (1:99, v/v) to give **12** (10.0 mg, 43%) and **13** (3.3 mg, 15%, a mixture of diastereomers) in the order of elution. **12**: Colorless oil. IR (film): 3370, 2930, 1613, 1483, 1473, 1297, 1163, 1138, 1100, 820, 755, 665 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.52—1.61 (2H, m), 1.78—1.86 (2H, m), 2.18 (1H, ddd, *J*=7.5, 9.4 and 12.5 Hz), 2.29 (1H, ddd, *J*=3.8, 6.3 and 12.5 Hz), 2.53 (3H, s), 2.86 (3H, s), 2.87—2.97 (2H, m), 3.09 (1H, ddd, *J*=5.6, 6.9 and 9.4 Hz), 3.14—3.24 (2H, m), 3.42 (1H, ddd, *J*=3.1, 8.1 and 10.0 Hz), 4.91 (1H, br s), 5.19 (1H, d, *J*=1.3 Hz), 6.65 (1H, d, *J*=7.5 Hz), 6.81 (1H, dt, *J*=1.3 and 7.5 Hz), 7.14 (1H, d, *J*=7.5 Hz), 7.19 (1H, dt, *J*=1.3 and 7.5 Hz), 7.35 (2H, d, *J*=8.1 Hz), 7.76 (2H, d, *J*=8.1 Hz). High resolution MS *m/z*: Calcd for $C_{22}H_{28}N_2O_5S_2$: 464.1440. Found: 464.1441 (M^+). **13** (a mixture of diastereomers, their separation was not easy): Colorless oil. IR (film): 3370, 3250, 2920, 1613, 1483, 1470, 1340, 1162, 1095, 1050 (br), 750, 662 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.50—1.63 (2H, m),

1.64—1.78 (2H, m), 2.19 (1H, ddd, *J*=8.5, 9.8 and 12.5 Hz), 2.29 (1H, ddd, *J*=3.9, 6.3 and 12.5 Hz), 2.45 (3H, s), 2.52 (3/2H, s), 2.53 (3/2H, s), 2.49—2.59 (1H, m), 2.60—2.67 (1H, m), 3.05—3.12 (1H, m), 3.14—3.24 (2H, m), 3.41 (1/2H, ddd, *J*=3.9, 8.5 and 10.0 Hz), 3.42 (1/2H, ddd, *J*=3.9, 8.5 and 10.0 Hz), 4.91 (1H, br s), 5.19 (1H, br s), 6.65 (1H, br d, *J*=8.1 Hz), 6.80 (1/2H, dt, *J*=1.0 and 8.1 Hz), 6.81 (1/2H, dt, *J*=1.0 and 8.1 Hz), 7.13 (1/2H, d, *J*=8.1 Hz), 7.14 (1/2H, d, *J*=8.1 Hz), 7.19 (1H, br t, *J*=8.1 Hz), 7.35 (2H, br d, *J*=8.5 Hz), 7.76 (2H, d, *J*=8.5 Hz). High resolution MS (FAB$^+$) *m/z*: Calcd for $C_{22}H_{29}N_2O_4S_2$: 449.1569. Found: 449.1565 (M^+).

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