Active thionium species mediated substitution reaction at 2α-position of indoles

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I. General

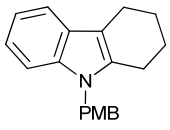
All melting points were measured on a Yanagimoto micro melting point apparatus, and are uncorrected. IR spectra were recorded on a Shimadzu IRPrestige-21 spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured on a JEOL JNM-AL300 (300 MHz) or a JEOL JMN-AL400 (400 MHz) spectrometer with tetramethylsilane as an internal standard. *J*-Values are given in Hertz. Mass spectra were recorded on a JEOL JMS 700 instrument with a direct inlet system. Elemental analyses were obtained using a Yanaco MT-6 elemental analyzer. Column chromatography was carried out on a silica gel [Kanto Chemical Co. Inc. (Silica Gel 60N, Spherical, neutral 40-50 μm) or Merck Ltd. (Silica Gel 60, 230-400 mesh)]. PTLC was performed Merck silica gel plates (60F-254). *N*-Acetyl tetrahydrocarbazole (**1b**), Ph_2SO, PhMeSO and *p*-TolMeSO are commercially available. DMSO and TFAA were purified by general method (distillation under drying agents) before use. The following compounds have been prepared previously and characterized: **1c**[1], **1i**[2], *p*-AnMeSO[3].

II. Experimental Procedures and Characterization Data

General procedure for synthesis of 1

Under nitrogen atmosphere, to a suspension of NaH in dry DMF (30 mL) was added starting material at 0 °C. After being stirred for time-1, tetrabutylammonium iodide and 4-methoxybenzyl chloride were added to the above reaction mixture, and stirred at room temperature for time-2. After the neutralization with saturated aqueous NH_4Cl, the mixture was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over $MgSO_4$ and evaporated. The residue was chromatographed on a column with *n*-hexane/AcOEt as an eluent to provide **1**.

9-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-9*H*-carbazole (1d)

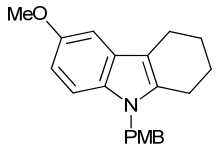


1d

NaH (0.36 g, 60%, 8.7 mmol); DMF (30 mL); 1,2,3,4-tetrahydrocarbazole (1.0 g, 5.8 mmol); time-1 = 20 min; tetrabutylammonium iodide (0.21 g, 0.58 mmol); 4-methoxybenzyl chloride (0.95 mL, 6.96 mmol); time-2 = 2.5 h; **1d** (1.6 g, 96%).
Colorless oil.
IR ($CHCl_3$): 3007, 2934, 1512, 1466, 1246, 1223 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.82-1.94 (4H, m), 2.63 (2H, t, *J* = 6.0 Hz), 2.75 (2H, t, *J* = 6.0 Hz), 3.74 (3H, s), 5.17 (2H, s), 6.72-6.88 (2H, m), 6.88-7.02 (2H, m), 7.04-7.12 (2H, m), 7.22 (1H, m), 7.49 (1H, dd, *J* = 7.1, 2.2 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 22.3, 23.3, 23.4, 45.7, 55.2, 108.9, 109.7, 113.9, 117.6, 118.6, 120.5, 127.2, 127.3, 130.2, 135.3, 136.3, 158.5.
MS (EI): *m/z* (%) 291 (M^+, 58), 121 (100).

HRMS (EI): *m/z* Calcd for $C_{20}H_{21}NO$: 291.1623; Found: 291.1623.

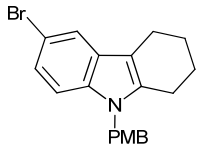
6-Methoxy-9-(4-methoxybenzyl)-1,2,3,4-tetrahydro-9*H*-carbazole (1e)



1e

NaH (0.24 g, 60%, 4.8 mmol); DMF (20 mL); 6-methoxy-1,2,3,4-tetrahydro-9*H*-carbazole (0.8 g, 4.0 mmol); time-1 = 15 min; tetrabutylammonium iodide (0.15 g, 0.40 mmol); 4-methoxybenzyl chloride (0.65 mL, 4.8 mmol); time-2 = 5 min; **1e** (1.2 g, 90%).
Colorless oil.
IR ($CHCl_3$): 3005, 2936, 1512, 1481, 1207 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.74-2.02 (4H, m), 2.62 (2H, t, *J* = 5.9 Hz), 2.71 (2H, t, *J* = 5.9 Hz), 3.74 (3H, s), 3.84 (3H, s), 5.13 (2H, s), 6.73 (1H, dd, *J* = 8.8, 2.4 Hz), 6.74-6.84 (2H, m), 6.84-6.94 (2H, m), 6.96 (1H, d, *J* = 2.4 Hz), 7.08 (1H, d, *J* = 8.8 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 22.3, 23.2, 45.8, 55.2, 56.0, 100.2, 109.4, 109.6, 110.2, 114.0, 127.3, 127.7, 129.4, 130.4, 131.7, 136.3, 153.7, 158.7.
MS (EI): *m/z* (%) 321 (M^+, 83), 121 (100).
HRMS (EI): *m/z* Calcd for $C_{21}H_{23}NO_2$: 321.1729; Found: 321.1730.

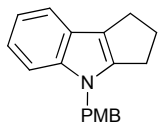
6-Bromo-9-(4-methoxybenzyl)-1,2,3,4-tetrahydro-9*H*-carbazole (1f)



1f

NaH (0.32 g, 60%, 8.1 mmol); DMF (27 mL); 6-bromo-1,2,3,4-tetrahydro-9*H*-carbazole (2.0 g, 5.4 mmol); time-1 = 30 min; tetrabutylammonium iodide (0.20 g, 0.54 mmol); 4-methoxybenzyl chloride (0.86 mL, 6.5 mmol); time-2 = 65 min; **1f** (2.5 g, 92%).
Yellowish oil.
IR ($CHCl_3$): 3009, 2938, 2839, 1512, 1466, 1246, 1207 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ 1.69-2.08 (4H, m), 2.62 (2H, t, *J* = 4.8 Hz), 2.69 (2H, t, *J* = 4.8 Hz), 3.75 (3H, s), 5.14 (2H, s), 6.70-6.84 (2H, m), 6.84-6.89 (2H, m), 7.05 (1H, d, *J* = 6.6 Hz), 7.15 (1H, dd, *J* = 6.6, 1.4 Hz), 7.59 (1H, d, *J* = 1.4 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 22.3, 23.16, 23.21, 45.9, 55.3, 109.5, 110.3, 112.0, 114.0, 120.3, 123.2, 127.2, 129.0, 129.6, 135.0, 136.8, 158.6.
MS (EI): *m/z* (%) 371 ([M^++2], 30), 369 (M^+, 30), 121 (100).
HRMS (EI): *m/z* Calcd for $C_{20}H_{20}BrNO$: 369.0728; Found: 369.0732.

4-(4-Methoxybenzyl)-1,2,3,4-tetrahydrocyclopenta[*b*]indole (1g)

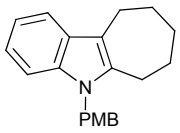


1g

NaH (0.39 g, 60%, 9.6 mmol); DMF (32 mL); 1,2,3,4-tetrahydrocyclopenta[*b*]indole (1.0 g, 6.4 mmol). time-1 = 15 min; tetrabutylammonium iodide

(0.24 g, 0.64 mmol): 4-methoxybenzyl chloride (1.0 mL, 7.7 mmol); time-2 = 15 min; **1g** (1.5 g, 84%).
White powder.
Mp: 62-64 °C.
IR ($CHCl_3$): 3007, 2955, 2936, 1512, 1458, 1246 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ 2.49 (2H, quint, *J* = 6.6 Hz), 2.73 (2H, t, *J* = 6.6 Hz), 2.85 (2H, t, *J* = 6.6 Hz), 3.72 (3H, s), 5.12 (2H, s), 6.66-6.83 (2H, m), 6.91-7.03 (2H, m), 7.03-7.12 (2H, m), 7.19 (1H, m), 7.42 (1H, m).
^{13}C NMR (100 MHz, $CDCl_3$): δ 24.7, 25.3, 28.5, 47.8, 55.2, 109.7, 113.9, 118.0, 118.4, 118.9, 119.9, 124.4, 127.8, 129.9, 140.9, 145.9, 158.7.
Anal Calcd for $C_{19}H_{19}NO$: C, 82.28; H, 6.90; N, 5.05; Found: C, 82.17; H, 7.04; N, 5.03.

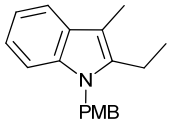
5-(4-Methoxybenzyl)-5,6,7,8,9,10-hexahydrocyclohepta[*b*]indole (1h)



1h

NaH (0.34 g, 60%, 8.6 mmol); DMF (28 mL); 5,6,7,8,9,10-hexahydrocyclohepta[*b*]indole (1.1 g, 5.7 mmol); time-1 = 10 min; tetrabutylammonium iodide (0.21 g, 0.57 mmol); 4-methoxybenzyl chloride (0.77 mL, 5.7 mmol); time-2 = 15 min; **1h** (1.4 g, 80%).
White needles.
Mp: 70-72 °C.
IR ($CHCl_3$): 3007, 2924, 1512, 1466, 1246 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ 1.65 (2H, quint, *J* = 5.4 Hz), 1.74 (2H, quint, *J* = 5.4 Hz), 1.83 (2H, quint, *J* = 5.4 Hz), 2.71 (2H, t, *J* = 5.6 Hz), 2.84 (2H, t, *J* = 5.6 Hz), 3.63 (3H, s), 5.13 (2H, s), 6.66-6.76 (2H, m), 6.76-6.86 (2H, m), 7.05 (2H, dd, *J* = 6.0, 3.2 Hz), 7.15 (1H, dt, *J* = 3.2, 6.0 Hz), 7.49 (1H, dt, *J* = 3.2, 6.0 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ 24.5, 26.5, 27.2, 28.5, 31.7, 45.7, 55.1, 108.9, 113.8, 113.9, 117.4, 118.6, 120.3, 126.8, 127.8, 130.3, 135.5, 138.6, 158.4.
Anal Calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59; N, 4.59; Found: C, 82.58; H, 7.74; N, 4.56.

2-Ethyl-1-(4-methoxybenzyl)-3-methyl-1*H*-indole (1j)



1j

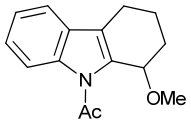
NaH (0.72 g, 60%, 18 mmol); DMF (60 mL); 2-ethyl-3-methyl-1*H*-indole (1.9 g, 12 mmol); time-1 = 10 min; tetrabutylammonium iodide (0.44 g, 1.2 mmol); 4-methoxybenzyl chloride (1.9 mL, 14 mmol); time-2 = 5 min; **1j** (2.5 g, 76%).
Colorless oil.
IR ($CHCl_3$): 3005, 2968, 2934, 1512, 1468, 1246 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.09 (3H, t, *J* = 7.5 Hz), 2.29 (3H, s), 2.72 (2H, q, *J* = 7.5 Hz), 3.73 (3H, s), 5.25 (2H, s), 6.63-6.80 (2H, m), 6.80-6.96 (2H, m), 7.00-7.20 (3H, m), 7.50 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 8.7, 14.5, 17.8, 45.9, 55.2, 106.3, 109.1, 114.0, 118.0, 118.8, 120.8, 127.1, 128.7, 130.5, 136.3, 138.3, 158.7. MS (EI): *m/z* (%) 279 (M^+, 45), 121 (100).
HRMS (EI): *m/z* Calcd for $C_{19}H_{21}NO$: 279.1623; Found: 279.1621.

General procedure for substitution reaction induced by thionium active species generated from sulfoxide (1 eq.)/TFAA (1 eq.)

Under argon atmosphere, to a solution of **1** (1 eq.) and sulfoxide (1 eq.) in CH_2Cl_2 (0.2 M) was added TFAA (1 eq.). After being stirred for 10 or 90 min at -40 °C or r.t., MeOH (10 eq.) was added to the above reaction mixture, and the reaction mixture was stirred for 10 min at same temperature. The reaction mixture was neutralized with saturated aqueous $NaHCO_3$, then extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography with *n*-hexane/AcOEt as an eluent to give **3** and **4**.

For Table 1

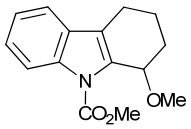
9-Acetyl-1-methoxy-1,2,3,4-tetrahydro-9*H*-carbazole (3b)



3b

Entry 2: **1b** (0.10 g, 0.47 mmol); Diphenyl sulfoxide (95 mg, 0.47 mmol); CH_2Cl_2 (2.3 mL); TFAA (65 µL, 0.47 mmol); 90 min; MeOH (0.19 mL, 4.7 mmol); **3b** (10 mg, 9 %). (recovery of **1b**, 87 mg, 87%)
Colorless oil.
IR ($CHCl_3$): 3007, 2943, 2824, 1730, 1456, 1443, 1375, 1364 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.71 (1H, tt, *J* = 13.2, 3.3 Hz), 1.80-2.20 (2H, m), 2.32 (1H, m), 2.57 (1H, ddd, *J* = 16.8, 10.8, 6.2 Hz), 2.83 (1H, m), 2.77 (3H, s), 3.46 (3H, s), 4.87 (1H, t, *J* = 3.3 Hz), 7.24 (1H, t, *J* = 7.5 Hz), 7.32 (1H, t, *J* = 7.5 Hz), 7.46 (1H, d, *J* = 7.5 Hz), 8.03 (1H, d, *J* = 7.5 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ 17.1, 21.1, 26.9, 53.4, 56.6, 70.9, 115.8, 118.6, 120.6, 122.7, 124.9, 129.0, 133.8, 136.2, 152.1.
MS (EI): *m/z* (%) 243 (M^+, 1), 211 (43), 170 (12), 169 (70), 168 (100), 167 (47).
HRMS (EI): *m/z* Calcd for $C_{15}H_{17}NO_3$: 243.1259; Found: 243.1263.

9-Methoxycarbonyl-1-methoxy-1,2,3,4-tetrahydro-9*H*-carbazole (3c)

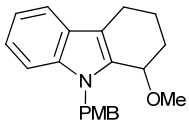


3c

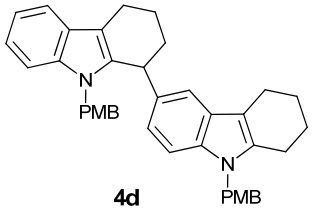
Entry 3: **1c** (97 mg, 0.42 mmol); Diphenyl sulfoxide (86 mg, 0.42 mmol); CH_2Cl_2 (2.1 mL); TFAA (59 µL, 0.42 mmol); 90 min; MeOH (0.17 mL, 4.2 mmol); **3c** (22 mg, 20 %). (recovery of **1c**, 69 mg, 71%)
Yellowish oil.
IR ($CHCl_3$): 3007, 2943, 1695, 1371, 1308 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.72 (1H, tt, *J* = 13.9, 3.3 Hz), 1.78-2.20 (2H, m), 2.32 (1H, ddt, *J* = 13.9, 4.8, 3.3 Hz), 2.57 (1H, ddd, *J* = 17.4, 12.1, 6.0 Hz), 2.81 (1H, ddd, *J* = 17.4, 5.3, 1.6 Hz), 3.48 (3H, s), 4.05 (3H, s), 4.90 (1H, t, *J* = 3.3 Hz), 7.24 (1H, dt, *J* = 1.0, 7.2 Hz), 7.30 (1H, ddd, *J* = 8.4, 7.2, 1.3 Hz), 7.46 (1H, ddd, *J* = 7.2, 1.3, 0.8 Hz), 8.03 (1H, dt, *J* = 8.4, 0.8 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ 17.1, 21.4, 26.5, 26.9, 60.0, 71.2, 115.6, 118.8, 121.4, 122.8, 125.1, 129.2, 133.8, 136.3, 169.6.
MS (EI): *m/z* (%) 259 (M^+, 2), 228 (23), 227 (100), 266 (15), 194 (16), 168 (37), 167 (56), 106 (27).

HRMS (EI): *m/z* Calcd for $C_{15}H_{17}NO_2$: 259.1208; Found: 259.1212.

1-Methoxy-9-(4-methoxybenzyl)-1,2,3,4-tetrahydro-9*H*-carbazole (3d) and Dimer 4d



3d



4d

Entry 4: **1d** (0.12 g, 0.42 mmol); Diphenyl sulfoxide (85 mg, 0.42 mmol); CH_2Cl_2 (2.1 mL); TFAA (59 μL, 0.42 mmol); 10 min; MeOH (0.17 mL, 4.2 mmol); **3d** (44 mg, 32 %); **4d** (40 mg, 33 %).

3d: Colorless oil.

IR ($CHCl_3$): 3007, 2940, 1512, 1464, 1246 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 1.70-1.82 (2H, m), 1.95 (1H, m), 2.17 (1H, m), 2.61 (1H, ddd, *J* = 15.6, 10.1, 5.1 Hz), 2.84 (1H, dt, *J* = 3.8, 15.6 Hz), 3.33 (3H, s), 3.65 (3H, s), 4.34 (1H, t, *J* = 3.8 Hz), 5.24 (2H, s), 6.66-6.80 (2H, m), 6.89-7.00 (2H, m), 7.01-7.11 (2H, m), 7.17 (1H, d, *J* = 8.0 Hz), 7.51 (1H, d, *J* = 8.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.1, 21.3, 27.2, 46.2, 55.0, 55.6, 70.7, 109.4, 112.7, 113.7, 118.61, 118.62, 121.8, 126.4, 127.3, 130.3, 133.6, 136.9, 158.3.

MS (EI): *m/z* (%) 321 (M^+, 3), 290 (10), 289 (42), 287 (13), 121 (100). HRMS (EI): *m/z* Calcd for $C_{21}H_{23}NO_2$: 321.1729; Found: 321.1730.

4d:Yellowish amorphous.

IR ($CHCl_3$): 3003, 2936, 2837, 1512, 1462, 1246 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 1.12-1.34 (2H, m), 1.48 (1H, m), 1.70-1.97 (5H, m), 2.10 (1H, m), 2.45-2.77 (5H, m), 3.70 (3H, s), 3.72 (3H, s), 4.50 (1H, d, *J* = 16.1 Hz), 4.63 (1H, d, *J* = 16.1 Hz), 4.75 (1H, t, *J* = 3.8 Hz), 4.96 (1H, d, *J* = 16.1 Hz), 5.10 (1H, d, *J* = 16.1 Hz), 6.39 (1H, d, *J* = 7.8 Hz), 6.66 (1H, d, *J* = 7.8 Hz), 6.68-6.72 (2H, m), 6.72-6.82 (2H, m), 6.82-6.93 (2H, m), 6.94 (1H, t, *J* = 7.8 Hz), 7.10-7.25 (2H, m), 7.25-7.32 (2H, m), 7.35 (1H, d, *J* = 7.8 Hz), 7.39 (1H, d, *J* = 7.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 17.6, 21.3, 22.3, 22.5, 23.3, 23.4, 33.5, 45.9, 46.7, 51.5, 55.3, 93.0, 105.6, 107.9, 109.4, 113.8, 113.9, 117.30, 117.33, 118.1, 122.6, 125.2, 127.1, 127.75, 127.83, 130.1, 130.4, 135.2, 136.3, 136.9, 137.7, 147.0, 150.1, 158.4, 158.48, 158.49.

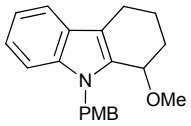
MS (EI): *m/z* (%) 580 (M^+, 42), 461 (13), 460 (37), 289 (23), 121 (100).

HRMS (EI): *m/z* Calcd for $C_{40}H_{40}N_2O_2$: 580.3090; Found: 580.3089.

General procedure for substitution reaction induced by thionium active species generated from DMSO (1 eq.)/TFAA (1 eq.).

Under argon atmosphere, to a solution of **1** (1 eq.) and DMSO (1 eq.) in CH_2Cl_2 (0.2 M) was added TFAA (1 eq.). After being stirred at -40 °C for 30 min, MeOH (5 eq.) was added to the above reaction mixture and, the mixture was stirred at same temperature for 10 min. The resulting mixture was neutralized with saturated aqueous $NaHCO_3$, then extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography with *n*-hexane/AcOEt as an eluent to give **3**.

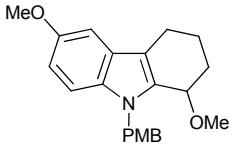
For Table 2
1-Methoxy-9-(4-methoxybenzyl)-1,2,3,4-tetrahydro-9*H*-carbazole (3d)



3d

Entry 2: **1d** (0.12 g, 0.40 mmol); DMSO (29 µL, 0.40 mmol); CH_2Cl_2 (2.0 mL); TFAA (56 µL, 0.40 mmol); MeOH (81 µL, 2.0 mmol); **3d** (0.12 g, 95%).

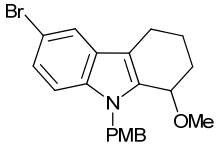
1,6-Dimethoxy-9-(4-methoxybenzyl)-1,2,3,4-tetrahydro-9*H*-carbazole (3e)



3e

1e (96 mg, 0.30 mmol); DMSO (21 µL, 0.30 mmol); CH_2Cl_2 (1.5 mL); TFAA (42 µL, 0.30 mmol); MeOH (61 µL, 1.5 mmol); **3e** (80 mg, 76 %).
Colorless oil.
IR ($CHCl_3$): 3005, 2940, 1512, 1483, 1246, 1207 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.65-2.10 (3H, m), 2.21 (1H, ddt, *J* = 13.7, 5.5, 2.8 Hz), 2.60 (1H, ddd, *J* = 15.5, 9.9, 5.5 Hz), 2.82 (1H, dt, *J* = 15.5, 5.5), 3.38 (3H, s), 3.74 (3H, s), 3.83 (3H, s), 4.37 (1H, t, *J* = 3.7 Hz), 5.25 (2H, s), 6.73-6.84 (2H, m), 6.79 (1H, d, *J* = 8.6 Hz), 6.94-7.03 (2H, m), 6.98 (1H, s), 7.07 (1H, d, *J* = 8.6 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ 19.0, 21.3, 27.2, 46.4, 55.2, 55.7, 55.9, 70.8, 100.8, 110.3, 112.0, 112.5, 113.9, 126.8, 127.5, 130.6, 132.5, 134.5, 153.6, 158.6.
MS (EI): *m/z* (%) 351 (M^+, 4), 321 (14), 320 (14), 319 (53), 317 (14), 121 (100).
HRMS (EI): *m/z* Calcd for $C_{22}H_{25}NO_3$: 351.1834; Found: 351.1837.

6-Bromo-1-methoxy-9-(4-methoxybenzyl)-1,2,3,4-tetrahydro-9*H*-carbazole (3f)

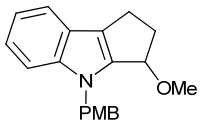


3f

1f (0.13 g, 0.35 mmol); DMSO (25 µL, 0.35 mmol); CH_2Cl_2 (1.8 mL); TFAA (49 µL, 0.35 mmol); MeOH (71 µL, 1.8 mmol); **3f** (98 mg, 70%).
Colorless oil.
IR ($CHCl_3$): 3007, 2938, 1512, 1464, 1246 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.66-2.04 (3H, m), 2.21 (1H, ddt, *J* = 13.5, 5.5, 2.9 Hz), 2.57 (1H, ddd, *J* = 15.2, 9.5, 5.5 Hz), 2.79 (1H, dt, *J* = 15.2, 5.5 Hz), 3.38 (3H, s), 3.73 (3H, s), 4.35 (1H, t, *J* = 3.5 Hz), 5.25 (2H, s), 6.72-6.87 (2H, m), 6.87-7.02 (2H, m), 7.04 (1H, d, *J* = 8.6 Hz), 7.18 (1H, dd, *J* = 8.6, 1.8 Hz), 7.64 (1H, d, *J* = 1.8 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ 18.8, 21.1, 27.0, 46.4, 55.2, 55.8, 70.6, 111.1, 112.1, 112.6, 114.0, 121.5, 124.7, 127.5, 128.3, 130.0, 135.1, 135.8, 158.8.
MS (EI): *m/z* (%) 401 ([M^++2], 7), 399 (M^+, 7), 369 (20), 367 (21), 121 (100).
HRMS (EI): *m/z* Calcd for $C_{21}H_{22}BrNO_2$: 399.0834; Found: 399.0831.

For Figure 1

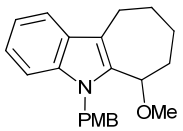
3-Methoxy-4-(4-methoxybenzyl)-1,2,3,4-tetrahydrocyclopenta[*b*]-indole (3g)



3g

1g (0.11 g, 0.39 mmol); DMSO (27 µL, 0.39 mmol); CH_2Cl_2 (1.9 mL); TFAA (54 µL, 0.39 mmol); MeOH (78 µL, 1.9 mmol); **3g** (0.11 g, 88%).
Purplish oil.
IR ($CHCl_3$): 3007, 2936, 1512, 1462, 1246 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ 2.44 (1H, m), 2.63-2.85 (2H, m), 2.99 (1H, m), 3.23 (3H, s), 3.71 (3H, s), 4.93 (1H, t, *J* = 3.9 Hz), 5.17 (1H, d, *J* = 15.6 Hz), 5,27 (1H, d, *J* = 15.6 Hz), 6.70-6.85 (2H, m), 7.00-7.17 (4H, m), 7.22 (1H, d, *J* = 7.6 Hz), 7.49 (1H, d, *J* = 7.6 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ 23.0, 35.1, 47.4, 54.5, 55.2, 110.2, 113.8, 113.9, 119.0, 119.5, 121.3, 121.5, 123.7, 128.0, 130.0, 141.7, 143.0, 158.6.
MS (EI): *m/z* (%) 307 (M^+, 3), 276 (11), 275(50), 121 (100).
HRMS (EI): *m/z* Calcd for $C_{20}H_{21}NO_2$: 307.1572; Found: 307.1575.

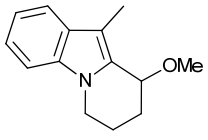
6-Methoxy-5-(4-methoxybenzyl)-5,6,7,8,9,10-hexahydrocyclohepta-[*b*]indole (3h)



3h

1h (0.12 g, 0.40 mmol); DMSO (29 µL, 0.40 mmol); CH_2Cl_2 (2.0 mL); TFAA (56 µL, 0.40 mmol); MeOH (81 µL, 2.0 mmol); **3h** (0.12 g, 90%).
Colorless oil.
IR ($CHCl_3$): 3005, 2930, 1512, 1466, 1248 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.56-1.80 (3H, m), 1.98-2.10 (2H, m), 2.28 (1H, m), 2.81-3.02 (2H, m), 3.22 (3H, s), 3.74 (3H, s), 4.55 (1H, dd, *J* = 6.0, 2.1 Hz), 5.30 (1H, d, *J* = 17.0 Hz), 5.37 (1H, d, *J* = 17.0 Hz), 6.66-6.84 (2H, m), 6.84-7.00 (2H, m), 7.08 (1H, dt, *J* = 1.3. 7.0 Hz), 7.14 (1H, dt, *J* = 1.3, 7.0 Hz), 7.22 (1H, d, *J* = 7.0 Hz), 7.56 (1H, d, *J* = 7.0 Hz)
^{13}C NMR (100 MHz, $CDCl_3$): δ 23.4, 23.6, 28.3, 29.8, 46.1, 55.3, 55.8, 73.5, 109.4, 113.9, 116.2, 118.6, 118.9, 121.6, 127.0, 127.4, 130.3, 136.0, 136.2, 158.5.
HRMS (FAB): *m/z* Calcd for $C_{22}H_{25}NO_2$: 335.1885; Found: 335.1885.

9-Methoxy-10-methyl-6,7,8,9-tetrahydropyrido[1,2-*a*]indole (3i)

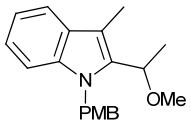


3i

1i (50 mg, 0.27 mmol); DMSO (19 µL, 0.27 mmol); CH_2Cl_2 (1.4 mL); TFAA (38 µL, 0.27 mmol); MeOH (55 µL, 1.4 mmol); **3i** (40 mg, 61%).
Colorless oil.
IR ($CHCl_3$): 3007, 2953, 2932, 2920, 1460, 1325, 1082 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.79 (1H, tt, *J* = 13.0, 3.3 Hz), 1.95 (1H, m), 2.18-2.60 (2H, m), 2.36 (3H, s), 3.37 (3H, s), 3.73 (1H, dt, *J* = 5.0, 11.5 Hz), 4.25 (1H, ddd, *J* = 11.5, 5.9, 2.6 Hz), 4.66 (1H, t, *J* = 3.3 Hz), 7.11 (1H, ddd, *J* = 8.0, 7.4, 1.1 Hz), 7.20 (1H, ddd, *J* = 8.0, 7.4, 1.3 Hz), 7.26 (1H, dt, *J* = 7.4, 1.1Hz), 7.65 (1H, ddd, *J* = 7.4, 1.3, 1.1 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ 8.8, 17.9, 27.0, 42.3, 55.8, 69.2, 109.1, 109.2, 118.8, 119.1, 121.6, 128.3, 131.3, 136.4.
MS (EI): *m/z* (%) 215 (M^+, 30), 185 (16), 184 (100), 183 (79), 182 (73), 180 (21), 169 (12), 168 (27), 167 (36).
HRMS (EI): *m/z* Calcd for $C_{14}H_{17}NO$: 215.1310; Found: 215.1311.

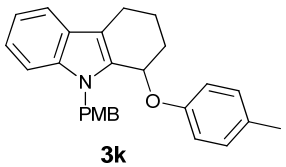
1-(4-Methoxybenzyl)-2-(1-methoxyethyl)-3-methyl-1*H*-indole (3j)



3j

Entry 3: **1j** (85 mg, 0.30 mmol); DMSO (21 μL, 0.30 mmol); CH_2Cl_2 (1.5 mL); TFAA (42 μL, 0.30 mmol); MeOH (61 μL, 1.5 mmol); **3j** (77 mg, 82%). Colorless oil.
IR ($CHCl_3$): 3005, 2986, 2932, 1512, 1466, 1246 cm^{-1}.
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43 (3H, d, *J* = 6.8 Hz), 2.36 (3H, s), 3.12 (3H, s), 3.74 (3H, s), 4.74 (1H, q, *J* = 6.8 Hz), 5.36 (1H, d, *J* = 17.0 Hz), 5.54 (1H, d, *J* = 17.0 Hz), 6.70-6.82 (2H, m), 6.82-6.98 (2H, m), 7.00-7.19 (3H, m), 7.57 (1H, m).
^{13}C NMR (75 MHz, $CDCl_3$): δ 8.7, 21.7, 46.7, 55.2, 56.3, 72.0, 109.3, 109.6, 113.9, 118.6, 119.0, 121.8, 127.1, 128.4, 130.5, 134.8, 137.2, 158.5.
MS (EI): *m/z* (%) 309 (M^+, 31), 277 (11), 121 (100).
HRMS (EI): *m/z* Calcd for $C_{20}H_{23}NO_2$: 309.1729; Found: 309.1726.

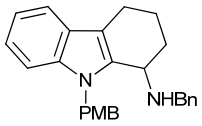
For Table 3
9-(4-Methoxybenzyl)-1-(4-methylphenyl)-1,2,3,4-tetrahydro-9*H*-carbazole (3k)



3k

Entry 1: **1d** (0.14 g, 0.47 mmol); DMSO (33 μL, 0.47 mmol); CH_2Cl_2 (2.3 mL); TFAA (65 μL, 0.47 mmol); *p*-cresol (0.25 g, 2.3 mmol); **3k** (0.13 g, 70%). Colorless amorphous.
IR ($CHCl_3$): 3007, 2936, 1612, 1508, 1464, 1246, 1225 cm^{-1}.
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.74-1.94 (2H, m), 2.00 (1H, m), 2.29 (3H, s), 2.50-2.83 (2H, m), 2.95 (1H, ddd, *J* = 15.9, 4.7, 2.7 Hz), 3.73 (3H, s), 5.16 (1H, d, *J* = 16.5 Hz), 5.26 (1H, d, *J* = 16.5 Hz), 5.35 (1H, t, *J* = 2.9 Hz), 6.65-6.77 (2H, m), 6.77-6.85 (2H, m), 6.85-6.98 (2H, m), 7.00-7.10 (2H, m), 7.10-7.30 (3H, m), 7.57 (1H, d, *J* = 7.7 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ 18.7, 20.4, 21.1, 28.2, 46.2, 55.1, 67.4, 109.6, 113.9, 114.0, 115.7, 119.0, 122.4, 126.5, 127.3, 127.6, 130.0, 130.2, 130.3, 132.5, 137.3, 155.1, 158.7.
MS (EI): *m/z* (%) 397 (M^+, 1), 290 (16), 289 (55), 121 (100), 108 (10), 107 (11).
HRMS (EI): *m/z* Calcd for $C_{27}H_{27}NO_2$: 397.2042; Found: 397.2038.

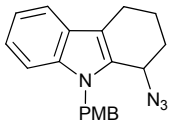
_N_-Benzylamino-9-(4-methoxybenzyl)-1,2,3,4-tetrahydro-9_H_-carbazole (3l)



3l

Entry 2: **1d** (0.11 g, 0.37 mmol); DMSO (26 µL, 0.37 mmol); CH_2Cl_2 (1.8 mL); TFAA (51 µL, 0.37 mmol); Benzyl amine 0.20 mL, 1.9 mmol); **3l** (0.12 g, 82%).
Colorless oil.
IR ($CHCl_3$): 3007, 2936, 2839, 1612, 1512, 1464, 1454, 1246, 1223, 1175 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.65-2.05 (3H, m), 2.23 (1H, m), 2.64 (1H, dt, *J* = 15.4, 8.0 Hz), 2.85 (1H, dt, *J* = 15.4, 3.8 Hz), 3.72 (3H, s), 3.73 (1H, d, *J* = 13.0 Hz), 3.86 (1H, t, *J* = 3.5 Hz), 3.93 (1H, d, *J* = 13.0 Hz), 5.44 (1H, d, *J* = 16.5 Hz), 5.22 (1H, d, *J* = 16.5 Hz), 6.62-6.79 (2H, m), 6.79-6.90 (2H, m), 7.05 (1H, dt, *J* = 1.3, 6.9 Hz), 7.11 (1H, dt, *J* = 1.3, 6.9Hz), 7.15-7.34 (6H, m), 7.51 (1H, dt, *J* = 7.9, 0.7 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ 18.4, 21.2, 27.1, 45.7, 48.8, 50.9, 55.2, 109.4, 111.5, 113.9, 118.4, 118.7, 121.5, 126.76, 126.84, 127.3, 128.2, 130.8, 136.2, 137.0, 140.5, 158.5.
HRMS (FAB): *m/z* Calcd for $C_{27}H_{29}N_2O$ $[M+H]^+$: 397.2280; Found: 397.2273.

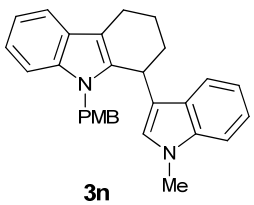
1-Azido-9-(4-methoxybenzyl)-1,2,3,4-tetrahydro-9_H_-carbazole (3m)



3m

Entry 3: **1d** (0.10 g, 0.35 mmol); DMSO (25 µL, 0.35 mmol); CH_2Cl_2 (1.7 mL); TFAA (48 µL, 0.35 mmol); Trimethylsilyl azide (0.23 mL, 1.8 mmol); **3m** (0.12 g, quant.).
Yellowish oil.
IR ($CHCl_3$): 3007, 2940, 2097, 1512, 1464, 1246 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.87-2.13 (3H, m), 2.15 (1H, m), 2.68 (1H, m), 2.92 (1H, m), 3.73 (3H, s), 4.43 (1H, t, *J* = 3.1 Hz), 5.27 (1H, d, *J* = 16.8 Hz), 5.37 (1H, d, *J* = 16.8 Hz), 6.72-6.82 (2H, m), 6.82-7.00 (2H, m), 7.06-7.26 (3H, m), 7.55 (1H, d, *J* = 7.5 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ 19.2, 20.9, 30.4, 46.2, 53.1, 55.2, 109.7, 113.9, 114.1, 119.0, 119.3, 122.6, 126.3, 127.3, 129.8, 130.8, 137.3, 158.8.
MS (EI): *m/z* (%) 332 (M^+, 1), 290 (14), 289 (47), 121 (100).
HRMS (EI): *m/z* Calcd for $C_{20}H_{20}N_4O$: 332.1637; Found: 332.1641.

9-(4-Methoxybenzyl)-1-(1-methyl-1_H_-indol-3-yl)-1,2,3,4-tetrahydro-9_H_-carbazole (3n)

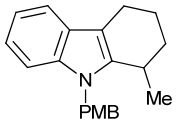


3n

Entry 8: **1d** (0.11 g, 0.37 mmol); DMSO (26 µL, 0.37 mmol); CH_2Cl_2 (1.8 mL); TFAA (51 µL, 0.37 mmol); *N*-Methylindole (0.24 mL, 1.9 mmol); **3n** (0.15 g, 97%).

Yellowish amorphous.
IR ($CHCl_3$): 3007, 2936, 1512, 1466, 1246 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.73-1.88 (2H, m), 2.03-2.20 (2H, m), 2.75 (1H, dt, *J* = 15.0, 7.7 Hz), 2.92 (1H, dt, *J* = 15.0, 4.1 Hz), 3.58 (3H, s), 3.72 (3H, s), 4.40 (1H, t, *J* = 4.1 Hz), 4.87 (1H, d, *J* = 16.5 Hz), 4.99 (1H, d, *J* = 16.5 Hz), 6.35 (1H, s), 6.58-6.70 (2H, m), 6.70-6.78 (2H, m), 7.06-7.17 (3H, m), 7.18-7.30 (3H, m), 7.52-7.63 (2H, m).
^{13}C NMR (100 MHz, $CDCl_3$): δ 19.2, 21.3, 29.8, 31.2, 32.5, 45.9, 55.1, 109.1, 109.2, 110.6, 113.5, 117.0, 117.9, 118.56, 118.63, 118.7, 120.8, 121.3, 126.5, 127.15, 127.16, 127.9, 130.4, 136.7, 136.9, 137.0, 158.2.
MS (EI): *m/z* (%) 420 (M^+, 100), 299 (13), 289 (39), 288 (29), 271 (18), 258 (16), 255 (11), 251 (16), 250 (13), 121 (68).
HRMS (EI): *m/z* Calcd for $C_{29}H_{28}N_2O$: 420.2202; Found: 420.2204.

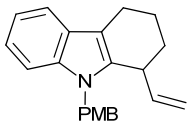
For Table 6
9-(4-Methoxybenzyl)-1-methyl-1,2,3,4-tetrahydro-9*H*-carbazole (3o)



3o

Entry 5: **2d** (0.10 g, 0.36 mmol); DMSO (25 µL, 0.36 mmol); TFAA (50 µL, 0.36 mmol); CH_2Cl_2 (1.8 mL); Methyl magnesium bromide (1.06 M in THF, 1.7 mL, 1.8 mmol); **3o** (0.11 g, 99 %).
White crystals.
Mp: 106-108 °C.
IR ($CHCl_3$): 3005, 2963, 2934, 1512, 1466, 1246 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ 1.20 (3H, d, *J* = 7.1 Hz), 1.76 (1H, m), 1.82-2.00 (3H, m), 2.66 (1H, m), 2.84 (1H, m), 2.99 (1H, m), 3.73 (3H, s), 5.18 (1H, d, *J* = 16.6 Hz), 5.28 (1H, d, *J* = 16.6 Hz), 6.70-6.82 (2H, m), 6.82-6.98 (2H, m), 7.03-7.13 (3H, m), 7.49 (1H, m).
^{13}C NMR (100 MHz, $CDCl_3$): δ 18.8, 21.0, 21.4, 26.5, 31.5, 45.9, 55.2, 109.0, 109.3, 113.9, 117.8, 118.7, 120.8, 126.9, 127.3, 130.2, 136.6, 139.8, 158.4.
Anal Calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59; N, 4.59; Found: C, 82.72; H, 7.75; N, 4.52.

9-(4-Methoxybenzyl)-1-vinyl-1,2,3,4-tetrahydro-9*H*-carbazole (3p)

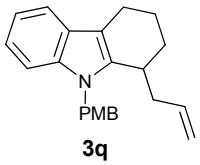


3p

Entry 6: **1d** (0.11 g, 0.38 mmol); DMSO (27 µL, 0.38 mmol); CH_2Cl_2 (1.9 mL); TFAA (53 µL, 0.38 mmol); Vinyl magnesium bromide (1.0 M solution in THF, 1.9 mL, 1.9 mmol); **3p** (0.12 g, quant.).
Colorless oil.
IR ($CHCl_3$): 3007, 2936, 1512, 1466, 1246, 1223 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.72-2.10 (4H, m), 2.46-2.95 (2H, m), 3.45 (1H, m), 3.70 (3H, s), 4.87 (1H, dt, *J* = 17.2, 1.5 Hz), 5.07 (1H, ddd, *J* = 10.3, 1.5, 1.1 Hz), 5.13 (1H, d, *J* = 16.7 Hz), 5.22 (1H, d, *J* = 16.7 Hz), 5.95 (1H, ddd, *J* = 17.2, 10.3, 6.9 Hz), 6.65-6.80 (2H, m), 6.80-6.92 (2H, m), 6.98-7.28 (3H, m), 7.50 (1H, m).
^{13}C NMR (75 MHz, $CDCl_3$): δ 18.9, 21.1, 30.3, 36.7, 45.7, 55.1, 109.3, 110.7, 113.9, 115.9, 118.0, 118.7, 121.0, 127.1, 127.2, 130.5, 135.6, 136.9, 140.6,

158.6.
MS (EI): *m/z* (%) 317 (M^+, 14), 121 (100).
HRMS (EI): *m/z* Calcd for $C_{22}H_{23}NO$: 317.1780; Found: 317.1781.

1-Allyl-9-(4-methoxybenzyl)-1,2,3,4-tetrahydro-9*H*-carbazole (3q)



3q

Entry 7: **1d** (95 mg, 0.33 mmol); DMSO (23 µL, 0.33 mmol); CH_2Cl_2 (1.6 mL); TFAA (45 µL, 0.33 mmol); Allyl magnesium bromide (0.70 M solution in THF, 2.3 mL, 1.6 mmol); **3q** (0.11 g, quant.).
Colorless oil.
IR ($CHCl_3$): 3005, 2936, 1612, 1512, 1466, 1246 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ 1.57-2.10 (4H, m), 2.10-2.50 (2H, m), 2.50-3.00 (3H, m), 3.73 (3H, s), 5.01 (2H, m), 5.19 (1H, d, *J* = 15.0 Hz), 5.28 (1H, d, *J* = 15.0 Hz), 5.80 (1H, m), 6.69-6.83 (2H, m), 6.83-6.98 (2H, m), 7.00-7.40 (3H, m), 7.53 (1H, m).
^{13}C NMR (75 MHz, $CDCl_3$): δ 18.2, 21.0, 26.5, 31.4, 38.4, 45.9, 55.2, 109.5, 109.9, 114.0, 116.4, 118.0, 118.9, 121.0, 127.1, 127.4, 130.2, 136.8, 136.9, 138.5, 158.7.
MS (EI): *m/z* (%) 331 (M^+, 30), 291 (29), 290 (100), 121 (78).
HRMS (EI): *m/z* Calcd for $C_{23}H_{25}NO$: 331.1936; Found: 331.1941.

References

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