Acid-Promoted Novel Skeletal Rearrangement Initiated by Intramolecular *ipso*-Friedel-Crafts-Type Addition to 3-Alkylidene Indolenium Cations

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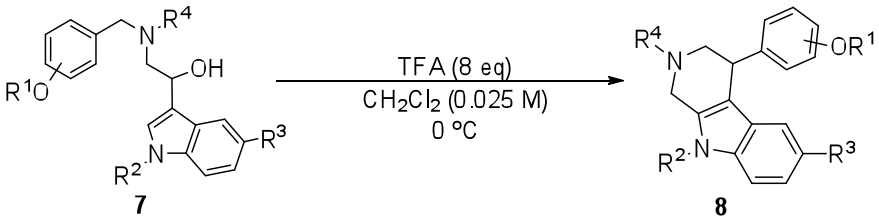
Supporting Information

Supporting Information (1)

1. General

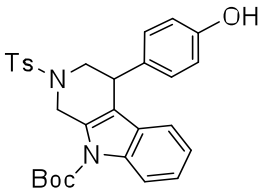
Infrared (IR) spectra were recorded on a JASCO FT/IR 230 Fourier transform infrared spectrophotometer, equipped with ATR (Smiths Detection, DuraSample IR II). NMR spectra were recorded on JEOL ecp 400 spectrometer, JEOL ecs 400 spectrometer, and JEOL eca 600 spectrometer. Chemical shifts in $CDCl_3$, were reported downfield from TMS (= 0 ppm) for ^{1}H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to the solvent signal [$CHCl_3$ (77.0 ppm)] as an internal reference. EI mass spectra were measured on JEOL GCmate MS-BU20. ESI mass spectra were measured on JEOL AccuTOF LC-plus JMS-T100LP. Analytical thin layer chromatography was performed on Merck Art. 5715, Kieselgel 60F254/0.25 mm thickness plates. Column chromatography was performed with silica gel 60 N (spherical, neutral 63-210 mesh). Reactions were carried out in dry solvent. Other reagents were purified by the usual methods.

2. General Procedure for the Acid-Promoted Novel Skeletal Rearrangement and Product Characterizations



7 **8**

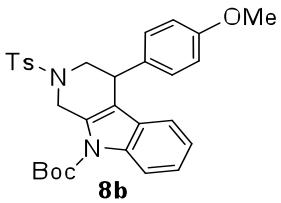
General Procedure: To a stirred solution of **7** (0.1 mmol) in CH_2Cl_2 (3.2 mL) at 0 °C was added TFA (0.8 mL, 1.0 M in CH_2Cl_2, 0.8 mmol). After being stirred for required time at 0 °C, the reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the desired products **8**.



8a

Reaction time 2.5 h;
White solid; melting point 88-91 °C;
Rf 0.21 (*n*-hexane/EtOAc = 3/1);
91% yield;

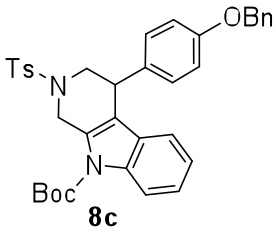
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.70 (s, 9H), 2.40 (s, 3H), 3.00 (dd, 1H, *J* = 12.0, 7.2 Hz), 3.83 (dd, 1H, *J* = 12.0, 5.2 Hz), 4.24 (br-dd, 1H, *J* = 7.2, 5.2 Hz), 4.41 (d, 1H, *J* = 16.4 Hz), 4.78 (d, 1H, *J* = 16.4 Hz), 5.33 (br-s, 1H), 6.72 (d, 2H, *J* = 8.0 Hz), 6.76 (d, 1H, *J* = 7.6 Hz), 6.98 (t, 1H, *J* = 7.6 Hz), 7.00 (d, 2H, *J* = 8.0 Hz), 7.20 (t, 1H, *J* = 7.6 Hz), 7.26 (d, 2H, *J* = 8.4 Hz), 7.67 (d, 2H, *J* = 8.4 Hz), 8.11 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.3 (×3), 39.4, 45.8, 51.4, 84.5, 115.3, 115.5 (×2), 117.4, 119.6, 122.6, 124.1, 127.6 (×2), 127.8, 129.5 (×2), 129.7 (×2), 131.0, 132.3, 133.7, 136.0, 143.7, 149.9, 154.9; IR (ATR) v 1725, 1515, 1452, 1370, 1355, 1320, 1253, 1228, 1144, 1115, 1093, 1043, 999, 959, 903, 836, 814, 765, 735, 711, 697, 657 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{29}H_{30}N_2NaO_5S$ 541.1773 (M+Na$^+$) found 541.1763.



8b

Reaction time 6 h;
White solid; melting point 126-131 °C;
Rf 0.40 (*n*-hexane/EtOAc = 3/1);
90% yield;

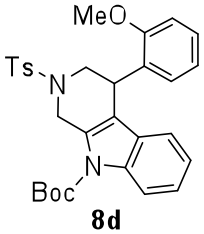
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.71 (s, 9H), 2.41 (s, 3H), 2.97 (dd, 1H, *J* = 12.0, 8.0 Hz), 3.79 (s, 3H), 3.88 (dd, 1H, *J* = 12.0, 5.6 Hz), 4.24 (br-dd, 1H, *J* = 8.0, 5.6 Hz), 4.37 (d, 1H, *J* = 16.8 Hz), 4.82 (d, 1H, *J* = 16.8 Hz), 6.74 (d, 1H, *J* = 7.6 Hz), 6.80 (d, 2H, *J* = 8.0 Hz), 6.99 (t, 1H, *J* = 7.6 Hz), 7.08 (d, 2H, *J* = 8.0 Hz), 7.20 (t, 1H, *J* = 7.6 Hz), 7.29 (d, 2H, *J* = 8.0 Hz), 7.68 (d, 2H, *J* = 8.0 Hz), 8.11 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.3 (×3), 39.4, 45.8, 51.4, 55.2, 84.4, 114.0 (×2), 115.3, 117.4, 119.6, 122.6, 124.1, 127.6 (×2), 127.9, 129.4 (×2), 129.7 (×2), 131.1, 132.3, 133.7, 136.0, 143.7, 149.9, 158.8; IR (ATR) v 1728, 1510, 1453, 1355, 1247, 1158, 1115, 1034, 960, 832, 764, 657 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{32}N_2NaO_5S$ 555.1930 (M+Na$^+$) found 555.1884.



8c

Reaction time 8 h;
White solid; melting point 87-91 °C;
Rf 0.38 (*n*-hexane/EtOAc = 3/1);
98% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.70 (s, 9H), 2.40 (s, 3H), 2.99 (dd, 1H, *J* = 12.0, 7.6 Hz), 3.87 (dd, 1H, *J* = 12.0, 5.6 Hz), 4.26 (dd, 1H, *J* = 7.6, 5.6 Hz), 4.38 (d, 1H, *J* = 16.4 Hz), 4.81 (d, 1H, *J* = 16.4 Hz), 5.02 (s, 2H), 6.75 (d, 1H, *J* = 7.6 Hz), 6.88 (d, 2H, *J* = 8.4 Hz), 6.99 (t, 1H, *J* = 7.6 Hz), 7.09 (d, 2H, *J* = 8.4 Hz), 7.20 (t, 1H, *J* = 7.6 Hz), 7.24-7.43 (m, 7H), 7.68 (d, 2H, *J* = 8.4 Hz), 8.11 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.2 (×3), 39.4, 45.8, 51.4, 70.0, 84.4, 114.9 (×2), 115.3, 117.4, 119.6, 122.6, 124.1, 127.5 (×2), 127.6 (×2), 127.8, 128.0, 128.5 (×2), 129.4 (×2), 129.7 (×2), 131.0, 132.6, 133.7, 136.0, 136.9, 143.7, 149.9, 158.0; IR (ATR) v 1727, 1508, 1453, 1355, 1227, 1163, 1115, 1018, 831, 735 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{36}H_{36}N_2NaO_5S$ 631.2243 (M+Na$^+$) found 631.2264.

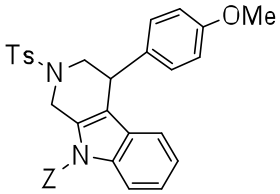


8d

Reaction time 3 h;
White solid; melting point 163 °C;
Rf 0.29 (*n*-hexane/EtOAc = 4/1);
83% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.71 (s, 9H), 2.39 (s, 3H), 3.33 (dd, 1H, *J* = 12.0, 5.2 Hz), 3.67 (dd, 1H, *J* = 12.0, 5.2 Hz), 3.91 (s, 3H), 4.60 (s, 2H), 4.74 (t, 1H, *J* = 5.2 Hz), 6.71-6.74 (m, 2H), 6.85 (d, 1H, *J* = 8.0 Hz), 6.91 (d, 1H, *J* = 8.4 Hz), 7.01 (t, 1H, *J* = 8.0

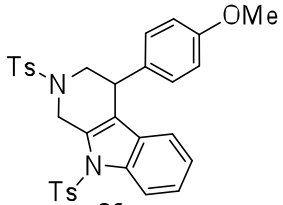
Hz), 7.19-7.25 (m, 4H), 7.63 (d, 2H, *J* = 8.4 Hz), 8.13 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.2 (×3), 32.4, 45.6, 49.2, 55.4, 84.3, 110.2, 115.3, 117.0, 119.3, 120.4, 122.6, 124.1, 127.6 (×2), 127.9, 128.1 (×2), 129.5, 129.6 (×2), 131.5, 134.0, 136.0, 143.4, 149.8, 156.9; IR (ATR) v1728, 1491, 1455, 1355, 1241, 1145, 1107, 1025, 961, 813, 733 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{32}N_2NaO_5S$ 555.1930 (M+Na$^+$) found 555.1916.



8e

Reaction time 7 h;
White solid; melting point 162 °C;
Rf 0.33 (*n*-hexane/EtOAc = 2/1);
75% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 2.91 (dd, 1H, *J* = 12.0, 8.0 Hz), 3.77 (s, 3H), 3.84 (dd, 1H, *J* = 12.0, 4.8 Hz), 4.24 (br-dd, 1H, *J* = 8.0, 4.8 Hz), 4.30 (d, 1H, *J* = 16.4 Hz), 4.78 (d, 1H, *J* = 16.4 Hz), 5.44 (d, 1H, *J* = 12.4 Hz), 5.47 (d, 1H, *J* = 12.4 Hz), 6.73 (d, 1H, *J* = 8.0 Hz), 6.80 (d, 2H, *J* = 8.4 Hz), 6.99 (t, 1H, *J* = 8.0 Hz), 7.06 (d, 2H, *J* = 8.4 Hz), 7.18-7.21 (m, 3H), 7.44-7.55 (m, 7H), 8.12 (d, 1H, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 39.4, 45.6, 51.4, 55.2, 69.2, 114.0 (×2), 115.4, 118.2, 119.8, 123.0, 124.4, 127.5 (×2), 128.0, 129.0 (×2), 129.0 (×2), 129.0, 129.4 (×2), 129.7 (×2), 131.0, 132.1, 133.6, 134.6, 136.0, 143.5, 151.1, 158.8; IR (ATR) v 1732, 1510, 1455, 1394, 1326, 1247, 1163, 1115, 815, 732 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{33}H_{30}N_2NaO_5S$ 589.1773 (M+Na$^+$) found 589.1743.

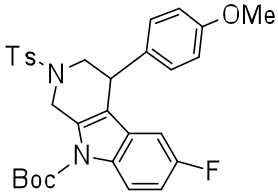


8f

Reaction time 5 h;
White solid; melting point 83-85 °C;
Rf 0.36 (*n*-hexane/EtOAc = 2/1);
99% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 2.41 (s, 3H), 2.95 (dd, 1H, *J* = 12.0, 7.6 Hz), 3.76 (s, 3H), 3.87 (dd, 1H, *J* = 12.0, 5.6 Hz), 4.18 (br-dd, 1H, *J* = 7.6, 5.6 Hz), 4.48 (d, 1H, *J* = 17.2 Hz), 4.93 (d, 1H, *J* = 17.2 Hz), 6.66 (d, 1H, *J* = 8.0 Hz), 6.76 (d, 2H, *J* = 8.4 Hz), 6.95 (d, 2H, *J* = 8.4 Hz), 6.98 (t, 1H, *J* = 8.0 Hz), 7.19-7.30 (m, 5H), 7.68 (d, 2H, *J* = 8.4 Hz), 7.71 (d, 2H, *J* = 8.4 Hz), 8.07 (d, 1H, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 21.6, 39.3, 44.8, 51.2, 55.2, 114.0 (×2), 114.1, 119.4, 120.1, 123.4, 124.4, 126.5 (×2), 127.5 (×2), 128.4, 129.2 (×2), 129.8 (×2), 130.1 (×2), 130.9, 131.6, 133.9, 135.1, 136.2, 143.8,

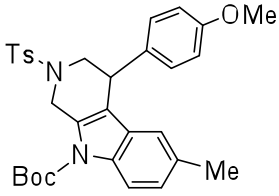
145.2, 158.8; IR (ATR) v 1733, 1510, 1450, 1242, 1164, 1092, 1038, 949, 812, 747 cm^{-1}; HRMS (ESI^+) calcd for $C_{32}H_{30}N_2NaO_5S$ 609.1494 ($M+Na^+$) found 609.1469.



8g

Reaction time 16 h;
White solid; melting point 92 °C;
Rf 0.29 (*n*-hexane/EtOAc = 4/1);
90% yield;

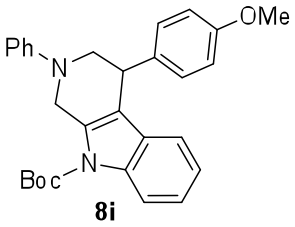
^1H NMR (400 MHz, $CDCl_3$) δ 1.70 (s, 9H), 2.40 (s, 3H), 2.94 (dd, 1H, J = 12.0, 8.0 Hz), 3.79 (s, 3H), 3.89 (dd, 1H, J = 12.0, 5.6 Hz), 4.22 (br-dd, 1H, J = 8.0, 5.6 Hz), 4.34 (d, 1H, J = 16.4 Hz), 4.82 (d, 1H, J = 16.4 Hz), 6.37 (dd, 1H, J = 8.8, 2.4 Hz), 6.82 (d, 2H, J = 8.4 Hz), 6.91 (td, 1H, J = 8.8, 2.4 Hz), 7.07 (d, 2H, J = 8.4 Hz), 7.29 (d, 2H, J = 8.4 Hz), 7.68 (d, 2H, J = 8.4 Hz), 8.06 (dd, 1H, J = 8.8, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.2 (×3), 39.3, 45.8, 51.3, 55.2, 84.7, 115.2 (d, J = 23.8 Hz), 111.7 (d, J = 24.8 Hz), 114.1 (×2), 116.3 (d, J = 8.6 Hz), 117.2 (d, J = 3.8 Hz), 127.5 (×2), 128.8 (d, J = 10.5 Hz), 129.3 (×2), 129.7 (×2), 131.6, 132.2, 132.6, 133.5, 143.8, 149.5, 158.8 (d, J = 238.3 Hz), 158.8; IR (ATR) v 1730, 1511, 1451, 1356, 1248, 1160, 1117, 1033, 903, 807, 754 cm^{-1}; HRMS (ESI^+) calcd for $C_{30}H_{31}FN_2NaO_5S$ 573.1835 ($M+Na^+$) found 573.1837.



8h

Reaction time 7 h;
White solid; melting point 105 °C;
Rf 0.24 (*n*-hexane/EtOAc = 4/1);
84% yield (2 steps);

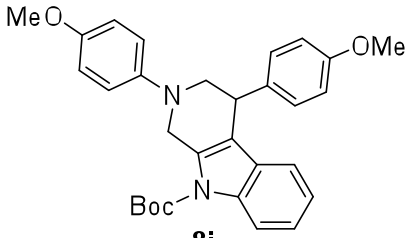
^1H NMR (400 MHz, $CDCl_3$) δ 1.70 (s, 9H), 2.22 (s, 3H), 2.40 (s, 3H), 3.04 (dd, 1H, J = 11.6, 7.6 Hz), 3.79 (s, 3H), 3.79 (dd, 1H, J = 11.6, 5.2 Hz), 4.23 (br-dd, 1H, J = 7.6, 5.2 Hz), 4.41 (d, 1H, J = 16.4 Hz), 4.73 (d, 1H, J = 16.4 Hz), 6.56 (s, 1H), 6.81 (d, 2H, J = 8.8 Hz), 7.02 (d, 1H, J = 8.0 Hz), 7.09 (d, 2H, J = 8.8 Hz), 7.28 (d, 2H, J = 8.0 Hz), 7.67 (d, 2H, J = 8.0 Hz), 7.98 (d, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 21.5, 28.2 (×3), 39.2, 45.8, 51.4, 55.2, 84.2, 113.9 (×2), 114.9, 117.0, 119.4, 125.4, 127.6 (×2), 128.0, 129.3 (×2), 129.7 (×2), 131.0, 132.1, 132.4, 133.6, 134.1, 143.6, 149.8, 158.6; IR (ATR) v 1727, 1510, 1456, 1350, 1247, 1163, 1127, 1035, 808, 735 cm^{-1}; HRMS (ESI^+) calcd for $C_{31}H_{34}N_2NaO_5S$ 569.2086 ($M+Na^+$) found 569.2050.



8i

Reaction time 24 h;
White solid; melting point 68 °C;
Rf 0.62 (*n*-hexane/EtOAc = 6/1);
68% yield;

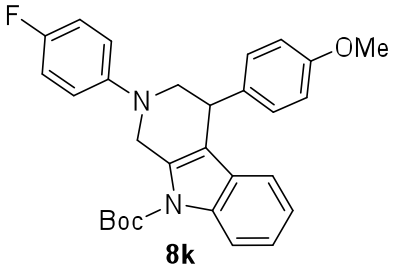
^{1}H NMR (600 MHz, $CDCl_3$) δ 1.74 (s, 9H), 3.50 (dd, 1H, *J* = 13.2, 6.6 Hz), 3.77 (s, 3H), 3.86 (dd, 1H, *J* = 13.2, 4.8 Hz), 4.24 (dd, 1H, *J* = 6.6, 4.8 Hz), 4.70 (d, 1H, *J* = 16.8 Hz), 4.75 (d, 1H, *J* = 16.8 Hz), 6.80 (t, 1H, *J* = 7.8 Hz), 6.81 (d, 2H, *J* = 8.4 Hz), 6.90 (d, 2H, *J* = 7.6 Hz), 6.90 (d, 1H, *J* = 7.6 Hz), 7.02 (t, 1H, *J* = 7.8 Hz), 7.20 (d, 2H, *J* = 8.4 Hz), 7.19-7.25 (m, 3H), 8.15 (d, 1H, *J* = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.3 (×3), 39.0, 48.5, 55.2, 56.4, 84.0, 113.8 (×2), 115.4, 116.0 (×2), 118.1, 119.2, 119.3, 122.5, 123.7, 128.5, 129.2 (×2), 129.3 (×2), 134.0, 134.1, 136.0, 150.1, 150.5, 158.4; IR (ATR) ν 1725, 1599, 1508, 1454, 1368, 1246, 1137, 1034, 830, 746 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{29}H_{31}N_2O_3$ 455.2335 (M+H$^+$) found 455.2351.



8j

Reaction time 24 h;
White solid; melting point 94 °C;
Rf 0.42 (*n*-hexane/EtOAc = 4/1);
62% yield;

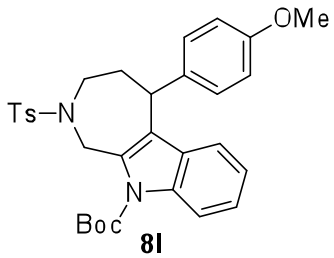
^{1}H NMR (600 MHz, $CDCl_3$) δ 1.73 (s, 9H), 3.36 (dd, 1H, *J* = 12.6, 7.2 Hz), 3.75 (dd, 1H, *J* = 12.6, 4.8 Hz), 3.75 (s, 3H), 3.78 (s, 3H), 4.20 (dd, 1H, *J* = 7.2, 4.8 Hz), 4.61 (d, 1H, *J* = 16.2 Hz), 4.67 (d, 1H, *J* = 16.2 Hz), 6.81 (d, 2H, *J* = 9.0 Hz), 6.82 (d, 2H, *J* = 9.0 Hz), 6.88 (d, 1H, *J* = 7.8 Hz), 6.89 (d, 2H, *J* = 9.0 Hz), 7.02 (t, 1H, *J* = 7.8 Hz), 7.20 (d, 2H, *J* = 9.0 Hz), 7.21 (t, 1H, *J* = 7.8 Hz), 8.15 (d, 1H, *J* = 7.8 Hz); ^{13}C NMR (100 MHz, 55°C, $CDCl_3$) δ 28.4 (×3), 39.3, 49.8, 55.2, 55.7, 57.9, 83.9, 114.0 (×2), 114.7 (×2), 115.4, 118.0, 118.4 (×2), 119.4, 122.5, 123.7, 128.7, 129.4 (×2), 134.4, 134.5, 136.2, 145.1, 150.4, 153.8, 158.6; IR (ATR) ν 1725, 1508, 1454, 1368, 1243, 1137, 1116, 1035, 825, 746 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{33}N_2O_4$ 485.2440 (M+H$^+$) found 485.2409.



8k

Reaction time 24 h;
White solid; melting point 58-61 °C;
Rf 0.58 (*n*-hexane/EtOAc = 4/1);
50% yield;

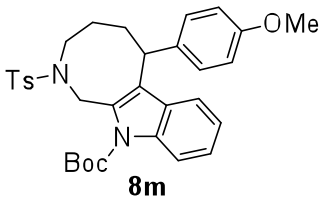
^{1}H NMR (400 MHz, 55 °C, $CDCl_3$) δ 1.73 (s, 9H), 3.42 (dd, 1H, *J* = 12.8, 6.4 Hz), 3.75 (dd, 1H, *J* = 12.8, 4.8 Hz), 3.77 (s, 3H), 4.21 (dd, 1H, *J* = 6.4, 4.8 Hz), 4.66 (s, 2H), 6.80-6.85 (m, 4H), 6.89-6.94 (m, 3H), 7.01 (t, 1H, *J* = 8.0 Hz), 7.16-7.24 (m, 3H), 8.13 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, 55 °C, $CDCl_3$) δ 28.4 (×3), 39.3, 49.5, 55.3, 57.5, 84.1, 114.0 (×2), 115.5, 115.6 (×2, d, *J* = 19.1 Hz), 117.9 (×2, d, *J* = 7.6 Hz), 118.0, 119.4, 122.6, 123.8, 128.6, 129.3, 134.1, 134.2, 136.2, 147.3, 147.3, 150.4, 157.1 (d, *J* = 237.4 Hz), 158.7; IR (ATR) ν 1726, 1507, 1454, 1368, 1246, 1138, 1117, 1034, 825, 747 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{29}H_{30}FN_2O_3$ 473.2240 (M+H$^+$) found 473.2202.



8l

Reaction time 7 h;
White solid; melting point 81-84 °C;
Rf 0.29 (*n*-hexane/EtOAc = 3/1);
88% yield;

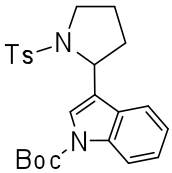
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.73 (s, 9H), 2.29-2.33 (m, 2H), 2.33 (s, 3H), 3.28-3.32 (m, 1H), 3.40-3.47 (m, 1H), 3.76 (s, 3H), 4.27 (br-t, 1H, *J* = 4.8 Hz), 4.78 (d, 1H, *J* = 17.2 Hz), 5.18 (d, 1H, *J* = 17.2 Hz), 6.79 (d, 2H, *J* = 8.4 Hz), 6.89 (d, 1H, *J* = 8.0 Hz), 7.01 (t, 1H, *J* = 8.0 Hz), 7.09 (d, 2H, *J* = 8.4 Hz), 7.16 (d, 2H, *J* = 8.4 Hz), 7.21 (t, 1H, *J* = 8.0 Hz), 7.58 (d, 2H, *J* = 8.4 Hz), 8.03 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 28.3 (×3), 33.4, 39.8, 43.8, 45.5, 55.1, 84.4, 113.8 (×2), 115.2, 119.1, 122.5, 122.9, 124.1, 127.0 (×2), 129.1 (×2), 129.2, 129.5 (×2), 133.7, 135.1, 135.5, 135.6, 143.1, 150.5, 158.1; IR (ATR) ν 1724, 1509, 1455, 1330, 1247, 1142, 1106, 1034, 812, 736, 664 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{31}H_{34}N_2NaO_5S$ 569.2086 (M+Na$^+$) found 569.2060.



8m

Reaction time 1 h;
White solid; melting point 136 °C;
Rf 0.19 (*n*-hexane/EtOAc = 6/1);
30% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.56-1.70 (m, 1H), 1.94-2.04 (m, 2H), 2.06-2.16 (m, 1H), 2.24 (s, 3H), 3.64-3.71 (m, 1H), 3.75 (s, 3H), 3.75-3.82 (m, 1H), 4.38 (d, 1H, J = 16.8 Hz), 4.59 (d, 1H, J = 16.8 Hz), 4.82 (t, 1H, J = 8.0 Hz), 6.78 (d, 2H, J = 8.4 Hz), 6.98 (d, 2H, J = 8.4 Hz), 6.98 (d, 2H, J = 8.0 Hz), 7.11 (t, 1H, J = 7.6 Hz), 7.22 (t, 1H, J = 7.6 Hz), 7.41 (d, 2H, J = 8.0 Hz), 7.48 (d, 1H, J = 7.6 Hz), 8.07 (d, 1H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 25.0, 27.8 (×3), 31.0, 34.0, 49.5, 55.2, 56.5, 83.8, 113.6 (×2), 115.4, 119.4, 119.5, 122.2, 123.5, 127.1, 127.2 (×2), 128.6 (×2), 128.9 (×2), 131.7, 134.9, 135.1, 136.4, 142.9, 150.0, 157.8; IR (ATR) ν 1726, 1510, 1454, 1322, 1244, 1155, 815, 737, 659 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{32}H_{36}N_2NaO_5S$ 583.2243 (M+Na$^+$) found 583.2235.



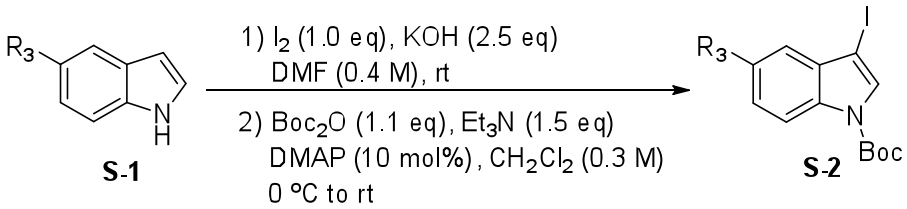
9

White solid; melting point 108 °C;
Rf 0.20(*n*-hexane/EtOAc = 6/1);
35% yield;

^{1}H NMR (600 MHz, $CDCl_3$) δ 1.67 (s, 9H), 1.71-1.87 (m, 1H), 1.87-1.94 (m, 2H), 1.95-2.01 (m, 1H), 2.40 (s, 3H), 3.44 (dt, 1H, J = 10.2, 7.8 Hz), 3.65 (ddd, 1H, J = 10.2, 6.6, 4.8 Hz), 5.02 (dd, 1H, J = 7.2, 4.2 Hz), 7.18 (t, 1H, J = 7.2 Hz), 7.24 (d, 2H, J = 8.8 Hz), 7.29 (t, 1H, J = 7.2 Hz), 7.46 (d, 1H, J = 7.2 Hz), 7.48 (s, 1H), 8.12 (br-s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 24.1, 28.2 (×3), 33.0, 48.8, 56.7, 83.6, 115.4, 119.1, 122.2, 122.3, 123.5, 124.3, 127.5 (×2), 128.1, 129.5 (×2), 134.9, 136.0, 143.3, 149.6; IR (ATR) ν 1728, 1451, 1369, 1250, 1152, 1091, 1019, 814, 736 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{24}H_{28}N_2NaO_4S$ 463.1667 (M+Na$^+$) found 463.1632.

3. Substrate Syntheses and Compound Characterizations

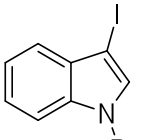
(3-1) Preparation of 3-iodo-indole derivatives **S-2**



S-1 **S-2**

Indole derivatives **S-2** were prepared according to the literature procedure[1] as followed. General Procedure: To a stirred solution of indole **S-1** (17.0 mmol) and KOH (2.40 g, 42.7 mmol) in DMF (20 mL) at room temperature was added I_2 (4.34 g, 17.0 mmol) in DMF (25 mL). After being stirred for 2 h, the reaction mixture was poured into ice and

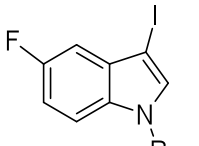
water (200 mL) containing ammonia (0.5%) and sodium sulfite (0.1% aqueous solution). The aqueous suspension was extracted with 3 times with Et_2O and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (60 mL) and added Boc_2O (4.17 g, 19 mmol), Et_3N (3.5 mL, 25 mmol), and DMAP (208 mg, 1.7 mmol) at 0 °C. After being stirred for 2 h at room temperature, the reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the desired products **S-2**.



S-2a

Colorless oil;
Rf 0.60 (*n*-hexane/EtOAc = 6/1);
89% yield (2 steps);

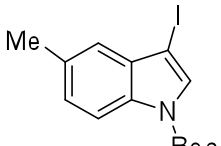
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.67 (s, 9H), 7.30-7.42 (m, 3H), 7.73 (s, 1H), 8.12 (d, 1H, J = 7.6 Hz). NMR spectra were identical with those reported previously[1,2].



S-2b

White solid; melting point 43 °C;
Rf 0.60 (*n*-hexane/EtOAc = 6/1);
91% yield (2 steps);

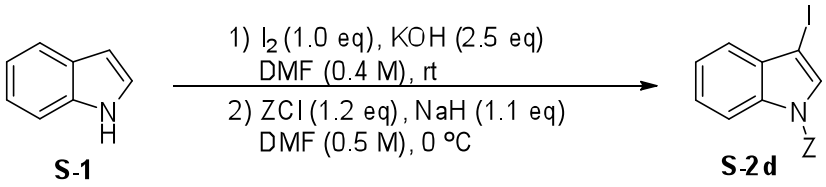
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.66 (s, 9H), 6.98 (d, 1H, J = 8.8 Hz), 7.00 (t, 1H, J = 8.8 Hz), 7.69 (s, 1H), 8.02 (br-s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0 (×3), 64.3 (d, J = 3.8 Hz), 84.4, 106.9 (d, J = 24.8 Hz), 113.0 (d, J = 24.8 Hz), 116.1 (d, J = 9.5 Hz), 131.0, 131.4, 133.1 (d, J = 9.5 Hz), 148.2, 159.4 (d, J = 239.3 Hz); IR (ATR) ν 1735, 1472, 1441, 1362, 1254, 1203, 1151, 1053, 851, 798 cm^{-1}; EI-LRMS m/z 361 (M^+), EI-HRMS calcd for $C_{13}H_{13}FINO_2$ 360.9975 (M^+) found 360.9987.



S-2c

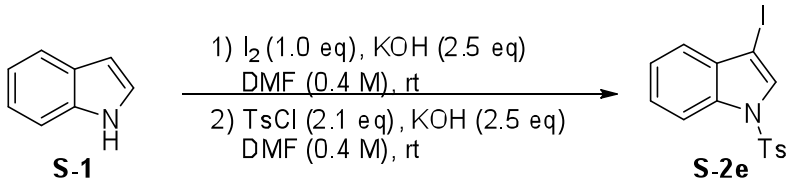
Red oil;
Rf 0.71 (*n*-hexane/EtOAc = 6/1);
99% yield (2 steps);

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 9H), 2.44 (s, 3H), 7.13 (d, 1H, J = 6.8 Hz), 7.13 (d, 1H, J = 6.8 Hz), 7.66 (s, 1H), 7.95 (br-s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 28.0 (×3), 65.2, 83.9, 114.6, 121.1, 126.6, 129.8, 132.0, 132.7, 132.8, 148.5; IR (ATR) ν 1735, 1474, 1359, 1251, 1211, 1155, 1054, 794, 762 cm^{-1}; EI-LRMS m/z 357 (M^+), EI-HRMS calcd for $C_{14}H_{16}INO_2$ 357.0226 (M^+) found 357.0235.



S-1 **S-2d**

To a stirred solution of indole **S-1** (351 mg, 3.0 mmol) and KOH (421 mg, 7.5 mmol) in DMF (4 mL) at room temperature was added I_2 (761 mg, 3.0 mmol) in DMF (4 mL). After being stirred for 2 h, the reaction mixture was poured into ice and water (40 mL) containing ammonia (0.5%) and sodium sulfite (0.1% aqueous solution). The aqueous suspension was extracted with 3 times with Et_2O and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was dissolved in DMF (6 mL) and added NaH (60% in oil, 132 mg, 3.3 mmol) at 0 °C. After being stirred for 2 h at the same temperature, the reaction mixture was quenched with saturated aqueous $NaHCO_3$, and extracted with 2 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 30:1) to give **S-2d** (919 mg, 81% in 2 steps) as a red oil: Rf 0.50 (*n*-hexane/EtOAc = 6/1); ^{1}H NMR (400 MHz, 55°C, $CDCl_3$) δ 5.42 (s, 2H), 7.21-7.46 (m, 8H), 7.74 (s, 1H), 8.13 (d, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, 55°C, $CDCl_3$) δ 66.5, 69.0, 115.1, 121.6, 123.7, 125.7, 128.5 (×2), 128.8, 128.8 (×2), 129.7, 132.2, 134.9, 135.0, 149.8; IR (ATR) ν 1739, 1449, 1390, 1352, 1306, 1231, 1049, 751, 696 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{16}H_{12}INNaO_2$ 399.9810 (M+Na$^+$) found 399.9795.



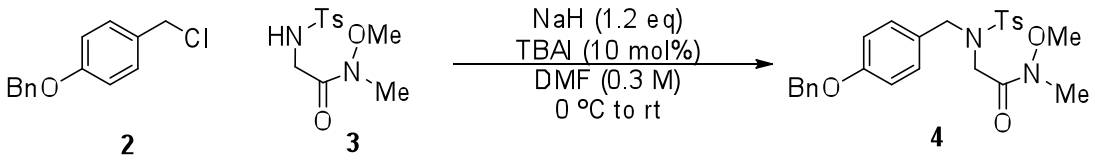
S-1 **S-2e**

S-2e was prepared according to the literature procedure[3] as followed.

General Procedure: To a stirred solution of indole **S-1** (17.0 mmol) and KOH (2.40 g, 42.7 mmol) in DMF (20 mL) at room temperature was added I_2 (4.34 g, 17.0 mmol) in DMF (25 mL). After being stirred for 2 h, the reaction mixture was added KOH (2.40 g, 42.7 mmol) and tosyl chloride (6.85 g, 35.9 mmol) and stirred for further 8 h. After the reaction was completed, the reaction mixture was diluted with water and extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by crystallization from Et_2O and *n*-hexane to give **S-2e** (3.32 g, 49% in 2 steps) as a white solid: Rf 0.14

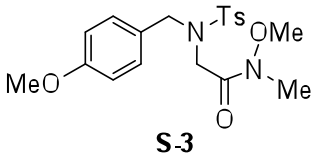
(*n*-hexane/EtOAc = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 7.23 (d, 2H, *J* = 8.0 Hz), 7.27-7.40 (m, 3H), 7.70 (s, 1H), 7.77 (d, 2H, *J* = 8.4 Hz), 7.95 (d, 1H, *J* = 8.8 Hz). NMR spectra were identical with those reported previously[3].

(3-2) Preparation of Compounds **7b**, **7c**, **7d**, **7e**, **7f**, **7g** and **7h**



2 was prepared according to the literature procedure[4].

General Procedure: To a stirred solution of **3** (1.36 g, 5.0 mmol) in DMF (17 mL) at 0 °C was added NaH (60% in oil, 240 mg, 6.0 mmol). After being stirred for 30 min at 0 °C, **2** (6.0 mmol) and TBAI (185 mg, 0.5 mmol) were added to the reaction mixture at the same temperature. After being stirred for 18 h at room temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl at 0 °C, and extracted with 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the desired products **4** (1.87 g, 72% in 2 steps) as a white solid: melting point 105 °C; Rf 0.26 (*n*-hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 3.04 (s, 3H), 3.45 (s, 3H), 4.10 (s, 2H), 4.46 (s, 2H), 5.03 (s, 2H), 6.90 (d, 2H, *J* = 8.4 Hz), 7.18 (d, 2H, *J* = 8.4 Hz), 7.29 (d, 2H, *J* = 8.4 Hz), 7.27-7.41 (m, 5H), 7.80 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 32.1, 45.1, 50.2, 61.1, 69.8, 114.8 (×2), 127.3 (×2), 127.4 (×2), 124.4, 127.8, 128.4 (×2), 129.2 (×2), 130.0 (×2), 136.7, 137.2, 143.0, 158.4, 168.8; IR (ATR) ν 1682, 1610, 1510, 1455, 1337, 1242, 1155, 1092, 999, 909, 814, 754, 698, 660 cm^{-1}; HRMS (ESI^+) calcd for $C_{25}H_{28}N_2NaO_5S$ 491.1617 ($M+Na^+$) found 491.1618.

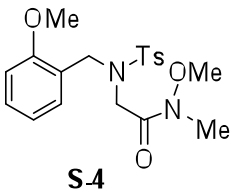


S-3

Yellow oil;
Rf 0.24 (*n*-hexane/EtOAc = 1/1);
84% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.06 (s, 3H), 3.50 (s, 3H), 3.77 (s, 3H), 4.10 (s, 2H), 4.46 (s, 2H), 6.83 (d, 2H, *J* = 8.8 Hz), 7.18 (d, 2H, *J* = 8.8 Hz), 7.30 (d, 2H, *J* = 7.6 Hz), 7.80 (d, 2H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 32.1, 45.1, 50.2, 55.1,

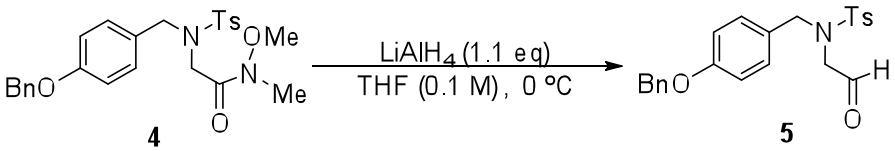
61.1, 113.8 (×2), 127.1, 127.4 (×2), 129.2 (×2), 130.0 (×2), 137.2, 143.0, 159.2, 168.9; IR (ATR) ν 2938, 1678, 1611, 1512, 1457, 1335, 1304, 1248, 1153, 1092, 1065, 1032, 997, 937, 908, 810, 745, 658 cm^{-1}; HRMS (ESI^+) calcd for $C_{19}H_{24}N_2NaO_5S$ 415.1304 ($M+Na^+$) found 415.1301.



S-4

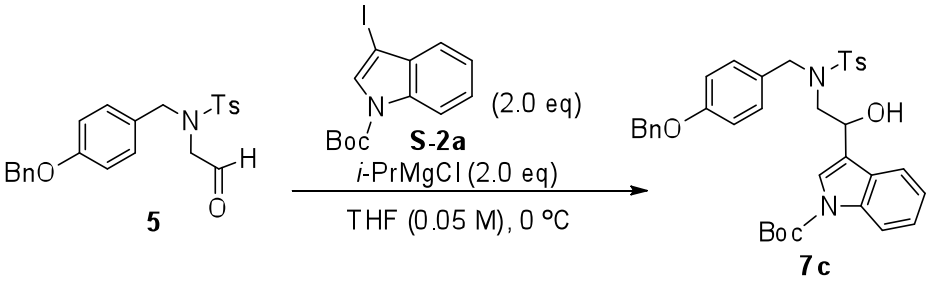
Pale yellow oil;
Rf 0.14 (*n*-hexane/EtOAc = 2/1);
32% yield (2 steps);

^1H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 3.09 (s, 3H), 3.55 (s, 3H), 3.69 (s, 3H), 4.91 (s, 2H), 4.56 (s, 2H), 6.80 (dd, 1H, *J* = 7.6, 1.2 Hz), 6.91 (dt, 1H, *J* = 7.6, 1.2 Hz), 7.24 (dt, 1H, *J* = 7.6, 1.2 Hz), 7.27 (d, 2H, *J* = 8.0 Hz), 7.33 (dd, 1H, *J* = 7.6, 1.2 Hz), 7.78 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 32.3, 45.9, 46.5, 55.1, 61.1, 110.1, 120.6, 123.7, 127.6 (×2), 129.0, 129.2 (×2), 130.4, 137.6, 142.8, 157.7, 169.4 ; IR (ATR) ν 1682, 1610, 1510, 1455, 1337, 1242, 1155, 1092, 999, 909, 814, 754, 698, 660 cm^{-1}; HRMS (ESI^+) calcd for $C_{19}H_{24}N_2NaO_5S$ 415.1304 ($M+Na^+$) found 415.1262.

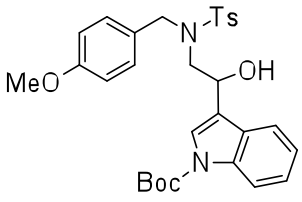


4 **5**

General Procedure: To a stirred suspension of $LiAlH_4$ (108 mg, 2.8 mmol) in THF (10mL) at 0 °C was added dropwise **4** (2.6 mmol) in THF (15 mL). After being stirred for 15 min at 0 °C, the reaction mixture was quenched with aqueous 2 M potassium sodium tartrate at the same temperature. The solution was warmed to room temperature and stirred until the organic and aqueous layers were separated. The aqueous layer was extracted with 2 times with EtOAc and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was passed through a short pad of silica gel. After concentration *in vacuo*, the obtained aldehyde **5** was utilized for the next reaction without further purification.



Grignard reagent **6** was prepared according to the literature procedure[5] as followed. General Procedure: To a stirred solution of 3-iodo-indole **S-2a** (1.0 mmol) in THF (5 mL) at 0 °C was added *i*-PrMgCl (0.5 mL, 2 M in THF, 1.0 mmol). After being stirred for 15 min, the reaction mixture was added aldehyde **5** (0.5 mmol) in THF (5 mL) at 0 °C. After being stirred for 10 min at the same temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl, and extracted with 2 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the desired products **7c** (235 mg, 75% in 2 steps) as a White solid; melting point 49 °C; Rf 0.27 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64 (s, 9H), 2.41 (s, 3H), 3.09 (br-s, 1H), 3.30 (dd, 1H, *J* = 15.2, 2.8 Hz), 3.44 (dd, 1H, *J* = 15.2, 9.2 Hz), 4.15 (d, 1H, *J* = 14.8 Hz), 4.55 (d, 1H, *J* = 14.8 Hz), 4.90 (br-d, 1H, *J* = 9.2 Hz), 5.04 (s, 2H), 6.93 (d, 2H, *J* = 8.8 Hz), 7.07-7.14 (m, 2H), 7.20-7.43 (m, 10H), 7.49 (s, 1H), 7.73 (d, 2H, *J* = 8.8 Hz), 8.09 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.1 (×3), 53.7, 54.9, 67.1, 70.0, 83.7, 115.1 (×2), 115.2, 119.2, 120.8, 122.4, 123.0, 124.3, 127.3 (×2), 127.3, 127.4 (×2), 128.0, 128.0, 128.5 (×2), 129.8 (×2), 129.9 (×2), 135.6, 135.7, 136.7, 143.7, 149.5, 158.7; IR (ATR) ν 1731, 1510, 1454, 1370, 1253, 1155, 1092, 749 cm^{-1}; HRMS (ESI^+) calcd for $C_{36}H_{38}N_2NaO_6S$ 649.2348 ($M+Na^+$) found 649.2299.

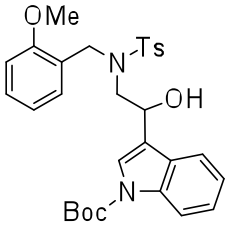


7b

White solid; melting point 52-53 °C;
Rf 0.33 (*n*-hexane/EtOAc = 2/1);
83% yield (2 steps);

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64 (s, 9H), 2.42 (s, 3H), 3.03 (s, 1H), 3.29 (dd, 1H, *J* = 15.2, 2.8 Hz), 3.44 (dd, 1H, *J* = 15.2, 9.2 Hz), 3.80 (s, 3H), 4.14 (d, 1H, *J* = 10.0 Hz), 4.55 (d, 1H, *J* = 10.0 Hz)), 4.89 (br-d, 1H, *J* = 9.2 Hz), 6.86 (d, 2H, *J* = 8.4 Hz), 7.11-7.14 (m, 2H), 7.21-7.28 (m, 3H), 7.31 (d, 2H, *J* = 8.4 Hz), 7.47 (s, 1H), 7.74 (d, 2H, *J* = 8.4 Hz), 8.09

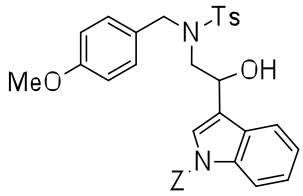
(d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.1 (×3), 53.8, 55.0, 55.3, 67.1, 83.7, 114.2 (×2), 115.3, 119.3, 120.9, 122.4, 123.0, 124.4, 127.3 (×2), 127.7, 128.0, 129.8 (×2), 130.0 (×2), 135.7, 135.8, 143.7, 149.5, 159.6; IR (ATR) ν 3512, 1730, 1611, 1513, 1452, 1369, 1251, 1153, 1091, 1019, 916, 815, 746, 660 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{34}N_2NaO_6S$ 573.2035 (M+Na$^+$) found 573.2047.



7d

White solid; melting point 63-66 °C;
Rf 0.24 (*n*-hexane/EtOAc = 3/1);
69% yield (2 steps);

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.65 (s, 9H), 2.40 (s, 3H), 3.23 (s, 1H), 3.37 (dd, 1H, J = 14.8, 2.8 Hz), 3.50 (dd, 1H, J = 14.8, 9.2 Hz), 3.71 (s, 3H), 4.41 (d, 1H, J = 14.4 Hz), 4.56 (d, 1H, J = 14.4 Hz), 4.94 (br-d, 1H, J = 9.2 Hz), 6.83 (d, 1H, J = 8.4 Hz), 6.97 (t, 1H, J = 8.4 Hz), 7.13 (t, 1H, J = 8.4 Hz), 7.21-7.32 (m, 5H), 7.40 (d, 1H, J = 7.2 Hz), 7.49 (s, 1H), 7.67 (d, 2H, J = 8.0 Hz), 8.10 (d, 1H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.2 (×3), 48.7, 55.2, 55.7, 66.9, 83.6, 110.5, 115.3, 119.3, 120.8, 120.9, 122.4, 123.0, 123.7, 124.3, 127.3 (×2), 128.1, 129.5, 129.6 (×2), 131.0, 135.7, 135.8, 143.5, 149.5, 157.4; IR (ATR) ν 1731, 1601, 1494, 1453, 1368, 1335, 1246, 1152, 1090, 1064, 1019, 917, 815, 749, 660 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{34}N_2NaO_6S$ 573.2035 (M+Na$^+$) found 573.1987.

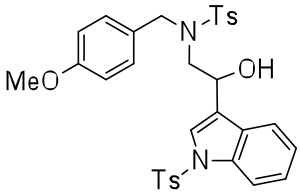


7e

White solid; melting point 47-50 °C;
Rf 0.29 (*n*-hexane/EtOAc = 2/1);
51% yield (2 steps);

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 3.06 (s, 1H), 3.28 (dd, 1H, J = 15.2, 2.8 Hz), 3.41 (dd, 1H, J = 15.2, 8.8 Hz), 3.77 (s, 3H), 4.12 (d, 1H, J = 14.8 Hz), 4.52 (d, 1H, J = 14.8 Hz), 4.89 (br-d, 1H, J = 8.8 Hz), 5.39 (s, 2H), 6.83 (d, 2H, J = 8.4 Hz), 7.10-7.49 (m, 13H), 7.73 (d, 2H, J = 8.0 Hz), 8.11 (d, 1H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 53.8, 54.9, 55.2, 67.1, 68.7, 114.2 (×2), 115.3, 119.4, 121.9, 122.6, 122.8, 124.7, 127.3 (×2), 127.7, 128.1, 128.5 (×2), 128.7 (×2), 128.7, 128.7, 129.8 (×2), 130.0 (×2), 135.0, 135.7, 143.7, 150.6, 159.6; IR (ATR) ν 1735, 1611, 1513, 1455, 1398, 1337, 1249, 1156, 1091, 1031, 816, 747, 699, 660 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{33}H_{32}N_2NaO_6S$ 607.1879

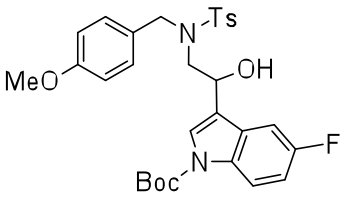
(M+Na$^+$) found 607.1882.



7f

White solid; melting point 73-76 °C;
Rf 0.24 (*n*-hexane/EtOAc = 2/1);
73% yield;

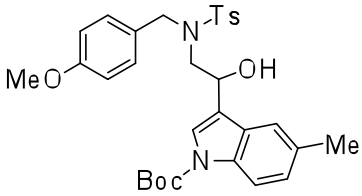
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 3H), 2.42 (s, 3H), 3.24 (dd, 1H, *J* = 15.2, 3.2 Hz), 3.37 (dd, 1H, *J* = 15.2, 9.2 Hz), 3.78 (s, 3H), 4.07 (d, 1H, *J* = 14.4 Hz), 4.47 (d, 1H, *J* = 14.4 Hz), 4.82 (dd, 1H, *J* = 9.2, 3.2 Hz), 6.82 (d, 2H, *J* = 8.4 Hz), 7.08-7.09 (m, 2H), 7.12 (d, 2H, *J* = 8.4 Hz), 7.16 (d, 2H, *J* = 8.4 Hz), 7.17-7.28 (m, 1H), 7.31 (d, 2H, *J* = 8.4 Hz), 7.45 (s, 1H), 7.71 (d, 2H, *J* = 8.4 Hz), 7.73 (d, 2H, *J* = 8.4 Hz), 7.90 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 53.8, 54.8, 55.2, 67.0, 113.5, 114.2 (×2), 119.8, 122.6, 123.0, 123.3, 124.6, 126.7 (×2), 126.7, 127.3 (×2), 127.5, 128.3, 129.8 (×2), 129.9 (×2), 129.9 (×2), 135.0, 135.1, 135.4, 143.9, 144.9, 159.5; IR (ATR) ν 1597, 1512, 1446, 1249, 1155, 1090, 813, 744, 703, 675 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{32}H_{32}N_2NaO_6S_2$ 627.1599 (M+Na$^+$) found 627.1556.



7g

White solid; melting point 65-67 °C;
Rf 0.24 (*n*-hexane/EtOAc = 3/1);
64% yield (2 steps);

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64 (s, 9H), 2.43 (s, 3H), 3.19 (dd, 1H, *J* = 14.8, 2.0 Hz), 3.25 (s, 1H), 3.39 (dd, 1H, *J* = 14.8, 9.2 Hz), 3.81 (s, 3H), 4.08 (d, 1H, *J* = 14.4 Hz), 4.56 (d, 1H, *J* = 14.4 Hz), 4.80 (br-d, 1H, *J* = 9.2 Hz), 6.64 (d, 1H, *J* = 8.8 Hz), 6.89 (d, 2H, *J* = 8.4 Hz), 6.95 (td, 1H, *J* = 8.8, 2.0 Hz), 7.22 (d, 2H, *J* = 8.4 Hz), 7.33 (d, 2H, *J* = 8.4 Hz), 7.51 (s, 1H), 7.75 (d, 2H, *J* = 8.4 Hz), 8.01 (br-s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.1 (×3), 53.9, 54.8, 55.2, 67.0, 83.9, 104.8 (d, *J* = 23.8 Hz), 112.0 (d, *J* = 24.7 Hz), 114.3 (×2), 116.1 (d, *J* = 9.6 Hz), 120.5 (d, *J* = 3.8 Hz), 124.5, 127.3 (×2), 127.3, 128.7 (d, *J* = 9.6 Hz), 129.9 (×2), 130.0 (×2), 131.9, 135.3, 143.9, 149.2, 158.8 (d, *J* = 238.4 Hz), 159.6; IR (ATR) ν 1733, 1612, 1513, 1472, 1450, 1372, 1337, 1252, 1154, 1065, 1035, 915, 810, 767, 744, 659 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{33}FN_2NaO_6S$ 591.1941 (M+Na$^+$) found 591.1910.

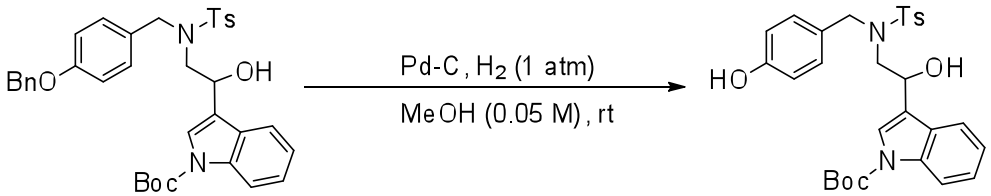


7h

White solid; melting point 65-68 °C;
Rf 0.36 (*n*-hexane/EtOAc = 2/1);
60% yield (2 steps);

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 9H), 2.36 (s, 3H), 2.42 (s, 3H), 3.10 (s, 1H), 3.27 (dd, 1H, *J* = 15.2, 2.8 Hz), 3.44 (dd, 1H, *J* = 15.2, 9.6 Hz), 3.79 (s, 3H), 4.18 (d, 1H, *J* = 14.0 Hz), 4.54 (d, 1H, *J* = 14.0 Hz), 4.80 (br-d, 1H, *J* = 9.2 Hz), 6.86 (d, 2H, *J* = 8.4 Hz), 6.86 (d, 1H, *J* = 8.4 Hz), 7.06 (d, 1H, *J* = 8.4 Hz), 7.22 (d, 2H, *J* = 8.4 Hz), 7.31 (d, 2H, *J* = 8.4 Hz), 7.45 (s, 1H), 7.75 (d, 2H, *J* = 8.4 Hz), 7.95 (br-s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 21.5, 28.1 (×3), 53.5, 54.6, 55.1, 66.8, 83.5, 114.2 (×2), 114.8, 119.0, 120.5, 123.0, 125.7, 127.3 (×2), 127.6, 128.1, 129.8 (×2), 129.9 (×2), 131.8, 133.8, 135.7, 143.7, 149.5, 159.4; IR (ATR) ν 1732, 1513, 1457, 1370, 1251, 1154, 1091, 805, 745, 658 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{31}H_{36}N_2NaO_6S$ 587.2192 (M+Na$^+$) found 587.2203.

(3-3) Preparation of Compound **7a**

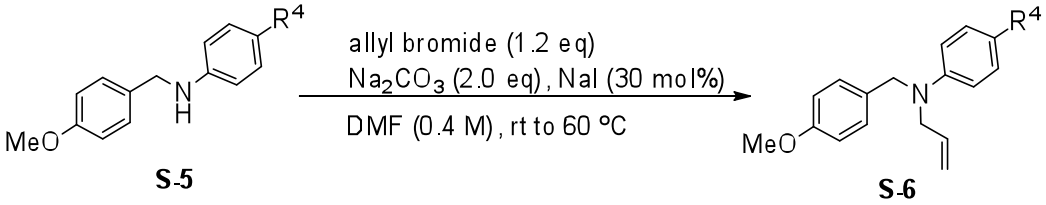


7c **7a**

To a suspension of Pd-C (40 mg) in MeOH (12mL) at room temperature was added **7c** (412 mg 0.66 mmol) and the reaction mixture was stirred for 21 h under an atmosphere of hydrogen. The reaction mixture was filtered through a Celite pad and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2/1) to give **7a** (181mg, 51%) as a white solid: melting point 77 °C; Rf 0.19 (*n*-hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 9H), 2.40 (s, 3H), 3.28 (br-d, 1H, *J* = 14.8 Hz), 3.45 (dd, 1H, *J* = 14.8, 8.0 Hz), 4.09 (d, 1H, *J* = 14.4 Hz), 4.51 (d, 1H, *J* = 14.4 Hz), 4.87 (br-d, 1H, *J* = 8.0 Hz), 6.78 (d, 2H, *J* = 8.0 Hz), 7.09-7.16 (m, 4H), 7.23 (t, 1H, *J* = 8.0 Hz), 7.29 (d, 2H, *J* = 8.0 Hz), 7.46 (s, 1H), 7.72 (d, 2H, *J* = 8.0 Hz), 8.06 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.1 (×3), 53.9, 55.1, 67.2, 83.8, 115.3, 115.8 (×2), 119.3, 120.6, 122.6, 123.0, 124.4, 127.3 (×2), 127.3, 128.0, 129.9 (×2), 130.1 (×2), 135.5, 135.6, 143.9, 149.6, 156.2; IR (ATR) ν 3425, 1731, 1516, 1452, 1369, 1333, 1256, 1224, 1152, 1091, 1064, 1018, 916, 815, 750, 660 cm^{-1}; HRMS (ESI$^+$)

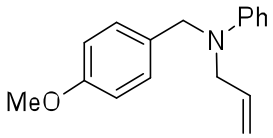
calcd for $C_{29}H_{32}N_2NaO_6S$ 559.1879 ($M+Na^+$) found 559.1873.

(3-4) Preparation of Compounds **7i**, **7j** and **7k**



S-5 **S-6**

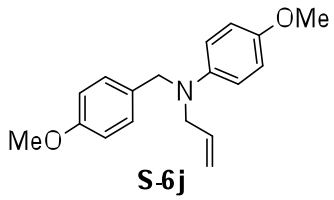
General Procedure: To a stirred solution of **S-5** (2.9 mmol), NaI (130 mg, 0.87 mmol) and Na_2CO_3 (421 mg, 5.8 mmol) in DMF (7 mL) at room temperature was added allyl bromide (0.30 mL, 3.5 mmol). After being stirred for 4.5 h at 60 °C, the reaction mixture was quenched with H_2O, and extracted with 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the desired products **S-6**.



S-6i

Colorless oil;
Rf 0.36 (*n*-hexane/EtOAc = 20/1);
63% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.97 (d, 2H, J = 3.6 Hz), 4.47 (s, 2H), 5.16 (dd, 1H, J = 10.0, 1.2 Hz), 5.17 (dd, 1H, J = 17.6, 1.2 Hz), 5.82-5.91 (m, 1H), 6.68 (t, 1H, J = 8.0 Hz), 6.72 (d, 2H, J = 8.0 Hz), 6.84 (d, 2H, J = 8.0 Hz), 7.14-7.19 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.8, 53.3, 55.2, 112.5 (×2), 114.0 (×2), 116.2, 116.4, 127.8 (×2), 129.1 (×2), 130.8, 133.7, 149.0, 158.5; IR (ATR) ν 1597, 1504, 1242, 1170, 1034, 987, 918, 811, 745, 690 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{17}H_{20}NO$ 254.1545 ($M+H^+$) found 254.1523.

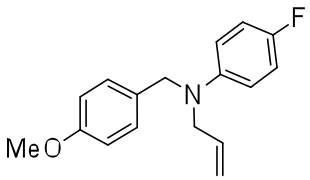


S-6j

Pale yellow oil;
Rf 0.24 (*n*-hexane/EtOAc = 20/1);
75% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (s, 3H), 3.76 (s, 3H), 3.89 (d, 2H, J = 5.2 Hz), 4.38 (s, 2H), 5.13-5.19 (m, 2H), 5.84 (ddt, 1H, J = 17.2, 10.4, 5.2 Hz), 6.69 (d, 2H, J = 9.2 Hz), 6.77 (d, 2H, J = 9.2 Hz), 6.83 (d, 2H, J = 8.0 Hz), 7.15 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.6, 54.3, 55.2, 55.6, 113.8 (×2), 114.6 (×2), 114.6 (×2), 116.3 (×2), 128.0, 131.0, 134.3, 143.7, 151.5, 158.5; IR (ATR) ν 1611, 1508, 1462, 1238, 1172, 1034, 920,

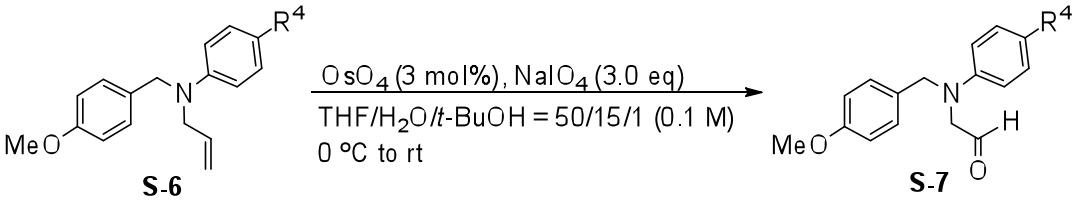
811, 715 cm^{-1}; HRMS (ESI+) calcd for $C_{18}H_{22}NO_2$ 284.1651 ($M+H^+$) found 284.1614.



S-6k

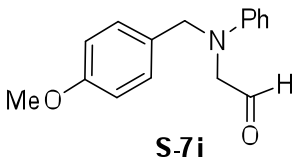
Colorless oil;
Rf 0.33 (*n*-hexane/EtOAc = 20/1);
66% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.92 (d, 2H, J = 5.2 Hz), 4.41 (s, 2H), 5.13-5.18 (m, 2H), 5.84 (ddt, 1H, J = 17.2, 10.0, 5.2 Hz), 6.62 (dd, 2H, J = 8.8, 4.4 Hz), 6.84 (d, 2H, J = 8.4 Hz), 6.86 (t, 2H, J = 8.8 Hz), 7.13 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.5, 54.1, 55.2, 113.7 (×2, d, J = 7.6 Hz), 113.9 (×2), 115.4 (×2, d, J = 21.9 Hz), 116.4, 127.8 (×2), 130.6, 133.7, 145.6, 155.3 (d, J = 233.6 Hz), 158.6; IR (ATR) ν 1611, 1506, 1357, 1224, 1170, 1034, 919, 808, 718 cm^{-1}; HRMS (ESI+) calcd for $C_{17}H_{19}FNO$ 272.1451 ($M+H^+$) found 272.1436.



S-6 **S-7**

General Procedure: To a stirred solution of **S-6** (3.4 mmol) in THF (25 mL) and H_2O (7.5 mL) at 0 °C was added OsO_4 (0.50 mL, 0.2 M in *t*-BiOH, 0.10 mmol) and $NaIO_4$ (2201 mg, 10.2 mmol). After being stirred for 8 h at room temperature, the reaction mixture was quenched with aqueous $Na_2S_2O_3$, and extracted with 2 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the desired products **S-7**.

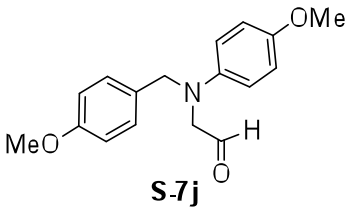


S-7i

Yellow oil;
Rf 0.27 (*n*-hexane/EtOAc = 6/1);
40% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 4.01 (s, 2H), 4.58 (s, 2H), 6.71 (d, 2H, J = 8.8 Hz), 6.78 (t, 1H, J = 7.6 Hz), 6.86 (d, 2H, J = 8.8 Hz), 7.18 (d, 2H, J = 8.8 Hz), 7.22 (dd, 2H, J = 8.8, 7.6 Hz), 9.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 55.4, 60.6, 112.9 (×2), 114.2 (×2), 118.2, 128.3 (×2), 129.5 (×2), 129.8, 148.6, 159.0, 202.3; IR (ATR) ν 1726,

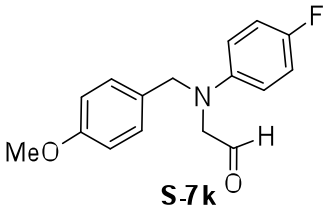
1597, 1504, 1353, 1243, 1173, 1032, 817, 748, 691 cm^{-1}; EI-LRMS m/z 255 (M^+), EI-HRMS calcd for $C_{16}H_{17}NO_2$ 255.1259 (M^+) found 255.1268.



S-7j

Yellow oil;
Rf 0.14 (*n*-hexane/EtOAc = 10/1);
43% yield;

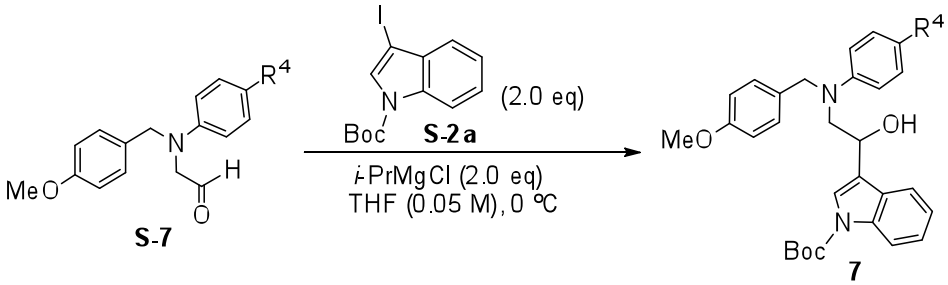
^1H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 3H), 3.79 (s, 3H), 3.92 (s, 2H), 4.47 (s, 2H), 6.70 (d, 2H, J = 9.2 Hz), 6.81 (d, 2H, J = 9.2 Hz), 6.85 (d, 2H, J = 8.8 Hz), 7.19 (d, 2H, J = 8.8 Hz), 9.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 55.6, 56.6, 61.2, 114.1 (×2), 114.8 (×2), 115.5 (×2), 128.7 (×2), 129.9, 143.2, 152.7, 158.9, 202.7; IR (ATR) ν 1726, 1610, 1507, 1462, 1239, 1173, 1033, 813 cm^{-1}; HRMS (ESI^+) calcd for $C_{17}H_{19}NNaO_3$ 308.1263 ($M+Na^+$) found 308.1249.



S-7k

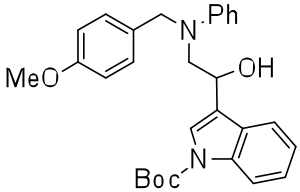
Pale yellow solid; melting point 88 °C;
Rf 0.17 (*n*-hexane/EtOAc = 6/1);
60% yield;

^1H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 3.98 (s, 2H), 4.50 (s, 2H), 6.63 (dd, 2H, J = 8.4, 4.0 Hz), 6.85 (d, 2H, J = 8.0 Hz), 6.91 (t, 2H, J = 8.4 Hz), 7.17 (d, 2H, J = 8.0 Hz), 9.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 56.1, 61.1, 114.1 (×2), 114.5 (×2, d, J = 7.6 Hz), 115.8 (×2, d, J = 21.9 Hz), 128.4 (×2), 129.5, 145.2, 156.1 (d, J = 236.4 Hz), 159.0, 201.8; IR (ATR) ν 1727, 1611, 1508, 1227, 1173, 1032, 813 cm^{-1}; HRMS (ESI^+) calcd for $C_{16}H_{16}FNNaO_2$ 296.1063 ($M+Na^+$) found 296.1058.



General Procedure: To a stirred solution of **S-2a** (1.0 mmol) in THF (5 mL) at 0 °C was

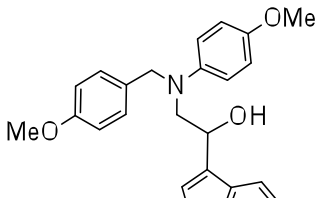
added *i*-PrMgCl (0.5 mL, 2 M in THF, 1.0 mmol). After being stirred for 15 min, the reaction mixture was added aldehyde **S-7** (0.5 mmol) in THF (5 mL) at 0 °C. After being stirred for 10 min at the same temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl, and extracted with 2 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the desired products **7**.



7i

White solid; melting point 58 °C;
Rf 0.21 (*n*-hexane/EtOAc = 6/1);
50% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.66 (s, 9H), 2.46 (s, 1H), 3.75-3.83 (m, 2H), 3.76 (s, 3H), 4.52 (d, 1H, *J* = 16.8 Hz), 4.59 (d, 1H, *J* = 16.8 Hz), 5.27 (br-dd, 1H, *J* = 7.6, 4.8 Hz), 6.77 (t, 1H, *J* = 6.8 Hz), 6.81 (d, 2H, *J* = 8.4 Hz), 6.89 (d, 2H, *J* = 8.4 Hz), 7.09 (d, 2H, *J* = 8.4 Hz), 7.12-7.26 (m, 3H), 7.37 (t, 1H, *J* = 7.6 Hz), 7.57 (s, 1H), 7.58 (d, 1H, *J* = 7.6 Hz), 8.15 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (×3), 55.1, 55.2, 57.9, 66.0, 83.8, 113.7 (×2), 114.0 (×2), 115.4, 117.6, 119.7, 121.4, 122.6, 122.9, 124.6, 128.0 (×2), 128.4, 129.3 (×2), 130.1, 135.8, 148.8, 149.6, 158.5; IR (ATR) ν 1731, 1598, 1505, 1450, 1369, 1245, 1152, 1090, 1033, 816, 737, 692 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{29}H_{32}N_2NaO_4$ 495.2260 (M+Na$^+$) found 495.2230.

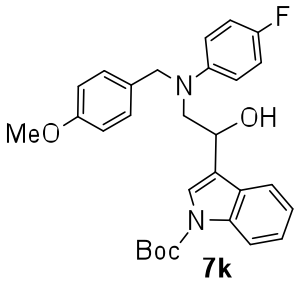


7j

Yellow solid; melting point 60-62 °C;
Rf 0.21 (*n*-hexane/EtOAc = 4/1);
43% yield;

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64 (s, 9H), 2.95 (s, 1H), 3.51-3.64 (m, 2H), 3.75 (br-s, 3H), 3.75 (br-s, 3H), 4.36 (d, 1H, *J* = 16.0 Hz), 4.41 (d, 1H, *J* = 16.0 Hz), 5.10 (br-d, 1H, *J* = 5.2 Hz), 6.79-6.83 (m, 4H), 6.91 (d, 2H, *J* = 7.6 Hz), 7.10 (d, 2H, *J* = 6.8 Hz), 7.18 (t, 1H, *J* = 7.2 Hz), 7.29 (t, 1H, *J* = 7.2 Hz), 7.49 (d, 1H, *J* = 7.2 Hz), 7.54 (s, 1H), 8.14 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.1 (×3), 55.1, 55.5, 57.1, 58.8, 65.5, 83.6, 113.9 (×2), 114.7 (×2), 115.3, 118.0 (×2), 119.7, 121.4, 122.5, 122.7, 124.4, 128.5, 128.7 (×2), 130.2,

135.7, 143.4, 149.6, 153.3, 158.6; IR (ATR) ν 1730, 1509, 1451, 1369, 1243, 1154, 1091, 1035, 811, 746 cm^{-1}; HRMS (ESI^+) calcd for $C_{30}H_{34}N_2NaO_5$ 525.2365 ($M+Na^+$) found 525.2364.

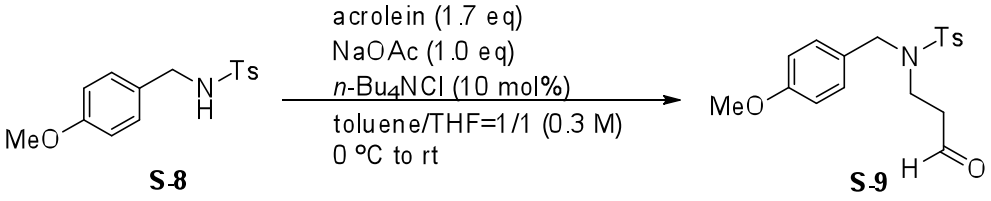


7k

White solid; melting point 54 °C;
Rf 0.17 (*n*-hexane/EtOAc = 6/1);
75% yield;

^1H NMR (400 MHz, $CDCl_3$) δ 1.64 (s, 9H), 2.76 (s, 1H), 3.66-3.68 (m, 2H), 3.73 (s, 3H), 4.40 (d, 1H, *J* = 16.4 Hz), 4.46 (d, 1H, *J* = 16.4 Hz), 5.15 (br-dd, 1H, *J* = 7.2, 5.6 Hz), 6.79 (d, 2H, *J* = 8.4 Hz), 6.79-6.82 (m, 2H), 6.91 (t, 2H, *J* = 8.8 Hz), 7.05 (d, 2H, *J* = 8.4 Hz), 7.18 (t, 1H, *J* = 7.6 Hz), 7.29 (t, 1H, *J* = 7.6 Hz), 7.51 (d, 1H, *J* = 7.6 Hz), 7.54 (s, 1H), 8.14 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.1 (×3), 55.1, 55.9, 58.4, 65.7, 83.7, 113.9 (×2), 115.3, 115.6 (×2, d, *J* = 21.9 Hz), 115.8 (×2, d, *J* = 6.6 Hz), 119.6, 121.4, 122.5, 122.8, 124.5, 128.2, 128.4, 129.8, 135.7, 145.4, 145.4, 149.5, 156.1 (d, *J* = 235.5 Hz), 158.6; IR (ATR) ν 1732, 1509, 1452, 1370, 1248, 1156, 1092, 813, 747 cm^{-1}; HRMS (ESI^+) calcd for $C_{29}H_{31}FN_2NaO_4$ 513.2166 ($M+Na^+$) found 513.2130.

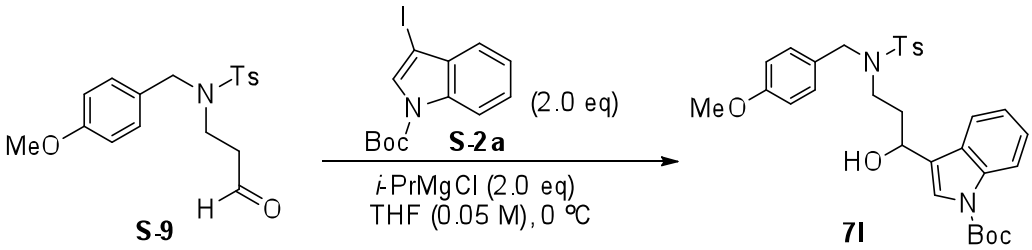
(3-5) Preparation of Compound **71**



S-8 **S-9**

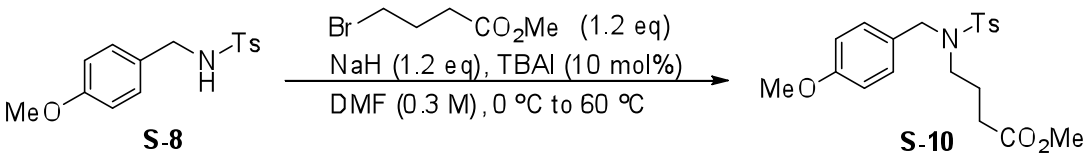
To a stirred solution of **S-8** (3.0 mmol), acrolein (0.33 mL, 5.0 mmol) and *n*-Bu_4NCl (83.4 mg, 0.3 mmol) in toluene (10 mL) and THF (10 mL) at 0 °C was added NaOAc (246 mg, 3.0 mmol). After being stirred for 50 min at rt, the reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2/1) to give the desired product **S-9** (496 mg, 48%) as a white solid: melting point 69-71 °C; Rf 0.29 (*n*-hexane/EtOAc = 2/1); ^1H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 2.43 (t, 2H, *J* = 7.2 Hz), 3.27 (t, 2H, *J* = 7.2 Hz), 3.70 (s, 3H), 4.13 (s, 2H), 6.76 (d, 2H, *J* = 8.4 Hz), 7.11 (d, 2H, *J* = 8.4 Hz), 7.25 (d, 2H, *J* = 8.4 Hz), 7.63 (d, 2H, *J* = 8.4 Hz), 9.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 41.6, 43.6, 52.5, 55.1, 114.0 (×2), 127.1 (×2),

127.7, 129.7 (×2), 129.8 (×2), 135.9, 143.5, 159.3, 200.2; IR (ATR) ν 1720, 1511, 1334, 1304, 1245, 1154, 1089, 1030, 907, 813, 744 cm^{-1}; HRMS (ESI^+) calcd for $C_{18}H_{21}NNaO_4S$ 370.1089 ($M+Na^+$) found 370.1050.



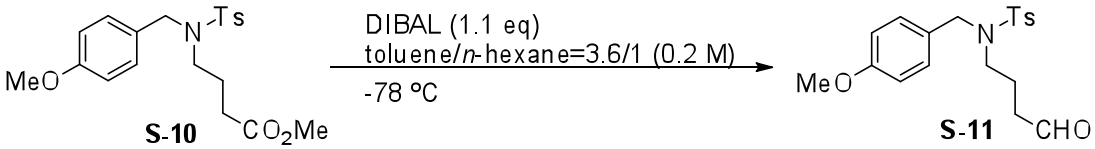
To a stirred solution of **S-2a** (343 mg, 1.0 mmol) in THF (5 mL) at 0 °C was added *i*-PrMgCl (0.5 mL, 2 M in THF, 1.0 mmol). After being stirred for 15 min, the reaction mixture was added aldehyde **S-9** (173 mg, 0.5 mmol) in THF (5 mL) at 0 °C. After being stirred for 10 min at the same temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl, and extracted with 2 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2/1) to give the desired product **7l** (263 mg, 93%) as a white solid: melting point 59 °C; Rf 0.24 (*n*-hexane/EtOAc = 2/1); ^1H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 9H), 1.69-1.86 (m, 2H), 2.41 (s, 3H), 3.00 (s, 1H), 3.02-3.08 (m, 1H), 3.48-3.56 (m, 1H), 3.74 (s, 3H), 4.01 (d, 1H, *J* = 14.4 Hz), 4.44 (d, 1H, *J* = 14.4 Hz), 4.89 (br-d, 1H, *J* = 8.4 Hz), 6.79 (d, 2H, *J* = 8.4 Hz), 7.13 (t, 1H, *J* = 7.6 Hz), 7.18 (d, 2H, *J* = 8.4 Hz), 7.22-7.27 (m, 2H), 7.28 (d, 2H, *J* = 8.4 Hz), 7.39 (s, 1H), 7.69 (d, 2H, *J* = 8.4 Hz), 8.10 (br-d, 1H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 28.0 (×3), 35.8, 45.4, 52.8, 55.1, 64.3, 83.4, 113.9 (×2), 115.0, 119.7, 122.0, 122.2, 123.2, 124.2, 127.0 (×2), 128.2 (×2), 129.7 (×2), 129.8 (×2), 135.6, 136.0, 143.4, 149.5, 159.2; IR (ATR) ν 1728, 1512, 1452, 1369, 1333, 1305, 1248, 1152, 1089, 1033, 814, 766, 735, 701, 654 cm^{-1}; HRMS (ESI^+) calcd for $C_{31}H_{36}N_2NaO_6S$ 587.2192 ($M+Na^+$) found 587.2146.

(3-5) Preparation of Compound **7m**

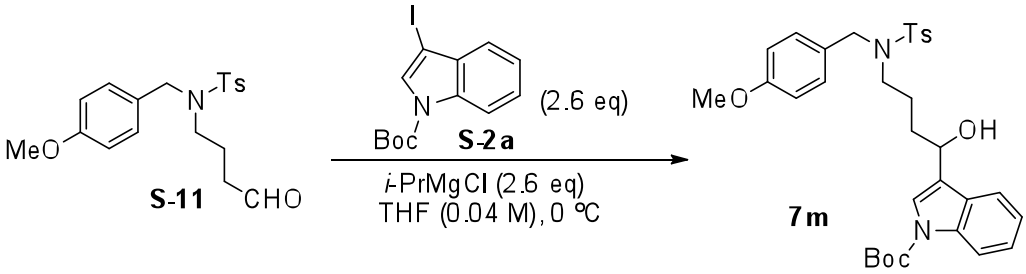


To a stirred solution of **S-8** (1000 mg, 3.4 mmol) in DMF (10 mL) at 0 °C was added NaH (60% in oil, 165 mg, 4.1 mmol). After being stirred for 30 min at 0 °C, methyl

4-bromobutyrate (0.52 mL, 4.1 mmol) and TBAI (126 mg, 0.34 mmol) were added to the reaction mixture at the same temperature. After being stirred for 8 h at 60 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl at 0 °C, and extracted with 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 3/1) to give the desired product **S-10** (1265 mg, 94%) as a Colorless oil: Rf 0.17 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64 (quintet, 2H, *J* = 7.2 Hz), 2.17 (t, 2H, *J* = 7.2 Hz), 2.44 (s, 3H), 3.10 (t, 2H, *J* = 7.2 Hz), 3.60 (s, 3H), 3.79 (s, 3H), 4.23 (s, 2H), 6.83 (d, 2H, *J* = 8.8 Hz), 7.19 (d, 2H, *J* = 8.8 Hz), 7.31 (d, 2H, *J* = 7.6 Hz), 7.71 (d, 2H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 23.3, 30.6, 47.1, 51.5, 51.7, 55.2, 113.9 (×2), 127.1 (×2), 128.1, 129.7 (×2), 129.7 (×2), 136.6, 143.2, 159.2, 173.2; IR (ATR) ν 1733, 1611, 1512, 1438, 1335, 1247, 1155, 1031, 815, 740 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{25}NNaO_5S$ 414.1351 (M+Na$^+$) found 414.1302.



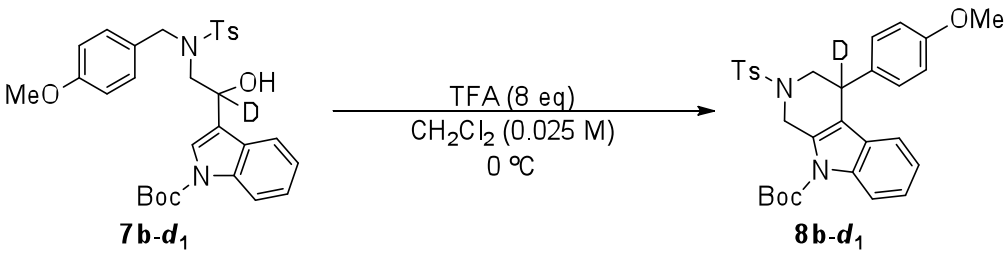
To a stirred solution of **S-10** (500 mg, 1.28 mmol) in toluene (5 mL) at -78 °C was added dropwise DIBAL (1.4 mL, 1.0 M in *n*-hexane). After being stirred for 1 h at -78 °C, the reaction mixture was quenched with aqueous 2 M potassium sodium tartrate at the same temperature. The solution was warmed to room temperature and stirred until the organic and aqueous layers were separated. The aqueous layer was extracted 3 times with EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2.3/1) to give the desired product **S-11** (350 mg, 76%) as a Colorless oil: Rf 0.21 (*n*-hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61 (quintet, 2H, *J* = 6.8 Hz), 2.33 (t, 2H, *J* = 6.8 Hz), 2.44 (s, 3H), 3.08 (t, 2H, *J* = 6.8 Hz), 3.79 (s, 3H), 4.21 (s, 2H), 6.83 (d, 2H, *J* = 8.8 Hz), 7.19 (d, 2H, *J* = 8.8 Hz), 7.32 (d, 2H, *J* = 8.0 Hz), 7.70 (d, 2H, *J* = 8.0 Hz), 9.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 21.5, 40.4, 47.3, 52.1, 55.2, 113.9 (×2), 127.1 (×2), 128.1, 129.7 (×2), 129.8 (×2), 136.4, 143.3, 159.2, 201.4; IR (ATR) ν 1720, 1611, 1511, 1333, 1246, 1154, 1089, 1030, 814, 734 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{19}H_{23}NNaO_4S$ 384.1245 (M+Na$^+$) found 384.1232.



To a stirred solution of **S-2a** (343 mg, 1.0 mmol) in THF (5 mL) at 0 °C was added *i*-PrMgCl (0.5 mL, 2 M in THF, 1.0 mmol). After being stirred for 15 min, the reaction mixture was added aldehyde **S-11** (140 mg, 0.38 mmol) in THF (5 mL) at 0 °C. After being stirred for 10 min at the same temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl, and extracted with 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2/1) to give the desired product **7m** (208 mg, 93%) as a white solid: melting point 51-54 °C; Rf 0.17 (*n*-hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36-1.56 (m, 2H), 1.65 (s, 9H), 1.65-1.73 (m, 2H), 2.13 (s, 1H), 2.37 (s, 3H), 3.11 (t, 2H, *J* = 7.2 Hz), 3.73 (s, 3H), 4.18 (s, 2H), 4.75 (t, 1H, *J* = 6.4 Hz), 6.75 (d, 2H, *J* = 8.0 Hz), 7.11 (d, 2H, *J* = 8.0 Hz), 7.17-7.24 (m, 3H), 7.29 (t, 1H, *J* = 8.0 Hz), 7.42 (s, 1H), 7.53 (d, 1H, *J* = 8.0 Hz), 7.64 (d, 2H, *J* = 8.0 Hz), 8.13 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 24.2, 28.1 (×3), 33.8, 47.5, 51.2, 55.1, 67.3, 83.6, 113.8 (×2), 115.2, 119.7, 122.2, 122.4, 123.7, 124.3, 127.0 (×2), 128.2, 128.4, 129.5 (×2), 129.5 (×2), 135.7, 136.9, 143.0, 149.6, 159.1; IR (ATR) ν 1728, 1512, 1452, 1368, 1248, 1153, 1089, 815, 736 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{32}H_{38}N_2NaO_6S$ 601.2348 ($M+Na^+$) found 601.2372.

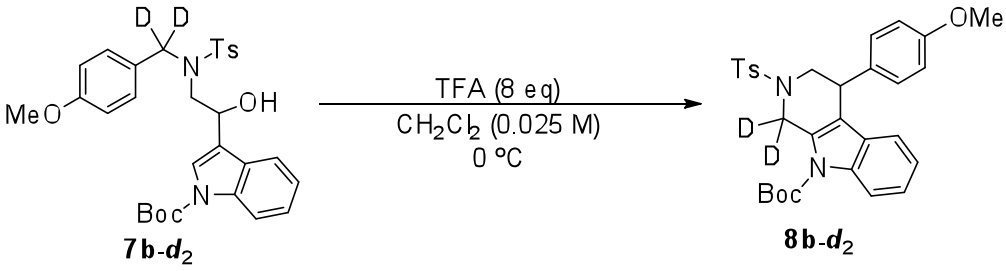
4. Deuterium Labelling Studies

(4-1) Acid-Promoted Novel Skeletal Rearrangement using Deuterium Labeling Compounds **7b-*d*$_1$** and **7b-*d*$_2$**



To a stirred solution of **7b-*d*$_1$** (71.7 mg, 0.13 mmol) in CH_2Cl_2 (4.2 mL) at 0 °C was added TFA (1.0 mL, 1.0 M in CH_2Cl_2, 1.0 mmol). After being stirred for 4 h at 0 °C, the reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel

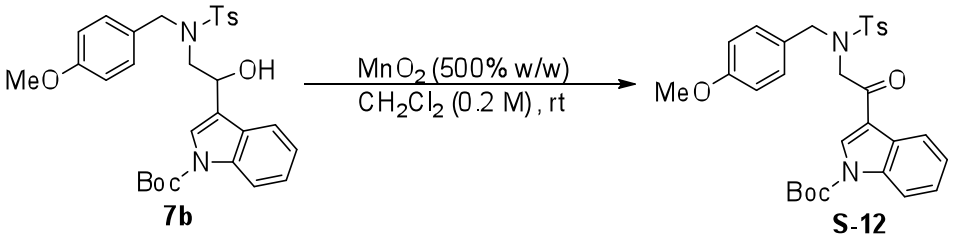
column chromatography (*n*-hexane/EtOAc = 4/1) to give the desired product **8b-*d*$_1$** (63.8 mg, 92%) as a white solid: melting point 98-101 °C; Rf 0.38 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.71 (s, 9H), 2.40 (s, 3H), 2.96 (d, 1H, *J* = 12.0 Hz), 3.78 (s, 3H), 3.87 (d, 1H, *J* = 12.0 Hz), 4.37 (d, 1H, *J* = 16.4 Hz), 4.82 (d, 1H, *J* = 16.4 Hz), 6.74 (d, 1H, *J* = 7.6 Hz), 6.81 (d, 2H, *J* = 7.6 Hz), 6.98 (t, 1H, *J* = 7.6 Hz), 7.09 (d, 2H, *J* = 7.6 Hz), 7.20 (t, 1H, *J* = 7.6 Hz), 7.29 (d, 2H, *J* = 7.6 Hz), 7.68 (d, 2H, *J* = 7.6 Hz), 8.11 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.2 (×3), 39.0 (t, *J* = 18.6 Hz), 45.8, 51.4, 55.2, 84.4, 113.9 (×2), 115.3, 117.3, 119.6, 122.6, 124.1, 127.6 (×2), 127.8, 129.3 (×2), 129.7 (×2), 131.1, 132.2, 133.6, 136.0, 143.7, 149.8, 158.7; IR (ATR) v 1731, 1509, 1455, 1371, 1248, 1155, 1117, 1036, 835, 748 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{31}DN_2NaO_5S$ 556.1992 (M+Na$^+$) found 556.1952.



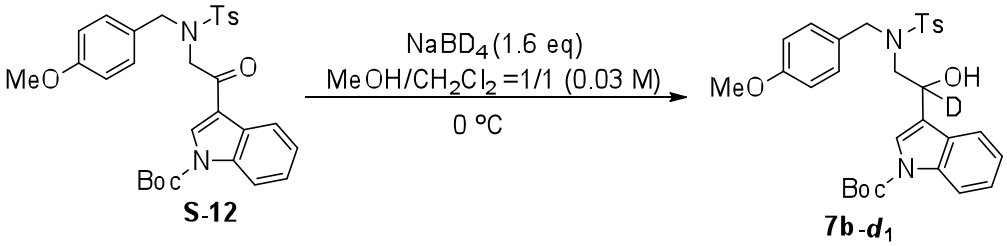
7b-*d*$_2$ **8b-*d*$_2$**

To a stirred solution of **7b-*d*$_2$** (0.20 mmol) in CH_2Cl_2 (6.3 mL) at 0 °C was added TFA (1.6 mL, 1.0 M in CH_2Cl_2, 1.6 mmol). After being stirred for 6 h at 0 °C, the reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 5/1) to give the desired product **8b-*d*$_2$** (79.8 mg, 76%) as a white solid: melting point 85 °C; Rf 0.19 (*n*-hexane/EtOAc = 6/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.71 (s, 9H), 2.40 (s, 3H), 2.97 (dd, 1H, *J* = 12.0, 8.4 Hz), 3.77 (s, 3H), 3.87 (dd, 1H, *J* = 12.0, 6.0 Hz), 4.26 (dd, 1H, *J* = 8.4, 6.0 Hz), 6.74 (d, 1H, *J* = 7.8 Hz), 6.80 (d, 2H, *J* = 8.4 Hz), 6.98 (t, 1H, *J* = 7.8 Hz), 7.08 (d, 2H, *J* = 8.4 Hz), 7.20 (t, 1H, *J* = 7.8 Hz), 7.29 (d, 2H, *J* = 8.4 Hz), 7.68 (d, 2H, *J* = 8.4 Hz), 8.12 (d, 1H, *J* = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.5, 28.2 (×3), 39.4, 45.3 (quintet, *J* = 18.9 Hz), 51.4, 55.2, 84.4, 114.0 (×2), 115.3, 117.5, 119.6, 122.6, 124.1, 127.6 (×2), 127.9, 129.4 (×2), 129.7 (×2), 130.9, 132.2, 133.7, 136.0, 143.7, 149.9, 158.7; IR (ATR) v 1728, 1510, 1455, 1368, 1251, 1149, 1034, 831, 735 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{30}D_2N_2NaO_5S$ 557.2055 (M+Na$^+$) found 557.2060.

(4-2) Preparation of Compound **7b-d_1**



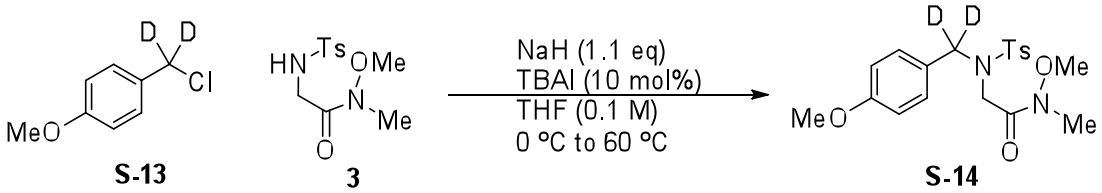
To a stirred solution of **7b** (110 mg, 0.2 mmol) in CH_2Cl_2 (10 mL) at room temperature was added MnO_2 (550 mg). After being stirred for 4.5h at room temperature, the reaction mixture was filtered through a pad of Celite and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 4/1) to give the desired product **S-12** (105 mg, 96%) as a White solid: melting point 53 °C; Rf 0.19 (*n*-hexane/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.69 (s, 9H), 2.42 (s, 3H), 3.69 (s, 3H), 4.45 (s, 2H), 4.48 (s, 2H), 6.71 (d, 2H, *J* = 8.4 Hz), 7.13 (d, 2H, *J* = 8.4 Hz), 7.28-7.37 (m, 4H), 7.78 (d, 2H, *J* = 8.0 Hz), 8.13 (t, 2H, *J* = 6.8 Hz), 8.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.0 (×3), 51.1, 52.0, 55.1, 85.5, 113.8 (×2), 114.8, 117.4, 122.3, 124.2, 125.5, 126.8, 127.1, 127.4 (×2), 129.5 (×2), 130.3 (×2), 131.9, 135.1, 136.8, 143.3, 148.7, 159.3, 190.1; IR (ATR) v 1743, 1450, 1359, 1237, 1150, 1192, 1032, 737, 656 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{32}N_2NaO_6S$ 571.1879 (M+Na$^+$) found 571.1832.



To a stirred solution of **S-12** (35.0 mg, 0.064 mmol) in MeOH (1 mL) and CH_2Cl_2 (1 mL) at 0 °C was added $NaBD_4$ (4.2 mg, 0.10 mmol). After being stirred for 1 h at 0 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with 2 times with EtOAc. The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2.5/1) to give the desired product **7b-d_1** (26.2 mg, 74%) as a White solid: melting point 55-58 °C; Rf 0.24 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64 (s, 9H), 2.42 (s, 3H), 3.07 (s, 1H), 3.27 (d, 1H, *J* = 15.2 Hz), 3.43 (d, 1H, *J* = 15.2 Hz), 3.80 (s, 3H), 4.13 (d, 1H, *J* = 14.0 Hz), 4.55 (d, 1H, *J* = 14.0 Hz), 6.86 (d, 2H, *J* = 8.0 Hz), 7.10-7.12 (m, 2H), 7.22 (d, 2H, *J* = 8.4 Hz), 7.24-7.27 (m, 1H), 7.30 (d,

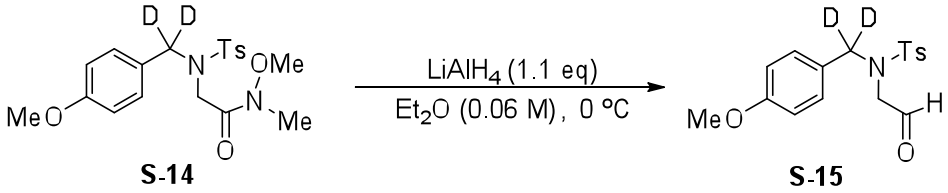
2H, J = 8.0 Hz), 7.47 (s, 1H), 7.74 (d, 2H, J = 8.0 Hz), 8.09 (d, 1H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.1 (×3), 53.8, 54.9, 55.2, 66.7 (t, J = 21.0 Hz), 83.7, 114.2 (×2), 115.2, 119.2, 120.7, 122.4, 123.0, 124.3, 127.3 (×2), 127.6, 128.0, 129.8 (×2), 129.9 (×2), 135.6, 135.6, 143.7, 149.5, 159.5; IR (ATR) v 1731, 1512, 1452, 1369, 1248, 1151, 1089, 912, 814, 742, 658 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{33}DN_2NaO_6S$ 574.2098 (M+Na$^+$) found 574.2084.

(4-3) Preparation of Compound **7b-*d*$_2$**

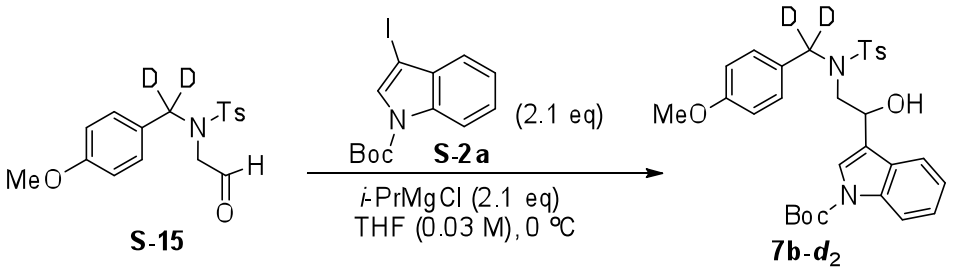


S-13 was prepared according to the literature procedure[6,7].

To a stirred solution of **3** (153 mg, 0.56 mmol) in THF (4 mL) at 0 °C was added NaH (60% in oil, 25 mg, 0.62 mmol). After being stirred for 30 min at 0 °C, **S-13** (88.2 mg, 0.56 mmol) in THF (1 mL) and TBAI (20.7 mg, 0.056 mmol) were added to the reaction mixture at the same temperature. After being stirred for 10 h at 60 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl at 0 °C, and extracted with 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2/1) to give the desired products **S-14** (117 mg, 51%) as a Yellow oil: Rf 0.10 (*n*-hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.06 (s, 3H), 3.50 (s, 3H), 3.77 (s, 3H), 4.10 (s, 2H), 6.83 (d, 2H, J = 8.8 Hz), 7.18 (d, 2H, J = 8.8 Hz), 7.30 (d, 2H, J = 7.6 Hz), 7.80 (d, 2H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 32.1, 45.0, 49.6 (quintet, J = 20.0 Hz), 55.1, 61.1, 113.8 (×2), 127.0, 127.4 (×2), 129.3 (×2), 130.0 (×2), 137.2, 143.0, 159.2, 168.9; IR (ATR) v 1680, 1611, 1513, 1463, 1337, 1304, 1250, 1157, 1105, 1029, 997, 929, 856, 811, 731, 657 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{19}H_{22}D_2N_2NaO_5S$ 417.1429 (M+Na$^+$) found 417.1387.



To a stirred suspension of $LiAlH_4$ (11.8 mg, 0.31 mmol) in Et_2O (2 mL) at 0 °C was added dropwise **S-14** (111.6 mg, 0.28 mmol) in Et_2O (3 mL). After being stirred for 15 min at 0 °C, the reaction mixture was quenched with aqueous 2 M potassium sodium tartrate at the same temperature. The solution was warmed to room temperature and stirred until the organic and aqueous layers were separated. The aqueous layer was extracted with 2 times with EtOAc and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was passed through a short pad of silica gel. After concentration *in vacuo*, the obtained aldehyde **S-15** was utilized for the next reaction without further purification.



To a stirred solution of **S-2a** (206 mg, 0.6 mmol) in THF (5 mL) at 0 °C was added *i*-PrMgCl (0.3 mL, 2 M in THF, 0.6 mmol). After being stirred for 15 min, the reaction mixture was added aldehyde **S-15** (0.28 mmol) in THF (5 mL) at 0 °C. After being stirred for 10 min at the same temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl, and extracted with 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 3/1) to give the desired product **7b-*d*$_2$** (110 mg, 71% in 2 steps) as a white solid: melting point 49-52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64 (s, 9H), 2.41 (s, 3H), 3.14 (s, 1H), 3.28 (dd, 1H, J = 14.8, 2.8 Hz), 3.43 (dd, 1H, J = 14.8, 8.8 Hz), 3.79 (s, 3H), 4.88 (d, 1H, J = 9.2 Hz), 6.85 (d, 2H, J = 8.4 Hz), 7.10-7.12 (m, 2H), 7.21 (d, 2H, J = 8.4 Hz), 7.23-7.27 (m, 1H), 7.29 (d, 2H, J = 8.4 Hz), 7.47 (s, 1H), 7.73 (d, 2H, J = 8.4 Hz), 8.09 (d, 1H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 28.1 (×3), 53.1 (quintet, J = 19.6 Hz), 54.8, 55.2, 67.0, 83.6, 114.1 (×2), 115.2, 119.2, 120.8, 122.4, 122.9, 124.3, 127.2 (×2), 127.5, 127.9, 129.8 (×2), 129.9 (×2), 135.6, 135.6, 143.7, 149.4, 159.5; IR (ATR) ν 1730, 1611, 1512, 1452, 1335, 1249, 1152, 1089, 812, 746 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{30}H_{32}D_2N_2NaO_6S$ 575.2161 (M+Na$^+$) found 575.2132.

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