Supplementary Material for Organic Biomolecular Chemistry

Supporting Information

Indole synthesis from *N*-allenyl-2-iodoanilines under mild conditions mediated by samarium(II) diiodide

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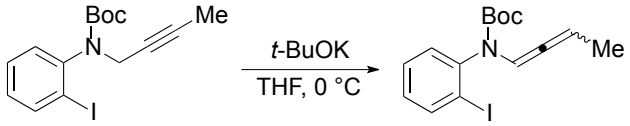
I. General remarks

All reactions were performed using oven-dried glasswares under an atmosphere of argon. Anhydrous THF was purchased from Kanto Chemicals Inc. and used without further purification. Anhydrous DMF was purchased from Wako Pure Chemical Industries, Ltd. and used without further purification. HMPA and DMPU were distilled from CaH_2 under reduced pressure. All other chemicals were purchased at the highest commercial grade and used without further purification. Melting points were measured with a Yanaco MP micro-melting apparatus and uncorrected. NMR spectra were measured on JEOL EX-270 (^{1}H: 270 MHz), JEOL AL-300 (^{1}H: 300 MHz; ^{13}C: 75.5 MHz), and Varian INOVA 400NB (^{1}H: 400 MHz, ^{13}C: 100 MHz) spectrometers with tetramethylsilane as an internal standard. Chemical shifts are reported in ppm. IR spectra were taken with Shimadu FTIR-8400 spectrophotometers. A JEOL JMS-GC mate spectrometer was used for low-resolution and high-resolution electron ionizations MS (LR-EIMS and HR-EIMS). Silica gel 60N (60-230 mesh, Kanto Chemical Co., Inc.) for column chromatography, silica gel 60 F_{254} pre-coated glass plates (0.25 mm-thickness, Merck) for analytical thin-layer chromatography (TLC) and silica gel 60 F_{254}

(0.5 mm and 1.0 mm-thickness, Merck) for preparative TLC were used.

Compounds **1a**, **1c**, **1d**, **5c** and **5d** were prepared according to reported procedures.[1] Compounds **S1**, **S2**, **2a'**, **2c**, **4b**, **4c**, **4f**, **4g**, **6a** and **6b** were known.[2]

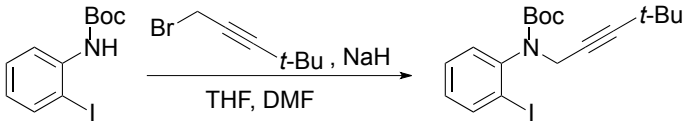
II. Preparation of starting material **5a** and **5b**.



S1 **5a**

***tert*-Butyl *N*-(Buta-1,2-dienyl)-*N*-(2-iodophenyl)-carbamate (5a)**

A solution of **S1** (300 mg, 0.808 mmol) in THF (4.0 mL) was added to *t*-BuOK (227 mg, 2.02 mmol) at 0 ºC. The mixture was stirred for 11 h at this temperature, and extracted with Et_2O. The extract was washed with H_2O and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduce pressure to leave a residue, which was purified by column chromatography over silica gel with *n*-hexane-EtOAc (7:1) to give **5a** (137 mg, 45%) as a mixture of conformer (1:1). Pale yellow oil: IR ($CHCl_3$) cm^{-1}: 1703 (C=O); ^1H NMR (400 MHz, $CDCl_3$) major; δ 1.38 (brs, 6H), 1.46 (dd, J = 6.8, 2.8 Hz, 3H), 1.54 (s, 3H), 5.30-5.41 (m, 1H), 6.74-6.79 (m, 1H), 6.99 (t, J = 7.2 Hz, 1H), 7.17 (t, J = 7.2 Hz, 1H), 7.29-7.35 (m, 1H), 7.84 (d, J = 7.2 Hz, 1H); minor; δ 1.38 (brs, 6H), 1.51 (dd, J = 7.2, 2.8 Hz, 3H), 1.54 (s, 3H), 5.30-5.41 (m, 1H), 6.99 (t, J = 7.2 Hz, 1H), 7.17 (t, J = 7.2 Hz, 1H), 7.29-7.35 (m, 1H), 7.73-7.76 (m, 1H), 7.84 (d, J = 7.2 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$) major; δ 15.5, 28.1 (2C), 28.3, 81.1, 97.9, 100.2, 120.1, 128.7, 129.1, 129.70, 138.8, 139.17, 196.2, 205.4; minor; δ 15.5, 28.1, 28.3 (2C), 81.1, 98.0, 100.6, 124.7, 128.9, 129.2, 129.72, 138.8, 139.19, 196.2, 205.4; MS (FAB) *m/z* (%) calcd for $C_{15}H_{19}INO_2$ (MH^+): 372.0461; found: 372.0456. ^{13}C NMR (100 MHz, $CDCl_3$)

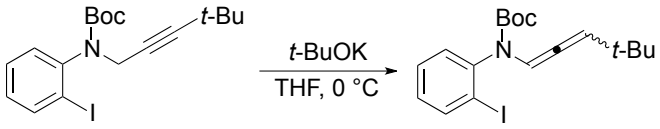


S2 **S3**

***tert*-Butyl *N*-(4,4-Dimethylpent-2-ynyl)-*N*-(2-iodophenyl)-carbamate (S3)**

A solution of **S2** (491 mg, 1.54 mmol) in THF (11.9 mL) and DMF (2.4 mL) was added to NaH (92.4 mg, 2.31 mmol, 60% in oil) at rt, and stirred for 30 min. After cooling to 0 ºC, 1-bromo-4,4-dimethyl-2-pentyne (674 mg, 3.85 mmol) in THF (1.5 mL) solution was added to the mixture, and stirring was continued for 2 h at rt. The mixture was extracted with EtOAc. The extract was washed with H_2O and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduce

pressure to leave a residue, which was purified by column chromatography over silica gel with *n*-hexane-EtOAc (12:1) to give **S3** (364 mg, 57%) as a mixture of conformer (7:3). Pale yellow oil: IR ($CHCl_3$) cm^{-1}: 1699 (C=O); ^1H NMR (400 MHz, $CDCl_3$) major; δ 1.10 (s, 9H), 1.36 (s, 6H), 1.55 (s, 3H), 4.03 (d, J = 17.2 Hz, 1H), 4.67 (d, J = 17.2 Hz, 1H), 6.98-7.02 (m, 1H), 7.29-7.42 (m, 2H), 7.85 (d, J = 8.0 Hz, 1H); minor; δ 1.15 (s, 9H), 1.36 (s, 6H), 1.55 (s, 3H), 3.91 (d, J = 17.2 Hz, 1H), 4.54 (d, J = 17.2 Hz, 1H), 6.74-6.78 (m, 1H), 7.29-7.42 (m, 2H), 7.74 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) major; δ 27.2, 28.2 (3C), 30.7 (3C), 38.1, 73.4, 80.6, 93.5, 100.7, 128.4, 128.8, 130.5, 139.0, 143.2, 153.5; minor; δ 27.9, 28.4 (3C), 30.8 (3C), 39.9, 73.8, 81.0, 93.0, 100.5, 120.1, 124.6, 129.1, 139.3, 143.9, 153.6. MS (EI) *m/z* (%) 413 (M^+, 2.4), 57 (100), 69 (29), 95 (24), 118 (27), 130 (20), 186 (40), 230 (27); HRMS (EI) calcd for $C_{18}H_{24}INO_2$ (M^+): 413.0852; found: 413.0850.



S3 **5b**

***tert*-Butyl *N*-(4,4-Dimethylpenta-1,2-dienyl)-*N*-(2-iodophenyl)-carbamate (5b)**

5b was synthesized with a similar manner to **5a** as a mixture of conformer (1:1). Yield: 71%. Pale yellow oil: IR ($CHCl_3$) cm^{-1}: 1703 (C=O); ^1H NMR (400 MHz, $CDCl_3$) major; δ 0.74 (s, 9H), 1.38 (s, 6H), 1.58 (s, 3H), 5.39 (d, J = 6.0 Hz, 1H), 6.96 (d, J = 7.6 Hz, 1H), 7.12-7.28 (m, 2H), 7.30-7.35 (m, 1H), 7.83 (d, J = 7.6 Hz, 1H); minor; δ 0.76 (s, 9H), 1.39 (s, 6H), 1.58 (s, 3H), 5.42 (d, J = 6.0 Hz, 1H), 6.98 (d, J = 7.6 Hz, 1H), 7.12-7.28 (m, 2H), 7.30-7.35 (m, 1H), 7.84 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) major; δ 28.1 (2C), 28.4, 29.3 (3C), 32.68, 81.2, 100.0, 102.2, 114.5, 128.4, 128.9, 129.6, 139.1, 142.0, 151.4, 191.8; minor; δ 28.1 (2C), 28.4, 29.5 (3C), 32.73, 81.3, 100.1, 102.5, 114.9, 128.7, 128.9, 130.0, 139.1, 142.2, 151.5, 192.0. MS (FAB) *m/z* (%) calcd for $C_{18}H_{25}INO_2$ (MH^+): 414.0935; found: 414.0930.

General procedure for samarium(II)-mediated cyclisation. Synthesis of *tert*-butyl 3-methyl-1*H*-indole-1-carboxylate (**2c**)

A mixture of samarium (141 mg, 0.938 mmol) and 1,2-diiodoethane (197 mg, 0.700 mmol) in THF (6.7 mL) was stirred for 1.5 h at rt. After cooling to 0 ºC, HMPA (0.44 mL, 2.52 mmol) was added to the mixture, and stirring was continued for 20 min at this temperature. A solution of allene **1c** (50.0 mg, 0.140 mmol) and *i*-PrOH (0.02 mL, 0.280 mmol) in THF (3.4 mL) was added to the mixture, and the mixture was stirred for 15 min at 0 ºC. After the mixture was exposed to air, saturated $NaHCO_3$ was added to the mixture, and the whole was extracted with Et_2O. The extract was washed

with saturated $NaHCO_3$ and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to leave a residue, which was purified by column chromatography over silica gel with *n*-hexane- EtOAc (8:1) to give **2c** (30.2 mg, 93% yield) as pale yellow oil.

***tert*-Butyl 3,5-Dimethyl-1*H*-indole-1-carboxylate (4a)**

4a was synthesized with a similar manner to **2c**. Yield: 82%. Colorless oil: IR ($CHCl_3$) cm^{-1}: 1724 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 1.65 (s, 9H), 2.23 (d, J = 1.6 Hz, 3H), 2.45 (s, 3H), 7.12 (dd, J = 11.2, 1.6 Hz, 1H), 7.27-7.28 (m, 1H), 7.31 (brs, 1H), 7.97 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.6, 21.3, 28.2 (3C), 82.9, 114.7, 116.0, 118.8, 122.8, 125.5, 131.6, 131.7, 133.6, 149.8; MS (EI) *m/z* (%) 245 (M^+, 34), 57 (16), 143 (20), 144 (53), 145 (100), 189 (75); HRMS (EI) calcd for $C_{15}H_{19}NO_2$ (M^+): 245.1416; found: 245.1414.

***tert*-Butyl 5-(Dimethylcarbamoyl)-3-methyl-1*H*-indole-1-carboxylate (4d)**

4d was synthesized with a similar manner to **2c**. Yield: 21%. Colorless oil: IR ($CHCl_3$) cm^{-1}: 1722 (C=O), 1634 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 1.67 (s, 9H), 2.27 (d, J = 1.6 Hz, 3H), 3.03 (brs, 3H), 3.13 (brs, 3H), 7.36 (dd, J = 11.6, 1.6 Hz, 1H), 7.39 (brs, 1H), 7.62-7.63 (m, 1H), 8.11 (d, J = 11.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.5, 28.2 (3C), 35.5, 39.9, 83.6, 114.7, 116.5, 118.4, 123.3, 123.7, 130.3, 131.2, 135.9, 149.6, 172.3; MS (EI) *m/z* (%) 302 (M^+, 16), 57 (17), 158 (100), 202 (91), 246 (41); HRMS (EI) calcd for $C_{17}H_{22}N_2O_3$ (M^+): 302.1630; found: 302.1633.

***tert*-Butyl 7-Methoxy-3-methyl-1*H*-indole-1-carboxylate (4e)**

4e was synthesized with a similar manner to **2c**. Yield: 79%. Colorless crystal: m.p. 70~71 ºC (*n*-hexane): IR (KBr) cm^{-1}: 1732 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 1.61 (s, 9H), 2.23 (d, J = 1.2 Hz, 3H), 3.93 (s, 3H), 6.83 (dd, J = 8.0, 1.2 Hz, 1H), 7.10 (dd, J = 8.0, 1.2 Hz, 1H), 7.19 (t, J = 8.0 Hz, 1H), 7.30-7.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.7, 28.0 (3C), 55.9, 82.7, 107.1, 111.6, 115.8, 123.3, 124.7, 125.4, 134.5, 148.4, 149.6; MS (EI) *m/z* (%) 261 (M^+, 12), 41 (24), 57 (24), 118 (42), 146 (46), 160 (23), 161 (100); HRMS (EI) calcd for $C_{15}H_{19}NO_3$ (M^+): 261.1365; found: 261.1362.

***tert*-Butyl 3-Methyl-2-(trimethylsilyl)-1*H*-indole-1-carboxylate (6c)**

6c was synthesized with a similar manner to **2c**. Yield: 93%. Colorless oil: IR ($CHCl_3$) cm^{-1}: 1728 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 0.39 (s, 9H), 1.69 (s, 9H), 2.36 (s, 3H), 7.19-7.23 (m, 1H), 7.27 (ddd, J = 8.4, 7.2, 1.2 Hz, 1H), 7.50 (ddd, J = 7.6, 0.8, 0.8 Hz, 1H), 7.93 (ddd, J = 8.4, 0.8, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 2.3 (3C), 11.2, 28.3 (3C), 83.4, 115.1, 118.7, 122.0, 124.5, 127.7, 132.6, 136.1, 137.0, 151.4; MS (EI) *m/z* (%) 303 (M^+, 12), 57 (17), 188 (67), 203 (100), 232

(56), 247 (16); HRMS (EI) calcd for $C_{17}H_{25}NO_2Si$ (M^+): 303.1654; found: 303.1658.

tert-Butyl 2-Benzyl-3-methyl-1*H*-indole-1-carboxylate (6d)

6d was synthesized with a similar manner to **2c**. Yield: 99%. Colorless crystal: m.p. 86~87 ºC (*n*-hexane): IR (KBr) cm^{-1}: 1720 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 1.43 (s, 9H), 2.25 (s, 3H), 4.46 (s, 2H), 6.99-7.08 (m, 2H), 7.15-7.31 (m, 5H), 7.49-7.52 (m, 1H), 8.10-8.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.9, 27.9 (3C), 32.1, 83.4, 108.4, 115.4, 115.9, 118.2, 122.3, 123.8, 125.8, 127.8 (2C), 128.2 (2C), 130.4, 131.8, 133.8, 139.8; MS (EI) *m/z* (%) 321 (M^+, 12), 41 (28), 57 (24), 144 (49), 206 (32), 218 (38), 221 (100), 265 (40); HRMS (EI) calcd for $C_{21}H_{23}NO_2$ (M^+): 321.1729; found: 321.1727.

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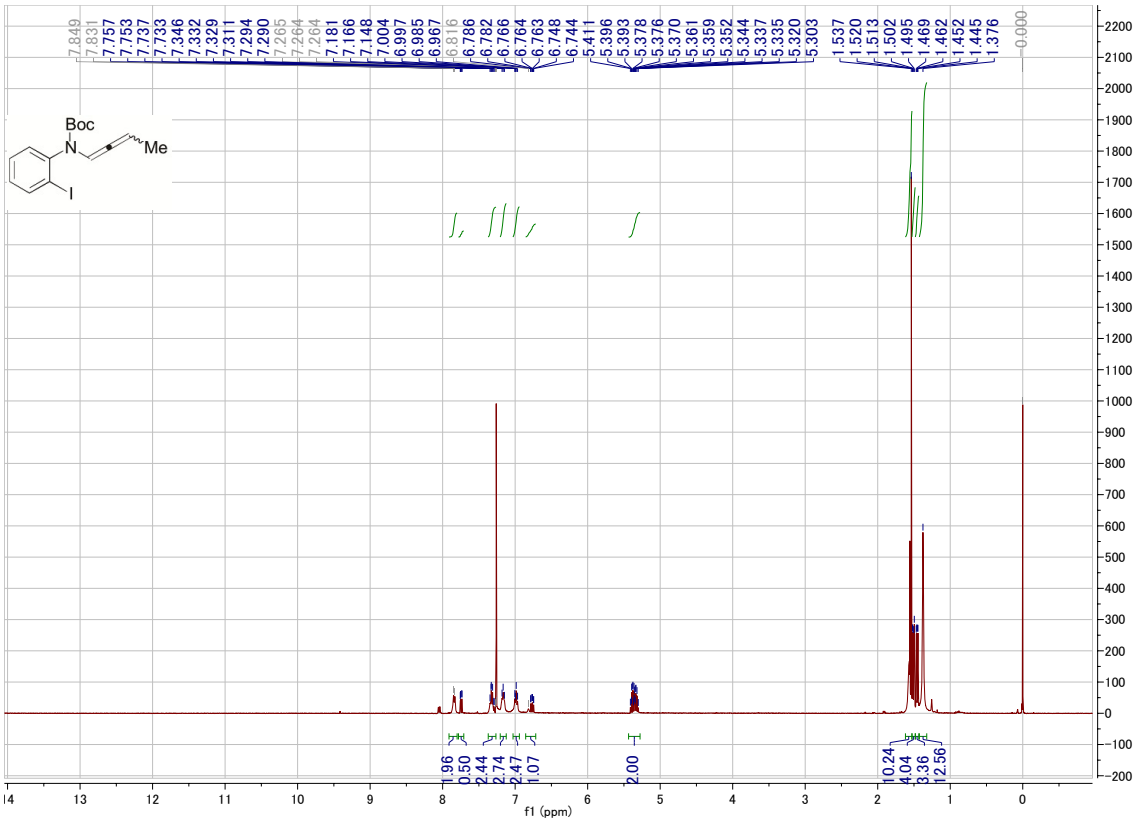
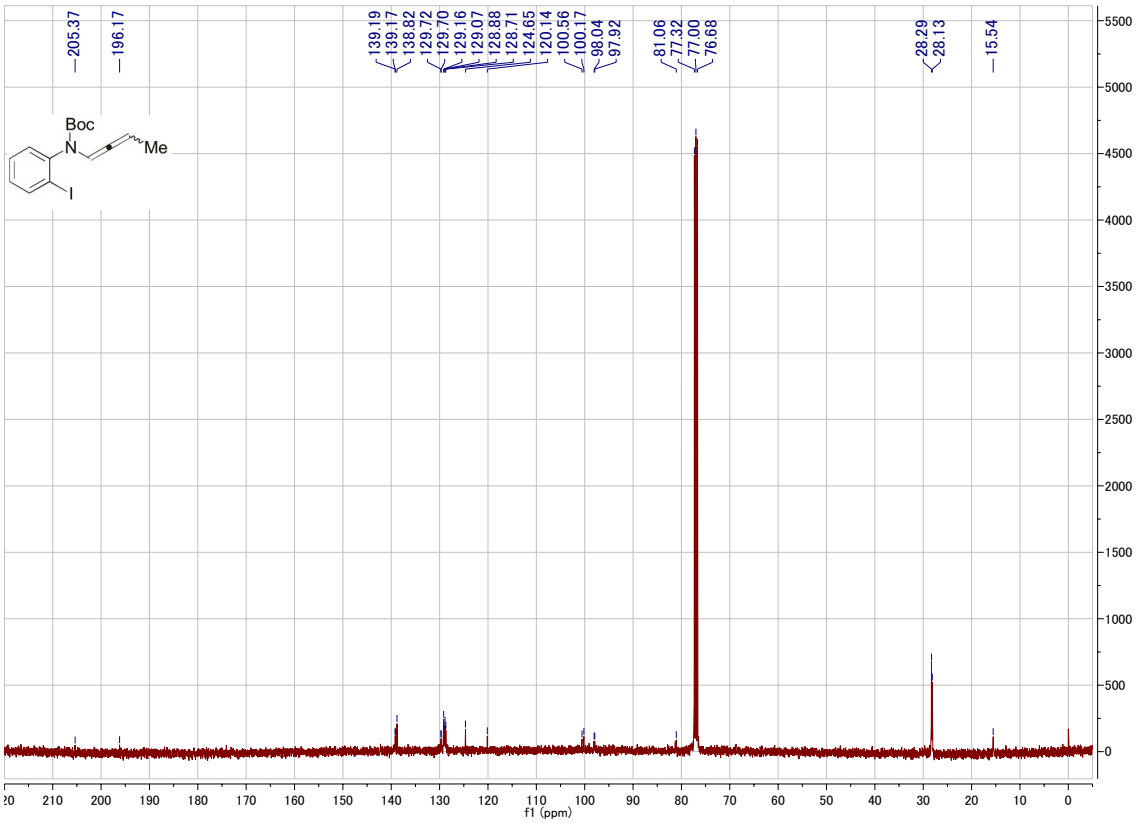
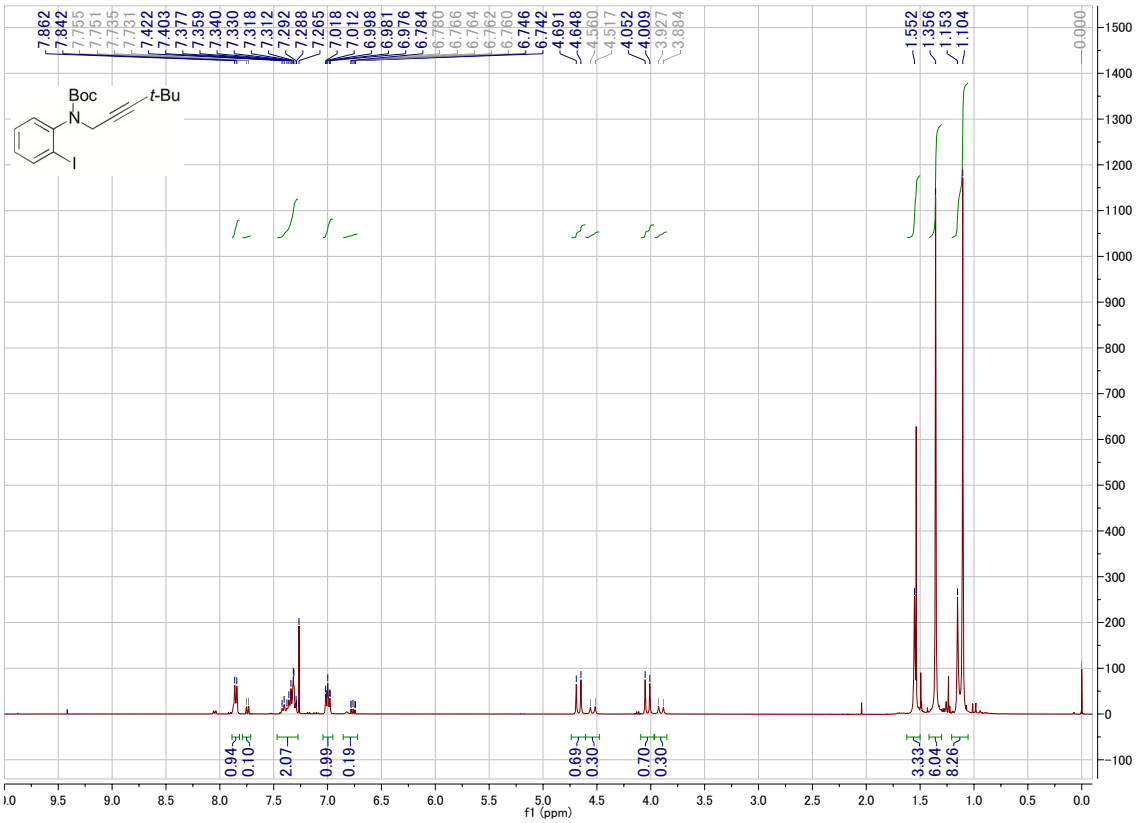
III. Copies of ^{1}H and ^{13}C NMR spectra

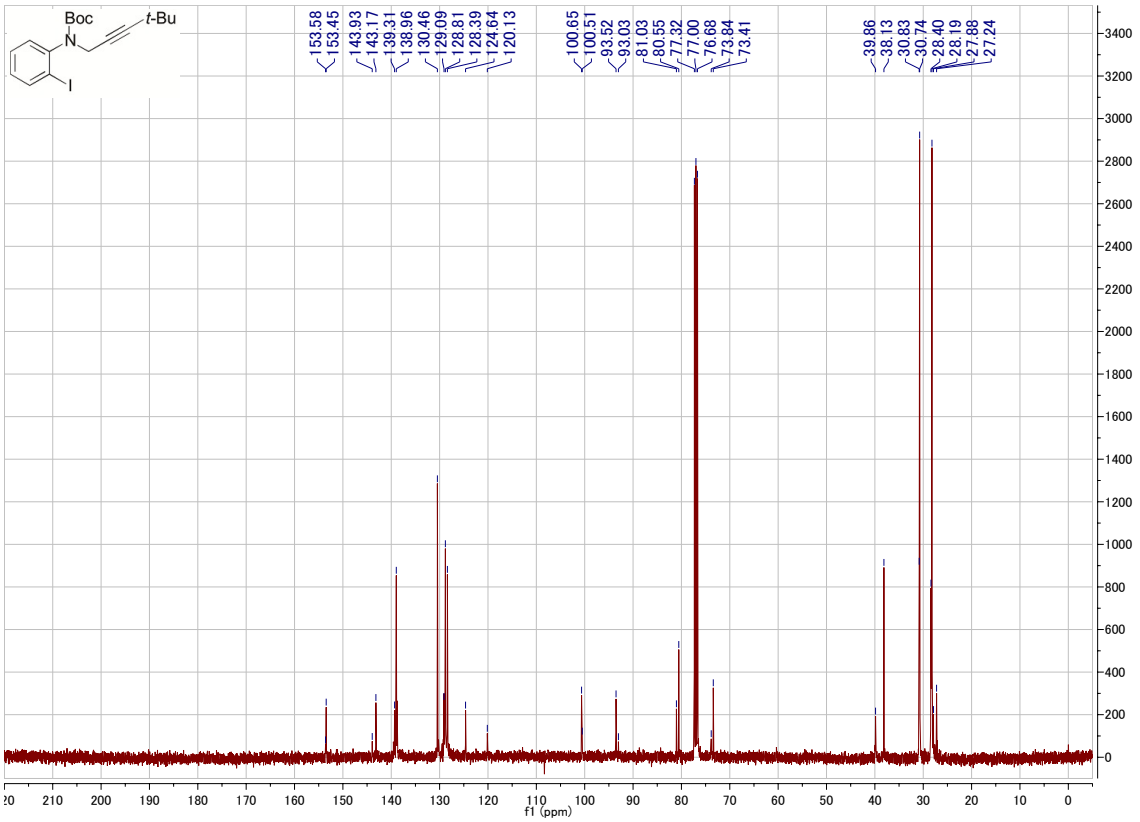
^{1}H NMR and ^{13}C NMR of **5a**



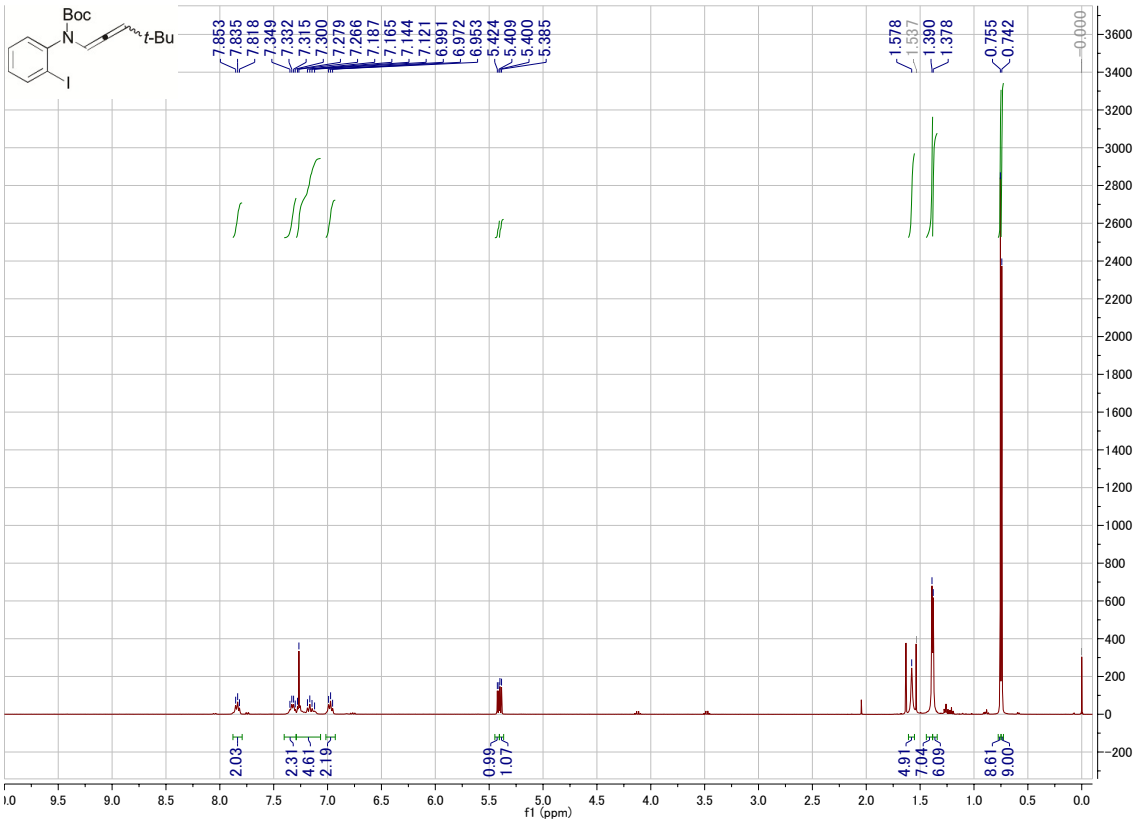


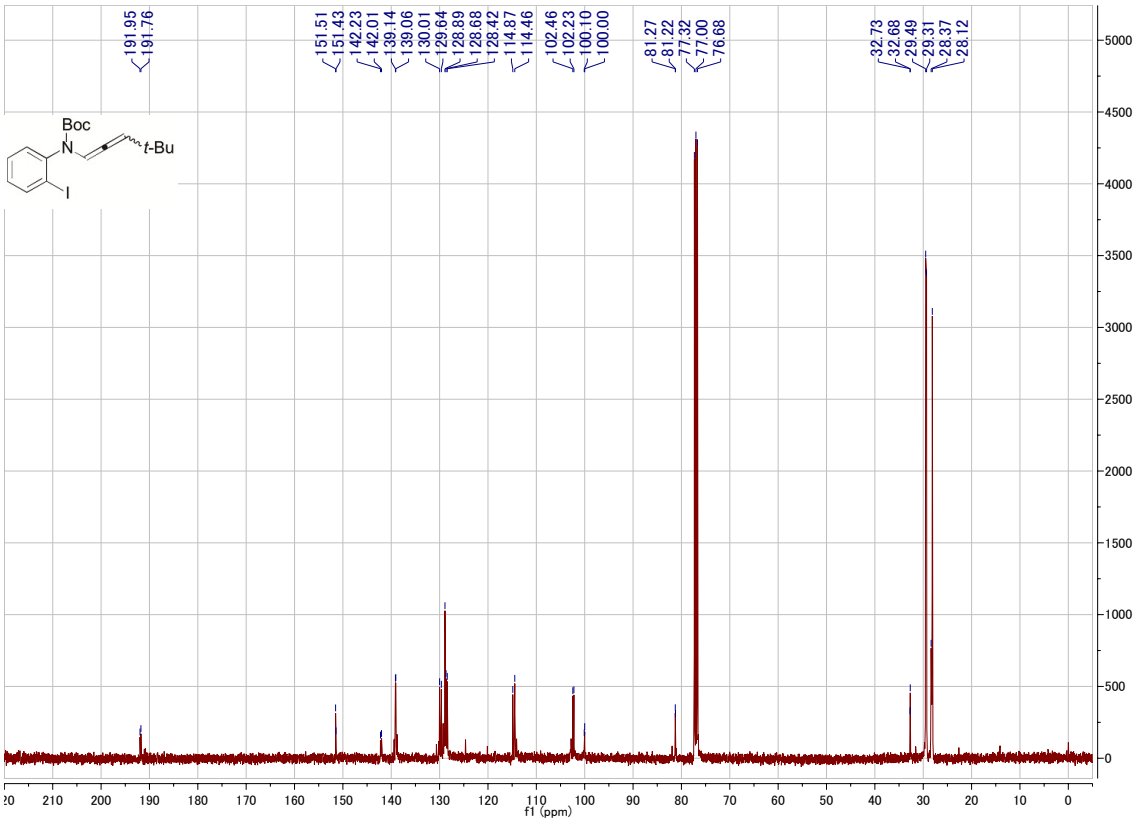
^{1}H NMR and ^{13}C NMR of **S3**



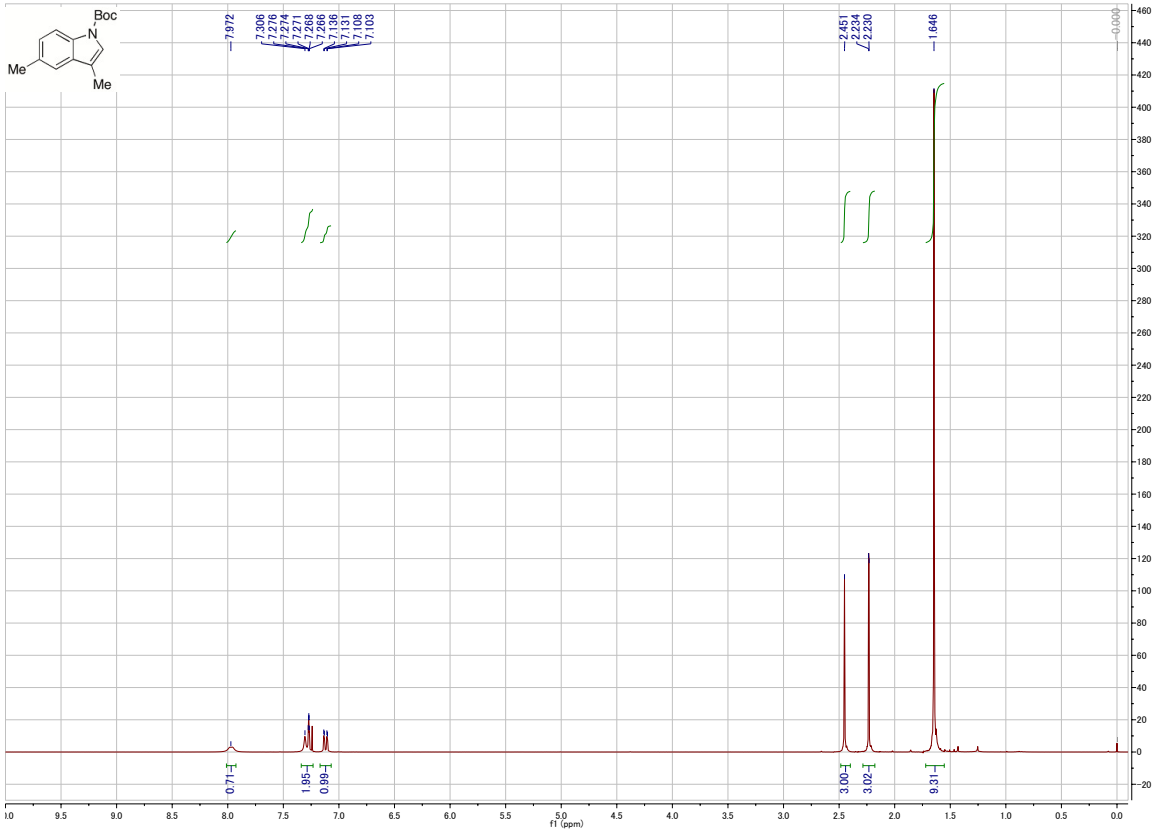


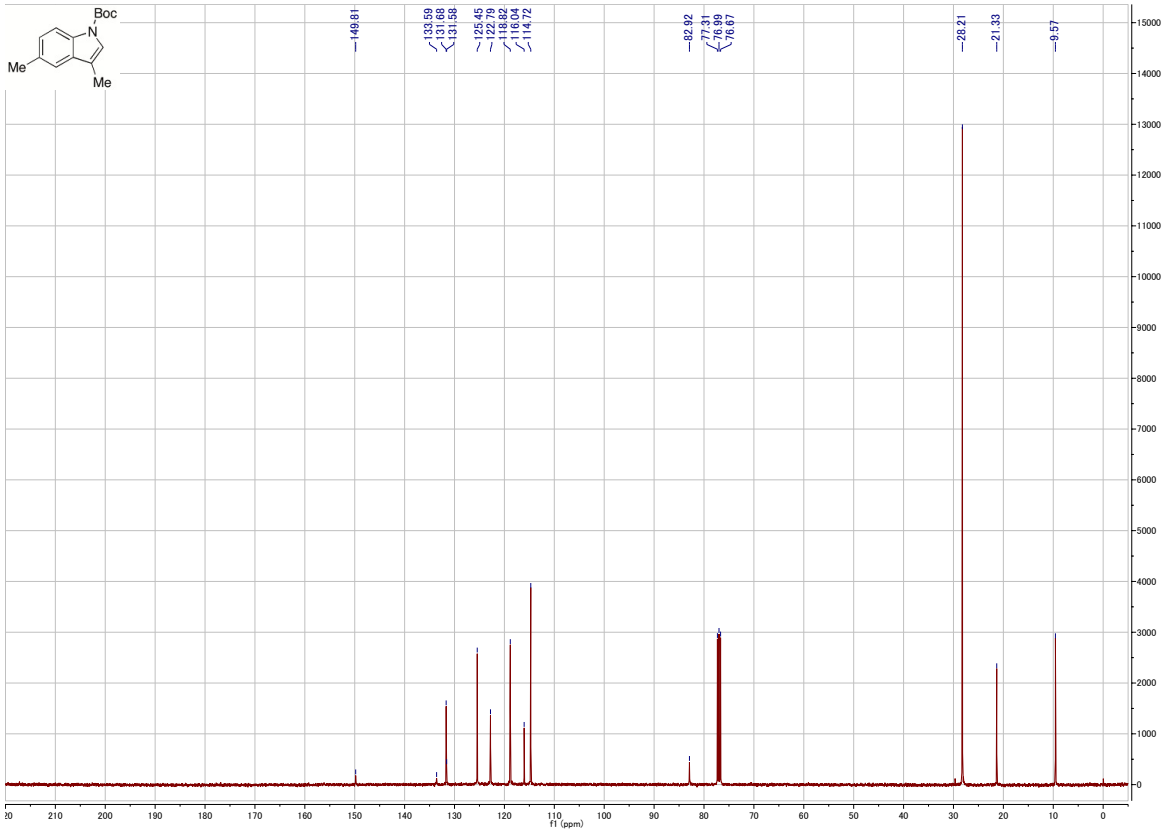
^{1}H NMR and ^{13}C NMR of **5b**



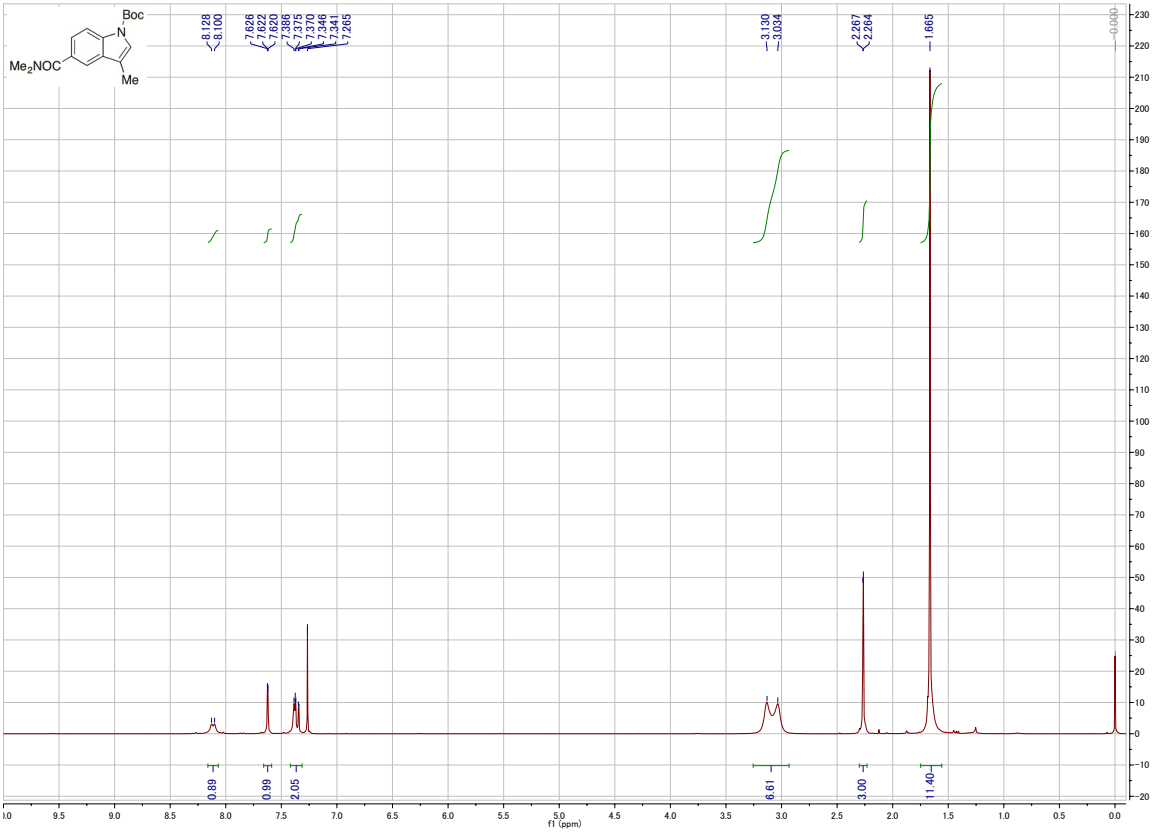


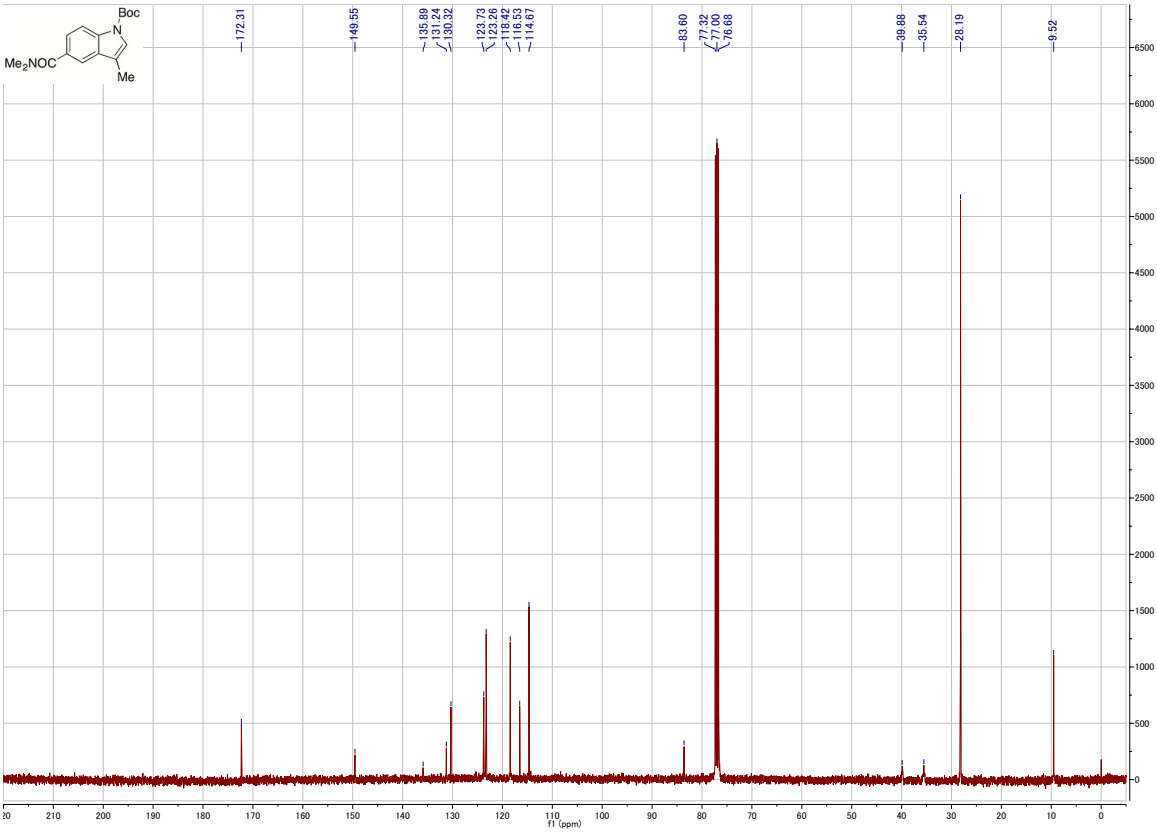
^{1}H NMR and ^{13}C NMR of **4a**





^{1}H NMR and ^{13}C NMR of **4d**





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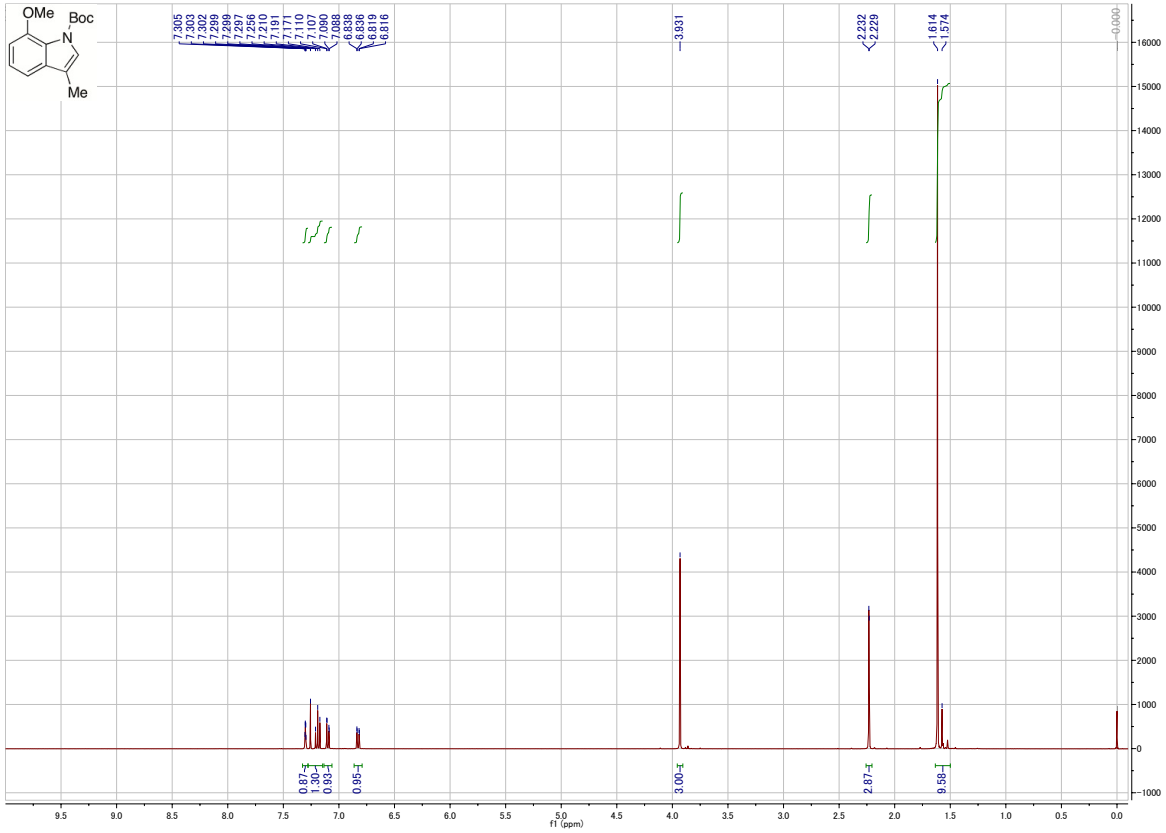
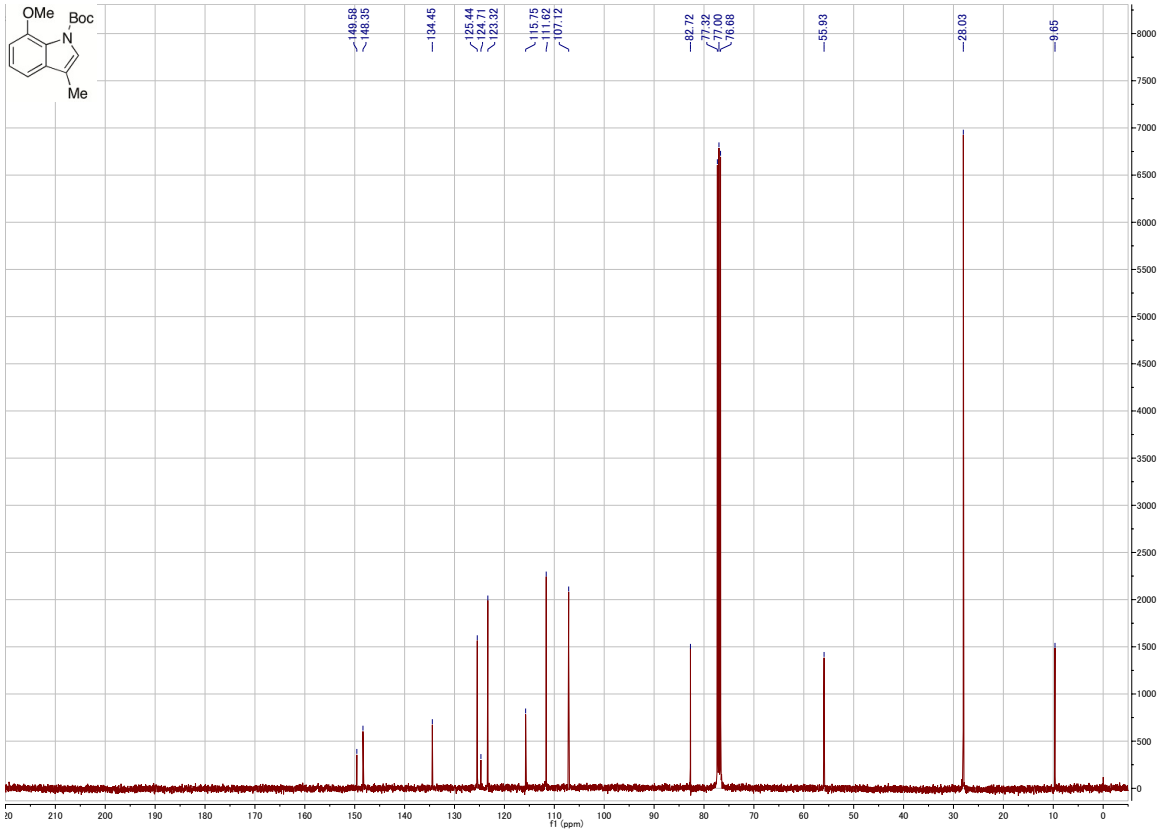
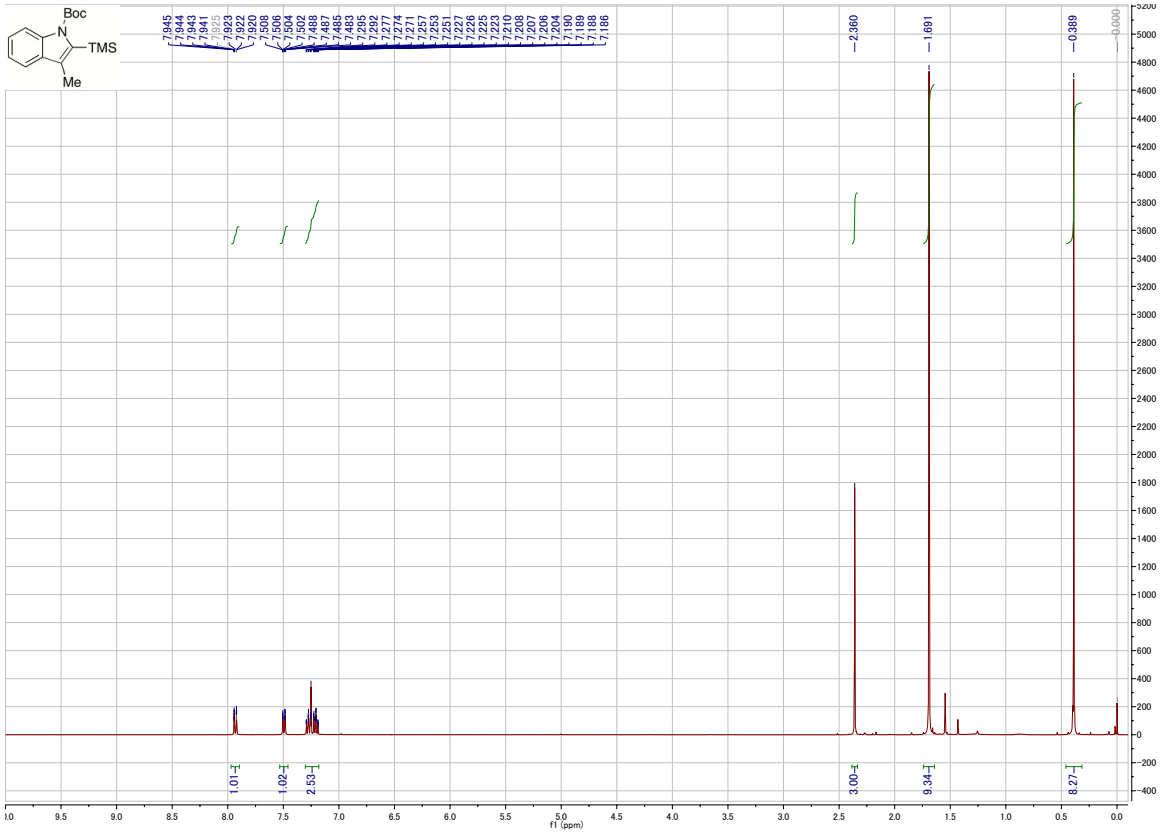
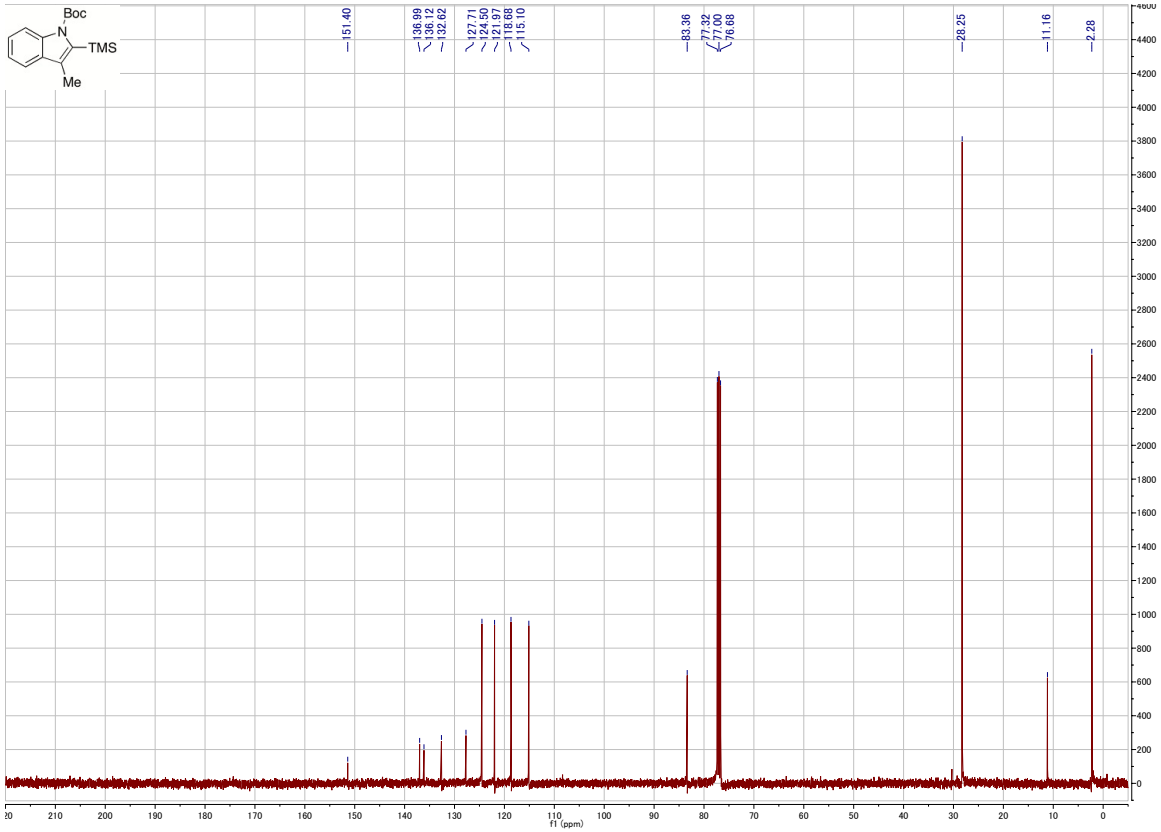




^{1}H NMR and ^{13}C NMR of **6c**





^{1}H NMR and ^{13}C NMR of **6d**