

# Supporting Information

Diastereoselective ring cleavage of azetidines with cyanogen bromide

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**General information:**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded at 300 and 75 MHz, respectively; chemical shifts ( $\delta$ ) are reported in ppm and coupling constants ( $J$ ) reported in Hertz and rounded up to 0.1 Hz. Splitting patterns are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), septuplet (sep), multiplet (m), broad (br), or a combination of these. Solvents were used as internal standard when assigning NMR spectra ( $\delta$  H:  $\text{CDCl}_3$  7.27 ppm;  $\delta$  C:  $\text{CDCl}_3$  77.0 ppm). IR data were collected with an ATR-FT-IR spectrometer. Optical rotations were determined with a Perkin Elmer 141 instrument. All reactions were carried out under argon. Column chromatography was performed on silica gel (230–400 mesh) with use of various mixtures of  $\text{CH}_2\text{Cl}_2$ , EtOAc, pentane, petroleum ether (35–60°C fraction) (PE) and methanol. TLC was performed on Merck Kieselgel 60 F254 plates. Melting points are uncorrected. Isomeric ratios were determined by NMR analysis of crude reaction mixtures before purification.

### General procedure for the formation of 3-hydroxy azetidines 5-8

To a solution of the required (*S*)-ethylamine in isopropanol (concentration: 1 mol.L<sup>-1</sup>) cooled to 0°C was added dropwise epichlorohydrin (1.0 equiv.). The reaction was stirred at 25°C for 24h. After solvent evaporation, the resulting chlorohydrin was dissolved in acetonitrile (concentration: 0.5 mol.L<sup>-1</sup>) and heated at reflux for 24h in the presence of sodium hydrogen carbonate (2.0 equiv.). The reaction mixture was filtered through Celite and the filtrate was concentrated in vacuo. The residue was purified by chromatography over silica gel.

**(*S*)-1-(1-Phenyl-ethyl)-azetidin-3-ol 5:** 77% yield as a white solid; Mp: 68–70°C; R<sub>f</sub> = 0.34 (MeOH/ $\text{CH}_2\text{Cl}_2$  10/90).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.31–7.19 (m, 5H), 4.44–4.36 (m, 1H), 3.77–3.66 (m, 2H), 3.39–3.29 (m, 2H), 2.95–2.85 (m, 2H), 1.22 (d,  $J$  = 6.5 Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 142.4, 128.4, 127.3, 127.1, 68.8, 63.0, 62.9, 61.3, 20.7; IR (film)  $\nu_{\text{max}}$  3048, 2961, 2838, 2746, 1496, 1473, 1453, 1335, 1215, 1187, 1174, 1153, 1089, 1046, 1030, 972, 796, 758, 700 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{11}\text{H}_{16}\text{NO}$  [ $\text{M} + \text{H}$ ]<sup>+</sup> 178.1227; found 178.1235. [ $\alpha$ ]<sub>578</sub><sup>20</sup>: - 90 (c 1.0,  $\text{CH}_2\text{Cl}_2$ ).

**(*S*)-1-(1-Naphthalen-1-yl-ethyl)-azetidin-3-ol 6:** 56% yield as colourless crystals; Mp: 113°C; R<sub>f</sub> = 0.51 (MeOH/DCM/ $\text{NEt}_3$  7.5/92/0.5).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.20 (d,  $J$  = 8.1 Hz 1H), 7.89–7.85 (m, 1H), 7.75 (d,  $J$  = 8.4 Hz 1H), 7.63 (d,  $J$  = 7.2 Hz 1H), 7.55–7.43 (m, 3H), 4.52–4.44 (m, 3H), 4.17 (q,  $J$  = 5.7 Hz, 1H), 3.82–3.77 (m, 1H), 3.59–3.54 (m, 1H), 3.34 (br s, 1H), 3.10–3.06 (m, 1H), 2.88–2.84 (m, 1H), 1.37 (d,  $J$  = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 138.7, 133.8, 131.0, 128.9, 127.2, 125.7, 125.6, 125.2, 123.3, 123.0, 64.6, 63.3, 63.2, 61.6, 20.6; IR (film)  $\nu_{\text{max}}$  3075, 2949, 2844, 2770, 1596, 1448, 1355, 1201, 1178, 1162, 1115, 1086, 1049, 1006, 979, 858, 793, 774 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{15}\text{H}_{18}\text{NO}$  [ $\text{M} + \text{H}$ ]<sup>+</sup> 228.1383; found 228.1384. [ $\alpha$ ]<sub>578</sub><sup>20</sup>: - 125 (c 1.0,  $\text{CH}_2\text{Cl}_2$ ).

**(*S*)-1-(1-Naphthalen-2-yl-ethyl)-azetidin-3-ol 7:** 47% yield as a white solid; Mp: 112°C; R<sub>f</sub> = 0.49 (MeOH/DCM/ $\text{NEt}_3$  7.5/92/0.5).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.83–7.79 (m, 3H), 7.72 (br s, 1H), 7.49–7.44 (m, 3H), 4.49–4.41 (m, 1H), 3.95 (br s, 1H), 3.78–3.73 (m, 1H), 3.51–3.37 (m, 2H), 3.00–2.90 (m, 2H), 1.32 (d,  $J$  = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 140.2, 133.2, 132.8, 128.1, 127.7, 125.9, 125.7, 125.5, 125.1, 69.0, 63.0, 61.4 20.8; IR (film)  $\nu_{\text{max}}$  3055, 2950, 2843, 2775, 1600, 1508, 1453, 1357, 1197, 1174, 1122, 1097, 1085, 1052, 976, 861, 821, 777, 750 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{15}\text{H}_{18}\text{NO}$  [ $\text{M} + \text{H}$ ]<sup>+</sup> 228.1383; found 228.1392. [ $\alpha$ ]<sub>578</sub><sup>20</sup>: - 110 (c 1.0,  $\text{CH}_2\text{Cl}_2$ ).

**(*S*)-1-(1-Cyclohexyl-ethyl)-azetidin-3-ol 8:** 72% yield as a colourless oil; R<sub>f</sub> = 0.39 ( $\text{NEt}_3$ /MeOH/ $\text{CH}_2\text{Cl}_2$  1/10/90).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 4.41–4.34 (m, 1H), 3.62–3.54 (m, 2H), 2.87–2.79 (m, 2H), 2.11–2.03 (m, 1H), 1.76–1.58 (m, 4H), 1.45–0.88 (m, 7H), 0.81 (d,  $J$  = 6.5 Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 68.4, 63.0, 62.8, 61.6, 39.3, 30.6, 26.8, 26.8, 26.5, 26.1, 12.0; IR (film)  $\nu_{\text{max}}$  3337, 2921, 2850, 1448, 1341, 1204, 1185, 1145, 1099, 980, 890, 840, 784, 767 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{11}\text{H}_{22}\text{NO}$  [ $\text{M} + \text{H}$ ]<sup>+</sup> 184.1696; found 184.1694. [ $\alpha$ ]<sub>578</sub><sup>20</sup>: - 33 (c 0.6,  $\text{CH}_2\text{Cl}_2$ ).

**Toluene-4-sulfonic acid (*S*)-1-(1-phenyl-ethyl)-azetidin-3-ylmethyl ester 9:** To a solution of 3-hydroxy azetidine **5** (90 mg, 0.50 mmol) in dichloromethane (5 mL) at 0°C was added triethylamine (0.14 mL, 1.00 mmol), DMAP (5 mg, 0.04 mmol) and tosyl chloride (143 mg, 0.75 mmol). The reaction mixture was stirred for 48h at 5°C. The mixture was concentrated under reduced pressure and the crude compound was purified by chromatography (EtOAc/Pentane 75/25) over silica gel to afford **9** (121 mg, 0.36 mmol, 73%) as a colourless oil; R<sub>f</sub> = 0.43 (EtOAc/Pentane 75/25).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.78–7.76 (d,  $J$  = 8.3 Hz, 2H), 7.35–7.22 (m, 7H), 4.87–4.79 (m, 1H), 3.70–3.65 (m, 1H), 3.31–3.25 (m, 2H), 3.10–3.06 (app t, 1H), 2.95–2.90 (app t, 1H), 2.45

(s, 3H), 1.19-1.17 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 145.1, 142.6, 133.1, 129.9, 128.4, 127.9, 127.3, 127.0, 68.7, 67.7, 59.8, 59.7, 21.7, 21.0; **IR** (film)  $\nu_{\text{max}}$  3320, 3037, 2967, 2922, 2852, 2632, 1597, 1494, 1452, 1369, 1218, 1158, 1119, 1031, 1008, 911, 815, 701, 679  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{18}\text{H}_{22}\text{NO}_3\text{S}$   $[\text{M} + \text{H}]^+$  332.1315; found 332.1327.  $[\alpha]_{578}^{20}$ : - 7 (c 0.3,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Phenyl-ethyl)-3-acetylthio-azetidone 10**: To a solution of tosylate **9** (80 mg, 0.24 mmol) in acetone (5 mL) was added potassium thioacetate (41 mg, 0.36 mmol) and the mixture was heated at  $60^\circ\text{C}$  for 24 h. The mixture was concentrated under reduced pressure and the crude compound was purified by chromatography (EtOAc/Pentane 50/70) over silica gel to afford **10** (40 mg, 0.17 mmol, 71%) as a yellow oil;  $R_f = 0.65$  (Et<sub>2</sub>O/Pentane 50/50).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.34-7.21 (m, 5H), 4.14-4.05 (m, 1H), 3.77-3.72 (app t, 1H), 3.56-3.51 (app t, 1H), 3.36-3.30 (q,  $J = 6.5$  Hz, 1H), 3.04-3.00 (m, 2H), 2.29 (s, 3H), 1.22-1.20 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 195.4, 142.7, 128.3, 127.2, 127.1, 68.5, 59.9, 59.8, 30.9, 30.4, 20.9; **IR** (film)  $\nu_{\text{max}}$  3026, 2964, 2926, 2820, 1688, 1492, 1450, 1352, 1219, 1135, 1113, 1031, 1007, 949, 762, 699, 681, 628  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{13}\text{H}_{18}\text{NOS}$   $[\text{M} + \text{H}]^+$  236.1104; found 236.1111.  $[\alpha]_{578}^{20}$ : - 55 (c 0.5,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Phenyl-ethyl)-3-(4-methoxybenzylthio)-azetidone 11**: 4-methoxybenzylthiol (0.13 mL, 0.94 mmol) was added to a stirred aqueous 1 M solution of sodium hydroxide (1 mL, 1.00 mmol). After 10 min, a solution of tosylate **9** (210 mg, 0.63 mmol) in EtOH (2.5 mL) was added. The reaction mixture was heated at  $80^\circ\text{C}$  for 2 hours. The mixture was allowed to cool, then diluted with DCM, washed with a mixture of brine and 0.5 M aqueous HCl solution (9:1), and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the crude compound was purified by chromatography (MeOH/ $\text{CH}_2\text{Cl}_2$  2/98) over silica gel to afford **11** (148 mg, 0.47 mmol, 75%) as a colourless oil;  $R_f = 0.35$  (iPrOH/ $\text{CH}_2\text{Cl}_2$  2/98).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.33-7.23 (m, 5H), 7.20-7.17 (m, 2H), 6.85-6.80 (m, 2H), 3.79 (s, 3H), 3.66-3.60 (m, 3H), 3.46-3.27 (m, 3H), 2.96-2.91 (app t, 1H), 2.88-2.84 (app t, 1H), 1.19-1.17 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 158.6, 142.9, 130.2, 129.7, 128.3, 127.1, 127.1, 113.9, 68.6, 61.0, 60.7, 55.2, 35.6, 32.3, 20.9; **IR** (film)  $\nu_{\text{max}}$  3028, 2959, 2923, 2831, 1608, 1583, 1509, 1492, 1451, 1368, 1300, 1246, 1174, 1106, 1031, 830, 761, 699  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{19}\text{H}_{24}\text{NOS}$   $[\text{M} + \text{H}]^+$  314.1574; found 314.1584.  $[\alpha]_{578}^{20}$ : - 38 (c 1.0,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Phenyl-ethyl)-3-(phthalimido)-azetidone 12**: To a solution of 3-tosyl azetidone **9** (210 mg, 0.63 mmol) in ethanol (2.5 mL) was added potassium phthalimide (235 mg, 1.26 mmol). The reaction mixture was stirred at  $80^\circ\text{C}$  for 1 h, then allowed to cool. The mixture was filtered to remove the resulting precipitate. The filtrate was concentrated in vacuo to give a crude compound which was purified by chromatography (MeOH/ $\text{CH}_2\text{Cl}_2$  2/98) over silica gel to afford **12** (102 mg, 0.33 mmol, 53%) as a white solid; Mp:  $103\text{-}105^\circ\text{C}$ ;  $R_f = 0.57$  (MeOH/ $\text{CH}_2\text{Cl}_2$  5/95).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.84-7.82 (m, 2H), 7.73-7.70 (m, 2H), 7.39-7.22 (m, 5H), 4.89-4.78 (m, 1H), 4.05-4.01 (m, 1H), 3.89-3.86 (app t, 1H), 3.75-3.72 (m, 1H), 3.65-3.53 (m, 2H), 1.35-1.33 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 168.1, 134.2, 131.7, 128.5, 127.3, 123.3, 68.3, 57.0, 56.8, 39.0, 20.7; **IR** (film)  $\nu_{\text{max}}$  3193, 3035, 2958, 2836, 1772, 1711, 1603, 1385, 1117, 1089, 1052, 969, 794, 763, 714, 698, 671  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_2$   $[\text{M} + \text{H}]^+$  307.1442; found 307.1442.  $[\alpha]_{578}^{20}$ : - 123 (c 0.5,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Phenyl-ethyl)-3-azido-azetidone 13**: To a solution of 3-tosyl azetidone **9** (140 mg, 0.42 mmol) in ethanol (2 mL) was added sodium azide (55 mg, 0.84 mmol). The reaction mixture was stirred at  $40^\circ\text{C}$  for 24 h, then allowed to cool. The mixture was allowed to cool, then diluted with DCM, washed with water and dried over magnesium sulfate. The solvent was evaporated to give a crude compound which was purified by chromatography (EtOAc/Pentane 25/75) over silica gel to afford **13** (64 mg, 0.32 mmol, 75%) as a colourless oil;  $R_f = 0.43$  (EtOAc/Pentane 25/75).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.35-7.23 (m, 5H), 4.03-3.95 (m, 1H), 3.70-3.65 (m, 1H), 3.40-3.27 (m, 2H), 3.06-3.01 (app t, 1H), 2.98-2.94 (app t, 1H), 1.25-1.23 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 142.7, 128.4, 127.3, 127.0, 68.5, 59.0, 59.0, 49.5, 20.9; **IR** (film)  $\nu_{\text{max}}$  3065, 3027, 2964, 2926, 2824, 2100, 1673, 1492, 1450, 1353, 1257, 1217, 1187, 1159, 1077, 1029, 760, 698  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{11}\text{H}_{15}\text{N}_4$   $[\text{M} + \text{H}]^+$  203.1292; found 203.1293.  $[\alpha]_{578}^{20}$ : - 117 (c 0.6,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Phenyl-ethyl)-3-(4-phenyl-1H-1,2,3-triazolo)-azetidone 14**: To a solution of **13** (40 mg, 0.20 mmol) in THF (1 mL) was added phenylacetylene (45  $\mu\text{L}$ , 0.4 mmol). A solution of copper sulfate (10 mg, 0.04 mmol) in

water (0.5 mL) was added, followed by sodium ascorbate (24 mg, 0.12 mmol). The mixture was stirred for 2 h, then diluted with DCM and washed with a mixture of brine and 28% aqueous ammonia solution (95:5). The aqueous phase was extracted twice with DCM, and the combined organic phases were dried over magnesium sulfate. The solvent was evaporated to give a crude compound which was purified by chromatography (MeOH/CH<sub>2</sub>Cl<sub>2</sub> 2/98) over silica gel to afford **14** (48 mg, 0.16 mmol, 79%) as a white solid; Mp: 72-74°C; R<sub>f</sub> = 0.51 (MeOH/CH<sub>2</sub>Cl<sub>2</sub> 5/95). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 8.06 (s, 1H), 7.89-7.86 (m, 2H), 7.47-7.42 (m, 2H), 7.38-7.28 (m, 6H), 5.28-5.20 (m, 1H), 3.89-3.84 (app t, 1H), 3.71-3.66 (app t, 1H), 3.56-3.45 (m, 3H), 1.32-1.29 (d, *J* = 6.5 Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 148.0, 142.4, 130.5, 128.8, 128.5, 128.2, 127.4, 127.1, 125.7, 118.4, 68.2, 59.9, 59.8, 49.7, 21.0; IR (film) ν<sub>max</sub> 3128, 3096, 2965, 2837, 2776, 1608, 1492, 1454, 1351, 1324, 1235, 1202, 1187, 1079, 1028, 991, 830, 789, 763, 725, 695, 689 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode) *m/z* calculated for C<sub>19</sub>H<sub>21</sub>N<sub>4</sub> [M + H]<sup>+</sup> 305.1761; found 305.1769. [α]<sub>578</sub><sup>20</sup>: - 15 (c 0.5, CH<sub>2</sub>Cl<sub>2</sub>).

**(S)-1-(1-Phenyl-ethyl)-3-(tert-butyloxycarbonylamino)-azetidine 15:** To a solution of **13** (167 mg, 0.83 mmol) in THF/H<sub>2</sub>O (5 mL/0.1mL) was added triphenylphosphine (262 mg, 1.0 mmol) in portions. The mixture was heated at 70°C for 45 minutes then allowed to cool and concentrated under reduced pressure. The residue was dissolved in MeCN (2 mL) and a solution of di-*tert*-butyl-dicarbonate (218 mg, 1.0 mmol) in MeCN (1 mL) was added. The reaction mixture was stirred for 24 h then concentrated in vacuo to give a crude compound which was purified by chromatography (MeOH/CH<sub>2</sub>Cl<sub>2</sub> 3/97) over silica gel to afford **15** (179 mg, 0.65 mmol, 78%) as a white solid; Mp: 109-111°C; R<sub>f</sub> = 0.38 ((MeOH/CH<sub>2</sub>Cl<sub>2</sub> 7.5/92.5). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 7.33-7.20 (m, 5H), 4.94 (bs, 1H), 4.29-4.19 (m, 1H), 3.71-3.67 (app t, 1H), 3.44-3.39 (app t, 1H), 3.29-3.23 (q, *J* = 6.4 Hz, 1H), 2.88-2.78 (m, 2H), 1.43 (s, 9H), 1.23-1.20 (d, *J* = 6.4 Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 155.0, 142.8, 128.4, 127.2, 127.1, 79.5, 68.7, 61.0, 60.8, 40.8, 28.3, 21.0; IR (film) ν<sub>max</sub> 3378, 2968, 2827, 1686, 1521, 1452, 1365, 1247, 1163, 1055, 1033, 875, 762, 640 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode) *m/z* calculated for C<sub>16</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub> [M + H]<sup>+</sup> 277.1911; found 277.1909. [α]<sub>578</sub><sup>20</sup>: - 56 (c 0.5, CH<sub>2</sub>Cl<sub>2</sub>).

**(S)-1-(1-Phenyl-ethyl)-3-(9-fluorenylmethoxycarbonylamino)-azetidine 16:** To a solution of **13** (64 mg, 0.32 mmol) in THF/H<sub>2</sub>O (1 mL/0.02 mL) was added triphenylphosphine (100 mg, 0.38 mmol) in portions. The mixture was heated at 70°C for 1 h then allowed to cool and concentrated under reduced pressure. The residue was dissolved in MeCN (1 mL) and 9-fluorenylmethyl chloroformate (103 mg, 0.40 mmol) was added. The reaction mixture was stirred for 24 h. The mixture was concentrated in vacuo to give a crude compound which was purified by chromatography (MeOH/CH<sub>2</sub>Cl<sub>2</sub> 5/95) over silica gel to afford **16** (95 mg, 0.24 mmol, 74%) as a white solid; Mp: 72-74°C; R<sub>f</sub> = 0.40 ((MeOH/CH<sub>2</sub>Cl<sub>2</sub> 10/90). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 7.74-7.72 (d, *J* = 6.5 Hz, 2H), 7.55-7.53 (d, *J* = 6.5 Hz, 2H), 7.40-7.35 (m, 2H), 7.33-7.19 (m, 7H), 5.22 (b, 1H), 4.38-4.17 (m, 3H), 4.18-4.14 (m, 1H), 3.71-3.65 (m, 1H), 3.44-3.39 (m, 1H), 3.30-3.28 (m, 1H), 2.91 (b, 2H), 1.21-1.19 (d, *J* = 5.5 Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 155.5, 143.8, 142.7, 141.3, 128.4, 127.7, 127.2, 127.1, 127.0, 124.9, 119.9, 68.6, 66.6, 60.7, 60.6, 47.1, 41.3 21.0; OIR (film) ν<sub>max</sub> 3332, 3064, 2948, 2812, 1683, 1535, 1451, 1351, 1319, 1252, 1183, 1138, 1085, 1041, 1017, 975, 759, 733, 696, 639 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode) *m/z* calculated for C<sub>26</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub> [M + H]<sup>+</sup> 399.2068; found 399.2074. [α]<sub>578</sub><sup>20</sup>: - 223 (c 0.5, CH<sub>2</sub>Cl<sub>2</sub>).

**(S)-1-(1-Phenyl-ethyl)-azetidine-3-carbonitrile 17:** To a solution of 3-tosyl azetidine **9** (331 mg, 2.07 mmol) in ethanol (10 mL) was added potassium cyanide (270 mg, 4.15 mmol). The reaction mixture was stirred at 80°C for 2h, then cooled to 23°C before evaporating the solvent. The residue was dissolved in DCM (20 mL). The organic layer was washed with 5% aqueous hydrogen carbonate (20 mL), dried over magnesium sulfate and concentrated in vacuo to give a crude compound which was purified by chromatography (EtOAc/Pentane 25/75) over silica gel to afford **17** (316 mg, 1.70 mmol, 82%) as a colourless oil; R<sub>f</sub> = 0.28 (EtOAc/Pentane 25/75). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 7.35-7.23 (m, 5H), 3.65-3.61 (m, 1H), 3.39-3.14 (m, 5H), 1.22-1.20 (d, *J* = 6.4 Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 141.9, 128.5, 127.4, 127.0, 120.2, 68.1, 56.3, 56.2, 20.6, 17.3; IR (film) ν<sub>max</sub> 3069, 3027, 2968, 2839, 2594, 2423, 2240, 2211, 1599, 1492, 1451, 1371, 1286, 1216, 1186, 1160, 1124, 1088, 1028, 962, 763, 700, 659 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode) *m/z* calculated for C<sub>12</sub>H<sub>15</sub>N<sub>2</sub> [M + H]<sup>+</sup> 187.1231; found 187.1229. [α]<sub>578</sub><sup>20</sup>: - 65 (c 0.5, CH<sub>2</sub>Cl<sub>2</sub>).

**(S)-1-(1-Phenyl-ethyl)-azetidine-3-carboxylic acid ethyl ester 18:** To a solution of 3-cyano azetidine **17** (257 mg, 1.38 mmol) in ethanol (10 mL) was added sulfuric acid (2.8 mL). The reaction mixture was stirred at 80°C for 16h, cooled to 0°C and poured slowly onto saturated aqueous hydrogen carbonate solution (60 mL), and then extracted with DCM (2 x 50 mL). The combined organic layers were washed with brine (20 mL), dried over magnesium sulfate and concentrated in vacuo to give a crude compound which was purified by chromatography

(EtOAc/Pentane 50/50) over silica gel to afford **18** (264 mg, 1.13 mmol, 82%) as a colourless oil;  $R_f = 0.26$  (EtOAc/Pentane 50/50).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.32-7.24 (m, 5H), 4.15 (q,  $J = 7.2$  Hz, 1H), 3.65-3.61 (m, 1H), 3.37-3.24 (m, 4H), 3.19-3.17 (m, 1H), 1.28-1.21 (m, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 173.0, 142.7, 128.2, 127.0, 68.2, 60.5, 55.5, 32.8, 20.6, 14.0; **IR** (film)  $\nu_{\text{max}}$  2955, 2921, 2852, 1741, 1459, 1376, 1239, 1167, 964, 721  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{14}\text{H}_{20}\text{NO}_2$   $[\text{M} + \text{H}]^+$  234.1489; found 234.1503.  $[\alpha]_{578}^{20}$ : - 28 (c 0.4,  $\text{CH}_2\text{Cl}_2$ ).

**[(S)-1-(1-Phenyl-ethyl)-azetidin-3-yl]-methanol 19**: To a suspension of lithium aluminium hydride (103 mg, 2.71 mmol) in THF (2 mL) cooled to  $0^\circ\text{C}$  was added dropwise a solution of **18** (264 mg, 1.13 mmol) in THF (2 mL). The reaction mixture was stirred at  $23^\circ\text{C}$  for 16 h and hydrolyzed at  $0^\circ\text{C}$  by successive additions of water (0.10 mL), 2 M aqueous sodium hydroxide (0.10 mL), and water (0.30 mL). After stirring at  $23^\circ\text{C}$  for 2 h, THF (3 mL) was added and the reaction mixture was filtered through Celite. The solid was washed with THF (3 x 3 mL), and the filtrate was concentrated in vacuo to give **19** (203 mg, 1.06 mmol, 94 %) as a clear oil that crystallized on standing to give a white solid; Mp:  $63\text{--}65^\circ\text{C}$ ;  $R_f = 0.25$  (DCM/MeOH 90/10).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.36-7.24 (m, 5H), 3.79-3.77 (m, 2H), 3.37-3.32 (m, 2H), 3.27-3.22 (m, 1H), 3.13-3.09 (m, 1H), 3.01-2.97 (m, 1H), 2.95-2.74 (m, 1H), 2.66-2.54 (m, 1H), 1.25 (d,  $J = 6.6$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 142.7, 128.3, 128.2, 127.1, 68.2, 64.4, 55.8, 55.6, 31.4, 20.8; **IR** (film)  $\nu_{\text{max}}$  3149, 2971, 2934, 2900, 2841, 2796, 1493, 1456, 1446, 1376, 1358, 1317, 1216, 1098, 1086, 1045, 1012, 986, 963, 797, 773, 751, 701, 657  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{12}\text{H}_{18}\text{NO}$   $[\text{M} + \text{H}]^+$  192.1383; found 192.1391.  $[\alpha]_{578}^{20}$ : - 76 (c 2.0,  $\text{CH}_2\text{Cl}_2$ ).

#### General procedure for the formation of 3-alkoxy azetidines **20**, **23-29**

To a suspension of sodium hydride in DMF (60% in mineral oil, 1.5 equiv, concentration:  $1.25 \text{ mol.L}^{-1}$ ) cooled to  $0^\circ\text{C}$  was added dropwise a solution of 3-hydroxy azetidine in DMF (1.0 equiv, concentration:  $0.85 \text{ mol.L}^{-1}$ ). After 10 min., a solution of alkyl bromide in DMF (1.5 equiv, concentration:  $1.25 \text{ mol.L}^{-1}$ ) cooled to  $0^\circ\text{C}$  was added dropwise to the reaction mixture which was stirred at  $23^\circ\text{C}$  for 24h. After quenching the reaction with ethanol (0.4 mL/mmol of 3-hydroxy azetidine) at  $0^\circ\text{C}$ , solvents were evaporated. The residue was dissolved in DCM. The organic layer was washed with water, dried over magnesium sulfate and concentrated in vacuo to give a crude compound which was purified by chromatography over silica gel.

**(S)-1-(1-Phenyl-ethyl)-3-benzyloxy-azetidine 20**: Following the general procedure from 3-hydroxy azetidine **5**, 65% yield as a colourless oil;  $R_f = 0.52$  (EtOAc/Pentane 75/25).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.34-7.18 (m, 10H), 4.39 (s, 2H), 4.21-4.13 (m, 1H), 3.72-3.67 (m, 1H), 3.34-3.26 (m, 2H), 2.97-2.93 (app t, 1H), 2.83-2.79 (app t, 1H), 1.22 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 143.1, 137.7, 128.4, 128.3, 127.9, 127.8, 127.1, 71.0, 68.9, 67.3, 60.7, 60.6, 21.0; **IR** (film)  $\nu_{\text{max}}$  3064, 3028, 2963, 2934, 2825, 2782, 1492, 1452, 1354, 1216, 1185, 1113, 1026, 734, 696  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{18}\text{H}_{22}\text{NO}$   $[\text{M} + \text{H}]^+$  268.1696; found 268.1695.  $[\alpha]_{578}^{20}$ : - 79 (c 1.0,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-3-Benzhydryloxy-1-(1-phenyl-ethyl)-azetidine 21**: To a solution of 3-hydroxy azetidine **5** (100 mg, 0.56 mmol) in DMF (3 mL) was added diisopropylethylamine (1.60 mL, 9.20 mmol) and benzhydryl chloride (0.40 mL, 2.03 mmol). The reaction mixture was stirred at  $60^\circ\text{C}$  for 4 days, cooled to  $23^\circ\text{C}$  and diluted with ethyl acetate (20 mL). The organic layer was washed with brine (2 x 10 mL), dried over magnesium sulfate and concentrated in vacuo to give a crude compound, which was purified by flash chromatography (EtOAc/Pentane 25/75) over silica gel to afford **21** (77 mg, 0.22 mmol, 40%) as a colourless oil;  $R_f = 0.45$  (EtOAc/Pentane 50/50).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.39-7.26 (m, 5H), 5.38 (s, 1H), 4.31-4.23 (m, 1H), 3.73-3.68 (m, 1H), 3.40-3.31 (m, 2H), 3.07-3.03 (m, 1H), 2.92-2.87 (m, 1H), 1.27 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 143.2, 141.7, 128.2, 127.9, 127.5, 127.4, 127.0, 126.9, 82.35, 68.8, 66.2, 60.9, 60.7, 21.0; **IR** (film)  $\nu_{\text{max}}$  3083, 3061, 2962, 2824, 1599, 1492, 1450, 1279, 1218, 1183, 1110, 1026, 1011, 754, 739, 696, 644  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{24}\text{H}_{26}\text{NO}$   $[\text{M} + \text{H}]^+$  344.2009; found 344.2010.  $[\alpha]_{578}^{20}$ : - 50 (c 1.8,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Phenyl-ethyl)-3-trityloxy-azetidine 22**: To a solution of 3-hydroxy azetidine **5** (100 mg, 0.56 mmol) in DMF (3 mL) was added diisopropylethylamine (1.60 mL, 9.20 mmol) and trityl chloride (272 mg, 0.97 mmol). The reaction mixture was stirred at  $60^\circ\text{C}$  for 4 days, cooled to  $23^\circ\text{C}$  and diluted with ethyl acetate (20 mL). The organic layer was washed with brine (2 x 10 mL), dried over magnesium sulfate and concentrated in vacuo to give a crude compound, which was purified by flash chromatography (EtOAc/Pentane 25/75) over silica gel to

afford **22** (157 mg, 0.37 mmol, 67%) as a yellow oil;  $R_f = 0.57$  (EtOAc/Pentane 50/50).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.51-7.47 (m, 6H), 7.30-7.26 (m, 14H), 4.36-4.27 (m, 1H), 3.31 (q,  $J = 6.6$  Hz, 1H), 3.23-3.19 (m, 1H), 3.09-3.05 (m, 1H), 2.83-2.76 (m, 2H), 1.20 (d,  $J = 6.6$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 144.3, 143.2, 128.3, 128.2, 127.7, 126.9, 87.1, 68.8, 63.3, 62.0, 61.4, 21.0; **IR** (film)  $\nu_{\text{max}}$  3083, 3058, 3024, 2963, 2824, 1596, 1491, 1448, 1369, 1217, 1177, 1102, 999, 906, 756, 697, 645, 630  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{30}\text{H}_{30}\text{NO}$   $[\text{M} + \text{H}]^+$  420.2322; found 420.2332.  $[\alpha]_{578}^{20}$ : - 25 (c 2.3,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Phenyl-ethyl)-3-allyloxy-azetidine 23**: Following the general procedure from 3-hydroxy azetidine **5**, 71% yield as a colourless oil;  $R_f = 0.35$  (EtOAc/Pentane 75/25).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.34-7.21 (m, 5H), 5.96-5.83 (m, 1H), 5.30-5.15 (m, 2H), 4.18-4.10 (m, 1H), 3.91-3.89 (m, 2H), 3.77-3.72 (m, 1H), 3.37-3.28 (m, 2H), 2.98-2.94 (app t, 1H), 2.82-2.78 (app t, 1H), 1.25-1.23 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 143.2, 134.4, 128.3, 127.1, 117.5, 70.0, 69.0, 67.3, 60.8, 60.7, 21.1; **IR** (film)  $\nu_{\text{max}}$  3026, 2967, 2937, 2928, 2777, 1646, 1492, 1451, 1351, 1278, 1218, 1186, 1112, 991, 922, 758, 699  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{14}\text{H}_{20}\text{NO}$   $[\text{M} + \text{H}]^+$  218.1540; found 218.1543.  $[\alpha]_{578}^{20}$ : - 83 (c 0.5,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Phenyl-ethyl)-3-(naphthalen-2-yl-methoxy)-azetidine 24**: Following the general procedure from 3-hydroxy azetidine **5**, 52% yield as a yellow oil;  $R_f = 0.36$  (EtOAc/Pentane 50/50).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.85-7.82 (m, 3H), 7.77 (s, 1H), 7.51-7.44 (m, 3H), 7.33-7.22 (m, 5H), 4.59 (s, 2H), 4.31-4.23 (m, 1H), 3.76-3.71 (m, 1H), 3.40-3.30 (m, 2H), 3.04-3.00 (app t, 1H), 2.91-2.86 (app t, 1H), 1.26-1.24 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 143.2, 135.2, 133.2, 133.0, 128.3, 128.2, 127.8, 127.6, 127.1, 126.7, 126.1, 125.9, 125.8, 71.1, 68.9, 67.4, 60.7, 60.6, 21.0; **IR** (film)  $\nu_{\text{max}}$  3055, 3024, 2962, 2932, 2824, 1601, 1508, 1491, 1450, 1361, 1340, 1278, 1217, 1184, 1124, 1076, 1027, 951, 854, 814, 750, 699  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{22}\text{H}_{24}\text{NO}$   $[\text{M} + \text{H}]^+$  318.1853; found 318.1851.  $[\alpha]_{578}^{20}$ : - 65 (c 0.6,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Phenyl-ethyl)-3-(anthracen-9-yl-methoxy)-azetidine 25**: Following the general procedure from 3-hydroxy azetidine **5**, 56% yield as a yellow solid; Mp: 51-53°C;  $R_f = 0.48$  (EtOAc/Pentane 75/25).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.47 (s, 1H), 8.36-8.33 (d,  $J = 8.7$  Hz, 2H), 8.04-8.01 (d,  $J = 8.2$  Hz, 2H), 7.60-7.47 (m, 4H), 7.36-7.24 (m, 5H), 5.42 (s, 2H), 4.44-4.36 (m, 1H), 3.74-3.69 (m, 1H), 3.44-3.39 (m, 1H), 3.34-3.28 (q,  $J = 6.4$  Hz, 1H), 3.03-2.99 (app t, 1H), 2.93-2.89 (app t, 1H), 1.22 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 143.2, 131.3, 130.9, 129.0, 128.6, 128.3, 127.9, 127.1, 126.3, 124.9, 124.0, 68.9, 67.4, 62.8, 60.8, 60.7, 21.1; **IR** (film)  $\nu_{\text{max}}$  3057, 3027, 2962, 2929, 2824, 1664, 1600, 1492, 1448, 1356, 1316, 1172, 1107, 931, 887, 759, 731, 698752  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{26}\text{H}_{26}\text{NO}$   $[\text{M} + \text{H}]^+$  368.2009; found 368.2013.  $[\alpha]_{578}^{20}$ : - 57 (c 0.5,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-3-Benzyloxy-1-(1-naphthalen-1-yl-ethyl)-azetidine 26**: Following the general procedure from 3-hydroxy azetidine **6**, 23% yield as a yellow oil;  $R_f = 0.49$  (MeOH/DCM 10/90).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.24 (d,  $J = 7.8$  Hz, 1H), 7.87 (d,  $J = 7.8$  Hz, 1H), 7.75 (d,  $J = 8.1$  Hz, 1H), 7.66 (d,  $J = 7.2$  Hz, 1H), 7.54-7.743 (m, 3H), 7.35-7.29 (m, 5H), 4.44 (s, 2H), 4.31-4.23 (m, 1H), 4.17 (q,  $J = 4.8$  Hz, 1H), 3.85-3.81 (m, 1H), 3.54-3.50 (m, 1H), 3.16-3.12 (m, 1H), 2.86-2.81 (m, 1H), 1.37 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 138.9, 137.6, 133.8, 131.0, 128.8, 128.4, 127.9, 127.8, 127.2, 125.6, 125.2, 123.8, 123.2, 71.0, 67.4, 64.9, 60.8, 20.6; **IR** (film)  $\nu_{\text{max}}$  3031, 2931, 2826, 1594, 1509, 1453, 1352, 1185, 1124, 1043, 1008, 800, 776, 734, 696  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{22}\text{H}_{24}\text{NO}$   $[\text{M} + \text{H}]^+$  318.1853; found 318.1865.  $[\alpha]_{578}^{20}$ : - 107 (c 0.6,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-3-Benzyloxy-1-(1-naphthalen-2-yl-ethyl)-azetidine 27**: Following the general procedure from 3-hydroxy azetidine **7**, 65% yield as a yellow oil;  $R_f = 0.54$  (MeOH/DCM 10/90).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.84-7.80 (m, 3H), 7.75 (s, 1H), 7.48-7.42 (m, 3H), 7.36-7.29 (m, 5H), 4.43 (s, 2H), 4.28-4.20 (m, 1H), 3.79-3.75 (m, 1H), 3.49 (q,  $J = 6.3$  Hz, 1H), 3.39-3.35 (m, 1H), 3.06-3.02 (m, 1H), 2.91-2.87 (m, 1H), 1.32 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 140.7, 137.6, 133.3, 132.8, 128.3, 128.0, 127.9, 127.8, 127.7, 127.5, 125.8, 125.7, 125.5, 125.3, 71.0, 69.1, 67.3, 60.7, 21.0; **IR** (film)  $\nu_{\text{max}}$  3055, 3034, 2962, 2939, 2826, 1677, 1600, 1498, 1453, 1352, 1281, 1194, 1113, 1026, 857, 819, 745, 697  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{22}\text{H}_{24}\text{NO}$   $[\text{M} + \text{H}]^+$  318.1853; found 318.1867.  $[\alpha]_{578}^{20}$ : - 12 (c 1.0,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Cyclohexyl-ethyl)-3-benzyloxy-azetidine 28**: Following the general procedure from 3-hydroxy azetidine **8**, 28% yield as a colourless oil;  $R_f = 0.43$  (EtOAc/Pentane 25/75).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.38-7.21 (m, 5H), 4.44 (s, 2H), 4.24-4.16 (m, 1H), 3.64-3.56 (m, 2H), 2.87-2.78 (m, 2H), 2.12-2.05 (m, 1H),

1.76-1.61 (m, 4H), 1.46-0.90 (m, 7H), 0.81 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 137.8, 128.4, 127.9, 127.8, 71.1, 68.4, 67.6, 60.7, 60.4, 39.3, 30.6, 26.9, 26.5, 26.2, 11.9; IR (film)  $\nu_{\text{max}}$  2921, 2850, 1450, 1382, 1352, 1205, 1186, 1147, 1117, 1027, 890, 732, 696, 609  $\text{cm}^{-1}$ ; HRMS (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{18}\text{H}_{28}\text{NO}$   $[\text{M} + \text{H}]^+$  274.2166; found 274.2167.  $[\alpha]_{578}^{20}$ : - 29 (c 1.0,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Naphthalen-1-yl-ethyl)-3-(naphthalen-2-yl-methoxy)-azetidine 29:** Following the general procedure from 3-hydroxy azetidine **6**, 8% yield as a yellow oil;  $R_f = 0.43$  (MeOH/DCM 10/90).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.26 (d,  $J = 7.9$  Hz, 1H), 7.75-7.90 (m, 6H), 7.68 (d,  $J = 7.0$  Hz, 1H), 7.46-7.756 (m, 6H), 4.62 (s, 2H), 4.29-4.37 (m, 1H), 4.17-4.23 (q,  $J = 4.2$  Hz, 1H), 3.83-3.87 (m, 1H), 3.53-3.57 (m, 1H), 3.17-3.21 (m, 1H), 2.87-2.92 (m, 2H), 1.39 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 139.0, 135.2, 133.9, 133.2, 133.0, 131.1, 128.9, 128.2, 127.8, 127.6, 127.2, 126.6, 126.1, 125.9, 125.8, 125.2, 123.9, 123.2, 71.1, 67.5, 65.0, 60.8, 20.6; IR (film)  $\nu_{\text{max}}$  3049, 2929, 2826, 2208, 1673, 1595, 1508, 1448, 1362, 1340, 1185, 1124, 1018, 892, 854, 816, 799, 749, 620  $\text{cm}^{-1}$ ; HRMS (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{26}\text{H}_{26}\text{NO}$   $[\text{M} + \text{H}]^+$  368.2009; found 368.2016.  $[\alpha]_{578}^{20}$ : - 7 (c 1.2,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Phenyl-ethyl)-3-acetyloxy-azetidine 30:** To a solution of 3-hydroxy azetidine **5** (90 mg, 0.50 mmol) in dichloromethane (4.5 mL) was added pyridine (0.5 mL) and acetic anhydride (0.10 mL, 1.00 mmol). The reaction mixture was stirred for 24h then evaporated under reduced pressure. The crude compound was purified by chromatography (EtOAc/Pentane 25/75) over silica gel to afford **30** (94 mg, 0.43 mmol, 85%) as a yellow oil;  $R_f = 0.38$  (EtOAc/Pentane 75/25).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.33-7.21 (m, 5H), 5.06-4.98 (m, 1H), 3.75-3.70 (m, 1H), 3.47-3.42 (m, 1H), 3.35-3.28 (q,  $J = 6.5$  Hz, 1H), 3.06-2.97 (m, 2H), 2.05 (s, 3H), 1.24-1.22 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 170.4, 142.9, 128.3, 127.1, 127.0, 68.7, 63.5, 59.8, 59.7, 21.1, 20.8; IR (film)  $\nu_{\text{max}}$  2966, 2829, 2777, 1739, 1492, 1450, 1359, 1229, 1171, 1090, 1026, 801, 760, 700, 609  $\text{cm}^{-1}$ ; HRMS (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{13}\text{H}_{18}\text{NO}_2$   $[\text{M} + \text{H}]^+$  220.1333; found 220.1331.  $[\alpha]_{578}^{20}$ : - 85 (c 0.5,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-2,2-Dimethyl-propionic acid 1-((1'S)-phenyl-ethyl)-azetid-3-yl ester 31:** To a solution of 3-hydroxy azetidine **5** (100 mg, 0.56 mmol) in dichloromethane (5 mL) was added pyridine (0.18 mL, 2.25 mmol), DMAP (69 mg, 0.56 mmol) and pivaloyl chloride (0.17 mL, 1.41 mmol). The reaction mixture was stirred for 24h, diluted with DCM (20 mL), washed with saturated aqueous ammonium chloride (15 mL) and brine (15 mL), and dried over magnesium sulfate. Solvent was evaporated under reduced pressure and the crude compound was purified by chromatography (EtOAc/Pentane 35/65) over silica gel to afford **31** (113 mg, 0.43 mmol, 77%) as a colourless oil;  $R_f = 0.74$  (EtOAc/Pentane 50/50).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.34-7.32 (m, 5H), 5.08-4.99 (m, 1H), 3.89-3.84 (m, 1H), 3.54-3.49 (m, 1H), 3.36 (q,  $J = 6.6$  Hz, 1H), 3.04-3.00 (m, 1H), 2.92-2.87 (m, 1H), 1.27 (d,  $J = 6.6$  Hz, 3H), 1.22 (s, 9H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 177.8, 142.8, 128.3, 127.1, 127.0, 68.8, 63.0, 60.0, 59.8, 38.3, 26.9, 20.9; IR (film)  $\nu_{\text{max}}$  2968, 2871, 2828, 1728, 1479, 1452, 1368, 1323, 1149, 1051, 759, 737  $\text{cm}^{-1}$ ; HRMS (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{16}\text{H}_{24}\text{NO}_2$   $[\text{M} + \text{H}]^+$  262.1802; found 262.1803.  $[\alpha]_{578}^{20}$ : - 80 (c 1.9,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Naphthyl-ethyl)-3-((S)- $\alpha$ -acetoxyphenylacetyloxy)-azetidine 32:** To a solution of hydroxy-azetidine **6** (91 mg, 0.40 mmol) and (*S*)- $\alpha$ -acetoxyphenylacetic acid (97 mg, 0.50 mmol) in  $\text{CH}_2\text{Cl}_2$  (3 mL) was added *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (115 mg, 0.60 mmol) and DMAP (10 mg, 0.08 mmol). The reaction mixture was stirred for 24 h, then diluted with  $\text{CH}_2\text{Cl}_2$  and washed with saturated aqueous ammonium chloride and brine, then dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the crude compound was purified by chromatography (EtOAc/Pentane 25/75) over silica gel to afford **32** (141 mg, 0.35 mmol, 87%) as a colourless oil;  $R_f = 0.33$  (EtOAc/Pentane 25/75).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.21-8.18 (d,  $J = 7.8$  Hz, 1H), 7.88-7.85 (m, 1H), 7.76-7.73 (d,  $J = 8.2$  Hz, 1H), 7.62-7.60 (d,  $J = 7.0$  Hz, 1H), 7.54-7.42 (m, 8H), 5.92 (s, 1H), 5.16-5.08 (m, 1H), 4.14-4.08 (q,  $J = 6.3$  Hz, 1H), 3.81-3.76 (app t, 1H), 3.67-3.62 (app t, 1H), 3.09-3.04 (m, 1H), 2.99-2.94 (m, 1H), 2.19 (s, 3H), 1.35-1.33 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 170.3, 168.2, 138.5, 133.9, 133.4, 131.0, 128.9, 128.8, 127.6, 127.3, 125.7, 125.6, 125.2, 123.8, 123.1, 74.4, 64.7, 59.8, 59.6, 20.7, 20.5; IR (film)  $\nu_{\text{max}}$  3340, 3046, 2963, 2924, 2849, 1740, 1509, 1455, 1370, 1228, 1205, 1172, 1081, 1045, 966, 801, 777, 736, 695  $\text{cm}^{-1}$ ; HRMS (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{25}\text{H}_{26}\text{NO}_4$   $[\text{M} + \text{H}]^+$  404.1857; found 404.1862.  $[\alpha]_{578}^{20}$ : - 13 (c 0.5,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1-(1-Naphthyl-ethyl)-3-((R)- $\alpha$ -acetoxyphenylacetyloxy)-azetidine 33:** To a solution of hydroxy-azetidine **6** (454 mg, 2.00 mmol) and (*R*)- $\alpha$ -acetoxyphenylacetic acid (428 mg, 2.20 mmol) in  $\text{CH}_2\text{Cl}_2$  (15 mL) was added

dicyclohexylcarbodiimide (498 mg, 2.40 mmol) and DMAP (49 mg, 0.40 mmol). The reaction mixture was stirred for 5 days, then diluted with CH<sub>2</sub>Cl<sub>2</sub> and filtered through Celite. The filtrate was washed with saturated aqueous ammonium chloride and brine, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the crude compound was purified by chromatography (EtOAc/Pentane 25/75) over silica gel to afford **33** (686 mg, 1.70 mmol, 85%) as a colourless oil; R<sub>f</sub> = 0.28 (EtOAc/Pentane 25/75). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 8.20 (d, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 7.0 Hz, 1H), 7.51-7.39 (m, 8H), 5.92 (s, 1H), 5.15-5.09 (m, 1H), 4.16-4.13 (m, 1H), 3.95-3.90 (app t, 1H), 3.60-3.56 (app t, 1H), 3.24-3.19 (app t, 1H), 2.87-2.82 (app t, 1H), 2.22 (s, 3H), 1.37-1.35 (d, *J* = 6.1 Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 170.4, 168.2, 138.4, 133.9, 133.3, 131.0, 129.3, 128.9, 128.8, 127.6, 127.4, 125.7, 125.6, 125.2, 123.8, 123.1, 74.4, 64.9, 64.6, 60.0, 59.4, 20.6, 20.5; **IR** (film) ν<sub>max</sub> 3050, 2965, 2832, 1740, 1595, 1509, 1455, 1370, 1228, 1205, 1173, 1085, 1045, 966, 801, 778, 735, 695 cm<sup>-1</sup>; **HRMS** (ESI-TOF positive mode) *m/z* calculated for C<sub>25</sub>H<sub>26</sub>NO<sub>4</sub> [M + H]<sup>+</sup> 404.1857; found 404.1877. [α]<sub>D</sub><sup>20</sup>: -102 (c 1.0, CH<sub>2</sub>Cl<sub>2</sub>).

### General procedure for the Von Braun reaction with azetidines

To a solution of the required azetidine in chloroform (concentration: 0.2 M) was added dropwise a 3 M solution of BrCN in CH<sub>2</sub>Cl<sub>2</sub> (3 equiv). The reaction was monitored by TLC. After completion, the solvent was evaporated under reduced pressure and the diastereomeric ratio of the crude product was determined using NMR spectroscopy.

**(R,S) Thioacetic acid (2-bromo-1-[[cyano-((1'S)-phenyl-ethyl)-amino]-methyl]-ethyl) ester 34:** colourless oil; R<sub>f</sub> = 0.70 (EtOAc/Pentane 25/75). T = -30°C *dr* = 55:45. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 55:45 diastereoisomeric mixture) δ: 7.43-7.35 (m, 5H<sup>M</sup> and 5H<sup>m</sup>), 4.24-4.14 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 4.05-3.92 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 3.75-3.65 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 3.61-3.56 (dd, *J* = 10.7, 6.3 Hz, 1H<sup>m</sup>), 3.52-3.37 (m, 2H<sup>M</sup>), 3.30-3.21 (m, 2H<sup>m</sup>), 3.15-3.09 (dd, *J* = 14.2 Hz, 6.1 Hz, 1H<sup>M</sup>), 2.39 (s, 3H<sup>M</sup>), 2.36 (s, 3H<sup>m</sup>), 1.70-1.65 (m, 3H<sup>m</sup> and 3H<sup>M</sup>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 193.6, 193.5, 140.2, 140.0, 129.1, 129.0, 128.6, 126.5, 126.4, 115.9, 60.2, 59.9, 52.1, 51.9, 43.8, 43.4, 33.2, 33.0, 30.7, 30.7, 21.2, 20.9; **IR** (film) ν<sub>max</sub> 3027, 2976, 2939, 2207, 1740, 1692, 1646, 1590, 1495, 1452, 1379, 1306, 1222, 1175, 1120, 1027, 955, 910, 762, 699, 660, 626 cm<sup>-1</sup>. **HRMS** (ESI-TOF positive mode) *m/z* calculated for C<sub>14</sub>H<sub>18</sub>BrN<sub>2</sub>OS [M + H]<sup>+</sup> 341.0318; found 341.0331.

**(1S, 2R,S)-[3-Bromo-2-(4-methoxy-benzylsulfanyl)-propyl]-(1-phenyl-ethyl)-cyanamide 35:** colourless oil; R<sub>f</sub> = 0.52 (EtOAc/Pentane 25/75). T = -30°C *dr* = 60:40. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 60:40 diastereoisomeric mixture) δ: 7.43-7.31 (m, 4H<sup>M</sup> and 4H<sup>m</sup>), 7.29-7.18 (m, 3H<sup>M</sup> and 3H<sup>m</sup>), 6.90-6.85 (m, 2H<sup>M</sup> and 2H<sup>m</sup>), 4.24-4.17 (q, *J* = 7.0 Hz, 1H<sup>M</sup>), 4.11-3.94 (m, 1H<sup>M</sup> and 2H<sup>m</sup>), 3.81 (s, 3H<sup>M</sup> and 3H<sup>m</sup>), 3.74-3.67 (m, 2H<sup>M</sup> and 2H<sup>m</sup>), 3.63-3.57 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 3.40-2.99 (m, 2H<sup>M</sup> and 2H<sup>m</sup>), 2.92-2.73 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 1.67-1.60 (m, 3H<sup>M</sup> and 3H<sup>m</sup>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 158.9, 140.4, 140.0, 130.0, 129.9, 129.1, 129.0, 128.5, 128.5, 126.5, 126.4, 114.2, 114.1, 60.8, 56.0, 55.3, 49.6, 36.3, 36.2, 21.3, 21.0; **IR** (film) ν<sub>max</sub> 2977, 2934, 2834, 2205, 1679, 1647, 1609, 1585, 1510, 1453, 1420, 1301, 1244, 1174, 1027, 819, 761, 699 cm<sup>-1</sup>. **HRMS** (ESI-TOF positive mode) *m/z* calculated for C<sub>20</sub>H<sub>24</sub>BrN<sub>2</sub>OS [M + H]<sup>+</sup> 419.0788; found 419.0782.

**(1S, 2R,S)-[3-Bromo-2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propyl]-(1'S)-phenyl-ethyl)-cyanamide 36:** colourless oil; R<sub>f</sub> = 0.89 (DCM/MeOH 95/5). T = -30°C *dr* = 60/40. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 60:40 diastereoisomeric mixture) δ: 7.90-7.85 (m, 2H<sup>M</sup> and 2H<sup>m</sup>), 7.80-7.74 (m, 2H<sup>M</sup> and 2H<sup>m</sup>), 7.35-7.29 (m, 5H<sup>M</sup> and 5H<sup>m</sup>), 4.78-4.65 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 4.25-4.13 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 3.86-3.54 (m, 3H<sup>M</sup> and 3H<sup>m</sup>), 3.50-3.44 (dd, *J* = 14.1, 5.9 Hz, 1H<sup>m</sup>), 3.32-3.26 (dd, *J* = 14.5, 4.2 Hz, 1H<sup>M</sup>), 1.61 (d, *J* = 6.9 Hz, 3H<sup>M</sup>), 1.58 (d, *J* = 6.9 Hz, 3H<sup>m</sup>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 167.9, 167.7, 139.9, 139.4, 134.4, 134.3, 131.4, 129.1, 128.7, 128.5, 126.7, 126.4, 123.7, 123.6, 115.7, 115.6, 60.3, 58.9, 51.2, 50.4, 49.7, 49.6, 28.9, 28.4, 21.5, 20.6; **IR** (film) ν<sub>max</sub> 3069, 3031, 2977, 2936, 2206, 1773, 1707, 1467, 1454, 1367, 1305, 1240, 1172, 1084, 873, 717, 699 cm<sup>-1</sup>. **HRMS** (ESI-TOF positive mode) *m/z* calculated for C<sub>20</sub>H<sub>19</sub>BrN<sub>3</sub>O<sub>2</sub> [M + H]<sup>+</sup> 412.0656; found 412.0676.

**(1S, 2R,S)-(2-Azido-3-bromo-propyl)-(1-phenyl-ethyl)-cyanamide 37:** colourless oil; R<sub>f</sub> = 0.73 (PE/EtOAc 75/25). T = -30°C *dr* = 65/35. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 65:35 diastereoisomeric mixture) δ: 7.45-7.33 (m, 5H<sup>M</sup> and 5H<sup>m</sup>), 4.26-4.18 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 3.93-3.82 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 3.49-3.47 (m, 1H<sup>M</sup> and 2H<sup>m</sup>), 3.38 (d, *J* = 5.6 Hz, 1H<sup>M</sup>), 3.27-3.21 (dd, *J* = 13.9, 4.1 Hz, 1H<sup>m</sup>), 3.13-3.09 (m, 2H<sup>M</sup>), 2.94-2.87 (dd, *J* = 14.1, 8.7 Hz, 1H<sup>m</sup>), 1.72-1.68 (m, 3H<sup>M</sup> and 3H<sup>m</sup>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 140.1, 139.7, 129.2, 128.8, 126.5, 126.4, 115.7, 115.5, 61.2, 60.6, 60.5, 60.2, 53.0, 52.0, 31.4, 31.2, 21.2, 20.9; **IR** (film) ν<sub>max</sub> 3026, 2996, 2984, 2933, 2211, 2142, 2118, 2069, 1713, 1493, 1453, 1417, 1386, 1304, 1274, 1232, 1198, 1122, 1113, 1071, 1028,



1005, 998, 789, 736, 705, 638, 614  $\text{cm}^{-1}$ . **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{12}\text{H}_{15}\text{BrN}_5$  [ $\text{M} + \text{H}$ ] $^+$  308.0506; found 308.0504.

**(1S, 2R,S)-[3-Bromo-2-(4-phenyl-[1,2,3]triazol-1-yl)-propyl]-(1-phenyl-ethyl)-cyanamide 38**: colourless oil;  $R_f = 0.78$  (DCM/MeOH 95/5).  $T = -30^\circ\text{C}$   $dr = 65/35$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 65:35 diastereoisomeric mixture)  $\delta$ : 7.95-7.84 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 7.50-7.34 (m,  $4\text{H}^{\text{M}}$  and  $4\text{H}^{\text{m}}$ ), 7.33-7.25 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 7.17-7.13 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 5.02-4.91 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 4.08 (dd,  $J = 13.7, 6.9$  Hz,  $1\text{H}^{\text{M}}$ ), 3.88-4.05 (m,  $4\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 1.59 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{M}}$ ), 1.48 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 147.6, 139.8, 139.0, 129.9, 129.9, 129.2, 129.1, 128.9, 128.9, 128.8, 128.7, 128.5, 128.4, 126.4, 126.3, 125.8, 125.8, 121.3, 120.4, 61.1, 60.9, 60.3, 52.6, 52.4, 30.6, 30.1, 21.1, 20.5; **IR** (film)  $\nu_{\text{max}}$  3091, 3059, 3028, 2977, 2931, 2205, 2142, 2118, 2069, 1493, 1454, 1404, 1380, 1338, 1354, 1274, 1230, 1197, 1125, 1085, 1028, 998, 917, 764, 756, 746, 736, 694, 640  $\text{cm}^{-1}$ . **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{20}\text{H}_{21}\text{BrN}_5$  [ $\text{M} + \text{H}$ ] $^+$  410.0975; found 410.0988.

**(2-Bromo-1-[[cyano-((1'S)-phenyl-ethyl)-amino]-methyl]-ethyl)-carbamic acid tert-butyl ester 39**: colourless oil;  $R_f = 0.74$  (DCM/MeOH 95/5).  $T = -30^\circ\text{C}$   $dr = 55/45$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 55:45 diastereoisomeric mixture)  $\delta$ : 7.41-7.34 (m,  $5\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 4.85 (b,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 4.28-4.14 (m,  $1\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 4.07-3.97 (m,  $1\text{H}^{\text{M}}$ ), 3.62-3.46 (m,  $2\text{H}^{\text{M}}$ ,  $2\text{H}^{\text{m}}$ ), 3.19-3.08 (m,  $2\text{H}^{\text{M}}$ ,  $1\text{H}^{\text{m}}$ ), 2.98-2.92 (dd,  $J = 13.9, 6.1$  Hz,  $1\text{H}^{\text{m}}$ ), 1.67-1.63 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 1.48, 1.45 (2s,  $9\text{H}^{\text{M}}$  and  $9\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 155.0, 154.7, 140.3, 139.9, 129.1, 129.0, 128.6, 128.5, 116.1, 80.5, 80.4, 60.0, 58.9, 52.5, 51.8, 49.4, 47.8, 34.9, 34.4, 28.2, 21.3, 20.7; **IR** (film)  $\nu_{\text{max}}$  3325, 2977, 2932, 2207, 1703, 1503, 1455, 1392, 1246, 1160, 1063, 910, 861, 763, 729, 699  $\text{cm}^{-1}$ . **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{17}\text{H}_{25}\text{BrN}_3\text{O}_2$  [ $\text{M} + \text{H}$ ] $^+$  382.1136; found 382.1141.

**(2-Bromo-1-[[cyano-((1'S)-phenyl-ethyl)-amino]-methyl]-ethyl)-carbamic acid 9H-fluoren-9-ylmethyl ester 40**: colourless oil;  $R_f = 0.67$  (DCM/MeOH 95/5).  $T = -30^\circ\text{C}$   $dr = 55/45$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 55:45 diastereoisomeric mixture)  $\delta$ : 7.79-7.76 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 7.71-7.29 (m,  $11\text{H}^{\text{M}}$  and  $11\text{H}^{\text{m}}$ ), 5.16-5.12 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 4.47-4.41 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 4.27-4.13 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 3.57 (m,  $1\text{H}^{\text{M}}$ ), 3.50-3.49 (m,  $1\text{H}^{\text{m}}$ ), 3.22-2.98 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 1.65 (d,  $J = 6.6$  Hz,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 155.6, 155.3, 143.5, 141.2, 140.7, 139.7, 132.0, 131.9, 129.1, 129.0, 128.6, 128.5, 128.4, 127.7, 127.0, 126.5, 126.4, 124.9, 119.9, 116.0, 67.1, 66.9, 60.2, 59.4, 52.1, 51.5, 50.0, 48.8, 47.0, 34.4, 33.9, 21.3, 20.8; **IR** (film)  $\nu_{\text{max}}$  3301, 3065, 2980, 2929, 2207, 1712, 1529, 1449, 1246, 1178, 1118, 1029, 908, 758, 725, 698, 646  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{27}\text{H}_{27}\text{BrN}_3\text{O}_2$  [ $\text{M} + \text{H}$ ] $^+$  504.1282; found 504.1277.

**(1S, 2R,S)-[3-Bromo-2-cyano-propyl]-(1-phenyl-ethyl)-cyanamide 41**: colourless oil;  $R_f = 0.49$  (EtOAc/Pentane 50/50).  $T = -30^\circ\text{C}$   $dr = 65:35$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 65:35 diastereoisomeric mixture)  $\delta$ : 7.46-7.35 (m,  $5\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 4.33-4.28 (m,  $1\text{H}^{\text{M}}$ ), 4.27-4.24 (m,  $1\text{H}^{\text{M}}$ ), 3.64-3.50 (m,  $2\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.45-3.40 (m,  $1\text{H}^{\text{m}}$ ), 3.37-3.22 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 1.71 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 139.4, 139.3, 129.3, 129.0, 126.5, 126.4, 117.3, 116.9, 114.8, 61.2, 61.1, 50.7, 49.9, 33.5, 33.2, 27.5, 27.3, 21.0, 20.9; **IR** (film)  $\nu_{\text{max}}$  3366, 3069, 3031, 2978, 2932, 2208, 1670, 1494, 1379, 1278, 1121, 1093, 1066, 765, 738, 700  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{13}\text{H}_{14}\text{N}_3\text{BrNa}$  [ $\text{M} + \text{Na}$ ] $^+$  314.0264; found 314.0266.

**3-Bromo-2-[[cyano-(1S-phenyl-ethyl)-amino]-methyl]-propionic acid ethyl ester 42**: colourless oil;  $R_f = 0.70$  (EtOAc/Pentane 25/75).  $T = -30^\circ\text{C}$   $dr = 65:35$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 65:35 diastereoisomeric mixture)  $\delta$ : 7.42-7.34 (m,  $5\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 4.28-4.12 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 3.70-3.60 (m,  $2\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.56-3.51 (dd,  $J = 10.5, 4.7$  Hz,  $1\text{H}^{\text{m}}$ ), 3.44-3.22 (m,  $1\text{H}^{\text{M}}$ ,  $2\text{H}^{\text{m}}$ ), 3.18-3.08 (m,  $2\text{H}^{\text{M}}$ ,  $1\text{H}^{\text{m}}$ ), 1.67-1.63 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 1.32-1.25 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 170.0, 169.7, 140.0, 129.0, 128.5, 126.4, 126.3, 61.7, 60.5, 49.9, 49.5, 45.6, 45.3, 29.9, 29.8, 20.9, 14.0; **IR** (film)  $\nu_{\text{max}}$  2979, 2933, 2206, 1731, 1494, 1454, 1376, 1237, 1200, 1181, 1157, 1122, 1093, 1028, 856, 762, 700  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{17}\text{H}_{25}\text{BrN}_3\text{O}_2$  [ $\text{M} + \text{H}$ ] $^+$  382.1125; found 382.1141.

**(1S, 2R,S)-[3-Bromo-2-hydroxymethyl-propyl]-(1-phenyl-ethyl)-cyanamide 43**: colourless oil;  $R_f = 0.50$  (EtOAc/Pentane 50/50).  $T = -30^\circ\text{C}$   $dr = 70:30$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 70:30 diastereoisomeric mixture)  $\delta$ : 7.42-7.32 (m,  $5\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 4.13 (q,  $J = 6.9$  Hz,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.74-3.64 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.54 (d,  $J = 4.8$  Hz,  $2\text{H}^{\text{M}}$ ), 3.53-3.44 (m,  $2\text{H}^{\text{m}}$ ), 3.07-2.98 (m,  $2\text{H}^{\text{M}}$ ), 2.91 (dd,  $J = 13.2$  Hz,  $J = 7.8$  Hz,  $2\text{H}^{\text{m}}$ ), 2.31-2.17 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 1.92-1.82 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 1.70-1.66 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 140.2, 140.1, 129.2, 128.5, 126.5, 126.4, 116.3, 116.1, 61.2, 61.1, 60.4, 49.7, 41.2, 41.0, 32.7, 32.3, 21.0, 20.7; **IR**

(film)  $\nu_{\max}$  3400, 2980, 2930, 2875, 2204, 1665, 1494, 1453, 1378, 1252, 1051, 1028, 763, 700  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{13}\text{H}_{18}\text{BrN}_2\text{O}$   $[\text{M} + \text{H}]^+$  297.0597; found 297.0598.

**(1S, 2R,S)-(2-Benzylloxy-3-bromo-propyl)-(1-phenyl-ethyl)-cyanamide 44:** white solid;  $R_f = 0.76$  (EtOAc/Pentane 25/75).  $T = -30^\circ\text{C}$   $dr = 70:30$ .  $T = -78^\circ\text{C}$   $dr = 80:20$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 70:30 diastereoisomeric mixture)  $\delta$ : 7.41-7.28 (m,  $10\text{H}^{\text{M}}$  and  $10\text{H}^{\text{m}}$ ), 4.70-4.52 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 4.23-4.16 (q,  $J = 6.9$  Hz,  $1\text{H}^{\text{m}}$ ), 4.14-4.07 (q,  $J = 6.9$  Hz,  $1\text{H}^{\text{M}}$ ), 3.89-3.83 (m,  $1\text{H}^{\text{m}}$ ), 3.82-3.75 (m,  $1\text{H}^{\text{M}}$ ), 3.52-3.37 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.28-3.09 (m,  $2\text{H}^{\text{M}}$ ,  $1\text{H}^{\text{m}}$ ), 3.05-2.98 (dd,  $J = 14.2$ , 7.9 Hz,  $1\text{H}^{\text{m}}$ ), 1.64-1.60 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 140.6, 140.2, 137.2, 137.1, 128.9, 128.6, 128.5, 128.4, 128.4, 128.1, 128.1, 128.0, 126.5, 126.5, 116.4, 116.3, 76.3, 75.5, 72.5, 72.1, 60.7, 60.0, 52.9, 52.1, 31.2, 31.0, 21.1, 21.0; **(1S, 2S)-(2-Benzylloxy-3-bromo-propyl)-(1-phenyl-ethyl)-cyanamide:** From reaction of 400mg, 1.50 mmol of azetidone **20** at  $-30^\circ\text{C}$ . Crystallisation of the crude residue from pentane/EtOAc gave white needles (yield 353 mg, 0.94 mmol, 63%);  $\text{Mp}$ :  $113\text{--}115^\circ\text{C}$ ;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.38-7.29 (m, 10H), 4.68 (d,  $J = 11.5$  Hz, 1H), 4.54 (d,  $J = 11.5$  Hz, 1H), 4.14-4.07 (q,  $J = 6.9$  Hz, 1H), 3.82-3.75 (m, 1H), 3.52-3.37 (m, 2H), 3.21-3.08 (m, 2H), 1.62 (d,  $J = 6.9$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 140.2, 137.1, 128.9, 128.5, 128.4, 128.1, 128.1, 126.5, 116.4, 75.5, 72.1, 60.0, 52.1, 31.2, 21.1; **IR** (film)  $\nu_{\max}$  3274, 3028, 2973, 2931, 2869, 2209, 1693, 1492, 1448, 1434, 1379, 1272, 1183, 1070, 1023, 760, 739, 698, 671  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{19}\text{H}_{22}\text{BrN}_2\text{O}$   $[\text{M} + \text{H}]^+$  373.0910; found 373.0917.  $[\alpha]_{578}^{20}$ : +44 (c 0.5,  $\text{CH}_2\text{Cl}_2$ ).

**(1S, 2R,S)-(2-Benzhydryloxy-3-bromo-propyl)-(1-phenyl-ethyl)-cyanamide 45:** colourless oil;  $R_f = 0.90$  (EtOAc/Pentane 50/50).  $T = -30^\circ\text{C}$   $dr = 70:30$ ;  $T = -78^\circ\text{C}$   $dr = 75:25$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 70:30 diastereoisomeric mixture)  $\delta$ : 7.48-7.23 (m,  $15\text{H}^{\text{M}}$  and  $15\text{H}^{\text{m}}$ ), 5.58 (s,  $1\text{H}^{\text{m}}$ ), 5.56 (s,  $1\text{H}^{\text{M}}$ ), 4.16 (q,  $J = 6.9$  Hz,  $1\text{H}^{\text{m}}$ ), 3.93-3.90 (m,  $1\text{H}^{\text{M}}$ ,  $1\text{H}^{\text{m}}$ ), 3.85-3.78 (m,  $1\text{H}^{\text{M}}$ ), 3.53-3.37 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.30-3.23 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.16-3.06 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 1.58 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 141.6, 141.4, 141.0, 140.9, 140.3, 140.1, 128.9, 128.6, 128.4, 128.1, 128.0, 127.7, 127.6, 127.5, 127.2, 126.8, 126.7, 126.4, 116.6, 116.3, 83.0, 82.4, 74.5, 73.2, 60.6, 59.4, 53.0, 52.3, 31.4, 31.1, 21.1, 21.0; **IR** (film)  $\nu_{\max}$  3028, 2976, 2929, 2869, 2206, 1658, 1493, 1453, 1278, 1061, 1028, 759, 742, 696  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{25}\text{H}_{26}\text{BrN}_2\text{O}$   $[\text{M} + \text{H}]^+$  449.1223; found 449.1224.

**(1S, 2R,S)-(3-Bromo-2-trityloxy-propyl)-(1-phenyl-ethyl)-cyanamide 46:** colourless oil;  $R_f = 0.92$  (EtOAc/Pentane 50/50).  $T = -30^\circ\text{C}$   $dr = 65:35$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 65:35 diastereoisomeric mixture)  $\delta$ : 7.55-7.46 (m,  $5\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 7.41-7.19 (m,  $15\text{H}^{\text{M}}$  and  $15\text{H}^{\text{m}}$ ), 4.01-3.95 (q,  $J = 6.9$  Hz,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.85-3.76 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.20-3.04 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.03-3.00 (m,  $1\text{H}^{\text{m}}$ ), 2.98-2.92 (m,  $1\text{H}^{\text{M}}$ ), 2.81-2.75 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 1.62-1.58 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 143.7, 143.6, 140.5, 140.2, 128.8, 128.7, 128.3, 128.2, 128.0, 127.8, 127.5, 127.2, 126.4, 126.2, 116.1, 88.0, 87.9, 70.5, 69.7, 60.7, 60.1, 51.8, 34.2, 33.3, 21.2, 20.6; **IR** (film)  $\nu_{\max}$  3091, 3058, 3029, 2975, 2932, 2850, 2206, 1691, 1596, 1490, 1447, 1245, 1177, 1085, 1040, 909, 764, 738, 696, 644, 629  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{31}\text{H}_{29}\text{BrN}_2\text{O}_3\text{Na}$   $[\text{M} + \text{Na}]^+$  547.1356; found 547.1367.

**(1S, 2R,S)-(2-Allyloxy-3-bromo-propyl)-(1-phenyl-ethyl)-cyanamide 47:** colourless oil;  $R_f = 0.90$  (EtOAc/Pentane 25/75).  $T = -30^\circ\text{C}$   $dr = 70:30$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 70:30 diastereoisomeric mixture)  $\delta$ : 7.14-7.00 (m,  $5\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 5.74-5.56 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 5.09-4.94 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.98-3.92 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.87-3.71 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.49-3.42 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.24-3.07 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 2.97 (dd,  $J = 14.4$  Hz,  $J = 3.6$  Hz,  $1\text{H}^{\text{m}}$ ), 2.87-2.85 (m,  $2\text{H}^{\text{M}}$ ), 2.71 (dd,  $J = 14.4$  Hz,  $J = 8.1$  Hz,  $1\text{H}^{\text{m}}$ ), 1.40-1.36 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 140.6, 140.2, 133.8, 128.9, 128.4, 126.5, 118.1, 116.3, 76.1, 75.7, 71.3, 71.2, 60.8, 60.2, 52.9, 51.9, 31.3, 31.0, 21.1, 21.0; **IR** (film)  $\nu_{\max}$  3065, 3031, 2977, 2930, 2863, 2206, 1646, 1494, 1455, 1378, 1339, 1378, 1339, 1237, 1070, 995, 925, 763, 733, 700  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{15}\text{H}_{20}\text{BrN}_2\text{O}$   $[\text{M} + \text{H}]^+$  323.0754; found 323.0758.

**(1S, 2R,S)-[3-Bromo-2-(naphthalen-2-ylmethoxy)-propyl]- (1-phenyl-ethyl)-cyanamide 48:** colourless oil;  $R_f = 0.76$  (EtOAc/Pentane 50/50).  $T = -30^\circ\text{C}$   $dr = 70:30$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 70:30 diastereoisomeric mixture)  $\delta$ : 7.93-7.84 (m,  $4\text{H}^{\text{M}}$  and  $4\text{H}^{\text{m}}$ ), 7.58-7.53 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 7.38-7.29 (m,  $5\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 4.89-4.84 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 4.79-4.71 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 4.25-4.19 (m,  $1\text{H}^{\text{m}}$ ), 4.16-4.09 (m,  $1\text{H}^{\text{M}}$ ), 3.97-3.82 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.58-3.42 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.33-3.27 (m,  $1\text{H}^{\text{m}}$ ), 3.25-3.14 (m,  $1\text{H}^{\text{M}}$ ), 3.11-3.04 (m,  $1\text{H}^{\text{m}}$ ), 1.66 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{m}}$ ), 1.62 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{M}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 140.5, 140.1, 134.6, 134.5, 133.0, 128.9, 128.3, 127.9, 127.6, 126.9, 126.8, 126.4, 126.2, 126.1, 125.8, 125.7, 116.4, 116.3, 76.2, 75.8, 72.5, 72.2, 60.7, 59.9, 52.9, 52.1, 31.2, 31.1, 21.1, 21.0; **IR** (film)  $\nu_{\max}$  3056, 3029, 2975, 2927, 2862, 2206, 1602, 1493,

1454, 1335, 1070, 907, 856, 816, 730, 700  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{23}\text{H}_{24}\text{BrN}_2\text{O}$   $[\text{M} + \text{H}]^+$  423.1067; found 423.1074.

**(1S, 2R,S)-[2-(Anthracen-9-ylmethoxy)-3-bromo-propyl]-(1-phenyl-ethyl)-cyanamide 49:** colourless oil;  $R_f = 0.85$  (EtOAc/Pentane 50/50).  $T = -30^\circ\text{C}$   $dr = 60:40$ .  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ , 60:40 diastereoisomeric mixture)  $\delta$ : 8.55-8.41 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 8.10-8.07 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 7.68-7.52 (m,  $4\text{H}^{\text{M}}$  and  $4\text{H}^{\text{m}}$ ), 7.32-7.14 (m,  $4\text{H}^{\text{M}}$  and  $4\text{H}^{\text{m}}$ ), 7.05-7.02 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 5.77-5.65 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 5.61-5.56 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 4.22-4.14 (m,  $1\text{H}^{\text{m}}$ ), 4.02-3.91 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.73 (q,  $J = 6.9$  Hz,  $1\text{H}^{\text{M}}$ ), 3.65-3.48 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.27-3.03 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 1.43 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{m}}$ ), 1.40 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{M}}$ );  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 140.4, 139.8, 131.3, 131.3, 130.9, 129.2, 128.9, 128.8, 128.7, 128.2, 127.3, 126.7, 126.6, 126.3, 125.3, 125.1, 124.0, 116.9, 75.1, 64.4, 63.9, 60.4, 59.5, 53.2, 52.3, 31.4, 31.3, 21.0, 20.7; **IR** (film)  $\nu_{\text{max}}$  3060, 3033, 2979, 2926, 2853, 2206, 1671, 1493, 1180, 1066, 907, 889, 763, 729, 699, 647  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{27}\text{H}_{26}\text{BrN}_2\text{O}$   $[\text{M} + \text{H}]^+$  473.1223; found 473.1232.

**Toluene-4-sulfonic acid 2-bromo-1-[[cyano-((1'S)-phenyl-ethyl)-amino]-methyl]-ethyl ester 50:** colourless oil;  $R_f = 0.78$  (EtOAc/Pentane 50/50).  $T = -30^\circ\text{C}$   $dr = 70:30$ .  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ , 70:30 diastereoisomeric mixture)  $\delta$ : 7.80-7.74 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 7.34-7.17 (m,  $8\text{H}^{\text{M}}$  and  $8\text{H}^{\text{m}}$ ), 4.71-4.64 (m,  $1\text{H}^{\text{m}}$ ), 4.61-4.54 (m,  $1\text{H}^{\text{M}}$ ), 4.06-3.97 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.46-3.35 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.26-3.11 (m,  $2\text{H}^{\text{M}}$ ,  $1\text{H}^{\text{m}}$ ), 3.03 (dd,  $J = 14.7$  Hz,  $J = 7.2$  Hz,  $1\text{H}^{\text{m}}$ ), 2.40 (s,  $3\text{H}^{\text{m}}$ ), 2.39 (s,  $3\text{H}^{\text{M}}$ ), 1.49 (m,  $J = 6.9$  Hz,  $3\text{H}^{\text{M}}$ ), 1.43 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{m}}$ );  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 145.6, 139.7, 132.8, 132.5, 130.1, 130.0, 129.1, 128.6, 128.0, 127.9, 126.4, 115.7, 115.3, 76.2, 60.8, 59.8, 52.0, 51.6, 29.9, 29.6, 21.6, 21.0, 20.8; **IR** (film)  $\nu_{\text{max}}$  3072, 3031, 2983, 2942, 2929, 2210, 1596, 1493, 1454, 1366, 1293, 1190, 1173, 1095, 998, 915, 813, 766, 703, 685, 662  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{19}\text{H}_{21}\text{BrN}_2\text{O}_3\text{SNa}$   $[\text{M} + \text{Na}]^+$  459.0343; found 459.0358.

**Acetic acid 2-bromo-1-[[cyano-((1'S)-phenyl-ethyl)-amino]-methyl]-ethyl ester 51:** colourless oil;  $R_f = 0.73$  (EtOAc/Pentane 25/75).  $T = -30^\circ\text{C}$   $dr = 55:45$ .  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ , 55:45 diastereoisomeric mixture)  $\delta$ : 7.43-7.21 (m,  $5\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 5.30-5.17 (m,  $1\text{H}^{\text{M}}$ ), 5.06-4.99 (m,  $1\text{H}^{\text{m}}$ ), 4.23-4.14 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.53-3.39 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.30-3.09 (m,  $2\text{H}^{\text{M}}$ ,  $2\text{H}^{\text{m}}$ ), 2.16 (s,  $3\text{H}^{\text{M}}$ ), 2.12 (s,  $3\text{H}^{\text{m}}$ ), 1.67 (d,  $J = 7.0$  Hz,  $3\text{H}^{\text{m}}$ ), 1.64 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{M}}$ );  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 170.2, 169.8, 140.0, 129.1, 128.6, 126.5, 126.4, 116.1, 116.0, 70.3, 69.1, 60.8, 59.4, 51.6, 51.5, 30.2, 30.2, 21.3, 20.9, 20.8, 20.8; **IR** (film)  $\nu_{\text{max}}$  3033, 2978, 2939, 2207, 1742, 1494, 1454, 1371, 1220, 1085, 1029, 935, 764, 736, 700  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{14}\text{H}_{17}\text{BrN}_2\text{O}_2\text{Na}$   $[\text{M} + \text{Na}]^+$  347.0366; found 347.0381.

**2,2-Dimethyl-propionic acid 2-bromo-1-[[cyano-((1'S)-phenyl-ethyl)-amino]-methyl]-ethyl ester 52:** colourless oil;  $R_f = 0.85$  (DCM/MeOH 90/10).  $T = -30^\circ\text{C}$   $dr = 60:40$ .  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ , 60:40 diastereoisomeric mixture)  $\delta$ : 7.39-7.33 (m,  $5\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 5.20-5.11 (m,  $1\text{H}^{\text{M}}$ ), 5.04-4.97 (m,  $1\text{H}^{\text{m}}$ ), 4.22-4.14 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.54 (dd,  $J = 11.4$  Hz,  $J = 6.0$  Hz,  $1\text{H}^{\text{m}}$ ), 3.46-3.37 (m,  $2\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.33-3.17 (m,  $1\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.12 (dd,  $J = 14.4$  Hz,  $J = 4.2$  Hz,  $1\text{H}^{\text{M}}$ ), 1.68-1.62 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 1.28 ( $3\text{H}^{\text{M}}$ ), 1.24 (s,  $3\text{H}^{\text{m}}$ );  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 177.7, 177.3, 140.0, 139.9, 129.1, 128.8, 127.1, 126.4, 125.9, 116.1, 115.9, 69.8, 68.5, 60.8, 59.0, 51.9, 51.7, 48.4, 39.0, 38.9, 30.4, 30.3, 27.5, 27.0, 21.6, 21.2, 20.9; **IR** (film)  $\nu_{\text{max}}$  2974, 2933, 2209, 1729, 1479, 1455, 1278, 1139, 1093, 1030, 764, 764, 700  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{17}\text{H}_{24}\text{BrN}_2\text{O}_2$   $[\text{M} + \text{H}]^+$  367.1016; found 367.1019.

**(1S, 2R,S)-(2-Benzyloxy-3-bromo-propyl)-(1-naphthalen-1-yl-ethyl)-cyanamide 53:** yellow oil;  $R_f = 0.80$  (EtOAc/Pentane 50/50).  $T = -30^\circ\text{C}$   $dr = 80:20$ .  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ , 80:20 diastereoisomeric mixture)  $\delta$ : 7.95-7.89 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 7.84 (d,  $J = 8.1$  Hz,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 7.61 (d,  $J = 7.2$  Hz,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 7.54-7.45 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 7.35-7.29 (m,  $5\text{H}^{\text{M}}$  and  $5\text{H}^{\text{m}}$ ), 5.16 (q,  $J = 6.9$  Hz,  $1\text{H}^{\text{m}}$ ), 5.04 (q,  $J = 6.9$  Hz,  $1\text{H}^{\text{M}}$ ), 4.69-4.44 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.91-3.64 (m,  $1\text{H}^{\text{m}}$ ), 3.76-3.68 (m,  $1\text{H}^{\text{M}}$ ), 3.42-3.32 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.26 (dd,  $J = 14.1$  Hz,  $J = 6.6$  Hz,  $1\text{H}^{\text{M}}$ ), 3.13 (dd,  $J = 14.1$  Hz,  $J = 4.2$  Hz,  $1\text{H}^{\text{M}}$ ), 3.00 (dd,  $J = 14.1$  Hz,  $J = 7.8$  Hz,  $1\text{H}^{\text{m}}$ ), 1.77 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 137.2, 137.0, 135.8, 135.3, 133.9, 130.6, 129.1, 128.9, 128.8, 128.5, 128.4, 128.0, 127.9, 126.6, 125.8, 125.4, 123.8, 123.6, 122.2, 116.8, 116.5, 75.6, 72.4, 72.1, 56.9, 56.1, 52.6, 51.7, 31.0, 20.5, 20.3; **IR** (film)  $\nu_{\text{max}}$  3065, 3031, 2980, 2930, 2869, 2205, 1597, 1511, 1496, 1453, 1395, 1377, 1237, 1207, 1168, 1066, 1027, 801, 777, 737, 697  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{23}\text{H}_{24}\text{BrN}_2\text{O}$   $[\text{M} + \text{H}]^+$  423.1067; found 423.1067.

**(1S, 2R,S)-(2-Benzyloxy-3-bromo-propyl)-(1-naphthalen-2-yl-ethyl)-cyanamide 54:** yellow oil;  $R_f = 0.80$  (EtOAc/Pentane 50/50).  $T = -30^\circ\text{C}$   $dr = 75:25$ .  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ , 75:25 diastereoisomeric mixture)  $\delta$ : 7.88-7.77 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 7.71-7.69 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 7.53-7.33 (m,  $8\text{H}^{\text{M}}$  and  $8\text{H}^{\text{m}}$ ), 4.70-4.52 (m,  $2\text{H}^{\text{M}}$  and

2H<sup>m</sup>), 4.37 (q,  $J = 6.6$  Hz, 1H<sup>m</sup>), 4.29 (q,  $J = 7.2$  Hz, 1H<sup>M</sup>), 3.92-3.78 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 3.53-3.36 (m, 2H<sup>M</sup> and 2H<sup>m</sup>), 3.28 (dd,  $J = 14.1$  Hz,  $J = 3.6$  Hz, 1H<sup>m</sup>), 3.19-3.17 (m, 2H<sup>M</sup>), 3.05 (dd,  $J = 14.1$  Hz,  $J = 7.8$  Hz, 1H<sup>m</sup>), 1.72-1.70 (m, 3H<sup>M</sup> and 3H<sup>m</sup>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 137.8, 137.5, 137.2, 137.0, 133.1, 133.0, 129.1, 128.5, 128.1, 128.1, 128.0, 127.8, 127.7, 126.5, 126.3, 125.7, 123.8, 116.5, 116.3, 76.3, 75.6, 72.5, 72.1, 60.8, 60.0, 52.9, 52.0, 31.1, 30.9, 21.1, 21.0; IR (film)  $\nu_{\max}$  3325, 3060, 2980, 2855, 2929, 1679, 1601, 1529, 1453, 1354, 1286, 1191, 1113, 1029, 820, 742, 697 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode)  $m/z$  calculated for C<sub>23</sub>H<sub>24</sub>BrN<sub>2</sub>O [M + H]<sup>+</sup> 423.1067; found 423.1053.

**(1S, 2R,S)-(2-Benzyloxy-3-bromo-propyl)-(1-cyclohexyl-ethyl)-cyanamide 55**: quantitative yield as a white solid;  $R_f = 0.80$  (EtOAc/Pentane 50/50). T = -30°C  $dr = 70:30$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 70:30 diastereoisomeric mixture)  $\delta$ : 7.39-7.30 (m, 5H<sup>M</sup> and 5H<sup>m</sup>), 4.72-4.59 (m, 2H<sup>M</sup> and 2H<sup>m</sup>), 3.90-3.80 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 3.51-3.49 (m, 2H<sup>M</sup> and 2H<sup>m</sup>), 3.36-3.32 (dd,  $J = 7.4$ , 4.6 Hz, 1H<sup>m</sup>), 3.32-3.28 (dd,  $J = 7.4$ , 4.6 Hz, 1H<sup>M</sup>), 3.25-3.14 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 2.77-2.65 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 1.89-1.65 (m, 5H<sup>M</sup> and 5H<sup>m</sup>), 1.56-1.42 (m, 1H<sup>M</sup> and 1H<sup>m</sup>), 1.30-1.08 (m, 6H<sup>M</sup> and 6H<sup>m</sup>), 1.03-0.86 (m, 1H<sup>M</sup> and 1H<sup>m</sup>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 137.1, 128.5, 128.1, 128.0, 128.0, 116.5, 116.5, 76.2, 76.2, 72.4, 72.3, 63.6, 63.2, 53.8, 53.4, 42.0, 41.9, 31.4, 30.1, 30.0, 29.0, 28.9, 26.1, 25.9, 15.9; IR (film)  $\nu_{\max}$  3240, 3072, 3034, 2924, 2852, 2204, 1690, 1601, 1512, 1449, 1266, 1095, 1067, 1026, 892, 739, 711, 698 cm<sup>-1</sup>. HRMS (ESI-TOF positive mode)  $m/z$  calculated for C<sub>19</sub>H<sub>28</sub>BrN<sub>2</sub>O [M + H]<sup>+</sup> 379.1380; found 379.1396.

**(1S, 2R,S)-(3-Bromo-2-(naphthalen-2-ylmethoxy)-propyl)-(1-naphthalen-1-yl-ethyl)-cyanamide 56**: yellow oil;  $R_f = 0.82$  (EtOAc/Pentane 50/50). T = -30°C  $dr = 80:20$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 80:20 diastereoisomeric mixture)  $\delta$ : 7.90-7.73 (m, 7H<sup>M</sup> and 7H<sup>m</sup>), 7.61-7.35 (m, 7H<sup>M</sup> and 7H<sup>m</sup>), 5.19-5.12 (q,  $J = 6.9$  Hz, 1H<sup>m</sup>), 5.05-4.98 (q,  $J = 6.6$  Hz, 1H<sup>M</sup>), 4.85-4.71 (m, 1H<sup>M</sup> and 2H<sup>m</sup>), 4.63-4.59 (d,  $J = 11.6$  Hz, 1H<sup>M</sup>), 3.96-3.88 (m, 1H<sup>m</sup>), 3.79-3.72 (m, 1H<sup>M</sup>), 3.42-3.26 (m, 3H<sup>M</sup> and 3H<sup>m</sup>), 3.19-3.13 (dd,  $J = 14.1$  Hz,  $J = 4.5$  Hz, 1H<sup>M</sup>), 3.08-3.01 (dd,  $J = 14.1$  Hz,  $J = 7.8$  Hz, 1H<sup>m</sup>), 1.74 (d,  $J = 6.9$  Hz, 3H<sup>M</sup> and 3H<sup>m</sup>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 135.8, 135.3, 134.6, 134.5, 133.8, 132.2, 133.0, 129.1, 128.9, 128.8, 128.3, 127.9, 127.6, 126.9, 126.7, 126.6, 126.2, 126.1, 125.9, 125.8, 125.7, 125.4, 123.7, 123.6, 122.1, 116.9, 76.7, 75.5, 72.6, 72.2, 56.9, 56.0, 52.7, 51.8, 31.0, 20.6, 20.3; IR (film)  $\nu_{\max}$  3050, 2977, 2926, 2853, 2206, 1670, 1598, 1437, 1395, 1169, 1068, 801, 777, 750 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode)  $m/z$  calculated for C<sub>26</sub>H<sub>27</sub>BrNO [M - CN + H]<sup>+</sup> 448.1271; found 448.1295.

**(2S)-Acetoxy-phenyl-acetic acid 2-bromo-1-[[cyano-(1'S)-naphthalen-1-yl-ethyl)-amino]-methyl)-ethyl ester 57**: colourless syrup;  $R_f = 0.34$  (*t*-Butyl methyl ether/Pentane 25/75). T = -30°C  $dr = 50:50$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 50:50 diastereoisomeric mixture)  $\delta$ : 8.02 (d,  $J = 8.4$  Hz, 1H<sup>M</sup>), 7.93-7.77 (m, 2H<sup>M</sup>, 3H<sup>m</sup>), 7.65-7.40 (m, 9H<sup>M</sup>, 9H<sup>m</sup>), 5.97 (s, 1H<sup>M</sup>), 5.95 (s, 1H<sup>m</sup>), 5.18-5.02 (m, 2H<sup>M</sup>, 1H<sup>m</sup>), 4.69-4.62 (m, 1H<sup>m</sup>), 3.46-3.23 (m, 3H<sup>M</sup>, 3H<sup>m</sup>), 3.16-3.10 (dd,  $J = 14.6$ , 4.6 Hz, 1H), 3.05-2.98 (dd,  $J = 14.8$ , 7.9 Hz, 1H), 2.24 (s, 3H<sup>M</sup>), 2.23 (s, 3H<sup>m</sup>), 1.76 (d,  $J = 6.9$  Hz, 3H<sup>M</sup>), 1.50 (d,  $J = 6.9$  Hz, 3H<sup>m</sup>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 170.4, 170.3, 168.2, 167.8, 135.5, 135.2, 134.0, 133.9, 133.1, 132.9, 130.5, 130.4, 129.7, 129.4, 129.2, 129.0, 128.8, 127.9, 127.6, 126.9, 126.7, 126.0, 125.9, 125.5, 123.7, 123.5, 122.0, 122.0, 116.4, 115.8, 74.5, 71.7, 70.0, 57.0, 55.6, 51.7, 51.1, 29.8, 29.4, 20.7, 20.6; IR (film)  $\nu_{\max}$  3043, 2983, 29325, 2359, 2337, 2209, 1740, 1511, 1496, 1371, 1227, 1167, 1081, 1049, 955, 802, 778, 733, 695, 648, 605 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode)  $m/z$  calculated for C<sub>26</sub>H<sub>26</sub>BrN<sub>2</sub>O<sub>4</sub> [M + H]<sup>+</sup> 509.1071; found 509.1064.

**(2R)-Acetoxy-phenyl-acetic acid 2-bromo-1-[[cyano-(1'S)-naphthalen-1-yl-ethyl)-amino]-methyl)-ethyl ester 58**: colourless syrup;  $R_f = 0.36$  (*t*-Butyl methyl ether/Pentane 25/75). T = -30°C  $dr = 70:30$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 70:30 diastereoisomeric mixture)  $\delta$ : 8.04 (d,  $J = 8.2$  Hz, 1H<sup>M</sup>), 7.94-7.83 (m, 2H<sup>M</sup>, 3H<sup>m</sup>), 7.65-7.40 (m, 9H<sup>M</sup>, 9H<sup>m</sup>), 5.92 (s, 1H<sup>m</sup>), 5.88 (s, 1H<sup>M</sup>), 5.16-5.08 (m, 2H<sup>M</sup>, 1H<sup>m</sup>), 4.69-4.62 (m, 1H<sup>m</sup>), 3.46-3.15 (m, 4H<sup>M</sup>, 3H<sup>m</sup>), 3.12-3.06 (dd,  $J = 14.6$ , 4.3 Hz, 1H<sup>m</sup>), 2.24 (s, 3H<sup>M</sup>), 2.22 (s, 3H<sup>m</sup>), 1.76 (d,  $J = 6.9$  Hz, 1H), 1.61 (d,  $J = 6.8$  Hz, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 170.6, 170.4, 168.4, 167.8, 135.5, 135.0, 134.0, 132.8, 130.6, 130.5, 129.7, 129.4, 129.2, 129.1, 129.0, 128.8, 127.7, 127.4, 126.9, 126.8, 126.0, 125.6, 125.5, 123.7, 123.6, 122.2, 121.9, 116.2, 74.6, 74.5, 71.6, 70.1, 57.1, 51.5, 50.9, 29.6, 29.5, 20.7, 20.6; IR (film)  $\nu_{\max}$  3043, 2983, 29325, 2359, 2337, 2209, 1740, 1511, 1496, 1371, 1227, 1167, 1081, 1049, 955, 802, 778, 733, 695, 648, 605 cm<sup>-1</sup>; HRMS (ESI-TOF positive mode)  $m/z$  calculated for C<sub>26</sub>H<sub>26</sub>BrN<sub>2</sub>O<sub>4</sub> [M + H]<sup>+</sup> 509.1071; found 509.1064.

**(S)-5-Bromomethyl-3-(1-phenyl-ethyl)-oxazolidin-2-ylideneamine hydrobromide 59a**: T = -30°C  $dr = 75:25$ ; T = -78°C  $dr = 80:20$ . The diastereomer products were separated by column chromatography using a gradient of MeOH/CH<sub>2</sub>Cl<sub>2</sub> 5/95 to 20/80 to afford firstly **diastereomer 1**: 57% yield as a colourless oil;  $R_f = 0.57$  (EtOAc/AcOH/H<sub>2</sub>O/nBuOH 70/10/10/10). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.31-7.19 (m, 5H), 5.25 (q,  $J =$

6.9 Hz, 1H), 4.59-4.47 (m, 3H), 3.46-3.34 (m, 2H), 3.27-3.16 (m, 2H), 1.51 (d,  $J = 6.9$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 159.2, 139.6, 128.6, 127.6, 127.0, 73.4, 51.9, 45.8, 32.5, 15.7; **IR** (film)  $\nu_{\text{max}}$  3338, 3033, 2974, 2934, 2871, 1663, 1485, 1429, 1274, 1162, 1053, 1021, 785, 742, 698, 649  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{12}\text{H}_{16}\text{BrN}_2\text{O}$   $[\text{M}]^+$  283.0441; found 283.0451.  $[\alpha]_{578}^{20}$ : - 74 (c 0.5,  $\text{CH}_2\text{Cl}_2$ ).

**Diastereomer 2:** 29% yield as a colourless oil;  $R_f = 0.49$  (EtOAc/AcOH/ $\text{H}_2\text{O}$ /nBuOH 70/10/10/10).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.40-7.28 (m, 5H), 5.46-5.38 (m, 1H), 5.29-4.92 (m, 2H), 4.82-4.74 (m, 1H), 3.70-3.65 (m, 1H), 3.42 (dd,  $J = 10.5$  Hz,  $J = 4.2$  Hz, 1H), 3.33 (dd,  $J = 10.5$  Hz,  $J = 6.9$  Hz, 1H), 3.06-3.01 (m, 1H), 1.60 (d,  $J = 6.9$  Hz, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 159.3, 139.1, 128.6, 127.8, 127.0, 126.9, 74.3, 52.1, 45.9, 32.1, 16.0; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{12}\text{H}_{16}\text{BrN}_2\text{O}$   $[\text{M}]^+$  283.0441; found 283.0455.  $[\alpha]_{578}^{20}$ : - 132 (c 0.3,  $\text{CH}_2\text{Cl}_2$ ).

**(S)-5-Bromomethyl-3-(1-naphthalen-1-yl-ethyl)-oxazolidin-2-ylideneamine hydrobromide 60a:** yellow oil;  $R_f = 0.55, 0.33$  MeOH/DCM (10/90).  $T = -30^\circ\text{C}$   $dr = 70:30$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 70:30 diastereoisomeric mixture)  $\delta$ : 8.24-8.17 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 7.88-7.82 (m,  $2\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 7.60-7.44 (m,  $4\text{H}^{\text{M}}$  and  $4\text{H}^{\text{m}}$ ), 5.99-5.89 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 4.88 (b,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 4.58-4.51 (m,  $1\text{H}^{\text{m}}$ ), 4.51-4.34 (m,  $1\text{H}^{\text{M}}$ ), 3.51-3.36 (m,  $2\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.23-3.12 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 2.95-2.89 (m,  $1\text{H}^{\text{m}}$ ), 2.82-2.76 (m,  $1\text{H}^{\text{M}}$ ), 2.50-2.46 (m,  $1\text{H}^{\text{m}}$ ), 1.74 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 158.3, 158.1, 135.1, 133.7, 131.7, 131.6, 128.8, 128.6, 126.8, 126.0, 124.8, 123.8, 123.6, 73.6, 73.2, 48.3, 45.9, 45.4, 32.6, 31.9, 14.7, 14.5; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{16}\text{H}_{18}\text{BrN}_2\text{O}$   $[\text{M}]^+$  333.0597; found 333.0605.

**(S)-5-Bromomethyl-3-(1-naphthalen-2-yl-ethyl)-oxazolidin-2-ylideneamine hydrobromide 61a:** yellow oil;  $R_f = 0.54, 0.35$  MeOH/DCM (10/90).  $T = -30^\circ\text{C}$   $dr = 70:30$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 70:30 diastereoisomeric mixture)  $\delta$ : 7.84-7.79 (m,  $4\text{H}^{\text{M}}$  and  $4\text{H}^{\text{m}}$ ), 7.53-7.48 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 5.53-5.47 (m,  $1\text{H}^{\text{M}}$ ,  $1\text{H}^{\text{m}}$ ), 5.08 (b,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 4.71-4.54 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.64-3.61 (m,  $1\text{H}^{\text{m}}$ ), 3.50-3.21 (m,  $4\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 2.97 (m,  $1\text{H}^{\text{m}}$ ), 1.70 (d,  $J = 6.9$  Hz,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 159.2, 137.1, 133.0, 132.7, 128.3, 127.9, 127.4, 126.2, 126.0, 125.6, 125.2, 73.7, 73.4, 51.9, 51.8, 45.8, 45.7, 32.5, 32.2, 15.7, 15.5; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{16}\text{H}_{18}\text{BrN}_2\text{O}$   $[\text{M}]^+$  333.0597; found 333.0612.

#### General procedure for the von Braun reaction of 3-hydroxy azetidines followed by acetylation

To a solution of the required azetidine in chloroform (concentration: 0.2 M) cooled to  $-28^\circ\text{C}$  was added dropwise a 3 M solution of BrCN in  $\text{CH}_2\text{Cl}_2$  (3 equiv). The reaction was monitored by TLC. After completion, triethylamine (3 equiv), acetic anhydride (2 equiv) and DMAP (0.2 equiv) were added at  $-28^\circ\text{C}$  to the reaction mixture. After 16h at  $-28^\circ\text{C}$ , solvent was evaporated under reduced pressure and the diastereomeric ratio was determined using NMR spectroscopy.

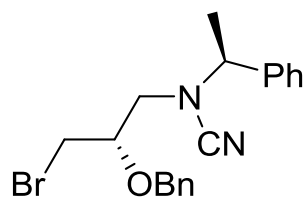
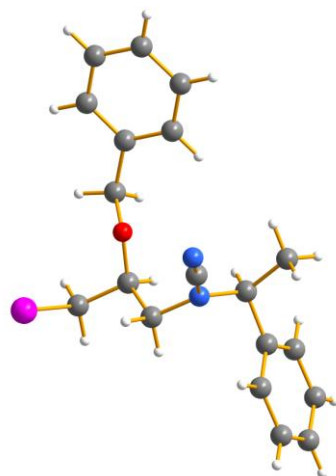
**Acetic acid 2-bromo-1-[[cyano-(1S-phenyl-ethyl)-amino]-methyl]-ethyl ester 51:** colourless oil;  $R_f = 0.74$  (EtOAc/Pentane 25/75).  $T = -30^\circ\text{C}$   $dr = 75:25$ . **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{14}\text{H}_{17}\text{BrN}_2\text{O}_2\text{Na}$   $[\text{M} + \text{Na}]^+$  347.0366; found 347.0361.

**Acetic acid (S)-2-bromo-1-[[cyano-(1-naphthalen-1-yl-ethyl)-amino]-methyl]-ethyl ester 60b:** yellow oil;  $R_f = 0.51$  (EtOAc/Pentane 30/70).  $T = -30^\circ\text{C}$   $dr = 70:30$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 70:30 diastereoisomeric mixture)  $\delta$ : 8.06-8.01 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 7.92 (d,  $J = 8.1$  Hz,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 7.86 (d,  $J = 8.1$  Hz,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 7.65-7.49 (m,  $4\text{H}^{\text{M}}$  and  $4\text{H}^{\text{m}}$ ), 5.22-5.07 (m,  $2\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 5.04-4.97 (m,  $1\text{H}^{\text{m}}$ ), 3.41-3.31 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 3.23-3.08 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 2.11 (s,  $1\text{H}^{\text{M}}$ ), 2.04 (s,  $1\text{H}^{\text{m}}$ ), 1.83-1.78 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 170.1, 169.7, 135.2, 135.0, 133.9, 130.6, 130.5, 129.2, 129.0, 126.8, 125.9, 125.4, 125.3, 123.8, 123.7, 122.0, 116.4, 70.3, 69.1, 57.1, 55.7, 51.4, 50.8, 30.2, 30.1, 20.7, 20.6, 20.1; **IR** (film)  $\nu_{\text{max}}$  3059, 2975, 2936, 2206, 1741, 1686, 1655, 1602, 1509, 1448, 1370, 1223, 1168, 1028, 803, 778  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{18}\text{H}_{19}\text{BrN}_2\text{O}_2\text{Na}$   $[\text{M} + \text{Na}]^+$  397.0523; found 397.0521.

**Acetic acid (S)-2-bromo-1-[[cyano-(1-naphthalen-2-yl-ethyl)-amino]-methyl]-ethyl ester 61b:** colourless oil;  $R_f = 0.65$  (EtOAc/Pentane 30/70).  $T = -30^\circ\text{C}$   $dr = 70:30$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , 70:30 diastereoisomeric mixture)  $\delta$ : 7.91-7.84 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 7.75 (s,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 7.54-7.47 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ ), 5.30-5.23 (m,  $1\text{H}^{\text{M}}$ ), 5.11-5.04 (m,  $1\text{H}^{\text{m}}$ ), 4.41-4.32 (m,  $1\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.54-3.49 (m,  $1\text{H}^{\text{m}}$ ), 3.45-3.38 (m,  $2\text{H}^{\text{M}}$  and  $1\text{H}^{\text{m}}$ ), 3.32-3.26 (m,  $1\text{H}^{\text{M}}$  and  $2\text{H}^{\text{m}}$ ), 3.18-3.11 (dd,  $J = 14.1$  Hz,  $J = 4.5$  Hz,  $1\text{H}^{\text{M}}$ ), 2.16 (s,  $3\text{H}^{\text{M}}$ ), 2.12 (s,  $3\text{H}^{\text{m}}$ ), 1.77-1.71 (m,  $3\text{H}^{\text{M}}$  and  $3\text{H}^{\text{m}}$ );  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 170.1, 169.7, 137.2, 133.2, 133.0, 129.2, 127.8, 127.7, 126.6, 126.4, 125.7, 123.7, 123.6, 116.1, 116.0, 70.2, 69.0, 60.9, 59.4, 51.5, 51.4, 30.2, 21.2, 20.9, 20.8, 20.7; **IR** (film)  $\nu_{\text{max}}$  3053, 2976, 2932, 2206, 174, 1685, 1655, 1602, 1508, 1447, 1370, 1223, 1054, 860,

820, 778, 752  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF positive mode)  $m/z$  calculated for  $\text{C}_{18}\text{H}_{19}\text{BrN}_2\text{O}_2\text{Na}$   $[\text{M} + \text{Na}]^+$  397.0523; found 397.0511.

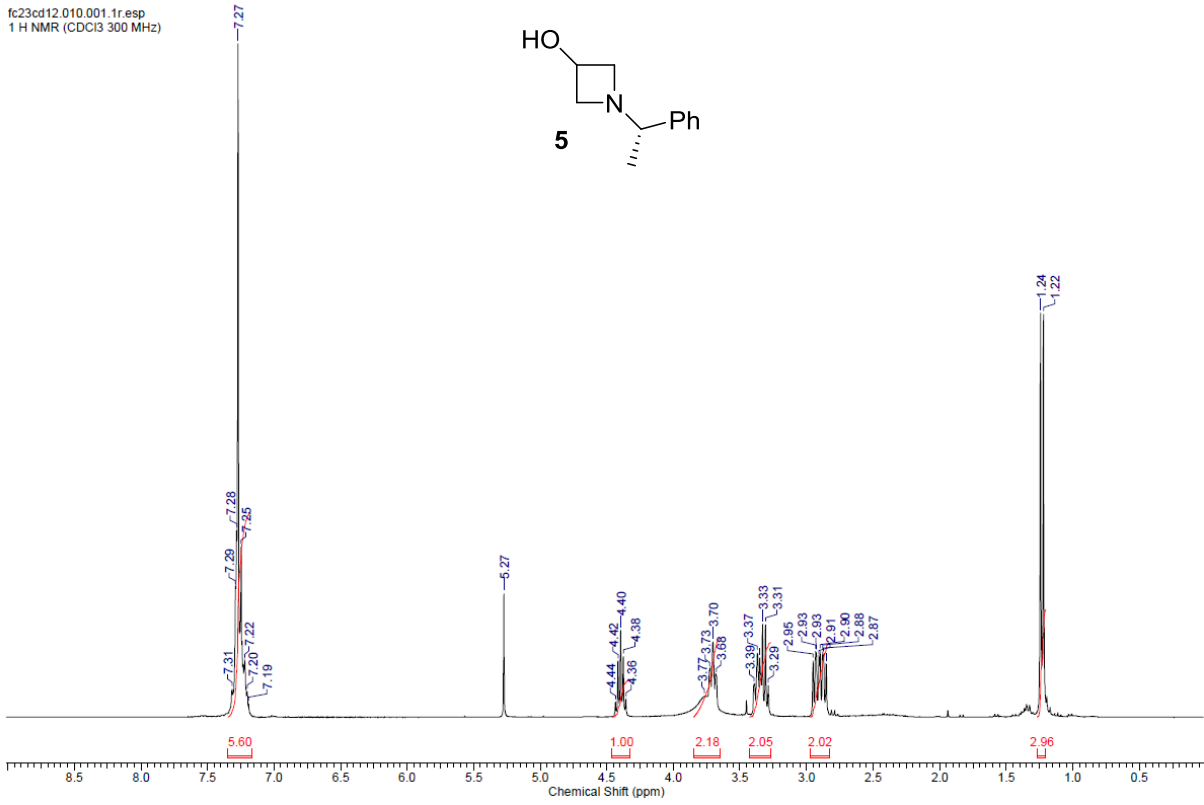
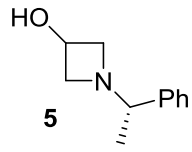
## X-ray structure of (1*S*, 2*S*)-44



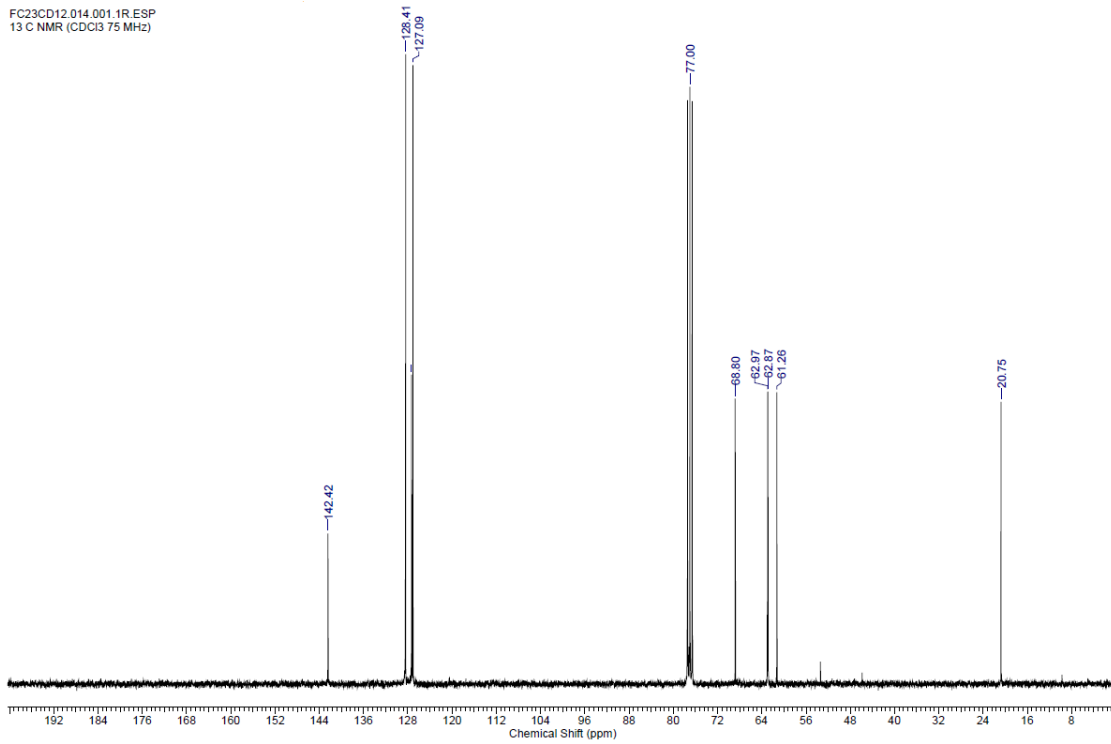
(1*S*, 2*S*)-44

Crystal data	Data collection	Refinement
<p><math>C_{19}H_{21}BrN_2O</math>  <math>M_r = 373.29</math>                      Monoclinic, <math>P2_1</math>  <math>a = 9.3946</math> (4) Å  <math>b = 9.3262</math> (5) Å  <math>c = 10.1302</math> (5) Å  <math>\beta = 93.507</math> (2)°  <math>V = 885.90</math> (7) Å<sup>3</sup>  <math>Z = 2</math>  <math>F(000) = 384</math>  <math>D_x = 1.399</math> Mg m<sup>-3</sup>                      Mo <math>K\alpha</math> radiation, <math>\lambda = 0.71073</math> Å                      Cell parameters from 9828 reflections  <math>\theta = 2.2</math>–<math>30.0</math>°  <math>\mu = 2.33</math> mm<sup>-1</sup>  <math>T = 200</math> K                      Parallelepiped, colorless  <math>0.30 \times 0.14 \times 0.10</math> mm</p>	<p>Bruker D8 VENTURE                      diffractometer                      Radiation source: microsource  <math>\varphi</math> and <math>\omega</math> scans                      Absorption correction: multi-scan                      SADABS (Sheldrick, V2016/2)                      52424 measured reflections                      5162 independent reflections                      4915 reflections with <math>I &gt; 2\sigma(I)</math>  <math>R_{int} = 0.067</math>  <math>\theta_{max} = 30.0</math>°, <math>\theta_{min} = 2.9</math>°  <math>h = -13 \rightarrow 13</math>  <math>k = -13 \rightarrow 13</math>  <math>l = -14 \rightarrow 14</math></p>	<p>Refinement on <math>F_2</math>                      Least-squares matrix: full  <math>R[F_2 &gt; 2\sigma(F_2)] = 0.024</math>  <math>wR(F_2) = 0.060</math>  <math>S = 1.05</math>                      5162 reflections                      209 parameters                      1 restraint                      Hydrogen site location: inferred from                      neighbouring sites                      H-atom parameters constrained  <math>w = 1/[\sigma_2(F_o2) + (0.0251P)_2 +</math>  <math>0.1347P]</math> where <math>P = (F_o2 + 2F_c2)/3</math>  <math>(\Delta/\sigma)_{max} = 0.002</math>  <math>\Delta\rho_{max} = 0.29</math> e Å<sup>-3</sup>  <math>\Delta\rho_{min} = -0.27</math> e Å<sup>-3</sup>                      Absolute structure: Flack <math>x</math> determined                      using 2180                      quotients <math>[(I^+)-(I^-)]/[(I^+)+(I^-)]</math>                      (Parsons, Flack and                      Wagner, Acta Cryst. B69 (2013) 249-                      259).                      Absolute structure parameter: <math>-0.005</math>                      (2)</p>

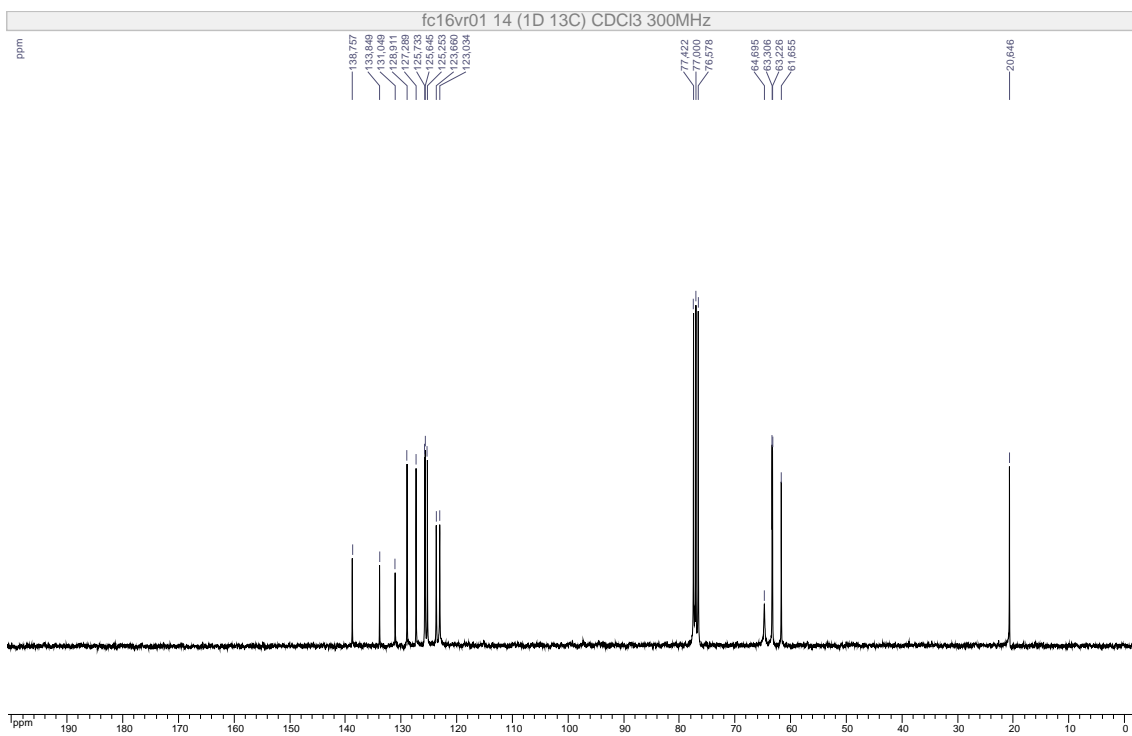
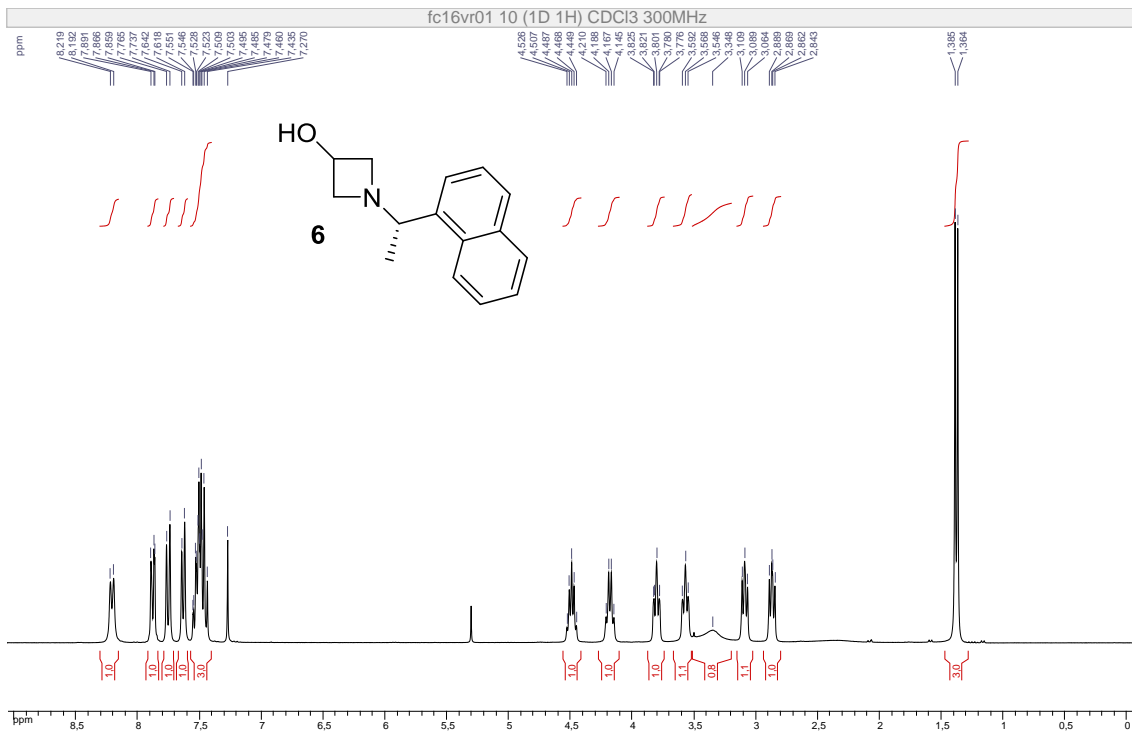
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1 H NMR (CDCl3 300 MHz)

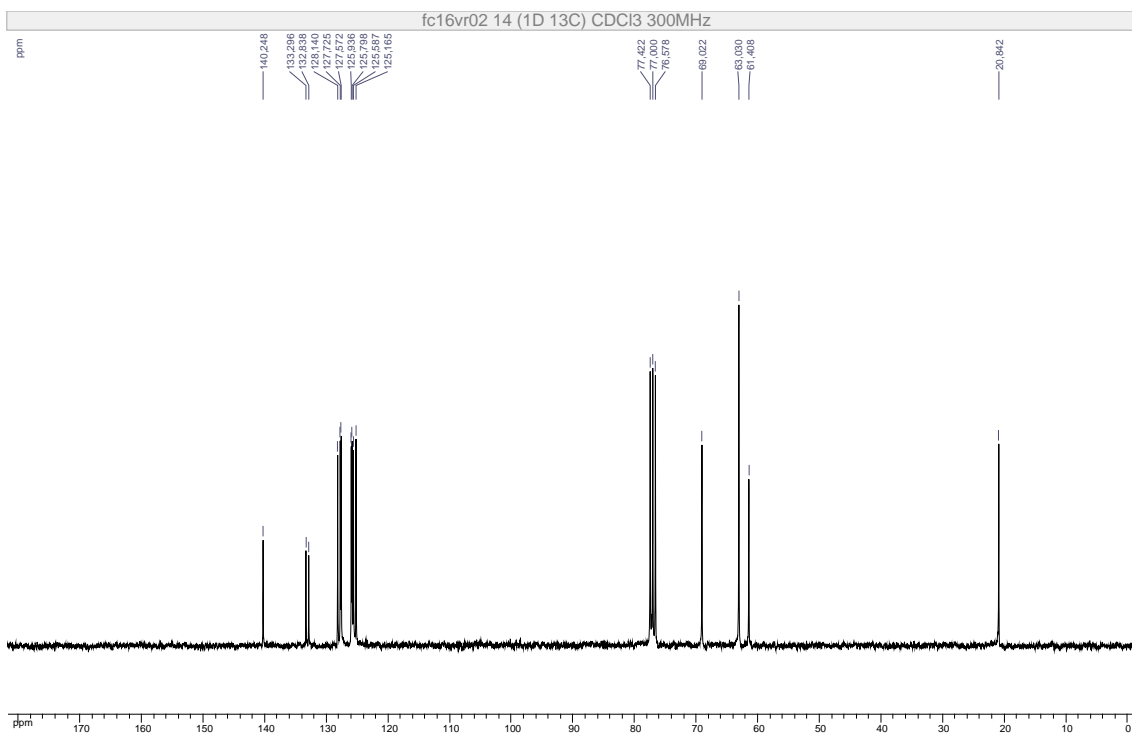
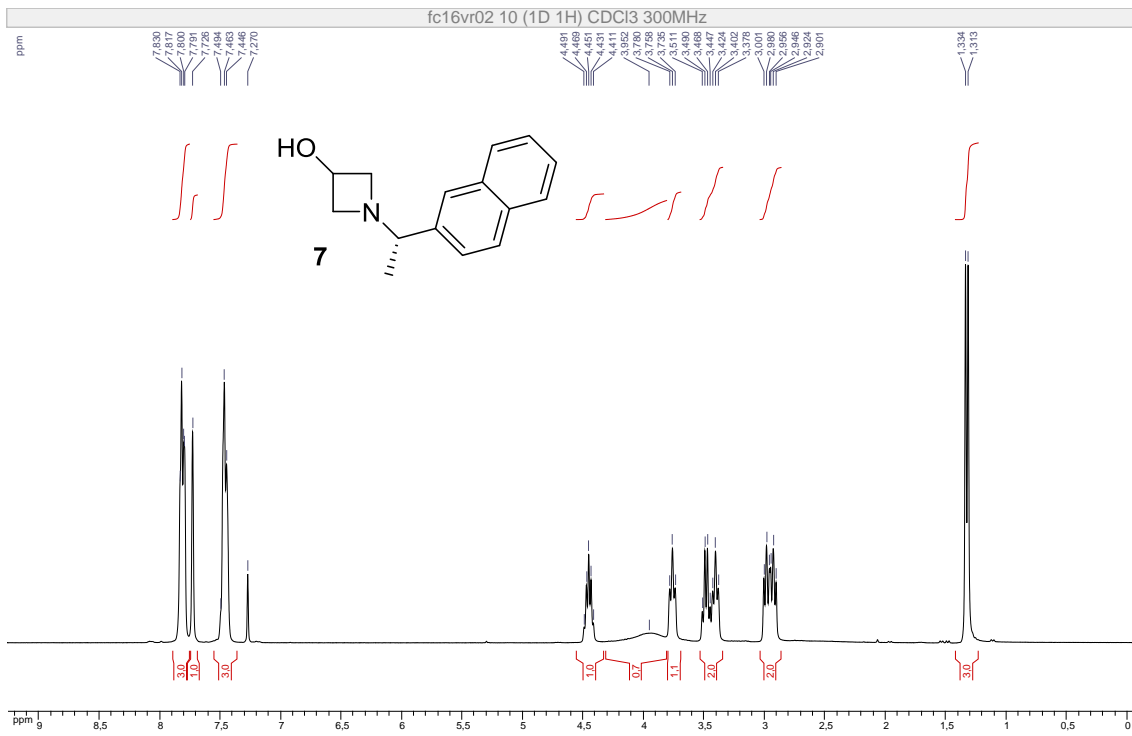


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13 C NMR (CDCl3 75 MHz)

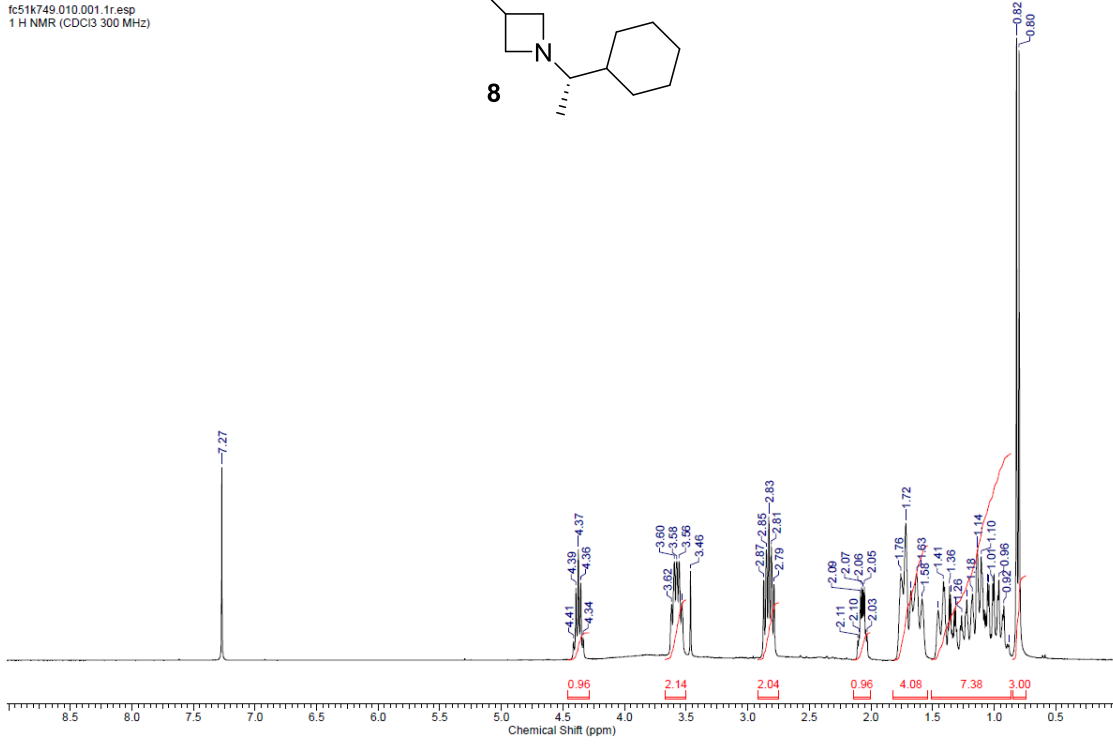
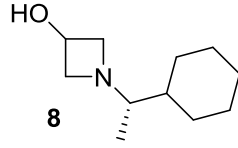




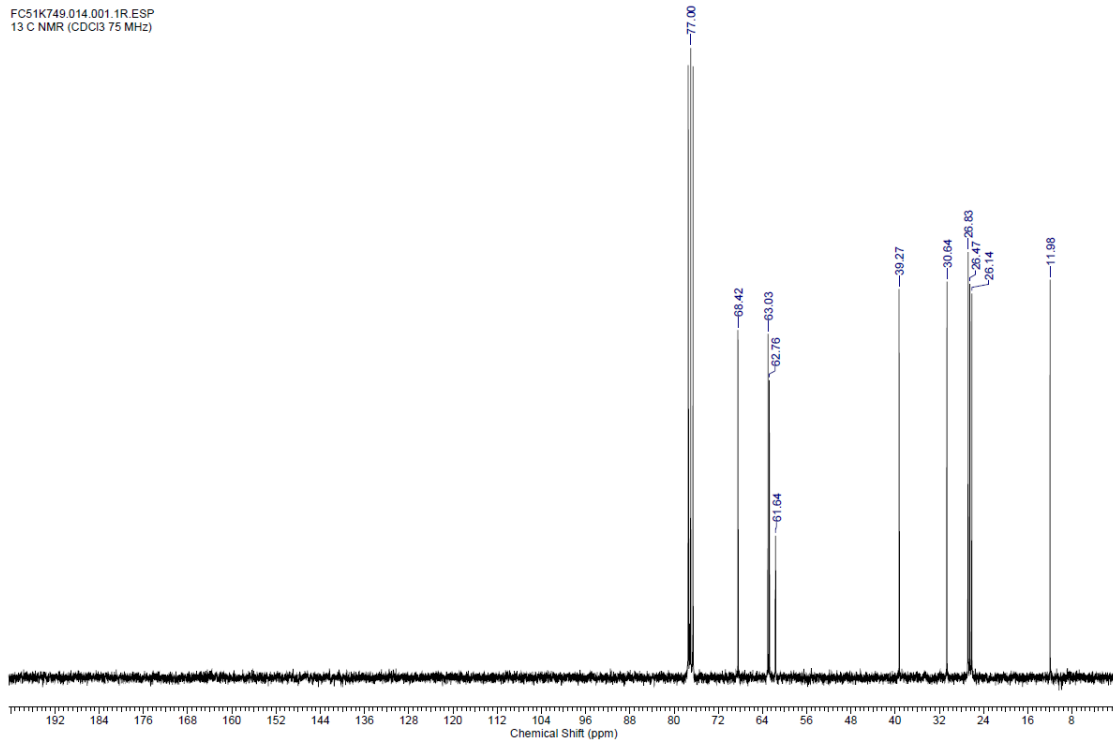




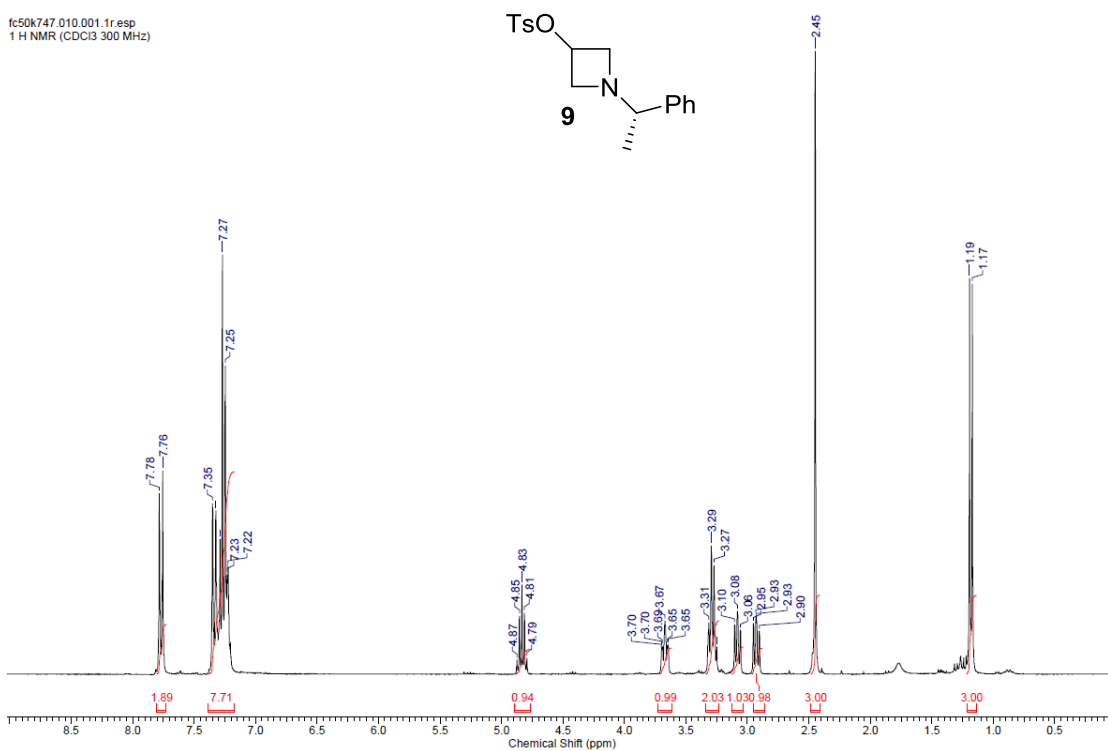
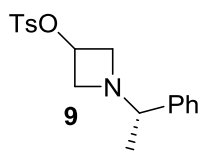
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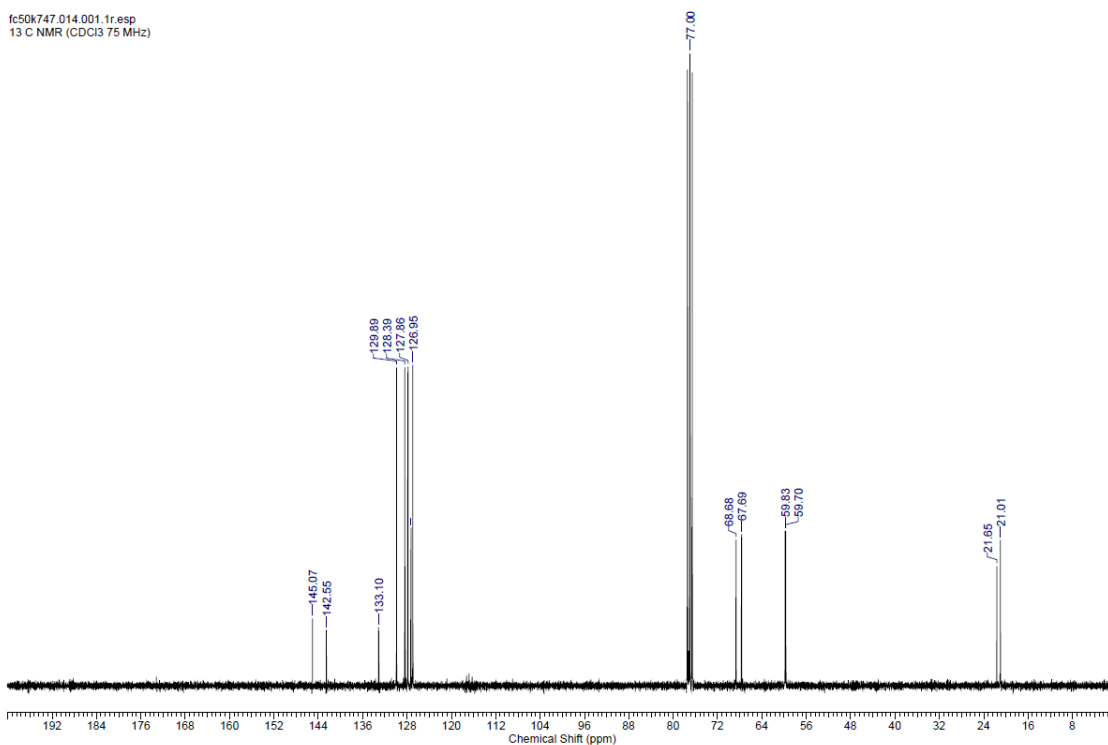
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13 C NMR (CDCl3 75 MHz)



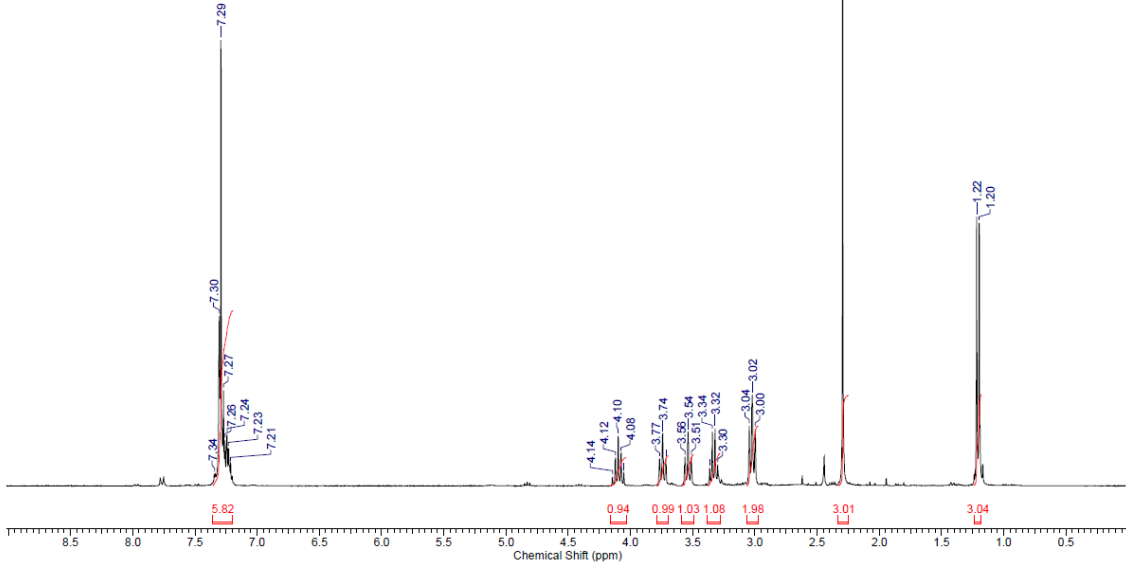
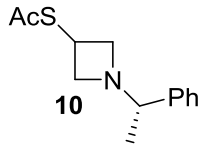
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1H NMR (CDCl3 300 MHz)



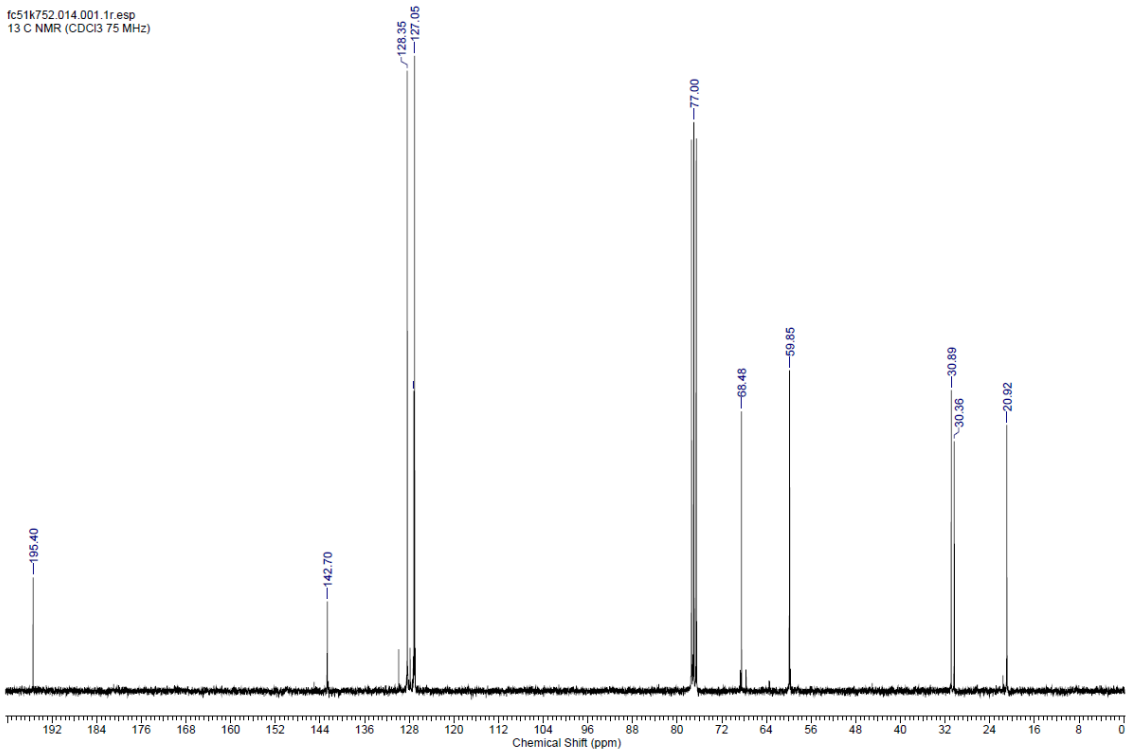
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13C NMR (CDCl3 75 MHz)



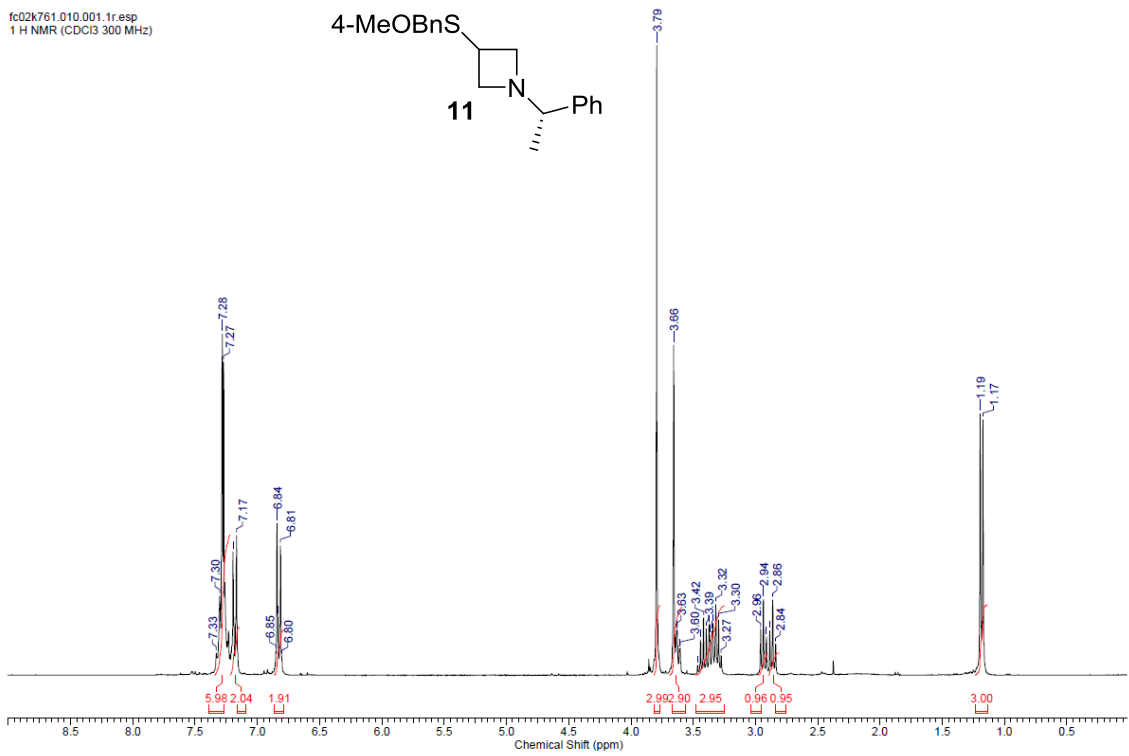
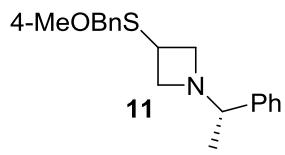
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1 H NMR (CDCl3 300 MHz)



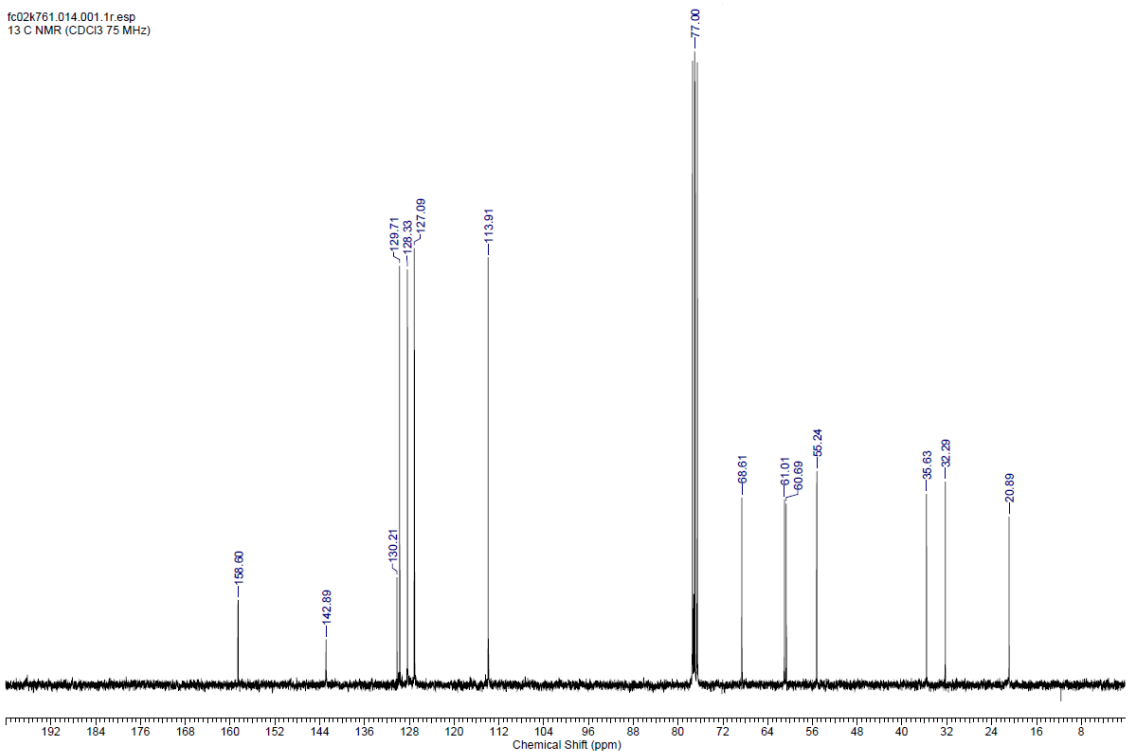
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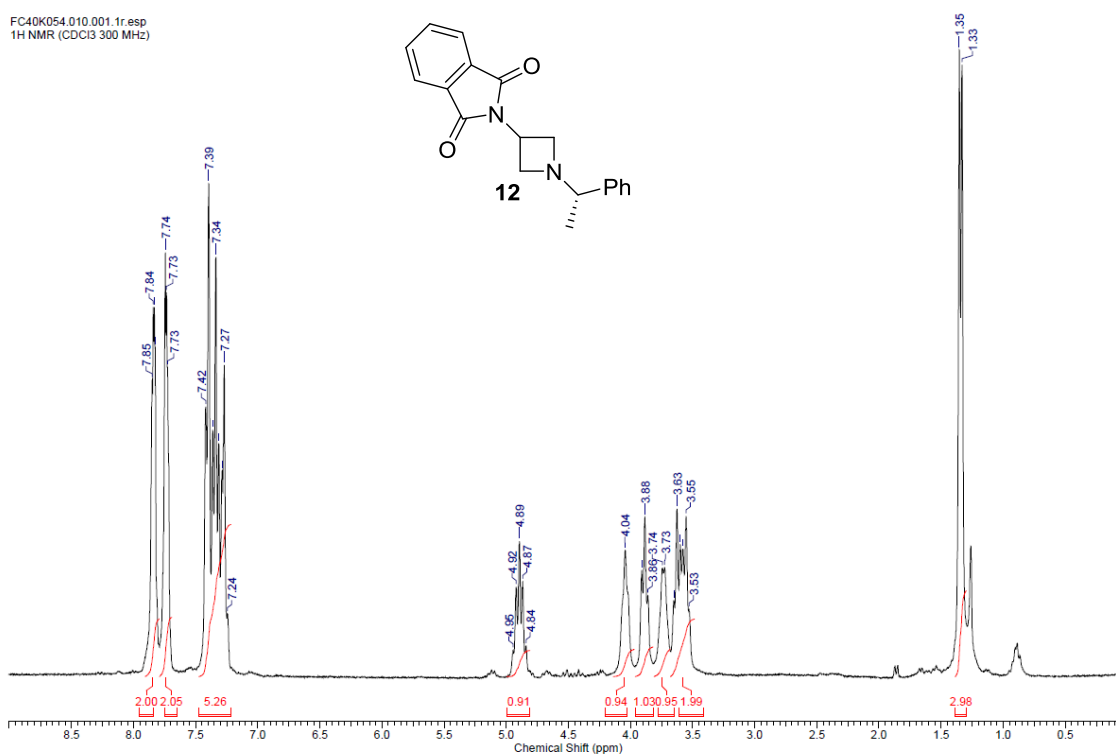
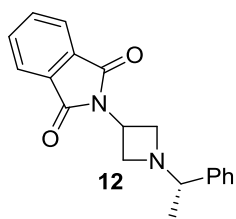
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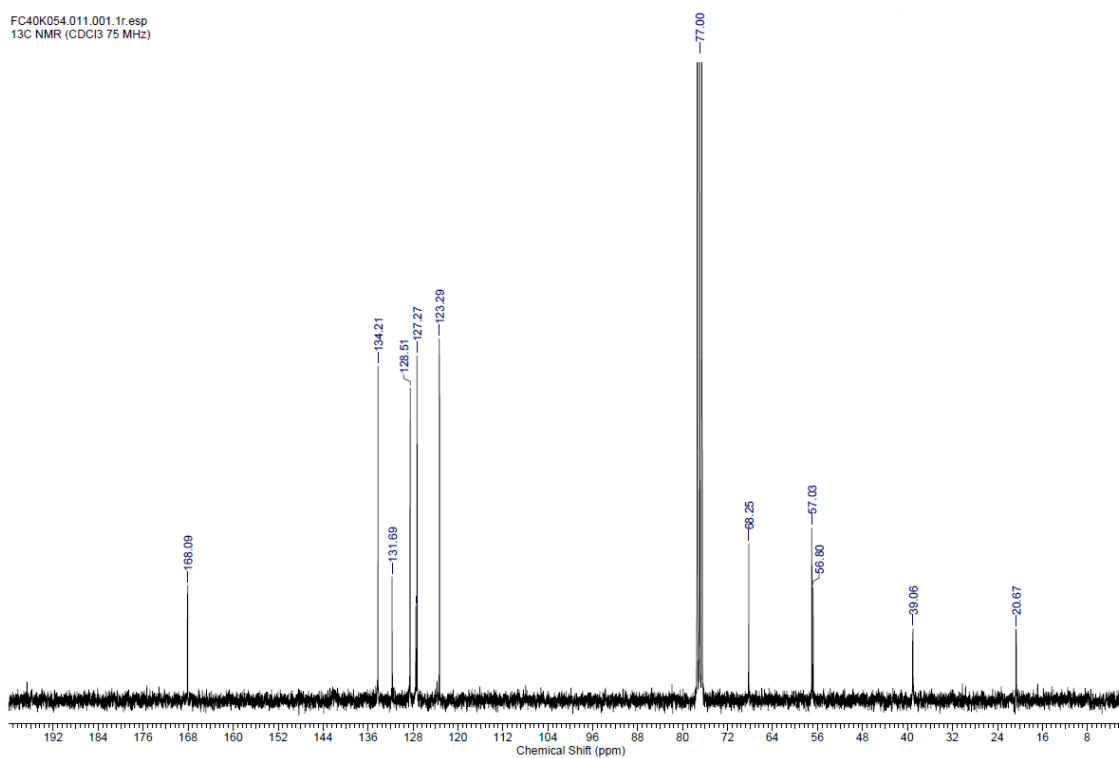
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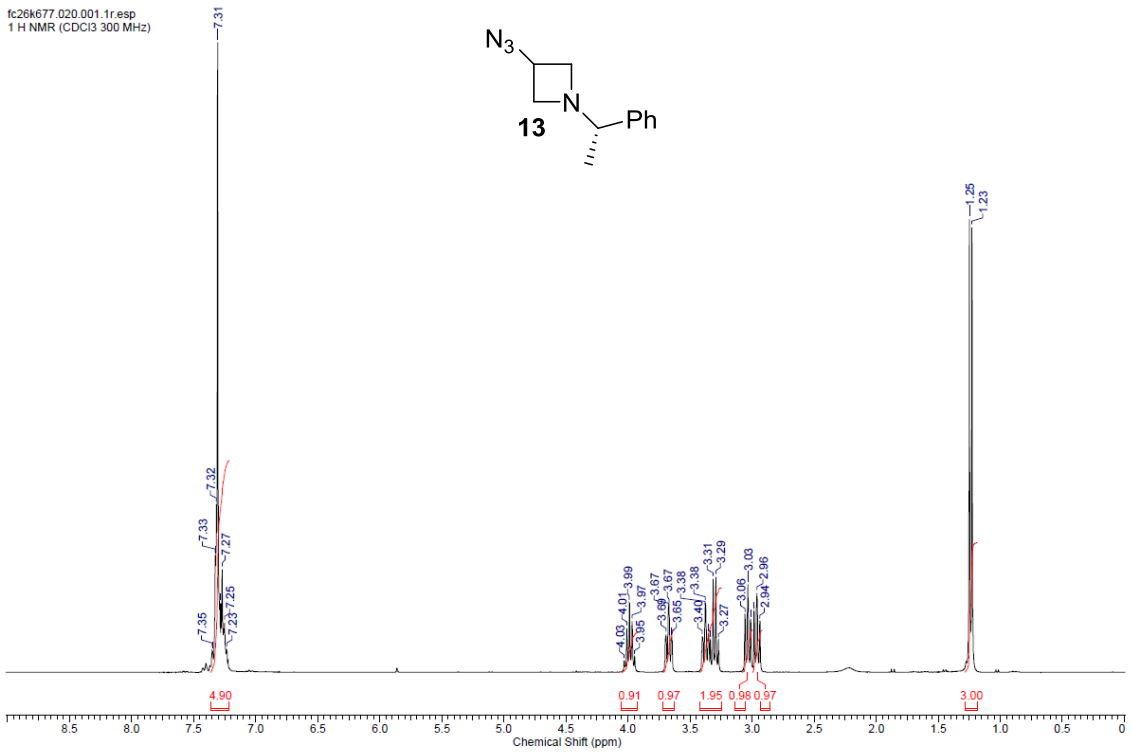
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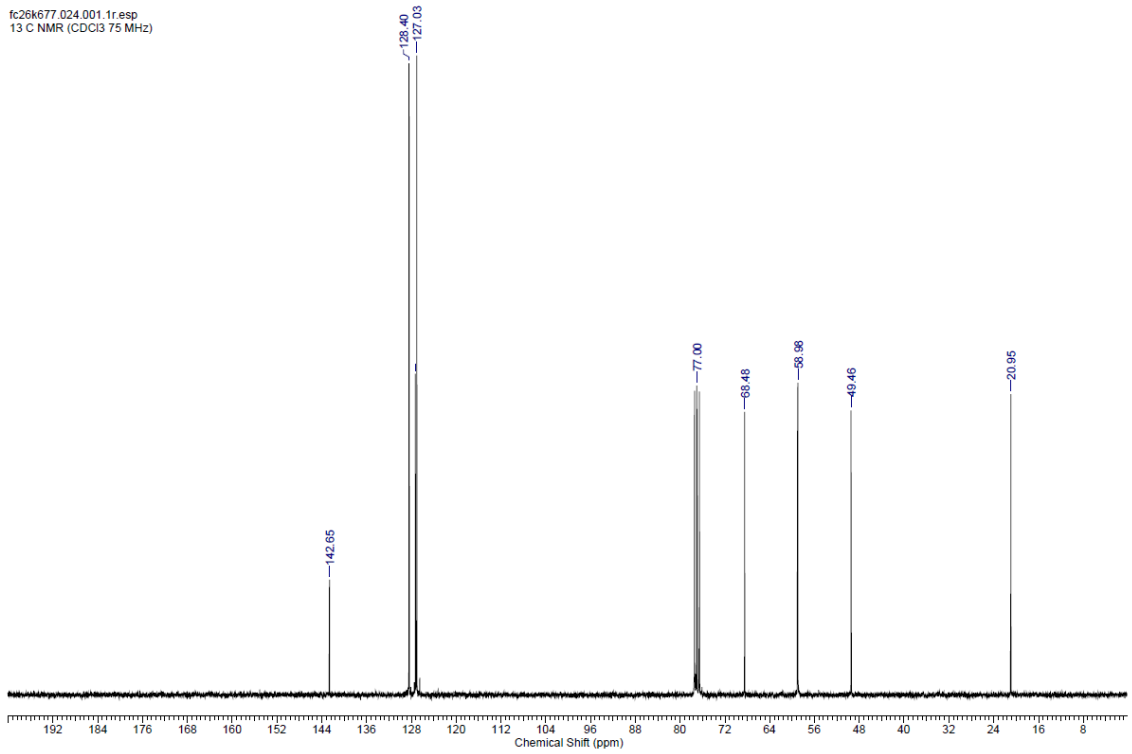
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13C NMR (CDCl3 75 MHz)



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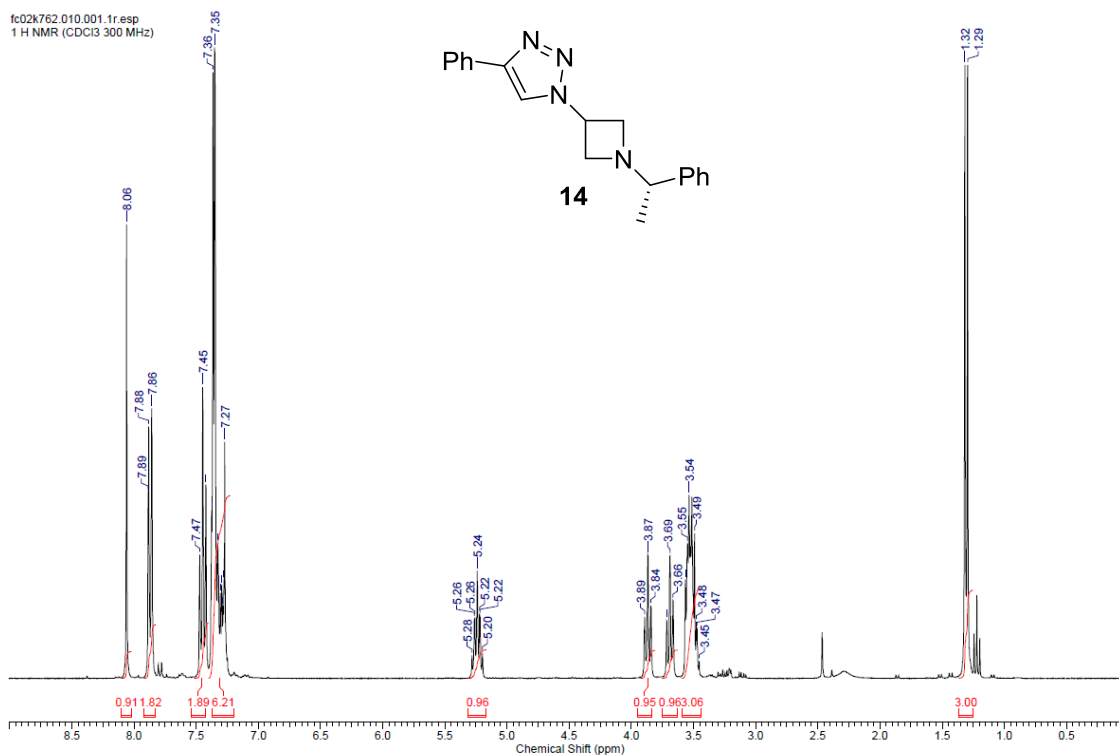


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13 C NMR (CDCl3 75 MHz)

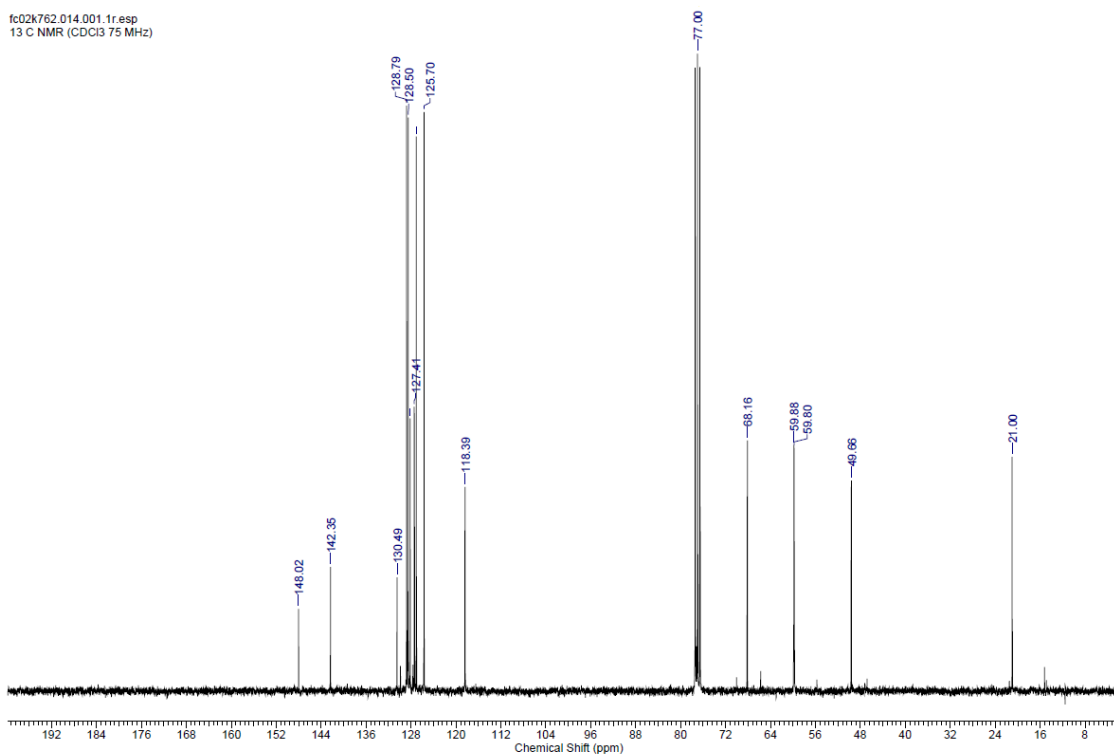




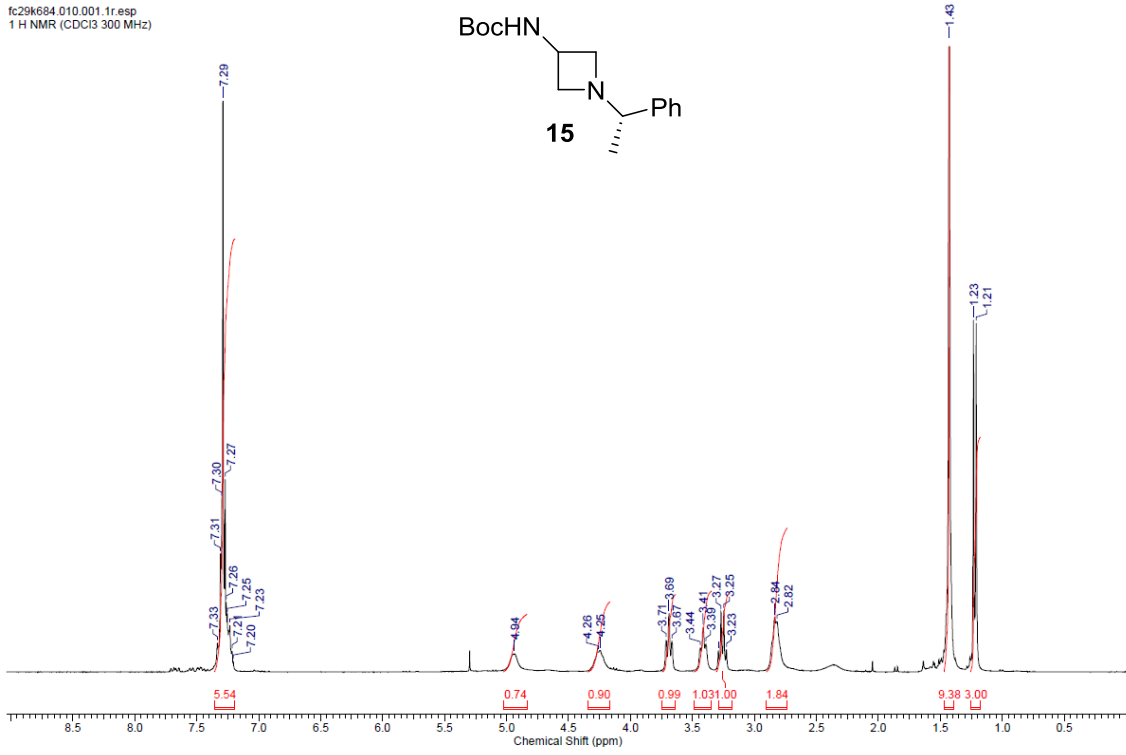
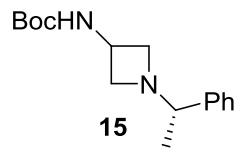
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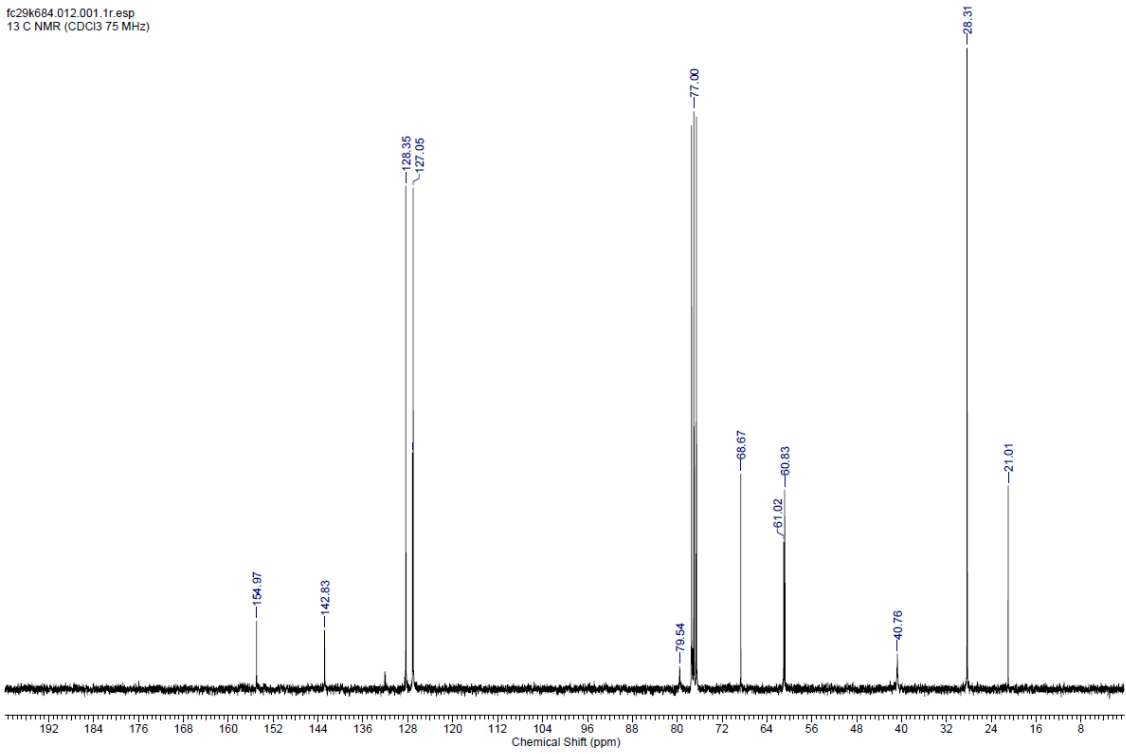
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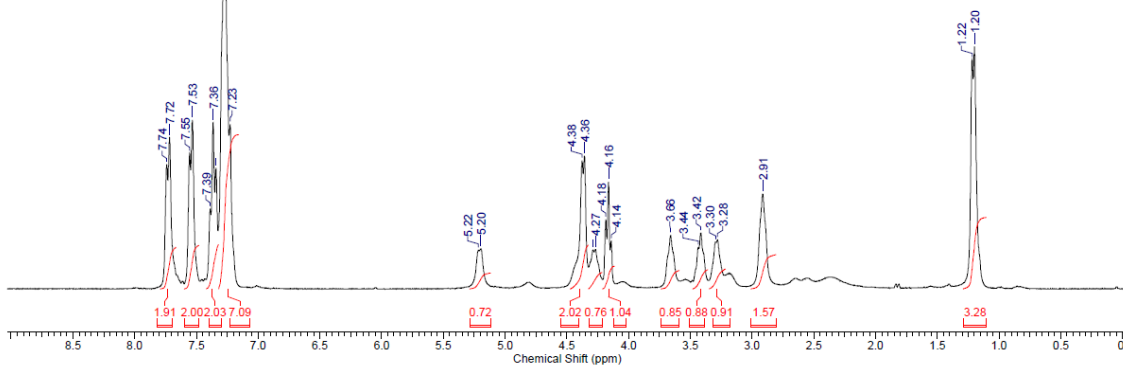
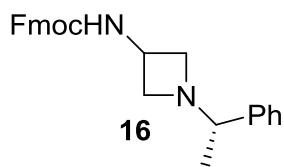
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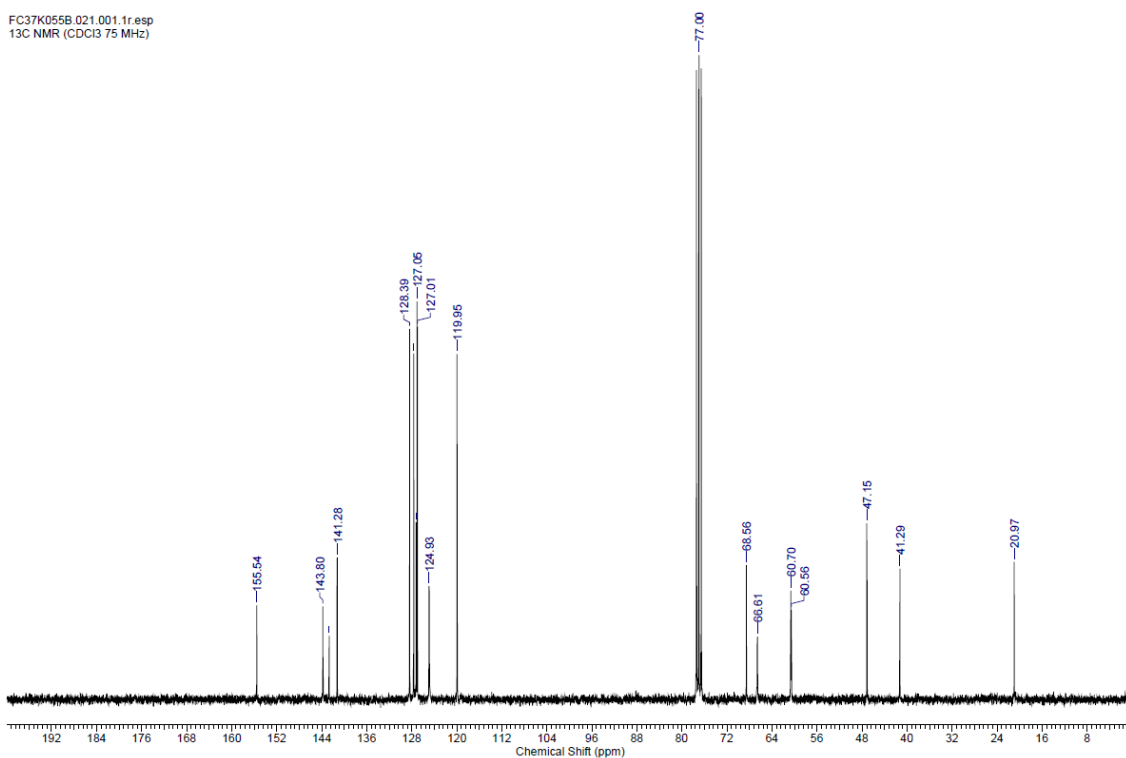
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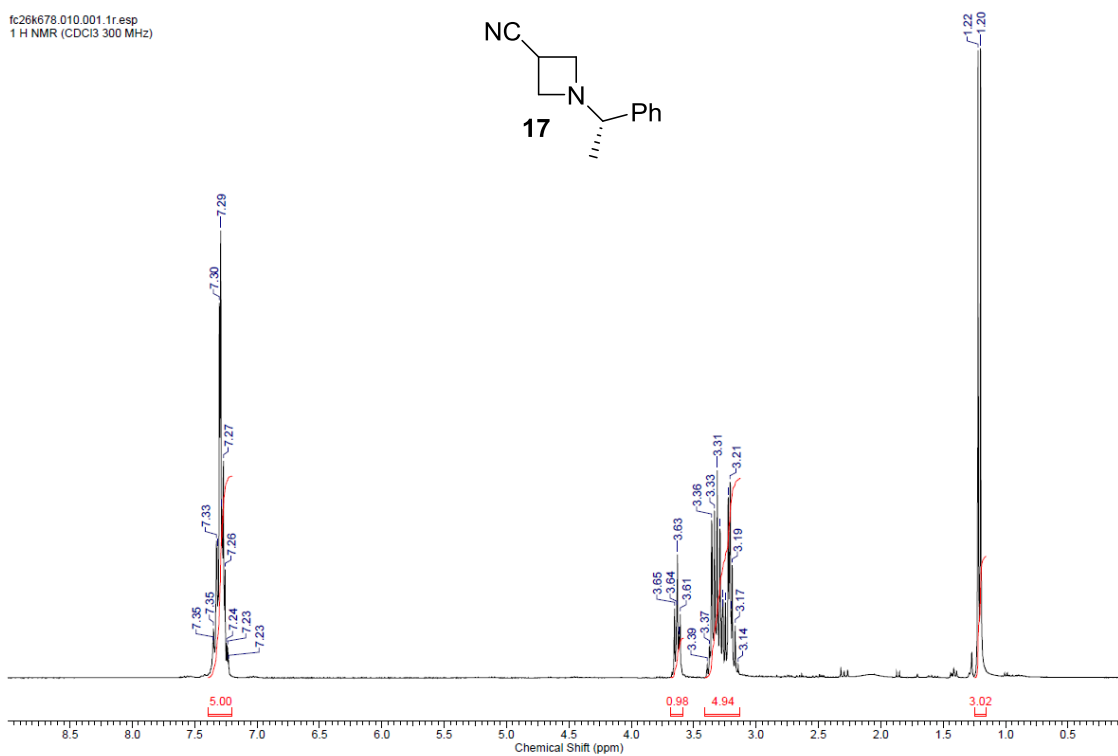
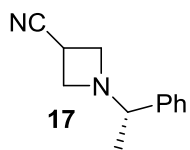
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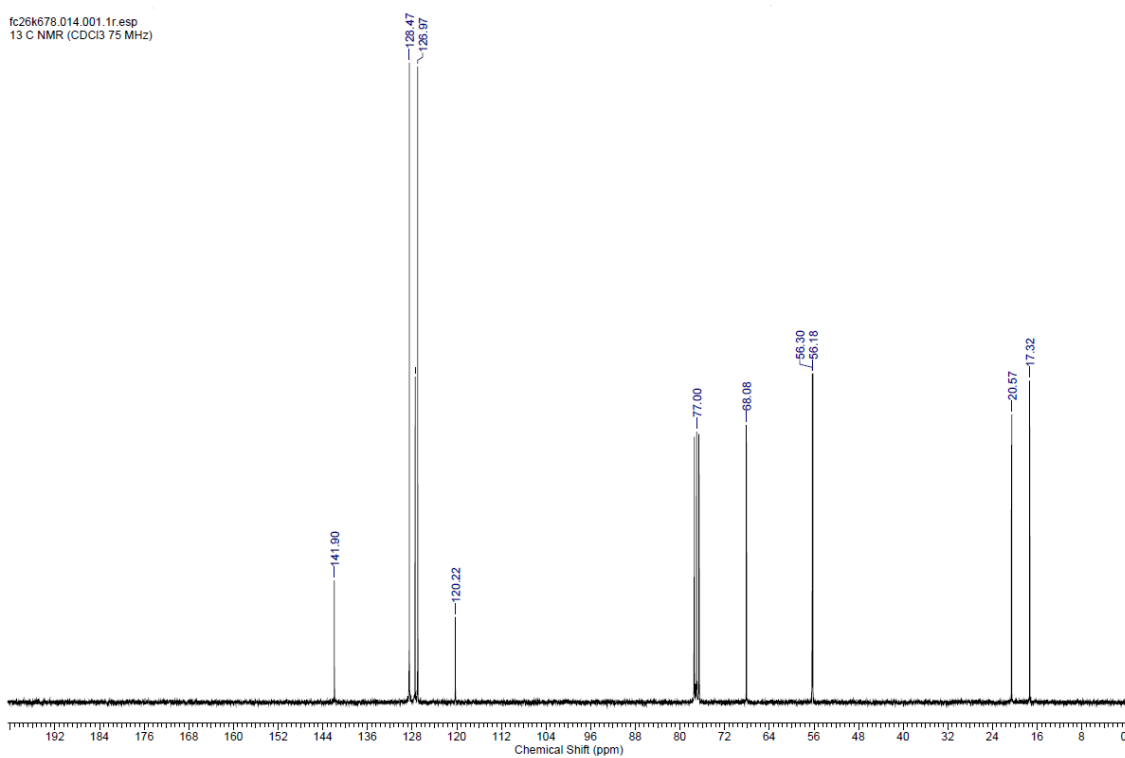
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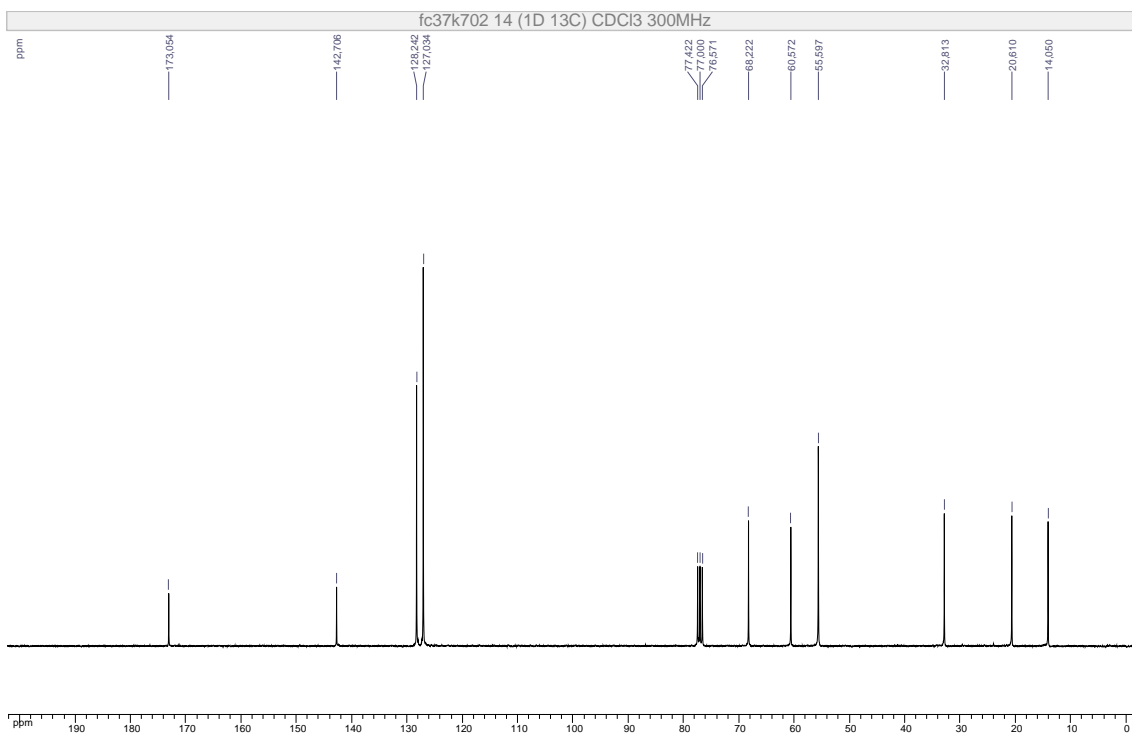
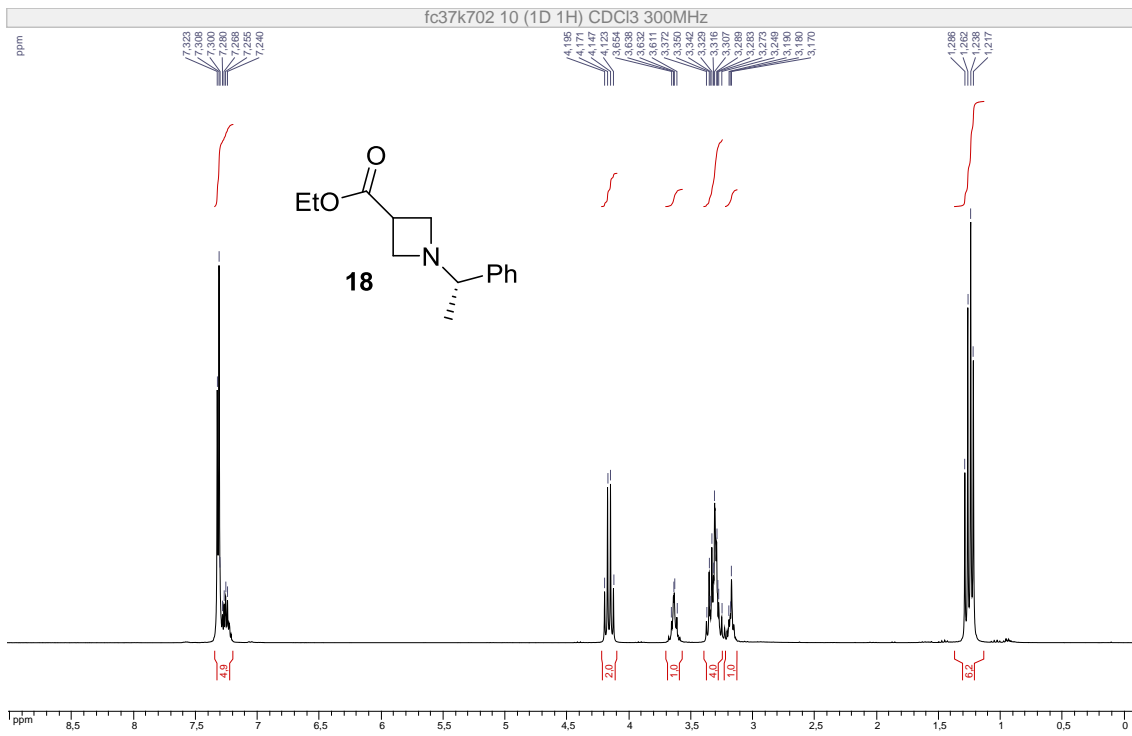


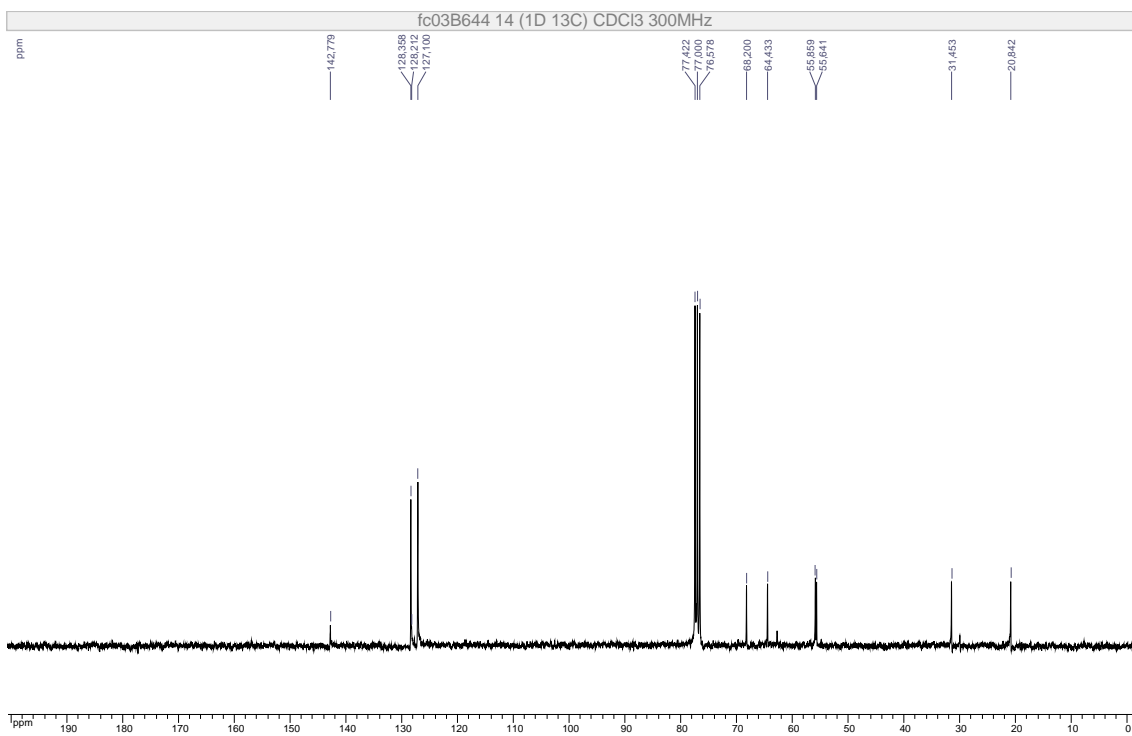
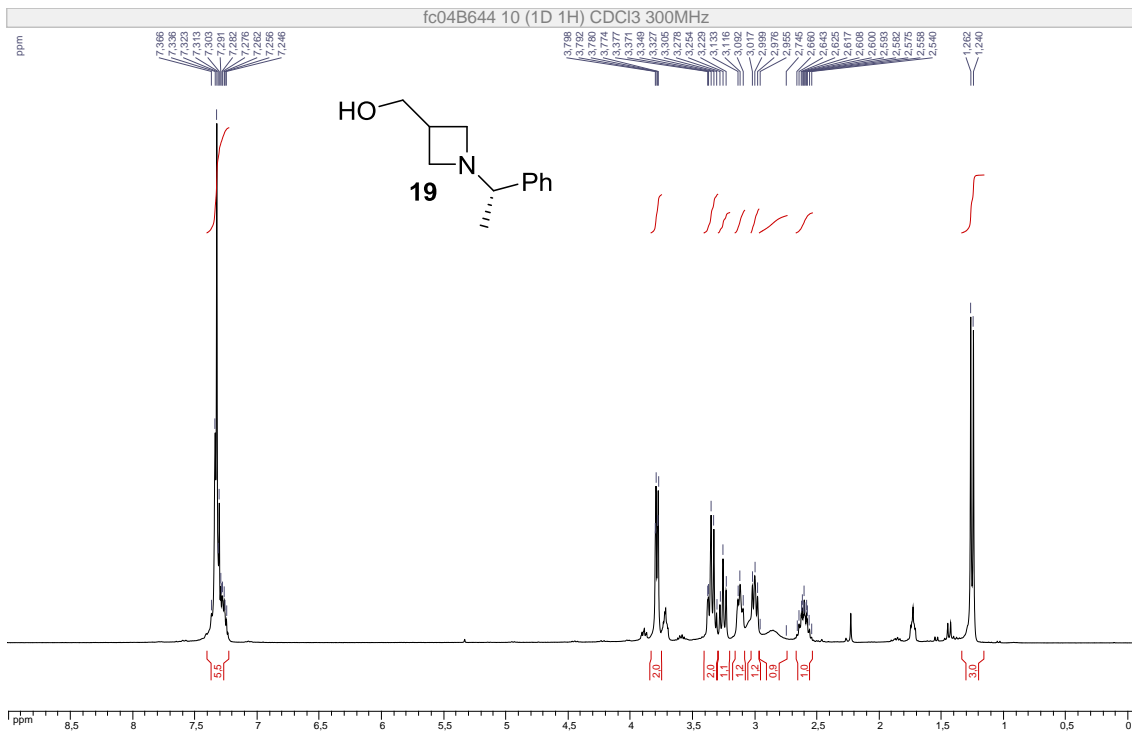
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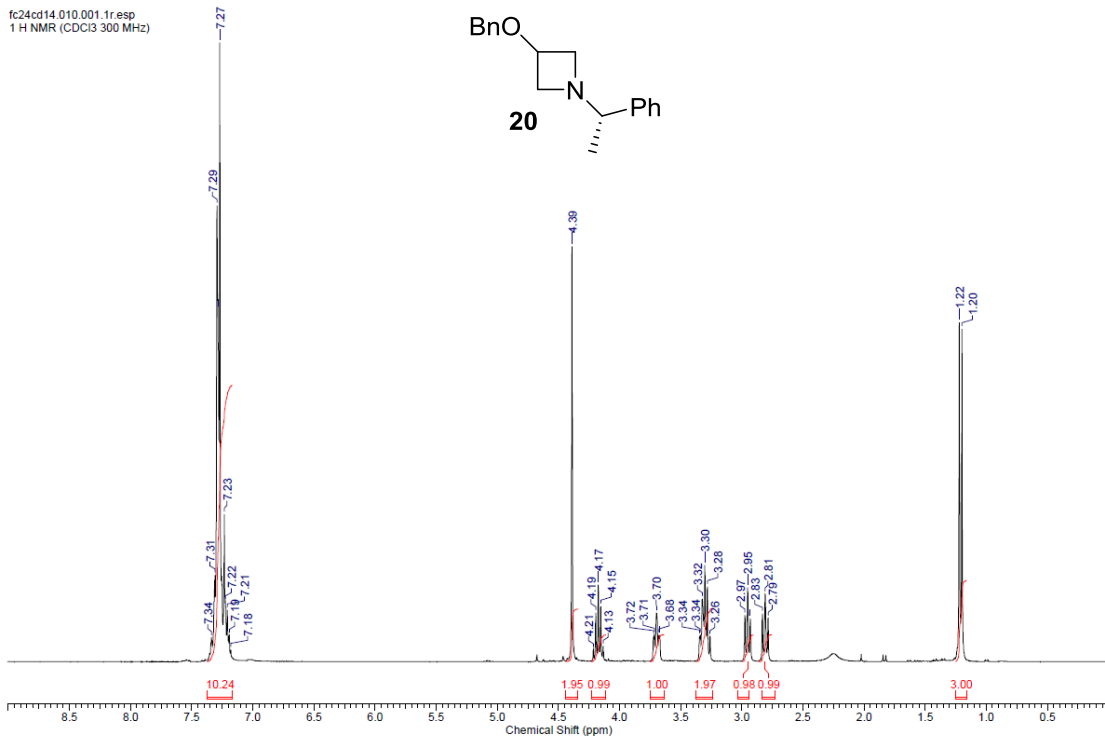
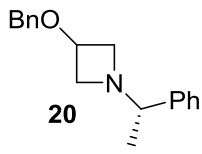
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13 C NMR (CDCl3 75 MHz)



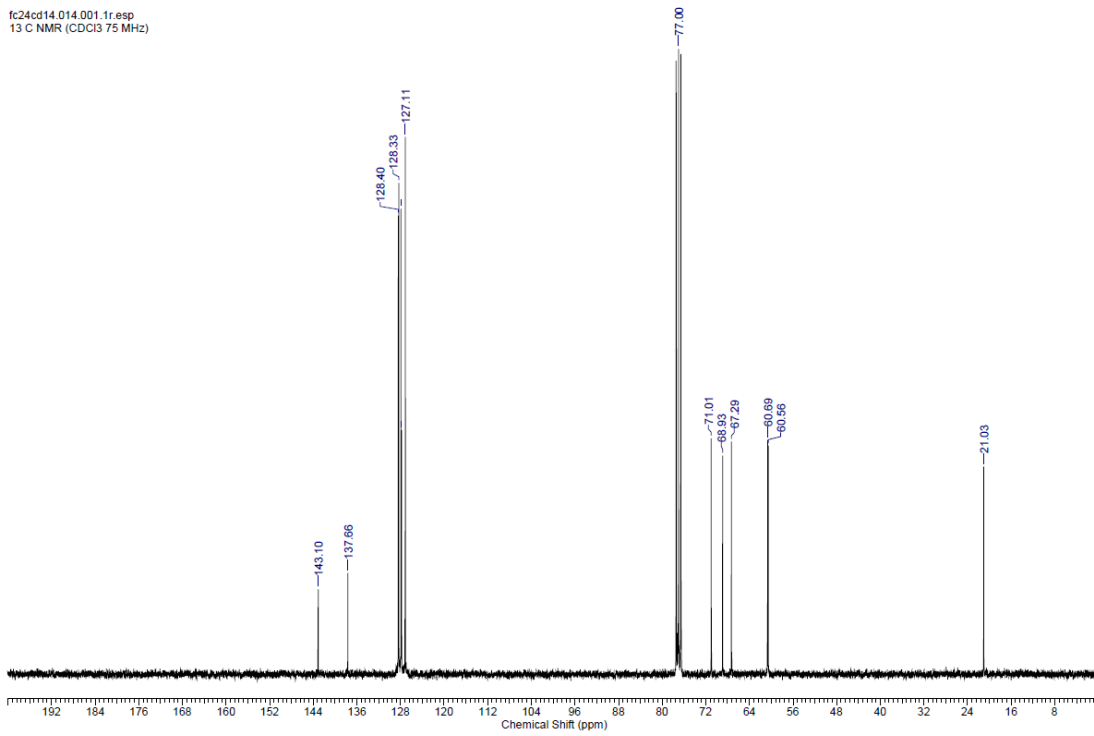


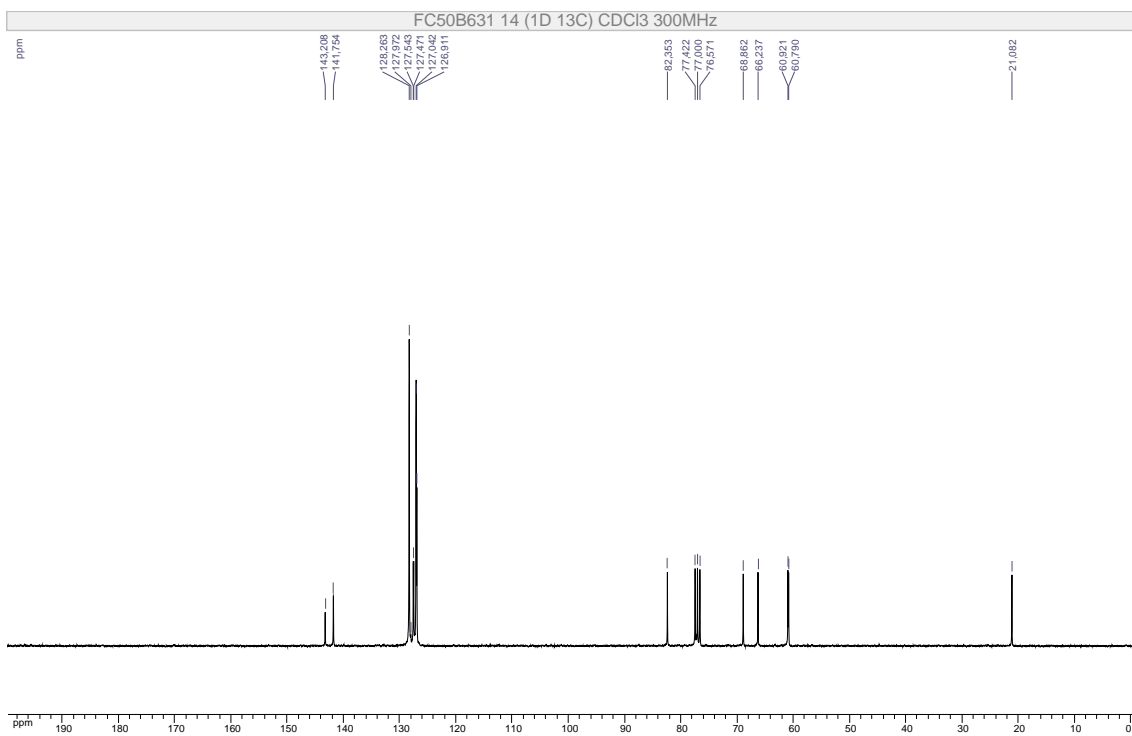
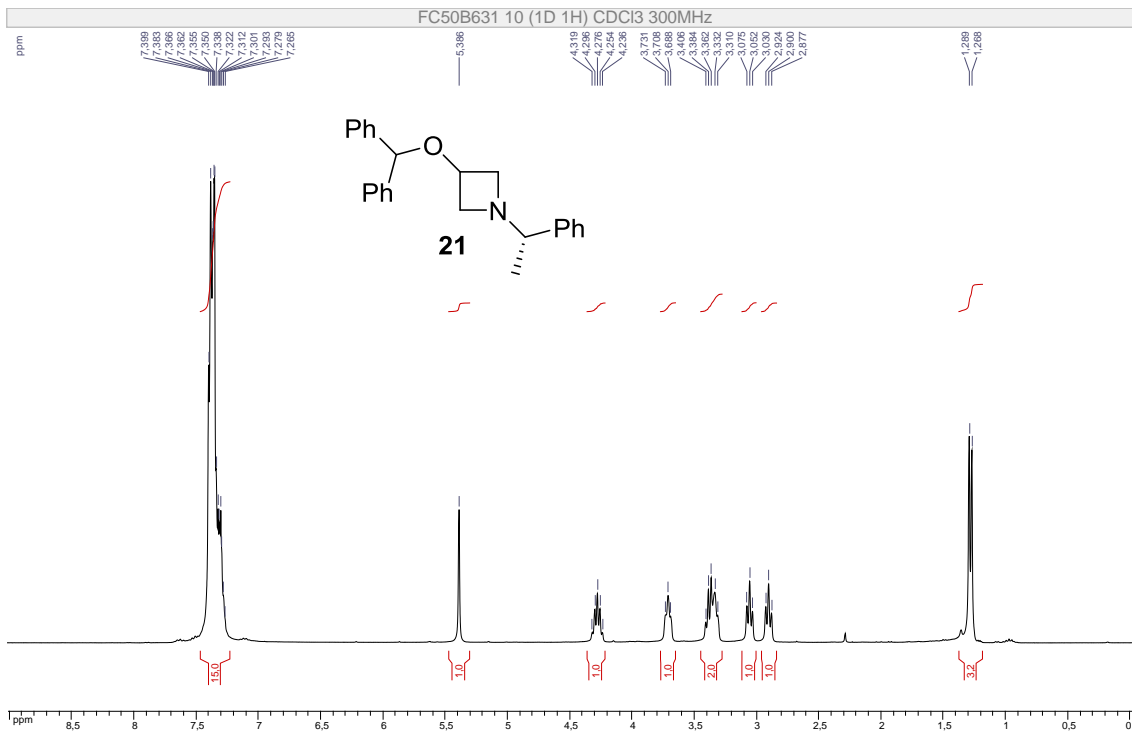


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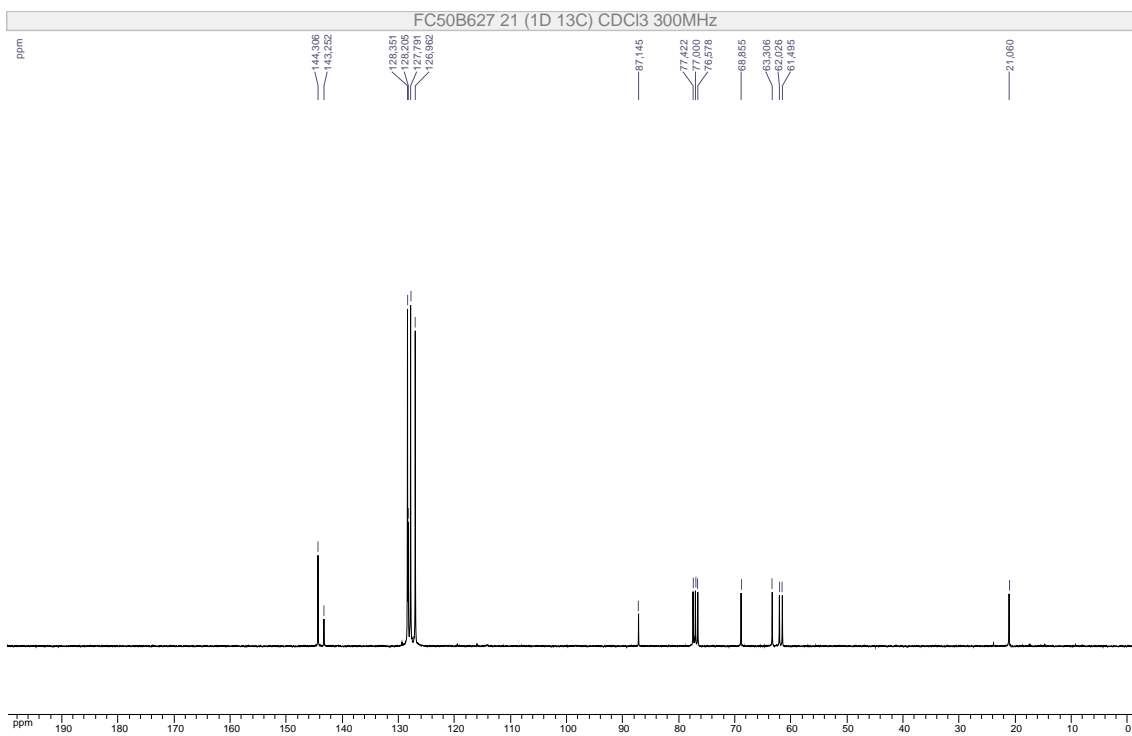
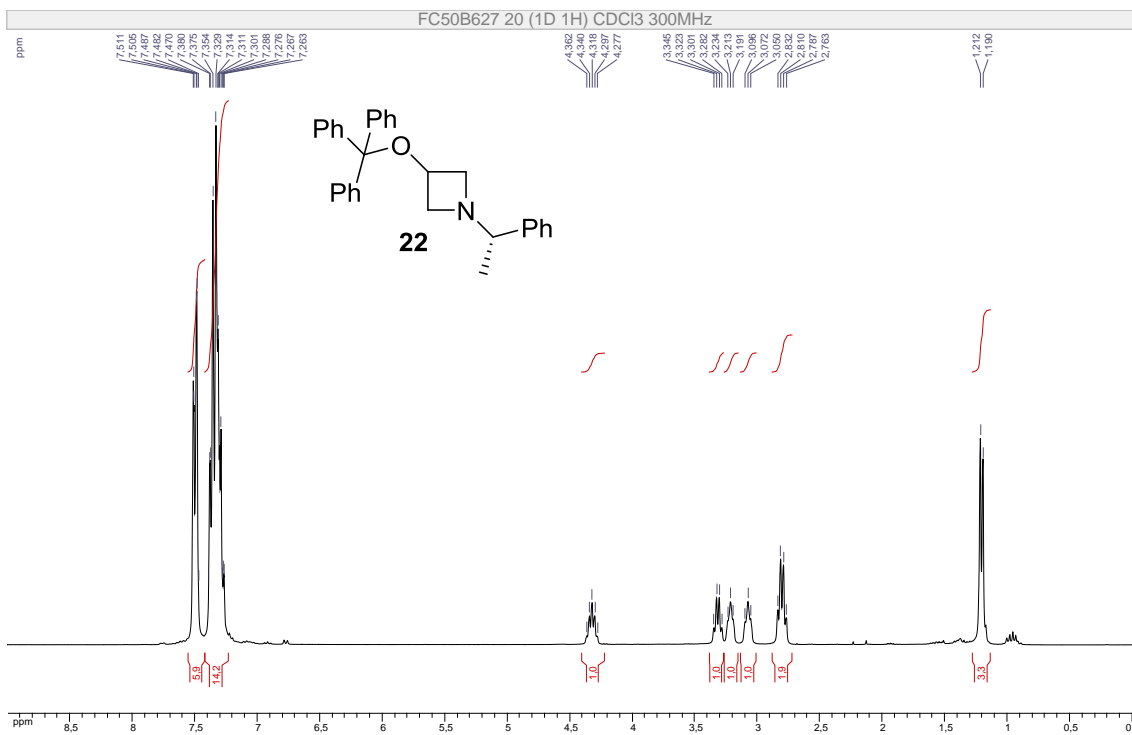


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13 C NMR (CDCl3 75 MHz)

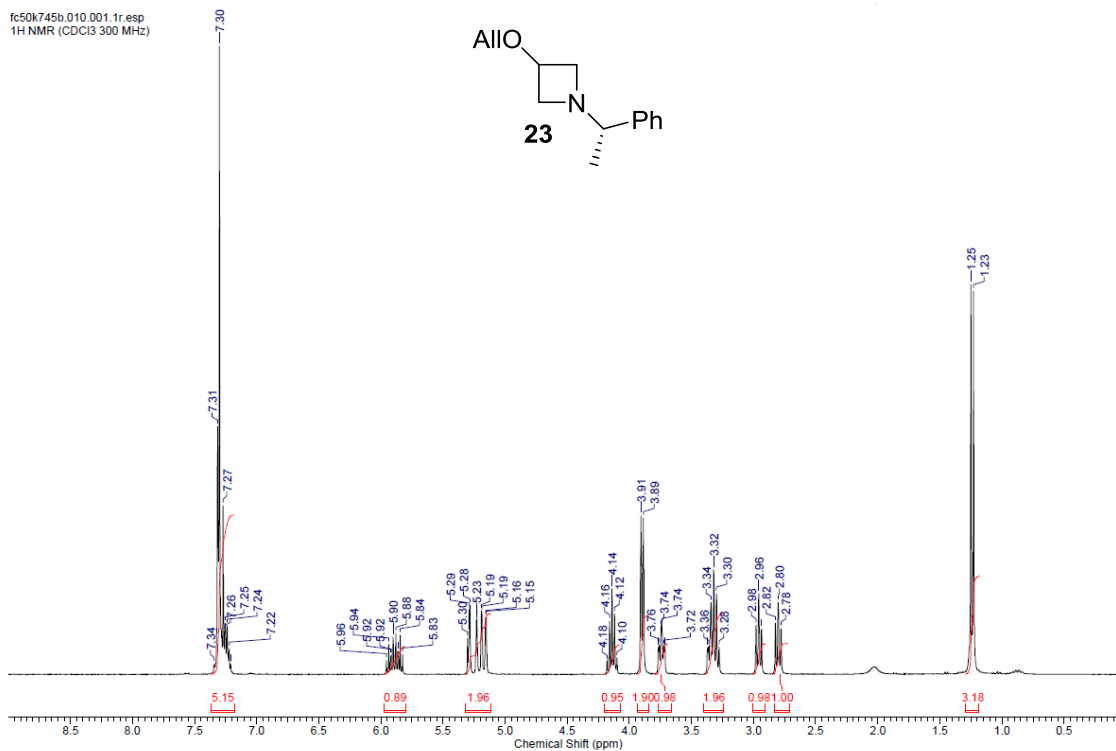
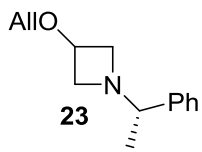




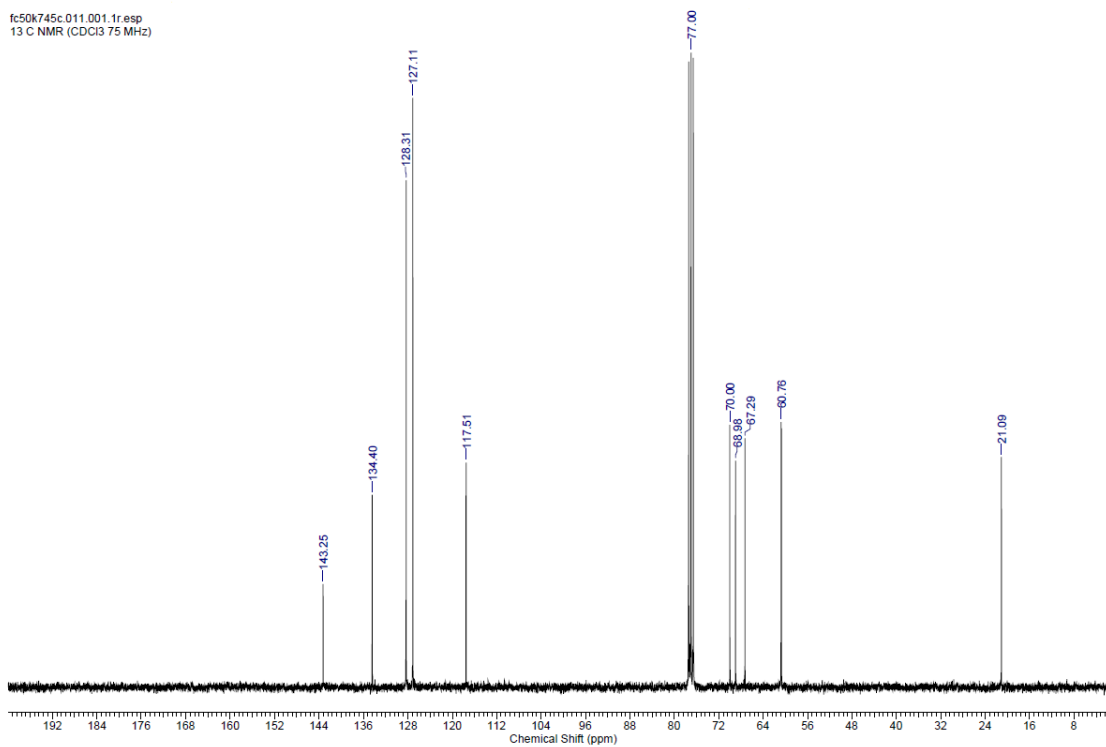




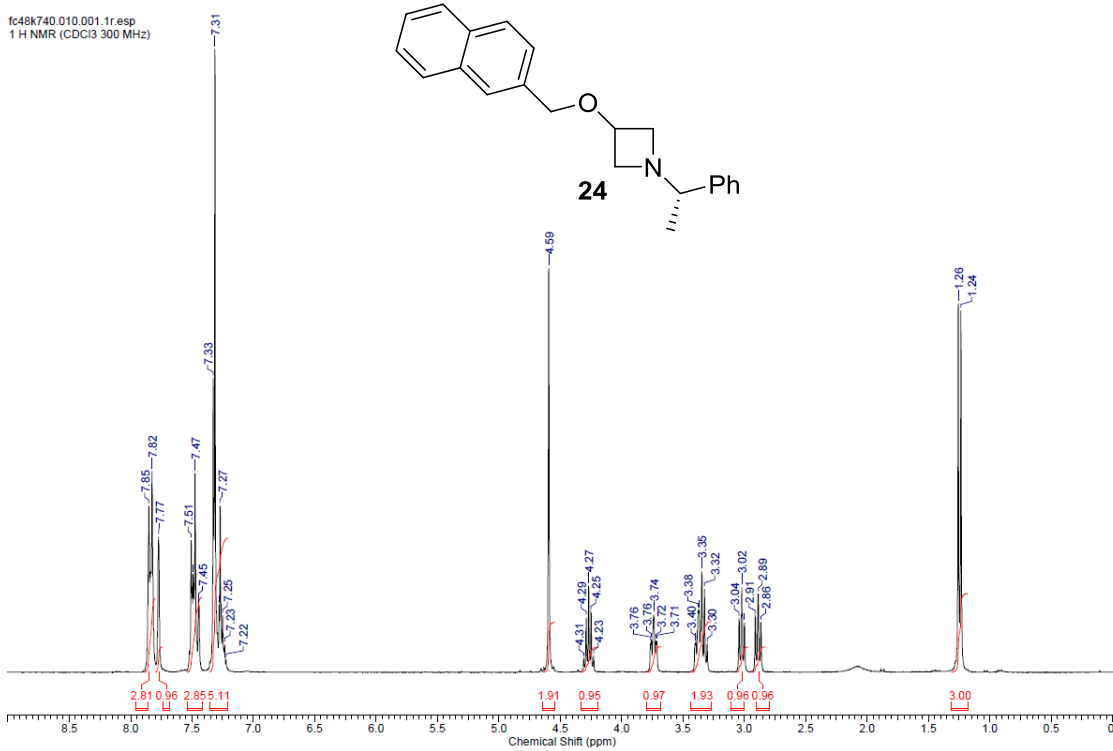
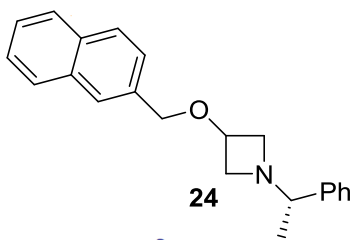
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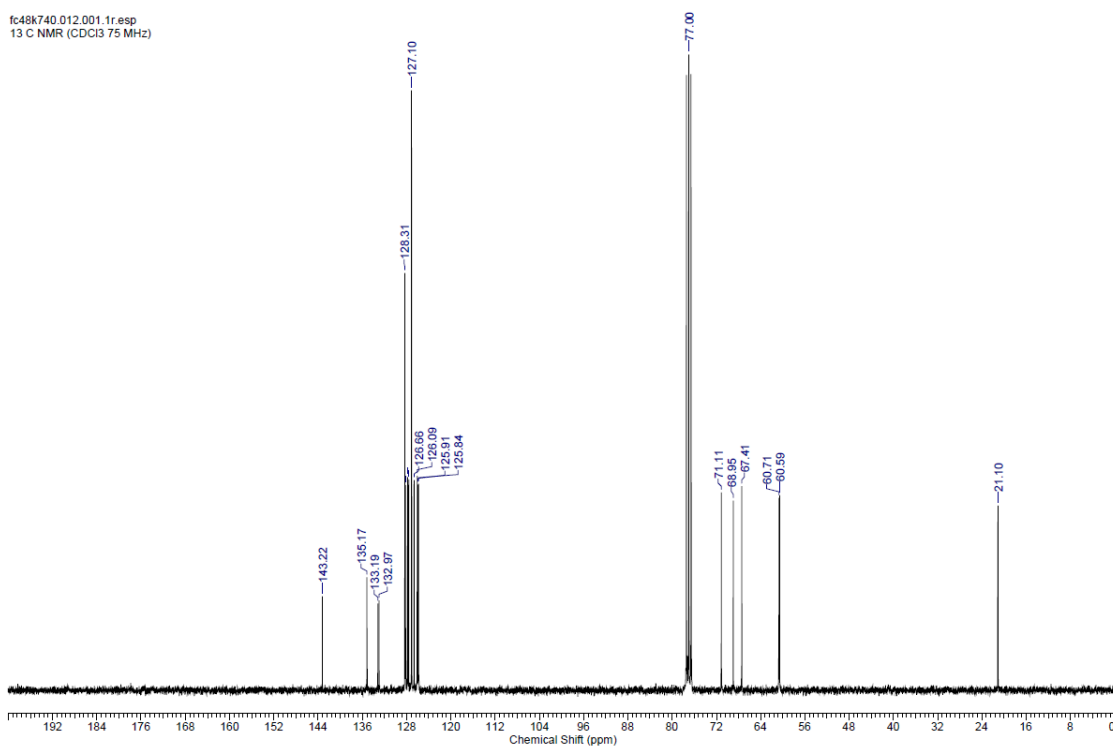
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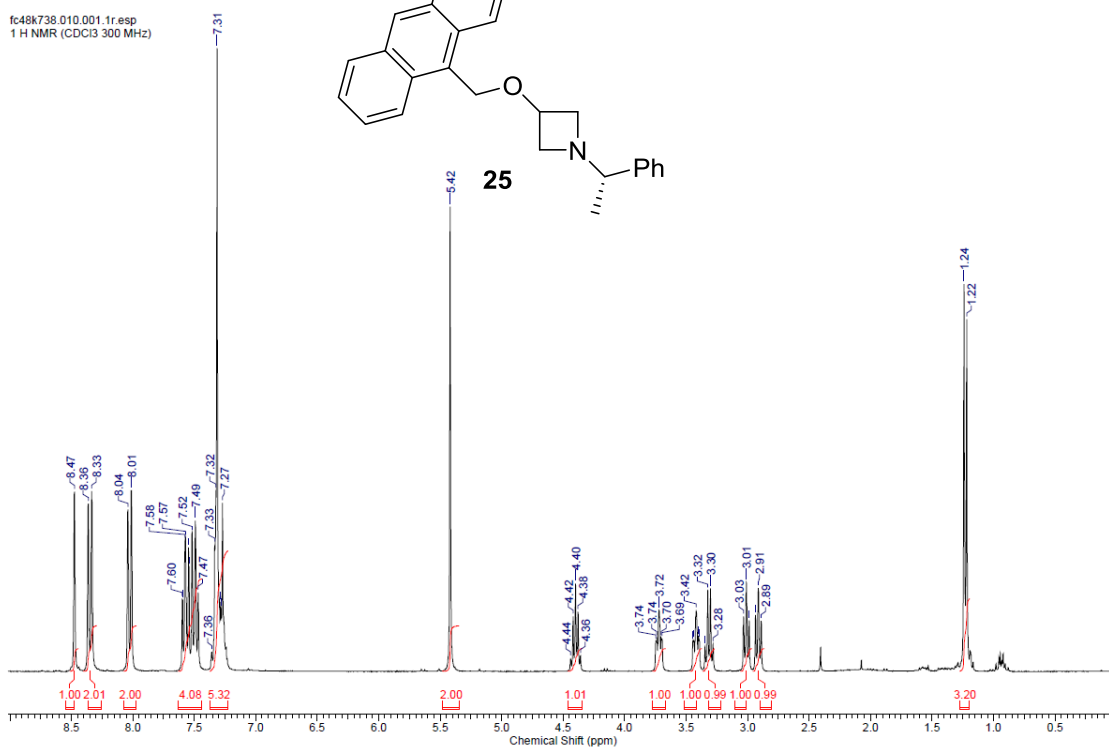
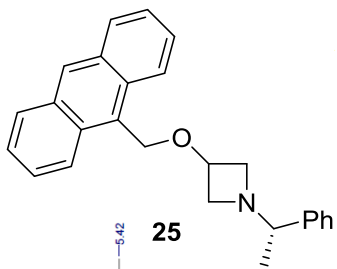
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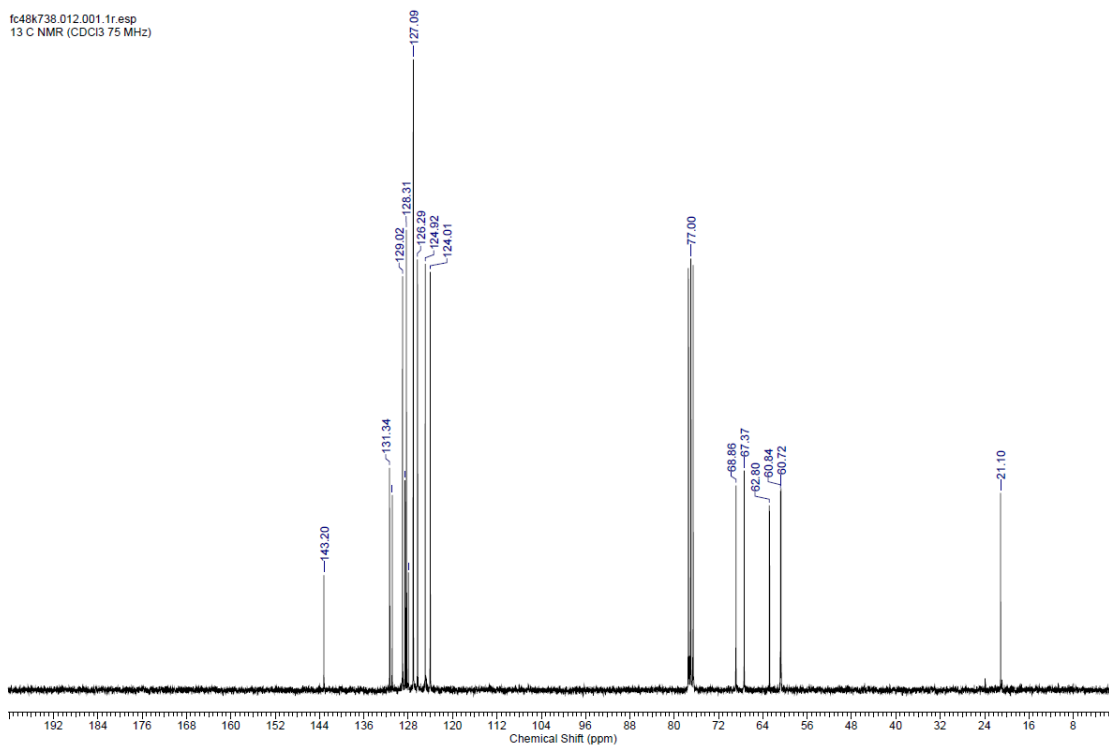
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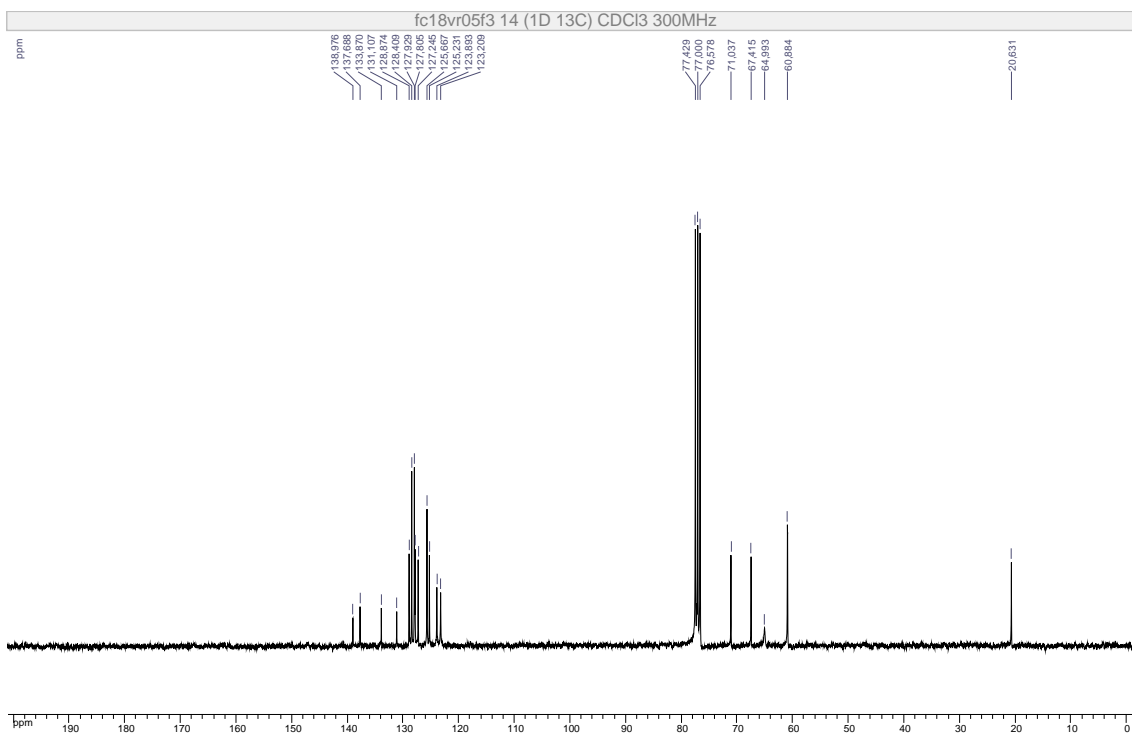
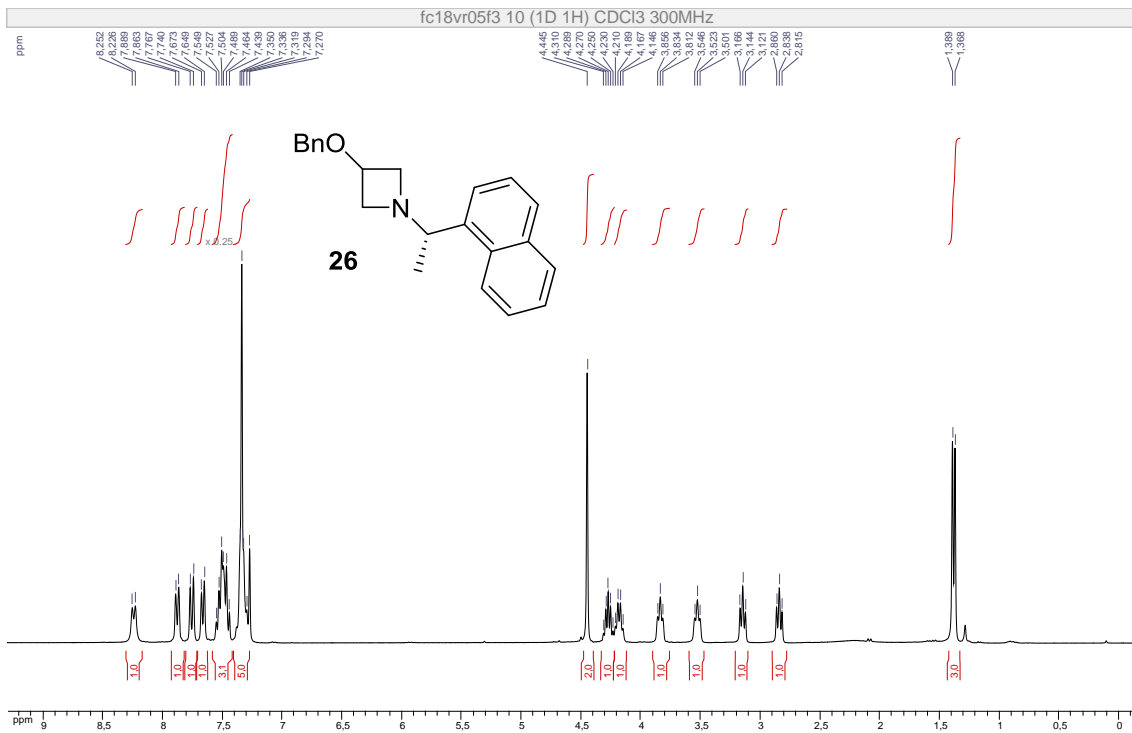


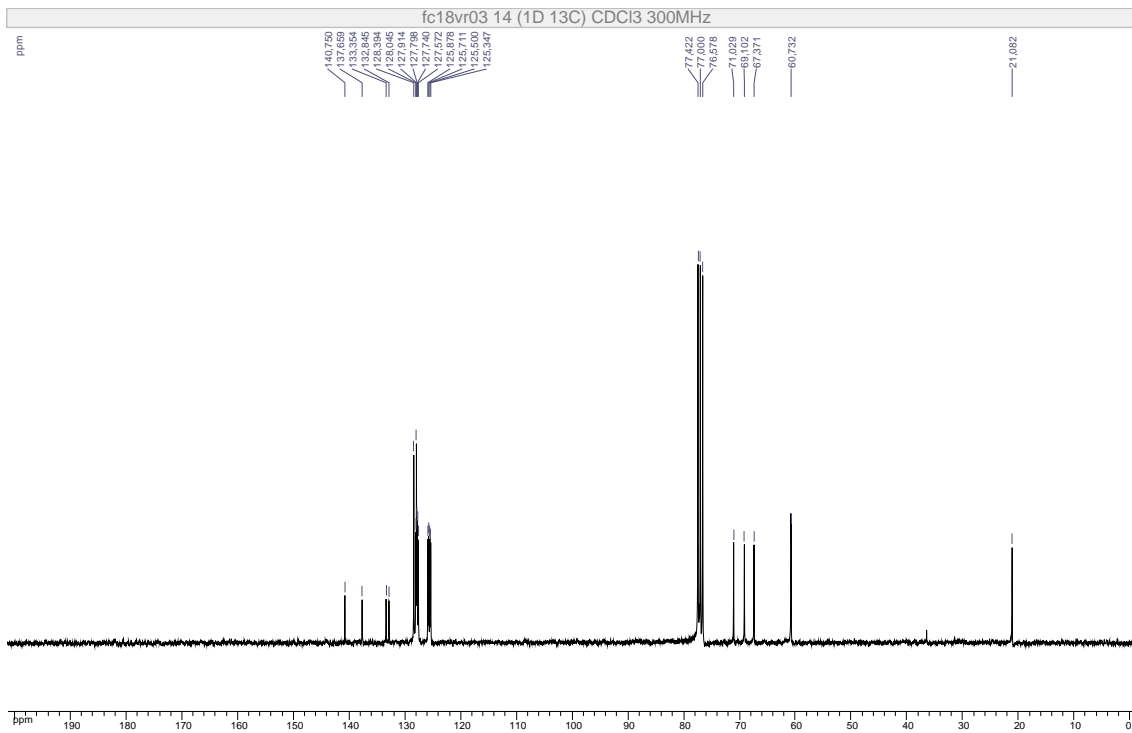
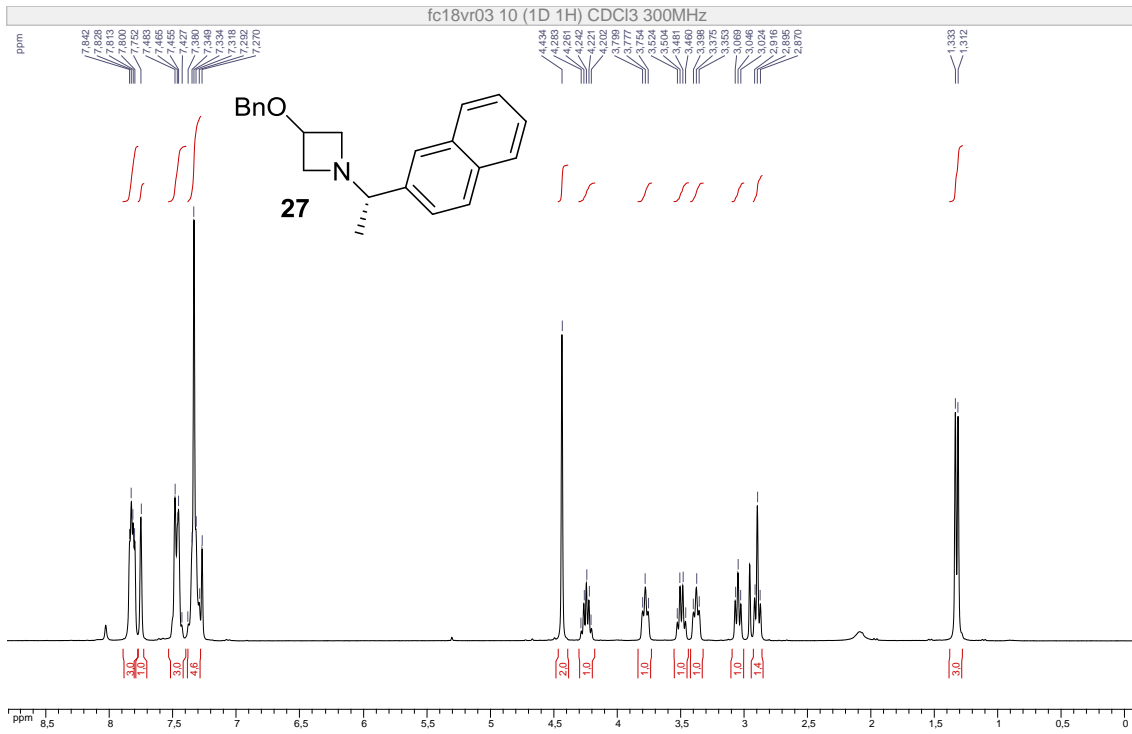
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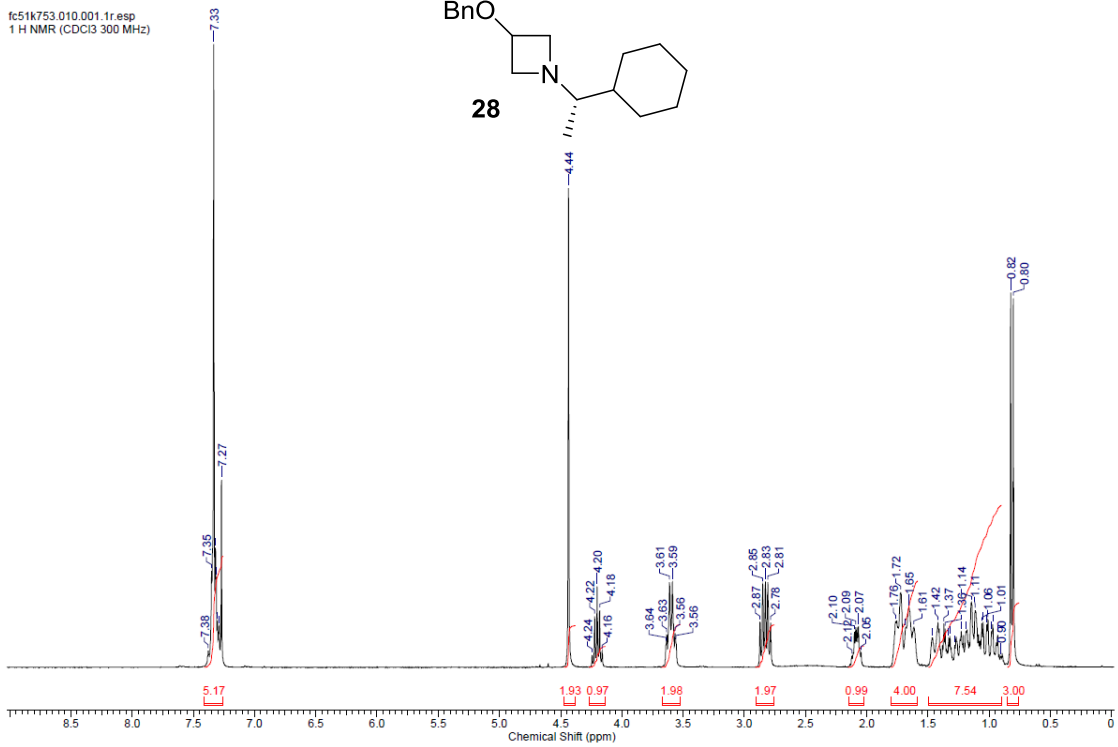
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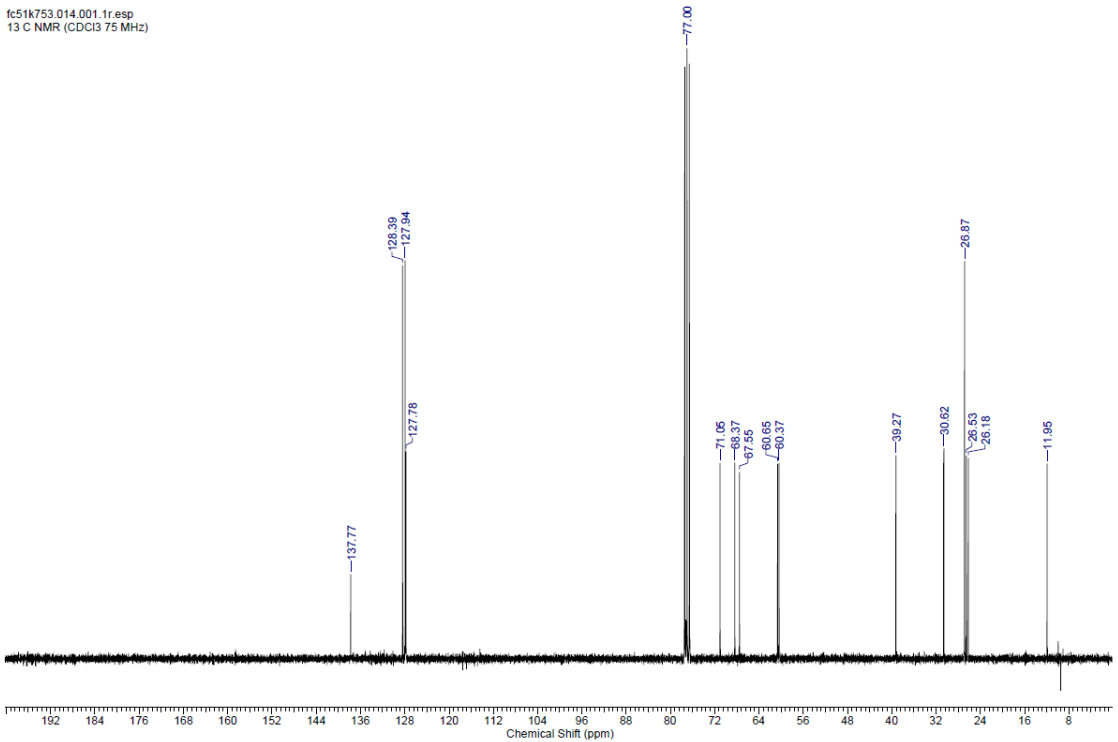


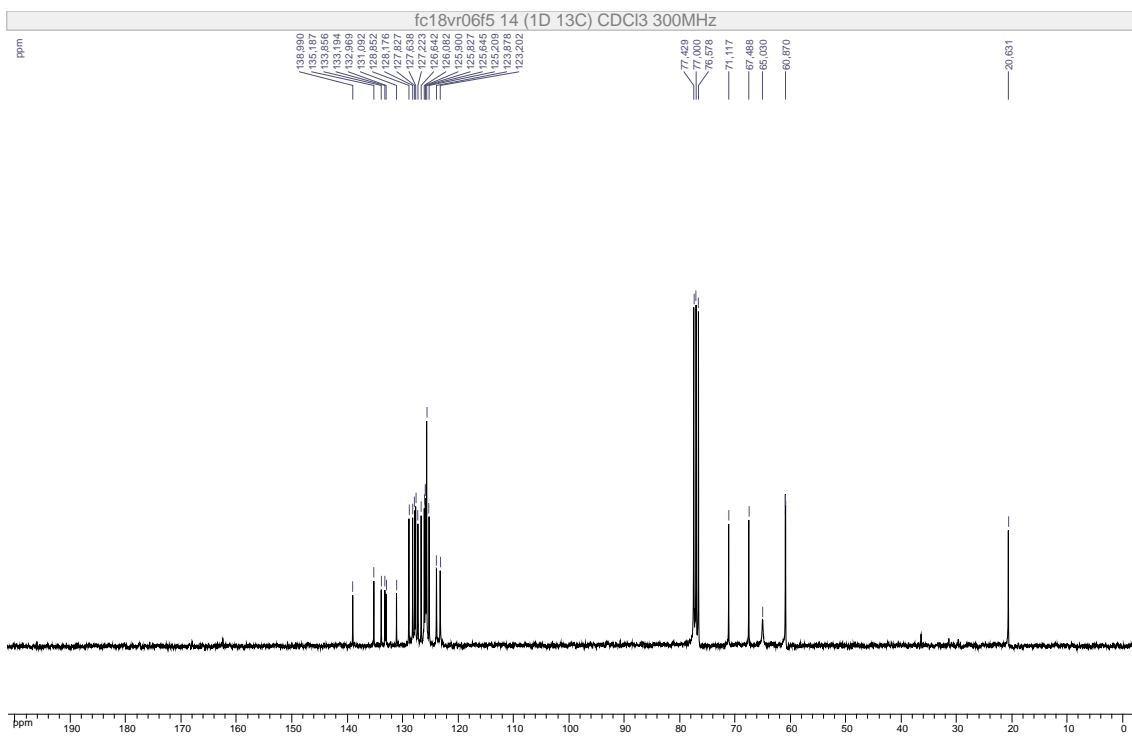
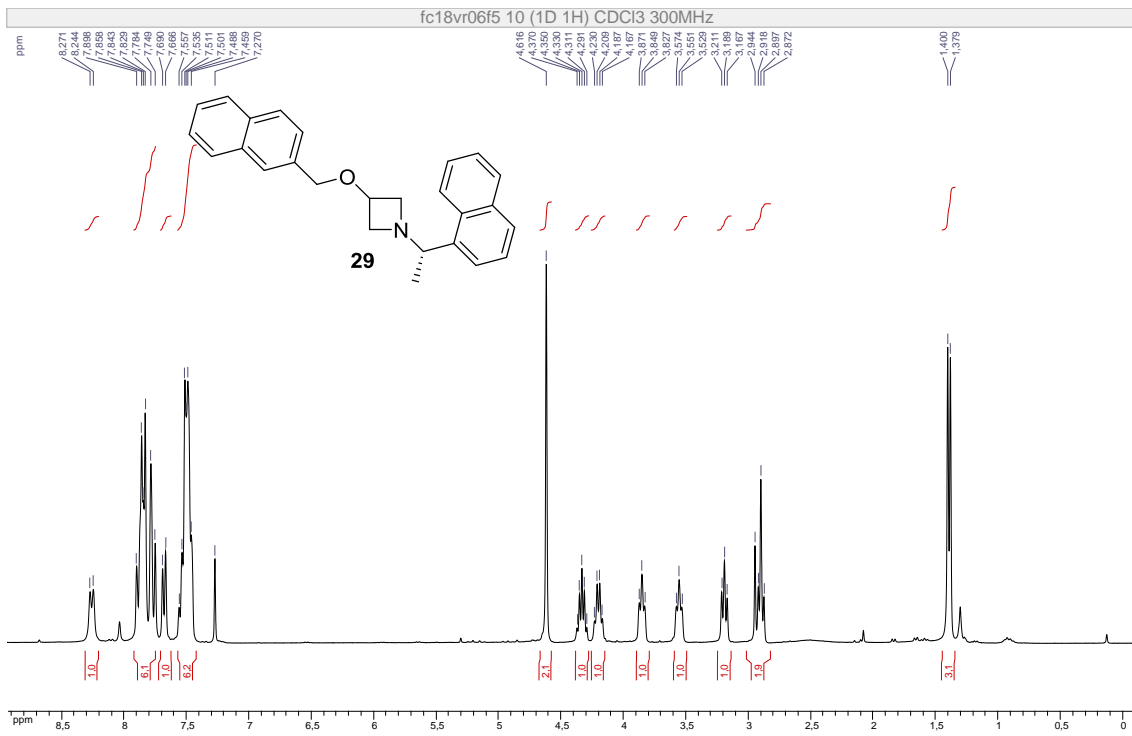


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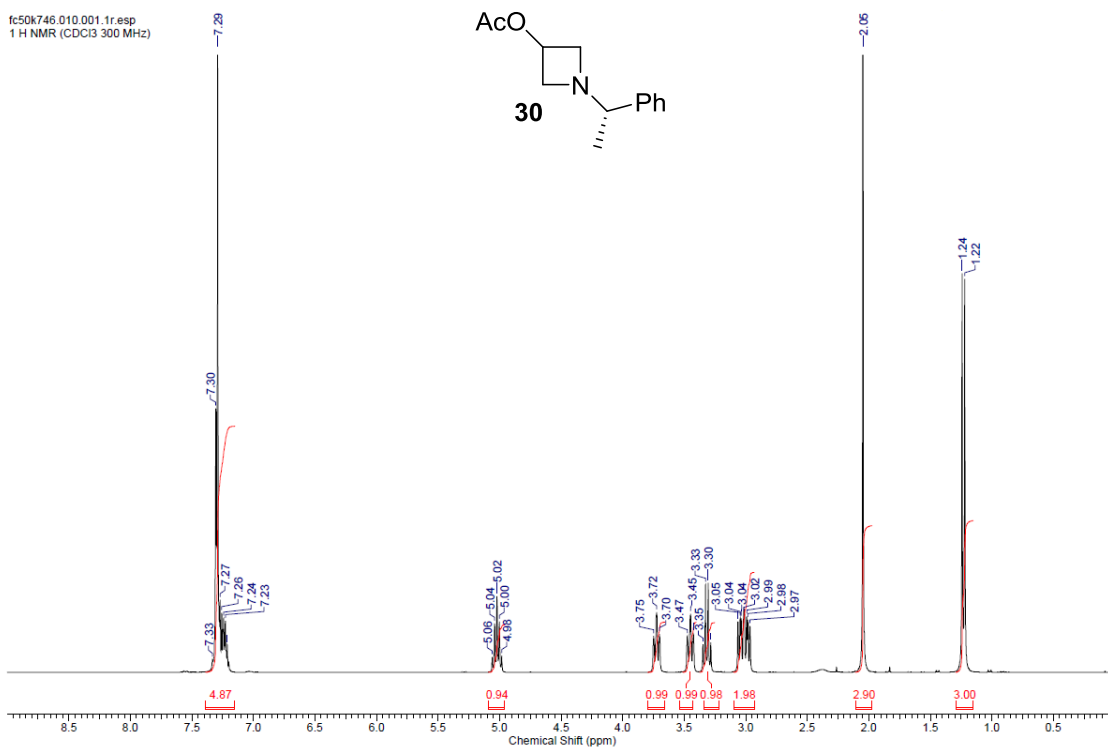
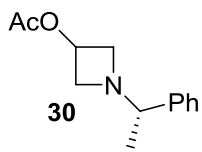
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13 C NMR (CDCl<sub>3</sub> 75 MHz)



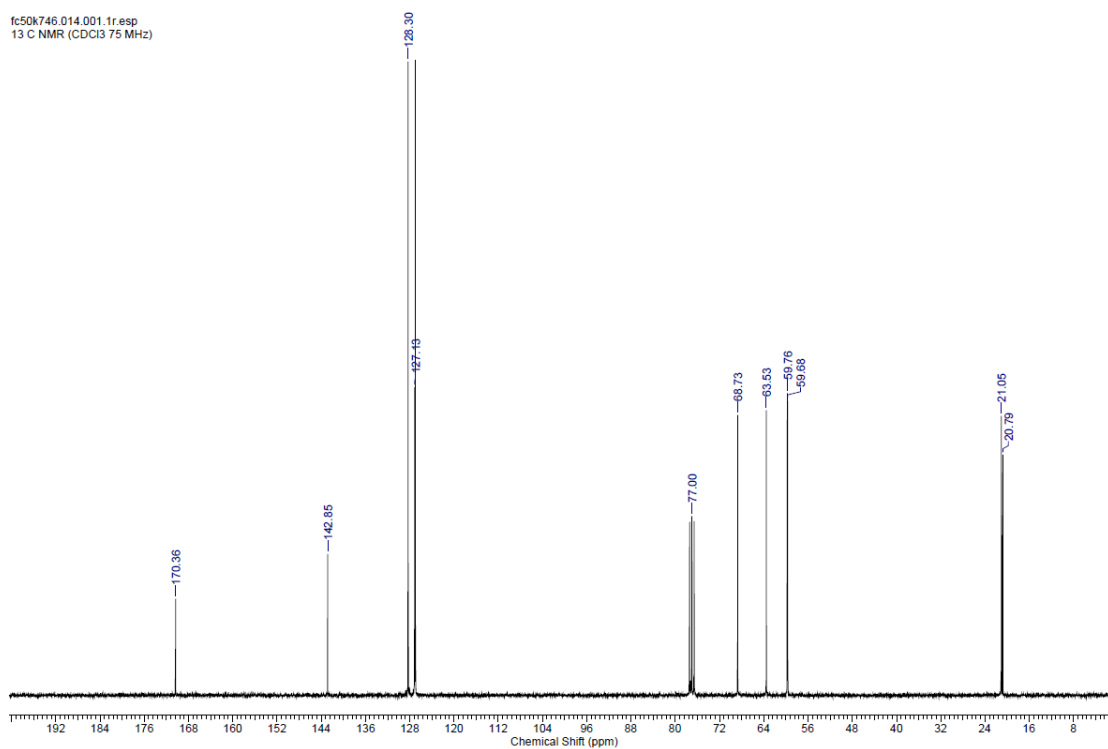


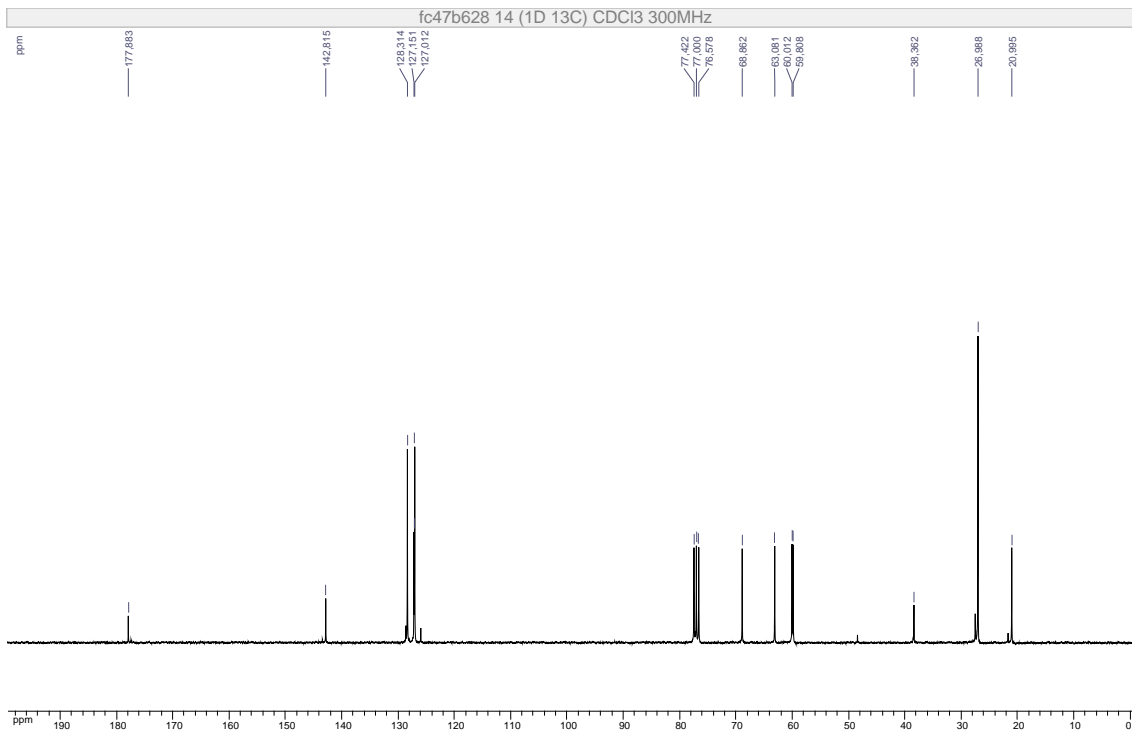
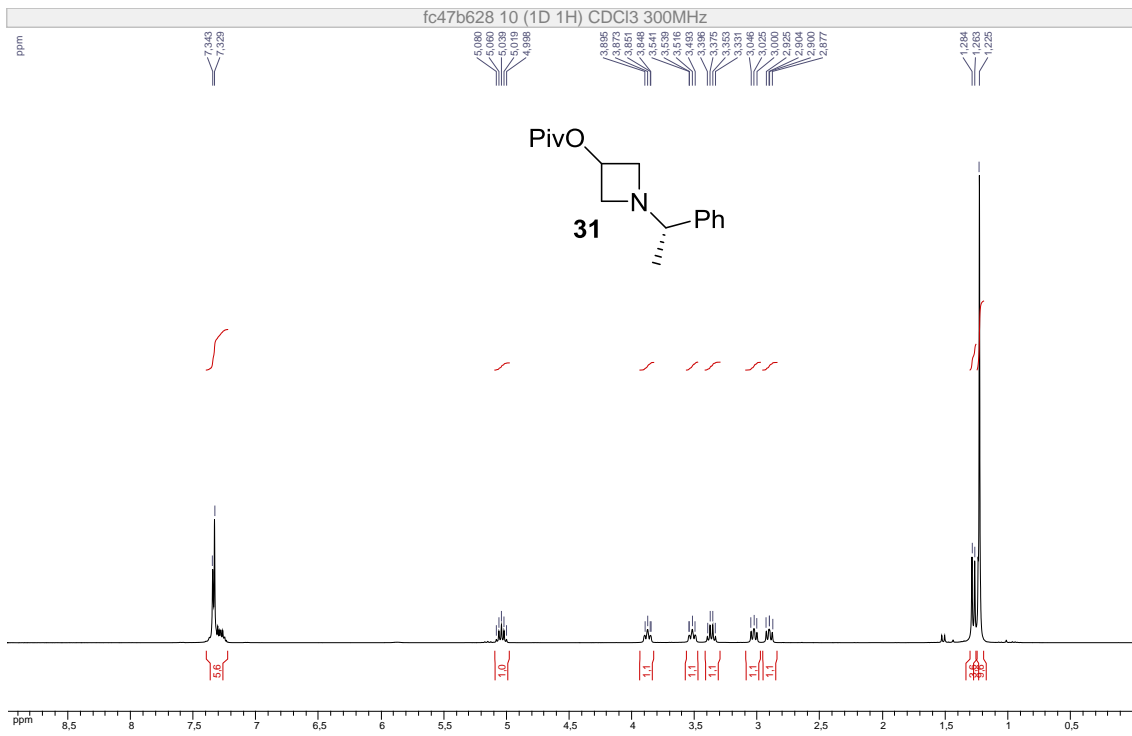


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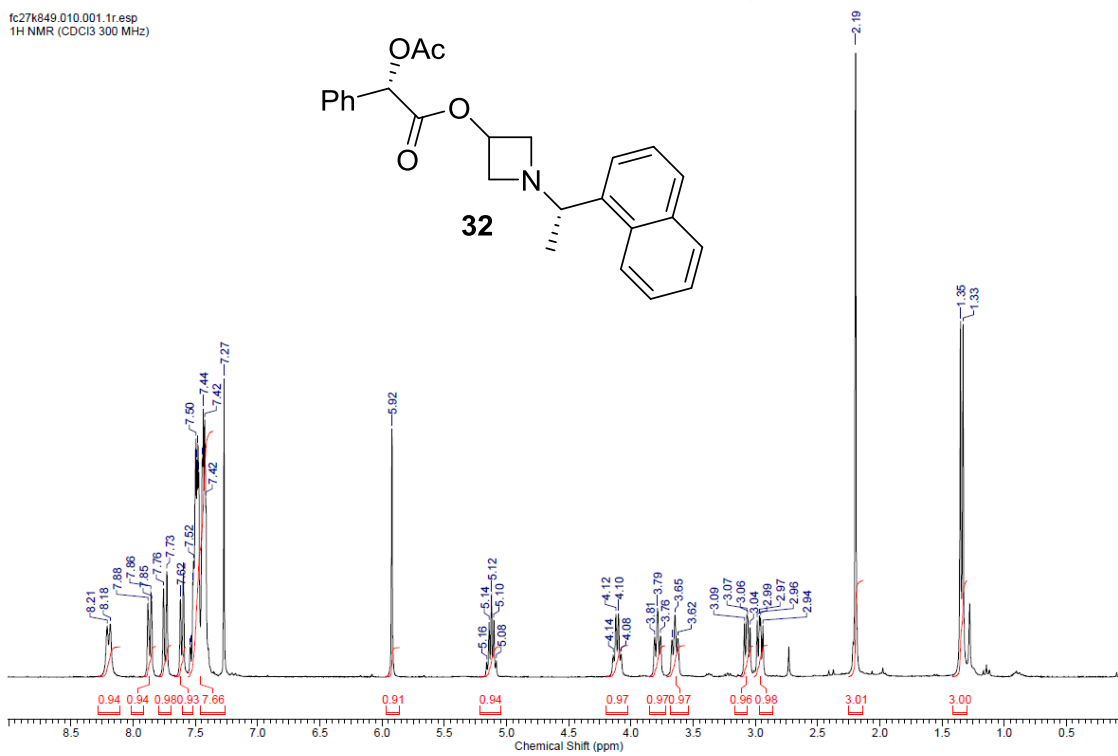
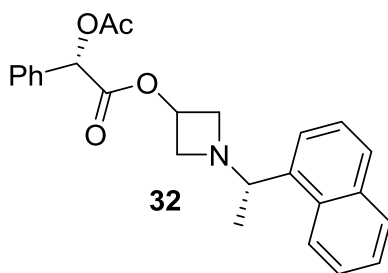


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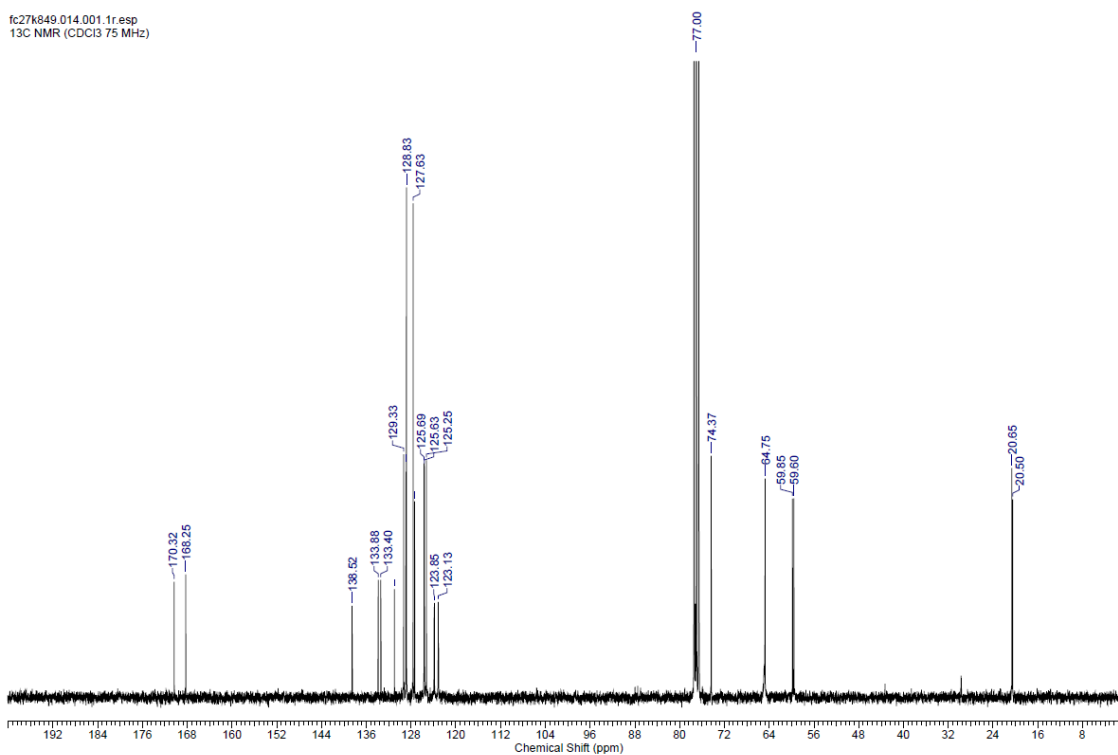




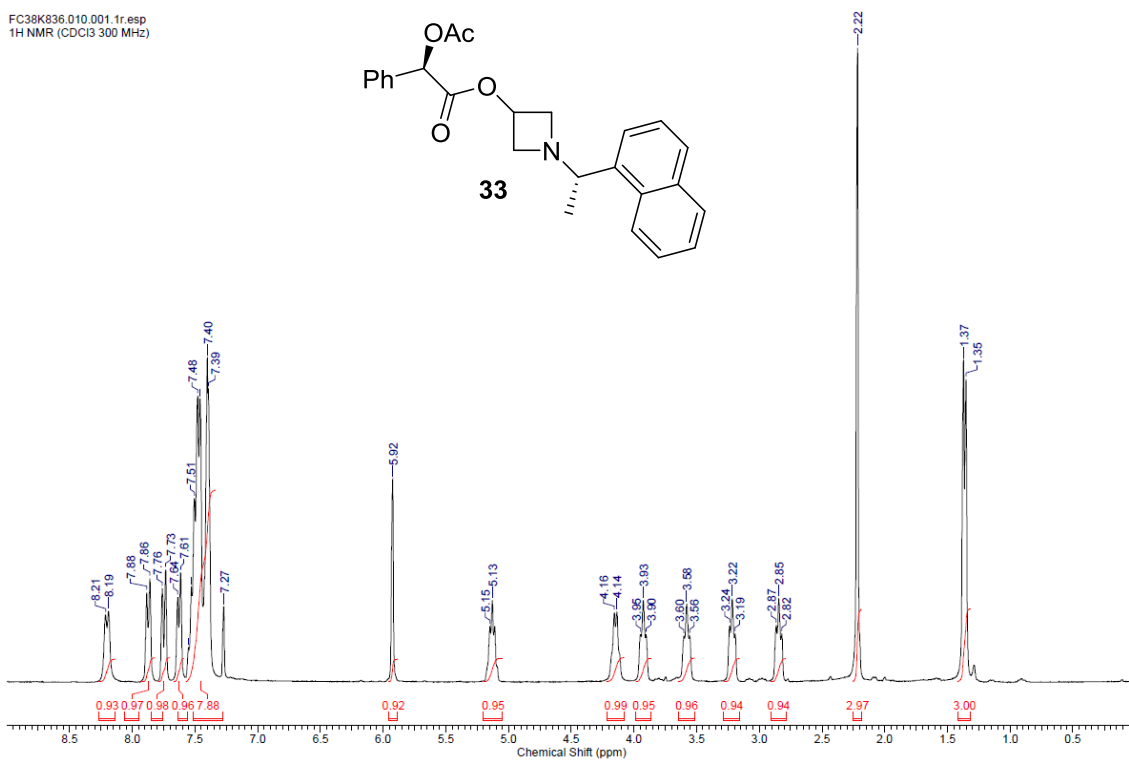
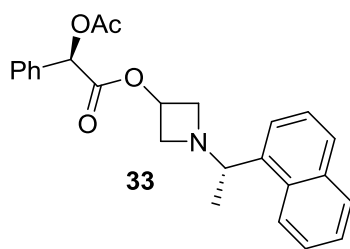
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1H NMR (CDCl3 300 MHz)



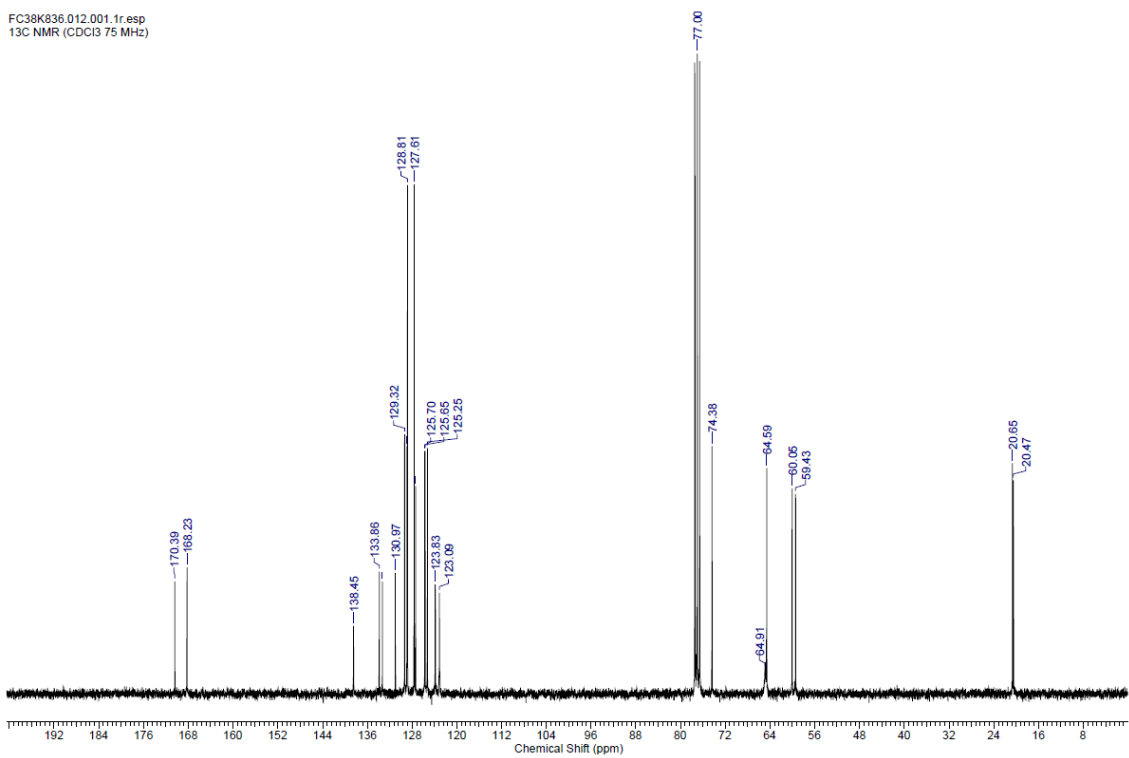
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13C NMR (CDCl3 75 MHz)



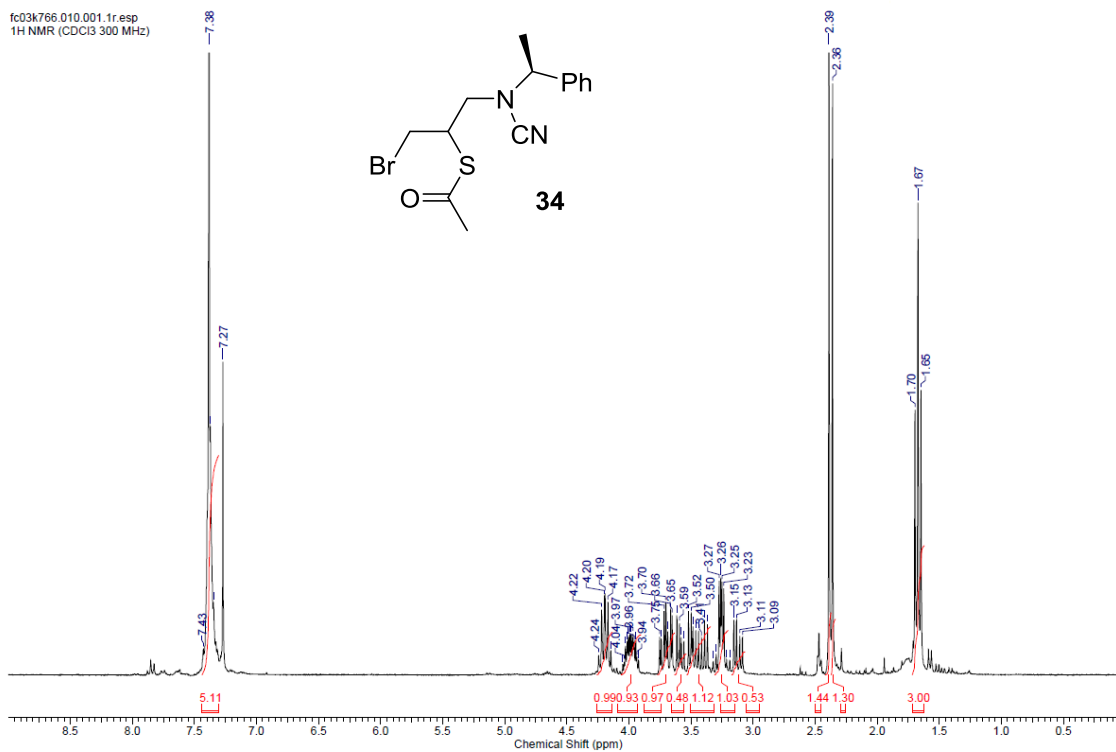
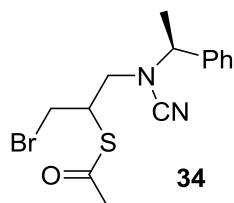
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1H NMR (CDCl3 300 MHz)



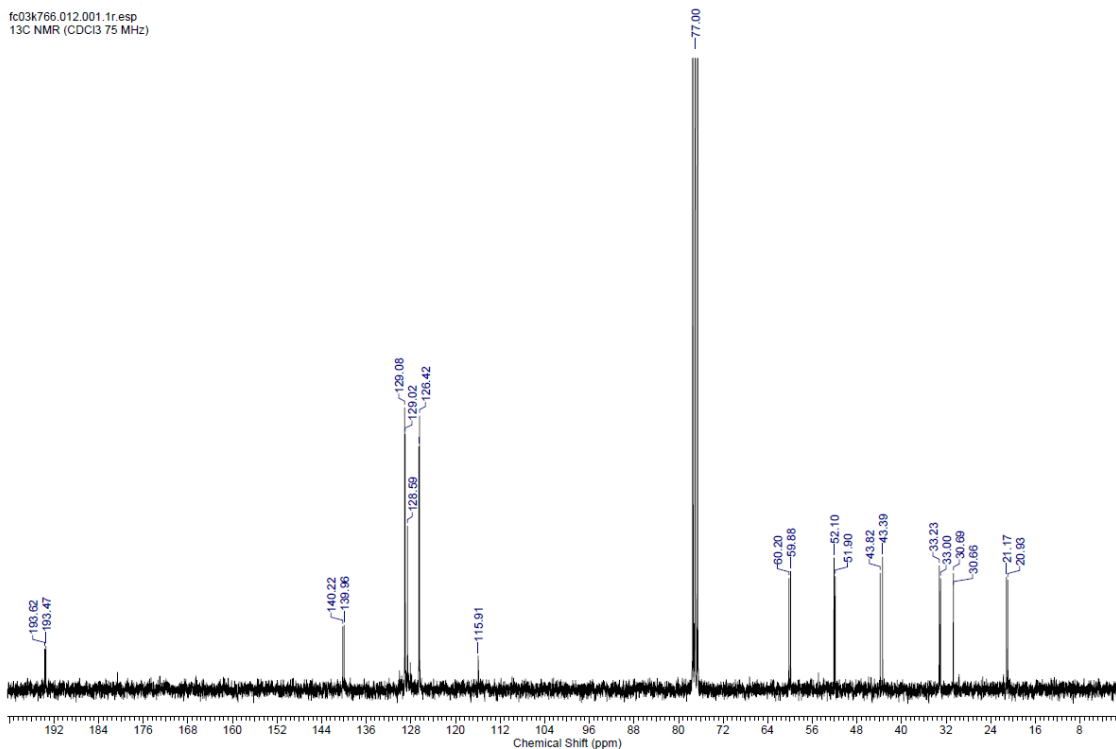
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13C NMR (CDCl3 75 MHz)



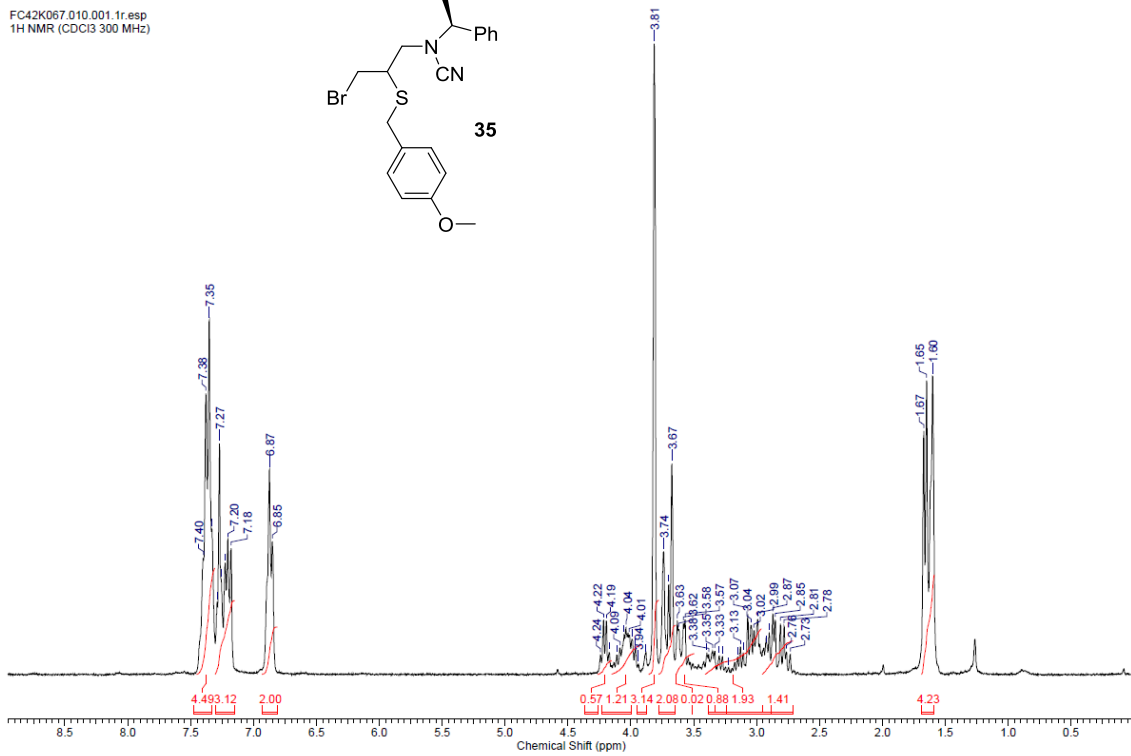
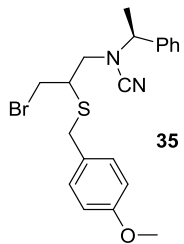
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1H NMR (CDCl3 300 MHz)



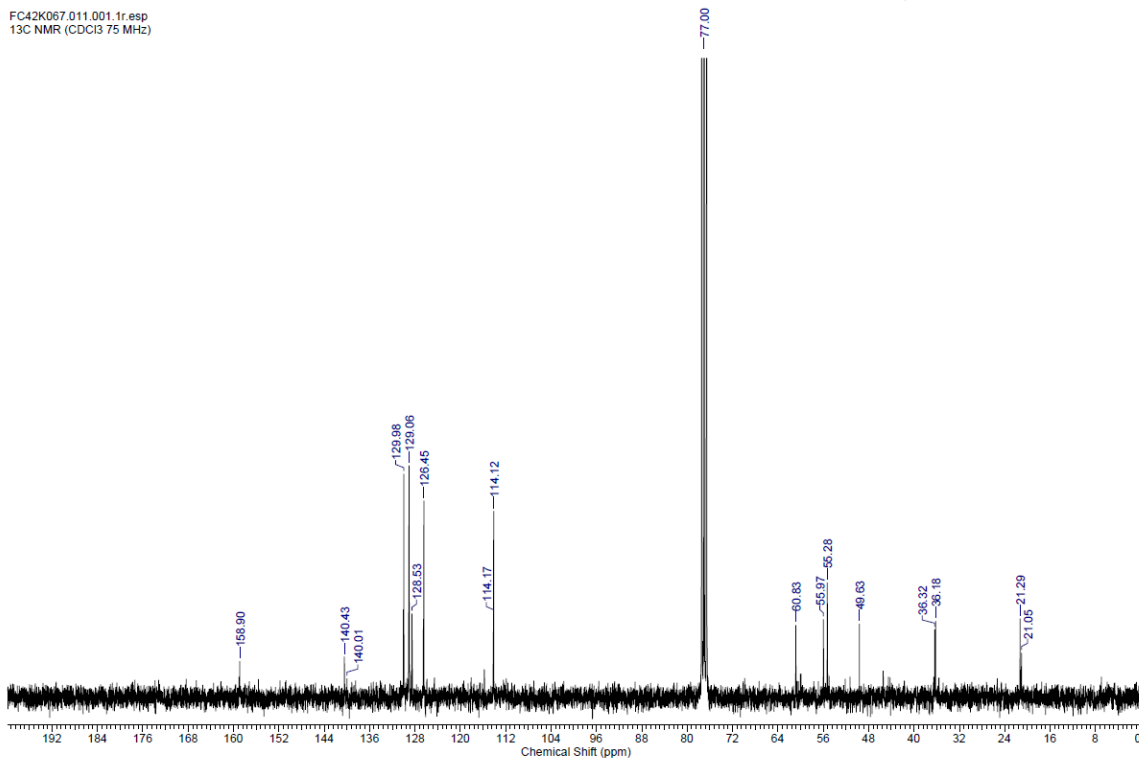
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13C NMR (CDCl3 75 MHz)



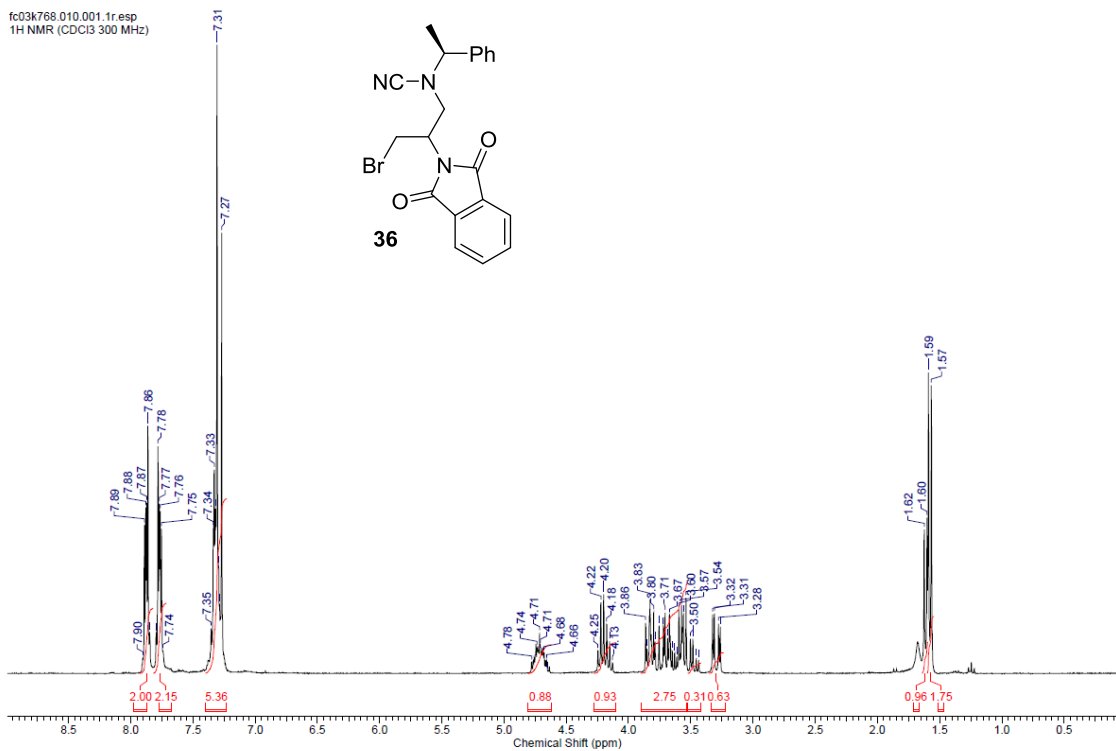
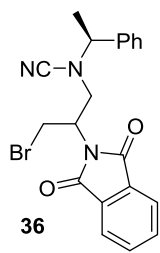
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1H NMR (CDCl3 300 MHz)



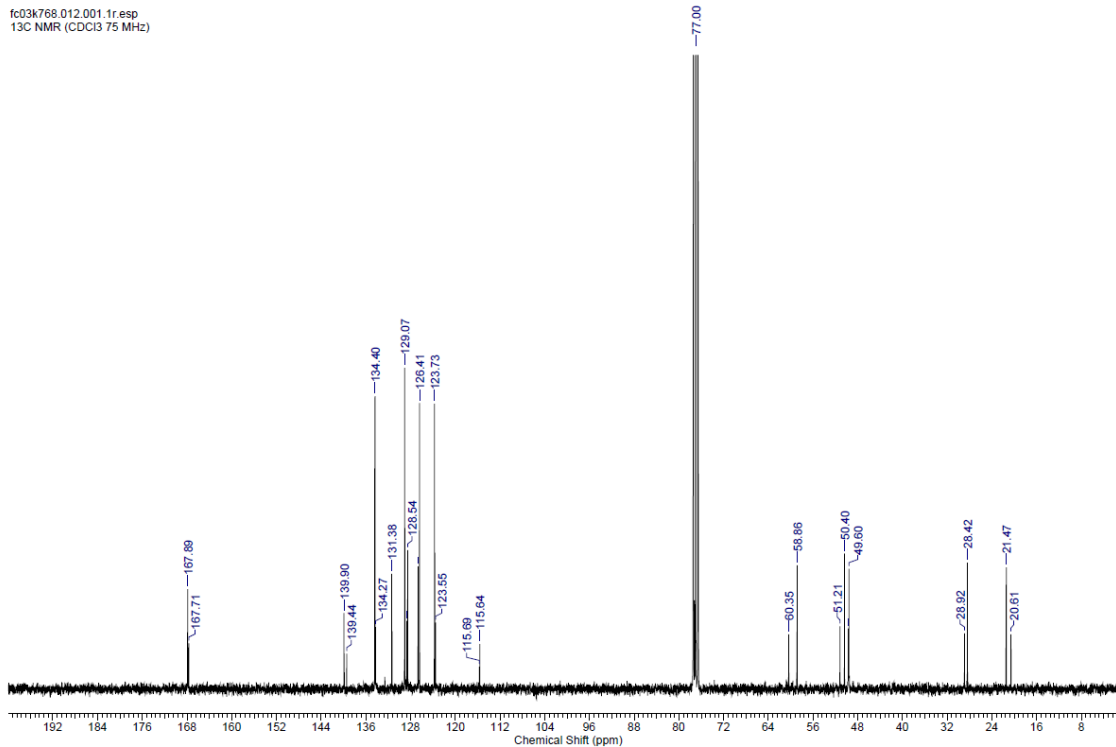
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13C NMR (CDCl3 75 MHz)



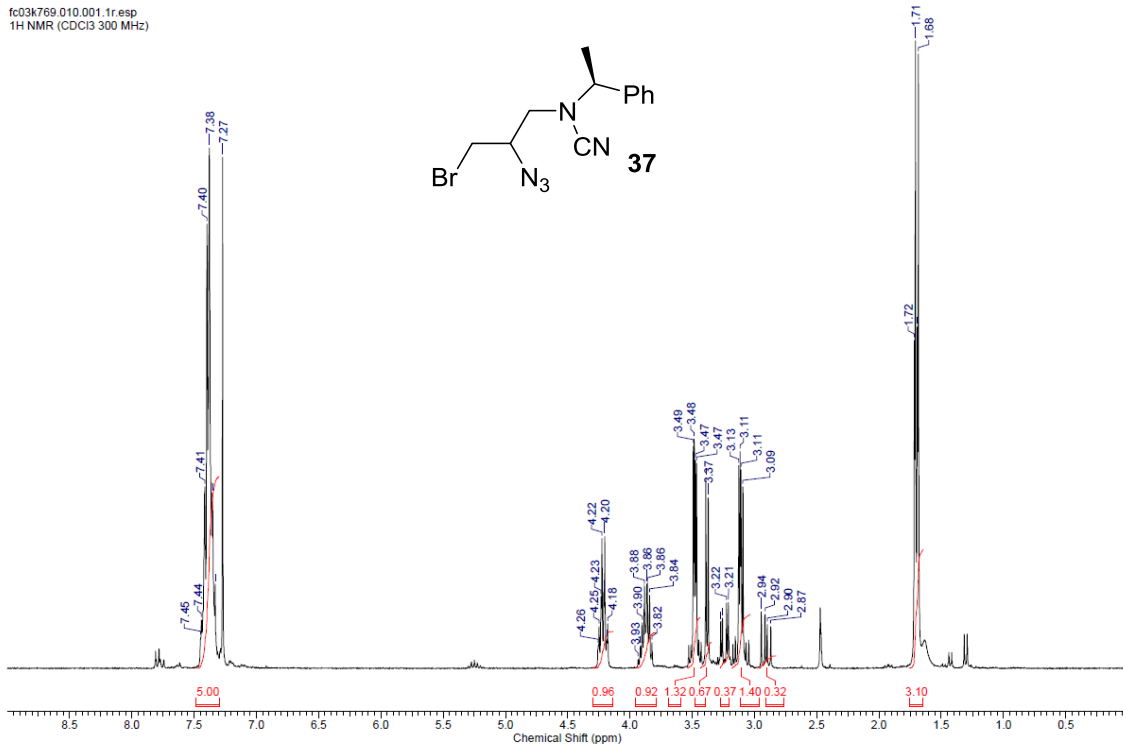
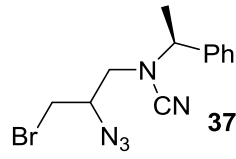
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1H NMR (CDCl3 300 MHz)



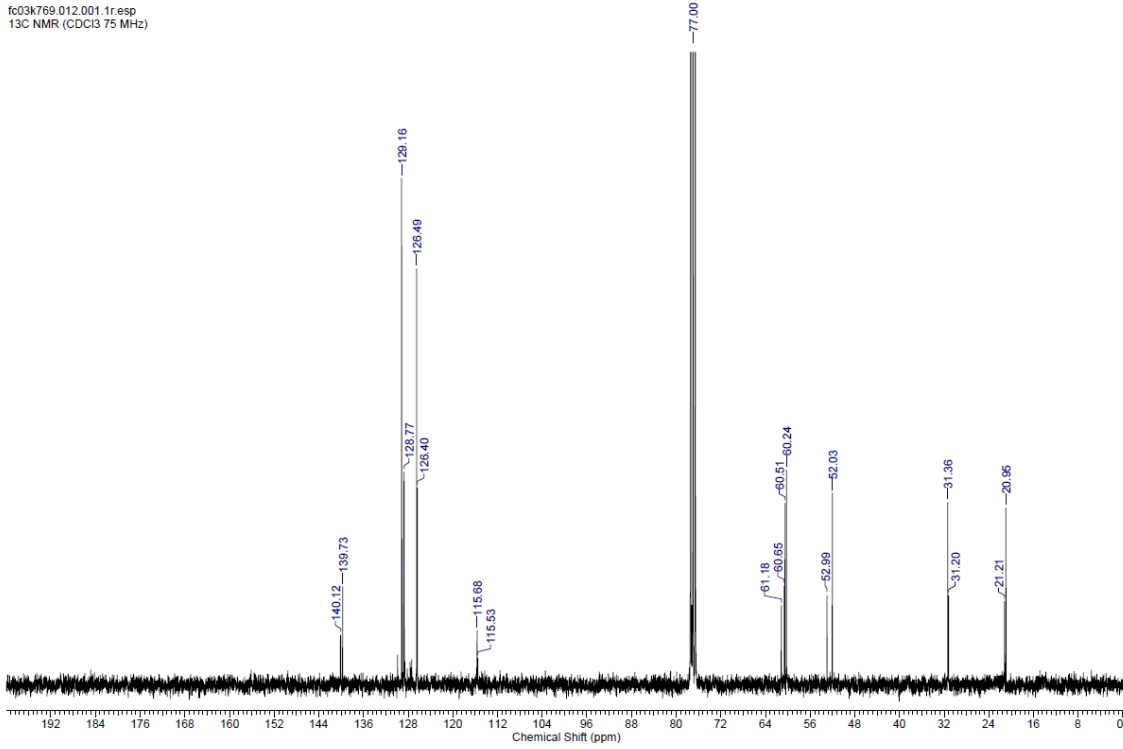
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13C NMR (CDCl3 75 MHz)



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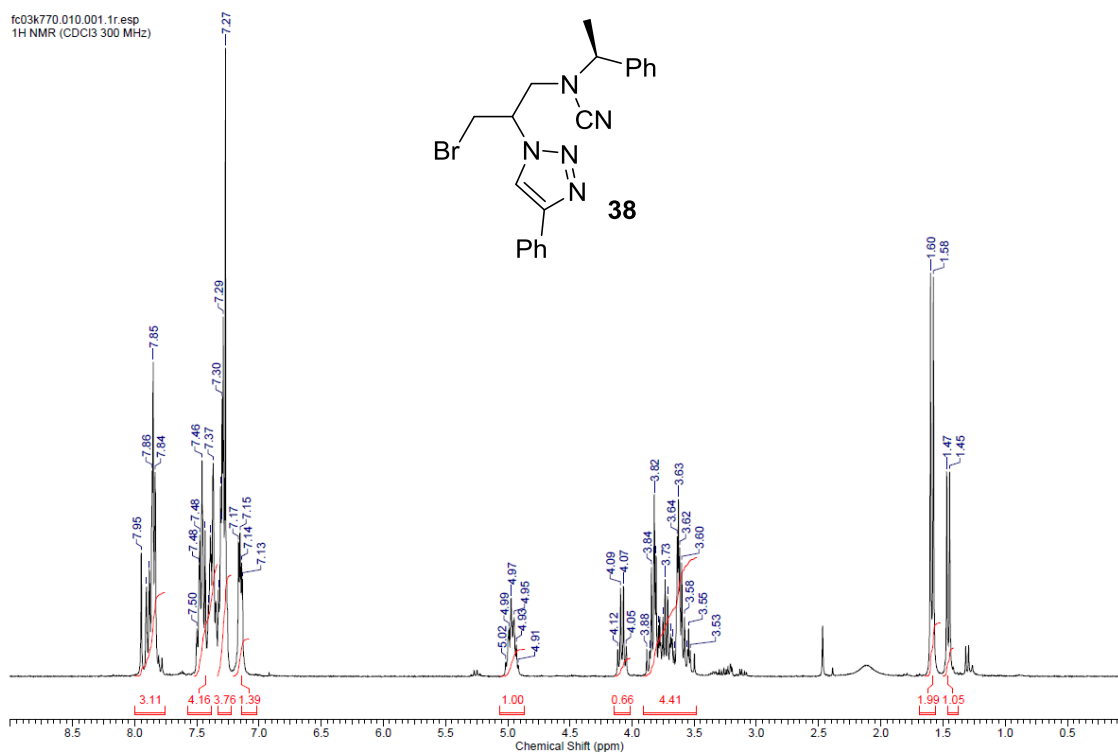
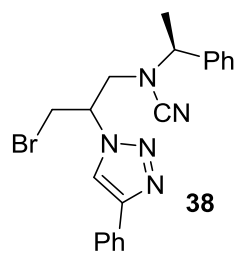


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13C NMR (CDCl3 75 MHz)

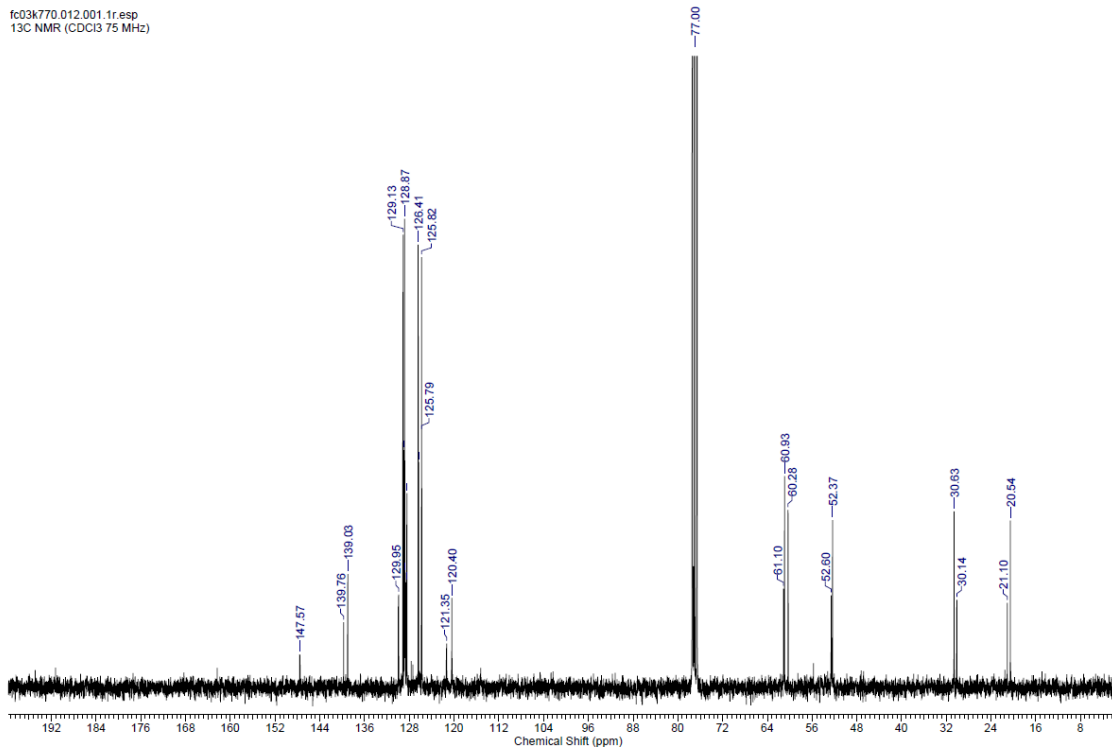




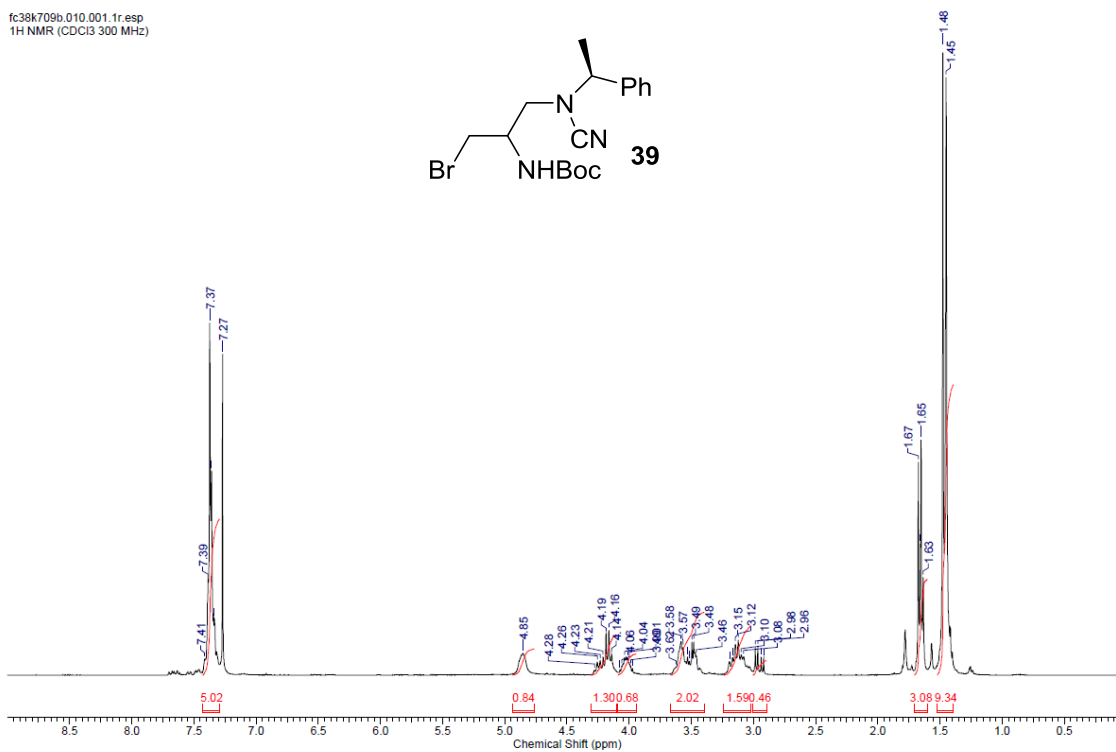
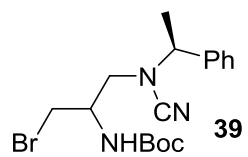
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1H NMR (CDCl3 300 MHz)



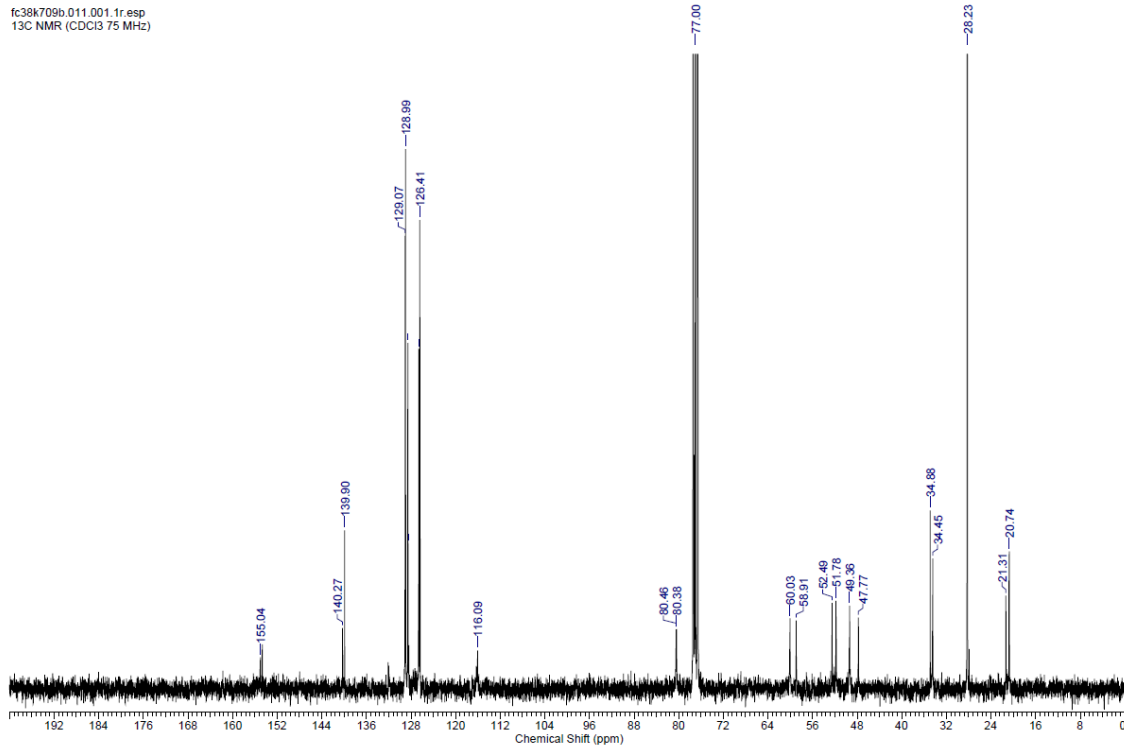
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13C NMR (CDCl3 75 MHz)

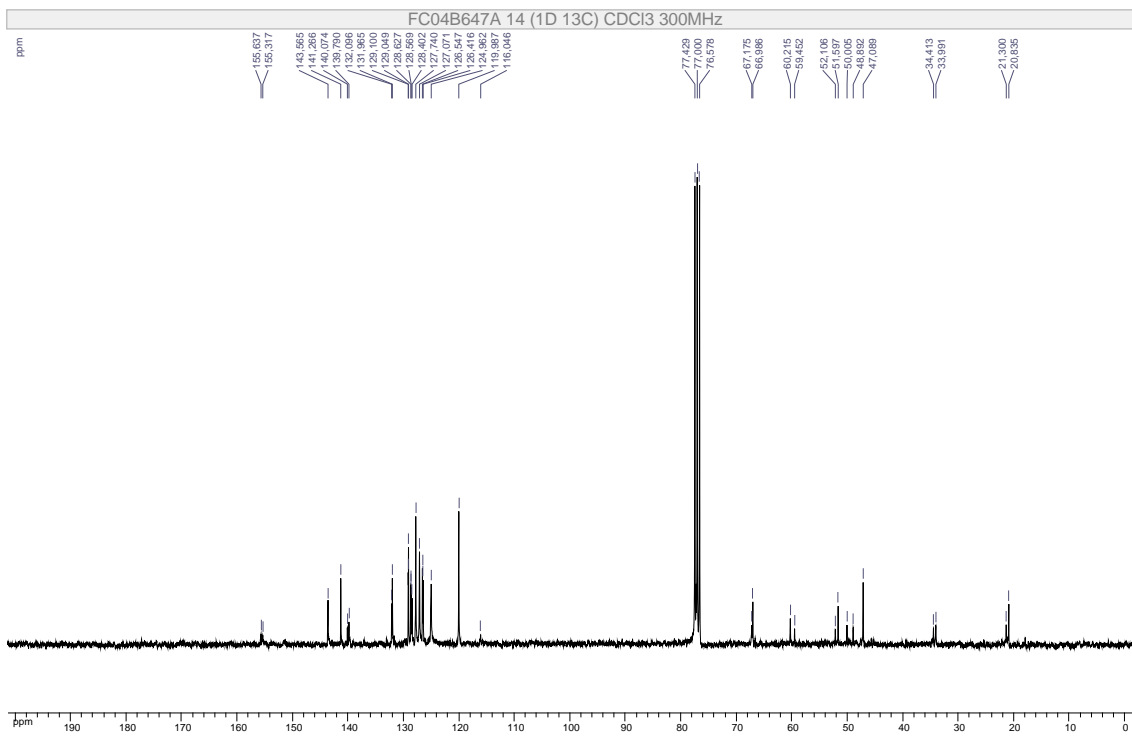
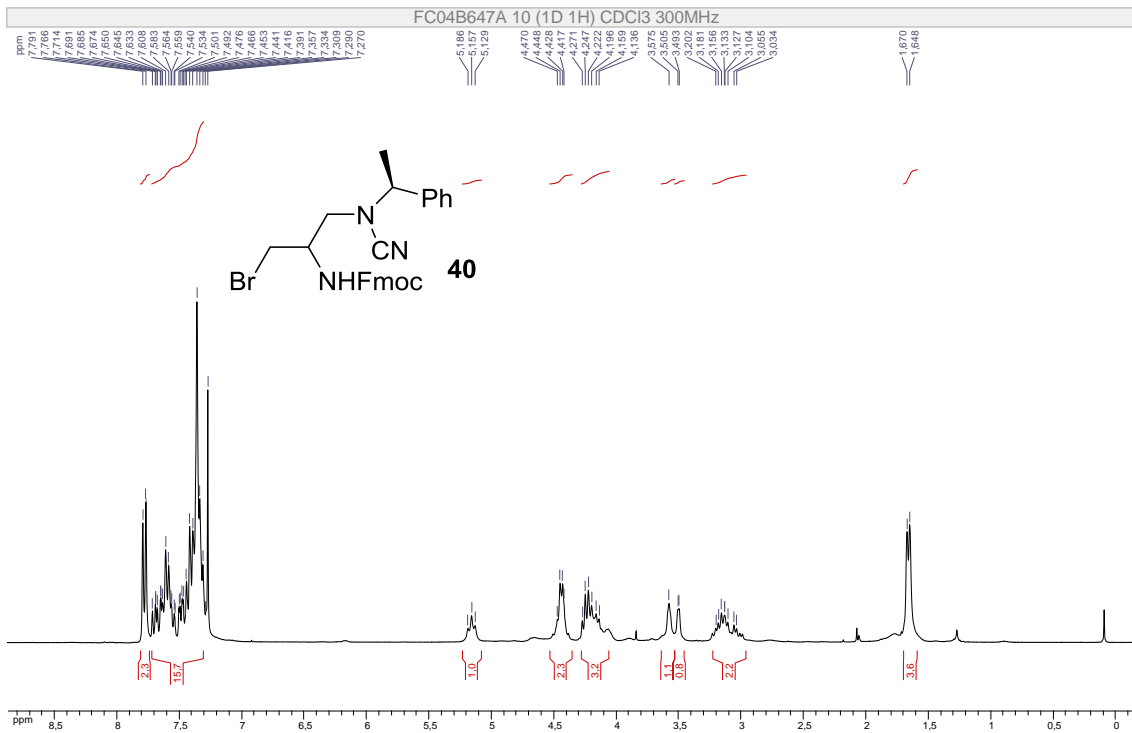


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1H NMR (CDCl3 300 MHz)

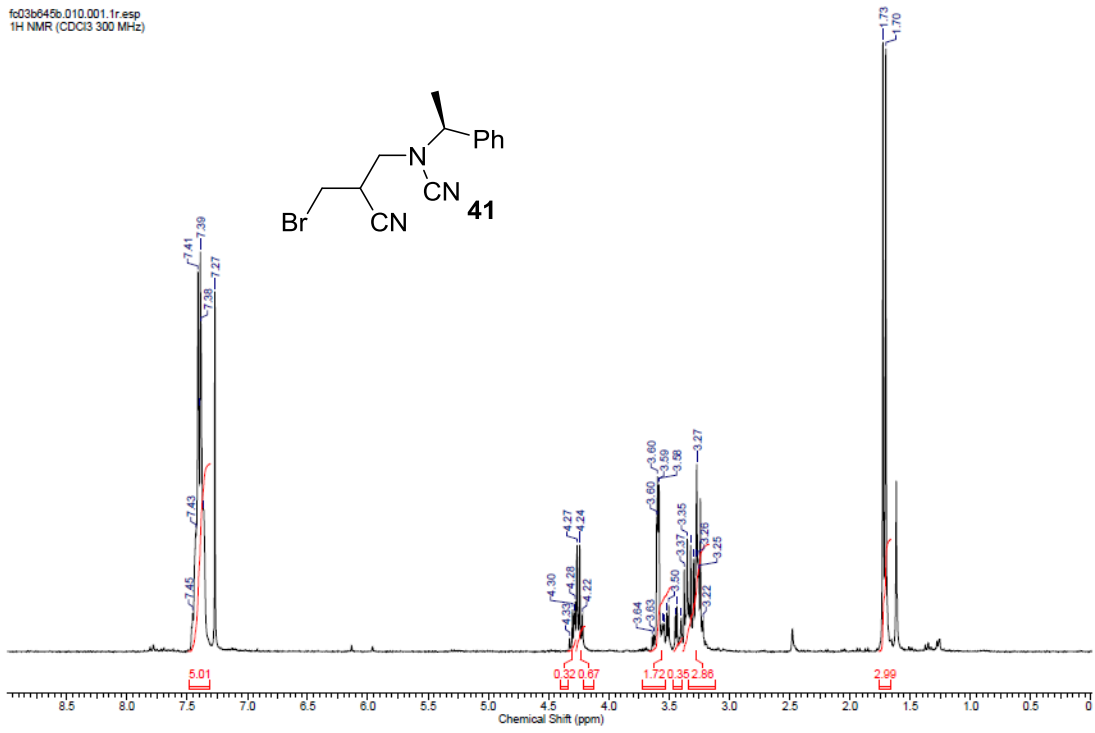
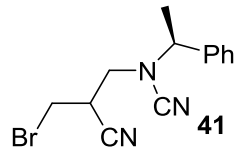


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13C NMR (CDCl3 75 MHz)

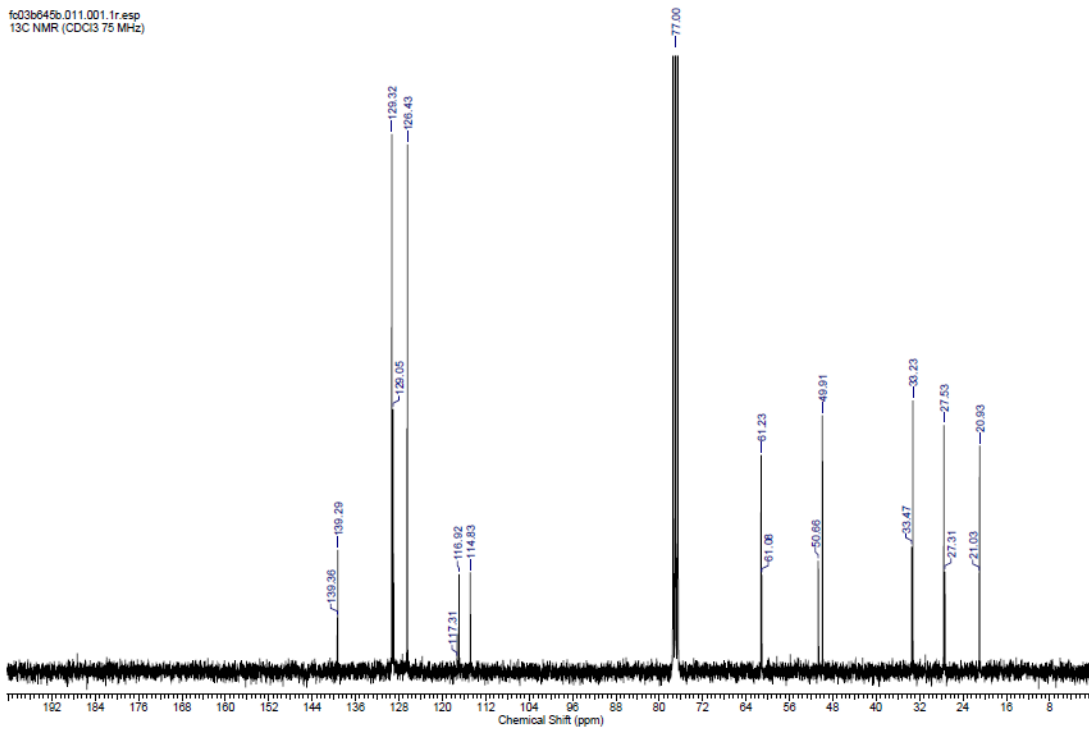




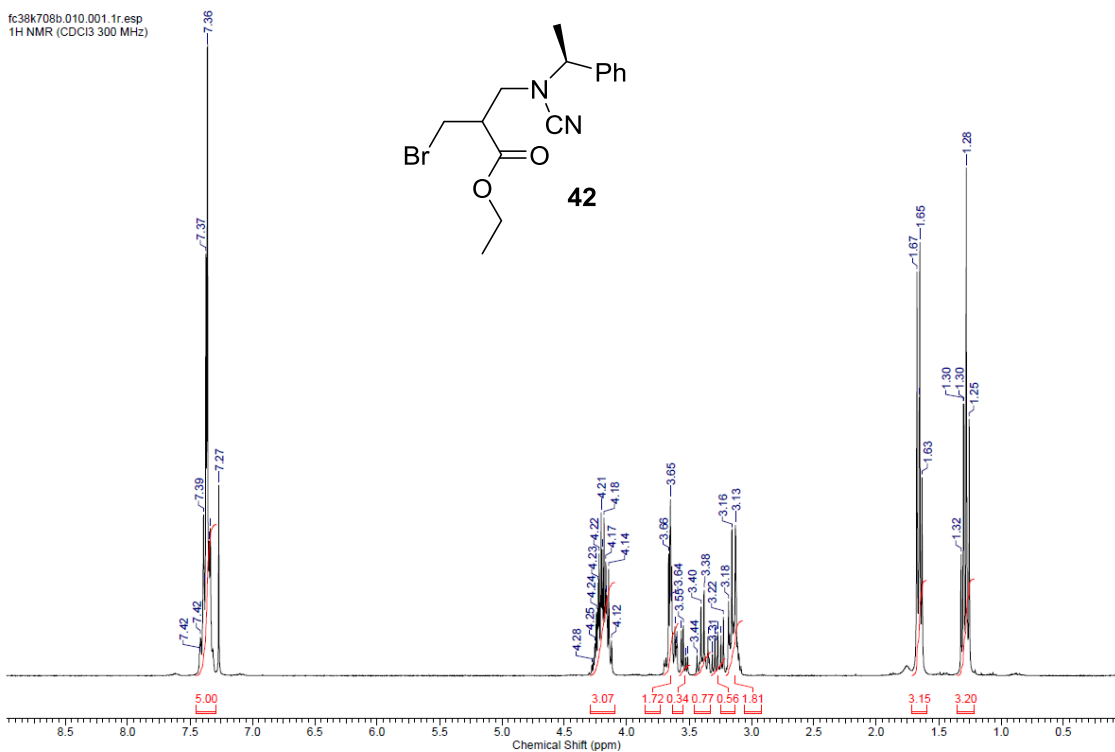
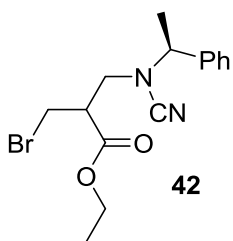
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1H NMR (CDCl3 300 MHz)



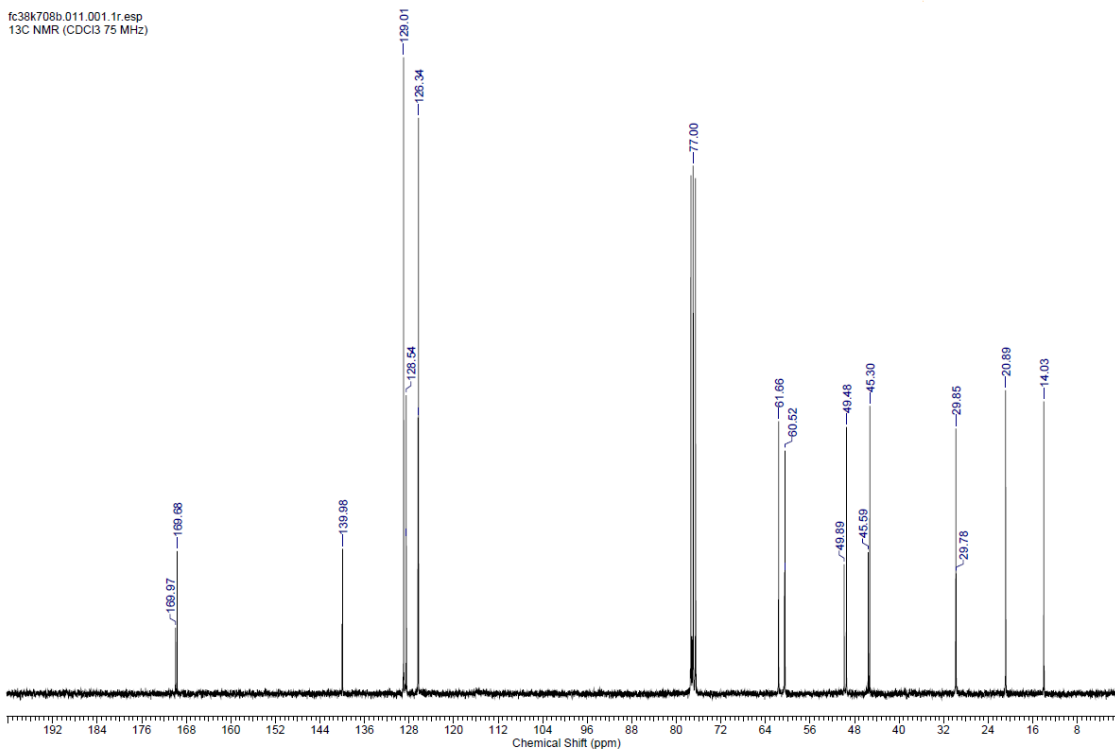
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13C NMR (CDCl3 75 MHz)

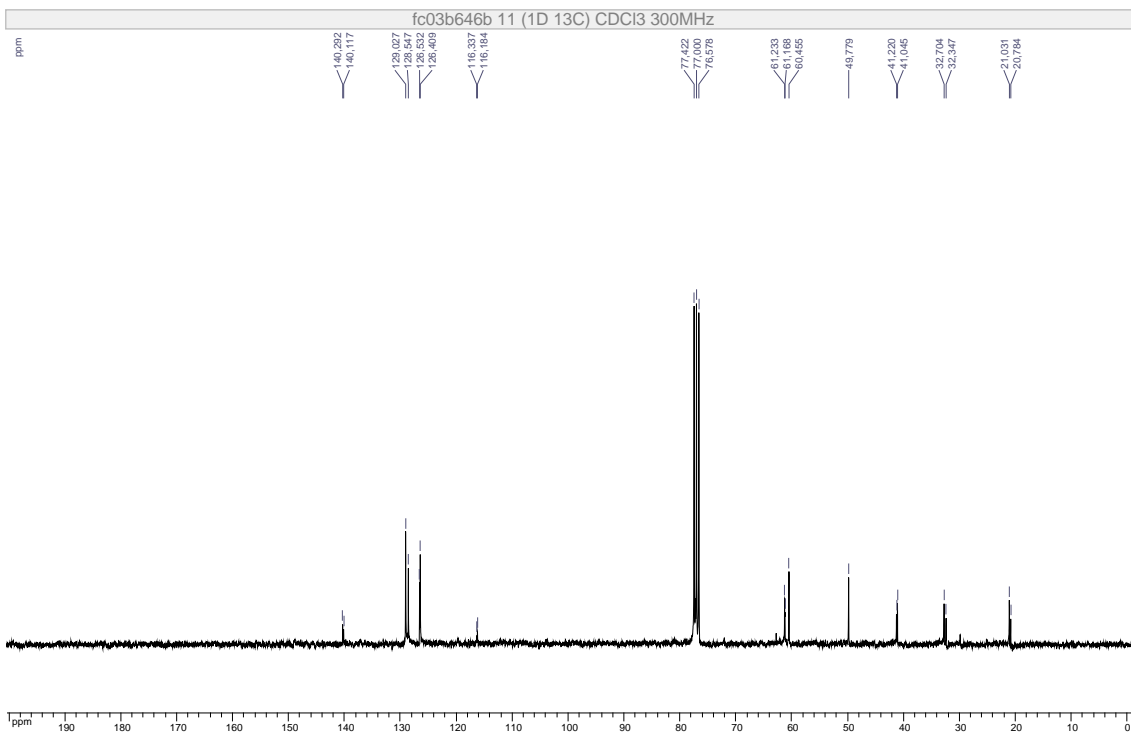
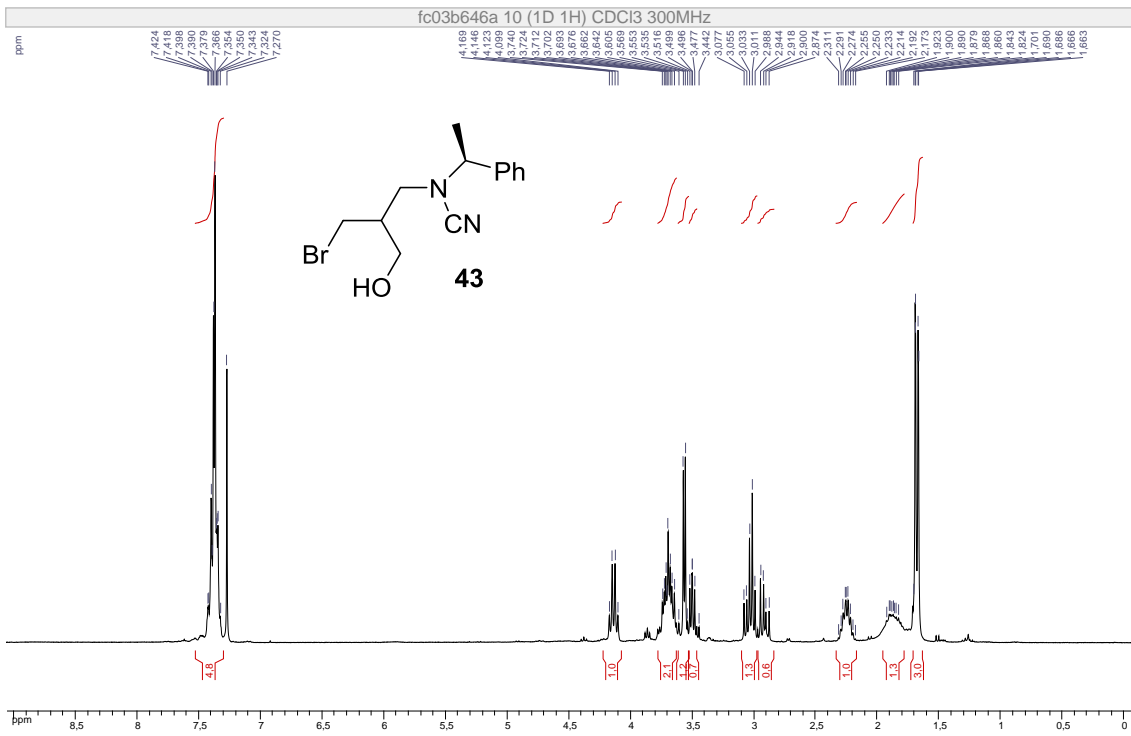


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1H NMR (CDCl3 300 MHz)

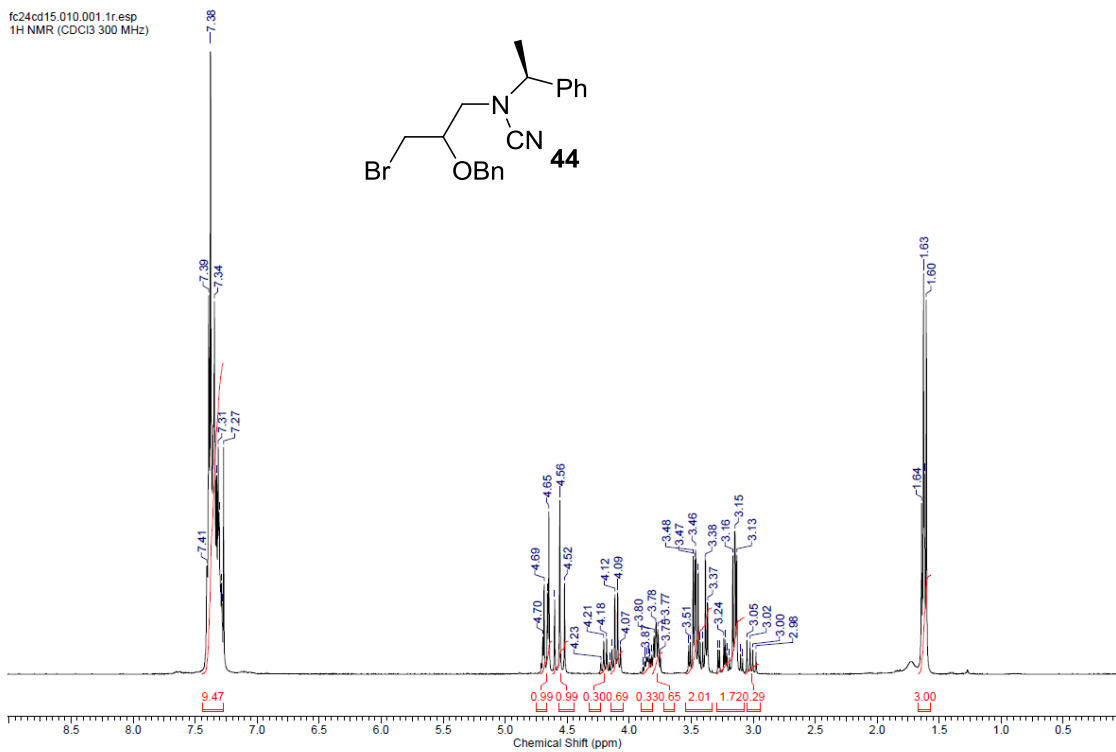
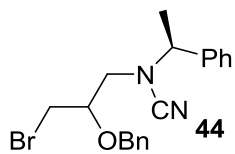


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13C NMR (CDCl3 75 MHz)

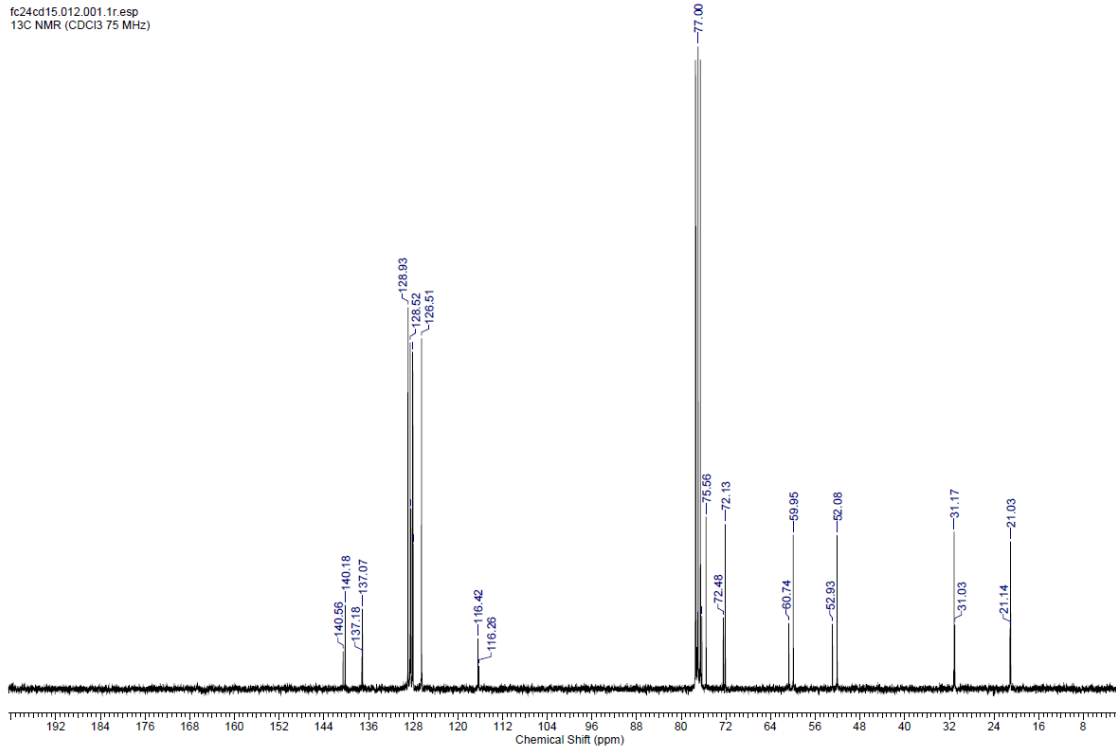




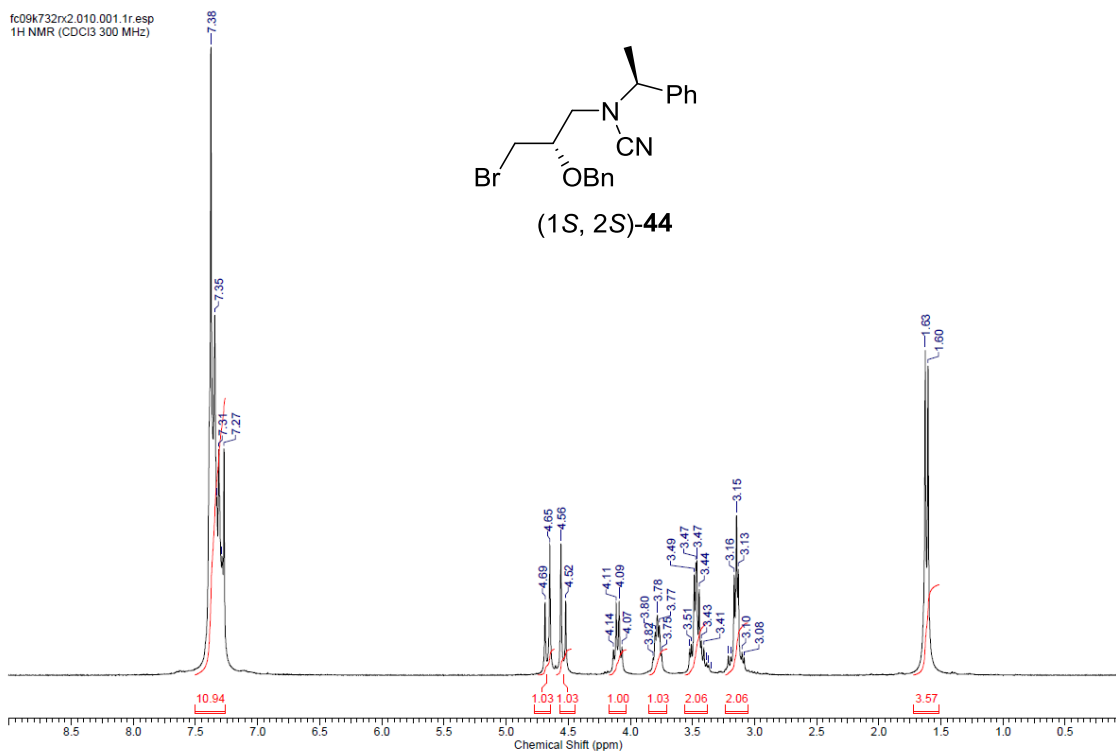
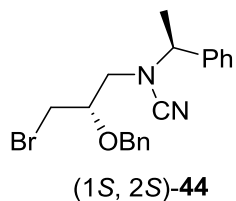
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1H NMR (CDCl3 300 MHz)



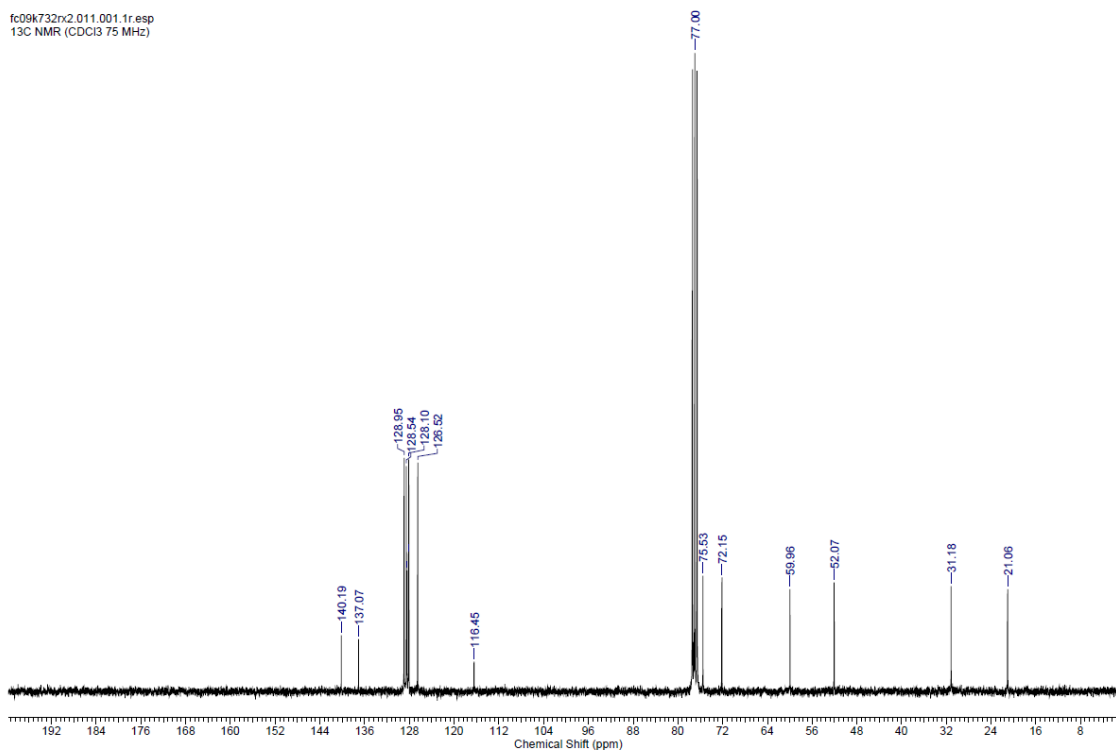
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13C NMR (CDCl3 75 MHz)



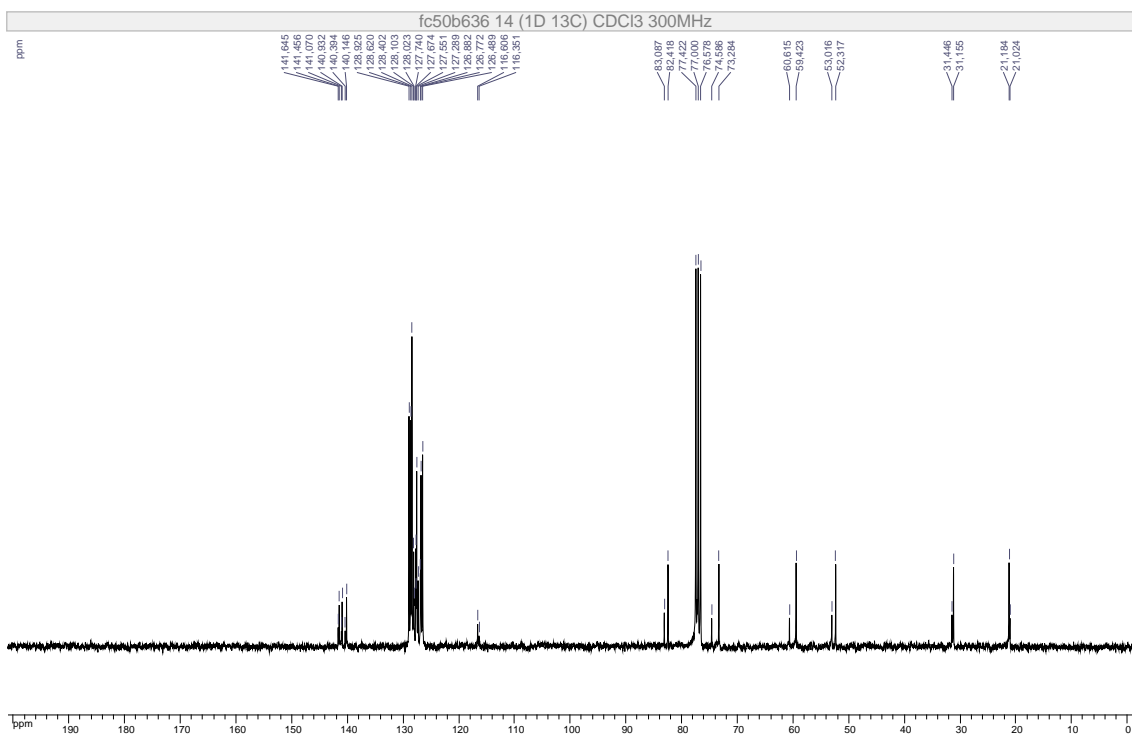
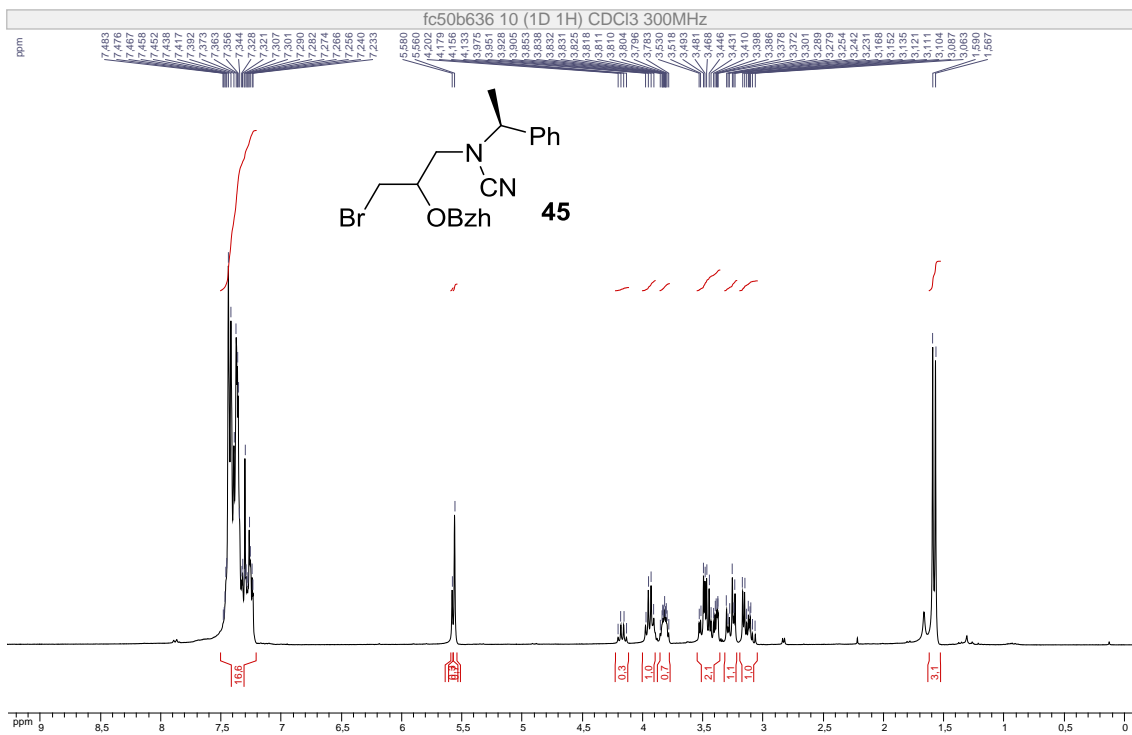
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1H NMR (CDCl3 300 MHz)



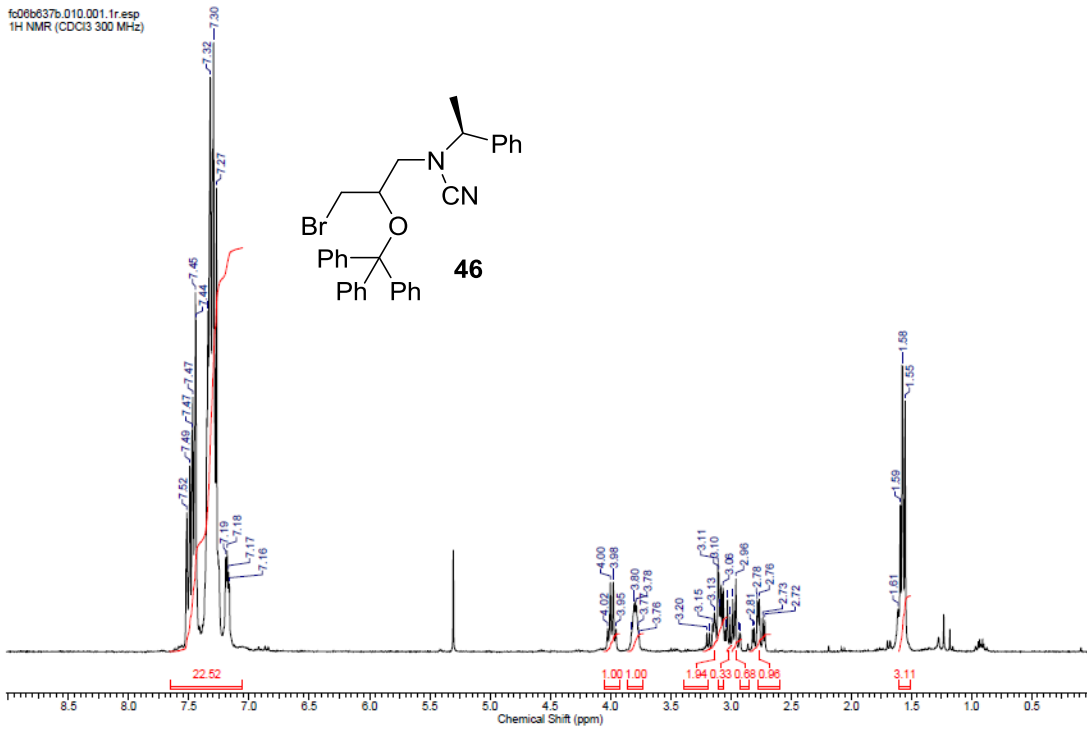
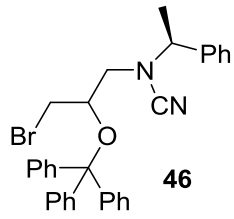
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13C NMR (CDCl3 75 MHz)



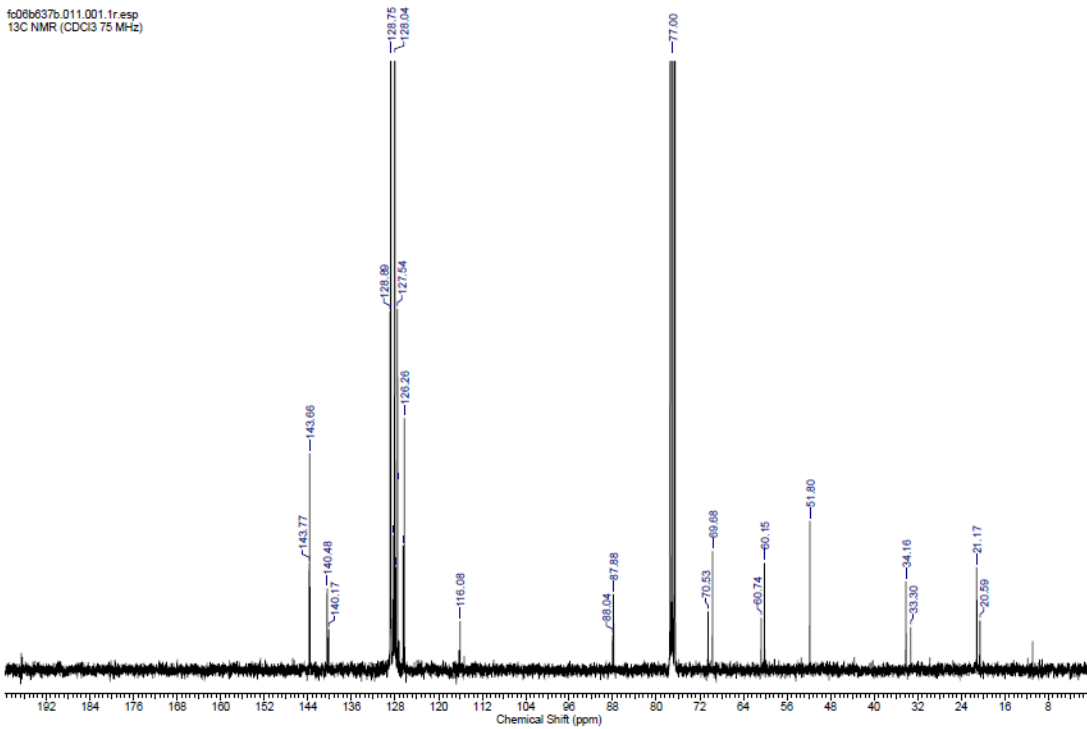


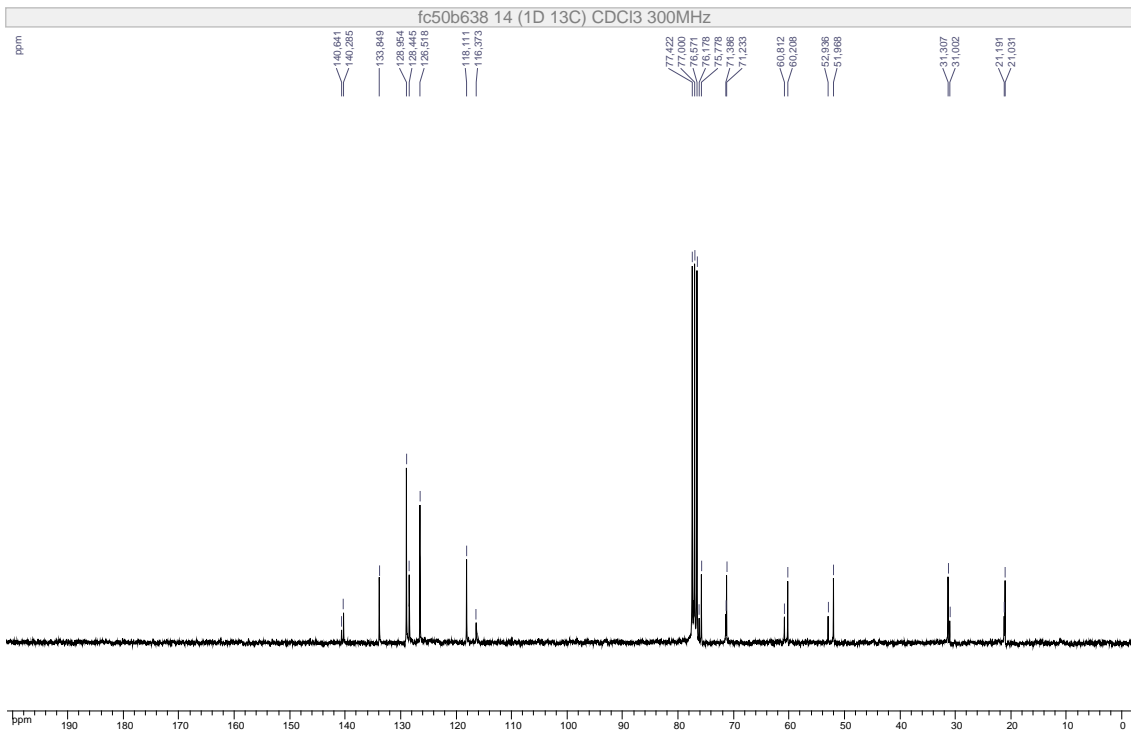
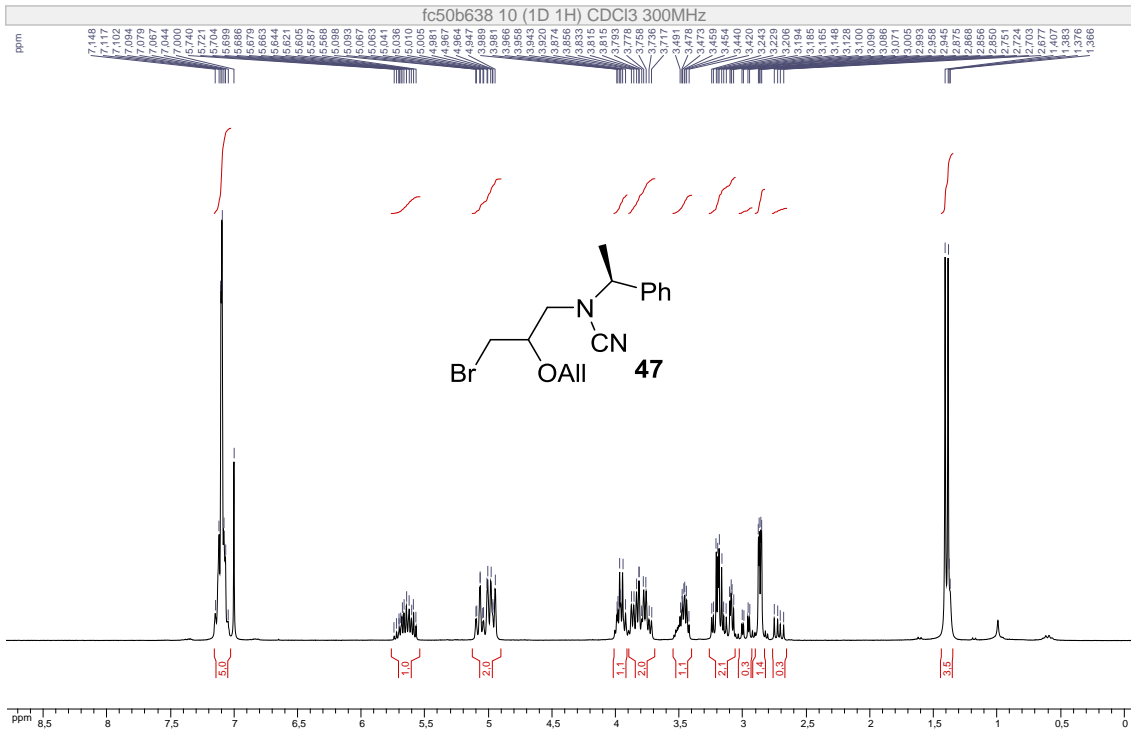


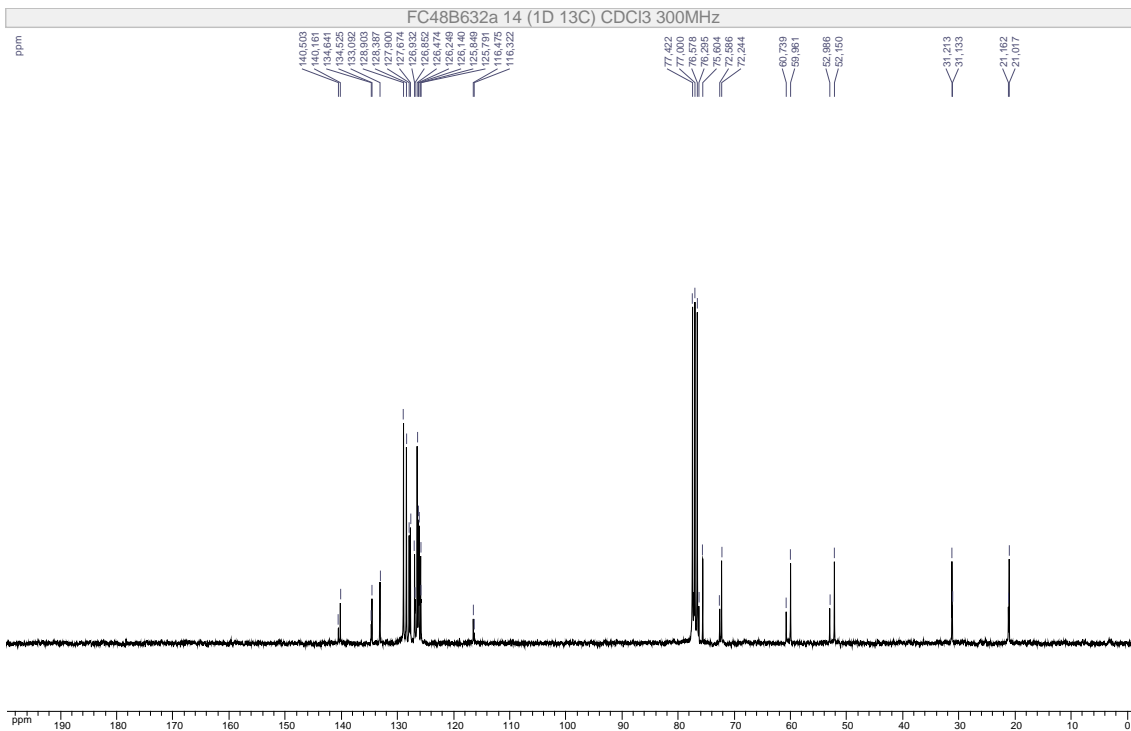
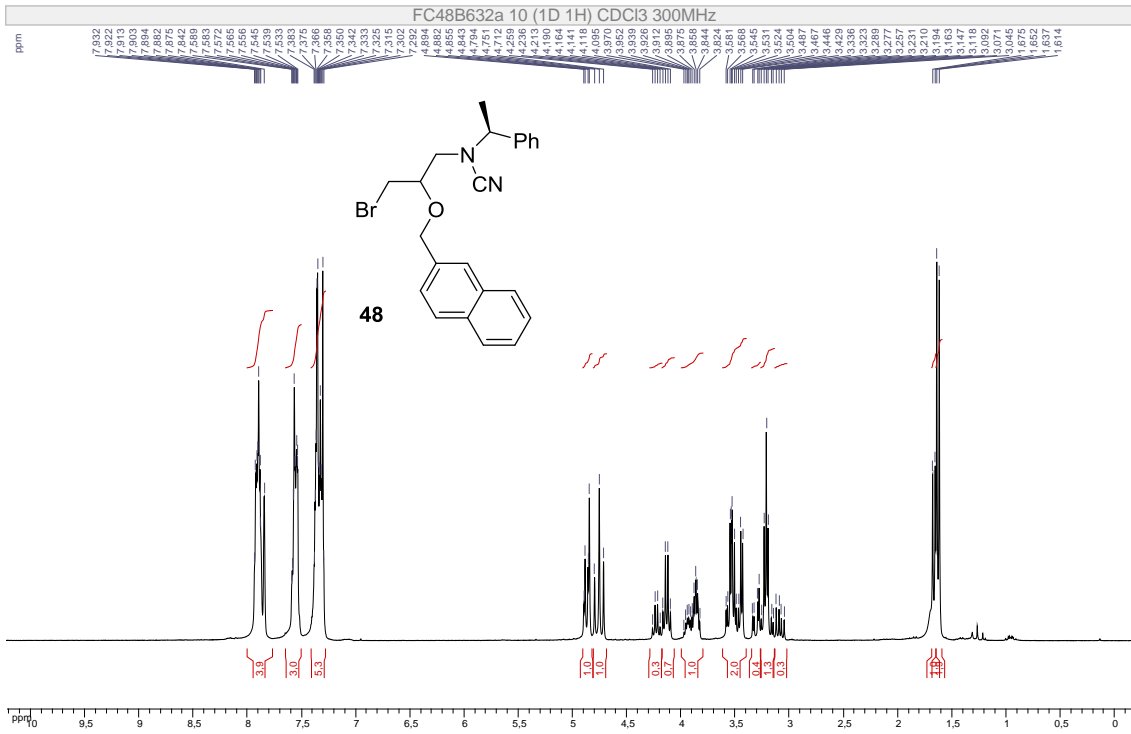
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1H NMR (CDCl3 300 MHz)

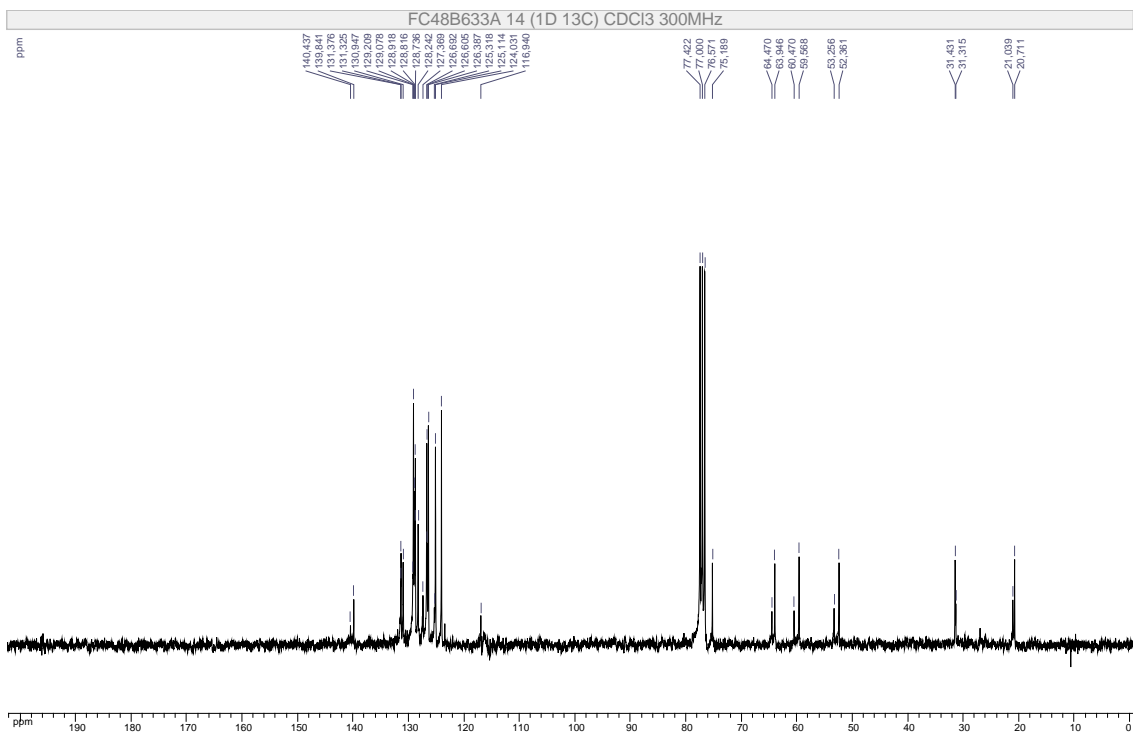
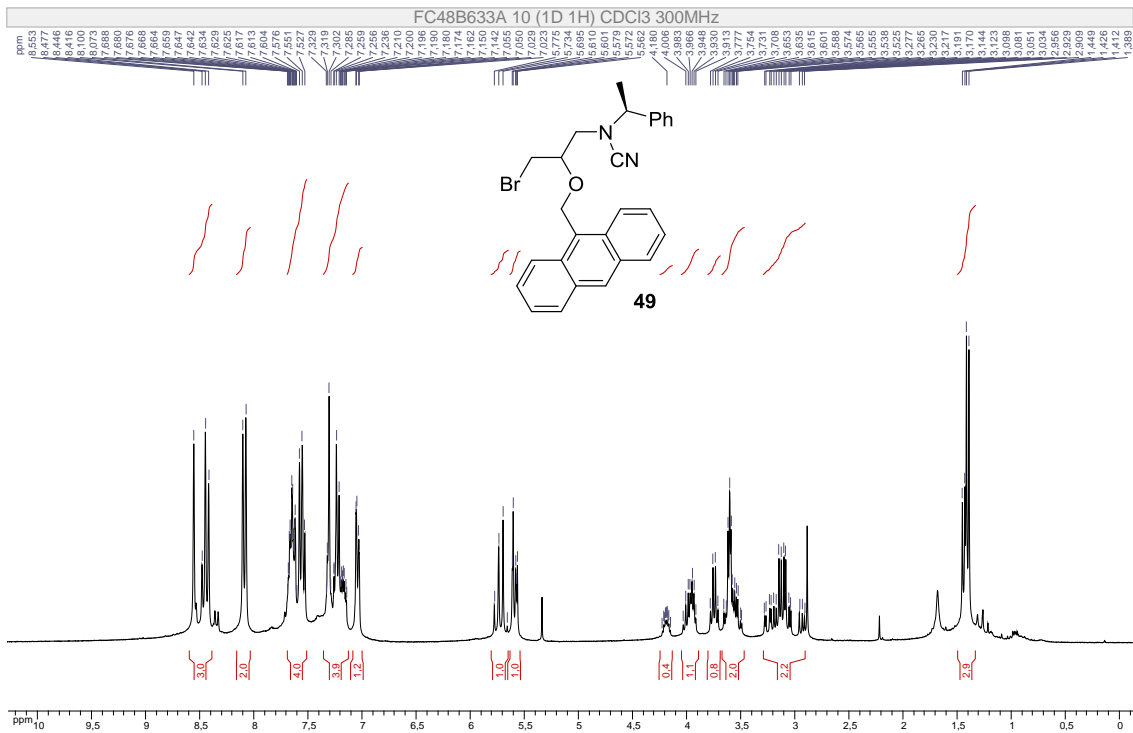


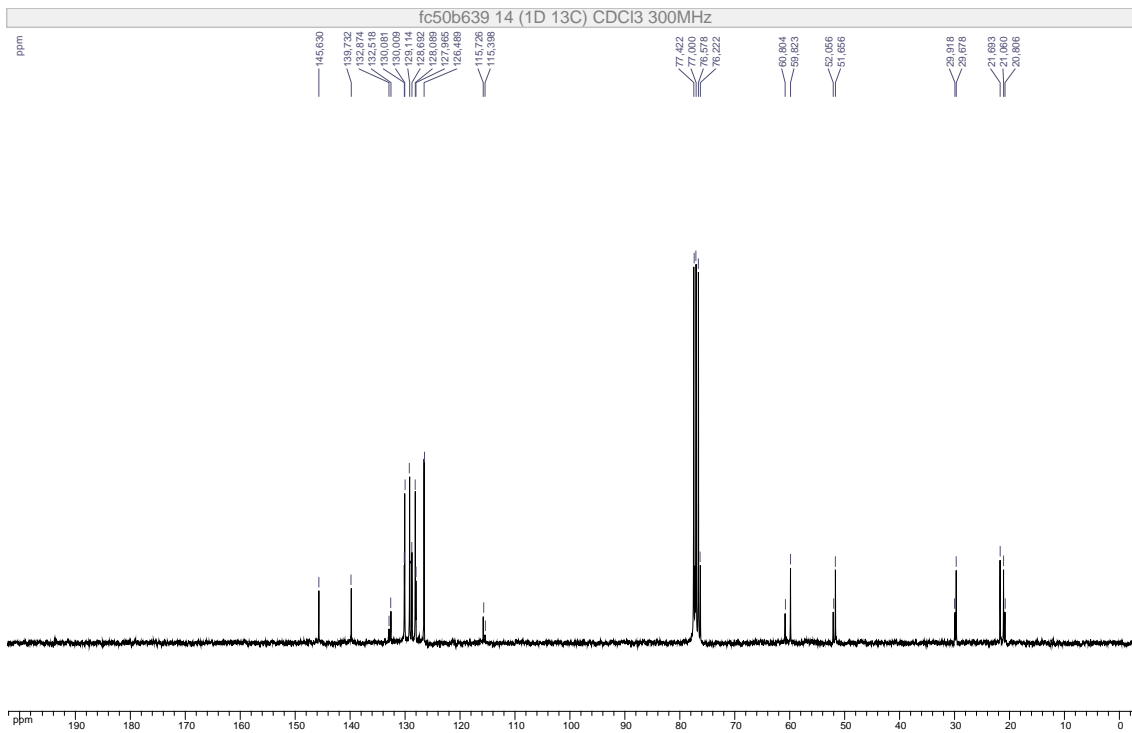
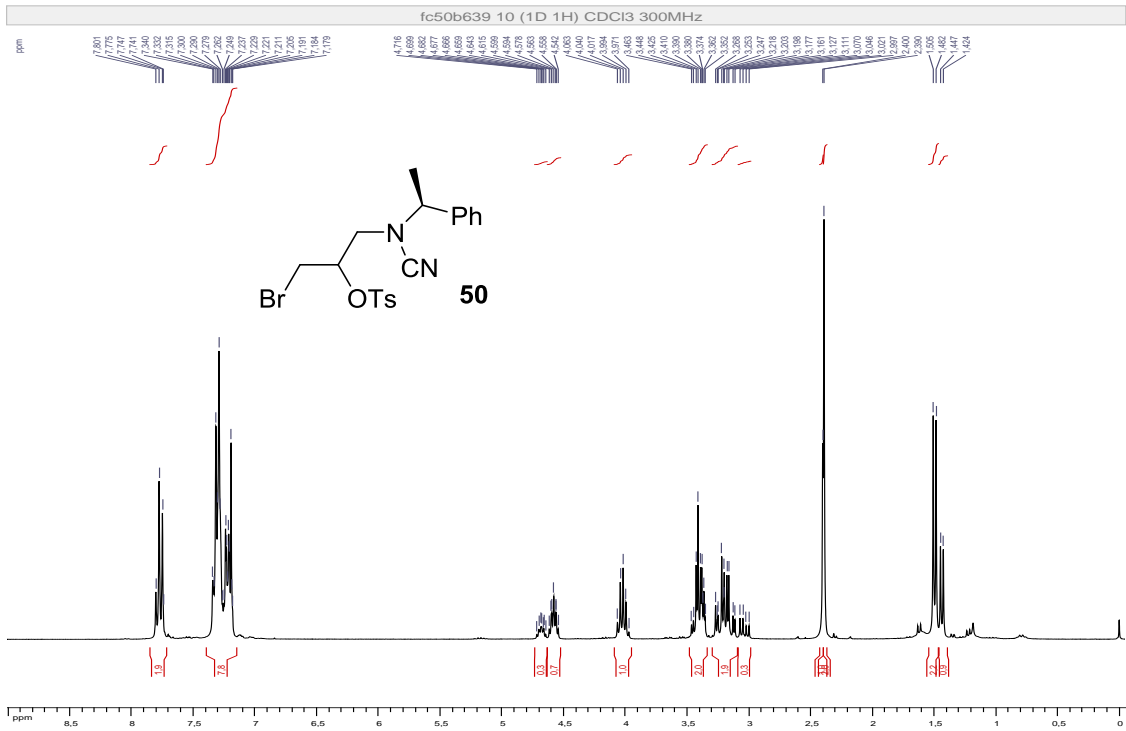
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13C NMR (CDCl3 75 MHz)



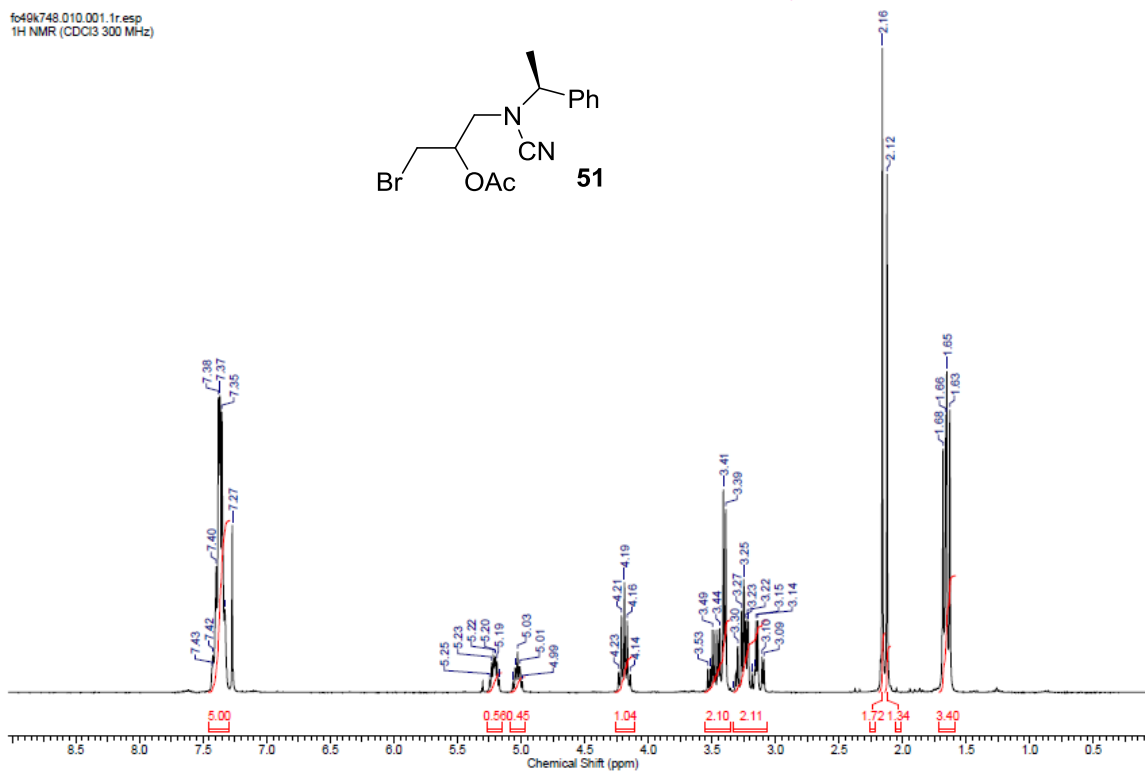
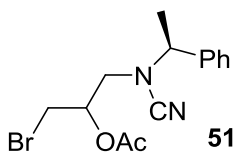




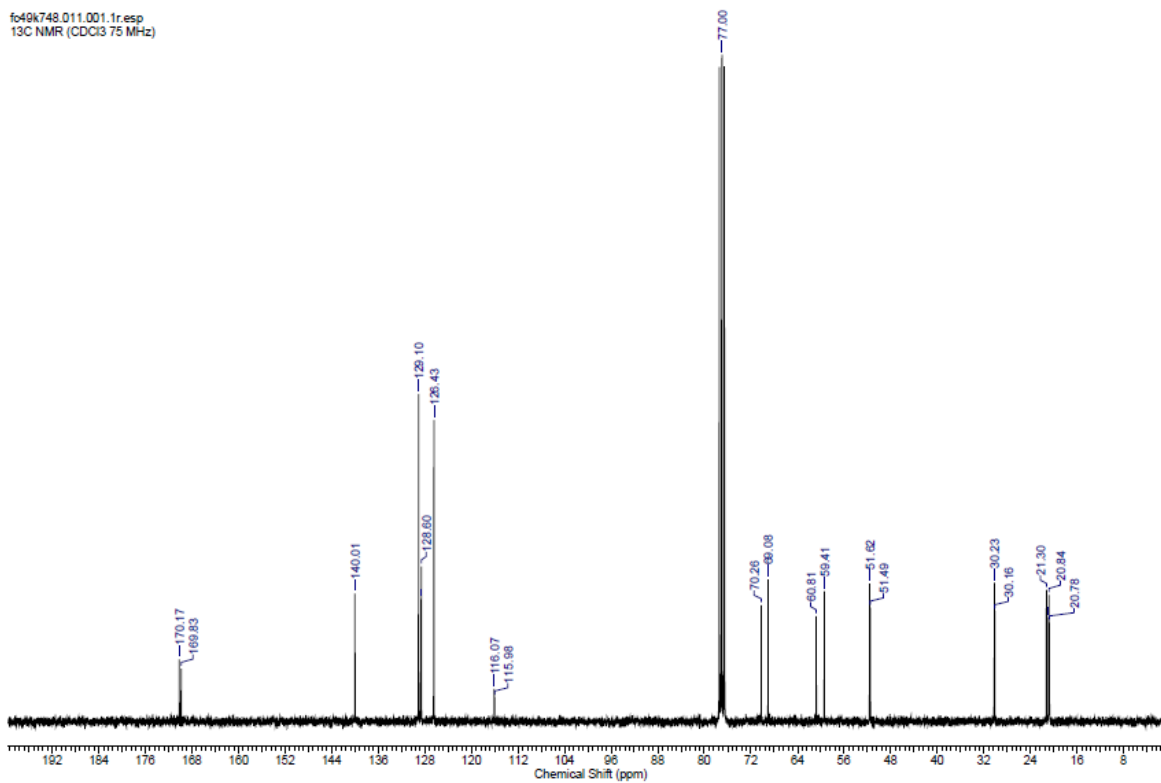


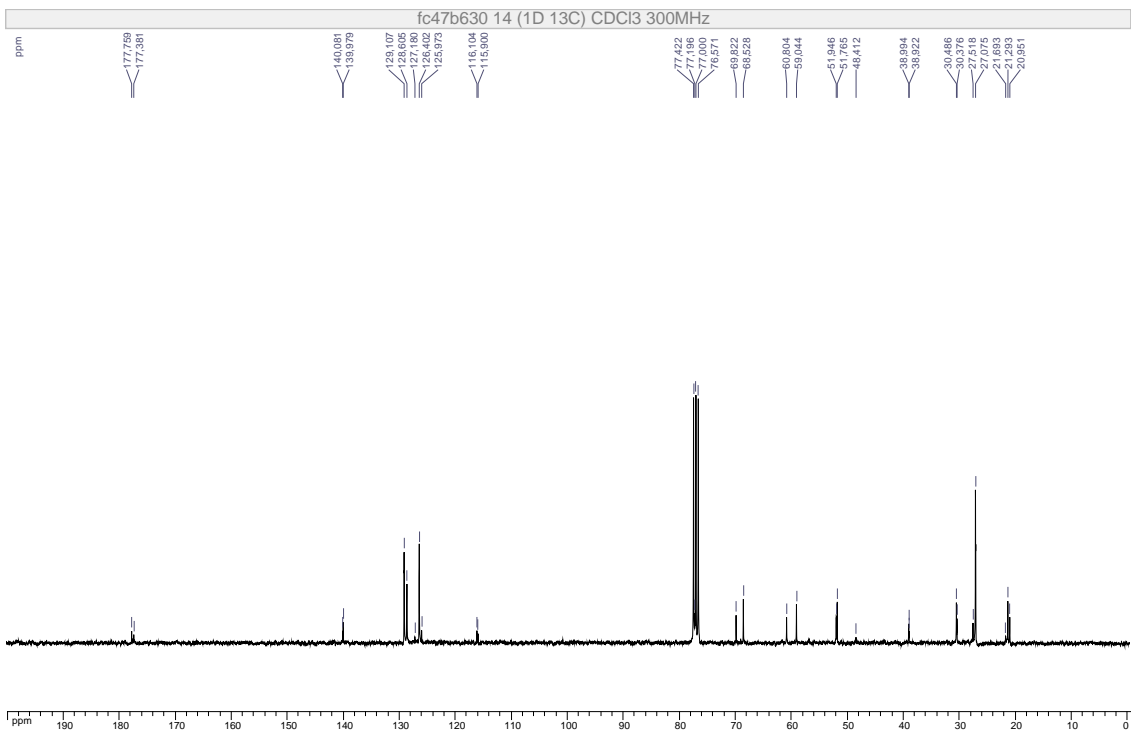
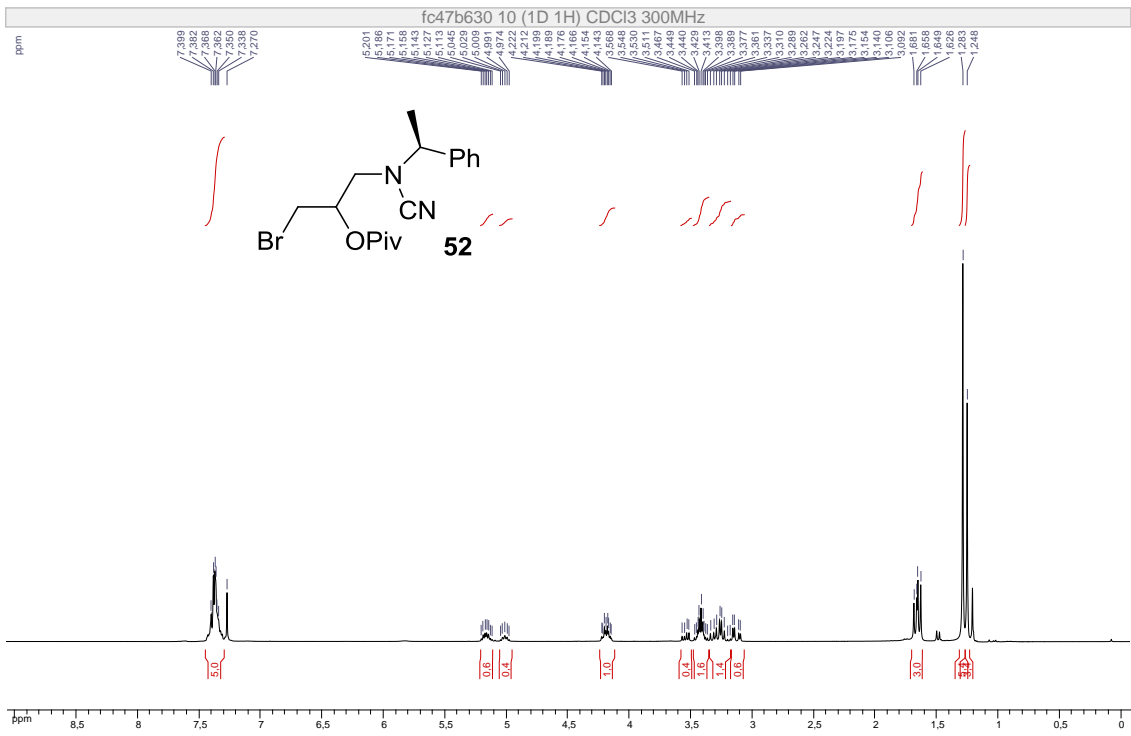


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1H NMR (CDCl3 300 MHz)

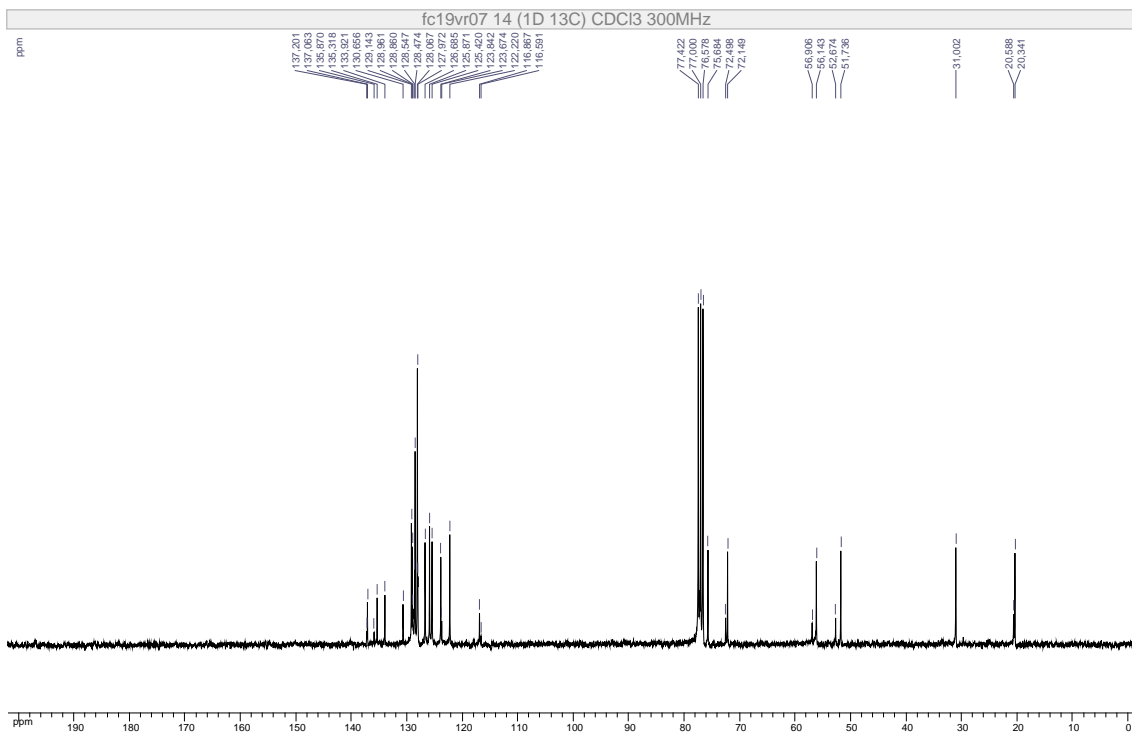
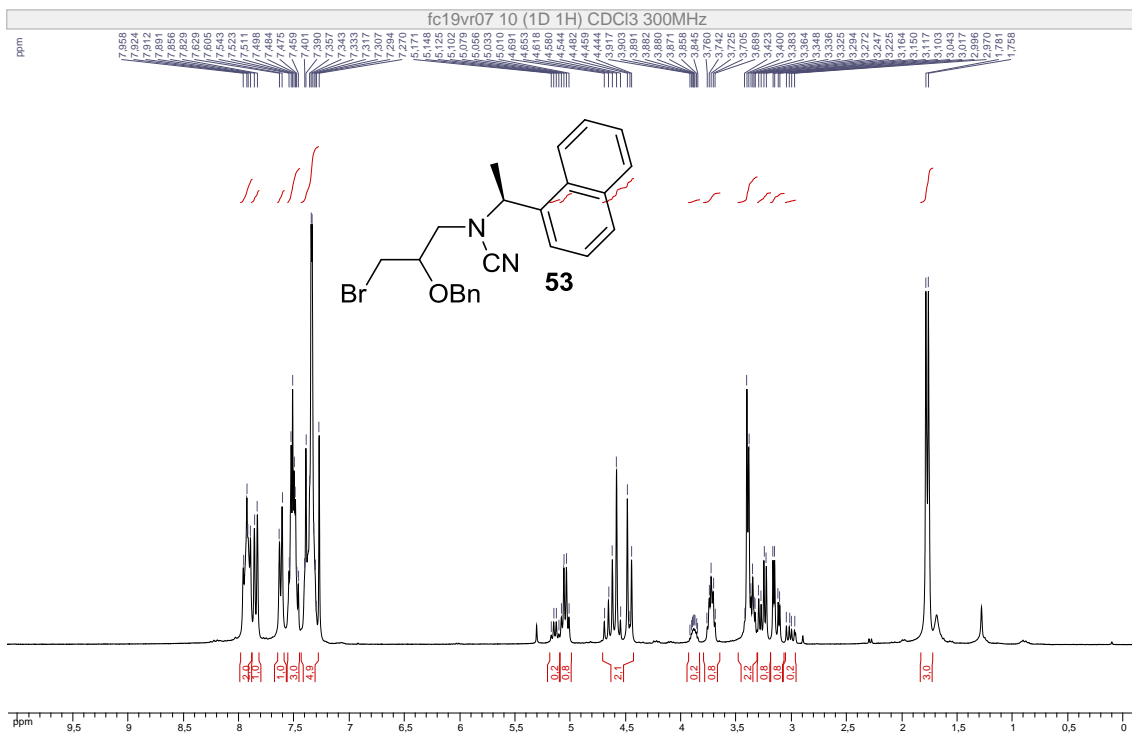


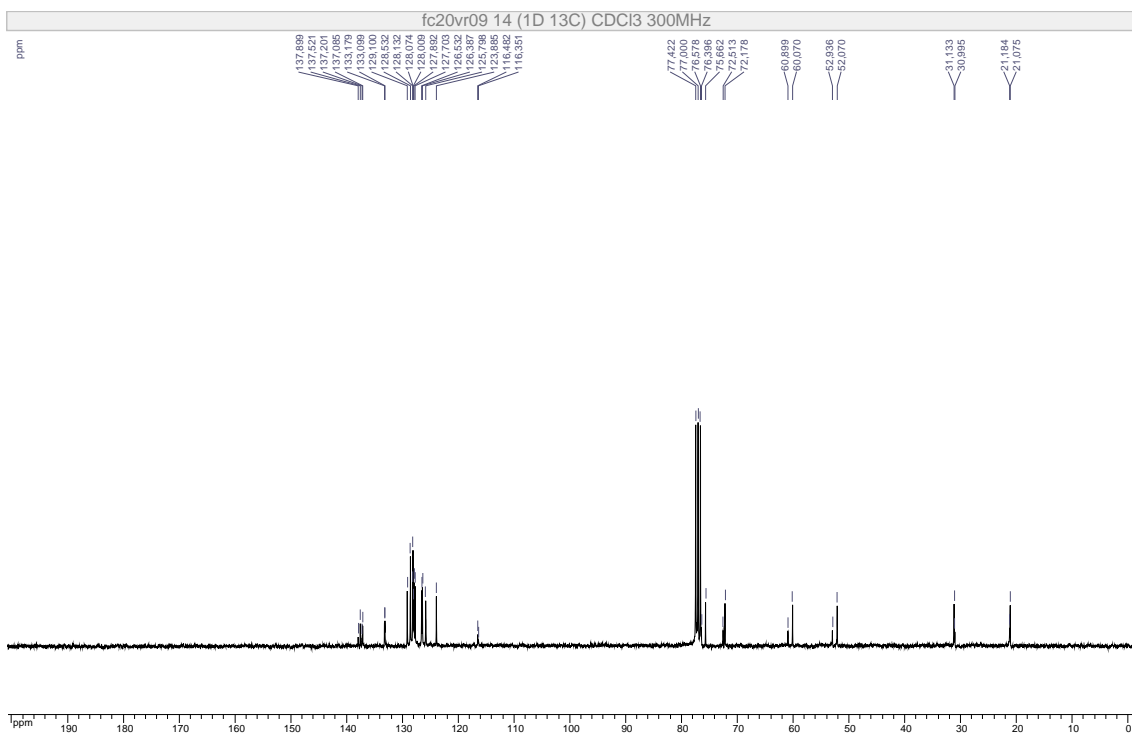
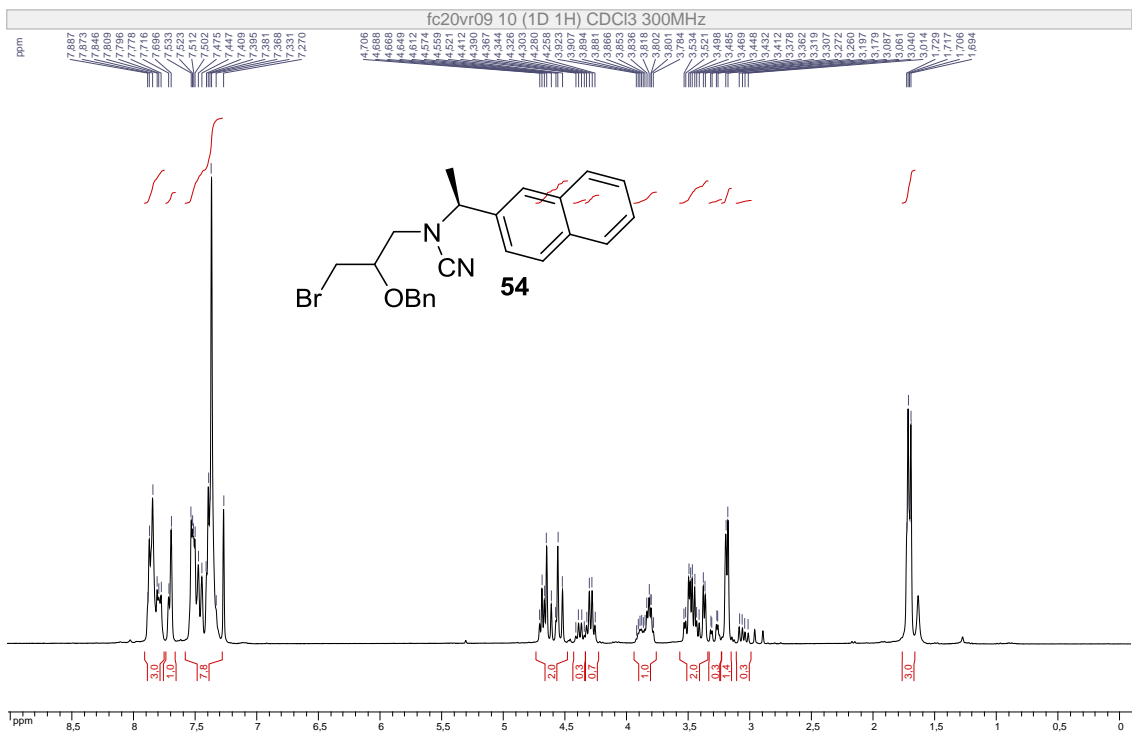
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13C NMR (CDCl3 75 MHz)



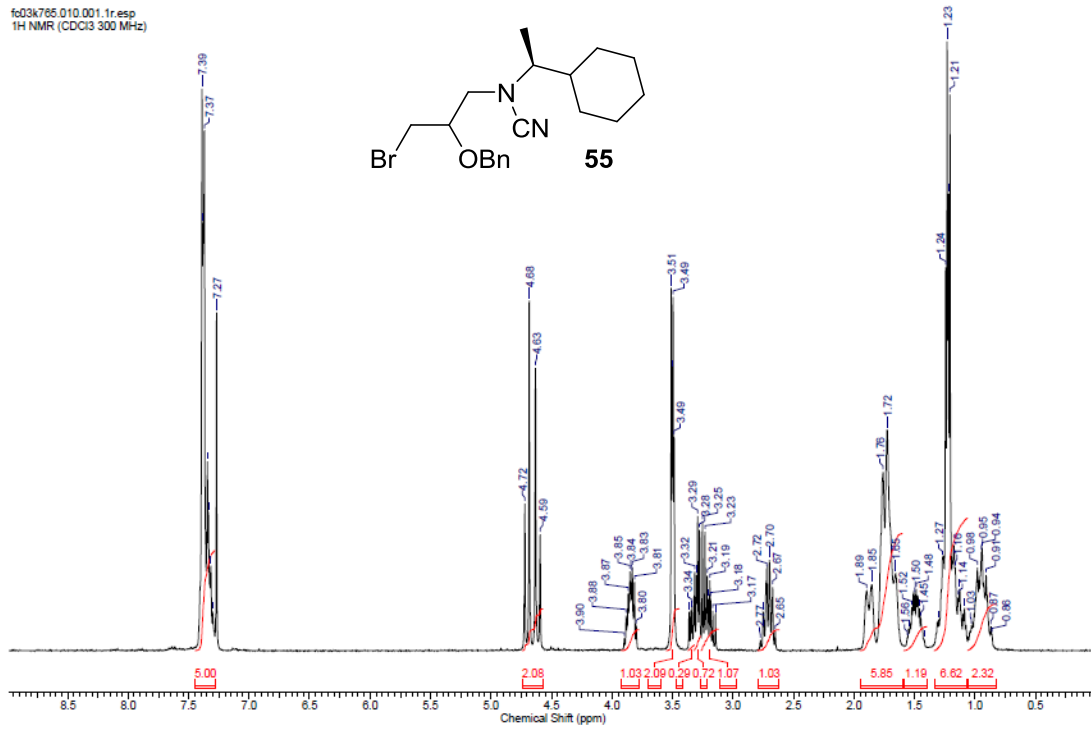
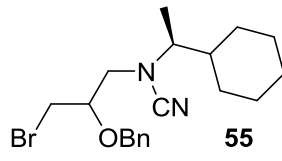




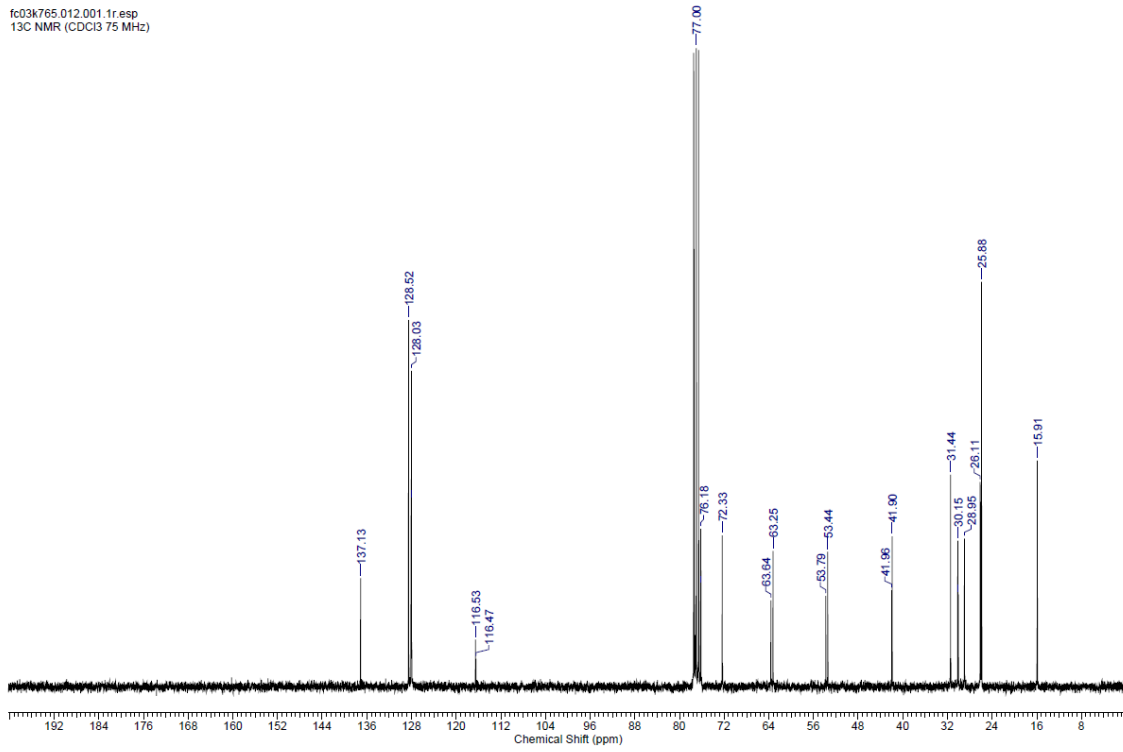


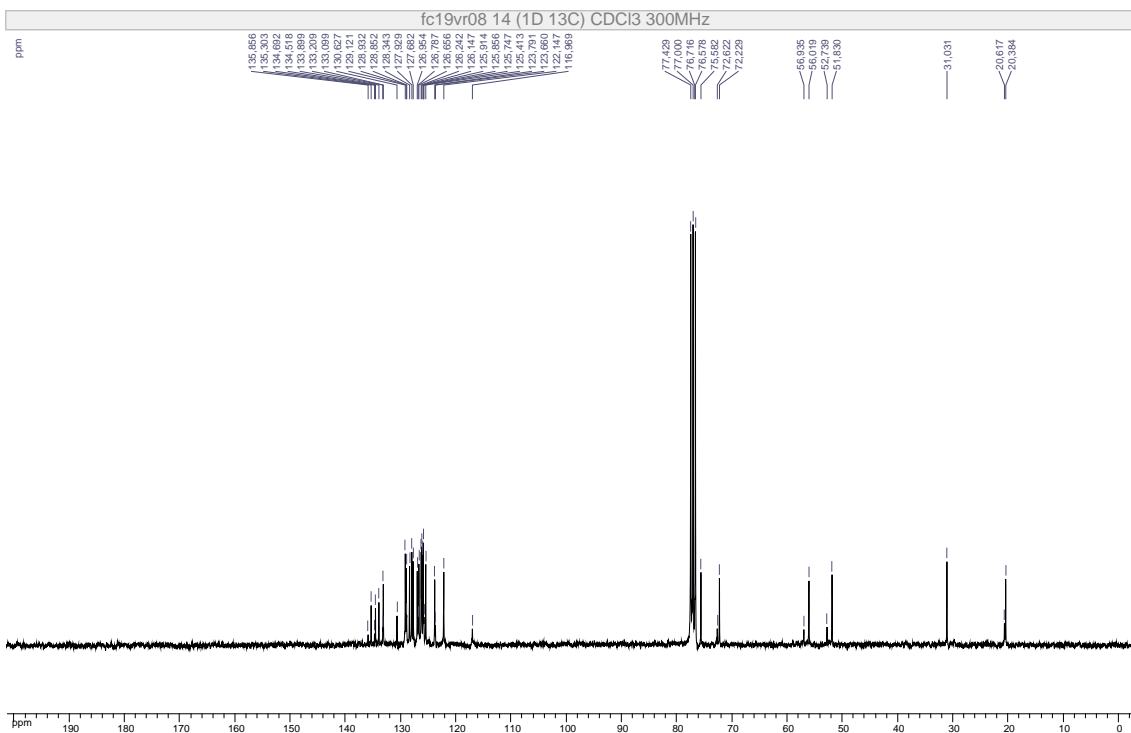
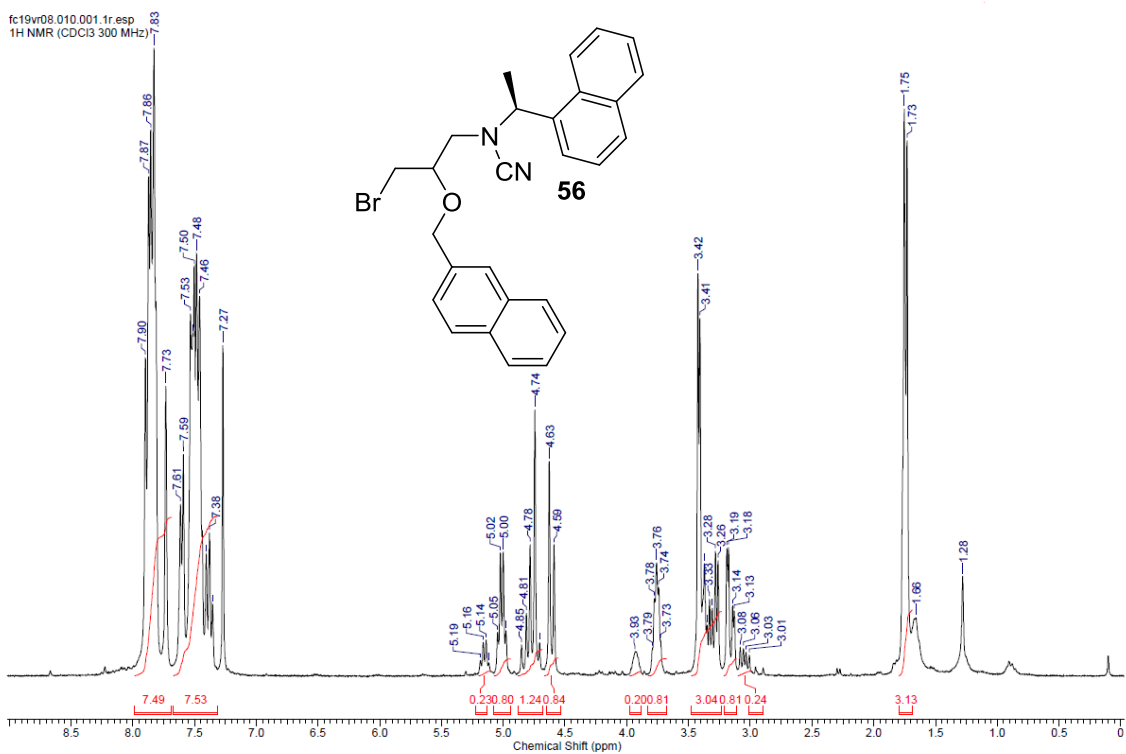


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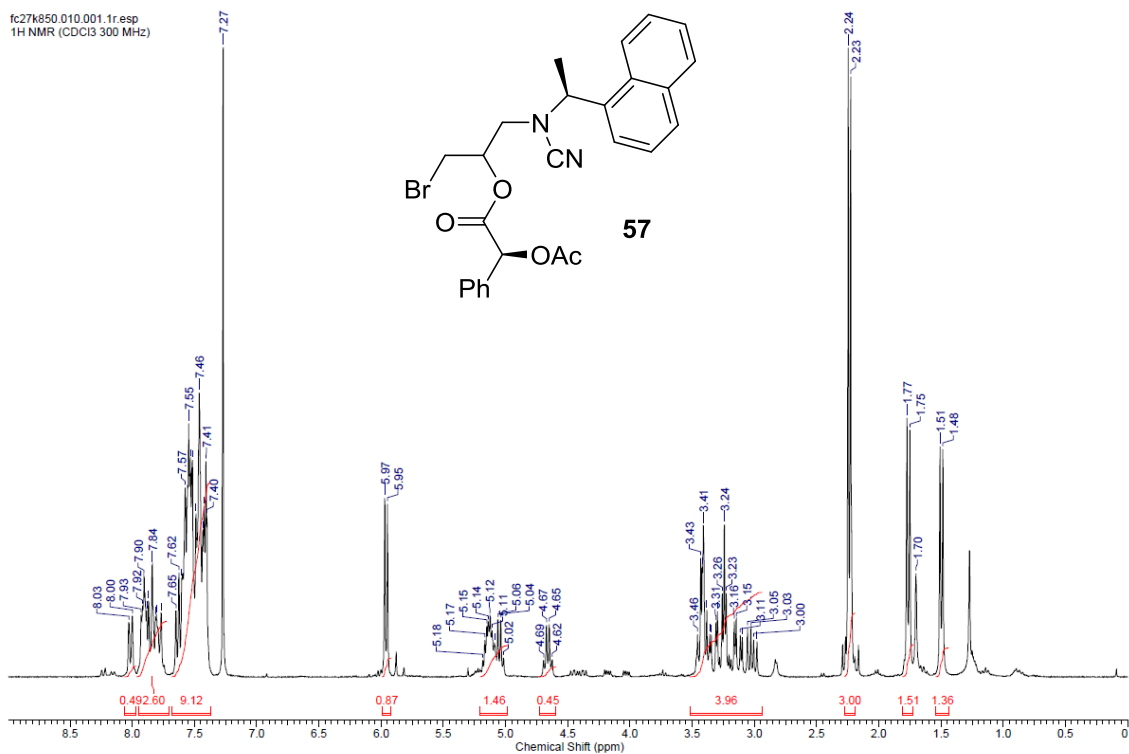


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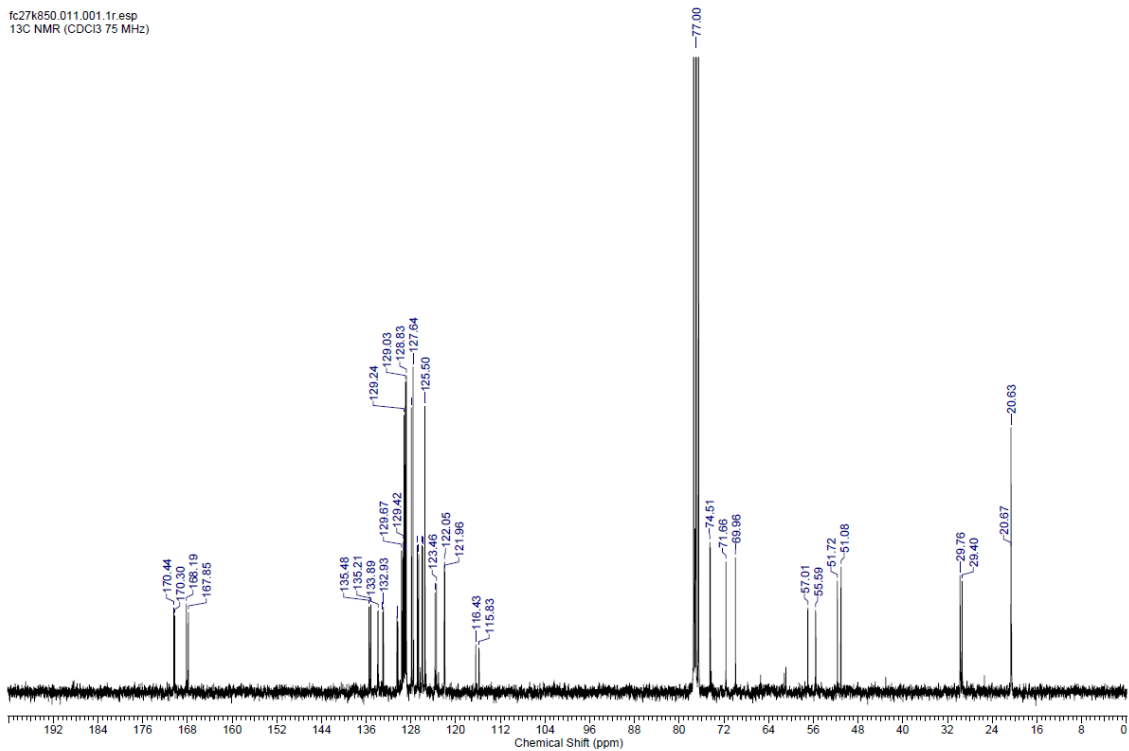




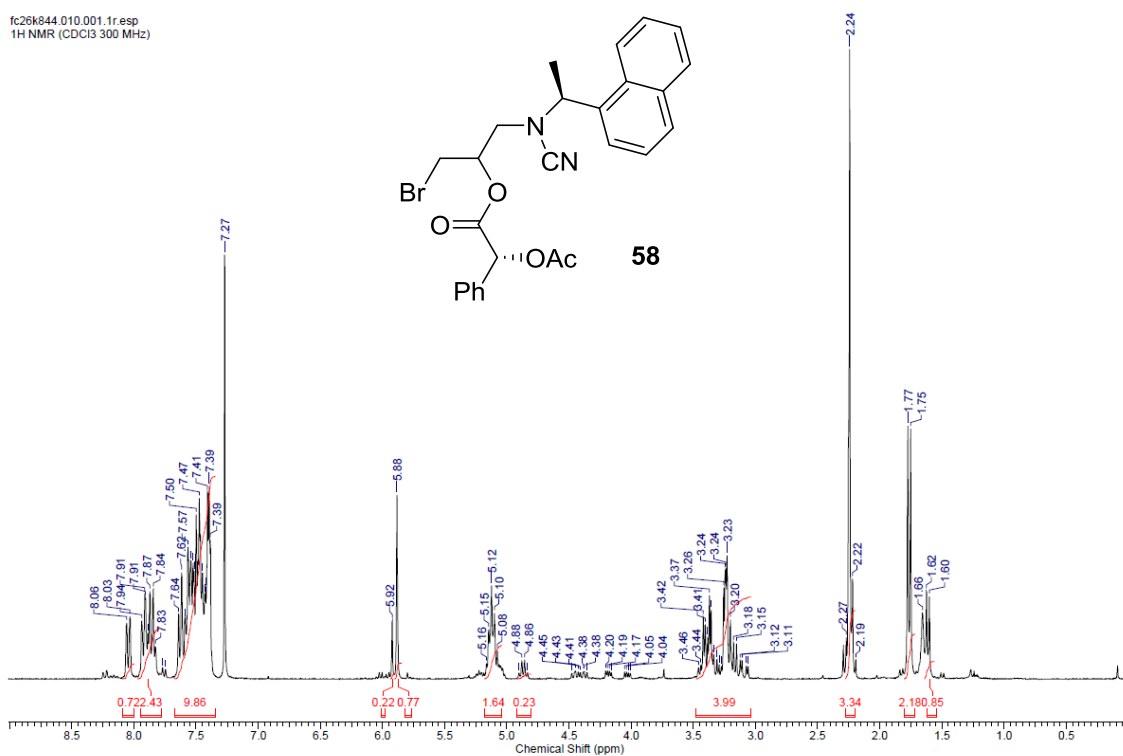
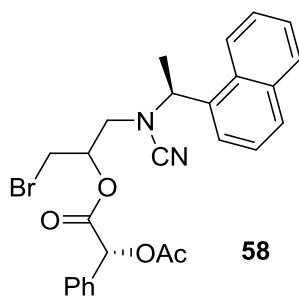
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fc27k850.011.001.1r.esp  
13C NMR (CDCl3 75 MHz)



fc26k844.010.001.1f.esp  
1H NMR (CDCl3 300 MHz)



fc26k844.011.001.1f.esp  
13C NMR (CDCl3 75 MHz)

