

Supporting Information

Cu(OAc)₂-Catalyzed Hydrazination of Cyclopropanols and Late-Stage Transformation to 4,5-Dihydropyrazoles

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1. General Information

All reactions were performed in dry solvents under an N₂ atmosphere and anhydrous conditions. All reagents were used as received from commercial sources. DCM, DMF, THF, and ethyl ether to be used in anhydrous reaction mixtures were dried by passage through activated alumina columns immediately prior to use. Reactions were monitored through thin layer chromatography (TLC) on 0.25-mm silica gel plates and visualized under UV light. Flash column chromatography (FCC) was performed using silica gel (60-Å pore size, 40–63 μm). NMR spectra were recorded Bruker Avance-400 and Bruker Avance-600 instrument, calibrated to CD(H)Cl₃ as the internal reference (7.26 and 77.0 ppm for ¹H and ¹³C NMR spectra, respectively). ¹H NMR spectral data are reported in terms of chemical shift (δ, ppm), multiplicity, coupling constant (Hz), and integration. ¹³C NMR spectral data are reported in terms of chemical shift (δ, ppm). The following abbreviations indicate the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. High-resolution mass spectra were performed on a SCIEX X500R LC-Q-TOF, ESI ion source.

2. Cyclopropanols Preparation

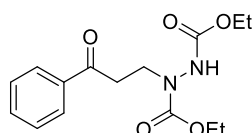
The cyclopropanols were prepared from the corresponding esters or ketones through Kulinkovich or Simmons-Smith reactions.¹

3. Experimental Procedures

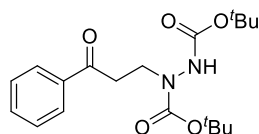
3.1 General Procedure for the Synthesis of the Hydrazine-1,2-dicarboxylates.

The cyclopropanol **3** (0.2 mmol), the **4** (0.24 mmol, 1.2 equiv), Cu(OAc)₂ (4 mg, 0.02 mmol, 0.1 equiv), and toluene (2 mL) were added sequentially to a flame-dried vial (4 mL) and then the reaction mixture was bubbled with nitrogen gas stirred at 50 °C until the starting material **1** was consumed. The solvent was evaporated under reduced pressure and the product was purified through silica gel flash column chromatography (petroleum ether/ethyl acetate 10:1 to 3:1) to yield the desired hydrazine-1,2-dicarboxylates **5a–5x**.

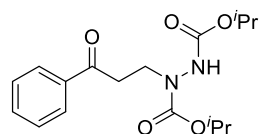
Characterization of the new compounds.



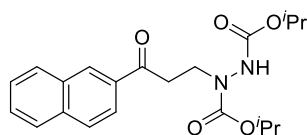
Following the general procedure, **5a** (56.7 mg, 92%) was obtained as a colorless oil ; $R_f = 0.40$ (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 7.97–7.95 (m, 2H), 7.59–7.55 (m, 1H), 7.48–7.44 (m, 2H), 6.99 (s, 1H), 4.20–4.14 (m, 4H), 3.96–3.93 (m, 2H), 3.37 (brs, 2H), 1.28–1.23 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 198.5, 157.0, 156.1, 136.6, 133.3, 128.6, 128.1, 62.4, 62.0, 46.6, 36.7, 14.5, 14.4; HRMS (ESI) Calcd for C₁₅H₂₁N₂O₅ [M + H]⁺ m/z 309.1445, found 309.1445.



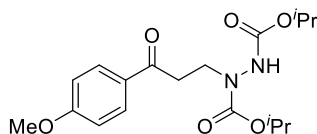
Following the general procedure, **5b** (66.2 mg, 91%) was obtained as a white solid, m. p. 94–97 °C; $R_f = 0.42$ (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 7.99–7.97 (m, 2H), 7.58–7.56 (m, 1H), 7.49–7.46 (m, 2H), 6.52 (s, 1H), 3.91–3.90 (m, 2H), 3.35 (brs, 2H), 1.48–1.47 (m, 18H); ¹³C NMR (100 MHz, CDCl₃) δ 198.8, 155.7, 155.0, 136.7, 133.2, 128.6, 128.1, 81.5, 81.2, 46.1, 36.8, 28.2 ; HRMS (ESI) Calcd for C₁₉H₂₉N₂O₅ [M + H]⁺ m/z 365.2071, found 365.2071.



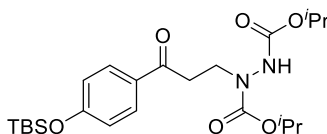
Following the general procedure, **5c** (63.8 mg, 95%) was obtained as a colorless oil ; $R_f = 0.41$ (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 7.97–7.95 (m, 2H), 7.58–7.55 (m, 1H), 7.48–7.44 (m, 2H), 6.65 (s, 1H), 4.94–4.93 (m, 2H), 3.93–3.92 (m, 2H), 3.35 (brs, 2H), 1.32–1.24 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 198.9, 156.0, 155.6, 136.6, 133.3, 128.6, 128.1, 69.8, 46.5, 36.8, 29.7, 22.0, 21.9; HRMS (ESI) Calcd for C₂₁H₂₇N₂O₅ [M + H]⁺ m/z 387.1915, found 387.1918.



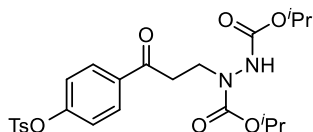
Following the general procedure, **5f** (72.0 mg, 94%) was obtained as a colorless oil ; $R_f = 0.42$ (petroleum ether/EtOAc, 3:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.49 (s, 1H), 8.04–8.01 (m, 2H), 7.97–7.96 (m, 1H), 7.90–7.86 (m, 2H), 7.62–7.54 (m, 2H), 6.81 (s, 1H), 4.99–4.94 (m, 2H), 4.03–3.99 (m, 2H), 3.51 (brs, 2H), 1.27–1.25 (m, 12H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 198.9, 156.4, 155.7, 135.7, 134.0, 132.5, 129.9, 129.6, 128.6, 128.5, 127.8, 126.8, 123.7, 70.0, 46.7, 36.8, 29.7, 22.1, 22.0; HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{27}\text{N}_2\text{O}_5$ $[\text{M} + \text{H}]^+$ m/z 387.1915, found 387.1906.



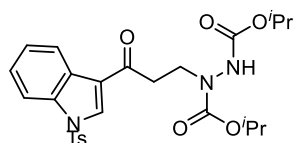
Following the general procedure, **5g** (67.3 mg, 92%) was obtained as a colorless oil ; $R_f = 0.25$ (petroleum ether/EtOAc, 3:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.95–7.93 (m, 2H), 6.94–6.92 (m, 2H), 6.76 (s, 1H), 4.93 (brs, 2H), 3.92 (brs, 2H), 3.87 (s, 3H), 3.30 (brs, 2H), 1.25–1.24 (m, 12H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 197.5, 163.6, 156.0, 155.6, 130.4, 113.8, 70.0, 55.5, 46.7, 36.4, 29.7, 22.0 (2C); HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{27}\text{N}_2\text{O}_5$ $[\text{M} + \text{H}]^+$ m/z 367.1864, found 367.1866.



Following the general procedure, **5h** (46.0 mg, 50%) was obtained as a colorless oil ; $R_f = 0.55$ (petroleum ether/EtOAc, 3:1); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.88–7.87 (m, 2H), 6.86–6.85 (m, 2H), 6.68 (s, 1H), 4.93–4.92 (m, 2H), 3.90 (brs, 2H), 3.28 (brs, 2H), 1.24–1.22 (m, 12H), 0.97 (s, 9H), 0.23 (s, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 197.6, 160.5, 156.0, 155.6, 130.3 (2C), 120.0, 77.3, 70.0, 46.7, 36.4, 25.6, 22.1, 22.0, 18.3, -4.4; HRMS (ESI) Calcd for $\text{C}_{23}\text{H}_{39}\text{N}_2\text{O}_6\text{Si}$ $[\text{M} + \text{H}]^+$ m/z 467.2572, found 467.2562.

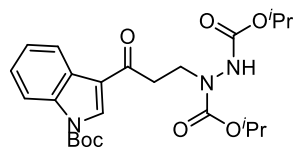


Following the general procedure, **5i** (46.1 mg, 55%) was obtained as a colorless oil ; $R_f = 0.41$ (petroleum ether/EtOAc, 3:1); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.92–7.90 (m, 2H), 7.72–7.71 (m, 2H), 7.34–7.33 (m, 2H), 7.10–7.09 (m, 2H), 6.66 (s, 1H), 4.94 (brs, 2H), 3.93–3.90 (m, 2H), 3.33 (brs, 2H), 2.47 (s, 3H), 1.26–1.24 (m, 12H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 197.5, 156.0, 155.5, 153.1, 145.8, 135.2, 132.1, 129.9, 129.8, 128.5, 122.6, 69.9, 46.4, 36.8, 29.7, 22.0, 21.9, 21.7; HRMS (ESI) Calcd for $\text{C}_{24}\text{H}_{31}\text{N}_2\text{O}_8\text{S}$ $[\text{M} + \text{H}]^+$ m/z 420.1270, found 420.1283.

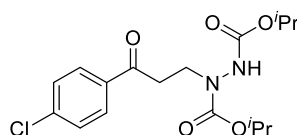


Following the general procedure, **5j** (52.0 mg, 49%) was obtained as a yellow oil ; $R_f = 0.35$ (petroleum ether/EtOAc, 3:1); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.32–8.30 (m, 2H), 7.95–7.93 (m,

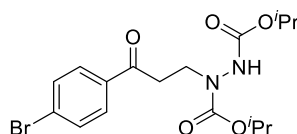
1H), 7.86–7.85 (m, 2H), 7.38–7.32 (m, 2H), 7.29–7.27 (m, 2H), 6.79 (s, 1H), 4.99–4.93 (m, 2H), 3.98–3.96 (m, 2H), 3.29 (brs, 2H), 2.36 (s, 3H), 1.25–1.24 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 194.5, 155.9, 155.6, 145.9, 134.9, 134.5, 132.3, 130.3, 127.5, 127.2, 125.8, 124.9, 123.0, 121.0, 113.1, 69.9, 68.5, 46.5, 38.1, 22.0 (2C), 21.6; HRMS (ESI) Calcd for C₂₆H₃₂N₃O₇S [M + H]⁺ *m/z* 530.1956, found 530.1950.



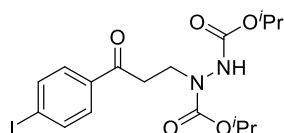
Following the general procedure, **5k** (78.9 mg, 83%) was obtained as a white solid, m.p. 71~73 °C; *R_f* = 0.35 (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 8.36–8.35 (m, 1H), 8.28 (s, 1H), 8.15–8.13 (m, 1H), 7.40–7.33 (m, 2H), 6.79 (s, 1H), 4.96–4.95 (m, 2H), 3.98 (brs, 2H), 3.27 (brs, 2H), 1.72 (s, 9H), 1.27–1.25 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 194.9, 155.9, 155.6, 149.0, 135.6, 132.3, 127.3, 125.5, 124.4, 122.6, 120.0, 115.0, 85.5, 70.0, 69.8, 46.6, 38.0, 28.1, 22.0 (2C); HRMS (ESI) Calcd for C₂₄H₃₄N₃O₇ [M + H]⁺ *m/z* 476.2392, found 476.2403.



Following the general procedure, **5l** (66.2 mg, 80%) was obtained as a colorless oil; *R_f* = 0.38 (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 7.93–7.91 (m, 2H), 7.46–7.44 (m, 2H), 6.65 (s, 1H), 4.95 (brs, 2H), 3.94 (brs, 2H), 3.35 (brs, 2H), 1.27–1.26 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 197.6, 156.0, 155.5, 139.7, 134.9, 129.5, 129.0, 69.9, 46.5, 36.8, 29.7, 22.0 (2C); HRMS (ESI) Calcd for C₁₇H₂₄N₂O₅Cl [M + H]⁺ *m/z* 371.1368, found 371.1362.

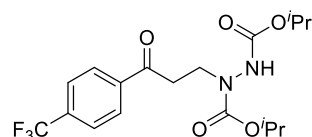


Following the general procedure, **5m** (62.9 mg, 76%) was obtained as a colorless oil; *R_f* = 0.38 (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 7.82–7.80 (m, 2H), 7.60–7.58 (m, 2H), 6.77 (s, 1H), 4.95–4.91 (m, 2H), 3.93–3.90 (m, 2H), 3.32 (brs, 2H), 1.24–1.23 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 197.8, 156.0, 155.5, 135.3, 132.0, 129.6, 128.5, 70.0, 46.4, 36.7, 29.7, 22.0, 21.9; HRMS (ESI) Calcd for C₁₇H₂₄N₂O₅ [M + H]⁺ *m/z* 415.0863, found 415.0854.

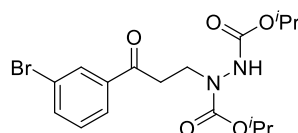


Following the general procedure, **5n** (60.1 mg, 65%) was obtained as a colorless oil; *R_f* = 0.38 (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 7.83–7.81 (m, 2H), 7.67–7.65 (m, 2H), 6.72 (s, 1H), 4.93 (brs, 2H), 3.93–3.90 (m, 2H), 3.31 (brs, 2H), 1.25–1.24 (m, 12H); ¹³C

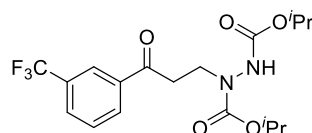
NMR (100 MHz, CDCl₃) δ 198.2, 156.0, 155.5, 138.0, 135.9, 129.5, 101.3, 70.1, 69.9, 46.4, 36.7, 22.0 (2C); HRMS (ESI) Calcd for C₁₇H₂₄N₂O₅I [M + H]⁺ m/z 463.0725, found 463.0722.



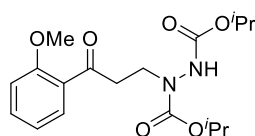
Following the general procedure, **5o** (52.5 mg, 65%) was obtained as a colorless oil ; R_f = 0.41 (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 8.22 (brs, 1H), 8.17–8.15 (m, 1H), 7.84–7.83 (m, 1H), 7.65–7.61 (m, 1H), 6.68 (s, 1H), 4.94 (brs, 2H), 3.98–3.95 (m, 2H), 3.40 (brs, 2H), 1.26–1.25 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 197.5, 156.0, 155.5, 137.1, 131.5, 131.3, 131.2, 130.8, 129.6, 129.4, 124.9 (2C), 124.8, 122.3, 77.2, 70.0, 46.3, 36.9, 22.0, 21.9; ¹⁹F (376 MHz, CDCl₃) δ -62.8; HRMS (ESI) Calcd for C₁₈H₂₄N₂O₅F₃ [M + H]⁺ m/z 405.1632, found 405.1625.



Following the general procedure, **5p** (57.1 mg, 69%) was obtained as a colorless oil ; R_f = 0.43 (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 8.05 (s, 1H), 7.86–7.84 (m, 1H), 7.67–7.65 (m, 1H), 7.34–7.30 (m, 1H), 6.70 (s, 1H), 4.91 (brs, 2H), 3.90–3.89 (m, 2H), 3.31 (brs, 2H), 1.23–1.22 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 197.5, 156.0, 155.5, 138.3, 136.1, 131.1, 130.3, 126.7, 123.0, 70.1, 46.3, 36.8, 29.7, 22.0 (2C); HRMS (ESI) Calcd for C₁₇H₂₄N₂O₅Br [M + H]⁺ m/z 415.0863, found 415.0851.

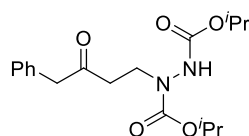


Following the general procedure, **5q** (46.1 mg, 57%) was obtained as a colorless oil ; R_f = 0.41 (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 8.19 (s, 1H), 8.14–8.13 (m, 1H), 7.82–7.80 (m, 1H), 7.62–7.59 (m, 1H), 6.66 (s, 1H), 4.95–4.92 (m, 2H), 3.94–3.93 (m, 2H), 3.38 (brs, 2H), 1.24–1.23 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 197.4, 156.4, 155.5, 137.1, 131.5, 131.3, 131.2, 129.6, 129.4, 125.0, 124.9 (2C), 124.8, 122.3, 77.2, 70.0, 46.3, 36.9, 22.0, 21.9; ¹⁹F (376 MHz, CDCl₃) δ -62.8; HRMS (ESI) Calcd for C₁₈H₂₄N₂O₅F₃ [M + H]⁺ m/z 405.1632, found 405.1622.

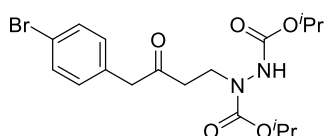


Following the general procedure, **5r** (70.2 mg, 95%) was obtained as a colorless oil ; R_f = 0.31 (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 7.70–7.68 (m, 1H), 7.48–7.44 (m, 1H), 7.01–6.95 (m, 2H), 6.74 (s, 1H), 4.95–4.92 (m, 2H), 3.91 (brs, 5H), 3.32–3.29 (m, 2H), 1.25–1.22 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 200.6, 158.7, 156.1, 155.8, 133.8, 130.4,

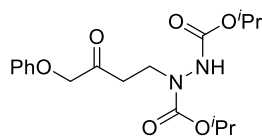
127.8, 120.7, 120.7, 111.6, 69.9, 69.6, 55.5, 46.2, 41.8, 22.0 (2C); HRMS (ESI) Calcd for $C_{18}H_{27}N_2O_6$ $[M + H]^+$ m/z 367.1864, found 367.1862.



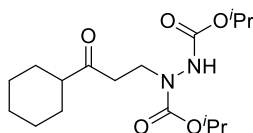
Following the general procedure, **5s** (35.0 mg, 50%) was obtained as a colorless oil ; $R_f = 0.35$ (petroleum ether/EtOAc, 3:1); 1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.29 (m, 2H), 7.26–7.24 (m, 1H), 7.19–7.17 (m, 2H), 6.73 (s, 1H), 4.94–4.87 (m, 2H), 3.70 (brs, 4H), 2.80 (s, 2H), 1.21–1.20 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8, 155.9, 155.5, 133.9, 129.5, 128.7, 127.1, 70.0, 69.7, 50.2, 45.6, 40.0, 22.0, 21.9; HRMS (ESI) Calcd for $C_{18}H_{27}N_2O_5$ $[M + H]^+$ m/z 351.1915, found 351.1916.



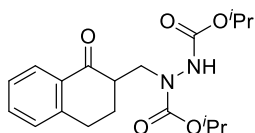
Following the general procedure, **5t** (57.4 mg, 67%) was obtained as a colorless oil ; $R_f = 0.35$ (petroleum ether/EtOAc, 3:1); 1H NMR (400 MHz, $CDCl_3$) δ 7.46–7.44 (m, 2H), 7.08–7.06 (m, 2H), 6.58 (s, 1H), 4.94–4.91 (m, 2H), 3.75–3.69 (m, 4H), 2.83 (s, 2H), 1.26–1.22 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.3, 156.0, 155.5, 132.8, 131.8, 131.2, 121.2, 70.2, 69.9, 49.3, 45.7, 40.3, 22.0, 21.9; HRMS (ESI) Calcd for $C_{18}H_{26}N_2O_5Br$ $[M + H]^+$ m/z 429.1020, found 429.1016.



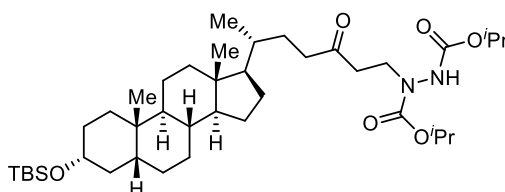
Following the general procedure, **5u** (54.9 mg, 75%) was obtained as a white solid, m. p. 57~60 °C; $R_f = 0.35$ (petroleum ether/EtOAc, 3:1); 1H NMR (600 MHz, $CDCl_3$) δ 7.30–7.28 (m, 2H), 7.00–6.98 (m, 1H), 6.89–6.88 (m, 2H), 6.70 (s, 1H), 4.93–4.91 (m, 2H), 4.58 (s, 2H), 3.84 (brs, 2H), 2.95 (brs, 2H), 1.25–1.22 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 157.7, 156.0, 155.5, 129.7, 121.7, 114.5, 114.5, 72.7, 70.2, 69.9, 45.2, 37.4, 22.0, 21.9; HRMS (ESI) Calcd for $C_{18}H_{27}N_2O_6$ $[M + H]^+$ m/z 367.1864, found 367.1859.



Following the general procedure, **5v** (62.2 mg, 91%) was obtained as a colorless oil ; $R_f = 0.37$ (petroleum ether/EtOAc, 3:1); 1H NMR (600 MHz, $CDCl_3$) δ 6.81 (s, 1H), 4.88–4.87 (m, 2H), 3.67 (s, 2H), 2.75 (s, 2H), 2.31–2.27 (m, 1H), 1.78–1.76 (m, 2H), 1.71–1.69 (m, 2H), 1.61–1.59 (m, 1H), 1.26–1.13 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.8, 156.0, 155.5, 69.9, 69.6, 50.8, 45.8, 38.4, 28.3, 25.7, 25.5, 22.0, 21.9; HRMS (ESI) Calcd for $C_{17}H_{31}N_2O_5$ $[M + H]^+$ m/z 343.2228, found 343.2238.



Following the general procedure, **5w** (61.5 mg, 85%) was obtained as a colorless oil ; $R_f = 0.37$ (petroleum ether/EtOAc, 3:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.01–7.99 (m, 1H), 7.50–7.46 (m, 1H), 7.32–7.24 (m, 2H), 6.85 (s, 1H), 4.96–4.95 (m, 2H), 3.93–3.83 (m, 2H), 3.04 (brs, 2H), 2.91 (brs, 1H), 2.39 (brs, 1H), 1.94 (brs, 1H), 1.28–1.24 (m, 12H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 198.8, 156.0, 144.1, 133.5, 132.3, 128.8, 127.3, 126.6, 70.0, 50.8, 46.2, 29.7, 28.4, 26.9, 22.0 (2C); HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{27}\text{N}_2\text{O}_5$ $[\text{M} + \text{H}]^+$ m/z 363.1915, found 363.1910.

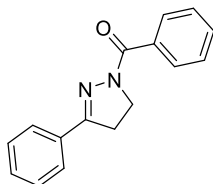


Following the general procedure, **5x** (27.5 mg, 78%) was obtained as a colorless oil ; $R_f = 0.40$ (petroleum ether/EtOAc, 3:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.58 (s, 1H), 4.96 (s, 2H), 3.77 (s, 2H), 3.62–3.56 (m, 1H), 2.79 (s, 2H), 2.50–2.45 (m, 1H), 2.39–2.31 (m, 1H), 1.96–1.93 (m, 1H), 1.82–1.71 (m, 7H), 1.46–1.33 (m, 7H), 1.28–1.27 (m, 15H), 1.16–1.05 (m, 6H), 0.91 (s, 16H), 0.64 (s, 3H), 0.07 (s, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 210.3, 156.5, 155.8, 72.8, 70.3, 69.8, 56.4, 56.0, 45.8, 42.7, 42.3, 40.2, 40.1, 39.9, 36.9, 35.9, 35.6, 35.3, 34.6, 31.0, 29.7, 29.6, 28.2, 27.3, 26.4, 26.0, 24.2, 23.4, 22.1, 22.0, 20.8, 18.4, 18.3, 12.0, -4.6; HRMS (ESI) Calcd for $\text{C}_{41}\text{H}_{75}\text{N}_2\text{O}_6\text{Si}$ $[\text{M} + \text{H}]^+$ m/z 705.5233, found 705.5216.

3.2 General Procedure for the Synthesis of the 4,5-dihydropyrazole.

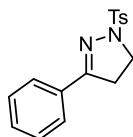
5b (0.22 mmol, 80 mg) was dissolved in DCM (10 mL) and HCl solution (4 M in dioxane, 4 mL) was added in the above reaction mixture at 0 °C, the solvent was evaporated under reduced pressure after the starting material was consumed. The crude product was used directly for the next step without any purification.

The crude product from last step was dissolved in DCM (10 mL) and cooled to 0 °C. Et_3N (2.2 eq., 67 μL) and acyl chloride or acid anhydride (1.1 eq) was added in the above solution subsequently. The reaction was monitored by TLC. After the reaction completed, the solvent was evaporated under reduced pressure and the reaction mixture was purified by FCC (petroleum ether/ethyl acetate 10:1 to 3:1) to yield the desired hydrazine-1,2-dicarboxylates **6a–6f**.

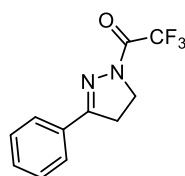


Following the general procedure, **6a** (46.8 mg, 85%) was obtained as a colorless oil ; $R_f = 0.30$ (petroleum ether/EtOAc, 3:1); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.02–8.01 (m, 2H), 7.72–7.70 (m, 2H), 7.52–7.50 (m, 1H), 7.48–7.45 (m, 2H), 7.43–7.40 (m, 3H), 4.27 (t, $J = 9.9$ Hz, 2H), 3.27 (t, $J = 9.9$ Hz, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 166.9, 156.7, 134.3, 131.5, 130.9, 130.3,

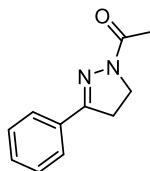
130.0, 128.7, 127.7, 126.7, 45.4, 31.1; HRMS (ESI) Calcd for C₁₆H₁₅N₂O [M + H]⁺ *m/z* 251.1179, found 251.1177.



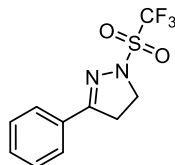
Following the general procedure, **6b** (56.8 mg, 86%) was obtained as a white solid, m.p. 122 °C; *R_f* = 0.40 (petroleum ether/EtOAc, 3:1); ¹H NMR (600 MHz, CDCl₃) δ 7.83 (d, *J* = 8.16 Hz, 2H), 7.72–7.69 (d, *J* = 6.72 Hz, 2H), 7.42–7.38 (m, 3H), 7.32–7.31 (m, 2H), 7.43–7.40 (m, 3H), 3.68 (t, *J* = 9.5 Hz, 2H), 3.08 (t, *J* = 9.5 Hz, 2H), 2.40 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 158.3, 144.4, 131.2, 130.9, 130.6, 129.6, 128.8, 128.6, 126.9, 48.7, 32.8, 21.6; HRMS (ESI) Calcd for C₁₆H₁₇N₂O₂S [M + H]⁺ *m/z* 301.1005, found 301.0998.



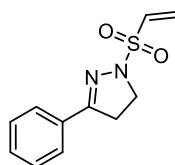
Following the general procedure, **6c** (43.7 mg, 82%) was obtained as a yellow solid, m.p. 110–112 °C; *R_f* = 0.32 (petroleum ether/EtOAc, 3:1); ¹H NMR (600 MHz, CDCl₃) δ 7.79–7.78 (m, 2H), 7.51–7.45 (m, 3H), 4.14 (t, *J* = 9.7 Hz, 2H), 3.31 (t, *J* = 9.5 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 159.6, 131.3, 130.3, 128.9, 128.8, 127.2, 45.1, 31.3; ¹⁹F NMR (376 MHz, CDCl₃) δ –71.3; HRMS (ESI) Calcd for C₁₁H₁₀N₂OF₃ [M + H]⁺ *m/z* 243.0740, found 243.0748.



Following the general procedure, **6d** (33.9 mg, 82%) was obtained as a white solid, m.p. 122 °C; *R_f* = 0.35 (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 7.76–7.75 (m, 2H), 7.45 (brs, 3H), 4.07 (t, *J* = 10.1 Hz, 2H), 3.26 (t, *J* = 10.1 Hz, 2H), 2.42 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 169.3, 155.7, 131.5, 130.3, 128.7, 126.5, 44.0, 31.9, 21.6; HRMS (ESI) Calcd for C₁₁H₁₃N₂O [M + H]⁺ *m/z* 189.1023, found 189.1028.



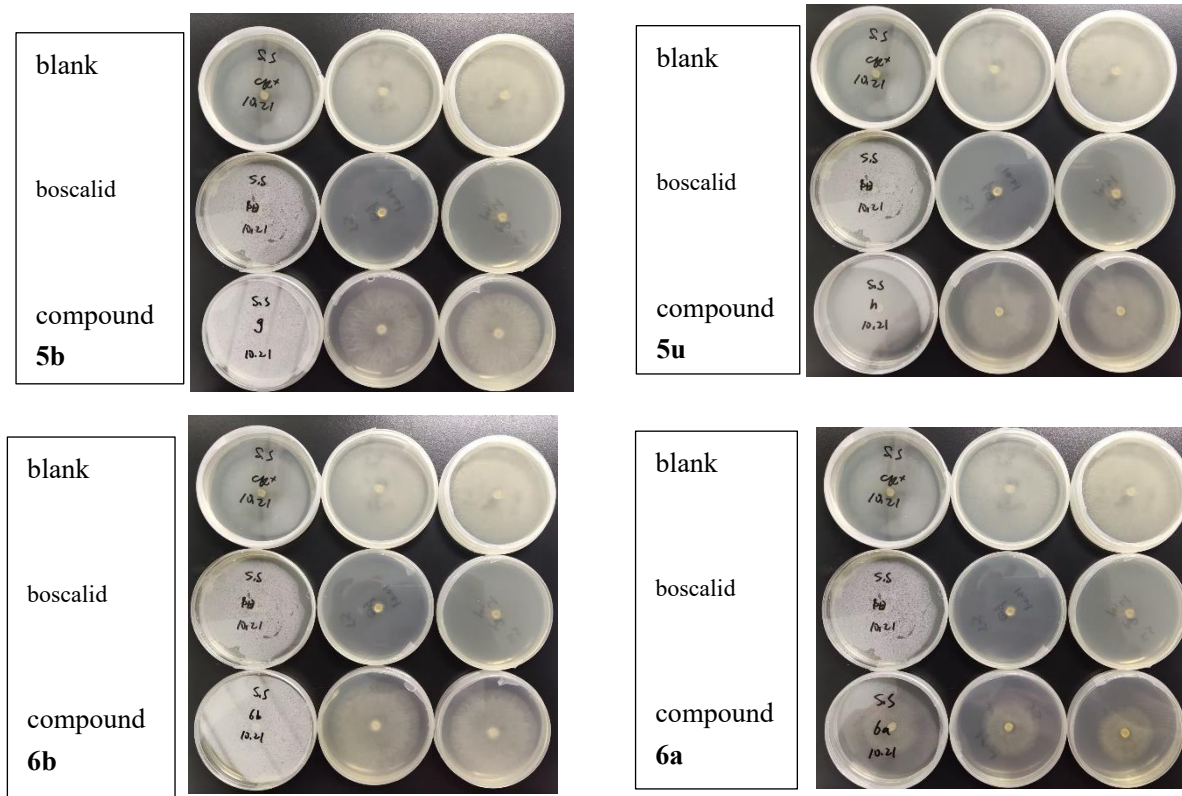
Following the general procedure, **6e** (50.8 mg, 83%) was obtained as a yellow solid, m.p. 98–100 °C; *R_f* = 0.38 (petroleum ether/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃) δ 7.79–7.77 (m, 2H), 7.51–7.44 (m, 3H), 4.21 (t, *J* = 9.8 Hz, 2H), 3.43 (t, *J* = 9.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 159.9, 131.4, 129.8, 128.9, 127.2, 48.5, 33.4; ¹⁹F NMR (376 MHz, CDCl₃) δ –72.3; HRMS (ESI) Calcd for C₁₀H₁₀N₂O₂S [M + H]⁺ *m/z* 279.0410, found 279.0411.



Following the general procedure, **6f** (38.9 mg, 75%) was obtained as a colorless oil ; $R_f = 0.40$ (petroleum ether/EtOAc, 3:1); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.77–7.75 (m, 2H), 7.47–7.41 (m, 3H), 6.60 (dd, $J = 10.0, 16.7$ Hz, 1H), 6.42 (d, $J = 16.7$ Hz, 1H), 6.16 (d, $J = 10.0$ Hz, 1H) 3.79 (t, $J = 9.7$ Hz, 2H), 3.26 (t, $J = 9.5$ Hz, 2H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 158.9, 131.2, 130.8, 130.7, 130.6, 128.7, 127.0, 48.4, 33.0; HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_{13}\text{N}_2\text{O}_2\text{S}$ [$\text{M} + \text{H}$] $^+$ m/z 237.0692, found 237.0695.

4. *In Vitro* Antifungal Activities of the Target Compounds

S. sclerotiorum

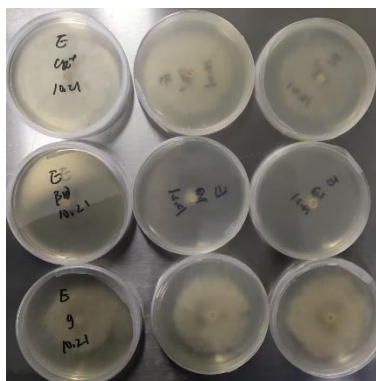


T. cucumeris

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boscalid

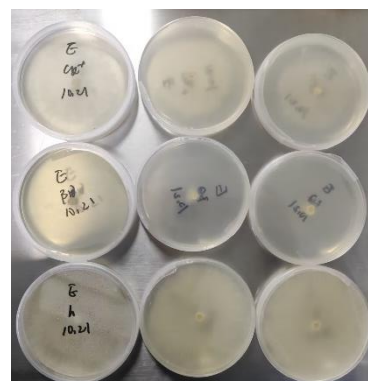
compound
5b



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boscalid

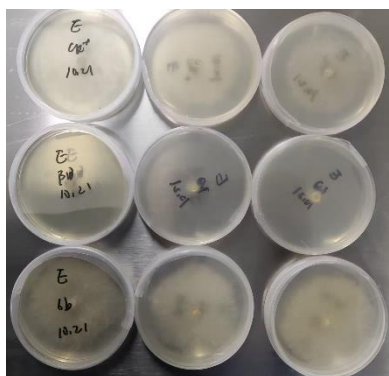
compound
5u



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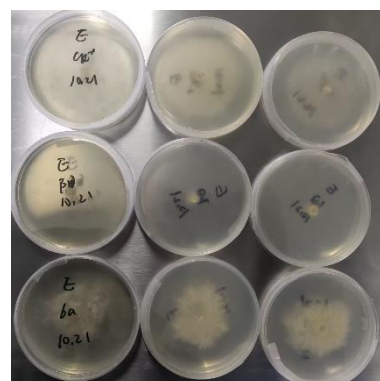
compound
6b



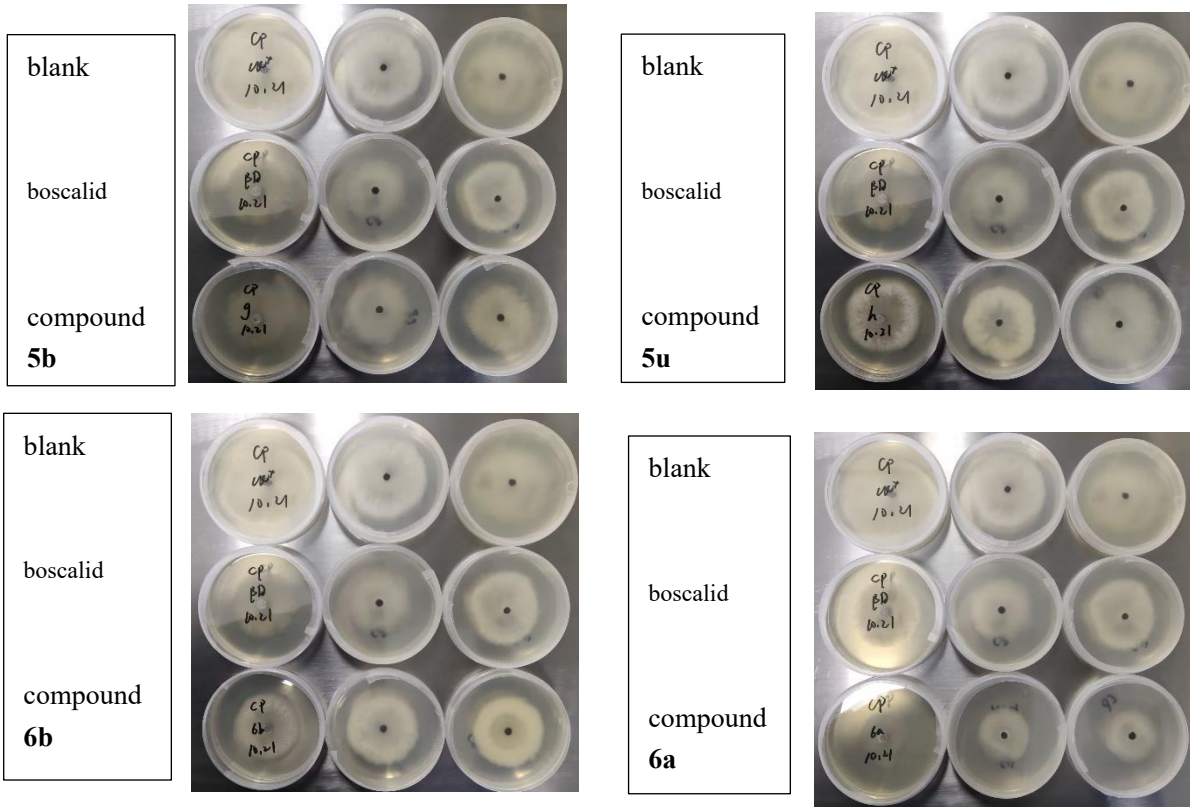
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boscalid

compound
6a



C. paradoxa

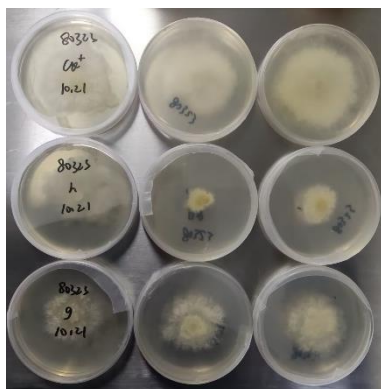


C. chrysosperma

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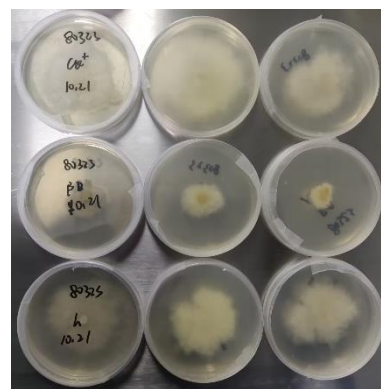
compound
5b



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boscalid

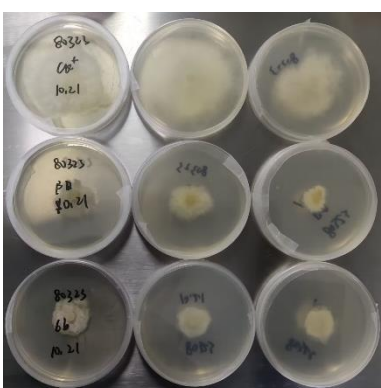
compound
5u



blank

boscalid

compound
6b



blank

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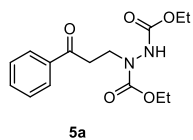
compound
6a



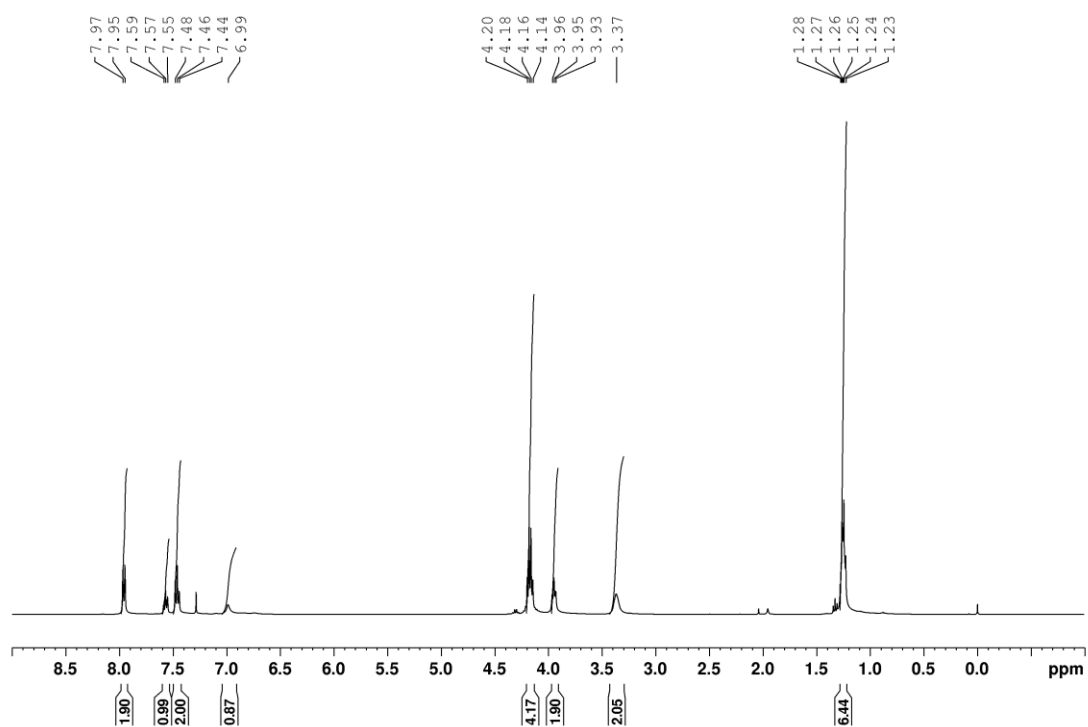
5. Reference

1. (a) Jia, K.; Zhang, F.; Huang, H.; Chen, Y. *J. Am. Chem. Soc.* **2016**, *138*, 1514. (b) Ye, Z.; Cai, X.; Li, J.; Dai, M. *ACS Catal.* **2018**, *8*, 5907. (c) He, X.-P.; Shu, Y.-J.; Dai, J.-J.; Zhang, W.-M.; Feng, Y.-S.; Xu, H.-J. *Org. Biomol. Chem.* **2015**, *13*, 7159. (d) Mills, L. R.; Zhou, C.; Fung, E.; Rousseaux, S. A. L. *Org. Lett.* **2019**, *21*, 8805. (e) Mills, L. R.; Monteith, J. J.; dos Passos Gomes, G.; Aspuru-Guzik, A.; Rousseaux, S. A. L. *J. Am. Chem. Soc.* **2020**, *142*, 13246.
(f) Rivera, R. M. H.; Jang, Y.; Poteat, C. M.; Lindsay, V. N. G. *Org. Lett.* **2020**, *22*, 6510.
(g) Li, Y.; Ye, Z.; Bellman, T. M.; Chi, T.; Dai, M. *Org. Lett.* **2015**, *17*, 2186.

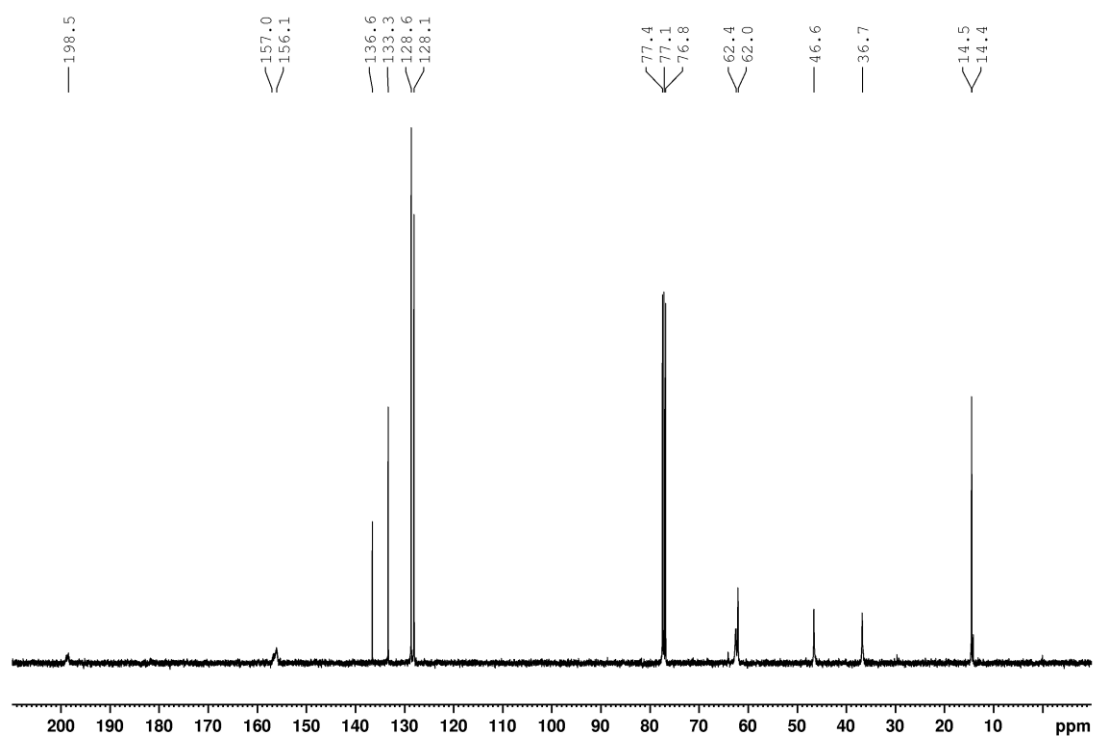
6. ^1H NMR and ^{13}C NMR Spectra

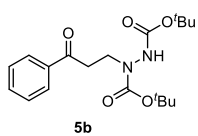


Compound 5a: ^1H NMR (400 MHz, CDCl_3)

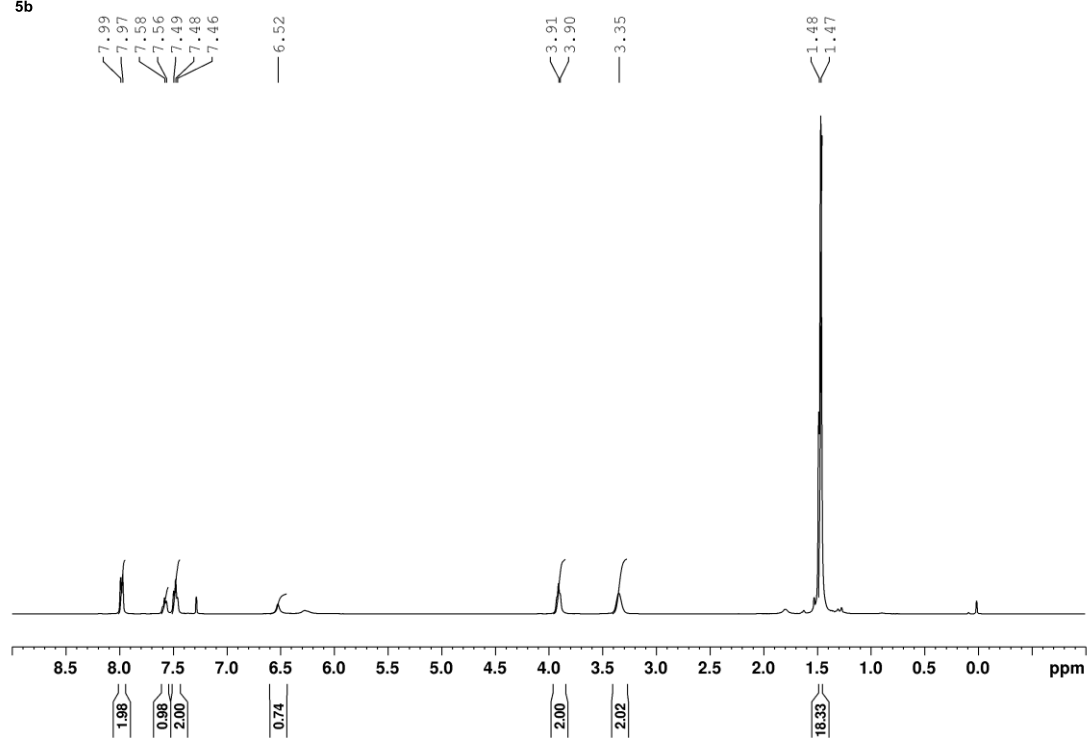


Compound 5a: ^{13}C NMR (100 MHz, CDCl_3)

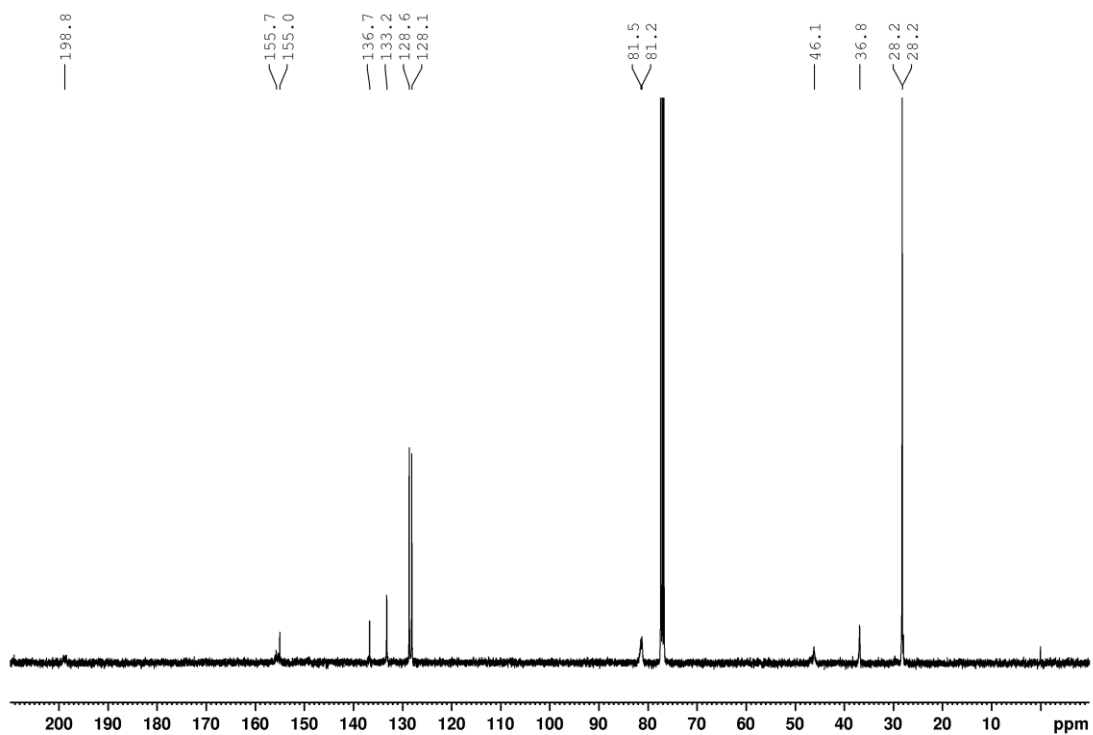


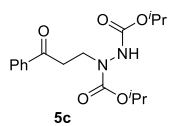


Compound **5b**: ^1H NMR (400 MHz, CDCl_3)

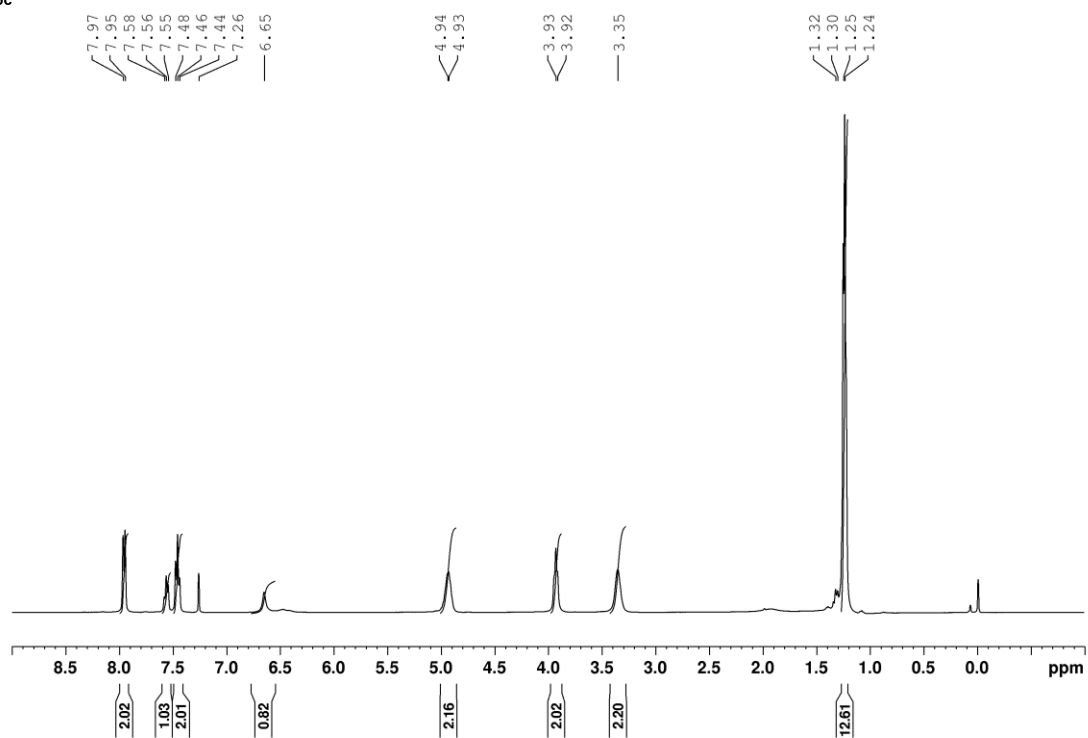


Compound **5b**: ^{13}C NMR (100 MHz, CDCl_3)

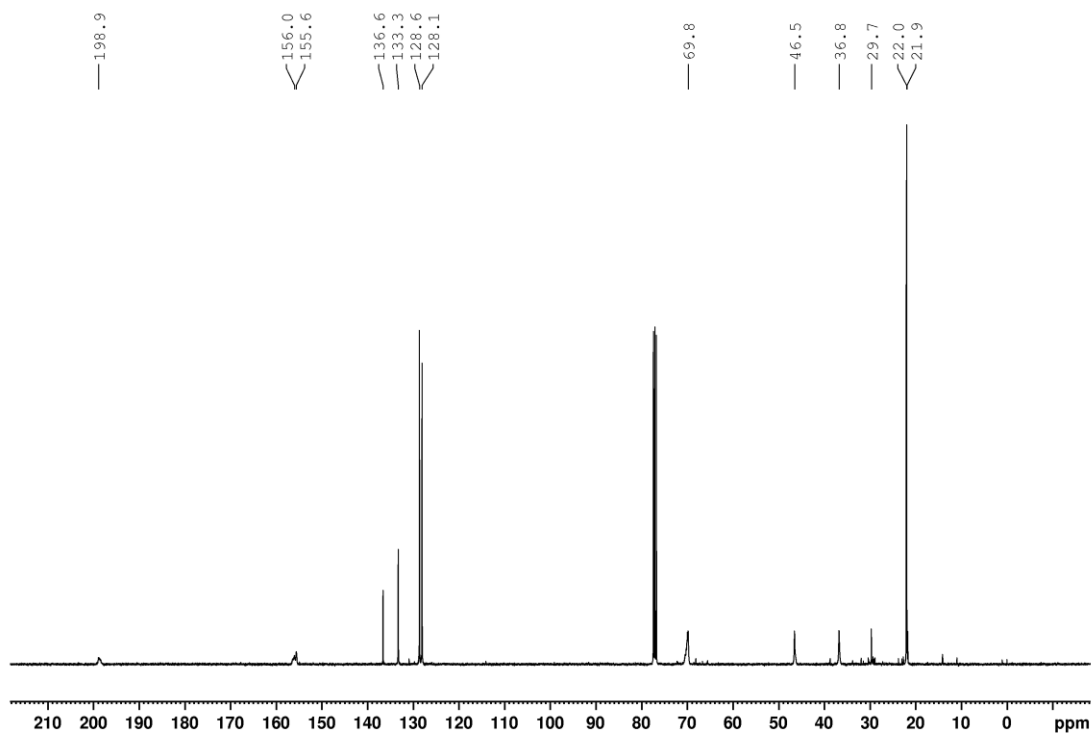


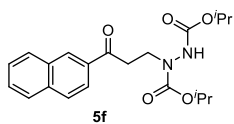


Compound 5c: ^1H NMR (400 MHz, CDCl_3)

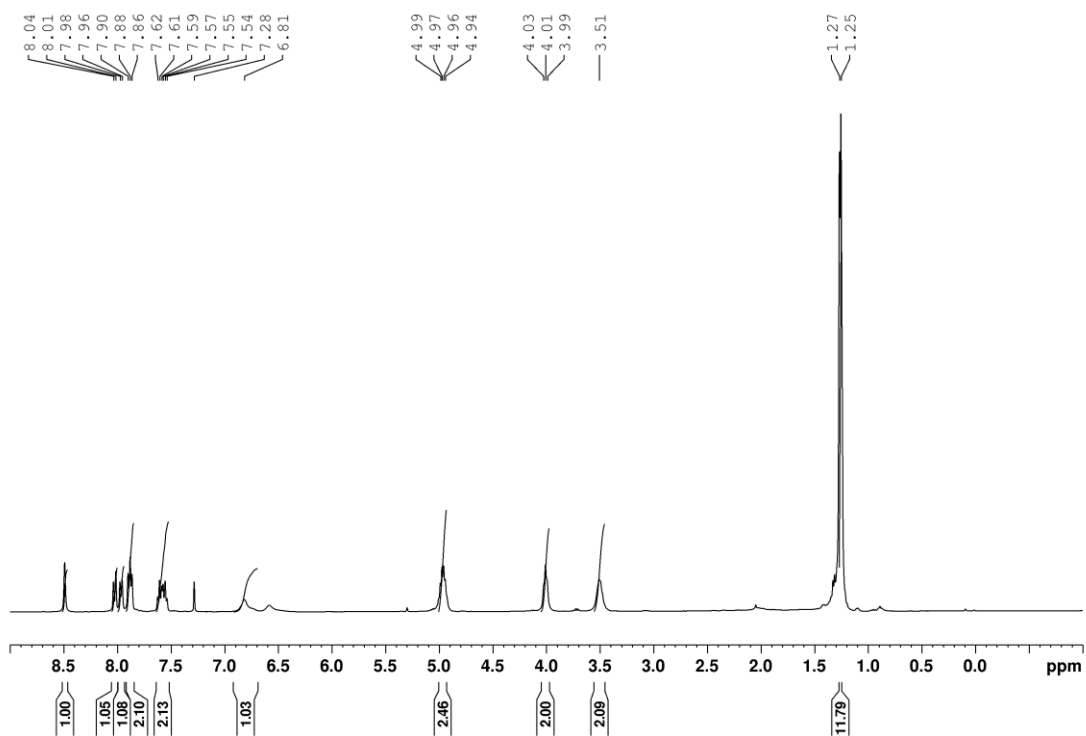


Compound 5c: ^{13}C NMR (100 MHz, CDCl_3)

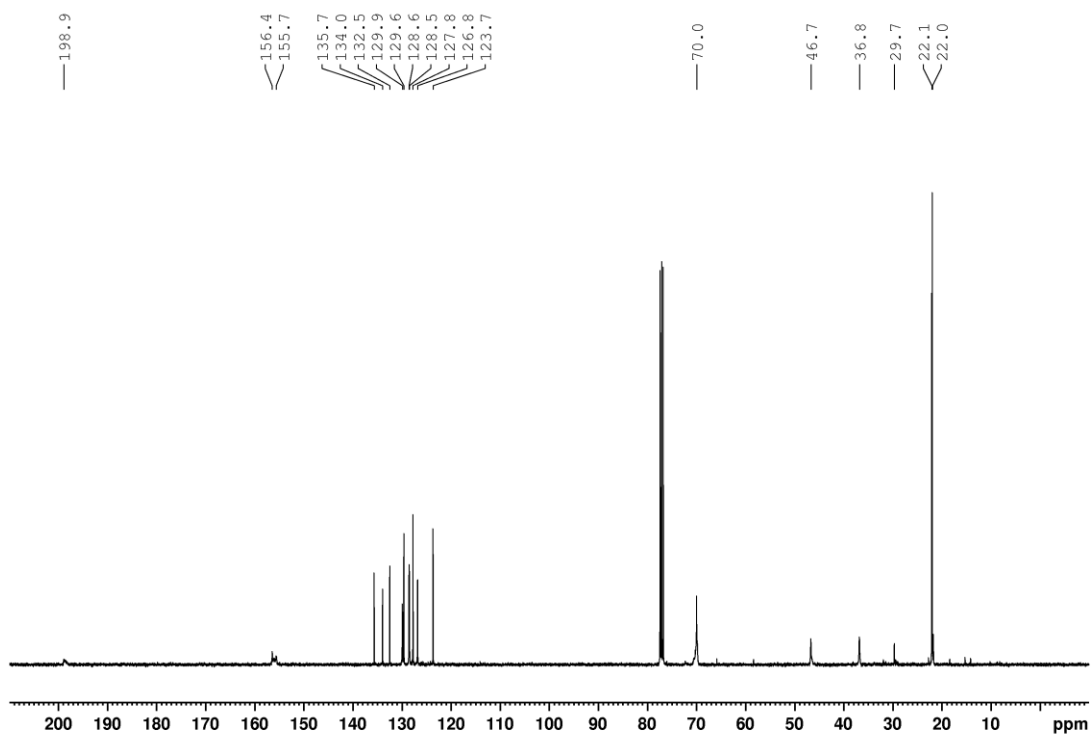




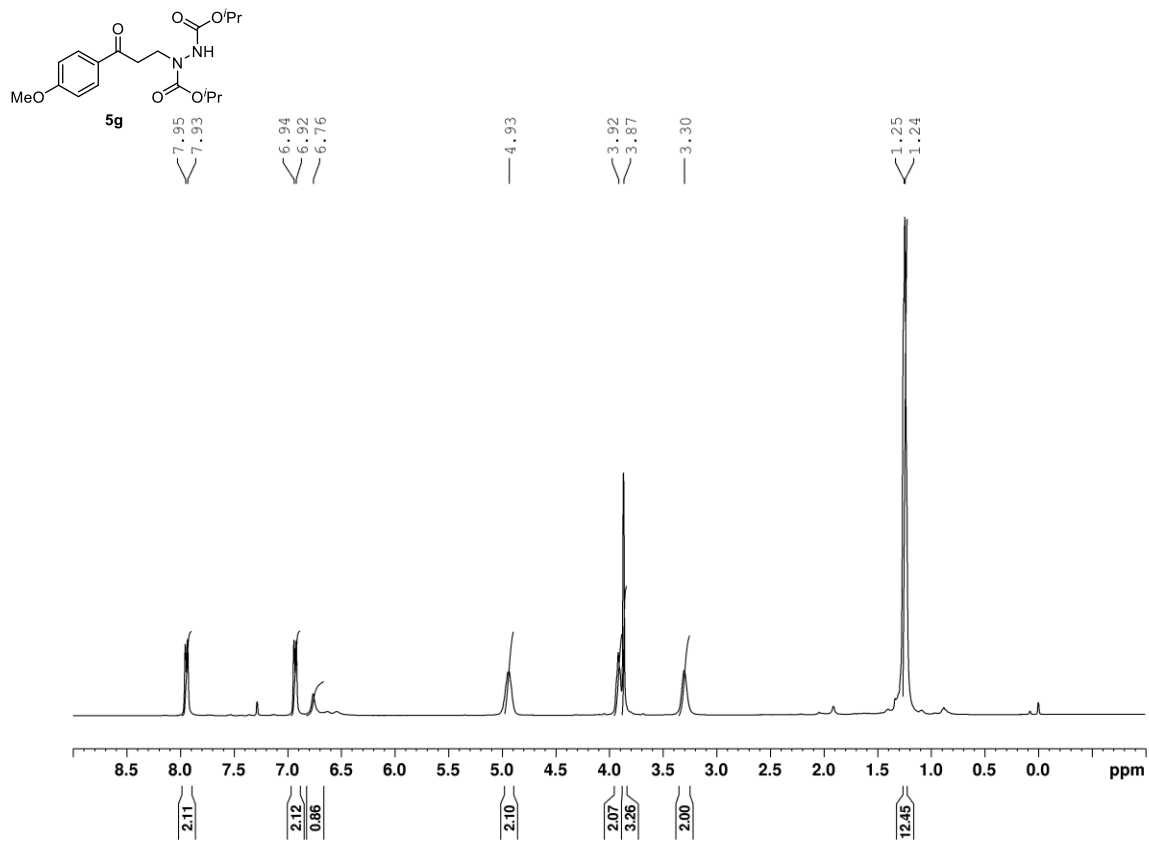
Compound **5f**: ^1H NMR (400 MHz, CDCl_3)



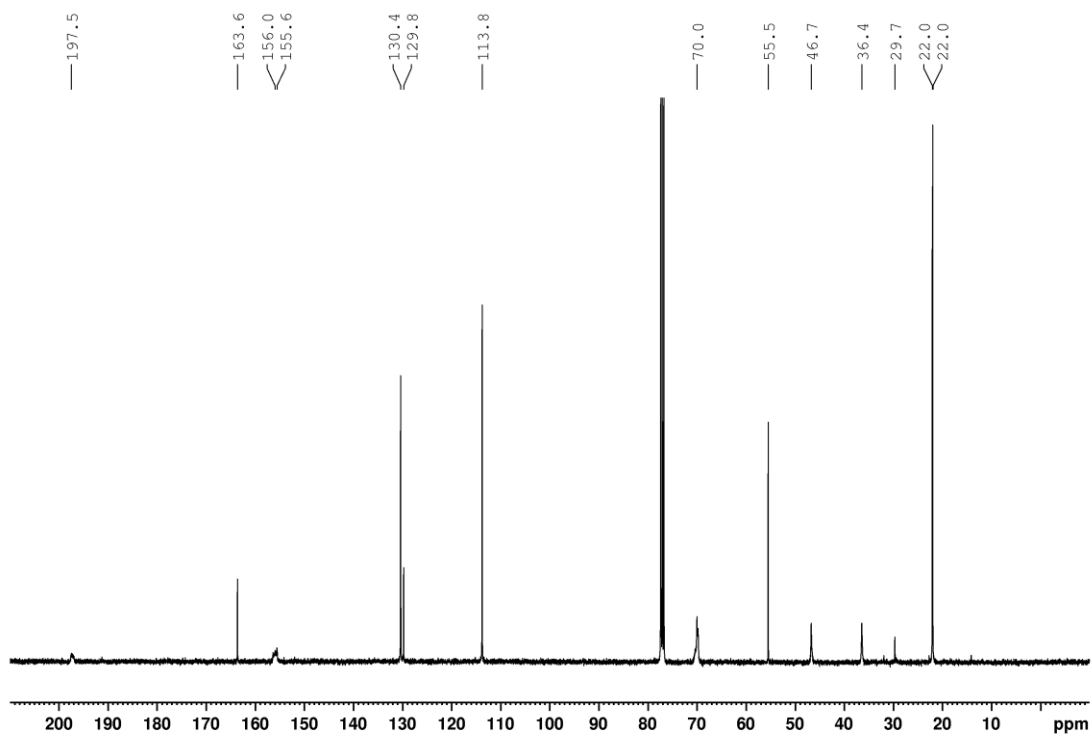
Compound **5f**: ^{13}C NMR (100 MHz, CDCl_3)



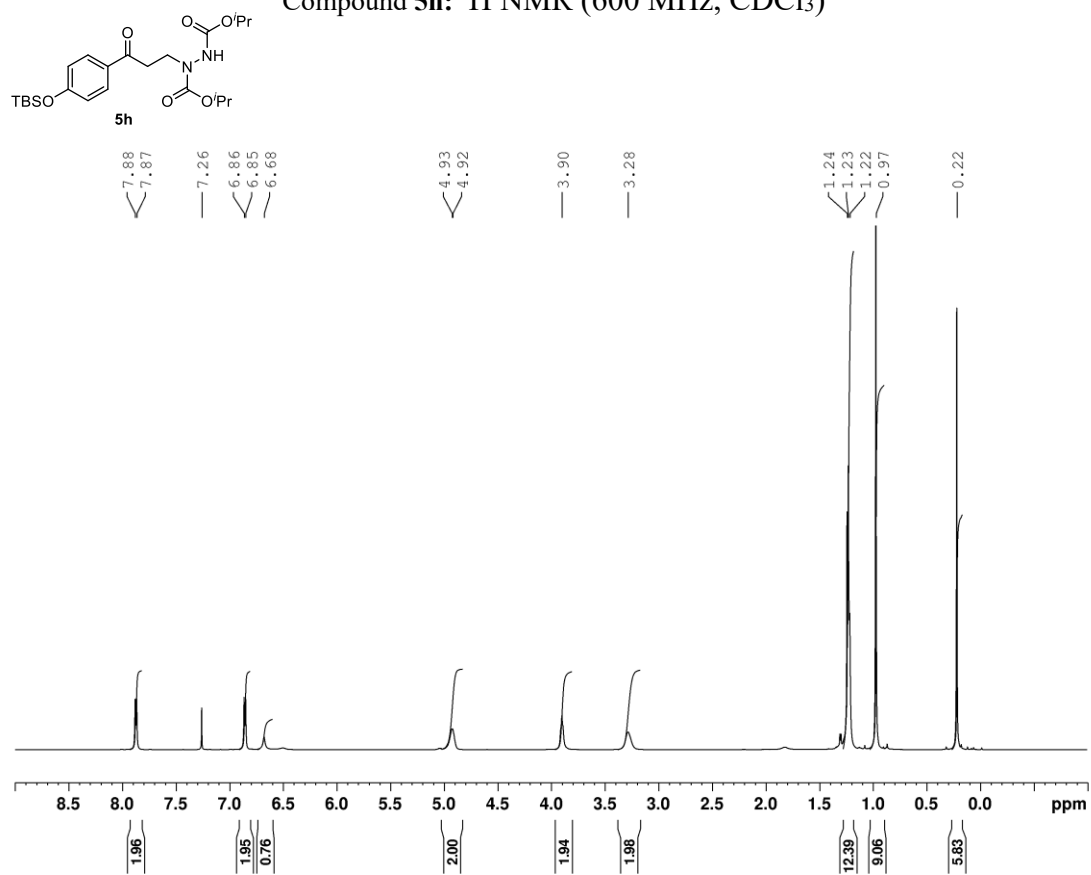
Compound **5g**: ^1H NMR (400 MHz, CDCl_3)



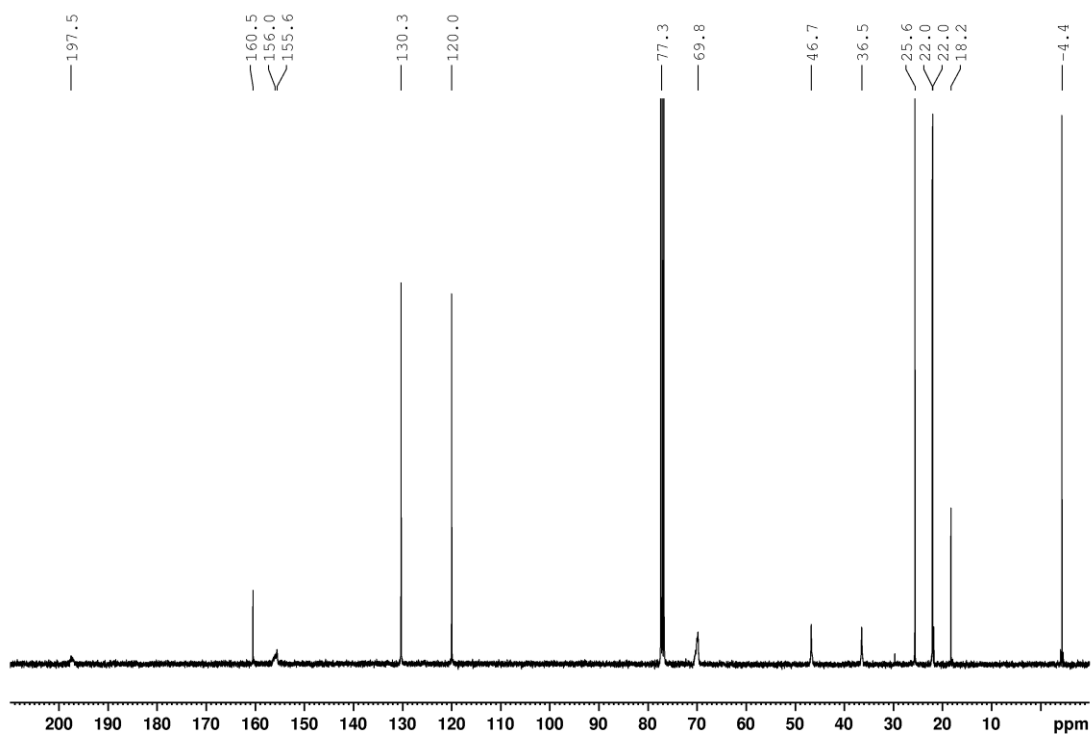
Compound **5g**: ^{13}C NMR (100 MHz, CDCl_3)



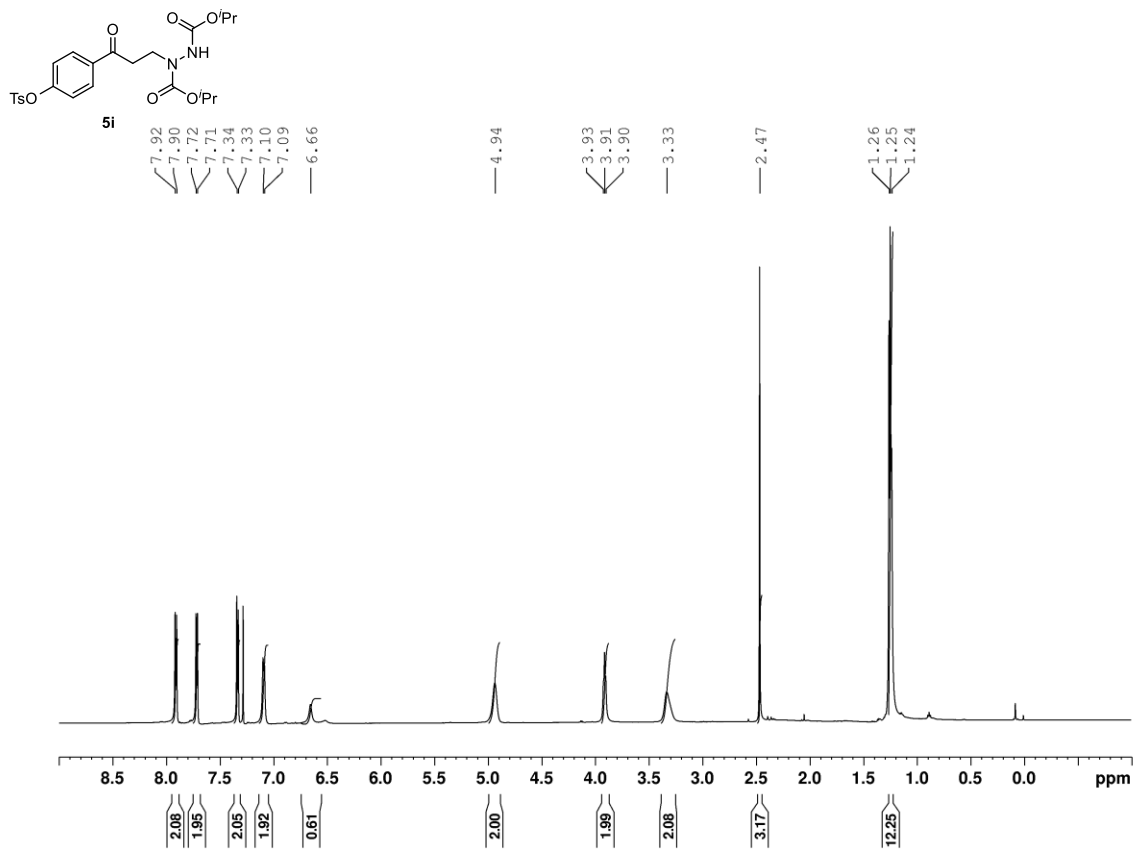
Compound **5h**: ^1H NMR (600 MHz, CDCl_3)



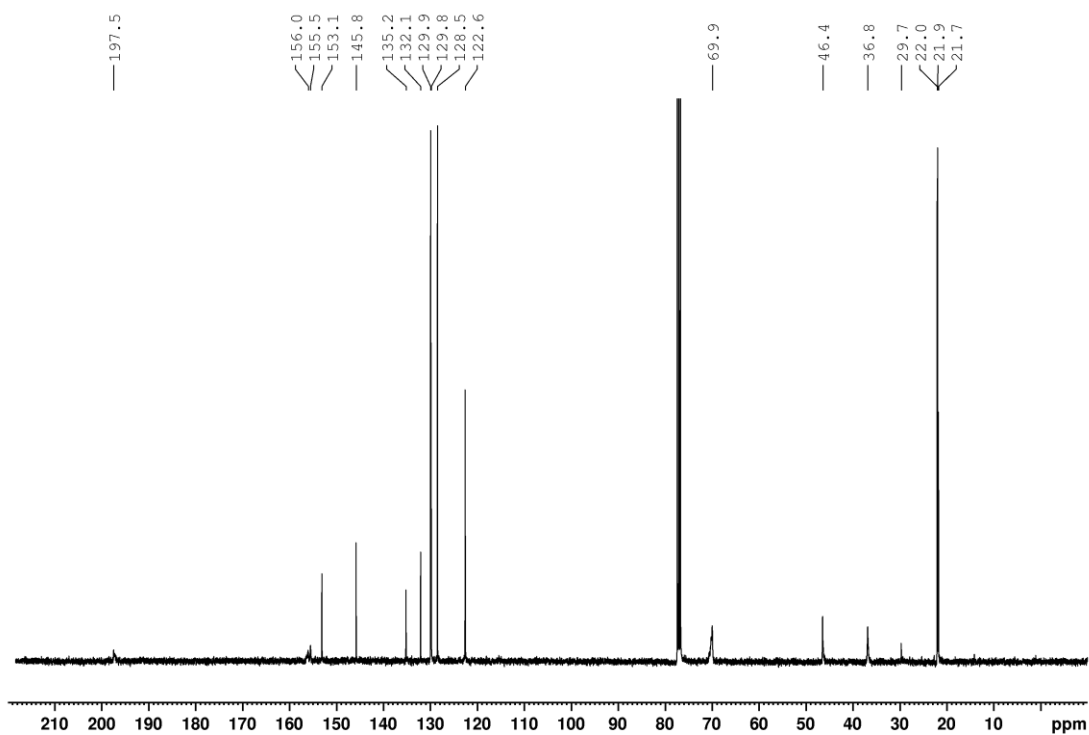
Compound **5h**: ^{13}C NMR (100 MHz, CDCl_3)



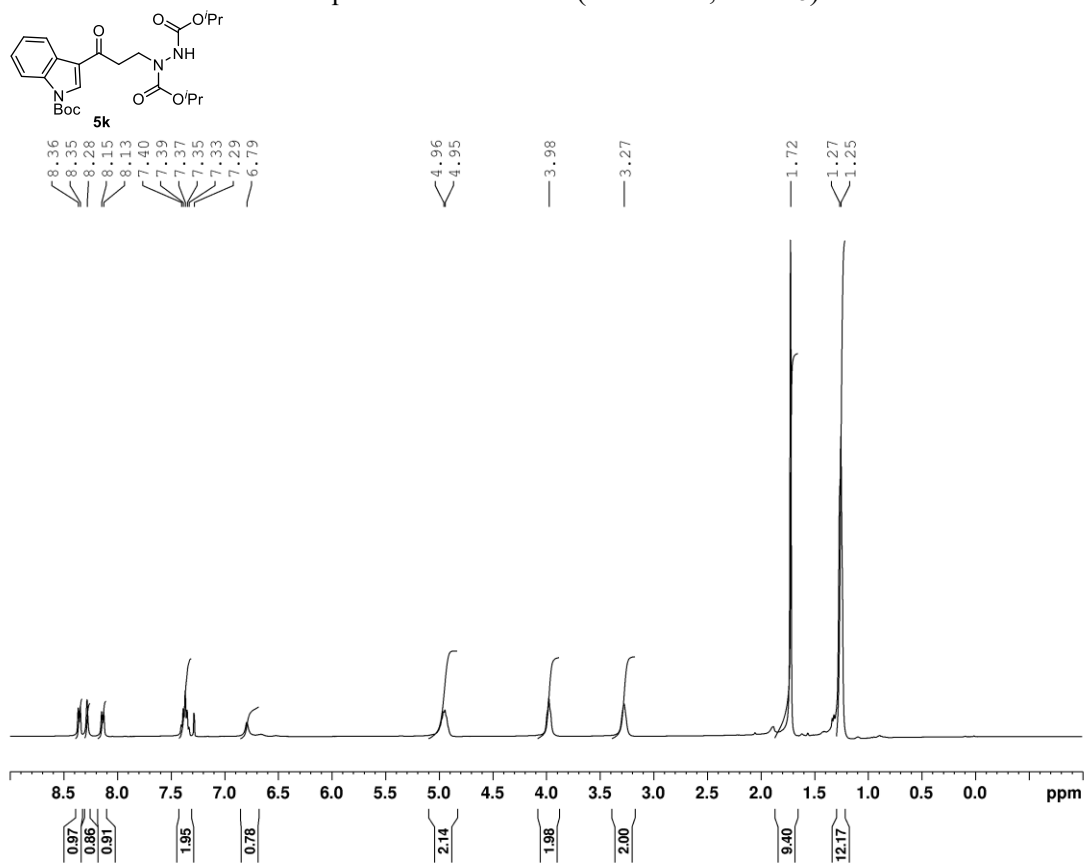
Compound **5i**: ^1H NMR (600 MHz, CDCl_3)



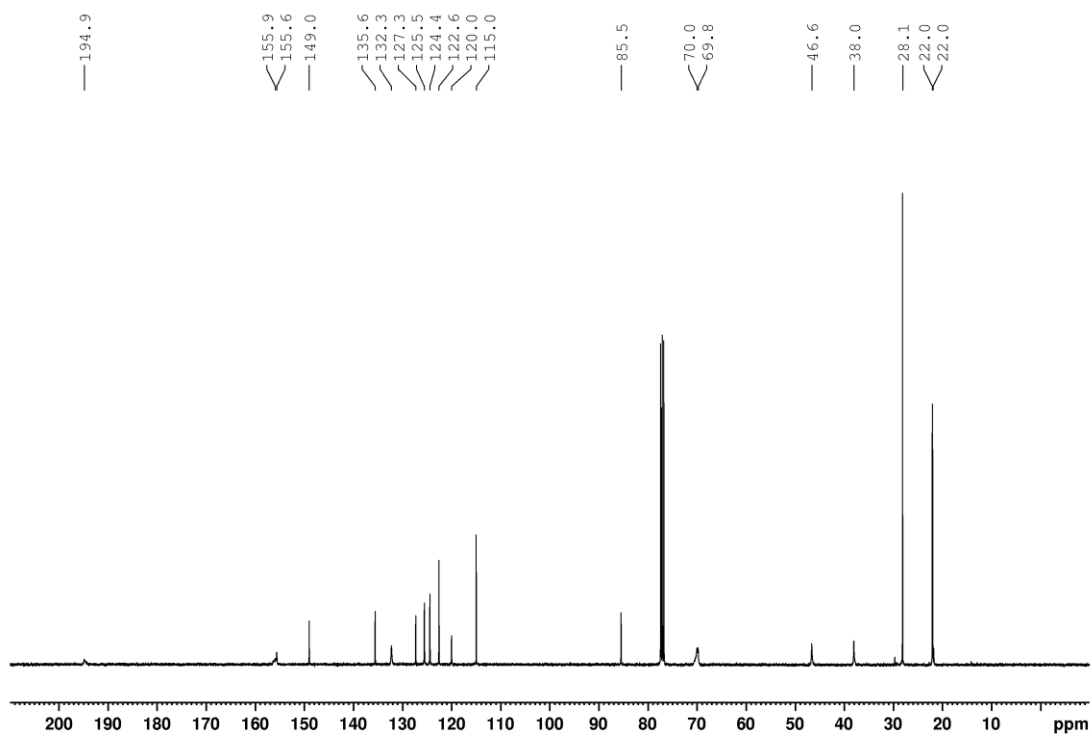
Compound **5i**: ^{13}C NMR (100 MHz, CDCl_3)



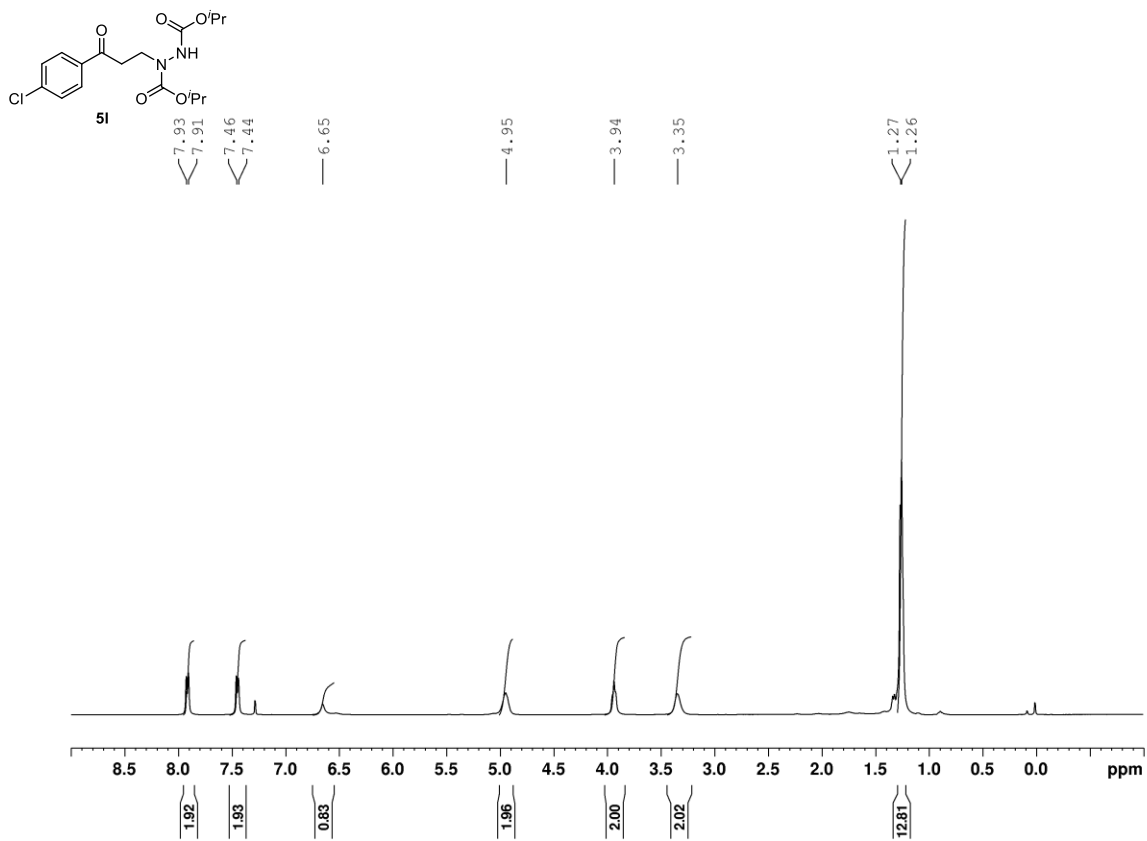
Compound **5k**: ^1H NMR (400 MHz, CDCl_3)



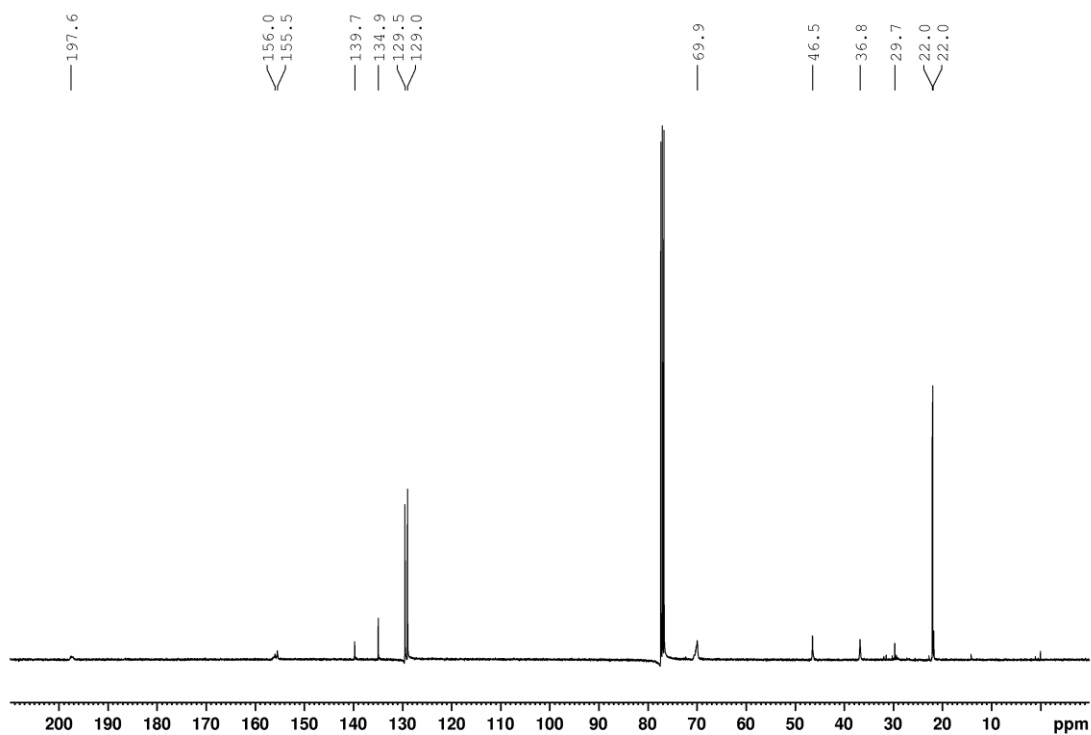
Compound **5k**: ^{13}C NMR (100 MHz, CDCl_3)

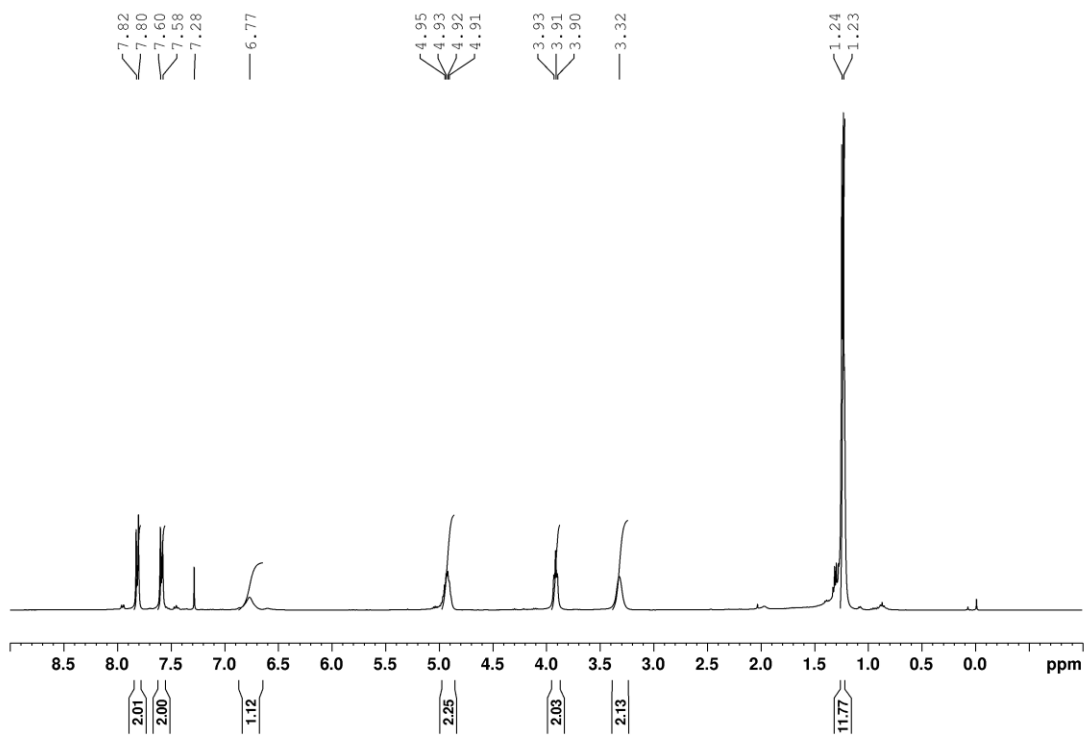
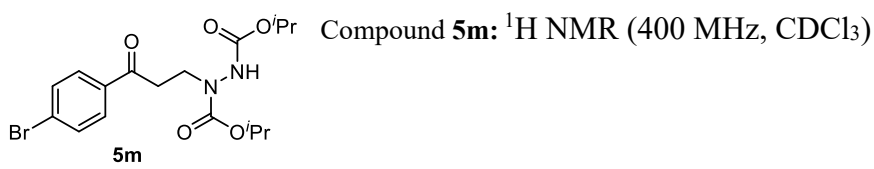


Compound **51**: ^1H NMR (400 MHz, CDCl_3)

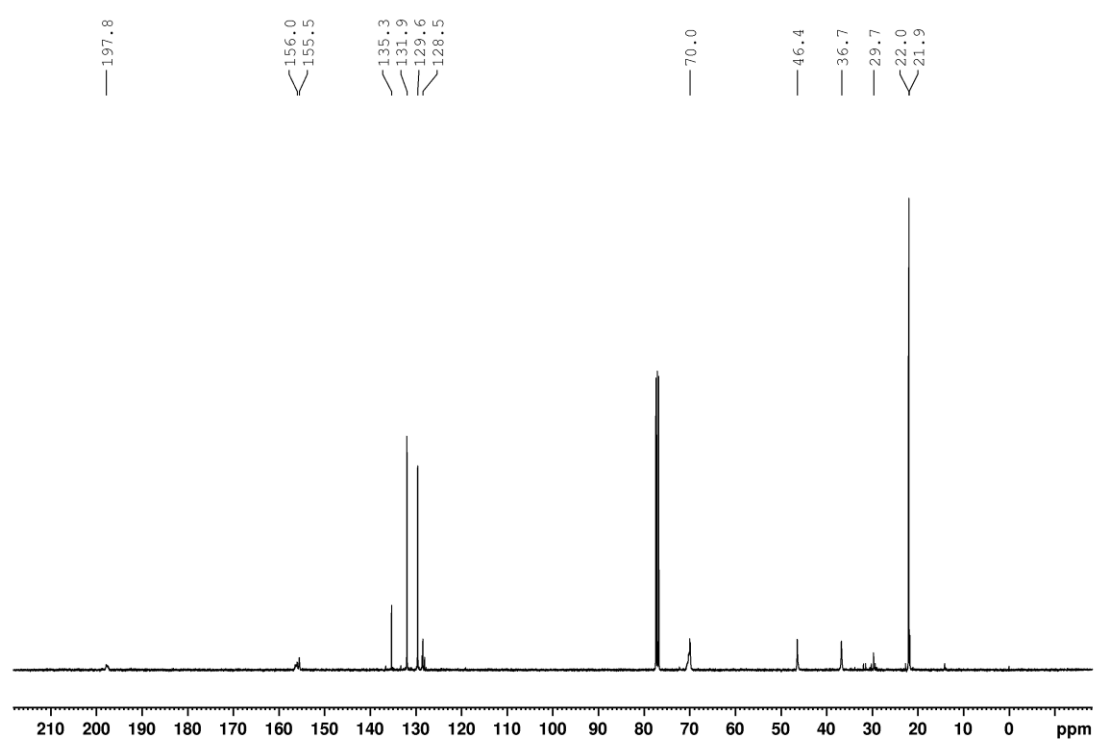


Compound **51**: ^{13}C NMR (100 MHz, CDCl_3)

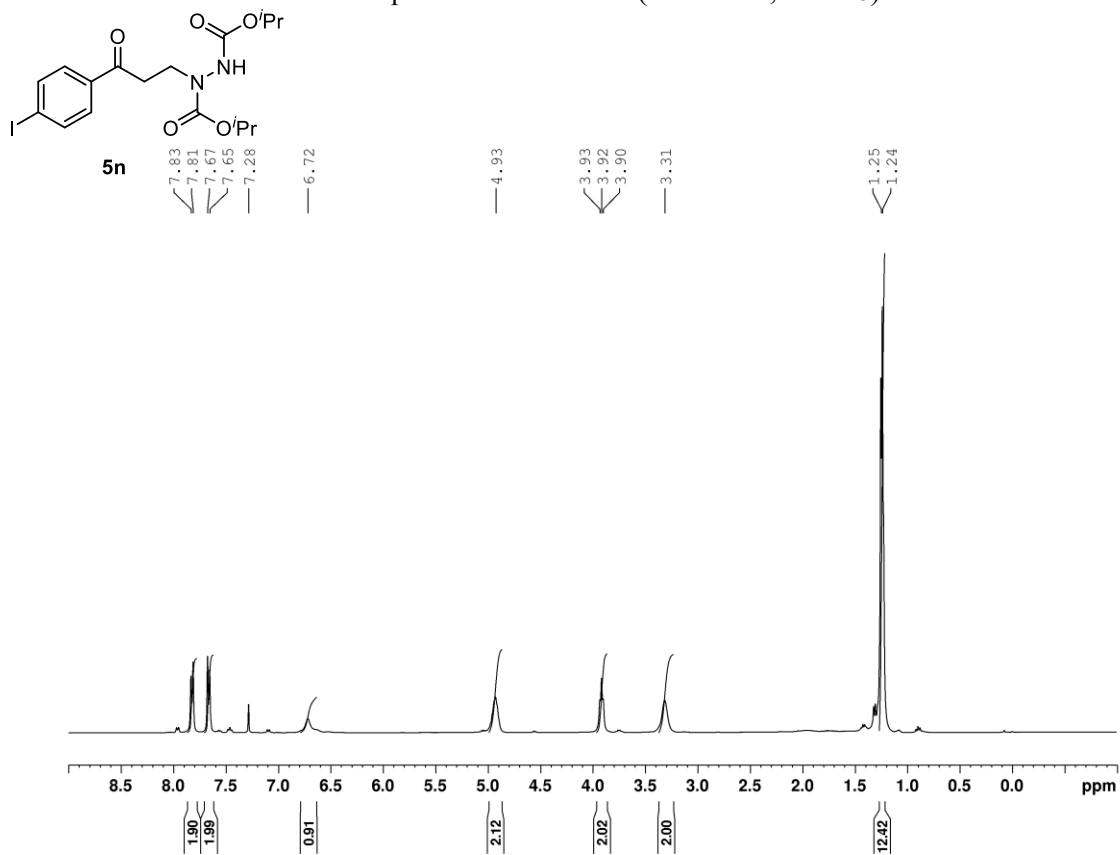




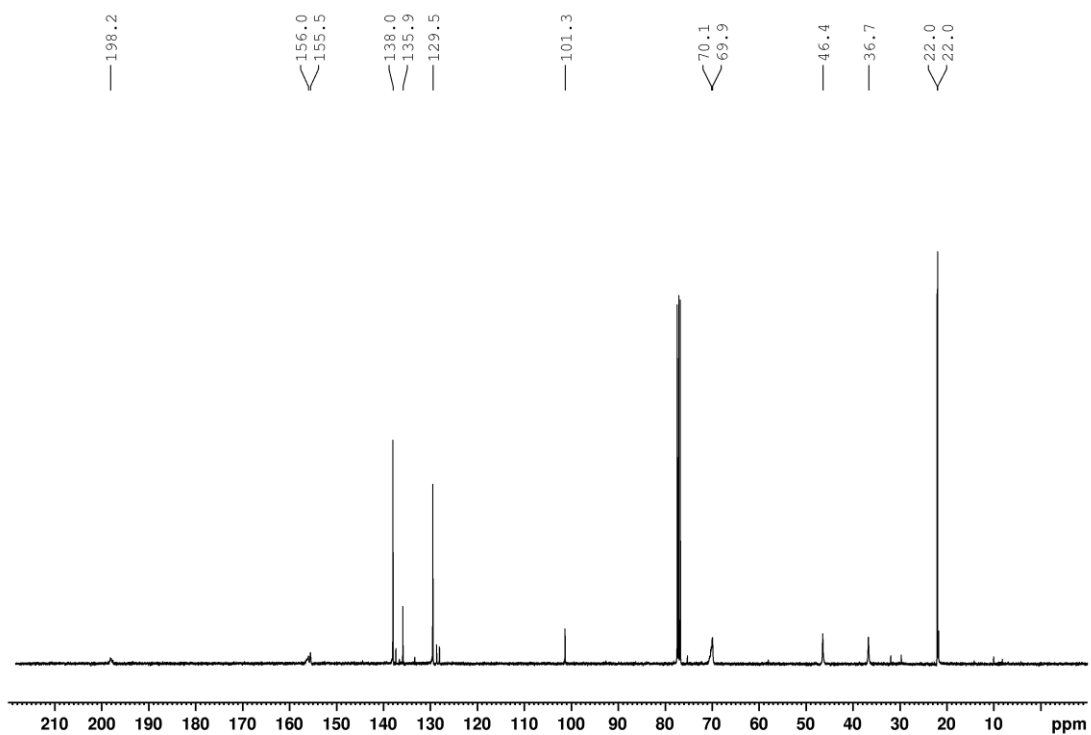
Compound **5m**: ^{13}C NMR (100 MHz, CDCl_3)

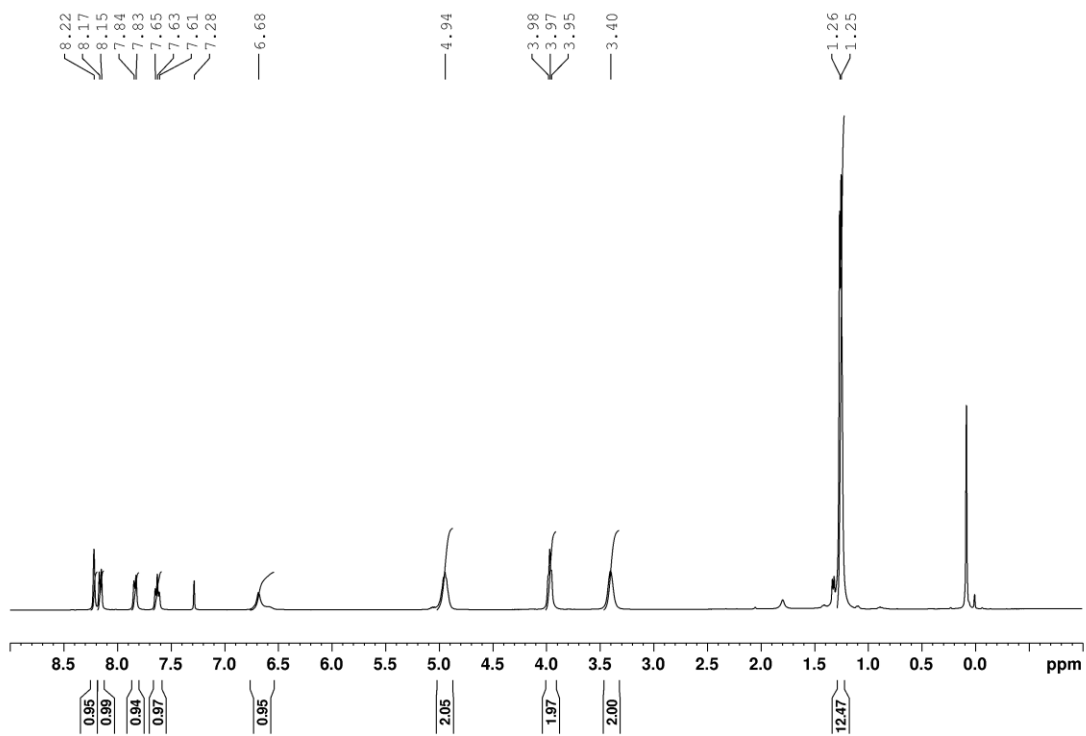
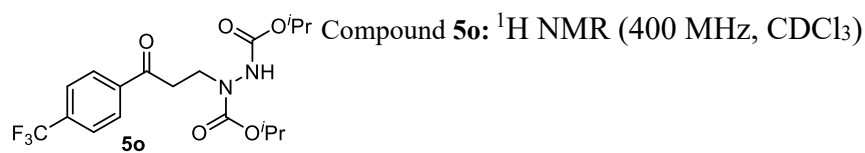


Compound **5n**: ^1H NMR (400 MHz, CDCl_3)

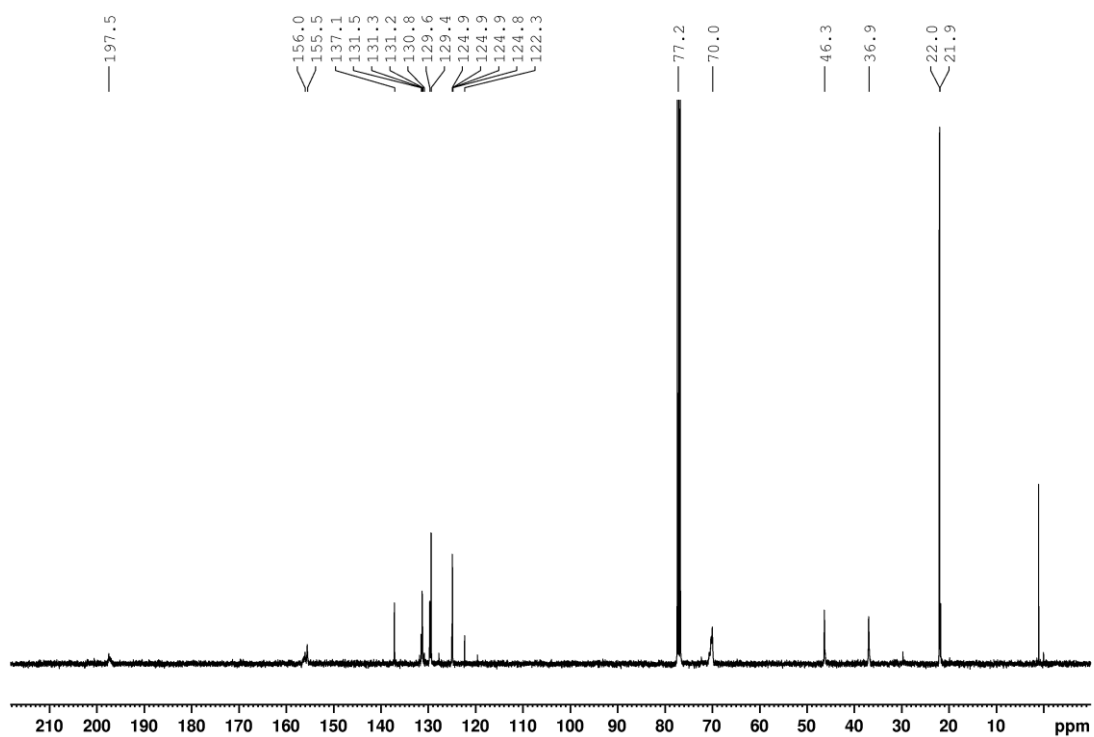


Compound **5n**: ^{13}C NMR (100 MHz, CDCl_3)

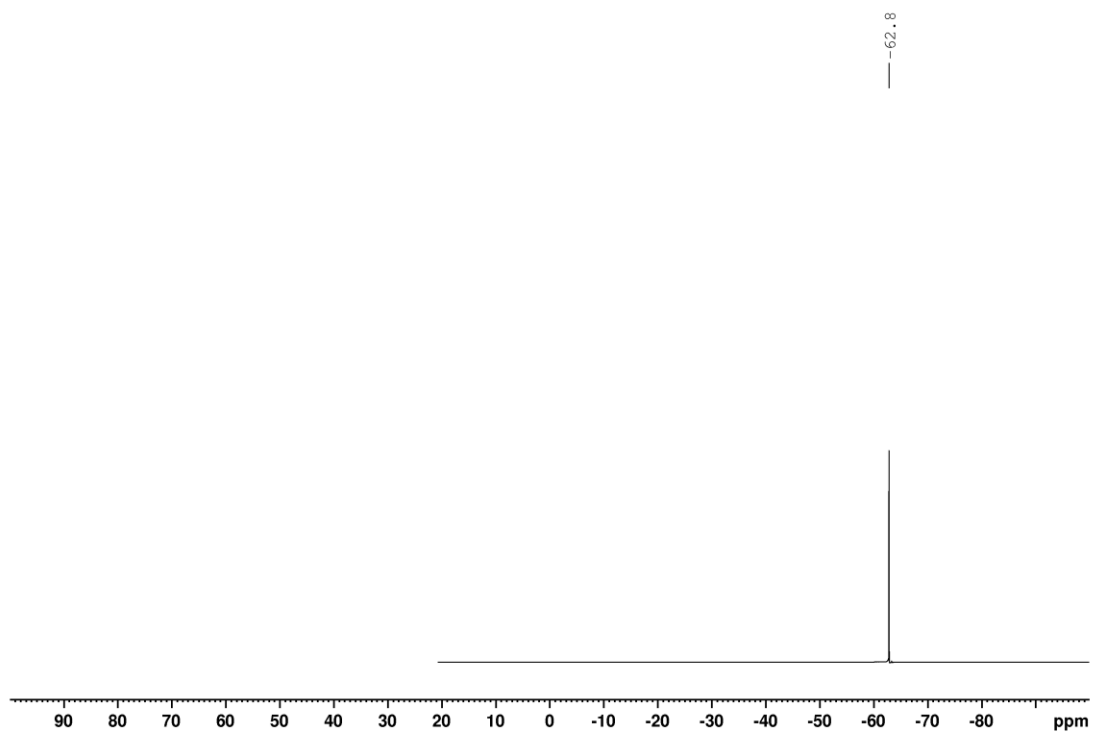


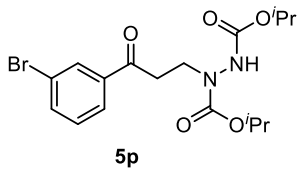


Compound **5o**: ^{13}C NMR (100 MHz, CDCl_3)

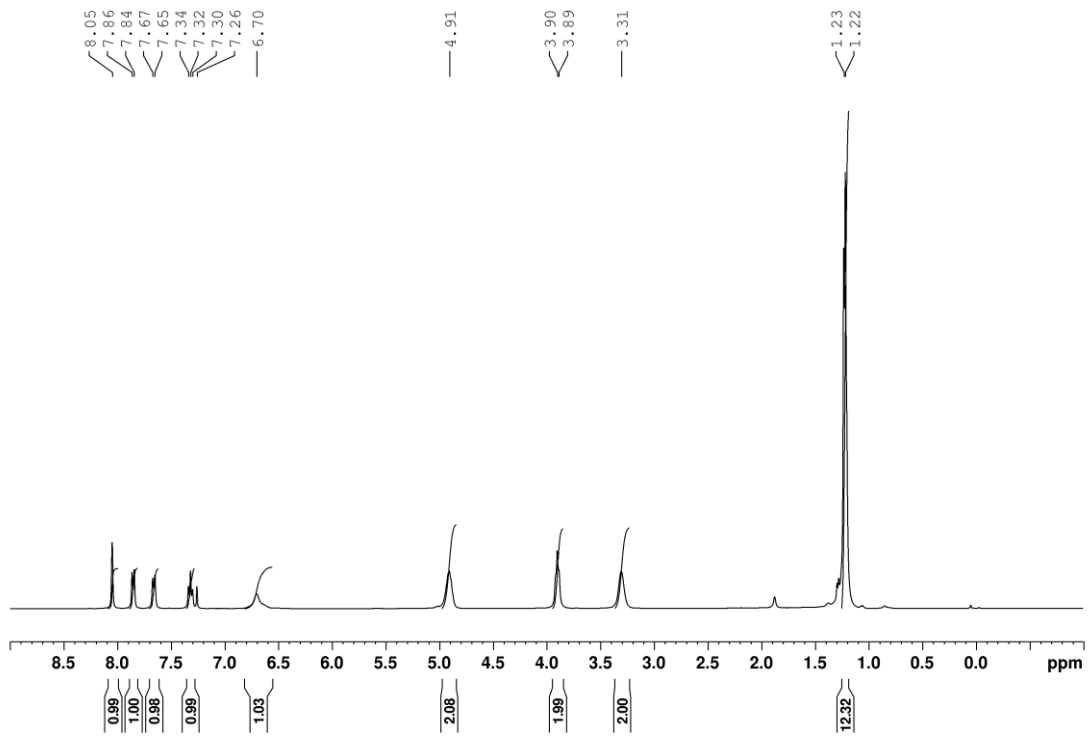


Compound **5o**: ^{19}F (376 MHz, CDCl_3)

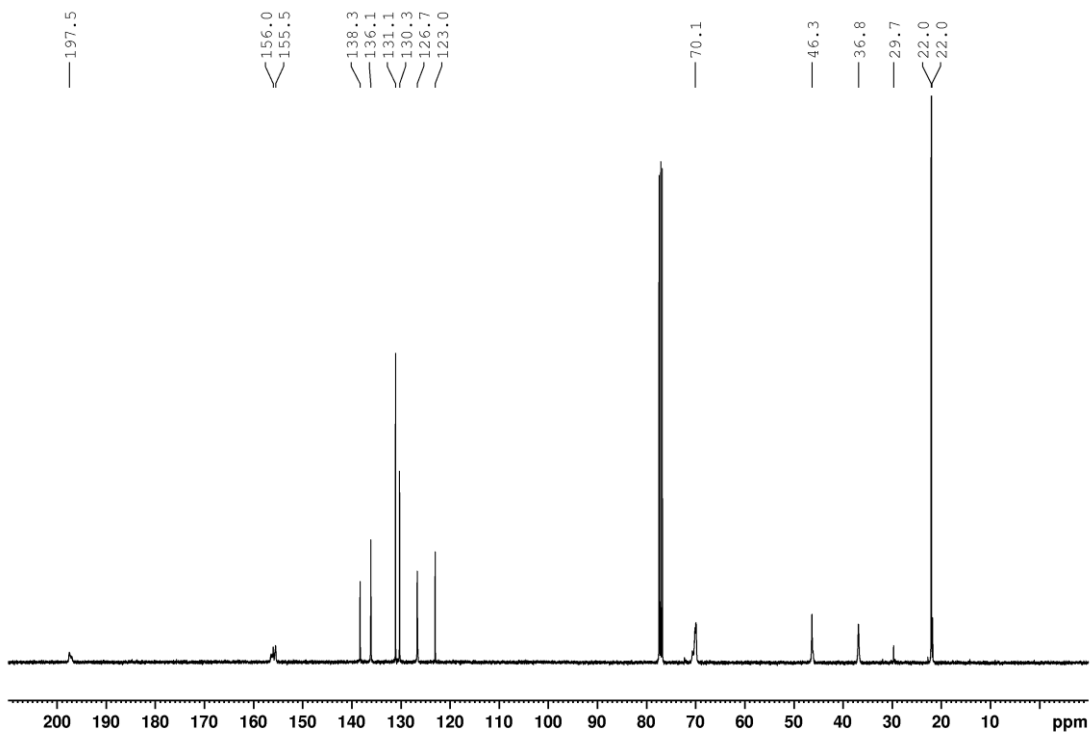


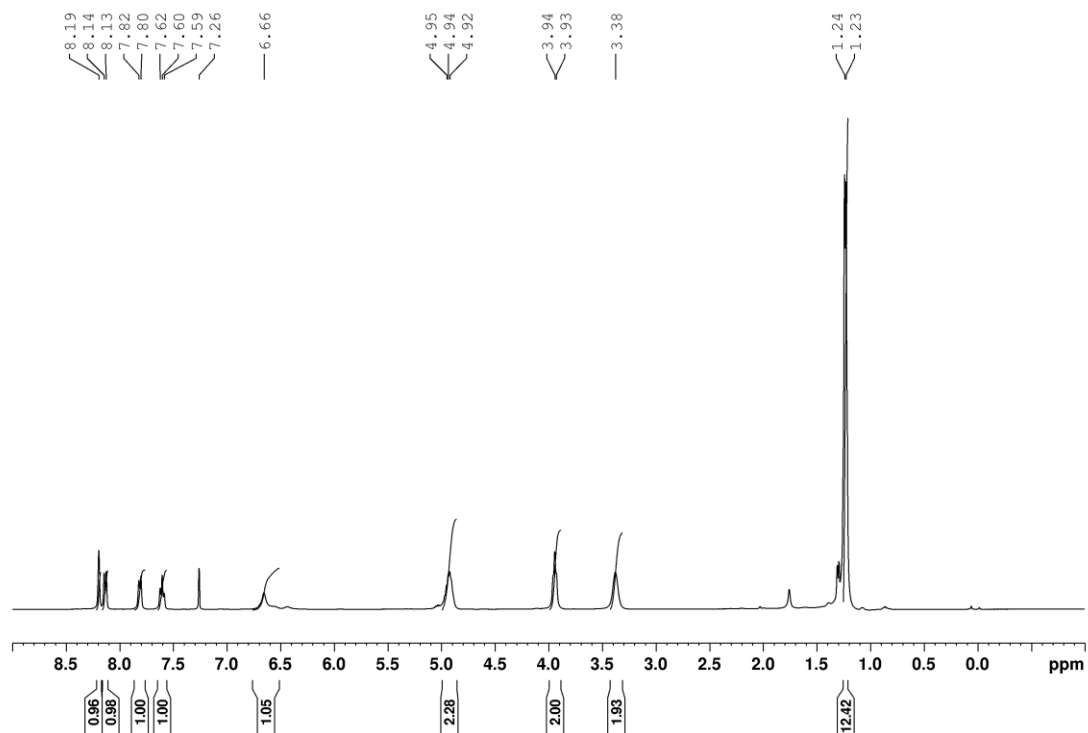
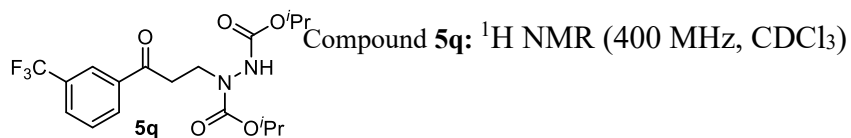


Compound **5p**: ^1H NMR (400 MHz, CDCl_3)

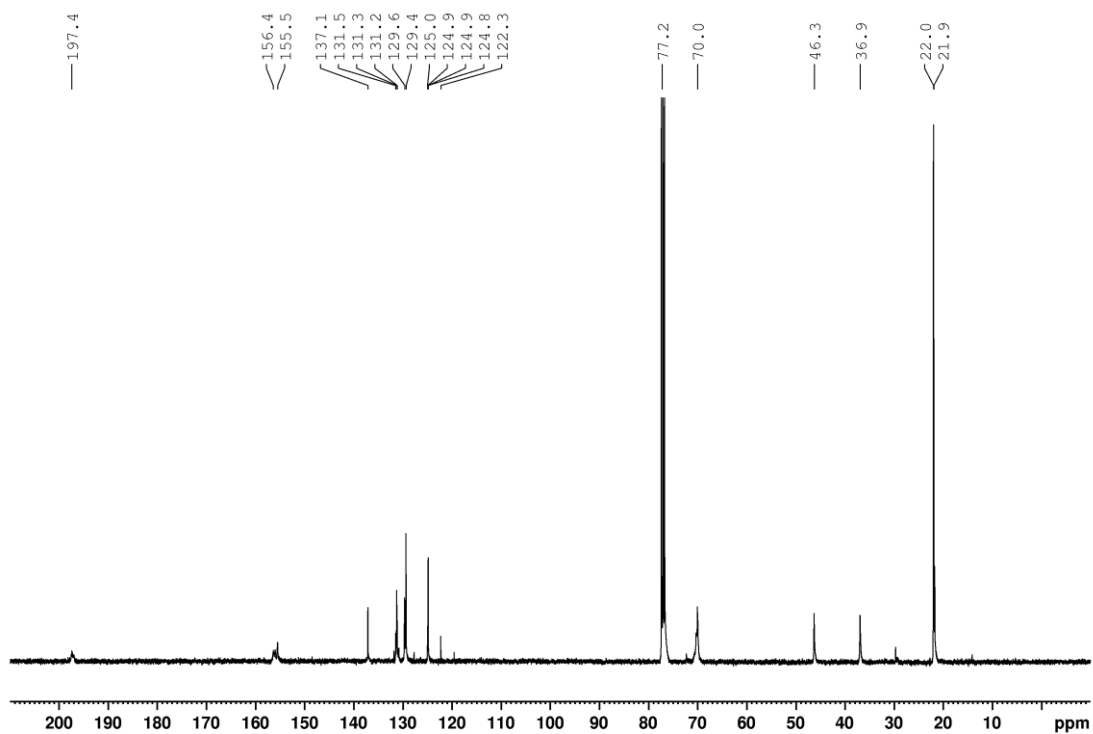


Compound **5p**: ^{13}C NMR (100 MHz, CDCl_3)

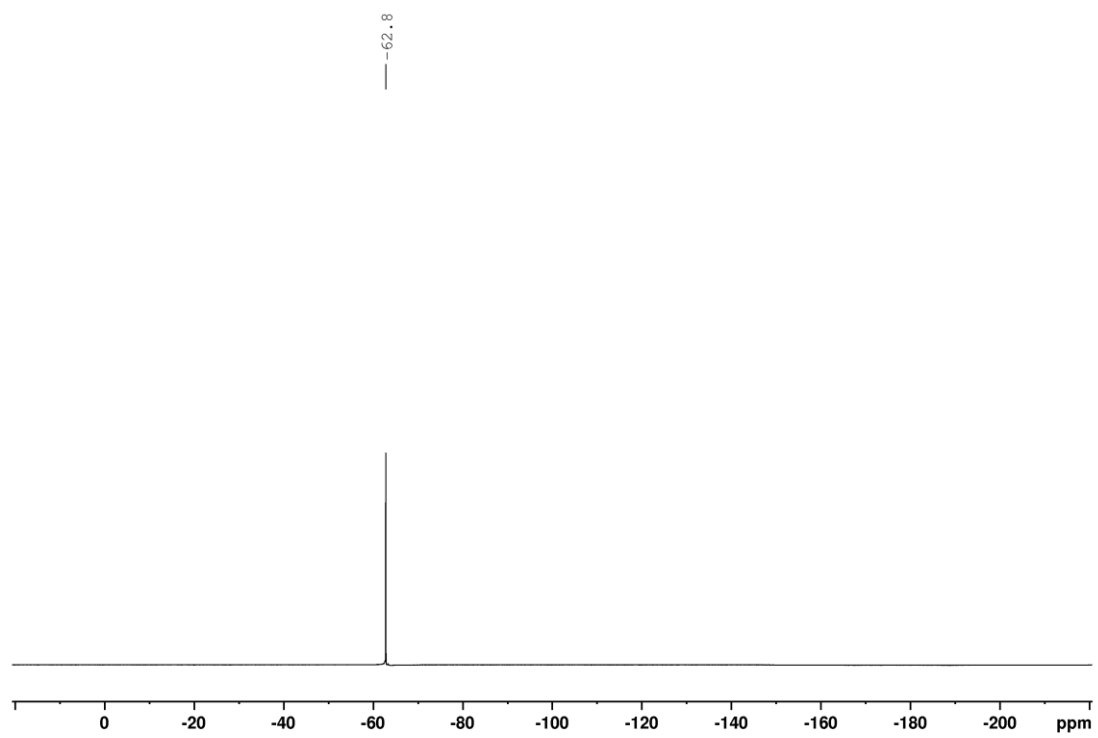


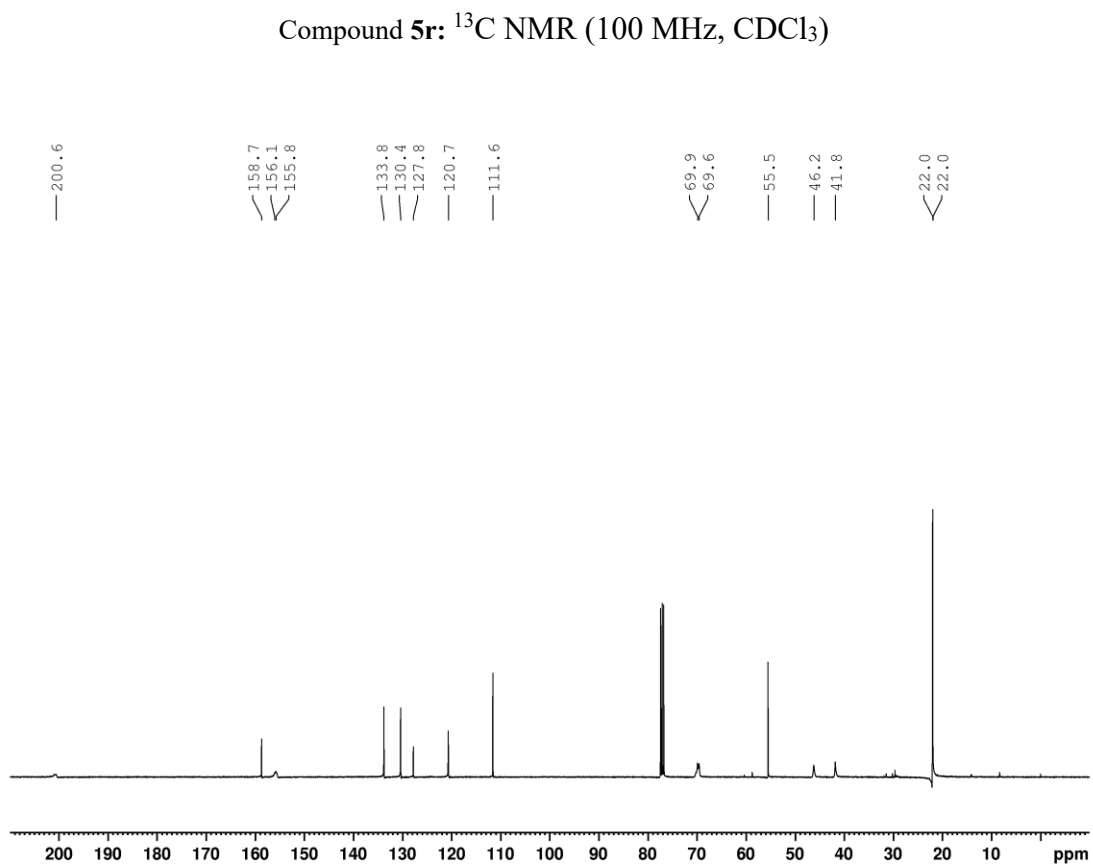
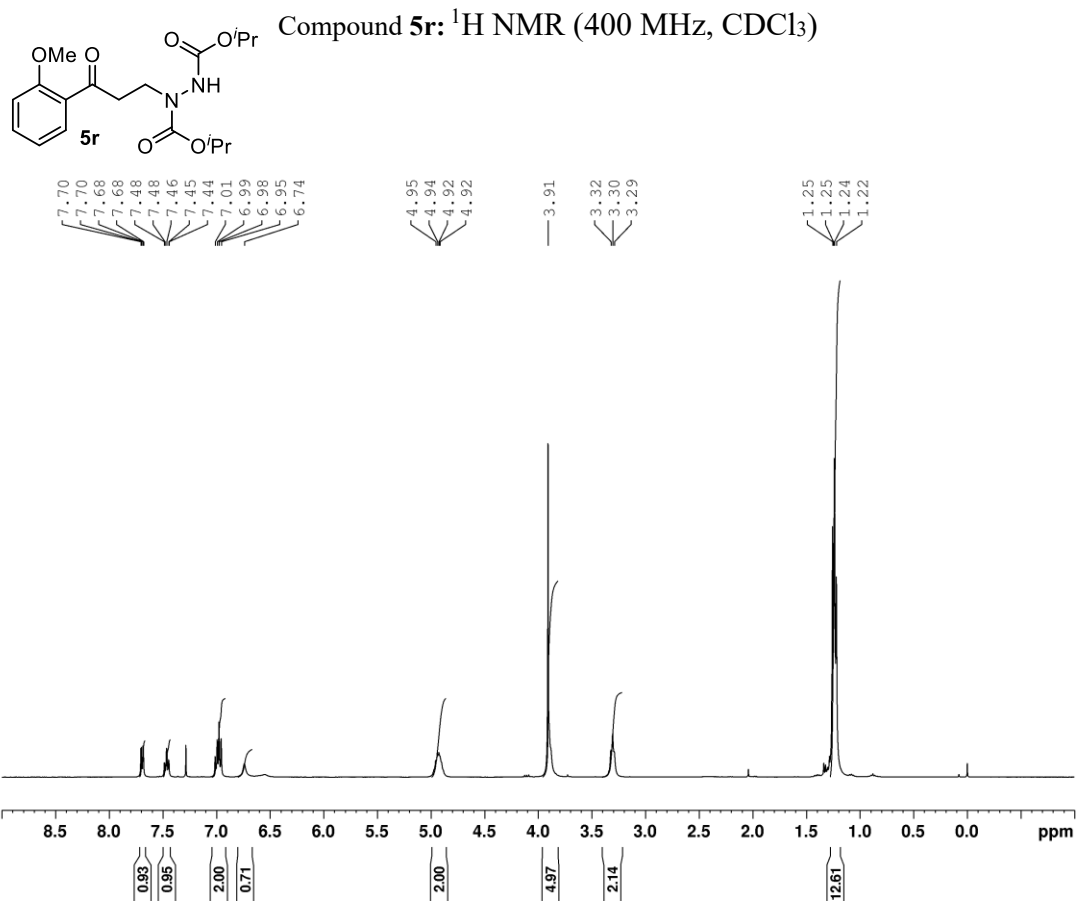


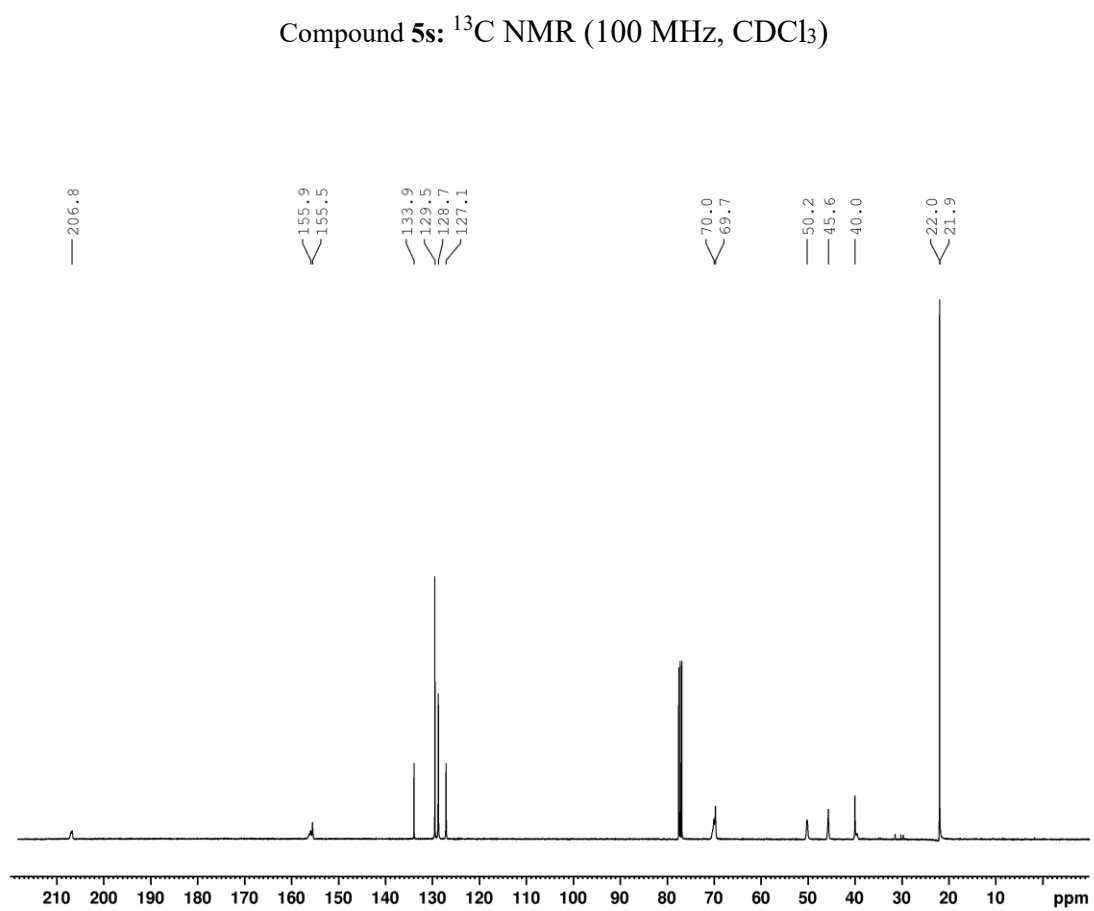
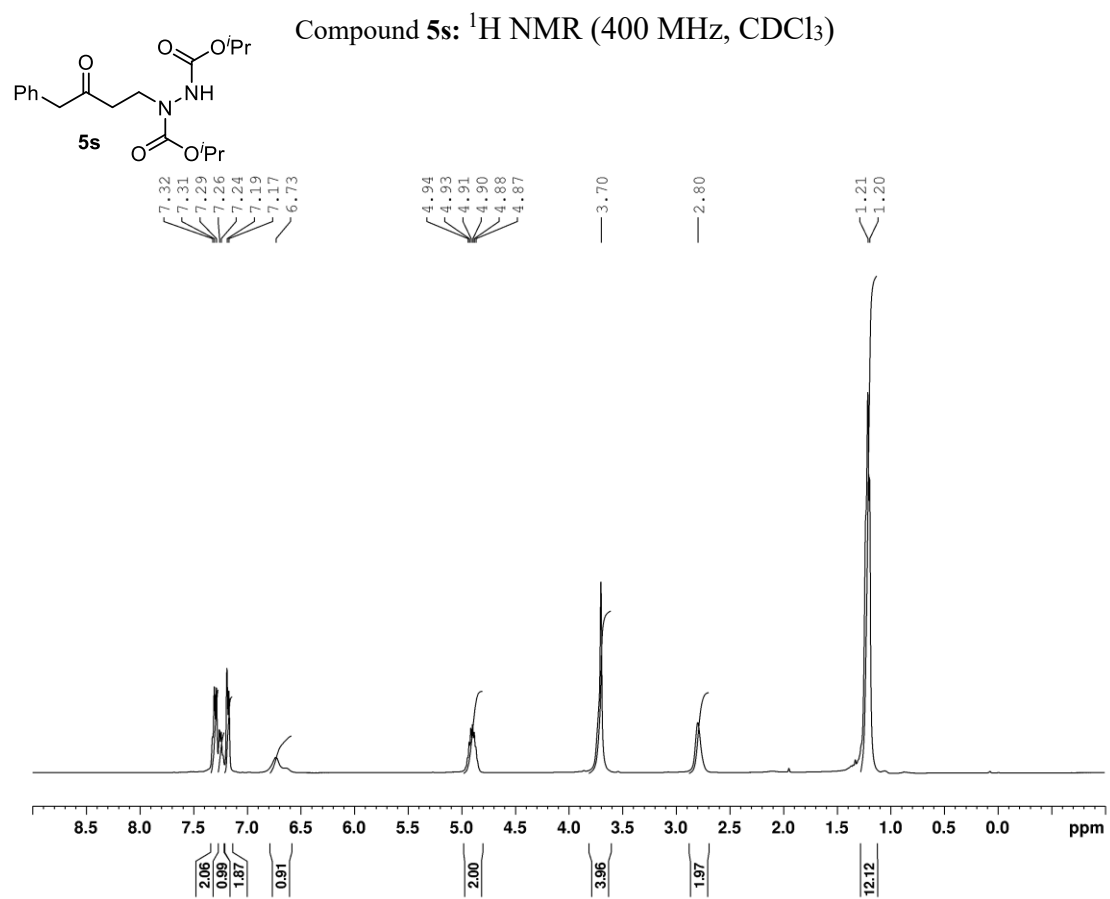
Compound **5q**: ^{13}C NMR (100 MHz, CDCl_3)

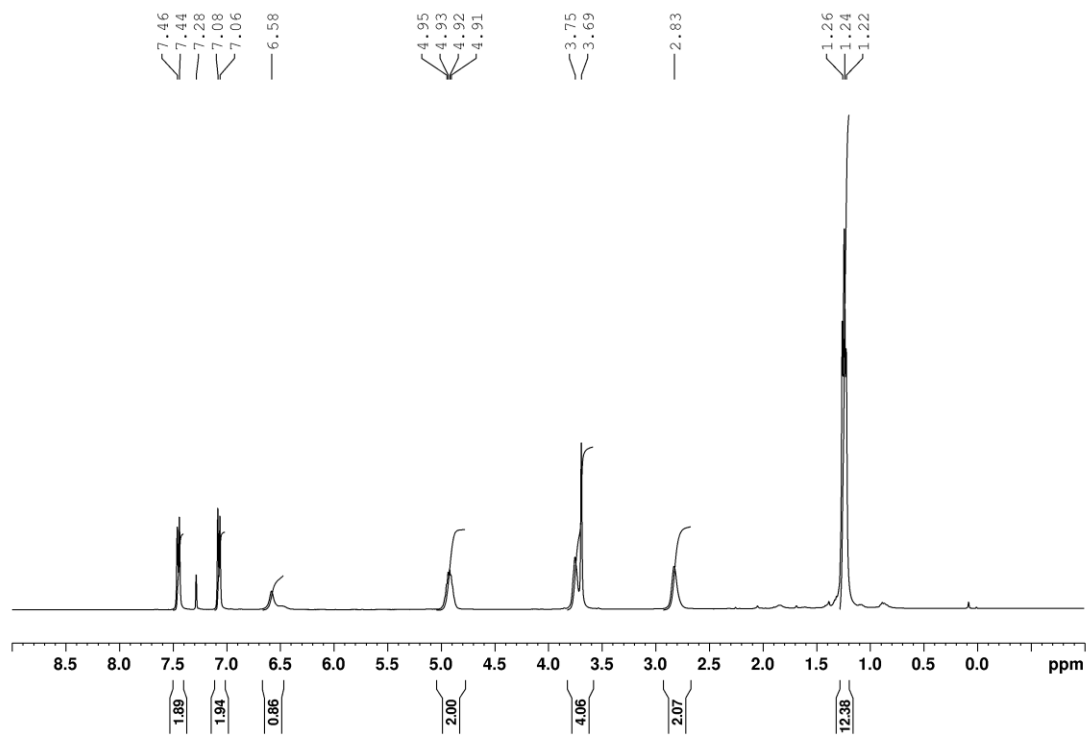
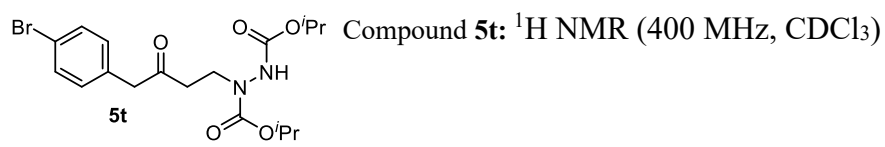


Compound **5q**: ^{19}F (376 MHz, CDCl_3)

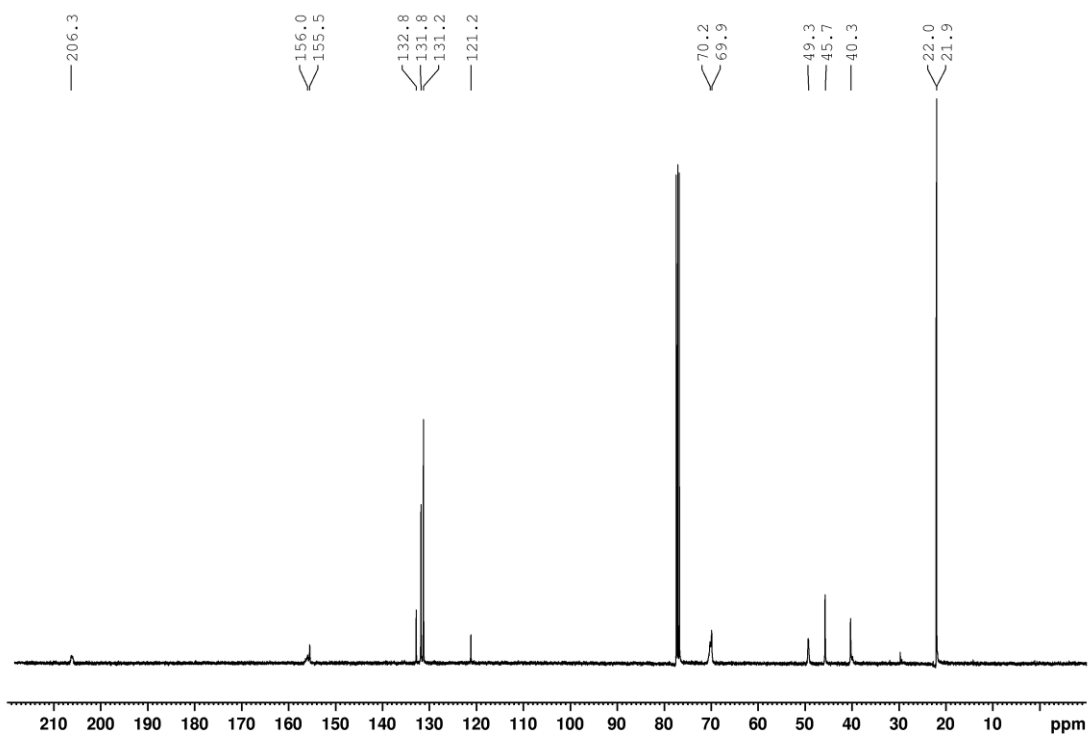




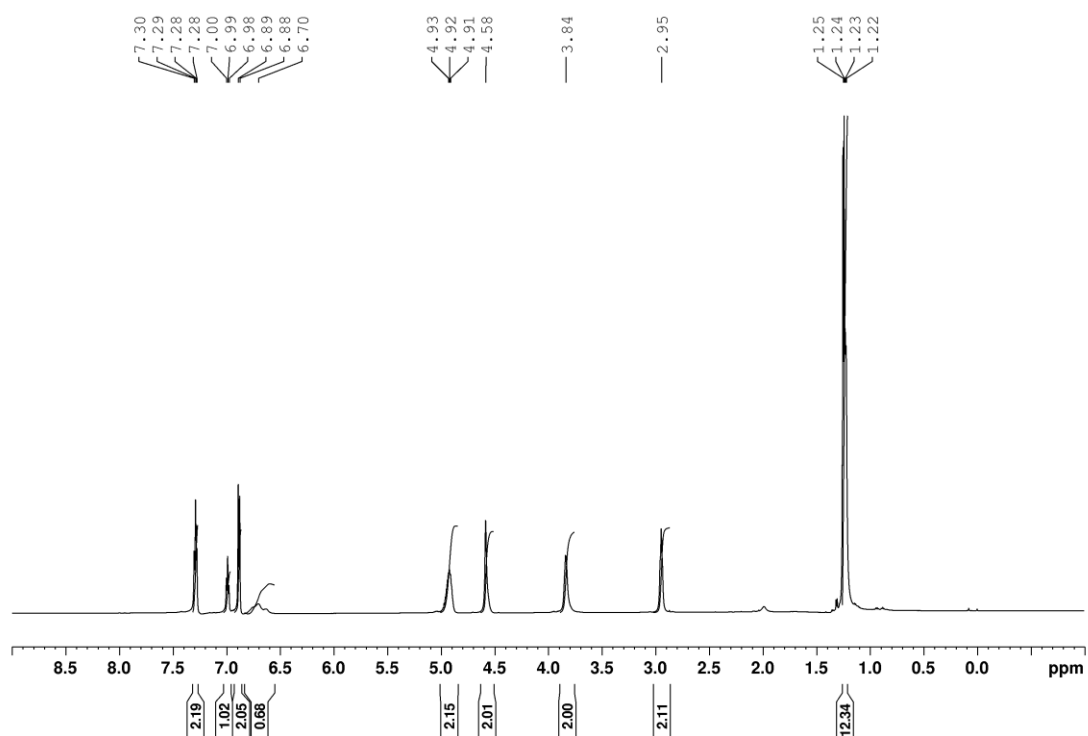
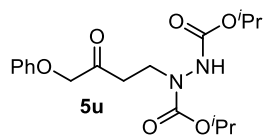




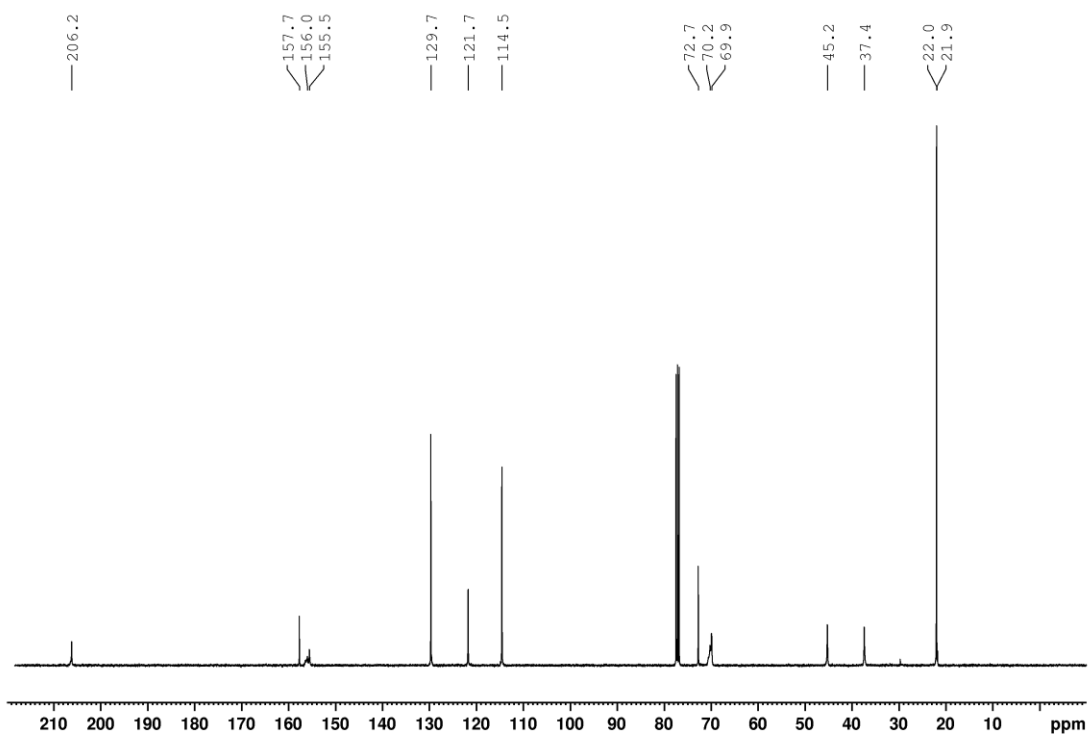
Compound **5t**: ^{13}C NMR (100 MHz, CDCl_3)



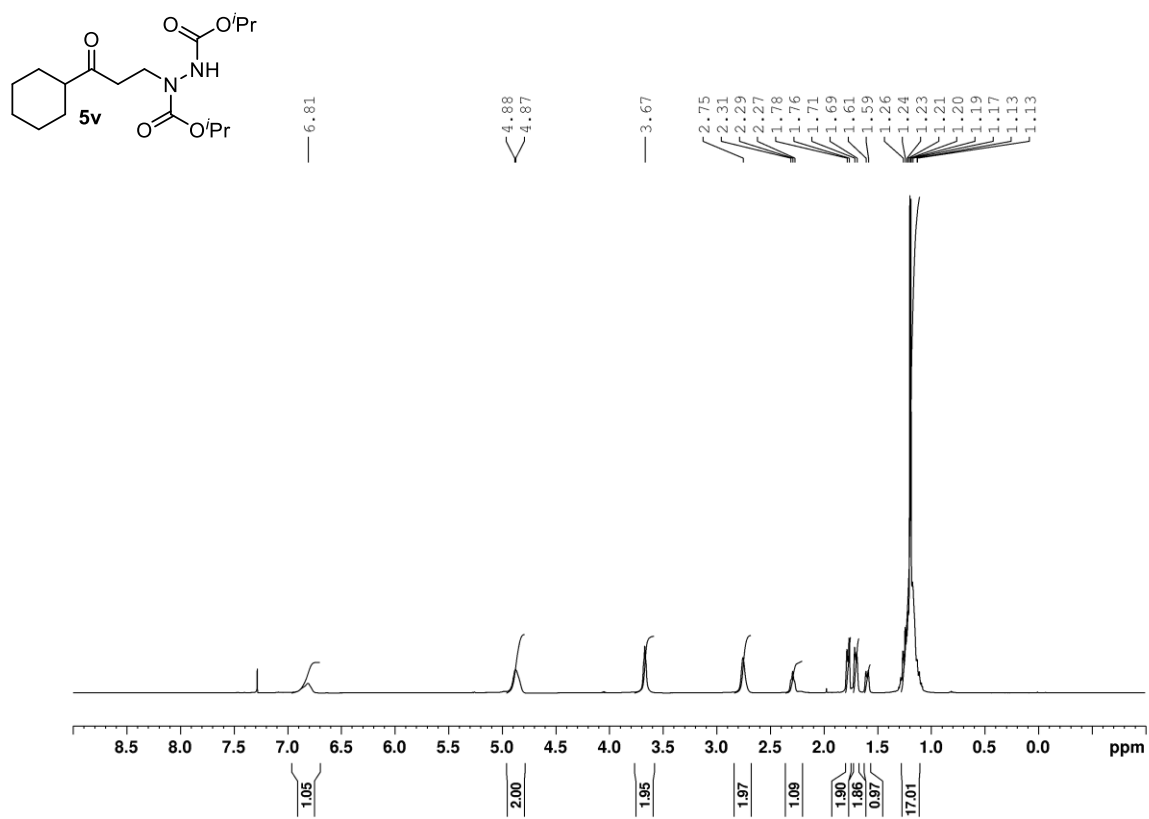
Compound **5u**: ^1H NMR (600 MHz, CDCl_3)



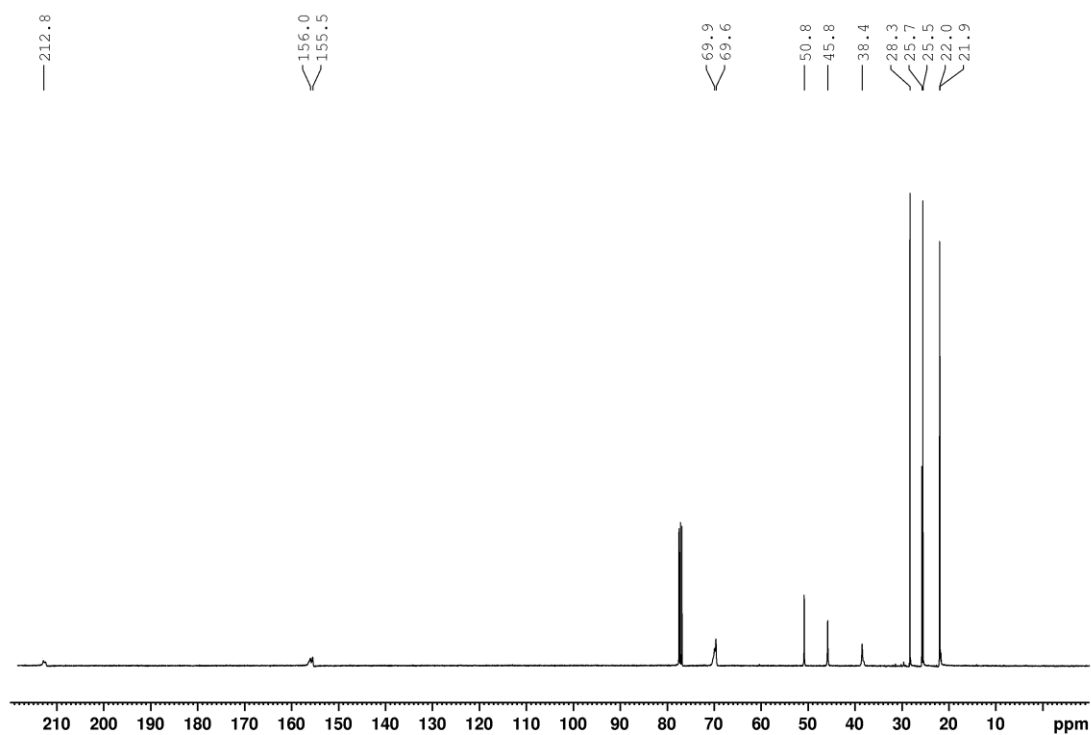
Compound **5u**: ^{13}C NMR (100 MHz, CDCl_3)

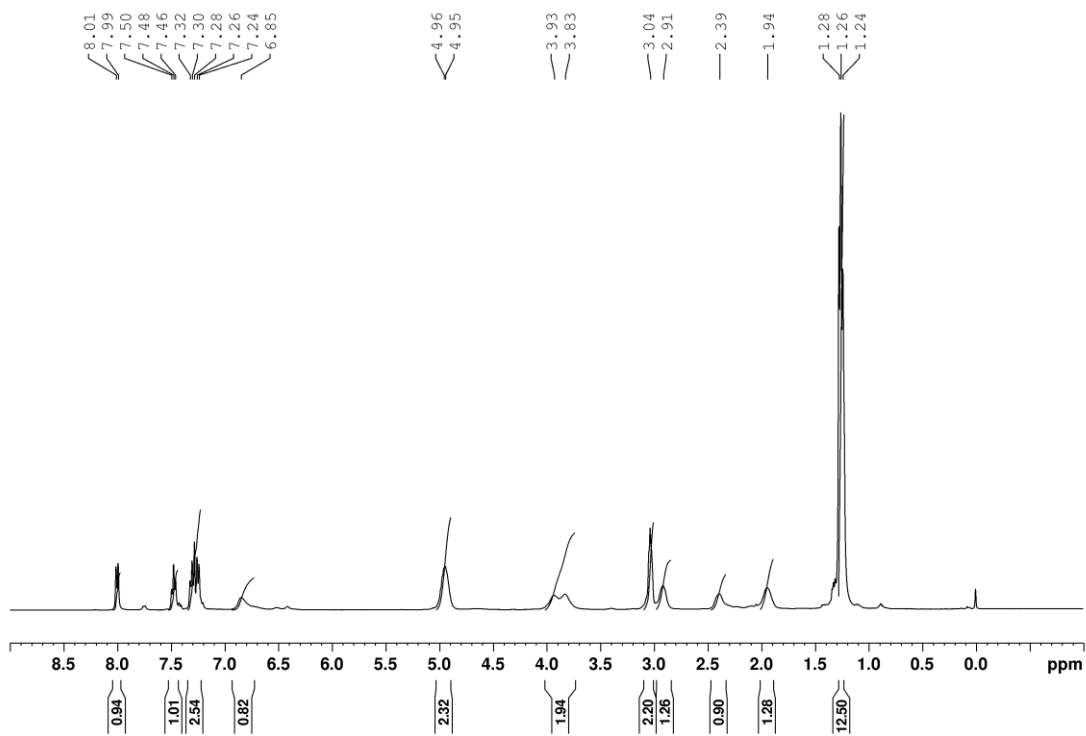
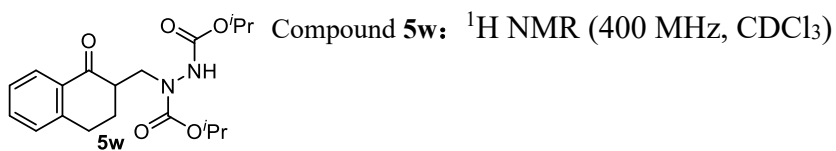


Compound **5v**: ^1H NMR (600 MHz, CDCl_3)

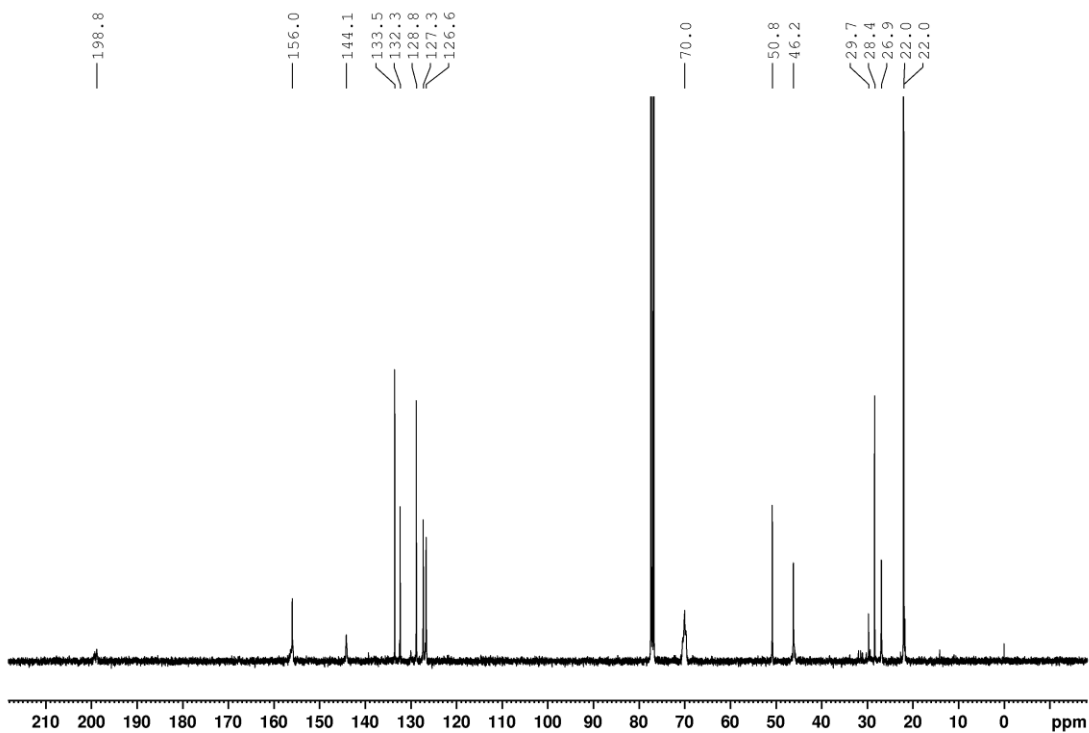


Compound **5v**: ^{13}C NMR (100 MHz, CDCl_3)

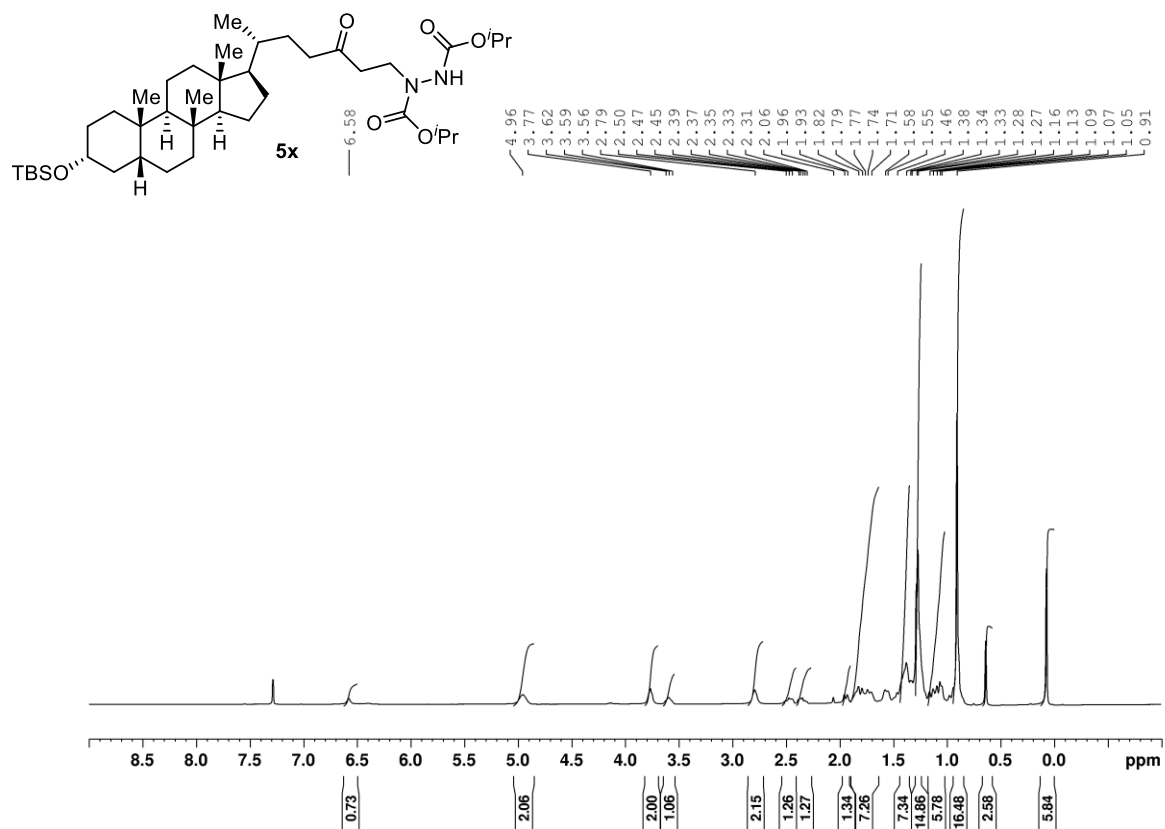




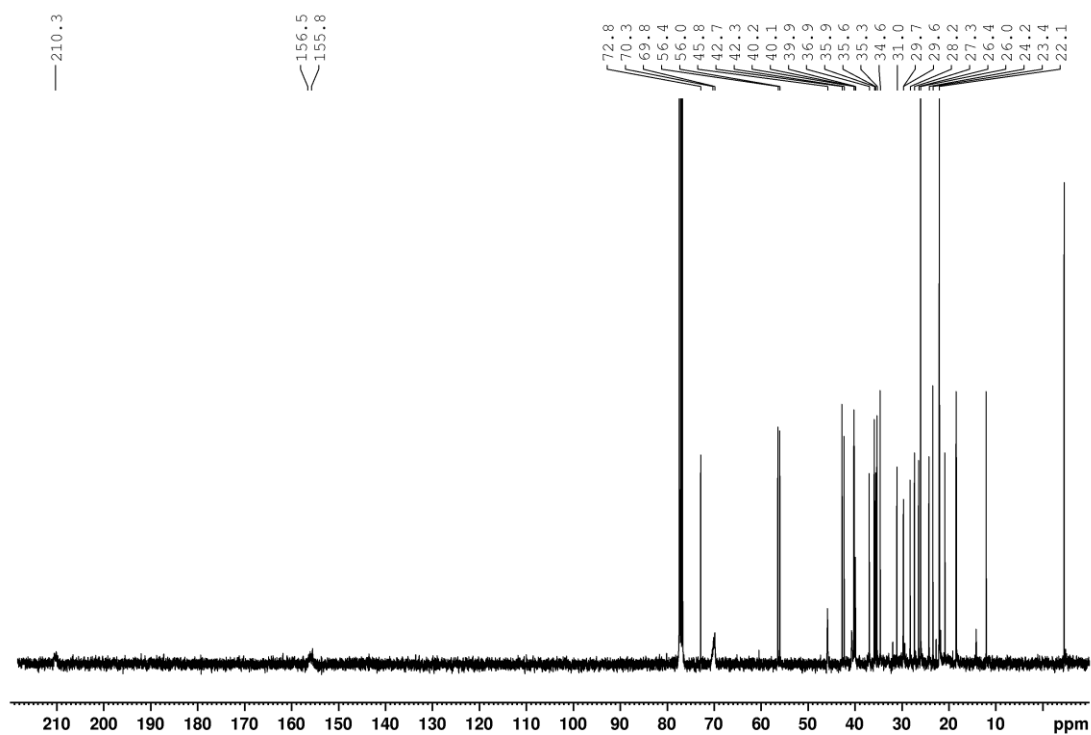
Compound **5w**: ^{13}C NMR (100 MHz, CDCl_3)

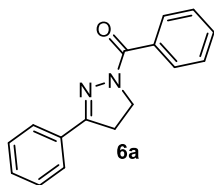


Compound **5x**: ^1H NMR (400 MHz, CDCl_3)

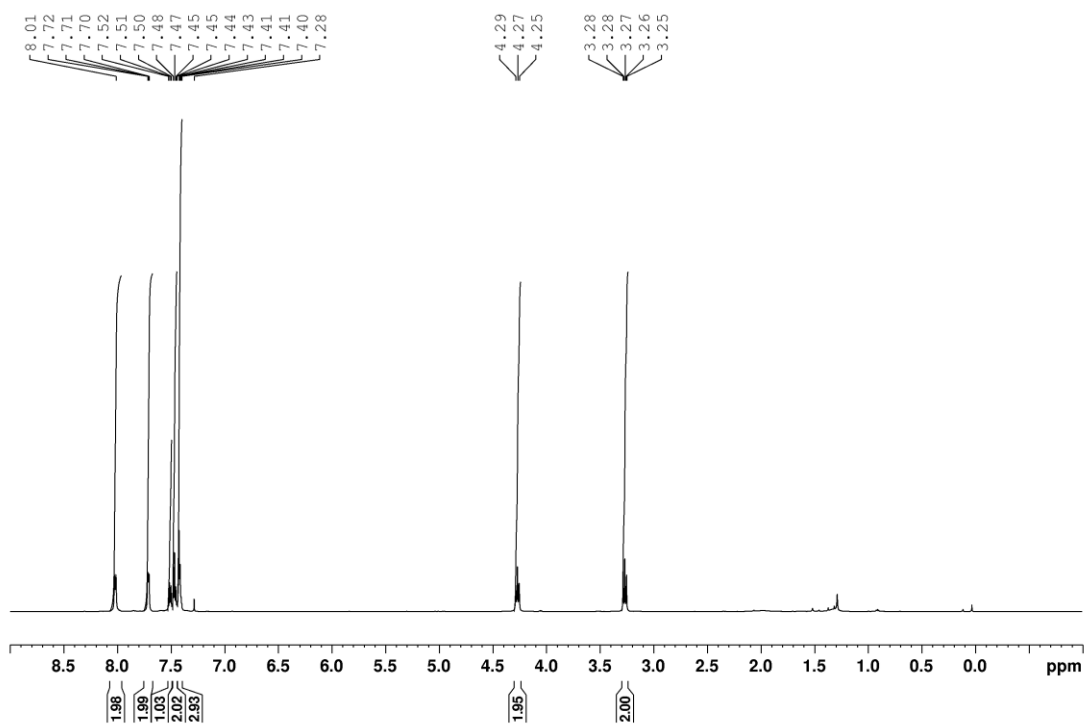


Compound **5x**: ^{13}C NMR (100 MHz, CDCl_3)

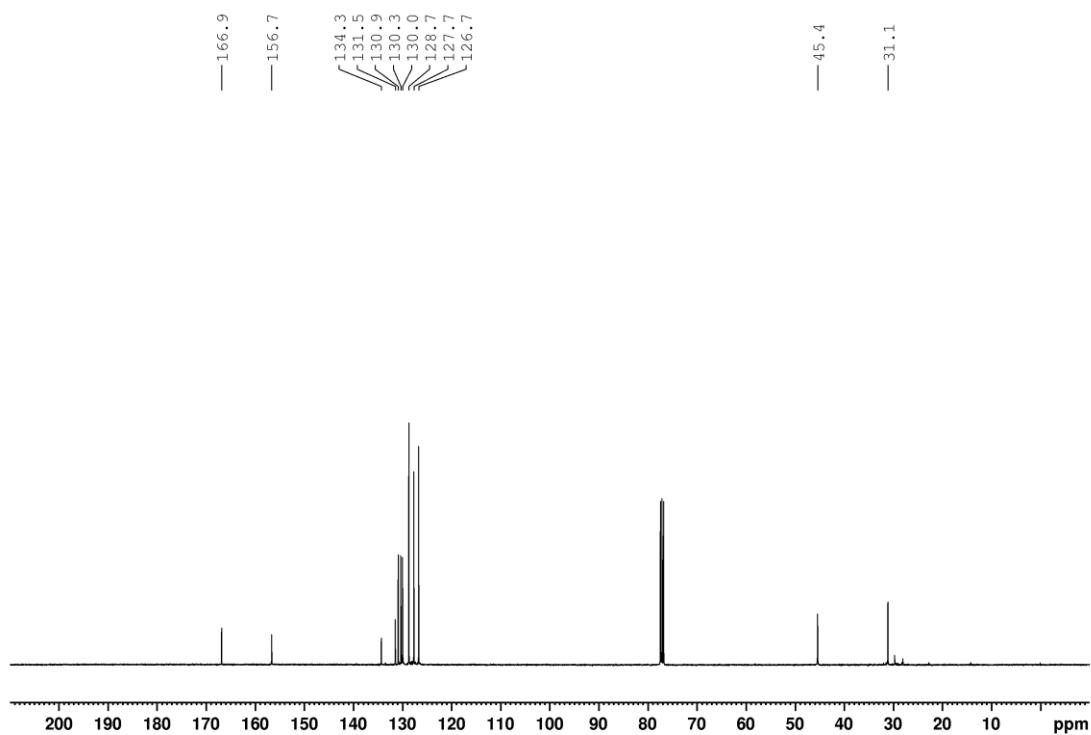


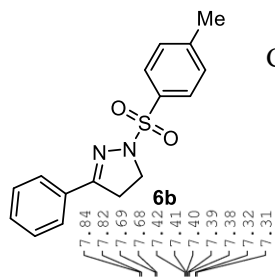


Compound **6a**: ^1H NMR (600 MHz, CDCl_3)

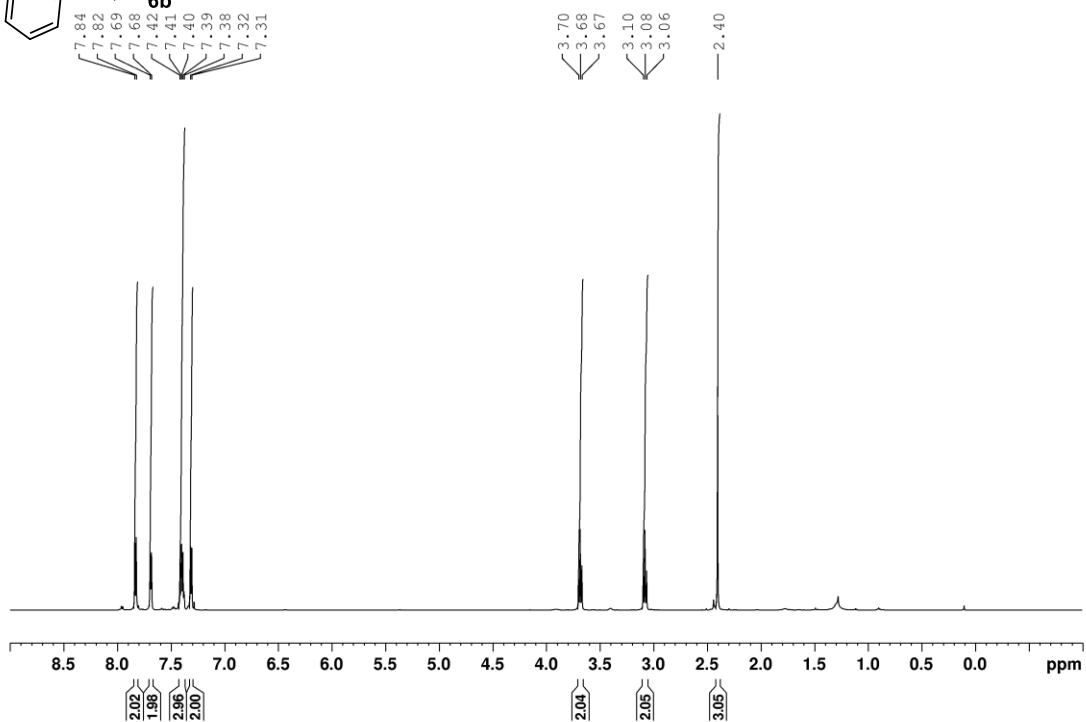


Compound **6a**: ^{13}C NMR (100 MHz, CDCl_3)

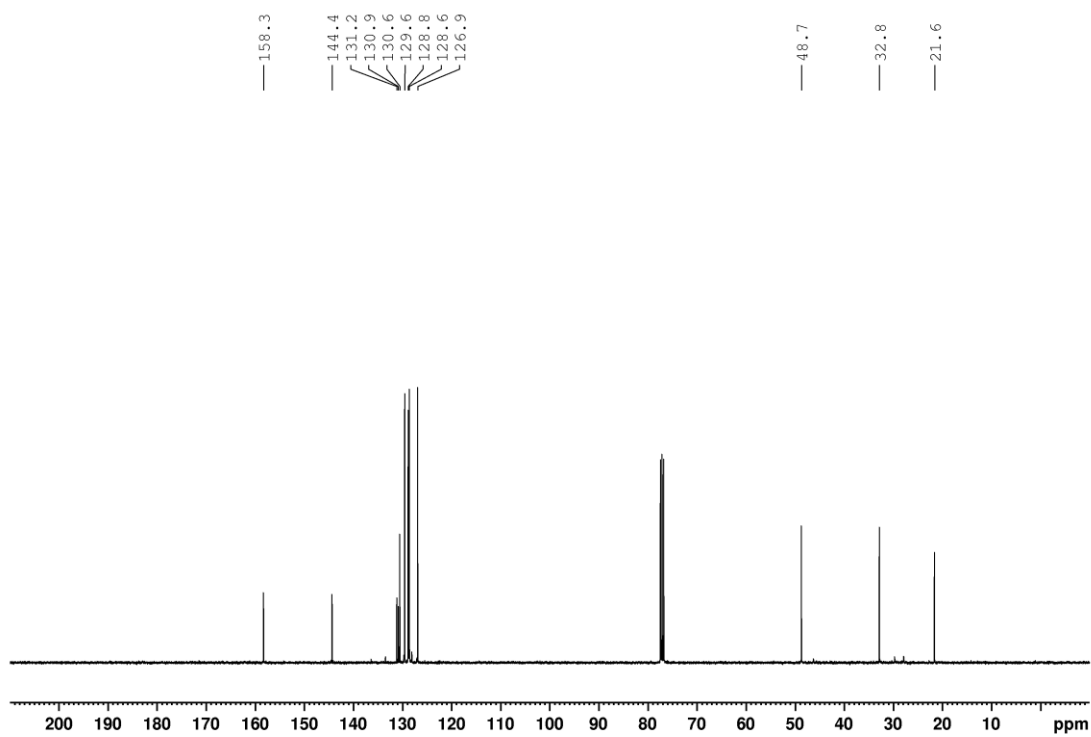


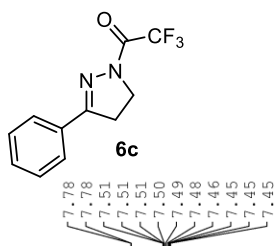


Compound **6b**: ^1H NMR (600 MHz, CDCl_3)

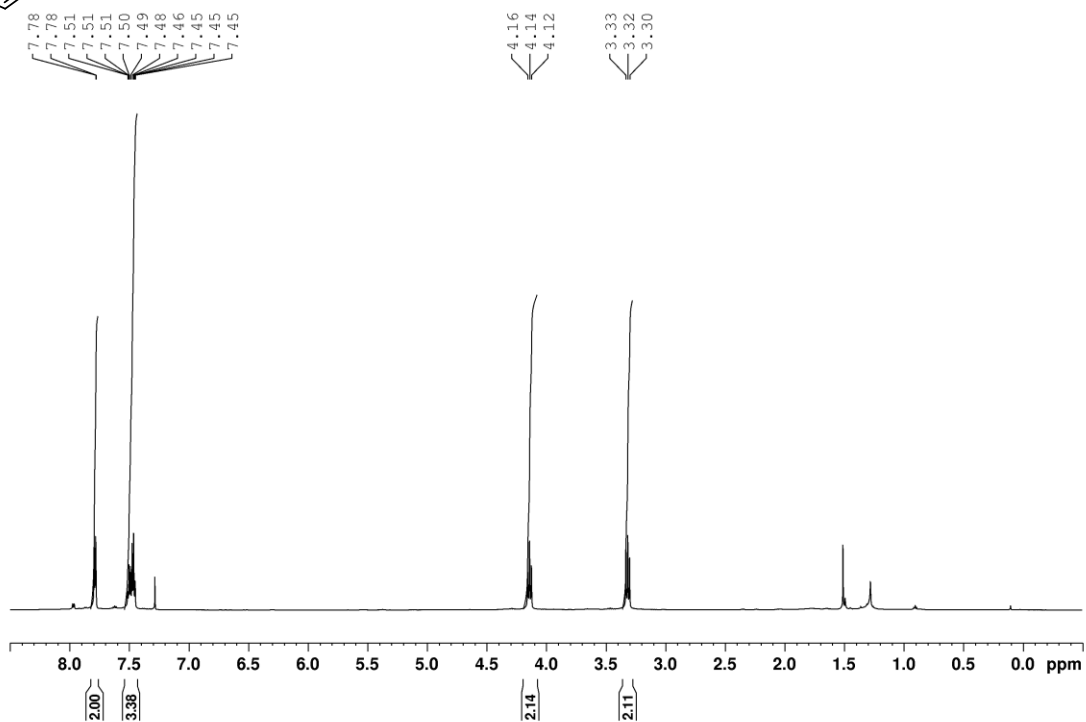


Compound **6b**: ^{13}C NMR (100 MHz, CDCl_3)

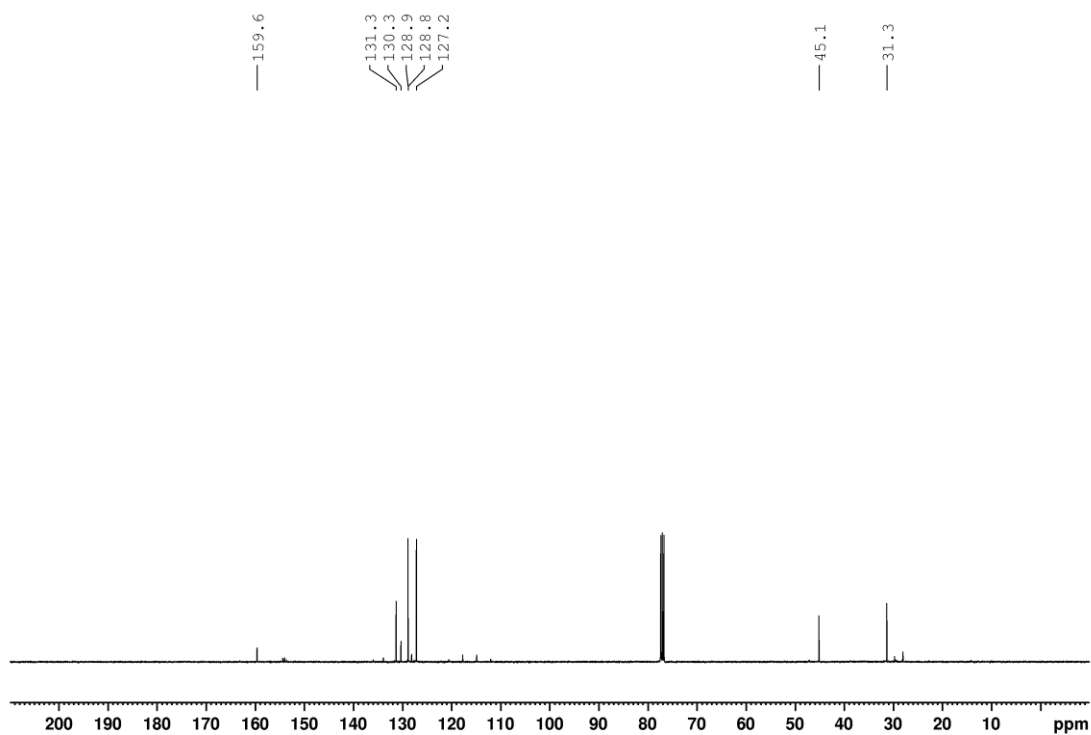




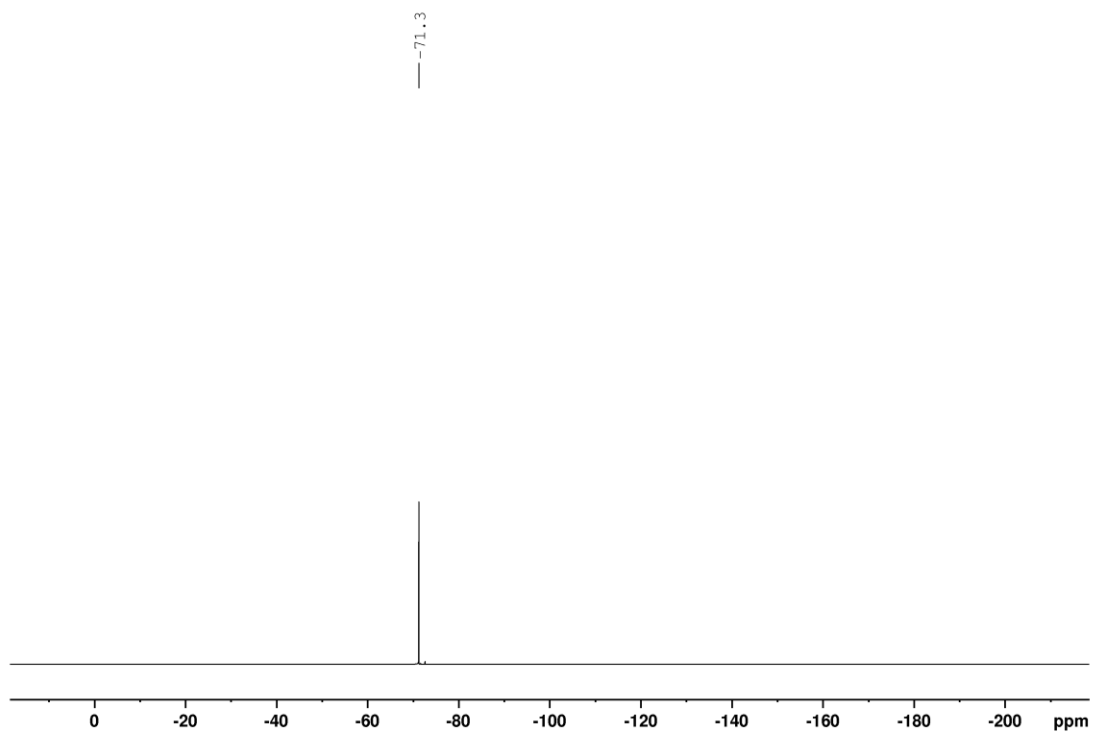
Compound **6c**: ^1H NMR (600 MHz, CDCl_3)

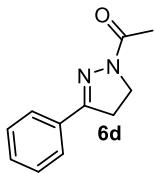


Compound **6c**: ^{13}C NMR (100 MHz, CDCl_3)

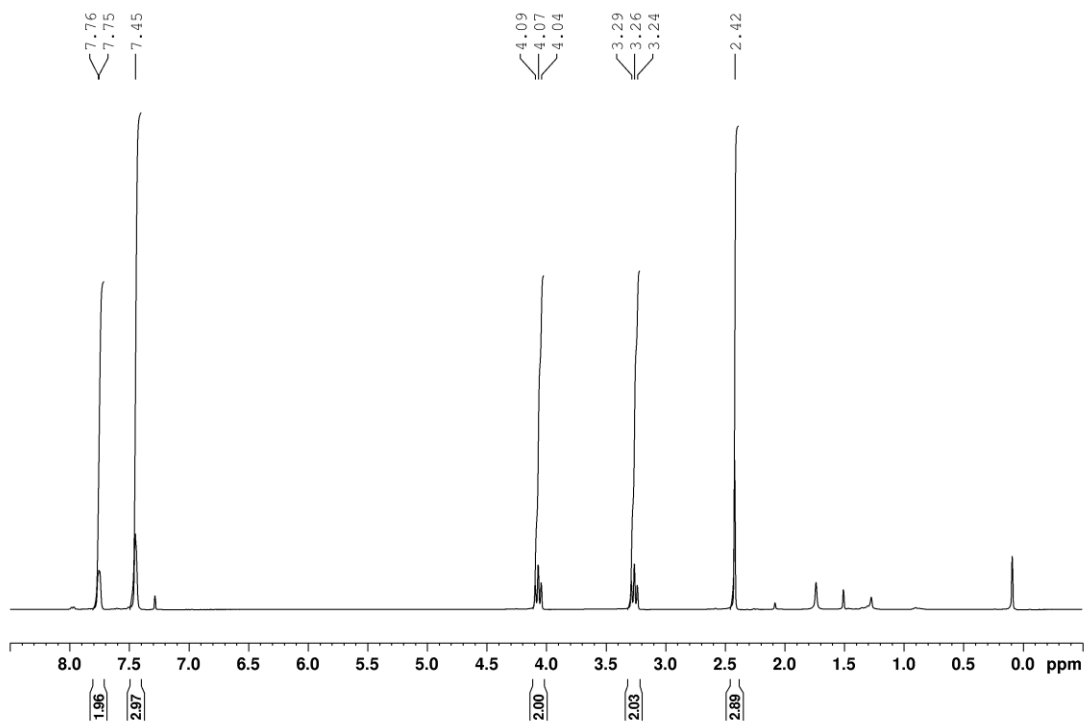


Compound **6c**: ^{19}F NMR (376 MHz, CDCl_3)

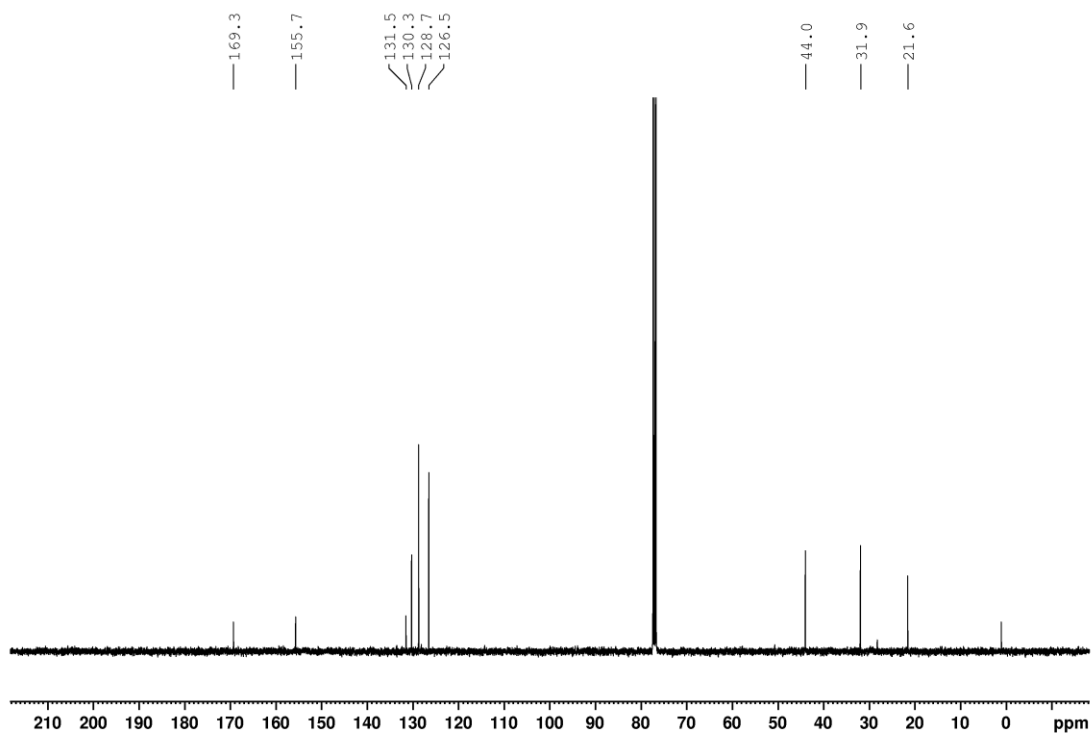


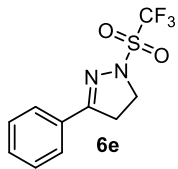


Compound **6d**: ^1H NMR (400 MHz, CDCl_3)

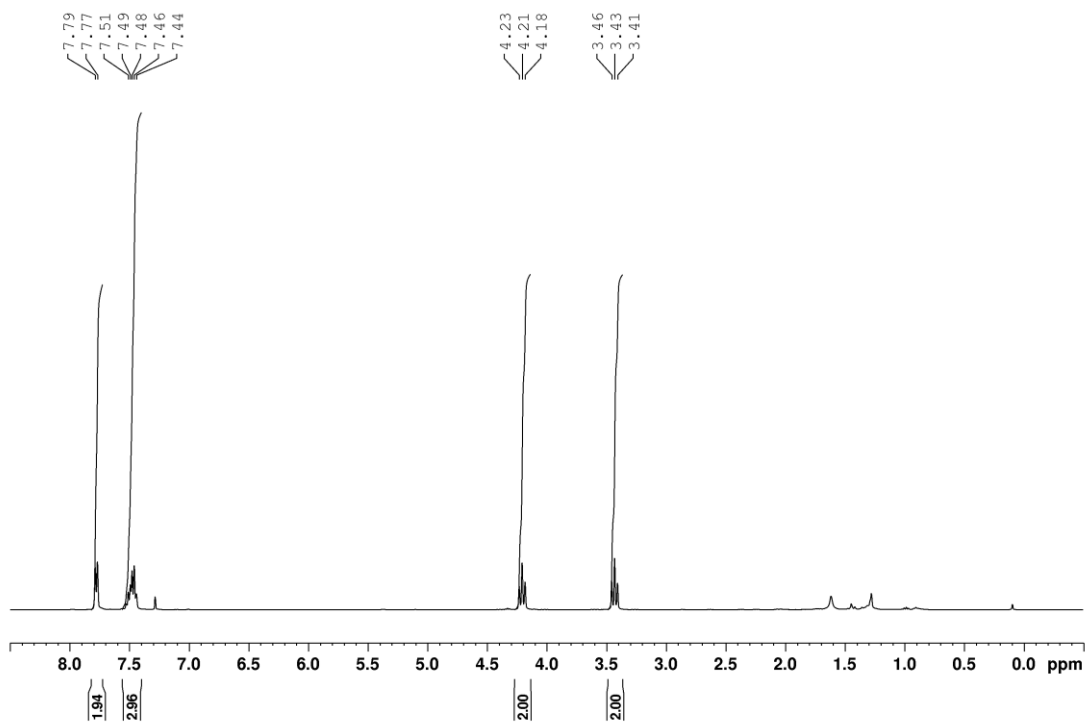


Compound **6d**: ^{13}C NMR (100 MHz, CDCl_3)

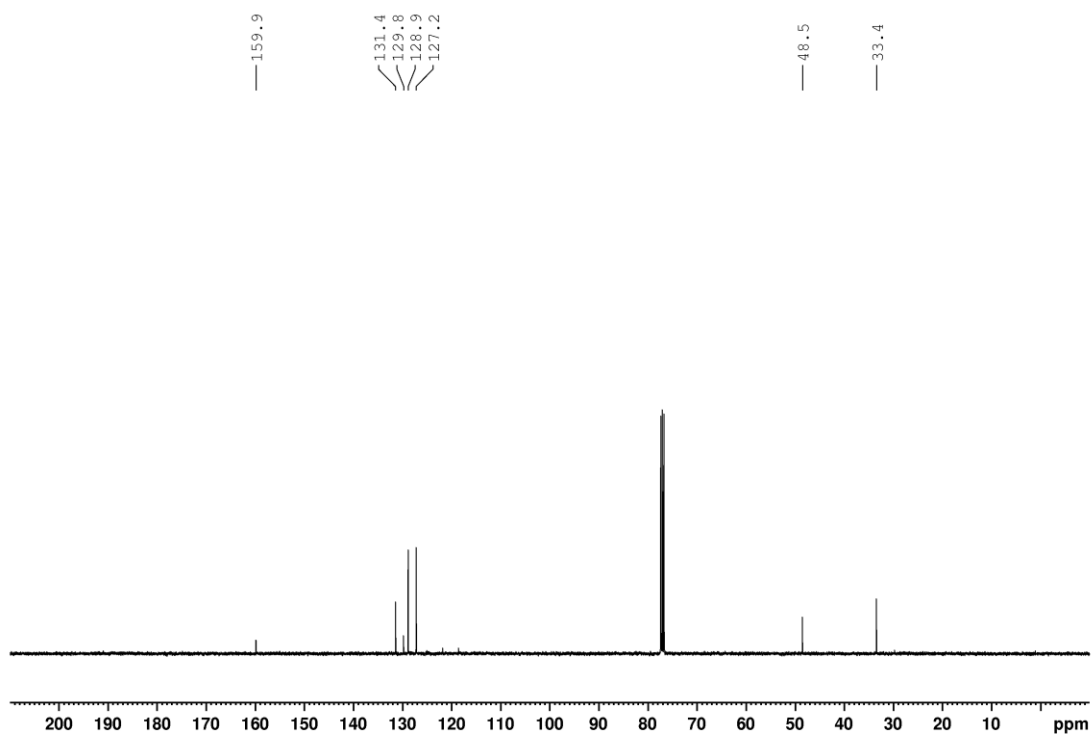




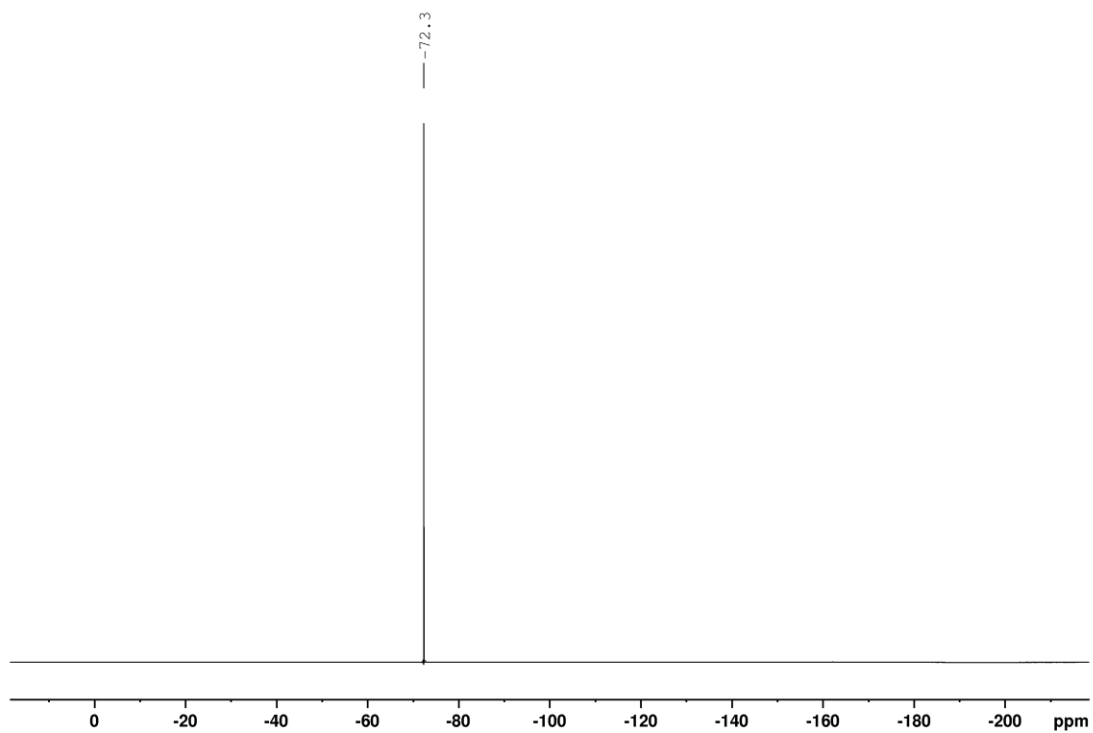
Compound **6e**: ^1H NMR (400 MHz, CDCl_3)

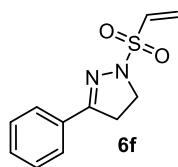


Compound **6e**: ^{13}C NMR (100 MHz, CDCl_3)

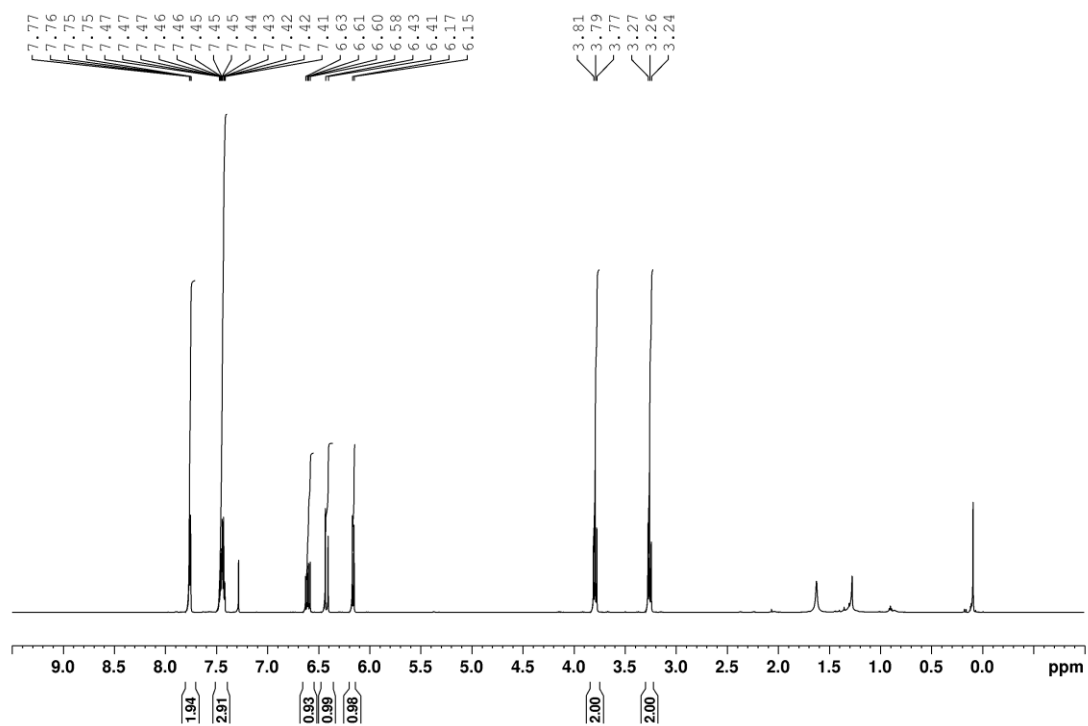


Compound **6e**: ^{19}F NMR (376 MHz, CDCl_3)





Compound **6f**: ^1H NMR (600 MHz, CDCl_3)



Compound **6f**: ^{13}C NMR (150 MHz, CDCl_3)

