Supporting Information to Accompany:

Nucleophilic Substitution of Oxazino-/Oxazolino-/Benzoxazin[3,2-*b*]indazoles: An effective route to 1*H*-Indazolones

Michael B. Donald,[†] Wayne E. Conrad,[†] James S. Oakdale,[†]
Jeffrey D. Butler,[†] Makhluf J. Haddadin,[‡] and Mark J. Kurth[†]

[†]*Department of Chemistry, University of California, One Shields Avenue, Davis, California 95616*

[‡]*Department of Chemistry, American University of Beirut, Beirut, Lebanon*

mjkurth@ucdavis.edu

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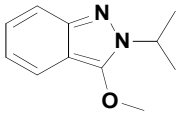
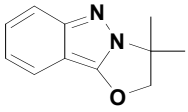
I. Experimental Procedures and Spectral Information

General Experimental Procedures. All chemicals were purchased from commercial suppliers and used without further purification. Analytical thin layer chromatography was carried out on pre-coated plates (Silica gel $60F_{254}$, 250 μm thickness) and visualized with UV light. Flash chromatography was performed with 60 Å, 32-63 μm silica gel (Scientific Absorbents). Concentration refers to rotary evaporation under reduced pressure. ^{1}H NMR spectra were recorded at 300, 400, or 600 MHz at ambient temperature with DMSO-d_6 or $CDCl_3$ as solvents. ^{13}C NMR spectra were recorded at 75, 100, or 150 MHz at ambient temperature with DMSO-d_6 or $CDCl_3$ as solvents. Chemical shifts are reported in parts per million relative to DMSO-d_6 (^{1}H, δ 2.50, ^{13}C, δ 39.52) or $CDCl_3$ (^{1}H, δ 7.26, ^{13}C, δ 77.16). Infrared spectra were recorded on an ATI-FTIR spectrometer. The specifications of the LC/MS are as follows: electrospray (+) ionization, mass range 150-1500 Da, 20 V cone voltage, and Xterra MS C_{18} column (2.1 mm x 50 mm x 3.5 μm). DMF refers to *N*,*N*-dimethylformamide.

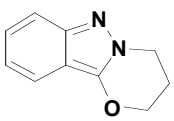
II. Preparation of Indazoles



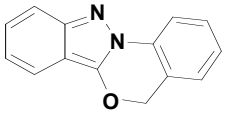
3,3-Dimethyl-2,3-dihydrooxazolo[3,2-b]indazole (**4**). Made via literature methods found in Mills, A.; Nazer, M.; Haddadin, M. and Kurth, M. *J. Org. Chem.* **2006**, *71*, 2687-2689. Spectral data is in accord with literature values.



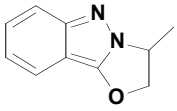
3,3-Dimethyl-2,3-dihydrooxazolo[3,2-*b*]indazole (**2c**). 2-Methyl-2-(2-nitrobenzylamino)-propan-1-ol (4.0 g, 17.85 mmol) was dissolved in 80 mL of 10% aqueous isopropanol. The solution was heated to 60 °C, then potassium hydroxide (4.4 g, 78.57 mmol) was added. The reaction was stirred at 60 °C for 10 hours and monitored by thin layer chromatography. When starting material was consumed, the reaction was removed from heat and concentrated. The residue was dissolved in ethyl acetate and added to a separatory funnel containing saturated ammonium chloride. The layers were separated and the aqueous layer was extracted with additional ethyl acetate. The combined organics were washed with water, brine, dried over sodium sulfate, and concentrated. The crude product was purified by flash chromatography (1:1 ethyl acetate:hexane) to afford **2c** (3.08 g, 92%). mp 94 – 95 °C; IR (neat) ν_{max} 3059, 2971, 1631, 1560, 1525, 1513, 1443, 1378, 1342, 1269, 1165, 1092, 1006, 986, 862, 829, 752 cm^{-1} ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 8.7, 14.8, 2H), 7.20 – 7.15 (m, 1H), 6.90 – 6.86 (m, 1H), 4.84 (s, 3H), 1.68 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.78, 149.98, 126.74, 119.57, 119.07, 117.89, 101.36, 88.02, 61.33, 25.97; ESI MS *m/z* 189.13 $(M + H)^{+}$.



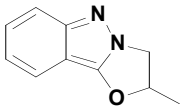
3,4-Dihydro-2*H*-[1,3]oxazino[3,2-*b*]indazole (**5**). Made via literature methods found in Oakdale, J.; Solano, D.; Fettinger, J.; Haddadin, M.; Kurth, M. *Org. Lett.* **2009**, *11*, 2760-2763. Spectral data is in accord with literature values.



5*H*-Indazolo[3,2-*b*]benzo[*d*]-1,3-oxazine (**6**). Made via literature methods found in Butler, J.; Solano, D.; Robins, L.; Haddadin, M.; Kurth, M. *J. Org. Chem.* **2008**, *73*, 234-240. Spectral data is in accord with literature values.

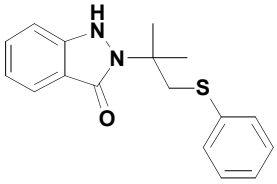


3-Methyl-2,3-dihydrooxazolo[3,2-*b*]indazole (**2b**). Made via literature methods found in Oakdale, J.; Solano, D.; Fettinger, J.; Haddadin, M.; Kurth, M. *Org. Lett.* **2009**, *11*, 2760-2763. Spectral data is in accord with literature values.

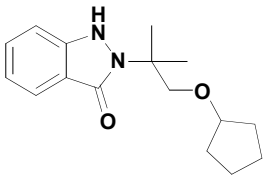


2-Methyl-2,3-dihydrooxazolo[3,2-*b*]indazole (**2d**). Made via literature methods found in Oakdale, J.; Solano, D.; Fettinger, J.; Haddadin, M.; Kurth, M. *Org. Lett.* **2009**, *11*, 2760-2763. Spectral data is in accord with literature values.

III. General Procedures for the Addition of Nucleophiles to Indazoles

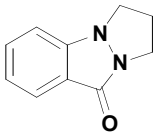


General procedure of Thiolate Nucleophiles: Synthesis of 2-(2-methyl-1-(phenylthio)propan-2-yl)-1*H*-indazol-3(2*H*)-one (**17**). Thiophenol (397 mg, 3.12 mmol) was added to a 10 mL microwave vial, sealed with a septum, and purged with N_2. 3 mL of dry DMF was added and the vessel was cooled to 0 ºC. Sodium hydride (84.0 mg, 2.08 mmol) was then added and stirred until the evolution of gas ceased. The vial was then removed from the ice bath and indazole **2c** (97.0 mg, 0.520 mmol), dissolved in DMF was added. The microwave vial was sealed and heated to 120 ºC for 20 minutes in a microwave reactor (Personal Chemistry, Emrys Optimizer). The mixture was diluted with H_2O, neutralized with 1N HCl, and extracted with 95:5 EtOAc:hexanes. The combined organic extracts were dried over sodium sulfate, concentrated, and the crude product was purified using flash column chromatography (EtOAc/hexanes) to afford a white solid **(5)** (154 mg, 99% yield). mp 142 – 144 °C; IR (neat) ν_{max} 2912, 1616, 1468, 1425, 1367, 1357, 1324, 1230, 749, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.67 (d, *J* = 7.8, 1H), 7.42 (t, *J* = 7.6, 1H), 7.32 (d, *J* = 7.7, 2H), 7.21 – 7.03 (m, 5H), 3.71 (s, 2H), 1.74 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.99, 147.02, 136.12, 131.71, 129.66, 128.91, 126.29, 123.54, 122.37, 120.59, 112.53, 61.40, 43.66, 25.41; ESI MS *m/z* 299.12 $(M + H)^+$.

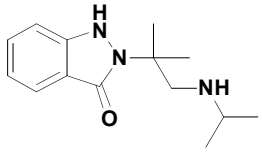


General procedure of Alkoxide Nucleophiles: Synthesis of 2-(1-(cyclopentyloxy)-2-methylpropan-2-yl)-1*H*-indazol-3(2*H*)-one (**20**). Cyclopentanol (271 mg, 3.15 mmol) was added to a 10 mL microwave vial, sealed with a septum, and purged with N_2. 3 mL dry DMF was added and the mixture was cooled to 0 ºC. Sodium hydride (84.0 mg, 2.10 mmol) was added and stirred until the evolution of gas ceased. The vial was removed from the ice bath and indazole **2c** (98.7 mg, 0.525 mmol), dissolved in DMF was added. The microwave vial was then sealed and heated to 120 ºC for 20 minutes in a microwave reactor (Personal Chemistry, Emrys Optimizer). The mixture was diluted with H_2O, neutralized with 1N HCl, and extracted with 95:5 EtOAc:hexanes. The combined organic extracts were dried over

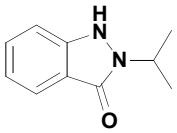
sodium sulfate, concentrated, and the crude product was purified using flash chromatography (1:1, EtOAc/hexanes) to afford a white solid **(10)** (115 mg, 80% yield). mp 132 – 133 °C; ; IR (neat) ν_{max} 2953, 2866, 1608, 1495, 1472, 1425, 1361, 1325, 1237, 1103, 787, 750 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.77 (d, *J* = 7.8, 1H), 7.44 (t, *J* = 7.74, 1H), 7.19 – 7.09 (m, 2H), 3.99 (m, 1H), 3.71 – 3.62 (m, 2H), 1.82 – 1.50 (m, 14H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.53, 146.28, 131.27, 123.54, 122.00, 120.78, 112.10, 82.40, 75.47, 60.34, 32.29, 23.55, 22.55; ESI MS *m/z* 275.19 $(M + H)^+$.



General procedure of ANRORC reaction: Synthesis of 2,3-dihydropyrazolo[1,2-*a*]indazol-9(1*H*)-one (**34'**). Indazole **5** (68.9 mg, 0.396 mmol) was added to a 10 mL microwave vial and dissolved in 6 mL of DMF. Potassium Iodide (263 mg, 1.58 mmol) was added, the vial was sealed, and heated to 170 ºC for 2 hours in a microwave reactor (Personal Chemistry, Emrys Optimizer). The mixture was diluted with H_2O, neutralized with 1N HCl, and extracted with 95:5 EtOAc:hexanes. The combined organic extracts were dried over sodium sulfate, concentrated, and the crude product was purified using flash chromatography (EtOAc/hexanes) to afford white amorphous solid **(34)** (26 mg, 38% yield). IR (neat) ν_{max} 2623, 1623, 1481, 1458, 1372, 1320, 1269, 1145, 1114, 752 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 1H), 7.51 – 7.48 (m, 1H), 7.19 – 7.14 (m, 2H), 3.93 (dd, *J* = 8.4, 5.9, 2H), 3.53 (t, *J* = 6.8, 2H), 2.71 – 2.64 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.87, 148.54, 131.57, 124.24, 122.43, 122.13, 112.20, 48.05, 40.90, 28.62; ESI MS *m/z* 175.10 $(M + H)^+$.



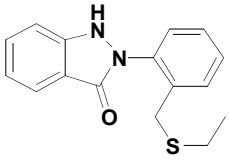
General procedure of Nitrogen Nucleophiles: Synthesis of 2-(1-(isopropylamino)-2-methylpropan-2-yl)-1*H*-indazol-3(2*H*)-one (**22**). Indazole **2c** (0.1 g, 0.52 mmol) was dissolved in 6 mL DMF containing isopropyl amine (0.071 mL, 1.14 mmol). The reaction was heated to 170 ºC for 2 hours in a microwave reactor (Personal Chemistry, Emrys Optimizer), cooled, diluted with water, and extracted with ethyl acetate. The combined organics were washed with water, dried, and concentrated. The crude product was purified by flash chromatography (1:1:0.01 Ethyl acetate:hexanes:HOAc) to yield a brown oil (**11)** (75 mg, 59%). IR (neat) ν_{max} 2967, 2926, 1726, 1615, 1580, 1547, 1532, 1464, 1388, 1370, 1163, 1062, 743 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.6, 1H), 7.45 (d, *J* = 8.8, 1H), 7.19 (m, 1H), 6.89 – 6.86 (m, 1H), 4.13 – 4.06 (m, 1H), 4.00 (s, 2H), 1.66 (s, 6H), 1.29 (d, *J* = 6.3, 8H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.01, 146.75, 126.46, 121.05, 119.32, 116.96, 112.97, 71.70, 63.18, 47.90, 29.92, 24.11, 23.88; ESI MS *m/z* 248.17 $(M + H)^+$.



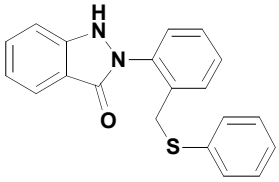
2-Isopropyl-1*H*-indazol-3(2*H*)-one (**7**). By following the general procedure of thiolate nucleophiles, with the exception of heating at 155 °C for 10 minutes, the target was synthesized furnishing a clear oil (90 mg, 62%). IR (neat) ν_{max} 3306, 3068, 2920, 1621, 1578, 1488, 1467, 1361, 1322, 1282, 1043, 1006, 746 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.02 (s, 1H), 7.70 (d, *J* = 7.8, 1H), 7.42 (t, *J* = 7.7, 1H), 7.21 (d, *J* = 8.2, 1H), 7.08 (t, *J* = 7.5, 1H), 4.85 – 4.69 (p, *J*=6.8, 1H), 1.38 (dd, *J* = 18.7, 6.9, 6H); ^{13}C

NMR (75 MHz, $CDCl_3$) δ 161.81, 146.76, 131.55, 123.46, 121.86, 118.73, 112.47, 46.05, 20.59; ESI MS *m/z* 177.14 $(M + H)^+$.

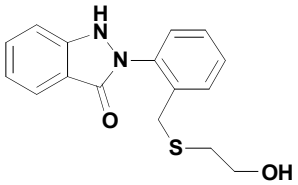
IV. Preparation of 2-(substituted)phenyl)-1*H*-indazol-3(2*H*)-ones



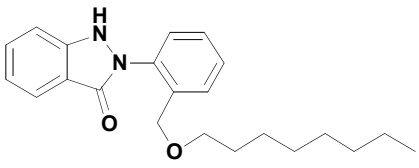
2-(2-(Ethylthiomethyl)phenyl)-1*H*-indazol-3(2*H*)-one (**8**). By following the general procedure of thiolate nucleophiles, the target was synthesized furnishing a clear oil (98 mg, 77%). IR (neat) ν_{max} 3063, 2959, 2922, 2853, 1628, 1578, 1486, 1466, 1452, 1356, 1320, 1266, 747 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.74 (s, 1H), 7.72 (d, *J* = 7.8, 1H), 7.50 – 7.46 (m, 1H), 7.38 (dd, *J* = 1.1, 7.6, 1H), 7.34 – 7.23 (m, 3H), 7.18 – 7.09 (m, 2H), 3.72 (s, 2H), 2.30 (q, *J* = 7.4, 2H), 1.08 – 1.01 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.33, 147.79, 137.07, 135.59, 132.42, 130.77, 129.21, 129.01, 128.45, 124.24, 122.67, 118.53, 112.76, 32.74, 25.97, 14.61; ESI MS *m/z* 285.08 $(M + H)^+$.



2-(2-(Phenylthiomethyl)phenyl)-1*H*-indazol-3(2*H*)-one (**9**). By following the general procedure of thiolate nucleophiles, the target was synthesized furnishing a brown oil (147 mg, 99%). IR (neat) ν_{max} 3060, 2959, 2922, 2853, 1628, 1578, 1486, 1466, 1452, 1356, 1320, 1266, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.60 (d, *J* = 7.9, 1H), 7.41 (dd, *J* = 14.9, 7.6, 2H), 7.33 – 6.97 (m, 10H), 4.16 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.09, 147.88, 135.96, 135.39, 135.23, 132.34, 131.35, 130.77, 129.00, 128.89, 128.33, 127.82, 126.95, 124.22, 122.79, 118.42, 112.59, 36.37; ESI MS *m/z* 333.07 $(M + H)^+$.

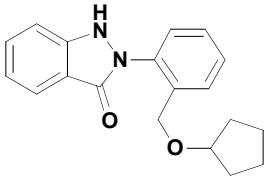


2-(2-((2-Hydroxyethylthio)methyl)phenyl)-1*H*-indazol-3(2*H*)-one (**10**). By following the general procedure of thiolate nucleophiles, the target was synthesized furnishing a clear oil (99 mg, 74%). IR (neat) ν_{max} 3306, 3068, 2920, 1621, 1578, 1488, 1467, 1361, 1322, 1282, 1043, 1006, 746 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ 10.63 (s, 1H), 7.73 (d, *J* = 7.8, 1H), 7.64 – 7.54 (m, 2H), 7.48 – 7.39 (m, 3H), 7.31 (d, *J* = 8.2, 1H), 7.18 (t, *J* = 7.5, 1H), 4.68 (s, 1H), 3.89 (d, *J* = 24.7, 2H), 3.37 (dd, *J* = 12.7, 5.9, 2H), 2.41 (t, *J* = 6.6, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.17, 147.02, 136.00, 135.42, 132.03, 130.39, 128.20, 127.74, 127.51, 123.39, 121.26, 116.49, 112.25, 60.34, 33.91, 32.19; ESI MS *m/z* 300.10 $(M + H)^+$.

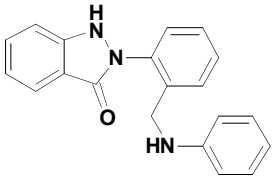


2-(2-(Octyloxymethyl)phenyl)-1*H*-indazol-3(2*H*)-one (**11**). By following the general procedure of alkoxide nucleophiles, the target was synthesized furnishing a brown oil (82 mg, 52%). IR (neat) ν_{max} 3069, 2924, 2853, 1639, 1620, 1581, 1488, 1467, 1358, 1321, 1097, 750 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.92 (s, 1H), 7.89 (dd, *J* = 16.1, 8.3, 1H), 7.59 – 7.46 (m, 4H), 7.44 – 7.35 (m, 3H), 7.24 – 7.10 (m, 3H), 4.72 – 4.37 (m, 3H), 3.57 – 3.31 (m, 3H), 1.76 – 1.47 (m, 4H), 1.47 – 1.07 (m, 18H), 1.07 – 0.79 (m, 4H); ^{13}C

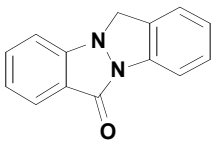
NMR (150 MHz, $CDCl_3$) δ 162.16, 147.33, 136.10, 135.21, 132.34, 130.66, 129.49, 128.97, 28.34, 124.40, 122.39, 118.54, 112.13, 71.01, 70.44, 31.89, 29.81, 29.52, 29.31, 26.35, 22.74, 14.21; ESI MS *m/z* 353.19 $(M + H)^+$.



2-(2-(Cyclopentyloxymethyl)phenyl)-1*H*-indazol-3(2*H*)-one (**12**). By following the general procedure of alkoxide nucleophiles, the target was synthesized as a white solid (48 mg, 35%). mp 105 – 107 °C; IR (neat) ν_{max} 2956, 2857, 1637, 1618, 1578, 1485, 1467, 1355, 1323, 1086, 1060, 749 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.83 (d, *J* = 24.6, 1H), 7.94 (d, *J* = 7.9, 1H), 7.63 – 7.53 (m, 2H), 7.52 – 7.39 (m, 3H), 7.29 – 7.17 (m, 2H), 4.46 (s, 2H), 4.03 – 3.99 (m, 1H), 1.82 – 1.48 (m, 8H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.22, 147.33, 136.57, 135.56, 132.38, 131.10, 129.77, 129.21, 128.79, 124.56, 122.51, 118.88, 112.08, 81.85, 68.88, 32.41, 23.70; ESI MS *m/z* 309.14 $(M + H)^+$.

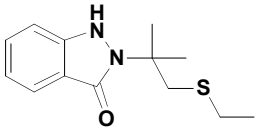


2-(2-((Phenylamino)methyl)phenyl)-1*H*-indazol-3(2*H*)-one (**14**). By following the general procedure of nitrogen nucleophiles, with the exception of heating at 140 °C for 30 minutes, the target was synthesized furnishing a brown solid (82 mg, 58%). Decomposes at 179 °C; IR (neat) ν_{max} 2919, 2850, 1705, 1626, 1599, 1543, 1524, 1494, 1475, 1455, 1366, 1303, 1279, 1253, 1218, 1175, 1162, 1008, 933, 769, 741 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ 8.18 (s, 1H), 7.66 (d, *J* = 7.7, 1H), 7.57 (d, *J* = 8.6, 1H), 7.50 (t, *J* = 7.4, 1H), 7.39 – 7.32 (m, 2H), 7.28 – 7.24 (m, 2H), 7.11 (t, *J* = 7.9, 2H), 6.94 (dd, *J* = 6.7, 8.3, 1H), 6.73 (t, *J* = 7.3, 1H), 6.68 (d, *J* = 7.6, 2H), 5.22 (t, *J* = 5.6, 1H), 4.29 (d, *J* = 5.6, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 148.49, 145.24, 139.77, 136.67, 135.24, 129.87, 129.77, 128.12, 127.81, 127.77, 127.15, 121.00, 120.97, 119.87, 118.37, 115.16, 114.63, 59.41; ESI MS *m/z* 316.13 $(M + H)^+$.



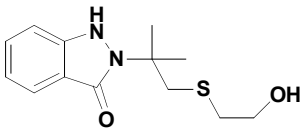
Indazolo[2,1-*a*]indazol-6(12*H*)-one (**15'**). By following the general procedure of the ANRORC reaction, the target was synthesized furnishing a white solid (32 mg, 65%). mp 133 – 136 °C; IR (neat) ν_{max} 3043, 2933, 2850, 1653, 1607, 1483, 1464, 1318, 1291, 1123, 1089 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 20.8, 7.9, 2H), 7.50 (t, *J* = 7.7, 1H), 7.35 (t, *J* = 7.7, 1H), 7.27 (d, *J* = 7.5, 1H), 7.16 – 7.07 (m, 3H), 4.96 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.52, 147.29, 135.33, 132.65, 129.52, 129.15, 125.03, 125.01, 123.77, 121.58, 120.23, 113.18, 110.48, 51.58; ESI MS *m/z* 223.13 $(M + H)^+$.

V. Preparation of 2-methylpropan-2-yl)-1*H*-indazol-3(2*H*)-ones

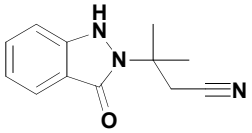


2-(1-(Ethylthio)-2-methylpropan-2-yl)-1*H*-indazol-3(2*H*)-one (**16**). By following the general procedure of thiolate nucleophiles, the target was synthesized as a white solid (112 mg, 85%). mp 89 – 91 °C; IR (neat) ν_{max} 2975, 2927, 1615, 1467, 1408, 1320, 1230

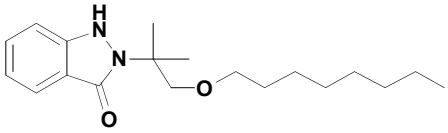
cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.8, 1H), 7.51 – 7.45 (m, 1H), 7.35 (s, 1H), 7.23 – 7.13 (m, 2H), 3.23 (s, 2H), 2.55 (q, *J* = 7.4, 2H), 1.70 (s, 6H), 1.23 (t, *J* = 7.4, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.07, 147.17, 131.79, 123.75, 122.68, 121.18, 112.61, 61.36, 42.26, 27.73, 25.38, 15.12; ESI MS *m/z* 251.13 $(M + H)^+$.



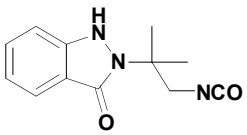
2-(1-(2-Hydroxyethylthio)-2-methylpropan-2-yl)-1*H*-indazol-3(2*H*)-one (**18**). By following the general procedure of thiolate nucleophiles, the target was synthesized furnishing a white solid (133 mg, 95%). mp 88 – 92 °C; IR (neat) ν_{max} 3230, 2980, 2920, 1615, 1492, 1469, 1423, 1361, 1321, 1227, 1046, 1008, 747 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ 9.73 (s, 1H), 7.58 (d, *J* = 7.8, 1H), 7.51 – 7.47 (m, 1H), 7.22 (d, *J* = 8.2, 1H), 7.08 (t, *J* = 7.4, 1H), 4.72 (t, *J* = 5.5, 1H), 3.45 (dd, *J* = 12.4, 6.8, 2H), 3.29 (s, 2H), 2.53 – 2.50 (t, *J*=7.0, 2H), 1.59 (d, *J* = 20.4, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.21, 147.12, 131.92, 123.66, 122.60, 120.68, 112.61, 61.41, 61.20, 41.95, 36.12, 25.48; ESI MS *m/z* 267.15 $(M + H)^+$.



3-Methyl-3-(3-oxo-1*H*-indazol-2(3*H*)-yl)butanenitrile (**19**). Indazole **2c** (0.12 g, 0.63 mmol) was dissolved in 6 mL DMF containing sodium cyanide (61 mg, 1.27 mmol). The reaction heated to 100 ºC for 6 minutes in a microwave reactor (Personal Chemistry, Emrys Optimizer). The cooled reaction was poured into water and extracted with ethyl acetate. The combined organics were washed with water, dried over sodium sulfate, and concentrated. The crude product was purified by flash chromatography (2:1 Ethyl acetate:hexanes) to yield a white solid **(8)** (43 mg, 38%). mp 115 – 118 °C; IR (neat) ν_{max} 3426, 2921, 1946, 1602, 1474, 1441, 1368, 1324, 1233, 1062 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.74 (d, *J* = 7.9, 1H), 7.52 – 7.44 (m, 1H), 7.24 – 7.10 (m, 2H), 3.92 (s, 2H), 2.15 (s, 2H), 1.55 (s, *J* = 13.0, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.25, 146.73, 132.14, 123.62, 122.54, 119.53, 112.40, 69.65, 63.21, 23.3; ESI MS *m/z* 216.20 $(M + H)^+$.

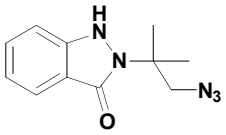


2-(2-Methyl-1-(octyloxy)propan-2-yl)-1*H*-indazol-3(2*H*)-one (**20**). By following the general procedure of alkoxide nucleophiles, the target was synthesized furnishing a beige oil (147 mg, 88%). IR (neat) ν_{max} 2654, 2923, 2852, 1612, 1473, 1426, 1361, 1325, 1127, 933, 787, 746, 682 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.74 (d, *J* = 7.8, 1H), 7.41 (dd, *J* = 8.1, 7.2, 1H), 7.18 – 7.07 (m, 2H), 3.69 (s, 2H), 3.51 (t, *J* = 6.5, 2H), 1.66 (s, 6H), 1.60 – 1.51 (m, 2H), 1.34 – 1.17 (m, 10H), 0.91 – 0.80 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.62, 146.34, 131.25, 123.44, 121.92, 120.63, 112.11, 77.25, 71.88, 60.41, 31.83, 29.55, 29.39, 29.30, 26.28, 22.69, 22.54, 14.14; ESI MS *m/z* 319.23 $(M + H)^+$.



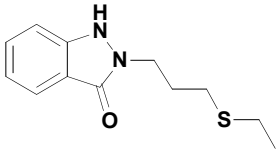
2-(1-Isocyanato-2-methylpropan-2-yl)-1*H*-indazol-3(2*H*)-one (**24**). Indazole **2c** (50 mg, 0.26 mmol) was dissolved in 6 mL DMF containing potassium cyanate (84 mg, 1.04 mmol) and potassium iodide (11 mg, 0.066 mmol). The reaction was heated to 100 ºC for 10 minutes in a microwave reactor (Personal Chemistry, Emrys Optimizer). The cooled reaction was poured into

water and extracted with ethyl acetate. The combined organics were washed with water, dried over sodium sulfate, and concentrated. The crude product was purified by flash chromatography (1:1 ethyl acetate:hexanes) to yield a white amorphous solid **(24)** (26 mg, 44%). IR (neat) ν_{max} 2955, 2869, 2691, 1611, 1479, 1461, 1391, 1344, 1323, 1257, 1104, 1086, 892, 790, 751, 677 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.3, 1H), 7.84 (d, *J* = 7.7, 1H), 7.61 (s, 1H), 7.28 (d, *J* = 8.0, 1H), 6.44 (s, 1H), 3.40 (s, 2H), 1.79 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.44, 149.84, 139.76, 133.17, 124.05, 123.38, 118.70, 115.42, 56.97, 51.63, 23.69; ESI MS *m/z* 232.09 $(M + H)^+$.

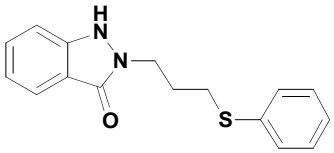


2-(1-Azido-2-methylpropan-2-yl)-1*H*-indazol-3(2*H*)-one (**25**). Indazole **2c** (50 mg, 0.26 mmol) was dissolved in 6 mL DMF containing sodium azide (70 mg, 1.04 mmol) and potassium iodide (11 mg, 0.066 mmol). The reaction was heated to 120 ºC for 10 minutes in a microwave reactor (Personal Chemistry, Emrys Optimizer). The cooled reaction was poured into water and extracted with ethyl acetate. The combined organics were washed with water, dried over sodium sulfate, and concentrated. The crude product was purified by flash chromatography (1:1 ethyl acetate : hexanes) to yield a white solid **(25)** (28 mg, 48%). mp 137 – 138 °C; IR (neat) ν_{max} 2899, 2095, 1615, 1469, 1434, 1359, 1322, 927, 788 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.8, 1H), 7.52 – 7.49 (m, 1H), 7.20 (dd, *J* = 7.7, 17.3, 2H), 7.12 (s, 1H), 3.93 (s, 2H), 1.63 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.41, 147.42, 132.18, 123.92, 123.01, 120.95, 112.72, 61.08, 58.13, 23.72; ESI MS *m/z* 232.09 $(M + H)^+$.

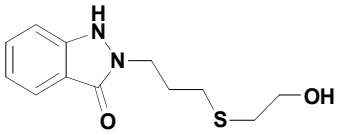
VI. Preparation of 2-(substituted)propyl)-1*H*-indazol-3(2*H*)-ones



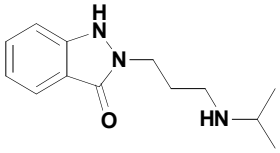
2-(3-(Ethylthio)propyl)-1*H*-indazol-3(2*H*)-one (**27**). By following the general procedure of thiolate nucleophiles, the target was synthesized furnishing a white solid (66 mg, 53%). mp 148 – 150 °C; IR (neat) ν_{max} 3043, 2931, 2886, 1627, 1541, 1442, 1421, 1367, 1329, 1269, 1151, 1108, 1054, 961, 825 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.77 (d, *J* = 7.9, 1H), 7.48 (t, *J* = 7.7, 1H), 7.19 (m, 2H), 3.99 (t, *J* = 6.8, 2H), 2.60 – 2.42 (m, 4H), 2.06 (dd, *J* = 6.9, 13.9, 2H), 1.19 (t, *J* = 7.4, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.75, 146.94, 131.97, 123.88, 122.62, 119.15, 112.58, 43.69, 28.93, 28.20, 26.09, 14.89; ESI MS *m/z* 237.16 $(M + H)^+$.



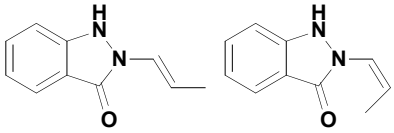
2-(3-(Phenylthio)propyl)-1*H*-indazol-3(2*H*)-one (**28**). By following the general procedure of thiolate nucleophiles, the target was synthesized furnishing a white solid (109 mg, 67%). mp 107 – 110 °C; IR (neat) ν_{max} 3044, 2922, 2851, 2747, 1618, 1584, 1478, 1381, 1256, 733 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.75 (d, *J* = 7.6, 1H), 7.47 (td, *J* = 7.2, 1.1, 1H), 7.32 – 7.11 (m, 7H), 4.00 (t, *J* = 6.7, 2H), 2.98 – 2.85 (m, 2H), 2.07 (p, *J* = 6.9, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.60, 146.76, 135.82, 131.91, 129.49, 129.07, 126.31, 123.70, 122.45, 118.75, 112.47, 77.37, 77.16, 76.95, 43.32, 30.96, 27.95; ESI MS *m/z* 285.08 $(M + H)^+$.



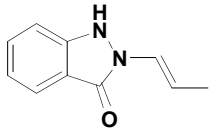
2-(3-(2-Hydroxyethylthio)propyl)-1*H*-indazol-3(2*H*)-one (**29**). By following the general procedure of thiolate nucleophiles, the target was synthesized furnishing a clear oil (68 mg, 47%). IR (neat) ν_{max} 3336, 3082, 2920, 2861, 1614, 1482, 1465, 1428, 1375, 1326, 1043, 1008, 747 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ 9.73 (s, 1H), 7.58 (d, *J* = 7.8, 1H), 7.51 – 7.47 (m, 1H), 7.22 (d, *J* = 8.2, 1H), 7.08 (t, *J* = 7.4, 1H), 4.72 (t, *J* = 5.5, 1H), 3.45 (dd, *J* = 12.4, 6.8, 2H), 3.29 (s, 2H), 2.52 (t, 2H), 1.61 – 1.53 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.23, 146.36, 131.90, 123.40, 122.07, 117.92, 112.35, 60.95, 43.14, 35.16, 29.06, 28.22; ESI MS *m/z* 253.11 $(M + H)^+$.



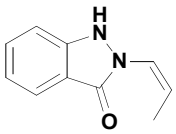
2-(3-(Isopropylamino)propyl)-1*H*-indazol-3(2*H*)-one (**33**). By following the general procedure of nitrogen nucleophiles, the target was synthesized furnishing a brown solid (51 mg, 38%). mp 135 – 139 °C; IR (neat) ν_{max} 3048, 2928, 1626, 1541, 1514, 1366, 1329, 1269, 1151, 961, 751 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.47 (dd, *J* = 8.6, 17.8, 2H), 7.23 (dd, *J* = 6.5, 13.1, 1H), 6.95 – 6.81 (m, 1H), 5.73 – 5.03 (br s, 1H), 4.47 (dd, *J* = 5.5, 10.4, 4H), 4.17 (d, *J* = 7.0, 1H), 2.47 – 2.29 (m, 2H), 1.18 (d, *J* = 6.6, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.48, 147.52, 127.34, 119.18, 119.08, 116.44, 66.21, 45.17, 40.54, 24.57, 22.95, 22.17. ESI MS *m/z* 234.31 $(M + H)^+$.



(E)-2-(Prop-1-enyl)-1*H*-indazol-3(2*H*)-one and (Z)-2-(prop-1-enyl)-1*H*-indazol-3(2*H*)-one (38 & 39). Cyclopentanol (271 mg, 3.15 mmol) was added to a 10 mL microwave vial under N_2 atmosphere. 3 mL dry DMF was added and the mixture was cooled to 0 ºC. NaH (84.0 mg, 2.10 mmol) was added and stirred until the evolution of gas ceased. Indazole **5** (98.7 mg, 0.56 mmol), dissolved in DMF, was added via syringe. The reaction was heated to 120 ºC for 15 minutes in a microwave reactor (Personal Chemistry, Emrys Optimizer) and then cooled. The reaction mixture was diluted with water and extracted with 95:5 ethyl acetate:hexanes. The combined organics were washed with water, dried over sodium sulfate, and concentrated. From the crude product, indazolones **38** and **39** were purified by flash chromatography (1:1 ethyl acetate:hexanes) to give (56 mg, 65%) combined yield, as a 3:2 ratio respectively.

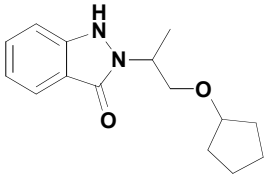


(E)-2-(Prop-1-enyl)-1*H*-indazol-3(2*H*)-one (**38**). mp 180 – 183°C; IR (neat) ν_{max} 3027, 2916, 2851, 1619, 1466, 1367, 1319, 1281, 1219, 932 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 7.76 – 7.70 (m, 1H), 7.56 – 7.52 (m, 1H), 7.27 – 7.21 (m, 1H), 7.12 – 7.07 (m, 1H), 7.04 (m, 1H), 5.52 – 5.45 (m, 1H), 4.89 (s, 1H), 1.90 – 1.78 (m, 3H); ^{13}C NMR (150 MHz, CD_3OD) δ 160.77, 148.03, 133.77, 124.24, 123.29, 121.83, 118.60, 113.26, 110.89, 15.34; ESI MS *m/z* 175.10 $(M + H)^+$.



(Z)-2-(Prop-1-enyl)-1*H*-indazol-3(2*H*)-one (**39**). mp 114 – 116 °C; IR (neat) ν_{max} 3036, 1627, 1467, 1433, 1318, 1230, 809, 748 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.79 (d, *J* = 9.1, 1H), 7.54 – 7.49 (m, 1H), 7.25 (d, 1H), 7.18 (t, *J* = 6.8, 14.3, 1H), 6.59 – 6.55 (m, 1H), 5.31 –

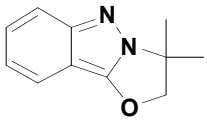
5.25 (m, 1H), 1.93 (dd, *J* = 1.7, 7.2, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.37, 147.63, 132.51, 124.16, 123.06, 121.09, 118.86, 115.70, 112.84, 13.36; ESI MS *m/z* 175.10 $(M + H)^+$.



2-(1-(Cyclopentyloxy)propan-2-yl)-1*H*-indazol-3(2*H*)-one (**40**). By following the general procedure of alkoxide nucleophiles, the racemic target was synthesized furnishing a beige solid (140 mg, 94%). Decomposes at 138 °C; IR (neat) ν_{max} 2956, 2869, 2689, 1610, 1478, 1461, 1390, 1344, 1323, 1256, 1104, 1085, 891, 789, 748, 677 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.8, 1H), 7.72 (s, 1H), 7.48 (t, *J* = 7.7, 1H), 7.20 (d, *J* = 8.2, 1H), 7.16 (t, *J* = 7.5, 1H), 4.91 – 4.83 (m, 1H), 3.91 (d, *J* = 5.5, 1H), 3.70 (dd, *J* = 3.4, 9.6, 1H), 3.60 (dd, *J* = 3.3, 9.6, 1H), 1.77 – 1.48 (m, 9H), 1.43 (d, *J* = 7.0, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.28, 146.63, 131.62, 124.06, 122.25, 119.27, 112.28, 82.35, 72.14, 48.59, 32.69, 32.30, 23.69, 23.67, 16.25; ESI MS *m/z* 261.09 $(M + H)^+$.

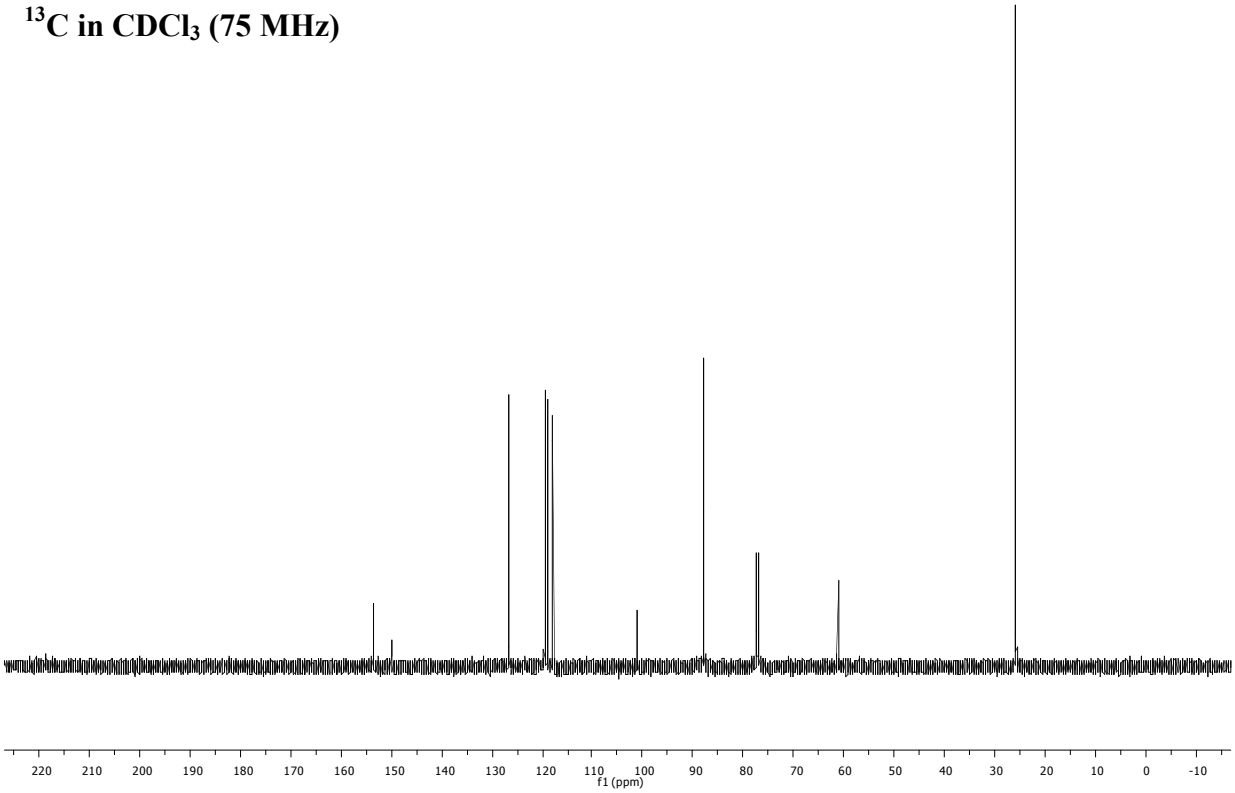
VII. ^{1}H and ^{13}C NMR Spectra

^{1}H in $CDCl_3$ (600 MHz)

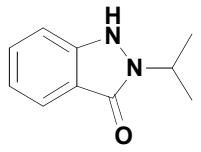


2c

^{13}C in $CDCl_3$ (75 MHz)

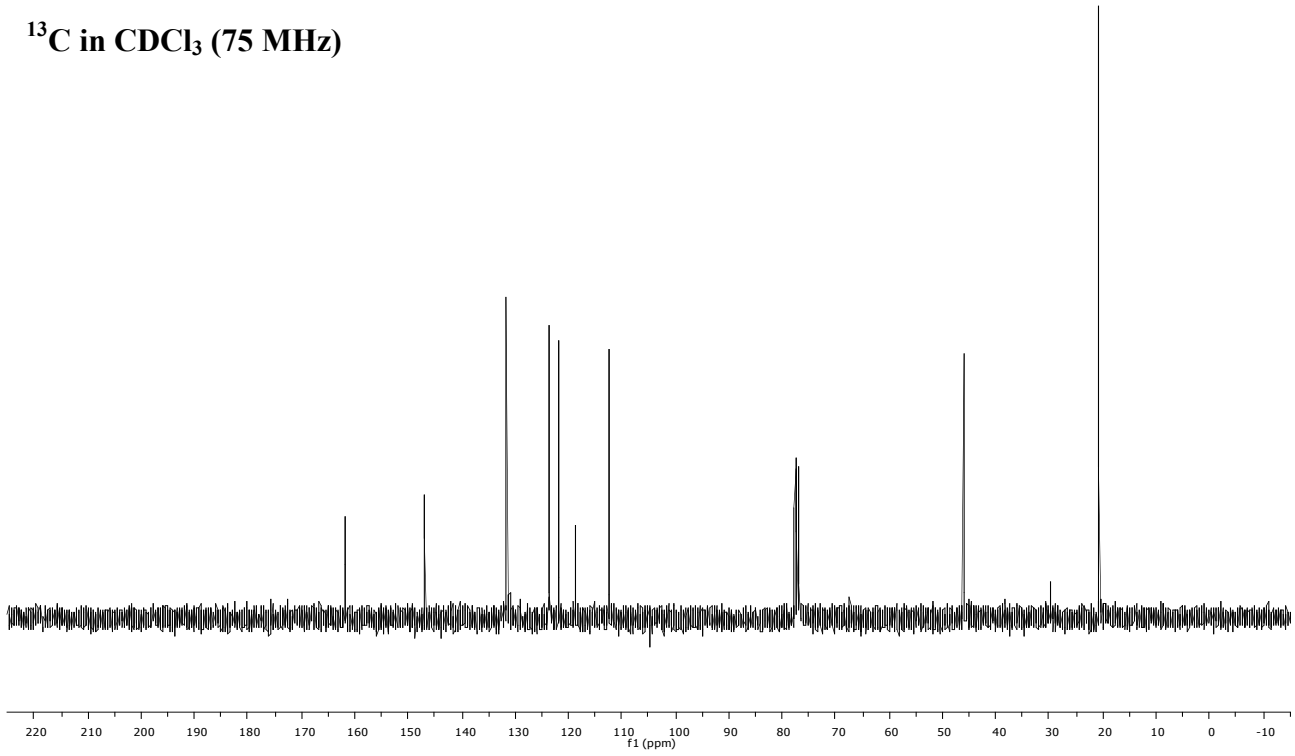


^{1}H in $CDCl_3$ (300 MHz)

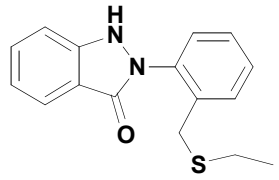


4

^{13}C in $CDCl_3$ (75 MHz)

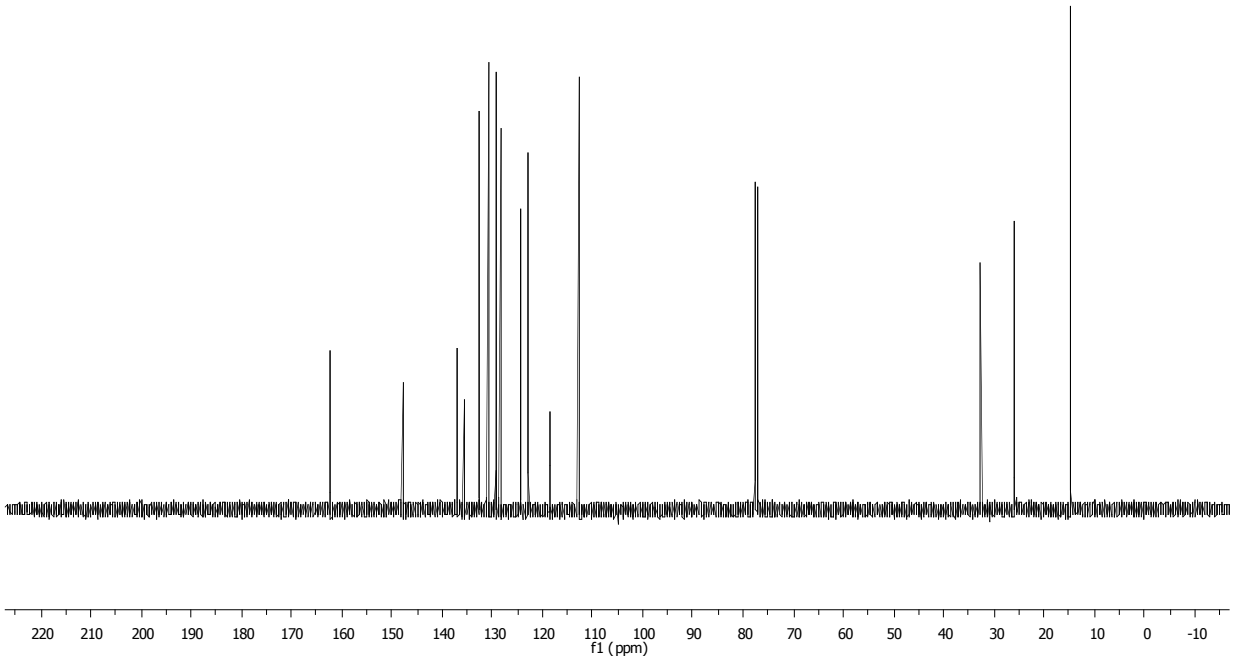


^{1}H in $CDCl_3$ (600 MHz)

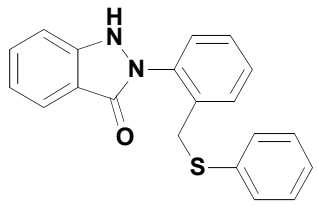


8

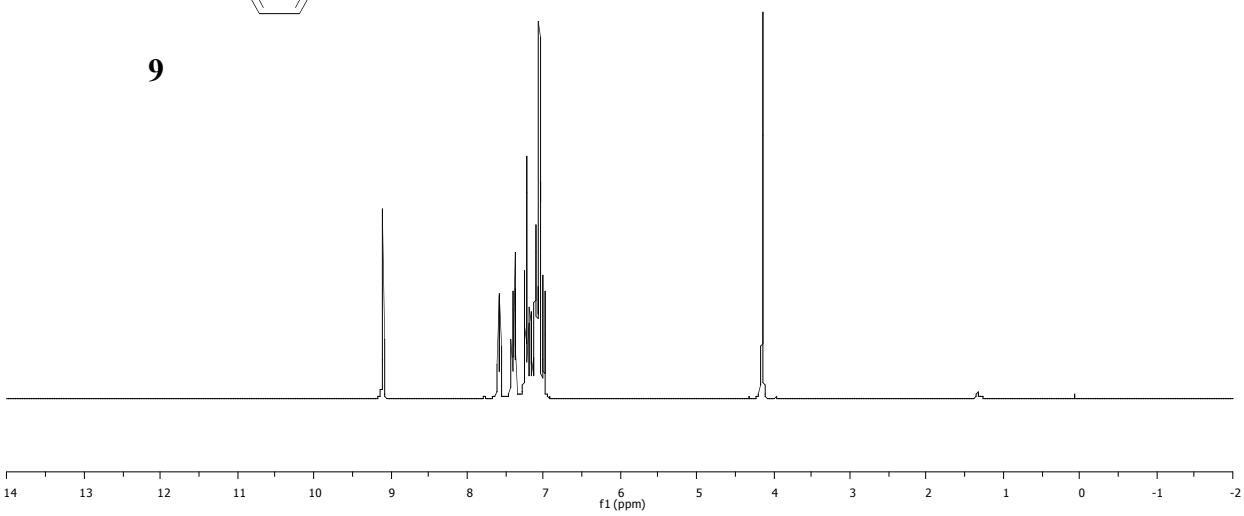
^{13}C in $CDCl_3$ (150 MHz)



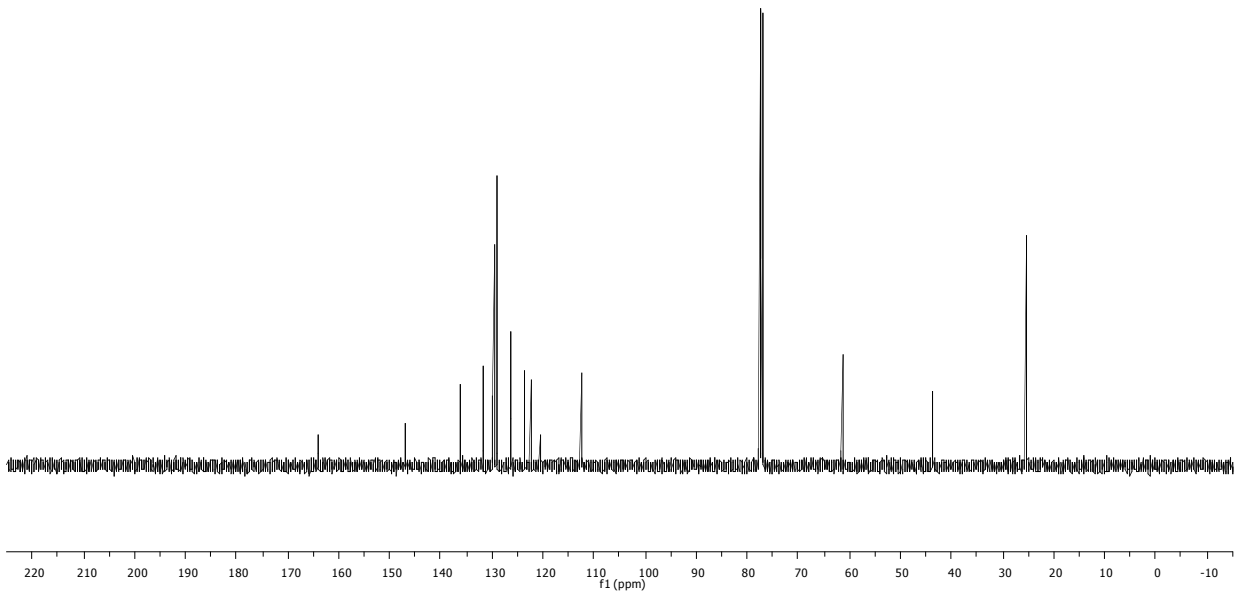
^{1}H in $CDCl_3$ (400 MHz)



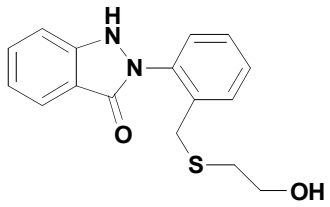
9



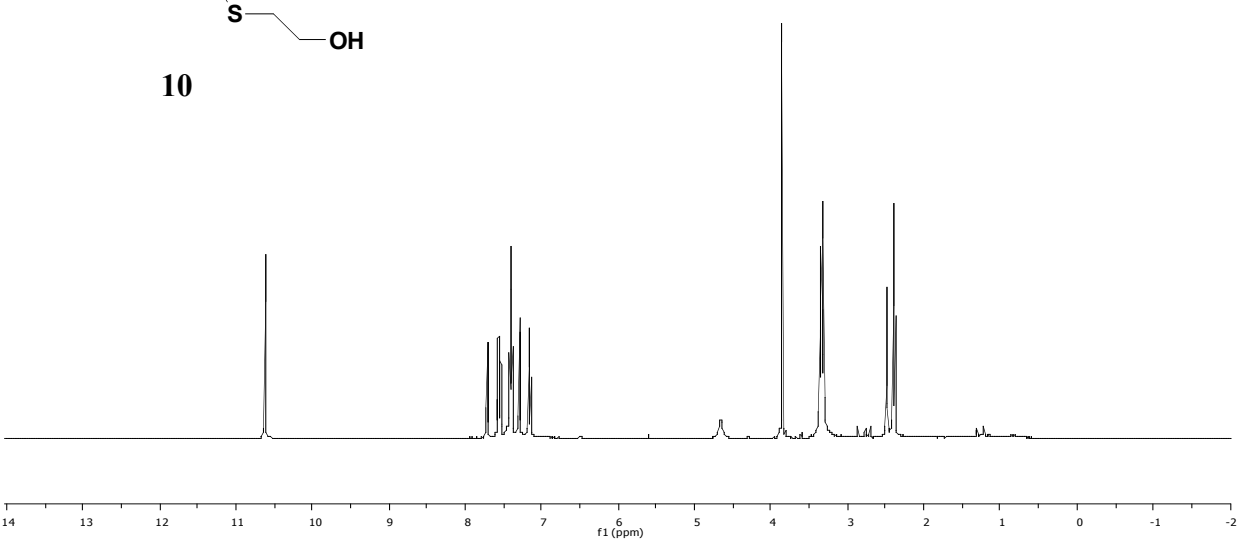
^{13}C in $CDCl_3$ (100 MHz)



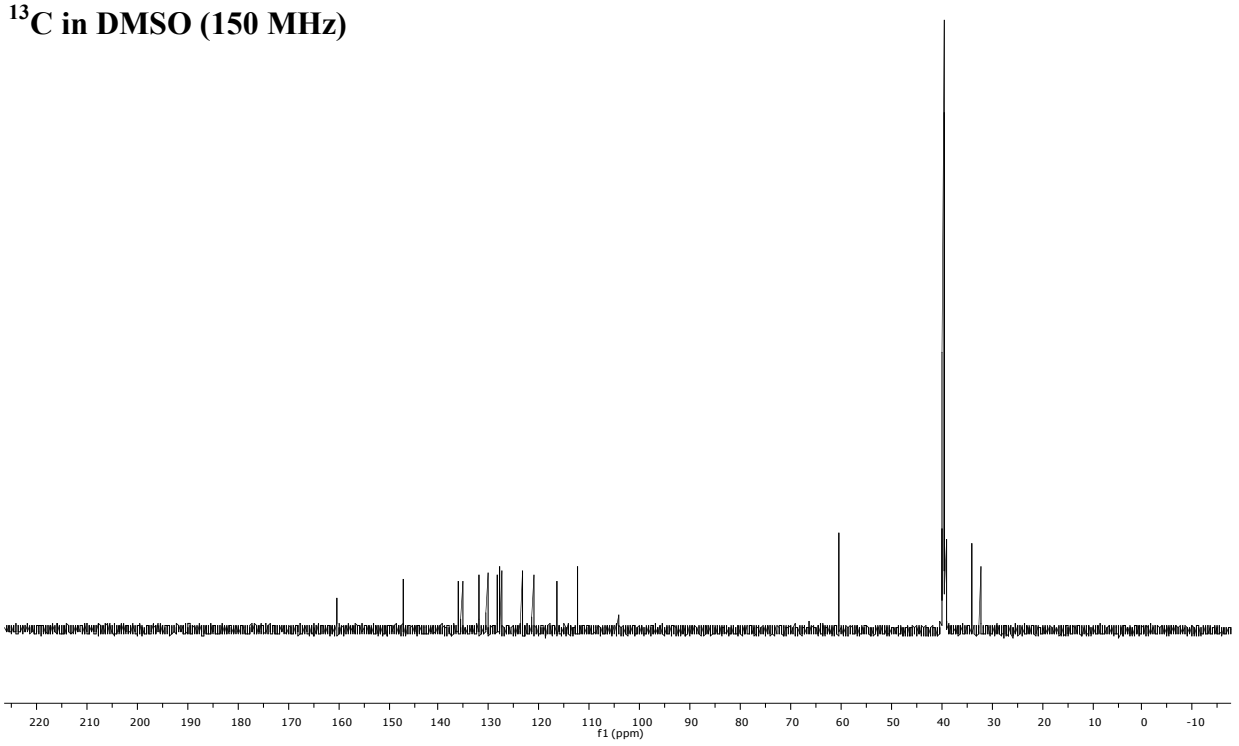
^{1}H in DMSO (600 MHz)



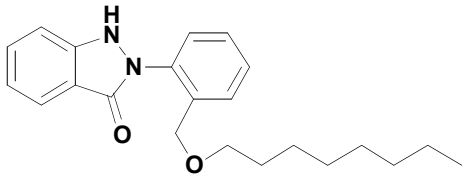
10



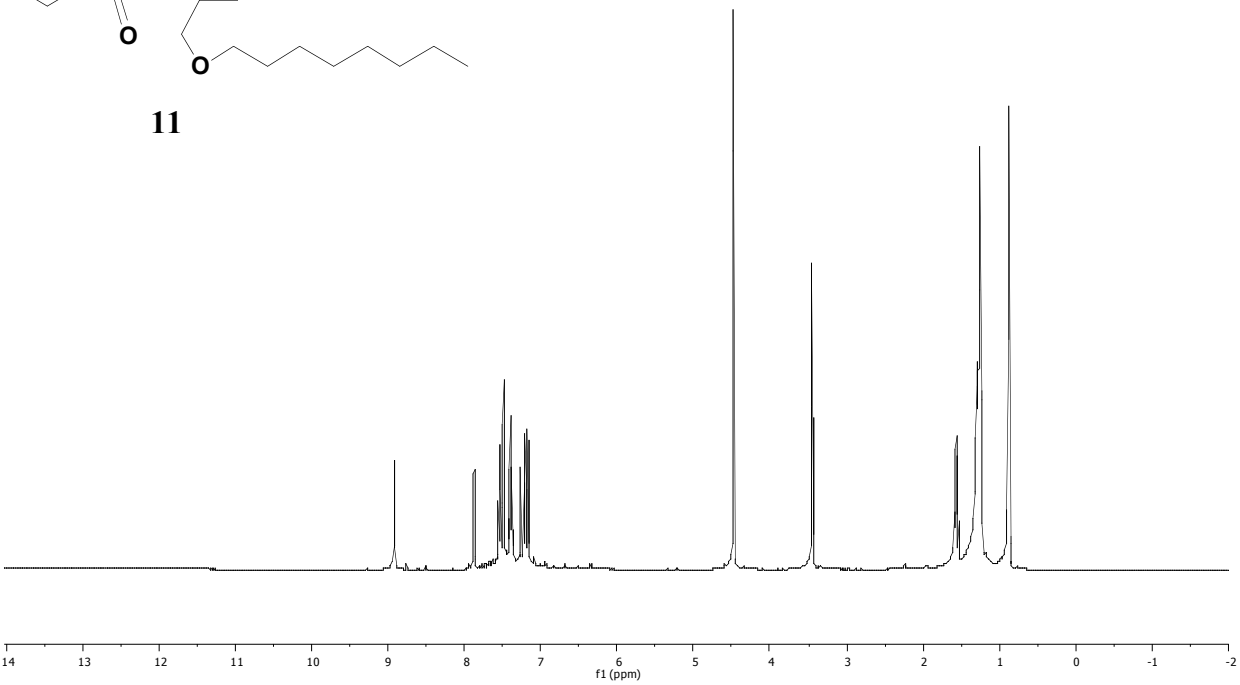
^{13}C in DMSO (150 MHz)



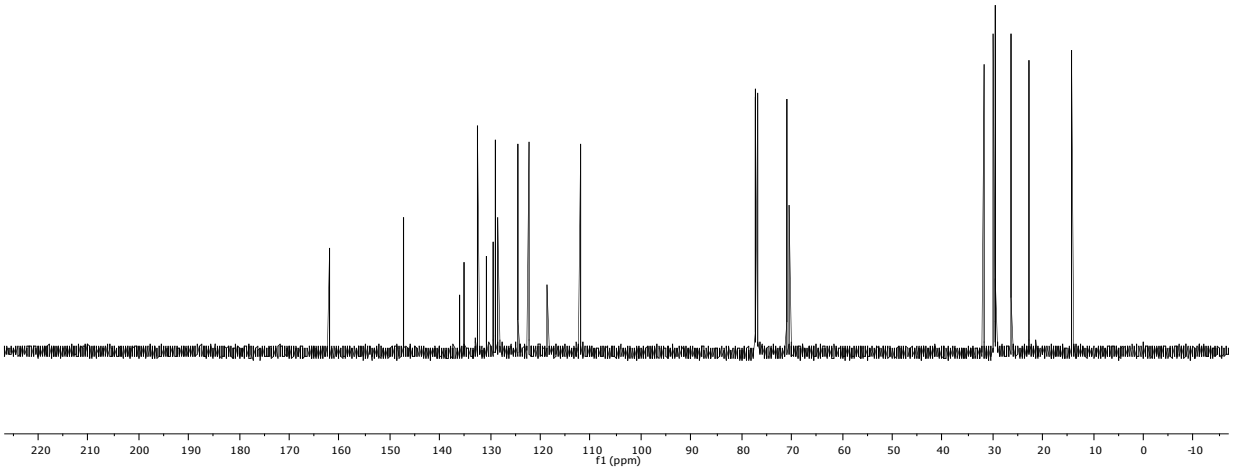
^{1}H in $CDCl_3$ (600 MHz)



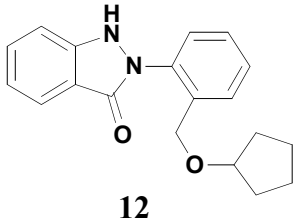
11



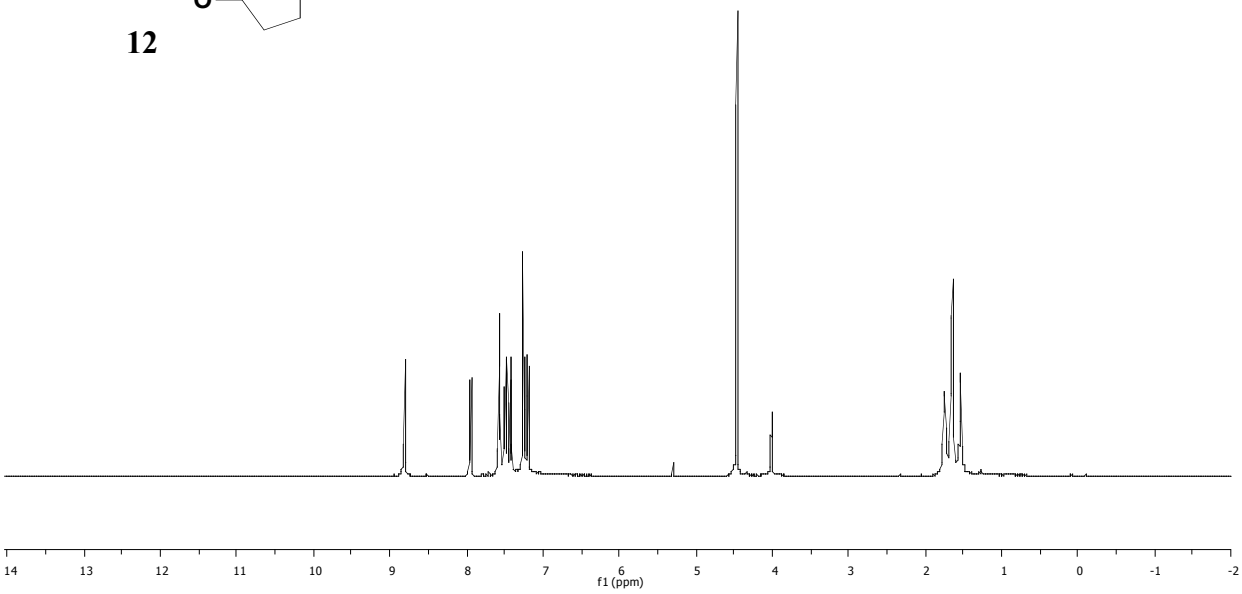
^{13}C in $CDCl_3$ (150 MHz)



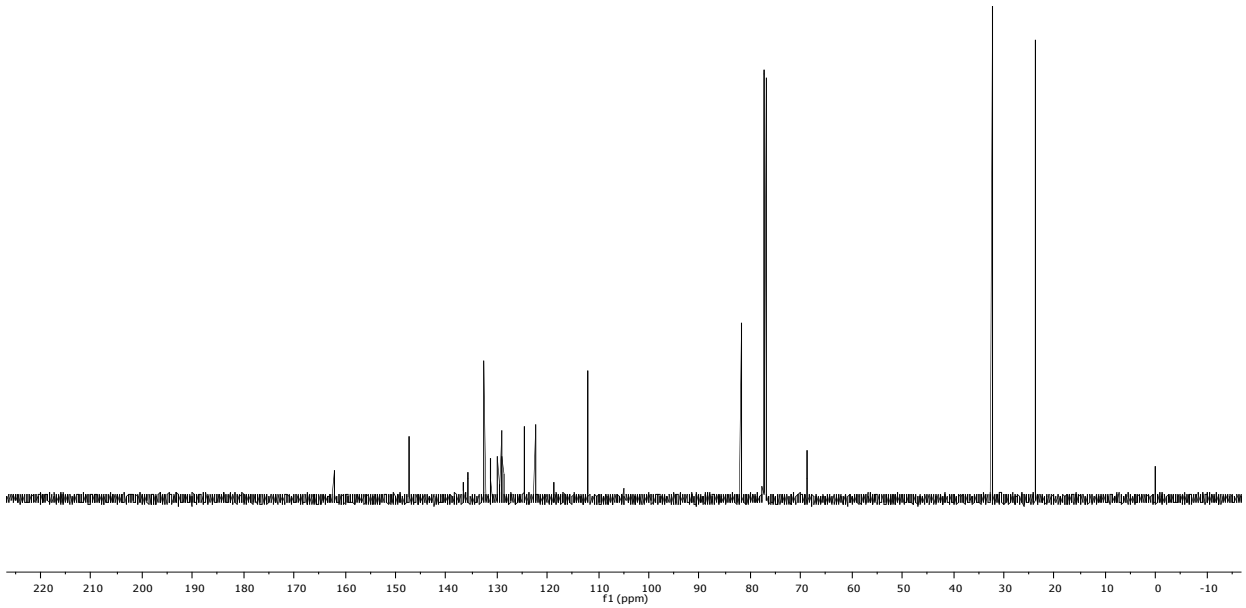
^{1}H in $CDCl_3$ (600 MHz)



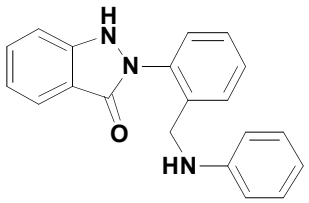
12



^{13}C in $CDCl_3$ (150 MHz)

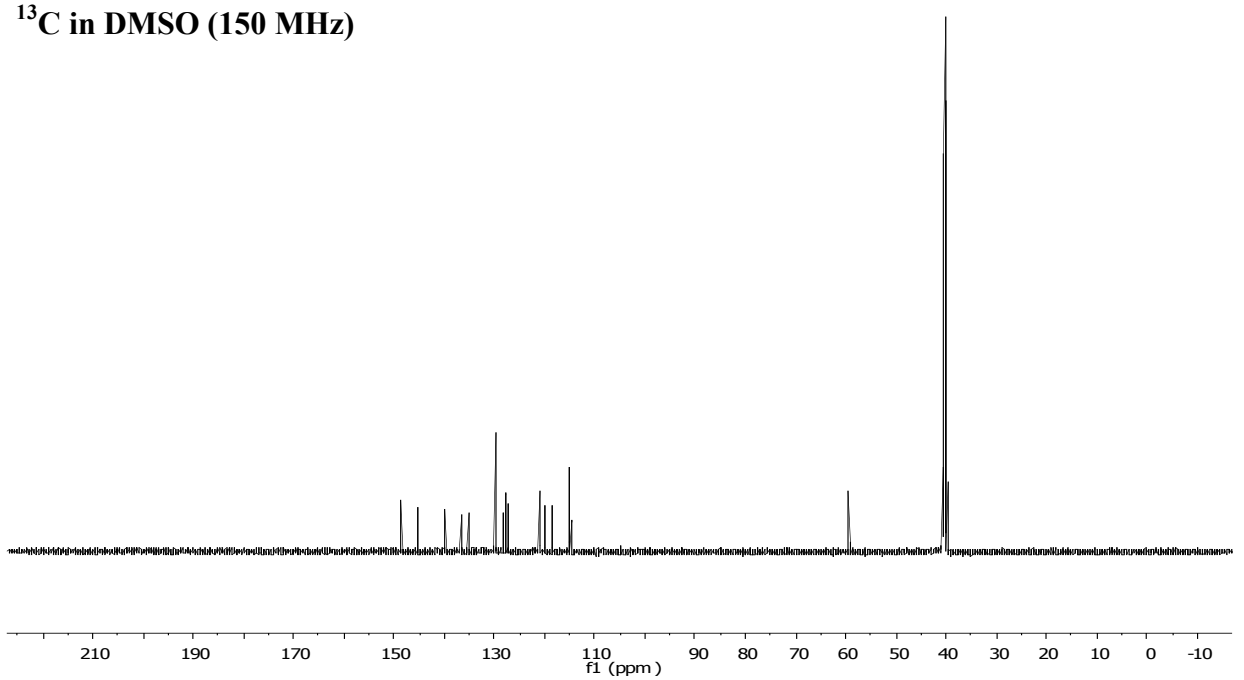


^{1}H in DMSO (600 MHz)

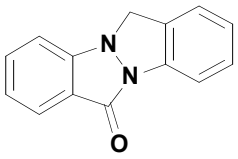


14

^{13}C in DMSO (150 MHz)



^{1}H in $CDCl_3$ (600 MHz)



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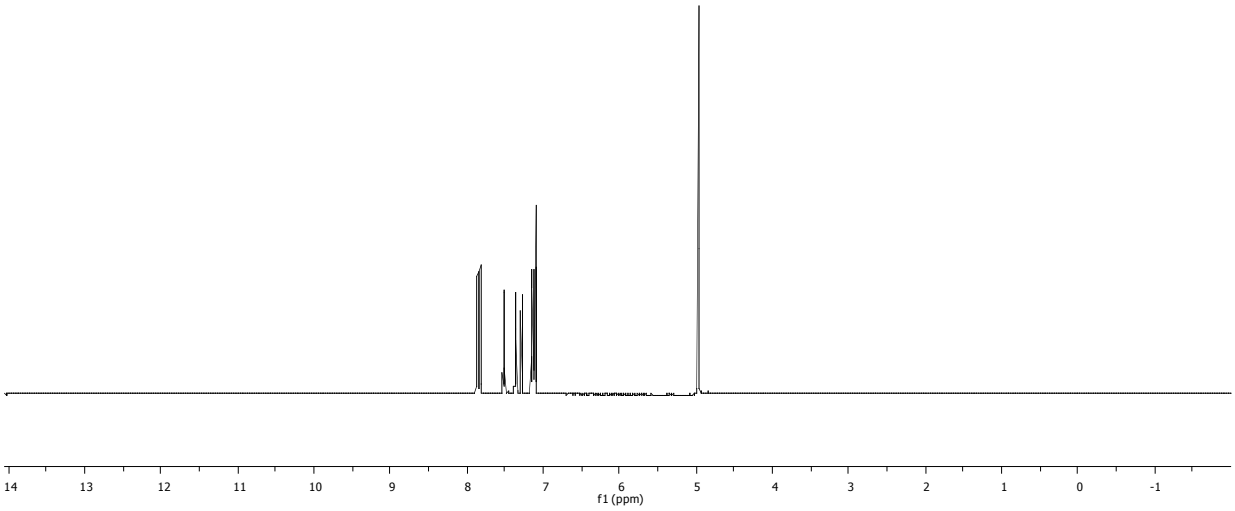
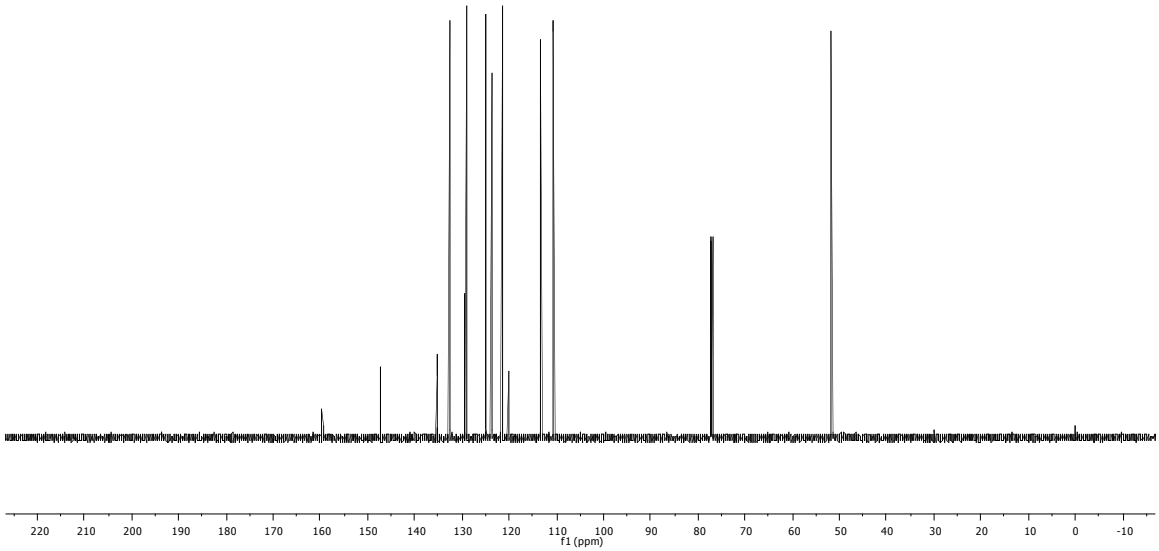
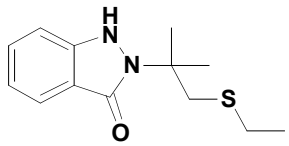


^{13}C in $CDCl_3$ (150 MHz)

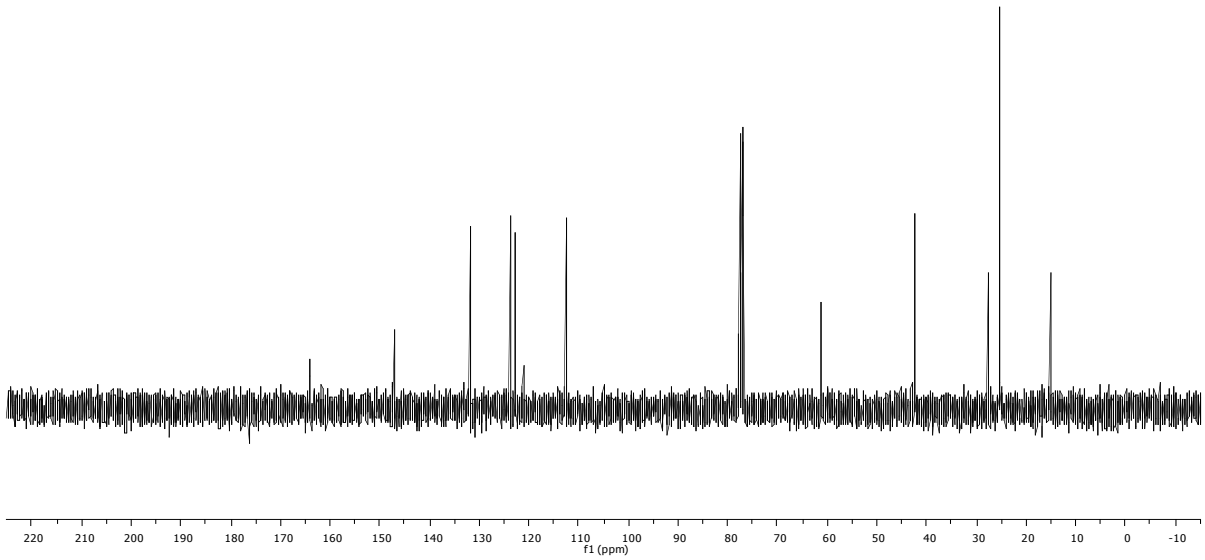


^{1}H in $CDCl_3$ (300 MHz)

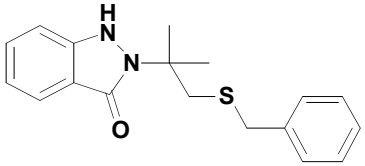


16

^{13}C in $CDCl_3$ (75 MHz)

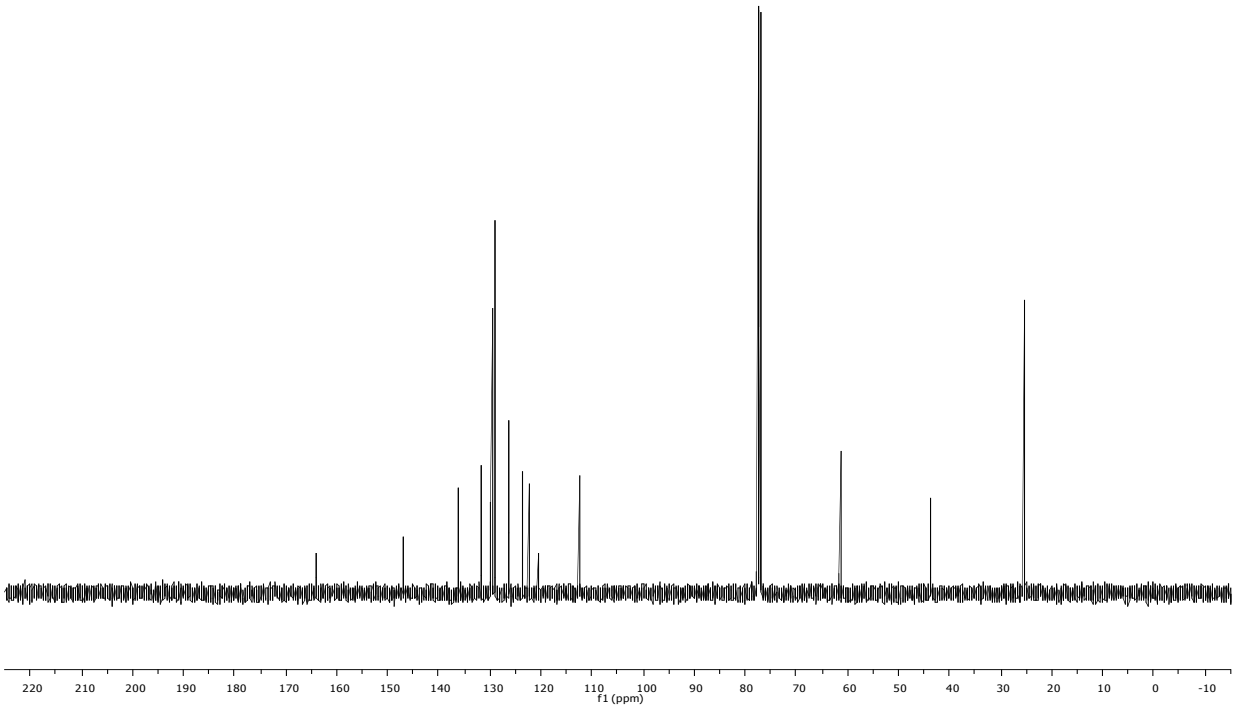


^{1}H in $CDCl_3$ (400 MHz)

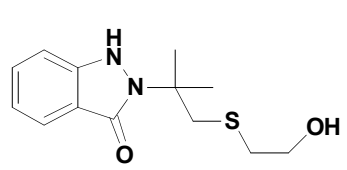


17

^{13}C in $CDCl_3$ (100 MHz)

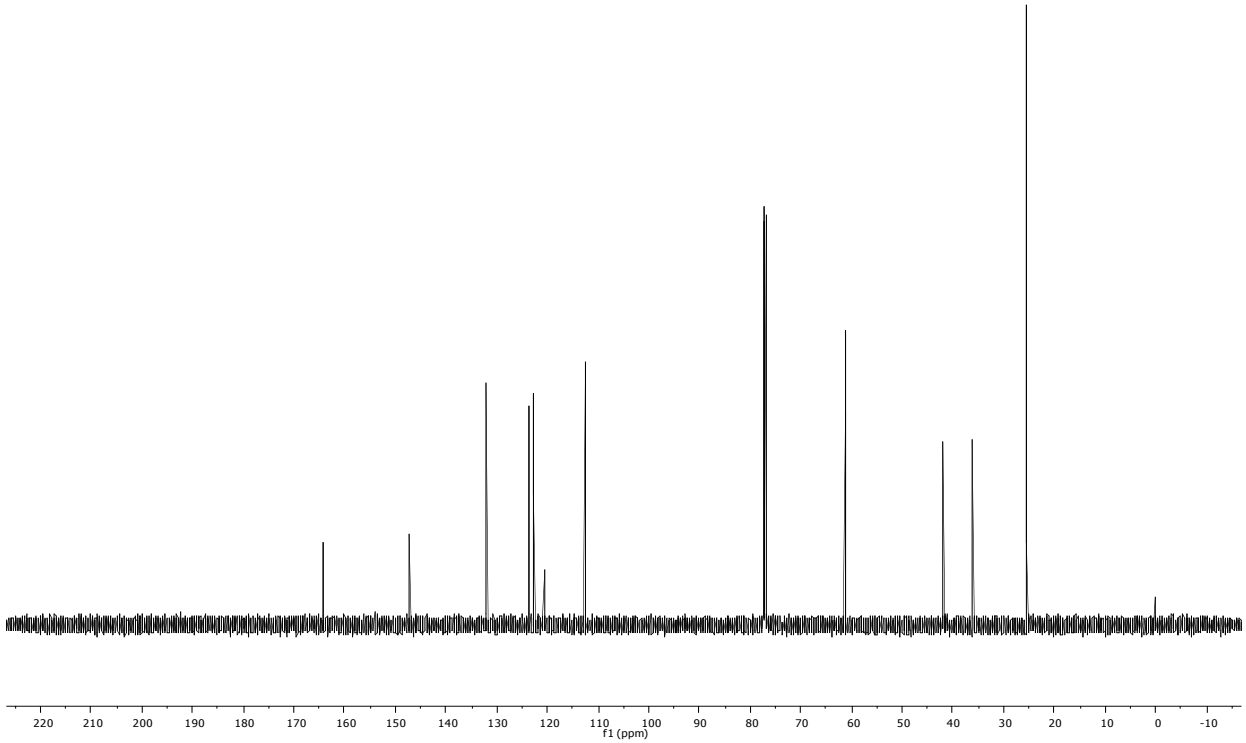


^{1}H in DMSO (600 MHz)

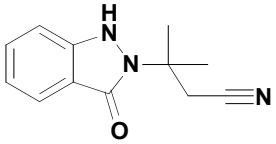


18

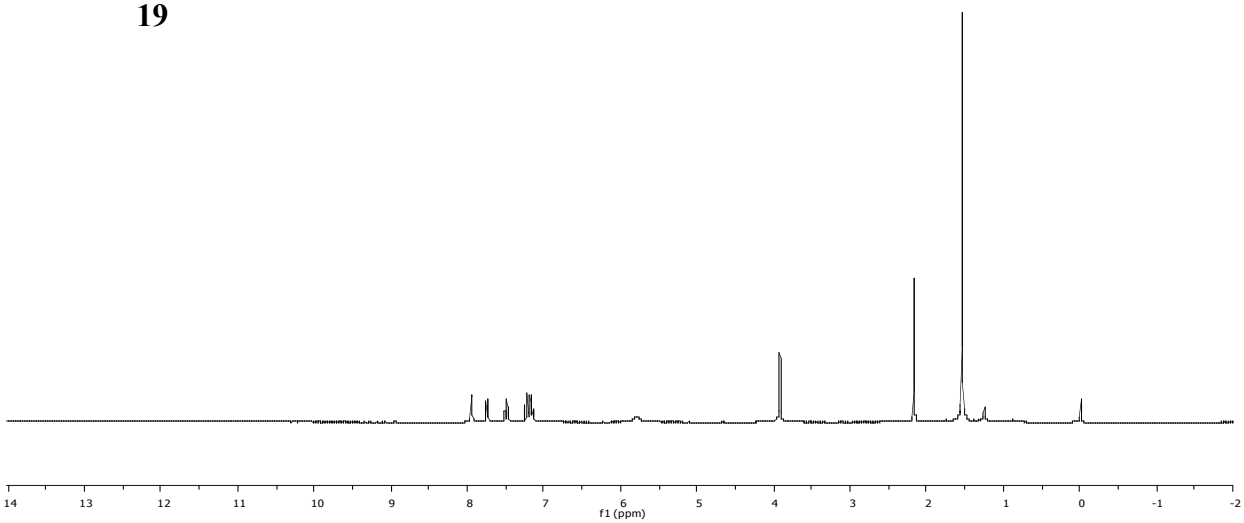
^{13}C in DMSO (150 MHz)



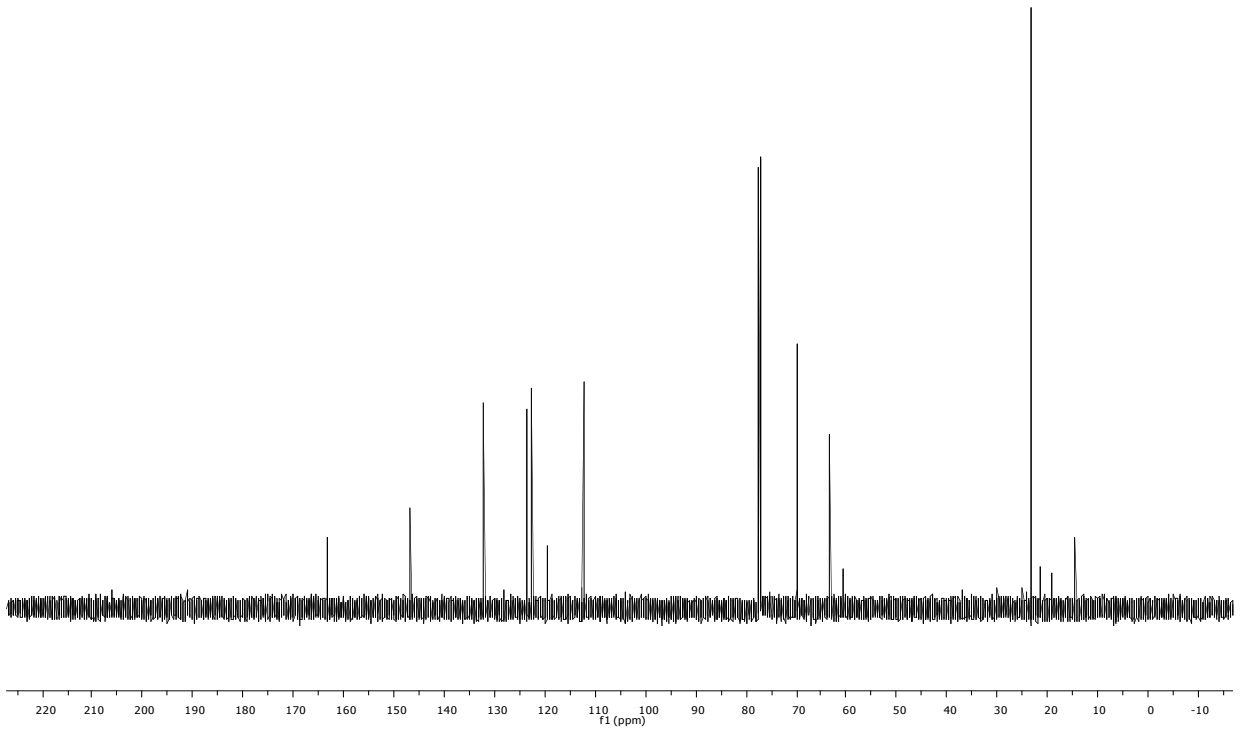
^{1}H in $CDCl_3$ (300 MHz)



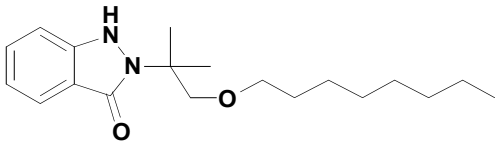
19



^{13}C in $CDCl_3$ (75 MHz)



^{1}H in $CDCl_3$ (600 MHz)



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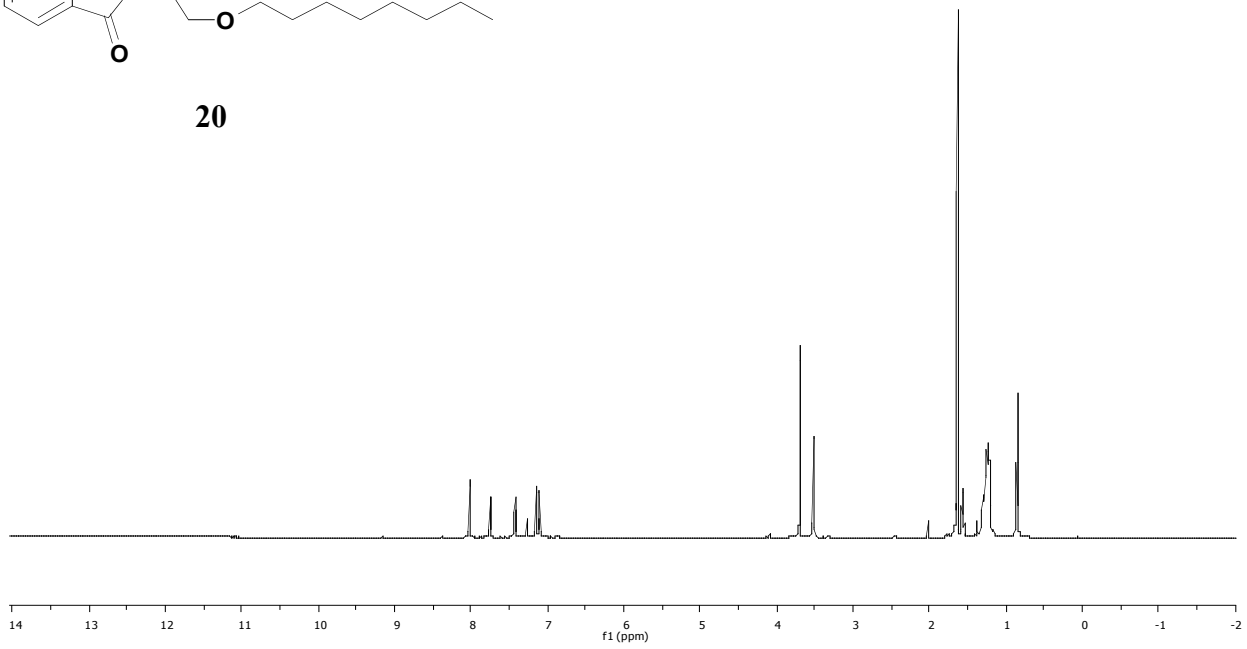
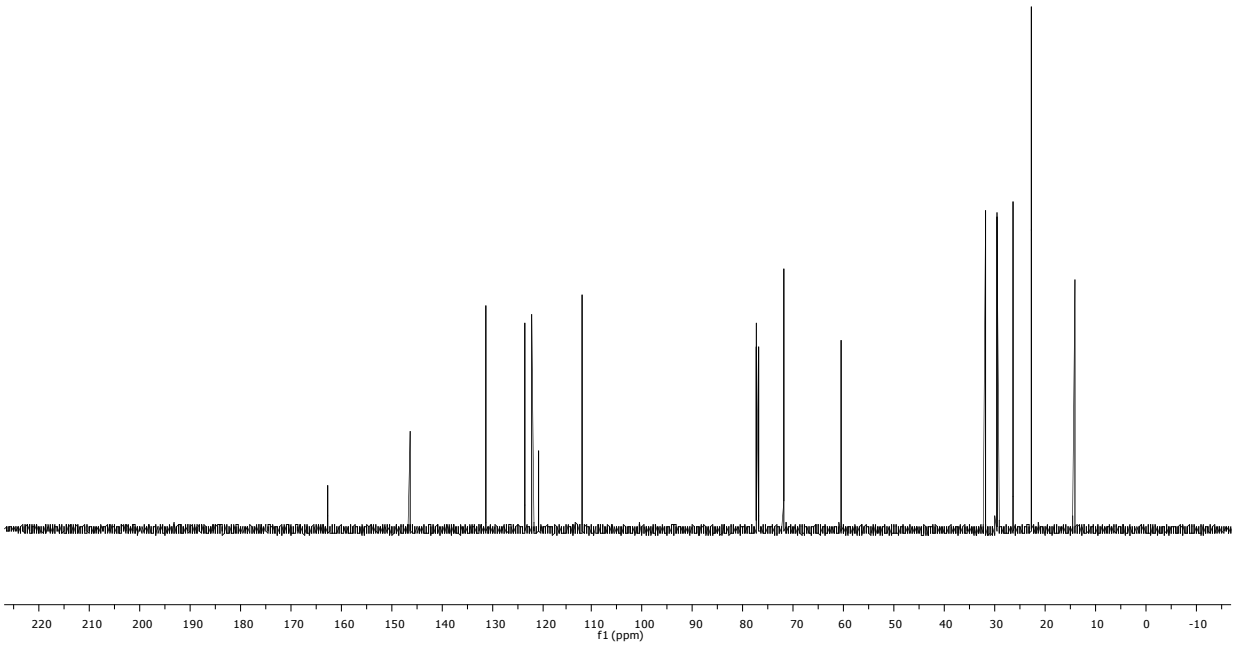
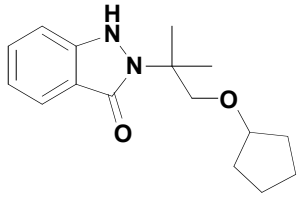


^{13}C in $CDCl_3$ (150 MHz)

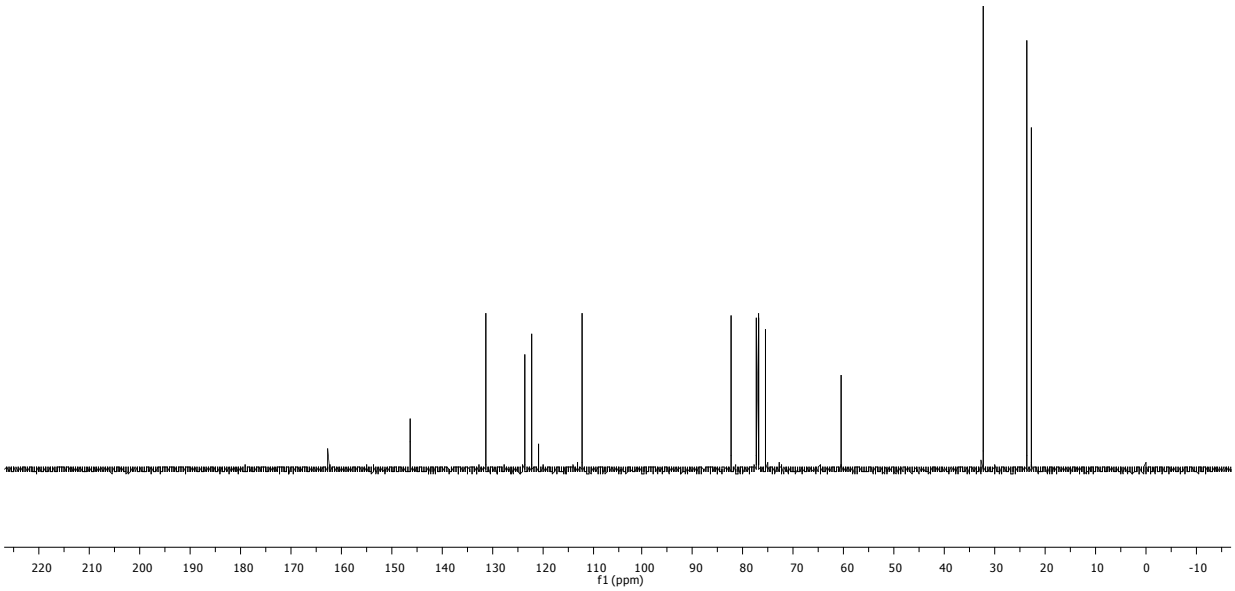


^{1}H in $CDCl_3$ (600 MHz)

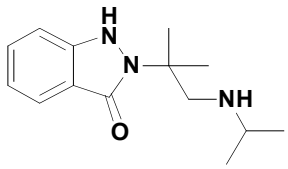


21

^{13}C in $CDCl_3$ (150 MHz)

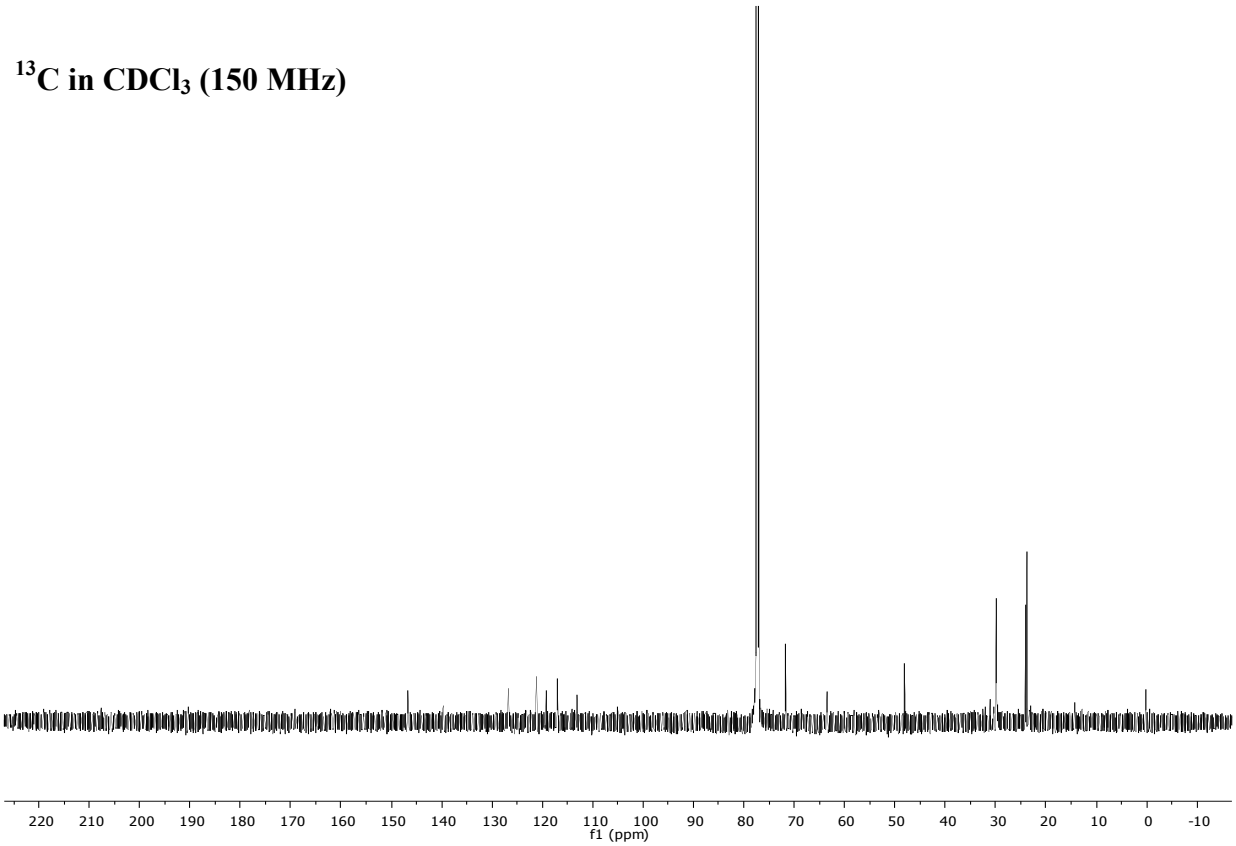


^{1}H in $CDCl_3$ (600 MHz)

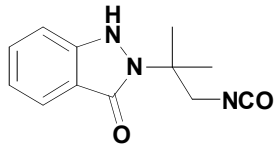


22

^{13}C in $CDCl_3$ (150 MHz)

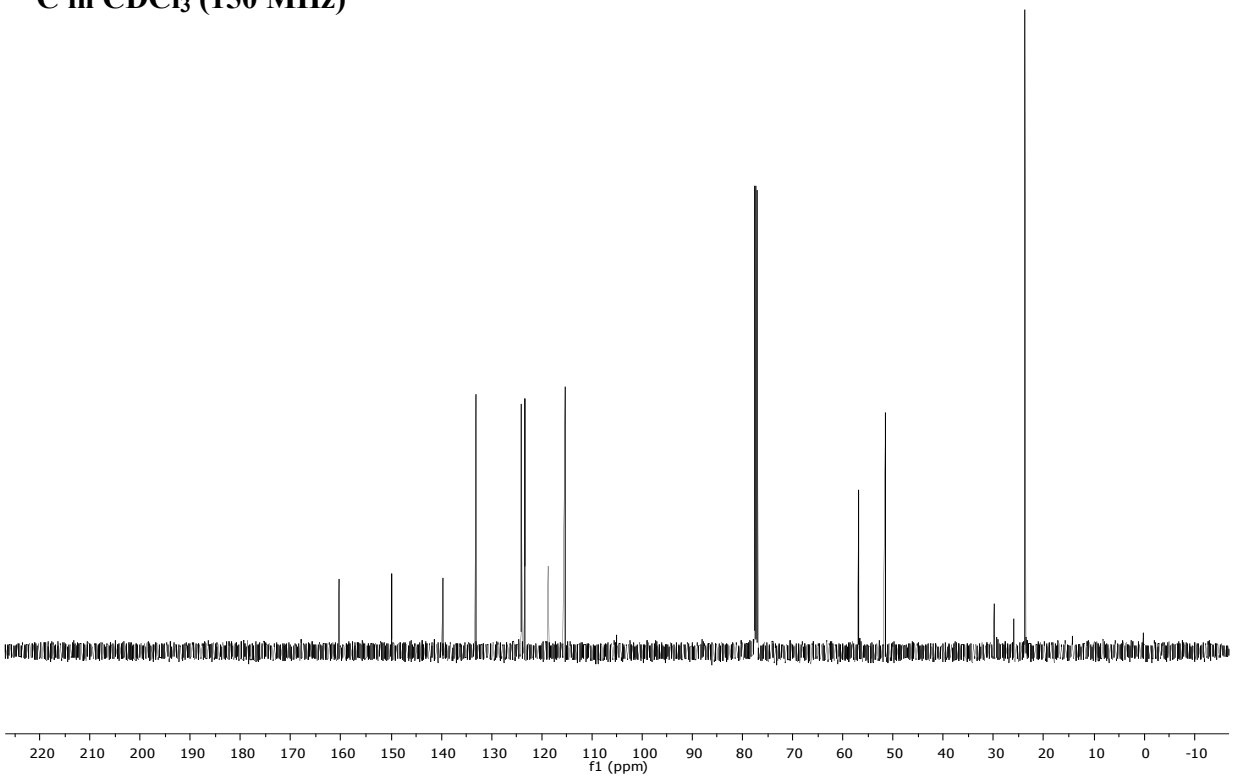


^{1}H in $CDCl_3$ (600 MHz)

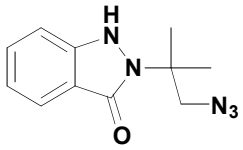


24

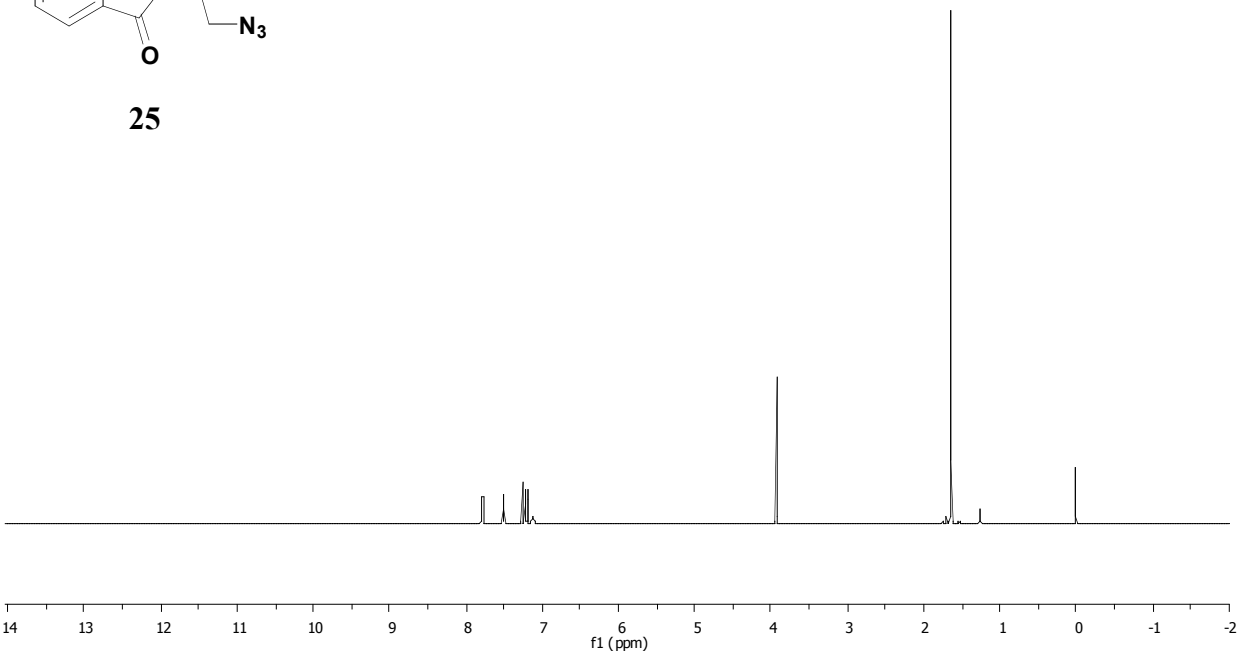
^{13}C in $CDCl_3$ (150 MHz)



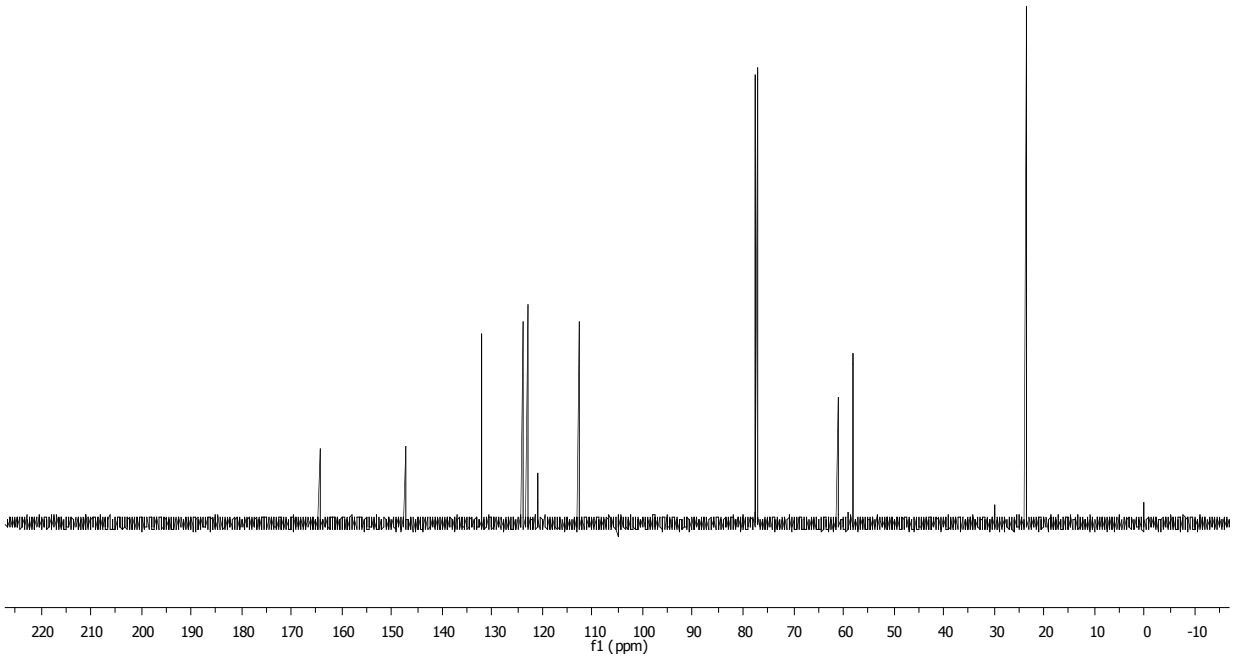
^{1}H in $CDCl_3$ (600 MHz)



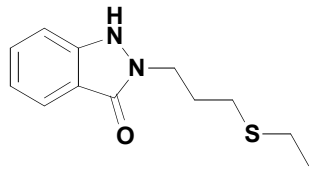
25



^{13}C in $CDCl_3$ (150 MHz)

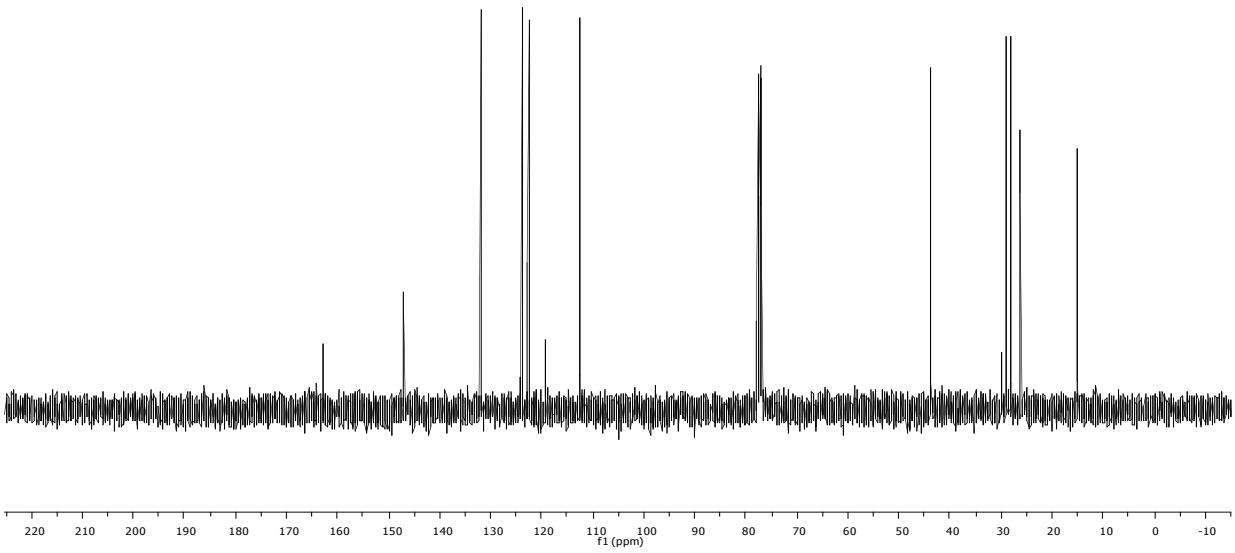


^{1}H in $CDCl_3$ (300 MHz)

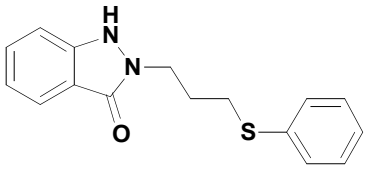


27

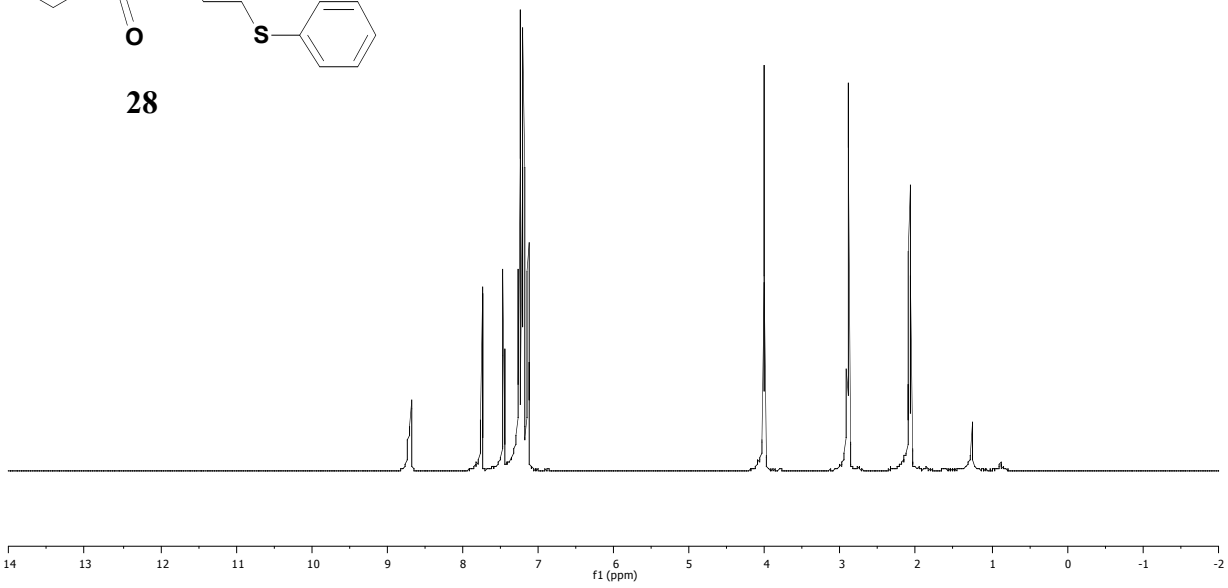
^{13}C in $CDCl_3$ (75 MHz)



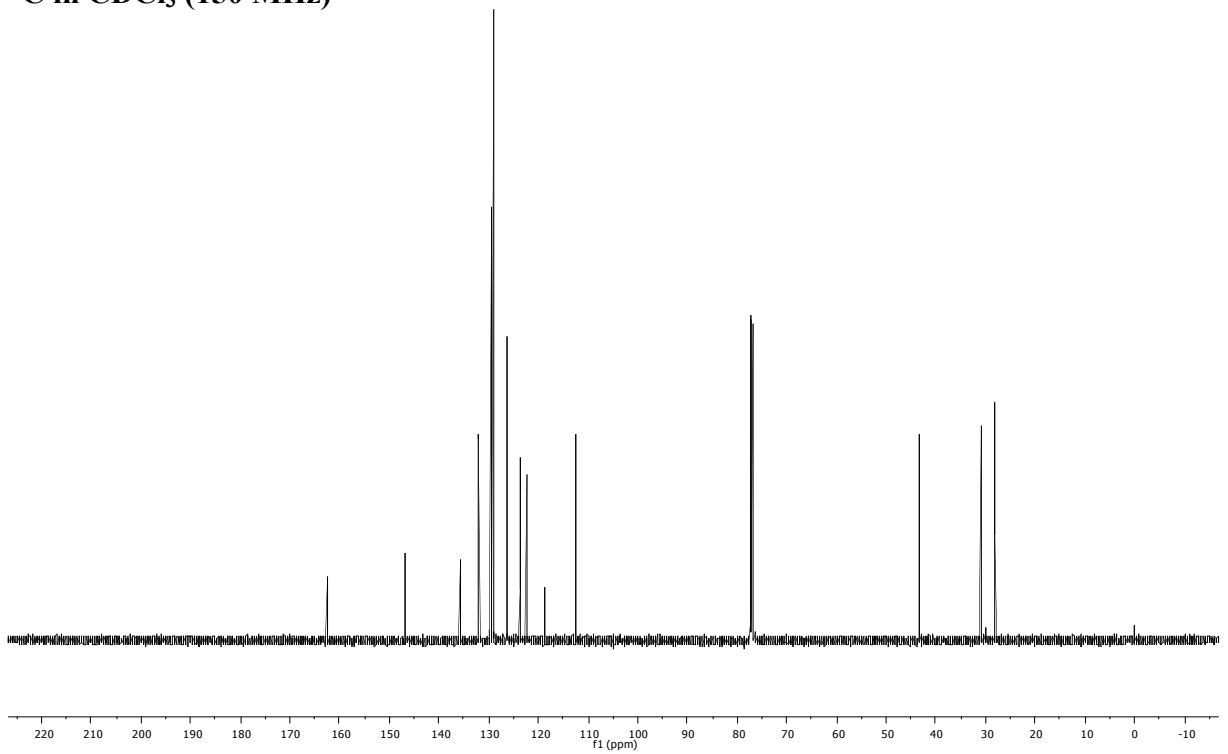
^{1}H in $CDCl_3$ (600 MHz)



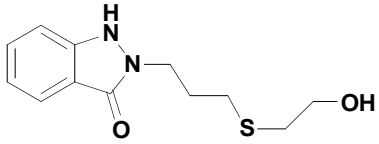
28



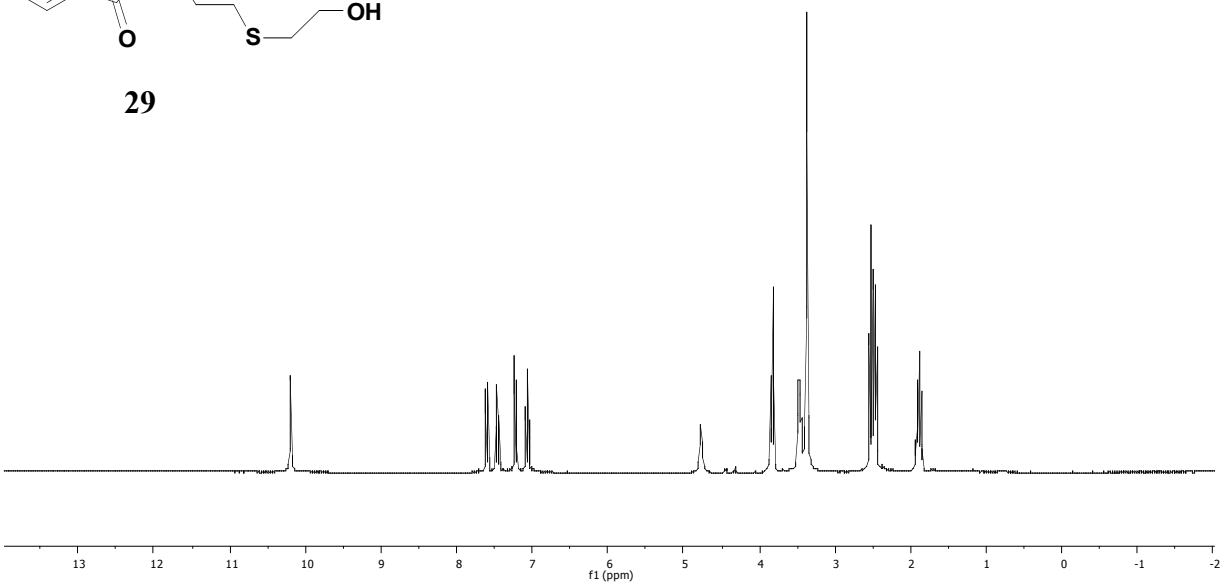
^{13}C in $CDCl_3$ (150 MHz)



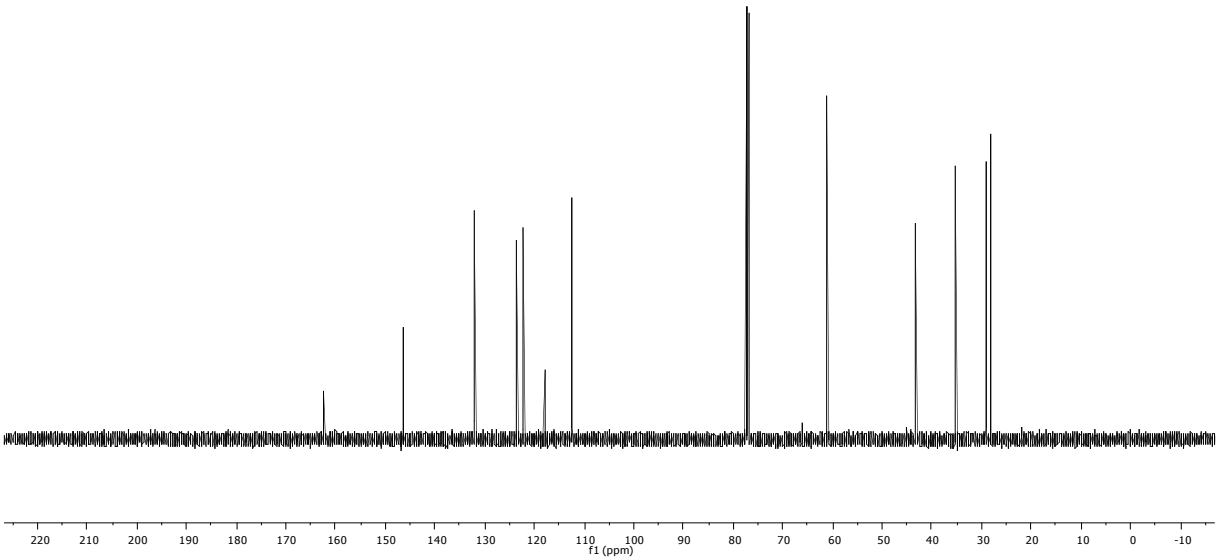
^{1}H in DMSO (600 MHz)



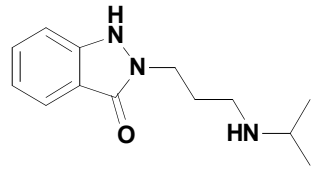
29



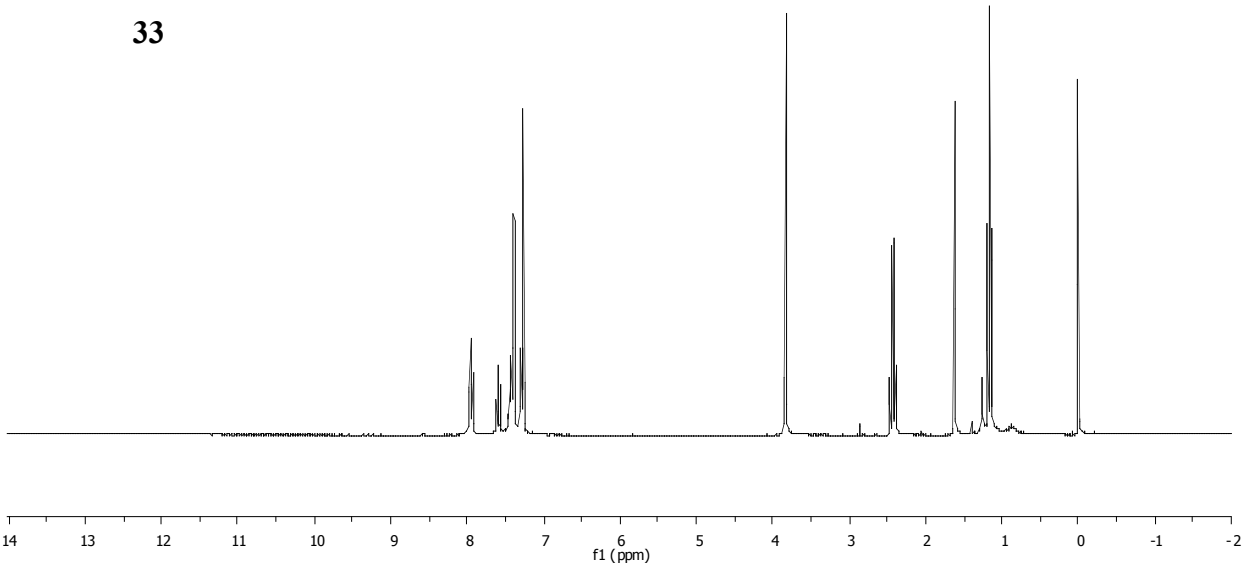
^{13}C in DMSO (150 MHz)



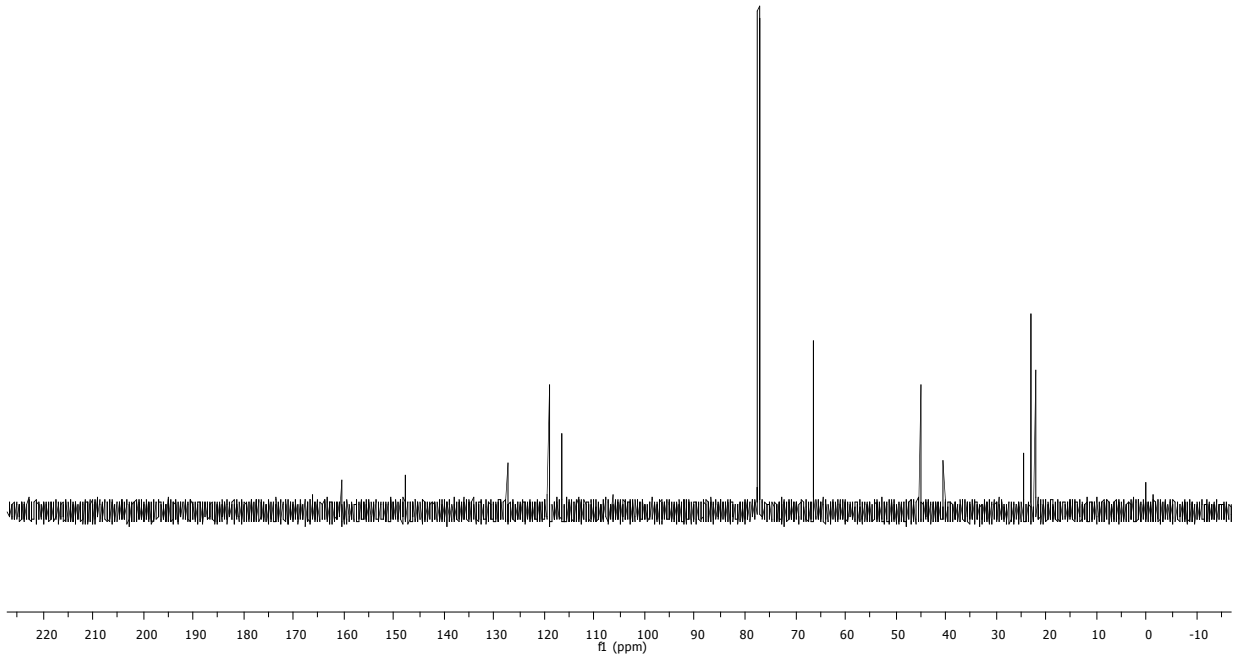
^{1}H in $CDCl_3$ (600 MHz)



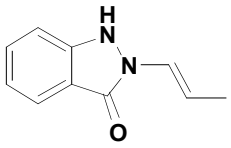
33



^{13}C in $CDCl_3$ (150 MHz)

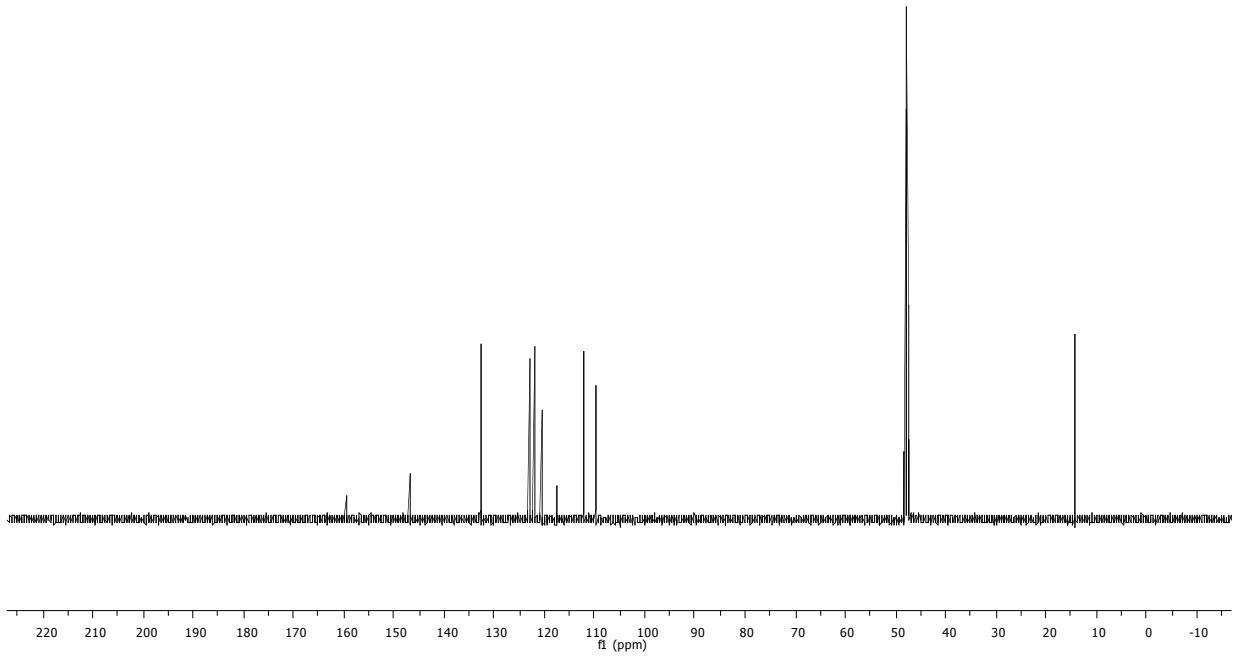


^{1}H in CD_3OD (600 MHz)

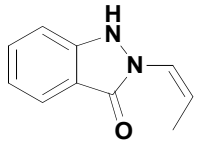


38

^{13}C in CD_3OD (150 MHz)

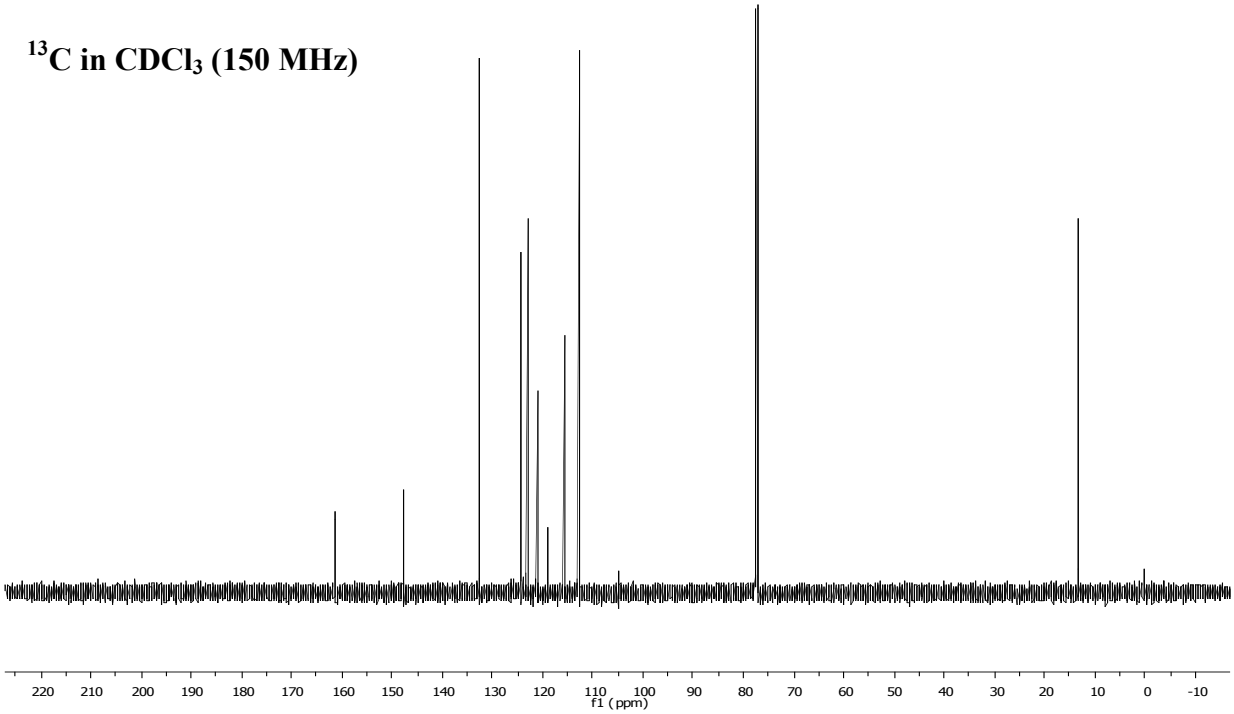


^{1}H in $CDCl_3$ (600 MHz)

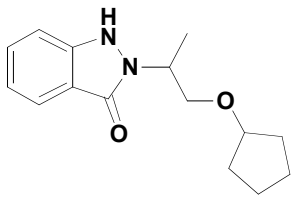


39

^{13}C in $CDCl_3$ (150 MHz)



^{1}H in $CDCl_3$ (600 MHz)



40

^{13}C in $CDCl_3$ (150 MHz)