# Supporting Information to Accompany:

# The Davis-Beirut Reaction: $N^1$,$N^2$-Disubstituted-1*H*-Indazolones via 1,6-Electrophilic Addition to 3-Alkoxy-2*H*-Indazoles

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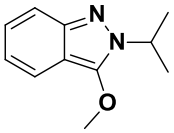
## I. General Methods and Materials

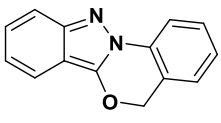
General Experimental Procedures. Acetonitrile was dried by distillation from $CaH_2$ prior to use. All other solvents and reagents were purchased from commercial suppliers and used without further purification. For reactions run in sealed microwave vials, oven-dried Biotage® 5-10 mL or 10-20 mL vials containing a Teflon-coated stirrer bar and sealed with a Teflon-lined septum were used. Analytical thin layer chromatography was carried out on pre-coated plates (Silica gel 60 $F_{254}$, 250 µm thickness) and visualized with UV light. Flash chromatography was performed with 60 Å, 35-70 µm silica gel (Acros Organics). Concentration refers to rotary evaporation under reduced pressure.

$^1$H NMR spectra were recorded on Varian spectrometers operating at 300, 400, or 600 MHz at ambient temperature with DMSO-d6 or $CDCl_3$ as solvents. $^{13}$C NMR spectra were recorded on Varian spectrometers operating at 75, 100, or 150 MHz at ambient temperature with DMSO-d6 or $CDCl_3$ as solvents. Data for $^1$H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet; br, broad), integration, coupling constant (Hz). Chemical shifts are reported in parts per million relative to DMSO-d6 ($^1$H, δ 2.50, $^{13}$C, δ 39.52), $CDCl_3$ ($^1$H, δ 7.26, $^{13}$C, δ 77.16), or TMS ($^1$H, δ 0.00, $^{13}$C, δ 0.00). 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 C18 column (2.1 mm x 50 mm x 3.5 µm).

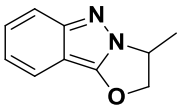
## II. Preparation of 2*H*-Indazoles



**3,3-Dimethyl-2,3-dihydrooxazolo[3,2-b]indazole (1a)**. 2-Nitrobenzyl bromide (3.307 g, 15.31 mmol) was dissolved in MeOH (115 mL) and added dropwise to a stirring solution of isopropylamine (5.25 mL, 61.2 mmol), DIEA (10.7 mL, 61.2 mmol), and 38 mL of MeOH over 6 hours and then left stirring overnight. Water (15 mL) and KOH (4.30 g, 76.6 mmol) were then added and this mixture was heated at 60 ºC for 24 hours and monitored by thin layer chromatography. When the starting material had been consumed, 50 mL of water was added and the methanol was removed under reduced pressure. This aqueous mixture was then extracted twice with dichloromethane. The combined organic extracts were washed with water, brine, dried over sodium sulfate, and concentrated. The crude mixture was purified by flash chromatography (20% ethyl acetate in hexanes) to afford **1a**, (2.513 g, 86%) as an orange oil. Spectral data is in accordance with literature values reported in Mills, A.; Nazer, M.; Haddadin, M. and Kurth, M*. J. Org. Chem***. 2006**, *71*, 2687-2689.

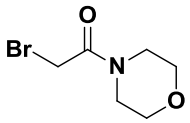


**5H-benzo[4,5][1,3]oxazino[3,2-b]indazole (1d)**. Made via literature methods found in Solano, D. M.; Butler, J. D.; Haddadin, M. J.; Kurth, M, J. *Org. Synth*. **2010**, *87*, 339. Spectral data is in accordance with literature values.

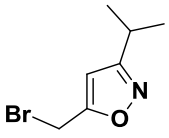


**3-Methyl-2,3-dihydrooxazolo[3,2-b]indazole (1e).** 2-Nitrobenzyl bromide (7.73 g, 35.80 mmol) was dissolved in isopropanol (179 mL) and added dropwise to a stirring solution of 2-amino-1-propanol (10.7 g, 143 mmol), DIEA (24.9 mL, 142 mmol), and 59 mL of isopropanol over 6 hours and then left stirring overnight. Water (24 mL) and KOH (10.0 g, 179 mmol) were added and this mixture was heated at 60 ºC for 24 hours and monitored by thin layer chromatography. When the starting material had been consumed, 50 mL of water was added and the methanol was removed under reduced pressure. This aqueous mixture was then extracted twice with dichloromethane. The combined organic extracts were washed with water, brine, dried over sodium sulfate, and concentrated. The crude mixture was purified by flash chromatography (90% ethyl acetate in hexanes) to afford **1e**, (4.48 g, 72%) as a pale yellow solid. Spectral data is in accordance with literature values reported in Oakdale, J.; Solano, D.; Fettinger, J.; Haddadin, M.; Kurth, M. *Org. Lett.* **2009**, *11*, 2760-2763. Removed sentence.

## III. Preparation of Electrophiles E8 and E9

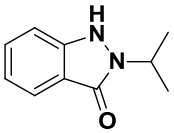


**2-bromo-1-morpholinoethanone (E8).** Morpholine (8.75 mL, 100 mmol) was dropwise added to a solution of bromoacetyl bromide (4.36 mL, 50.0 mmol) in dry dichloromethane (250 mL) at -42 ºC. This was stirred for 15 minutes at -42 ºC, then allowed to warm to room temperature over 1 hour. This solution was then washed successively with saturated ammonium chloride, saturated sodium carbonate, water, brine, and dried over sodium sulfate. The organic extracts were then concentrated to afford **E8**, (8.663 g, 83%) as a colorless oil, which was used without further purification: **IR** (neat) $\nu_{max}$ 2965, 2921, 2901, 2855, 1638, 1459, 1437, 1274, 1259, 1218, 1109, 1037, 964 $cm^{-1}$; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 3.82 (s, 1.3 H), 3.81 (s, 0.7 H), 3.72-3.62 (m, 4H), 3.61-3.55 (m, 2H), 3.51-3.45 (m, 2H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 165.4, 66.6, 66.4, 47.2, 42.4, 25.6, 25.4; **ESI MS** calc'd. for $[C_6H_{10}BrNO_2 + H]^+$: 207.99, found: 207.91.

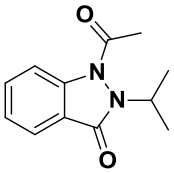


**5-(bromomethyl)-3-isopropylisoxazole (E9).** Made via literature methods found in Liu, Y.; Cui, Z., Liu; B.; Cai, B.; Li, Y.; and Wang, Q. *J. Agric. Food Chem*. **2010,** *58*, 2685-2689: **IR** (neat) $\nu_{max}$ 2969, 2933, 2903, 2877, 1604, 1463, 1418, 1258, 1216, 1002, 985, 912 $cm^{-1}$; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 6.19 (s, 1H), 4.43 (s, 2H), 3.05 (m, *J* = 6.9 Hz, 1H), 1.28 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.8, 167.1, 102.1, 26.7, 21.8, 19.0; **ESI MS** calc'd. for $[C_7H_{10}BrNO + H]^+$: 203.99, found: 204.08.

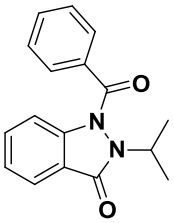
## IV. Preparation of Indazolones (2-10)



**2-isopropyl-1H-indazol-3(2H)-one (2).** Indazole **1a** (192 mg, 1.01 mmol) was added to a 25 mL round-bottom flask fitted with a water-cooled reflux condenser and dissolved in acetic acid (5 mL). This solution was heated to reflux for 17 hours at which time TLC analysis showed consumption of the indazole. The crude mixture was then diluted with water (20 mL) and slowly neutralized with sodium bicarbonate. This neutral aqueous mixture was then extracted with ethyl acetate (3 x 30 mL) and the combined organic extracts were washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was then purified by flash chromatography (5% methanol in ethyl acetate) to afford **2** as a pale yellow solid (0.153 g, 86%): **mp** 152-153 ºC; **IR** (neat) $\nu_{max}$ 3027, 2869, 2734, 1615,m 1457, 1321, 1243, 1216, 1065 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 9.49 (br s, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.44-7.40 (m, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.08 (dd, *J* = 7.7 Hz, 1H), 4.79 (m, *J* = 6.9 Hz, 1H), 1.37 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 161.65, 146.64, 131.51, 123.35, 121.68, 118.42, 112.41, 46.06, 20.60 (2C).; **ESI MS** calc'd. for $[C_{10}H_{12}N_2O + H]^+$: 177.09, found: 177.08.

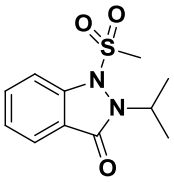


**1-acetyl-2-isopropyl-1H-indazol-3(2H)-one (3).** Indazole **1a** (198 mg, 1.04 mmol) was added to a 25 mL round-bottom flask fitted with a water-cooled reflux condenser and dissolved in acetic anhydride (5 mL). This solution was then heated to reflux for 2 days at which time TLC analysis showed consumption of the indazole. The crude mixture was then poured into saturated sodium carbonate (50 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were washed with water (20 mL) and brine (20 mL), dried over sodium sulfate, and concentrated. This crude material was then purified by flash chromatography ( 25-30% ethyl acetate in hexanes) to afford **3** as a yellow amorphous solid (0.200 g, 89%): **IR** (neat) $\nu_{max}$ 2965, 2931, 16980, 1452, 1284, 1243, 1183, 1131, 1011 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 7.7 Hz, 1H), 7.64 (ddd, *J* = 8.3, 7.7, 1.3 Hz, 1H), 7.34 (dd, *J* = 7.7, 7.7 Hz, 1H), 4.16 (m, *J* = 6.9 Hz, 1H), 2.55 (s, 3H), 1.54 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 170.2, 169.0, 144.9, 134.0, 125.1, 124.0, 120.4, 115.1, 56.2, 24.5, 19.2 (2C); **ESI MS** calc'd. for $[C_{12}H_{14}N_2O_2 + H]^+$: 219.11, found: 219.11.

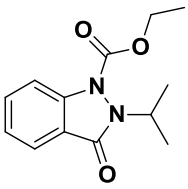


**1-benzoyl-2-isopropyl-1H-indazol-3(2H)-one (4).** Indazole **1a** (195 mg, 1.03 mmol) was added to a 25 mL 2-neck round-bottom flask fitted with a water-cooled reflux condenser and an $N_2$ balloon, then dissolved in dry acetonitrile (10 mL). Benzoyl chloride (478 µL, 4.12 mmol) was added and the solution was heated to reflux for 8 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then poured into saturated sodium carbonate (30 mL) and the layers were

separated. The organic extracts were then washed with water (20 mL) and brine (20 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (20-30% ethyl acetate in hexanes) to afford **4** as a yellow solid (0.271 g, 94%): **mp** 104-105 ºC; **IR** (neat) $\nu_{max}$ 2980, 2933, 1704, 1672, 1609, 1458, 1364, 1258, 1171, 1152 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.92-7.89 (m, 2H), 7.87-7.84 (m, 1H), 7.74-7.71 (m, 1H), 7.60 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.34-7.30 (m, 1H), 7.25 (dd, *J* = 7.42, 7.42 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 4.35 (m, *J* = 6.9 Hz, 1H), 1.58 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 168.6, 165.6, 143.8, 134.8, 133.8, 132.7, 129.9 (2C), 129.3 (2C), 124.7, 124.0, 120.1, 113.3, 53.4, 19.7 (2C); **ESI MS** calc'd. for $[C_{17}H_{16}N_2O_2 + H]^+$: 281.12, found: 281.11.

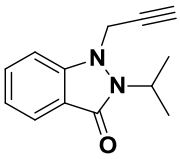


**2-isopropyl-1-(methylsulfonyl)-1H-indazol-3(2H)-one (5).** Indazole **1a** (205 mg, 1.08 mmol) was added to a two-neck round bottom flask fitted with a water-cooled reflux condenser and an $N_2$ balloon, then dissolved in dry acetonitrile (10 mL). Methanesulfonyl chloride (334 µL, 4.32 mmol) was added and the solution was heated at reflux for 6.5 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then poured into saturated sodium carbonate (20 mL) and the layers were separated. The organic extracts were then washed with water, brine, dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (20-30% ethyl acetate in hexanes gradient) to afford **5** as a yellow oil (0.192 g, 70%): **IR** (neat) $\nu_{max}$ 3015, 2980, 2935, 1703, 1476, 1461, 1361, 1187, 1171, 1100, 961 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.69 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.47 (d, *J* = 7.8, 7.8 Hz, 1H), 4.61 (m, *J* = 6.9 Hz, 1H), 2.53 (s, 3H), 1.53 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 168.2, 146.2, 134.0, 127.3, 124.4, 122.7, 118.0, 55.9, 31.2, 19.5 (2C); **ESI MS** calc'd. for $[C_{11}H_{14}N_2O_3S + H]^+$: 255.07, found: 255.10.

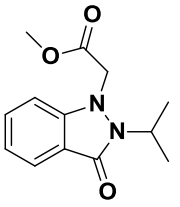


**Ethyl 2-isopropyl-3-oxo-2,3-dihydro-1H-indazole-1-carboxylate (6).** Indazole **1a** (209 mg, 1.10 mmol) was added to a 25 mL two-neck round bottom flask fitted with a water-cooled reflux condenser and an $N_2$ balloon. Dry acetonitrile (10 mL) and ethyl chloroformate (419 µL, 4.40 mmol) were added and this solution was heated to 80 ºC for 16 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then poured into saturated sodium carbonate (30 mL) and the layers were separated. The organic extracts were then washed with water (30 mL) and brine (30 mL), dried over sodium carbonate, and concentrated. This crude material was purified by flash chromatography (20% ethyl acetate in hexanes) to afford **6** as a pale yellow oil (0.271 g, 95%): **IR** (neat) $\nu_{max}$ 2979, 2938, 1740, 1460, 1310, 1198, 1092, 1034 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.86-7.80 (m, 2H), 7.61 (ddd, *J* = 7.8, 7.8, 1.3 Hz, 1H), 7.31 (dd, *J* = 7.8, 7.2 Hz, 1H), 4.46 (m, *J* = 6.9 Hz, 1H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.55 (d, *J* = 6.9 Hz, 6H), 1.47 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 166.4, 152.4, 144.3,

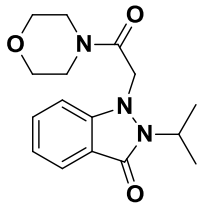
133.2, 124.8, 123.5, 120.3, 115.6, 64.1, 54.2, 19.5 (2C), 14.4; **ESI MS** calc'd. for $[C_{13}H_{16}N_2O_3 + H]^+$: 249.12, found 249.10.



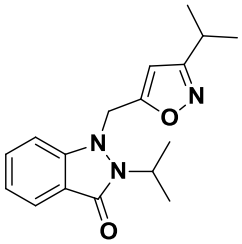
**2-isopropyl-1-(prop-2-yn-1-yl)-1H-indazol-3(2H)-one (7).** Indazole **1a** (1.92 g, 10.1 mmol) was added to a 250 mL round bottom flask fitted with a water-cooled reflux condenser and an $N_2$ balloon. Dry acetonitrile (100 mL) and propargyl bromide (465 µL, 4.32 mmol, 80% solution in toluene) were added and this solution was heated to reflux for 2 days at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (100 mL). This solution was washed with water (100 mL) and brine (100 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (35-40% ethyl acetate in hexanes) to afford **7** as an off-white solid (1.80 g, 83%): **mp** 97-98 ºC; **IR** (neat) $\nu_{max}$ 3416, 3278, 2973, 2166, 2119, 1644, 1613, 1464, 1313, 1247 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.54 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.23-7.16 (m, 2H), 4.53 (m, *J* = 6.9 Hz, 1H), 4.41 (d, *J* = 2.2 Hz, 2H), 2.01 (t, *J* = 2.2 Hz, 1H), 1.49 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.0, 150.7, 132.3, 123.9, 123.5, 121.6, 122.7, 75.2, 74.4, 48.2, 42.6, 20.7 (2C); **ESI MS** calc'd. for $[C_{13}H_{14}N_2O + H]^+$: 215.11, found: 215.09.



**Methyl 2-(2-isopropyl-3-oxo-2,3-dihydro-1H-indazol-1-yl)acetate (8).** Indazole **1a** (194 mg, 1.02 mmol) was added to a 25 mL two-neck round bottom flask fitted with a water-cooled reflux condenser and an $N_2$ balloon. Dry acetonitrile (10 mL) and methyl bromoacetate (386 µL, 4.08 mmol) were added and this solution was heated to reflux for 18 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then poured into water (30 mL) and the layers were separated. The organic extracts were then washed with brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (70% ethyl acetate in hexanes) to afford **8** as a white solid (0.242 g, 95%): **mp** 100-101 ºC; **IR** (neat) $\nu_{max}$ 2972, 2934, 1749, 1660, 1617, 1481, 1464, 1207, 1179, 1146 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.8 Hz, 1H), 7.53 (ddd, *J* = 7.8, 7.2, 1.2 Hz, 1H), 7.18 (ddd, *J* = 7.8, 7.5, 0.8 Hz, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 4.56 (m, *J* = 7.0 Hz, 1H), 4.47 (s, 2H), 3.60 (s, 3H), 1.46 (d, *J* = 7.0 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 167.8, 165.2, 150.7, 132.5, 124.2, 122.5, 119.7, 111.1, 52.3, 52.3, 48.5, 20.6 (2C); **ESI MS** calc'd. for $[C_{13}H_{16}N_2O_3 + H]^+$: 249.12, found: 249.10.

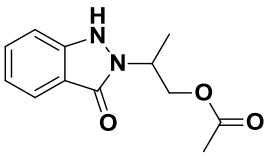


**2-isopropyl-1-(2-morpholino-2-oxoethyl)-1H-indazol-3(2H)-one (9)**. Indazole **1a** (195 mg, 1.03 mmol) was added to a 25 mL two-neck round bottom flask fitted with a water-cooled reflux condenser and an $N_2$ balloon. Dry acetonitrile (10 mL) and 2-bromo-1-morpholinoethanone **E8** (0.427 g, 2.05 mmol) were added and this solution was heated to reflux for 24 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and this crude material was purified by flash chromatography (5-10% methanol in ethyl acetate) to afford **9** as a white solid (0.260 g, 84%): **mp** 205-206 ºC (decomp); **IR** (neat) $\nu_{max}$ 2977, 2920, 2893, 2853, 1640, 1462, 1429, 1316, 1271, 1232, 1114, 1029 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.7 Hz, 1H), 7.50 (ddd, *J* = 8.3, 7.4, 1.2 Hz, 1H), 7.15 (dd, *J* = 7.8, 7.4 Hz, 1H), 7.09 (d, *J* = 8.3 Hz, 1H), 4.53 (m, *J* = 6.9 Hz, 1H), 4.49 (s, 2H), 3.70-3.64 (m, 4H), 3.60-3.55 (m, 2H), 3.52-3.47 (m, 2H), 1.47 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.2, 165.1, 151.3, 132.6, 124.2, 122.4, 119.6, 111.2, 67.0, 66.6, 52.1, 48.7, 45.7, 42.4, 20.7 (2C); **ESI MS** calc'd. for $[C_{16}H_{21}N_3O_3 + H]^+$: 304.16, found: 304.09.



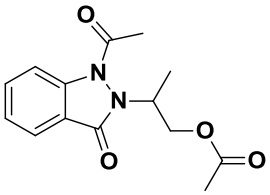
**2-isopropyl-1-((3-isopropylisoxazol-5-yl)methyl)-1H-indazol-3(2H)-one (10).** Indazole **1a** (195 mg, 1.03 mmol) was added to a 25 mL two-neck round bottom flask fitted with a water-cooled reflux condenser and an $N_2$ balloon. Dry acetonitrile (10 mL) and 5-(bromomethyl)-3-isopropylisoxazole **E9** (0.420 g, 2.06 mmol) were added and this solution was heated to reflux for 36 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then poured into water (30 mL) and the layers were separated. The organic extracts were then washed with brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (40-55% ethyl acetate in hexanes) to afford **10** as a brown oil (0.279 g, 91%): **IR** (neat) $\nu_{max}$ 2970, 2934, 2875, 1663, 1614, 1480, 1464, 1340, 1312, 1250 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.56 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.25-7.19 (m, 2H), 5.53 (s, 1H), 4.94 (s, 2H), 4.48 (m, *J* = 6.9, 1H), 2.88 (m, *J* = 6.9 Hz, 1H), 1.50 (d, *J* = 6.9 Hz, 6H), 1.14 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.4, 165.8, 164.7, 150.6, 132.8, 124.3, 123.4, 120.7, 112.4, 101.2, 49.3, 47.1, 26.6, 21.6 (2C), 20.6 (2C); **ESI MS** calc'd. for $[C_{17}H_{21}N_3O_2 + H]^+$: 300.16, found: 300.14.

## V. Preparation of Indazolones (11-20)

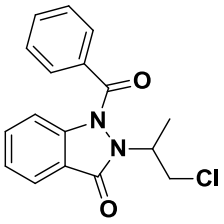


**2-(3-oxo-1H-indazol-2(3H)-yl)propyl acetate (11).** Indazole **1e** (181 mg, 1.04 mmol) was added to a 15 mL round bottom flask fitted with a water-cooled reflux condenser. Acetic acid (5.2 mL) was added and this solution was heated to reflux for 18 hours at which time TLC analysis showed consumption of the indazole. The crude mixture was then diluted with water (30 mL) and slowly neutralized with sodium

bicarbonate. This neutral aqueous mixture was then extracted with ethyl acetate (3 x 30 mL) and the combined organic extracts were washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was then purified by flash chromatography (100% ethyl acetate) to afford **11** as a white solid (0.229 g, 94%): **mp** 132-133 ºC; **IR** (neat) $\nu_{max}$ 3052, 2921, 2832, 2693, 2608, 1735, 1606, 1480,1234, 1213, 1041 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 9.24 (br s, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.46 (ddd, *J* = 8.1, 7.5, 1.0 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 7.11 (dd, *J* = 7.5, 7.5 Hz, 1H), 4.97-4.89 (m, 1H), 4.49 (dd, *J* = 11.6, 9.0 Hz, 1H), 4.22 (dd, *J* = 11.6, 4.6 Hz, 1H) 1.93 (s, 3H), 1.39 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 171.3, 163.5, 147.6, 132.1, 123.6, 122.2, 118.5, 112.8, 64.9, 49.4, 20.8, 15.3; **ESI MS** calc'd. for $[C_{12}H_{14}N_2O_3 + H]^+$: 235.10, found: 235.06.

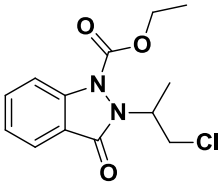


**2-(1-acetyl-3-oxo-1H-indazol-2(3H)-yl)propyl acetate (12).** Indazole **1e** (176 mg, 1.01 mmol) was added to a 15 mL round bottom flask fitted with a water-cooled reflux condenser. Acetic anhydride (5.1 mL) was added and this solution was heated to reflux for 18 hours at which time TLC analysis showed consumption of the indazole. The crude mixture was then diluted with water (30 mL) and slowly sodium carbonate was added until the solution was alkaline. This aqueous mixture was then extracted with ethyl acetate (3 x 30 mL) and the combined organic extracts were washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was then purified by flash chromatography (40% ethyl acetate in hexanes) to afford **12** as a pale yellow oil (0.276 g, 99%): **IR** (neat) $\nu_{max}$ 2994, 2985, 1738, 1693, 1611, 1462, 1368, 1263, 1235, 1041 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.63 (dd, *J* = 8.3, 7.5 Hz, 1H), 7.33 (dd, J = 7.5, 7.5 Hz, 1H) 4.68 (td, *J* = 10.7, 2.6 Hz, 1H), 4.44-4.35 (m, 2H), 2.55 (s, 3H), 1.85 (s, 3H) 1.49 (d, *J* = 6.5 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 170.7, 169.3, 168.2, 144.5, 134.1, 125.2, 124.2, 119.9, 114.9, 64.4, 57.4, 24.6, 20.7, 14.6; **ESI MS** calc'd. for $[C_{14}H_{16}N_2O_4 + H]^+$: 277.11, found: 277.12.

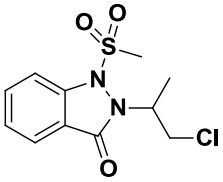


**1-benzoyl-2-(1-chloropropan-2-yl)-1H-indazol-3(2H)-one (13).** Indazole **1e** (183 mg, 1.05 mmol) was added to 10-20 mL microwave vial. Dry acetonitrile (10 mL) and benzoyl chloride (488 µL, 4.20 mmol) were added and this solution was heated at 90 ºC for 6 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then poured into saturated sodium carbonate (30 mL) and the layers were separated. The organic extracts were then washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (10-20% ethyl acetate in hexanes) to afford **13** as a white solid (0.297 g, 90%): **mp** 84-86 ºC; **IR** (neat) $\nu_{max}$ 3003, 2991, 1673, 1613, 1460, 1297, 1269, 1237, 1172, 1050 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.92-7.87 (m, 3H), 7.77-7.72 (m, 1H), 7.64-7.58 (m, 2H), 7.31 (ddd, *J* = 8.4, 7.3, 1.4 Hz, 1H), 7.28-7.24 (m, 1H), 6.43 (d, *J* = 8.4 Hz, 1H), 4.50-4.43 (m, 1H), 4.39 (dd, *J* = 10.9, 8.7, 1H), 3.86

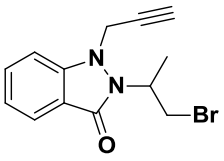
(dd, *J* = 10.9, 6.0, 1H), 1.77 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 168.0, 164.8, 143.2, 134.2, 134.0, 133.0, 129.9 (2C), 129.5 (2C), 124.9, 124.2, 119.4, 113.2, 58.3, 44.7, 16.5; **ESI MS** calc'd. for $[C_{17}H_{15}ClN_2O_2 + H]^+$: 315.08, found: 315.04.



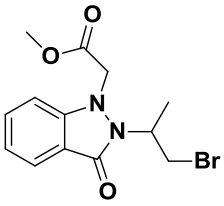
**Ethyl 2-(1-acetoxypropan-2-yl)-3-oxo-2,3-dihydro-1H-indazole-1-carboxylate (14).** Indazole **1e** (178 mg, 1.02 mmol) was added to a 10-20 mL microwave vial. Dry acetonitrile (10 mL) and ethyl chloroformate (392 µL, 4.10 mmol) were added and this solution was heated at 82 ºC for 6 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then washed with water (30 mL and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (20% ethyl acetate in hexanes) to afford **14** as a white solid (0.281 g, 97%): **mp** 75-77 ºC; **IR** (neat) $\nu_{max}$ 2984, 2969, 2921, 2906, 1726, 1684, 1458, 1224, 1156, 1034 cm-1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.87-7.80 (m, 2H), 7.66-7.59 (m, 1H), 7.34 (dd, *J* = 7.6, 7.6 Hz, 1H), 4.63-4.52 (m, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 4.28 (dd, *J* = 10.9, 7.7 Hz, 1H), 3.89 (dd, *J* =10.9, 7.2 Hz, 1H) 1.63 (d, *J* = 6.9 Hz, 3H), 1.47 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 166.0, 152.1, 144.1, 133.7, 125.0, 123.8, 119.6, 115.9, 64.5, 59.2, 44.8, 15.9, 14.5; **ESI MS** calc'd. for $[C_{13}H_{15}ClN_2O_3 + H]^+$: 283.08, found: 282.99.



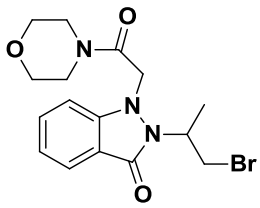
**2-(1-chloropropan-2-yl)-1-(methylsulfonyl)-1H-indazol-3(2H)-one (15).** Indazole **1e** (171 mg, 0.983 mmol) was added to a 10-20 mL . Dry acetonitrile (10 mL) and methanesulfonyl chloride (305 µL, 3.93 mmol) were added and this solution was heated at 82 ºC for 6 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then poured into saturated sodium carbonate (30 mL) and the layers were separated. The organic extracts were then washed with water (30 mL and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (30% ethyl acetate in hexanes) to afford **15** as a white solid (0.266 g, 94%): **mp** 89-90 ºC; **IR** (neat) $\nu_{max}$ 3008, 2950, 2927, 1689, 1359, 1168, 1153, 1125, 964 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.72 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.51 (ddd, *J* = 7.5, 7.5, 0.8 Hz, 1H), 4.80-4.73 (m, 1H), 4.40 (dd, *J* = 11.2, 9.4 Hz, 1H), 3.78 (dd, *J* = 11.2, 6.0 Hz, 1H), 2.63 (s, 3H), 1.54 (d, *J* = 6.9, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 167.8, 146.1, 134.4, 127.4, 124.5, 121.8, 118.0, 60.1, 44.9, 31.7, 15.9; **ESI MS** calc'd. for $[C_{11}H_{13}ClN_2O_3S + H]^+$: 289.03, found: 288.99.



**2-(1-bromopropan-2-yl)-1-(prop-2-yn-1-yl)-1H-indazol-3(2H)-one (16).** Indazole **1e** (216 mg, 1.24 mmol) was added to a 10-20 mL microwave vial. Dry acetonitrile (10 mL) and propargyl bromide (535 µL, 4.96 mmol, 80% solution in toluene) were added and this solution was heated to 82 ºC for 15 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then poured into saturated sodium carbonate (30 mL) and the layers were separated. The organic extracts were then washed with water (30 mL and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (35% ethyl acetate in hexanes) to afford **16** as a yellow solid (0.357 g, 98%): **mp** 85-86 ºC; **IR** (neat) $\nu_{max}$ 3236, 3227, 2162, 1657, 1615, 1480, 1462, 1312, 1248, 1236, 933 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.7 Hz, 1H), 7.59 (dd, *J* = 8.2, 7.3 Hz, 1H), 7.28-7.23 (m, 2H), 4.45-4.37 (m, 3H), 4.02 (dd, *J* = 10.4, 7.6 Hz, 1H), 3.74 (dd, *J* = 10.4, 7.1 Hz, 1H), 2.09 (t, *J* = 2.3 Hz, 1H) 1.65 (d, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.8, 151.3, 132.9, 124.2, 124.0, 121.3, 113.2, 75.2, 74.7, 54.6, 42.3, 33.6, 17.0; **ESI MS** calc'd. for $[C_{13}H_{13}BrN_2O + H]^+$: 293.02, found: 202.95.

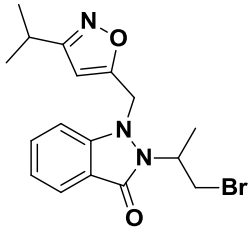


**Methyl 2-(2-(1-bromopropan-2-yl)-3-oxo-2,3-dihydro-1H-indazol-1-yl)acetate (17).** Indazole **1e** (206 mg, 1.18 mmol) was added to a 10-20 mL microwave vial. Dry acetonitrile (12 mL) and methyl bromoacetate (447 µL, 4.72 mmol, 80% solution in toluene) were added and this solution was heated to 82 ºC for 2 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (50% ethyl acetate in hexanes) to afford **17** as a white solid (0.357 g, 98%): **mp** 112-113 ºC; **IR** (neat) $\nu_{max}$ 3002, 2982, 2951, 1737, 1649, 1617, 1483, 1267, 1208, 1178, 1158 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.55-7.50 (m, 1H), 7.16 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.11 (d, *J* = 8.3 Hz, 1H), 4.47 (d, *J* = 18.0 Hz, 1H), 4.40 (d, *J* = 18.0 Hz, 1H), 4.34-4.27 (m, 1H), 4.09 (dd, *J* = 10.3, 8.6 Hz, 1H), 3.64 (dd, *J* = 6.0, 10.3 Hz, 1H), 3.59 (s, 3H), 1.51 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 167.7, 165.9, 151.2, 132.9, 124.0, 122.7, 119.3, 114.4, 55.2, 52.3, 51.7, 33.7, 16.8; **ESI MS** calc'd. for $[C_{13}H_{15}BrN_2O_3 + H]^+$: 327.03, found: 327.01.



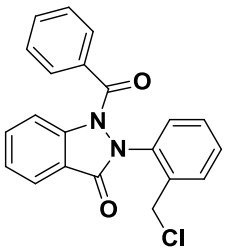
**2-(1-bromopropan-2-yl)-1-(2-morpholino-2-oxoethyl)-1H-indazol-3(2H)-one (18).** Indazole **1e** (194 mg, 1.11 mmol) was added to a 10-20 mL microwave vial. Dry acetonitrile (11 mL) and 2-bromo-1-morpholinoethanone **E8** (462 mg, 2.22 mmol) were added and this solution was heated to 82 ºC for 6 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in hot ethyl acetate. Upon cooling, a white precipitate formed, which was collected using vacuum filtration to furnish **18** (365

mg, 86%): **mp** 186-187 (decomp); **IR** (neat) $\nu_{max}$ 2972, 2902, 2854, 1657, 1619, 1484, 1447, 1275, 1239, 1116, 1034 cm-1; at 25 ºC, **18** exists as a mixture of rotational isomers. **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.5 Hz, 1H), 7.855-7.51 (m, 1H), 7.18 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.11 (d, *J* = 8.3 Hz, 1H), 4.55-4.49 (m, 1H), 4.45-4.40 (m, 1H), 4.34 (dd, *J* = 11.1, 8.6 Hz, 1H), 4.30-4.23 (m, 1H), 3.80 (dd, *J* = 11.1, 5.1 Hz, 1H), 3.71-3.65 (m, 4H), 3.63-3.55 (m, 2H), 3.52-3.44 (m, 2H), 1.56 (d, *J* = 6.8 Hz, 0.5H), 1.53 (d, *J* = 6.8 Hz, 2.5H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 166.8, 166.3, 152.0, 132.9, 132.9, 124.1, 122.7, 119.4, 111.6, 66.9, 66.4, 56.0, 56.0, 52.4, 46.0, 45.5, 42.4, 34.4, 16.6, 15.8; **ESI MS** calc'd. for $[C_{16}H_{20}BrN_3O_3 + H]^+$: 382.07, found: 381.99.



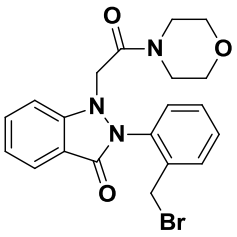

**2-(1-bromopropan-2-yl)-1-((3-isopropylisoxazol-5-yl)methyl)-1H-indazol-3(2H)-one (19).** Indazole **1e** (1.02 g, 5.78 mmol) was added to a 100 mL round bottom flask and dissolved in acetonitrile (58 mL). 5-(bromomethyl)-3-isopropylisoxazole **E9** (2.36 g,11.6 mmol) was added and this solution was heated to reflux for 6 hours at which time TLC analysis showed consumption of the indazole. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (35% ethyl acetate in hexanes) to afford **19** as a dark red solid (2.08 g, 95%): **mp** 83-86 ºC; **IR** (neat) $\nu_{max}$ 2966, 2933, 1660, 614, 1480, 1452, 1314, 1226, 1241 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 7.7 Hz, 1H), 7.58 (ddd, *J* = 7.6, 7.6, 0.8 Hz, 1H), 7.25-7.20 (m, 2H), 5.66 (s, 1H), 4.93 (d, *J* = 16.9 Hz, 1H), 4.87 (d, *J* = 16.9 Hz, 1H), 4.35 (m, *J* = 6.9 Hz, 1H), 4.04 (dd, *J* = 16.9, 8.7 Hz, 1H), 3.72 (dd, *J* = 10.4, 6.6 Hz, 1H), 2.89 (m, *J* = 6.9 Hz, 1H), 1.59 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.3, 166.2, 164.6, 150.9, 133.1, 124.2, 123.6, 120.3, 112.6, 101.5, 55.5, 46.8, 33.5, 26.5, 21.6, 21.5, 16.9; **ESI MS** calc'd. for $[C_{17}H_{20}BrN_3O_2 + H]^+$: 378.07, found: 378.03.

**VI. Preparation of Indazolones 20 and 21**



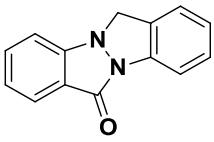

**1-benzoyl-2-(2-(chloromethyl)phenyl)-1H-indazol-3(2H)-one (20).** Indazole **1d** (1.09 g, 4.91 mmol) was added to a 100 mL round-bottom flask. Dry acetonitrile (49 mL) and benzoyl chloride (2.28 mL, 19.6 mmol) were added, the vial was sealed, and this solution was heated at 60 ºC for 12 hours. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate. This solution was then poured into saturated sodium carbonate (60 mL) and the layers were separated. The organic extracts were then washed with water (60 mL) and brine (60 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (25% ethyl acetate in hexanes) to afford **20** as a yellow solid (1.75 g, 99%): **mp** 133-136

ºC; **IR** (neat) $\nu_{max}$ 3071, 3038, 2979, 2919, 1691, 1602, 1452, 1306, 1284, 1152, 1212, 1126, 1044 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.7 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 2H), 7.73 (d, *J* = 7.7 Hz, 1H), 7.67 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.54 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.46 (dd, *J* = 7.9, 7.9 Hz, 1H), 7.41-7.34 (m, 2H), 7.33-7.28 (m, 2H), 6.86 (d, *J* = 8.5 Hz, 1H), 4.94 (s, 1H), 4.93 (s, 1H) ; **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 167.1, 163.4, 143.9, 135.3, 135.0, 133.8, 133.8, 133.7, 130.3, 130.2, 129.6, 129.3, 129.0, 128.8, 128.5, 125.3, 125.0, 124.8, 117.9, 113.5, 42.3; **ESI MS** calc'd. for $[C_{21}H_{15}ClN_2O_2 + H]^+$: 363.08, found: 363.08.



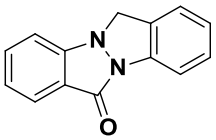
**2-(2-(bromomethyl)phenyl)-1-(2-morpholino-2-oxoethyl)-1H-indazol-3(2H)-one (21).** Indazole **1d** (223 mg, 1.00 mmol) was added to 10-20 mL microwave vial. Dry acetonitrile (10 mL) and 2-bromo-1-morpholinoethanone **E8** (832 mg, 4.00 mmol) were added and this solution was heated at 82 ºC for 6 hours. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL) and washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (70-90% ethyl acetate in hexanes gradient) to afford **21** as a white solid (121 mg, 28%, 43% BORSM): **mp** 148-150 ºC; **IR** (neat) $\nu_{max}$ 30032970, 2917, 2861, 1669, 1650, 1613, 1482, 1454, 1274, 1236, 1112, 1030 cm-1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.7 Hz, 1H), 7.66-7.58 (m, 2H), 7.45-7.38 (m, 2H), 7.36-7.30 (m, 1H), 7.28-7.24 (m, 2H), 4.88 (d, *J* = 7.7 Hz, 1H), 4.58 (d, *J* = 10.7 Hz, 1H), 4.49 (d, *J* = 17.0 Hz, 1H), 4.25 (d, *J* = 17.0 Hz, 1H), 3.68-3.61 (m, 1H), 3.60-3.51 (m, 3H), 3.51-3.41 (m, 2H), 3.26-3.18 (m, 2H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 164.9, 163.3, 151.8, 136.6, 133.4, 133.3, 131.9, 129.8, 129.3, 127.4, 124.8, 122.8, 117.9, 111.5, 66.7, 66.3, 50.6, 45.3, 42.2, 30.8; **ESI MS** calc'd. for $[C_{20}H_{20}BrN_3O_3 + H]^+$: 430.07, found: 430.02.

### VII. Preparation of Indazoloindazolone 22



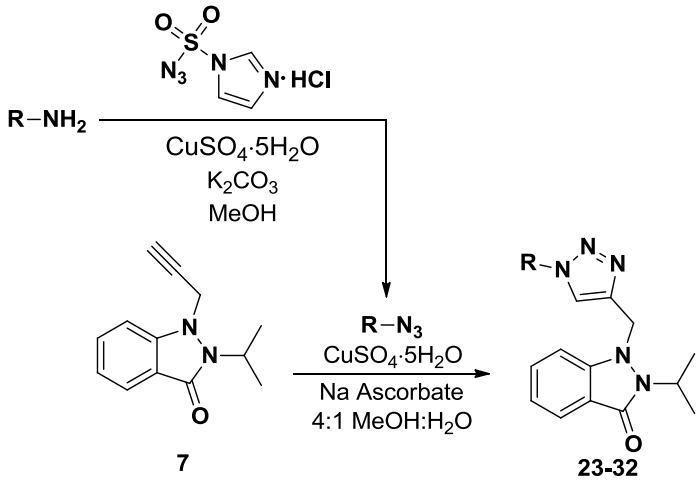
**Indazolo[2,1-a]indazol-6(12H)-one (22); Procedure A (Thermal Heating)** Indazole **1d** (216 mg, 0.972 mmol) was added to a 10-20 mL microwave vial. Dry acetonitrile (10 mL) and 2-bromo-1-morpholinoethanone **E8** (20.2 mg, 97.2 µmol) were added, the vial was sealed, and this solution was heated at 82 ºC for 7 days. The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (40% ethyl acetate in hexanes) to afford **22** as a pale yellow solid (170 mg, 79%): **mp** 135-136 ºC (decomp); **IR** (neat) $\nu_{max}$ 3050, 2927, 2902, 2852, 1653, 1605, 1482, 1464, 1384, 1314, 1289, 1205, 1121 cm-1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.54 (dd, *J* = 8.0, 7.3 Hz, 1H), 7.39 (dd, *J*= 7.8, 7.8 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 1H), 7.15-7.11 (m, 2H), 5.00 (s, 2H);

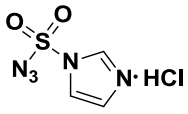
**$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 159.5, 147.3, 135.3, 132.6, 129.5, 129.1, 125.0, 125.0, 123.8, 121.6, 120.2, 113.2, 110.5, 51.6; **ESI MS** calc'd. for $[C_{14}H_{10}N_2O + H]^+$: 223.08, found: 223.07.



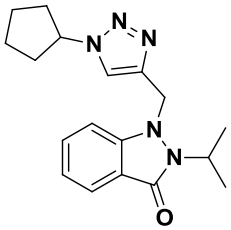
**Indazolo[2,1-a]indazol-6(12H)-one (22); Procedure B (microwave heating)** Indazole **1d** (123 mg, 0.553 mmol) was added to a 5-10 mL microwave vial. Dry acetonitrile (5.0 mL) and 2-bromo-1-morpholinoethanone **E8** (11.5 mg, 55.2 µmol) were added, the vial was sealed, and this solution was heated at 150 ºC for 5 hours in a microwave reactor (Personal Chemistry, Emrys Optimizer). The acetonitrile was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (40% ethyl acetate in hexanes) to afford **22** as a white solid (113 mg, 92%): See spectral data above.

## VIII. Preparation of Triazolyl-Indazolones (23-32).



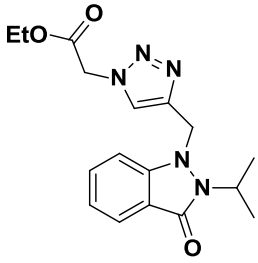



**1H-imidazole-1-sulfonyl azide hydrochloride.** Made via literature methods reported in Goddard-Borger, E. D.; Stick, R. V. *Org. Lett*. **2007**, *9*, 3797. Spectral data is in accordance with literature values.

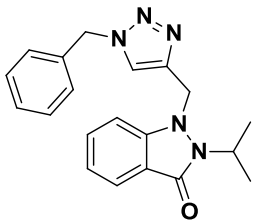


**General Procedure for the Synthesis of Triazolyl-Indazolones 23-32: 1-((1-cyclopentyl-1H-1,2,3-triazol-4-yl)methyl)-2-isopropyl-1H-indazol-3(2H)-one (23).** Cyclopentylamine (93 µL, .944 mmol) was added to a 5-10 mL microwave vial and dissolved in methanol (2.4 mL). To this solution was added 1H-imidazole-1-sulfonyl azide hydrochloride (218 mg, 1.04 mmol), $K_2CO_3$ (176 mg, 1.27 mmol), and $CuSO_4·5H_2O$ (1.18 mg, 4.72 µmol). After stirring for 24 hours at room temperature, indazolone **7** (101 mg, .472 mmol), water (720 µL), $CuSO_4·5H_2O$ (11.8 mg, 47.2 µmol), and

(+)-Sodium L-ascorbate (18.7 mg, 94.4 µmol) were added and this mixture was stirred vigorously for 24 hours at room temperature. The contents of the vial were then poured into 1 M $NH_4OH$ (30 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were washed with brine (30 mL), dried over sodium sulfate, and concentrated. The crude material was then purified by flash chromatography (70-90% ethyl acetate in hexanes gradient) to afford **23** as a colorless oil (138 mg, 90%): **IR** (neat) $\nu_{max}$ 3097, 3049, 2971, 2874, 1661, 1615, 1482, 1464, 1453, 1343, 1317, 1248, 1134, 1054 cm-1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.8 Hz, 1H), 7.54 (ddd, *J* = 8.3, 7.4, 1.2 Hz, 1H), 7.30 (d, *J* = 8.3 Hz, 1H), 7.17 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.73 (s, 1H), 5.06 (s, 2H), 4.72-4.63 (m, 1H), 4.50 (m, *J* = 6.9 Hz, 1H), 2.15 (m, 2H), 1.88-2.04 (m, 6H), 1.50 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.5, 150.5, 140.1, 132.4, 124.0, 122.8, 120.7, 119.9, 112.7, 61.9, 49.0, 47.2, 33.3 (2C), 24.0 (2C), 20.5 (2C); **ESI MS** calc'd. for $[C_{18}H_{23}N_5O + H]^+$: 326.19, found: 326.12.

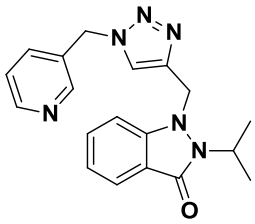


**Ethyl 2-(4-((2-isopropyl-3-oxo-2,3-dihydro-1H-indazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)acetate (24).** The general procedure for the synthesis of triazolyl-indazolones 23-32 was employed using glycine ethyl ester hydrochloride (135 mg, 966 mmol), indazolone **7** (103 mg, 483 mmol), and ethanol was used in place of methanol to avoid transesterification. When the reaction was complete, the mixture was poured into water instead of dilute $NH_4OH$ to avoid hydrolysis of the ester. After extraction with ethyl acetate, the crude material was purified by flash chromatography (80% ethyl acetate in hexanes) to afford **24** as a yellow oil (86.2 mg, 52%): **IR** (neat) $\nu_{max}$ 3097, 3049, 2971, 2874, 1661, 1615, 1482, 1464, 1453, 1343, 1317, 1248, 1134, 1054 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.5 Hz, 1H), 7.55-7.52 (m, 1H), 7.32 (d, *J* = 8.3 Hz, 1H), 7.16 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.98 (s, 1H), 5.09 (s, 2H), 4.96 (s, 2H), 4.50 (m, *J* = 7.0 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 1.50 (d, *J* = 7.0 Hz, 6H), 1.22 (t, *J*= 7.1 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 166.0, 165.7, 150.4, 140.7, 132.5, 124.0, 123.0, 122.9, 120.8, 112.8, 62.6, 50.9, 49.1, 47.1, 20.5 (2C), 14.1; **ESI MS** calc'd. for $[C_{17}H_{21}N_5O_3 + H]^+$: 344.16, found: 344.13.

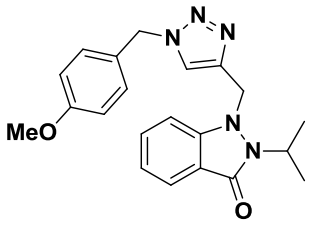


**1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-2-isopropyl-1H-indazol-3(2H)-one (25).** The general procedure for the synthesis of triazolyl-indazolones 23-32 was employed using benzylamine (104 mg, 966 mmol) and indazolone **7** (483 mmol). The crude material was purified by flash chromatography (80% ethyl acetate in hexanes) to afford **25** as an off-white solid (161 mg, 96%): **mp** 115-117 ºC; **IR** (neat) $\nu_{max}$ 3105, 3044, 2978, 2938, 1653, 1481, 1430, 1323, 1254, 1052, 1029 cm-1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.41 (d, *J* = 1.7 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.52 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 7.31-7.21 (m, 4H), 7.18-7.13 (m, 1H), 6.76 (s, 1H), 5.36 (s, 2H), 5.05 (s, 2H), 4.48 (m, *J* = 6.9 Hz, 1H), 1.49 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.7, 150.5, 140.6, 134.5,

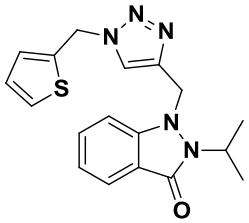
132.4, 129.2 (2C), 128.7, 127.6 (2C), 124.0, 122.9, 121.5, 120.9, 112.9, 54.1, 49.1, 47.2, 20.5 (2C); **ESI MS** calc'd. for $[C_{20}H_{21}N_5O + H]^+$: 348.17, found: 348.09.



**2-isopropyl-1-((1-(pyridin-3-ylmethyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-indazol-3(2H)-one (26)**. The general procedure for the synthesis of triazolyl-indazolones 23-32 was employed using 3-(aminomethyl)pyridine (109 mg, 1.01 mmol) and indazolone **7** (108 mg, 0.506 mmol). The crude material was purified by flash chromatography (10% methanol in ethyl acetate) to afford **26** as a brown amorphous solid (175 mg, 99%): **IR** (neat) $\nu_{max}$ 3106, 3040, 2997, 2976, 2951, 1655, 1482, 1322, 1253, 1051 cm-1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.8 Hz, 1H), 7.49 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 7.32-7.26 (m, 3H), 7.17-7.11 (m, 1H), 7.02-6.97 (m, 2H), 6.73 (s, 1H), 5.33 (s, 2H), 5.03 (s, 2H), 4.47 (m, *J* = 6.9 Hz, 1H), 1.48 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.8, 150.5, 150.3, 148.8, 140.9, 135.3, 132.6, 130.4, 124.0, 123.9, 123.1, 121.5, 120.8, 112.9, 52.5, 49.2, 47.1, 20.5 (2C); **ESI MS** calc'd. for $C_{19}H_{20}N_6O$+ H]$^+$: 349.17, found: 349.14.

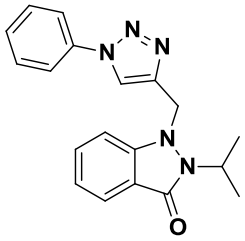


**2-isopropyl-1-((1-(4-methoxybenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-indazol-3(2H)-one (27)**. The general procedure for the synthesis of triazolyl-indazolones 23-32 was employed using 4-methoxybenzylamine (129 mg, 0.943 mmol) and indazolone **7** (101 mg, 0.472 mmol). The crude material was purified by flash chromatography (80% ethyl acetate in hexanes) to afford **27** as a pale yellow amorphous solid (176 mg, 99%). **IR** (neat) $\nu_{max}$ 3994, 3485, 3423, 1626, 1514, 1282, 1248, 1057 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.49 (ddd, *J* = 8.3, 7.3, 1.2 Hz, 1H), 7.26 (d, *J* = 8.3 Hz, 1H), 7.13 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.99-6.96 (m, 2H), 6.81 (dd, J = *6.7,* 1.9 Hz, 2H), 6.71 (s, 1H), 5.25 (s, 2H), 5.02 (s, 2H), 4.47 (m, *J* = 6.9 Hz, 1H), 3.78 (s, 3H), 1.48 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.4, 159.7, 150.2, 140.3, 132.2, 129.0 (2C), 126.4, 123.7, 122.7, 121.3, 120.6, 114.3 (2C), 112.7, 55.3, 53.4, 48.9, 46.9, 20.3 (2C); **ESI MS** calc'd. for $[C_{21}H_{23}N_5O_2$ + H]$^+$: 378.19, found: 378.10.

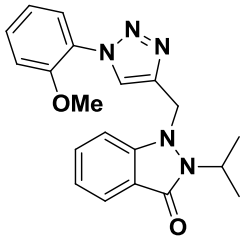


**2-isopropyl-1-((1-(thiophen-2-ylmethyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-indazol-3(2H)-one (28).** The general procedure for the synthesis of triazolyl-indazolones 23-32 was employed using thiophene-2-methylamine (103 µL, 1.00 mmol) and indazolone **7** (107 mg, 0.500 mmol). The crude material was purified by flash chromatography (85% ethyl acetate in hexanes) to afford **28** as a white solid (163 mg, 92%): **mp** 133-134 ºC; **IR** (neat) $\nu_{max}$ 3046, 2940, 1673, 1638, 1481, 1427, 1124, 1030 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.53-7.49 (m, 1H), 7.28-7.25 (m, 2H), 7.15 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.93 (dd, *J* = 4.9, 3.7 Hz, 1H), 6.90-6.88 (m, 1H), 6.78 (s, 1H), 5.50 (s, 2H), 5.03 (s, 2H), 4.47 (m, *J* = 6.9 Hz, 1H), 1.48 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.7, 150.5,

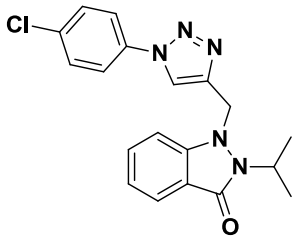
140.7, 136.0, 132.4, 127.9, 127.3, 127.1, 124.0, 122.9, 121.1, 120.8, 112.8, 49.1, 48.6, 47.2, 20.5 (2C); **ESI MS** calc'd. for $[C_{18}H_{19}N_5OS + H]^+$: 354.13, found: 354.09.



**2-isopropyl-1-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)-1H-indazol-3(2H)-one (29).** The general procedure for the synthesis of triazolyl-indazolones 23-32 was employed using aniline (91.2 µL, 0.999 mmol) and indazolone **7** (107 mg, 0.499 mmol). The crude material was purified by flash chromatography (70% ethyl acetate in hexanes) to afford **29** as a tan solid (163 mg, 98%): **mp** 182-183 ºC; **IR** (neat) $\nu_{max}$ 3115, 3061, 2969, 2931, 1664, 1478, 1461, 1335, 1302, 1249, 1241, 1048 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.58-7.54 (m, 1H), 7.51-7.48 (m, 2H), 7.44 (dd, *J* = 10.2, 5.4 Hz, 2H), 7.40-7.36 (m, 2H), 7.21 (m, 2H), 5.15 (s, 2H), 4.55 (m, *J* = 6.9 Hz, 1H), 1.54 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.6, 150.3, 140.9, 136.5, 132.5, 129.6 (2C), 128.9, 123.9, 122.9, 120.6, 120.5 (2C), 119.5, 112.7, 49.1, 46.9, 20.4 (2C); **ESI MS** calc'd. for $[C_{19}H_{19}N_5O + H]^+$: 334.16, found: 334.20.

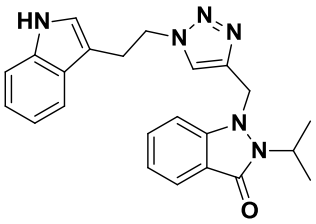


**2-isopropyl-1-((1-(2-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-indazol-3(2H)-one (30).** The general procedure for the synthesis of triazolyl-indazolones 23-32 was employed using *o*-anisidine (107 µL, 0.954 mmol) and indazolone **7** (102 mg, 0.477 mmol). The crude material was purified by flash chromatography (75% ethyl acetate in hexanes) to afford **30** as a brown solid (126 mg, 73%): **mp** 148-149 ºC; **IR** (neat) $\nu_{max}$ 2983, 2966, 1666, 1455, 1313, 1255, 1234, 1123, 1097, 1049 cm-1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.8 Hz, 1H), 7.65 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.55 (ddd, *J* = 8.3, 7.3, 1.2 Hz, 1H), 7.40-7.32 (m, 3H), 7.17 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.03 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 1H), 6.99-6.95 (m, 1H), 5.15 (s, 2H), 4.54 (m, *J*= 6.9 Hz, 1H), 3.71 (s, 3H), 1.54 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.6, 151.0, 150.7, 139.7, 132.5, 130.3, 126.1, 125.3, 124.0, 123.9, 122.9, 121.3, 121.1, 113.0, 112.4, 56.0, 49.1, 47.3, 20.6 (2C); **ESI MS** calc'd. for $[C_{20}H_{21}N_5O_2 + H]^+$: 364.17, found: 364.12.



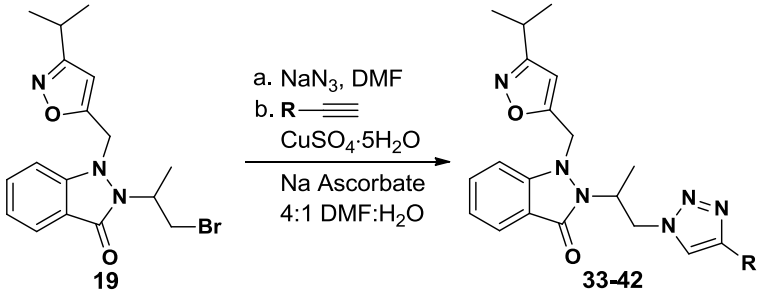
**1-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)-2-isopropyl-1H-indazol-3(2H)-one (31).** The general procedure for the synthesis of triazolyl-indazolones 23-32 was employed using 4-chloroaniline (129 mg, 1.01 mmol) and indazolone **7** (108 mg, 0.505 mmol). The crude material was purified by flash chromatography (60% ethyl acetate in hexanes) to afford **31** as a tan solid (153 mg, 81%): **mp** 169-171 ºC; **IR** (neat) $\nu_{max}$ 3108, 3064, 2959, 1665, 1503, 1239, 1095, 1048, 990 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.78-7.76 (m, 1H), 7.57 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 7.47-7.39 (m, 4H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.21-7.17 (m, 2H), 5.14 (s, 2H), 4.55 (m, *J* = 6.9 Hz, 1H), 1.54 (d, *J*= 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 165.9, 150.5, 141.2, 135.2, 134.9,

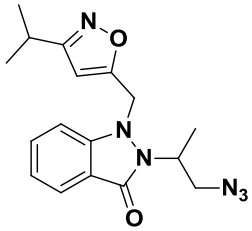
132.7, 130.0 (2C), 124.2, 123.2, 121.9 (2C), 120.8, 119.4, 112.7, 49.3, 47.1, 20.6 (2C); **ESI MS** calc'd. for $[C_{19}H_{18}ClN_5O + H]^+$: 368.12, found: 368.07.



**1-((1-(2-(1H-indol-3-yl)ethyl)-1H-1,2,3-triazol-4-yl)methyl)-2-isopropyl-1H-indazol-3(2H)-one (32).** The general procedure for the synthesis of triazolyl-indazolones 23-32 was employed using tryptamine (156 mg, 0.976 mmol) and indazolone **7** (105 mg, 0.488 mmol). The crude material was purified by flash chromatography (80% ethyl acetate in hexanes) to afford **32** as a white solid (172 mg, 88%): **mp** 69-70; **IR** (neat) $\nu_{max}$ 3103, 2987, 2978, 2940, 1656, 1618, 1482, 1310, 1254, 1088, 1051, 1028 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 8.97 (br s, 1H), 7.72-7.70 (m, 1H), 7.49 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 7.47-7.44 (m, 2H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.22 (m, 1H), 7.10-7.07 (m, 2H), 5.99 (d, *J* = 2.4 Hz, 1H), 5.96 (s, 1H) 4.97 (s, 2H), 4.44 (m, *J* = 6.9 Hz, 1H), 4.40-4.36 (m, 2H), 3.14-3.11 (m, 2H), 1.43 (d, *J* = 6.9 Hz, 6H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 166.3, 150.2, 138.5, 136.4, 132.6, 126.2, 124.2, 123.5, 123.0, 123.0, 122.0, 120.5, 119.3, 117.8, 113.1, 112.0, 109.7, 50.8, 49.2, 46.7, 26.4, 20.6 (2C); **ESI MS** calc'd. for $[C_{23}H_{24}N_6O + H]^+$: 401.20, found: 401.19.

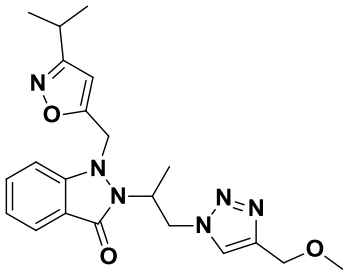
## IX. Preparation of Triazolyl-Indazolones (33-42)



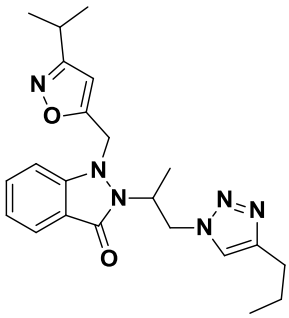



**2-(1-azidopropan-2-yl)-1-((3-isopropylisoxazol-5-yl)methyl)-1H-indazol-3(2H)-one.** Indazolone **19** (149, 394 mmol) was added to a 5-10 mL microwave vial and dissolved in DMF (2.0 mL). Sodium azide (30.7 mg, 473 mmol) was added and the vial was sealed and placed in an oil bath at 60 ºC for 3 hours. The DMF was then removed under reduced pressure and the crude material was dissolved in ethyl acetate (30 mL). This solution was then washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated. This crude material was purified by flash chromatography (40% ethyl acetate in hexanes) to afford **33** as a pale yellow solid (133 mg, 99%): **mp** 86-87 ºC; **IR** (neat) $\nu_{max}$ 2969, 2930, 2904, 2876, 2091, 1675, 1607, 1461, 1334, 1312, 1251, 1235 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.8 Hz, 1H), 7.52 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 7.22-7.14 (m, 2H), 5.57 (s, 1H), 4.88 (d, *J* = 16.9 Hz, 1H), 4.82 (d, *J* = 16.9 Hz, 1H), 4.21-4.14 (m, 1H), 4.03 (dd, *J* = 12.5, 8.7 Hz, 1H), 3.51 (dd, *J* =

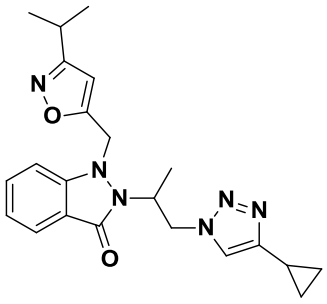
12.5, 5.5 Hz, 1H), 2.82 (m, *J* = 6.9 Hz, 1H), 1.42 (d, *J* = 7.0 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 1.07 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.3, 166.4, 164.5, 150.9, 133.1, 124.2, 123.6, 120.2, 112.6, 101.4, 53.5, 53.4, 46.7, 26.5, 21.5, 21.5, 15.8; **ESI MS** calc'd. for $[C_{17}H_{20}N_6O_2 + H]^+$: 341.16, found: 341.16.



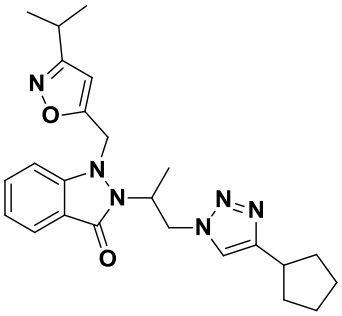
**General Procedure for the Synthesis of Triazolyl-Indazolones 33-42: 1-((3-isopropylisoxazol-5-yl)methyl)-2-(1-(4-(methoxymethyl)-1H-1,2,3-triazol-1-yl)propan-2-yl)-1H-indazol-3(2H)-one (33).** Indazolone **19** (176 mg, 465 mmol) was added to a 5-10 mL microwave vial and dissolved in DMF (2.3 mL). Sodium azide (36.2 mg, 558 mmol) was added and the vial was sealed and placed in an oil bath at 60 ºC for 3 hours. The vial was then removed from the oil bath and water (575 µL),$CuSO_4 \cdot 5H_2O$ (11.6 mg, 46.5 µmol), and (+)-sodium L-ascorbate (18.4 mg, 93.0 µmol) were added. This mixture was then stirred vigorously at room temperature for 24 hours. The contents of the vial were then poured into 1 M $NH_4OH$ (30 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were washed with brine (30 mL), dried over sodium sulfate, and concentrated. The crude material was then purified by flash chromatography (5% methanol in ethyl acetate) to afford **33** as a white solid (171 mg, 90%): **mp** 92-94 ºC; **IR** (neat) $\nu_{max}$ 2989, 2963, 2932, 2894, 2872, 1670, 1616, 1463, 1340, 1264, 1149, 1087, 1051 cm-1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.59-7.52 (m, 2H), 7.24-7.19 (m, 1H), 7.15 (d, *J* = 8.3, 1H), 5.61 (s, 1H), 5.30 (dd, *J* = 13.7 9.6 Hz, 1H), 4.74 (dd, *J* = 13.7, 5.7, 1H), 4.67-4.59 (m, 2H), 4.46 (s, 2H), 3.37 (s, 3H), 2.90 (m, *J* = 6.9 Hz, 1H), 1.54 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.3, 166.6, 164.5, 151.0, 144.7, 133.2, 124.1, 124.0, 123.5, 119.9, 112.6, 101.7, 65.8, 58.1, 51.6, 46.0, 26.5, 21.6, 21.5, 21.4 15.3; **ESI MS** calc'd. for $[C_{21}H_{26}N_6O_3 + H]^+$: 411.21, found: 411.15.



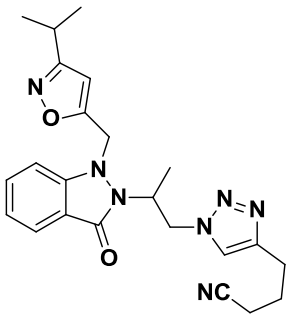
**1-((3-isopropylisoxazol-5-yl)methyl)-2-(1-(4-propyl-1H-1,2,3-triazol-1-yl)propan-2-yl)-1H-indazol-3(2H) (34).** The general procedure for the synthesis of triazolyl-indazolones 33-42 was employed using indazolone **19** (193 mg, 0.510 mmol) and 1-pentyne (69.5 mg, 1.02 mmol). The crude material was purified by flash chromatography (70% ethyl acetate in hexanes) to afford **34** as a colorless oil (198 mg, 95%): **IR** (neat) $\nu_{max}$ 2964, 2933, 2872, 1668, 1615, 1480, 1463, 1341, 1313, 1253 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.8 Hz, 1H), 7.57-7.52 (m, 1H), 7.22 (s, 1H), 7.20 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 1H), 5.,62 (s, 1H), 5.23 (dd, *J* = 13.8, 9.6 Hz, 1H), 4.72-4.59 (m, 4H), 2.90 (m, *J* = 6.9 Hz, 1H), 2.60-2.50 (m, 2H), 1.55 (d, *J* = 6.9 Hz, 3H), 1.51-1.43 (m, 2H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 3H), 0.82 (t, *J* = 7.4, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.2, 166.3, 164.5, 150.7, 147.8, 133.1, 123.8, 123.4, 122.3, 119.8, 112.5, 101.7, 54.2, 51.2, 45.9, 27.5, 26.5, 22.5, 21.5, 21.4, 15.3, 13.6; **ESI MS** calc'd. for $[C_{22}H_{28}N_6O_2 + H]^+$: 409.23, found: 409.17.



**2-(1-(4-cyclopropyl-1H-1,2,3-triazol-1-yl)propan-2-yl)-1-((3-isopropylisoxazol-5-yl)methyl)-1H-indazol-3(2H)-one (35).** The general procedure for the synthesis of triazolyl-indazolones 33-42 was employed using indazolone **19** (193 mg, 0.510 mmol) and cyclopropylacetylene (85.0 µL, 1.00 mmol). The crude material was purified by flash chromatography (80% ethyl acetate in hexanes) to afford **35** as a white solid (202 mg, 99%): **mp** 99-101 ºC; **IR** (neat) $\nu_{max}$ 3082, 2964, 2938, 1671, 1613, 1463, 1339, 1310, 1252 cm-1; **$^{1}$H NMR** (600 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.8, 0.5 Hz, 1H), 7.56 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.21 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.18-7.14 (m, 2H), 5.58 (s, 1H), 5.21 (dd, *J* = 13.7, 9.6 Hz, 1H), 4.69-4.57 (m, 4H), 2.90 (m, *J* = 6.9 Hz, 1H), 1.85-1.79 (m, 1H), 1.54 (d, *J* = 6.9 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 3H), 0.87-0.81 (m, 2H), 0.68-0.63 (m, 1H), 0.57-0.52 (m, 1H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.2, 166.6, 164.5, 150.9, 150.0, 133.2, 123.8, 123.4, 121.2, 119.8, 112.6, 101.7, 54.2, 51.3, 45.8, 26.5, 21.5, 21.4, 15.3, 7.9, 7.6, 6.6; **ESI MS** calc'd. for $[C_{22}H_{26}N_6O_2 + H]^+$: 407.21, found: 407.20.

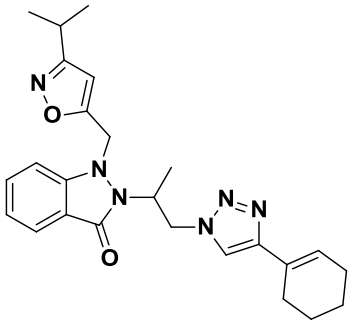


**2-(1-(4-cyclopentyl-1H-1,2,3-triazol-1-yl)propan-2-yl)-1-((3-isopropylisoxazol-5-yl)methyl)-1H-indazol-3(2H)-one (36).** The general procedure for the synthesis of triazolyl-indazolones 33-42 was employed using indazolone **19** (114 mg, 0.301 mmol) and cyclopentylacetylene (69.8 µL, 0.602 mol). The crude material was purified by flash chromatography (60% ethyl acetate in hexanes) to afford **36** as a colorless oil (107 mg, 82%): **IR** (neat) $\nu_{max}$ 2961, 2868, 1668, 1614, 1463, 1313, 1253, 1048 cm-1; **$^{1}$H NMR** (600 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.8 Hz, 1H), 7.54 (dd, *J* = 8.2, 7.5 Hz, 1H), 7.20 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.15-7.11 (m, 2H), 5.64 (s, 1H), 5.18 (dd, *J* = 13.7, 9.7 Hz, 1H), 4.71-4.57 (m, 4H), 3.01 (p, *J* = 8.1 Hz, 1H), 2.90 (m, *J* = 6.9 Hz, 1H), 1.97-1.86 (m, 2H), 1.64-1.51 (m, 7H), 1.45-1.32 (m, 2H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.2, 166.1, 164.5, 152.4, 150.6, 133.0, 123.7, 123.3, 121.1, 119.8, 112.4, 54.2, 51.0, 45.8, 36.5, 33.0, 26.4, 33.0, 33.0, 26.4, 25.0, 21.5, 21.4, 15.5; **ESI MS** calc'd. for $[C_{24}H_{30}N_6O_2 + H]^+$: 435.24, found: 435.17.

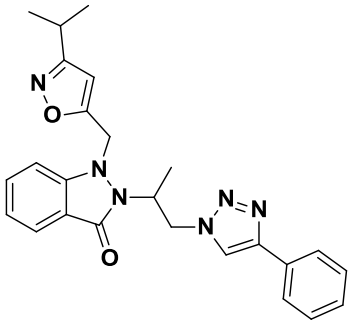


**4-(1-(2-(1-((3-isopropylisoxazol-5-yl)methyl)-3-oxo-1H-indazol-2(3H)-yl)propyl)-1H-1,2,3-triazol-4-yl)butanenitrile (37).** The general procedure for the synthesis of triazolyl-indazolones 33-42 was employed using indazolone **19** (185 mg, 0.489 mmol) and 5-hexynenitrile (102 µL, 0.978 mmol). The crude material was purified by flash chromatography (60% ethyl acetate in hexanes) to afford **37** as a colorless oil (191 mg, 99%): **IR** (neat) $\nu_{max}$ 2967, 2936, 2877, 1667, 1614, 1480, 1463, 1342, 1313, 1253, 1222, 1153, 1050, 2245 cm-1; **$^{1}$H NMR** (600 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.58 (dd, *J* = 8.3, 7.2 Hz, 1H), 7.30-7.28 (m, 1H),

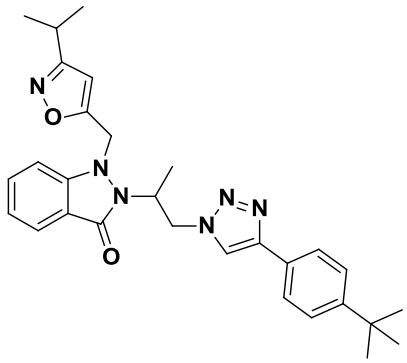
7.23 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.15 (d, *J* = 8.3 Hz, 1H), 5.62 (s, 1H), 5.24 (dd, *J* = 13.7, 9.7 Hz, 1H), 4.72-4.69 (m, 3H), 4.66-4.62 (m, 1H), 2.90 (m, *J* = 6.9 Hz, 1H), 2.76-2.66 (m, 2H), 2.24 (t, *J* = 7.3 Hz, 2H), 1.91-1.80 (m, 2H), 1.58 (d, *J* = 6.8 Hz, 3H), 1.16 (d, J = 6.9 Hz, 3H), 1.16 (d, J = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.2, 166.2, 164.3, 150.6, 145.2, 133.3, 123.9, 123.6, 122.8, 119.8, 119.3, 112.4, 101.7, 54.2, 51.2, 45.9, 26.5, 24.9, 24.2, 21.5, 21.4, 16.3, 15.6; **ESI MS** calc'd. for $[C_{23}H_{27}N_7O_2 + H]^+$: 434.22, found: 434.18.



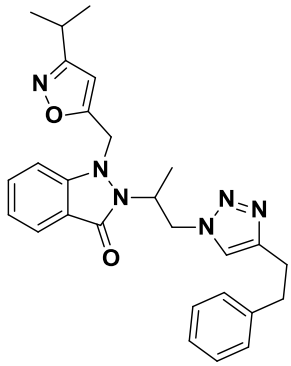
**2-(1-(4-(cyclohex-1-en-1-yl)-1H-1,2,3-triazol-1-yl)propan-2-yl)-1-((3-isopropylisoxazol-5-yl)methyl)-1H-indazol-3(2H)-one (38).** The general procedure for the synthesis of triazolyl-indazolones 33-42 was employed using indazolone **19** (188 mg, 0.497 mmol) and 1-ethynylcyclohexene (117 µL, 0.994 mmol). The crude material was purified by flash chromatography (60% ethyl acetate in hexanes) to afford **38** as a pale yellow solid (182 mg, 82%): **mp** 113-114 ºC; **IR** (neat) $\nu_{max}$ 3128, 2963, 2929, 2893, 2876, 2834, 1669, 1613, 1606, 1478, 1460, 1447, 1430, 1335, 1306, 1239, 1153, 1129, 1054, 1000 cm-1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.8, 1H), 7.55 (ddd, *J* = 8.4, 7.4, 1.2 Hz, 1H), 7.37 (s, 1H), 7.19 (dd, *J* = 7.4, 0.5 Hz, 1H), 7.16 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.43-6.38 (m, 1H), 5.47 (s, 1H), 5.33 (dd, *J* = 13.9, 9.6 Hz, 1H), 4.73-4.57 (m, 4H), 2.86 (m, *J* = 6.9 Hz, 1H), 2.32-2.30 (m, 1H), 2.18-2.06 (m, 3H), 1.73-1.65 (m, 2H), 1.65-1.56 (m, 2H), 1.53 (d, *J* = 6.7 Hz, 3H), 1.15 (d, J = 6.9 Hz, 3H), 1.13 (d, J = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.2, 166.9, 164.4, 151.0, 149.0, 133.1, 127.0, 125.0, 123.8, 123.4, 120.1, 119.8, 112.7, 101.7, 54.3, 51.4, 45.6, 26.4, 26.2, 25.2, 22.4, 22.2, 21.5, 21.3, 15.1; **ESI MS** calc'd. for $[C_{25}H_{30}N_6O_2 + H]^+$: 447.24, found: 447.18.



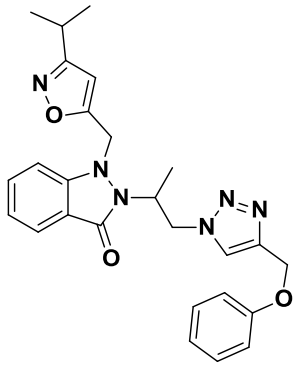
**1-((3-isopropylisoxazol-5-yl)methyl)-2-(1-(4-phenyl-1H-1,2,3-triazol-1-yl)propan-2-yl)-1H-indazol-3(2H)-one (39).** The general procedure for the synthesis of triazolyl-indazolones 33-42 was employed using indazolone **19** (193 mg, 0.510 mmol) and phenylacetylene (112 µL, 1.02 mmol). The crude material was purified by flash chromatography (60% ethyl acetate in hexanes) to afford **39** as a white solid (214 mg, 95%): **mp** 145-147 ºC; **IR** (neat) $\nu_{max}$ 3133, 2979, 2965, 2937, 1662, 1615, 1604, 1482, 1461, 1450, 1438, 1343, 1309, 1242 cm-1; **$^1$H NMR** (600 MHz, $CDCl_3$) δ 7.80-7.76 (m, 2H), 7.70-7.65 (m, 2H), 7.55-7.50 (m, 1H), 7.39-7.33 (m, 2H), 7.32-7.26 (m, 1H), 7.20 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 1H), 5.49-5.40 (m, 2H), 4.77 (dd, *J* = 13.8, 5.4 Hz, 1H), 4.72-4.57 (m, 3H), 2.68 (m, *J* = 6.9 Hz, 1H), 1.56 (d, *J* = 6.8 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H), 1.01 (d, J = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.2, 167.2, 164.4, 151.2, 147.4, 133.3, 130.4, 128.8 (2C), 128.2, 125.7 (2C), 123.9, 123.5, 121.4, 119.9, 112.8, 101.7, 54.5, 51.7, 45.8, 26.4, 21.5, 21.2, 15.2; **ESI MS** calc'd. for $[C_{25}H_{26}N_6O_2 + H]^+$: 443.21, found: 443.15.



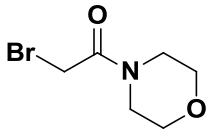
**2-(1-(4-(4-(tert-butyl)phenyl)-1H-1,2,3-triazol-1-yl)propan-2-yl)-1-((3-isopropylisoxazol-5-yl)methyl)-1H-indazol-3(2H)-one (40).** The general procedure for the synthesis of triazolyl-indazolones 33-42 was employed using indazolone **19** (184 mg, 0.486 mmol) and 4-*tert*-butylphenylacetylene (175 µL, 0.972 mmol). The crude material was purified by flash chromatography (50% ethyl acetate in hexanes) to afford **40** as a white solid (240 mg, 99%): **mp** 161-163 ºC; **IR** (neat) $\nu_{max}$ 2963, 2869, 1683, 1613, 1465, 1451, 1367, 1337, 1307, 1236 cm-1; **$^{1}$H NMR** (600 MHz, $CDCl_3$) δ 7.79-7.76 (m, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.52 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.20 (dd, *J* = 7.7, 7.3 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 1H), 5.48-5.42 (m, 2H), 4.76 (dd, *J* = 13.9, 5.3 Hz, 1H), 4.68-4.60 (m, 1H), 4.66 (d, *J* = 16.7 Hz, 1H), 4.57 (d, *J* = 16.7 Hz, 1H), 2.62 (m, *J* = 6.9 Hz, 1H), 1.54 (d, *J* = 6.8 Hz, 3H), 1.31 (s, 9H), 1.01-0.97 (m, 6H); at 25 ºC, **40** exists as a mixture of rotational isomers. **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.2, 167.3, 164.4, 151.4, 151.2, 147.4, 133.4, 133.3, 127.5, 125.8, 125.7, 125.5, 125.4, 123.9, 123.8, 123.6, 123.4, 121.2, 121.0, 119.9, 112.8, 101.8, 101.7, 54.7, 54.6, 51.7, 51.6, 45.8, 45.7, 45.7, 34.7, 31.4, 31.3, 26.4, 26.3, 21.5, 21.4, 21.2, 21.1, 15.1, 15.1; **ESI MS** calc'd. for $[C_{29}H_{34}N_6O_2 + H]^+$: 499.27, found: 499.24.



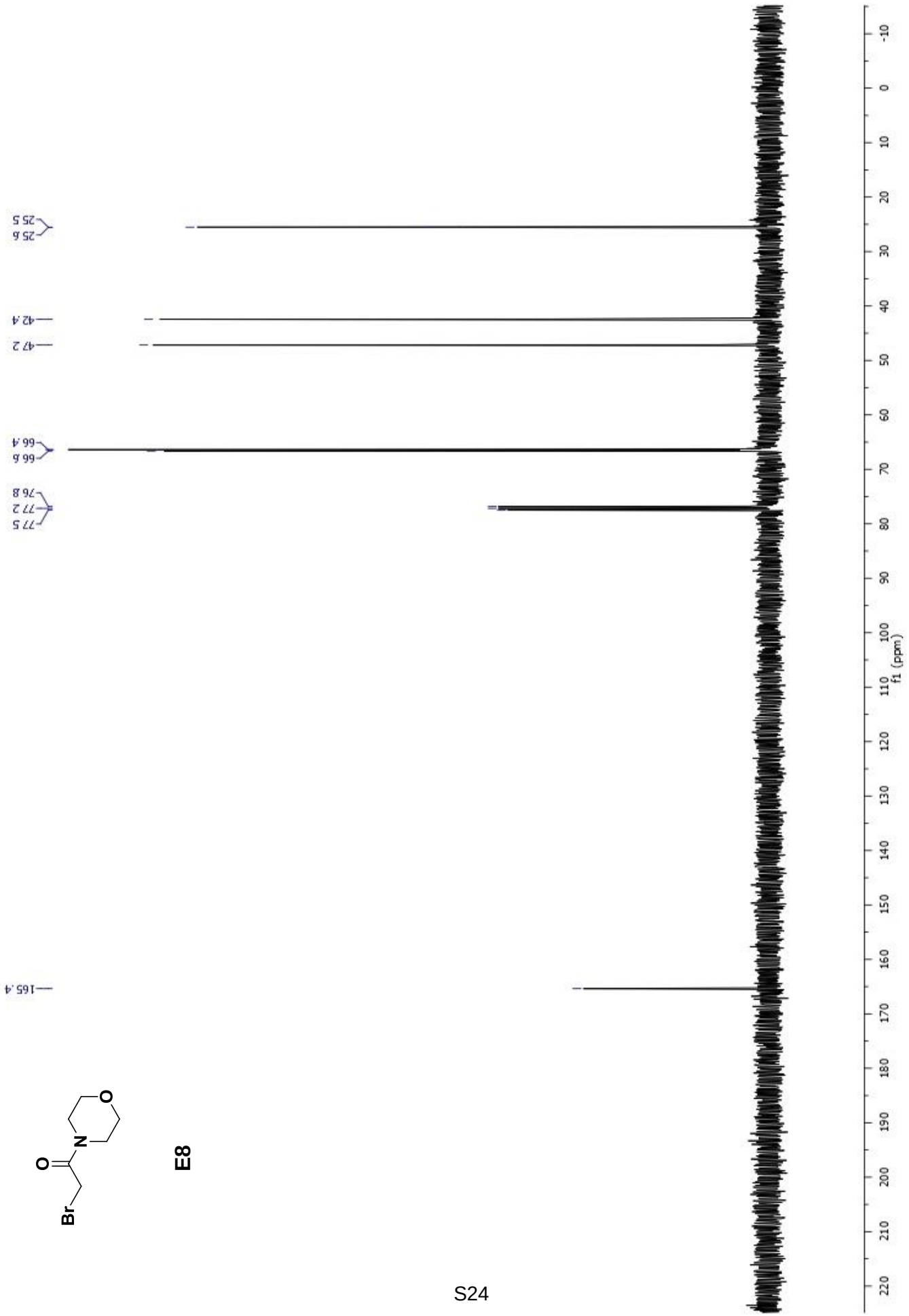
**1-((3-isopropylisoxazol-5-yl)methyl)-2-(1-(4-phenethyl-1H-1,2,3-triazol-1-yl)propan-2-yl)-1H-indazol-3(2H)-one (41).** The general procedure for the synthesis of triazolyl-indazolones 33-42 was employed using indazolone **19** (194 mg, 0.513 mmol) and 4-phenyl-1-butyne (145 µL, 1.03 mmol). The crude material was purified by flash chromatography (80% ethyl acetate in hexanes) to afford **41** as a colorless oil (234 mg, 97%): **IR** (neat) $\nu_{max}$ 2967, 2938, 1673, 1615, 1481, 1341, 1254 cm-1; **$^{1}$H NMR** (600 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.56 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.22 (dd, *J* = 7.8, 7.2 Hz, 1H), 7.20-7.17 (m, 2H), 7.15-7.11 (m, 3H), 7.09 (d, *J* = 8.0 Hz, 2H), 5.65 (s, 1H), 5.19 (dd, *J* = 13.8, 9.7 Hz, 1H), 4.67 (dd, *J* = 13.8, 5.6 Hz, 1H), 4.61-4.55 (m, 1H), 4.53 (d, *J* = 6.8 Hz, 2H), 2.97-2.87 (m, 3H), 2.80 (t, *J* = 7.8 Hz, 2H), 1.52 (d, *J* = 6.8 Hz, 3H), 1.18 (d, J = 6.9 Hz, 3H), 1.17 (d, J = 6.9 Hz, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.2, 166.3, 164.6, 150.9, 146.9, 141.0, 138.1, 128.4 (2C), 128.3 (2C), 126.1, 123.8, 123.4, 122.6, 119.8, 112.5, 101.7, 54.3, 51.3, 46.0, 35.3, 27.2, 26.5, 21.5, 21.5, 15.2; **ESI MS** calc'd. for $[C_{27}H_{30}N_6O_2 + H]^+$: 471.24, found: 471.20.



**1-((3-isopropylisoxazol-5-yl)methyl)-2-(1-(4-(phenoxymethyl)-1H-1,2,3-triazol-1-yl)propan-2-yl)-1H-indazol-3(2H)-one (42).** The general procedure for the synthesis of triazolyl-indazolones 33-42 was employed using indazolone **19** (183 mg, 0.484 mmol) and phenyl propargyl ether (124 µL, 0.968 mmol). The crude material was purified by flash chromatography (80% ethyl acetate in hexanes) to afford **42** as a colorless oil (178 mg, 78%): **IR** (neat) $\nu_{max}$ 2969, 2934, 2878, 1668, 1613, 1599, 1482, 1464, 1341, 1311, 1239 cm-1; **$^{1}$H NMR** (600 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.60 (s, 1H), 7.54 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 7.23-7.18 (m, 3H), 7.09 (d, *J* = 8.3 Hz, 1H), 6.93-6.86 (m, 3H), 5.60 (s, 1H), 5.31 (dd, *J* = 13.9, 9.8 Hz, 1H), 5.12 (d, *J* = 12.3 Hz, 1H), 5.08 (d, *J* = 12.3 Hz, 1H), 4.73 (dd, *J* = 13.9, 5.5 Hz, 1H), 4.61-4.54 (m, 1H), 4.52 (d, *J* = 16.8 Hz, 1H), 4.47 (d, *J* = 16.8 Hz, 1H), 2.89 (m, *J* = 6.9 Hz, 1H), 1.53 (d, *J* = 6.8 Hz, 3H), 1.16 (d, J = 6.9 Hz, 3H), 1.16 (d, J = 6.9 Hz, 3H); at 25 ºC, **42** exists as a mixture of rotational isomers. **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 169.3, 166.3, 164.6, 158.1, 151.1, 144.0, 133.3, 133.2, 129.6, 129.5, 124.5, 124.4, 124.0, 123.9, 123.6, 123.5, 121.3, 119.9, 114.9, 112.7, 112.6, 101.7, 61.8, 54.5, 54.4, 51.7, 46.1, 26.6, 26.5, 21.6, 21.5, 21.4, 15.2, 15.2,; **ESI MS** calc'd. for $[C_{26}H_{28}N_6O_3 + H]^+$: 473.22, found: 473.24.



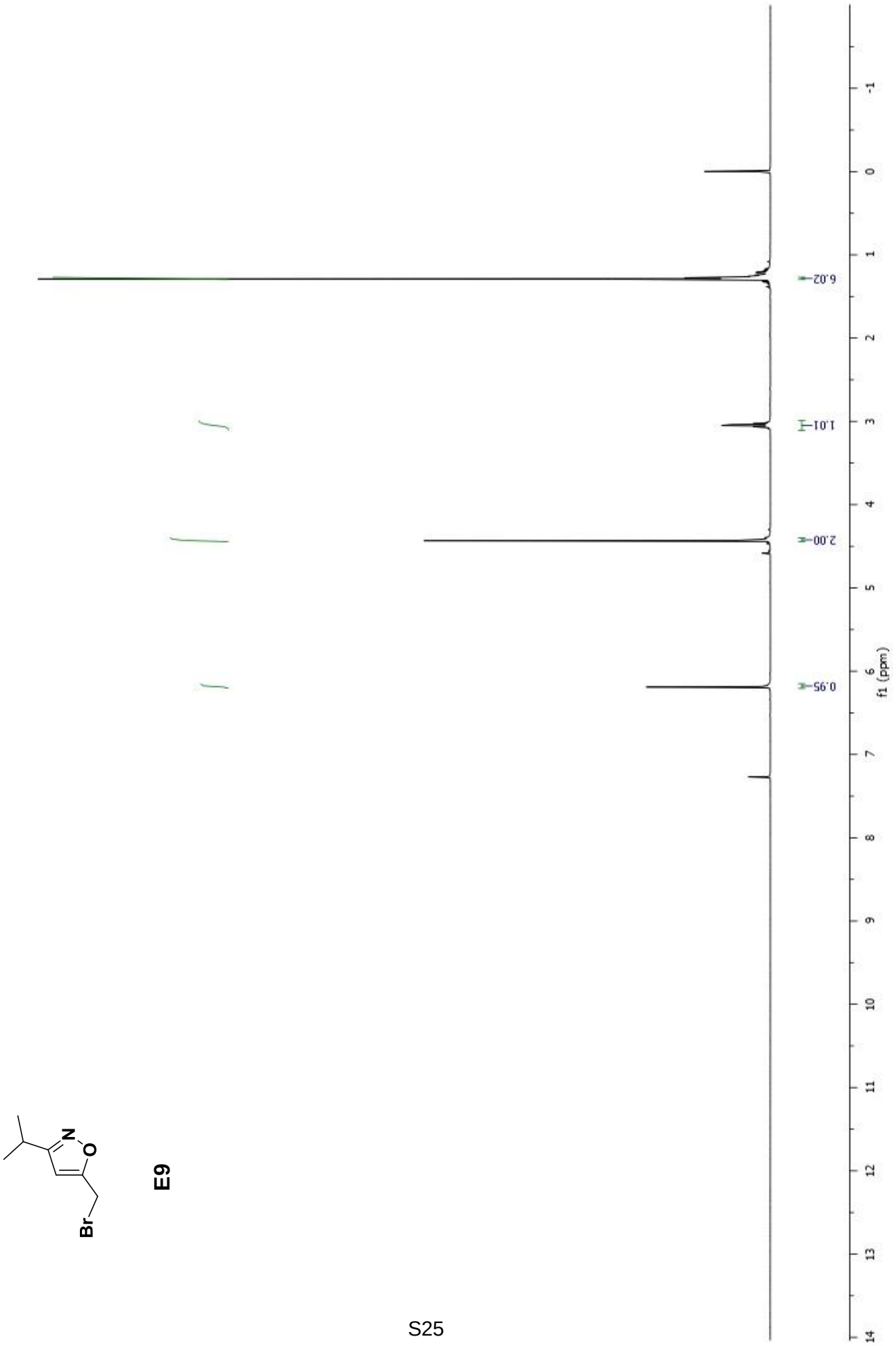

**E8**







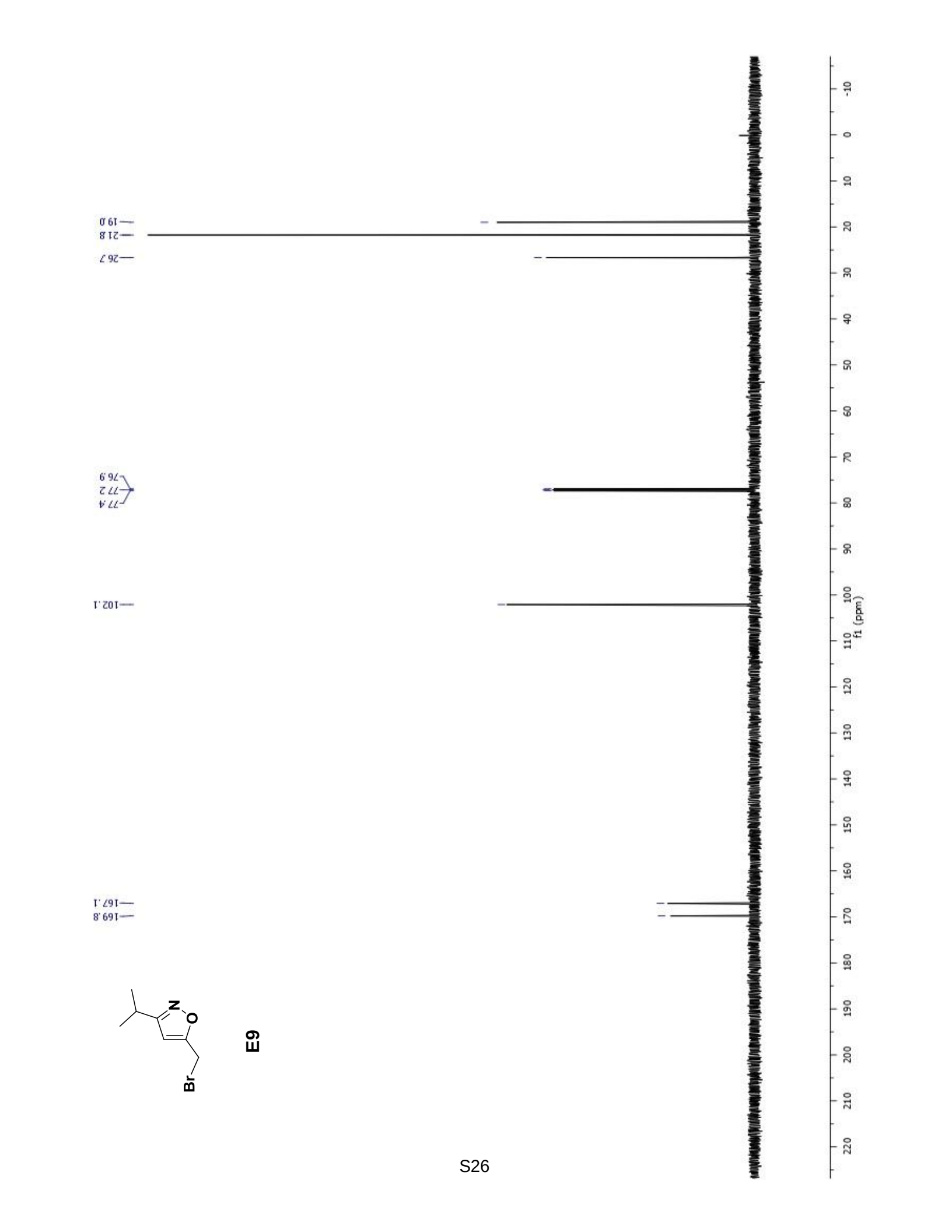
**E8**



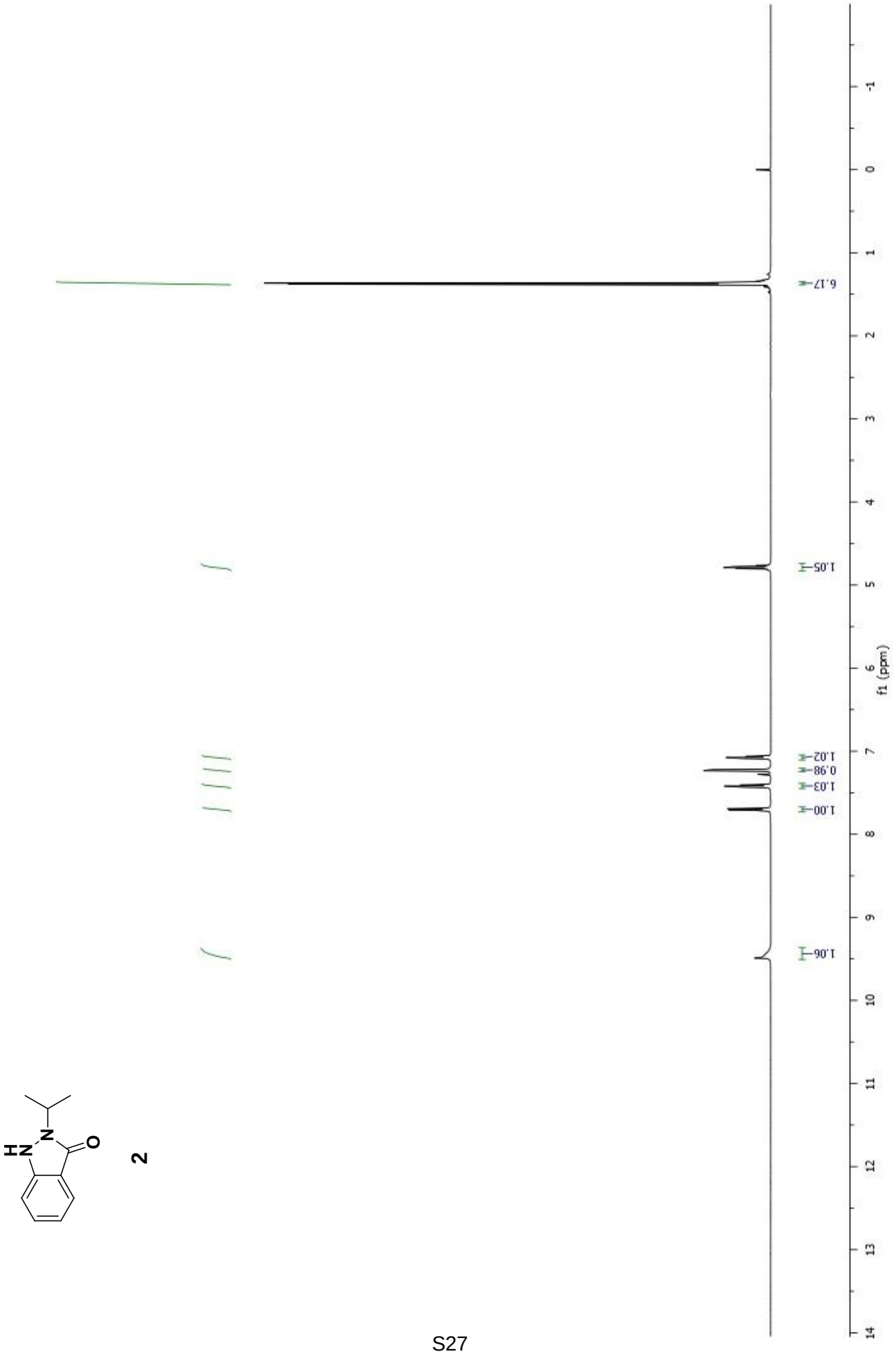




**E9**

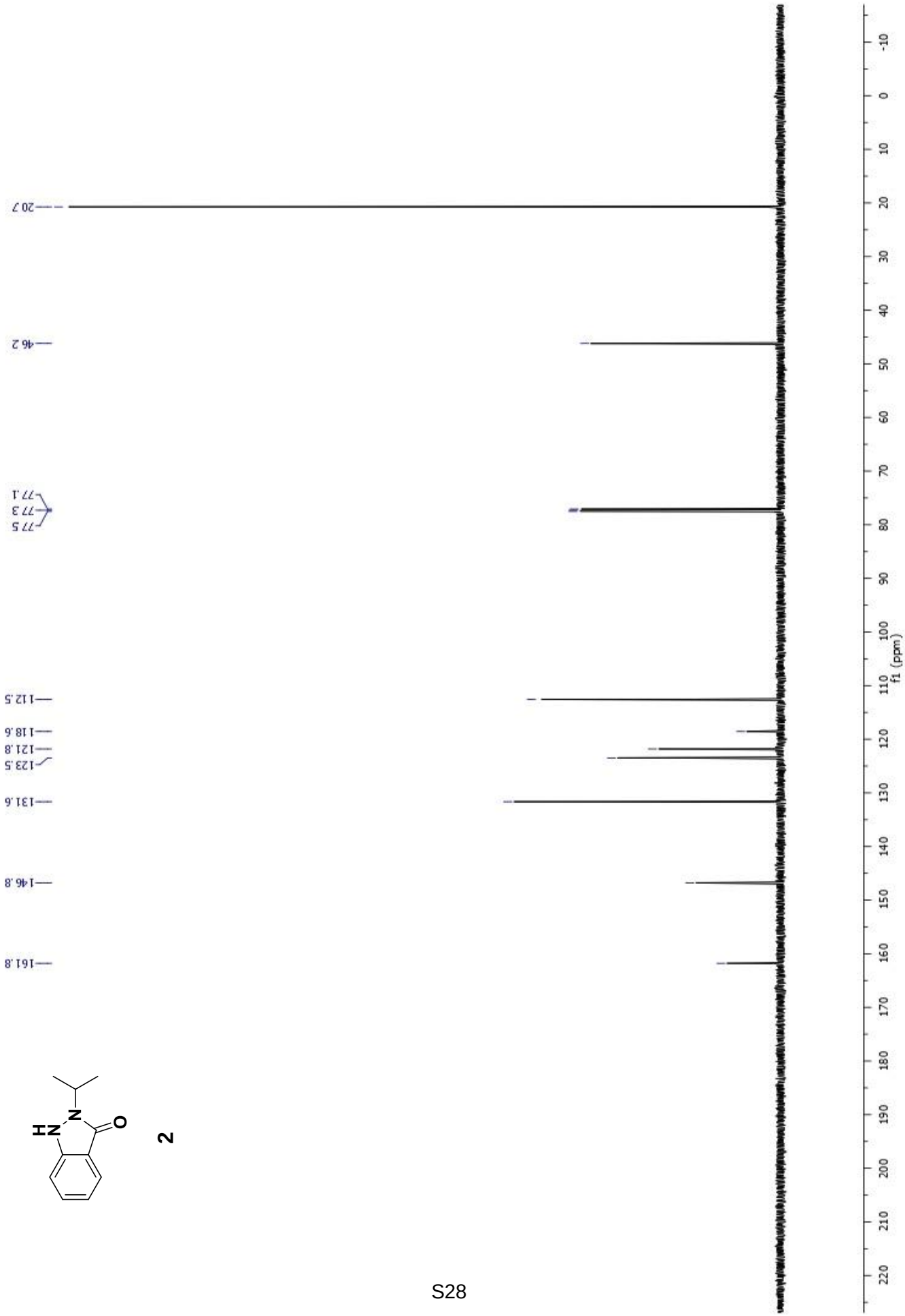



**E9**



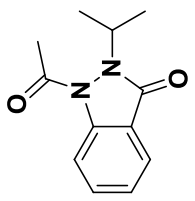



**2**

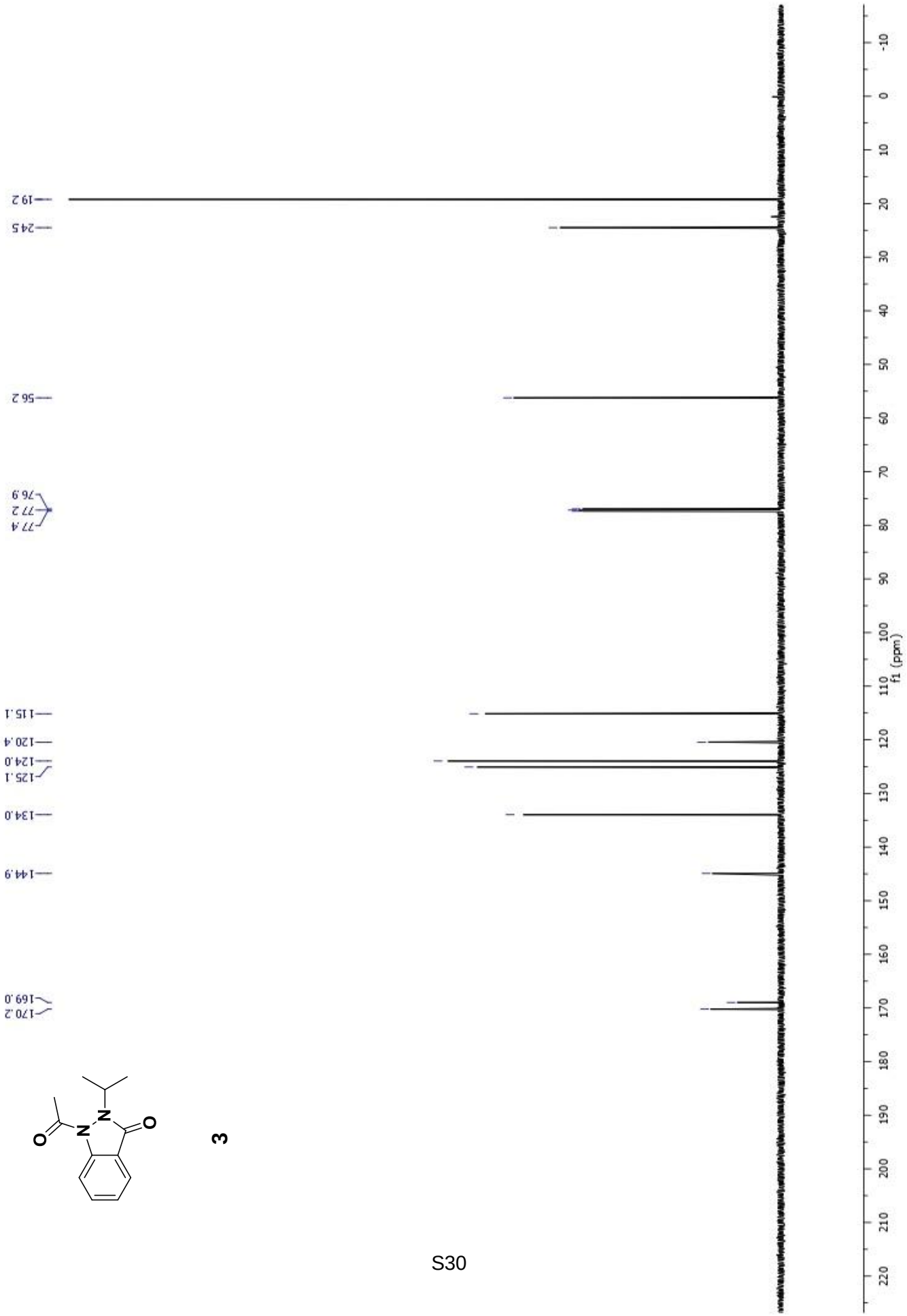





2



**3**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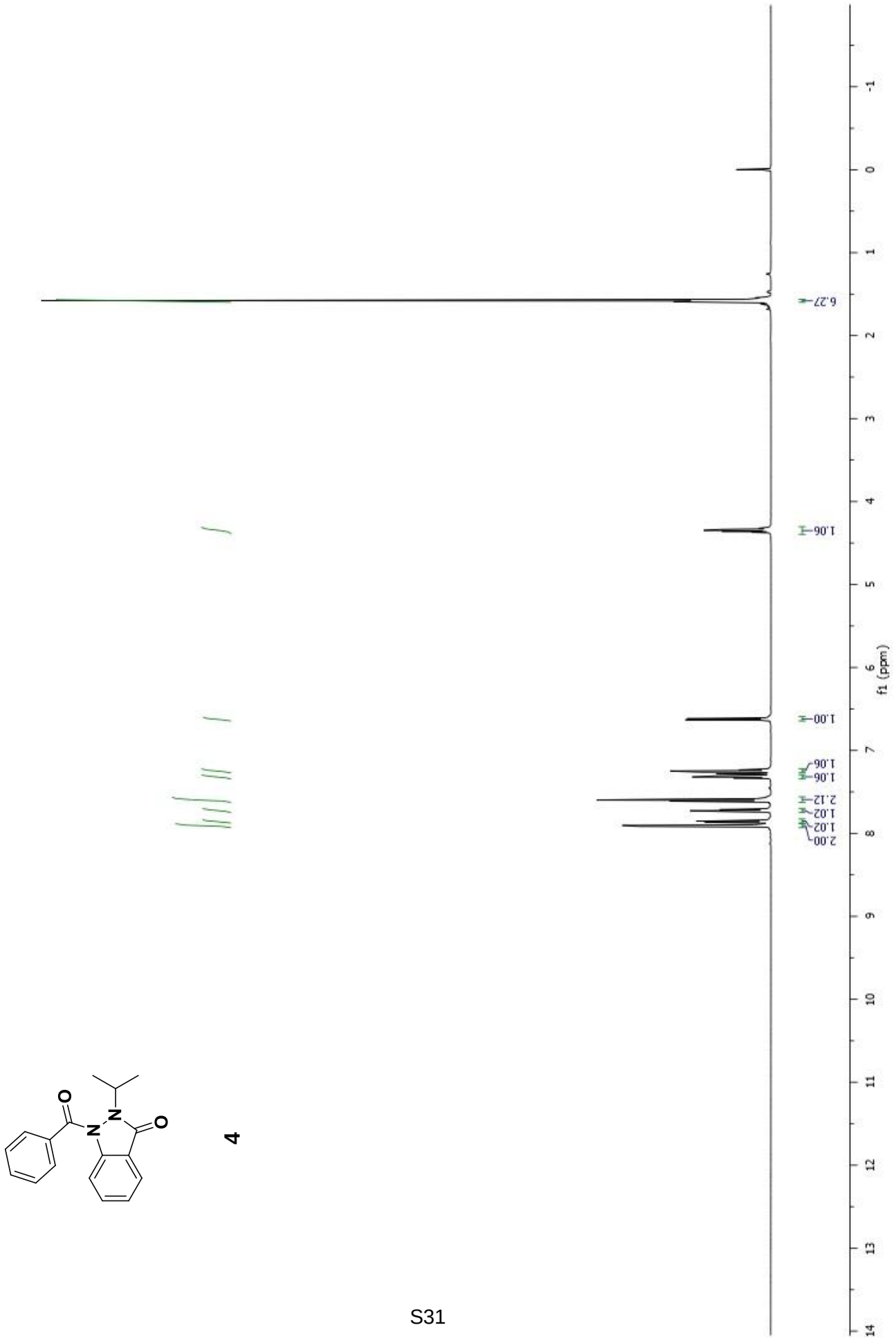
24.5
56.2
76.9
77.2
77.4
115.1
120.4
124.0
125.1
134.0
144.9
169.0
170.2
f1 (ppm)

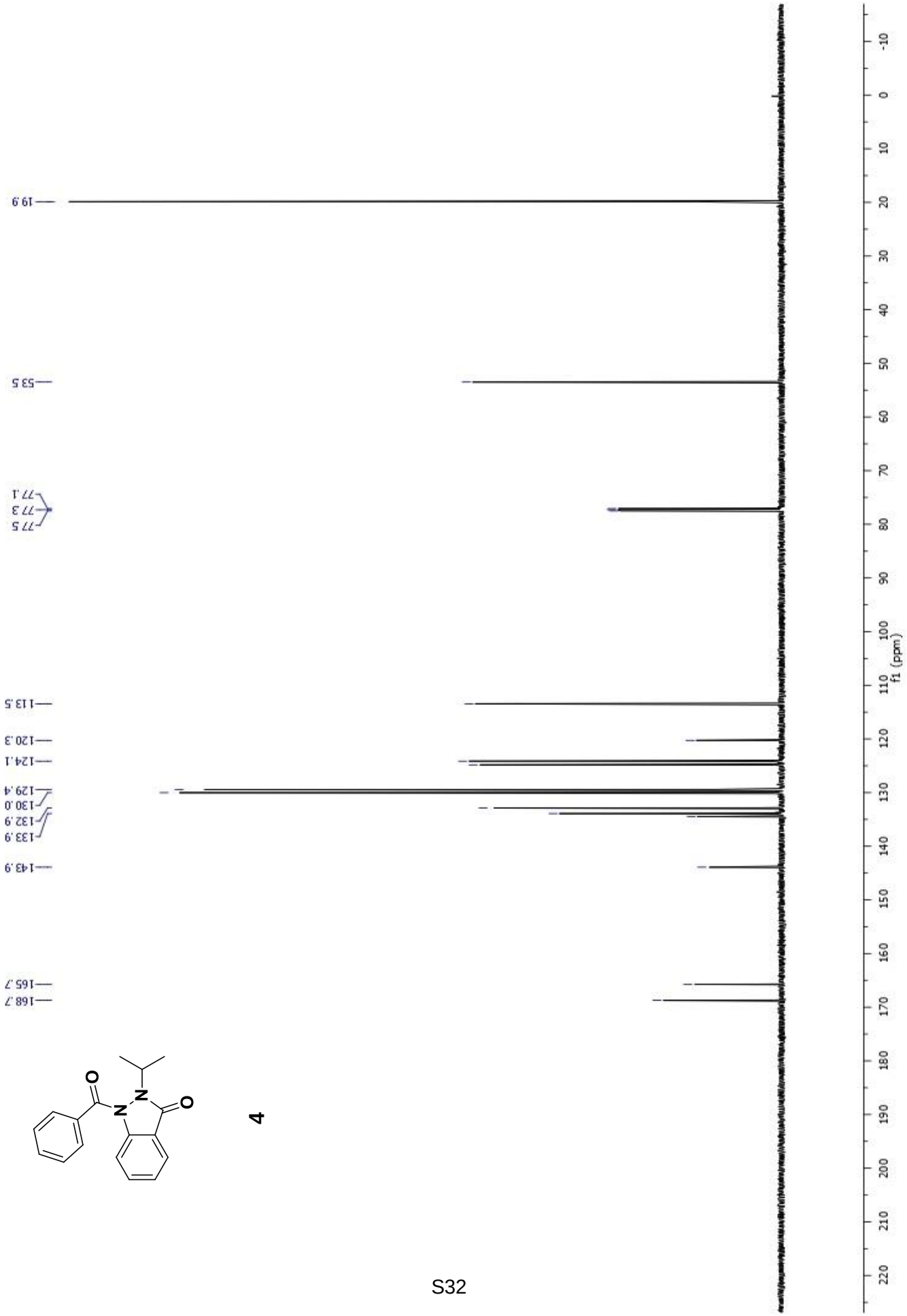


**3**



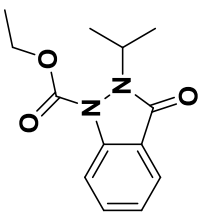



**4**

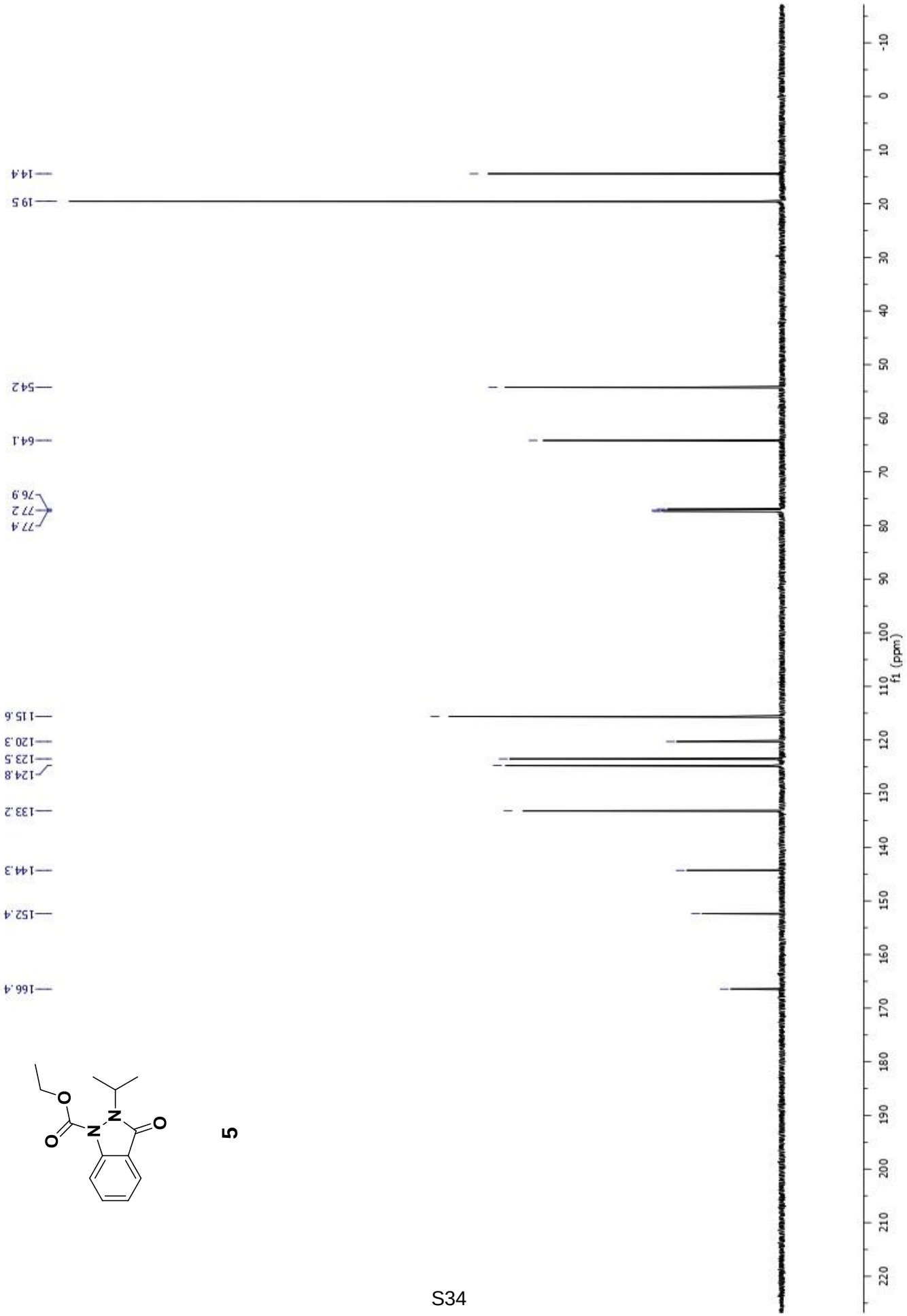

19.9
53.5
77.5
77.3
77.1
113.5
120.3
124.1
129.4
130.0
132.9
133.9
143.9
165.7
168.7
f1 (ppm)



**4**

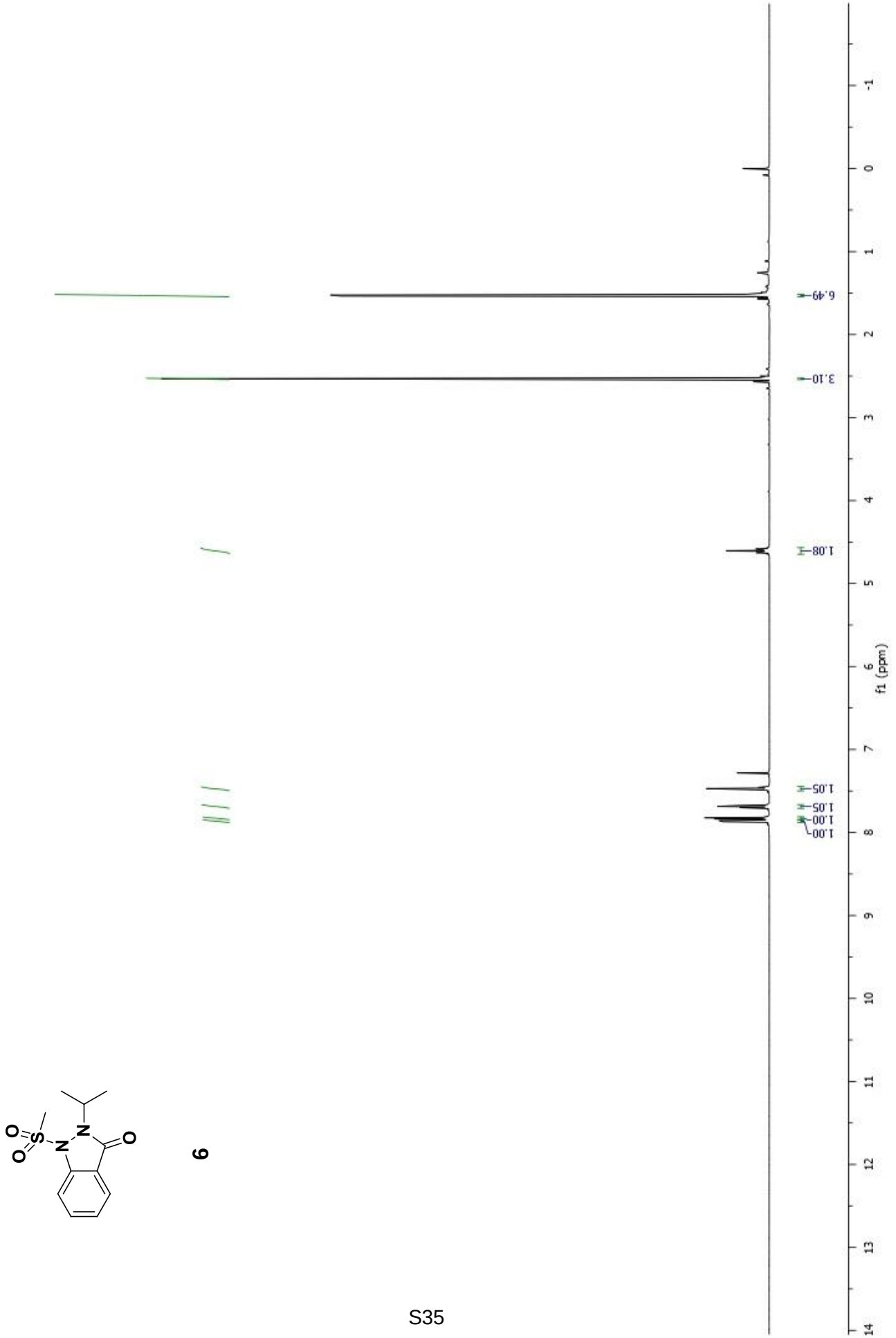


**5**


144
19.5
54.2
64.1
77.4
77.2
76.9
115.6
120.3
123.5
124.8
133.2
144.3
152.4
166.4
f1 (ppm)

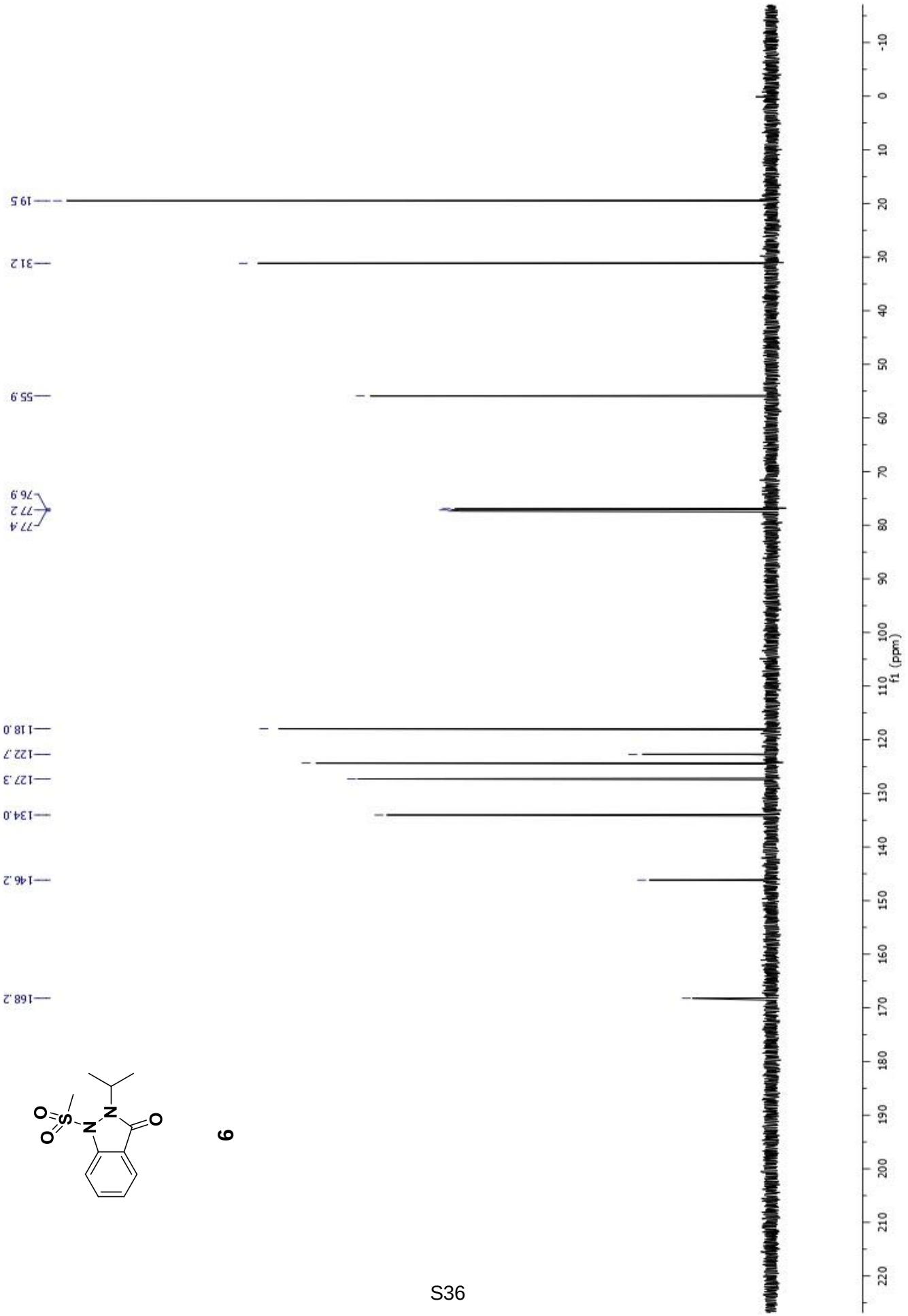


**5**



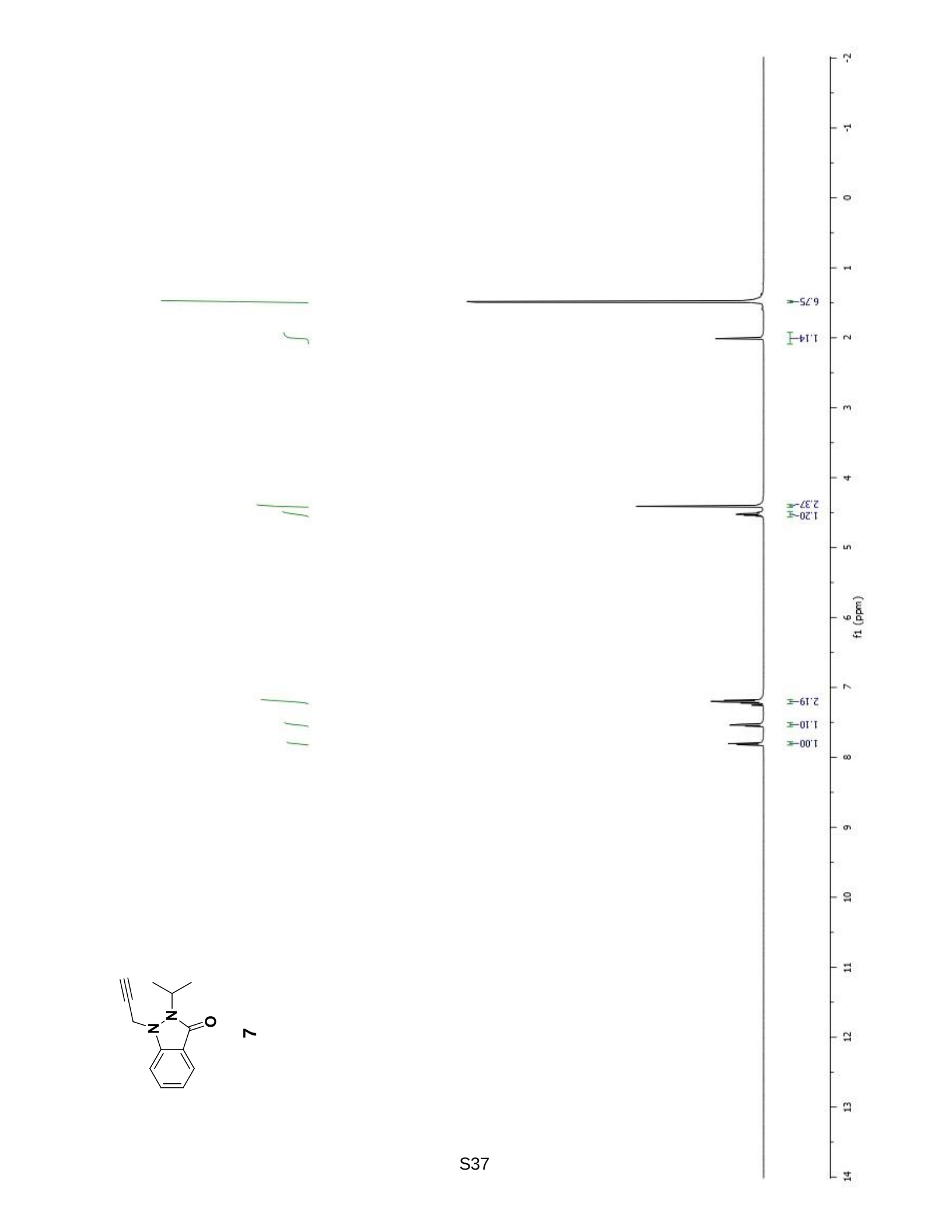



**6**



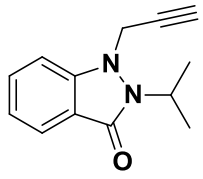



**6**



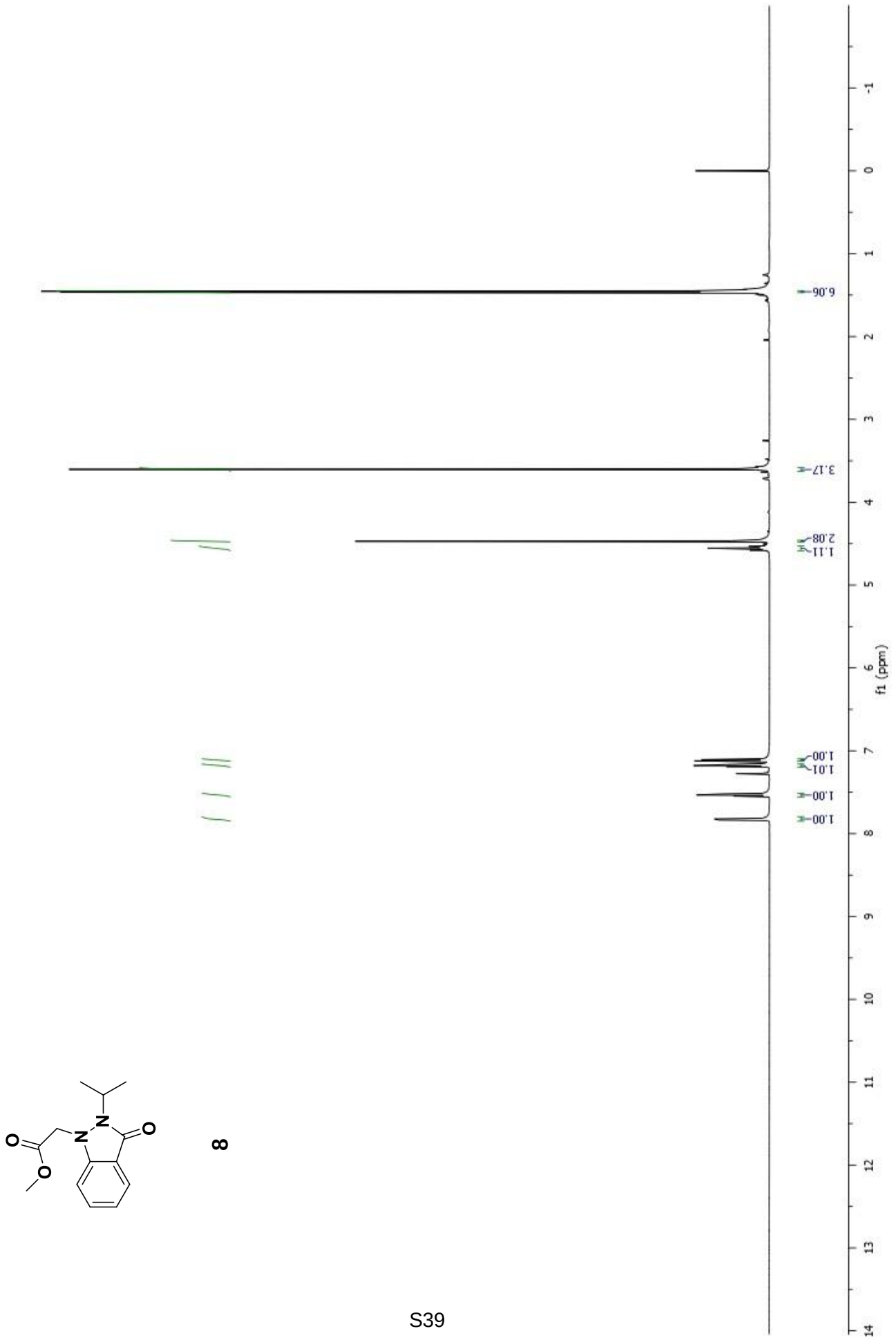



**7**



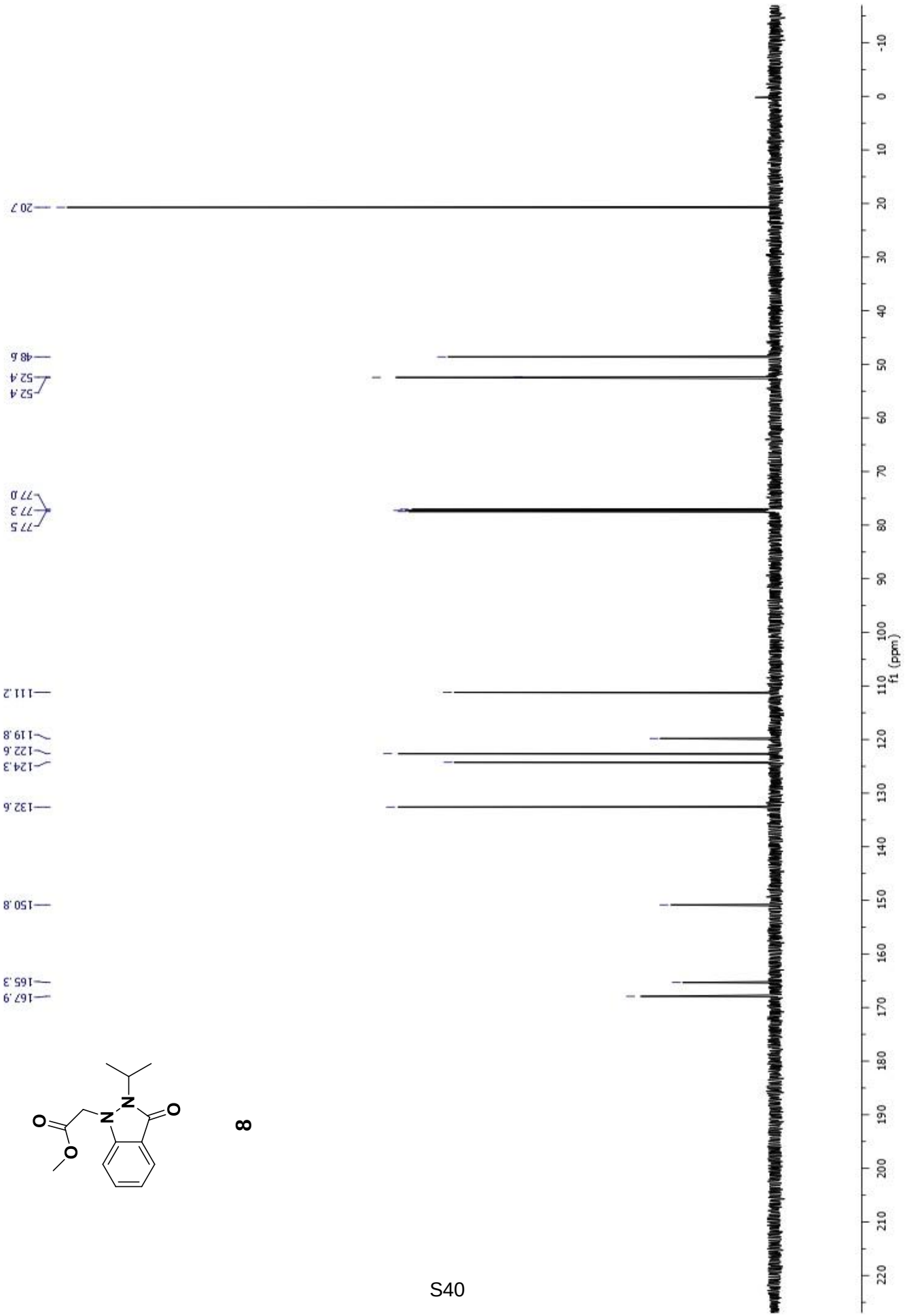
**7**


165.0
150.7
132.3
123.9
123.5
121.6
112.7
77.4
77.2
76.9
75.2
74.4
48.2
42.6
20.7
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)






8


207
48.6
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52.4
77.5
77.3
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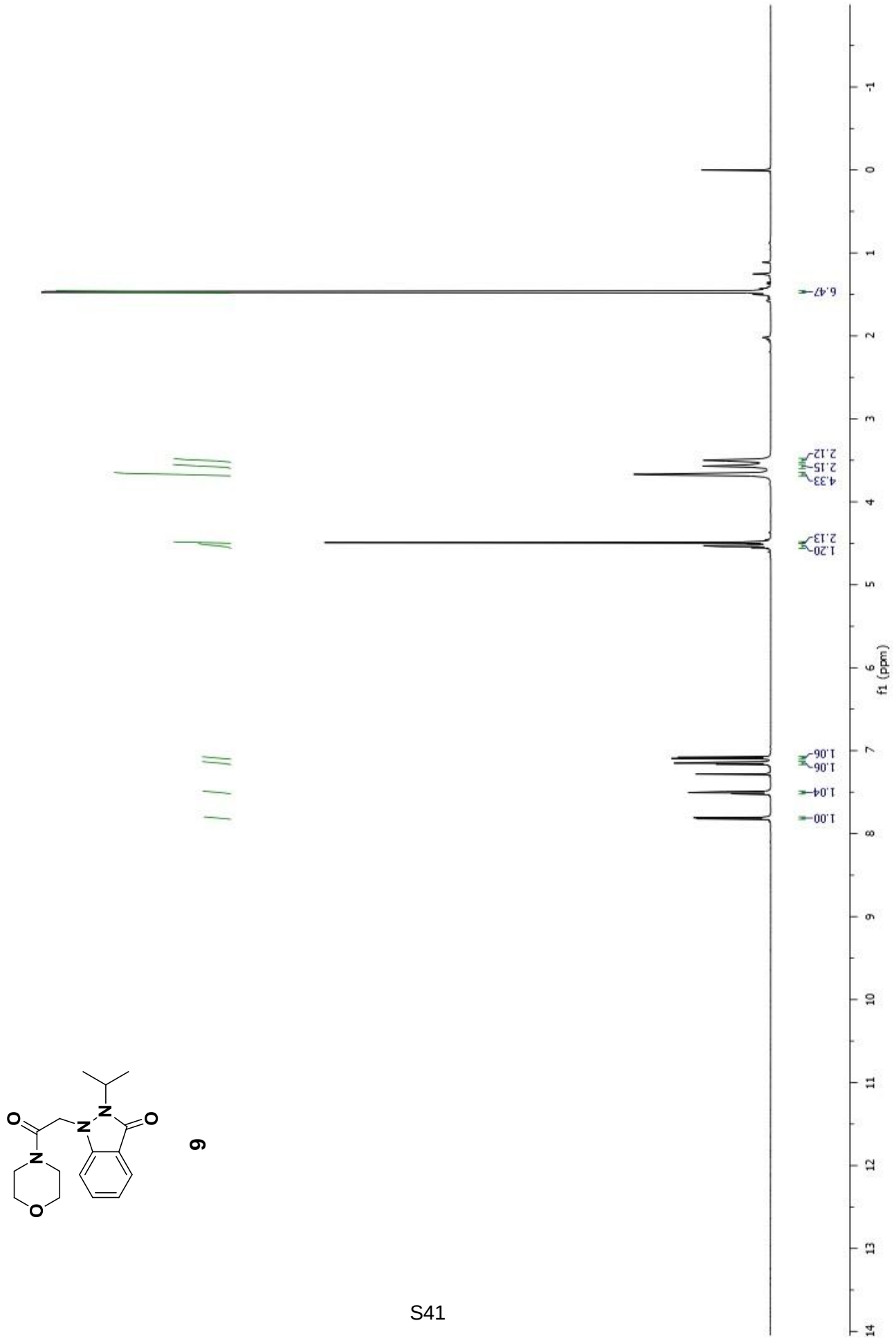
122.6
124.3
132.6
150.8
165.3
167.9
f1 (ppm)



**8**



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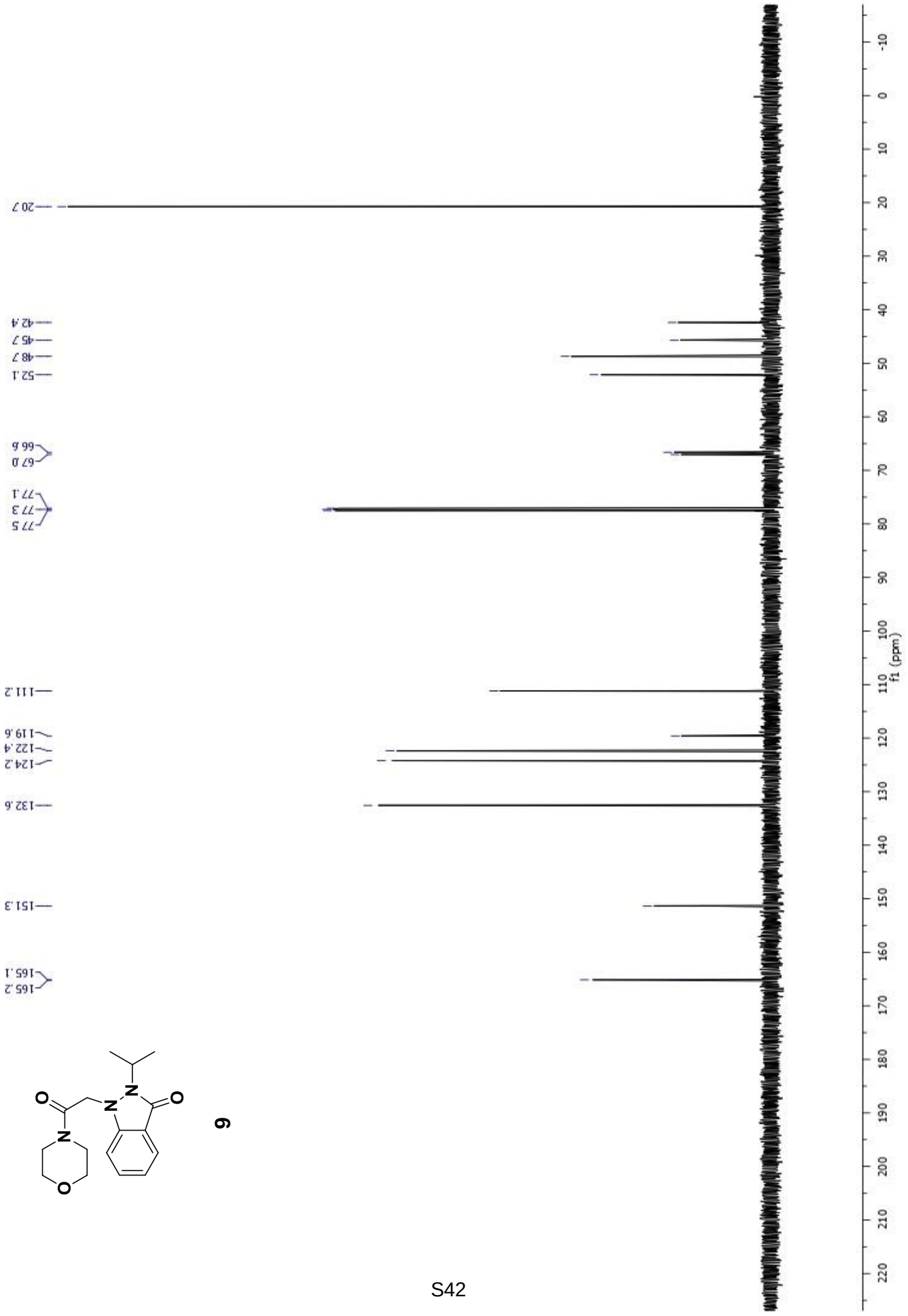
207
42.4
45.7
48.7
52.1
66.6
67.0
77.1
77.3
77.5
111.2
119.6
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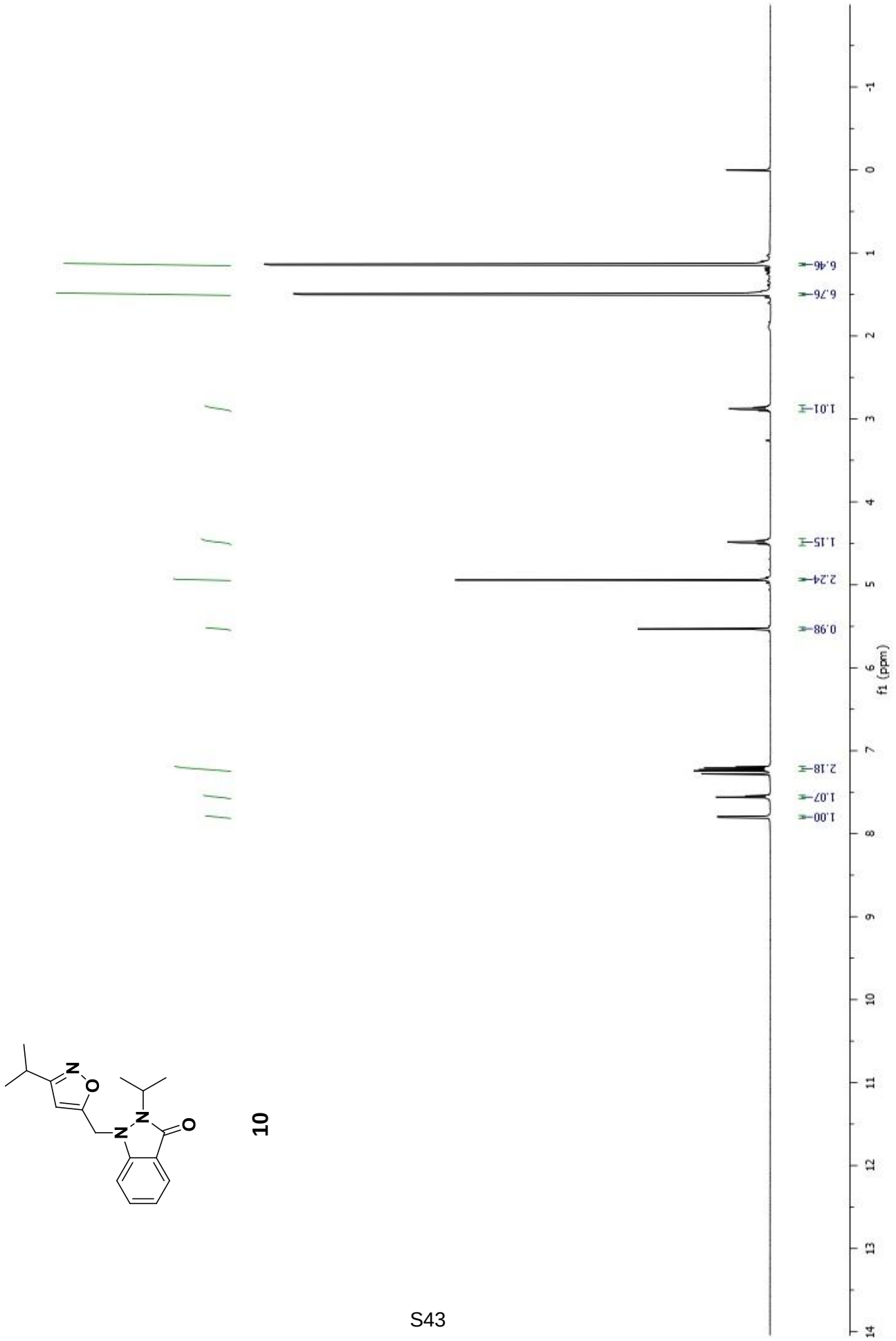
124.2
132.6
151.3
165.1
165.2
f1 (ppm)

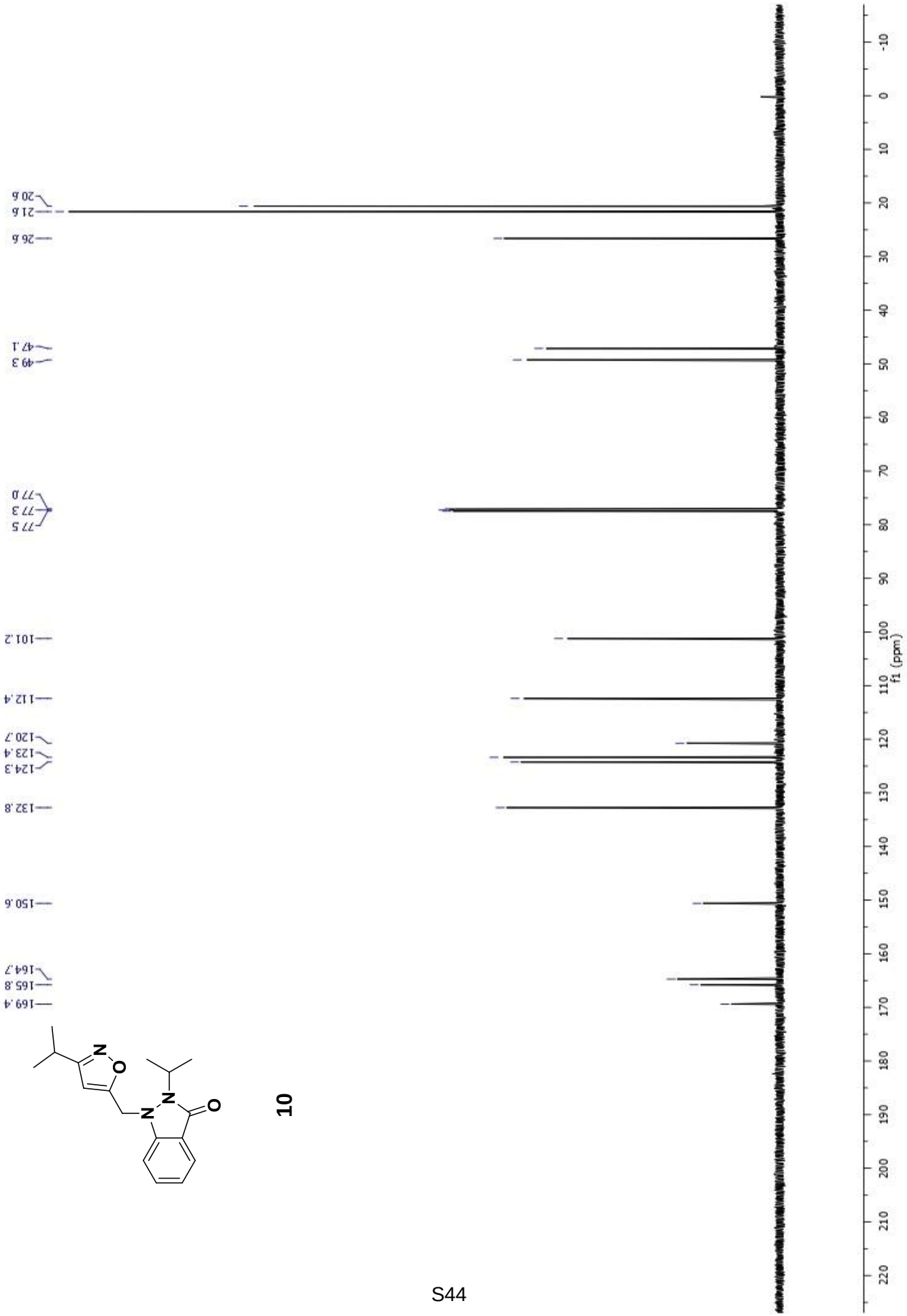


**6**






**10**


169.4
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150.6
132.8
124.3
123.4
120.7
112.4
101.2
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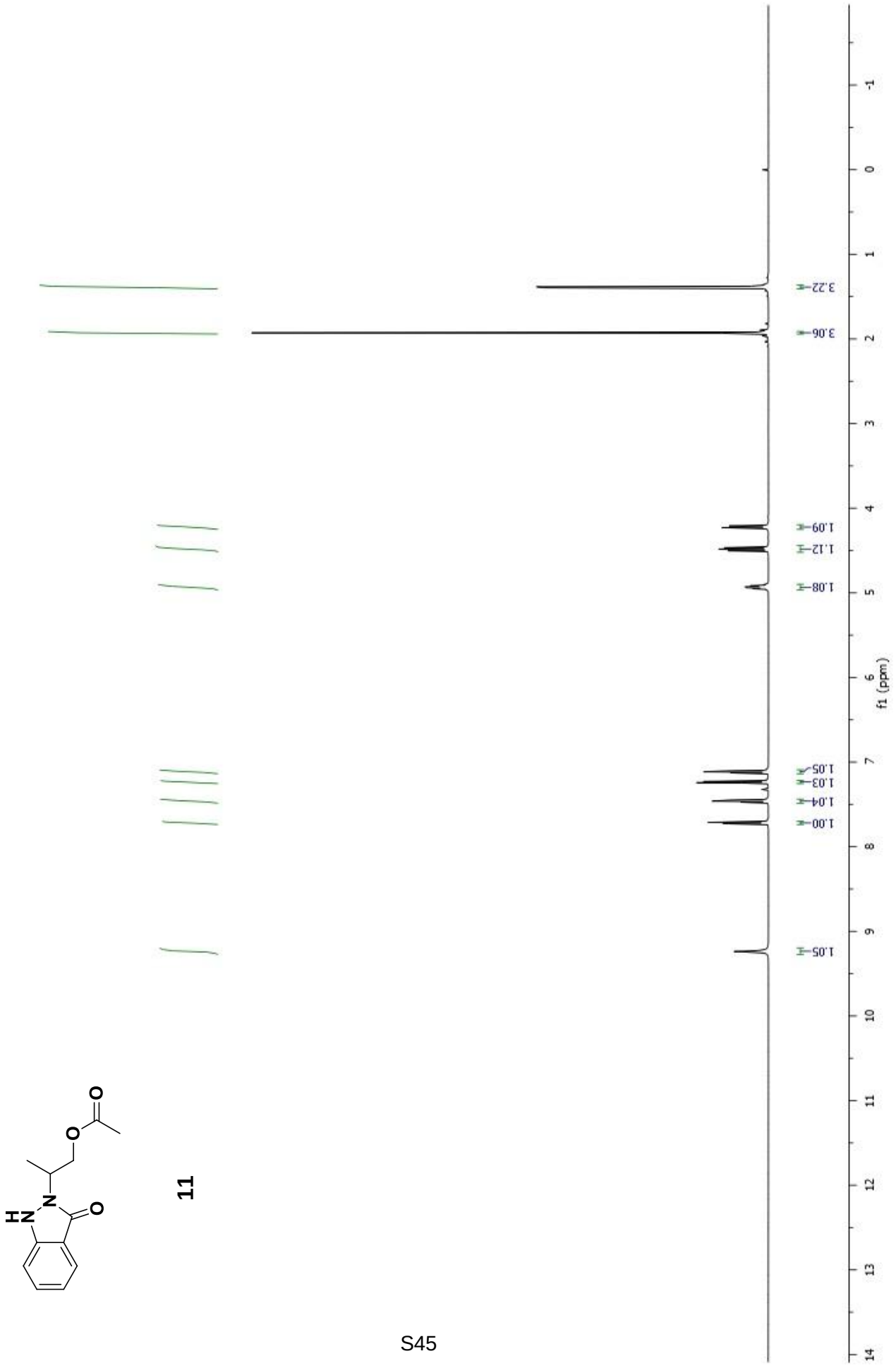
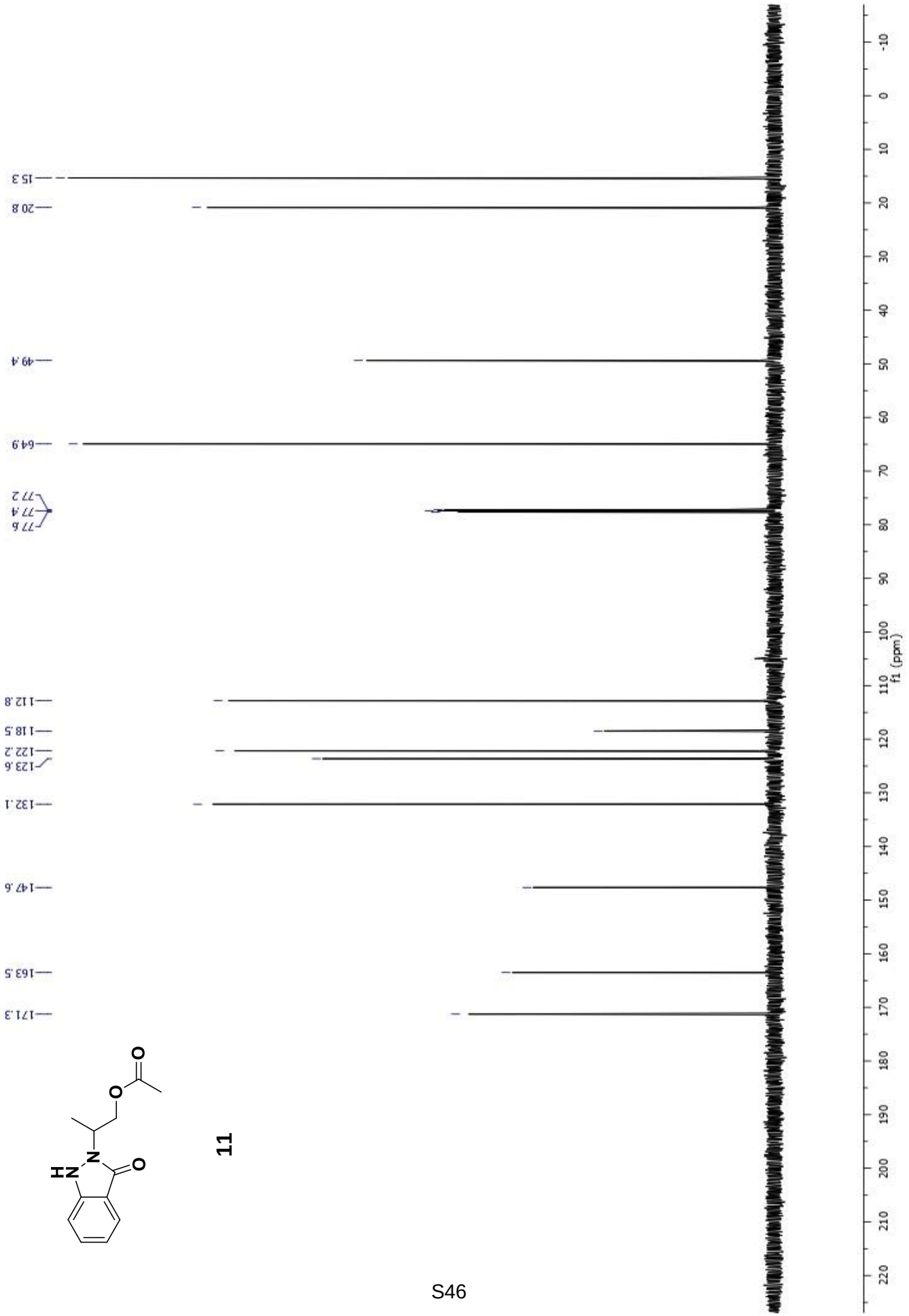
77.3
77.0
49.3
47.1
26.6
21.6
20.6
f1 (ppm)

**10**



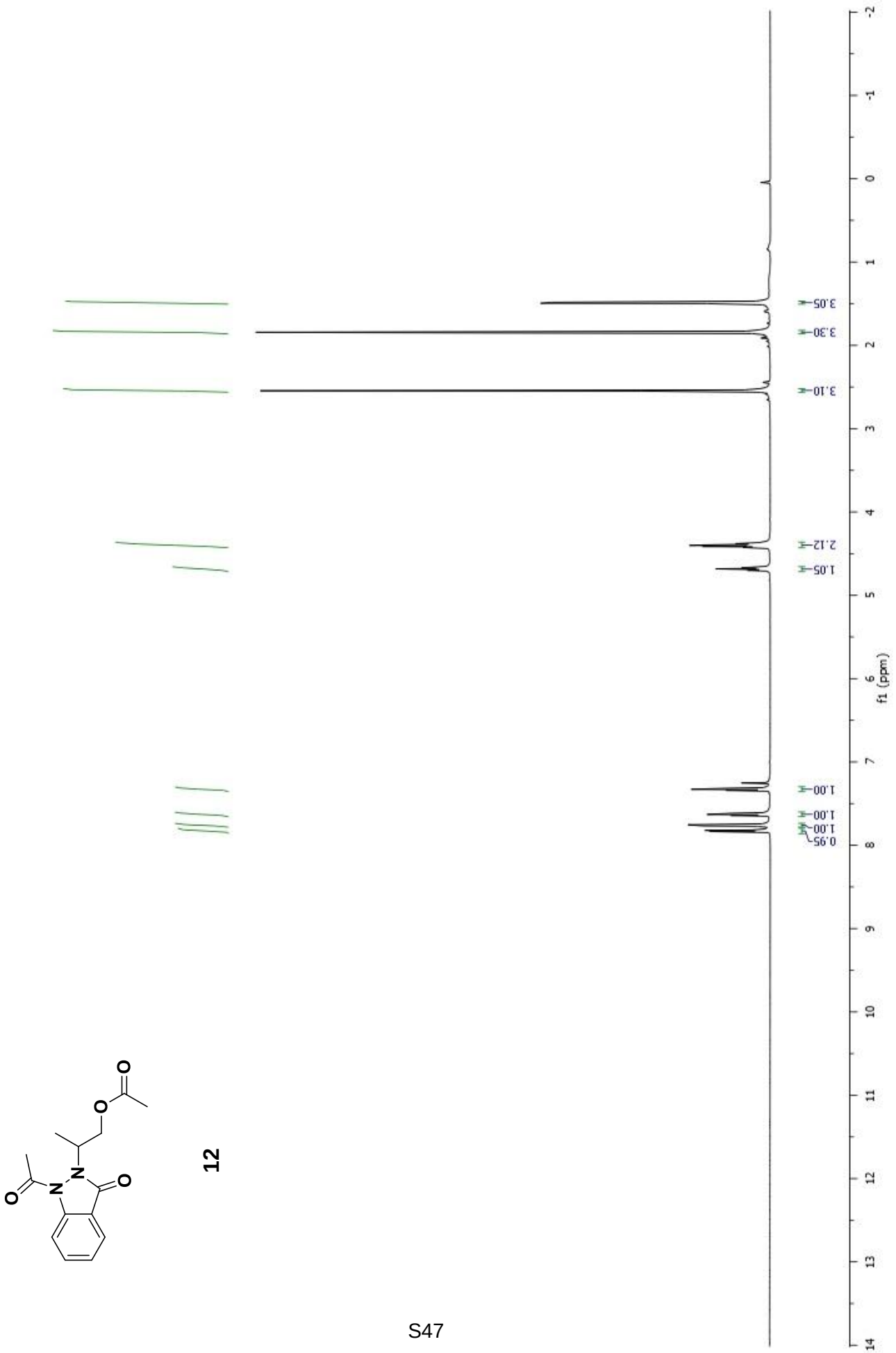



**11**


15.3
20.8
49.4
64.9
77.6
77.4
77.2
112.8
118.5
122.2
123.6
132.1
147.6
163.5
171.3
f1 (ppm)

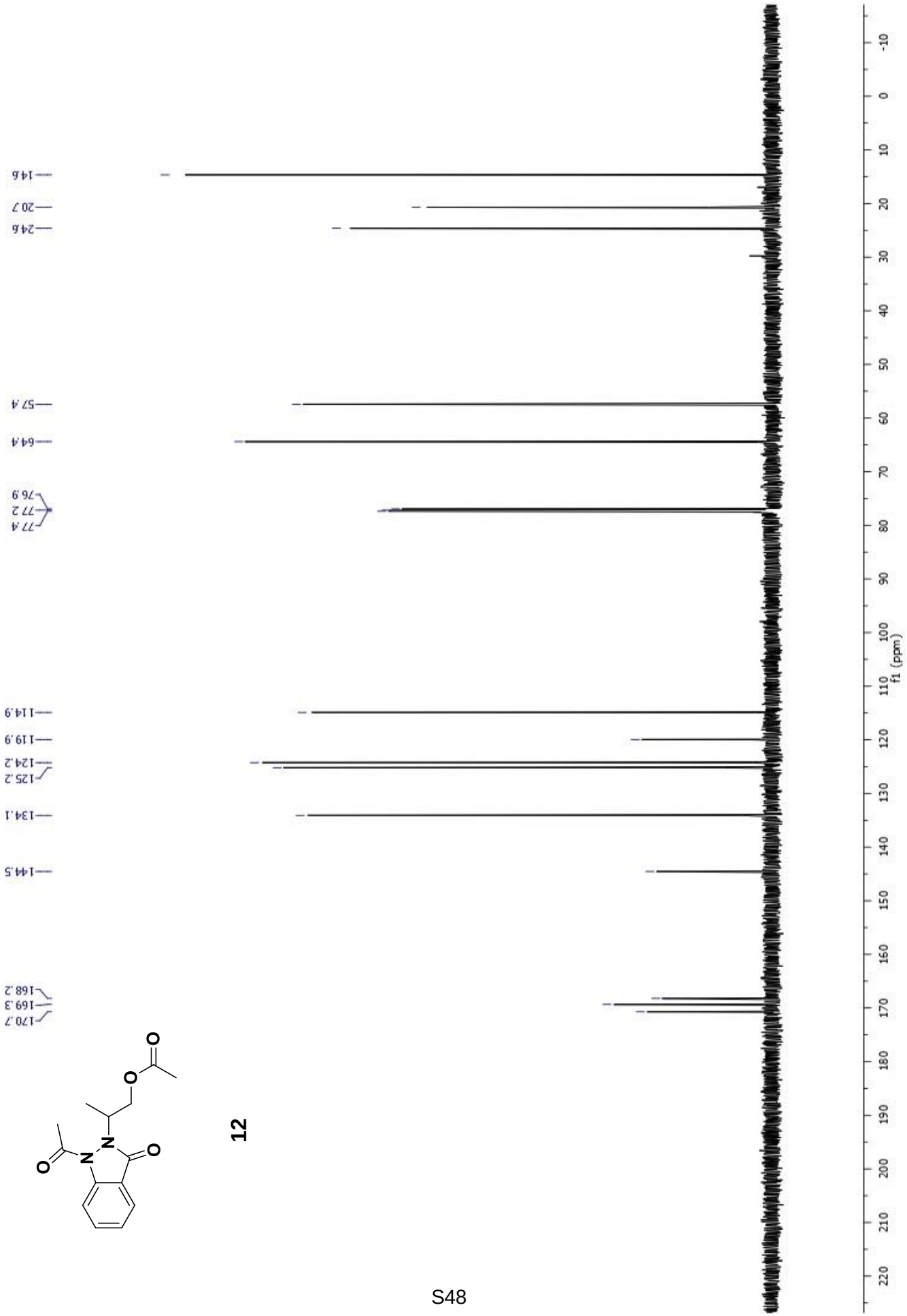


**11**

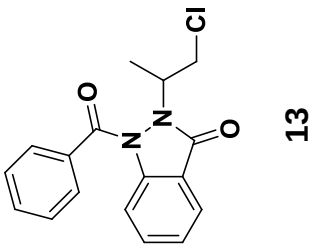




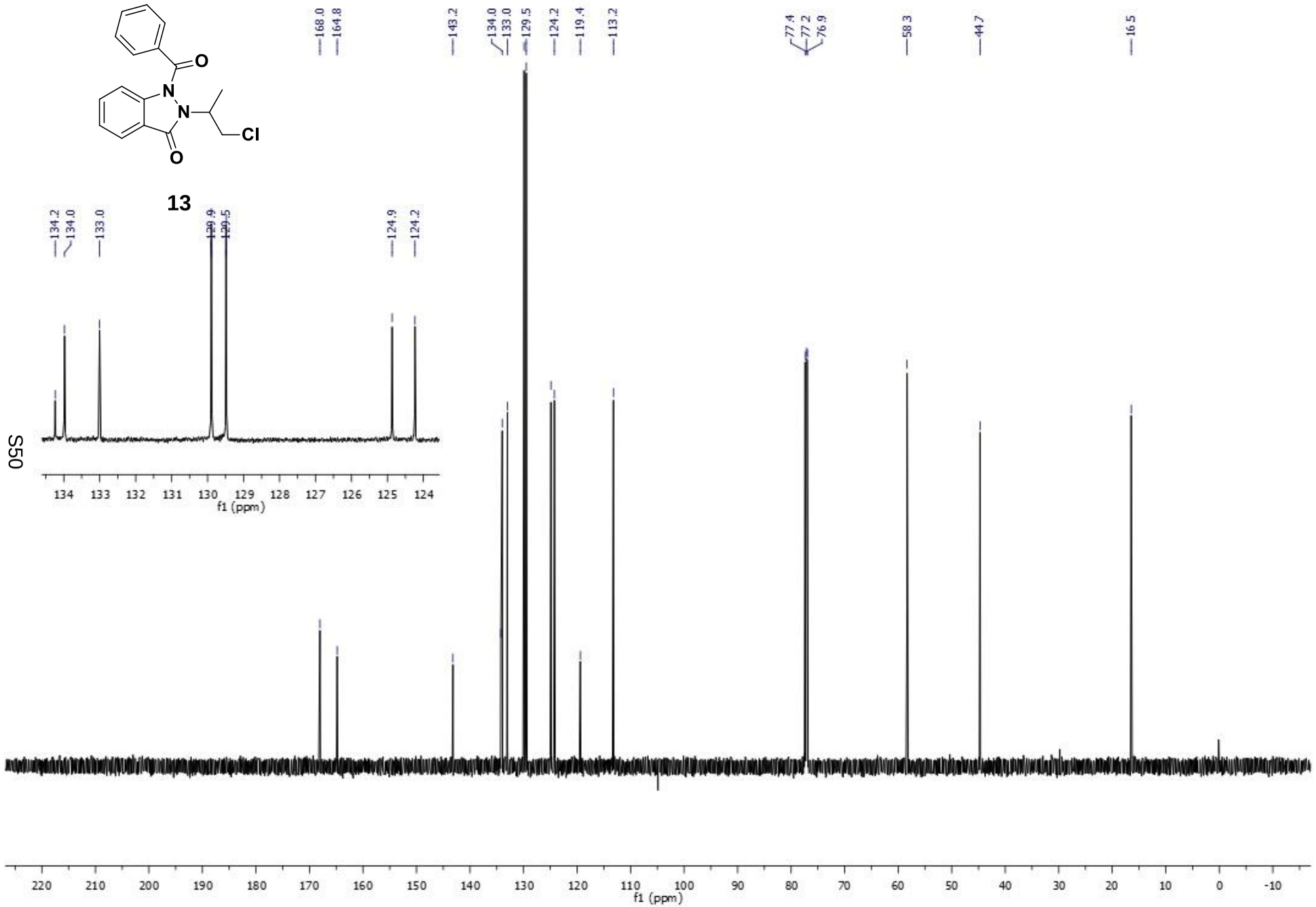

**12**

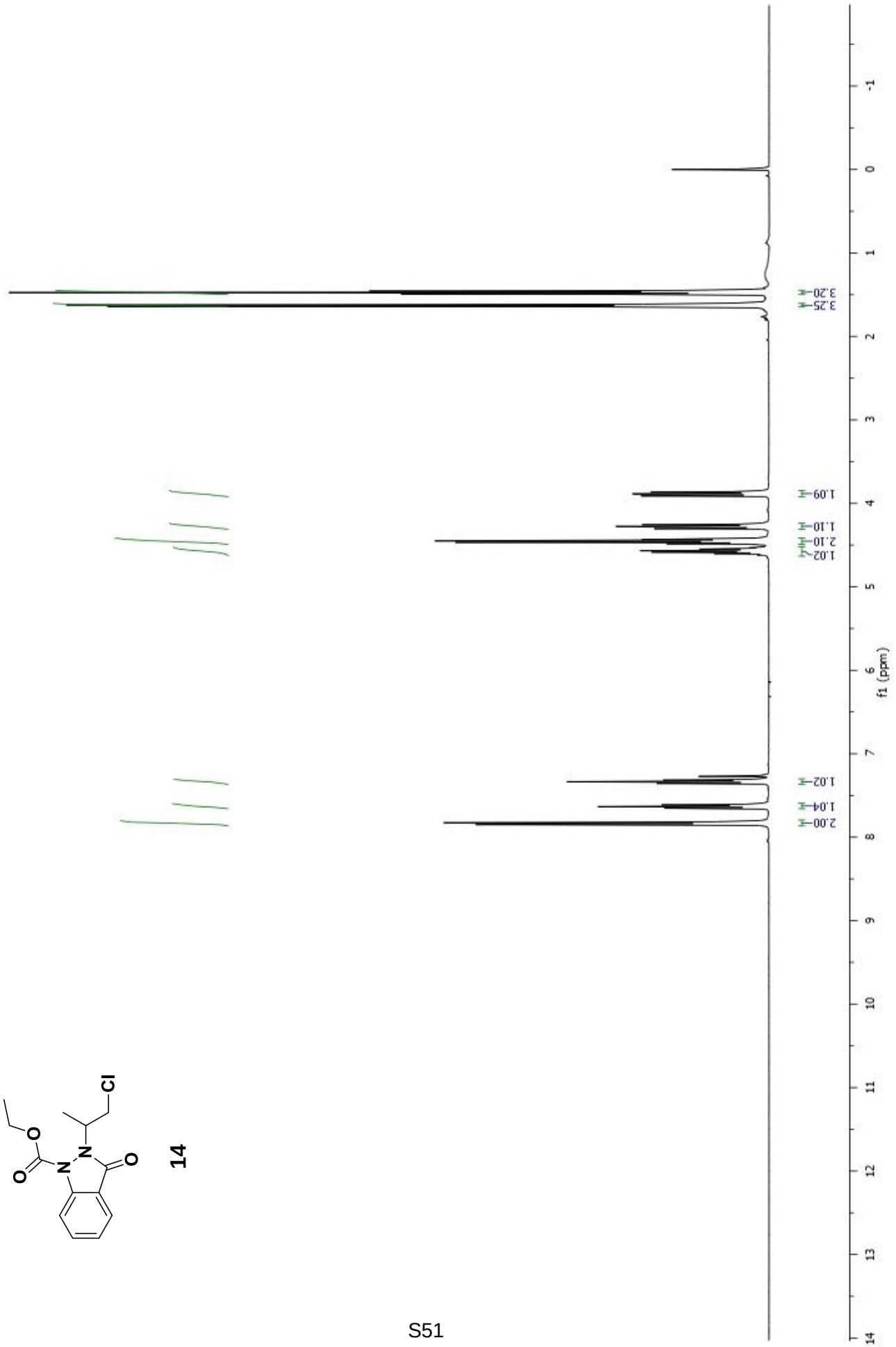

14.6
20.7
24.6
57.4
64.4
76.9
77.2
77.4
114.9
119.9
124.2
125.2
134.1
144.5
168.2
169.3
170.7
f1 (ppm)

**12**




**13**

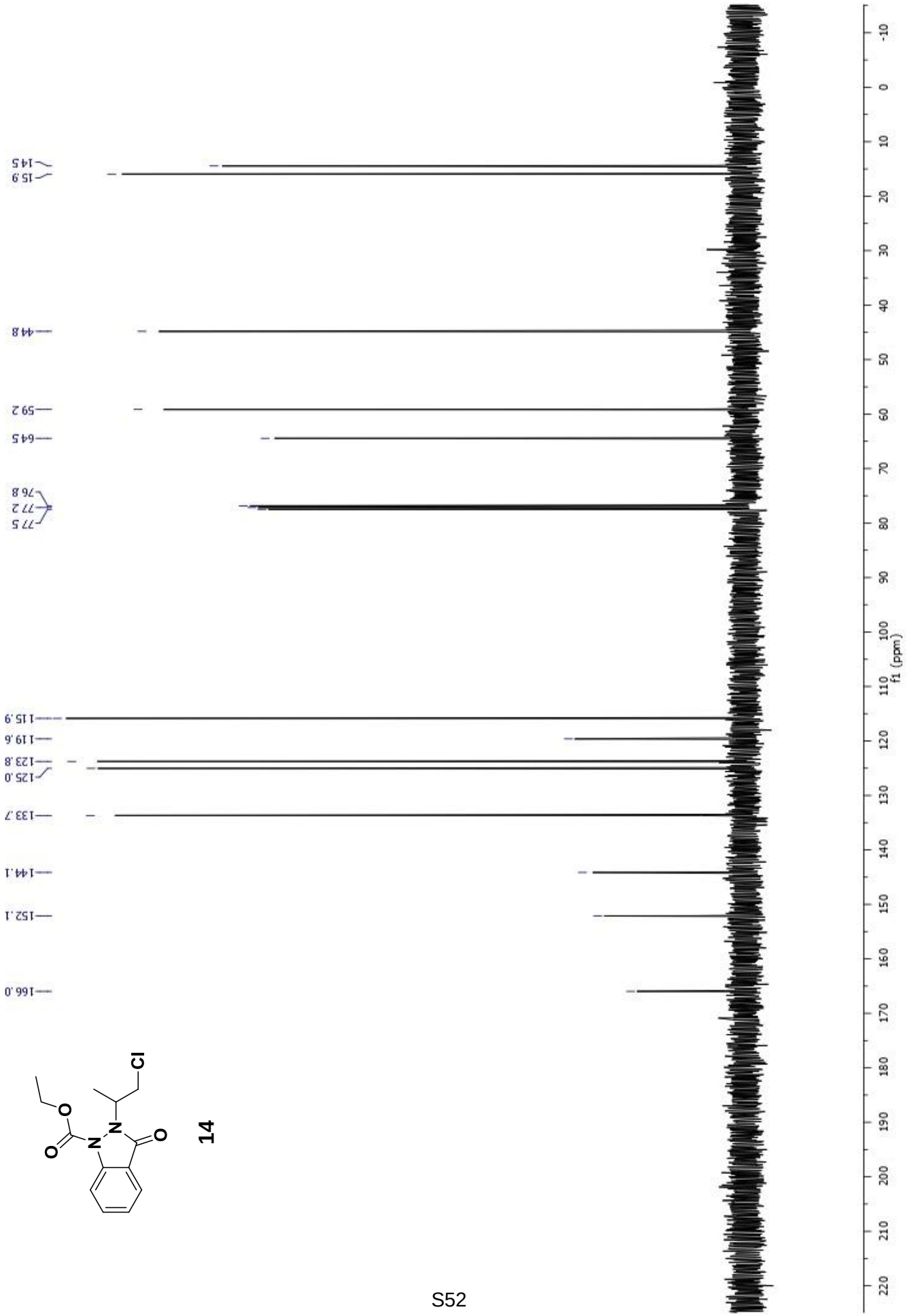

O
N
N
Cl
O
13
168.0
164.8
143.2
134.0
133.0
129.5
124.2
119.4
113.2
77.4
77.2
76.9
58.3
44.7
16.5
134.2
134.0
133.0
129.9
129.5
124.9
124.2
134 133 132 131 130 129 128 127 126 125 124
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)





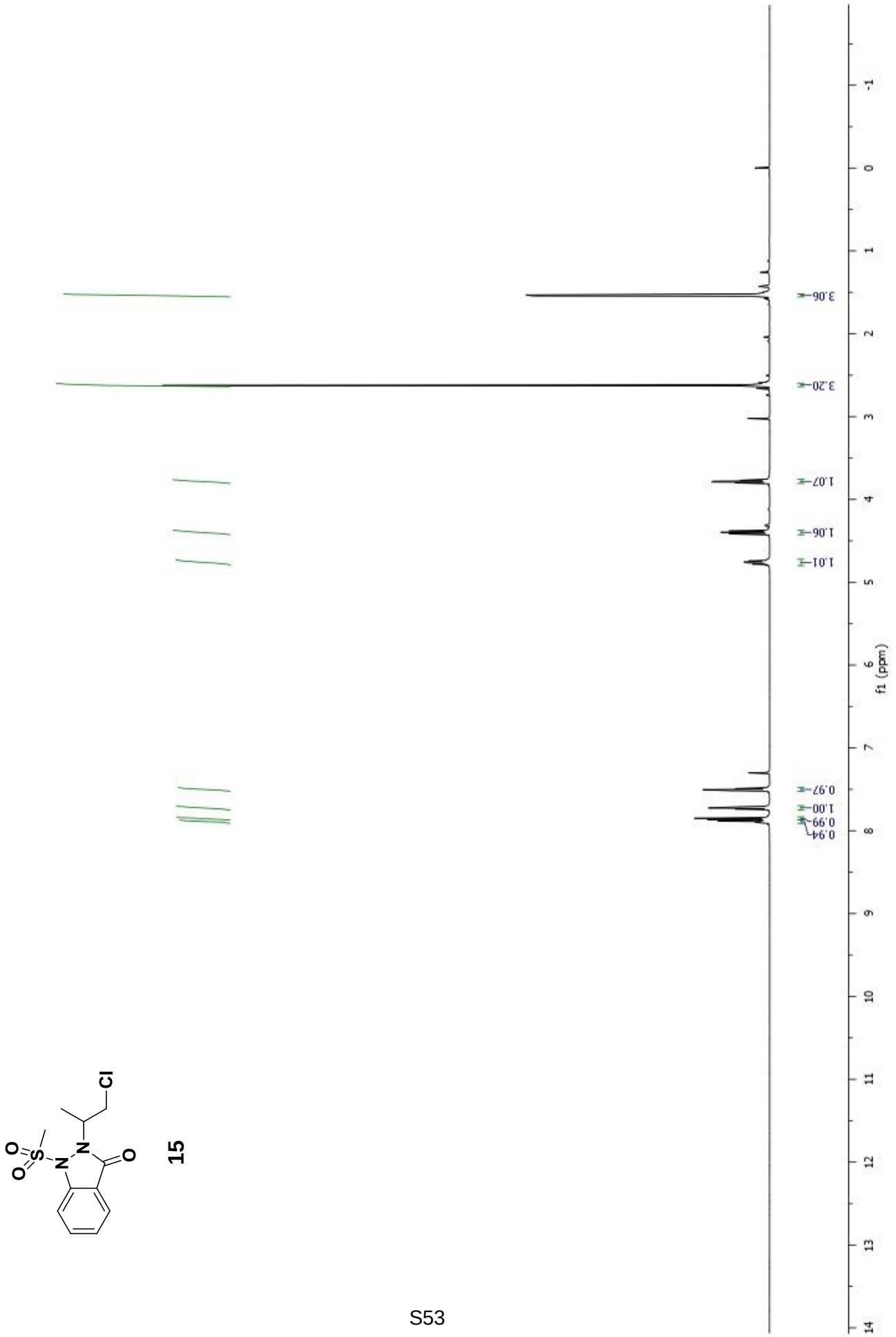


**14**


145.9
44.8
59.2
64.5
76.8
77.2
77.5
115.9
119.6
123.8
125.0
133.7
144.1
152.1
166.0
f1 (ppm)


Cl
O
O
N
N
O

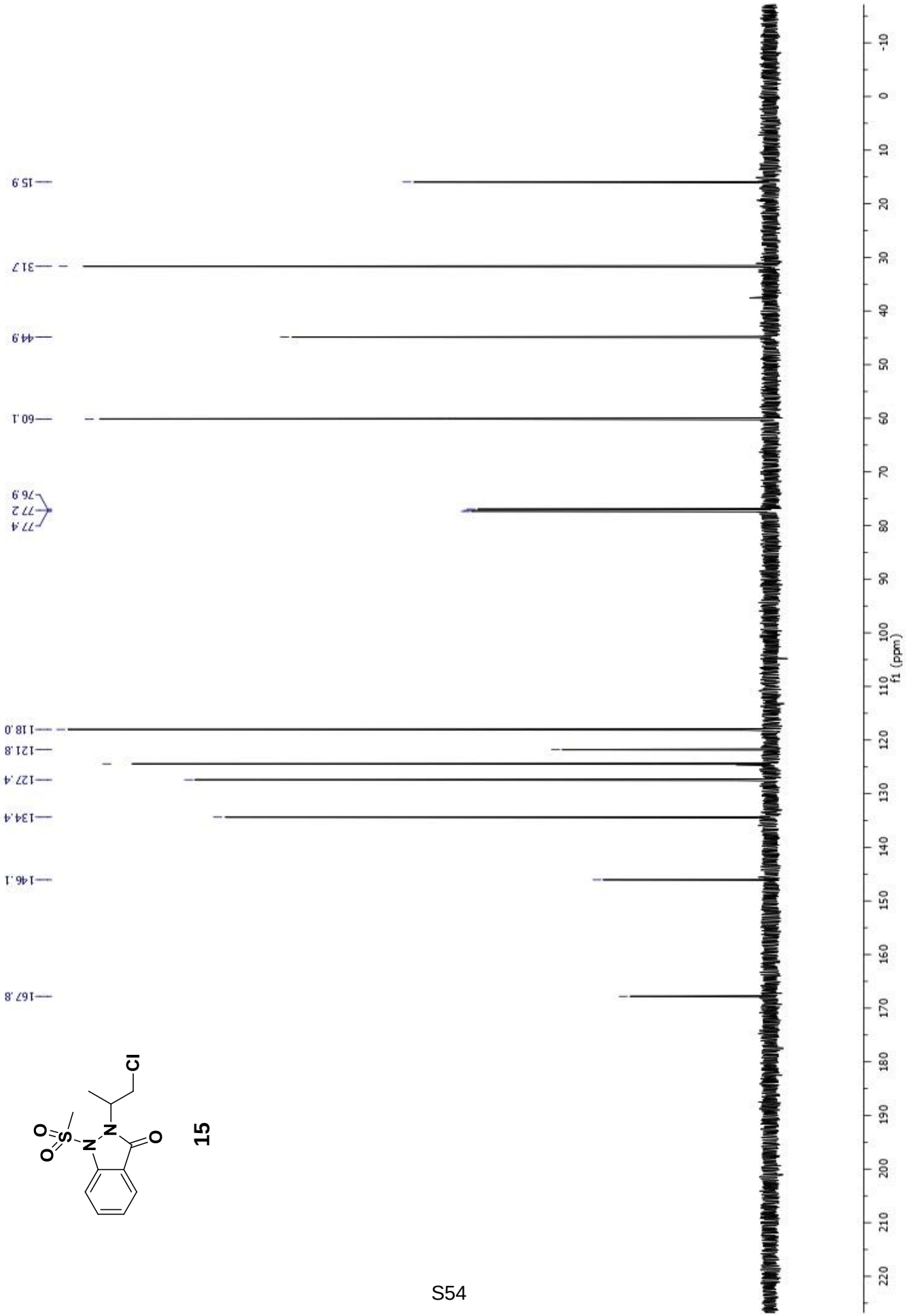
**14**





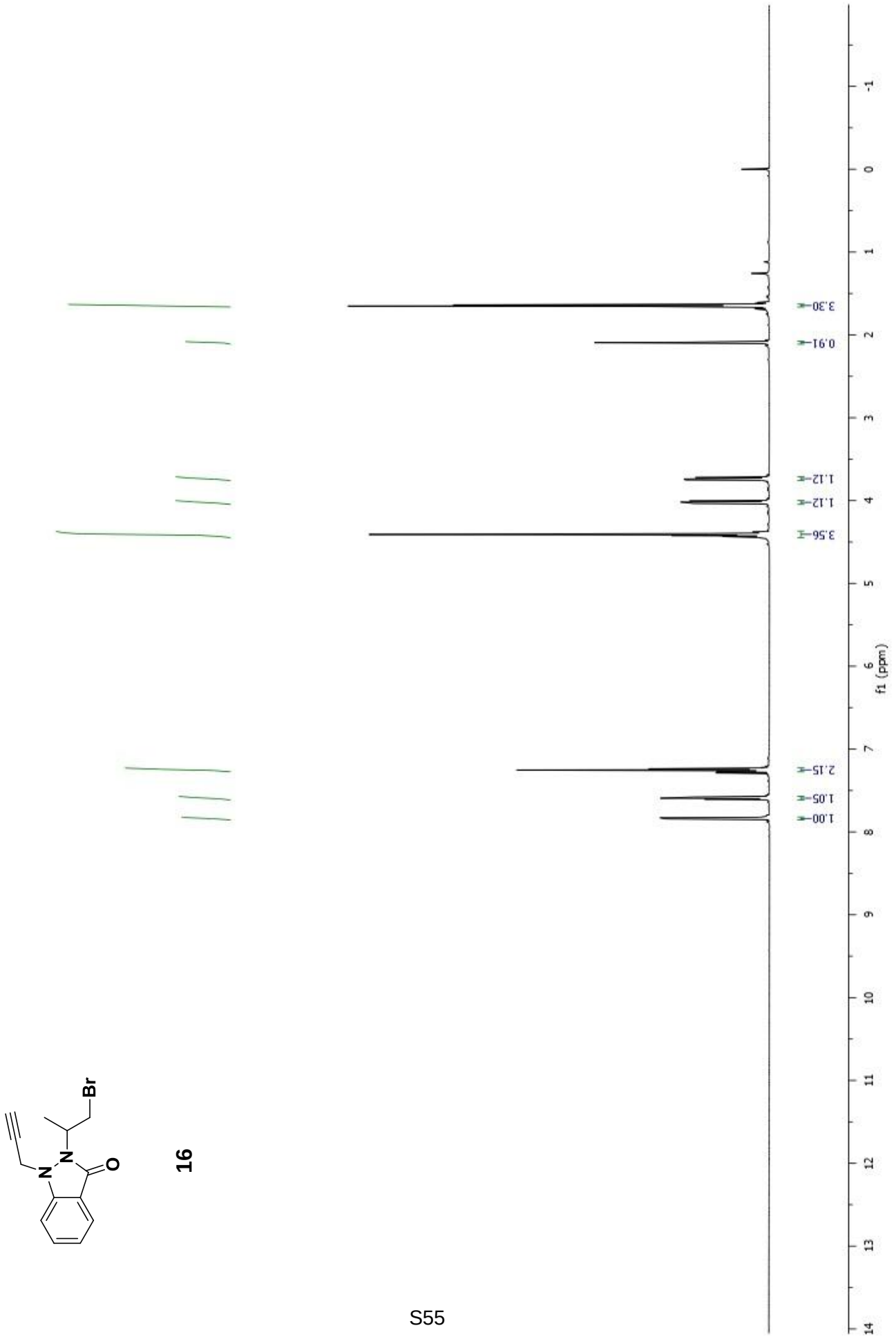


**15**


15.9
31.7
44.9
60.1
76.9
77.2
77.4
118.0
121.8
127.4
134.4
146.1
167.8
f1 (ppm)



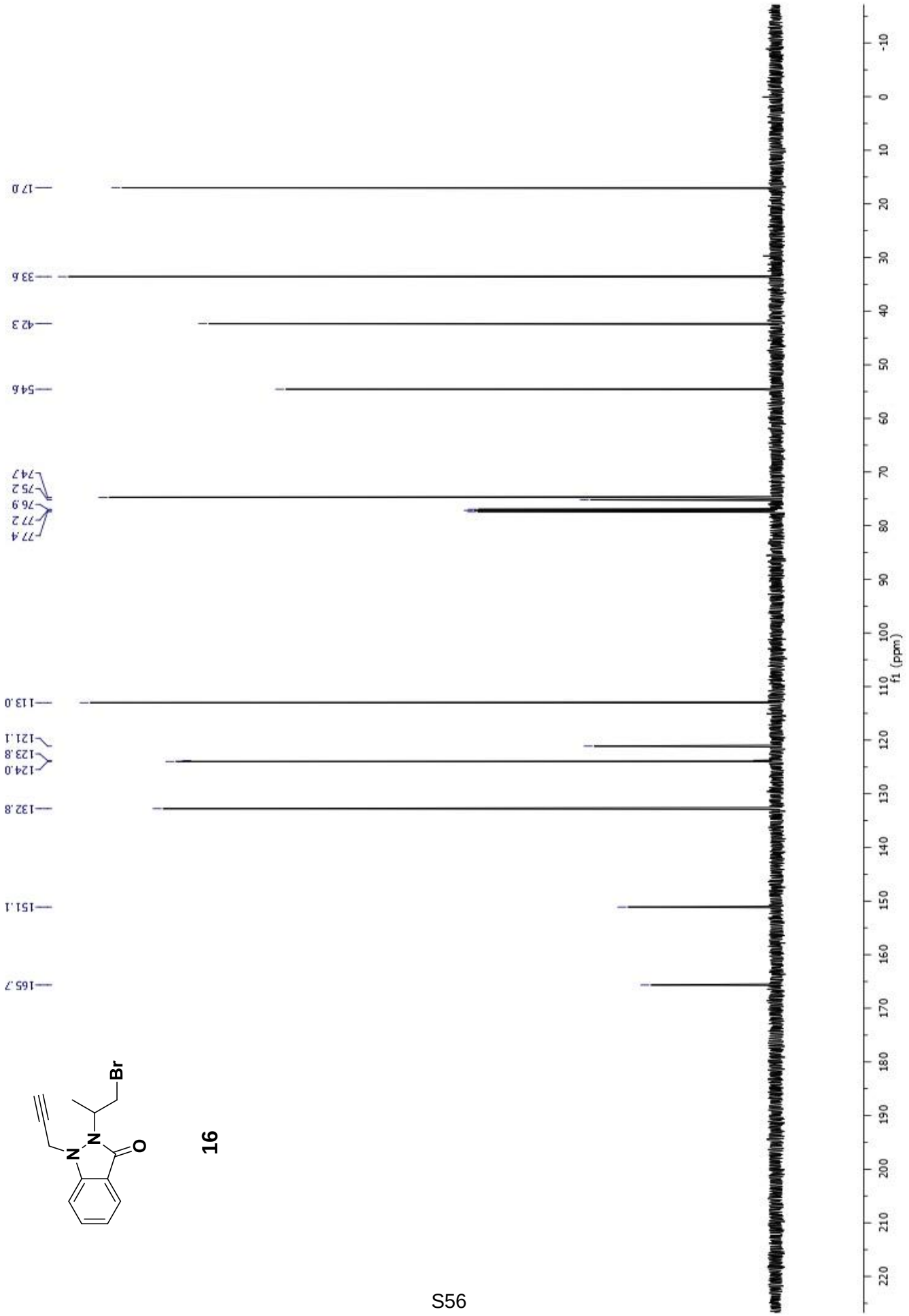
**15**





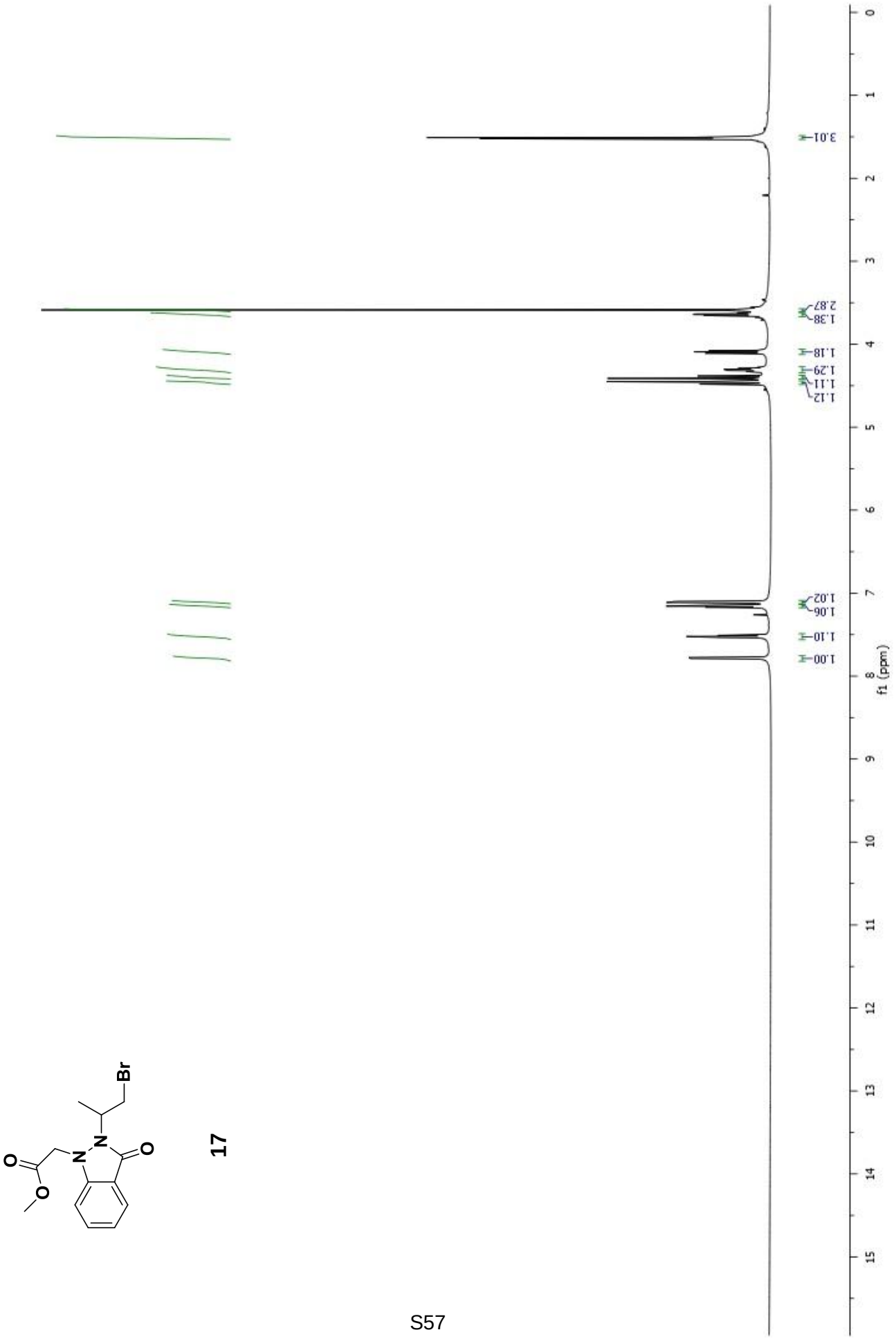


**16**


17.0
33.6
42.3
54.6
77.4
77.2
76.9
75.2
74.7
113.0
121.1
123.8
124.0
132.8
151.1
165.7
f1 (ppm)


Br
N
N
O

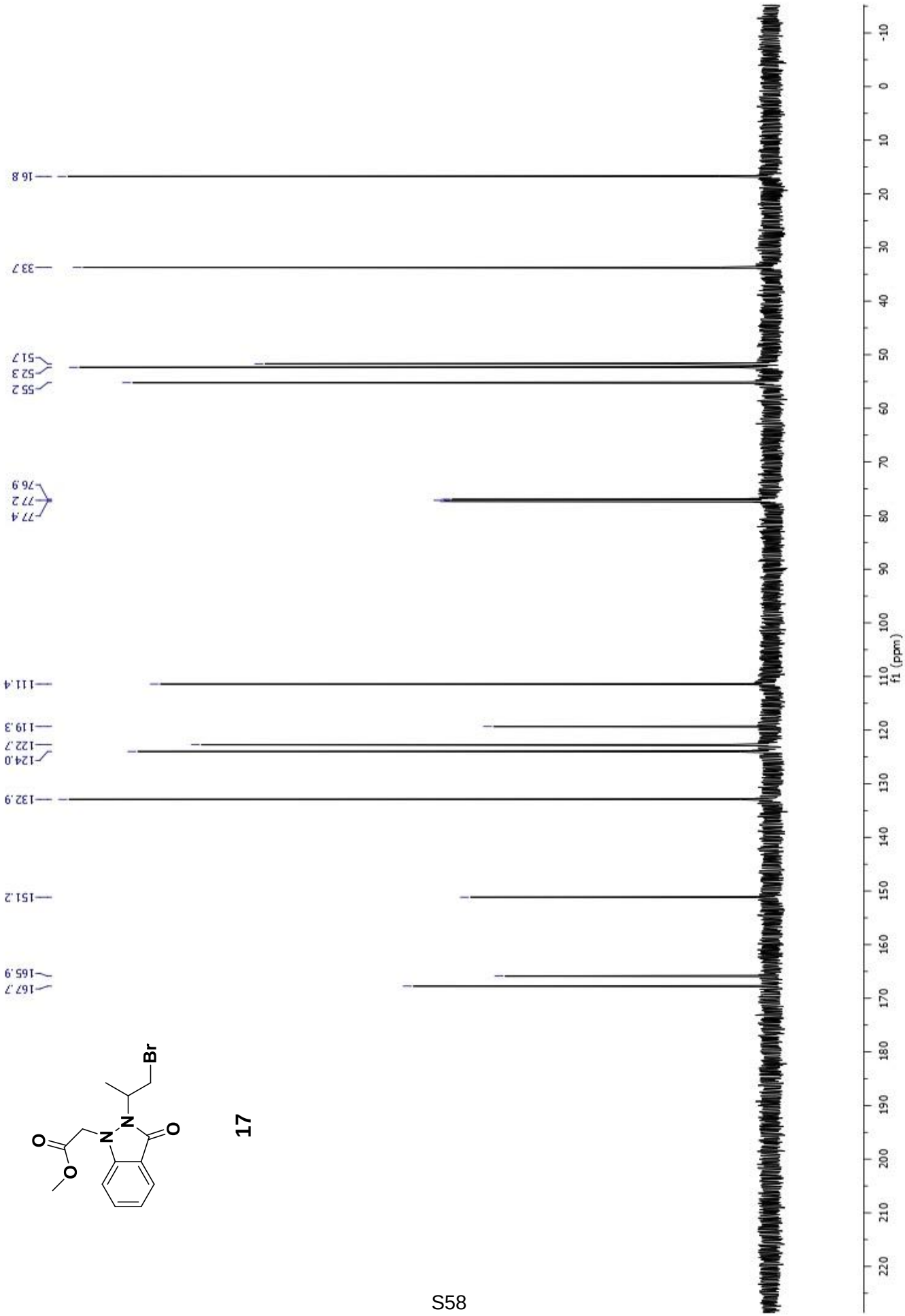
**16**





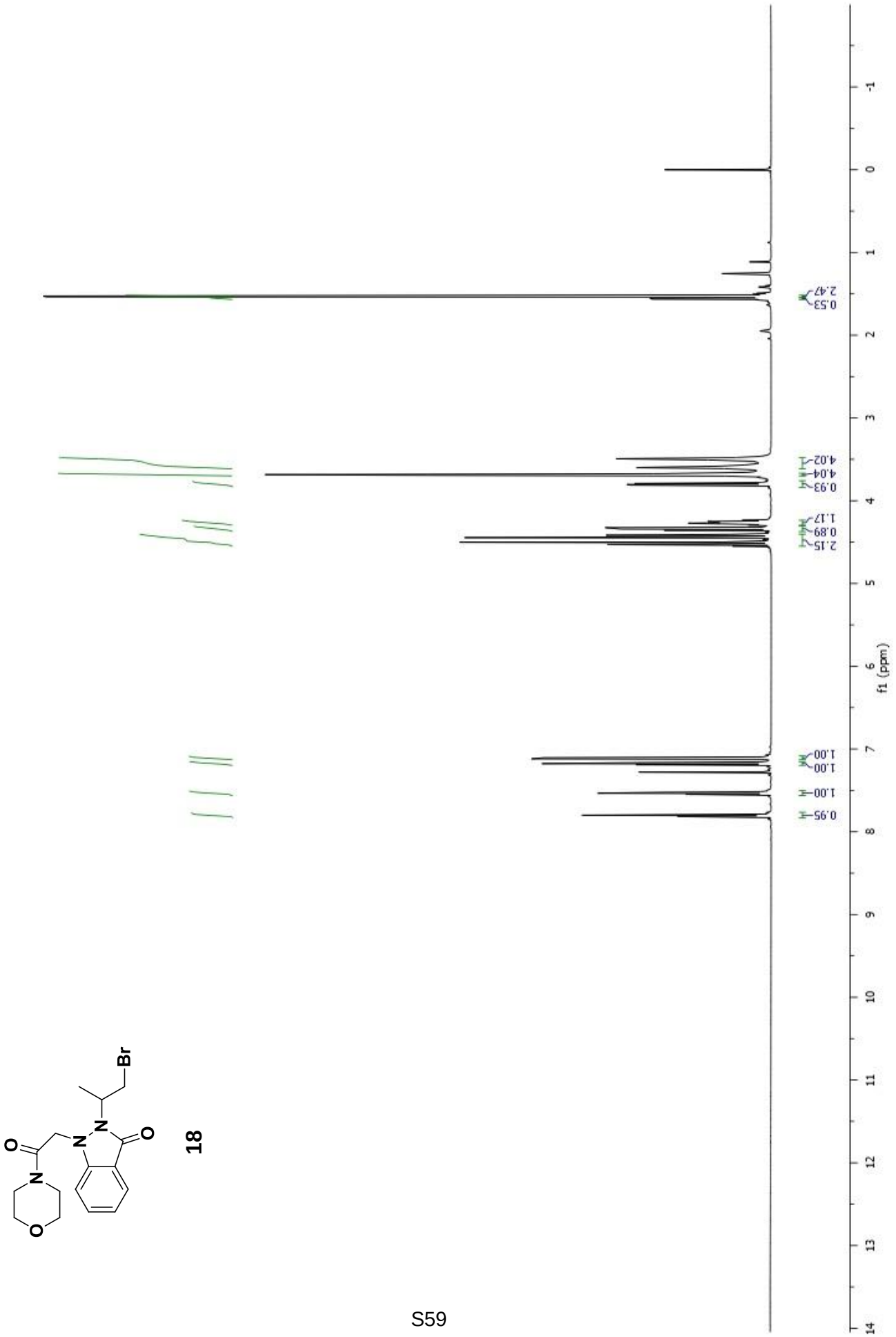


**17**


16.8
33.7
51.7
52.3
55.2
76.9
77.2
77.4
111.4
119.3
122.7
124.0
132.9
151.2
165.9
167.7
f1 (ppm)

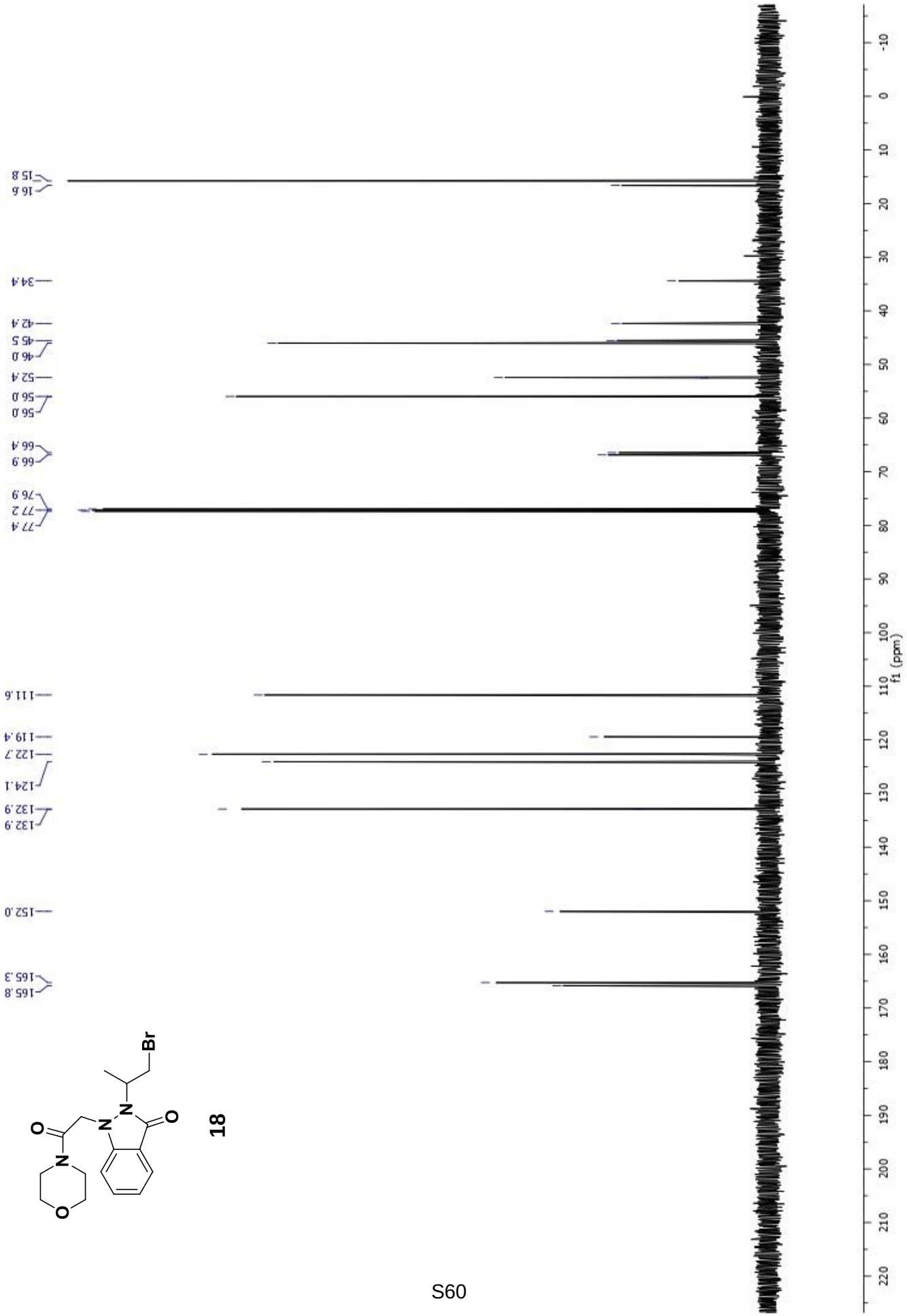

Br
N
N
O
O
O

**17**

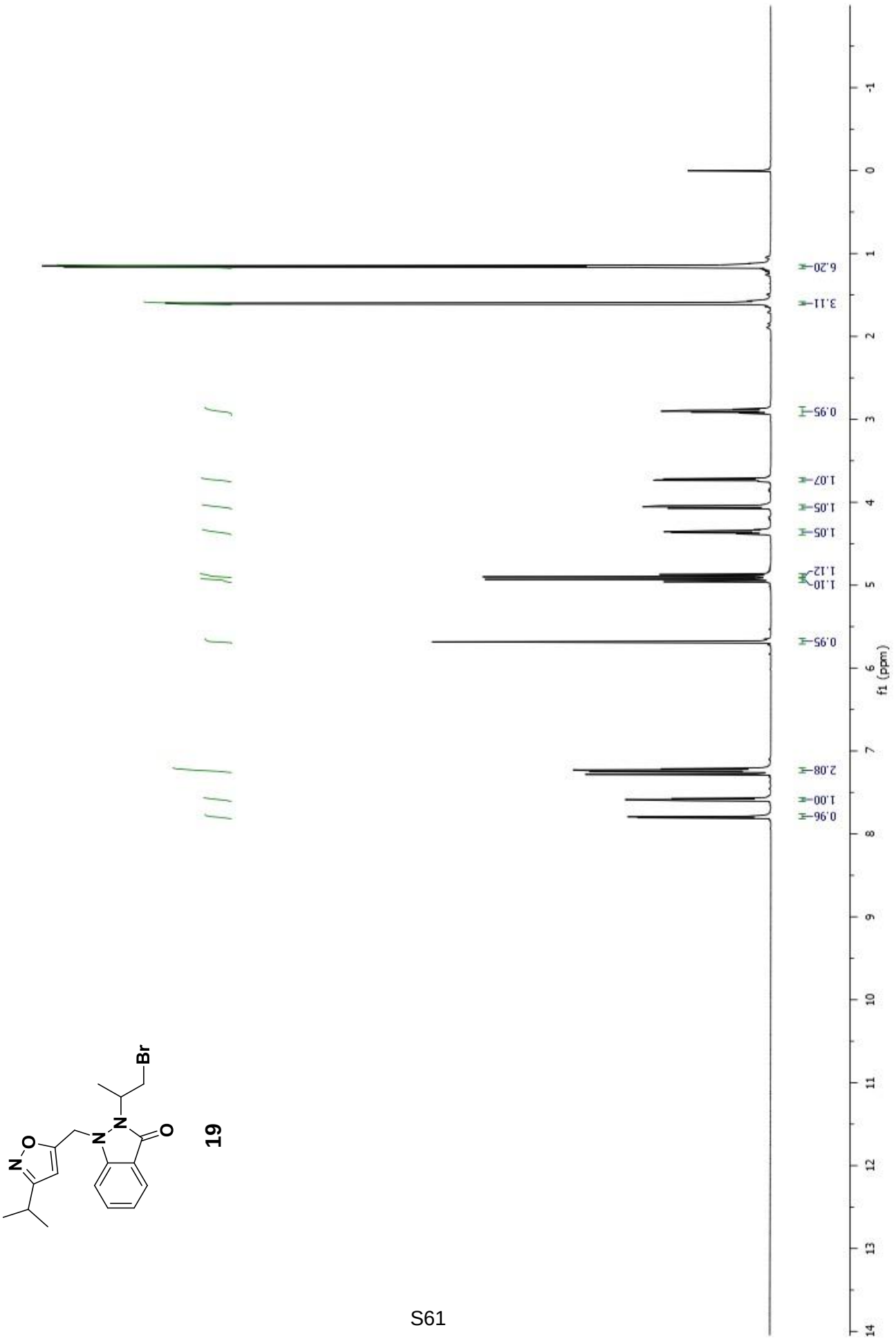





**18**


15.8
16.6
34.4
42.4
45.5
46.0
52.4
56.0
56.0
66.4
66.9
76.9
77.2
77.4
111.6
119.4
122.7
124.1
132.9
132.9
152.0
165.3
165.8
f1 (ppm)
Br
O
N
N
N
O
O

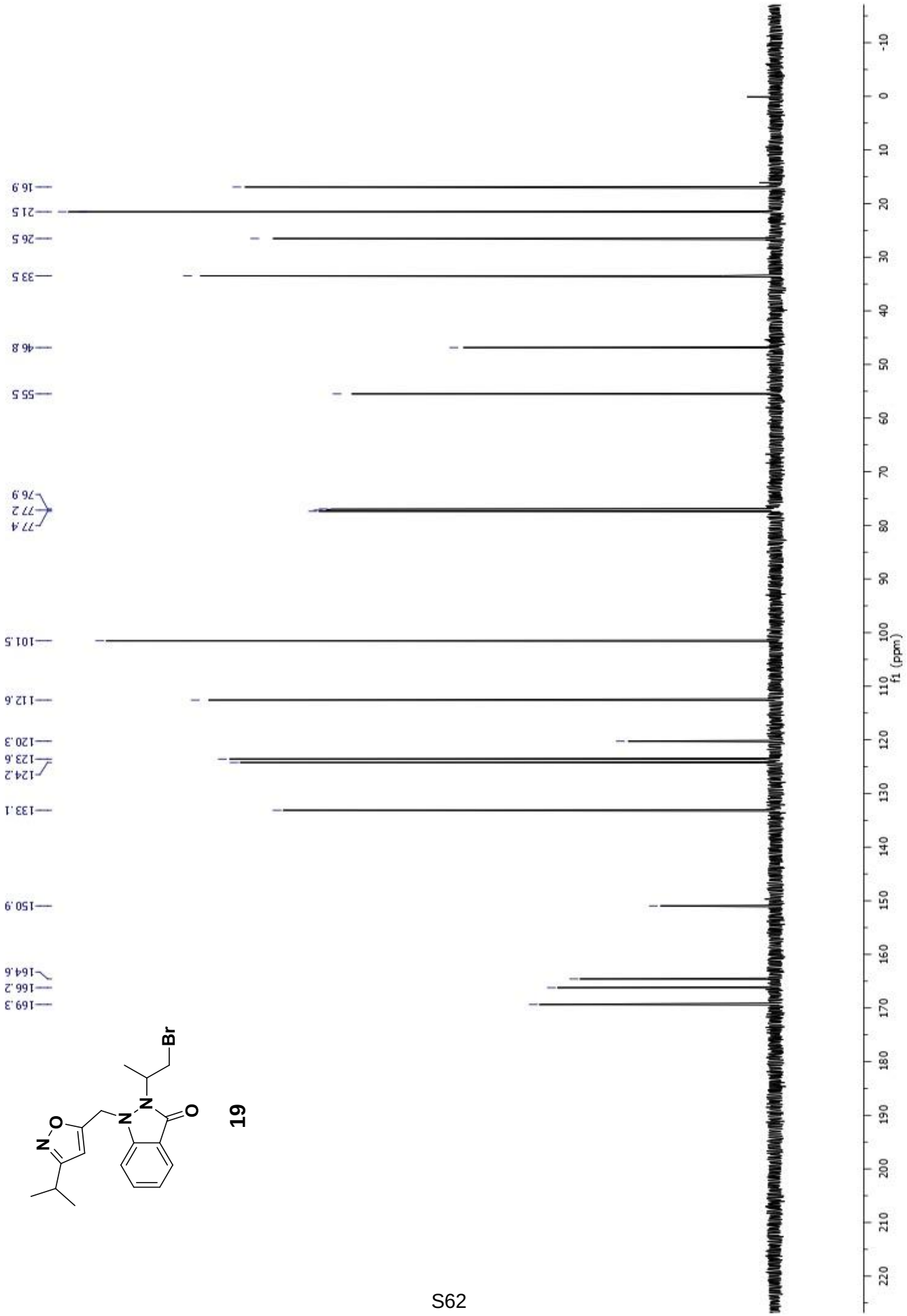
**18**



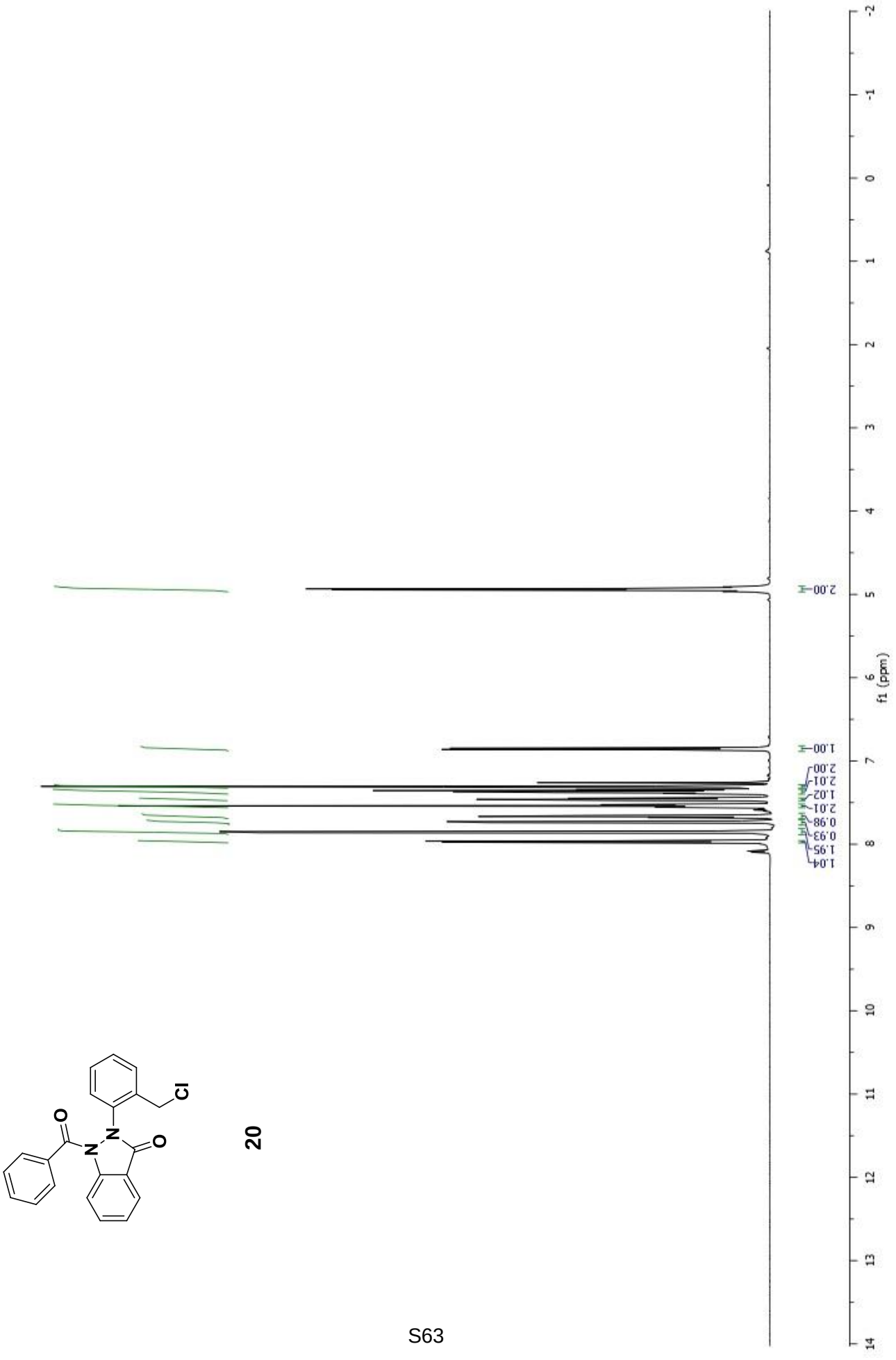




**19**


16.9
21.5
26.5
33.5
46.8
55.5
76.9
77.2
77.4
101.5
112.6
120.3
123.6
124.2
133.1
150.9
164.6
166.2
169.3
f1 (ppm)
Br
O
N
N
N
O

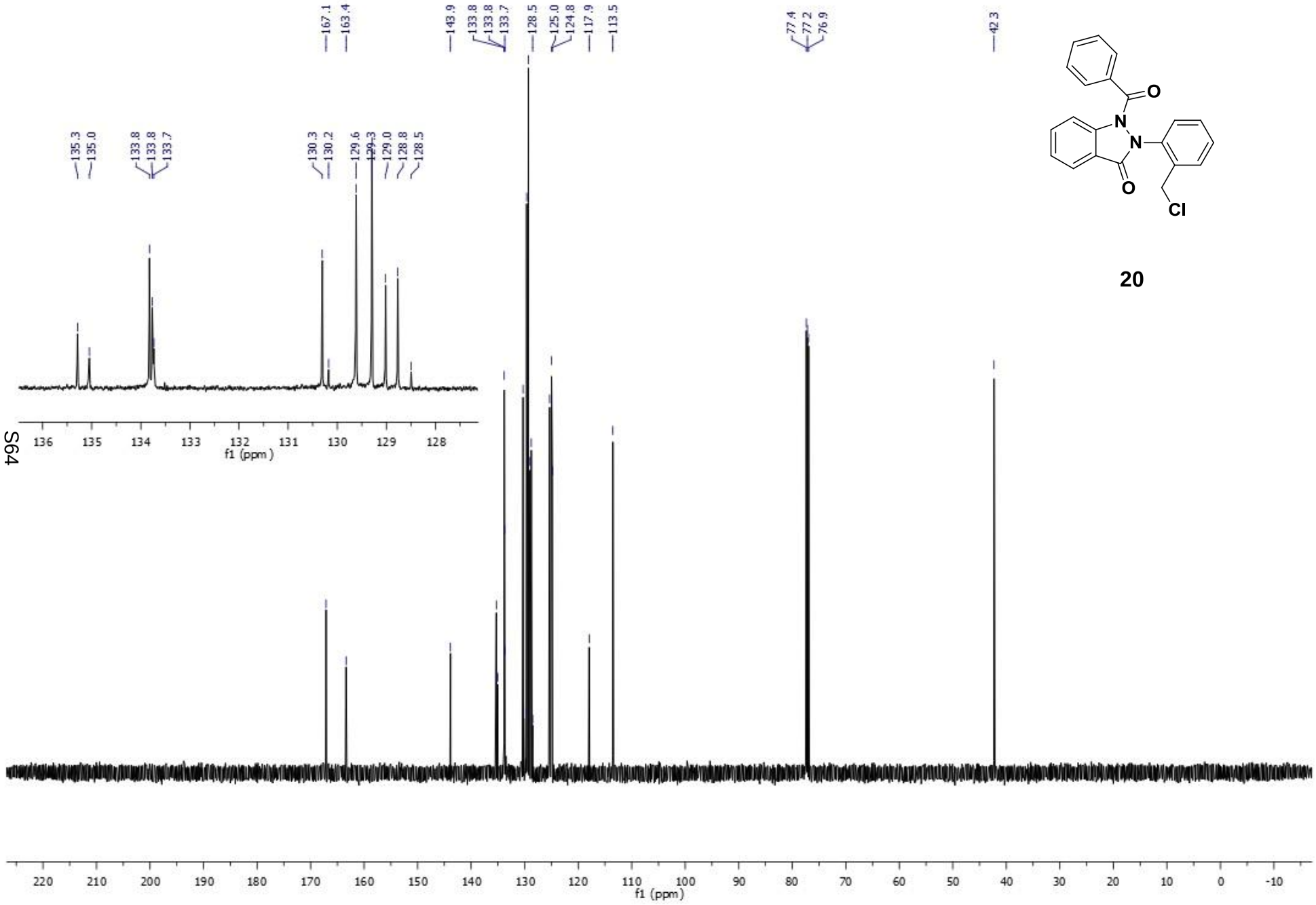
**19**



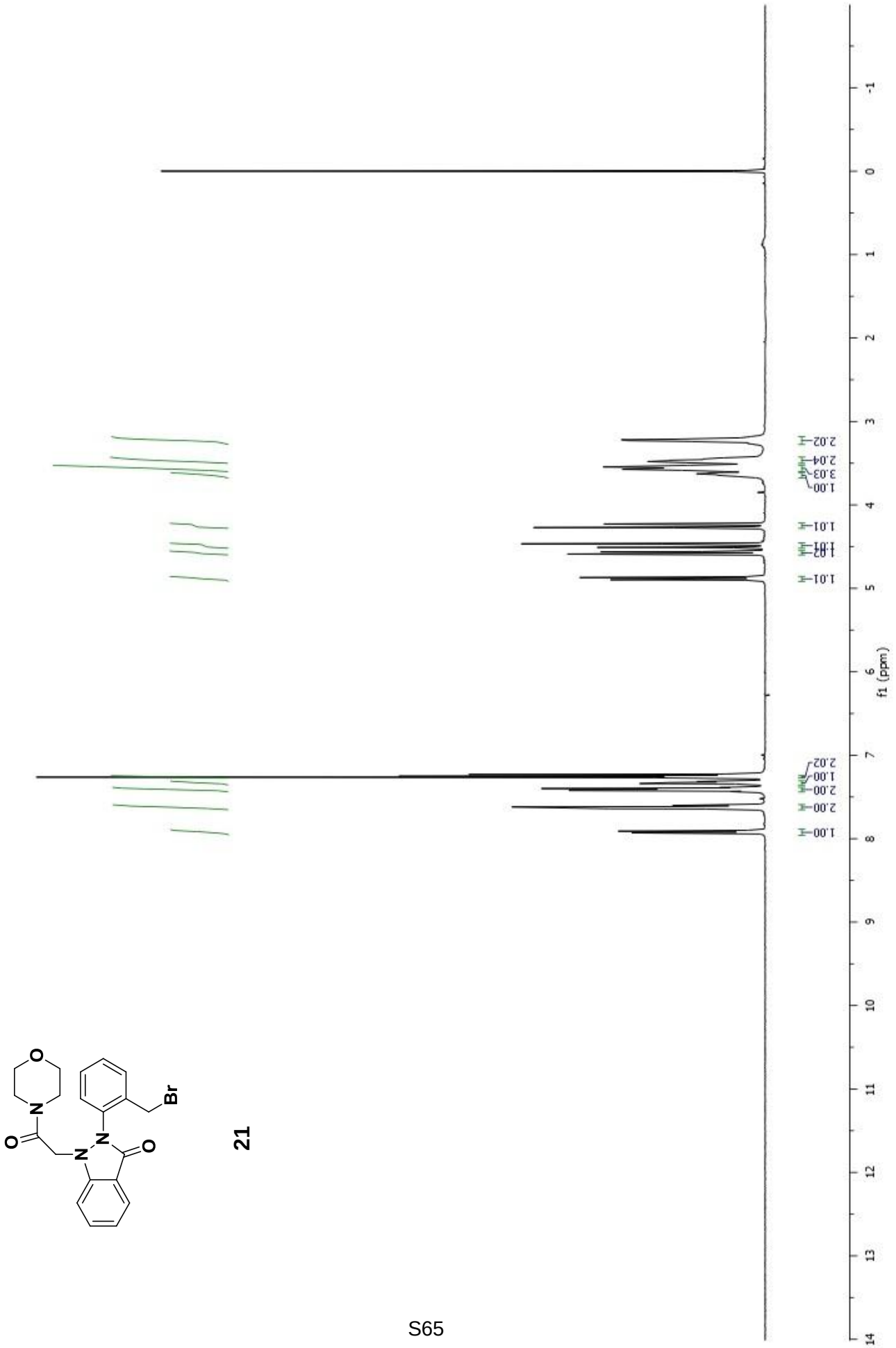




**20**


167.1
163.4
143.9
133.8
133.8
133.7
128.5
125.0
124.8
117.9
113.5
77.4
77.2
76.9
42.3
135.3
135.0
133.8
133.8
133.7
130.3
130.2
129.6
129.3
129.0
128.8
128.5
O
N
N
O
Cl
136
135
134
133
132
131
130
129
128
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

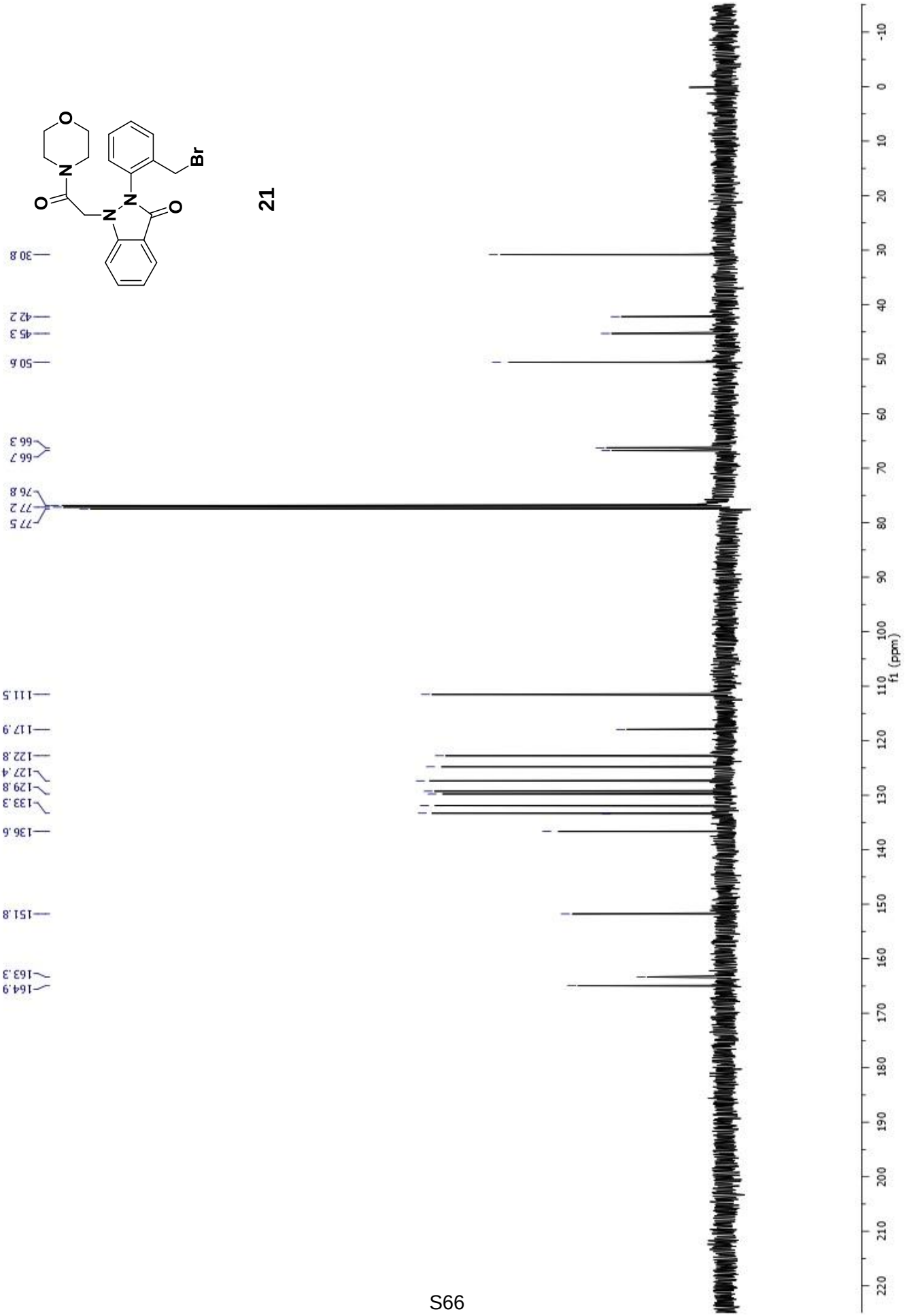
**20**

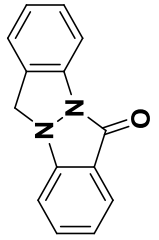




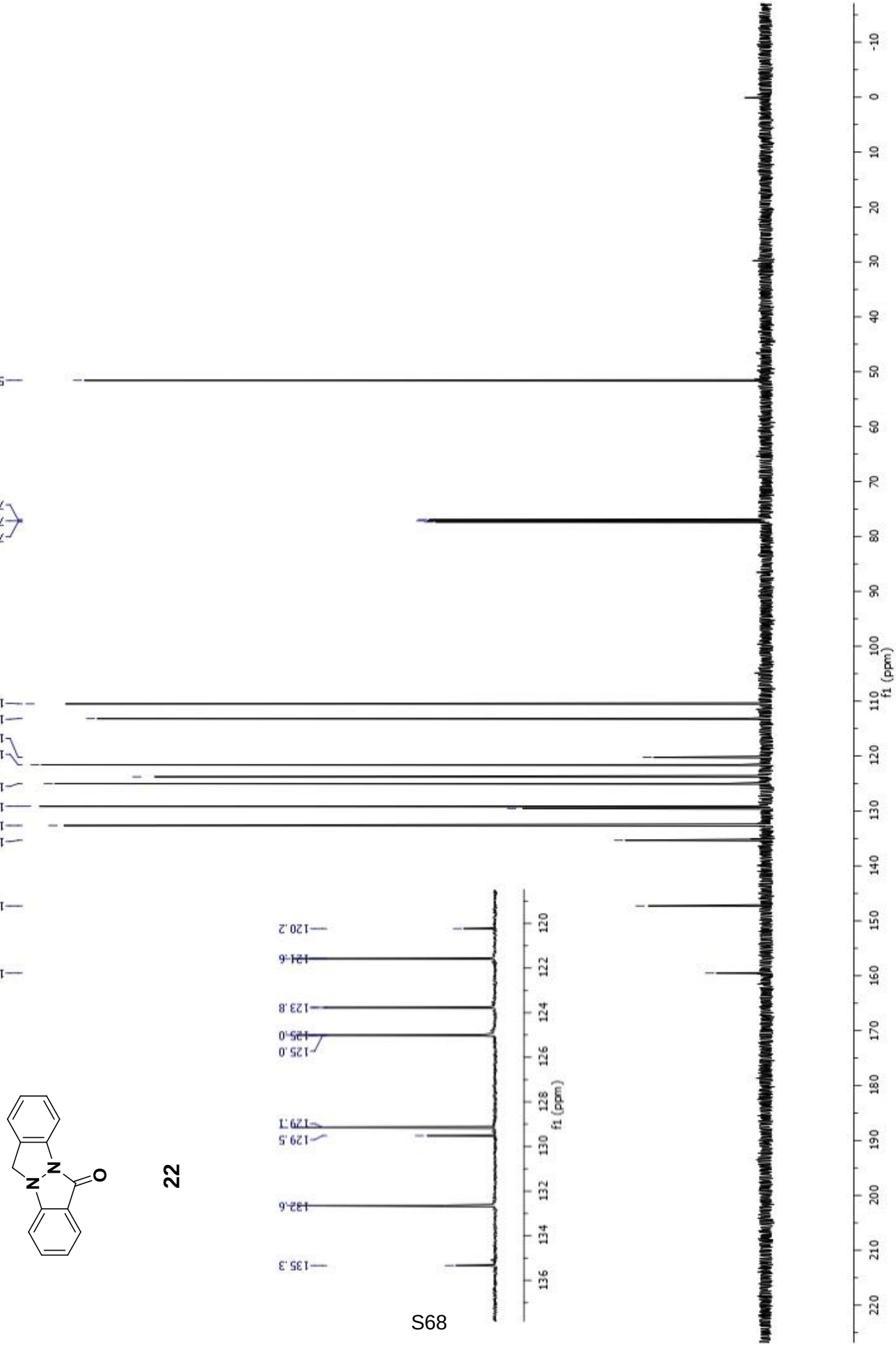


**21**


21
Br
O
N
O
N
N
O
30.8
42.2
45.3
50.6
66.3
66.7
76.8
77.2
77.5
111.5
117.9
122.8
127.4
129.8
133.3
136.6
151.8
163.3
164.9
f1 (ppm)

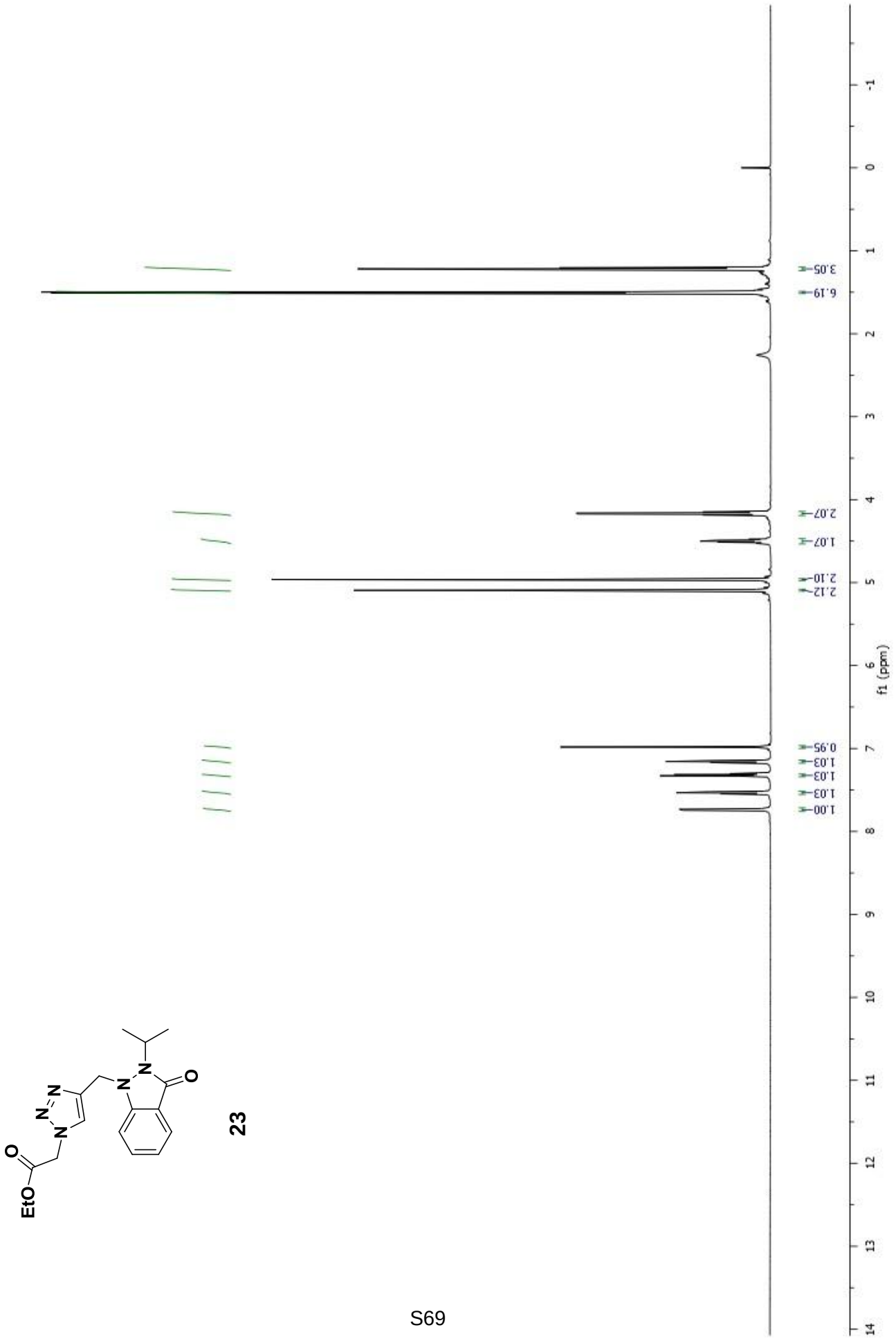


**22**


51.6
77.4
77.2
76.9
110.5
113.2
120.2
121.6
125.0
129.1
132.6
135.3
147.3
159.5
f1 (ppm)
120.2
121.6
123.8
125.0
125.0
129.1
129.5
132.6
135.3
f1 (ppm)



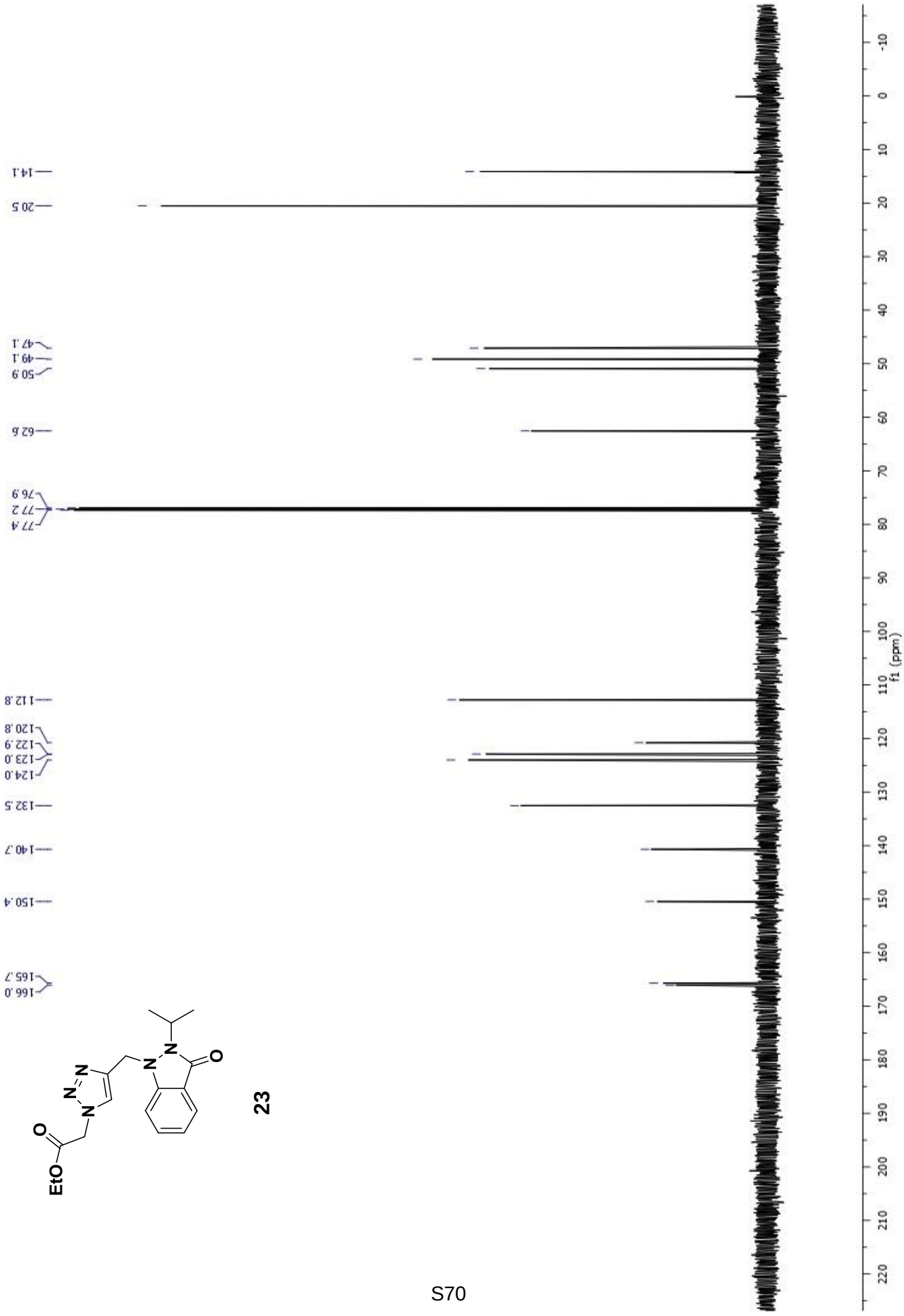
**22**



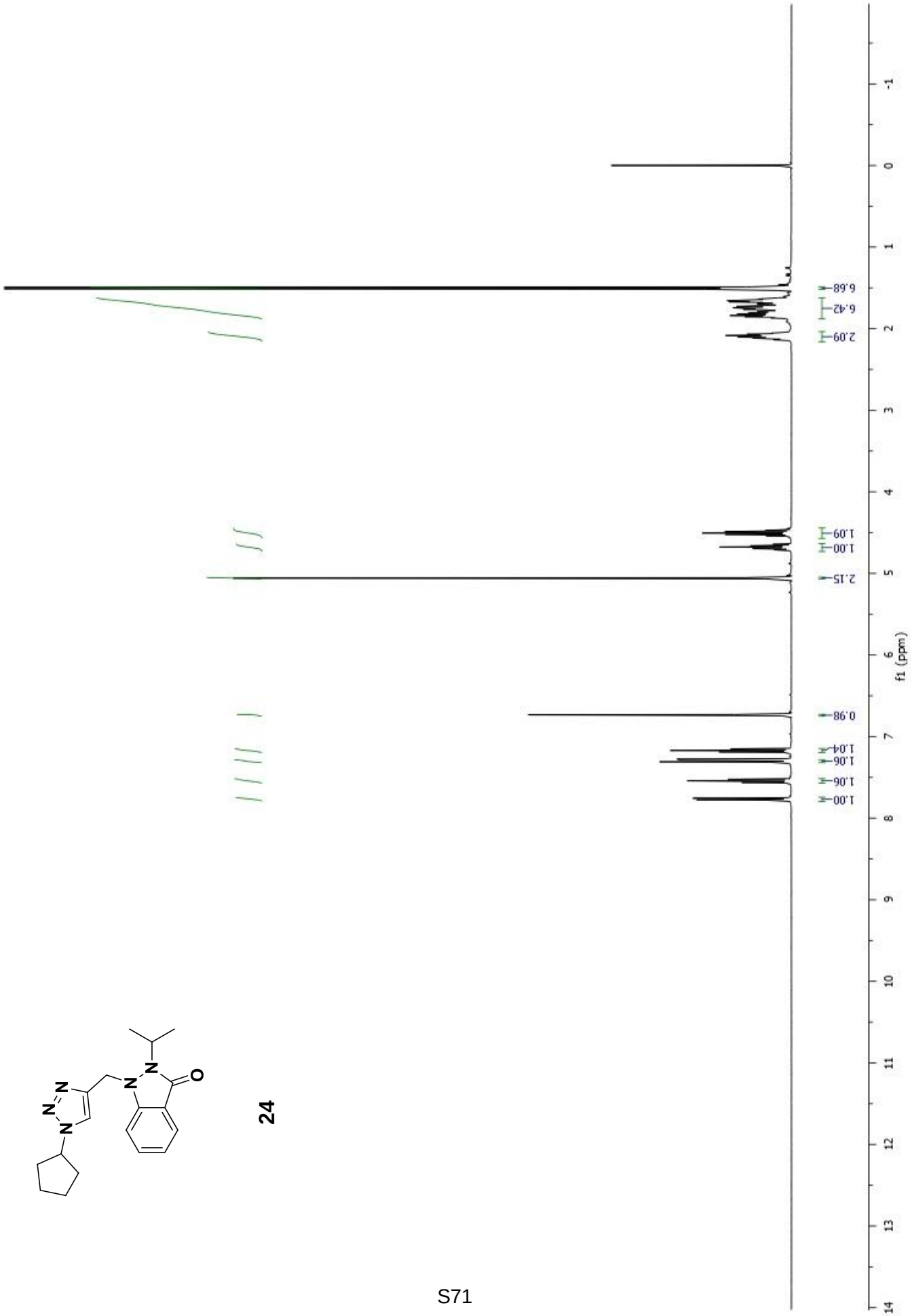




**23**

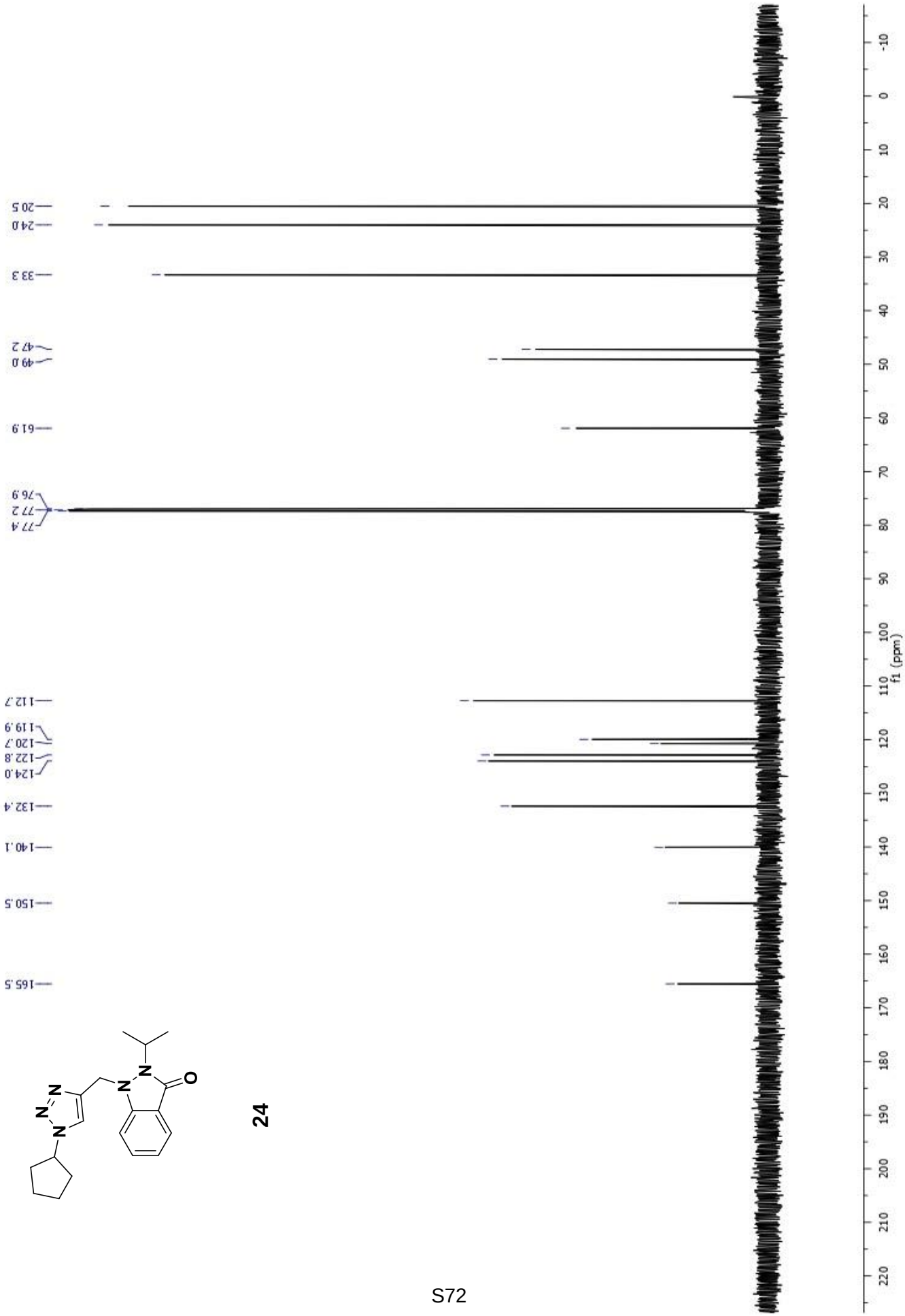

14.1
20.5
47.1
49.1
50.9
62.6
76.9
77.2
77.4
112.8
120.8
122.9
123.0
124.0
132.5
140.7
150.4
165.7
166.0
f1 (ppm)
EtO
O
N
N
N
N
O

23

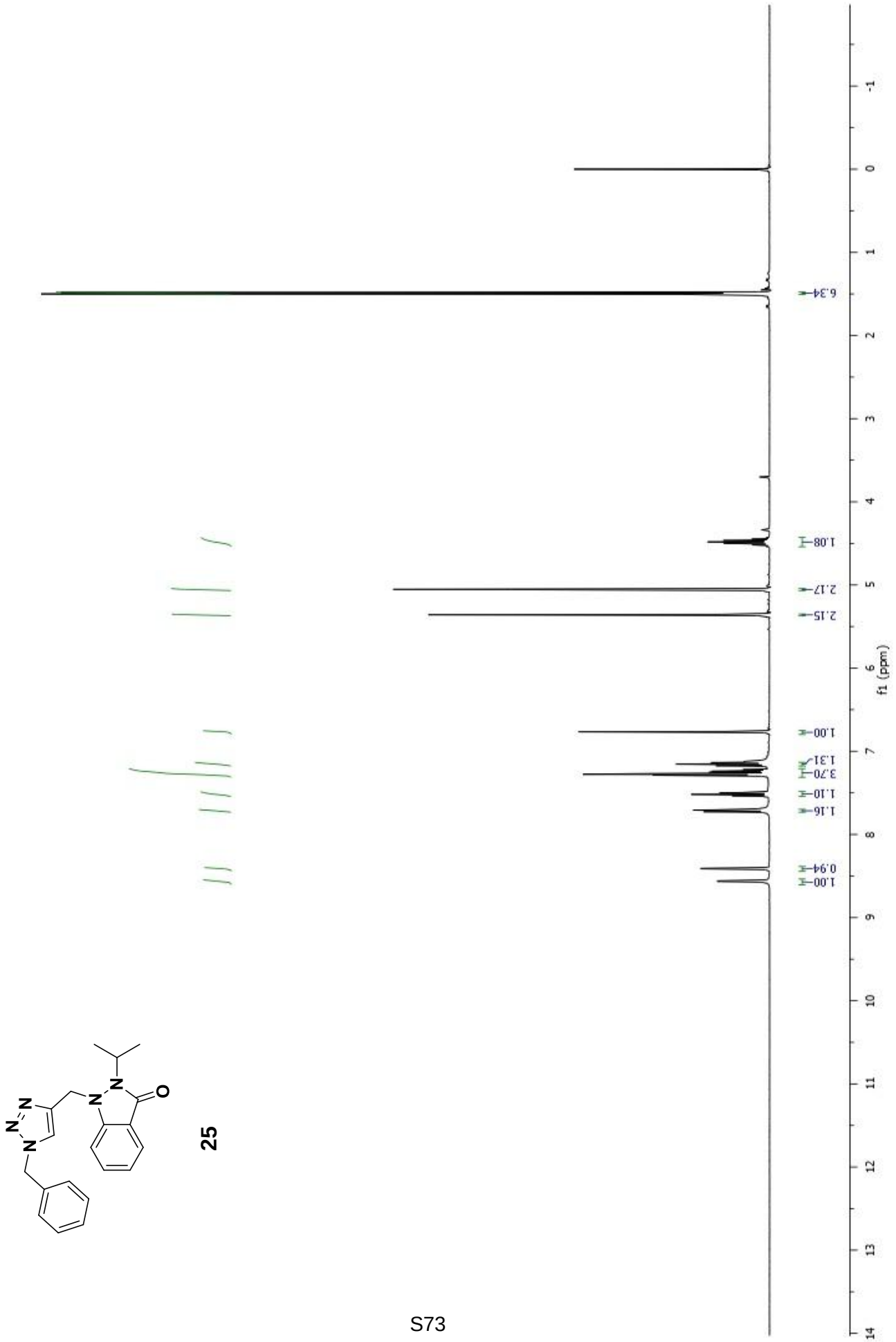





**24**

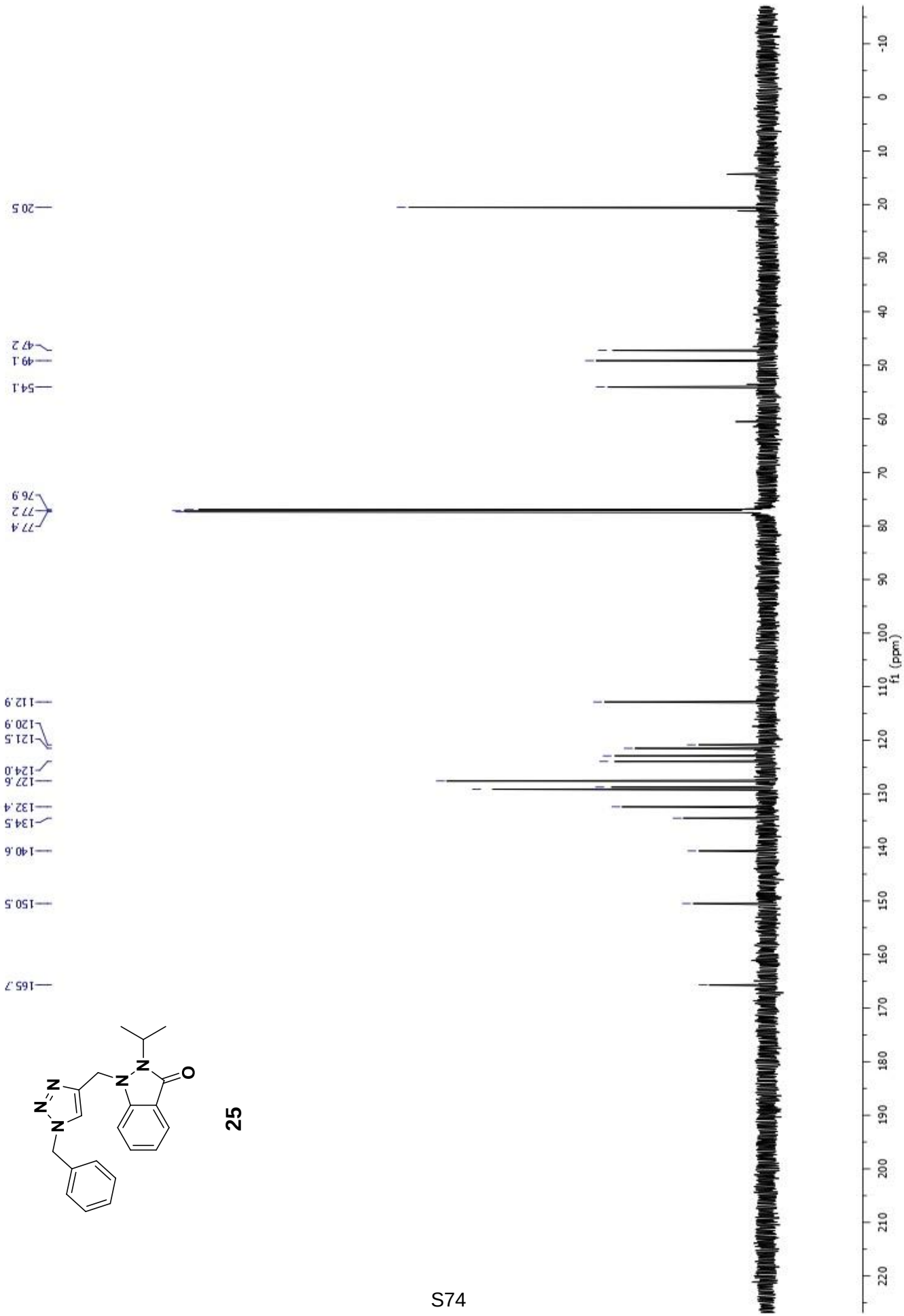

20.5
24.0
33.3
47.2
49.0
61.9
76.9
77.2
77.4
112.7
119.9
120.7
122.8
124.0
132.4
140.1
150.5
165.5
f1 (ppm)

**24**

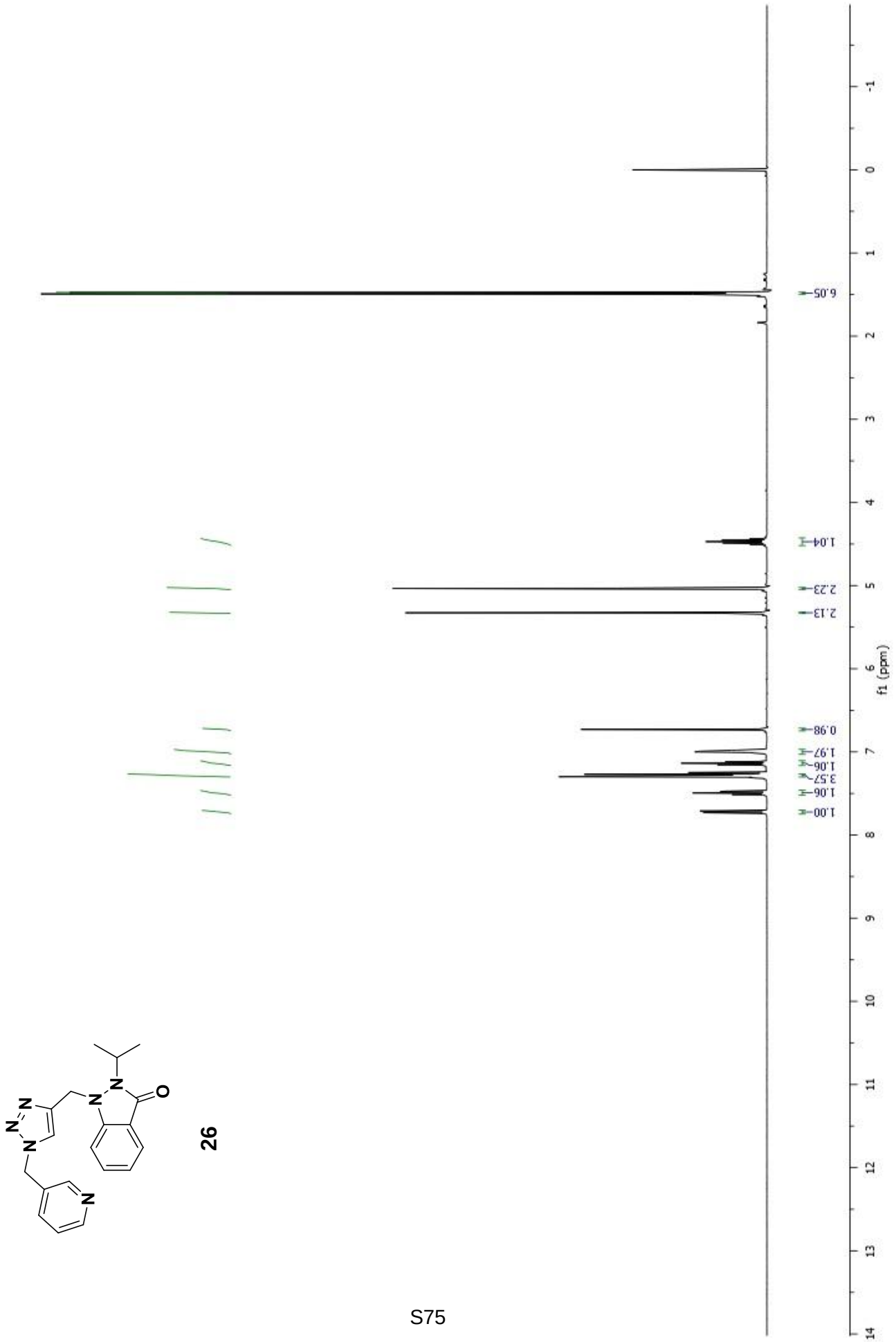





**25**

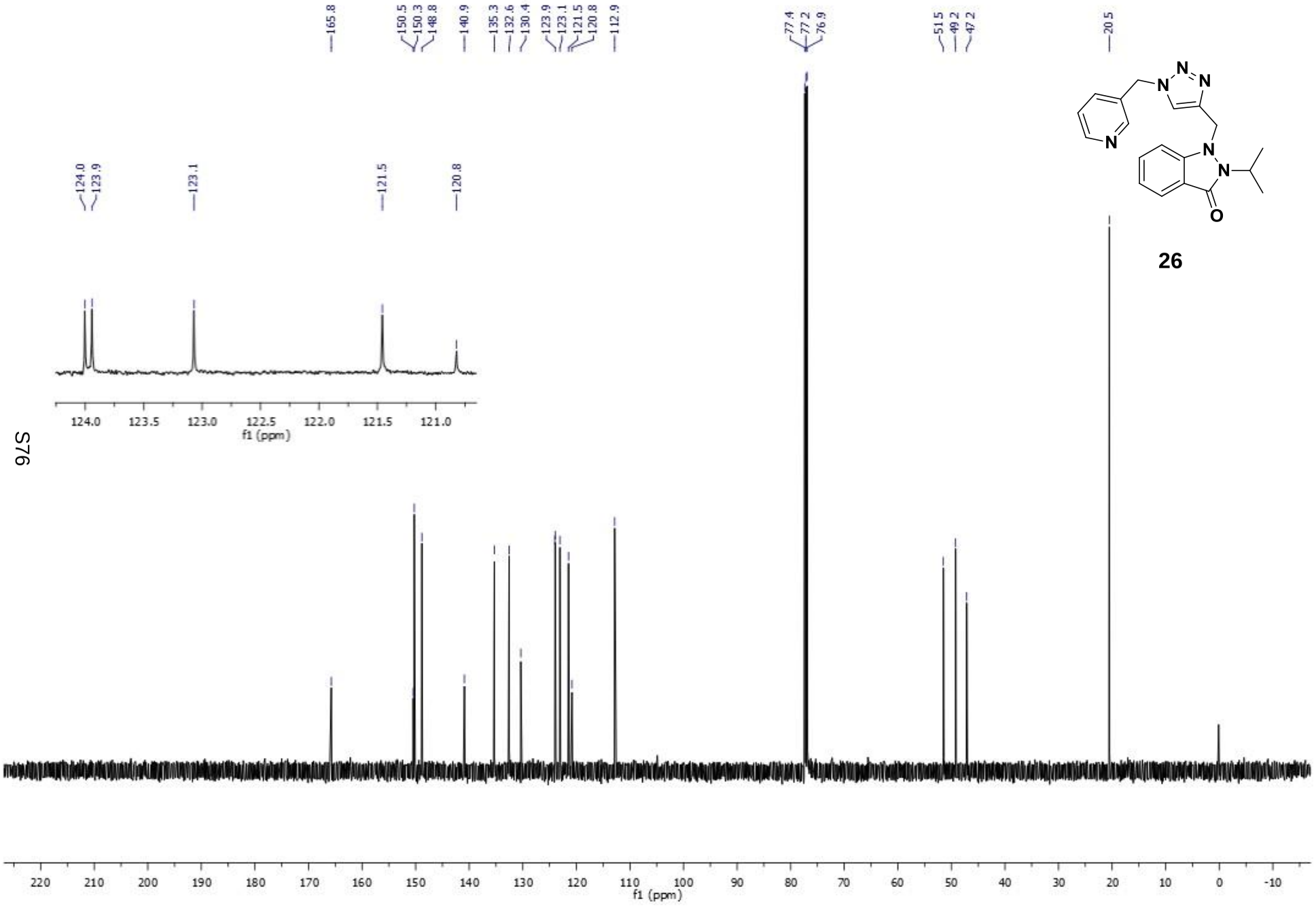

20.5
47.2
49.1
54.1
76.9
77.2
77.4
112.9
120.9
121.5
124.0
127.6
132.4
134.5
140.6
150.5
165.7
f1 (ppm)

**25**

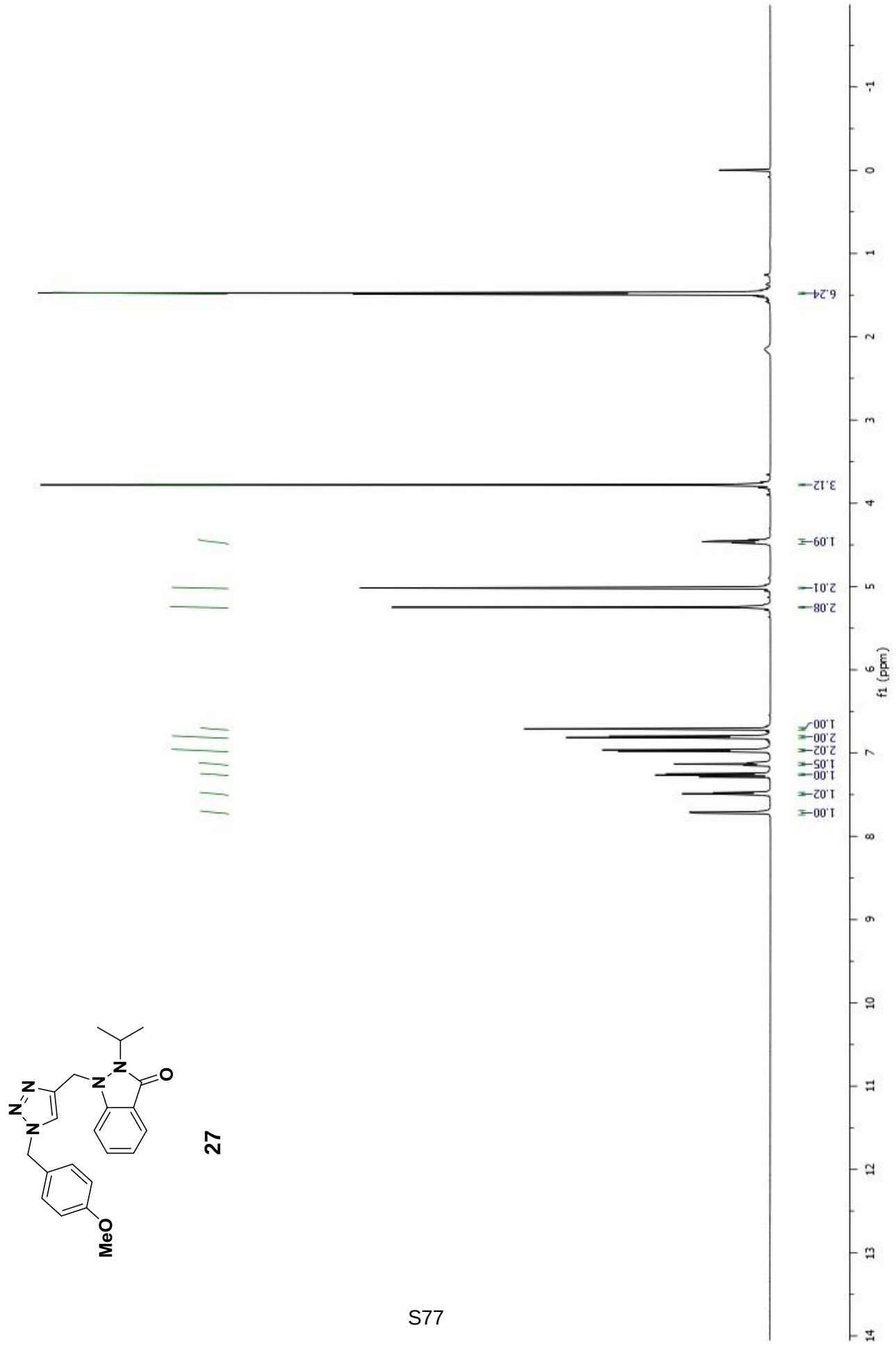




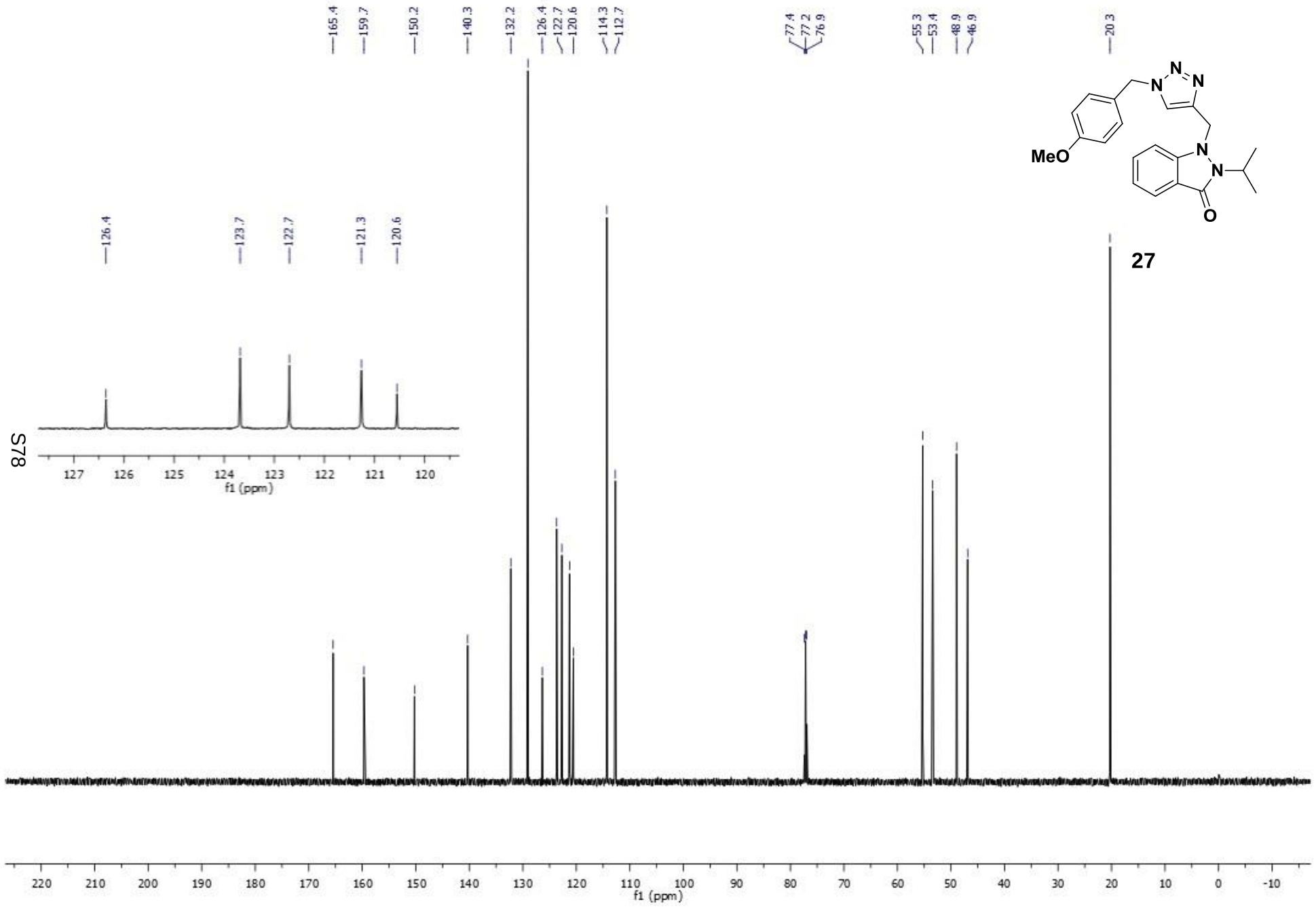

**26**

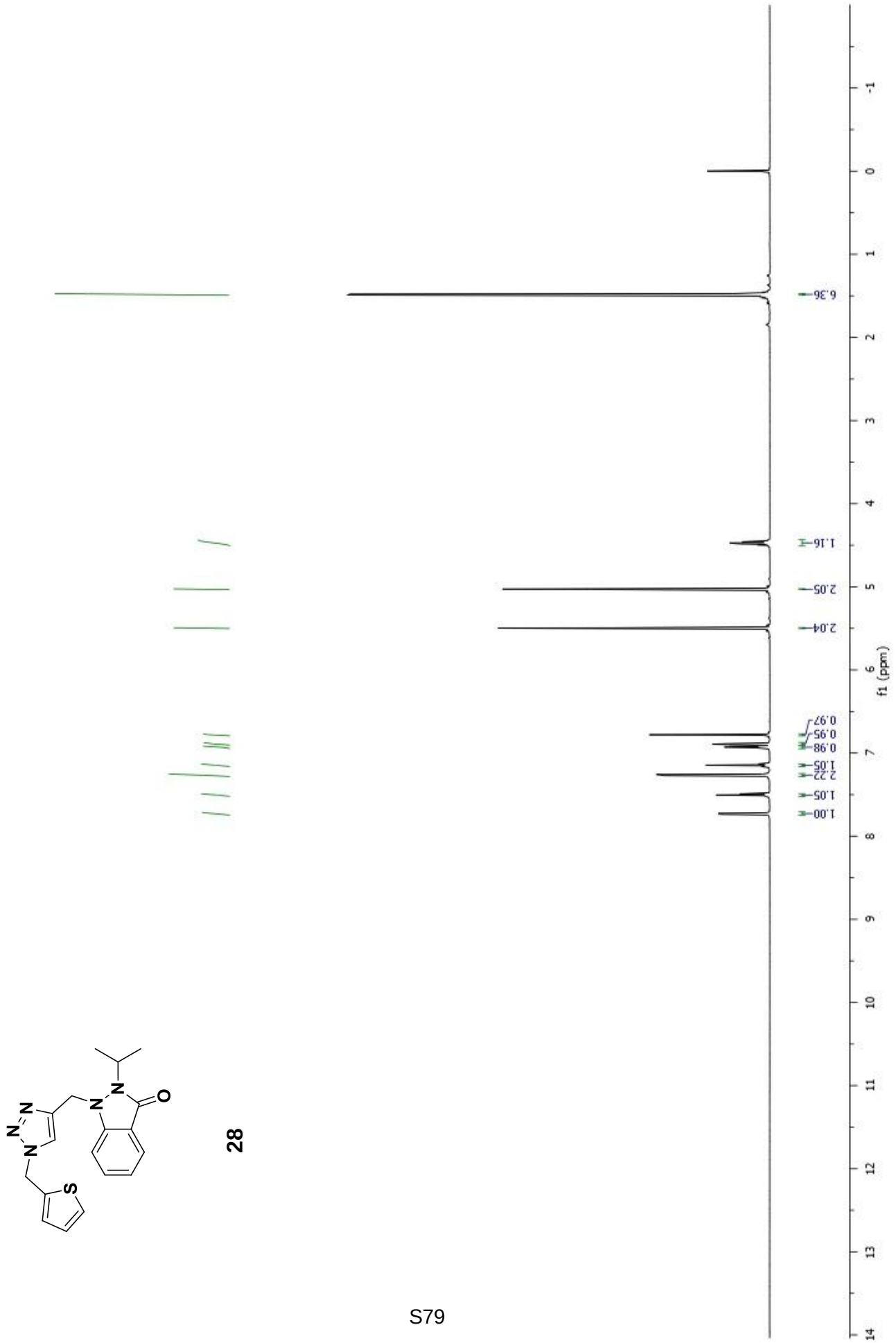

165.8
150.5
150.3
148.8
140.9
135.3
132.6
130.4
123.9
123.1
121.5
120.8
112.9
77.4
77.2
76.9
51.5
49.2
47.2
20.5
124.0
123.9
123.1
121.5
120.8
124.0 123.5 123.0 122.5 122.0 121.5 121.0
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
N
N
N
N
N
O

**26**


6.24
3.12
1.09
2.01
2.08
1.00
2.00
2.02
1.05
1.00
1.02
1.00
f1 (ppm)
MeO
O
N
N
N
N
N

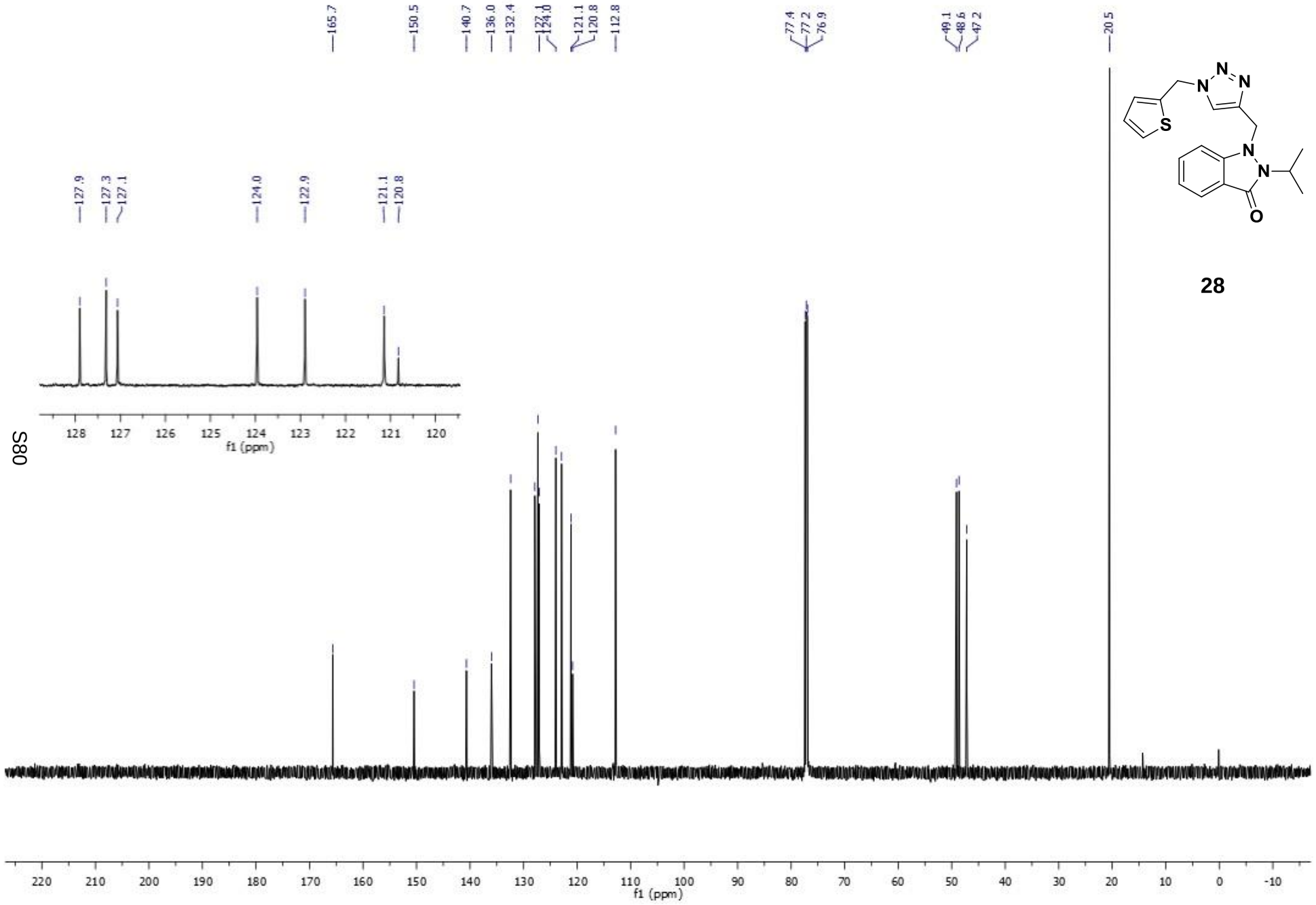
**27**

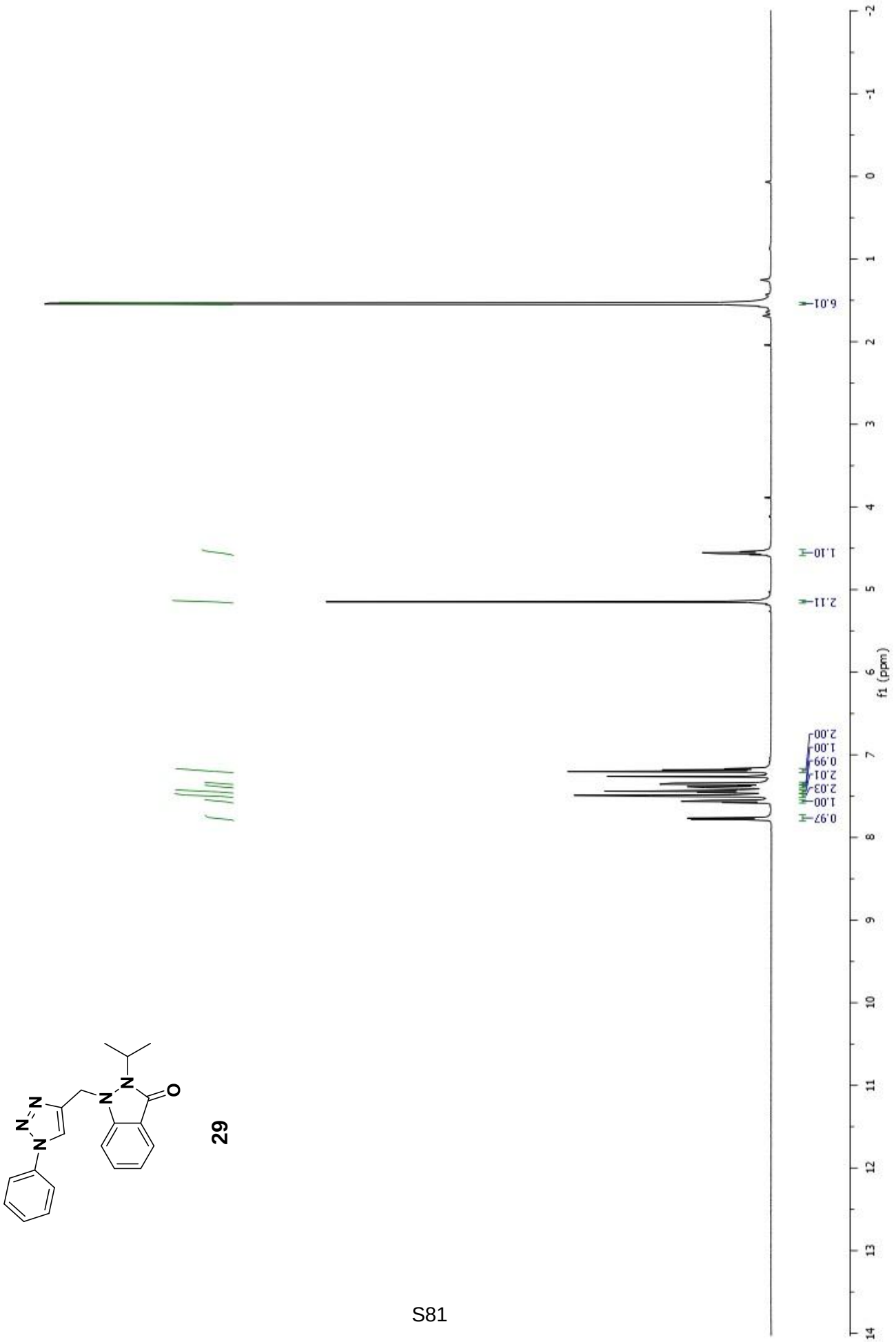

165.4
159.7
150.2
140.3
132.2
126.4
122.7
120.6
114.3
112.7
77.4
77.2
76.9
55.3
53.4
48.9
46.9
20.3
MeO
N
N
N
N
O
27
126.4
123.7
122.7
121.3
120.6
127
126
125
124
123
122
121
120
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)





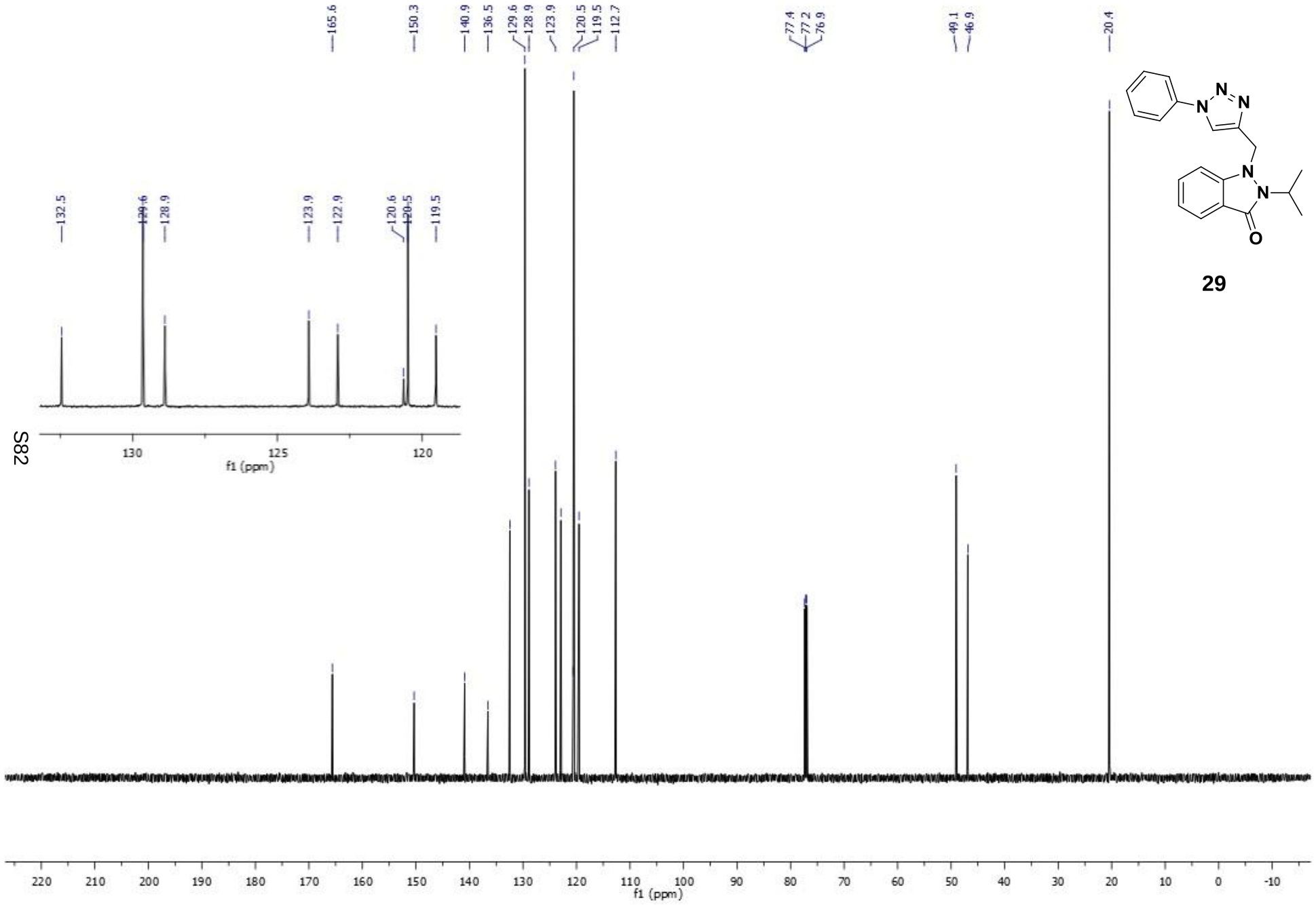

**28**


165.7
150.5
140.7
136.0
132.4
127.1
124.0
121.1
120.8
112.8
77.4
77.2
76.9
49.1
48.6
47.2
20.5
127.9
127.3
127.1
124.0
122.9
121.1
120.8
128
127
126
125
124
123
122
121
120
f1 (ppm)
S
N
N
N
N
O
28
S80
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

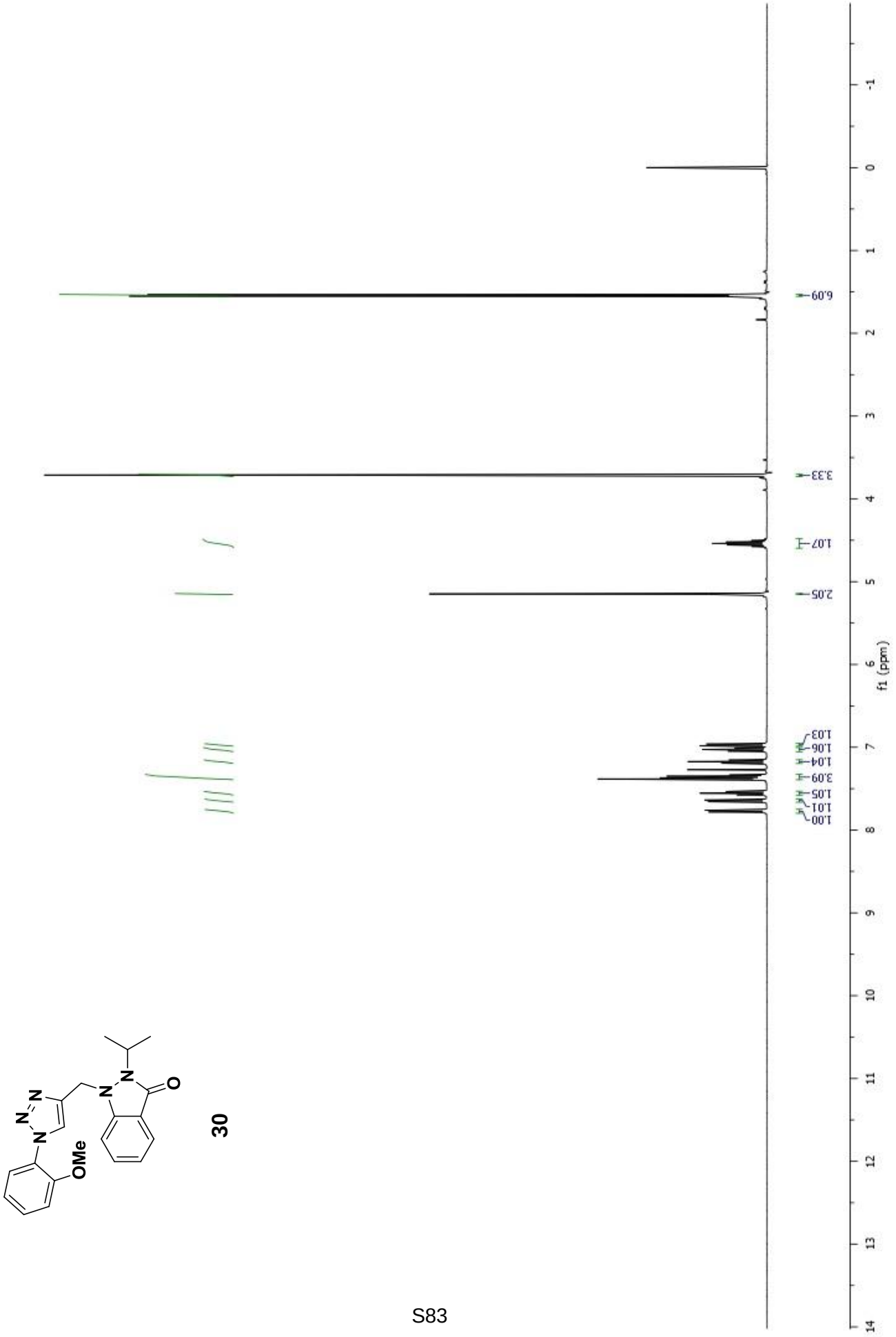




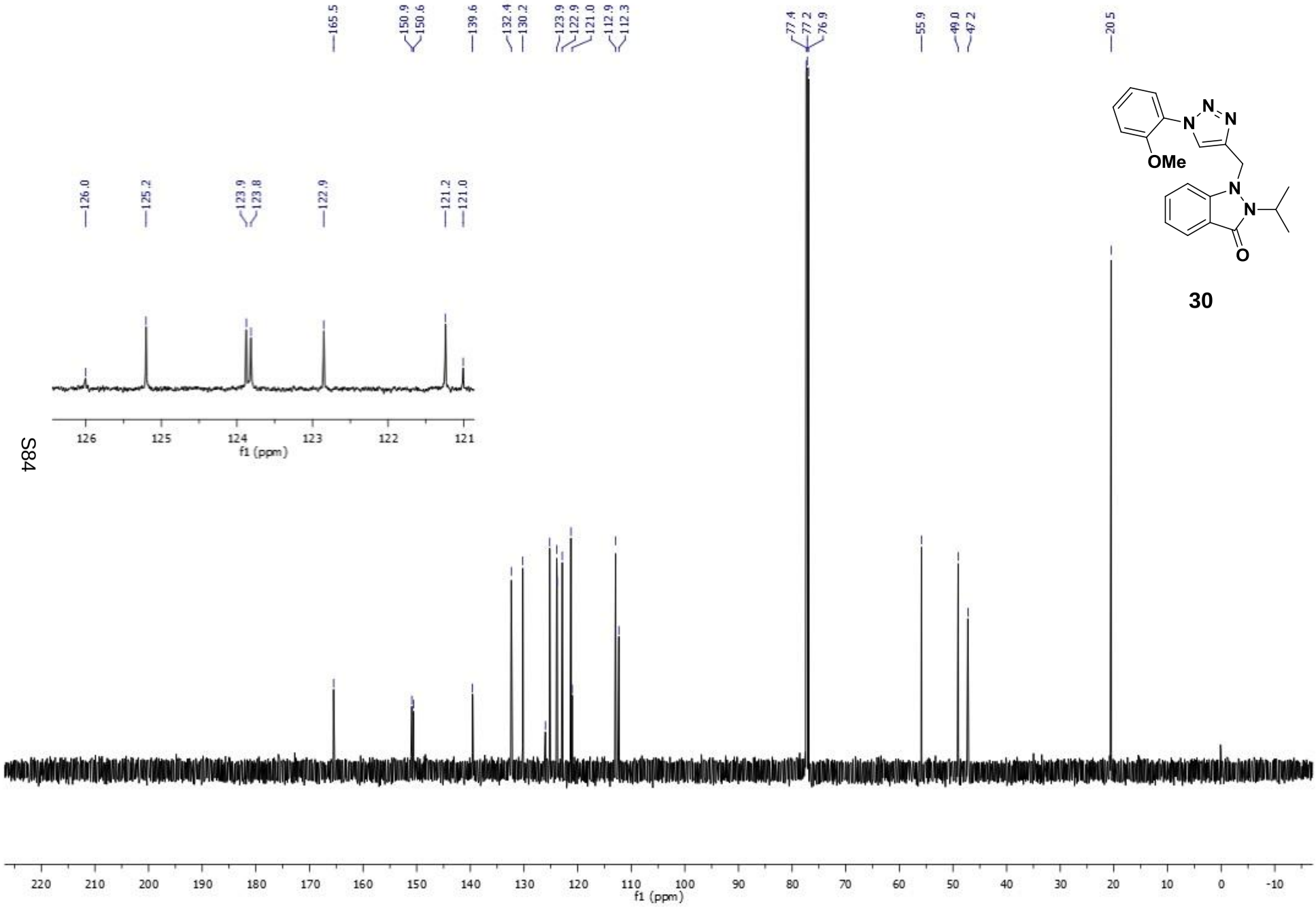

**29**

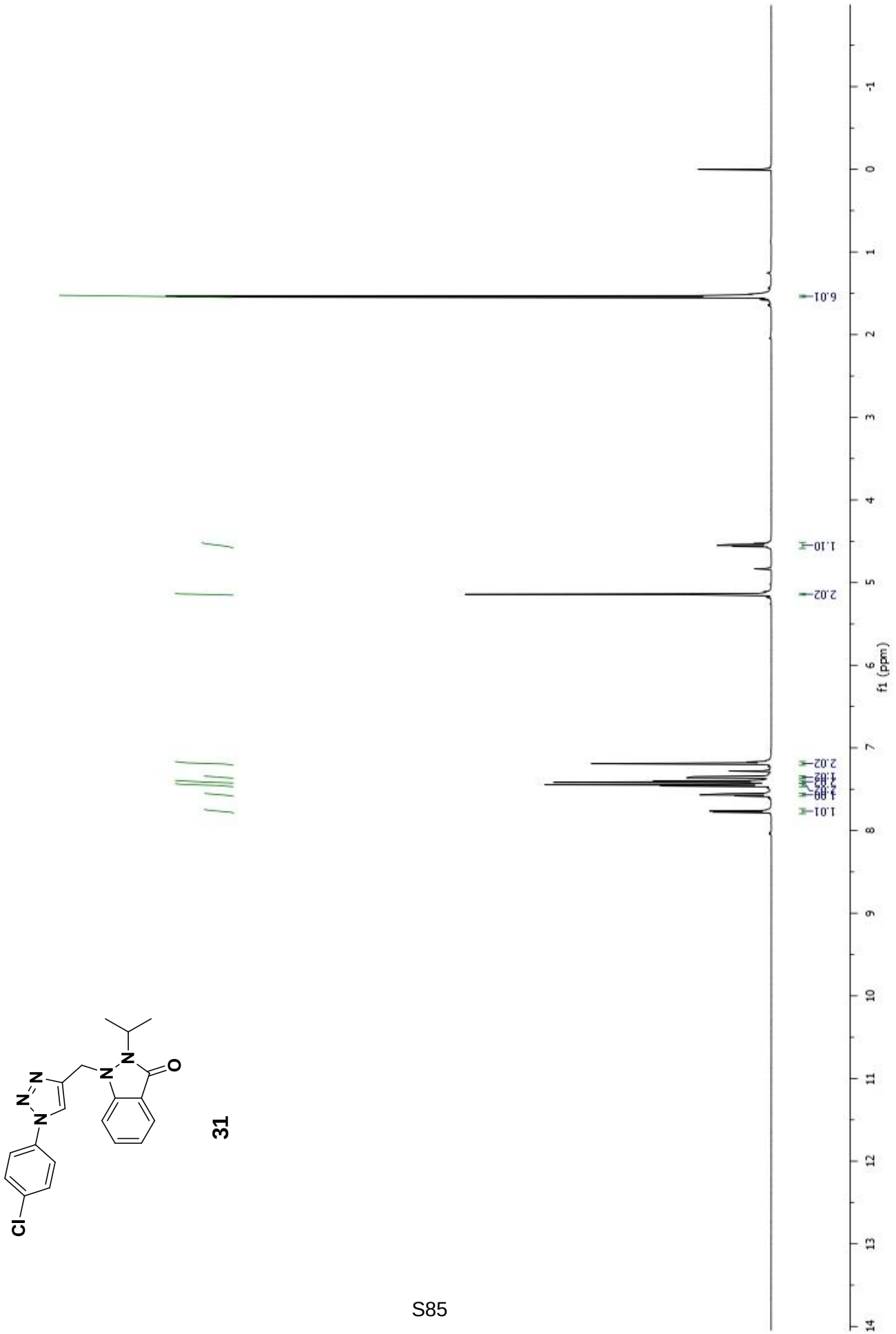

165.6
150.3
140.9
136.5
129.6
128.9
123.9
120.5
119.5
112.7
77.4
77.2
76.9
49.1
46.9
20.4
132.5
129.6
128.9
123.9
122.9
120.6
120.5
119.5
130
125
120
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

**29**




**30**

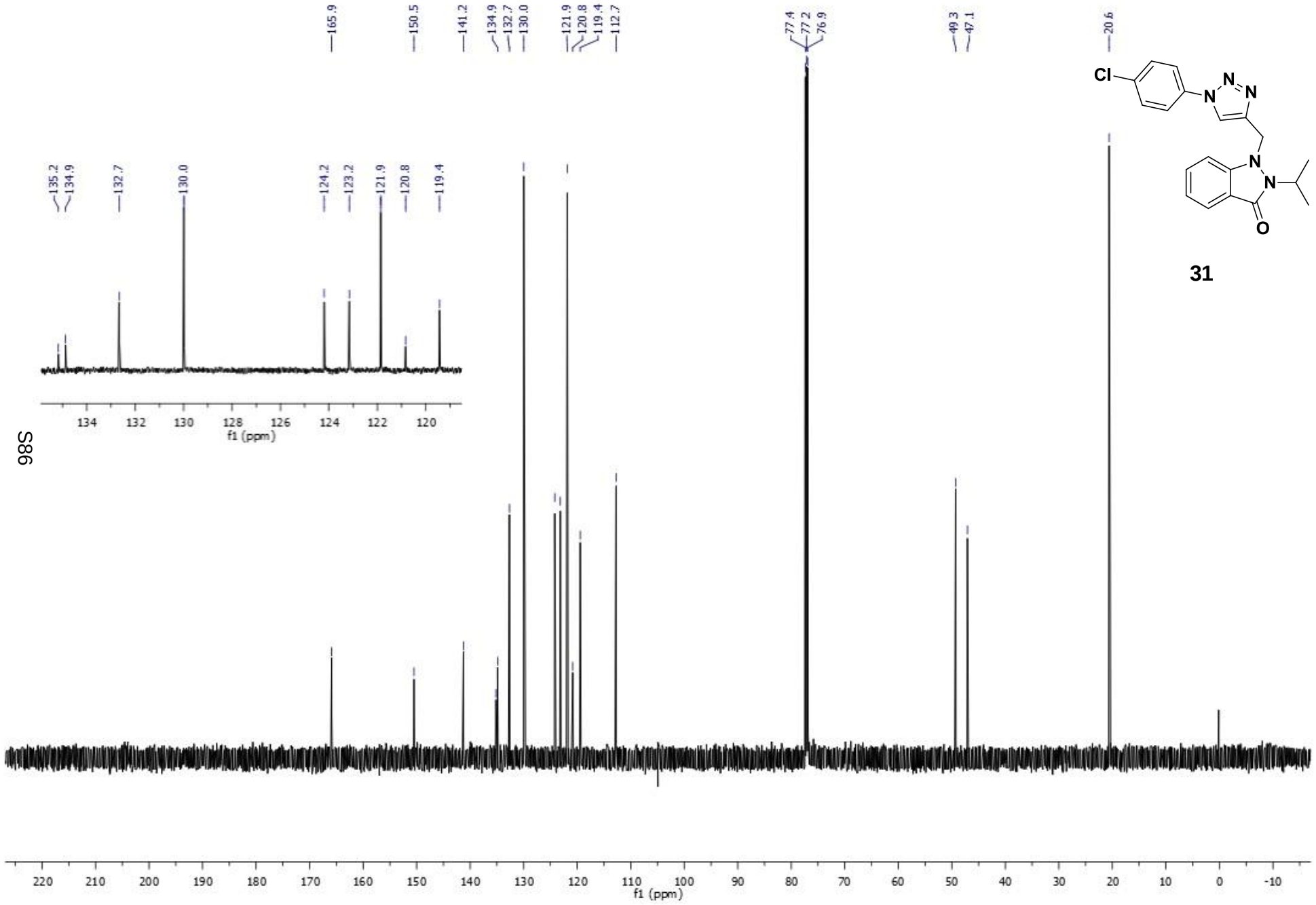

165.5
150.9
150.6
139.6
132.4
130.2
123.9
122.9
121.0
112.9
112.3
77.4
77.2
76.9
55.9
49.0
47.2
20.5
126.0
125.2
123.9
123.8
122.9
121.2
121.0
126
125
124
123
122
121
f1 (ppm)
OMe
N
N
N
N
N
O
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

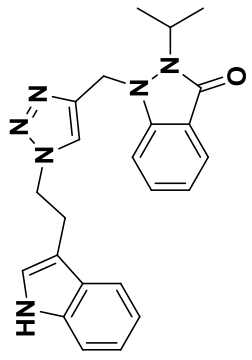




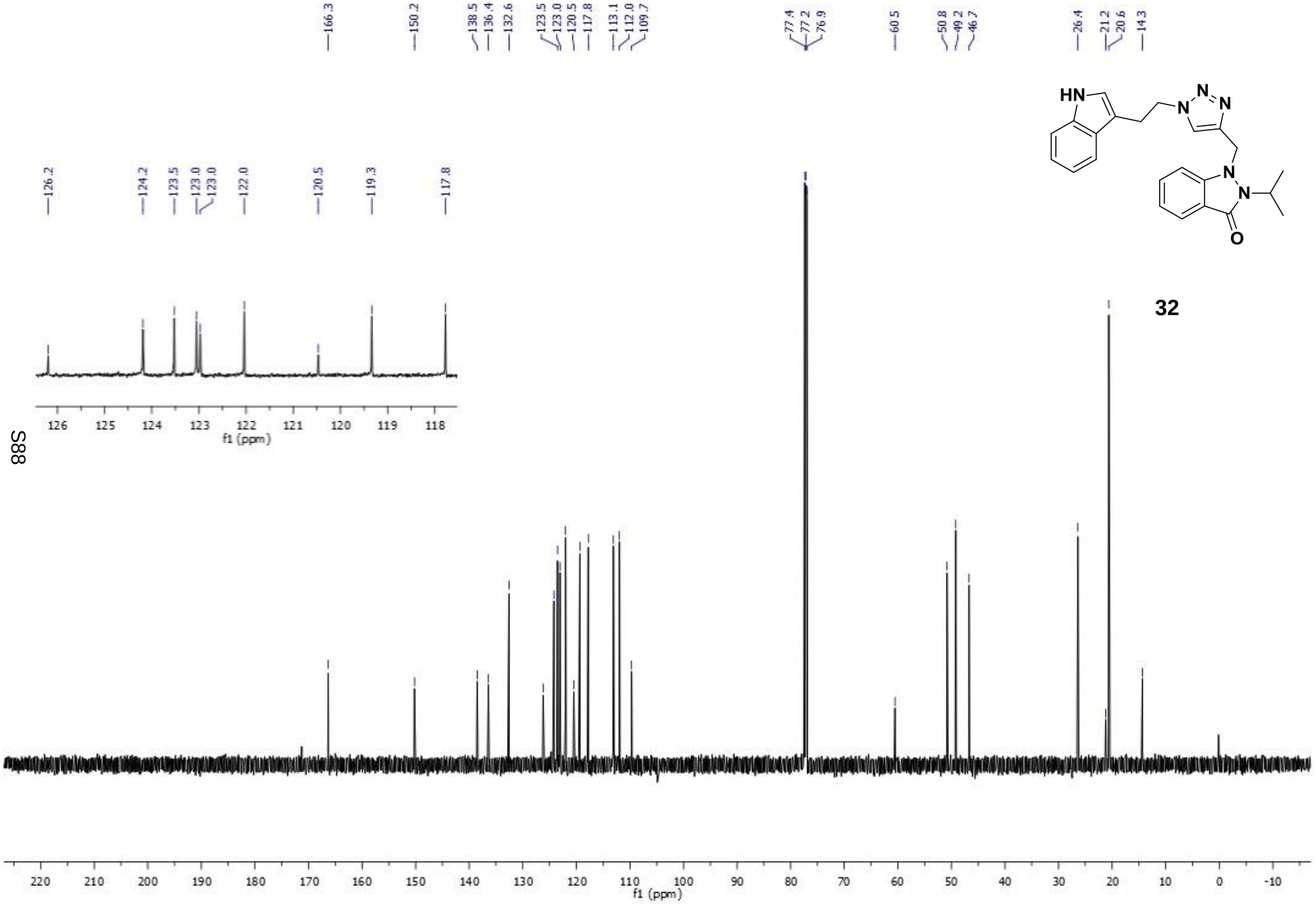


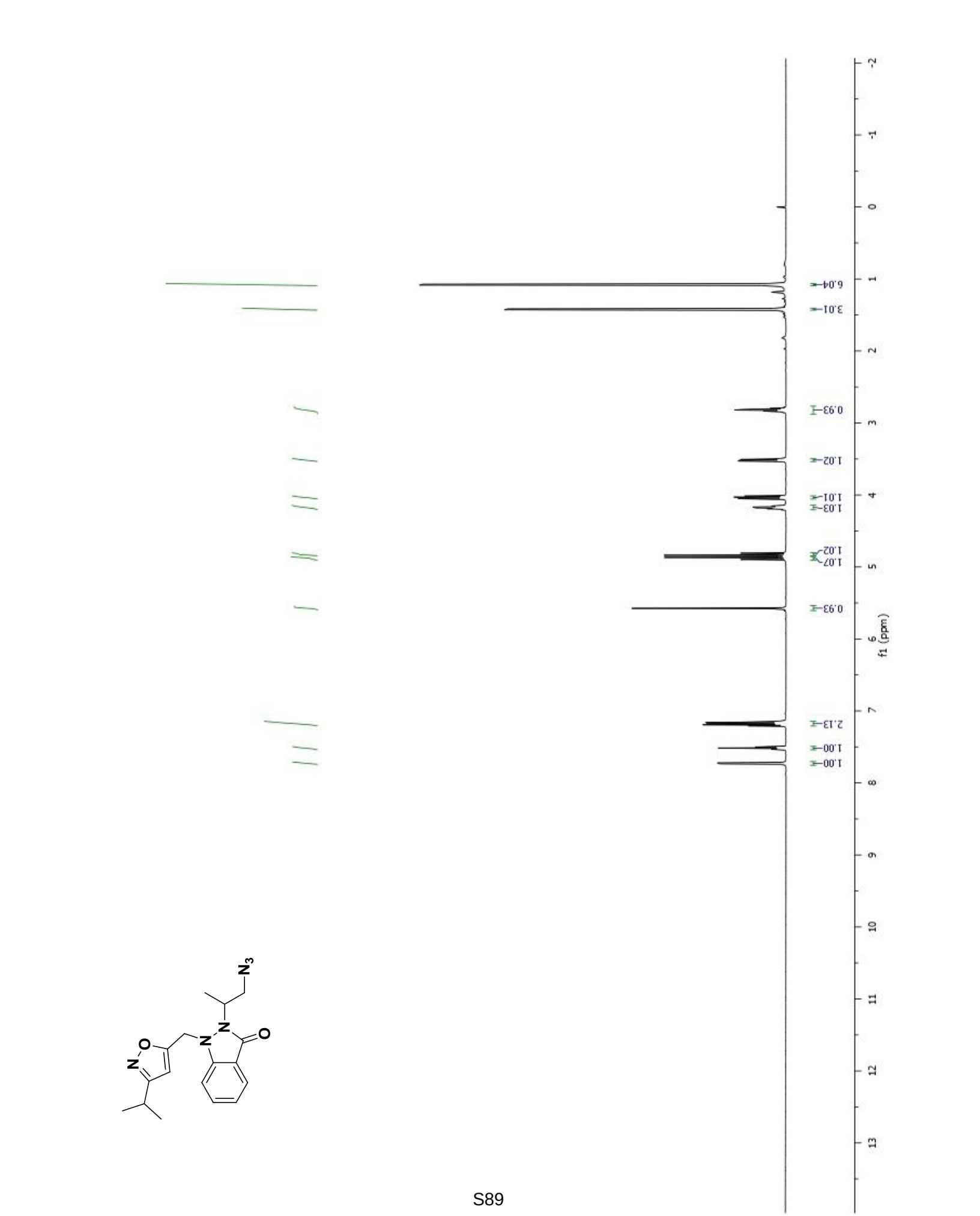
**31**

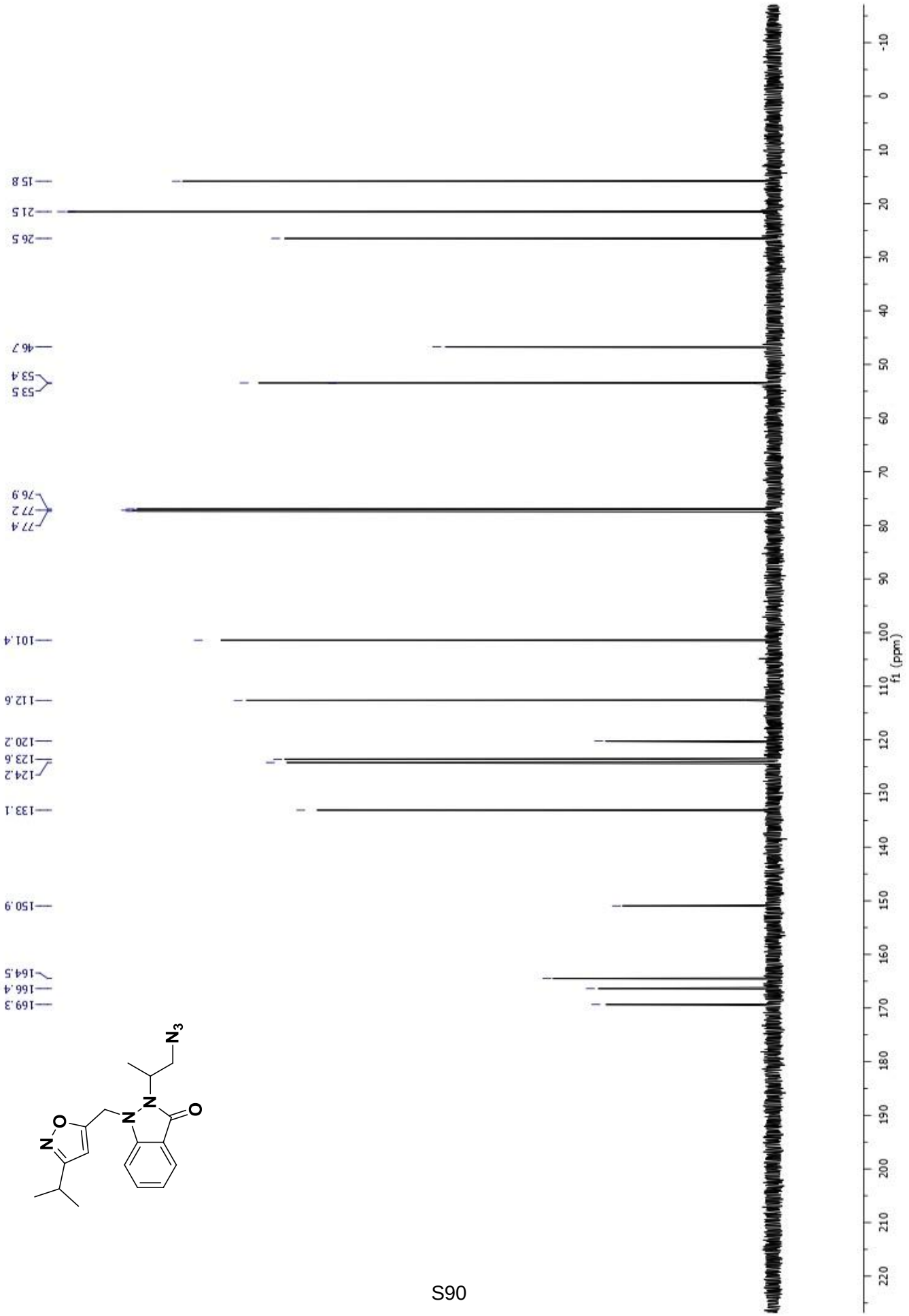

165.9
150.5
141.2
134.9
132.7
130.0
121.9
120.8
119.4
112.7
77.4
77.2
76.9
49.3
47.1
20.6
135.2
134.9
132.7
130.0
124.2
123.2
121.9
120.8
119.4
134
132
130
128
126
124
122
120
f1 (ppm)
Cl
N
N
N
N
N
O
31
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

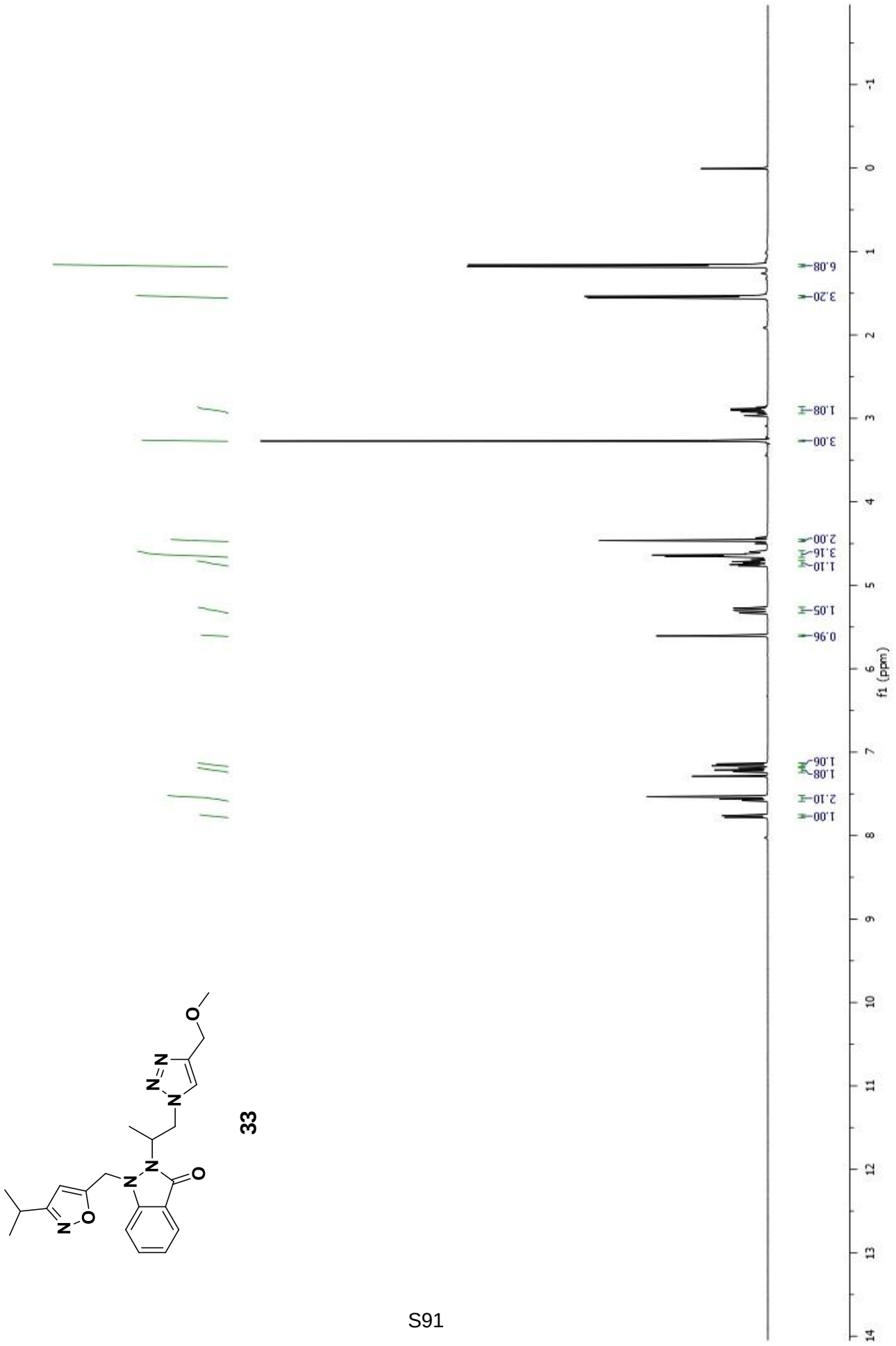


**32**

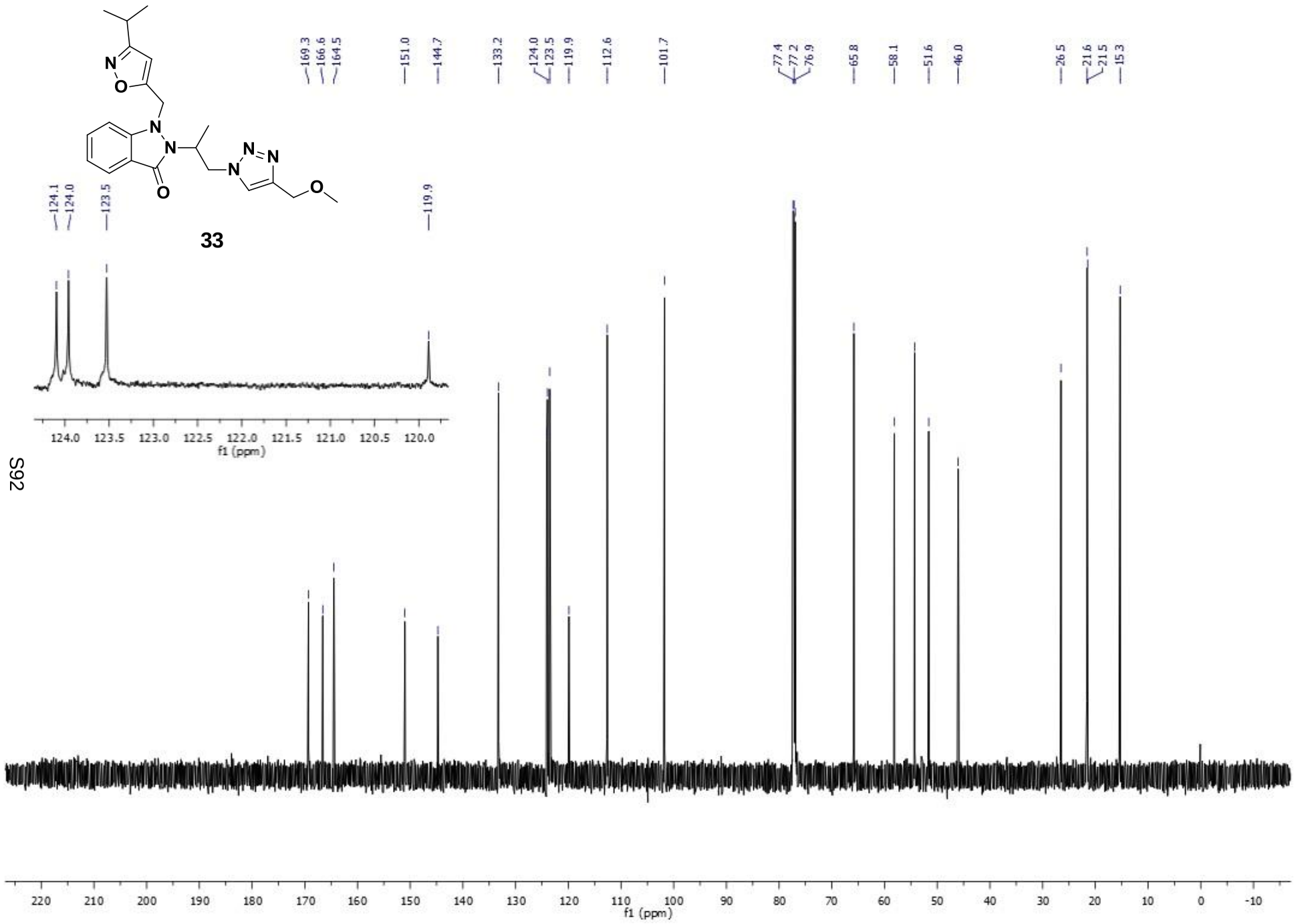

166.3
150.2
138.5
136.4
132.6
123.5
123.0
120.5
117.8
113.1
112.0
109.7
77.4
77.2
76.9
60.5
50.8
49.2
46.7
26.4
21.2
20.6
14.3
126.2
124.2
123.5
123.0
123.0
122.0
120.5
119.3
117.8
HN
N
N
N
N
O
32
f1 (ppm)
f1 (ppm)

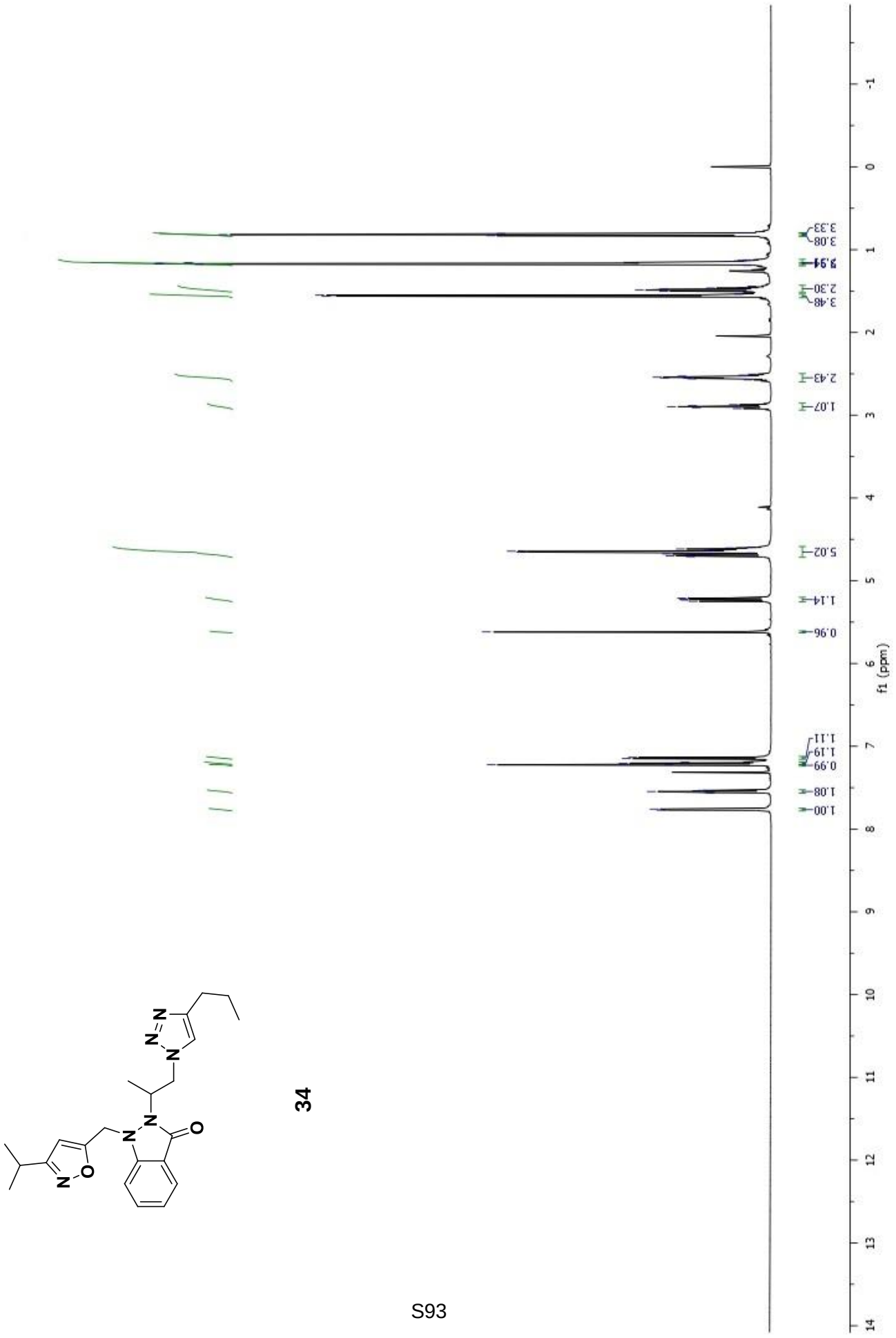

6.04
3.01
0.93
1.02
1.01
1.03
1.07
1.02
0.93
2.13
1.00
1.00
f1 (ppm)


15.8
21.5
26.5
46.7
53.4
53.5
76.9
77.2
77.4
101.4
112.6
120.2
123.6
124.2
133.1
150.9
164.5
166.4
169.3
f1 (ppm)

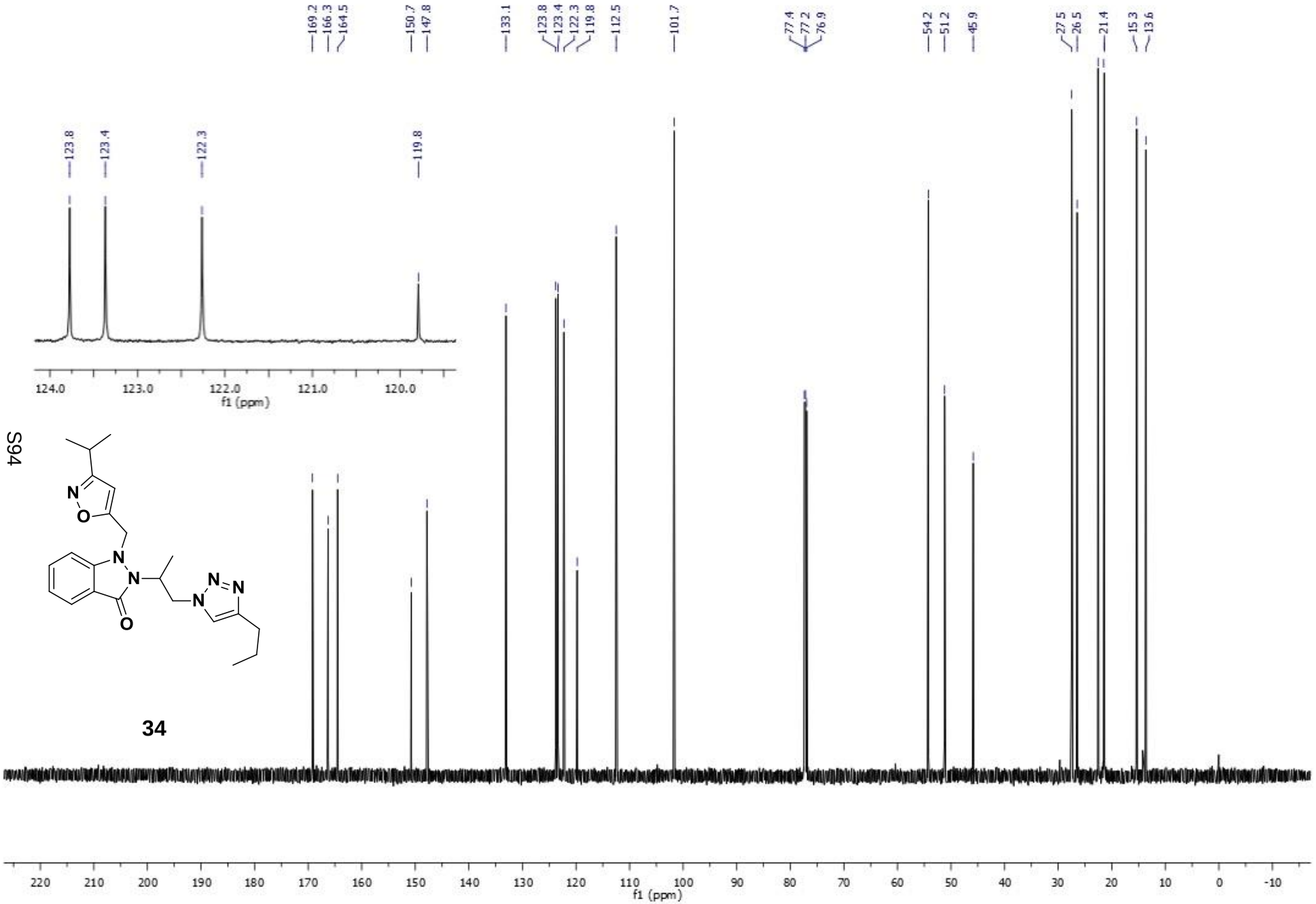



**33**

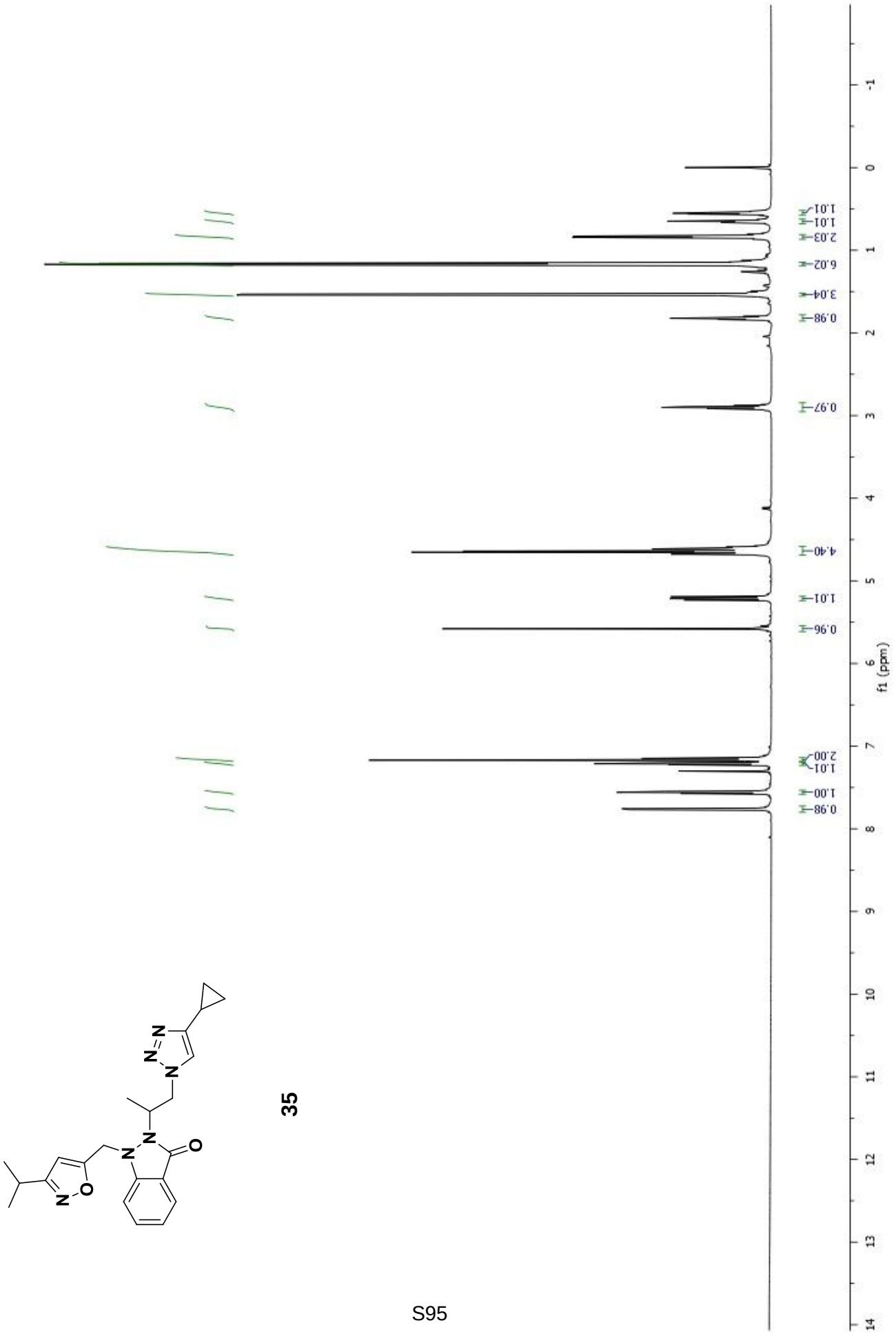

169.3
166.6
164.5
151.0
144.7
133.2
124.0
123.5
119.9
112.6
101.7
77.4
77.2
76.9
65.8
58.1
51.6
46.0
26.5
21.6
21.5
15.3
124.1
124.0
123.5
119.9
33
124.0 123.5 123.0 122.5 122.0 121.5 121.0 120.5 120.0
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



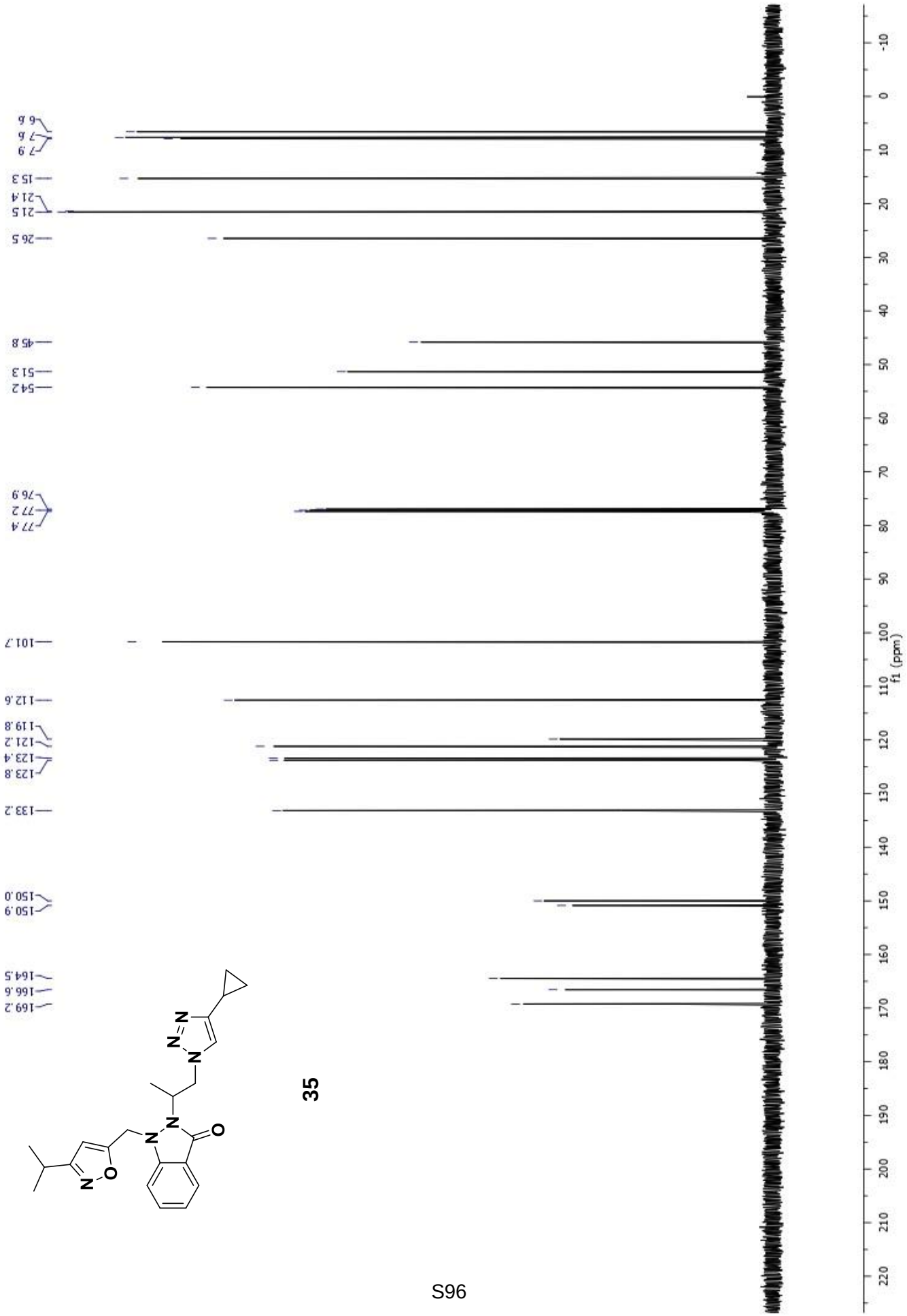

**34**


169.2
166.3
164.5
150.7
147.8
133.1
123.8
123.4
122.3
119.8
112.5
101.7
77.4
77.2
76.9
54.2
51.2
45.9
27.5
26.5
21.4
15.3
13.6
123.8
123.4
122.3
119.8
124.0
123.0
122.0
121.0
120.0
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

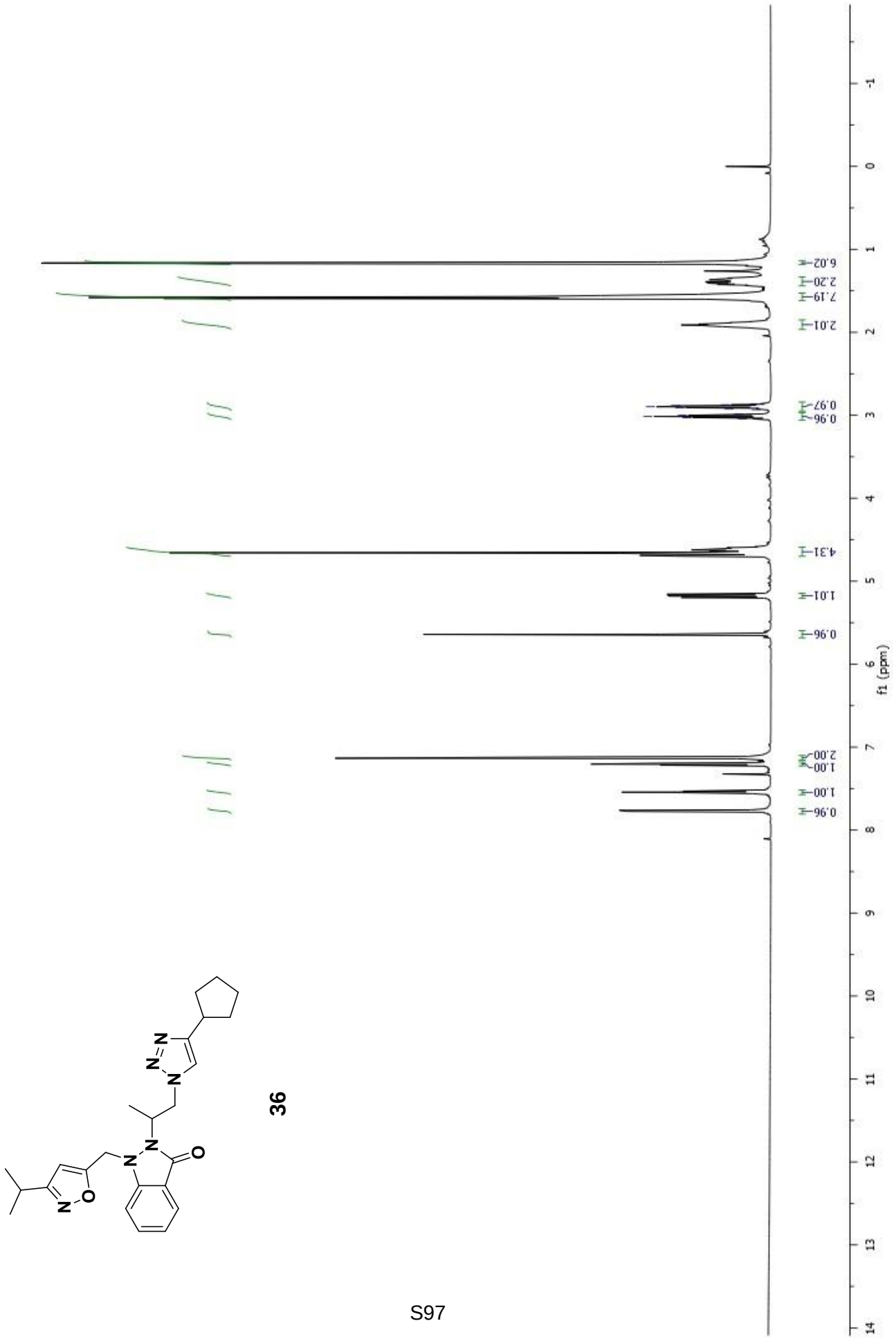
**34**



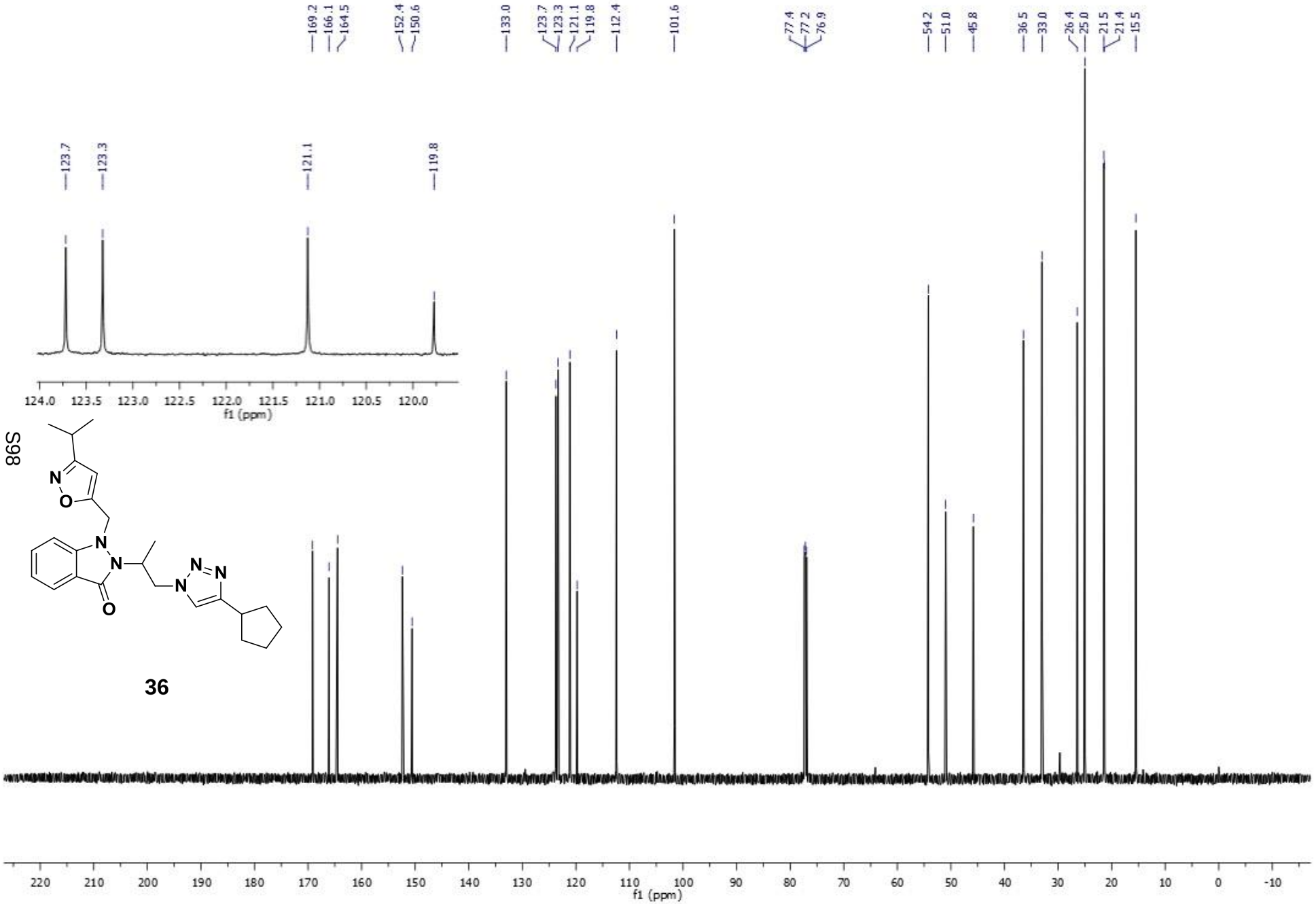

**35**


169.2
166.6
164.5
150.9
150.0
133.2
123.8
123.4
121.2
119.8
112.6
101.7
77.4
77.2
76.9
54.2
51.3
45.8
26.5
21.5
21.4
15.3
7.9
7.6
6.6
f1 (ppm)

**35**

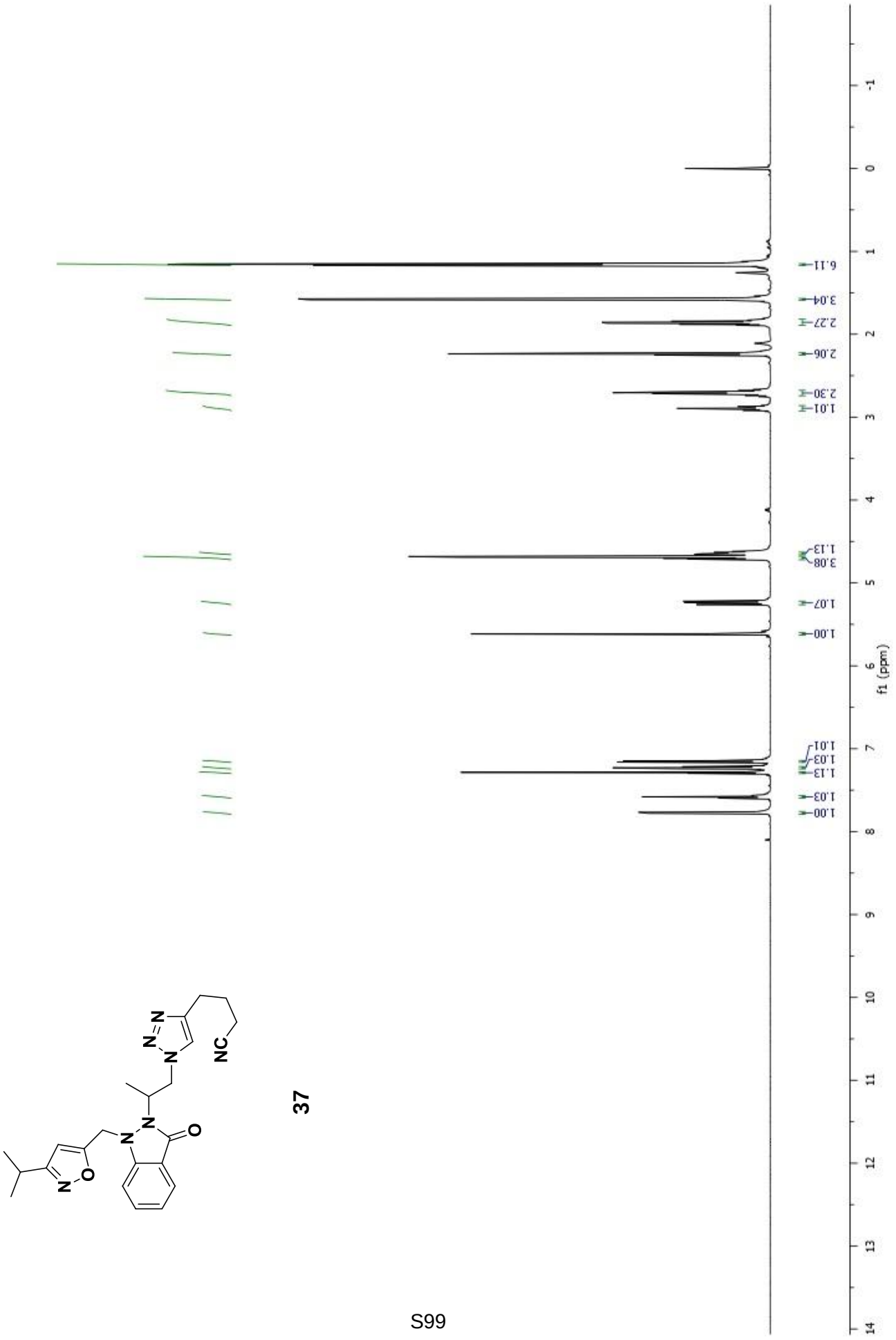



**36**


169.2
166.1
164.5
152.4
150.6
133.0
123.7
123.3
121.1
119.8
112.4
101.6
77.4
77.2
76.9
54.2
51.0
45.8
36.5
33.0
26.4
25.0
21.5
21.4
15.5
123.7
123.3
121.1
119.8
124.0 123.5 123.0 122.5 122.0 121.5 121.0 120.5 120.0
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

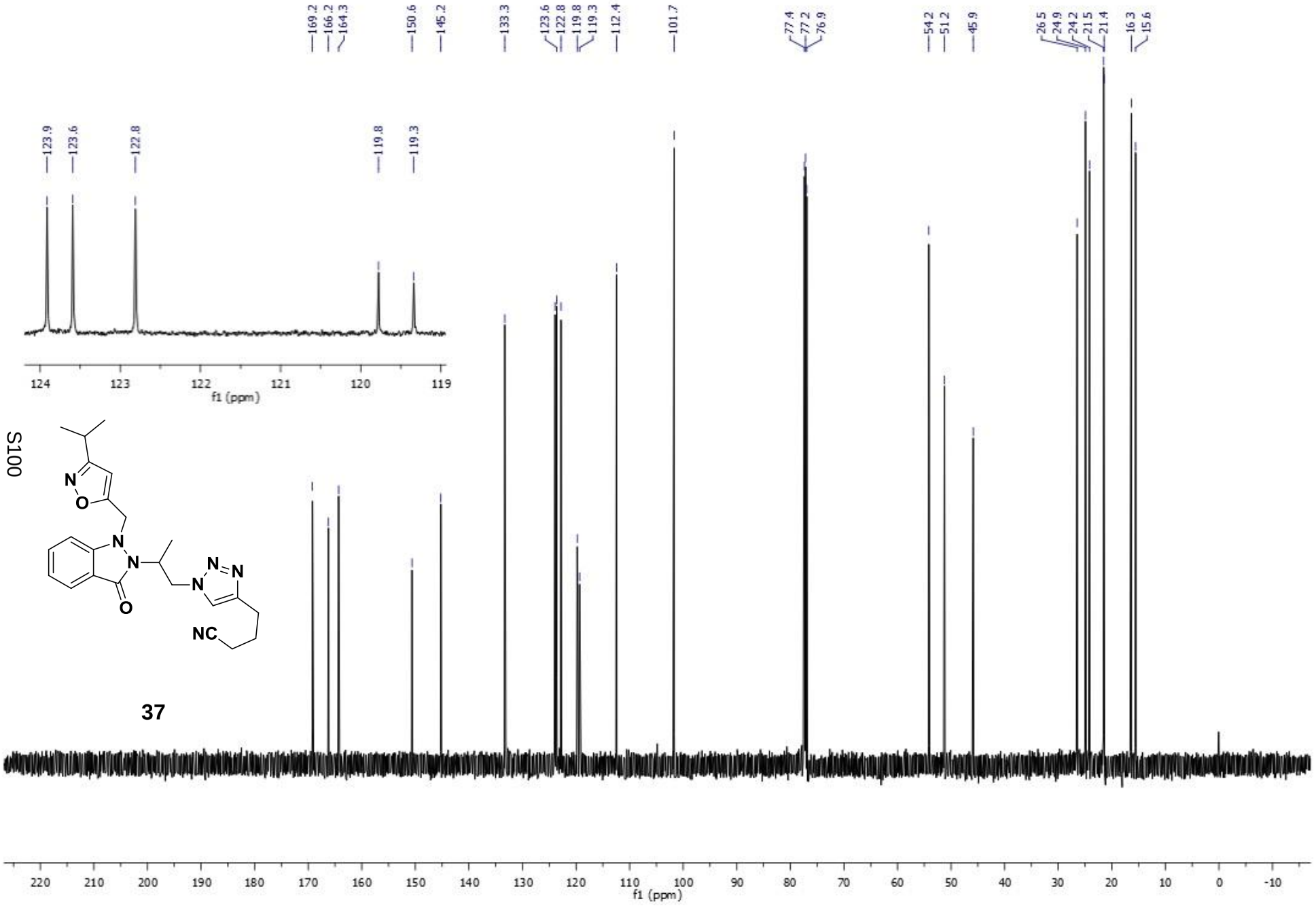
S98

**36**


6.11
3.04
2.27
2.06
2.30
1.01
3.08
1.13
1.07
1.00
1.01
1.03
1.13
1.03
1.00
f1 (ppm)

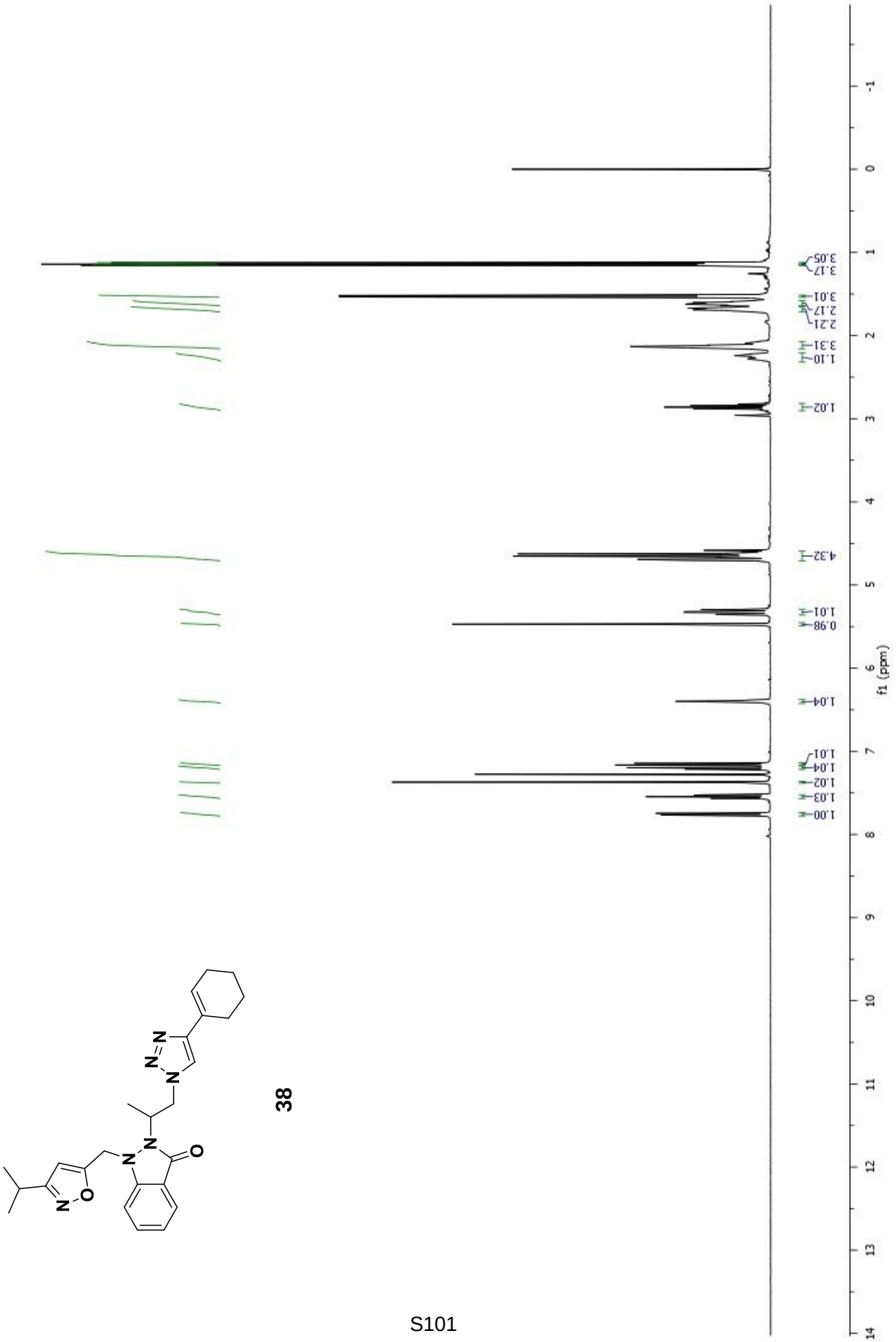


**37**

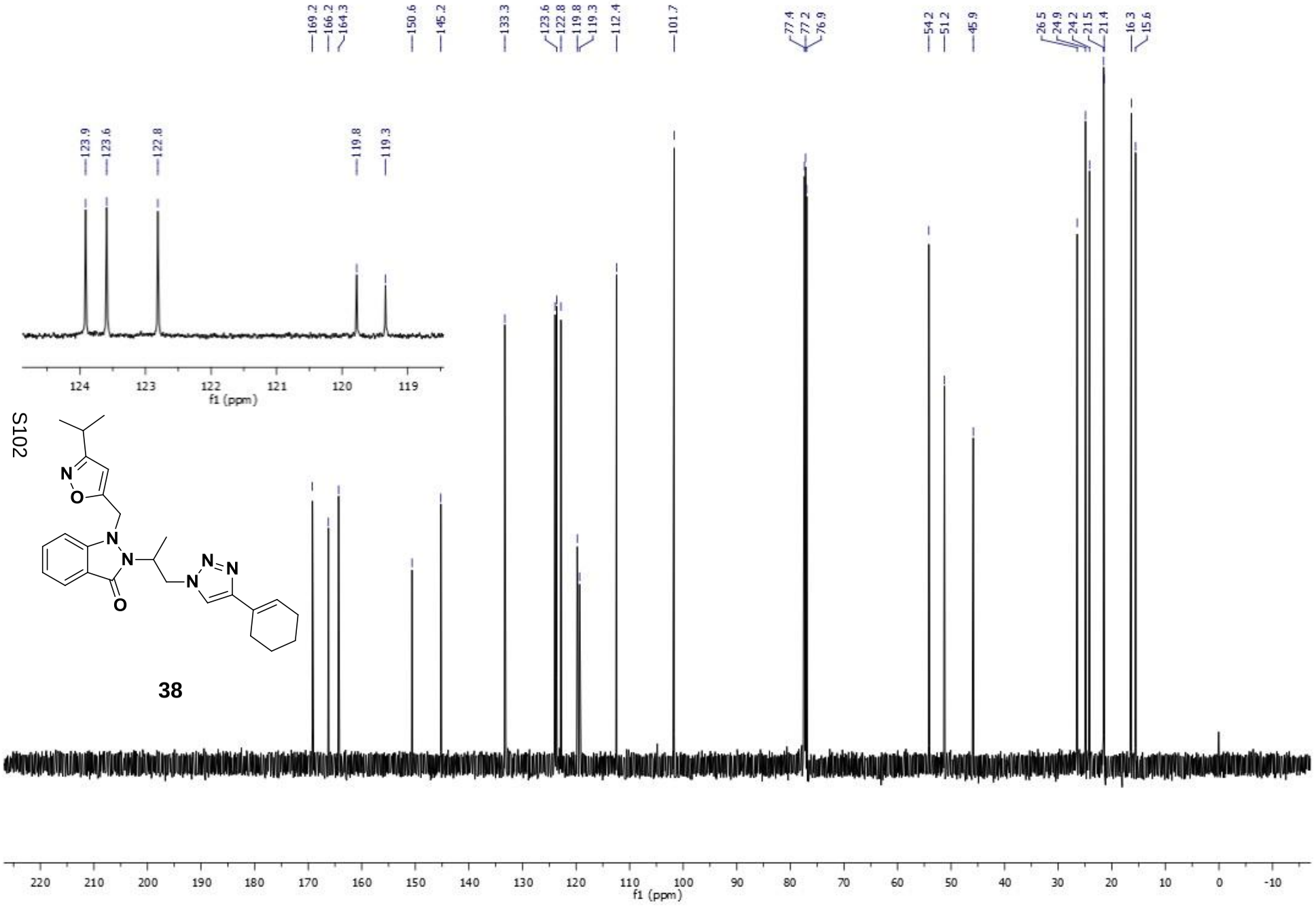

169.2
166.2
164.3
150.6
145.2
133.3
123.6
122.8
119.8
119.3
112.4
101.7
77.4
77.2
76.9
54.2
51.2
45.9
26.5
24.9
24.2
21.5
21.4
16.3
15.6
123.9
123.6
122.8
119.8
119.3
124
123
122
121
120
119
f1 (ppm)
N
O
N
N
O
N
N
N
NC
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

S100

**37**

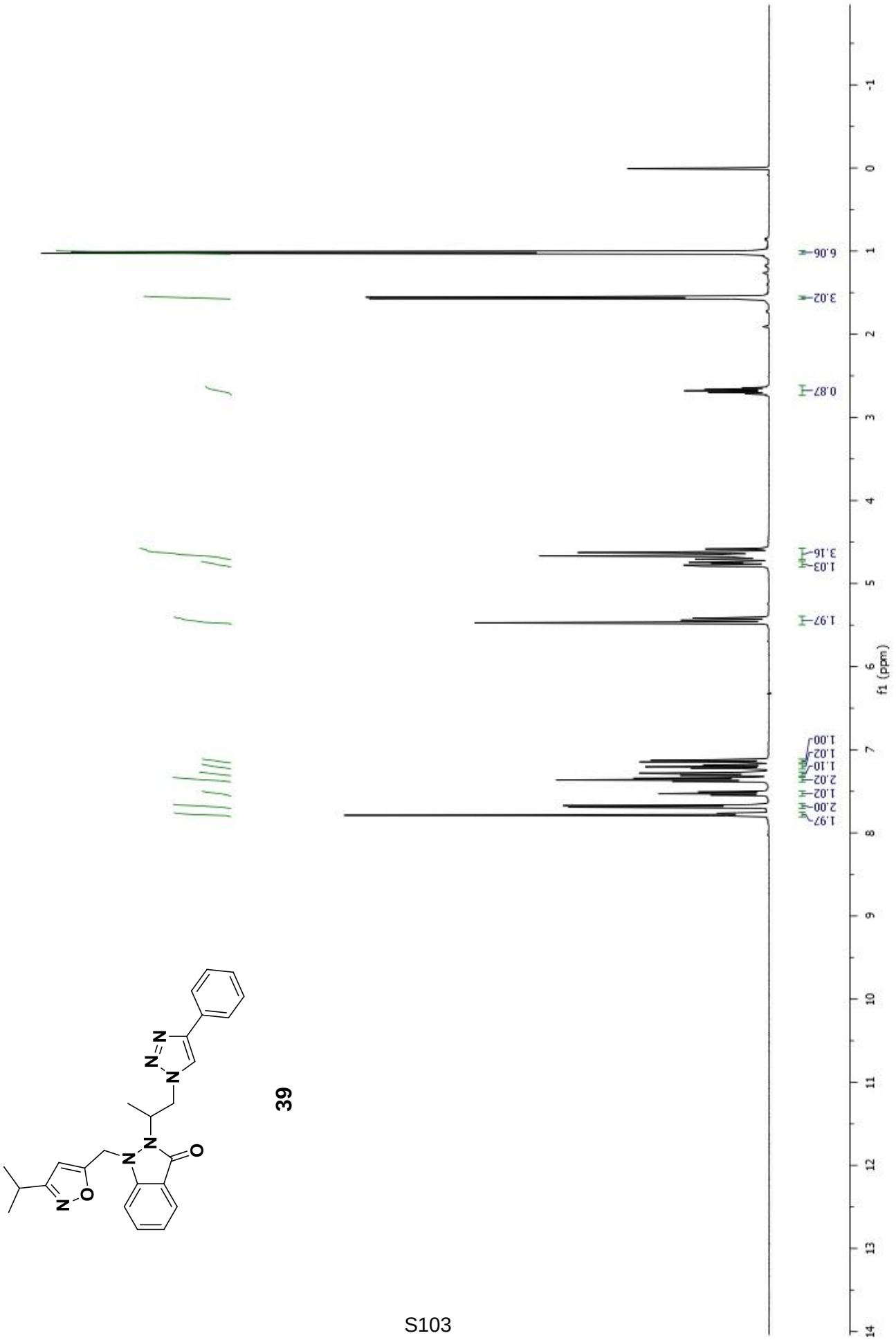

3.05
3.17
3.01
2.17
2.21
3.31
1.10
1.02
4.32
1.01
0.98
1.04
1.01
1.04
1.02
1.03
1.00
f1 (ppm)

**38**

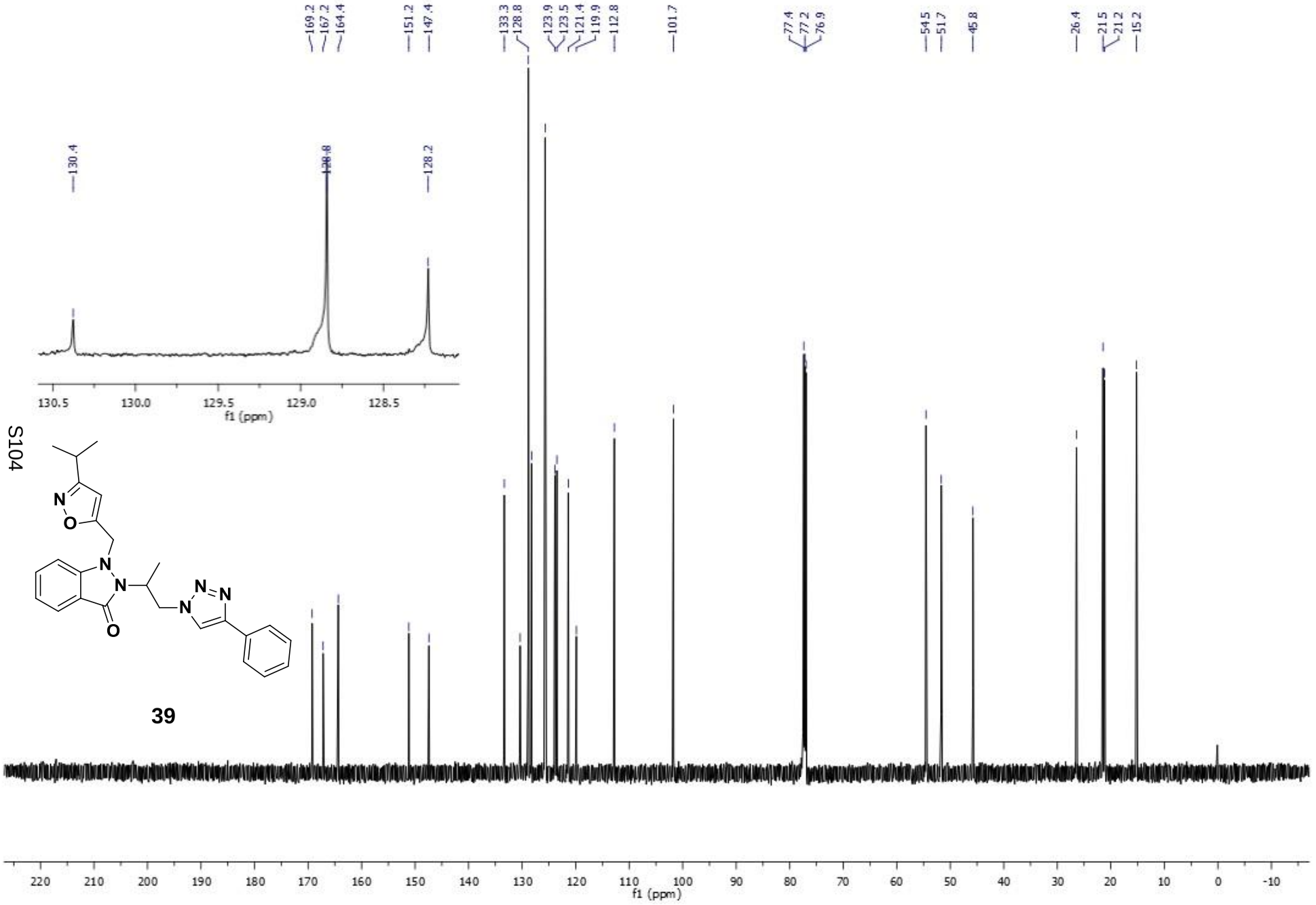

169.2
166.2
164.3
150.6
145.2
133.3
123.6
122.8
119.8
119.3
112.4
101.7
77.4
77.2
76.9
54.2
51.2
45.9
26.5
24.9
24.2
21.5
21.4
16.3
15.6
123.9
123.6
122.8
119.8
119.3
124
123
122
121
120
119
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

S102

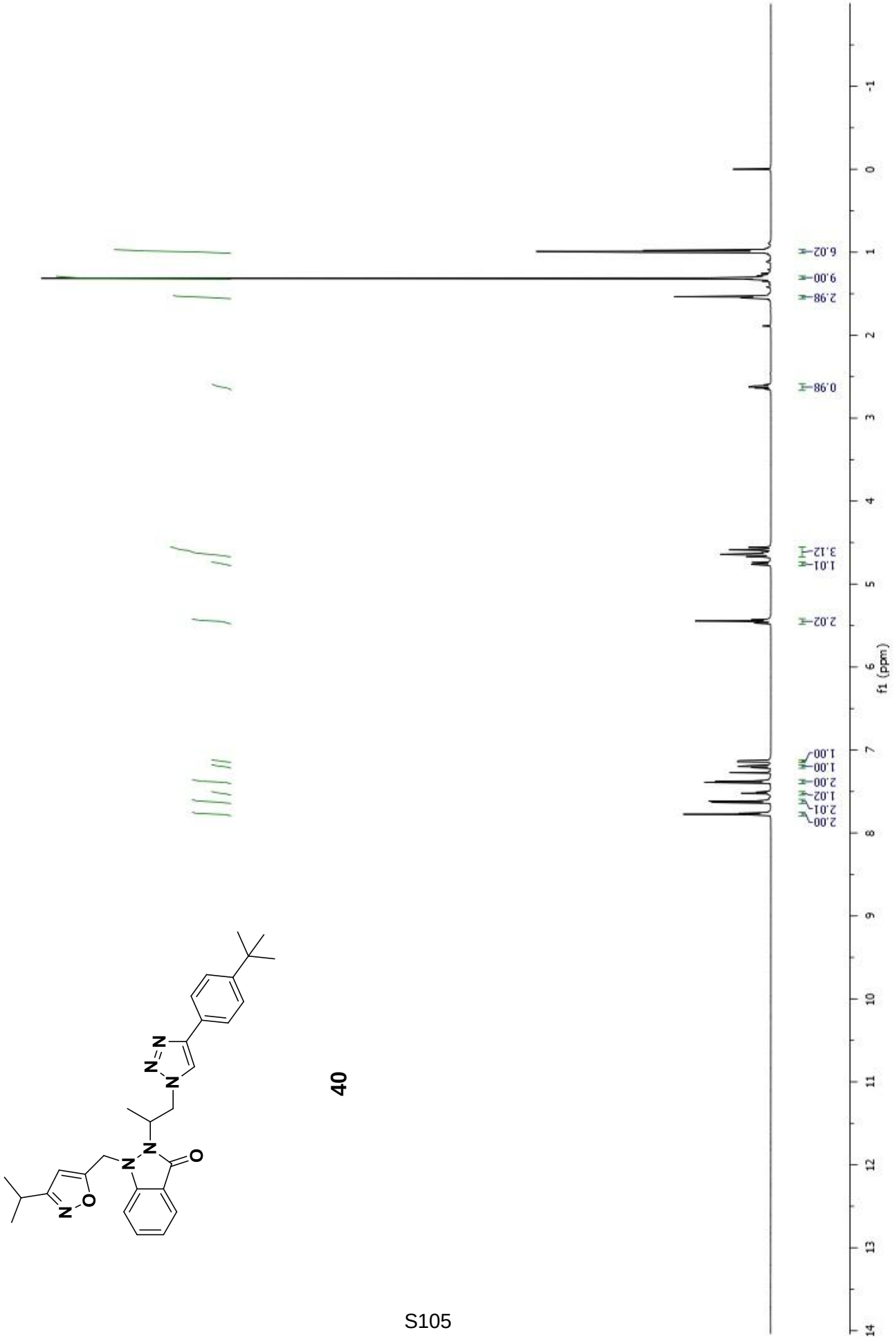
**38**



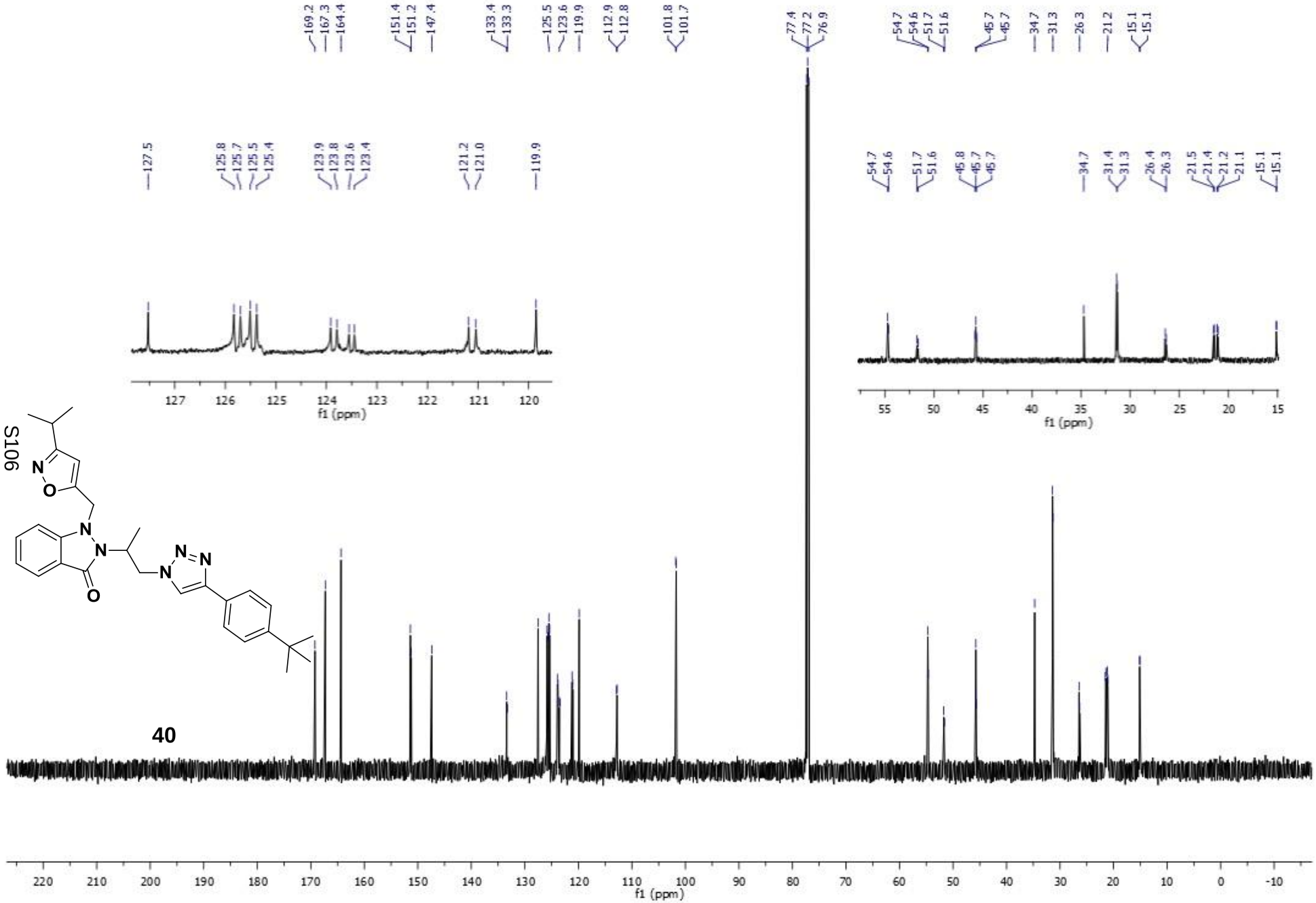

**39**

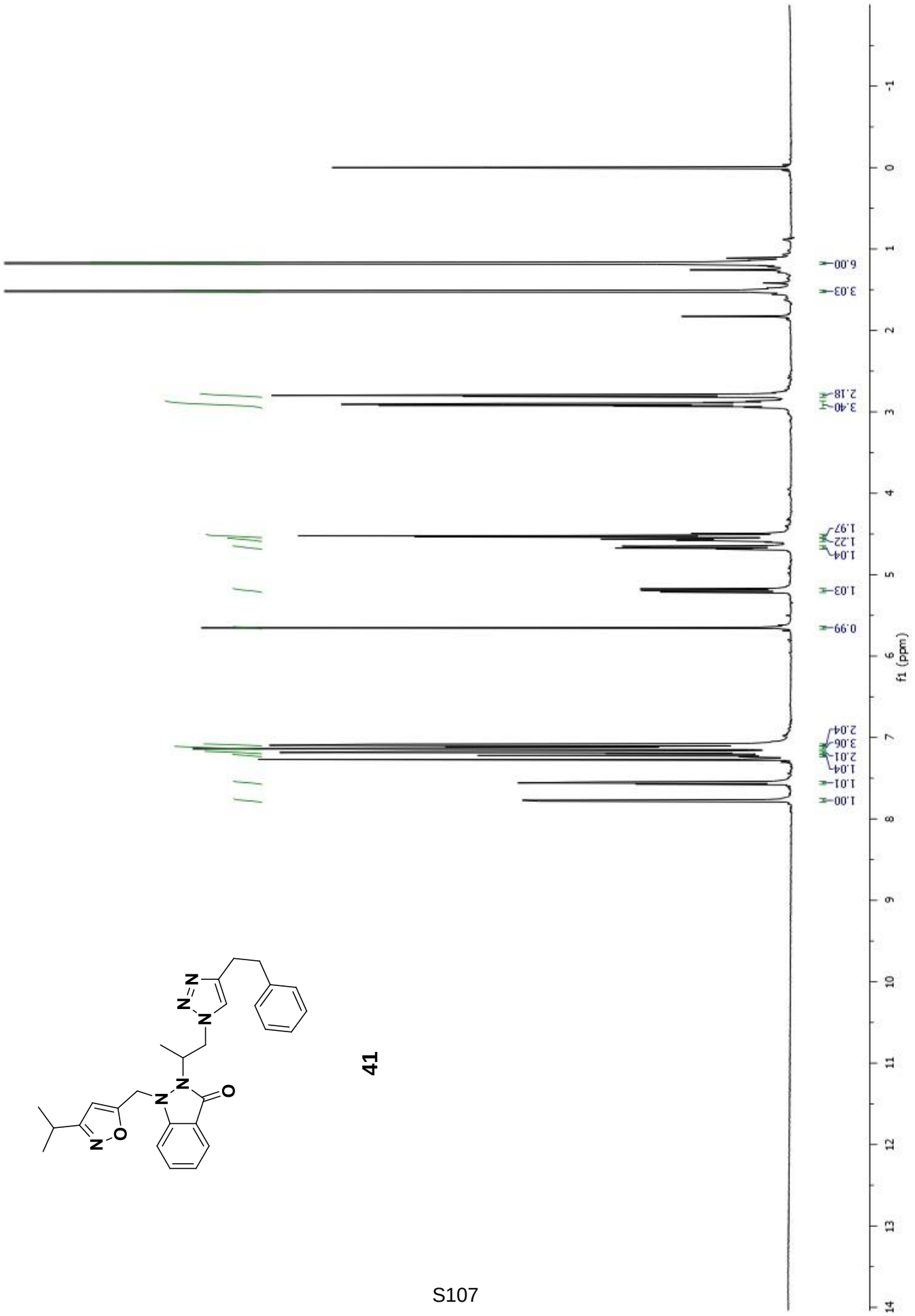

169.2
167.2
164.4
151.2
147.4
133.3
128.8
123.9
123.5
121.4
119.9
112.8
101.7
77.4
77.2
76.9
54.5
51.7
45.8
26.4
21.5
21.2
15.2
130.4
128.8
128.2
130.5
130.0
129.5
129.0
128.5
f1 (ppm)
N
O
N
N
N
N
N
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

**39**



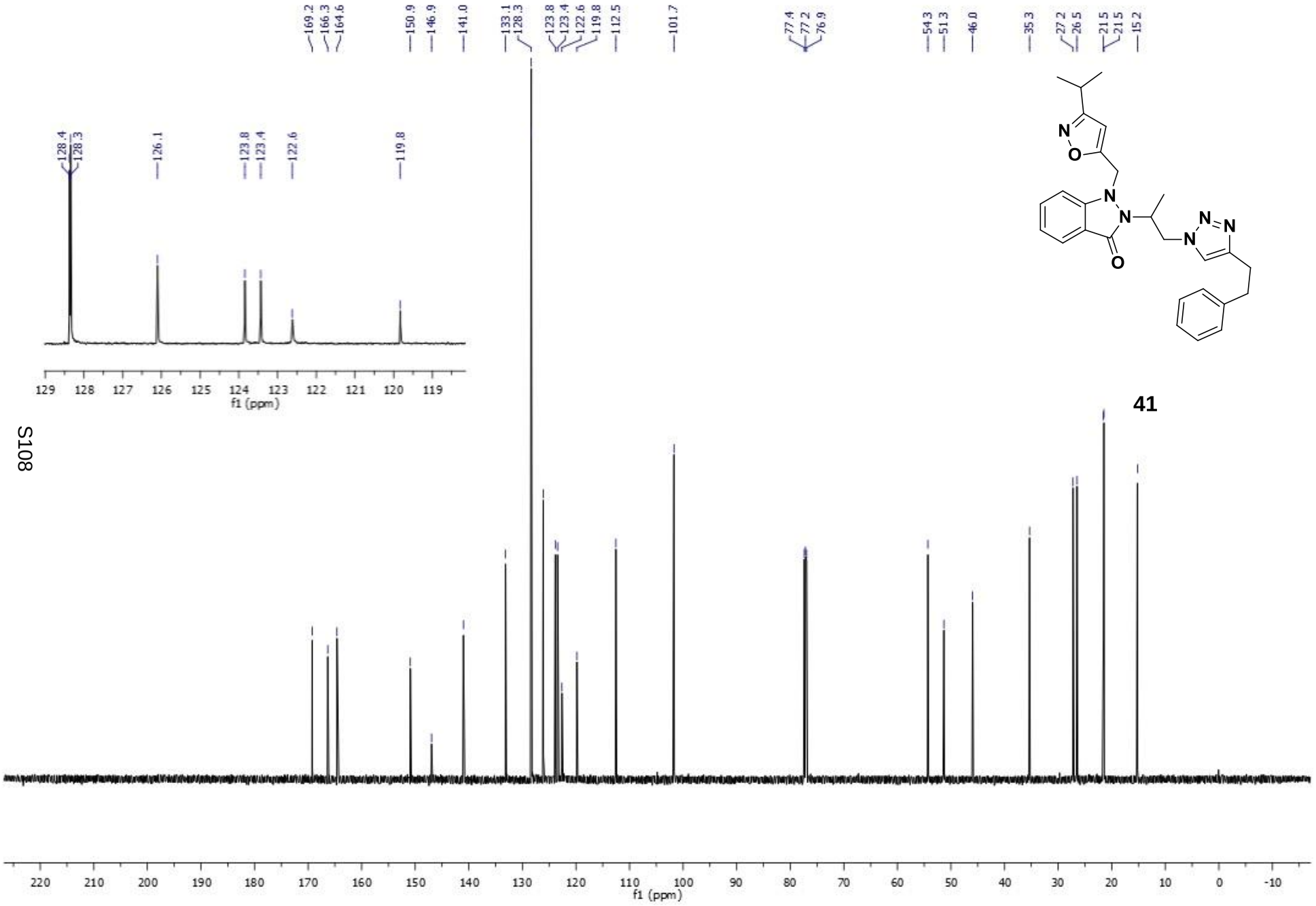

**40**

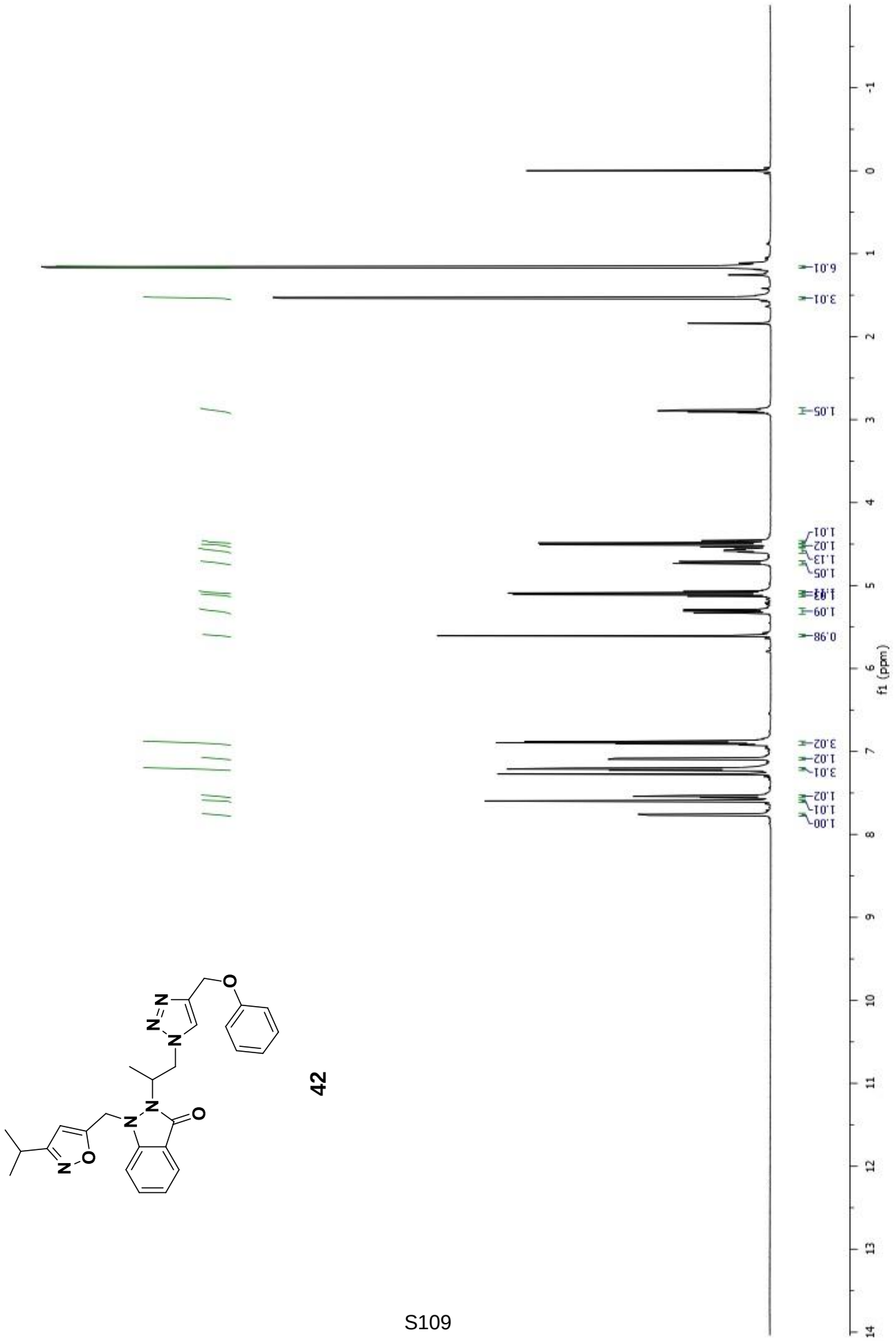

169.2
167.3
164.4
151.4
151.2
147.4
133.4
133.3
125.5
123.6
119.9
112.9
112.8
101.8
101.7
77.4
77.2
76.9
54.7
54.6
51.7
51.6
45.7
45.7
34.7
31.3
26.3
21.2
15.1
15.1
127.5
125.8
125.7
125.5
125.4
123.9
123.8
123.6
123.4
121.2
121.0
119.9
54.7
54.6
51.7
51.6
45.8
45.7
45.7
34.7
31.4
31.3
26.4
26.3
21.5
21.4
21.2
21.1
15.1
15.1
f1 (ppm)
f1 (ppm)
f1 (ppm)
S106
40


6.00
3.03
2.18
3.40
1.97
1.22
1.04
1.03
0.99
2.04
3.06
2.01
1.04
1.01
1.00
f1 (ppm)



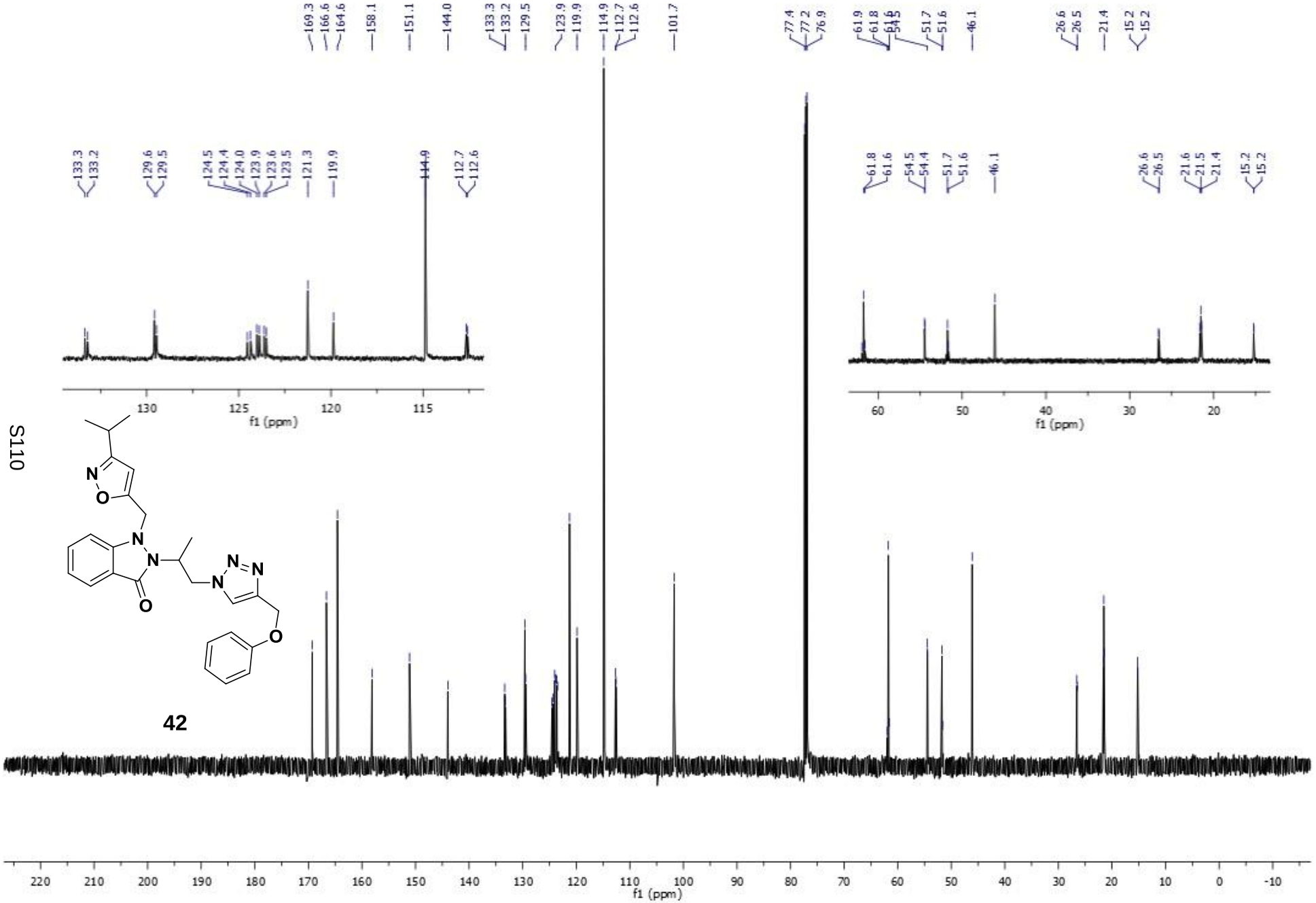
**41**


169.2
166.3
164.6
150.9
146.9
141.0
133.1
128.3
123.8
123.4
122.6
119.8
112.5
101.7
77.4
77.2
76.9
54.3
51.3
46.0
35.3
27.2
26.5
21.5
21.5
15.2
128.4
128.3
126.1
123.8
123.4
122.6
119.8
129 128 127 126 125 124 123 122 121 120 119
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
N
O
N
N
O
N
N
N
41


6.01
3.01
1.05
1.01
1.02
1.13
1.05
1.09
0.98
3.02
1.02
3.01
1.02
1.01
1.00
f1 (ppm)



**42**


169.3
166.6
164.6
158.1
151.1
144.0
133.3
133.2
129.5
123.9
119.9
114.9
112.7
112.6
101.7
77.4
77.2
76.9
61.9
61.8
54.5
51.7
51.6
46.1
26.6
26.5
21.4
15.2
15.2
f1 (ppm)

**42**