Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Dual catalysis by Cu(I): Facile single step click and intramolecular C-O bond formation leading to triazole tethered dihydrobenzodioxines/ benzoxazines/ benzoxathiines/ benzodioxepines

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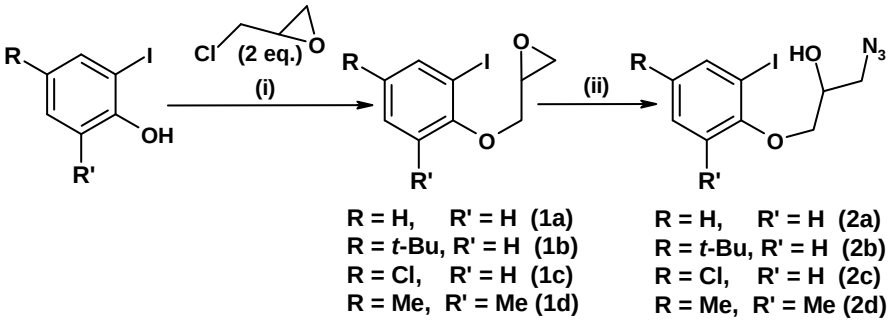
Supporting Information

General experimental details

Chemicals were purified when required according to standard procedures.[1] All reactions, unless stated otherwise, were performed in a dry nitrogen atmosphere. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded using a 400 MHz spectrometer in $CDCl_3$ (unless stated otherwise) with shifts referenced to $SiMe_4$ ($\delta = 0$) or 85 % H_3PO_4 ($\delta = 0$). Infrared spectra were recorded neat or by using KBr pellets on an FT/IR spectrometer. Melting points were determined by using a local hot-stage melting point apparatus and are uncorrected. Microanalyses were performed using a CHNS analyzer. For TLC, glass microslides were coated with silica-gel-GF_{254} (mesh size 75μ) and spots were identified using iodine or UV chamber as appropriate. For column chromatography, silica gel of100-200 mesh size was used. LC-MS and HRMS equipment was used to record mass spectra for isolated compounds where appropriate. LC-MS data were obtained using electrospray ionization (positive mode) on a C-18 column at a flow rate 0.2 mL/ min using MeOH/water (90:10) as eluent. Required 2-iodophenols,[2] 2-iodoanilines,[3] 2-iodothiophenol[3] 2-iodo-cyclohexeneol[4] and 2-iodo sulfonamide[5] were prepared following literature procedures.

General procedure for the synthesis of compounds 1a-1e and 2a-2e



R = H, R' = H (1a)
R = *t*-Bu, R' = H (1b)
R = Cl, R' = H (1c)
R = Me, R' = Me (1d)

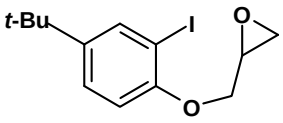
R = H, R' = H (2a)
R = *t*-Bu, R' = H (2b)
R = Cl, R' = H (2c)
R = Me, R' = Me (2d)

Conditions: (i). K_2CO_3 (1.5 eq.), CH_3CN, reflux, 12h
(ii). NH_4Cl (2.0 eq.), NaN_3 (4.0 eq.), MeOH, 50 ^oC, 10h.

Step (i): To a stirred solution of 2-iodophenol (4.5 mmol) and potassium carbonate (5.4 mmol) in anhydrous CH_3CN (10 mL) was added epichlorohydrin (9.0 mmol) at once under nitrogen atmosphere with continuous stirring at room temperature. The reaction mixture was heated under reflux for 12 h. After completion of reaction (tlc), water was added to the mixture and the product extracted into diethyl ether (3x30 mL). The combined organic layer was washed with aqueous brine (15 mL), dried over anhydrous sodium sulfate and evaporated to dryness to give crude product. The product was purified by column chromatography (silica gel, hexane). Compounds **1b-1e** were prepared similarly using the same molar quantities of reactants. Compounds **1a** and **1c** are known; [6] the spectroscopic data were identical to that reported in the literature.

Step (ii): A literature procedure was slightly modified.[7] To a stirred mixture of 2-((2-iodophenoxy)methyl)oxirane **1a** (3.0 mmol) in methanol (20 mL) was added ammonium chloride (6.0 mmol) and sodium azide (12.0 mmol) at room temperature. The resulting reaction mixture was stirred at 50 ^oC for 10 h. After completion of reaction (tlc), methanol was removed under reduced pressure. Then water was added to the slurry and the product extracted into ethyl acetate (3x30 mL). The combined organic layer was washed with aqueous brine (15 mL), dried over anhydrous sodium sulfate and evaporated to dryness to give crude product. The product **2a** was purified by column chromatography (silica gel, hexane). Compounds **2b-2e** were prepared similarly using the same molar quantities of reactants.

Compound 1b:



Yield: 1.19 g (80%).

IR (neat): 2960, 2867, 1594, 1495, 1480, 1288, 1252, 1164, 1050, 916, 807 cm^{-1}.

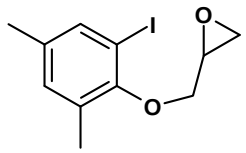
^{1}H NMR: δ 1.28 (s, 9H, C(CH_3)$_3$), 2.86-2.92 (m, 2H, OCH_2), 3.36-3.39 (m, 1H, O-C*H*), 4.04 (dd, *J* = 11.2 and 4.8 Hz, 1H, OCH_aH_b), 4.26 (dd, *J* = 11.2 and 3.2 Hz, 1H, OCH_aH_b), 6.78 (d, *J* = 8.8 Hz, 1H, Ar-*H*), 7.30 (dd, *J* ~ 8.8 and 2.3 Hz, 1H, Ar-*H*), 7.77 (d, *J* ~ 2.3 Hz, 1H, Ar-*H*).

^{13}C NMR: δ 31.4, 34.1, 44.8, 50.2, 69.6, 86.7 (*C*I), 112.3, 126.4, 136.6, 146.3, 154.9.

LC-MS: *m/z* 333 $[M+1]^+$.

Anal. Calc. for $C_{13}H_{17}IO_2$: C, 47.01; H, 5.16. Found: C, 47.12; H, 5.23.

Compound 1d:



Yield: 1.16 g (85%).

IR (neat): 2998, 2924, 2870, 1557, 1470, 1341, 1273, 1219, 1125, 1013, 912, 855 cm^{-1}.

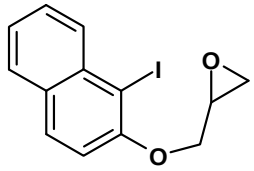
^{1}H NMR: δ 2.23 and 2.30 (2 s, 6H, 2 CH_3), 2.75 (dd, *J* = 4.8 and 2.4 Hz, 1H, OCH_aH_b), 2.90 (dd→t, *J* = 4.8 Hz, 1H, OCH_aH_b), 3.43-3.47 (m, 1H, O-C*H*), 3.83 (dd, *J* = 10.8 and 6.0 Hz, 1H, OCH_aH_b), 4.08 (dd, *J* = 10.8 and 3.6 Hz, 1H, OCH_aH_b), 6.95-6.96 (s, 1H, Ar-*H*), 7.43 (s, 1H, Ar-*H*).

^{13}C NMR: δ 16.9, 20.2, 44.9, 50.4, 73.6, 91.6 (*C*I), 131.8, 132.4, 135.9, 137.4, 154.3.

LC-MS: *m/z* 305 $[M+1]^+$.

Anal. Calc. for $C_{11}H_{13}IO_2$: C, 43.44; H, 4.31. Found: C, 43.56; H, 4.23.

Compound 1e:



Yield: 1.11 g (76%).

Mp: 80-82 ^oC

IR (neat): 2999, 2922, 1698, 1589, 1501, 1325, 1265, 1242, 1145, 1059, 864, 764, 743 cm^{-1}.

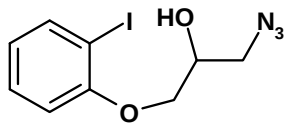
^1H NMR: δ 2.94-2.95 (d, *J* = 2.4 Hz, 2H, OCH_2), 3.46-3.47 (m, 1H, O-C*H*), 4.22 (dd, *J* ~ 11.2 and 4.8 Hz, 1H, OCH_aH_b), 4.44 (dd, *J* = 11.2 and 2.8 Hz, 1H, OCH_aH_b), 7.21 (d, *J* ~ 8.4 Hz, 1H, Ar-*H*), 7.41 (t, *J* ~ 7.6 Hz, 1H, Ar-*H*), 7.55 (t, *J* ~ 7.6 Hz, 1H, Ar-*H*), 7.75 (d, *J* = 7.6 Hz, 1H, Ar-*H*), 7.81 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 8.15 (d, *J* = 8.4 Hz, 1H, Ar-*H*).

^{13}C NMR: δ 44.9, 50.3, 70.7, 89.2 (*C*I), 114.8, 124.8, 128.2, 130.3, 130.4 131.4, 135.6, 155.8.

LC-MS: *m/z* 327 $[M+1]^+$.

Anal. Calc. for $C_{13}H_{11}IO_2$: C, 47.88; H, 3.40. Found: C, 47.72; H, 3.51.

Compound 2a:



Yield: 0.69 g (72%).

IR (neat): 3414, 2934, 2534, 2104, 1711, 1581, 1474, 1439, 1277, 1248, 1053, 1019, 937, 750 cm^{-1}.

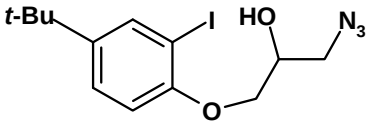
^{1}H NMR: δ 2.72 (d, *J* = 6.0 Hz, 1H, O*H*), 3.60-3.62 (m, 2H, NCH_2), 4.06-4.08 (m, 2H, OCH_2), 4.18-4.25 (m, 1H, OC*H*), 6.76 (dt, *J* = 7.6 and 1.2 Hz, 1H, Ar-*H*), 6.83 (dd, *J* ~ 8.4 and 1.2 Hz, 1H, Ar-*H*), 7.31 (dt, *J* = 7.6 and 1.2 Hz, 1H, Ar-*H*), 7.77 (dd, *J* = 8.0 and 1.6 Hz, 1H, Ar-*H*).

^{13}C NMR: δ 53.3, 69.3, 70.3, 86.8 (*C*I), 112.6, 123.5, 129.7, 139.5, 156.6.

LC-MS: *m/z* 320 $[M+1]^+$.

Anal. Calc. for $C_9H_{10}IN_3O_2$: C, 33.88; H, 3.16; N, 13.17. Found: C, 33.81; H, 3.25; N, 13.06.

Compound 2b:



Yield: 0.78 g (69%).

IR (neat): 3400, 2960, 2867, 2101, 1594, 1495, 1288, 1257, 1050, 812 cm^{-1}.

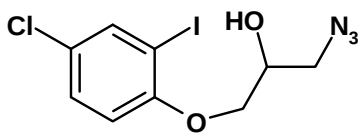
^{1}H NMR: δ 1.30 (s, 9H, C(CH_3)$_3$), 2.74 (br s, 1H, O*H*), 3.59-3.60 (m, 2H, NCH_2), 4.04-4.07 (m, 2H, OCH_2), 4.19-4.21 (m, 1H, HOC*H*), 6.77 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.32 (dd, *J* = 8.4 and 2.2 Hz, 1H, Ar-*H*), 7.76-7.77 (d, *J* ~ 2.2 Hz, 1H, Ar-*H*).

^{13}C NMR: δ 31.4, 34.2, 53.4, 69.3, 70.5, 86.8 (*C*I), 112.3, 126.6, 136.5, 146.7, 154.5.

LC-MS: *m/z* 374 $[M-1]^+$.

Anal. Calc. for $C_{13}H_{18}IN_3O_2$: C, 41.62; H, 4.84; N, 11.20. Found: C, 41.75; H, 4.81; N, 11.09.

Compound 2c:



Yield: 0.76g (72%).

IR (neat): 3394, 2934, 2877, 2101, 1578, 1469, 1283, 1242, 1045, 807, 714 cm^{-1}.

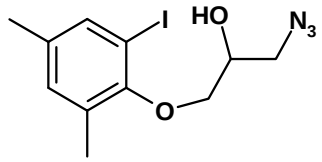
^{1}H NMR: δ 2.57 (br s, 1H, O*H*), 3.60-3.62(m, 2H, NCH_2), 4.02-4.06 (m, 2H, OCH_2), 4.20-4.27 (m, 1H, OC*H*), 6.75 (d, *J* ~ 8.4 Hz, 1H, Ar-*H*), 7.29 (dd, *J* ~ 8.4 and 2.4 Hz, 1H Ar-*H*), 7.75 (d, *J* = 2.4 Hz, 1H, Ar-*H*).

^{13}C NMR: δ 53.3, 69.2, 70.6, 86.9 (*C*I), 112.9, 127.4, 129.5, 138.6, 155.5.

LC-MS: *m/z* 354 $[M+1]^+$.

Anal. Calc. for $C_9H_9ClIN_3O_2$: C, 30.58; H, 2.57; N, 11.89. Found: C, 30.45; H, 2.65; N, 11.76.

Compound 2d:



Yield: 0.84 g (81%).

IR (neat): 3420, 2923, 2101, 1464, 1273, 1221, 1112, 1014, 854, 776 cm^{-1}.

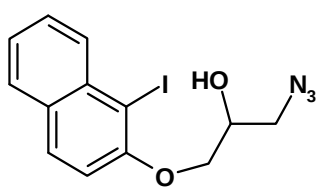
^{1}H NMR: δ 2.25 and 2.30 (2 s, 6H, 2 CH_3), 2.71 (br s, 1H, O*H*), 3.58-3.60 (m, 2H, NCH_2), 3.91 (d, *J* = 4.8 Hz, 2H, OCH_2), 4.20-4.24 (m, 1H, HOC*H*), 6.96 (s, 1H, Ar-*H*), 7.44 (s, 1H, Ar-*H*).

^{13}C NMR: δ 17.1, 20.2, 53.4, 69.9, 73.2, 91.6 (*C*I), 131.5, 132.7, 136.2, 137.5, 153.5.

LC-MS: *m/z* 348 $[M+1]^+$.

Anal. Calc. for $C_{11}H_{14}IN_3O_2$: C, 38.06; H, 4.06; N, 12.10. Found: C, 38.17; H, 3.95; N, 12.22.

Compound 2e:



Yield: 0.74 g (67%).

IR (neat): 3432, 2934, 2525, 2105, 1721, 1593, 1502, 1454, 1265, 1150, 1065, 1024, 941, 802, 764 cm^{-1}.

^{1}H NMR: δ 2.75 (br s, 1H, O*H*), 3.66-3.67 (m, 2H, NCH_2), 4.22-4.27 (m, 3H, OCH_2 + HOC*H*), 7.19 (d, *J* = 8.8 Hz, 1H, Ar-*H*), 7.43 (t, *J* ~ 7.6 Hz, 1H, Ar-*H*), 7.58 (t, *J* ~ 7.6 Hz, 1H, Ar-*H*), 7.77 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 7.84 (d, *J* = 8.8 Hz, 1H, Ar-*H*), 8.13 (d, *J* = 8.4 Hz, 1H, Ar-*H*),

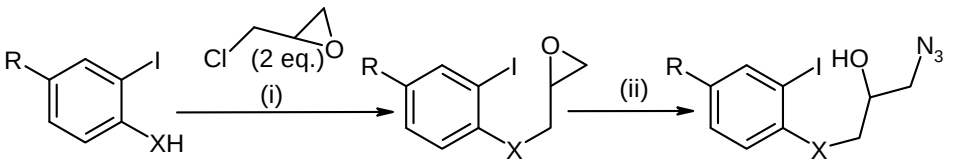
^{13}C NMR: δ 53.4, 69.5, 71.5, 89.1 (*C*I), 114.4, 124.9, 128.3, 128.4, 130.4, 130.6, 131.2, 135.5, 155.2.

LC-MS: *m/z* 368 $[M-1]^+$.

Anal. Calc. for $C_{13}H_{12}IN_3O_2$: C, 42.30; H, 3.28; N, 11.38. Found: C, 42.21; H, 3.21; N, 11.48.

General procedure for the synthesis of compounds 1f-1h and 2f-2h:

Compounds **1f-1h** and **2f-2h** were prepared by following the procedure (i) and (ii) mentioned above with same molar quantities. In the case of **1f**, **1g**, **2f** and **2g**, ^{1}H and ^{13}C spectra shows multiple peaks due to the possibility of rotamers/flip isomers (nearly 1:1 ratio).[8]



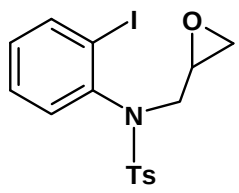
X = N-Ts, S

R = H, X = N-Ts, (**1f**)
R = Me, X = N-Ts (**1g**)
R = H, X = S, (**1h**)

R = H, X = N-Ts, (**2f**)
R = Me, X = N-Ts (**2g**)
R = H, X = S, (**2h**)

Conditions: (i). K_2CO_3 (1.5 eq.), CH_3CN, reflux, 6-12h.
(ii). NH_4Cl (2.0 eq.), NaN_3 (4.0 eq.), MeOH, 50 °C, 10h.

Compound 1f (rotamers/ flip isomers nearly 1:1 ratio):



Yield: 1.45 g (75%).

Mp: 98-100 ^{o}C.

IR (KBr): 3068, 2997, 2915, 1584, 1458, 1342, 1156, 1096, 871, 718 cm^{-1}.

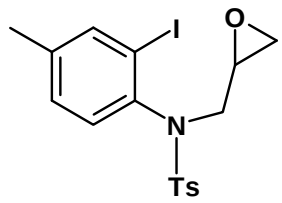
^{1}H NMR: δ 2.27 (dd, *J* = 4.8 and 2.4 Hz, 1H, C*H*$_a$H$_b$), 2.41 (dd, *J* = 4.8 and 2.8 Hz, 1H, CH$_a$*H*$_b$), 2.44 (s, 6H, C*H*$_3$), 2.68 (dd→t, *J* = 4.4 Hz, 1H, C*H*$_a$H$_b$), 2.72 (dd→t, *J* = 4.4 Hz, 1H, CH$_a$*H*$_b$), 3.17-3.18 (m, 1H, OC*H*), 3.28-3.29 (m, 1H, OC*H*), 3.54-3.61 (m, 2H, NC*H*$_2$), 3.71-3.80 (m, 2H, NC*H*$_2$), 6.95 (dd, *J* ~ 8.0 and 1.6 Hz, 1H, Ar-*H*), 7.01 (t, *J* = 7.6 Hz, 2H, Ar-*H*), 7.12 (dd, *J* = 8.0 and 1.6 Hz, 1H, Ar-*H*),7.27-7.34 (m, 6H, Ar-*H*), 7.64-7.66 (m, 4H, Ar-*H*), 7.89 (dd, *J* ~ 8.0 and 1.6 Hz, 1H, Ar-*H*), 7.93 (dd, *J* ~ 8.0 and 1.6 Hz, 1H, Ar-*H*). Due to the presence of isomers, number of protons is doubled in the assignment.

^{13}C NMR: δ 21.7, 46.0, 46.1, 49.7, 50.0, 54.4, 54.7, 102.3, 102.8, 128.2, 129.0, 129.1, 129.6$_7$, 129.7$_1$, 130.3, 130.7, 131.0, 136.1, 136.2, 140.5, 140.6, 141.6, 141.9, 144.1. Due to the presence of isomers, number of carbons is more in the spectrum

LC-MS: *m/z* 428 [M-1]$^{+}$.

Anal. Calc. for $C_{16}H_{16}INO_3S$: C, 44.77; H, 3.76; N, 3.26. Found: C, 44.65; H, 3.72; N, 3.31.

Compound 1g (rotamers/ flip isomers nearly 1:1 ratio):



Yield: 1.44 g (72%).

Mp: 106-108 ^{o}C.

IR (KBr): 3052, 2915, 2860, 1600, 1490, 1348, 1156, 1085, 811, 685, 586 cm^{-1}.

^{1}H NMR: δ 2.27 (dd, *J* ~ 4.8 and 2.4 Hz, 1H, C*H*$_a$H$_b$), 2.31 (s, 6H, C*H*$_3$), 2.41 (dd, *J* = 4.8

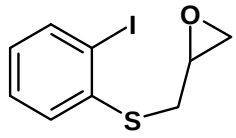
and 2.8 Hz, 1H, CH_aH_b), 2.44 (s, 6H, CH_3), 2.68 (dd→t, J ~ 4.4 Hz, 1H, CH_aH_b), 2.72 (dd→t, J ~ 4.4 Hz, 1H, CH_aH_b), 3.18-3.20 (m, 1H, OC*H*), 3.30-3.35 (m, 1H, OC*H*), 3.51-3.58 (m, 2H, NCH_2), 3.69-3.85 (m, 2H, NCH_2), 6.79 (d, J = 8.0 Hz, 1H, Ar-*H*), 6.97 (d, J = 8.0 Hz, 1H, Ar-*H*), 7.07-7.12 (m, 2H, Ar-*H*), 7.29-7.31 (m, 4H, Ar-*H*), 7.61-7.66 (m, 4H, Ar-*H*), 7.72-7.76 (m, 2H, Ar-*H*). Due to the presence of isomers, number of protons is doubled in the assignment.

^{13}C NMR: δ 20.7, 21.7, 45.9, 46.1, 49.8, 50.1, 54.4, 54.7, 102.1, 102.7, 128.1, 128.2, 128.4, 129.6, 129.7, 129.8, 129.9, 130.4, 136.1, 136.3, 138.9, 139.1, 140.7, 140.9, 141.0, 144.0. Due to the presence of isomers, number of carbons is more in the spectrum.

LC-MS: *m/z* 444 $[M+1]^+$.

Anal. Calc. for $C_{17}H_{18}INO_3S$: C, 46.06; H, 4.09; N, 3.16. Found: C, 46.15; H, 4.15; N, 3.23.

Compound 1h:



Yield: 1.12 g (85%).

IR (neat): 3052, 2986, 2921, 1643, 1573, 1441, 1255, 1096, 1008, 921, 844, 751 cm^{-1}.

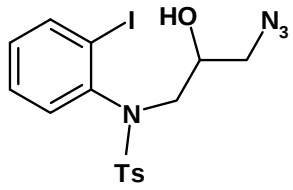
^{1}H NMR: δ 2.57 (dd, J = 4.8 and 2.4 Hz, 1H, CH_aH_b), 2.80 (dd→t, J ~ 4.8 Hz, 1H, CH_aH_b), 2.99 (dd, J = 13.6 and 5.2 Hz, 1H, CH_aH_b), 3.16-3.24 (m, 2H, CH_aH_b + OC*H*), 6.88-6.92 (m, 1H, Ar-*H*), 7.30-7.41 (m, 2H, Ar-*H*), 7.82-7.84 (m, 1H, Ar-*H*).

^{13}C NMR: δ 36.7, 47.4, 50.5, 101.0 (*C*I), 127.7, 128.8, 128.9, 139.8, 140.3.

LC-MS: *m/z* 293 $[M+1]^+$.

Anal. Calc. for C_9H_9IOS: C, 37.00; H, 3.11. Found: C, 37.12; H, 3.18.

Compound 2f (rotamers/ flip isomers nearly 1:1 ratio):



Yield: 0.98 g (69%).

Mp: 108-110 ^{o}C.

IR (KBr): 3534, 2908, 2096, 1583, 1449, 1340, 1288, 1154, 1071, 823, 704, 652 cm^{-1}.

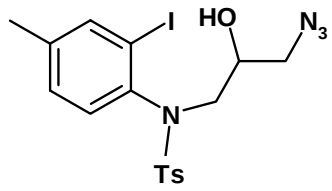
^{1}H NMR: δ 2.44 and 2.45 (s, 6H, C*H*$_3$), 2.93-3.90 (m, 12H, multiple peaks), 6.82 (dd, *J* ~ 8.0 and 1.6 Hz, 1H, Ar-*H*), 7.04-7.08 (m, 3H, Ar-*H*), 7.28-7.35 (m, 6H, Ar-*H*), 7.59-7.62 (m, 4H, Ar-*H*), 7.90 (dd, *J* ~ 8.0 and 1.6 Hz, 1H, Ar-*H*), 7.94 (dd, *J* = 8.0 and 1.6 Hz, 1H, Ar-*H*). Due to the presence of isomers, number of protons is doubled in the assignment.

^{13}C NMR: δ 21.7, 53.7, 54.4, 55.3, 56.7, 68.5, 101.9, 103.7, 128.3$_8$, 128.4$_3$, 129.2, 129.3, 129.4, 129.7, 129.8, 130.3, 130.4, 131.1, 134.7, 135.3, 140.7, 141.8, 142.5, 144.4, 144.5. Due to the presence of isomers, number of carbons is more in the spectrum.

LC-MS: *m/z* 473 [M+1]$^{+}$.

Anal. Calc. for $C_{16}H_{17}IN_4O_3S$: C, 40.69; H, 3.63; N, 11.86. Found: C, 40.52; H, 3.68; N, 11.92.

Compound 2g (rotamers/ flip isomers nearly 1:1 ratio):



Yield: 1.05 g (72%).

Mp: 120-122 ^{o}C.

IR (KBr): 3529, 2909, 2865, 2098, 1594, 1479, 1347, 1150, 1073, 816, 679 cm^{-1}.

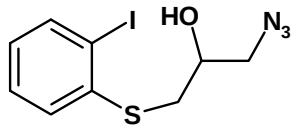
^{1}H NMR: δ 2.32 (s, 6H, C*H*$_3$), 2.45 and 2.46 (s, 6H, C*H*$_3$), 2.88-3.92 (m, 12H, multiple peaks), 6.67 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 6.92 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 7.08-7.13 (m, 2H, Ar-*H*), 7.13-7.33 (m, 4H, Ar-*H*), 7.61-7.63 (m, 4H, Ar-*H*), 7.73 (s, 1H, Ar-*H*), 7.78 (s, 1H, Ar-*H*). Due to the presence of isomers, number of protons is doubled in the spectrum.

^{13}C NMR: δ 20.6, 21.7, 53.6, 54.4, 55.3, 56.7, 68.4, 68.5, 101.5, 103.4, 128.3$_6$, 128.4$_2$, 129.7, 129.8, 130.0, 130.2, 130.5, 134.8, 135.5, 139.1, 139.8, 140.8, 140.9, 144.0, 144.2, 144.4. Due to the presence of isomers, number of carbons is more in the spectrum.

LC-MS: *m/z* 487 $[M+1]^+$.

Anal. Calc. for $C_{17}H_{19}IN_4O_3S$: C, 41.99; H, 3.94; N, 11.52. Found: C, 41.85; H, 4.02; N, 11.43.

Compound 2h:



Yield: 0.79g (79%).

IR (neat): 3425, 2915, 2099, 1573, 1441, 1293, 1101, 1014, 926, 745 cm^{-1}.

^{1}H NMR: δ 2.68 (d, *J* = 4.0 Hz, 1H, O*H*), 2.99-3.14 (m, 2H, C*H*$_2$), 3.41-3.52 (m, 2H, C*H*$_2$), 3.85-3.92 (m, 1H, HOC*H*), 6.93 (dd, *J* = 8.0 and 7.2 Hz, 1H, Ar-*H*), 7.32-7.39 (m, 2H, Ar-*H*), 7.85 (d, *J* = 8.0 Hz, 1H, Ar-*H*).

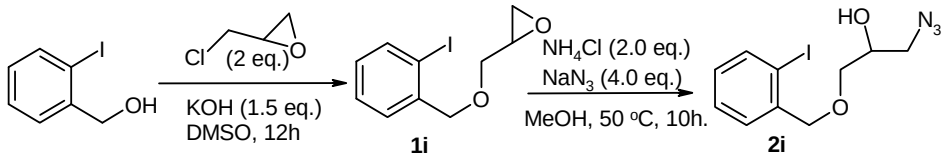
^{13}C NMR: δ 39.3, 55.2, 68.7, 101.9 (*C*I), 128.2, 129.1, 129.5, 139.6, 140.0.

LC-MS: *m/z* 336 $[M+1]^+$.

Anal. Calc. for $C_9H_9IN_3OS$: C, 32.25 H, 3.01; N, 12.54. Found: C, 32.15; H, 3.12; N, 12.43.

General procedure for the synthesis of compounds 1i and 2i:

Epichlorohydrin (0.95 g, 10.2 mmol) was added to a suspension of 2-iodobenzyl alcohol (1.2 g, 5.1 mmol) and potassium hydroxide (3.43 g, 6.12 mmol) in DMSO (5 mL) at room temperature and the mixture stirred for 12 h. After completion of reaction (tlc), water (20 mL) was added and the product extracted into diethyl ether (3x30 mL). The organic layer was washed with brine solution (20 mL) and dried over anhydrous sodium sulfate. Removal of solvent afforded an oily material. This was purified by silica gel column chromatography (hexane: EtOAc; 97:3) to give 2-((2-iodobenzyloxy)methyl)oxirane **1i** as a yellow oil. Compound **2i** was prepared following step (ii) for **2a** by using 2-((2-iodobenzyloxy)methyl)oxirane (**1i**) (0.87 g, 3.0 mmol), ammonium chloride (0.32 g, 6.0 mmol) and sodium azide (0.78 g, 12.0 mmol).



Compound 1i:

Yield: 0.99 g (67%).

IR (neat): 2923, 1728, 1583, 1433, 1283, 1247, 1133, 1097, 1014, 740 cm^{-1}.

^{1}H NMR: δ 2.68 (dd, *J* = 4.8 and 1.6 Hz, 1H, C*H*$_a$H$_b$), 2.84 (dd→t, *J* = 4.4 Hz, 1H, CH$_a$*H*$_b$), 3.23-3.27 (m, 1H, OC*H*), 3.54 (dd, *J* ~ 11.2 and 5.6 Hz, 1H, CH$_a$*H*$_b$), 3.87 (dd, *J* = 11.2 and 2.8 Hz, 1H, C*H*$_a$H$_b$), 4.53-4.62 (m, 2H, OC*H*$_2$), 7.00 (t, *J* ~ 7.6 Hz, 1H, Ar-*H*), 7.36 (t, *J* ~ 7.2 Hz, 1H, Ar-*H*), 7.45 (d, *J* ~ 7.2 Hz, 1H, Ar-*H*), 7.83 (d, *J* = 7.6 Hz, 1H, Ar-*H*).

^{13}C NMR: δ 44.4, 50.8, 71.4, 76.9, 97.8 (*C*I), 128.3, 128.9, 129.3, 139.2, 140.2.

LC-MS: *m/z* 291 $[M+1]^+$.

Anal. Calc. for $C_{10}H_{11}IO_2$: C, 41.40; H, 3.82. Found: C, 41.52; H, 3.75.

Compound 2i:

Yield: 0.81 g (81%).

IR (neat): 3441, 2913, 2867, 2101, 1563, 1433, 1273, 1097, 1009, 745 cm^{-1}.

^{1}H NMR: δ 2.59-2.60 (m, 1H, O*H*), 3.41-3.42 (m, 2H, NCH_2), 3.59-3.63 (m, 2H, OCH_2), 3.99-4.03 (m, 1H, HOC*H*), 4.55 (s, 2H, OCH_2), 7.00-7.04 (m, 1H, Ar-*H*), 7.34-7.40 (m, 2H, Ar-*H*), 7.84 (d, *J* = 8.0 Hz, 1H, Ar-*H*).

^{13}C NMR: δ 53.5, 69.7, 71.7, 77.1, 98.3 (*C*I), 128.3, 129.3, 129.7, 139.5, 139.8.

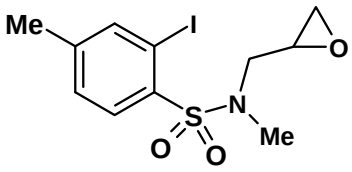
LC-MS: *m/z* 332 $[M-1]^+$.

Anal. Calc. for $C_{10}H_{12}IN_3O_2$: C, 36.06; H, 3.63; N, 12.61. Found: C, 36.12; H, 3.58; N, 12.51.

General procedure for the synthesis of compounds 1j and 2j:

Compounds **1j** and **2j** were prepared by following the steps (i) - (ii) mentioned above for **2a** using the same molar quantities of 2-iodo-*N*,4-dimethylbenzennesulfonamide and epichlorohydrin.

Compound 1j:



Yield: 1.02 g (62%).

IR (neat): 2926, 1584, 1457, 1321, 1260, 1156, 1025, 931, 844, 745 cm^{-1}.

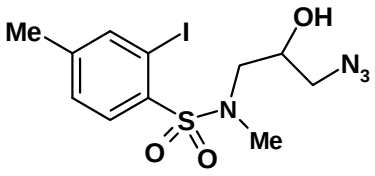
^{1}H NMR: δ 2.37 (s, 3H, CH_3), 2.55-2.57 (m, 1H, CH_aH$_b$), 2.79-2.81 (m, 1H, CH$_a$$H_b$), 2.95 (s, 3H, NC$H_3$), 3.08 (dd, *J* ~ 14.8 and 6.8 Hz, 1H, CH_aH$_b$), 3.11-3.19 (m, 1H, OC*H*), 3.81 (dd, *J* = 14.8 and 2.8 Hz, 1H, CH$_a$$H_b$), 7.30 (m, 1H, Ar-*H*), 7.94 (s, 1H, Ar-*H*), 8.01 (d, *J* = 8.0 Hz, 1H, Ar-*H*).

^{13}C NMR: δ 20.7, 29.2, 44.5, 50.7, 52.4, 92.3(*C*I), 129.0, 131.9, 137.9, 143.6, 144.7.

LC-MS: *m/z* 368 $[M+1]^+$.

Anal. Calc. for $C_{11}H_{14}INO_3S$: C, 35.98; H, 3.84; N, 3.81. Found: C, 35.86; H, 3.91; N, 3.75.

Compound 2j:



Yield: 0.83 g (67%).

IR (neat): 3503, 2981, 2929, 2096, 1718, 1588, 1449, 1335, 1159, 1097, 978, 760 cm^{-1}.

^{1}H NMR: δ 2.37 (s, 3H, ArC*H*$_3$), 2.82 (bs, 1H, O*H*), 2.97 (s, 3H, NC*H*$_3$), 3.31-3.43 (m, 4H, 2 C*H*$_2$), 4.03 (br s, 1H, HOC*H*), 7.30 (d, *J* ~ 8.0 Hz, 1H, Ar-*H*), 7.94 (s, 1H, Ar-*H*), 7.97 (d, *J* = 8.0 Hz, 1H, Ar-*H*).

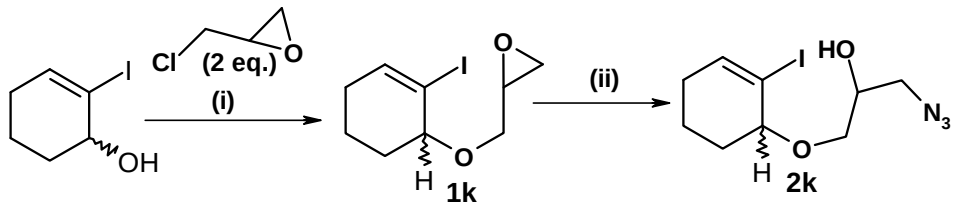
^{13}C NMR: δ 20.8, 36.4, 53.8, 54.3, 68.9, 92.2 (*C*I), 129.2, 132.0, 137.7, 143.7, 145.0.

LC-MS: *m/z* 411 $[M+1]^{+}$.

Anal. Calc. for $C_{11}H_{15}IN_4O_3S$: C, 32.21; H, 3.69; N, 13.66. Found: C, 32.29; H, 3.61; N, 13.56.

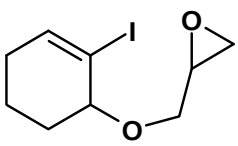
General procedure for the synthesis of compounds 1k and 2k:

Compounds **1k** and **2k** were prepared by following the procedures for **1i** and **2i** mentioned above with same molar quantities.



Conditions: (i). KOH (1.5 eq.), DMSO, r.t., 8h
(ii). NH_4Cl (2.0 eq.), NaN_3 (4.0 eq.), MeOH, 50 °C, 10h.

Compound 1k (approx. 1:1 diastereomeric ratio)**:**



Yield: 0.96 g (67%).

IR (neat): 3047, 2992, 2921, 1605, 1468, 1386, 1337, 1227, 1162, 1079, 932, 899, 745 cm^{-1}.

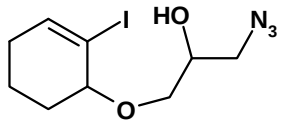
^1H NMR: δ 1.63-2.11 (m, 12H, C*H*$_2$), 2.66-2.68 (m, 2H), 2.80-2.85 (m, 2H), 3.22-3.26 (m, 2H), 3.52-3.58 (m, 2H), 3.78-3.83 (m, 2H), 3.88 (br s, 1H), 3.97 (bs, 1H), 6.53-6.56 (m, 2H, vinyl-*H*). Due to the presence of isomers, number of protons is doubled in the assignment.

^{13}C NMR: δ 17.0, 28.7, 29.2, 44.2, 44.6, 50.8, 69.7, 71.1, 79.3, 79.9, 98.7, 98.8, 141.8, 141.9. Due to the presence of isomers, number of carbons is more in the spectrum.

LC-MS: *m/z* 281 $[M+1]^+$.

Anal. Calc. for $C_9H_{13}IO_2$: C, 38.59; H, 4.68. Found: C, 38.52; H, 4.56.

Compound 2k (approx. 1:1 diastereomeric ratio)**:**



Yield: 0.69 g (71%).

IR (neat): 3436, 2932, 2860, 2099, 1627, 1436, 1293, 1096, 964, 734 cm^{-1}.

^1H NMR: δ 1.66-2.13 (m, 12H, C*H*$_2$), 2.66-2.67 (m, 1H), 2.72-2.73 (m, 1H), 3.40-3.53 (m, 6H), 3.66-3.72 (m, 2H), 3.87-3.88 (m, 2H), 3.98-4.01 (m, 2H), 6.55-6.57 (m, 2H, vinyl-*H*). Due to the presence of isomers, number of protons is doubled in the assignment.

^{13}C NMR: δ 17.1_9, 17.2_3, 28.7, 29.3, 53.2, 53.4, 69.6, 69.9, 70.3, 70.6, 79.6, 79.8, 98.8, 142.0_7, 142.1_1. Due to the presence of isomers, number of carbons is more in the spectrum.

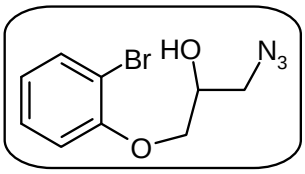
LC-MS: *m/z* 324 $[M+1]^+$.

Anal. Calc. for $C_9H_{14}IN_3O_2$: C, 33.45; H, 4.37; N, 13.00. Found: C, 32.56; H, 4.29; N, 13.12.

General procedure for the synthesis of compounds 1l and 2l:

Compounds **1l** and **2l** were prepared by following the steps (i) - (ii) mentioned above for **2a** using the same molar quantities of 2-bromo phenol and epichlorohydrin. Compound **1l** is a known compound.[9]

Compound 2l:



Yield: 0.636 g (78 %).

IR (neat): 3364, 3047, 2010, 1567, 1485, 1441, 1239, 1244, 1123, 1047, 767, 734 cm^{-1}.

^{1}H NMR: δ 3.10 (br, 1H, O*H*), 3.54-3.60 (m, 2H, CH_2), 4.06 (d, *J* = 5.2 Hz, 2H, CH_2), 4.19-4.22 (m, 1H, OC*H*), 6.85-6.90 (m, 2H, Ar-*H*), 7.24-7.29 (m, 1H, Ar-*H*), 7.53 (dd, *J* ~ 8.0 and 1.6 Hz, 1H, Ar-*H*).

^{13}C NMR: δ 53.3, 69.1, 70.2, 112.3, 113.7, 122.7, 128.6, 133.3, 154.5.

LC-MS: *m/z* 272, 274 $[M]^+$.

Anal. Calcd. for $C_9H_{10}BrN_3O_2$: C, 39.73; H, 3.70; N, 15.44; Found: C, 39.65; H, 3.76; N, 15.39.

References:

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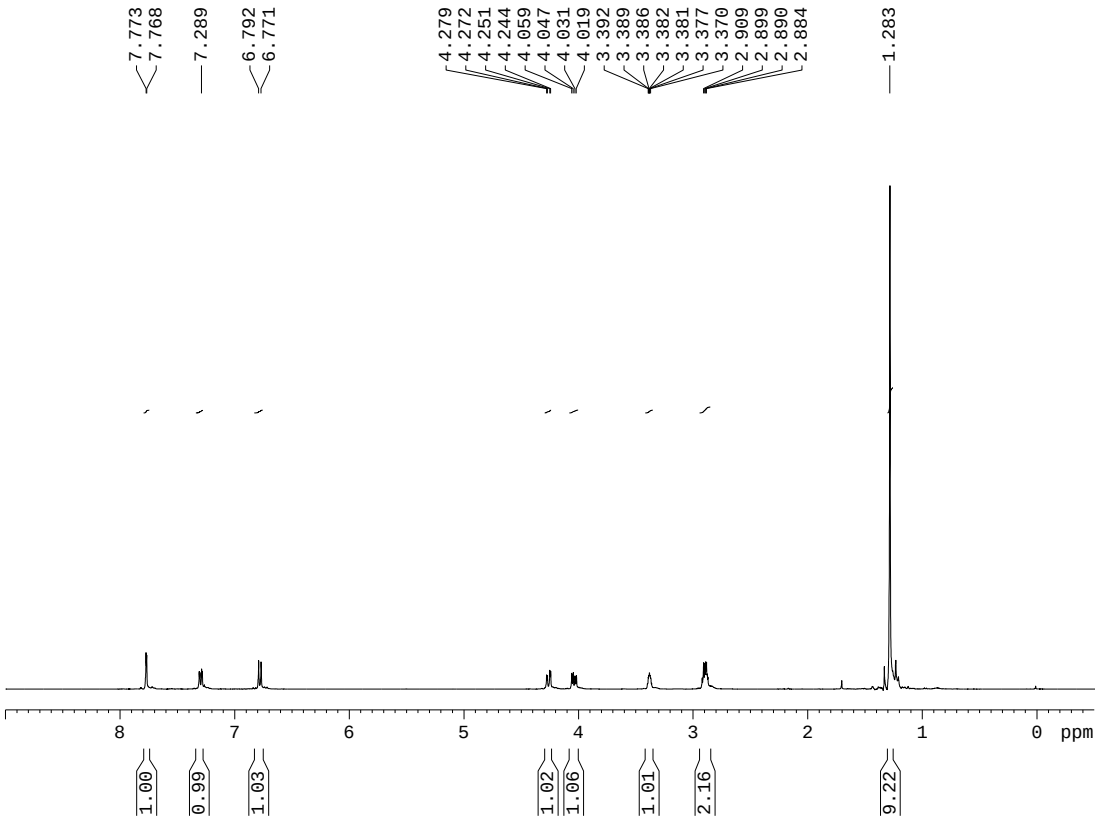

Figure S1. ^{1}H NMR spectrum of compound **1b**

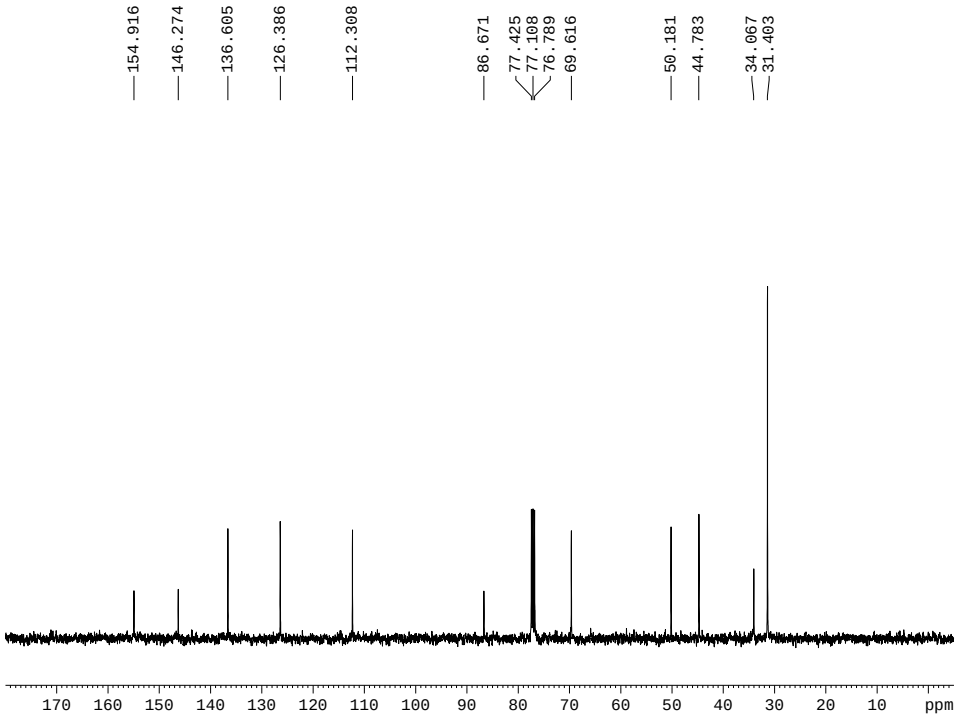

Figure S2. ^{13}C NMR spectrum of compound **1b**

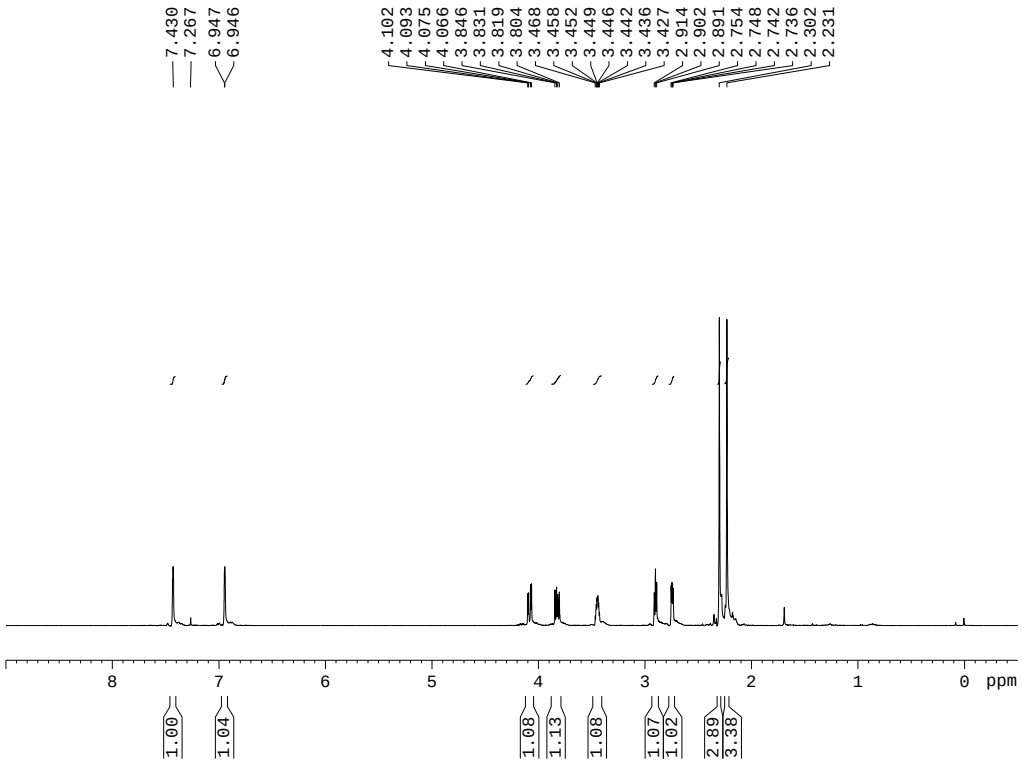

Figure S3. ^{1}H NMR spectrum of compound **1d**

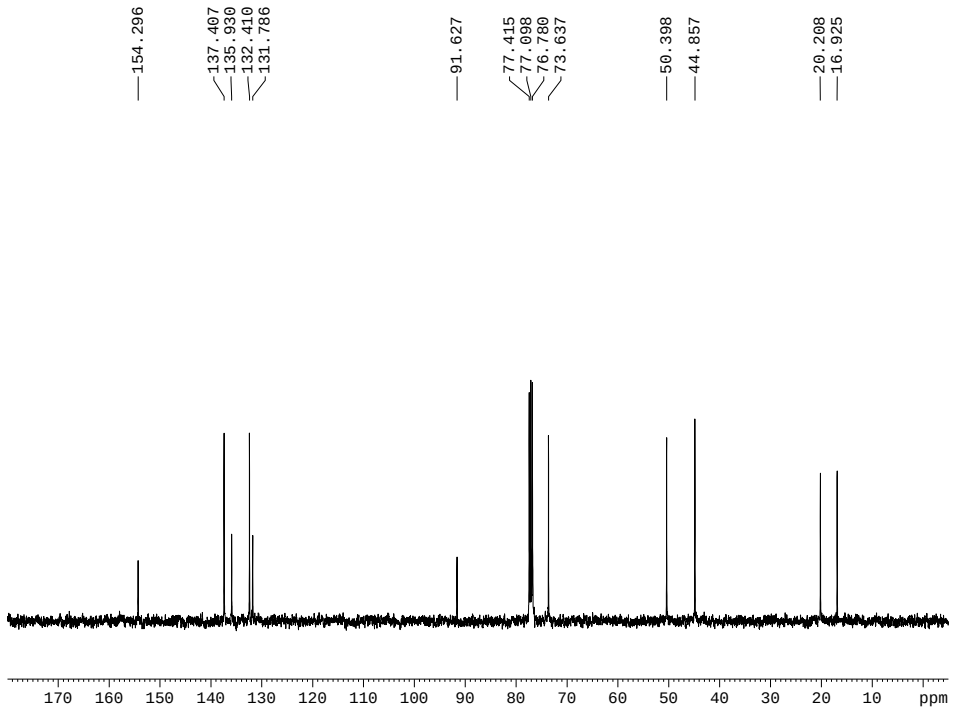

Figure S4. ^{13}C NMR spectrum of compound **1d**

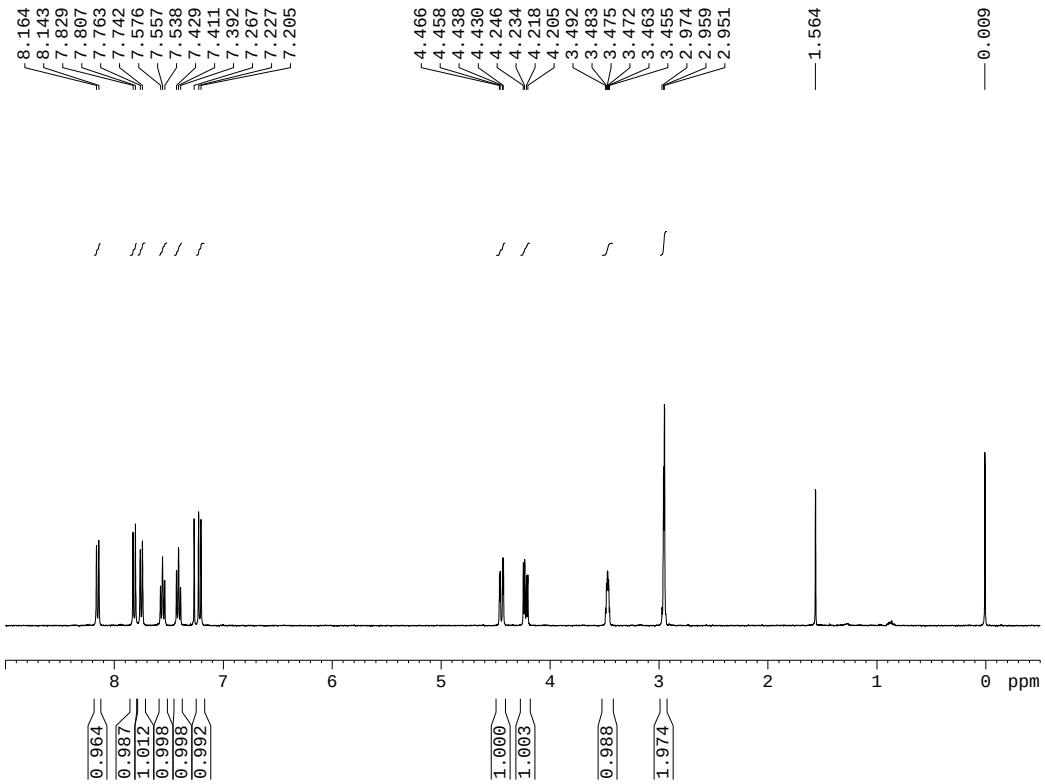

Figure S5. ^{1}H NMR spectrum of compound **1e**

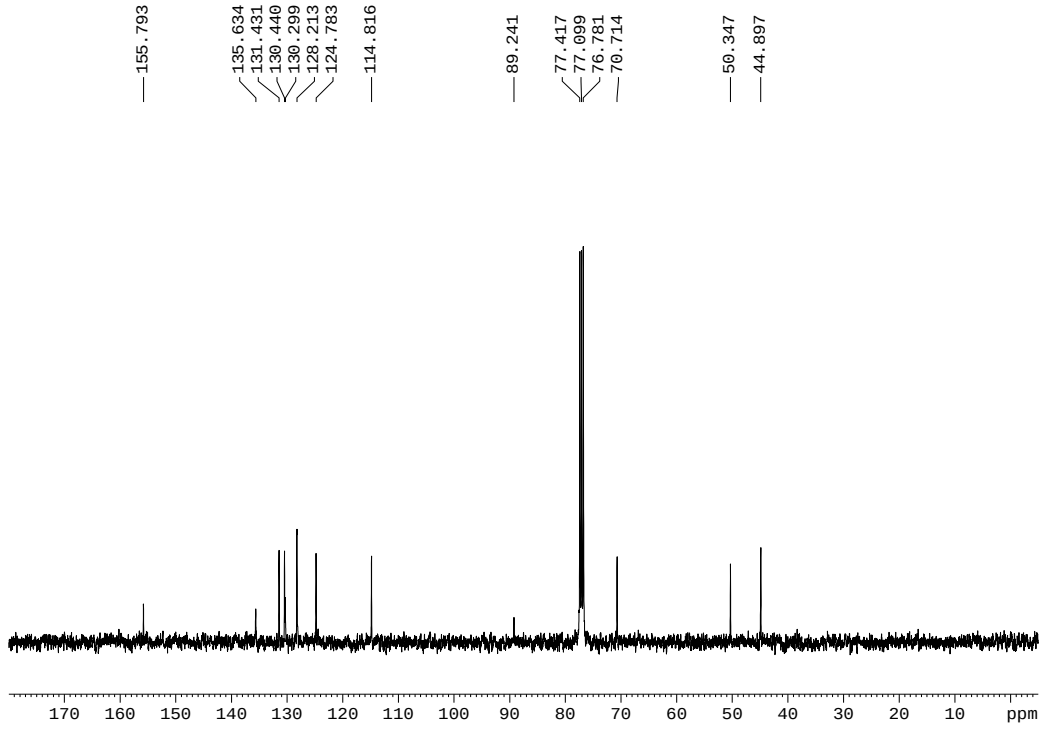

Figure S6. ^{13}C NMR spectrum of compound **1e**

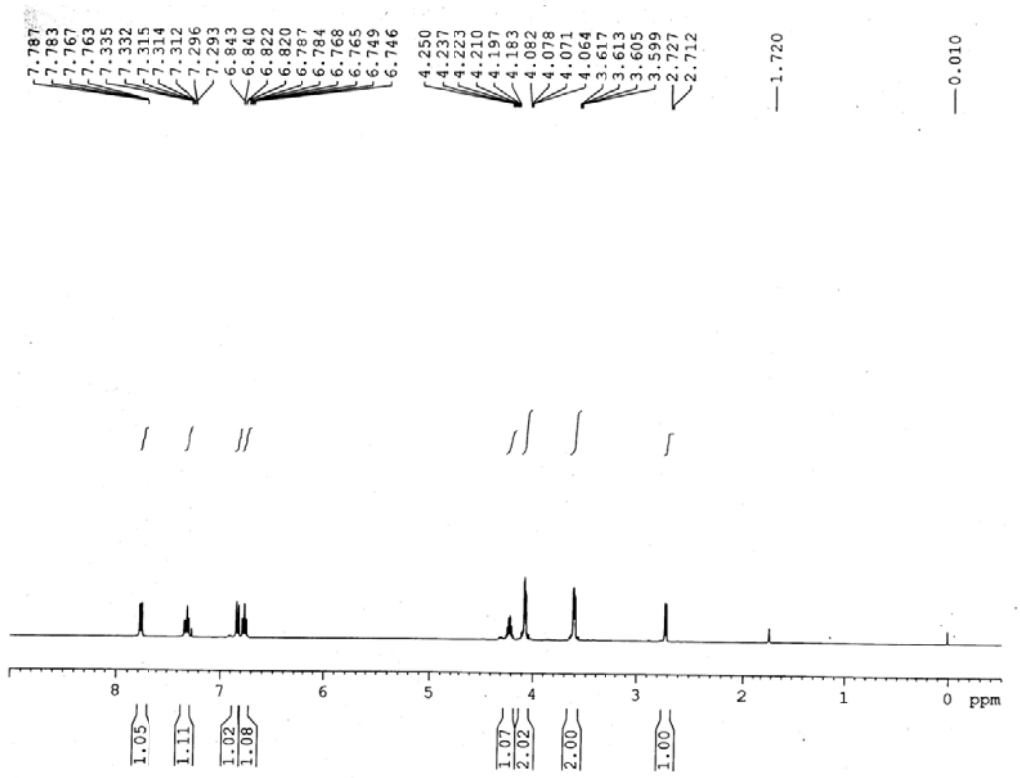

Figure S7. ^{1}H NMR spectrum of compound **2a**

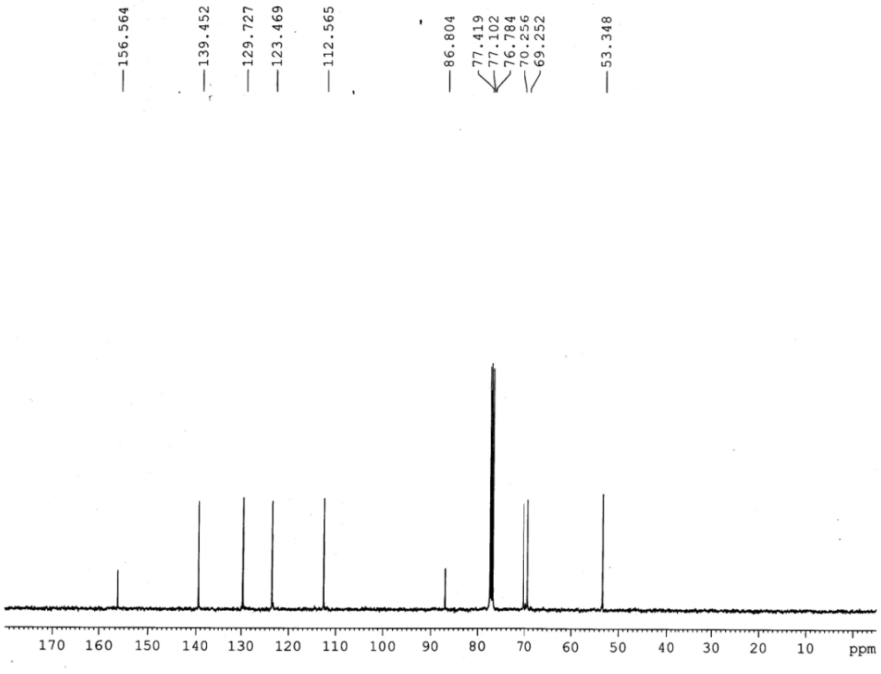

Figure S8. ^{13}C NMR spectrum of compound **2a**

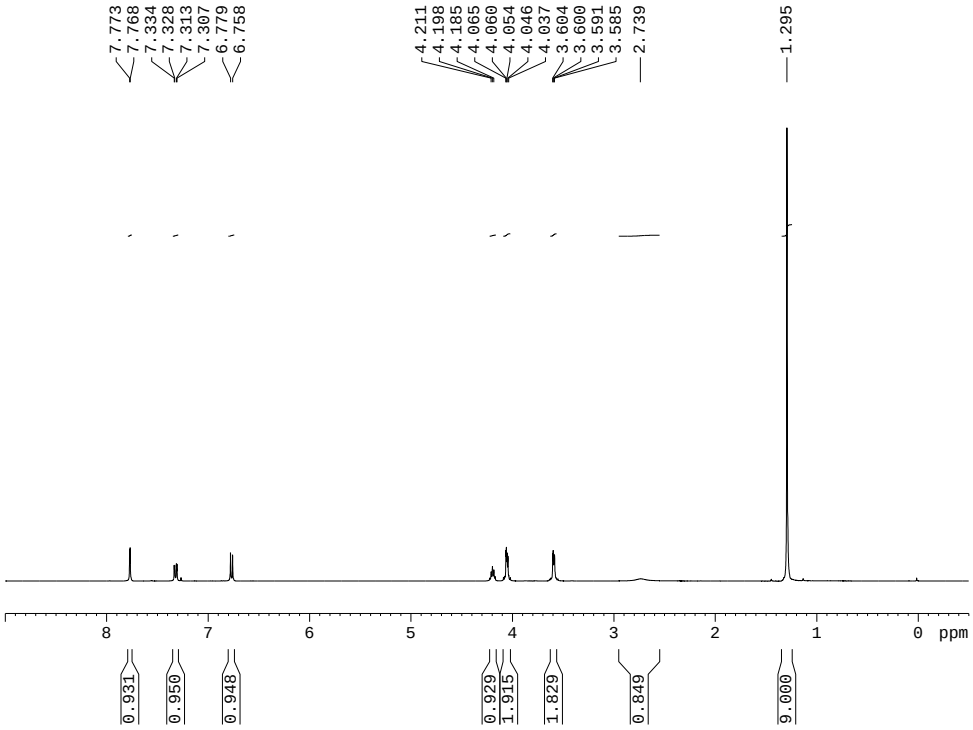

Figure S9. ^{1}H NMR spectrum of compound **2b**

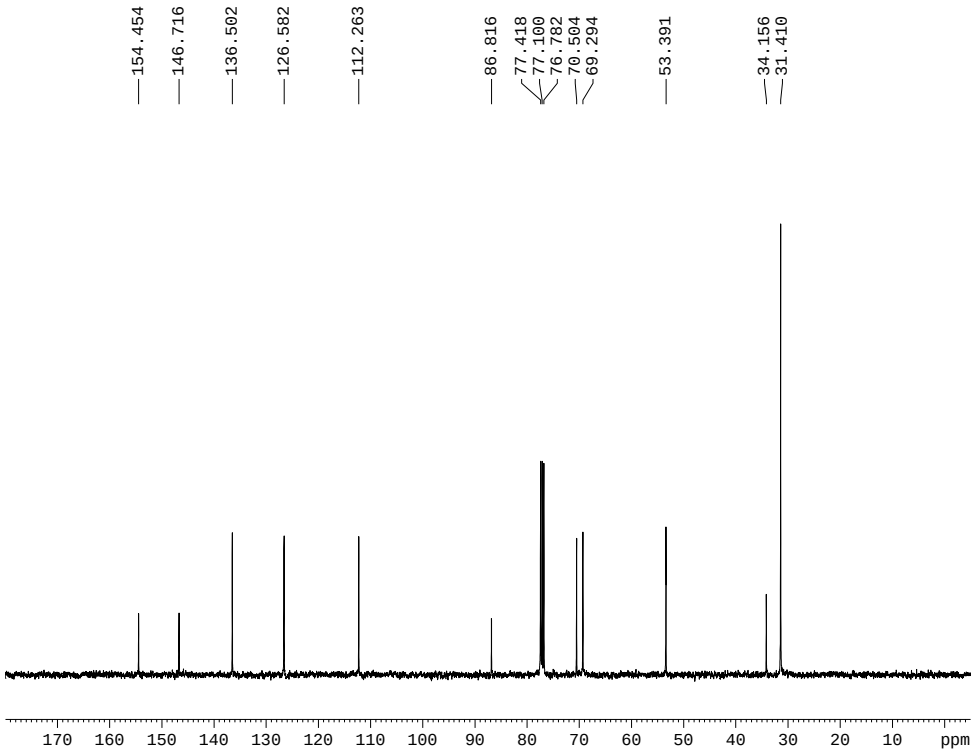

Figure S10. ^{13}C NMR spectrum of compound **2b**

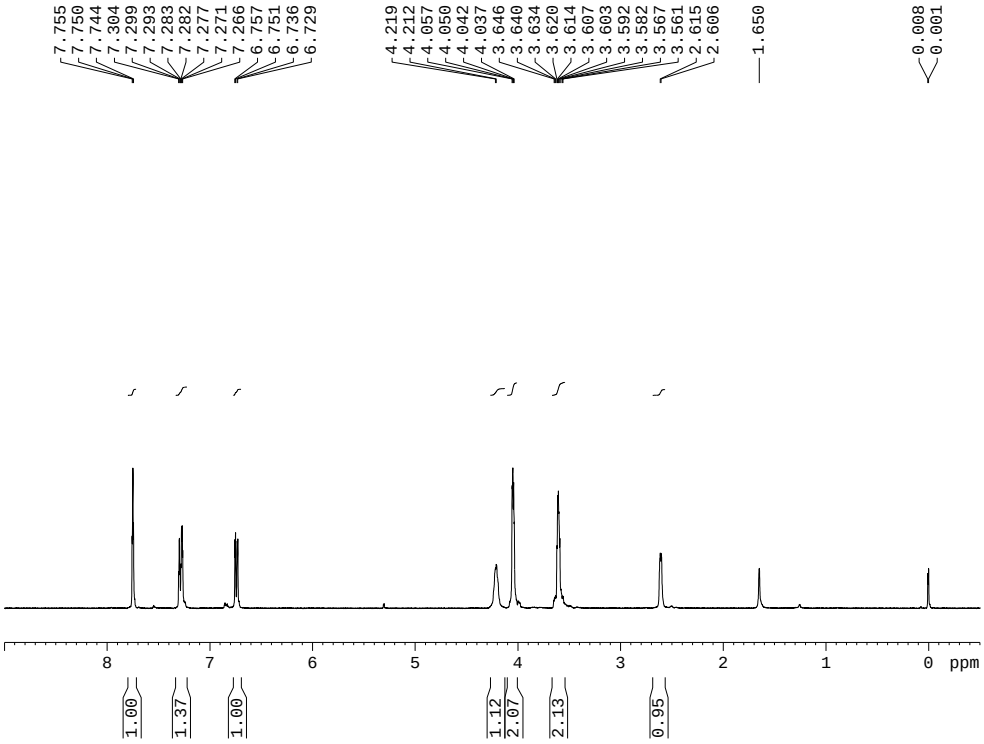

Figure S11. ^{1}H NMR spectrum of compound **2c**

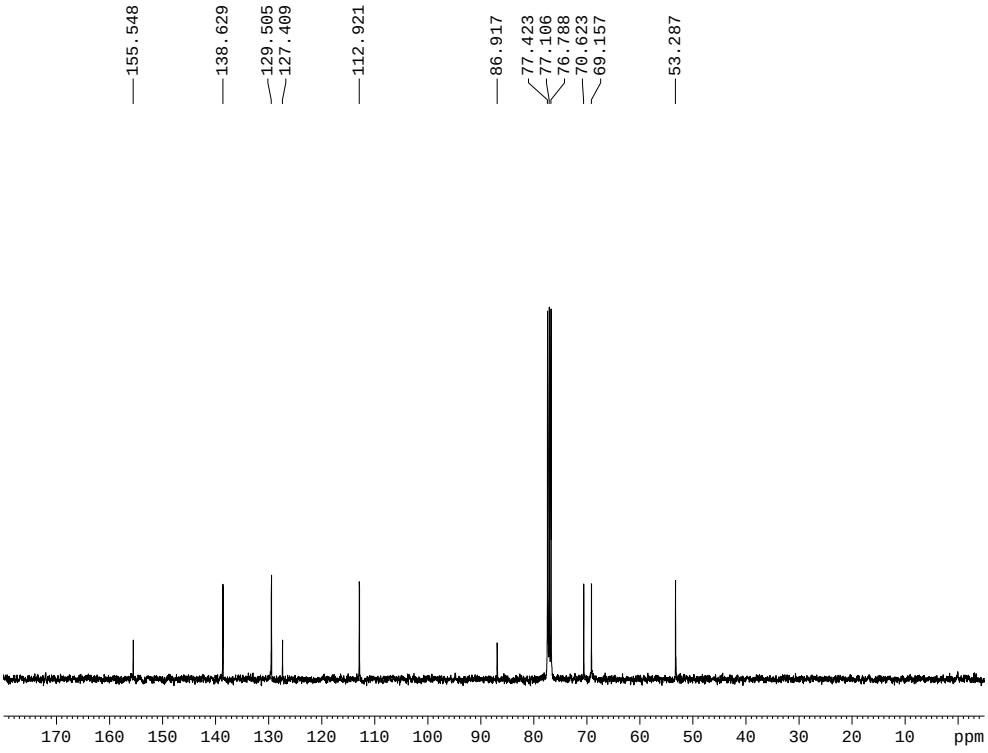

Figure S12. ^{13}C NMR spectrum of compound **2c**

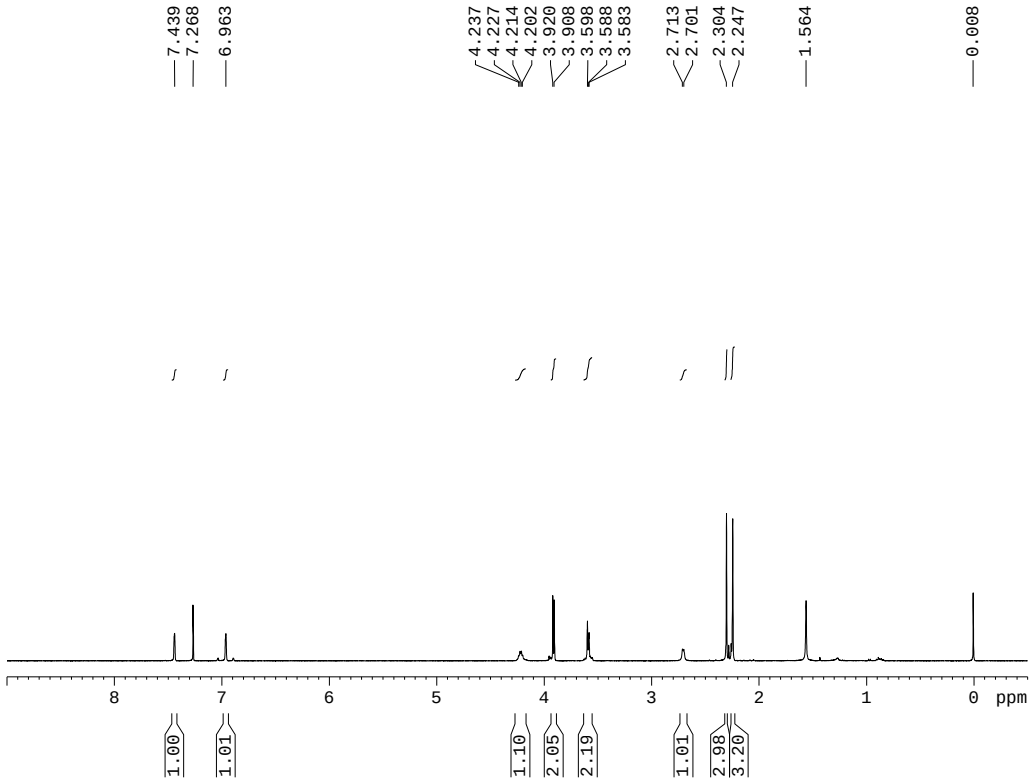

Figure S13. ^{1}H NMR spectrum of compound **2d**

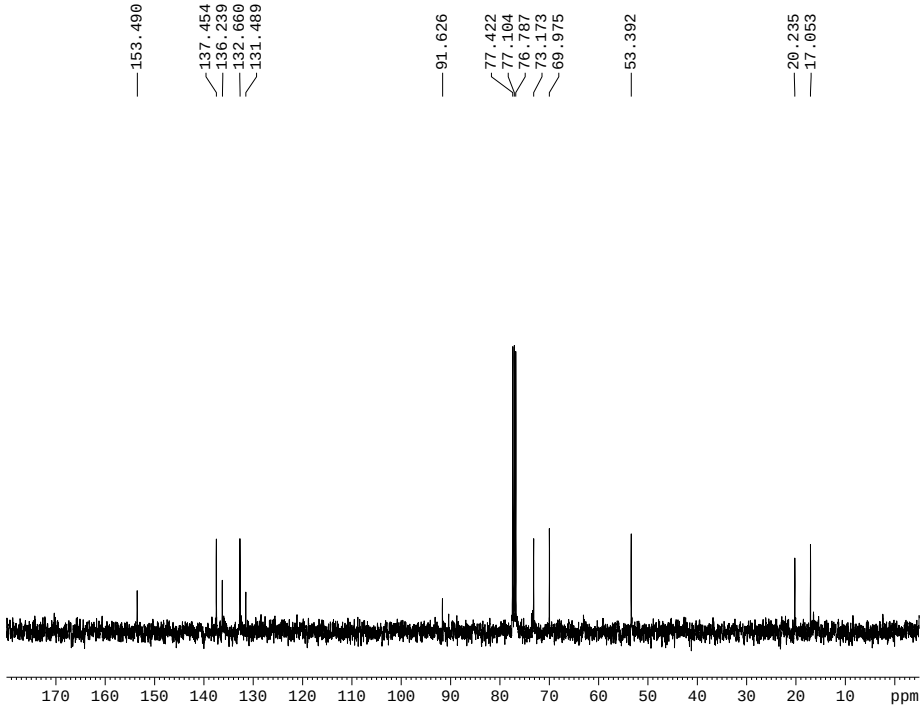

Figure S14. ^{13}C NMR spectrum of compound **2d**

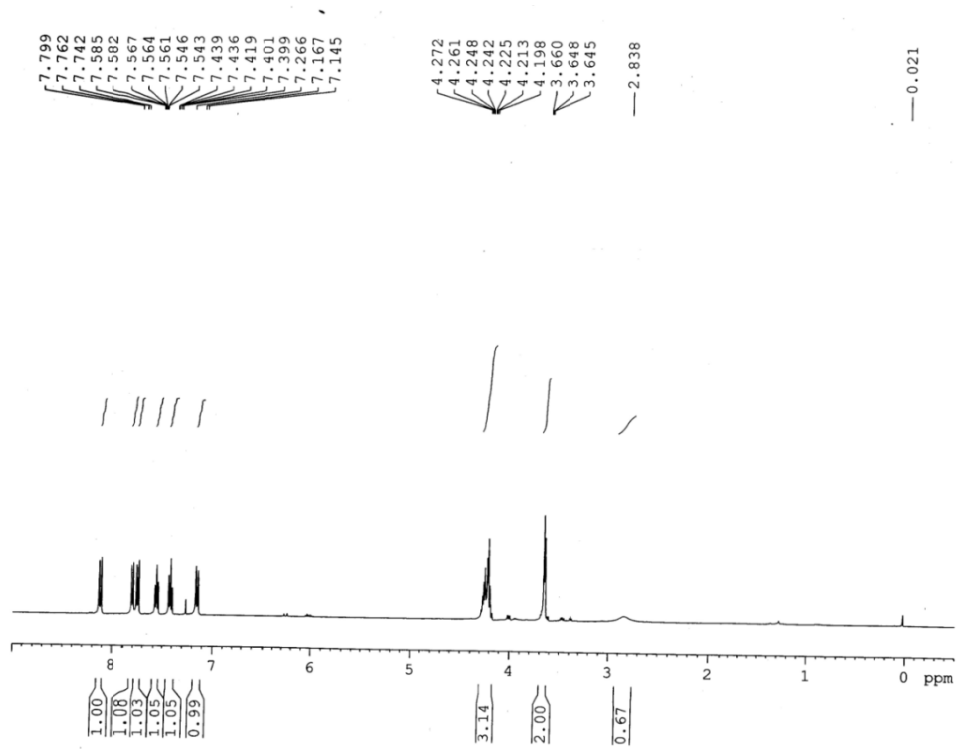

Figure S15. ^{1}H NMR spectrum of compound **2e**

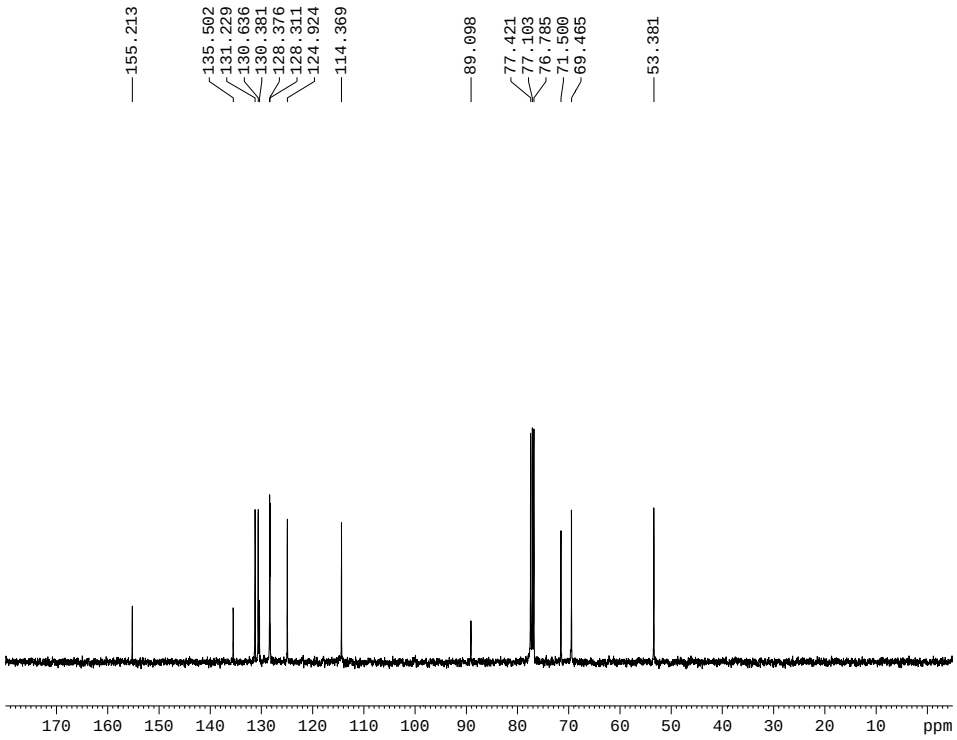

Figure S16. ^{13}C NMR spectrum of compound **2e**

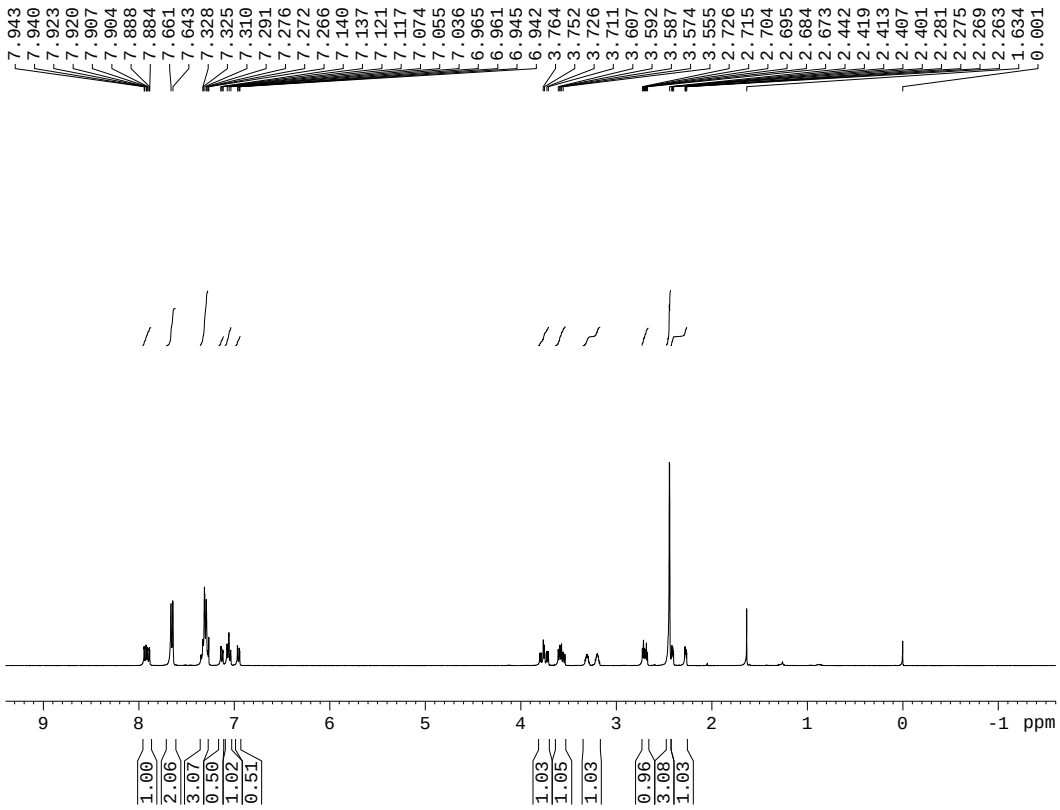

Figure S17. ^{1}H NMR spectrum of compound **1f**

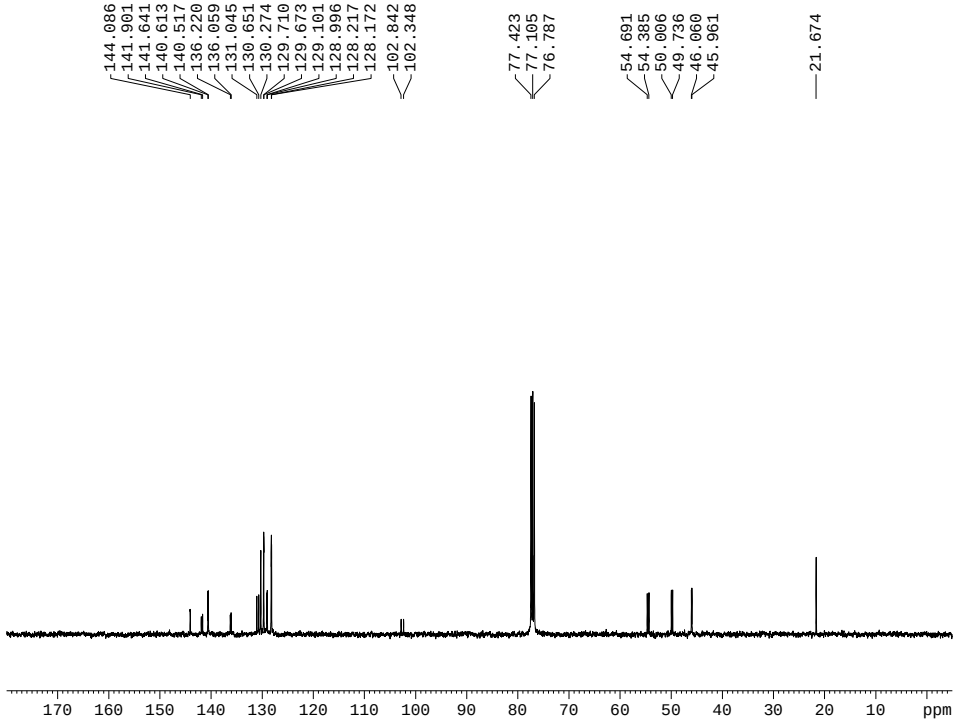

Figure S18. ^{13}C NMR spectrum of compound **1f**

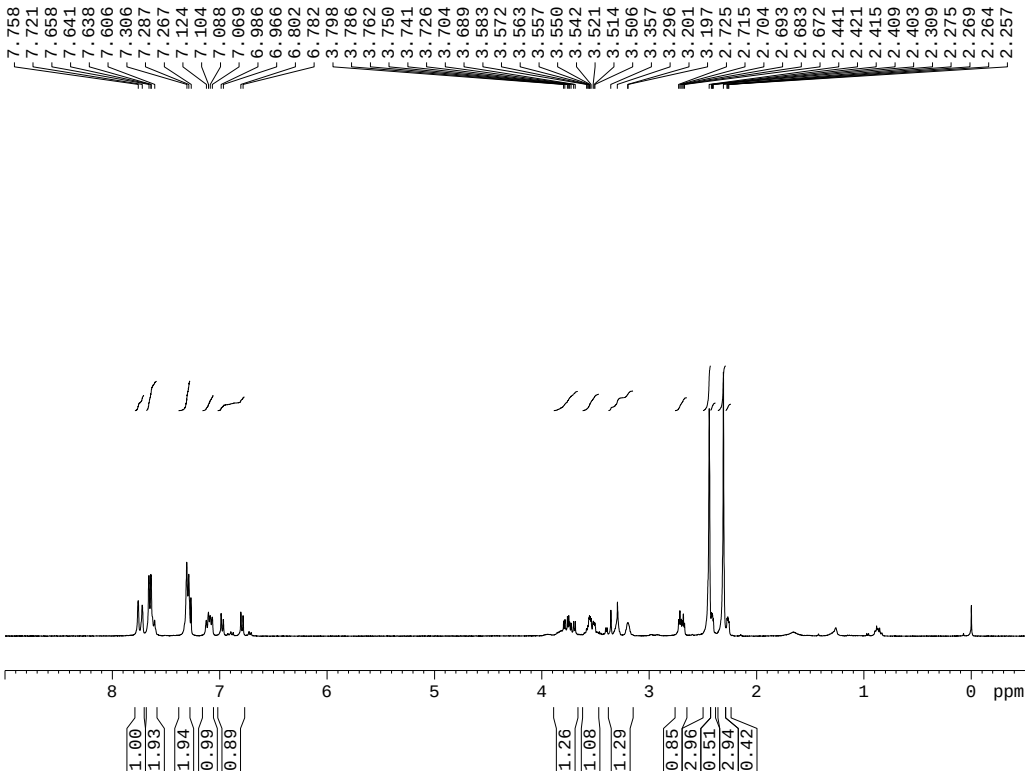

Figure S19. ^{1}H NMR spectrum of compound **1g**

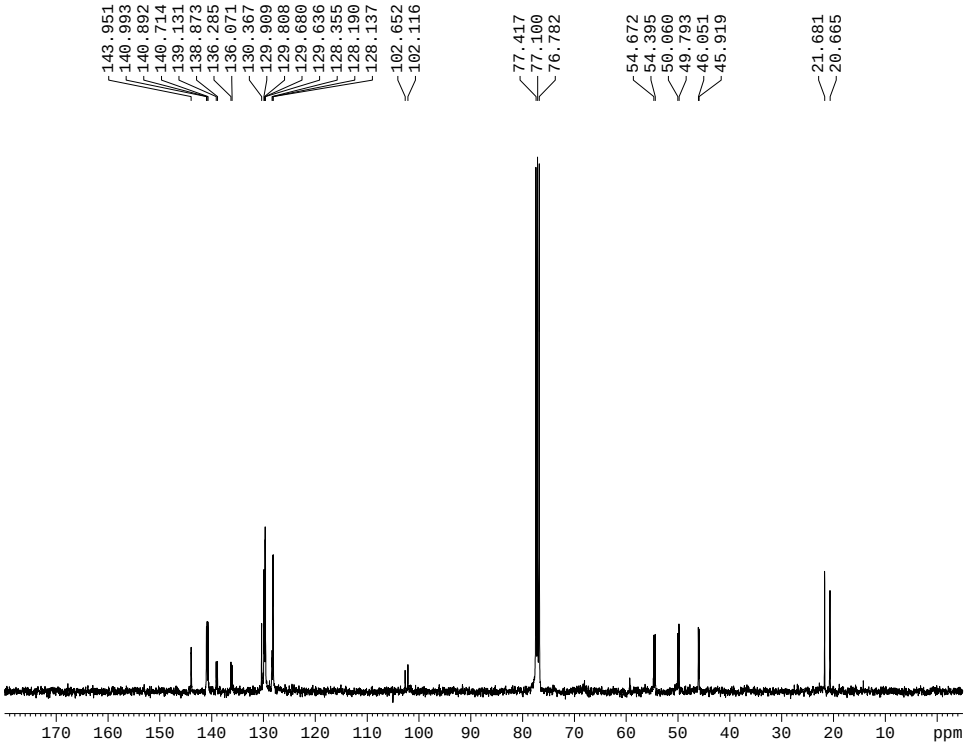

Figure S20. ^{13}C NMR spectrum of compound **1g**

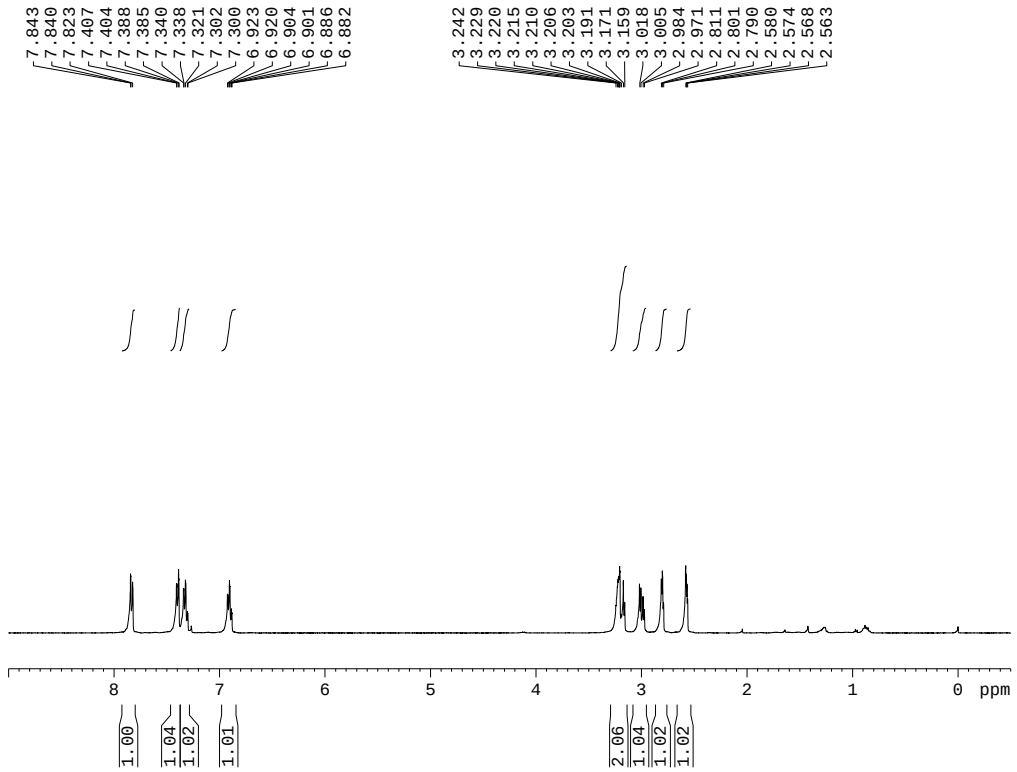

Figure S21. ^{1}H NMR spectrum of compound **1h**

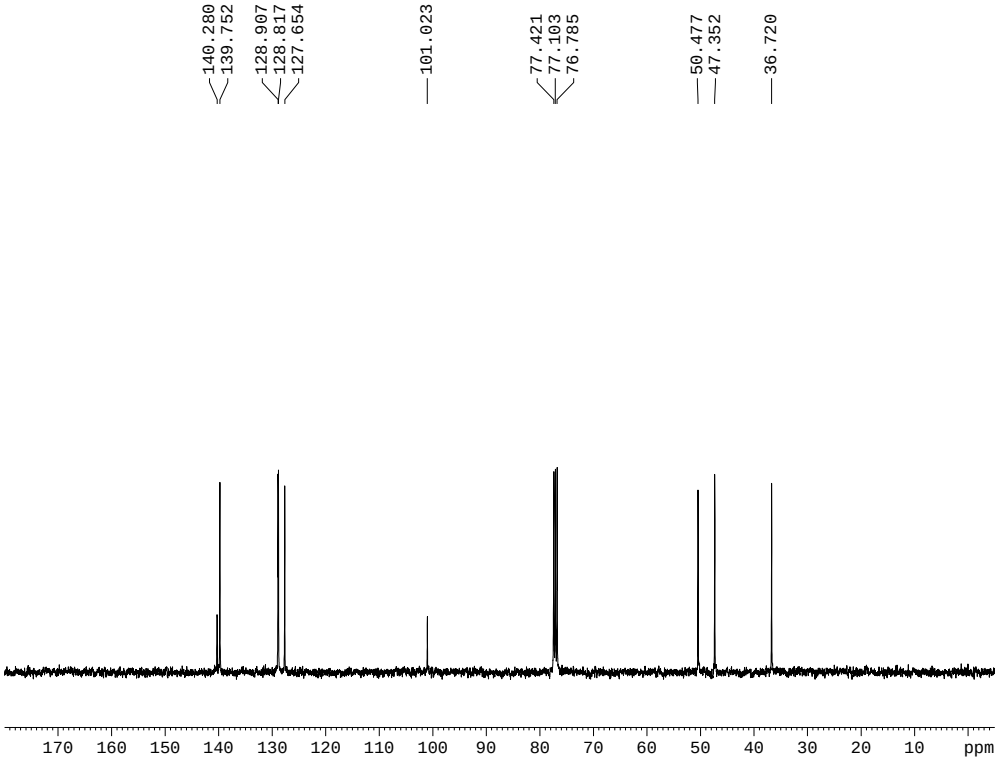

Figure S22. ^{13}C NMR spectrum of compound **1h**

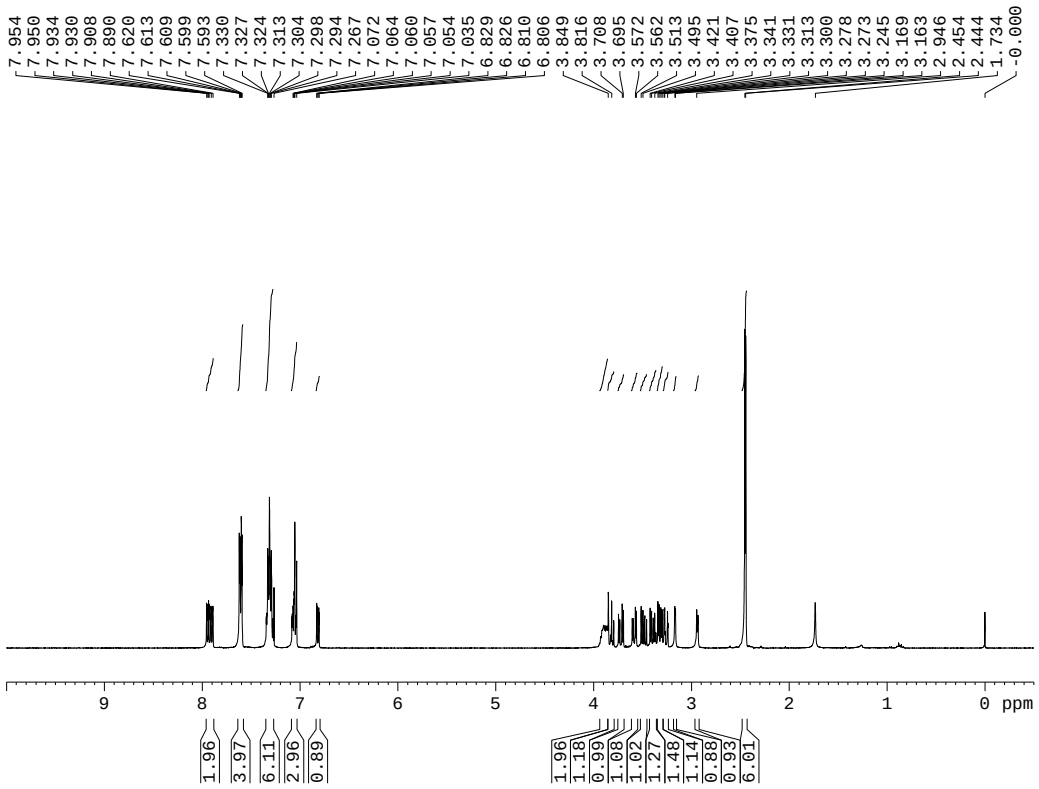

Figure S23. ^{1}H NMR spectrum of compound **2f**

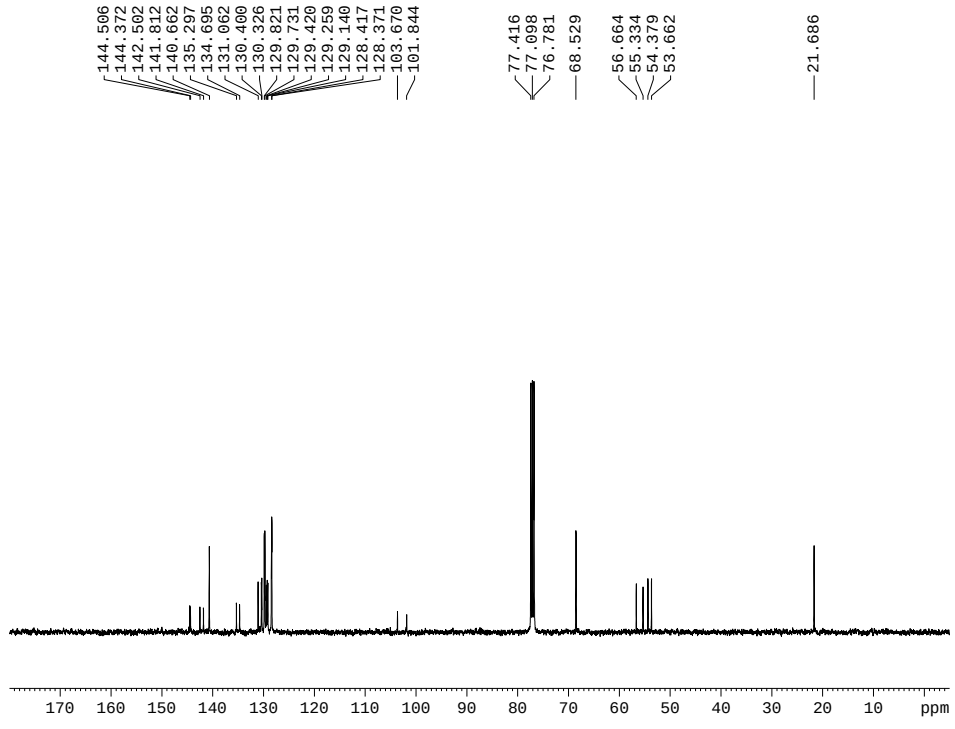

Figure S24. ^{13}C NMR spectrum of compound **2f**

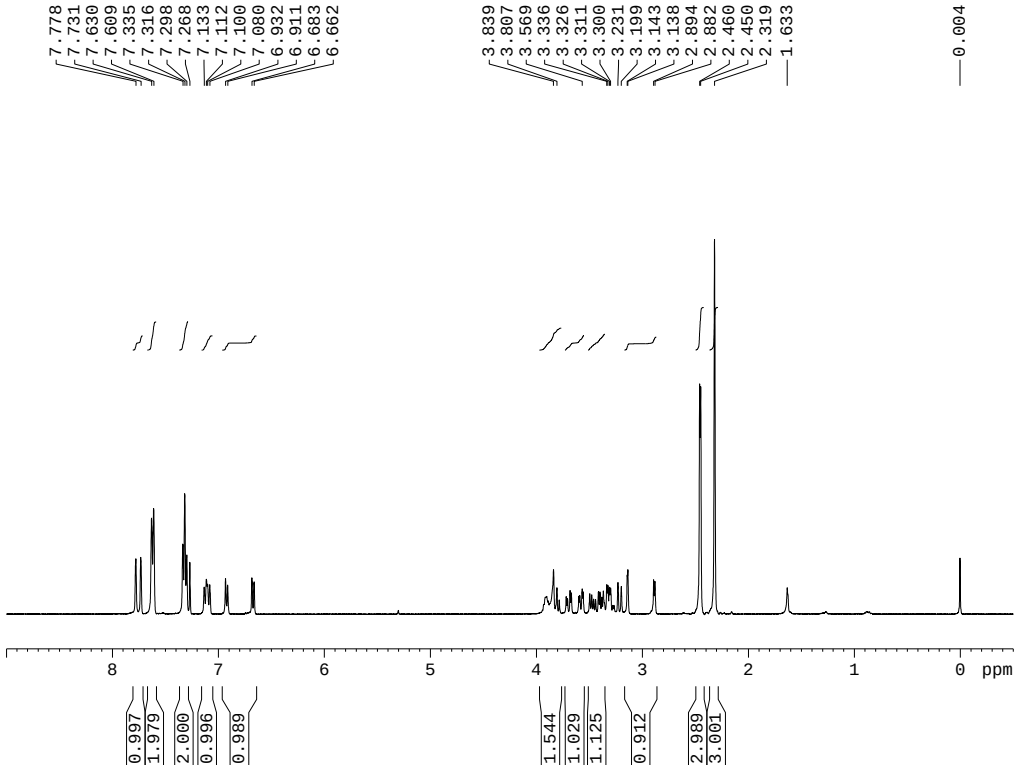

Figure S25. ^{1}H NMR spectrum of compound **2g**

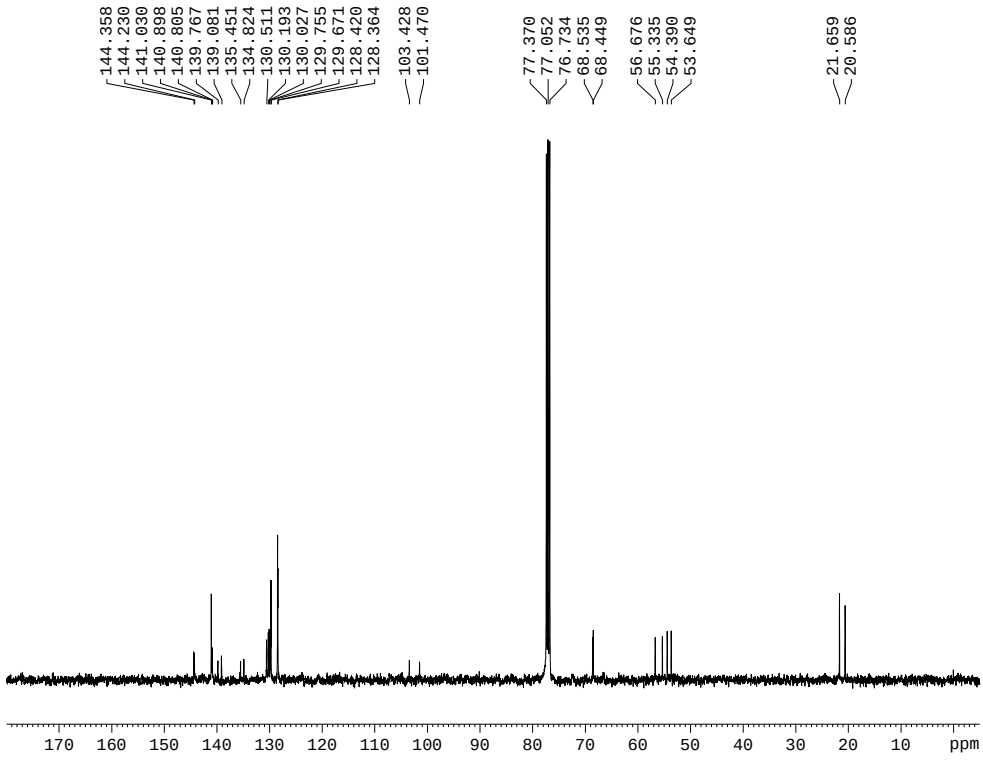

Figure S26. ^{13}C NMR spectrum of compound **2g**

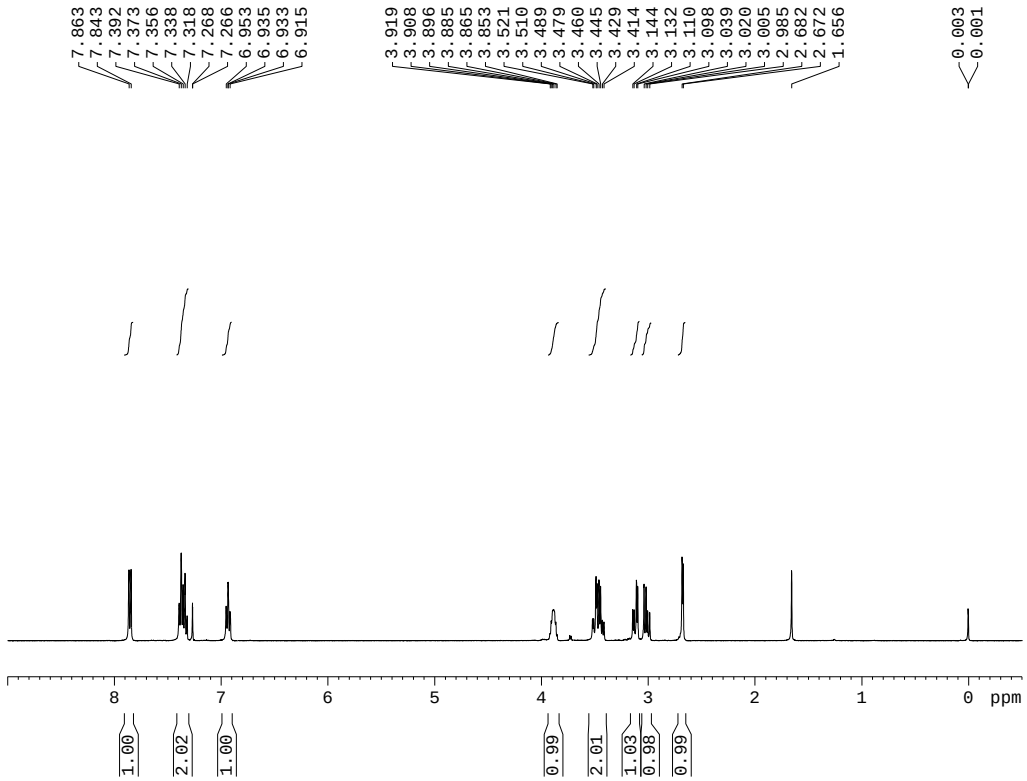

Figure S27. ^{1}H NMR spectrum of compound **2h**

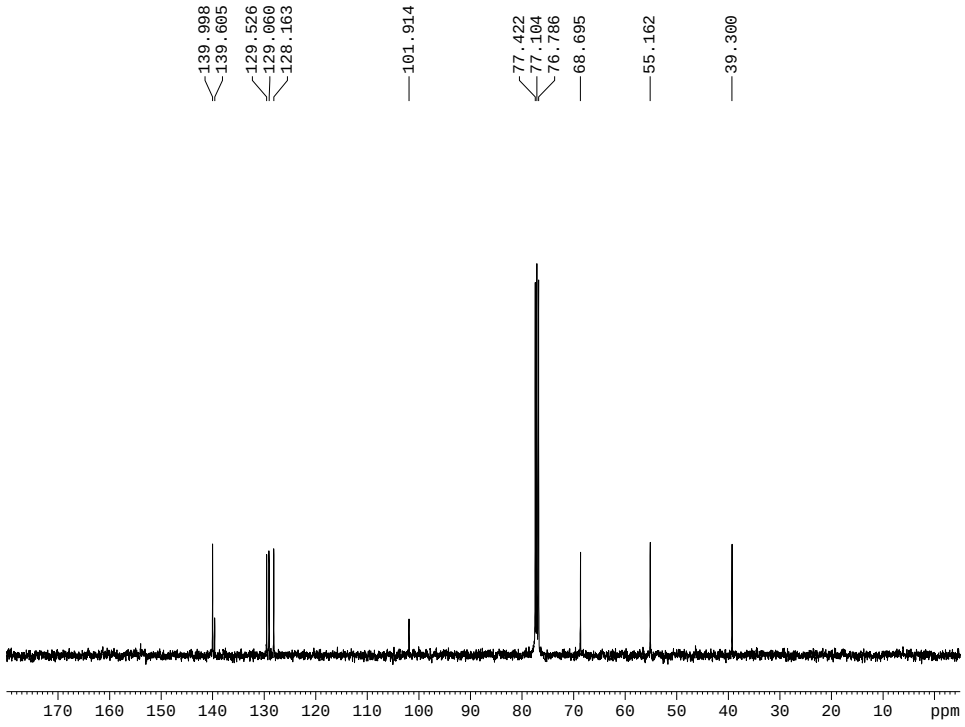

Figure S28. ^{13}C NMR spectrum of compound **2h**

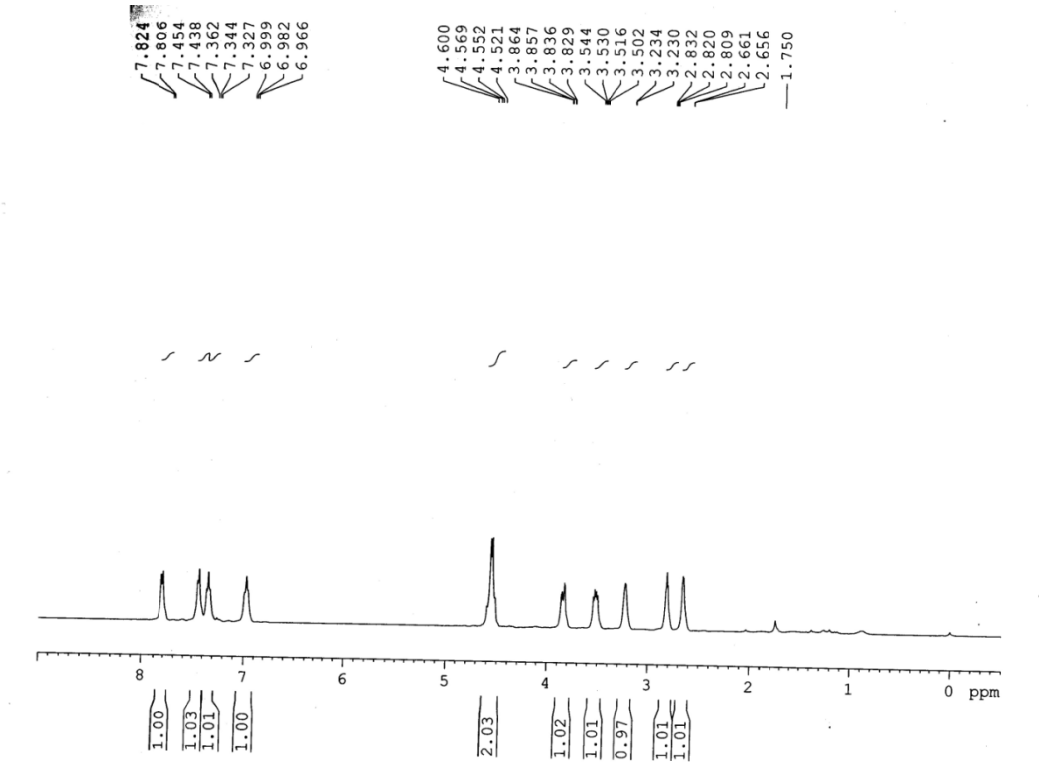

Figure S29. ^{1}H NMR spectrum of compound **1i**

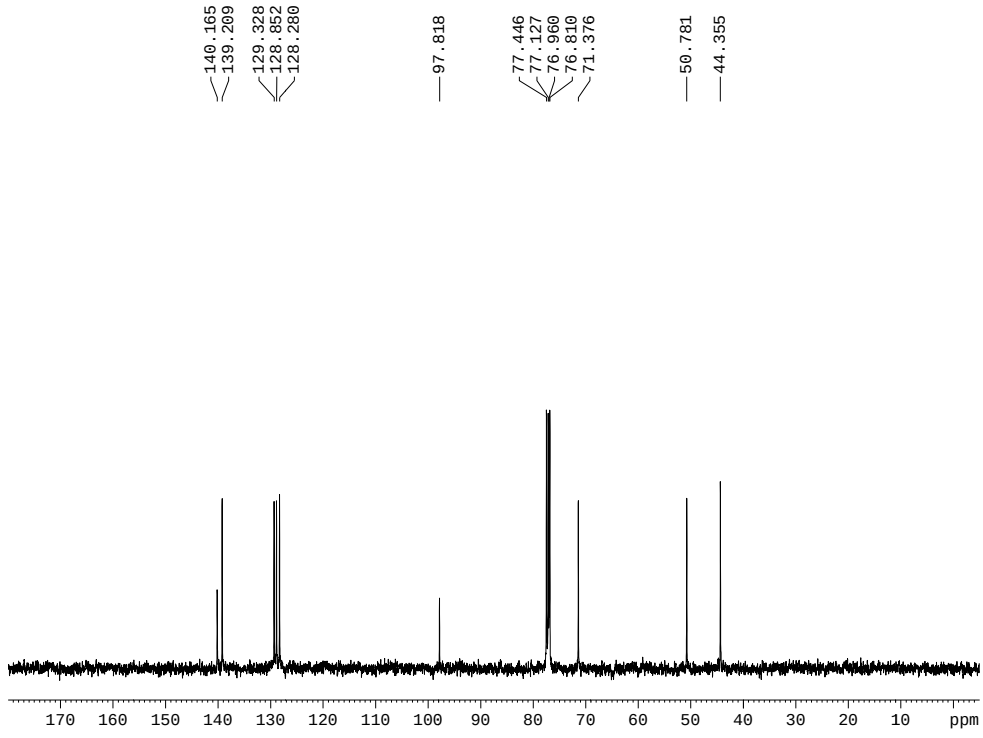

Figure S30. ^{13}C NMR spectrum of compound **1i**

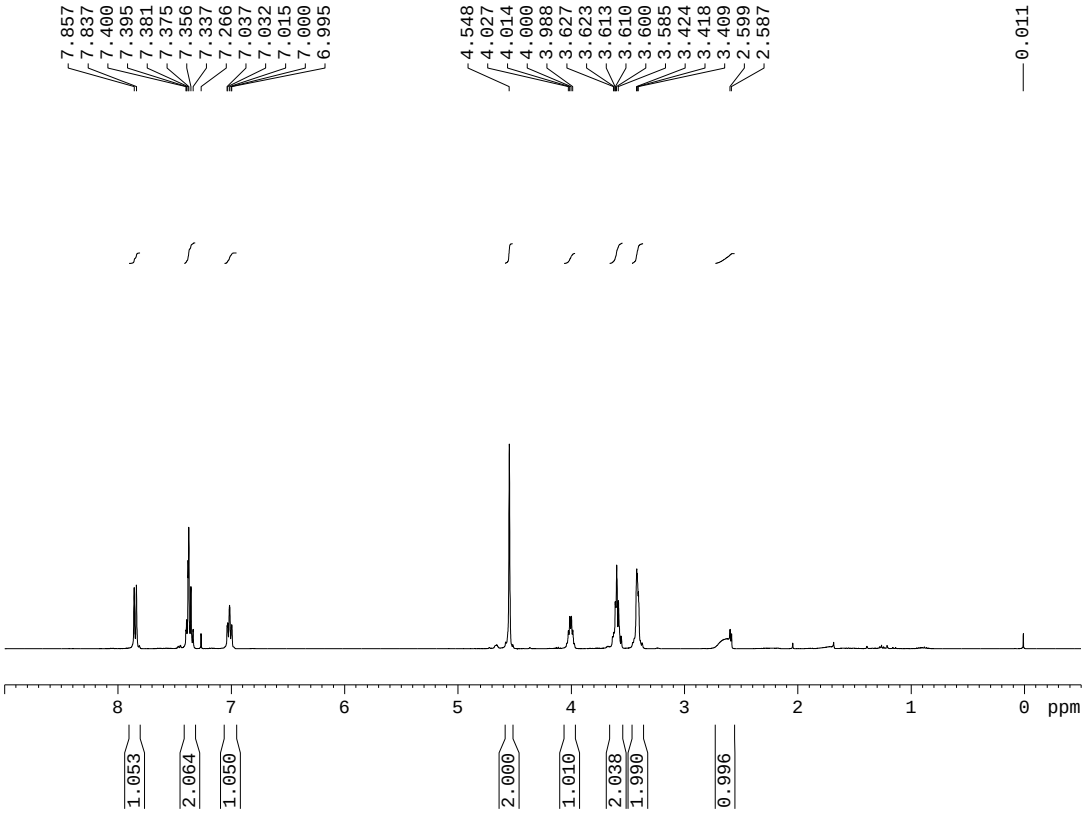

Figure S31. ^{1}H NMR spectrum of compound **2i**

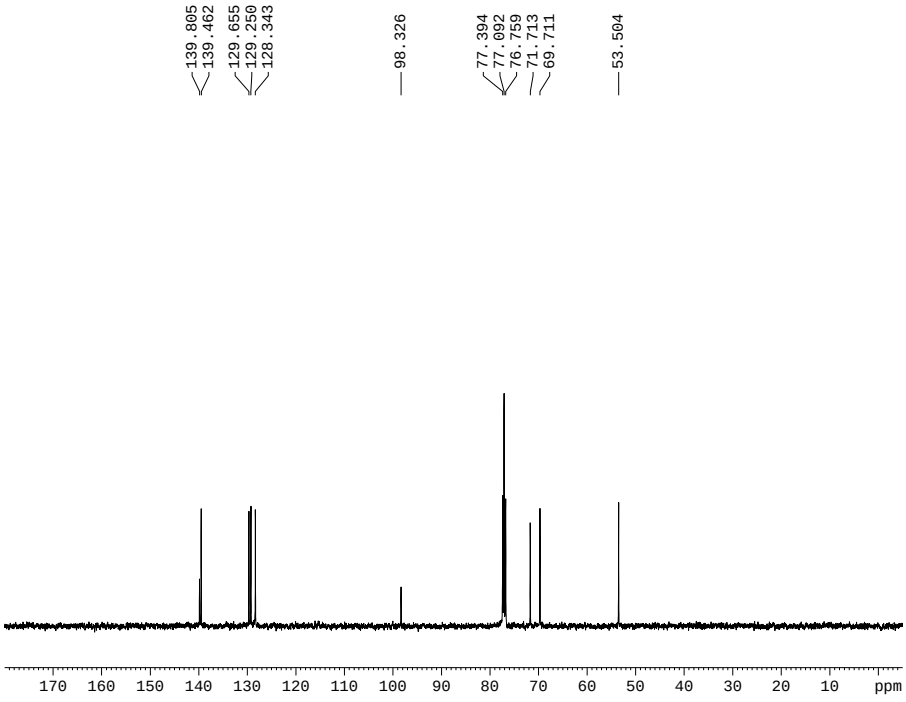

Figure S32. ^{13}C NMR spectrum of compound **2i**

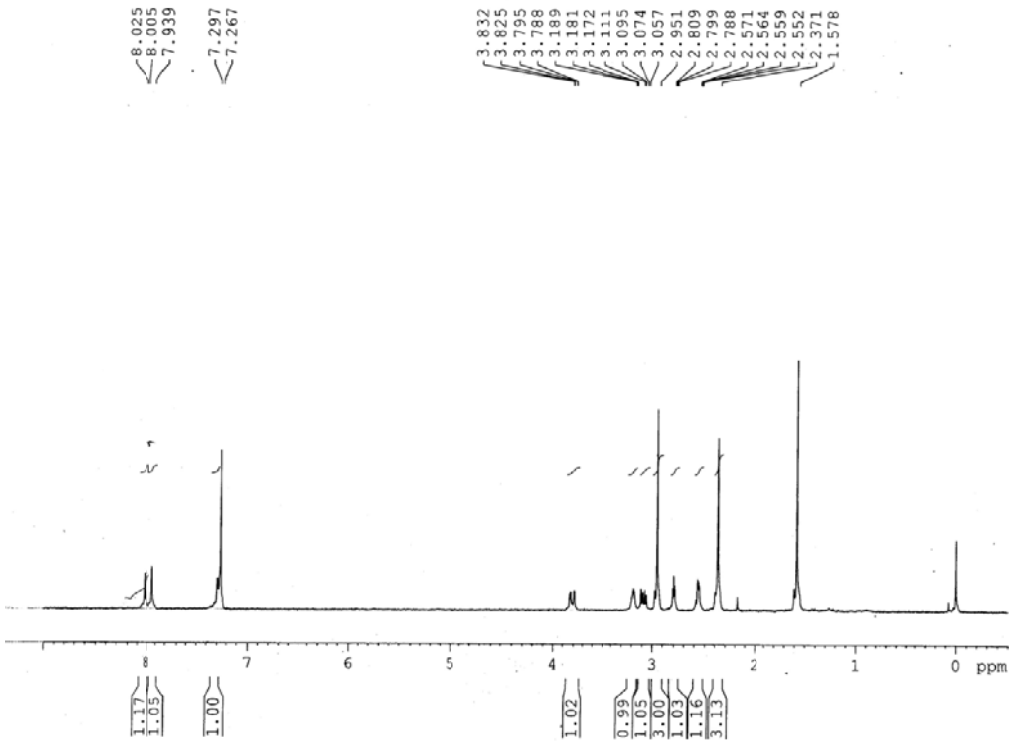

Figure S33. ^{1}H NMR spectrum of compound **1j**

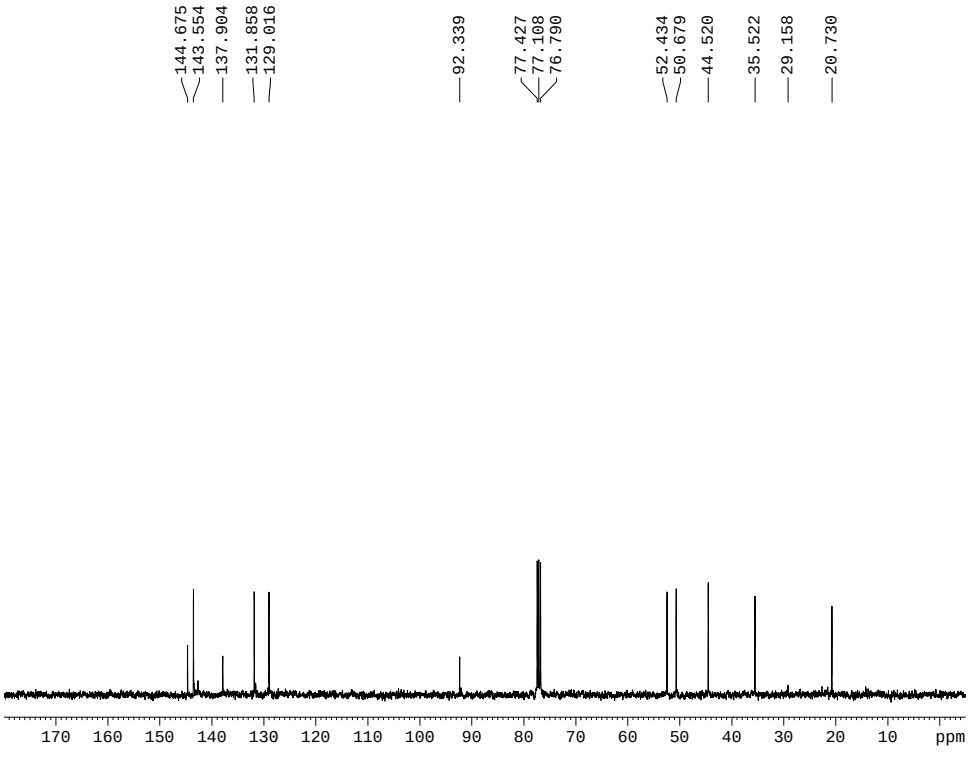

Figure S34. ^{13}C NMR spectrum of compound **1j**

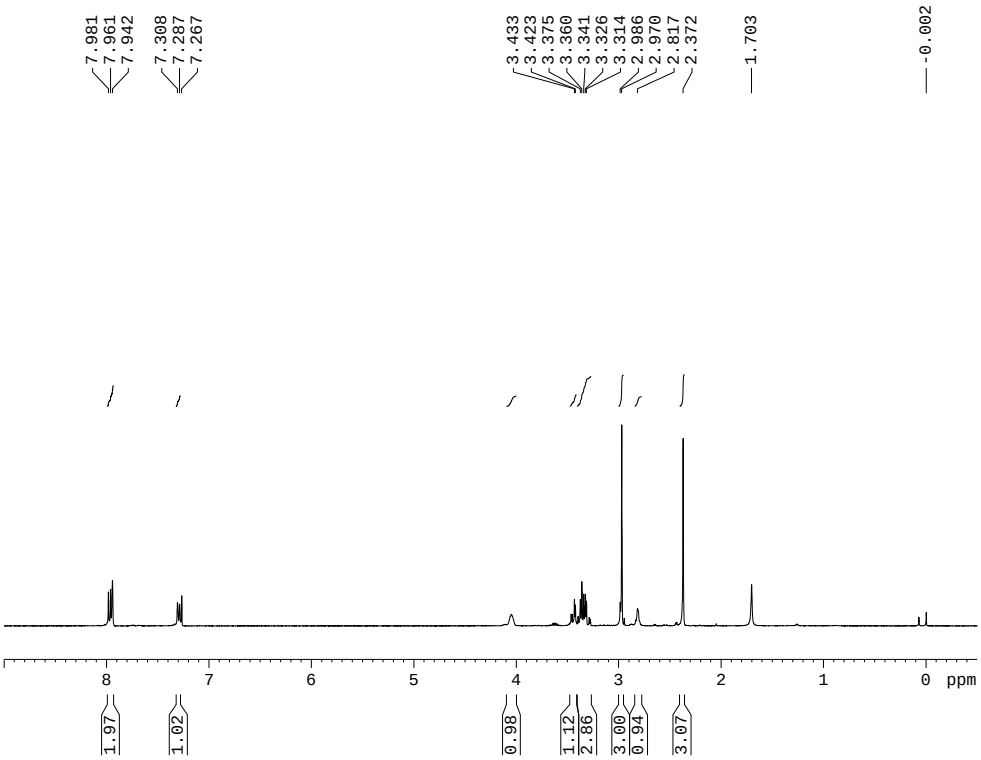

Figure S35. ^{1}H NMR spectrum of compound **2j**

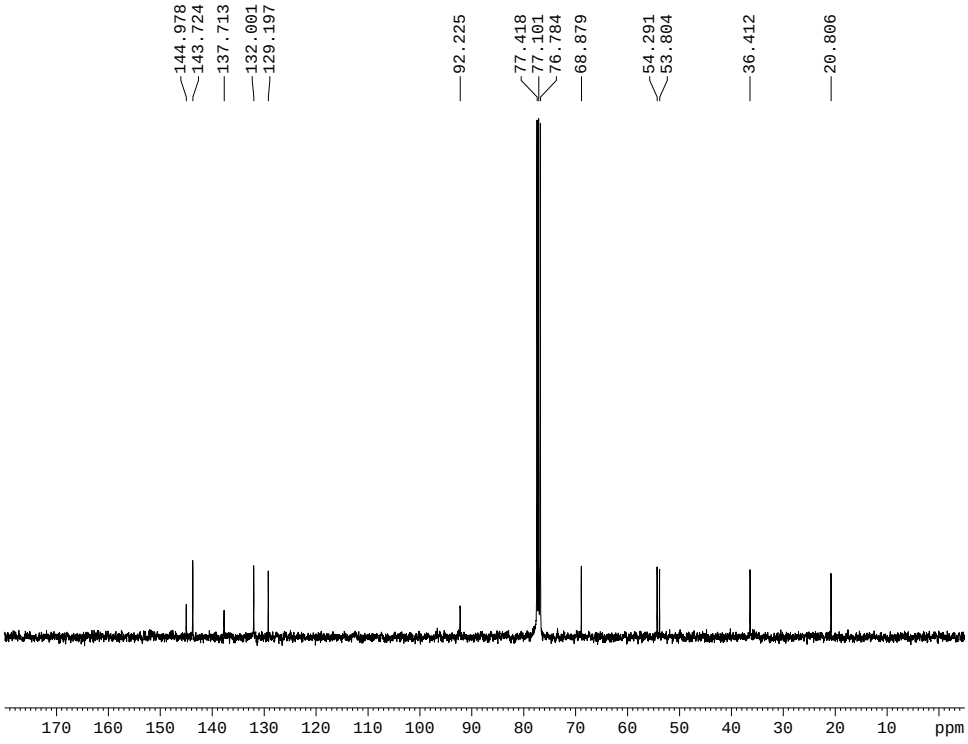

Figure S36. ^{13}C NMR spectrum of compound **2j**

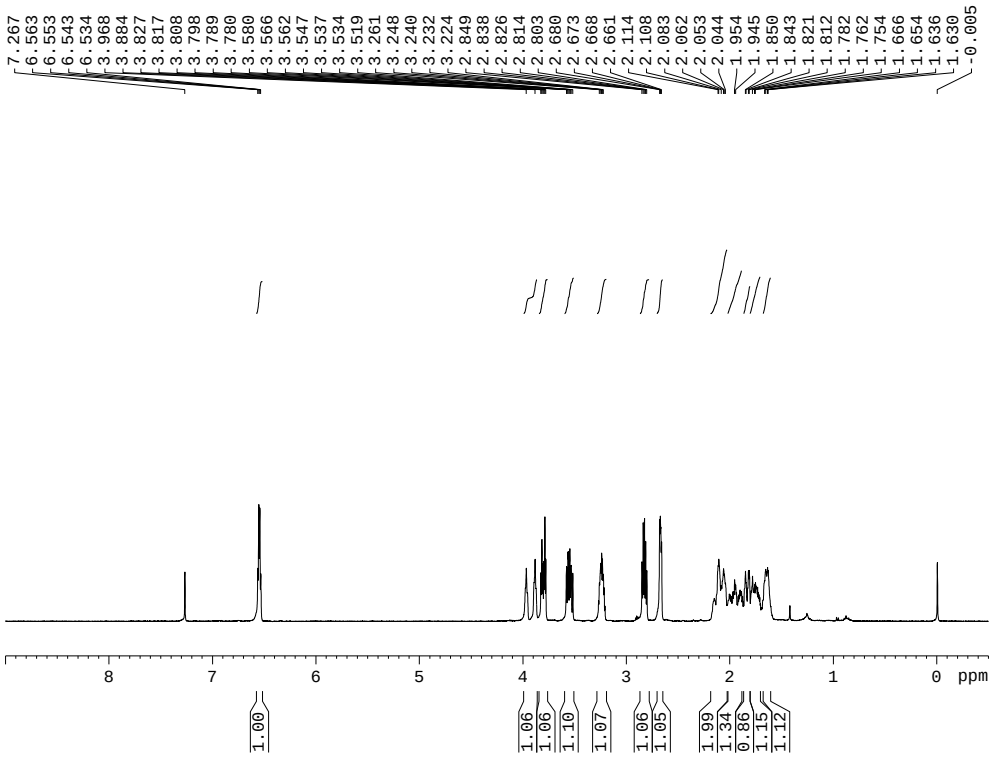

Figure S37. ^{1}H NMR spectrum of compound **1k**

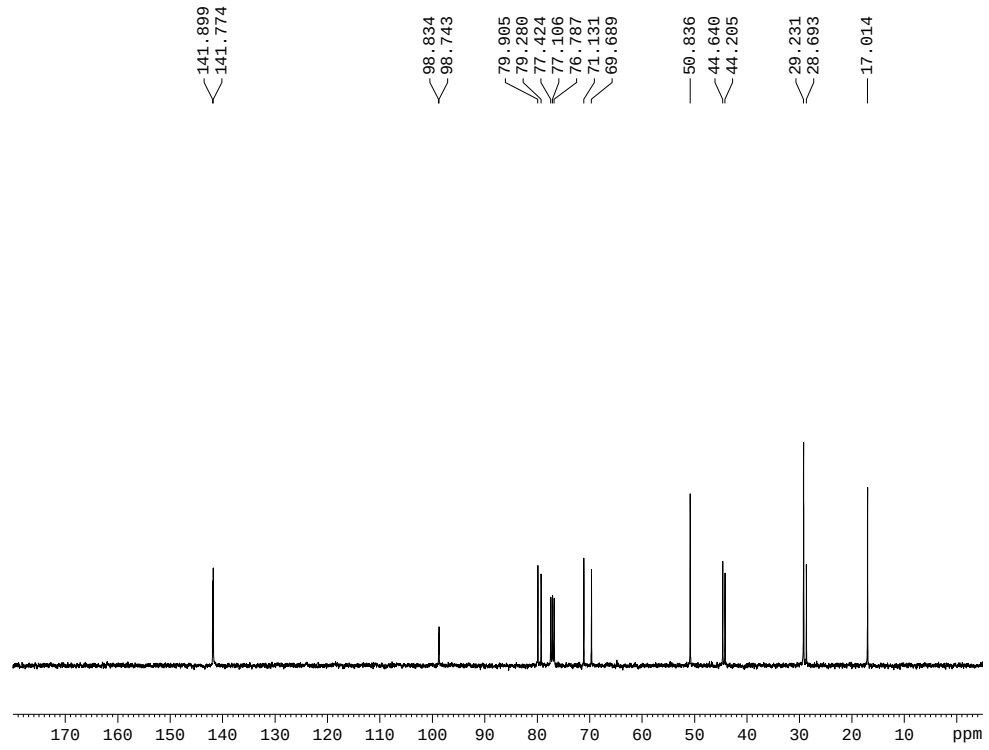

Figure S38. ^{13}C NMR spectrum of compound **1k**

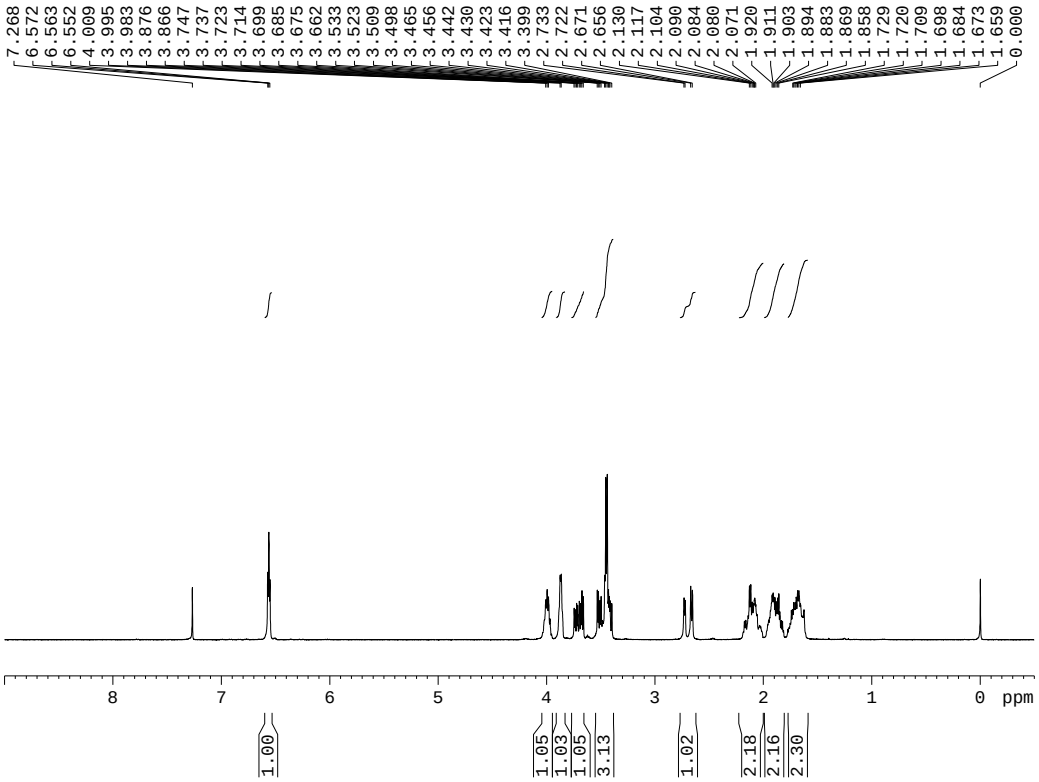

Figure S39. ^{1}H NMR spectrum of compound **2k**

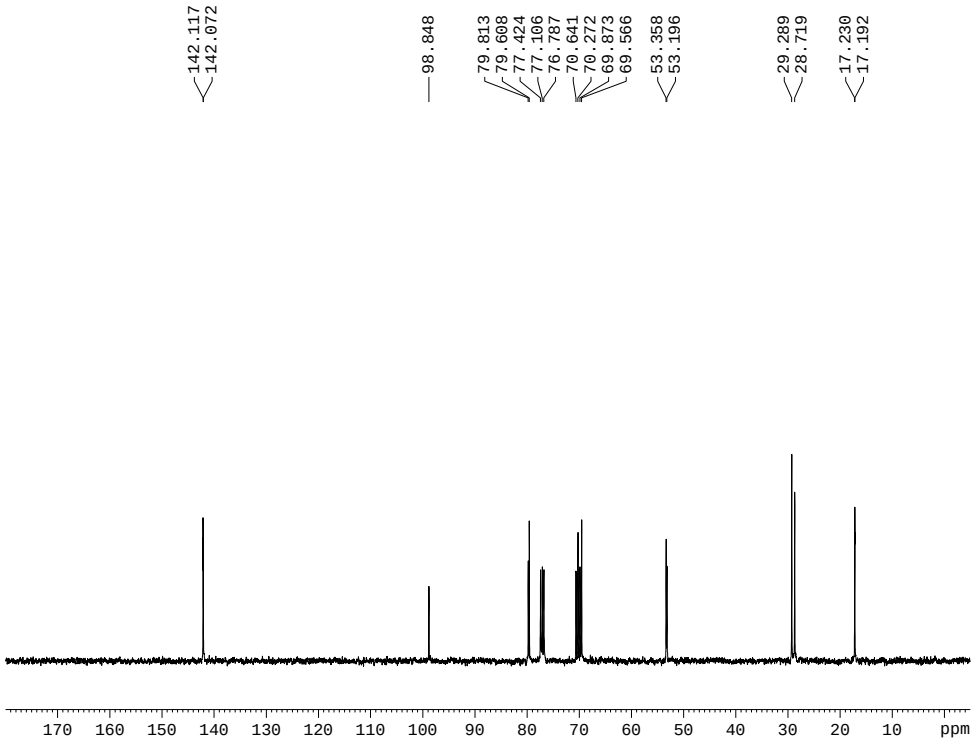

Figure S40. ^{13}C NMR spectrum of compound **2k**

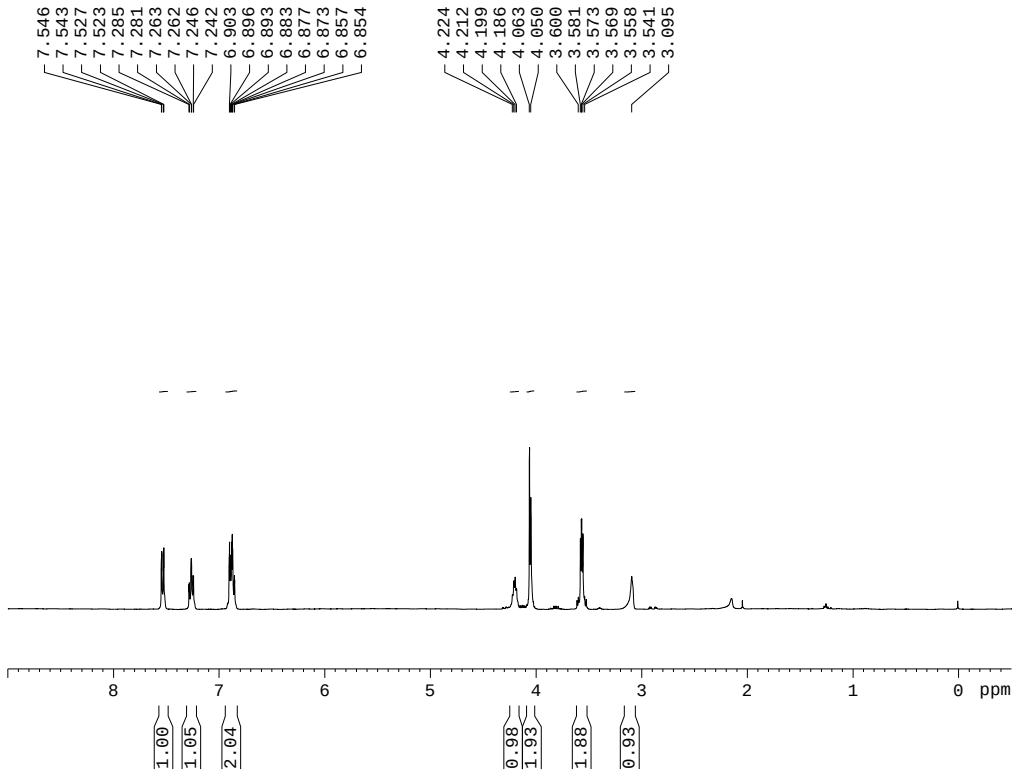

Figure S41. ^{1}H NMR spectrum of compound **2l**

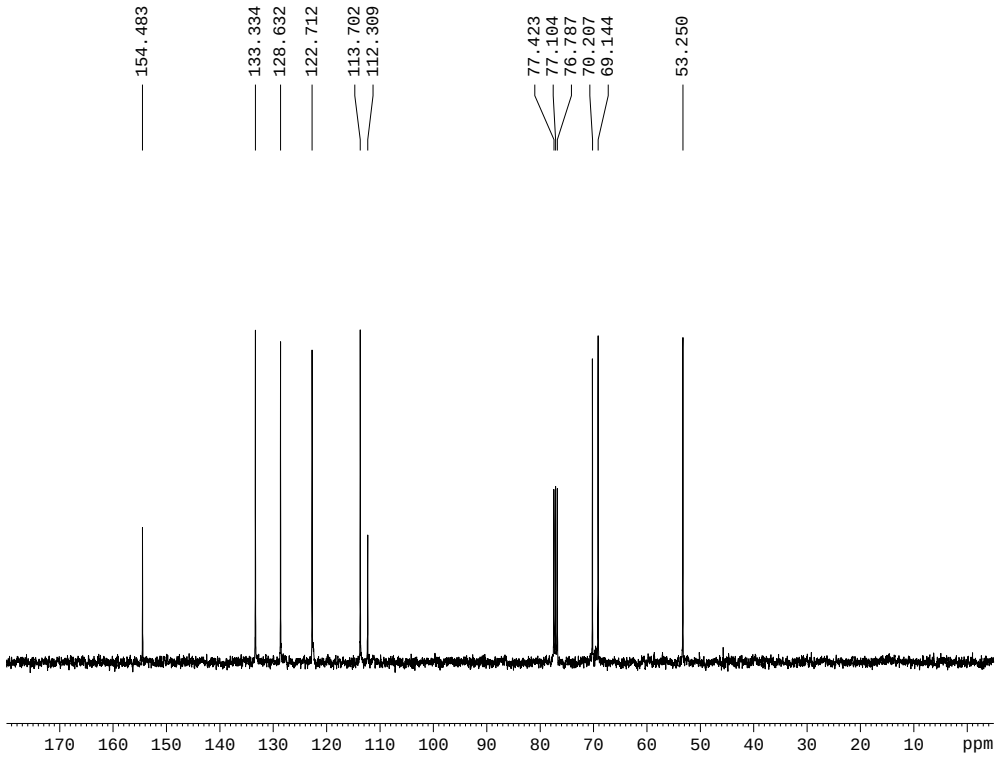

Figure S42. ^{13}C NMR spectrum of compound **2l**

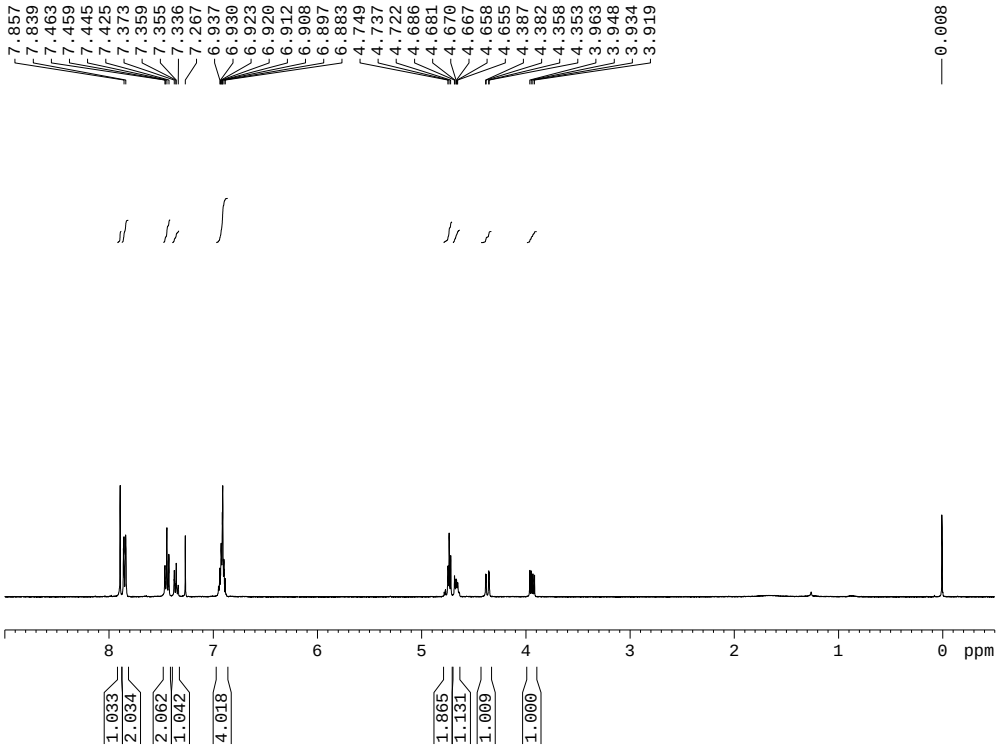

Figure S43. ^{1}H NMR spectrum of compound **3**

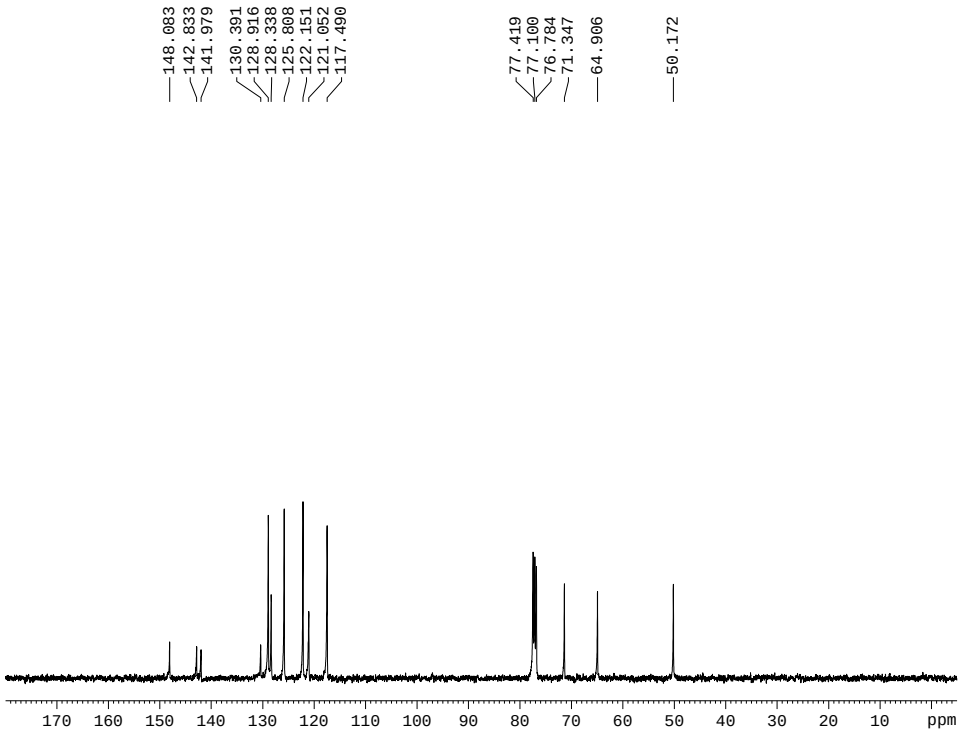

Figure S44. ^{13}C NMR spectrum of compound **3**

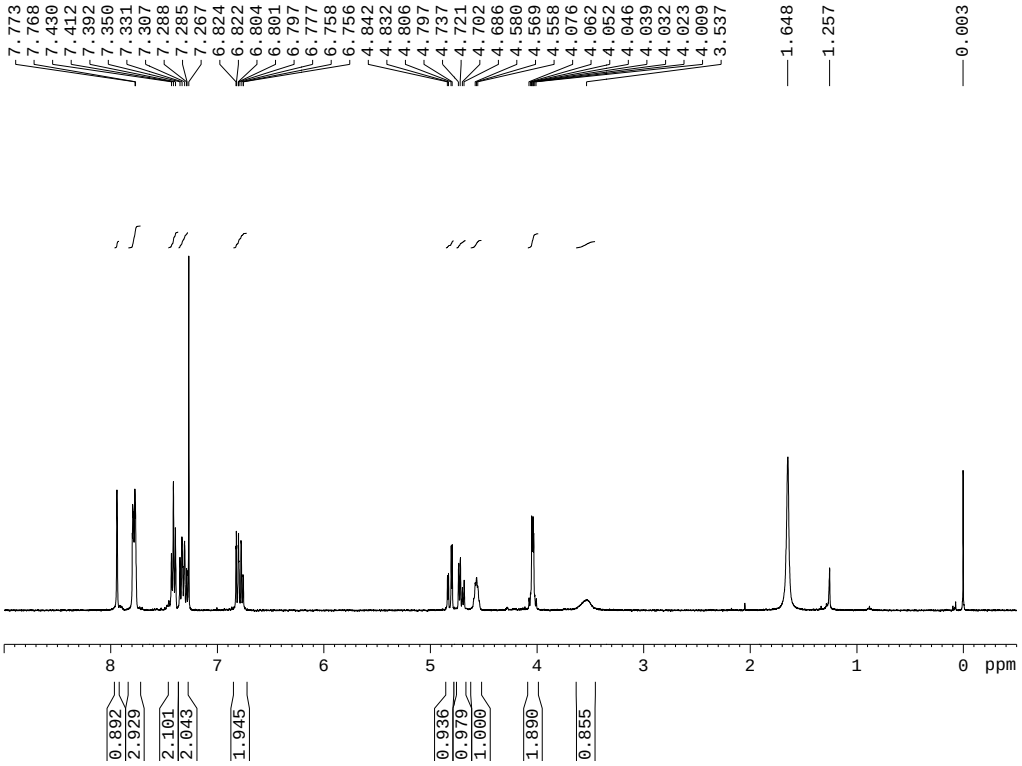

Figure S45. ^{1}H NMR spectrum of compound **4**

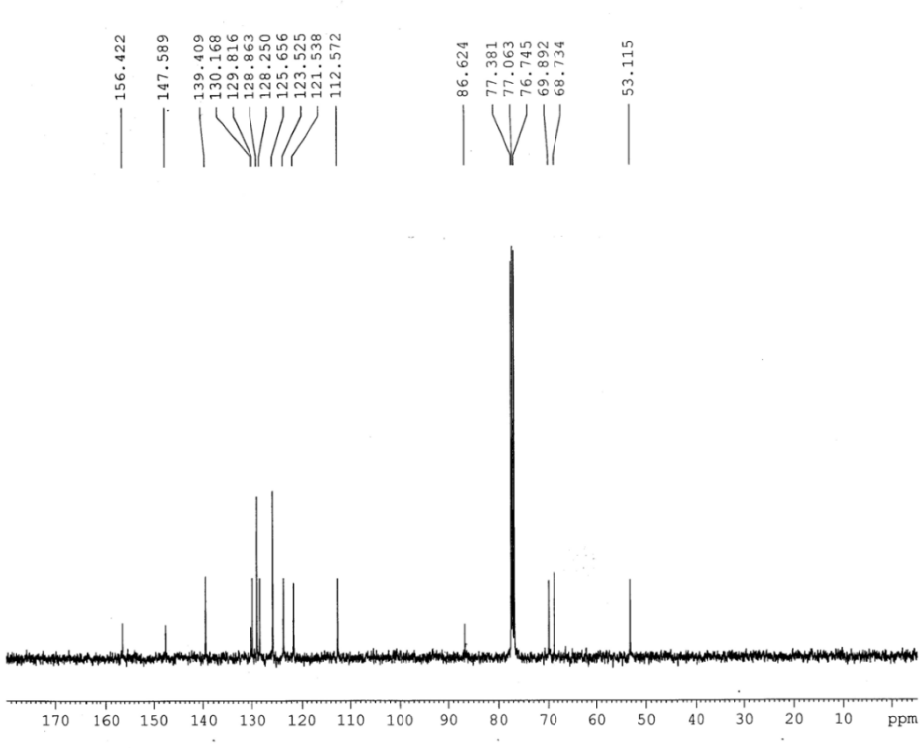

Figure S46. ^{13}C NMR spectrum of compound **4**

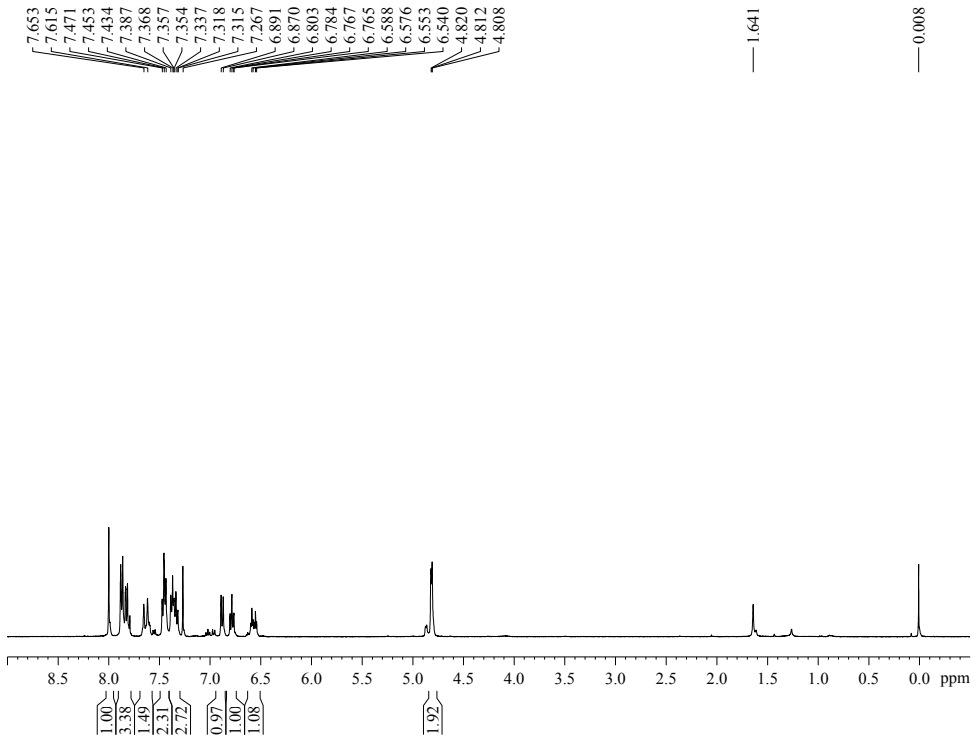

Figure S47. ^{1}H NMR spectrum of compound **5**

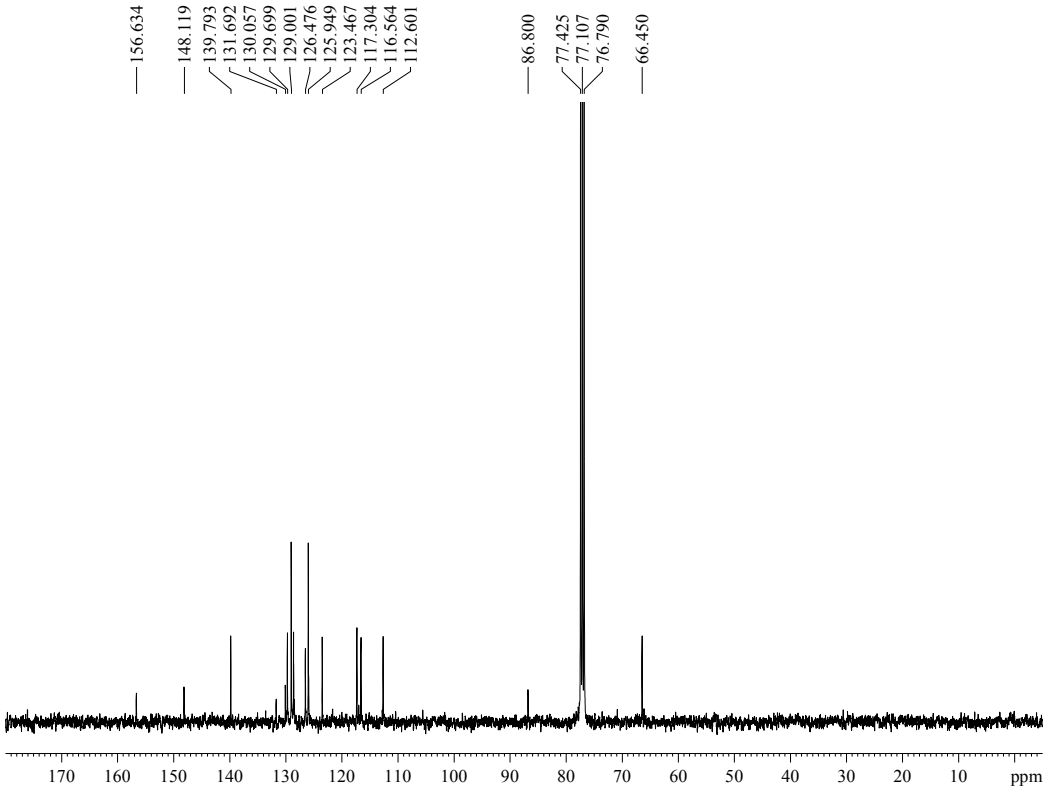

Figure S48. ^{13}C NMR spectrum of compound **5**

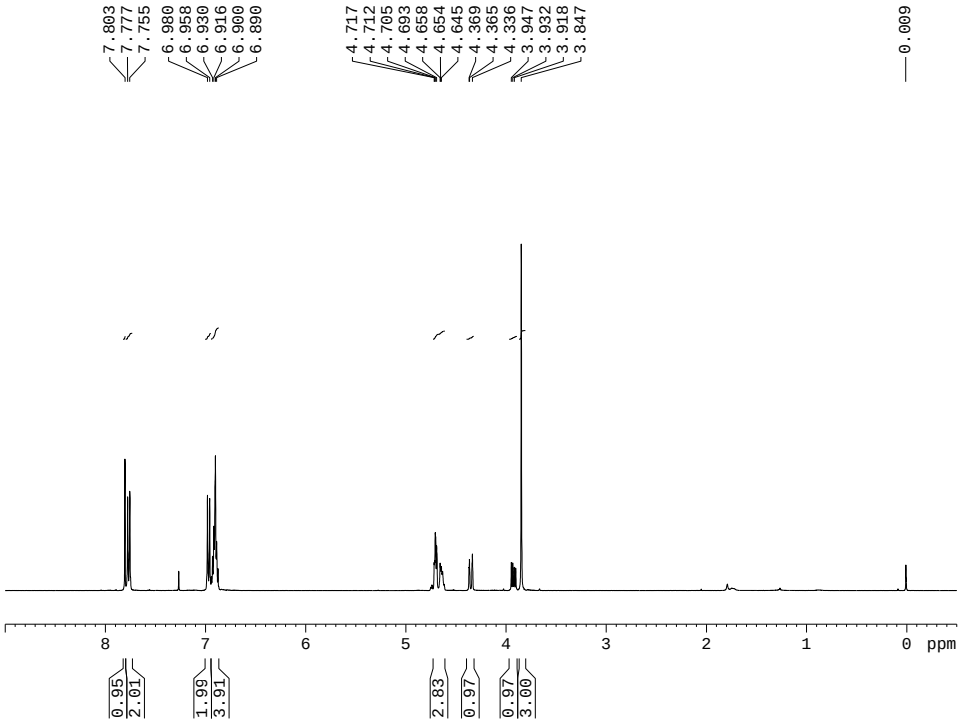

Figure S49. ^{1}H NMR spectrum of compound **6**

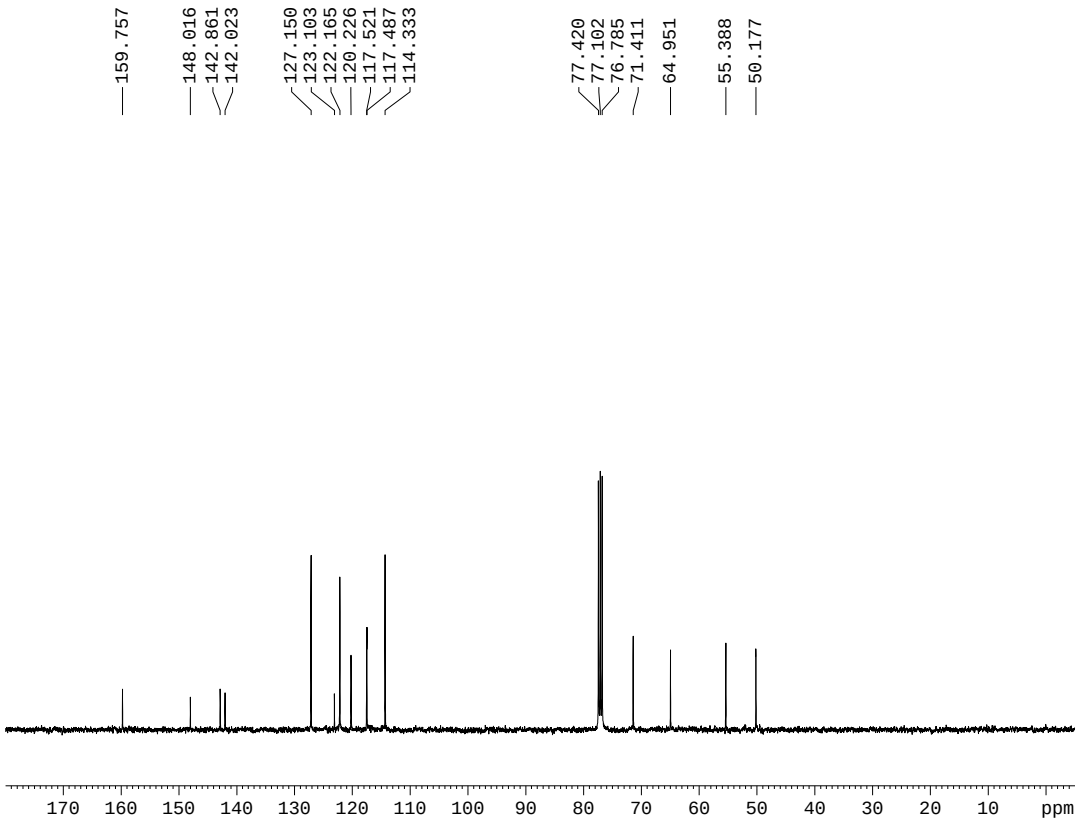

Figure S50. ^{13}C NMR spectrum of compound **6**

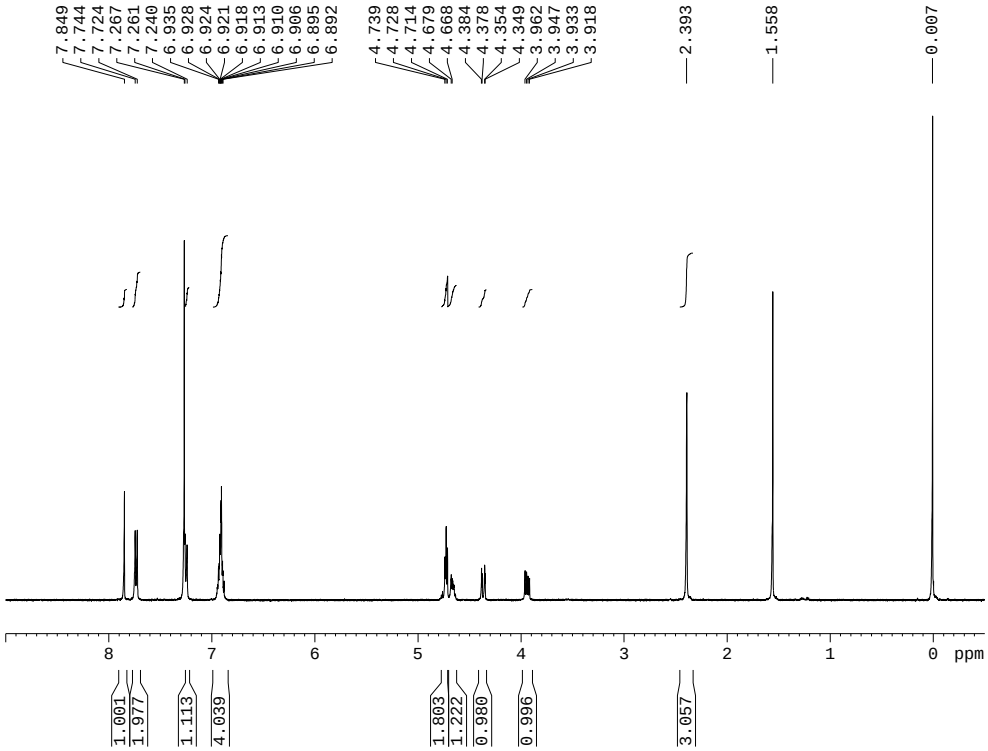

Figure S51. ^{1}H NMR spectrum of compound **7**

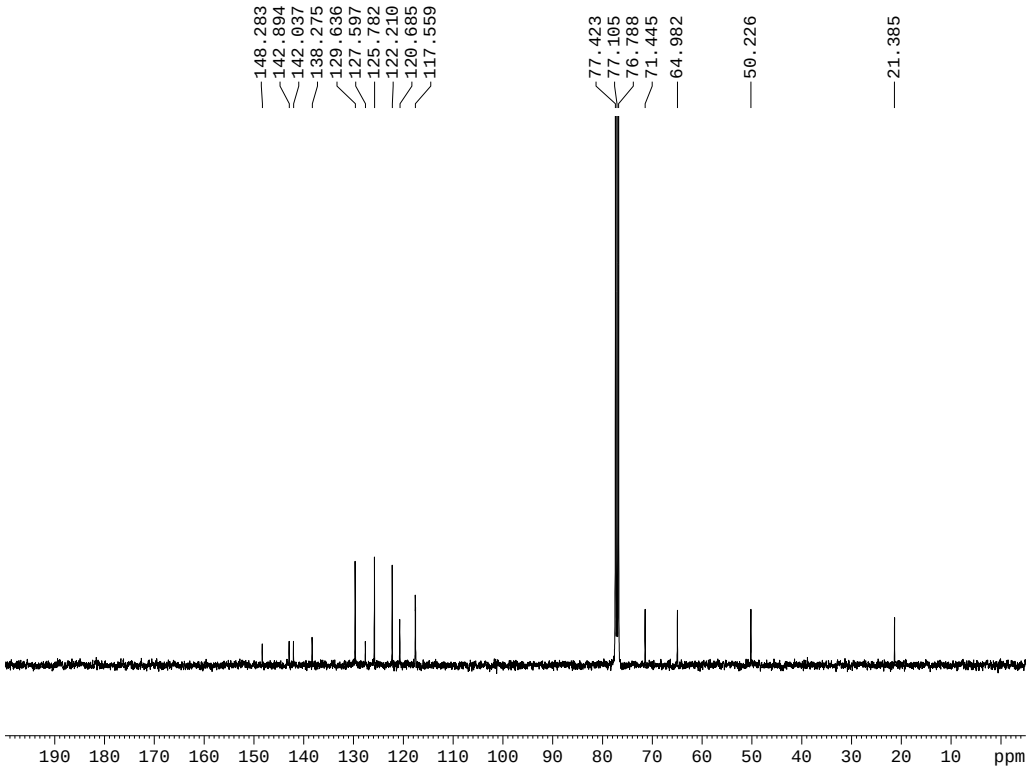

Figure S52. ^{13}C NMR spectrum of compound **7**

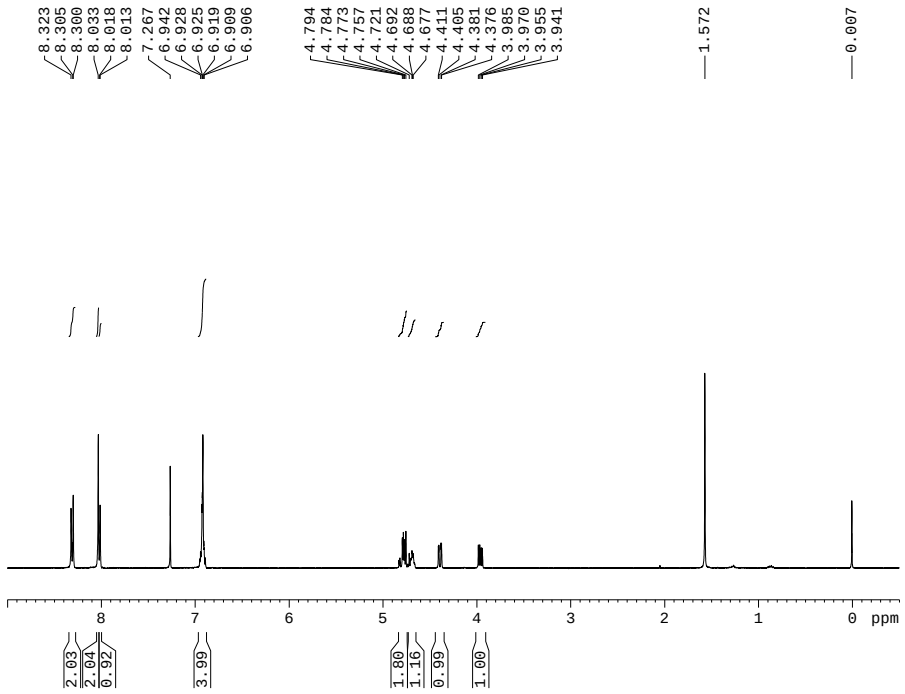

Figure S53. ^{1}H NMR spectrum of compound **8**

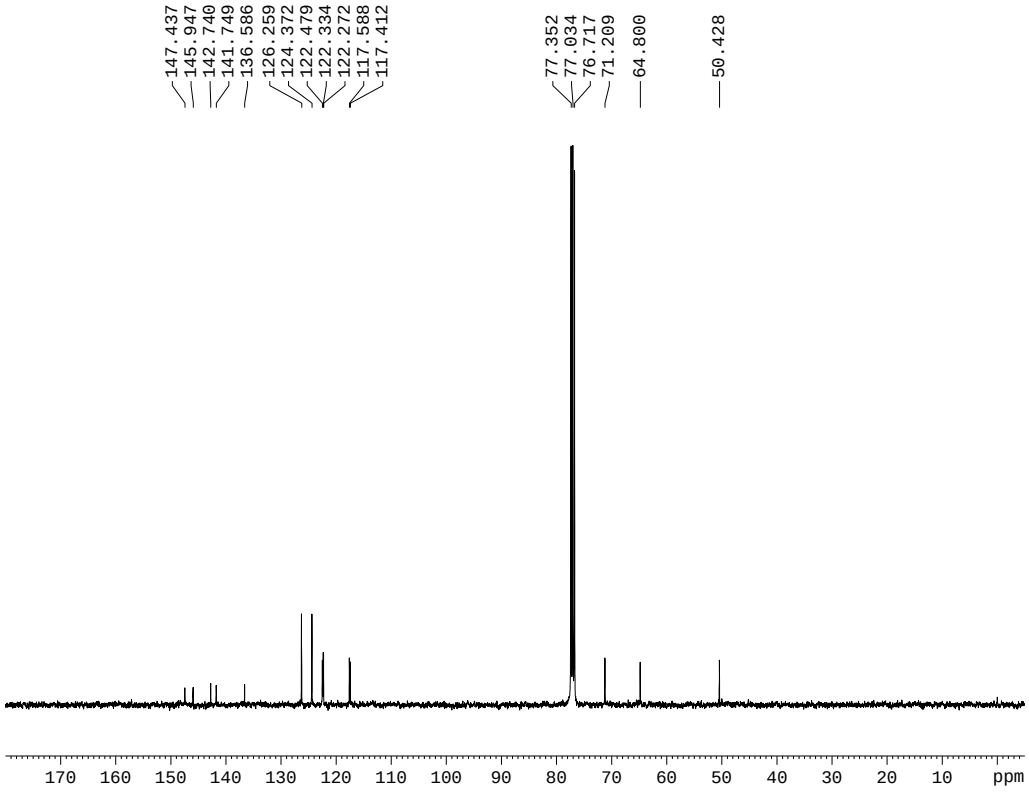

Figure S54. ^{13}C NMR spectrum of compound **8**

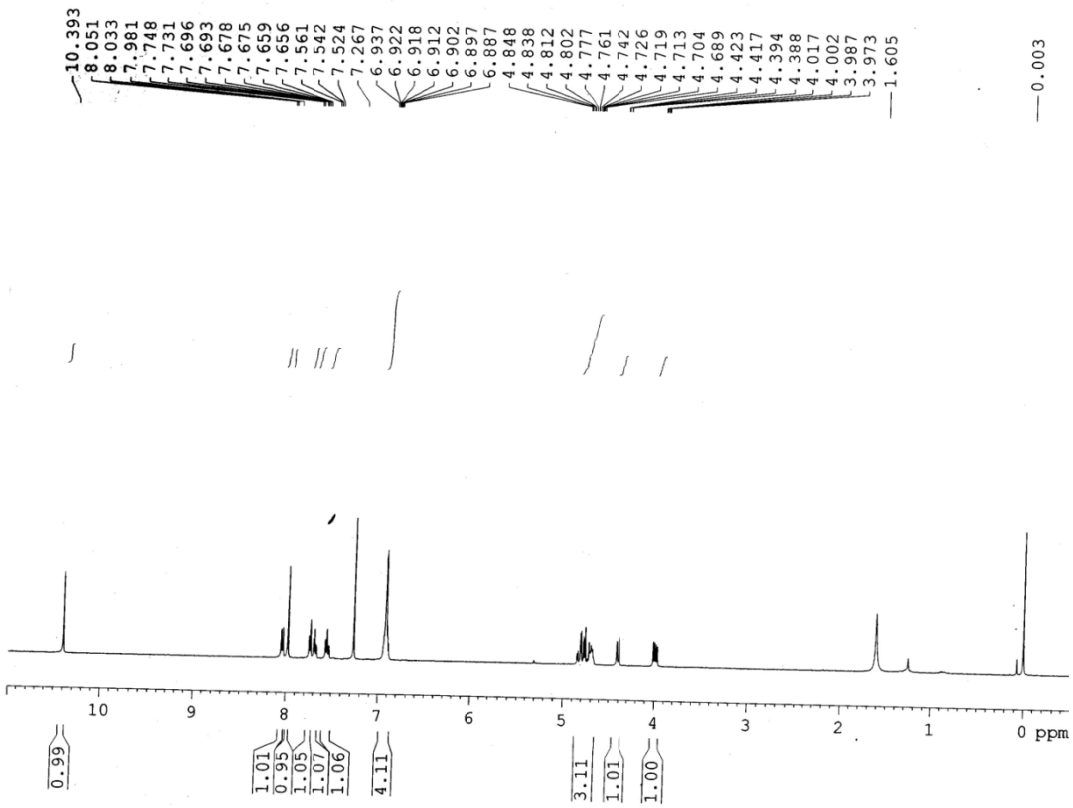

Figure S55. ^{1}H NMR spectrum of compound **9**

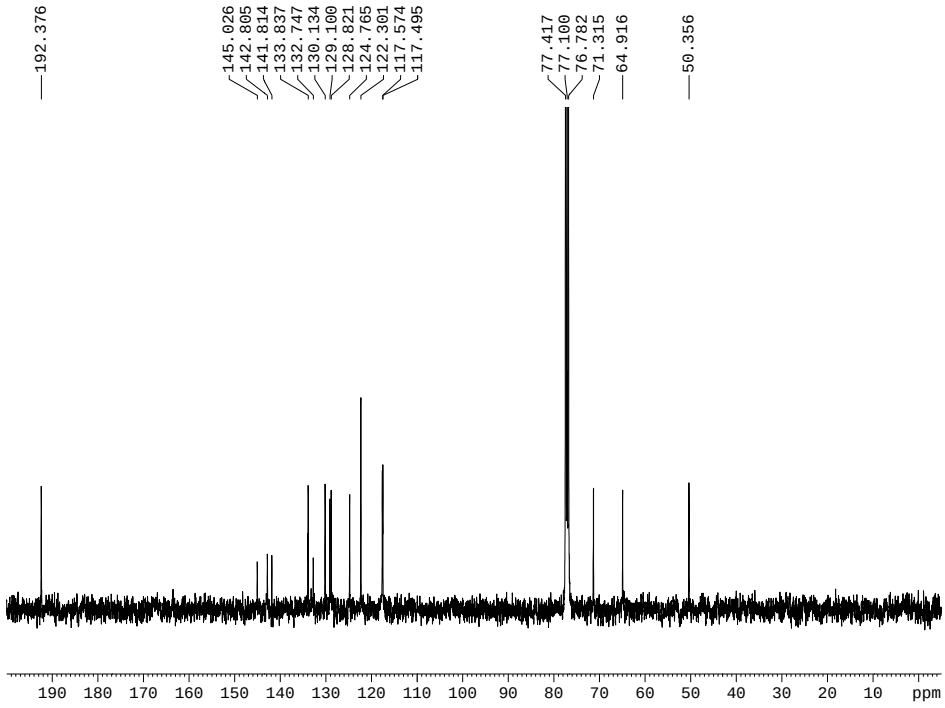

Figure S56. ^{13}C NMR spectrum of compound **9**

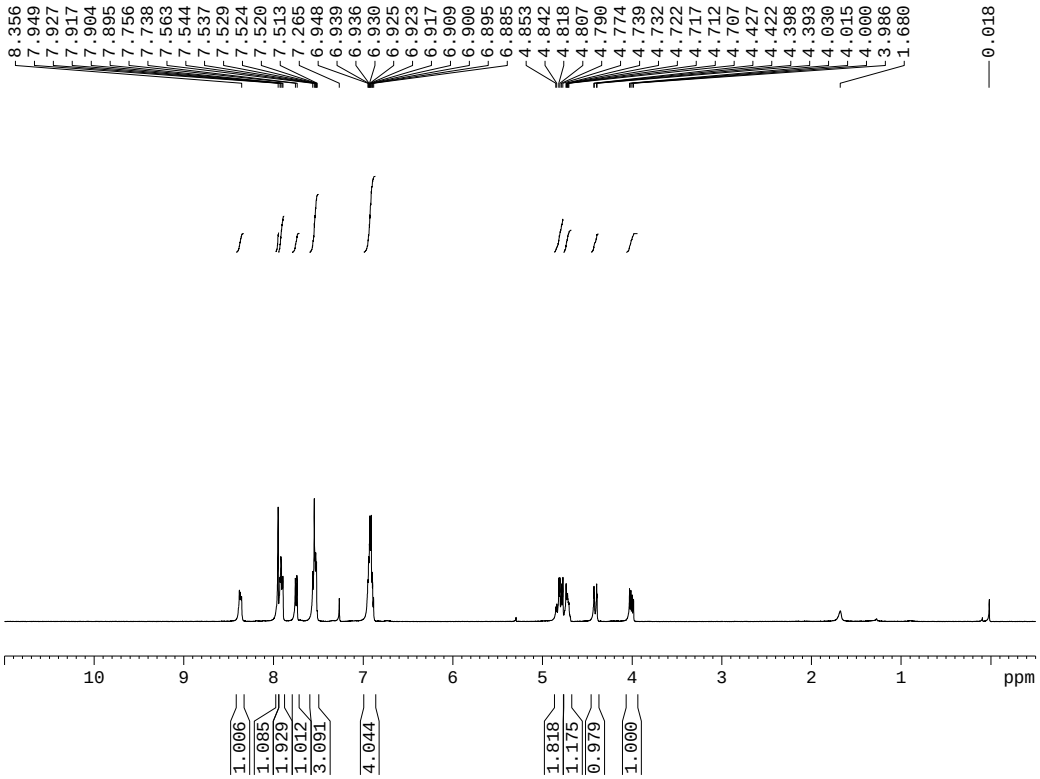

Figure S57. ^{1}H NMR spectrum of compound **10**

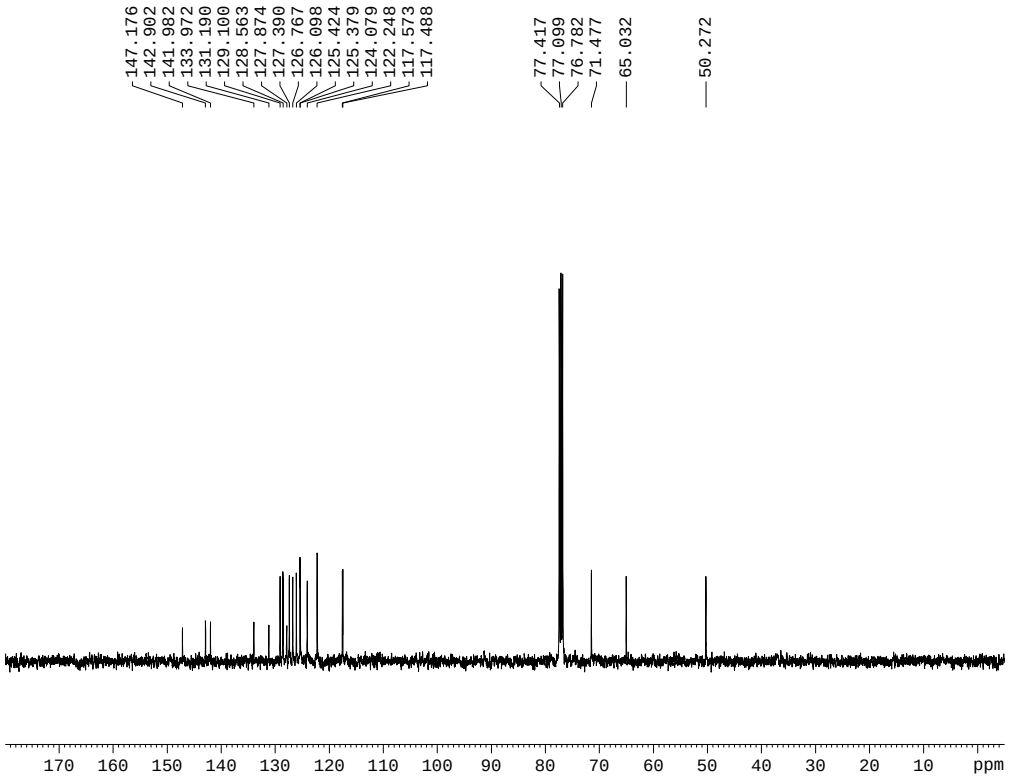

Figure S58. ^{13}C NMR spectrum of compound **10**

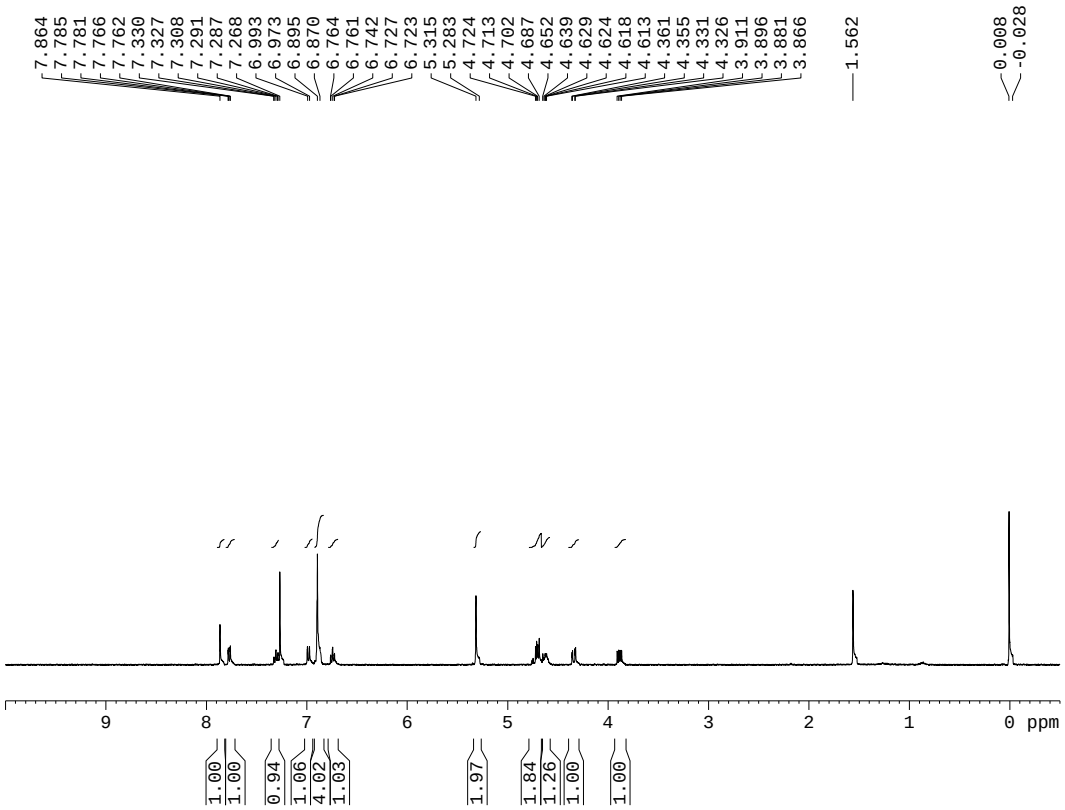

Figure S59. ^{1}H NMR spectrum of compound **11**

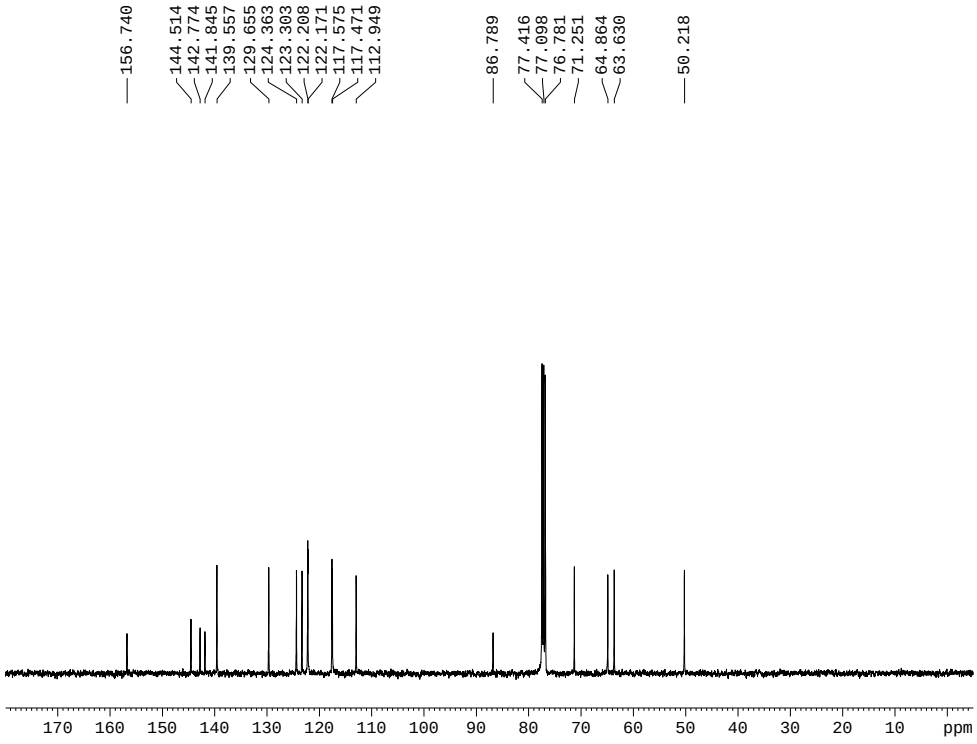

Figure S60. ^{13}C NMR spectrum of compound **11**

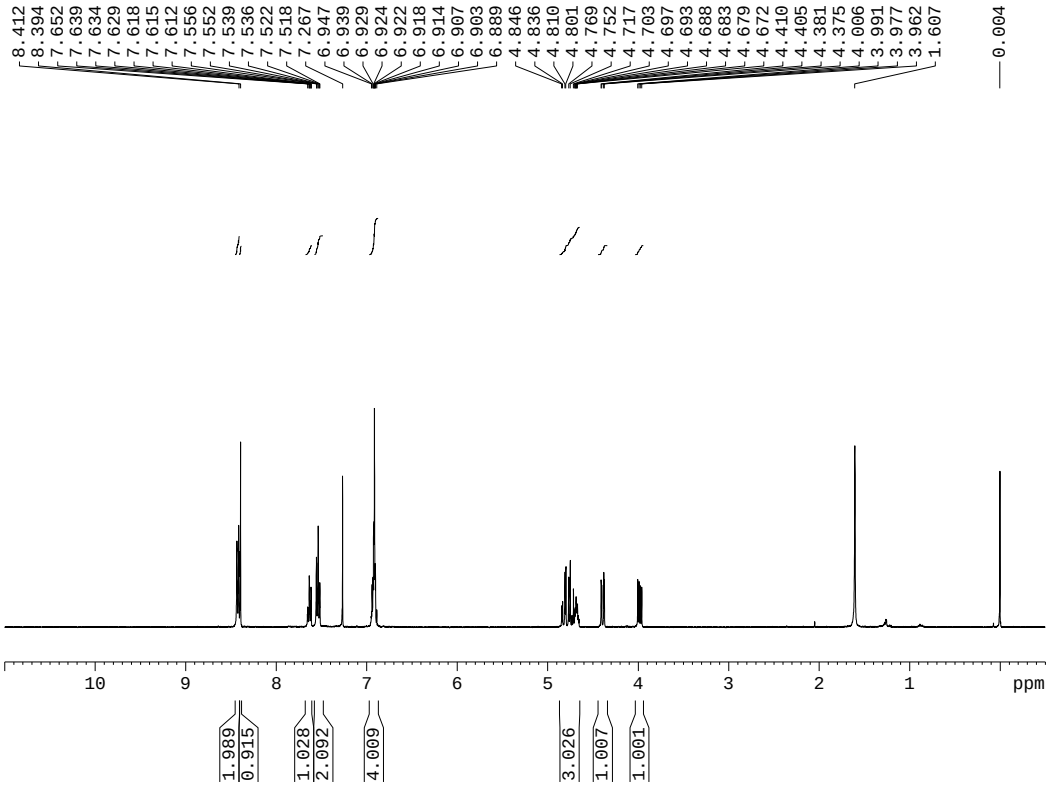

Figure S61. ^{1}H NMR spectrum of compound **12**

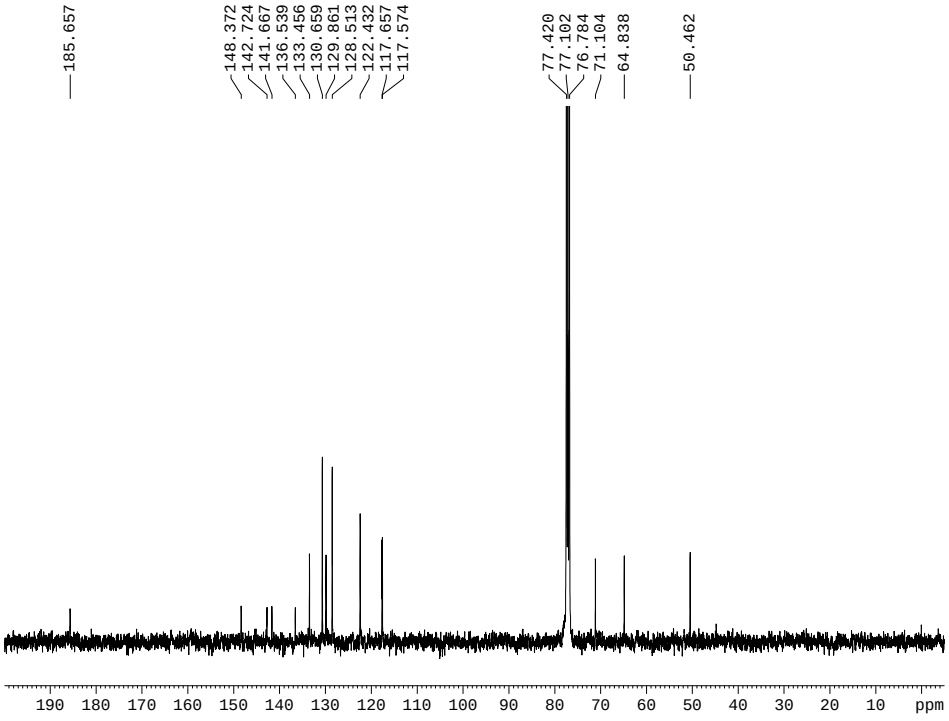

Figure S62. ^{13}C NMR spectrum of compound **12**

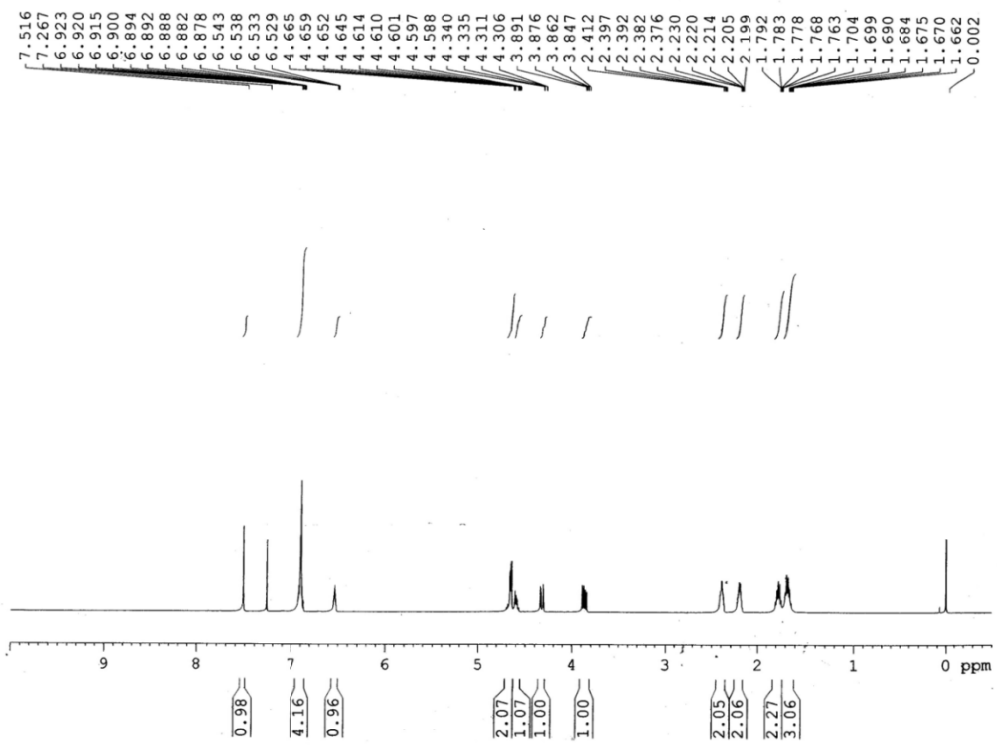

Figure S63. ^{1}H NMR spectrum of compound **13**

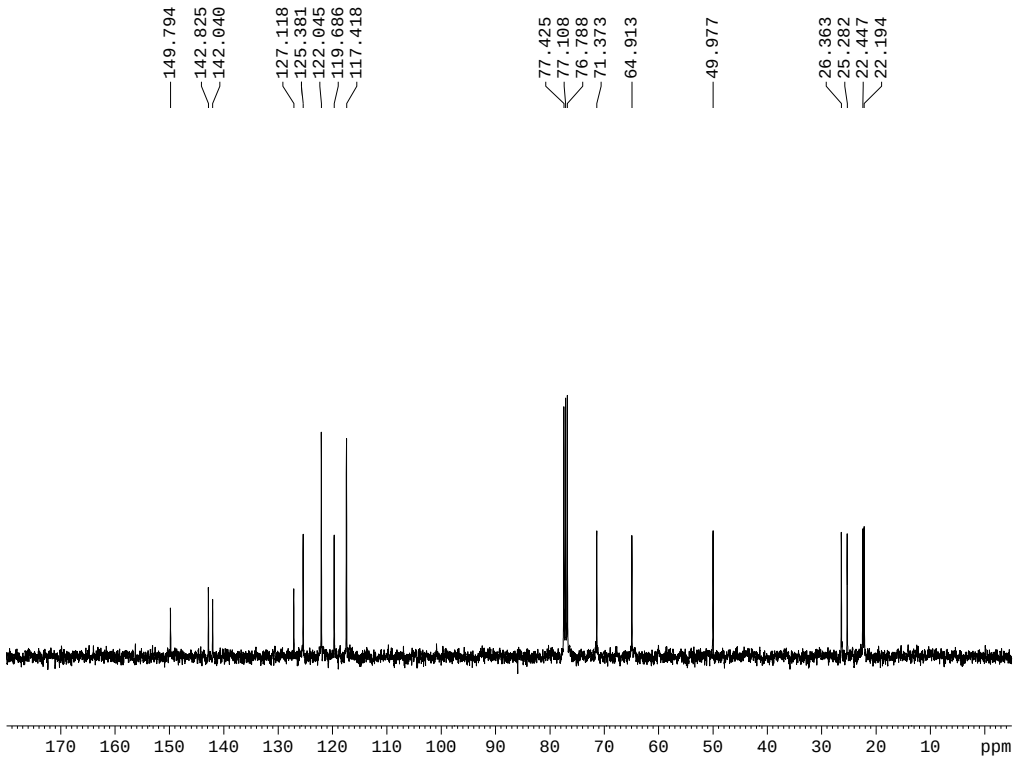

Figure S64. ^{13}C NMR spectrum of compound **13**

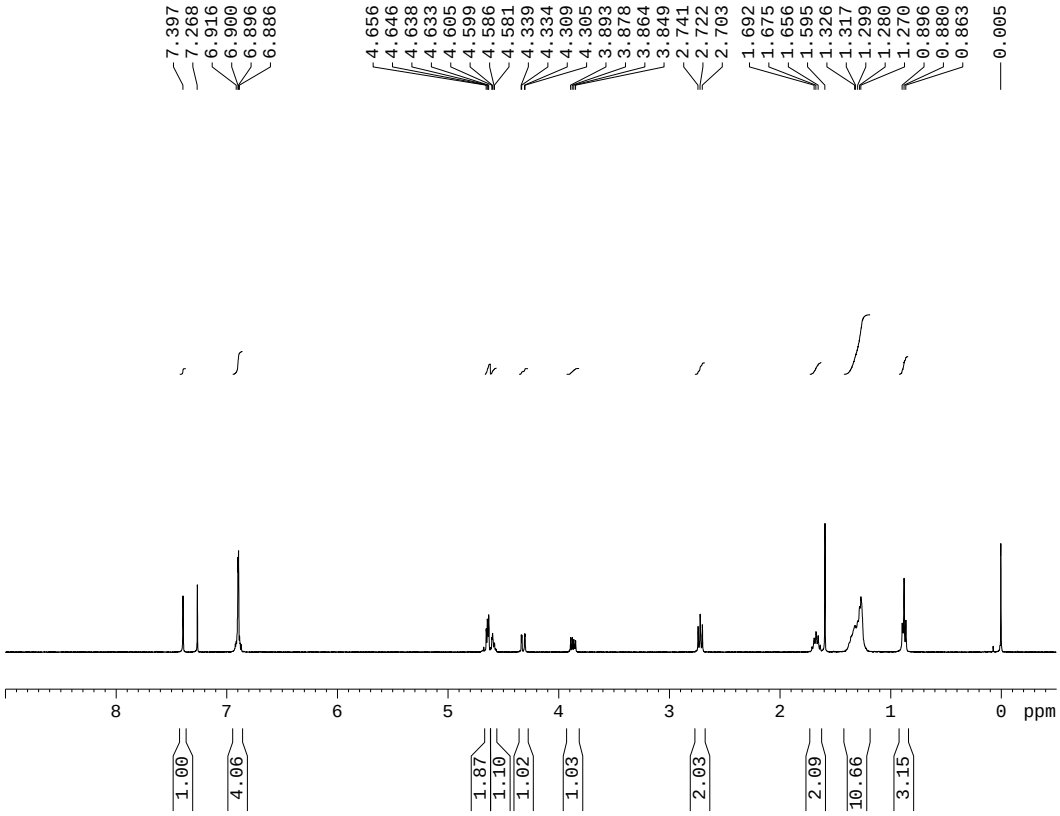

Figure S65. ^{1}H NMR spectrum of compound **14**

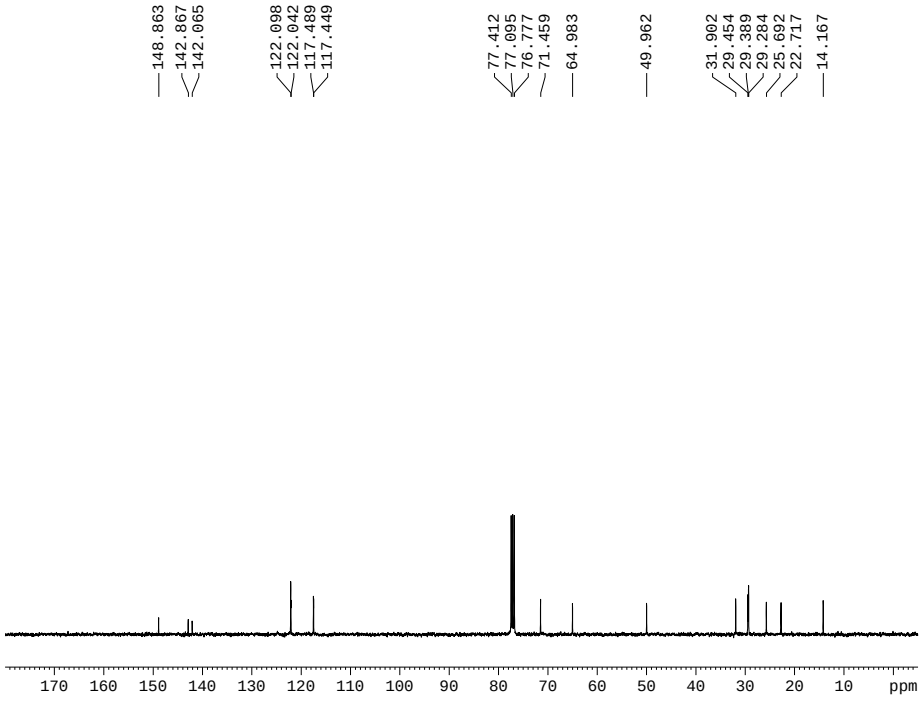

Figure S66. ^{13}C NMR spectrum of compound **14**

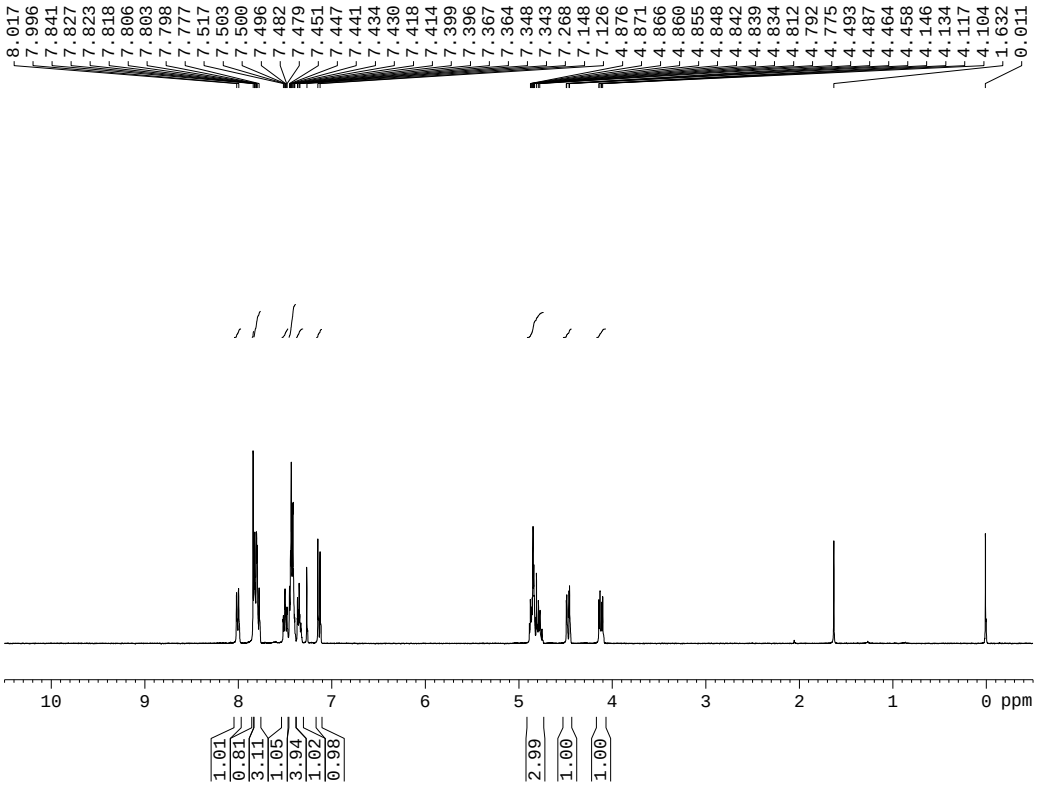

Figure S67. ^{1}H NMR spectrum of compound **15**

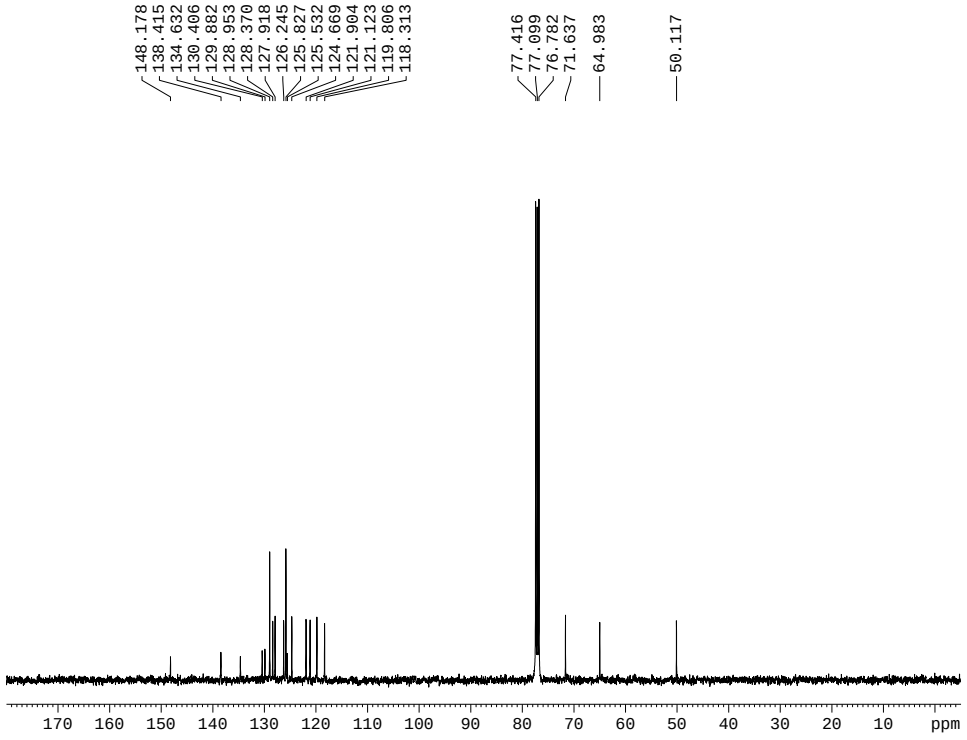

Figure S68. ^{13}C NMR spectrum of compound **15**

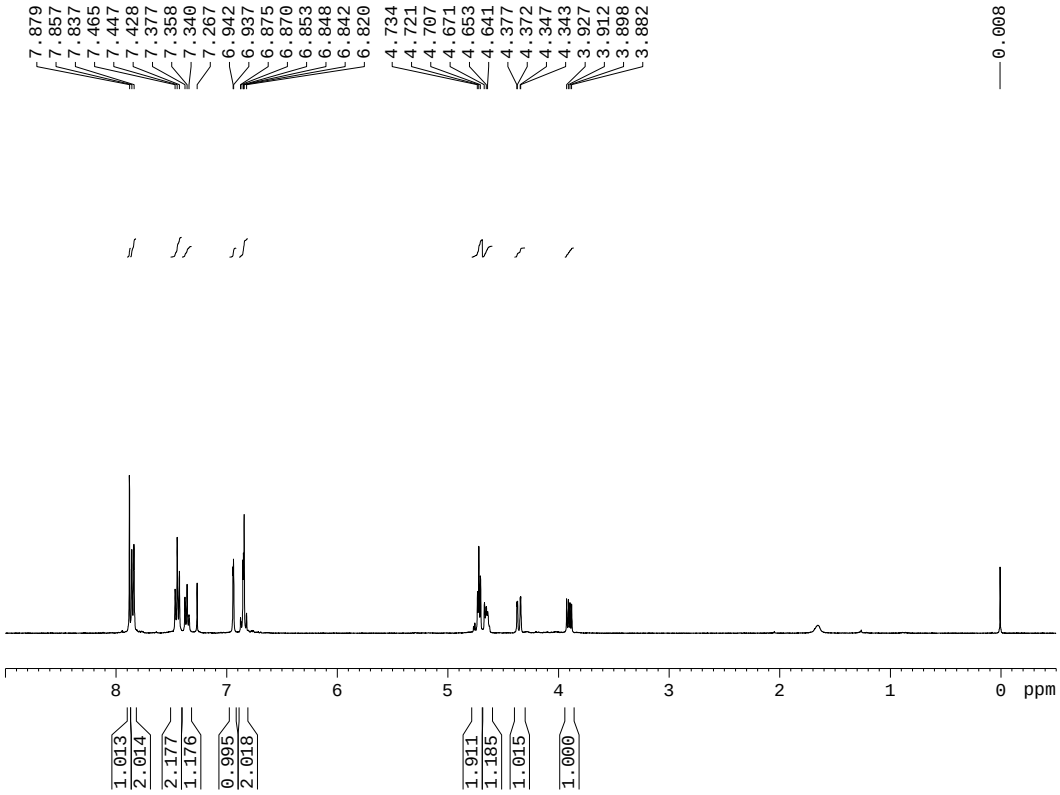

Figure S69. ^{1}H NMR spectrum of compound **16**

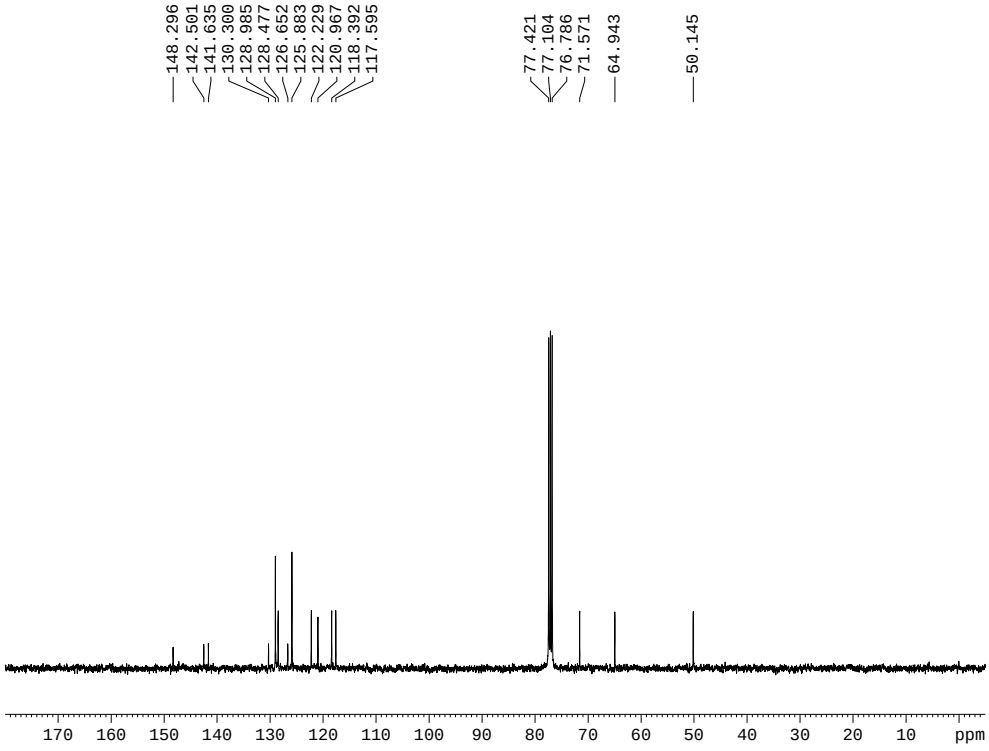

Figure S70. ^{13}C NMR spectrum of compound **16**

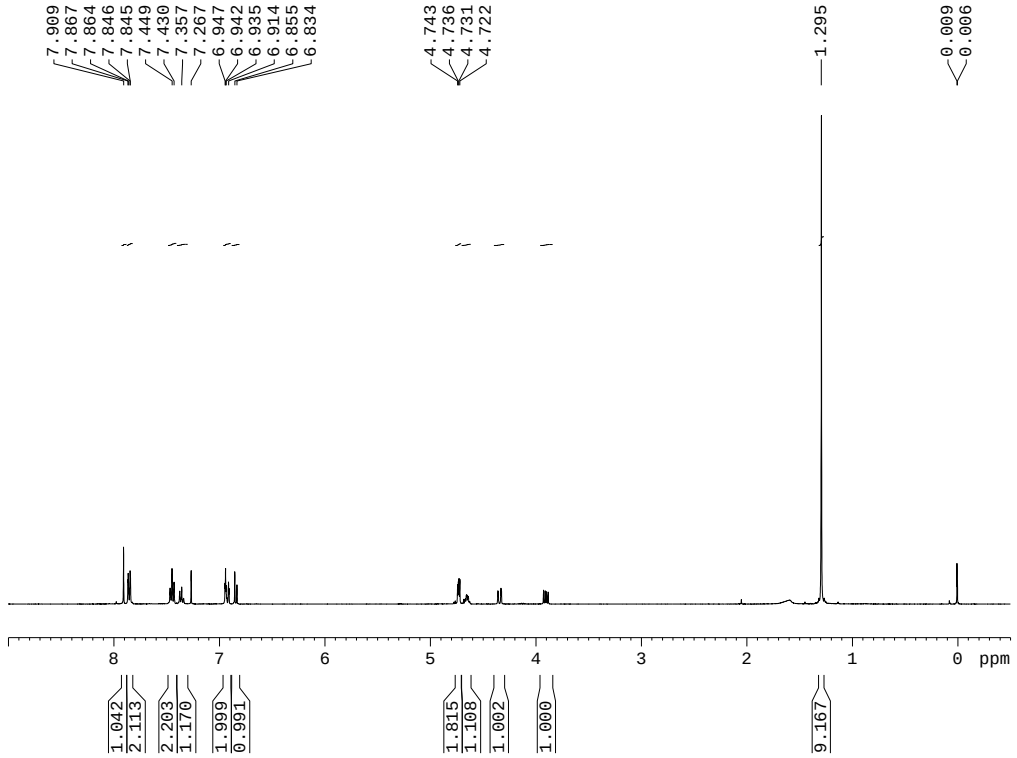

Figure S71. ^{1}H NMR spectrum of compound **17**

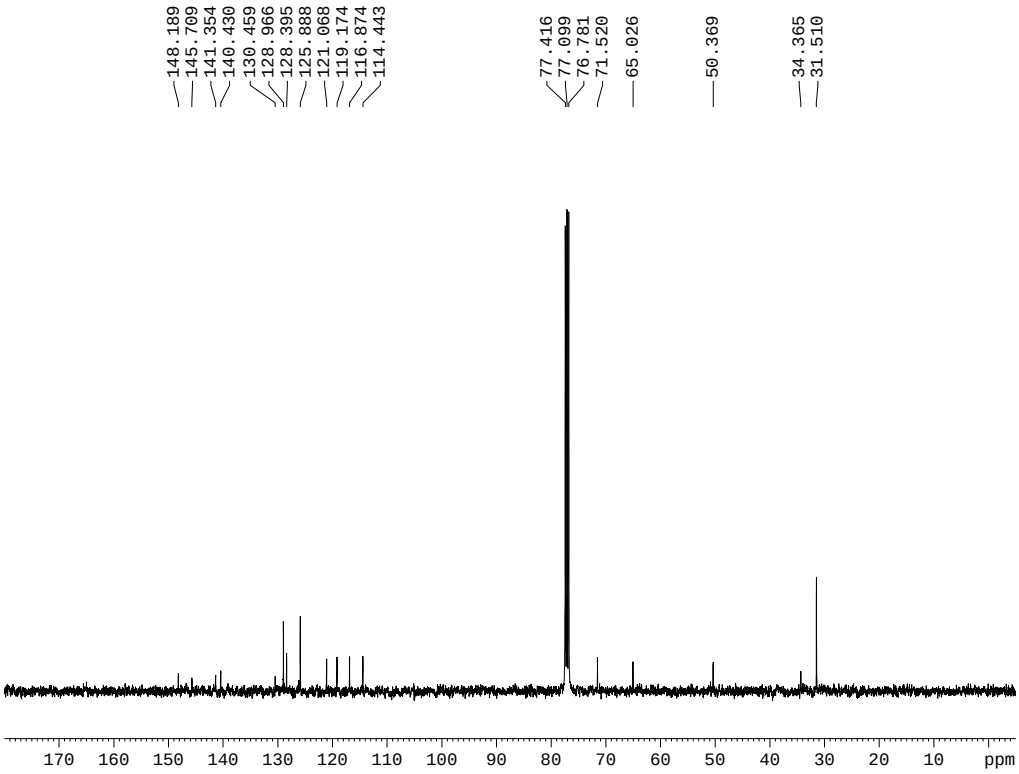

Figure S72. ^{13}C NMR spectrum of compound **17**

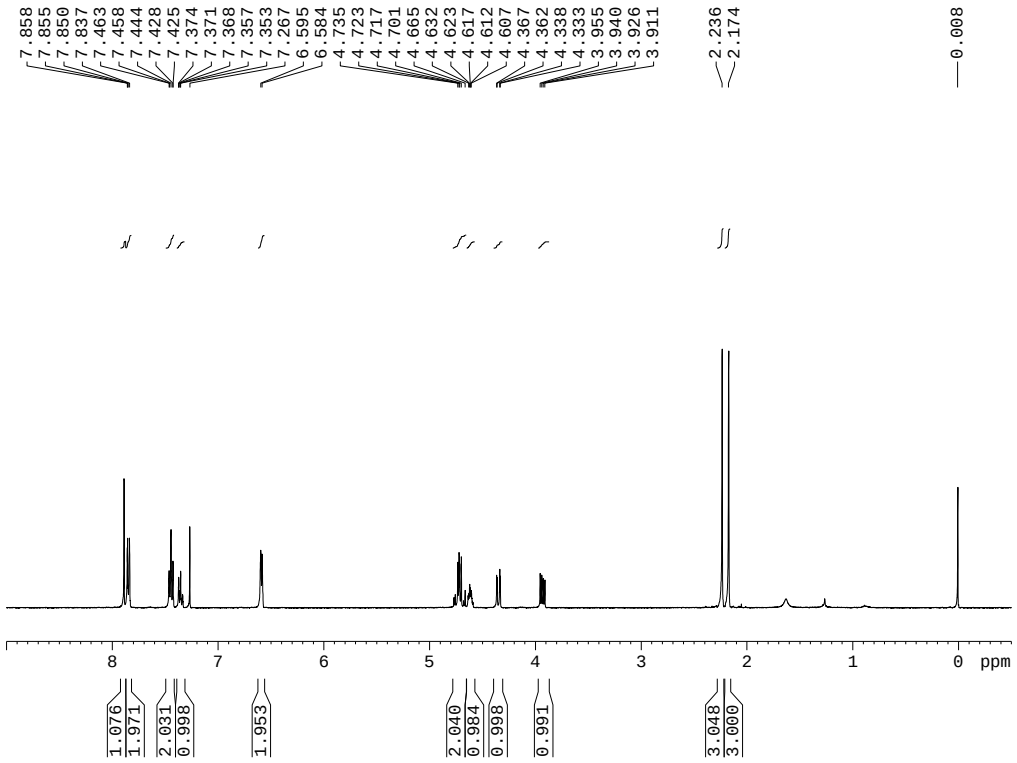

Figure S73. ^{1}H NMR spectrum of compound **18**

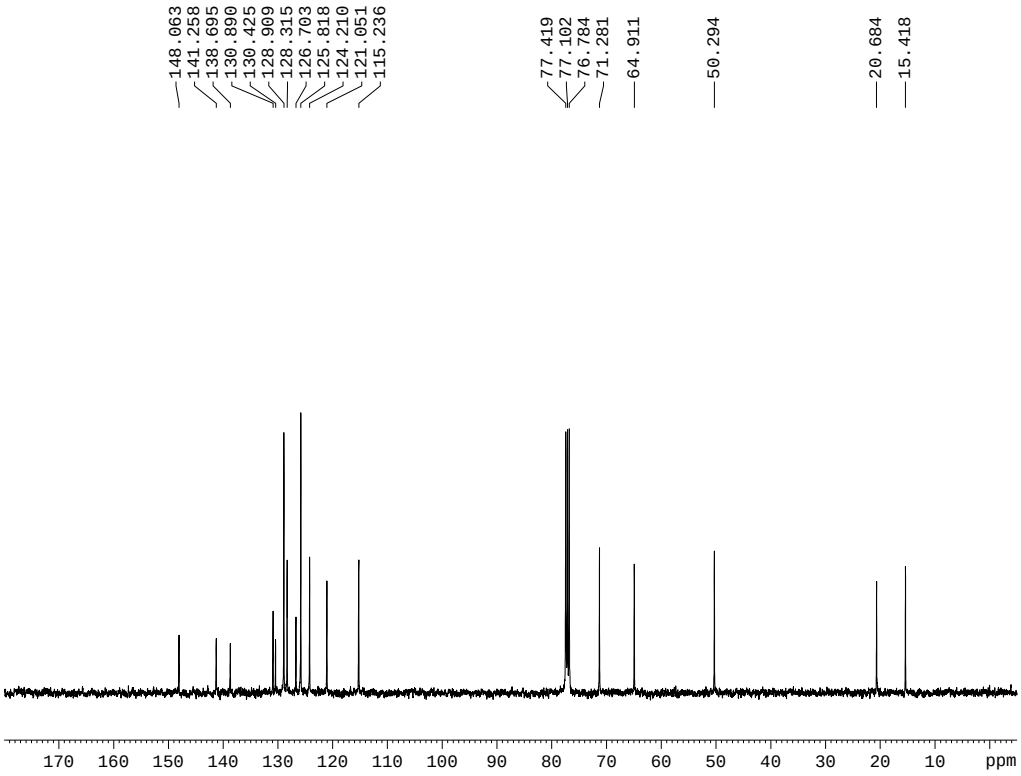

Figure S74. ^{13}C NMR spectrum of compound **18**

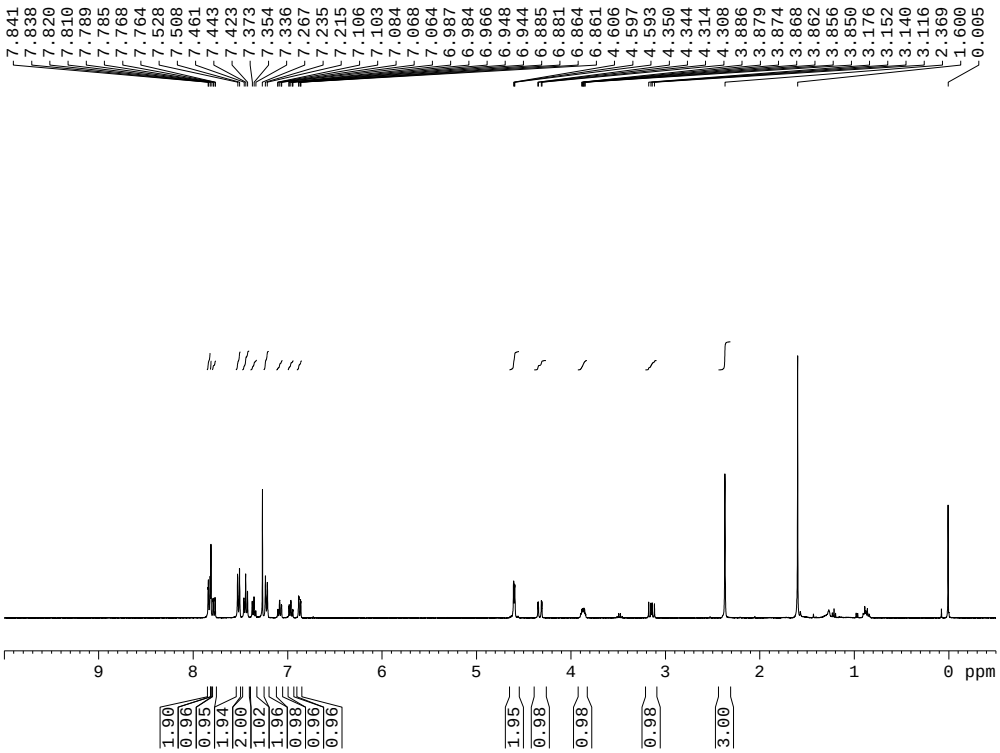

Figure S75. ^{1}H NMR spectrum of compound **19**

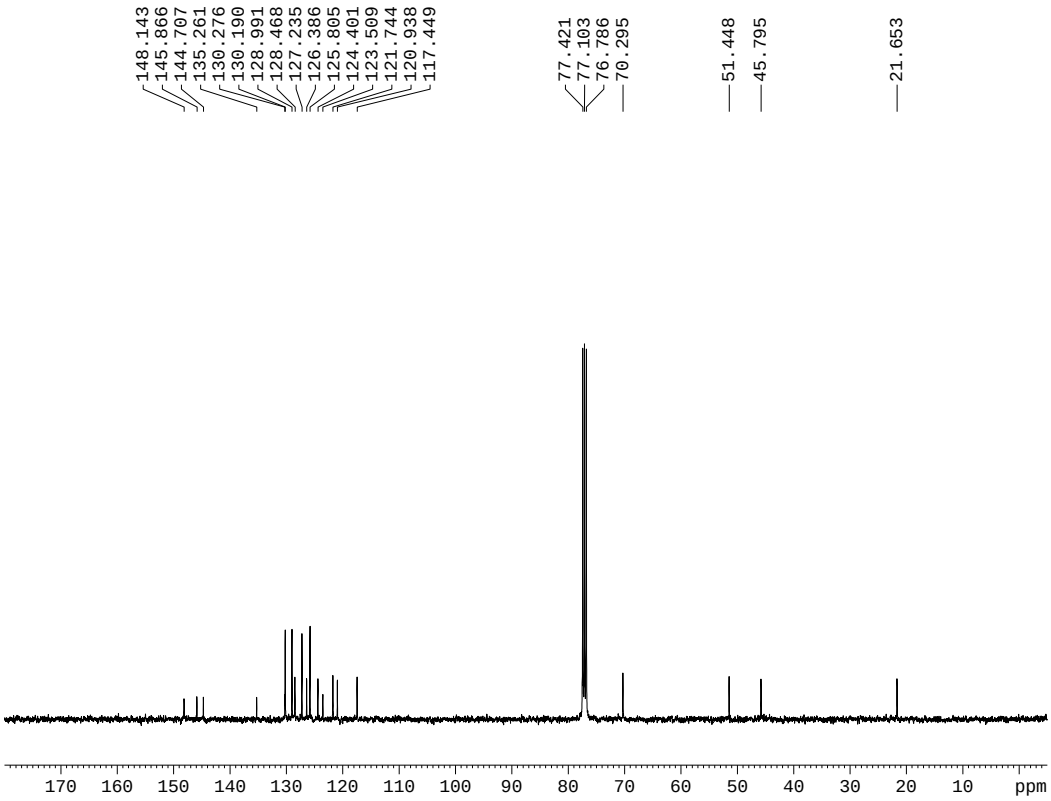

Figure S76. ^{13}C NMR spectrum of compound **19**

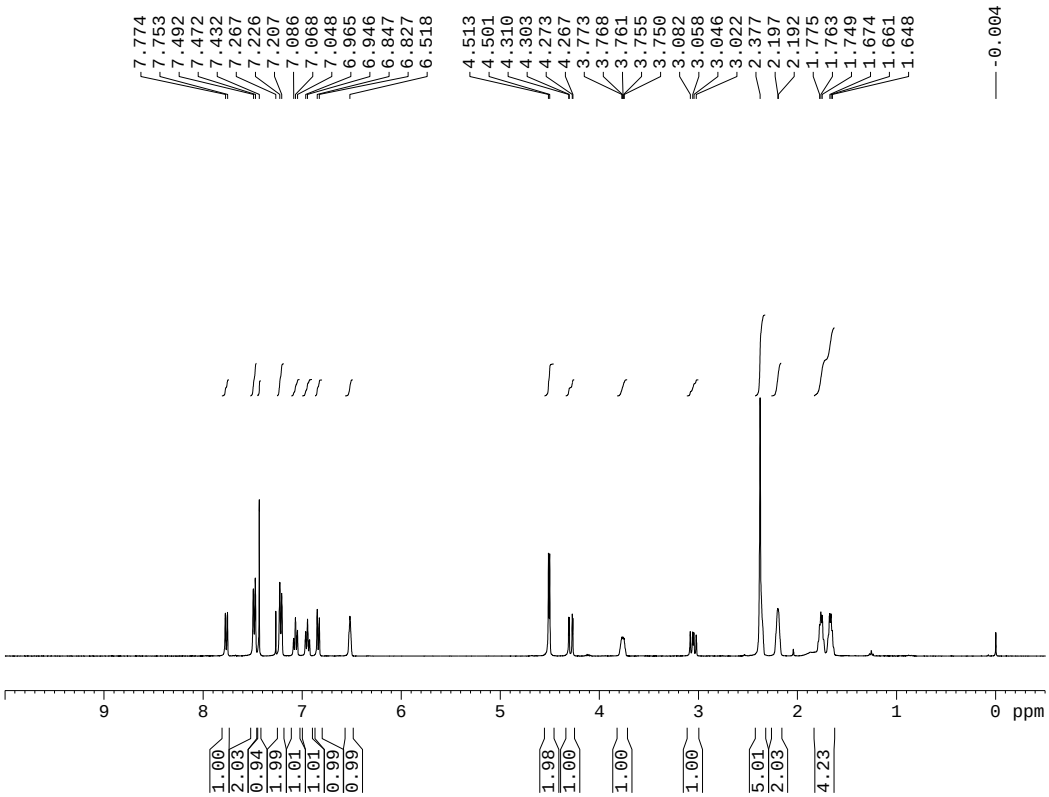

Figure S77. ^{1}H NMR spectrum of compound **20**

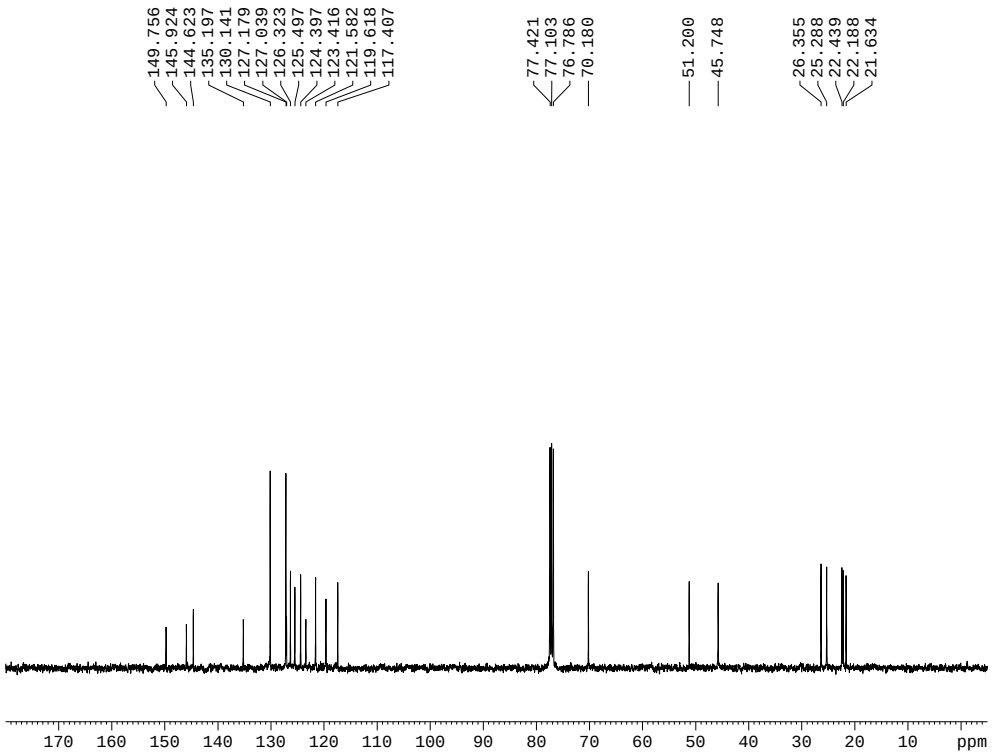

Figure S78. ^{13}C NMR spectrum of compound **20**

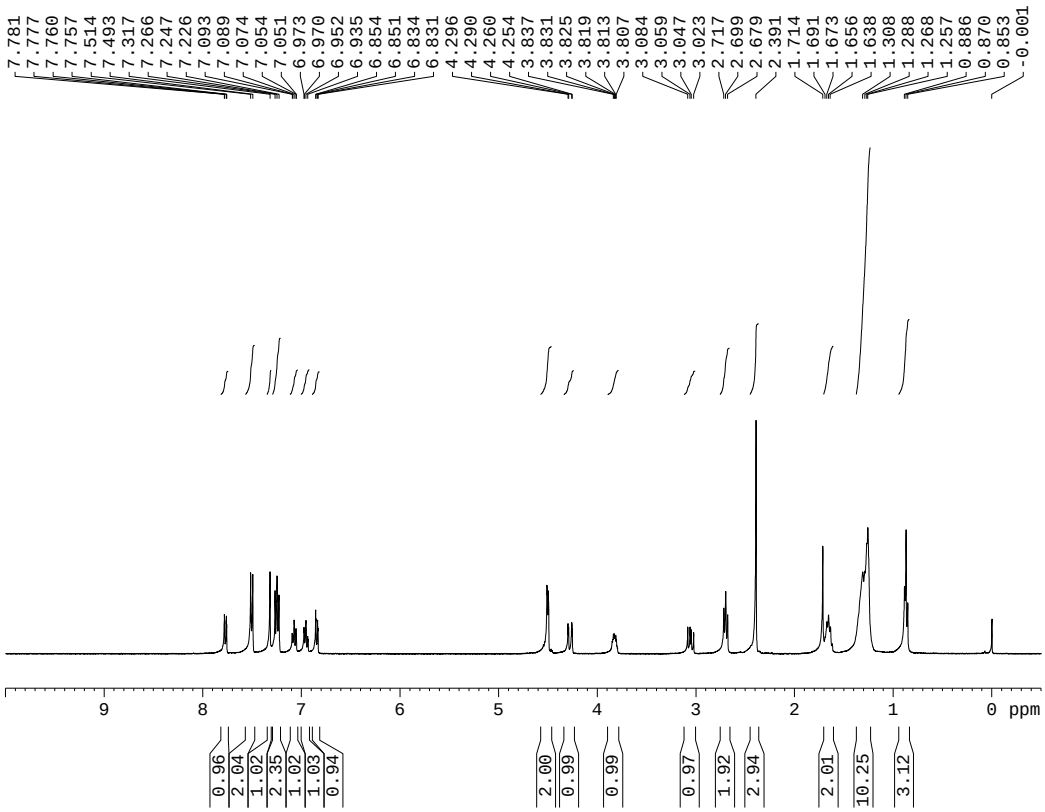

Figure S79. ^{1}H NMR spectrum of compound **21**

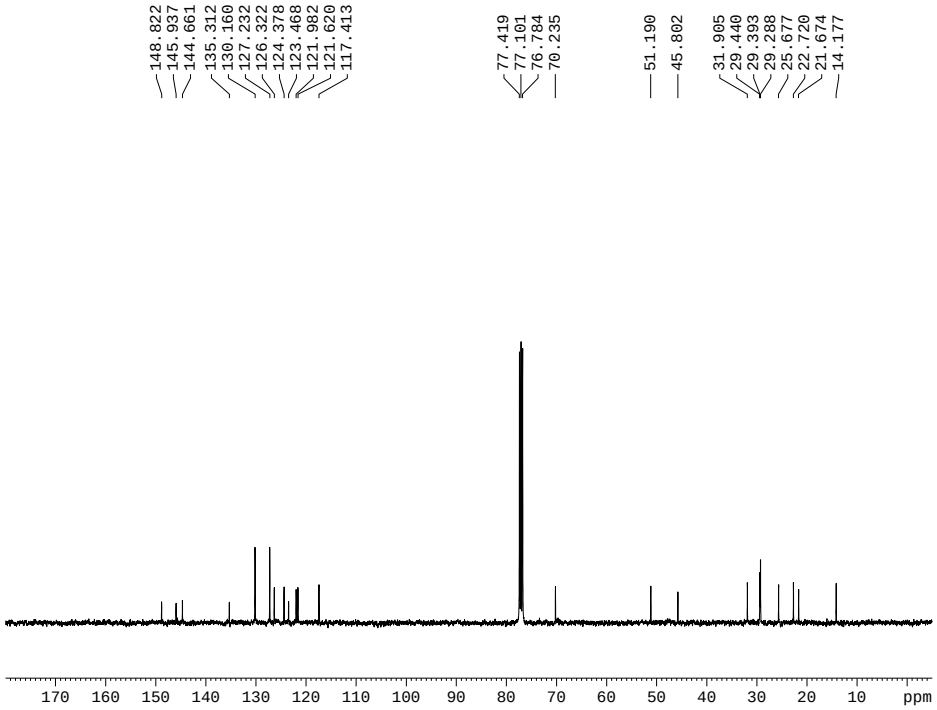

Figure S80. ^{13}C NMR spectrum of compound **21**

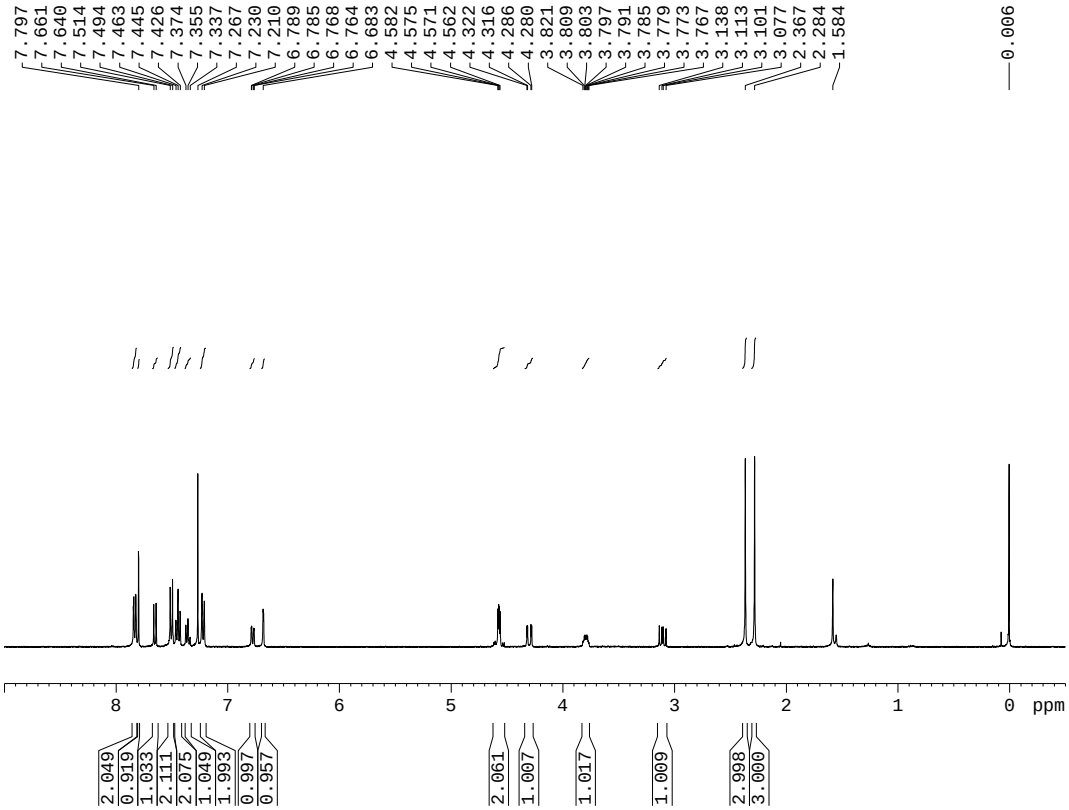

Figure S81. ^{1}H NMR spectrum of compound **22**

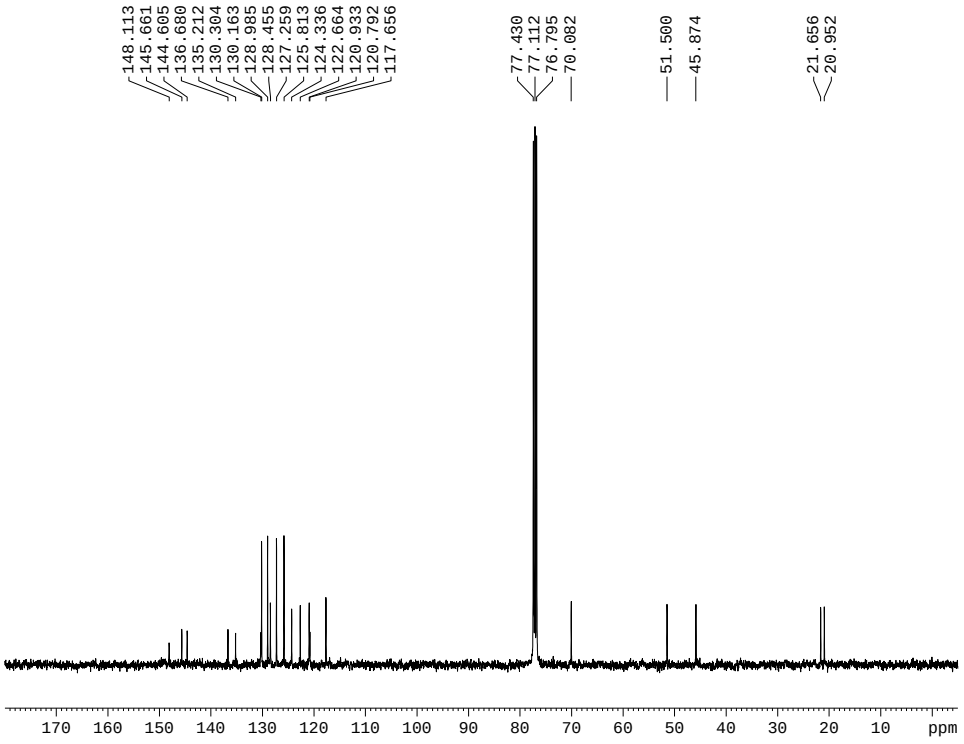

Figure S82. ^{13}C NMR spectrum of compound **22**

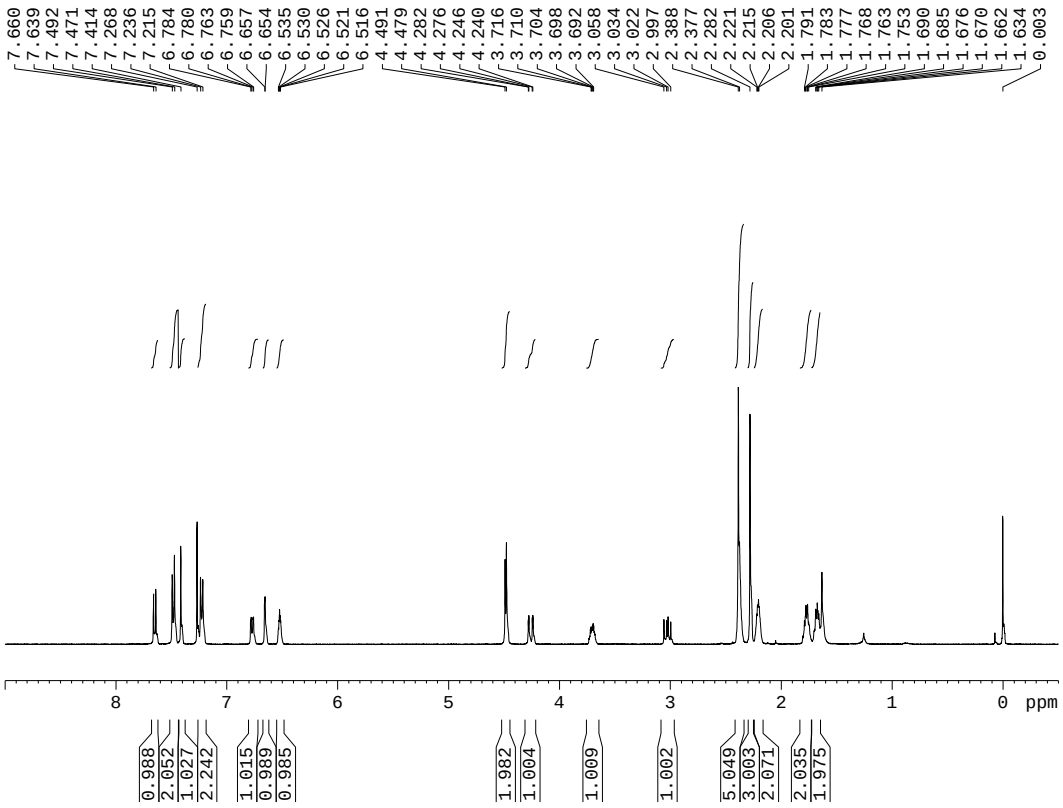

Figure S83. ^{1}H NMR spectrum of compound **23**

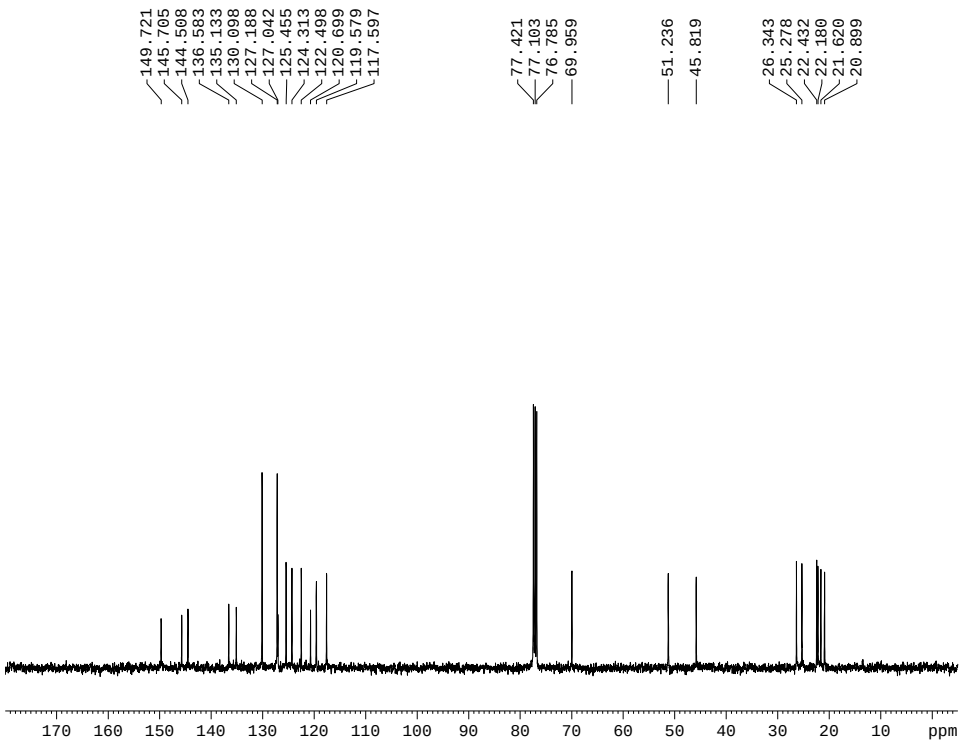

Figure S84. ^{13}C NMR spectrum of compound **23**

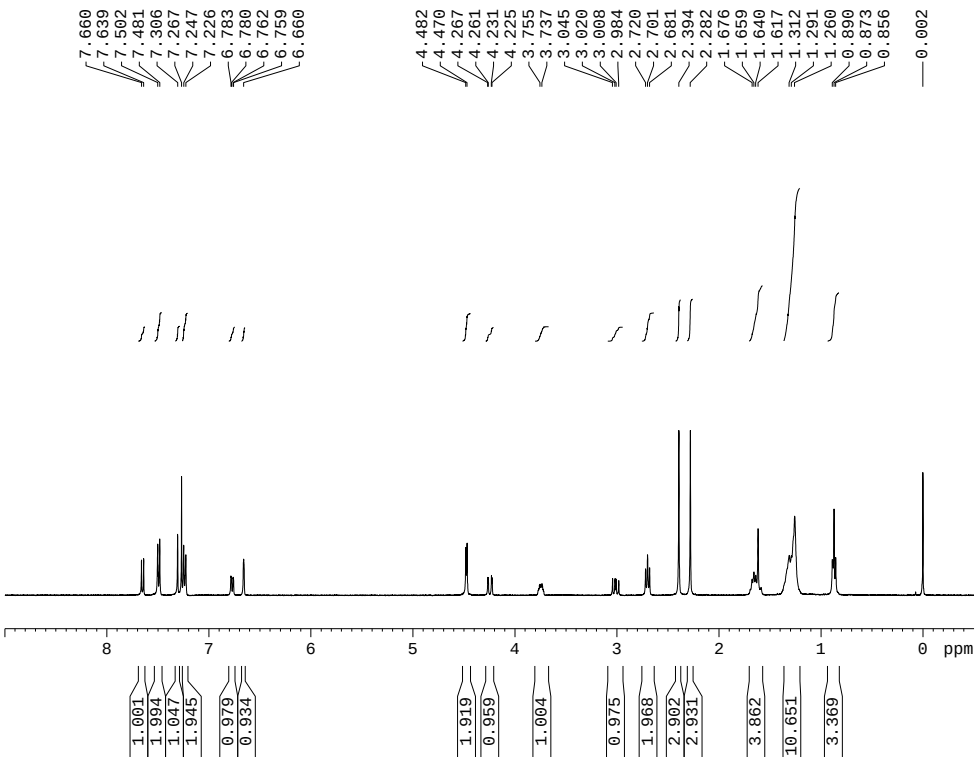

Figure S85. ^{1}H NMR spectrum of compound **24**

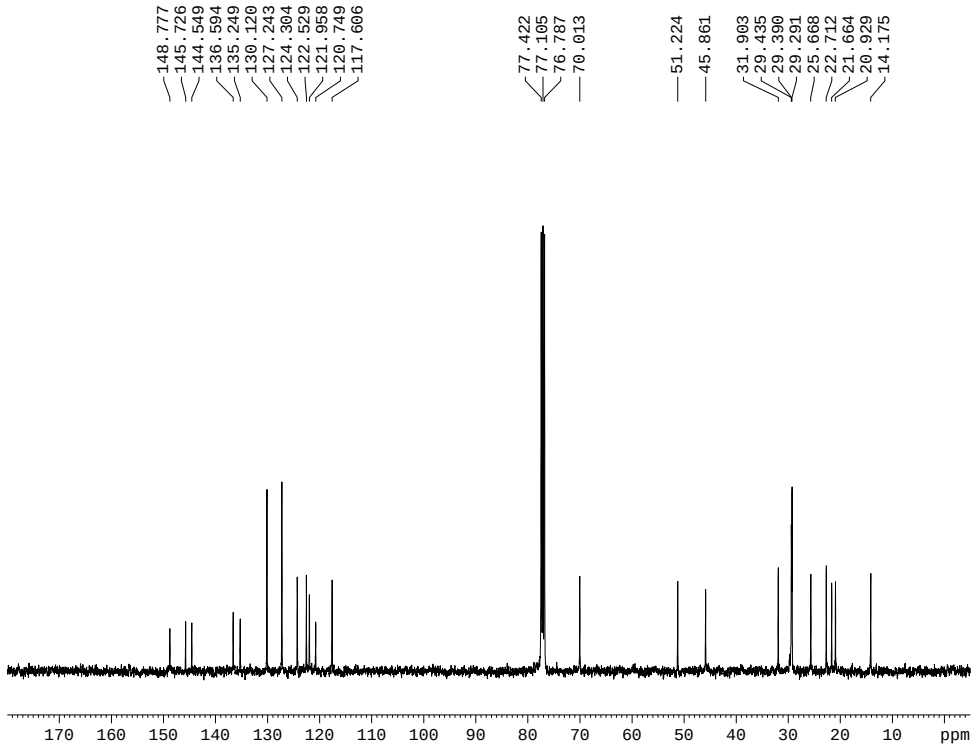

Figure S86. ^{13}C NMR spectrum of compound **24**

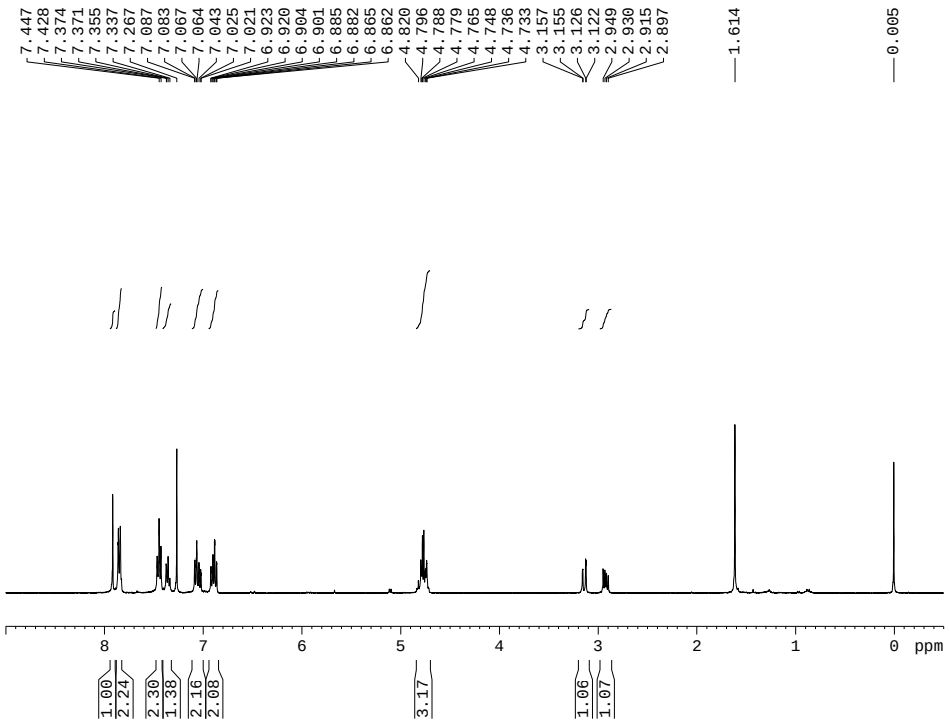

Figure S87. ^{1}H NMR spectrum of compound **25**

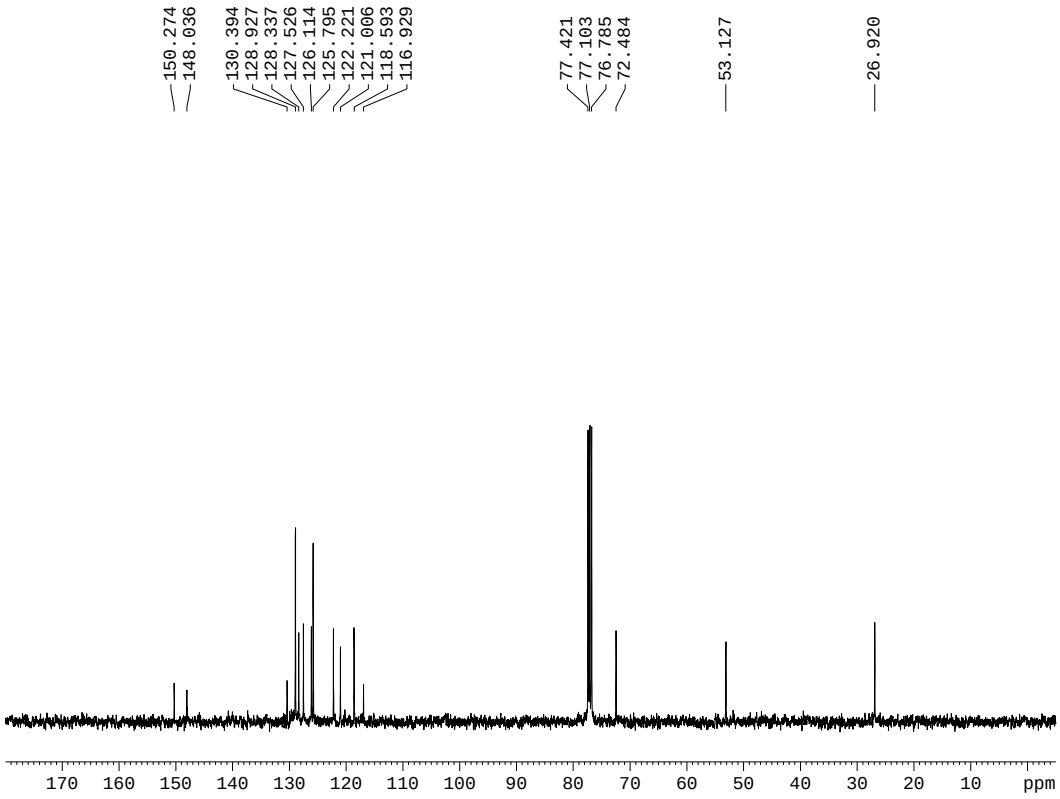

Figure S88. ^{13}C NMR spectrum of compound **25**

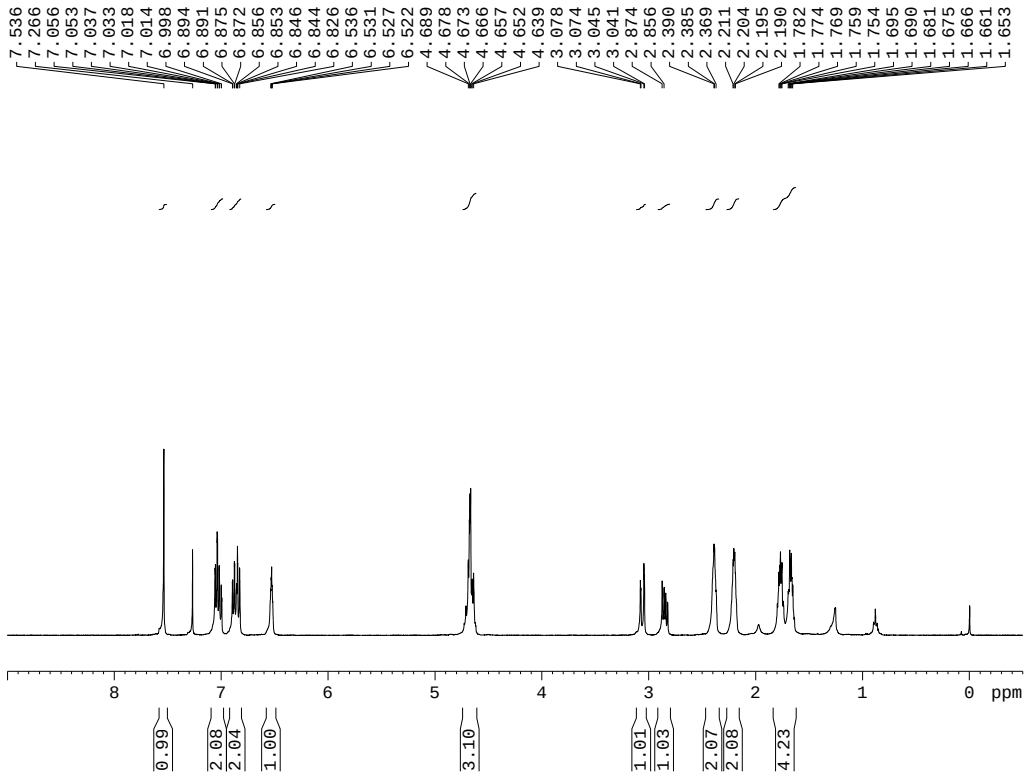

Figure S89. ^{1}H NMR spectrum of compound **26**

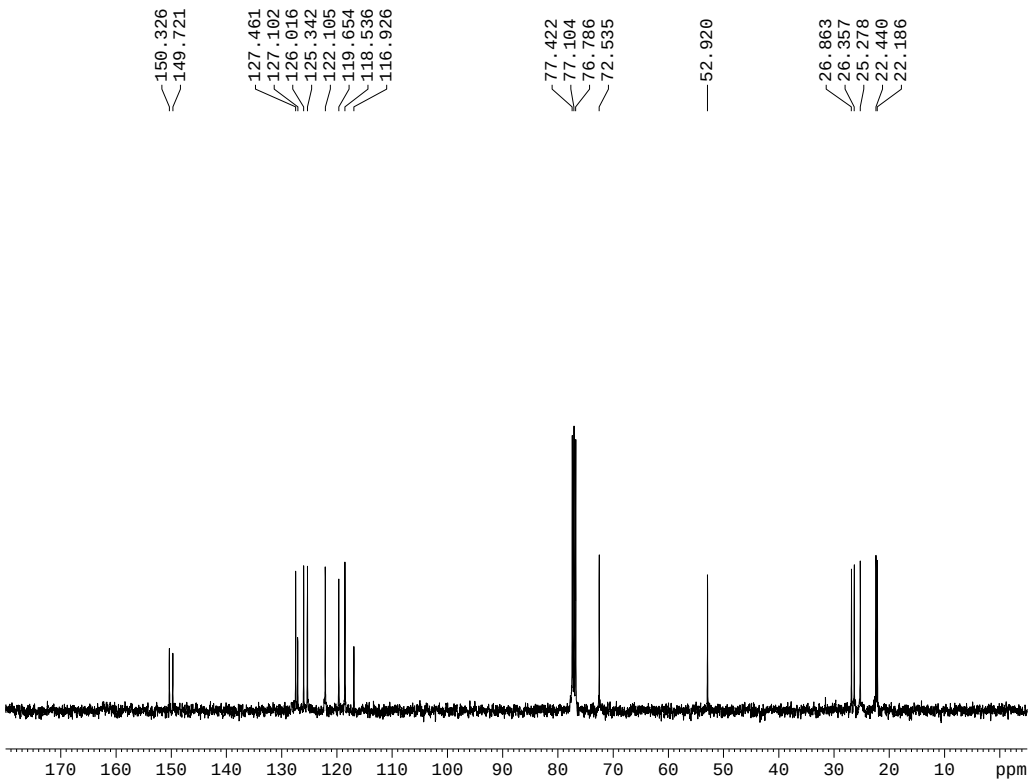

Figure S90. ^{13}C NMR spectrum of compound **26**

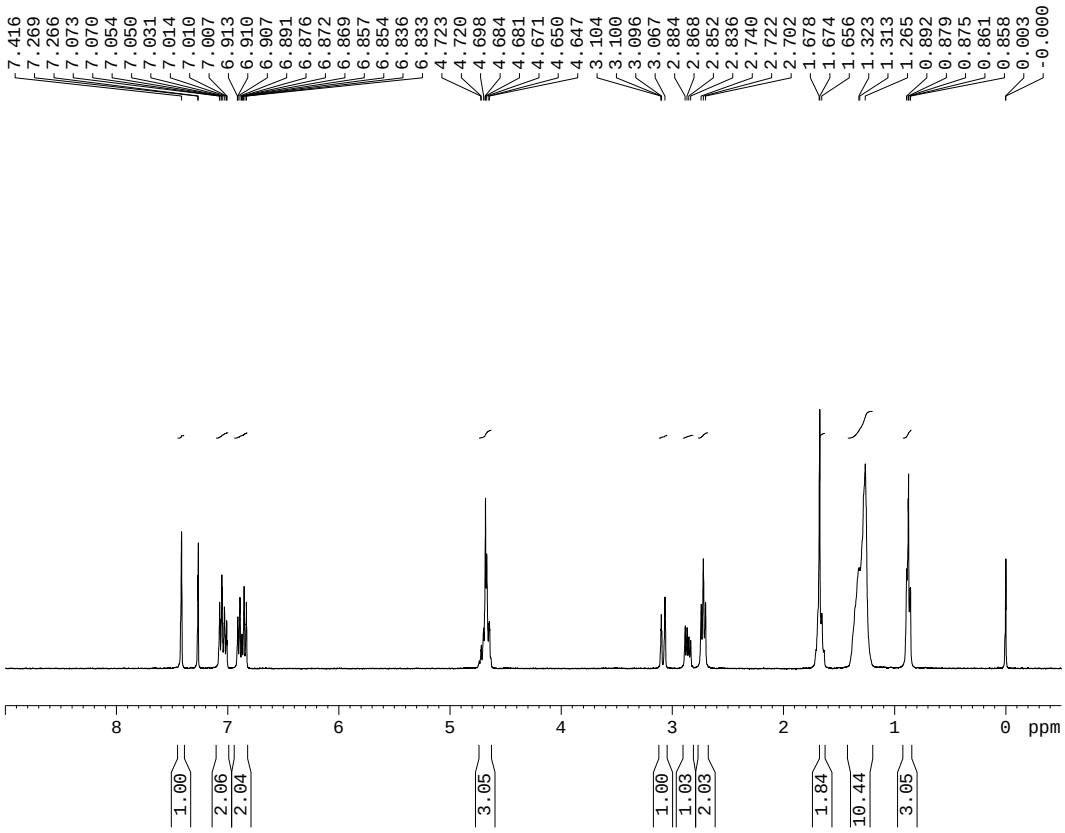

Figure S91. ^{1}H NMR spectrum of compound **27**

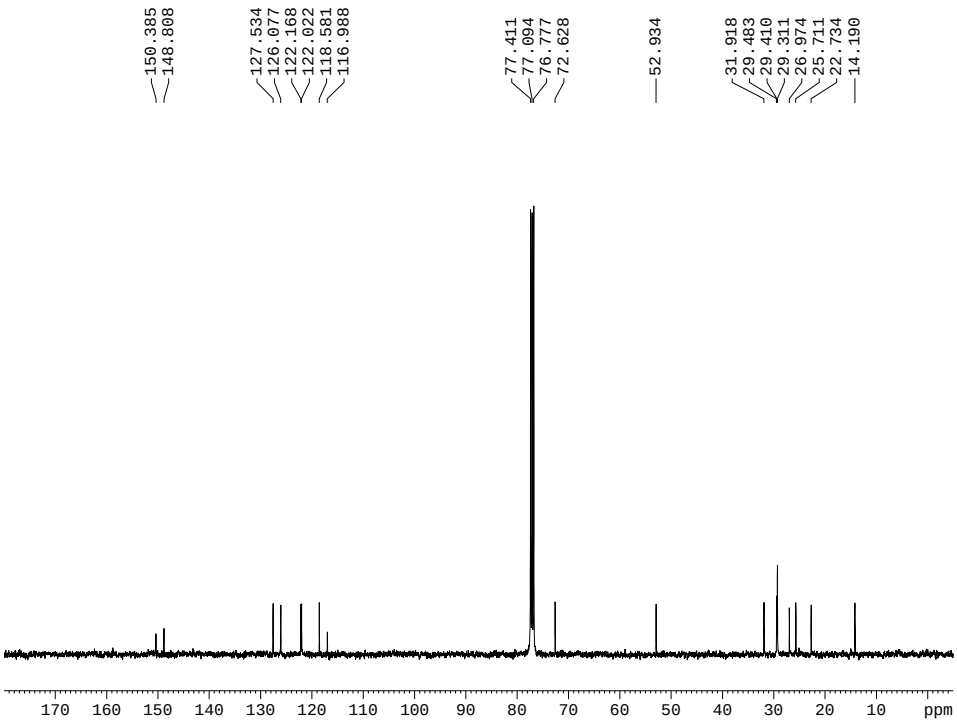

Figure S92. ^{13}C NMR spectrum of compound **27**

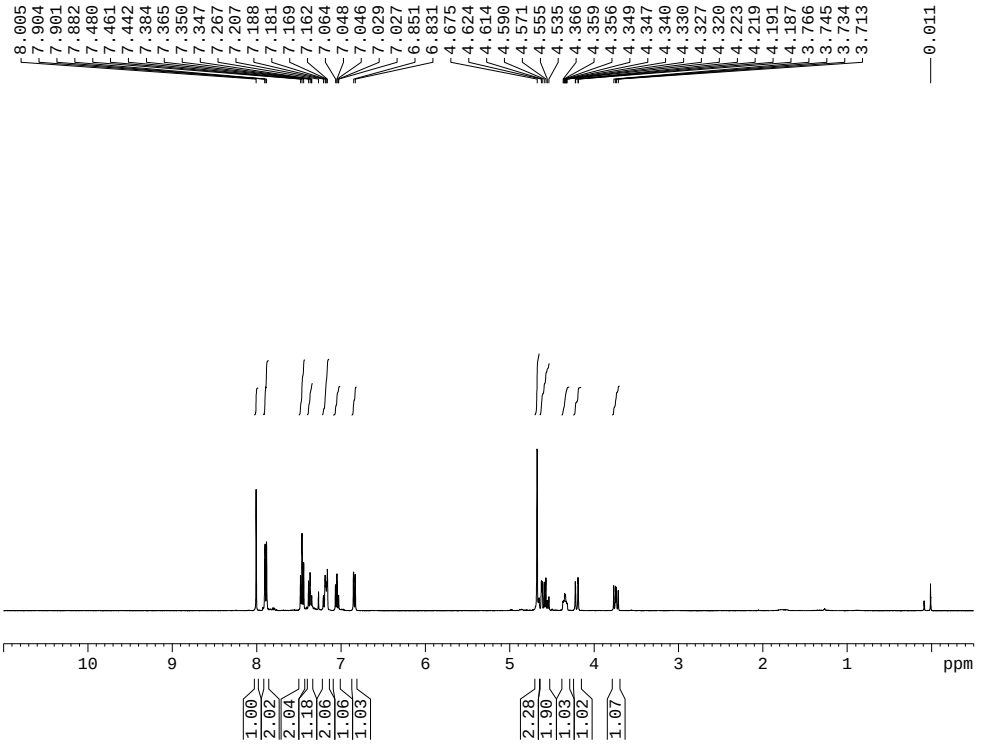

Figure S93. ^{1}H NMR spectrum of compound **28**

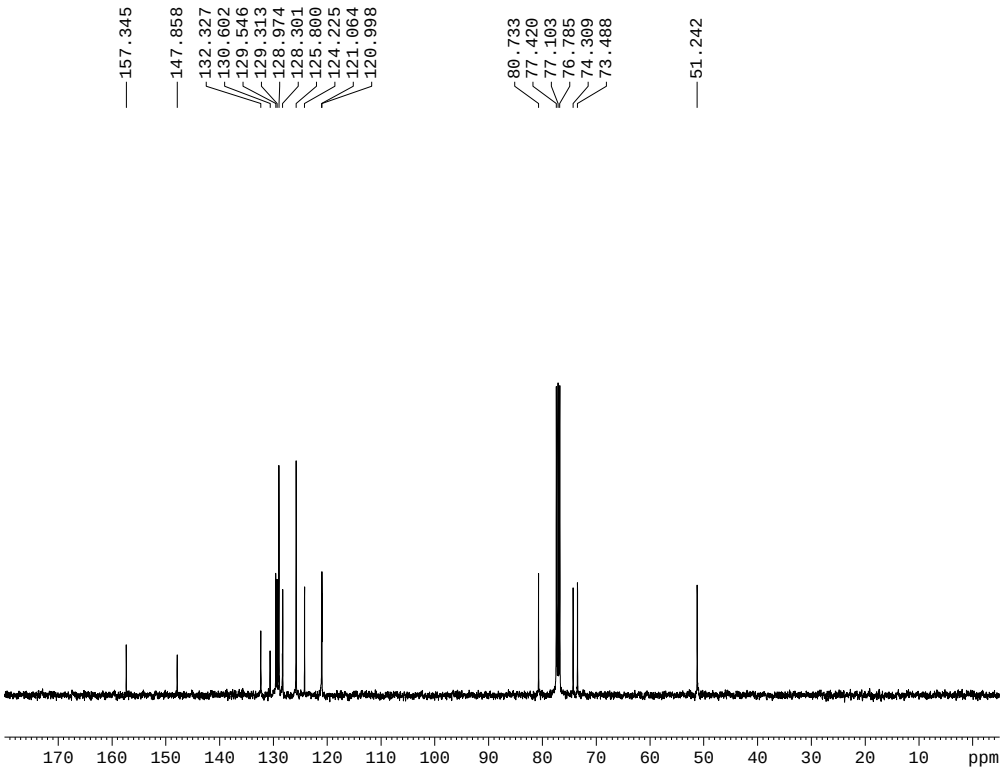

Figure S94. ^{13}C NMR spectrum of compound **28**

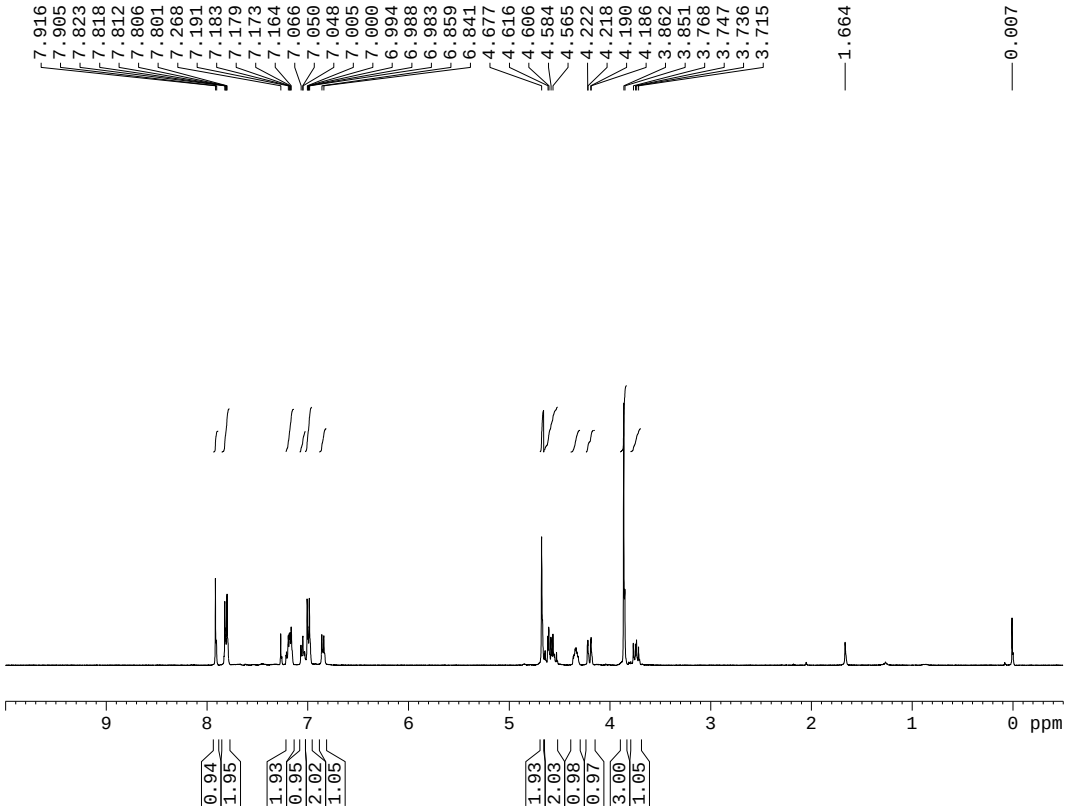

Figure S95. ^{1}H NMR spectrum of compound **29**

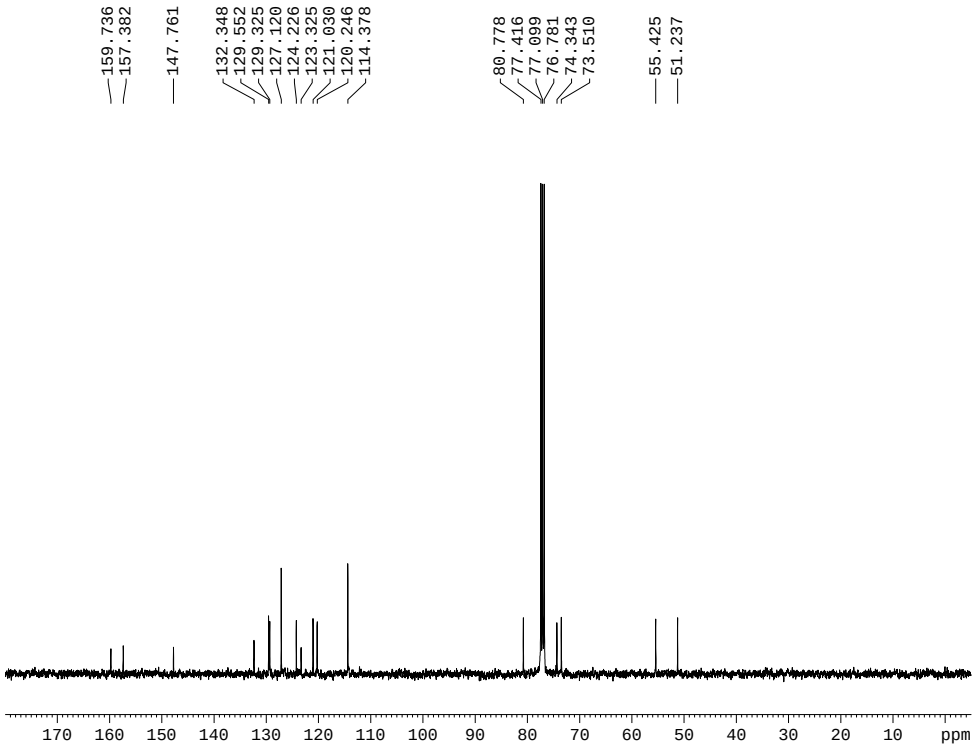

Figure S96. ^{13}C NMR spectrum of compound **29**

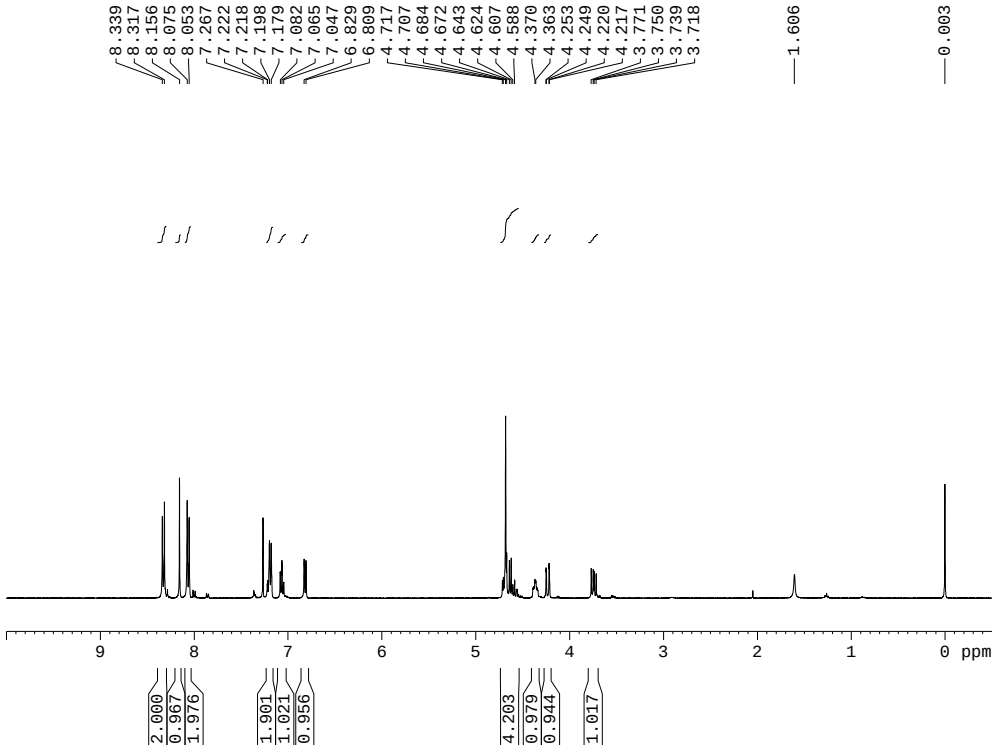

Figure S97. ^{1}H NMR spectrum of compound **30**

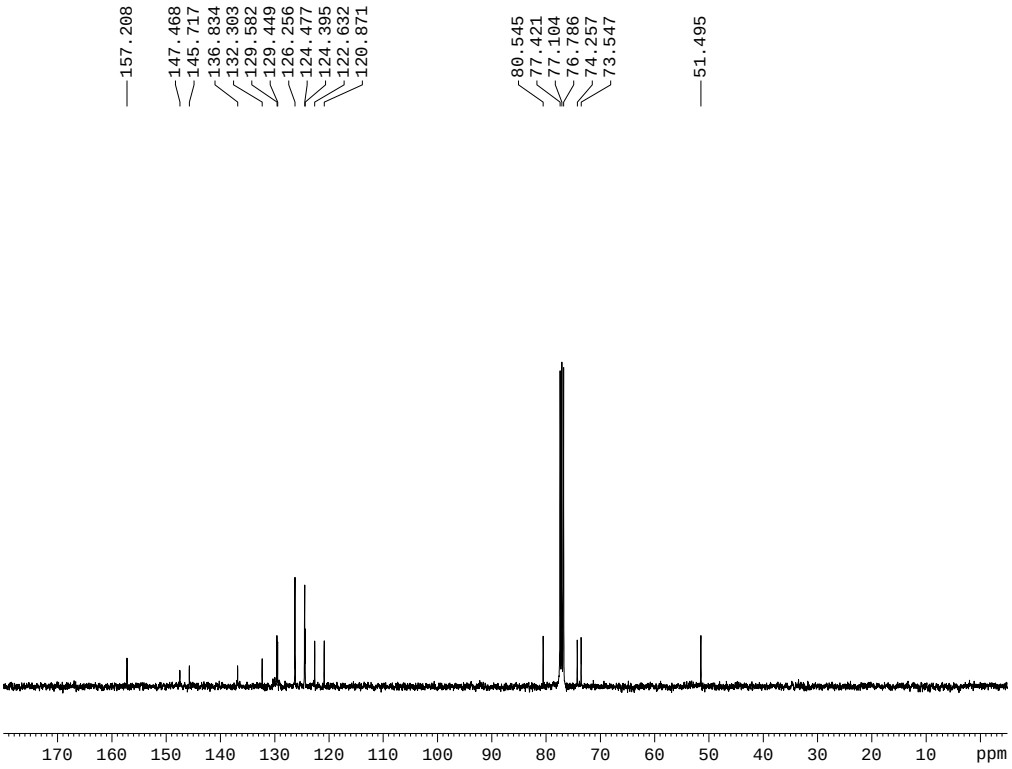

Figure S98. ^{13}C NMR spectrum of compound **30**

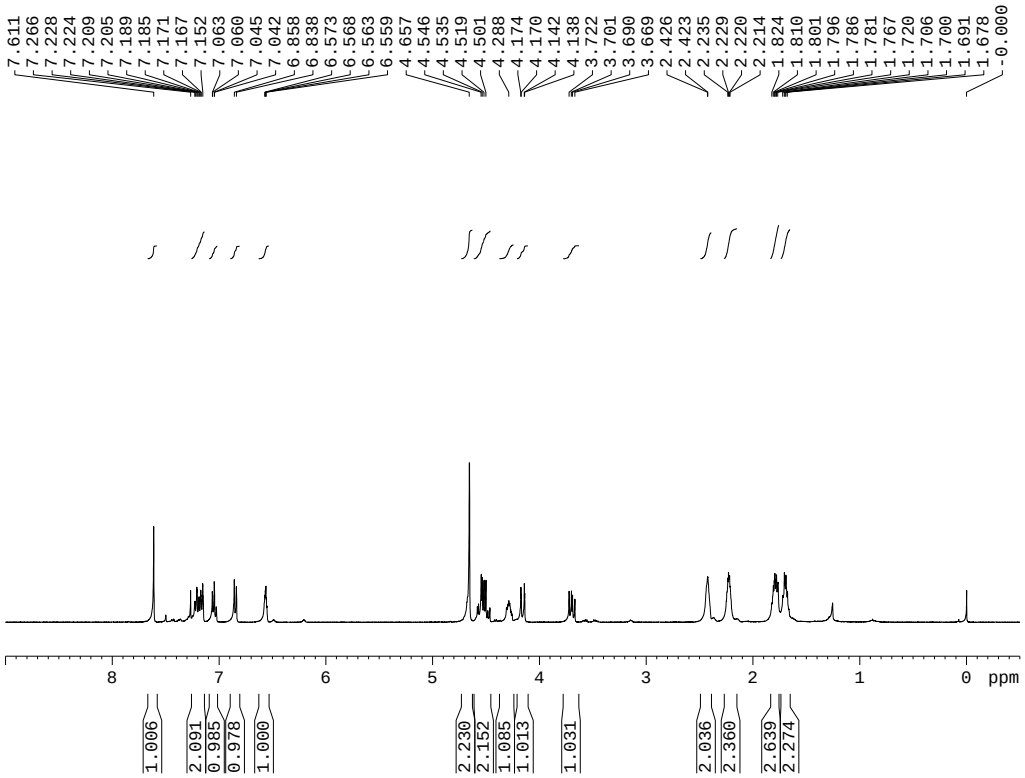

Figure S99. ^{1}H NMR spectrum of compound **31**

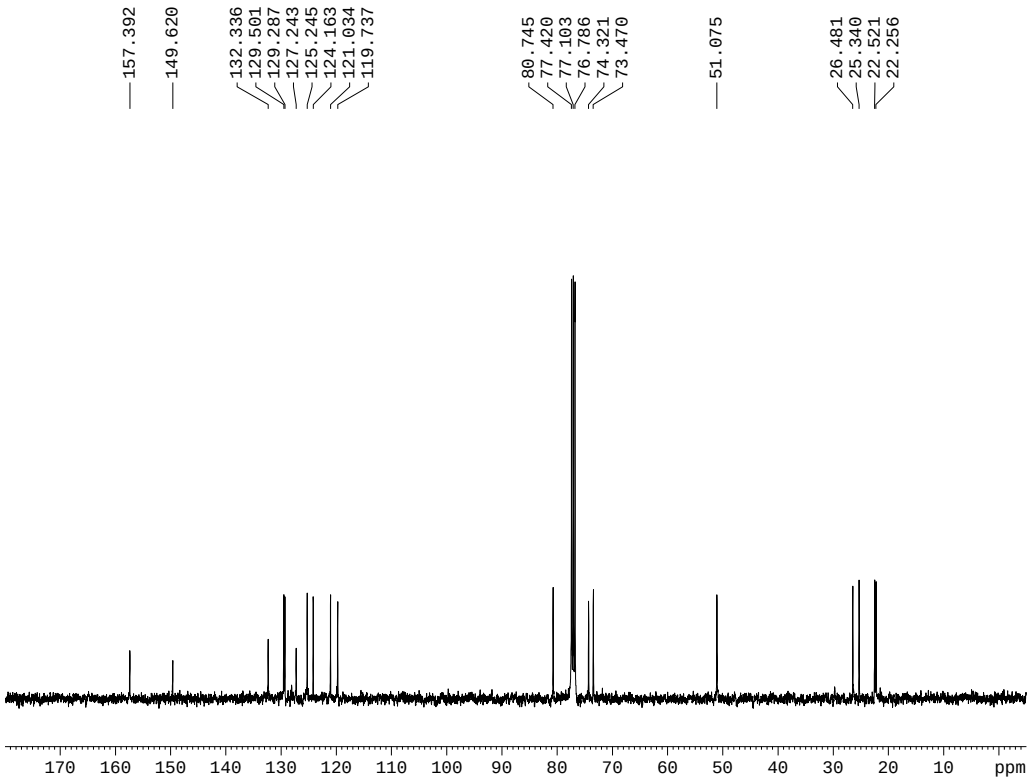

Figure S100. ^{13}C NMR spectrum of compound **31**

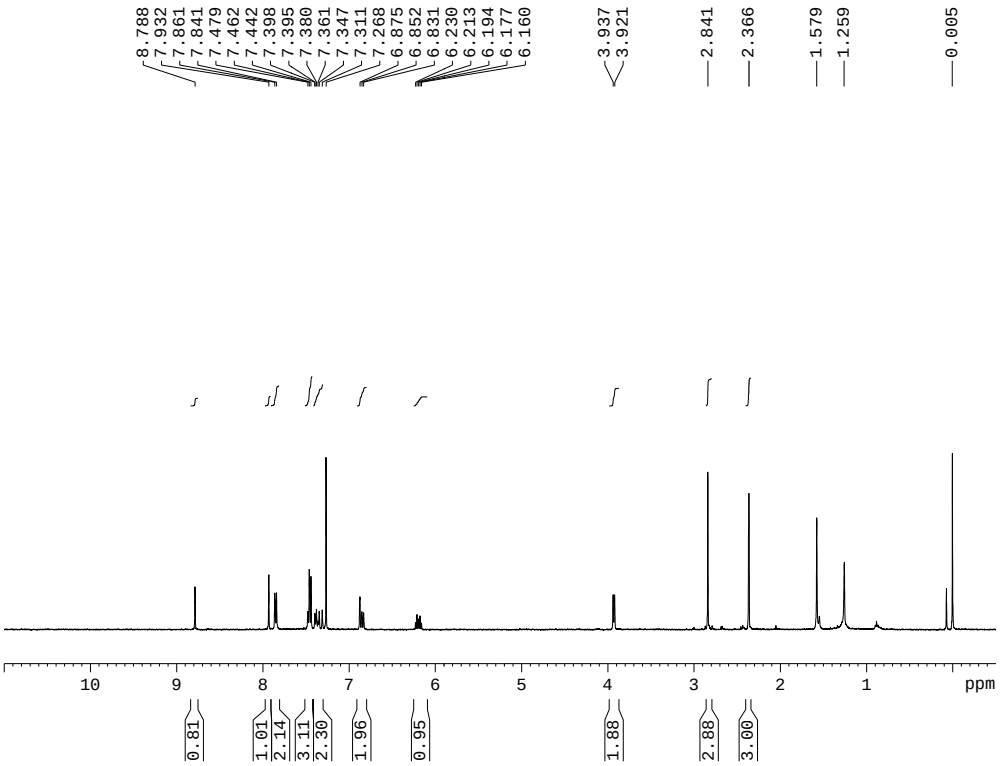

Figure S101. ^{1}H NMR spectrum of compound **32**

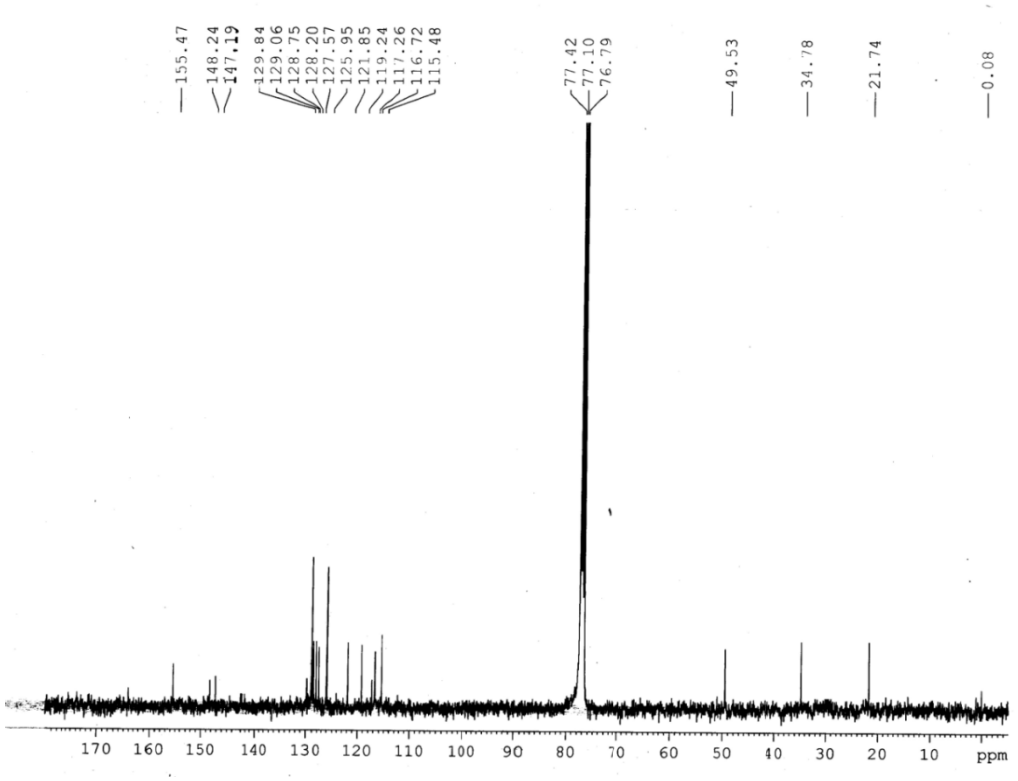

Figure S102. ^{13}C NMR spectrum of compound **32**

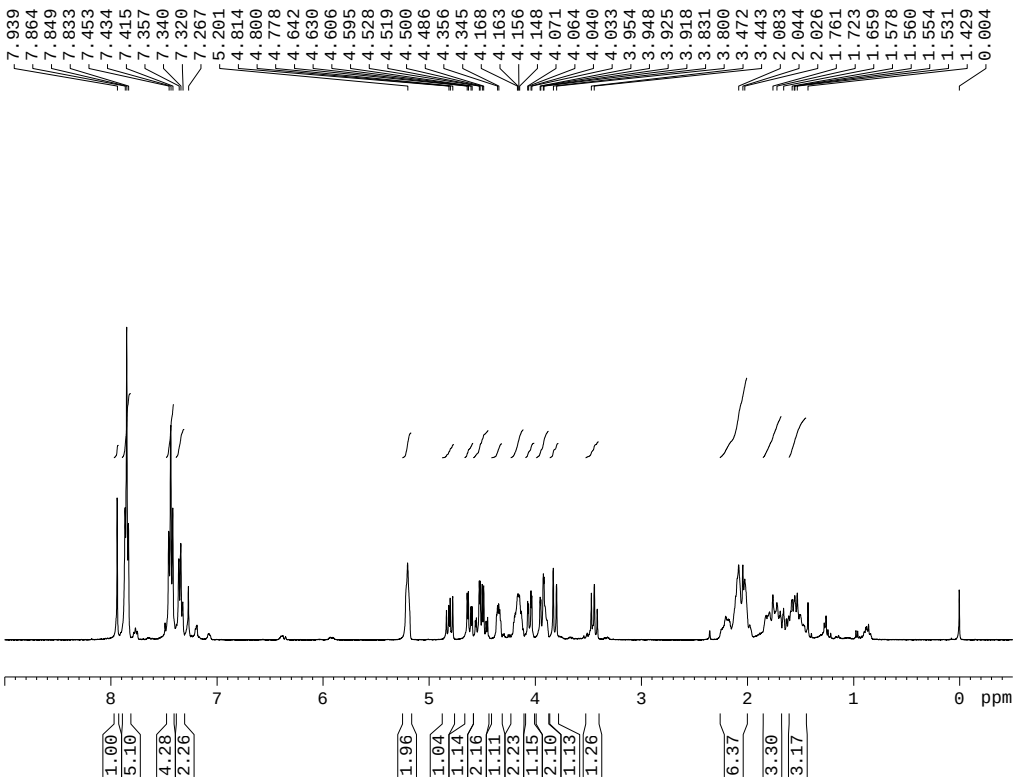

Figure S103. ^{1}H NMR spectrum of compound **33**

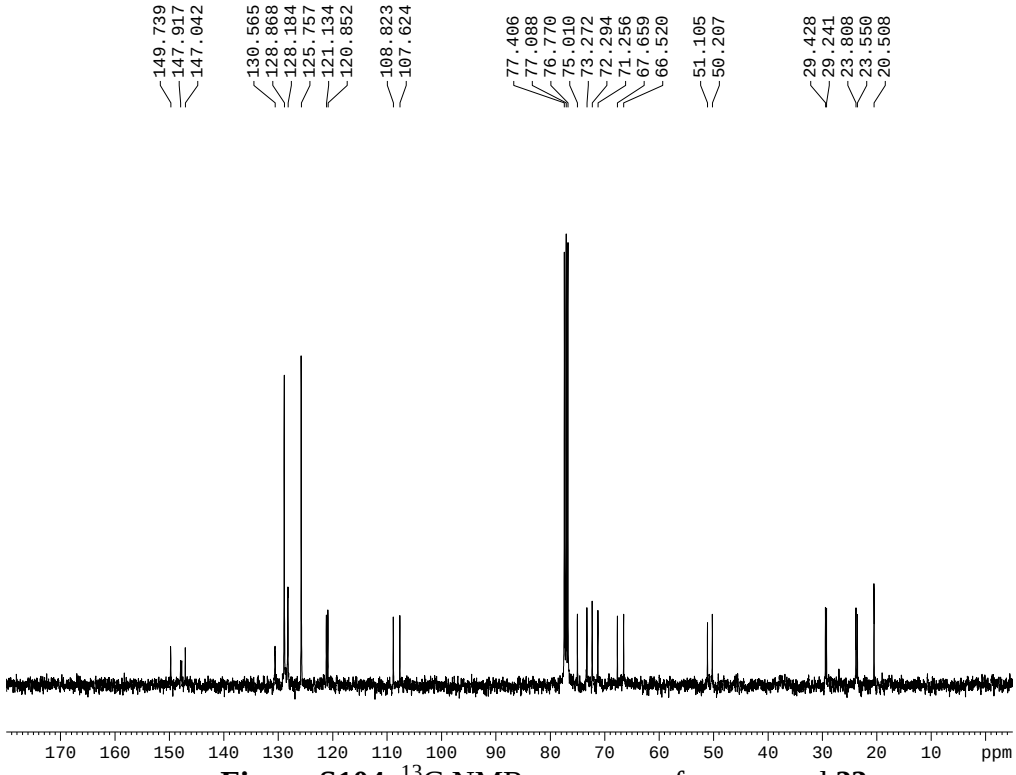

Figure S104. ^{13}C NMR spectrum of compound **33**

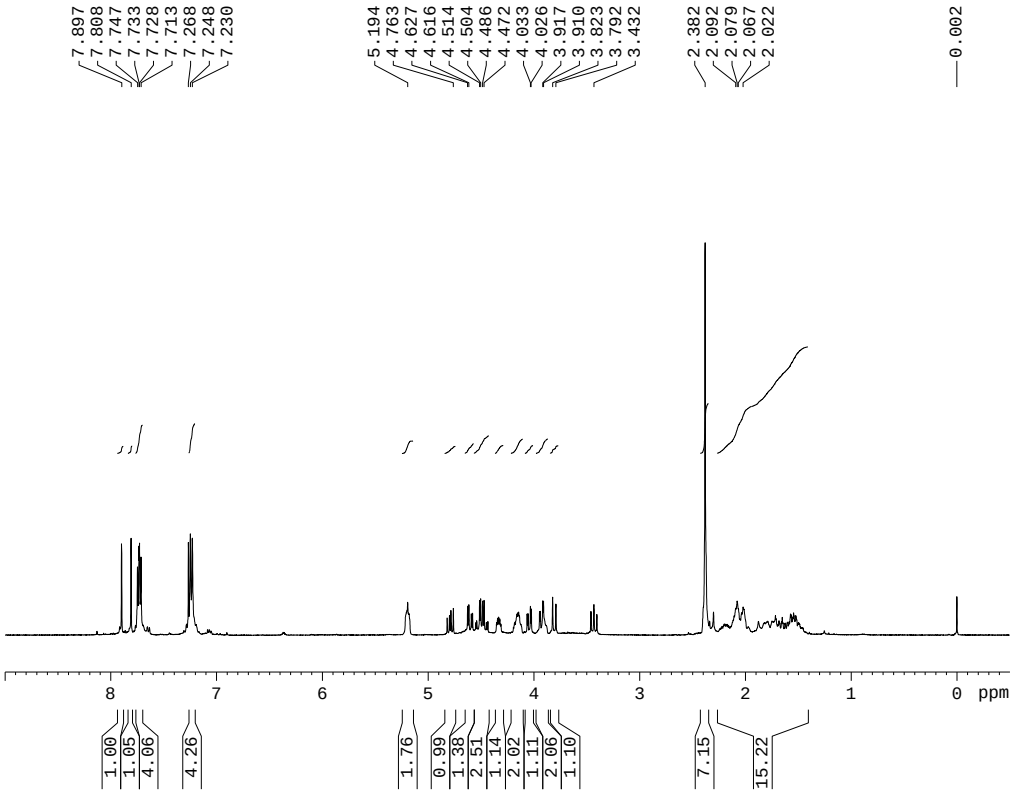

Figure S105. ^{1}H NMR spectrum of compound **34**

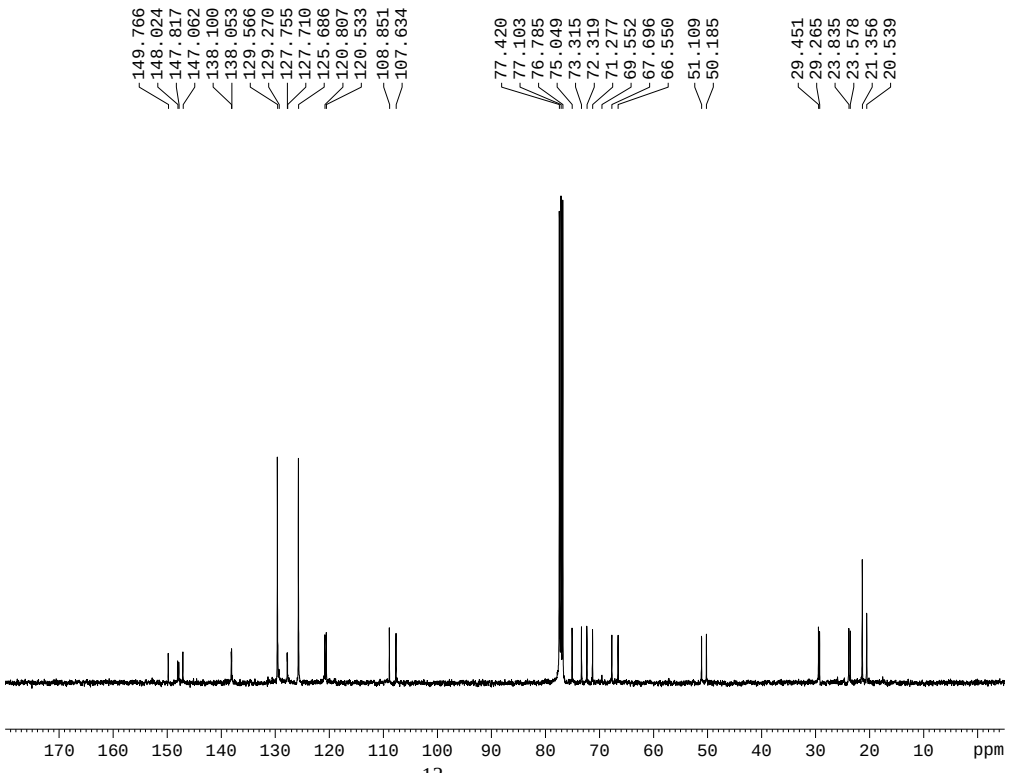

Figure S106. ^{13}C NMR spectrum of compound **34**

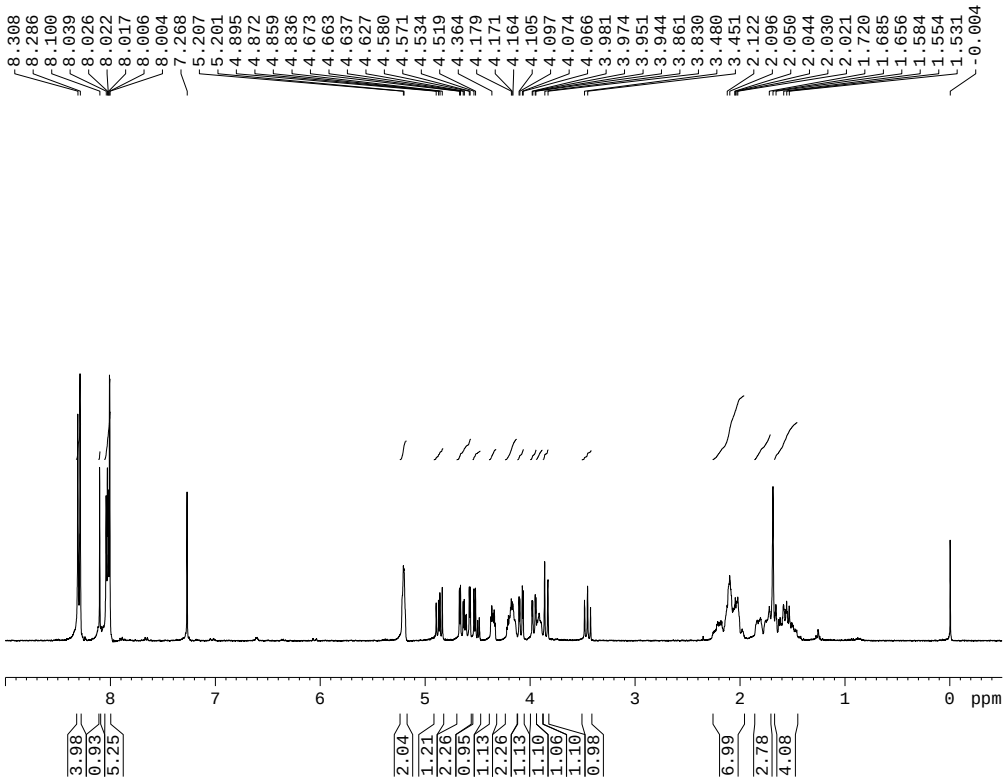

Figure S107. ^{1}H NMR spectrum of compound **35**

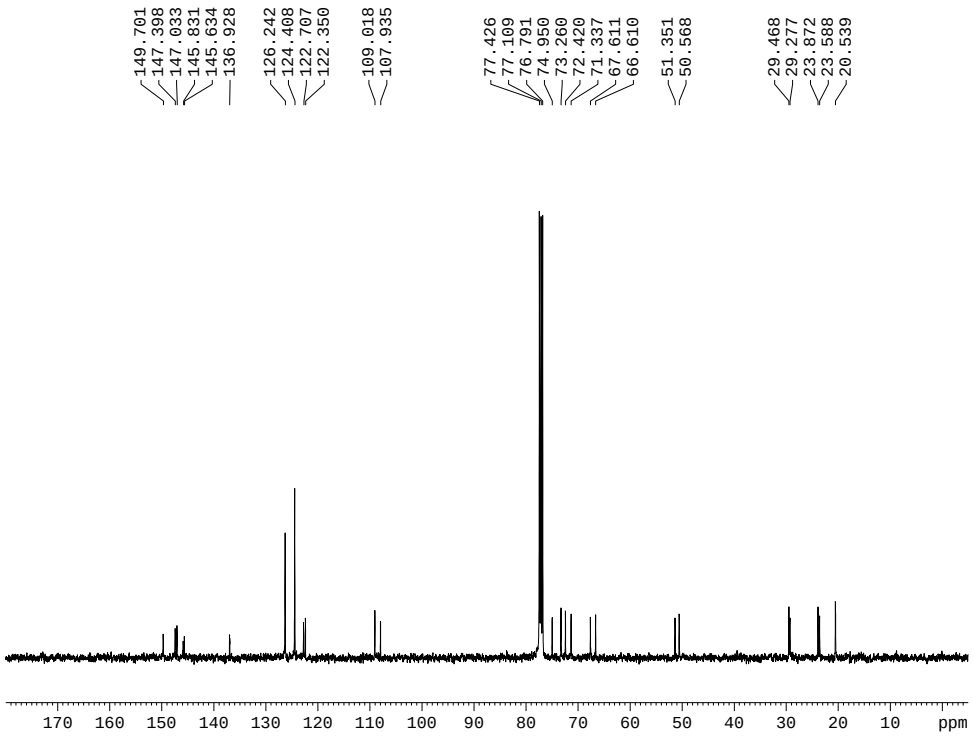

Figure S108. ^{13}C NMR spectrum of compound **35**

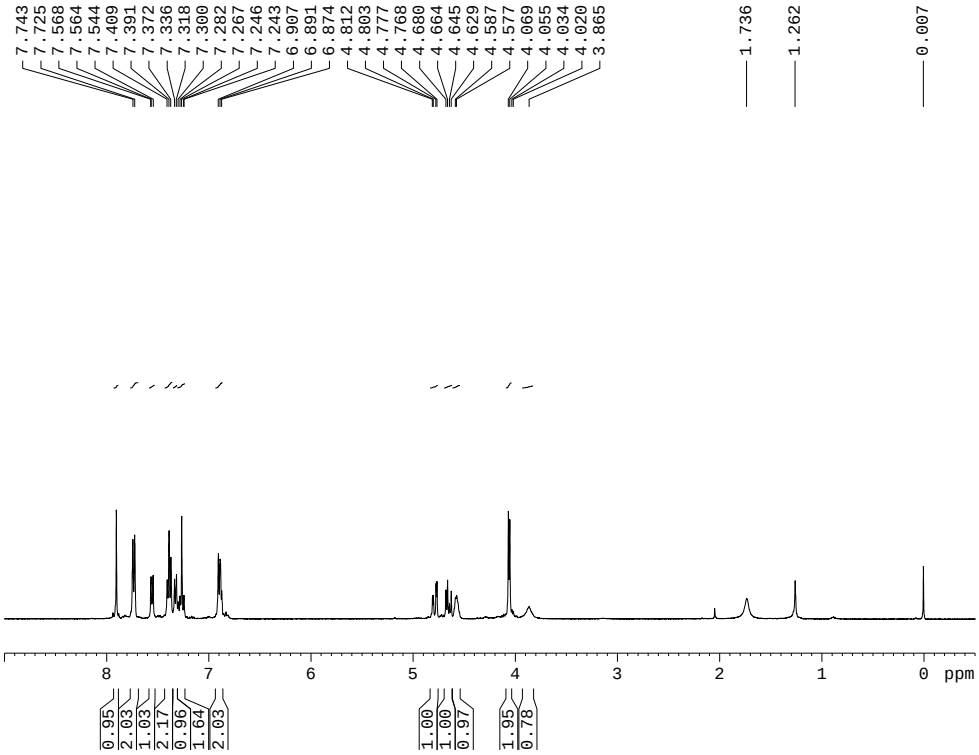

Figure S109. ^{1}H NMR spectrum of compound **36**

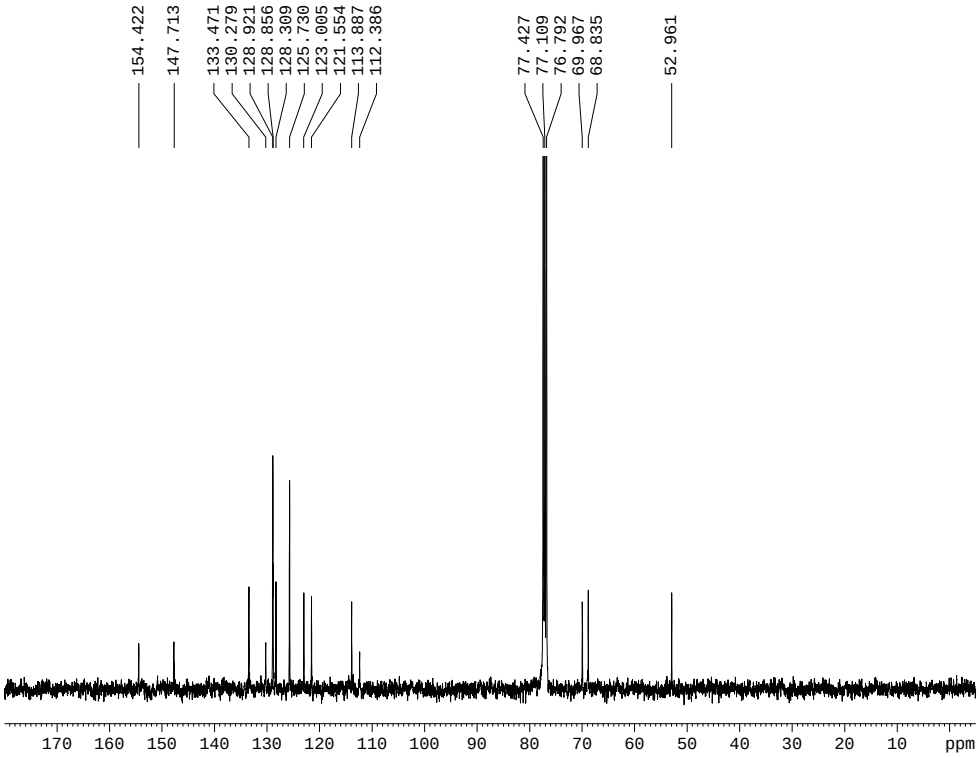

Figure S110. ^{13}C NMR spectrum of compound **36**

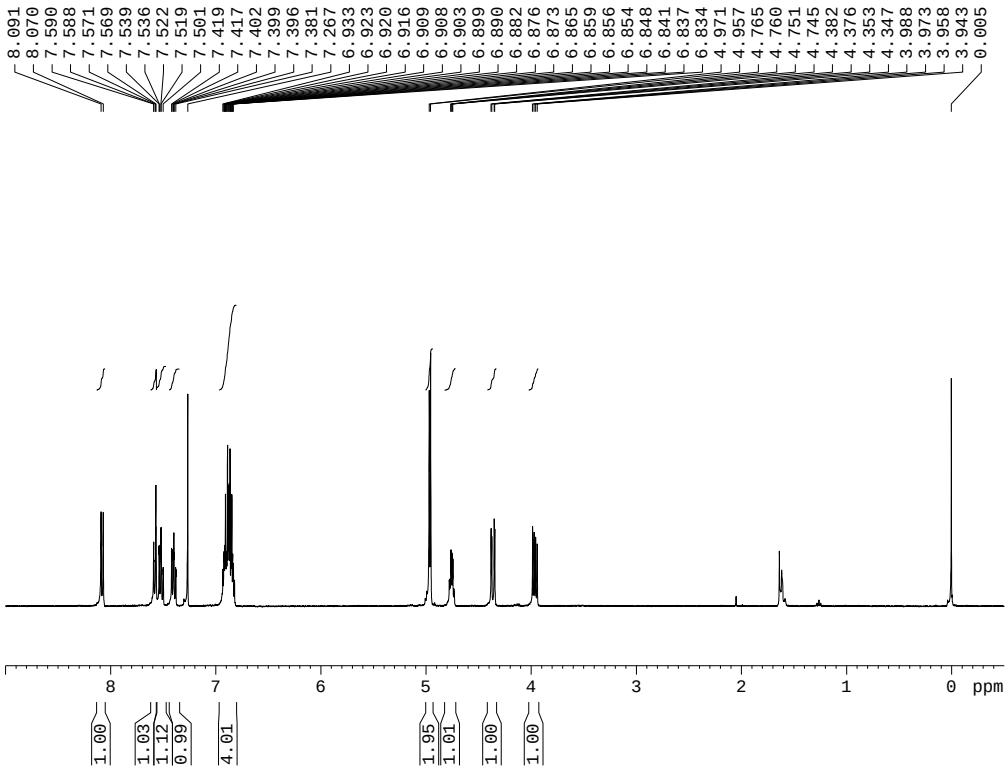

Figure S111. ^{1}H NMR spectrum of compound **37**

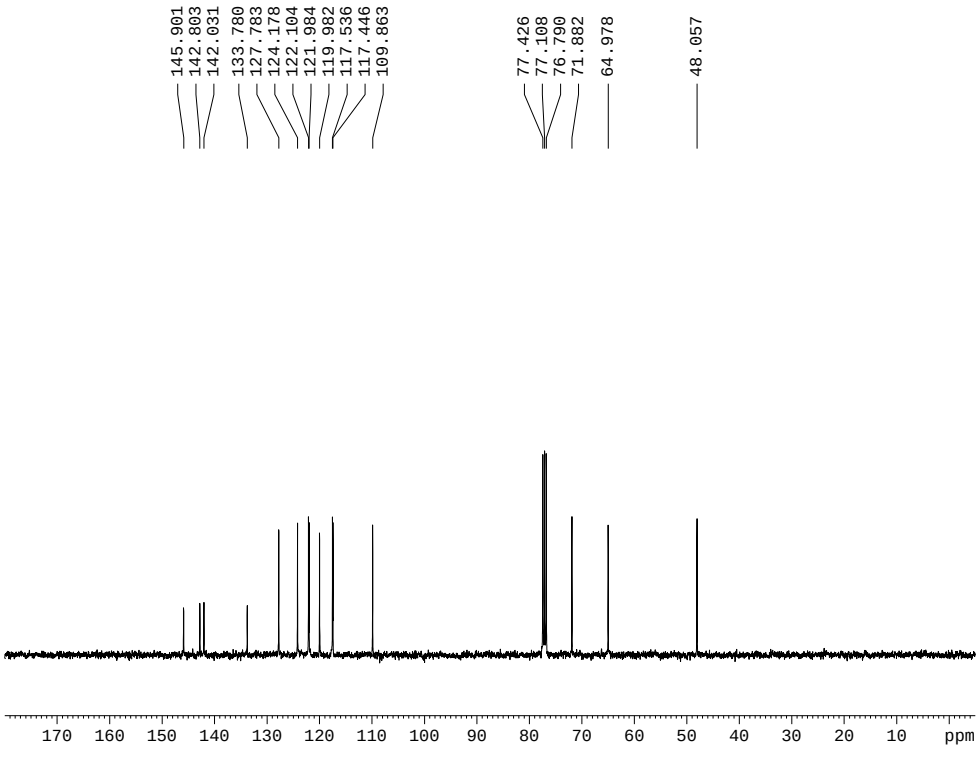

Figure S112. ^{13}C NMR spectrum of compound **37**

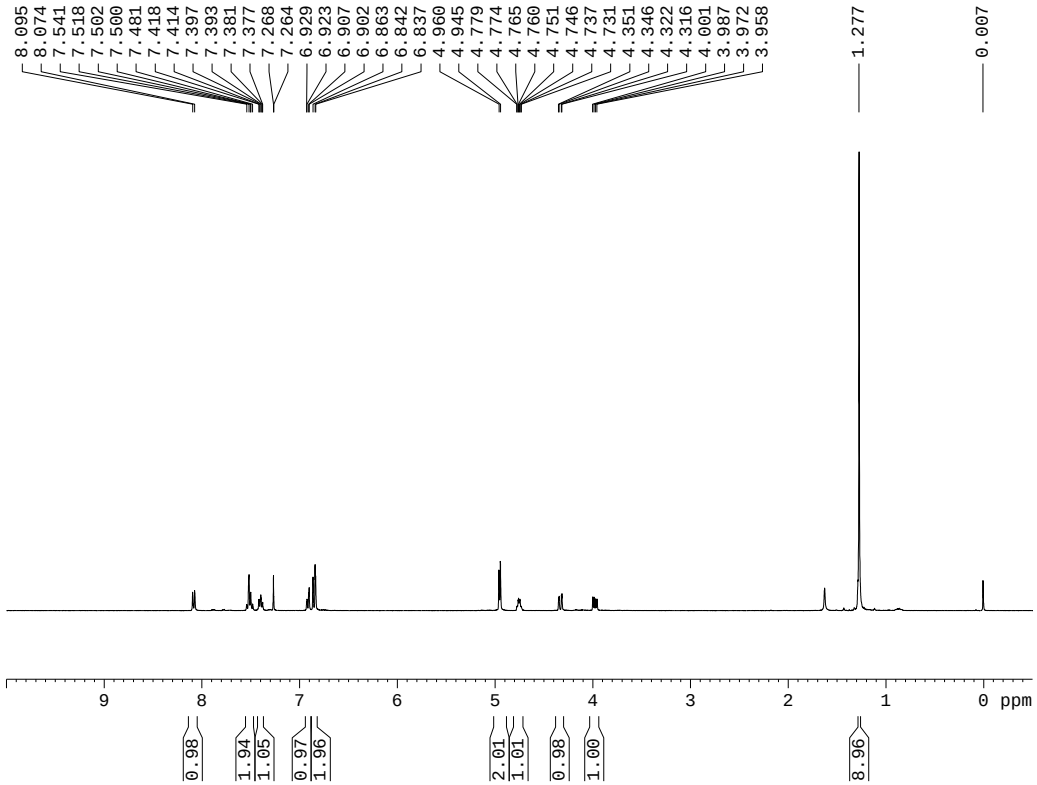

Figure S113. ^{1}H NMR spectrum of compound **38**

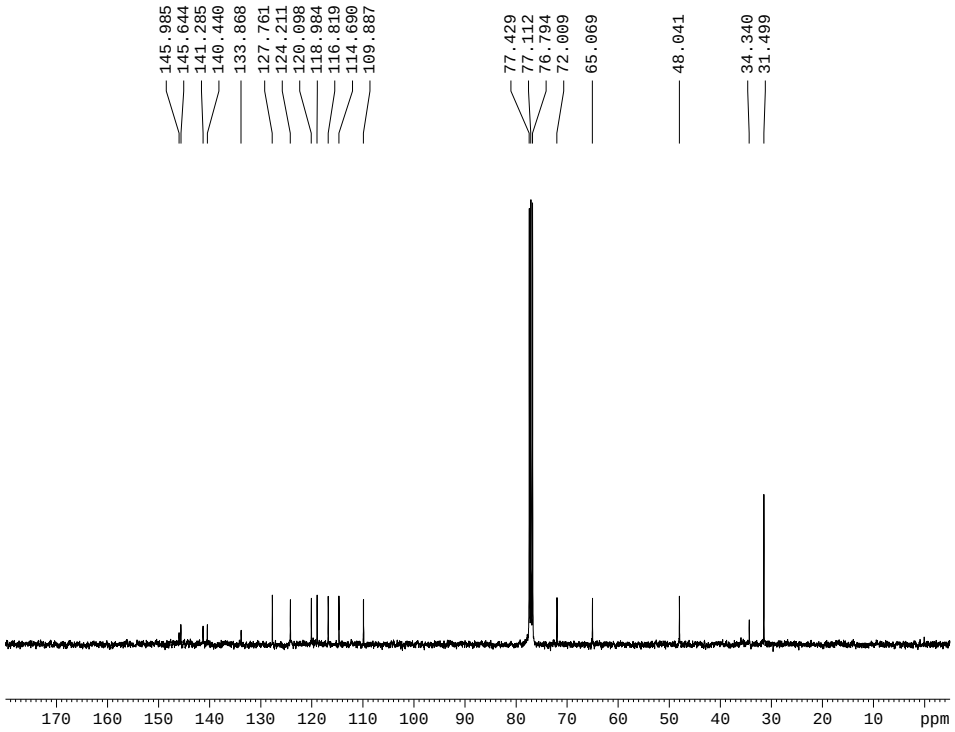

Figure S114. ^{13}C NMR spectrum of compound **38**

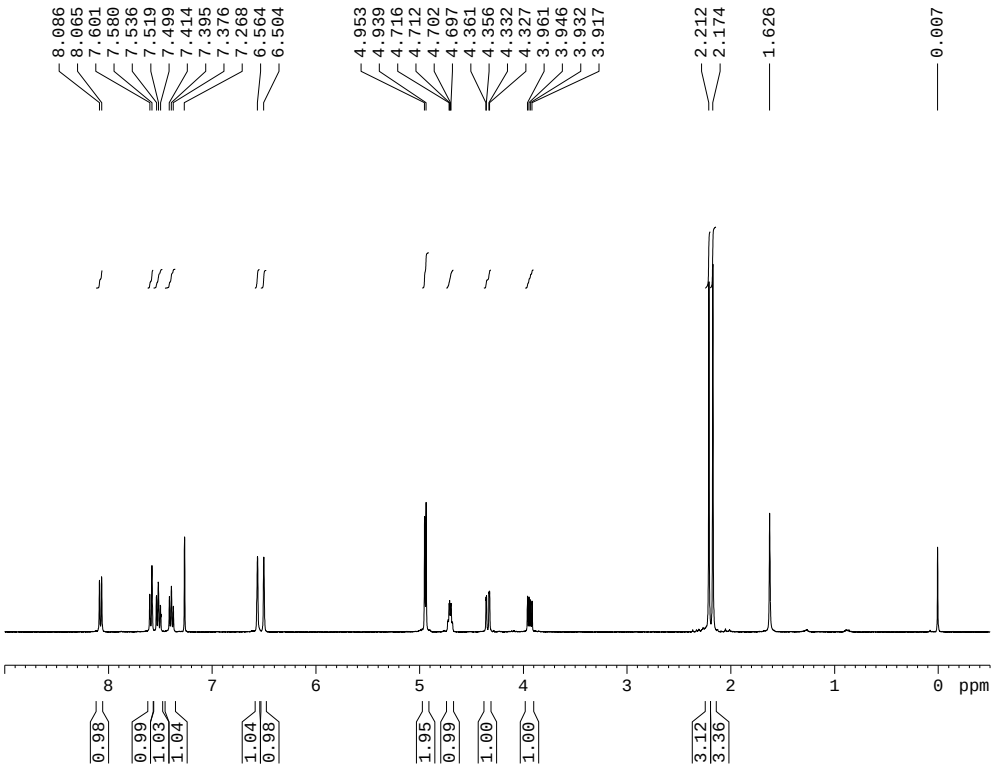

Figure S115. ^{1}H NMR spectrum of compound **39**

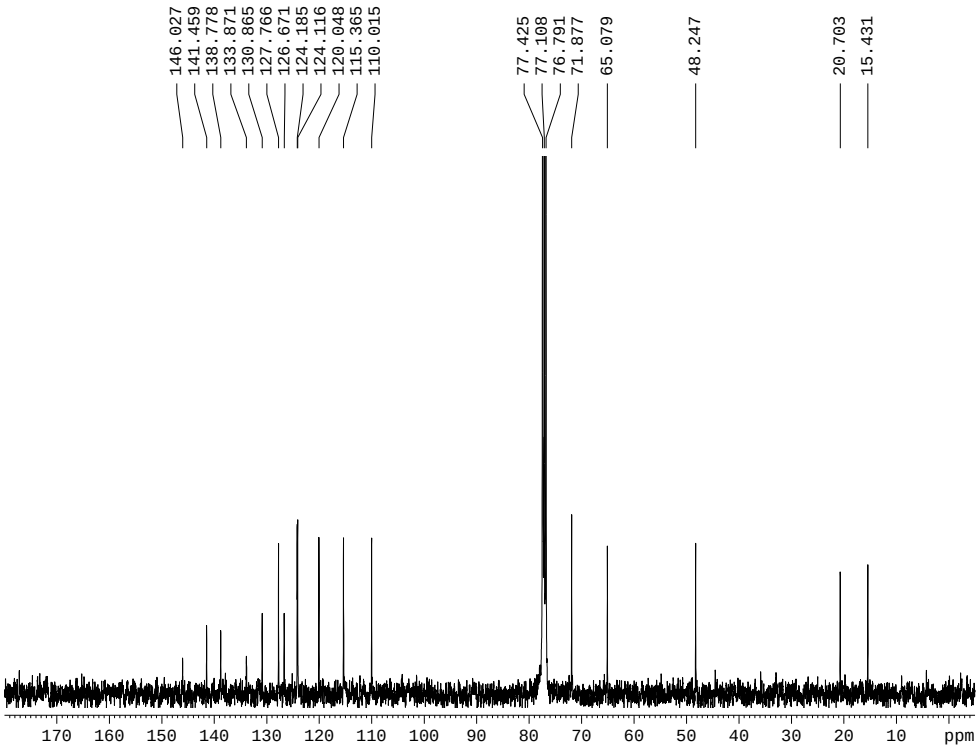

Figure S116. ^{13}C NMR spectrum of compound **39**

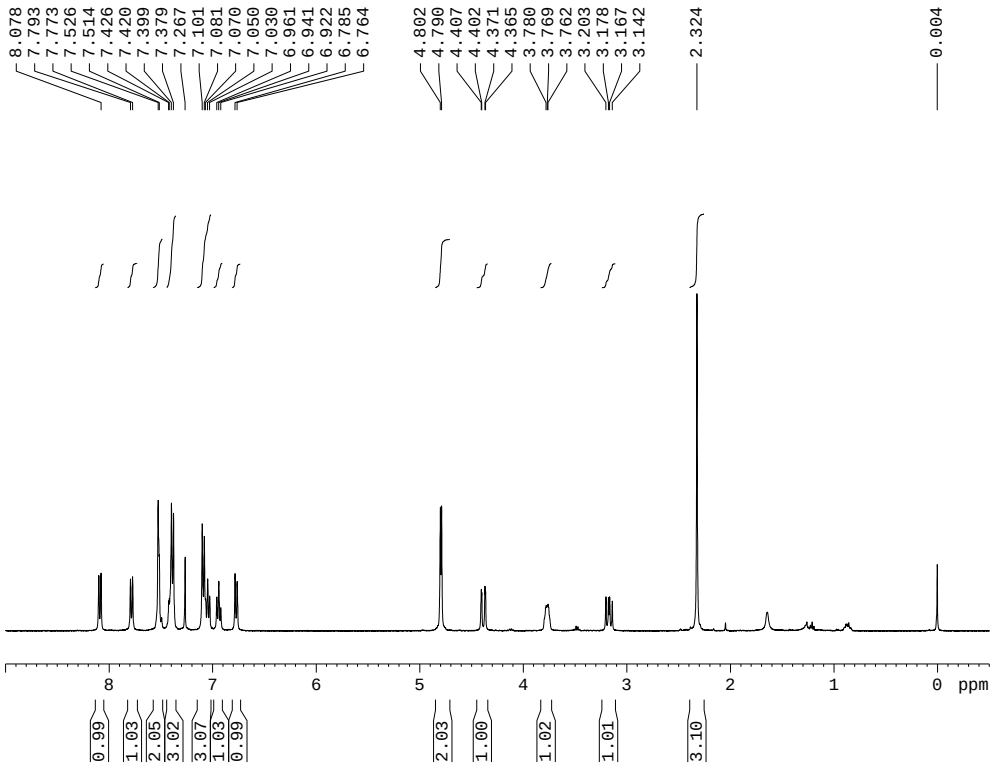

Figure S117. ^{1}H NMR spectrum of compound **40**

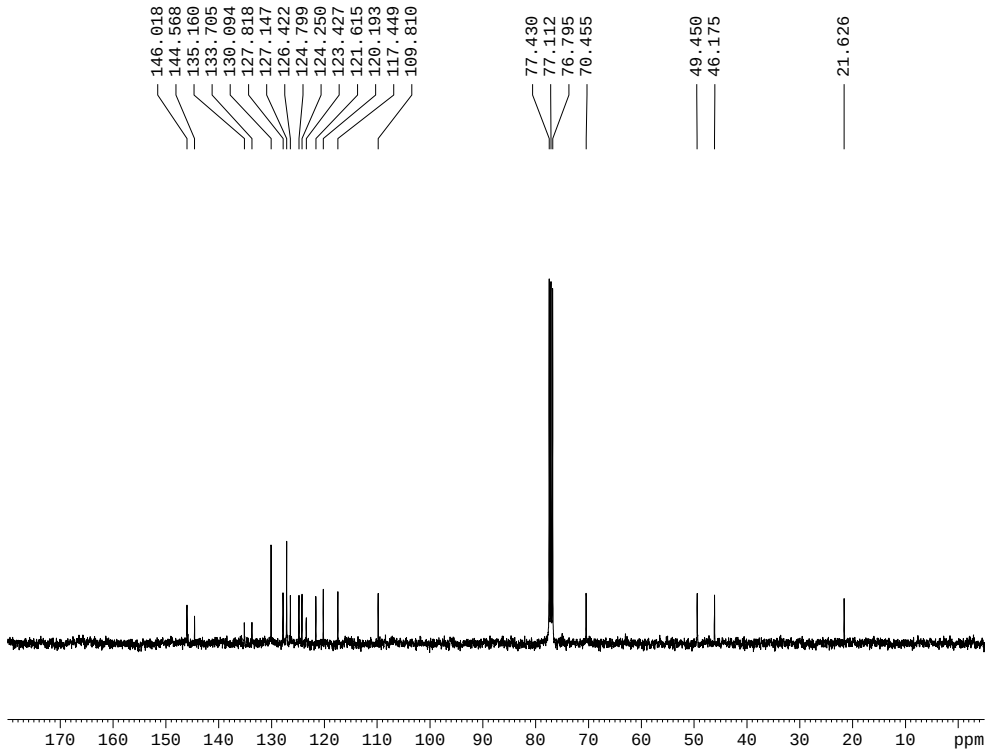

Figure S118. ^{13}C NMR spectrum of compound **40**

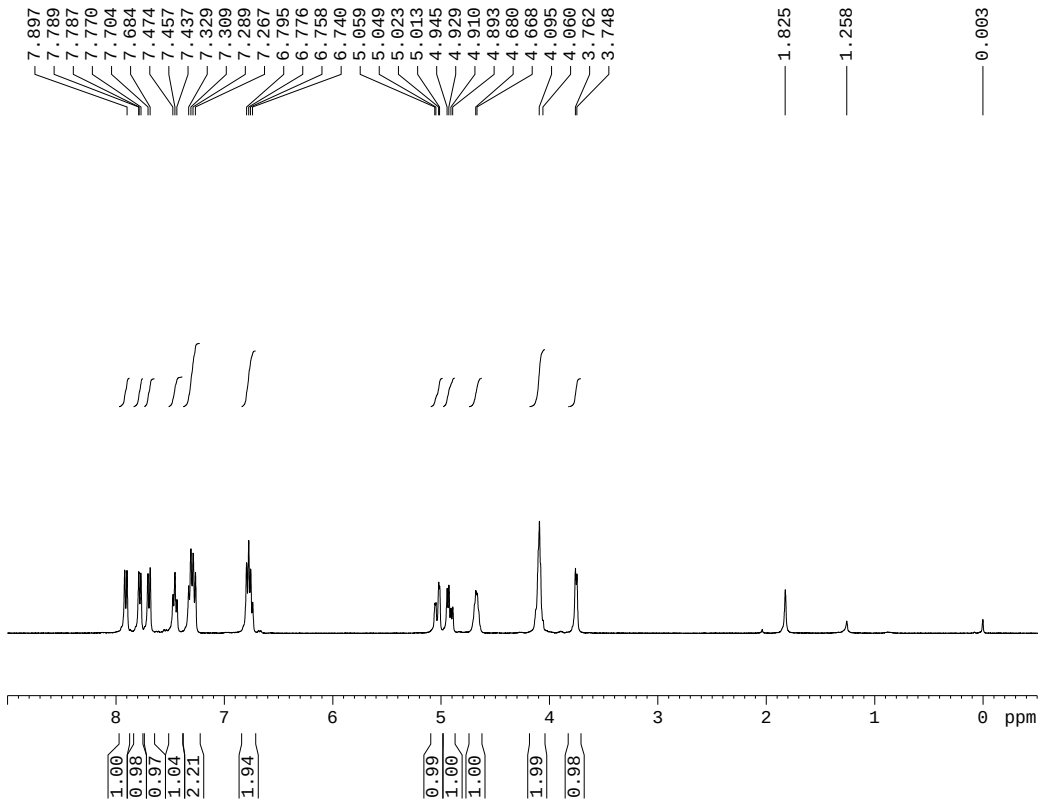

Figure S119. ^{1}H NMR spectrum of compound **41**

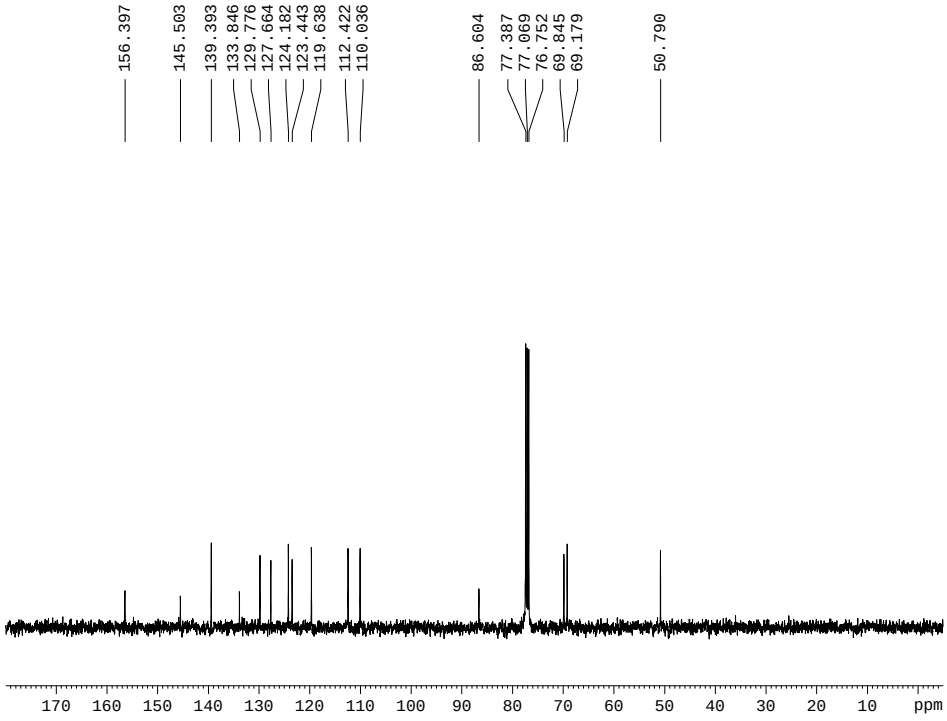

Figure S120. ^{13}C NMR spectrum of compound **41**