Supplementary data

Discovery of new benzothiazole-1,2,3-triazole hybrids-based hydrazone/thiosemicarbazone derivatives as potent EGFR inhibitors with cytotoxicity against breast cancer

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I. General methods:

The solvents and reagents used in this study were of the highest quality of analytical reagent grade and were used without undergoing any purification. The fine chemicals and solvents were acquired from BDH Chemicals Ltd. and Sigma-Aldrich. The melting temperatures were uncorrected and were determined with a Stuart Scientific SMP1. UV fluorescent Silica gel Merck 60 F254 plates were employed for thin layer chromatography (TLC) to monitor the reactions. A UV lamp (254 nm) was used to visualize the resulting spots. Fourier transform infrared spectroscopy (FT-IR) was conducted on FT-IR spectrometer type Perkin-Elmer 1430 series. The ^{1}H and ^{13}C nuclear magnetic resonance spectroscopy were gathered on a Bruker spectrometer (400 MHz) using the TMS as an internal reference. A GmbH-Vario EL III Elemental Analyzer was employed to conduct elemental analyses.

II. Characterization of the newly designed compounds:

II.1. Characterization of 1,2,3-triazoles 5a-c:

Characterization of N-(benzo[d]thiazol-2-yl)-2-(4-((4-formylphenoxy)methyl)-1H-1,2,3-triazol-1-yl)acetamide (5a)

IR (υ, cm^{-1}): 3240 (N-H), 3090 (C-H ar), 1720 (C=O), 1640 (C=N), 1560 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 12.81 (1H, s, N**H**), 9.86 (1H, s, C**H**O), 8.36 (1H, s, 1,2,3-triazole **H-5**), 7.99 (2H, d, *J* = 8 Hz, Ar-**H**), 7.90 (2H, d, *J* = 8 Hz, Ar-**H**), 7.78 (1H, d, *J* = 4 Hz, Ar-**H**), 7.46 (1H, d, *J* = 4 Hz, Ar-**H**), 7.33-7.28 (2H, m, Ar-**H**), 5.58 (2H, s, NC$\mathbf{H}_2$CO), 5.33 (2H, s, OC$\mathbf{H}_2$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 192.5 (H**C**=O); 162.9, 161.5, 152.6, 142.4, 139.5, 136.7, 132.4, 132.2, 131.7, 130.8, 125.9, 122.5, 121.9, 115.8 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 62.3 (O**C**H_2); 52.8 (N**C**H_2) ppm.

Characterization of 2-(4-((4-formylphenoxy)methyl)-1H-1,2,3-triazol-1-yl)-N-(6-(methylsulfonyl)benzo[d]thiazol-2-yl)acetamide (5b)

IR (υ, cm^{-1}): 3290 (N-H), 3060 (C-H ar), 1715 (C=O), 1630 (C=N), 1550 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 12.86 (1H, s, N**H**), 9.88 (s, 1H, C**H**O), 8.36 (s, 1H, 1,2,3-triazole **H-5**), 7.90 (d, 2H, *J* = 8 Hz, Ar-**H**), 7.77 (s, 1H, Ar-**H**), 7.65 (d, 1H, Ar-**H**), 7.27 (d, 3H, *J* = 4 Hz, Ar-**H**), 5.56 (s, 2H, NC$\mathbf{H}_2$CO), 5.32 (s, 2H, OC$\mathbf{H}_2$), 2.40 (s, 3H, C$\mathbf{H}_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 191.9 (H**C**=O); 163.4, 142.5, 133.8, 132.2, 130.3, 128.1, 127.2, 121.8, 120.8, 115.6 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.7 (O**C**H_2); 52.1 (N**C**H_2); 21.4 (**C**H_3) ppm.

Characterization of 2-(4-((4-formylphenoxy)methyl)-1H-1,2,3-triazol-1-yl)-N-(6-(methylsulfonyl)benzo[d]thiazol-2-yl)acetamide (5c)

IR (υ, cm^{-1}): 3220 (N-H), 3050 (C-H ar), 1725 (C=O), 1630 (C=N), 1570 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 12.80 (1H, br, N**H**), 9.88 (s, 1H, C**H**O), 8.66 (s, 1H, Ar-**H**), 8.37 (s, 1H, 1,2,3-triazole **H-5**), 7.97 (s, 2H, Ar-**H**), 7.90 (d, 2H, *J* = 8 Hz, Ar-**H**), 7.28 (d, 2H, *J* = 8 Hz, Ar-**H**), 5.62 (s, 2H, NC$\mathbf{H}_2$CO), 5.33 (s, 2H, OC$\mathbf{H}_2$), 3.25 (s, 3H, C$\mathbf{H}_3$). ^{13}C NMR (100

MHz, DMSO-d_6): δ_C = 191.9 (H**C**=O); 166.9, 163.4, 162.1, 152.3, 142.5, 136.0, 132.4, 132.3, 132.2, 130.3, 125.5, 122.8, 121.4, 115.6 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.7 (O**C**H_2); 52.2 (N**C**H_2); 44.3 (**C**H_3) ppm.

II.2. Characterization of Schiff bases 7a-d:

Characterization of (Z)-N'-(4-(prop-2-yn-1-yloxy)benzylidene)benzohydrazide (7a)

IR (υ, cm^{-1}): 3200-3310 (N-H, ≡CH), 3035 (C-H ar), 2150 (C≡C), 1700 (C=O), 1610 (C=N), 1540 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 11.75 (0.90H, s, N**H**), 11.75 (0.90H, s, N**H**), 8.41 (0.90H, s, **H**C=N), 8.06 (0.10H, bs, **H**C=N), 7.92 (1.80H, d, *J* = 8 Hz, Ar-**H**), 7.81 (0.20H, d, *J* = 8 Hz, Ar-**H**), 7.70 (1.80H, d, *J* = 8 Hz, Ar-**H**), 7.58-7.50 (3.20H, m, Ar-**H**), 7.08 (2H, d, *J* = 8 Hz, Ar-**H**), 4.86 (2H, s, OC**H**$_2$), 3.61 (1H, s, ≡C**H**). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 163.4, 159.2, 148.0, 134.0, 132.1, 129.0, 128.9, 128.0, 115.6 (Ar-**C**, **C**=N, **C**=O); 79.4, 78.9 (**C**≡**C**H); 56.0 (O**C**H_2) ppm. Calculated for $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07; N, 10.07. Found: C, 73.56; H, 5.13; N, 10.21.

Characterization of (Z)-N'-(4-(prop-2-yn-1-yloxy)benzylidene)isonicotino-hydrazide (7b)

IR (υ, cm^{-1}): 3230-3340 (N-H, ≡CH), 3055 (C-H ar), 2160 (C≡C), 1690 (C=O), 1620 (C=N), 1560 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 11.95 (0.87H, s, N**H**), 11.91 (0.13H, s, N**H**), 8.78 (1.74H, d, *J* = 4 Hz, Ar-**H**), 8.73 (0.26H, s, Ar-**H**), 8.41 (0.87H, s, **H**C=N), 8.04 (0.13H, s, **H**C=N), 7.81 (1.74H, d, *J* = 4 Hz, Ar-**H**), 7.72 (1.74H, d, *J* = 8 Hz, Ar-**H**), 7.66 (0.26H, d, *J* = 4 Hz, Ar-**H**), 7.48 (0.25H, d, *J* = 8 Hz, Ar-**H**), 7.09 (1.76H, d, *J* = 8 Hz, Ar-**H**), 7.01 (0.25H, d, *J* = 8 Hz, Ar-**H**), 4.87 (1.75H, s, OC**H**$_2$), 4.82 (0.25H, s, OC**H**$_2$), 3.61 and 3.58 (1H, 2s, ≡C**H**). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 161.9, 159.4, 150.7, 149.2, 141.0, 129.3, 127.7, 121.9, 115.7 (Ar-**C**, **C**=N, **C**=O); 79.4, 79.0 (**C**≡**C**H); 56.0 (O**C**H_2) ppm. Calculated for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.65; H, 4.61; N, 15.17

Characterization of (Z)-1-(2,4-dinitrophenyl)-2-(4-(prop-2-yn-1-yloxy)benzylidene)hydrazine (7c)

IR (υ, cm^{-1}): 3240-3320 (N-H, ≡CH), 3075 (C-H ar), 2140 (C≡C), 1625 (C=N), 1550 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 11.59 (1H, s, N**H**), 8.85 (1H, d, *J* = 4 Hz, Ar-**H**), 8.63 (1H, s, **H**C=N), 8.33 (1H, d, *J* = 8 Hz, Ar-**H**), 8.06 (1H, d, *J* = 8 Hz, Ar-**H**), 7.76 (2H, d, *J* = 8 Hz, Ar-**H**), 7.10 (2H, d, *J* = 8 Hz, Ar-**H**), 4.87 (2H, s, OC**H**$_2$), 3.61 (1H, s, ≡C**H**). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 159.6, 149.7, 144.9, 137.2, 129.6, 127.5, 123.5, 117.1, 115.8 (Ar-**C**, **C**=N); 79.3, 79.0 (**C**≡**C**H); 56.0 (O**C**H_2) ppm. Calculated for $C_{16}H_{12}N_4O_5$: C, 56.47; H, 3.55; N, 16.46. Found: C, 56.59; H, 3.59; N, 16.53.

Characterization of (Z)-2-(4-(prop-2-yn-1-yloxy)benzylidene)hydrazine-1-carbothioamide (7d)

IR (υ, cm^{-1}): 3260-3350 (N-H, ≡CH), 3065 (C-H ar), 2150 (C≡C), 1620 (C=N), 1570 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 11.33 (1H, s, N**H**), 8.11 (1H, s, **H**C=N), 7.99 (1H, s, N**H**), 7.92 (1H, s, N**H**), 7.75 (2H, d, *J* = 8 Hz, Ar-**H**), 7.01 (2H, d, *J* = 8 Hz, Ar-**H**), 4.83 (2H, s,

OC**H**$_2$), 3.56 (1H, s, ≡C**H**). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 178.1 (**C**=S); 159.0, 142.5, 129.2, 127.9, 115.4 (Ar-**C**, **C**=N); 79.4, 78.9 (**C**≡**C**H); 56.0 (O**C**H$_2$) ppm. Calculated for $C_{11}H_{11}N_3OS$: C, 56.63; H, 4.75; N, 18.01. Found: C, 56.45; H, 4.83; N, 18.14.

II.3 Characterization of 1,2,3-triazole-benzothiazole molecular conjugates 8a-l:

Characterization of (E)-N-(benzo[d]thiazol-2-yl)-2-(4-((4-((2-benzoylhydrazono)-methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)acetamide (8a)

IR (υ, cm^{-1}): 3290 (N-H), 3050 (C-H ar), 1700 (C=O), 1615 (C=N), 1565 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 11.76 (0.80H, s, N**H**), 9.88 (0.20H, s, N**H**), 8.42 (1H, s, **H**C=N), 8.35 (1H, s, 1,2,3-triazole **H-5**), 7.91-7.69 (4H, m, Ar-**H**), 7.57-7.52 (4H, m, Ar-**H**), 7.28-7.16 (6H, m, Ar-**H**), 5.58 (2H, s, NC**H**$_2$CO), 5.26 (2H, s, OC**H**$_2$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 168.1, 166.3, 163.4, 160.0 (2 x **C**=O); 148.7, 148.3, 143.0, 129.1, 128.1, 126.7, 123.3, 121.2, 115.6 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.6 (O**C**H$_2$); 53.0, 52.2 (N**C**H$_2$) ppm. Calculated for$C_{26}H_{21}N_7O_3S$: C, 61.05; H, 4.14; N, 19.17. Found: C, 61.26; H, 4.19; N, 19.05.

Characterization of (E)-2-(4-((4-((2-benzoylhydrazono)methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)-N-(6-methylbenzo[d]thiazol-2-yl)acetamide (8b)

IR (υ, cm^{-1}): 3310 (N-H), 3075 (C-H ar), 1710 (C=O), 1620 (C=N), 1570 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 11.75 (0.80H, s, N**H**), 11.61 (0.20H, s, N**H**), 8.43 (1H, s, **H**C=N), 8.33 (1H, s, 1,2,3-triazole **H-5**), 7.91 (2H, d, J = 4 Hz, Ar-**H**), 7.78-7.52 (7H, m, Ar-**H**), 7.26-7.15 (3H, m, Ar-**H**), 5.55 (2H, s, NC**H**$_2$CO), 5.32 (0.20H, s, OC**H**$_2$), 5.25 (1.80H, s, OC**H**$_2$), 2.40 (3H, s, C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 166.4, 159.8 (2 x **C**=O); 147.8, 145.0, 142.4, 133.6, 131.9, 129.1, 128.9, 115.7 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.4 (O**C**H$_2$); 53.3, 52.3 (N**C**H$_2$); 29.3 (**C**H$_3$) ppm. Calculated for $C_{27}H_{23}N_7O_3S$: C, 61.70; H, 4.41; N, 18.66. Found: C, 61.86; H, 4.47; N, 18.78.

Characterization of (E)-2-(4-((4-((2-benzoylhydrazono)methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)-N-(6-(methylsulfonyl)benzo[d]thiazol-2-yl)acetamide (8c)

IR (υ, cm^{-1}): 3330 (N-H), 3040 (C-H ar), 1695 (C=O), 1625 (C=N), 1555 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 11.75 (0.80H, s, N**H**), 9.88 (0.20H, s, N**H**), 8.66 (1H, s, Ar-**H**), 8.42 (1H, bs, **H**C=N), 8.35 (1H, bs, 1,2,3-triazole **H-5**), 7.95-7.89 (3H, m, Ar-**H**), 7.69 (2H, bs, Ar-**H**), 7.58-7.52 (3H, m, Ar-**H**), 7.27-7.16 (3H, m, Ar-**H**), 5.60 (2H, s, NC**H**$_2$CO), 5.33 (0.40H, s, OC**H**$_2$), 5.26 (1.60H, s, OC**H**$_2$), 3.23 (3H, s, C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 160.8, 160.3 (2 x **C**=O); 152.2, 149.2, 142.7, 136.2, 132.2, 129.3, 127.1, 122.8, 121.8, 115.6 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.6 (O**C**H$_2$); 53.2 (N**C**H$_2$); 44.8 (**C**H$_3$) ppm. Calculated for $C_{27}H_{23}N_7O_5S_2$: C, 55.00; H, 3.93; N, 16.63. Found: C, 55.26; H, 3.86; N, 16.53.

Characterization of (E)-N-(benzo[d]thiazol-2-yl)-2-(4-((4-((2-isonicotinoylhydrazono)methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)acetamide **(8d)**

IR (υ, cm^{-1}): 3300 (N-H), 3035 (C-H ar), 1695 (C=O), 1610 (C=N), 1585 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 12.91 (1H, s, CH$_2$CON**H**), 11.97 (0.90H, s, N**H**), 11.93 (0.10H, s, N**H**), 9.88 (0.10H, s, N**H**), 8.43 (1H, s, **H**C=N), 8.35 (1H, m, 1,2,3-triazole **H-5**), 7.99-7.88 (3H, m, Ar-**H**), 7.79-7.72 (4H, m, Ar-**H**), 7.48-7.33 (2H, m, Ar-**H**), 7.19-7.10 (3H, m, Ar-**H**), 5.62 (2H,

s, NC**H**$_2$CO), 5.34 (0.25H, s, OC**H**$_2$), 5.27 (1.75H, s, OC**H**$_2$), 3.24 (3H, s, C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 162.0, 160.3 (2 x **C**=O); 150.5, 149.3, 142.8, 129.4, 128.9, 127.3, 127.0, 126.7, 124.2, 122.3, 121.0, 115.6 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.6 (O**C**H$_2$); 52.3 (N**C**H$_2$) ppm. Calculated for $C_{25}H_{20}N_8O_3S$: C, 58.58; H, 3.93; N, 21.86. Found: C, 58.75; H, 3.99; N, 21.96

Characterization of (E)-2-(4-((4-((2-isonicotinoylhydrazono)methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)-N-(6-methylbenzo[d]thiazol-2-yl)acetamide (8e)

IR (υ, cm^{-1}): 3325 (N-H), 3020 (C-H ar), 1700 (C=O), 1610 (C=N), 1555 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 12.86 (1H, s, CH$_2$CON**H**), 12.03 (0.80H, s, N**H**), 11.95 (0.10H, s, N**H**), 9.90 (0.10H, s, N**H**), 8.48 (1H, bs, **H**C=N), 8.35 (1H, m, 1,2,3-triazole **H-5**), 7.89-7.66 (5H, m, Ar-**H**), 7.49-7.10 (6H, m, Ar-**H**), 5.57 (2H, s, NC**H**$_2$CO), 5.33 (0.25H, s, OC**H**$_2$), 5.27 (1.75H, s, OC**H**$_2$), 2.41 (3H, s, C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 166.7, 163.0, 159.9 (2 x **C**=O); 147.6, 145.6, 142.6, 133.9, 131.8, 128.6, 125.6, 121.1, 115.7 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.4 (O**C**H$_2$); 53.2, 52.7 (N**C**H$_2$); 29.5 (**C**H$_3$) ppm. Calculated for $C_{26}H_{22}N_8O_3S$: C, 59.31; H, 4.21; N, 21.28. Found: C, 59.55; H, 4.29; N, 21.17.

Characterization of (E)-2-(4-((4-((2-isonicotinoylhydrazono)methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)-N-(6-(methylsulfonyl)benzo[d]thiazol-2-yl)acetamide (8f)

IR (υ, cm^{-1}): 3350 (N-H), 3055 (C-H ar), 1690 (C=O), 1620 (C=N), 1570 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 13.22 (1H, s, CH$_2$CON**H**), 11.98 (0.80H, s, N**H**), 11.91 (0.10H, s, N**H**), 9.88 (0.10H, s, N**H**), 8.67 (1H, s, Ar-**H**), 8.44 (0.70H, bs, **H**C=N), 8.32-8.36 (1.30H, m, **H**C=N and 1,2,3-triazole **H-5**), 7.99-7.88 (5H, m, Ar-**H**), 7.72 (2H, d, J = 4 Hz, Ar-**H**), 7.49 (0.30H, d, J = 8 Hz, Ar-**H**), 7.28-7.16 (2.70H, m, Ar-**H**), 5.62 (2H, s, NC**H**$_2$CO), 5.34 (0.25H, s, OC**H**$_2$), 5.27 (1.75H, s, OC**H**$_2$), 3.24 (3H, s, C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 166.9, 162.0, 160.3 (2 x **C**=O); 152.3, 149.3, 142.9, 136.2, 132.2, 127.3, 125.4, 121.5, 115.6 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.6 (O**C**H$_2$); 52.2 (N**C**H$_2$); 44.8 (**C**H$_3$) ppm. Calculated for $C_{26}H_{22}N_8O_5S_2$: C, 52.87; H, 3.75; N, 18.97. Found: C, 52.71; H, 3.80; N, 18.86

Characterization of (Z)-N-(benzo[d]thiazol-2-yl)-2-(4-((4-((2-(2,4-dinitrophenyl)hydrazono)methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)acetamide (8g)

IR (υ, cm^{-1}): 3320 (N-H), 3055 (C-H ar), 1690 (C=O), 1620 (C=N), 1580 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 12.69 (1H, bs, CH$_2$CON**H**), 11.62 (1H, s, N**H**), 8.83 (1H, s, Ar-**H**), 8.63 (1H, s, **H**C=N), 8.31 (2H, s, 1,2,3-triazole **H-5** and Ar-**H**), 8.05 (2H, d, J = 4 Hz, Ar-**H**), 7.84-7.75 (3H, m, Ar-**H**), 7.79-7.72 (4H, m, Ar-**H**), 7.40 (1H, s, Ar-**H**), 7.19-7.15 (3H, m, Ar-**H**), 5.51 (2H, bs, NC**H**$_2$CO), 5.27 (2H, s, OC**H**$_2$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 165.4 (**C**=O); 149.8, 146.1, 145.2, 142.6, 136.9, 135.0, 130.0, 129.5, 127.1, 126.0, 123.5, 117.1, 115.7 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.7 (O**C**H$_2$); 52.9 (N**C**H$_2$) ppm. Calculated for $C_{25}H_{19}N_9O_6S$: C, 52.35; H, 3.34; N, 21.98. Found: C, 52.52; H, 3.39; N, 21.89

Characterization of (Z)-2-(4-((4-((2-(2,4-dinitrophenyl)hydrazono)methyl)phenoxy)-methyl)-1H-1,2,3-triazol-1-yl)-N-(6-methylbenzo[d]thiazol-2-yl) acetamide (8h)

IR (υ, cm^{-1}): 3340 (N-H), 3055 (C-H ar), 1700 (C=O), 1615 (C=N), 1565 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 12.82 (1H, s, CH$_2$CON**H**), 11.60 (1H, s, N**H**), 8.85 (1H, s, Ar-**H**), 8.64

(1H, s, **H**C=N), 8.34 (2H, s, 1,2,3-triazole **H-5** and Ar-**H**), 8.08 (1H, bd, *J* = 4 Hz, Ar-**H**), 7.76-7.66 (3H, m, Ar-**H**), 7.26-7.10 (4H, m, Ar-**H**), 5.56 (2H, s, NC**H**$_2$CO), 5.28 (2H, s, OC**H**$_2$), 2.40 (3H, s, C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 160.5 (**C**=O); 149.8, 144.9, 137.2, 133.8, 130.1, 129.5, 128.0, 126.9, 123.5, 121.8, 117.1, 115.7 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.6 (O**C**H$_2$); 52.1 (N**C**H$_2$); 21.4 (**C**H$_3$) ppm. Calculated for C26H21N9O6S: C, 53.15; H, 3.60; N, 21.45. Found: C, 53.39; H, 3.52; N, 21.57.

Characterization of (Z)-2-(4-((4-((2-(2,4-dinitrophenyl)hydrazono)methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)-N-(6-(methylsulfonyl)benzo[d]thiazol-2-yl)acetamide (8i)

IR (υ, cm^{-1}): 3315 (N-H), 3080 (C-H ar), 1705 (C=O), 1610 (C=N), 1560 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 12.76 (1H, bs, CH$_2$CON**H**), 11.55 (1H, s, N**H**), 8.85 (1H, s, Ar-**H**), 8.64 (2H, s, **H**C=N and Ar-**H**), 8.35 (2H, s, 1,2,3-triazole **H-5** and Ar-**H**), 8.08-8.76 (4H, m, Ar-**H**), 7.19-7.10 (3H, m, Ar-**H**), 5.61 (2H, s, NC**H**$_2$CO), 5.29 (2H, s, OC**H**$_2$), 3.62 (3H, s, C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 162.7 (**C**=O); 159.6, 149.7, 144.9, 142.8, 137.2, 136.0, 130.2, 129.6, 129.5, 127.5, 123.5, 117.2, 115.8 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.6 (O**C**H$_2$); 52.1 (N**C**H$_2$); 21.4 (**C**H$_3$) ppm. Calculated for $C_{26}H_{21}N_9O_8S_2$: C, 47.92; H, 3.25; N, 19.35. Found: C, 47.74; H, 3.17; N, 19.49.

Characterization of (Z)-N-(benzo[d]thiazol-2-yl)-2-(4-((4-((2-carbamothioylhydrazono)methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)acetamide (8j)

IR (υ, cm^{-1}): 3280 (N-H), 3050 (C-H ar), 1700 (C=O), 1625 (C=N), 1575 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 13.00 (1H, bs, CH$_2$CON**H**), 11.48 (1H, s, N**H**), 8.34 (1H, s, 1,2,3-triazole **H-5**), 8.25 (1H, s, **H**C=N), 8.04 (1H, s, N**H**), 7.98 (1H, d, *J* = 8 Hz, N**H**), 7.76 (3H, t, *J* = 4 Hz, Ar-**H**), 7.32-7.25 (3H, m, Ar-**H**), 7.10 (2H, d, *J* = 8 Hz, Ar-**H**), 5.61 (2H, s, NC**H**$_2$CO), 5.32 (0.20H, s, OC**H**$_2$), 5.23 (1.80H, s, OC**H**$_2$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 166.2 (**C**=S); 160.0 (**C**=O); 143.4, 142.8, 131.8, 129.5, 127.3, 126.9, 126.7, 124.3, 122.3, 121.1, 115.3 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.5 (O**C**H$_2$); 52.2 (N**C**H$_2$) ppm. Calculated for $C_{20}H_{18}N_8O_2S_2$: C, 51.49; H, 3.89; N, 24.02. Found: C, 51.70; H, 3.94; N, 24.17.

Characterization of (Z)-2-(4-((4-((2-carbamothioylhydrazono)methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)-N-(6-methylbenzo[d]thiazol-2-yl)acetamide (8k)

IR (υ, cm^{-1}): 3260 (N-H), 3040 (C-H ar), 1700 (C=O), 1605 (C=N), 1555 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H= 12.78 (1H, bs, CH$_2$CON**H**), 11.73 (0.70H, s, N**H**), 9.87 (0.30H, s, N**H**), 8.42-8.28 (3H, m, 1,2,3-triazole **H-5**, **H**C=N and Ar-**H**), 7.89 (1H, bd, *J* = 8 Hz, Ar-**H**), 7.80-7.65 (4H, m, N**H** and Ar-**H**), 7.26 (1H, bd, *J* = 4 Hz, Ar-**H**), 7.11-7.08 (2H, m, *J* = 4 Hz, Ar-**H**), 5.55 (2H, s, NC**H**$_2$CO), 5.32 (0.60H, s, OC**H**$_2$), 5.25 (1.40H, s, OC**H**$_2$), 3.38 (3H, s, C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 166.1 (**C**=S); 163.4, 160.3 (**C**=O); 146.7, 133.8, 132.3, 130.3, 129.8, 128.1, 126.9, 121.8, 120.8, 115.6, 115.4 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.8, 61.6 (O**C**H$_2$); 52.1 (N**C**H$_2$), 21.4 (**C**H$_3$) ppm. Calculated for $C_{21}H_{20}N_8O_2S_2$: C, 52.49; H, 4.20; N, 23.32. Found: C, 52.76; H, 4.27; N, 23.20.

Characterization of (Z)-2-(4-((4-((2-carbamothioylhydrazono)methyl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)-N-(6-(methylsulfonyl)benzo[d]thiazol-2-yl)acetamide (8l)

IR (υ, cm^{-1}): 3290 (N-H), 3075 (C-H ar), 1710 (C=O), 1615 (C=N), 1570 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H = 13.31 (1H, bs, $CH_2CON\mathbf{H}$), 11.51 (1H, s, N**H**), 9.89 (1H, s, N**H**), 8.62 (1H, s, Ar-**H**), 8.35-8.25 (2H, m, 1,2,3-triazole **H-5** and **H**C=N), 8.25 (1H, s, **H**C=N), 8.03 (1H, s, N**H**), 7.93-7.88 (3H, m, Ar-**H**), 7.77 (2H, bd, *J* = 4 Hz, Ar-**H**), 7.27 (1H, bd, *J* = 4 Hz, Ar-**H**), 7.11 (1H, bd, *J* = 4 Hz, Ar-**H**), 5.59 (2H, s, $NC\mathbf{H}_2CO$), 5.33 (0.60H, s, $OC\mathbf{H}_2$), 5.24 (1.40H, s, $OC\mathbf{H}_2$), 3.38 (3H, s, $C\mathbf{H}_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C = 167.5 (**C**=S); 163.4, 160.0 (**C**=O); 152.6, 143.4, 142.8, 135.7, 132.2, 130.3, 129.5, 127.3, 127.1, 126.9, 125.2, 122.5, 121.2, 115.6, 115.3 (Ar-**C**, 1,2,3-triazole **C-5**, **C**=N); 61.8, 61.6 ($O\mathbf{C}H_2$); 52.6 ($N\mathbf{C}H_2$), 44.5 ($\mathbf{C}H_3$) ppm. Calculated for $C_{21}H_{20}N_8O_4S_3$: C, 46.31; H, 3.70; N, 20.57. Found: C, 46.50; H, 3.65; N, 20.68.

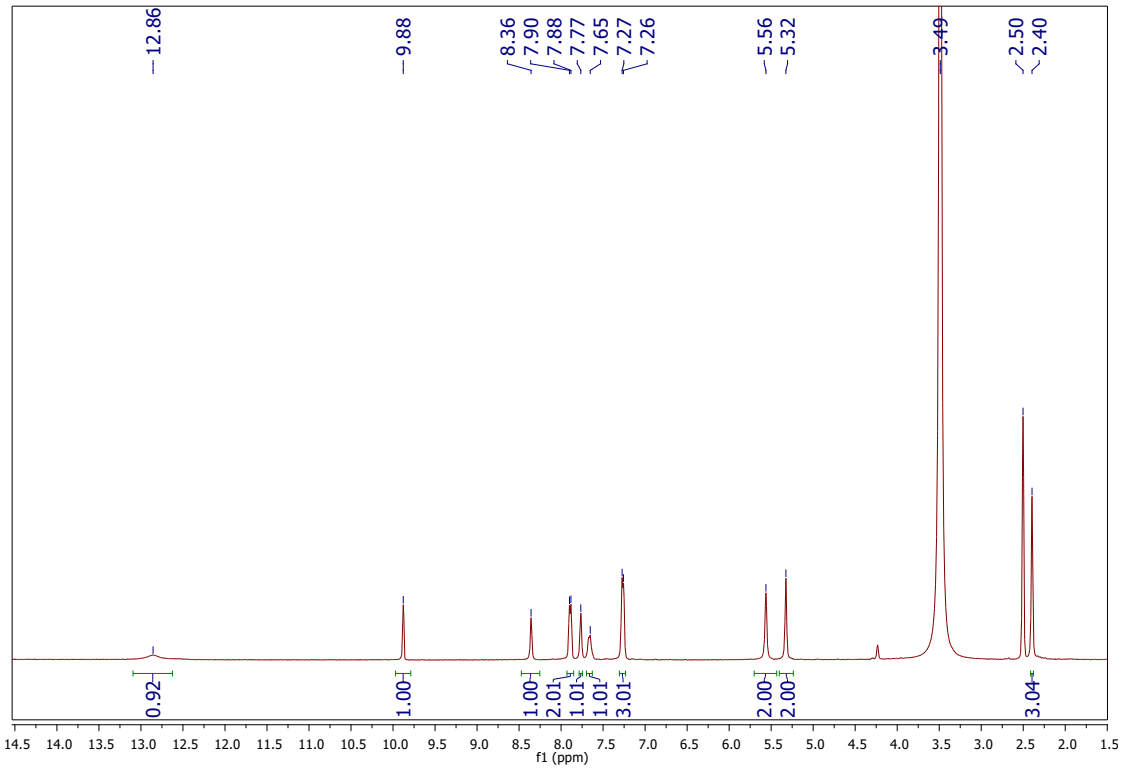

Figure S1: ^{1}H NMR spectrum of compound **5b**.

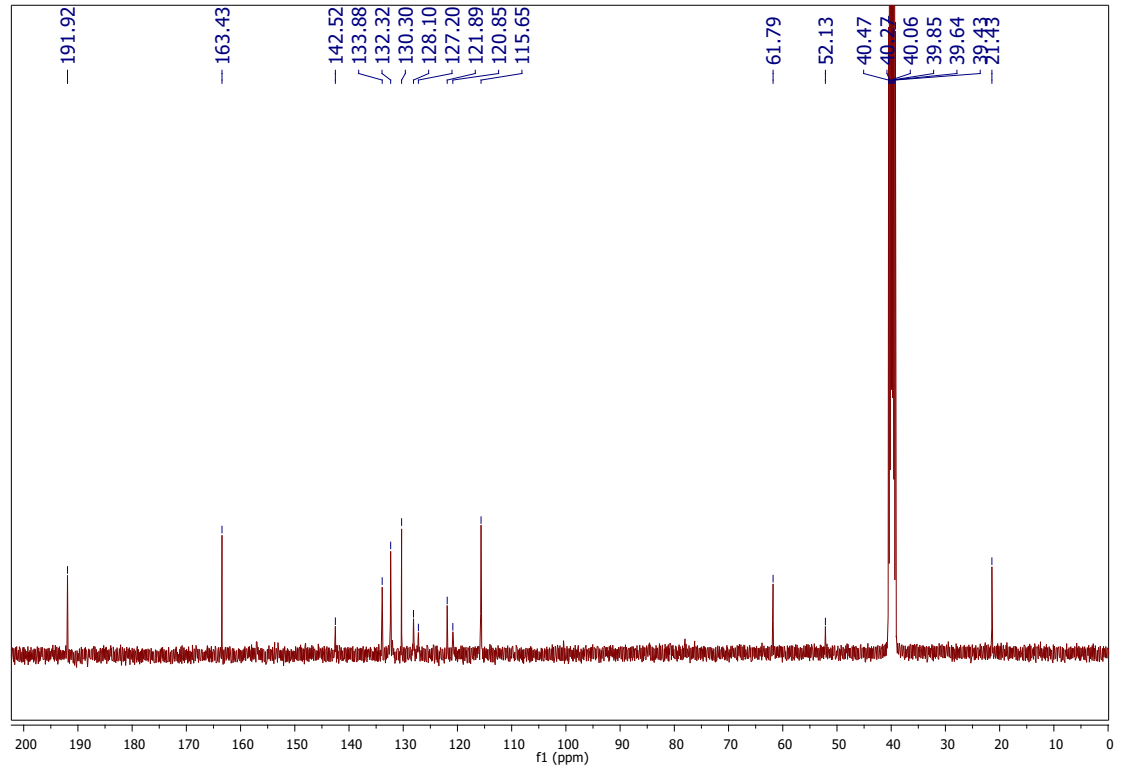

Figure S2: ^{13}C NMR spectrum of compound **5b**.

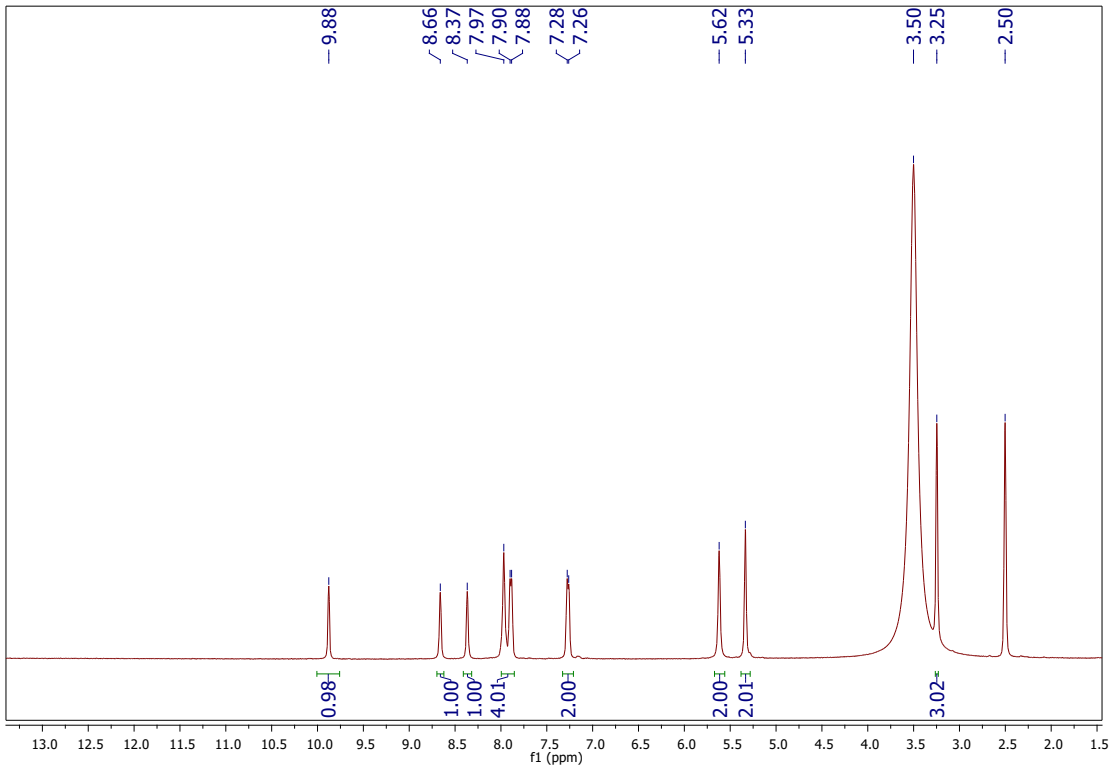

Figure S3: ^{1}H NMR spectrum of compound **5c**.

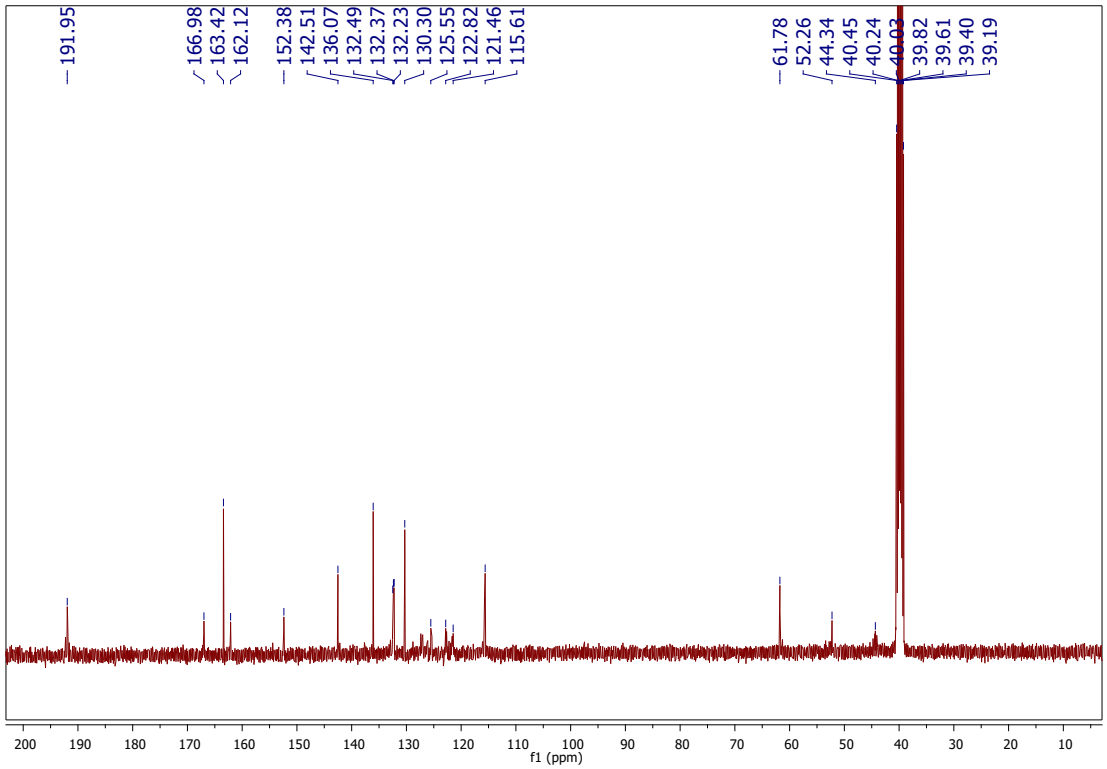

Figure S4: ^{13}C NMR spectrum of compound **5c**.

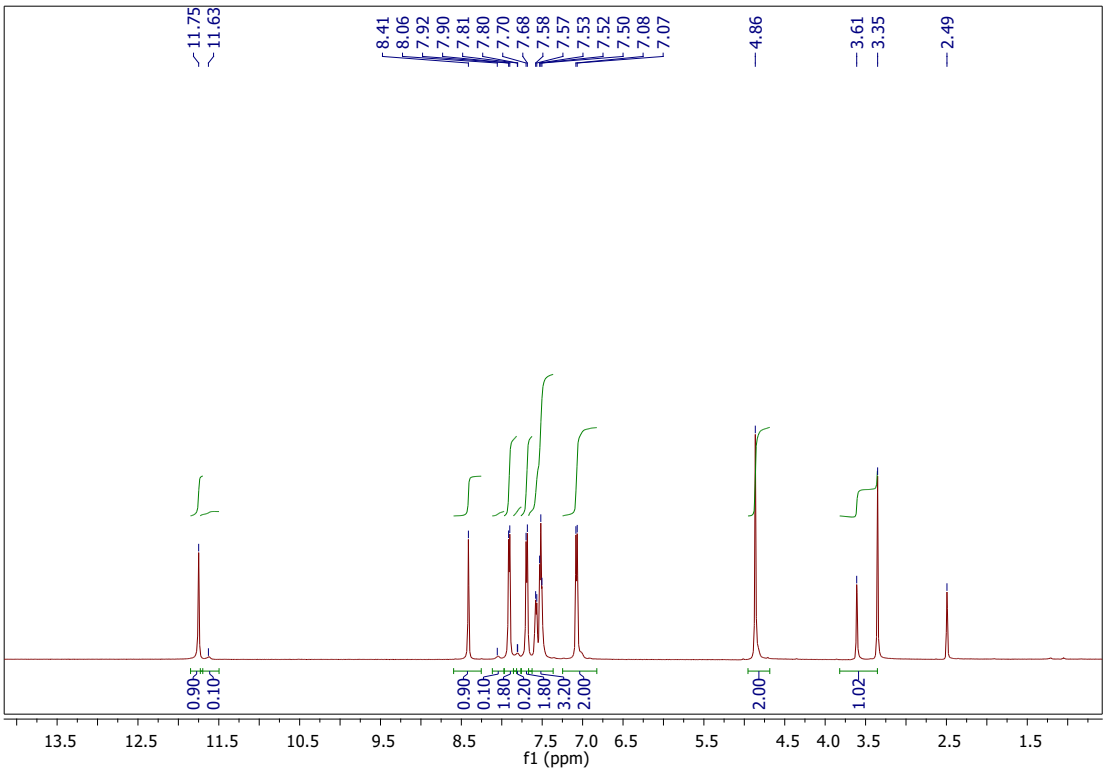

Figure S5: ^{1}H NMR spectrum of compound **7a**.

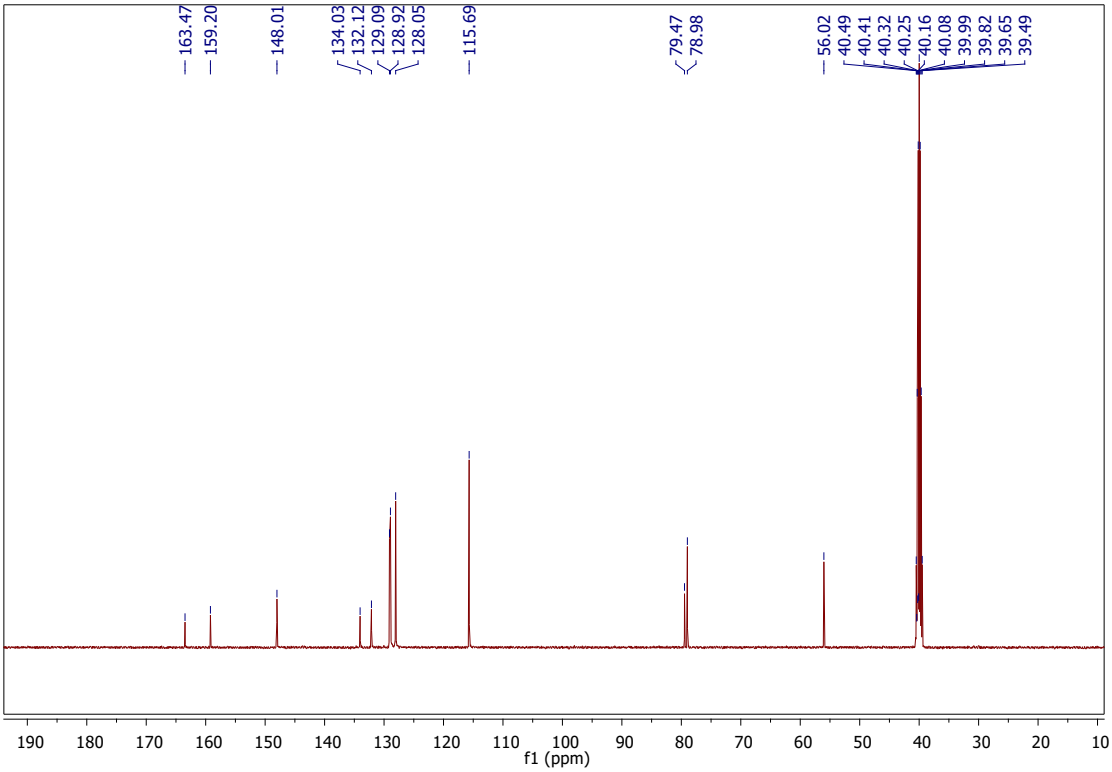

Figure S6: ^{13}C NMR spectrum of compound **7a**.

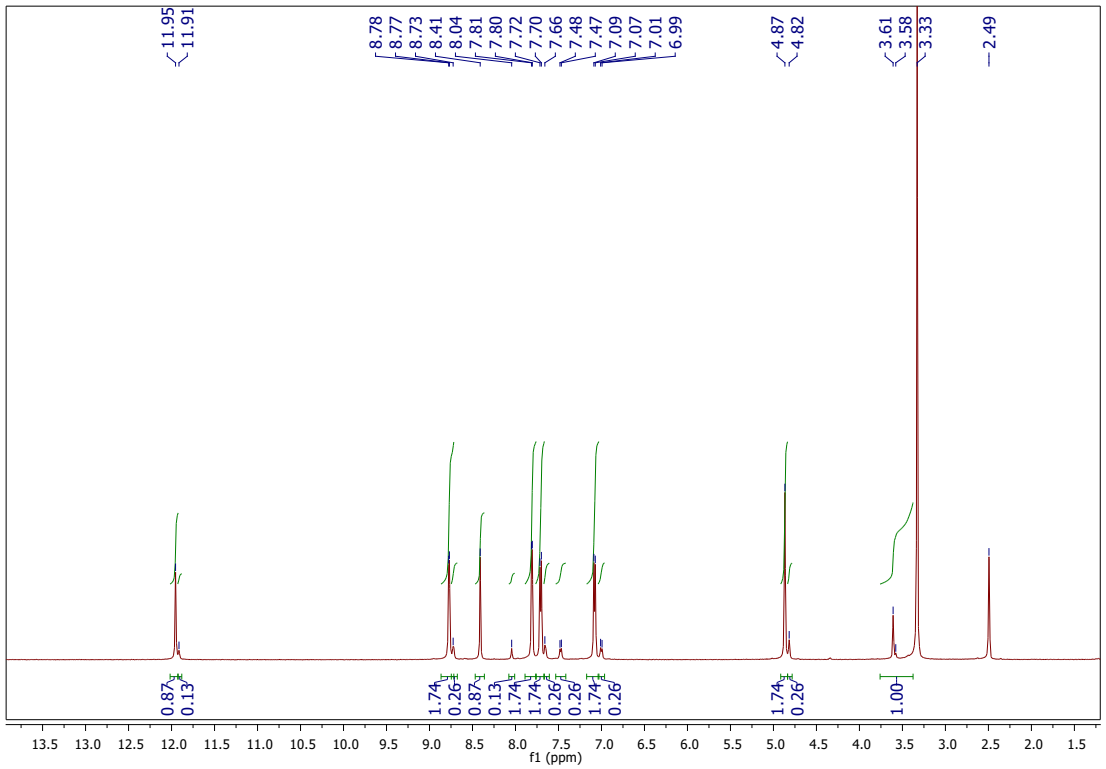

Figure S7: ^{1}H NMR spectrum of compound **7b**.

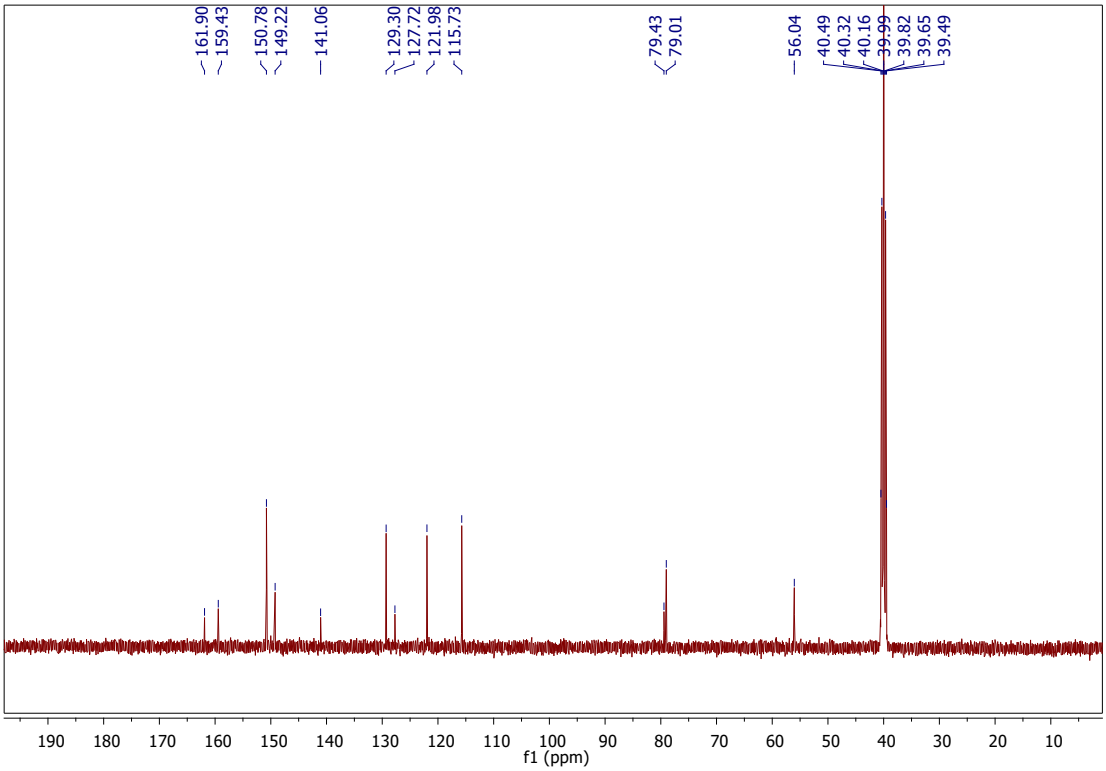

Figure S8: ^{13}C NMR spectrum of compound **7b**.

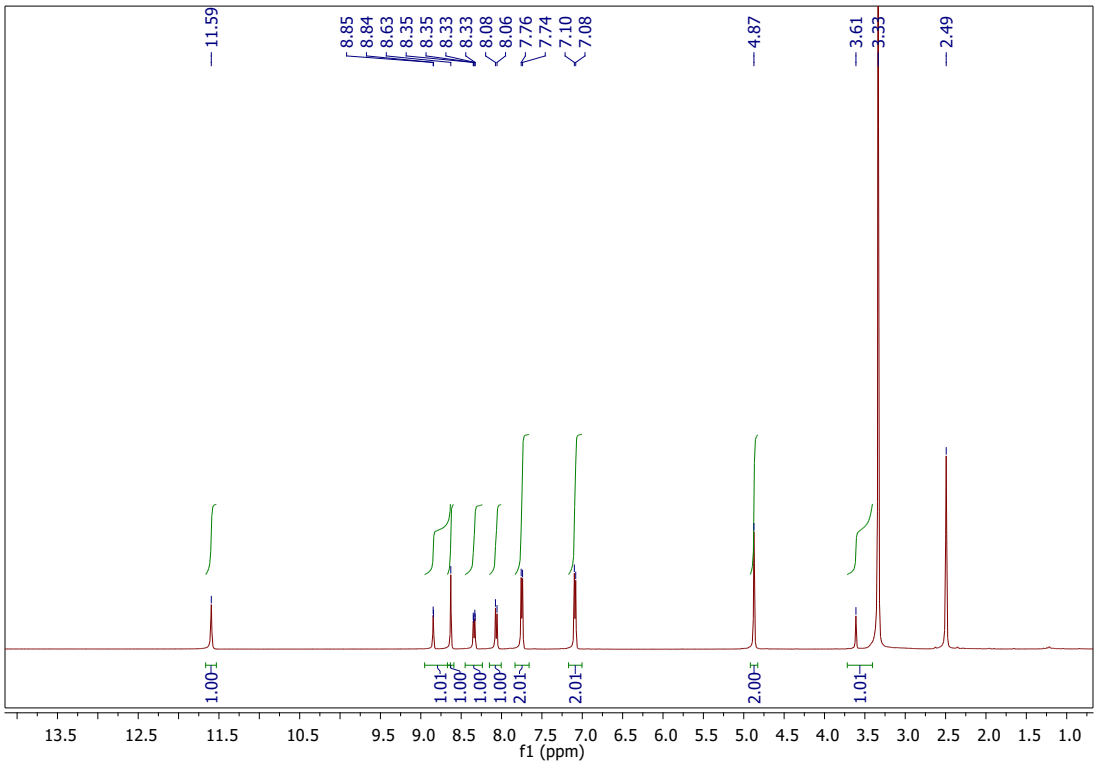

Figure S9: ^{1}H NMR spectrum of compound **7c**.

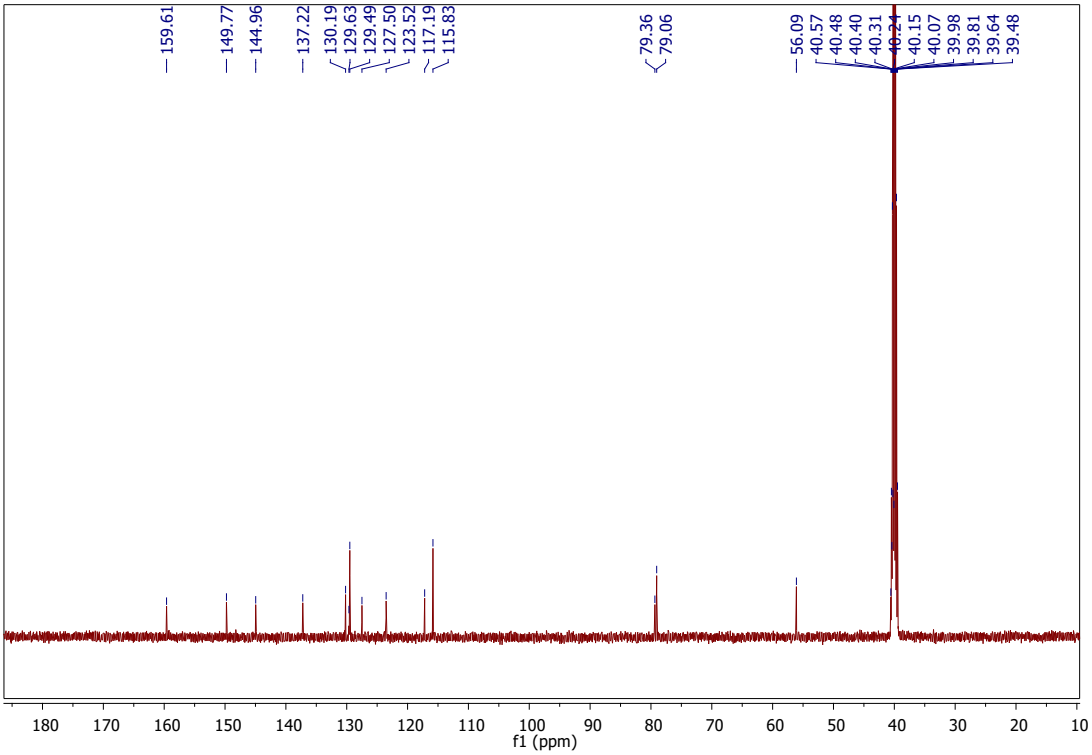

Figure S10: ^{13}C NMR spectrum of compound **7c**.

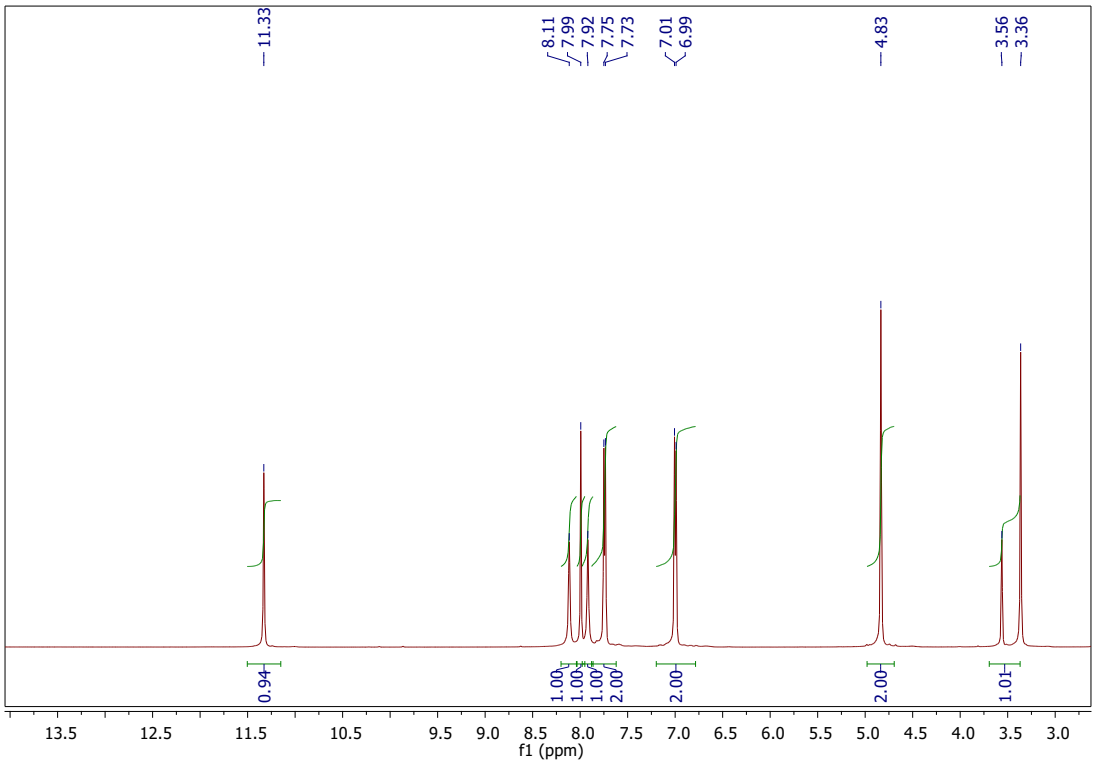

Figure S11: ^{1}H NMR spectrum of compound **7d**.

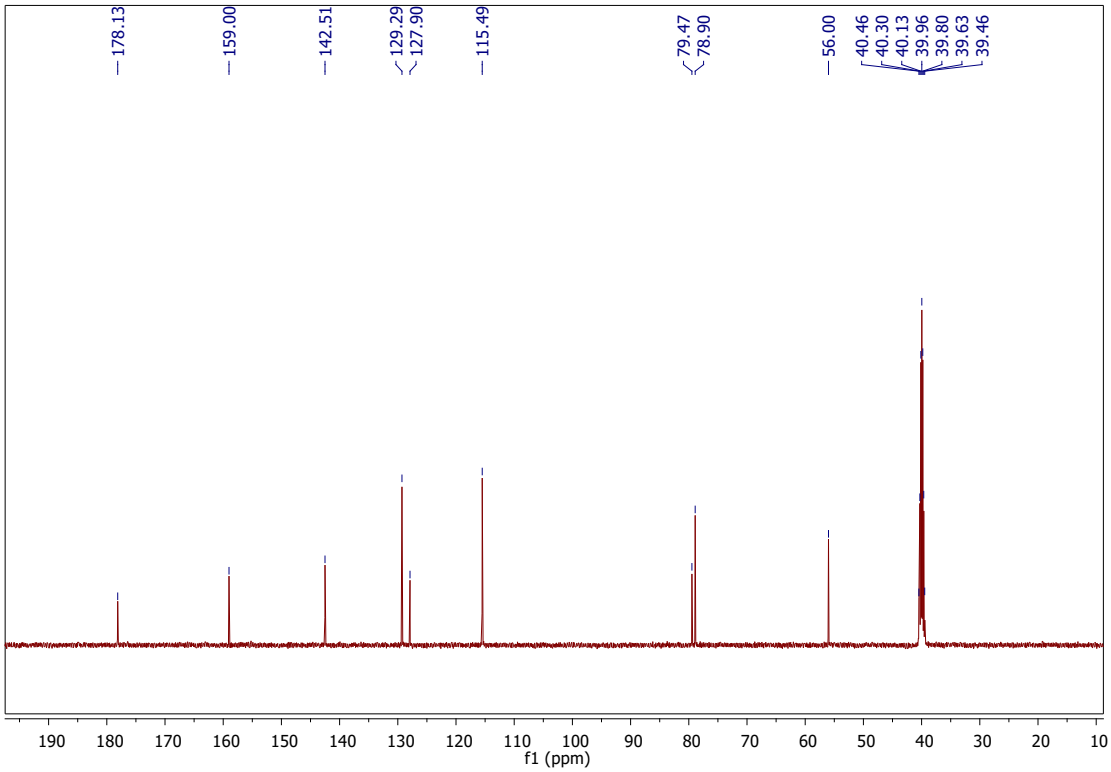

Figure S12: ^{13}C NMR spectrum of compound **7d**.

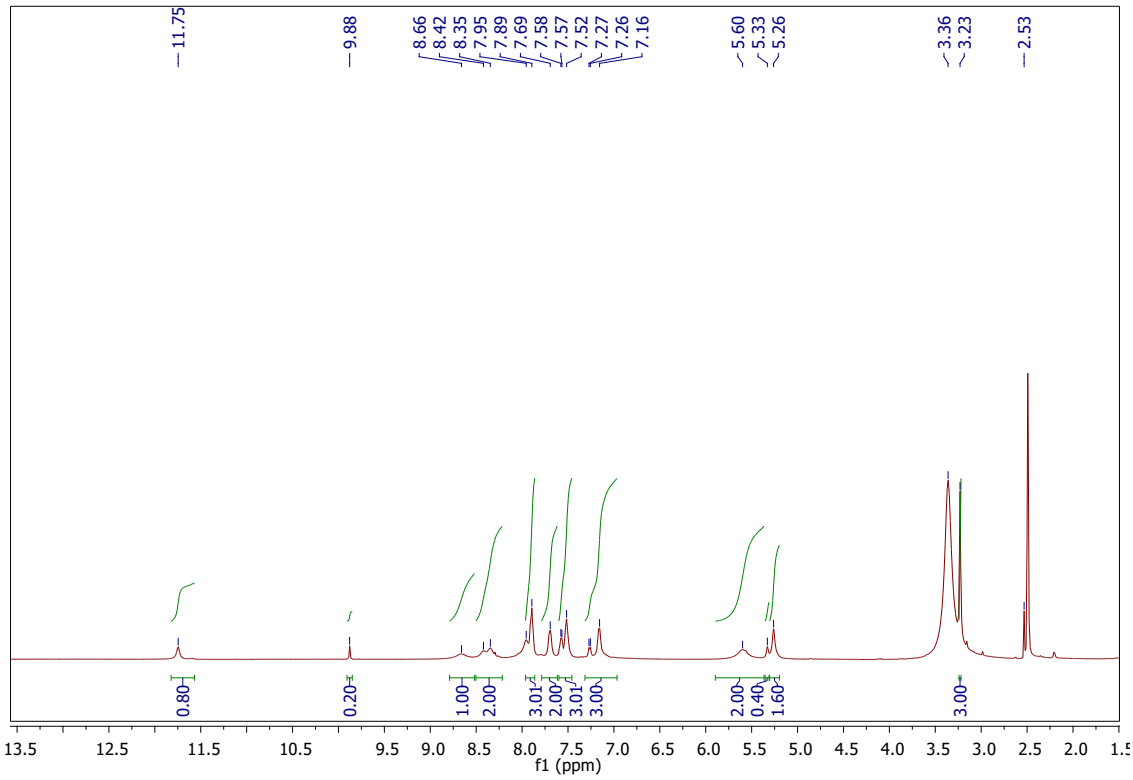

Figure S13: ^{13}C NMR spectrum of compound **8c**.

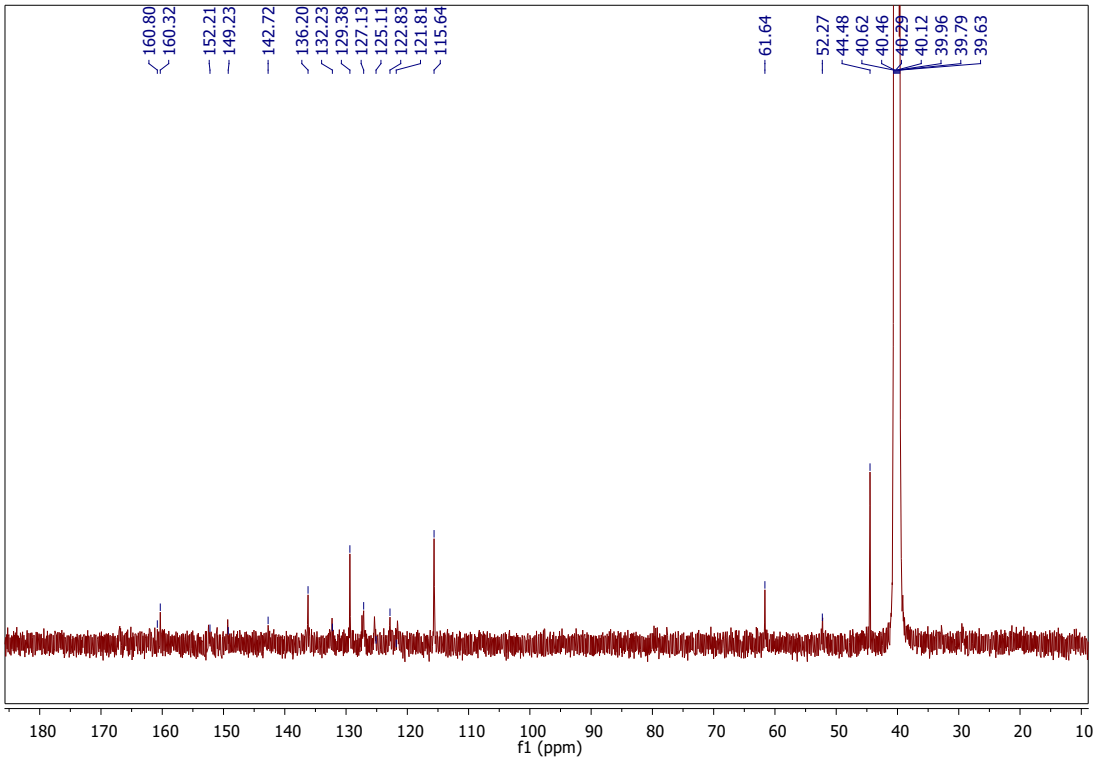

Figure S14: ^{13}C NMR spectrum of compound **8c**.

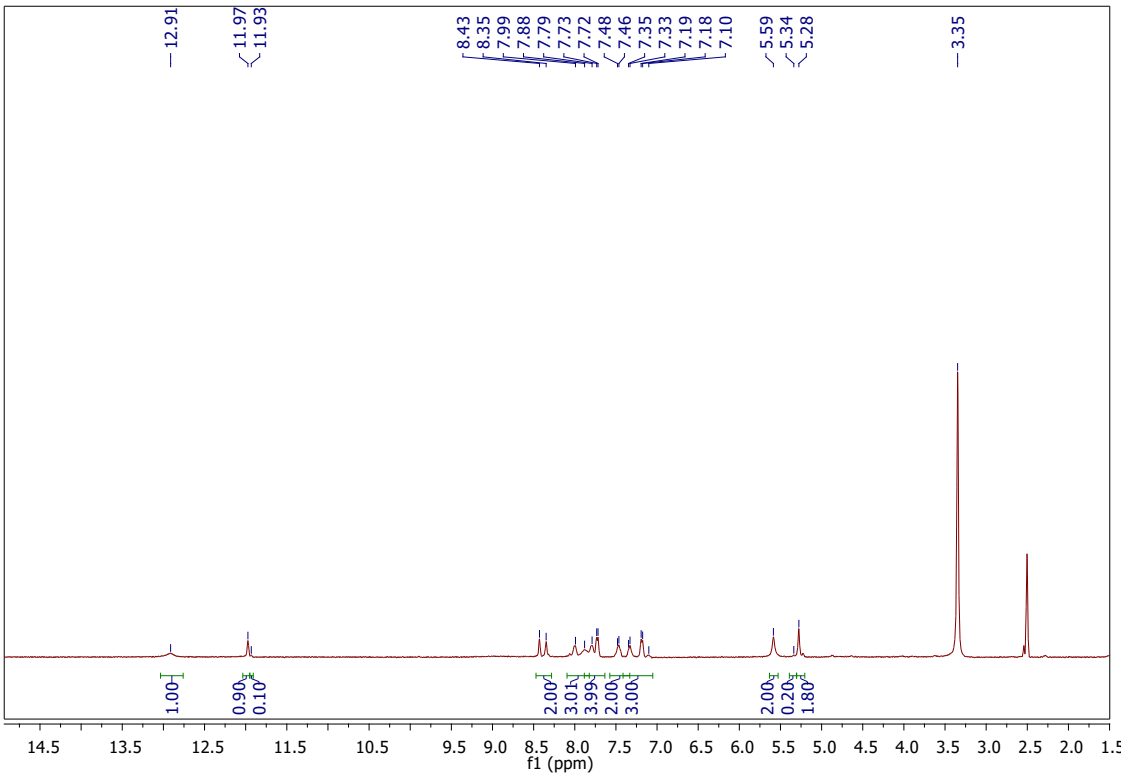

Figure S15: ^{13}C NMR spectrum of compound **8d**.

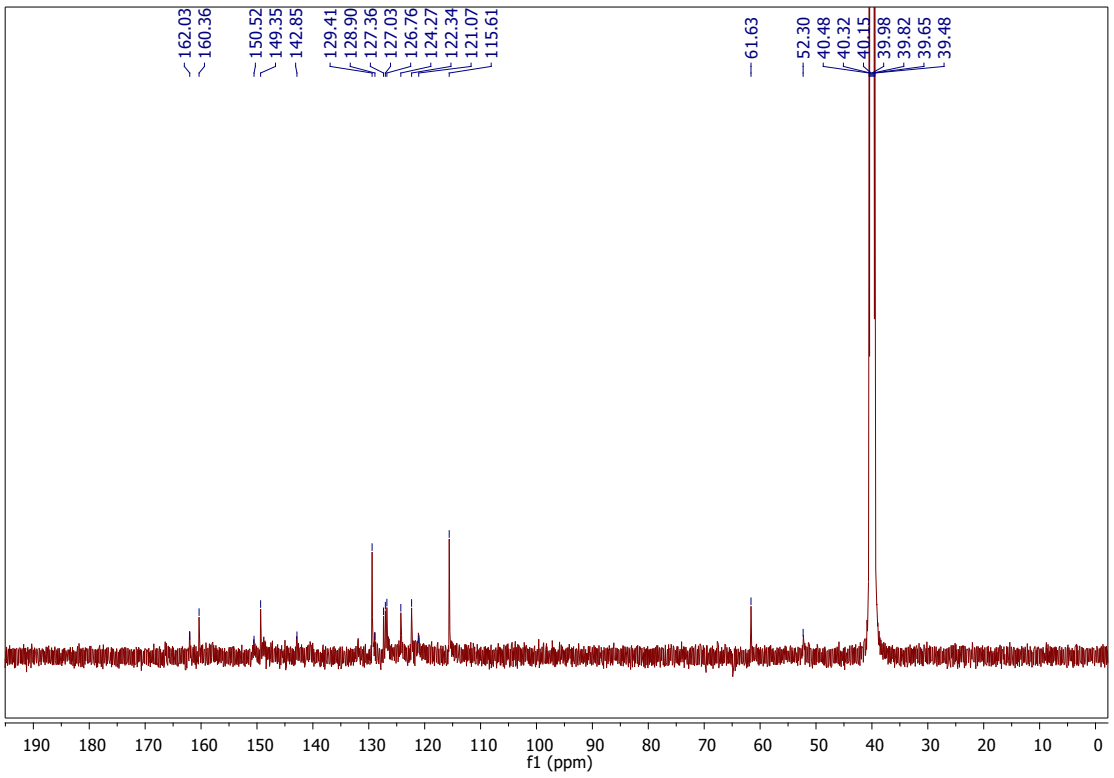

Figure S16: ^{13}C NMR spectrum of compound **8d**.

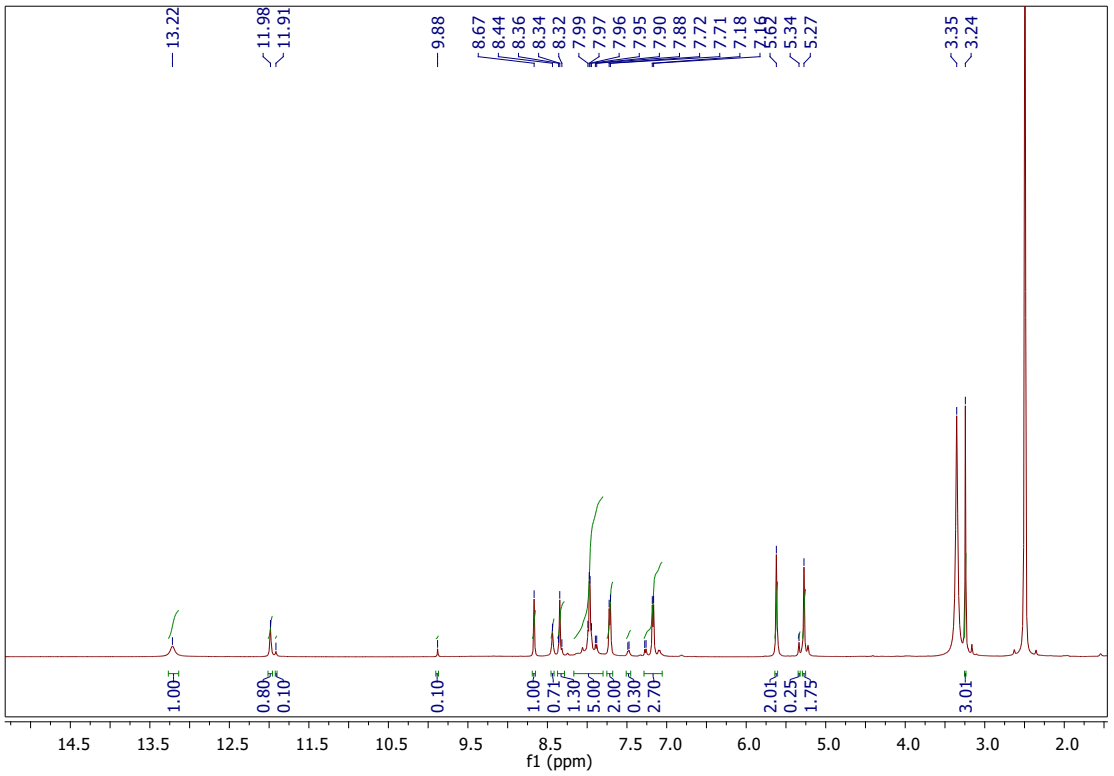

Figure S17: ^{13}C NMR spectrum of compound **8f**.

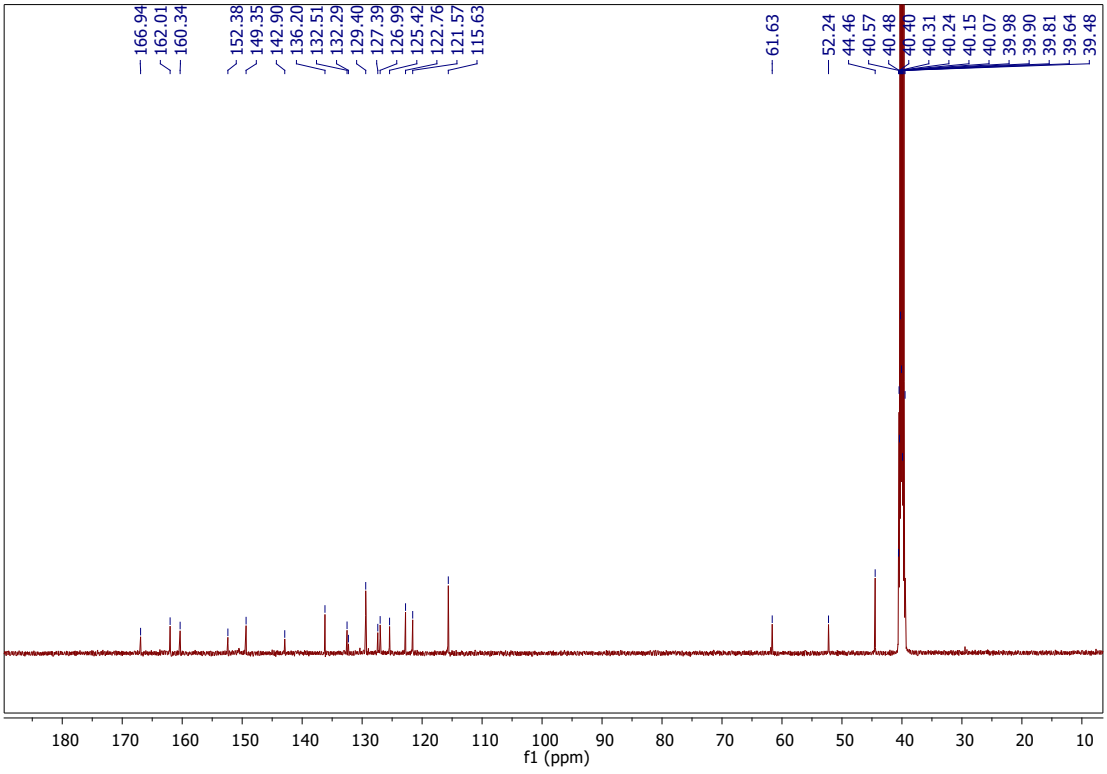

Figure S18: ^{13}C NMR spectrum of compound **8f**.

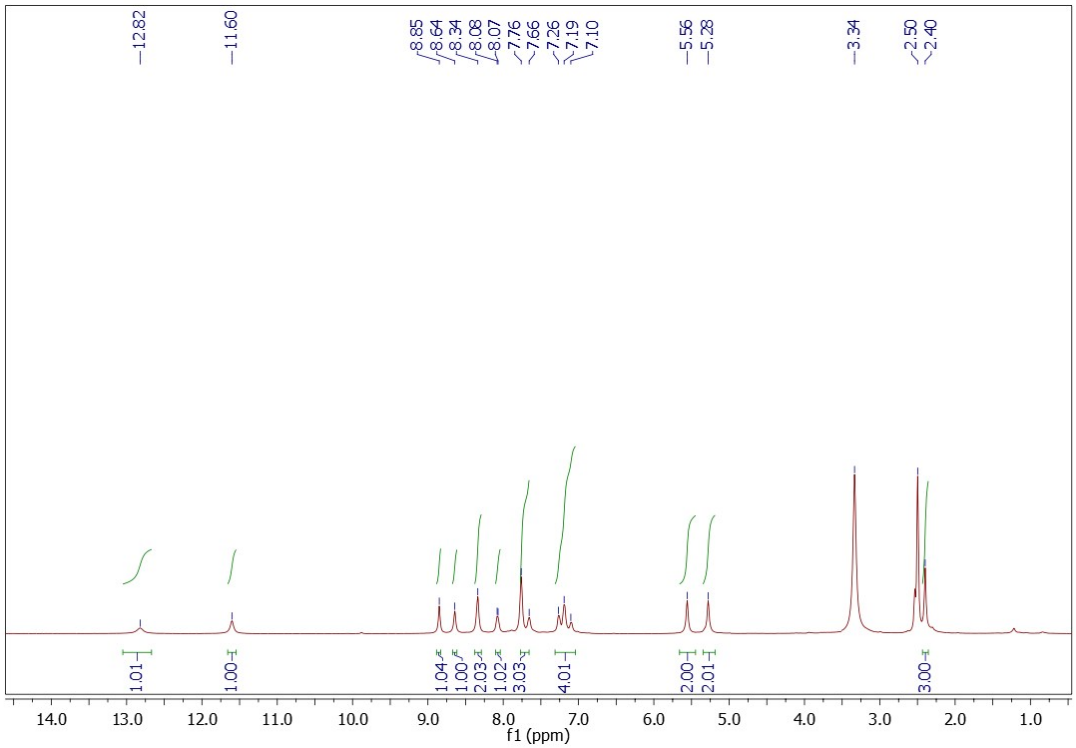

Figure S19: ^{13}C NMR spectrum of compound **8h**.

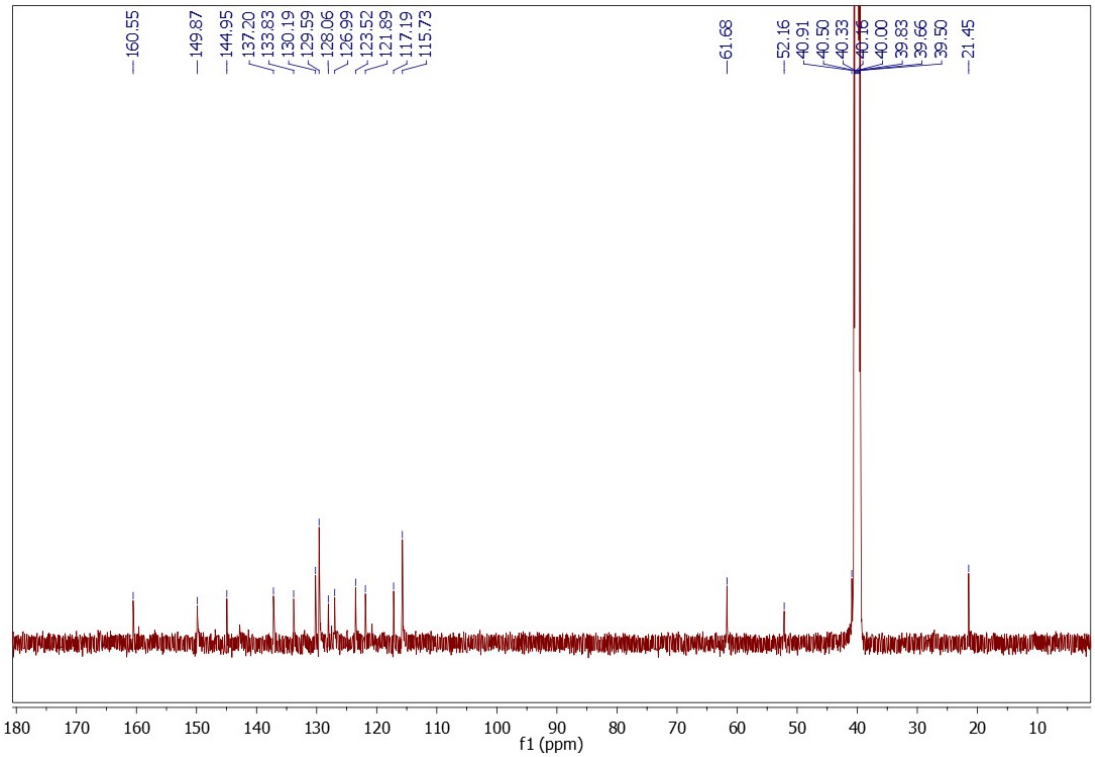

Figure S20: ^{13}C NMR spectrum of compound **8h**.

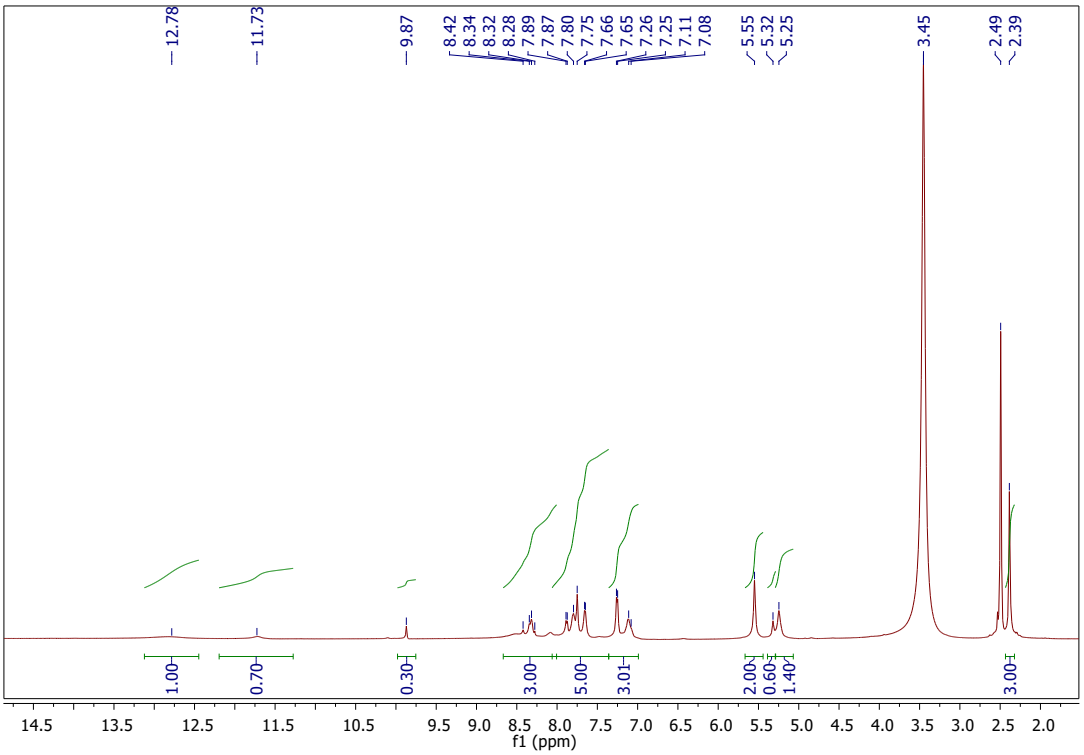

Figure S21: ^{13}C NMR spectrum of compound **8k**.

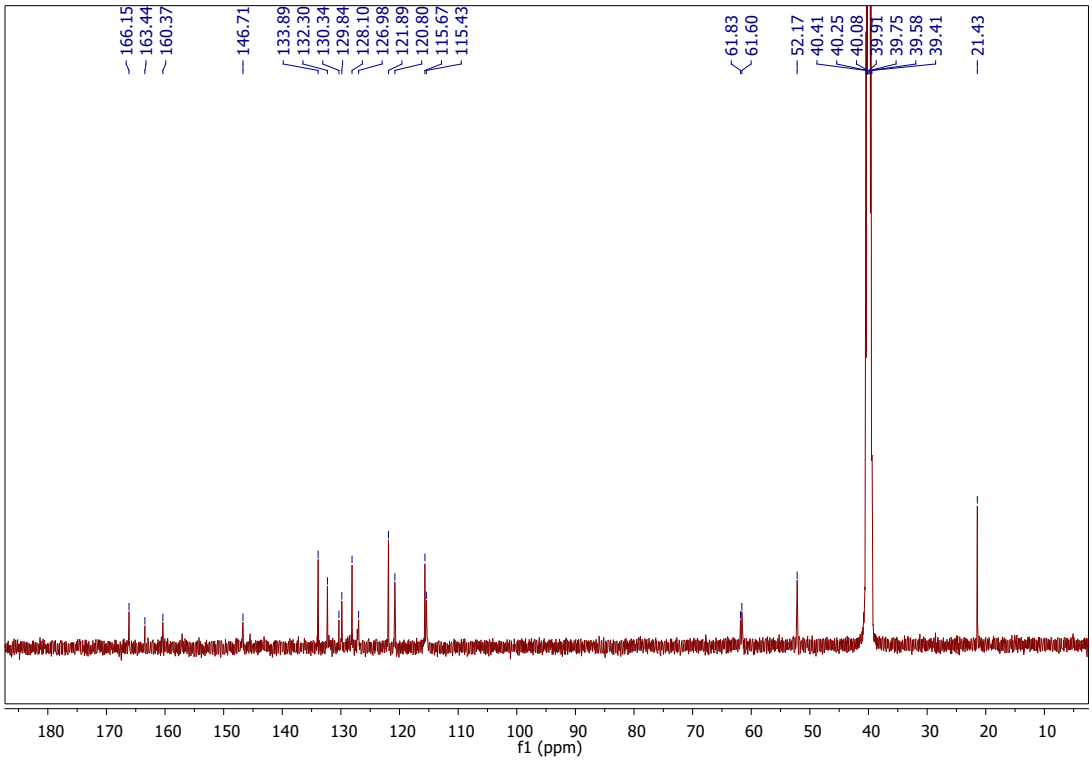

Figure S22: ^{13}C NMR spectrum of compound **8k**.

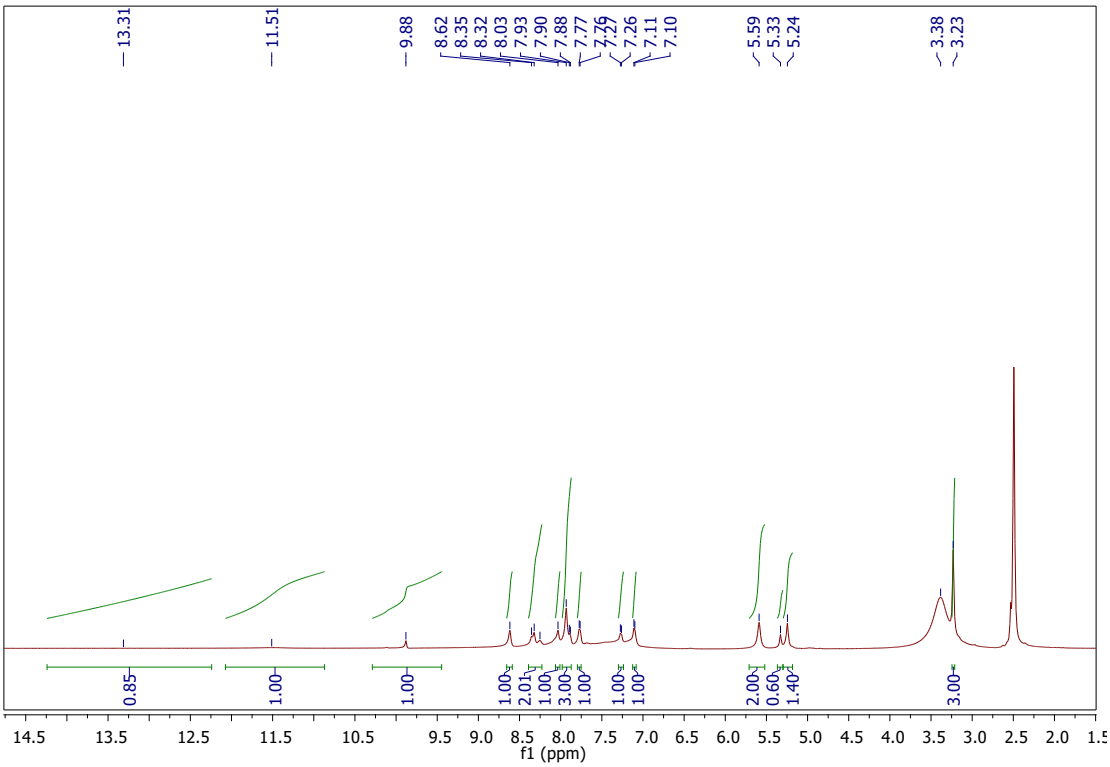

Figure S23: ^{13}C NMR spectrum of compound **8l**.

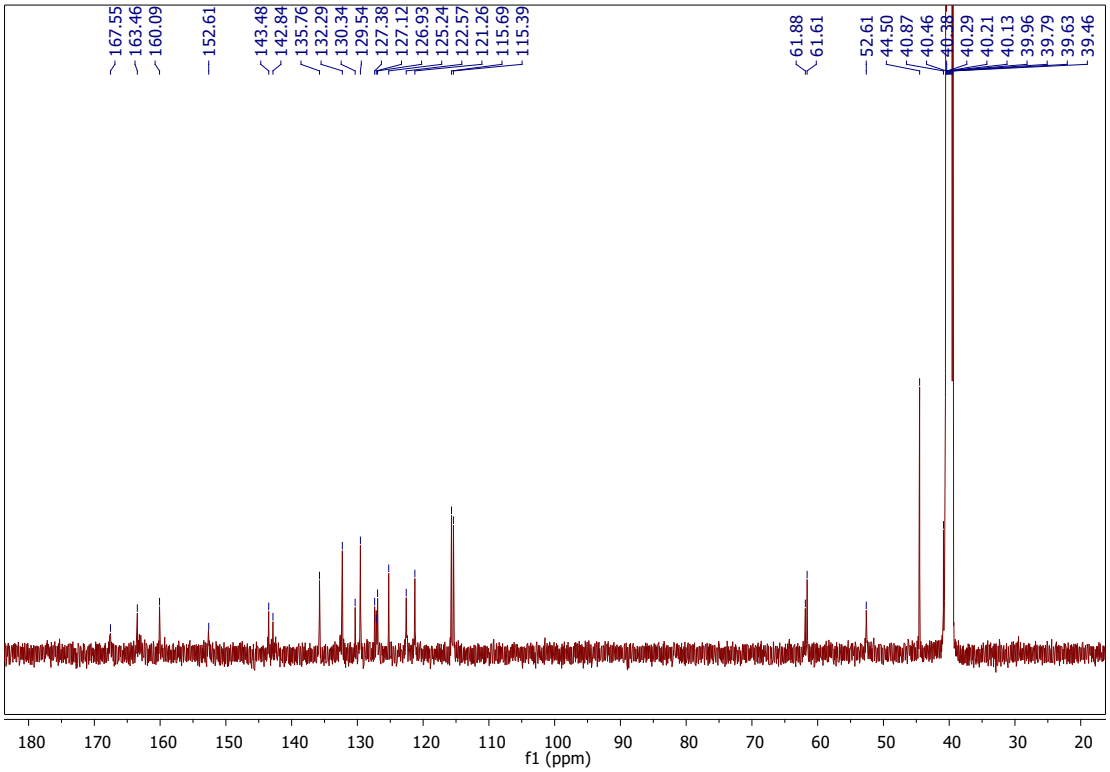

Figure S24: ^{13}C NMR spectrum of compound **8l**.

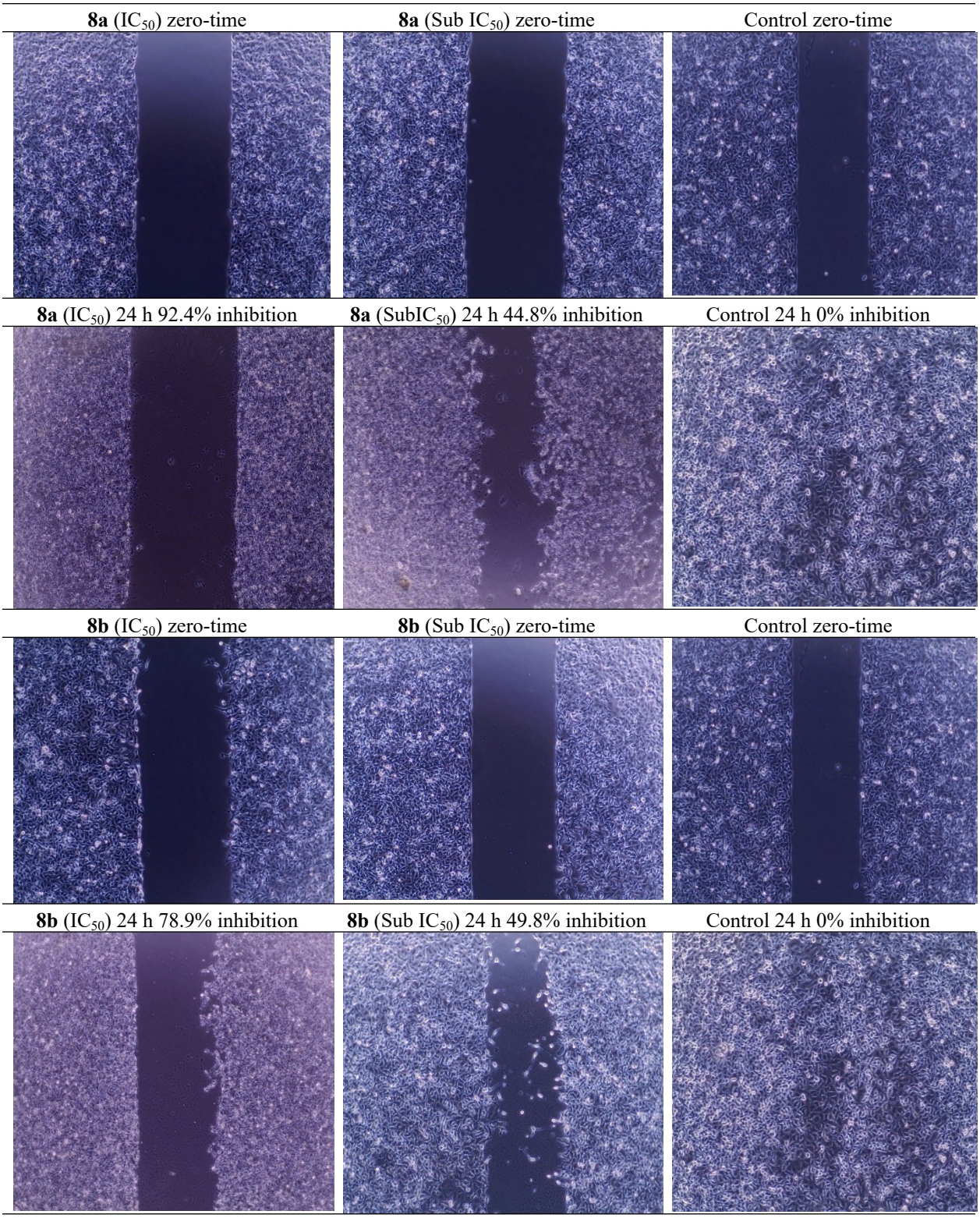

Fig. S25: Effect of **8a** and **8b** treatment on A549 cell migration. A549 cells were seeded in inserts and incubated for 24 hrs. Afterward, inserts were removed, and cells were treated with mitomycin C for 1 hour to stop cell proliferation. Then, A549 cells were treated with either **8a** or **8b** at IC_{50} and sub-IC_{50} concentrations for 24 hr. Images of the wound at 0 and 24 h at 10x magnification using EVOS XL Core imaging system.