Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information

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Synthesis of ligands

Materials and methods:

All commercial reagents were used as delivered, without further purification. Solvents used for purification (Ethyl Acetate, Hexane, Petroleum Ether) were distilled before using. Thin layer chromatographic (TLC) analyses were carried out on pre-coated silica gel on aluminium sheets. All the solvents used for chromatographic separation were distilled before use. The NMR spectra were measured with a Bruker Ascend^{TM} 600 spectrometer (^{1}H NMR at 600 MHz, ^{13}C NMR at 150 MHz). Chemical shifts are cited with respect to Me_4Si as internal standard (^{1}H and ^{13}C).

Synthesis of 1,4-bis(bromomethyl)-2,5-dimethylbenzene:[1] HBr in acetic acid (20 ml, 30-33 wt%)was added to a solution of *p*-xylene (2.6 g, 24.33 mmol) and para-formaldehyde (3.07 g, 102.19 mmol) in 10 ml glacial acetic acid. The mixture was refluxed for 16 h at 120 °C, poured into 100 ml of distilled water and the product was filtered through a sintered glass funnel. The crude product was air dried, and purified using silica gel column chromatography (60-120 mesh) using ethyl acetate and petroleum ether as solvent. R_f = 0.5 (100% petroleum ether). Yield: 6.8 g (97 %). ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) = 7.13 (s, 2H), 4.45 (s, 4H), 2.36 (s, 6H); ^{13}C NMR ($CDCl_3$, 150MHz): δ (ppm) = 136.6, 135.4, 132.6, 32.0, 18.4.

Synthesis of 1,3-bis(bromomethyl)mesitylene:[1] HBr in acetic acid (8.6 ml, 30-33 wt%) was added to a solution of mesitylene (2.6 g, 21.59 mmol) and para-formaldehyde (1.3 g, 43.29 mmol) in 12 ml glacial acetic acid. The mixture was refluxed for 8 h at 80 ºC. The reaction was monitored by TLC analysis. After completion, the reaction mixture was poured into 50 ml of distilled water and the product was filtered through a sintered glass funnel and air dried. The crude product was directly used for next step without further purification. R_f = 0.5 (2% ethyl acetate in petroleum ether). Yield: 5.80 g (87 %). ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) = 6.92 (s, 1H), 4.58 (s, 4H), 2.46 (s, 3H), 2.40 (s, 6H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ (ppm) = 138.3, 137.4, 132.8, 131.0, 30.1, 19.7, 14.9.

Preparation of 1,3,5-tris(bromomethyl)benzene:[2] Mesitylene (2.6 g, 21.59 mmol), *N*-bromosuccinimide (13.45 g, 75.56 mmol), and benzoyl peroxide (2.7 g, 11.23 mmol) were taken in 30 ml carbon tetrachloride and the resultant mixture was heated under reflux for 6 h at 70 ºC. The imide was filtered off through a pad of silica, the solvent was evaporated under reduced pressure and the remaining solid was extracted with ethyl acetate. The organic part was washed with brine and concentrated *in vacuo*. R_f = 0.5 (100% Hexane). Yield: 4.23 g (59 %).^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) = 7.35 (s, 3H), 4.45 (s, 6H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ (ppm) = 139.3, 129.8, 32.6.

Preparation of 1,3,5-tris(bromomethyl)mesitylene:[1] HBr in acetic acid (35 ml, 30-33 wt%) was added to a solution of mesitylene (6.0 g, 50.37 mmol) and para-formaldehyde (5.0 g, 166.5 mmol) in 25 ml glacial acetic acid. The mixture was refluxed for 12 h at 95 ºC, poured into 100 ml of distilled water and the product was filtered off on a sintered glass funnel and air dried. The crude product was used directly for the next step without purification. R_f = 0.5 (4% ethyl acetate in petroleum ether). Yield: 17.9 g (93 %).^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) = 4.58 (s, 6H), 2.47 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ (ppm) = 138.1, 133.5, 30.2, 15.6.

Preparation of 1,2,3,4,5,6-hexakis(bromomethyl)benzene:[3] A solution of hexamethyl benzene (0.5 g, 3.08 mmol) in 13 ml 1,2-dibromoethane was heated under reflux for 30 min. Then bromine solution (2 ml, 39.04 mmol) was added to this dropwise for 20 min. The mixture was then heated for 30 h, cooled to room temperature, filtered, washed with dibromoethane and diethyl ether, and dried *in vacuo*. R_f= 0.7 (100 % Hexane). Yield: 1.38 g (72 %). ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) = 4.70 (s, 12H).

Plots for % Proliferation by MTT assay in MDA-MB-231 cells

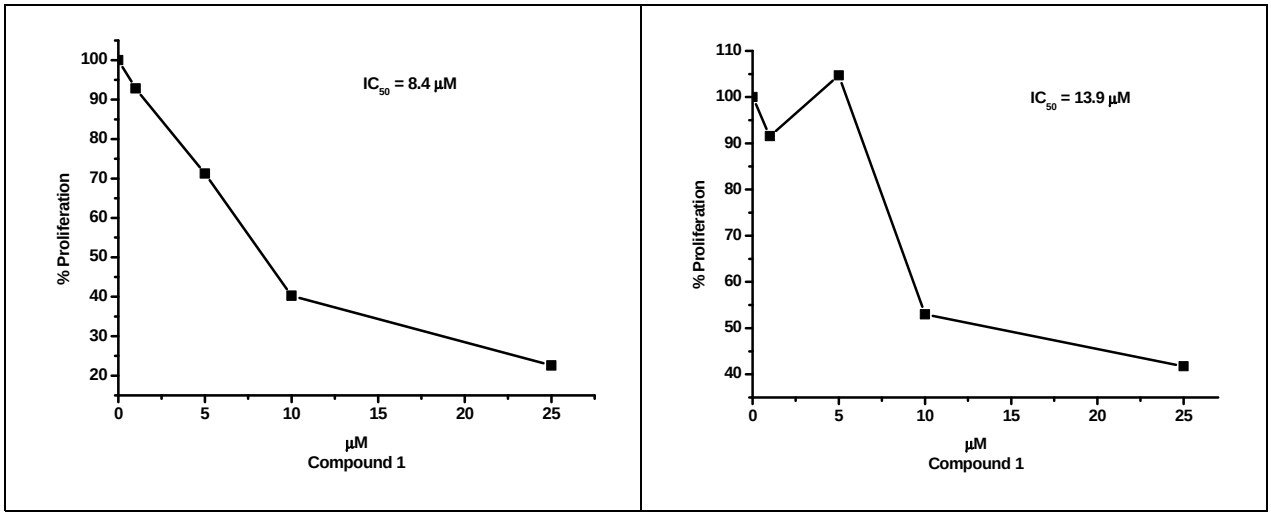


Fig S1: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **1**.

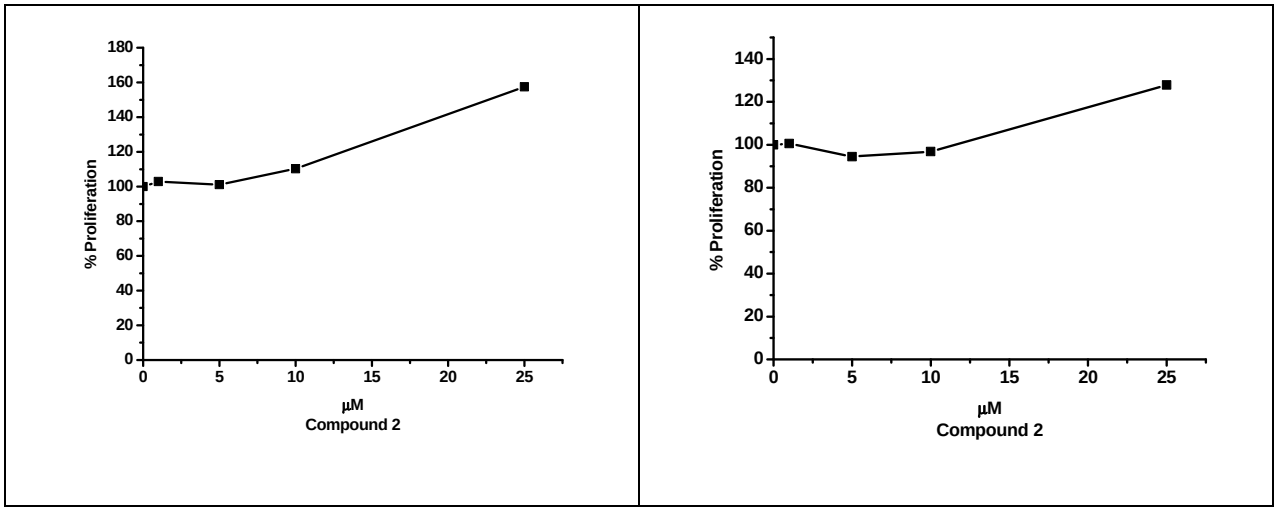


Fig S2: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **2**.

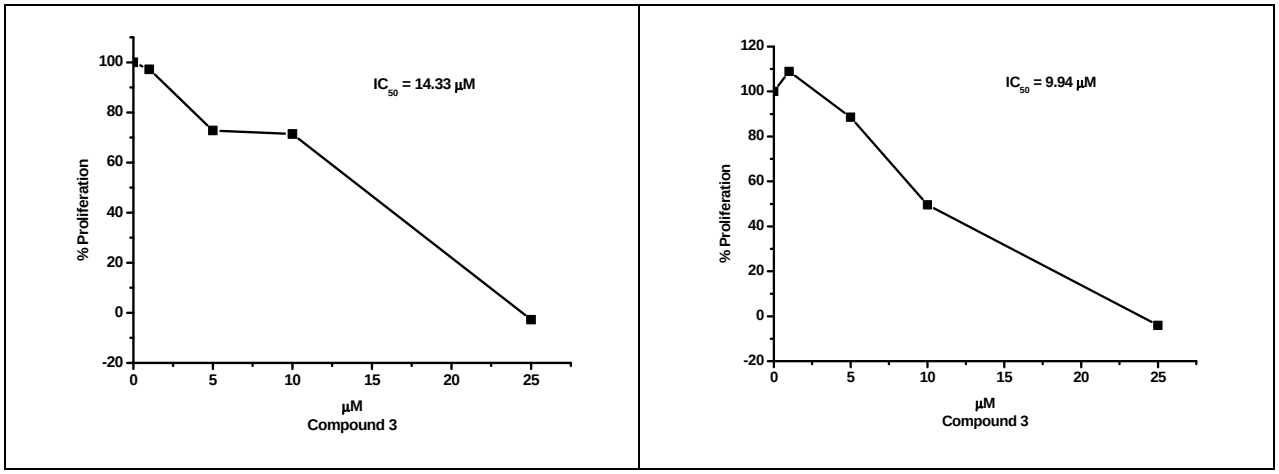


Fig S3: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **3.**

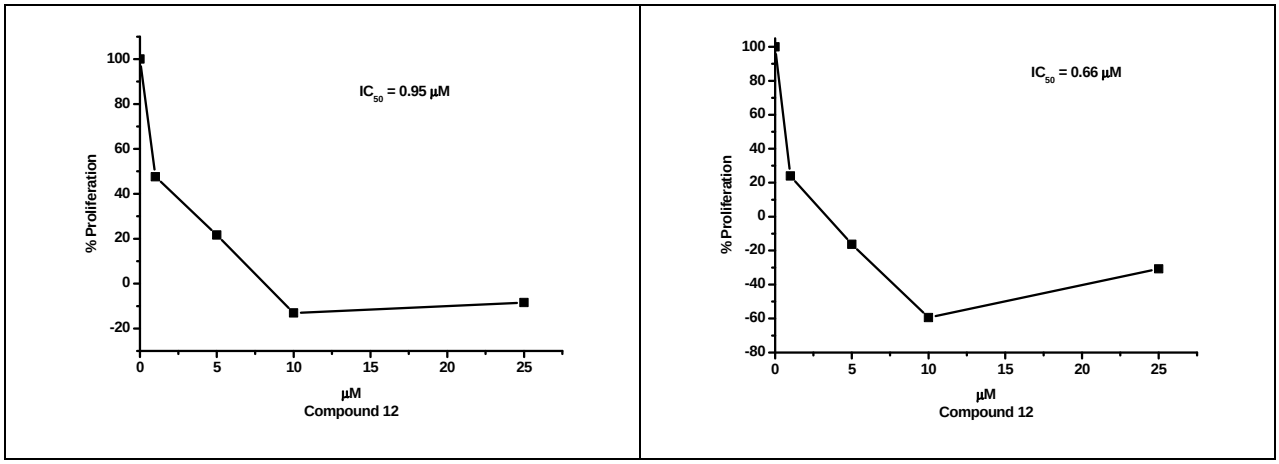


Fig S4: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **12.**

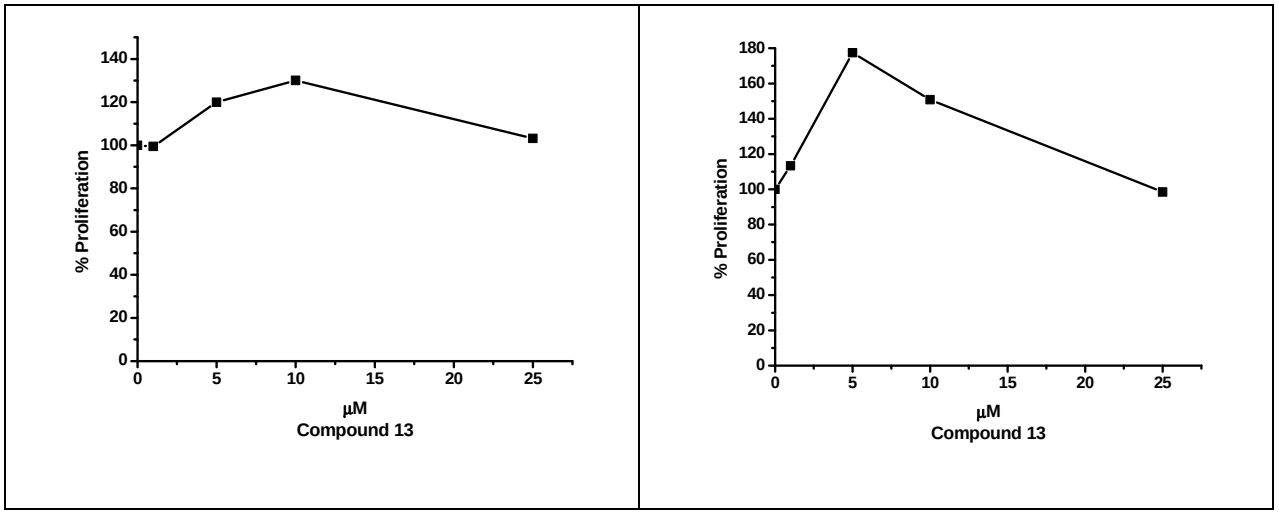


Fig S5: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **13.**

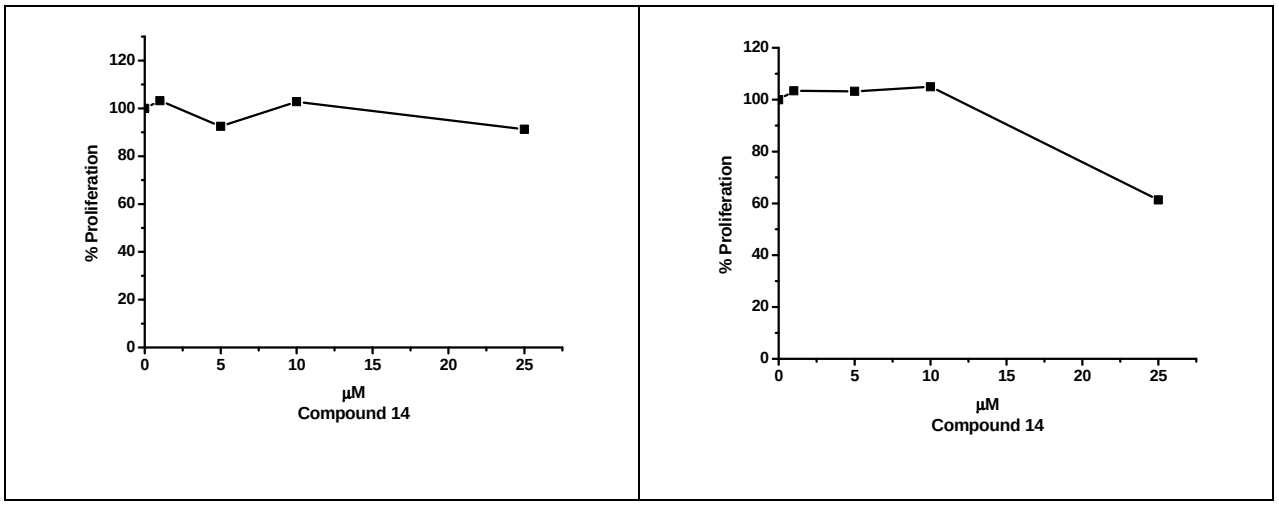


Fig S6: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **14.**

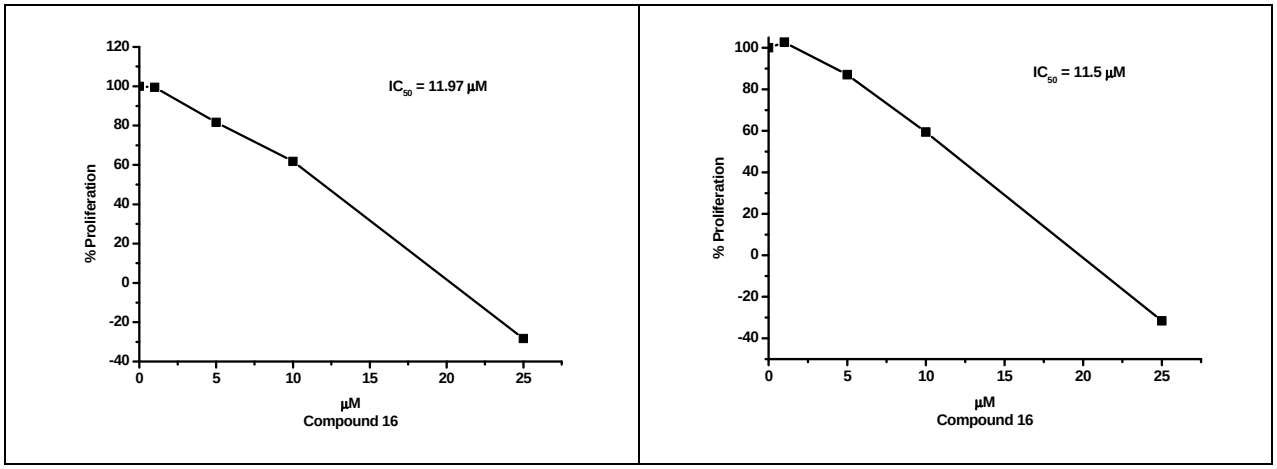


Fig S7: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **16**.

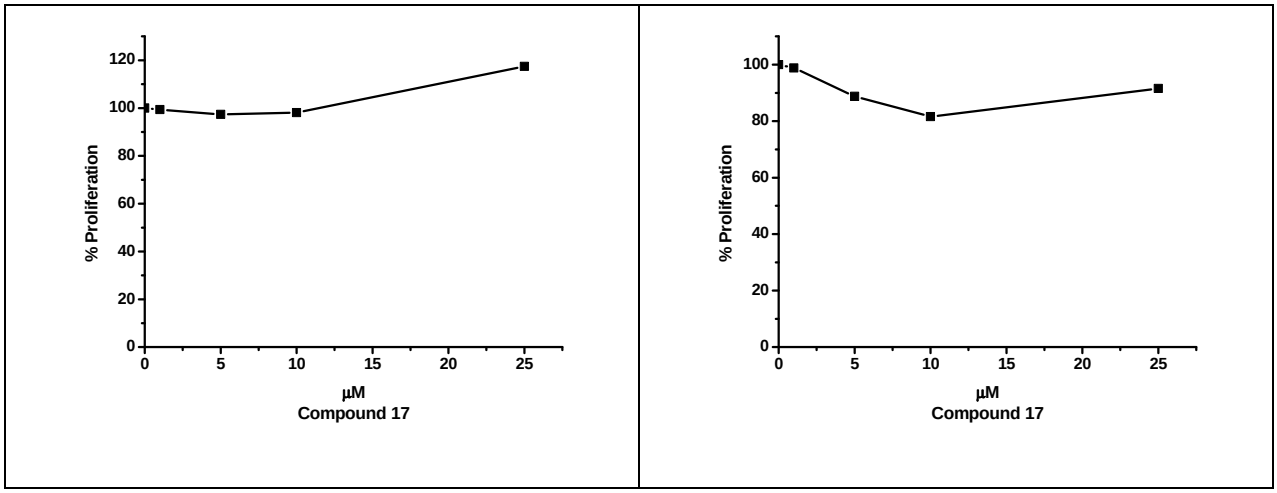


Fig S8: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **17**.

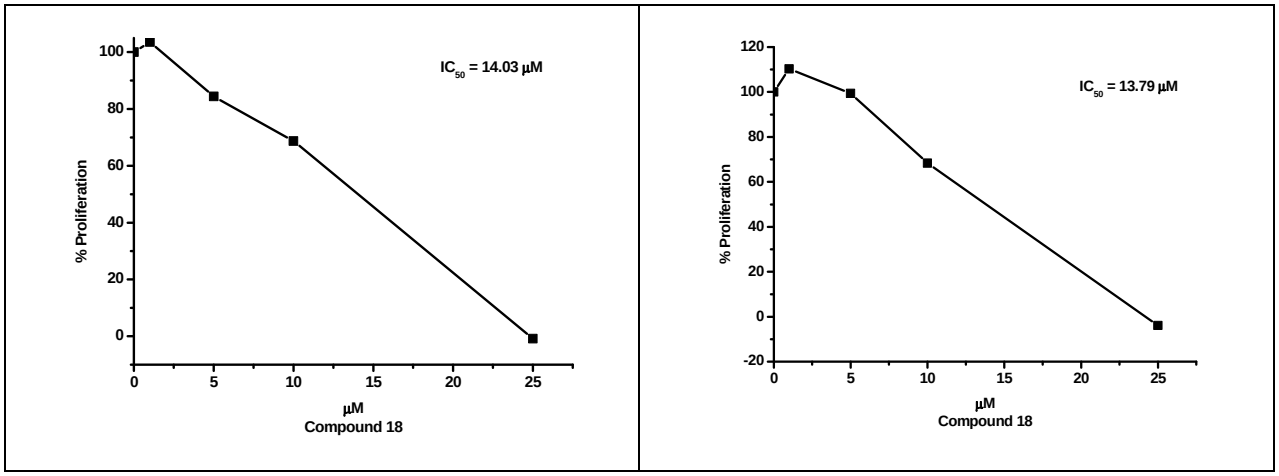


Fig S9: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **18**.

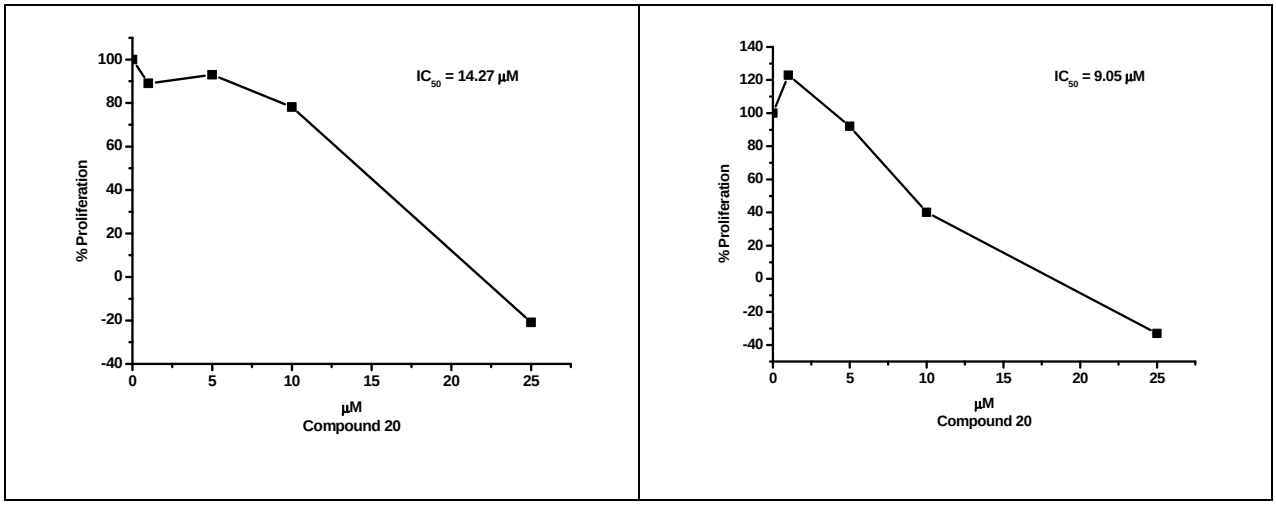


Fig S10: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **20**.

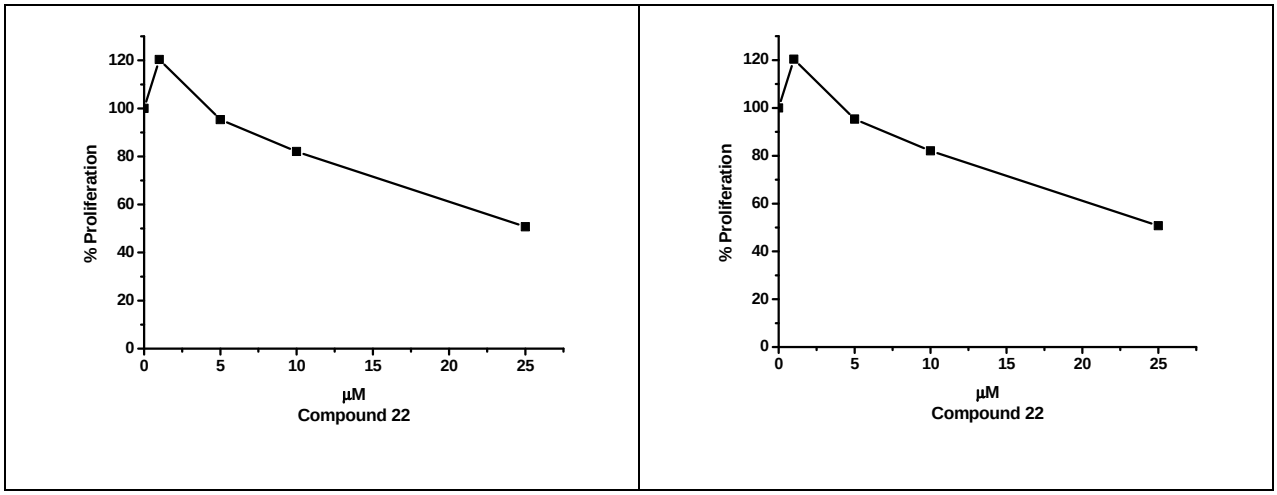


Fig S11: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **22**.

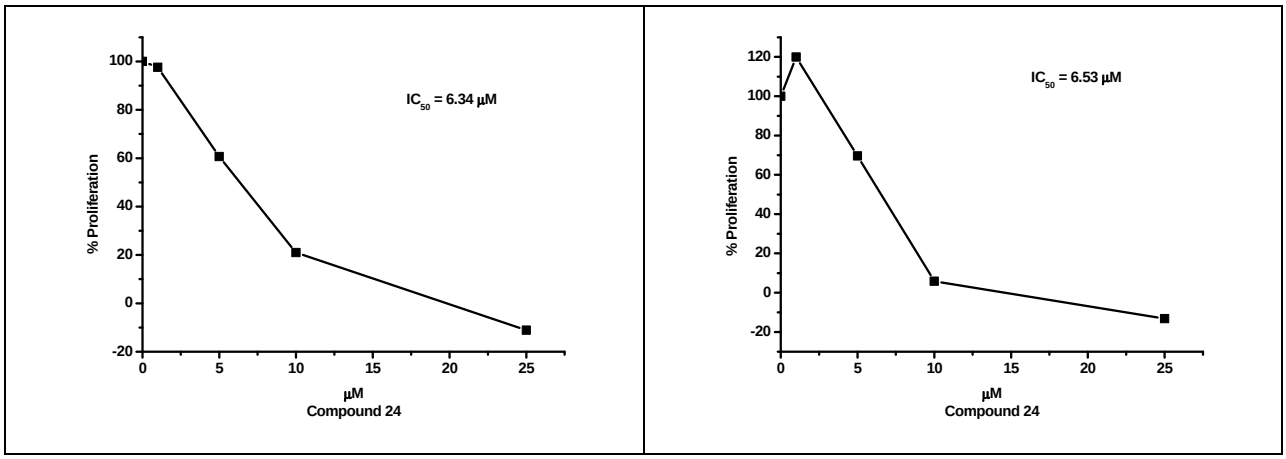


Fig S12: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **24**.

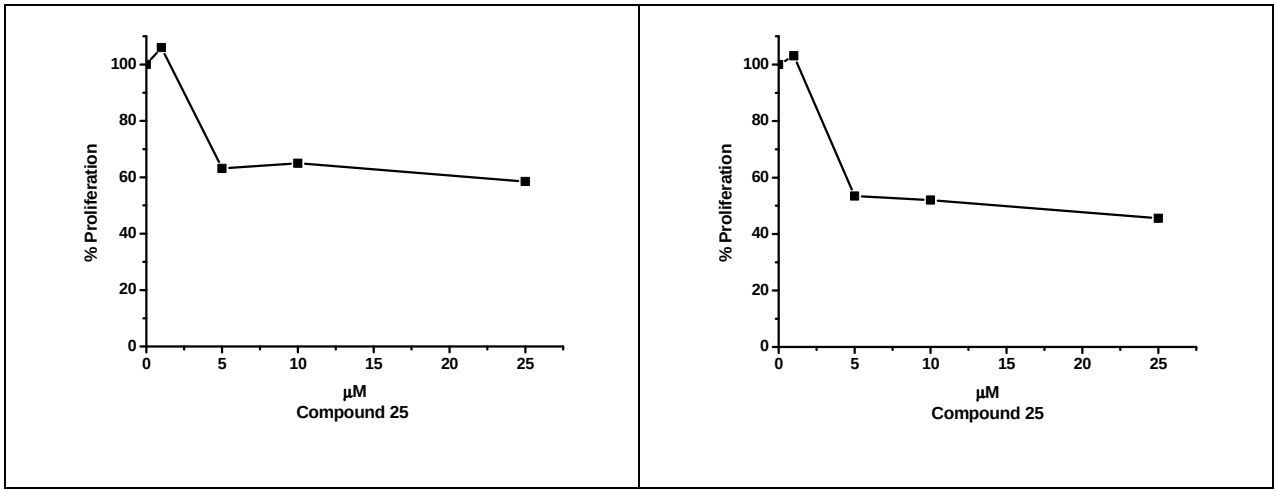


Fig S13: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **25**.

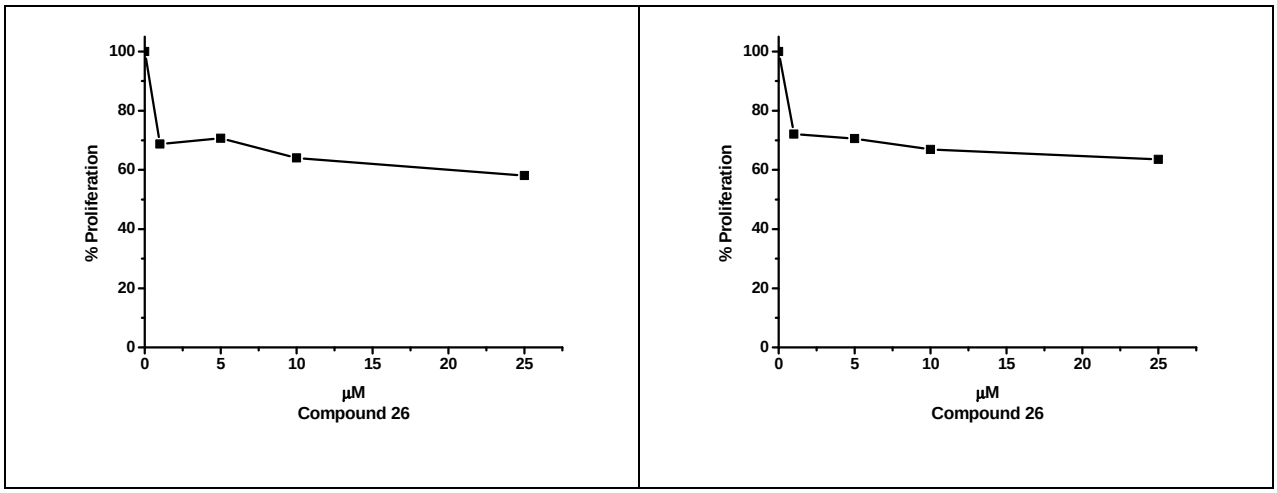


Fig S14: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **26**.

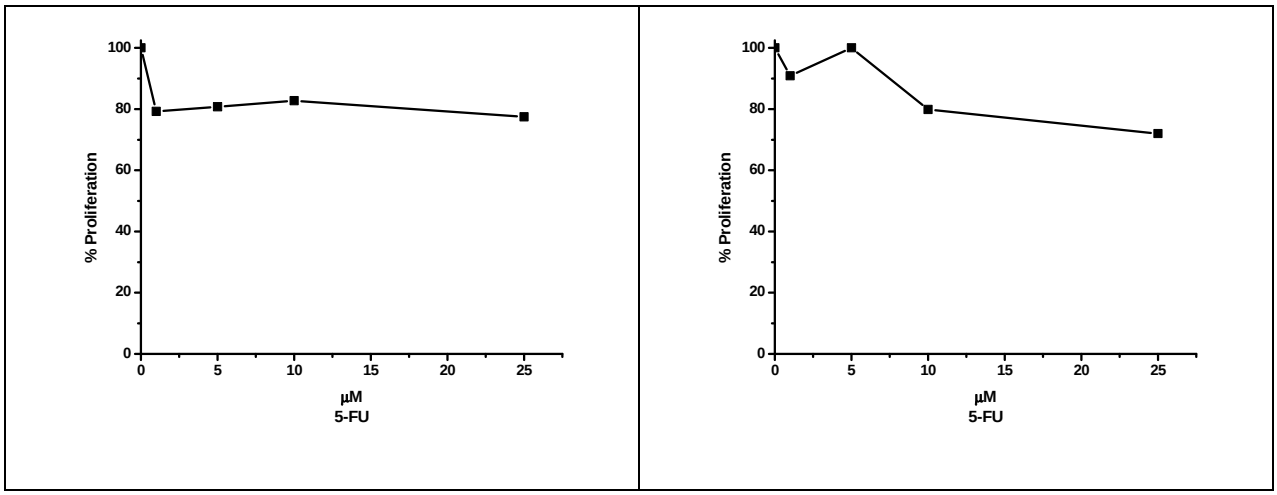


Fig S15: Plots for the % proliferation of MDA-MB-231 cells in the presence of compound **5-FU**.

Plots for % Proliferation by MTT assay in MCF-7 and T47D cells

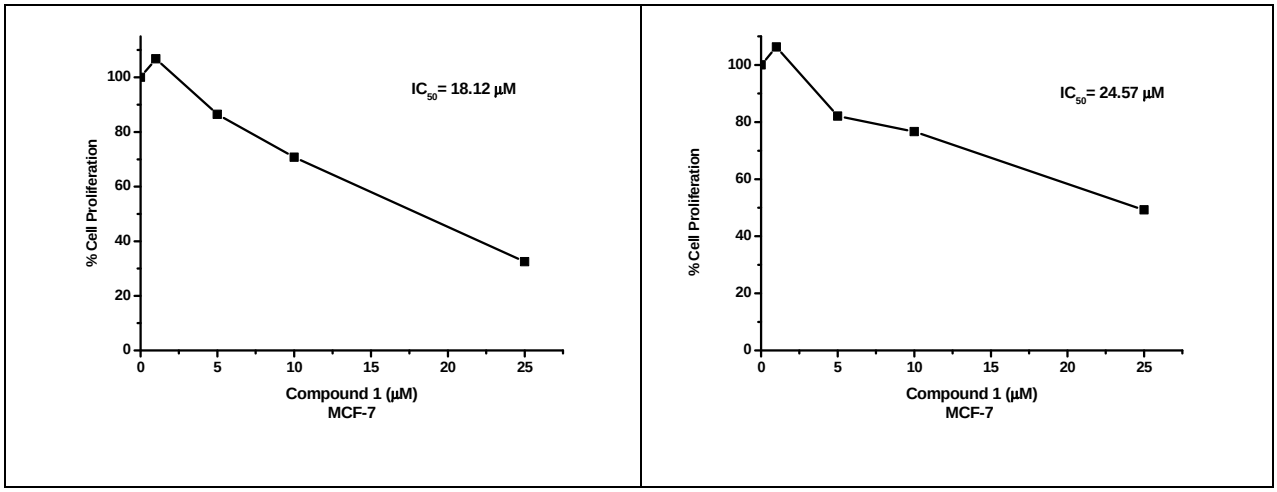


Fig S16: Plots for the % proliferation of MCF-7 cells in the presence of compound **1**.

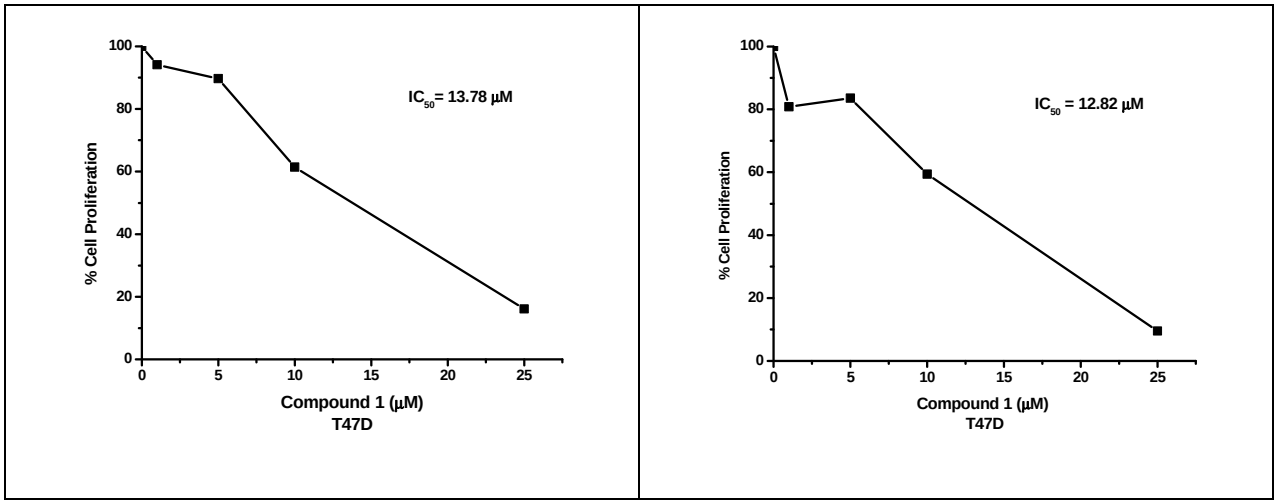


Fig S17: Plots for the % proliferation of T47D cells in the presence of compound **1**

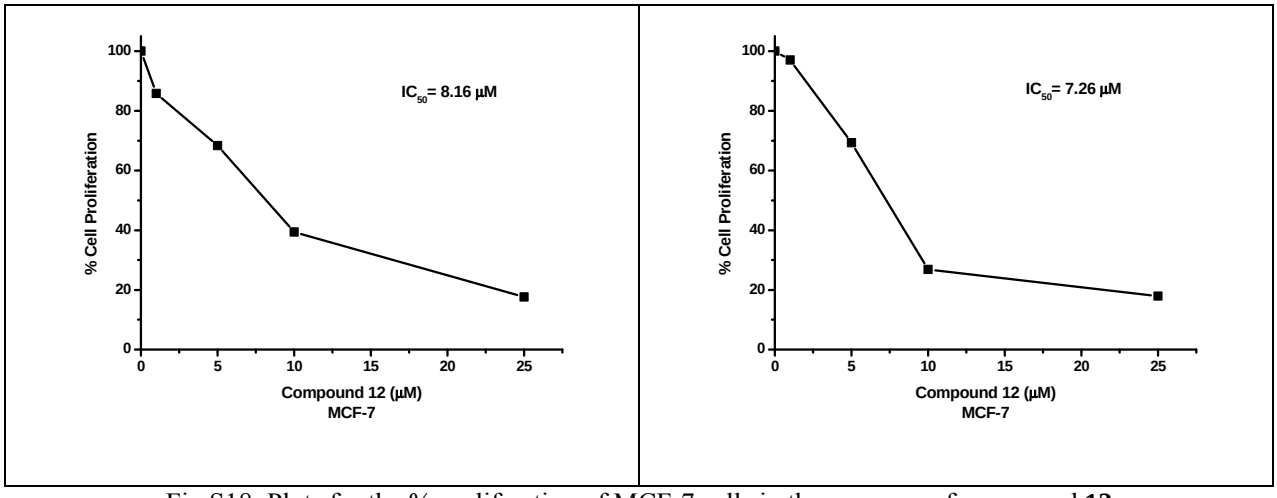


Fig S18: Plots for the % proliferation of MCF-7 cells in the presence of compound **12**

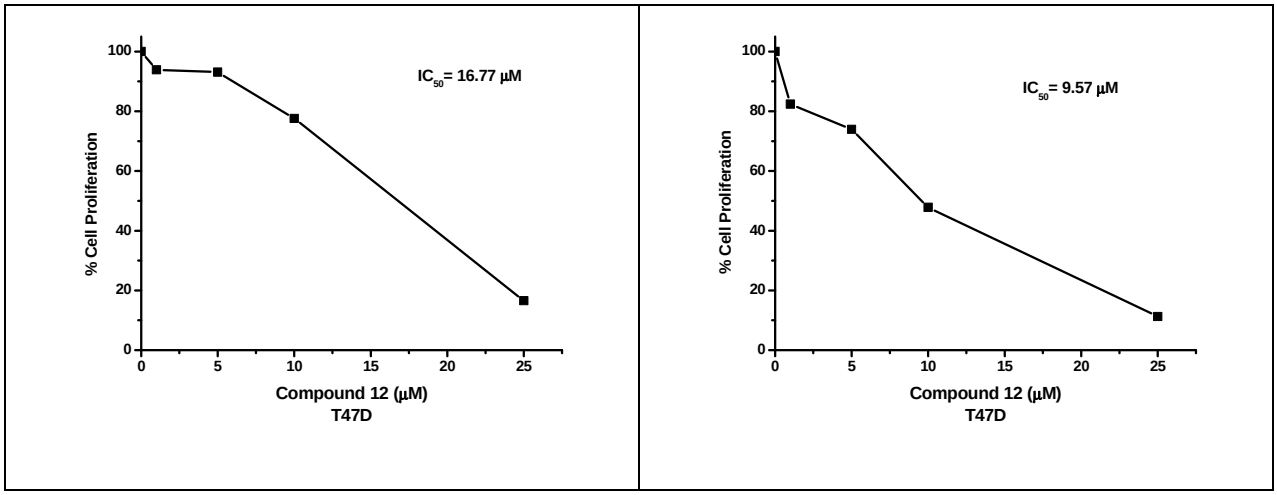


Fig S19: Plots for the % proliferation of T47D cells in the presence of compound **12**

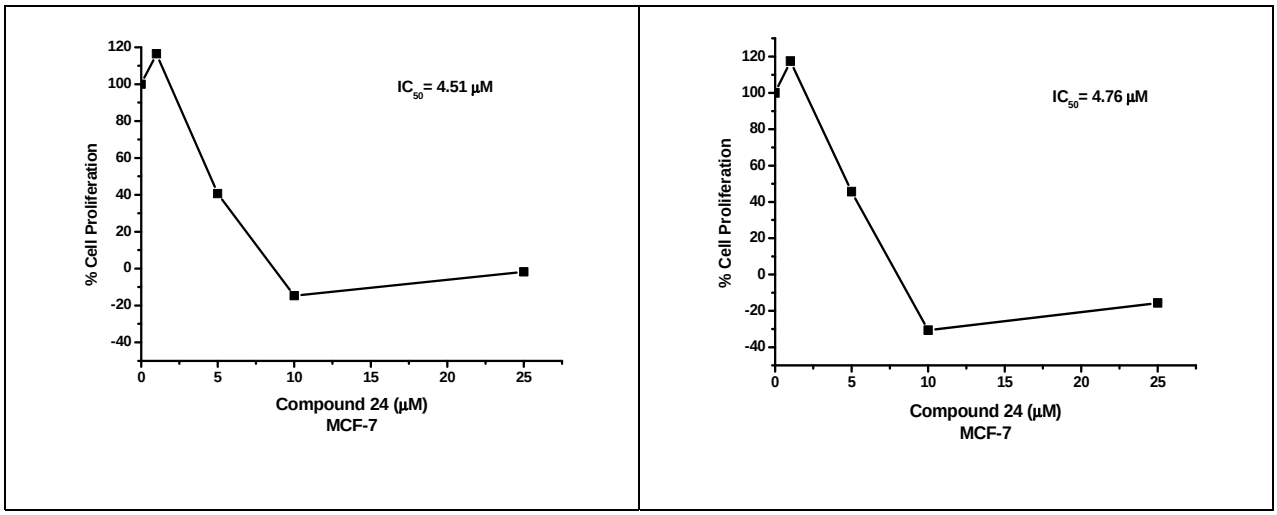


Fig S20: Plots for the % proliferation of MCF-7 cells in the presence of compound **24**

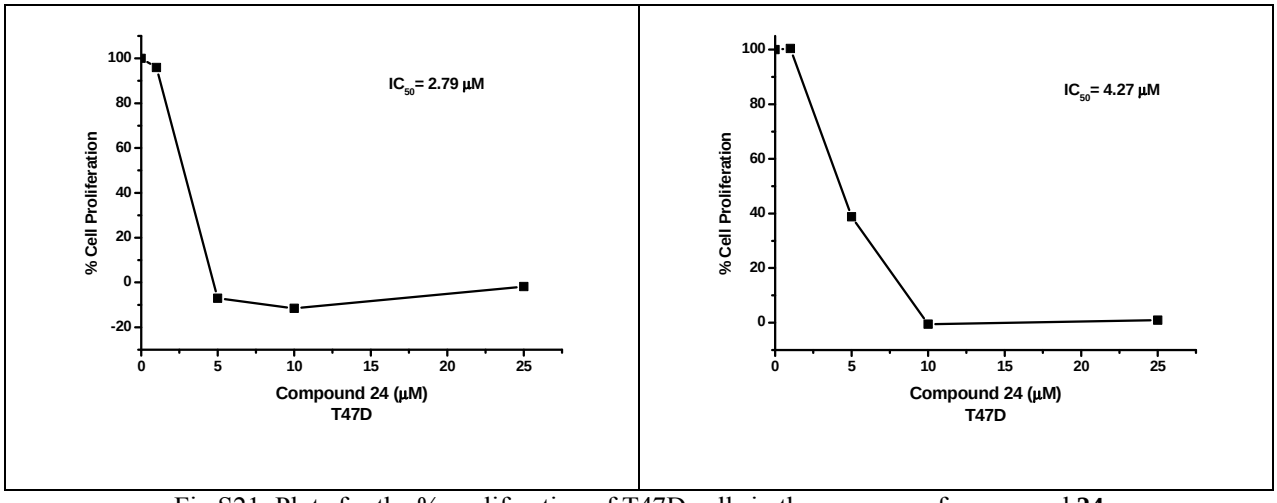


Fig S21: Plots for the % proliferation of T47D cells in the presence of compound **24**

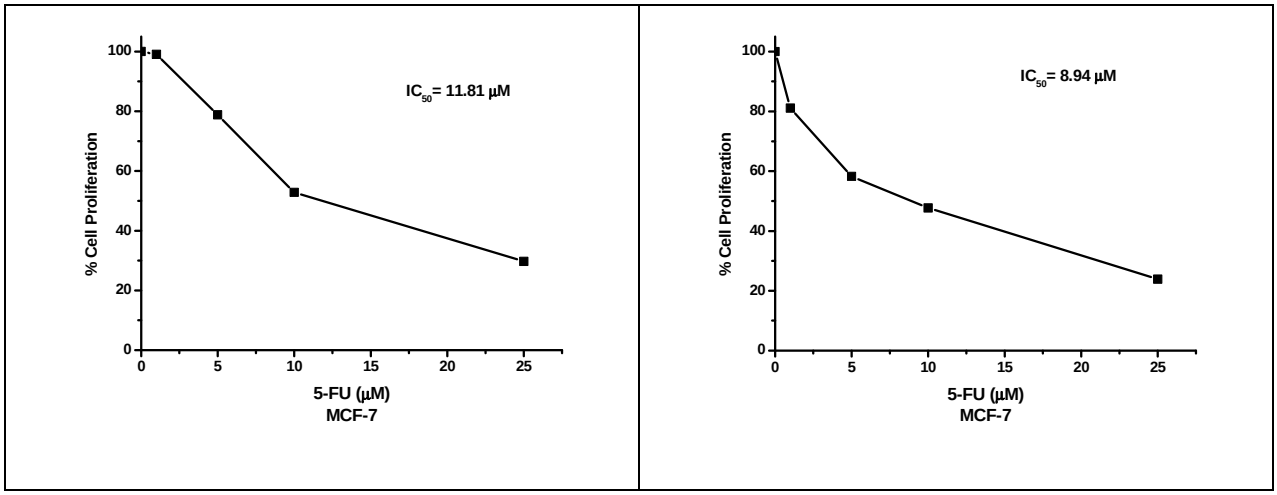


Fig S22: Plots for the % proliferation of MCF-7 cells in the presence of 5-FU.

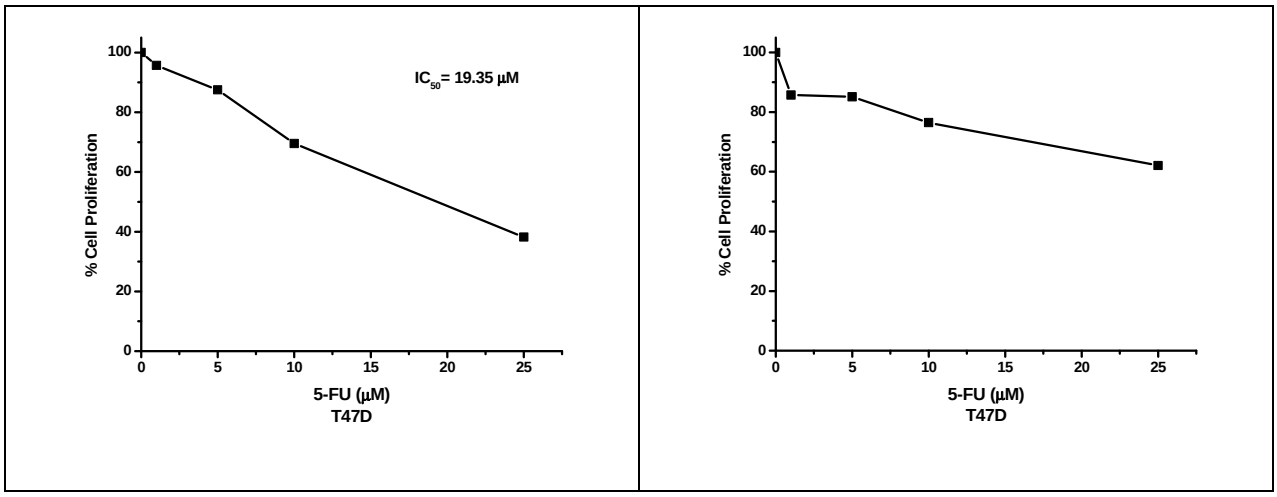


Fig S23: Plots for the % proliferation of T47D cells in the presence of 5-FU.

IC_{50} values for selected compounds in other cell lines

	IC_{50} values (µM)	
Compounds	**MCF-7**	**T47D**
1	21.34 ± 3.22	13.3 ± 0.48
12	7.71 ± 0.45	13.17 ± 3.6
24	4.64 ± 0.13	3.53 ± 0.74
5-FU	10.38 ± 1.44	-

Table 1: IC_{50} values of selected compounds on ER+ breast cancer cell lines.

Anti-proliferative activity of compound 12 in breast cancer cells (MDA-MB-231) and normal cells (L-132)

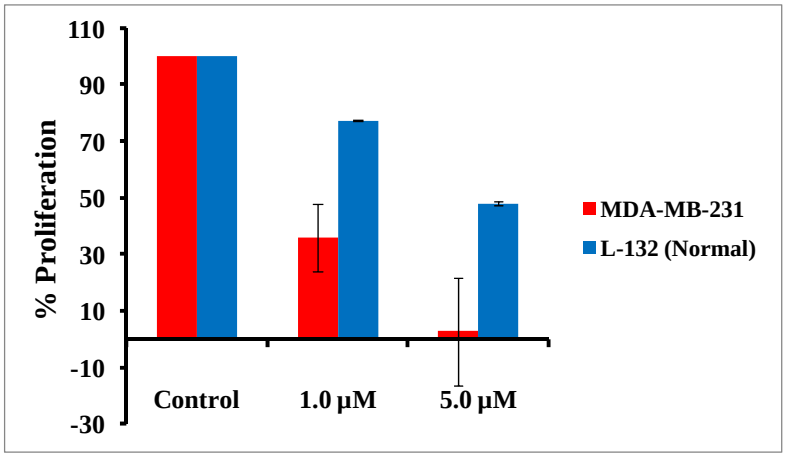


Fig S24. Percentage proliferation of MDA-MB-231 and L-132 cells in the presence of compound **12** at two different concentrations (1.0 µM and 5.0 µM).

Hydrogen peroxide scavenging ability of test compounds

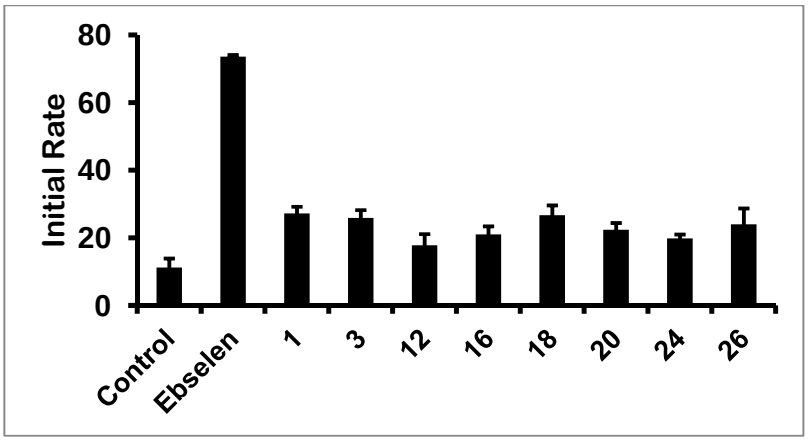


Fig S25: Initial rates (v_o) for the reduction of H_2O_2 using GSH as co-substrate in the presence and absence of some selected test compounds. The assay mixture contains GSH (2.0 mM), EDTA (1.0 mM), Glutathione reductase (2.0 units/ml), NADPH (0.4 mM) in phosphate buffer (0.1 M, pH = 7.5). The sample concentrations were maintained at 50 µM, and the reaction was started by the addition of 0.16 mM H_2O_2.

Peroxynitrite scavenging activity of test compounds

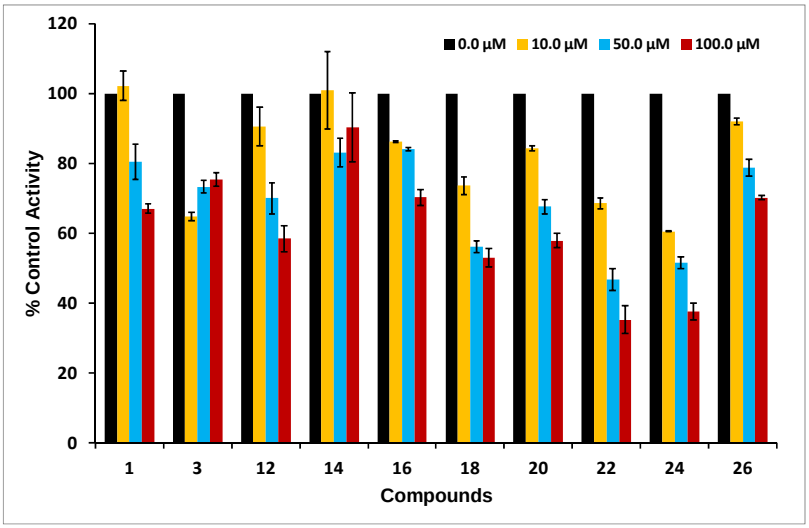


Fig S26: Peroxynitrite scavenging activity of some selected selenocyanates at different concentrations (0.0 µM, 10.0 µM, 50.0 µM and 100.0 µM). The assay mixture contained DHR-123 (1.0 µM), with variable concentration of test compounds in phosphate buffer (0.1 M, pH = 7.4) with appropriate concentration of PN to have fluorescence emission of rhodamine-123 in the range of (7.0-9.0)x10^6.

Peroxynitrite scavenging activity of ebselen

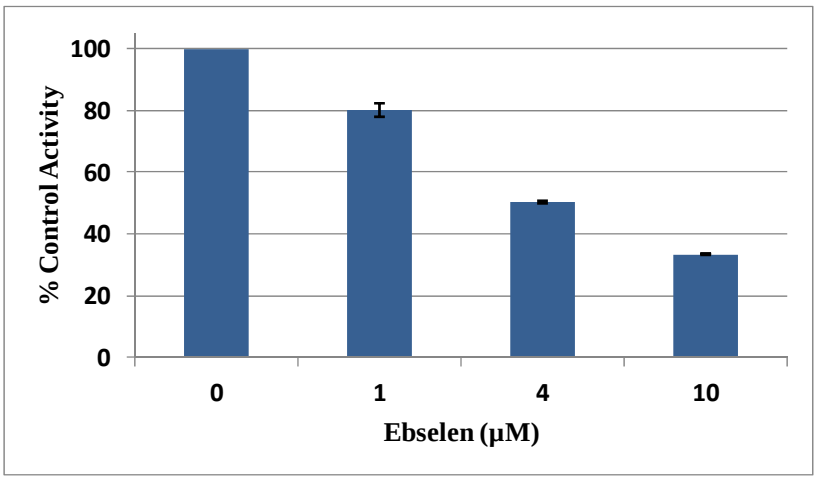
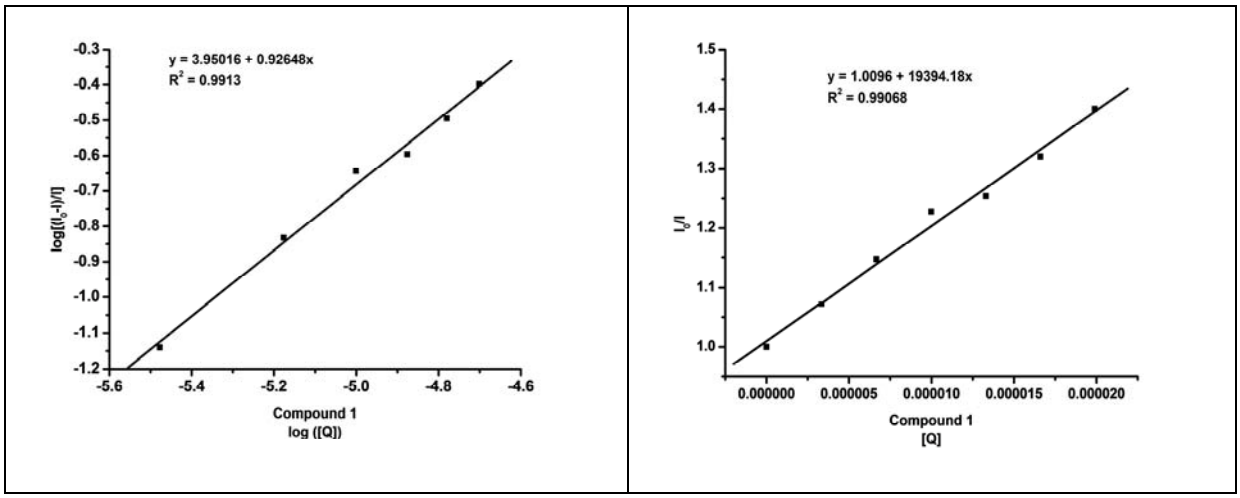


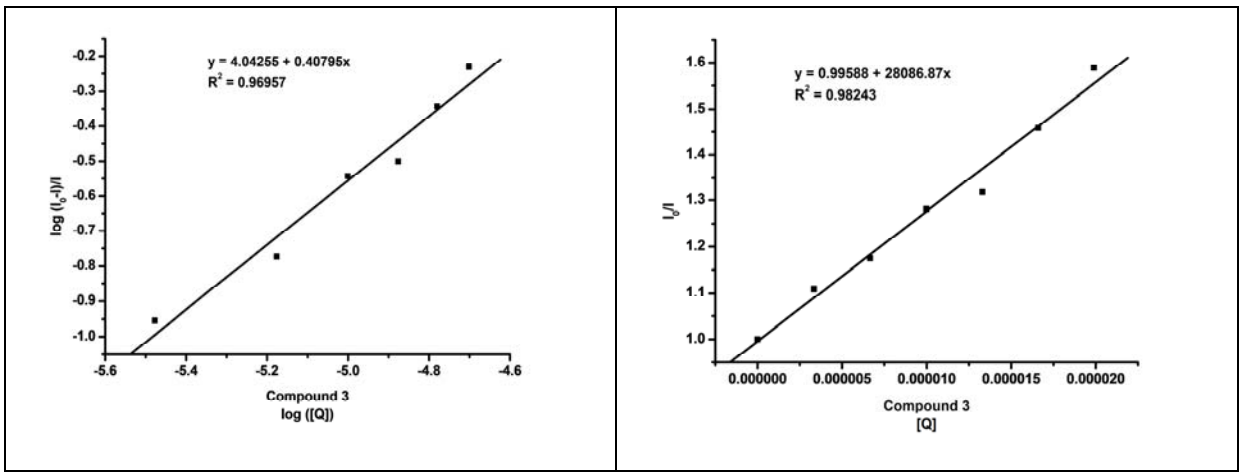
Fig S27: Effect of ebselen on the peroxynitrite-mediated oxidation of DHR-123.

Plots for the interaction of test compounds with BSA



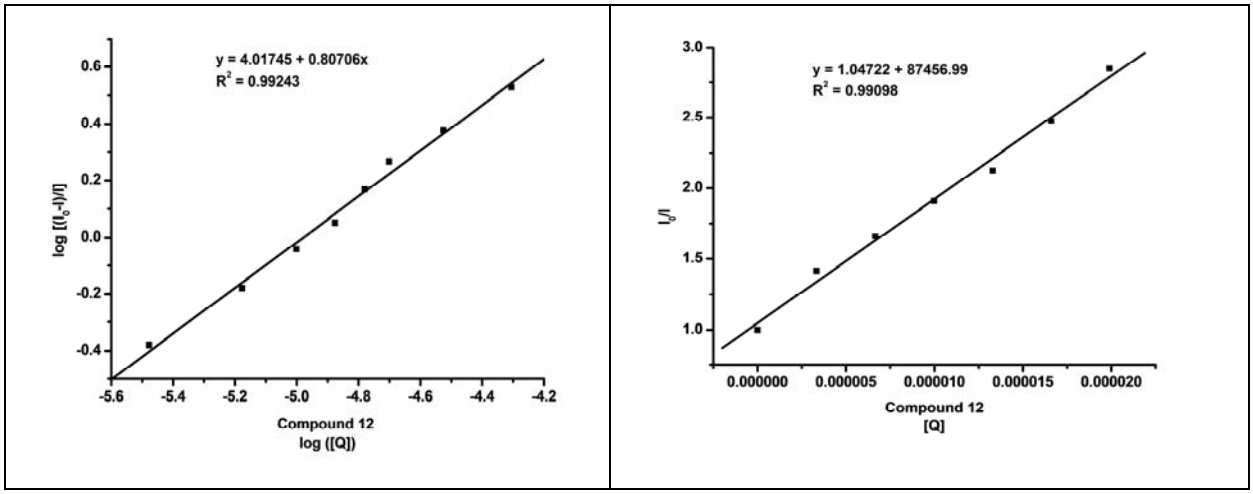
(a) (b)

Fig S28: (a) Scatchard plot and (b) Stern-Volmer plot of compound **1**.



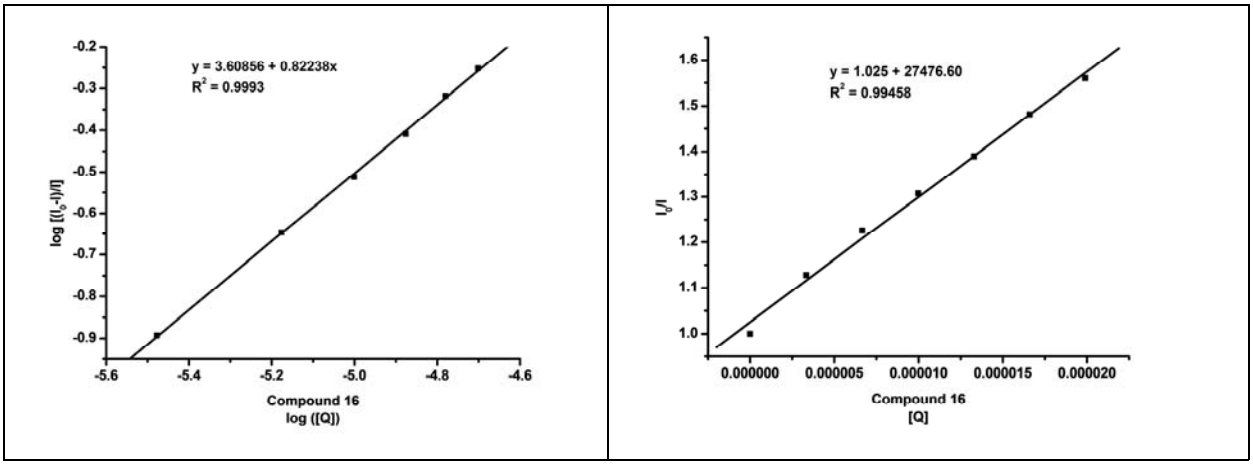
(a) (b)

Fig S29: (a) Scatchard plot and (b) Stern-Volmer plot of compound **3**.



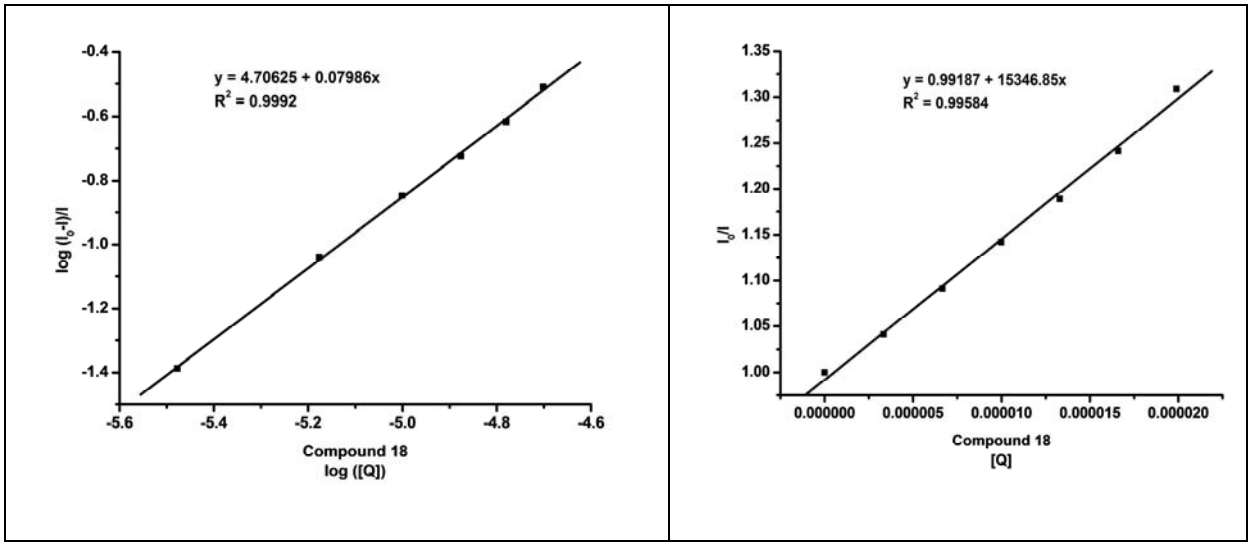
(a) (b)

Fig S30: (a) Scatchard plot and (b) Stern-Volmer plot of compound **12**.



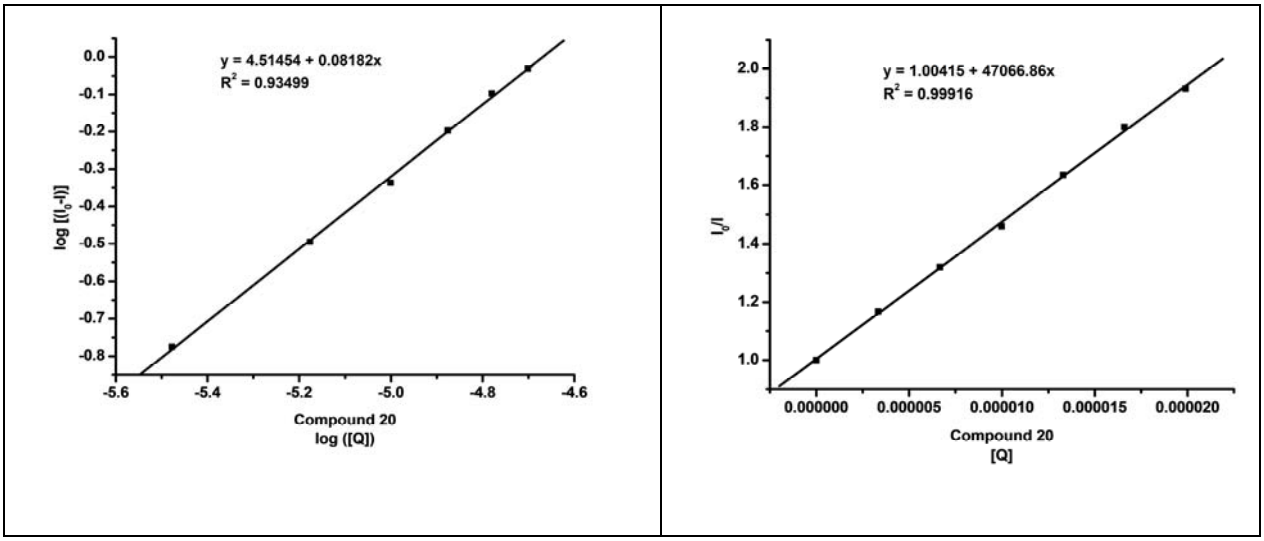
(a) (b)

Fig S31: (a) Scatchard plot and (b) Stern-Volmer plot of compound **16**.



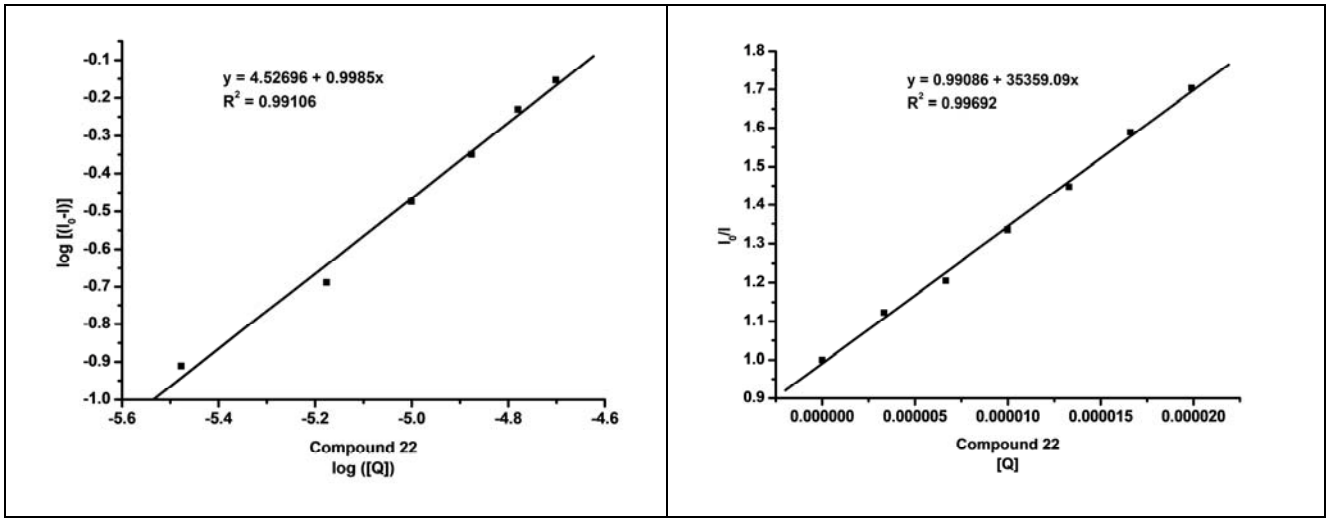
(a) (b)

Fig S32: (a) Scatchard plot and (b) Stern-Volmer plot of compound **18**.



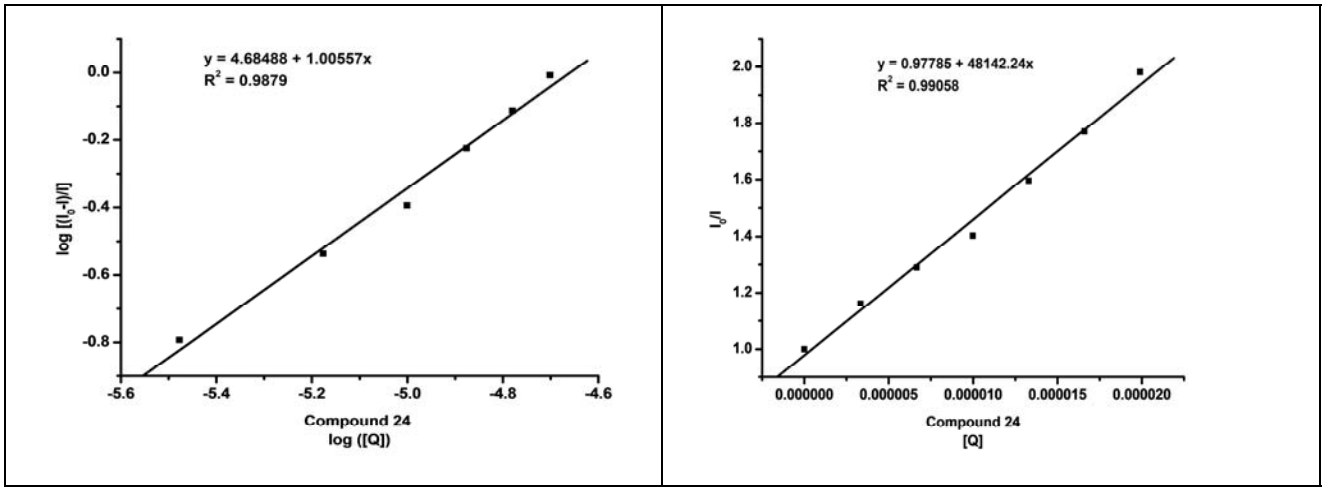
(a) (b)

Fig S33: (a) Scatchard plot and (b) Stern-Volmer plot of compound **20**.



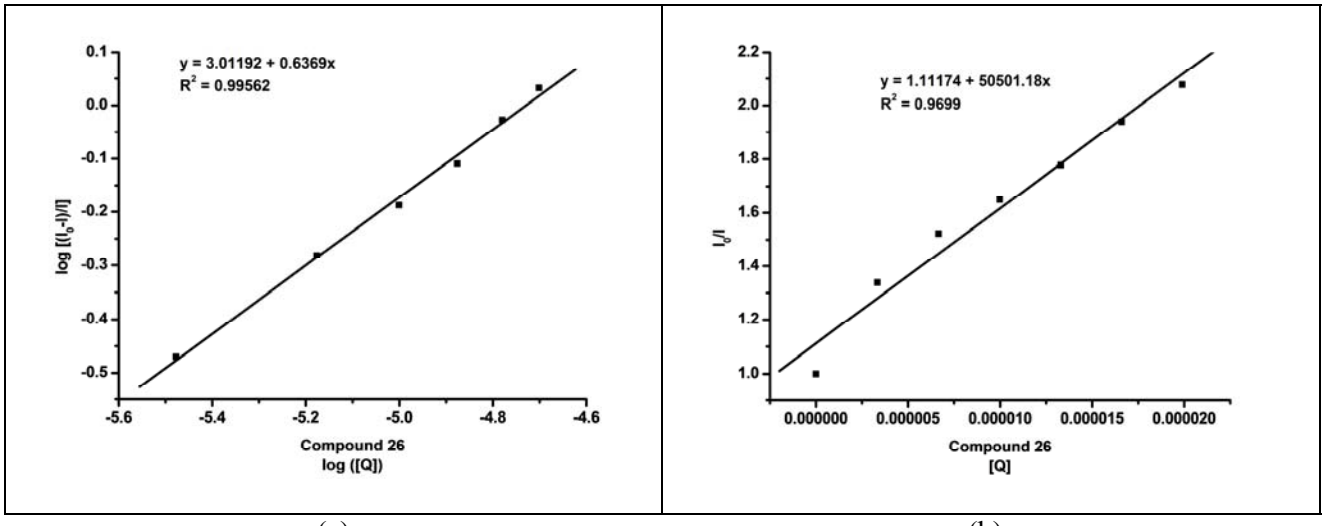
(a) (b)

Fig S34: (a) Scatchard plot and (b) Stern-Volmer plot of compound **22**.



(a) (b)

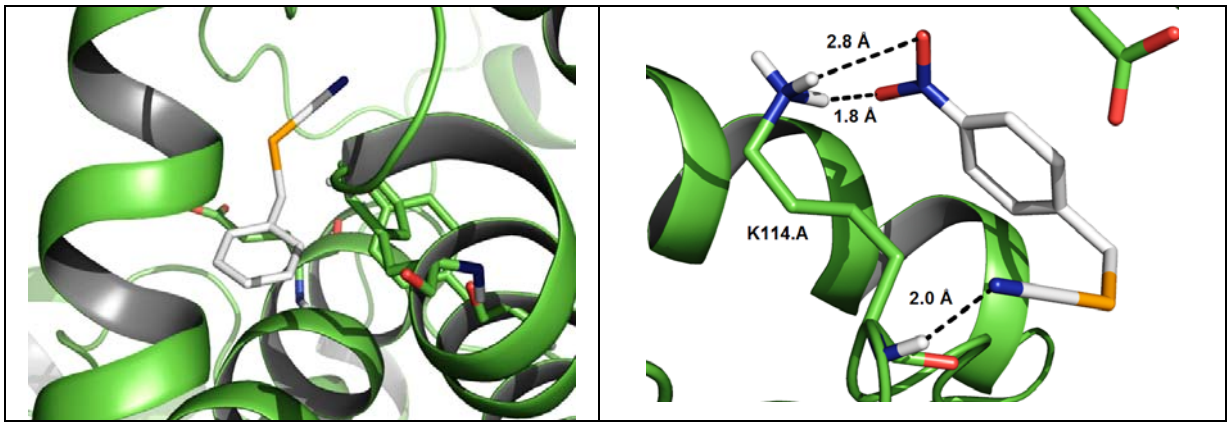
Fig S35: (a) Scatchard plot and (b) Stern-Volmer plot of compound **24**.



(a) (b)

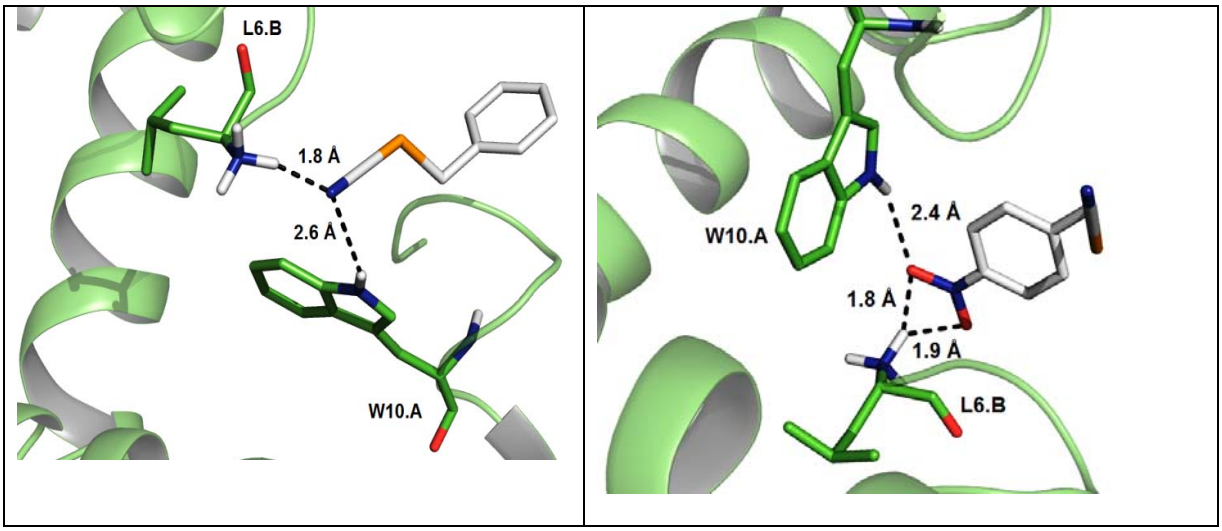
Fig S36: (a) Scatchard plot and (b) Stern-Volmer plot of compound **26**.

Protein-ligand interactions of compounds 1 and 12 with BSA, Survivin, Bcl-2 and COX-2



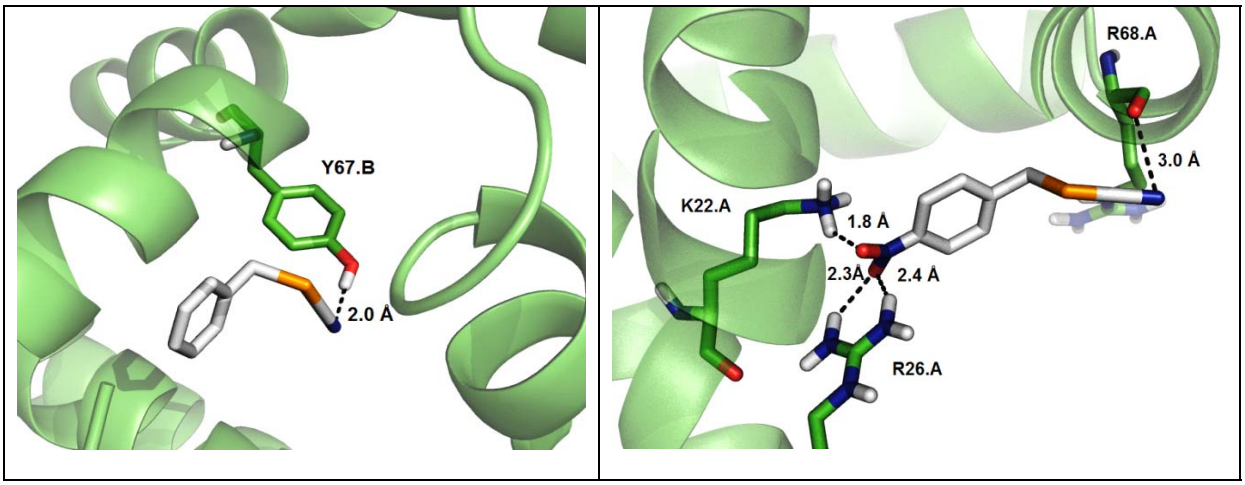
(a) (b)

Fig S37: Molecular interactions of (a) Compound **1** and (b) Compound **12** with BSA.



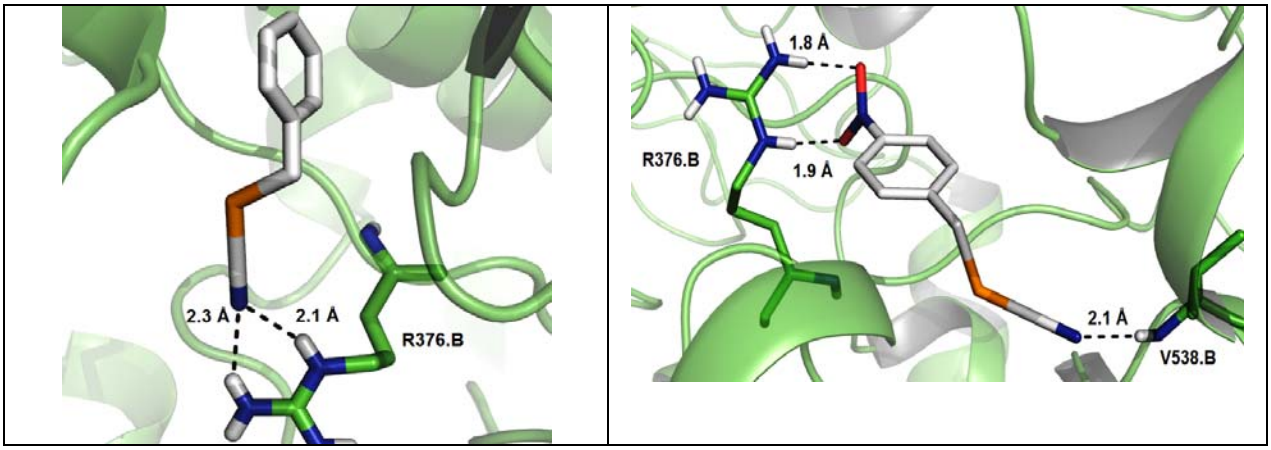
(a) (b)

Fig S38: Molecular interactions of (a) Compound **1** and (b) Compound **12** with Survivin.



(a) (b)

Fig S39: Molecular interactions of (a) Compound **1** and (b) Compound **12** with Bcl-2.

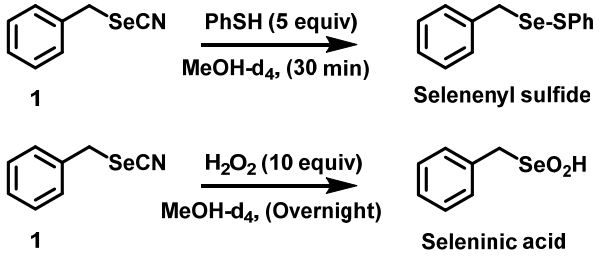


(a) **(b)**

Fig S40**:** Molecular interactions of (a) Compound **1** and (b) Compound **12** with COX-2.

Reaction of selenocyanate 1 with thiophenol and hydrogen peroxide

Compound **1** was treated with 5 equivalents of thiophenol (PhSH) in NMR tube with methanol-d4 and the mixture was incubated at room temperature for 30 min. The product formation was monitored by ^{77}Se-NMR spectroscopy. In another experiment, compound **1** was treated with an excess amount of hydrogen peroxide (H_2O_2, 10 equiv) in NMR tube with methanol-d4 and the product formation was monitored by ^{77}Se NMR spectroscopy after an incubation of 12 h at room temperature (Figure S23).



Scheme S1: Reaction of selenocyanate **1** with thiophenol and hydrogen peroxide.

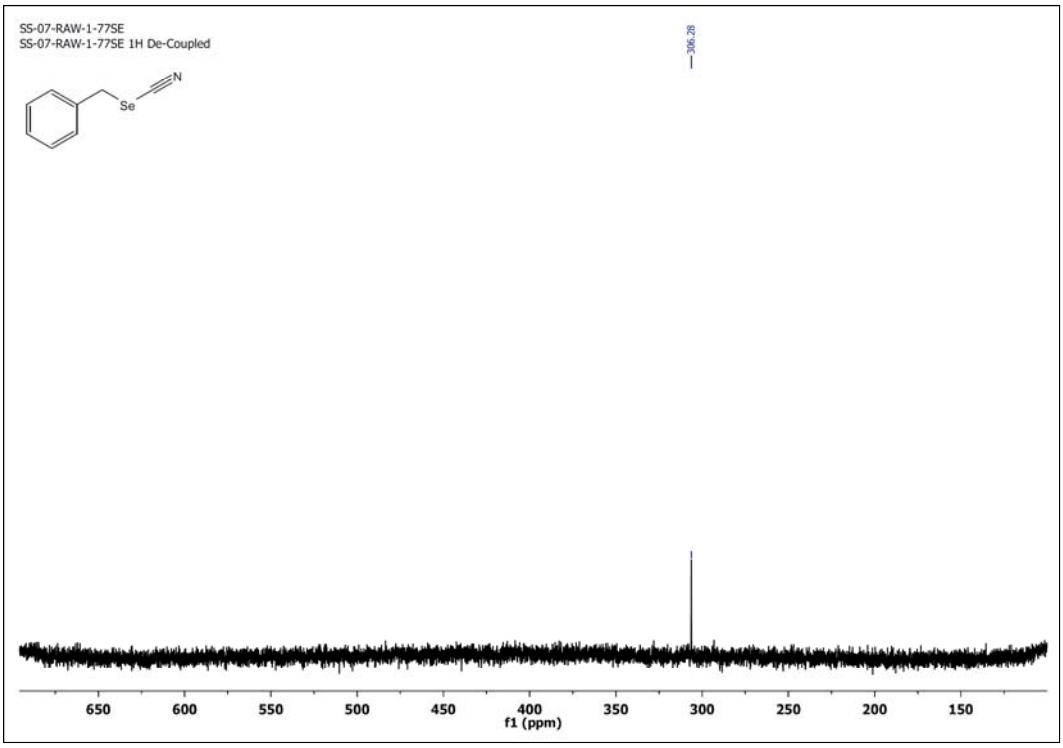


Fig S41: ^{77}Se NMR (76 MHz) spectrum of benzyl selenocyanate **1** in MeOH-d_4.

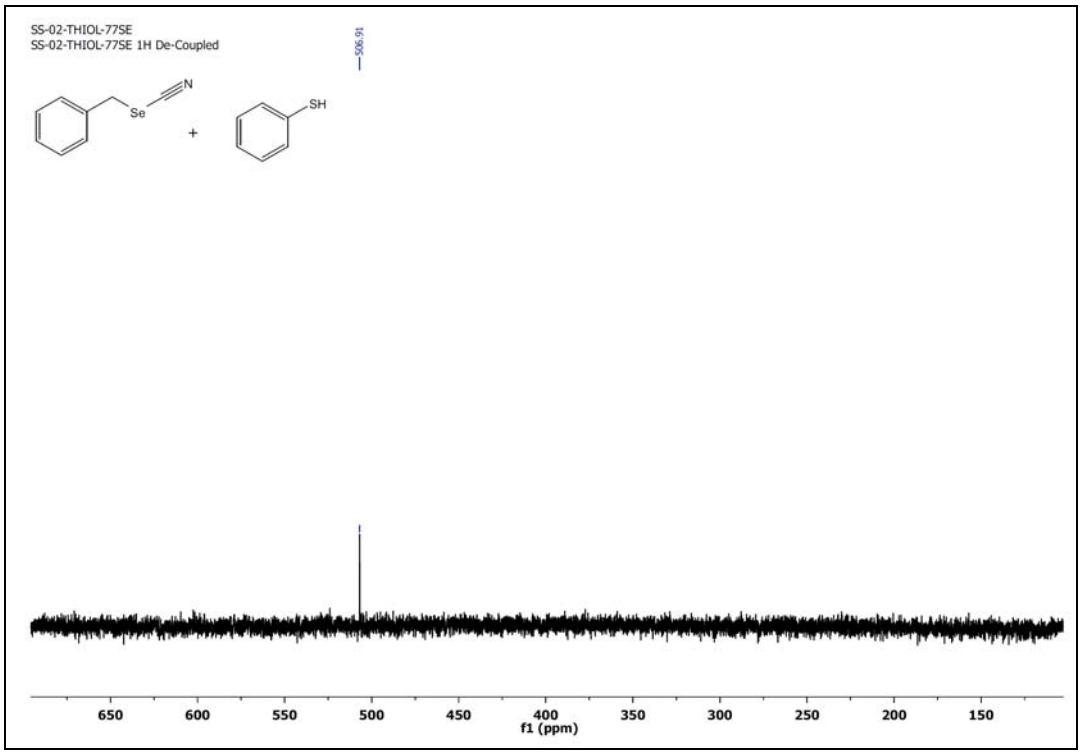


Fig S42: ^{77}Se NMR (76 MHz) spectrum of the mixture after addition of PhSH to compound **1** in MeOH-d_4.

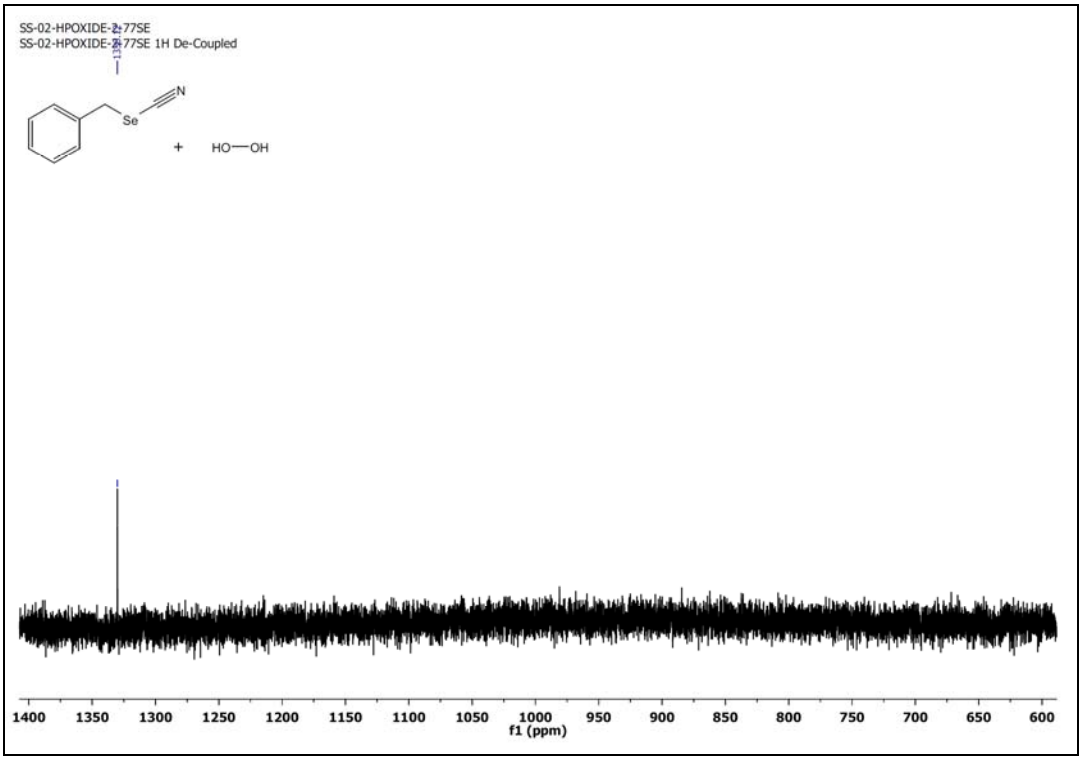


Fig S43: ^{77}Se NMR (76 MHz) spectrum of the mixture after addition of H_2O_2 to compound **1** in MeOH-d_4.

NMR spectra of synthesised selenocyanates and thiocyanates

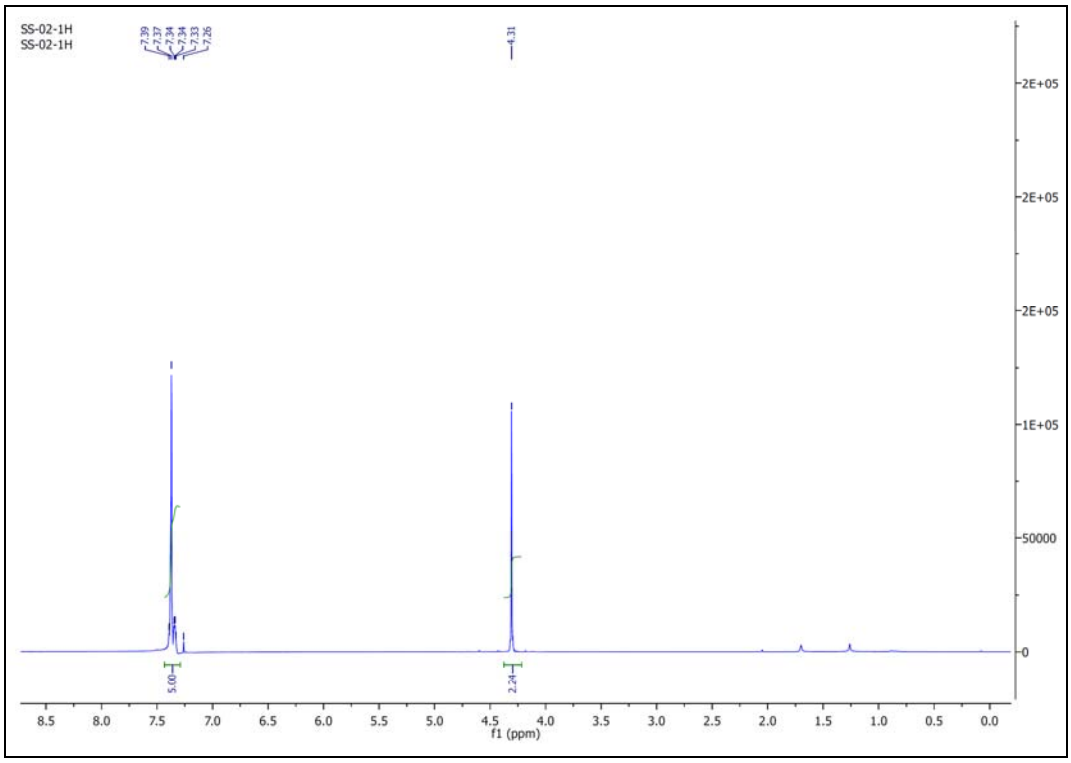


Fig S44: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **1**.

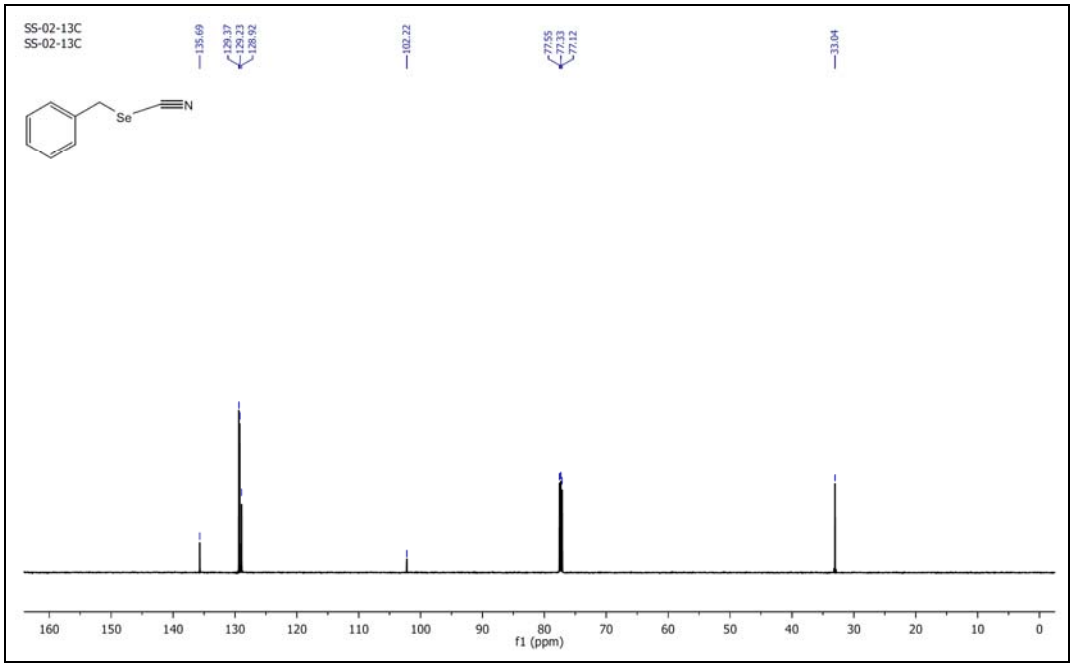


Fig S45: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **1.**

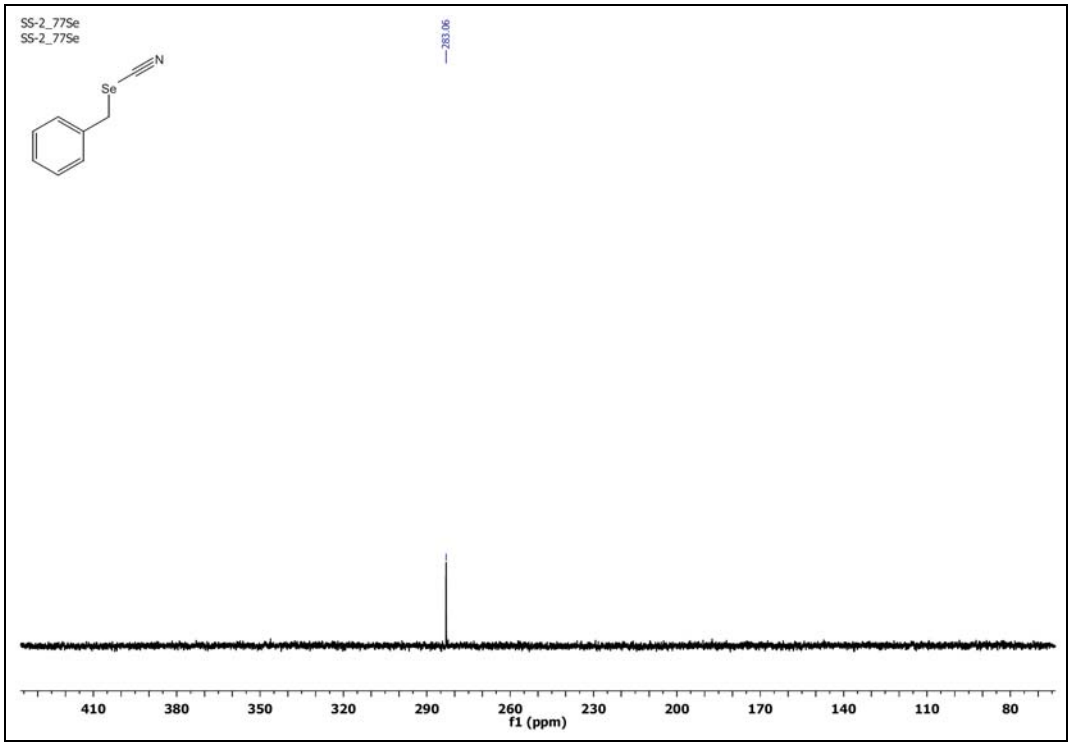


Fig S46: ^{77}Se NMR spectrum (114 MHz, $CDCl_3$) of Compound **1**.

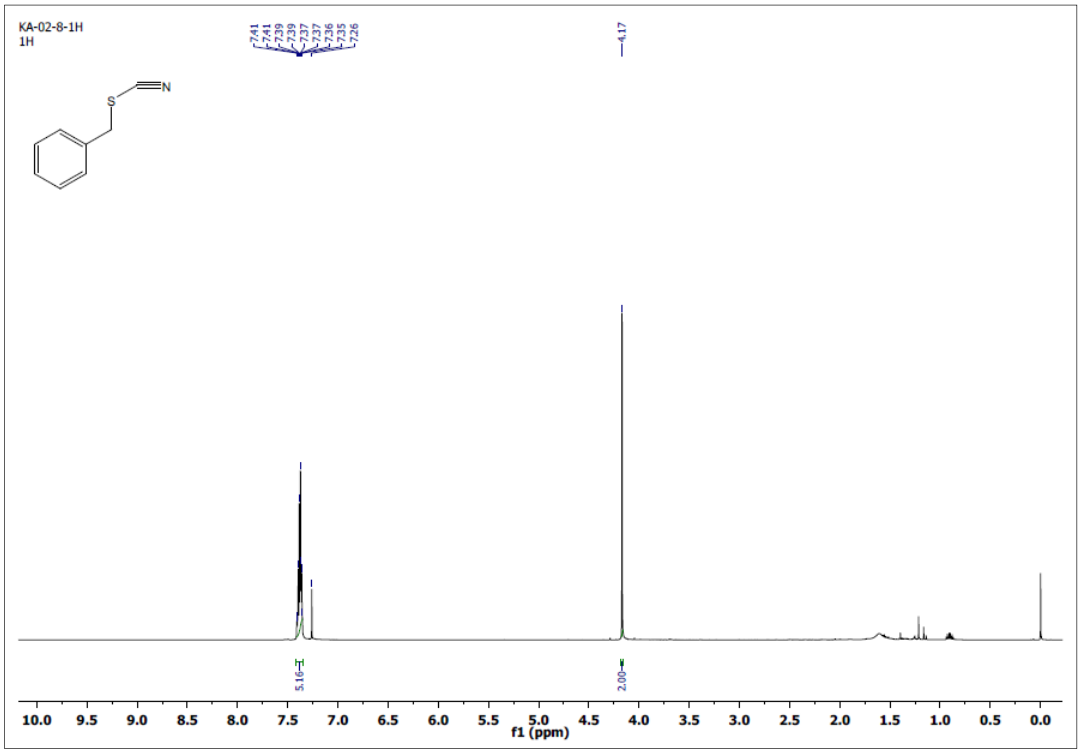


Fig S47: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **2**.

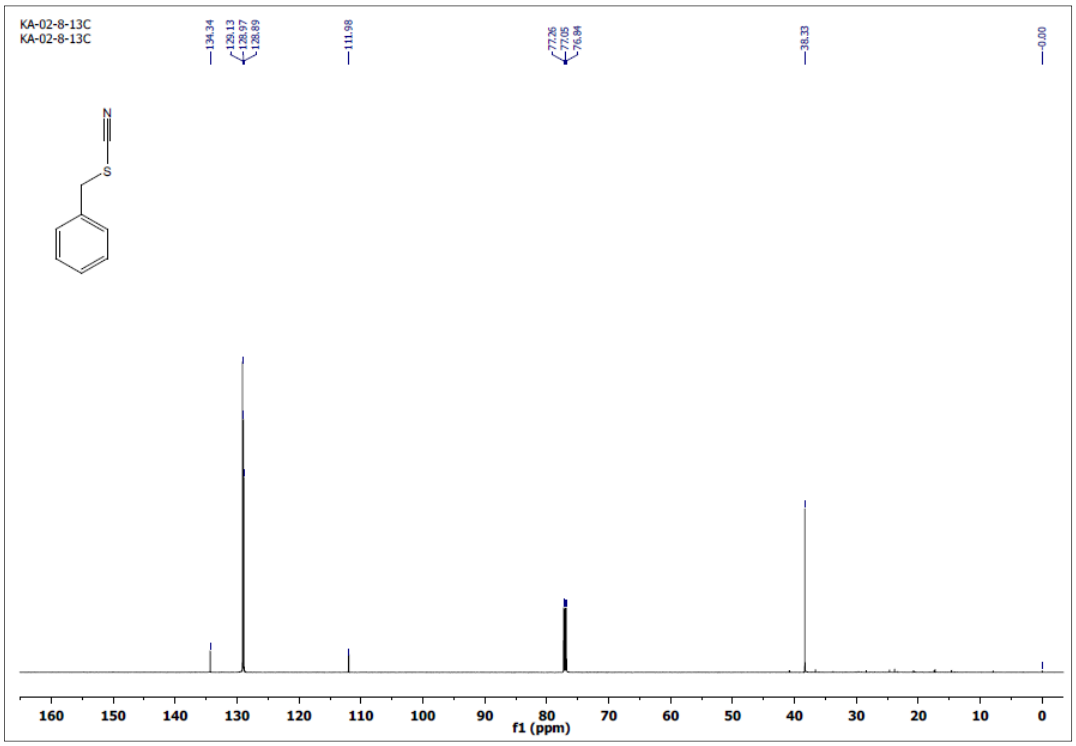


Fig S48: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **2**.

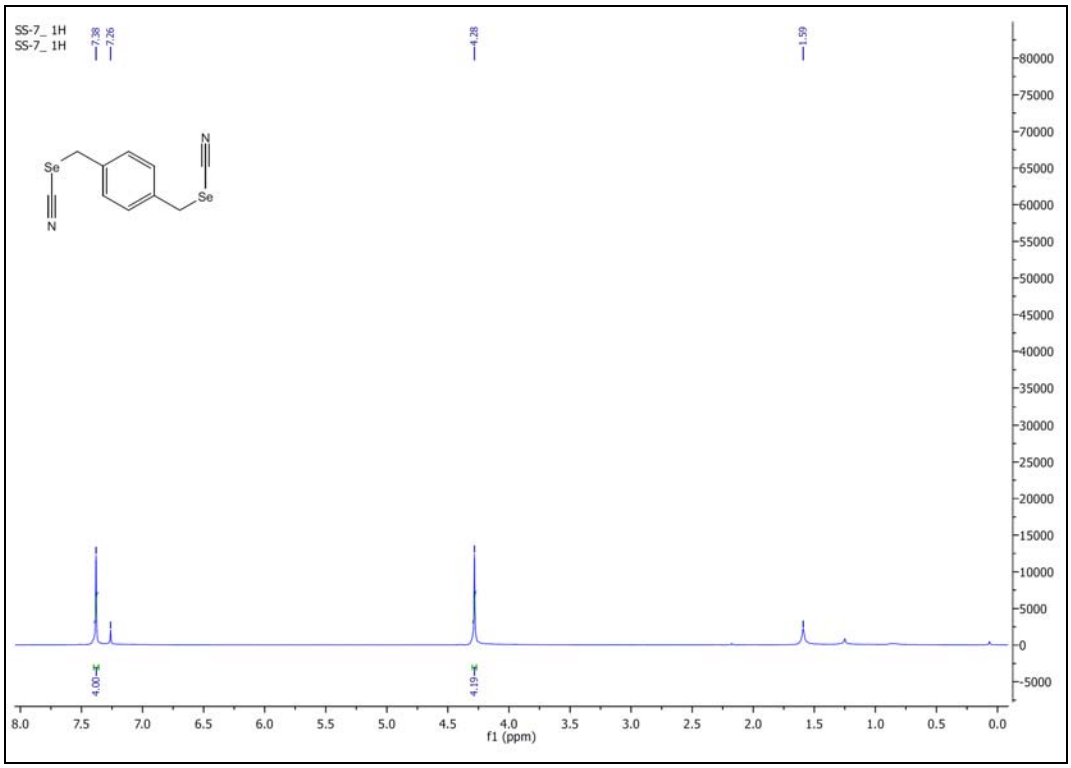


Fig S49: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **3.**

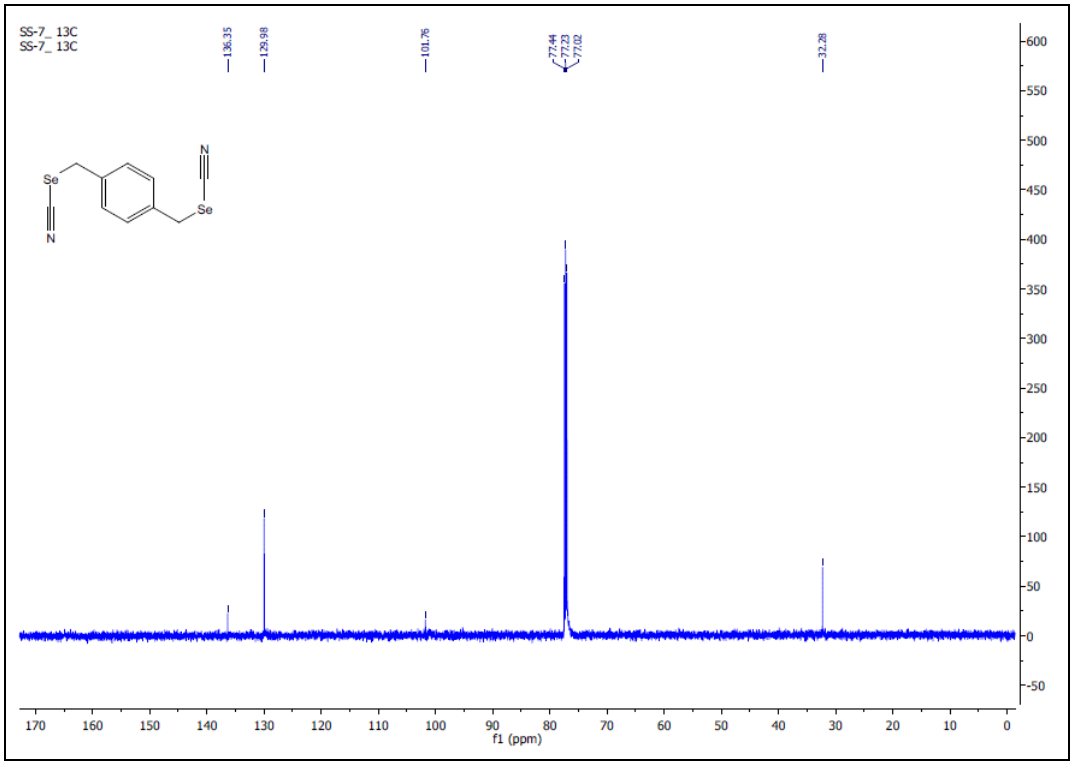


Fig S50: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **3.**

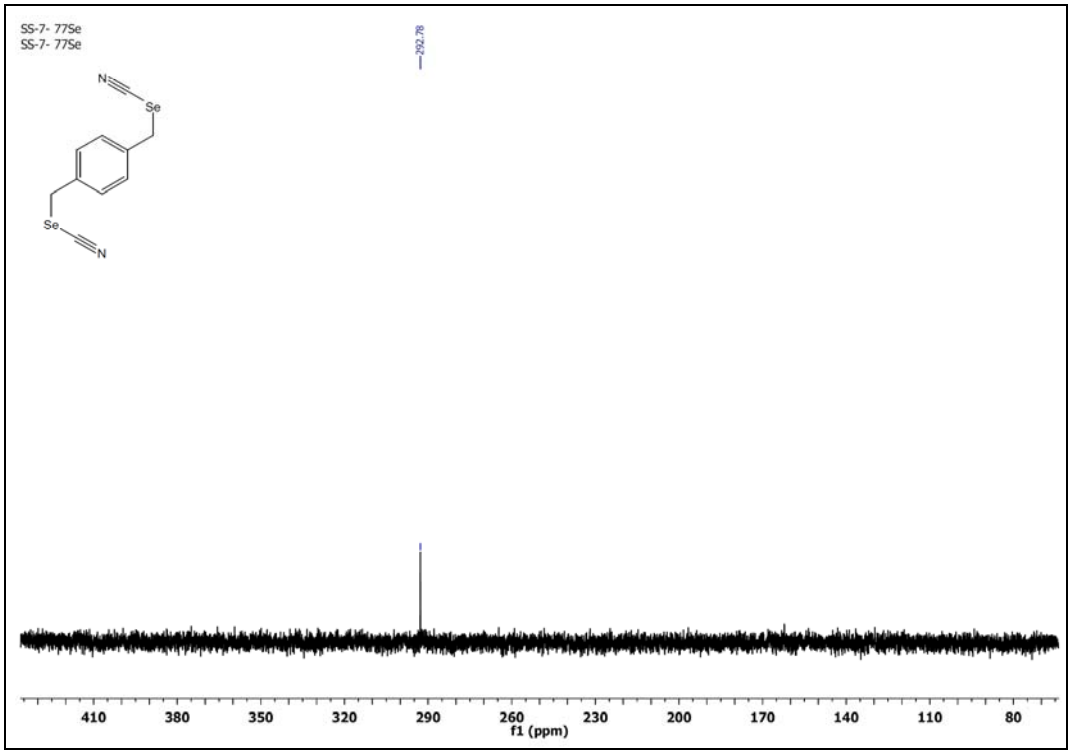


Fig S51: ^{77}Se NMR spectrum (114 MHz, $CDCl_3$) of Compound **3.**

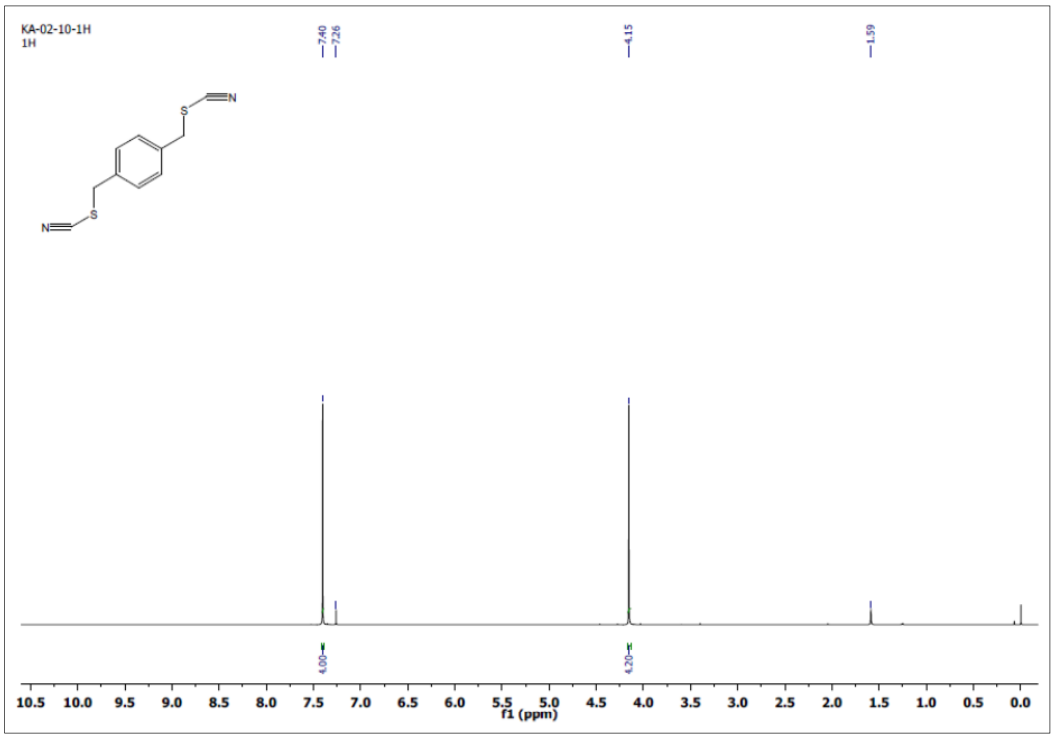


Fig S52: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **4.**

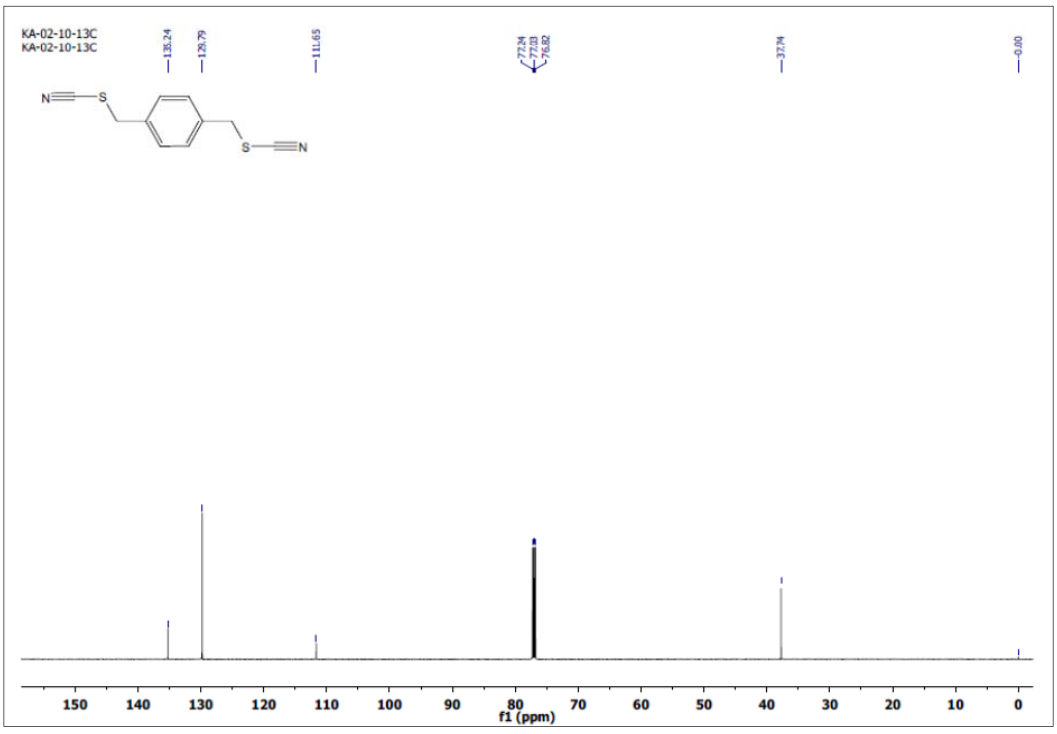


Fig S53: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **4.**

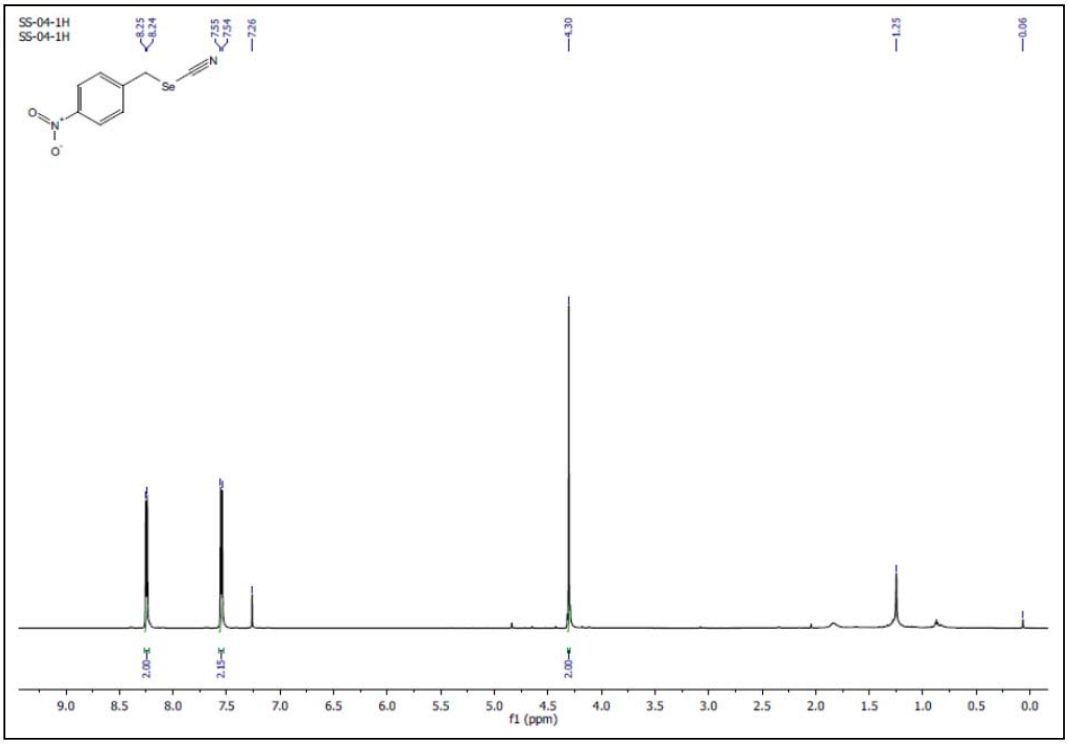


Fig S54: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **12.**

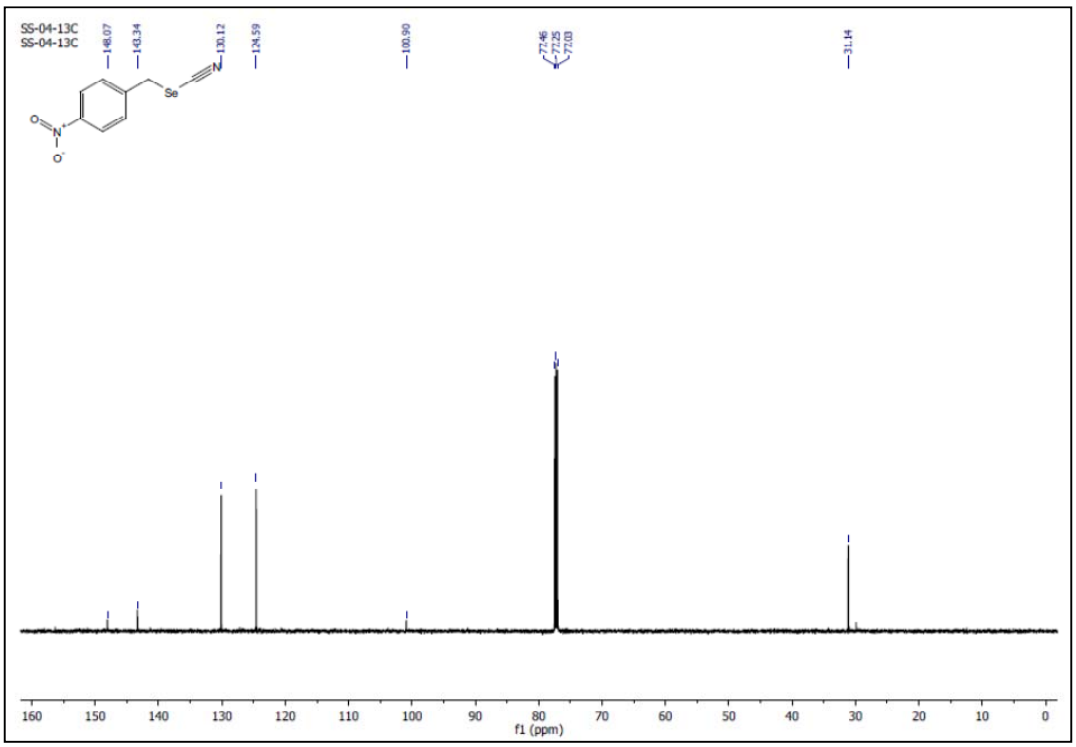


Fig S55: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **12.**

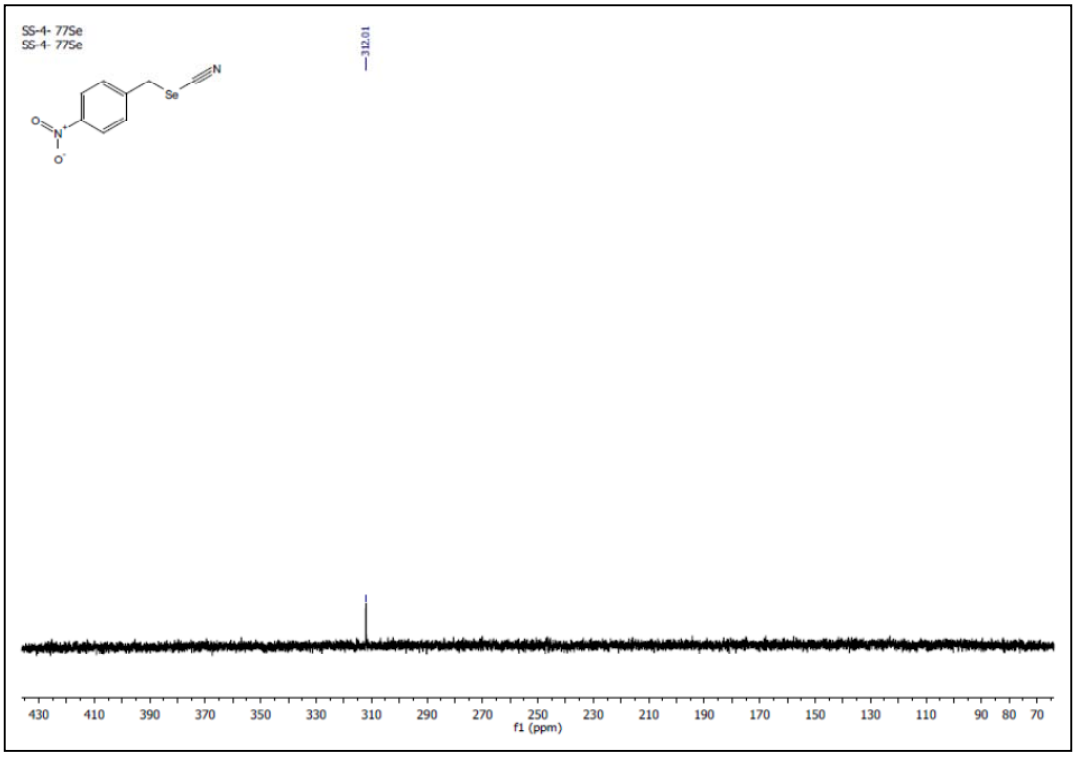


Fig S56: ^{77}Se NMR spectrum (114 MHz, $CDCl_3$) of Compound **12.**

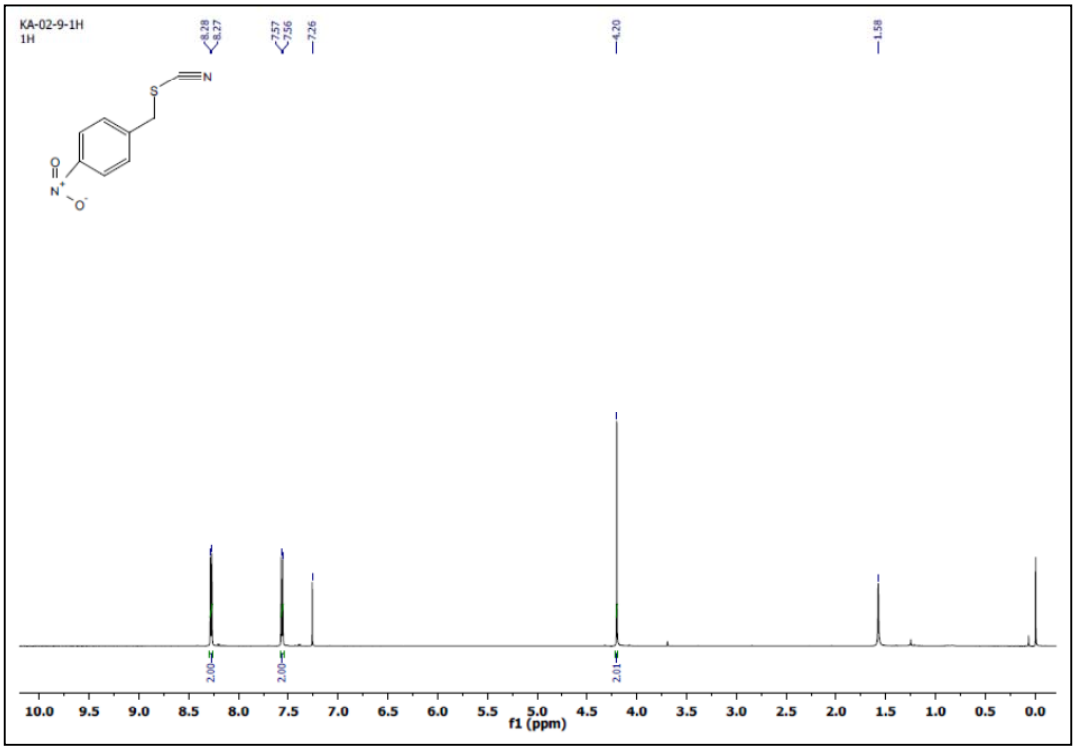


Fig S57: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **13.**

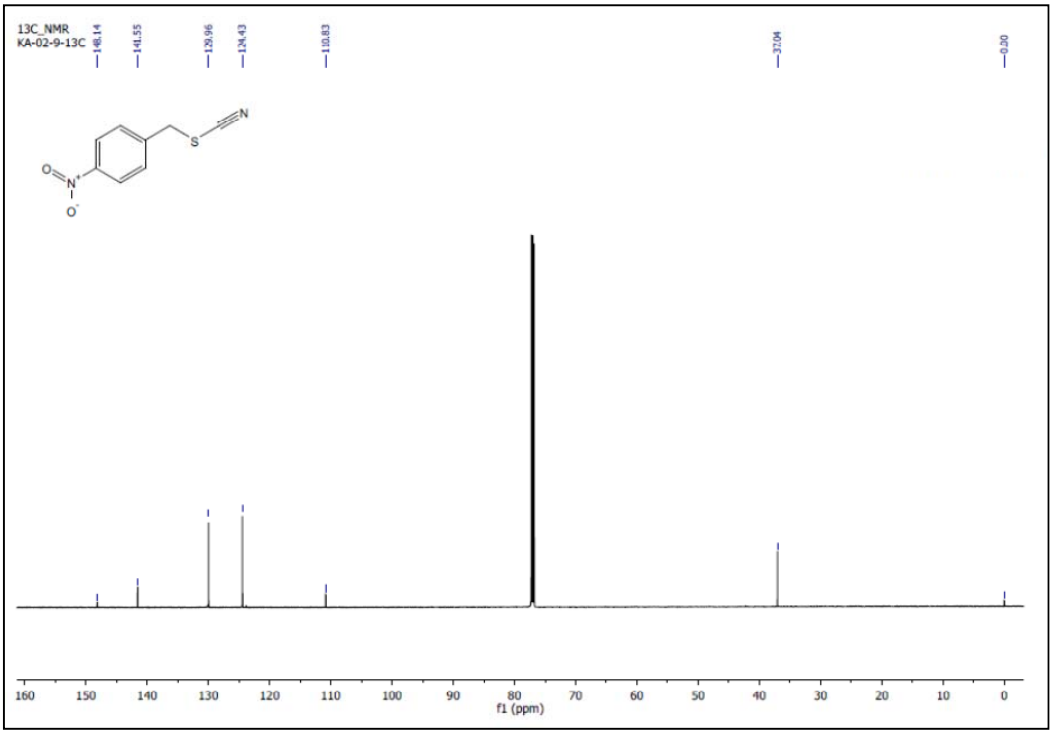


Fig S58: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **13.**

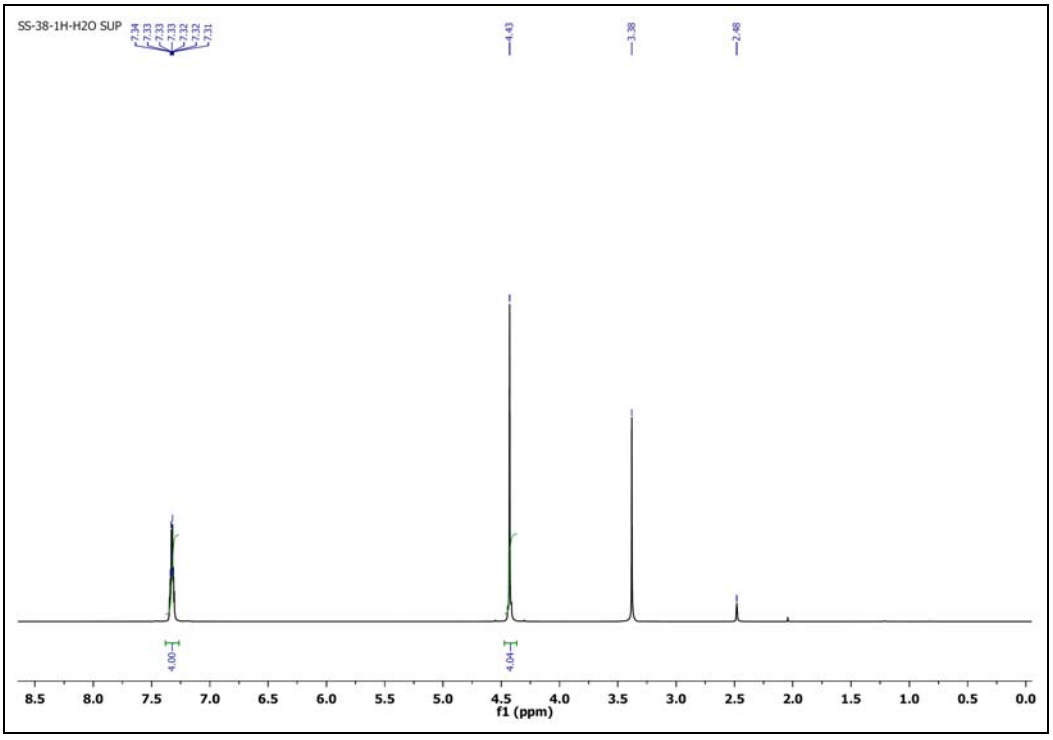


Fig S59: ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of Compound **14.**

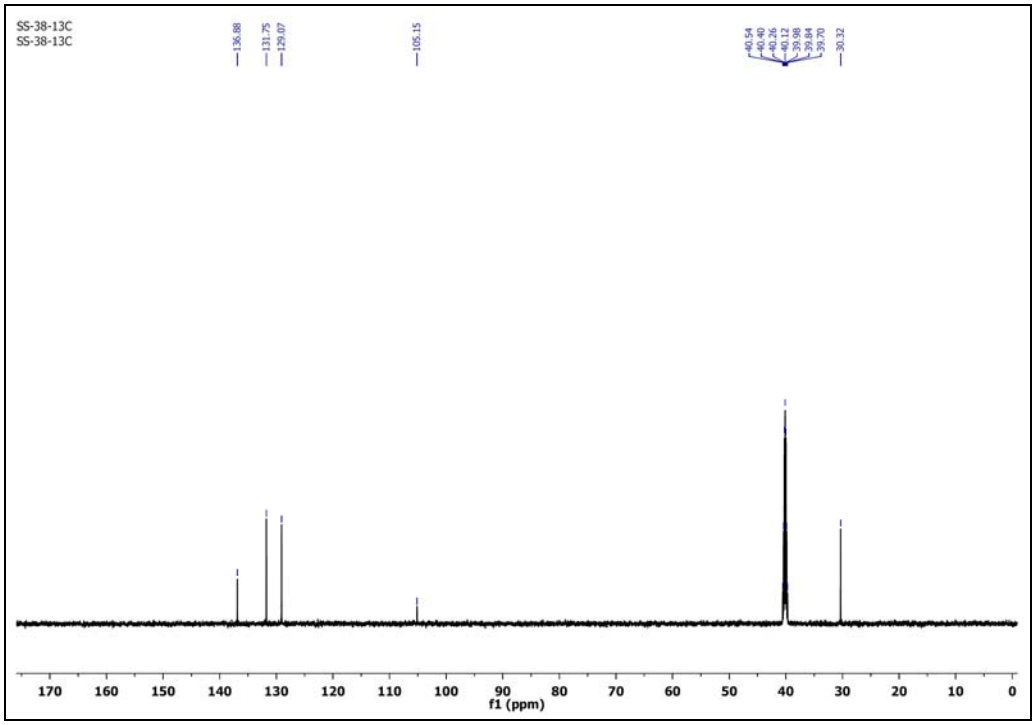


Fig S60: ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of Compound **14.**

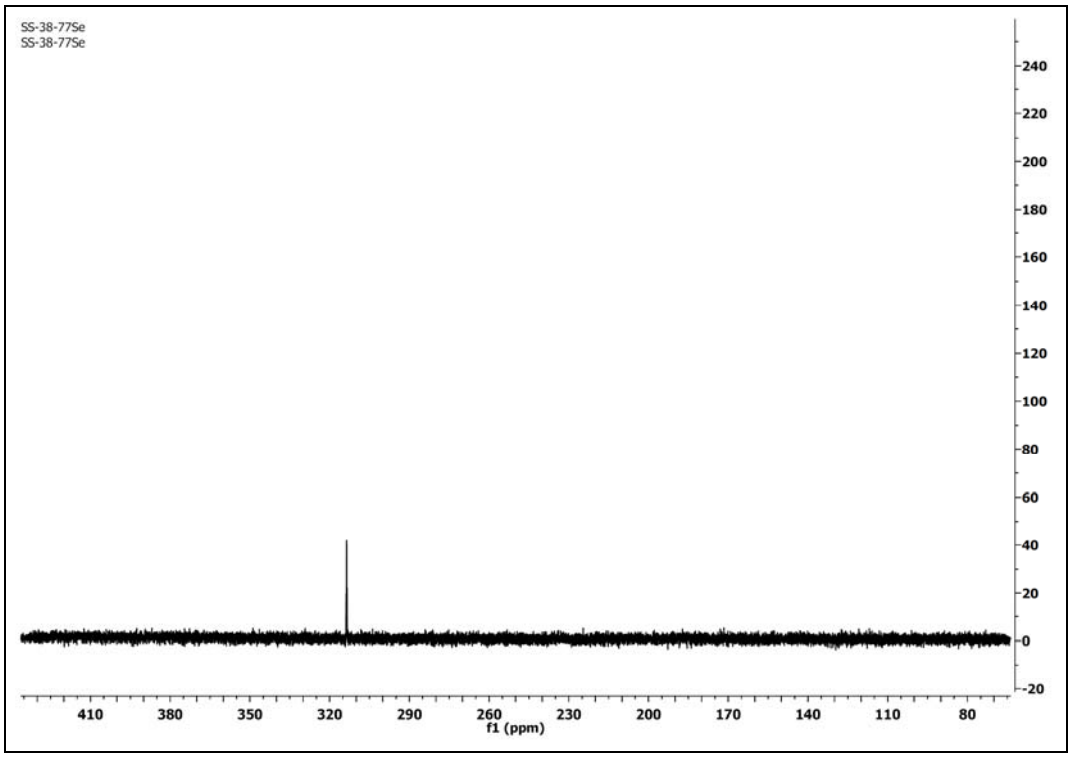


Fig S61: ^{77}Se NMR spectrum (114 MHz, DMSO-d_6) of Compound **14.**

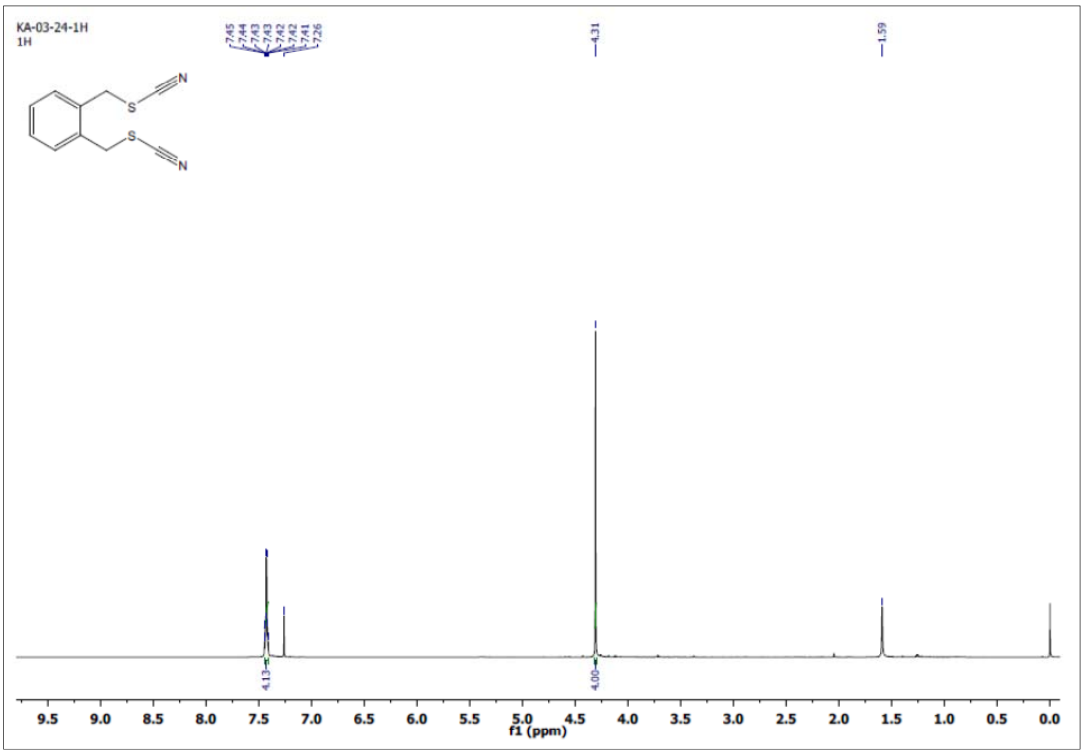


Fig S62: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **15.**

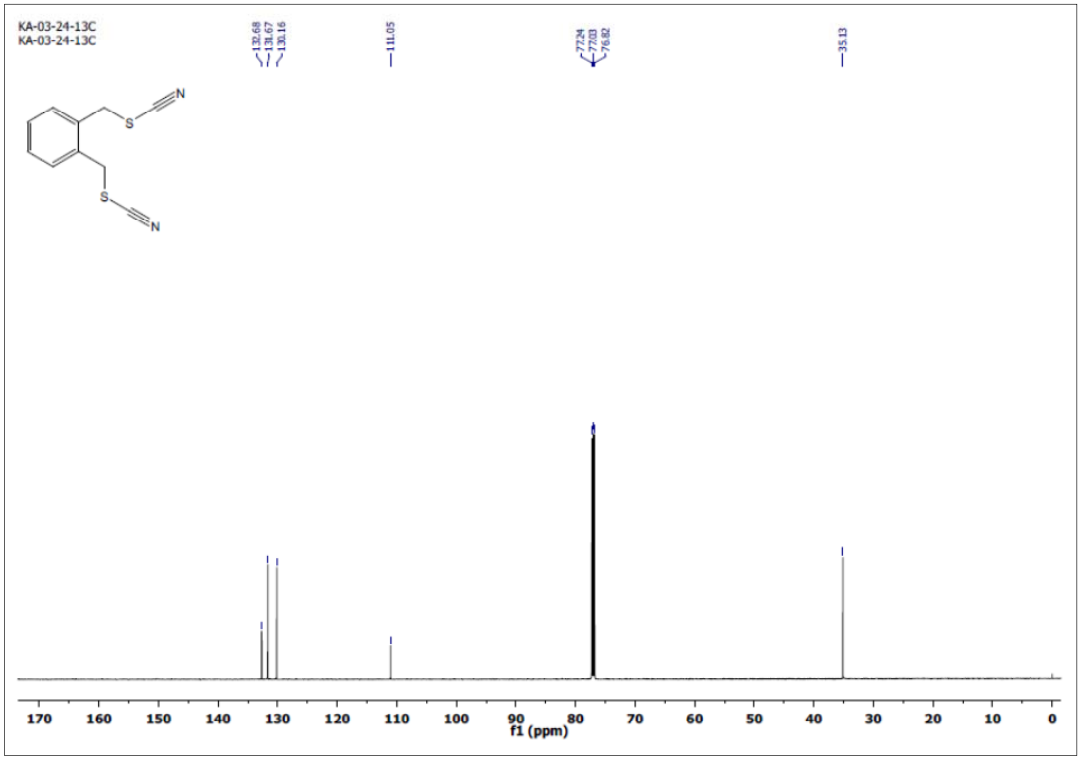


Fig S63: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **15.**

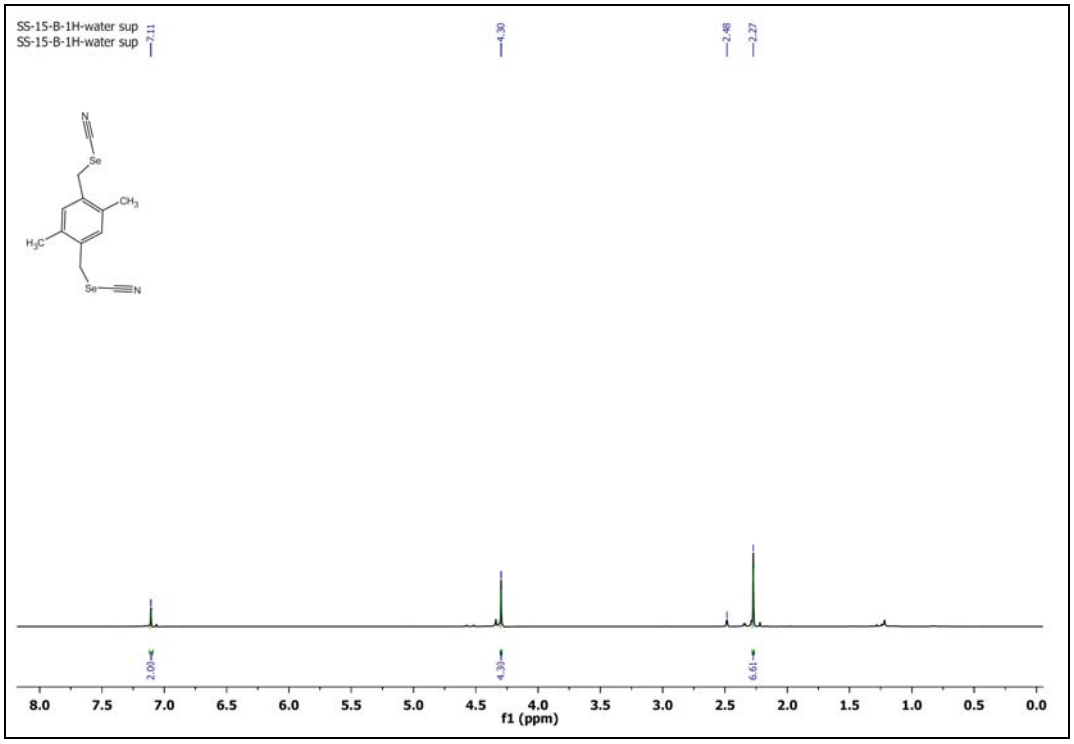


Fig S64: ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of Compound **16.**

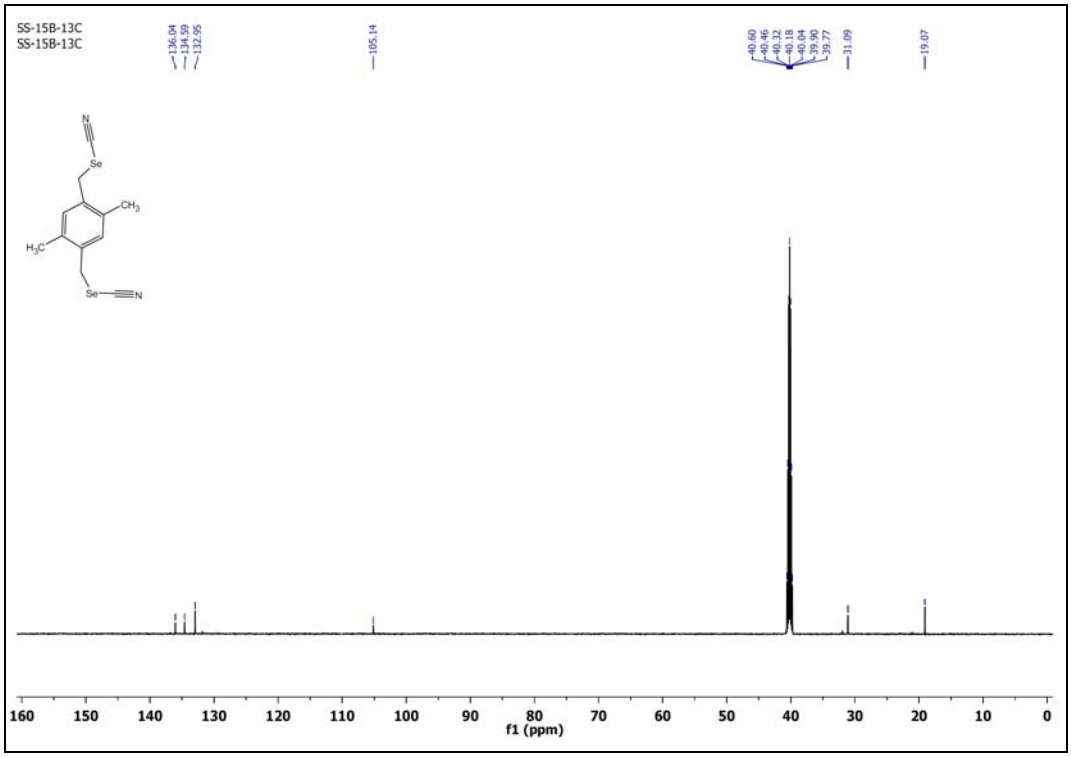


Fig S65: ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of Compound **16.**

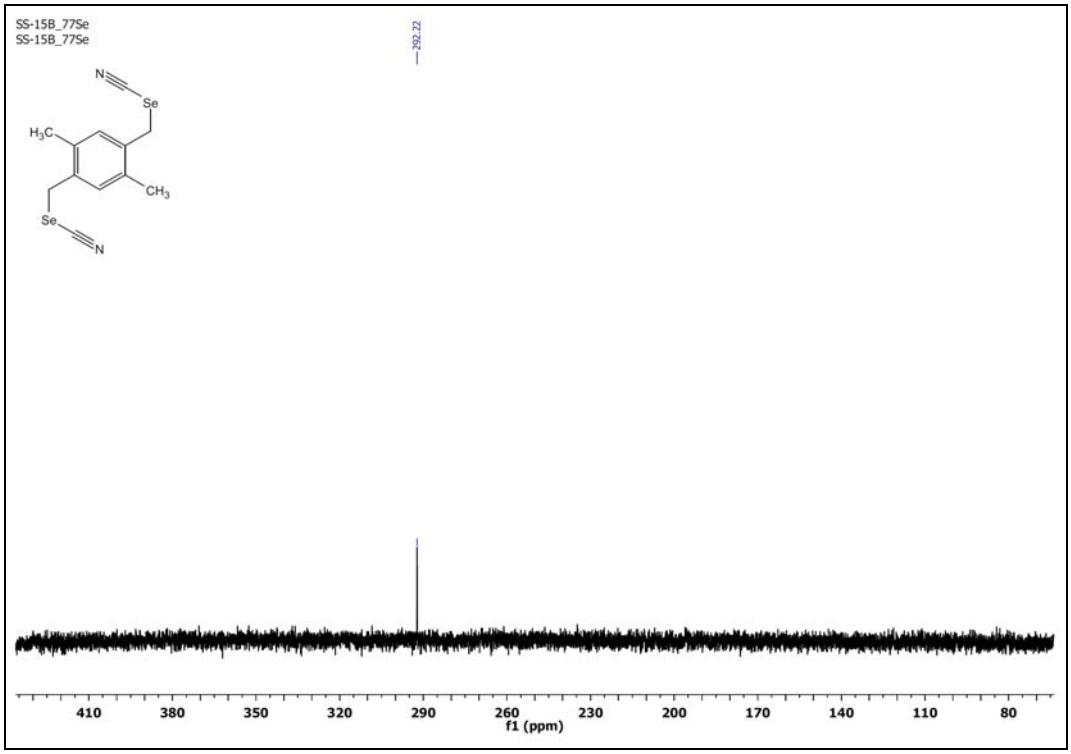


Fig S66: ^{77}Se NMR spectrum (114 MHz, DMSO-d_6) of Compound **16.**

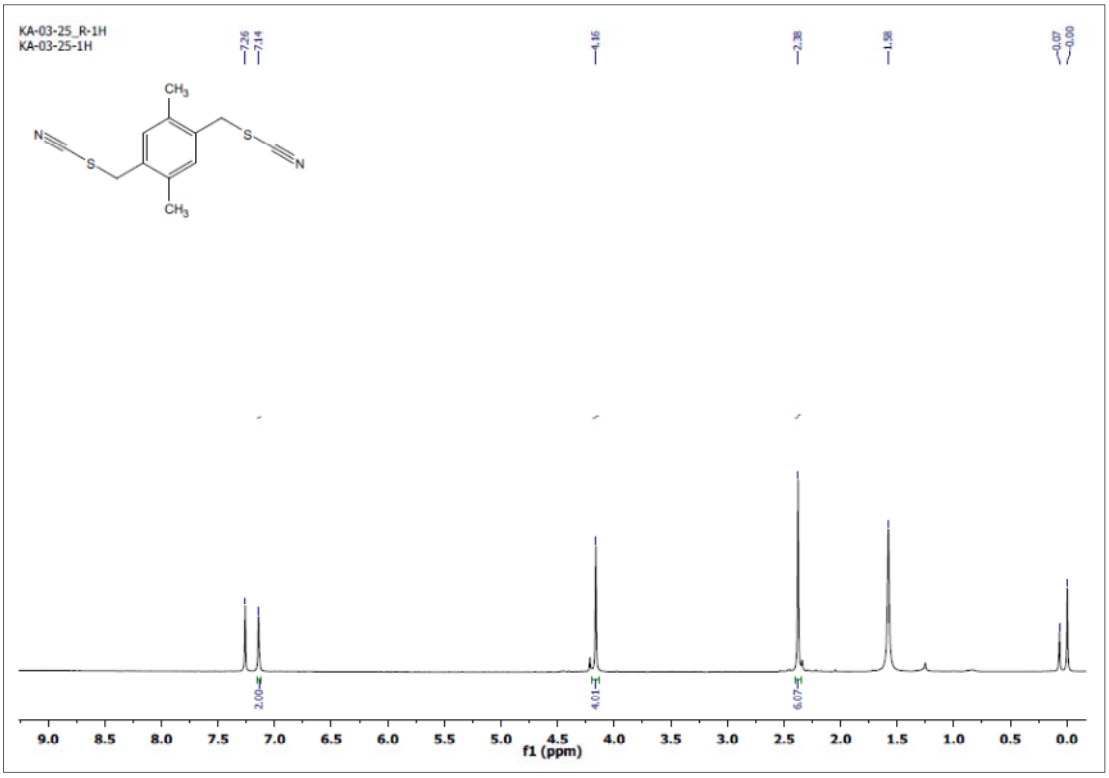


Fig S67: ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of Compound **17.**

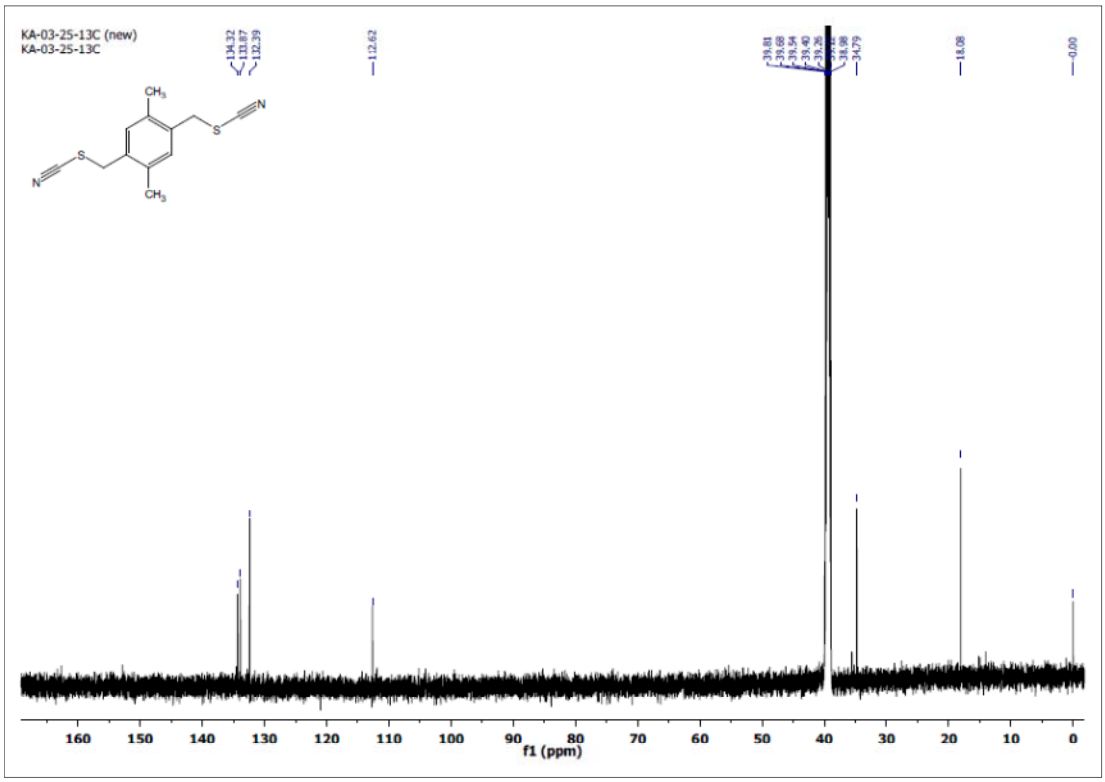


Fig S68: ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of Compound **17.**

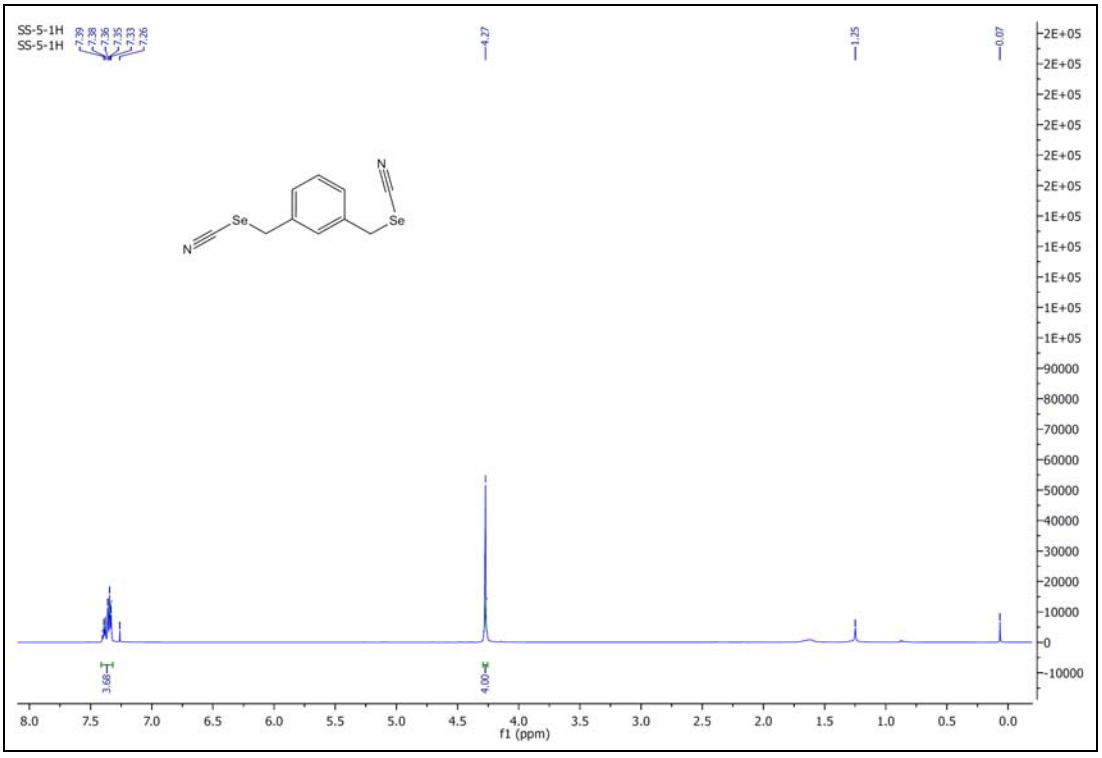


Fig S69: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **18.**

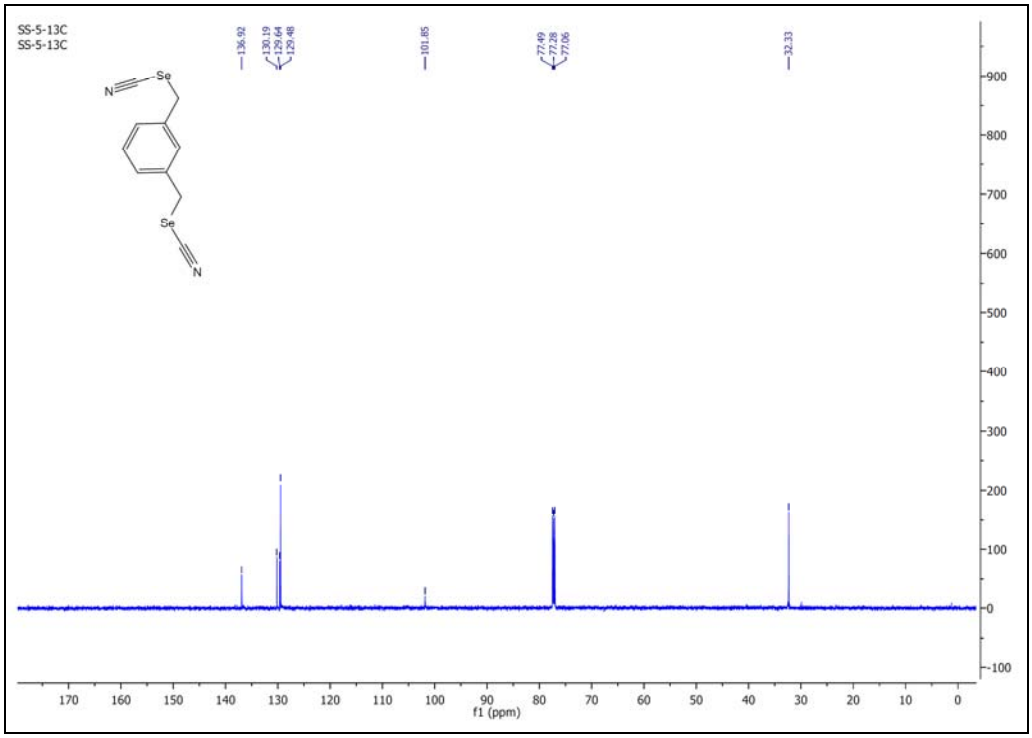


Fig S70: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **18.**

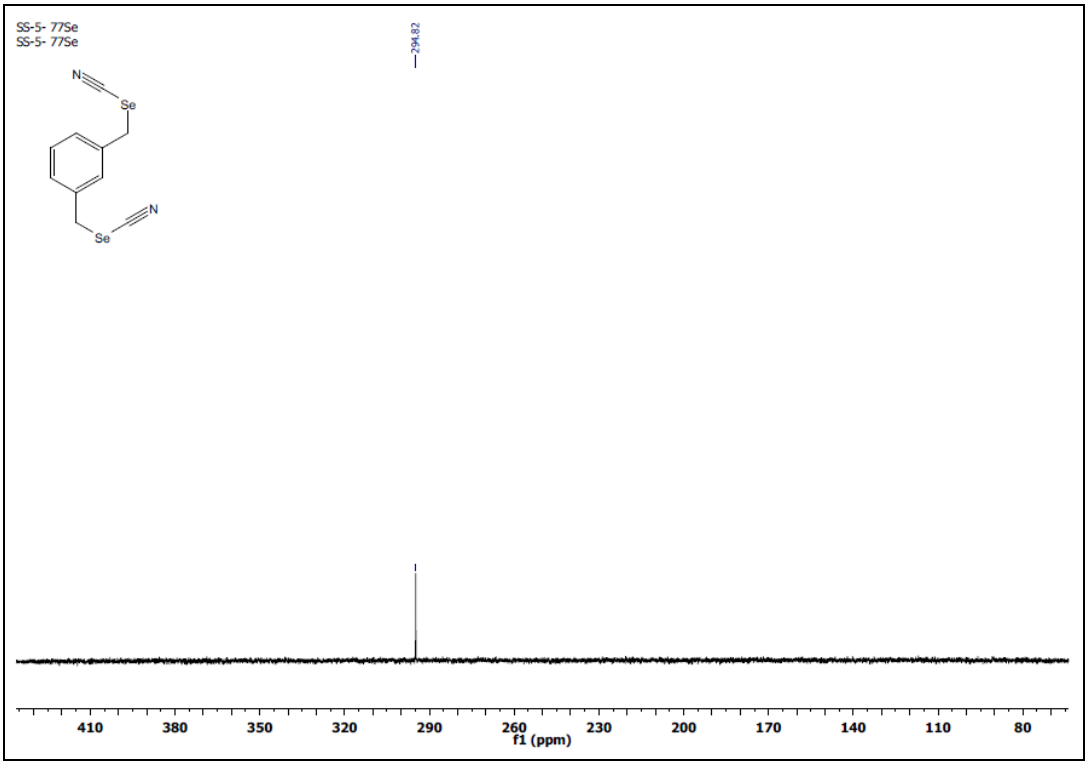


Fig S71: ^{77}Se NMR spectrum (114 MHz, $CDCl_3$) of Compound **18.**

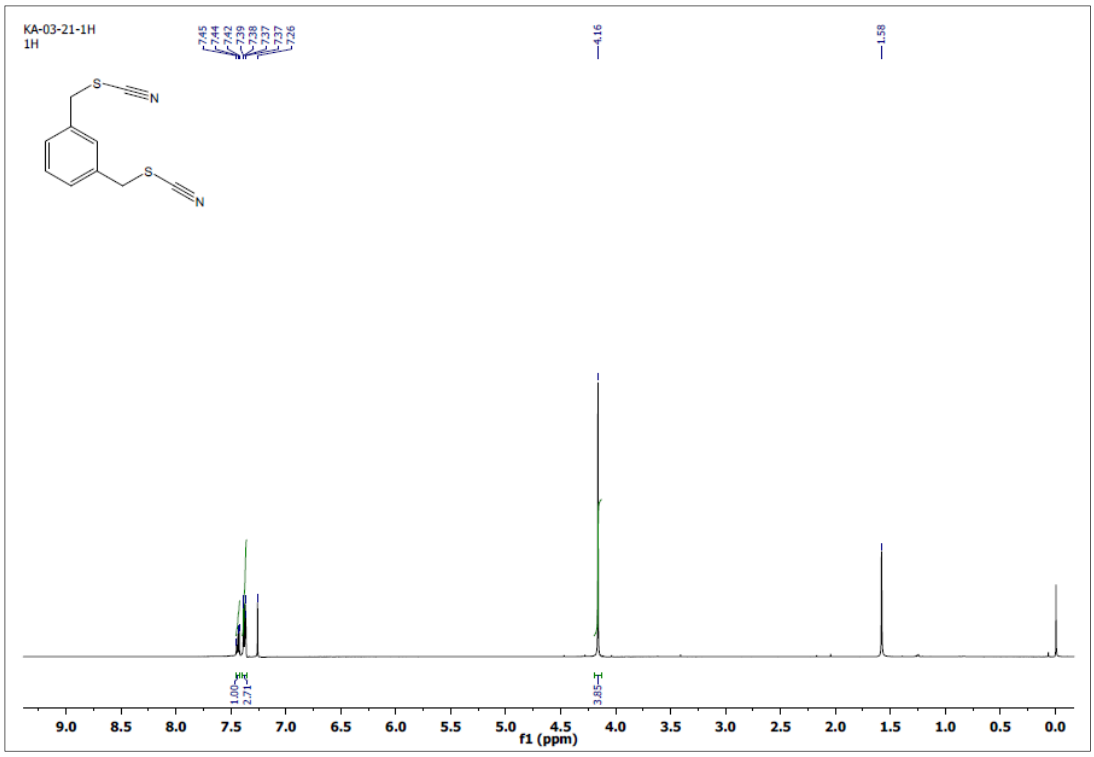


Fig S72: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **19.**

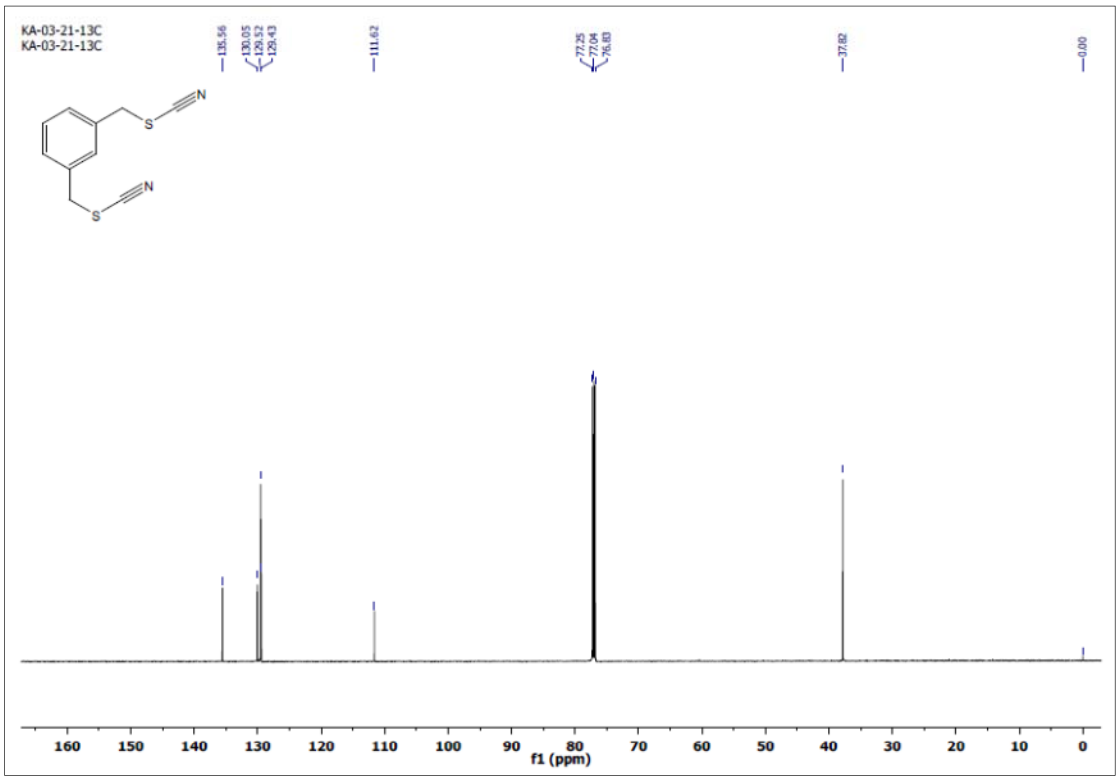


Fig S73: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **19.**

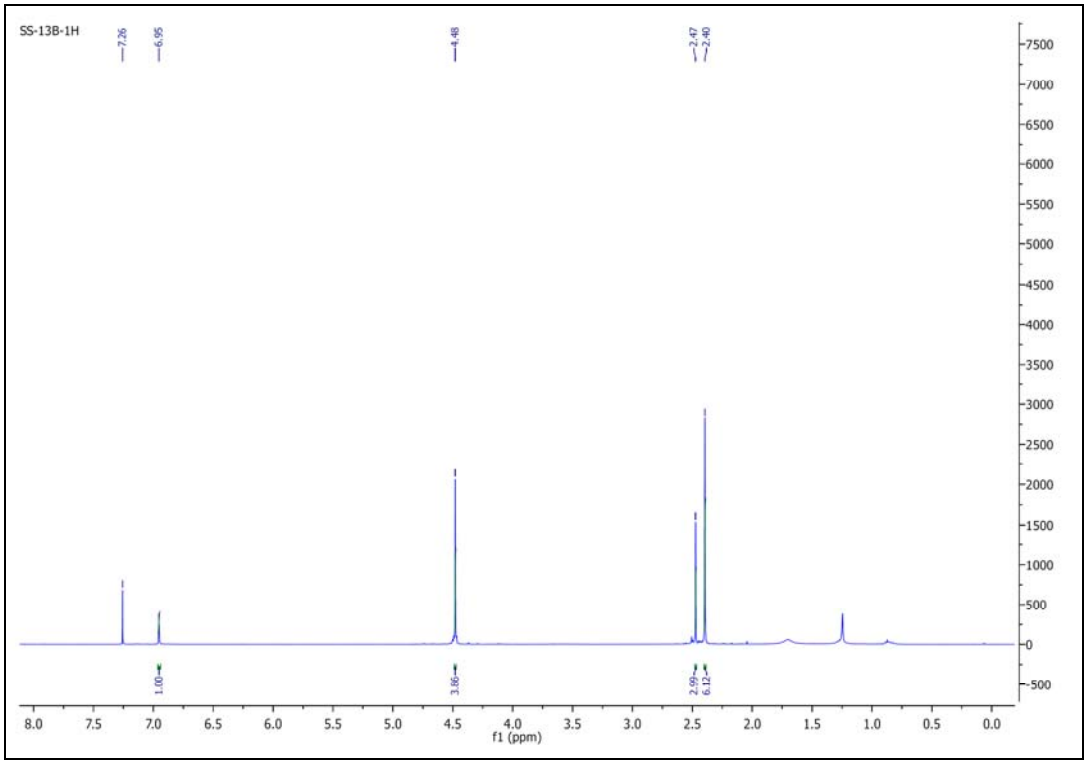


Fig S74: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **20.**

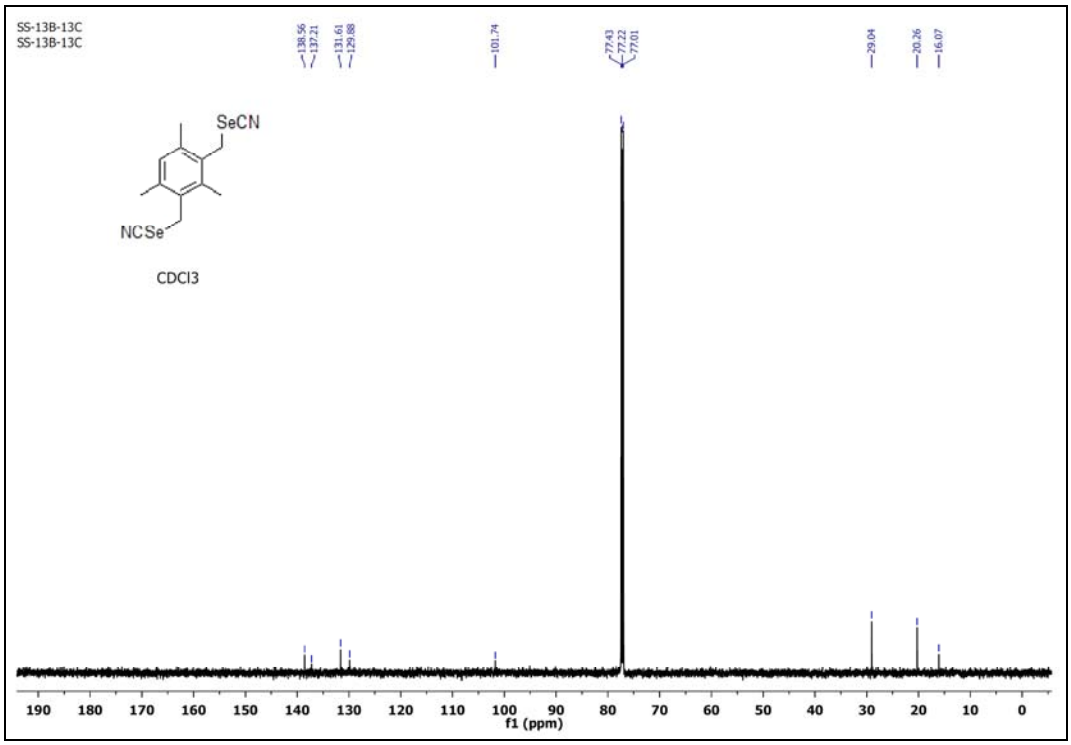


Fig S75: ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of Compound **20.**

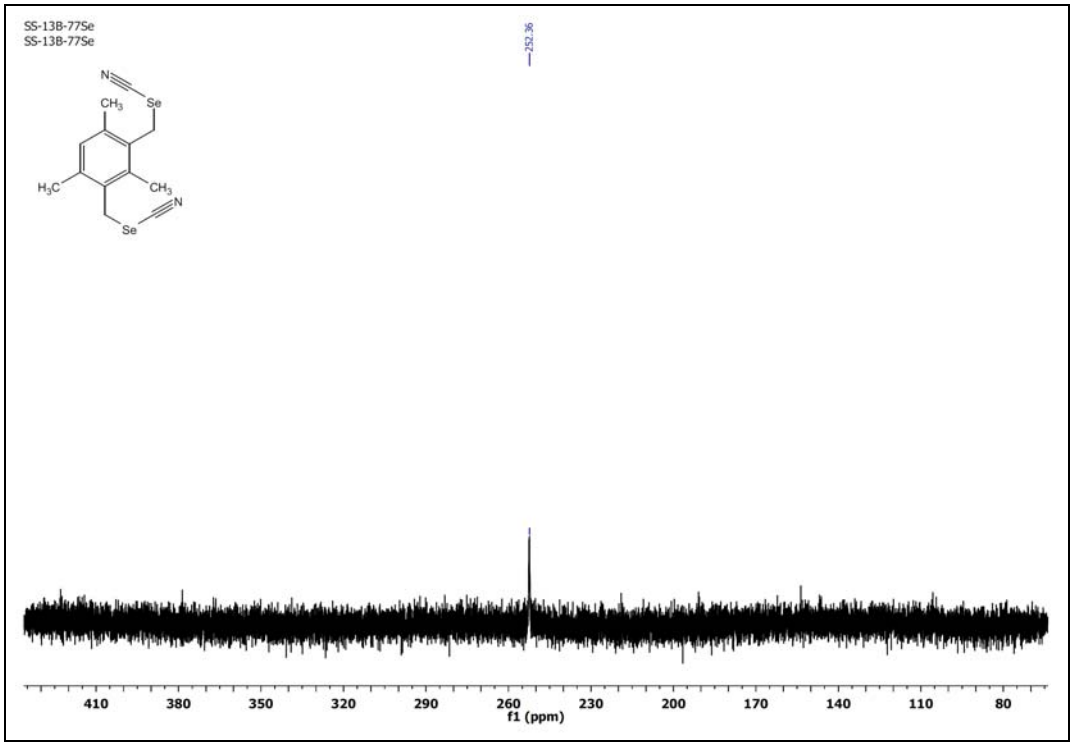


Fig S76: ^{77}Se NMR spectrum (114 MHz, DMSO-d_6) of Compound **20.**

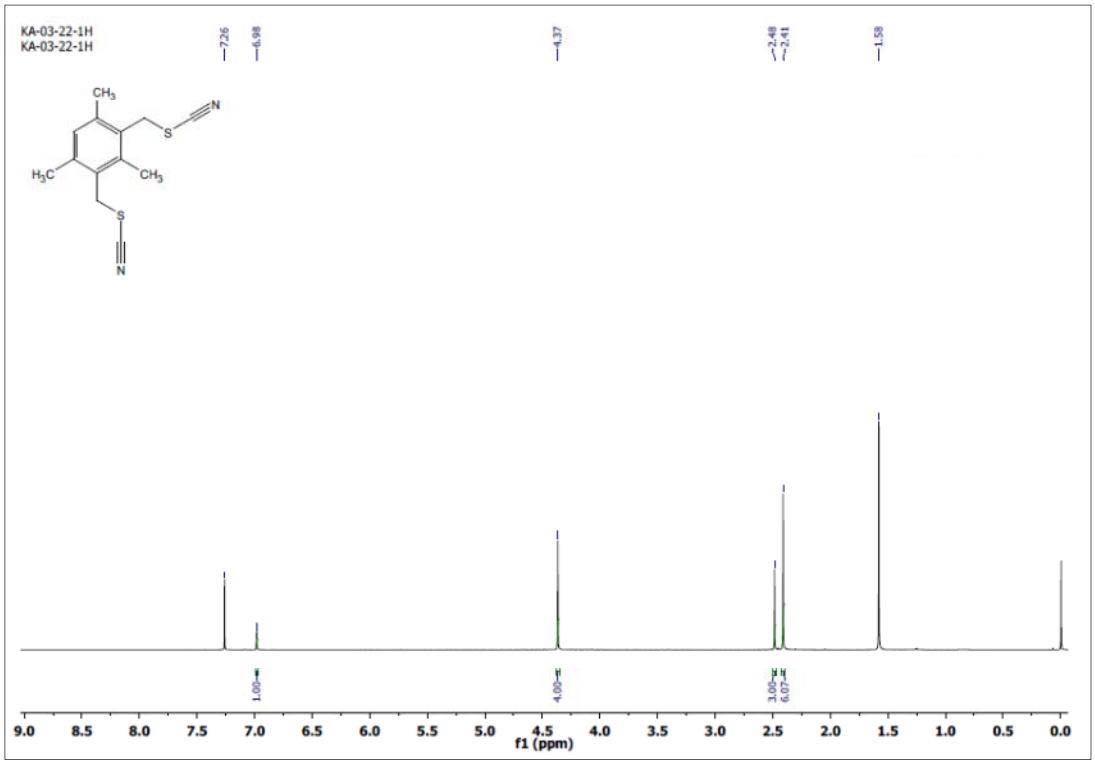


Fig S77: ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of Compound **21.**

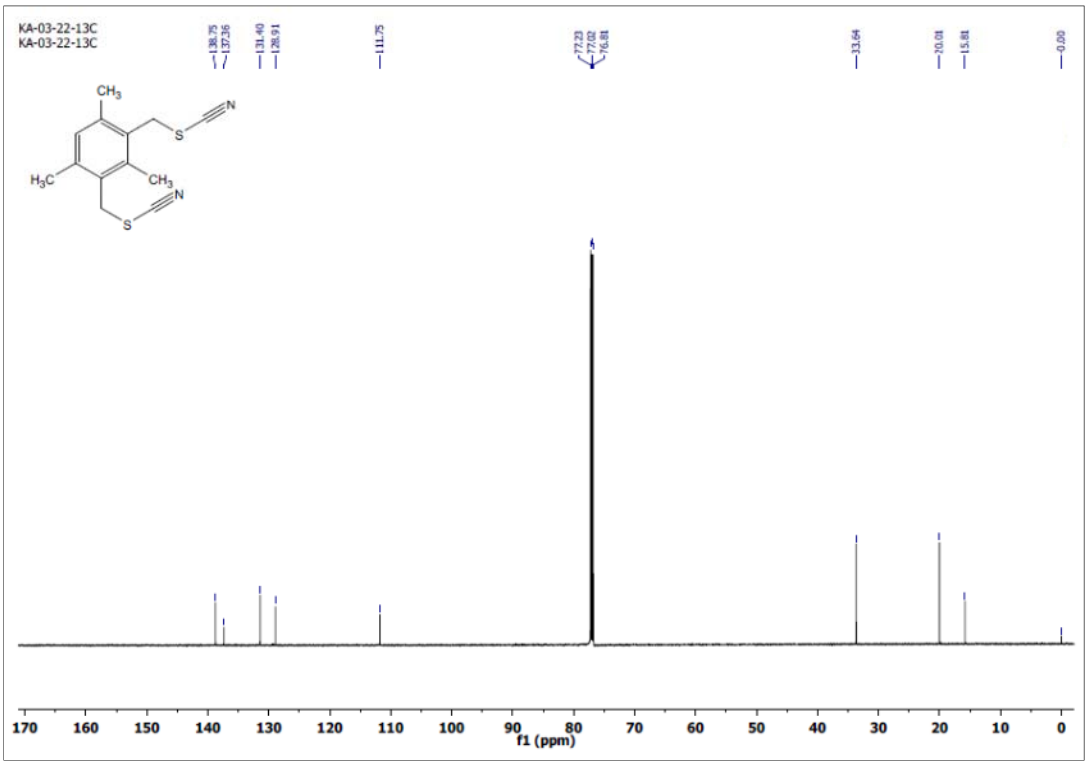


Fig S78: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **21.**

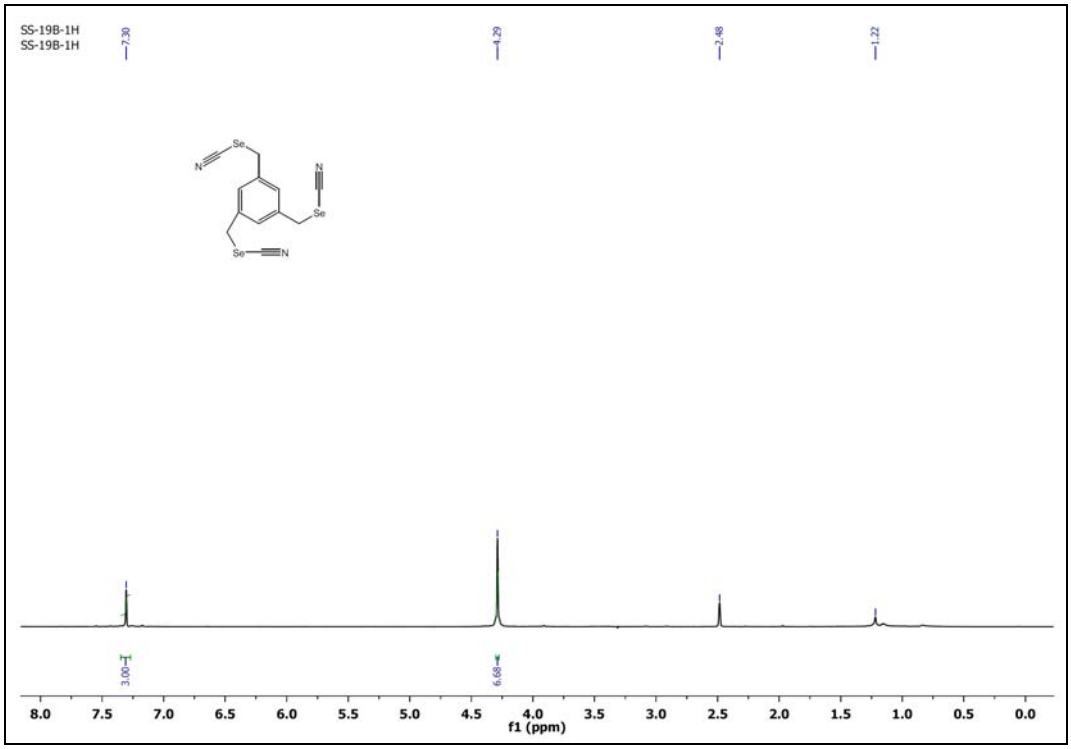


Fig S79: ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of Compound **22.**

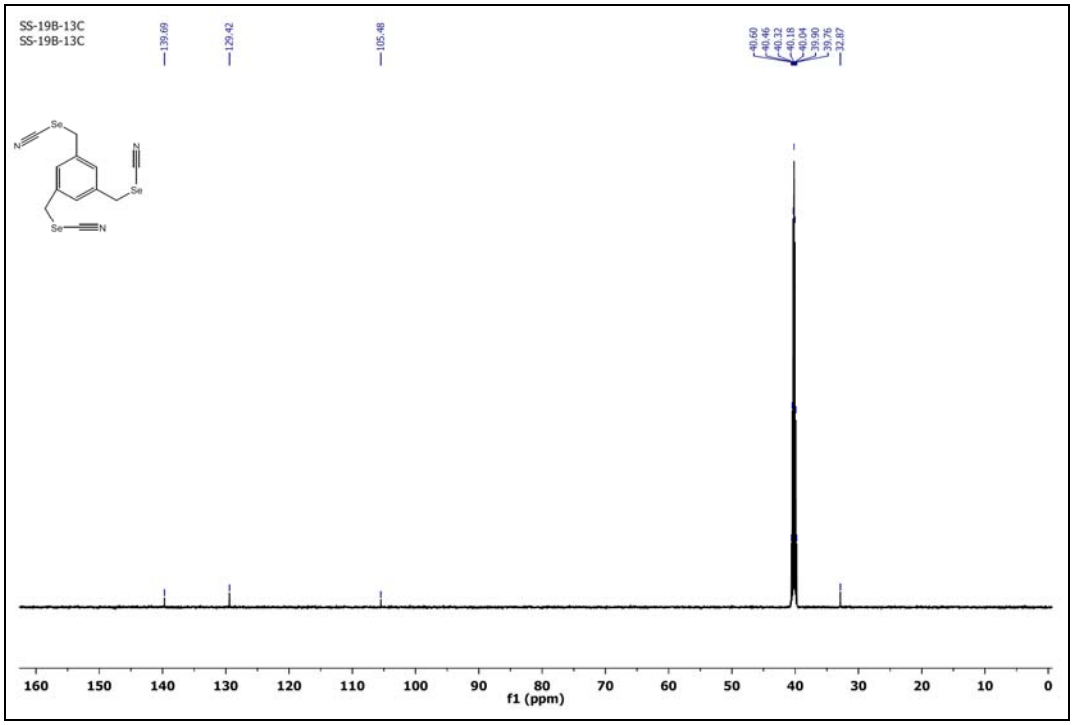


Fig S80: ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of Compound **22**.

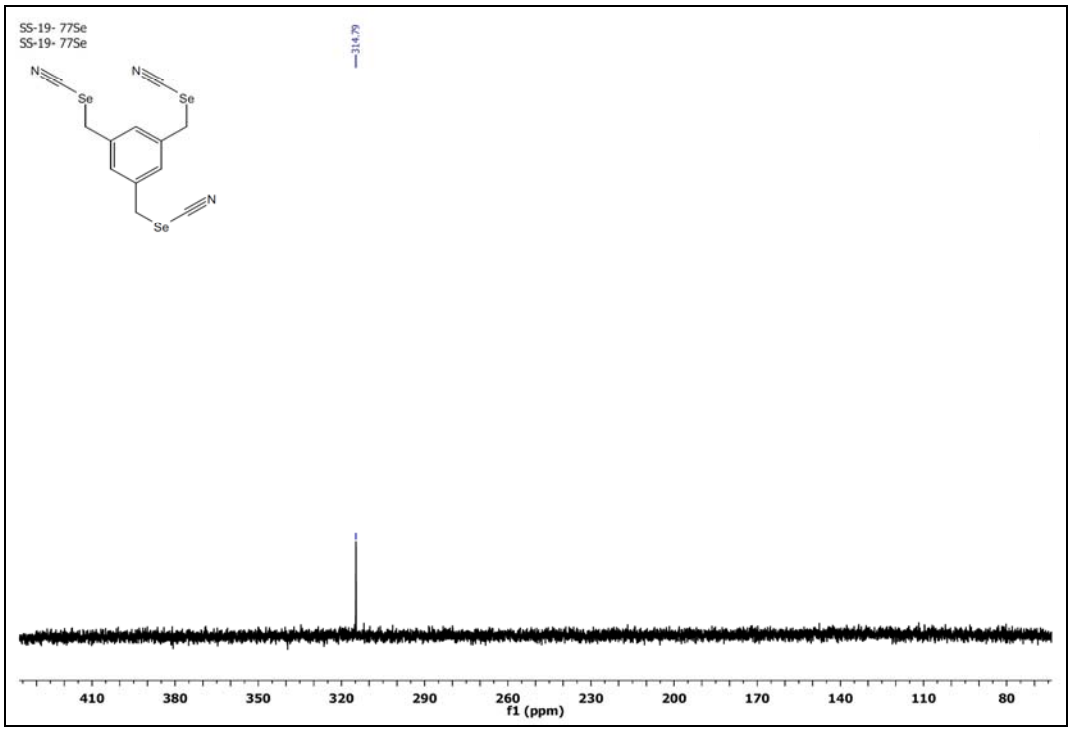


Fig S81: ^{77}Se NMR spectrum (114 MHz, DMSO-d_6) of Compound **22.**

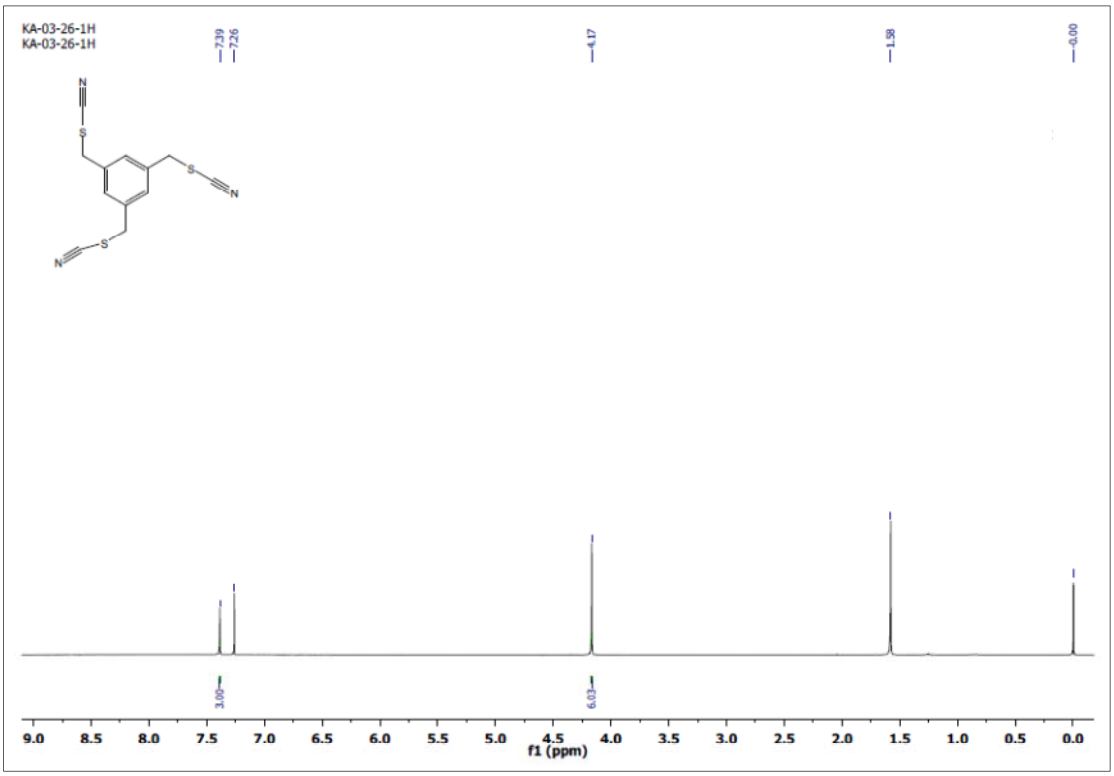


Fig S82: ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of Compound **23.**

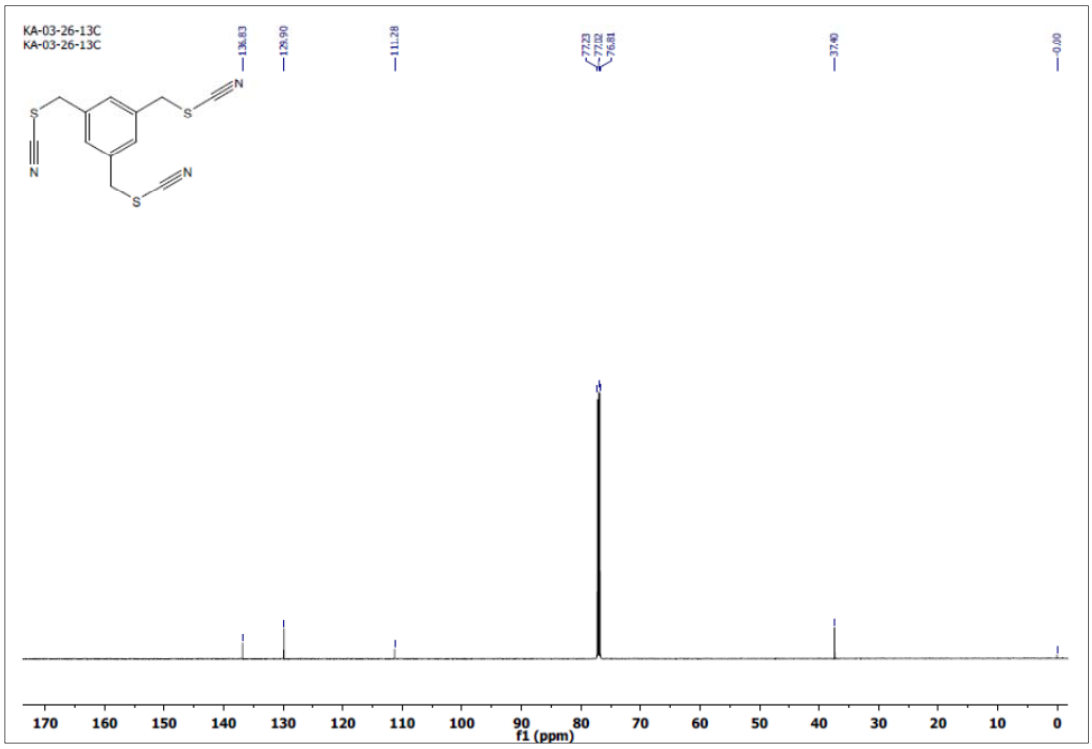


Fig S83: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **23.**

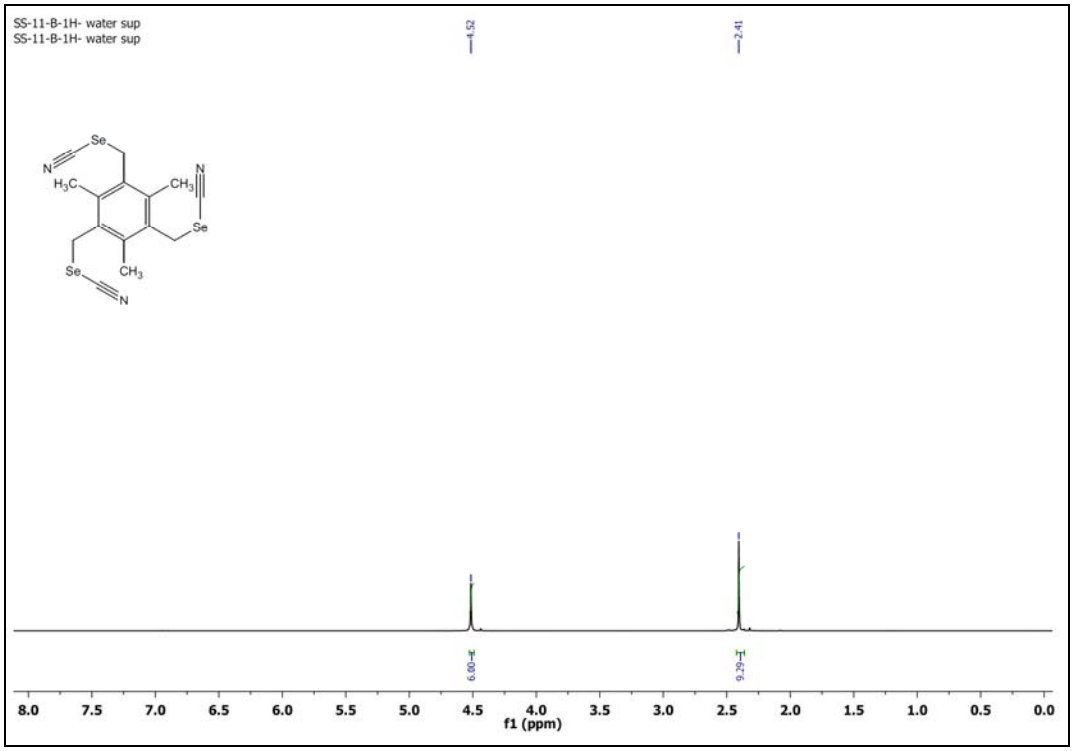


Fig S84: ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of Compound **24.**

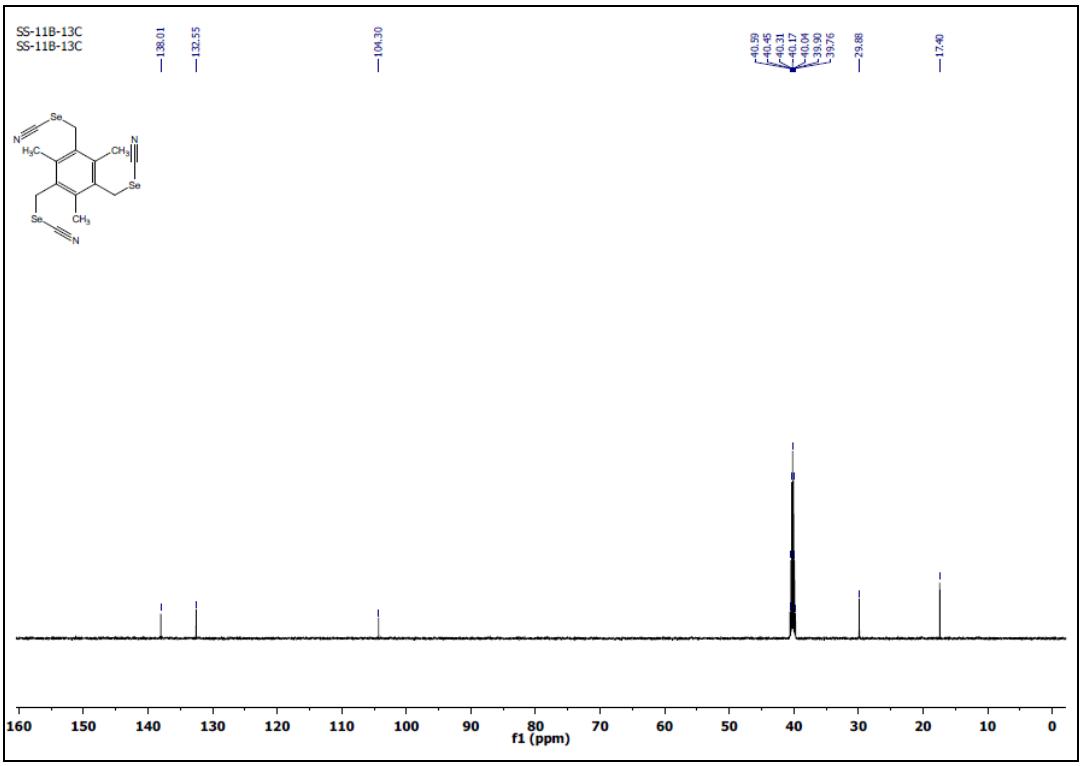


Fig S85: ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of Compound **24.**

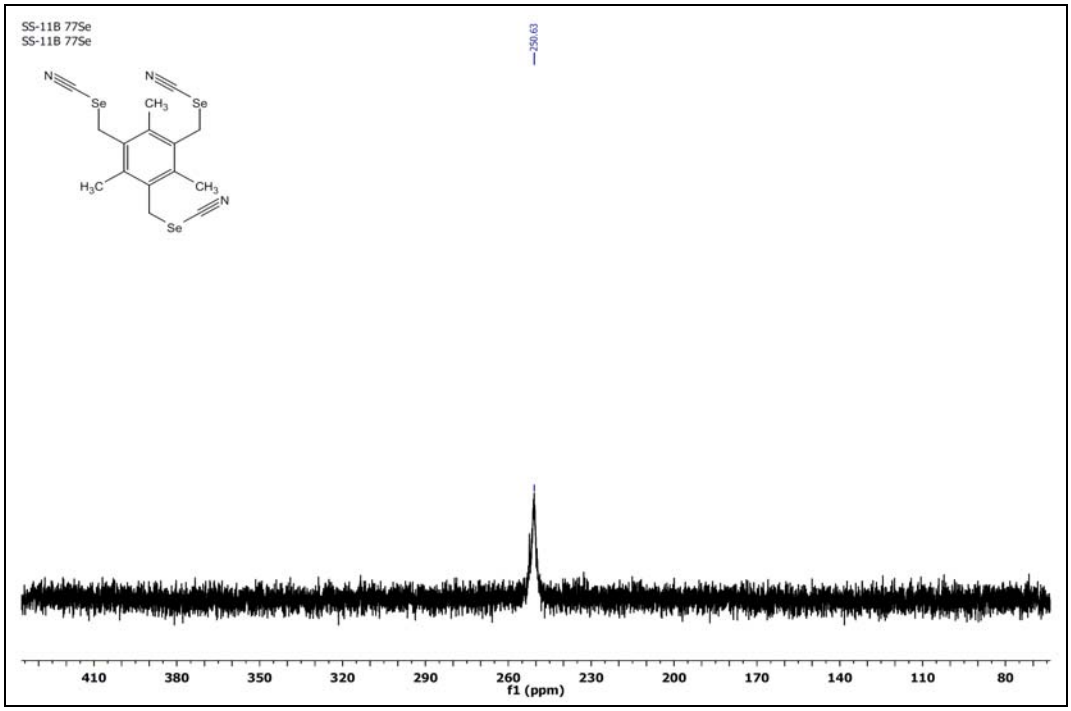


Fig S86: ^{77}Se NMR spectrum (114 MHz, DMSO-d_6) of Compound **24.**

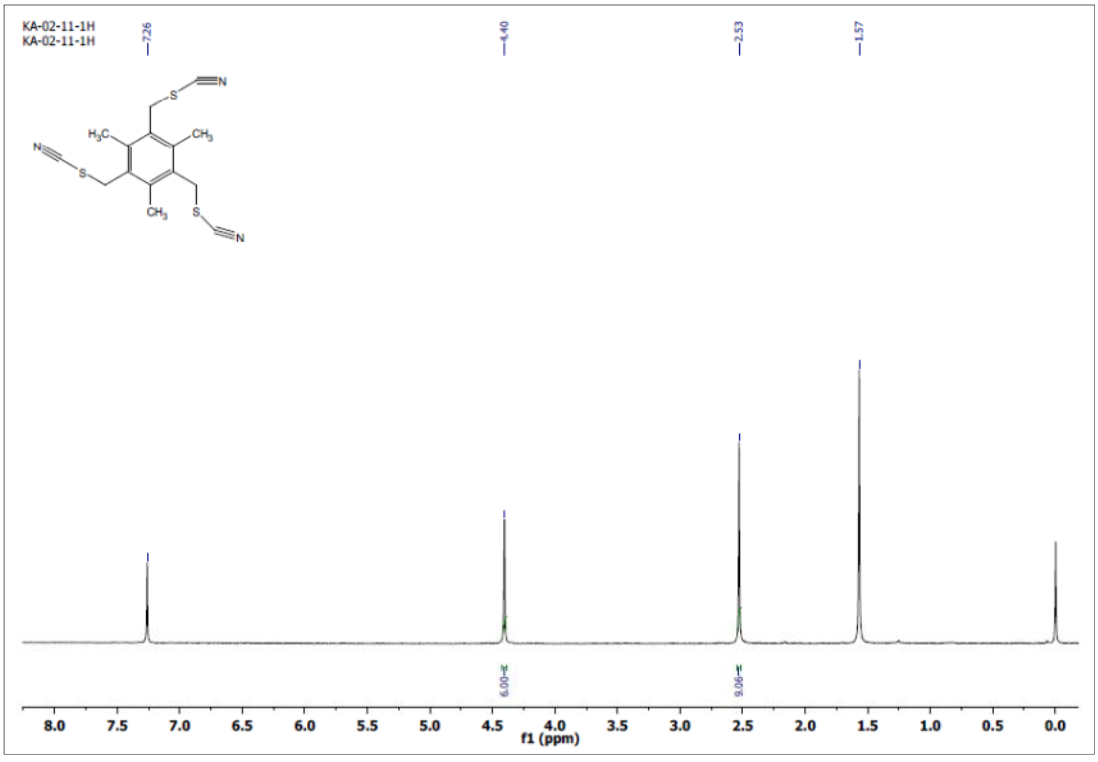


Fig S87: ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of Compound **25.**

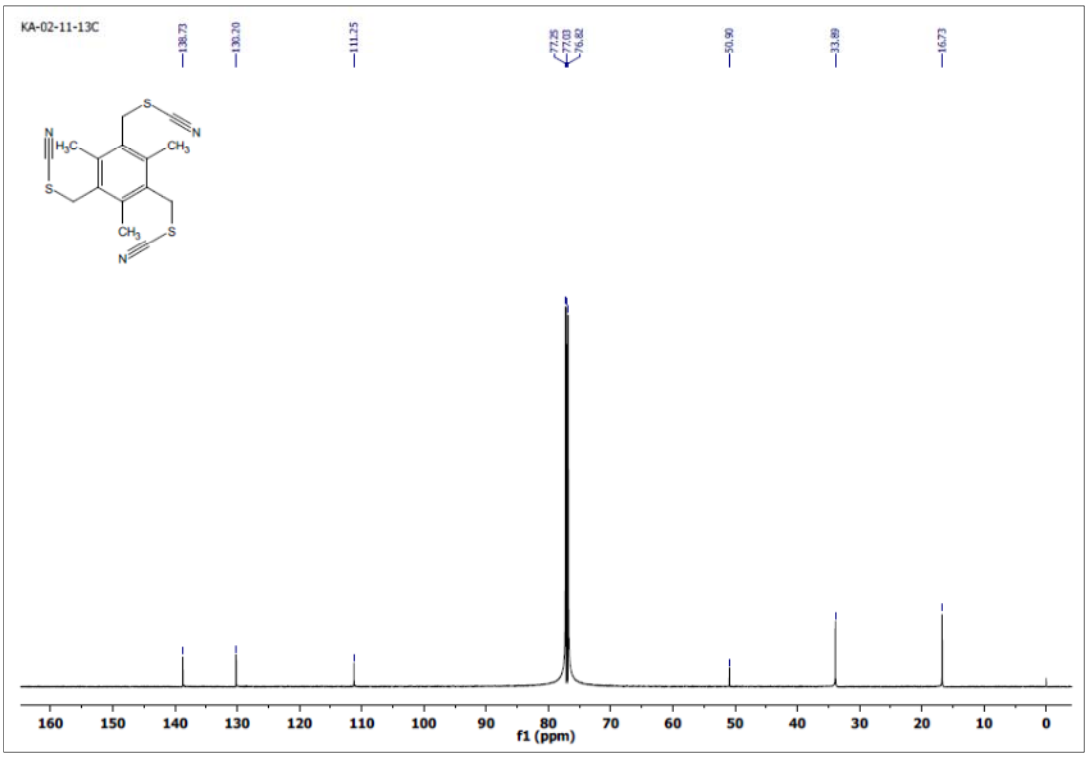


Fig S88: ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of Compound **25.**

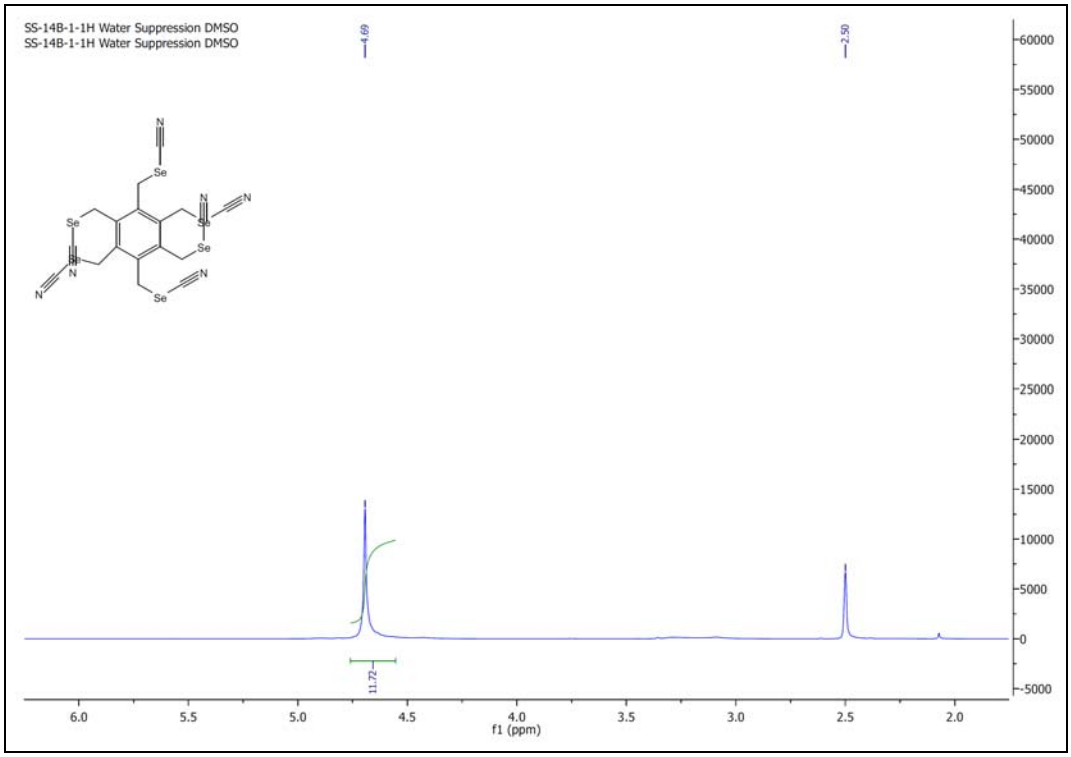


Fig S89: ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of Compound **26.**

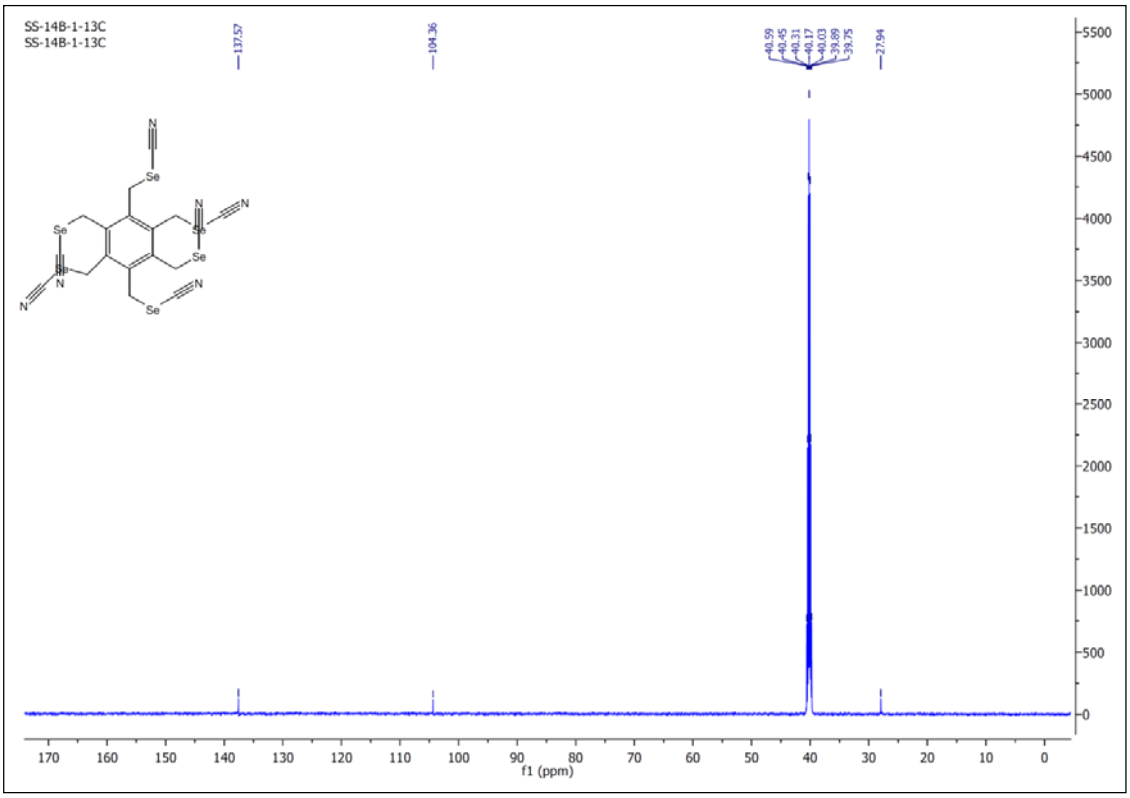


Fig S90: ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of Compound **26.**

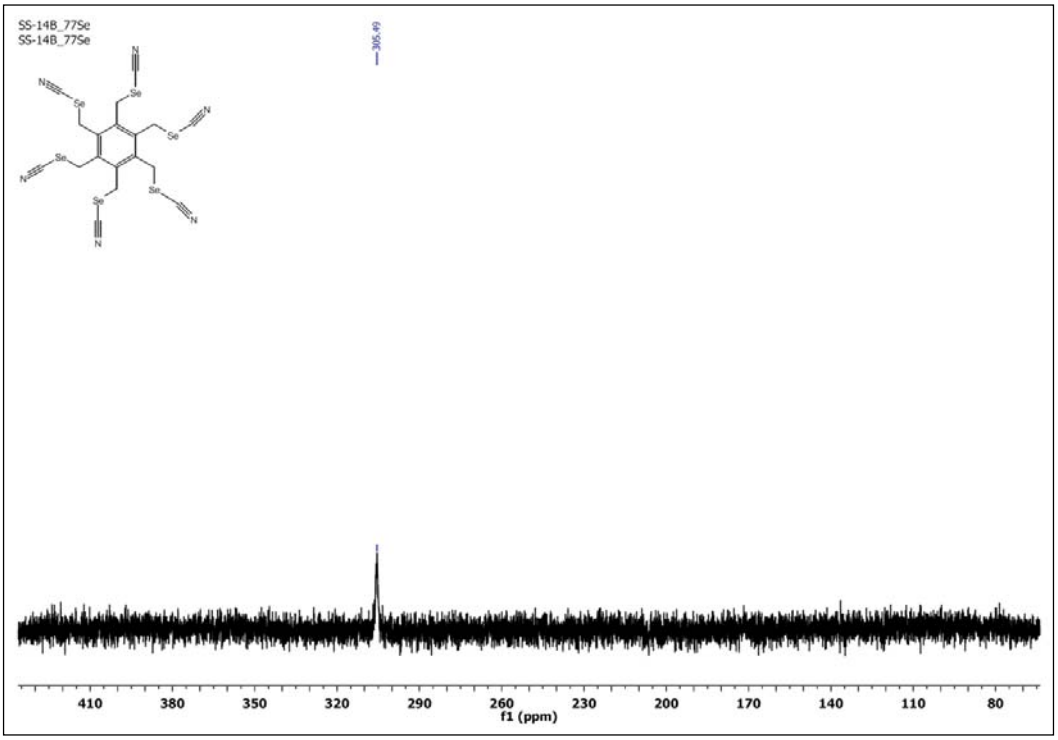


Fig S91: ^{77}Se NMR spectrum (114 MHz, DMSO-d_6) of Compound **26.**

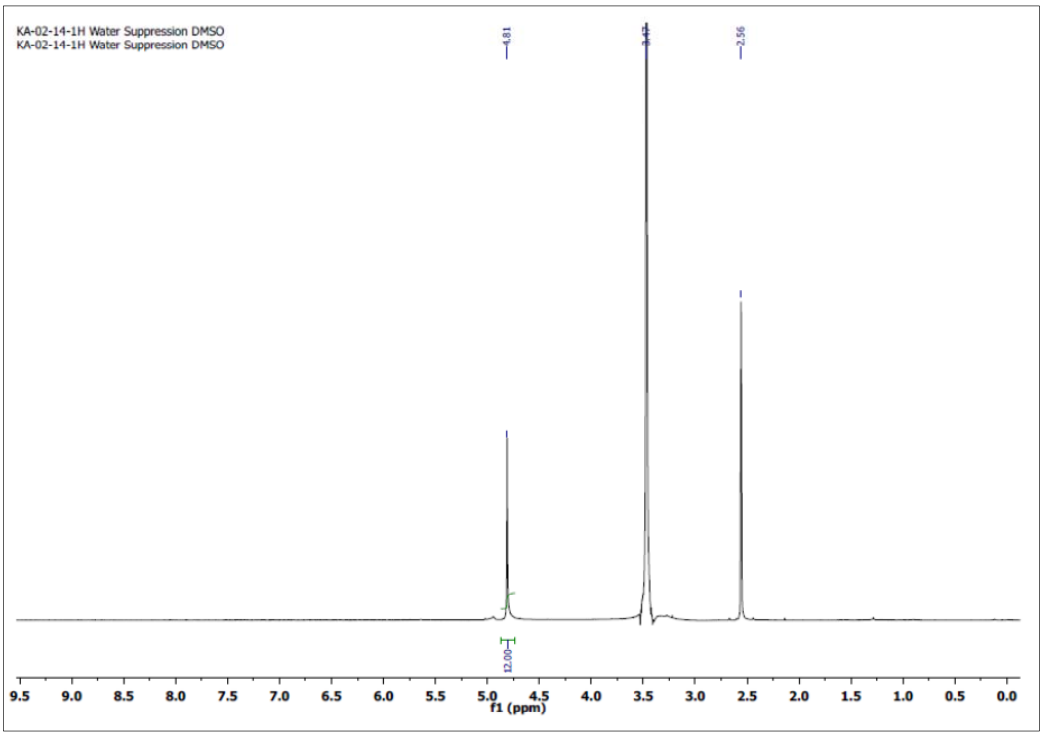


Fig S92: ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of Compound **27.**

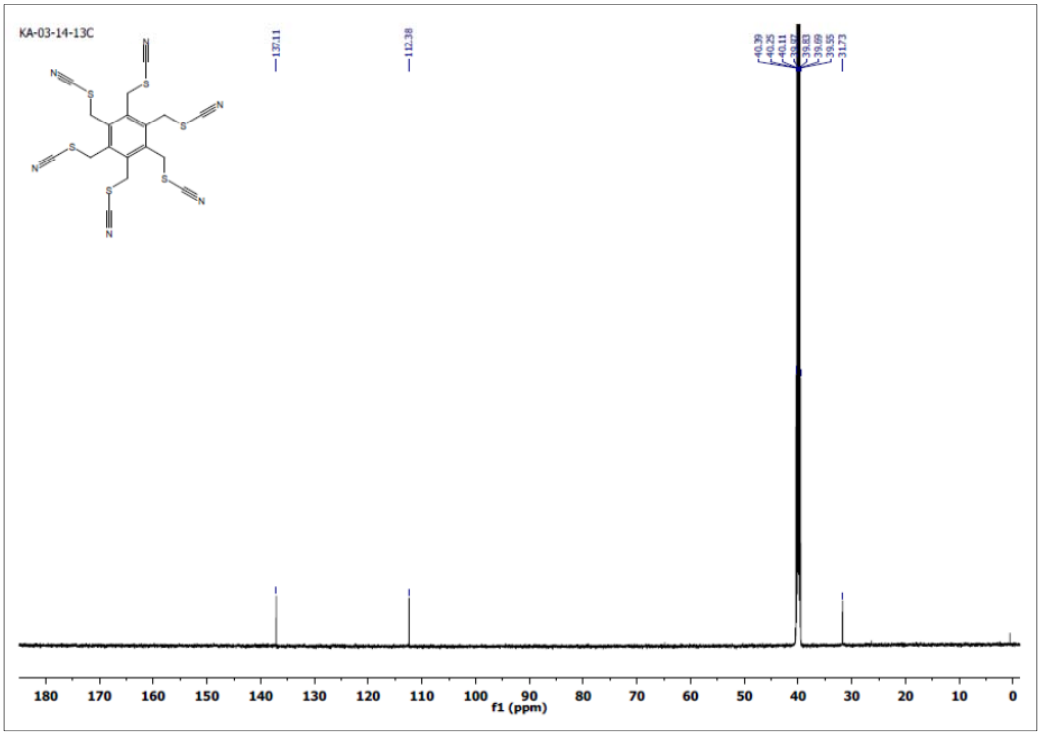


Fig S93: ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of Compound **27.**

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