

Introduction of Catalytic Triad Increases the Glutathione Peroxidase-like Activity of Diaryl Diselenides

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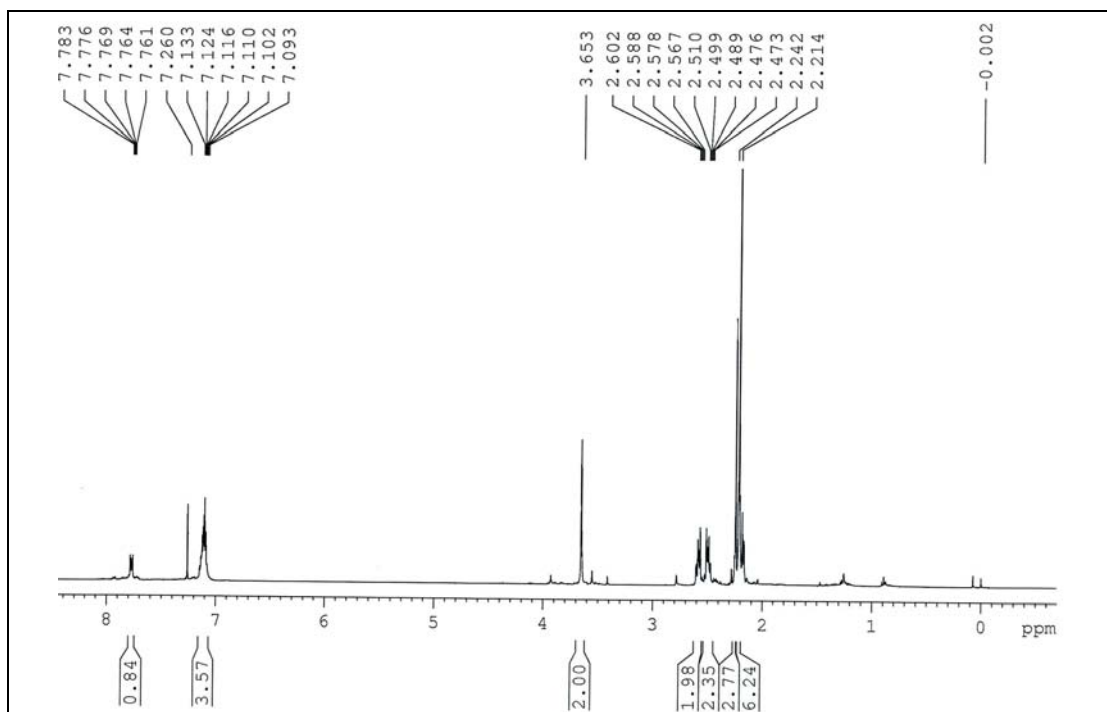


Figure S1. ¹H NMR of compound **7a** in CDCl₃

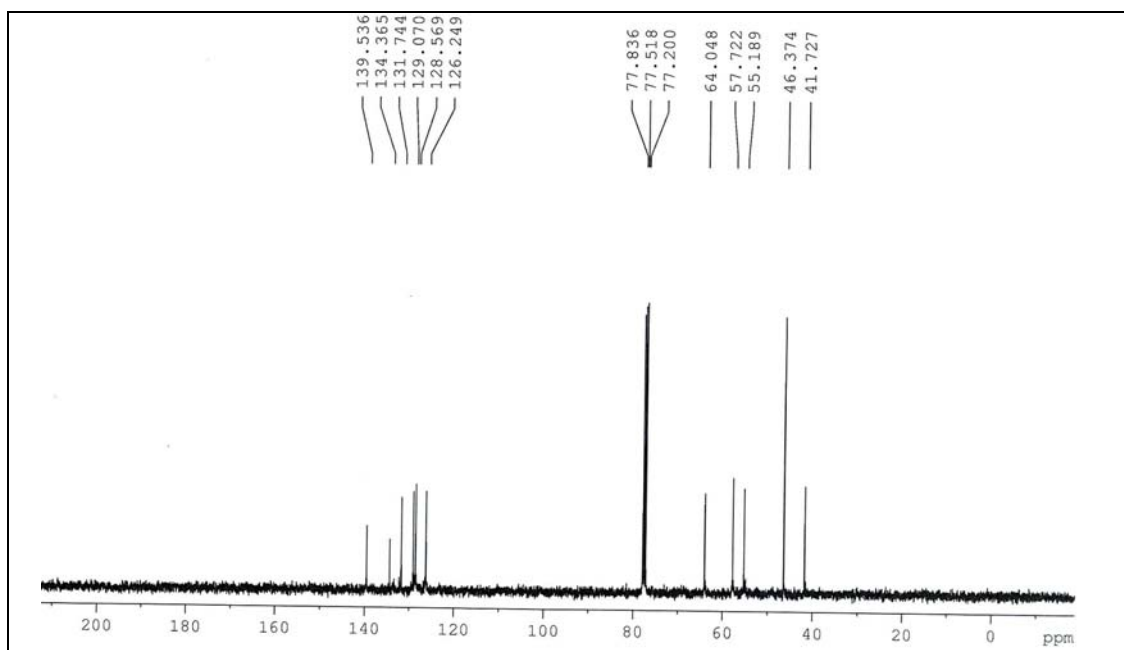


Figure S2. ¹³C NMR of compound **7a** in CDCl₃

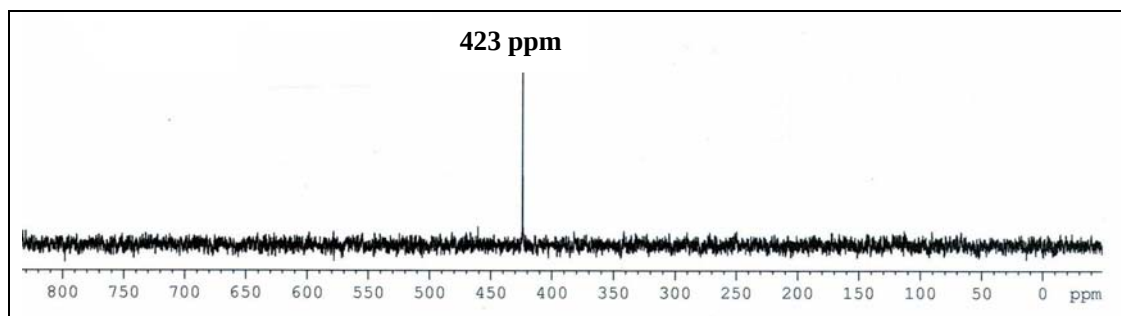


Figure S3. ⁷⁷Se NMR of compound 7a in CDCl₃

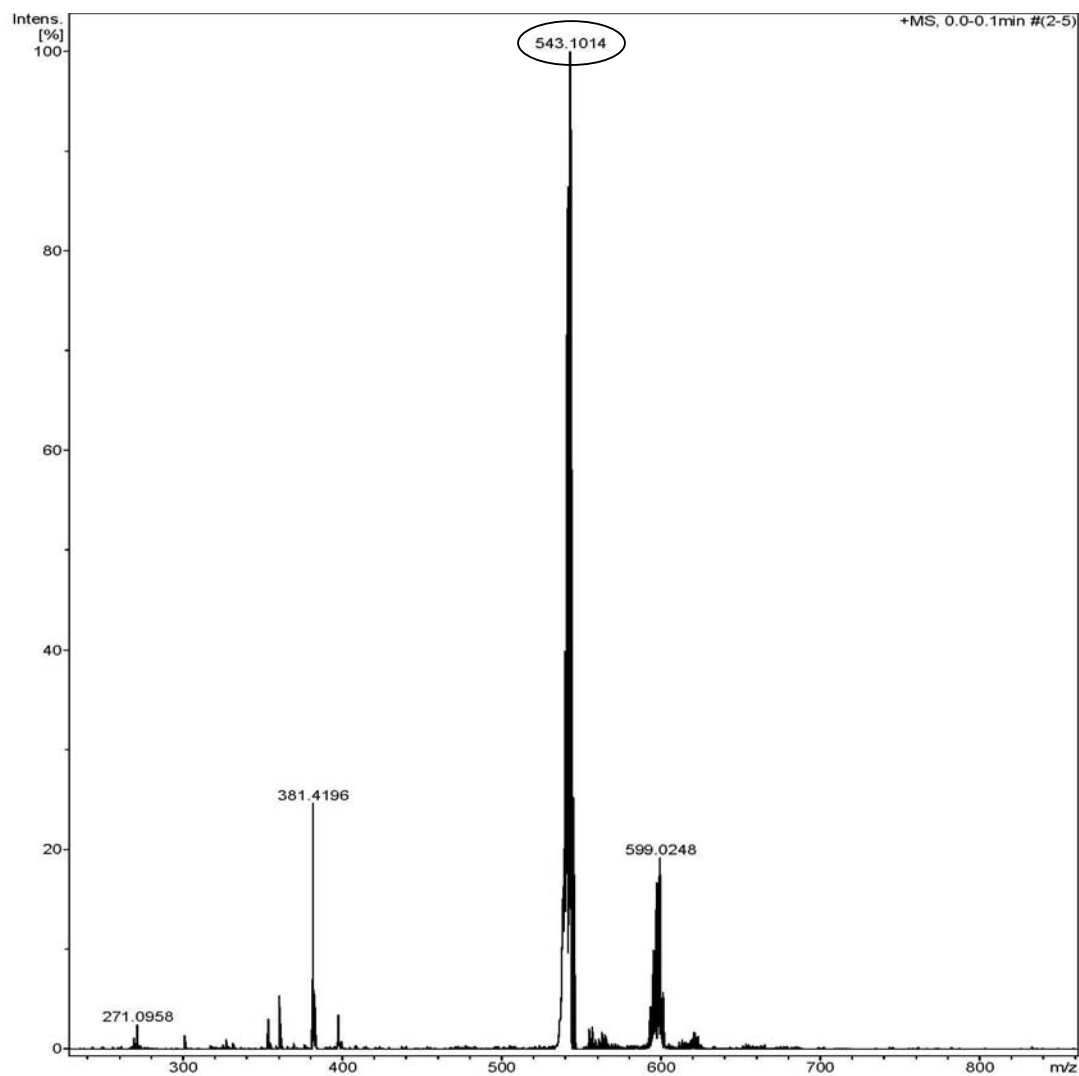


Figure S4. ESI-Mass spectrum of compound 7a. ESI-MS: m/z calcd for C₂₄H₃₉N₄Se₂[M+H]⁺: 543.1505; found: 543.1014.

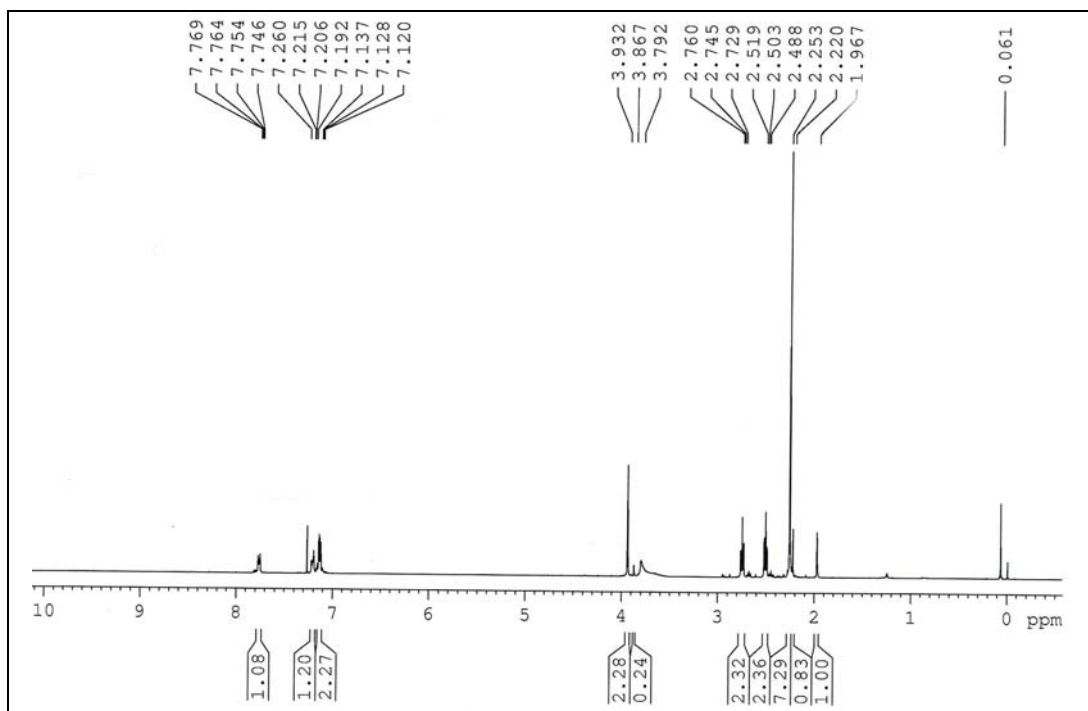


Figure S5. ¹H NMR of compound **7b** in CDCl₃

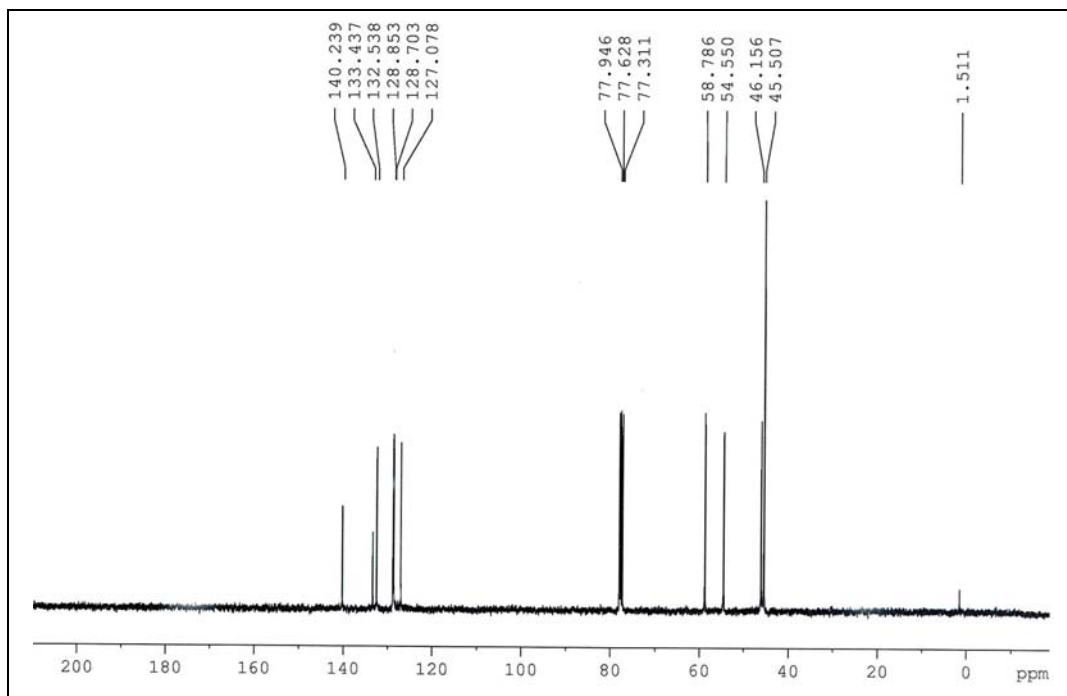


Figure S6. ¹³C NMR of compound **7b** in CDCl₃

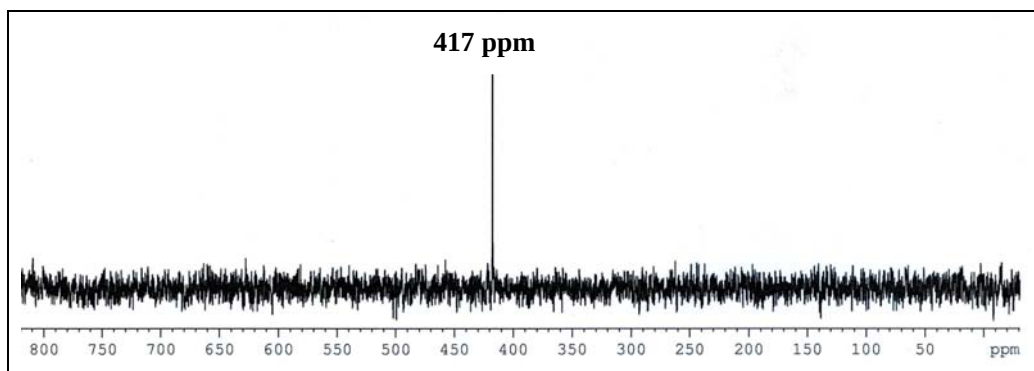


Figure S7. ⁷⁷Se NMR of compound **7b** in CDCl₃

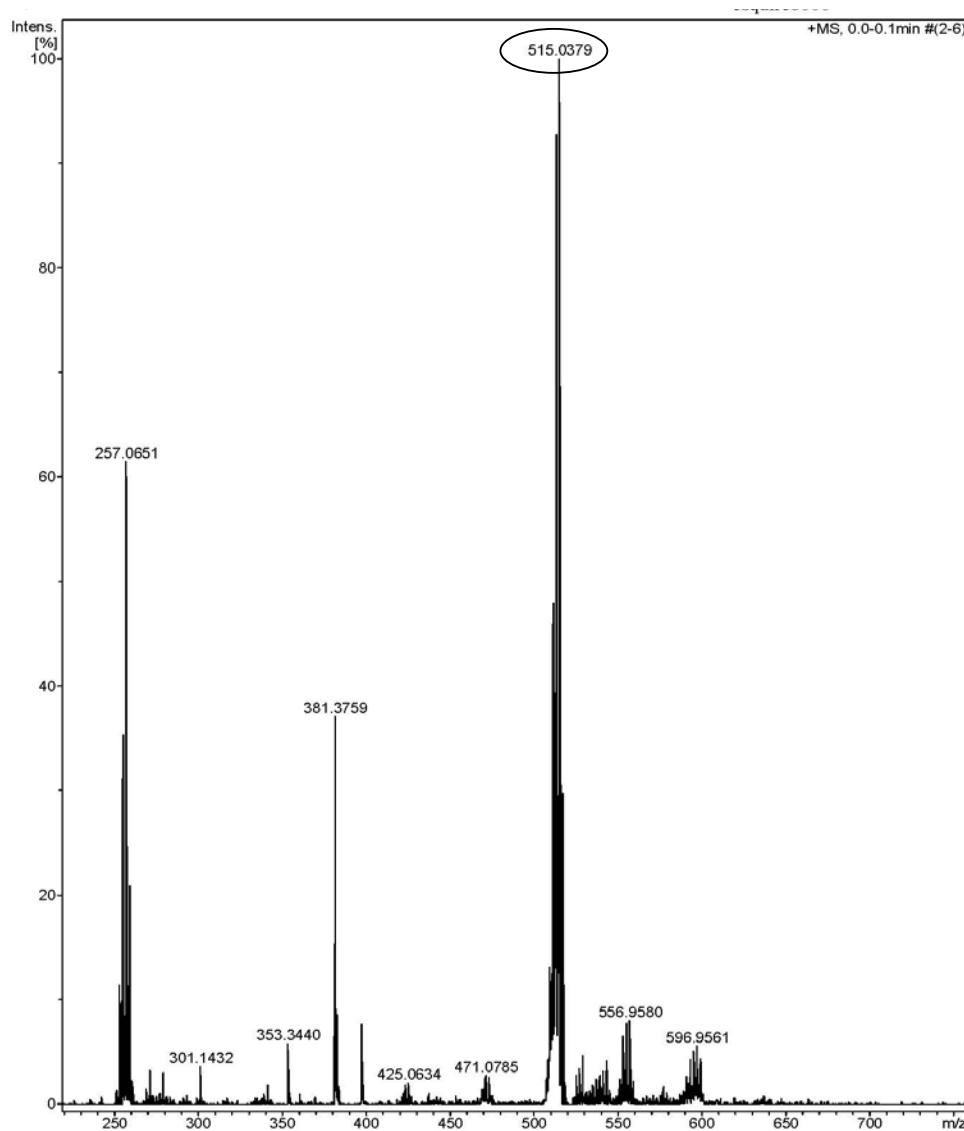


Figure S8. ESI-Mass spectrum of compound **7b**. ESI-MS: m/z calcd for C₂₂H₃₅N₄Se₂[M+H]⁺: 515.1192; found: 515.0397.

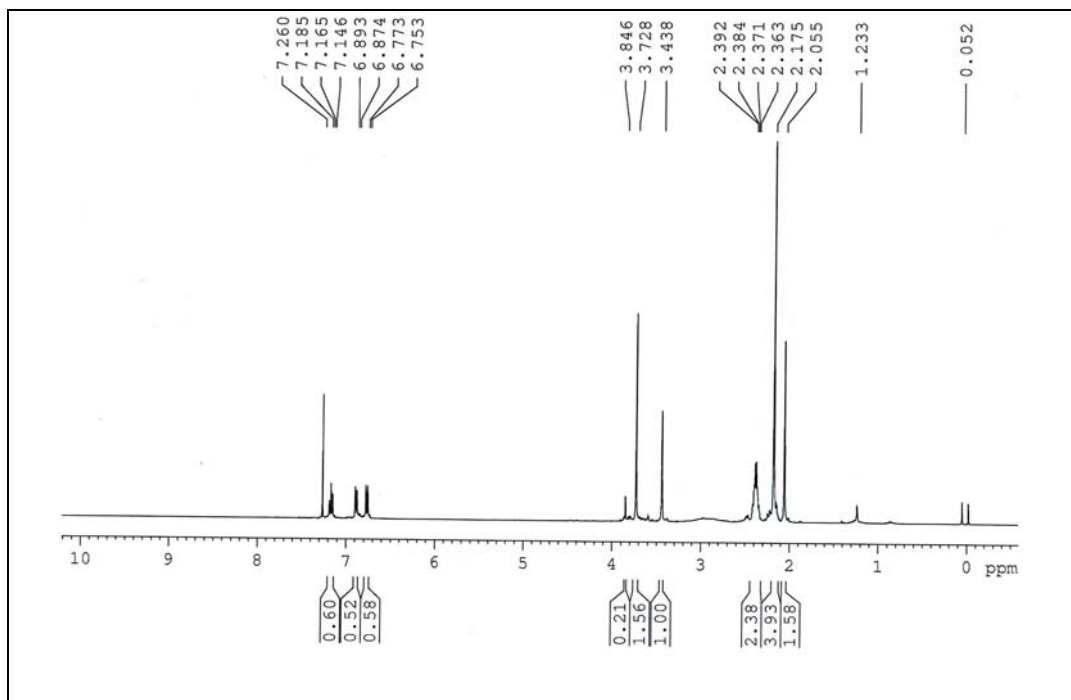


Figure S9. ¹H NMR of compound **8a** in CDCl₃

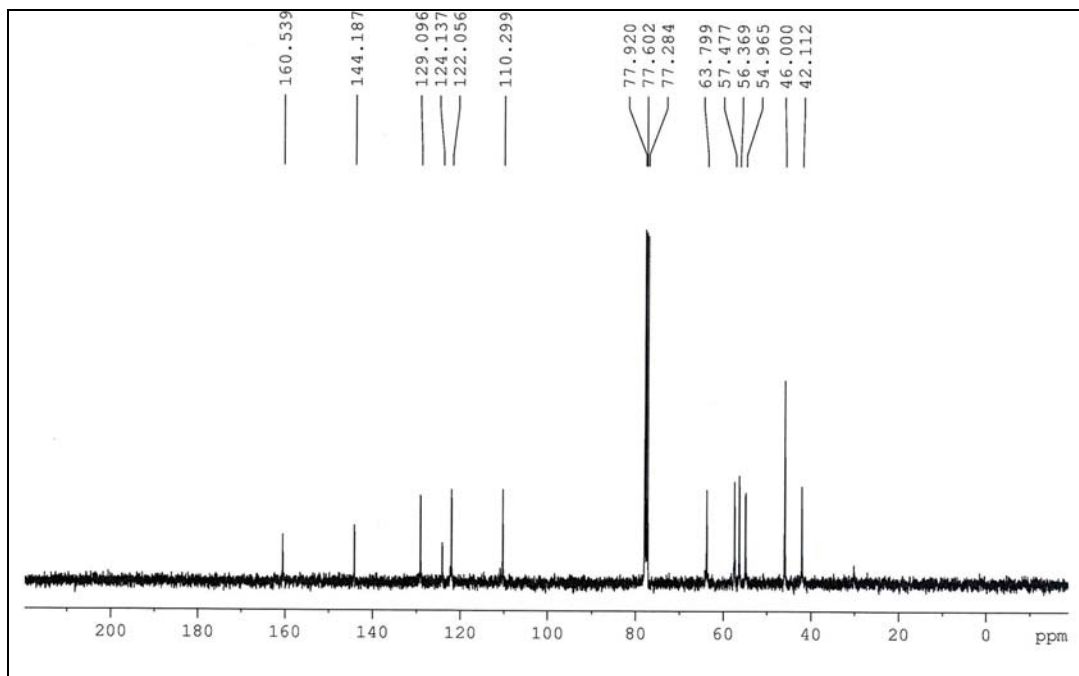


Figure S10. ¹³C NMR of compound **8a** in CDCl₃

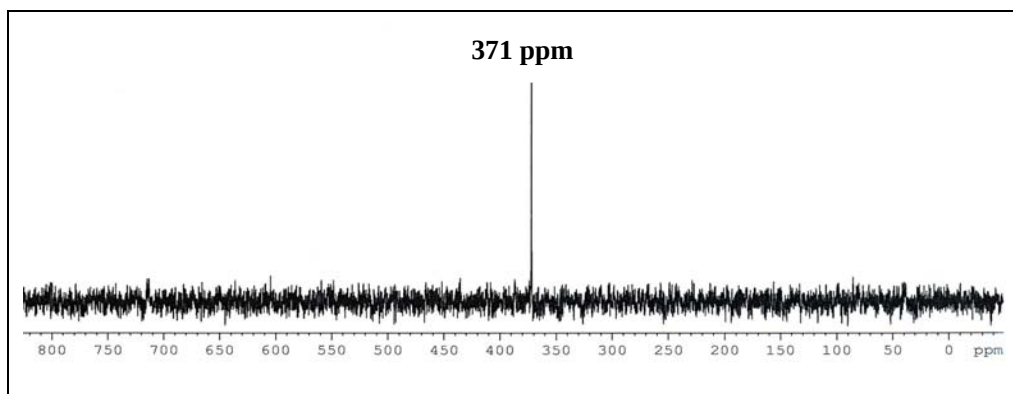


Figure S11. ^{77}Se NMR of compound **8a** in CDCl_3

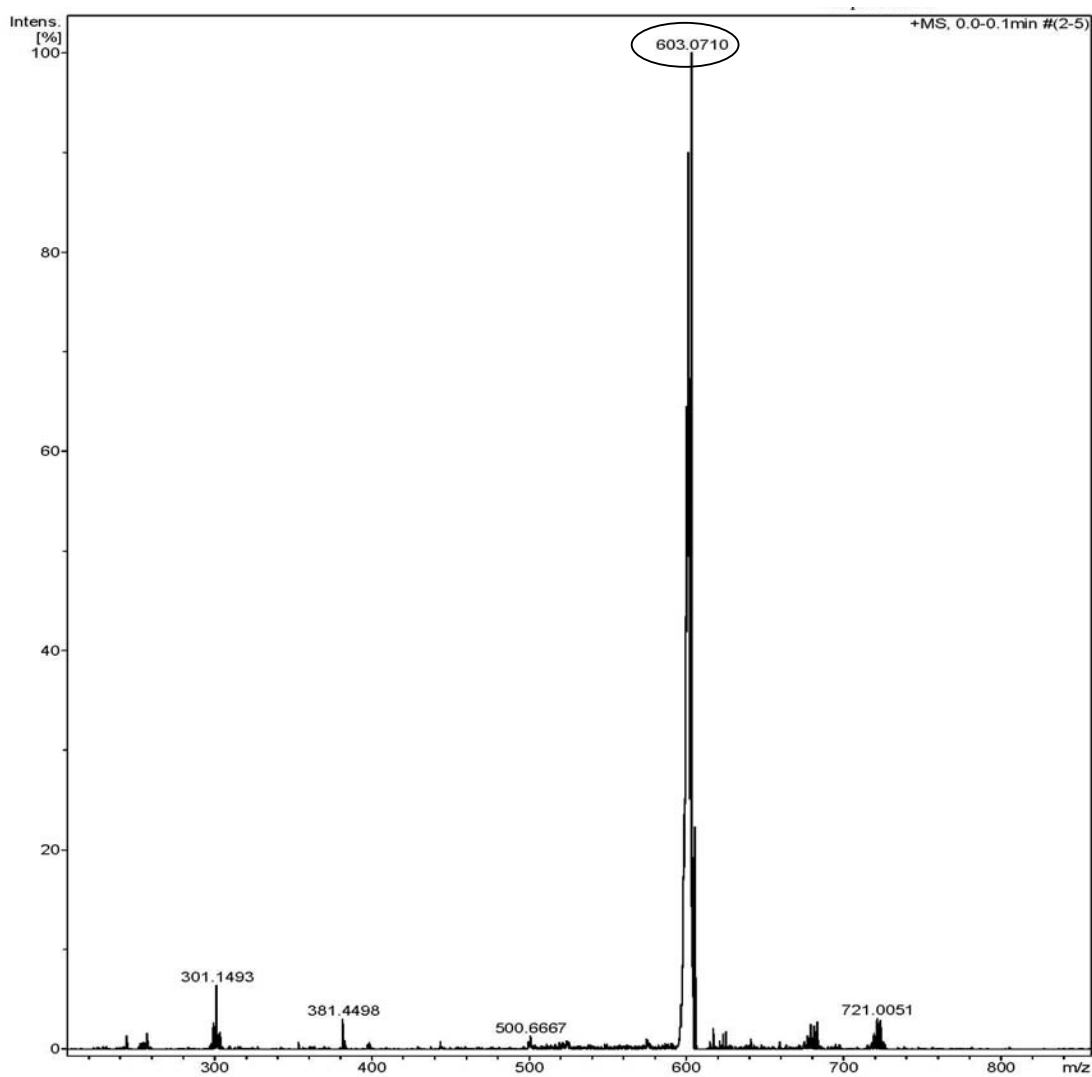


Figure S12. ESI-Mass spectrum of compound **8a**. ESI-MS: m/z calcd for $\text{C}_{26}\text{H}_{43}\text{N}_4\text{O}_2\text{Se}_2[\text{M}+\text{H}]^+$: 603.1716; found: 603.0710.

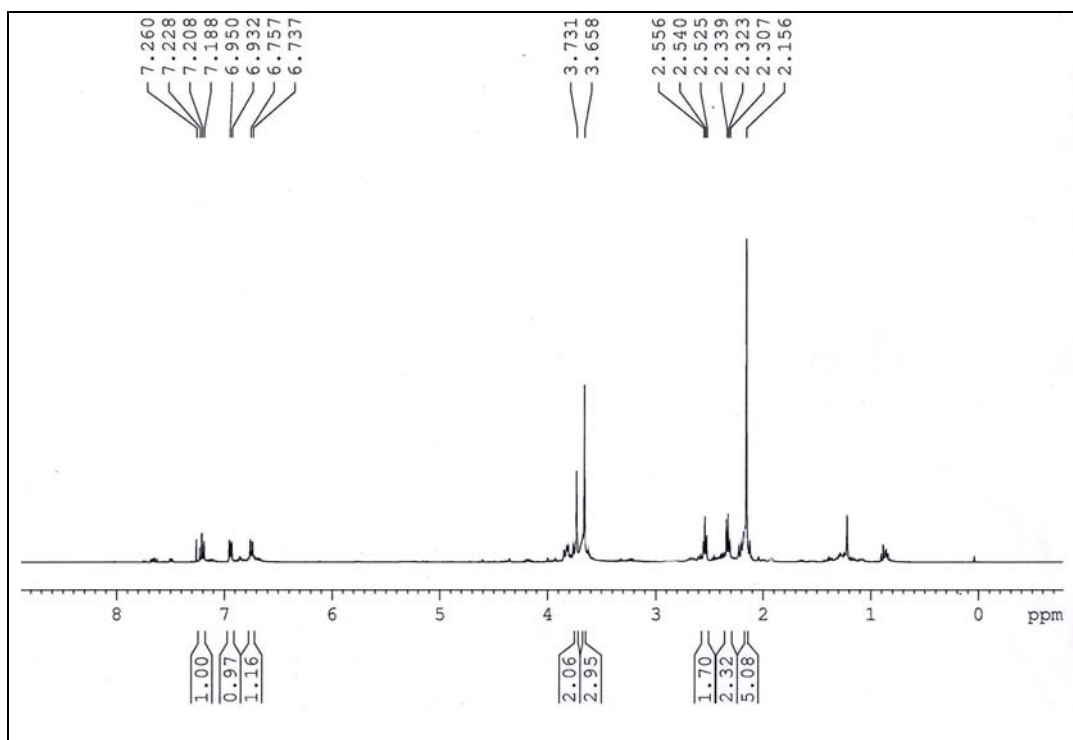


Figure S13. ¹H NMR of compound **8b** in CDCl₃

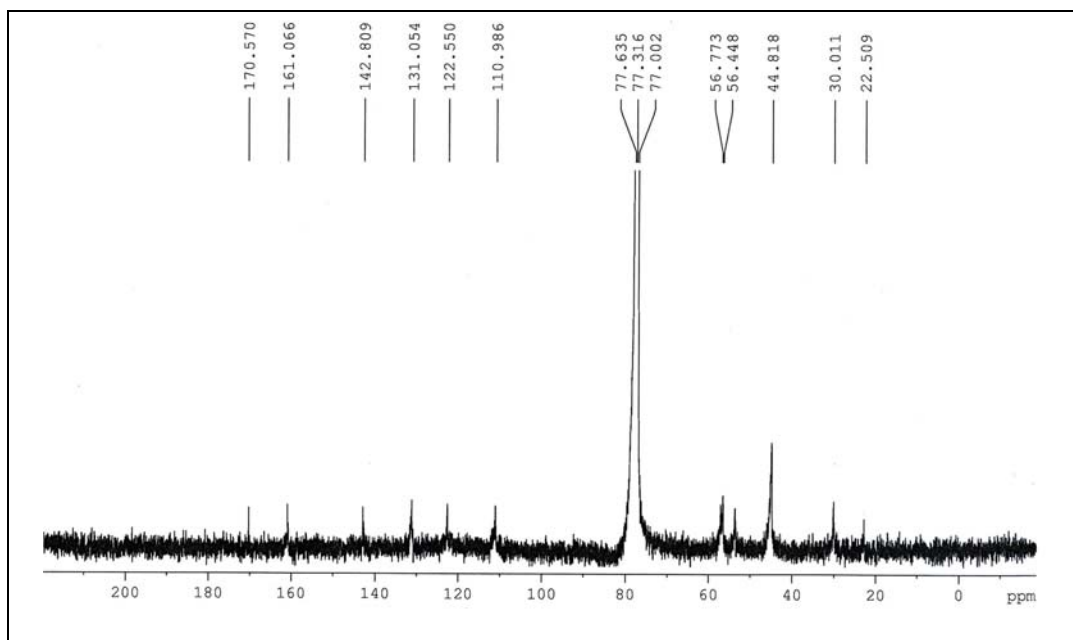


Figure S14. ¹³C NMR of compound **8b** in CDCl₃

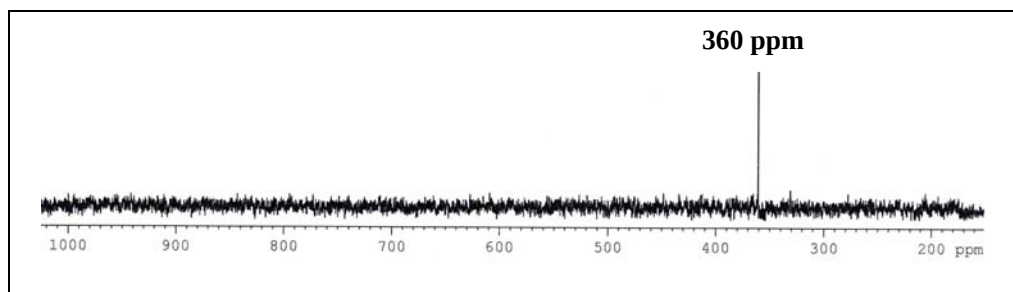


Figure S15. ⁷⁷Se NMR of compound **8b** in CDCl₃

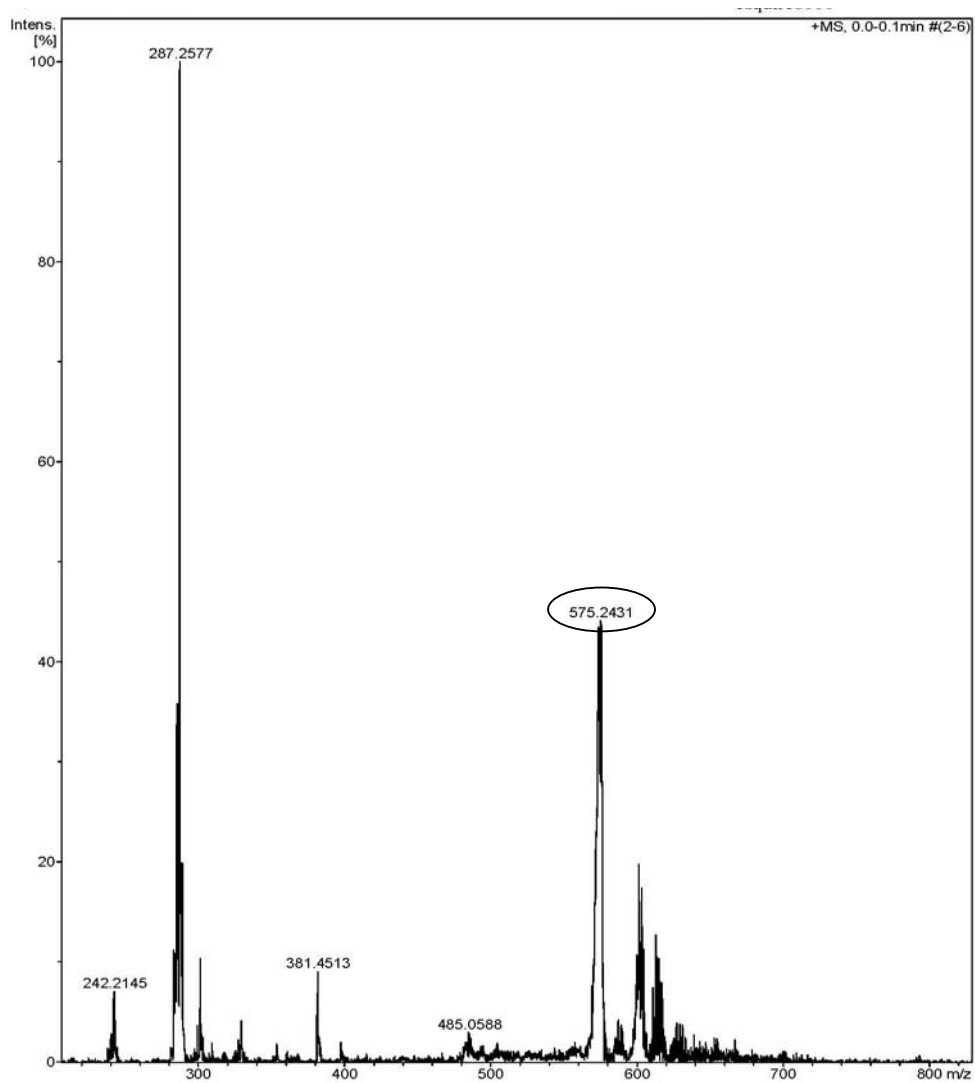


Figure S16. ESI-Mass spectrum of compound **8b**. ESI-MS: m/z calcd for C₂₄H₃₉N₄O₂Se₂[M+H]⁺: 575.1403; found: 575.2431.

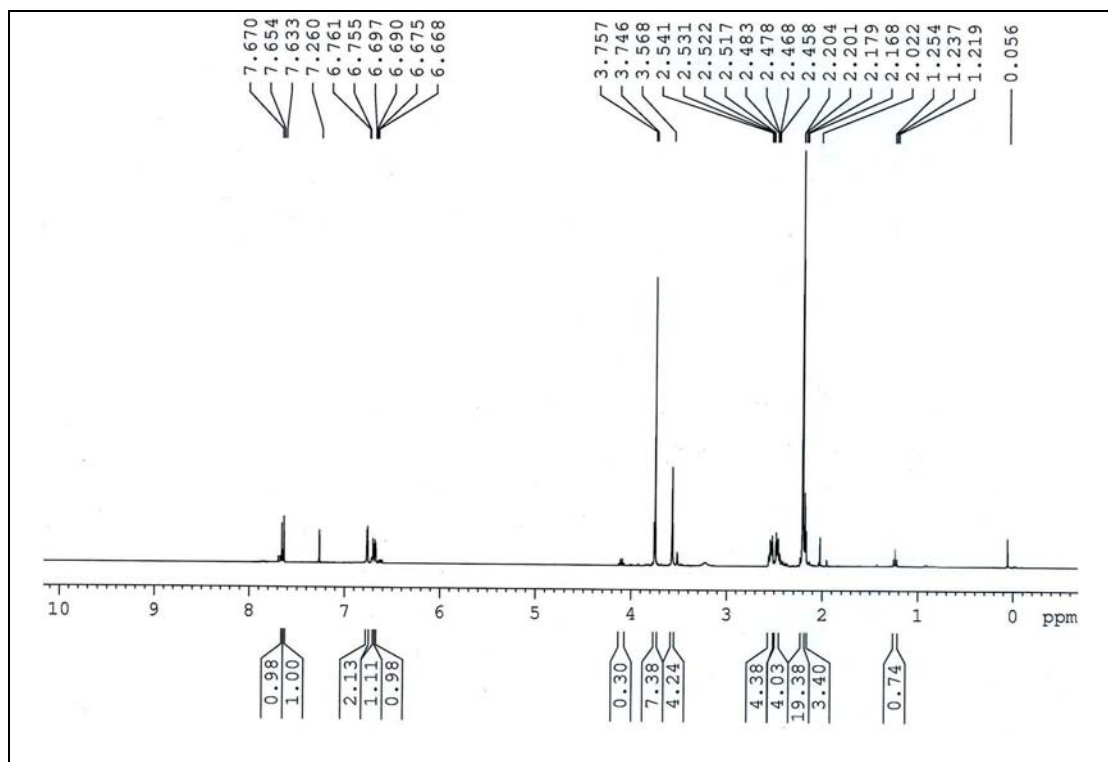


Figure S17. ¹H NMR of compound **9** in CDCl₃

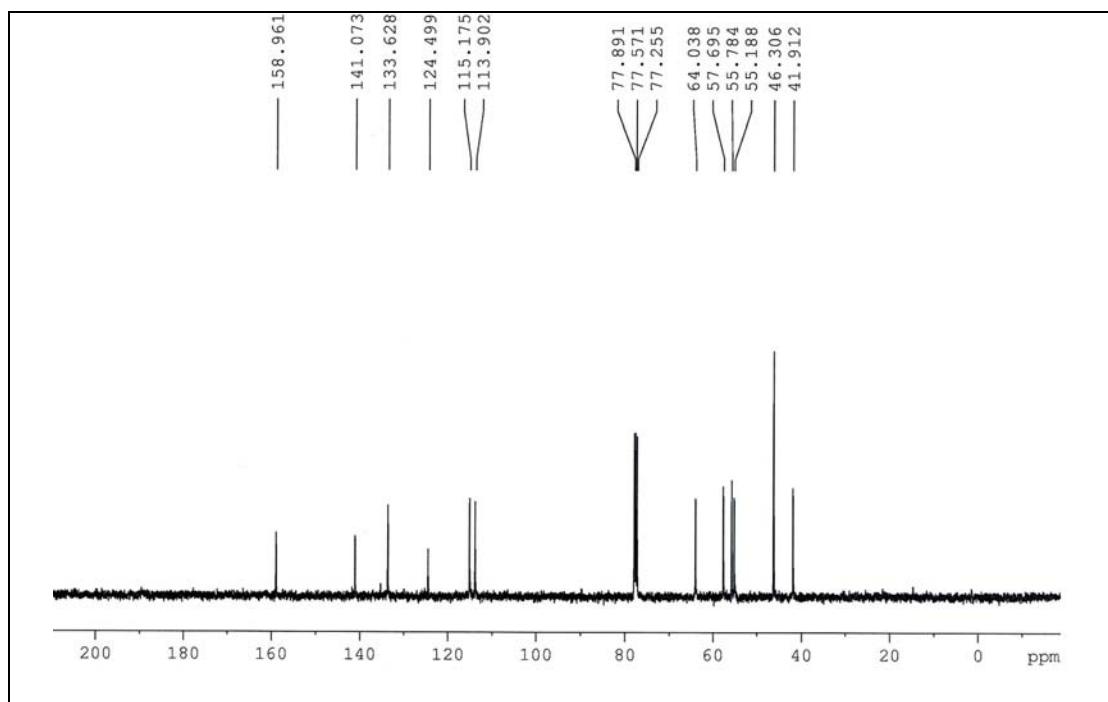


Figure S18. ¹³C NMR of compound **9** in CDCl₃

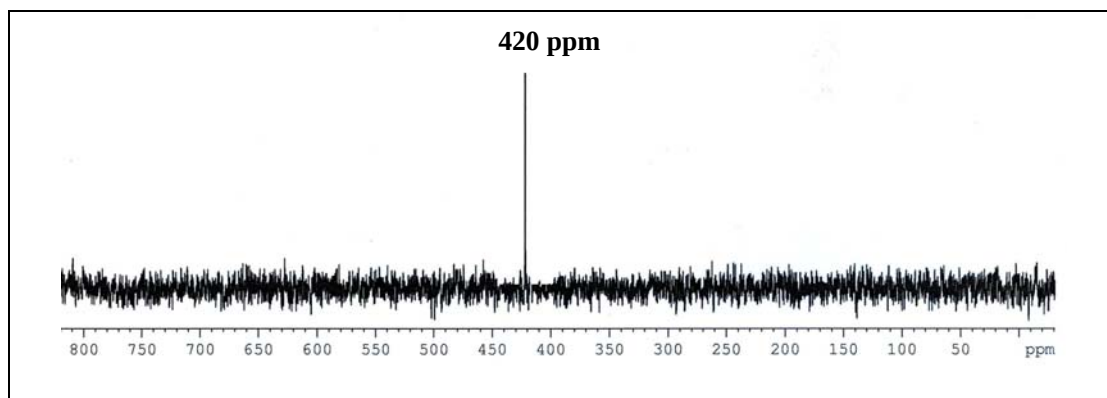


Figure S19. ^{77}Se NMR of compound **9** in CDCl_3

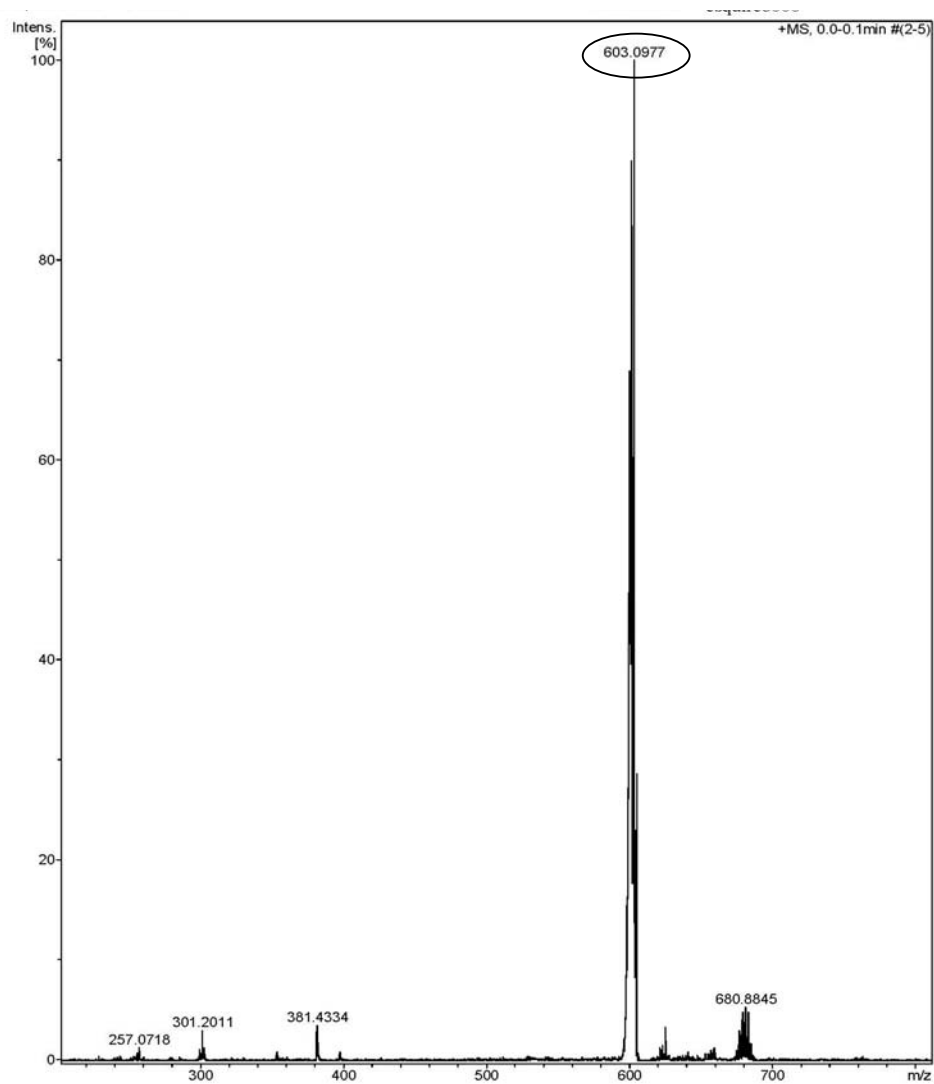


Figure S20. ESI-Mass spectrum of compound **9**. ESI-MS: m/z calcd for $\text{C}_{26}\text{H}_{43}\text{N}_4\text{O}_2\text{Se}_2[\text{M}+\text{H}]^+$: 603.1716; found: 603.0977.

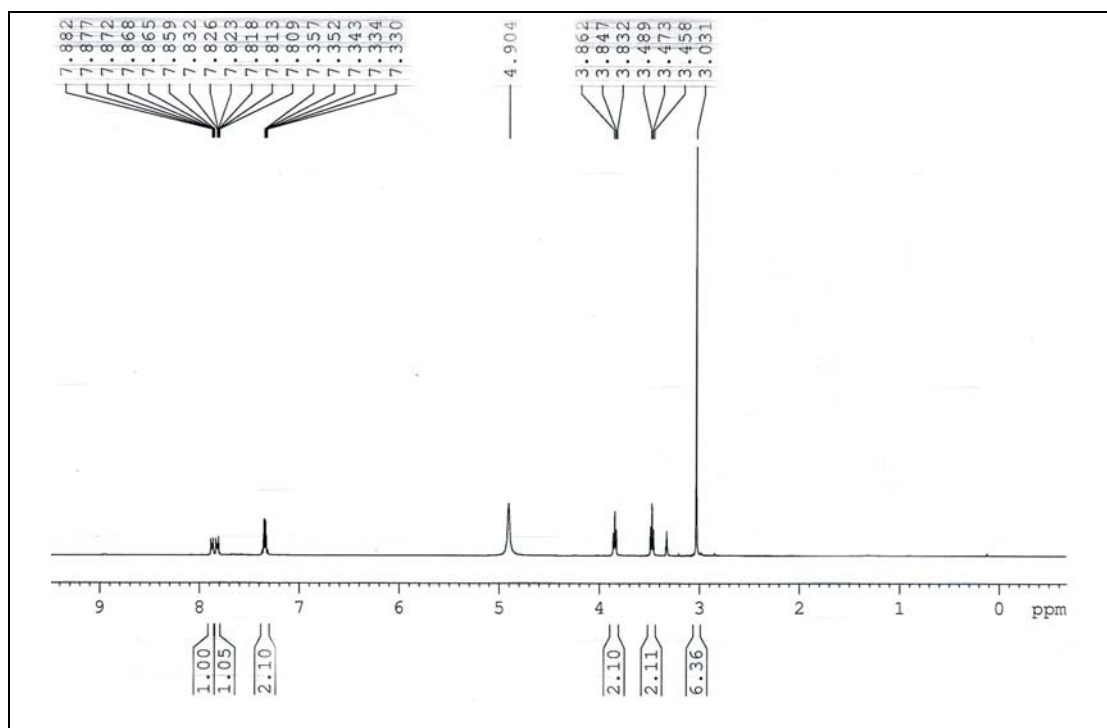


Figure S21. ¹H NMR of compound **10** in CDCl₃

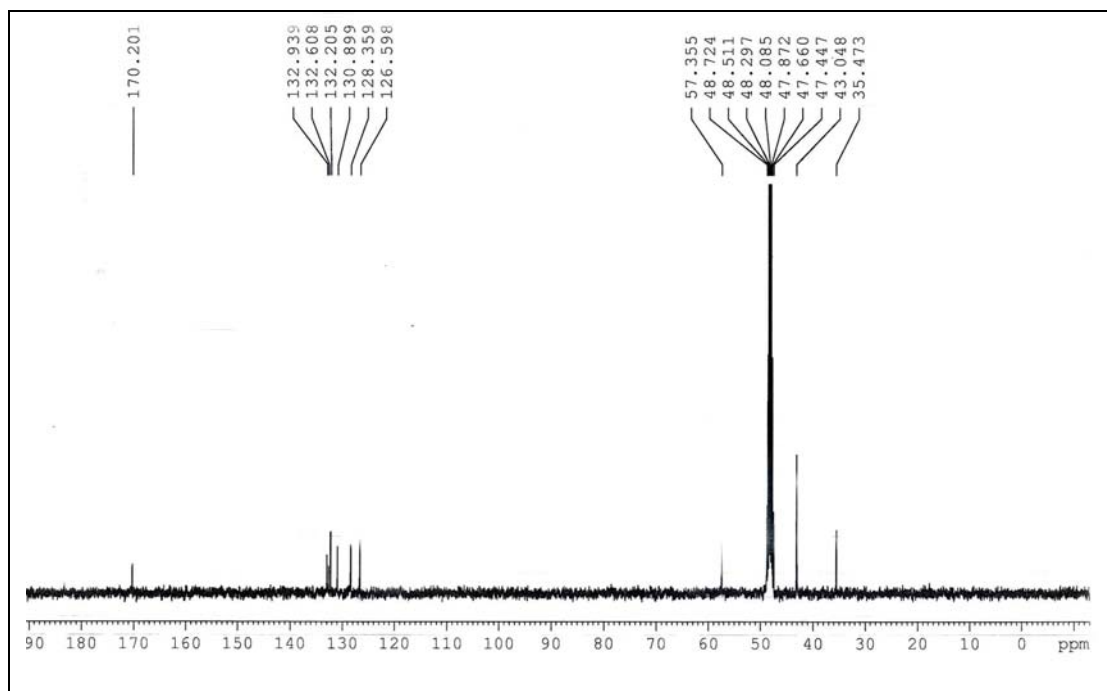


Figure S22. ¹³C NMR of compound **10** in CDCl₃

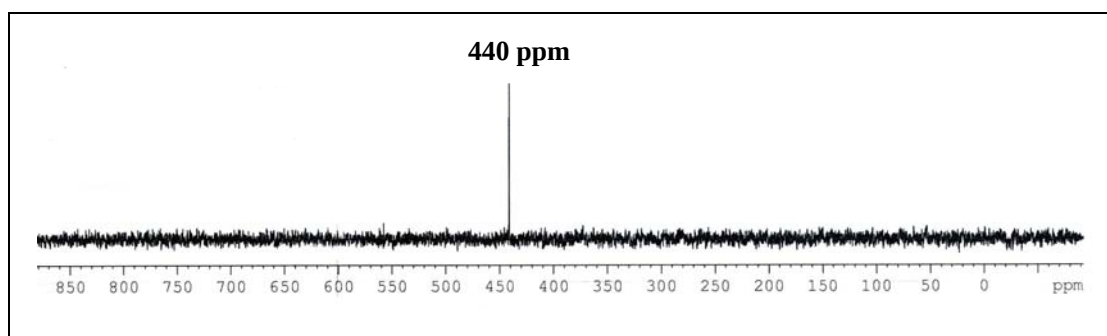


Figure S23. ⁷⁷Se NMR of compound **10** in CDCl₃

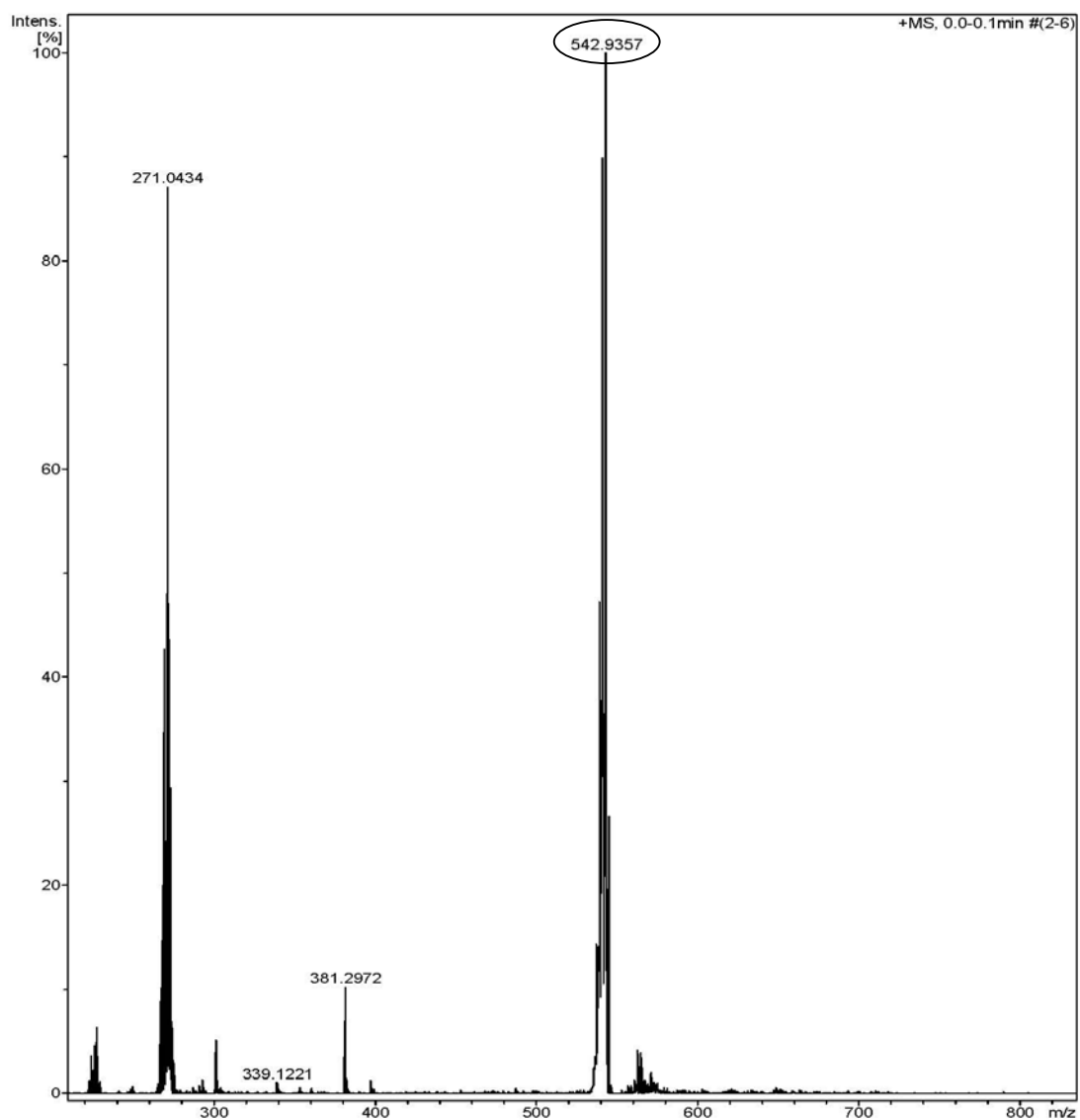


Figure S24. ESI-Mass spectrum of compound **10**. ESI-MS: m/z calcd for C₂₂H₃₁N₄O₂Se₂[M+H]⁺: 543.0777; found: 542.9357.

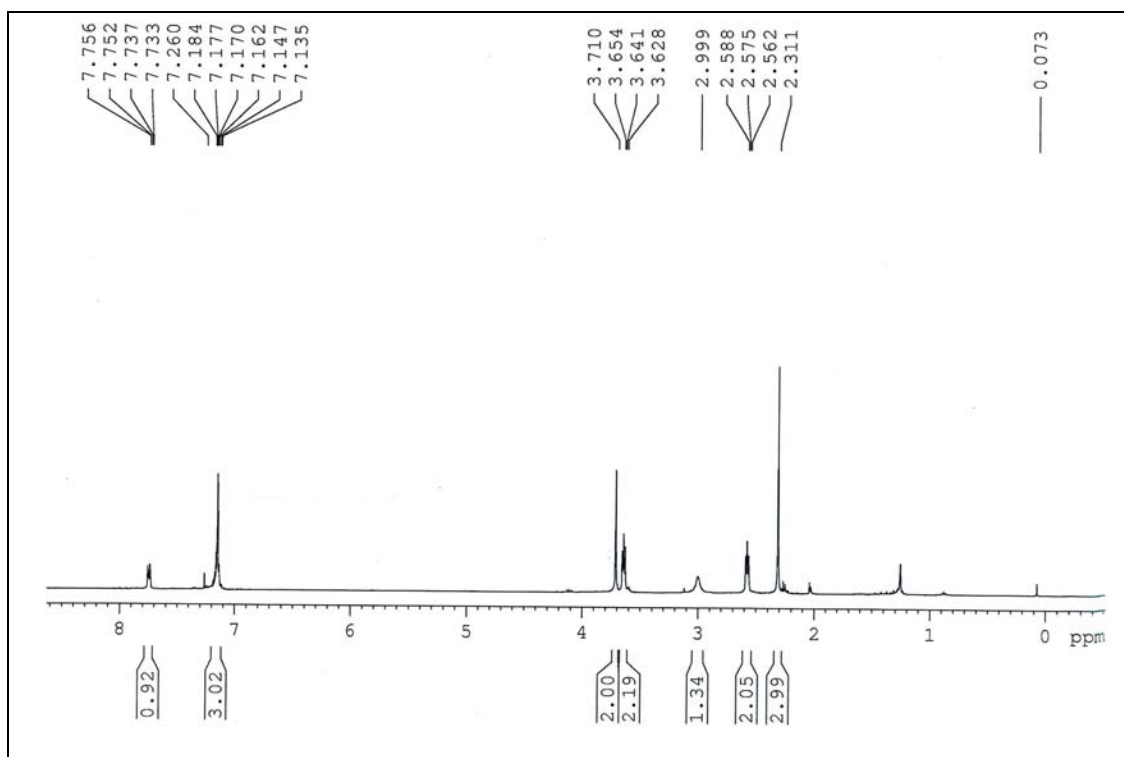


Figure S25. ¹H NMR of compound **11a** in CDCl₃

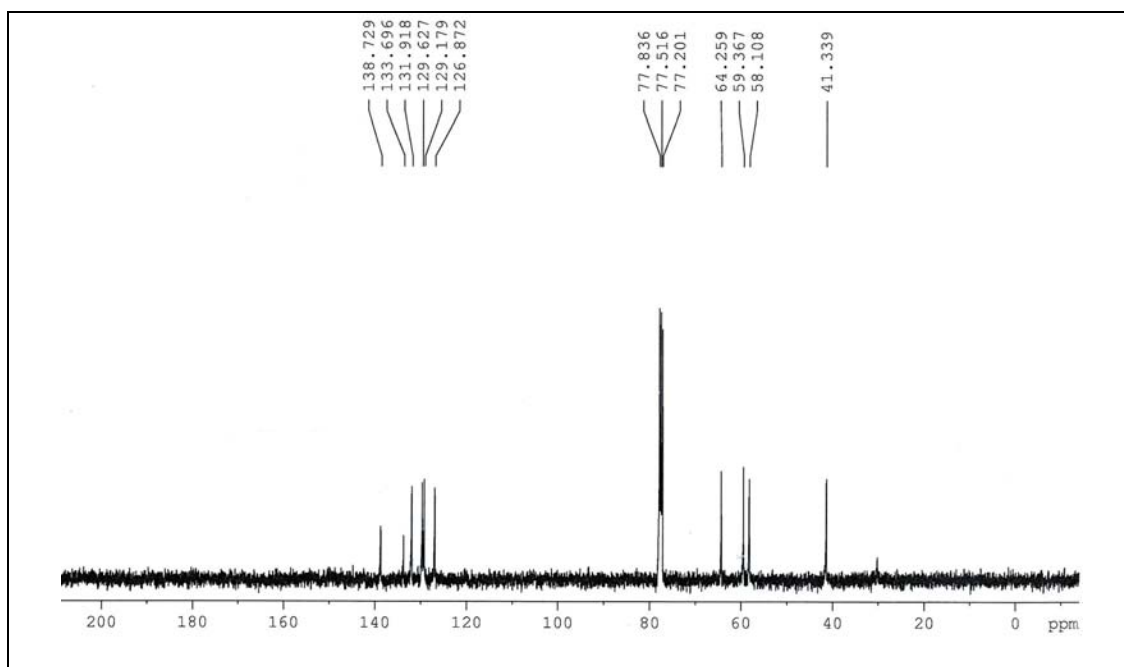


Figure S26. ¹³C NMR of compound **11a** in CDCl₃

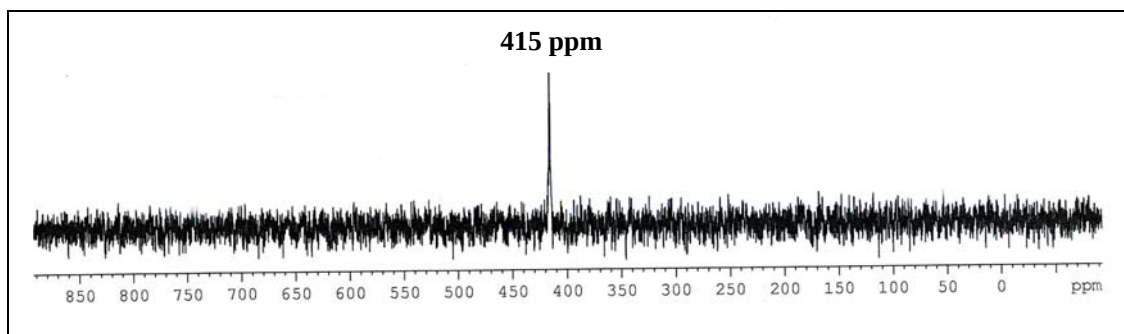


Figure S27. ^{77}Se NMR of compound **11a** in CDCl_3

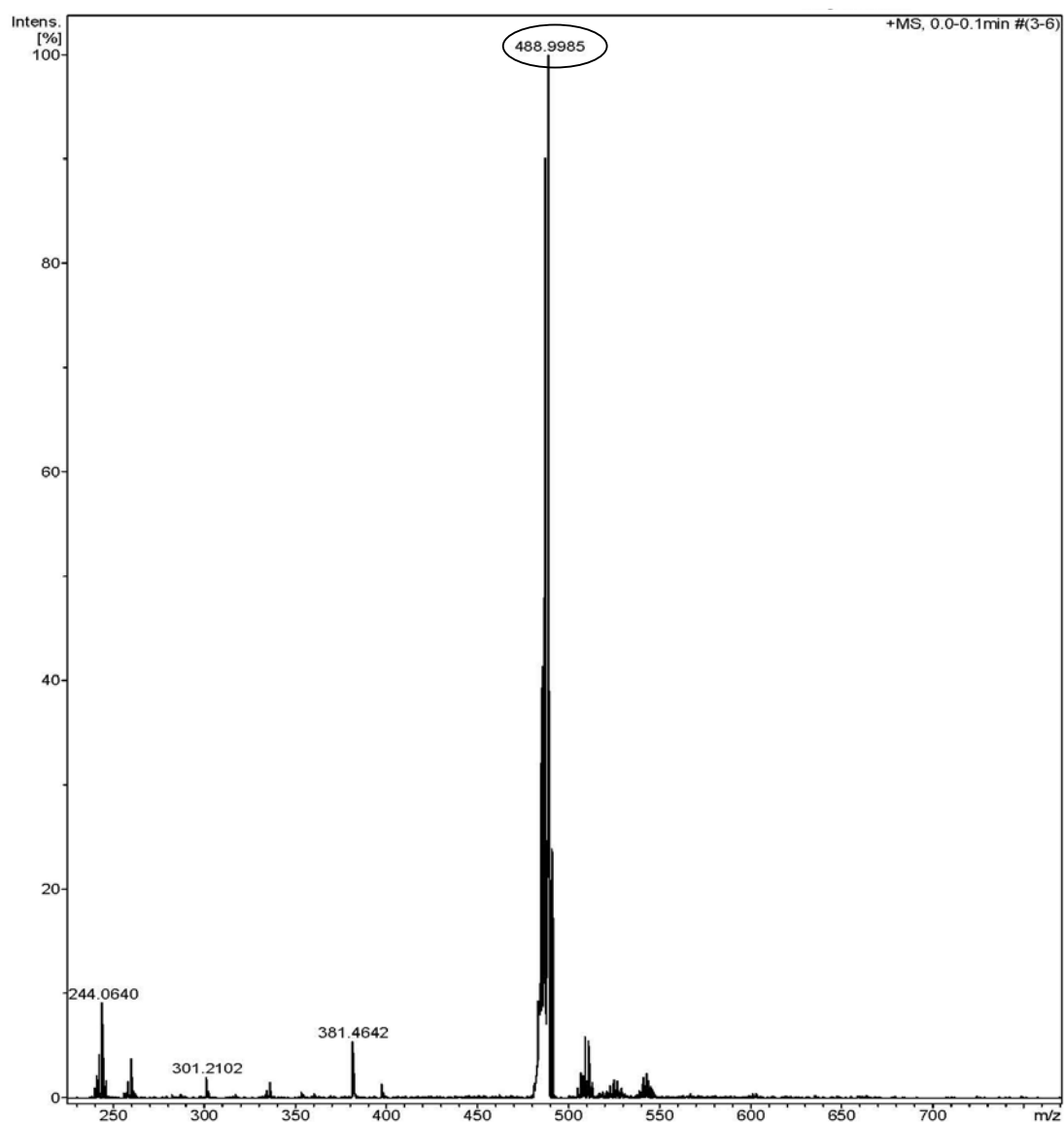


Figure S28. ESI-Mass spectrum of compound **11a**. ESI-MS: m/z calcd for $\text{C}_{20}\text{H}_{29}\text{N}_2\text{O}_2\text{Se}_2[\text{M}+\text{H}]^+$: 489.0559; found: 488.9985.

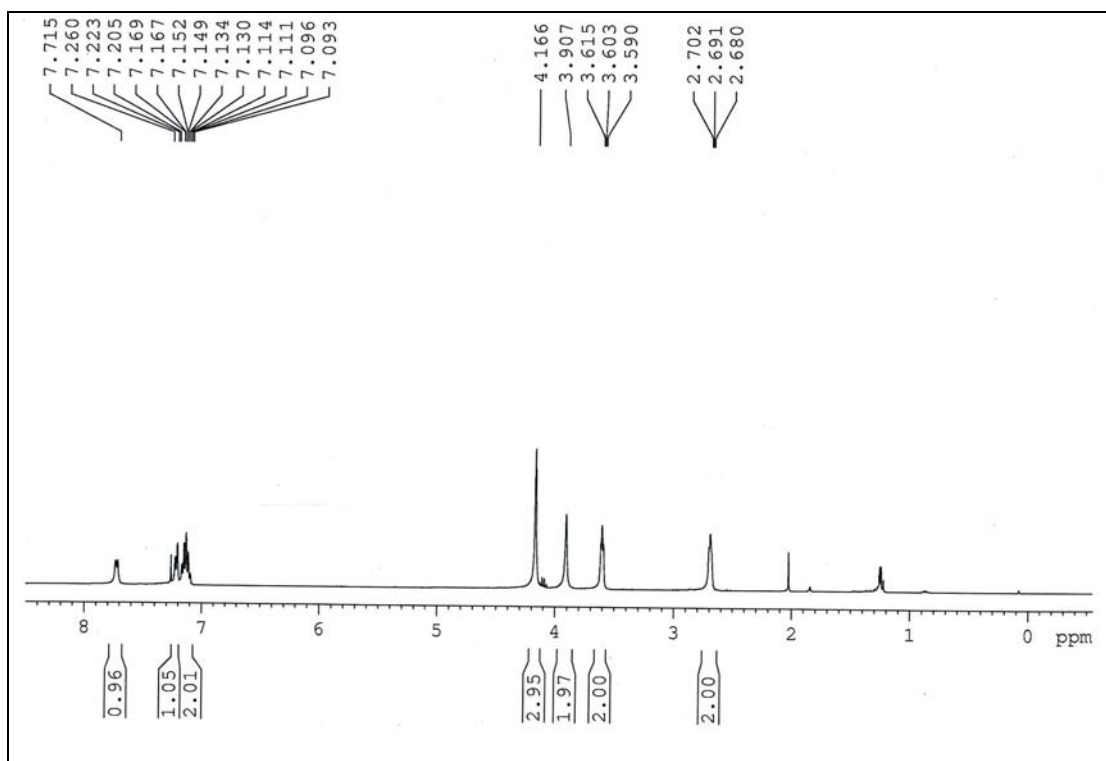


Figure S29. ¹H NMR of compound **11b** in CDCl₃

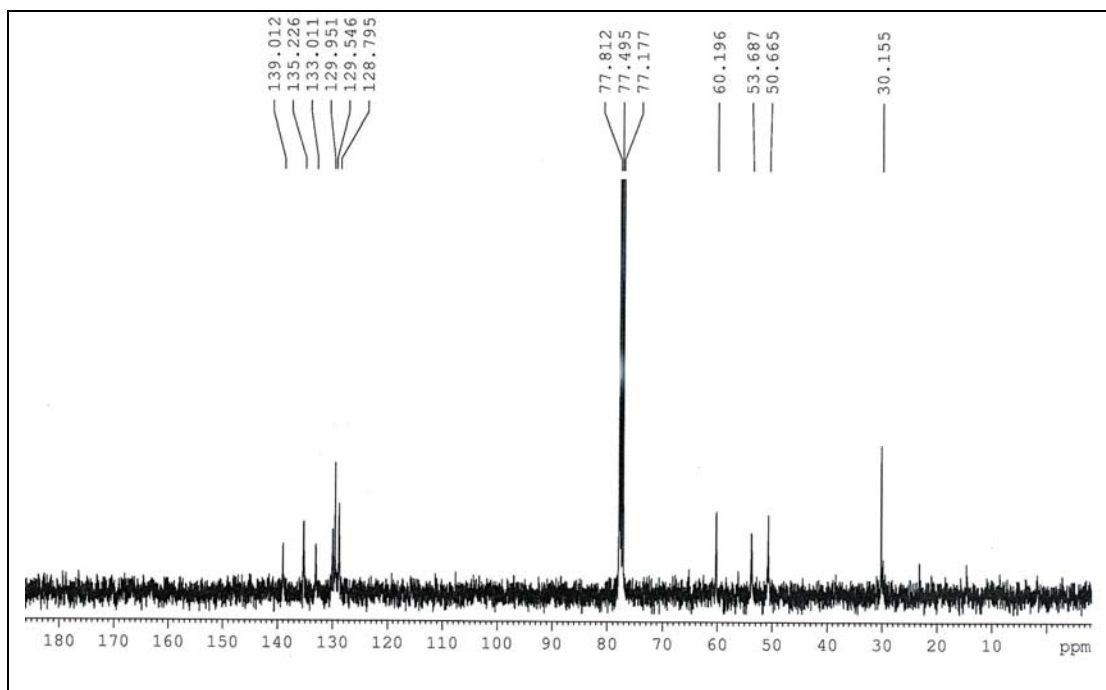


Figure S30. ¹³C NMR of compound **11b** in CDCl₃

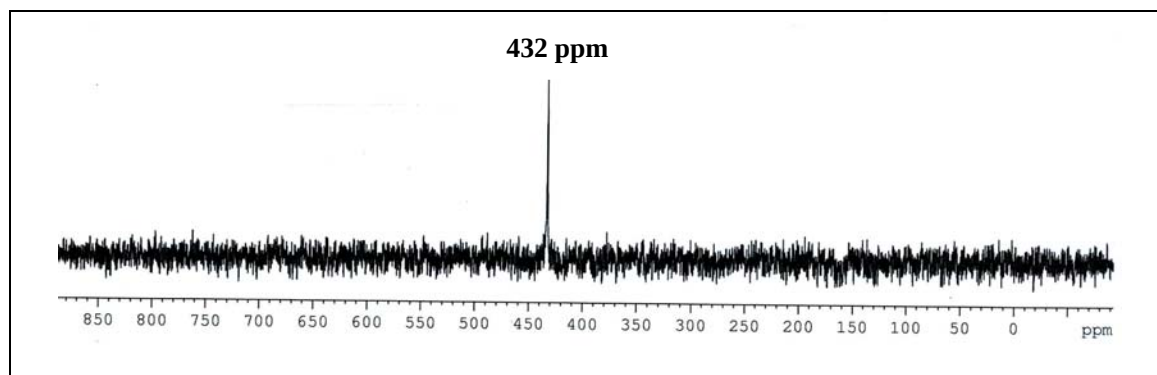


Figure S31. ⁷⁷Se NMR of compound **11b** in CDCl₃

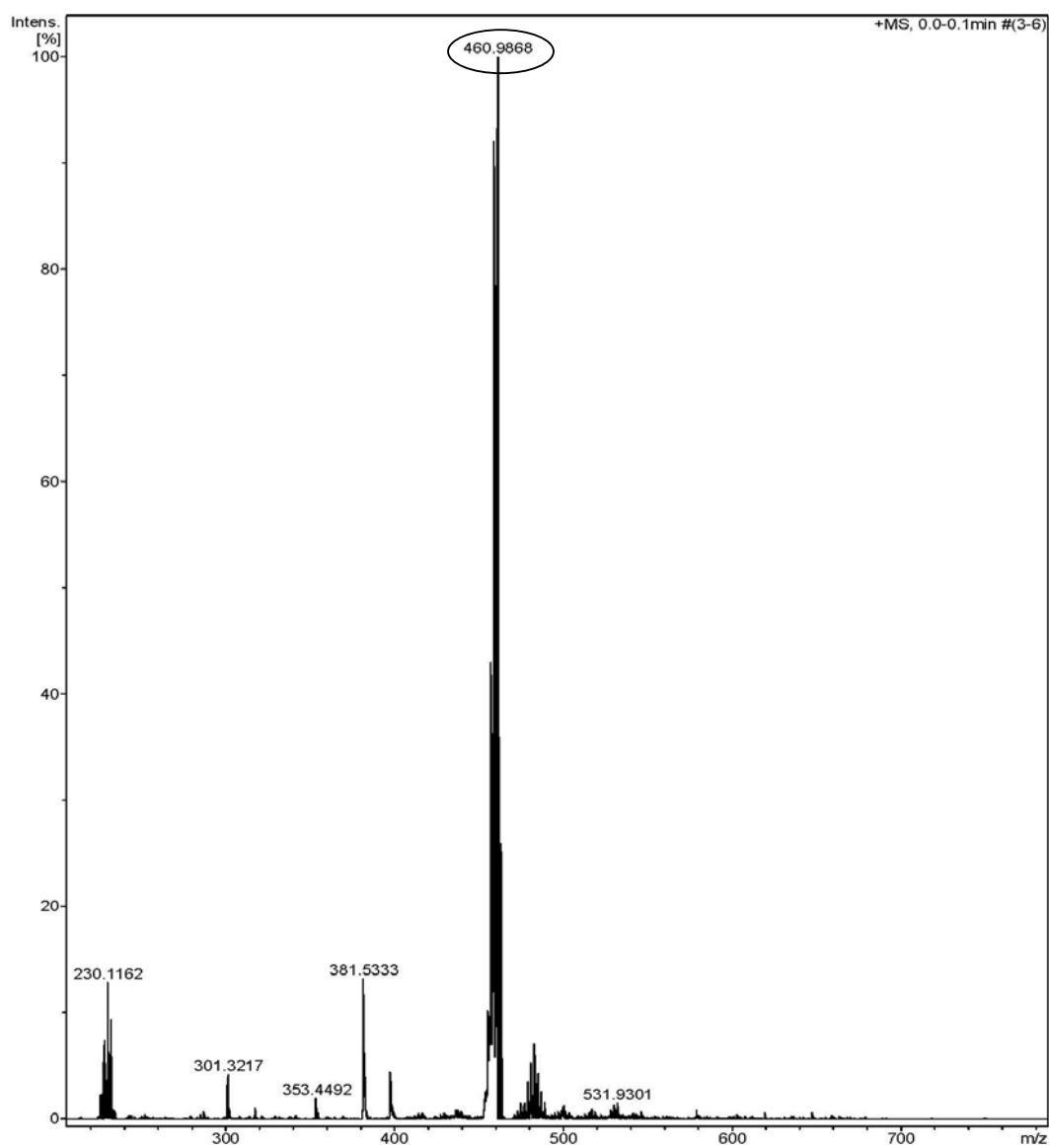


Figure S32. ESI-Mass spectrum of compound **11b**. ESI-MS: m/z calcd for C₁₈H₂₅N₂O₂Se₂[M+H]⁺: 461.0246; found: 460.9868.

Figure S33. ^{77}Se NMR spectrum of compound **7a** with H_2O_2 to produce the (a) selenenic acid **18c** (1 equiv of H_2O_2) (b) seleninic acid **19c** (2 equiv of H_2O_2) and (c) the selenonic acid **20c** (20 equiv of H_2O_2).

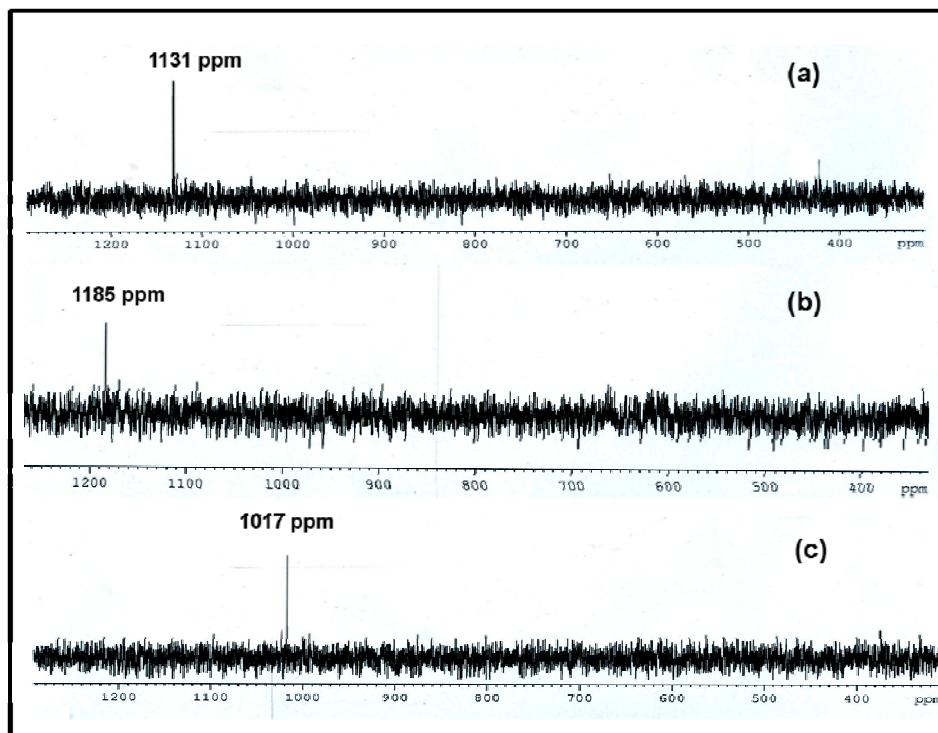


Figure S34. ^{77}Se NMR spectrum of compound **7b** with H_2O_2 to produce the (a) selenenic acid **18d** (1 equiv of H_2O_2) (b) seleninic acid **19d** (2 equiv of H_2O_2) and (c) the selenonic acid **20d** (20 equiv of H_2O_2).

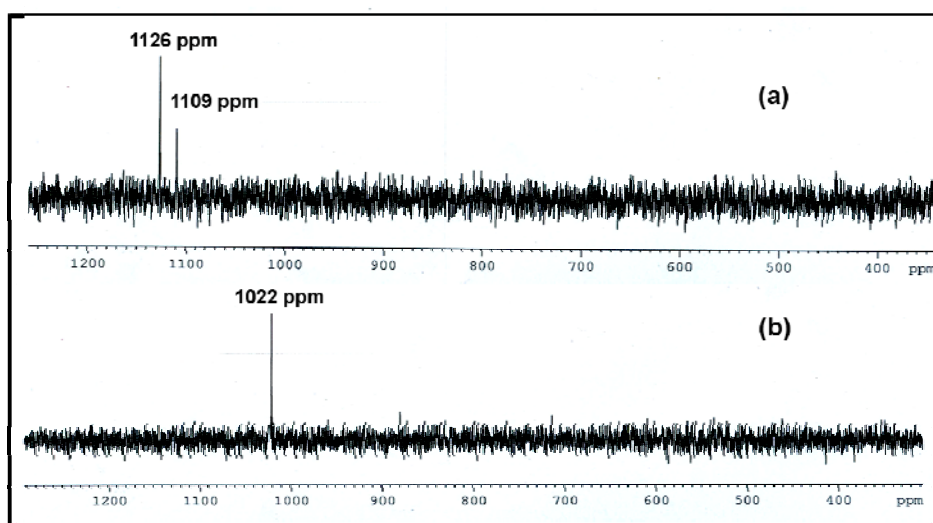


Figure S35. ^{77}Se NMR spectrum of compound **8a** with H_2O_2 to produce the (a) selenenic acid **21b** (1 equiv of H_2O_2) (b) seleninic acid **22b** (2 equiv of H_2O_2) and (c) the selenonic acid **23b** (20 equiv of H_2O_2).

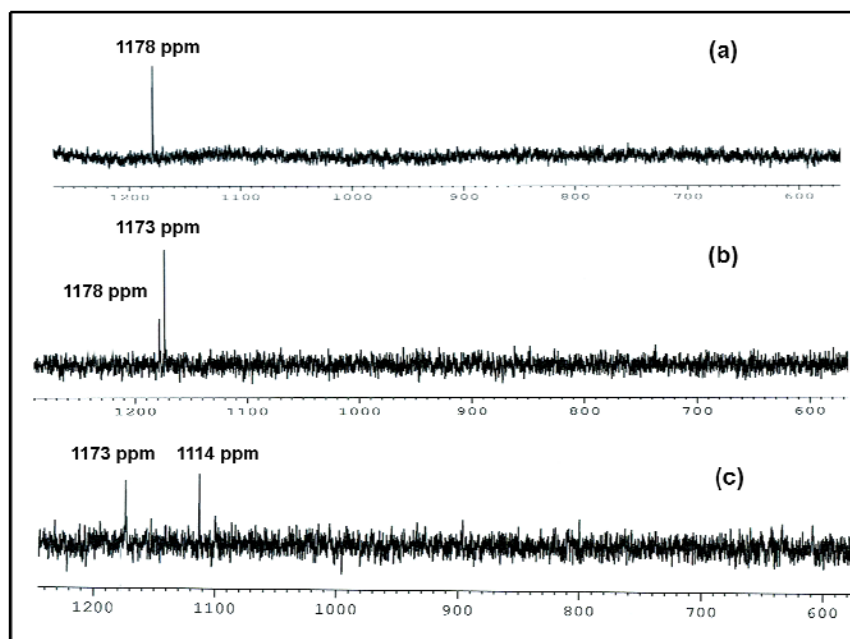


Figure S36. ^{77}Se NMR spectrum of compound **8b** with H_2O_2 to produce the (a) selenenic acid **21c** (1 equiv of H_2O_2) (b) seleninic acid **22c** (2 equiv of H_2O_2) and (c) the selenonic acid **23c** (20 equiv of H_2O_2). A new peak was observed at 1122 ppm for the selenoxide **25**.

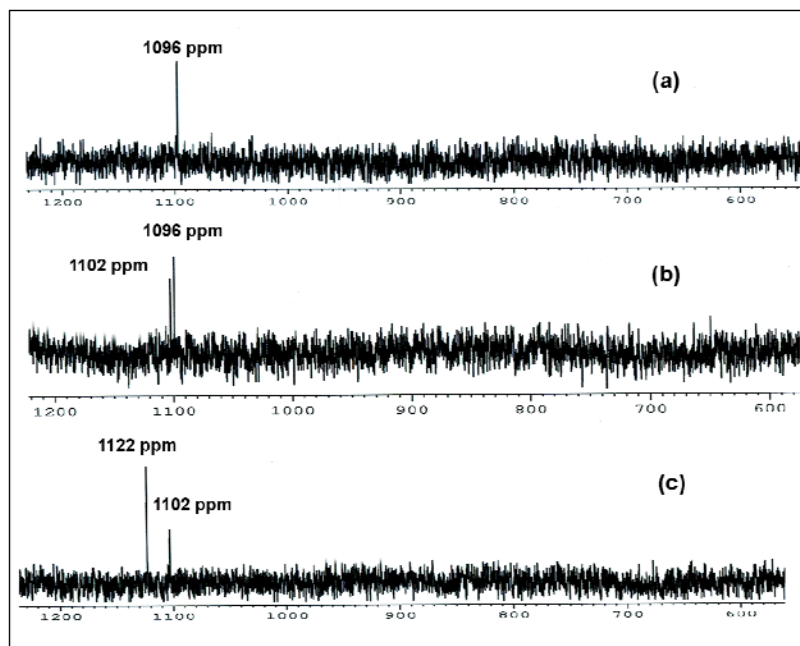


Figure S37. ^{77}Se NMR spectrum of compound **24** with H_2O_2 to produce the selenoxide **25**.

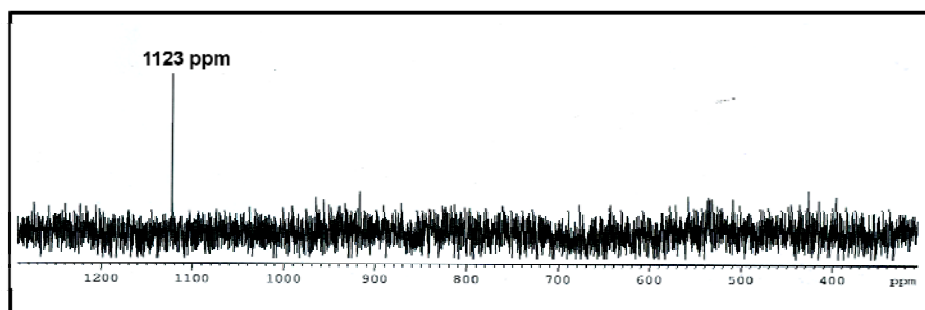


Figure S38. ^{77}Se NMR spectrum of compound **9** with H_2O_2 to produce the (a) selenenic acid **26b** and seleninic acid **27b** (1 equiv of H_2O_2) and (c) the selenonic acid **28b** (20 equiv of H_2O_2).

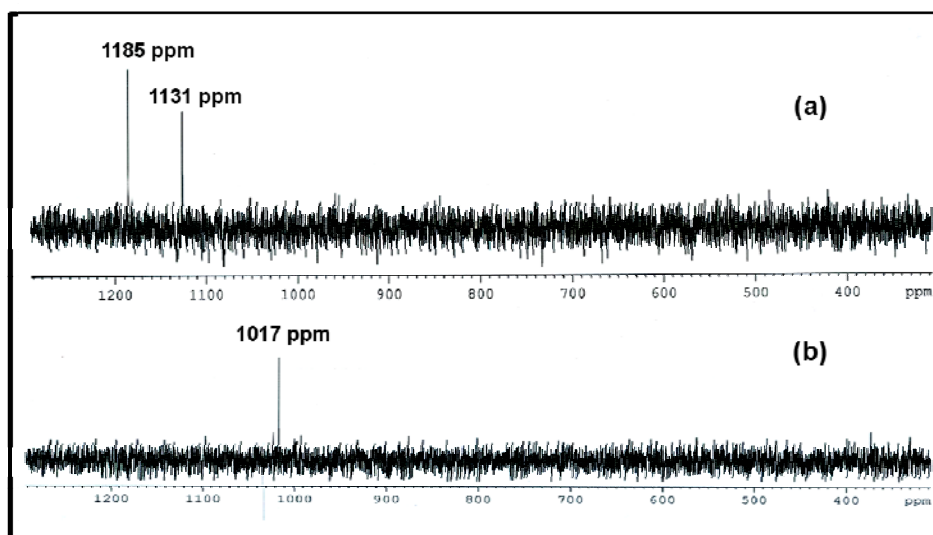


Figure S39. ^{77}Se NMR spectrum of (a) compound **4a** with H_2O_2 to produce the ebselen analogue and seleninic acid (b) compound **10** with H_2O_2 to produce the ebselen analogue **32** and seleninic acid **33**.

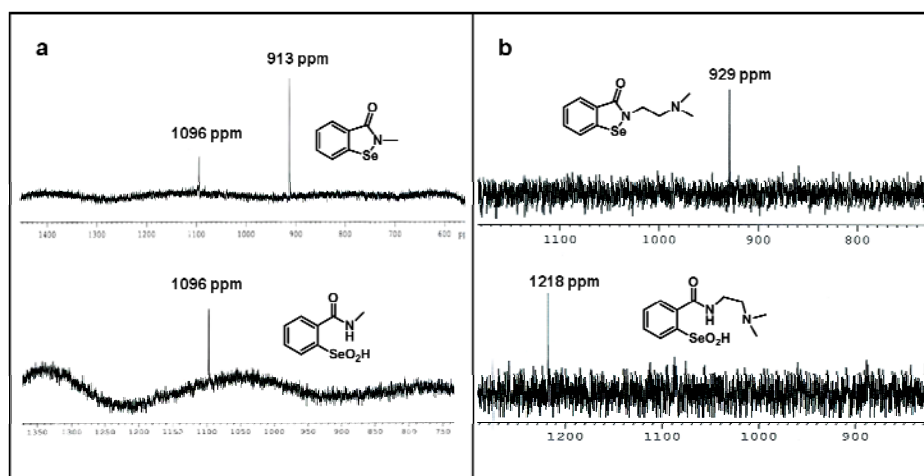


Figure S40. ^{77}Se NMR spectrum of (a) compound **7a** with PhSH to produce the selenenyl sulphide **26a** and selenol **27a** (b) compound **7b** with PhSH to produce the selenenyl sulphide **26b** and selenol **27b**, however, the peak for selenol **27b** was not detected.

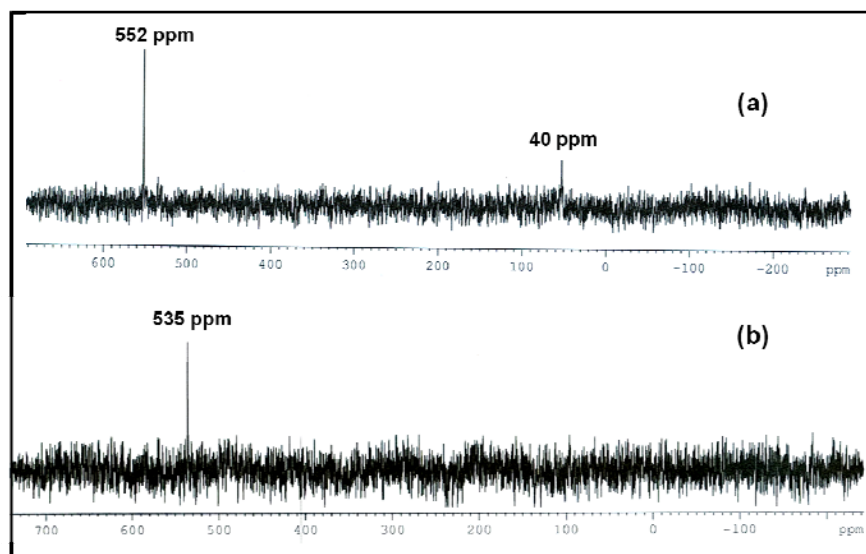


Figure S41. ^{77}Se NMR spectrum of (a) compound **8a** with PhSH to produce the selenenyl sulphide **26c** and selenol **27c** (b) compound **8b** with PhSH to produce the selenenyl sulphide **26d** and selenol **27d**, however, the peak for selenol **27d** was not detected.

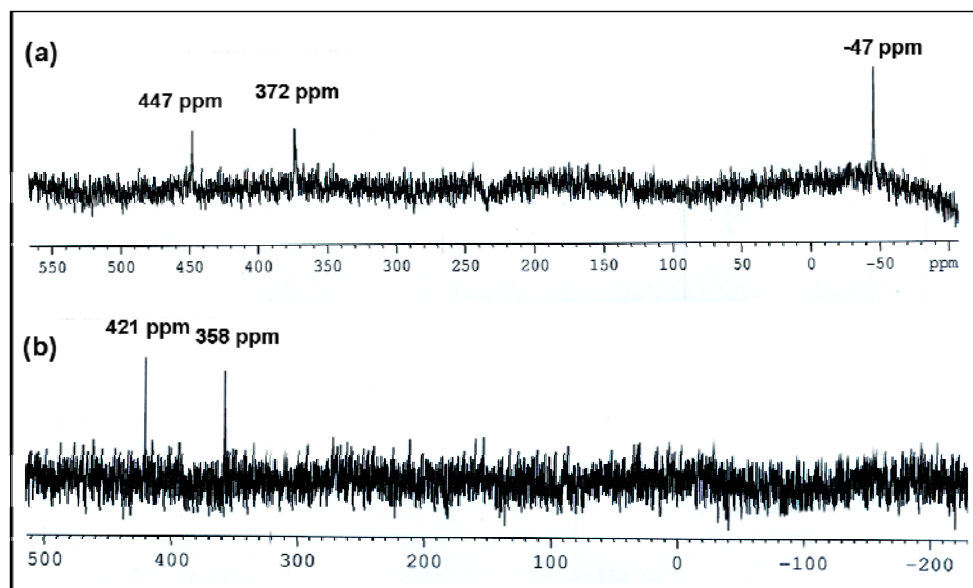


Figure S42. ^{77}Se NMR spectrum of compound **9** with PhSH to produce the selenenyl sulphide **26e** and the selenol **27e**.

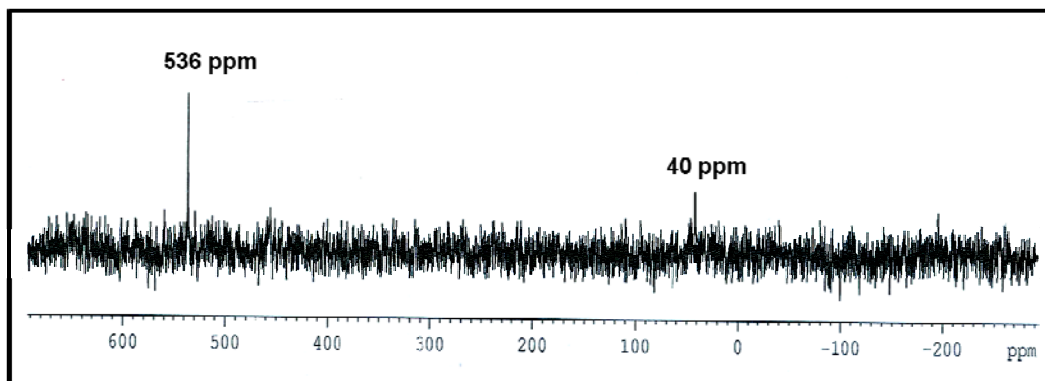


Figure S43. The ^{77}Se NMR spectra of compound **10** (a) without PhSH, (b) 2 equiv of PhSH, (c) 4 equiv of PhSH, which indicates the complete conversion of the diselenide to the selenenyl sulfide **28**. (d) Excess of PhSH leads to the formation of the selenol **29**, which is trapped by iodoacetic acid to obtain the monoselenide **30**.

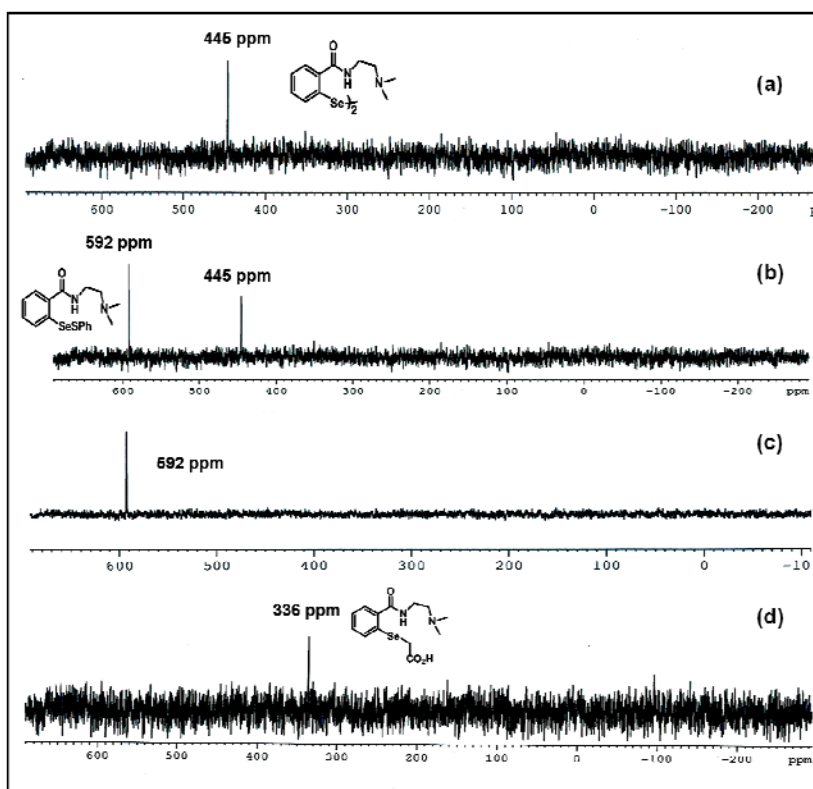


Table S40. The energy optimized structures and the coordinates of the compounds **2d**, **5d**, **6d** and **26a-d**. The compounds are optimized by DFT calculation using B3LYP/6-31+G(d) basis set in Gaussian 98 program.

Compound 2d				Compound 5d			
34	0.347310000	-0.873794000	-0.606544000	6	1.555784000	3.046499000	-0.841844000
16	-1.545451000	-0.218069000	-1.638518000	6	2.576724000	3.134562000	0.106778000
1	4.393356000	-0.225784000	0.227953000	6	0.929113000	1.822442000	-1.087347000
7	2.698901000	-1.500464000	0.517497000	1	3.075921000	4.081511000	0.294044000
6	-2.793124000	-0.142495000	-0.345239000	1	0.137211000	1.759810000	-1.827505000
6	-4.127321000	-0.108534000	-0.781599000	6	2.957234000	1.990393000	0.811421000
1	-4.348893000	-0.161066000	-1.845023000	6	1.296740000	0.683618000	-0.368003000
6	-5.169435000	0.004490000	0.139760000	1	3.756509000	2.048567000	1.547752000
1	-6.196440000	0.034752000	-0.216117000	34	0.511896000	-1.068739000	-0.728031000
6	-4.897315000	0.059371000	1.510391000	6	2.327701000	0.759909000	0.589210000
1	-5.708499000	0.140146000	2.229088000	1	1.252304000	3.925780000	-1.404574000
6	-3.570606000	0.010330000	1.944954000	6	2.739829000	-0.471827000	1.361367000
1	-3.343538000	0.050118000	3.007817000	1	3.627964000	-0.258334000	1.980924000
6	-2.521384000	-0.097950000	1.027677000	7	2.938839000	-1.587202000	0.434590000
1	-1.495470000	-0.144542000	1.378199000	1	3.691740000	-1.374908000	-0.217629000
1	3.725818000	-1.502026000	2.393152000	6	3.136127000	-2.888550000	1.065079000
6	2.709279000	-1.383891000	1.973995000	1	3.988847000	-2.914294000	1.765565000
1	2.322963000	-0.404914000	2.270578000	1	2.228600000	-3.157010000	1.618154000
1	2.061581000	-2.154583000	2.403841000	1	1.933649000	-0.772578000	2.047083000
6	3.369767000	-0.387534000	-0.157248000	16	-1.464345000	-0.475753000	-1.622053000
6	2.557839000	0.883238000	-0.043175000	6	-2.580129000	-0.157906000	-0.249230000
6	3.190580000	2.110922000	0.184631000	6	-2.169987000	0.262807000	1.021985000
1	4.269106000	2.129980000	0.328984000	6	-3.950955000	-0.263461000	-0.533135000
6	2.460796000	3.300260000	0.234578000	1	-1.113676000	0.356345000	1.251353000
1	2.966984000	4.244559000	0.416330000	1	-4.274947000	-0.595604000	-1.516475000

6	1.076913000	3.261946000	0.050267000	6	-3.125112000	0.571574000	1.994381000
1	0.492473000	4.177707000	0.090229000	6	-4.897932000	0.052044000	0.442816000
6	0.431830000	2.045799000	-0.189006000	1	-2.795362000	0.898391000	2.977851000
1	-0.640559000	2.029351000	-0.352672000	1	-5.956207000	-0.037299000	0.209641000
6	1.165309000	0.857020000	-0.239554000	6	-4.490037000	0.464413000	1.714864000
1	3.462340000	-0.661765000	-1.217276000	1	-5.226772000	0.705119000	2.476689000
6	3.159514000	-2.809439000	0.067098000	1	3.296816000	-3.645021000	0.290847000
1	4.211213000	-3.006549000	0.344947000				
1	2.532184000	-3.588527000	0.512568000				
1	3.065916000	-2.876691000	-1.021489000				

Compound 26a				Compound 26b			
6	-1.758750000	3.840662000	-0.266940000	6	-1.724511000	3.775459000	-0.530029000
6	-0.940118000	4.379075000	0.728404000	6	-0.919954000	4.391536000	0.430689000
6	-1.512555000	2.556613000	-0.759148000	6	-1.479960000	2.452615000	-0.906874000
1	-1.121147000	5.380921000	1.108594000	1	-1.095788000	5.425008000	0.716997000
1	-2.151989000	2.140111000	-1.531510000	1	-2.106229000	1.978750000	-1.656602000
6	0.120145000	3.620539000	1.229763000	6	0.122133000	3.669452000	1.016753000
6	-0.468013000	1.791900000	-0.236851000	6	-0.451713000	1.726209000	-0.303727000
1	0.768120000	4.037249000	1.998450000	1	0.758639000	4.145208000	1.760438000
34	-0.028246000	0.020433000	-0.919261000	34	-0.006261000	-0.092863000	-0.850336000
6	0.373696000	2.329055000	0.754761000	6	0.365161000	2.336243000	0.667925000
1	-2.582303000	4.421954000	-0.673951000	1	-2.534242000	4.326005000	-1.002368000
6	1.507345000	1.496045000	1.306855000	6	1.494620000	1.559296000	1.303437000
1	2.120153000	2.092422000	2.007455000	1	2.100006000	2.217061000	1.949843000
7	2.313670000	0.921576000	0.219853000	7	2.274577000	0.900105000	0.255300000
6	3.097757000	-0.235012000	0.668897000	1	2.708711000	1.594527000	-0.352390000

1	3.861862000	0.073330000	1.408037000	6	3.250059000	-0.090181000	0.707531000
1	2.399130000	-0.904766000	1.182775000	1	3.986798000	0.343431000	1.407052000
6	3.758367000	-1.004626000	-0.497694000	1	2.695892000	-0.863315000	1.254265000
1	4.608408000	-0.434675000	-0.892410000	6	3.959286000	-0.708422000	-0.515950000
1	3.024717000	-1.093995000	-1.308626000	1	4.433475000	0.097741000	-1.095150000
7	4.247942000	-2.345909000	-0.186032000	1	3.193064000	-1.152806000	-1.162937000
6	5.341808000	-2.384064000	0.773343000	7	4.978712000	-1.718892000	-0.256593000
1	6.117068000	-1.667372000	0.478408000	6	6.175657000	-1.224044000	0.407265000
1	5.037543000	-2.154799000	1.813487000	1	6.541370000	-0.329369000	-0.109726000
1	5.789557000	-3.385074000	0.773390000	1	6.029206000	-0.969937000	1.475319000
6	3.207679000	-3.320429000	0.112503000	1	6.960433000	-1.988021000	0.354702000
1	3.642455000	-4.326806000	0.096089000	6	4.471276000	-2.945438000	0.341740000
1	2.726708000	-3.182386000	1.100487000	1	5.246360000	-3.719377000	0.294359000
1	2.426670000	-3.274516000	-0.653950000	1	4.171293000	-2.837774000	1.402600000
1	1.093219000	0.652301000	1.874820000	1	3.602803000	-3.300118000	-0.224174000
16	-2.027277000	-0.641313000	-1.702479000	1	1.088889000	0.761530000	1.942803000
6	-2.934193000	-1.302533000	-0.297732000	16	-1.983967000	-0.788675000	-1.664321000
6	-2.657048000	-1.006078000	1.042143000	6	-2.951301000	-1.350890000	-0.257657000
6	-4.029466000	-2.123093000	-0.611610000	6	-2.752841000	-0.929351000	1.062736000
1	-1.815846000	-0.370834000	1.298571000	6	-4.024108000	-2.206157000	-0.555930000
1	-4.243815000	-2.364879000	-1.649904000	1	-1.931610000	-0.263204000	1.305061000
6	-3.477234000	-1.519188000	2.051091000	1	-4.180545000	-2.540448000	-1.578731000
6	-4.843936000	-2.628595000	0.402655000	6	-3.620009000	-1.364122000	2.069051000
1	-3.255921000	-1.278393000	3.088339000	6	-4.887469000	-2.631118000	0.455002000
1	-5.687978000	-3.263346000	0.143849000	1	-3.457098000	-1.029528000	3.090978000
6	-4.568551000	-2.334604000	1.741612000	1	-5.712138000	-3.295827000	0.209190000
1	-5.199815000	-2.730979000	2.532415000	6	-4.686356000	-2.217799000	1.775426000
6	3.110594000	1.936251000	-0.470020000	1	-5.355789000	-2.551615000	2.563753000

1	3.916238000	2.337097000	0.174395000	
1	3.562344000	1.517022000	-1.372068000	
1	2.464968000	2.765547000	-0.771550000	

Compound 6d				Compound 26c			
34	0.404476000	-1.064532000	-0.197850000	6	2.638025000	-3.149430000	0.567061000
16	-1.382149000	-0.725528000	-1.513126000	6	2.000252000	-3.489515000	1.762469000
1	4.490776000	-0.385753000	-0.708653000	6	2.079855000	-2.172229000	-0.269410000
7	3.146618000	-1.513738000	0.518765000	1	2.436851000	-4.253298000	2.400798000
6	-2.808289000	-0.583193000	-0.428340000	6	0.800901000	-2.877786000	2.122851000
6	-4.055283000	-0.476418000	-1.065915000	6	0.902607000	-1.502620000	0.128087000
1	-4.109806000	-0.466541000	-2.152356000	1	0.286071000	-3.173621000	3.033545000
6	-5.225584000	-0.369812000	-0.311707000	34	0.087787000	-0.140926000	-0.973939000
1	-6.182249000	-0.281287000	-0.821111000	6	0.243254000	-1.886640000	1.304028000
6	-5.171081000	-0.388483000	1.085650000	1	3.552502000	-3.658899000	0.284661000
1	-6.082920000	-0.312684000	1.672235000	6	-1.092182000	-1.259412000	1.635970000
6	-3.930178000	-0.508171000	1.717350000	1	-1.491473000	-1.685290000	2.574939000
1	-3.870690000	-0.528621000	2.803313000	7	-2.039829000	-1.411542000	0.519397000
6	-2.754314000	-0.609484000	0.969558000	6	-3.127388000	-0.431450000	0.600726000
1	-1.795674000	-0.696556000	1.468965000	1	-3.766491000	-0.621951000	1.485094000
1	4.846338000	-1.045557000	1.735265000	1	-2.654410000	0.546020000	0.746953000
6	3.739757000	-1.069844000	1.776742000	6	-3.987056000	-0.378337000	-0.681745000
1	3.383171000	-0.066296000	2.025988000	1	-4.648817000	-1.252074000	-0.732271000
1	3.440633000	-1.752914000	2.578483000	1	-3.313353000	-0.431982000	-1.546384000
6	3.410095000	-0.591697000	-0.594829000	7	-4.829448000	0.806892000	-0.840587000
6	2.651680000	0.705001000	-0.418478000	6	-5.865527000	0.948198000	0.172002000
6	3.322023000	1.933499000	-0.451392000	1	-6.415286000	0.005037000	0.272456000
1	4.395089000	1.953579000	-0.624466000	1	-5.482006000	1.232089000	1.171627000

6	2.619781000	3.121071000	-0.253701000	1	-6.576325000	1.722284000	-0.141428000
1	3.140061000	4.074850000	-0.285405000	6	-4.098691000	2.046998000	-1.064870000
6	1.250025000	3.095802000	0.015043000	1	-4.799926000	2.821292000	-1.398257000
1	0.721715000	4.024932000	0.195958000	1	-3.576564000	2.434483000	-0.168674000
6	0.570072000	1.870296000	0.059129000	1	-3.353404000	1.899981000	-1.853790000
6	1.265873000	0.669769000	-0.193655000	1	-0.960888000	-0.181926000	1.795295000
1	3.072901000	-1.089836000	-1.512668000	16	1.828342000	1.211918000	-1.421139000
6	3.523573000	-2.884751000	0.194159000	6	1.808320000	2.433507000	-0.105607000
1	4.609960000	-2.996789000	0.013367000	6	1.507888000	2.131603000	1.229923000
1	3.244589000	-3.545838000	1.021423000	6	2.244613000	3.725327000	-0.437874000
1	2.985072000	-3.209449000	-0.702563000	1	1.190648000	1.130145000	1.501726000
8	-0.749290000	1.754237000	0.359216000	1	2.469397000	3.968632000	-1.473291000
6	-1.528596000	2.927973000	0.552234000	6	1.659450000	3.106785000	2.217354000
1	-1.172410000	3.505073000	1.415809000	6	2.389586000	4.696930000	0.555760000
1	-1.520666000	3.560617000	-0.344487000	1	1.435471000	2.857069000	3.251982000
1	-2.543003000	2.574525000	0.741663000	1	2.725441000	5.694581000	0.283090000
				6	2.088908000	4.396107000	1.886783000
				1	2.199640000	5.152400000	2.659390000
				8	2.597295000	-1.826967000	-1.477323000
				6	3.844463000	-2.376528000	-1.881040000
				1	3.781375000	-3.465722000	-2.004107000
				1	4.068835000	-1.915001000	-2.844041000
				1	4.636682000	-2.129317000	-1.163079000
				6	-2.505487000	-2.790202000	0.383442000
				1	-3.132206000	-3.106258000	1.240659000
				1	-3.088992000	-2.904868000	-0.533401000
				1	-1.645155000	-3.462576000	0.320119000

Compound 26d				
6	2.782977000	-2.875797000	0.913796000	
6	2.152724000	-2.976907000	2.156409000	
6	2.227176000	-2.064353000	-0.085484000	
1	2.585324000	-3.615245000	2.922630000	
6	0.970504000	-2.282847000	2.409388000	
6	1.054062000	-1.326415000	0.182508000	
1	0.470210000	-2.384014000	3.369470000	
34	0.261392000	-0.219518000	-1.173433000	
6	0.414952000	-1.454734000	1.424541000	
1	3.688908000	-3.441508000	0.726643000	
6	-0.912146000	-0.769195000	1.653013000	
1	-1.235961000	-0.914347000	2.698608000	
7	-1.893851000	-1.260710000	0.678571000	
6	-3.157852000	-0.526123000	0.675566000	
1	-3.620496000	-0.481647000	1.679017000	
1	-2.931415000	0.506022000	0.378855000	
6	-4.128923000	-1.173006000	-0.332985000	
1	-4.381444000	-2.185503000	0.016210000	
1	-3.597783000	-1.289706000	-1.285746000	
7	-5.383298000	-0.475117000	-0.599729000	
6	-6.278349000	-0.372164000	0.543188000	
1	-6.389624000	-1.355937000	1.013876000	
1	-5.940900000	0.344145000	1.317573000	
1	-7.268429000	-0.047443000	0.200946000	
6	-5.227783000	0.789259000	-1.304224000	
1	-6.210066000	1.134062000	-1.648757000	
1	-4.787093000	1.597613000	-0.688574000	

1	-4.590433000	0.645205000	-2.183568000	
1	-0.812313000	0.311342000	1.488086000	
16	1.950345000	1.227749000	-1.564078000	
6	1.658768000	2.461642000	-0.292263000	
6	2.217542000	2.303411000	0.985272000	
6	0.918133000	3.616424000	-0.584195000	
1	2.799209000	1.413689000	1.207765000	
1	0.492010000	3.740675000	-1.575719000	
6	2.024108000	3.283570000	1.961707000	
6	0.729708000	4.595781000	0.394209000	
1	2.459314000	3.152878000	2.949584000	
1	0.154585000	5.488247000	0.159542000	
6	1.280541000	4.431280000	1.668920000	
1	1.134439000	5.194889000	2.428783000	
8	2.745389000	-1.944397000	-1.336120000	
6	3.959684000	-2.611808000	-1.650827000	
1	3.851688000	-3.701264000	-1.566498000	
1	4.177255000	-2.348058000	-2.687092000	
1	4.779756000	-2.270307000	-1.006133000	
1	-2.057625000	-2.256298000	0.832321000	