

# First Generation of Antioxidant Precursors for Bioisosteric Se-NSAIDs: Design, Synthesis and In Vitro and In Vivo Anticancer Evaluation

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## Biological evaluation

### GI<sub>50</sub>, TGI and LD<sub>50</sub> values

**Table S1.** GI<sub>50</sub>, TGI and LD<sub>50</sub> values (in μM)<sup>a</sup> for the Se-NSAID analogs in colon (HT-29, HCT-116), prostate (DU-145, PC-3), breast (MDA-MB-231, T-47D, 184B5) and lung (H1299, A549, BEAS-2B) cell lines.

Compounds	Colon cell lines		Prostate cell lines		Breast cell lines			Lung cell lines			
	HT-29	HCT-116	DU-145	PC-3	MDA-MB-231	T-47D	184B5	H1299	A549	BEAS-2B	
<b>1</b>	GI <sub>50</sub>	3.9 ± 0.4	21.0 ± 4.0	4.4 ± 0.5	2.8 ± 0.2	6.6 ± 2.2	1.6 ± 0.3	7.0 ± 1.1	7.7 ± 1.2	>100	3.9 ± 1.3
	TGI	6.2 ± 1.9	44.5 ± 7.1	5.1 ± 0.2	3.0 ± 0.3	15.3 ± 4.6	2.9 ± 0.6	11.3 ± 1.4	9.4 ± 0.8	26.2 ± 5.8	8.4 ± 2.4
	LD <sub>50</sub>	>100	88.0 ± 3.5	6.1 ± 0.7	3.3 ± 0.4	>100	6.0 ± 1.9	21.1 ± 3.9	>100	74.6 ± 5.9	17.0 ± 5.7
<b>2</b>	GI <sub>50</sub>	>100	44.5 ± 3.4	58.4 ± 8.4	>100	23.1 ± 14.3	25.5 ± 10.2	>100	53.2 ± 1.2	>100	>100
	TGI	>100	81.5 ± 2.3	>100	>100	>100	39.0 ± 8.5	>100	>100	>100	>100
	LD <sub>50</sub>	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100
<b>3</b>	GI <sub>50</sub>	6.8 ± 1.4	9.3 ± 4.7	5.0 ± 0.2	4.4 ± 0.3	5.2 ± 0.2	1.8 ± 0.2	7.1 ± 0.5	6.7 ± 1.1	3.3 ± 0.4	7.0 ± 2.5
	TGI	>100	30.9 ± 16.7	6.1 ± 0.6	5.0 ± 0.1	5.6 ± 0.8	3.1 ± 0.3	9.4 ± 0.2	>100	>100	9.0 ± 1.2
	LD <sub>50</sub>	>100	>100	10.4 ± 2.4	5.9 ± 0.9	>100	6.3 ± 0.7	>100	>100	>100	12.3 ± 2.1
<b>4</b>	GI <sub>50</sub>	24.4 ± 2.6	4.3 ± 0.6	19.5 ± 3.5	4.8 ± 0.4	2.4 ± 0.5	>100	4.8 ± 0.3	24.6 ± 1.8	8.1 ± 0.4	4.2 ± 0.6
	TGI	36.2 ± 3.0	6.7 ± 1.9	28.5 ± 2.9	5.5 ± 0.5	4.2 ± 1.7	9.5 ± 2.3	5.4 ± 0.4	33.6 ± 1.6	19.9 ± 3.4	4.7 ± 0.3
	LD <sub>50</sub>	62.5 ± 14.3	>100	39.6 ± 2.4	6.7 ± 1.2	>100	27.2 ± 2.3	>100	43.5 ± 1.8	>100	5.4 ± 0.4
<b>5</b>	GI <sub>50</sub>	4.8 ± 1.0	4.6 ± 1.5	6.0 ± 1.3	4.7 ± 0.2	4.8 ± 1.1	1.8 ± 0.4	6.6 ± 1.5	8.1 ± 1.0	2.3 ± 0.2	7.8 ± 2.3
	TGI	7.2 ± 1.8	10.3 ± 3.8	7.3 ± 0.9	6.1 ± 0.5	7.9 ± 3.8	2.7 ± 0.3	11.1 ± 1.4	10.2 ± 1.0	>100	9.8 ± 1.6
	LD <sub>50</sub>	>100	>100	9.0 ± 0.4	8.9 ± 1.9	>100	4.2 ± 0.3	>100	16.5 ± 5.1	>100	14.8 ± 4.7

<sup>a</sup>GI<sub>50</sub>, TGI and LD<sub>50</sub> values are presented as the mean ± SD of at least three independent experiments determined by the MTT assay.

## Chemical characterization – NMR spectra

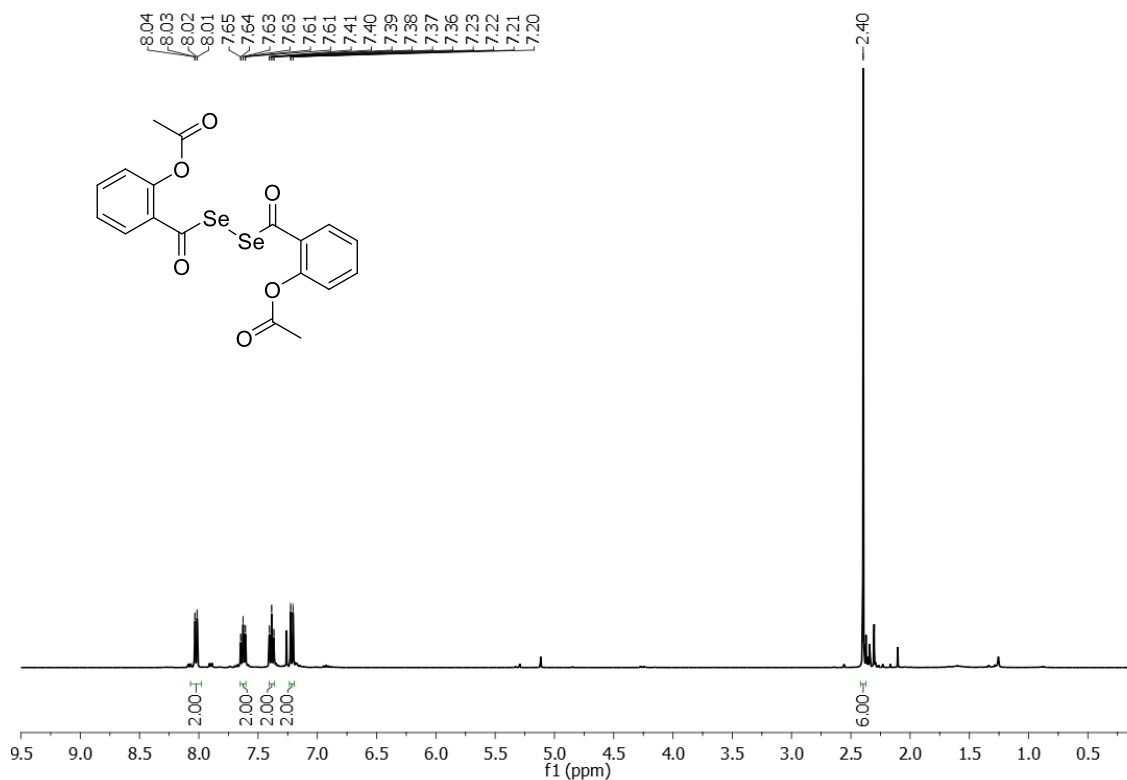


Figure S1. <sup>1</sup>H-NMR spectrum of compound 1.

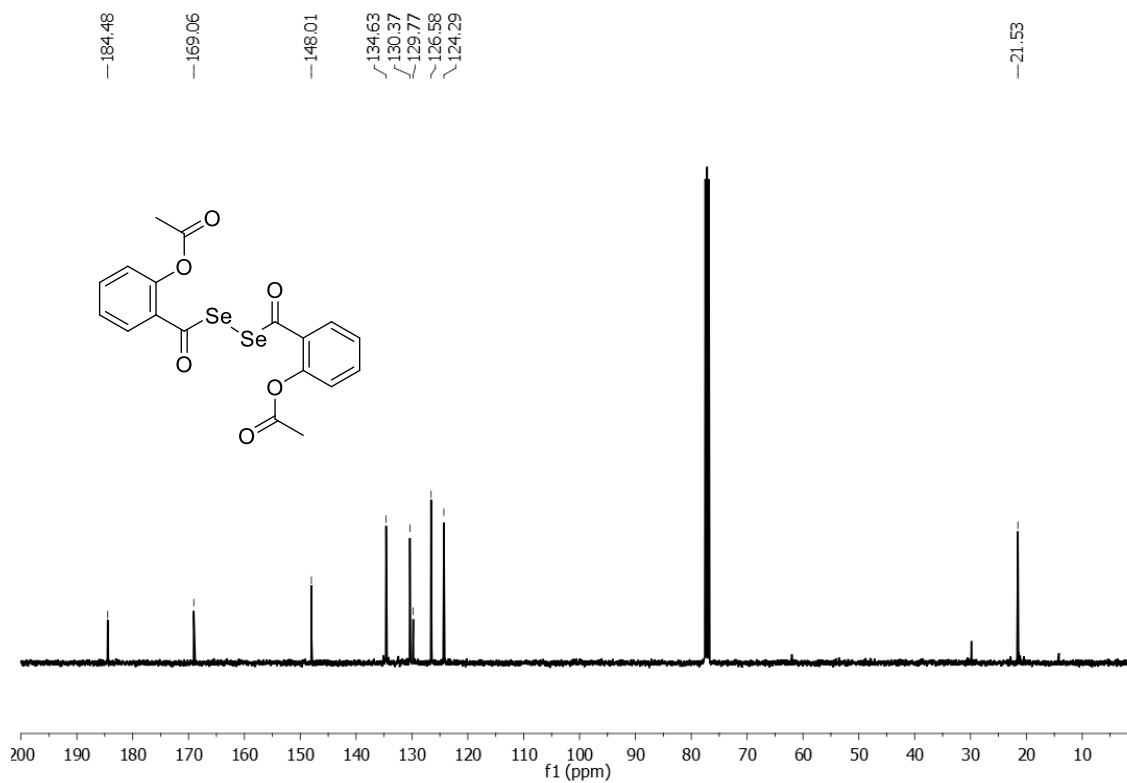


Figure S2. <sup>13</sup>C-NMR spectrum of compound 1.

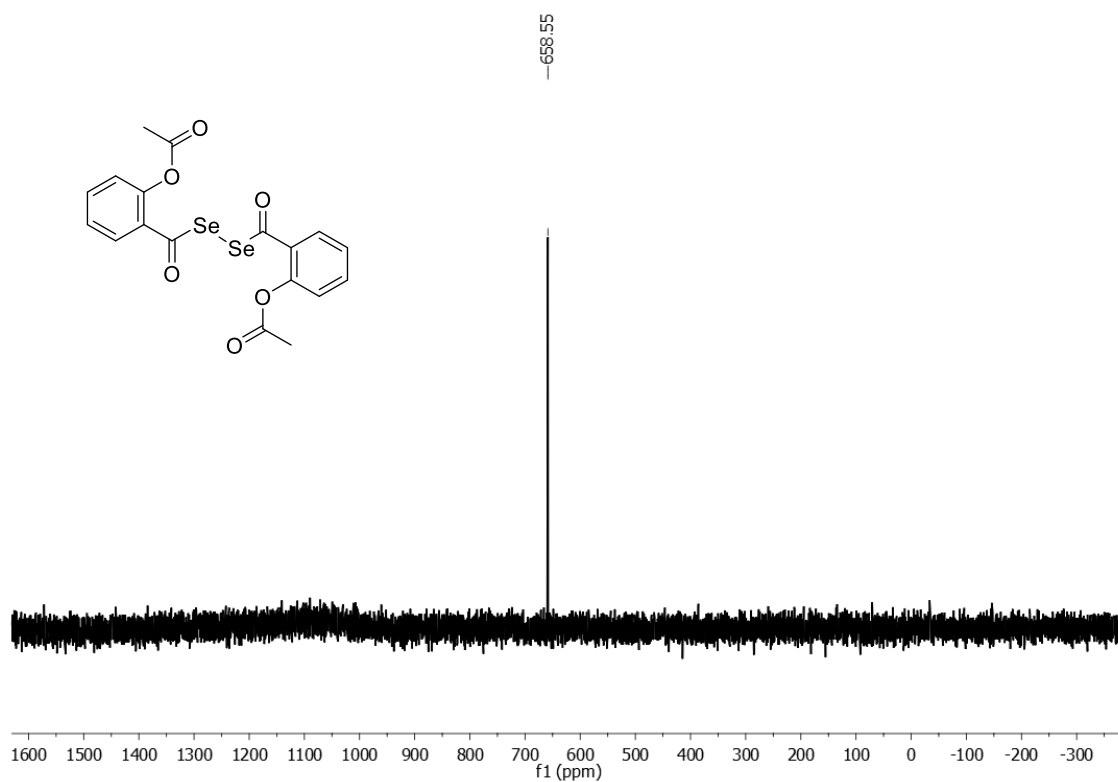


Figure S3.  $^{77}\text{Se}$ -NMR spectrum of compound 1.

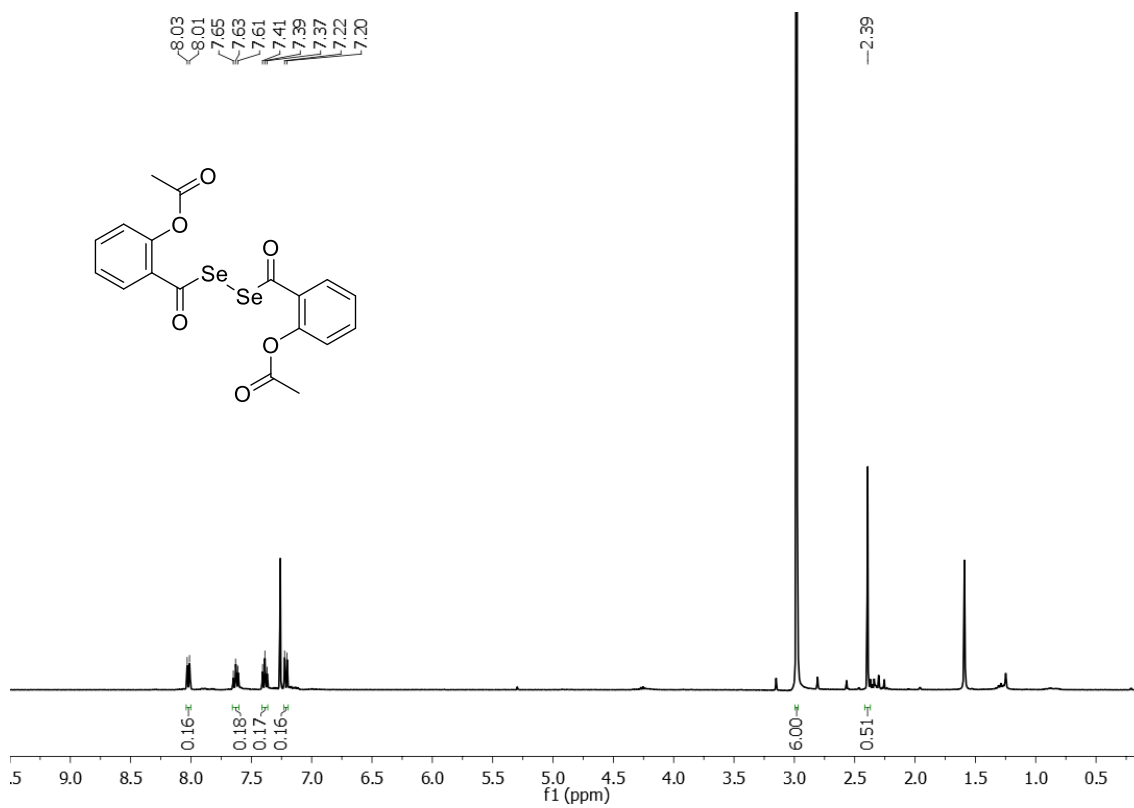


Figure S4. qNMR spectrum of compound 1.

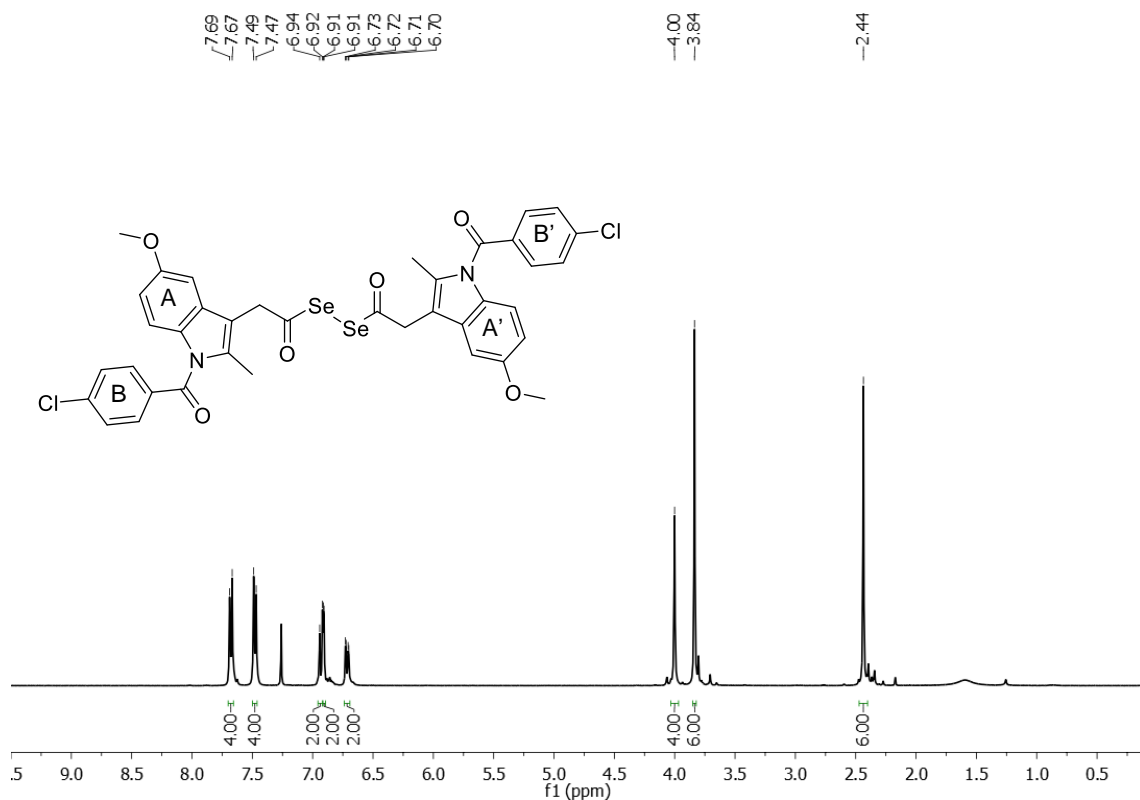


Figure S5.  $^1\text{H-NMR}$  spectrum of compound 2.

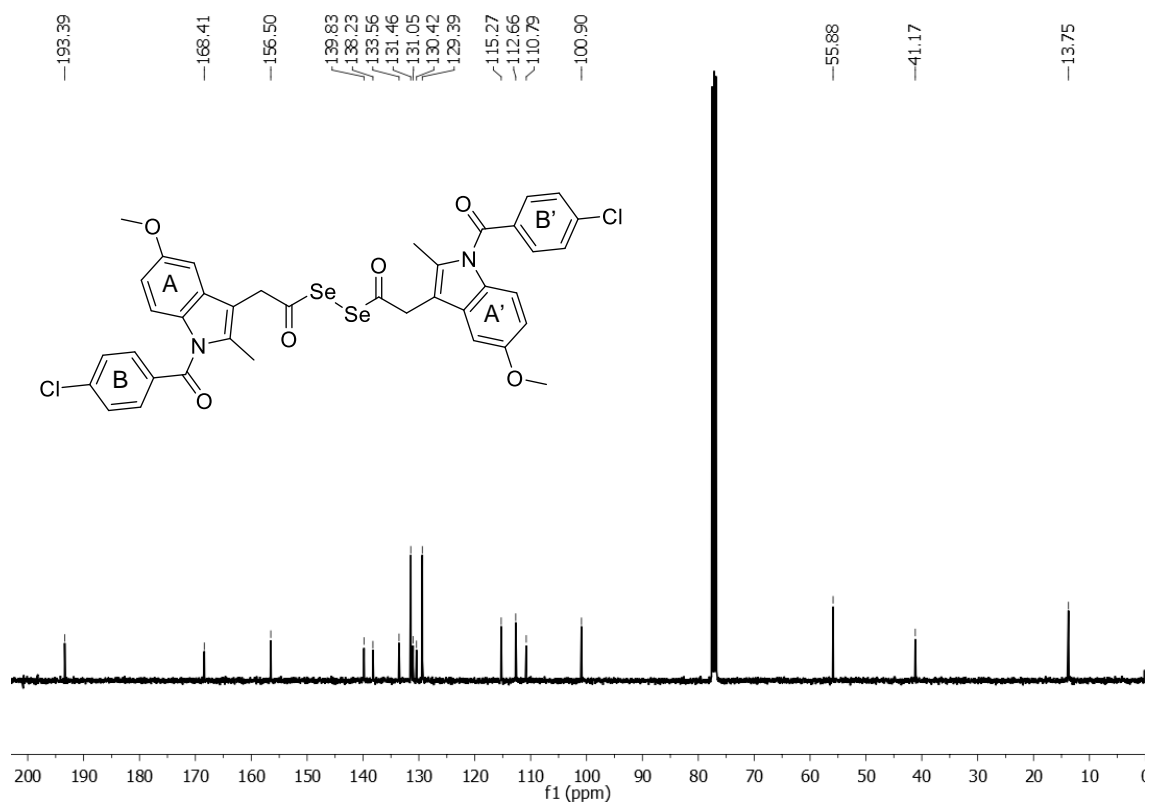


Figure S6.  $^{13}\text{C-NMR}$  spectrum of compound 2.

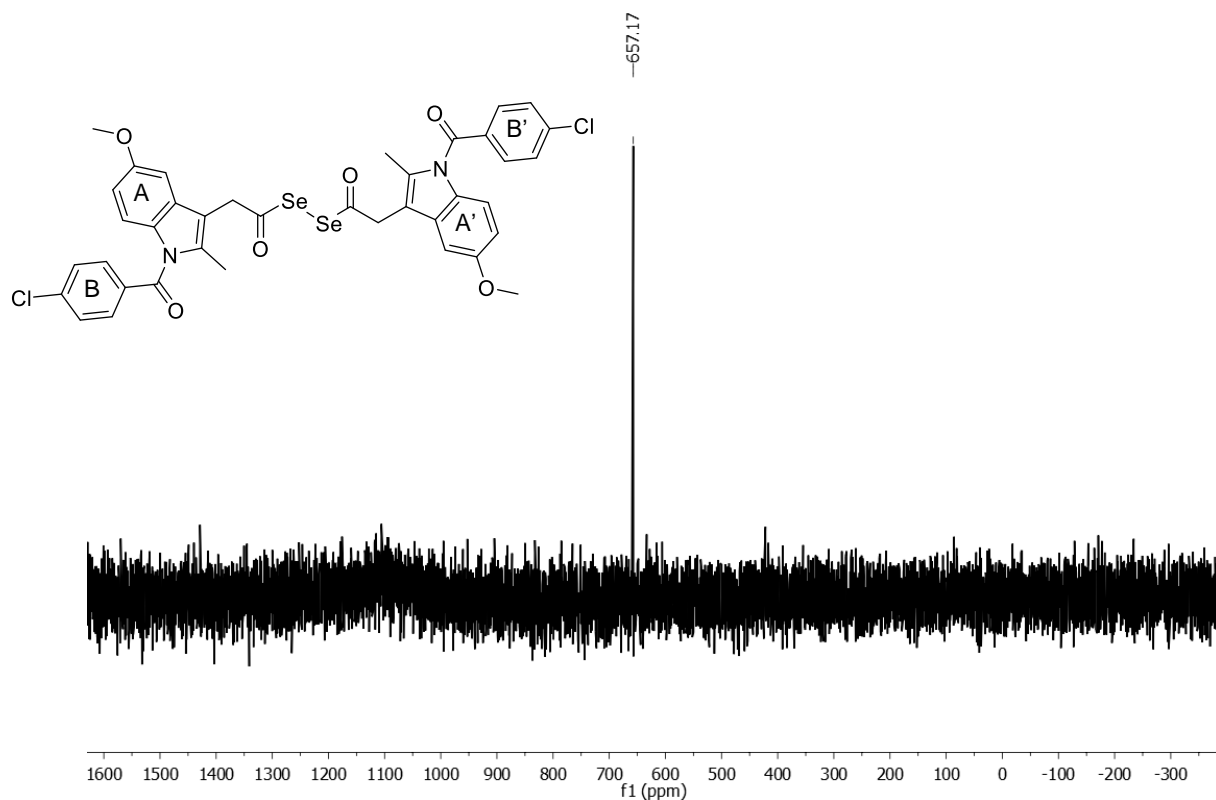


Figure S7.  $^{77}\text{Se}$ -NMR spectrum of compound 2.

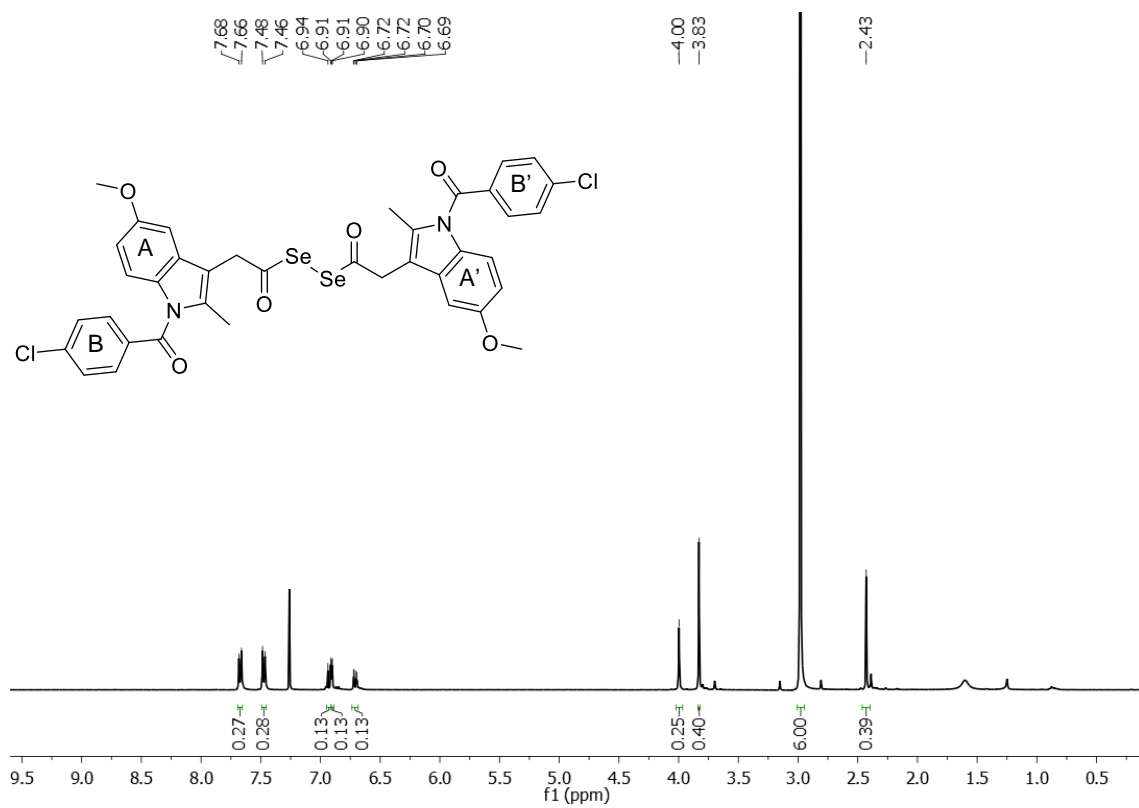


Figure S8. qNMR spectrum of compound 2.

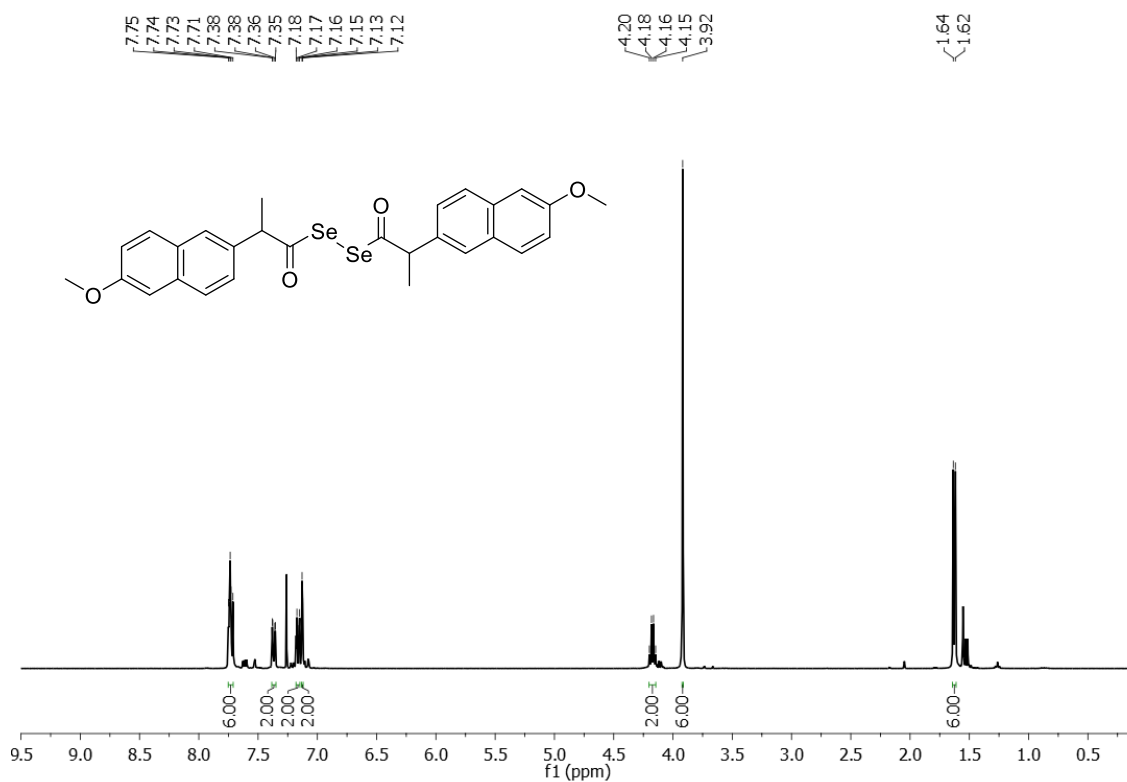


Figure S9. <sup>1</sup>H-NMR spectrum of compound 3.

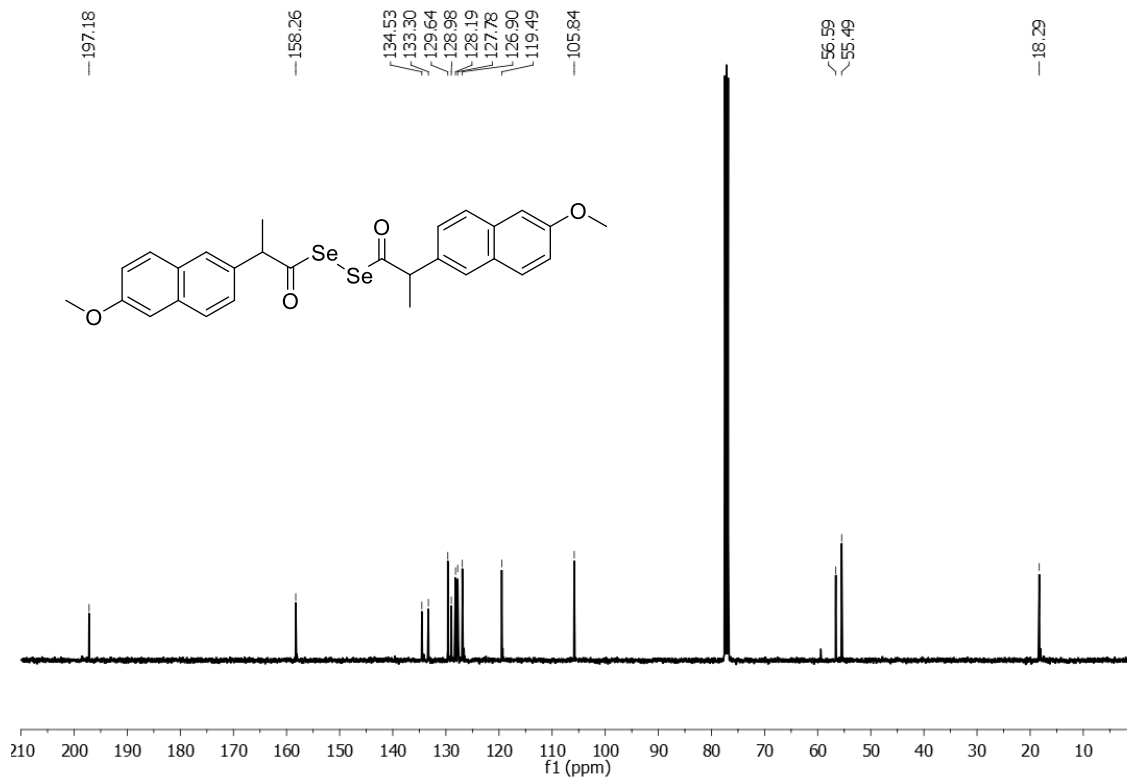


Figure S10. <sup>13</sup>C-NMR spectrum of compound 3.

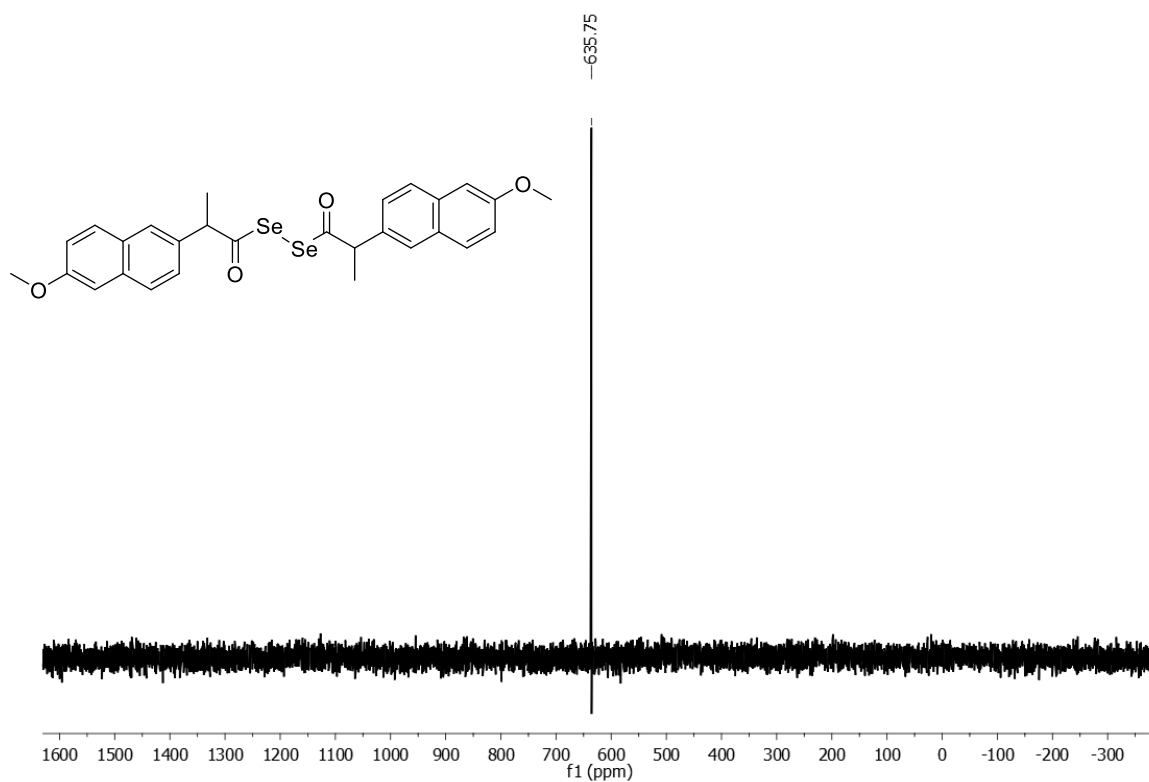


Figure S11.  $^{77}\text{Se}$ -NMR spectrum of compound 3.

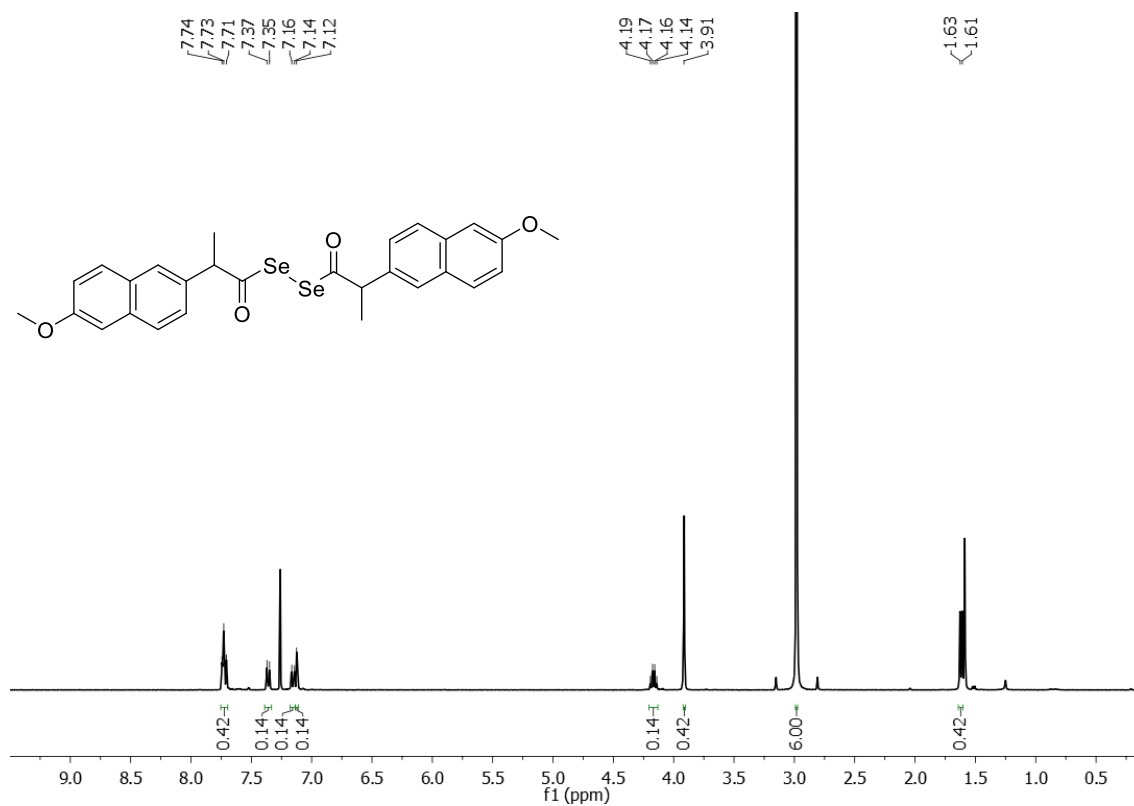


Figure S12. qNMR spectrum of compound 3.



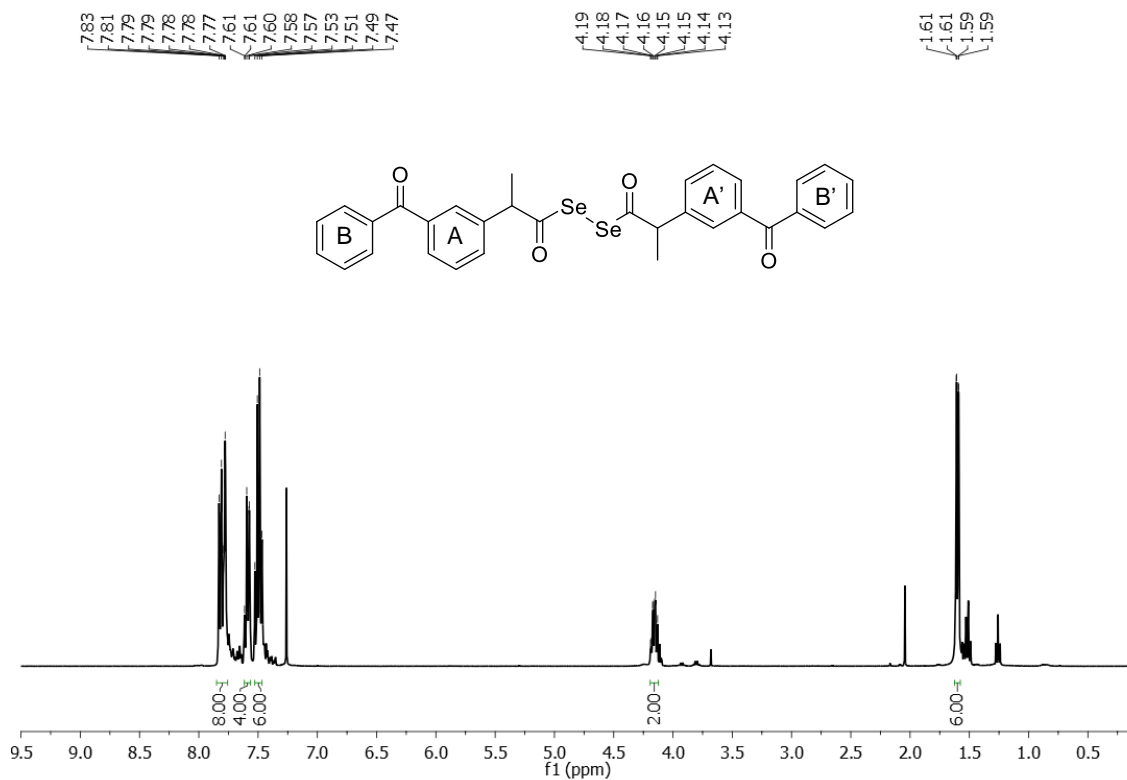


Figure S13. <sup>1</sup>H-NMR spectrum of compound 4.

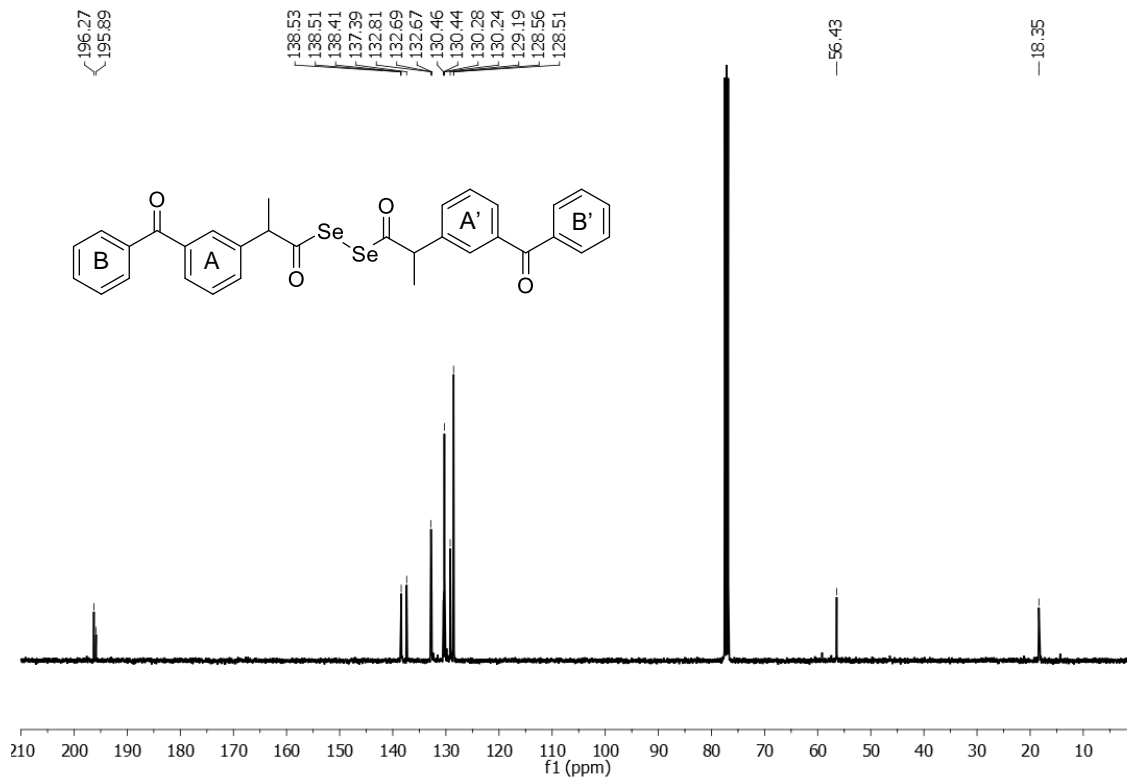


Figure S14. <sup>13</sup>C-NMR spectrum of compound 4.

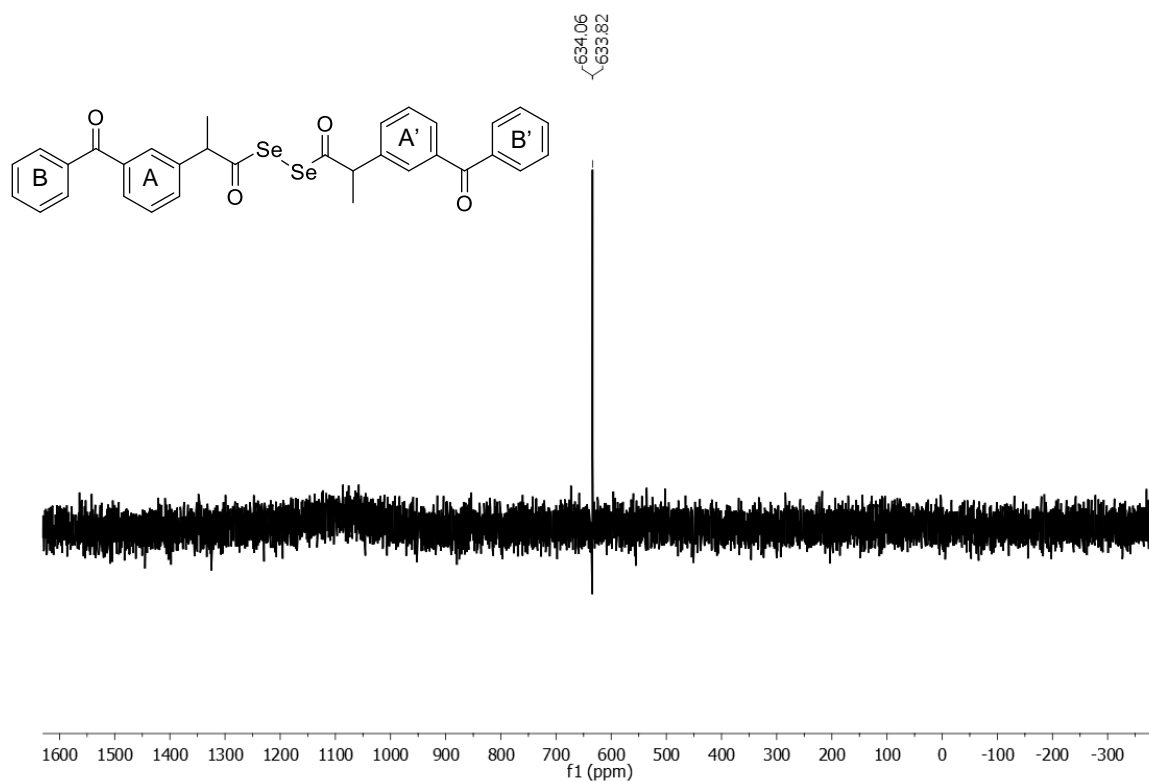


Figure S15.  $^{77}\text{Se}$ -NMR spectrum of compound 4.



Figure S16. qNMR spectrum of compound 4.

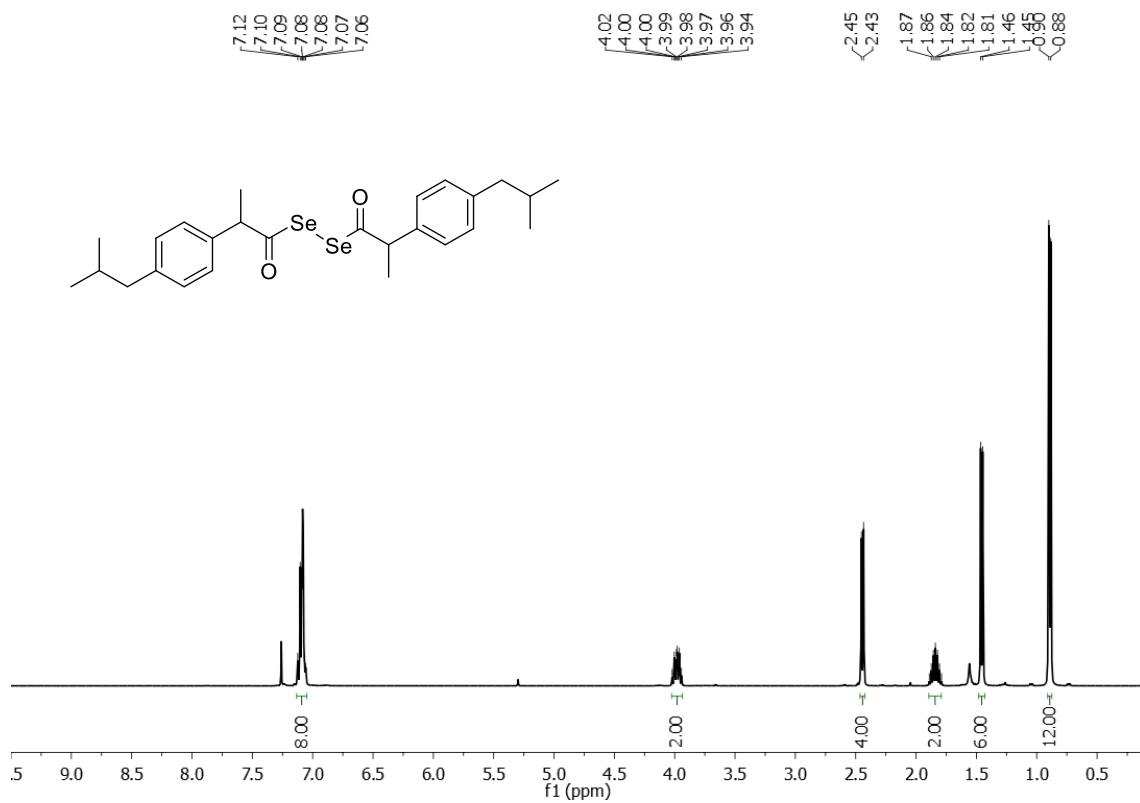


Figure S17. <sup>1</sup>H-NMR spectrum of compound 5.

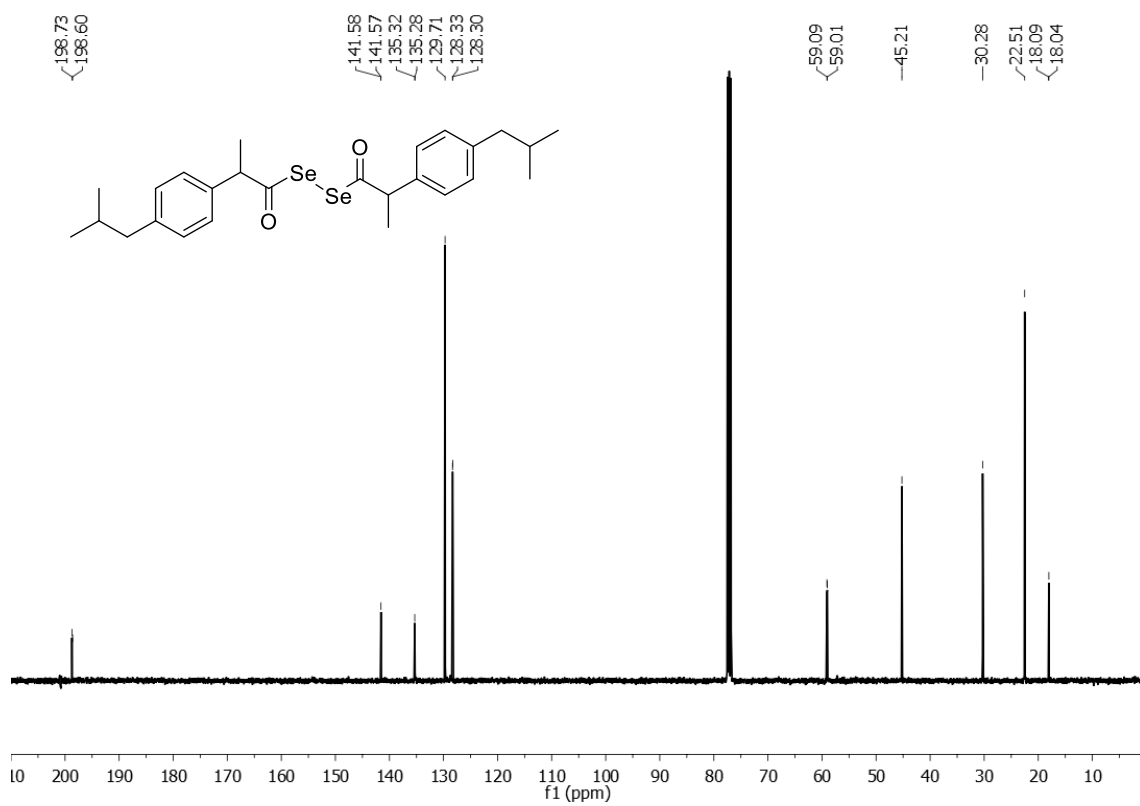


Figure S18. <sup>13</sup>C-NMR spectrum of compound 5.

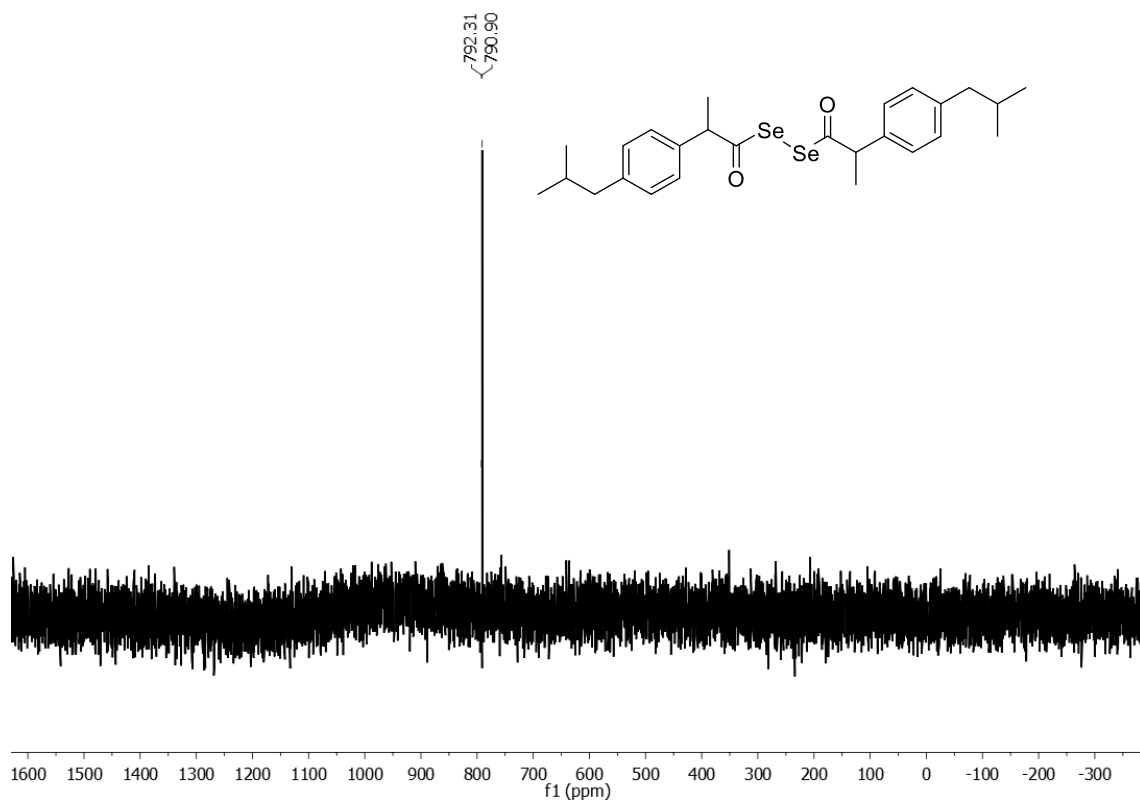


Figure S19.  $^{77}\text{Se}$ -NMR spectrum of compound 5.

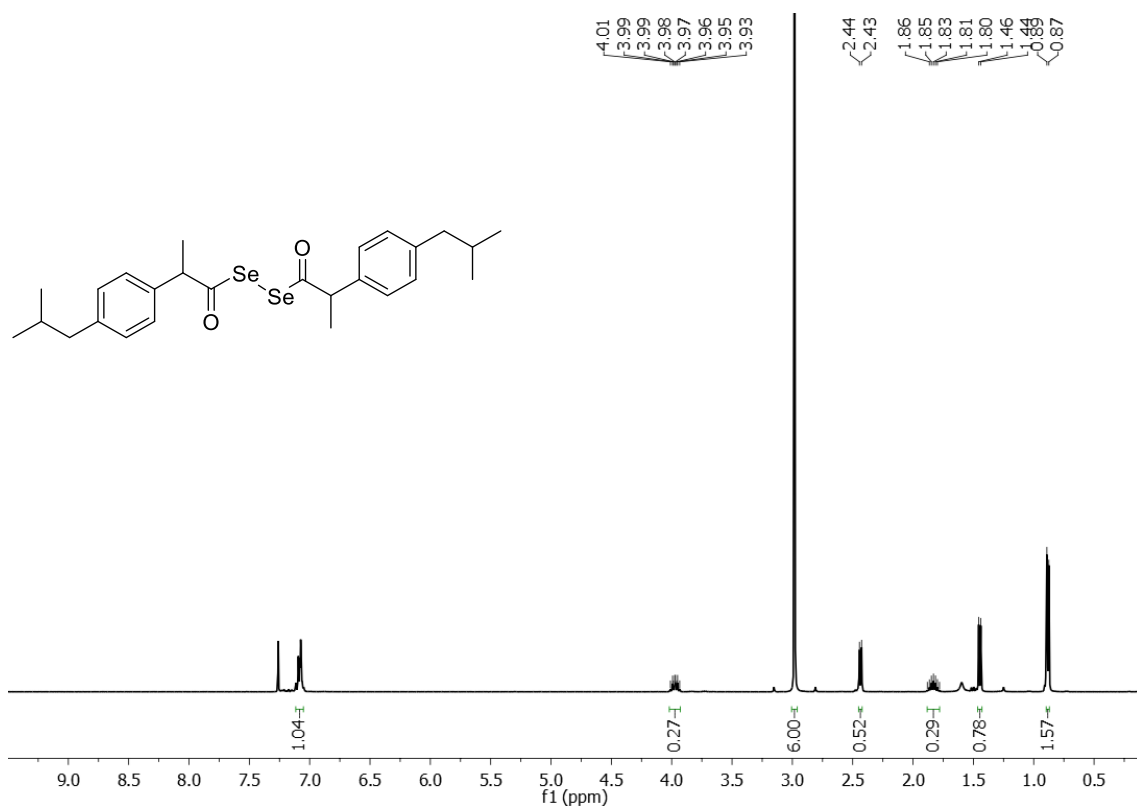
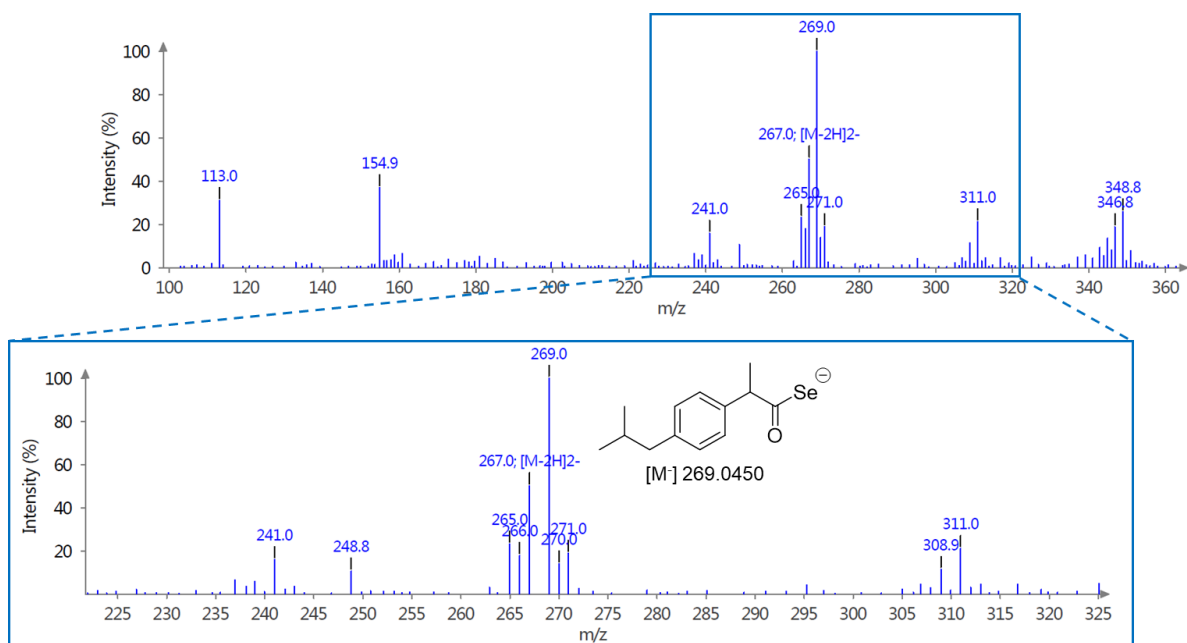


Figure S20. qNMR spectrum of compound 5.



**Figure S21.** Mass spectrum of compound 5 obtained with a negative ionization mode.