Electronic Supplementary Material (ESI) for Dalton Transactions.

Supporting Information

for

Computer-Assisted Designed "selenoxy-chinolin": New Catalytic Mechanism of GPx-like and inhibition of metal-free and metal-associated A*β* aggregation

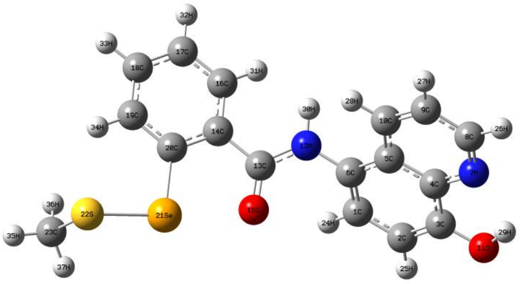
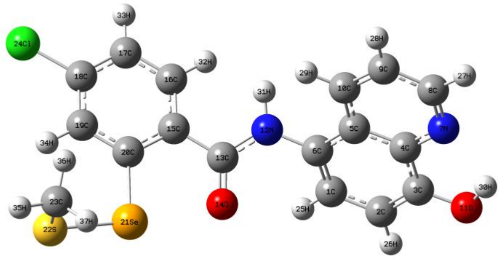
Zhiren Wang, Yali Wang, Wenrui Li, Zhihong Liu, Zonghua Luo, Yang Sun, Ruibo Wu, Ling Huang,* Xingshu Li*

School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, 510006, China

Contents

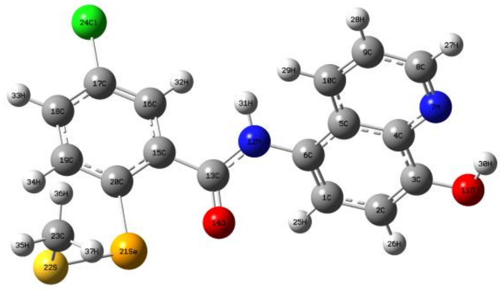
1. Computation Design

All calculations were performed by using the Gaussian 09 suite of quantum chemical programs. The computational models are fully optimized using DFT calculations at B3LYP/6-311+g(d,p) level of theory and characterized by frequency calculation. As glutathione was very flexible, the G group replaced with a Me group according to the reported method in literature.[1, 2]

<table>
<tr><td colspan="4">
Selenenyl sulfides for 11a
Electronic Energy = - 3716.2103362</td><td colspan="4">
Selenenyl sulfides for 11b
Electronic Energy = - 4175.834644</td></tr>
<tr><td>C</td><td>2.507237</td><td>-1.037350</td><td>-1.519108</td><td>C</td><td>3.025375</td><td>-0.598322</td><td>-1.689178</td></tr>
<tr><td>C</td><td>3.721191</td><td>-1.750193</td><td>-1.555088</td><td>C</td><td>4.332409</td><td>-1.104983</td><td>-1.821232</td></tr>
<tr><td>C</td><td>4.769630</td><td>-1.375772</td><td>-0.745395</td><td>C</td><td>5.301008</td><td>-0.775905</td><td>-0.900044</td></tr>
<tr><td>C</td><td>4.608216</td><td>-0.279362</td><td>0.153018</td><td>C</td><td>4.964327</td><td>0.059357</td><td>0.206465</td></tr>
<tr><td>C</td><td>3.364552</td><td>0.417192</td><td>0.216361</td><td>C</td><td>3.629874</td><td>0.540779</td><td>0.360812</td></tr>
<tr><td>C</td><td>2.315340</td><td>0.029514</td><td>-0.665970</td><td>C</td><td>2.663301</td><td>0.212705</td><td>-0.633245</td></tr>
<tr><td>N</td><td>5.678184</td><td>0.028034</td><td>0.930340</td><td>N</td><td>5.965349</td><td>0.336768</td><td>1.080745</td></tr>
<tr><td>C</td><td>5.559553</td><td>1.008751</td><td>1.799937</td><td>C</td><td>5.690847</td><td>1.076294</td><td>2.134079</td></tr>
<tr><td>C</td><td>4.365533</td><td>1.744779</td><td>1.970536</td><td>C</td><td>4.398681</td><td>1.580427</td><td>2.403355</td></tr>
<tr><td>C</td><td>3.276779</td><td>1.448309</td><td>1.184804</td><td>C</td><td>3.377041</td><td>1.311084</td><td>1.523391</td></tr>
<tr><td>O</td><td>5.951811</td><td>-2.025493</td><td>-0.777317</td><td>O</td><td>6.566791</td><td>-1.227627</td><td>-1.016602</td></tr>
<tr><td>N</td><td>1.098369</td><td>0.765198</td><td>-0.663554</td><td>N</td><td>1.350708</td><td>0.748807</td><td>-0.526789</td></tr>
<tr><td>C</td><td>-0.158174</td><td>0.219299</td><td>-0.585920</td><td>C</td><td>0.186236</td><td>0.040534</td><td>-0.683515</td></tr>
<tr><td>C</td><td>-1.314505</td><td>1.158940</td><td>-0.634531</td><td>O</td><td>0.174723</td><td>-1.171314</td><td>-0.880801</td></tr>
<tr><td>O</td><td>-0.339345</td><td>-0.988746</td><td>-0.459237</td><td>C</td><td>-1.091107</td><td>0.801430</td><td>-0.582878</td></tr>
<tr><td>C</td><td>-1.199354</td><td>2.465762</td><td>-1.135901</td><td>C</td><td>-1.156733</td><td>2.190337</td><td>-0.770938</td></tr>
</table>

C	-2.283129	3.331776	-1.154235
C	-3.509477	2.892992	-0.655782
C	-3.650346	1.596875	-0.174630
C	-2.572090	0.708001	-0.173913
Se	-2.777207	-1.135991	0.447457
S	-4.885172	-1.102739	1.248349
C	-5.870990	-1.590131	-0.222875
H	1.701387	-1.340000	-2.175717
H	3.843043	-2.589180	-2.230204
H	6.433449	1.232146	2.406519
H	4.316127	2.524016	2.722871
H	2.345602	1.986965	1.325301
H	6.528404	-1.594750	-0.120216
H	1.171022	1.769657	-0.648453
H	-0.258738	2.808292	-1.556013
H	-2.174944	4.333225	-1.556173
H	-4.366468	3.559216	-0.650398
H	-4.607050	1.271034	0.215592
H	-6.903772	-1.690472	0.117853
H	-5.824559	-0.831030	-1.003636
H	-5.531109	-2.546593	-0.617392

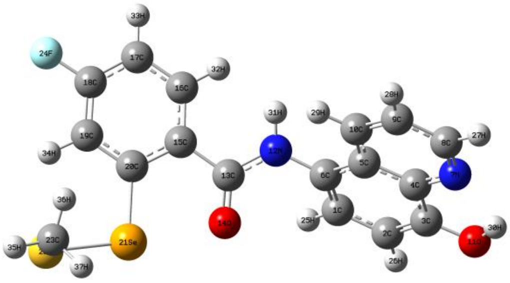
C	-2.352845	2.885724	-0.676168
C	-3.509754	2.166446	-0.386504
C	-3.488096	0.789845	-0.215782
C	-2.284416	0.090857	-0.322849
Se	-2.242838	-1.857364	-0.143080
S	-4.326084	-2.272124	0.603816
C	-4.158671	-2.031319	2.416109
Cl	-5.038068	3.020718	-0.256799
H	2.284536	-0.859371	-2.433886
H	4.588077	-1.745614	-2.657117
H	6.513438	1.282992	2.813840
H	4.223809	2.162042	3.301556
H	2.374978	1.668836	1.735360
H	7.064143	-0.874910	-0.256380
H	1.273509	1.714325	-0.250412
H	-0.265512	2.749376	-1.037858
H	-2.392007	3.956096	-0.834491
H	-4.408272	0.255052	-0.014810
H	-5.117341	-2.316614	2.854337
H	-3.952660	-0.988971	2.658831
H	-3.375080	-2.670346	2.820552



Selenenyl sulfides for 11c

Electronic Energy = -4175.8337781

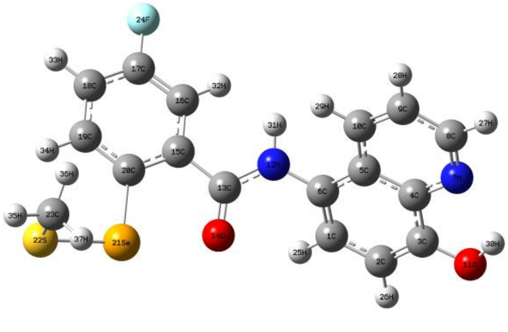
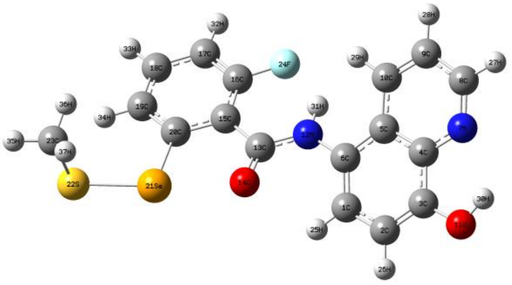
C	2.763137	-0.826068	-1.649568
C	4.052127	-1.366400	-1.820546
C	5.052049	-1.080309	-0.919039
C	4.765882	-0.254432	0.208322
C	3.449906	0.262547	0.403193
C	2.450089	-0.021394	-0.572628
N	5.795470	-0.020200	1.061808
C	5.569370	0.710100	2.132822
C	4.299852	1.247080	2.441887



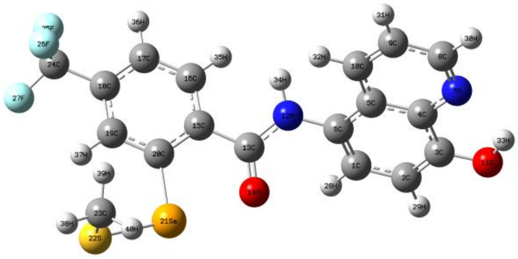
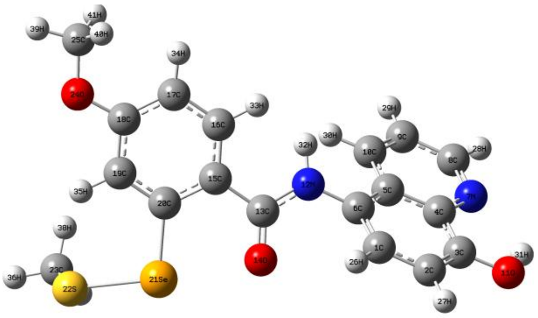
Selenenyl sulfides for 11d

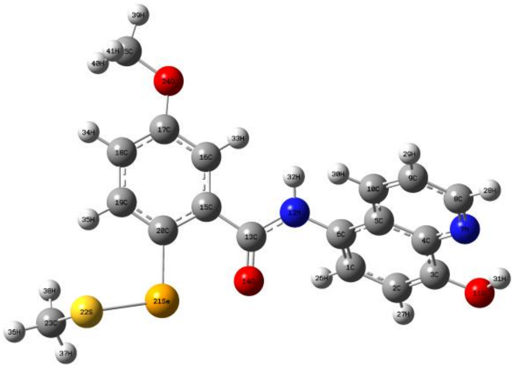
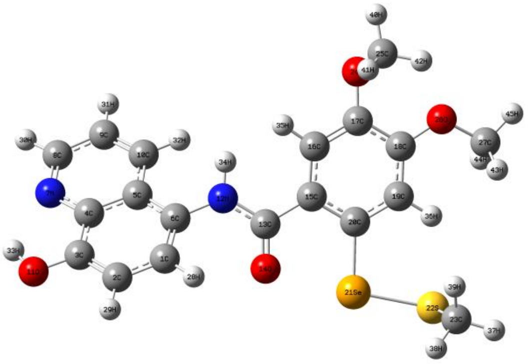
Electronic Energy = -3815.4809875

C	2.775407	-0.754078	-1.637807
C	4.048497	-1.347135	-1.739528
C	5.038559	-1.026532	-0.838486
C	4.757238	-0.110824	0.218566
C	3.455326	0.460086	0.344405
C	2.467215	0.137061	-0.630265
N	5.775900	0.153636	1.076391
C	5.550699	0.967414	2.085730
C	4.292858	1.564671	2.325211

C	3.249484	1.020976	1.583784	C	3.254028	1.309008	1.461409
O	6.301247	-1.565861	-1.073964	O	6.274043	-1.561131	-0.929046
N	1.161450	0.557711	-0.423214	N	1.193100	0.762478	-0.555545
C	-0.035979	-0.067013	-0.657014	C	-0.017455	0.131239	-0.695500
O	-0.116282	-1.248001	-0.981385	O	-0.111577	-1.083814	-0.847405
C	-1.272687	0.750209	-0.474987	C	-1.238307	0.981973	-0.632618
C	-1.248562	2.151687	-0.543502	C	-1.204963	2.365125	-0.870491
C	-2.411736	2.882923	-0.366593	C	-2.349227	3.146524	-0.806943
C	-3.620439	2.237138	-0.123266	C	-3.543039	2.509550	-0.499242
C	-3.654307	0.849266	-0.075885	C	-3.631766	1.147909	-0.279422
C	-2.498835	0.085193	-0.259305	C	-2.479867	0.364036	-0.354685
Se	-2.565392	-1.870138	-0.251510	Se	-2.574147	-1.573520	-0.106858
S	-4.645180	-2.232329	0.531767	S	-4.684664	-1.809781	0.643555
C	-4.404867	-2.159359	2.350187	C	-4.502487	-1.514380	2.446196
Cl	-2.359971	4.636462	-0.467319	F	-4.671981	3.249810	-0.429089
H	1.998416	-1.055553	-2.379541	H	2.017845	-1.010998	-2.366771
H	4.268611	-2.000008	-2.672715	H	4.261642	-2.048733	-2.537549
H	6.414356	0.881896	2.794564	H	6.386528	1.161341	2.753004
H	4.163743	1.819769	3.352385	H	4.156531	2.205722	3.188975
H	2.265245	1.405285	1.830235	H	2.276454	1.738652	1.653465
H	6.827094	-1.239146	-0.321392	H	6.794580	-1.197054	-0.190055
H	1.127303	1.495660	-0.057976	H	1.180566	1.739933	-0.313271
H	-0.333976	2.683879	-0.778007	H	-0.275230	2.848734	-1.152101
H	-4.529584	2.811811	0.010526	H	-2.329138	4.211795	-1.001642
H	-4.600531	0.349238	0.095114	H	-4.596563	0.701573	-0.068312
H	-5.365973	-2.418718	2.799201	H	-5.481812	-1.704459	2.890376
H	-4.120678	-1.157021	2.670144	H	-4.213267	-0.483443	2.649677
H	-3.653394	-2.879554	2.670420	H	-3.773712	-2.198282	2.878796
 				 			
Selenenyl sulfides for 11e Electronic Energy = -3815.4791866				**Selenenyl sulfides for 11f** Electronic Energy = -3815.4812844			
C	2.641164	-0.874458	-1.597332	C	2.347951	-1.506523	-0.976072
C	3.904761	-1.482010	-1.727808	C	3.538094	-2.259970	-0.982868

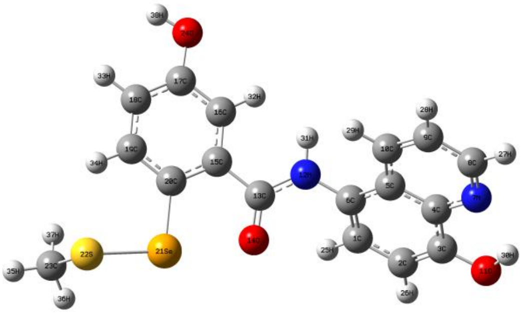
C	4.917243	-1.179902	-0.845816	C	4.692012	-1.748116	-0.436211
C	4.669152	-0.266879	0.221716	C	4.669894	-0.453188	0.161171
C	3.377682	0.320531	0.377668	C	3.458424	0.300621	0.196886
C	2.365216	0.015597	-0.578792	C	2.288102	-0.248002	-0.409824
N	5.708924	-0.020449	1.059269	N	5.840915	-0.013646	0.689626
C	5.516844	0.791662	2.076665	C	5.862344	1.164096	1.276348
C	4.272864	1.404747	2.345303	C	4.718430	1.983975	1.392392
C	3.212547	1.166637	1.502797	C	3.526856	1.552500	0.858357
O	6.143589	-1.729856	-0.964743	O	5.848622	-2.444104	-0.446911
N	1.105484	0.662807	-0.472937	N	1.112882	0.548887	-0.435519
C	-0.120975	0.086742	-0.682473	C	-0.172554	0.097332	-0.356487
O	-0.260246	-1.105060	-0.939704	O	-0.440566	-1.100235	-0.248391
C	-1.312997	0.977468	-0.560409	C	-1.296321	1.083931	-0.402199
C	-1.212655	2.370007	-0.712640	C	-1.161683	2.469738	-0.572585
C	-2.341297	3.154714	-0.592251	C	-2.215759	3.354952	-0.633041
C	-3.585836	2.605182	-0.326392	C	-3.503615	2.83823	-0.5148200
C	-3.691495	1.225905	-0.193988	C	-3.701886	1.476216	-0.335426
C	-2.574604	0.394096	-0.316210	C	-2.622440	0.591948	-0.272128
Se	-2.746220	-1.552915	-0.187457	Se	-2.930973	-1.324547	-0.011622
S	-4.840520	-1.753415	0.613925	S	-5.180394	-1.381636	0.225270
C	-4.593709	-1.580480	2.424763	C	-5.390078	-1.091693	2.026399
F	-2.227576	4.495556	-0.752234	F	0.090335	3.017961	-0.694454
H	1.866543	-1.118950	-2.311698	H	1.458856	-1.930371	-1.420351
H	4.092193	-2.181141	-2.534412	H	3.553477	-3.246715	-1.430938
H	6.369363	0.971056	2.726628	H	6.815164	1.488452	1.686842
H	4.163271	2.044185	3.213994	H	4.787011	2.936289	1.906185
H	2.246524	1.609874	1.720925	H	2.640226	2.168148	0.965741
H	6.684167	-1.376273	-0.235133	H	6.515456	-1.88921	-0.0030110
H	1.114699	1.619983	-0.159963	H	1.240602	1.541001	-0.549494
H	-0.277759	2.854631	-0.970915	H	-2.021261	4.411352	-0.772446
H	-4.456164	3.246313	-0.243429	H	-4.358428	3.504384	-0.566232
H	-4.662742	0.785018	-0.002959	H	-4.708978	1.085887	-0.257562
H	-5.565690	-1.762980	2.888034	H	-6.453668	-1.217547	2.239208
H	-4.258713	-0.575929	2.682812	H	-5.088209	-0.081595	2.303390
H	-3.878747	-2.316556	2.789421	H	-4.821519	-1.819222	2.603893

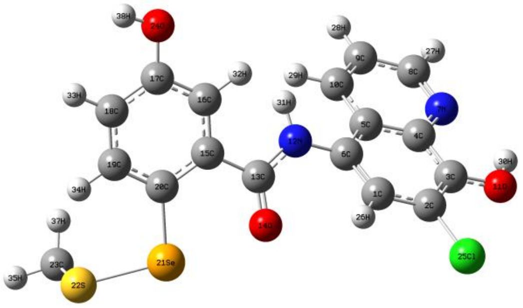
<table>
<tr><td colspan="4">
Selenenyl sulfides for 11g
Electronic Energy = -4053.3875676</td><td colspan="4">
Selenenyl sulfides for 11h
Electronic Energy = -4779.4812504</td></tr>
<tr><td>C</td><td>3.457253</td><td>-0.596870</td><td>-1.646513</td><td>C</td><td>-2.994920</td><td>-0.675034</td><td>-1.636472</td></tr>
<tr><td>C</td><td>4.808322</td><td>-0.970807</td><td>-1.776404</td><td>C</td><td>-4.305562</td><td>-1.167882</td><td>-1.786107</td></tr>
<tr><td>C</td><td>5.746028</td><td>-0.511995</td><td>-0.879149</td><td>C</td><td>-5.294313</td><td>-0.793718</td><td>-0.904800</td></tr>
<tr><td>C</td><td>5.334671</td><td>0.322488</td><td>0.202516</td><td>C</td><td>-4.975197</td><td>0.073828</td><td>0.181187</td></tr>
<tr><td>C</td><td>3.959382</td><td>0.670990</td><td>0.356678</td><td>C</td><td>-3.637722</td><td>0.540902</td><td>0.356059</td></tr>
<tr><td>C</td><td>3.023427</td><td>0.211076</td><td>-0.614990</td><td>C</td><td>-2.648453</td><td>0.167771</td><td>-0.599826</td></tr>
<tr><td>N</td><td>6.309564</td><td>0.729959</td><td>1.054767</td><td>N</td><td>-5.995139</td><td>0.395388</td><td>1.018165</td></tr>
<tr><td>C</td><td>5.970920</td><td>1.473566</td><td>2.086269</td><td>C</td><td>-5.737433</td><td>1.164881</td><td>2.054119</td></tr>
<tr><td>C</td><td>4.636647</td><td>1.852788</td><td>2.354377</td><td>C</td><td>-4.445083</td><td>1.657277</td><td>2.343031</td></tr>
<tr><td>C</td><td>3.640137</td><td>1.451306</td><td>1.496204</td><td>C</td><td>-3.404588</td><td>1.344088</td><td>1.500244</td></tr>
<tr><td>O</td><td>7.049939</td><td>-0.836385</td><td>-0.995477</td><td>O</td><td>-6.564195</td><td>-1.231579</td><td>-1.041105</td></tr>
<tr><td>N</td><td>1.666801</td><td>0.622185</td><td>-0.511794</td><td>N</td><td>-1.335372</td><td>0.694143</td><td>-0.476545</td></tr>
<tr><td>C</td><td>0.568448</td><td>-0.173742</td><td>-0.706375</td><td>C</td><td>-0.168370</td><td>-0.018335</td><td>-0.620999</td></tr>
<tr><td>O</td><td>0.650265</td><td>-1.375055</td><td>-0.941633</td><td>O</td><td>-0.165632</td><td>-1.233305</td><td>-0.805519</td></tr>
<tr><td>C</td><td>-0.768375</td><td>0.484632</td><td>-0.596678</td><td>C</td><td>1.106440</td><td>0.737313</td><td>-0.525623</td></tr>
<tr><td>C</td><td>-0.939280</td><td>1.862527</td><td>-0.793645</td><td>C</td><td>1.179928</td><td>2.124845</td><td>-0.696442</td></tr>
<tr><td>C</td><td>-2.185579</td><td>2.461453</td><td>-0.689186</td><td>C</td><td>2.378251</td><td>2.822207</td><td>-0.611511</td></tr>
<tr><td>C</td><td>-3.289661</td><td>1.664991</td><td>-0.384961</td><td>C</td><td>3.552435</td><td>2.108250</td><td>-0.346748</td></tr>
<tr><td>C</td><td>-3.1486520</td><td>0.292407</td><td>-0.209693</td><td>C</td><td>3.507534</td><td>0.719401</td><td>-0.193113</td></tr>
<tr><td>C</td><td>-1.898247</td><td>-0.317730</td><td>-0.324634</td><td>C</td><td>2.310231</td><td>0.025804</td><td>-0.290065</td></tr>
<tr><td>Se</td><td>-1.706227</td><td>-2.255562</td><td>-0.141810</td><td>Se</td><td>2.263477</td><td>-1.925242</td><td>-0.126419</td></tr>
<tr><td>S</td><td>-3.732840</td><td>-2.819677</td><td>0.653843</td><td>S</td><td>4.366755</td><td>-2.358606</td><td>0.553834</td></tr>
<tr><td>C</td><td>-3.547275</td><td>-2.548804</td><td>2.460003</td><td>C</td><td>4.259162</td><td>-2.118275</td><td>2.370687</td></tr>
<tr><td>C</td><td>-4.646336</td><td>2.295602</td><td>-0.202916</td><td>O</td><td>4.784115</td><td>2.670318</td><td>-0.236433</td></tr>
<tr><td>F</td><td>-4.760396</td><td>3.464048</td><td>-0.872925</td><td>C</td><td>4.919405</td><td>4.073442</td><td>-0.420588</td></tr>
<tr><td>F</td><td>-4.891218</td><td>2.572721</td><td>1.104122</td><td>H</td><td>-2.238477</td><td>-0.972771</td><td>-2.350738</td></tr>
<tr><td>F</td><td>-5.647294</td><td>1.494259</td><td>-0.621925</td><td>H</td><td>-4.547532</td><td>-1.833981</td><td>-2.606115</td></tr>
<tr><td>H</td><td>2.741455</td><td>-0.959327</td><td>-2.372415</td><td>H</td><td>-6.574855</td><td>1.406318</td><td>2.703797</td></tr>
<tr><td>H</td><td>5.121101</td><td>-1.611296</td><td>-2.592716</td><td>H</td><td>-4.284946</td><td>2.263953</td><td>3.227353</td></tr>
<tr><td>H</td><td>6.774188</td><td>1.785949</td><td>2.748485</td><td>H</td><td>-2.402741</td><td>1.691934</td><td>1.729054</td></tr>
</table>

H 4.411036 2.443929 3.234837 H 2.609378 1.713345 1.711070 H 7.515681 -0.409775 -0.253316 H 1.5014360 1.571024 -0.216732 H -0.0948230 2.482595 -1.076237 H -2.300004 3.524650 -0.858648 H -4.019355 -0.317551 0.000429 H -4.473915 -2.899419 2.919112 H -3.414886 -1.491644 2.689430 H -2.711112 -3.124548 2.853964	H -7.075352 -0.846659 -0.306238 H -1.256323 1.660978 -0.206693 H 0.287798 2.692030 -0.943937 H 2.385508 3.893281 -0.764592 H 4.437734 0.192417 -0.015831 H 5.228197 -2.412036 2.779853 H 3.482343 -2.749921 2.799368 H 4.069439 -1.074114 2.619291 H 5.978795 4.287030 -0.294034 H 4.606942 4.375248 -1.425213 H 4.345970 4.631438 0.326514
 **Selenenyl sulfides for 11i** Electronic Energy = -3830.7638115	 **Selenenyl sulfides for 11j** Electronic Energy = -3945.3145056
C 2.784981 -0.945341 -1.601612 C 4.062576 -1.512768 -1.771850 C 5.101888 -1.144081 -0.948123 C 4.869078 -0.204425 0.099578 C 3.565308 0.341311 0.295713 C 2.522682 -0.031725 -0.601415 N 5.935339 0.106623 0.880771 C 5.756755 0.943221 1.880831 C 4.503332 1.518779 2.187007 C 3.416702 1.216461 1.400493 O 6.341762 -1.653800 -1.105122 N 1.240833 0.564319 -0.457882 C 0.043048 -0.103891 -0.480886 O -0.025903 -1.324880 -0.589450 C -1.196448 0.715778 -0.338589 C -1.202447 2.093287 -0.580400 C -2.359325 2.854090 -0.423621 C -3.532381 2.220834 -0.007008 C -3.536564 0.846018 0.216064	C -3.162981 -1.248460 1.268978 C -4.467696 -1.763247 1.397382 C -5.522825 -1.153782 0.757866 C -5.281570 -0.012236 -0.062234 C -3.954087 0.486750 -0.223934 C -2.890916 -0.144539 0.486288 N -6.365300 0.533529 -0.671946 C -6.184196 1.567888 -1.465145 C -4.911849 2.124929 -1.722745 C -3.806673 1.584816 -1.108075 O -6.786205 -1.613204 0.884308 N -1.583731 0.401527 0.388976 C -0.418606 -0.310988 0.257525 O -0.415526 -1.540441 0.179747 C 0.855463 0.445658 0.191744 C 0.940696 1.831724 0.418576 C 2.126578 2.531597 0.311796 C 3.297601 1.829104 -0.054601 C 3.239017 0.451001 -0.244797

C	-2.394507	0.068492	0.040372
Se	-2.423394	-1.872438	0.303599
S	-4.502333	-2.173345	1.120740
C	-5.484145	-2.475050	-0.402248
O	-2.242080	4.185390	-0.700992
C	-3.396112	5.005685	-0.583454
H	1.986764	-1.240205	-2.270325
H	4.239317	-2.232860	-2.562309
H	6.629474	1.174121	2.486348
H	4.408219	2.180024	3.041019
H	2.443434	1.629185	1.643859
H	6.899352	-1.257068	-0.411297
H	1.215947	1.550822	-0.256353
H	-0.320189	2.612345	-0.939235
H	-4.450120	2.776921	0.139355
H	-4.453900	0.374107	0.547779
H	-6.495386	-2.724432	-0.073304
H	-5.075807	-3.312686	-0.965831
H	-5.522471	-1.588423	-1.035052
H	-3.077064	6.008479	-0.860846
H	-4.189764	4.677493	-1.262547
H	-3.775025	5.018266	0.443715

C	2.039988	-0.252675	-0.116102
Se	1.989349	-2.192821	-0.373714
S	4.163680	-2.628393	-0.827550
C	4.854288	-2.9235690	0.848893
O	2.109960	3.891718	0.479680
C	2.843569	4.405198	1.597896
O	4.423031	2.571851	-0.203509
C	5.613514	1.930938	-0.653423
H	-2.352597	-1.737904	1.792141
H	-4.650963	-2.635658	2.013820
H	-7.071257	1.983627	-1.936199
H	-4.817572	2.960408	-2.407363
H	-2.822339	1.986887	-1.323674
H	-7.351707	-1.034512	0.341266
H	-1.515955	1.405571	0.386686
H	0.074824	2.421336	0.701500
H	4.129650	-0.096925	-0.523675
H	5.892699	-3.231986	0.709825
H	4.310629	-3.720141	1.354810
H	4.826863	-2.017449	1.454306
H	2.671202	5.480580	1.599977
H	2.467865	3.973992	2.532002
H	3.910988	4.203619	1.498153
H	5.959952	1.184584	0.067414
H	5.462441	1.457289	-1.627175
H	6.355776	2.721434	-0.743069





Selenenyl sulfides for 11k

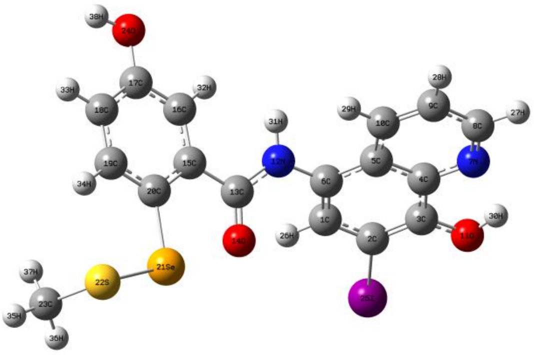
Electronic Energy = -3791.4860181

Selenenyl sulfides for 12k

Electronic Energy = -4251.0722251

C	2.580291	-1.113833	-1.480216
C	3.814714	-1.782951	-1.588602
C	4.886055	-1.394853	-0.816599
C	4.729445	-0.328026	0.117272

C	-2.453372	-0.851912	-0.958881
C	-3.766441	-1.350163	-0.844315
C	-4.711326	-0.709278	-0.071016
C	-4.320878	0.463554	0.641453

C	3.467900	0.324758	0.254629	C	-2.985649	0.957554	0.56373
C	2.392144	-0.075794	-0.590568	C	-2.055502	0.281068	-0.281432
N	5.823175	-0.004372	0.853900	N	-5.289587	1.045233	1.394240
C	5.713681	0.950597	1.752780	C	-4.980266	2.112118	2.100286
C	4.506081	1.642486	1.995511	C	-3.683364	2.669587	2.121727
C	3.392527	1.328643	1.252345	C	-2.694459	2.091861	1.359550
O	6.086478	-2.003314	-0.918493	O	-5.975005	-1.153173	0.036987
N	1.157872	0.623088	-0.511915	N	-0.750367	0.812108	-0.423854
C	-0.087791	0.050430	-0.489296	C	0.414130	0.092762	-0.545512
O	-0.252396	-1.166582	-0.497244	O	0.442206	-1.132149	-0.491680
C	-1.259981	0.972024	-0.423503	C	1.671046	0.876898	-0.722646
C	-1.153508	2.329676	-0.756843	C	1.655722	2.183381	-1.230370
C	-2.247685	3.178496	-0.659706	C	2.834368	2.899913	-1.392020
C	-3.469195	2.669113	-0.218223	C	4.048169	2.305238	-1.045582
C	-3.589337	1.320344	0.092421	C	4.073244	1.003067	-0.561215
C	-2.506382	0.446999	-0.018619	C	2.900283	0.264740	-0.397681
Se	-2.693608	-1.463776	0.370698	Se	2.945809	-1.589893	0.233396
S	-4.807663	-1.545406	1.151528	S	5.067605	-1.747908	0.965712
C	-5.779105	-1.859961	-0.375559	C	4.954798	-1.082809	2.673001
O	-2.062677	4.488860	-1.011197	O	2.736501	4.167645	-1.898392
H	1.756718	-1.428176	-2.107709	Cl	-4.201109	-2.794026	-1.723121
H	3.933020	-2.599386	-2.291463	H	-1.751708	-1.382084	-1.586413
H	6.607015	1.187992	2.324750	H	-5.778805	2.554940	2.689790
H	4.465999	2.401870	2.768380	H	-3.477544	3.534511	2.741964
H	2.453281	1.833811	1.451381	H	-1.688726	2.497407	1.394225
H	6.6777310	-1.569574	-0.276639	H	-6.434447	-0.537774	0.638003
H	1.208616	1.622705	-0.401269	H	-0.663433	1.814099	-0.376041
H	-0.231449	2.753828	-1.139113	H	0.736691	2.656246	-1.559350
H	-4.334654	3.320778	-0.123382	H	4.981387	2.849760	-1.169088
H	-4.543065	0.942677	0.441316	H	5.025826	0.549727	-0.312651
H	-6.813450	-2.009500	-0.058251	H	5.940519	-1.217924	3.123512
H	-5.427069	-2.758960	-0.879381	H	4.216133	-1.633020	3.254041
H	-5.733913	-1.012312	-1.059313	H	4.707748	-0.021234	2.666735
H	-2.891224	4.977489	-0.939261	H	3.613071	4.551242	-2.021029
							

Selenenyl sulfides for 13k

Electronic Energy = -3802.2265049

C	-1.955010	-0.187471	0.533886
C	-3.307601	-0.450012	0.234005
C	-4.079798	0.484628	-0.421016
C	-3.476224	1.718087	-0.817333
C	-2.100686	1.974096	-0.551723
C	-1.351514	0.994281	0.161605
N	-4.286511	2.592236	-1.467018
C	-3.772976	3.729927	-1.885763
C	-2.415717	4.074332	-1.702855
C	-1.586084	3.199003	-1.041343
O	-5.377181	0.281542	-0.706226
N	0.001521	1.264145	0.498100
C	1.057126	0.410734	0.287966
O	0.919156	-0.676339	-0.263522
C	2.403558	0.872709	0.734517
C	2.555478	1.908743	1.666813
C	3.815846	2.346276	2.050663
C	4.945179	1.745823	1.493143
C	4.803577	0.703823	0.585199
C	3.545579	0.235818	0.202468
Se	3.349555	-1.266595	-1.039257
S	5.490213	-1.609092	-1.653874
C	6.058728	-2.847340	-0.421831
O	3.879090	3.357392	2.971353
I	-4.165358	-2.293101	0.828000
H	-1.377342	-0.932641	1.063289
H	-4.447752	4.409036	-2.400257
H	-2.040789	5.014085	-2.092157
H	-0.535256	3.438167	-0.917790
H	-5.688078	1.079861	-1.173082
H	0.209239	2.183286	0.853972
H	1.701795	2.371709	2.149424
H	5.940827	2.083088	1.771662
H	5.691225	0.255155	0.155321
H	7.069707	-3.135294	-0.718230
H	5.418409	-3.728042	-0.435613
H	6.086550	-2.426951	0.583366
H	4.796790	3.556426	3.192016

2. Chemistry-Synthesis

The NMR spectra were recorder using TMS (^1H, ^{13}C NMR) as the internal standard and Me_2Se (^{77}Se NMR) as external standards on a Bruker AvanceIII spectrometer at 400.13 (^1H NMR), 100.61 (^{13}C NMR) and 76.31 (^{77}Se NMR) MHz. MS spectra were generated on an Agilent LC−MS 6120 instrument with an ESI and APCI mass selective detector. The high-resolution mass spectra were obtained using a Shimadzu LCMS-IT-TOF or LTQ Orbitrap XL (Thermo Scientific) mass spectrometer. The melting points were determined using an SRS-Opti Melt automated melting point instrument. The reactions were followed by thin-layer chromatography (TLC) on glass-packed precoated silica gel plates and visualized in an iodine chamber or with a UV lamp. Flash column chromatography was performed using silica gel (200–300 mesh) purchased from Qingdao Haiyang Chemical Co. Ltd. The purity (≥95%) of the samples was determined by HPLC, conducted on a Shimadzu LC-20AT series system, TC-C18 column (4.6×250 mm, 5 μm), eluted with CH_3OH/PBS (25 mM NaH_2PO_4 pH 3.0), 30/70, at a flow rate of 0.5 mL/min.

5-Nitroquinolin-8-ol (2)

Compound **2** were synthesised according to the literature.[3, 4] ^1H NMR (400 MHz, DMSO) δ 9.14 (d, J = 8.8 Hz, 1H), 9.02 (d, J = 3.5 Hz, 1H), 8.54 (d, J = 8.7 Hz, 1H), 7.88 (dd, J = 8.7, 3.9 Hz, 1H), 7.21 (d, J = 8.8 Hz, 1H).

***Tert*-butyl (5-nitroquinolin-8-yl) carbonate (3a)**

Compound **3a** was synthesised by following a previously reported procedure.[5] 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (d, *J* = 8.9 Hz, 1H), 9.03 (s, 1H), 8.44 (d, *J* = 8.4 Hz, 1H), 7.68 (dd, *J* = 5.5, 3.3 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 1.60 (s, 9H).

General Procedures for the Synthesis of 3b-3c

DMAP (2.10 g, 17.20 mmol) and DIPEA (12 mL, 68.90 mmol) were added at room temperature to a stirred suspension of nitroxoline (10.0 g, 34.45 mmol) and di-*tert*-butyl dicarbonate (15.03 g, 68.90 mmol) in a 1:2 mixture of hexanes-DCM (500 mL). The mixture was stirred for 72 h at 50℃, filtered, and concentrated under reduced pressure to provide a crude product which was purified by flash column chromatography on silica gel (eluent: petroleum ether /DCM = 8:2).

***Tert*-butyl (7-chloro-5-nitroquinolin-8-yl) carbonate (3b)**

Yellow solid, 62% yield. R_f = 0.58 (petrolem/EtOAc=10/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (d, *J* = 8.8 Hz, 2H), 8.50 (s, 1H), 7.62 (dd, *J* = 8.7, 4.1 Hz, 1H), 1.59 (s, 9H).

***Tert*-butyl (7-iodo-5-nitroquinolin-8-yl) carbonate (3c)**

Yellow solid, 76% Yield. R_f = 0.67 (petrolem/EtOAc=10/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (dd, *J* = 8.7, 1.3 Hz, 1H), 8.98 (d, *J* = 2.5 Hz, 1H), 8.82 (s, 1H), 7.64 (dd, *J* = 8.8, 4.1 Hz, 1H), 1.66 (s, 9H).

5-Aminoquinolin-8-yl *tert*-butyl carbonate (4a)[5]

Tert-butyl(5-nitroquinolin-8-yl) carbonate (**3a)** (14.0 g, 66.8 mmol) was dissolved in 200 mL of ethyl acetate, 8.0 equiv of $SnCl_2 \cdot 2H_2O$ (120 g, 535.1 mmol) was added to the solution in one portion, and the reaction was stirred at room temperature for 3 h.

The solution was adjusted to pH=8 with a saturated $NaHCO_3$ solution, extracted (ethyl acetate), washed (brine), and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded the pure product as a yellow solid in 78% yield. Mp 172.4-173.3 ℃. R_f = 0.32 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.20 – 8.05 (m, 1H), 7.38 – 7.29 (m, 2H), 6.72 (dd, *J* = 7.9, 3.4 Hz, 1H), 4.12 (s, 2H), 1.59 (s, 9H). LC/MS (ESI): 261.1 $[M+H]^+$.

General Procedures for the Synthesis of 4b-4c

To a solution of *tert*-butyl (7-chloro-5-nitroquinolin-8-yl) carbonate **(3b)** or *tert*-butyl(7-iodo-5-nitroquinolin-8-yl) carbonate **(3c)** (1.0 equiv) in 20 mL of ethanol was added 5.0 equiv of $Na_2S·9H_2O$ in one portion. The mixture was stirred at room temperature for 3 h.

5-Amino-7-chloroquinolin-8-yl *tert*-butyl carbonate (4b)

Yellow solid, 86%Yield. R_f = 0.54 (petrolem/EtOAc=5/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.89 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.08 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.30 (dd, *J* = 8.5, 4.1 Hz, 2H), 6.81 (s, 1H), 1.50 (s, 9H). LC/MS (ESI): 251.1 $[M–CO_2+H]^+$.

5-Amino-7-iodoquinolin-8-yl *tert*-butyl carbonate (4c)

Yellow solid, 84% Yield. Mp 123.8-124.9 ℃. R_f = 0.67 (petrolem/EtOAc=5/1).^1H NMR (400 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 4.0, 1.5 Hz, 1H), 8.08 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.34 (dd, *J* = 8.5, 4.1 Hz, 1H), 7.23 (s, 1H), 3.96 (s, 2H), 1.57 (s, 9H). LC/MS (ESI): 343.0 $[M–CO_2+H]^+$.

General Procedures for the Synthesis of 6a-6l and 7a-7l

Compound **6a-6l** and **7a-7l** were synthesized according to literature procedures.[6]

General Procedures for the Synthesis of 8a-8k, 9k and 10k

To a solution of 20 mL of anhydrous DCM, 10.0 equiv of anhydrous triethylamine and 1.0 equiv of (**4**), a solution of 1.5 equiv of the corresponding chloride in 2 mL of anhydrous DCM was added dropwise. The reaction was stirred at room temperature for 16 h. Saturated $NaHCO_3$ was added to the mixture, which was then extracted with DCM, washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica-column chromatography.

***Tert*-butyl (5-(3-oxobenzo[*d*][1,2]selenazol-2(3*H*)-yl)quinolin-8-yl) carbonate (8a)**

White solid, 81% yield. R_f = 0.51 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 9.03 – 8.82 (m, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 8.08 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.73 – 7.56 (m, 4H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.42 (dd, *J* = 8.6, 4.1 Hz, 1H), 1.62 (s, 9H). LC/MS (ESI):443.0 $[M+H]^+$.

***Tert*-butyl (5-(6-chloro-3-oxobenzo[*d*][1,2]selenazol-2(3*H*)-yl)quinolin-8-yl) carbonate (8b)**

Pale yellow solid, 78% yield. R_f = 0.57 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.92 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.02 (dd, *J* = 12.8, 4.8 Hz, 2H), 7.73 (d, *J* = 1.6 Hz, 1H), 7.57 (q, *J* = 8.1 Hz, 2H), 7.46 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.40 (dd, *J* = 8.6, 4.2 Hz, 1H), 1.61 (s, 9H). LC/MS (ESI): 477.0 $[M+H]^+$.

***Tert*-butyl (5-(5-chloro-3-oxobenzo[*d*][1,2]selenazol-2(3*H*)-yl)quinolin-8-yl) carbonate (8c)**

Pale yellow solid, 84% yield. R_f = 0.58 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 9.02 – 8.91 (m, 1H), 8.15 (s, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.71 – 7.62 (m, 3H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.47 (dd, *J* = 8.6, 4.2 Hz, 1H), 1.62 (s, 9H). LC/MS (ESI): 477.0 $[M+H]^+$.

Tert-butyl (5-(6-fluoro-3-oxobenzo[_d_][1,2]selenazol-2(3_H_)-yl)quinolin-8-yl) carbonate (8d)

White solid, 89% yield. R_f = 0.53 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.14 (dd, *J* = 8.6, 5.2 Hz, 1H), 8.08 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.60 (s, 1H), 7.46 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.42 (dd, *J* = 7.8, 2.2 Hz, 1H), 7.23 (dd, *J* = 8.6, 2.2 Hz, 1H), 1.62 (s, 9H). . LC/MS (ESI): 461.0 $[M+H]^+$.

Tert-butyl (5-(5-fluoro-3-oxobenzo[_d_][1,2]selenazol-2(3_H_)-yl)quinolin-8-yl) carbonate (8e)

White solid, 80% yield. R_f = 0.56 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.94 (t, *J* = 3.6 Hz, 1H), 8.11 (dt, *J* = 8.8, 4.9 Hz, 1H), 8.05 (dd, *J* = 8.5, 3.2 Hz, 1H), 7.59 (ddd, *J* = 17.3, 8.0, 4.8 Hz, 2H), 7.43 (dd, *J* = 8.3, 4.6 Hz, 2H), 7.25 – 7.17 (m, 1H), 1.62 (s, 9H). LC/MS (ESI): 461.0 $[M+H]^+$.

Tert-butyl (5-(4-fluoro-3-oxobenzo[_d_][1,2]selenazol-2(3_H_)-yl)quinolin-8-yl) carbonate (8f)

Pale yellow solid, 71% yield. R_f = 0.51 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.13 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.63 (d, *J* = 2.9 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.49 (d, *J* = 3.0 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.17 (dd, *J* = 9.6, 8.4 Hz, 1H), 1.62 (s, 9H). LC/MS (ESI): 461.0 $[M+H]^+$.

Tert-butyl (5-(3-oxo-6-(trifluoromethyl)benzo[_d_][1,2]selenazol-2(3_H_)-yl)quinolin-8-yl) carbonate (8g)

yellow solid, 82% yield. R_f = 0.59 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, _J_ = 4.2, 1.6 Hz, 1H), 8.28 (d, _J_ = 8.2 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.77 (dd, _J_ = 8.2, 0.8 Hz, 1H), 7.62 (dd, _J_ = 20.8, 8.1 Hz, 2H), 7.46 (dd, _J_ = 8.6, 4.2 Hz, 1H), 1.62 (s, 9H). LC/MS (ESI): 510.0 $[M+H]^+$.

Tert-butyl (5-(5-methoxy-3-oxobenzo[_d_][1,2]selenazol-2(3_H_)-yl)quinolin-8-yl) carbonate (8i)

Pale yellow solid, 77% yield. R_f = 0.54 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, _J_ = 4.1, 1.5 Hz, 1H), 8.09 (dd, _J_ = 8.6, 1.6 Hz, 1H), 7.65 (dd, _J_ = 5.3, 2.7 Hz, 2H), 7.58 (dd, _J_ = 8.4, 4.2 Hz, 2H), 7.45 (dd, _J_ = 8.6, 4.2 Hz, 1H), 7.34 (dd, _J_ = 8.7, 2.7 Hz, 1H), 3.92 (s, 3H), 1.62 (s, 9H). LC/MS (ESI): 473.0 $[M+H]^+$.

Tert-butyl (5-(5,6-dimethoxy-3-oxobenzo[_d_][1,2]selenazol-2(3_H_)-yl)quinolin-8-yl) carbonate (8j)

White solid, 69% yield. R_f = 0.55 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, _J_ = 4.1 Hz, 1H), 8.10 (d, _J_ = 8.6 Hz, 1H), 7.65 (d, _J_ = 8.0 Hz, 1H), 7.58 (t, _J_ = 3.9 Hz, 2H), 7.46 (dd, _J_ = 8.2, 4.1 Hz, 1H), 7.13 (s, 1H), 4.02 (s, 3H), 4.00 (s, 3H), 1.62 (s, 9H). LC/MS (ESI): 503.1 $[M+H]^+$.

2-(8-((_Tert_-butoxycarbonyl)oxy)quinolin-5-yl)-3-oxo-2,3-dihydrobenzo[_d_][1,2]selenazol-5-yl acetate (8k)

Pale yellow solid, 76% yield. R_f = 0.49 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.09 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.90 (d, *J* = 2.3 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.52 – 7.45 (m, 2H), 2.37 (s, 3H), 1.62 (s, 9H). LC/MS (ESI): 501.1 $[M+H]^+$.

***Tert*-butyl (5-(5-hydroxy-3-oxobenzo[*d*][1,2]selenazol-2(3*H*)-yl)quinolin-8-yl) carbonate (8l)**

The solution of 1.0 equiv of **8k**, 1.0 equiv of anhydrous potassium carbonate in 20mL of methyl alcohol was stirred at room temperature and monitored by TLC. After the completion of the reaction, the mixture was adjusted to pH=7 with acetic acid, 150mL of water was added, filtrated, and the product was recrystallized from ethyl acetate to afford a white solid, 78% yield. R_f = 0.38 (CH_2Cl_2/CH_3OH=20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.92 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.07 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.67 (d, *J* = 2.4 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.43 – 7.40 (m, 1H), 7.14 (dd, *J* = 8.6, 2.4 Hz, 1H), 1.60 (s, 9H). LC/MS (ESI): 459.0 $[M+H]^+$.

2-(8-((*Tert*-butoxycarbonyl)oxy)-7-chloroquinolin-5-yl)-3-oxo-2,3-dihydrobenzo[*d*][1,2]selenazol-5-yl acetate (9k)

White solid, 71% yield. R_f = 0.34 (petrolem/EtOAc=5/1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.00 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.89 (d, *J* = 2.2 Hz, 1H), 7.72 (d, *J* = 8.6 Hz, 1H), 7.67 (s, 1H), 7.49 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.40 (dd, *J* = 8.5, 4.1 Hz, 1H), 2.37 (s, 3H), 1.59 (s, 9H). LC/MS (ESI): 491.0 $[M–CO_2+H]^+$.

***Tert*-butyl (7-chloro-5-(5-hydroxy-3-oxobenzo[*d*][1,2]selenazol-2(3*H*)-yl)quinolin-8-yl) carbonate (9l)**

To a solution 1.0 equiv of **9k** in 20 mL of methyl alcohol containing, 1.0 equiv of anhydrous potassium carbonate was added in portion. The reaction was stirred at room temperature and monitored by TLC. After the completion of the reaction, the mixture was adjusted to pH 7 with acetic acid. Water (150 mL) was added, extracted by ethyl acetate, washed with brine, dried over anhydrous Na_2SO_4, evaporated the solvent under reduced pressure, purified by silica-column chromatography to afford a white solid, 82% yield. R_f = 0.34 (petrolem/EtOAc=2/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (dd, *J* = 4.1, 1.6 Hz, 1H), 7.99 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.68 (s, 1H), 7.67 (d, *J* = 2.5 Hz, 1H), 7.46 (d, *J* = 8.6 Hz, 1H), 7.37 (dd, *J* = 8.5, 4.1 Hz, 1H), 7.16 (dd, *J* = 8.6, 2.5 Hz, 1H), 1.58 (s, 9H). LC/MS (ESI): 449.0 $[M–CO_2+H]^+$.

2-(8-((*Tert*-butoxycarbonyl)oxy)-7-iodoquinolin-5-yl)-3-oxo-2,3-dihydrobenzo[*d*][1,2]selenazol-5-yl acetate (10k)

Pale yellow solid, 84% yield. R_f = 0.39 (petroleum/EtOAc=5/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, *J* = 2.1 Hz, 1H), 8.02 (s, 1H), 7.99 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.88 (d, *J* = 1.8 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.49 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.42 (dd, *J* = 8.4, 3.7 Hz, 1H), 2.37 (s, 3H), 1.66 (s, 9H). LC/MS (ESI): 583.0 $[M–CO_2+H]^+$.

Tert-butyl (5-(5-hydroxy-3-oxobenzo[*d*][1,2]selenazol-2(3*H*)-yl)-7-iodoquinolin-8-yl) carbonate (10l)

The procedure are same as **9l**. Pale yellow solid, 76% yield. R_f = 0.35 (petroleum/EtOAc=2/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.01 (s, 1H), 7.97 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.67 (d, *J* = 2.5 Hz, 1H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.39 (dd, *J* = 8.5, 4.1 Hz, 1H), 7.19 (dd, *J* = 8.6, 2.6 Hz, 1H), 1.64 (s, 9H). LC/MS (ESI): 541.0 $[M–CO_2+H]^+$.

General Procedure for the Synthesis of 11a-11c, 11e, 11i and 11j

Piperidine (1.5 equiv) was added to a solution of 5 mL anhydrous DCM containing 1.0 equiv of **8a**, **8b**, **8c**, **8e**, **8i** or **8j** at ambient temperature. After 20 minutes, the mixture was filtered, washed with DCM, and dried under reduced pressure to obtain the pure product.

General Procedures for the Synthesis of 11d, 11f, 11g, 11k, 12k and 13k

To a solution of 300 mg of **8**, **9** or **10** in 12 mL CH_2Cl_2, HCl gas was bubbled at room temperature for 4 h. The reaction was stirred under an HCl atmosphere overnight at 0 ℃. The mixture was filtered and dried under reduced pressure to yield the product.

2-(8-Hydroxyquinolin-5-yl)benzo[*d*][1,2]selenazol-3(2*H*)-one (11a)

Yellow solid, 86% yield. Mp 247.4-248.1 ℃. R_f = 0.19 (CH_2Cl_2/CH_3OH=5/1). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.91 (d, *J* = 3.9 Hz, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 7.94 (s, 1H), 7.93 – 7.90 (m, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.59 (dd, *J* = 8.4, 4.1 Hz, 1H), 7.53 (t, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (101 MHz, d_6-DMSO) δ

166.40, 153.51, 148.58, 140.42, 138.48, 132.13, 128.37, 127.99, 127.04, 126.19, 125.94, 125.24, 122.34, 110.61. ^{77}Se NMR (d_6-DMSO): δ = 886 ppm. HRMS (ESI) m/z [M+Cl]$^-$ for $C_{16}H_{10}N_2O_2Se$ pred. 376.9602, meas. 376.9586; HPLC purity: 99.45%.

6-Chloro-2-(8-hydroxyquinolin-5-yl)benzo[*d*][1,2]selenazol-3(2*H*)-one (11b)

Yellow solid, 88% yield. Mp 244.6-245.1 ℃. R_f = 0.22 (CH_2Cl_2/CH_3OH=5/1). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.88 (s, 1H), 8.15 (s, 1H), 7.90 (t, *J* = 7.3 Hz, 2H), 7.55 (d, *J* = 7.2 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 7.9 Hz, 1H). ^{13}C NMR (101 MHz, d_6-DMSO) δ 165.48, 153.65, 148.58, 142.06, 138.47, 137.13, 132.11, 129.46, 128.44, 126.62, 126.17, 126.11, 125.32, 124.86, 122.39, 110.61. ^{77}Se NMR (d_6-DMSO): δ = 864 ppm. HRMS (ESI) m/z [M+Cl]$^-$ for $C_{16}H_9N_2O_2ClSe$ pred. 410.9210, meas. 410.9205; HPLC purity: 98.80%.

5-Chloro-2-(8-hydroxyquinolin-5-yl)benzo[*d*][1,2]selenazol-3(2*H*)-one (11c)

Yellow solid, 81% yield. Mp 248.3-249.4 ℃. R_f = 0.21 (CH_2Cl_2/CH_3OH=5/1). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.91 (dd, *J* = 3.9, 1.3 Hz, 1H), 8.15 (dd, *J* = 8.5, 3.2 Hz, 1H), 7.94 (dd, *J* = 6.4, 2.1 Hz, 1H), 7.89 (d, *J* = 2.2 Hz, 1H), 7.83 – 7.75 (m, 1H), 7.59 (dd, *J* = 8.5, 4.1 Hz, 1H), 7.52 (dd, *J* = 7.4, 2.8 Hz, 1H), 7.16 (dd, *J* = 8.1, 3.6 Hz, 1H).^{13}C NMR (101 MHz, d_6-DMSO) δ 165.15, 153.68, 148.57, 139.10, 138.48, 132.12, 131.93, 131.34, 128.89, 128.34, 127.92, 127.12, 126.08, 124.91, 122.37, 110.59. ^{77}Se NMR (d_6-DMSO): δ = 870 ppm. HRMS (ESI) m/z [M+Cl]$^-$ for $C_{16}H_9N_2O_2ClSe$ pred. 410.9210, meas. 410.9188; HPLC purity: 99.35%.

5-Fluoro-2-(8-hydroxyquinolin-5-yl)benzo[*d*][1,2]selenazol-3(2*H*)-one (11e)

Yellow solid, 75% yield. Mp 249.1-250.3 ℃. R_f = 0.20 (CH_2Cl_2/CH_3OH=5/1). ^1H NMR (400 MHz, d_6-DMSO) δ 8.91 – 8.86 (m, 1H), 8.04 – 7.81 (m, 3H), 7.57 (dd, *J* = 8.4, 3.9 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.36 (t, *J* = 8.7 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 1H).^{13}C NMR (101 MHz, d_6-DMSO) δ 165.56 (d, $J_{\text{C-F}}$= 17.9 Hz), 163.15 (s), 153.60 (s), 148.56 (s), 142.52 (d, $J_{\text{C-F}}$ = 11.0 Hz), 138.47 (s), 132.11 (s), 130.17 (d, $J_{\text{C-F}}$ = 9.3 Hz), 128.46 (s), 126.22 (s), 125.01 (s), 123.87 (s), 122.37 (s), 114.45 (d, $J_{\text{C-F}}$ = 23.6 Hz), 112.46 (d, $J_{\text{C-F}}$ = 26.1 Hz), 110.59 (s). ^{77}Se NMR (d_6-DMSO): δ = 933 ppm. HRMS (ESI) m/z $[M+Cl]^-$ for $C_{16}H_9N_2O_2FSe$ pred. 394.9508, meas. 394.9464; HPLC purity: 95.14%.

6-Fluoro-2-(8-hydroxyquinolin-5-yl)benzo[*d*][1,2]selenazol-3(2*H*)-one hydrochloride (11d)

Yellow solid, 92% yield. Mp 237.4-238.6 ℃. R_f = 0.25 (CH_2Cl_2/CH_3OH=5/1). ^1H NMR (400 MHz, d_6-DMSO) δ 9.17 (dd, *J* = 5.2, 1.0 Hz, 1H), 8.77 (dd, *J* = 8.6, 0.9 Hz, 1H), 8.51 (dd, *J* = 10.0, 2.4 Hz, 1H), 8.08 (dd, *J* = 8.6, 5.3 Hz, 1H), 7.93 (dd, *J* = 8.5, 5.6 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.33 (td, *J* = 8.6, 2.4 Hz, 1H). ^{13}C NMR (101 MHz, d_6-DMSO) δ 165.38 (d, *J* = 28.3 Hz), 162.77 (s), 147.38 (s), 144.46 (s), 144.33 (d, *J* = 10.5 Hz), 143.24 (s), 130.29 (s), 129.58 (d, *J* = 9.6 Hz), 128.80 (s), 127.66 (s), 127.06 (s), 125.34 (s), 122.49 (s), 115.73 (s), 113.96 (d, *J* = 12.6 Hz), 113.70 (d, *J* = 9.0 Hz). ^{77}Se NMR (d_6-DMSO): δ = 860 ppm. HRMS (ESI) m/z $[M+H]^+$ for $C_{16}H_9N_2O_2FSe$ pred. 360.9887, meas. 360.9871; HPLC purity: 98.23%.

4-Fluoro-2-(8-hydroxyquinolin-5-yl)benzo[*d*][1,2]selenazol-3(2*H*)-one hydrochloride (11f)

Yellow solid, 92% yield. Mp 274.1-275.0 ℃. R_f = 0.18 (CH_2Cl_2/CH_3OH=5/1). ^1H NMR (400 MHz, *d*$_6$-DMSO) δ 9.13 (dd, *J* = 5.2, 1.2 Hz, 1H), 8.75 (dd, *J* = 8.6, 1.0 Hz, 1H), 8.41 (d, *J* = 8.1 Hz, 1H), 8.04 (dd, *J* = 8.6, 5.2 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.63 (td, *J* = 8.1, 5.0 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.24 (dd, *J* = 10.6, 8.2 Hz, 1H). ^{13}C NMR (101 MHz, *d*$_6$-DMSO) δ 163.72 (d, $J_{C\text{-}F}$ = 3.1 Hz), 161.84 (d, $J_{C\text{-}F}$ = 259.8 Hz), 147.58 (s), 144.53 (s), 144.21 (s), 143.13 (s), 131.88 (d, $J_{C\text{-}F}$ = 8.3 Hz), 130.58 (s), 128.94 (s), 127.21 (d, $J_{C\text{-}F}$ = 8.7 Hz), 123.41 (d, $J_{C\text{-}F}$ = 3.3 Hz), 122.58 (s), 116.13 (d, $J_{C\text{-}F}$ = 10.8 Hz), 115.59 (s), 112.47 (d, $J_{C\text{-}F}$ = 19.8 Hz). ^{77}Se NMR (*d*$_6$-DMSO): *δ* = 879 ppm. HRMS (ESI) m/z $[M+H]^+$ for $C_{16}H_9FN_2O_2Se$ pred. 360.9886, meas. 360.9886; HPLC purity: 98.21%.

2-(8-Hydroxyquinolin-5-yl)-6-(trifluoromethyl)benzo[*d*][1,2]selenazol-3(2*H*)-one (11g)

Yellow solid, 96% yield. Mp 251.1-252.0 ℃. R_f = 0.23 (CH_2Cl_2/CH_3OH=5/1). ^1H NMR (400 MHz, *d*$_6$-DMSO) δ 9.16 (dd, *J* = 5.3, 1.3 Hz, 1H), 9.13 (s, 1H), 8.78 (dd, *J* = 8.6, 1.3 Hz, 1H), 8.12 – 8.08 (m, 1H), 8.08 – 8.05 (m, 1H), 7.81 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.62 (d, *J* = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, *d*$_6$-DMSO) δ 165.27 (s), 147.48 (s), 144.49 (s), 143.28 (s), 142.93 (s), 132.26 (s), 131.08 (q, *J* = 31.5 Hz), 130.21 (s), 128.81 (s), 128.36 (s), 127.47 (s), 126.93 (s), 124.74 (d, *J* = 4.0 Hz), 124.12 (q, *J* = 273.0 Hz), 122.54 (s), 122.24 (d, *J* = 3.0 Hz), 115.71 (s). ^{77}Se NMR (d_6-DMSO): δ = 855 ppm. HRMS (ESI) m/z $[M+H]^+$for $C_{17}H_9N_2O_3F_3Se$ pred. 410.9855, meas. 410.9836; HPLC purity: 99.73%.

2-(8-Hydroxyquinolin-5-yl)-6-methoxybenzo[*d*][1,2]selenazol-3(2*H*)-one hydrobromide (11h)

To a solution of 20mL hydrobromic acid (47%) 100mg of **10h** was added. After refluxed for 24h, the mixture was filtrated and dried under reduced pressure to get the product as a brown solid. 62% yield. Mp 316.3-317.2 ℃. R_f = 0.16 (CH_2Cl_2/CH_3OH=5/1). ^{1}H NMR (400 MHz, d_6-DMSO) δ 9.13 (dd, *J* = 5.2, 1.3 Hz, 1H), 8.68 (dd, *J* = 8.6, 1.1 Hz, 1H), 8.08 (d, *J* = 2.3 Hz, 1H), 8.05 (dd, *J* = 8.7, 5.2 Hz, 1H), 7.79 (dd, *J* = 15.1, 8.4 Hz, 2H), 7.51 (d, *J* = 8.3 Hz, 1H), 7.08 (dd, *J* = 8.6, 2.4 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (101 MHz, d_6-DMSO) δ 166.05, 162.18, 147.44, 144.65, 142.92, 142.64, 130.58, 129.05, 128.78, 127.70, 127.24, 122.63, 120.86, 115.46, 113.95, 111.24, 55.61. ^{77}Se NMR (d_6-DMSO): δ = 899 ppm. HRMS (ESI) m/z $[M+H]^+$for $C_{17}H_{12}N_2O_3Se$ pred. 373.0086, meas. 373.0086; HPLC purity: 98.76%.

2-(8-Hydroxyquinolin-5-yl)-5-methoxybenzo[*d*][1,2]selenazol-3(2*H*)-one (11i)

Yellow solid, 72%yield. Mp 225.5-226.2 ℃. R_f = 0.18 (CH_2Cl_2/CH_3OH=5/1). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.90 (d, *J* = 3.6 Hz, 1H), 8.00 (d, *J* = 8.8 Hz, 1H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.58 (dd, *J* = 8.5, 4.0 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 2.5 Hz, 1H), 7.37 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, d_6-DMSO) δ 166.17, 158.48, 153.66, 148.50, 138.55, 132.13, 131.26, 128.23, 128.06, 126.91, 126.13, 125.35, 122.27, 121.14, 110.59, 110.29, 55.50. ^{77}Se NMR (d_6-DMSO): δ = 941 ppm. HRMS (ESI) m/z [M+Cl]$^-$ for $C_{17}H_{12}N_2O_3Se$ pred. 406.9708, meas. 406.9701; HPLC purity: 99.40%.

2-(8-Hydroxyquinolin-5-yl)-5,6-dimethoxybenzo[*d*][1,2]selenazol-3(2*H*)-one (11j)

Yellow solid, 83% yield. Mp 276.5-277.1 ℃. R_f = 0.18 (CH_2Cl_2/CH_3OH=5/1). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.90 (d, *J* = 3.8 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.64 (s, 1H), 7.59 (dd, *J* = 8.4, 4.0 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.36 (s, 1H), 7.14 (d, *J* = 8.1 Hz, 1H), 3.89 (s, 3H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, d_6-DMSO) δ 166.39, 153.42, 152.93, 148.53, 138.48, 132.94, 132.14, 128.37, 126.28, 125.54, 122.28, 119.05, 110.55, 109.05, 107.49, 55.80, 55.65. ^{77}Se NMR (d_6-DMSO): δ = 938 ppm. HRMS (ESI) m/z [M+Cl]$^-$ for $C_{18}H_{14}N_2O_4Se$ pred. 436.9814, meas. 436.9778; HPLC purity: 98.16%.

5-Hydroxy-2-(8-hydroxyquinolin-5-yl)benzo[*d*][1,2]selenazol-3(2*H*)-one hydrochloride (11k)

Yellow solid, 83% yield. Mp 294.4-294.9 ℃. R_f = 0.24 (CH_2Cl_2/CH_3OH=3/1). ^{1}H NMR (400 MHz, d_6-DMSO) δ 9.12 (dd, *J* = 5.1, 1.2 Hz, 1H), 8.65 (dd, *J* = 8.6, 0.9 Hz, 1H), 8.20 (d, *J* = 8.7 Hz, 1H), 8.02 (dd, *J* = 8.6, 5.2 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.54 (d, *J* = 8.3 Hz, 1H), 7.31 (d, *J* = 2.6 Hz, 1H), 7.17 (dd, *J* = 8.7, 2.7 Hz, 1H). ^{13}C NMR (101 MHz, d_6-DMSO) δ 166.31, 156.22, 147.41, 144.48, 143.14, 130.27, 130.26, 128.88, 128.79, 128.01, 127.81, 127.00, 122.50, 120.53, 115.63, 112.79. ^{77}Se NMR (d_6-DMSO): δ = 899 ppm. HRMS (ESI) m/z [M+H]$^+$ for $C_{16}H_{10}N_2O_3Se$ pred. 358.9929, meas. 358.9928; HPLC purity: 98.73%.

2-(7-Chloro-8-hydroxyquinolin-5-yl)-5-hydroxybenzo[*d*][1,2]selenazol-3(2*H*)-one hydrochloride (12k)

Yellow solid, 95% yield. Mp 262.3-263.6 °C. R_f = 0.28 (CH_2Cl_2/CH_3OH=5/1). ^1H NMR (400 MHz, d_6-DMSO) δ 9.05 (dd, *J* = 4.5, 1.3 Hz, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 8.23 (d, *J* = 8.7 Hz, 1H), 7.80 (dd, *J* = 8.5, 4.6 Hz, 1H), 7.71 (s, 1H), 7.32 (d, *J* = 2.4 Hz, 1H), 7.17 (dd, *J* = 8.6, 2.5 Hz, 1H). ^{13}C NMR (101 MHz, d_6-DMSO) δ 166.38, 156.22, 146.86, 145.31, 139.79, 133.19, 130.34, 129.58, 128.88, 128.78, 128.04, 125.76, 122.48, 120.57, 119.61, 112.82. ^{77}Se NMR (d_6-DMSO): δ = 903 ppm. HRMS (ESI) m/z $[M+H]^+$ for $C_{16}H_9ClN_2O_3Se$ pred. 392.9540, meas. 392.9543; HPLC purity: 98.89%.

5-Hydroxy-2-(8-hydroxy-7-iodoquinolin-5-yl)benzo[*d*][1,2]selenazol-3(2*H*)-one hydrochloride (13k)

Yellow solid, 92% yield. Mp 229.4-230.1 °C. R_f = 0.27 (CH_2Cl_2/CH_3OH=5/1). ^1H NMR (400 MHz, d_6-DMSO) δ 8.95 (d, *J* = 4.2 Hz, 1H), 8.11 (d, *J* = 8.7 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.84 (s, 1H), 7.69 (dd, *J* = 8.5, 4.3 Hz, 1H), 7.31 (d, *J* = 2.5 Hz, 1H), 7.18 (dd, *J* = 8.7, 2.6 Hz, 1H). ^{13}C NMR (101 MHz, d_6-DMSO) δ 166.29, 156.22, 151.17, 147.59, 137.07, 136.65, 134.01, 130.10, 128.73, 128.61, 127.85, 126.28, 122.56, 120.62, 112.79, 83.06. ^{77}Se NMR (d_6-DMSO): δ = 925 ppm. HRMS (ESI) m/z $[M+H]^+$ for $C_{16}H_9IN_2O_3Se$ pred. 484.8896, meas. 484.8897; HPLC purity: 99.31%.

3. Coupled Reductase Assay

Procedure: Phosphate buffer solutions of pH 7.5, GSH, NADPH, GR were added into cuvette contained buffer solution. Finally, peroxide was added to initiate the reaction in a cuvette having mixture of all and immediately start the experiment for the control values in absence of any catalyst. For the test samples, solution was made in appropriate solvent and added into cuvette containing the mixture of buffer solution, GSH, NADPH and GR. Now, peroxide was added to initiate the reaction. Each of the measurement was carried out in triplicates. The initial reduction rate (5-10% consumption of NADPH) was expressed as µM of NADPH depleting per minute (µM/min) after the addition of peroxide. A plot of inverse of initial reaction rate v_0 inverse of GSH and peroxide concentration gave the catalytic parameters such as maximum velocities ($V_{\max}$), Michaelis constants (K_m), catalytic constants (k_{cat}) and catalytic efficiencies (η) for the reduction of peroxide by GSH in presence of compound.

Initial reaction rate (v_0) = $\Delta A/6.22 \times 1000$ ($\mu M \bullet min^{-1}$)

$$\frac{1}{v_0} = \frac{K_m}{V_{\max}} \cdot \frac{1}{[S]} + \frac{1}{V_{max}}$$

$$k_{cat} = \frac{V_{\max}}{[S]_0}$$

$$\eta = \frac{k_{cat}}{K_m}$$

$$\text{Slope} = \frac{K_m}{V_{\max}}$$

$$\text{Intercept} = \frac{1}{V_{\max}}$$

Where, ΔA = Difference in absorbance for one minute obtained from the initial 5-10%

of the NADPH consumption measured at 340 nm. It is obtained from the graph of absorbance in the first 10 s.

v_0 = Initial reaction rate

η = Catalytic efficiency

k_{cat} = Catalytic constant

K_m = Michaelis constant

$[S]_0$ = The concentration of catalyst

material	Sample (µL)	Control (µL)
PBS	140	150
GSH	20	20
NADPH	5	5
GR	5	5
Catalyst	10	0
Peroxide	20	20

Total volume of the solution was taken 200 µL. GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), catalyst (80 µM) and peroxide (1.6 mM).

Effect of increasing GSH on initial rate for the reduction of H_2O_2

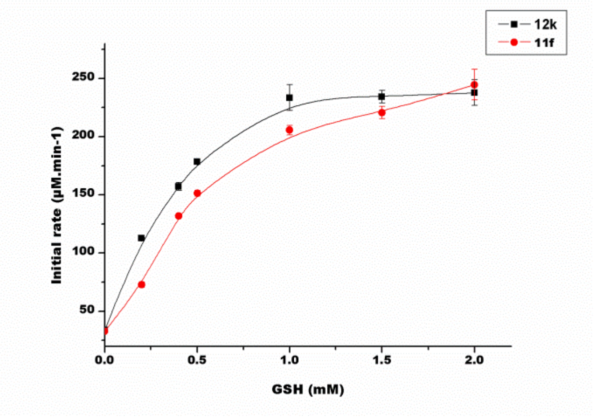


Figure S1. Effect of increasing GSH on initial rate for the reduction of H_2O_2 (1.6 mM) in the presence of **11f** and **12k** (80 µM).

4. Determination of the Catalytic Parameters

Table S1. Summary for the effect of substrate (H_2O_2) concentration on the initial rate of **12k**

$[H_2O_2]$ (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	$1/[H_2O_2]$ (mM^{-1})	$1/v_0$ (μM^{-1} ·min)
1.6	198.88 211.34 192.66	200.96 ±9.51	0.6250	0.0049761
1.4	187.75 184.33 189.93	187.33 ±2.82	0.7142	0.0053379
1.2	182.40 182.14 182.66	182.40 ±0.26	0.8333	0.0054824
1.0	169.35 172.41 176.78	172.84 ±3.73	1.0000	0.0057854
0.8	158.62 165.86 163.64	162.70 ±3.70	1.2500	0.0061460
0.4	118.95	115.36 ±7.96	2.5000	0.0086682

	120.90 106.24			

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), H_2O_2 (variable) and **12k** (80 μM).

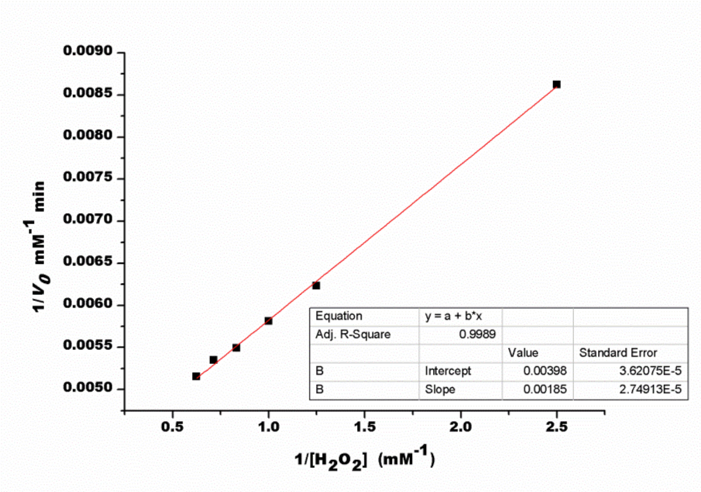


Figure S2. The Lineweaver-Burk (double-reciprocal) plots obtained for **12k** with the variation of H_2O_2 at the fixed concentration of GSH.

Intercept = 0.00398 ±0.0000362

Slop = 0.00185 ±0.0000274

V_{max} = 251.25 ±1.24

K_m = 0.46 ±0.02

k_{cat} = 3.14 ±0.01

η = 6.83 ±0.04

Table S2. Summary for the effect of substrate (*t*-BuOOH) concentration on the initial rate of **12k**

[*t*-BuOOH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[*t*-BuOOH] (mM^{-1})	1/v_0 (μM^{-1} ·min)
1.6	70.04 67.45 72.21	69.90 ±2.38	0.6250	0.014306
1.4	69.23 60.41 68.13	65.92 ±4.80	0.7142	0.015169
1.2	69.77 61.47 65.24	65.49 ±4.15	0.8333	0.015268
1.0	60.24 61.21 59.53	60.32 ±0.84	1.0000	0.016576
0.8	54.02 52.79 55.69	54.16 ±1.45	1.2500	0.018461
0.4	37.97 30.78 35.17	34.64 ±4.06	2.5000	0.028868

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), *t*-BuOOH (variable) and **12k** (80 μM).

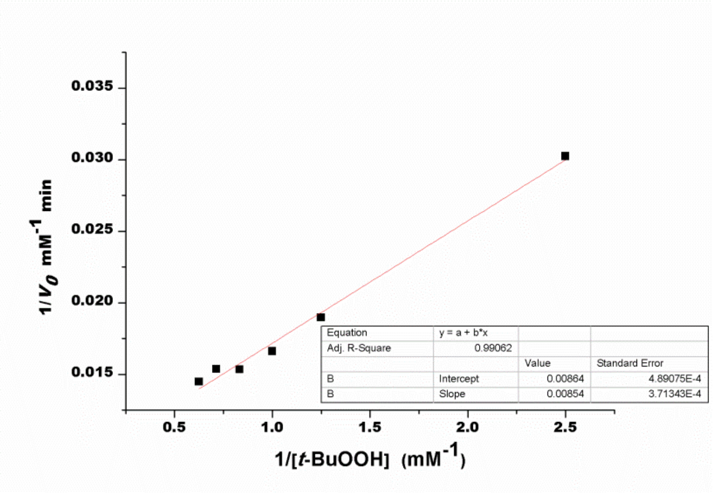


Figure S3. The Lineweaver-Burk (double-reciprocal) plots obtained for **12k** with the variation of *t*-BuOOH at the fixed concentration of GSH.

Intercept = 0.00884 ±0.000489

Slop = 0.00854 ±0.000371

V_{max} = 113.12 ±4.42

K_{m} = 0.96 ±0.03

k_{cat} = 1.41 ±0.05

η = 1.46 ±0.05

Table S3. Summary for the effect of substrate (Cum-OOH) concentration on the initial rate of **12k**

[Cum-OOH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[Cum-OOH] (mM^{-1})	1/v_0 (μM^{-1} ·min)

1.6	186.78 188.01 191.58	188.79 ±2.49	0.6250	0.0052968
1.4	184.73 180.91 176.32	180.65 ±4.21	0.7142	0.0055354
1.2	173.02 178.55 168.44	173.33 ±5.06	0.8333	0.0057691
1.0	167.93 168.99 169.01	168.64 ±0.61	1.0000	0.0059296
0.8	151.62 153.45 150.87	151.98 ±1.32	1.2500	0.0065798
0.4	103.14 98.50 100.83	100.82 ±2.32	2.5000	0.0099183

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL),Cum-OOH (variable) and **12k** (80 μM).

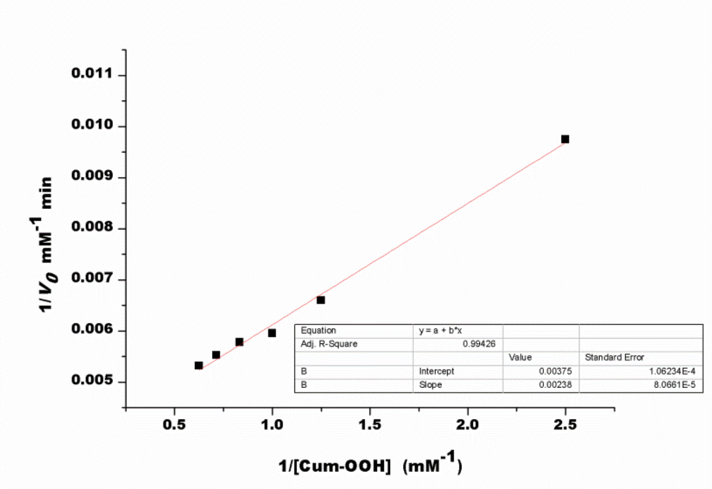


Figure S4. The Lineweaver-Burk (double-reciprocal) plots obtained for **12k** with the variation of Cum-OOH at the fixed concentration of GSH.

Intercept = 0.00375 ±0.000106

Slop = 0.00238 ±0.0000806

V_{max} = 266.67 ±3.51

K_{m} = 0.63 ±0.08

k_{cat} = 3.33 ±0.04

η = 5.28 ±0.06

Table S4. Summary for the effect of substrate (H_2O_2) concentration on the initial rate of **11f**

[H_2O_2] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[H_2O_2] (mM^{-1})	1/v_0 (μM^{-1} ·min)
1.6	253.08	251.09 ±4.79	0.6250	0.0039826

	254.57 245.63			
1.4	190.38 198.10 196.32	194.93 ±4.02	0.7142	0.0051300
1.2	169.24 168.46 169.01	168.90 ±0.40	0.8333	0.0059206
1.0	154.42 156.27 157.34	156.01 ±1.47	1.0000	0.0064098
0.8	127.85 120.66 128.65	125.72 ±4.40	1.2500	0.0079541
0.4	81.37 81.90 85.67	82.98 ±2.34	2.5000	0.0120511

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), H_2O_2 (variable) and **11f** (80 μM).

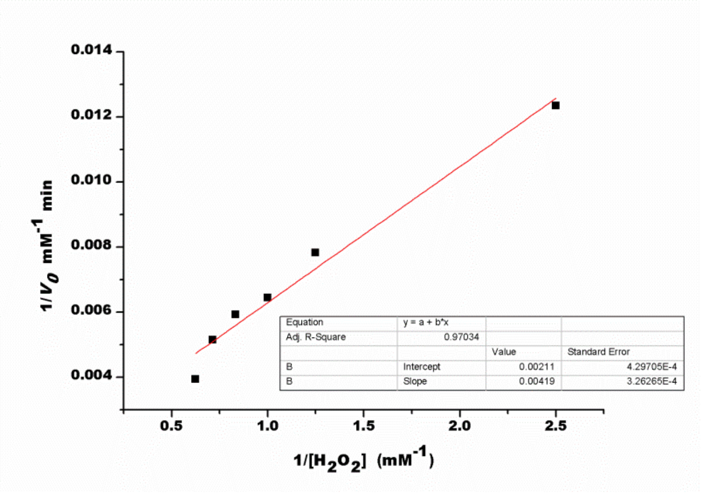


Figure S5. The Lineweaver-Burk (double-reciprocal) plots obtained for **11f** with the variation of H_2O_2 at the fixed concentration of GSH.

Intercept = 0.00211 ±0.000429

Slop = 0.00419 ±0.000326

$V_{\max}$ = 473.93 ±8.01

K_{m} = 1.98 ±0.15

k_{cat} = 5.92 ±0.10

η = 2.99 ±0.05

Table S5. Summary for the effect of substrate (*t*-BuOOH) concentration on the initial rate of **11f**

[*t*-BuOOH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[*t*-BuOOH] (mM^{-1})	1/v_0 (μM^{-1} min)
1.6	58.22	64.53 ±5.69	0.6250	0.0154966

	69.27 66.12			
1.4	56.82 55.34 53.22	55.12 ±1.81	0.7142	0.0181422
1.2	56.82 44.98 45.33	49.04 ±6.73	0.8333	0.02039151
1.0	30.78 47.26 38.98	39.00 ±8.24	1.0000	0.0256410
0.8	27.88 33.76 32.44	31.36 ±3.08	1.2500	0.0318877
0.4	13.94 12.97 13.88	13.59 ±0.54	2.5000	0.0735835

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), *t*-BuOOH (variable) and **11f** (80 µM).

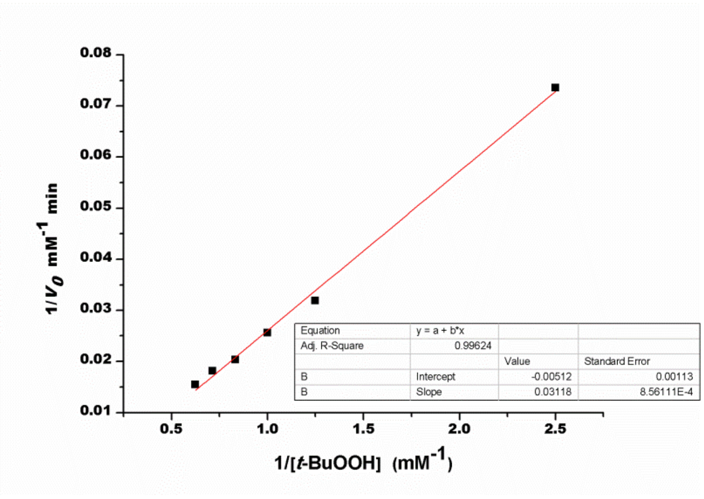


Figure S6. The Lineweaver-Burk (double-reciprocal) plots obtained for **11f** with the variation of *t*-BuOOH at the fixed concentration of GSH.

Intercept = –0.00512 ±0.00113

Slop = 0.03118 ±0.000856

$V_{\max}$ = 195.31 ±8.10

K_{m} = 6.08 ±0.25

k_{cat} = 2.44 ±0.10

η = 0.40 ±0.10

Table S6. Summary for the effect of substrate (Cum-OOH) concentration on the initial rate of **11f**

[Cum-OOH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[Cum-OOH] (mM^{-1})	1/v_0 (μM^{-1} ·min)
1.6	182.49	180.91 ±1.62	0.6250	0.0055276

	180.99 179.24			
1.4	150.04 148.99 156.44	151.82 ±4.03	0.7142	0.0066370
1.2	133.99 126.01 135.92	131.97 ±5.25	0.8333	0.0075774
1.0	122.68 129.61 118.73	123.67 ±5.50	1.0000	0.0080860
0.8	105.84 104.35 105.14	105.11 ±0.74	1.2500	0.0095138
0.4	55.51 57.96 59.36	57.61 ±1.95	2.5000	0.0173580

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL),Cum-OOH (variable) and **11f** (80 µM).

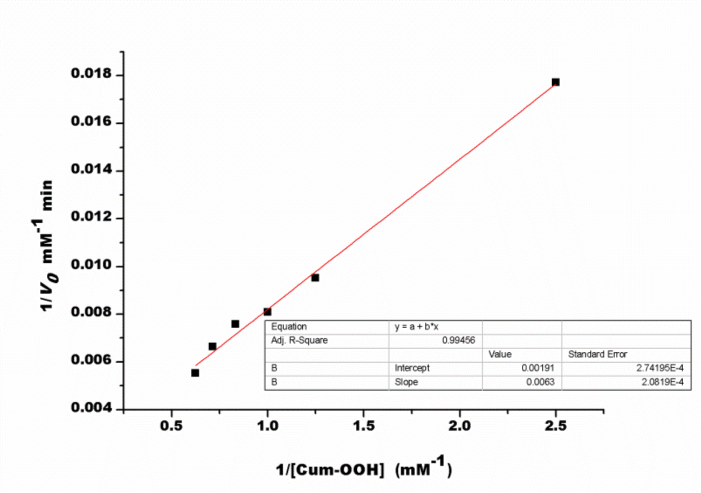


Figure S7. The Lineweaver-Burk (double-reciprocal) plots obtained for **11f** with the variation of Cum-OOH at the fixed concentration of GSH.

Intercept = 0.00191 ±0.000274

Slop = 0.0063 ±0.000208

$V_{\max}$ =523.56 ±10.21

K_m = 3.30 ±0.06

k_{cat} = 6.54 ±0.12

η = 1.98 ±0.03

Table S7. Summary for the effect of substrate (H_2O_2) concentration on the initial rate of **ebselen**

$[H_2O_2]$ (mM)	$v_0(\mu M\cdot min^{-1})$	Mean $v_0(\mu M\cdot min^{-1})$	$1/[H_2O_2]$ (mM^{-1})	$1/v_0$ ($\mu M^{-1}\cdot min$)
1.6	128.64	129.25 ±0.66	0.6250	0.0077369

	129.17 129.96			
1.4	128.38 124.70 132.85	128.64 ±4.08	0.7142	0.0077736
1.2	116.72 116.63 110.31	114.55 ±3.67	0.8333	0.0087298
1.0	109.70 113.03 111.42	111.38 ±1.66	1.0000	0.0089782
0.8	111.45 99.44 104.98	105.29 ±6.01	1.2500	0.0094975
0.4	65.24 61.12 63.04	63.13 ±2.06	2.5000	0.0158277

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), H_2O_2 (variable) and **ebselen** (80 µM).

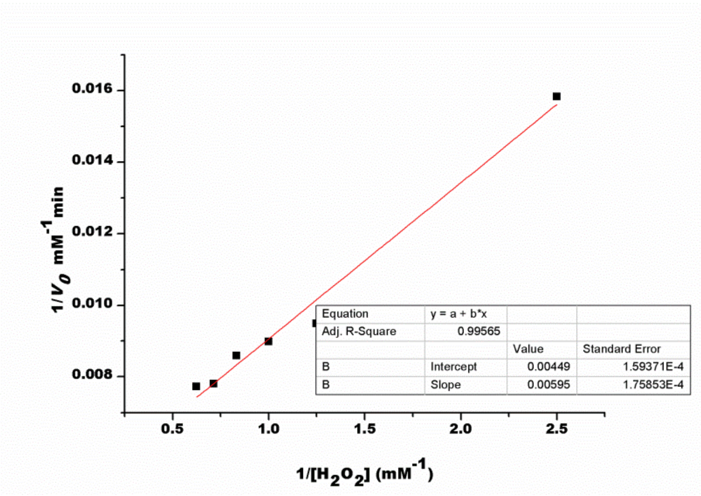


Figure S8. The Lineweaver-Burk (double-reciprocal) plots obtained for **ebselen** with the variation of H_2O_2 at the fixed concentration of GSH.

Intercept = 0.00449 ±0.0001593

Slop = 0.00595 ±0.000175

V_{max} = 222.71 ±3.46

K_m = 1.32 ±0.04

k_{cat} = 2.78 ±0.20

η = 2.10 ±0.1

Table S8. Summary for the effect of substrate (*t*-BuOOH) concentration on the initial rate of **ebselen**

[*t*-BuOOH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[*t*-BuOOH] (mM^{-1})	$1/v_0$ ($μM^{-1}$ ·min)
1.6	52.04	51.75 ±2.30	0.6250	0.0193236

	49.32 53.89			
1.4	49.02 39.81 37.70	42.17 ±6.01	0.7142	0.0237090
1.2	32.35 33.14 34.63	33.37 ±1.15	0.8333	0.0299640
1.0	27.44 30.69 25.99	28.04 ±2.40	1.0000	0.0356633
0.8	17.62 14.90 20.08	17.53 ±2.59	1.2500	0.05703422
0.4	6.84 9.03 8.93	8.26 ±1.23	2.5000	0.12096774

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), *t*-BuOOH (variable) and **ebselen** (80 μM).

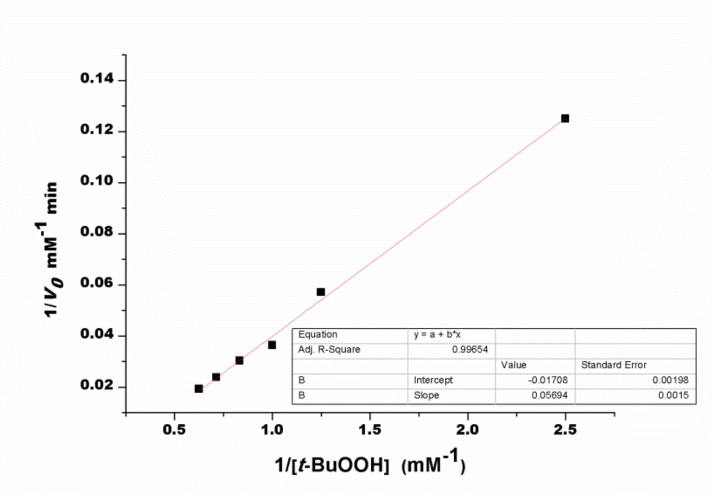


Figure S9. The Lineweaver-Burk (double-reciprocal) plots obtained for **ebselen** with the variation of *t*-BuOOH at the fixed concentration of GSH.

Intercept = –0.01708 ±0.00198

Slop = 0.05694 ±0.0015

V_{max} = 58.55 ±3.00

K_m = 3.33 ±0.17

k_{cat} = 0.73 ±0.03

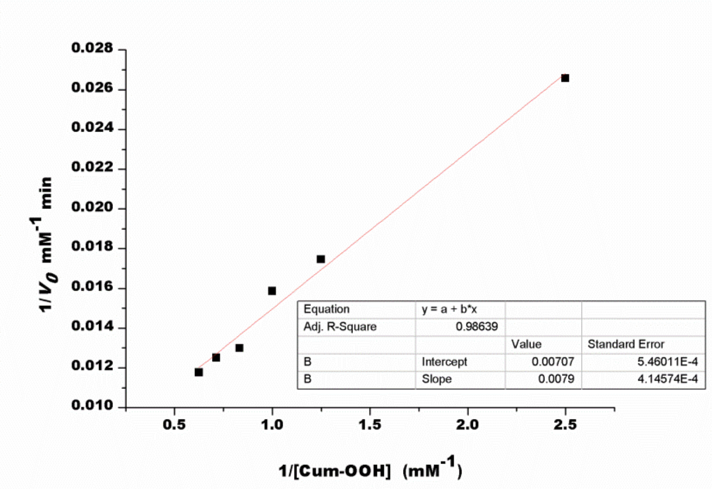
η = 0.22 ±0.01

Table S9. Summary for the effect of substrate (Cum-OOH) concentration on the initial rate of **ebselen**

[Cum-OOH] (mM)	$v_0(\mu M \cdot min^{-1})$	Mean $v_0(\mu M \cdot min^{-1})$	1/[Cum-OOH] (mM^{-1})	$1/v_0$ $(\mu M^{-1} \cdot min)$
1.6	87.60	86.41 ±1.33	0.6250	0.0115727

	84.97 86.66			
1.4	73.66 83.04 84.35	80.35 ±5.83	0.7142	0.0124455
1.2	77.69 77.97 79.62	78.42 ±1.04	0.8333	0.0127507
1.0	62.96 65.06 61.12	63.04 ±1.97	1.0000	0.0158612
0.8	59.45 56.12 56.29	57.28 ±1.87	1.2500	0.0174560
0.4	39.63 38.32 34.98	37.64 ±2.39	2.5000	0.0265651

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL),Cum-OOH (variable) and **ebselen** (80 μM).



Equation	y = a + b*x		
Adj. R-Square	0.98639		
		Value	Standard Error
B	Intercept	0.00707	5.46011E-4
B	Slope	0.0079	4.14574E-4

Figure S10. The Lineweaver-Burk (double-reciprocal) plots obtained for **ebselen** with the variation of Cum-OOH at the fixed concentration of GSH.

Intercept = 0.00707 ±0.000546

Slop = 0.0079 ±0.000414

V_{max} = 141.44 ±8.10

K_m = 1.11 ±0.06

k_{cat} = 1.77 ±0.10

η = 1.59 ±0.09

Table S10. Summary for the effect of substrate (GSH) concentration on the initial rate of **11f•HCl**.

[GSH] (mM)	$v_0(\mu M\cdot min^{-1})$	Mean $v_0(\mu M\cdot min^{-1})$	1/[GSH] (mM^{-1})	$1/v_0$ $(\mu M^{-1}\cdot min)$
0.2	70.68	72.98 ±2.28	5.0000	0.0137023

	75.24 73.02			
0.4	130.57 132.06 133.05	131.89 ±1.24	2.5000	0.0075818
0.5	150.65 154.32 149.54	151.50 ±2.50	2.0000	0.00660151
1	213.97 209.32 217.65	213.64 ±4.17	1.0000	0.00468062
1.5	215.98 210.22 220.89	215.69 ±5.34	0.6667	0.00463614
2	240.28 233.96 259.23	244.49 ±13.15	0.5000	0.00409014

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (variable), NADPH (0.4 mM), GR (1.3 unit/mL), H_2O_2 (1.6 mM) and **11f•HCl** (80 μM).

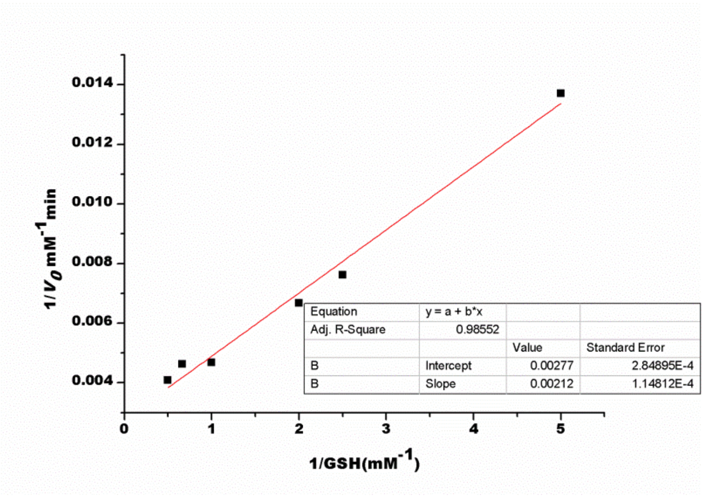


Figure S11. The Lineweaver-Burk (double-reciprocal) plots obtained for **11f•HCl** with the variation of GSH at the fixed concentration of H_2O_2.

Intercept = 0.00277 ±0.00028

Slop = 0.00212 ±0.00011

$V_{\max}$ = 361.01 ±7.21

K_m = 0.76 ±0.01

k_{cat} = 4.51 ±0.09

η = 5.90 ±0.12

Table S11. Summary for the effect of substrate (GSH) concentration on the initial rate of **11f•HCl**.

[GSH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[GSH] (mM^{-1})	1/v_0 (μM^{-1} ·min)

0.2	10.12 12.34 8.89	10.45 ±1.74	5.0000	0.09569378
0.4	15.87 17.65 14.20	15.90 ±1.72	2.5000	0.06286672
0.5	19.11 21.57 17.32	19.33 ±2.13	2.0000	0.05172413
1	23.32 24.81 22.45	23.53 ±4.06	1.0000	0.04250495
1.5	30.78 39.11 27.53	32.47 ±5.97	0.6667	0.03079449
2	37.18 30.95 34.46	34.19 ±3.12	0.5000	0.02924261

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (variable), NADPH (0.4 mM), GR (1.3 unit/mL), *t*-BuOOH (1.6 mM) and **11f•HCl** (80 µM).

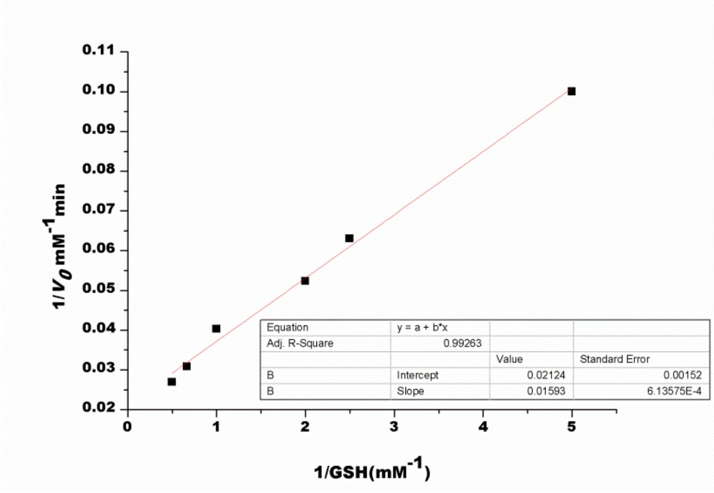


Figure S12. The Lineweaver-Burk (double-reciprocal) plots obtained for **11f•HCl** with the variation of GSH at the fixed concentration of *t*-BuOOH.

Intercept = 0.02124 ±0.00152

Slop = 0.01593 ±0.00061

V_{max} = 62.77 ±0.30

K_{m} = 0.75 ±0.01

k_{cat} = 0.78 ±0.01

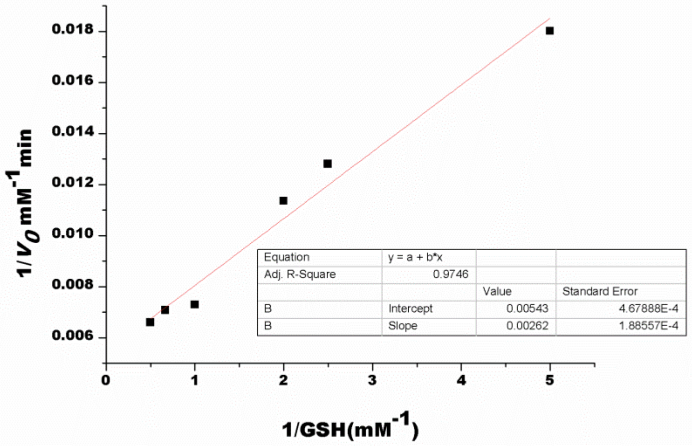
η = 1.05 ±0.01

Table S12. Summary for the effect of substrate (GSH) concentration on the initial rate of **11f•HCl**.

[GSH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[GSH] (mM^{-1})	1/v_0 (μM^{-1} ·min)

0.2	55.51 48.40 62.32	55.41 ±6.96	5.0000	0.0180472
0.4	78.03 80.21 76.02	78.08 ±2.09	2.5000	0.0128062
0.5	85.06 88.83 90.01	87.96 ±2.58	2.0000	0.0011367
1	135.74 128.73 147.06	137.17 ±9.24	1.0000	0.00728987
1.5	140.13 142.67 141.10	141.30 ±1.28	0.6667	0.00707714
2	153.46 151.44 149.95	151.61 ±1.76	0.5000	0.00659558

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (variable), NADPH (0.4 mM), GR (1.3 unit/mL), Cum-OOH (1.6 mM) and **11f•HCl** (80 µM).



Equation	y = a + b*x		
Adj. R-Square	0.9746		
		Value	Standard Error
B	Intercept	0.00543	4.67888E-4
B	Slope	0.00262	1.88557E-4

Figure S13. The Lineweaver-Burk (double-reciprocal) plots obtained for **11f•HCl** with the variation of GSH at the fixed concentration of Cum-OOH.

Intercept = 0.00543 ±0.00034

Slop = 0.00262 ±0.00014

V_{max} = 184.16 ±8.72

K_{m} = 0.48 ±0.01

k_{cat} = 2.30 ±0.02

η = 4.78 ±0.04

Table S13. Summary for the effect of substrate (GSH) concentration on the initial rate of **12k•HCl**.

[GSH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[GSH] (mM^{-1})	1/v_0 (μM^{-1} min)

0.2	112.07 112.94 113.01	112.67 ±0.52	5.0000	0.0088752
0.4	153.57 160.06 158.27	157.30 ±3.35	2.5000	0.00635729
0.5	180.82 176.17 178.67	178.55 ±2.32	2.0000	0.00560056
1	236.50 221.25 242.64	233.46 ±11.01	1.0000	0.00428332
1.5	234.34 232.65 236.07	234.35 ±5.34	0.6667	0.00426706
2	250.28 233.96 229.23	237.82 ±11.04	0.5000	0.00420480

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (variable), NADPH (0.4 mM), GR (1.3 unit/mL), H_2O_2 (1.6 mM) and **12k•HCl** (80 μM).

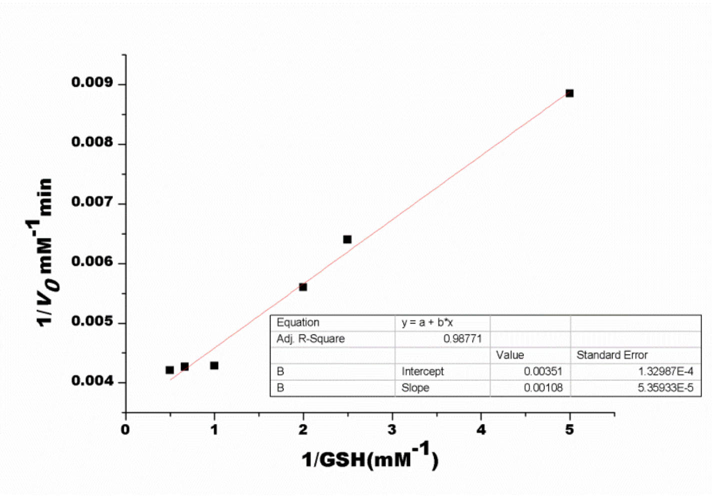


Figure S14. The Lineweaver-Burk (double-reciprocal) plots obtained for **12k•HCl** with the variation of GSH at the fixed concentration of H_2O_2.

Intercept = 0.00351 ±0.00013

Slop = 0.00108 ±0.00005

V_{max} = 284.90 ±7.12

K_{m} = 0.30 ±0.01

k_{cat} = 3.56 ±0.09

η = 11.87 ±0.30

Table S14. Summary for the effect of substrate (GSH) concentration on the initial rate of **12k•HCl**.

[GSH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[GSH] (mM^{-1})	1/v_0 (μM^{-1} ·min)
0.2	29.89	29.99 ±2.82	5.0000	0.03333703

	27.23 32.87			
0.4	43.20 42.12 43.61	42.97 ±0.76	2.5000	0.02326284
0.5	47.02 46.91 47.07	47.00 ±0.10	2.0000	0.02127659
1	55.12 59.54 51.43	55.36 ±4.06	1.0000	0.01806249
1.5	62.69 64.32 60.55	62.52 ±1.89	0.6667	0.01599488
2	68.82 66.66 67.34	67.60 ±1.10	0.5000	0.01479144

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (variable), NADPH (0.4 mM), GR (1.3 unit/mL), *t*-BuOOH (1.6 mM) and **12k•HCl** (80 μM).

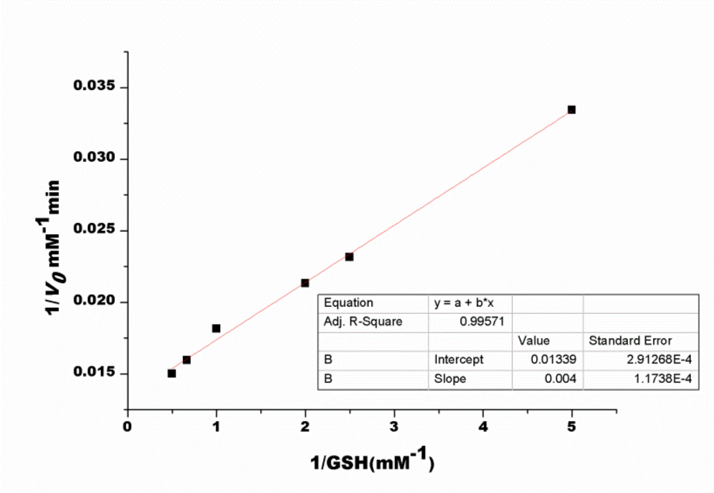


Figure S15. The Lineweaver-Burk (double-reciprocal) plots obtained for **12k•HCl** with the variation of GSH at the fixed concentration of *t*-BuOOH.

Intercept = 0.01339 ±0.00029

Slop = 0.004 ±0.00017

$V_{\max}$ = 74.68 ±0.60

K_m = 0.30 ±0.01

k_{cat} = 0.94 ±0.01

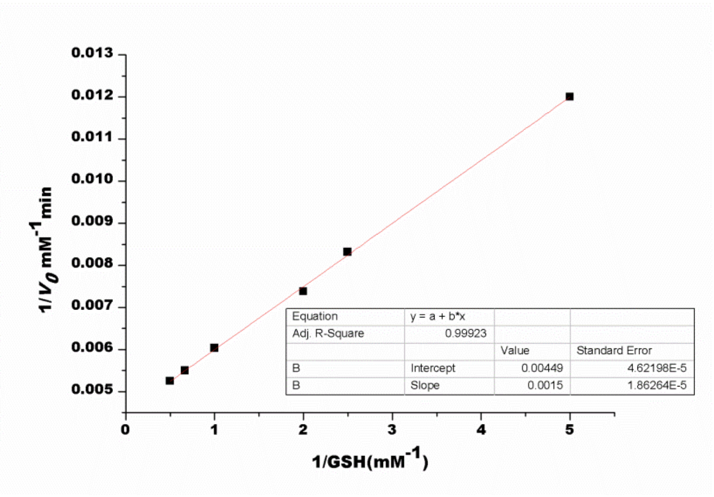
η = 3.13 ±0.30

Table S15. Summary for the effect of substrate (GSH) concentration on the initial rate of **12k•HCl**.

[GSH] (mM)	$v_0(\mu M \cdot min^{-1})$	Mean $v_0(\mu M \cdot min^{-1})$	1/[GSH] (mM^{-1})	$1/v_0$ ($\mu M^{-1} \cdot min$)
0.2	83.83	83.29 ±0.46	5.0000	0.01200528

	83.04 83.02			
0.4	120.75 128.03 112.05	120.27 ±8.00	2.5000	0.00831416
0.5	132.28 150.31 124.04	135.54 ±13.43	2.0000	0.00737771
1	167.18 169.87 160.57	165.87 ±4.78	1.0000	0.00602869
1.5	179.53 183.38 182.59	181.83 ±2.03	0.6667	0.00549954
2	191.35 187.67 192.49	190.50 ±2.51	0.5000	0.00524925

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (variable), NADPH (0.4 mM), GR (1.3 unit/mL), Cum-OOH (1.6 mM) and **12k•HCl** (80 μM).



Equation	y = a + b*x		
Adj. R-Square	0.99923		
		Value	Standard Error
B	Intercept	0.00449	4.62198E-5
B	Slope	0.0015	1.86264E-5

Figure S16. The Lineweaver-Burk (double-reciprocal) plots obtained for **12k•HCl** with the variation of GSH at the fixed concentration of Cum-OOH.

Intercept = 0.00449 ±0.000046

Slop = 0.00150 ±0.000018

$V_{\max}$ = 222.71 ±1.79

K_{m} = 0.33 ±0.01

k_{cat} = 2.78 ±0.01

η = 8.42 ±0.03

Table S16. Summary for the effect of substrate (GSH) concentration on the initial rate of **ebselen**.

[GSH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[GSH] (mM^{-1})	1/v_0 (μM^{-1} min)

1.0	94.67 92.51 92.21	93.13 ±1.34	1.0000	0.01073767
1.5	107.33 105.49 111.72	108.18 ±3.20	0.6667	0.00924385
2.0	120.40 117.33 123.43	120.38 ±3.05	0.5000	0.00830656
3.0	138.73 138.82 132.57	136.70 ±3.58	0.3333	0.00731493
4.0	150.56 153.21 147.32	150.36 ±2.94	0.2500	0.00665055
5.0	160.21 162.32 158.46	160.33 ±1.93	0.2000	0.00623713

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (variable), NADPH (0.4 mM), GR (1.3 unit/mL), H_2O_2 (1.6 mM) and **ebselen** (80 μM).

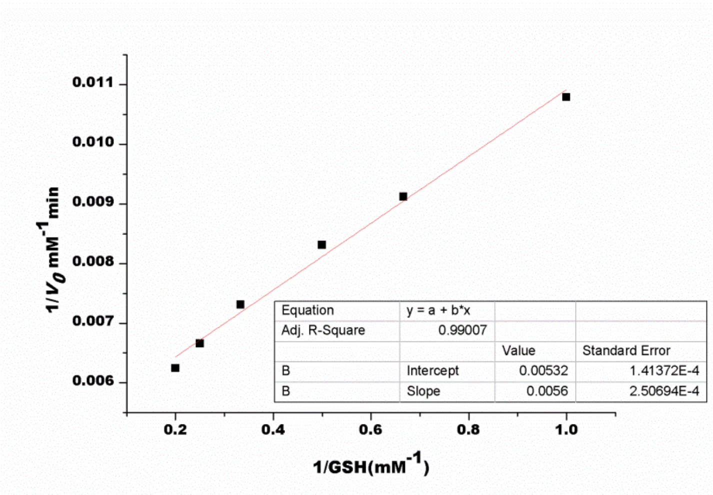


Figure S17. The Lineweaver-Burk (double-reciprocal) plots obtained for **ebselen** with the variation of GSH at the fixed concentration of H_2O_2.

Intercept = 0.00532 ±0.00014

Slop = 0.0056 ±0.00025

$V_{\max}$ = 187.96 ±2.77

K_m = 1.05 ±0.01

k_{cat} = 2.35 ±0.03

η = 2.23 ±0.02

Table S17. Summary for the effect of substrate (GSH) concentration on the initial rate of **ebselen**.

[GSH]	v_0(μM·min^{-1})	Mean	1/[GSH]	1/v_0

(mM)		v_0(μM·min^{-1})	(mM^{-1})	(μM^{-1} ·min)
0.2	6.40 11.66 7.27	8.44 ±2.81	5.0000	0.11843663
0.5	13.41 17.62 15.50	15.51 ±2.10	2.0000	0.06447453
1	21.30 14.11 30.95	22.12 ±8.44	1.0000	0.04520795
1.5	27.88 28.50 28.20	28.19 ±0.31	0.6667	0.03546937
2	33.41 32.34 34.52	33.42 ±1.10	0.5000	0.02991921
3	34.32 35.23 33.56	34.37 ±1.10	0.3333	0.02909514

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (variable), NADPH (0.4 mM), GR (1.3 unit/mL), *t*-BuOOH (1.6 mM) and **ebselen** (80 μM).

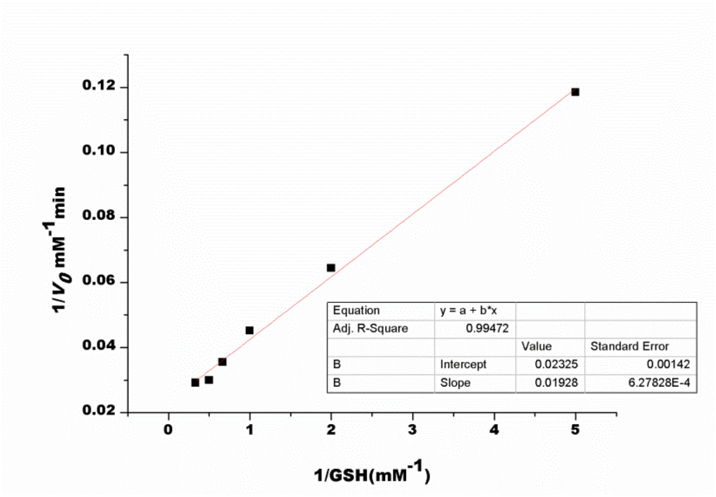


Figure S18. The Lineweaver-Burk (double-reciprocal) plots obtained for **ebselen** with the variation of GSH at the fixed concentration of *t*-BuOOH.

Intercept = 0.02325 ±0.00142

Slop = 0.01928 ±0.00062

$V_{\max}$ = 43.01 ±0.60

K_{m} = 0.83 ±0.01

k_{cat} = 0.54 ±0.07

η = 0.65 ±0.08

Table S18. Summary for the effect of substrate (GSH) concentration on the initial rate of **ebselen**.

[GSH] (mM)	v_0(μM·min^{-1})	Mean v_0(μM·min^{-1})	1/[GSH] (mM^{-1})	1/v_0 (μM^{-1}·min)

0.2	8.41 13.15 13.24	11.60 ±2.76	5.0000	0.08620689
0.5	19.99 20.87 19.46	20.10 ±0.71	2.0000	0.04973474
1	32.53 32.62 32.79	32.64 ±0.13	1.0000	0.03063099
1.5	46.38 48.93 47.96	47.75 ±1.28	0.6667	0.02093948
2	51.73 47.88 51.82	50.47 ±2.24	0.5000	0.01981112
3	58.31 58.75 58.49	58.51 ±0.22	0.3333	0.01708914

Assay conditions: phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (variable), NADPH (0.4 mM), GR (1.3 unit/mL), Cum-OOH (1.6 mM) and **ebselen** (80 μM).

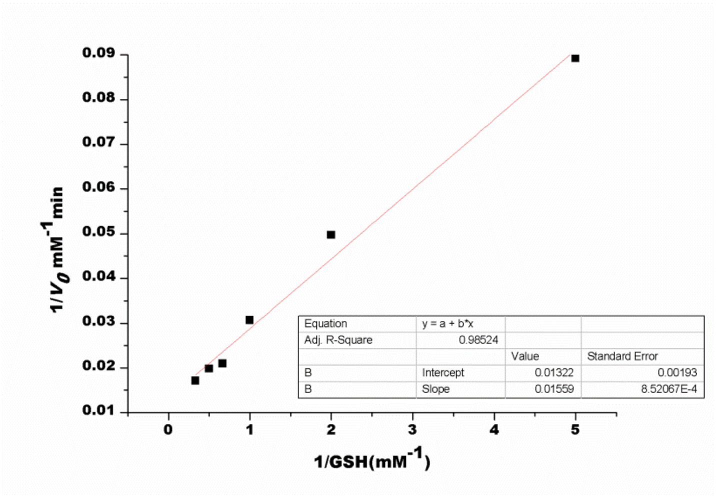


Figure S19. The Lineweaver-Burk (double-reciprocal) plots obtained for **ebselen** with the variation of GSH at the fixed concentration of Cum-OOH.

Intercept = 0.01322 ±0.00193

Slop = 0.01559 ±0.00085

V_{max} = 75.64 ±4.21

K_{m} = 1.18 ±0.06

k_{cat} = 0.95 ±0.05

η = 0.80 ±0.04

5. Scavenging peroxide by GSH in the Presence of Compound

Scavenging H_2O_2

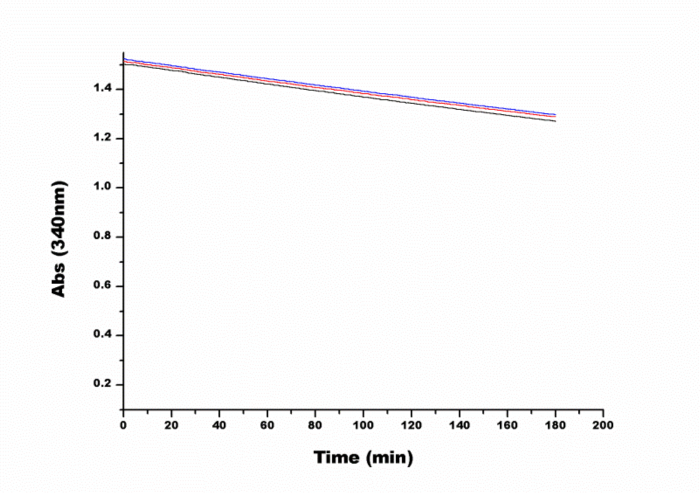


Figure S20. (**Control**) Rate of consumption for H_2O_2 in the absence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and H_2O_2(0.20 mM).

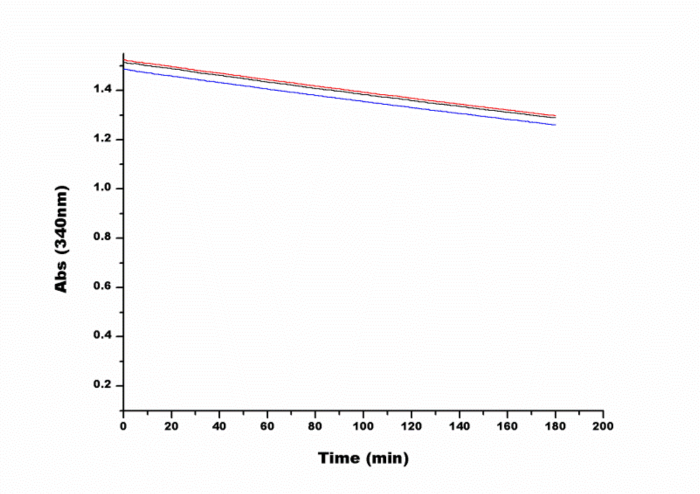


Figure S21. (**CQ**) Rate of consumption for H_2O_2 in the absence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and H_2O_2(0.20 mM).

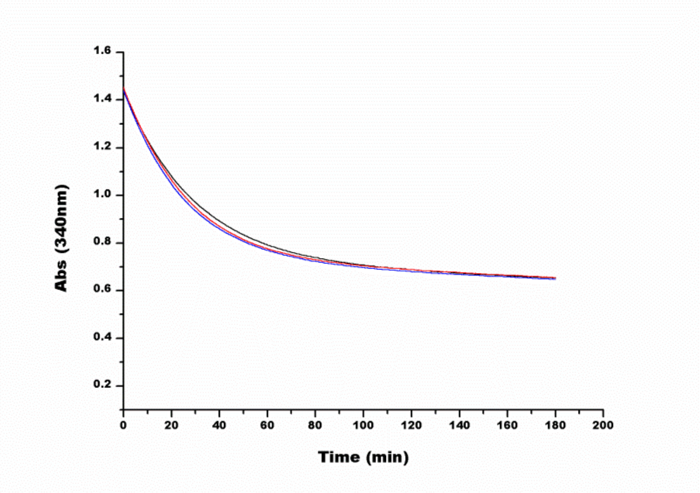


Figure S22. (**ebselen**) Rate of consumption for H_2O_2 in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and H_2O_2(0.20 mM).

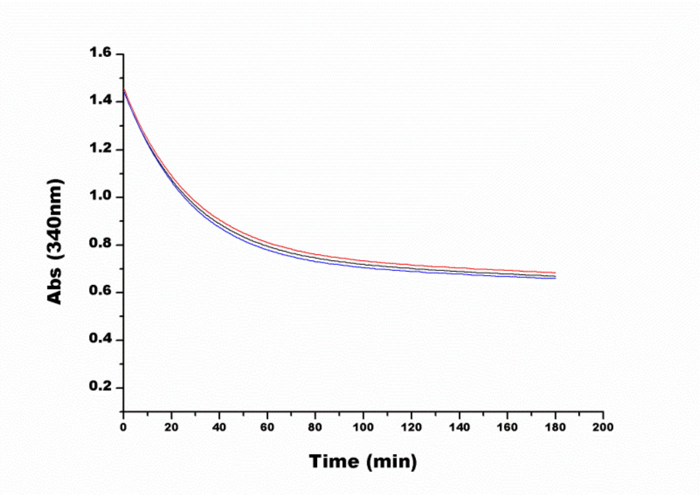


Figure S23. (**11f•HCl**) Rate of consumption for H_2O_2 in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and H_2O_2(0.20 mM).

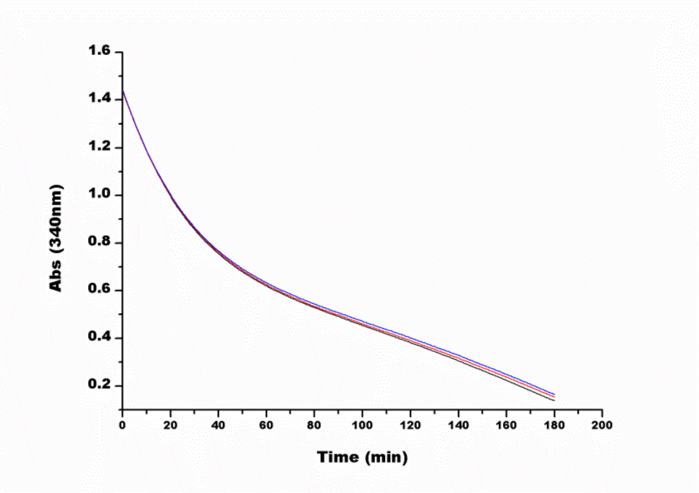


Figure S24. (**12k•HCl**) Rate of consumption for H_2O_2 in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and H_2O_2(0.20 mM).

Scavenging *t*-BuOOH

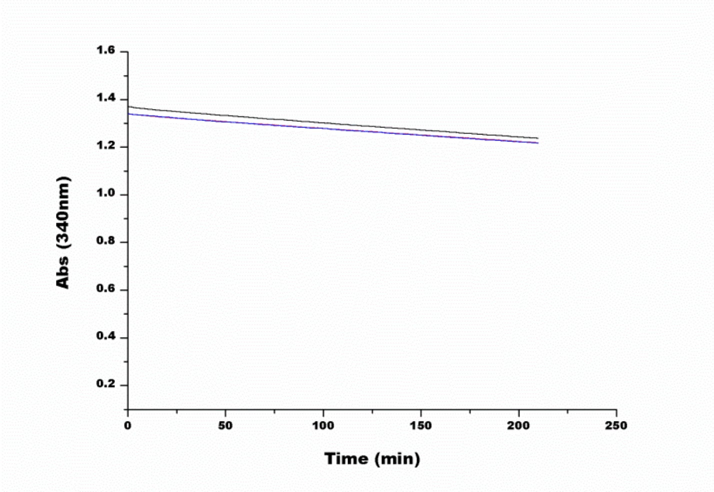


Figure S25. (**Control**) Rate of consumption for *t*-BuOOH in the absence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and *t*-BuOOH (0.20 mM).

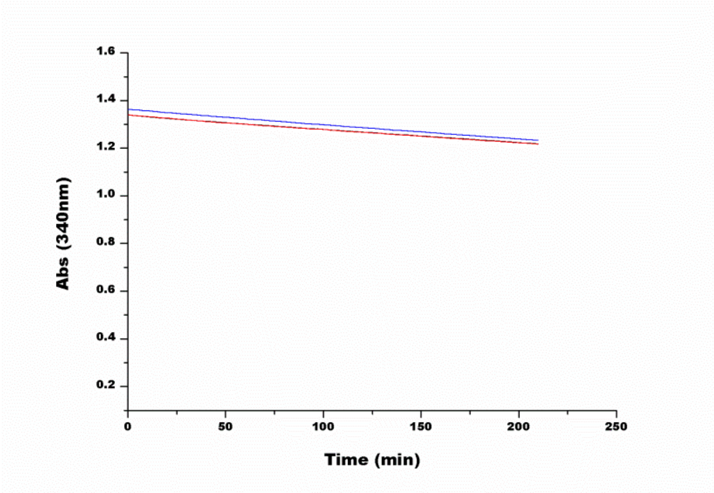


Figure S26. (**CQ**) Rate of consumption for *t*-BuOOH in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and *t*-BuOOH (0.20 mM).

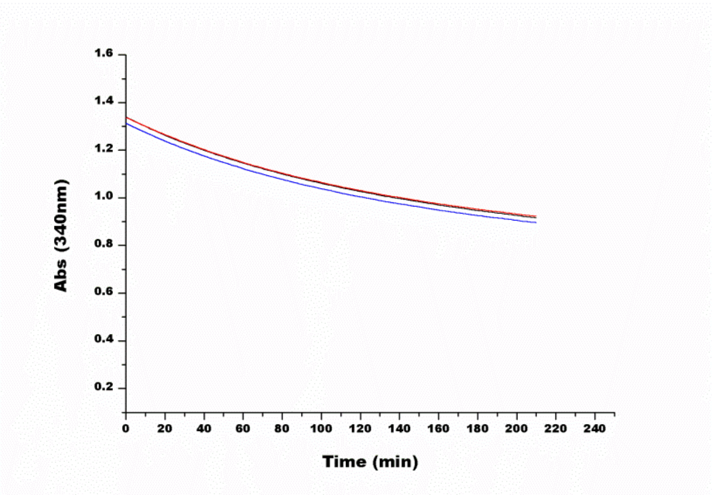


Figure S27. (**ebselen**) Rate of consumption for *t*-BuOOH in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and *t*-BuOOH (0.20 mM).

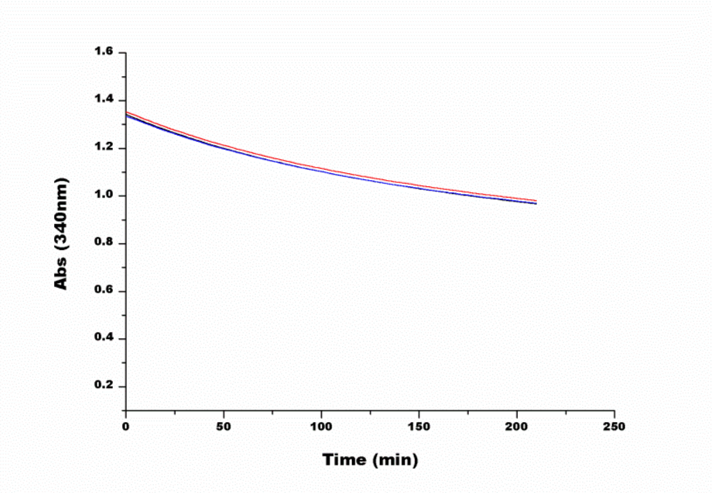


Figure S28. (**11f•HCl**) Rate of consumption for *t*-BuOOH in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and *t*-BuOOH (0.20 mM).

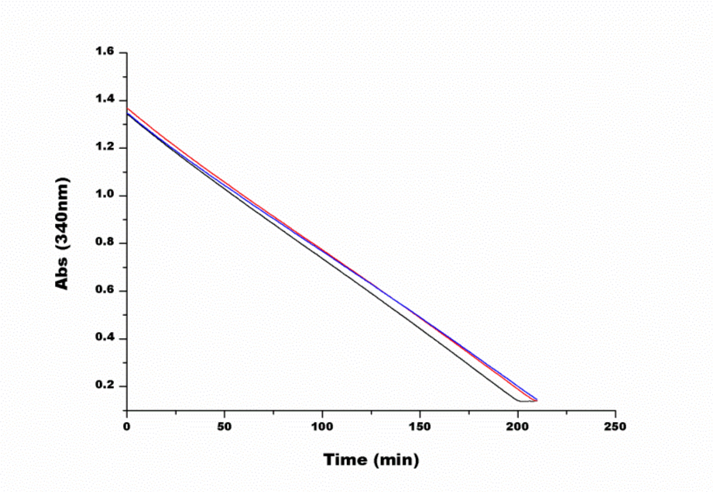


Figure S29. (**12k•HCl**) Rate of consumption for *t*-BuOOH in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and *t*-BuOOH (0.20 mM).

Scavenging Cum-OOH

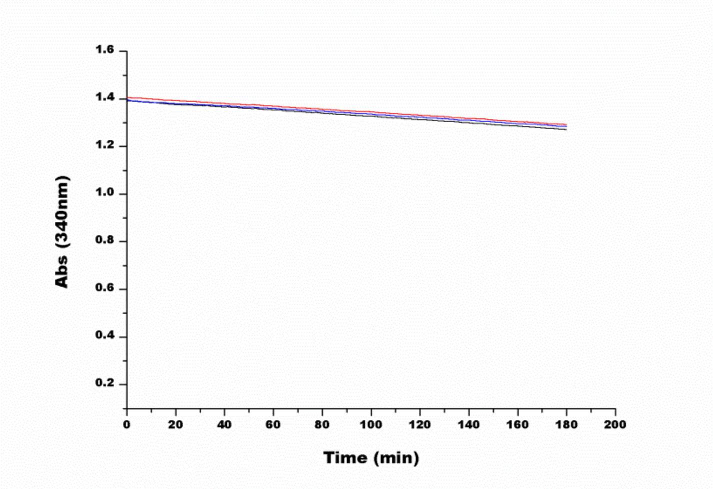


Figure S30. (**Control**) Rate of consumption for Cum-OOH in the absence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and Cum-OOH

(0.20 mM).

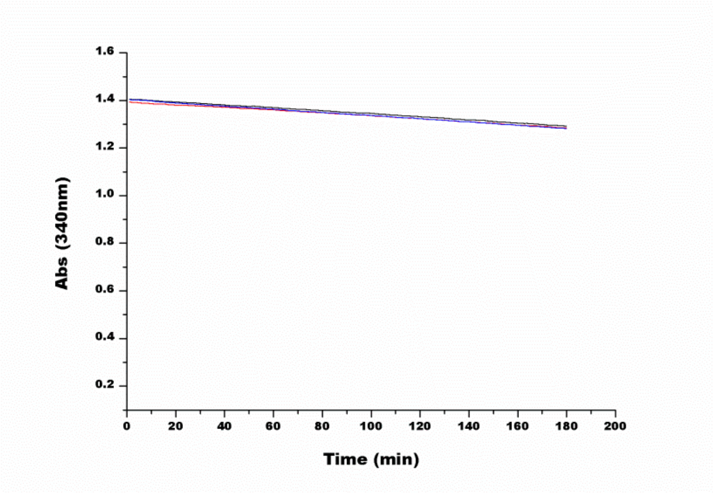


Figure S31. (**CQ**) Rate of consumption for Cum-OOH in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and Cum-OOH (0.20 mM).

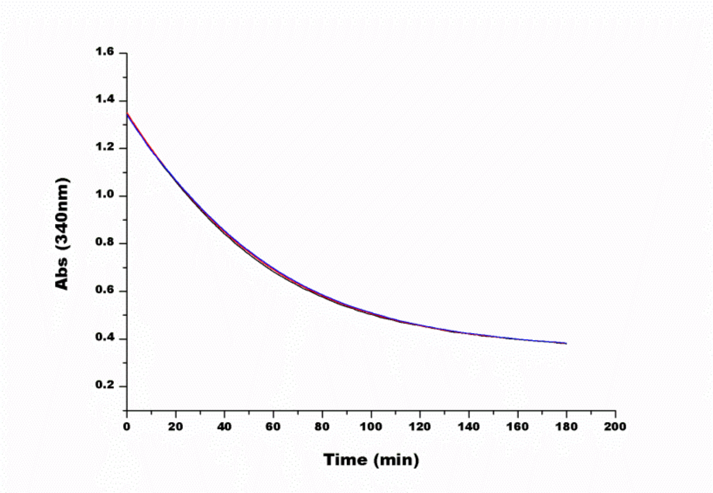


Figure S32. (**Ebselen**) Rate of consumption for Cum-OOH in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and Cum-OOH

(0.20 mM).

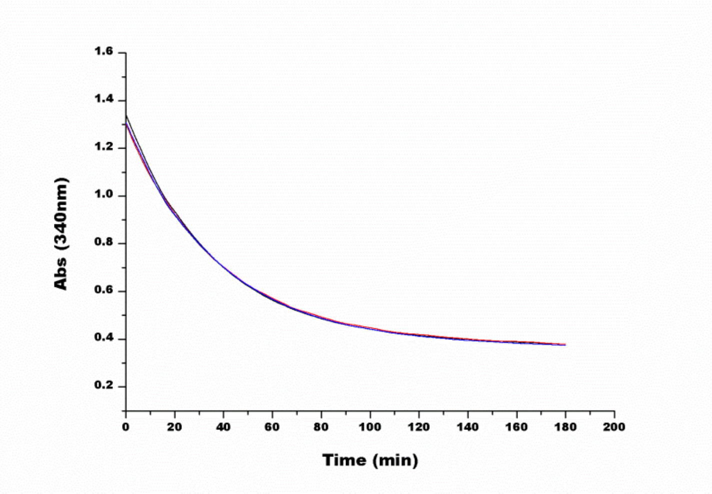


Figure S33. (**11f•HCl**) Rate of consumption for Cum-OOH in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and Cum-OOH (0.20 mM).

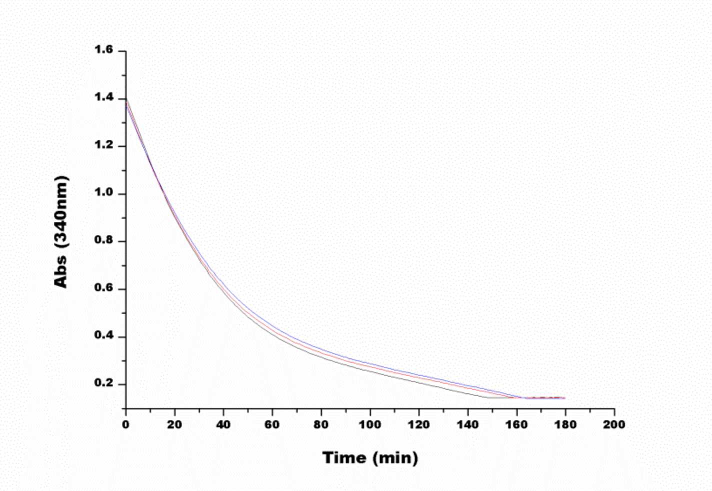


Figure S34. (**12k•HCl**) Rate of consumption for Cum-OOH in the presence of catalyst with time. Assay conditions: reactions were carried out with phosphate buffer (100 mM), pH 7.5, with EDTA (1 mM), GSH (0.25 mM), NADPH (0.50 mM), glutathione reductase(1.3 unit/ml), and Cum-OOH

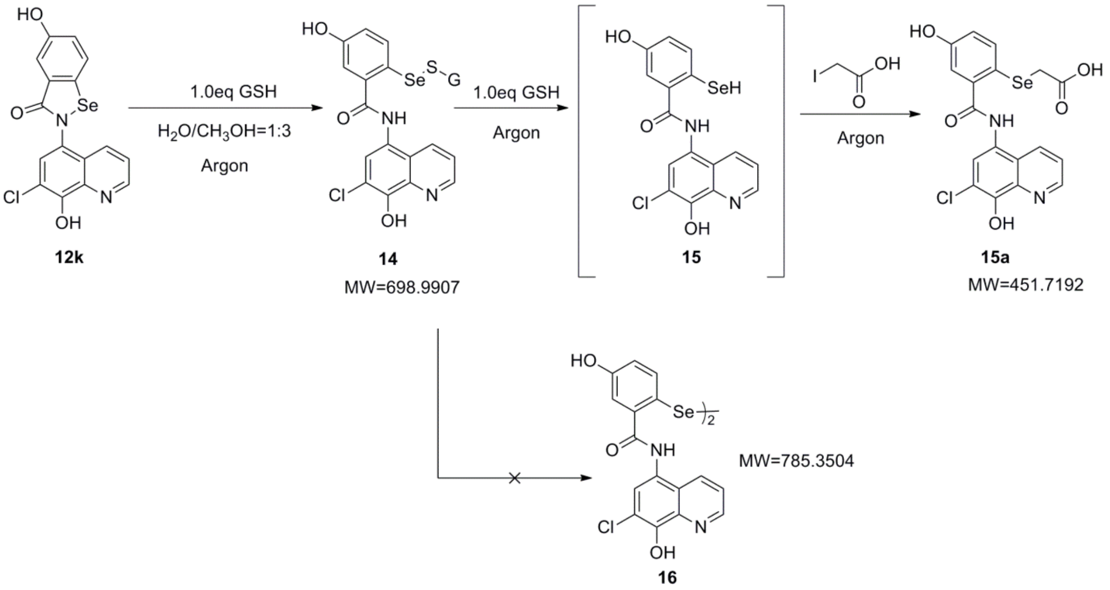
(0.20 mM).

6. Mechanism of the GPx-like catalytic cycle

The ^{77}Se NMR spectra were recorder using Me_2Se as external standards on a Bruker AvanceIII spectrometer at 76 MHz. The high-resolution mass spectra (HRMS) were obtained using a Shimadzu LCMS-IT-TOF mass spectrometer.

Isolation of Selenol

Hybrid compound (5 mg) in a three-necked round-bottomed flask (4 mL CH_3OH/H_2O (3:1) kept under argon atmosphere was treated with 1 equivalent of GSH. The reaction mixture was stirred for 20 minutes. After the hybrid compound completely converted to the selenenyl sulfides, another equivalent of GSH and 1 equivalent of iodoacetic acid was added, the reaction mixture was further stirred for 24 h. The reaction was analyzed by the HRMS. The results showed only selenenyl sulfides and selenol (trapped by generating selenide with iodoacetic acid) preduced in the cycle. It indicates that the production diselenide intermediated is not facile using GSH as a substrate.



Scheme S1. Trapped selenol by generating selenide **15a** with iodoacetic acid in argon atmosphere.

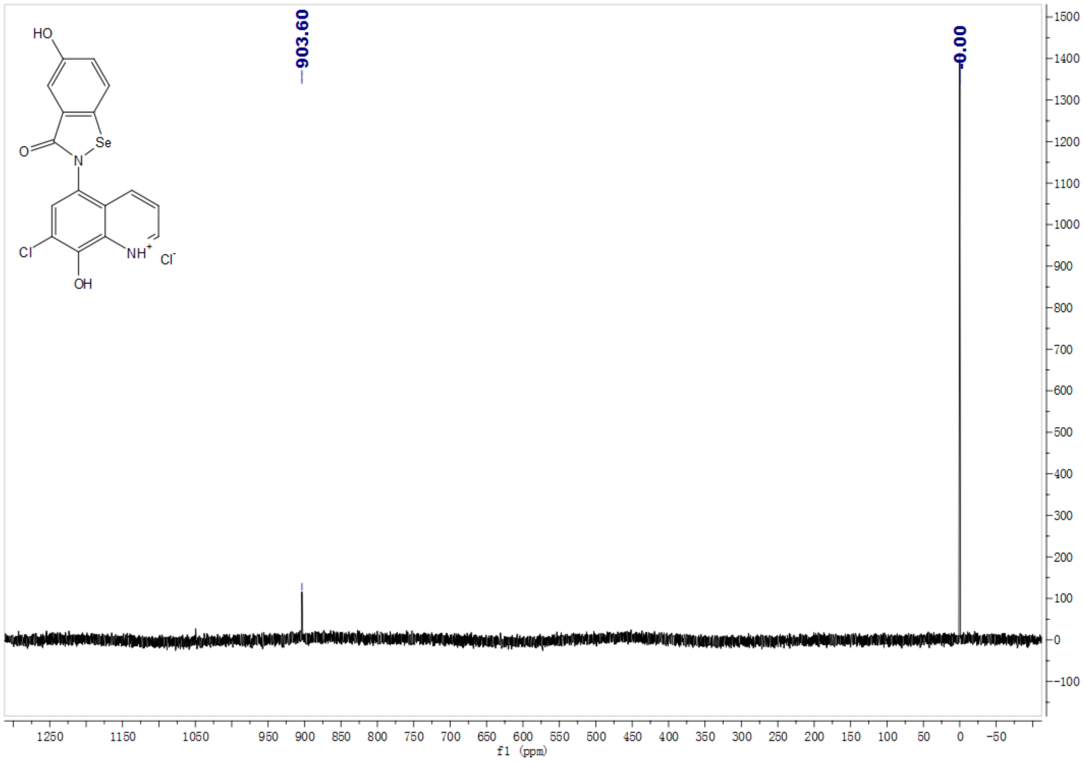


Figure S35. ^{77}Se NMR spectra of **12k** in DMSO-d_6

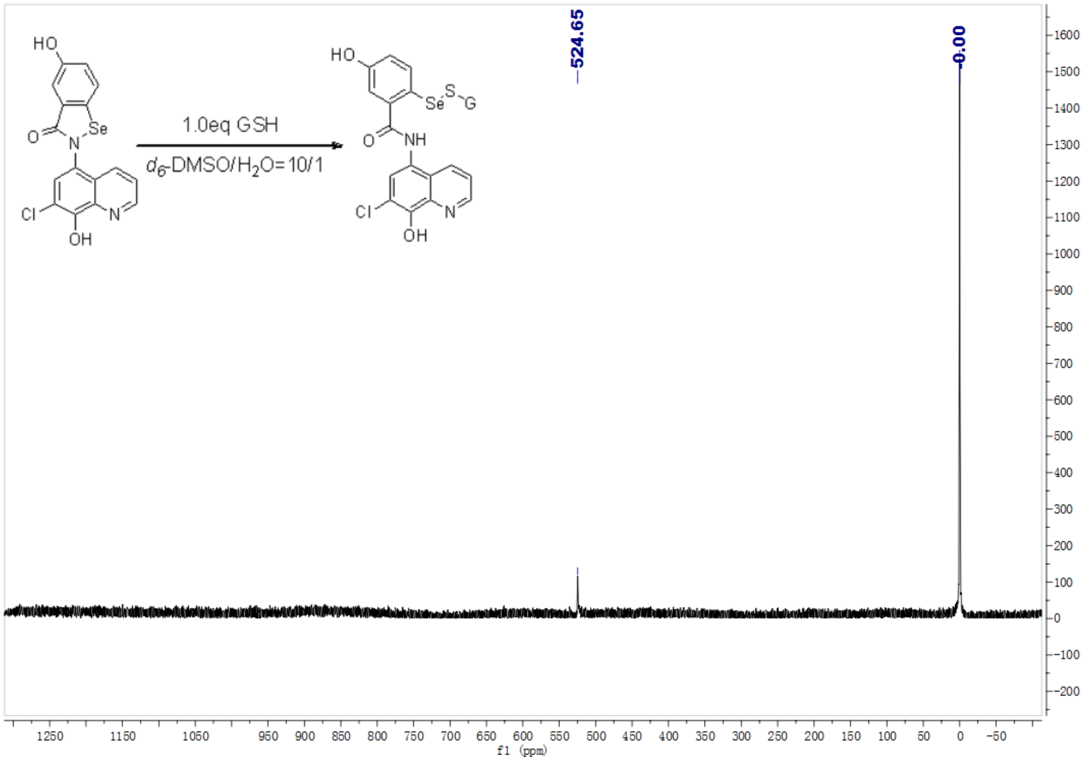


Figure S36. ^{77}Se NMR spectra of selenenyl sulfides **14** obtained from the the reaction of **12k** with GSH (1.0 equiv).

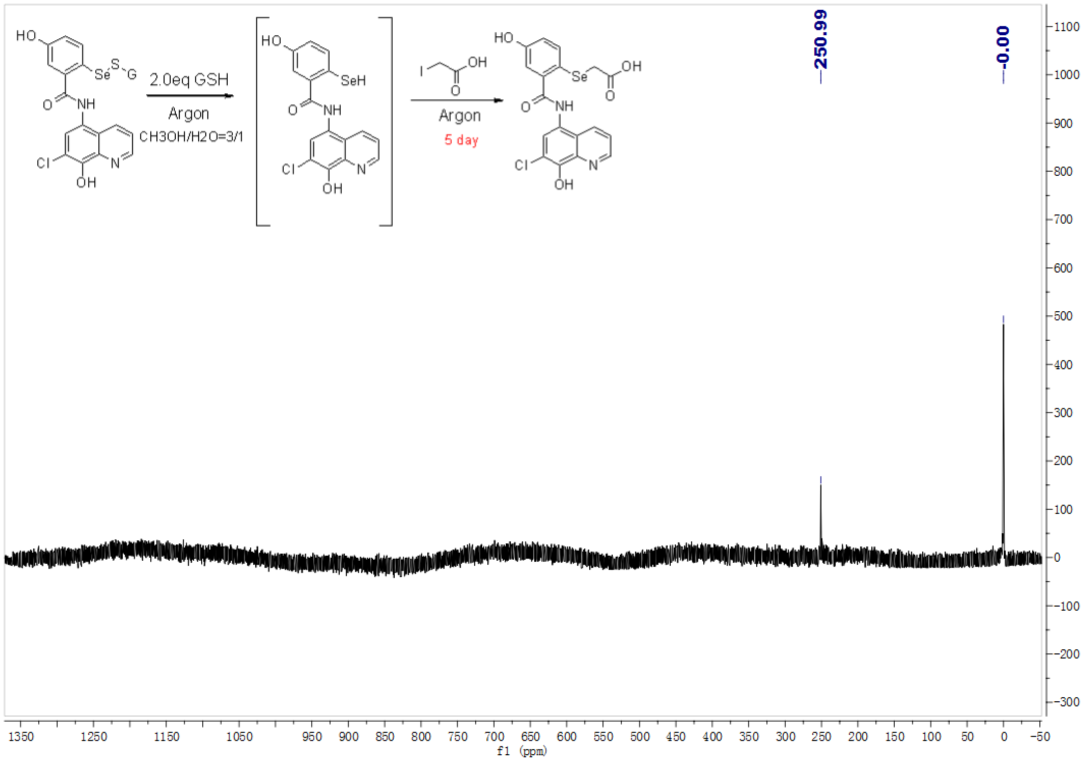


Figure S37. ^{77}Se NMR spectra of selenide **15a** (in DMSO-d_6) obtained from the the reaction of selenenyl sulfides **14** with GSH (2.0 equiv) and iodoacetic acid (1.0 equiv) under argon atmosphere for 5 days.

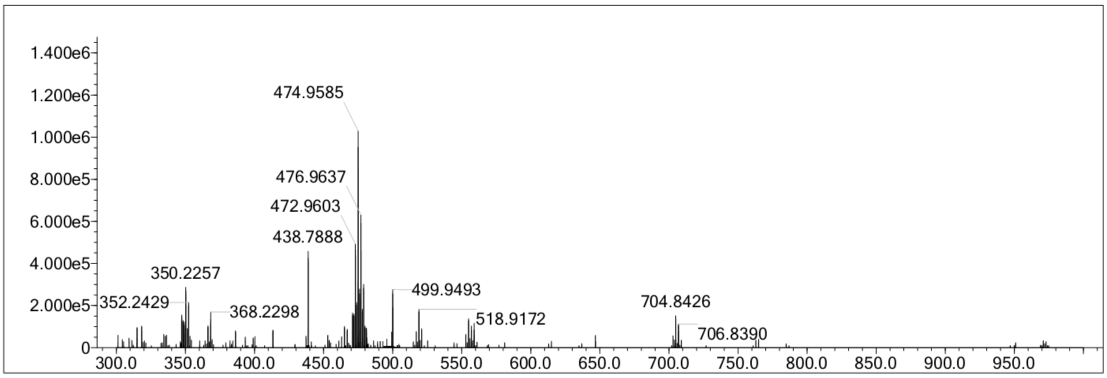


Figure S38. HRMS spectra of **15a** obtained from the the reaction of selenenyl sulfides **14** with GSH (2.0 equiv) and iodoacetic acid (1.0 equiv) under argon atmosphere for 12 h.

[M+Na]$^+$ for **15a** $C_{18}H_{13}N_2O_5ClSe$ pred. 474.9585, meas. 474.9569

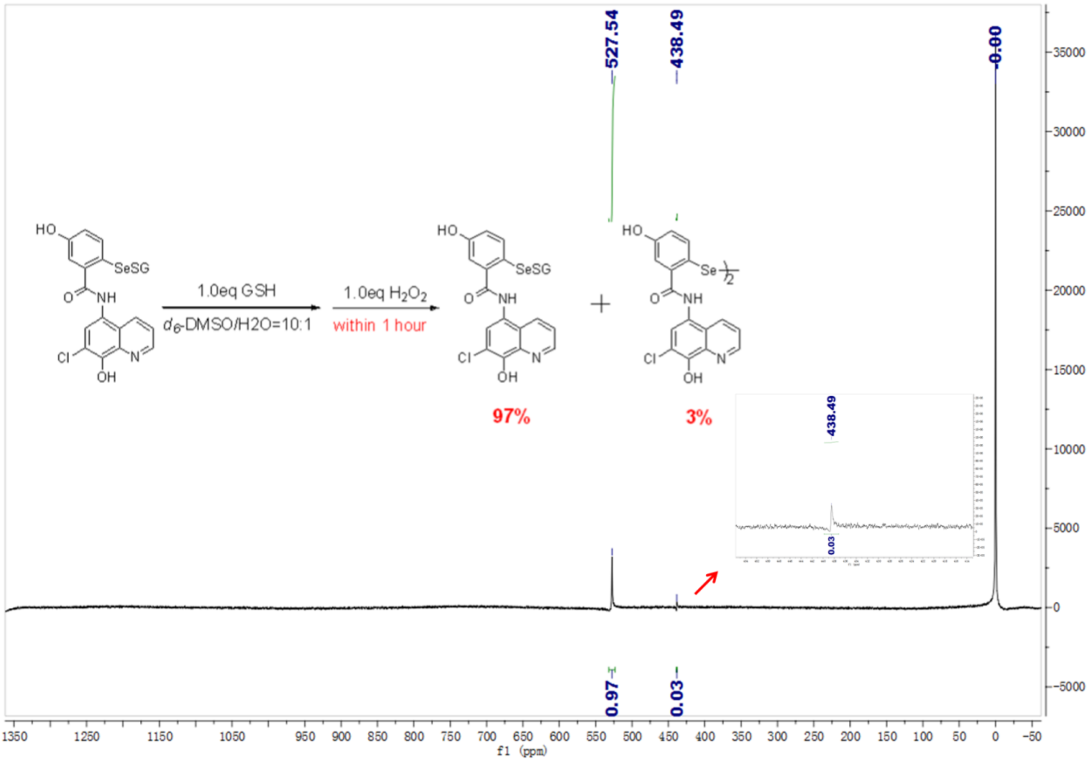


Figure S39. ^{77}Se NMR spectra of selenenyl sulfides **14** (δ 527 ppm) and diselenide **16** (δ 438 ppm) obtained from the the reaction of selenenyl sulfides **14** and GSH (1.0 equiv) with H_2O_2 (1.0 equiv) in DMSO-d_6/H_2O = 10/1 mixture within 1 hour.

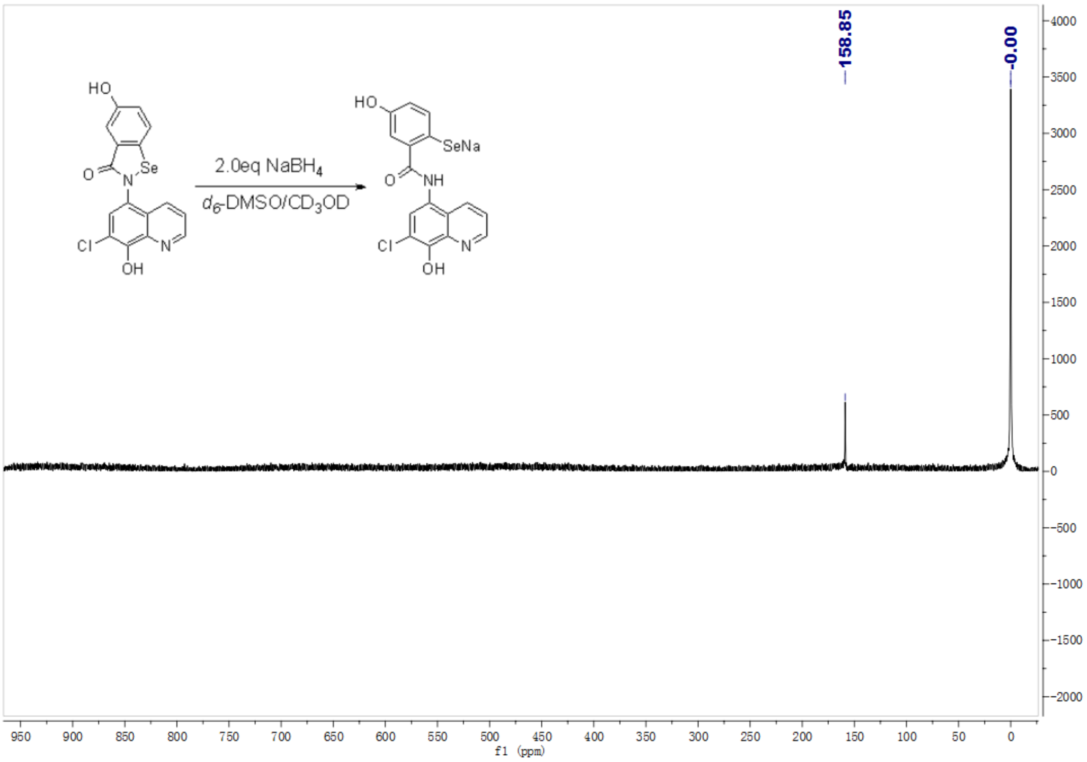


Figure S40. ^{77}Se-NMR spectra of sodium selenolate obtained from the reduction of **12k** with NaBH4 in DMSO-d_6/CD$_3$OD = 10/1 mixture

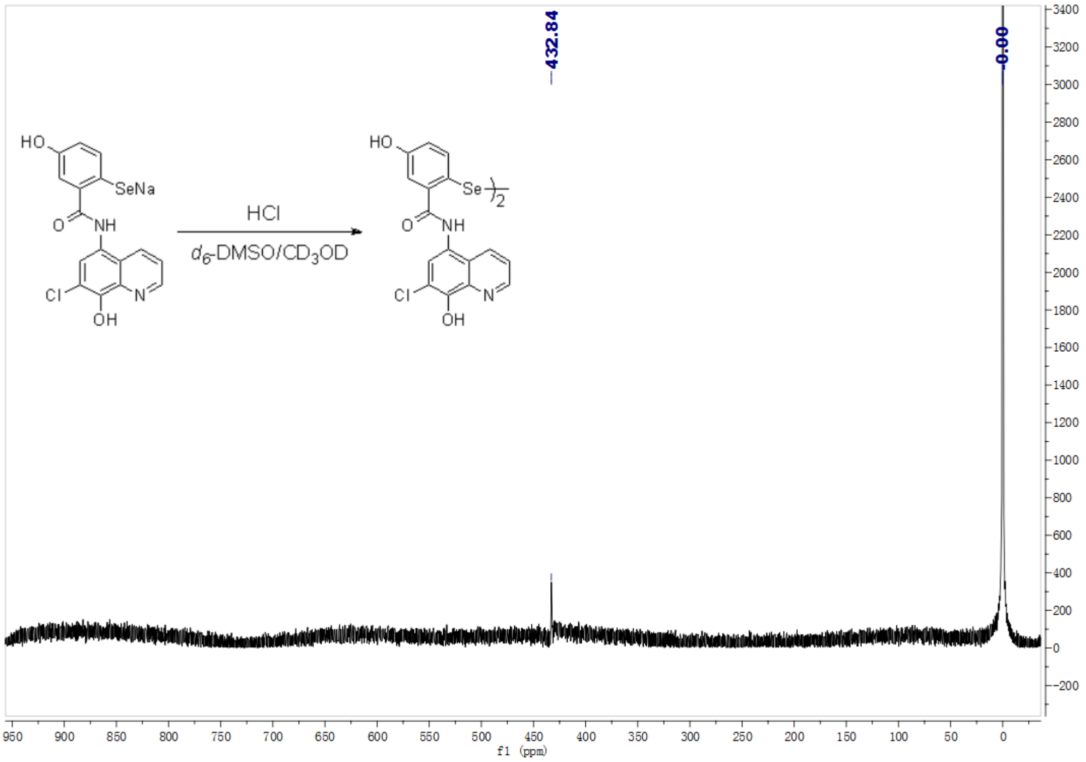


Figure S41. ^{77}Se-NMR spectra of diselenide **16** obtained from the acidification of the sodium selenolate with HCl solution (10%) in DMSO-d_6/CD$_3$OD = 10/1 mixture under air atmosphere.

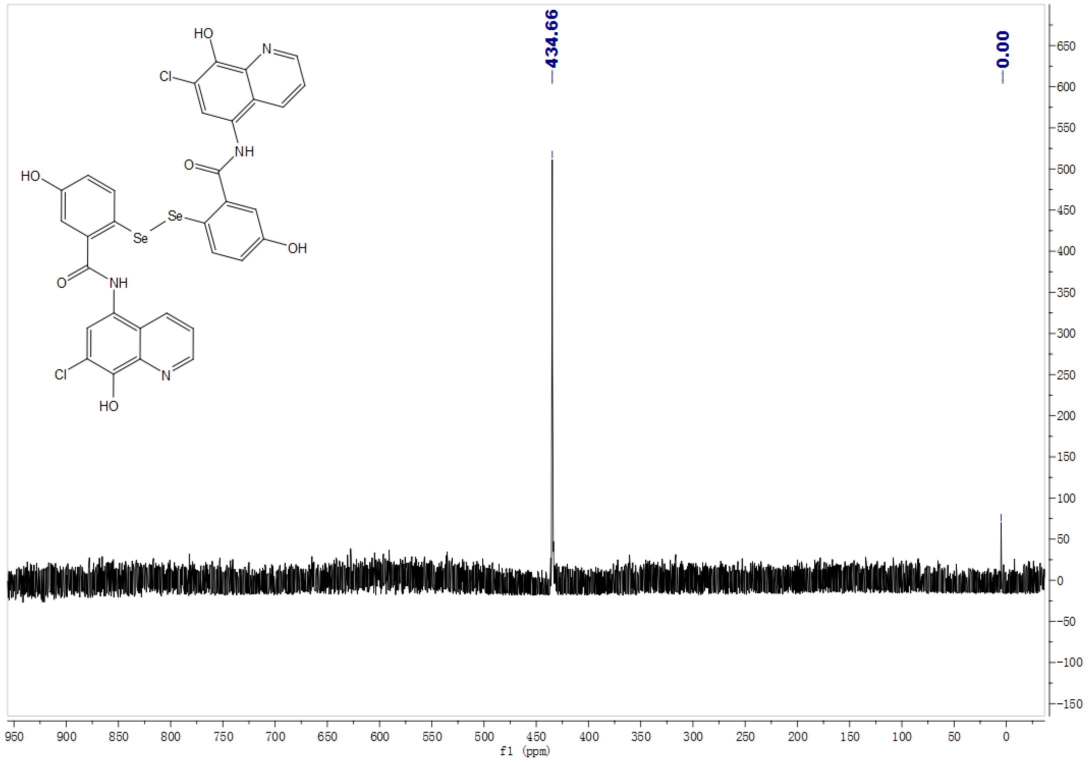


Figure S42. ^{77}Se-NMR spectra of pure diselenide **16** (in DMSO-d_6) obtained from the acidification of the sodium selenolate with HCl solution (10%) in CH$_3$OH mixture under air atmosphere.

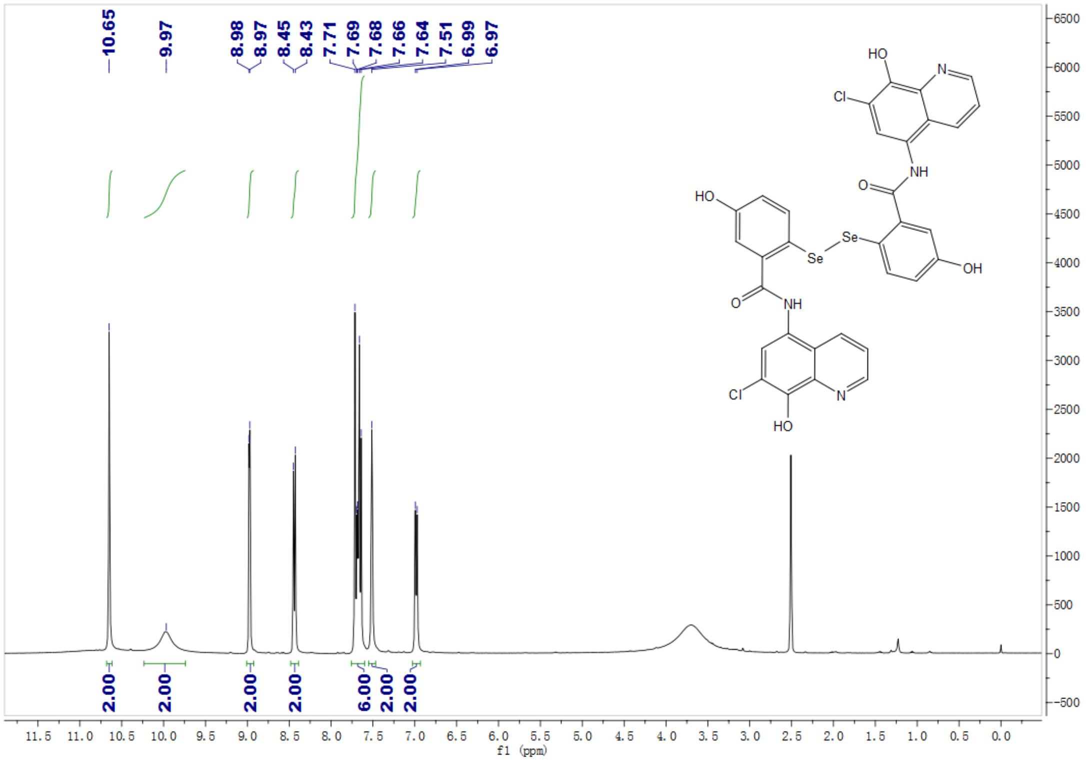


Figure S43. ^{1}H-NMR spectra of pure diselenide **16** (in DMSO-d_6) obtained from the acidification of the sodium selenolate with HCl solution (10%) in CH_3OH mixture under air atmosphere.

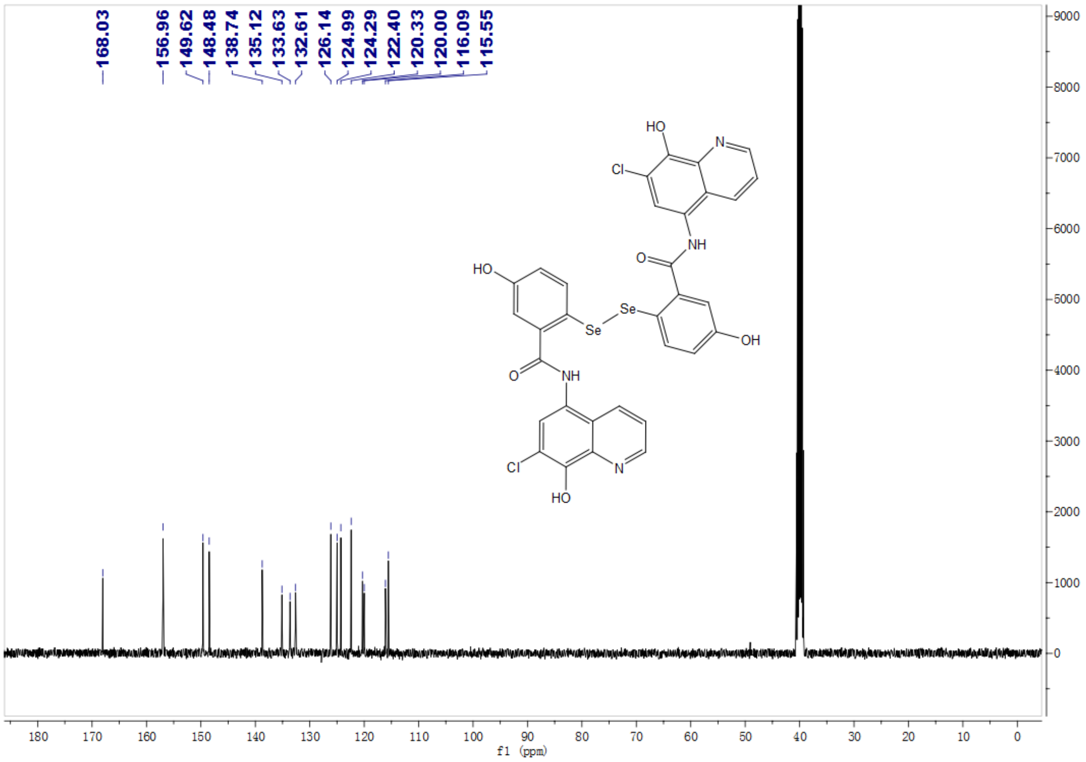


Figure S44. ^{13}C-NMR spectra of pure diselenide **16** (in DMSO-d_6) obtained from the acidification of the sodium selenolate with HCl solution (10%) in CH_3OH mixture under air atmosphere.

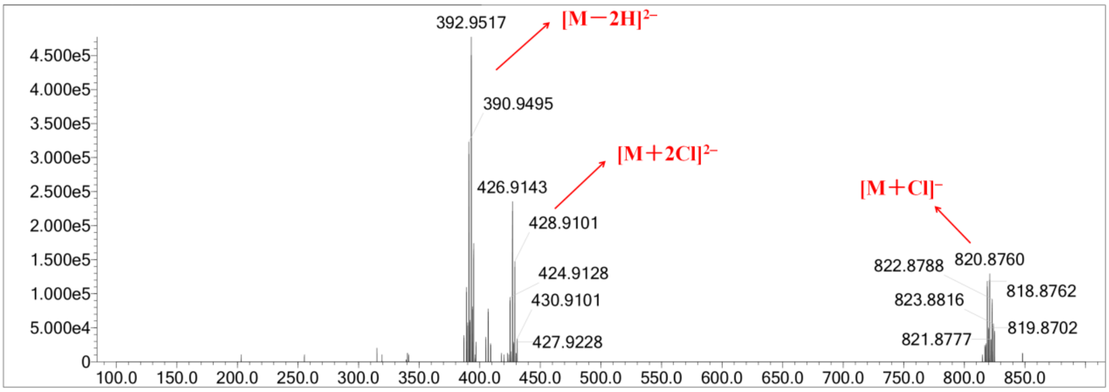


Figure S45. HRMS spectra of pure diselenide **16**. [M+Cl]$^-$ for **16** $C_{32}H_{20}N_4O_6Cl_2Se_2$ pred. 820.8783, meas. 820.8760

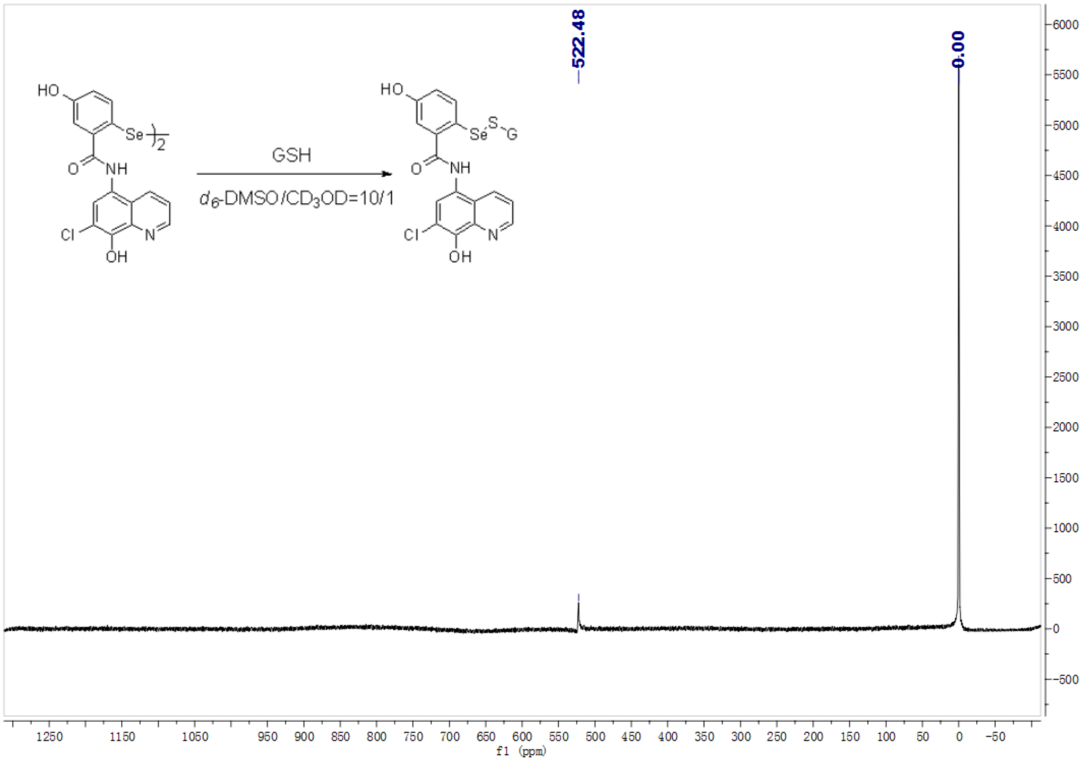


Figure S46. ^{77}Se NMR spectra of selenenyl sulfides **14** obtained f rom the the reaction of diselenide **16** with GSH (2.0 equiv) in DMSO-d_6/H_2O = 10/1 mixture.

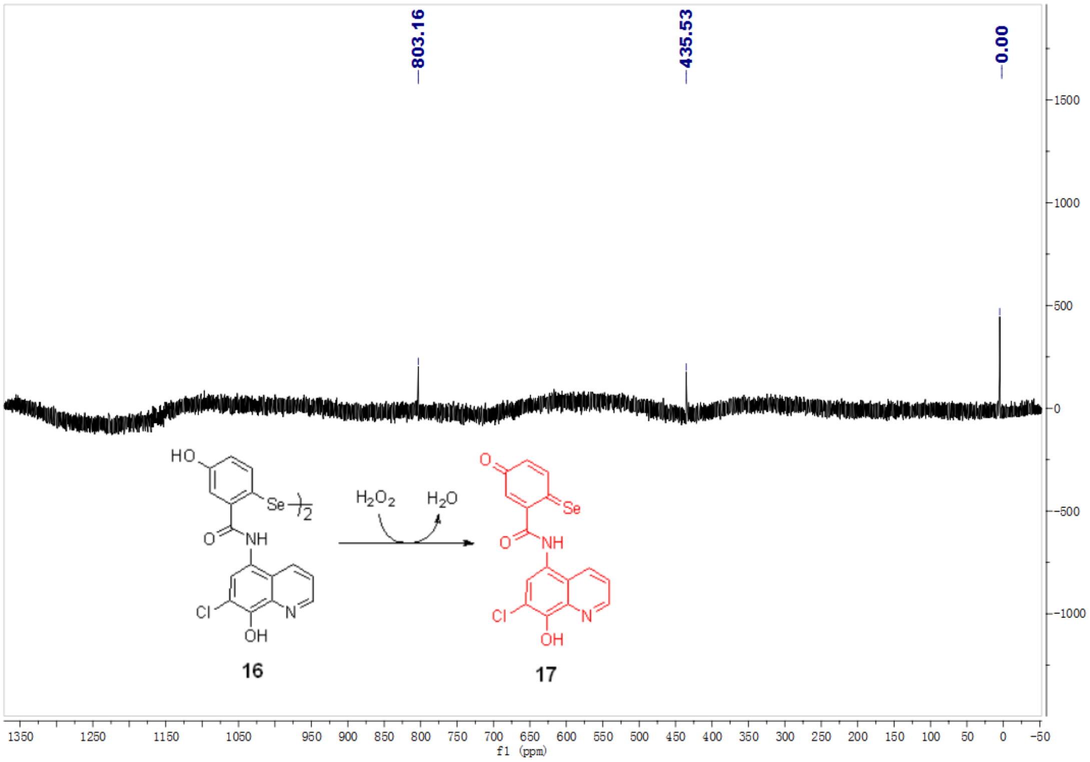


Figure S47. ^{77}Se NMR spectra of diselenide **16** (δ 435 ppm) and selenium quinone **17** (δ 803 ppm) obtained from the the reaction of diselenide **16** with H_2O_2 (2.0 equiv) in DMSO-d_6 within 2 h.

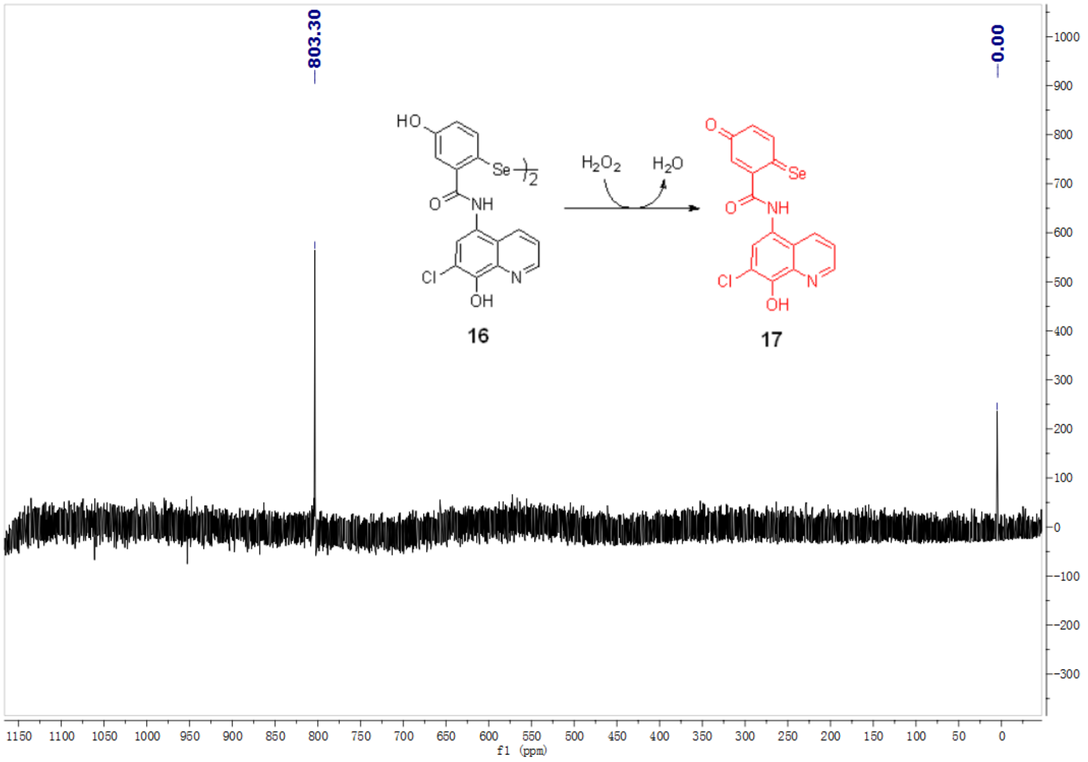


Figure S48. ^{77}Se NMR spectra of selenium quinone **17** (δ 803 ppm) obtained from the the reaction of diselenide **16** with H_2O_2 (4.0 equiv) in DMSO-d_6 after 12 h.

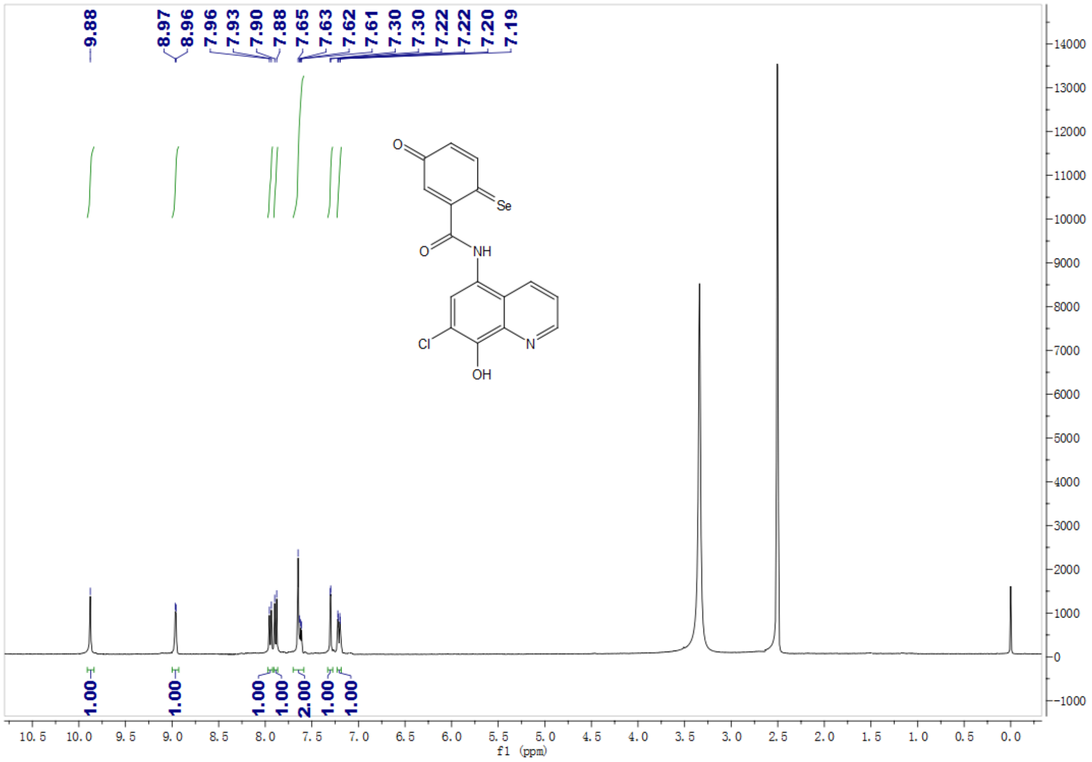


Figure S49. ^{1}H NMR spectra of selenium quinone **17** (in DMSO-d_6).

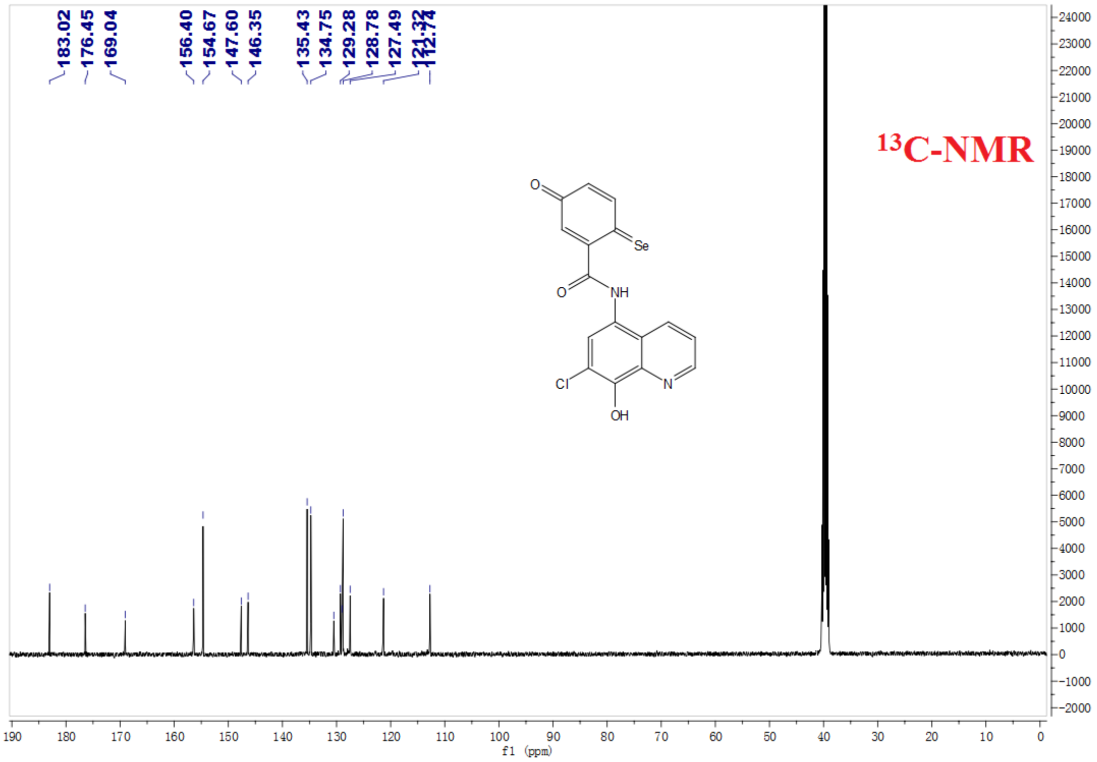


Figure S50. ^{13}C NMR spectra of selenium quinone **17** (in DMSO-d_6). (^{13}C NMR δ 183 ppm and 176ppm demonstrated the quinone structure)

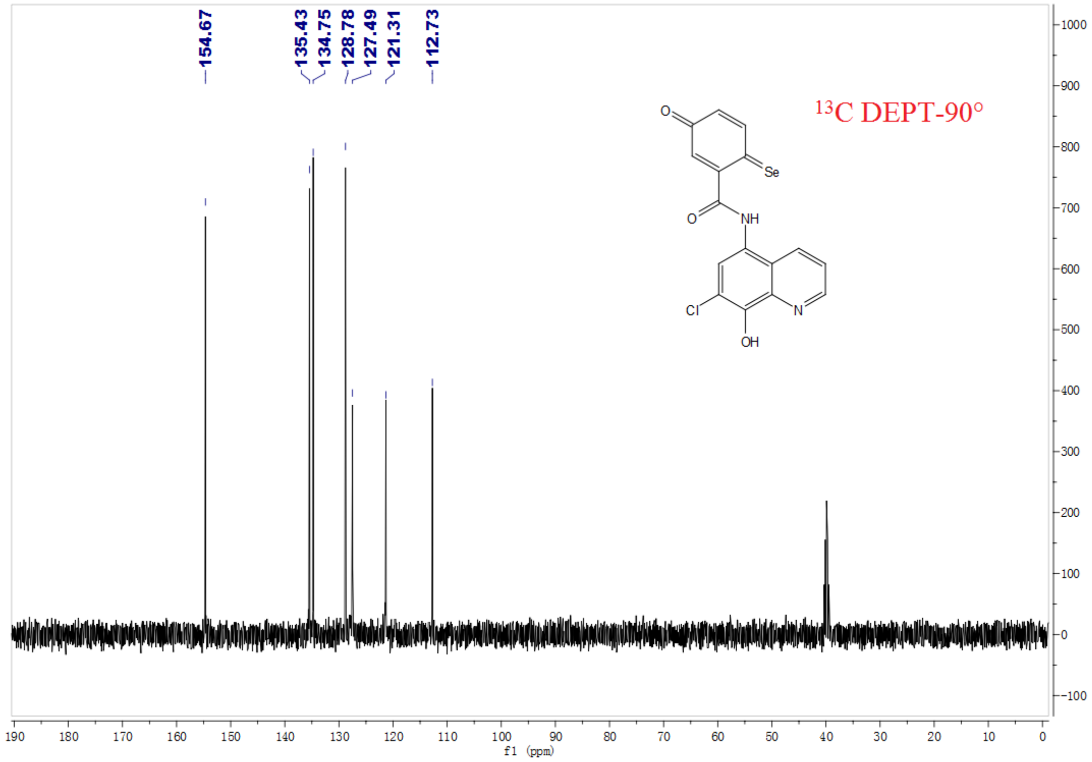


Figure S51. ^{13}C DEPT-90 °NMR spectra of selenium quinone **17** (in DMSO-d_6).

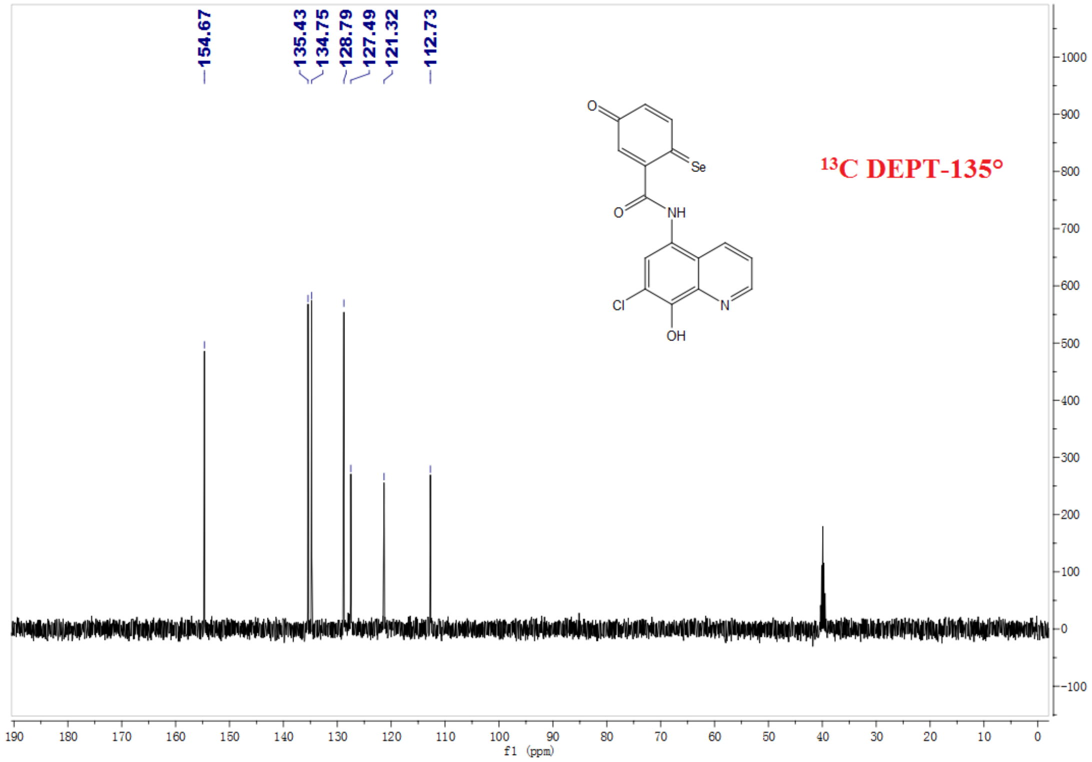


Figure S52. ^{13}C DEPT-135 °NMR spectra of selenium quinone **17** (in DMSO-d_6).

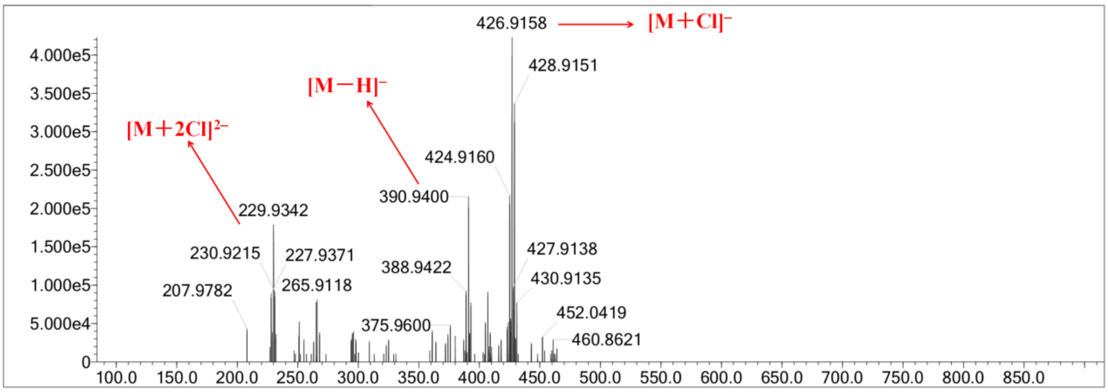


Figure S53. HRMS spectra of selenium quinone **17**. [M+Cl]⁻ for **17** $C_{16}H_9N_2O_3ClSe$ pred. 426.9159, meas. 426.9158.

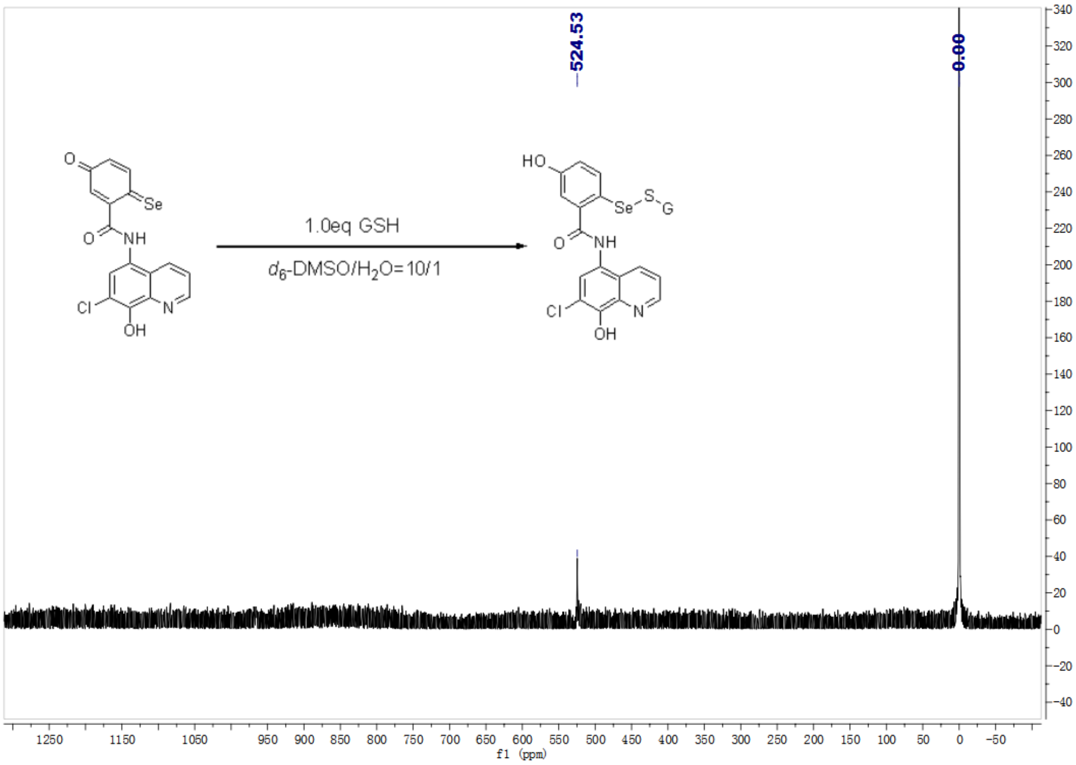


Figure S54. ^{77}Se NMR spectra of selenenyl sulfides **14** obtained from the the reaction of selenium quinone **17** with GSH (1.0 equiv) in DMSO-d_6/H_2O = 10/1.

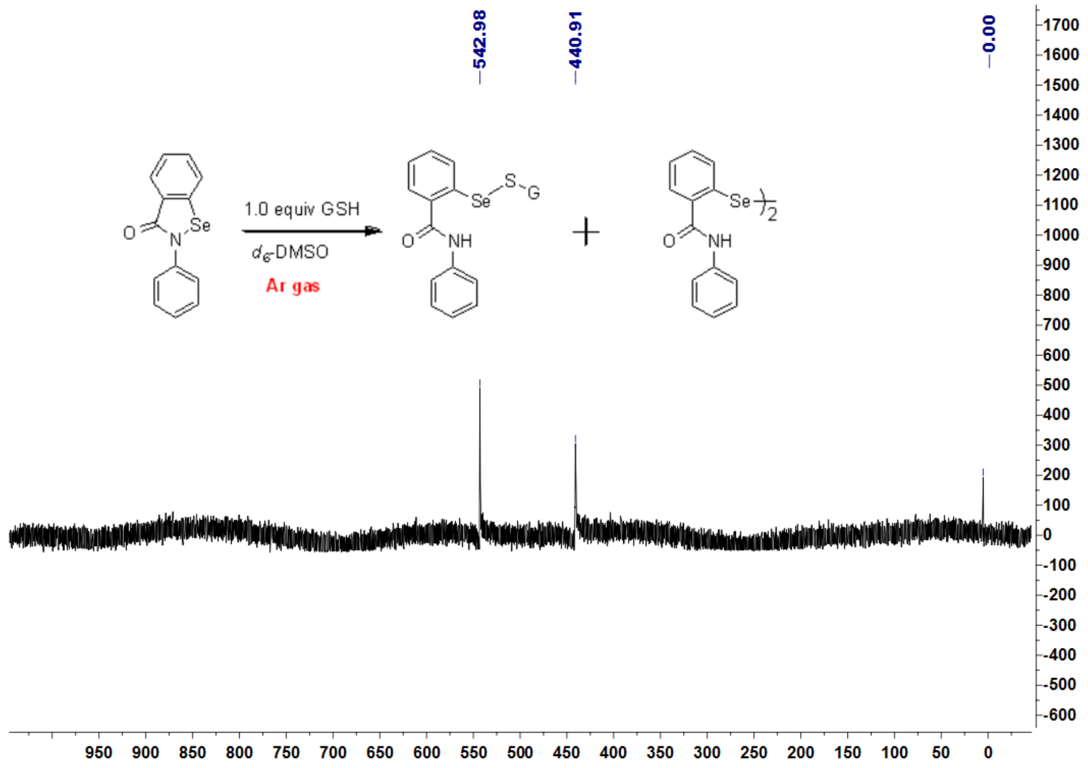


Figure S55. ^{77}Se NMR spectra of selenenyl sulfides and diselenide obtained from the disproportionation reaction of **ebselen** with GSH (1.0 equiv) under Ar condition in d_6-DMSO.

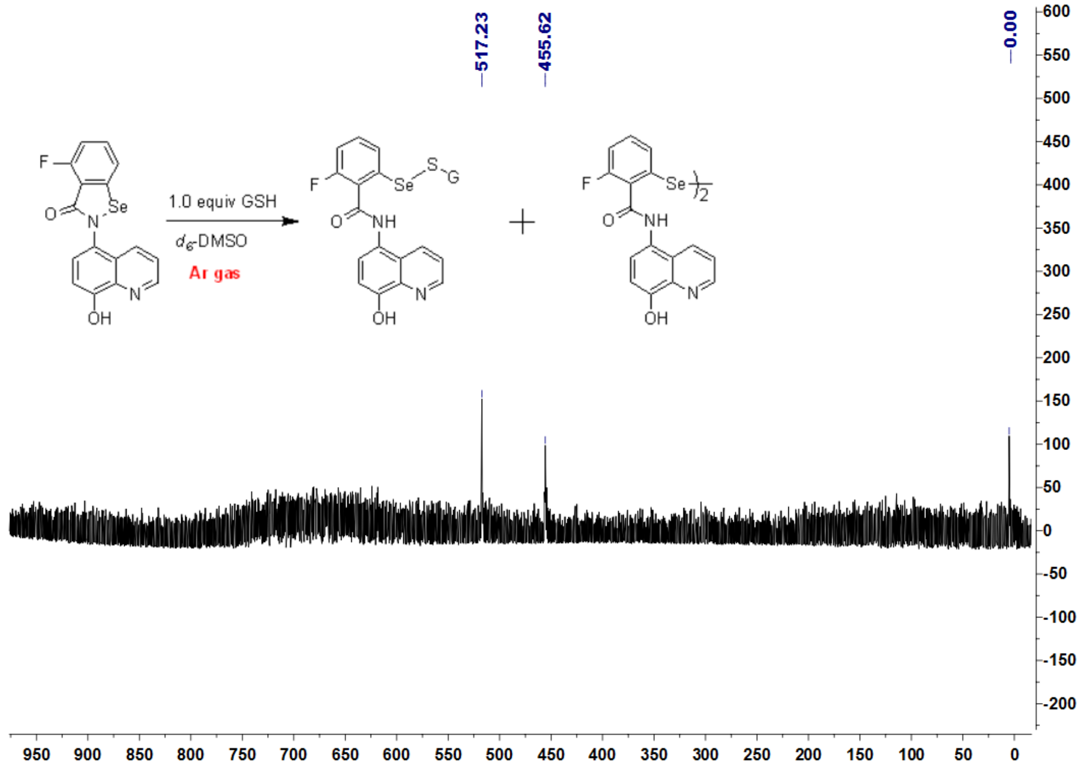


Figure S56. ^{77}Se NMR spectra of selenenyl sulfides and diselenide obtained from the disproportionation reaction of **11f** with GSH (1.0 equiv) under Ar condition in d_6-DMSO.

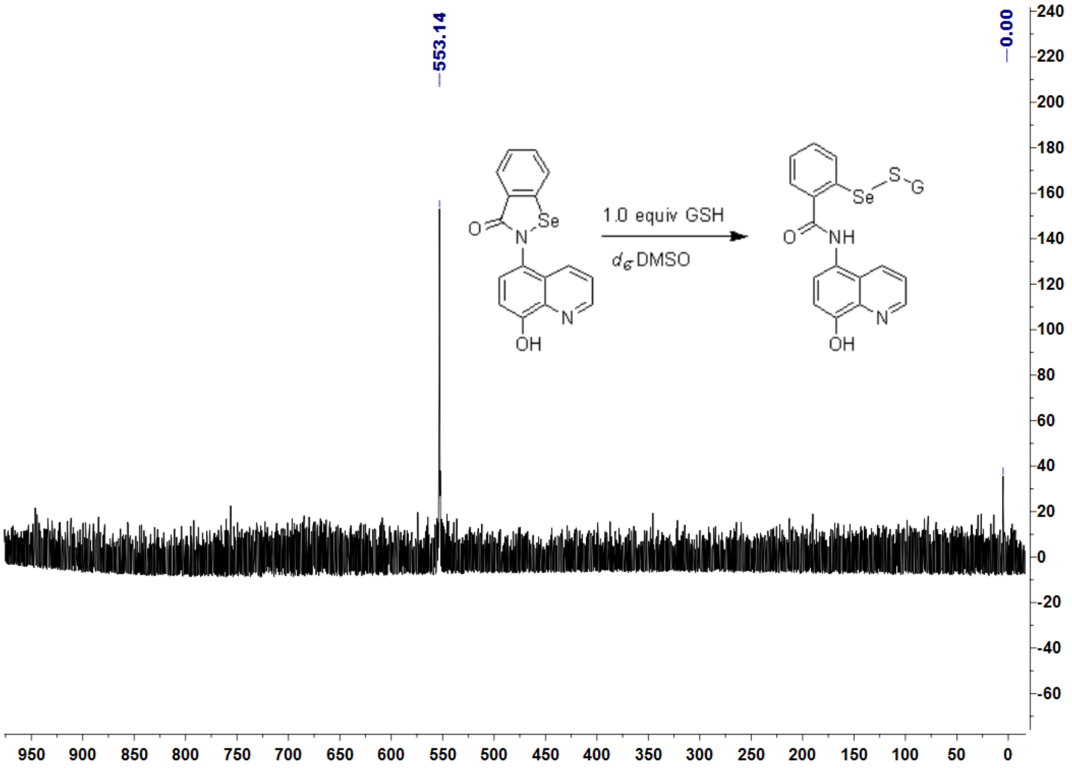


Figure S57. ^{77}Se NMR spectra of selenenyl sulfides obtained from the reaction of **11a** with GSH (1.0 equiv) in d_6-DMSO.

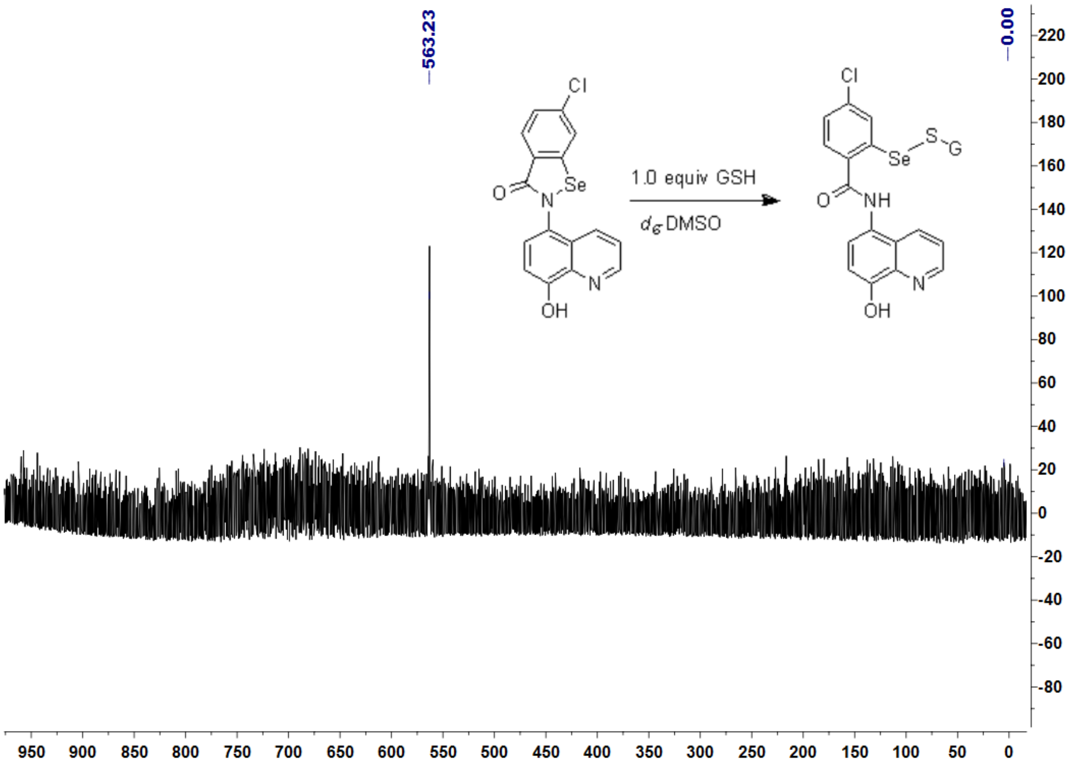


Figure S58. ^{77}Se NMR spectra of selenenyl sulfides obtained from the reaction of **11b** with GSH (1.0 equiv) in d_6-DMSO.

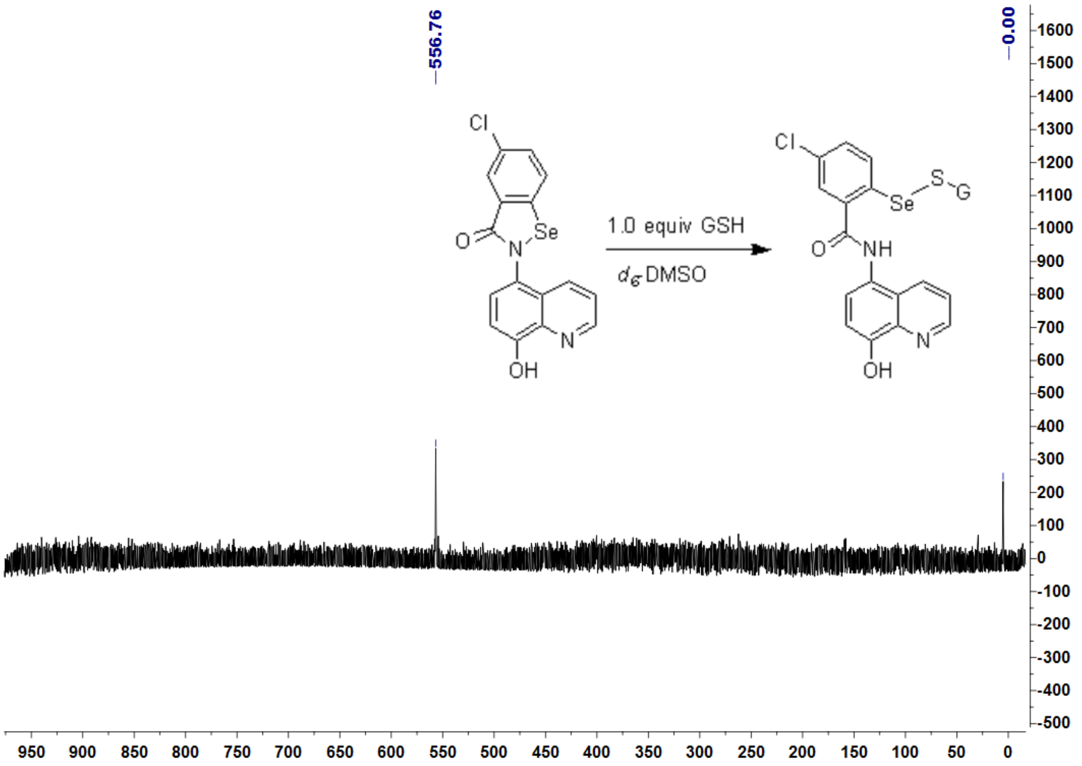


Figure S59. ^{77}Se NMR spectra of selenenyl sulfides obtained from the reaction of **11c** with GSH (1.0 equiv) in d_6-DMSO.

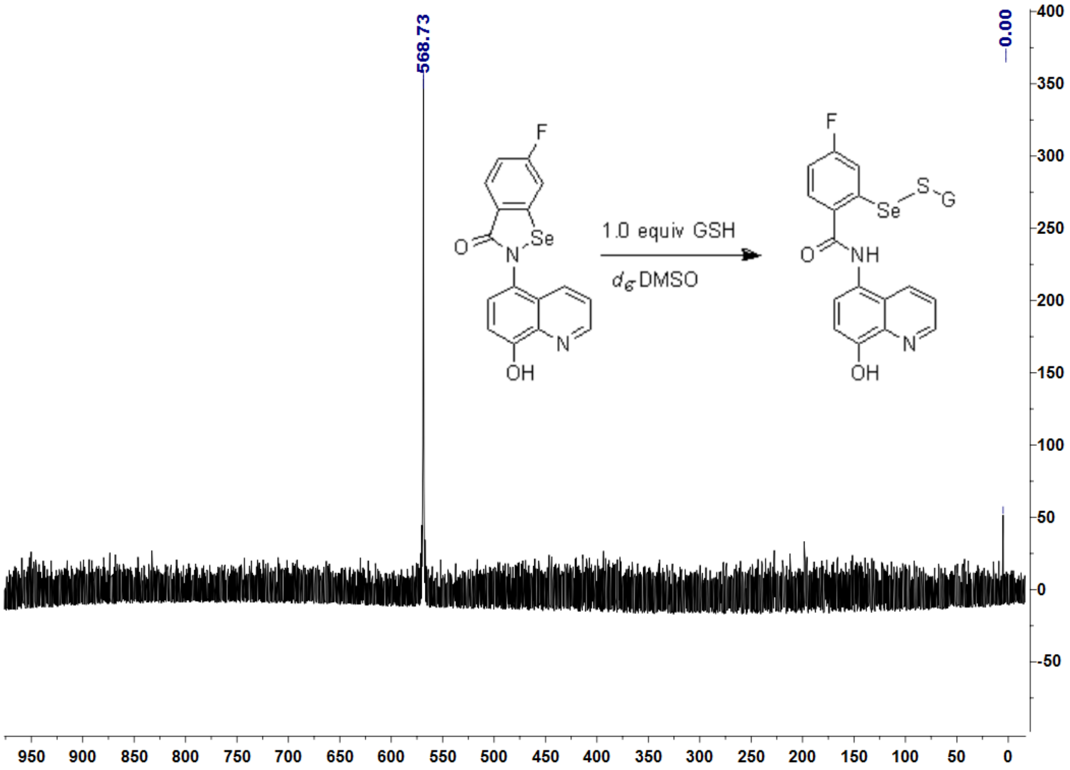


Figure S60. ^{77}Se NMR spectra of selenenyl sulfides obtained from the reaction of **11d** with GSH (1.0 equiv) in d_6-DMSO.

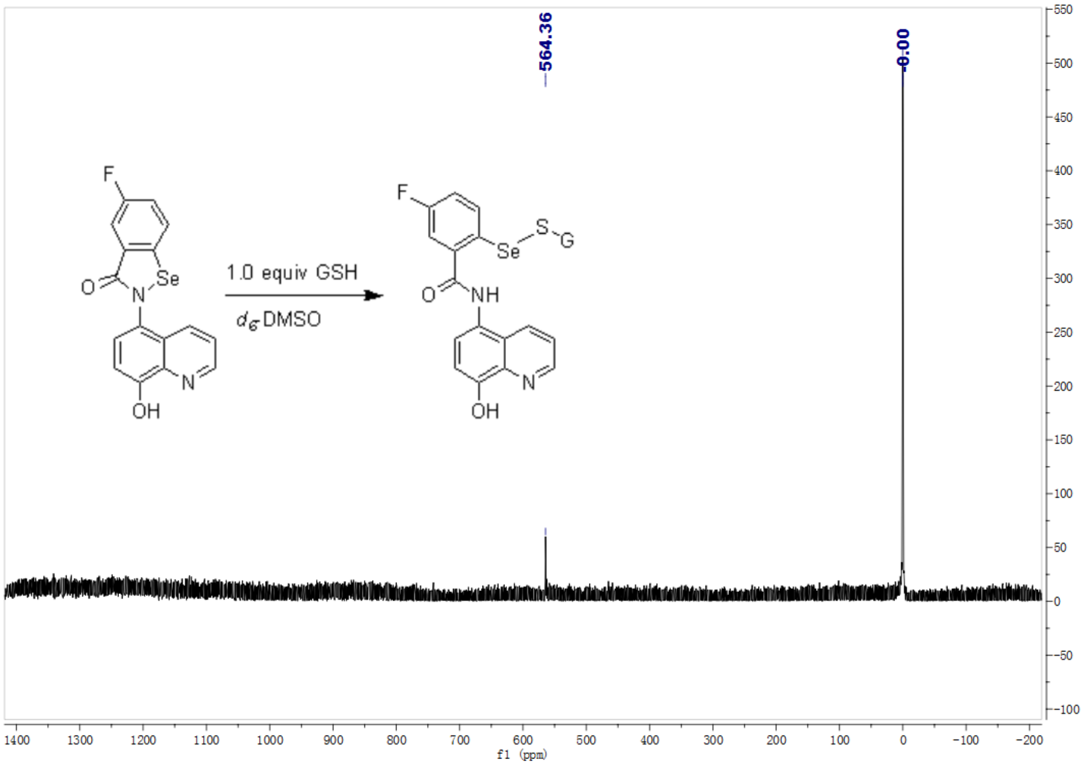


Figure S61. ^{77}Se NMR spectra of selenenyl sulfides obtained from the reaction of **11e** with GSH (1.0 equiv) in d_6-DMSO.

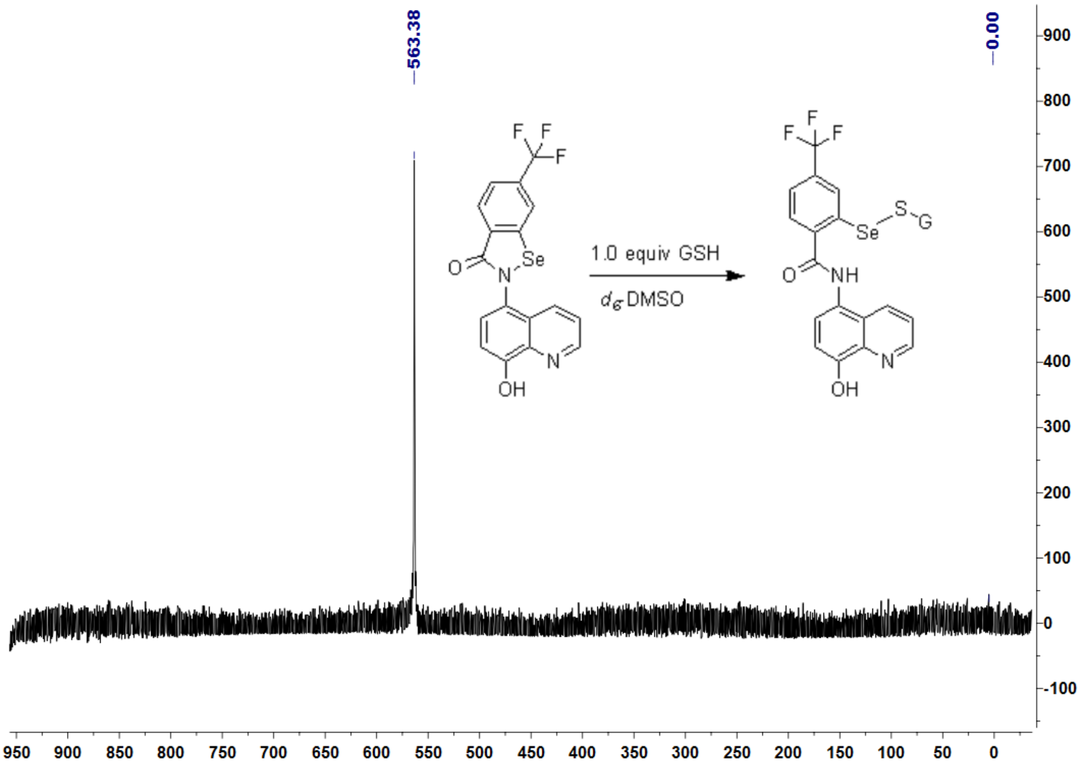


Figure S62. ^{77}Se NMR spectra of selenenyl sulfides obtained from the reaction of **11g** with GSH (1.0 equiv) in d_6-DMSO.

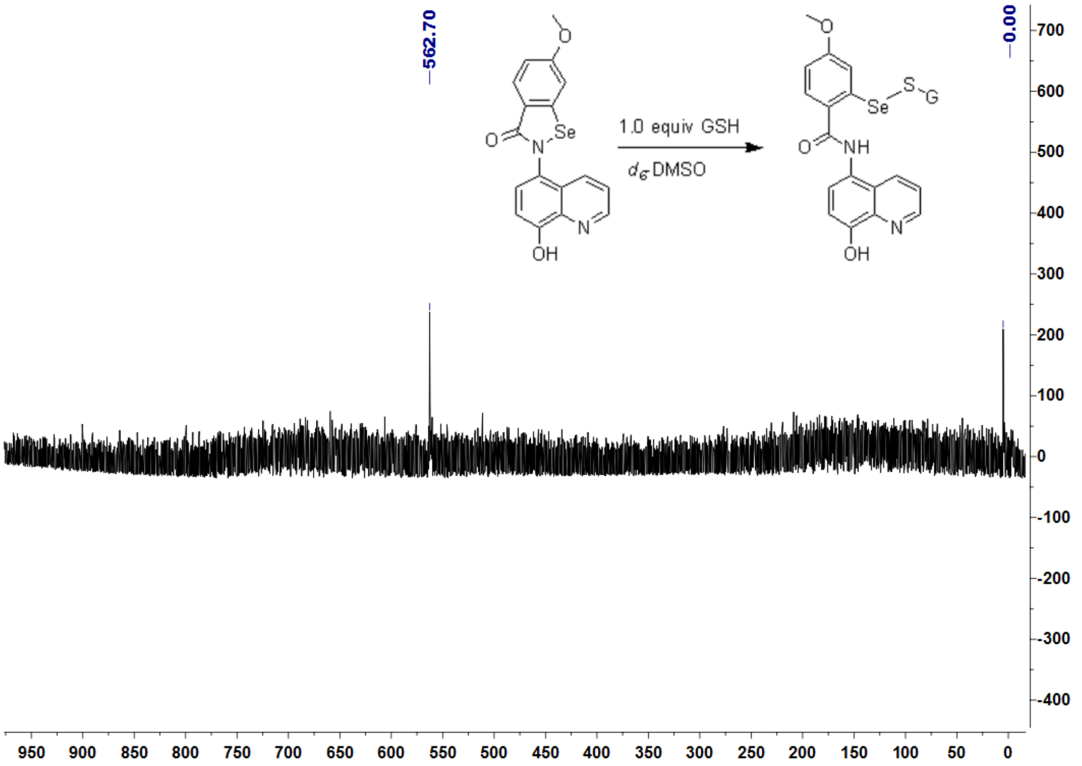


Figure S63. ^{77}Se NMR spectra of selenenyl sulfides obtained from the reaction of **11h** with GSH (1.0 equiv) in d_6-DMSO.

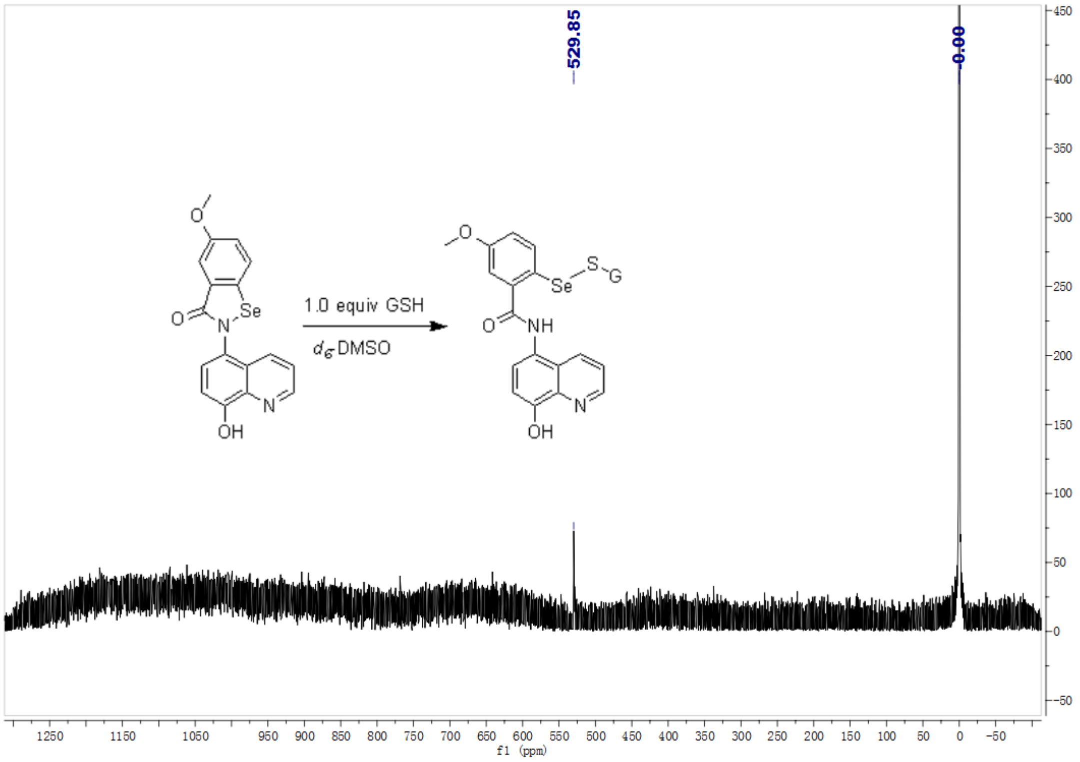


Figure S64. ^{77}Se NMR spectra of selenenyl sulfides obtained from the reaction of **11i** with GSH (1.0 equiv) in d_6-DMSO.

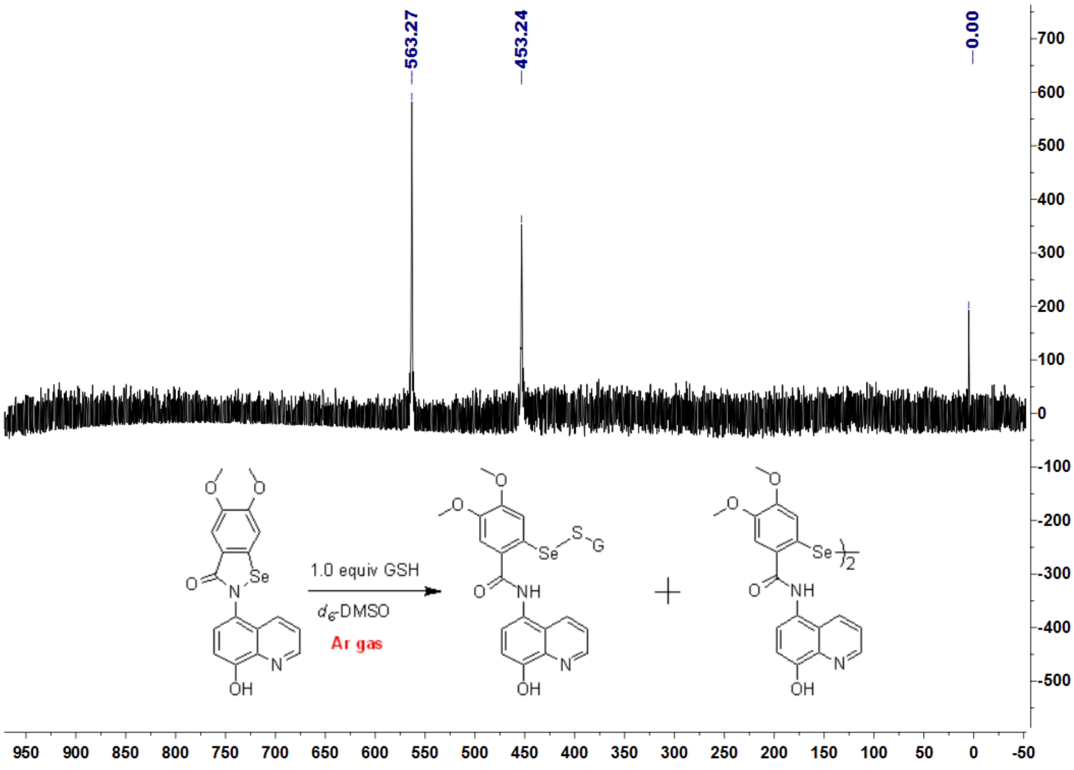


Figure S65. ^{77}Se NMR spectra of selenenyl sulfides and diselenide obtained from the disproportionation reaction of **11j** with GSH (1.0 equiv) under Ar condition in d_6-DMSO.

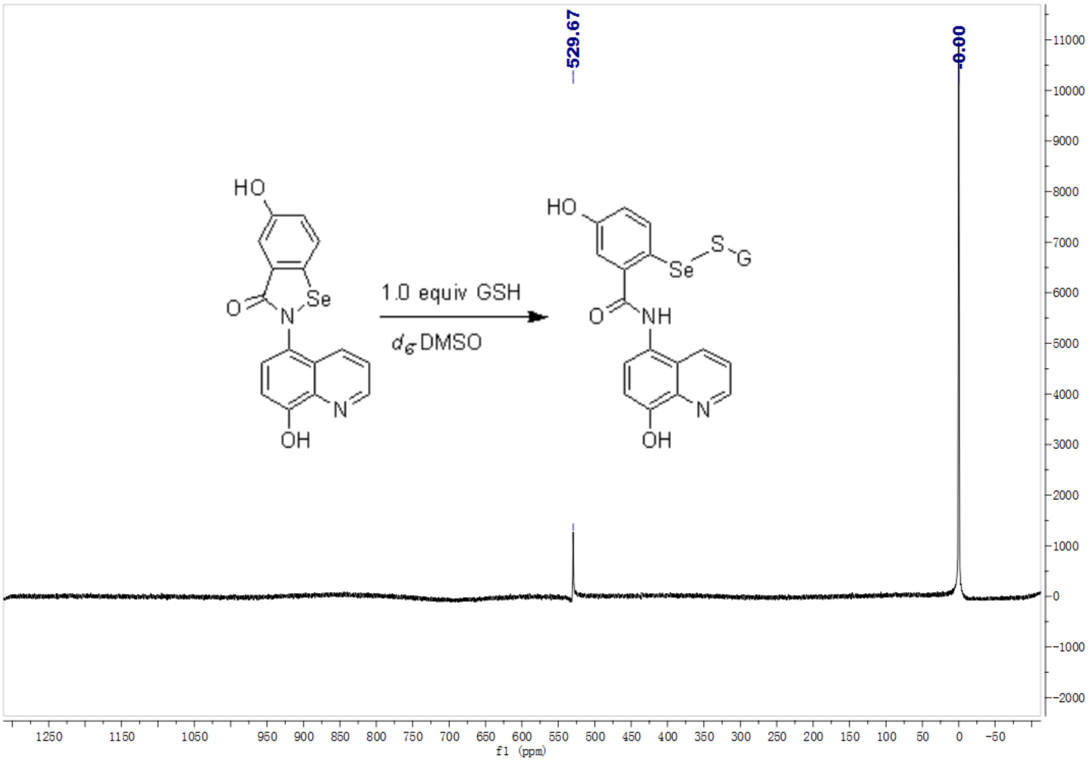


Figure S66. ^{77}Se NMR spectra of selenenyl sulfides obtained from the reaction of **11k** with GSH (1.0 equiv) in d_6-DMSO.

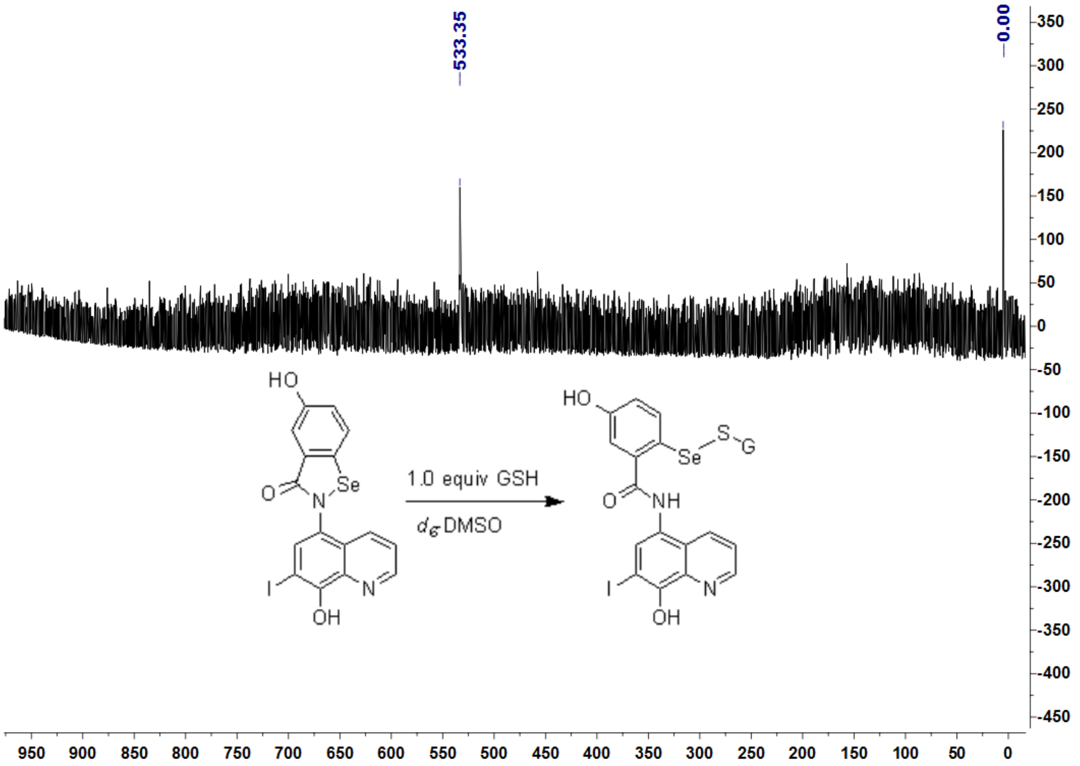


Figure S67. ^{77}Se NMR spectra of selenenyl sulfides obtained from the reaction of **13k** with GSH (1.0 equiv) in *d*$_6$-DMSO.

7. UV spectrum of Metal binding

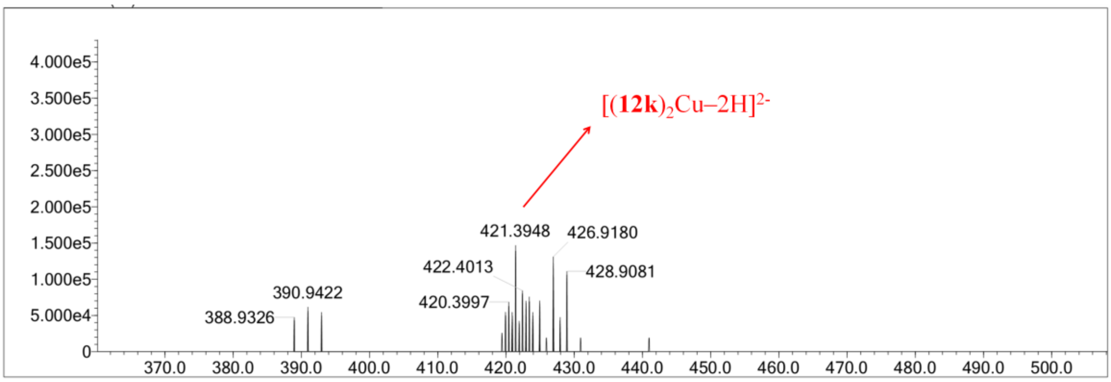


Figure S68. High-resolution mass spectra (HRMS) of the **12k**-Cu complex.

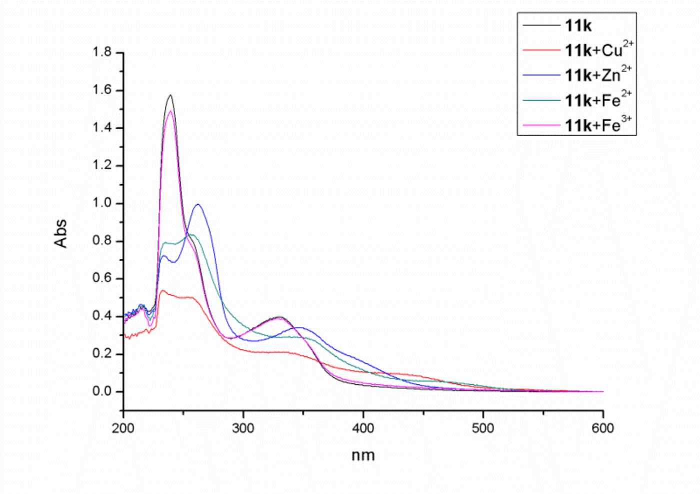


Figure S69. UV spectrum of compound **11k** (50 μM) alone or in the presence of CuSO$_4$ (50 μM), ZnCl$_2$ (50 μM) or FeSO$_4$(50 μM) in buffer (20 mM HEPES, 150 mM NaCl, pH 7.4).

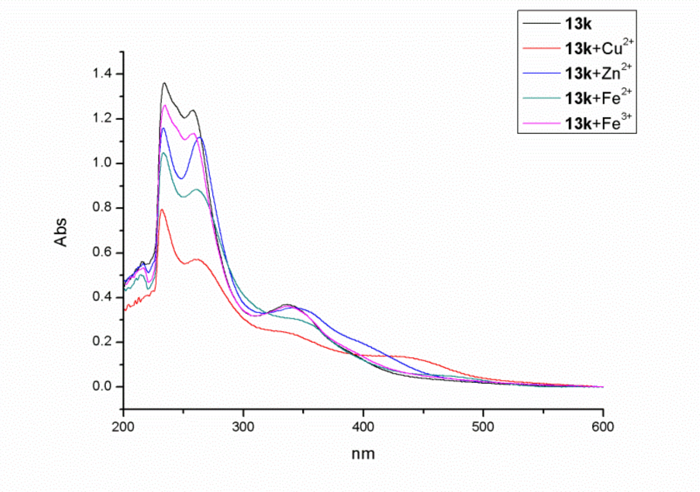


Figure S70. UV spectrum of compound **13k** (50 μM) alone or in the presence of $CuSO_4$ (50 μM), $ZnCl_2$ (50 μM) or $FeSO_4$(50 μM) in buffer (20 mM HEPES, 150 mM NaCl, pH 7.4).

8. Tables of results for the PAMPA

Table S19. Permeability ($P_e \times 10^{-6}$ cm s^{-1}) in the PAMPA-BBB assay for 13 commercial drugs, used in the Experiment Validation.

Commercial drugs	Bibl [a]	PBS : EtOH (70 : 30) [b]
testosterone	17	22.3 ± 1.4
verapamil	16	21.2 ± 1.9
desipramine	12	16.4 ± 1.2
progesterone	9.3	17.7 ± 1.2
promazine	8.8	14.3 ± 0.5
chlorpromazine	6.5	6.0 ± 0.3
clonidine	5.3	5.1 ± 0.3
piroxicam	2.5	0.24 ± 0.01
hydrocortisone	1.9	0.65 ± 0.01
lomefloxacin	1.1	0.37 ± 0.02
atenolol	0.8	0.78 ± 0.02
ofloxacin	0.8	0.37 ± 0.02
theophylline	0.1	0.26 ± 0.01

[a] Taken from reference.[7] [b] Data are the mean ± SD of three independent experiments

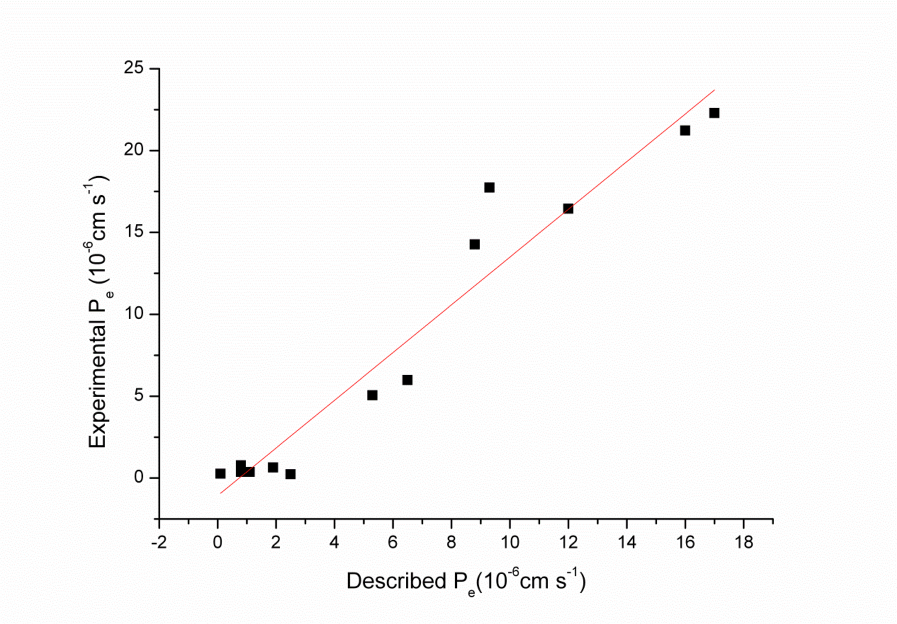


Figure S71. Lineal correlation between experimental and reported permeability of commercial drugs using the PAMPA-BBB assay. P_e (exp.)=1.4574Pe (bibl.) -1.0773 (R^2=0.9427)

Table S20. Ranges of Permeability of PAMPA-BBB Assays (P_e, 10^{-6} cm s^{-1})

Compounds of high BBB permeation (CNS+)	$P_e > 4.7$
Compounds of uncertain BBB permeation (CNS+/-)	$4.7 > P_e > 1.8$
Compounds of low BBB permeation (CNS-)	$P_e < 1.8$

Table S21. Permeability ($P_e \times 10^{-6}$ cm s^{-1}) determined by the PAMPA-BBB assay for target compounds and predicted penetration of the CNS.

Compound[a]	P_e($\times 10^{-6}$ cm s^{-1})[b]	Prediction	Compound[a]	P_e($\times 10^{-6}$ cm s^{-1})[b]	Prediction
11a	6.8 ± 0.3	CNS+	**11h•HBr**	8.8 ± 0.1	CNS+
11b	12.7 ± 0.5	CNS+	**11i**	7.3 ± 0.1	CNS+

11c	12.9 ± 0.2	CNS+	**11j**	1.1 ± 0.1	CNS–
11d•HCl	10.8 ± 0.3	CNS+	**11k•HCl**	1.2 ± 0.1	CNS–
11e	11.9 ± 0.2	CNS+	**12k•HCl**	5.3 ± 0.1	CNS+
11f•HCl	3.2 ± 0.1	CNS±	**13k•HCl**	3.0 ± 0.1	CNS±
11g•HCl	13.3 ± 0.4	CNS±	Chlorpromazine	5.1 ± 0.2	CNS+

[a] Compounds were dissolved in DMSO at 5 mg mL^{-1} and diluted with PBS / EtOH (70:30).

[b] Values are expressed as the means ± SD of three independent experiments.

References

1. B. K. Sarma and G. Mugesh, *J. Am. Chem. Soc.*, 2005, **127**, 11477-11485.
2. K. Selvakumar, P. Shah, H. B. Singh and R. J. Butcher, *Chem. Eur. J.*, 2011, **17**, 12741-12755.
3. N. B. Patel, J. C. Patel and S. H. Modi, *J. Saudi. Chem. Soc.*, 2011, **15**, 167-176.
4. U. K. Mazumder, M. Gupta, S. Bhattacharya, S. S. Karki, S. Rathinasamy and S. Thangavel, *J. Enzyme. Inhib. Med. Chem.*, 2004, **19**, 185-192.
5. Z. Wang, Y. Wang, W. Li, F. Mao, Y. Sun, L. Huang and X. Li, *ACS Chem. Neurosci.*, 2014, **5**, 952-962.
6. J. He, D. Li, K. Xiong, Y. Ge, H. Jin, G. Zhang, M. Hong, Y. Tian, J. Yin and H. Zeng, *Bioorg. Med. Chem.*, 2012, **20**, 3816-3827.
7. L. Di, E. H. Kerns, K. Fan, O. J. McConnell and G. T. Carter, *Eur. J. Med. Chem.*, 2003, **38**, 223-232.