Supplementary Material

Molecular modeling and DFT studies on the antioxidant activity of *Centaurea scoparia* flavonoids and molecular dynamics simulation of their interaction with β-lactoglobulin

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Cartesian coordinates of all neutral flavonoids represented in this study.

3'-geranyl-5,7,4'-trihydroxyisoflavone (**1**)

C	-7.30474	-0.55215	-0.34762
C	-6.21597	0.28329	-0.57437
C	-4.90183	-0.15678	-0.24226
C	-4.76302	-1.44147	0.30927
C	-5.83642	-2.2859	0.54005
C	-7.10931	-1.82252	0.20449
H	-8.29552	-0.1969	-0.60803
C	-3.74723	0.69733	-0.46049
H	-5.69424	-3.27002	0.96294
C	-2.44015	-1.12722	0.44242
C	-2.45175	0.13491	-0.04867
H	-1.53683	-1.64719	0.73107
C	-1.19345	0.9088	-0.15158
C	-0.22555	0.83561	0.86256
C	-0.92115	1.72082	-1.2589
C	0.99201	1.50775	0.7946
H	-0.43739	0.25629	1.75598
C	0.2827	2.40829	-1.34623
H	-1.6554	1.82525	-2.04458
C	1.23793	2.30229	-0.33567
H	0.48154	3.03826	-2.20901
O	-3.5213	-1.9124	0.63604
O	-3.86101	1.83072	-0.96325
O	-6.41765	1.49342	-1.10166
O	-8.14722	-2.66571	0.43887
H	-8.97007	-2.24386	0.16921
H	-5.52332	1.91786	-1.18079
C	2.02837	1.39051	1.89643
H	1.5141	1.09055	2.81701
H	2.4698	2.36978	2.08338
C	3.09228	0.36696	1.57382
C	4.40921	0.54861	1.41863
H	2.70814	-0.64436	1.44614
C	5.29841	-0.62941	1.07484
H	6.1373	-0.67913	1.78086
H	4.73334	-1.55879	1.19618
C	5.11391	1.87507	1.5546
H	5.5786	2.16873	0.60763
H	4.44859	2.68404	1.85094
H	5.91943	1.80444	2.29478
C	5.87705	-0.58519	-0.36243
H	5.03574	-0.4913	-1.06068
H	6.4851	0.31232	-0.48983
C	6.66156	-1.82299	-0.69824
C	7.96935	-1.94144	-0.95774
H	6.06975	-2.73821	-0.71461
C	8.57724	-3.28801	-1.26794
H	7.83113	-4.08472	-1.24707
H	9.04862	-3.28804	-2.25817
H	9.36516	-3.53913	-0.54772
C	8.9526	-0.79786	-0.97852
H	8.50438	0.16273	-0.7266
H	9.7705	-0.98279	-0.27231
H	9.41378	-0.70508	-1.96907

O	2.42784	2.97489	-0.38725
H	2.46006	3.49617	-1.19598

6-prenyl-5,7,4'-trihydroxyisoflavone (**2**)

C	2.7961	0.64764	-0.62424
C	1.57656	-0.03283	-0.66436
C	0.35676	0.62455	-0.335
C	0.42096	1.97721	0.03481
C	1.61037	2.68065	0.08366
C	2.78464	2.00243	-0.244
C	-0.91223	-0.08087	-0.37323
H	1.63499	3.7229	0.36825
C	-1.90607	2.0101	0.33212
C	-2.09058	0.70421	0.0228
H	-2.71307	2.68187	0.59191
C	-3.4417	0.10234	0.09728
C	-4.31343	0.42744	1.14853
C	-3.89984	-0.793	-0.87905
C	-5.59849	-0.09233	1.21551
H	-3.97197	1.07989	1.94462
C	-5.18367	-1.32112	-0.81851
H	-3.24262	-1.08486	-1.68574
C	-6.04178	-0.97084	0.22598
H	-6.26353	0.15549	2.03367
H	-5.51893	-2.01162	-1.58728
O	-0.72304	2.65694	0.35565
O	-0.98718	-1.2755	-0.72004
O	1.56422	-1.32451	-1.02443
O	3.93118	2.7303	-0.17522
O	-7.31084	-1.4602	0.33733
H	4.6763	2.19065	-0.45993
H	0.61263	-1.61408	-0.99911
H	-7.48328	-2.06378	-0.39272
C	4.08507	-0.07895	-0.96109
C	4.85623	-0.52163	0.26315
H	4.72388	0.57103	-1.57908
H	3.84176	-0.9275	-1.59712
H	5.22789	0.28597	0.89306
C	5.1137	-1.77264	0.66028
C	4.65555	-3.01633	-0.05798
C	5.91334	-2.02931	1.91412
H	3.94186	-2.81507	-0.85469
H	5.51133	-3.55631	-0.4808
H	4.17368	-3.70019	0.64916
H	6.24125	-1.10148	2.38677
H	5.323	-2.5957	2.64376
H	6.80134	-2.63367	1.69417

3'-geranyl-5,7,2',4'-tetrahydroxyisoflavone (**3**)

C	-7.111	-0.78987	-0.35495
C	-6.07719	0.11829	-0.55921
C	-4.73543	-0.25356	-0.25532
C	-4.51438	-1.54511	0.24822
C	-5.53216	-2.46207	0.45636

C	-6.8336	-2.06557	0.14778
H	-8.12418	-0.48605	-0.59371
C	-3.63489	0.67427	-0.45492
H	-5.32582	-3.44946	0.84369
C	-2.21197	-1.096	0.37509
C	-2.30083	0.17406	-0.08919
H	-1.28428	-1.55943	0.67246
C	-1.10104	1.03546	-0.2235
C	-0.07881	1.06192	0.74764
C	-0.9496	1.87577	-1.33244
C	1.04643	1.88951	0.63125
C	0.15667	2.6991	-1.47976
H	-1.72568	1.89313	-2.08319
C	1.14841	2.70547	-0.50105
H	0.24651	3.3407	-2.35085
O	-3.2444	-1.94663	0.55267
O	-3.82983	1.81844	-0.9089
O	-6.35682	1.33249	-1.03974
O	-7.81748	-2.97819	0.35849
H	-8.66588	-2.59592	0.11008
H	-5.48837	1.8114	-1.10719
C	2.14707	1.89225	1.67882
H	1.70344	1.86066	2.68667
H	2.66596	2.84712	1.63276
C	3.11298	0.73931	1.51948
C	4.42052	0.79338	1.23961
H	2.66818	-0.24865	1.63284
C	5.21782	-0.48777	1.09755
H	6.15805	-0.40181	1.6562
H	4.66219	-1.31659	1.54716
C	5.20105	2.06931	1.04187
H	5.80866	2.01377	0.13349
H	4.5666	2.94966	0.95359
H	5.89745	2.22451	1.8747
C	5.55373	-0.85591	-0.37018
H	4.60881	-0.92182	-0.92362
H	6.12563	-0.04975	-0.83388
C	6.28119	-2.16766	-0.47552
C	7.52668	-2.4023	-0.90579
H	5.70315	-3.02892	-0.1406
C	8.08489	-3.80469	-0.93002
H	7.36358	-4.53538	-0.55914
H	8.37254	-4.09538	-1.94757
H	8.99134	-3.87783	-0.31721
C	8.48218	-1.34644	-1.40296
H	8.07199	-0.33783	-1.36328
H	9.40576	-1.35743	-0.81243
H	8.77486	-1.55021	-2.43979
O	2.2572	3.50382	-0.59956
H	2.19845	4.01848	-1.41086
O	-0.21232	0.23164	1.83206
H	0.45791	0.45346	2.48649

6-prenyl-3,5,7,4'-tetrahydroxyflavone (**4**)

C	-2.75401	-0.68847	-0.7524
C	-2.0392	0.50374	-0.65575

C	-0.63178	0.49487	-0.45787
C	0.03063	-0.73843	-0.3559
C	-0.65365	-1.94009	-0.4445
C	-2.03391	-1.89632	-0.63828
C	0.12753	1.70598	-0.36018
H	-0.14142	-2.88832	-0.36465
C	2.15254	0.3414	-0.06806
C	1.55695	1.56946	-0.15808
O	1.37583	-0.78789	-0.16703
O	-0.3601	2.86142	-0.44049
O	-2.6904	1.67551	-0.75779
O	-2.6615	-3.10055	-0.71217
H	-3.59834	-2.96829	-0.89177
H	-2.01769	2.39438	-0.67224
C	-4.25848	-0.66591	-0.94809
C	-5.02879	-0.86962	0.33806
H	-4.54745	-1.44167	-1.67416
H	-4.52743	0.27764	-1.41856
H	-4.88474	-1.83861	0.81487
C	-5.83753	-0.00036	0.95396
C	-6.13365	1.39569	0.46782
C	-6.53424	-0.37843	2.23812
H	-5.50019	1.70795	-0.36048
H	-7.18224	1.48313	0.15896
H	-5.98747	2.11357	1.28219
H	-6.30815	-1.40293	2.53993
H	-6.23865	0.2921	3.0534
H	-7.62168	-0.2841	2.13496
O	2.23042	2.7433	-0.07425
C	3.56919	0.02815	0.12159
C	3.99667	-1.31133	0.13564
C	4.54441	1.03176	0.29247
C	5.33345	-1.63697	0.30899
H	3.27265	-2.10349	0.00776
C	5.87969	0.70797	0.46636
H	4.25042	2.06988	0.28832
C	6.28575	-0.62834	0.4753
H	5.63878	-2.67935	0.31445
H	6.62621	1.48158	0.59757
H	1.53509	3.42132	-0.1792
O	7.61139	-0.88508	0.6489
H	7.75779	-1.83686	0.63607

5,7,2’-trihydroxyflavone (**5**)

C	-3.94857	-0.44035	0.0988
C	-3.21737	0.72929	-0.08386
C	-1.7971	0.68785	-0.0476
C	-1.17524	-0.55145	0.1734
C	-1.88867	-1.72519	0.3568
C	-3.28195	-1.65101	0.31598
C	-1.0013	1.88789	-0.24096
H	-1.38437	-2.66597	0.52382
C	0.96104	0.45392	0.02817
C	0.43299	1.68002	-0.20095
O	0.18974	-0.64498	0.22842

O	-1.51633	3.00493	-0.43896
O	-3.85597	1.88438	-0.29247
O	-3.96001	-2.81476	0.49744
H	-4.90646	-2.64325	0.44839
H	-3.15329	2.57965	-0.3964
C	2.40693	0.17098	0.11681
C	2.99678	-0.91214	-0.56539
C	3.23041	1.0097	0.87777
C	4.3719	-1.1319	-0.46134
C	4.59941	0.79095	0.97781
H	2.77367	1.83384	1.41273
C	5.16757	-0.28801	0.30535
H	4.81714	-1.96684	-0.99468
H	5.21257	1.44893	1.58089
H	6.23267	-0.47683	0.37452
O	2.20196	-1.69774	-1.34013
H	2.74342	-2.3644	-1.77557
H	-5.03135	-0.39001	0.06887
H	1.07995	2.52684	-0.38162

5,7,4'-trihydroxy-6,3’-dimethoxyflavone (**6**)

C	4.15356	-0.25876	-0.12101
C	3.33787	0.86513	-0.22919
C	1.93066	0.7225	-0.19368
C	1.4314	-0.58826	-0.07671
C	2.23888	-1.72092	-0.00983
C	3.61452	-1.54772	-0.03754
C	0.98303	1.85821	-0.27881
H	1.80322	-2.70781	0.05721
C	-0.82233	0.1709	-0.12775
C	-0.42014	1.45478	-0.25749
O	0.08663	-0.84281	-0.03246
O	1.31568	3.0327	-0.36313
O	4.43889	-2.6233	0.01841
H	5.33073	-2.30852	-0.18545
C	-2.20758	-0.32043	-0.08495
C	-2.49058	-1.68028	-0.24588
C	-3.27622	0.57718	0.11321
C	-3.80325	-2.14377	-0.22447
C	-4.57945	0.11531	0.13299
C	-4.85448	-1.25851	-0.0378
O	5.5369	-0.10423	-0.14432
H	-1.68021	-2.37934	-0.39579
C	6.11808	0.08736	1.16544
H	5.9185	-0.77513	1.8074
H	7.19148	0.19333	1.01113
H	5.72033	0.98954	1.63782
O	3.9127	2.0785	-0.36631
H	4.85323	1.91947	-0.53214
H	-1.14167	2.25231	-0.35968
O	-6.13398	-1.70411	-0.01311
H	-6.70401	-0.93571	0.12866
H	-3.07538	1.62763	0.26656
O	-5.70407	0.87717	0.32037
C	-5.55409	2.28127	0.5001
H	-6.56083	2.67765	0.61818

H	-4.96736	2.50397	1.39724
H	-5.08059	2.74236	-0.37275
H	-4.02886	-3.19513	-0.35375

5,7,4’,5’-tetrahydroxy-6,3’-dimethoxyflavone (**7**)

C	-4.32489	0.32103	-0.11074
C	-3.56686	-0.83892	-0.25108
C	-2.15424	-0.76861	-0.21031
C	-1.59007	0.51152	-0.0546
C	-2.33938	1.68117	0.04423
C	-3.72191	1.57845	0.01009
C	-1.26528	-1.94751	-0.32837
H	-1.85387	2.64207	0.14027
C	0.6214	-0.35864	-0.12338
C	0.15676	-1.61597	-0.2938
O	-0.23437	0.69625	-0.0002
O	-1.65592	-3.10086	-0.44801
O	-4.49144	2.6919	0.09606
H	-5.39731	2.42856	-0.11861
C	2.03223	0.05811	-0.06263
C	2.37079	1.40678	-0.20895
C	3.04259	-0.90089	0.13799
C	3.70439	1.80331	-0.16995
C	4.36973	-0.49833	0.17314
C	4.70507	0.8524	0.01808
O	-5.71418	0.23697	-0.13951
H	1.61031	2.15869	-0.36052
C	-6.3069	0.0384	1.164
H	-6.06703	0.87237	1.82942
H	-7.38386	-0.01095	1.00596
H	-5.95448	-0.8946	1.61187
O	-4.20193	-2.01727	-0.42397
H	-5.13276	-1.80591	-0.58607
H	0.83875	-2.4442	-0.42023
O	6.0018	1.28371	0.05134
H	6.56441	0.51018	0.18947
H	2.78512	-1.93903	0.28371
O	5.4593	-1.30859	0.36307
C	5.24418	-2.70723	0.525
H	6.23115	-3.14986	0.64581
H	4.64096	-2.91306	1.41494
H	4.75722	-3.13574	-0.35671
O	4.02539	3.11718	-0.31926
H	4.98657	3.19661	-0.26778

5,4'-dihydroxy-6,7-dimethoxyflavone (**8**)

C	3.44532	-0.05771	0.15725
C	2.64244	1.0835	0.17634
C	1.22795	0.96067	0.11827
C	0.67101	-0.31948	0.05483
C	1.44727	-1.47022	0.03007
C	2.83871	-1.33162	0.0702
C	0.36515	2.13185	0.14985
H	0.96187	-2.43223	-0.03218

C	-1.52754	0.57851	0.03267
C	-1.05229	1.84824	0.11211
O	-0.68998	-0.49304	0.0049
O	0.81908	3.29092	0.21362
C	-2.94188	0.18164	-0.01589
C	-3.32736	-1.14103	0.26063
C	-3.9446	1.10786	-0.33634
C	-4.65887	-1.5216	0.2332
C	-5.28001	0.73478	-0.36726
H	-3.68358	2.12903	-0.58371
C	-5.64609	-0.58373	-0.07963
H	-6.04022	1.46606	-0.62475
O	4.80394	0.0236	0.27432
H	-2.57013	-1.87299	0.5064
H	-1.72806	2.68898	0.16783
O	3.21804	2.29126	0.25082
O	-6.93708	-1.01046	-0.09374
H	-7.51835	-0.27554	-0.31665
H	2.47616	2.95194	0.25567
H	-4.95611	-2.53938	0.4534
O	3.69872	-2.37421	0.03461
C	3.171	-3.69429	-0.01313
H	2.58121	-3.85796	-0.92147
H	4.03583	-4.35485	-0.02049
H	2.55659	-3.91014	0.86718
C	5.49155	0.53027	-0.87623
H	5.18989	1.55743	-1.09361
H	6.55196	0.50621	-0.62664
H	5.3107	-0.10693	-1.74881

Calculated thermodynamic parameters of isolated flavonoids (1-8).

Calculated thermodynamic parameters of compound 1.

	Total Energy	ZPE	TC Energy	TC enthalpy	TCGE
H·	-0.50215590	0	0.001416	0.00236	-0.010654
Flavonoid 1	-1344.77399636	0.455551	0.484509	0.485453	0.391976
Radicals					
4'-O	-1344.13507116	0.442719	0.471384	0.472328	0.378733
5-O	-1344.10312745	0.441122	0.470499	0.471443	0.375445
7-O	-1344.12021009	0.441862	0.470666	0.47161	0.377409
Anions					
4'-O	-1344.22349685	0.440985	0.469596	0.470541	0.377724
5-O	-1344.20212430	0.440537	0.469926	0.47087	0.375834
7-O	-1344.23060825	0.441927	0.4707	0.471644	0.378528
Cation					
	-1344.51743627	0.455121	0.484144	0.485089	0.390738

Calculated thermodynamic parameters of compound 2

	Total Energy	ZPE	TC Energy	TC enthalpy	TCGE
H·	-0.50215590	0	0.001416	0.00236	-0.010654
Flavonoid 2	-1149.38410856	0.337874	0.360301	0.361245	0.284692

Radicals					
4'-O	-1148.74144902	0.324945	0.347122	0.348066	0.271207
5-O	-1148.71796722	0.32386	0.34655	0.347494	0.269622
7-O	-1148.73451168	0.324166	0.346484	0.347428	0.269952
Anions					
4'-O	-1148.82612754	0.32358	0.345678	0.346622	0.271265
5-O	-1148.81684675	0.323014	0.345635	0.346579	0.270017
7-O	-1148.84561786	0.324319	0.346498	0.347443	0.271859
Cation					
	-1149.12264674	0.337645	0.360013	0.360957	0.284189

Calculated thermodynamic parameters of compound 3

	Total Energy	ZPE	TC Energy	TC enthalpy	TCGE
H·	-0.50215590	0	0.001416	0.00236	-0.010654
Flavonoid 3	-1420.01581765	0.45985900	0.49006800	0.49101200	0.39458200
Radicals					
2'-O	-1419.38051855	0.44668500	0.47672300	0.47766700	0.38029000
4'-O	-1419.37802897	0.44709000	0.47691900	0.47786300	0.38165400
5-O	-1419.34493301	0.44549800	0.47607900	0.47702300	0.37851100
7-O	-1419.33728392	0.44567000	0.47569600	0.47664000	0.37948400
Anions					
2'-O	-1419.47383516	0.44500200	0.47501800	0.47596300	0.38011000
4'-O	-1419.46681507	0.44559300	0.47533400	0.47627800	0.38123800
5-O	-1419.45015824	0.44509300	0.47560100	0.47654500	0.37882900
7-O	-1419.46872785	0.44619100	0.47626500	0.47720900	0.38095100
Cation					
	-1419.76165382	0.45984900	0.48984800	0.49079200	0.39493500

Calculated thermodynamic parameters of compound 4

	Total Energy	ZPE	TC Energy	TC enthalpy	TCGE
H·	-0.50215590	0	0.001416	0.00236	-0.010654
Flavonoid 4	-1224.63697330	0.34239200	0.36599800	0.36694200	0.28748100
Radicals					
3-O	-1223.99649052	0.32932800	0.35281100	0.35375500	0.27342900
4'-O	-1223.99589345	0.32941100	0.35274000	0.35368500	0.27409100
5-O	-1223.97640727	0.32850700	0.35218700	0.35313100	0.27294200
7-O	-1223.98922770	0.32884700	0.35222300	0.35316700	0.27352600
Anions					
3-O	-1224.08180006	0.32715100	0.35064900	0.35159300	0.27330600
4'-O	-1224.09645046	0.32833800	0.35170500	0.35264900	0.27440900
5-O	-1224.07837140	0.32778600	0.35131800	0.35226200	0.27373800
7-O	-1224.10213883	0.32895300	0.35226100	0.35320600	0.27494300
Cation					
	-1224.38066610	0.34269600	0.36617100	0.36711500	0.28756200

Calculated thermodynamic parameters of compound 5

	Total Energy	ZPE	TC Energy	TC enthalpy	TCGE
H·	-0.50215590	0	0.001416	0.00236	-0.01065
Flavonoid 5	-953.99081258	0.220691	0.236313	0.237257	0.177474
Radicals					
2'-O	-953.34550796	0.207553	0.222927	0.223871	0.163803
5-O	-953.30925051	0.207084	0.22276	0.223704	0.163145
7-O	-953.33789434	0.207065	0.222505	0.223449	0.163143
Anions					
2'-O	-953.44985537	0.206481	0.221851	0.222796	0.163397
5-O	-953.41162709	0.205644	0.221743	0.222687	0.161374
7-O	-953.44140423	0.206993	0.222465	0.223409	0.163664
Cation					
	-953.71200005	0.219429	0.234993	0.235937	0.175658

Calculated thermodynamic parameters of compound 6

	Total Energy	ZPE	TC Energy	TC enthalpy	TCGE
H·	-0.50215590	0	0.001416	0.00236	-0.010654
Flavonoid 6	-1183.08113878	0.285491	0.306807	0.307751	0.234378
Radicals					
4'-O	-1182.45869430	0.27273	0.293501	0.294445	0.22113
5-O	-1182.44252201	0.272278	0.293573	0.294517	0.219723
7-O	-1182.45568043	0.272757	0.293534	0.294478	0.221358
Anions					
4'-O	-1182.56103573	0.271535	0.292114	0.293058	0.221956
5-O	-1182.53177733	0.271348	0.292539	0.293483	0.219738
7-O	-1182.55139318	0.271781	0.292688	0.293632	0.220812
Cation					
	-1182.84173997	0.284443	0.305469	0.306413	0.233089

Calculated thermodynamic parameters of compound 7

	Total Energy	ZPE	TC Energy	TC enthalpy	TCGE
H·	-0.50215590	0	0.001416	0.00236	-0.010654
Flavonoid 7	-1258.32450438	0.28957600	0.31221500	0.31315900	0.23709700
Radicals					
5'-O	-1257.69980438	0.27740800	0.29928600	0.30023000	0.22467900
4'-O	-1257.71591373	0.27786500	0.29953500	0.30047900	0.22528000
5-O	-1257.68596860	0.27635000	0.29897900	0.29992300	0.22226200
7-O	-1257.68200099	0.27633000	0.29887400	0.29981800	0.22258800
Anions					
5'-O	-1257.78698413	0.27559100	0.29759800	0.29854200	0.22354800
4'-O	-1257.81550055	0.27626800	0.29786100	0.29880500	0.22543600
5-O	-1257.77452589	0.27548100	0.29800600	0.29895000	0.22276900
7-O	-1257.78097538	0.27586200	0.29830400	0.29924800	0.22310600
Cation					
	-1258.06176149	0.28886000	0.31154000	0.31248400	0.23572800

Calculated thermodynamic parameters of compound 8

	Total Energy	ZPE	TC Energy	TC enthalpy	TCGE
H·	-0.50215590	0	0.001416	0.00236	-0.01065
Flavonoid 8	-1107.84745381	0.280735	0.300782	0.301726	0.231208
Radicals					
4'-O	-1107.20278723	0.267534	0.287392	0.288336	0.217356
5-O	-1107.19017057	0.267626	0.287835	0.288779	0.216589
Anions					
4'-O	-1107.31332809	0.266746	0.286452	0.287396	0.217896
5-O	-1107.27196199	0.265674	0.286068	0.287012	0.214902
Cation					
	-1107.60543538	0.281549	0.301445	0.30239	0.231861

Characterization of spectral data of isolated flavonoids (1-8)

*3'-geranyl-5,7,4'-trihydroxyisoflavone (**1**)*

Compound **1** was obtained as pale yellow oil, IR ν_{max} (KBr) cm^{-1}: 3418, 1705, 1661, 1509 and 1402; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.74 (3H, s, H-9"), 1.77 (3H, s, H-8"), 1.82 (3H, s, H-10"), 2.24 (4H, m, H-4",H-5"), 3.73 (2H, d, H-1"), 5.38 (1H, m, H-6"), 5.64 (1H, m, H-2"), 5.96 (1H, d, H-6), 6.06 (1H, d, H-8), 6.59 (1H, d, H-2'), 6.78 (1H, d, H-5'), 7.22 (1H, dd, H-6'), 7.78 (1H, s, H-2); ^{13}C NMR (125 MHz, $CDCl_3$): δ_c 16.44 (C-8"), 18.43 (C-9"), 22.43 (C-10"), 25.98 (C-5"), 28.80 (C-1"), 39.43 (C-4"), 93.28 (C-8), 98.78 (C-6), 106.44 (C-4a), 114.53 (C-5'), 121.74 (C-2"), 122.51 (C-3), 123.28 (C-6"), 127.43 (C-6'), 128.02 (C-2'), 132.02 (C-3'), 133.43 (C-1'), 137.03 (C-7"), 140.02 (C-3"), 152.42 (C-2), 155.13 (C-4'), 158.03 (C-8a), 162.70 (C-5), 164.84 (C-7), 180.99 (C-4).

*6-prenyl-5,7,4'-trihydroxyisoflavone (**2**)*

Compound **2** was obtained as yellow amorphous powder, IR ν_{max} (KBr) cm^{-1}: 3425, 1718, 1652, 1517, 1402 and 1391; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.75 (3H, s, H-4"), 1.81 (3H, s, H-5"), 3.57 (2H, m, H-1"), 5.47 (1H, t, H-2"), 6.38 (1H, s, H-8), 6.41 (1H, d, H-3',-5'), 7.15 (1H, d, H-2',-6'), 7.89 (1H, s, H-2); ^{13}C NMR (125 MHz, $CDCl_3$): δ_c 18.31 (C-4"), 27.71 (C-1"), 29.79 (C-5"), 93.29 (C-8), 106.36 (C-4a), 115.19 (C-6), 118.67 (C-3', -5'), 120.68 (C-2"), 123.99 (C-3), 127.42 (C-1'), 133.29 (C-2', -6'), 137.48 (C-3"), 152.12 (C-2), 154.93 (C-8a), 158.02 (C-4'), 162.65 (C-5), 164.88 (C-7) and 180.87 (C-4).

*3'-geranyl-5,7,2',4'-tetrahydroxyisoflavone (**3**)*

Compound **3** was obtained as pale yellow oil, IR ν_{max} (KBr) cm^{-1}: 3432, 1721, 1648, 1513, 1412 and 1386; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.75 (3H, s, H-9"), 1.79 (3H, s, H-8"), 1.85 (3H, s, H-10"), 2.25 (4H, m, H-4",H-5"), 3.68 (2H, m, H-1"), 5.26 (1H, m, H-6"), 5.53 (1H, m, H-2"), 5.95 (1H, d, H-6), 5.98 (1H, d, H-8), 6.74 (1H, d, H-5'), 7.12 (1H, d, H-6'), 8.13 (1H, s, H-2); ^{13}C NMR (125 MHz, $CDCl_3$): δ_c 17.03 (C-8"), 18.80 (C-9"), 22.53 (C-10"), 27.03 (C-5"), 29.42 (C-1"), 37.57 (C-4"), 94.08 (C-8), 99.04 (C-6), 103.02 (C-4a), 106.52 (C-5'), 108.22 (C-1'), 117.33 (C-3'), 122.32 (C-3), 123.43 (C-2"), 124.44 (C-6"), 130.03 (C-6'), 131.40 (C-7"), 134.13 (C-3"), 152.03 (C-2),154.13 (C-2'), 157.40 (C-4'),159.99 (C-8a),164.80 (C-5),167.39 (C-7), 181.41 (C-4).

*6-prenyl-3,5,7,4'-tetrahydroxyflavone (**4**)*

Compound **4** was obtained as yellow crystalline needles, IR ν_{max} (KBr) cm^{-1}: 3441, 1728, 1633, 1519, 1423 and 1389; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.77 (3H, s, H-4"), 1.82 (3H, s, H-5"), 3.62 (2H, m, H-1"), 5.51 (1H, t, H-2"), 6.58 (1H, s, H-8), 6.78 (1H, d, H-3',-5'), 7.37 (1H, d, H-2',-6'); ^{13}C NMR (125 MHz, $CDCl_3$): δ_c 19.29 (C-4"), 23.31 (C-1"), 26.36 (C-5"), 92.12 (C-8), 104.42 (C-4a), 110.02 (C-6), 115.67 (C-3', -5'), 121.68 (C-1'), 123.69 (C-2"), 128.02 (C-2', -6'), 132.48 (C-3"), 135.69 (C-3), 146.03 (C-2), 156.02 (C-8a), 158.88 (C-4'), 163.89 (C-5), 166.08 (C-7) and 177.55 (C-4).

*5,7,2'-trihydroxyflavone (**5**)*

Compound **5** was obtained as yellow amorphous powder, IR ν_{max} (KBr) cm^{-1}: 3462, 1733, 1621 and 1509; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 5.97 (1H, d, H-6), 6.05 (1H, d, H-8), 6.62 (1H, d, H-3'), 7.03 (1H, dd, H-5'), 7.07 (1H, m, H-4'), 7.74 (1H, d, H-6'); ^{13}C NMR (125 MHz, $CDCl_3$): δ_c 95.73 (C-8), 98.46 (C-8), 103.78 (C-4a), 117.78 (C-3'), 118.48 (C-1'), 122.23 (C-5'), 128.70 (C-6'), 129.25 (C-4'), 136.25 (C-3), 149.48 (C-2), 156.54 (C-2'), 157.73 (C-8a), 161.77 (C-5), 166.55 (C-7), 175.57 (C-4).

*5,7,4'-trihydroxy-6,3'-dimethoxyflavone (**6**)*

Compound **6** was obtained as yellow amorphous powder, IR ν_{max} (KBr) cm^{-1}: 3482, 1738, 1631, 1401 and 1511; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.76 (3H, s, 6-OMe), 3.83 (3H, s, 3'-OMe), 6.04 (1H, s, H-8), 6.28, (1H, d, H-2'), 6.57 (1H, d, H-3), 6.96 (1H, d, H-5'), 7.09 (1H, dd, H-6'); ^{13}C NMR (125 MHz, $CDCl_3$): δ_c 56.56 (C-3'-OMe), 61.28 (C-6-OMe), 96.35 (C-8), 104.08 (C-3), 106.02 (C-4a), 112.56 (C-2'), 113.90 (C-5'), 121.66 (C-6'), 122.36 (C-1'), 131.96 (C-6), 144.96 (C-4'), 148.38 (C-3'), 151.45 (C-8a), 154.98 (C-5), 162.66 (C-7), 182.69 (C-4).

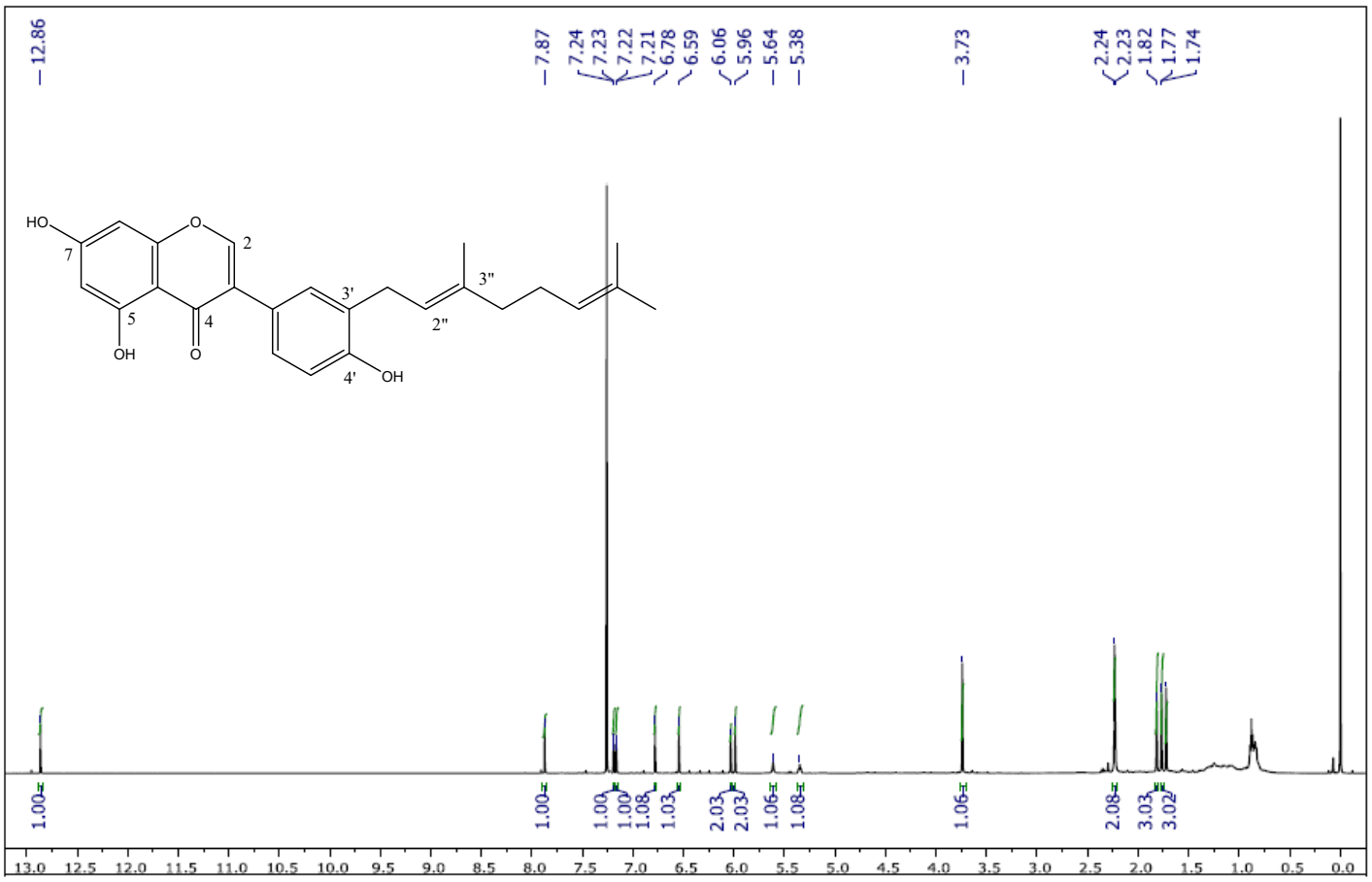
*5,7,4',5'-tetrahydroxy-6,3'-dimethoxyflavone (**7**)*

Compound **7** was obtained as yellow amorphous powder, IR ν_{max} (KBr) cm^{-1}: 3396, 1742, 1645, 1408 and 1516; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.79 (3H, s, 6-OMe), 3.87 (3H, s, 3'-OMe), 6.10 (1H, s, H-8), 6.27 (1H, d, H-6') 6.32 (1H, d, H-2'), 6.88 (1H, s, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): δ_c 58.02 (C-3'-OMe), 63.38 (C-6-OMe), 94.08 (C-8), 104.22 (C-3), 105.02 (C-2'), 106.65 (C-4a), 108.45 (C-6'), 127.48 (C-1'), 131.69 (C-6), 135.66 (C-4'), 146.67 (C-5'), 150.04 (C-3'), 153.65 (C-8a), 156.67 (C-5), 161.59 (C-7), 164.76 (C-2), 184.56 (C-4).

*5,4'-dihydroxy-6,7-dimethoxyflavone (**8**)*

Compound **8** was obtained as yellow amorphous powder, IR ν_{max} (KBr) cm^{-1}: 3425, 1729, 1632, 1389 and 1507; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.74 (3H, s, 6-OMe), 3.80 (3H, s, 7-OMe), 6.11 (1H, s, H-8), 6.41 (1H, d, H-3', -5'), 6.69 (1H, s, H-3), 7.38 (1H, d, H-2', -6'); ^{13}C NMR (125 MHz, $CDCl_3$): δ_c 56.70 (C-7-OMe), 62.54 (C-6-OMe), 93.27 (C-8), 104.39 (C-3), 108.90 (C-4a), 115.17 (C-3', -5'), 120.68 (C-1'), 126.70 (C-2', -6'), 132.48 (C-6), 150.39 (C-8a), 152.27 (C-5), 155.03 (C-4'), 158.33 (C-7), 163.02 (C-2), 182.87 (C-4).

^{1}H NMR and ^{13}C NMR Spectral data of isolated compounds (1-8)



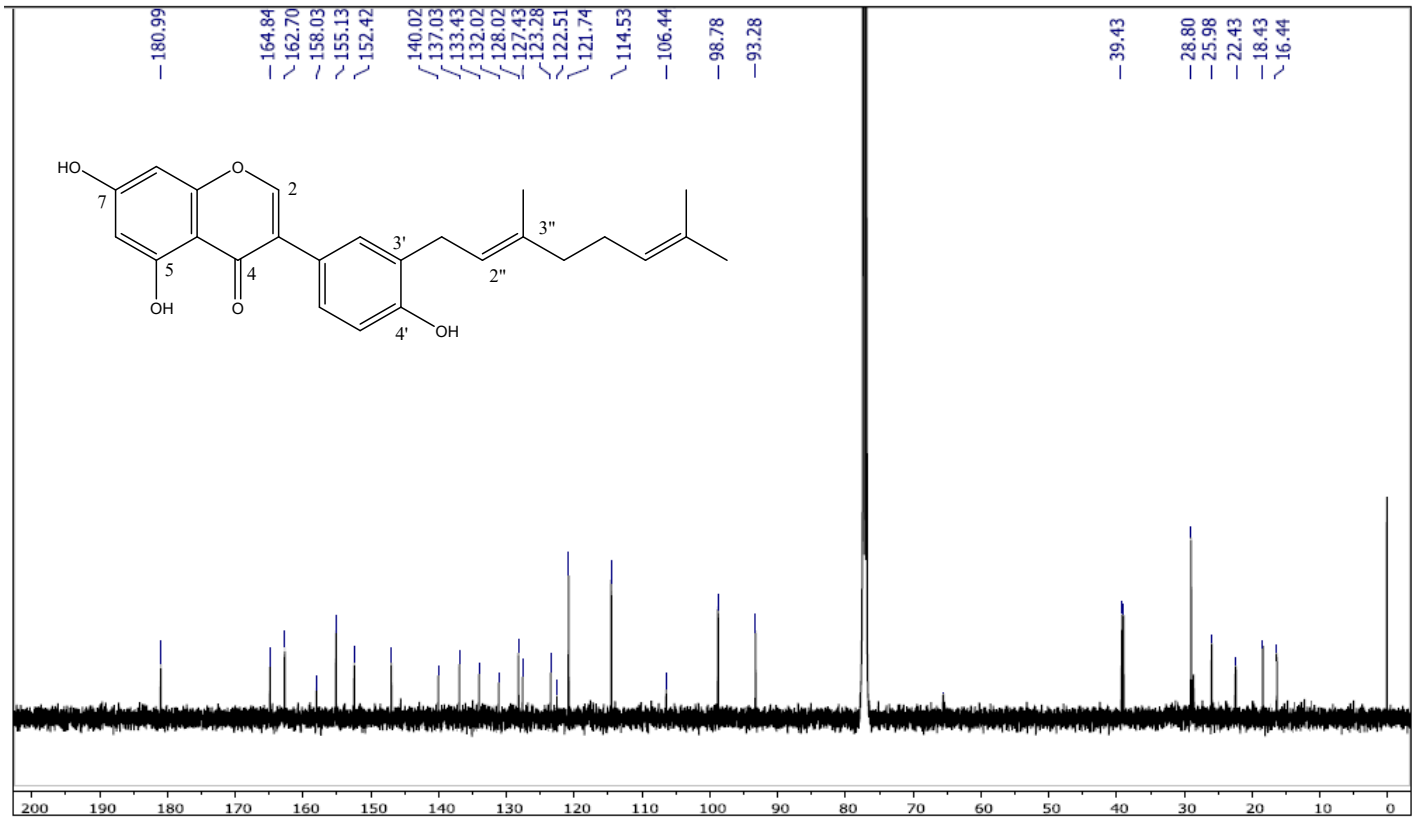


Figure S1. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **1**

Figure S2. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) compound **1**

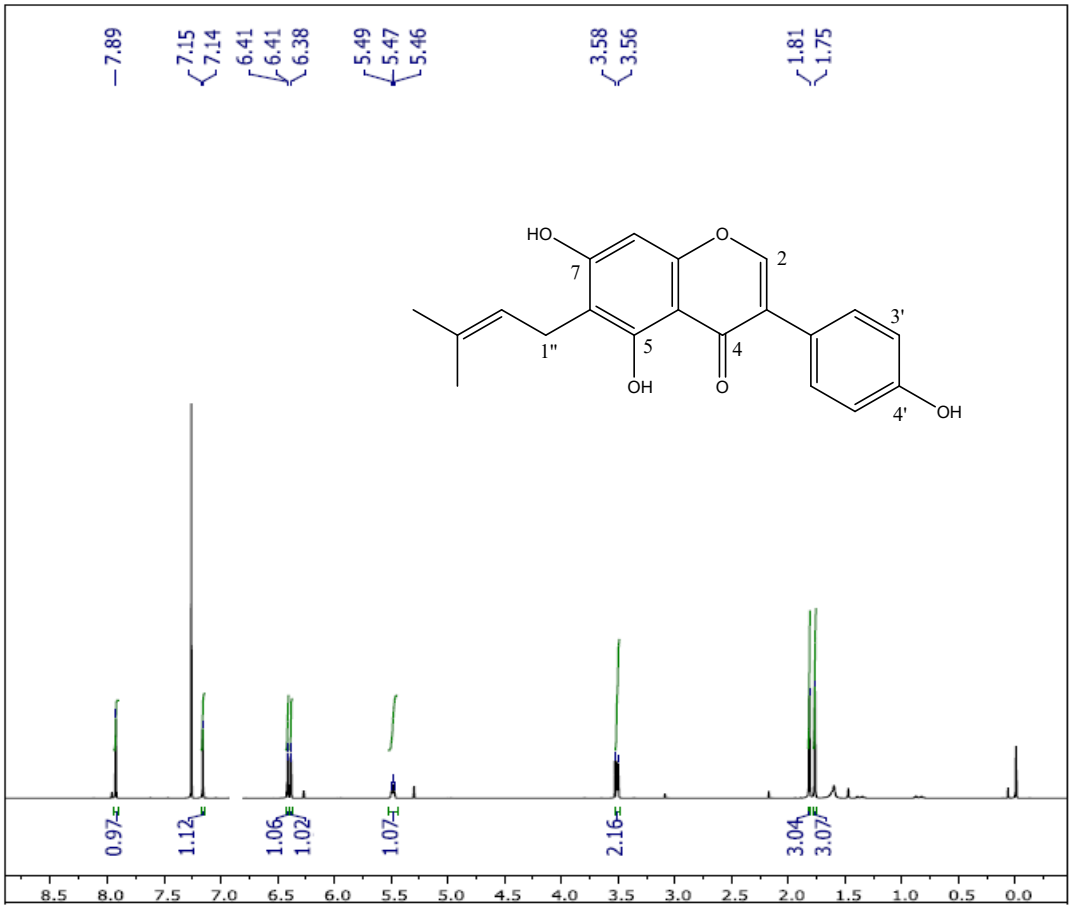


Figure S3. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **2**

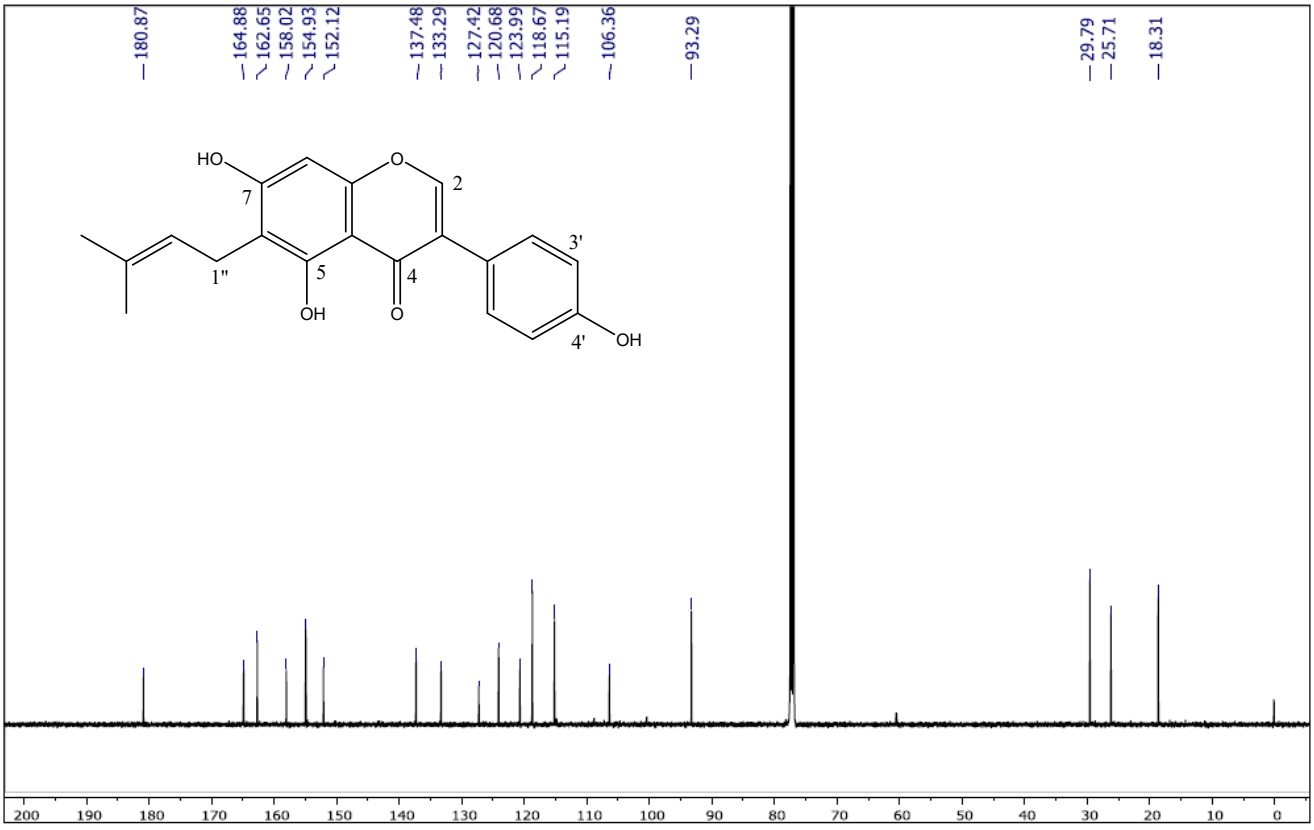
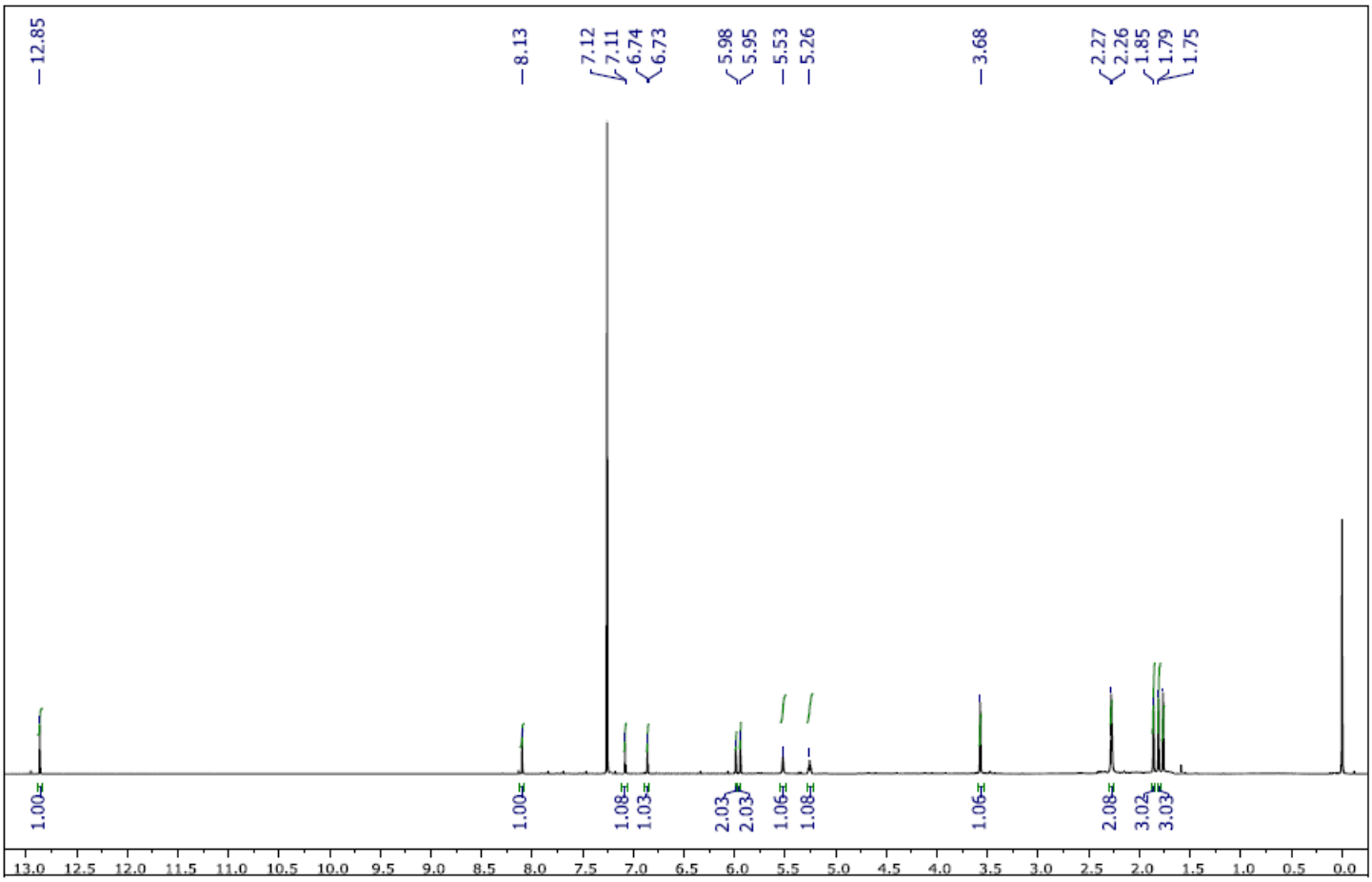


Figure S4. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) compound **2**



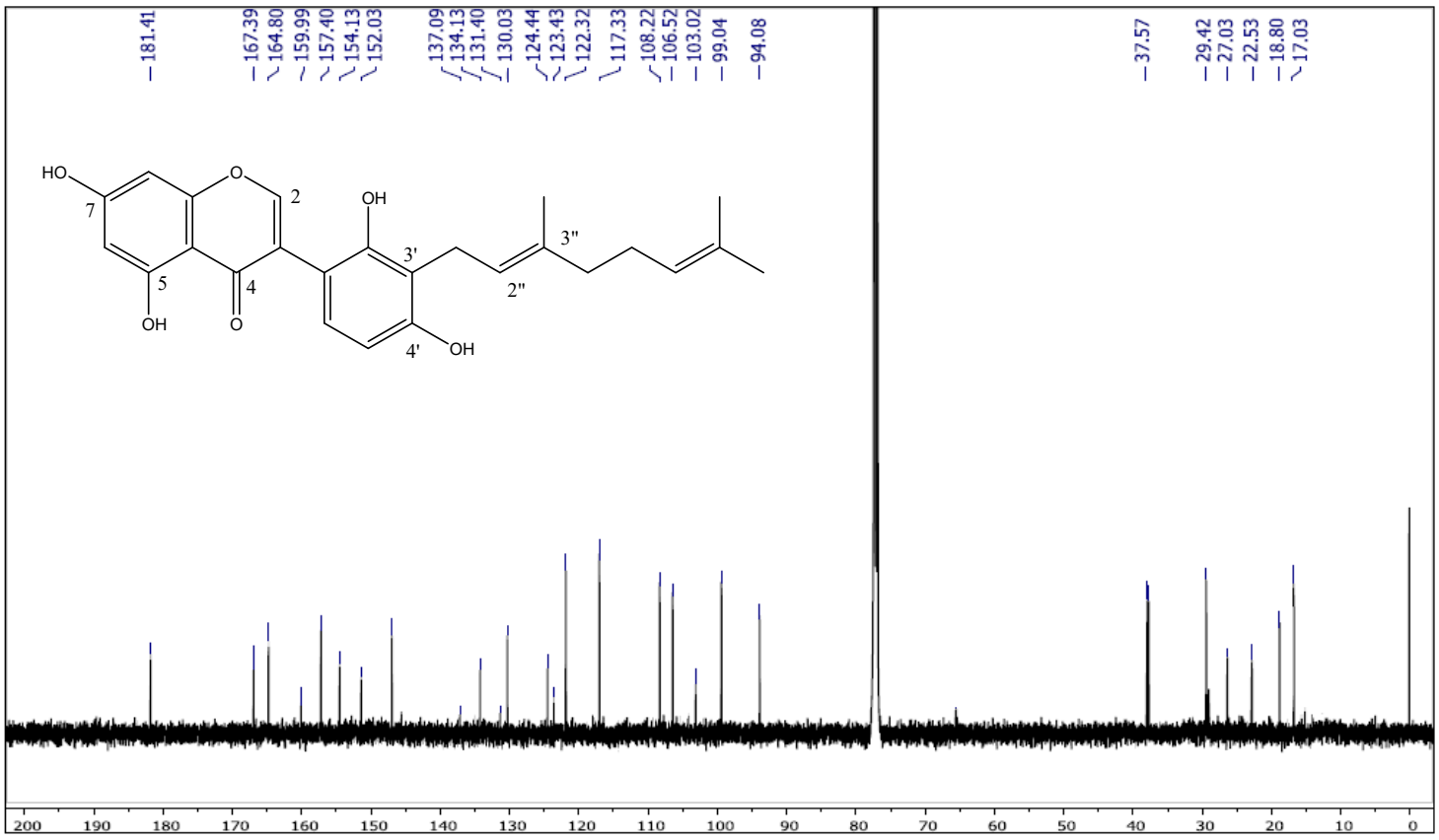
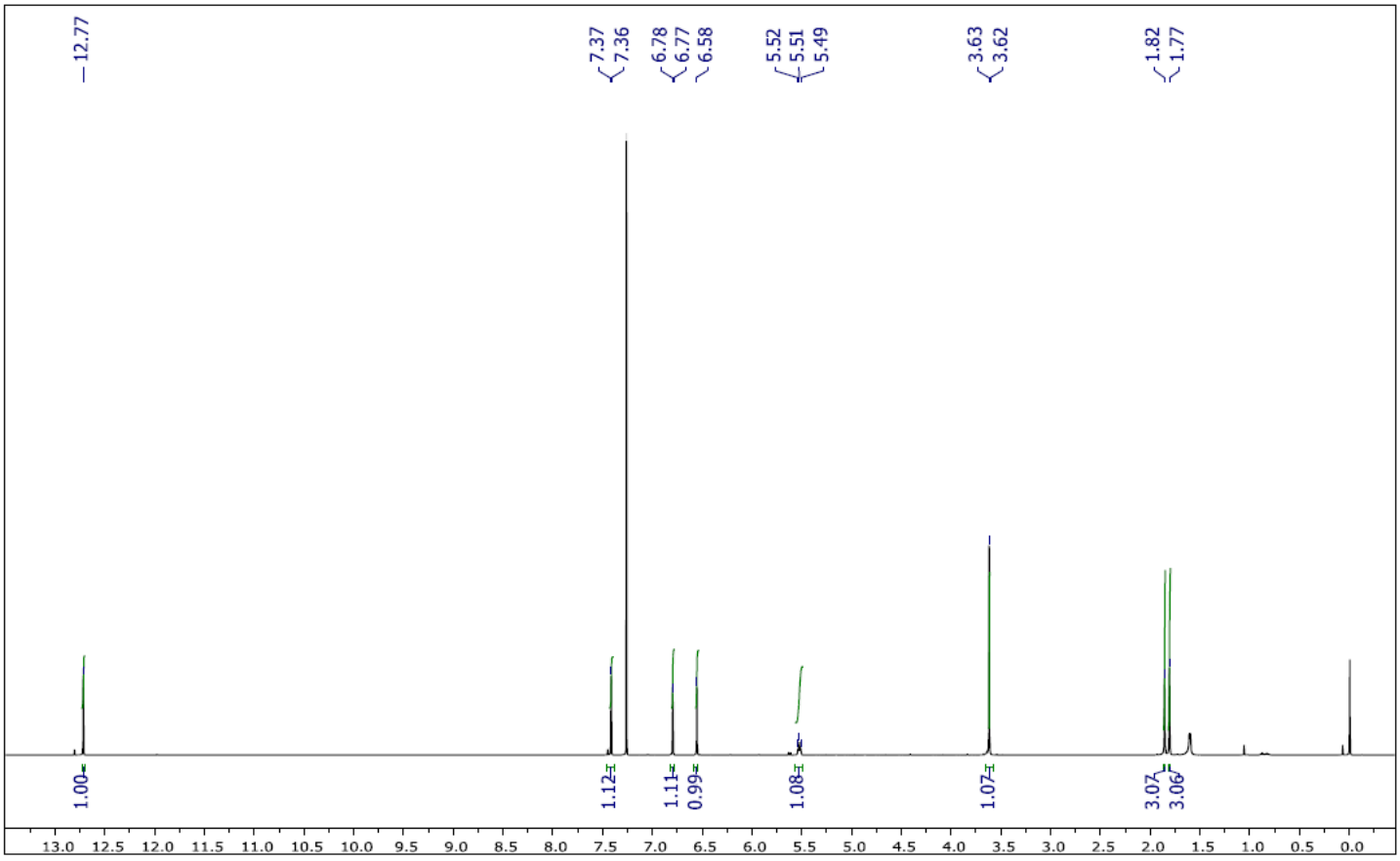


Figure S5. ^{1}H NMR spectrum (5 00 MHz, $CDCl_3$) of compound **3**

Figure S6. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) compound **3**



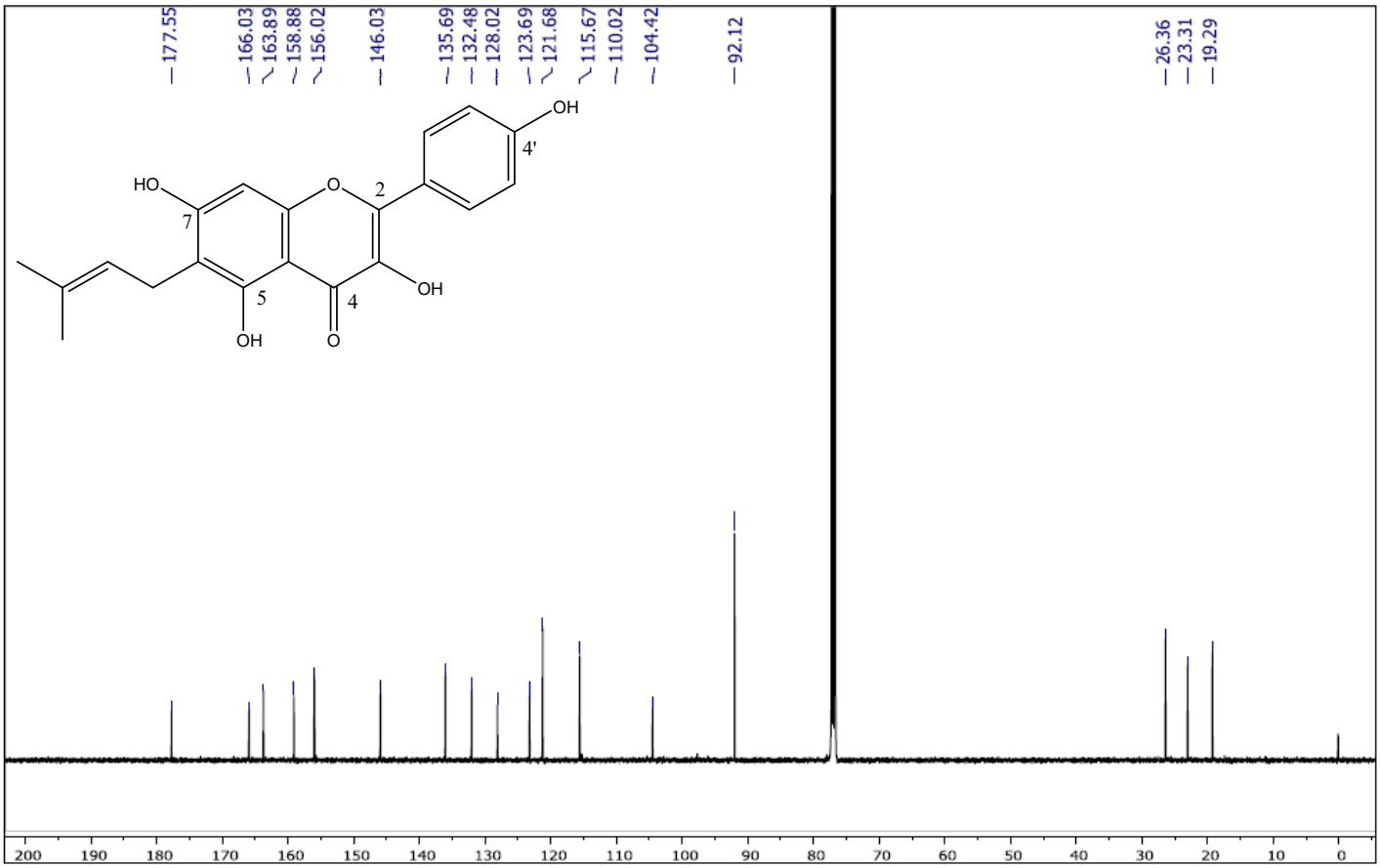


Figure S7. ^{1}H NMR spectrum (5 00 MHz, $CDCl_3$) of compound **4**

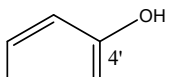


Figure S8. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) compound **4**

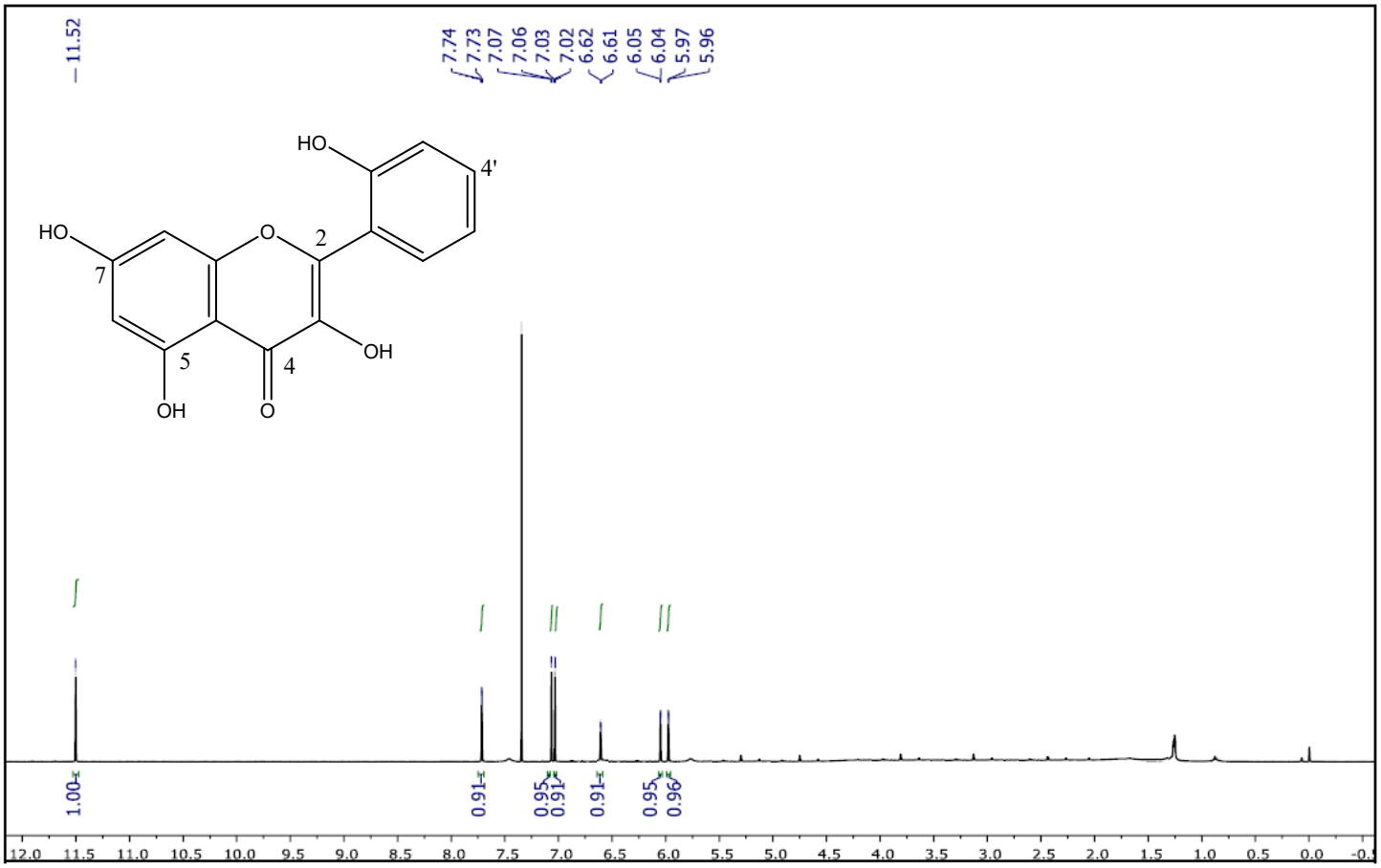


Figure S9. ^{1}H NMR spectrum (5 00 MHz, $CDCl_3$) of compound **5**

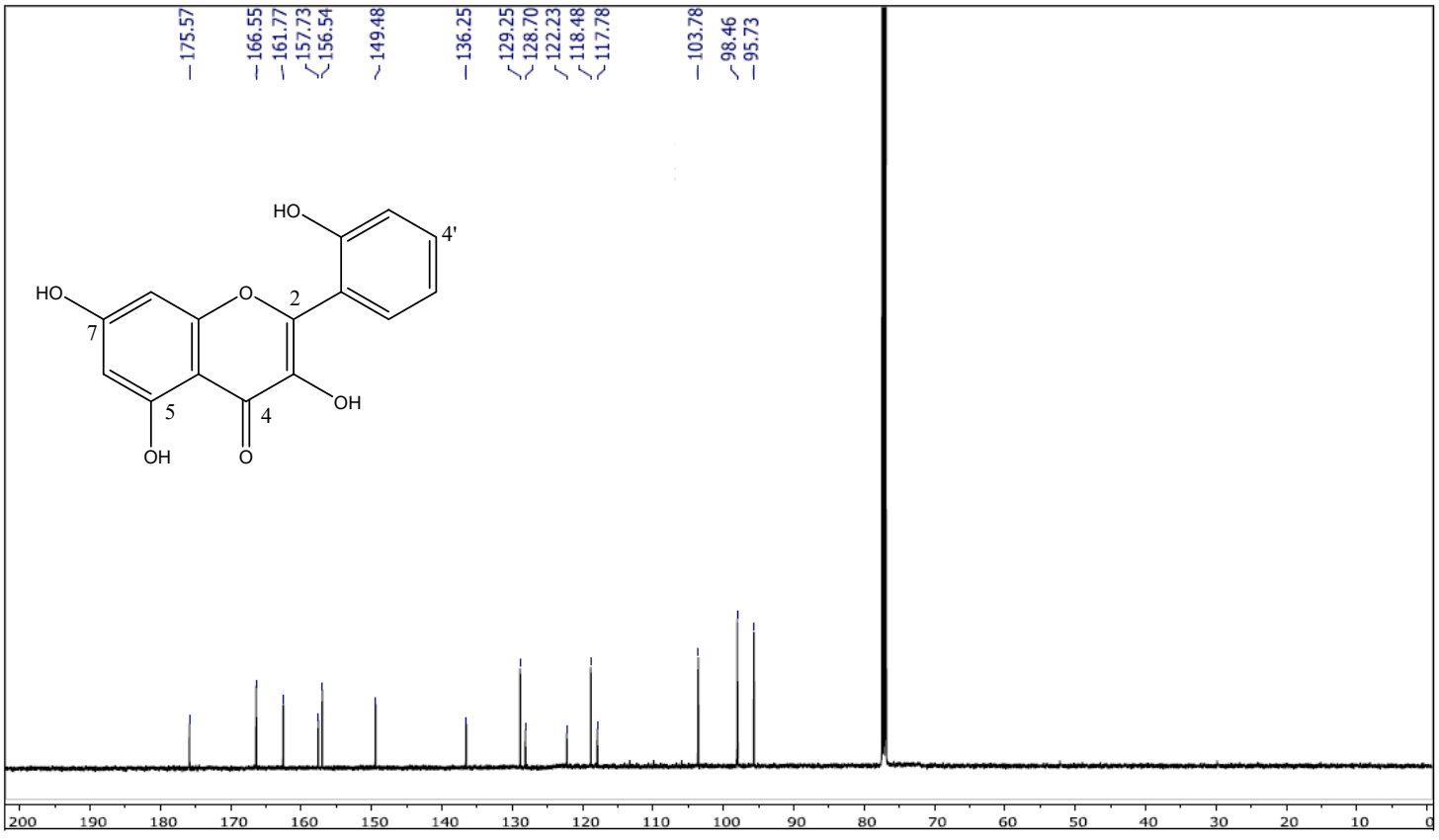


Figure S10. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) compound **5**

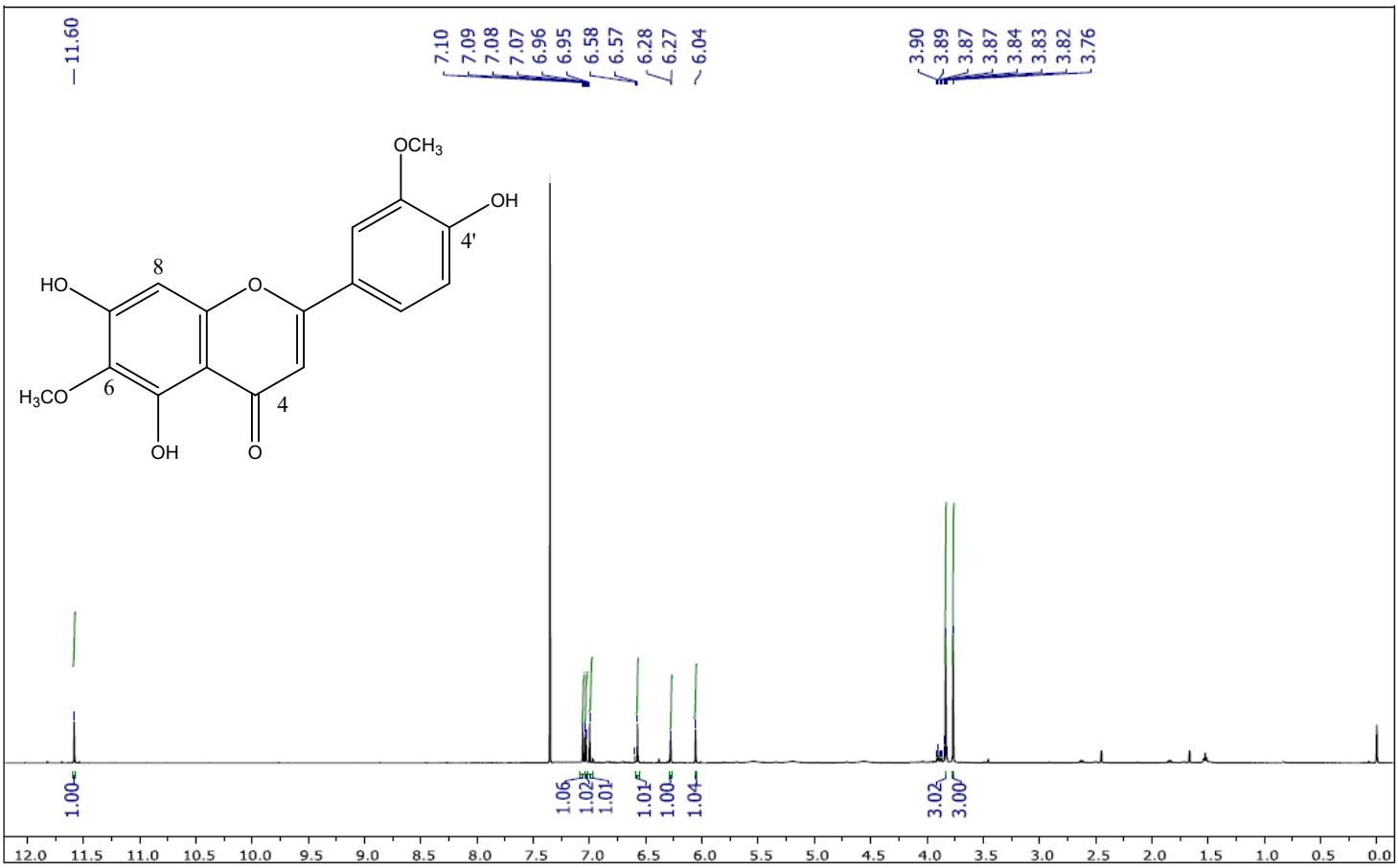


Figure S11. ^{1}H NMR spectrum (5 00 MHz, $CDCl_3$) of compound **6**

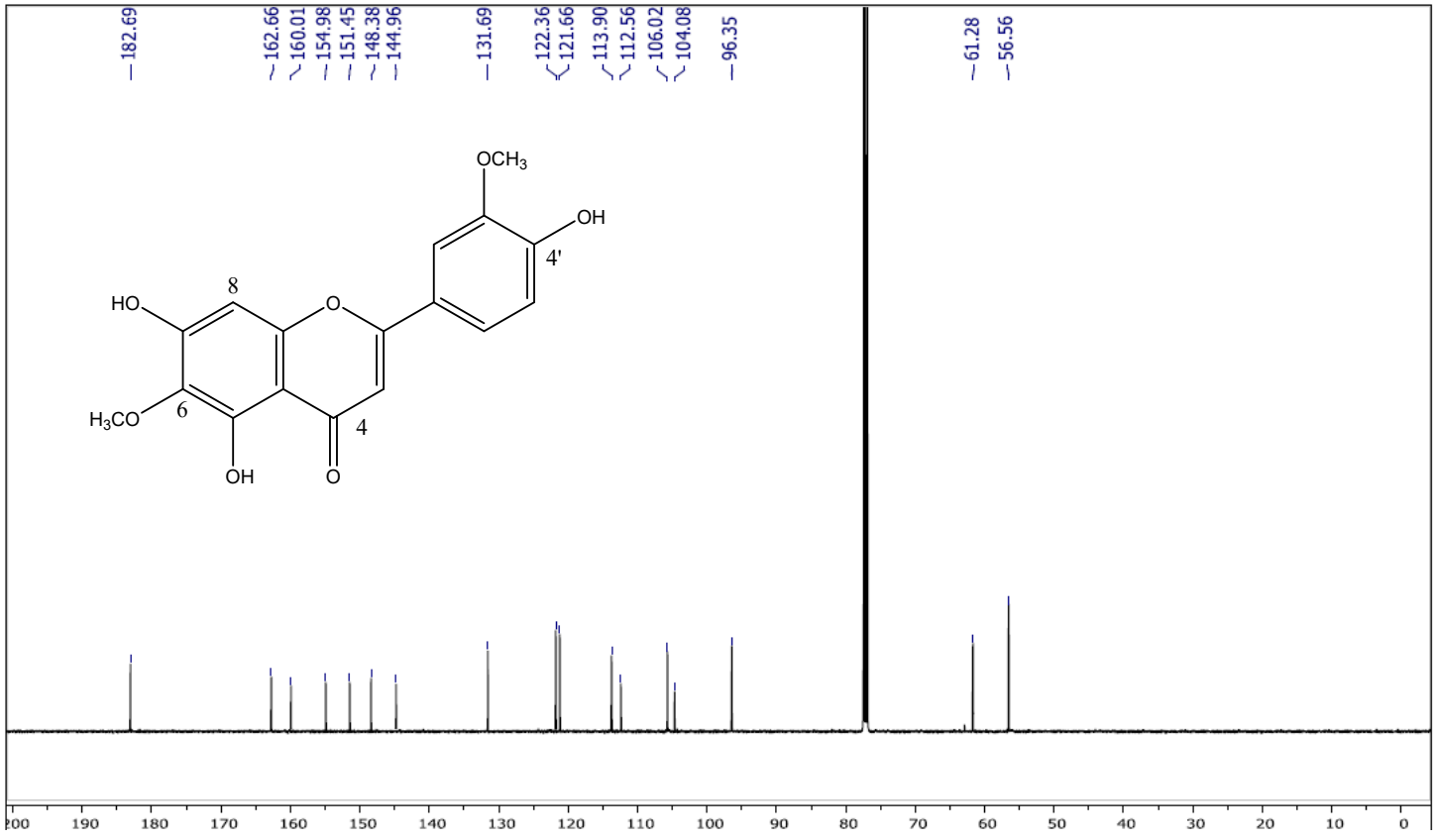
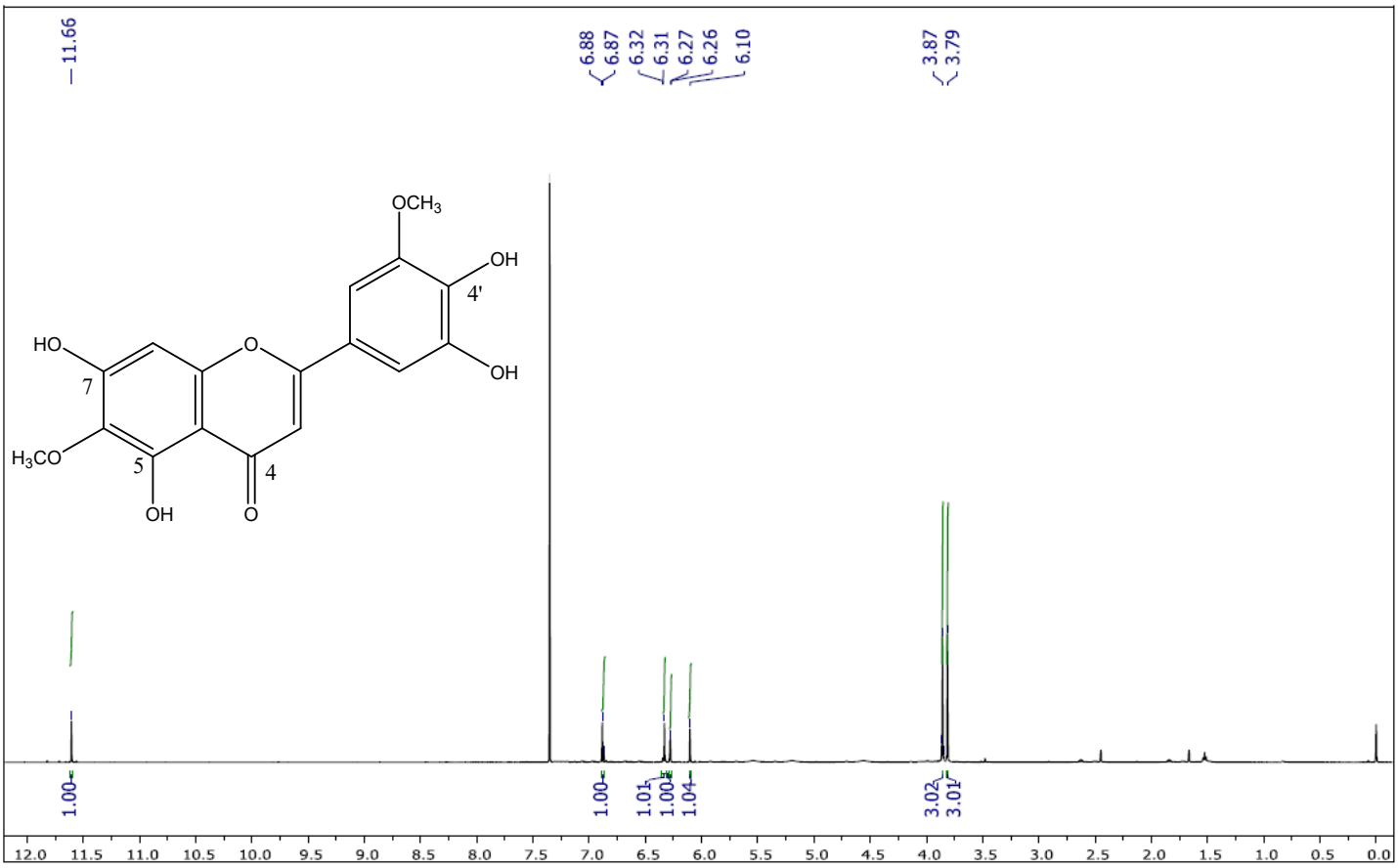


Figure S12. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) compound **6**



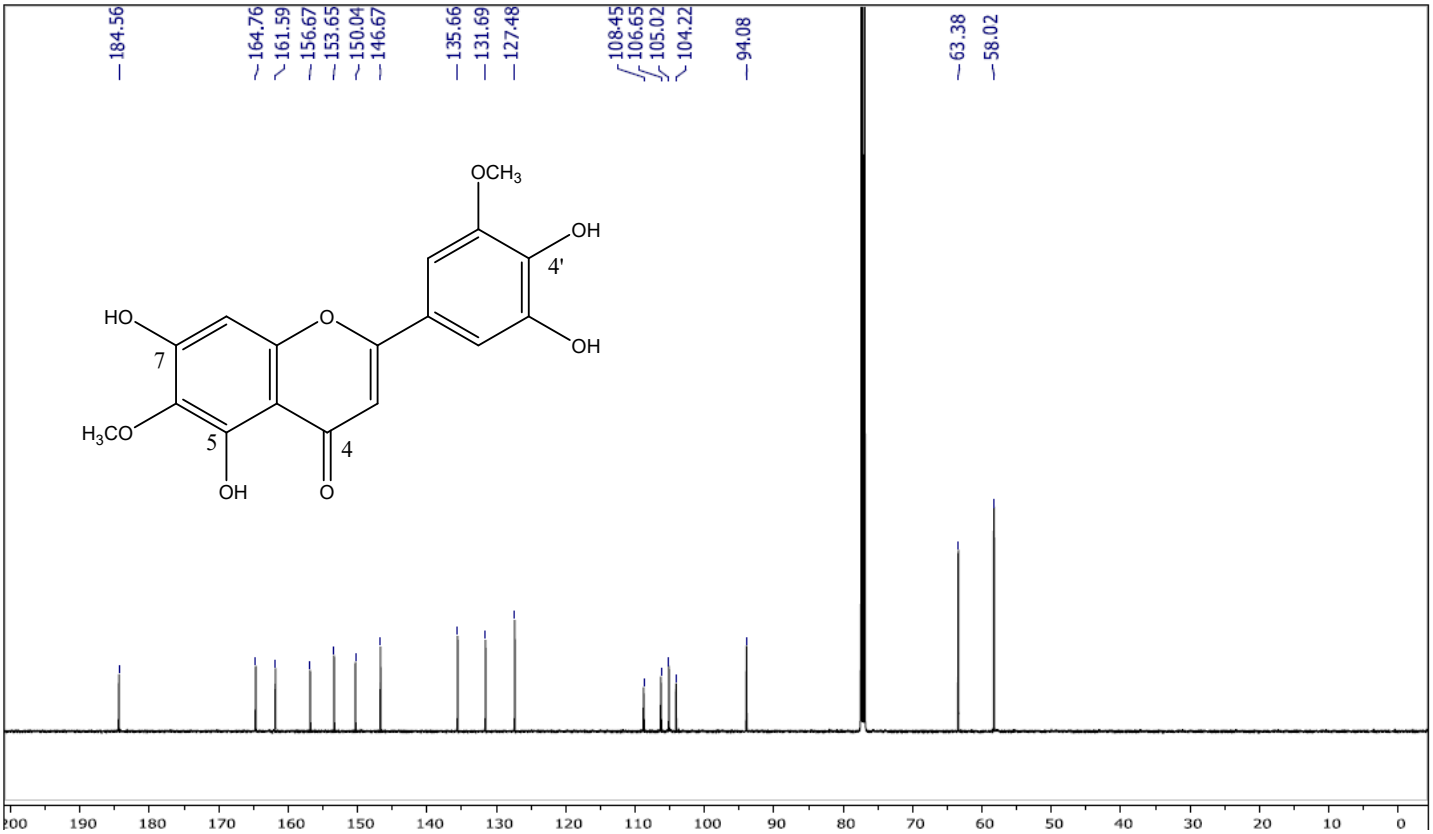
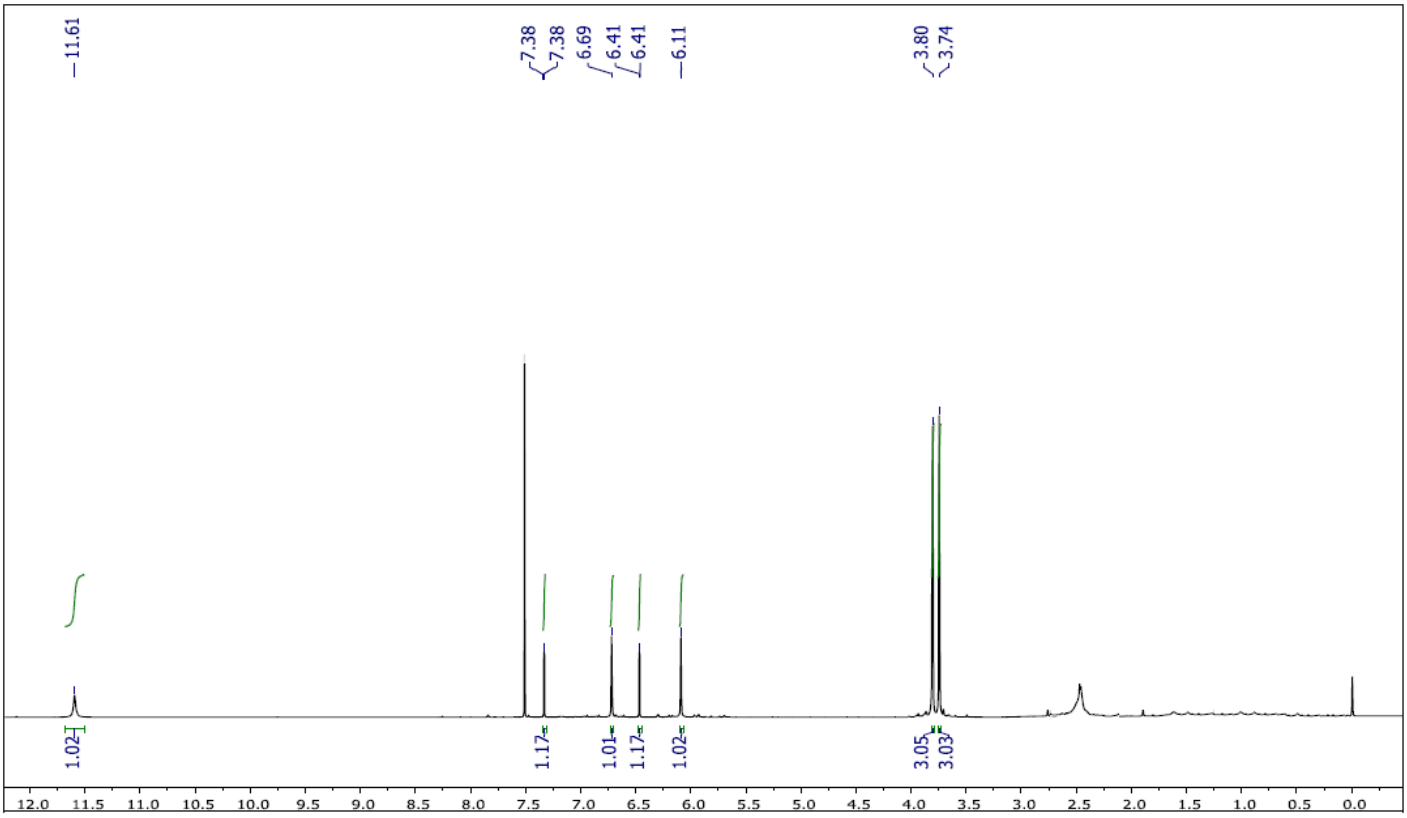


Figure S13. ^{1}H NMR spectrum (5 00 MHz, $CDCl_3$) of compound **7**

Figure S14. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) compound **7**



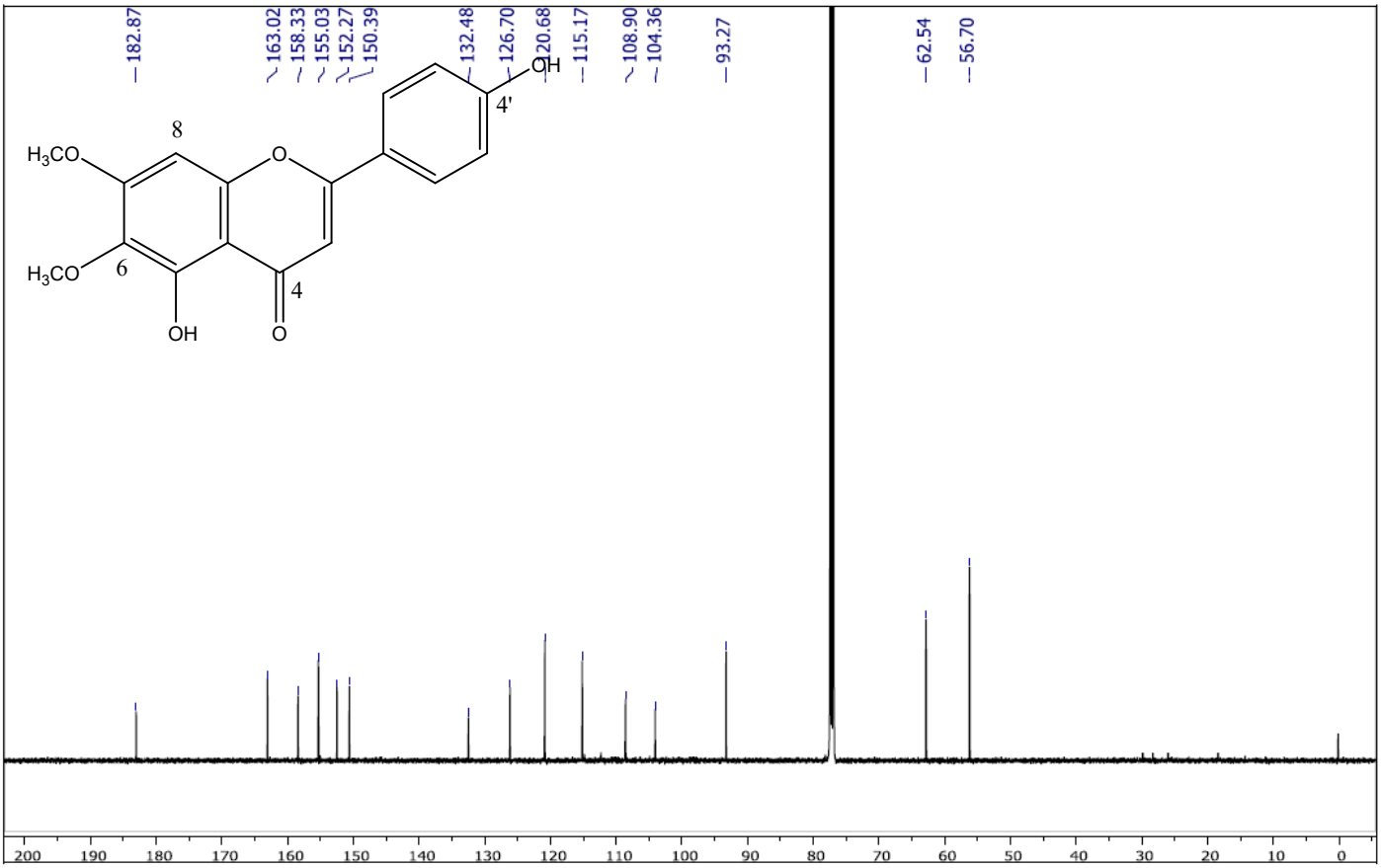
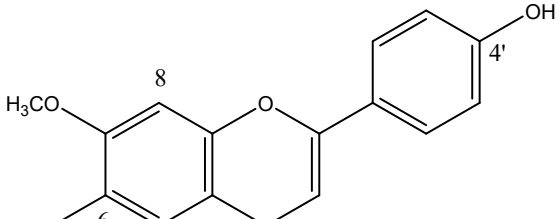


Figure S15. ^{1}H NMR spectrum (5 00 MHz, $CDCl_3$) of compound **8**

Figure S16. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) compound **8**



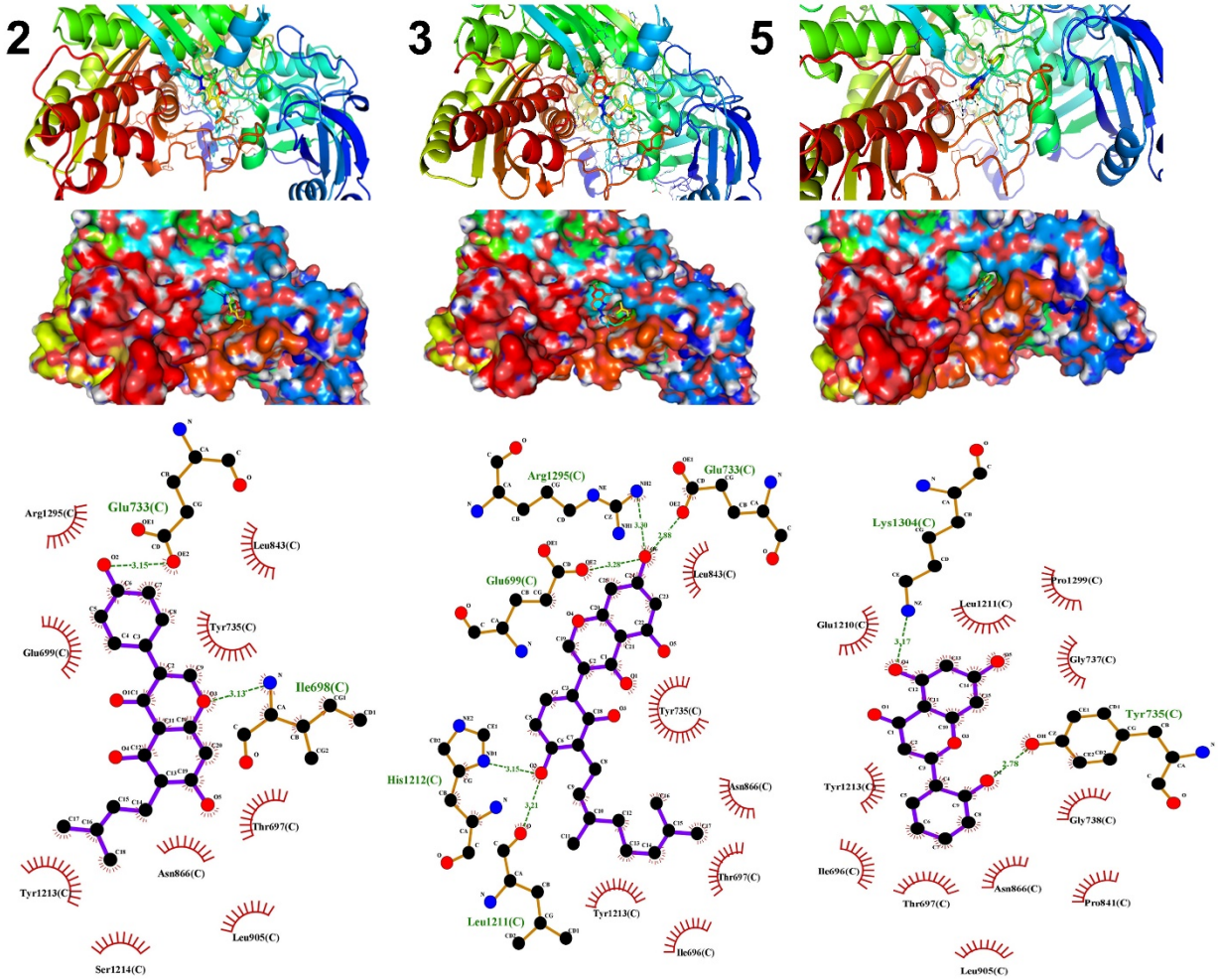


Figure S17. Molecular docking outputs showing the binding modes of compounds **2**, **3**, and **5** with XO.

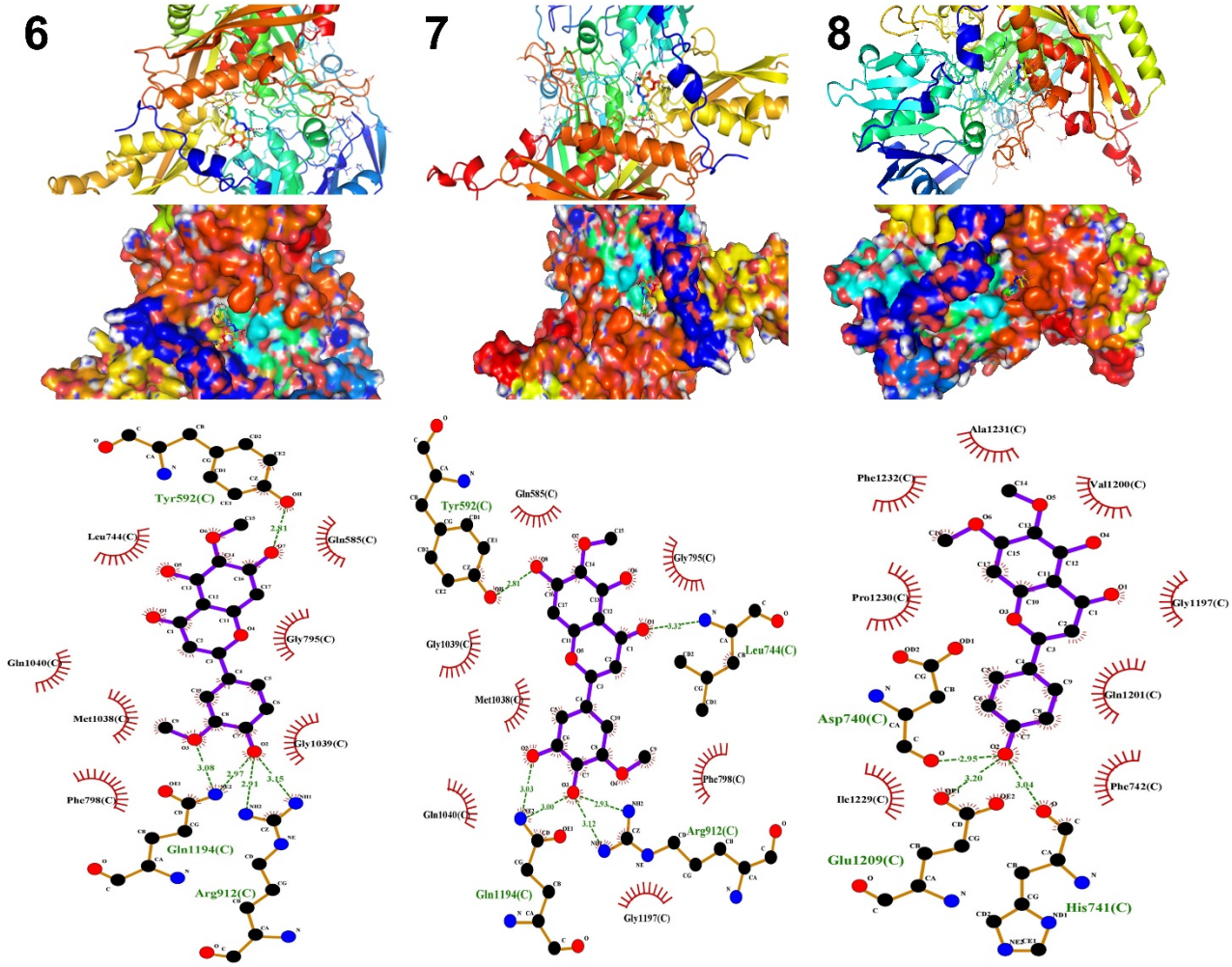


Figure S18. Molecular docking outputs showing the binding modes of compounds **6**, **7**, and **8**.

Thermodynamic parameters calculation equations

The homolytic bonding dissociation enthalpy (BDE) of O-H characterizes better the HAT mechanism and can be calculated by the following equation:

$$BDE = H_{(Flav—O^{\bullet})} + H_{(H)} - H_{(Flav—OH)} \quad (1)$$

Where $H_{(Flav—O^{\bullet})}$, $H_{(H)}$ and $H_{(Flav—OH)}$ are the enthalpies of phenoxyl radical, hydrogen atom and the flavonoids molecule, respectively.

According to the SET-PT mechanism, the flavonoid donates an electron to the radical forming $Flav—OH^{\bullet+}$ and consequently the interaction of both $Flav—O^{\bullet}$ and $Flav—OH^{\bullet+}$ causes the radicals to be stabilized which suppresses or attenuates the radical chain reaction. This electron transfer process is expressed by the variation of the ionization potential (IP) as follow:

$$IP = H_{(Flav—OH^{\bullet+})} + H_{(e)} - H_{(Flav—OH)} \quad (2)$$

Where $H_{(Flav—OH^{\bullet+})}$ and $H_{(e)}$ are the enthalpies of flavonoid radical cation and electron, respectively. Subsequent to the single electron transfer process the deprotonation of the previously formed flavonoid radical cation. This step can be descried as the hydroxyl proton dissociation enthalpy (PDE) and can be deduce from the following equation:

$$PDE = H_{(Flav—O^{\bullet})} + H_{(H+)} - H_{(Flav—OH^{\bullet+})} \quad (3)$$

Where $H_{(H+)}$ is the enthalpy of proton

In the SPLET mechanism, the flavonoid molecule is deprotonated in the first step to afford a phenoxide anion, this step needs the evaluation of the proton affinity (PA) of the phenoxide anion as follow:

$$PA = H_{(Flav—O^{-})} + H_{(H+)} - H_{(Flav—OH)} \quad (4)$$

Where $H_{(Flav—O^{-})}$ is the enthalpy of the flavonoid anion. The next step is the electron transfer from the phenoxide anion, this step reveals the electron transfer enthalpy (ETE) and can be evaluated by the following equation:

$$ETE = H_{(Flav—O^{\bullet})} + H_{(e^{-})} - H_{(Flav—O^{-})} \quad (5)$$

Optimized geometries and Mulliken spin populations of all radical flavonoids

Compound 1

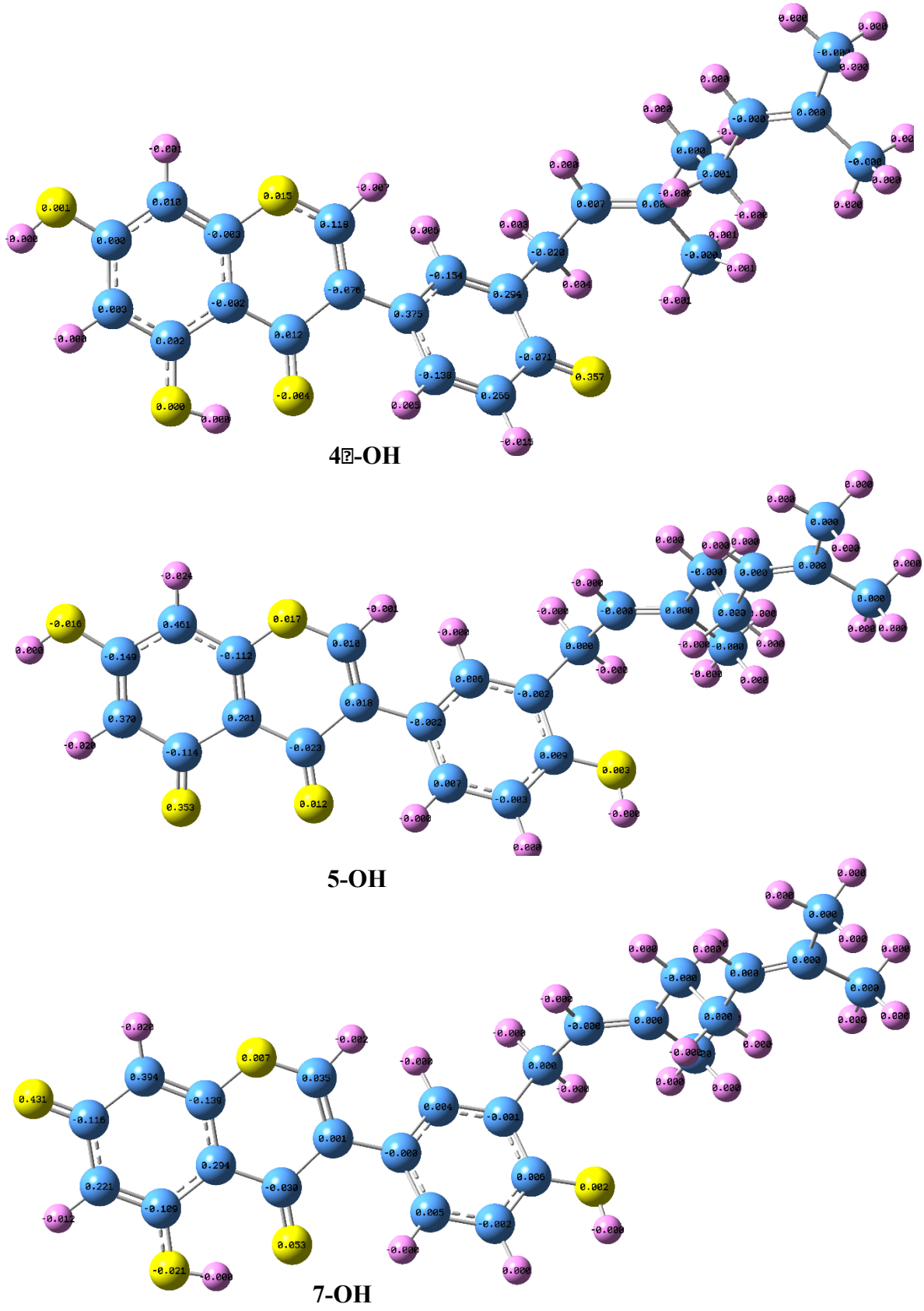
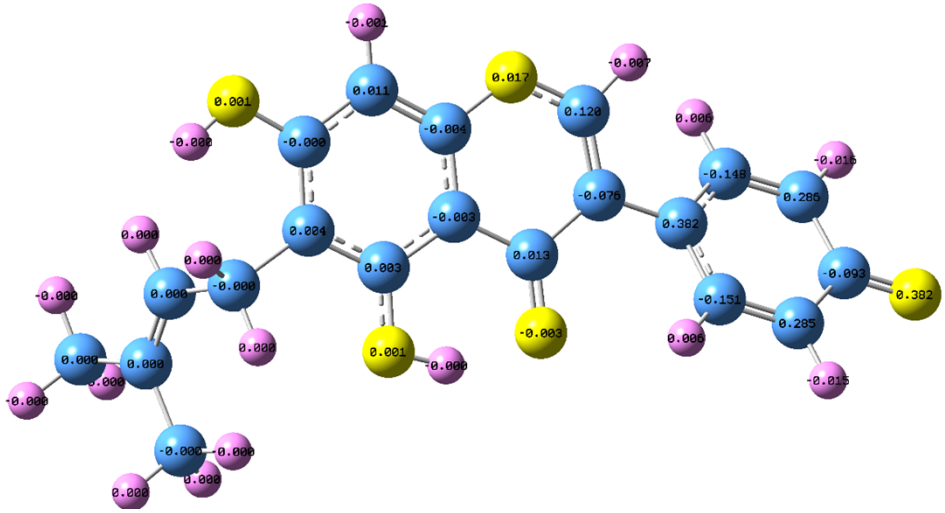
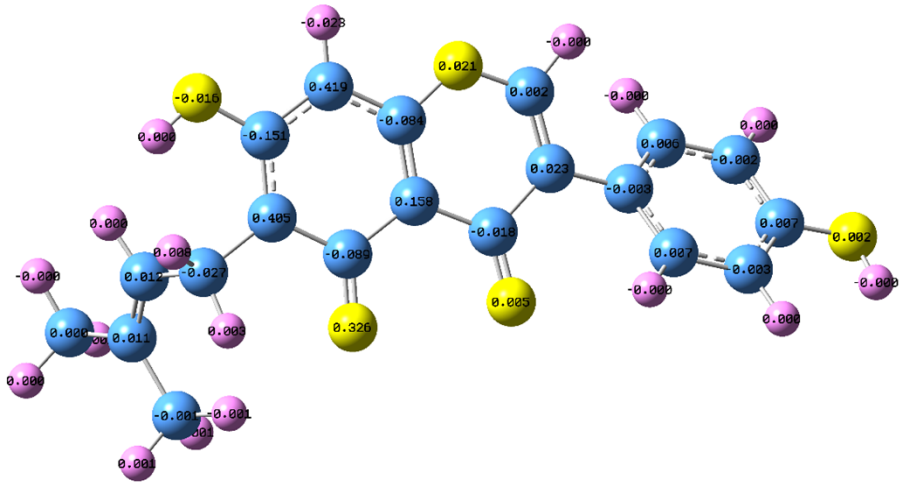


Figure S19. Distribution of spin densities in the radical species formed by H-removal from the neutral form of compound **1**.

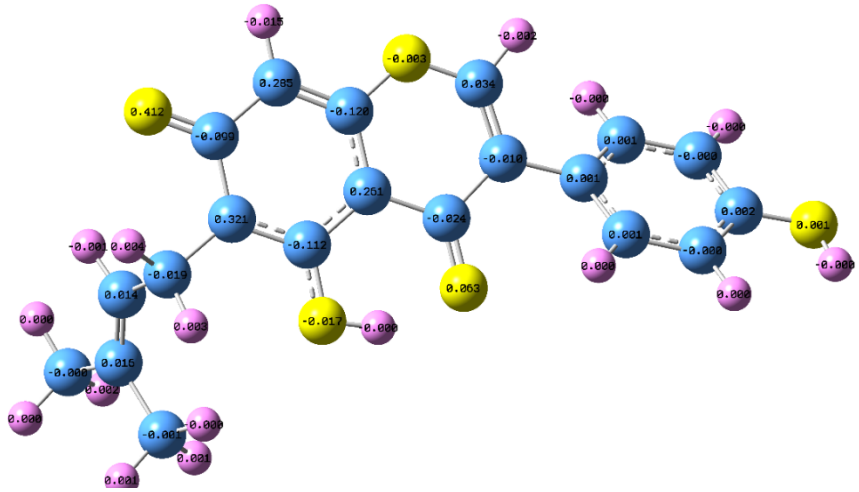
Compound 2



4'-OH



5-OH



7-OH

Figure S20. Distribution of spin densities in the radical species formed by H-removal from the neutral form of compound **2**.

Compound 3

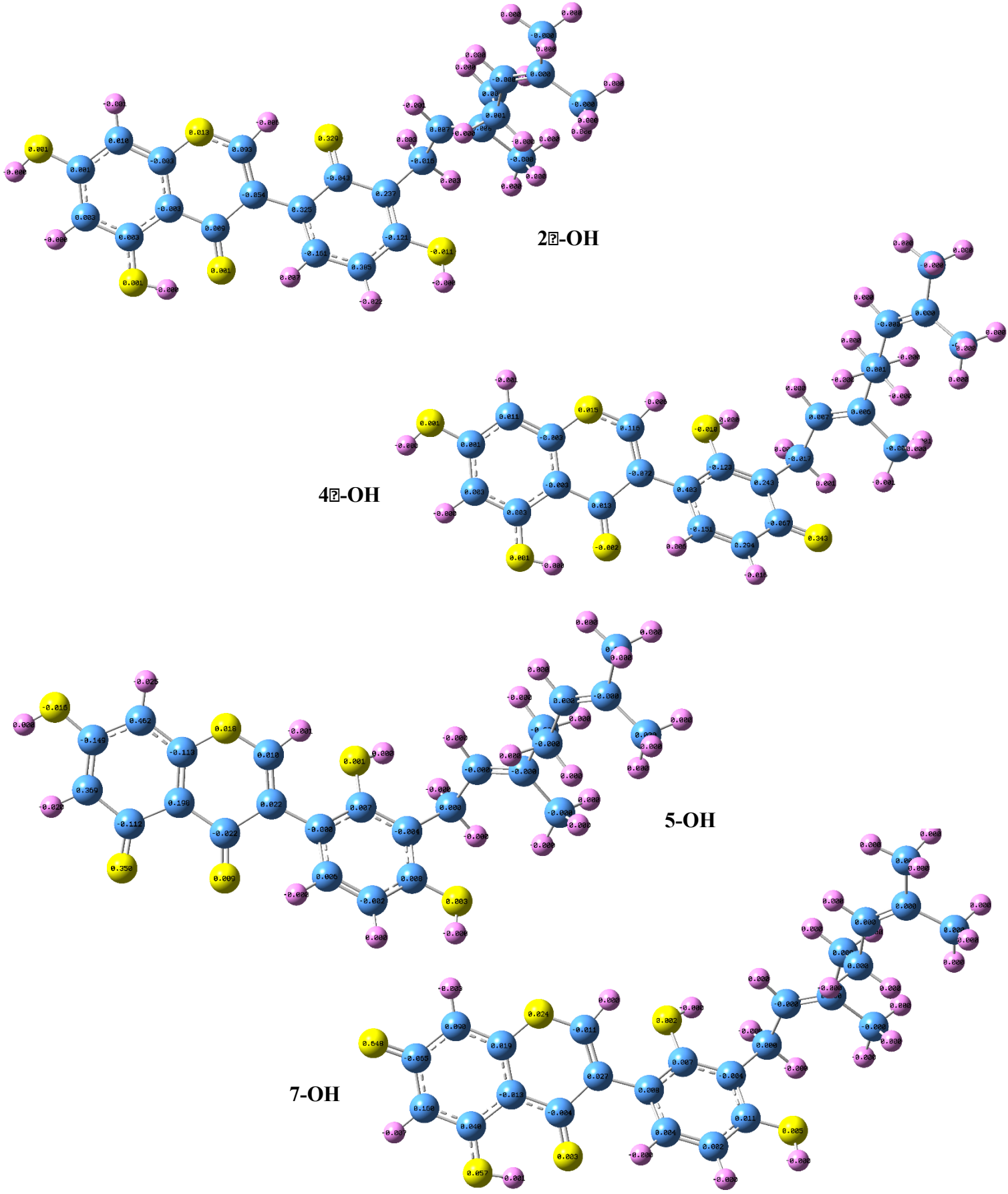
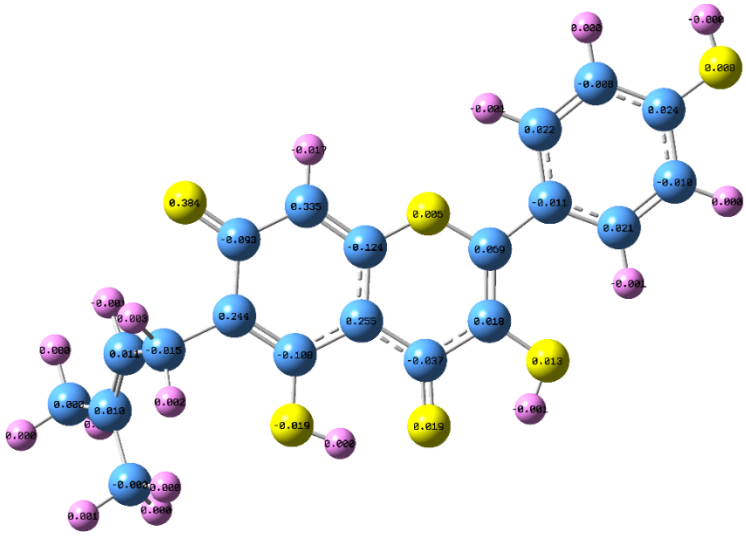
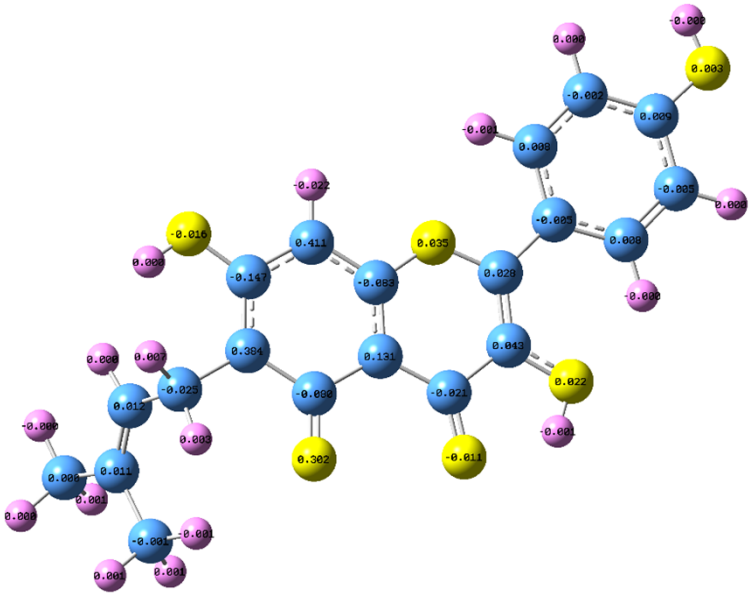


Figure S21. Distribution of spin densities in the radical species formed by H-removal from the neutral form of compound **3**.

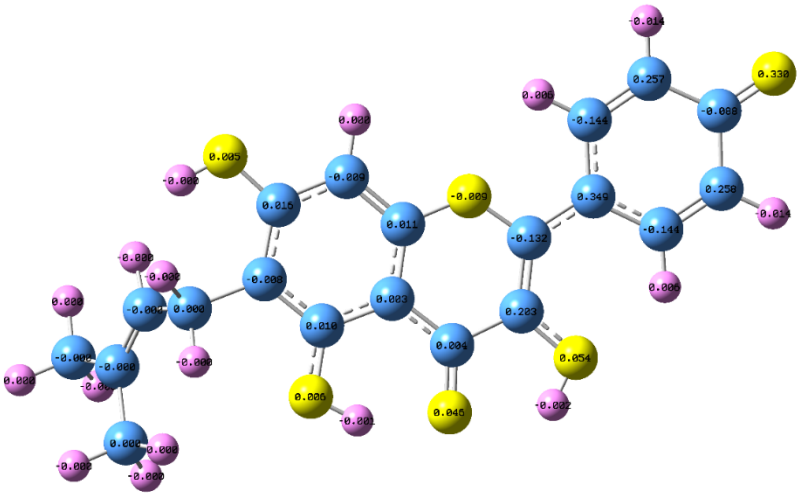
Compound 4



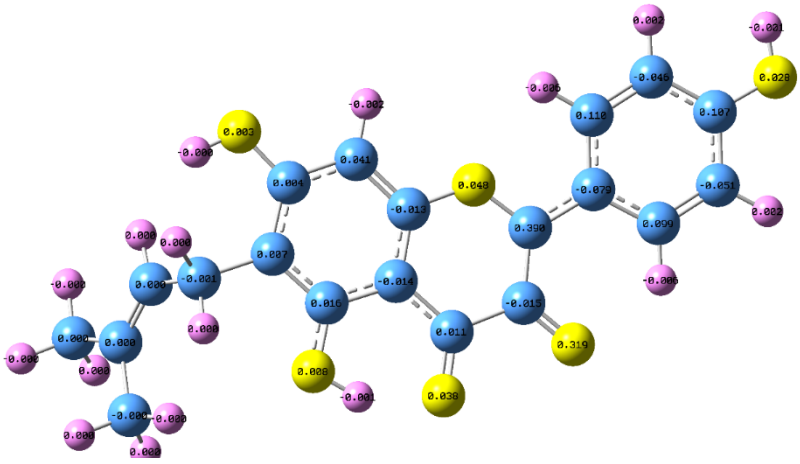
7-OH



5-OH



4-OH



3-OH

Figure S22. Distribution of spin densities in the radical species formed by H-removal from the neutral form of compound **4**.

Compound 5

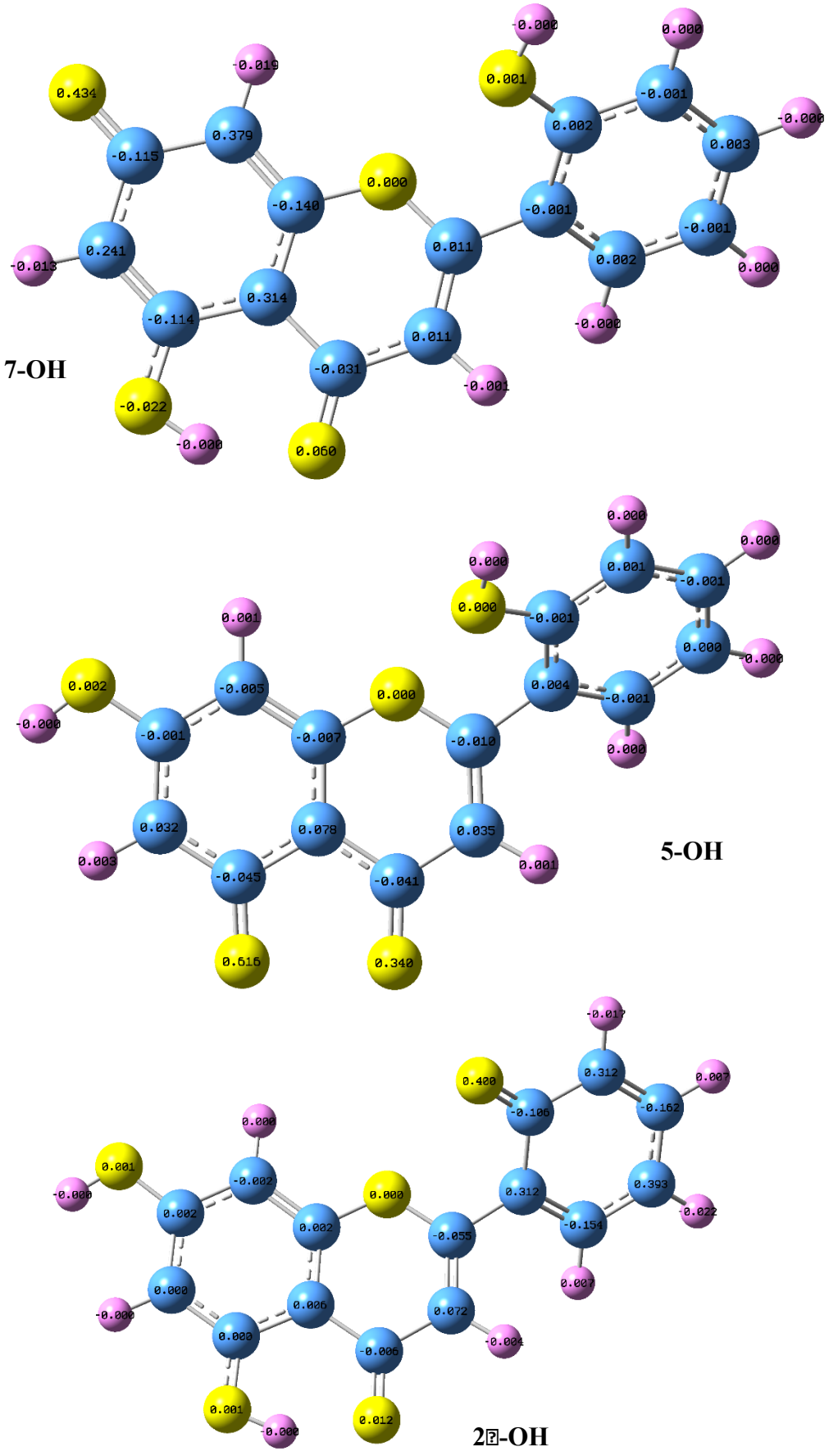


Figure S23. Distribution of spin densities in the radical species formed by H-removal from the neutral form of compound **5**.

Compound 6

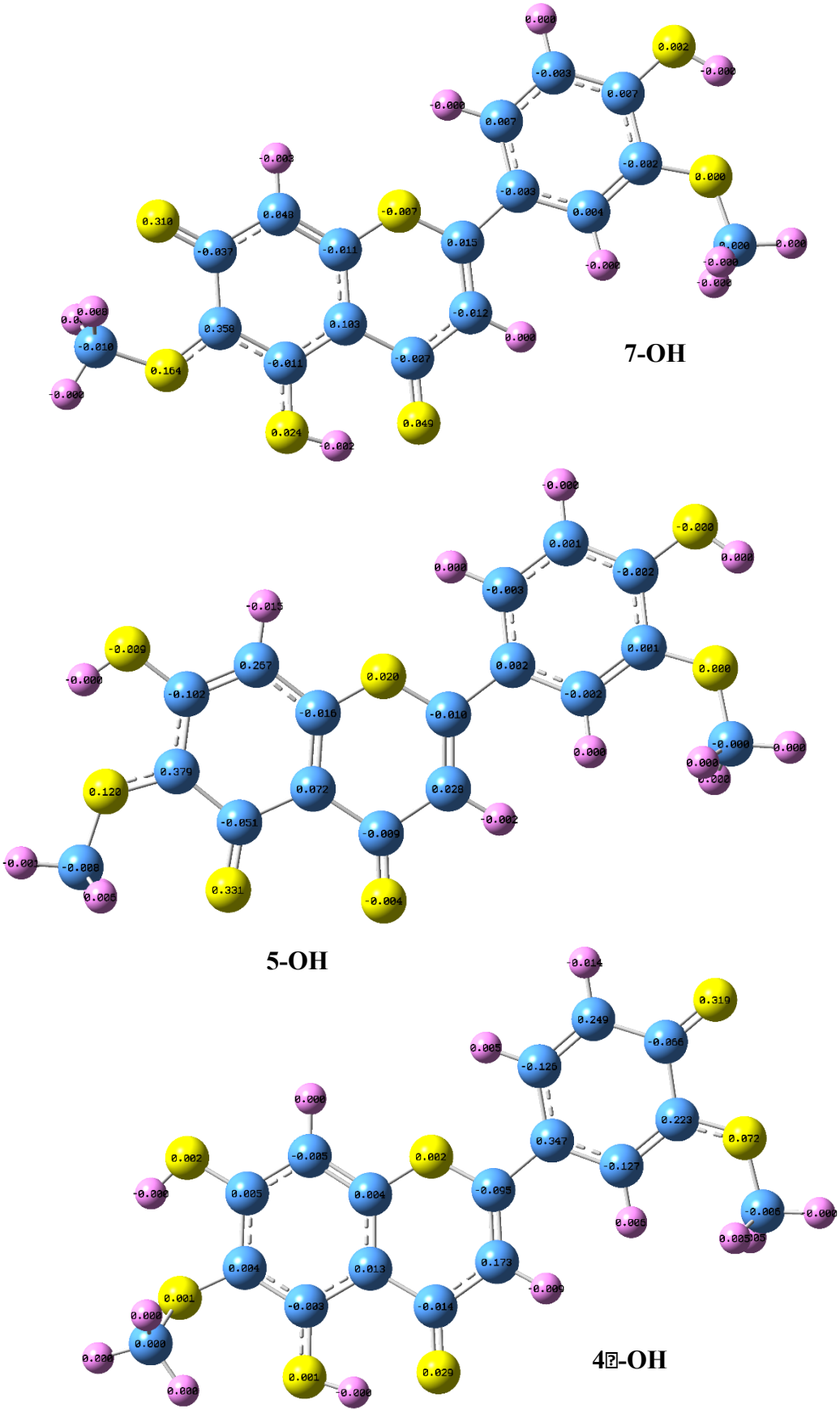
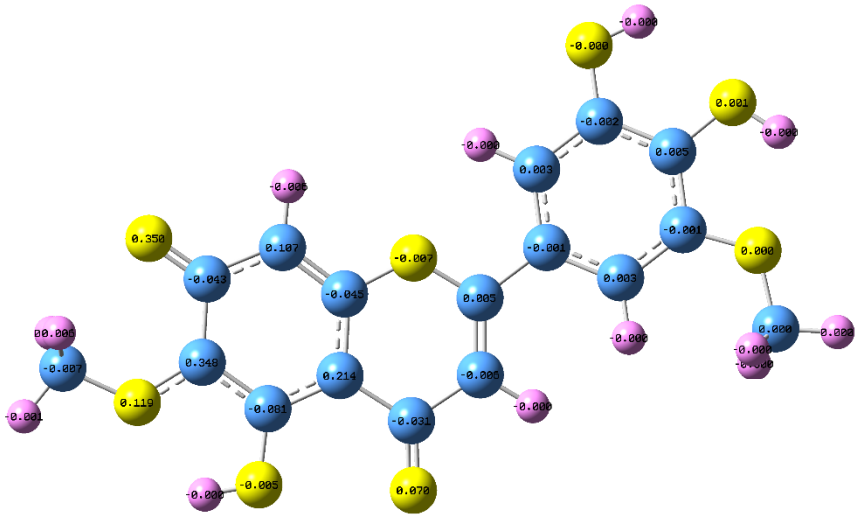
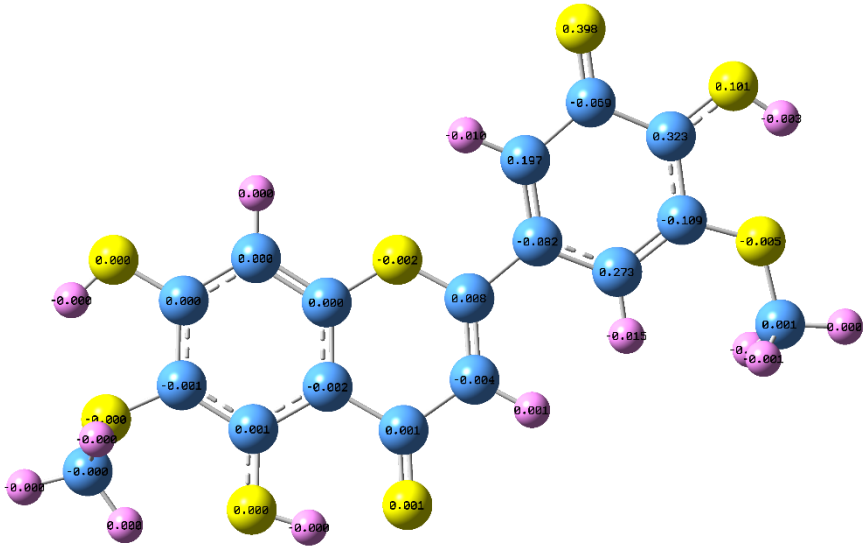
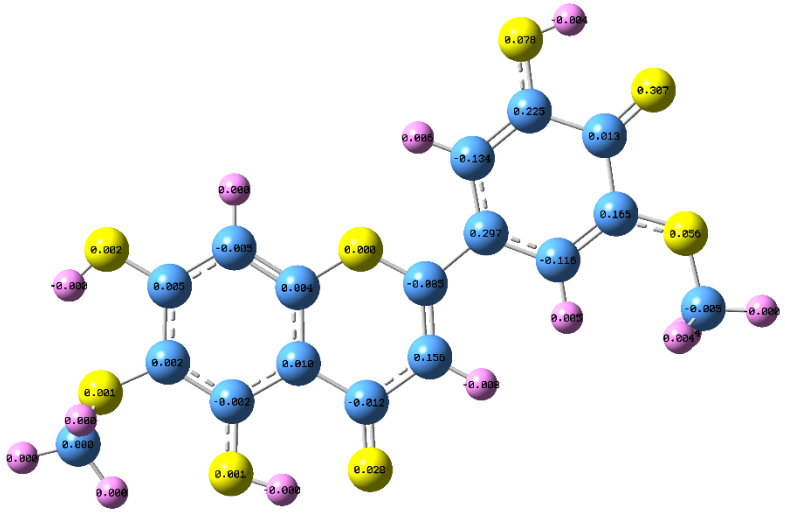


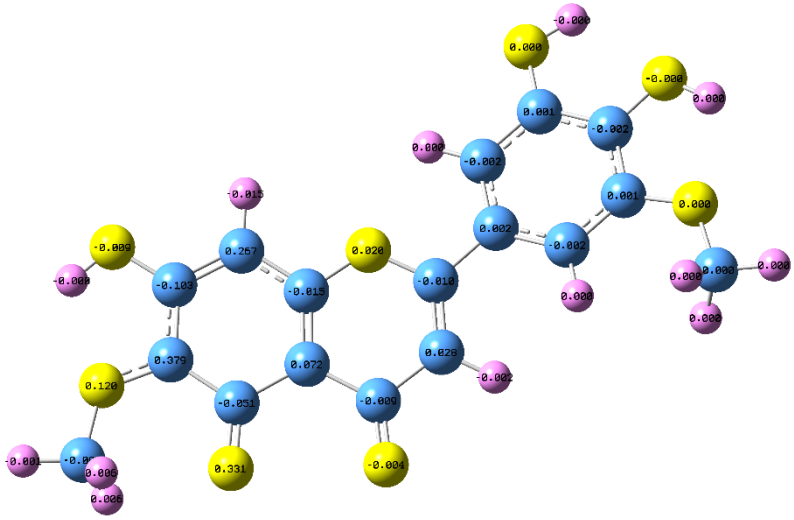
Figure S24. Distribution of spin densities in the radical species formed by H-removal from the neutral form of compound **6**.







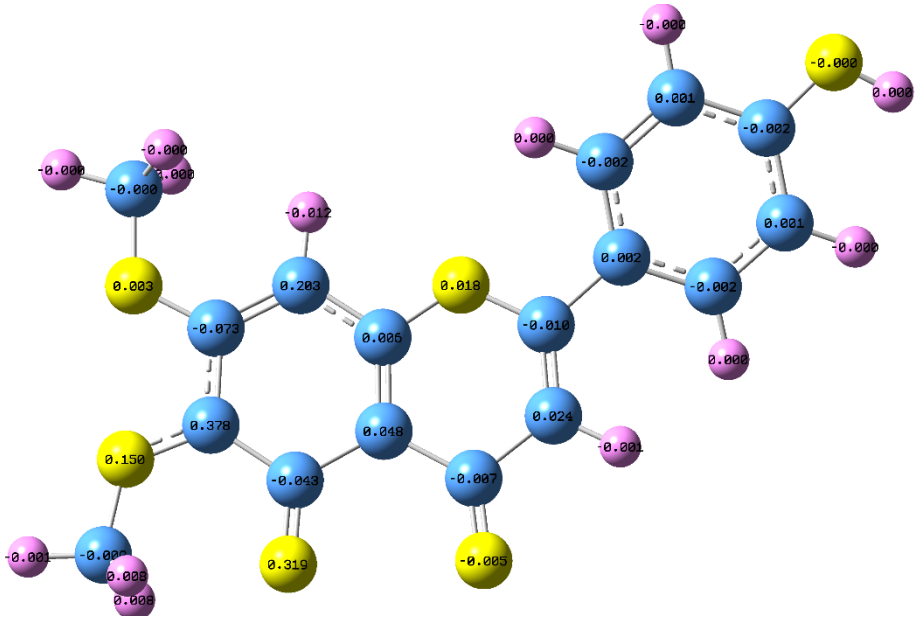
7-OH



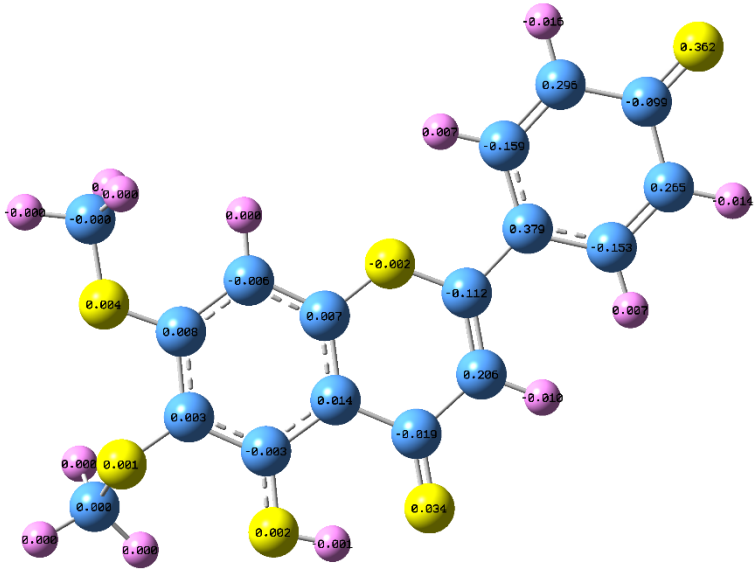
Compound 7

5-OH

Compound 8



5-OH



4□ -OH

Figure S26. Distribution of spin densities in the radical species formed by H-removal from the neutral form of compound **8**.

Figure S25. Distribution of spin densities in the radical species formed by H-removal from the neutral form of compound **7**.