Supporting Information

Exploring the effect of the axial ligands on the anticancer activity of [C,N,N'] Pt(IV) cyclometallated compounds

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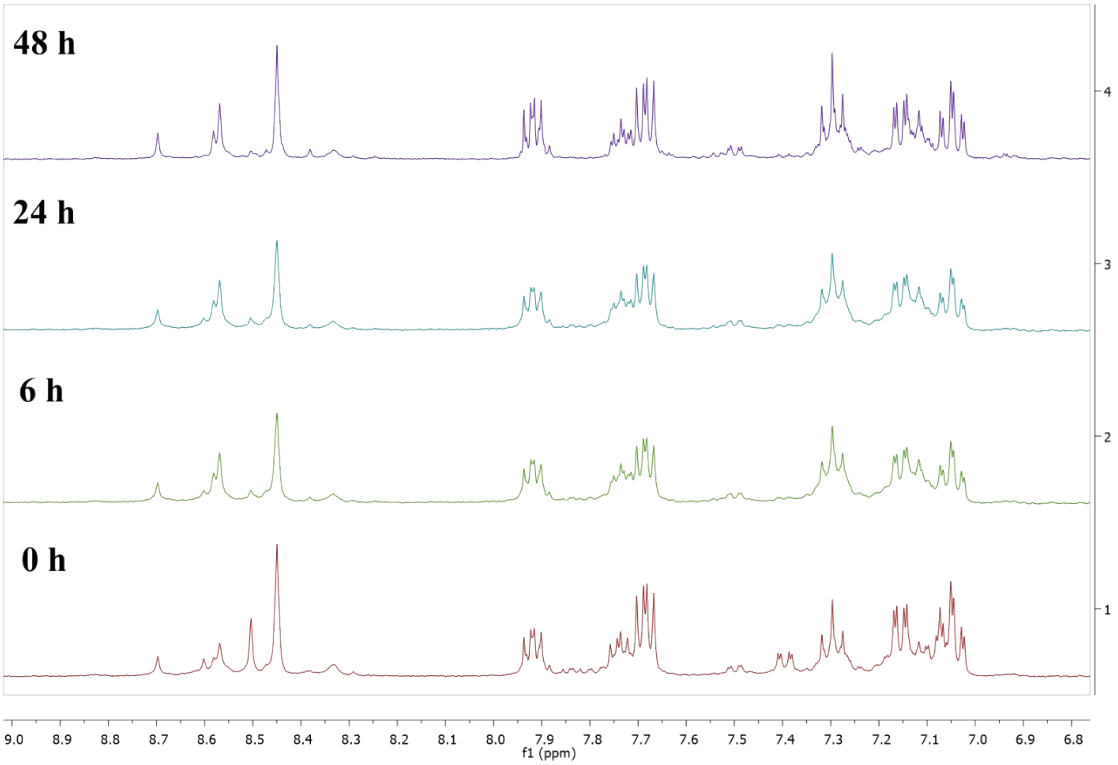

Figure S1. Partial view of ^{1}H NMR spectrum of compound **2** in a DMSO/D_2O mixture freshly prepared and after 6 h, 24 h and 48 h of storage at 298 K.

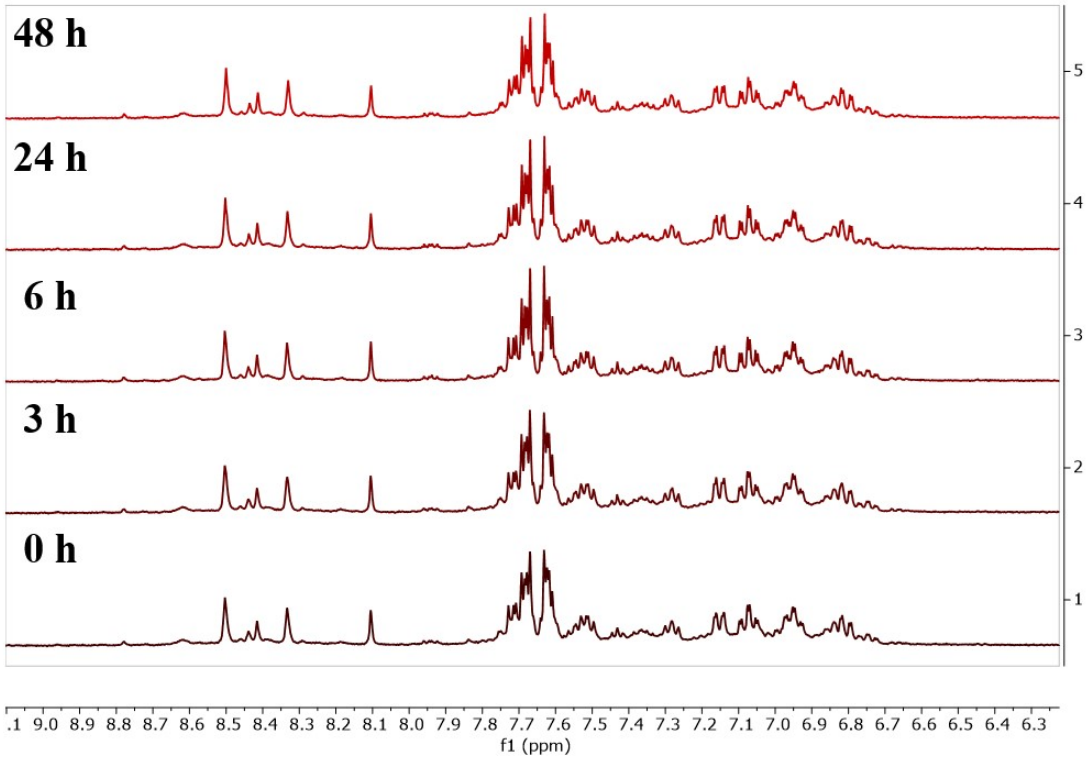

Figure S2. Partial view of ^{1}H NMR spectrum of compound **3** in a DMSO/D_2O mixture freshly prepared and after 3h, 6h, 24 h and 48 h of storage at 298 K.

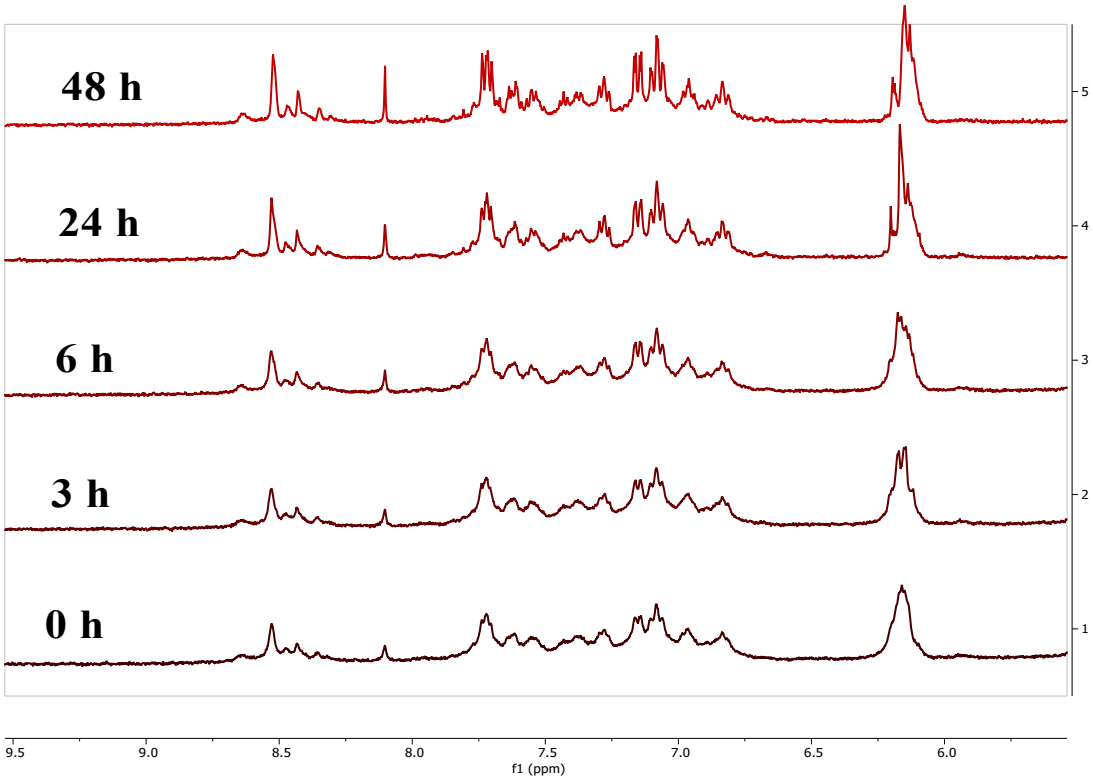

Figure S3. Partial view of ^{1}H NMR spectrum of compound **4** in a DMSO/D_2O mixture freshly prepared and after 3h, 6h, 24 h and 48 h of storage at 298 K.

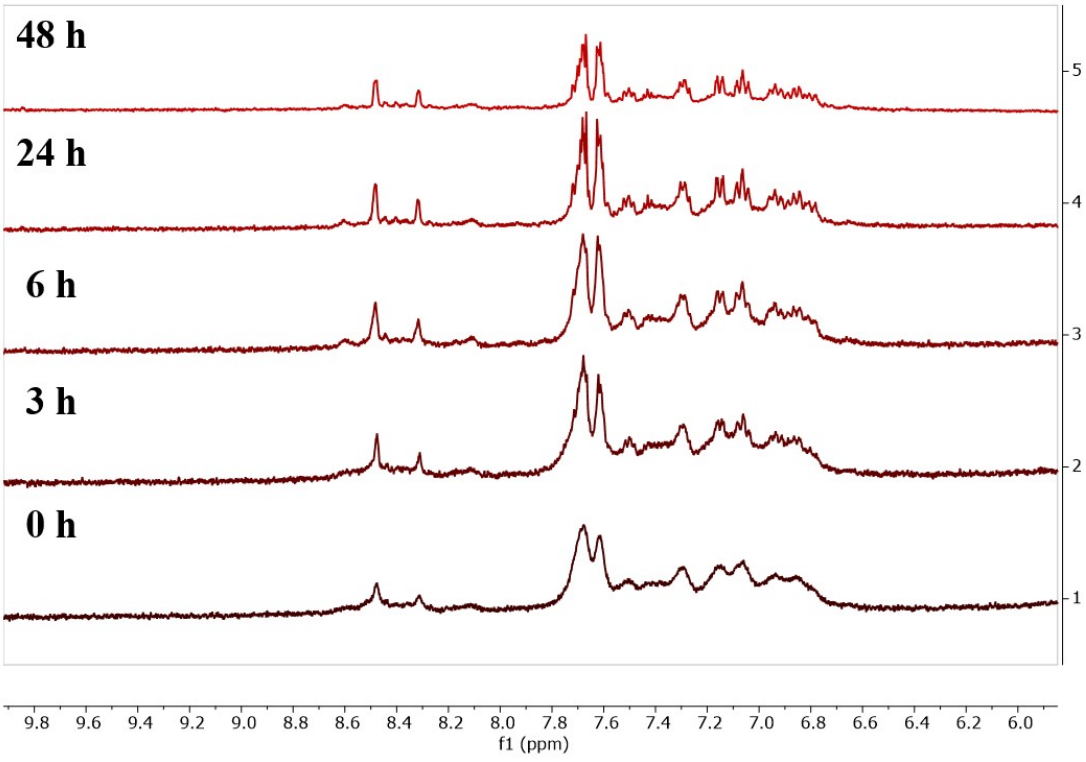

Figure S4. Partial view of ^{1}H NMR spectrum of compound **5** in a DMSO/D_2O mixture freshly prepared and after 24 h and 48 h of storage at 298 K.

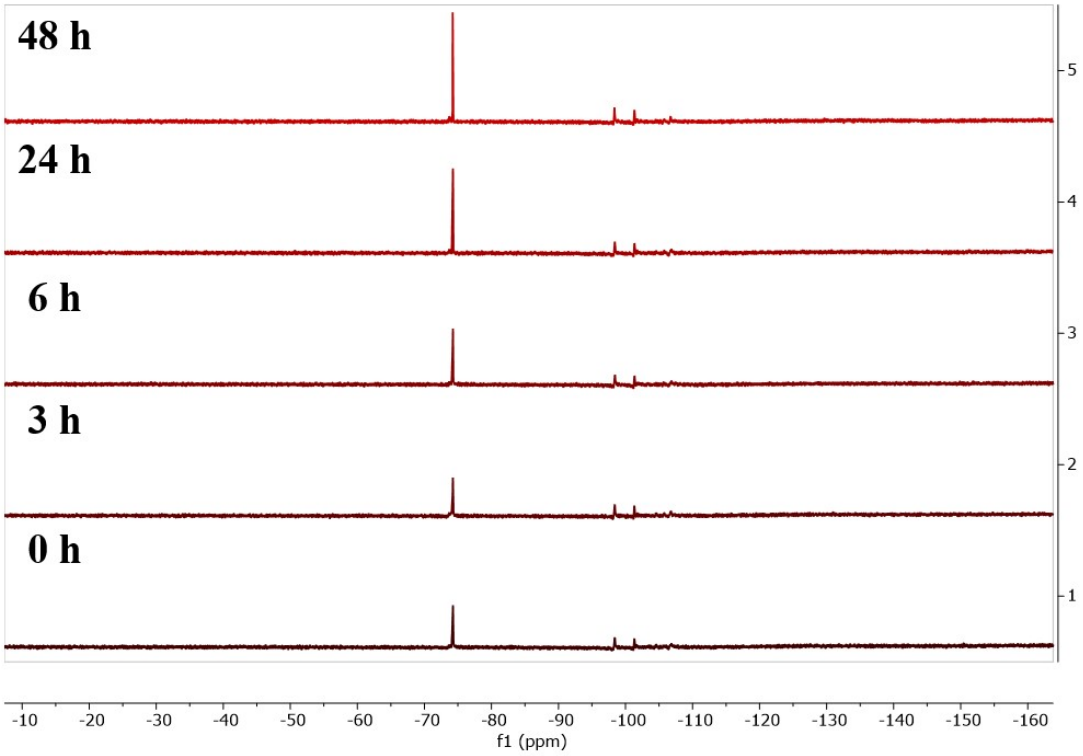

Figure S5. Partial view of ^{19}F NMR spectrum of compound **5** in a DMSO/D_2O mixture freshly prepared and after 24 h and 48 h of storage at 298 K.

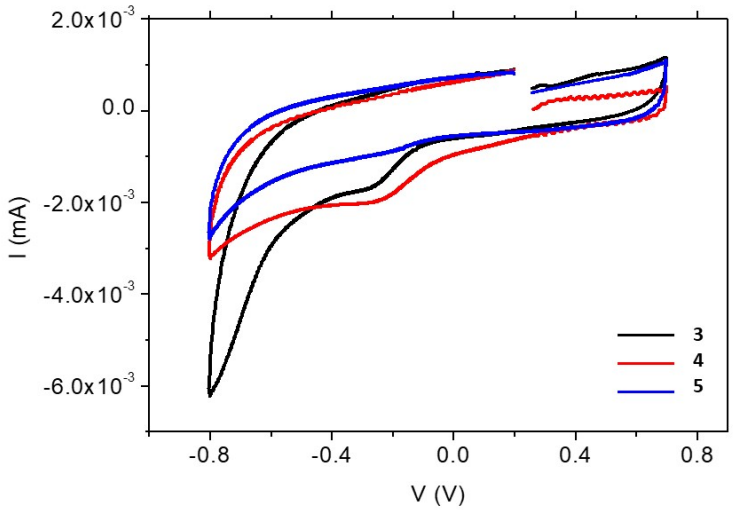

Figure S6. First cycle of the cyclic voltammogram of compounds **3**, **4** and **5** in a dimethyl sulfoxide/water (1:1) solution at a scan rate of 100mV/s.

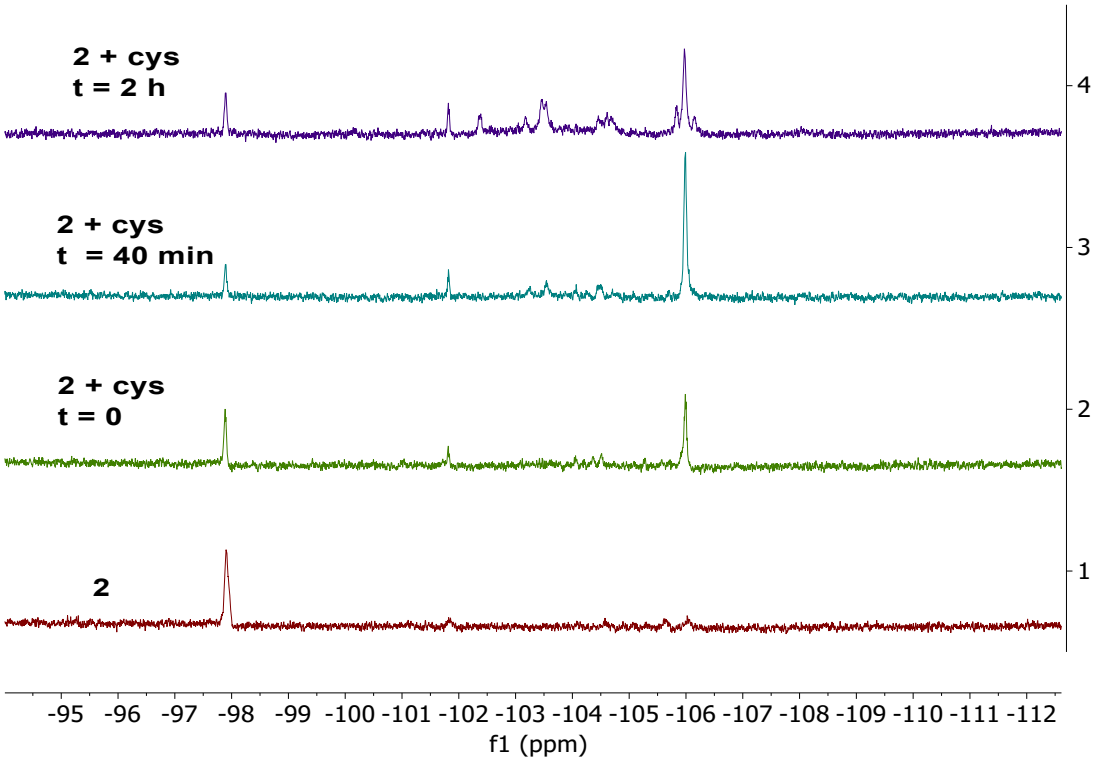

Figure S7. Partial view of ^{19}F NMR spectrum of compound **2** in a DMSO/D_2O mixture and upon addition of L-cysteine at different reaction times at 298 K.

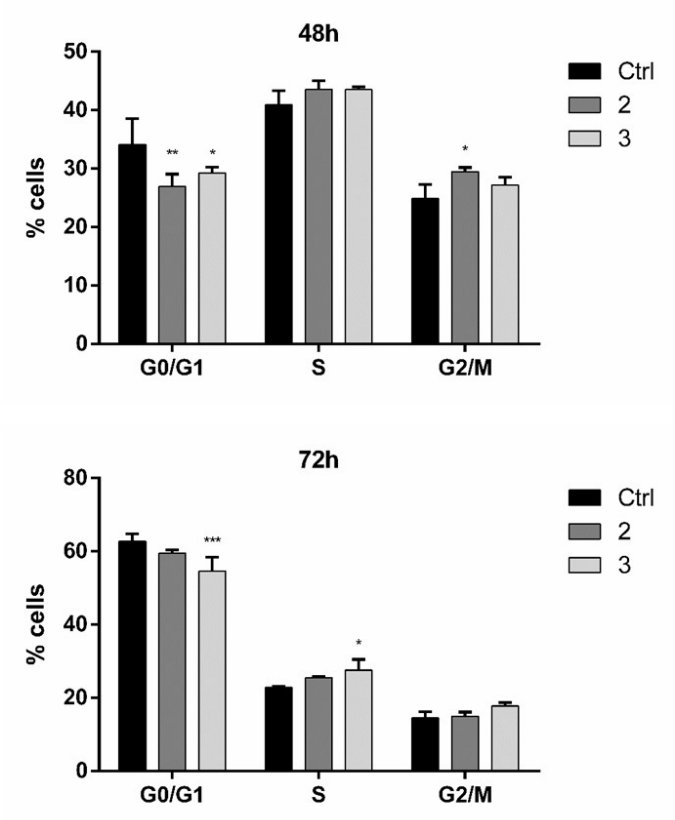

Figure S8. Cell cycle phase distribution at 48 and 72 h incubation with compounds **2** and **3** at their IC_{50} concentration in HCT116 CRC cell line. Mean ± standard deviation are shown. Two-way ANOVA was used to evaluate significance between treated and control cells, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

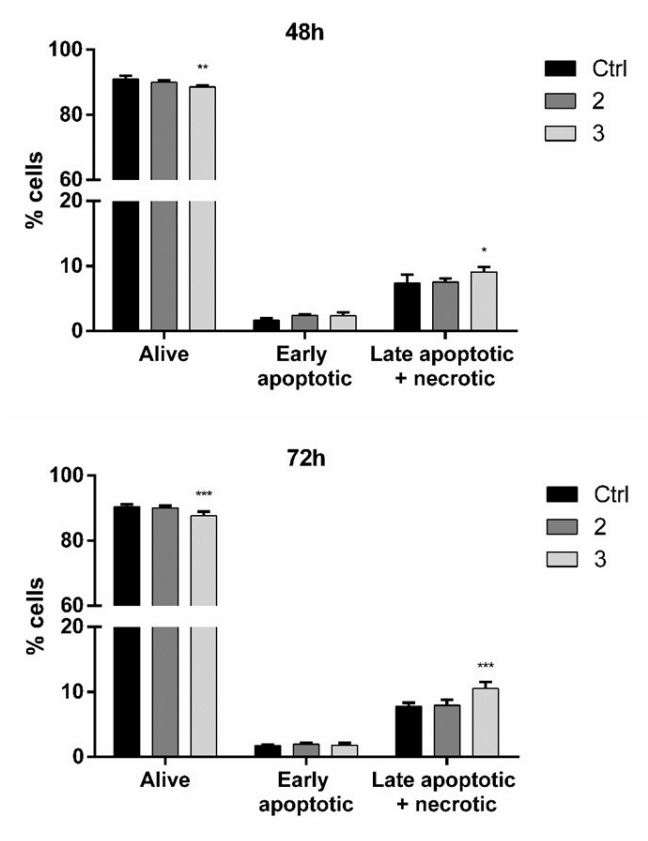

Figure S9. Percentage variations of alive, early apoptotic and late apoptotic/necrotic cell populations at 48 and 72 h incubation with compounds **2** and **3** at their IC_{50} concentration in HCT116 CRC cell line. Mean ± standard deviation are shown. Two-way ANOVA was used to evaluate significance between treated and control cells, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

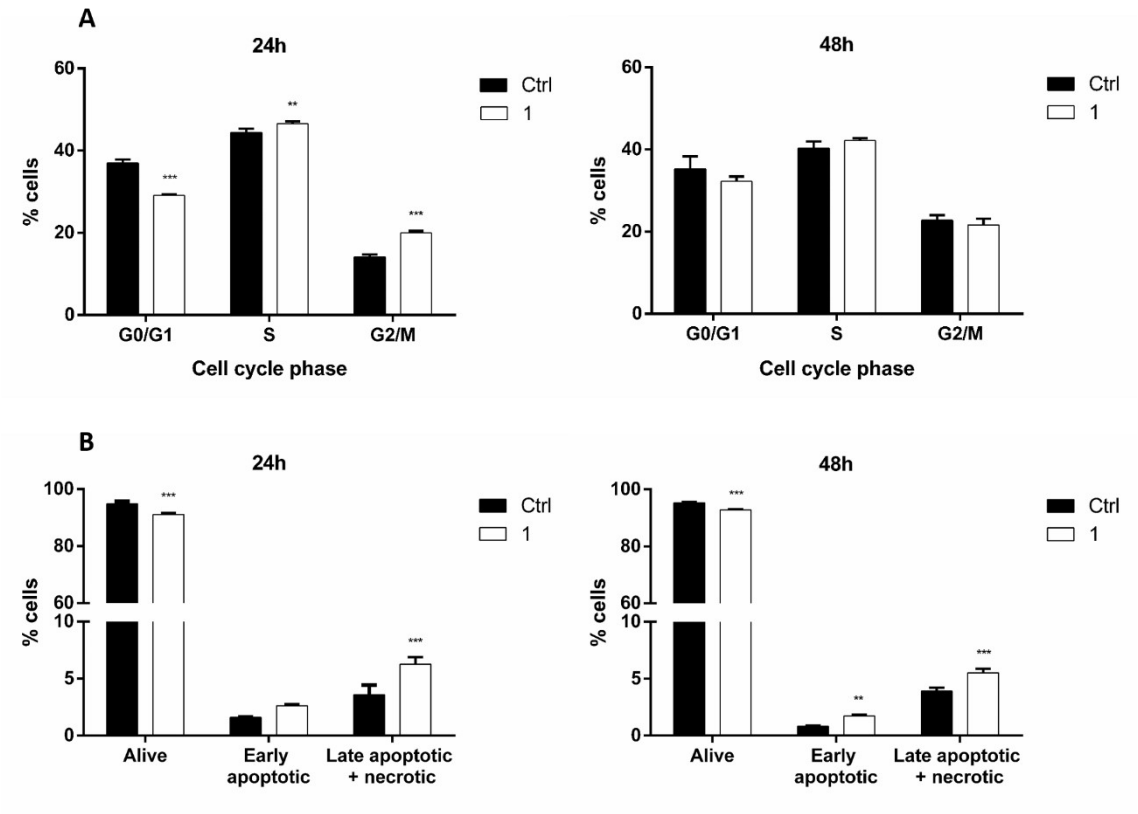

Figure S10. A) Cell cycle phase distribution at 24 and 48 h incubation with compound **1** at its IC_{50} concentration in HCT116 CRC cell line. B) Percentage variations of alive, early apoptotic and late apoptotic/necrotic cell populations at 24 and 48 h incubation with compound **1** at its IC_{50} concentration in HCT116 CRC cell line. Mean ± standard deviation are shown. Two-way ANOVA was used to evaluate significance between treated and control cells, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

Table S1. Optimised coordinates of compounds **1**-**5** and $X(H_2O)_3^-$ anions

1

30

H	2.799148	0.110864	-3.481120
C	2.944685	0.047839	-2.405782
C	3.289696	-0.122664	0.388104
C	1.838500	0.018554	-1.544465
C	4.233302	-0.006126	-1.879880
C	4.368512	-0.091174	-0.496394
C	1.991662	-0.064585	-0.120808
H	5.115046	0.015367	-2.511052
H	3.483315	-0.187964	1.453952
F	5.618650	-0.142080	0.019357
C	0.466142	0.050357	-2.002065
H	0.183734	0.091597	-3.053836
N	-0.437539	0.009398	-1.073468
Pt	0.207241	-0.050279	0.812405
N	-2.000291	0.056381	1.241332
C	-2.551368	0.598220	-0.045975
H	-2.346559	1.672042	-0.054449
H	-3.638985	0.453228	-0.081054
C	-1.888812	-0.045446	-1.265634
H	-2.181931	-1.096993	-1.366116
H	-2.181199	0.479502	-2.181057
Cl	0.982317	-0.141871	3.089490
C	-2.543531	-1.296228	1.524237
H	-2.287558	-1.980650	0.713707
H	-3.636443	-1.255730	1.633524
H	-2.100582	-1.667118	2.450861
C	-2.367576	0.967530	2.351748
H	-1.945918	0.579398	3.280134
H	-3.459933	1.039043	2.445572
H	-1.953726	1.959588	2.158732

2

32

H	2.797378	0.126628	-3.540774
C	2.947672	0.064648	-2.466798
C	3.306177	-0.108434	0.334310
C	1.841006	0.031915	-1.602946
C	4.234415	0.012967	-1.942284
C	4.381489	-0.072877	-0.559951
C	2.031759	-0.052169	-0.197340
H	5.113192	0.036306	-2.576849
H	3.492151	-0.173507	1.400302
F	5.626339	-0.120042	-0.051445
C	0.467877	0.056413	-2.049860
H	0.186506	0.098818	-3.101601
N	-0.443378	0.008970	-1.134535
Pt	0.234516	-0.057665	0.762426
N	-2.054236	0.041568	1.205169
C	-2.569118	0.589289	-0.094400
H	-2.357108	1.660017	-0.103870
H	-3.655618	0.450435	-0.154076
C	-1.897666	-0.069906	-1.300202
H	-2.166843	-1.128742	-1.378840
H	-2.193999	0.433070	-2.225940
Cl	1.015978	-0.141058	3.043862
Cl	0.287317	-2.460851	0.646059
Cl	0.347738	2.350392	0.791244
C	-2.661279	-1.281675	1.496743
H	-2.473575	-1.977138	0.680239
H	-3.743828	-1.166458	1.637701
H	-2.215657	-1.683052	2.408648
C	-2.406428	0.965848	2.312409
H	-2.008652	0.561442	3.244854
H	-3.497379	1.059314	2.390068
H	-1.966747	1.945534	2.127677

3

34

H	2.746275	0.123866	-3.594028
C	2.896934	0.052917	-2.520499
C	3.258118	-0.143402	0.276912
C	1.793291	0.014766	-1.654244
C	4.185048	-0.003827	-1.997981
C	4.332142	-0.101774	-0.616037
C	1.975165	-0.080231	-0.244319
H	5.063575	0.024019	-2.633072
H	3.446050	-0.216470	1.342312
F	5.580208	-0.154402	-0.109566
C	0.417638	0.042145	-2.097906
H	0.129507	0.097278	-3.147280
N	-0.486317	-0.024893	-1.175494
Pt	0.193697	-0.074761	0.707604
N	-2.069012	0.062947	1.171208
C	-2.572200	0.618138	-0.125727
H	-2.296203	1.674228	-0.148083
H	-3.665393	0.535026	-0.172206
C	-1.941198	-0.082554	-1.329289
H	-2.233661	-1.137218	-1.377238
H	-2.240291	0.405018	-2.262374
Cl	1.016953	-0.064709	2.989380
C	-2.673735	-1.255057	1.467143
H	-2.351623	-1.984105	0.725120
H	-3.769219	-1.176817	1.481715
H	-2.321670	-1.589621	2.445185
C	-2.376877	1.018634	2.259813
H	-2.041111	0.593060	3.207042
H	-3.457311	1.210426	2.308288
H	-1.835290	1.945601	2.067370
O	0.114025	-2.123761	0.711805
H	0.378516	-2.393812	-0.183289
O	0.165310	1.979818	0.705035
H	0.638658	2.209529	1.522702

4

44

H	1.082294	2.743600	-3.433866
C	0.766119	2.872463	-2.402732
C	-0.047304	3.179030	0.287748
C	0.519974	1.752262	-1.598617
C	0.609207	4.151882	-1.874069
C	0.210183	4.273420	-0.546892
C	0.107981	1.915282	-0.249174
H	0.791010	5.041786	-2.466465
H	-0.357682	3.345968	1.313058
F	0.060248	5.507700	-0.030364
C	0.678616	0.387129	-2.042376
H	1.002322	0.125535	-3.048995
N	0.429478	-0.540926	-1.181623
Pt	-0.191562	0.100603	0.627208
N	-0.396176	-2.183661	0.972550
C	-0.465241	-2.678364	-0.443739
H	-1.470401	-2.464351	-0.813253
H	-0.314963	-3.764577	-0.467806
C	0.562282	-1.989661	-1.343064
H	1.586495	-2.269385	-1.073897
H	0.395319	-2.264367	-2.389408
Cl	-0.923380	0.860093	2.812037
C	0.767409	-2.768085	1.686437
H	1.695118	-2.541719	1.161756
H	0.646235	-3.856548	1.756392
H	0.817687	-2.339602	2.688366
C	-1.638315	-2.558134	1.692942
H	-1.560033	-2.219422	2.727292
H	-1.768965	-3.647885	1.675923
H	-2.492239	-2.076098	1.217451
O	1.670652	0.049443	1.482699
O	-2.198714	0.126667	0.167492
C	2.817617	0.279411	0.903626
C	-2.758301	0.294614	-0.994684
O	-2.254587	0.366058	-2.102864
O	3.068126	0.553306	-0.254088
C	3.939646	0.131684	1.966390
H	3.543272	-0.039027	2.962694
C	-4.299672	0.419042	-0.892786
H	-4.715574	0.504065	-1.892829
Cl	-4.756889	1.920748	-0.000654
Cl	-5.043362	-1.039347	-0.133497
Cl	4.961605	-1.296515	1.548314
Cl	4.924465	1.635883	2.027369

5

44

H	1.109542	2.798754	-3.427413
C	0.786919	2.928563	-2.398450
C	-0.042196	3.237287	0.287474
C	0.545859	1.809031	-1.591847
C	0.616521	4.208228	-1.874987
C	0.209951	4.330954	-0.550204
C	0.126332	1.973839	-0.244868
H	0.793515	5.097556	-2.469599
H	-0.359541	3.404846	1.310438
F	0.046064	5.565341	-0.039121
C	0.720195	0.444295	-2.029597
H	1.059514	0.181392	-3.030744
N	0.468892	-0.483547	-1.167880
Pt	-0.178333	0.158674	0.632331
N	-0.416286	-2.131870	0.967051
C	-0.431241	-2.625612	-0.451770
H	-1.423129	-2.417705	-0.859066
H	-0.274866	-3.710920	-0.470537
C	0.624263	-1.932094	-1.313833
H	1.639076	-2.196738	-0.997715
H	0.505200	-2.215517	-2.364257
Cl	-0.925607	0.917061	2.808069
C	0.710150	-2.728693	1.728859
H	1.663257	-2.494489	1.256723
H	0.583941	-3.817742	1.777191
H	0.709915	-2.315832	2.738760
C	-1.692754	-2.497233	1.632104
H	-1.664662	-2.146479	2.665138
H	-1.822005	-3.587112	1.621174
H	-2.523790	-2.023201	1.110503
O	1.675169	0.059362	1.489853
O	-2.168836	0.170194	0.146020
C	2.820507	0.330262	0.937330
C	-2.725693	0.304073	-1.021219
O	-2.244124	0.469713	-2.124313
O	3.094616	0.743334	-0.171833
C	3.955399	-0.011968	1.942984
C	-4.265742	0.183693	-0.845519
F	-4.901709	0.395519	-2.004259
F	-4.725760	1.070880	0.056698
F	-4.590123	-1.053432	-0.409658
F	5.137584	0.437513	1.502648
F	4.046107	-1.352103	2.089887
F	3.727910	0.521924	3.157451

$Cl(H_2O)_3^-$

10

Cl	0.854094	0.022520	0.302969
H	-0.236077	-1.854916	1.062800
H	-0.232361	1.897367	1.073681
H	0.849314	0.026430	-1.995949
O	-0.695221	-2.657923	1.386832
H	-0.780322	-2.488117	2.337904
O	-0.694802	2.696686	1.402176
H	-0.783063	3.237816	0.602651
O	0.854338	0.032053	-2.976060
H	0.864100	-0.911915	-3.197005

$OH(H_2O)_3^-$

11

H	-0.744151	0.357778	-1.145410
O	-0.167586	0.393310	-0.364794
H	-0.941482	-0.735697	0.612863
H	0.763980	-0.895431	-0.589144
H	0.043552	1.999107	-0.209311
O	-1.180704	-1.607090	1.055099
H	-0.482654	-2.154555	0.651887
O	1.238522	-1.801380	-0.631241
H	1.833630	-1.766868	0.134615
O	0.131739	3.004975	-0.112698
H	-0.494847	3.205851	0.598134

$DCA(H_2O)_3^-$

16

C	-0.418657	0.336495	-1.082774
O	-0.658091	0.111268	-2.279266
C	-0.146595	1.810347	-0.636949
H	-0.462210	1.984548	0.388576
Cl	-0.990246	3.033159	-1.659443
Cl	1.650288	2.097913	-0.662947
O	-0.331483	-0.491948	-0.123195
H	-0.765491	-2.344429	-0.988920
H	1.513184	-1.012151	0.647402
H	-0.347163	0.104700	1.585504
O	2.105239	-1.007159	1.422224
H	1.554202	-0.505752	2.056204
O	-0.102018	0.464401	2.471563
H	-0.649279	-0.040528	3.094874
O	-0.993478	-2.693193	-1.870732
H	-0.958200	-1.847670	-2.362121

$TFA(H_2O)_3^-$

16

C	0.722154	0.767794	-1.914737
F	-0.190031	1.769920	-1.846081
F	1.790288	1.154330	-1.176269
F	1.131120	0.687048	-3.194754
C	0.104455	-0.560699	-1.385953
O	-0.148285	-1.440854	-2.211344
O	-0.096690	-0.545472	-0.128022
H	1.143526	0.155157	1.099546
H	-0.998286	1.052798	0.654127
H	-1.017588	-1.949817	0.545595
O	-1.054732	1.727648	1.357002
H	-0.186510	1.589720	1.786830
O	-1.551105	-2.652296	0.984354
H	-2.455919	-2.309617	0.918651
O	1.511645	0.590469	1.900483
H	1.295957	-0.036128	2.610572