Electronic Supplementary Information

Metal Center and Aromatic Moiety in Schiff Base Complexes: Impact on G-Quadruplex Stabilization and Oncogene Downregulation.

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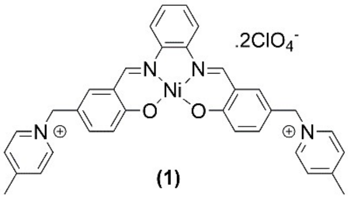
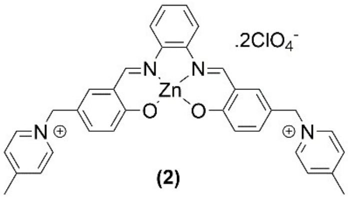
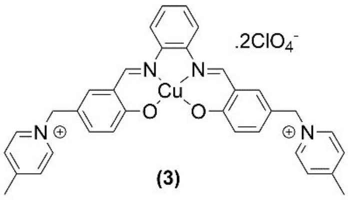
Figure S1. Structures of the complexes synthetized in this study.



(1)



(2)



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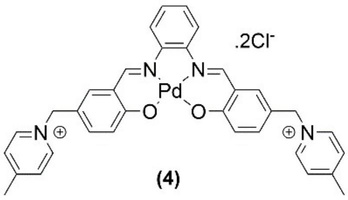

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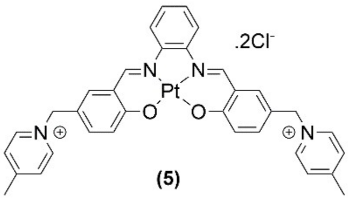

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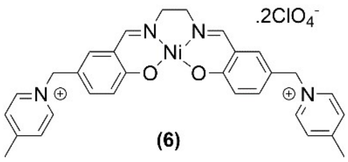

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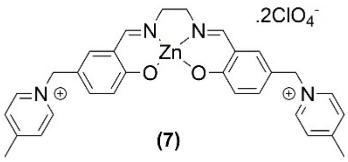

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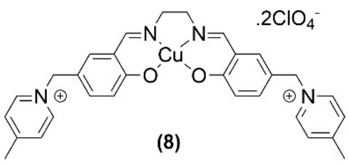

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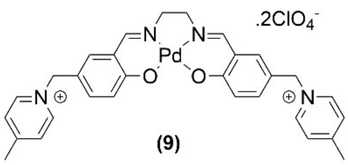

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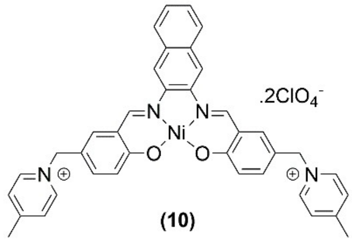
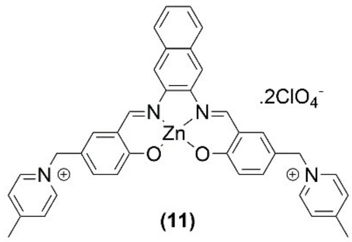


(10)



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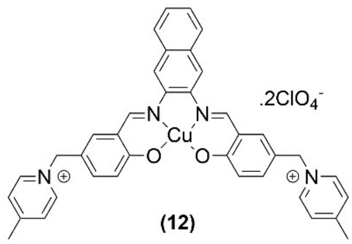
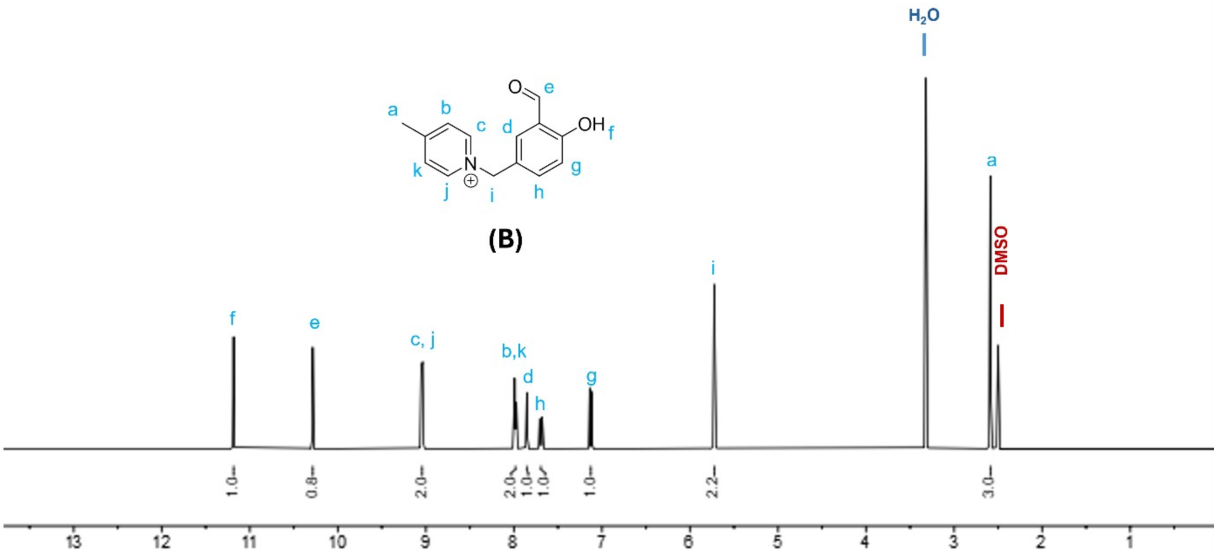
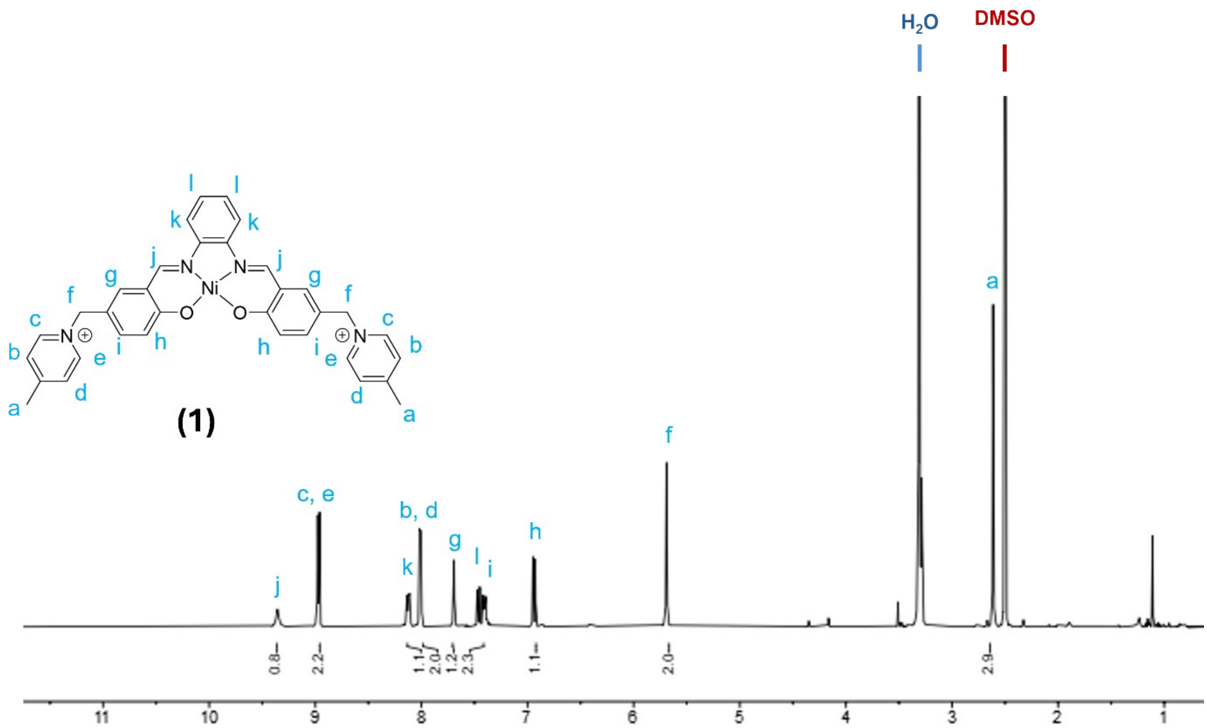
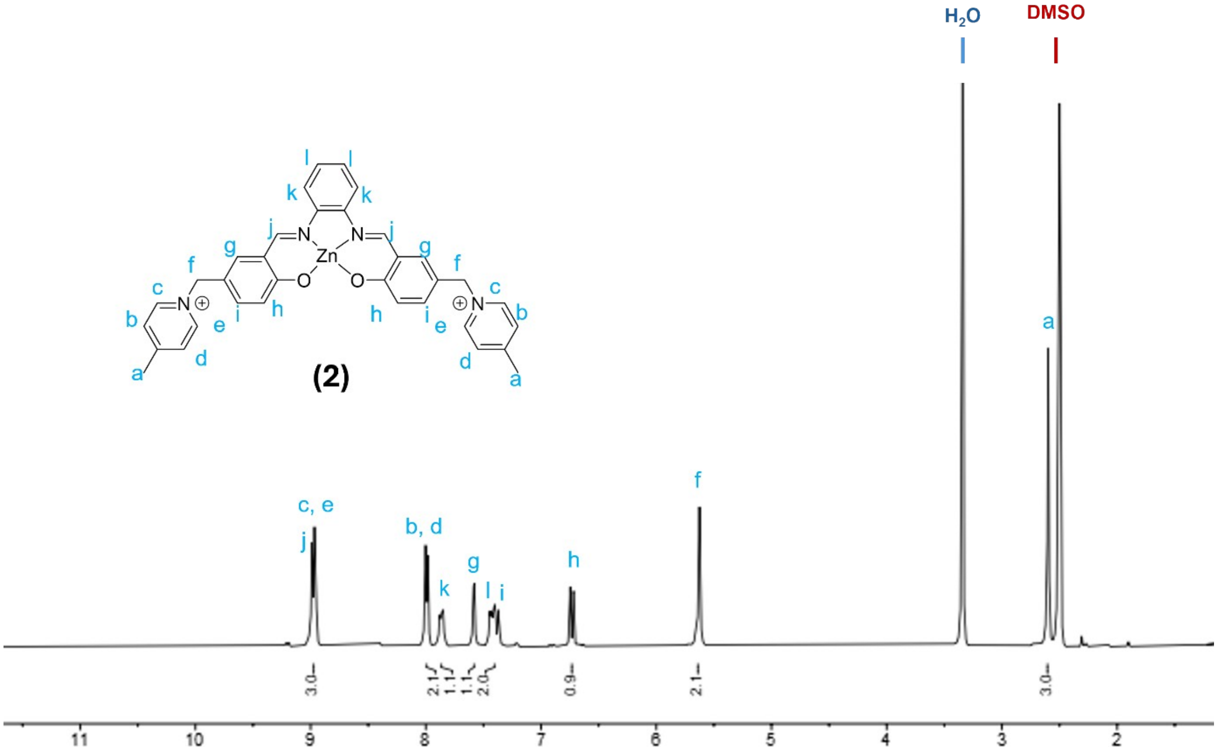


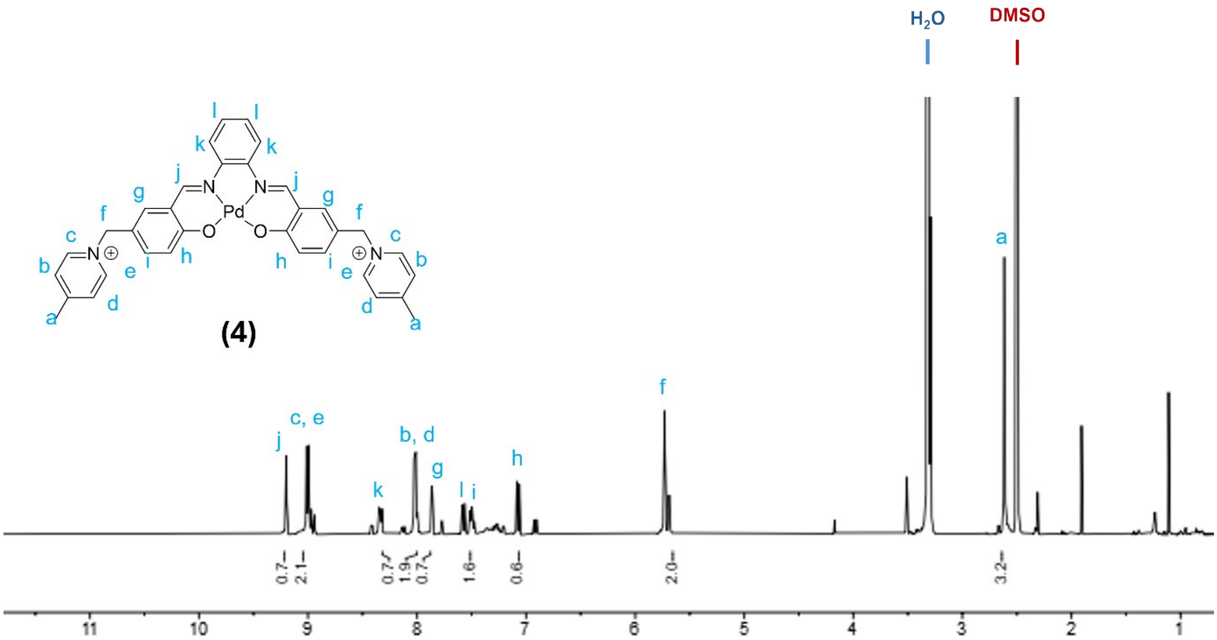
(12)

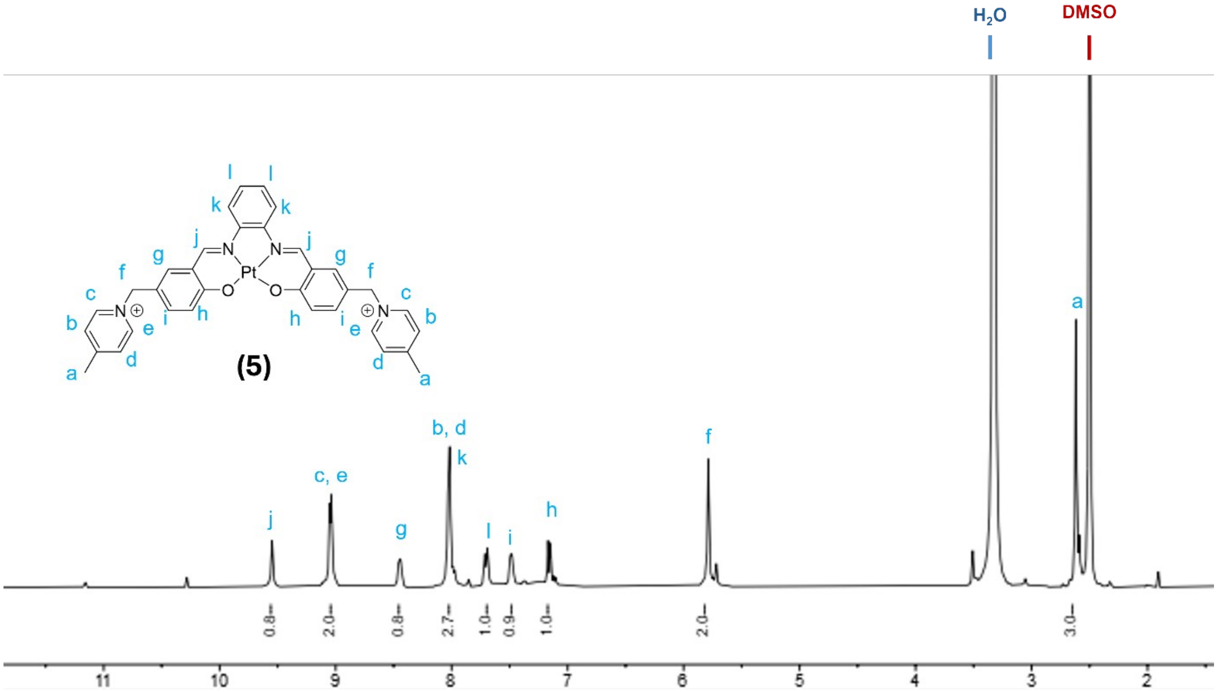
Figure S2. [1]H-NMR spectra of the new pyridinium **(B)** and metal complexes **1, 2, 4, 5, 6, 7, 8, 10** and **11** in d_6-DMSO.

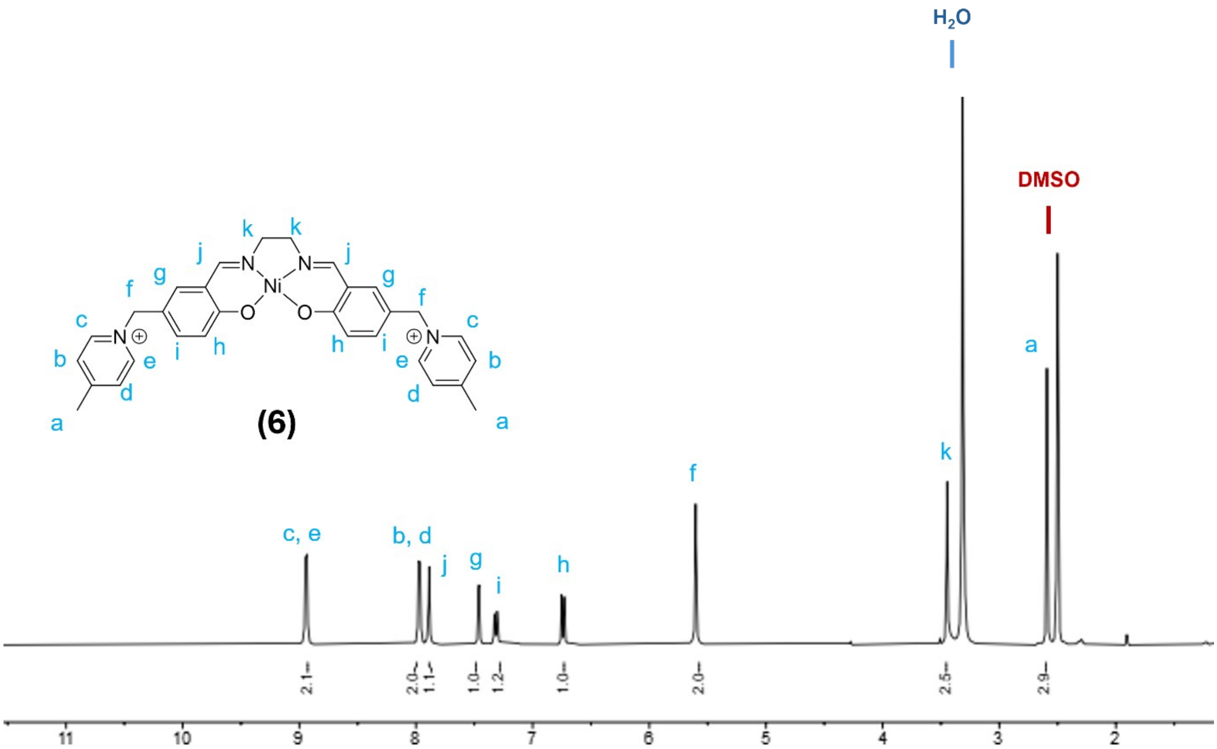


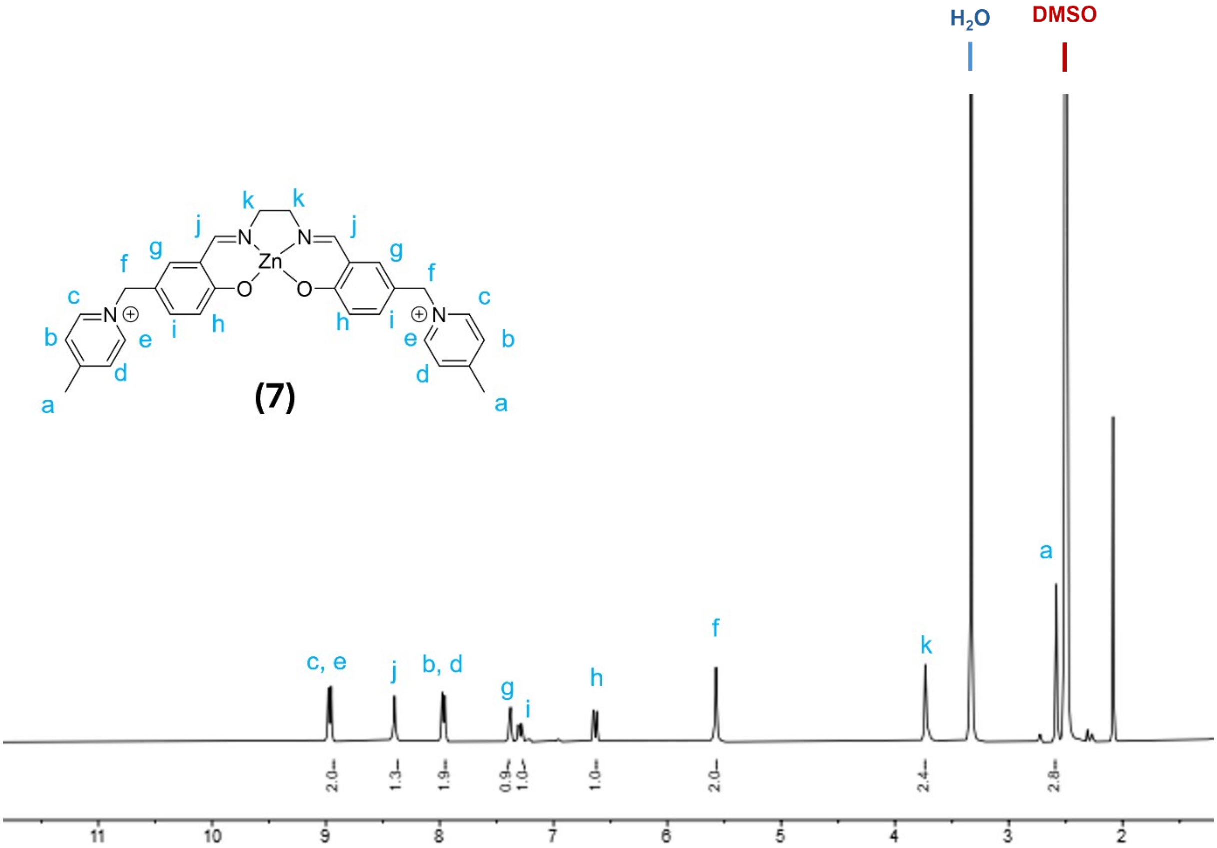


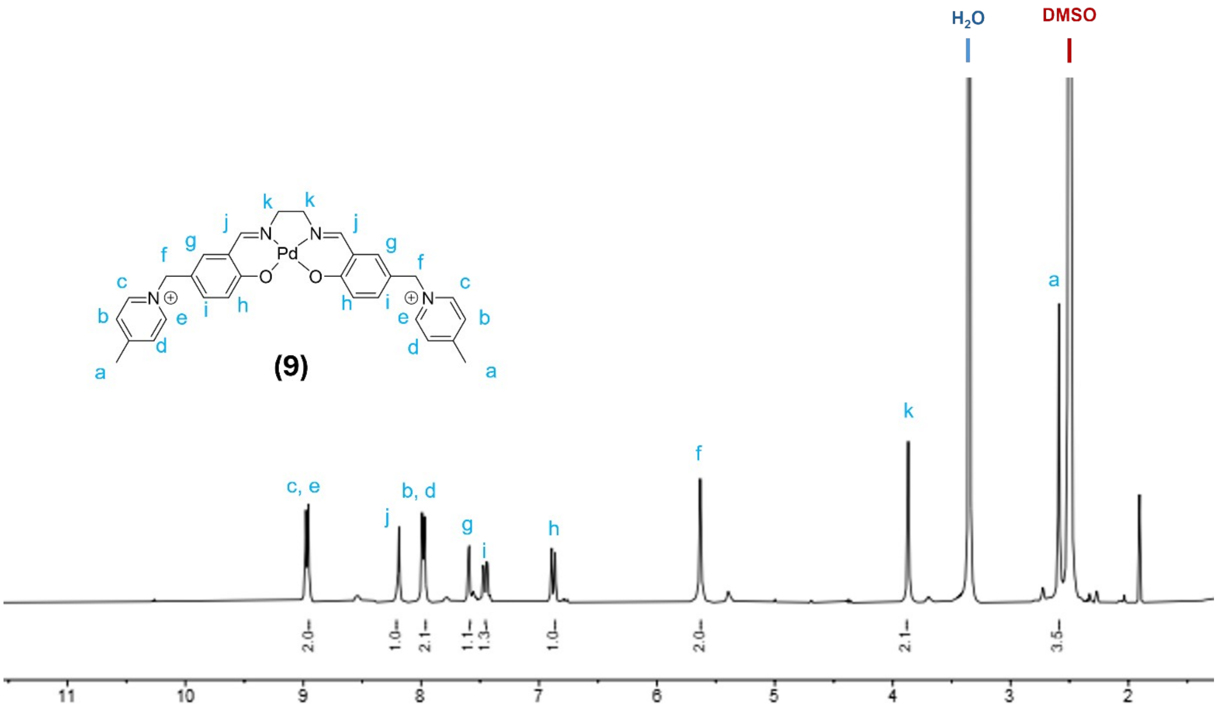

(2)
Zn
H2O
DMSO
a
f
c, e
j
b, d
k
g
l
i
h
3.0
2.1
1.1
1.1
2.0
0.9
2.1
3.0
11 10 9 8 7 6 5 4 3 2


(4)
Pd
H2O
DMSO
a
f
j
c, e
b, d
k
g
l
i
h
0.7
2.1
0.7
1.9
0.7
1.6
0.6
2.0
3.2
11 10 9 8 7 6 5 4 3 2 1


H2O
DMSO
(5)
a
b, d
k
c, e
j
g
l
i
h
f
0.8
2.0
0.8
2.7
1.0
0.9
1.0
2.0
3.0
11
10
9
8
7
6
5
4
3
2


H2O
DMSO
(6)
a
k
f
c, e
b, d
j
g
i
h
2.1
2.0
1.1
1.0
1.2
1.0
2.0
2.5
2.9
11
10
9
8
7
6
5
4
3
2


H2O
DMSO
(7)
Zn
c, e
j
b, d
g
i
h
f
k
a
2.0
1.3
1.9
0.9
1.0
1.0
2.0
2.4
2.8
11
10
9
8
7
6
5
4
3
2


H2O
DMSO
(9)
Pd
c, e
j
b, d
g
i
h
f
k
a
2.0
1.0
2.1
1.1
1.3
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2.1
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11
10
9
8
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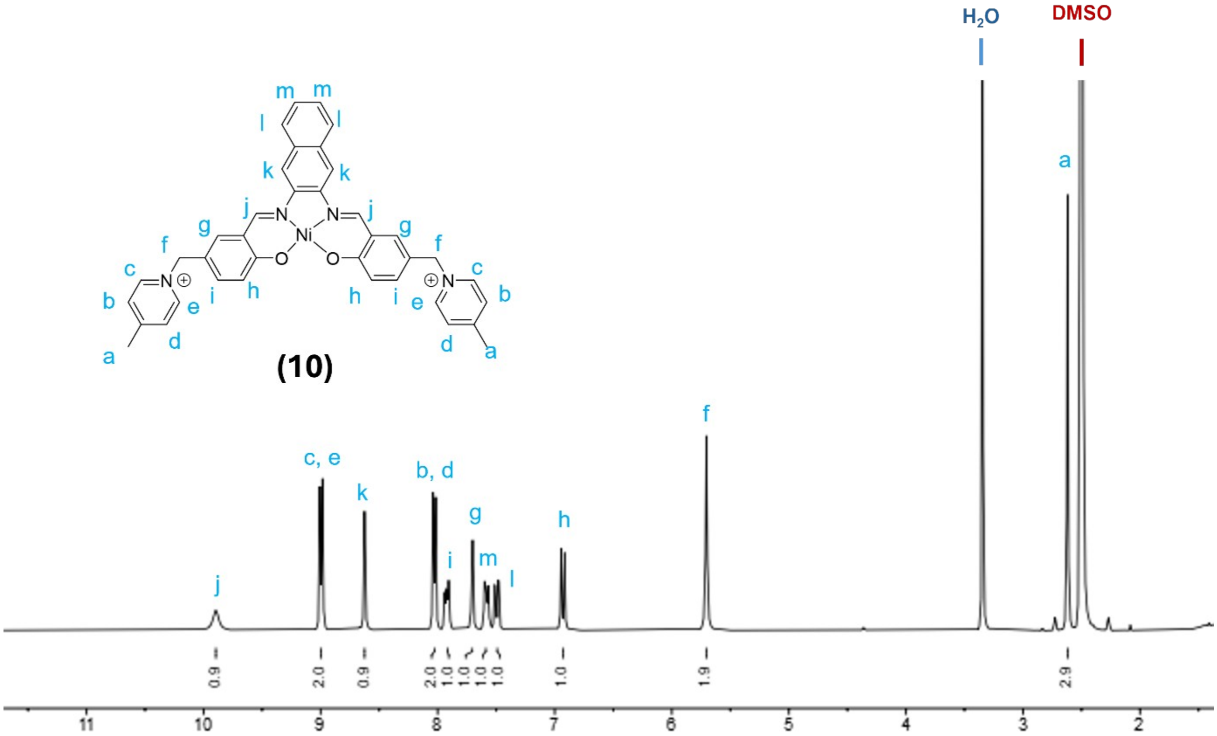
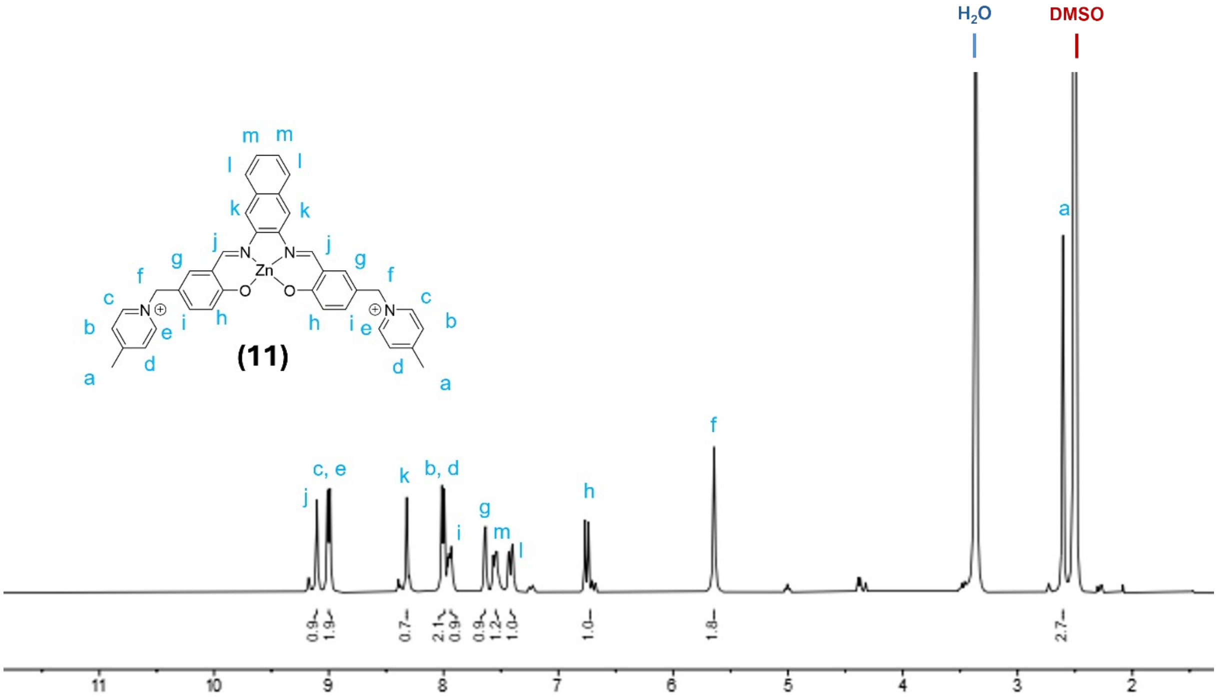
6
5
4
3
2



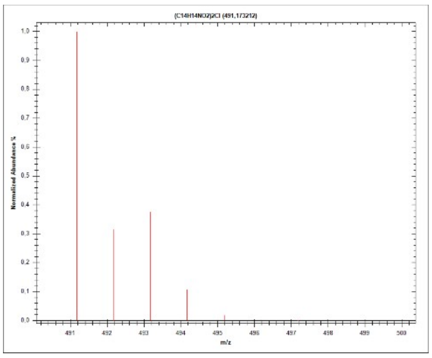
(10)
Ni
H2O
DMSO
a
f
c, e
k
b, d
g
i
m
l
h
j
0.9
2.0
0.9
2.0
1.0
1.0
1.0
1.0
1.0
1.9
2.9
11
10
9
8
7
6
5
4
3
2



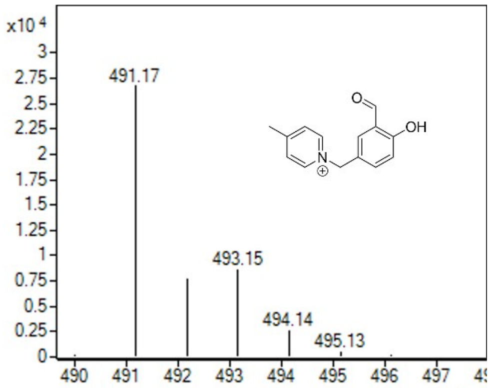
(11)
Zn
H2O
DMSO
a
f
c, e
j
k
b, d
g
i
m
l
h
0.9
1.9
0.7
2.1
0.9
0.9
1.2
1.0
1.0
1.8
2.7
11
10
9
8
7
6
5
4
3
2

Figure S3. Mass spectra of compound **B** and metal complexes **1-12.** In each figure, calculated values (table), theorical spectrum (left) and experimental spectrum (right) are reported.

Compound **B**
Calculated for $C_{14}H_{14}NO_2$ $[2M + Cl]^+$ 491.17; found 491.17



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
491,17	100	54,93	100
492,18	31,49	17,3	31,49
493,17	37,61	20,66	37,61
494,17	10,8	5,93	10,8
495,18	1,87	1,03	1,87
496,18	0,24	0,13	0,24
497,18	0,02	0,01	0,02

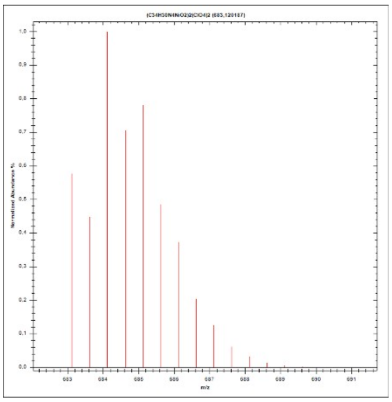


Calculated

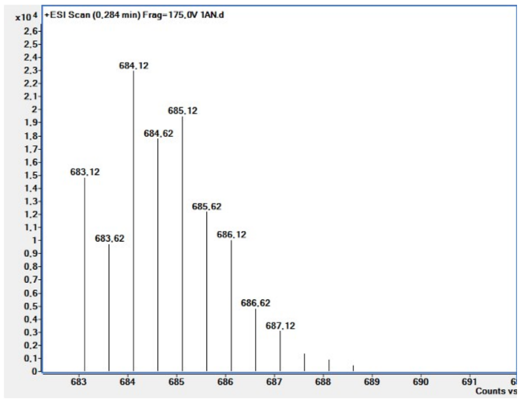
Found

Compound **1**

Calculated for $(C_{34}H_{30}N_4O_2Ni)_2(ClO_4)_2$ $[M]^{2+}$ 684.12; found 684.12



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
683,12	57,73	11,99	100
683,62	44,81	9,31	77,62
684,12	100	20,77	173,22
684,62	70,55	14,65	122,21
685,12	78,05	16,21	135,19
685,62	48,6	10,09	84,19
686,12	37,26	7,74	64,53
686,62	20,34	4,22	35,22
687,12	12,5	2,6	21,65
687,62	6,09	1,27	10,55
688,12	3,16	0,66	5,48
688,62	1,39	0,29	2,41
689,12	0,62	0,13	1,07
689,62	0,24	0,05	0,42
690,12	0,09	0,02	0,16
690,62	0,03	0,01	0,05

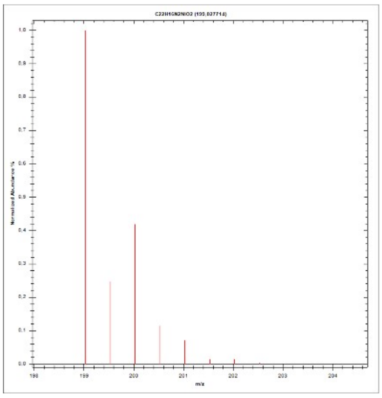


Calculated

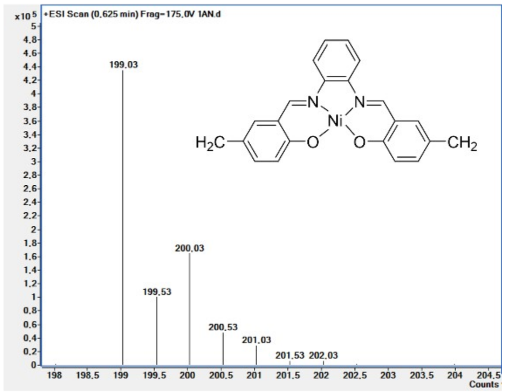
Found

Compound **1**

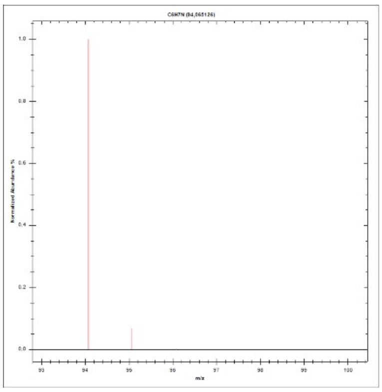
Calculated for $C_{22}H_{16}N_2NiO_2$ $[M]^{2+}$ 199.03; found 199.03



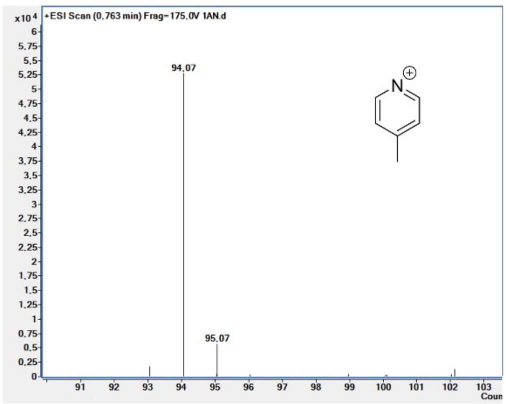
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
199,03	100	52,98	100
199,53	24,79	13,13	24,79
200,03	41,87	22,19	41,87
200,53	11,55	6,12	11,55
201,03	7,07	3,75	7,07
201,53	1,51	0,8	1,51
202,02	1,55	0,82	1,55
202,53	0,36	0,19	0,36
203,03	0,05	0,02	0,05
203,53	0	0	0



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.07



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

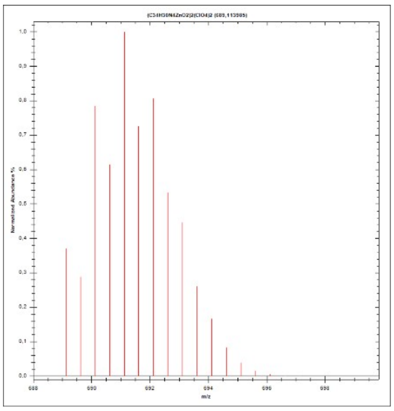


Calculated

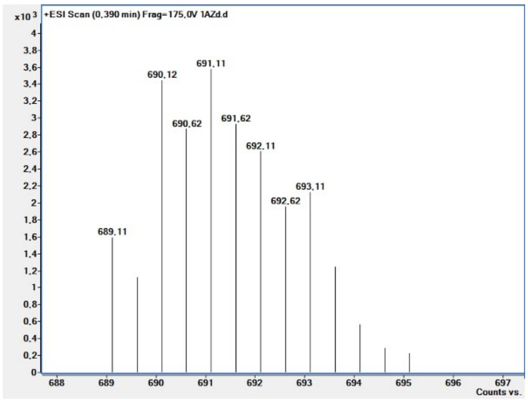
Found

Compound **2**

Calculated for $(C_{34}H_{30}N_4O_2Zn)_2(ClO_4)_2$ $[M]^{2+}$ 691.11; found 691.11



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
689,11	37,03	6,03	100
689,62	28,74	4,68	77,62
690,11	78,53	12,78	212,09
690,61	61,47	10,01	166,03
691,11	100	16,28	270,08
691,61	72,68	11,83	196,29
692,11	80,64	13,13	217,8
692,61	53,36	8,69	144,12
693,11	44,62	7,26	120,5
693,61	26,12	4,25	70,54
694,11	16,66	2,71	45
694,61	8,25	1,34	22,29
695,11	3,88	0,63	10,49
695,61	1,54	0,25	4,15
696,11	0,53	0,09	1,42
696,61	0,16	0,03	0,42
697,11	0,04	0,01	0,11

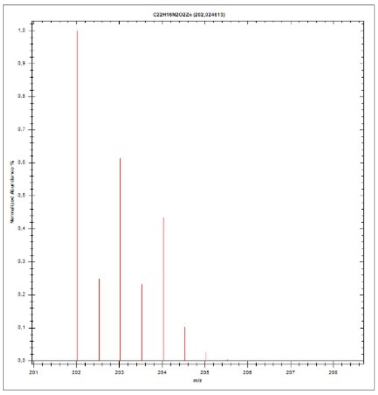


Calculated

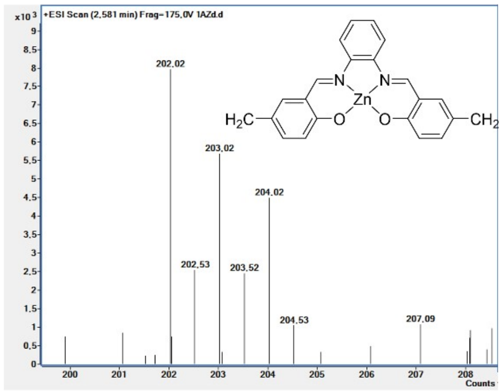
Found

Compound **2**

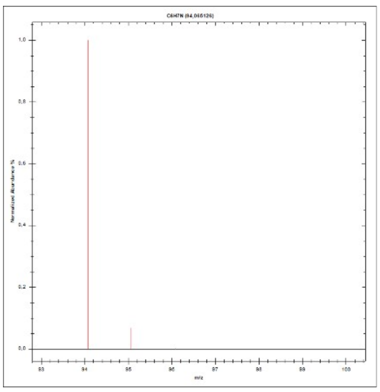
Calculated for $C_{22}H_{16}N_2ZnO_2$ $[M]^{2+}$ 202.02; found 202.02



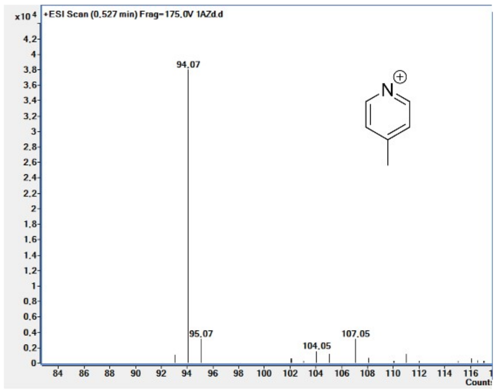
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
202,02	100	37,57	100
202,53	24,79	9,31	24,79
203,02	61,31	23,03	61,31
203,52	23,19	8,71	23,19
204,02	43,49	16,34	43,49
204,52	10,24	3,85	10,24
205,02	2,67	1	2,67
205,53	0,45	0,17	0,45
206,03	0,05	0,02	0,05



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.07



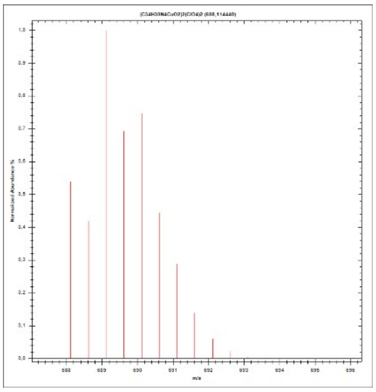
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0



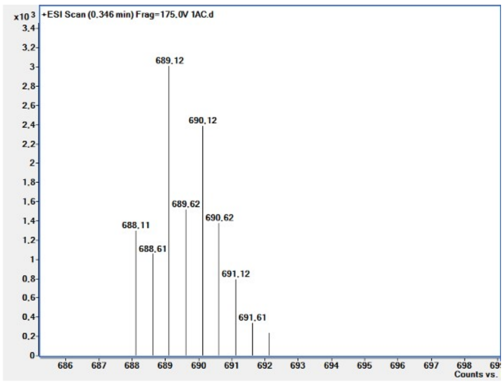
Calculated

Found

Compound **3**
Calculated for $(C_{34}H_{30}N_4O_2Cu)_2(ClO_4)_2$ $[M]^{2+}$ 689.11; found 689.12



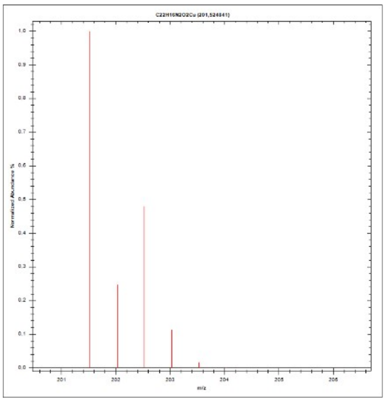
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
688,11	53,94	12,37	100
688,62	41,86	9,6	77,62
689,11	100	22,94	185,4
689,62	69,21	15,88	128,32
690,11	74,81	17,16	138,7
690,61	44,51	10,21	82,52
691,11	28,76	6,6	53,32
691,61	13,92	3,19	25,81
692,11	5,97	1,37	11,06
692,61	2,16	0,5	4,01
693,11	0,64	0,15	1,19
693,62	0,16	0,04	0,29
694,12	0,03	0,01	0,06
694,62	0,01	0	0,01



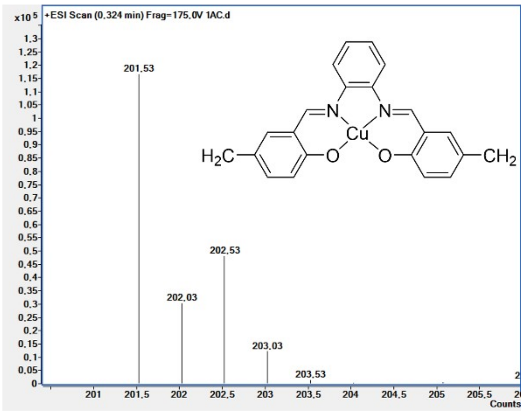
Calculated

Found

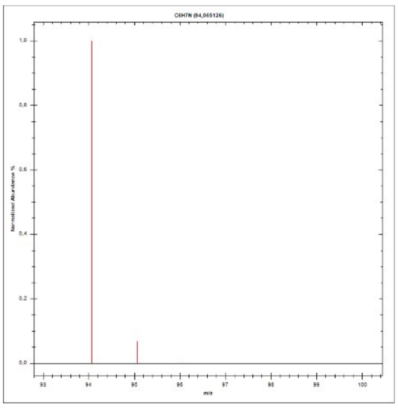
Compound **3**
Calculated for $C_{22}H_{16}N_2CuO_2$ $[M]^{2+}$ 201.52; found 201.53



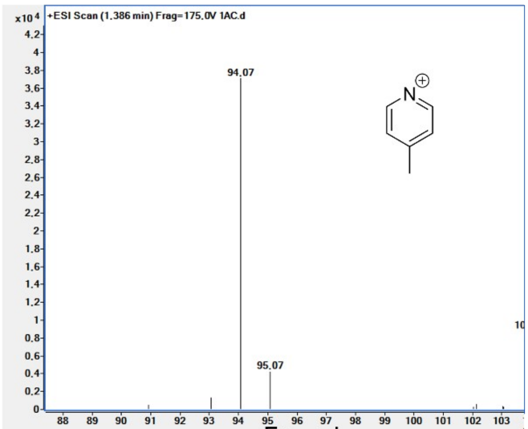
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
201,52	100	53,82	100
202,03	24,79	13,34	24,79
202,52	47,97	25,81	47,97
203,03	11,38	6,13	11,38
203,53	1,52	0,82	1,52
204,03	0,15	0,08	0,15
204,53	0,01	0,01	0,01
205,03	0	0	0
205,53	0	0	0



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.07



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

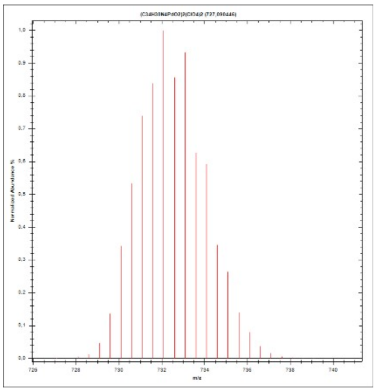


Calculated

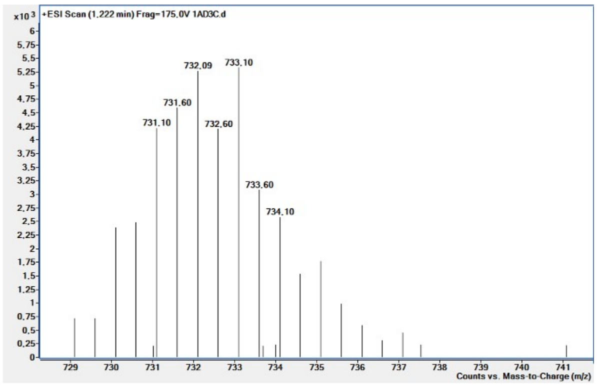
Found

Compound **4**

Calculated for $(C_{34}H_{30}N_4O_2Pd)_2(ClO_4)_2$ $[M]^{2+}$ 732.09; found 732.09



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
727,09	0,02	0	100
727,59	0,02	0	77,62
728,09	0,46	0,06	2280,49
728,59	1,25	0,17	6132,89
729,09	4,64	0,61	22819,06
729,59	13,57	1,8	66752,4
730,09	34,29	4,54	168694,72
730,59	53,25	7,05	261929,45
731,09	73,97	9,79	363863,41
731,59	83,83	11,1	412332,06
732,09	100	13,24	491894,66
732,59	85,67	11,34	421389,09
733,09	93,26	12,35	458759,66
733,59	62,75	8,31	308670,97
734,09	59,3	7,85	291692,22
734,59	34,55	4,57	169930,06
735,09	26,4	3,5	129869,48
735,59	13,98	1,85	68760,91
736,09	8,05	1,07	39593,71
736,59	3,7	0,49	18178,14
737,09	1,54	0,2	7561,02
737,59	0,55	0,07	2701,35
738,09	0,16	0,02	794,59
738,59	0,04	0,01	193,39
739,09	0,01	0	39,79

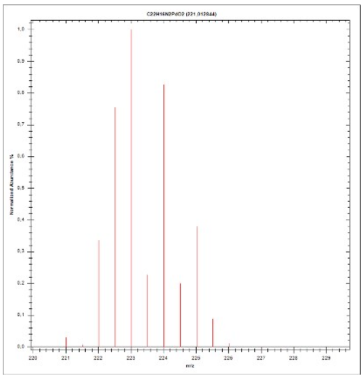


Calculated

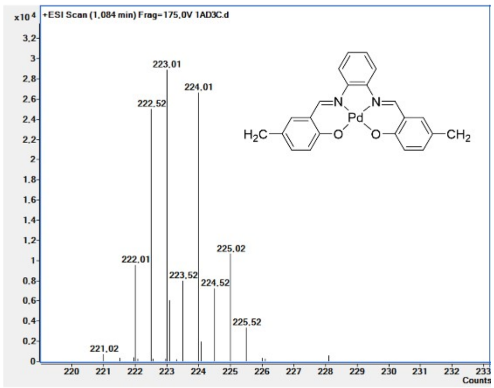
Found

Compound **4**

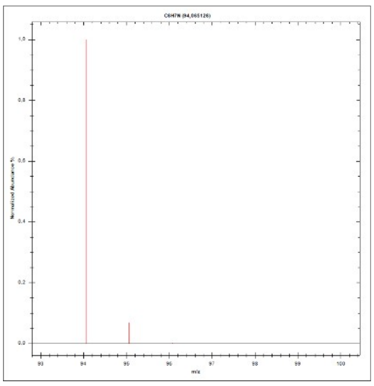
Calculated for $C_{22}H_{16}N_2PdO_2$ $[M]^{2+}$ 223.01; found 223.01



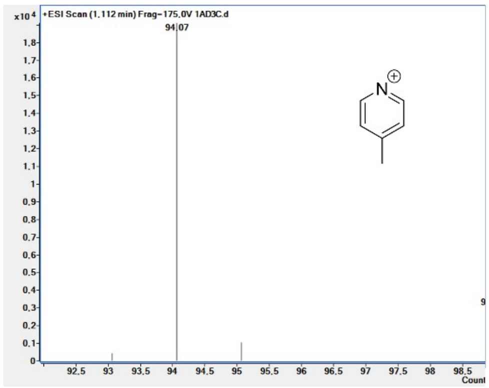
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
221,01	3,07	0,79	100
221,51	0,76	0,2	24,79
222,01	33,62	8,7	1095,51
222,51	75,5	19,53	2460,24
223,01	100	25,87	3258,66
223,51	22,74	5,88	741,04
224,01	82,59	21,36	2691,31
224,51	20,01	5,18	652,2
225,01	37,95	9,82	1236,68
225,51	9	2,33	293,24
226,02	1,2	0,31	39,16
226,52	0,12	0,03	3,76
227,02	0,01	0	0,28



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.07



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

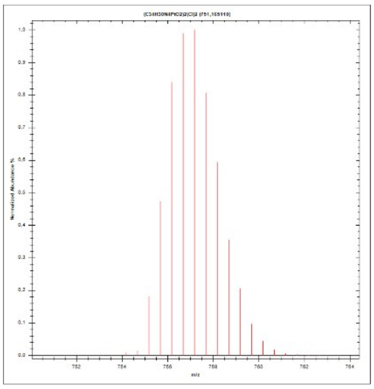


Calculated

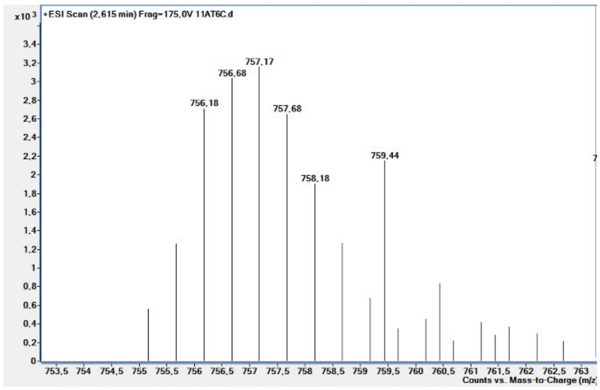
Found

Compound **5**

Calculated for $(C_{34}H_{30}N_4O_2Pt)_2(Cl)_2$ $[M]^{2+}$ 757.17; found 757.17



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
751,17	0	0	100
751,67	0	0	77,31
752,17	0	0	11265,72
752,67	0	0	8694,36
753,17	0,02	0	793524,62
753,67	0,03	0,01	1095073
754,17	0,81	0,14	27782374
754,67	1,41	0,25	48520740
755,17	18,09	3,21	621286464
755,67	47,26	8,39	1623495296
756,17	83,97	14,92	2884638720
756,67	98,96	17,58	3399493888
757,17	100	17,76	3435235584
757,67	80,56	14,31	2767489792
758,17	59,27	10,53	2035922048
758,67	35,47	6,3	1218424832
759,17	20,6	3,66	707687040
759,67	9,66	1,72	331954944
760,17	4,38	0,78	150623472
760,67	1,68	0,3	57688952
761,17	0,57	0,1	19728486
761,67	0,17	0,03	5998175

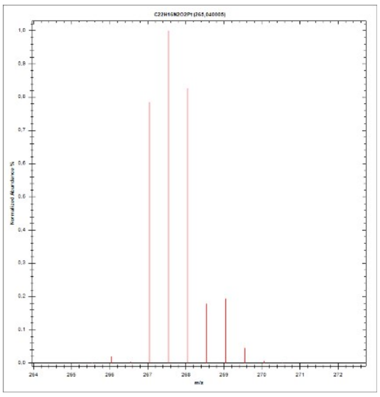


Calculated

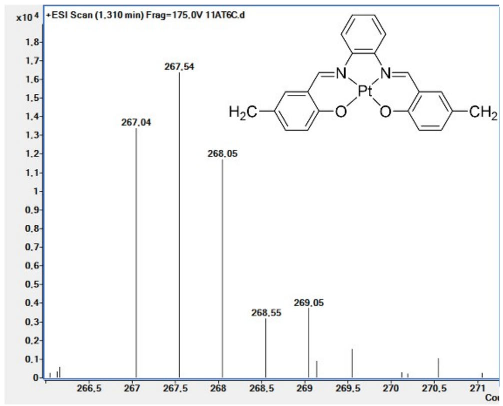
Found

Compound **5**

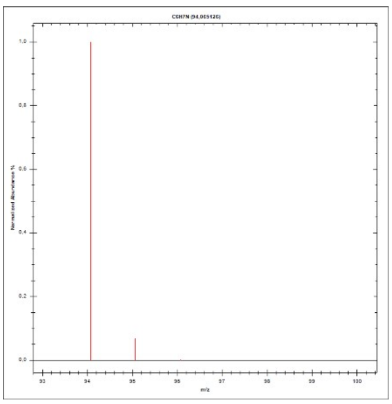
Calculated for $C_{22}H_{16}N_2PtO_2$ $[M]^{2+}$ 267.54; found 267.54



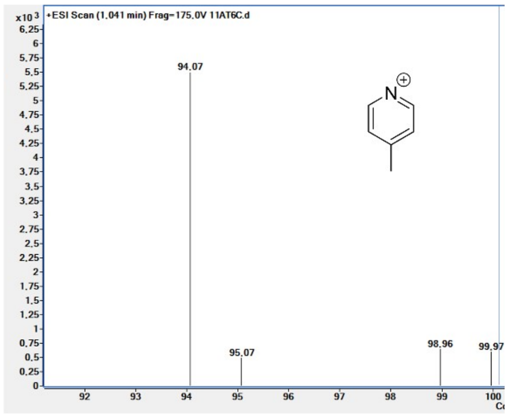
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
265,04	0,03	0,01	100
265,54	0,01	0	24,79
266,04	1,86	0,61	5589,07
266,54	0,46	0,15	1384,77
267,04	78,54	25,68	235665,88
267,54	100	32,69	300039,72
268,04	82,69	27,03	248091,8
268,54	17,85	5,84	53553,36
269,04	19,35	6,33	58050,08
269,55	4,44	1,45	13328,6
270,05	0,59	0,19	1763,34
270,55	0,06	0,02	168,78
271,05	0	0	12,69



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.07



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

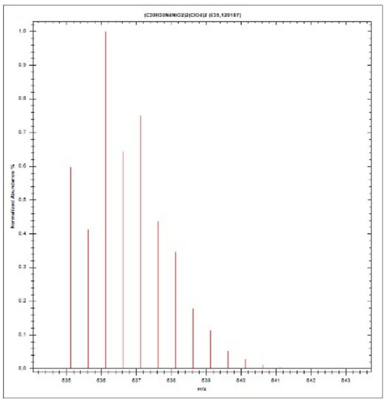


Calculated

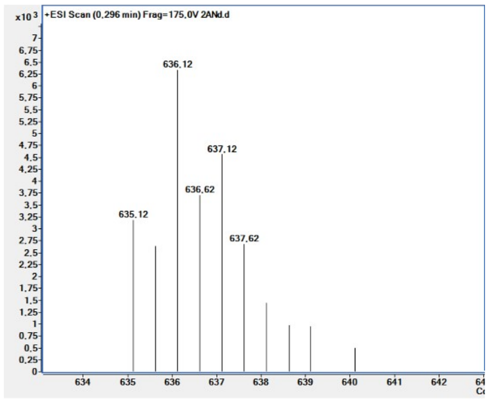
Found

Compound **6**

Calculated for $(C_{30}H_{30}N_4O_2Ni)_2(ClO_4)_2$ $[M]^{2+}$ 636.12; found 636.12



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
635,12	59,91	13,07	100
635,62	41,32	9,01	68,96
636,12	100	21,81	166,92
636,62	64,42	14,05	107,53
637,12	75,09	16,38	125,34
637,62	43,72	9,54	72,98
638,12	34,63	7,55	57,8
638,62	17,96	3,92	29,97
639,12	11,3	2,46	18,86
639,62	5,28	1,15	8,82
640,12	2,79	0,61	4,65
640,62	1,19	0,26	1,98
641,12	0,53	0,11	0,88
641,62	0,2	0,04	0,33

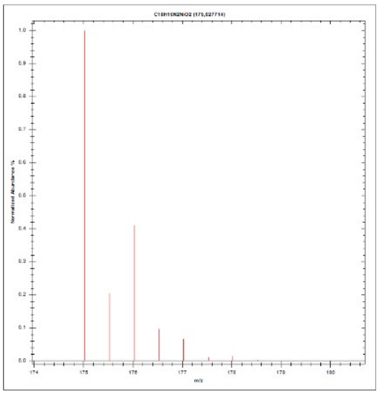


Calculated

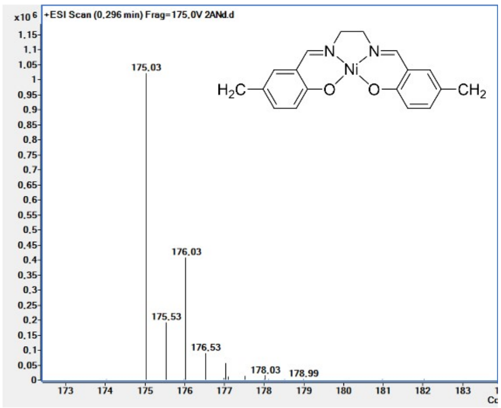
Found

Compound **6**

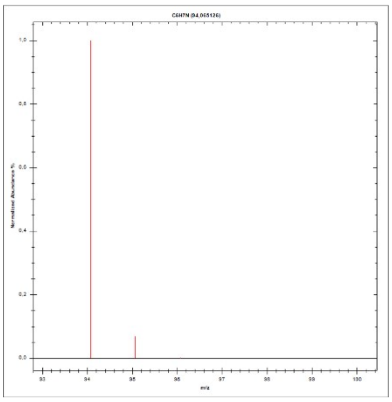
Calculated for $C_{18}H_{16}N_2NiO_2$ $[M]^{2+}$ 175.03; found 175.03



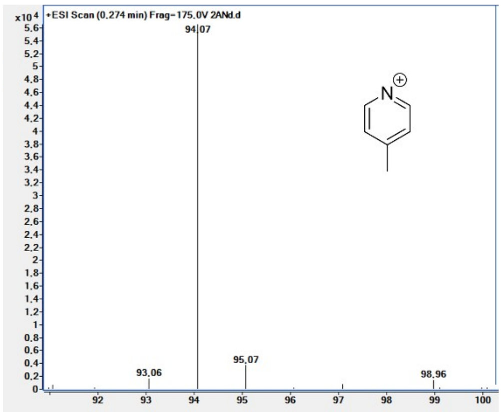
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
175,03	100	55,31	100
175,53	20,46	11,32	20,46
176,03	40,92	22,63	40,92
176,53	9,76	5,4	9,76
177,02	6,62	3,66	6,62
177,53	1,21	0,67	1,21
178,02	1,5	0,83	1,5
178,53	0,29	0,16	0,29
179,03	0,03	0,02	0,03



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.07

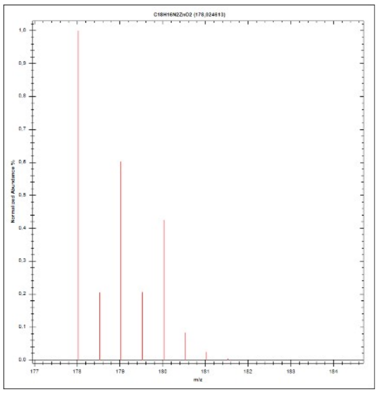


m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

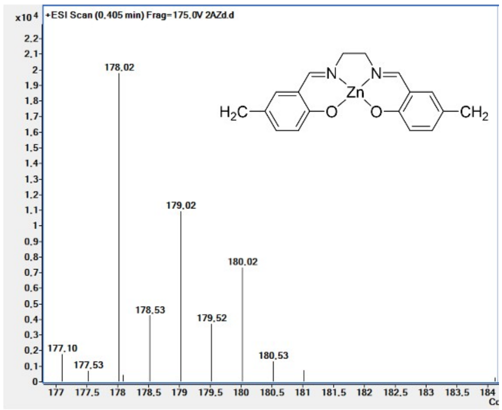


Compound **7**

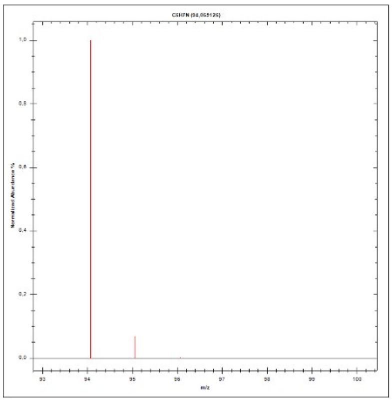
Calculated for $C_{18}H_{16}N_2ZnO_2$ $[M]^{2+}$ 178.02; found 178.02



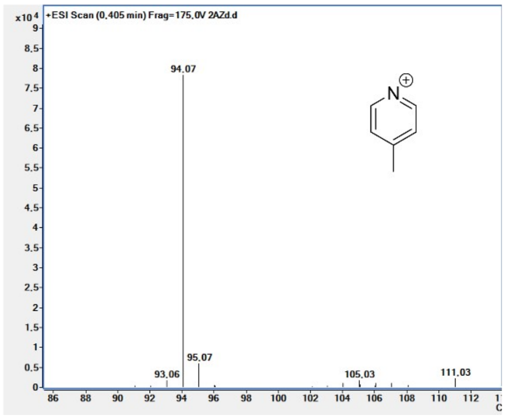
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
178,02	100	39,22	100
178,53	20,46	8,02	20,46
179,02	60,35	23,67	60,35
179,52	20,56	8,06	20,56
180,02	42,56	16,69	42,56
180,52	8,39	3,29	8,39
181,02	2,28	0,89	2,28
181,52	0,35	0,14	0,35
182,03	0,04	0,01	0,04
182,53	0	0	0



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.07

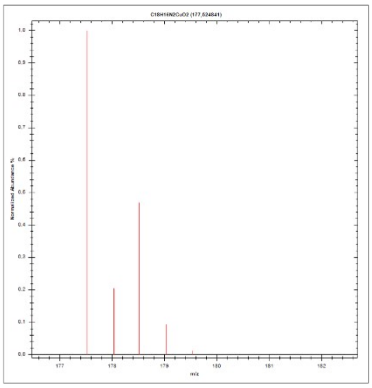


m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

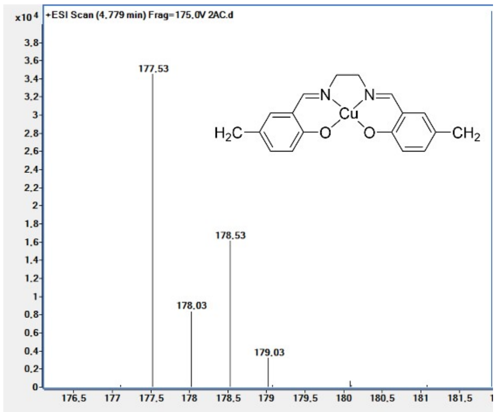


Compound **8**

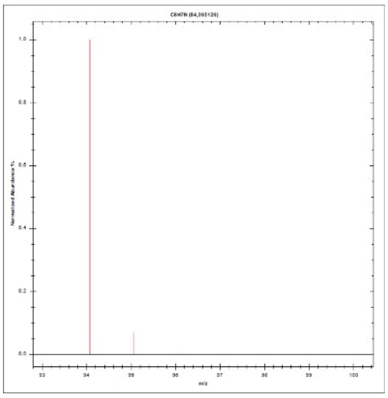
Calculated for $C_{18}H_{16}N_2CuO_2$ $[M]^{2+}$ 177.52; found 177.53



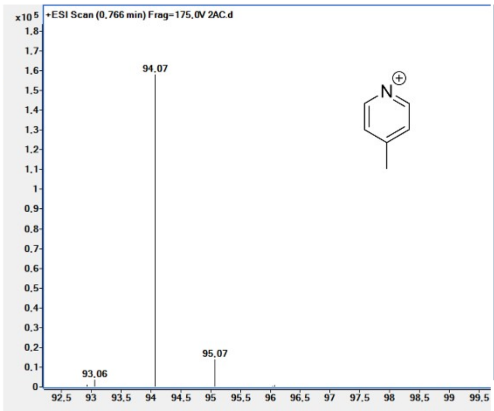
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
177,52	100	56,18	100
178,03	20,46	11,49	20,46
178,52	47,01	26,41	47,01
179,03	9,33	5,24	9,33
179,53	1,08	0,61	1,08
180,03	0,09	0,05	0,09
180,53	0,01	0	0,01



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.07

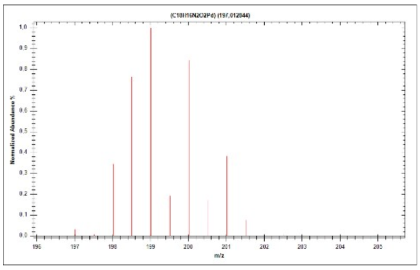


m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

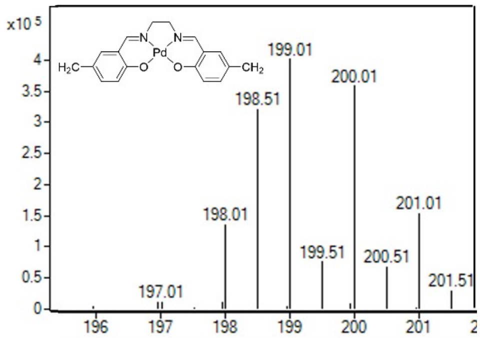


Compound **9**

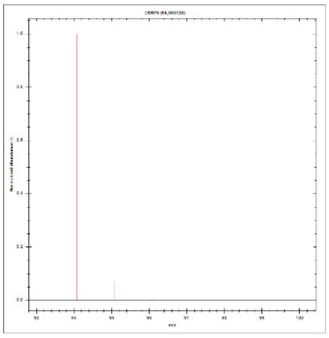
Calculated for $C_{18}H_{16}N_2PdO_2$ $[M]^{2+}$ 199.01; found 199.01



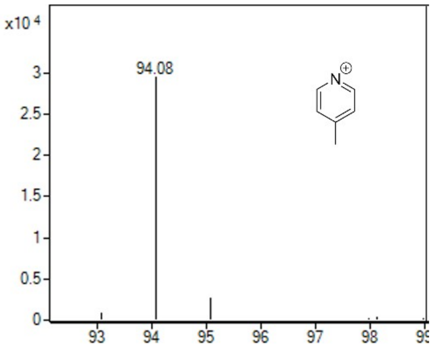
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
197,01	3,17	0,83	100
197,51	0,65	0,17	20,46
198,01	34,71	9,07	1094,55
198,51	76,51	20	2412,87
199,01	100	26,13	3153,5
199,51	19,12	5	602,91
200,01	84,45	22,07	2663
200,51	17,01	4,45	536,56
201,01	38,42	10,04	1211,59
201,51	7,62	1,99	240,43
202,02	0,88	0,23	27,9
202,52	0,08	0,02	2,38
203,02	0,01	0	0,16
203,52	0	0	0,01



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.08

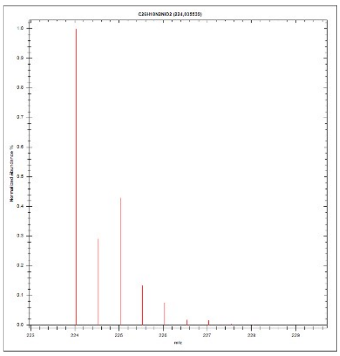


m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

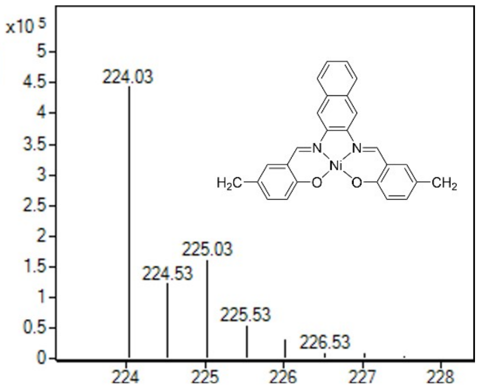


Compound **10**

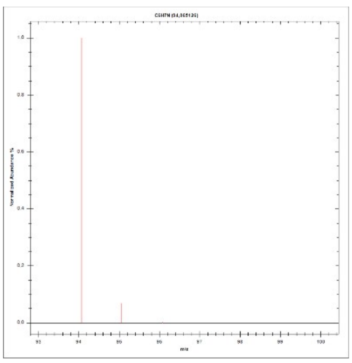
Calculated for $C_{26}H_{18}N_2NiO_2$ $[M]^{2+}$ 224.04; found 224.03



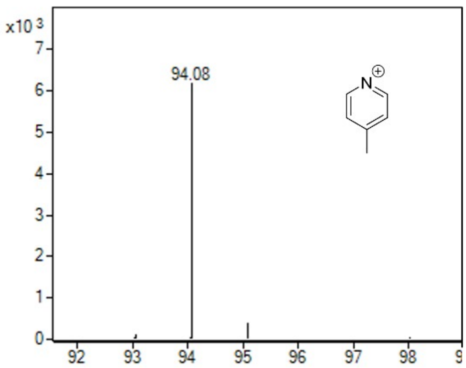
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
224,04	100	50,74	100
224,54	29,13	14,78	29,13
225,03	43,02	21,83	43,02
225,53	13,39	6,79	13,39
226,03	7,6	3,86	7,6
226,53	1,82	0,92	1,82
227,03	1,62	0,82	1,62
227,53	0,42	0,22	0,42
228,04	0,06	0,03	0,06
228,54	0,01	0	0,01



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.08

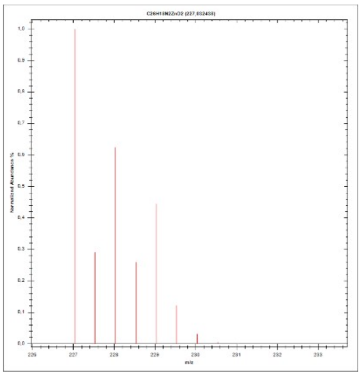


m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

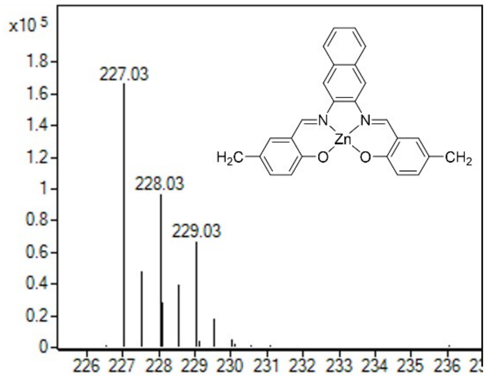


Compound **11**

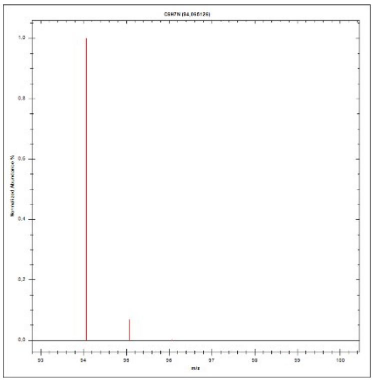
Calculated for $C_{26}H_{18}N_2ZnO_2$ $[M]^{2+}$ 227.03; found 227.03



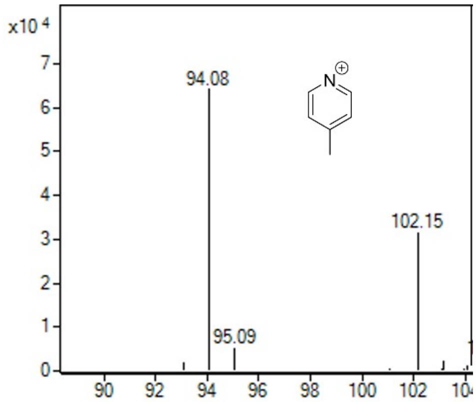
m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
227,03	100	35,98	100
227,53	29,13	10,48	29,13
228,03	62,46	22,47	62,46
228,53	25,87	9,31	25,87
229,03	44,54	16,02	44,54
229,53	12,15	4,37	12,15
230,03	3,15	1,13	3,15
230,53	0,58	0,21	0,58
231,03	0,08	0,03	0,08
231,54	0,01	0	0,01



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.08

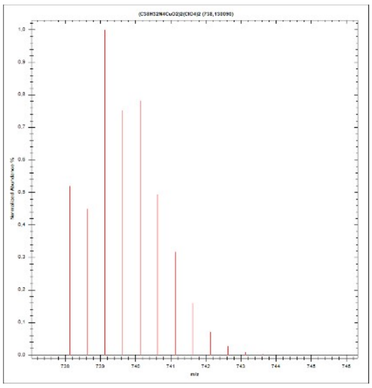


m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

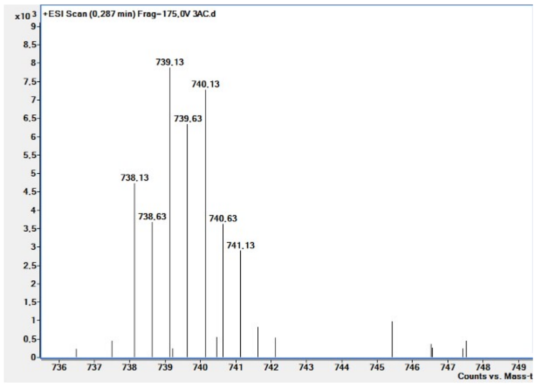


Compound **12**

Calculated for $(C_{38}H_{32}N_4O_2Cu)_2(ClO_4)_2$ $[M]^{2+}$ 739.13; found 739.13



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
738,13	51,95	11,35	100
738,63	44,84	9,79	86,32
739,13	100	21,84	192,49
739,63	75,18	16,42	144,71
740,13	78,18	17,07	150,49
740,63	49,37	10,78	95,02
741,13	31,67	6,92	60,96
741,63	15,97	3,49	30,73
742,13	7,01	1,53	13,49
742,63	2,63	0,57	5,06
743,13	0,82	0,18	1,58
743,63	0,21	0,05	0,41
744,13	0,05	0,01	0,09
744,63	0,01	0	0,02

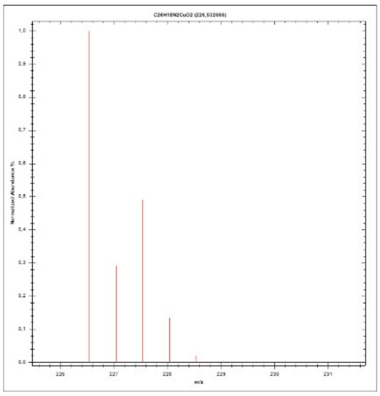


Calculated

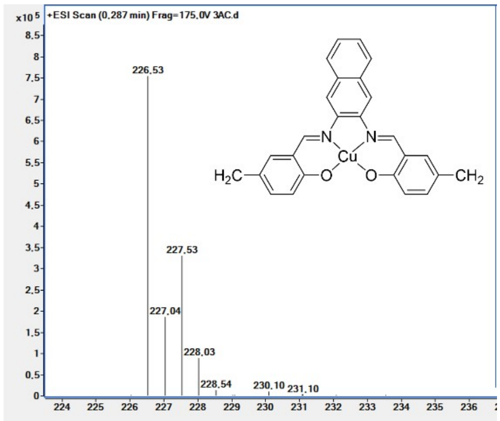
Found

Compound **12**

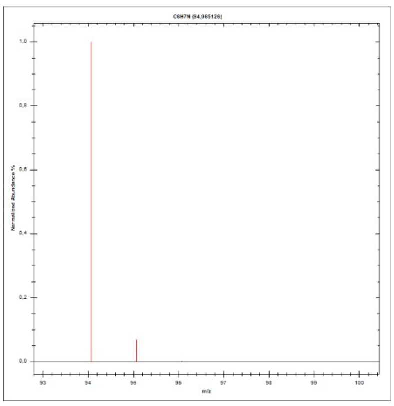
Calculated for $C_{26}H_{18}N_2CuO_2$ $[M]^{2+}$ 226.53; found 226.53



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
226,53	100	51,54	100
227,03	29,13	15,02	29,13
227,53	49,11	25,31	49,11
228,03	13,49	6,95	13,49
228,53	2,05	1,06	2,05
229,04	0,22	0,11	0,22
229,54	0,02	0,01	0,02
230,04	0	0	0
230,54	0	0	0



Calculated for C_6H_7N $[M + H]^+$ 94.07; found 94.07



m/z	Abund (% largest)	Abund (% sum)	Abund (% first)
94,07	100	93,32	100
95,07	6,95	6,48	6,95
96,07	0,21	0,19	0,21
97,07	0	0	0

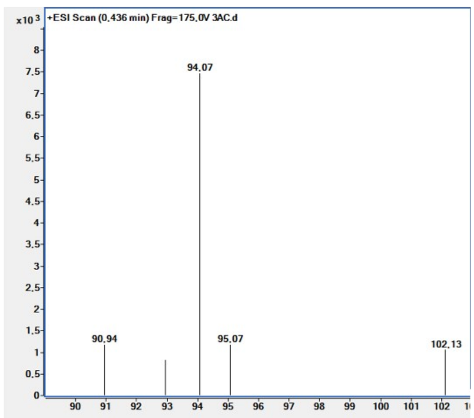


Figure S4. Example of FRET melting profile of cMYC G4 (0.2 µM, black line) upon interaction with compound **1** (1 µM, red line) in a [G4 DNA]:[compound **1**] ratio of 1:5 in 10 mM potassium cacodylate buffer, pH 7.2, showing that in such conditions the melting temperature cannot be reached.

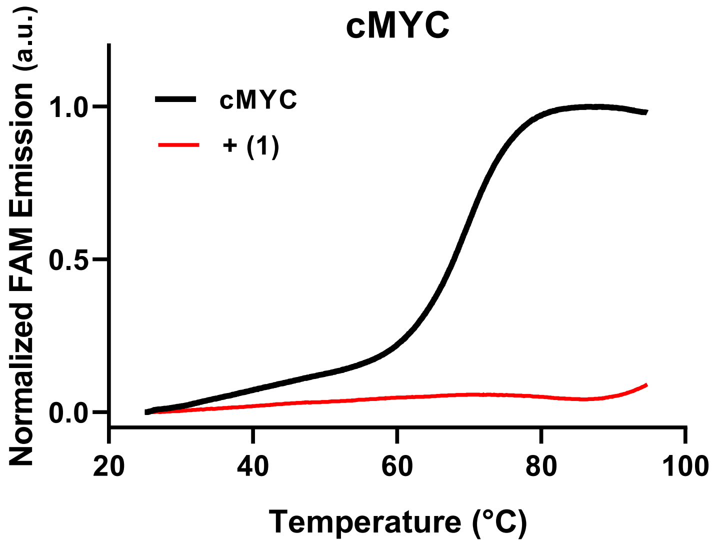


Figure S5. Circular dichroism spectra of ctDNA, *kRAS*, *BCL2* or *cMYC* quadruplexes in presence of increasing concentrations of complex **(6)** in 50 mM Tris HCl 100 mM KCl pH 7.4.

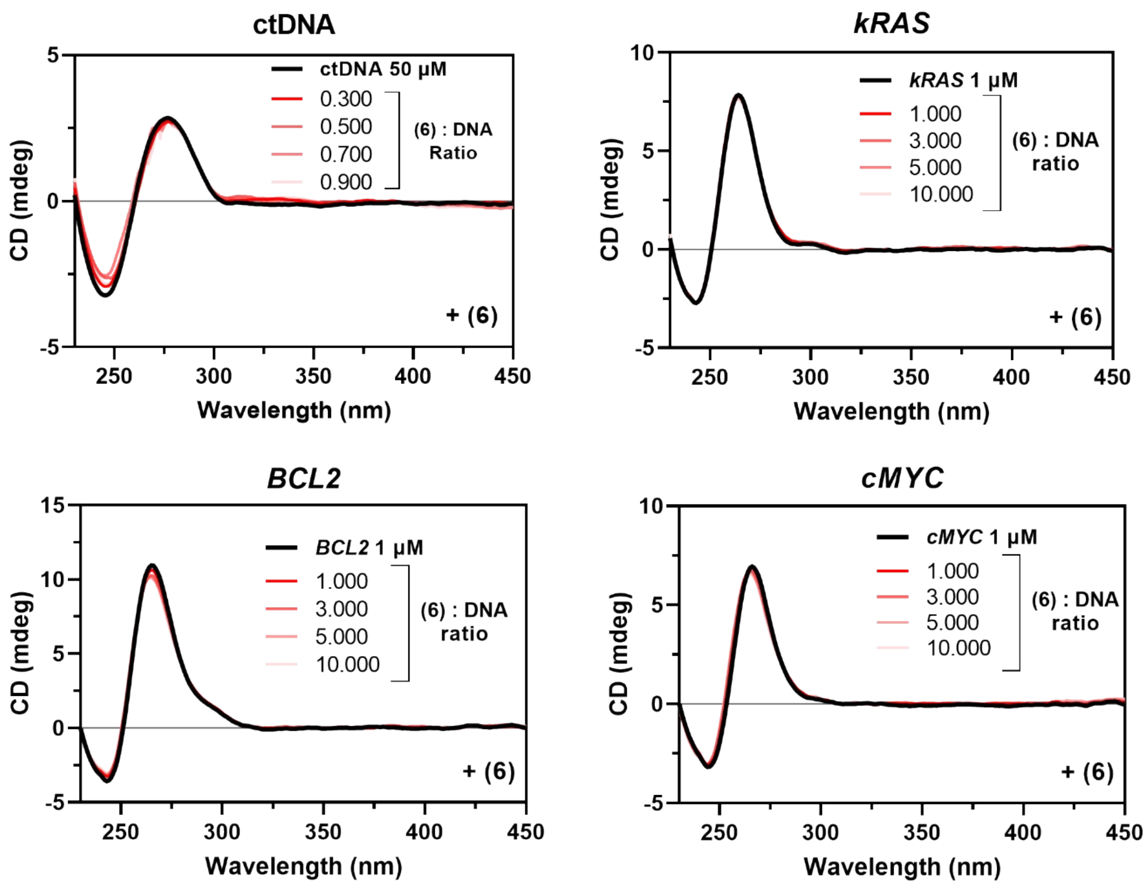


Figure S6. UV-vis spectra of compound **(1)** at 20 µM in presence of increasing concentration of ctDNA, *kRAS*, *BCL2* or *cMYC* quadruplexes in 50 mM Tris HCl 100 mM KCl pH 7.4.

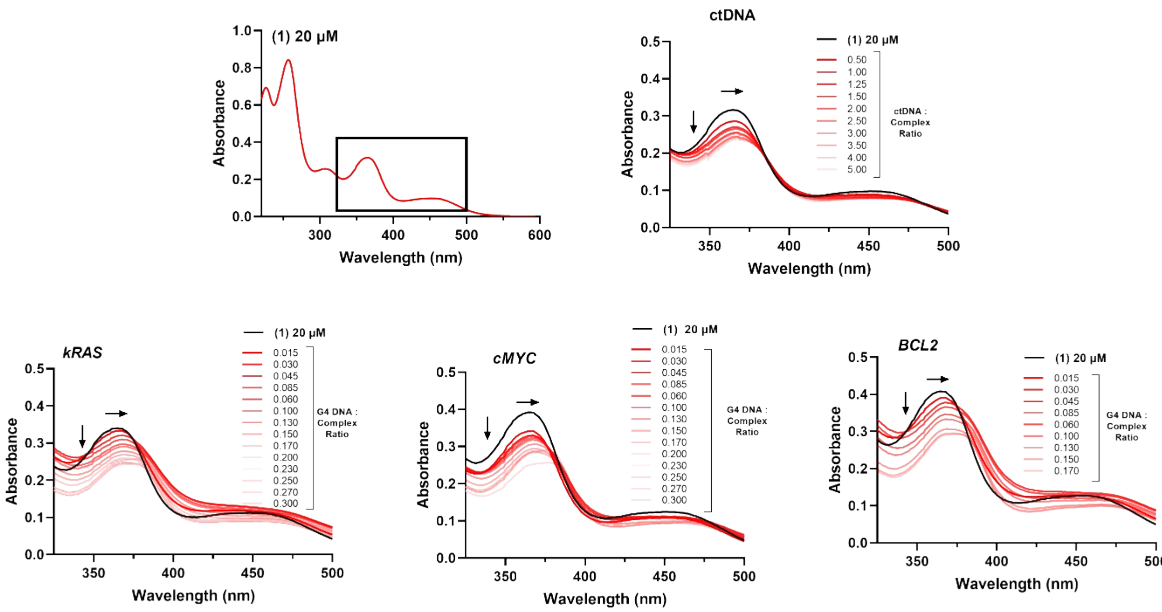


Figure S7. UV-vis spectra of compound **(6)** at 20 µM in presence of increasing concentration of ctDNA, *kRAS*, *BCL2* or *cMYC* quadruplexes in 50 mM Tris HCl 100 mM KCl pH 7.4.

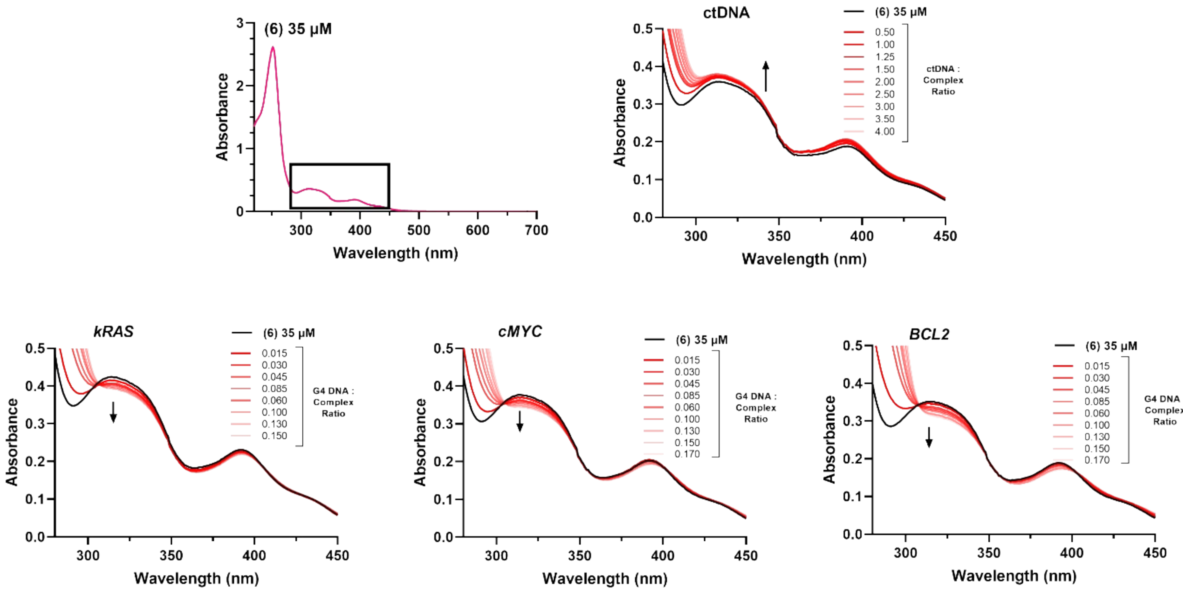


Figure S8. UV-vis spectra of compound **(10)** at 20 µM in presence of increasing concentration of ctDNA, *kRAS*, *BCL2* or *cMYC* quadruplexes in 50 mM Tris HCl 100 mM KCl pH 7.4.

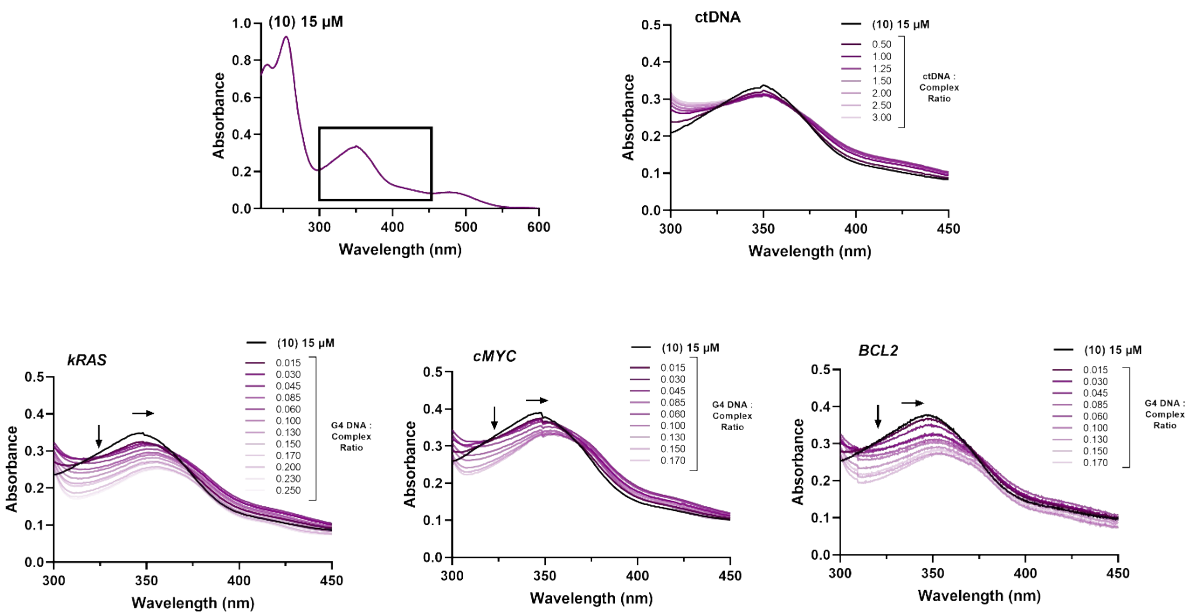


Figure S9. IC50 determination of metal complexes 1 – 12 on T3M4 cells. Relative viability (%) of T3M4 cell line at 48 hours of treatment of the considered complex metal, obtained by crystal violet assay. *Mean* ± *SEM* (n=5).

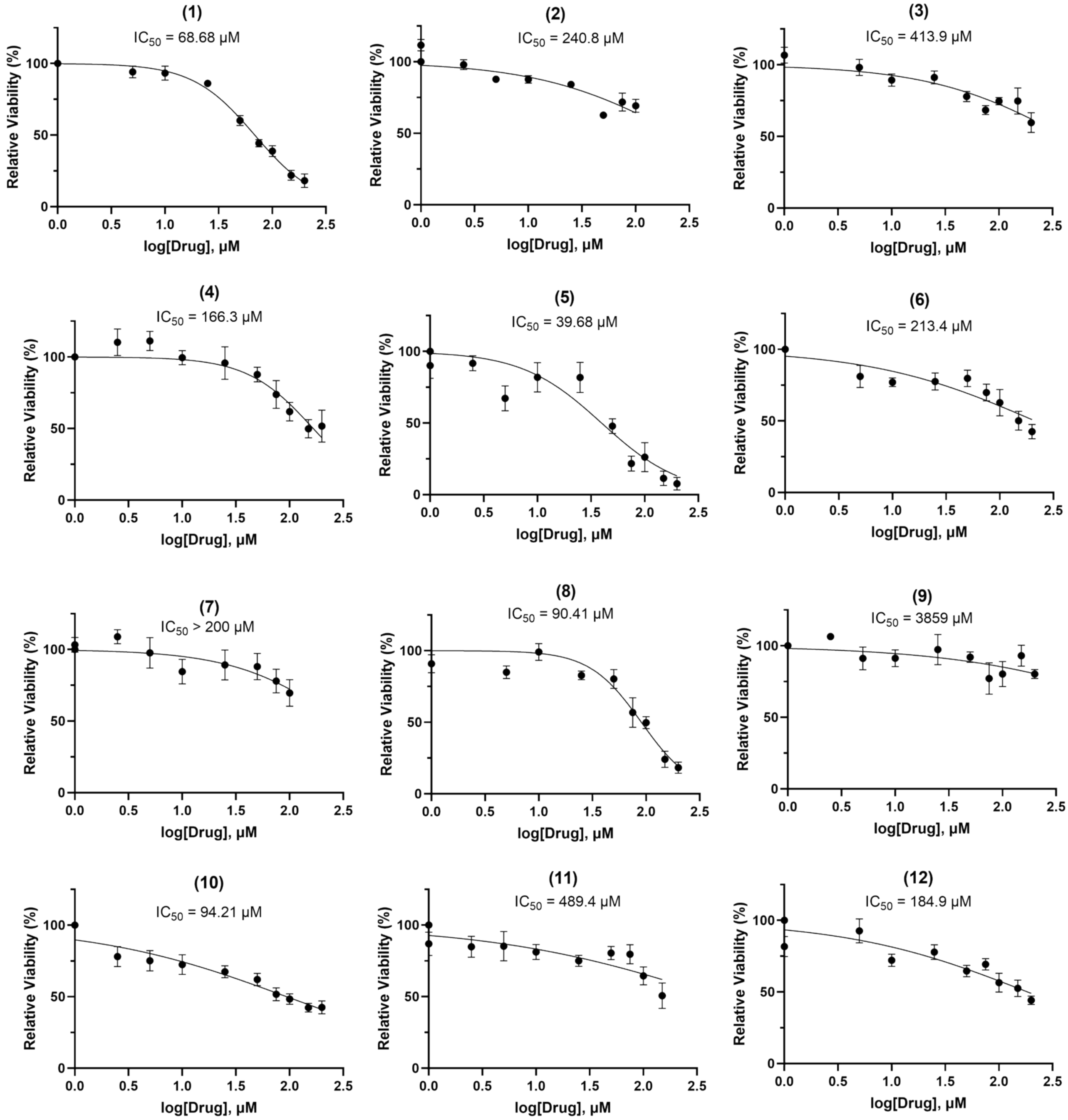


Figure S10. IC50 determination of metal complexes 1 – 12 on T47D cells. Relative viability (%) of T47D cell line at 48 hours of treatment of the considered complex metal, obtained by crystal violet assay. *Mean* ± *SEM* (n=5).

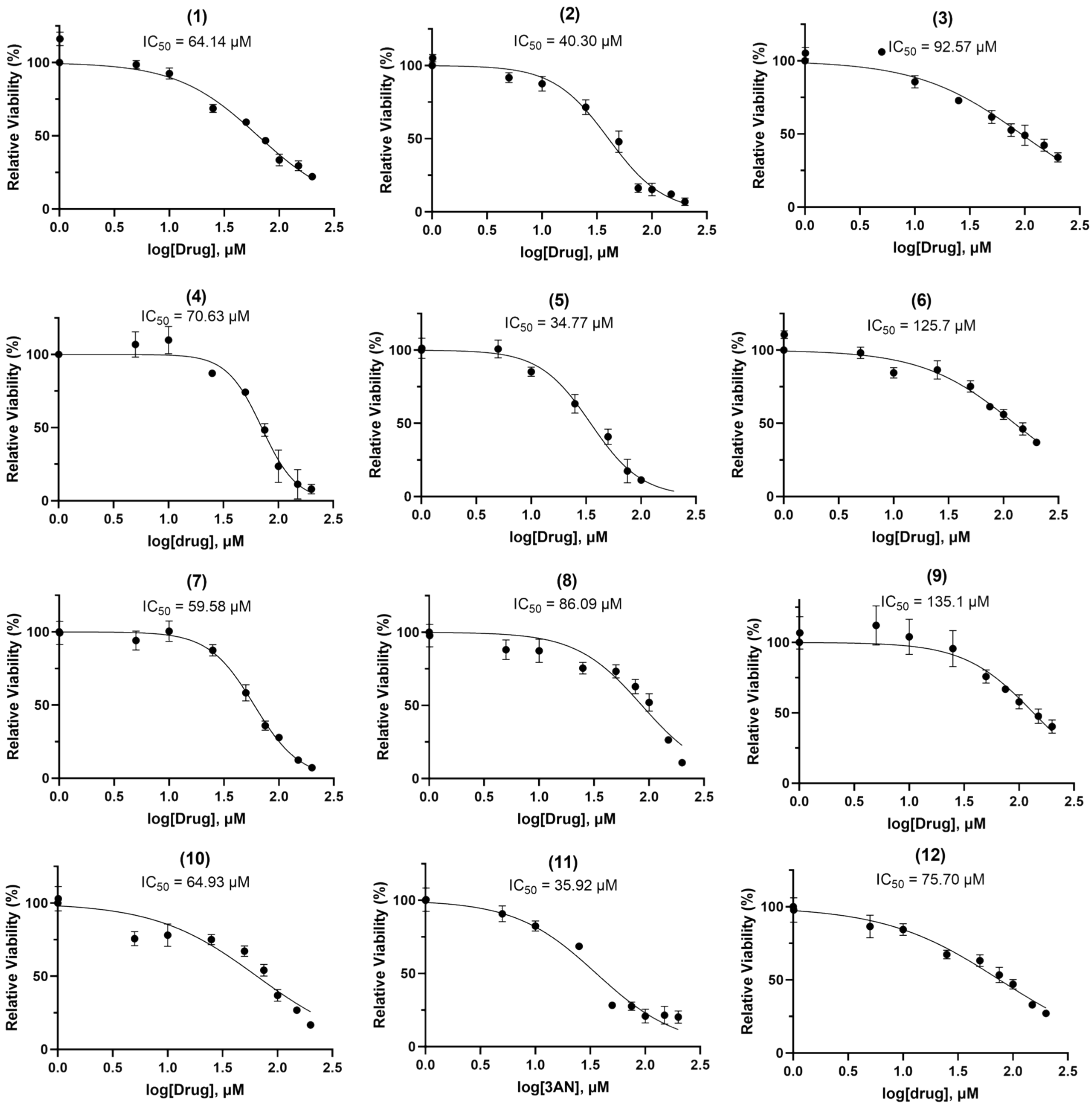


Figure S11. IC50 determination of metal complexes 1 – 12 on MDA-MB-231 cells. Relative viability (%) of MDA-MB-231 cell line at 48 hours of treatment of the considered complex metal, obtained by crystal violet assay. *Mean* ± *SEM* (n=5).

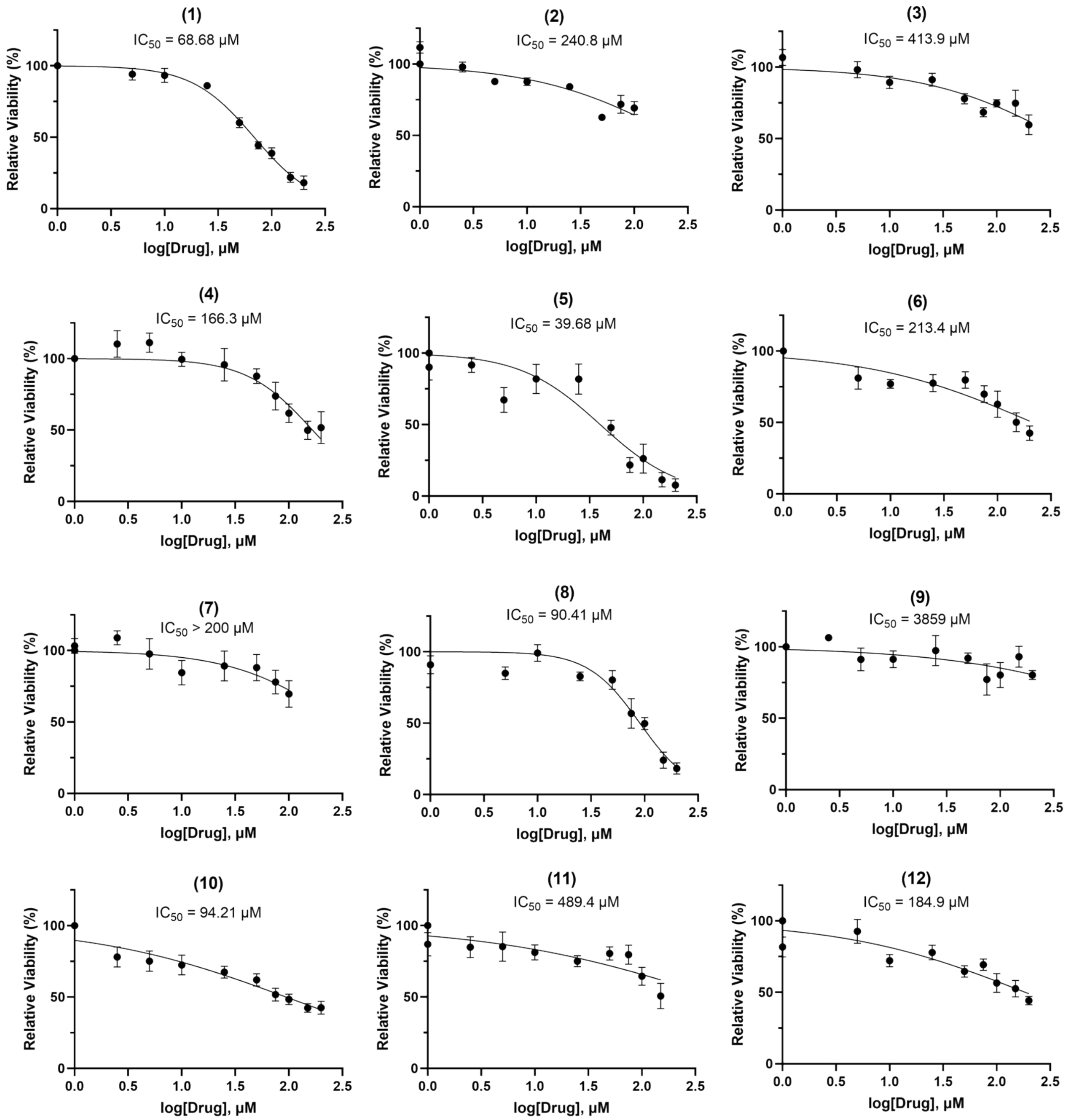
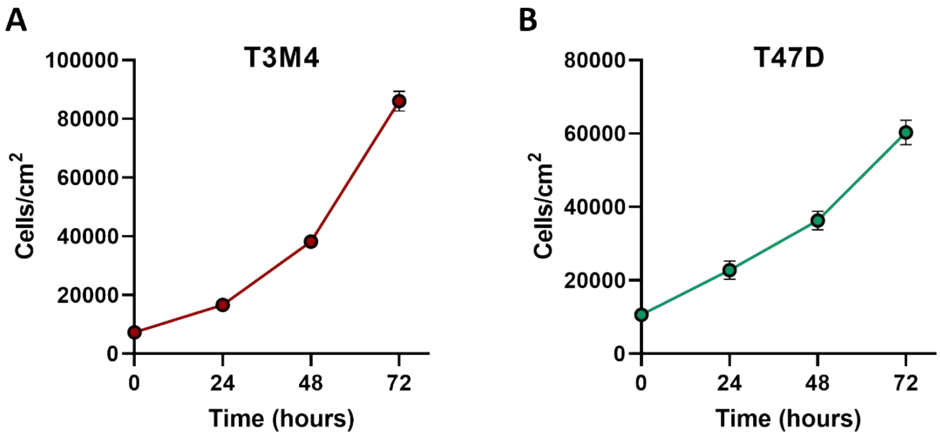
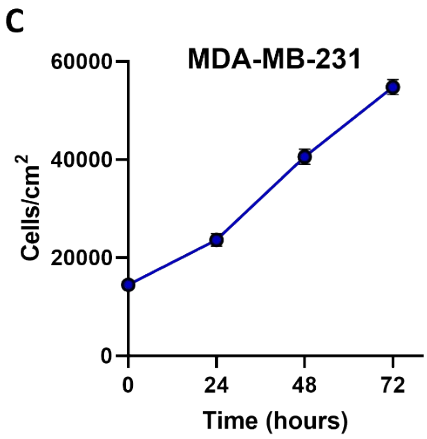


Figure S12. Doubling time of T3M4, T47D and MDA-MB-231 cell lines. Doubling time of T3M4 (A), T47D (B), and MDA-MB-231 (C) cell lines was determined from the proliferation follow-up of untreated cells over 72 hours using the equation: $T = \frac{t\ ln2}{\ln(day\ 1) - ln(day\ 2)}$. *Mean ± SEM* (n=6).





D

	Doubling time	± SEM
T3M4	20 hours	0,5
T47D	30 hours	1,3
MDA-MB-231	44 hours	4,6

Table S1. DNA sequences (5' – 3') of the G4 motifs used for the DNA binding studies. The oligonucleotides were used free for the UV-visible and Circular Dichroism assays, and fluorolabelled with FAM and TAMRA probes for FRET experiments. dsDNA was used only for the FRET experiment.

Oligonucleotide	Sequence
dsDNA	5'-/56-FAM/TATAGCTA/iSp18/TATAGCTATA/36 TAMSp/-3'
hTelo	5'-AGGGTTAGGGTTAGGGTTAGGG-3'
BCL2	5'-AGGGGCGGGCGCGGGAGGAAGGGGGCGGGA-3'
cKIT-1	5'-AGGGAGGGCGCTGGGAGGAGGG-3'
cKIT-2	5'-CGGGCGGGCGCGAGGGAGGGG-3'
cKIT-SP	5'-GGCGAGGAGGGGCGTGGCCGGC-3'
cMYC	5'-TGGGGAGGGTGGGGAGGGTGGGGAAGG-3'
RET	5'-AGGGGCGGGGGCGGGGCGGGGT-3'
kRAS	5'-AGGGCGGTGTGGGAAGAGGGAAGAGGGGGAGG-3'

Table S2. ΔTM values of nucleic acid sequences upon interaction with metal complexes 1 – 12. Numerical values of ΔTM obtained by FRET melting assay of the considered nucleic acid sequences (dsDNA and G4 molecules) at 0.2 μM in presence of 1 μM of the tested metal complex (ratio [DNA]:[complex] = 1:5). Values are expressed as Mean ± SEM.

	dsDNA	hTelo	*cKIT-1*	*cKIT-2*	*cKIT-SP*	*BCL2*	*kRAS*	*cMYC*	*RET*
1	1.75 ± 0.72	27.36 ± 0.17	28.10 ± 0.13	> 35	14.08 ± 1.14	> 35	22.30 ± 0.16	> 35	> 35
2	0.27 ± 0.36	9.32 ± 0.05	13.92 ± 0.37	16.71 ± 0.13	5.05 ± 0.98	8.18 ± 0.06	8.71 ± 0.19	12.66 ± 0.05	13.94 ± 1.39
3	1.69 ± 0.25	22.17 ± 0.10	23.46 ± 0.34	21.54 ± 0.11	11.84 ± 0.09	14.16 ± 0.02	17.61 ± 0.17	> 35	> 35
4	1.58 ± 0.06	13.40 ± 1.87	27.00 ± 0.06	18.39 ± 0.35	15.25 ± 1.60	12.00 ± 0.52	30.49 ± 0.71	19.66 ± 0.67	15.28 ± 0.18
5	0.75 ± 0.24	2.49 ± 0.03	11.39 ± 0.27	16.10 ± 0.06	10.46 ± 0.71	5.30 ± 0.26	14.58 ± 0.26	-2.11 ± 0.29	10.01 ± 0.20
6	0.15 ± 0.49	6.95 ± 0.06	8.36 ± 0.07	14.12 ± 0.03	-0.51 ± 1.07	5.61 ± 0.09	10.99 ± 0.05	13.14 ± 0.16	14.06 ± 0.19
7	0.27 ± 0.01	0.62 ± 0.13	1.09 ± 0.01	1.45 ± 0.06	1.28 ± 0.85	0.59 ± 0.04	0.79 ± 0.28	1.66 ± 0.11	1.11 ± 0.06
8	1.18 ± 0.22	2.08 ± 0.60	6.02 ± 0.01	7.11 ± 0.09	1.52 ± 0.35	2.91 ± 0.05	5.33 ± 0.18	8.74 ± 0.18	9.77 ± 0.03
9	1.22 ± 0.45	9.71 ± 0.16	11.44 ± 0.14	13.33 ± 0.11	2.09 ± 0.92	6.98 ± 0.09	12.20 ± 0.10	9.64 ± 0.03	> 35
10	1.75 ± 0.65	26.59 ± 0.16	28.94 ± 0.10	> 35	11.84 ± 0.08	> 35	24.68 ± 0.22	> 35	> 35
11	0.83 ± 0.98	9.60 ± 2.60	16.38 ± 1.37	31.00 ± 0.04	4.07 ± 2.21	7.35 ± 0.43	4.00 ± 0.10	> 35	11.05 ± 0.28
12	1.41 ± 0.11	29.91 ± 0.35	30.73 ± 0.58	> 35	9.71 ± 0.07	17.81 ± 0.10	20.21 ± 0.58	> 35	> 35

Table S3. Proliferation inhibition rate of cancer cells by metal complexes 1 - 12. Proliferation inhibition rate (%) in T3M4, T47D and MDA-MB-231 cell lines with 10 or 50 µM of the corresponding complex for 48 or 72 hours. Proliferation inhibition of each condition was calculated relatively to its time-control and was expressed in percentage (%). *Mean* ± *SEM* (n=3).

		T3M4		T47D		MDA-MB-231	
		10 µM	50 µM	10 µM	50 µM	10 µM	50 µM
1	**48 h**	12.4 ± 0.8	61.9 ± 0.4	-13.6 ± 3.8	59.3 ± 1.5	-3.9 ± 5.1	32.0 ± 1.1
	72 h	13.9 ± 3.7	83.8 ± 0.2	-0.5 ± 2.3	76.4 ± 2.2	-3.1 ± 5.9	35.4 ± 3.4
2	**48 h**	16.8 ± 5.6	57.6 ± 4.7	11.7 ± 2.9	62.9 ± 0.9	10.6 ± 2.4	30.9 ± 6.9
	72 h	17.2 ± 9.1	72.9 ± 6.7	7.0 ± 2.0	86.5 ± 0.4	13.2 ± 1.5	40.3 ± 1.5
3	**48 h**	28.8 ± 0.5	59.0 ± 3.5	-0.1 ± 2.8	18.3 ± 1.2	-2.1 ± 1.9	5.2 ± 1.5
	72 h	58.4 ± 1.3	87.7 ± 0.7	-2.6 ± 4.5	33.5 ± 4.6	1.1 ± 2.2	-4.5 ± 3.9
4	**48 h**	24.9 ± 4.8	62.0 ± 0.2	3.7 ± 1.6	81.9 ± 1.4	5.7 ± 1.1	69.0 ± 5.0
	72 h	27.6 ± 2.7	86.7 ± 0.4	7.6 ± 1.7	97.8 ± 0.3	2.2 ± 1.9	76.2 ± 3.4
5	**48 h**	22.7 ± 1.6	60.6 ± 4.5	13.9 ± 3.8	62.4 ± 0.7	17.8 ± 9.7	77.3 ± 2.4
	72 h	24.8 ± 8.6	75.7 ± 8.6	6.1 ± 3.6	87.8 ± 1.9	13.8 ± 9.1	93.9 ± 1.9
6	**48 h**	13.8 ± 3.3	47.6 ± 3.9	-5.9 ± 3.2	51.8 ± 3.5	7.1 ± 1.6	39.6 ± 2.9
	72 h	14.7 ± 4.1	49.4 ± 2.4	5.0 ± 2.1	57.5 ± 3.4	7.9 ± 1.9	51.7 ± 5.7
7	**48 h**	15.2 ± 9.6	29.5 ± 15.0	4.9 ± 6.3	50.9 ± 3.3	18.9 ± 1.4	25.5 ± 1.4
	72 h	17.2 ± 12.0	51.7 ± 14.0	6.3 ± 3.7	72.9 ± 1.5	19.4 ± 1.5	29.4 ± 2.6
8	**48 h**	6.2 ± 5.3	41.0 ± 3.2	9.9 ± 2.1	21.4 ± 3.6	11.1 ± 0.5	48.2 ± 6.1
	72 h	13.8 ± 3.0	54.2 ± 0.4	11.0 ± 2.7	52.5 ± 4.4	21.2 ± 7.0	64.9 ± 3.7
9	**48 h**	13.0 ± 3.0	15.89 ± 5.84	9.4 ± 2.5	32.9 ± 0.9	17.9 ± 4.9	17.4 ± 4.9
	72 h	18.9 ± 3.8	33.57 ± 6.48	9.3 ± 3.9	46.6 ± 2.3	16.1 ± 2.6	14.8 ± 1.2
10	**48 h**	20.6 ± 5.5	50.76 ± 0.28	11.1 ± 2.9	89.3 ± 0.7	2.2 ± 2.6	51.1 ± 3.3
	72 h	19.6 ± 3.1	66.78 ± 2.36	11.9 ± 0.7	97.2 ± 0.2	-2.2 ± 3.8	54.4 ± 3.6
11	**48 h**	22.4 ± 12.3	43.84 ± 11.02	30.8 ± 5.0	27.4 ± 1.8	24.2 ± 4.9	38.2 ± 6.5
	72 h	29.3 ± 15.4	65.02 ± 11.60	27.8 ± 5.5	67.5 ± 4.1	26.3 ± 1.7	54.6 ± 9.2
12	**48 h**	12.2 ± 1.7	45.50 ± 1.71	13.5 ± 0.2	39.7 ± 2.7	7.3 ± 2.1	26.6 ± 5.3
	72 h	14.9 ± 1.8	58.26 ± 1.08	8.5 ± 4.2	46.6 ± 4.5	13.2 ± 7.9	28.4 ± 8.5

Table S4. RT-qPCR primers sequences (5' - 3').

GENE	Sens	Primer sequence	Temp. (°C)
UBB	Forward	5' – GCTTTGTTGGGTGAGCTTGT – 3'	60°C
	Reverse	5' – CGAAGATCTGCATTTTGACCT – 3'	
TBP	Forward	5' – GAGCTGTGATGTGAAGTTTCC – 3'	60°C
	Reverse	5' - TCTGGGTTTGATCATTCTGTAG - 3'	
RPL13A	Forward	5' - GTTCCTGCTCTCAAG – 3'	58°C
	Reverse	5' – GTCACTGCCTGGTACTTCC - 3'	
kRAS	Forward	5' – TCTTGCCTCCCTACCTTCCACAT - 3'	61°C
	Reverse	5' – CTGTCAGATTCTCTTGAGCCCTG - 3'	
cMYC	Forward	5' -GGCTCCTGGCAAAAGGTCA - 3'	61°C
	Reverse	5' – CTGCGTAGTTGTGCTGATGT - 3'	
BCL2	Forward	5' – GTCATGTGTGTGGAGAGCGTCAACC - 3'	60°C
	Reverse	5' – CCAGGGCCAAACTGAGCAGAGTC - 3'	
RET	Forward	5' – GCAGCATTGTTGGGGGACA - 3'	61°C
	Reverse	5' - CACCGGAAGAGGAGTAGCTG - 3'	