Electronic Supplementary Information (ESI)

Silver(I) complexes of 3-methoxy-4-hydroxybenzaldehyde thiosemicarbazones and triphenylphosphine: structural, cytotoxic and apoptotic studies

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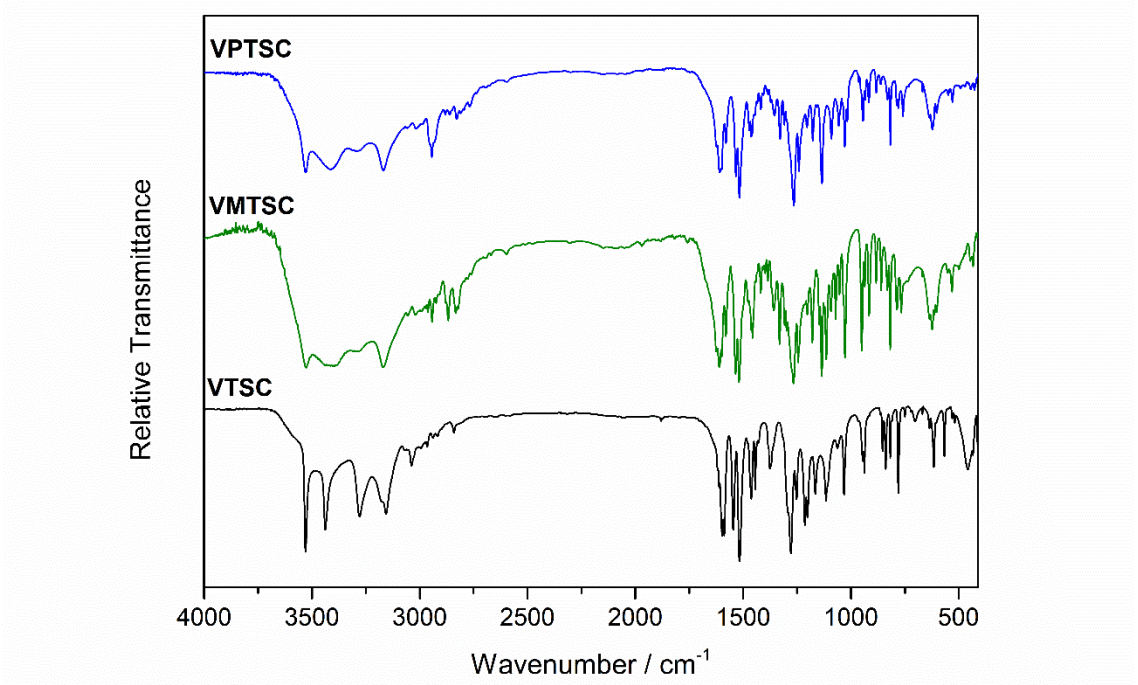
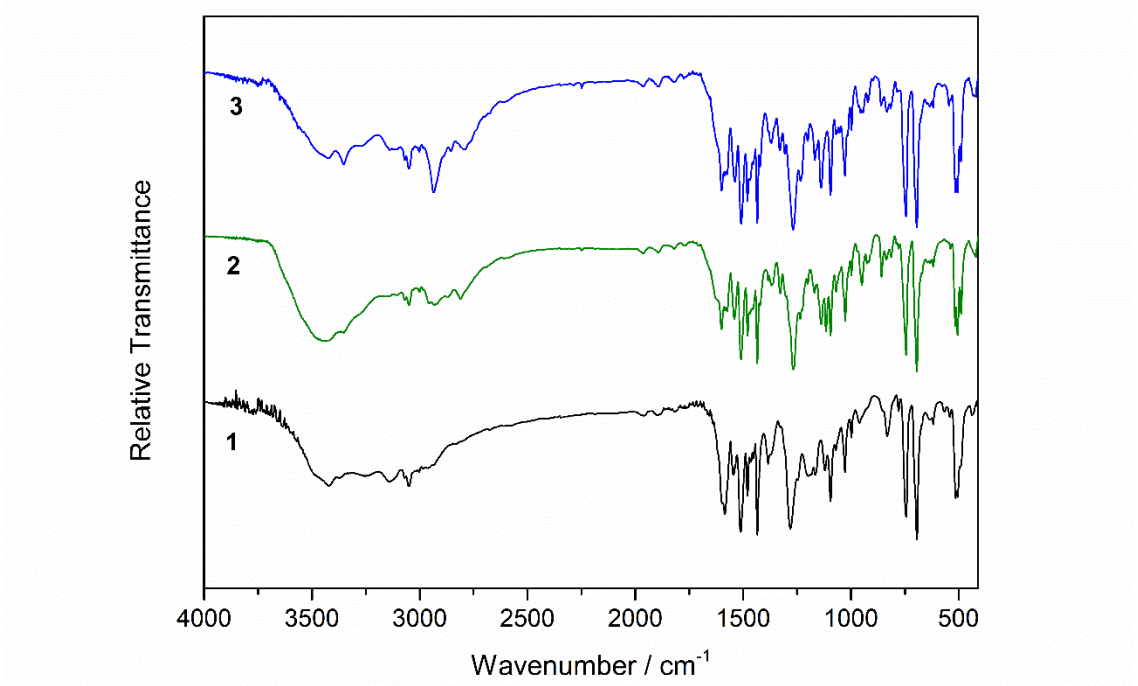


(A)

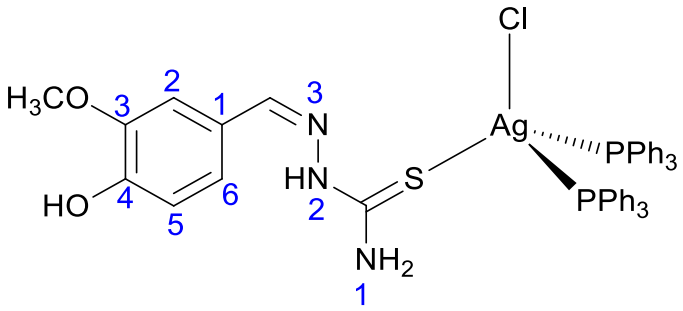


(B)

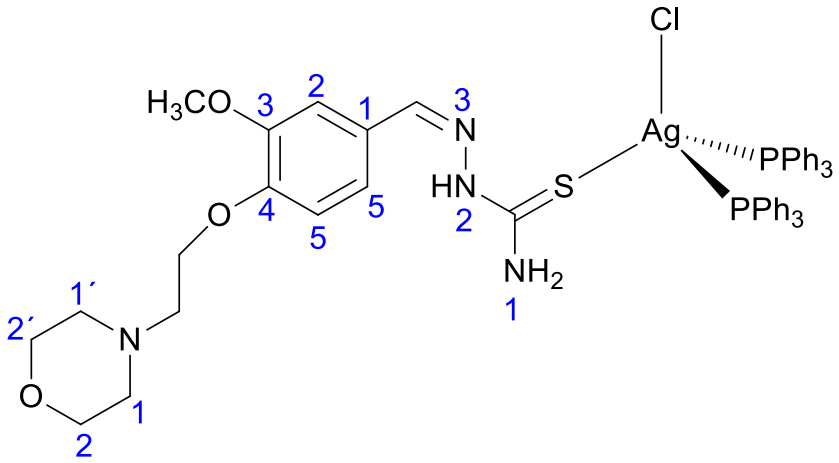
Fig. S1. IV spectra of (A) thiosemicarbazones and (B) complexes **1**-**3**.

Table S1 Selected bond lengths (Å) and bond angles (°) of complexes **2** and **3**.

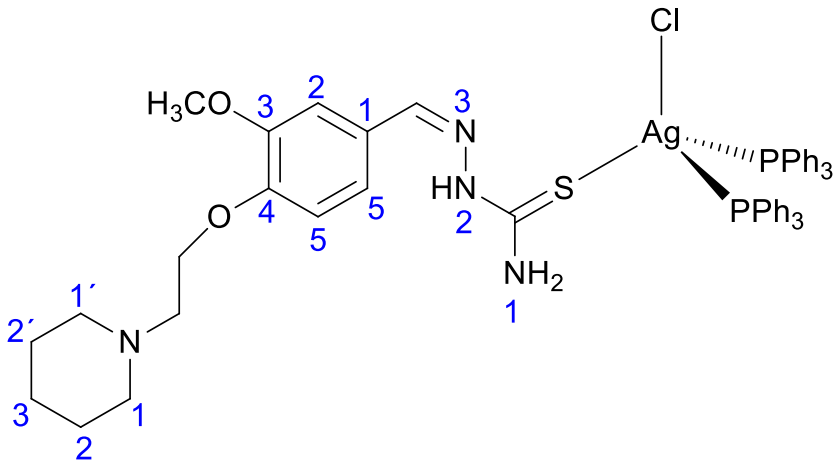
2	Length (Å)		Angle (°)
Ag(1) – S(21)	2.6013(7)	P(31) – Ag(1) – S(21)	107.06(2)
Ag(1) – P(31)	2.4917(7)	P(31) – Ag(1) – Cl(44)	103.89(3)
Ag(1) – Cl(44)	2.5892(8)	Cl44 – Ag(1) – S(21)	107.86(2)
Ag(1) – P(51)	2.4759(7)	P(51) – Ag(1) – S(21)	109.04(2)
		P(51) – Ag(1) – P(31)	115.35(3)
		P(51) – Ag(1) – Cl(44)	113.21(3)
3			
Ag(1) – S(1)	2.6325(8)	P(8) – Ag(1) – Cl(40)	100.72(2)
Ag(1) – P(8)	2.4794(7)	P8 – Ag(1) – S(1)	114.40(3)
Ag(1) – Cl(40)	2.5723(7)	P(27) – Ag(1) – P(8)	124.21(2)
Ag(1) – P(27)	2.4661(6)	P(27) – Ag(1) – Cl(40)	113.22(2)
		P(27) – Ag(1) – S(1)	99.80(2)
		Cl(40) – Ag(1) – S(1)	103.09(2)



(1)

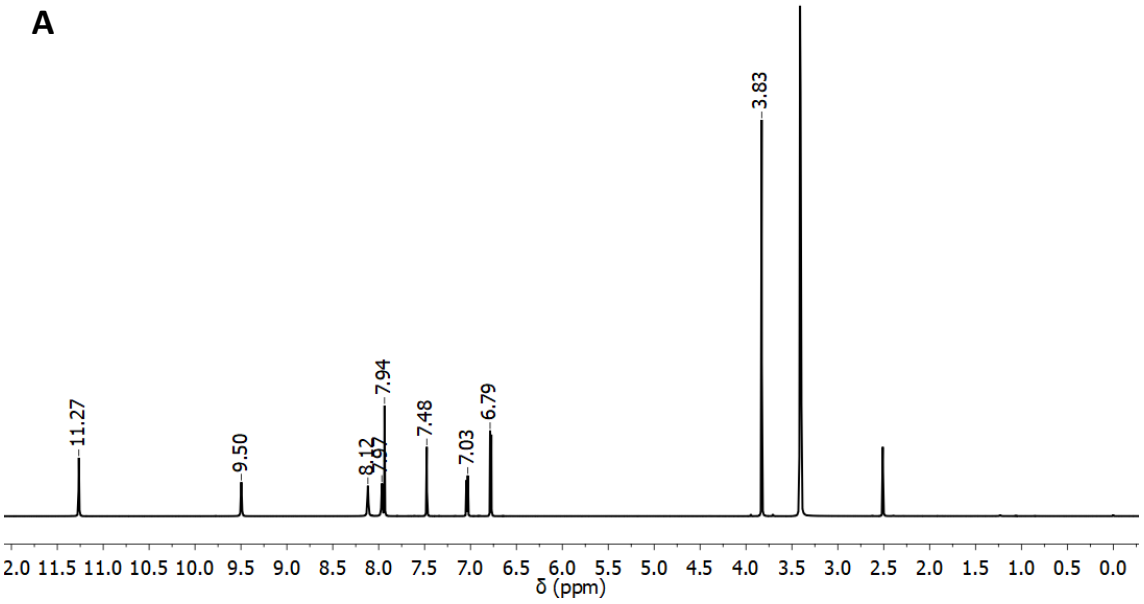


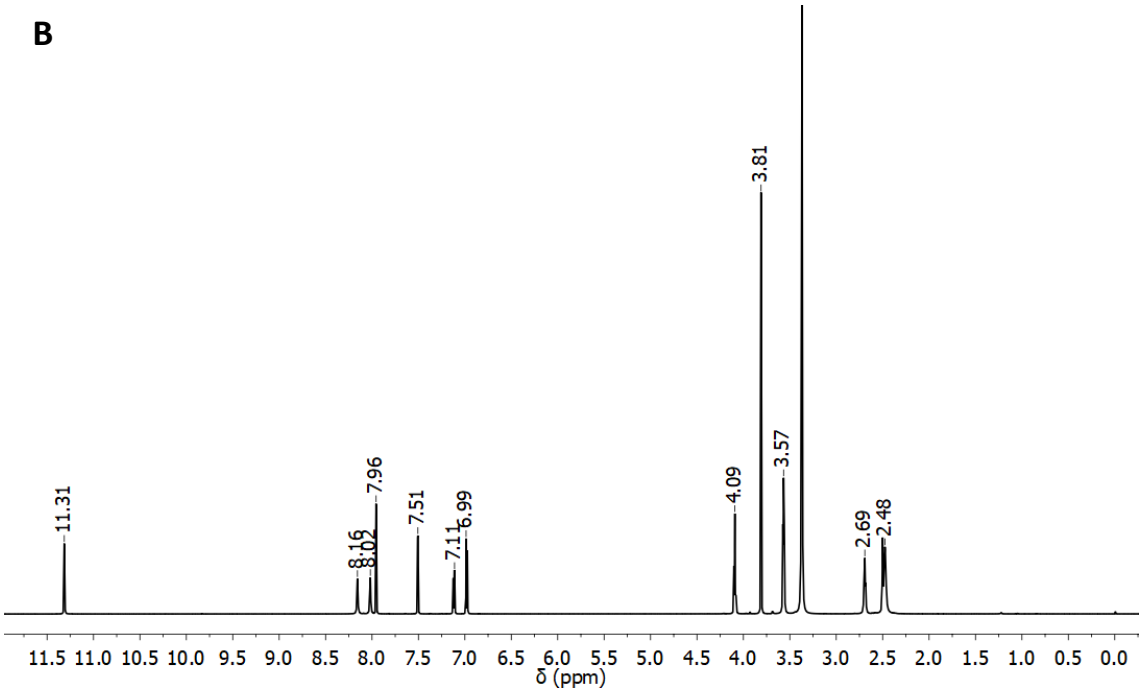
(2)



(3)

Fig. S2. Numbering scheme of complexes **1-3** for NMR data.


A
11.27
9.50
8.12
7.97
7.94
7.48
7.03
6.79
3.83
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)


B
11.31
8.16
8.02
7.96
7.51
7.11
6.99
4.09
3.81
3.57
2.69
2.48
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)

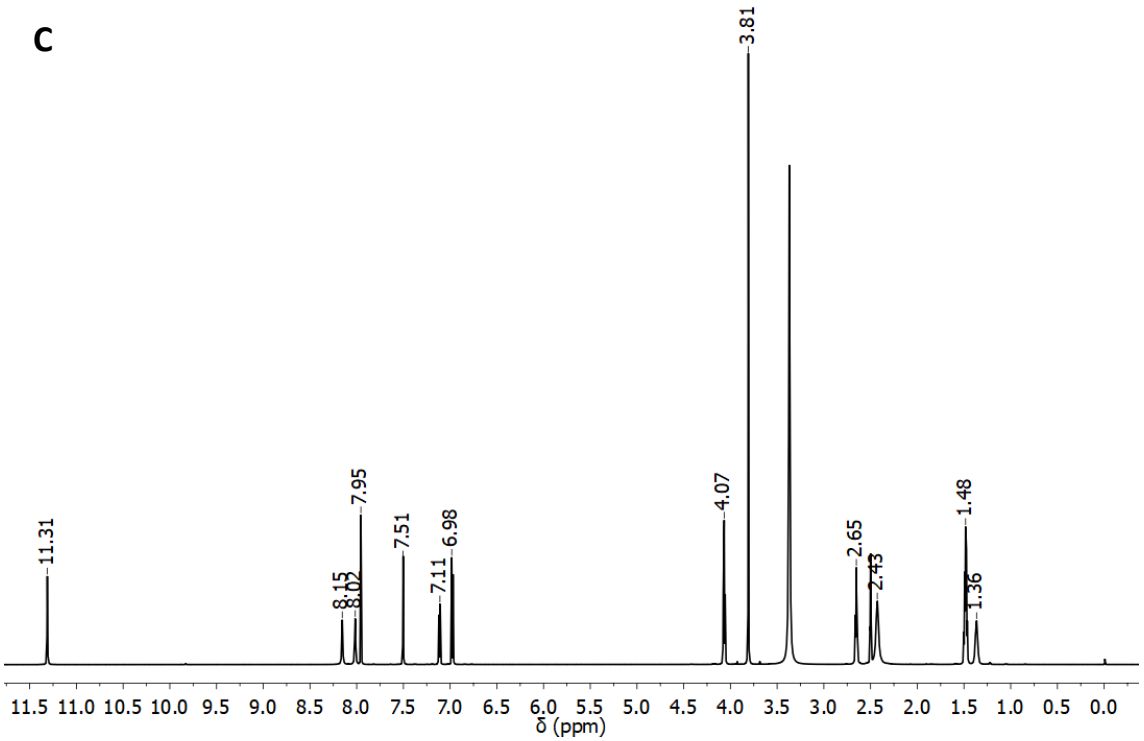
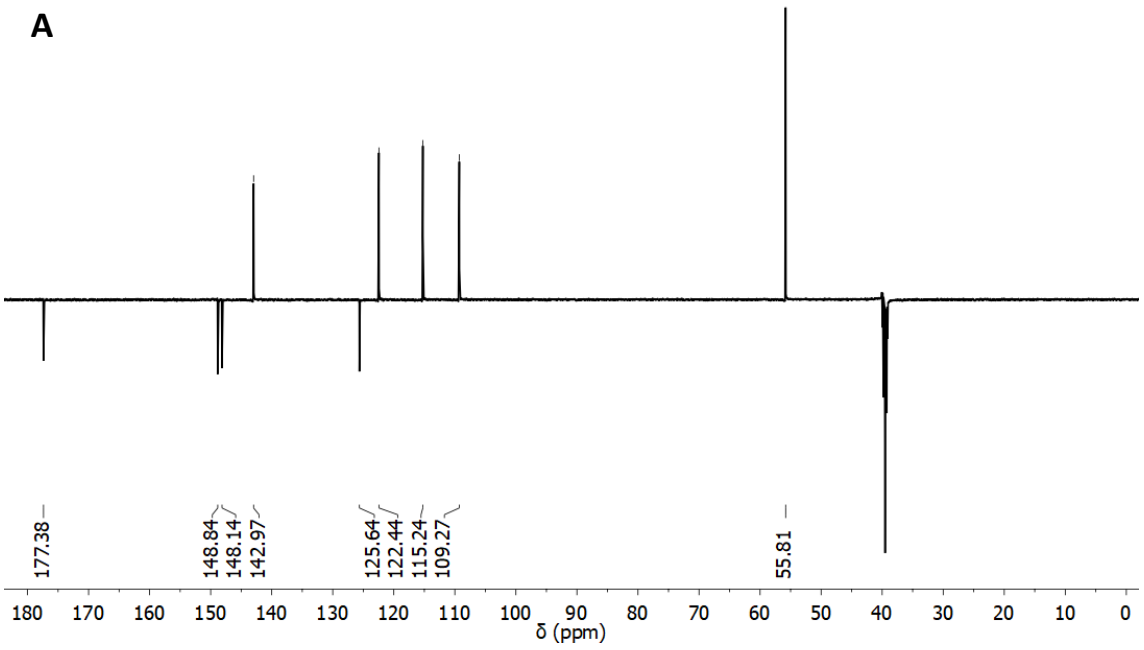


Fig. S3. ^{1}H NMR spectra of thiosemicabazones (A) VTSC; (B) VMTSC and (C) VPTSC in DMSO-d_6.



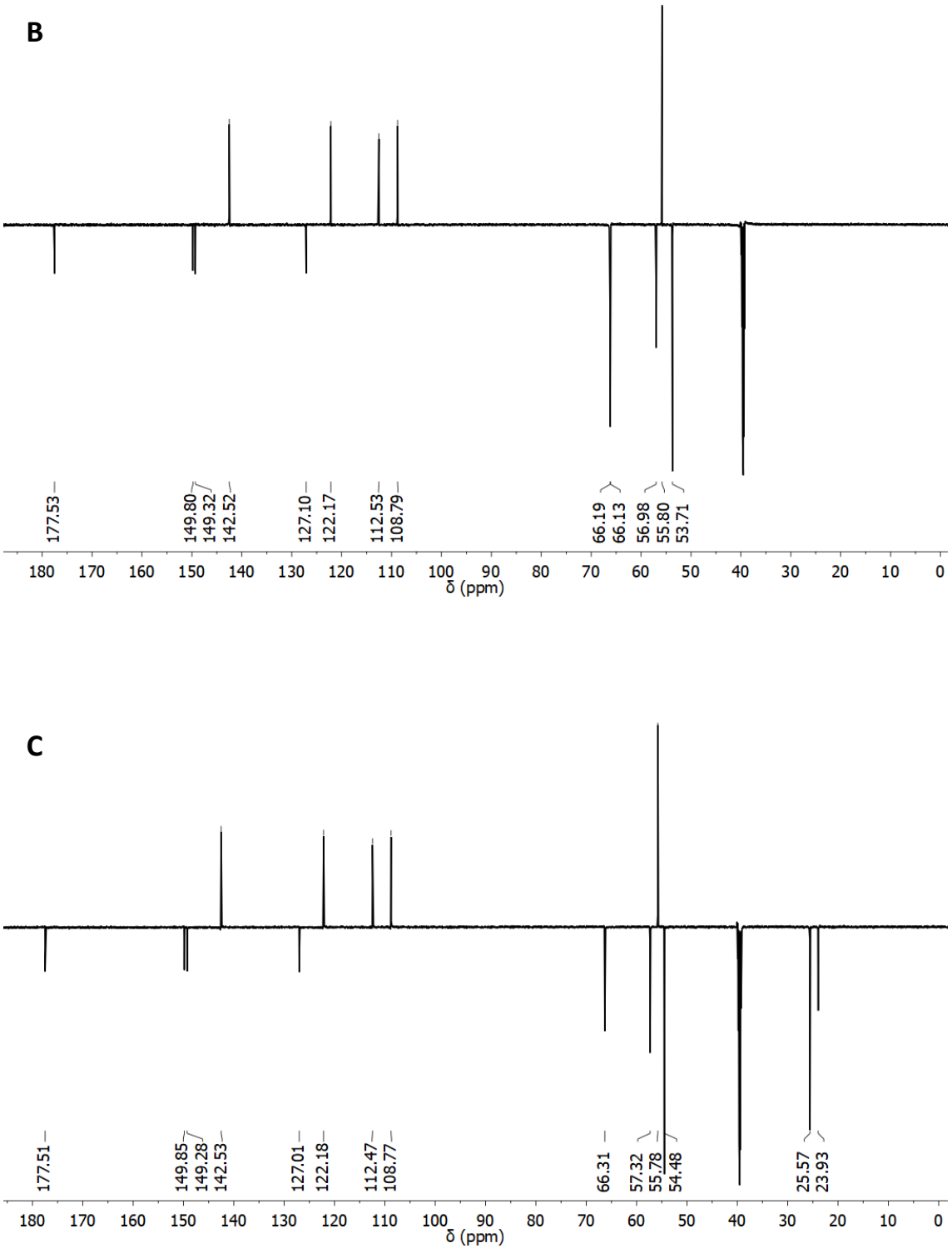


Fig. S4. DEPTQ NMR spectra of thiosemicabazones (A) VTSC; (B) VMTSC and (C) VPTSC in DMSO-d_6.

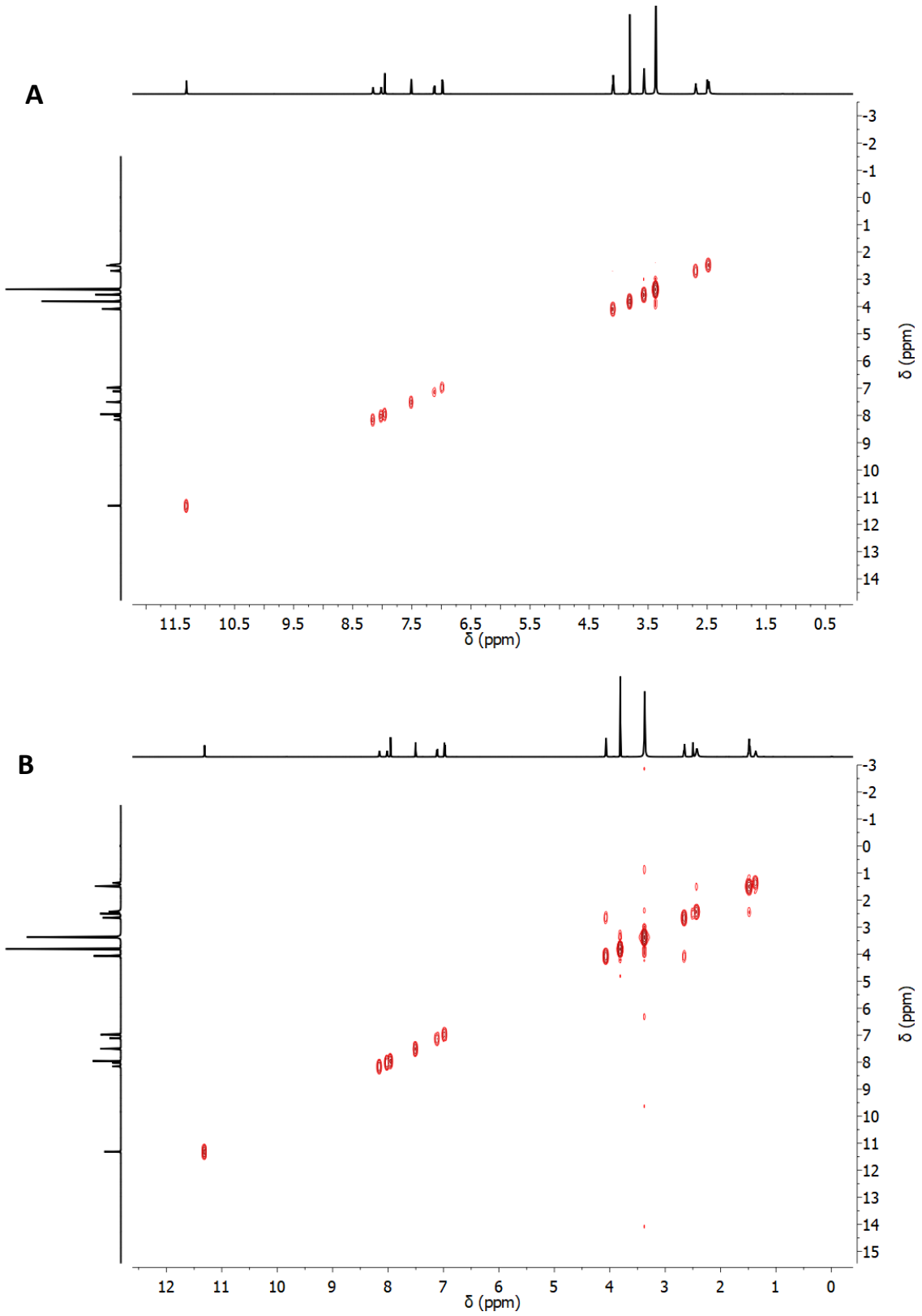
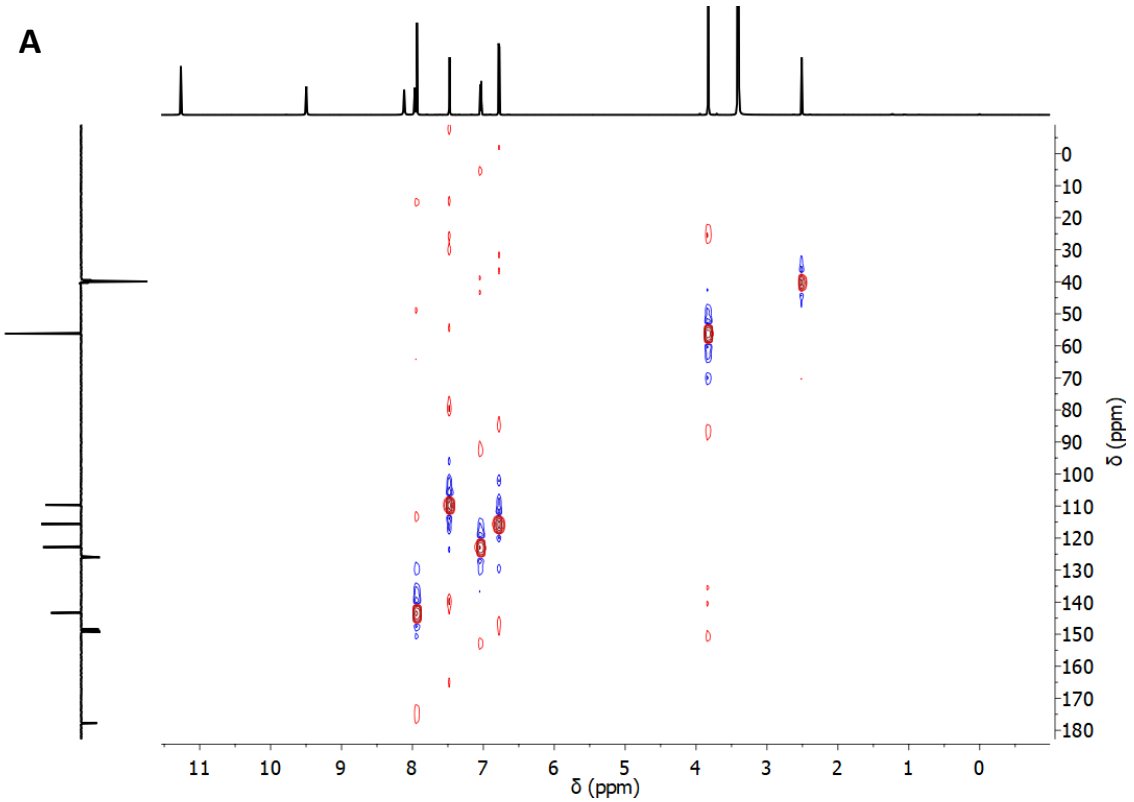
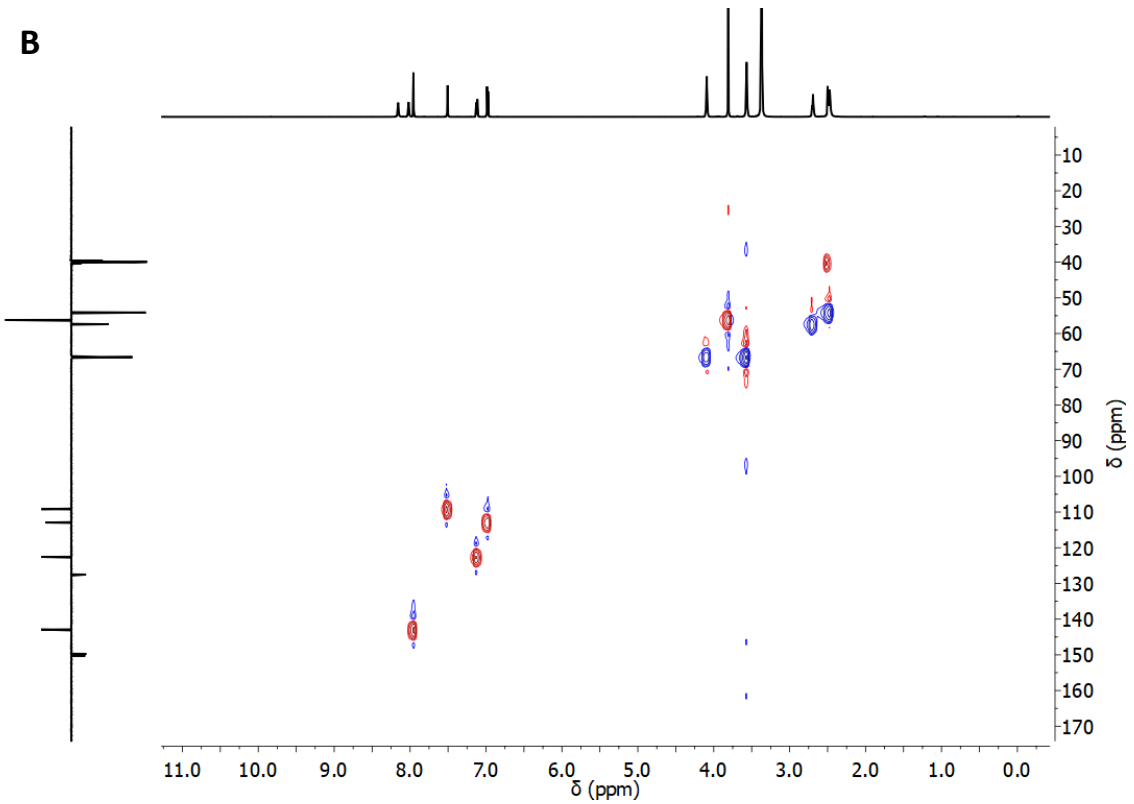


Fig. S5. COSY ^{1}H-^{1}H NMR spectra of thiosemicabazones (A) VMTSC and (B) VPTSC in DMSO-d_6.


A
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
δ (ppm)
11
10
9
8
7
6
5
4
3
2
1
0
δ (ppm)


B
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
δ (ppm)
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
δ (ppm)

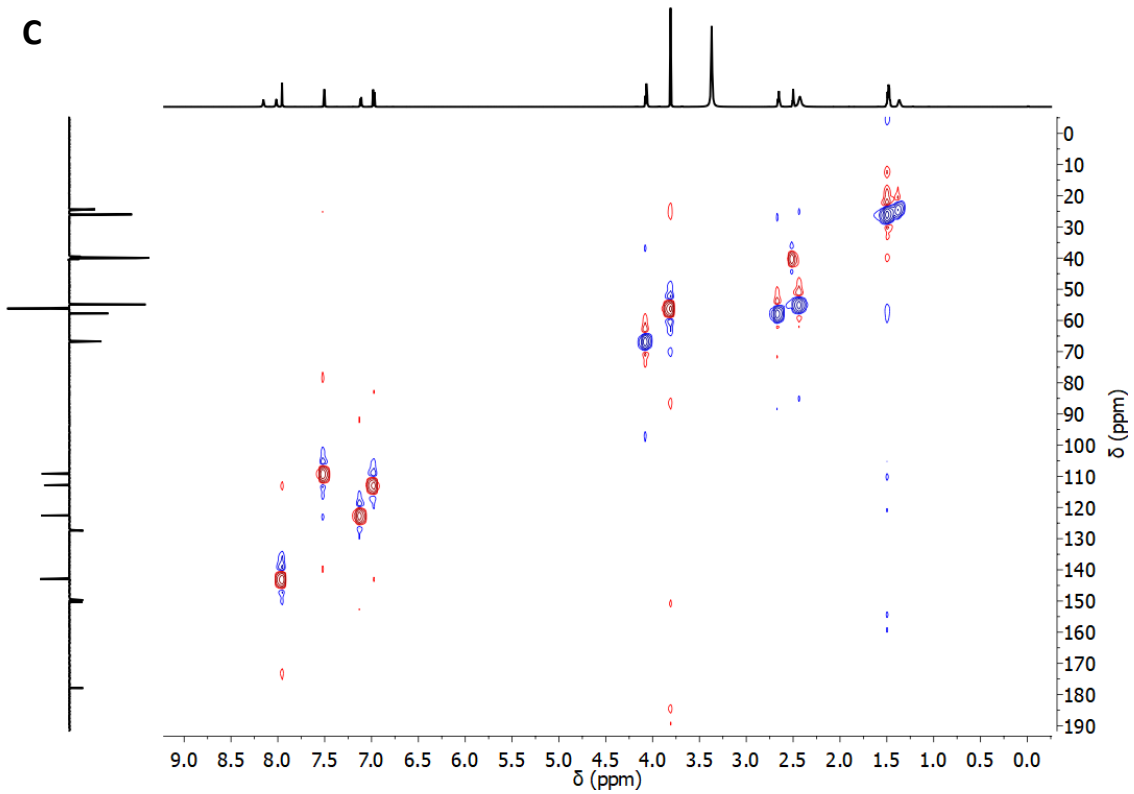
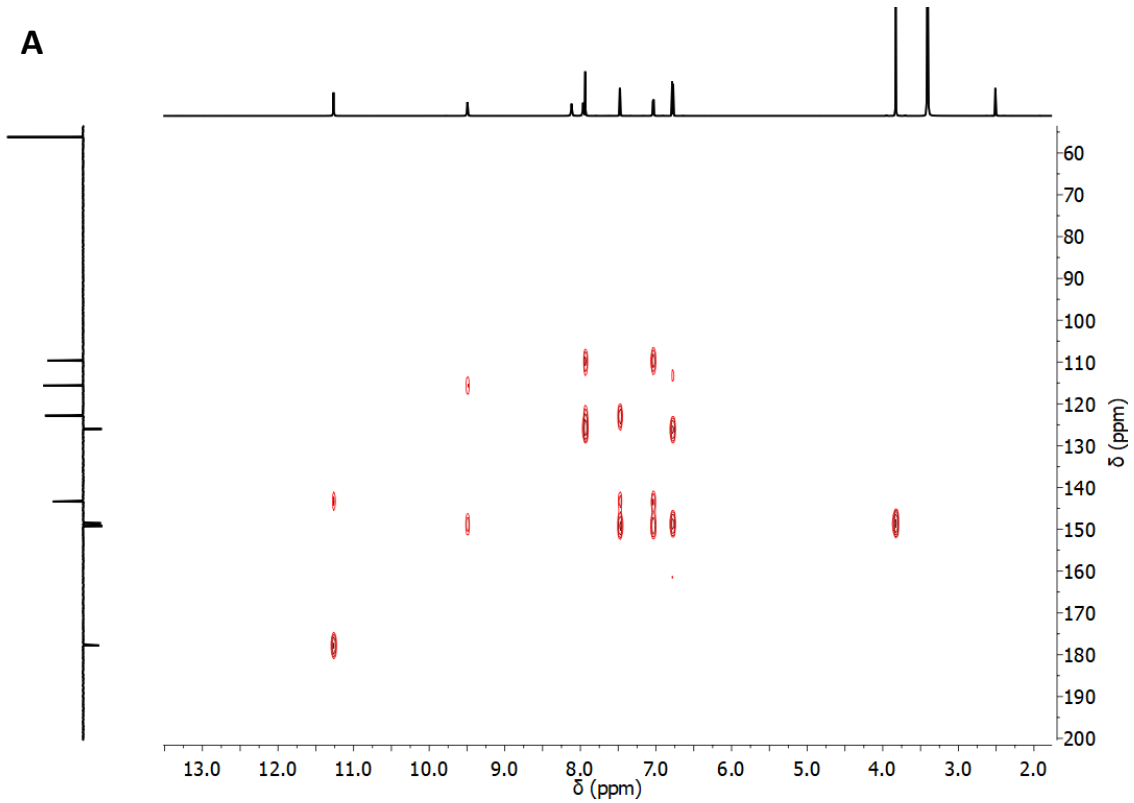


Fig. S6. ^{1}H-^{13}C HSQC spectra of thiosemicabazones (A) VTSC; (B) VMTSC and (C) VPTSC in DMSO-d_6.



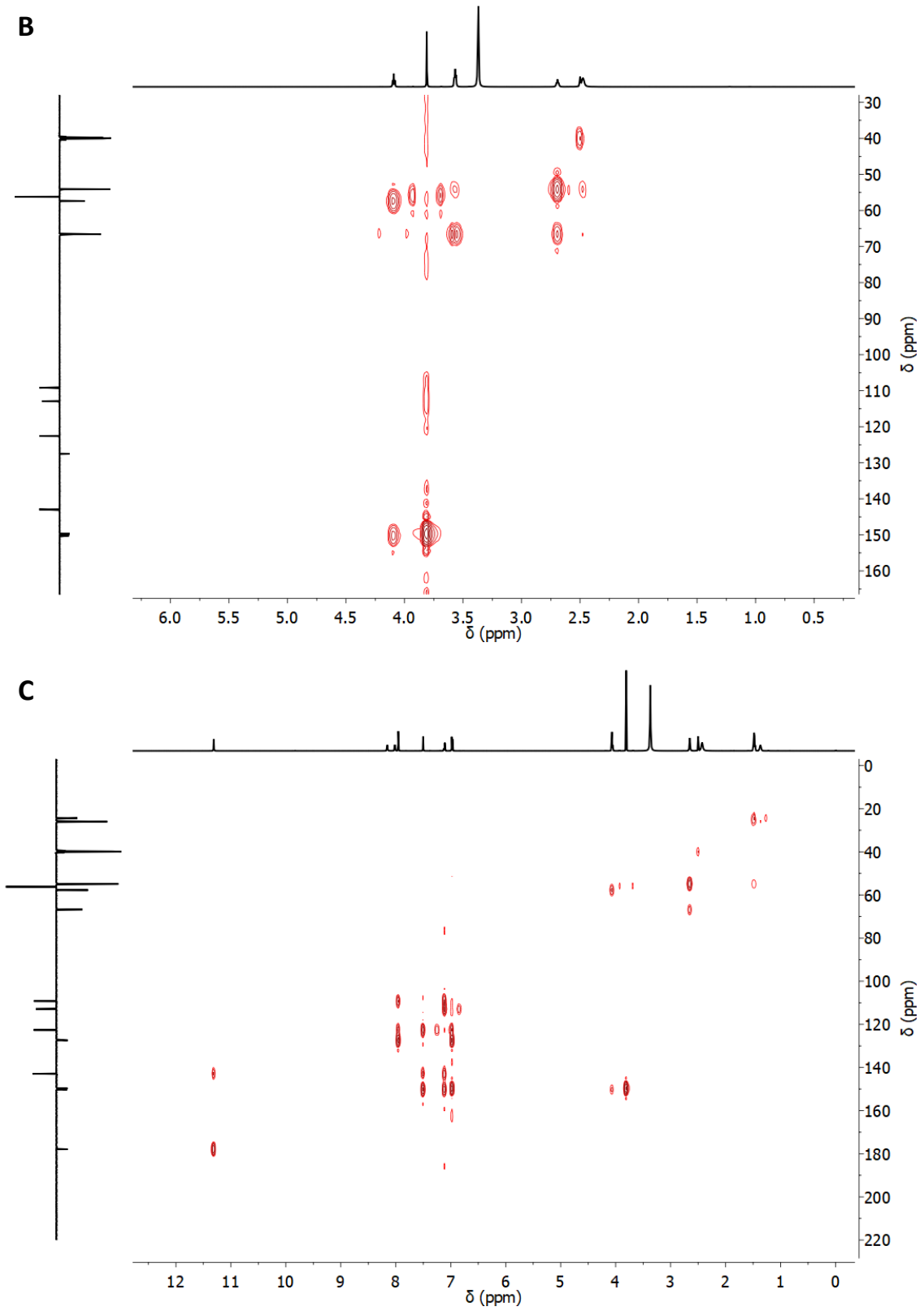
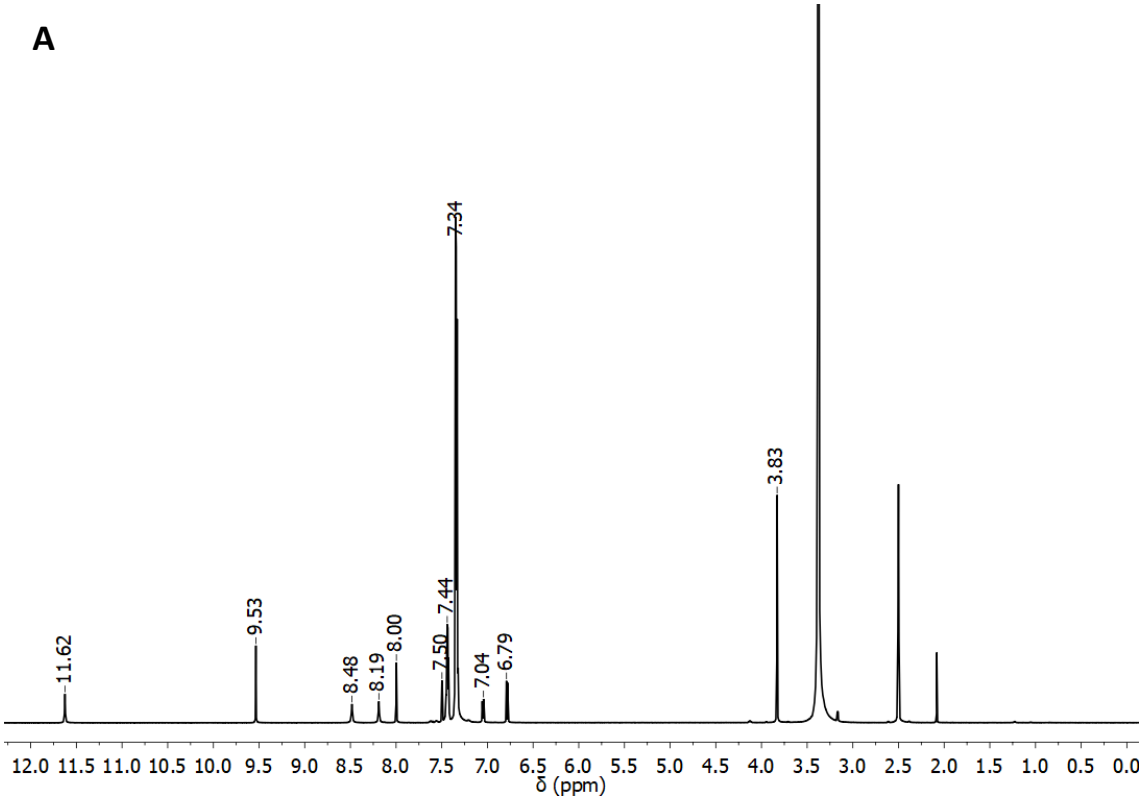
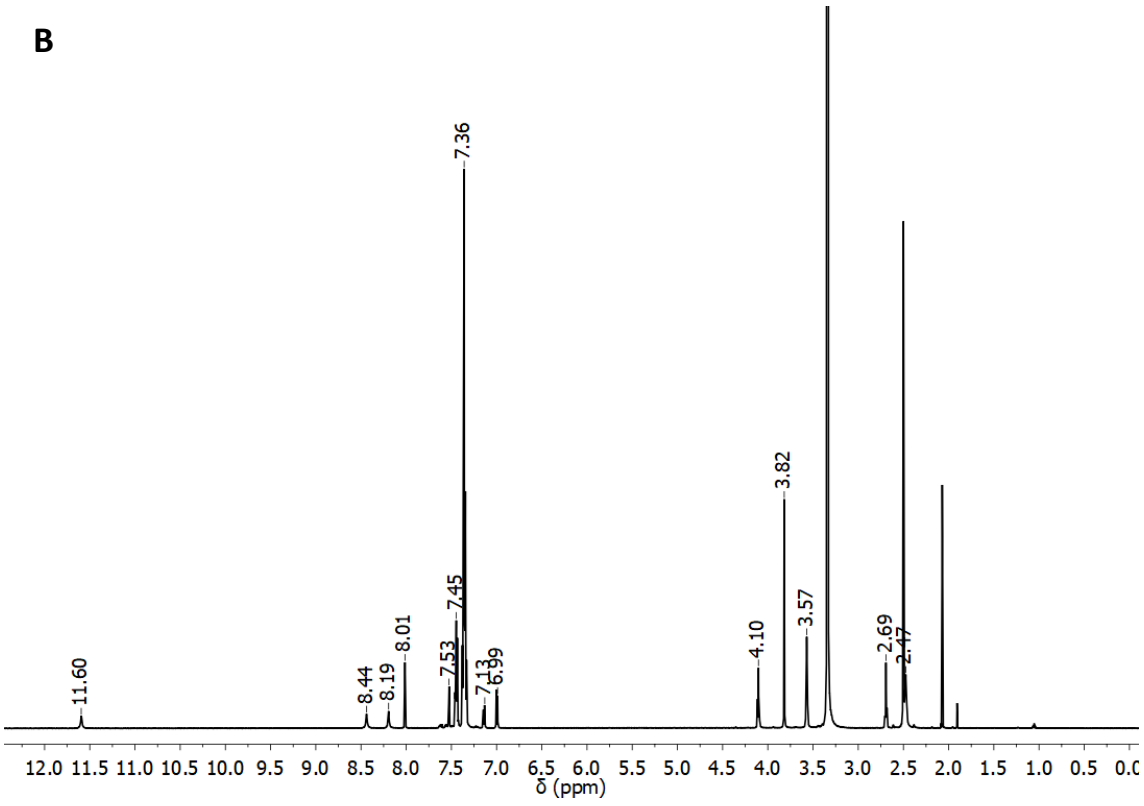


Fig. S7. ^{1}H-^{13}C HMBC spectra of thiosemicabazones (A) VTSC; (B) VMTSC and (C) VPTSC in DMSO-d_6.

A


11.62
9.53
8.48
8.19
8.00
7.50
7.44
7.34
7.04
6.79
3.83
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)

B


11.60
8.44
8.19
8.01
7.53
7.45
7.36
7.13
6.99
4.10
3.82
3.57
2.69
2.47
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)

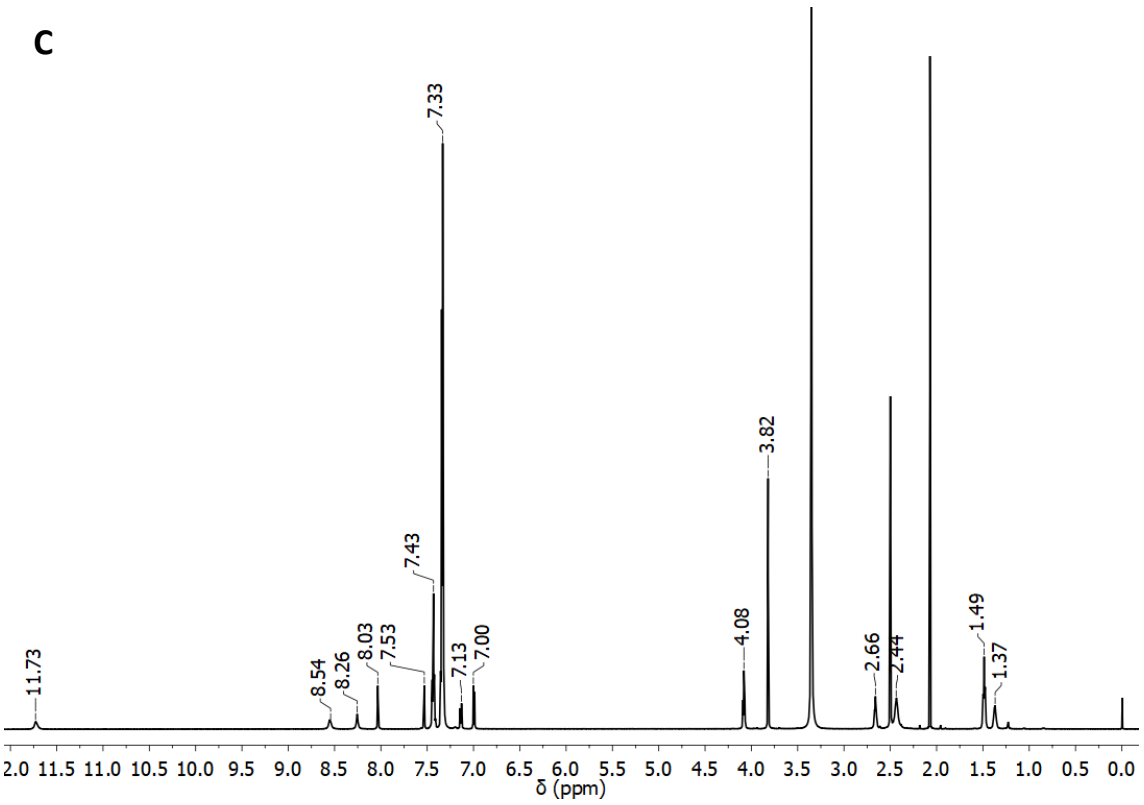
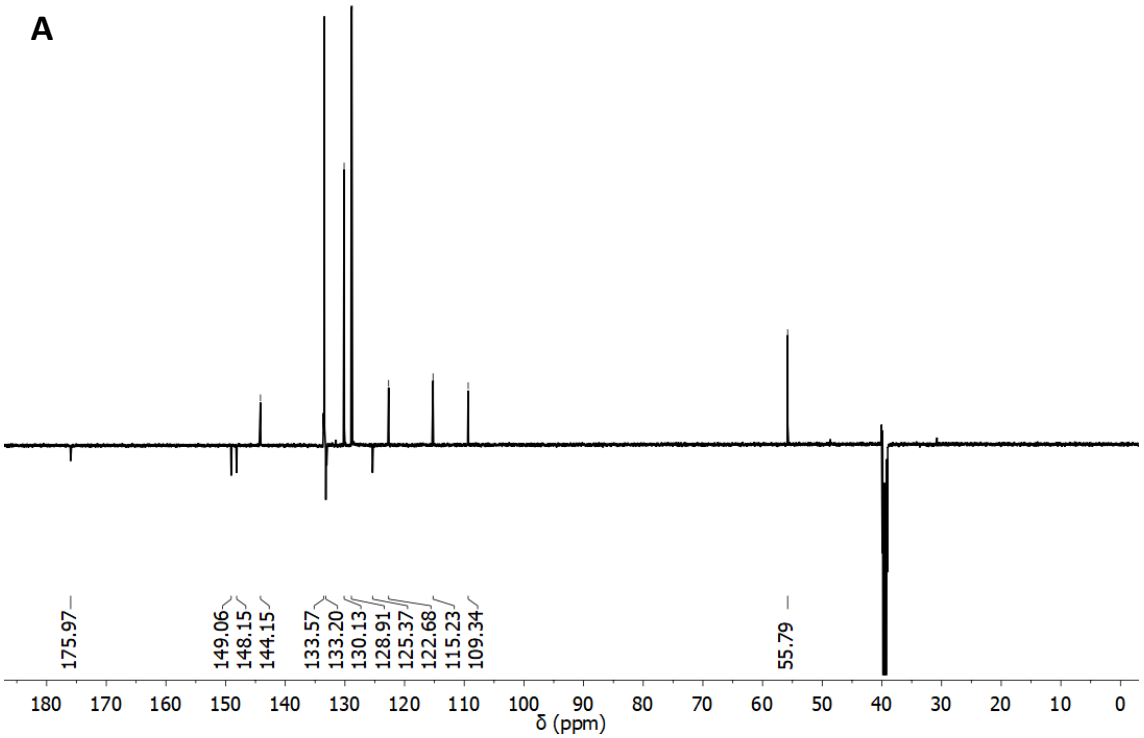


Fig. S8. ^{1}H NMR spectra of complexes (A) **1**; (B) **2** and (C) **3**.



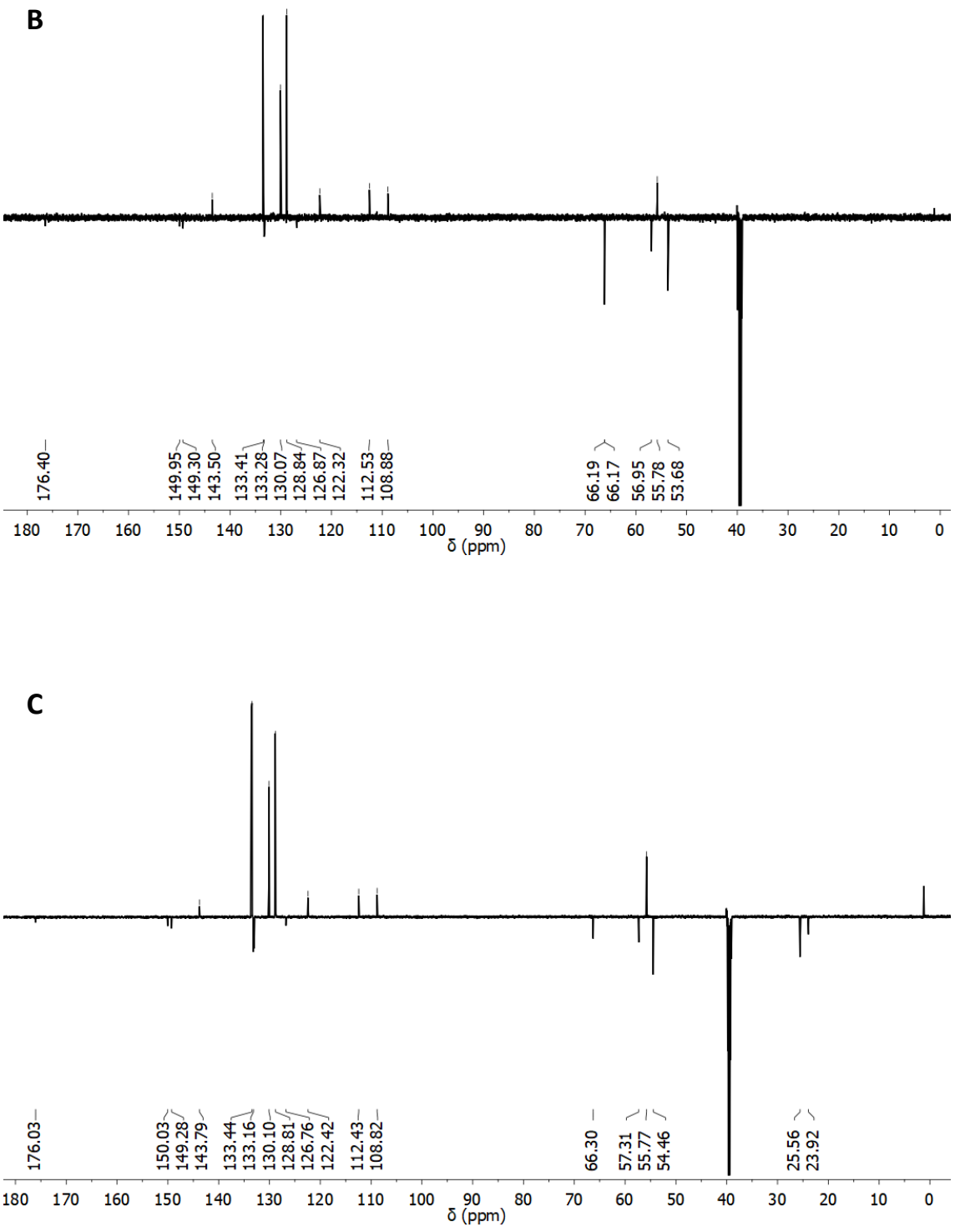
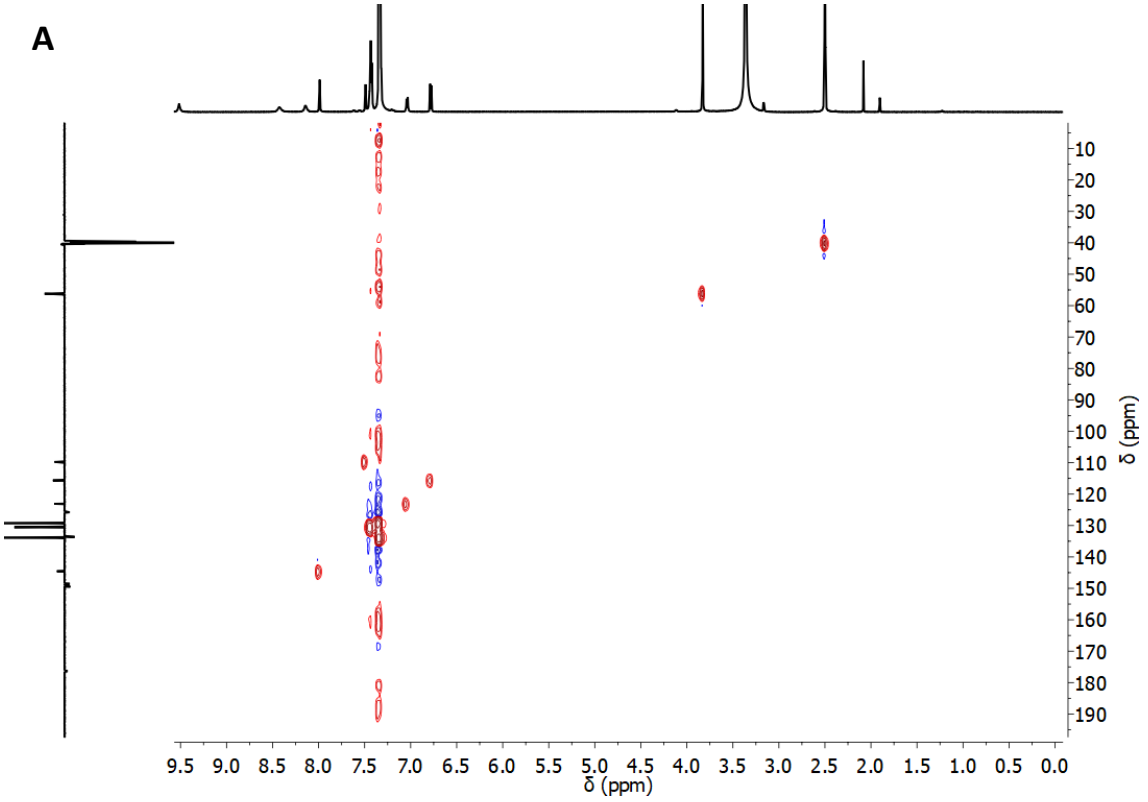
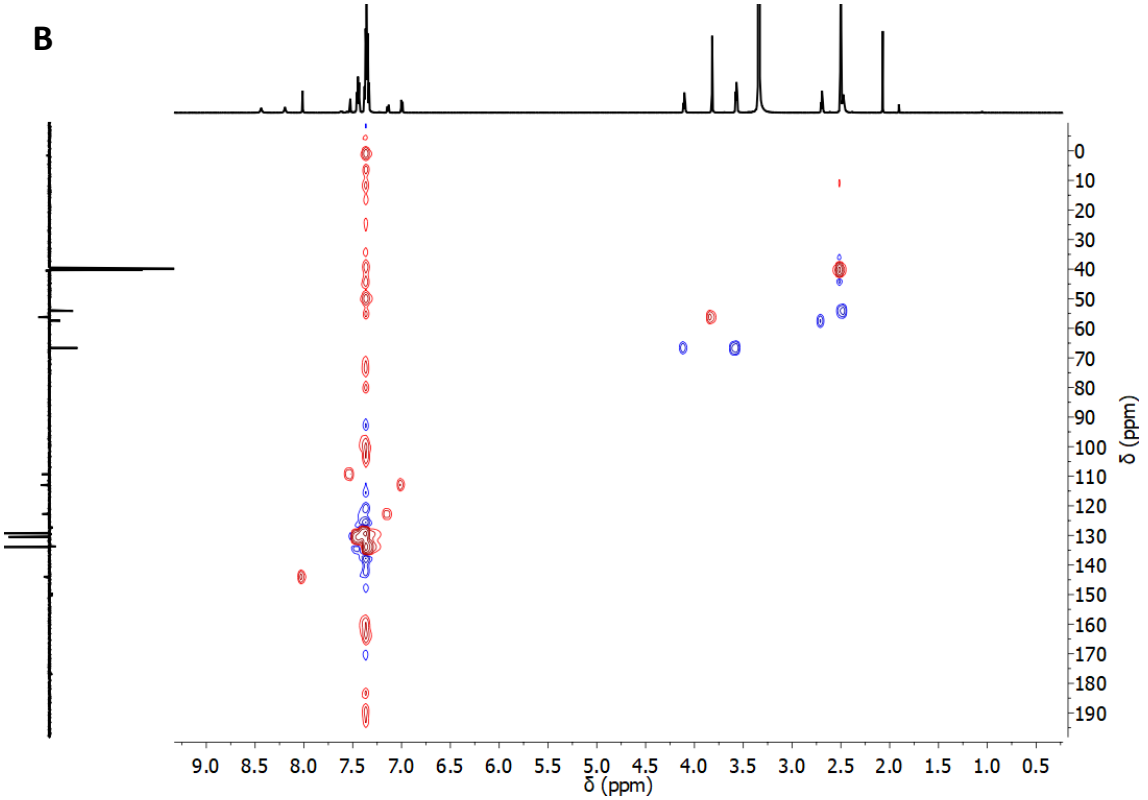


Fig. S9. DEPTQ NMR spectra of complexes (A) **1**; (B) **2** and (C) **3** in DMSO-d_6.


A
δ (ppm)
δ (ppm)


B
δ (ppm)
δ (ppm)

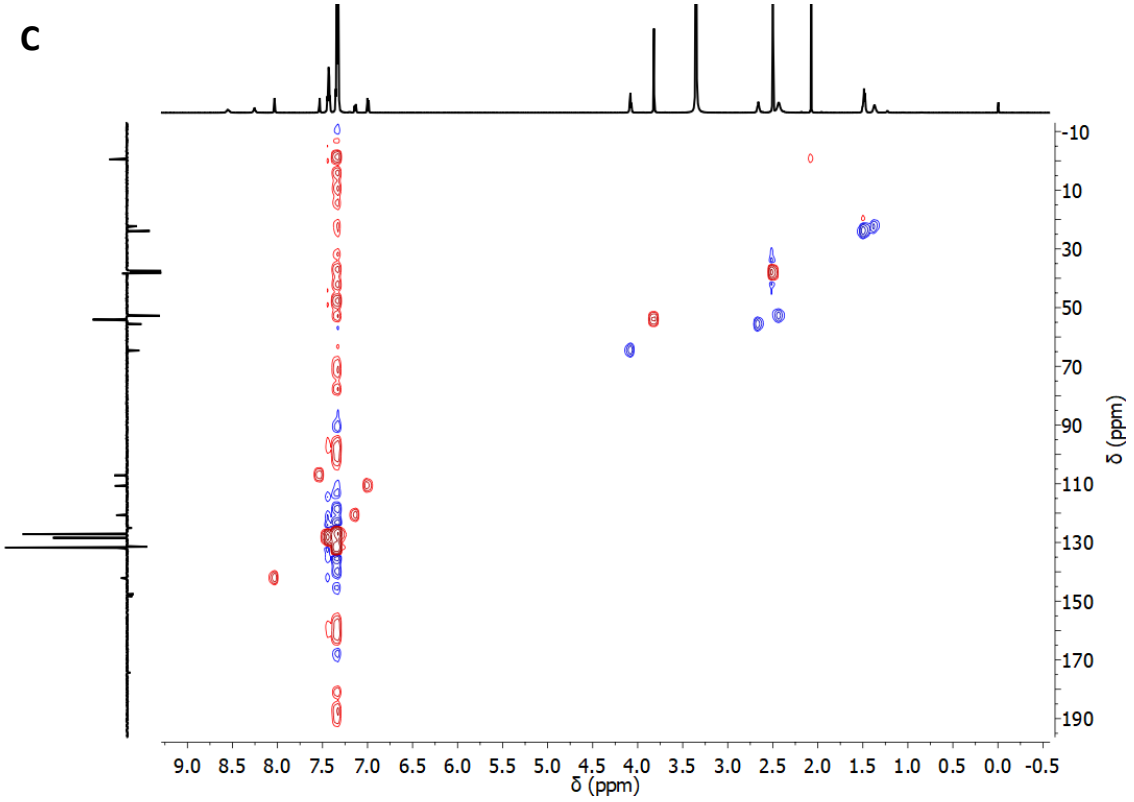
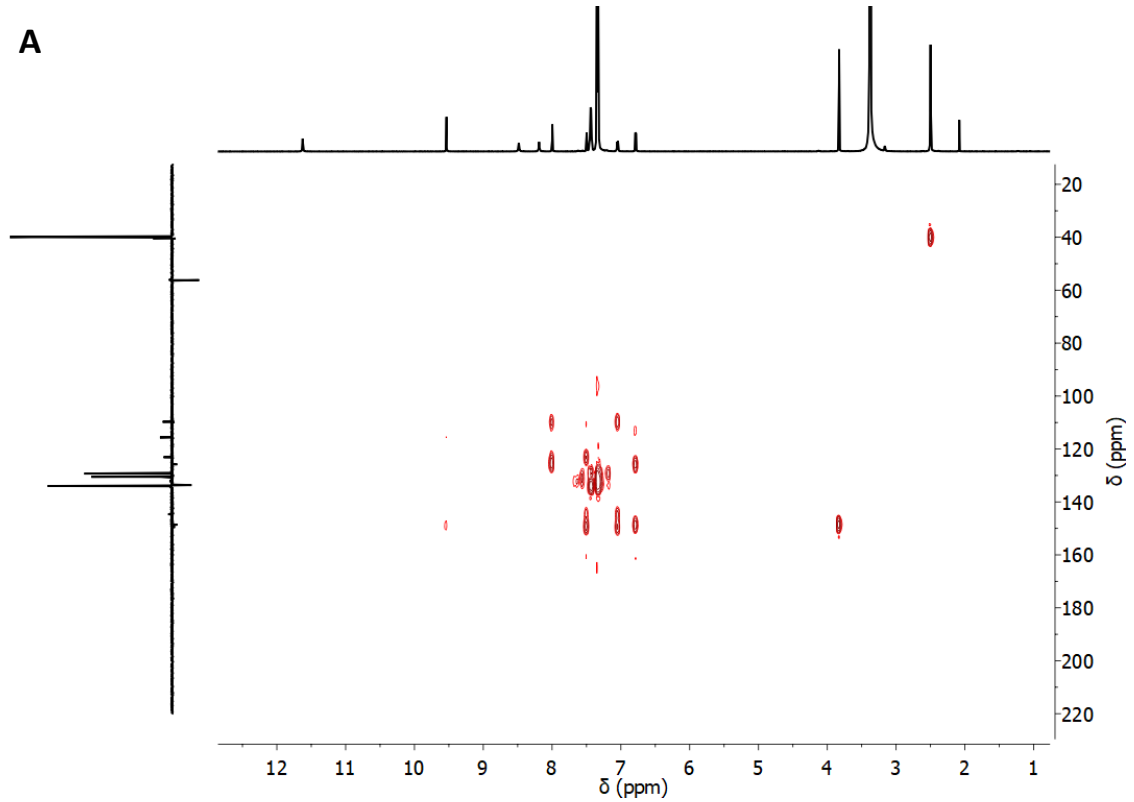


Fig. S10. ^{1}H-^{13}C HSQC spectra of complexes (A) **1**; (B) **2** and (C) **3** in DMSO-d_6.



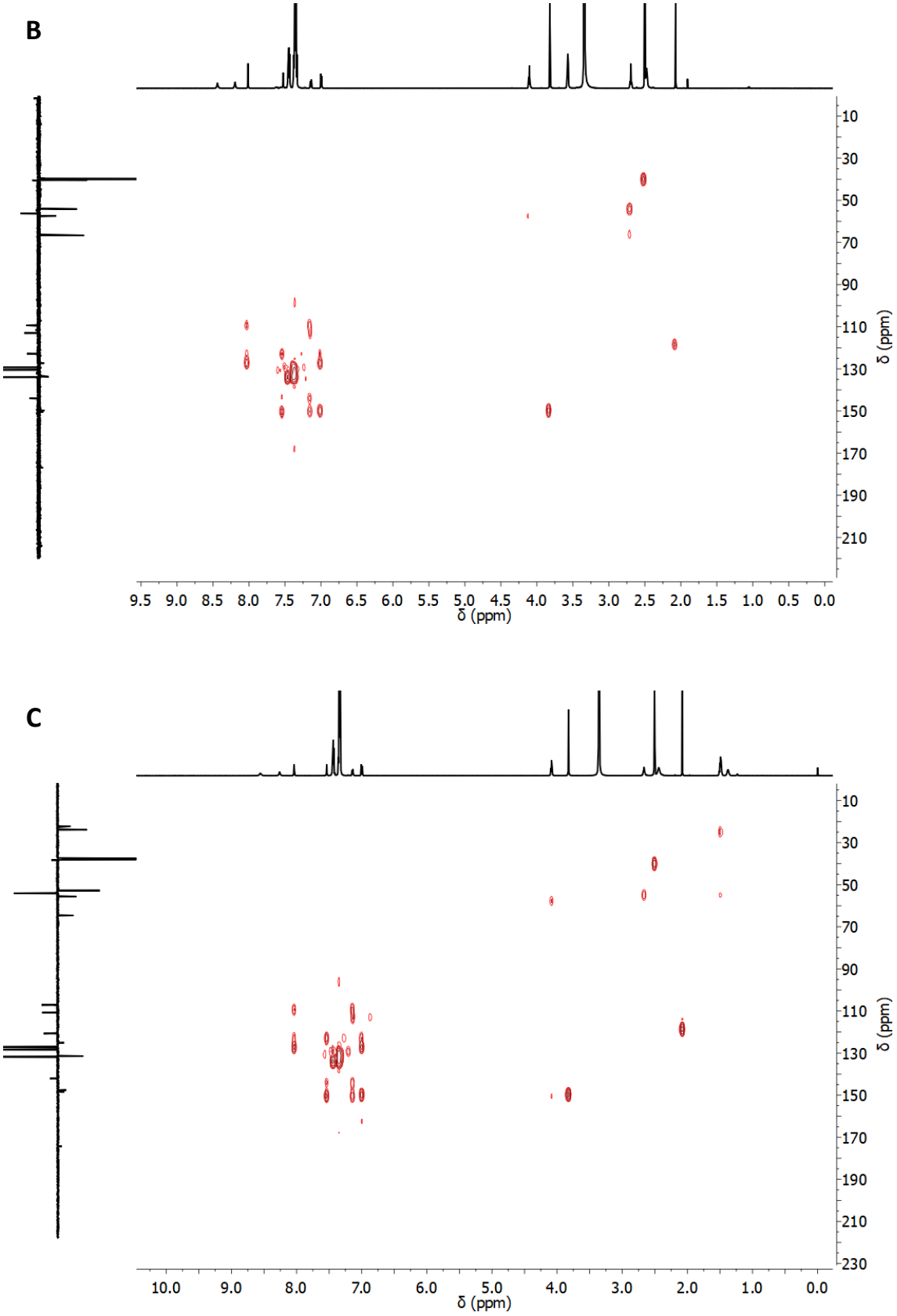


Fig. S11. ^{1}H-^{13}C HMBC spectra of complexes (A) **1**; (B) **2** and (C) **3** in DMSO-d_6.

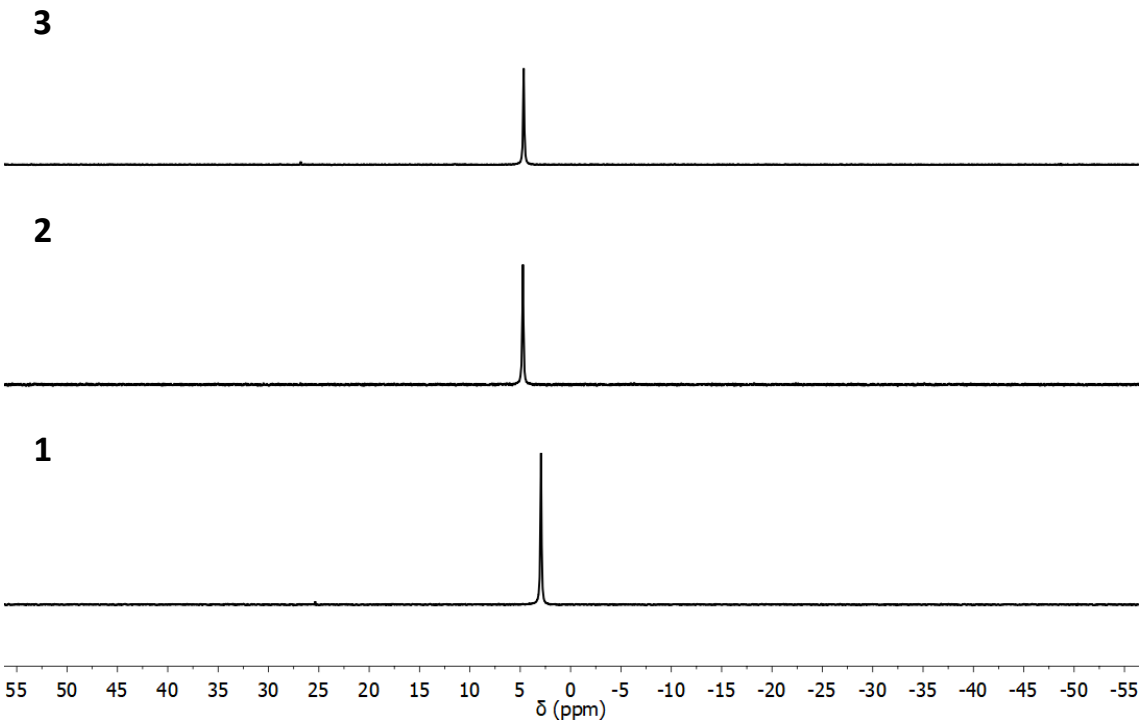
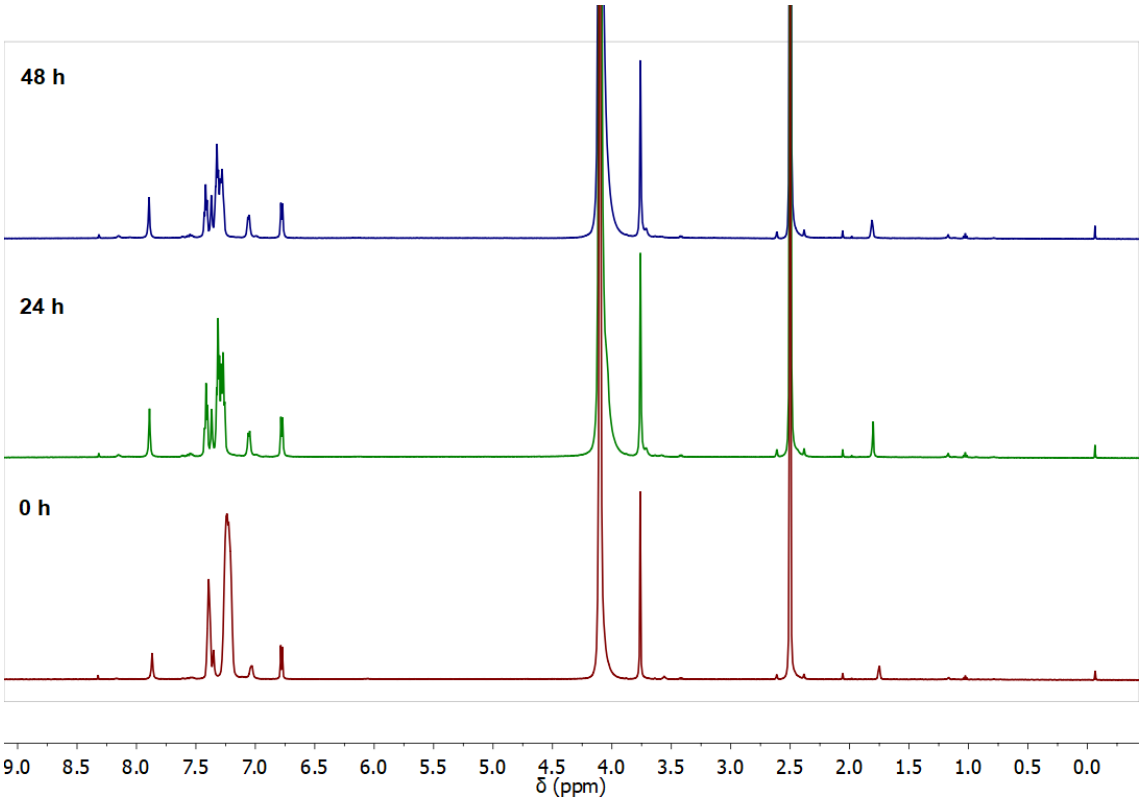
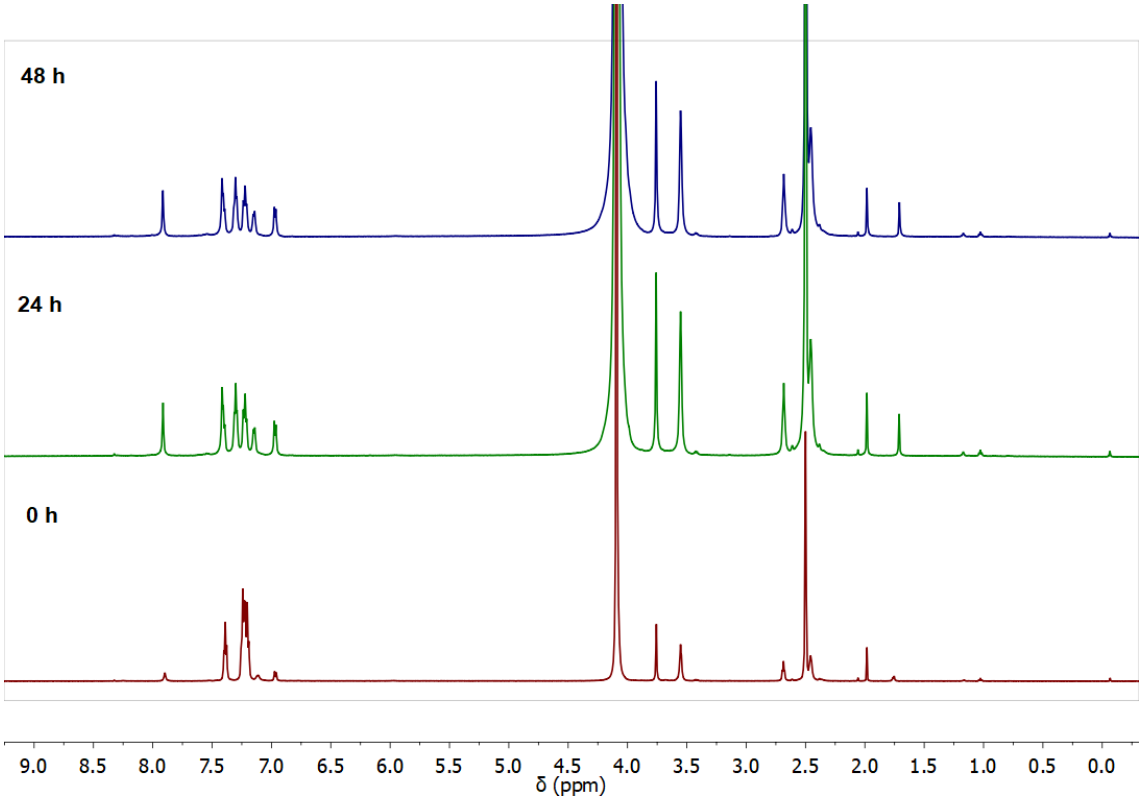


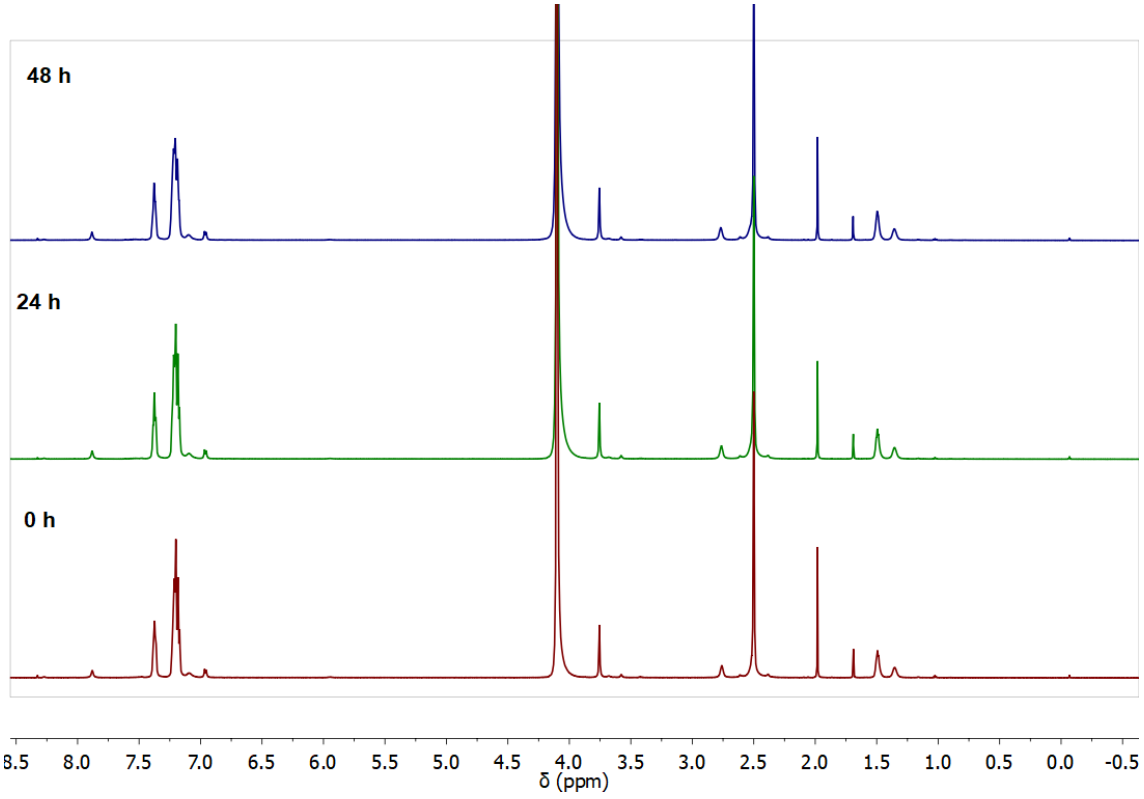
Fig. S12. ^{31}P NMR spectra of complexes **1-3** in DMSO-d_6.



(A)



(B)



(C)

Fig. S13. ^{1}H NMR spectra of complexes (A) **1**, (B) **2** and (C) **3** recorded in DMSO-d_6/D_2O (80; 20% v/v) over a period of 48 hours.

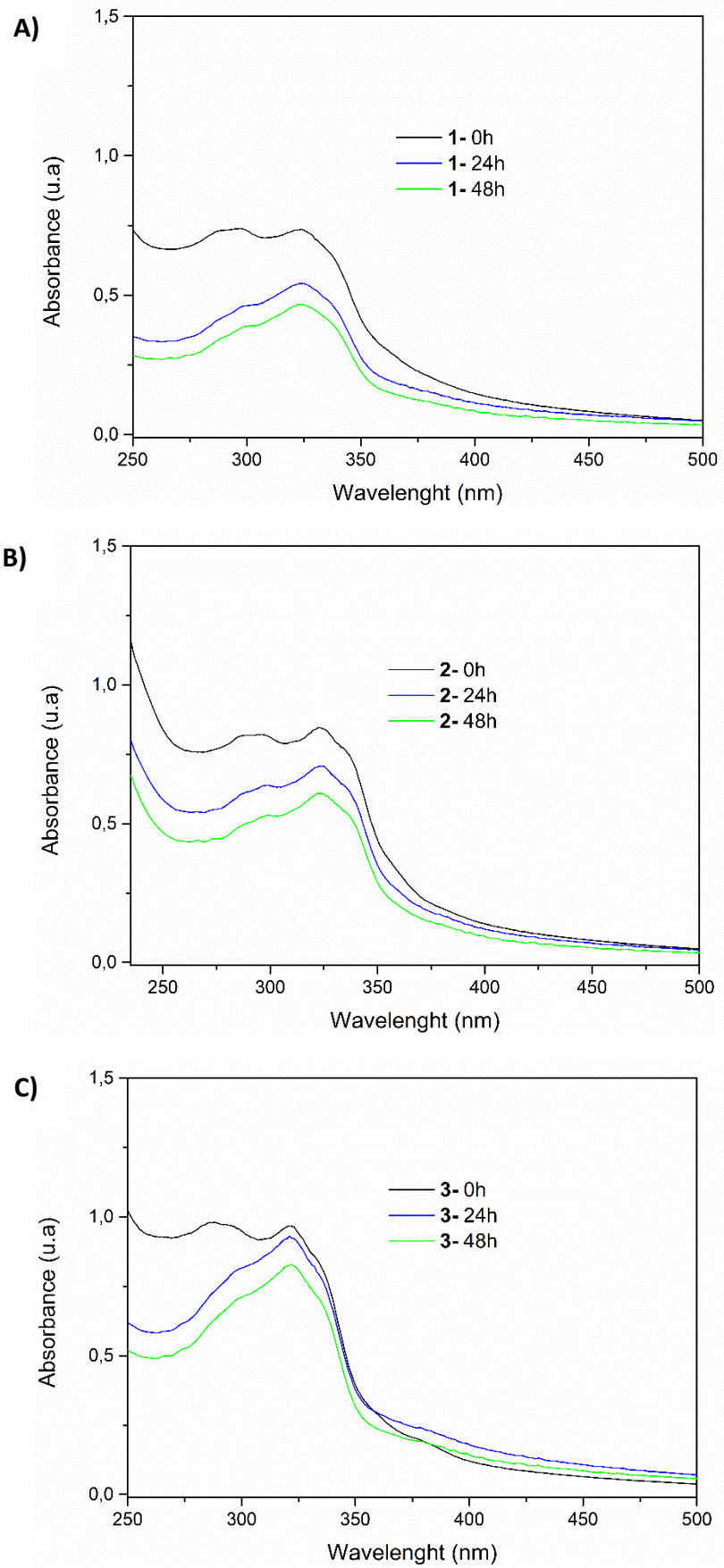


Fig. S14. UV-Vis spectra of complexes (A) **1**, (B) **2** and (C) **3** in Tris-HCl buffer (2% DMSO) recorded at 0, 24h and 48h after preparation of solutions.

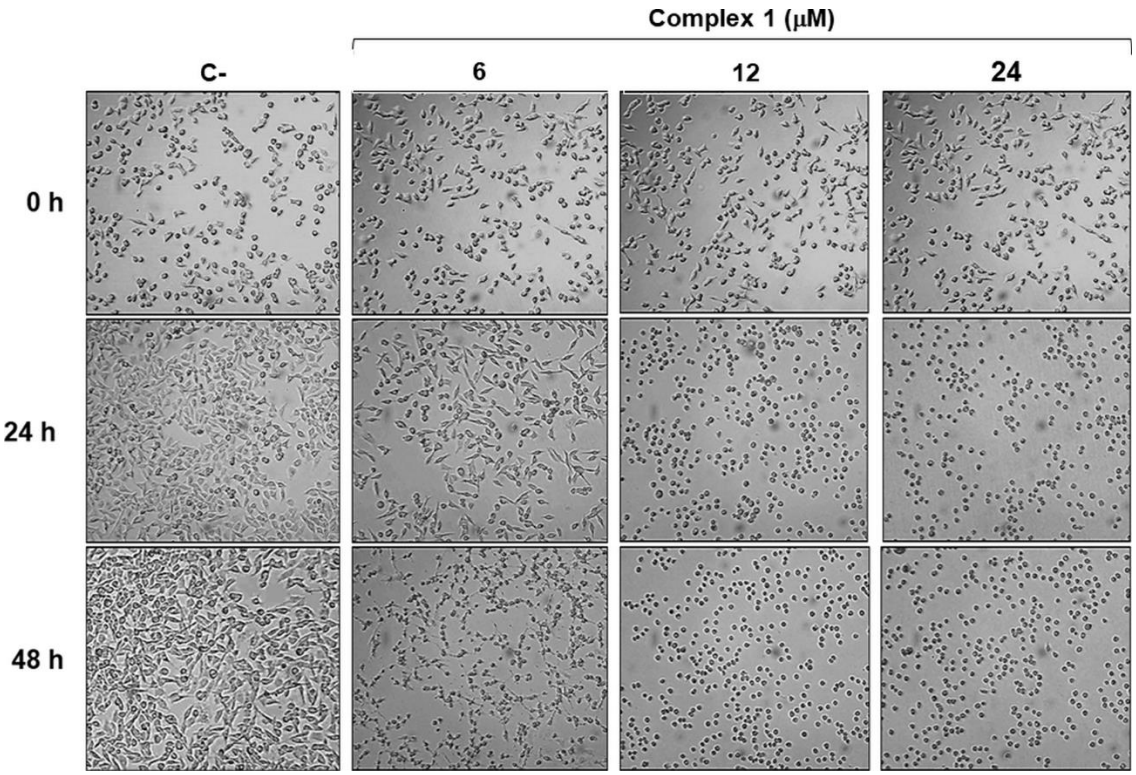


Fig. S15. Morphological changes in MDA-MB-231 cells incubated with complex **1** at a period of 48 hours. Amplification 10 x.

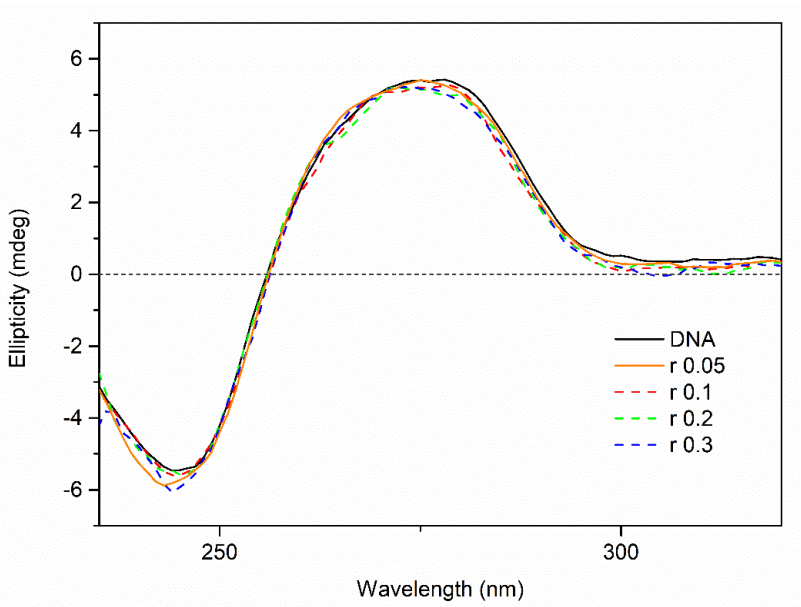


Fig. S16. CD spectrum of ct-DNA in the presence of **1**. r = [complex **1**]/ [DNA].

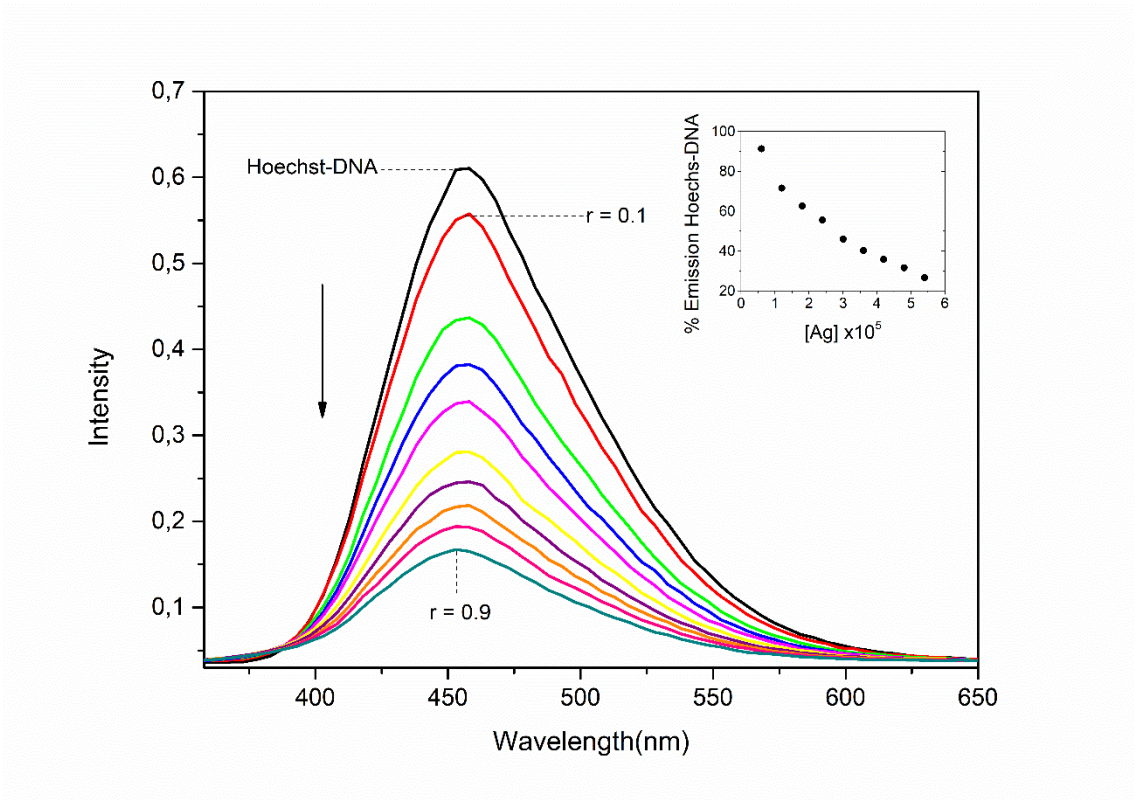


Fig S17. Emission spectra of Hoechst-bound DNA (λ_{ex} = 350 nm) in the presence of increasing concentrations of **1** (6 - 60 μM) in Tris-HCl buffer. [DNA] = 60 μM; [Hoechst] = 6 μM. Inset: plot [Ag] vs relative emission of Hoechst-bound DNA.

Determination of Ag uptake in the cell by HR-CS GFAAS

Table S2. Instrumental parameters and temperature program used in the determination of Ag in cell suspension by HR-CS GFAAS.

Wavelength (nm)	328.0683
Read time (s)	5
Integration mode of absorbance signal	Area
Evaluation pixels	3 (CP ± 1)
Purge gas	Argon
Gas flow during atomization	Stop
Working range (pg)	0 – 750

Step	Name	Temp. (°C)	Ramp. (°C s^{-1})	Hold (s)
1	Drying	125	7	30
2	Pyrolysis	800	60	35
3	Gas adaption	800	0	5
4	Atomize	1800	1500	5
5	Clean	2600	1000	3

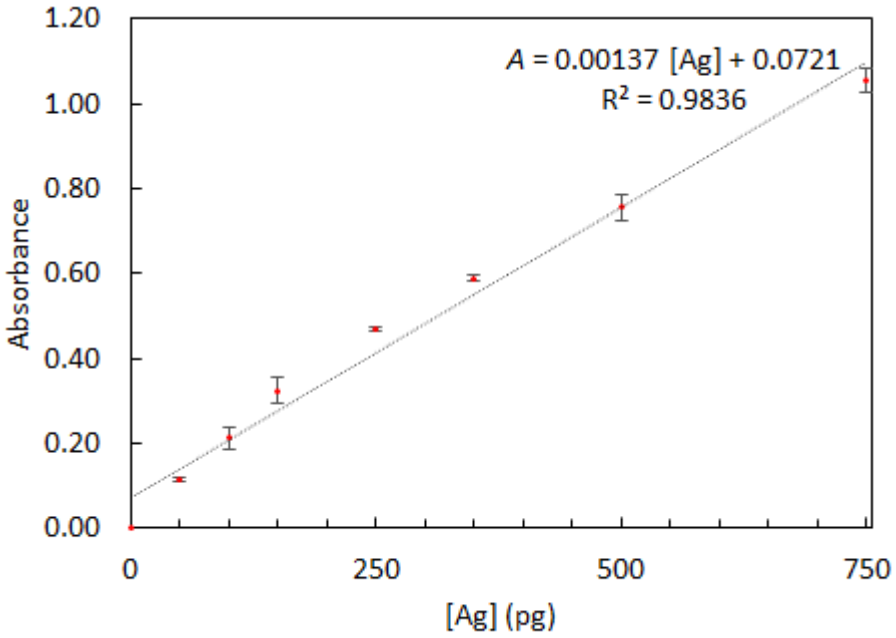


Fig. S18. Calibration curve obtained for Ag determination by HR-CS GFAAS.

Table S3. Percentage of Ag uptake in the cells determined by HR-CS GFAAS (n = 3).

Sample	[Ag] (pg)	Initial concentration (pg)	Uptake percentage (%)
1	2938 ± 172	9572 ± 119	30.7
	2916 ± 144		30.5
	3004 ± 92		31.4
2	2572 ± 170	7578 ± 211	33.9
	2594 ± 198		34.4
	2480 ± 135		32.7
3	3151 ± 105	8848 ± 408	35.6
	3138 ± 210		35.5
	3028 ± 291		34.2