Supplementary Information

Platinum(II/IV) complexes with *N*-substituted carboxylate ethylenediamine/propylenediamine ligands: preparation, characterization and *in vitro* activity

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Contents

Synthesis

Synthesis of 4-[(2-aminoethylamino)methyl]benzoic acid ethyl ester hydrochloride (L1·HCl)

A solution of ethyl 4-(bromomethyl)benzoate (11.6 g, 48 mmol) in dichloromethane (10 mL) was added dropwise over 6 h to a solution of 1,2-diaminoethane (28.8 g, 480 mmol, 32 mL) in dichloromethane (40 mL) at 0 °C. After 2 h of stirring at 0 °C, the protonated 1,2-diaminoethane precipitated as a white solid. After complete addition, the mixture was stirred for an additional hour at 0 °C, then warmed to room temperature and stirred overnight. The white suspension was treated with a saturated NaCl solution (50 mL) and washed with water (3 × 30 mL). The combined aqueous layers were extracted with dichloromethane (2 × 30 mL). The combined organic phases were dried over Na_2SO_4. Then the solvent was evaporated yielding the greenish product.

Yield: 9.5 g (90%). Properties: Greenish oil; soluble in dichloromethane; poorly soluble in water; insoluble in diethyl ether.

^{1}H NMR (300 MHz, DMSO-*d*$_6$, in ppm): δ 1.22 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_3^a), 2.42 (t, $^3J_{H,H}$ = 6.0 Hz, 2H, CH_2^b), 2.62 (m, 3H, CH_2^c), 3.67 (s, 2H, CH_2^d), 4.21 (q, $^3J_{H,H}$ = 7.12 Hz, CH_2^e), 7.38 (d, $^3J_{H,H}$ = 8.0 Hz, 2H, CH^f), 7.82 (d, $^3J_{H,H}$ = 8.1 Hz, 2H, CH^h).

^{13}C{^{1}H} NMR (75 MHz, D_2O, in ppm): δ 14.2 (s, CH_3^a), 41.3 (s, CH_2^b), 51.6 (s, CH_2^c), 52.5 (s, CH_2^d), 60.5 (s, CH_2^e), 127.9 (s, CH^f), 128.1 (s, C^g), 129.0 (s, CH^h), 147.0 (s, C^j), 165.7 (s, CO).

IR ($\tilde{\nu}$ in cm^{-1}): 3310 (w), 3297 (w, br), 2980 (w), 2934 (m), 2906 (m), 2835 (m), 1715 (s), 1643 (w), 1611 (m), 1575 (w), 1544 (w), 1464 (m), 1367 (m), 1308 (m), 1277 (s), 1175 (m), 1107 (s), 1021 (m), 854 (w), 756 (s).

Synthesis of 4-[(3-aminopropylamino)methyl]benzoic acid ethyl ester hydrochloride (L2·HCl)

A solution of ethyl-4-(bromomethyl)benzoate (3.90 g, 16.36 mmol) in dichloromethane (5 mL) was added dropwise over 6 h to a solution of 1,3-diaminopropane (10.56 g, 143.74 mmol, 12 mL) in dichloromethane (20 mL) at 0 °C. After stirring for 2 h at 0 °C, the protonated 1,3-diaminopropane precipitated as a white solid. After complete addition, the mixture was stirred for an additional hour at 0 °C, then warmed to room temperature and stirred overnight. The white suspension was treated with a saturated NaCl solution (20 mL) and washed with water (3 × 20 mL). The combined aqueous phases were extracted with dichloromethane (2 × 10 mL). The combined organic phases were dried over Na_2SO_4. Then the solvent was evaporated yielding a clear yellow oil.

Yield: 3.6 g (91%). Properties: clear yellow oil; soluble in dichloromethane, chloroform, methanol; moderately soluble in DMSO; poorly soluble in water; insoluble in diethyl ether.

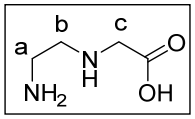
^{1}H NMR (400 MHz, $CDCl_3$, in ppm): δ 1.37 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, CH_3^{a}), 1.64 (p, $^{3}J_{H,H}$ = 6.8 Hz, 2H, CH_2^{b}), 2.67 (t, $^{3}J_{H,H}$ = 6.9 Hz, 2H, CH_2^{c}), 2.76 (t, $^{3}J_{H,H}$ = 6.8 Hz, 2H, CH_2^{d}), 3.81 (s, 2H, CH_2^{e}), 4.35 (q, $^{3}J_{H,H}$ = 7.1 Hz, 2H, CH_2^{f}), 7.38 (d, $^{3}J_{H,H}$ = 8.1 Hz, 2H, CH^{g}), 7.98 (d, $^{3}J_{H,H}$ = 8.2 Hz, 2H, CH^{j}).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, in ppm): δ 14.4 (s, CH_3^{a}), 33.7 (s, CH_2^{b}), 40.5 (s, CH_2^{c}), 47.4 (s, CH_2^{d}), 53.7 (s, CH_2^{e}), 60.8 (s, CH_2^{f}), 127.9 (s, CH^{g}), 129.1 (s, C^{h}), 129.6 (s, CH^{j}), 145.9 (s, C^{k}), 166.5 (s, CO).

IR ($\tilde{\nu}$ in cm^{-1}): 3416 (m), 2979 (m), 1717 (s), 1612 (m), 1539 (m), 1405 (m), 1276 (s), 1175 (m), 1106 (s), 1021 (m).

Synthesis of 2-(2-aminoethylamino)acetic acid hydrochloride (L3·HCl)

The compound is already known in the literature, but the synthesis herein was slightly modified. Bromoacetic acid (9.5 g, 0.07 mol) was added in portions over 6 h to a solution of 1,2-diaminoethane (42.0 g, 47.0 mL, 0.70 mol) in ethanol (40 mL) at 0 °C resulting in cloudiness after a few portions. The mixture was stirred overnight at room temperature, then concentrated to give a clear oil. This oil was acidified with aqueous HCl (3 M, 20 mL). After keeping the resulting solution at 4 °C for 24 h, a white precipitate formed, which was filtered off, washed with ethanol (10 mL) and diethyl ether (20 mL), and air-dried.



Yield: 5.8 g (70%). Properties: White powder; very soluble in water; soluble in chloroform; poorly soluble in DMSO; insoluble in diethyl ether.

^{1}H NMR (300 MHz, D_2O, in ppm): δ 3.29–3.47 (m, 4H, C$H_2^{a,b}$), 3.95 (s, 2H, CH_2^{c}).

^{1}H NMR (300 MHz, DMSO-d_6, in ppm): δ 3.17–3.24 (m, 4H, C$H_2^{a,b}$), 3.86 (s, 2H, CH_2^{c}).

^{13}C{^{1}H} NMR (75 MHz, D_2O, in ppm): δ 35.4 and 43.9 (s, $CH_2^{a,b}$), 47.8 (s, CH_2^{c}), 168.6 (s, CO).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, in ppm): δ 36.0 and 44.6 (s, $CH_2^{a,b}$), 48.1 (s, CH_2^{c}), 168.6 (s, CO).

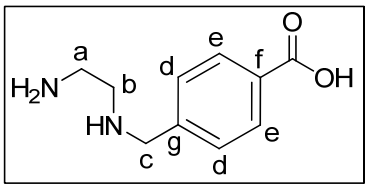
IR ($\tilde{\nu}$ in cm^{-1}): 3436 (s, br), 3012 (s, br), 2526 (w), 1909 (m, br), 1722 (s), 1605 (s), 1497 (s), 1445 (s), 1428 (m), 1379 (s), 1349 (m), 1326 (s), 1257 (s), 1144 (w), 1050 (m), 1031 (m), 999 (s), 950 (m), 913 (m), 870 (m), 789 (s).

Synthesis of 4-[(2-aminoethylamino)methyl]benzoic acid hydrochloride (L4·HCl)

L4·HCl is described in the literature, but the synthesis in this work was carried out using the respective brominated starting materials.

A suspension of 4-(bromomethyl)benzoic acid (7.5 g, 0.035 mol) in ethanol (25 mL) was added dropwise over 8 h with ice-cooling to a solution of 1,2-diaminoethane (0.37 mol, 25 mL) in ethanol (50 mL) at 0°C. After stirring for an additional 14 h at 0 °C, the solvent and excess 1,2-diaminoethane were removed under vacuum at 60 °C. The resulting white viscous residue was recrystallized from DMSO (20 mL), ethanol (30 mL), and diethyl ether (15 mL). The resulting

white powder was filtered off, washed with ethanol (20 mL) and diethyl ether (20 mL), and air-dried.



Yield: 3.8 g (52%). Properties: White powder; soluble in water; moderately soluble in DMSO; insoluble in diethyl ether.

^{1}H NMR (300 MHz, D_2O, in ppm): δ 2.69 (t, $^{3}J_{H,H}$ = 6.5 Hz, 2H, CH_2^{a}), 2.89 (t, $^{3}J_{H,H}$ = 6.5 Hz, 2H, CH_2^{b}), 3.58 (s, 2H, CH_2^{c}), 7.14 (d, $^{3}J_{H,H}$ = 8.0 Hz, 2H, CH^{d}), 7.61 (d, $^{3}J_{H,H}$ = 8.0 Hz, 2H, CH^{e}).

^{1}H NMR (300 MHz, DMSO-*d*$_6$, in ppm): δ 2.17 (s, 1H, N*H*), 2.36 (m, 1.9H, CH_2^{a}), 2.55 (m, 2H, CH_2^{b}), 3.34 (s, 2H, CH_2^{c}), 6.91 (d, $^{3}J_{H,H}$ = 7.7 Hz, 2H, CH^{d}), 7.39 (d, $^{3}J_{H,H}$ = 7.8 Hz, 2H, CH^{e}).

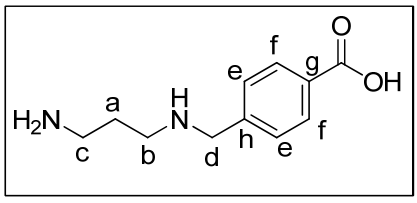
^{13}C{^{1}H} NMR (75 MHz, DMSO-*d*$_6$, in ppm): δ 39.0 (s, *C*H_2^{a}), 46.2 (s, *C*H_2^{b}), 52.7 (s, *C*H_2^{c}), 128.4 (s, *C*H^{d}), 130.0 (s, *C*H^{e}), 137.7 (s, *C*^{f}), 141.8 (s, *C*^{g}), 172.3 (s, *C*O).

^{13}C{^{1}H} NMR (75 MHz, D_2O, in ppm): δ 38.2 (s, *C*H_2^{a}), 45.3 (s, *C*H_2^{b}), 51.6 (s, *C*H_2^{c}), 128.2 (s, *C*H^{d}), 129.1 (s, *C*H^{e}), 135.3 (s, *C*^{f}), 140.5 (s, *C*^{g}), 175.0 (s, *C*O).

IR ($\tilde{\nu}$ in cm^{-1}): 3446 (s, br), 2850 (s, br), 2363 (w), 1624 (s), 1507 (s, br), 1381 (s), 1261 (w), 1173 (w), 1118 (w), 1093 (w), 1064 (w), 1017 (m), 867 (w), 846 (w), 788 (m), 763 (m).

Synthesis of 4-[(3-aminopropylamino)methyl]benzoic acid hydrochloride (L5·HCl)

1,3-Diaminopropane (0.36 mol, 30 mL) was dissolved in ethanol (50 mL) and cooled to 0 °C. A suspension of 4-(bromomethyl)benzoic acid (8.0 g, 0.04 mol) in ethanol (25 mL) was added dropwise to this clear solution over 6 h and stirred for an additional 12 h at room temperature. Excess 1,3-diaminopropane and solvent were removed under reduced pressure (2 mbar) at 60 °C. The remaining white viscous mass was stirred in hot DMSO (15 mL) and ethanol (30 mL). Upon cooling to room temperature, a white viscous solid precipitated, which was filtered off, washed with ethanol (15 mL) and diethyl ether (15 mL), and dried in vacuo.



Yield: 4.0 g (76%). Properties: white powder; soluble in water; moderately soluble in DMSO; insoluble in diethyl ether.

^{1}H NMR (300 MHz, D_2O, in ppm): δ 1.46–1.87 (m, 2H, CH_2^{a}), 2.50 (t, $^{3}J_{H,H}$ = 6.4 Hz, 2H, CH_2^{b}), 2.78 (t, $^{3}J_{H,H}$ = 6.9 Hz, 2H, CH_2^{c}), 3.58 (s, 2H, CH_2^{d}), 7.18 (d, $^{3}J_{H,H}$ = 6.6 Hz, 2H, CH^{e}), 7.67 (d, $^{3}J_{H,H}$ = 7.0 Hz, 2H, CH^{f}).

^{1}H NMR (300 MHz, DMSO-*d*$_6$, in ppm): δ 1.99 (p, $^{3}J_{H,H}$ = 7.8 Hz 2H, CH_2^{a}), 2.90 (t, $^{3}J_{H,H}$ = 7.6 Hz, 2H, CH_2^{b}), 3.04 (t, $^{3}J_{H,H}$ = 7.8 Hz, 2H, CH_2^{c}), 4.16 (s, 2H, CH_2^{d}), 7.53 (d, $^{3}J_{H,H}$ = 8.0 Hz, 2H, CH^{e}), 7.88 (d, $^{3}J_{H,H}$ = 7.8 Hz 2H, CH^{f}).

^{13}C{^{1}H} NMR (75 MHz, D_2O, in ppm): δ 26.6 (s, *C*H_2^{a}), 37.7 (s, *C*H_2^{b}), 44.9 (s, *C*H_2^{c}), 51.7 (s, *C*H_2^{d}), 128.4 (s, *C*H^{e}), 129.1 (s, *C*H^{f}), 135.3 (s, *C*^{g}), 140.7 (s, *C*^{h}), 175.1 (s, *C*O).

^{13}C{^{1}H} NMR (75 MHz, DMSO-*d*$_6$, in ppm): δ 24.4 (s, *C*H_2^{a}), 37.1 (s, *C*H_2^{b}), 45.0 (s, *C*H_2^{c}), 50.9 (s, *C*H_2^{d}), 130.7 (s, *C*H^{e}), 130.9 (s, *C*H^{f}), 134.0 (s, *C*^{g}), 136.3 (s, *C*^{h}), 169.6 (s, *C*O).

IR ($\tilde{\nu}$ in cm^{-1}): 3435 (s), 2961 (m), 2821 (m), 2146 (w), 1608 (m), 1587 (m), 1550 (s), 1382 (s), 1176 (w), 1119 (w), 1016 (w).

Table S1. Fundamental structure parameters

Compound	**3** · DMSO · 0.5 H_2O	**4** · H_2O	**6**
Empirical formula	$C_{15}H_{27}Cl_4N_2O_{3.50}PtS$	$C_4H_{12}Cl_2N_2O_3Pt$	$C_4H_9Br_{0.22}Cl_{2.78}N_2O_2Pt$
Formula weight	660.33	402.15	428.53
Temperature [K]	130(2)	130(2)	130(2)
Wavelength [Å]	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/c$	$C2/c$
Unit cell dimensions			
a [Å]	11.7909(1)	8.0288(2)	12.5082(2)
b [Å]	25.2517(2)	7.4126(2)	7.2732(2)
c [Å]	29.6625(2)	16.7813(4)	21.4594(4)
α [deg]	90	90	90
β [deg]	94.966(1)	97.874(3)	99.959(2)
γ [deg]	90	90	90
Volume [$Å^3$]	8798.6(1)	989.31(4)	1922.84(7)
Z	16	4	8
$\rho_{(calculated)}$ [Mg/m^3]	1.994	2.700	2.961
μ [mm^{-1}]	6.980	14.696	16.258
F(000)	5136	744	1568
Crystal size [mm^3]	0.35 · 0.23 · 0.03	0.29 · 0.15 · 0.01	0.13 · 0.09 · 0.03
Θ_{Min} - Θ_{Max} [deg]	2.122 - 30.508	2.450 - 28.192	1.927 - 32.541
Index ranges	$-16 \le h \le 16$ $-36 \le k \le 36$ $-42 \le l \le 42$	$-10 \le h \le 10$ $-9 \le k \le 9$ $-21 \le l \le 22$	$-17 \le h \le 18$ $-10 \le k \le 10$ $-30 \le l \le 31$
Reflections collected	180108	10532	17991
Indp. reflections (R_{int})	26843 (0.0629)	2296 (0.0278)	3268 (0.0487)
Completeness (Θ_{Max})	99.9 % (25.24°)	100.0 % (26.38°)	100.0 % (30.51°)
T_{Max} / T_{Min}	0.828 / 0.286	0.864 / 0.112	0.605 / 0.224
Restraints / parameters	0 / 967	0 / 110	2 / 113
Gof on F^2	1.020	1.068	1.080
R1 / wR2 ($I>2\sigma(I)$)	0.0372 / 0.0675	0.0226 / 0.0474	0.0284 / 0.0460
R1 / wR2 (all data)	0.0758 / 0.0789	0.0300 / 0.0504	0.0433 / 0.0491
Residual electron density [$e \cdot Å^{-3}$]	1.918 / -1.686	1.197 / -1.338	1.585 / -1.854
Comments	†[1]	†[2]	†[3]
CCDC No	2390314	2390315	2390316

†[1]: Pseudo symmetry detectable. With the exception of the COOEt substituent and solvent molecules, the structure could be described in a smaller (b' = ½ b) A-centered monoclinic cell (non-standard space group setting A2/a; see Figure S1, top left). These moieties represent approximately 3/4 of the total electron density. The additional weaker

reflections (Figure S1, top right marked in light blue) led to the correct primitive cell and a completely non-disordered structure (Figure S1, bottom left and right). †[2] The water molecule O(3) is located in the vicinity of a center of inversion with symmetry related disordered hydrogen atoms H(2O3) and H(2OF). †[3]: Small bromine impurities: Cl(3):Br(3F) disorder detectable with ratio 0.776(4):0.224(4)). The atoms Cl(1) and Cl(2) are not affected.

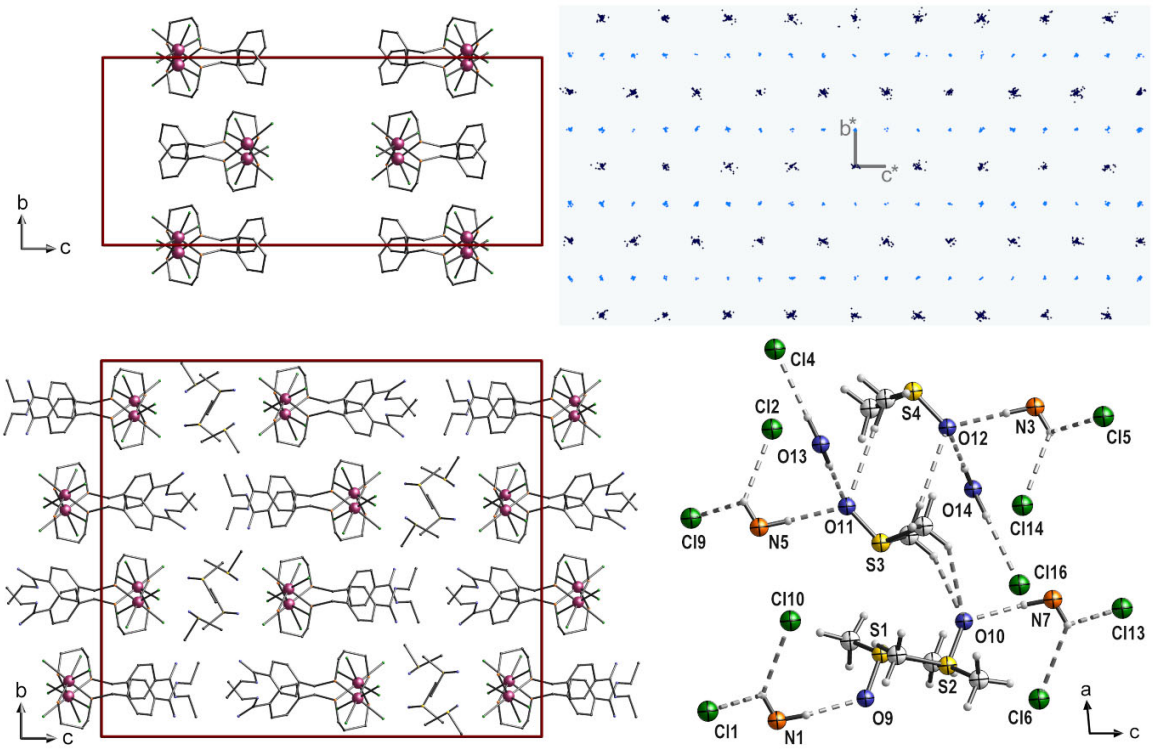


Figure S1. Remarkably, unusual diffraction pattern of **3** viewing along a* (top right). The strong dark blue marked reflections feigned a smaller A-centered lattice (top left). The less intensive light blue marked reflections (top right) reveal the the correct unit cell (bottom left). Water and DMSO, located in solvent channals along (100), are not disordered at all as they interact intensively with adjacent molecules via hydrogen donor-acceptor bonds (bottom right).

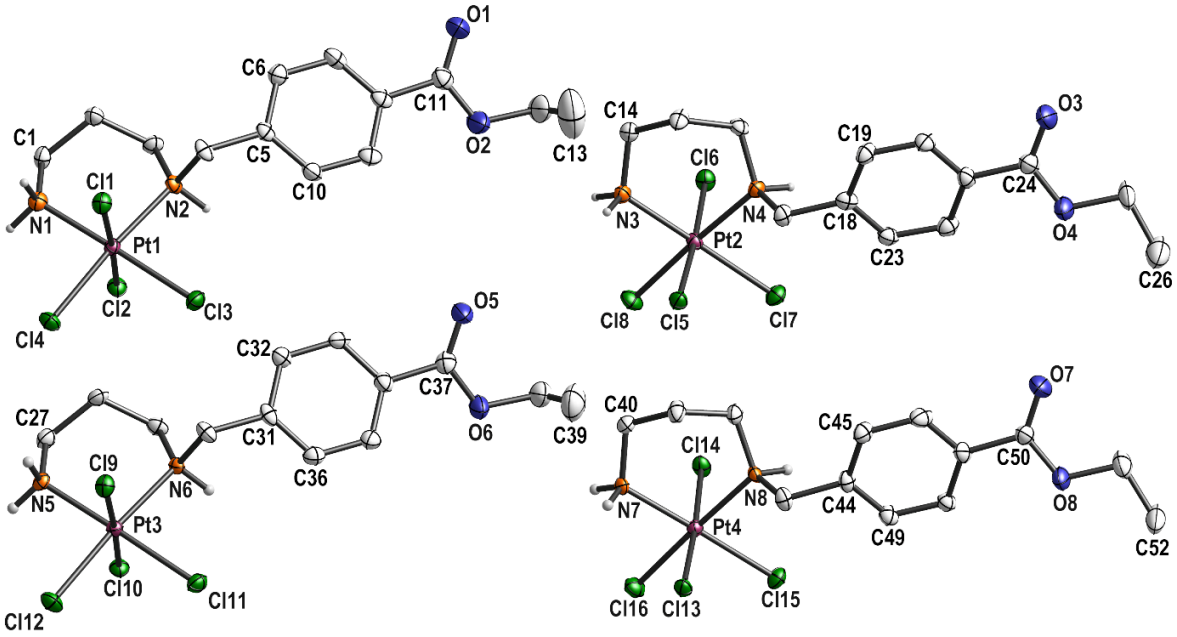


Figure S2. Labelling scheme of all four independent complex molecules of **3**. Hydrogen atoms, except NH, were omitted for clarity. Displacement ellipsoids are drawn at the 50 % probability level.

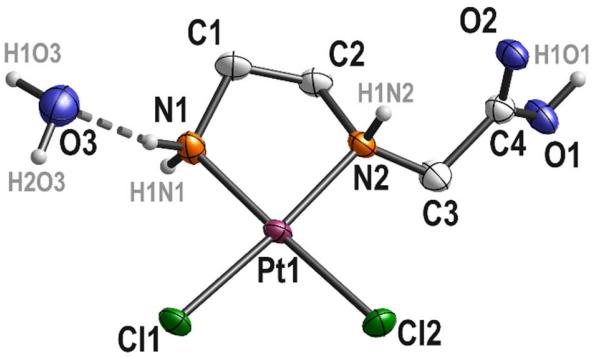


Figure S3. Labelling scheme of **4**. Hydrogen atoms, except NH, OH, and the disordered atom H(2OF) were omitted for clarity. Displacement ellipsoids are drawn at the 50 % probability level.

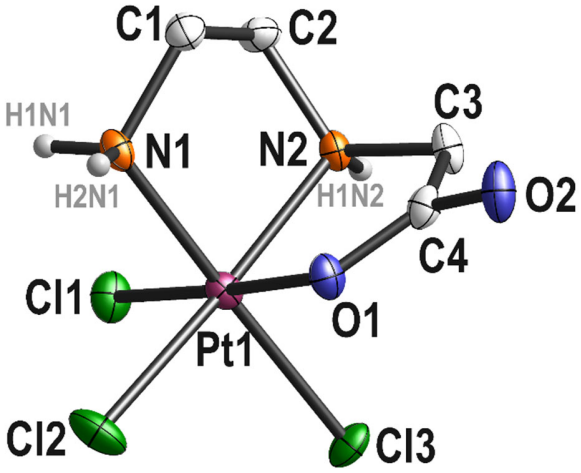


Figure S4. Labelling scheme of **6**. Hydrogen atoms, except NH and the disordered atom Br(3F) were omitted for clarity. Displacement ellipsoids are drawn at the 50 % probability level.

Table S2. Hydrogen donor-acceptor bonds.

	D-H···A	d(D-H) [Å]	d(H···A) [Å]	d(D···A) [Å]	<(DHA) [deg]
Compound **3**	N(1)-H(1N1)···O(9)#1	0.91	1.92	2.788(5)	159.9
	N(3)-H(1N3)···O(12)#2	0.91	1.88	2.754(5)	161.3
	N(5)-H(1N5)···O(11)	0.91	1.88	2.753(5)	161.3
	N(7)-H(1N7)···O(10)	0.91	1.93	2.796(5)	159.5
	O(13)-H(26O)···O(11)	0.99	1.88	2.863(7)	175.2
	O(13)-H(25O)···Cl(4)#3	0.99	2.46	3.445(6)	175.5
	O(14)-H(27O)···O(12)	0.99	1.87	2.862(7)	176.0
	O(14)-H(28O)···Cl(16)	0.99	2.50	3.493(6)	176.5
Compound **4**	O(1)-H(1O1)···O(2)#4	0.84	1.80	2.639(5)	176.5
	N(1)-H(2N1)···O(3)	0.91	1.97	2.871(6)	168.3
Compound **6**	N(1)-H(1N1)···O(2)#5	0.91	2.03	2.842(4)	148.8
	N(1)-H(2N1)···O(2)#6	0.91	1.93	2.839(4)	174.3

Symmetry transformations used to generate equivalent atoms: #1: x+1/2, -y+1/2, z+1/2; #2: x-1/2, -y+1/2, z+1/2; #3: x+1/2, -y+1/2, z-1/2; #4: -x+1,-y,-z+1; #5: x-1/2,y+1/2,z; #6: -x+3/2,-y+1/2,-z+1

Biological Studies

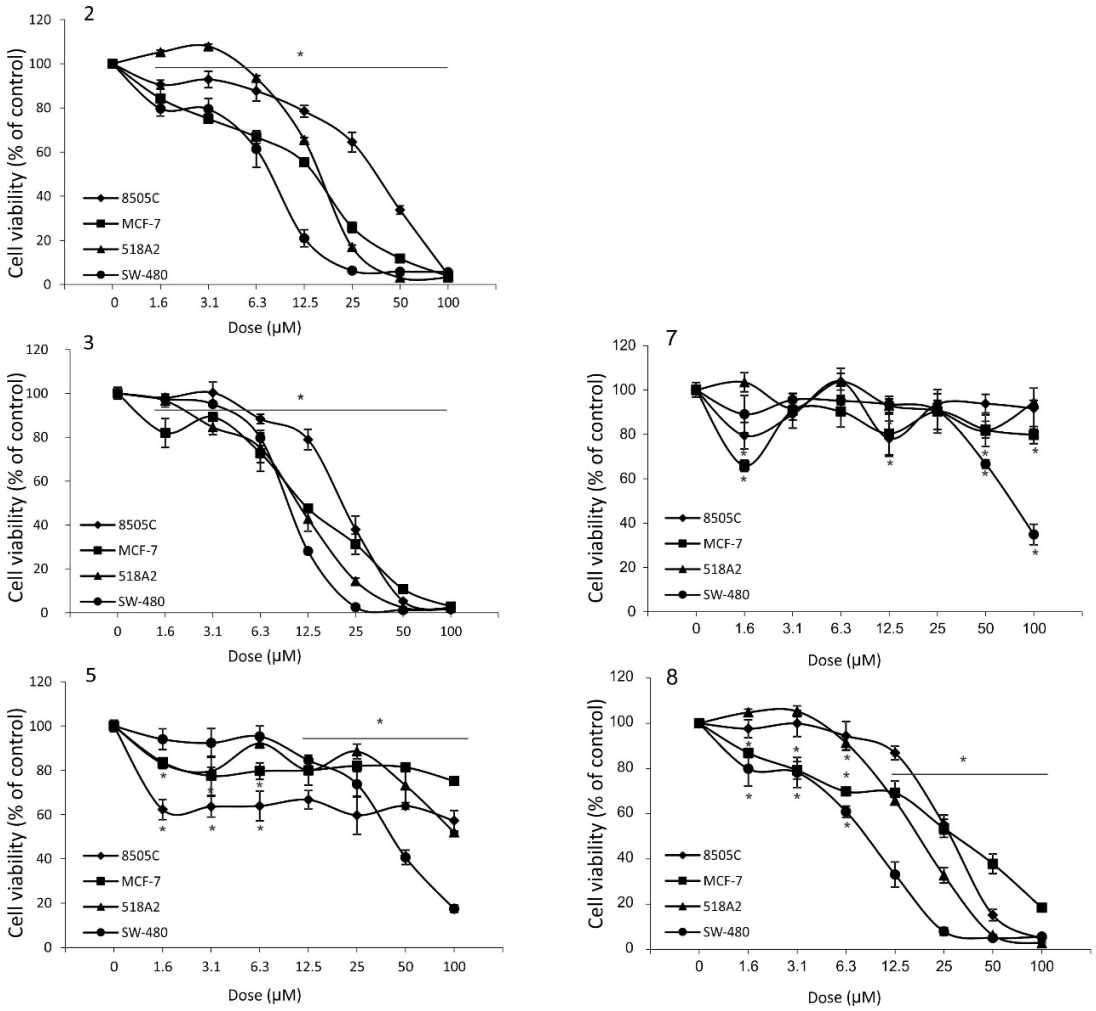


Figure S5. Viability curves. 8505C, MCF-7, 518A2, and SW-480 cell lines were treated with a dose range of complexes **2**, **3**, **5**, **7**, and **8** and the viability was estimated using an SRB assay after 96 h. The data are presented as a mean ± SD from one representative out of three independent experiments. *$p<0.05$ refers to untreated cultures.

Table S3. IC_{50} values (μM) of compounds **2**, **3**, **5**, **7**, and **8** prepared in DMSO stock solution (96 h, SRB assay).

Cell line	Biological replicate	**2**	**3**	**5**	**7**	**8**
8505C	1st	12.9	13.1	/	/	17
	2nd	7.7	25	/	/	34.9
MCF-7	1st	14.2	9.5	/	/	18.6
	2nd	10.1	16	/	/	50
518A2	1st	12.3	18.1	/	/	16
	2nd	22.6	71.9	/	/	65
SW-480	1st	6.5	9.6	19.6	/	1.9
	2nd	16.3	4.8	36.3	/	3

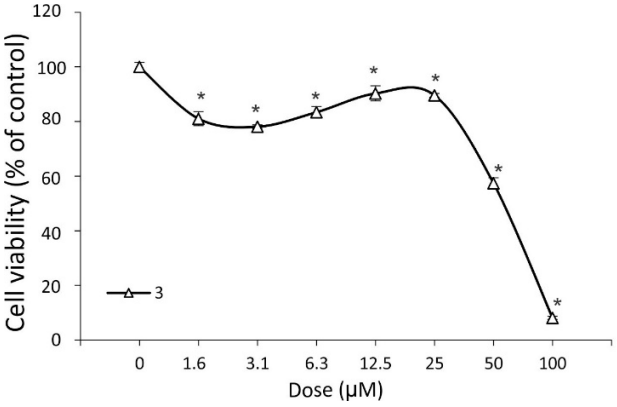


Figure S6. The influence of **3** on the viability of MRC5 cell line. Cells were treated with a dose range of **3** and the viability was estimated using an SRB assay after 96 h. The data are presented as a mean ± SD from one representative out of three independent experiments. *$p<0.05$ refers to untreated cultures.

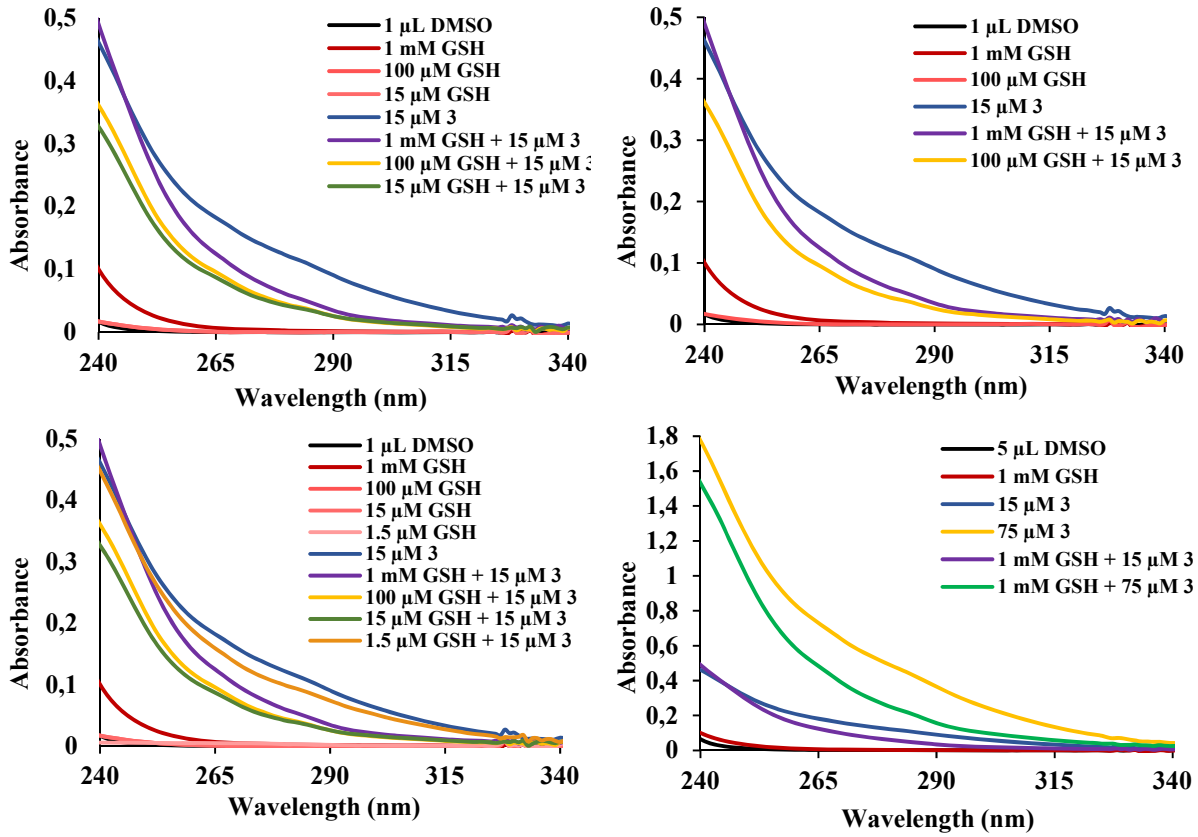


Figure S7. UV-vis spectra of compound **3** at concentrations indicated (15 µM, 75 µM) in the presence of glutathione (GSH). Conditions: GSH 50 mM, pH 7, phosphate buffer (room temperature). Since compound **3** was employed as a stock solution in DMSO, control spectra are also shown illustrating the lack of effect of DMSO at the employed concentrations/volumes.

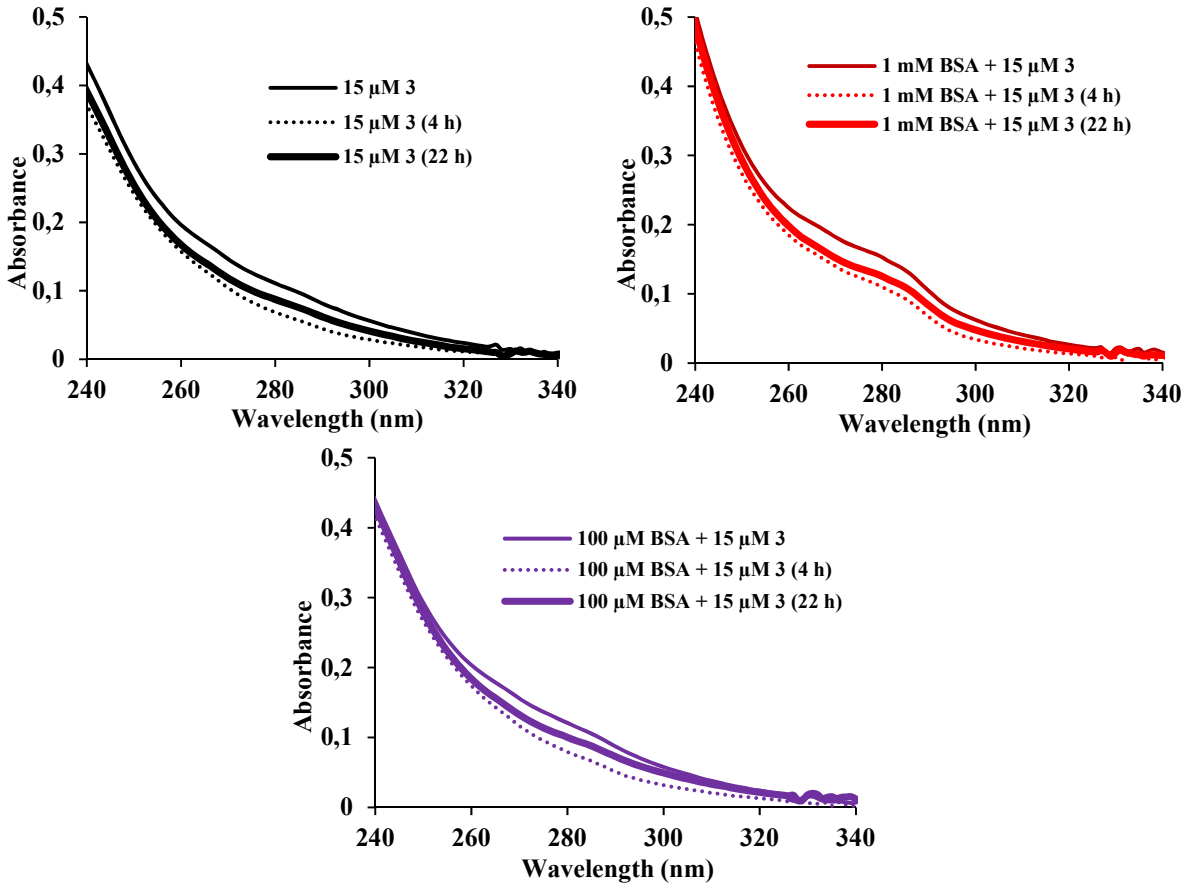


Figure S8. UV-vis spectra of compound **3** in the presence of bovine serum albumin (BSA). Conditions: BSA 50 mM, pH 7, phosphate buffer (room temperature), concentrations indicated in Figure legends.

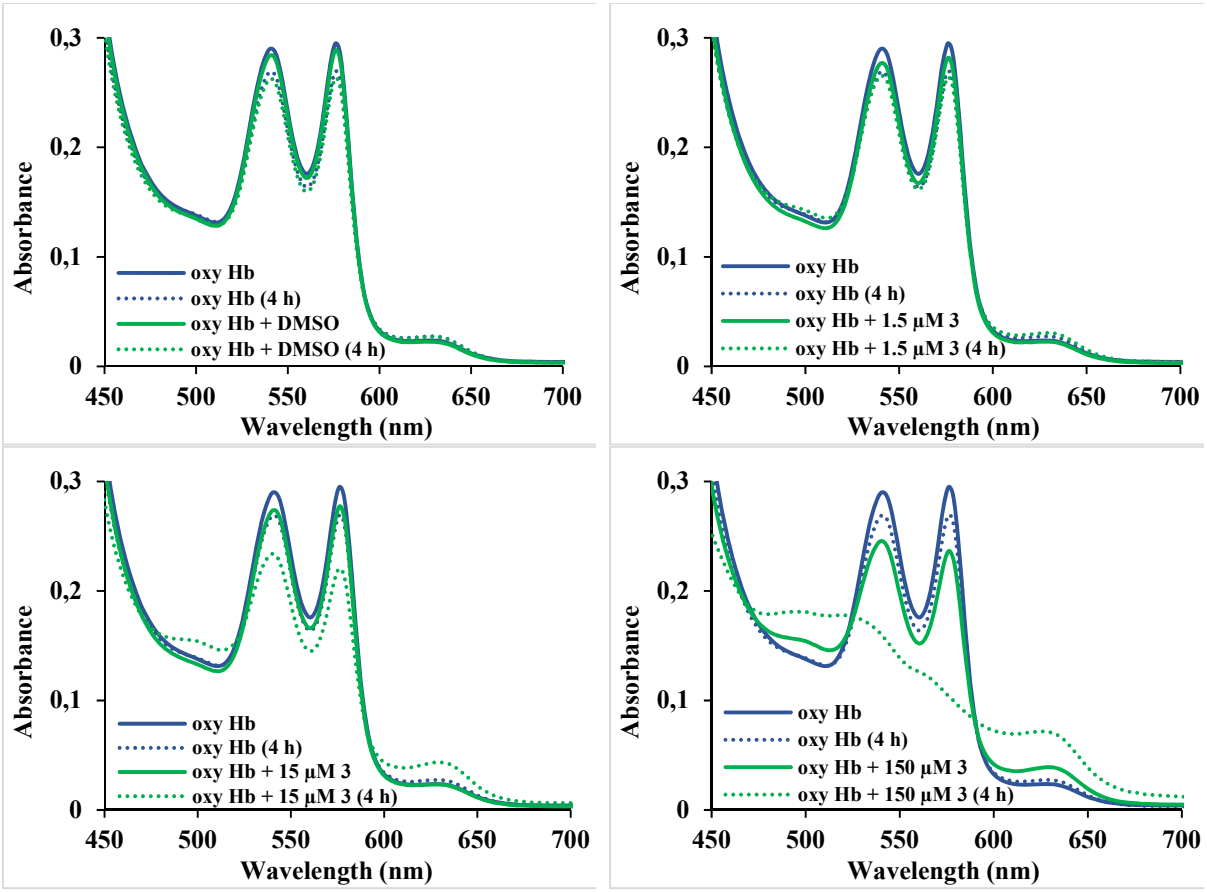


Figure S9. UV-vis spectra of oxy Hb (15 µM) in the presence of varying concentrations of compound **3**, before and after incubation for 4 h at 37 °C. Conditions: oxy Hb 50 mM, pH 7, phosphate buffer, concentrations indicated in Figure legends. Since compound **3** was employed as a stock solution in DMSO, control spectra are also shown illustrating the lack of effect of DMSO at the employed concentrations/volumes.

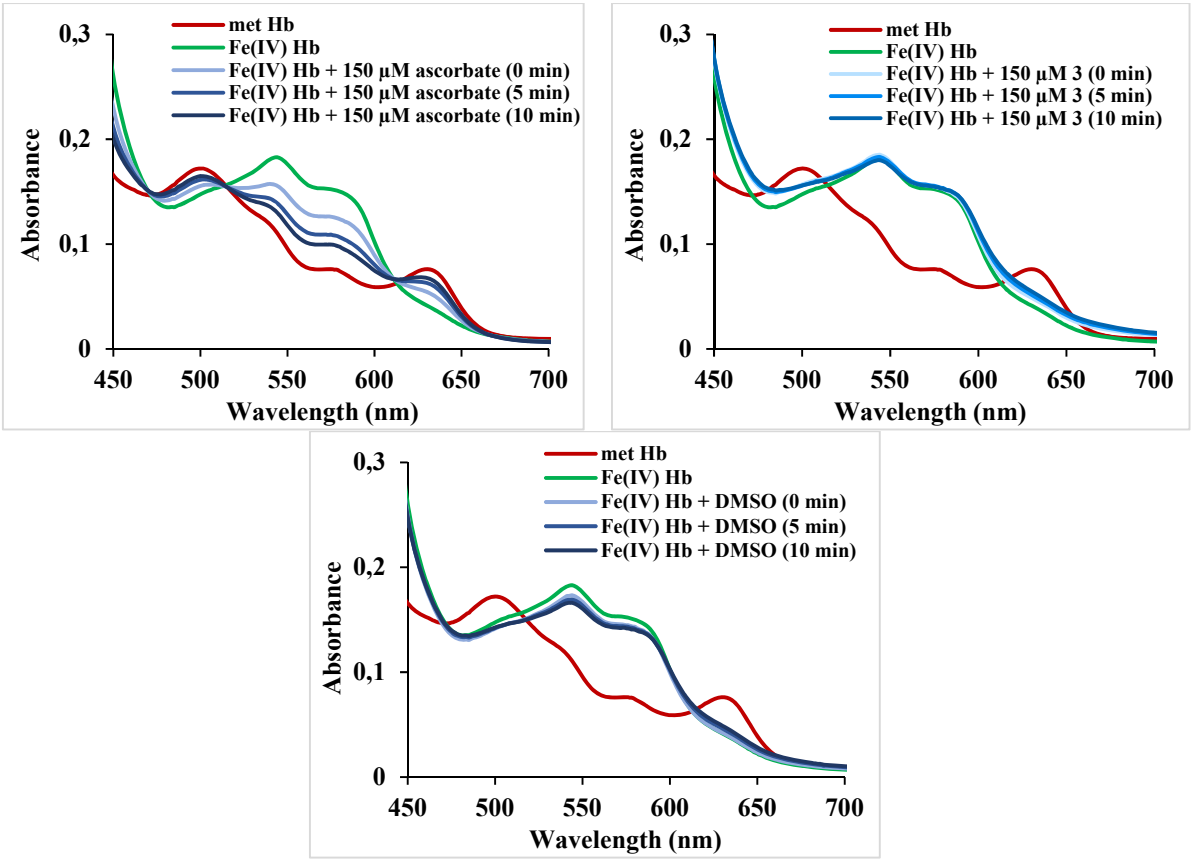


Figure S10. UV-vis spectra of iron(IV) Hb (15 µM) in the presence of compound **3** and ascorbate. Conditions: Iron(IV) Hb 50 mM, pH 7, phosphate buffer, concentrations indicated in Figure legends. Since compound **3** was employed as a stock solution in DMSO, control spectra are also shown illustrating the lack of effect of DMSO at the employed concentrations/volumes.

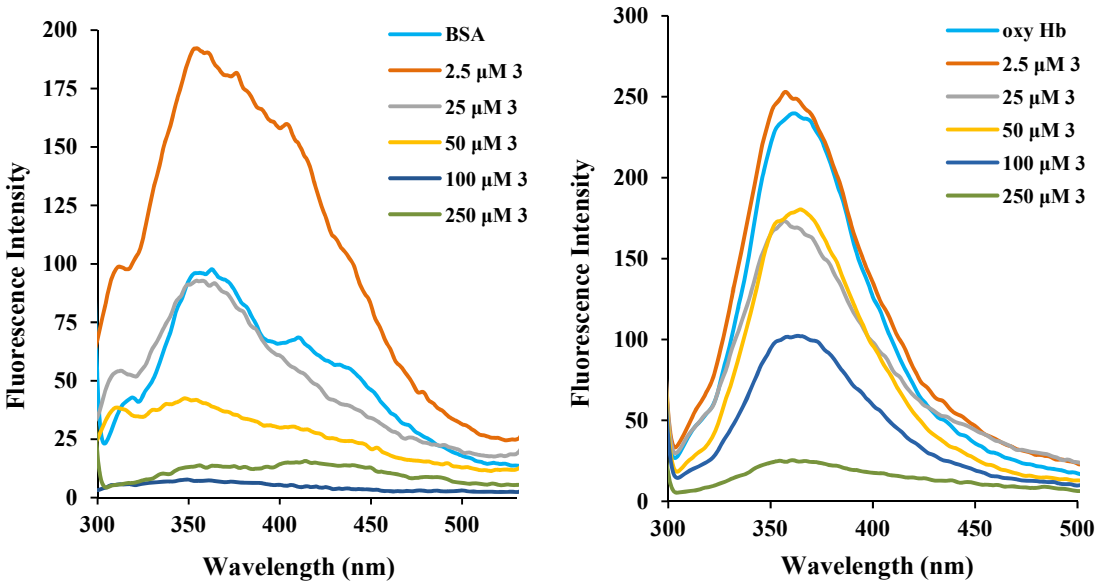


Figure S11. Fluorescence emission spectra collected with excitation at 280 nm for bovine serum albumin (BSA, left) and oxy Hb (right) in the presence of varying concentrations of compound **3**. Conditions: BSA 50 mM, oxy Hb 0.15 µM, pH 7, phosphate buffer (room temperature); concentrations of **3** are indicated in Figure legends. Since compound **3** was employed as a stock solution in DMSO, control spectra were also collected illustrating the lack of effect of DMSO at the employed concentrations/volumes (not shown).

Electrochemical studies

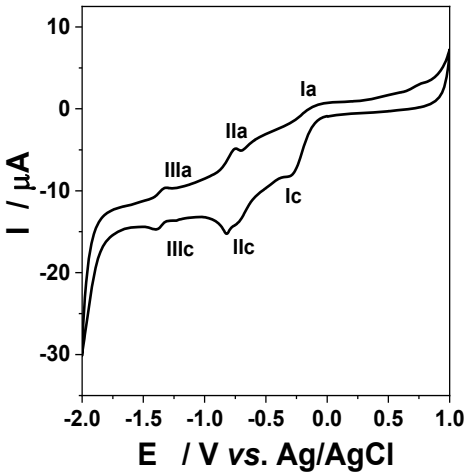


Figure S12. Cyclic voltammograms obtained at a glassy carbon (GC) electrode with compound **3** (10^{-3} M). Experimental conditions: electrolyte, in 0.1 M (*n*-Bu_4N)[BF_4]) in DMF solution; scan rate, 0.1 V s^{-1}; starting potential 0 V vs. Ag/AgCl.

NMR Spectra

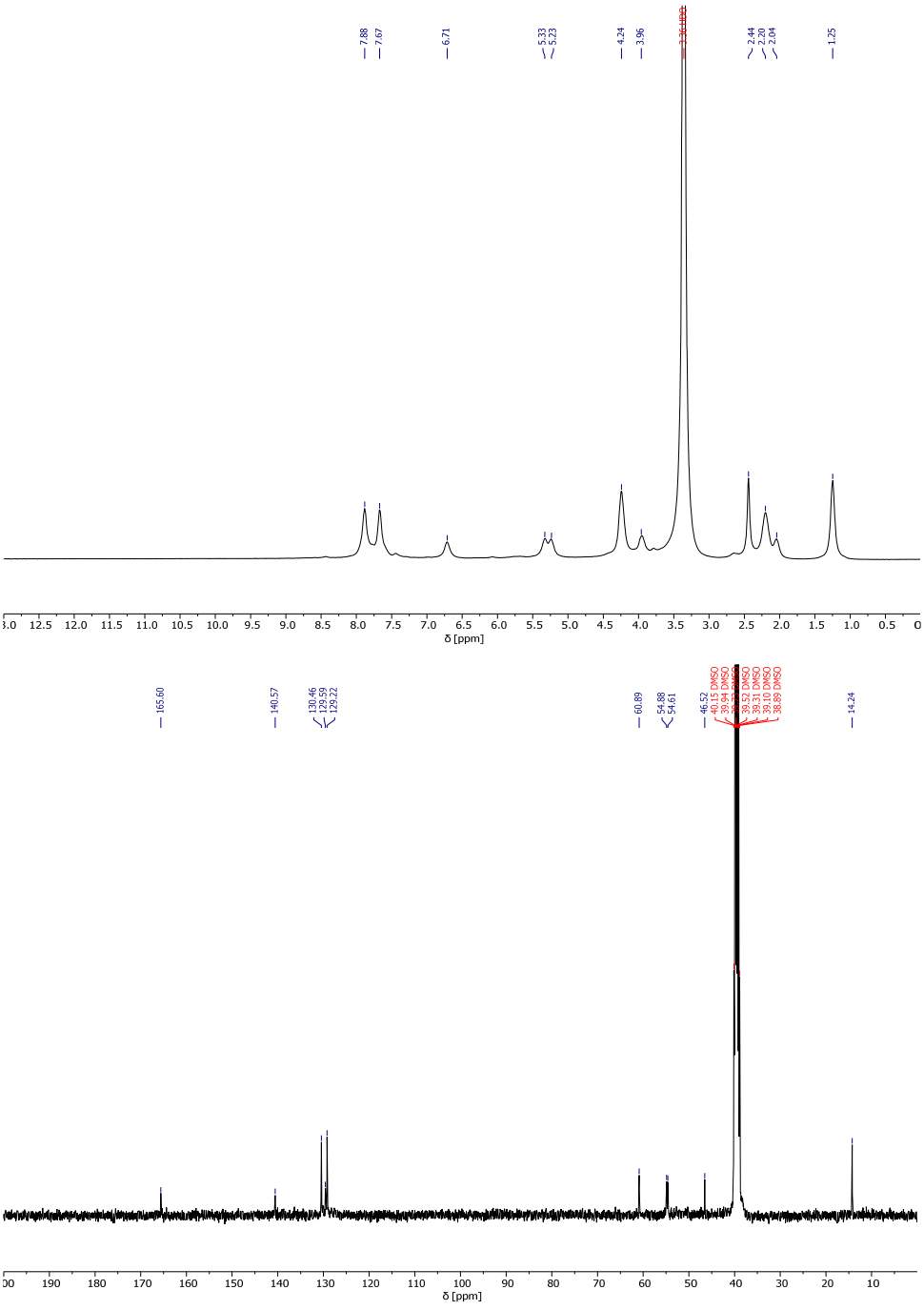


Figure S13. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of **1** (400 and 100 MHz, respectively, DMSO-d_6).

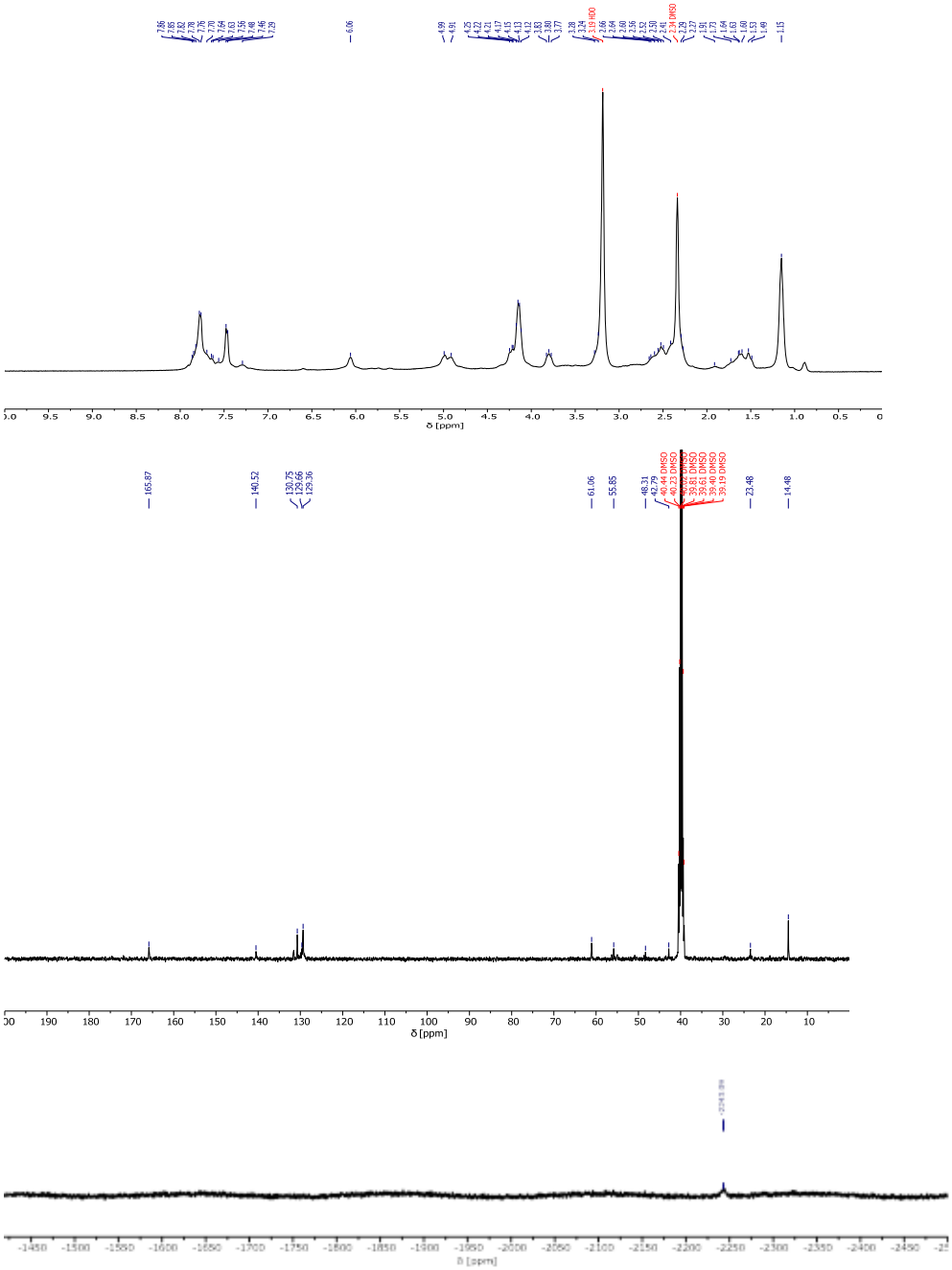


Figure S14. ^{1}H, $^{13}C\{^{1}H\}$ and ^{195}Pt NMR spectra of **2** (400, 100 and 85 MHz, respectively, DMSO-d_6).

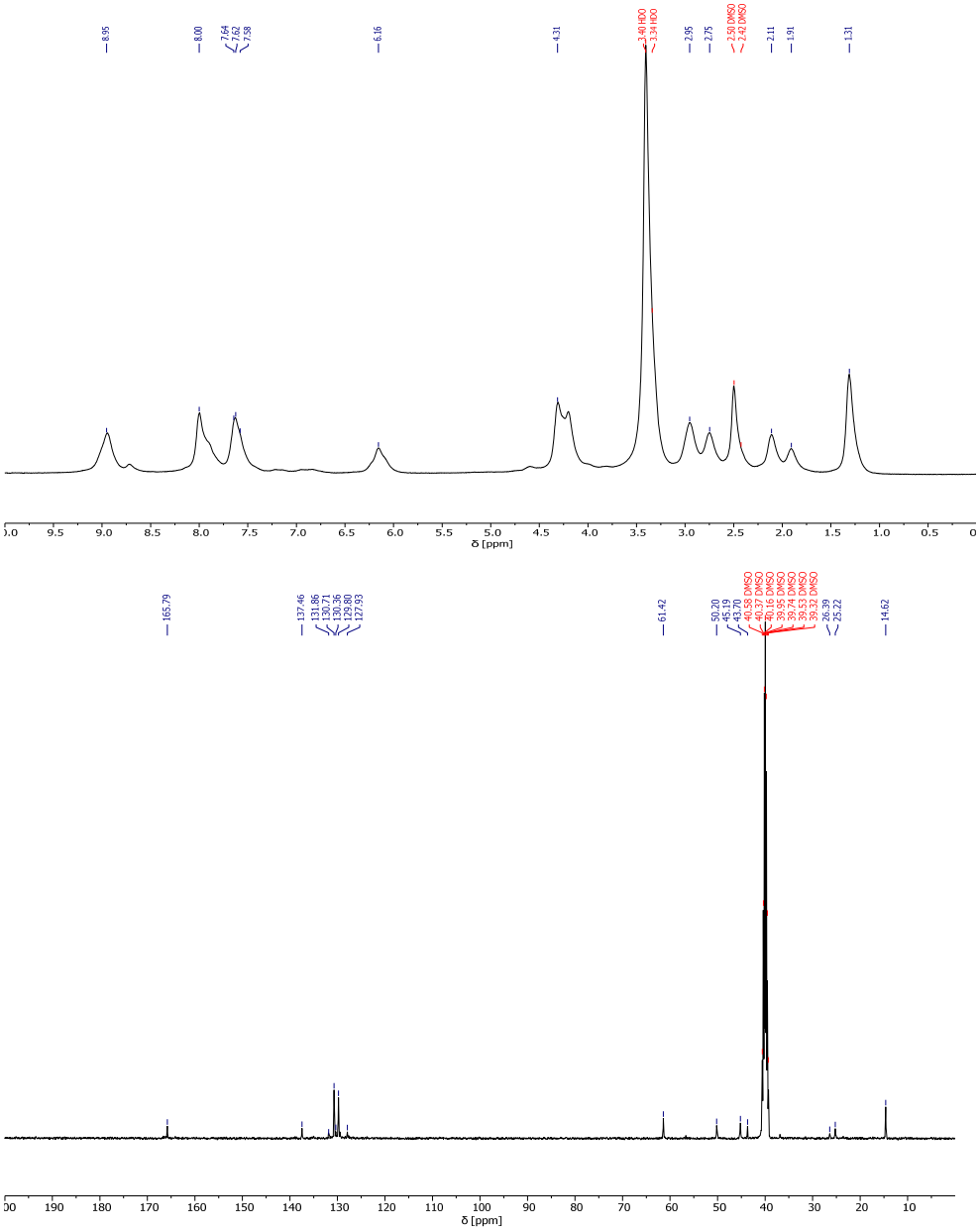


Figure S15. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of **3** (400 and 100 MHz, respectively, DMSO-d_6).

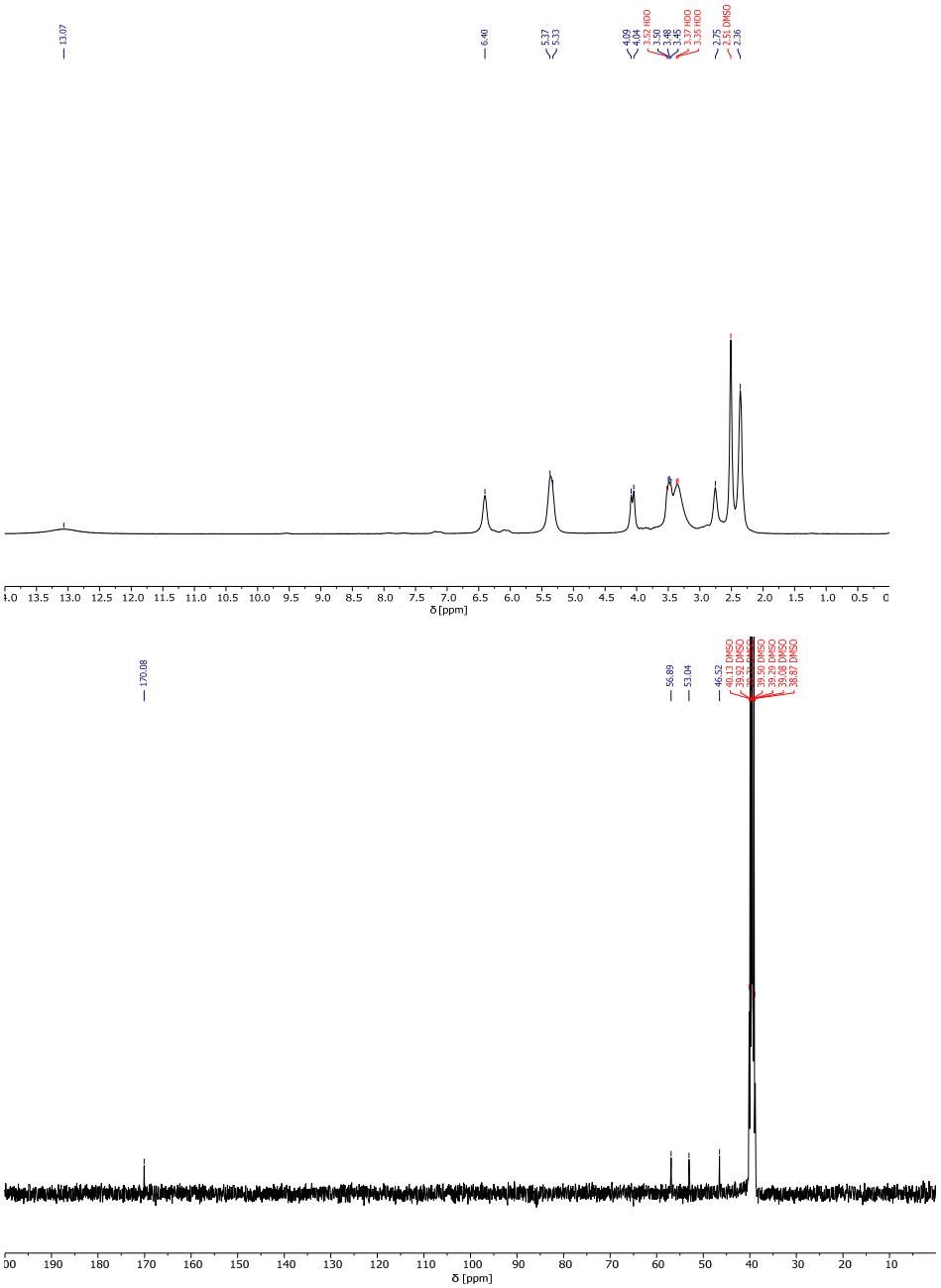


Figure S16. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of **4** (400 and 100 MHz, respectively, DMSO-d_6).

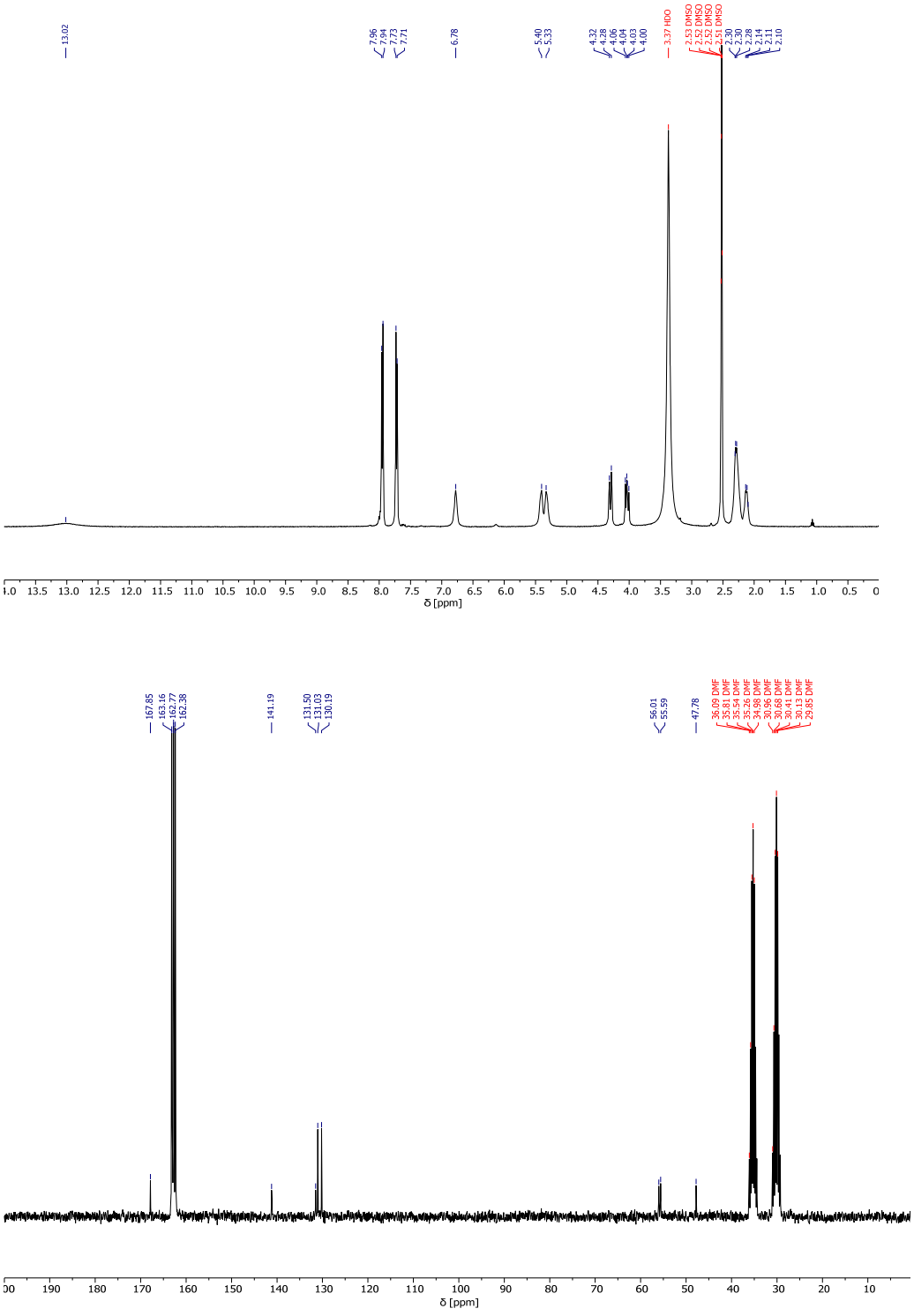


Figure S17. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of **5** (400 and 75 MHz, DMSO-d_6 and DMF-d_7, respectively).

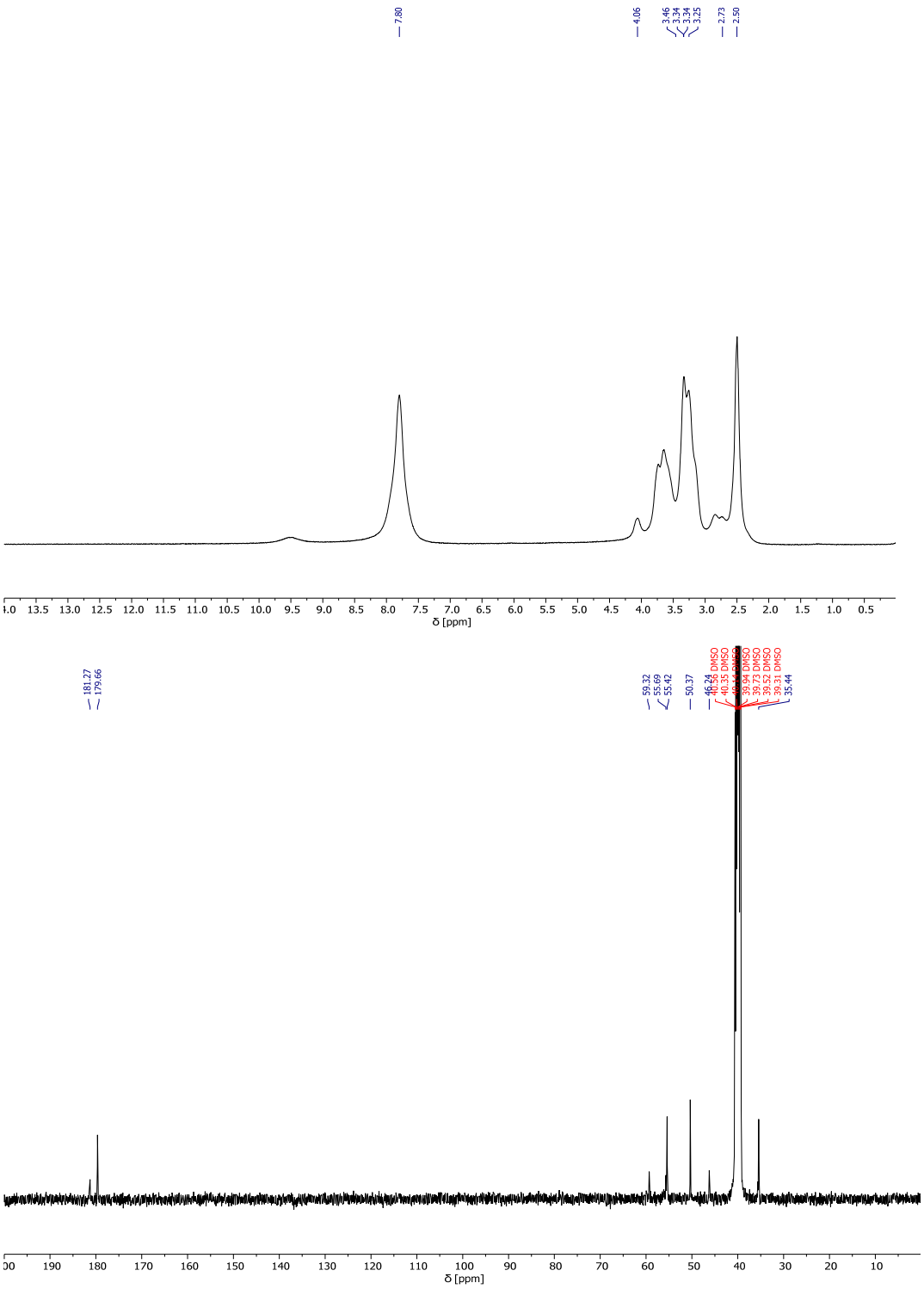


Figure S18. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of **6** (400 and 100 MHz, respectively, DMSO-d_6).

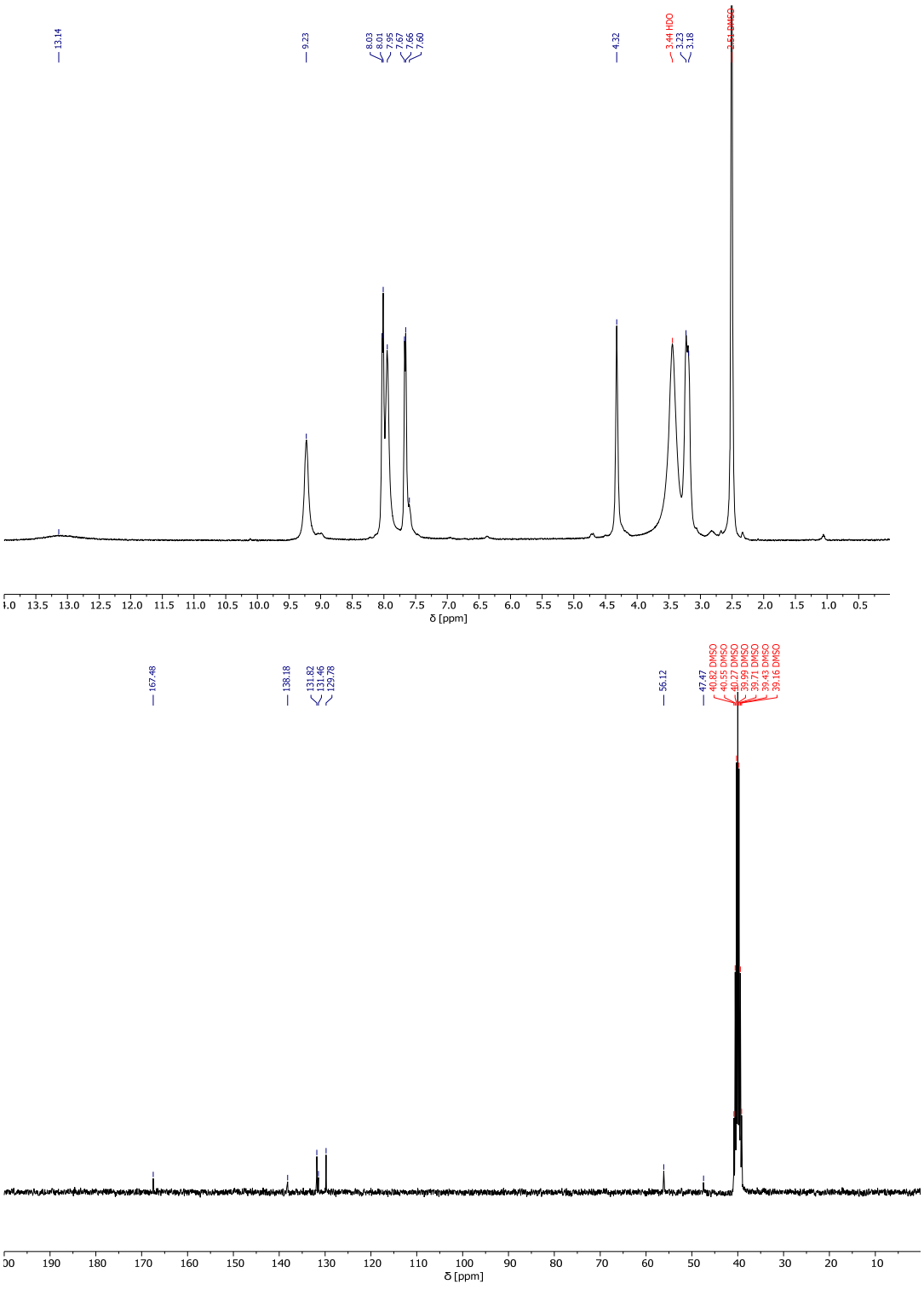


Figure S19. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of **7** (400 and 100 MHz, respectively, DMSO-d_6).