Electronic Supplementary Material (ESI) for Inorganic Chemistry Frontiers.

Supporting Information for

A new class of platinum(II) complexes with phosphine ligand pta which show potent anticancer activity

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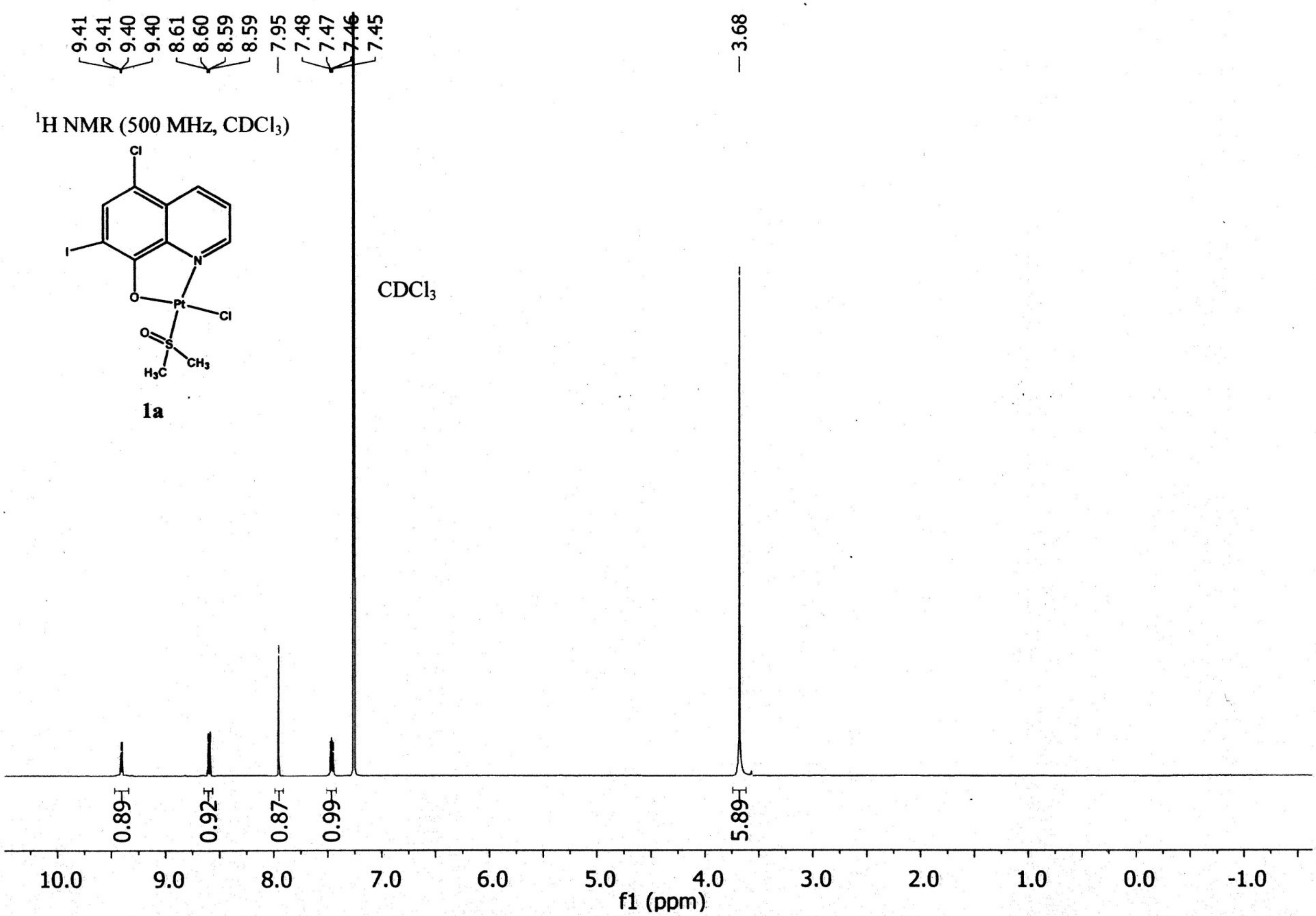
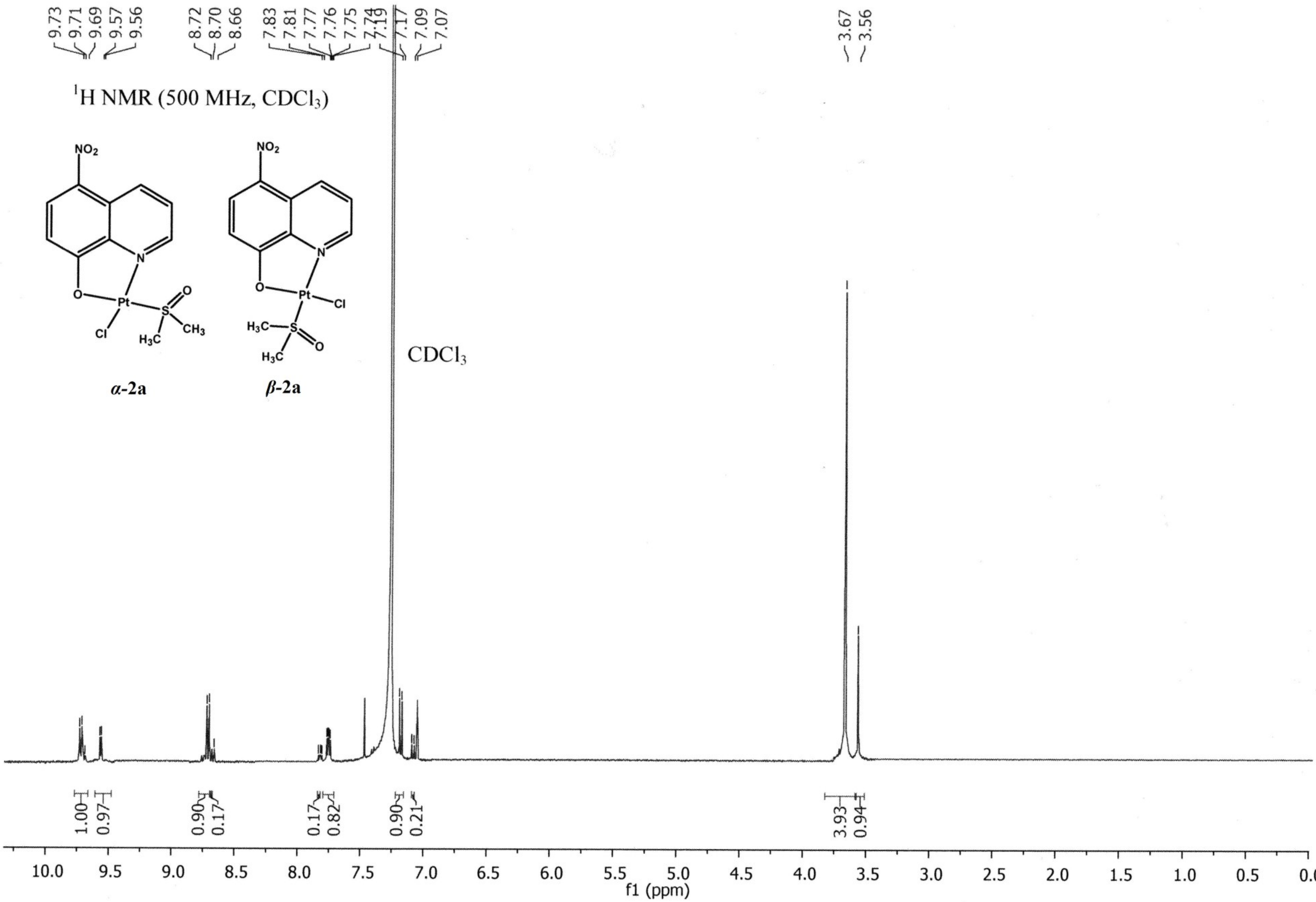
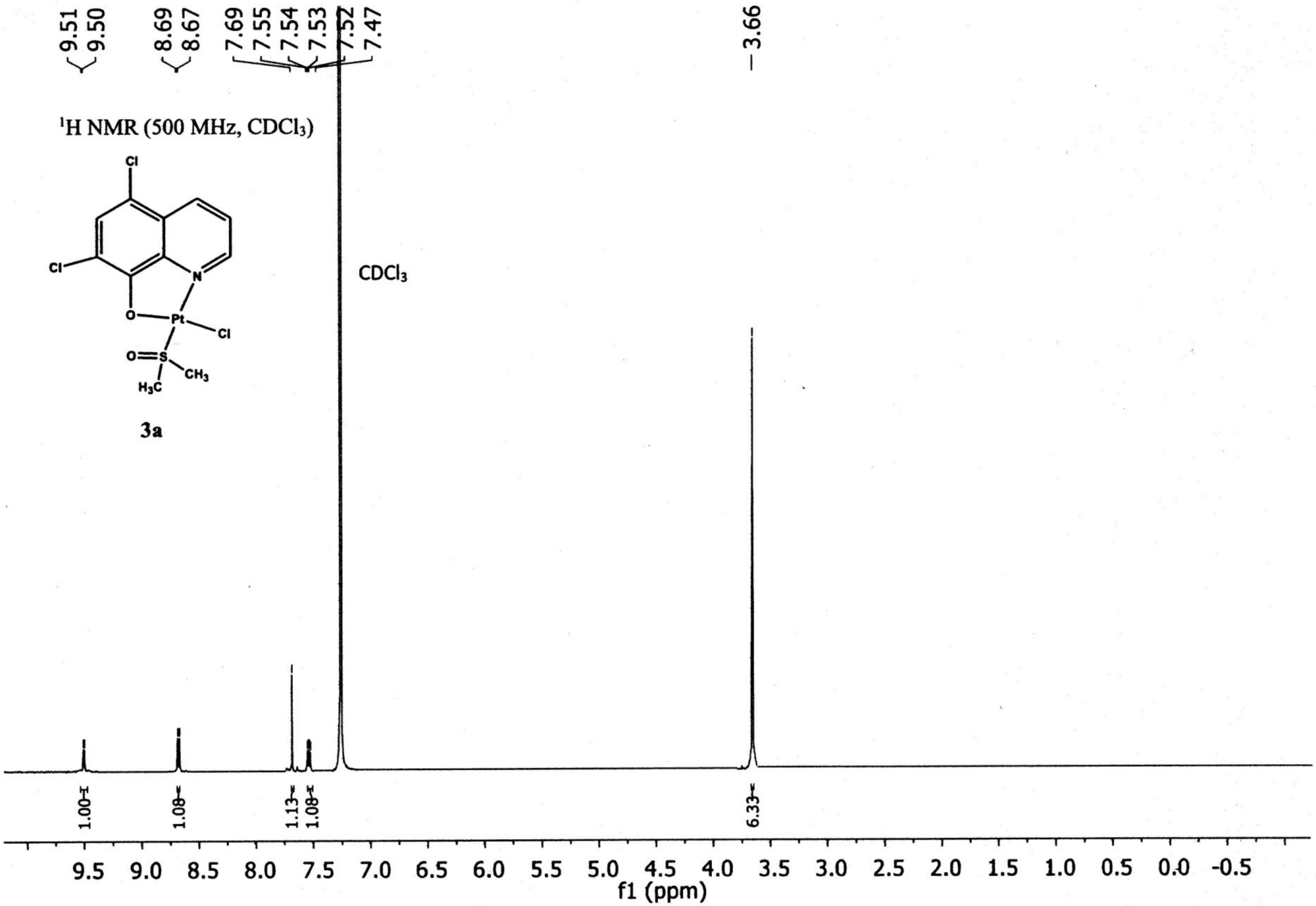
Contents:



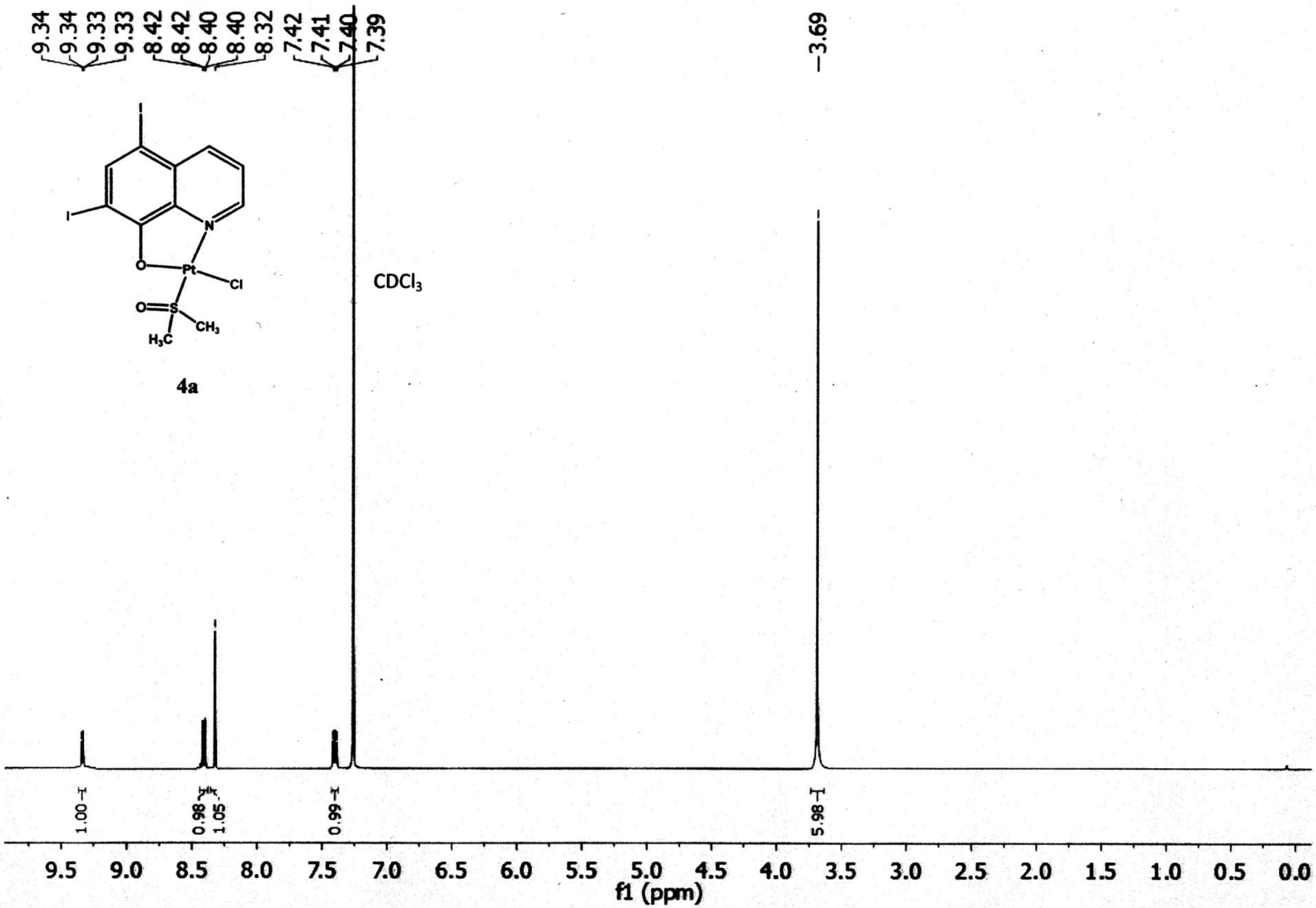
9.41
9.41
9.40
9.40
8.61
8.60
8.59
8.59
7.95
7.48
7.47
7.46
7.45
3.68
¹H NMR (500 MHz, CDCl3)
Cl
I
N
O
Pt
Cl
O
S
CH3
H3C
1a
CDCl3
0.89
0.92
0.87
0.99
5.89
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)

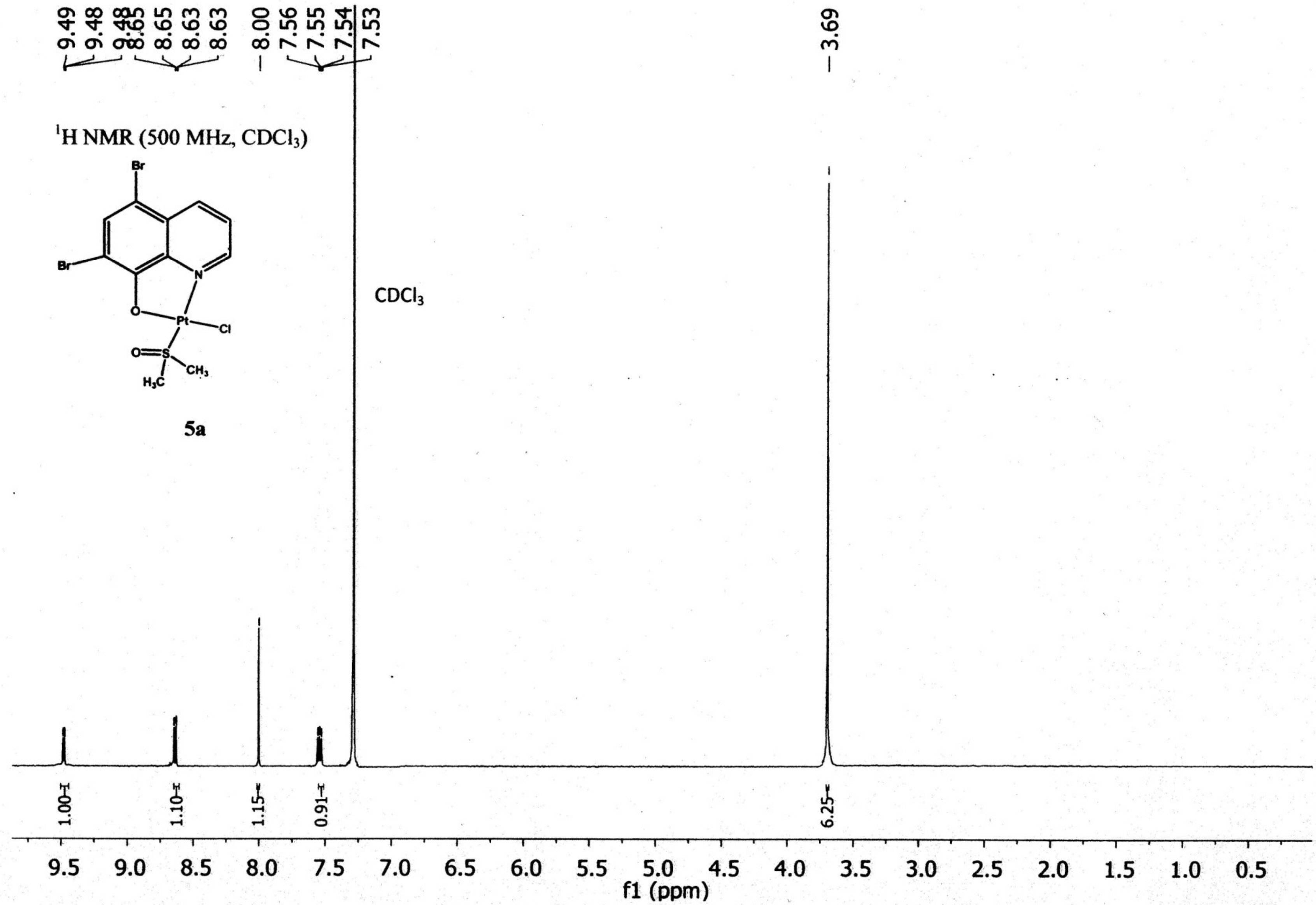


9.73
9.71
9.69
9.57
9.56
8.72
8.70
8.66
7.83
7.81
7.77
7.76
7.75
7.74
7.19
7.17
7.09
7.07
3.67
3.56
¹H NMR (500 MHz, CDCl3)
NO2
N
O
Pt
Cl
S
O
H3C
CH3
α-2a
β-2a
CDCl3
1.00
0.97
0.90
0.17
0.17
0.82
0.90
0.21
3.93
0.94
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



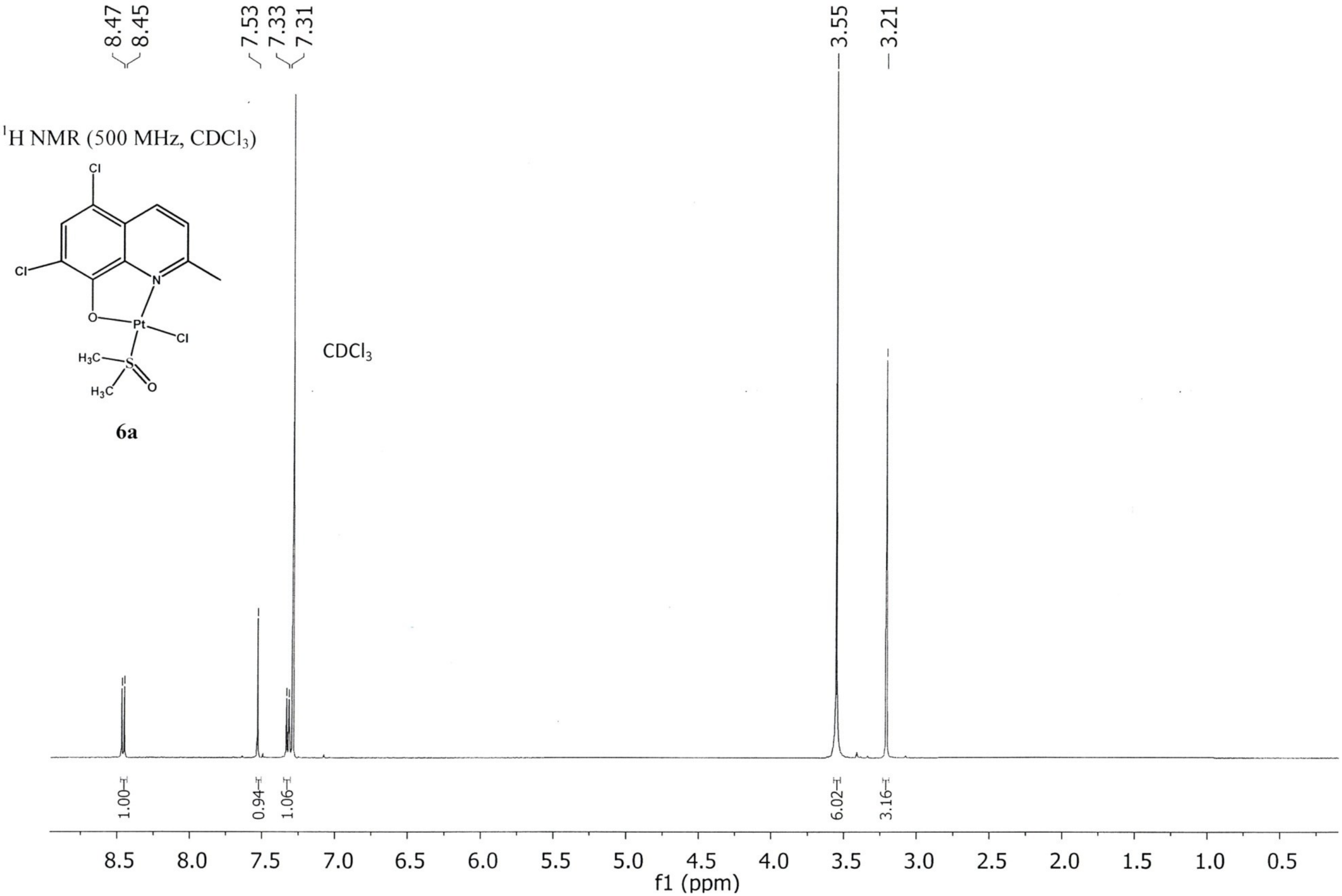
9.51
9.50
8.69
8.67
7.69
7.55
7.54
7.53
7.52
7.47
3.66
¹H NMR (500 MHz, CDCl₃)
Cl
Cl
N
O
Pt
Cl
O
S
CH₃
H₃C
3a
CDCl₃
1.00
1.08
1.13
1.08
6.33
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


9.34
9.34
9.33
9.33
8.42
8.42
8.40
8.40
8.32
7.42
7.41
7.40
7.39
3.69
CDCl3
4a
1.00
0.98
1.05
0.99
5.98
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
f1 (ppm)



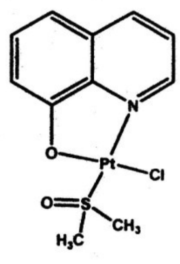
9.49 9.48 9.48 8.65 8.65 8.63 8.63
8.00
7.56 7.55 7.54 7.53
3.69
^{1}H NMR (500 MHz, $CDCl_3$)
Br
Br
N
O
Pt
Cl
O=S
CH_3
H_3C
5a
$CDCl_3$
1.00
1.10
1.15
0.91
6.25
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

^{1}H NMR (500 MHz, $CDCl_3$)

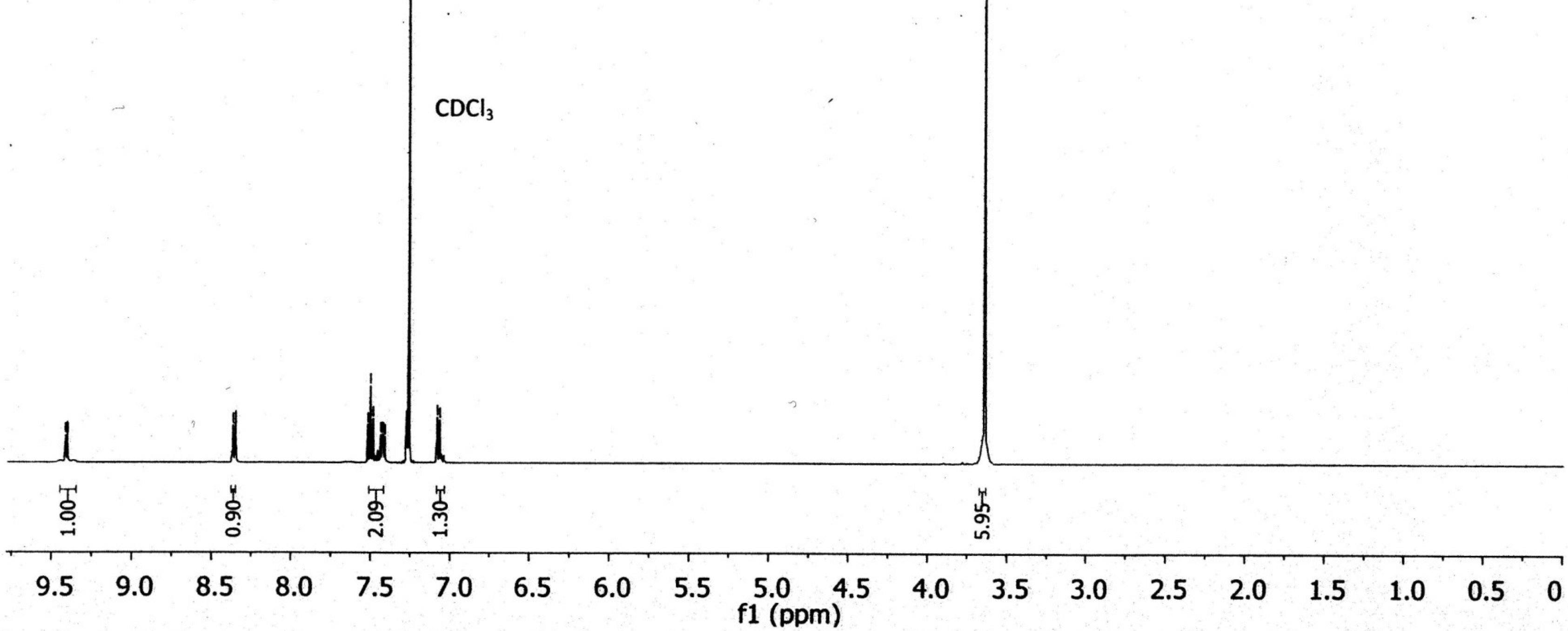


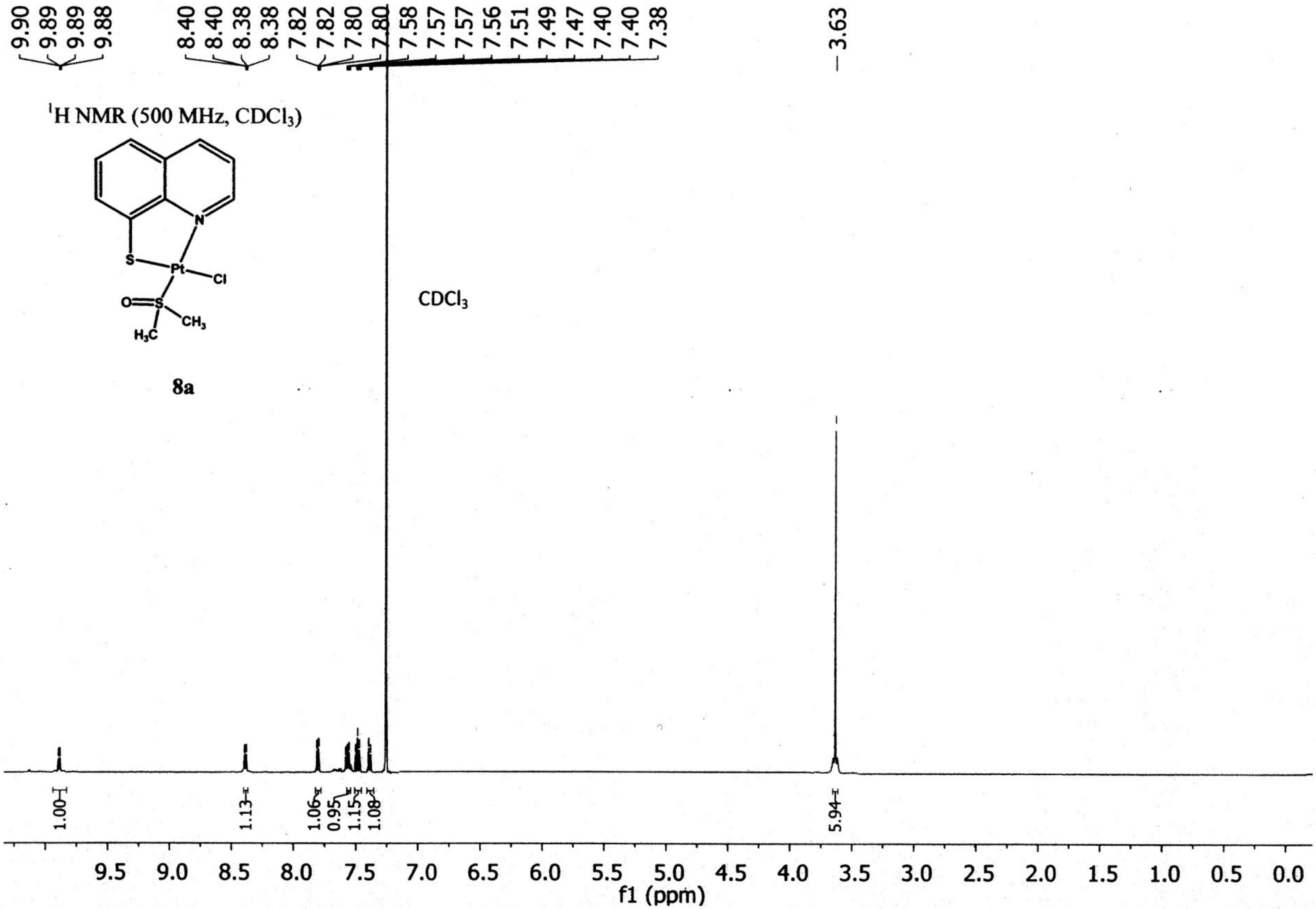
6a

[1]H NMR (500 MHz, $CDCl_3$)

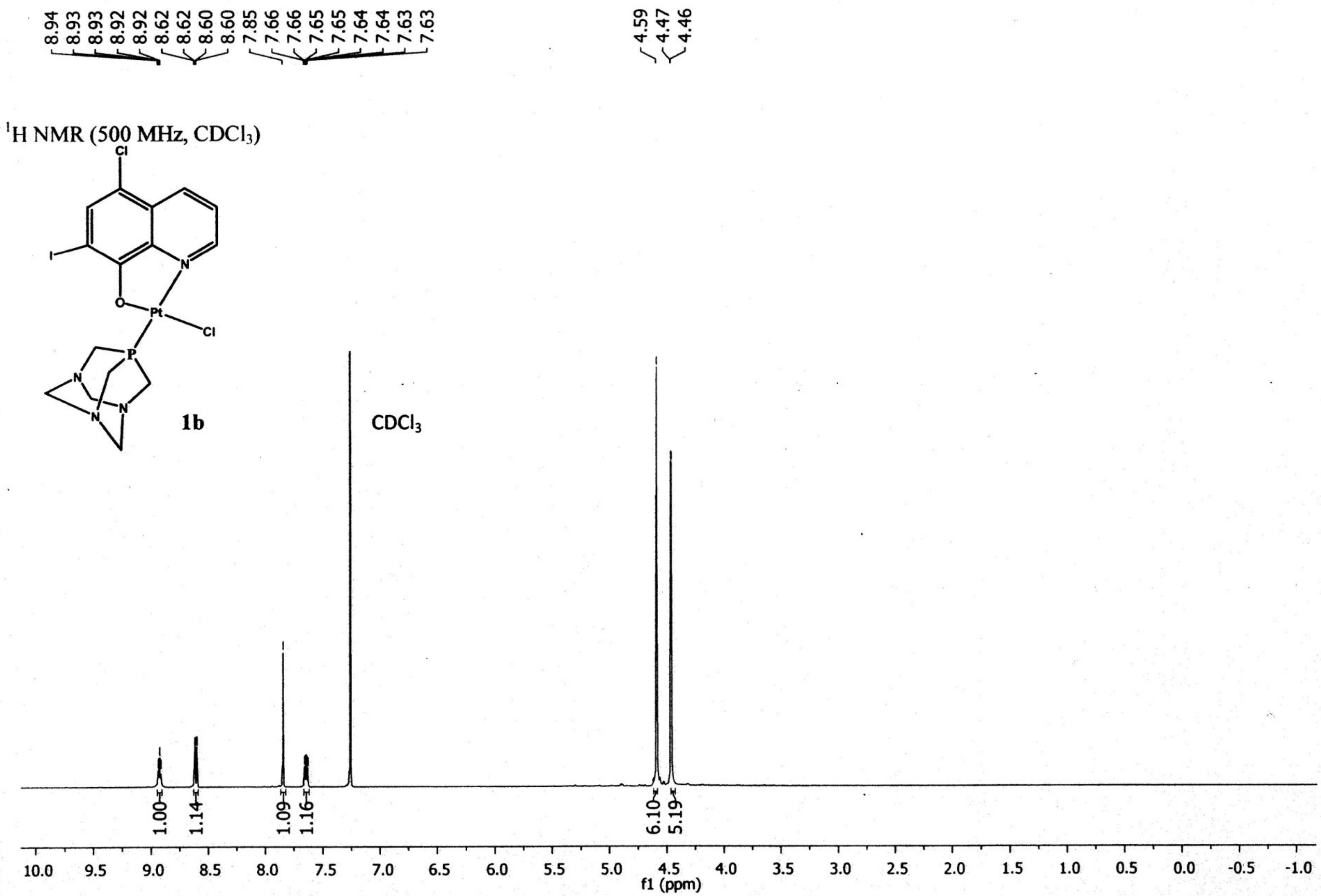


7a

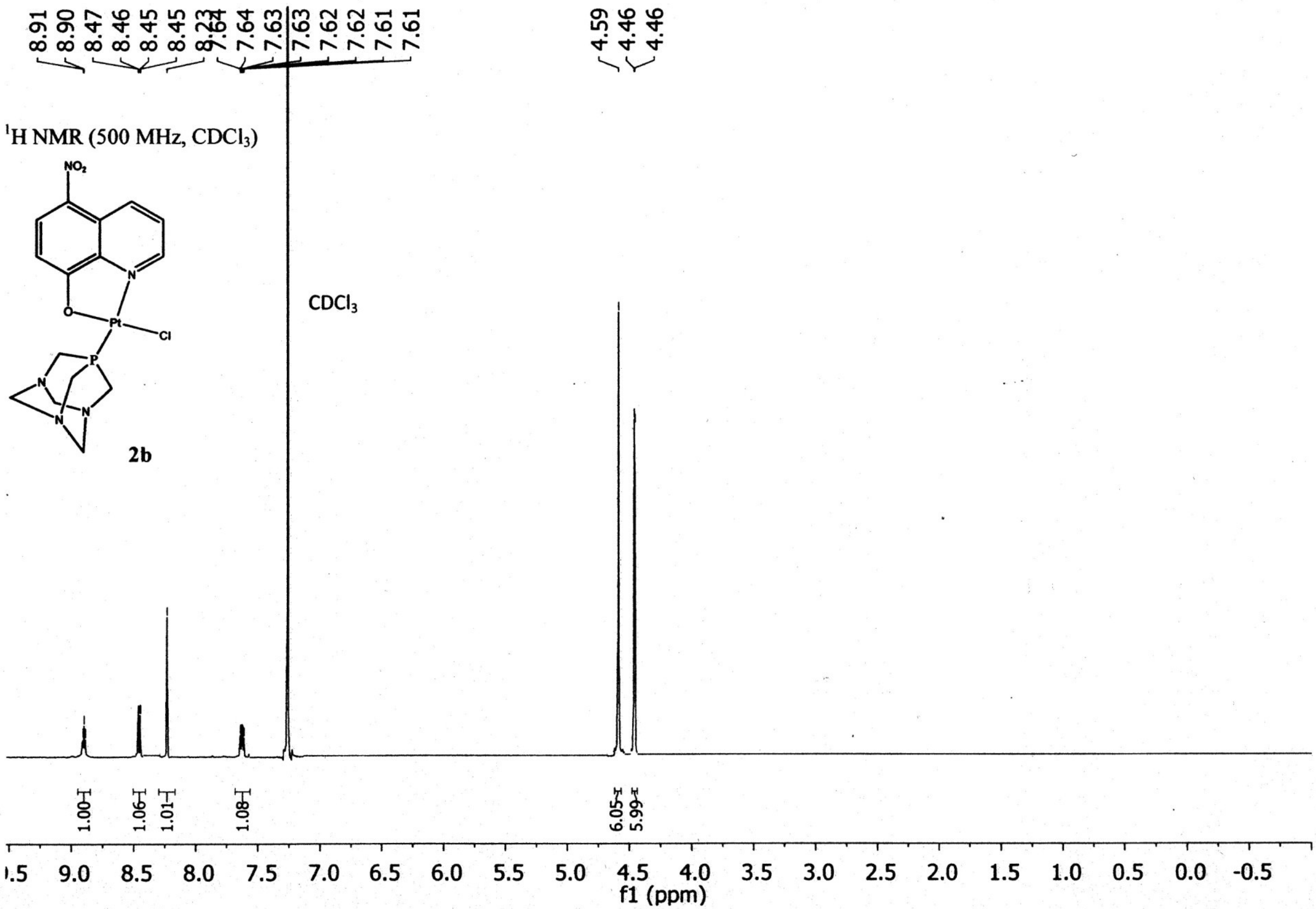




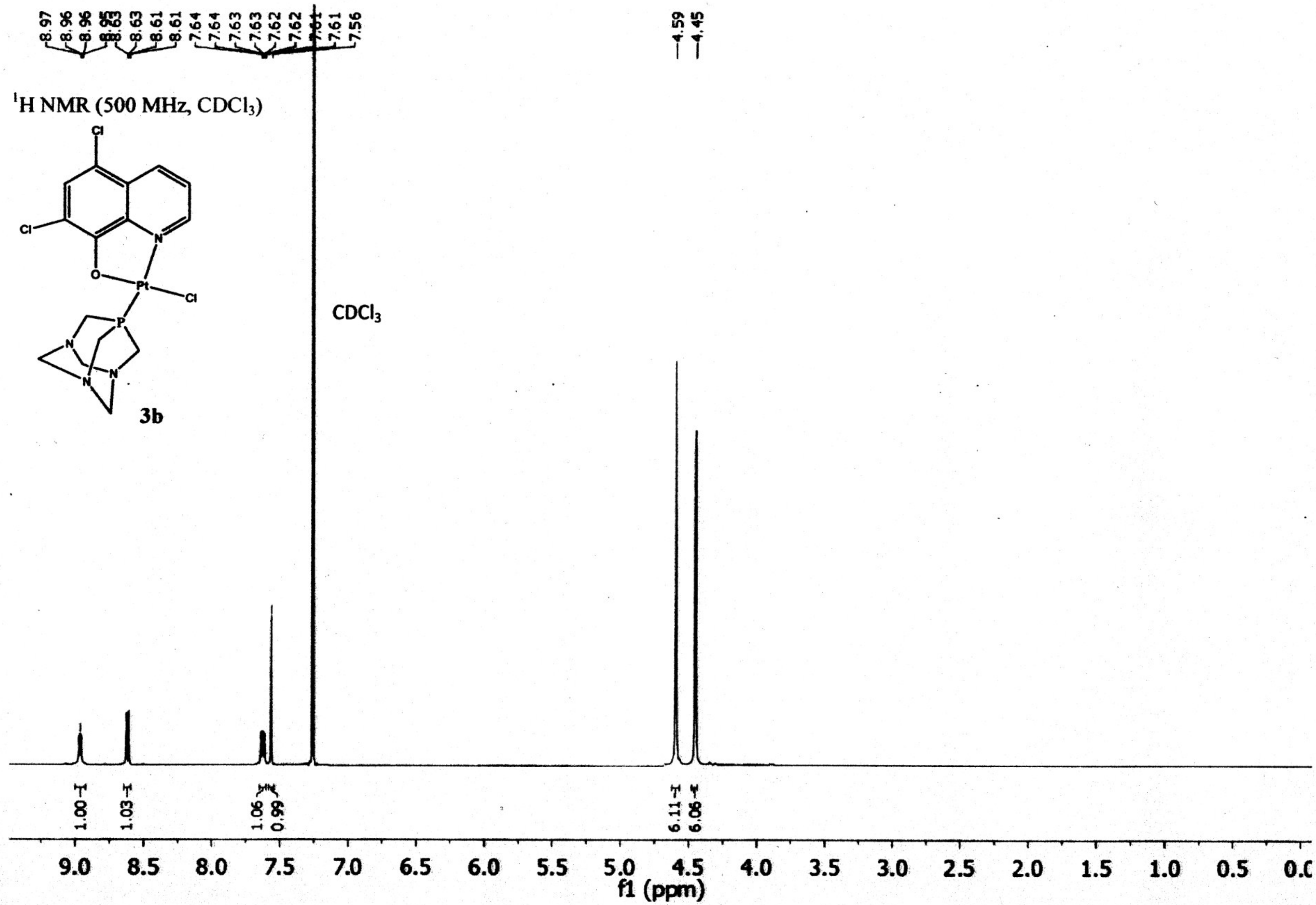
9.90 9.89 9.89 9.88
8.40 8.40 8.38 8.38
7.82 7.82 7.80 7.80 7.58 7.57 7.57 7.56 7.51 7.49 7.47 7.40 7.40 7.38
3.63
¹H NMR (500 MHz, CDCl₃)
8a
CDCl₃
1.00 1.13 1.06 0.95 1.15 1.08 5.94
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



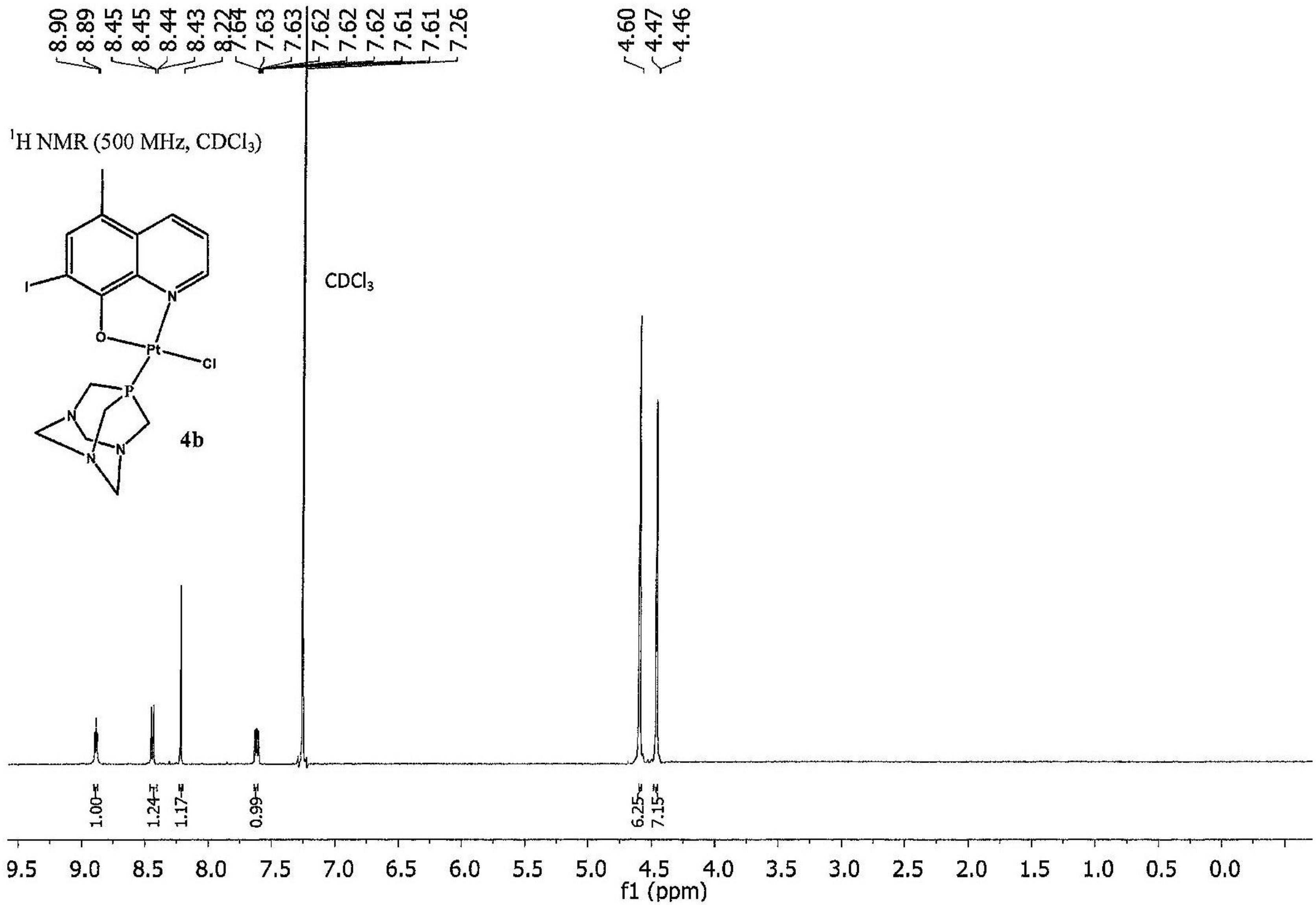
1H NMR (500 MHz, CDCl3)
8.94
8.93
8.93
8.92
8.92
8.62
8.62
8.60
8.60
7.85
7.66
7.66
7.65
7.65
7.64
7.64
7.63
7.63
4.59
4.47
4.46
Cl
I
N
O
Pt
Cl
P
N
N
N
1b
CDCl3
1.00
1.14
1.09
1.16
6.10
5.19
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

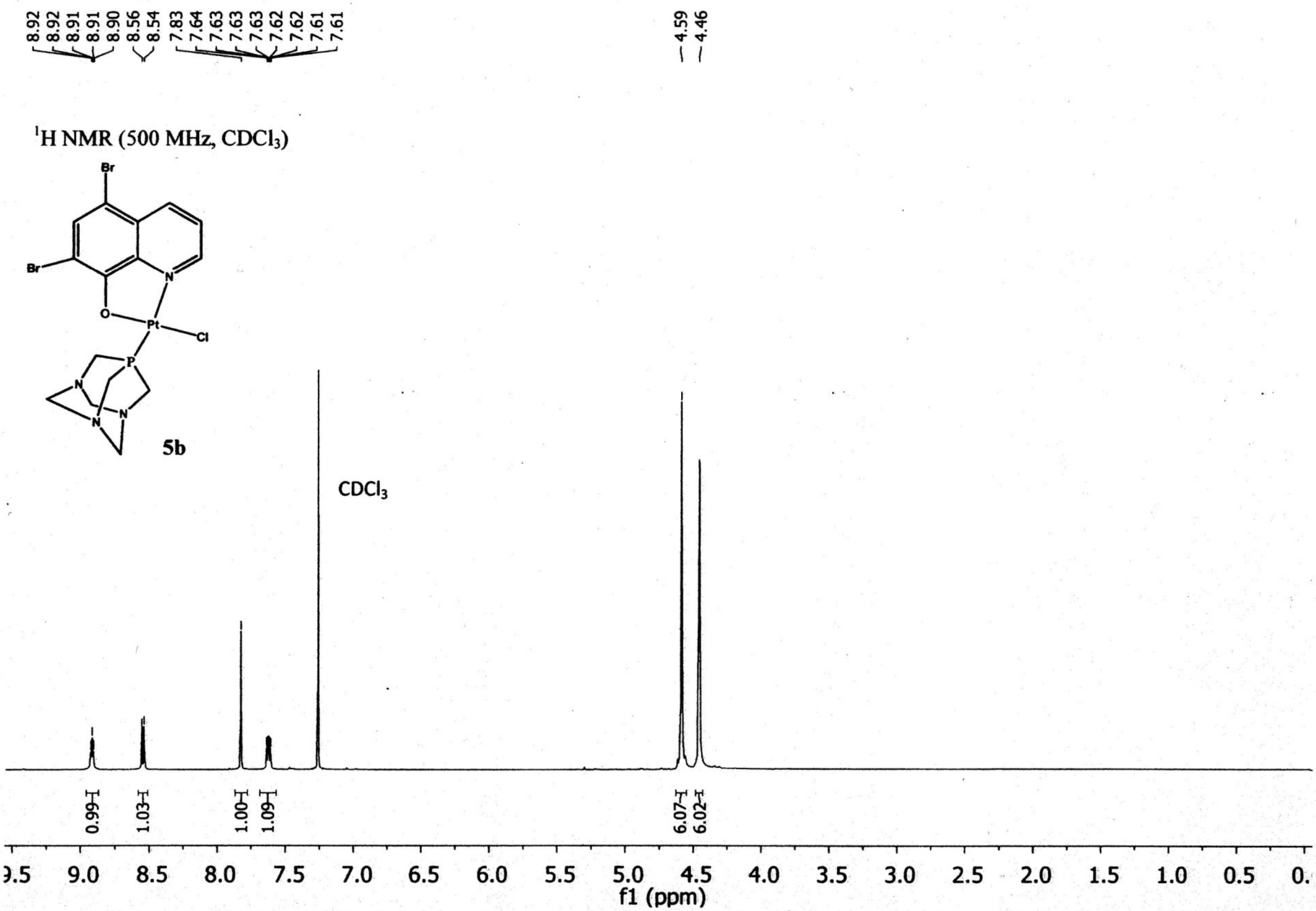


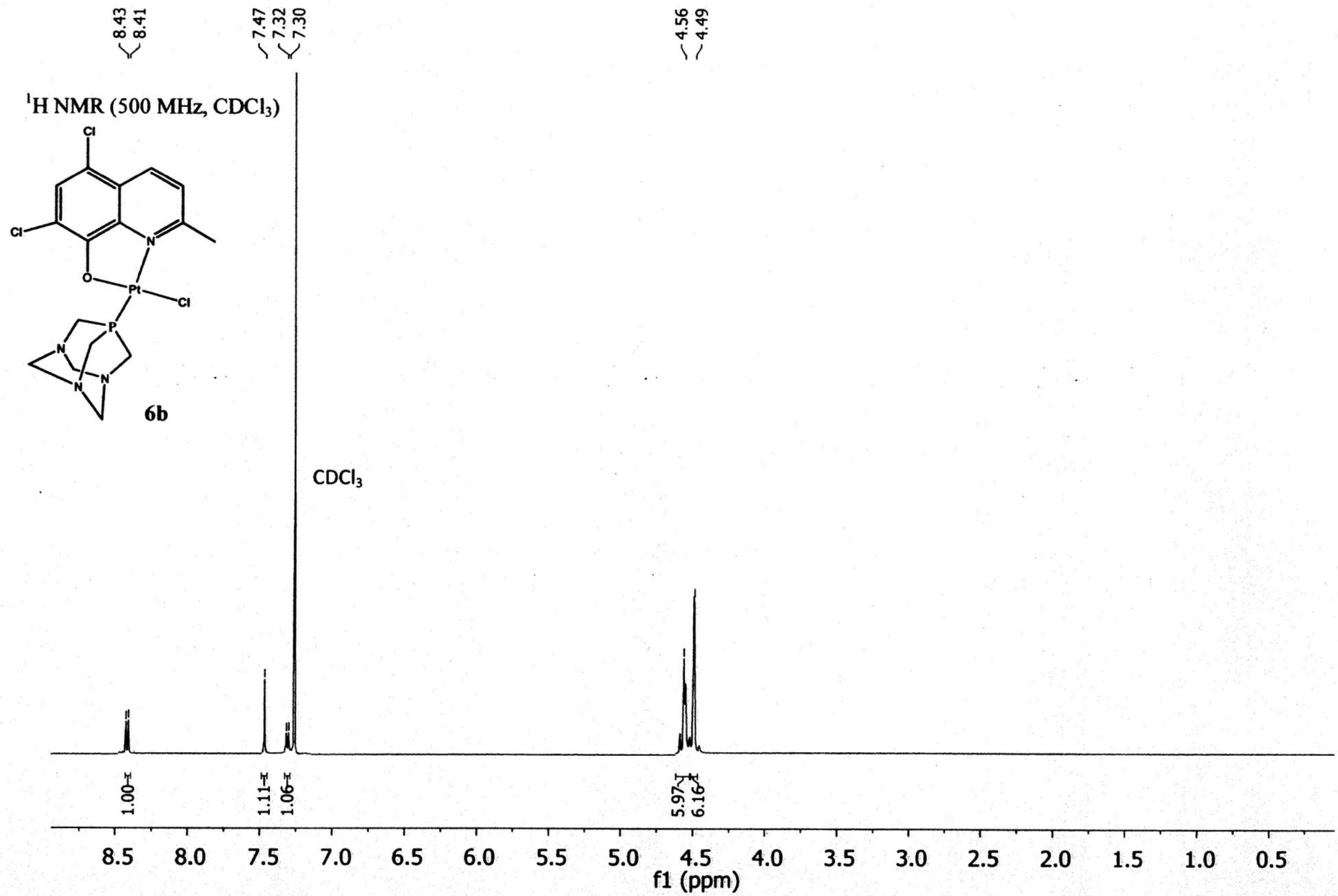
8.91
8.90
8.47
8.46
8.45
8.45
8.23
7.64
7.64
7.63
7.63
7.62
7.62
7.61
7.61
4.59
4.46
4.46
¹H NMR (500 MHz, CDCl₃)
NO₂
N
O
Pt
Cl
P
N
N
N
2b
CDCl₃
1.00
1.06
1.01
1.08
6.05
5.99
.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



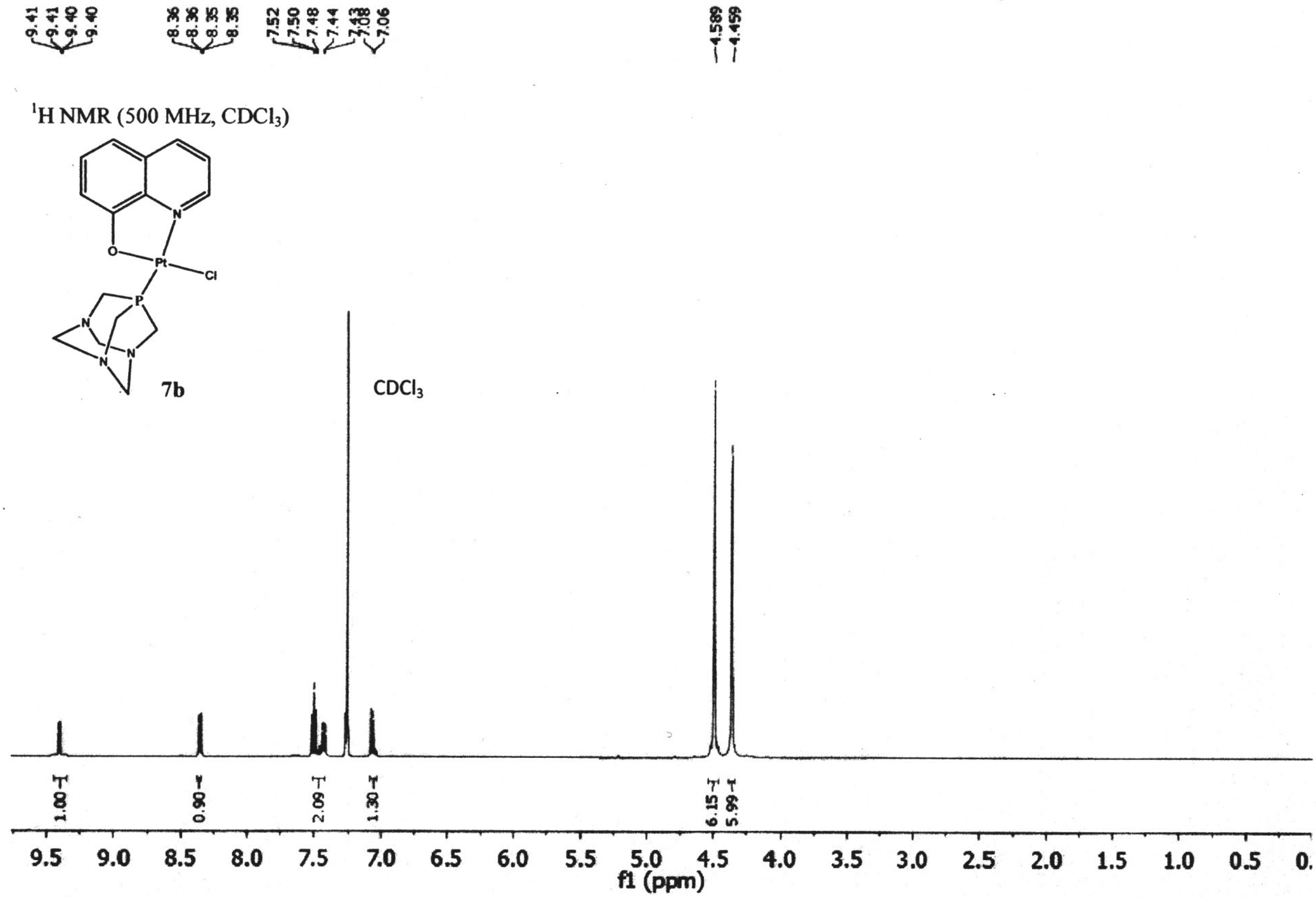
8.97
8.96
8.96
8.95
8.63
8.63
8.61
8.61
7.64
7.64
7.63
7.63
7.62
7.62
7.61
7.61
7.56
4.59
4.45
^{1}H NMR (500 MHz, $CDCl_3$)
Cl
Cl
N
O
Pt
Cl
P
N
N
N
3b
$CDCl_3$
1.00
1.03
1.06
0.99
6.11
6.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

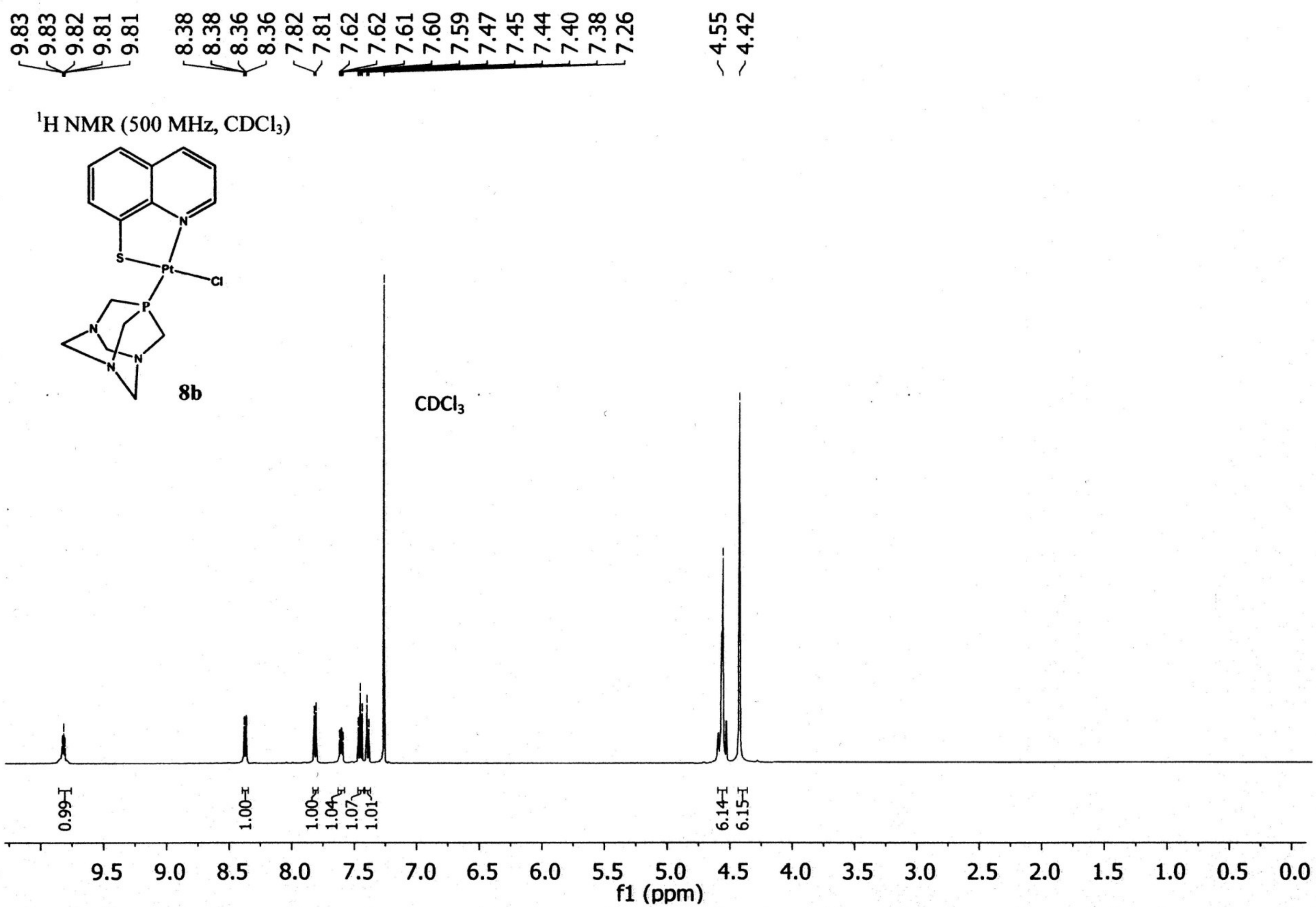

8.90
8.89
8.45
8.45
8.44
8.43
8.22
7.64
7.63
7.63
7.62
7.62
7.62
7.61
7.61
7.26
4.60
4.47
4.46
1H NMR (500 MHz, CDCl3)
CDCl3
I
O
N
Pt
Cl
P
N
N
N
4b
1.00
1.24
1.17
0.99
6.25
7.15
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


8.92
8.92
8.91
8.91
8.90
8.56
8.54
7.83
7.64
7.63
7.63
7.63
7.62
7.62
7.61
7.61
4.59
4.46
^1H NMR (500 MHz, $CDCl_3$)
Br
Br
N
O
Pt
Cl
P
N
N
N
5b
$CDCl_3$
0.99
1.03
1.00
1.09
6.07
6.02
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.
f1 (ppm)



8.43
8.41
7.47
7.32
7.30
4.56
4.49
^1H NMR (500 MHz, $CDCl_3$)
Cl
Cl
N
O
Pt
Cl
P
N
N
N
6b
$CDCl_3$
1.00
1.11
1.06
5.97
6.16
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
f1 (ppm)


9.41
9.41
9.40
9.40
8.36
8.36
8.35
8.35
7.52
7.50
7.48
7.44
7.43
7.08
7.06
4.589
4.459
¹H NMR (500 MHz, CDCl₃)
N
O
Pt
Cl
P
N
N
N
7b
CDCl₃
1.00
0.90
2.09
1.30
6.15
5.99
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.
f1 (ppm)



9.83
9.83
9.82
9.81
9.81
8.38
8.38
8.36
8.36
7.82
7.81
7.62
7.62
7.61
7.60
7.59
7.47
7.45
7.44
7.40
7.38
7.26
4.55
4.42
1H NMR (500 MHz, CDCl3)
S
N
Pt
Cl
P
N
N
N
8b
CDCl3
0.99
1.00
1.00
1.04
1.07
1.01
6.14
6.15
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
f1 (ppm)

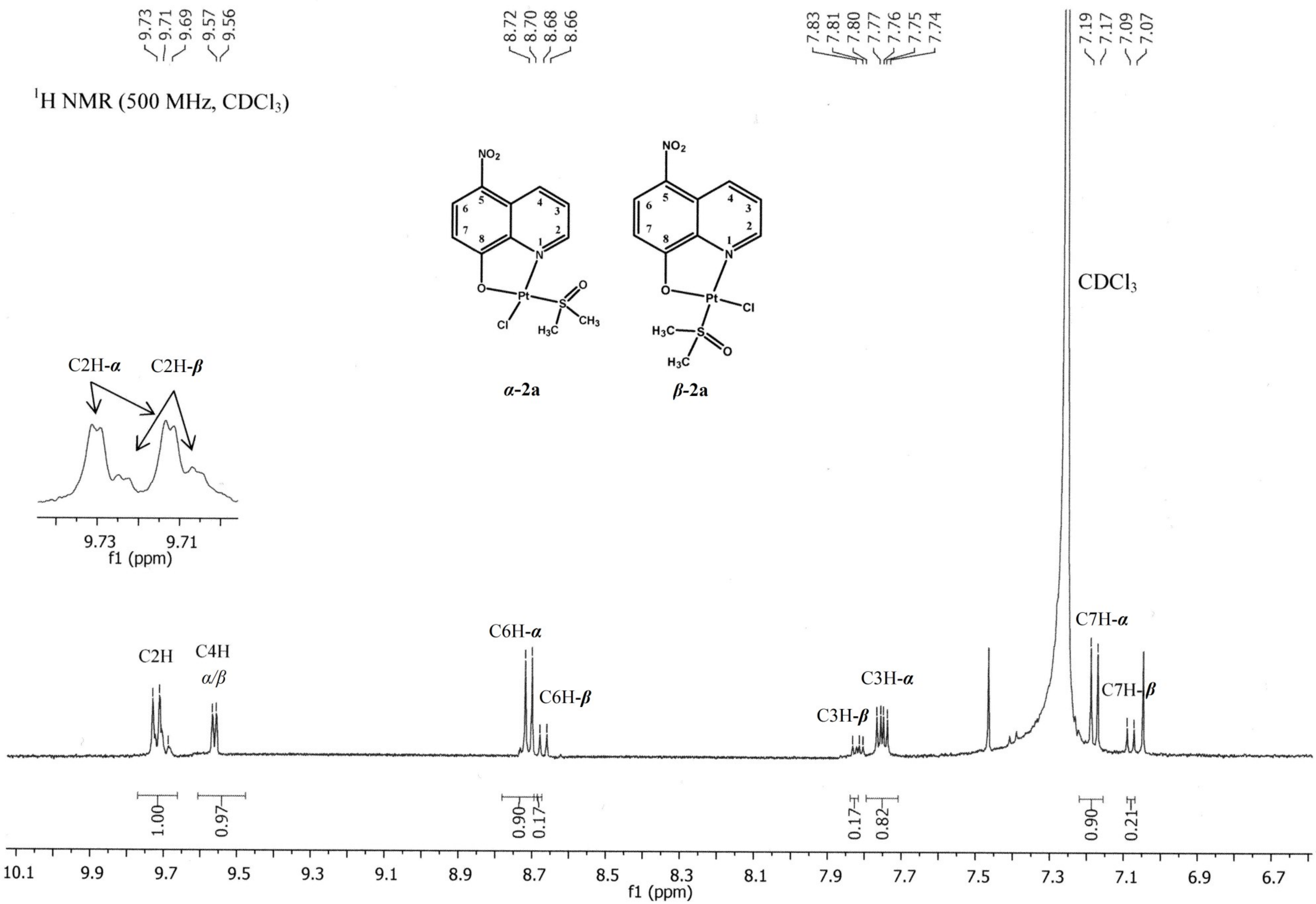


Figure S1. A mixture of ***α*** and ***β*** isomer of complex **2a** evidenced in the ^{1}H NMR spectrum.

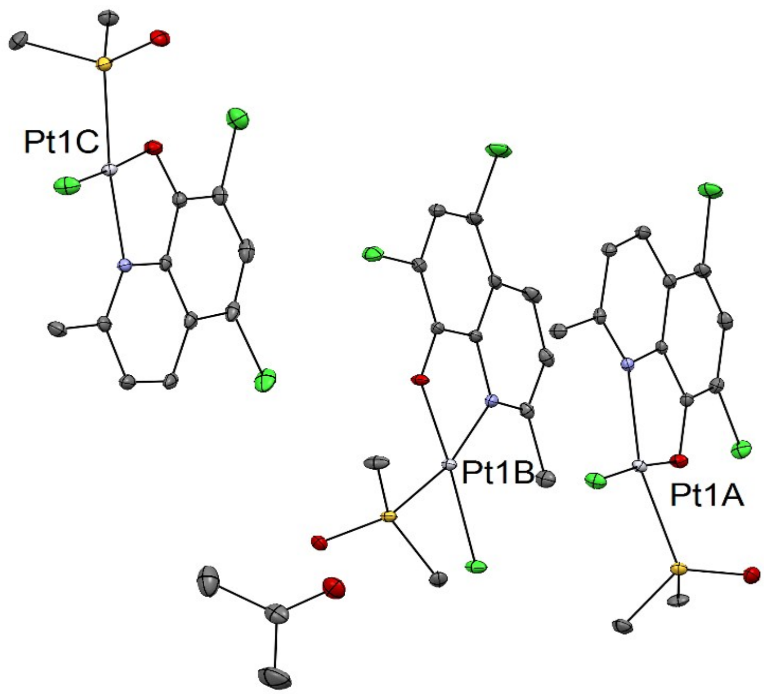
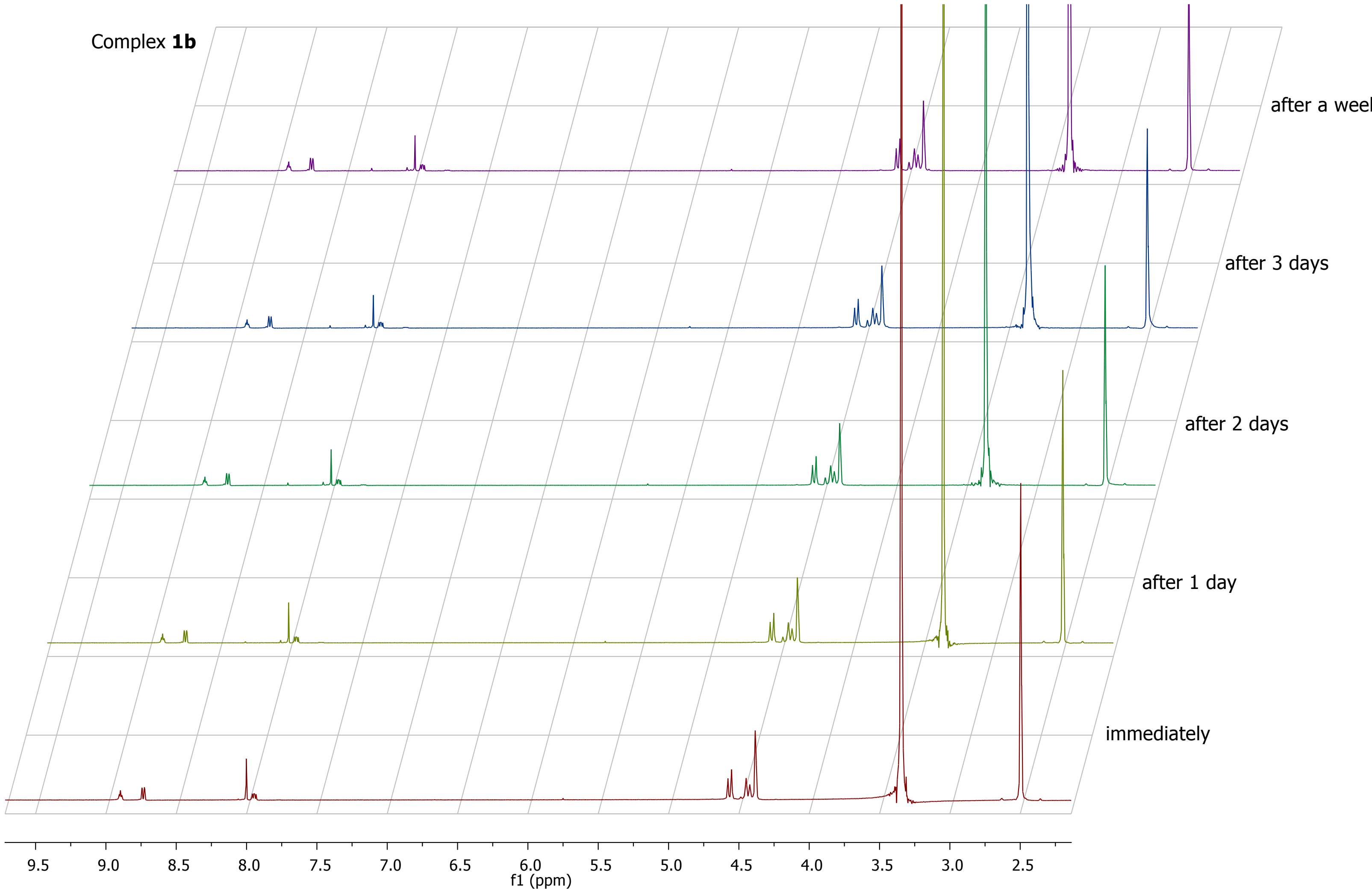


Figure S2. Three crystallographically independent molecules of complex **6a**. Thermal ellipsoids are shown at 30% probability level and hydrogen atoms are omitted for better clarity of presentation.


Complex **1b**
after a week
after 3 days
after 2 days
after 1 day
immediately
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
f1 (ppm)

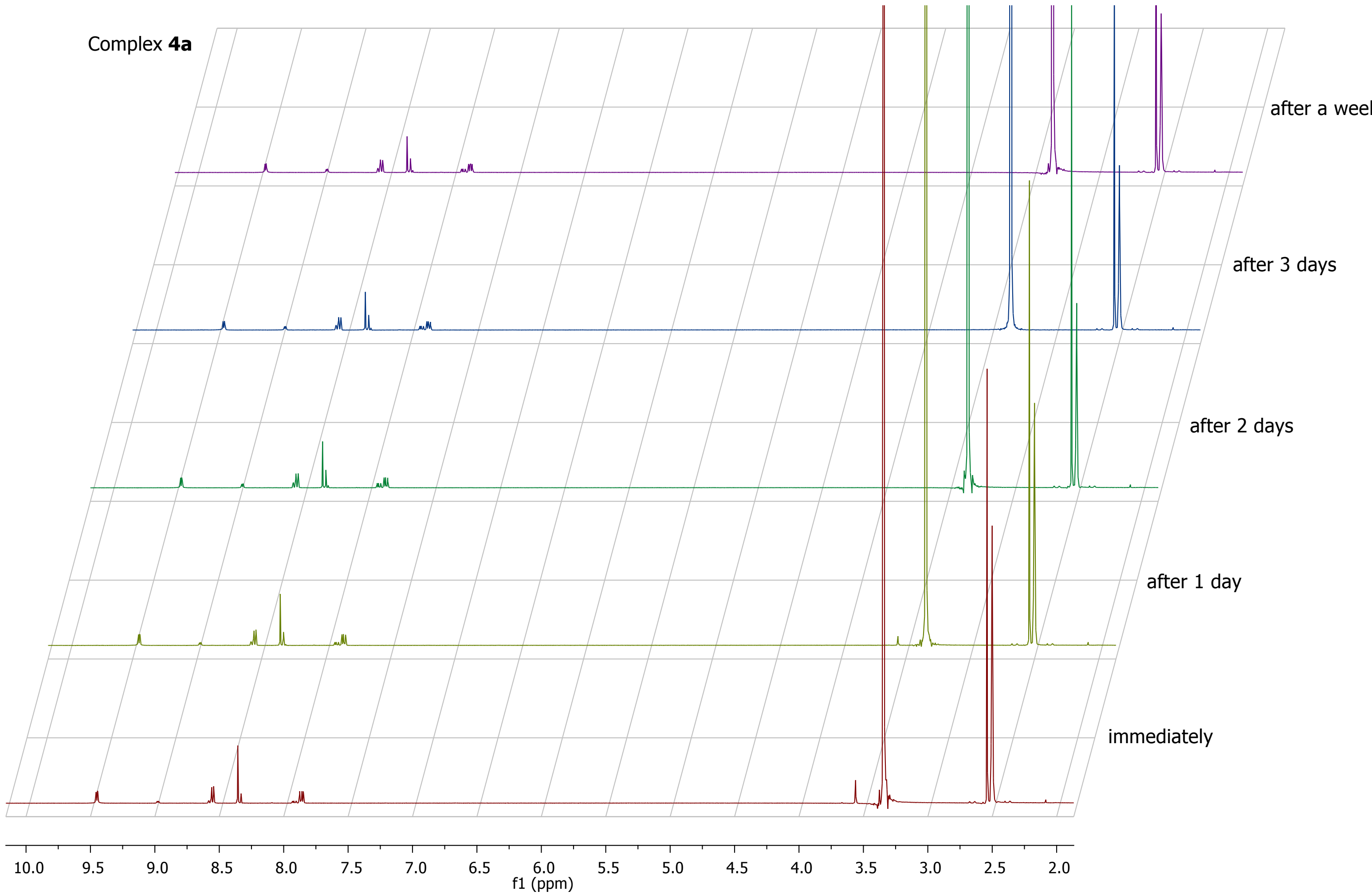


Figure S3. Stability of complexes **1b** and **4a** in dmso solution over a period of 7 days followed by ^{1}H NMR spectroscopy. Spectra were taken 1) immediately, 2) after 1 day, 3) after 2 days, 4) after 3 days and d) after a week indicating that no degradation of complexes was observed.

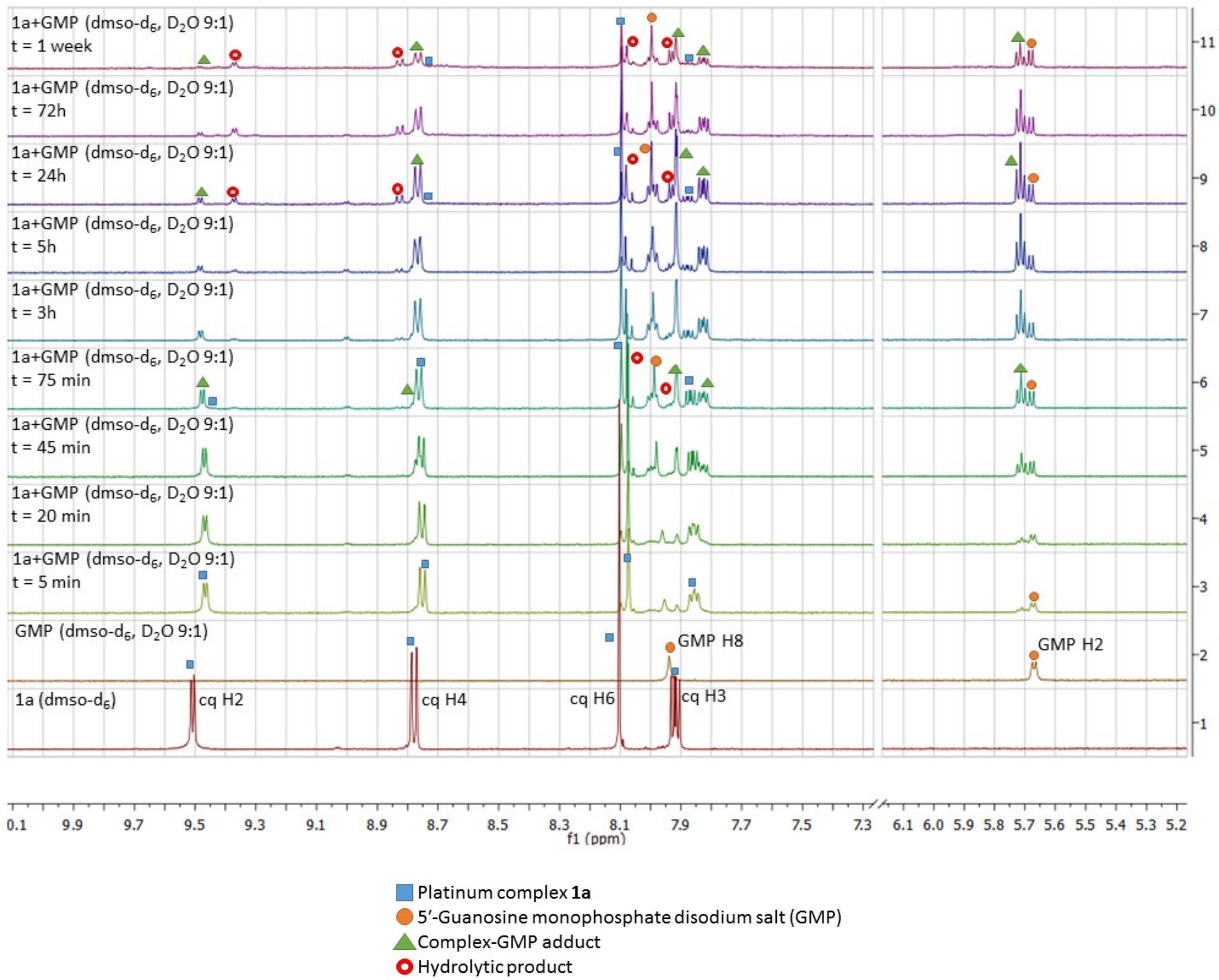


Figure S4: Reactivity of complex **1a** towards GMP in dmso-d_6/D_2O 9:1.

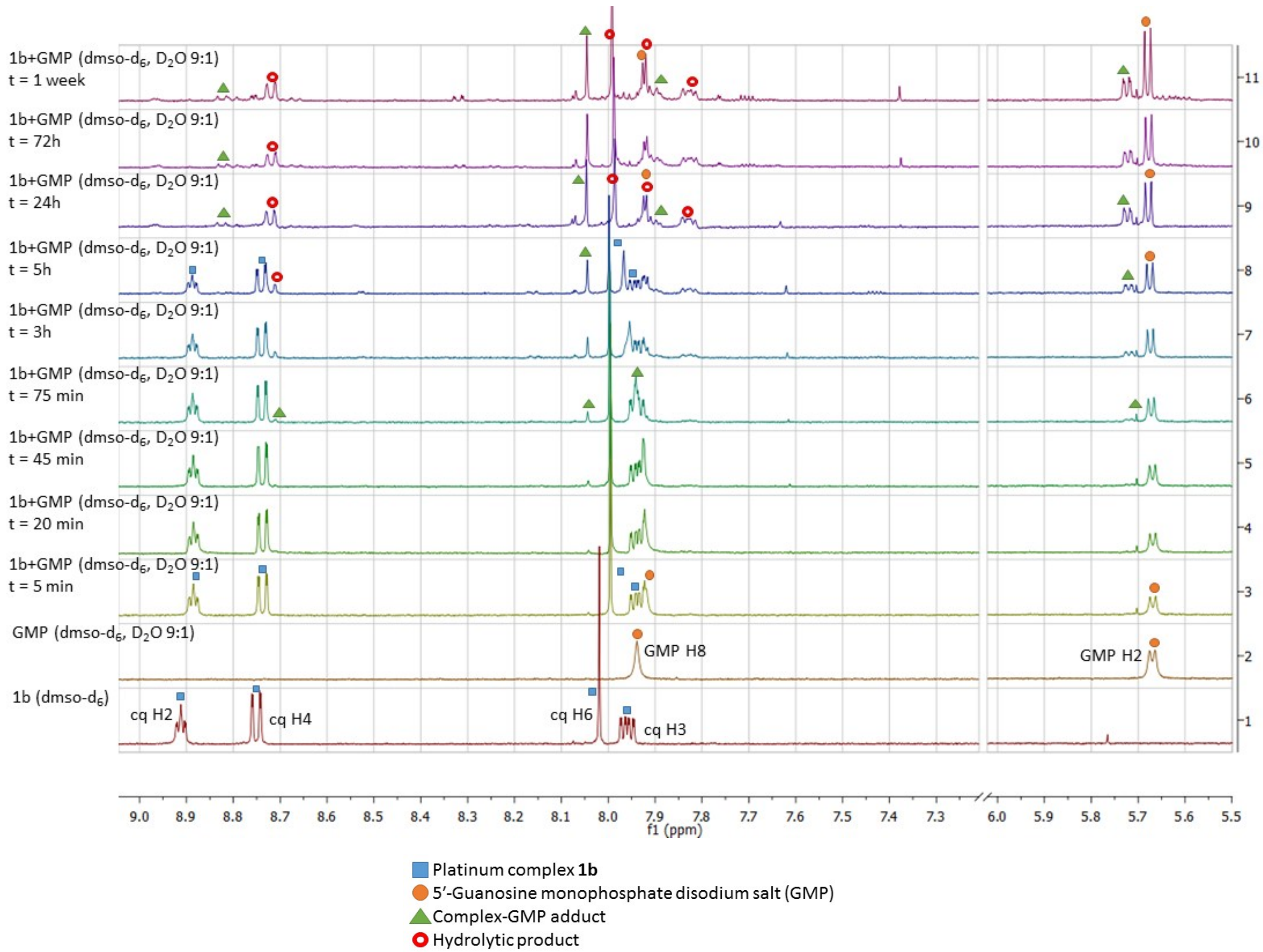


Figure S5: Reactivity of complex **1b** towards GMP in dmso-d$_6$/D$_2$O 9:1.

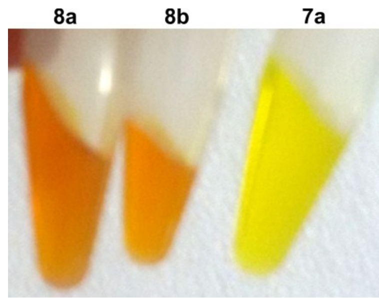


Figure S6. Visual appearance of **8a** and **8b** in comparison to **7a** showing bright orange color of these two complexes in comparison to yellow or pale yellow of all other complexes.

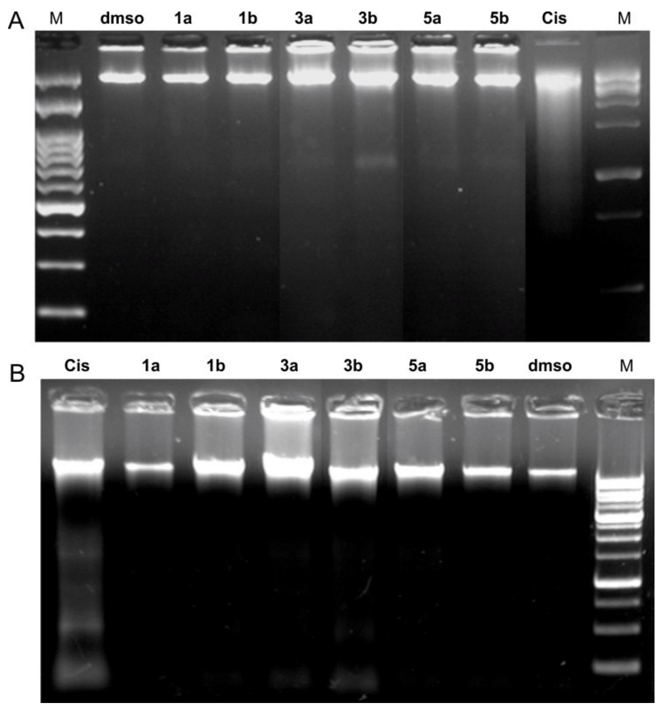


Figure S7. Cellular DNA degradation in **A)** carcinoma A549 cells and **B)** zebrafish embryos, induced by complexes **1a, 1b, 3a, 3b, 5a and 5b** in comparison to cisplatin (**Cis**) and dmso treated cells. DNA molecular weight marker in lane M (1 kb ladder, Nippon Genetics).

Table S1: Compound nomenclature according to IUPAC recommendations.*

Cpd	*Isomer*	IUPAC	**Cpd**	*Isomer*	IUPAC
1a-7a	*α*	SP-4-4	**1b-7b**	*α*	SP-4-4
	β	SP-4-3		*β*	SP-4-3
8a	*α*	SP-4-3	**8b**	*α*	SP-4-4
	β	SP-4-4		*β*	SP-4-2

* In *Nomenclature of Inorganic Chemistry*, IUPAC Recommendations, ed. N. G. Connelly, T. Damhus, R. M. Hartshorn, A. T. Hutton, Royal Society of Chemistry, Cambridge, 2005, IR-9.3, 180.

Table S2. Crystallographic data for compounds *β*-**1b**, *α*-**2a**, and *β*-**2a**.

Compound	*β*-**1b**	*α*-**2a**$\cdot CH_2Cl_2$*	*β*-**2a***
Empirical formula	$C_{15}H_{16}Cl_2IN_4OPPt$	$C_{12}H_{13}Cl_3N_2O_4PtS$	$C_{11}H_{11}ClN_2O_4PtS$
M_w	692.18	582.74	497.82
T, K	150(2)	150(2)	150(2)
Crystal system	*Triclinic*	*Monoclinic*	*Monoclinic*
Space group	*P -1*	*C 2/c*	*P 2₁/m*
a, Å	5.810(5)	19.3571(7) A	9.4359(6)
b, Å	12.770(5)	6.8349(3)	6.7378(4)
c, Å	12.865(5)	25.1990(10)	10.5414(5)
α, deg.	84.543(5)	90	90
β, deg.	81.308(5)	95.245(4)	97.352(5)
γ, deg.	78.412(5)	90	90
V, $Å^3$	922.2(9)	3320.0(2)	664.68(7)
Z	2	8	2
D_{calc}, g/cm^3	2.493	2.332	2.487
μ, mm^{-1}	9.670	9.080	10.926
F(000)	644	2208	468
Crystal size, mm	0.2×0.15×0.10	0.25×0.25×0.20	0.15×0.05×0.05
Color	yellow	orange	yellow
Data collected / unique	7153 / 4237	7110 / 3800	3476 / 1655
R_{int}	0.0271	0.0250	0.0326
Restraints / parameters	0 / 226	0 / 208	0 / 118
S	1.022	1.047	1.103
R_1, wR_2 [$I>2\sigma(I)$]	0.0288 / 0.0544	0.0248 / 0.0506	0.0384 / 0.0814
R_1, wR_2 (all data)	0.0348 / 0.0580	0.0295 / 0.0527	0.0429 / 0.0833
Larg. diff. peak/hole ($e\cdot Å^{-3}$)	1.452 / -1.359	0.705 / -1.125	5.411 / -2.641

* for *α*/*β* notations see Table 1.

Table S3. Crystallographic data for compounds *β*-**4b** and *β*-**6a**.

Compound	*β*-**4b**	(3·*β*-**6a**)·acetone
Empirical formula	$C_{15}H_{16}ClI_2N_4OPPt$	$C_{39}H_{42}Cl_9N_3O_7Pt_3S_3$
M_w	783.63	1665.25
T, K	150(2)	150(2)
Crystal system	*Triclinic*	*Monoclinic*
Space group	*P -1*	*P 21/c*
a, Å	5.8236(3)	23.9829(5)
b, Å	9.9683(6)	10.1789(3)
c, Å	17.4696(9)	20.8153(5)
α, deg.	86.328(4)	90
β, deg.	88.630(4)	103.822(2)
γ, deg.	73.328(5)	90
V, $Å^3$	969.49(9)	4934.3(2)
Z	2	4
D_{calc}, g/cm^3	2.684	2.242
μ, mm^{-1}	10.653	9.149
F(000)	716	3152
Crystal size, mm	0.15×0.05×0.05	0.15×0.05×0.05
Color	yellow	yellow
Data collected / unique	7583 / 4435	36804 / 11011
R_{int}	0.0323	0.0403
Restraints / parameters	0 / 226	0 / 588
S	1.011	0.983
R_1, wR_2 [I>2σ(I)]	0.0327 / 0.0599	0.0247 / 0.0423
R_1, wR_2 (all data)	0.0422 / 0.0652	0.0358 / 0.0448
Larg. diff. peak/hole ($e·Å^{-3}$)	2.258 / -1.579	0.973 / -1.111

* for *α*/*β* notations see Table 1.

Table S4. Instrument operating conditions for ICP-QMS

Rf power (W)	1548
Gas flows (L/min)	13.9; 1.09; 0.8
Acquisition time	3 x 50s
Points per peak	3
Dwell time (ns)	10
Detector mode	Pulse
Measured isotopes	^{194}Pt

Table S5. Lethal and teratogenic effects observed in zebrafish (*Danio rerio*) embryos at different hours post fertilization (hpf).

Category	Developmental endpoints	Exposure time (hpf)			
		24	48	72	96
Lethal effect	Egg coagulation[a]	•	•	•	•
	No somite formation	•	•	•	•
	Tail not detached	•	•	•	•
	No heart-beat		•	•	•
Teratogenic effect	Malformation of head	•	•	•	•
	Malformation of eyes[b]	•	•	•	•
	Malformation of sacculi/otoliths[c]	•	•	•	•
	Malformation of chorda	•	•	•	•
	Malformation of tail[d]	•	•	•	•
	Scoliosis	•	•	•	•
	Heart beat frequency		•	•	•
	Blood circulation		•	•	•
	Pericardial edema	•	•	•	•
	Yolk edema	•	•	•	•
	Yolk deformation	•	•	•	•
	Growth retardation[e]	•	•	•	•

[a] No clear organs structure are recognized

[b] Malformation of eyes was recorded for the retardation in eye development and abnormality in shape and size.

[c] Presence of no, one or more than two otoliths per sacculus, as well as reduction and enlargement of otoliths and/or sacculi (otic vesicles).

[d] Tail malformation was recorded when the tail was bent, twisted or shorter than to control embryos as assessed by optical comparation.

[e] Growth retardation was recorded by comparing with the control embryos in development or size (before hatching, at 24 hpf and 48 hpf) or in a body length (after hatching, at and onwards 72 hpf) using by optical comparation using a inverted microscope (CKX41; Olympus, Tokyo, Japan).