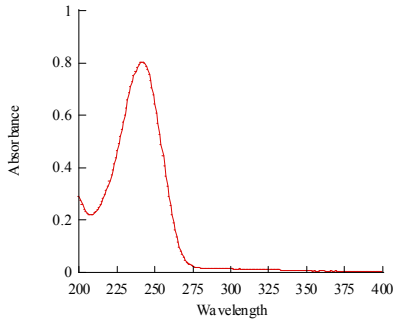
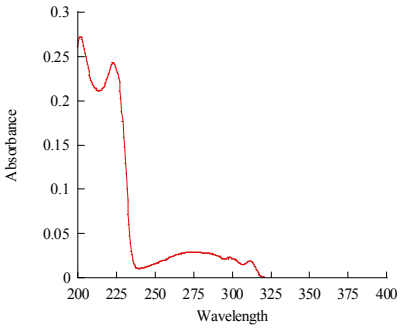
Supplementary information

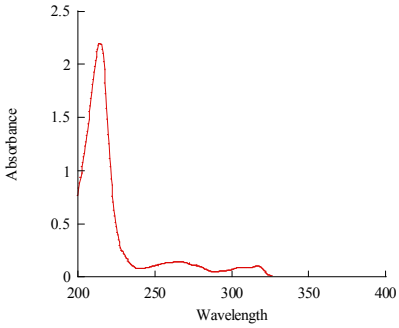
1. UV/Vis of the complexes:



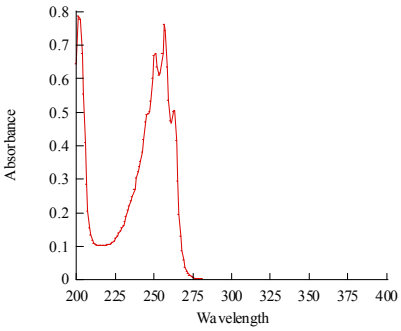
Ethisterone



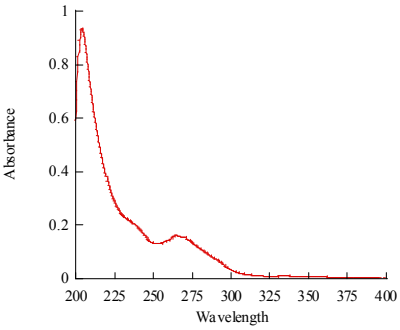
Quinoline



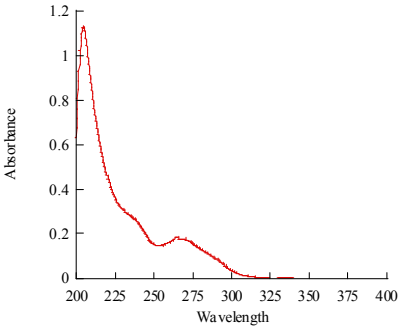
Isoquinoline



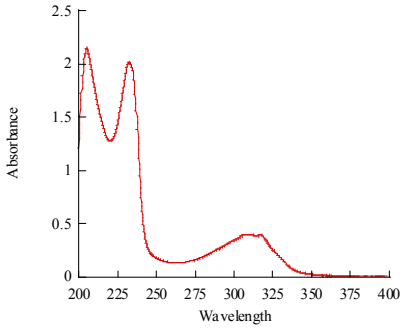
Pyridine



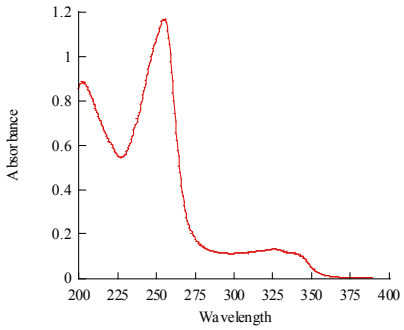
Py.Pt-trans



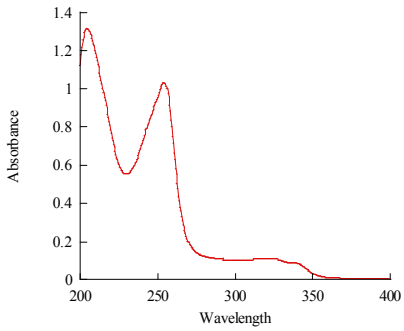
py.Pt-cis



Quin.Pt-trans



5.Pt-trans



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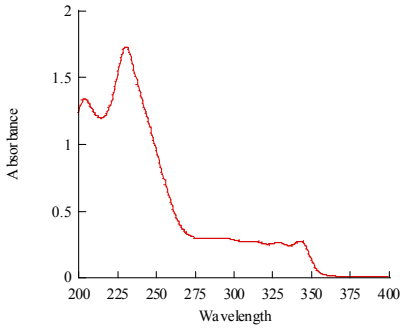

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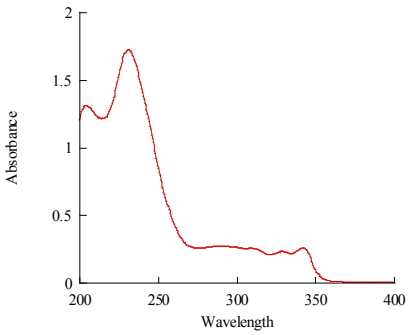

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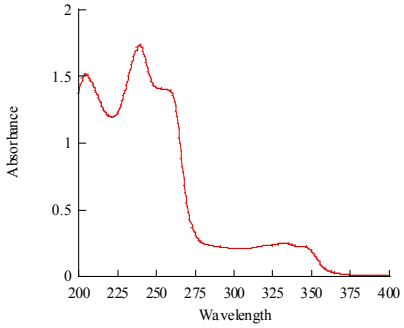
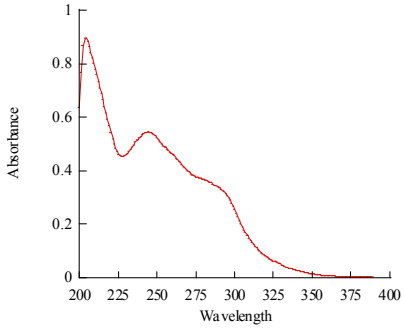
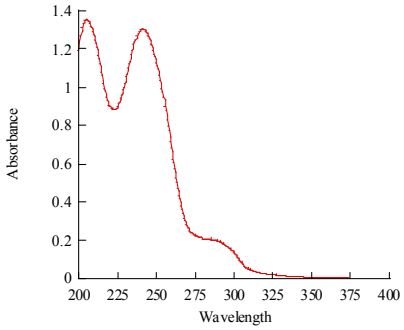


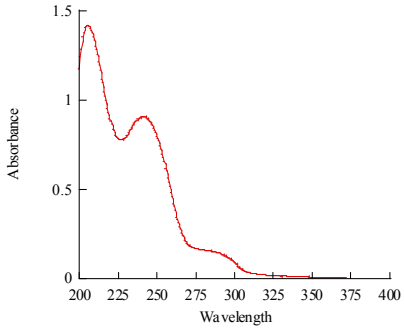
3.Pt-trans



2.Pt-trans



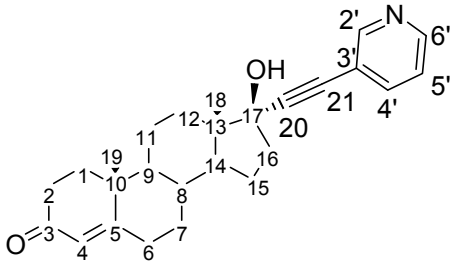
1.Pt-trans



1.Pt-cis

2. Additional spectroscopy of Ligands:

2.1. ET-3-Py (1)



$C_{26}H_{31}NO_2$

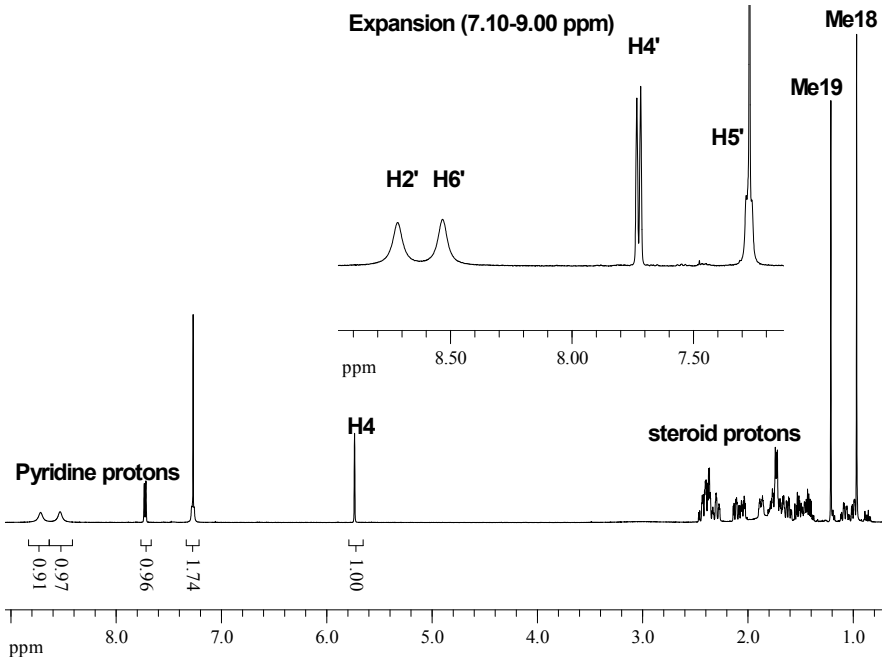


Figure 2.1.1 The ^{1}H NMR spectrum of 1 in $CDCl_3$.

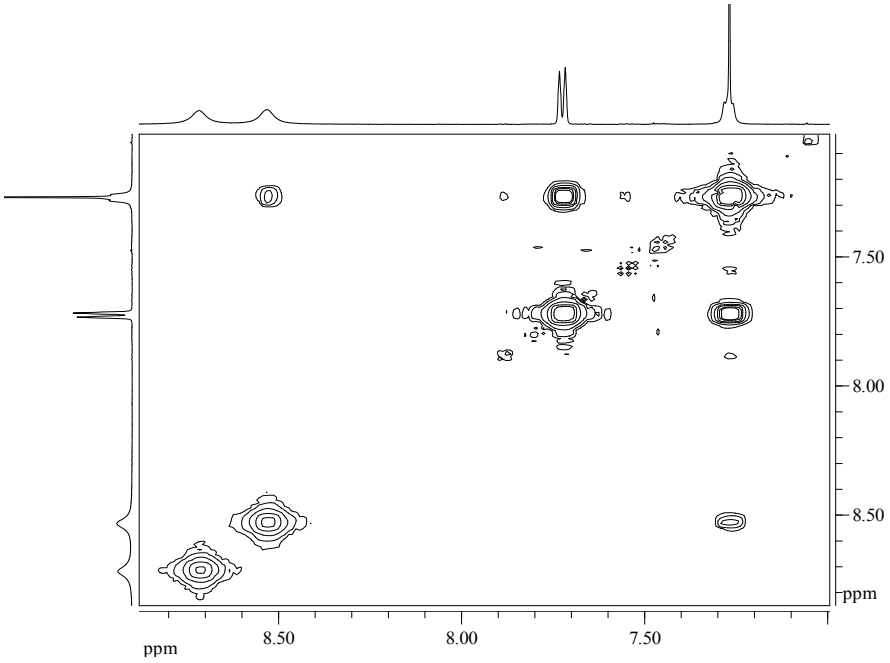
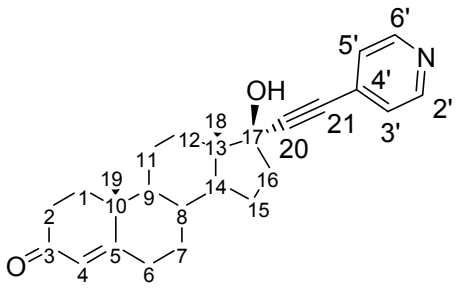


Figure 2.1.2 The COSY spectrum of 1 in $CDCl_3$.

2.2. ET-4-Py (2)



$C_{26}H_{31}NO_2$

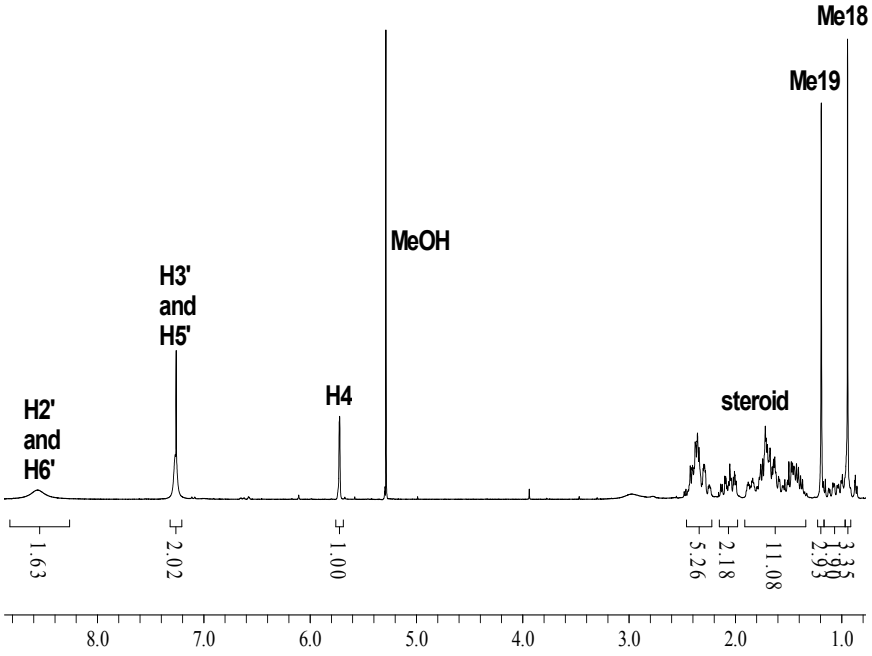
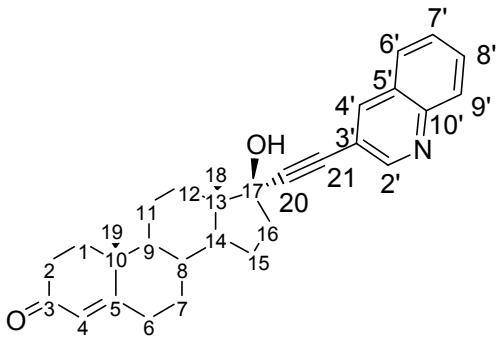


Figure 2.2.1 The ^{1}H NMR of 2 in CD_3OD.

2.3. ET-3-Q (3)



$C_{30}H_{33}NO_2$

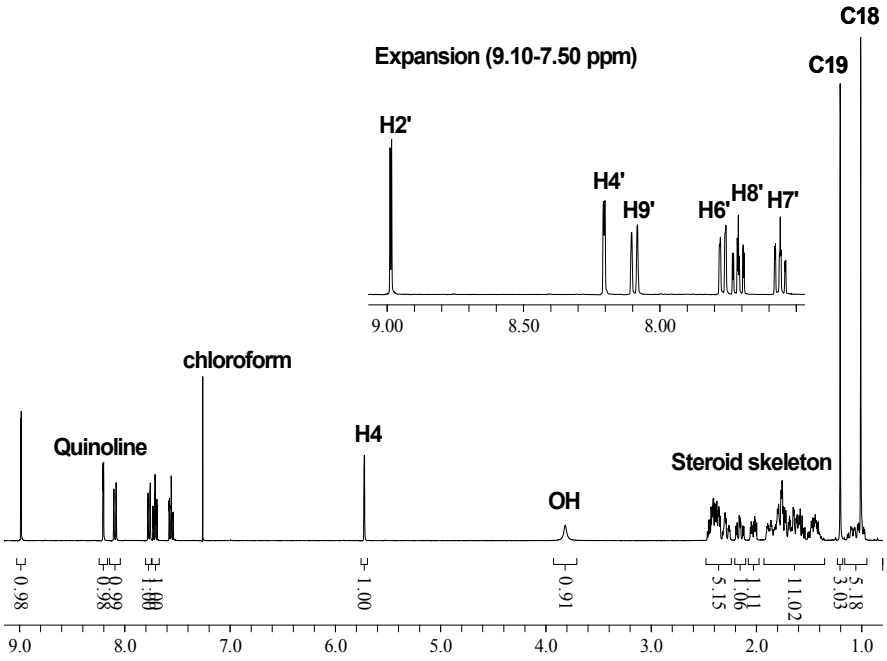


Figure 2.3.1 The ^{1}H NMR spectrum of 3 in $CDCl_3$.

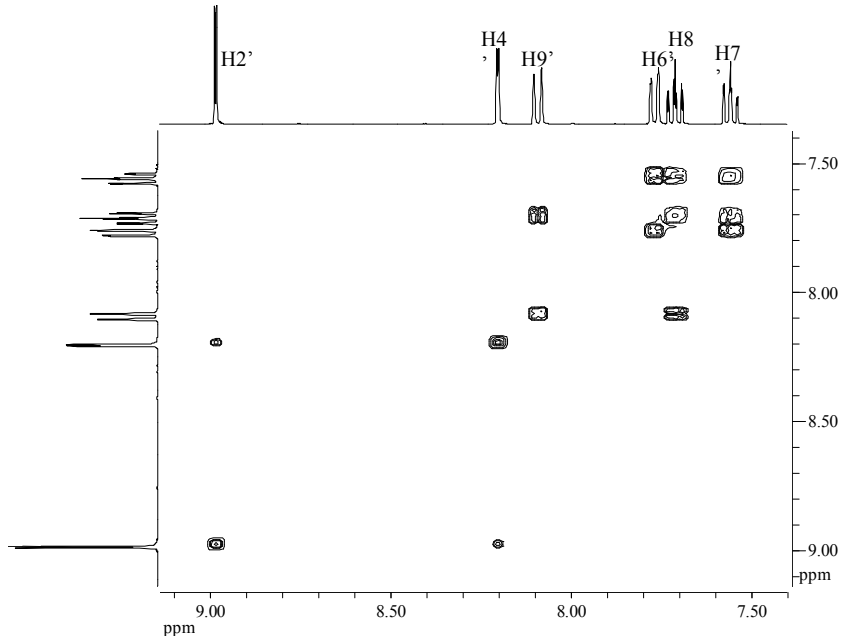


Figure 2.3.2 The COSY spectrum of 3 in $CDCl_3$

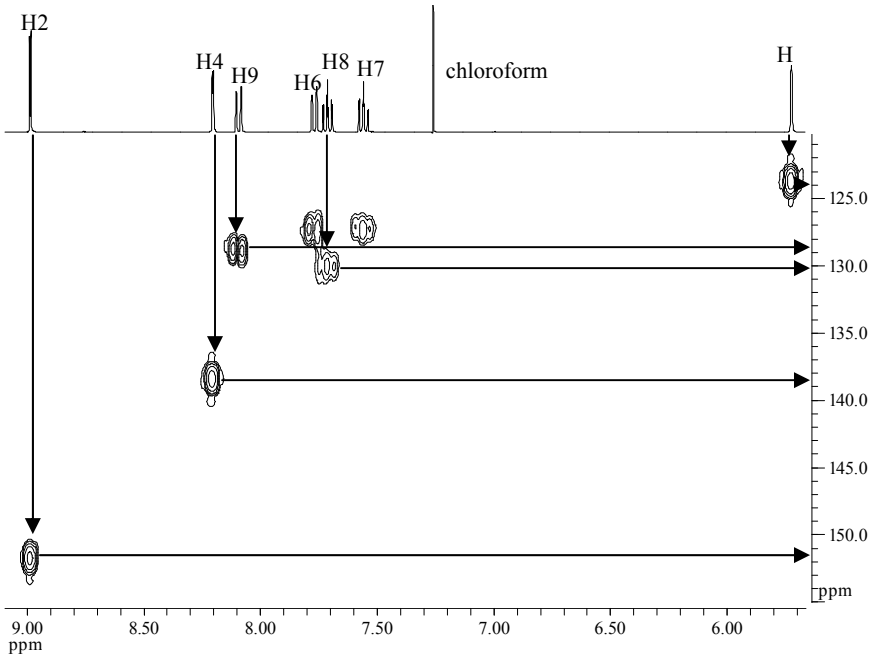


Figure 2.3.3 The low field region in the ^{1}H-^{13}C HMQC spectrum of 3 in $CDCl_3$

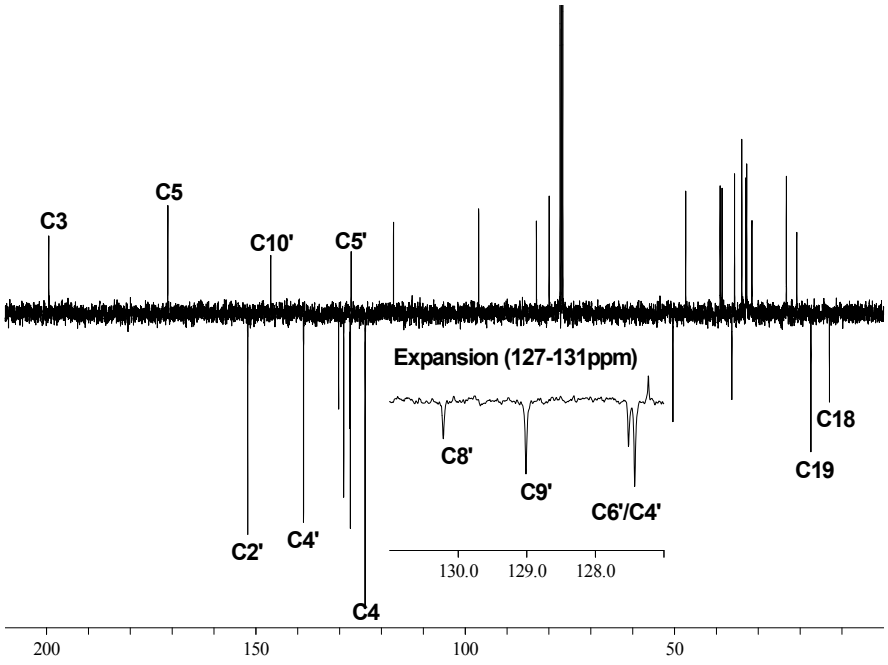
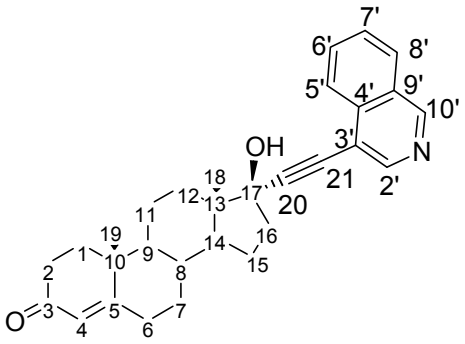


Figure 2.3.4 The ^{13}C DEPT NMR spectrum of 3 in $CDCl_3$.

2.4. ET-4-IQ (4)



$C_{30}H_{33}NO_2$

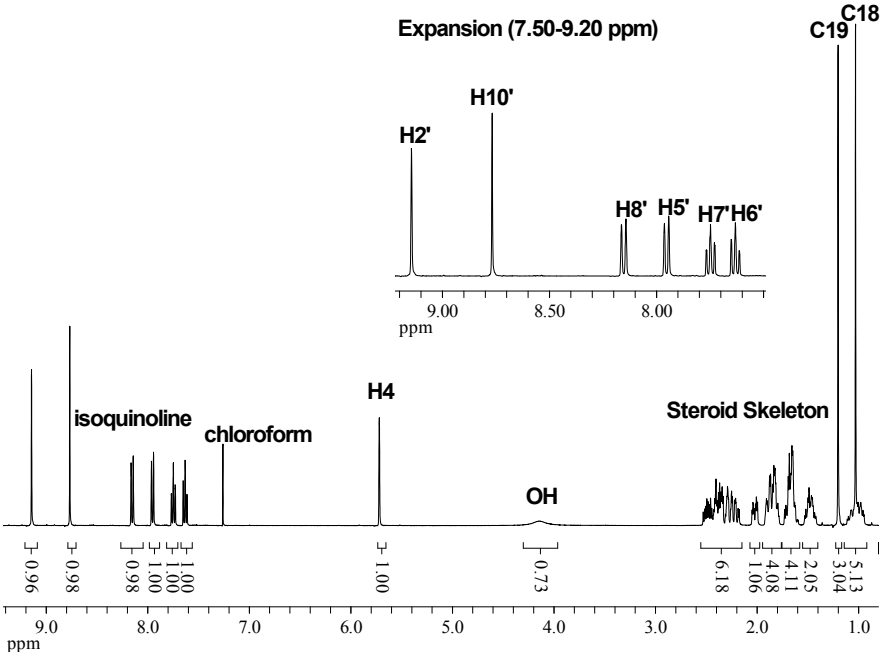


Figure 2.4.1 The ^{1}H NMR spectrum of 4 in $CDCl_3$.

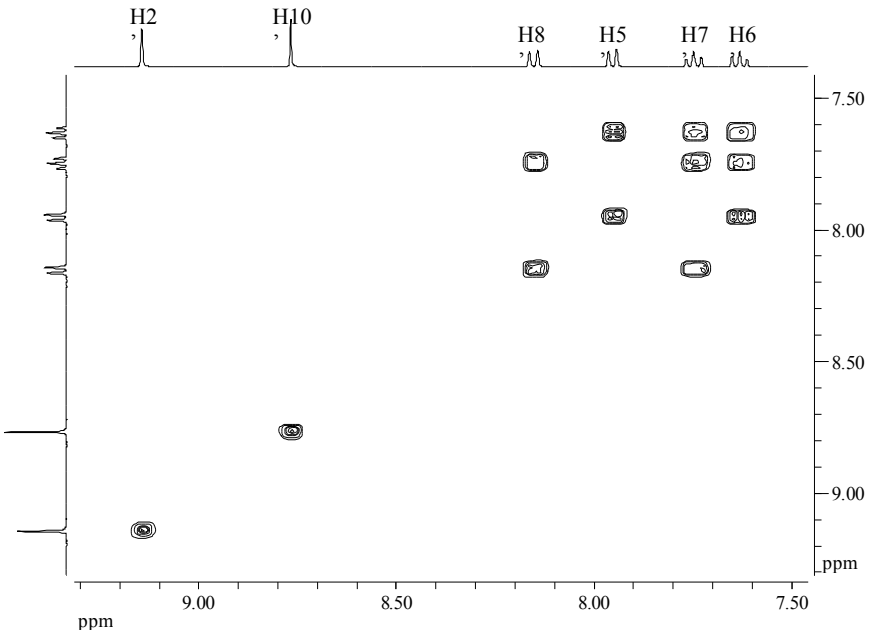


Figure 2.4.2 The aromatic region in the COSY spectrum for 4 in $CDCl_3$

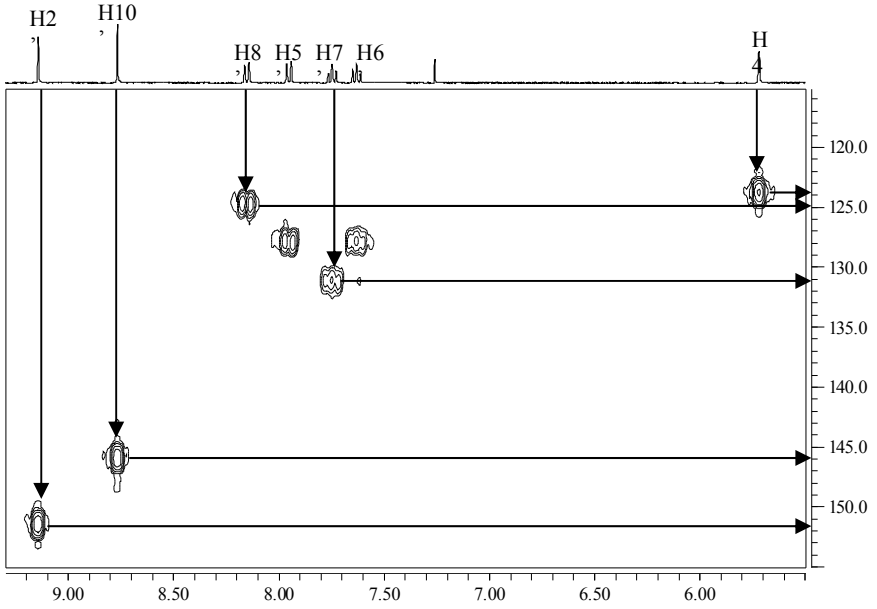


Figure 2.4.3 The low field ^{1}H-^{13}C HMQC spectrum of 4 in $CDCl_3$

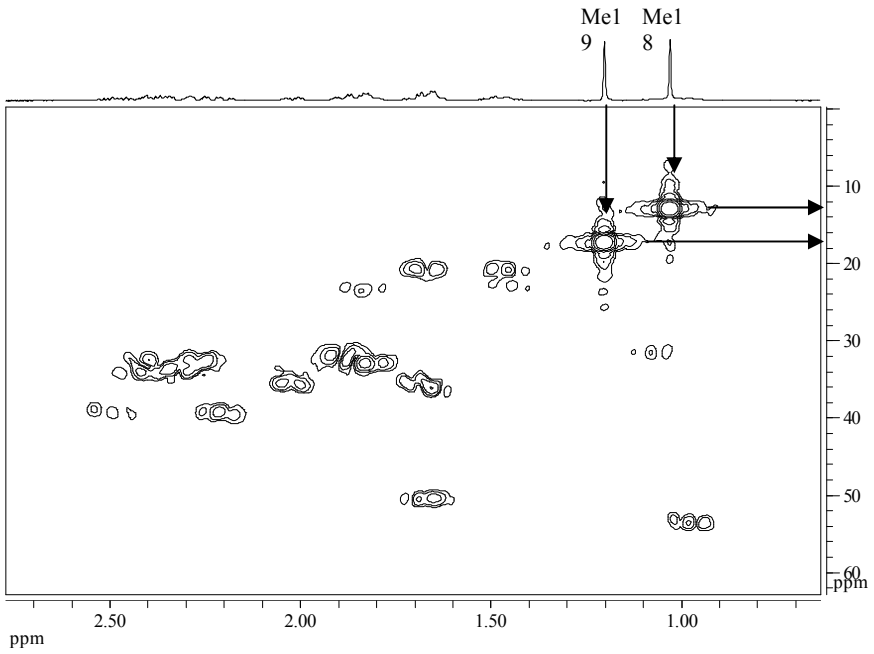


Figure 2.4.4 The aliphatic region in the ^{1}H-^{13}C HMQC spectrum of 4 in $CDCl_3$

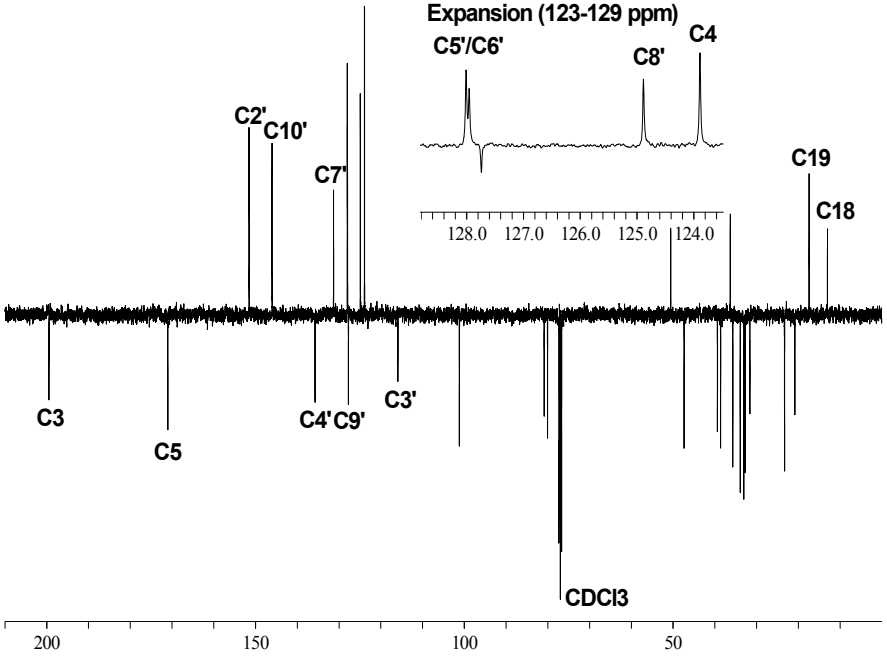
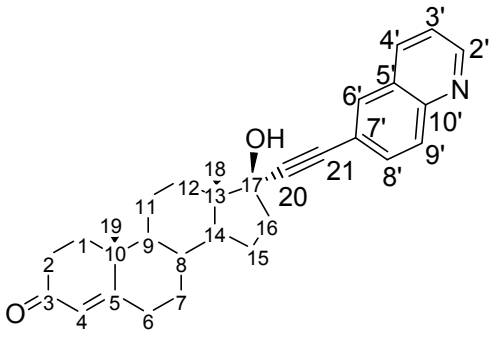


Figure 2.4.5 The ^{13}C NMR spectrum of 4 in $CDCl_3$.

2.5. ET-6-Q (5)



$C_{30}H_{33}NO_2$

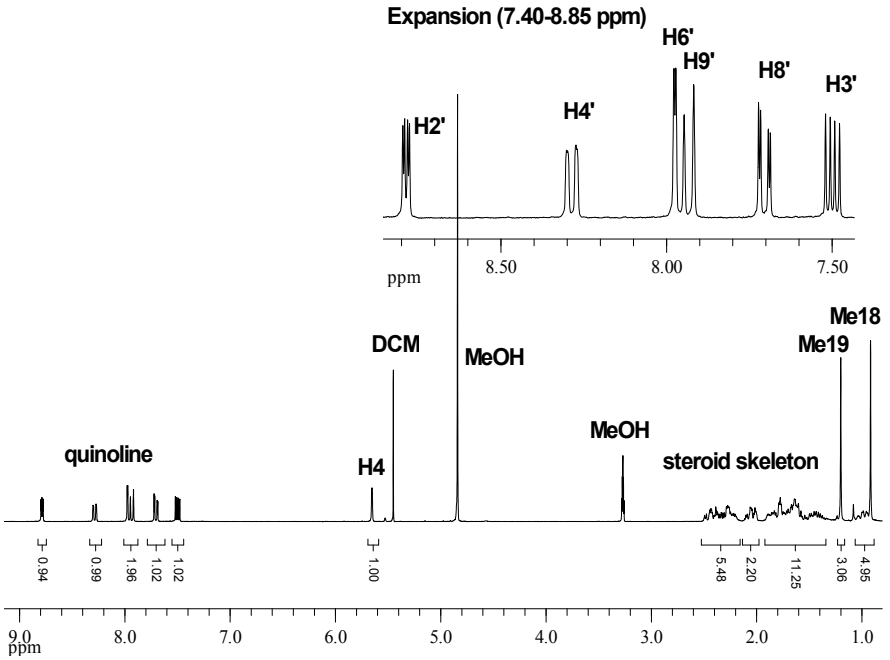


Figure 2.5.1 The ^{1}H NMR spectrum of 5 in CD_3OD

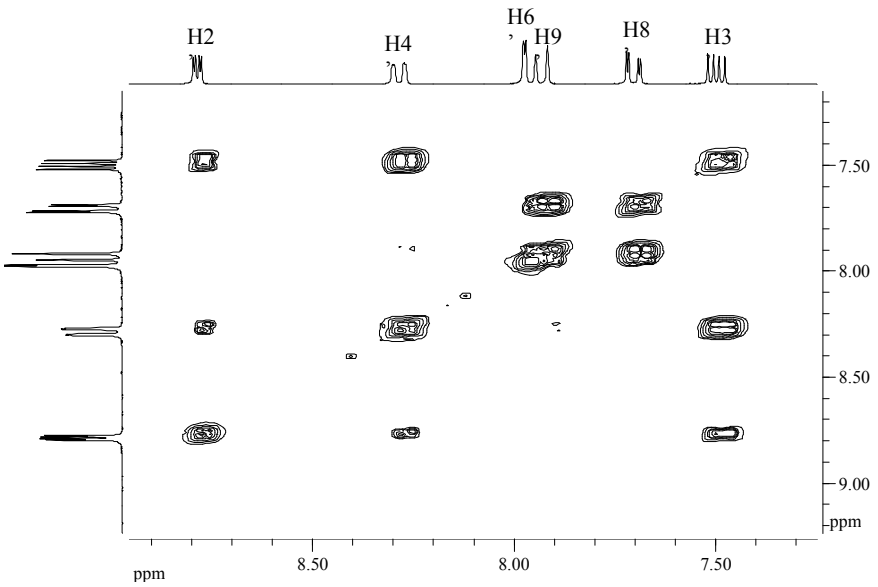
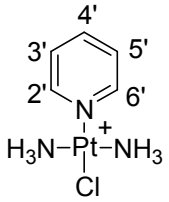


Figure 2.5.2 The aromatic region in the COSY spectrum of 5.

3. Additional spectroscopy of trans complexes:

3.1. Py.Pt-trans



$[C_5H_{11}ClN_3Pt][NO_3]$

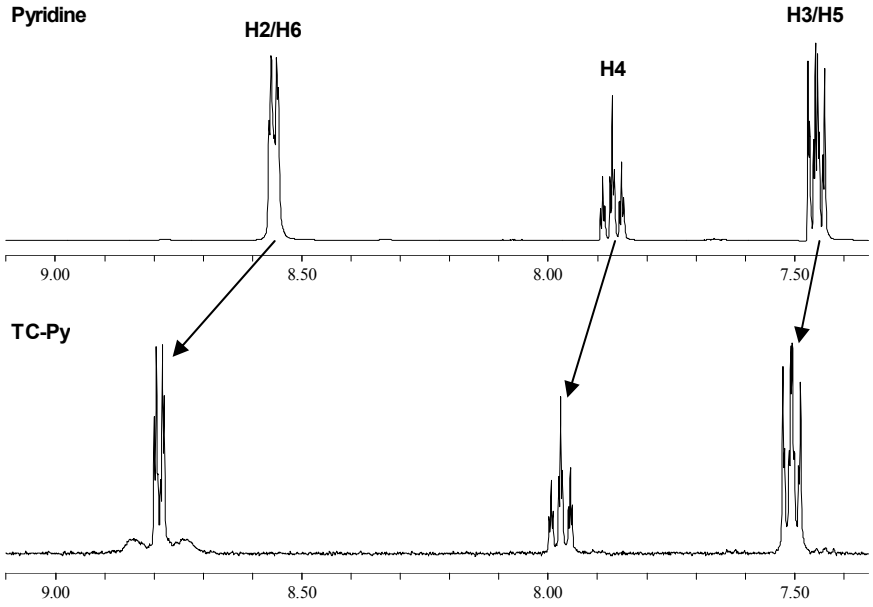
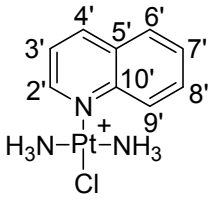


Figure 3.1.1 Comparison of the chemical shifts of free pyridine and Py.Pt-trans

3.2. Qui.Pt-trans



$[C_9H_{13}N_3Pt][NO_3]$

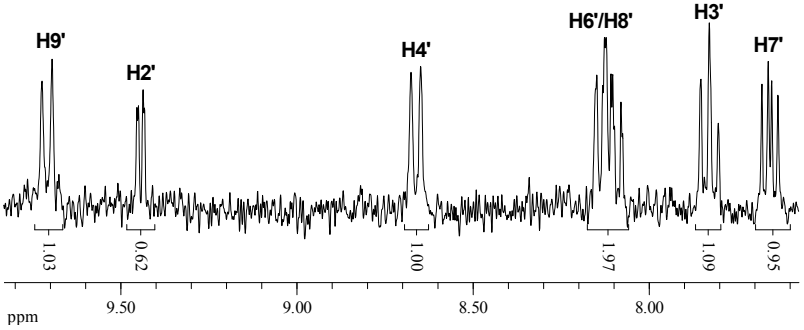
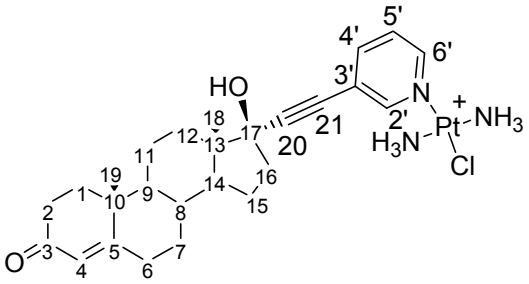


Figure 3.2.1 The ^{1}H NMR spectrum of qui.Pt-trans in CD_3OD.

3.3. 1.Pt-trans



$[C_{26}H_{37}ClN_3O_2Pt][NO_3]$

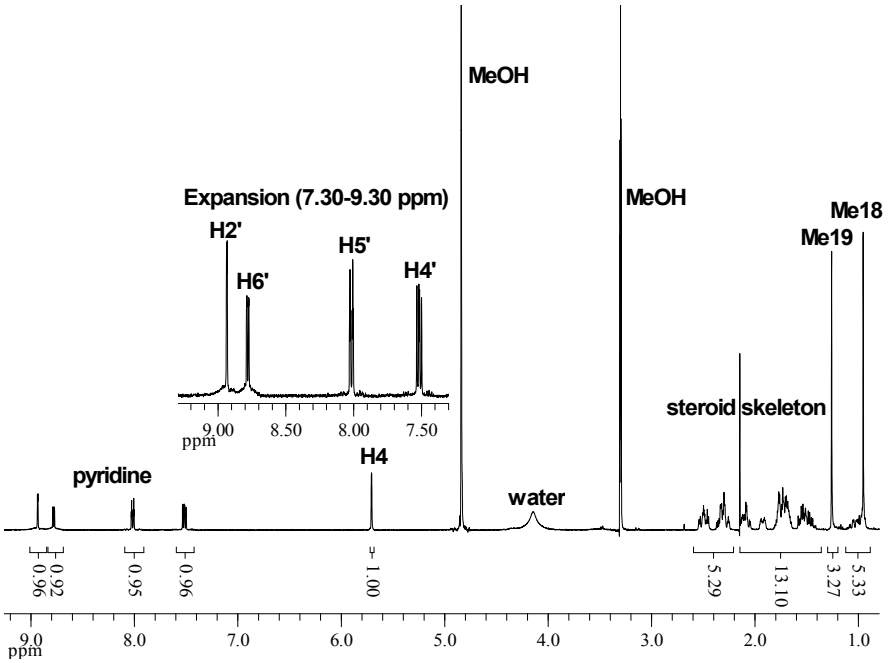


Figure 3.3.1 The ^{1}H NMR spectrum of 1.Pt-trans in CD_3OD.

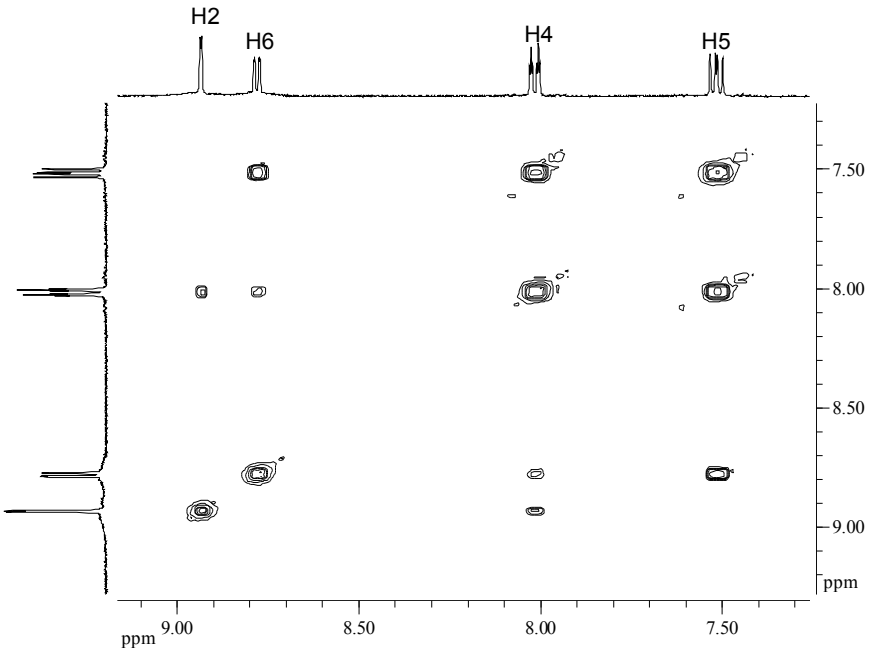


Figure 3.3.2 The COSY spectrum for 1.Pt-trans in CD_3OD

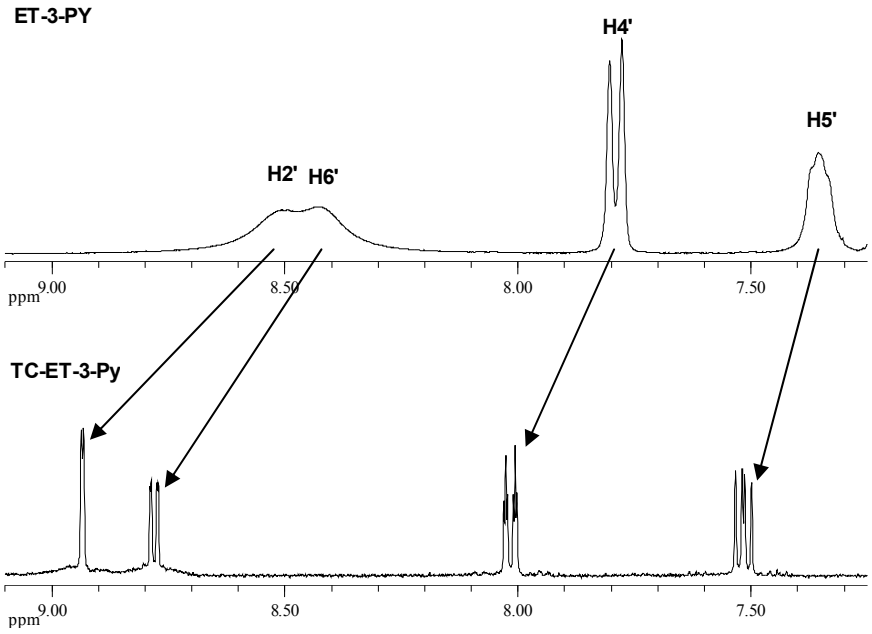
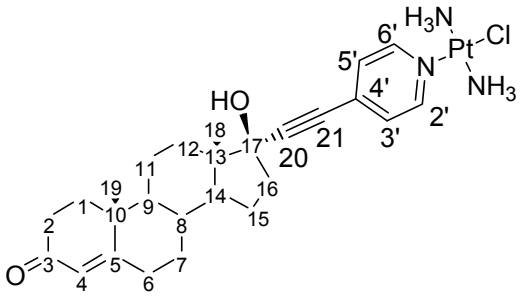


Figure 3.3.3 The aromatic region in ^1H NMR spectra of 1 (top) and 1.Pt-trans(bottom) in CD_3OD

3.4. 2.Pt-trans



$[C_{26}H_{37}ClN_3O_2Pt][NO_3]$

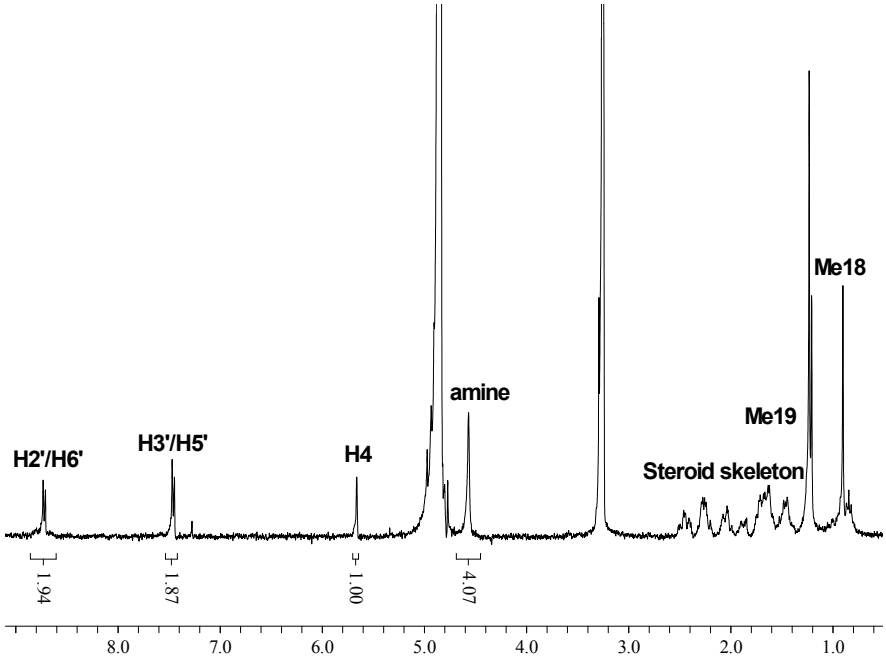


Figure 3.4.1 The ^{1}H NMR spectrum of 2.Pt-trans in CD_3OD.

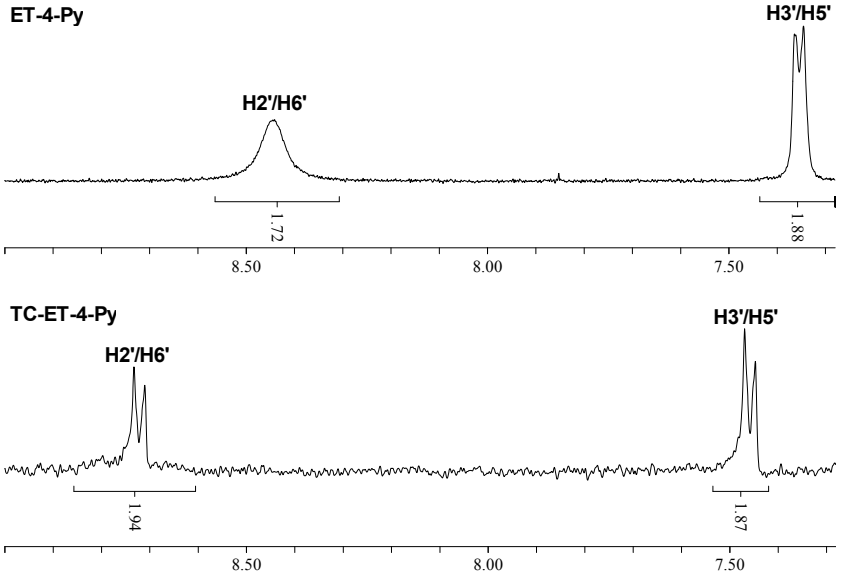
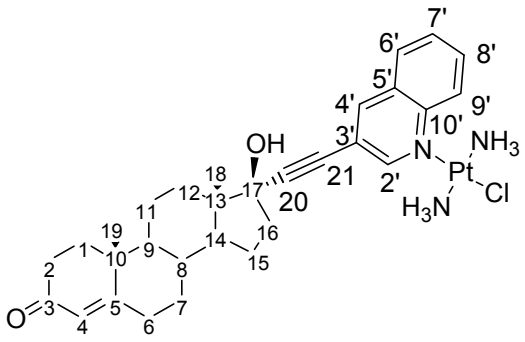


Figure 3.4.2 The aromatic region of the ^{1}H NMR spectrum of 2 and 2.Pt-trans in CD_3OD

3.5. 3.Pt-trans



$[C_{30}H_{39}ClN_3O_2Pt][NO_3]$

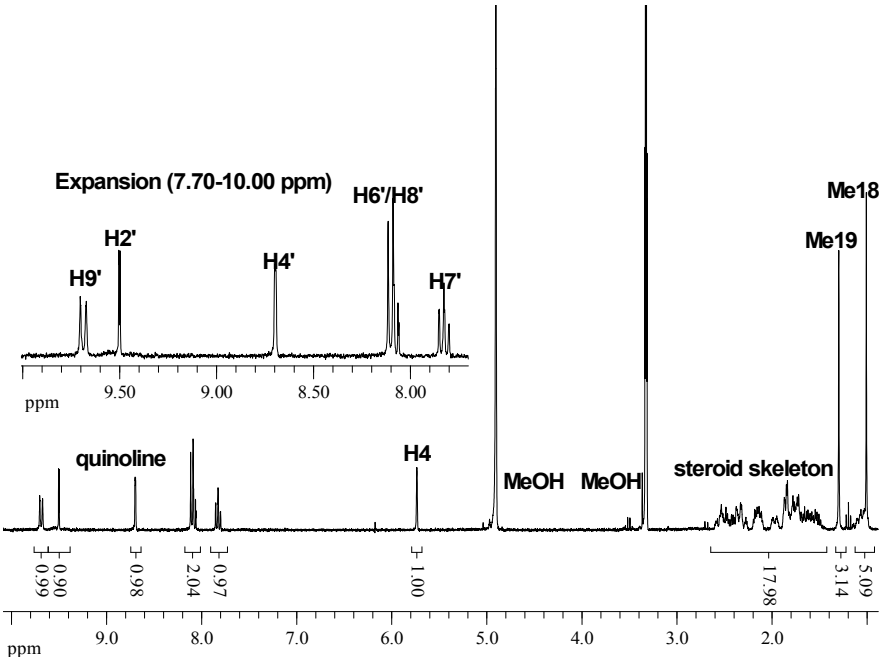


Figure 3.5.1 The ^{1}H NMR spectrum of 3.Pt-trans in CD_3OD.

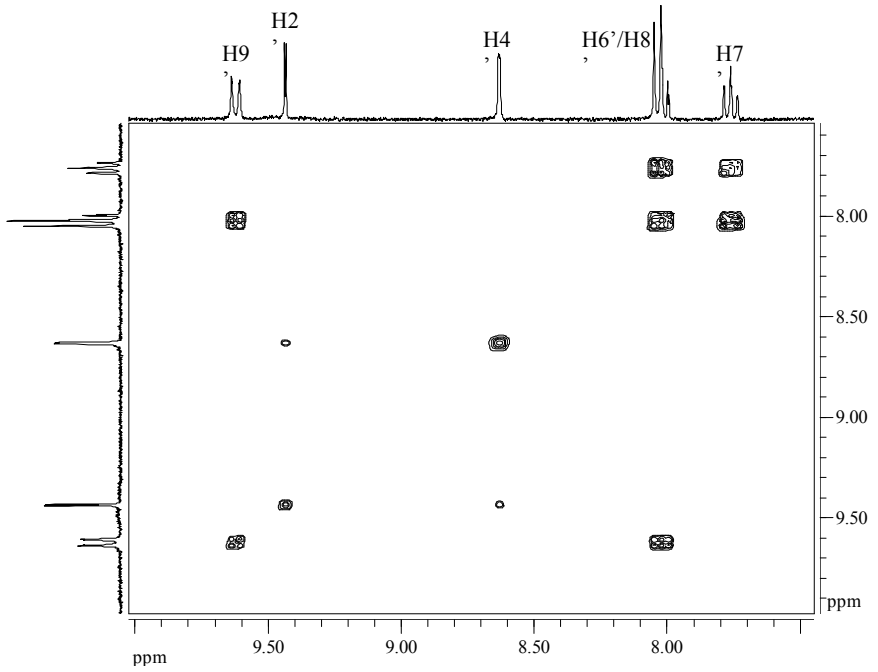


Figure 3.5.2 The ^{1}H NMR COSY spectrum of 3.Pt-trans

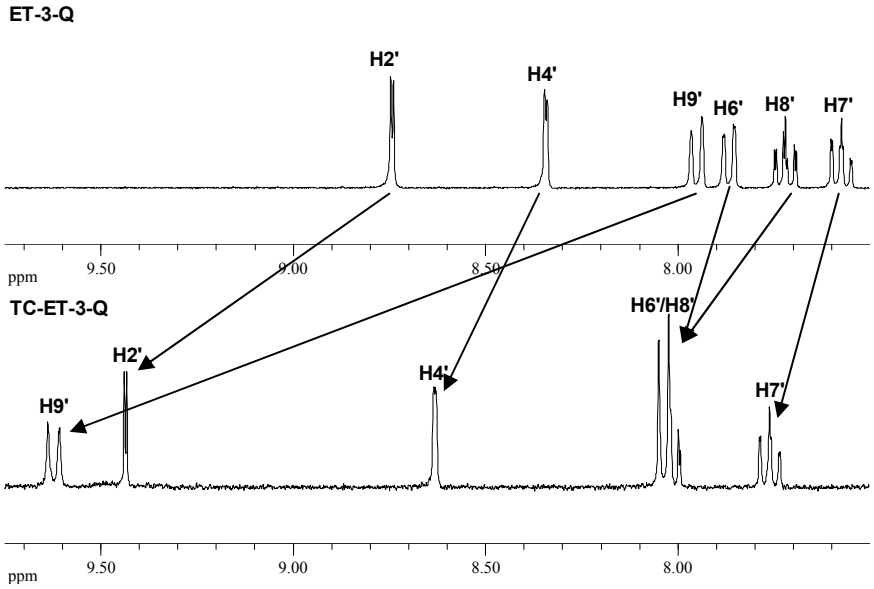
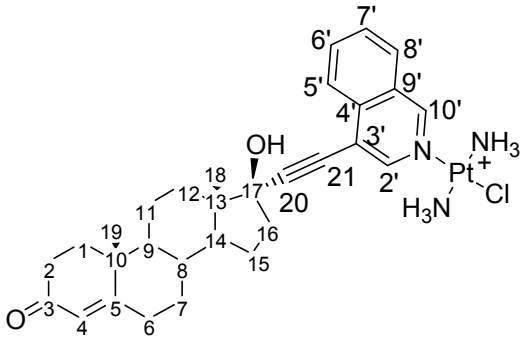


Figure 3.5.3 The ^{1}H NMR spectrum of 3 (top) and 3.Pt-trans (bottom) in CD_3OD

3.6. 4.Pt-trans



$[C_{30}H_{39}ClN_3O_2Pt][NO_3]$

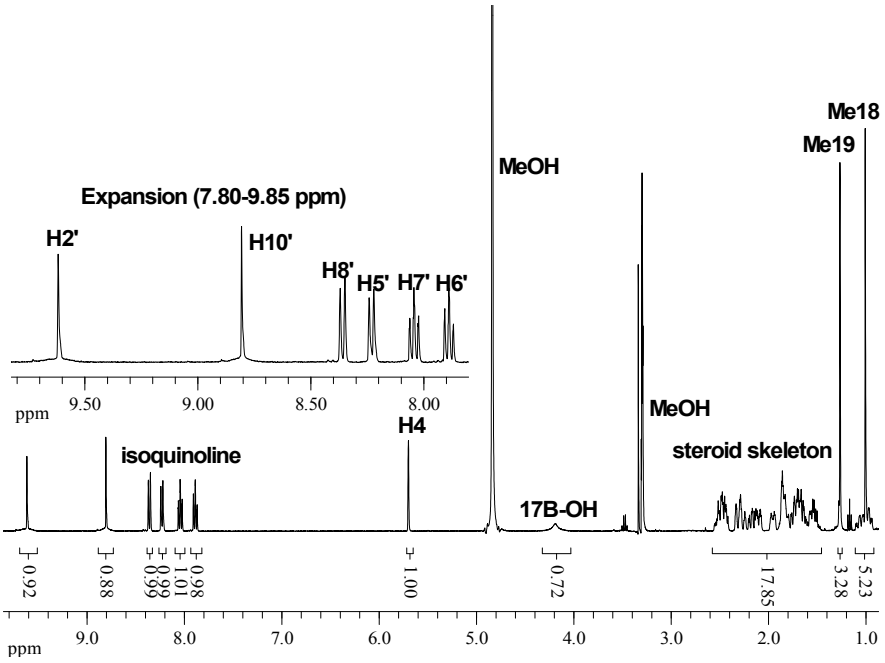


Figure 3.6.1 The ^{1}H NMR spectrum of 4.Pt-trans in CD_3OD.

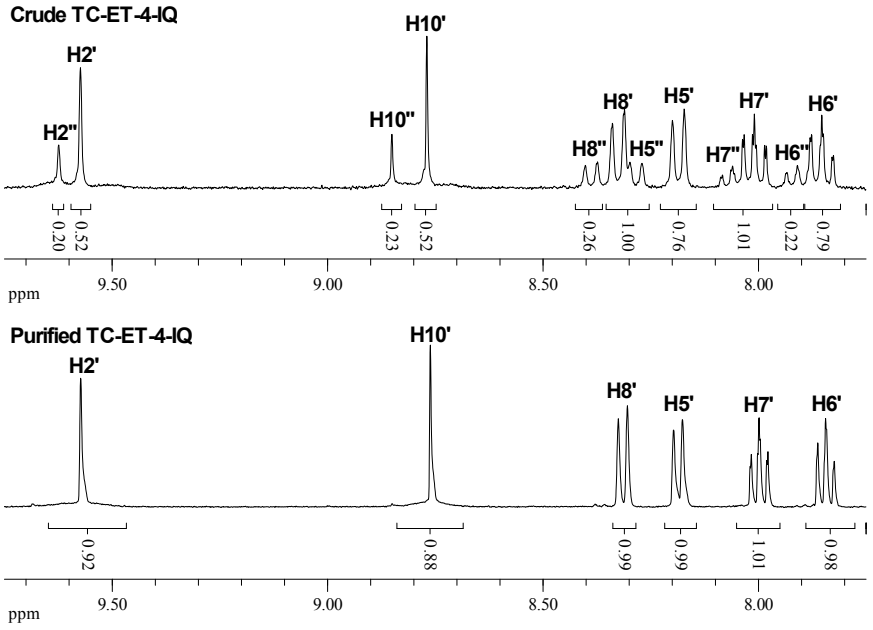


Figure 3.6.2 Comparison of the aromatic region of the ^{1}H NMR spectrum of crude (upper) and pure (lower) 4.Pt-trans.

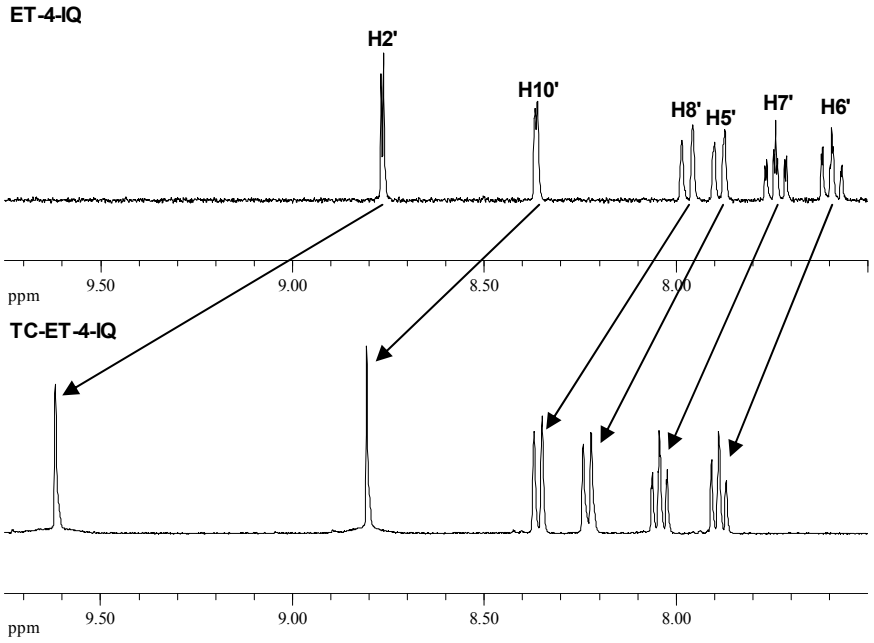
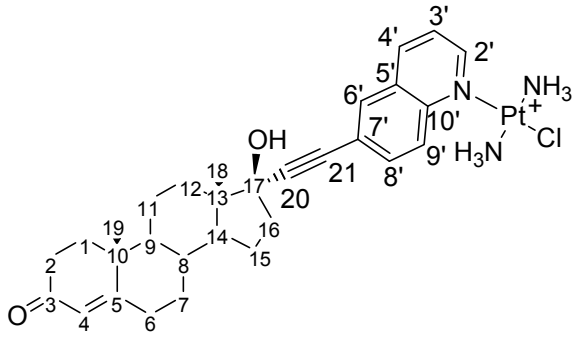


Figure 3.6.3 The aromatic region of the ^{1}H NMR spectrum of 4 (top) and 4.Pt-cis (bottom) in CD_3OD

3.7. 5.Pt-trans



$[C_{30}H_{39}ClN_3O_2Pt][NO_3]$

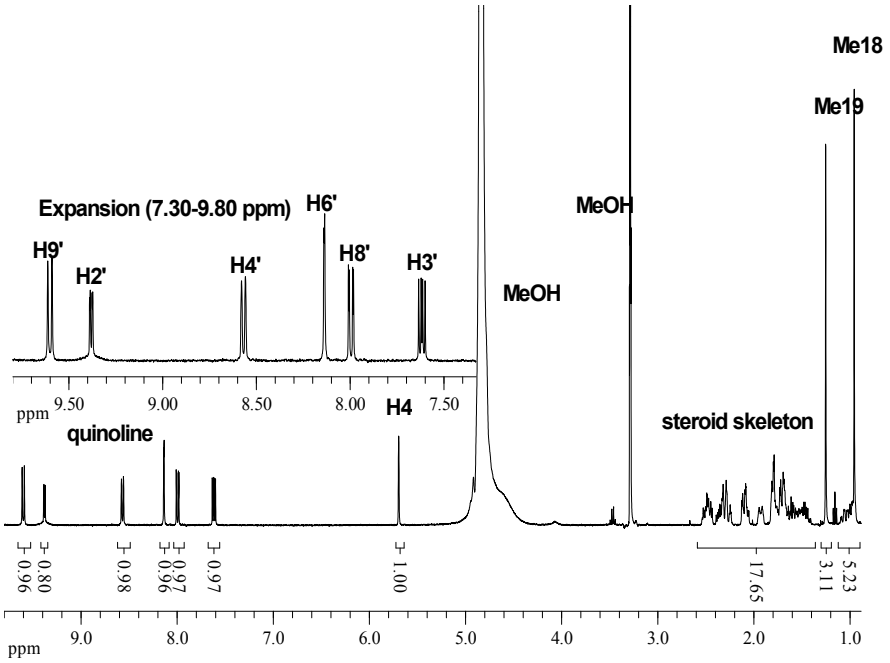


Figure 3.7.1 The ^{1}H NMR spectrum of 5.Pt-trans in CD_3OD.

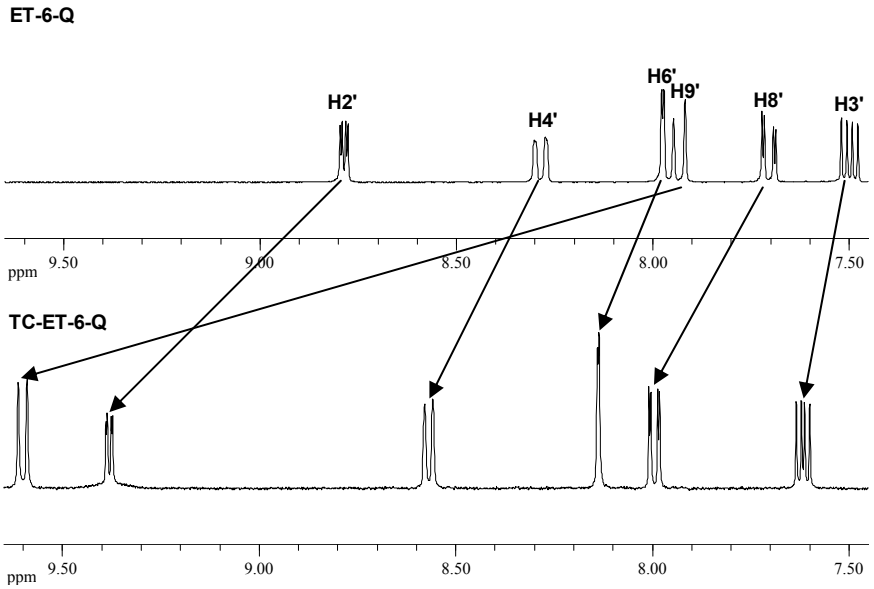
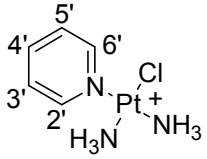


Figure 3.7.2 The comparison of the ^{1}H NMR spectra of 5 and 5.Pt-trans

4. Additional spectroscopy of cis complexes:

4.1. Py.Pt-cis



$[C_5H_{11}ClN_3][NO_3]$

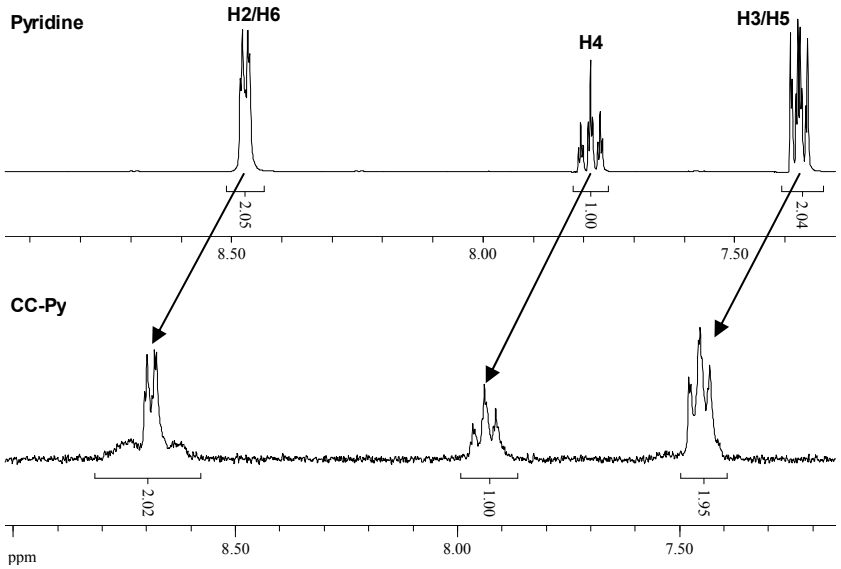
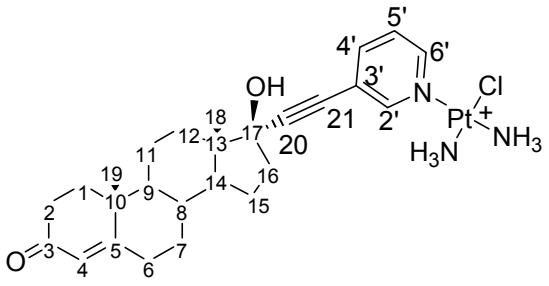


Figure 4.1.1 The ^{1}H NMR spectra of pyridine (upper) and Py.Pt-cis (lower) in CD_3OD

4.2. 1.Pt-cis



$[C_{26}H_{37}ClN_3O_2Pt][NO_3]$

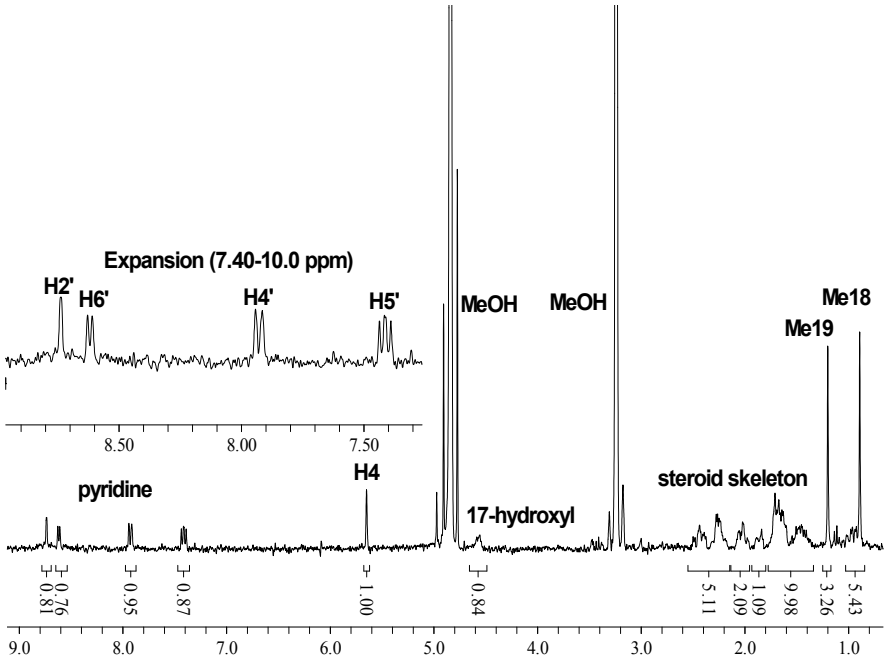


Figure 4.2.1 The ^{1}H NMR spectrum of 1.Pt-cis in CD_3OD.

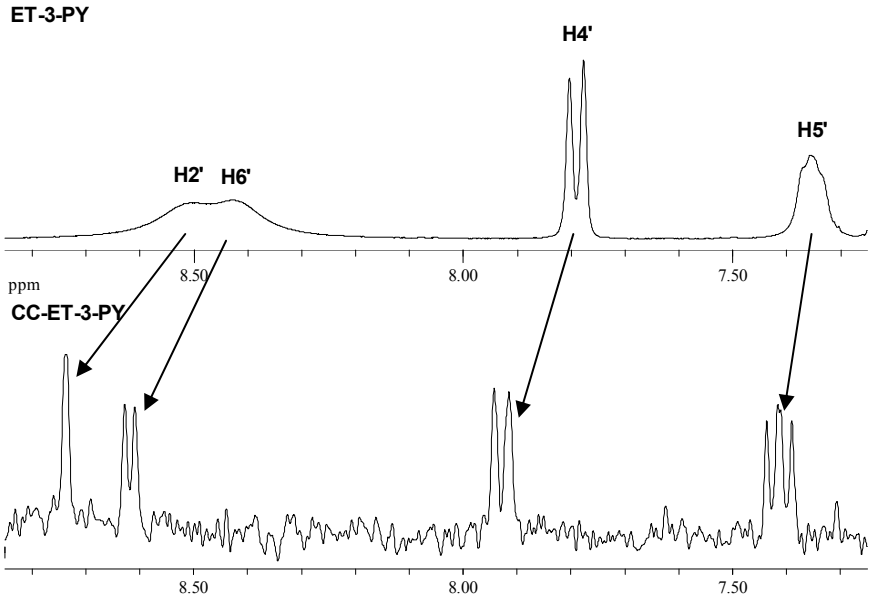
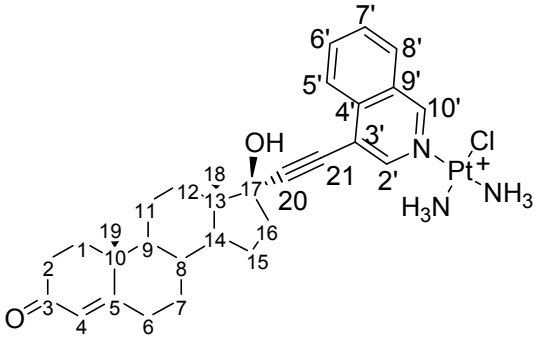


Figure 4.2.2 The ^{1}H NMR spectra of 1 (upper) and 1.Pt-cis (lower) in CD_3OD

4.3. 4.Pt-cis



$[C_{30}H_{39}ClN_3O_2Pt][NO_3]$

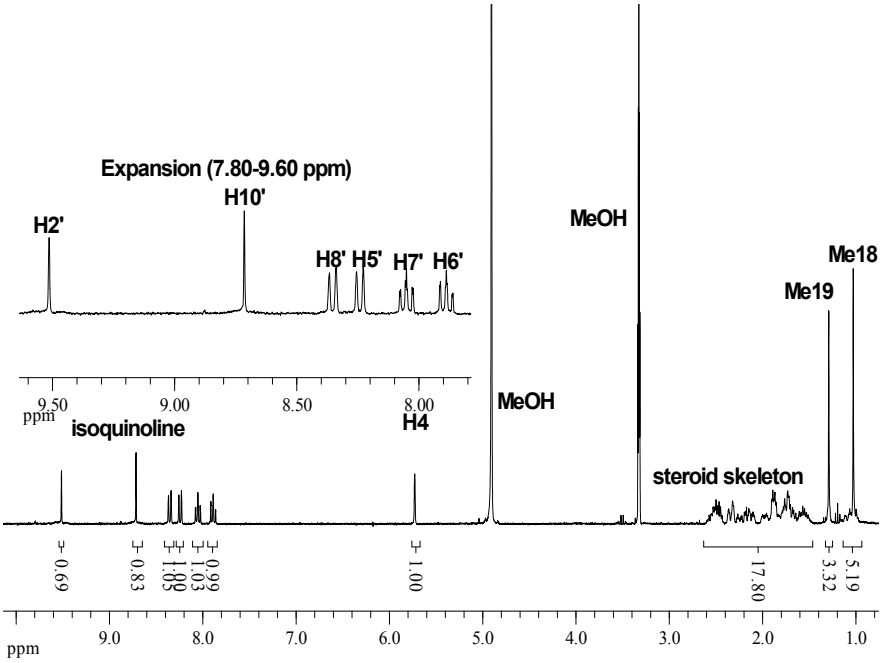


Figure 4.3.1 The ^{1}H NMR spectrum of 4.Pt.cis in CD_3OD

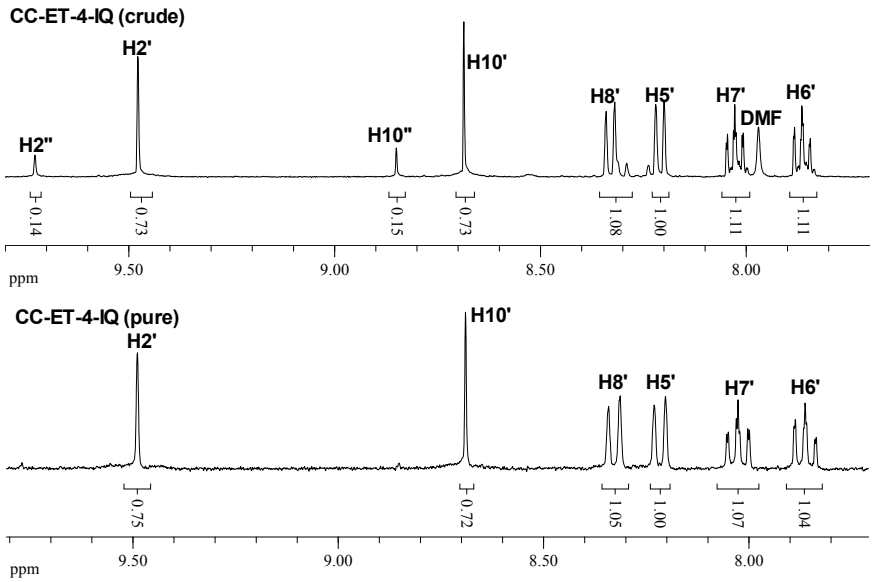


Figure 4.3.2 The ^{1}H NMR spectra of 4.Pt-cis showing the crude(top) spectrum and purified(bottom) spectrum. Those signals marked double prime represent the disubstituted complex in CD_3OD.

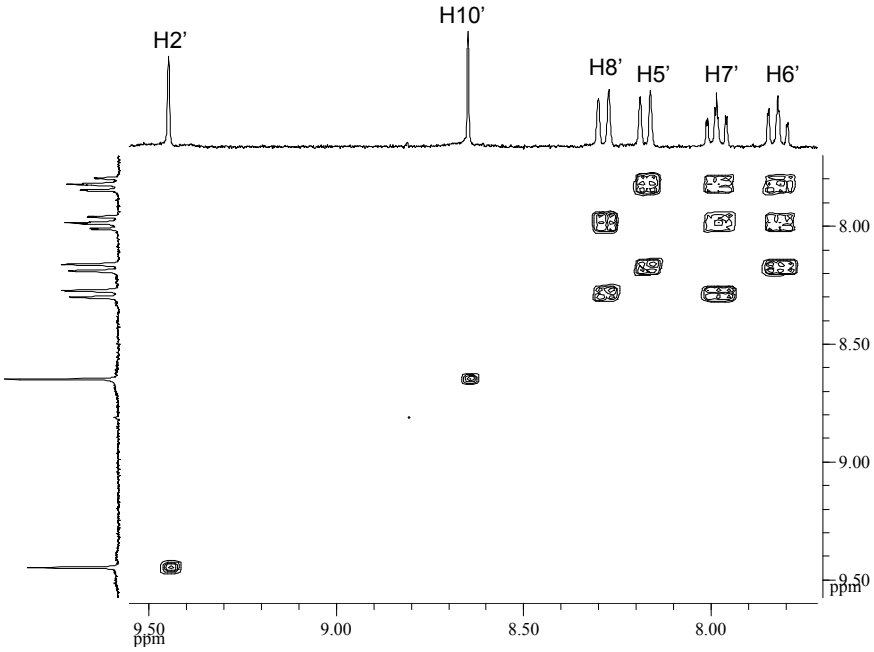


Figure 4.3.3 The aromatic region in the COSY spectrum of 4.Pt-cis in CD_3OD

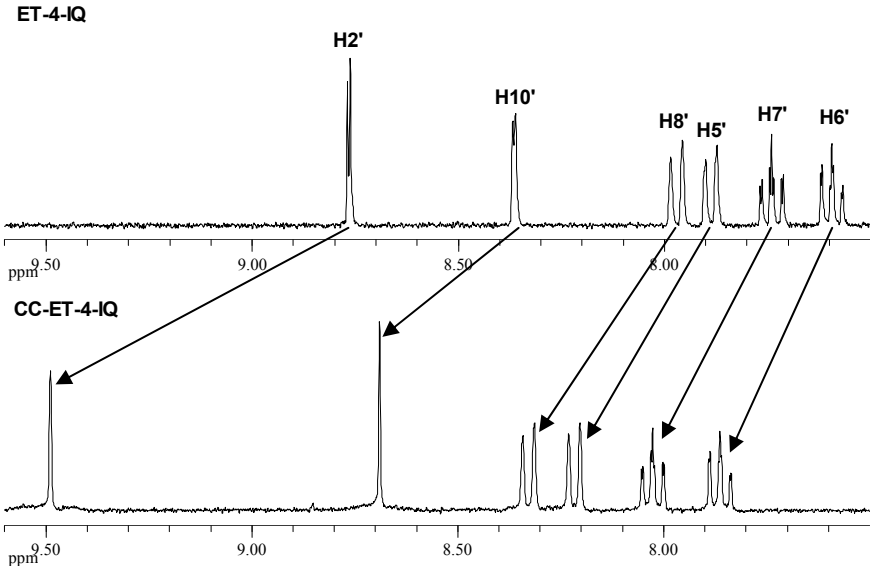
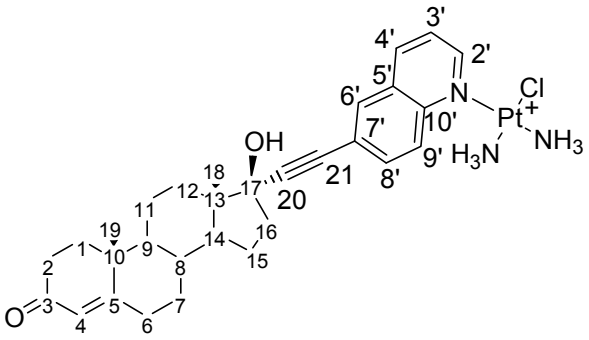


Figure 4.3.4 The ^{1}H NMR spectra of 4 and 4.Pt-cis in CD_3OD

4.4. 5.Pt-cis



$[C_{30}H_{39}ClN_3O_2Pt][NO_3]$

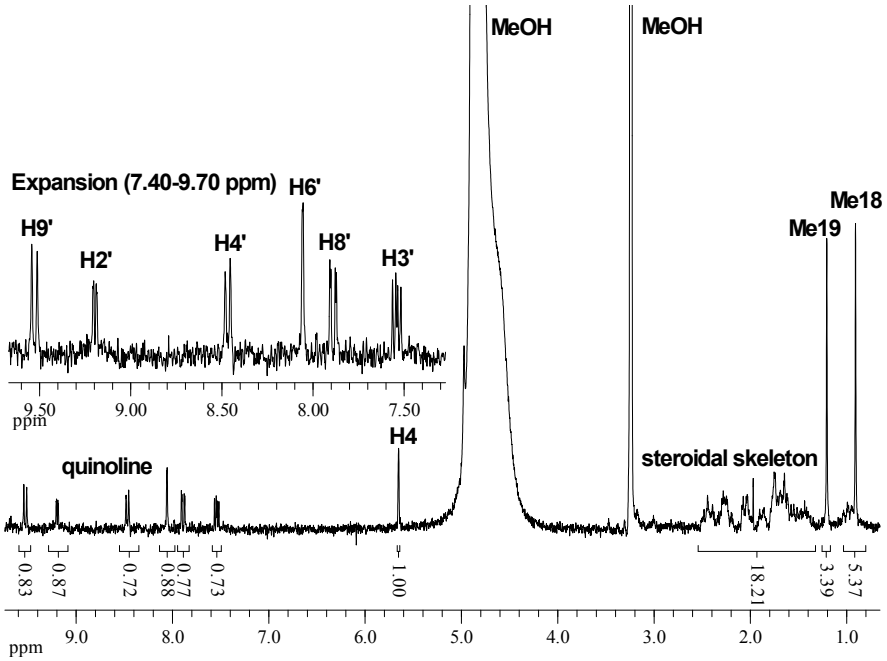


Figure 4.4.1 The ^{1}H NMR spectrum of 5.Pt-cis in CD_3OD.

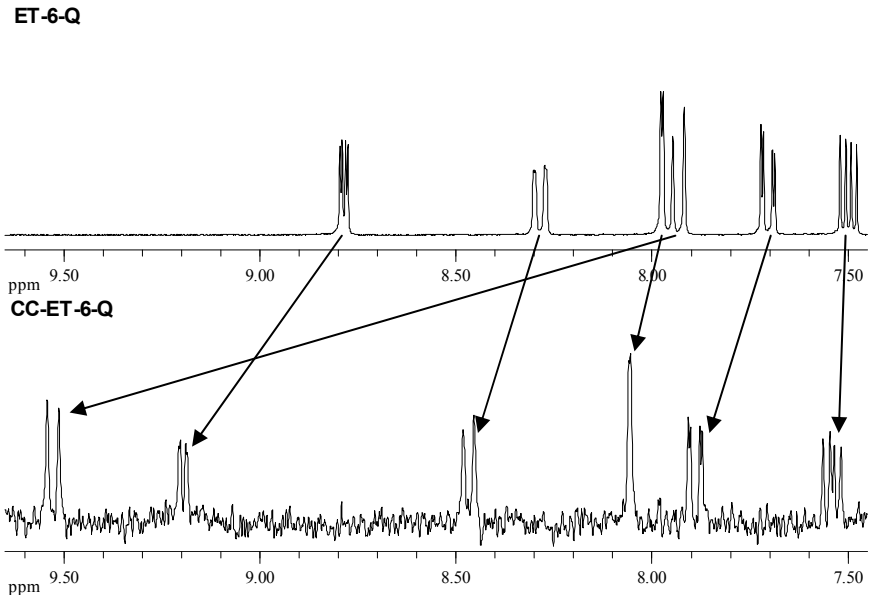


Figure 4.4.2 The ^{1}H NMR spectra of 5 (upper) and 5.Pt.cis (bottom) in CD_3OD

5. Geometry of trans and cis complexes:

5.1. Py.Pt-trans and Py.Pt-cis

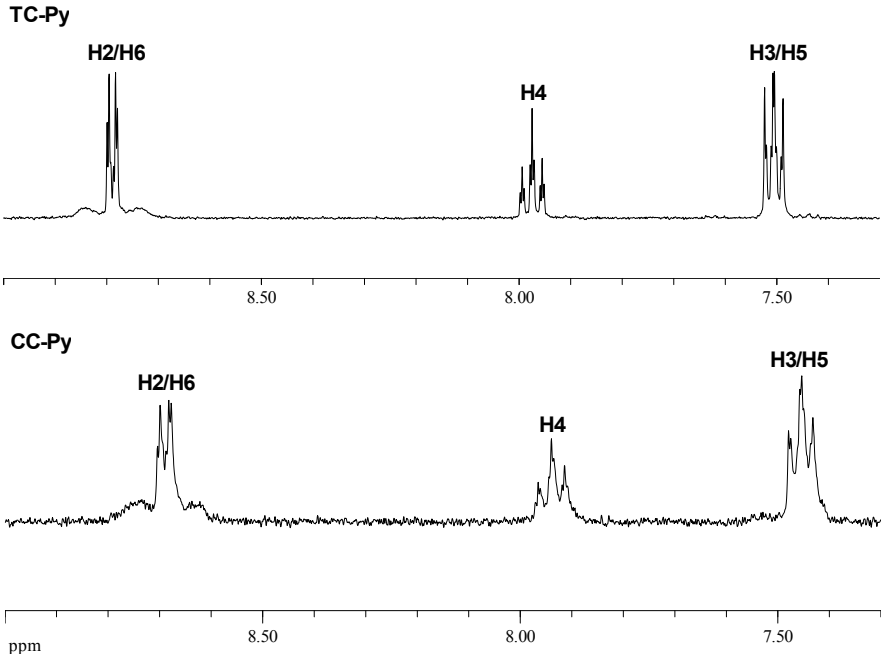


Figure 5.1.1 Comparison of the ^{1}H NMR spectra of Py.Pt-trans (upper) and Py.Pt-cis (lower) in CD_3OD.

5.2. 1.Pt-trans and 1.Pt-cis

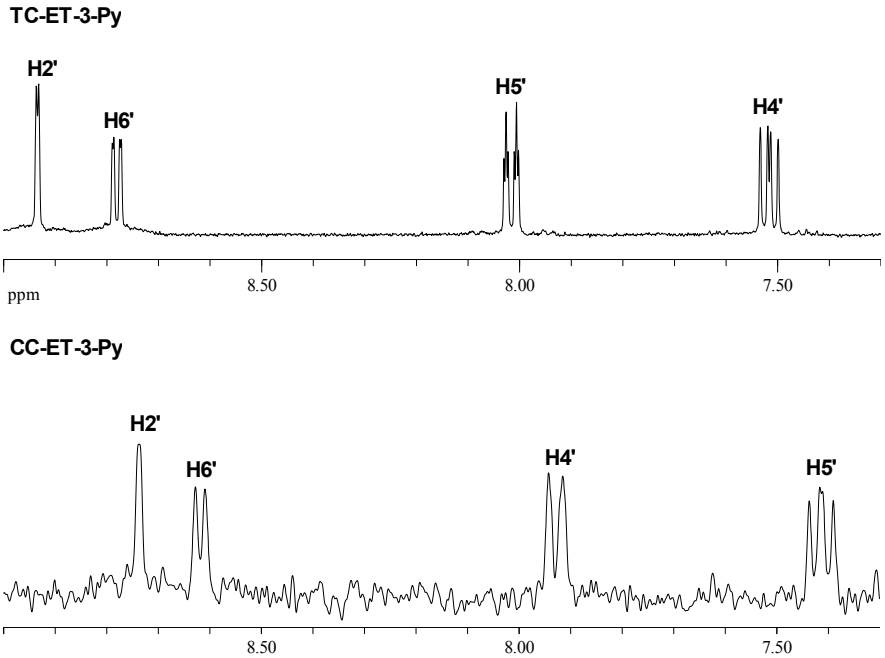
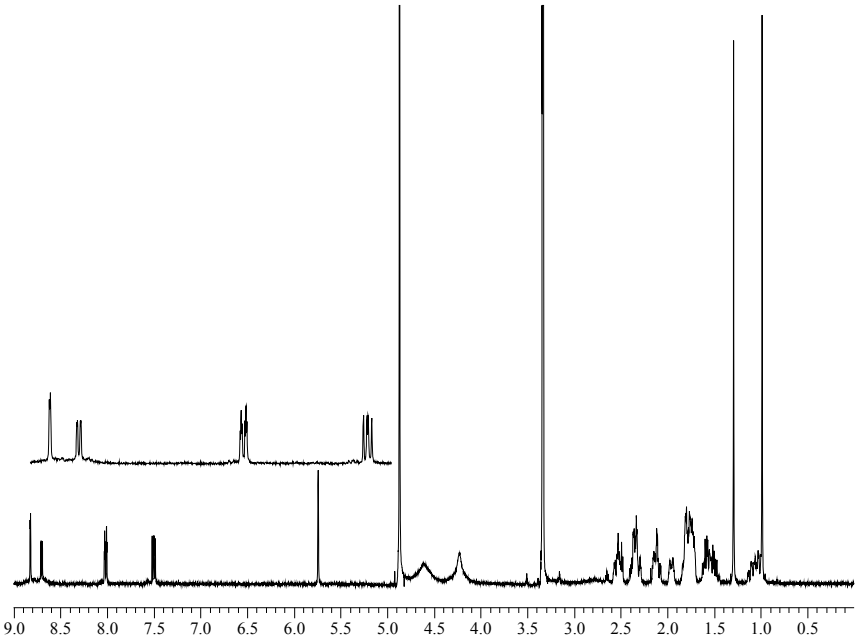


Figure 5.2.1 Comparison of the aromatic fraction of the ^{1}H NMR spectra of 1.Pt-trans (upper) and 1.Pt-cis (lower) in CD_3OD.

1.Pt-cis:



1.Pt-trans:

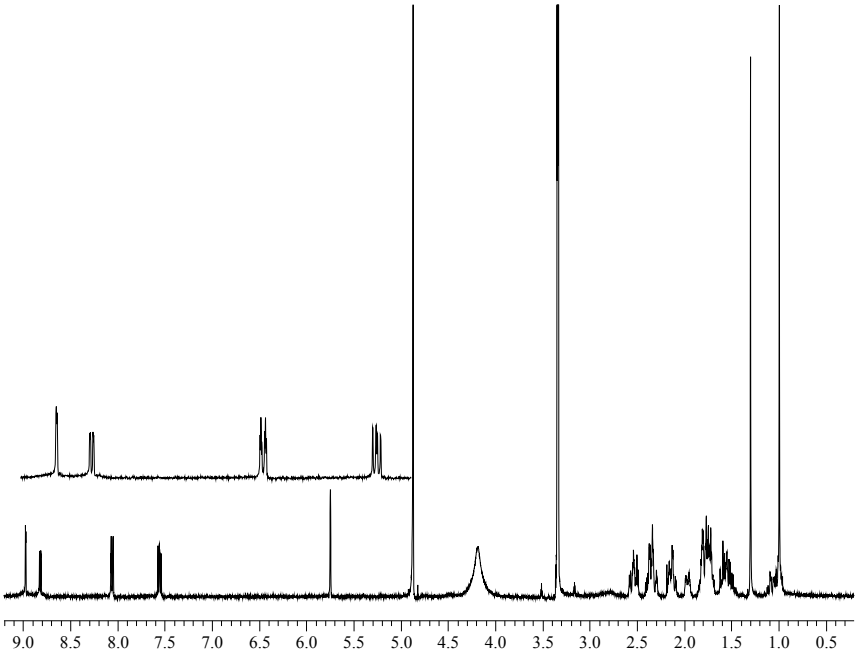


Figure 5.2.2 Comparison of the full ^{1}H NMR spectra of 1.Pt-trans and 1.Pt-cis in CD_3OD, showing the difference between the ammine groups (around 4ppm).

5.3. 4.Pt-trans and 4.Pt-cis

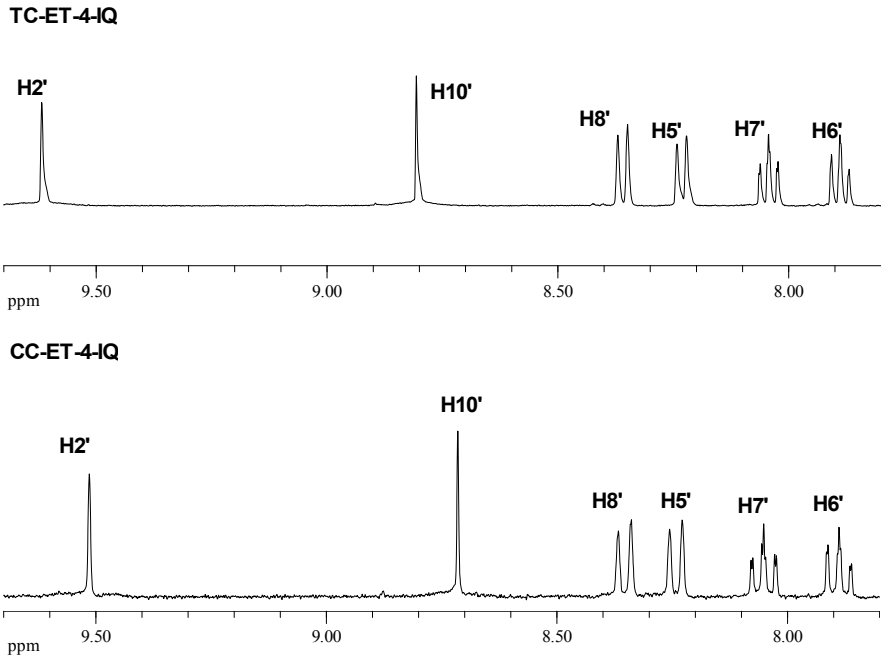


Figure 5.3.1 Comparison of the ^{1}H NMR spectra of 4.Pt-trans (upper) and 4.Pt-cis (lower) in CD_3OD.

5.4. 5.Pt-trans and 5.Pt-cis

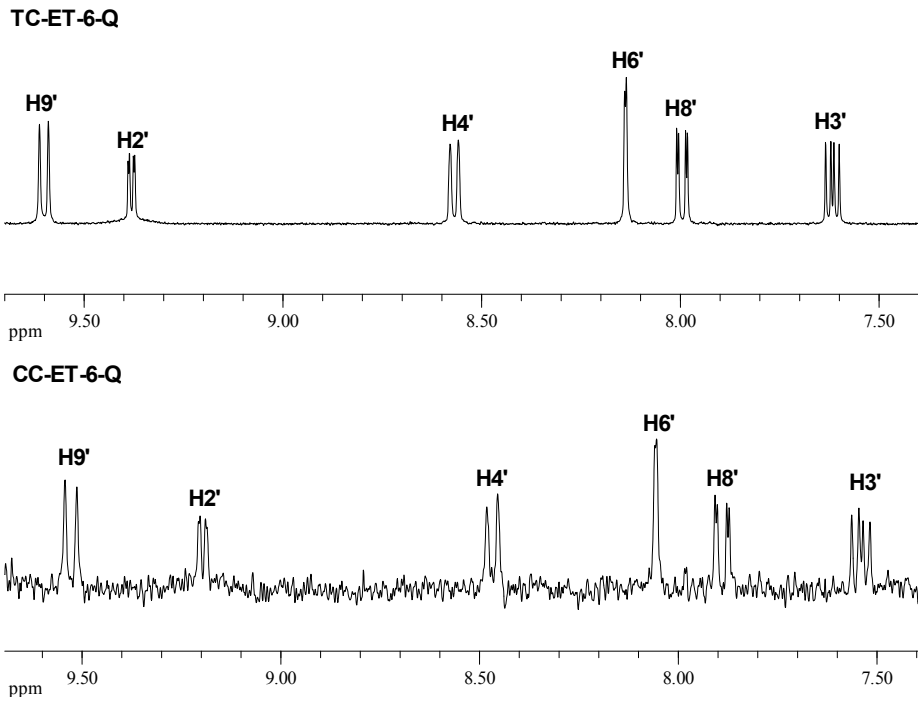


Figure 5.4.1 Comparison of the ^{1}H NMR spectra of 5.Pt-trans (upper) and 5.Pt-cis (lower) in CD_3OD.

6. Cytotoxicity

Molecule	T47D	MDA-MB-231	SKOV-3	HBL-100	A2780	A2780cisR	Rx[a]
1.Pt-cis	15.9 ± 0.5	29.2 ± 8.1	15.7 ± 0.5	7.4 ± 1	17.4 ± 3.1	33.3 ± 4.3	1.9
1.Pt-trans	63 ± 8	27.3 ± 4.7	39.1 ± 2	27.3 ± 1.9	35.3 ± 4.2	88 ± 2	2.5
2.Pt-trans	19.2 ± 0.1		26.8 ± 1.8	12.1 ± 0.8			
3.Pt-trans	51.4 ± 1.9		49.9 ± 4.5	24 ± 1.2			
4.Pt-cis	32.8 ± 0.7		26.3 ± 0.3	27.7 ± 1			
4.Pt-trans	51.4 ± 3.6		70.7 ± 2.7	28 ± 1.8			
5.Pt-cis	14.4 ± 1		16.4 ± 0.7	12.4 ± 1.4			
5.Pt-trans	38.6 ± 2.4		45.4 ± 3.5	26.3 ± 2.8			
py.Pt-cis	197 ± 17	186 ± 14	115 ± 5	210 ± 15	25.0 ± 1.2	105 ± 3	4.2
py.Pt-trans	181 ± 11	334 ± 54	98 ± 6	198± 10	72 ± 7	157 ± 2	2.2
quin.Pt-trans	75 ± 4.6		243.3 ± 7.1	98 ± 9.7			
1	>200		>200	>170			
4EE*	40		35	9			
3	48.6	20.3	21.1				
5	38.7	23.2	30.6				
Cisplatin	32.0 ± 4.8	31.3 ± 4.7	6.0 ± 1.3	7.7 ± 0.5	3.0 ± 0.5	12.8 ± 1.4	4.3

[a] Rx is ratio of IC50 for a compound in A2780cisR compared to A2780. * indicate a oestradiol derivative.

7. Cellular uptake

	SKOV-3			T47D			MDA-MB-231		
	whole cell	cytoplasm	nuclei	whole cell	cytoplasm	nuclei	whole cell	cytoplasm	nuclei
1.Pt-cis	4.96	4.08	0.09	12.63	4.46	0.26	12.75	9.57	2.21
1.Pt-trans	8.09	8.36	0.51	23.38	8.87	0.21	8.34	8.9	0.89
py.Pt-cis	114.04	9.1	15.89	69.39	3.74	5.64	92.99	6.04	6.59
py.Pt-trans	57.49	37.02	5.93	3.79	2.35	0.74	11.95	5.27	0.48
cisplatin	36.09	16.78	4.29	15.51	6.68	0.21	13.18	10.8	1.88

Table 7.1 pmoles of Pt in T47D, SKOV-3 and MDA-MB-231 per million cells after 3 hours of treatment with 30 μM of complexes.

	SKOV-3				T47D				HBL-100			
	Pt added (µmol)	**Pt in cells (nmol)**	**% Pt delivered**	**nmol Pt/µmol DNA (bp)**	**Pt added (µmol)**	**Pt in cells (nmol)**	**% Pt delivered**	**nmol Pt/µmol DNA (bp)**	**Pt added (µmol)**	**Pt in cells (nmol)**	**% Pt delivered**	**nmol Pt/µmol DNA (bp)**
1.Pt-cis	0.08	0.05	0.06	0.49	0.08	0.10	0.13	0.20	0.04	0.03	0.08	-
1.Pt-trans	0.2	0.14	0.07	-	0.31	0.80	0.25	0.56	0.14	0.14	0.10	0.20
4.Pt-cis	0.13	0.12	0.09	-	0.14	0.30	0.18	-	0.14	0.22	0.16	-
py.Pt-cis	0.57	0.05	0.01	0.73	0.98	0.18	0.02	0.51	1.05	0.11	0.01	-
py.Pt-trans	0.49	0.05	0.01	6.39	0.91	0.12	0.01	0.44	0.99	0.16	0.02	0.59
cisplatin	0.03	0.03	0.1	0.93	0.16	0.03	0.02	0.30	0.04	0.03	0.08	0.25

Table 7.2 nmoles of Pt in T47D, SKOV3 and HBL-100 per million cells after 72 hours of treatment with IC_{50} µM of complexes.