Supporting Information

Synthesis of fused tetrahydropyrido[2,3-c]coumarin derivatives as potential inhibitors for dopamine d3 receptors, catalyzed by hydrated ferric sulfate

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Experimental General

Melting points were recorded on a Büchi melting point apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer 281 IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Varian 400 spectrometer by using TMS as internal reference; chemical shifts (δ scale) are reported in parts per million (ppm). Elemental analyses were carried out using Perkin-Elmer 2400 Series II CHNS/O analyzer at the Department of Chemistry, Indian Institute of Technology Guwahati. Column chromatographic separations were performed using Merck silica gel (60-120 mesh).

Crystallographic Description

Crystal data were collected with Bruker Smart Apex-II CCD diffractometer using graphite monochromated MoKα radiation (λ = 0.71073 Å) at 296 K. Cell parameters were retrieved using SMART software and refined with SAINT on all observed reflections. Data reduction was performed with the SAINT software and corrected for Lorentz and polarization effects. Absorption corrections were applied with the program SADABS. The structure was solved by direct methods implemented in SHELX-97 program and refined by full-matrix least-squares methods on F2. All non-hydrogen atomic positions were located in difference Fourier maps and refined anisotropically. The hydrogen atoms were placed in their geometrically generated positions. Compound **4c** empirical formula $C_{21}H_{18}ClNO_3$, colorless crystal, formula wt 367.81, Triclinic, P-1, a = 9.4104(10) Å, b = 9.6627(9) Å, c = 10.6311(10) Å, V = 866.08(15) $Å^3$, Z = 2, F (0 0 0) = 384, GOF(S) = 1.004. Final indices R_{obs} = 0.0384, wR_{obs} = 0.0815 with I > 2r(I); R_{all} = 0.0504, wR_{all} = 0.0865 for all data. Compound **5o** empirical formula $C_{18}H_{15}NO_4$, colorless crystal, formula wt 309.31, Monoclinic, P 21/c, a = 11.8099(5) Å, b = 9.7399(5) Å, c = 12.7370(6) Å, V = 1461.83(12) $Å^3$, Z = 4, F (0 0 0) = 648, GOF(S) = 1.031. Final indices R_{obs} = 0.0503, wR_{obs} = 0.1131 with I > 2r(I); R_{all} = 0.0920, wR_{all} = 0.1292 for all data.

Table S1. Crystal data and structure refinement for **4c** and **5o**. For atomic coordinates and equivalent isotropic displacement parameters and bond angles, please check the CIF.

	Compound 4c (trans CCDC811857)	Compound 5o (cis CCDC 838311)
Identification code	Cl-AC-DHP	Fur-AC-DHP
Empirical formula	$C_{21}H_{18}ClNO_3$	$C_{18}H_{15}NO_4$
Formula weight	367.81	309.31
Temperature	296(2) K	296(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system	Triclinic	Monoclinic
Space group	P-1	'P 21/c'
Unit cell dimensions		
a	9.4104(10) Å	11.8099(5) Å
b	9.6627(9) Å	9.7399(5) Å

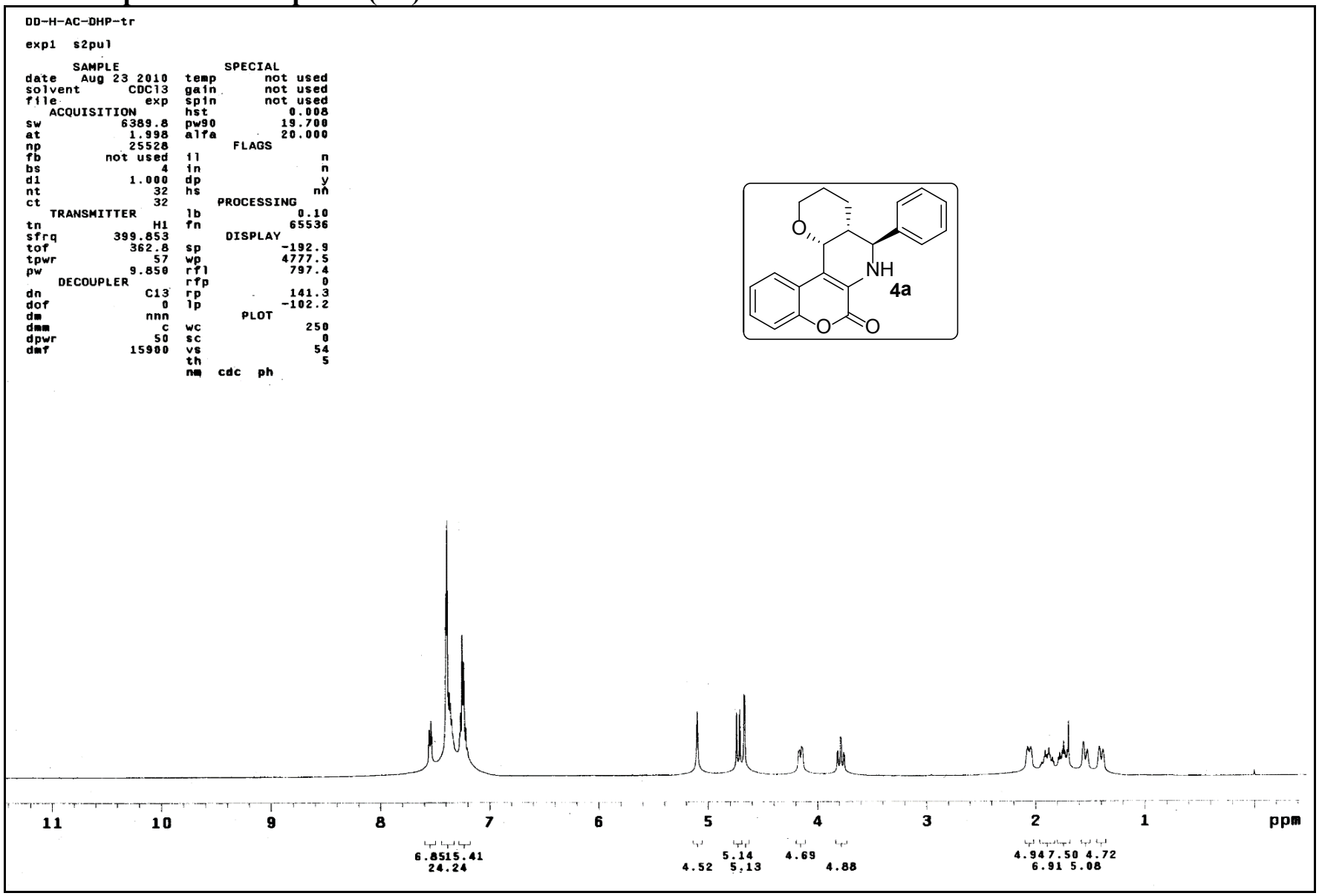
c	10.6311(10) Å	12.7370(6) Å
α	78.191(5)	90.00º
β	66.629(6)º	93.828º(2)
γ	89.263(5)º	90.00º
Volume	866.08(15) $Å^3$	1461.83(12) $Å^3$
Z	2	4
Density (calculated)	1.410 g/cm^3	1.405 g/cm^3
Absorption coefficient	0.242 mm^{-1}	0.100 mm^{-1}
F(000)	384	648
Theta range for data collection	2.14 to 28.34º	1.73 to 34.04º
Index ranges	-11 <=h<=11, -11<=k<=12, -12<=l<=14	-18<=h<=18, -13<=k<=13, -18<=l<=19
Reflections collected	6806	22111
Independent reflections	4322 R_{int} = 0.0415	5974 R_{int} = 0.0273
Completeness to θº	98.4% (θ = 28.34º)	97.8% (θ = 34.04º)
Refinement method	Full-matrix least-squares on F2	Full-matrix least-squares on F2
Data / restraints / parameters	4322 / 0 / 240	5448 / 0 / 212
Goodness-of-fit on F2	1.004	1.031
Final R indices [>2sigma(I)]	R_{obs} = 0.0384, wR_{obs} = 0.0815	R_{obs} = 0.0503, wR_{obs} = 0.1131
R indices (all data)	R_{all} = 0.0504, wR_{all} = 0.0865	R_{all} = 0.0920, wR_{all} = 0.1292
Largest diff. peak and hole	0.216 and -0.210e.$Å^{-3}$	0.173 and -0.210e.$Å^{-3}$

Table SI2. Docking analysis of the synthesized compounds on chain A of human dopamine D3 receptor (PDB Id: 3PBL)

Product	Score	Substituents, n	Conformations in the largest cluster [out of 100]	H-bond interactions	Pi interactions	Hydrophobic contact residues
5r	-10.56	Me($C_{4'}$), NO_2(C_{10}), n=2	100	S192	F345	V86
5g	-10.46	OMe($C_{4'}$), OMe($C_{3'}$), H(C_{10}), n=2	100	-	F345	V86, L89, V111, I183
5d	-9.94	Br($C_{4'}$), H(C_{10}), n=2	100	-	F345	V86, V111, I183
5c	-9.73	Cl($C_{4'}$), H(C_{10}), n=2	100	-	F345	V86, V111, I183
5b	-9.6	Me($C_{1'}$), H(C_{10}), n=2	100	-	F345	V86, V111, I183
5f	-9.54	OMe($C_{4'}$), H(C_{10}), n=2	100	-	F345	V86, L89, V111, I183
5m	-9.51	Br ($C_{4'}$), H(C_{10}), n=1	100	-	F345	V86, V111
5l	-9.28	Cl ($C_{4'}$), H(C_{10}), n=1	100	-	F345	V86, V111, F345
4f	-9.26	OMe($C_{4'}$), H(C_{10}), n=2	100	Y365	-	V86, L89, F106, V107, T369
5p	-9.24	Cl($C_{4'}$), Br(C_{10}), n=2	100	-	F345	V107, I183, F345
5a	-9.11	H($C_{4'}$), H(C_{10}), n=2	100	-	F345	V86, L89, V111, I183
5e	-9.10	F($C_{4'}$), H(C_{10}), n=2	100	-	F345	V86, V111, I183
5n	-9.09	MeO($C_{4'}$), H(C_{10}), n=1	100	-	F345	V86, V111, I183
5k	-8.92	H($C_{4'}$), H(C_{10}), n=1	100	-	F345	V111, C114, F346
5s	-8.80	Cl, ($C_{4'}$), MeO (C_{10}), n=2	100	-	F345	V86, V107, I183, F345
5o	-8.39	Furfuryl (C_4), H(C_{10}), n=1	100	I183	-	V111, C114, S196
5h	-8.36	Furfuryl(C_4), H(C_{10}), n=2	100	-	F345	I183
5q	-8.11	Furfuryl(C_4), Br (C_{10}), n=2	100	-	F345	V107, I183
4g	-8.10	OMe($C_{4'}$), OMe($C_{3'}$), H(C_{10}), n=2	100	D110	F345	I183, F345, H349, T369
4s	-8.01	Cl, ($C_{4'}$), MeO (C_{10}), n=2	100	Y365	-	V86, L89, F106, V107, T369
4d	-7.99	Br($C_{4'}$), H(C_{10}), n=2	100	Y365	-	V86, L89, F106, V107, T369

4o	-7.98	Furfuryl (C_4), H(C_{10}), n=1	100	Y365	-	V86, L89, F106, V107, T369
4k	-7.94	H($C_{4'}$), H(C_{10}), n=1	100	D110	F345	I183, F345, H349
4h	-7.91	Furfuryl(C_4), H(C_{10}), n=2	100	Y365	F345	S182, F345, T369, F345
4b	-7.89	Me($C_{4'}$), H(C_{10}), n=2	100	Y365	-	V86, L89, F106, V107, T369
4c	-7.86	Cl($C_{4'}$), H(C_{10}), n=2	100	Y365	-	V86, L89, F106, V107, T369
4l	-7.64	Cl ($C_{4'}$), H(C_{10}), n=1	100	D110	F345	S182, W342, F345, T369, F345
4p	-7.32	Cl($C_{4'}$), Br(C_{10}), n=2	100	Y365	-	V86, T369
4q	-7.30	Furfuryl(C_4), Br (C_{10}), n=2	100	D110	F345	I183, F345
4m	-7.28	Br ($C_{4'}$), H(C_{10}), n=1	100	D110	F345	L89, F345
4c	-7.27	Cl($C_{4'}$), H(C_{10}), n=2	100	Y365	-	V86, L89, F106, V107, T369
4e	-7.12	F($C_{4'}$), H(C_{10}), n=2	100	Y365	-	V86, L89, F106, V107, T369
4a	-7.04	H($C_{4'}$), H(C_{10}), n=2	72	D110	F345	S182, F345, H349, T369
4r	-6.95	Me($C_{4'}$), NO_2(C_{10}), n=2	100	D110	F345	L89, S182, W342, F345, T369
4n	-6.40	MeO($C_{4'}$), H(C_{10}), n=1	85	D110	F345	L89, F345
ETQ*	-8.207	compute_AutoDock41_score.py				

^{1}HNMR Spectra of Compound(4a)



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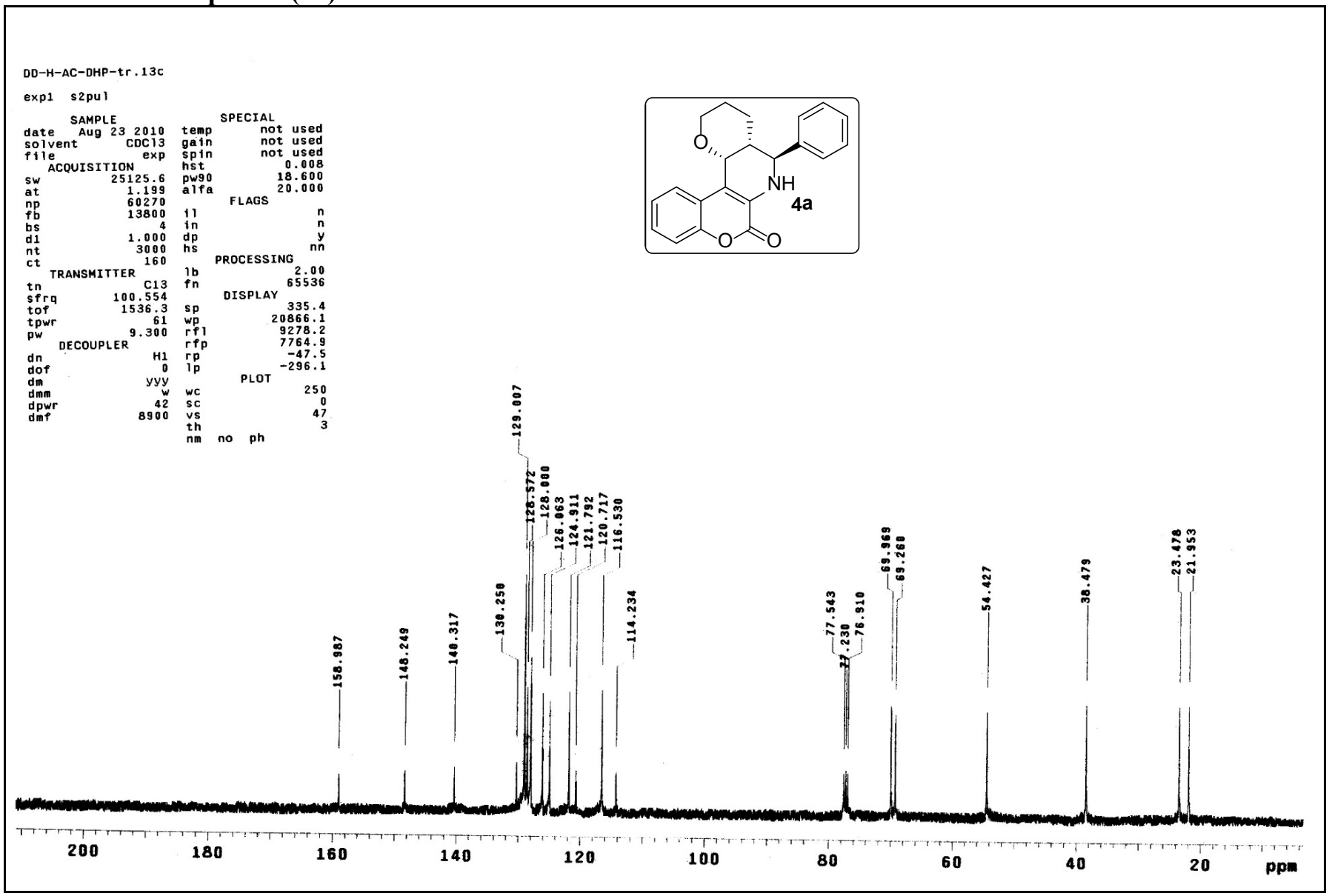

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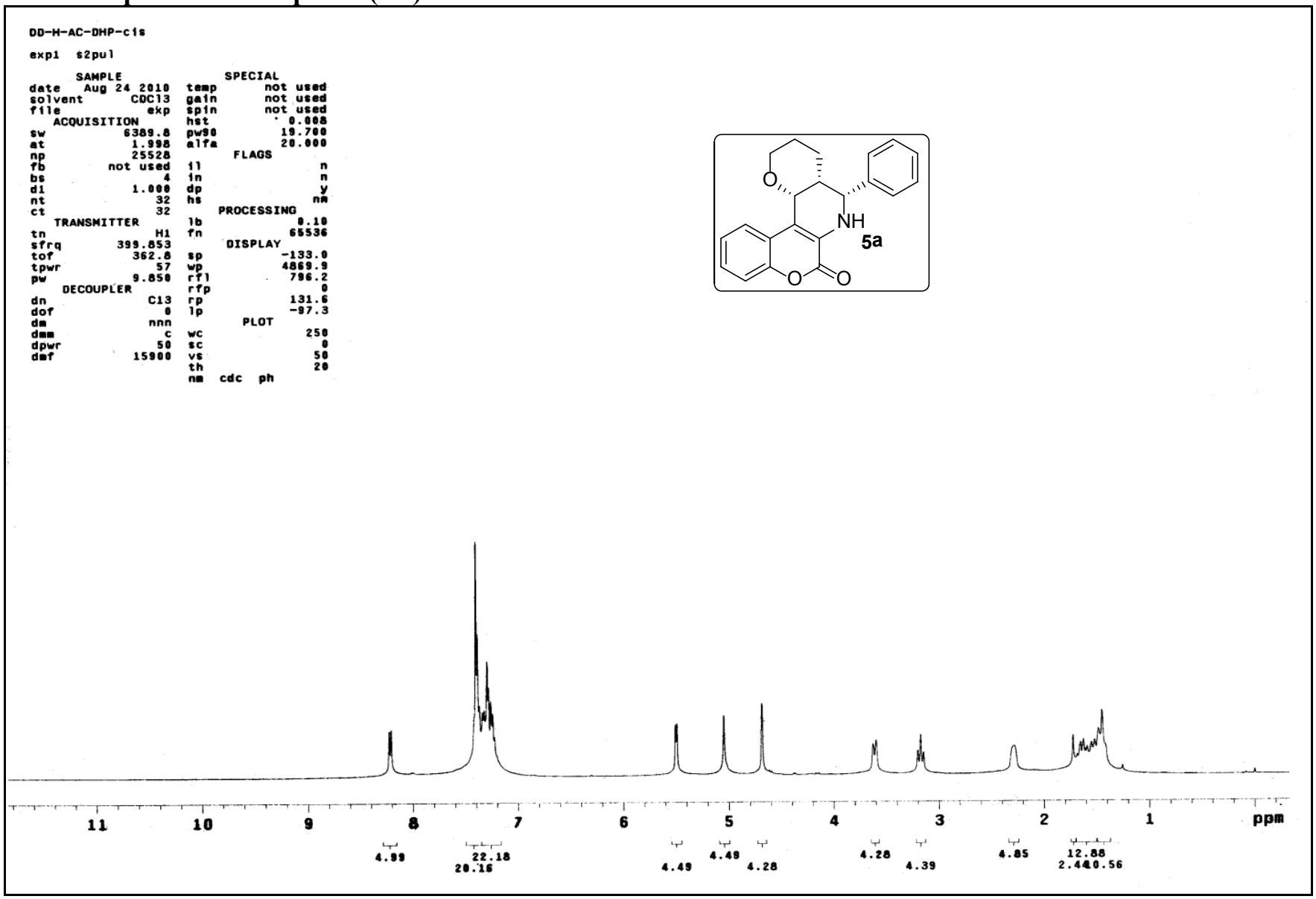
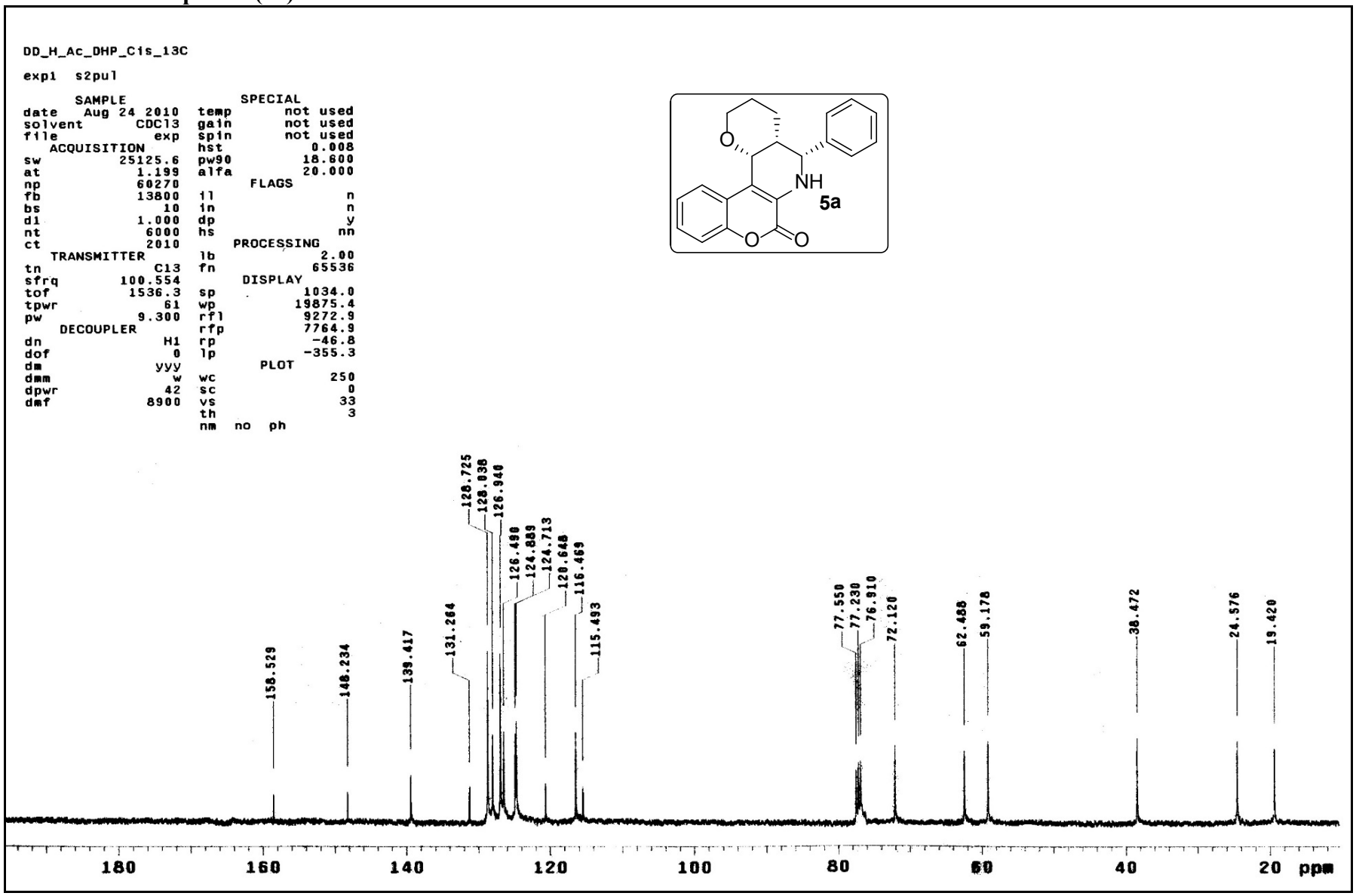
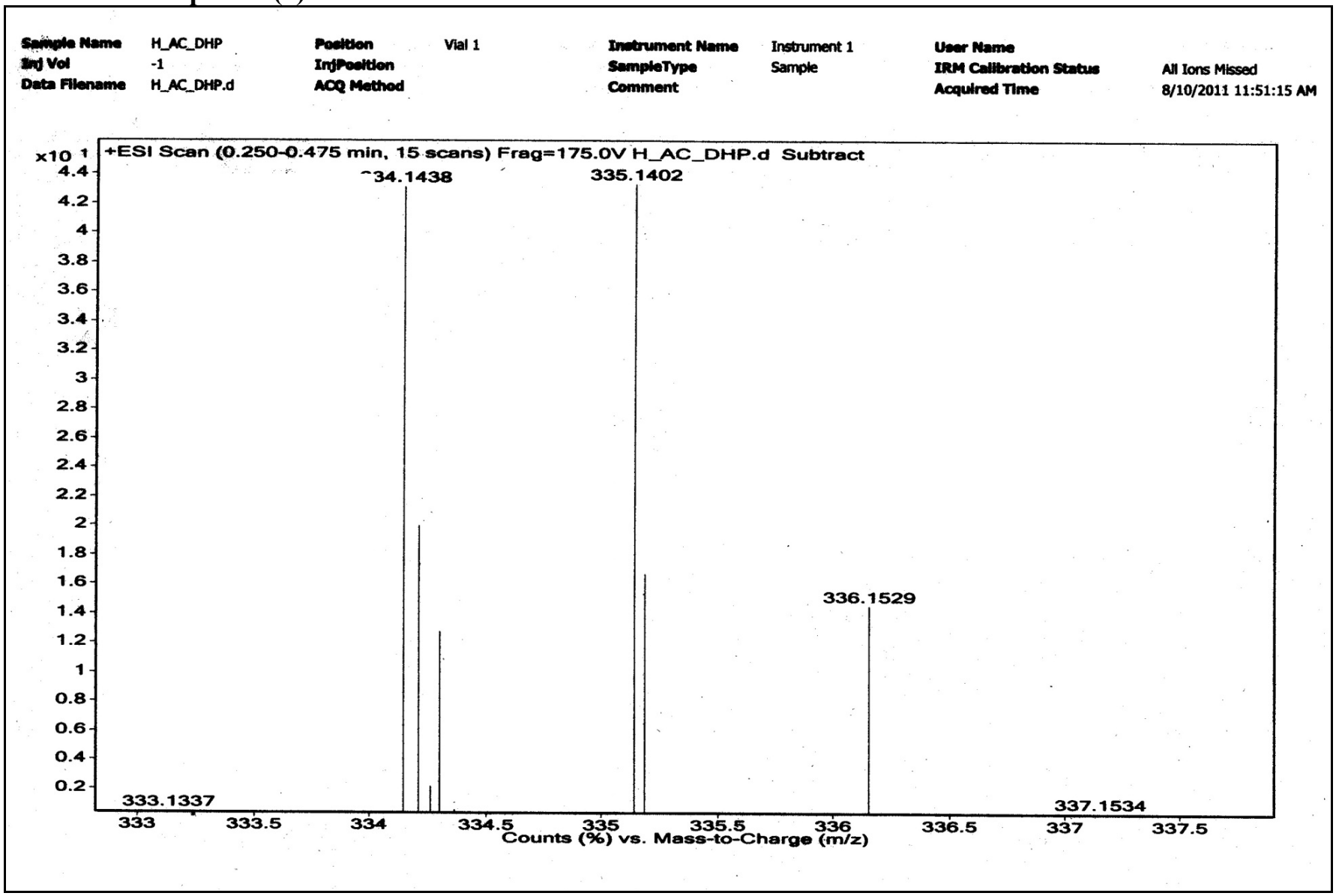


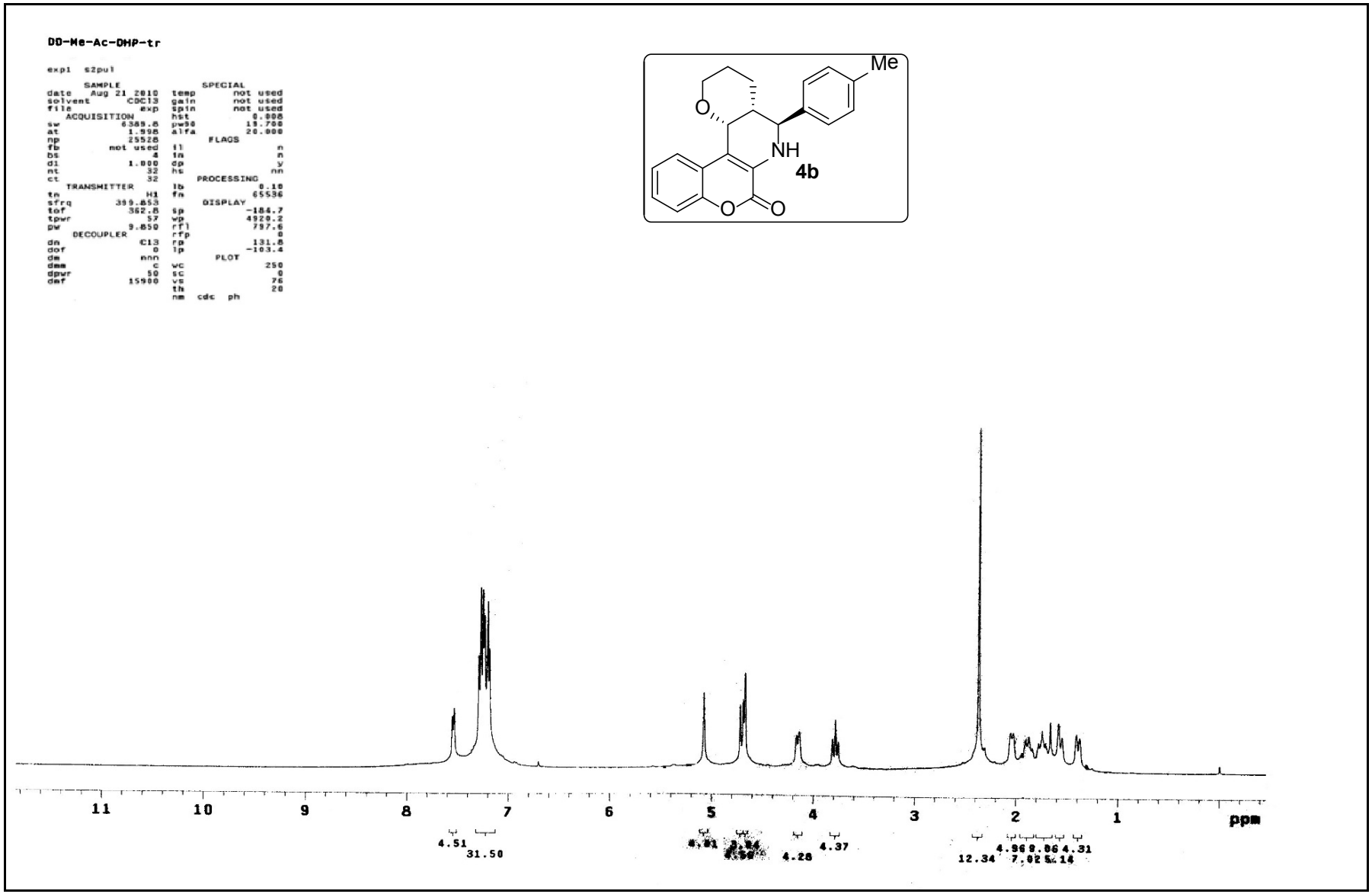
^{13} CNMR of Compound (5a)



HRMS of Compound (a)



[1]HNMR Spectra of Compound(4b)



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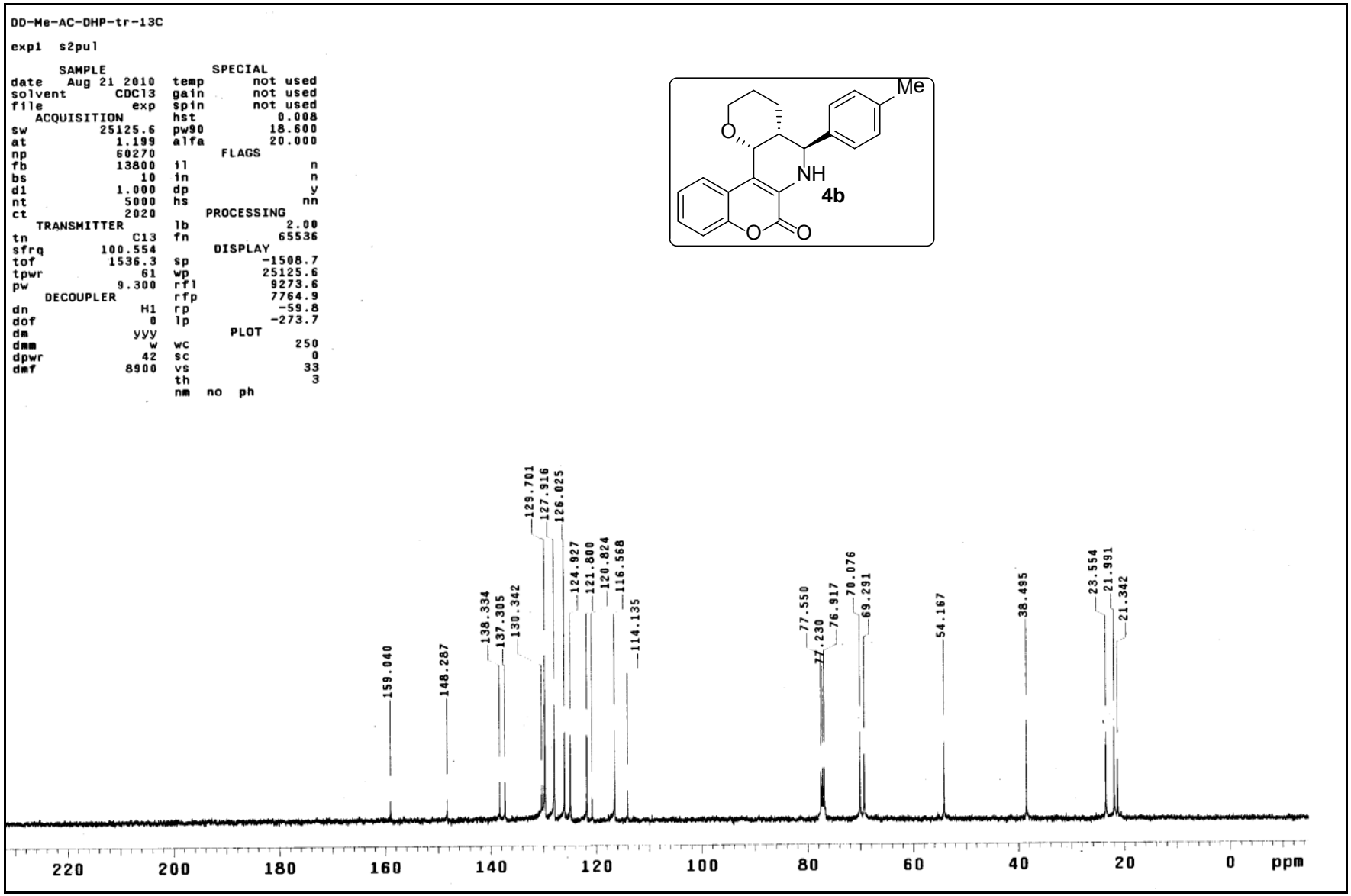
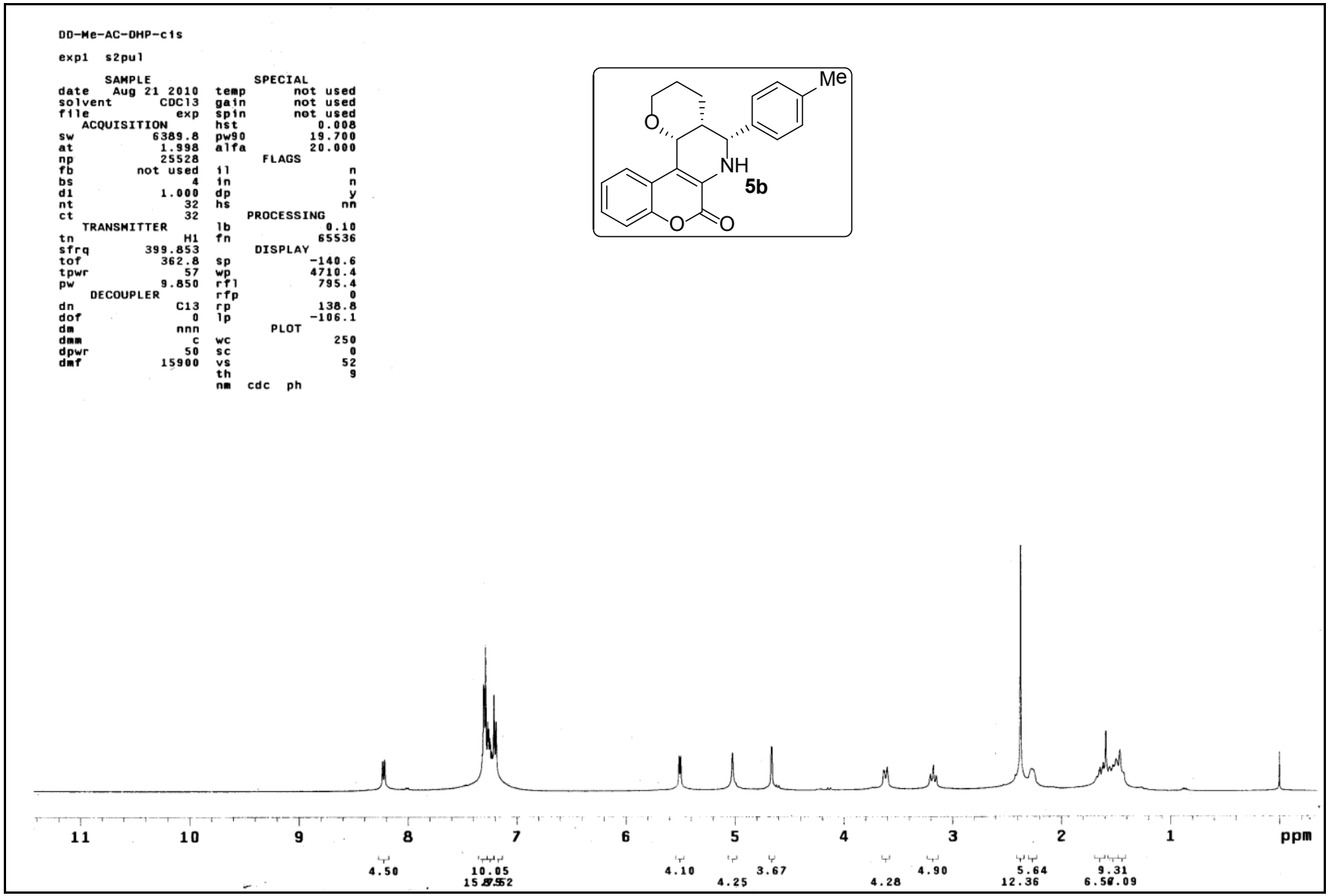


^{1}HNMR Spectra of Compound(5b)



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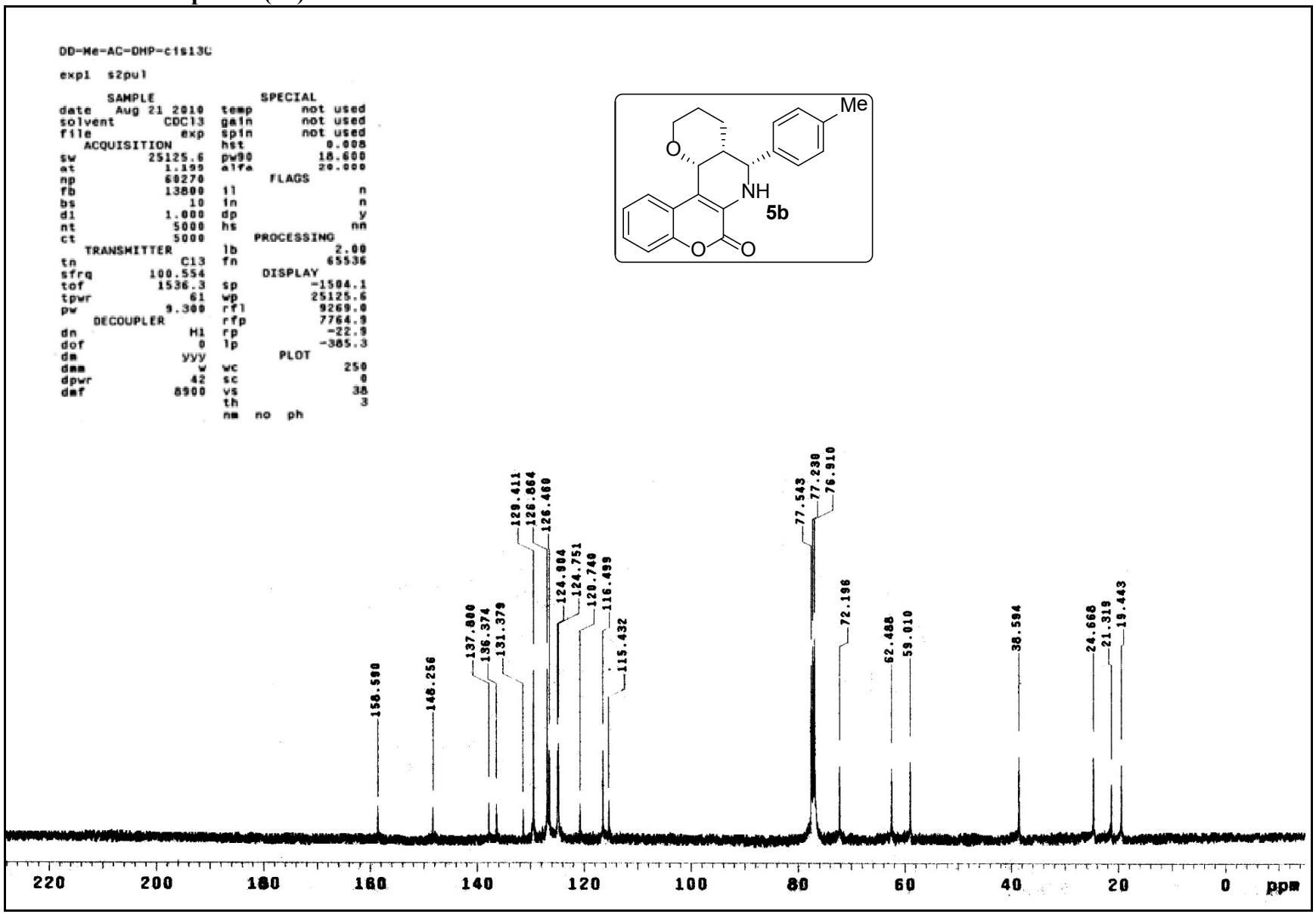
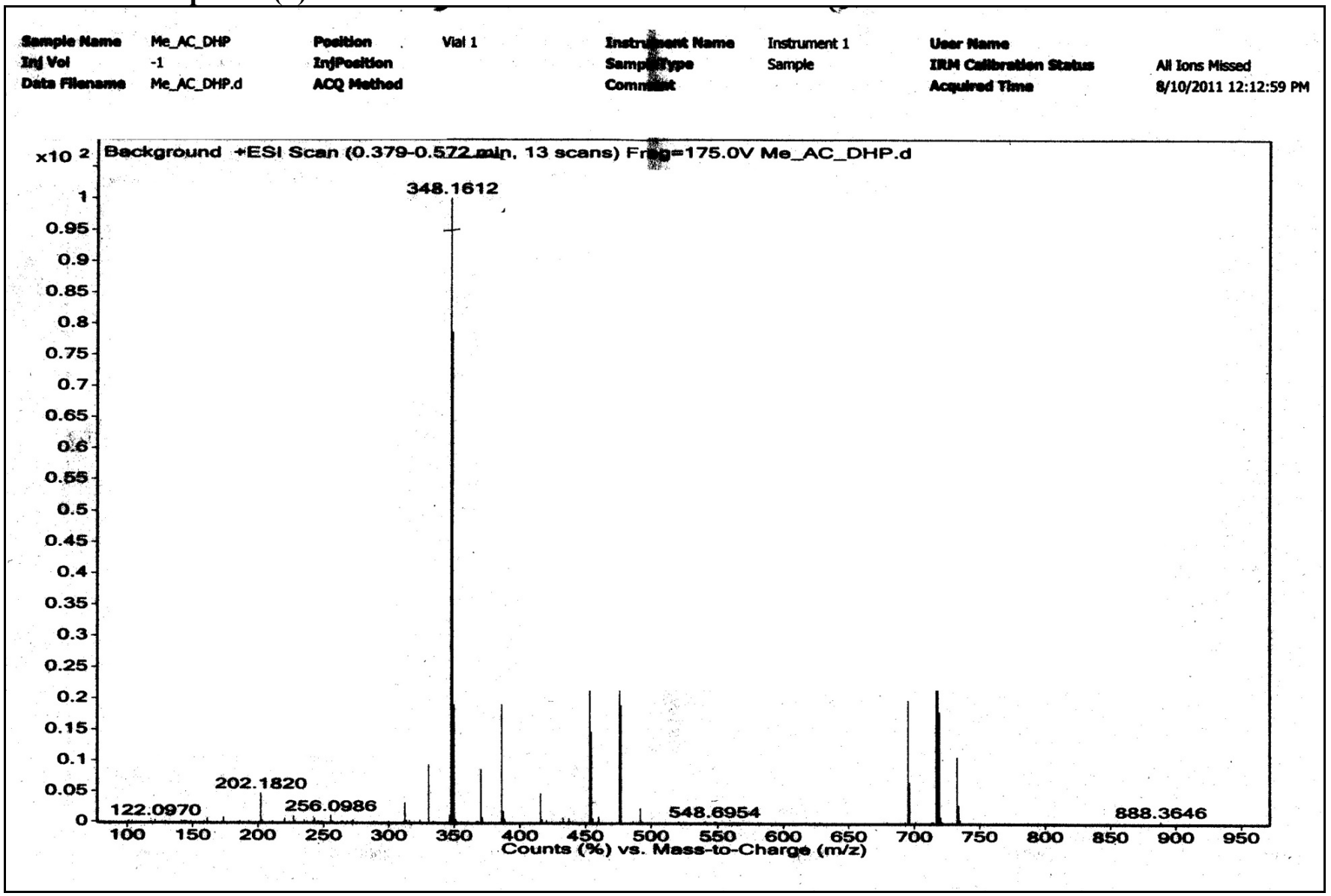
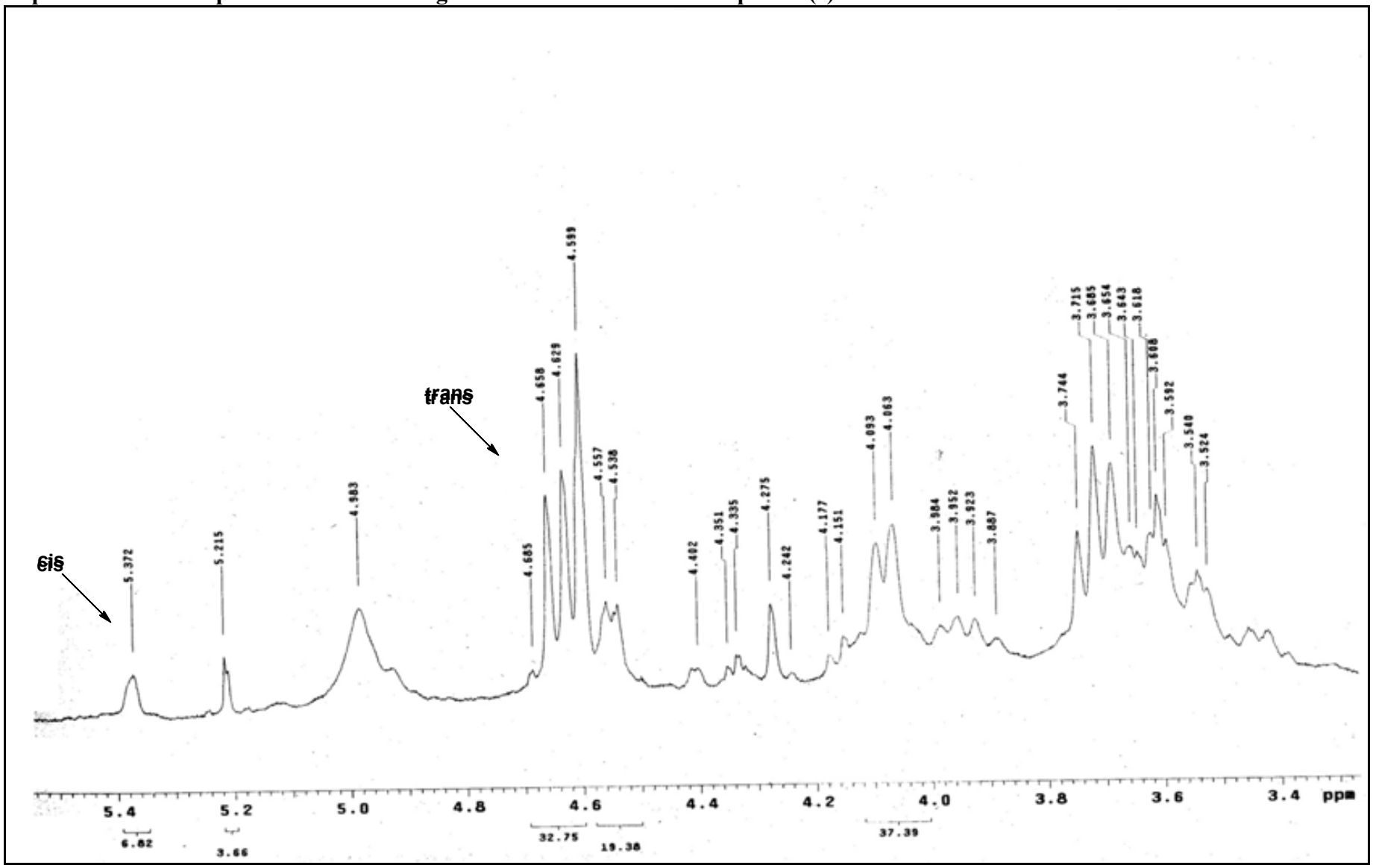


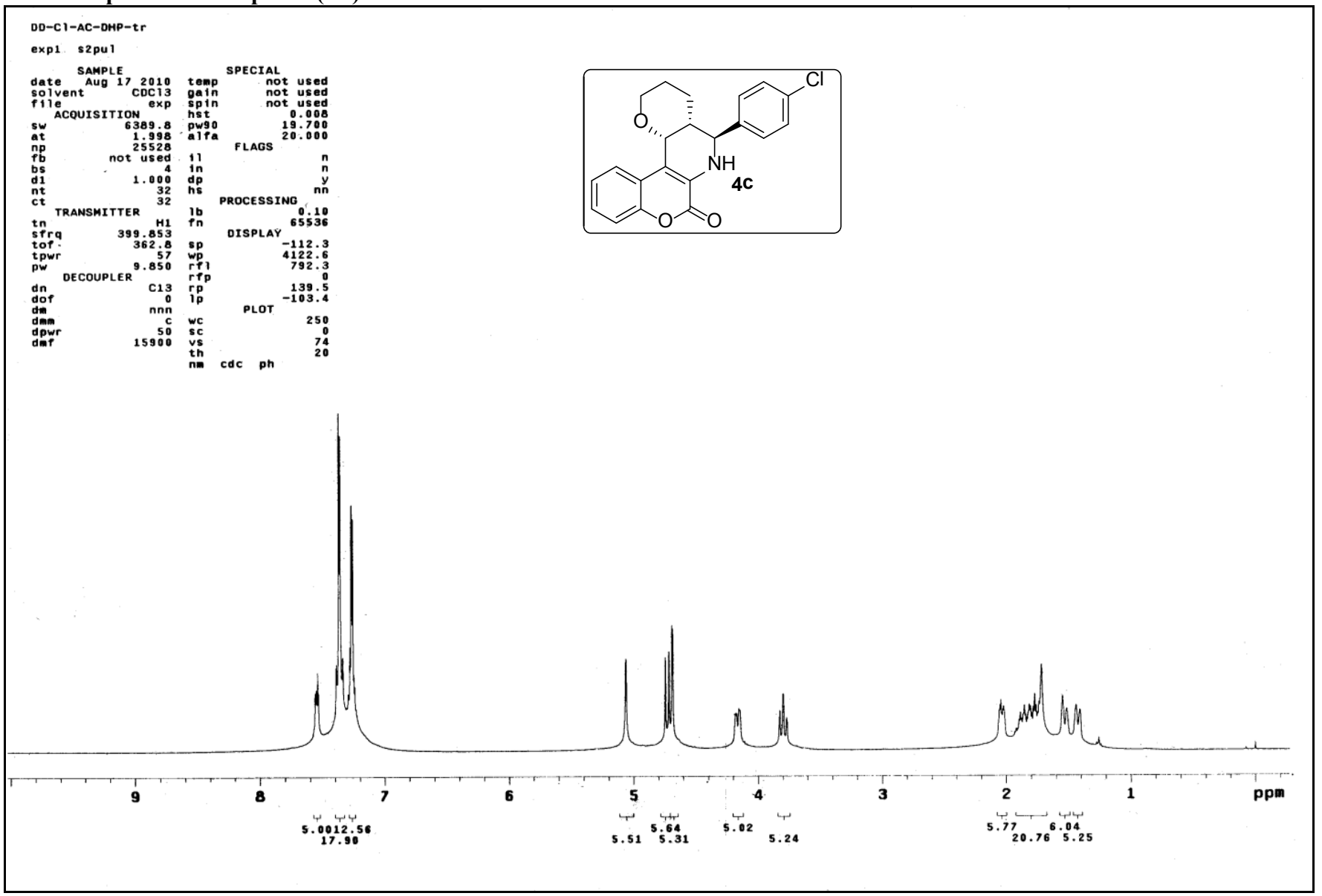
HRMS of Compound (b)



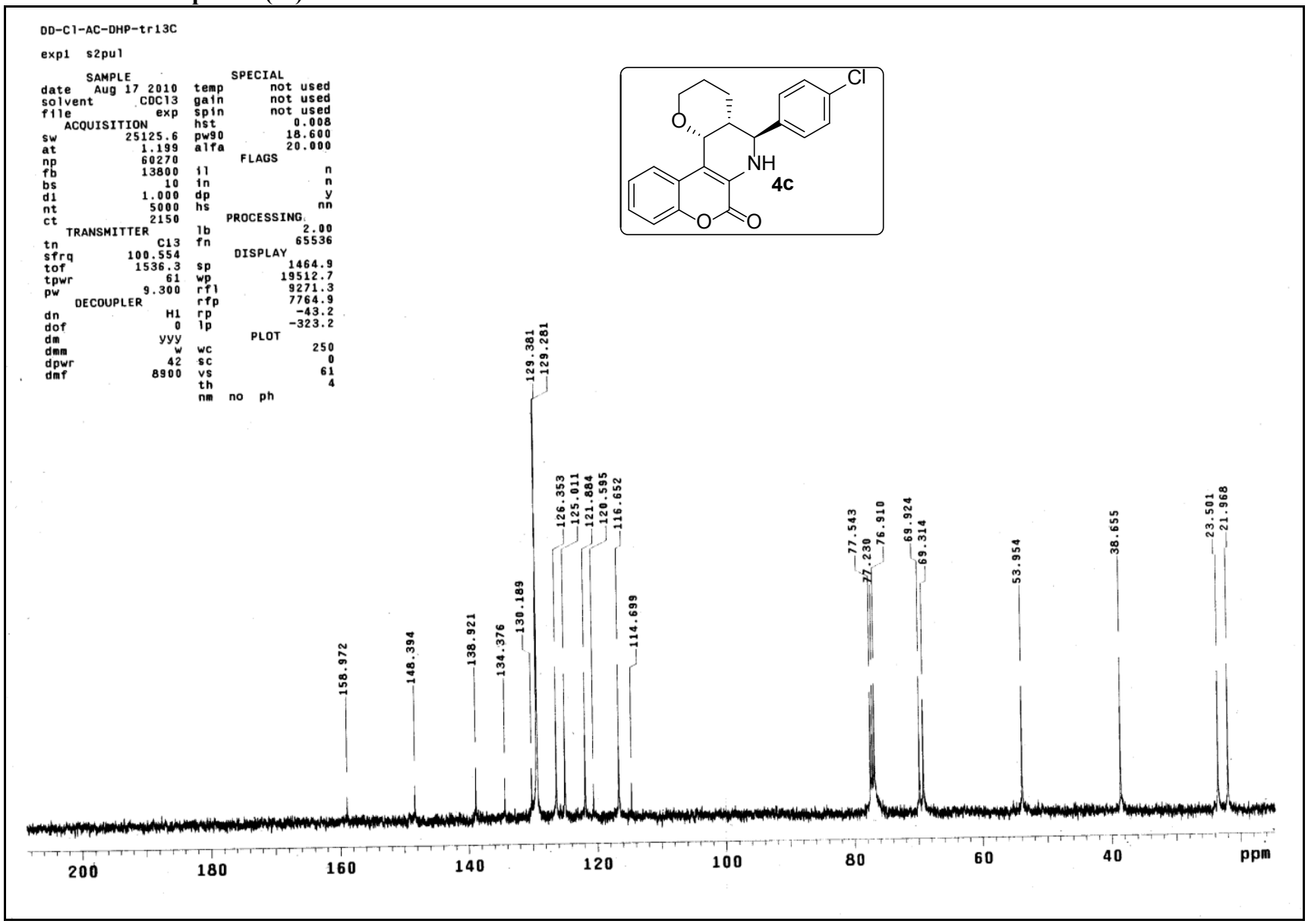
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (c)



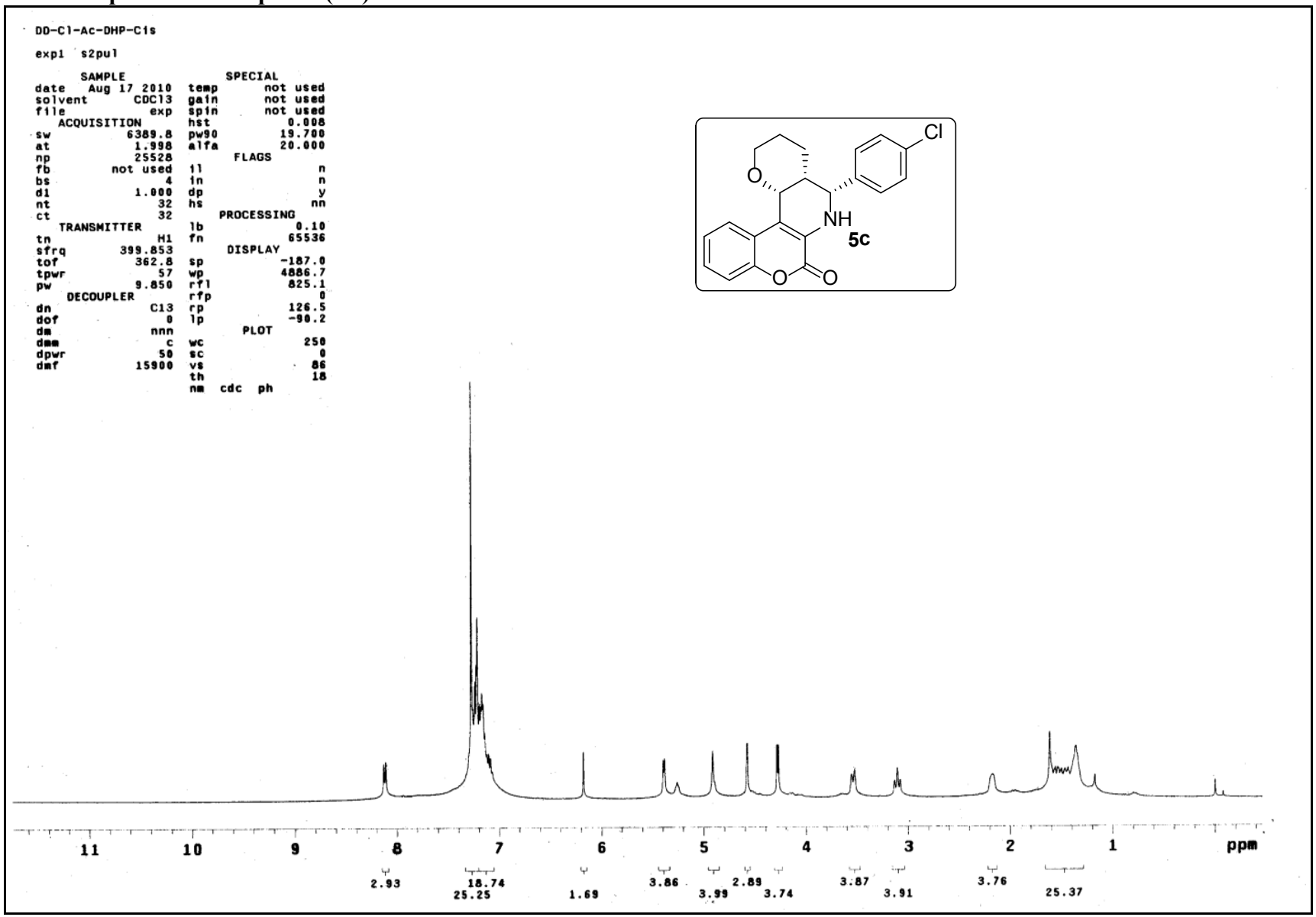
[1]HNMR Spectra of Compound(4c)



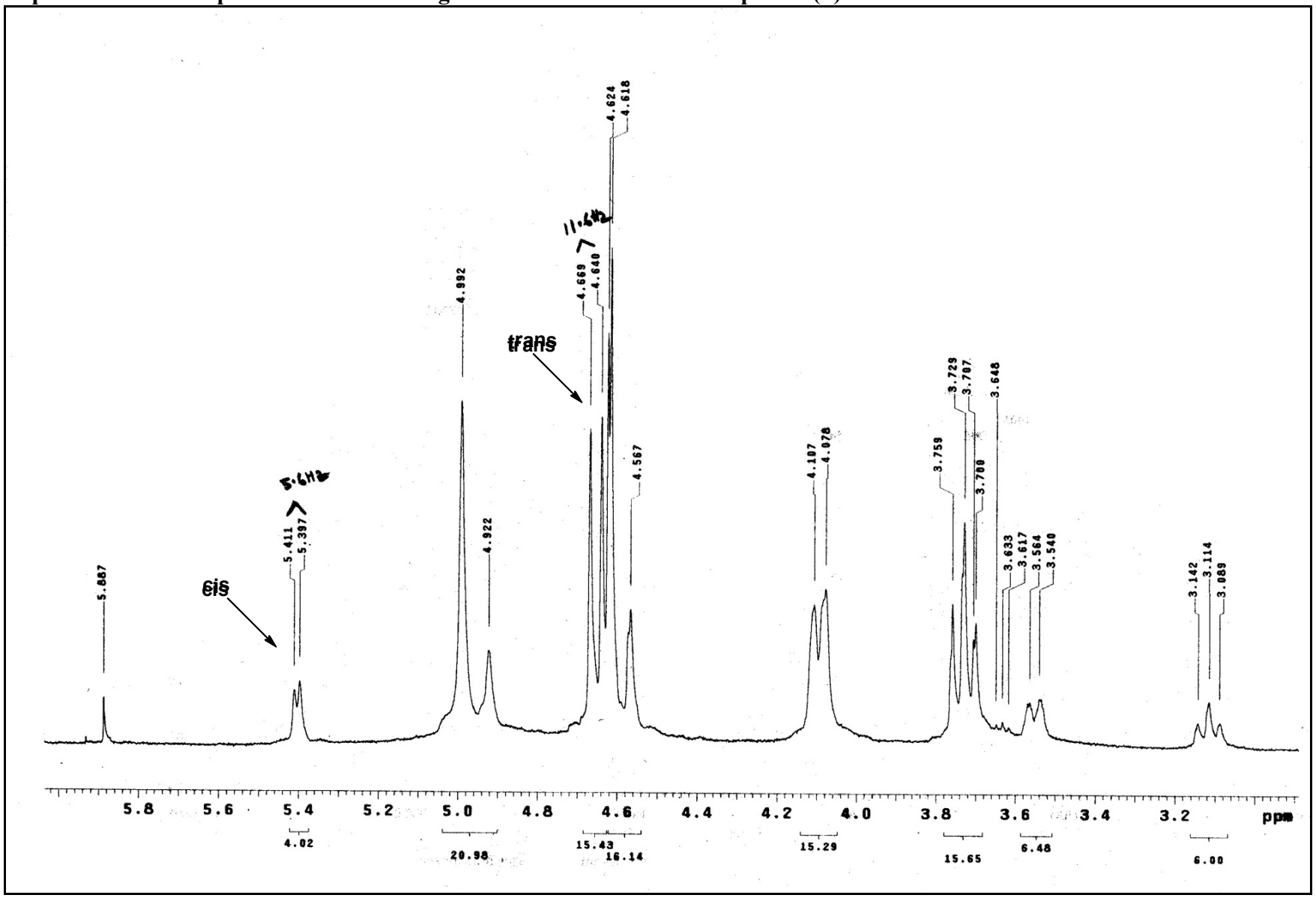
13 CNMR of Compound (4c)



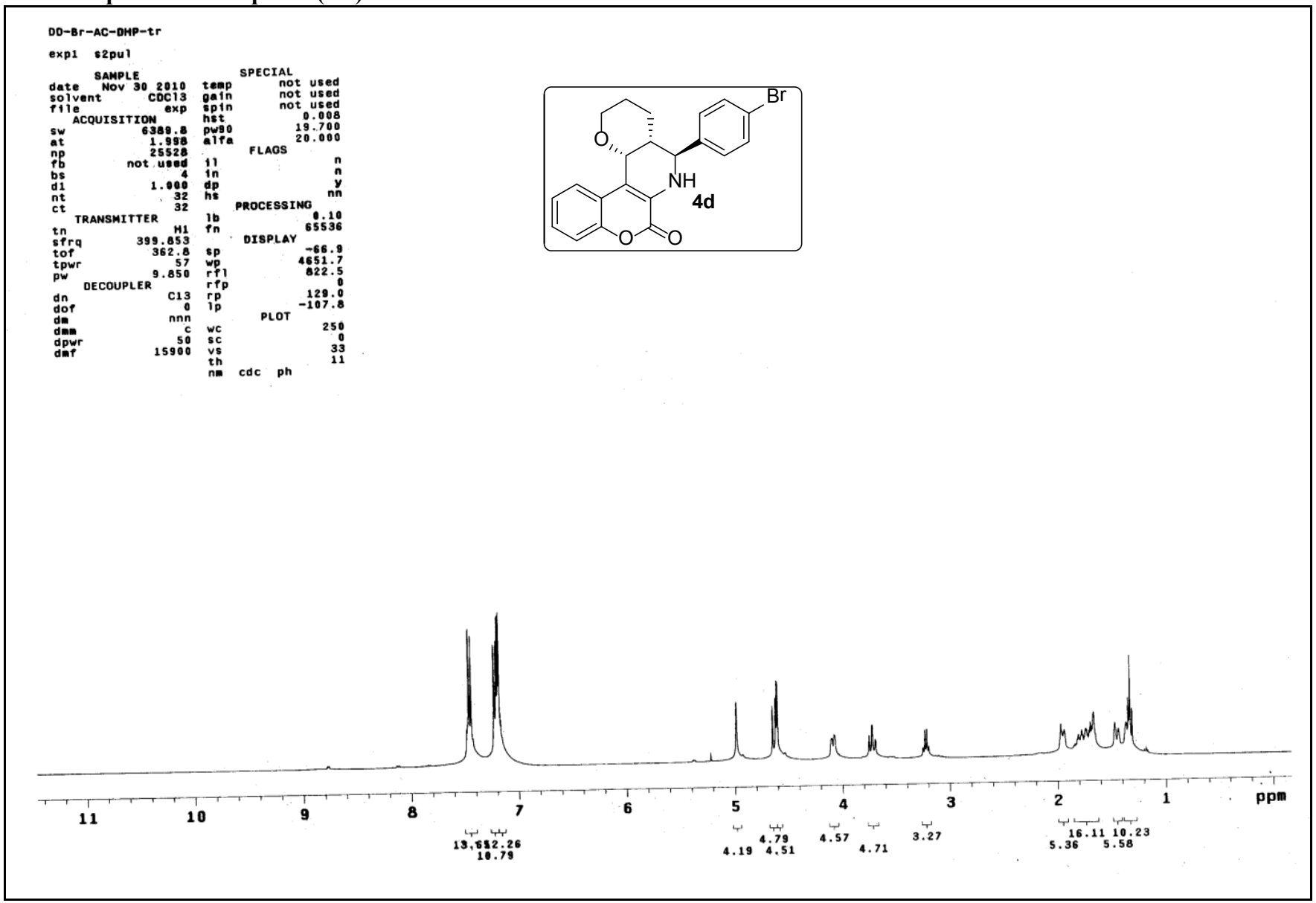
[1]HNMR Spectra of Compound(5c)



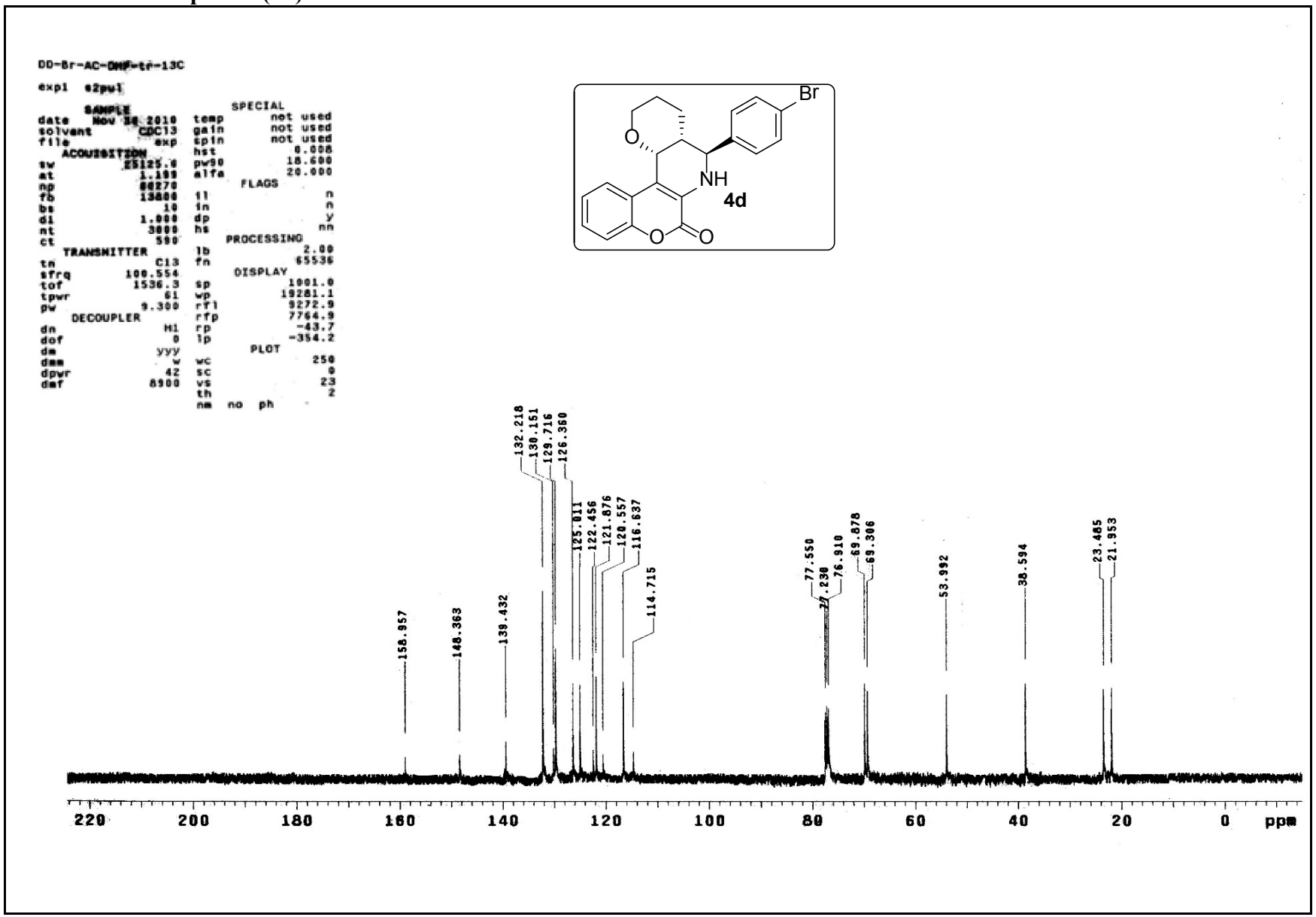
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (d)



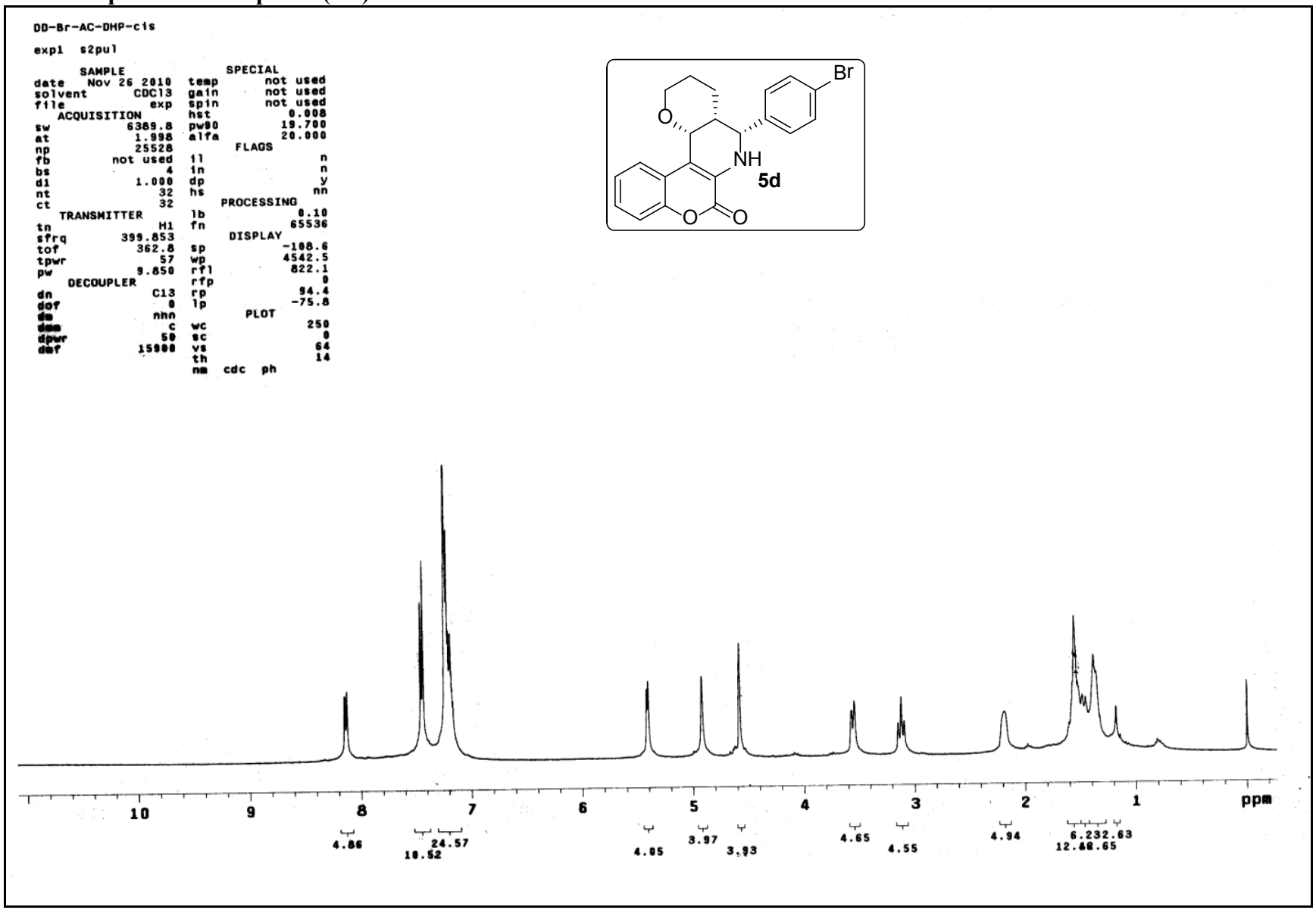
^{1}HNMR Spectra of Compound(4d)



13 CNMR of Compound (4d)



[1]HNMR Spectra of Compound(5d)



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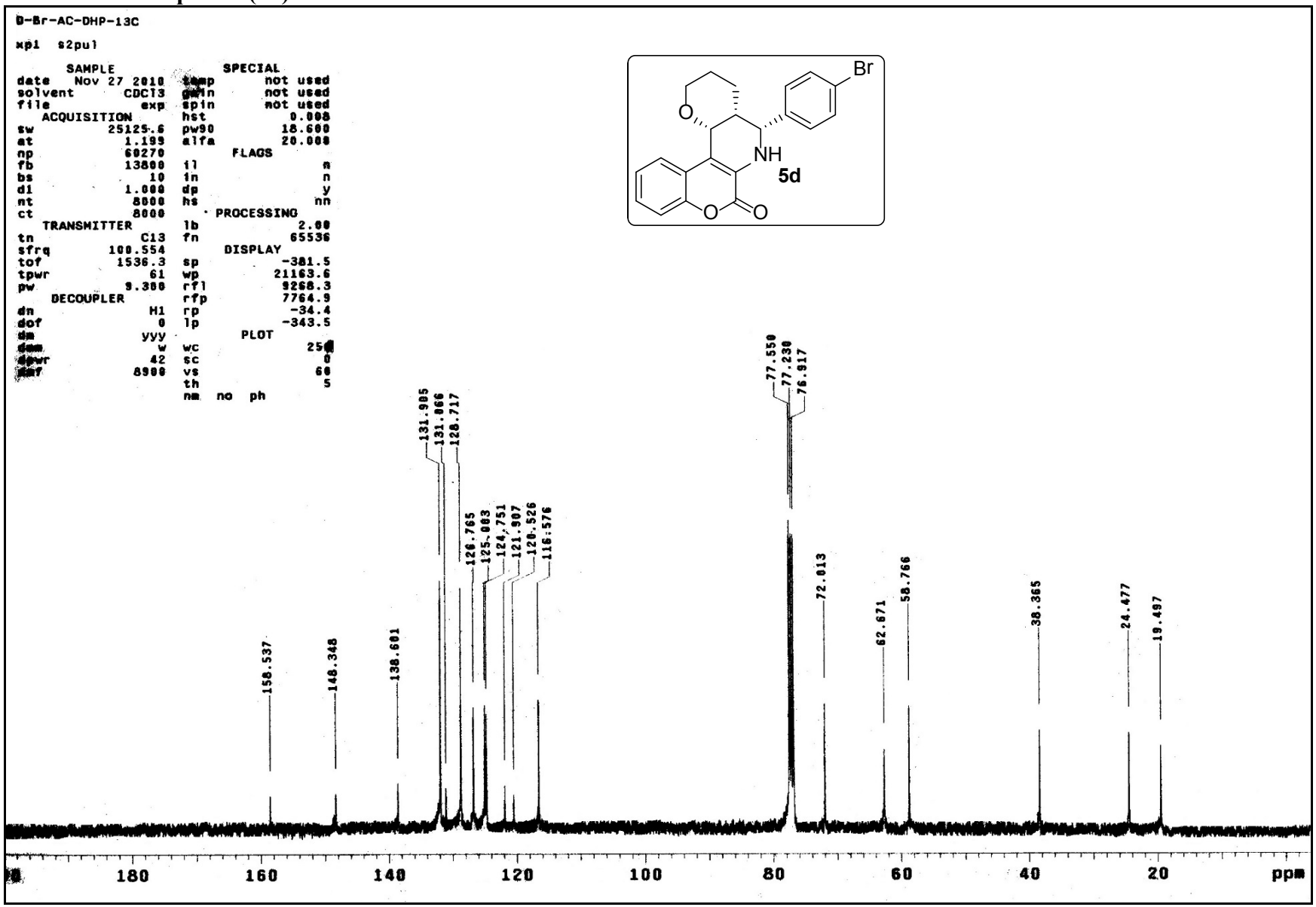
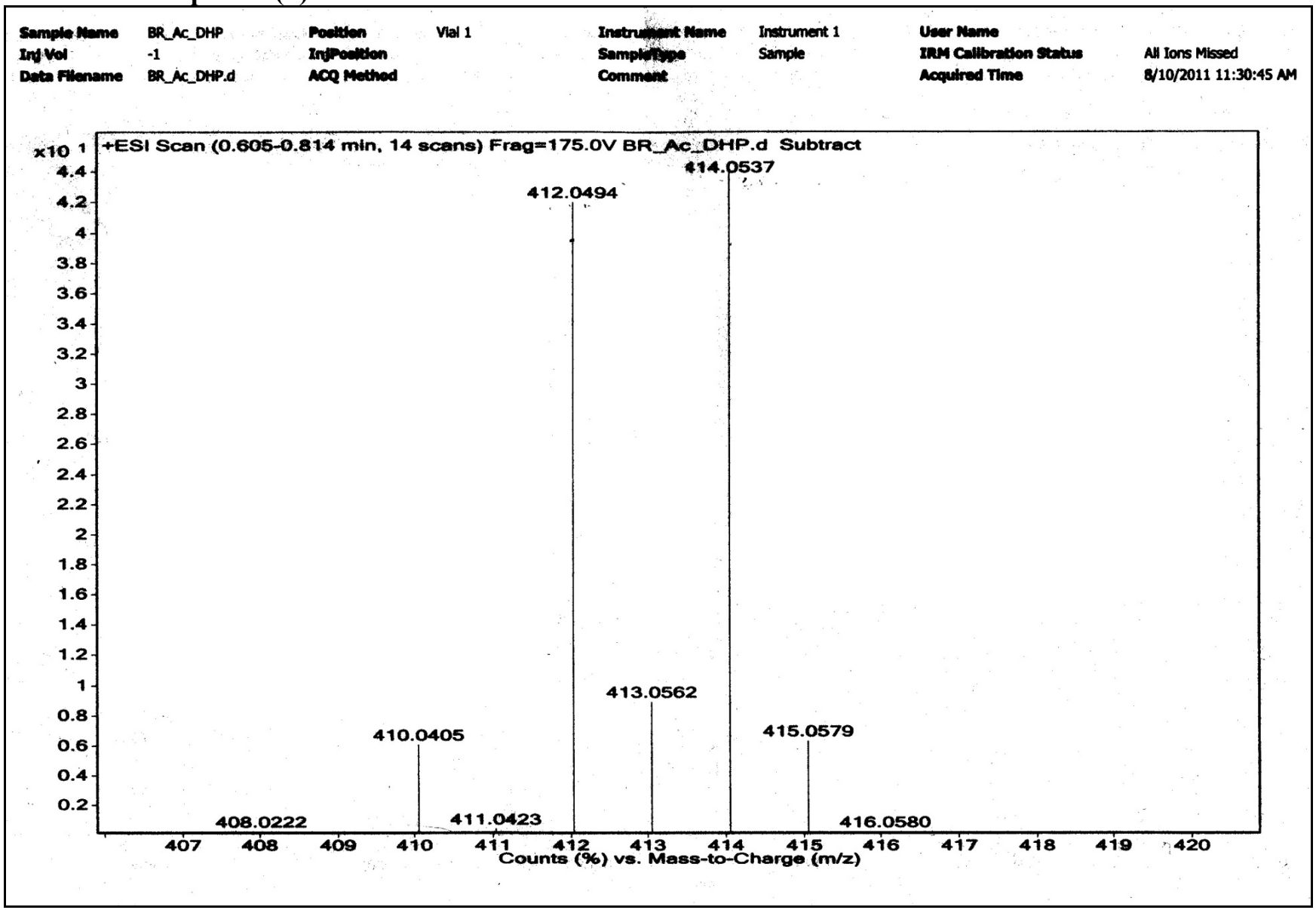
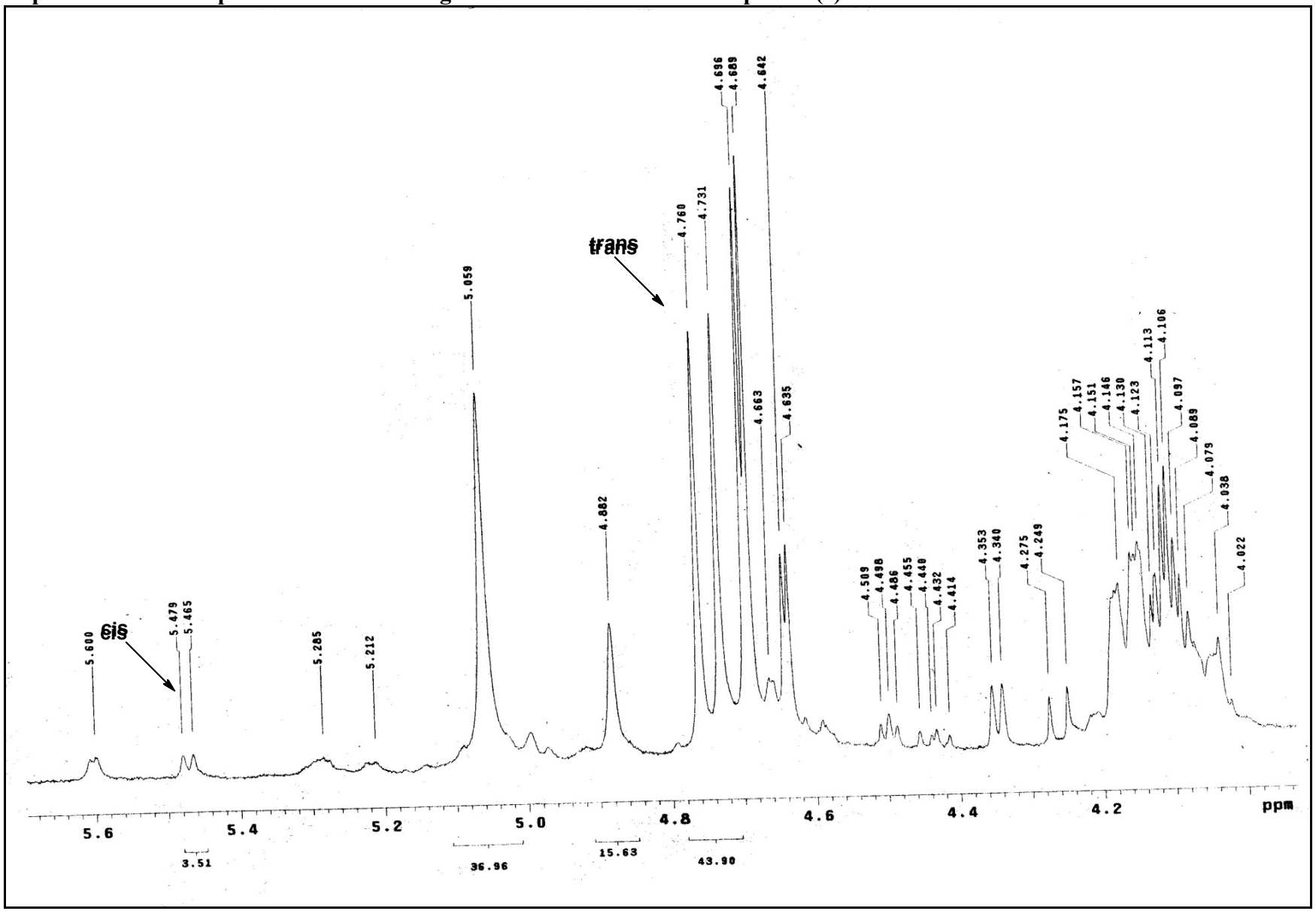


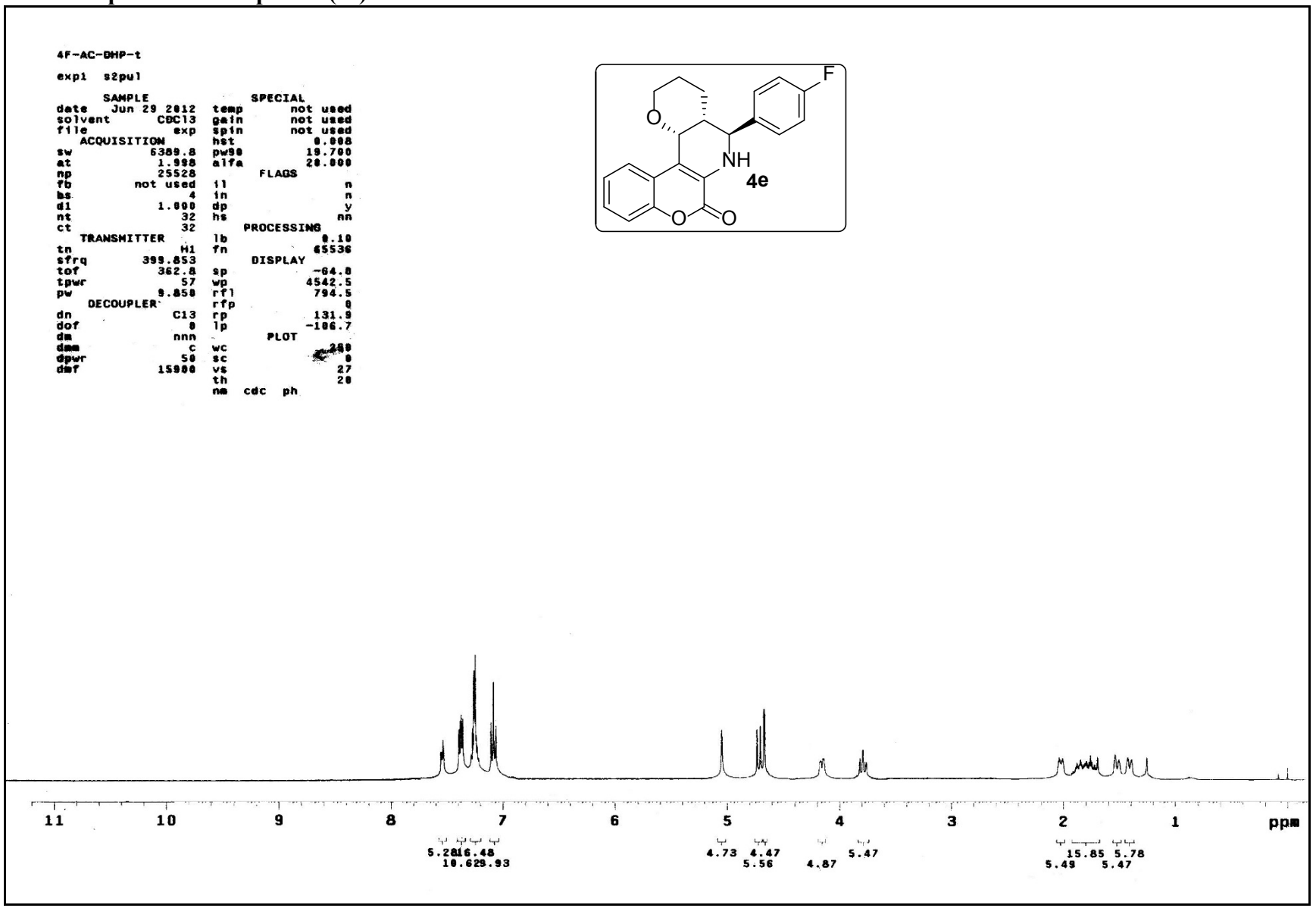
HRMS of Compound (d)



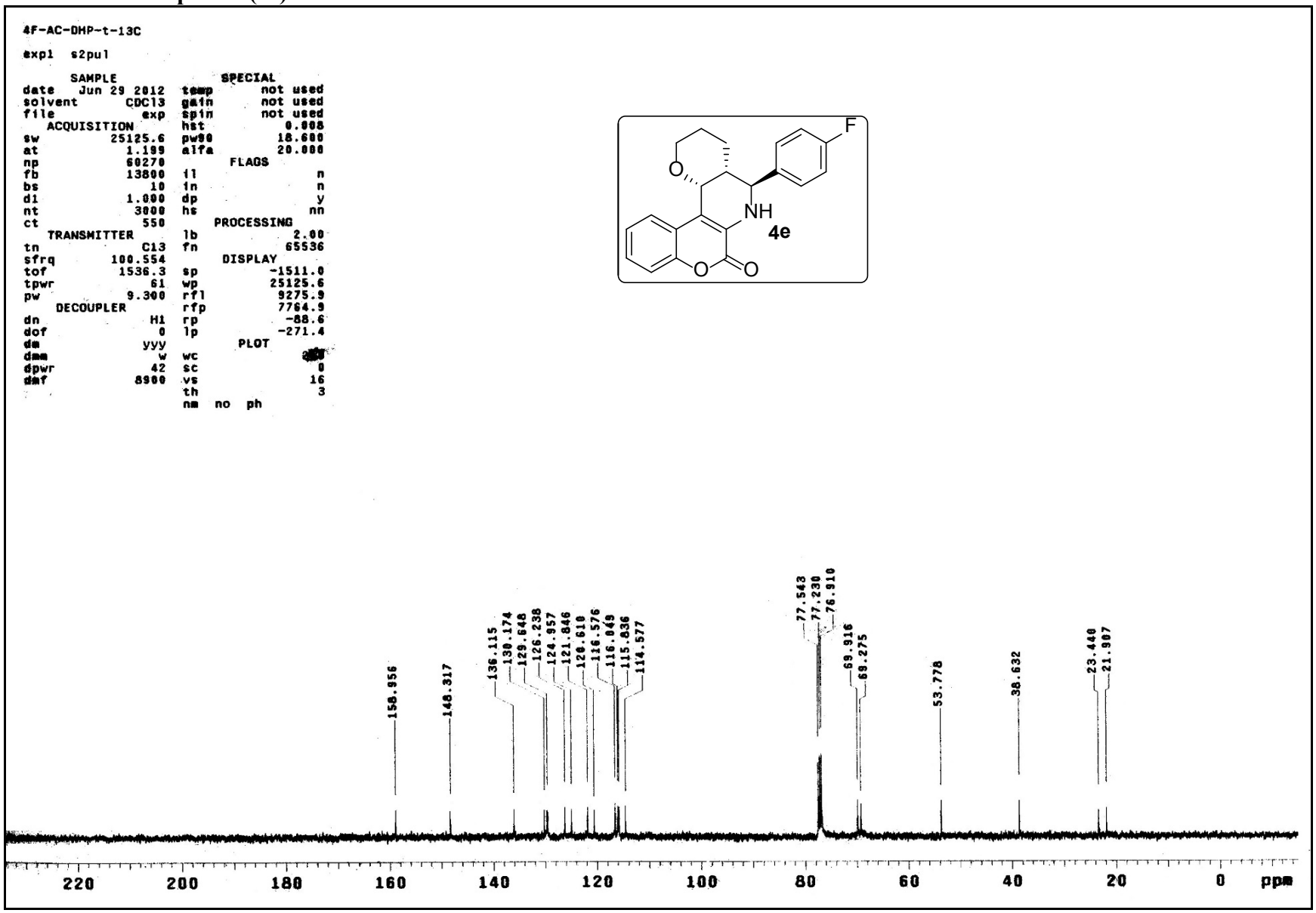
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (e)



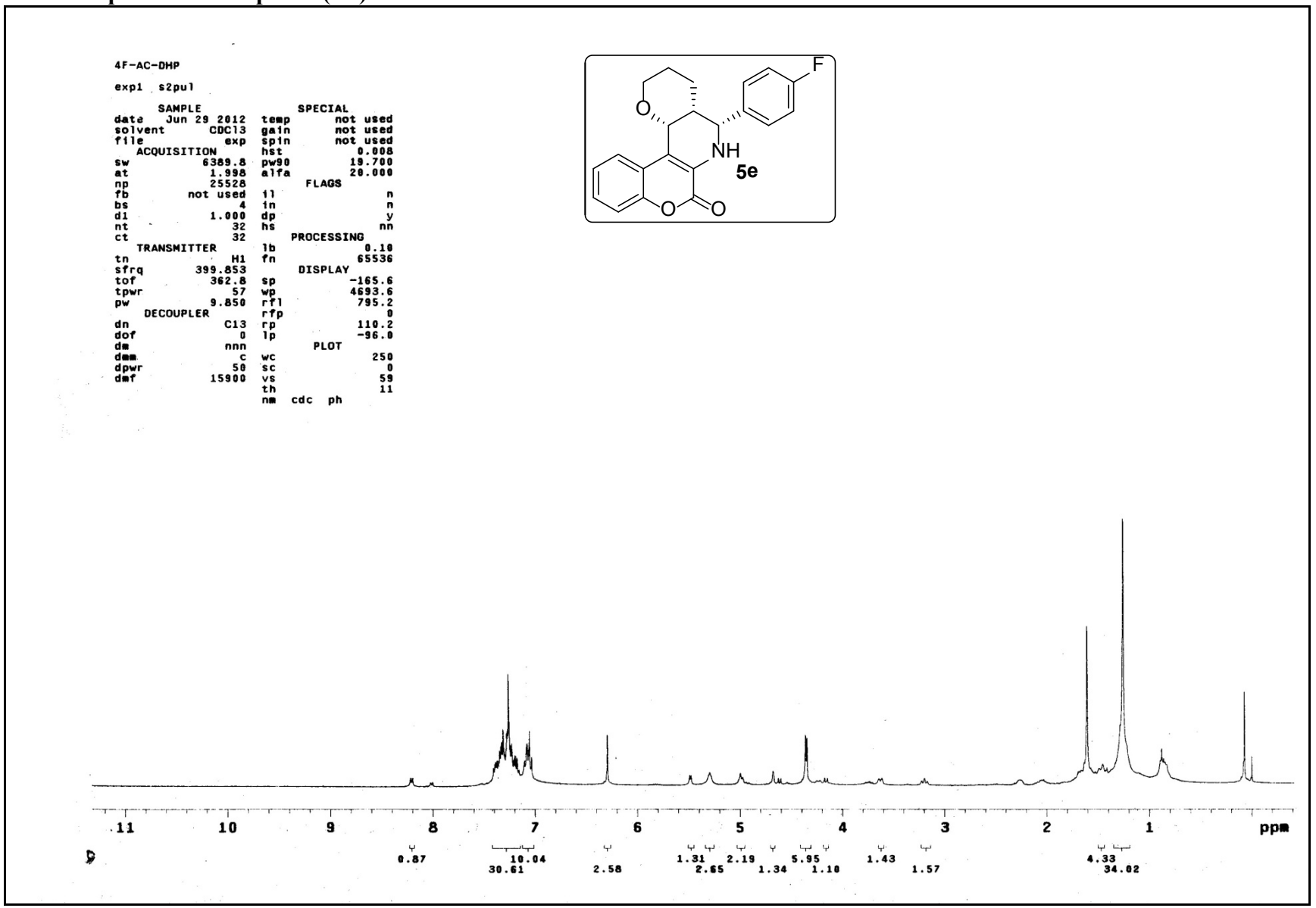
^{1}HNMR Spectra of Compound (4e)



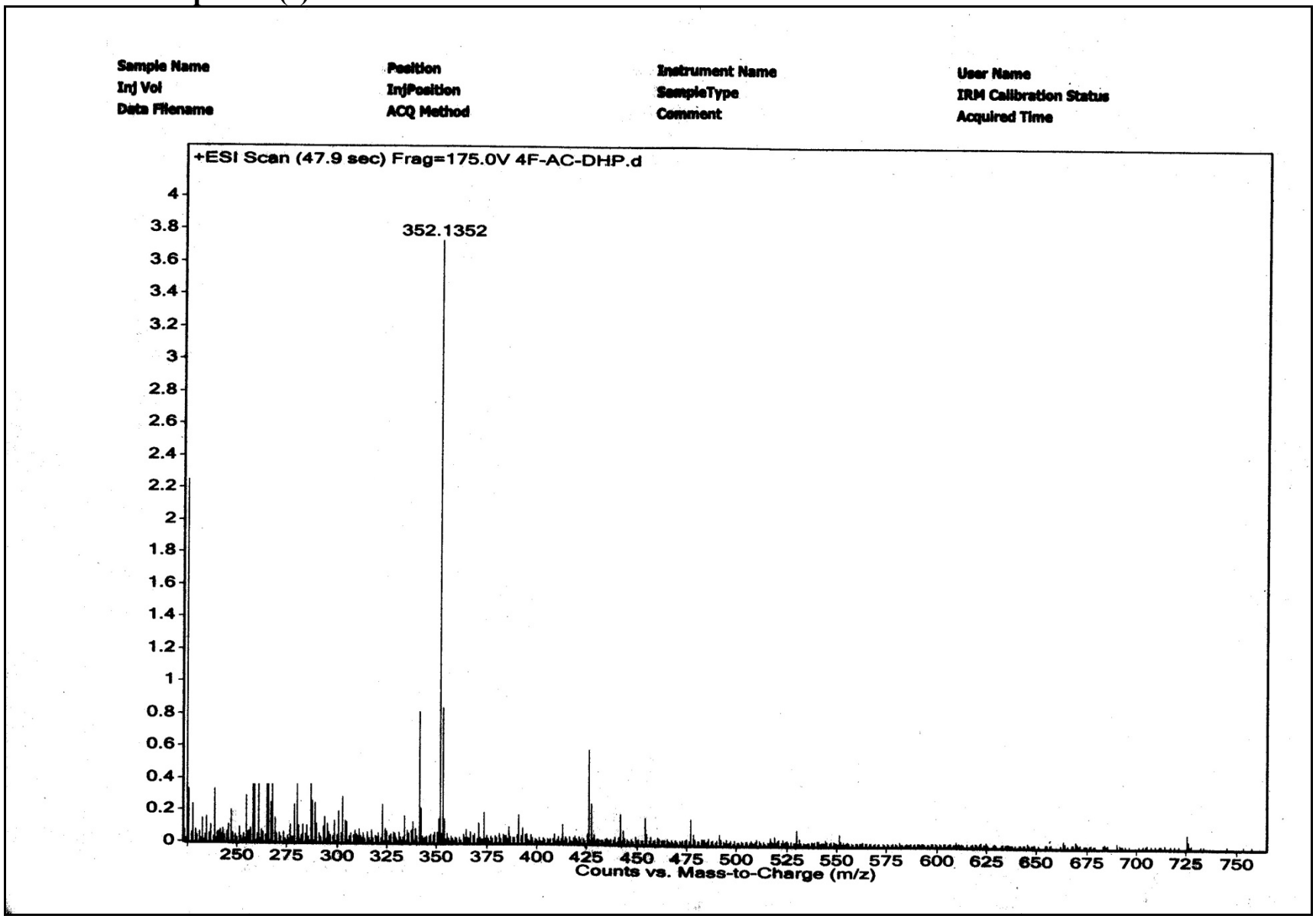
^{13}CNMR of Compound (4e)



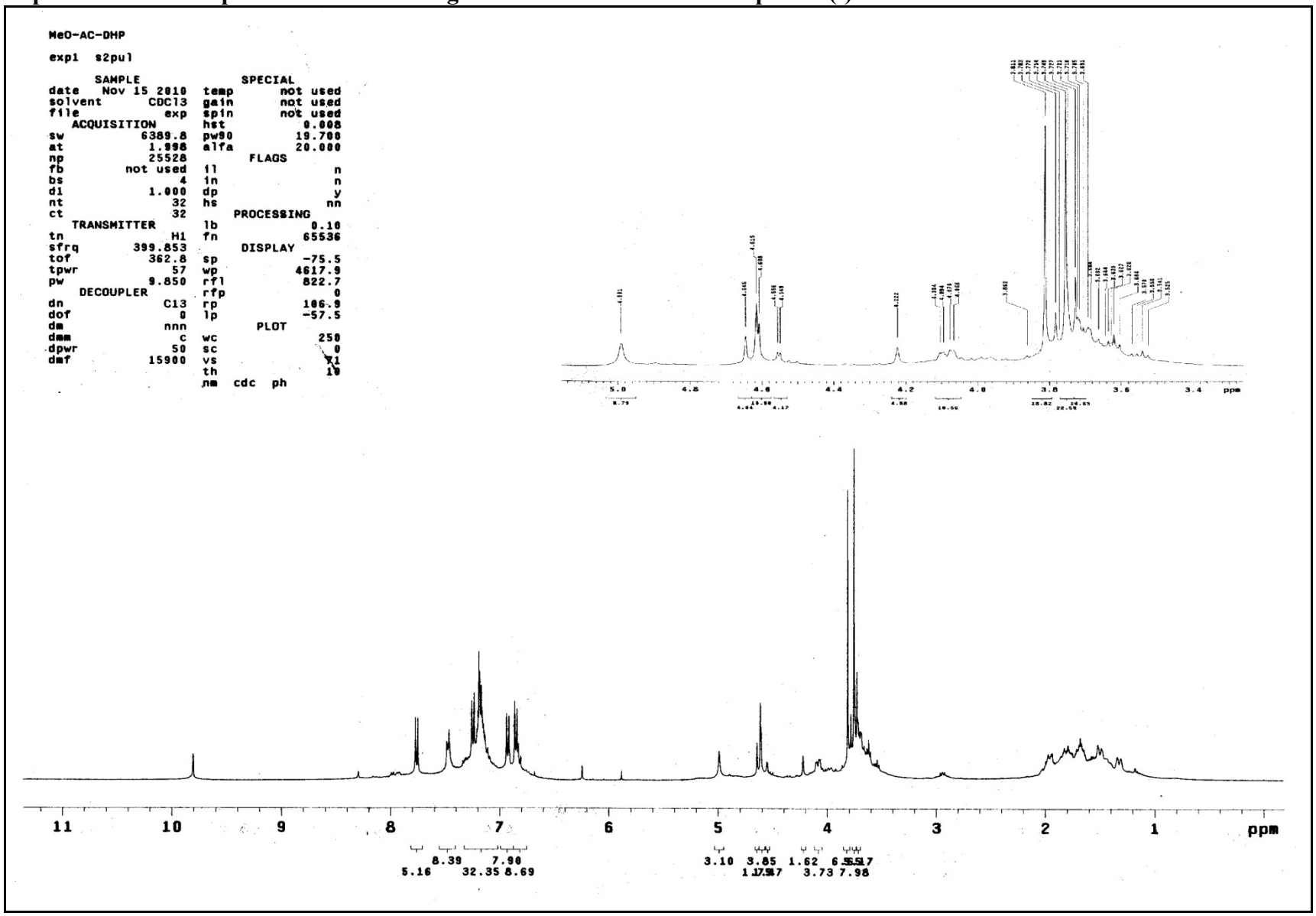
^{1}HNMR Spectra of Compound(5e)



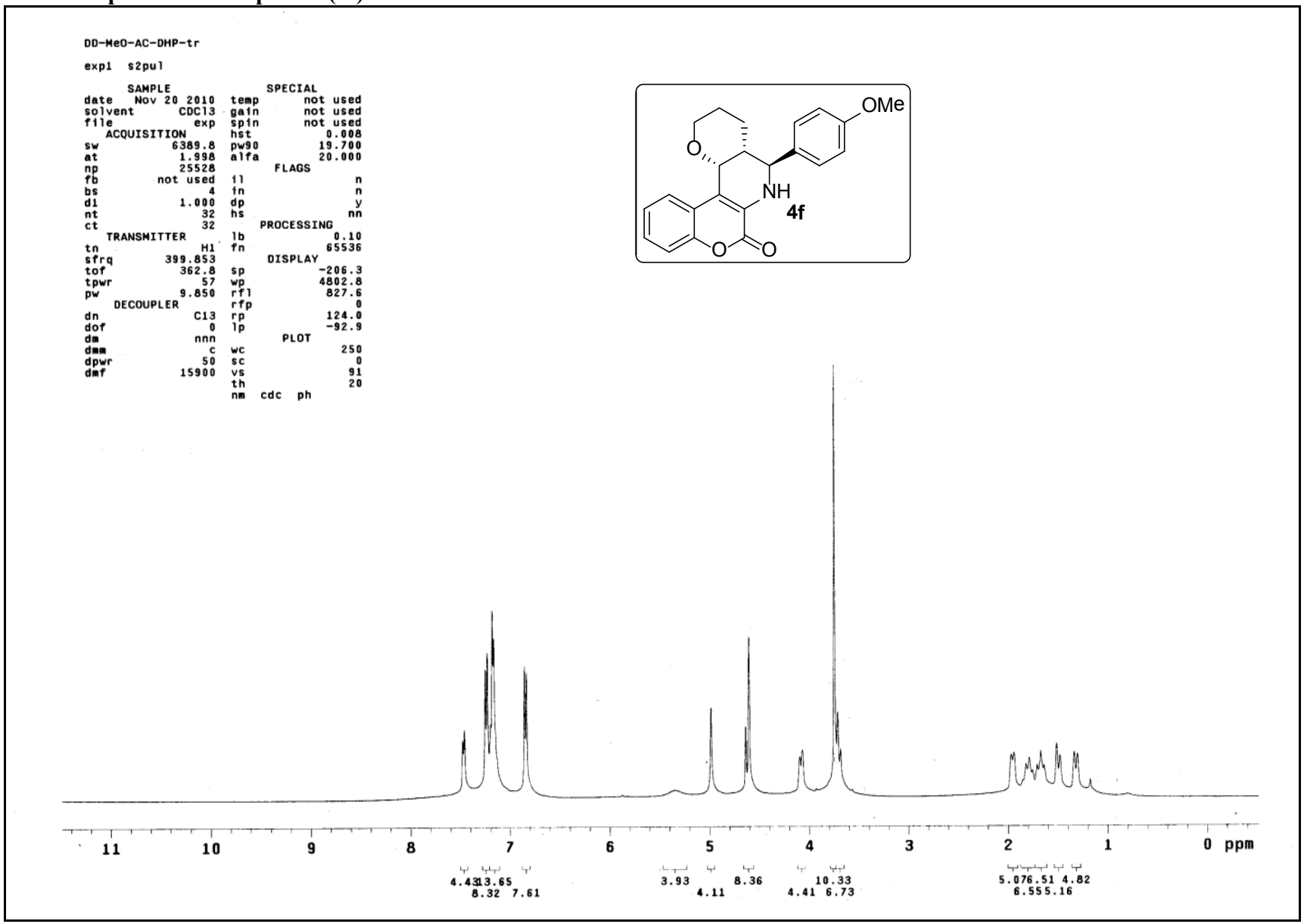
HRMS of Compound (e)



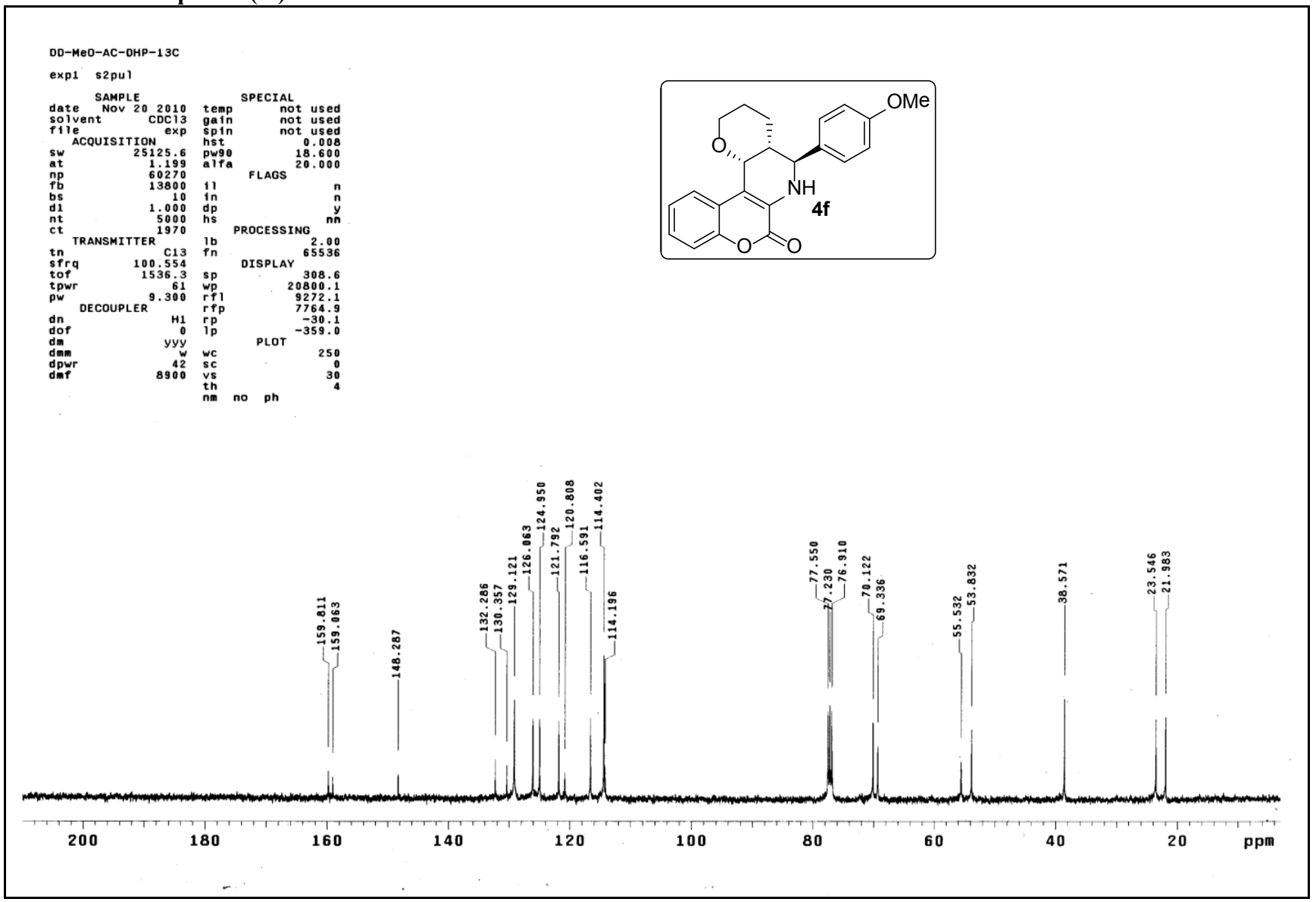
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (f)



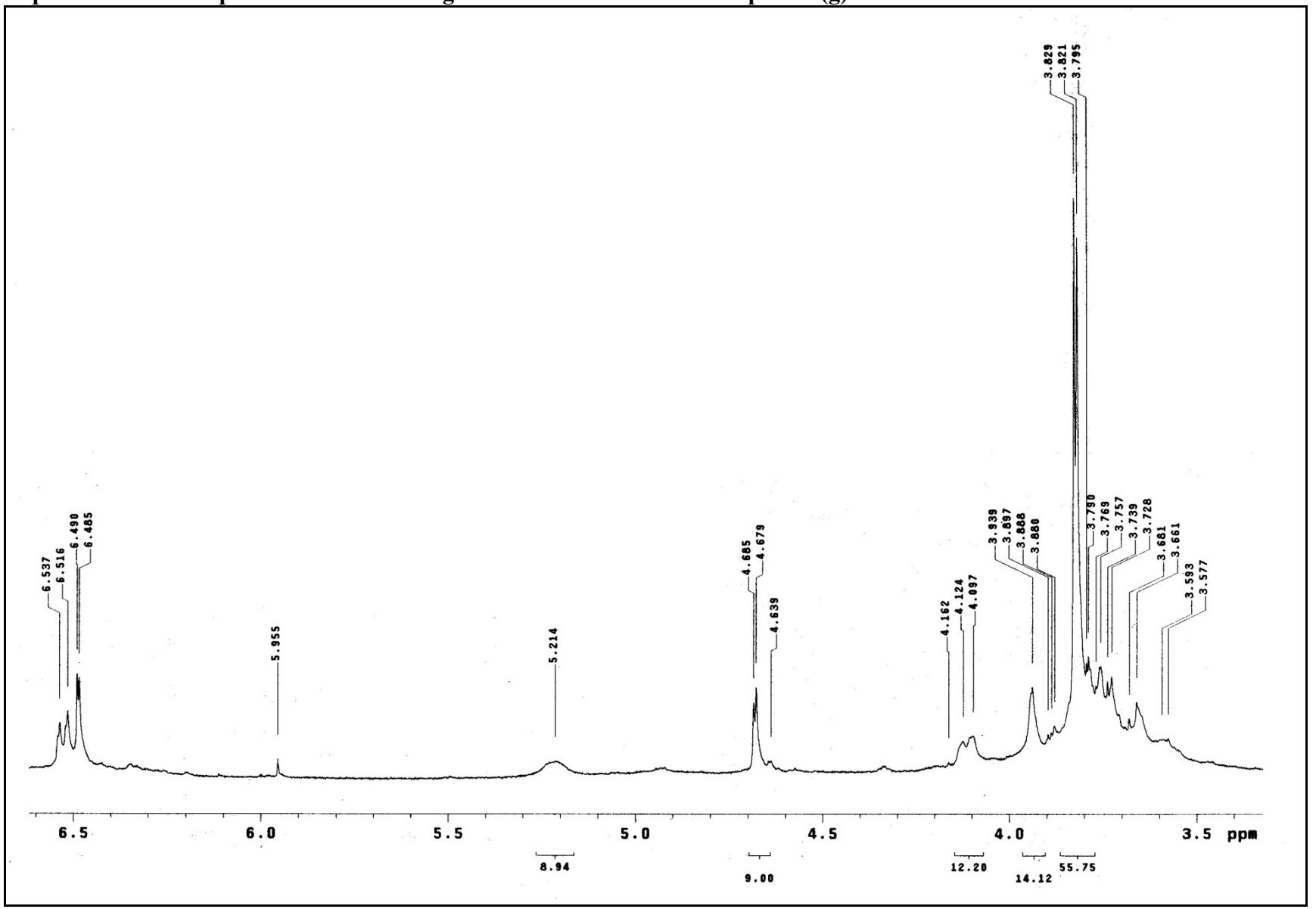
^{1}HNMR Spectra of Compound (4f)



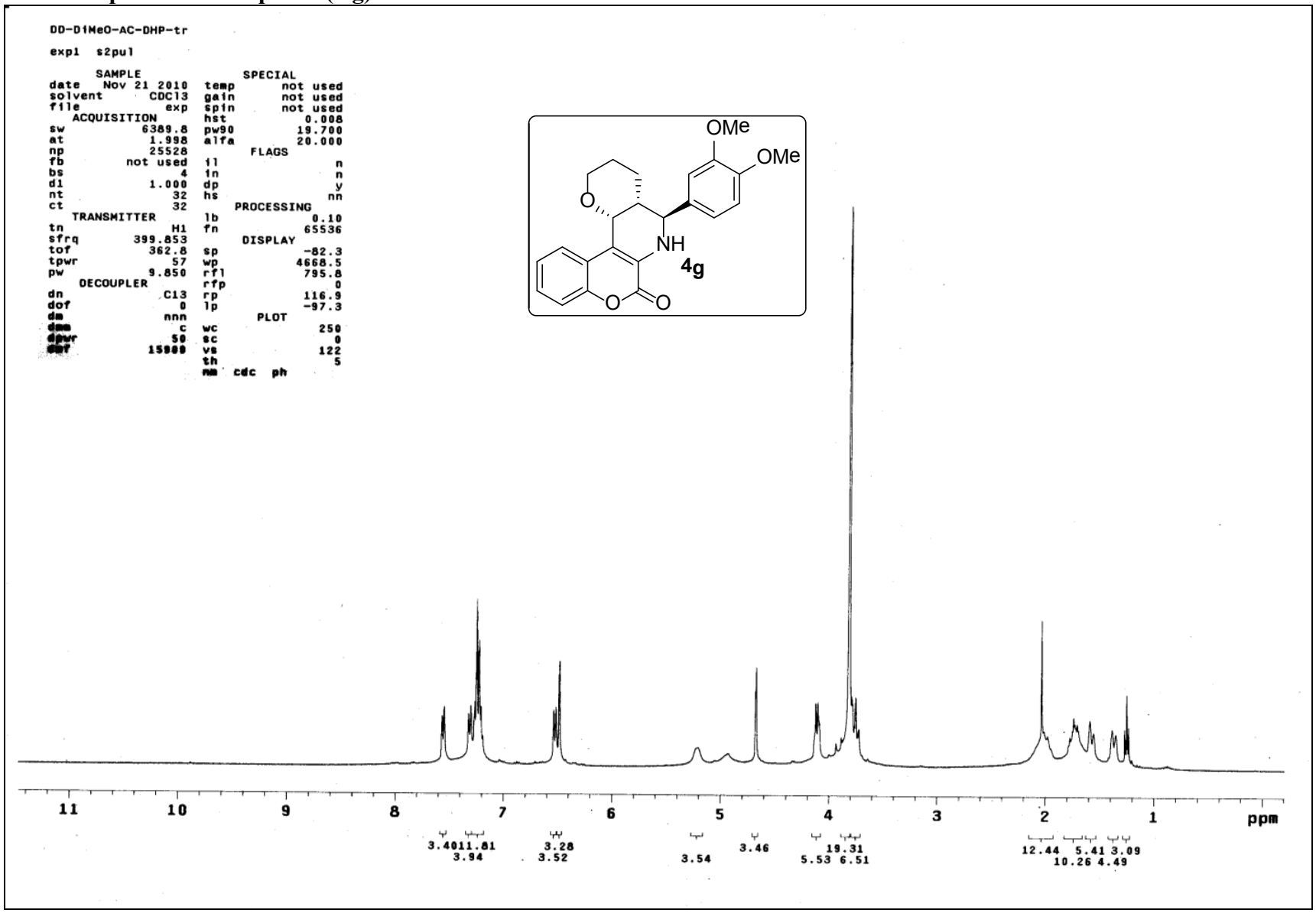
^{13}CNMR of Compound (4f)



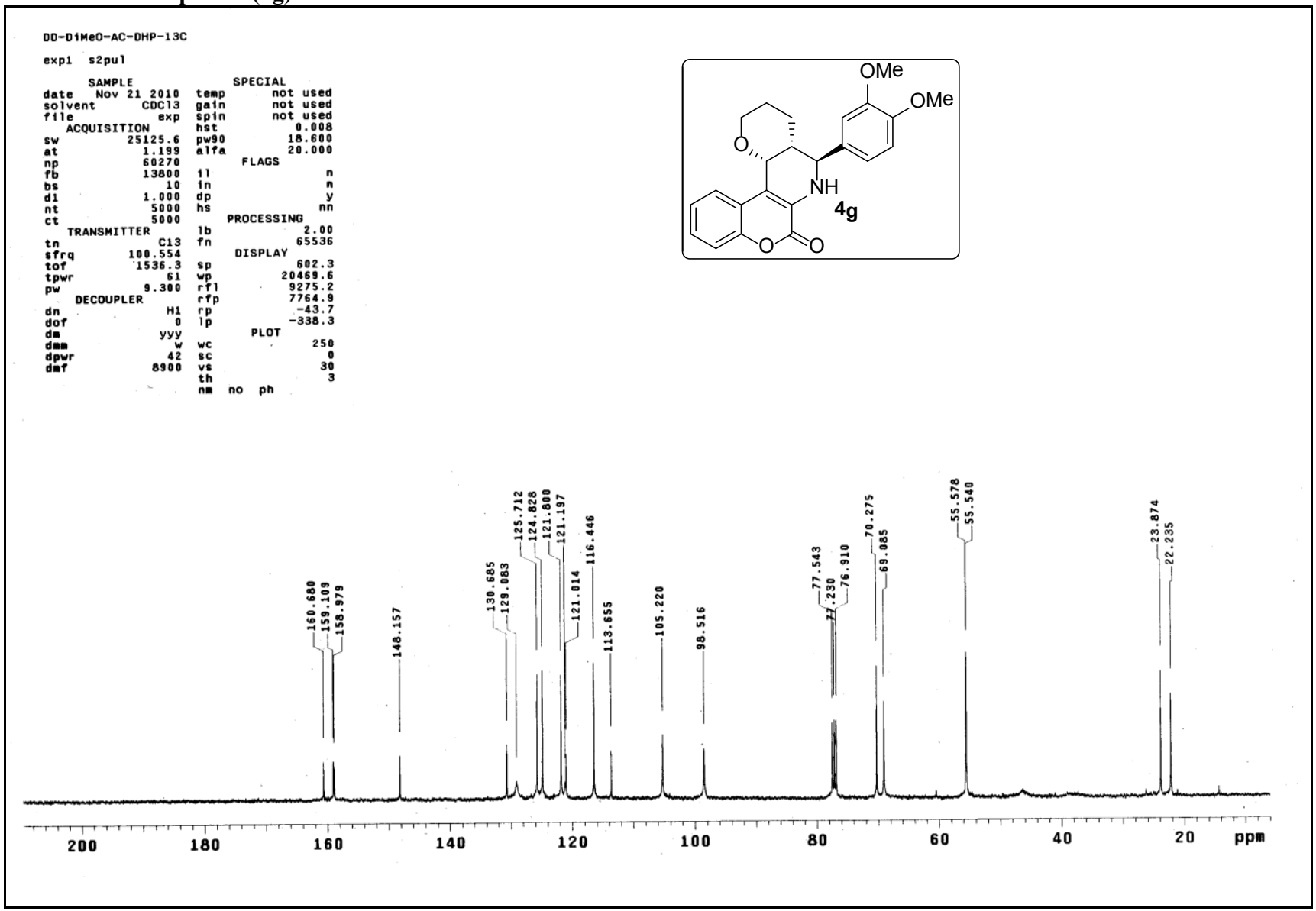
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (g)



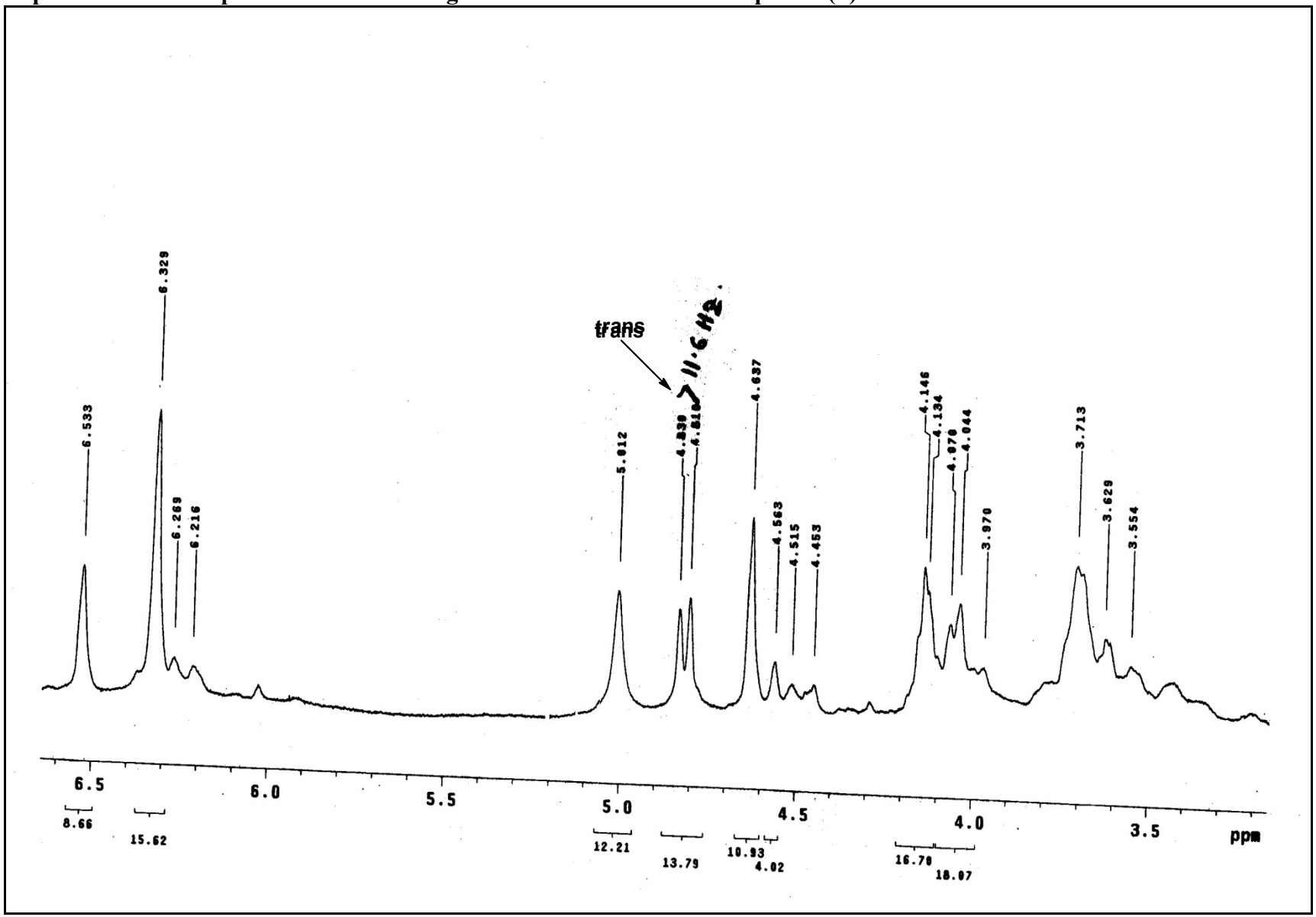
[1]HNMR Spectra of Compound(4g)



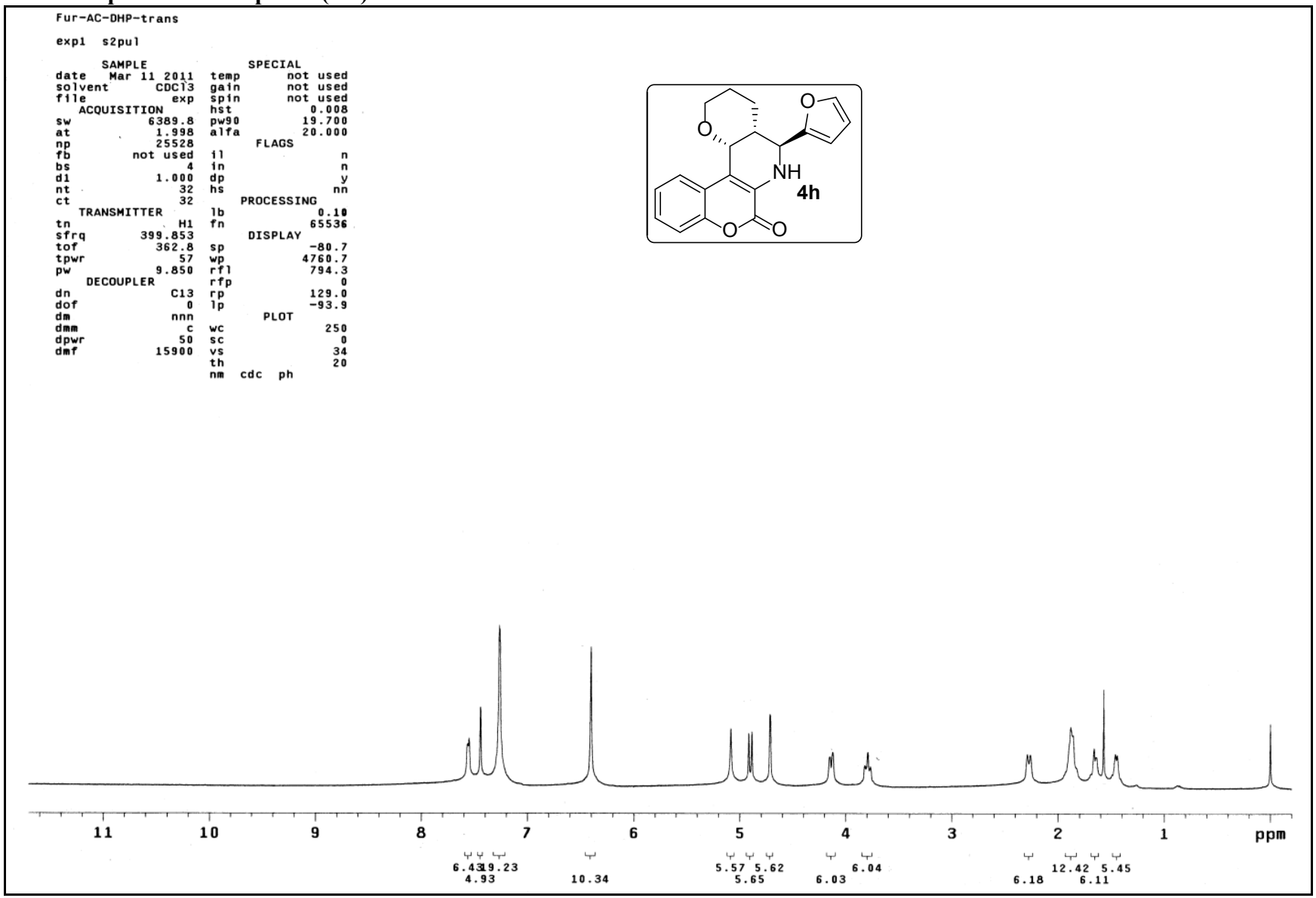
^{13}CNMR of Compound (4g)



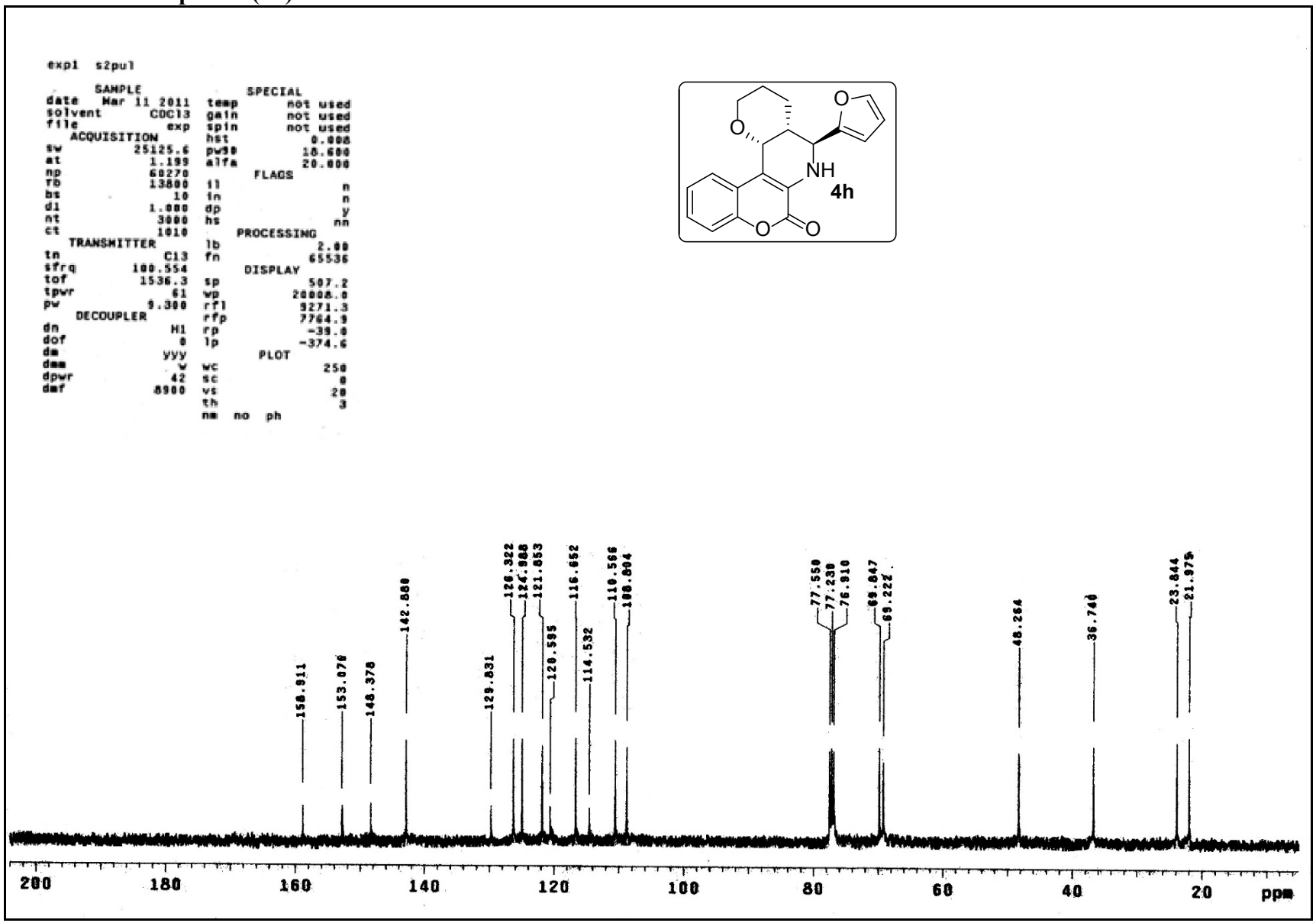
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (h)



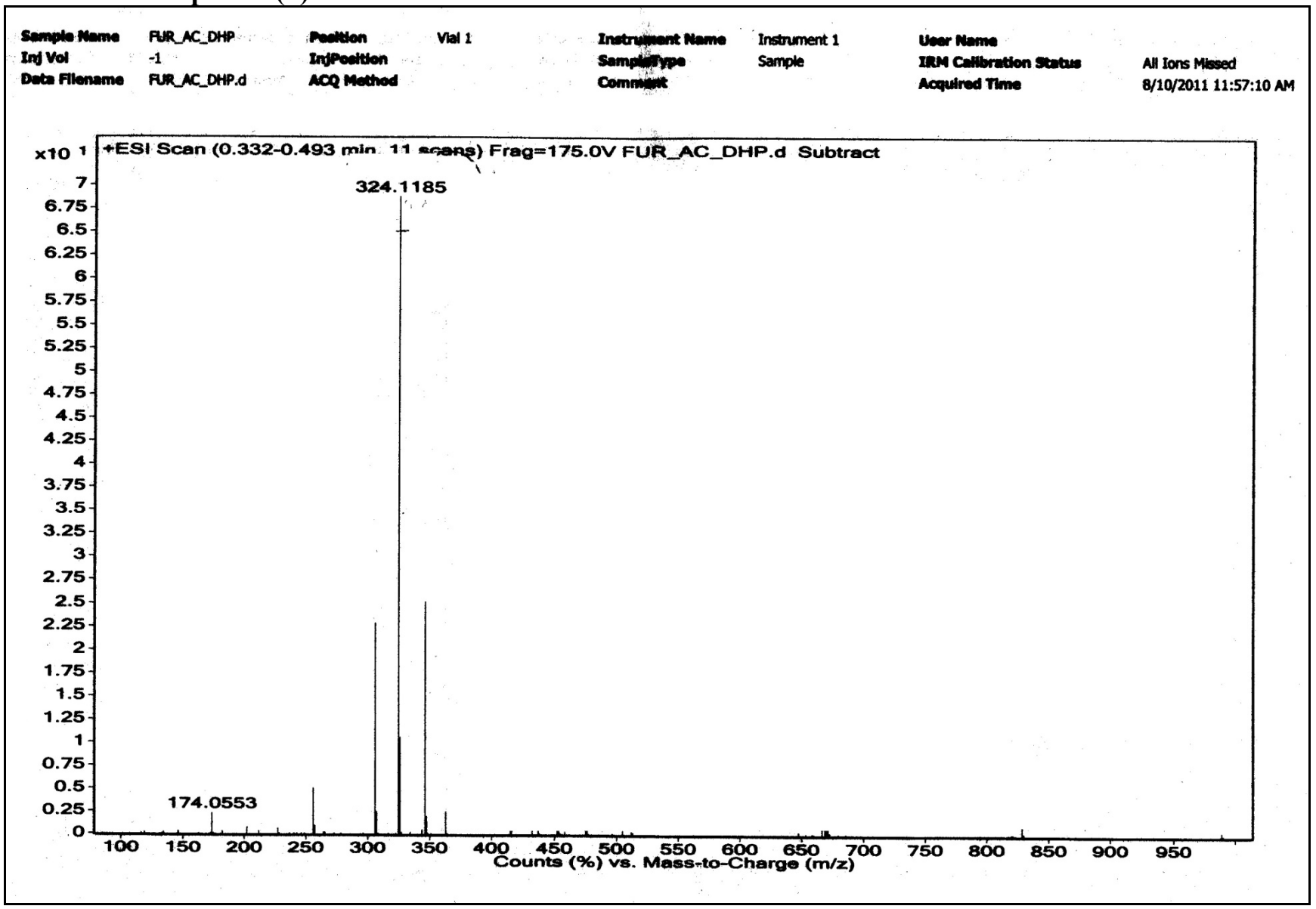
^{1}HNMR Spectra of Compound(4h)



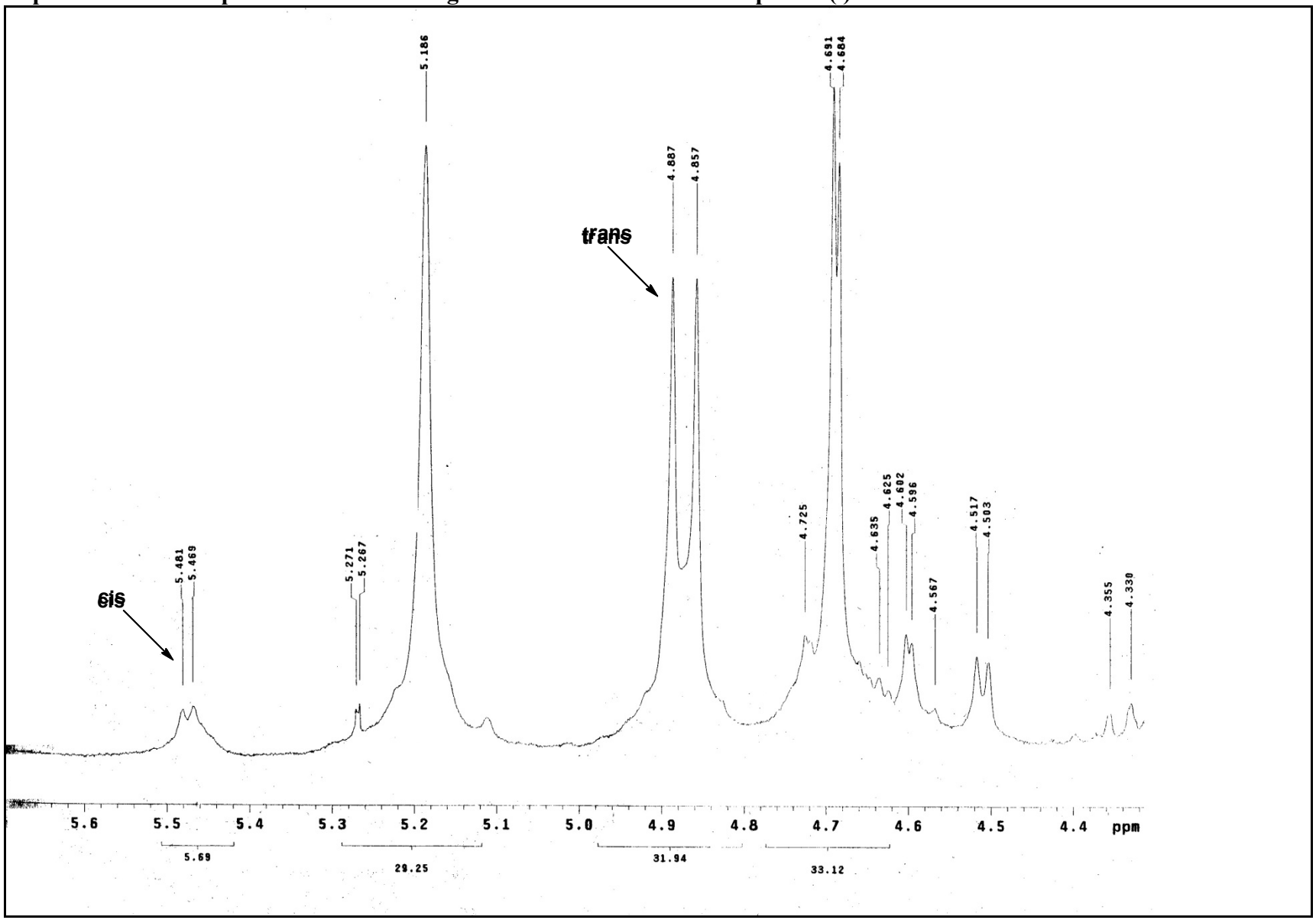
^{13}CNMR of Compound (4h)



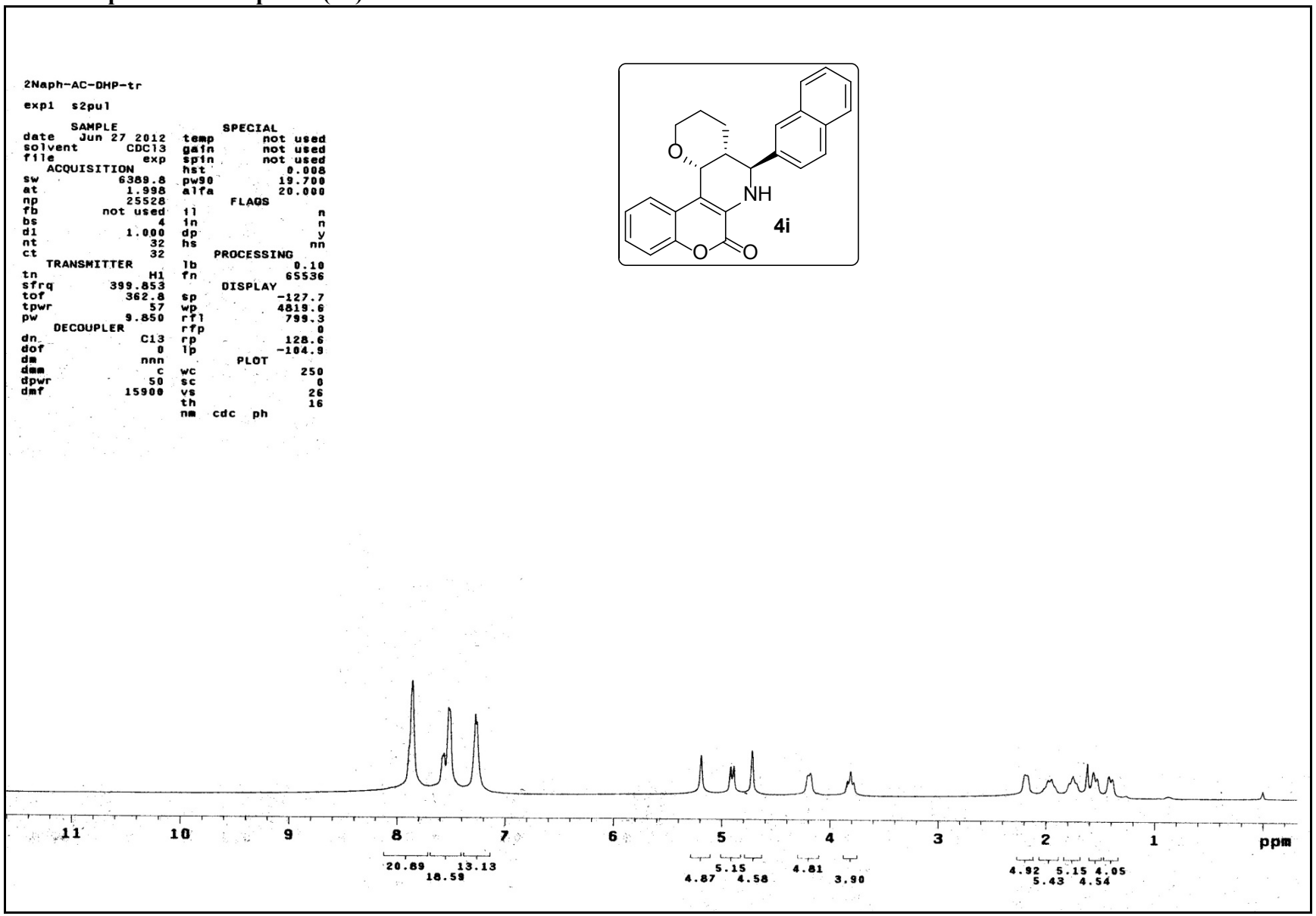
HRMS of Compound (h)



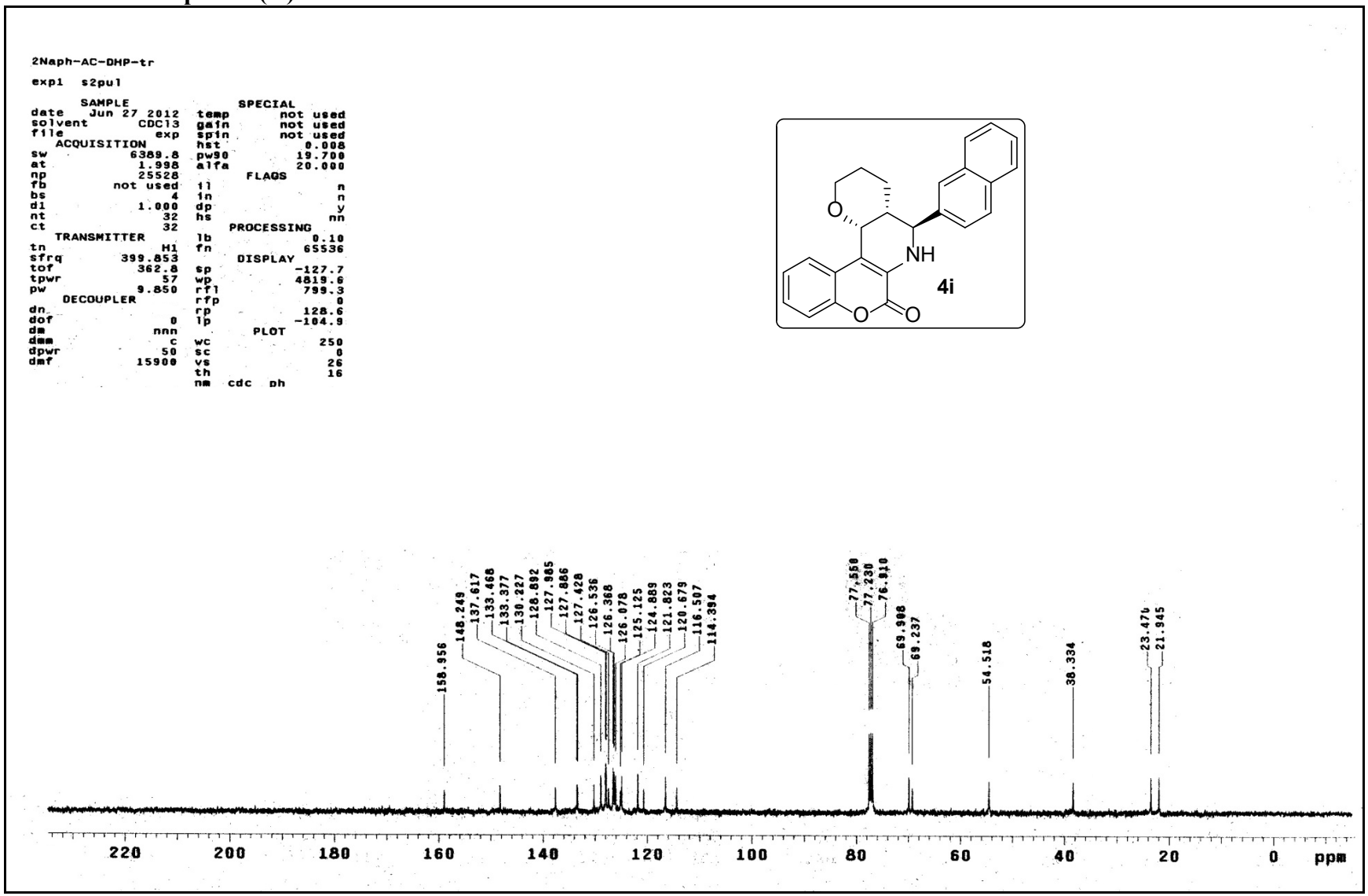
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (i)



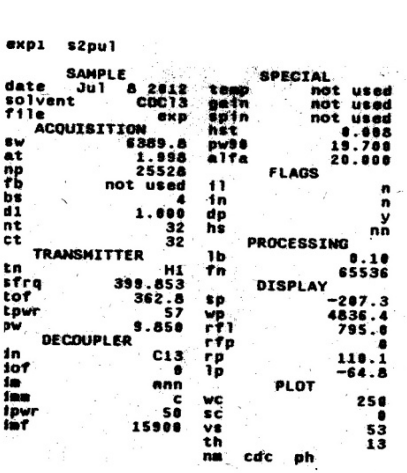
^{1}HNMR Spectra of Compound(4i)

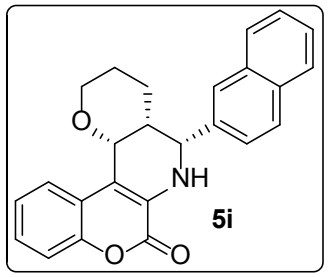


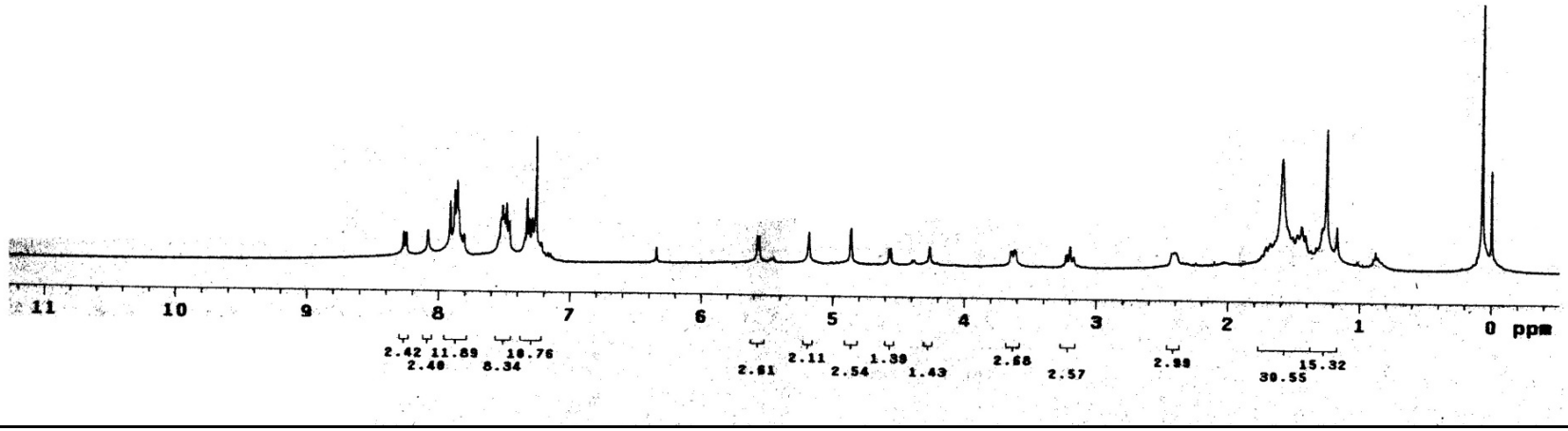
^{13}CNMR of Compound (4i)



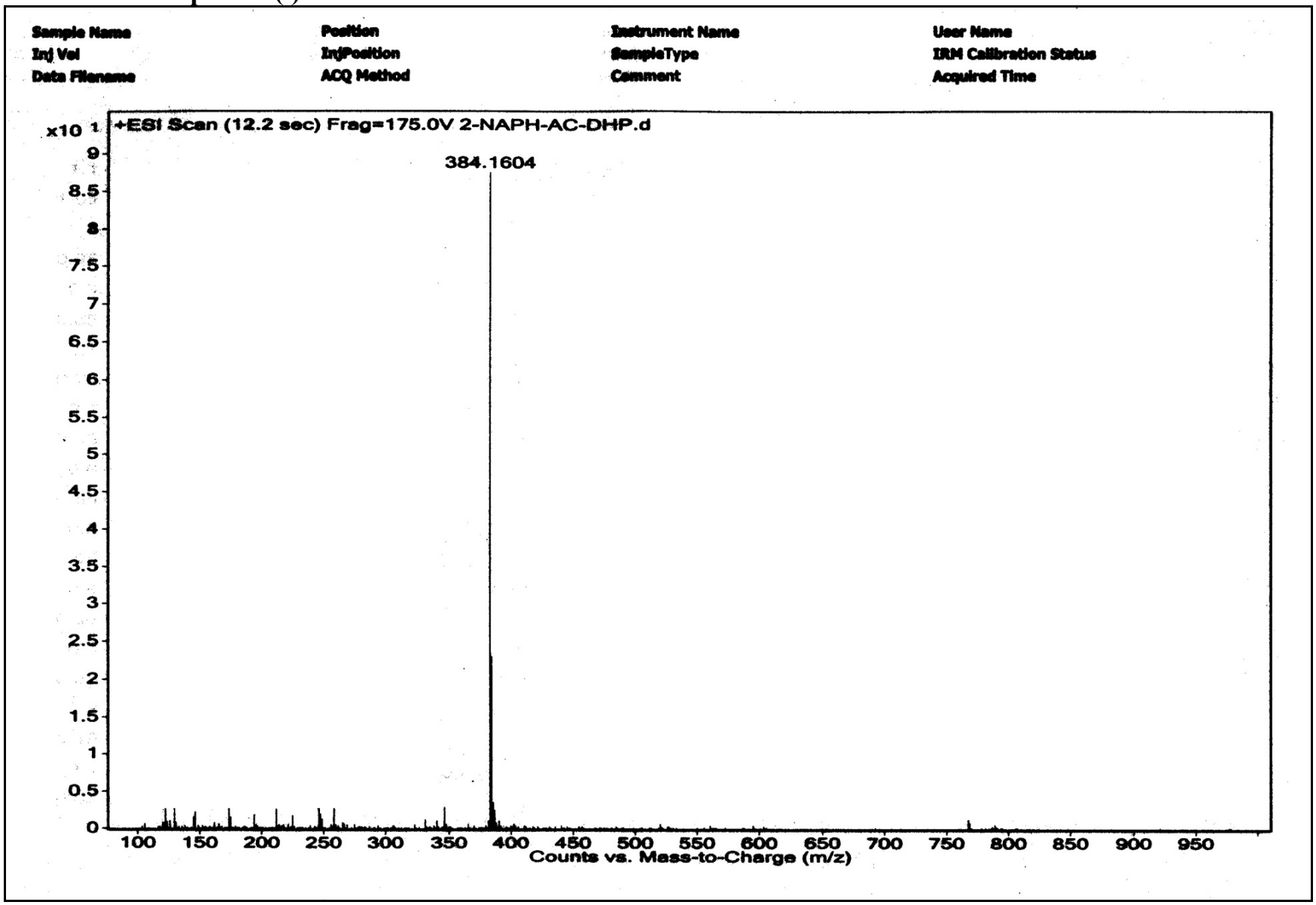
^{1}HNMR Spectra of Compound(5i)



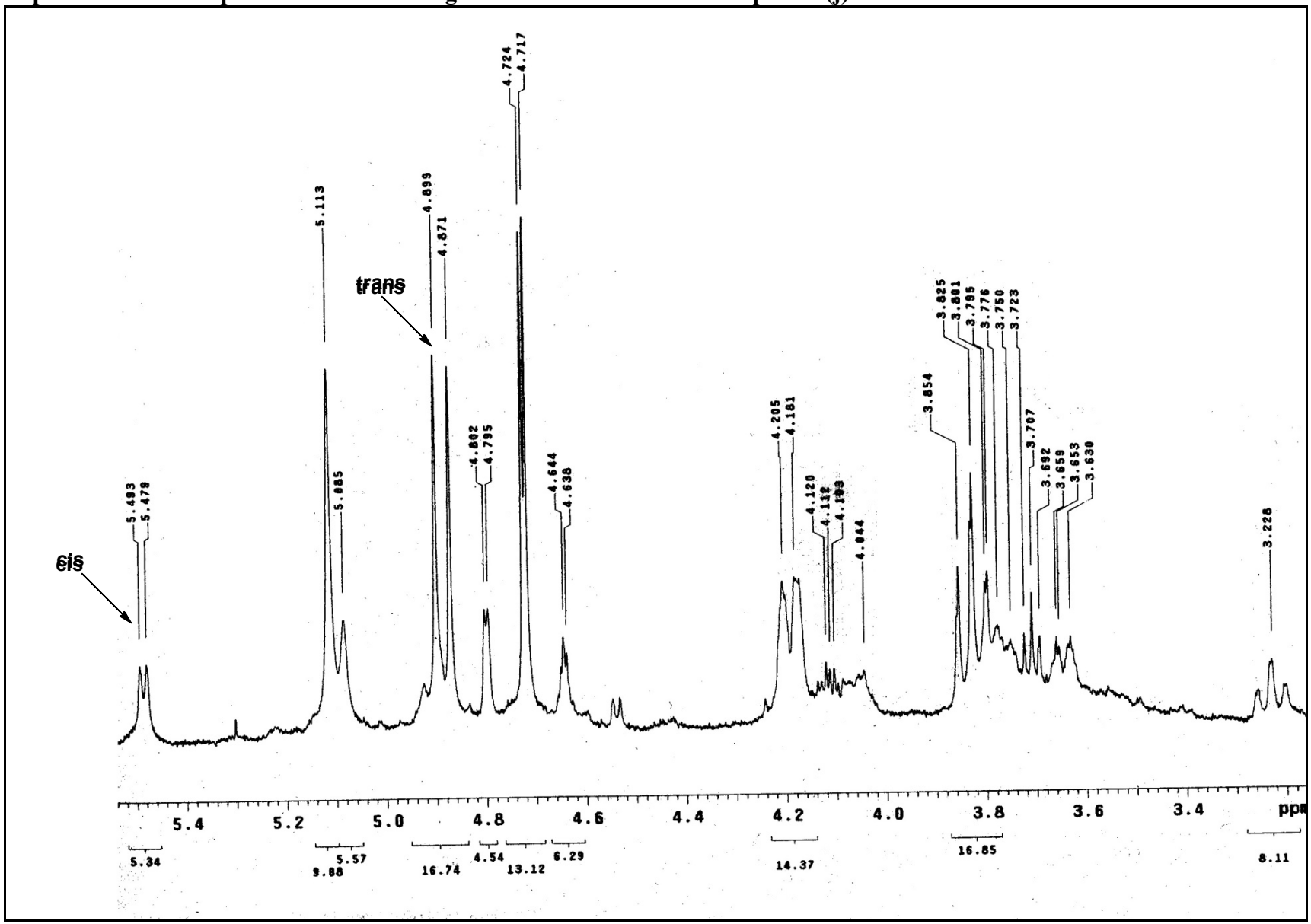




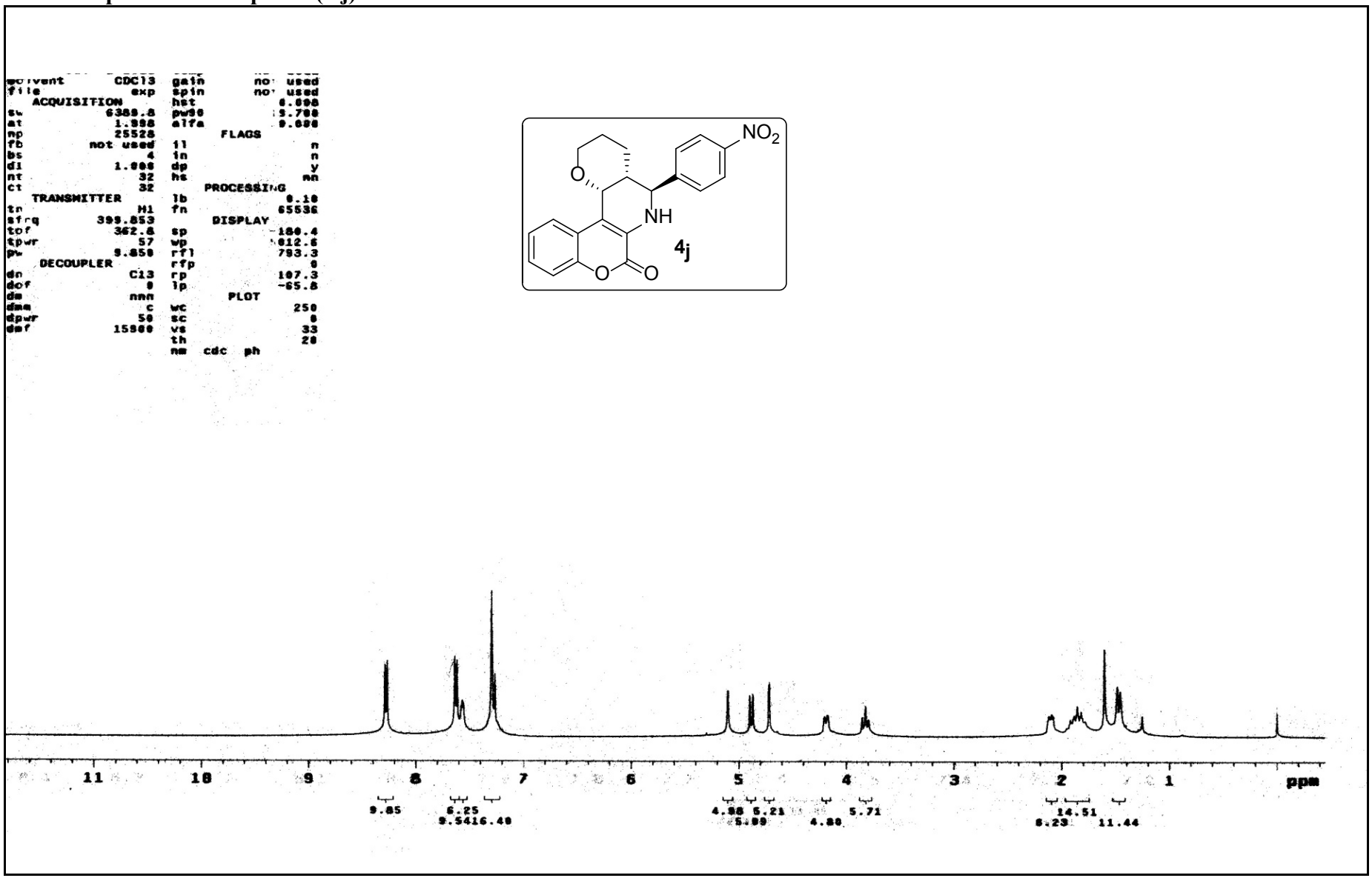
HRMS of Compound (i)



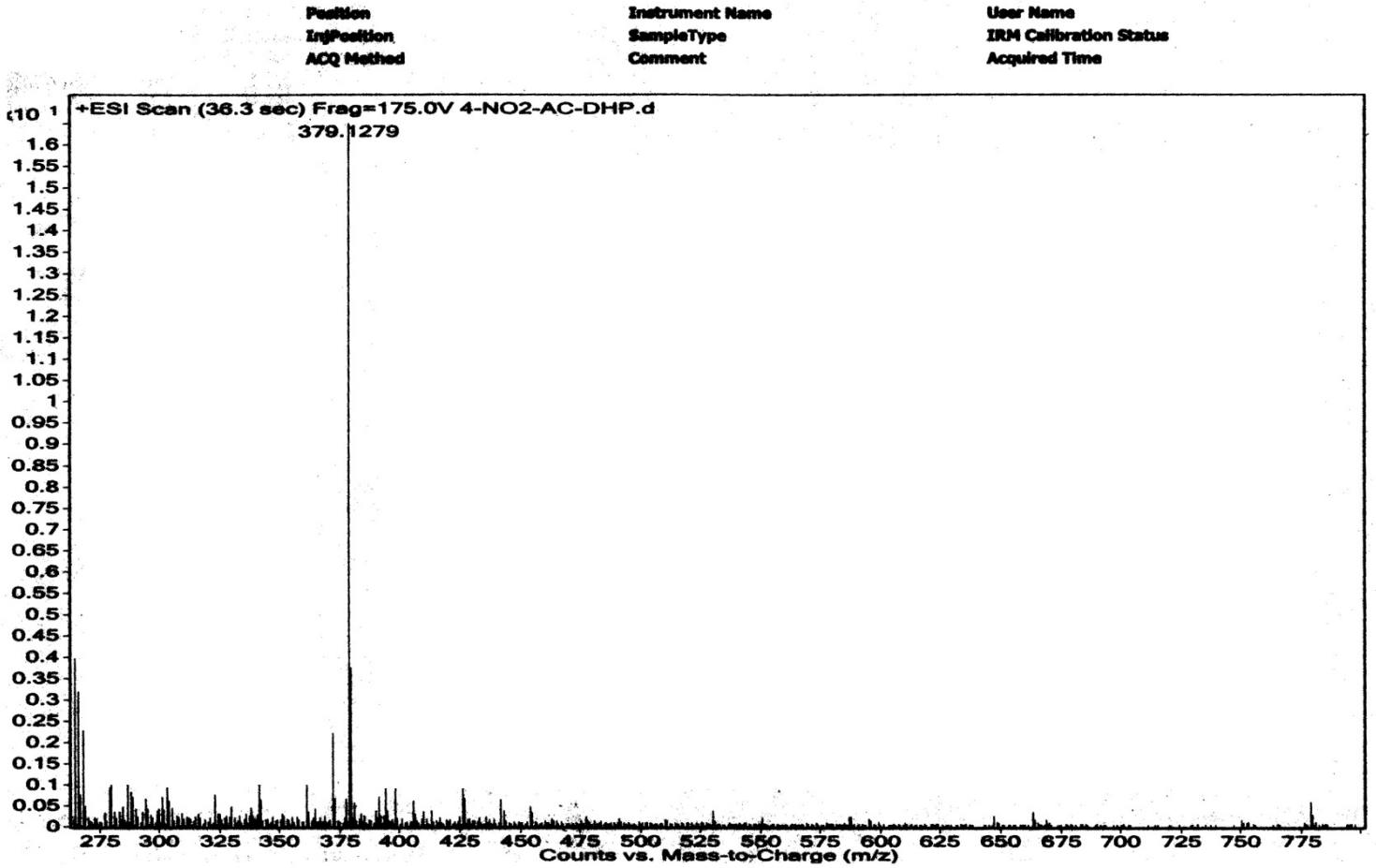
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (j)



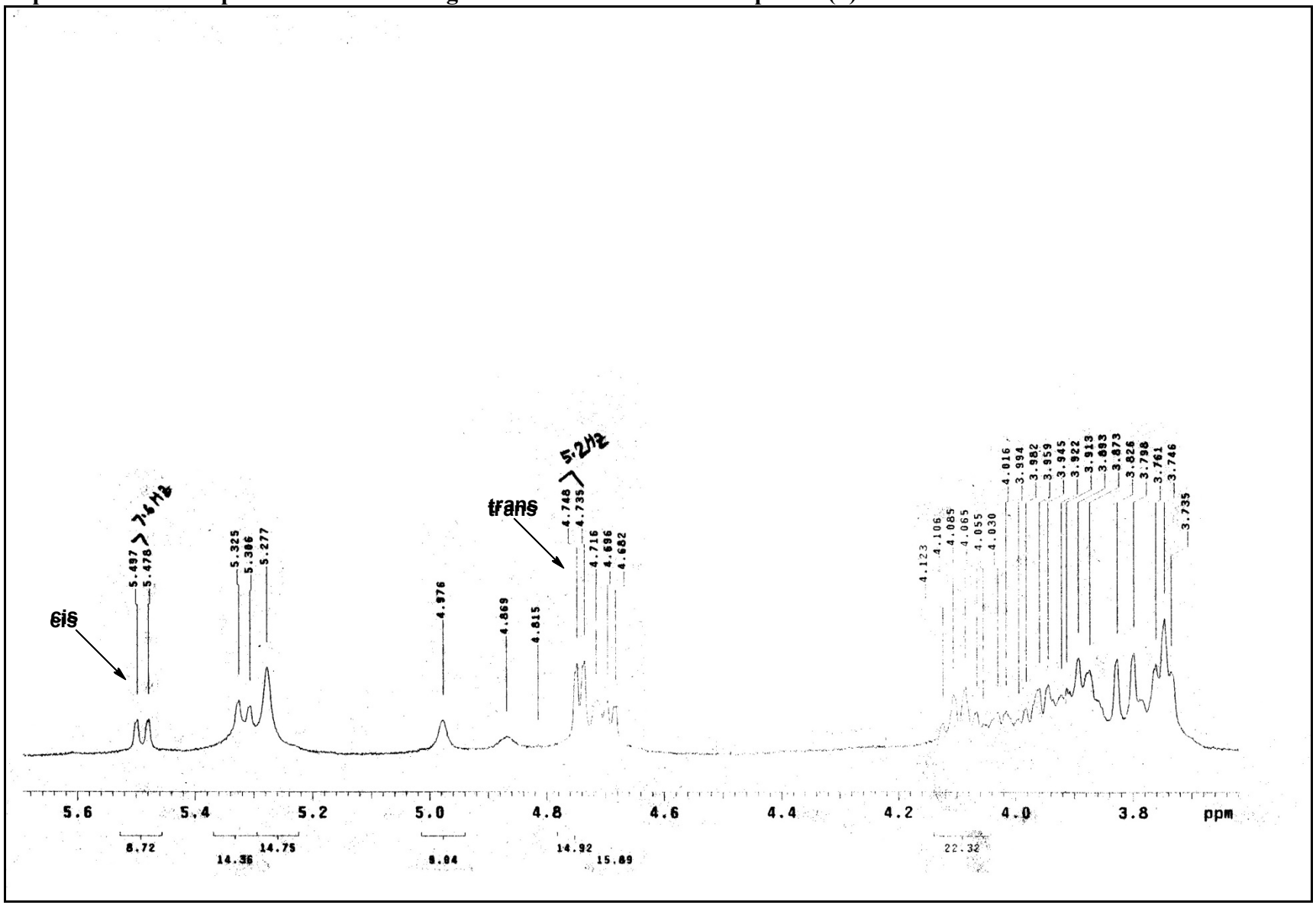
[1]HNMR Spectra of Compound(4j)



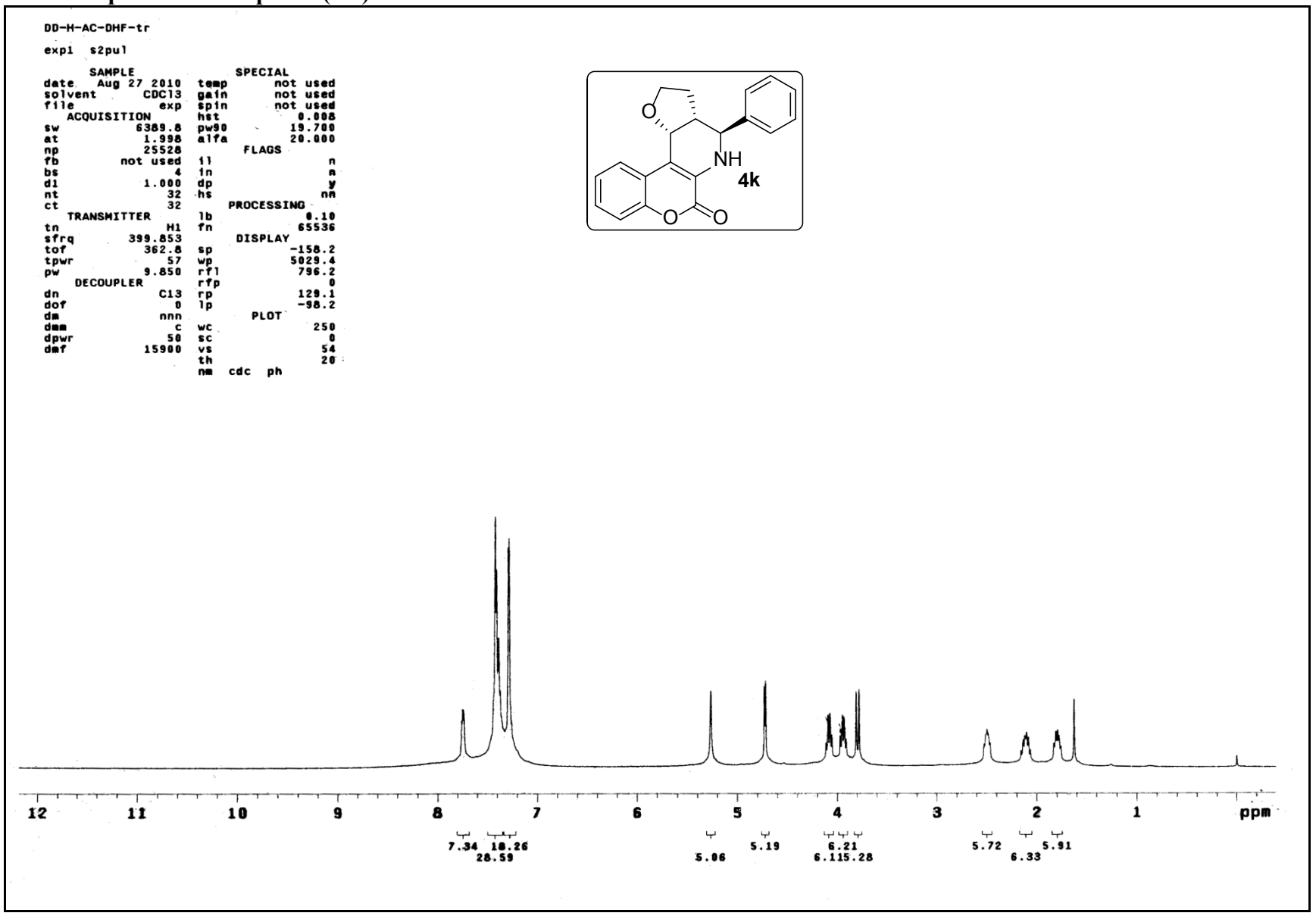
HRMS of Compound (j)



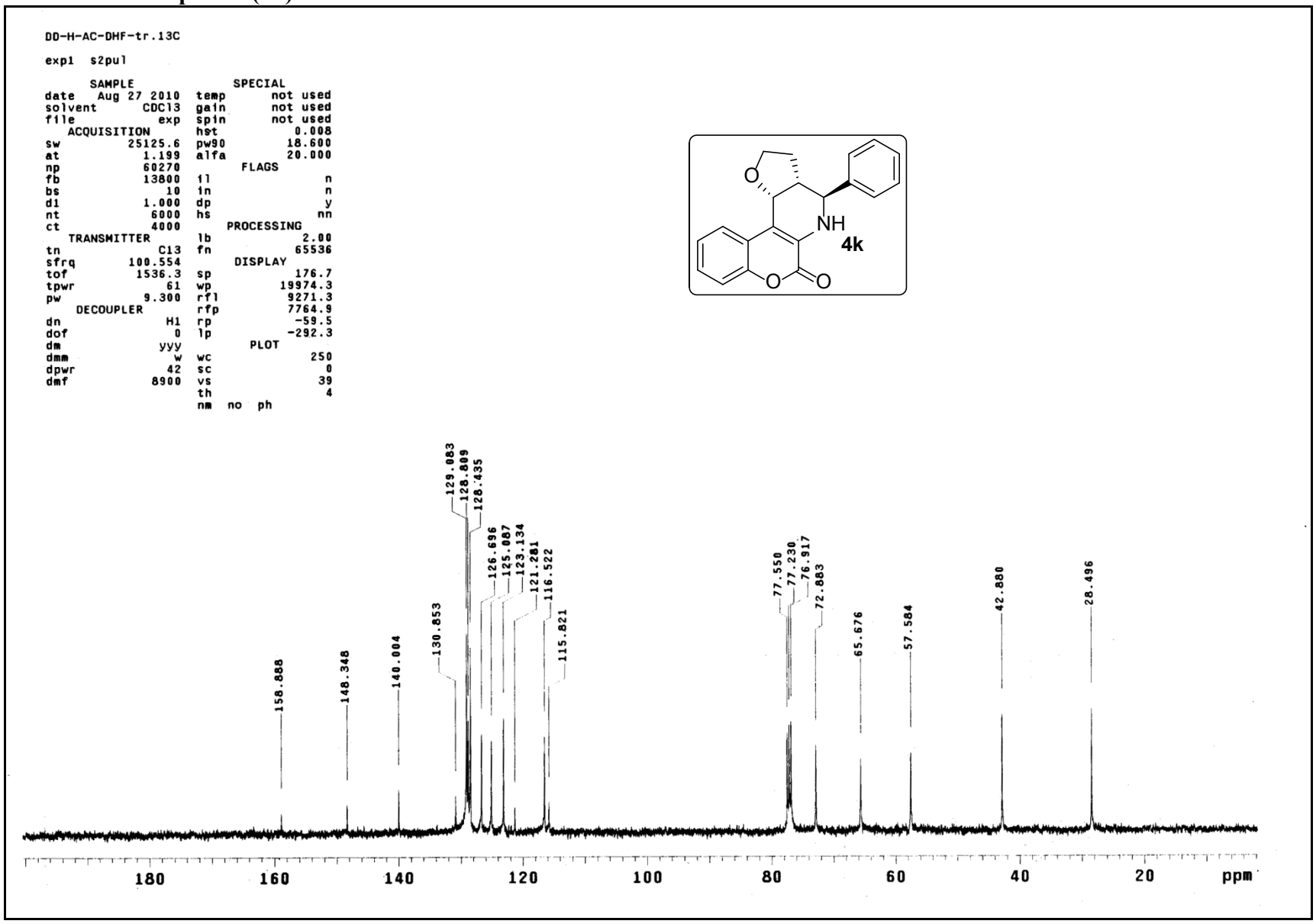
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (k)



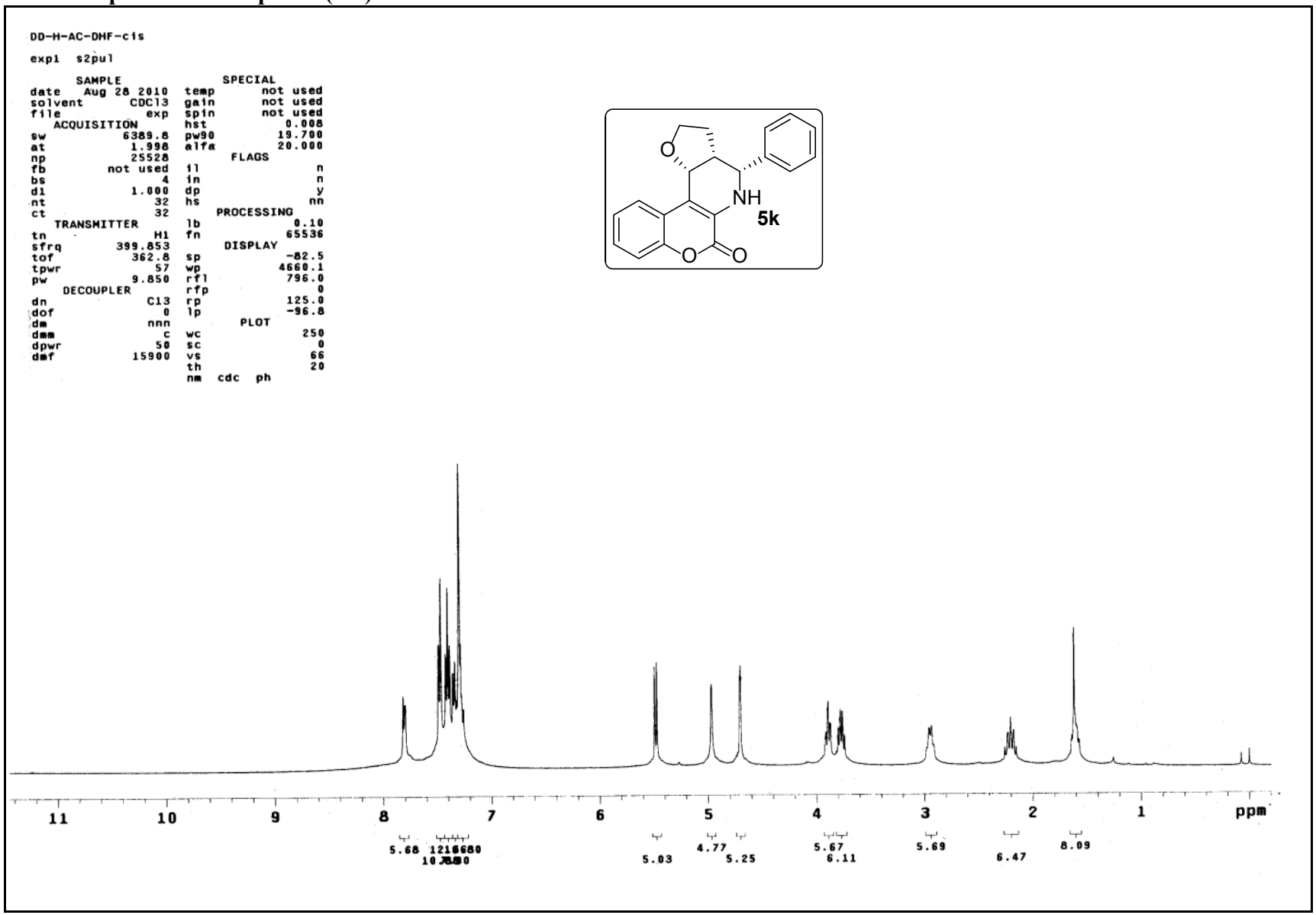
^{1}HNMR Spectra of Compound(4k)



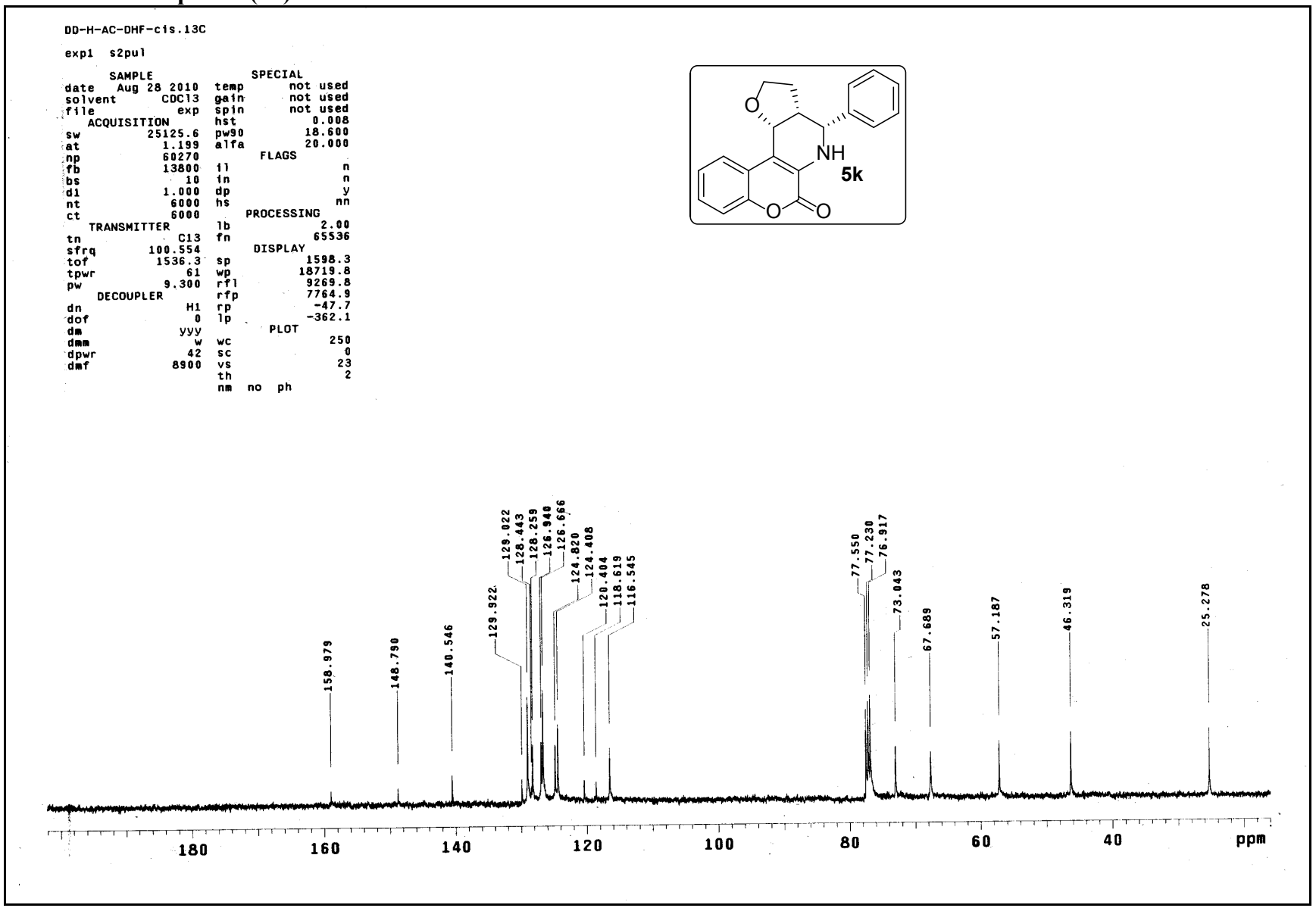
^{13}CNMR of Compound (4k)



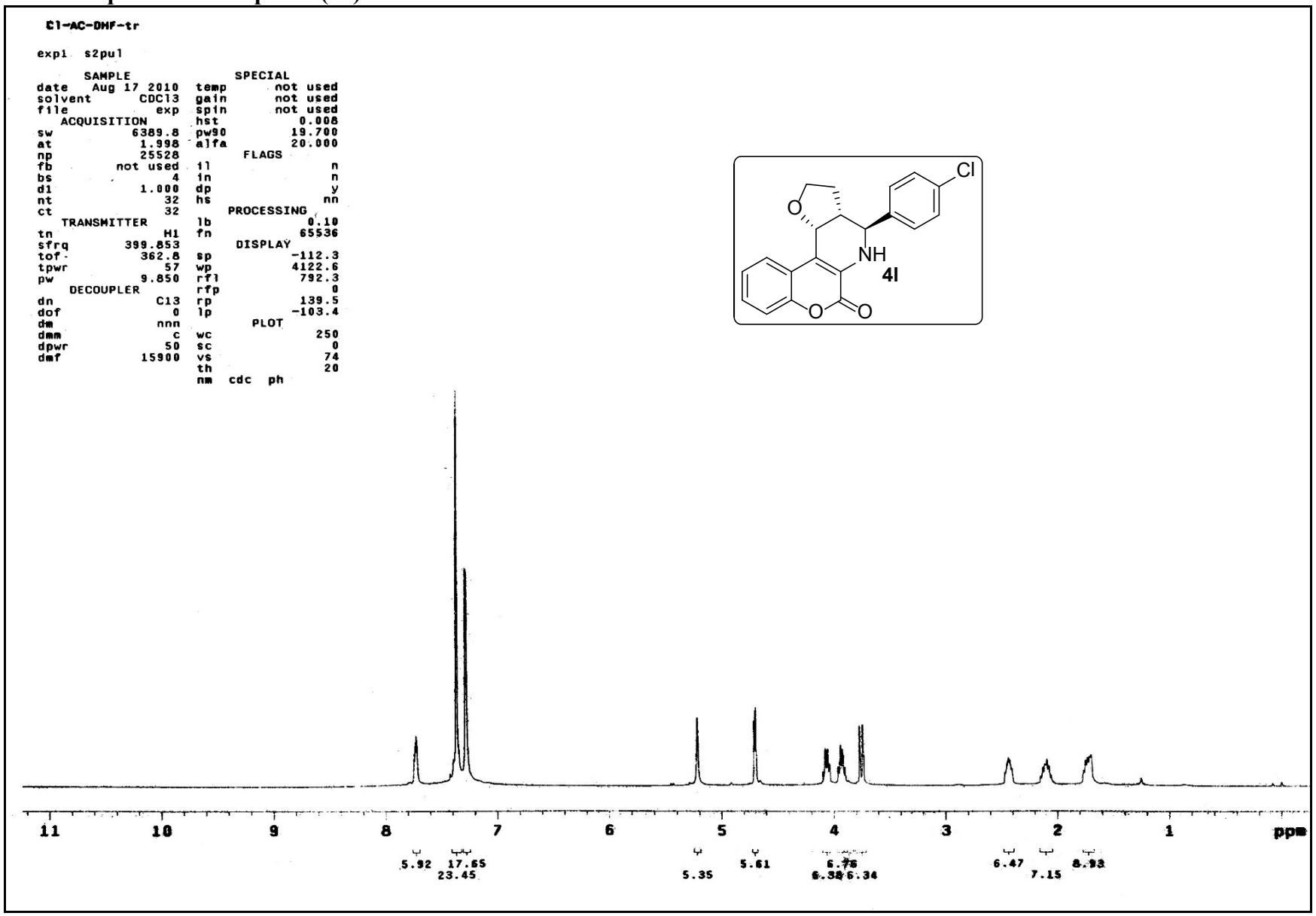
[1]HNMR Spectra of Compound(5k)



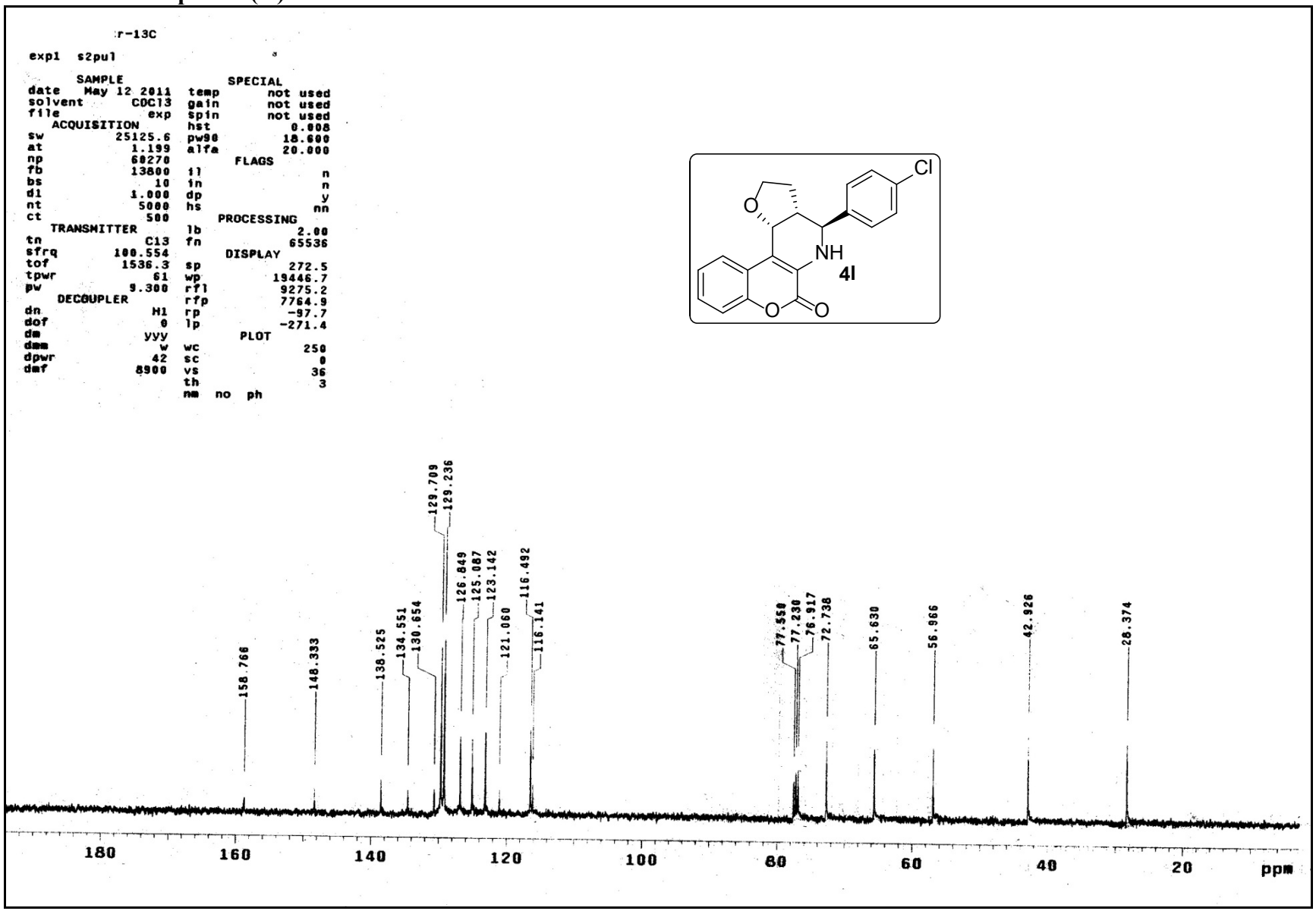
^{13}CNMR of Compound (5k)



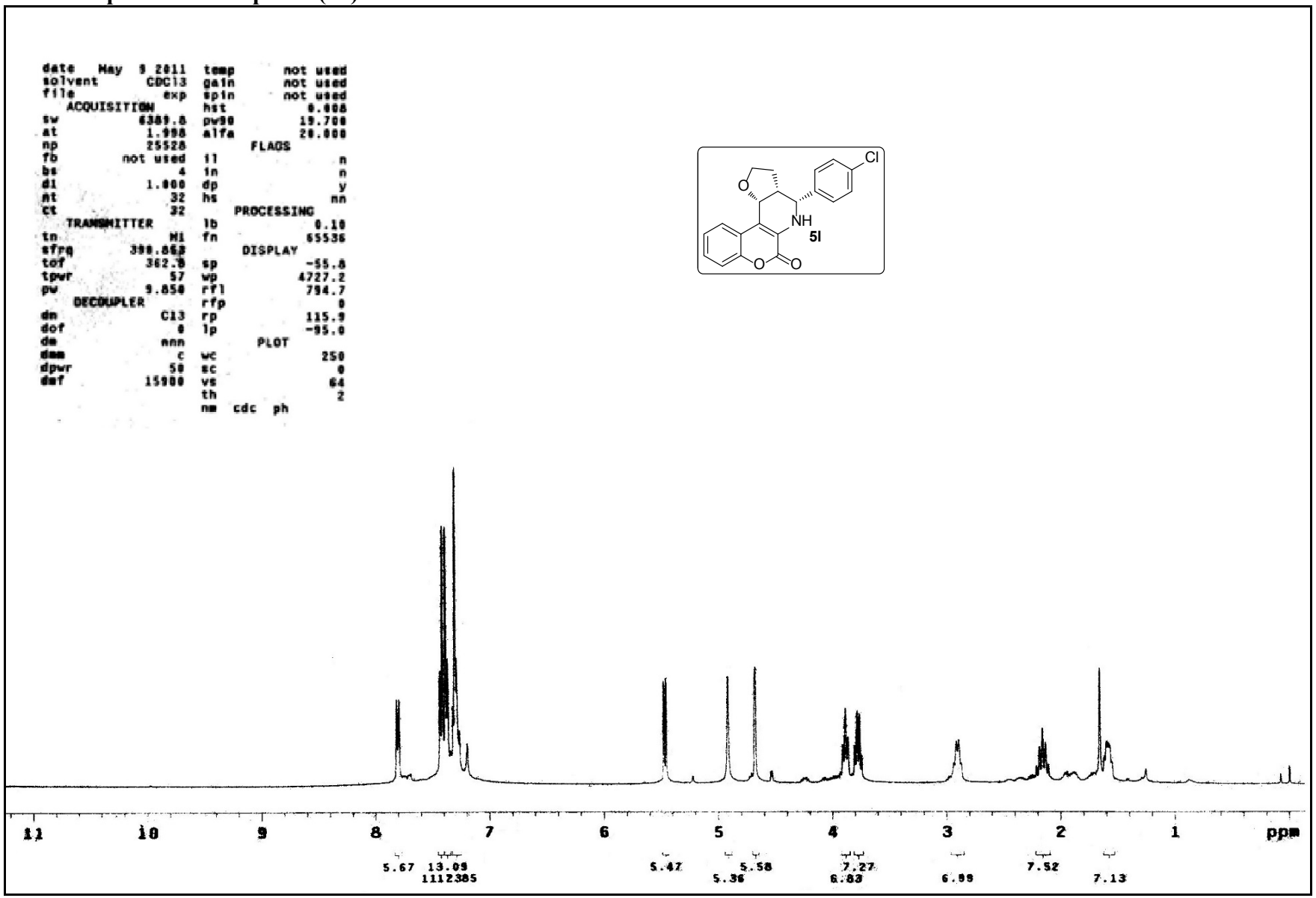
[1]HNMR Spectra of Compound(4l)



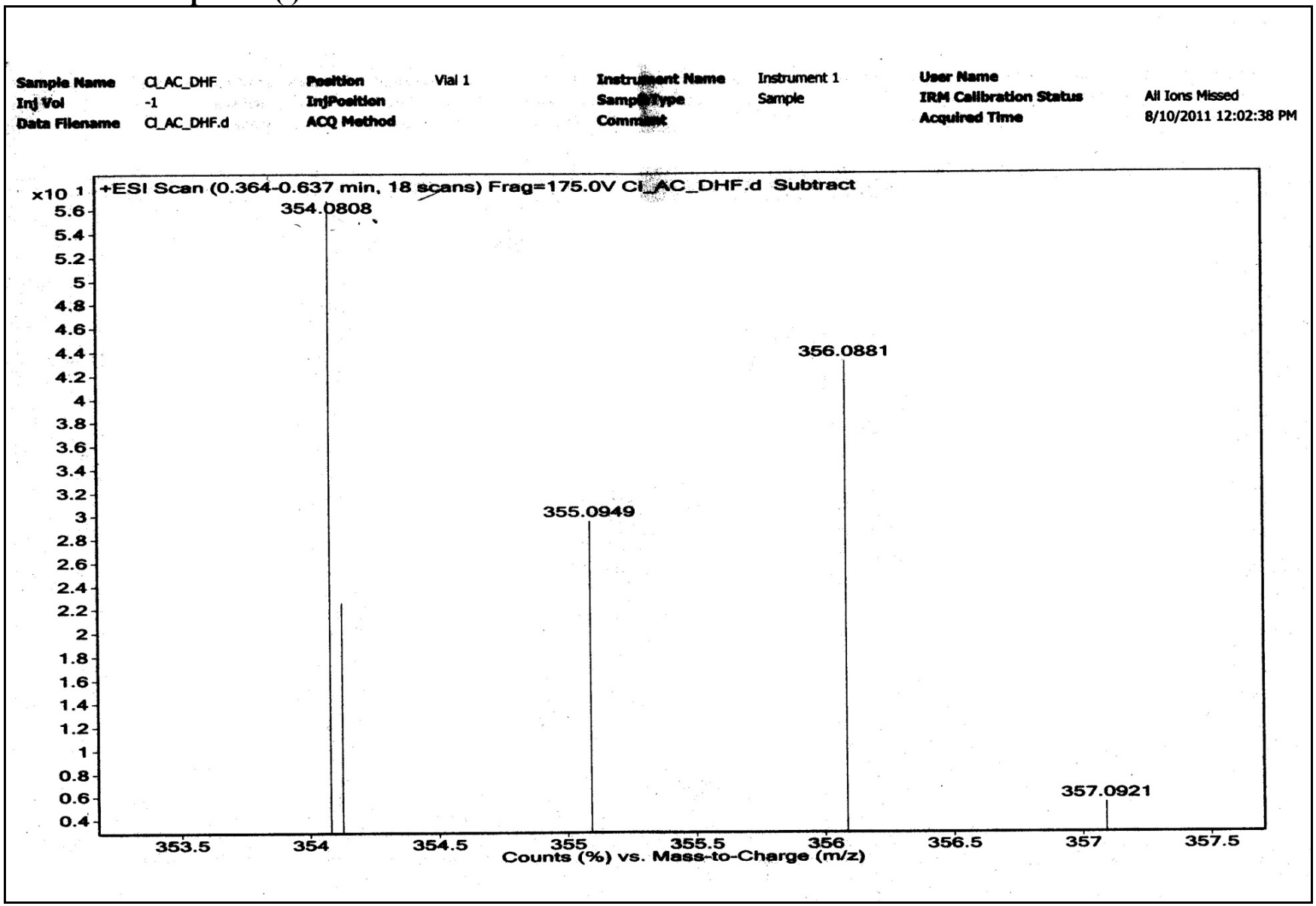
^{13}CNMR of Compound (4l)



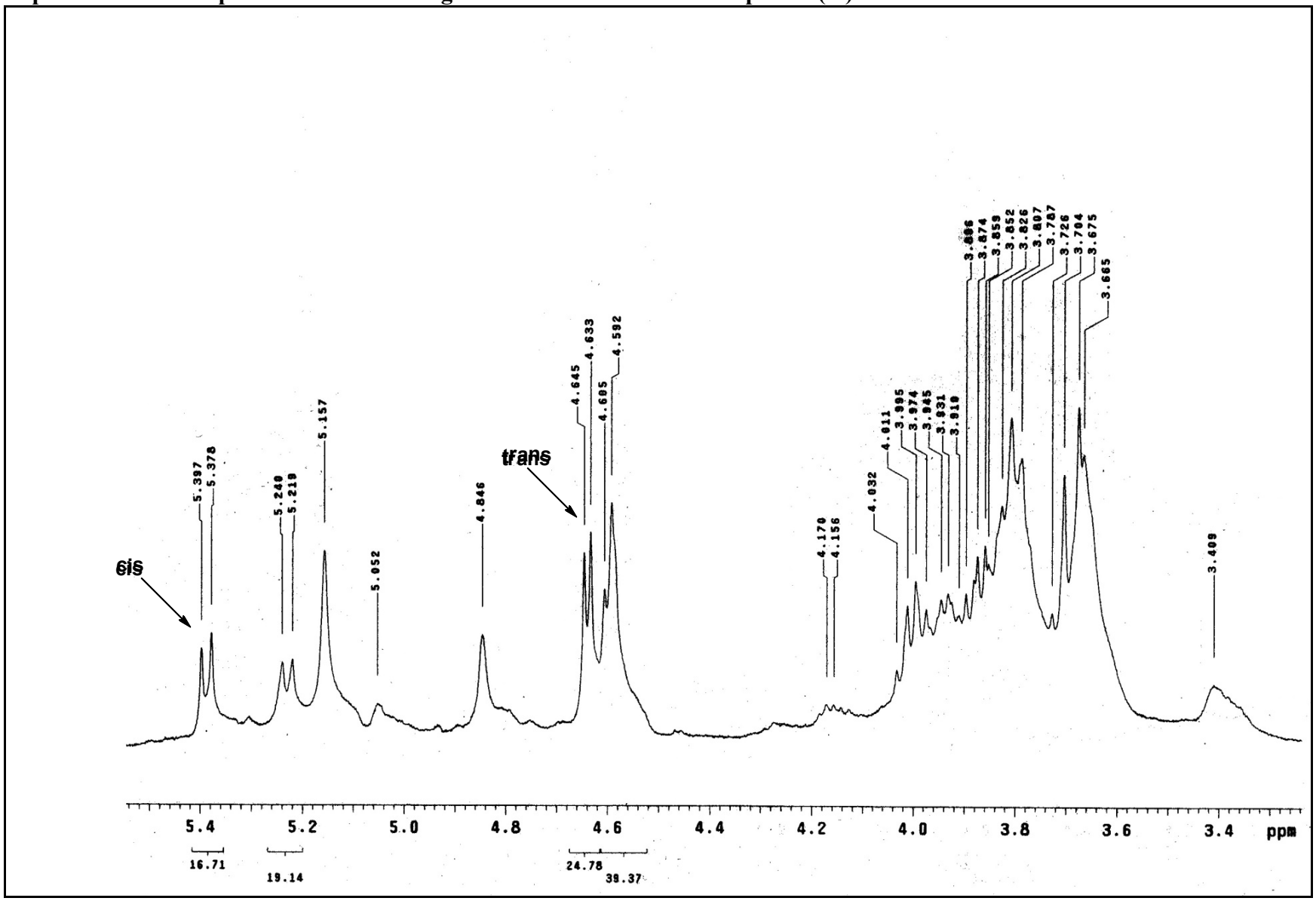
[1]HNMR Spectra of Compound(5l)



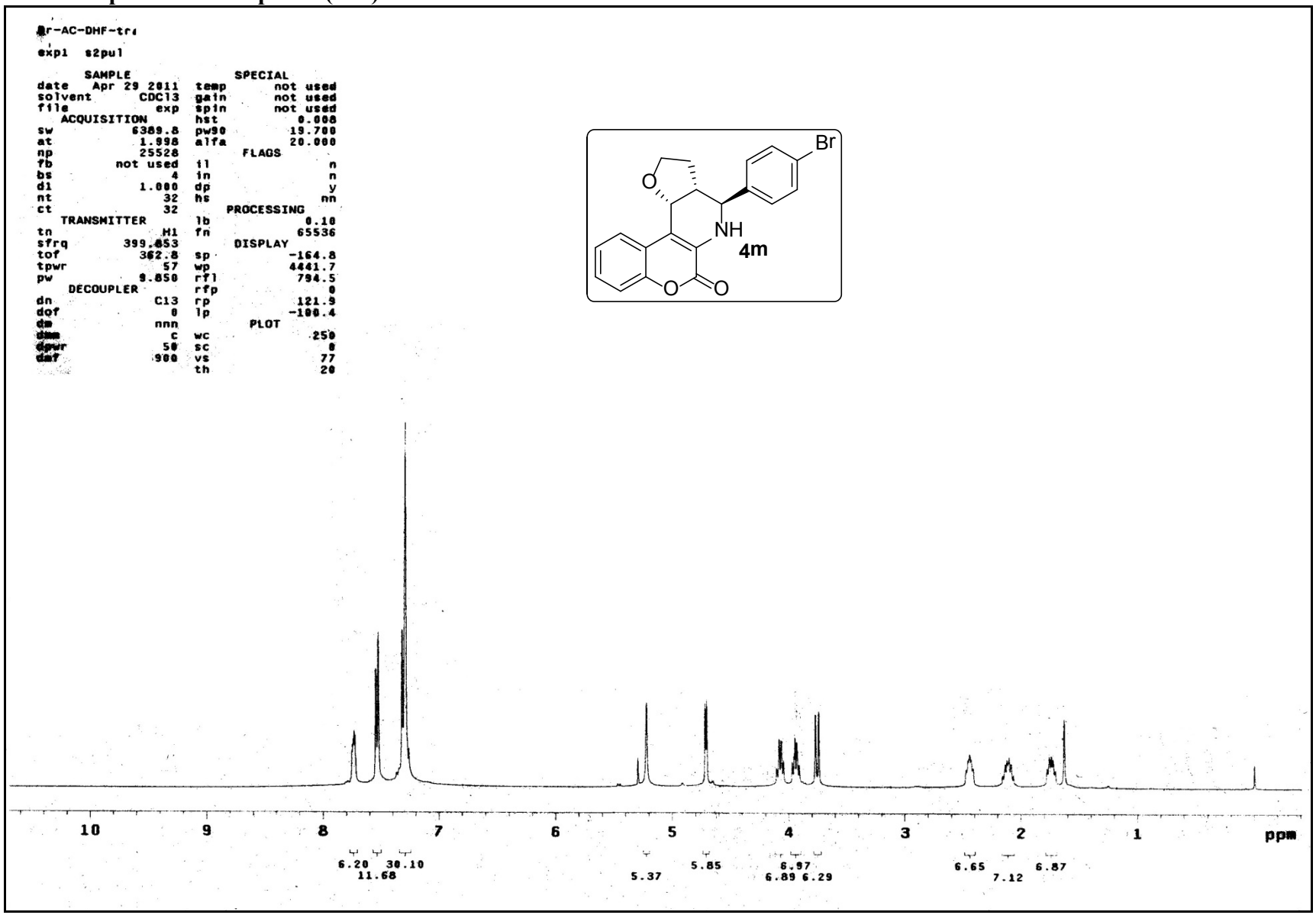
HRMS of Compound (l)



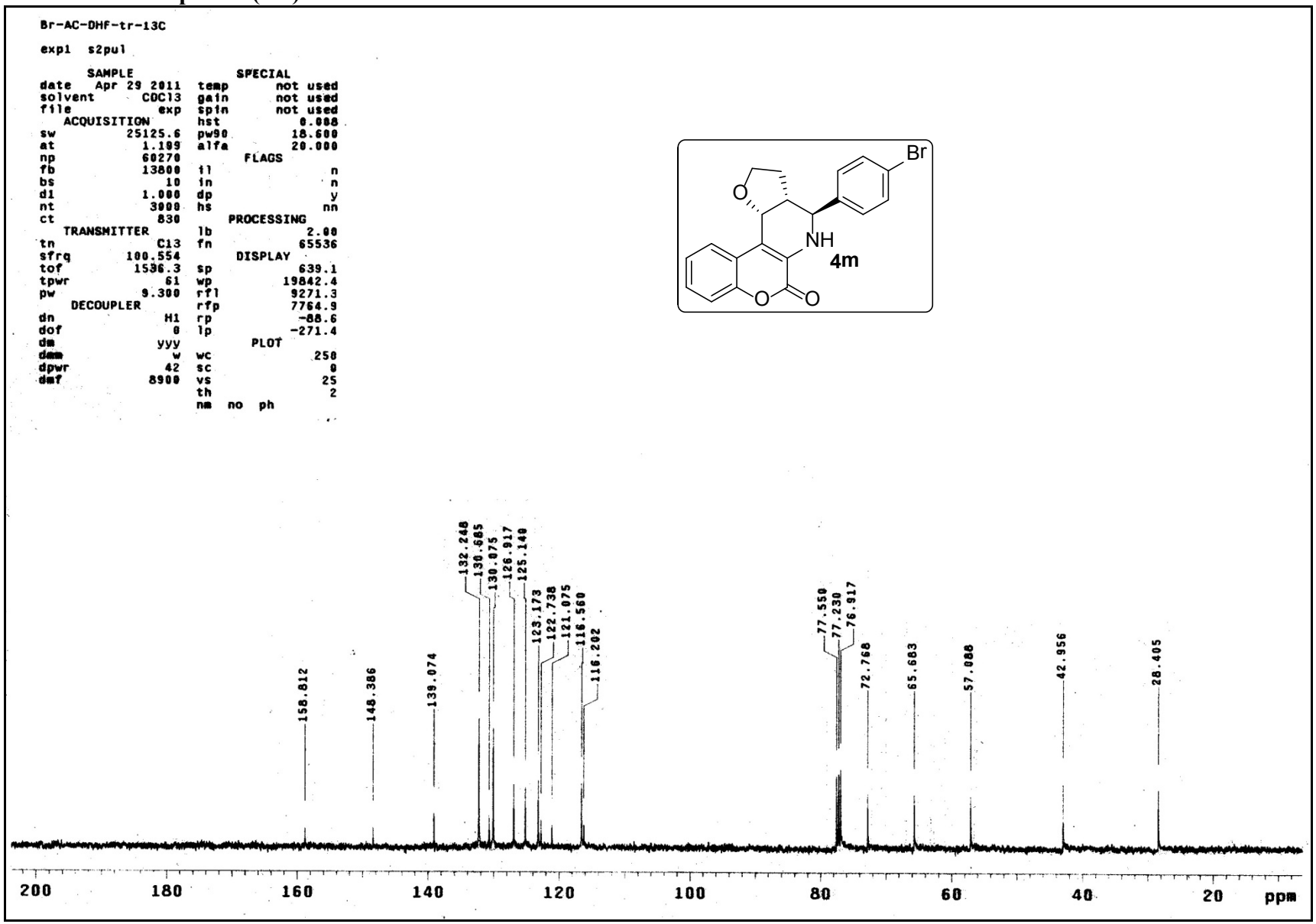
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (m)



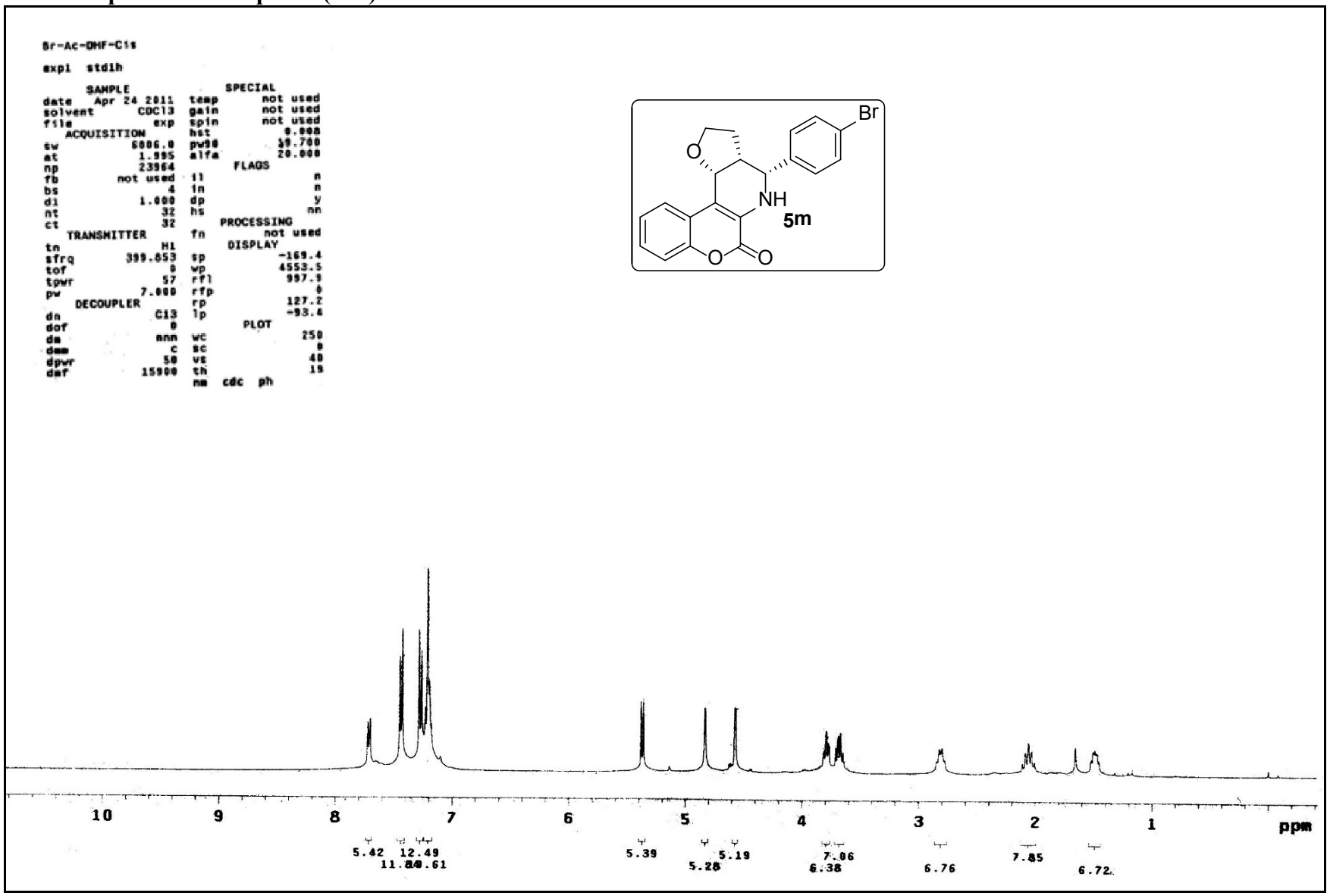
[1]HNMR Spectra of Compound(4m)



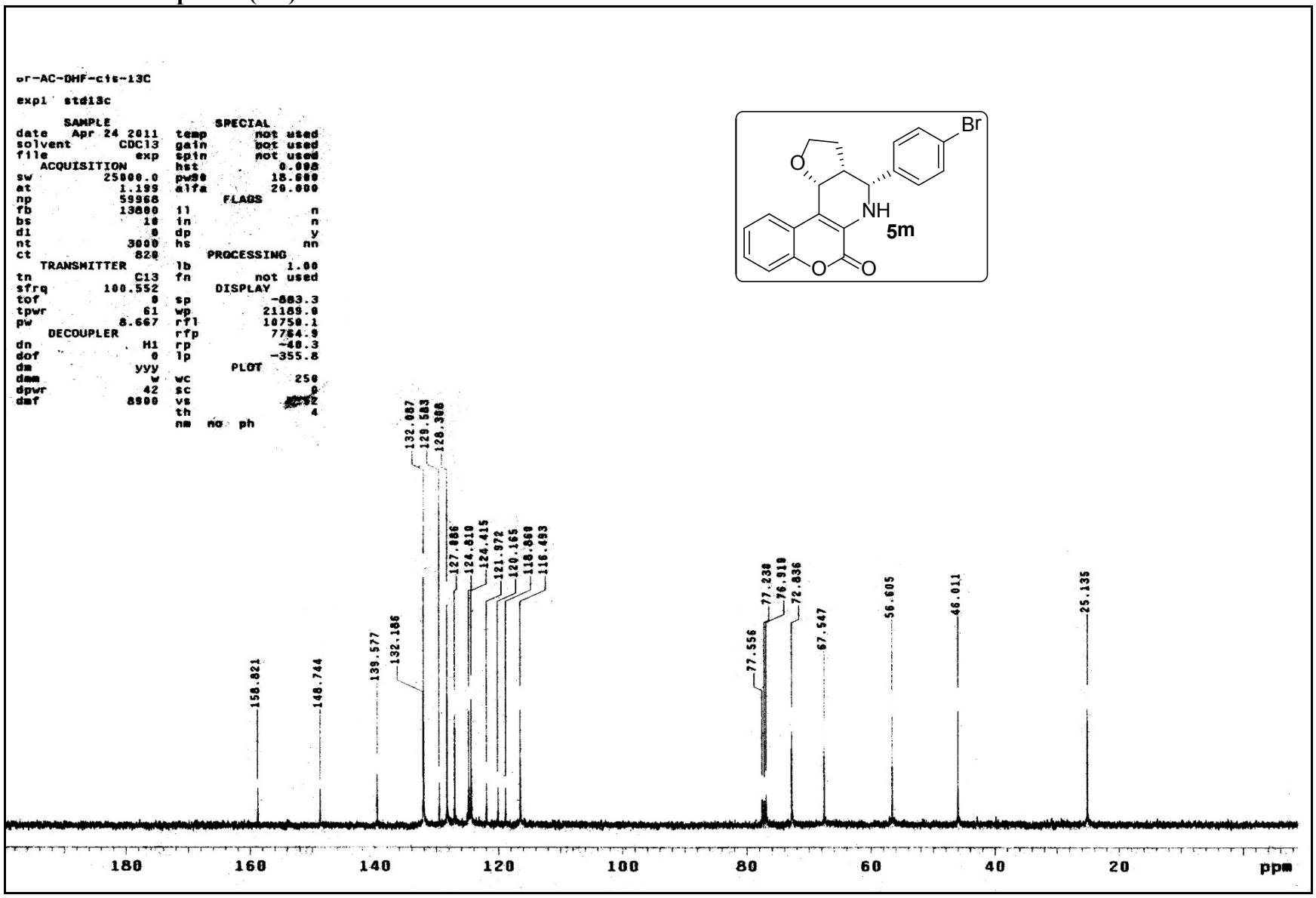
^{13}CNMR of Compound (4m)



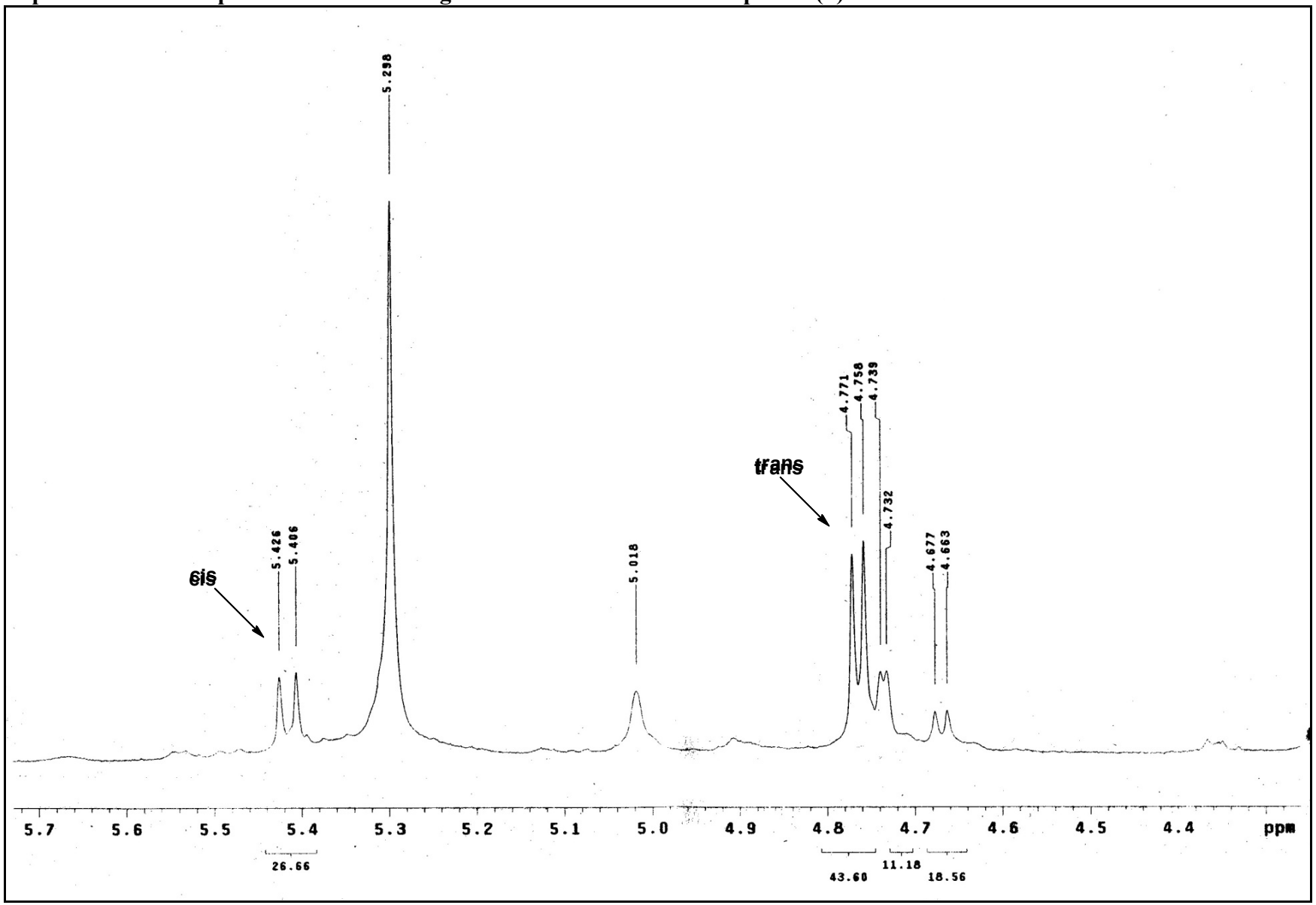
^{1}HNMR Spectra of Compound(5m)



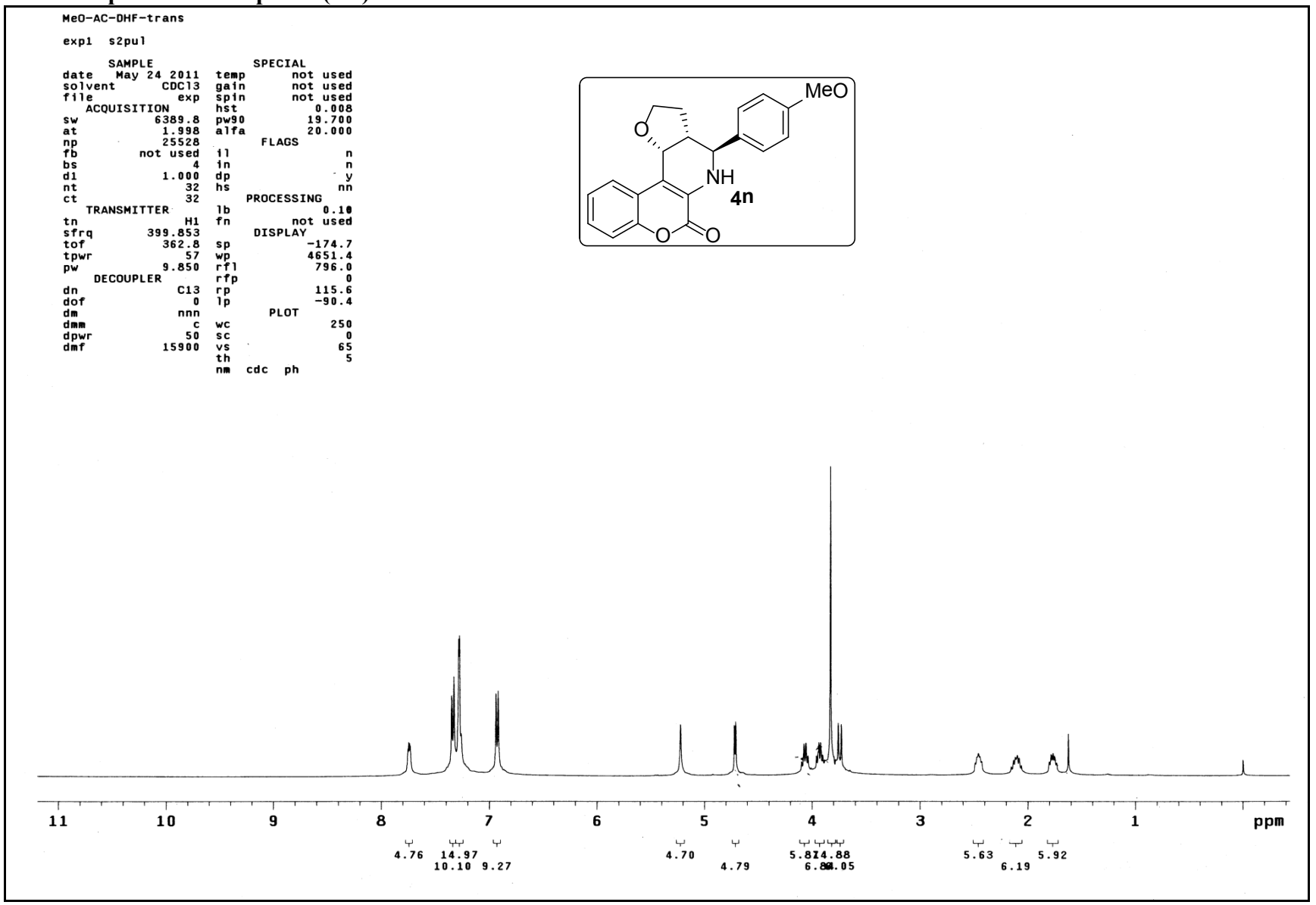
^{13}CNMR of Compound (5m)



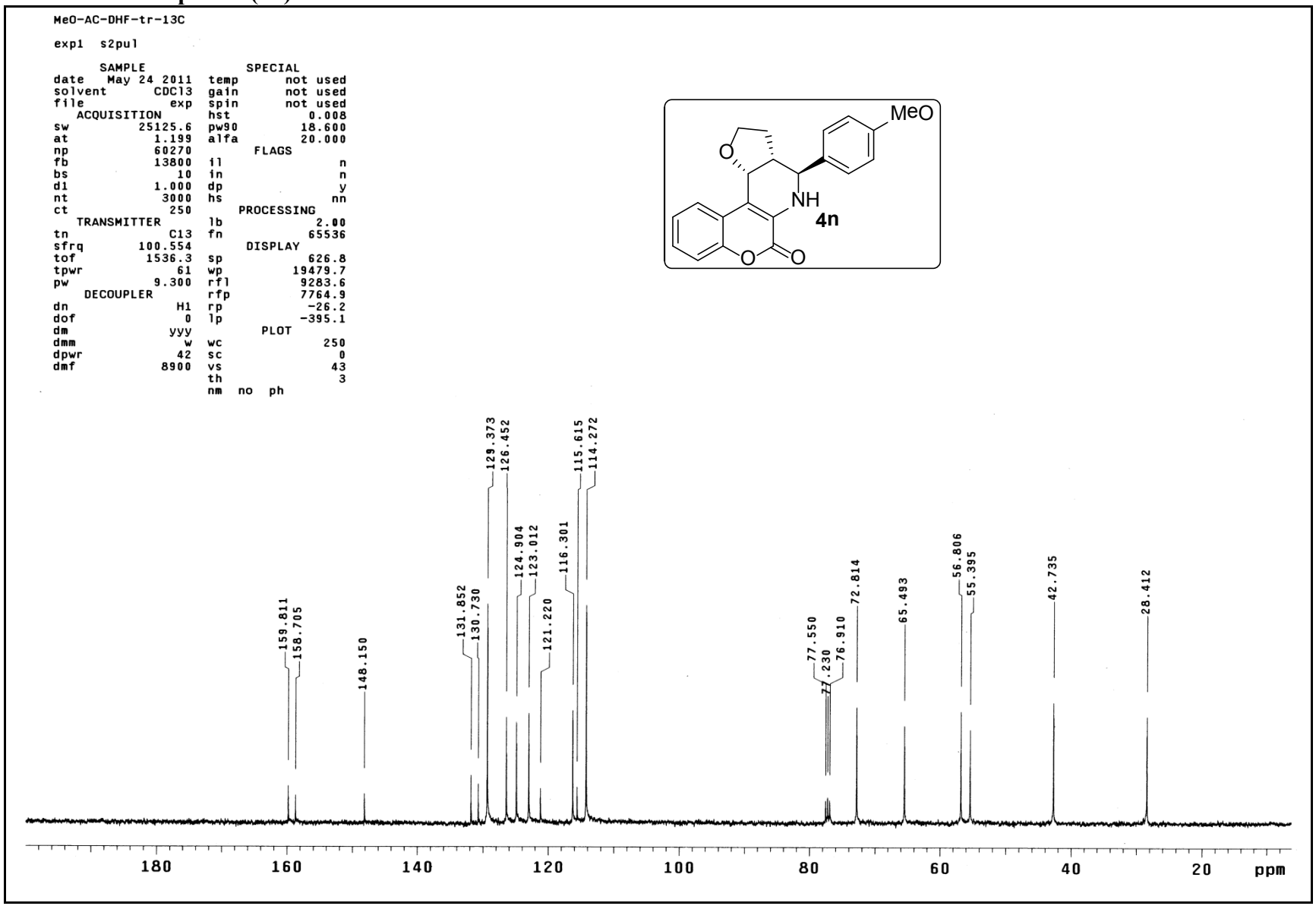
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (n)



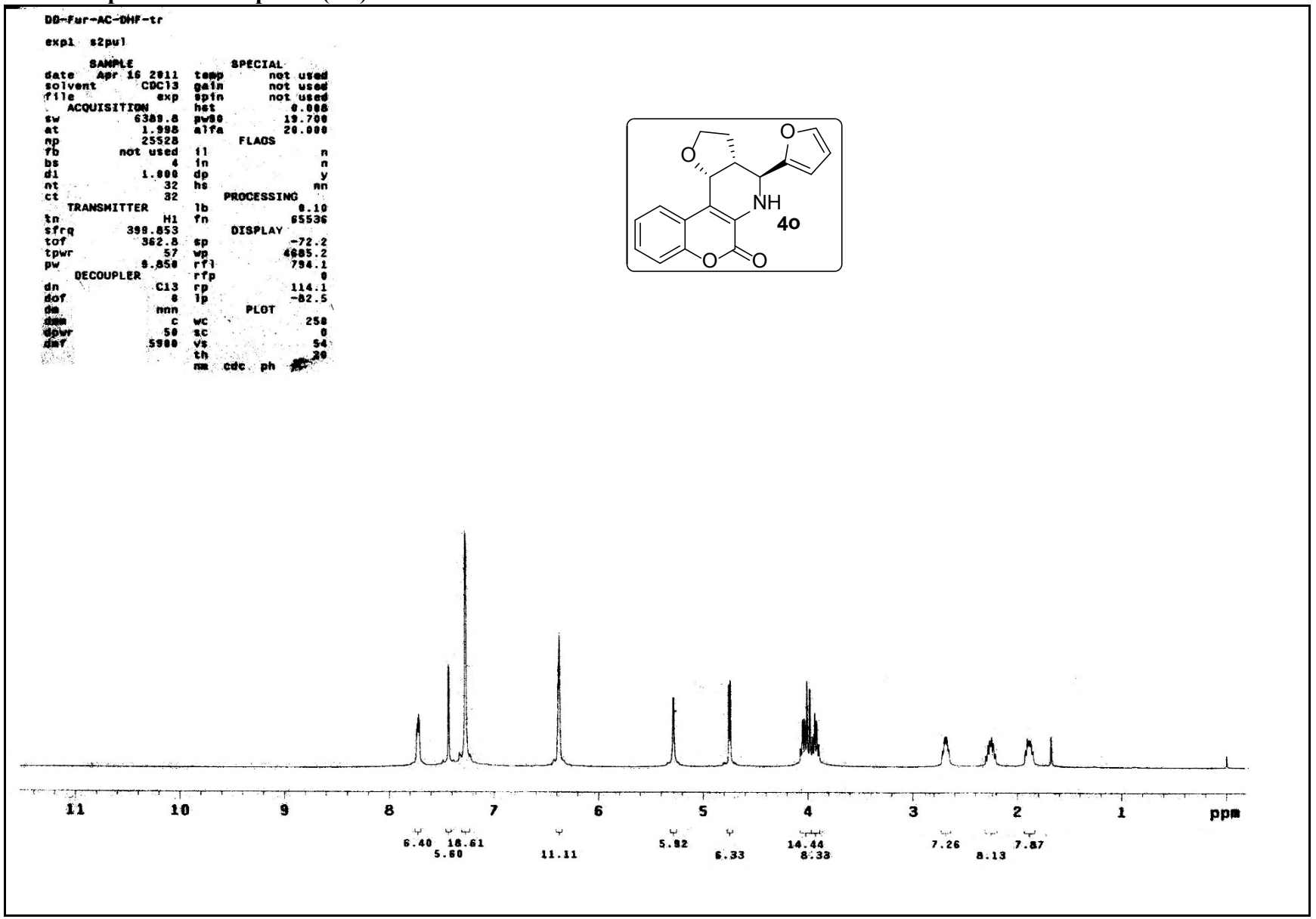
^{1}HNMR Spectra of Compound(4n)



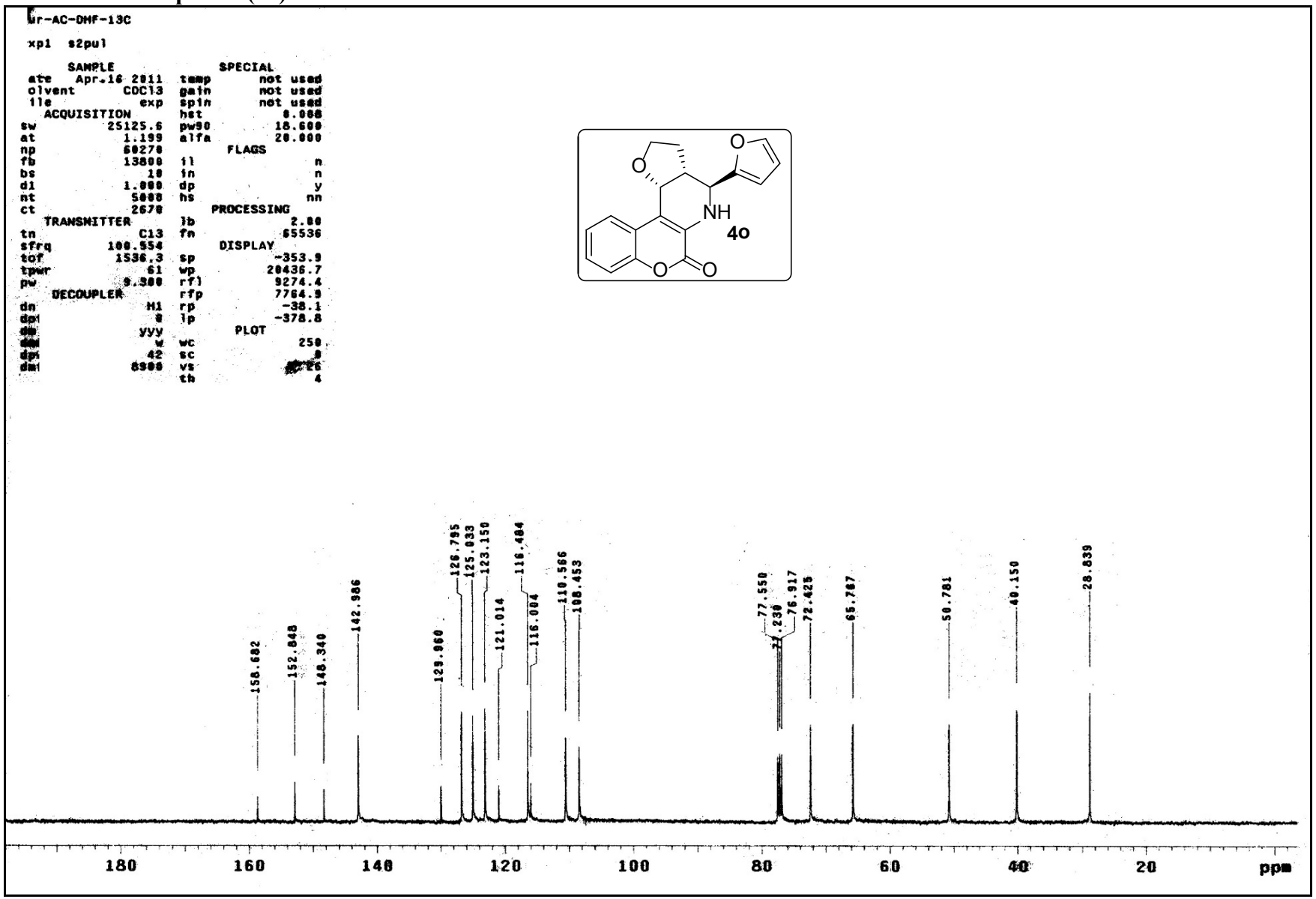
^{13}CNMR of Compound (4n)



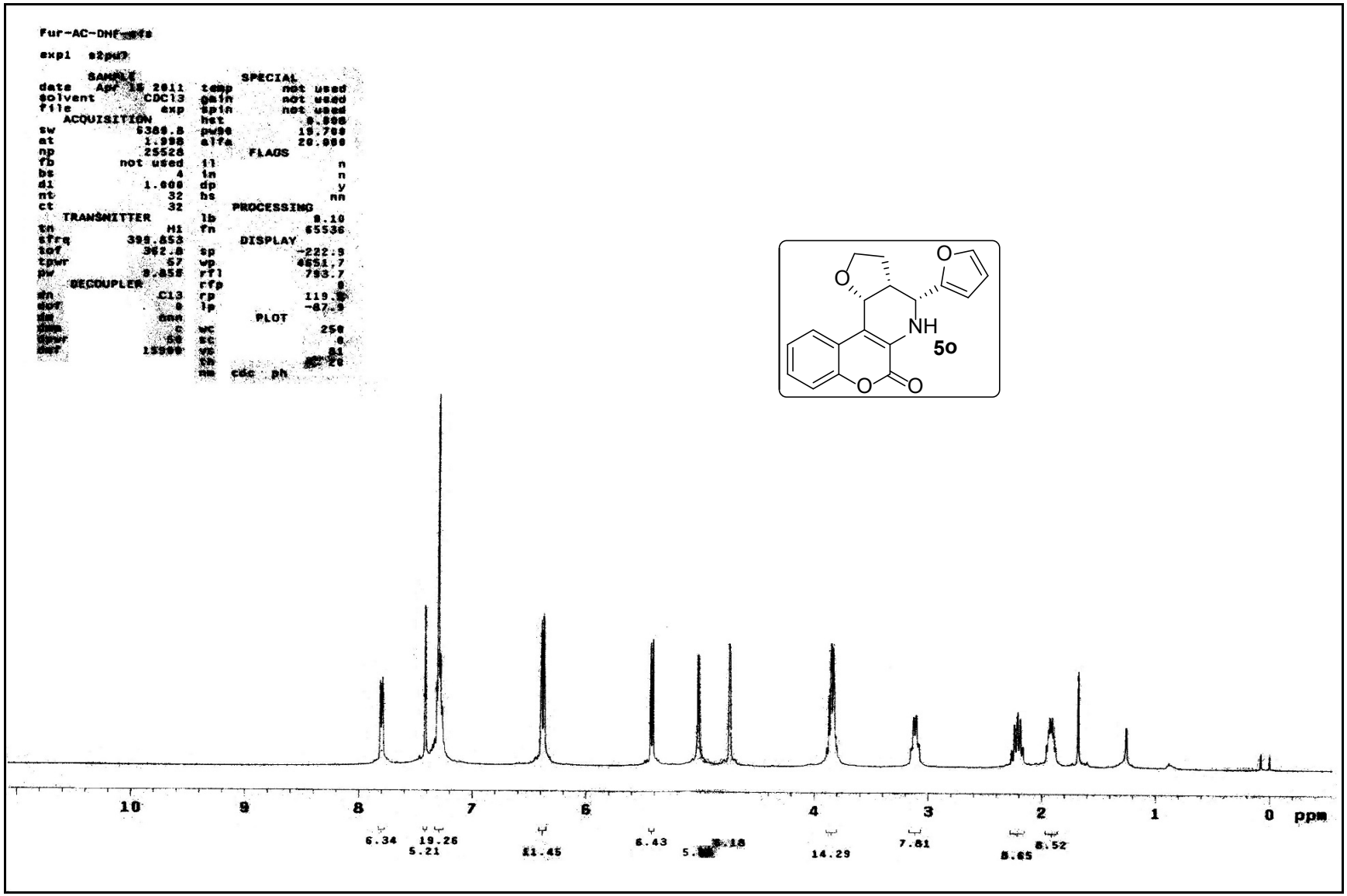
^{1}HNMR Spectra of Compound(4o)



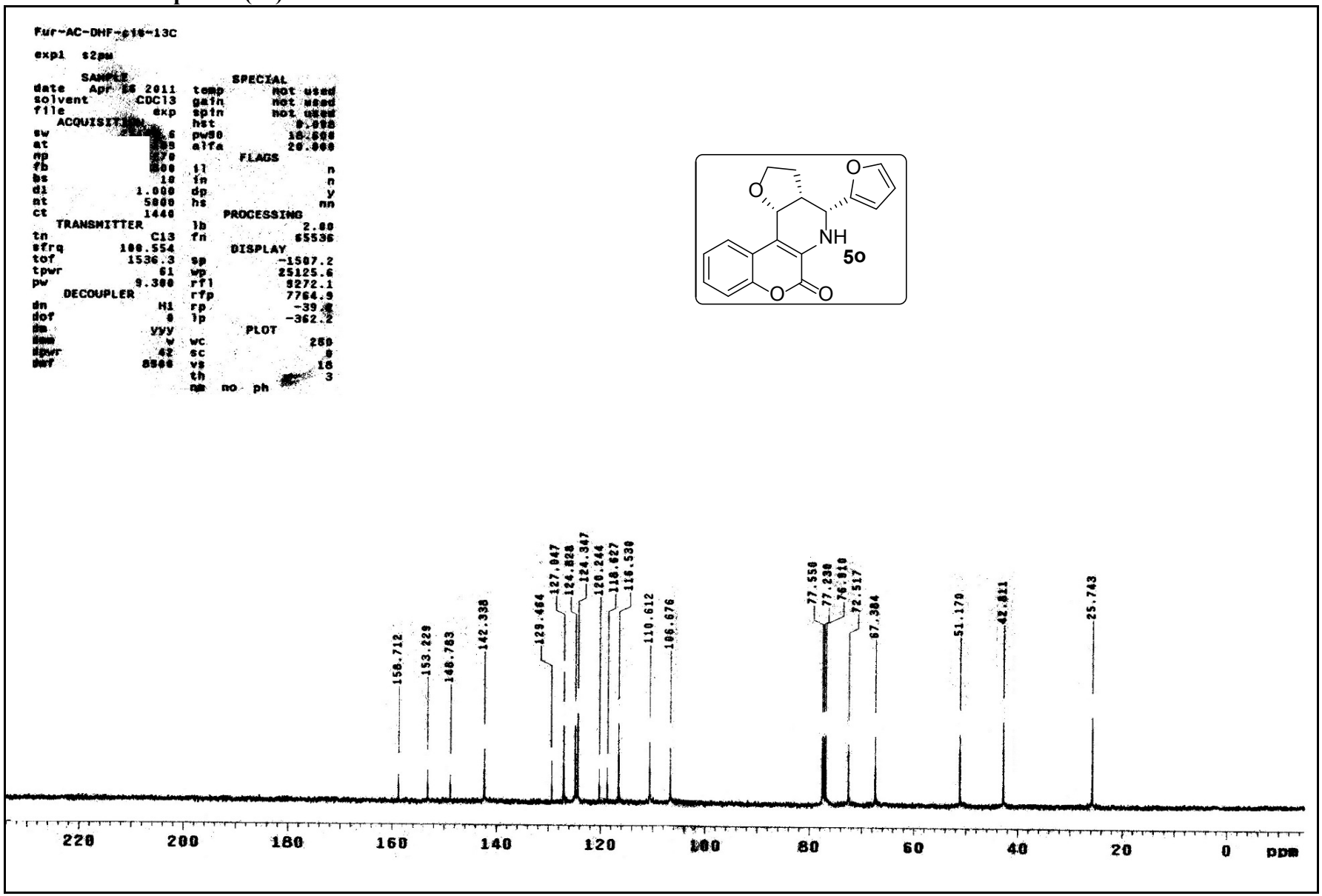
^{13}CNMR of Compound (4o)



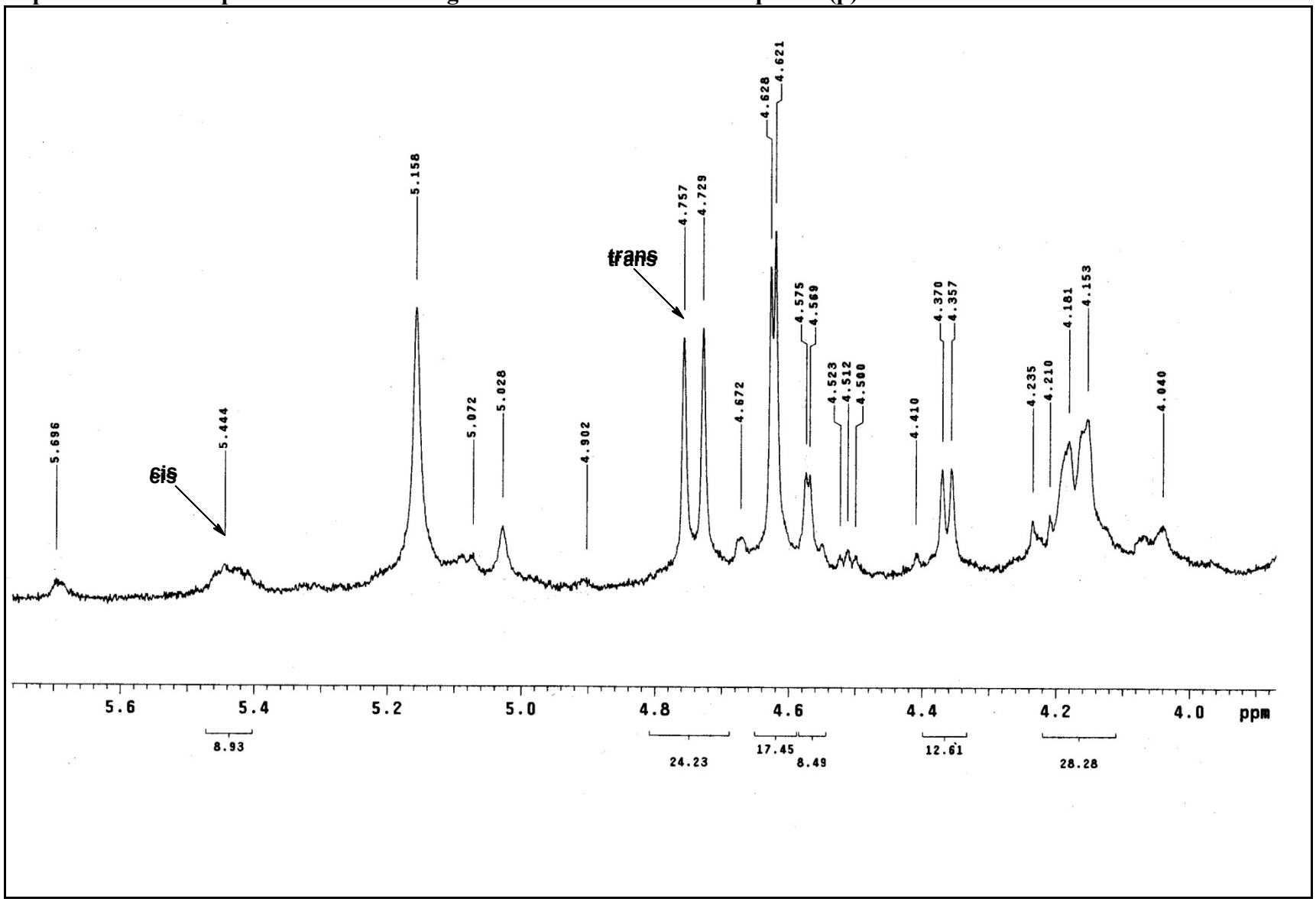
[1]HNMR Spectra of Compound(5o)



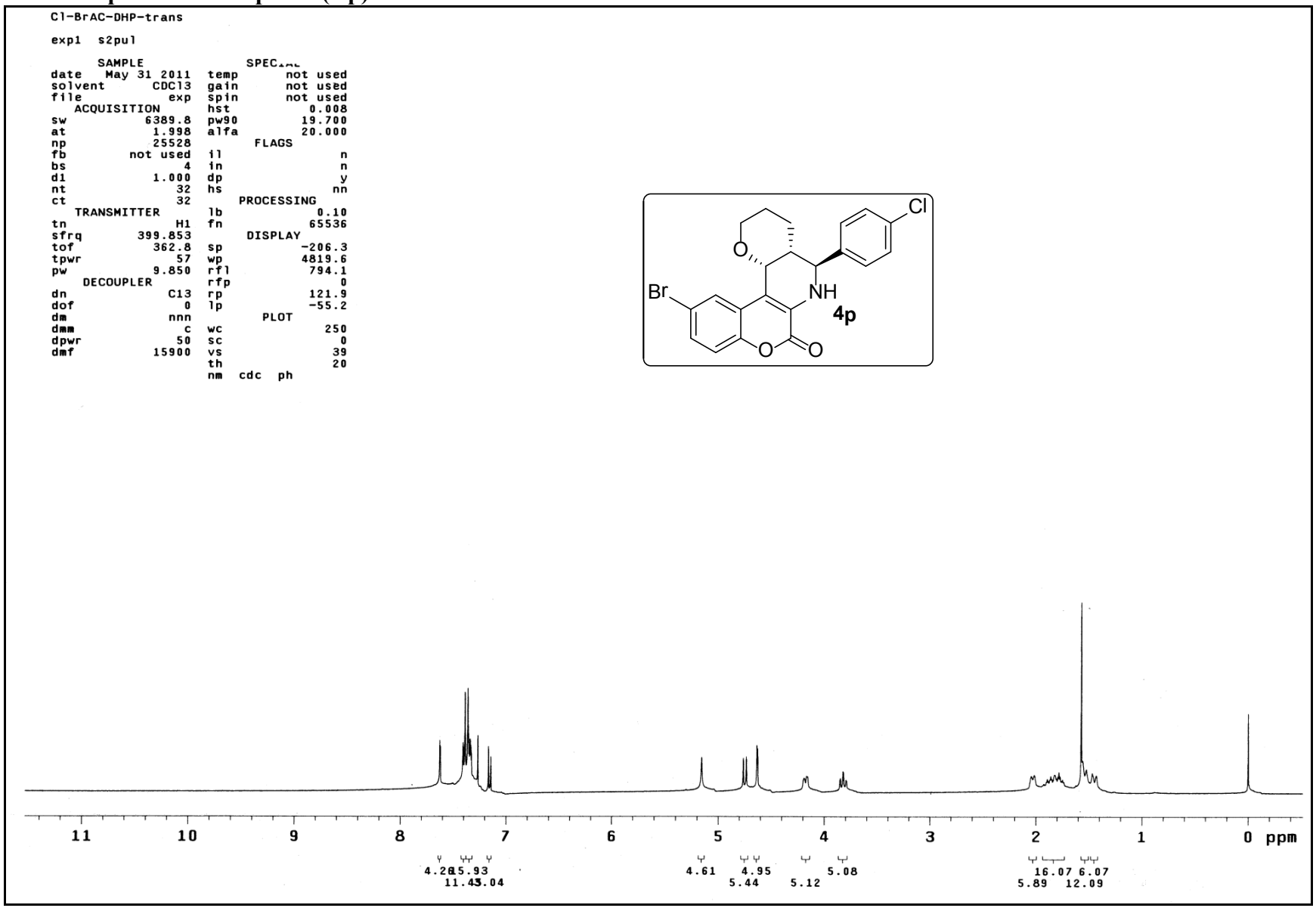
^{13}CNMR of Compound (5o)



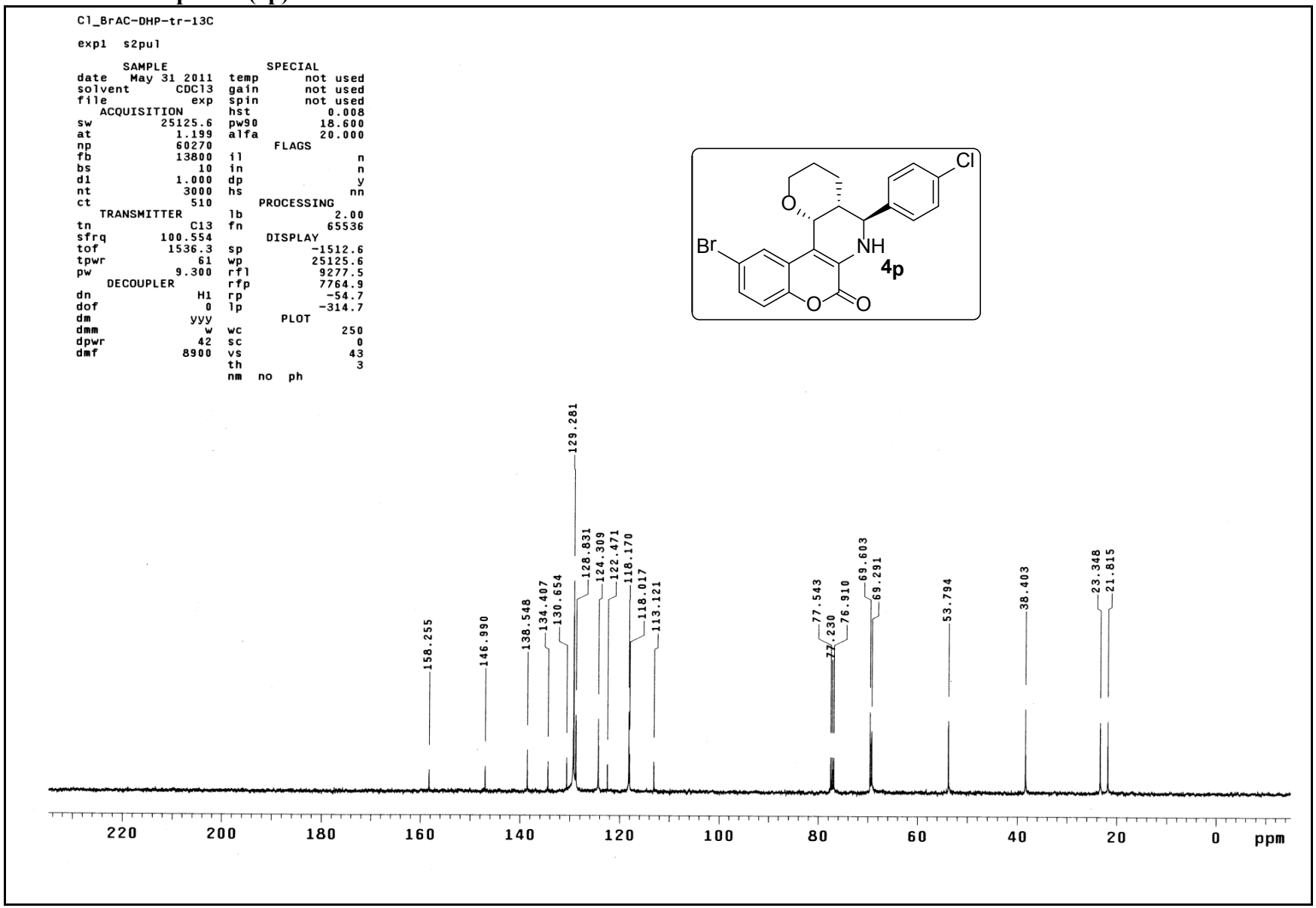
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (p)



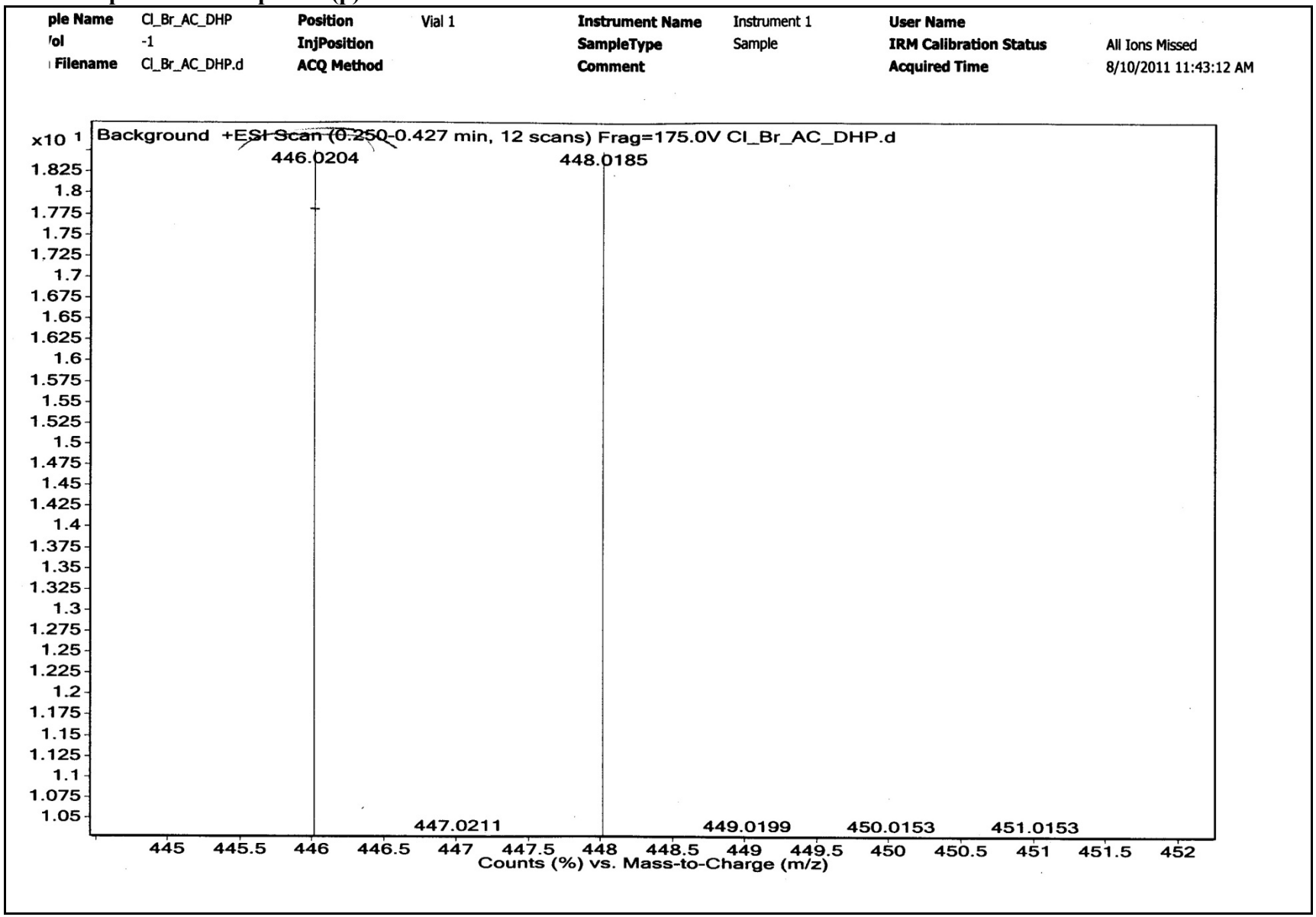
^{1}HNMR Spectra of Compound(4p)



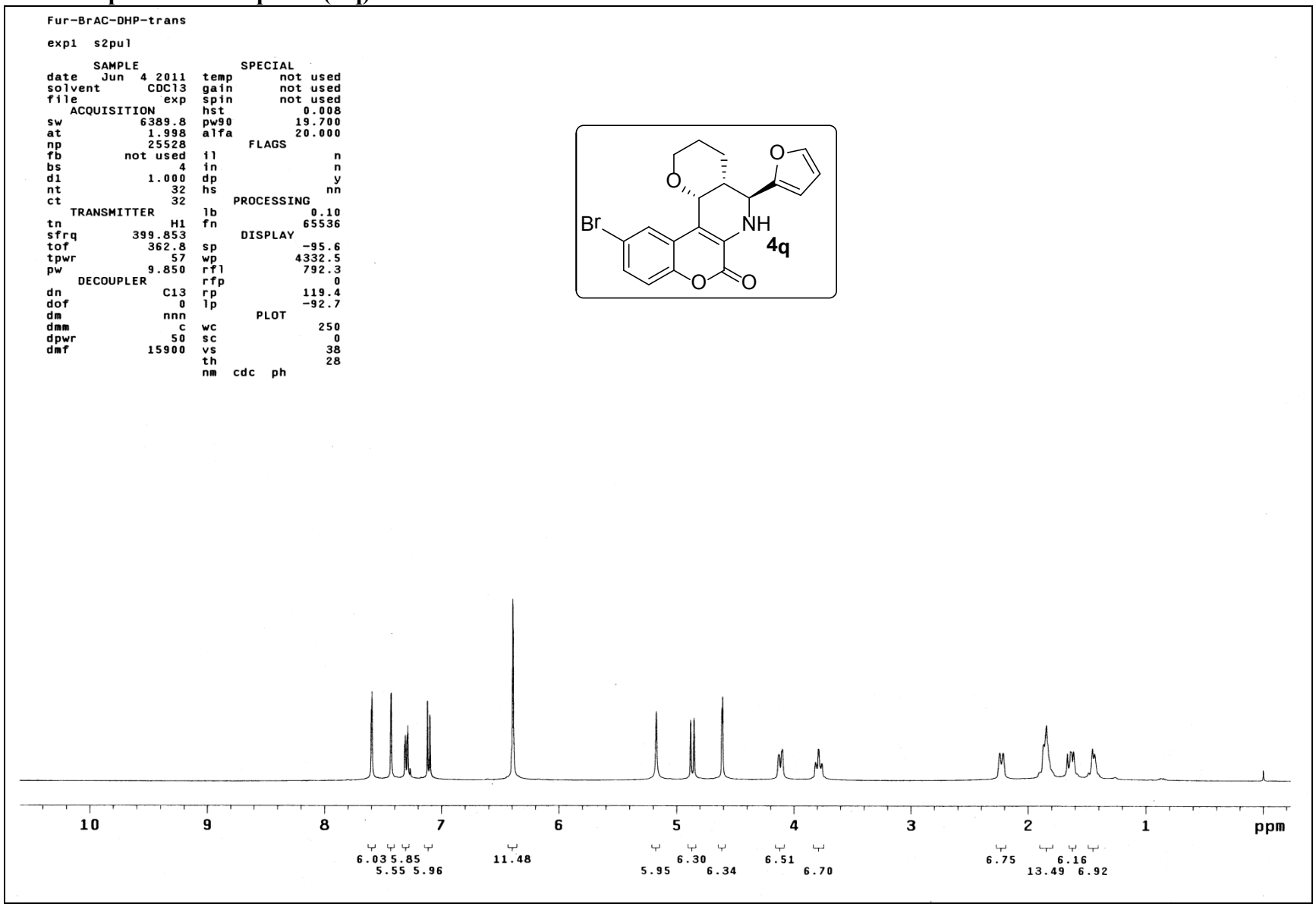
^{13}CNMR of Compound (4p)



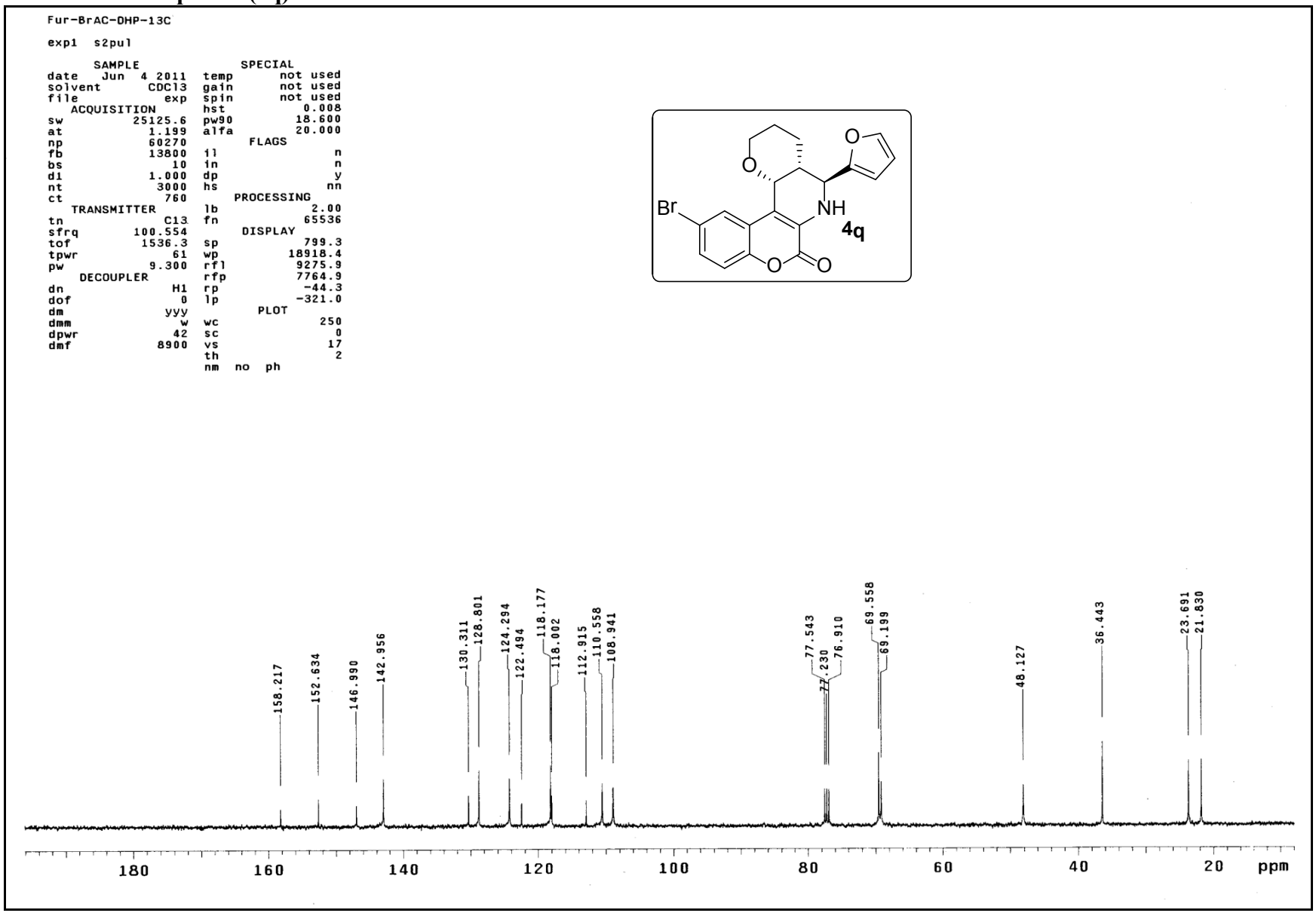
^{1}HNMR Spectra of Compound (p)



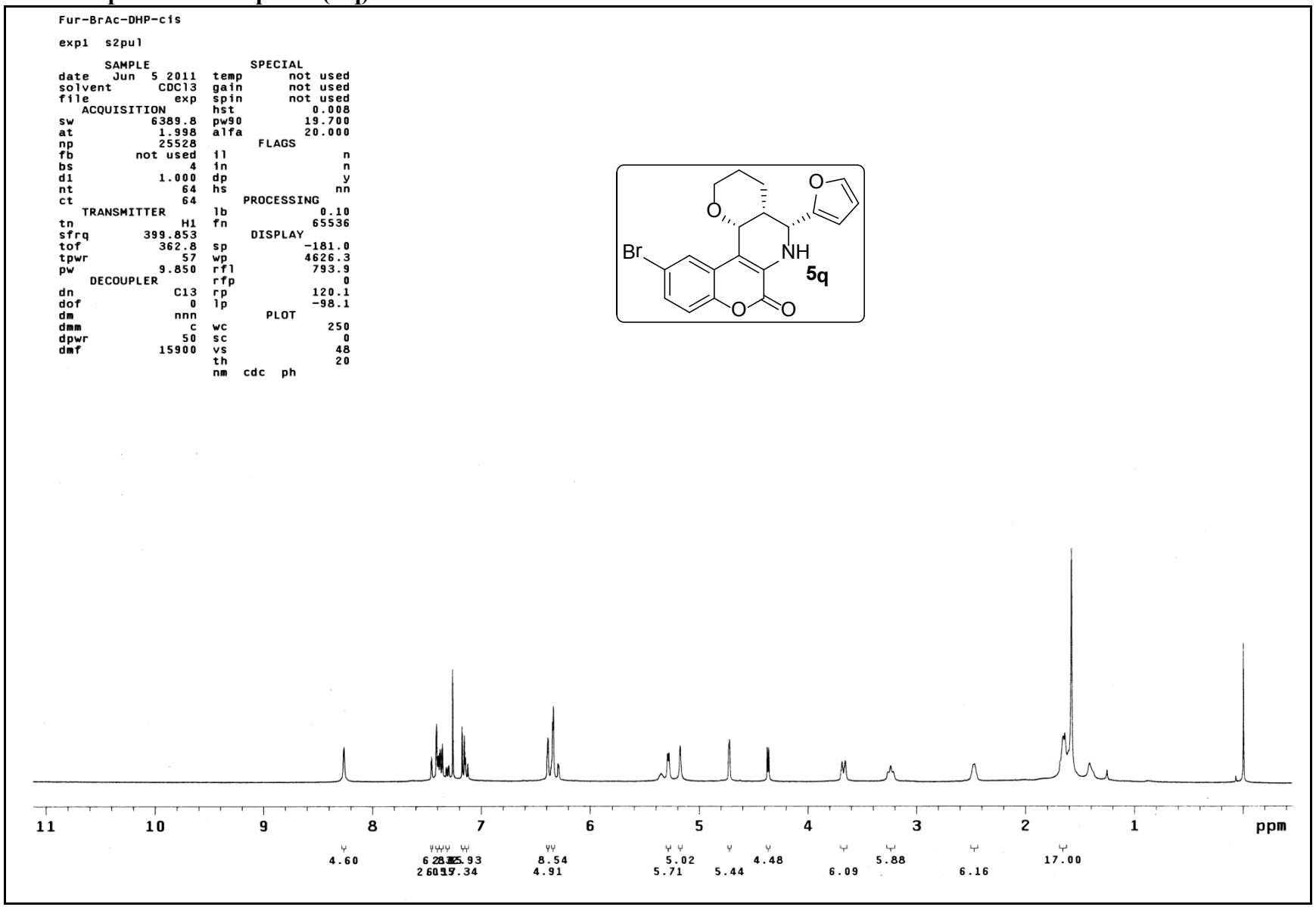
^{1}HNMR Spectra of Compound(4q)



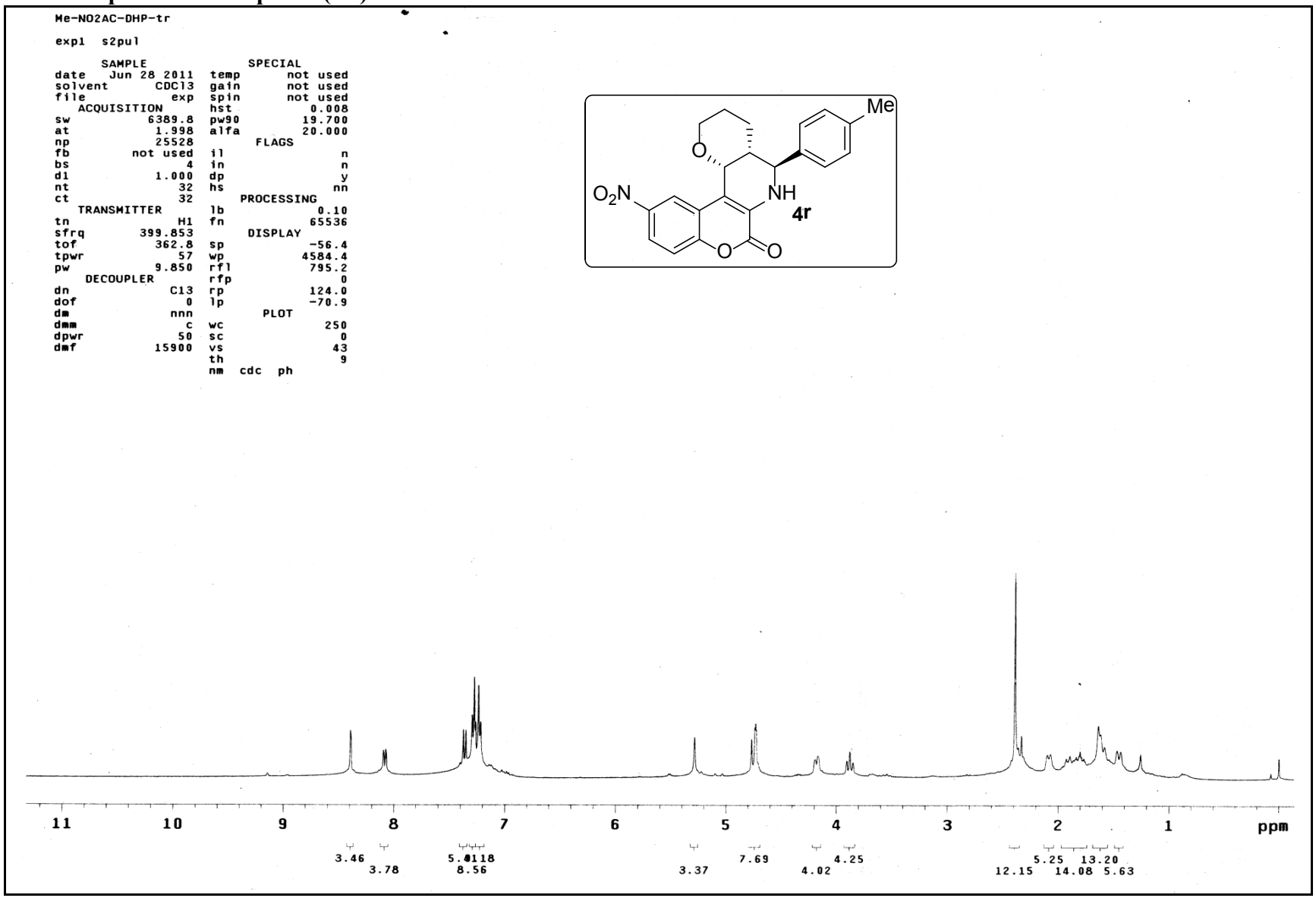
^{13}CNMR of Compound (4q)



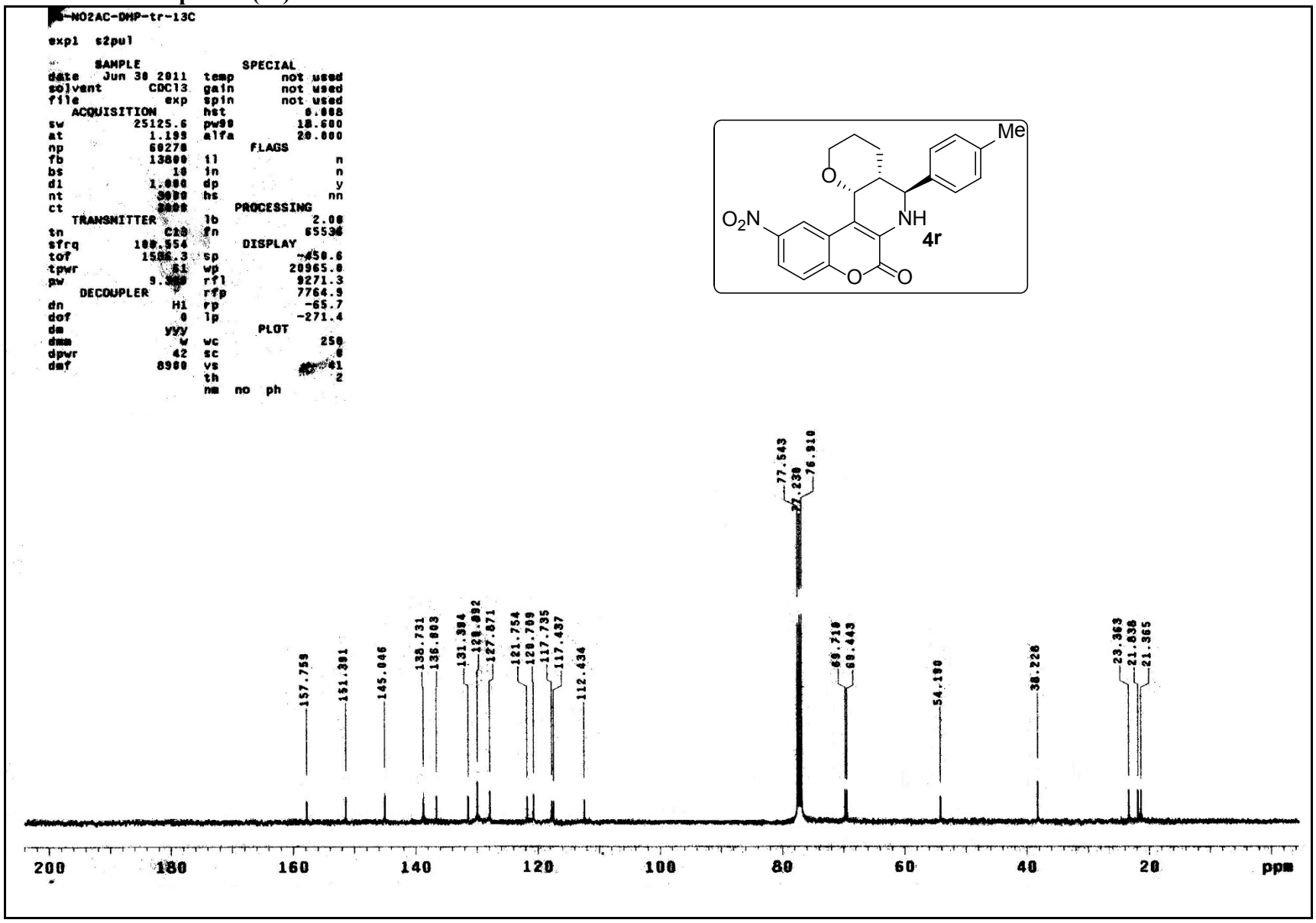
^{1}HNMR Spectra of Compound(5q)



^{1}HNMR Spectra of Compound(4r)

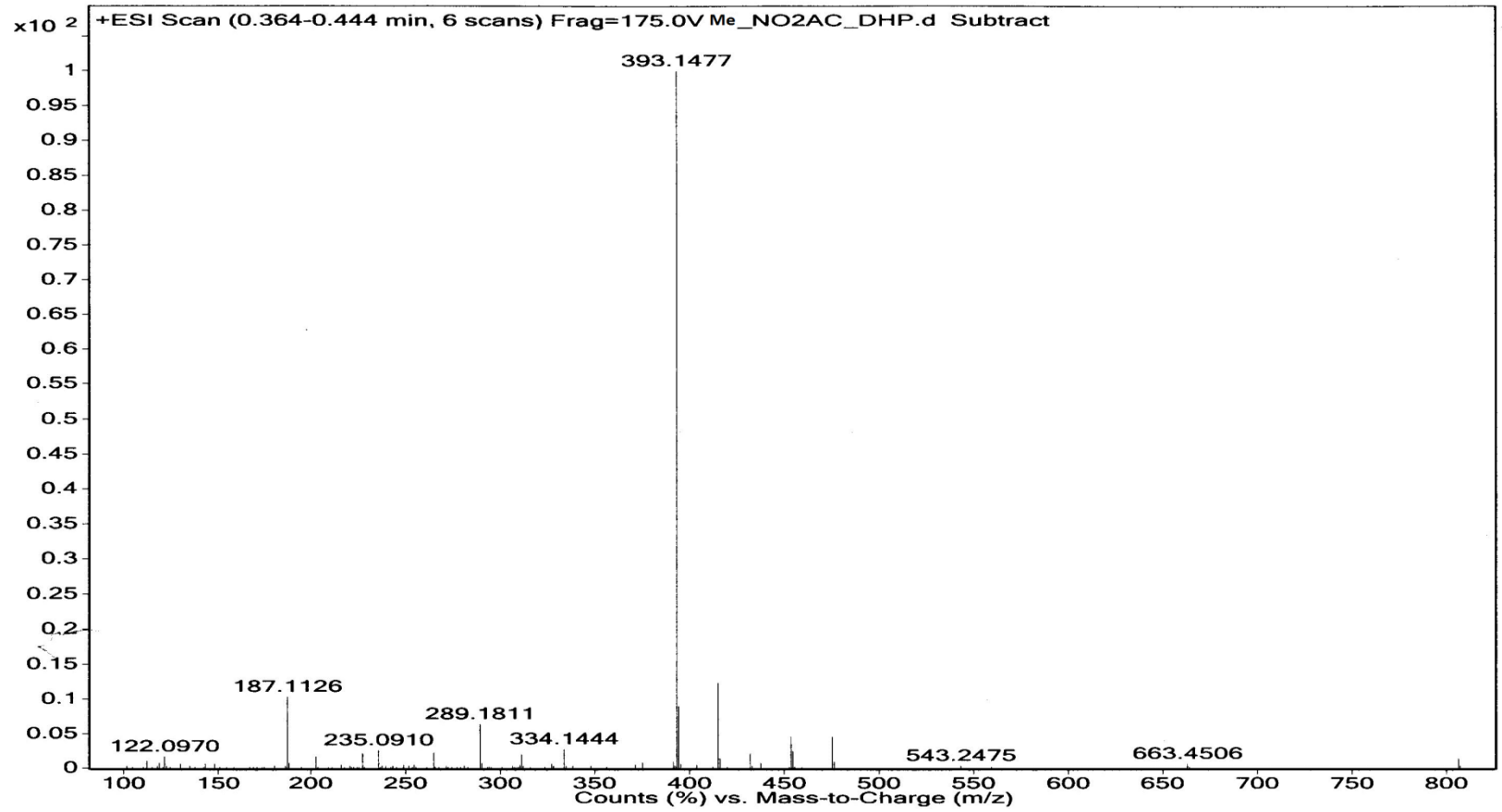


^{13}CNMR of Compound (4r)

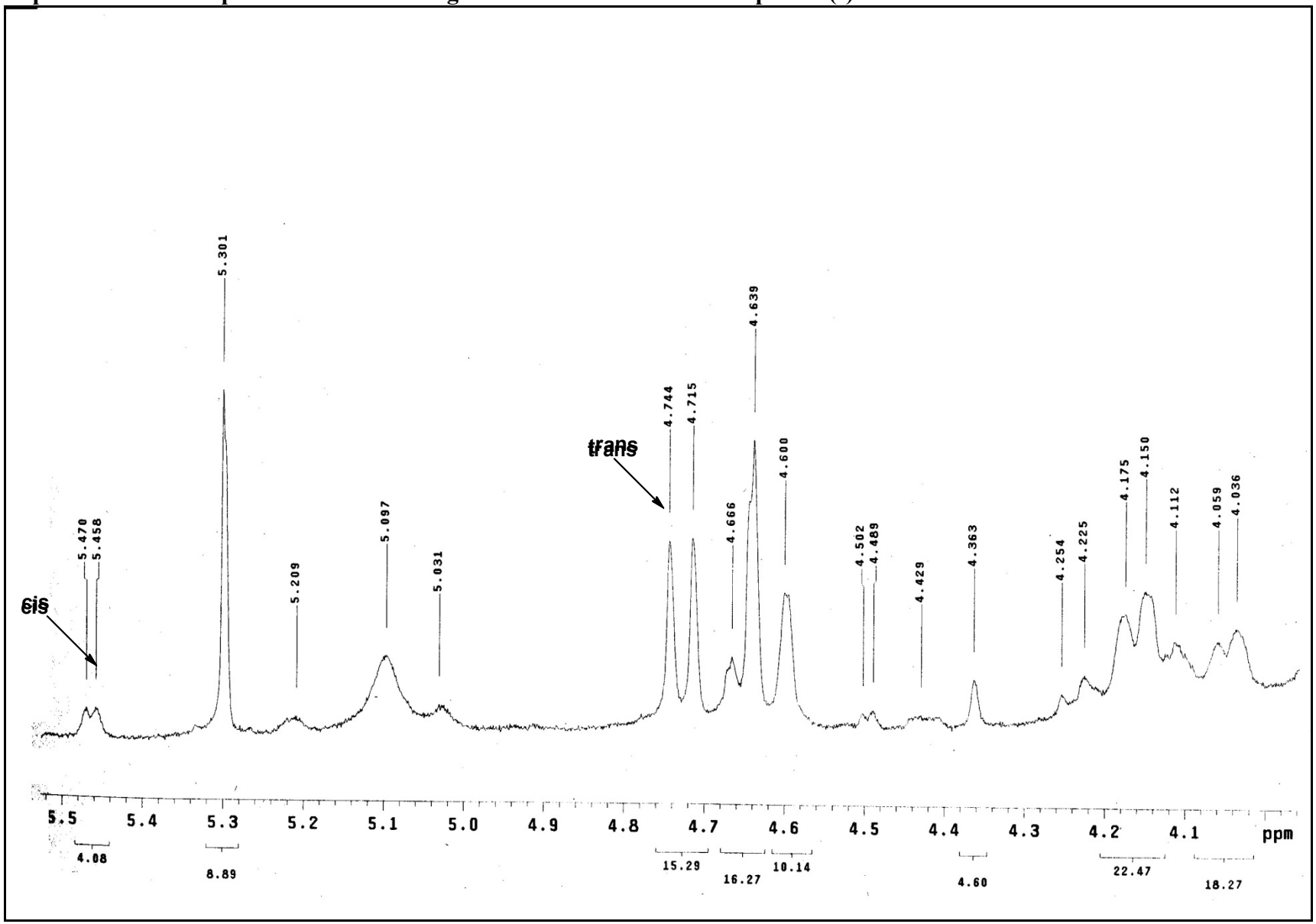


HRMS Spectra of Compound (r)

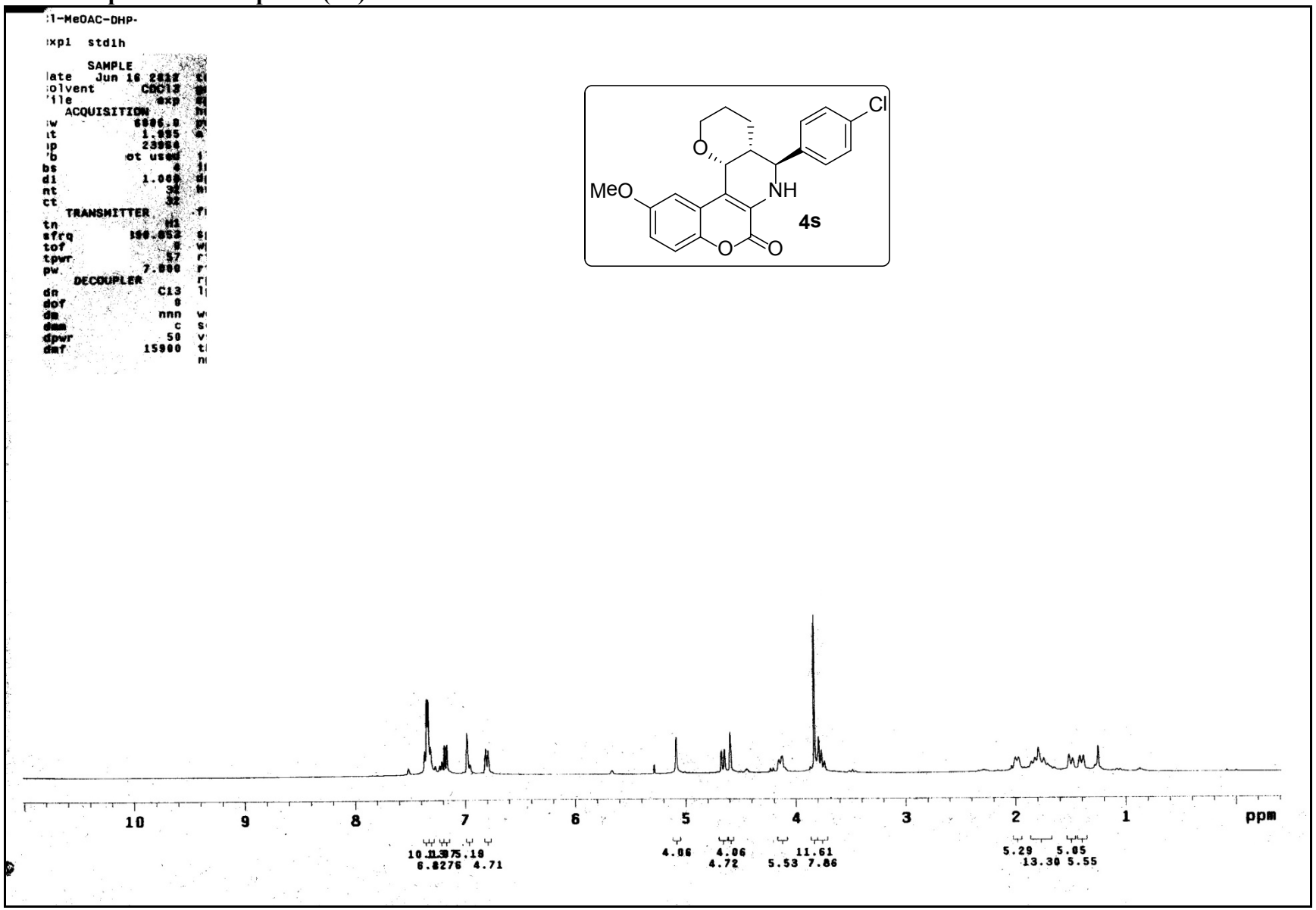
Sample Name	Cl_NO2AC_DHP	**Position**	Vial 1	**Instrument Name**	Instrument 1	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Some Ions Missed
Data Filename	Cl_NO2AC_DHP.d	**ACQ Method**		**Comment**		**Acquired Time**	8/10/2011 12:26:44 PM



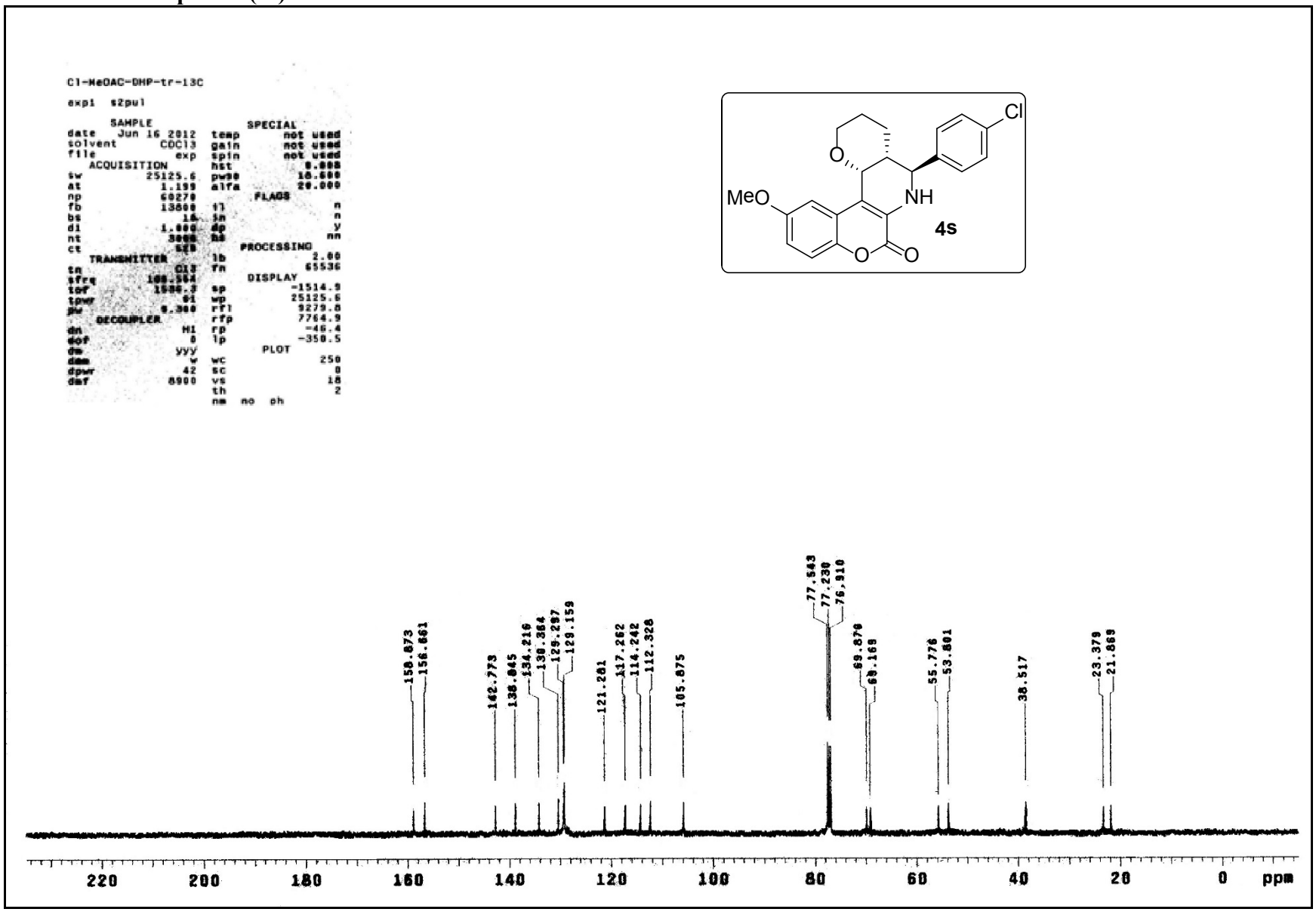
Expansion ^{1}HNMR spectra for determining the trans : cis ratio for Compound (s)



[1]HNMR Spectra of Compound(4s)



^{13}CNMR of Compound (4s)



HRMS Spectra of Compound (s)