Synthesis and biochemical evaluation of benzoylbenzophenone thiosemicarbazone analogues as potent and selective inhibitors of cathepsin L

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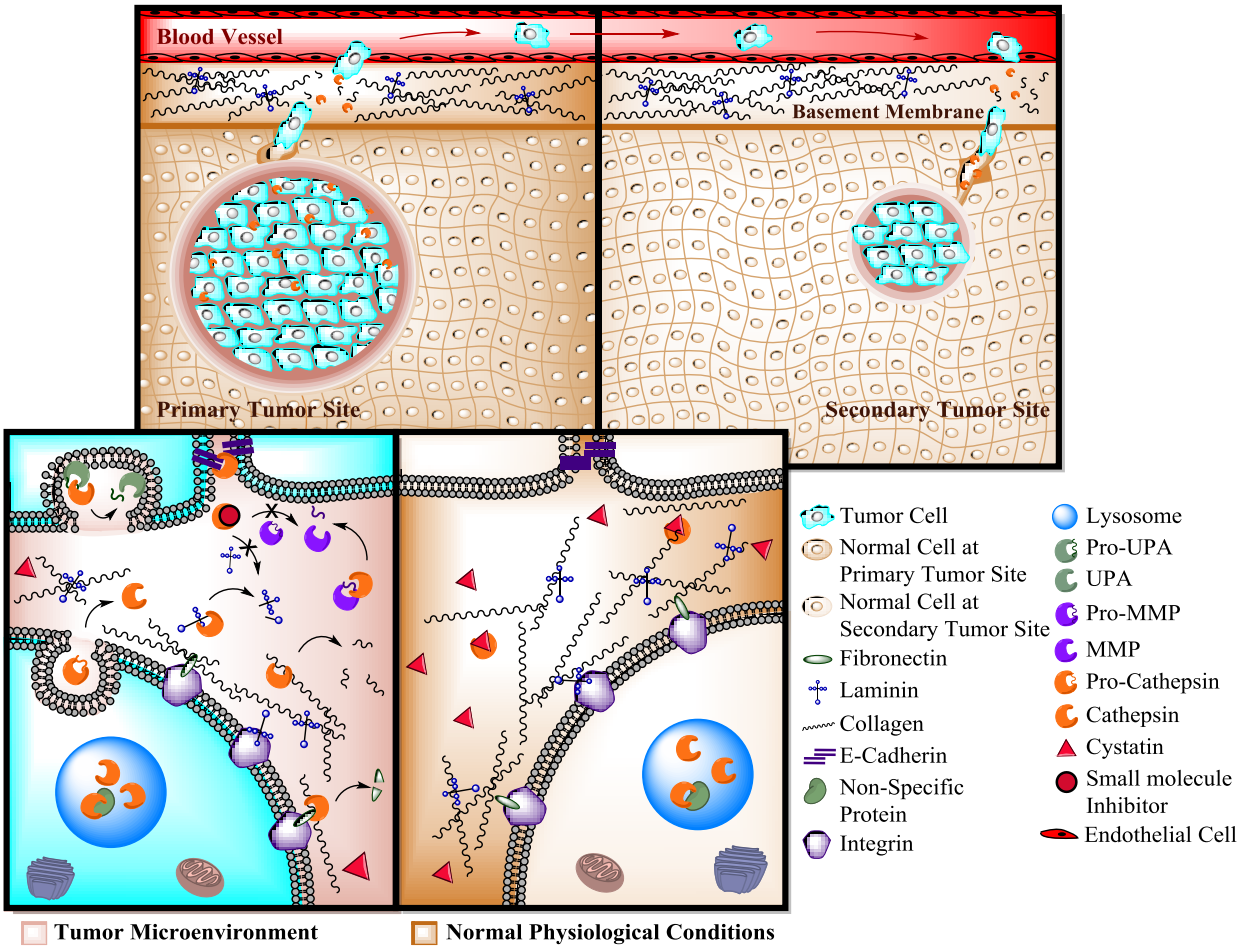
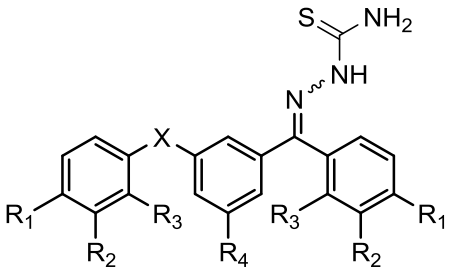


Figure S1. (Corresponds to Figure 1 in the manuscript) Overview of cysteine cathepsins in invasion and metastasis**.** Compared to normal physiological conditions, certain cathepsins are upregulated in the tumor microenvironment. Additionally, changes occur within the tumor microenvironment such as downregulation of endogenous inhibitors including the cystatins, extracellular acidification increasing the proteolytic capability of cathepsins, and extracellular secretion of cathepsins. Degradation of the extracellular matrix through the direct proteolysis of matrix and cell-adhesion proteins such as laminin, fibronectin, collagen, E-cadherin and activation of other proteases including pro-uPA and pro-MMPs facilitates tumor cell invasion from the primary tumor site, intravasation into blood vessels or lymphatic vessels allowing cells to travel to a distant site, extravasation out of the blood vessels or lymphatic vessels, and ultimately migration to a secondary tumor site. Small-molecule cathepsin inhibitors have the potential to inhibit the invasive nature of malignant cells and may provide increased effectiveness in combination with known chemotherapeutics.

Table 1. Inhibitory Activity of Benzoylbenzophenone Thiosemicarbazones Against Cathepsins L and B



Compd	R_1	R_2	R_3	R_4	X	IC_{50} Values (nM) ± S.E.	
						Cat L	Cat B
1	H	H	H	H	C=O	9.85±0.60	>10000
2	H	H	H	Bz	C=O	56.0±19.5	>10000
4	H	H	H	H	CH(OH)	23.80±0.78	>10000
8	F	H	H	H	C=O	14.4±4.5	>10000
9	Br	H	H	H	C=O	1522±325	>10000
10	Br	H	H	H	C=NNHC(S)NH_2	>10000	>10000
11	OCH_3	H	H	H	C=O	5117±600	>10000
13	OH	H	H	H	C=O	340.5±30	>10000
14	$OCH(CH_3)_2$	H	H	H	C=O	>10000	>10000
20	H	CH_3	H	H	C=O	654±162	>10000
22	H	Br	H	OH	C=O	~10000[a]	>10000
31	H	OH	H	Br	C=O	71.6±6.8	>10000
32	H	H	F	Br	C=O	8.12±0.5	>10000
33	H	Br	H	Br	C=O	10347±1864	>10000
Ethyl Acetate[b]	-	-	-	-	-	>>10000	ND

[a]Compound **22** inhibited cathepsin L activity by 56.9% at 10000 nM.

[b]Ethyl Acetate inhibited cathepsin L activity by 10% at a concentration of 5 % by volume (0.5 M).

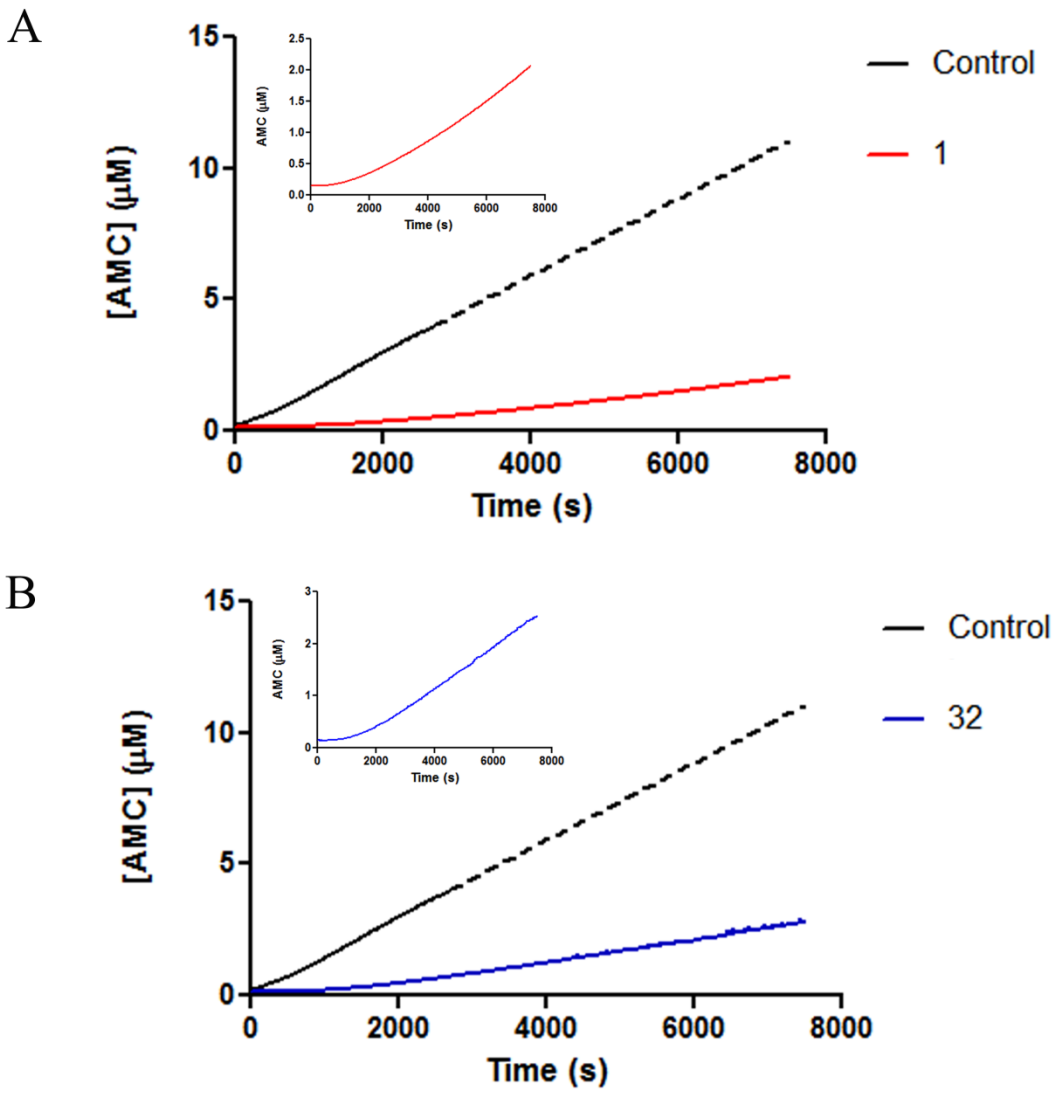


Figure S2. Reversibility studies of cathepsin L inhibition with analogues **1** and **32**. Inhibition of cathepsin L with analogues **1** (**A**) and **32** (**B**) was found to be reversible. Inhibitors (5 μM) were pre-incubated at 25 ^{o}C with 100 nM cathepsin L for 3 h, and then diluted 100 fold with 10 μM Z-FR-AMC substrate. Enzyme activity was monitored by determining the release of the fluorescent product AMC as a function of time for the untreated enzyme reaction (Control) and the reactions of enzyme that had been pre-treated with inhibitors. The results for each inhibitor demonstrate a slow recovery of enzyme activity (increasing reaction rates) as a function of time. The insets for each graph show an expanded view.

Reversibility Studies:

Compounds **1** and **32** were investigated to determine if these time dependent inhibitors were reversible inhibitors of cathepsin L. Pre-incubation of 100 nM of cathepsin L with either 5

μM compound **1** or 5 μM compound **32** was followed by a 100 fold dilution of the enzyme-inhibitor solution with substrate to give a final reaction concentration of 50 nM inhibitor and 1 nM cathepsin L in 10 μM substrate. Observation of the reaction rate as a function of time showed complete inhibition of enzyme activity by both compounds for approximately the first 1000 s. This was followed by a slow increase in enzyme reaction rate as a function of time (Figure S2). Cathepsin L activity for the uninhibited reaction was found to be 1.47 nM/s, compared to 0.26 nM/s and 0.38 nM/s at 7500 s for compounds **1** and **32** respectively (the rates were still increasing at 7500 s). These results indicate that cathepsin L showed a slow recovery of enzyme activity.

Experimental Section:

The pre-incubation buffer contained 100 mM NaOAc, pH 5.5, 1 mM EDTA, 3 mM DTT, 2% DMSO, and 0.01% Brij 35. A 100 μM solution of Z-FR-AMC was also prepared. Cathepsin L was pre-incubated with an equal amount of a 10 μM solution of inhibitor to make an enzyme-inhibitor pre-incubation solution with 100 nM cathepsin L and 5 μM inhibitor which was incubated at 25 °C for 3 h. Control enzyme solution was also incubated under the same conditions. Each reaction was initiated by addition of 2 μl of enzyme-inhibitor solution to 178 μl of assay buffer and 20 μl of Z-FR-AMC solution to make up a 200 μl total reaction solution per well in a 96 well Corning 3686 assay microplate. The final reaction conditions were: 100 mM NaOAc, pH 5.5, 1 mM EDTA, 3 mM DTT, 0.2% DMSO, 0.01% Brij 35, 1 nM cathepsin L, 50 nM inhibitor and 10 μM of Z-FR-AMC. The reaction was monitored fluorometrically at 15 second intervals for 7500 seconds with a Thermo Fluoroskan Ascent FL microplate reader. Data analysis was performed with Graphpad Prism 5.0 software.

Molecular modeling:

For docking studies, the 1.45 Å resolution crystal structure 2XU1 (PDB) was used.[S1] For this crystal structure the enzyme was obtained from recombinant human cathepsin L with Thr110 of the mature enzyme mutated to an alanine residue (T223A in CatL1_human.sw) that had been pre-incubated with a 2 mM solution of the covalent inhibitor,(4R)-1-{[1-(4-chlorophenyl)cyclolpropyl]carbonyl}-4-[(2-chlorophenyl)sulfonyl]-*N*-(1-cyanocyclopropyl)-L-prolinamide, prior to crystallization. 2XU1 was imported into Discovery Studio (Accelrys) 4.1 and water molecules and the ligand were then removed. The Prepare Protein function was used to check the amino acid sequence, correct for missing atoms, and protonate the protein. Individual ligands for docking were imported from ChemDraw molefiles and protonated. The binding site on the enzyme was defined from the PDB data in the Define and Edit Binding Site mode. The CDOCKER program in Receptor-Ligand Interactions which uses a CHARMm based molecular dynamics scheme was used to dock ligands into the binding/active site of cathepsin L. In this program, random ligand conformations are generated using high-temperature molecular dynamics, and in fact we observed both *E* and *Z* isomers of individual ligands in the results. The ligand conformations generated are then translated into the binding site for creation of poses using random rigid-body rotations followed by simulated annealing. The ligand poses are refined by an additional minimization. The results (10-20) for each ligand were ranked by interaction energies, and the poses with the most favorable interaction energies were examined for orientation, H-bonding, non-polar interactions and distance from the Cys25 thiolate. To validate this protocol, KGP94, which had been docked into cathepsin L and characterized,[S2] was docked and its top pose confirmed as very close to the conformation reported previously.

S1. Hardegger, L. A., Kuhn, B., Spinnler, B., Anselm, L., Ecabert, R., Stihle, M., Gsell, B., Thoma, R., Diez, J., Benz, J., Plancher, J.-M., Hartmann, G., Banner, D. W., Haap, W. and Diederich, F. Systematic Investigation of Halogen Bonding in Protein–Ligand Interactions. *Angew. Chem. Int. Ed*. **2011**, *50*, 314–318. doi: 10.1002/anie.201006781

S2. Chavarria, G. E.; Horsman, M. R.; Arispe, W. M.; Kishore Kumar, G. D; Chen, S.-E.; Strecker, T. E.; Parker, E. N.; Chaplin, D. J.; Pinney, K.G.; Trawick, M.L. Initial evaluation of the antitumor activity of KGP94, a functionalized benzophenone thiosemicarbazone inhibitor of cathepsin L. *Eur. J. Med. Chem.* **2012,** *58*, 568-572.

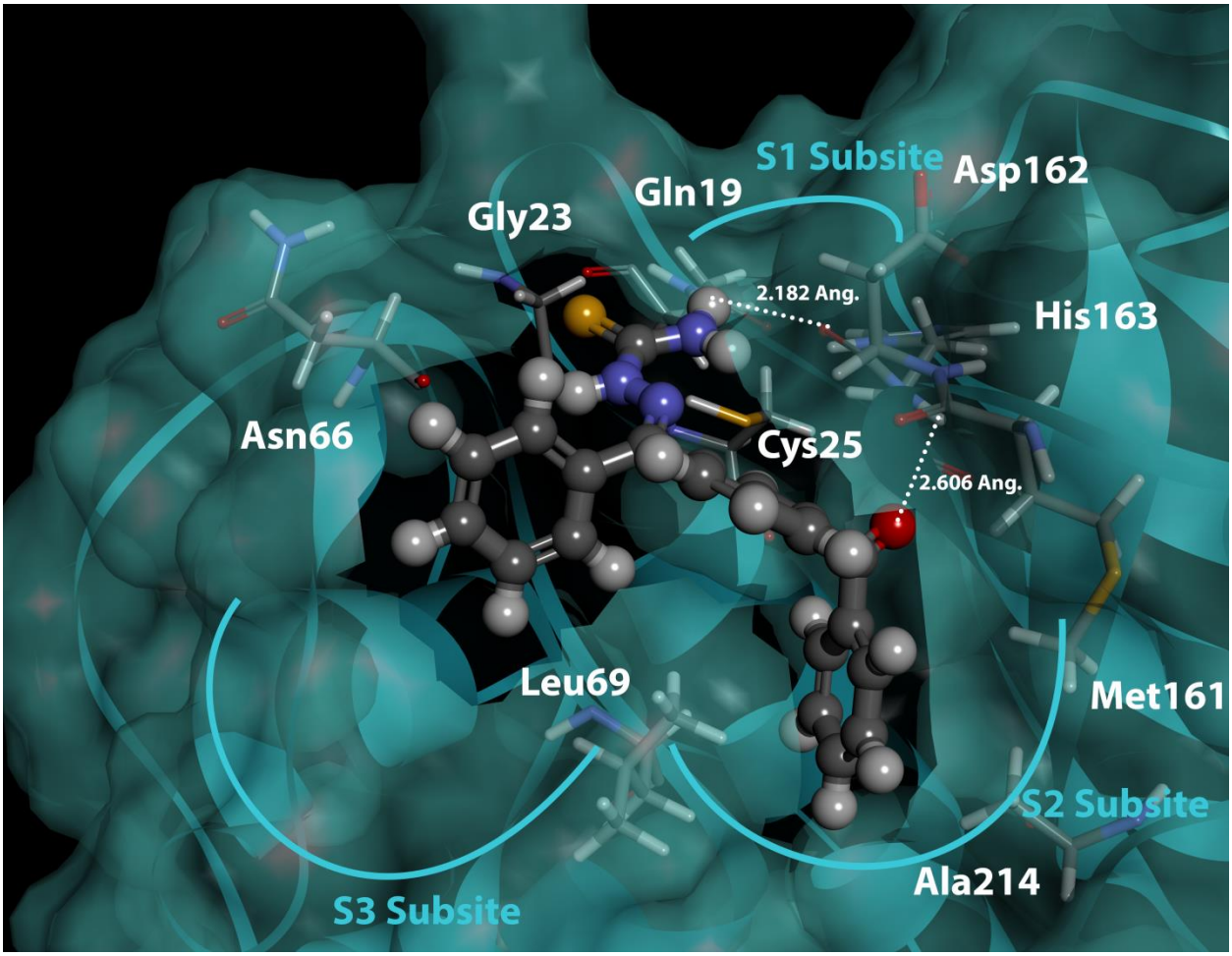


Figure S3. Molecular docking of analogue **1** within the active site of cathepsin L. Same as Figure 6A in corresponding article except the binding subsites of cathepsin L are labeled and hydrogen bonding between cathepsin L and the inhibitor are shown. Analogue **1** is shown in ball and stick mode (C, gray; H, white; O, red; N, blue; S, yellow). Cathepsin L is shown in ribbon mode with a transparent molecular surface (Green) and enzyme active site amino acid residues are labeled and shown in stick mode (C, gray; H, white; O, red; N, blue; S, yellow).

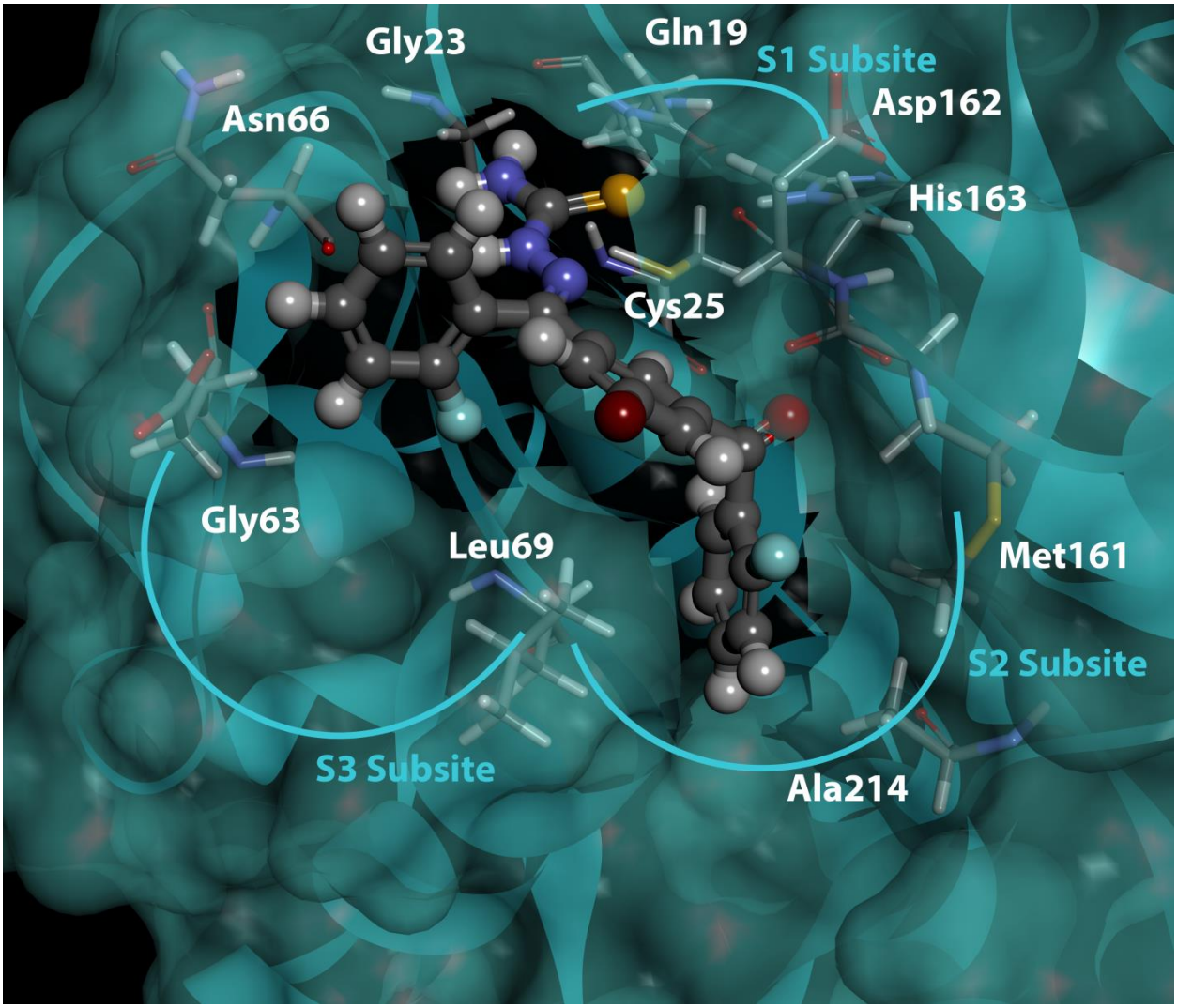


Figure S4. Molecular docking of analogue **32** within the active site of cathepsin L. Same as Figure 6B in corresponding article except the binding subsites of cathepsin L are labeled. Analogue **32** is shown in ball and stick mode (C, gray; H, white; O, red; N, blue; S, yellow; F, light blue; Br, brown). Cathepsin L is shown in ribbon mode with a transparent molecular surface (Green) and enzyme active site amino acid residues are labeled and shown in stick mode (C, gray; H, white; O, red; N, blue; S, yellow).

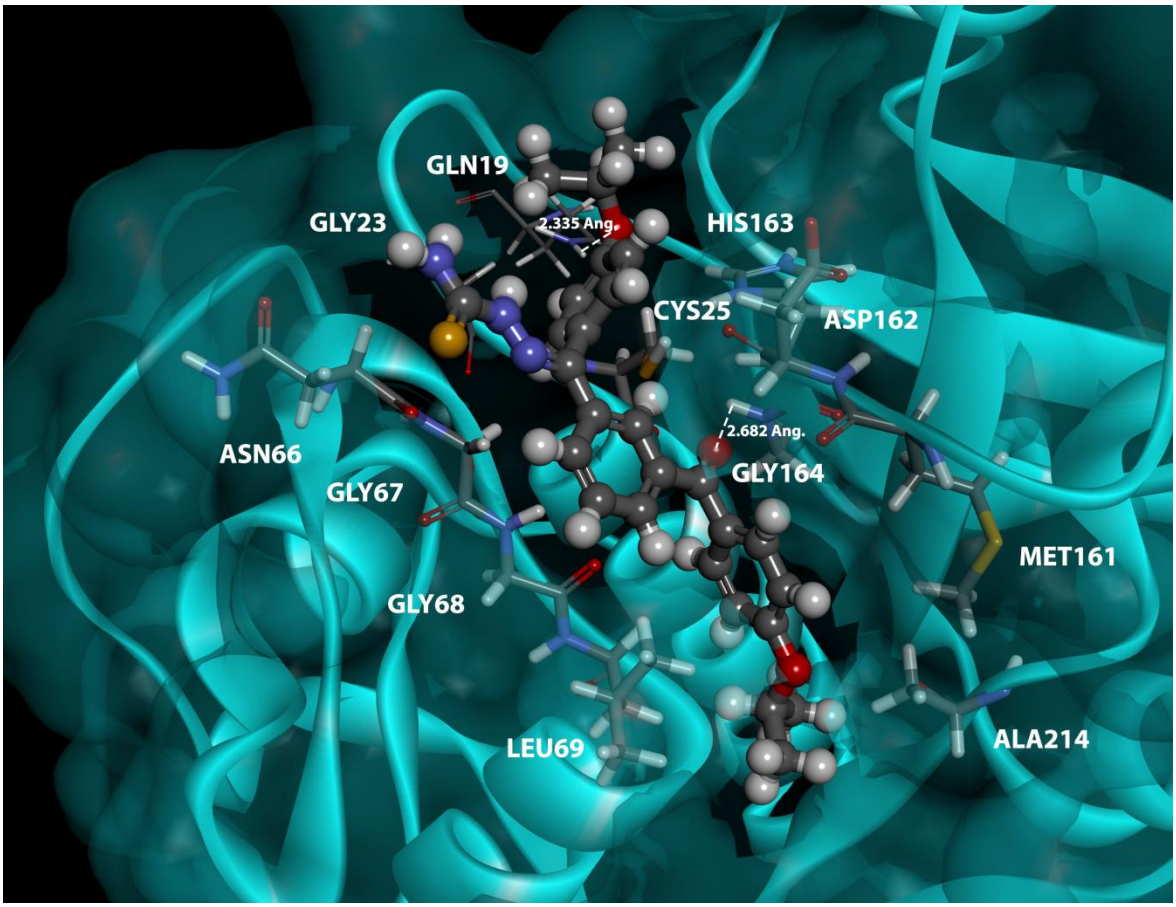


Figure S5. Molecular docking of analogue **14** within the active site of cathepsin L. Analogue **14** is shown in ball and stick mode (C, gray; H, white; O, red; N, blue; S, yellow). Cathepsin L is shown in ribbon mode with a transparent molecular surface (Green) and enzyme active site amino acid residues are labeled and shown in stick mode (C, gray; H, white; O, red; N, blue; S, yellow).

Figure S5 shows the most favorable binding orientation for analogue **14** (inactive against cathepsin L) as determined by interaction energy. The *p*-isopropoxy analogue **14** did not bind in the active site of cathepsin L in a manner that would facilitate formation of a covalent bond. In each of the top binding orientations, the thiocarbonyl carbon atom of analogue **14** was not in close proximity (separated by 7.9 Å in the pose shown in Figure S5) to the Cys25 thiolate ion of cathepsin L. Multiple nonpolar interactions and two hydrogen bonds one between the carbonyl oxygen of analogue **14** and the NH backbone of Gly164 and another between the *p*-isopropoxy oxygen atom of analogue **14** and the sidechain NH of Gln19 were observed for the top binding orientation. Interestingly, the benzophenone portion resides in the S2 pocket of cathepsin L in a similar fashion to that observed for active cathepsin L inhibitors **1** and **32**. However, the remaining outermost ring resides in the S1 subsite instead of being oriented towards the S3 subsite and the thiosemicarbazone moiety is oriented towards the solvent instead of residing in the S1 subsite. Active cathepsin L inhibitors **1** and **32** bind in a manner that facilitates formation of a transient covalent bond between the enzyme and inhibitor. This comparison emphasizes that formation of a transient covalent bond is necessary for activity against cathepsin L in this series of compounds.

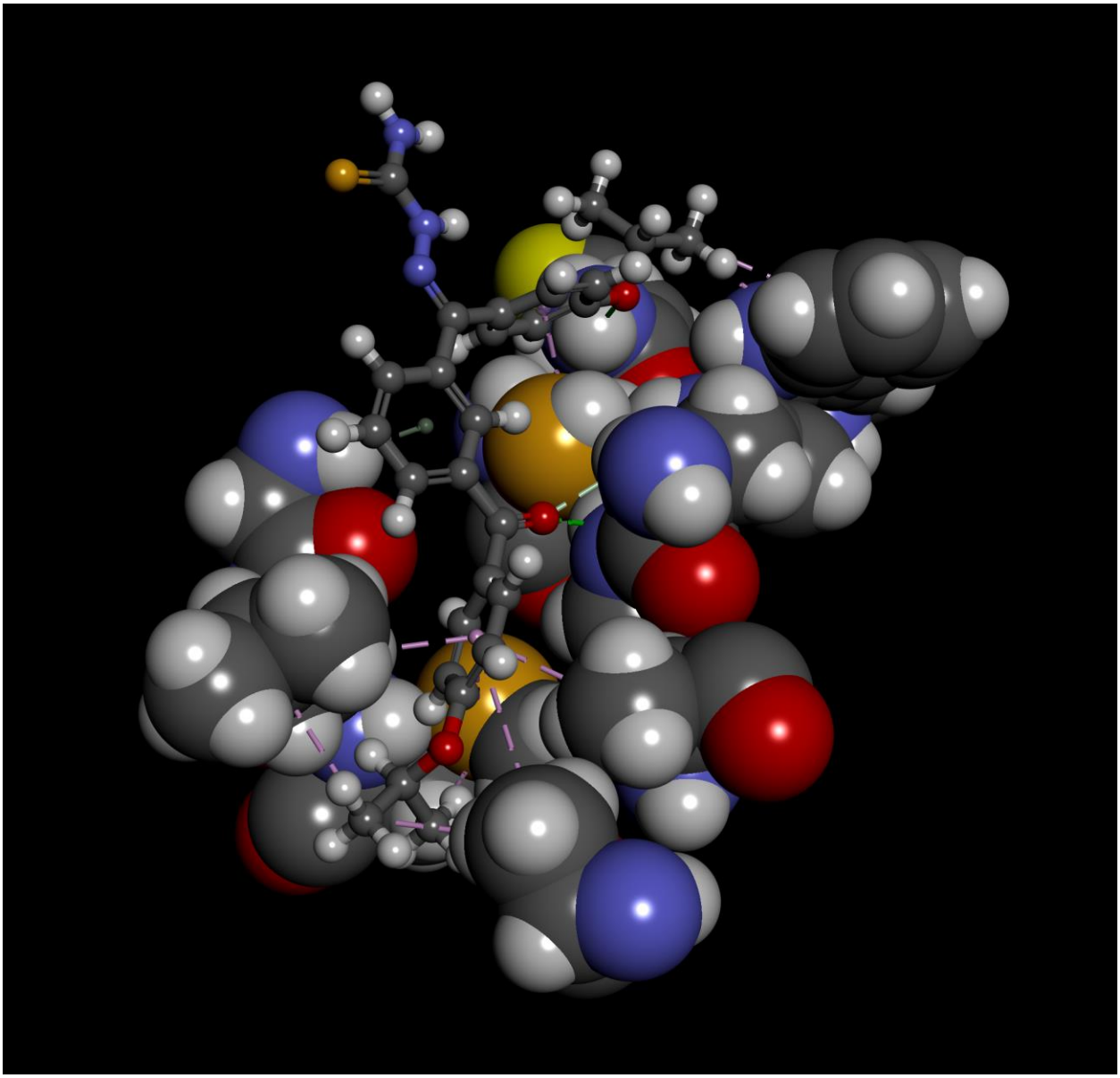


Figure S6. Molecular docking of analogue **14** with cathepsin L showing interactions with active site amino acid residues. Analogue **14** is shown in ball and stick mode and amino acid residues of cathepsin L are shown in CPK mode (C, gray; H, white; O, red; N, blue; S, yellow). This view shows the close interactions between compound **14** and the amino acid residues of cathepsin L. The thiosemicarbazone moiety of compound **14** is oriented towards solvent.

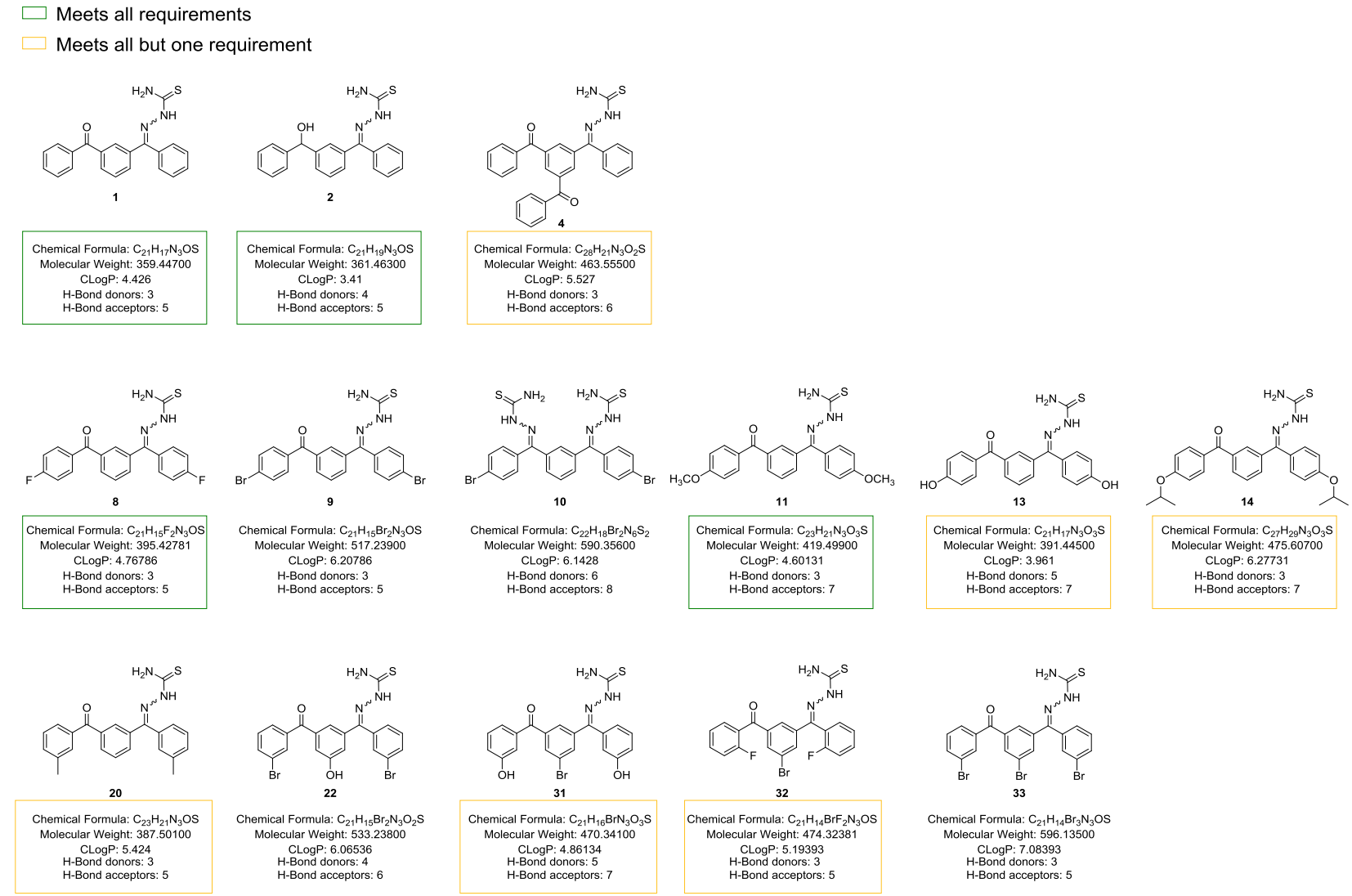
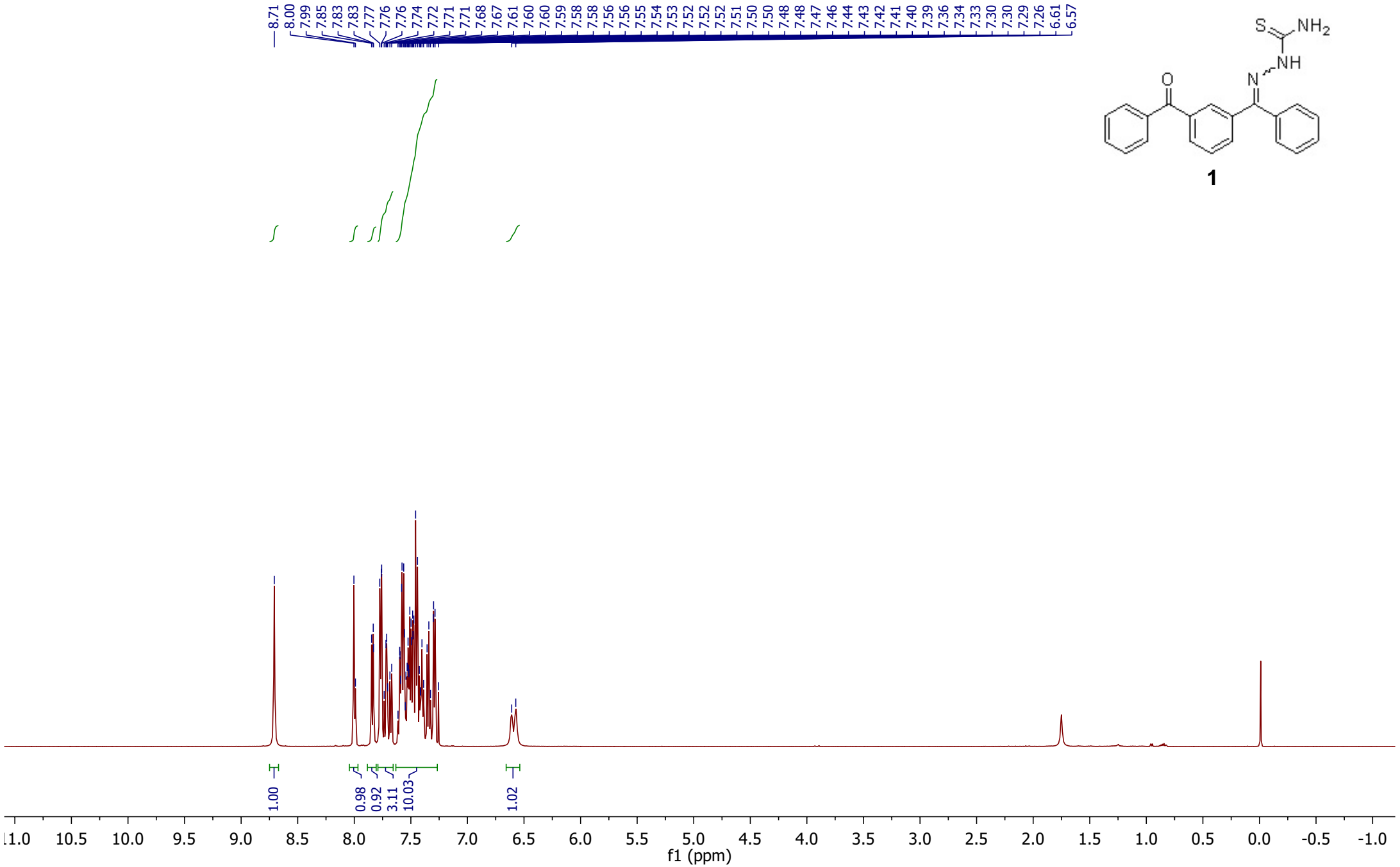


Figure S7. Lipinski rule of five analysis for benzoylbenzophenone thiosemicarbazones.

The Lipinski rule of five was used as a preliminary analysis for predicting pharmacokinetic properties of benzoylbenzophenone thiosemicarbazone analogues. The Lipinski rule of five[S3] predicts the likelihood of whether or not a particular molecular entity will exhibit suitable solubility and permeability properties which are applicable to predicting oral bioavailability. CLogP, chemical formula, and molecular weight were calculated using ChemBioDraw Ultra Version 14.0.0.117. Four of the fourteen described analogues met all of the requirements for the Lipinski rule of five including benzoylbenzophenone analogues **1, 2**, **8** which were potent inhibitors of cathepsin L with IC_{50} values less than 25 nM. An additional six analogues met all but one requirement including 1,3-bis(2-fluorobenzoyl)-5-bromobenzene thiosemicarbazone (**32**) which was the most potent cathepsin L inhibitor in this series.

S3. Lipinski, C. A.; Lombardo, F.; Dominy, B.W.; Feeney, P.J. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Adv. Drug Deliv. Rev.* **2001**, *46*, 3-26.

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



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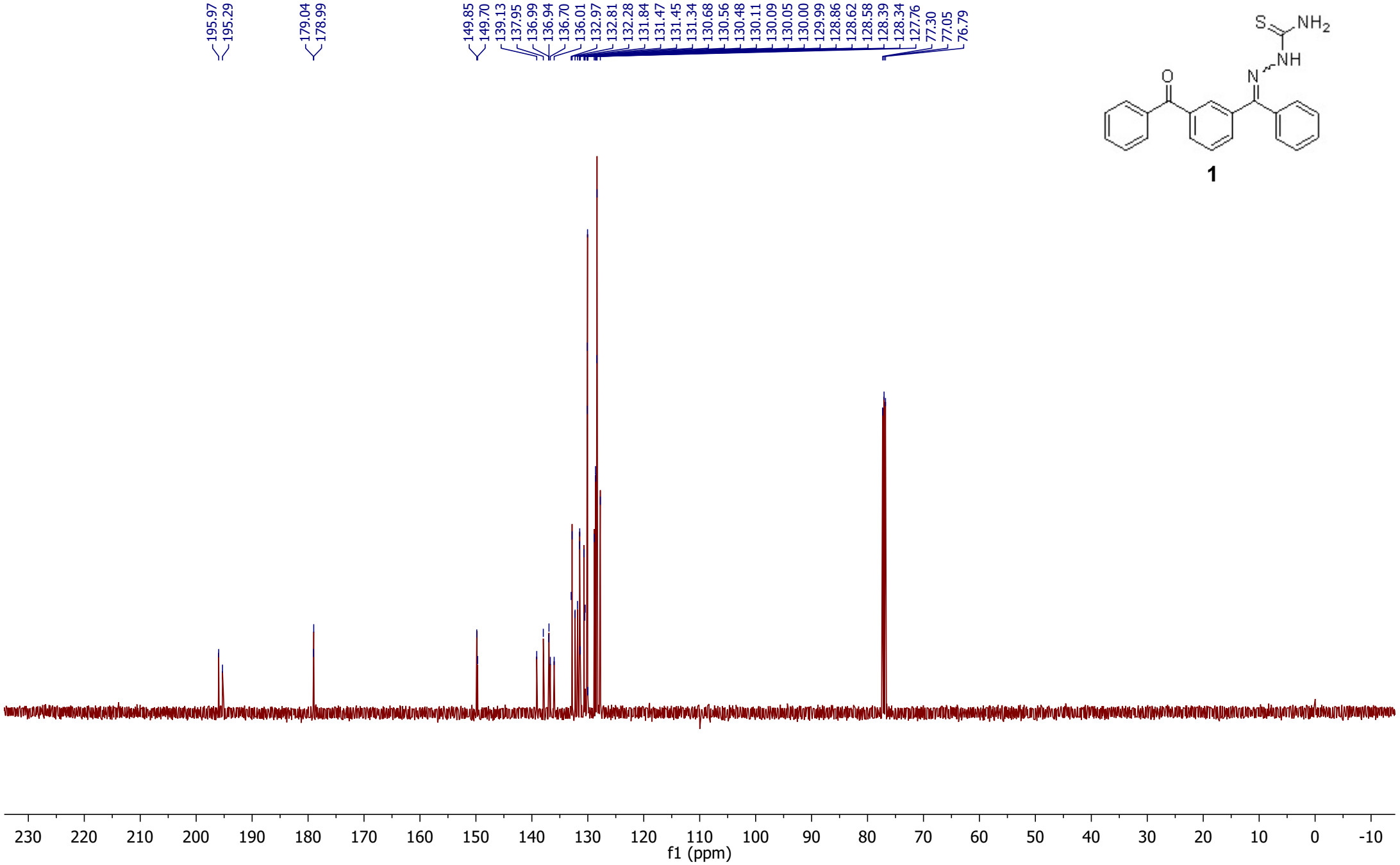

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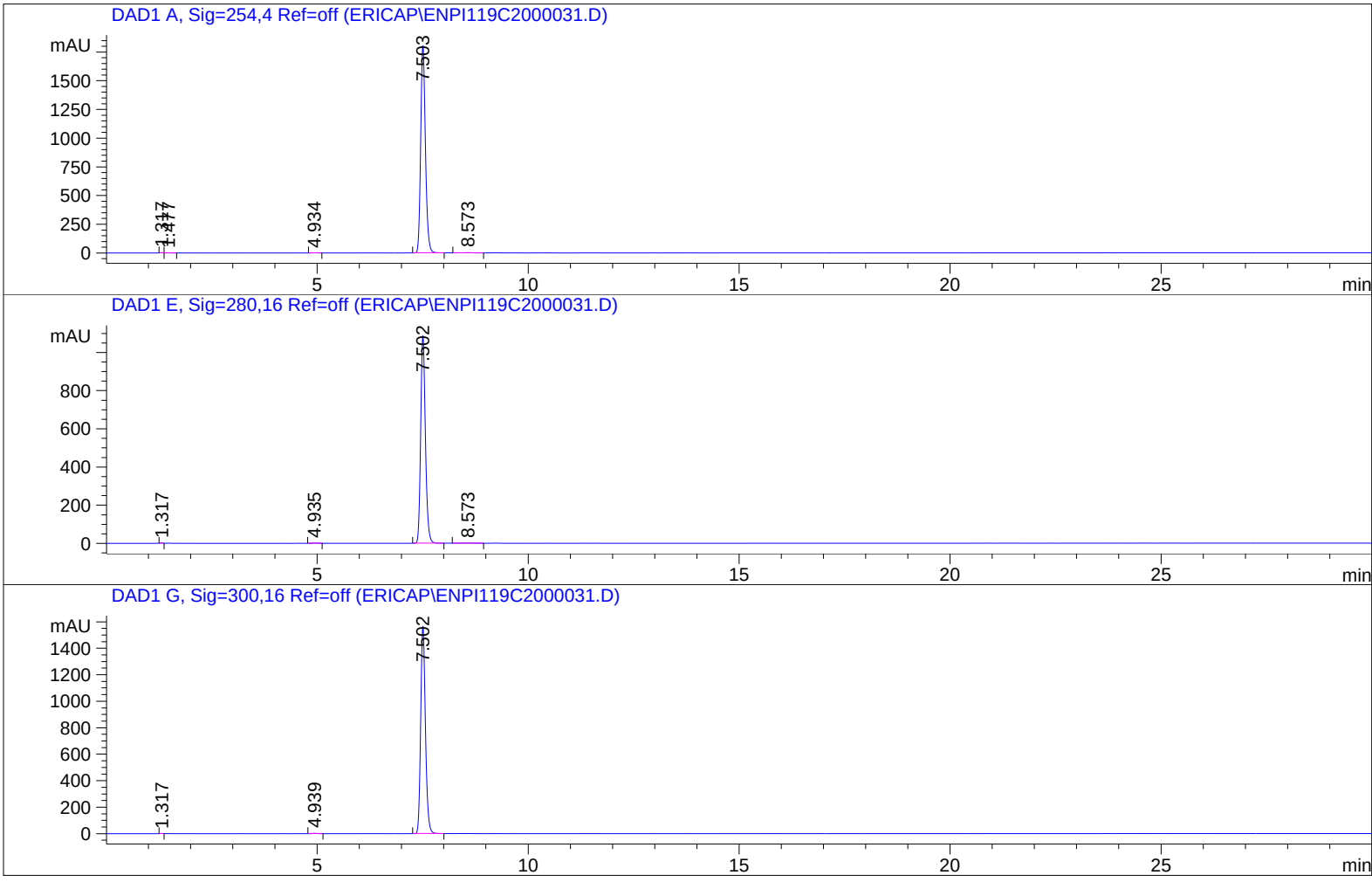

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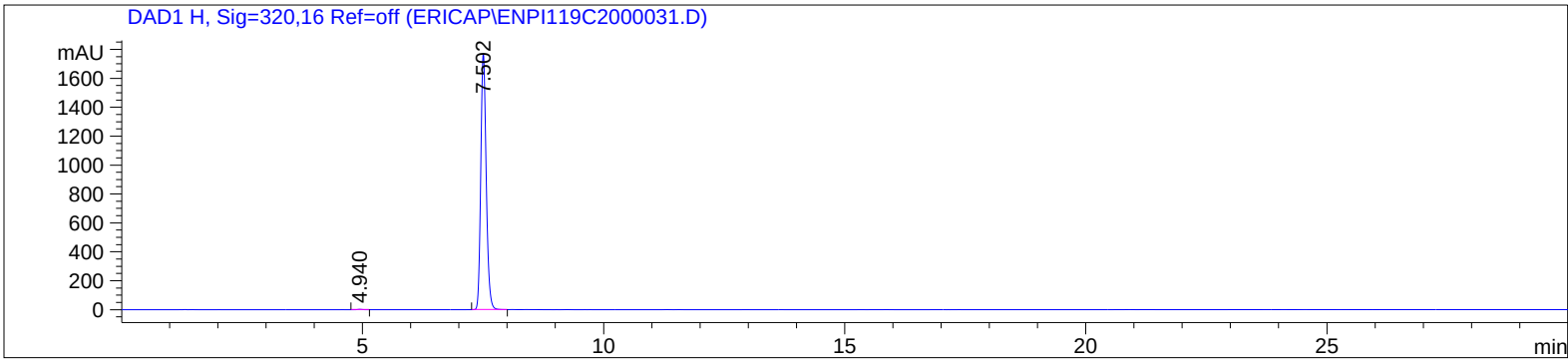

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HPLC trace for Compound 1

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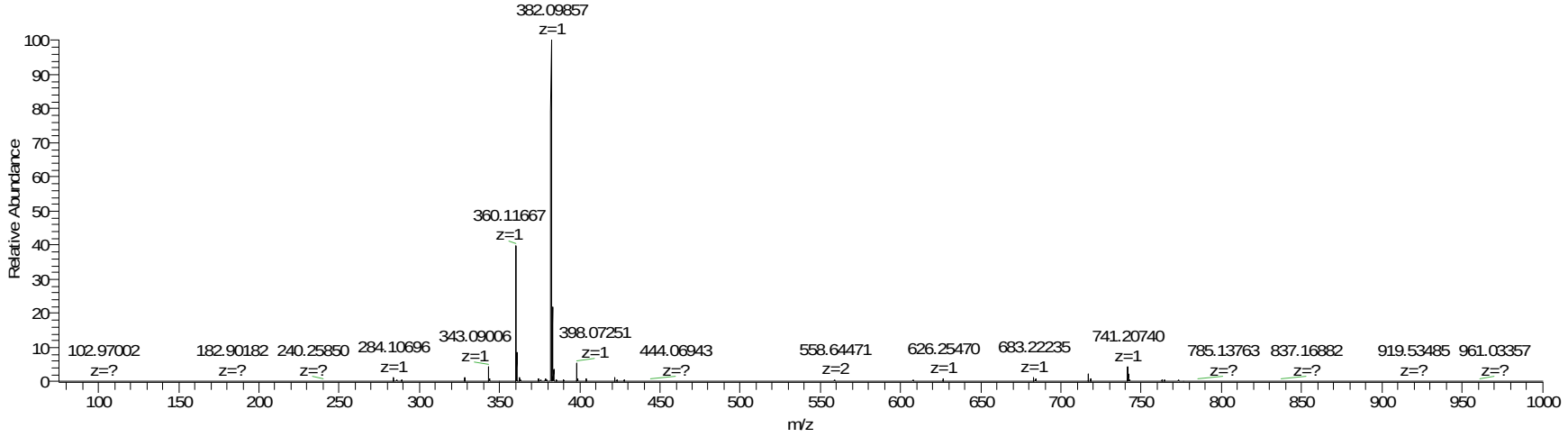
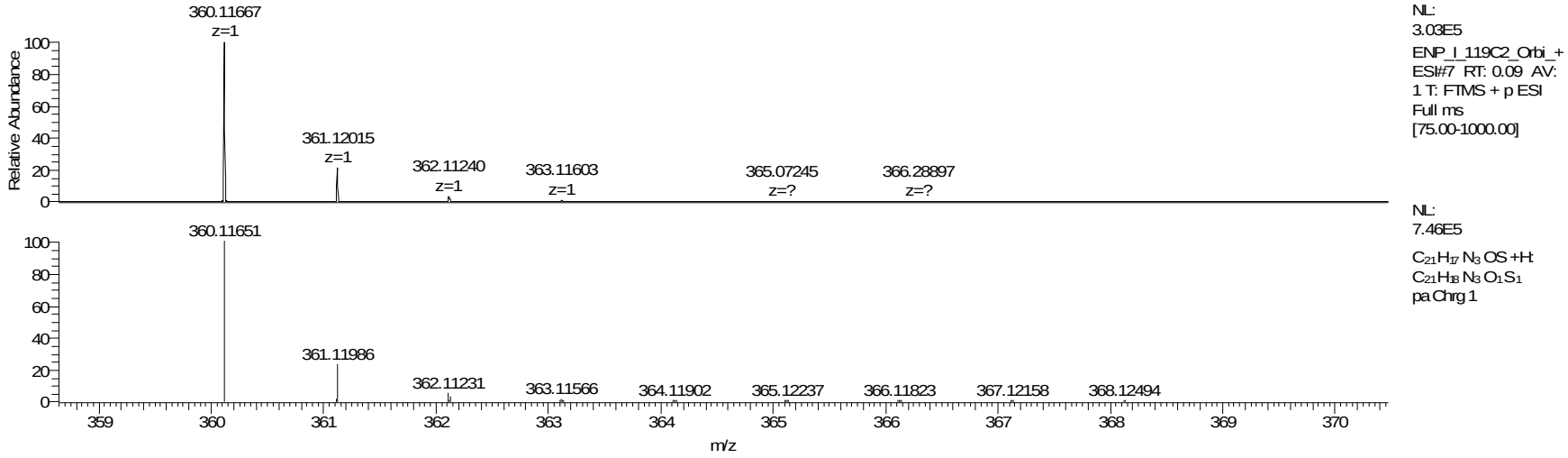
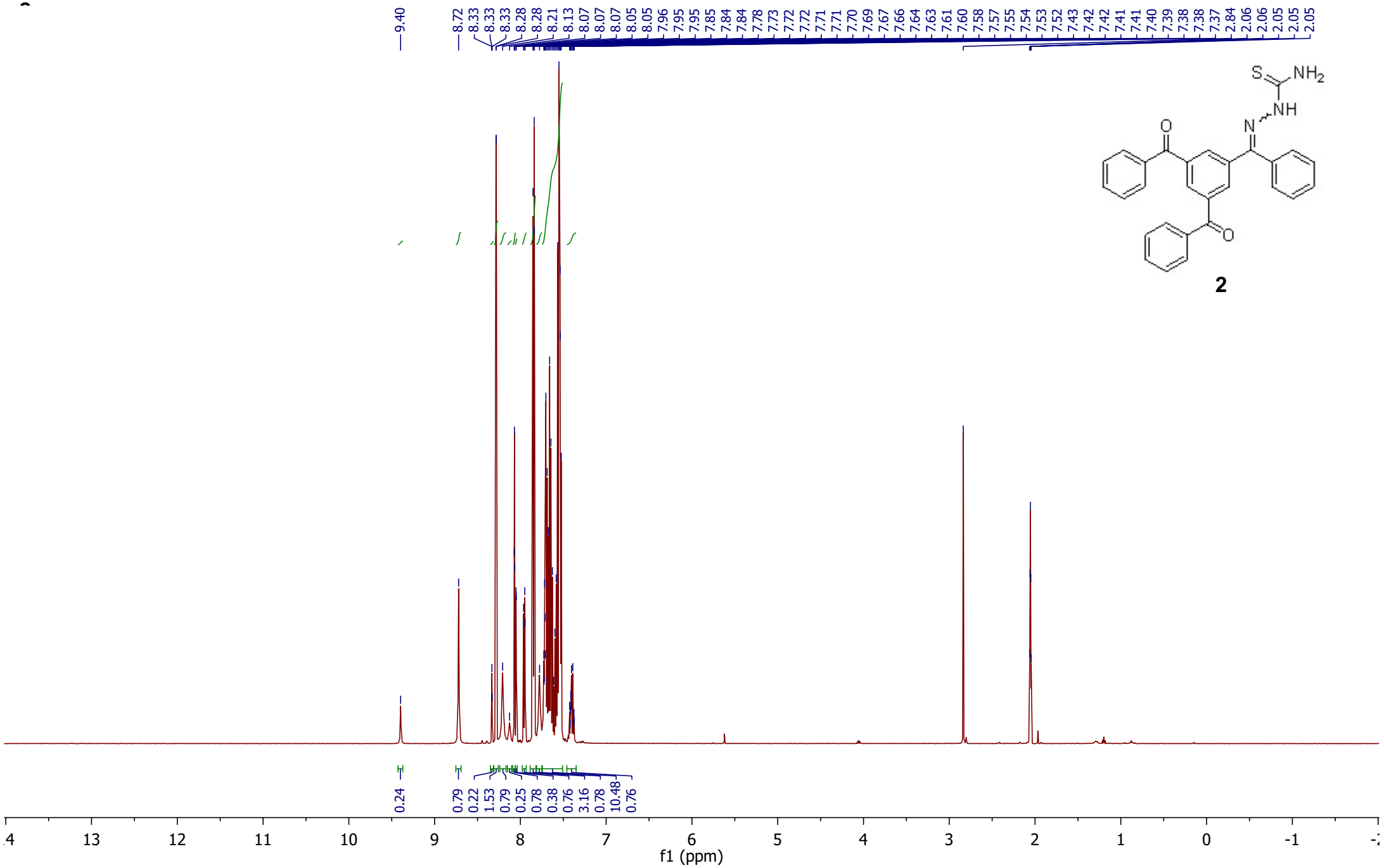




^{1}H NMR (500 MHz, Acetone-d_6) of Compound



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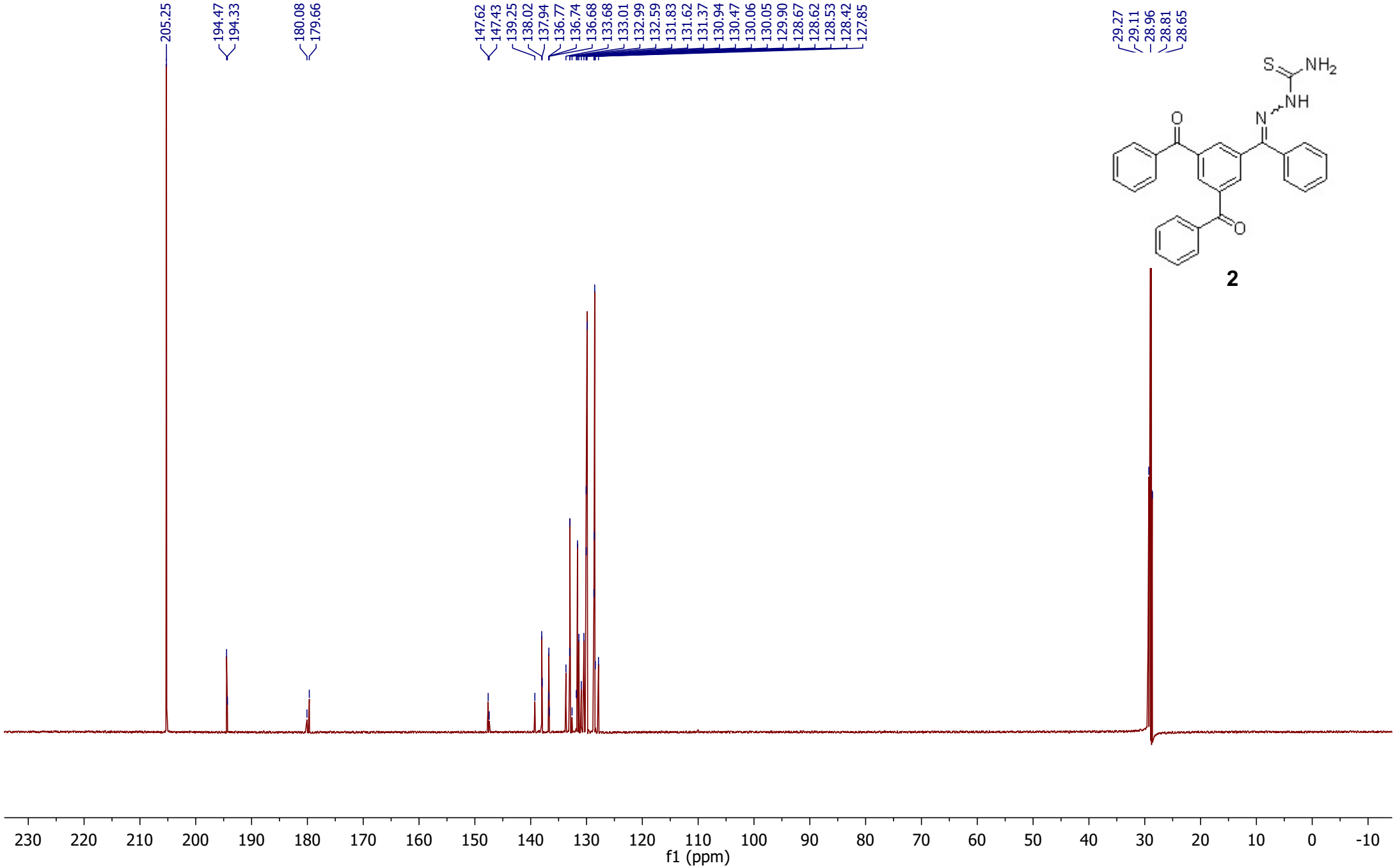

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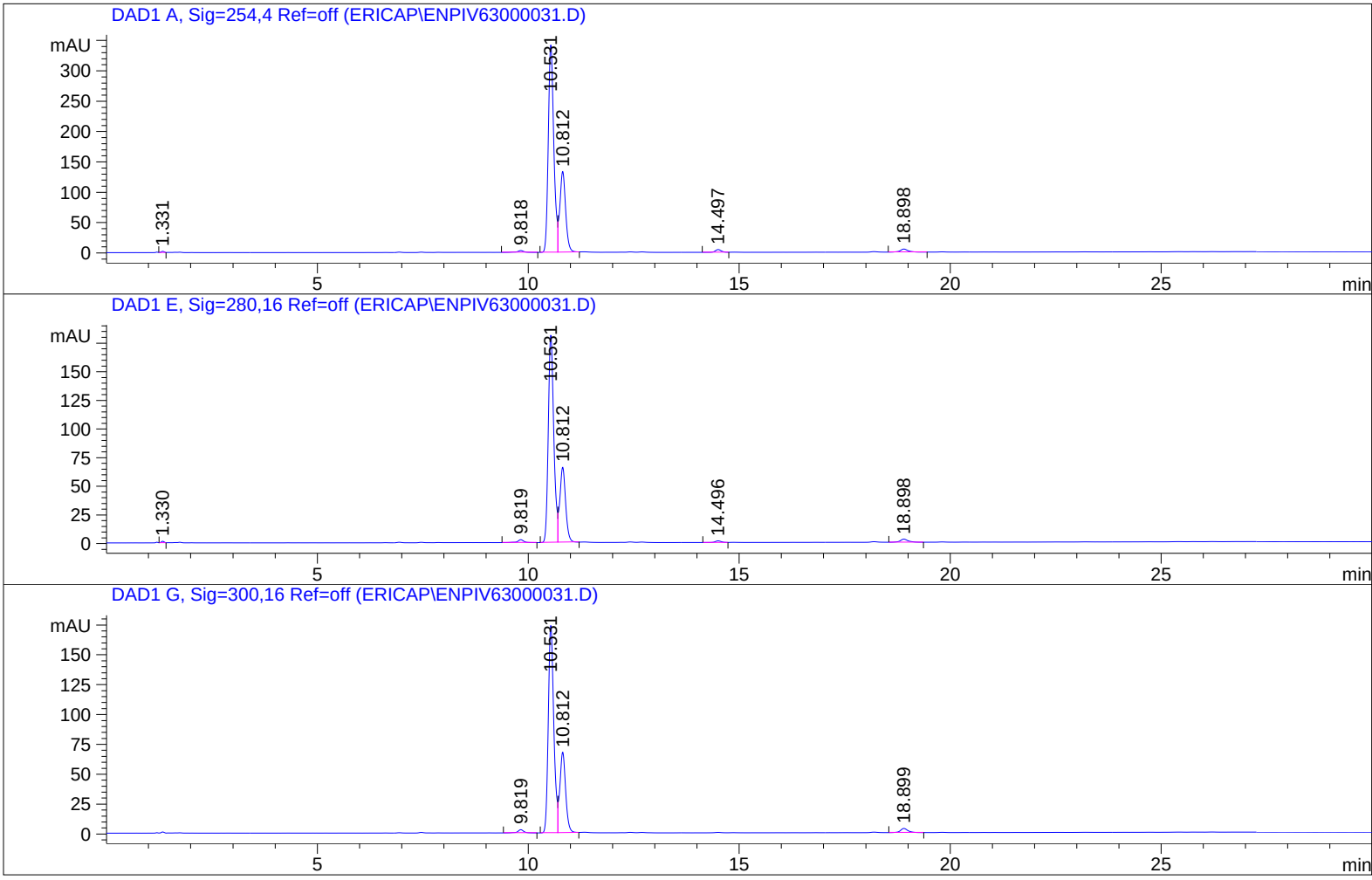

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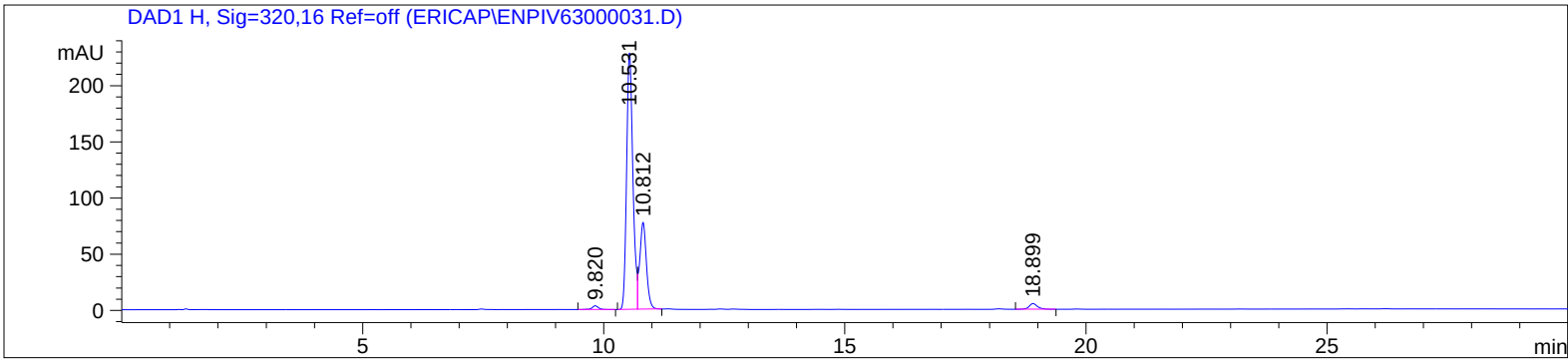

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Signal 3: DAD1 G, Sig=300,16 Ref=off

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Sample Name: ENPIV63

HPLC trace for Compound 2

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.819	BB	0.1446	26.63732	2.71282	1.1641
2	10.531	BV	0.1378	1575.84021	173.70177	68.8695
3	10.812	VB	0.1433	642.73590	67.37366	28.0897
4	18.899	BB	0.1838	42.94009	3.48465	1.8766
Totals :				2288.15352	247.27291	

Signal 4: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.820	BB	0.1406	31.34613	3.30553	1.0816
2	10.531	BV	0.1377	2067.92480	228.21864	71.3532
3	10.812	VB	0.1433	737.39844	77.28585	25.4438
4	18.899	BB	0.1815	61.48148	5.06982	2.1214
Totals :				2898.15085	313.87985	

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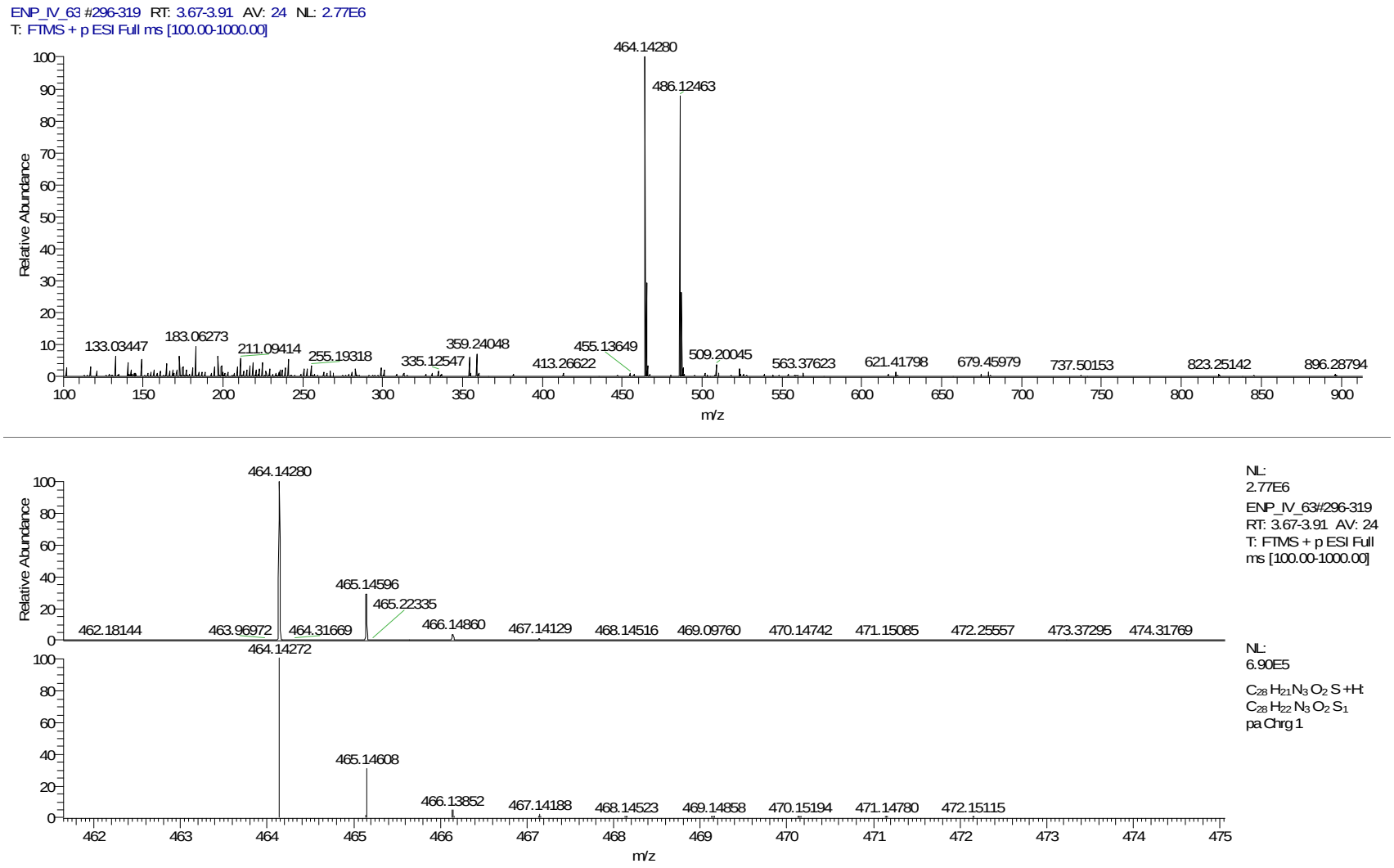
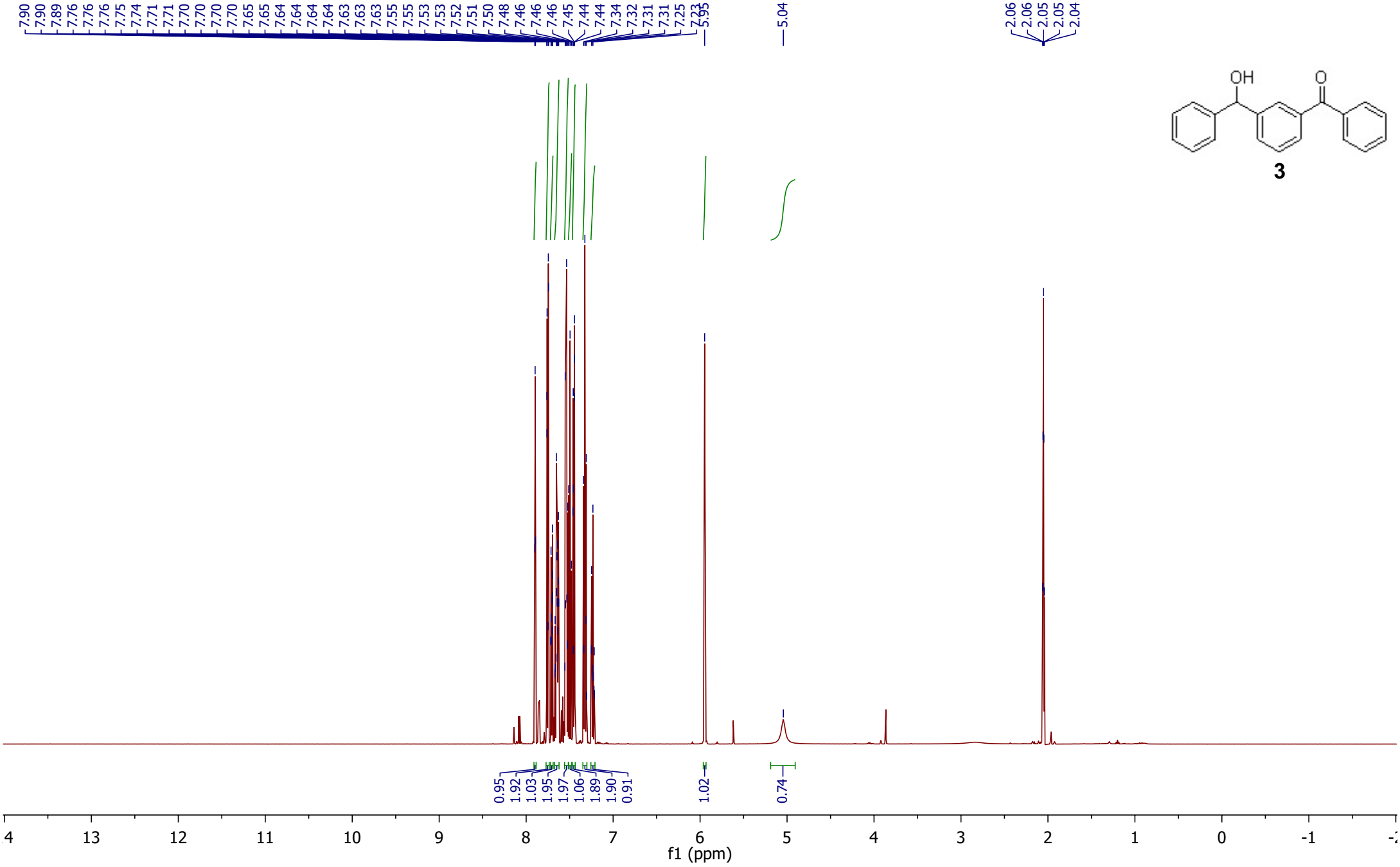
*** End of Report ***

HRMS(ESI) for Compound **2**

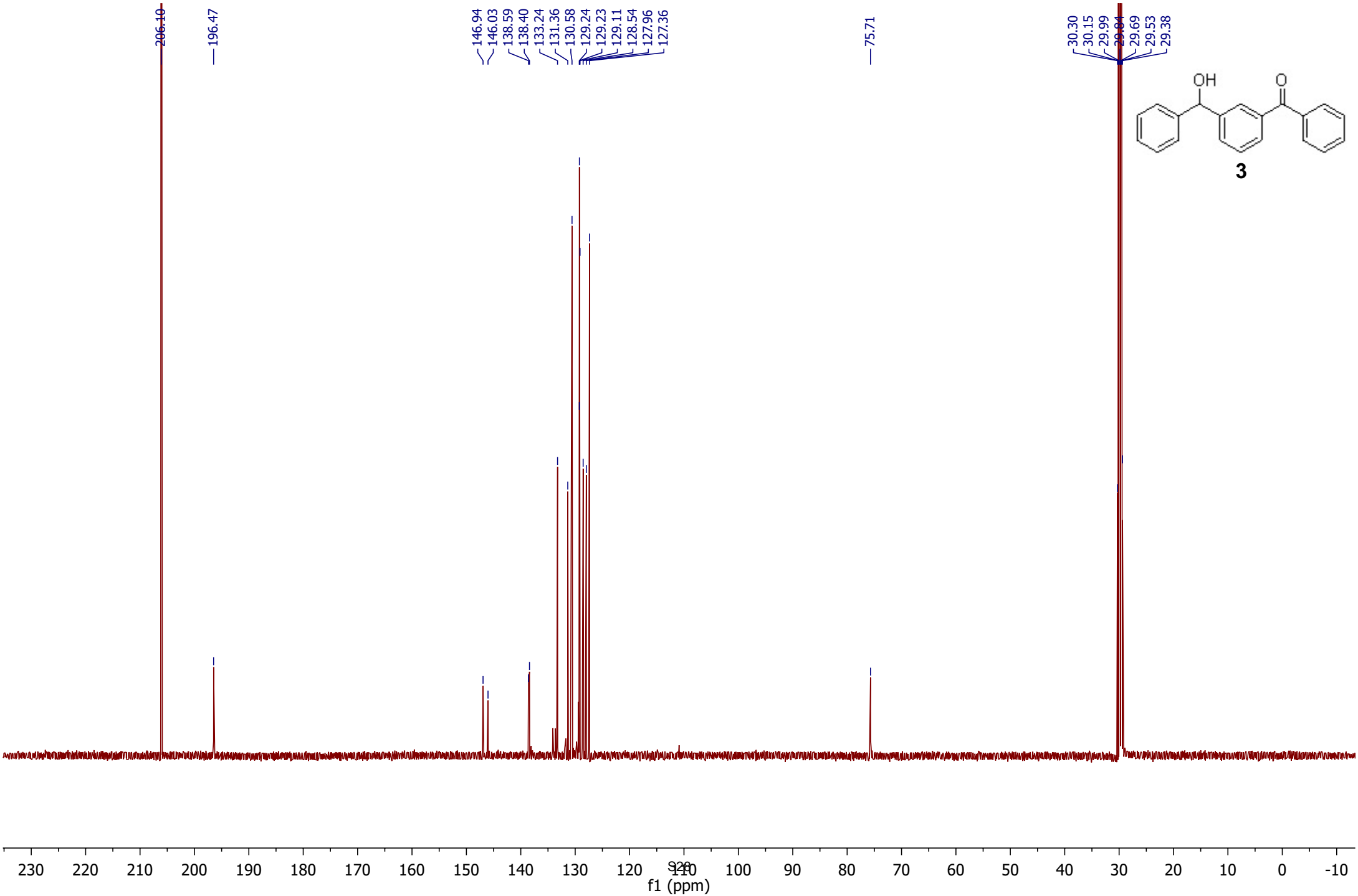
C:\Xcalibur\...\01-02-2015\ENP_IV_63 1/2/2015 9:35:32 PM



^{1}H NMR (500 MHz, Acetone-d_6) of Compound **3**

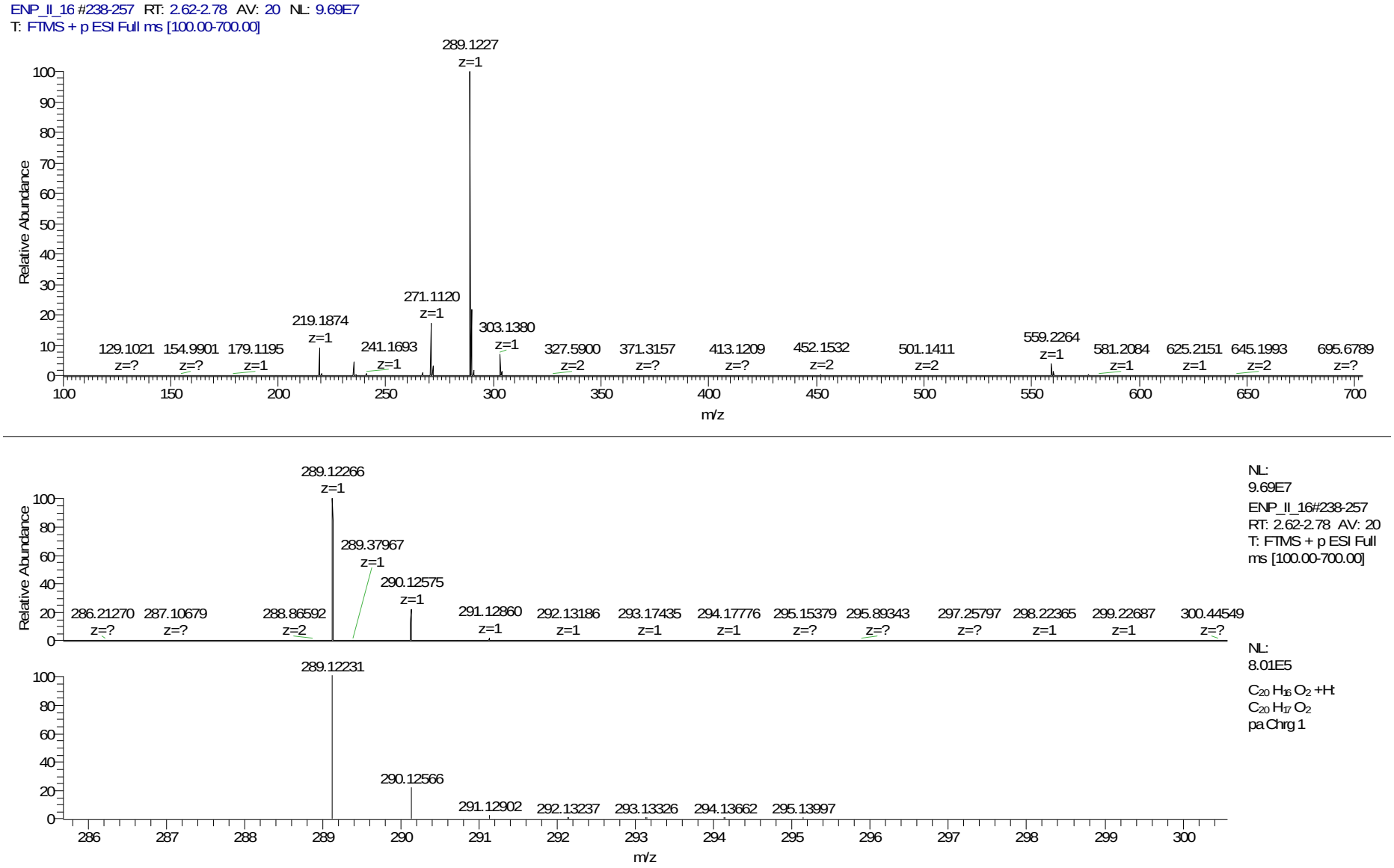


^{1}H NMR (125 MHz, Acetone-d_6) of Compound **3**

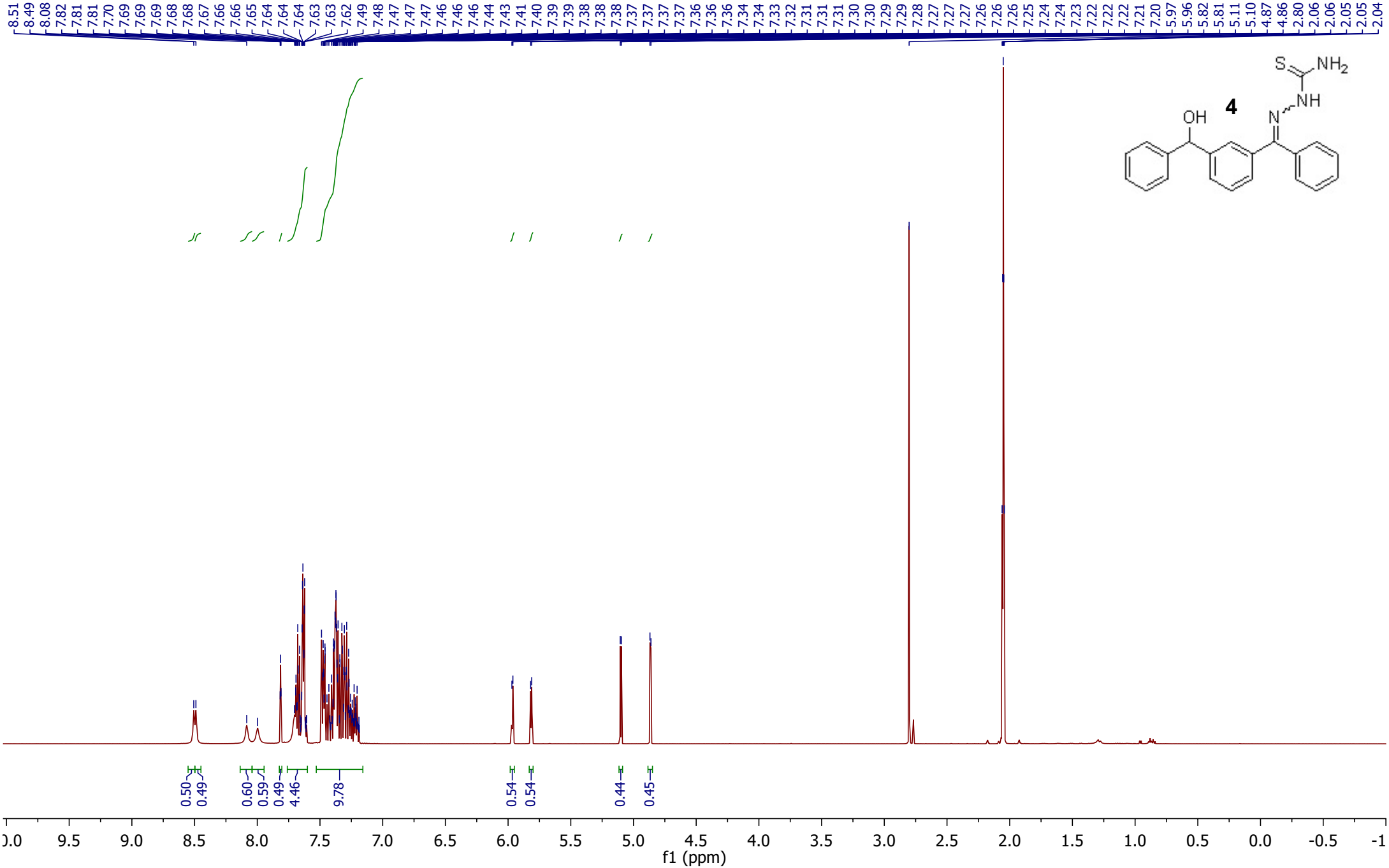


HRMS(ESI) for Compound **3**

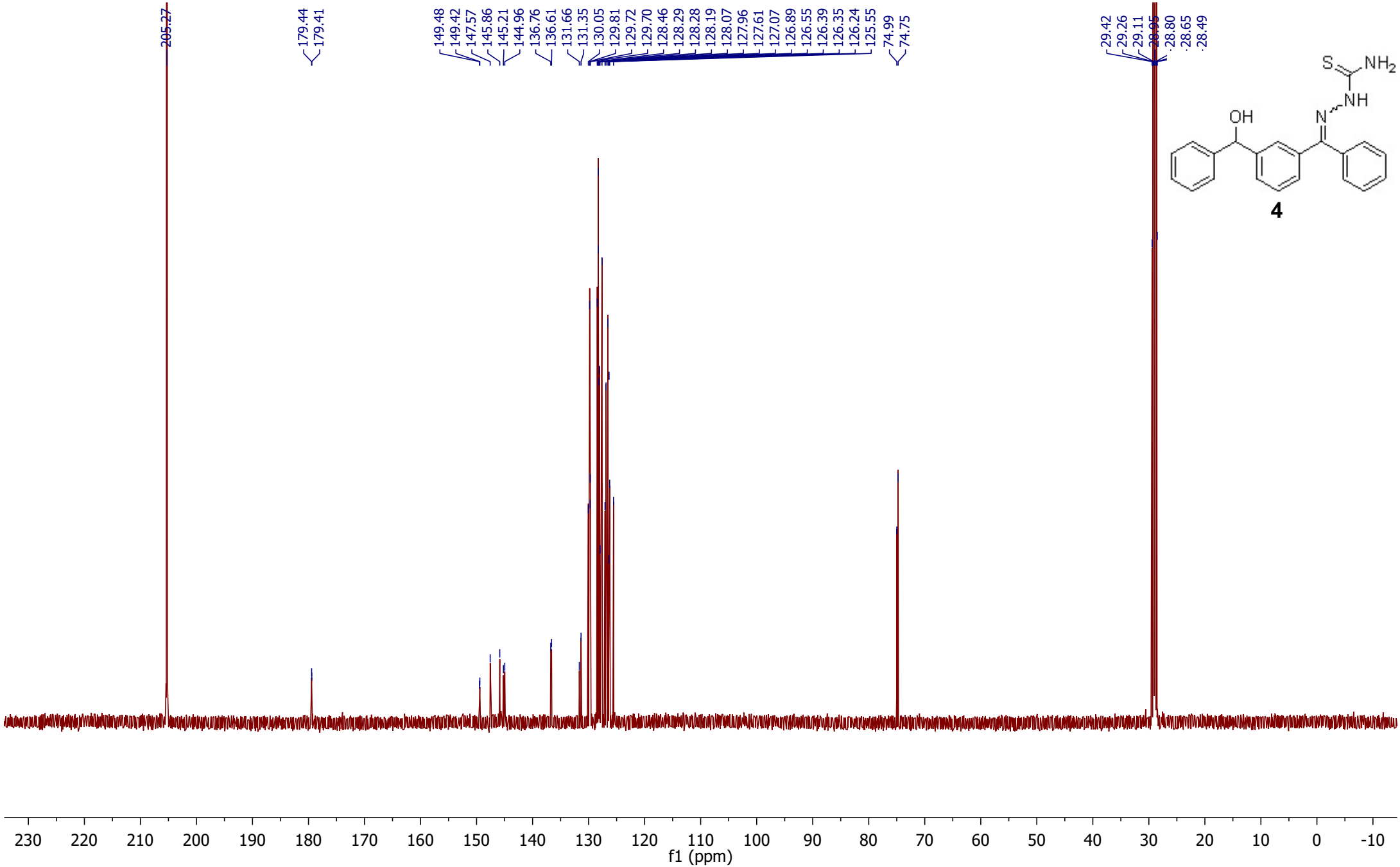
C:\Xcalibur\...\Erica\12-19-14\ENP_II_16 12/19/2014 9:23:59 AM



^{1}H NMR (500 MHz, Acetone-d_6) of Compound **4**



^{13}C NMR (125 MHz, Acetone-d_6) of Compound **4**



Data File C:\CHEM32\1\DATA\ERICAP\ENPII21000030.D
Sample Name: ENPII21

HPLC trace for Compound 4

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Acq. Operator   : ERICAP
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 4/23/2014 6:20:58 PM
Acq. Method     : C:\CHEM32\1\METHODS\GRAD 2 30-90 ACN.M
Last changed    : 4/23/2014 6:03:32 PM by ERICAP
Analysis Method : C:\CHEM32\1\DATA\ERICAP\ENPII21000030.D\DA.M (GRAD 2 30-90 ACN.M)
Last changed    : 6/12/2014 10:09:58 PM by ERICAP
                  (modified after loading)
Sample Info     : ENP-II-21

                  Method:

                  0-25 Min. 30:70 to 90:10 ACN:Water
                  25-30 min 90:10 ACN:Water
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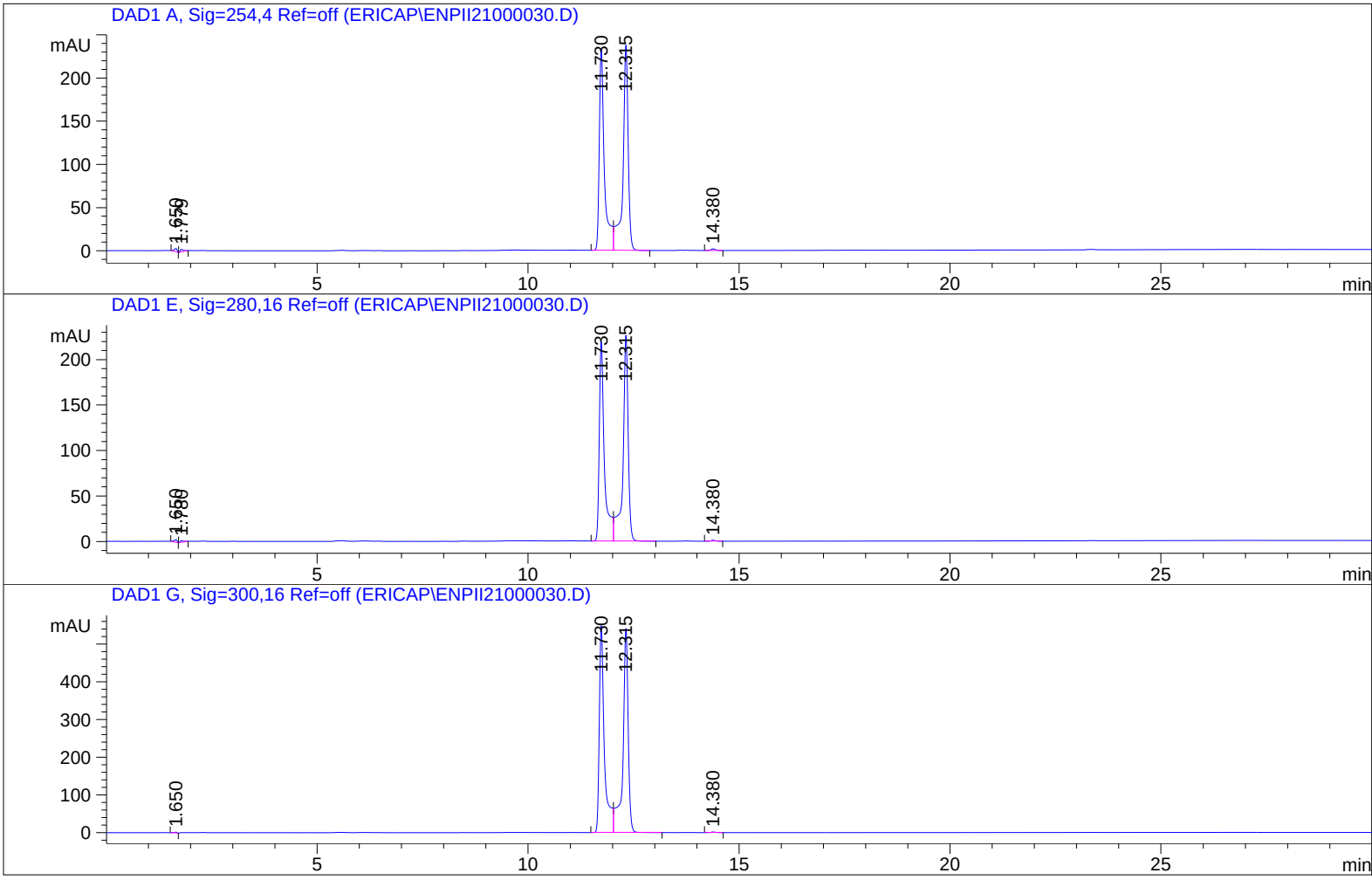
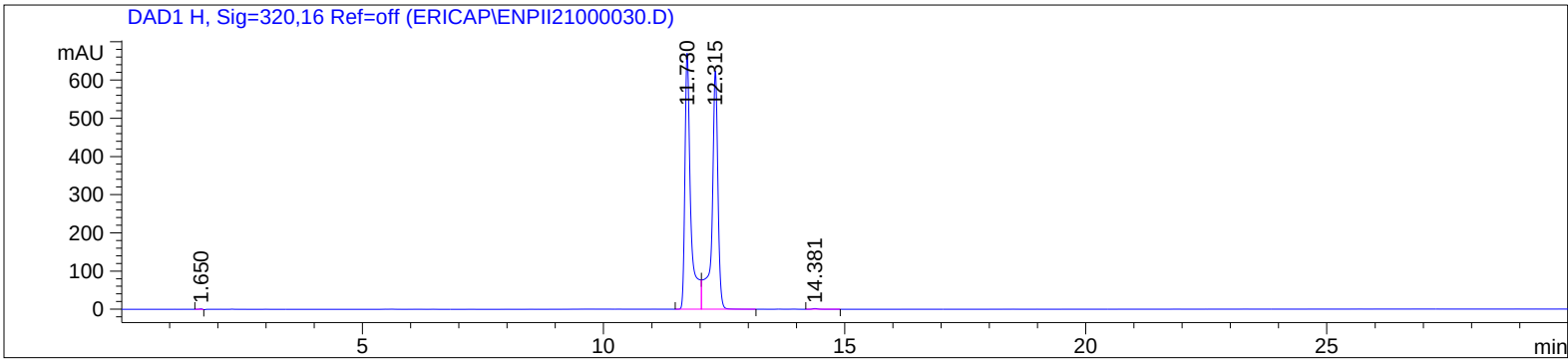
Two peaks observed in the HPLC traces are due to the presence of both E and Z geometrical isomers.



Data File C:\CHEM32\1\DATA\ERICAP\ENPII21000030.D
Sample Name: ENPII21

HPLC trace for Compound 4



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.650	BB	0.0769	18.23187	3.87769	0.4449
2	1.779	BB	0.0828	17.08805	3.07529	0.4170
3	11.730	BV	0.1226	1977.19495	233.86279	48.2460
4	12.315	VB	0.1256	2072.02637	238.03497	50.5600
5	14.380	BB	0.1131	13.60941	1.86607	0.3321

Totals : 4098.15064 480.71681

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.650	BB	0.0781	13.92746	2.89825	0.3603
2	1.780	BB	0.0894	11.38207	1.85881	0.2945
3	11.730	BV	0.1227	1857.43726	219.44960	48.0557
4	12.315	VB	0.1256	1974.17249	226.70097	51.0759
5	14.380	BB	0.1116	8.25262	1.12419	0.2135

Totals : 3865.17190 452.03182

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.650	BB	0.0803	10.63423	2.12782	0.1132
2	11.730	BV	0.1226	4635.96777	548.51636	49.3507
3	12.315	VB	0.1259	4735.43945	541.91022	50.4096

Data File C:\CHEM32\1\DATA\ERICAP\ENPII21000030.D
Sample Name: ENPII21

HPLC trace for Compound 4

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
4	14.380	BB	0.1111	11.88297	1.62996	0.1265
Totals :				9393.92443	1094.18435	

Signal 4: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.650	BB	0.0794	9.00574	1.83150	0.0808
2	11.730	BV	0.1223	5650.26221	670.28705	50.6806
3	12.315	VB	0.1262	5475.74316	625.02753	49.1153
4	14.381	BB	0.1141	13.74645	1.86303	0.1233
Totals :				1.11488e4	1299.00910	

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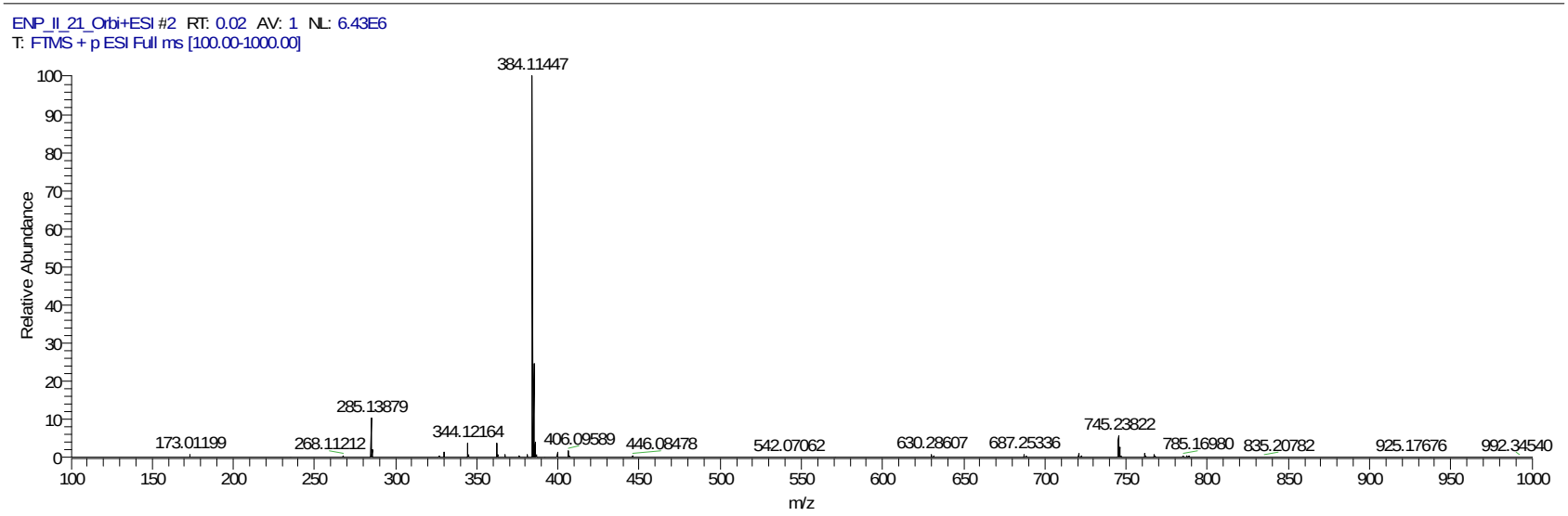
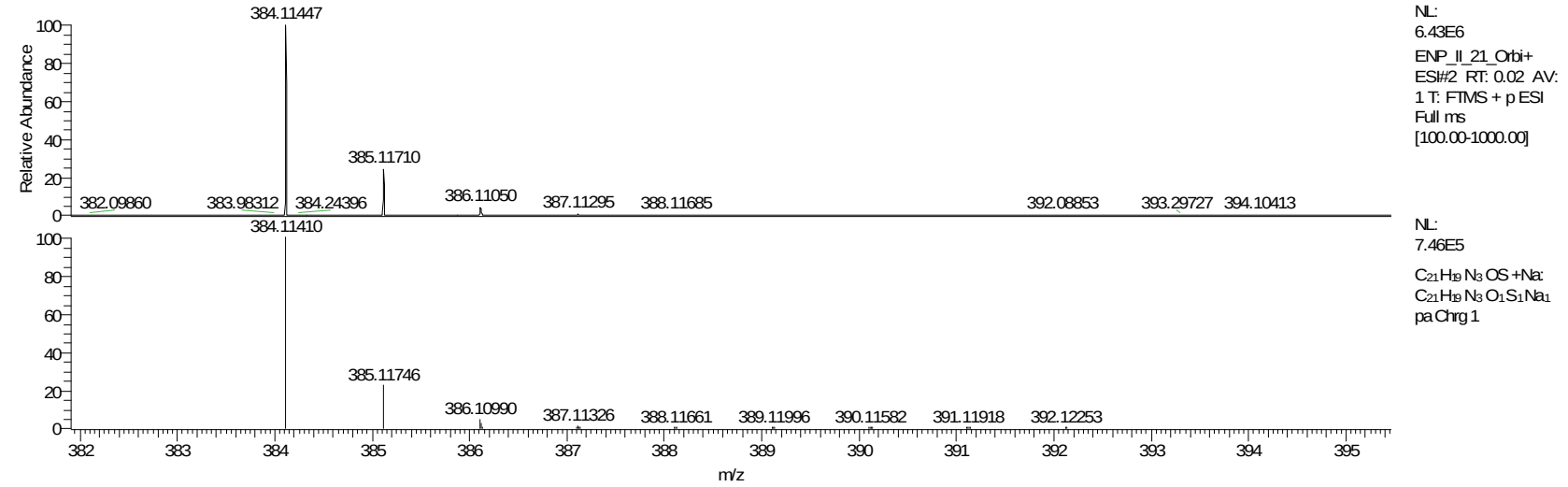
*** End of Report ***

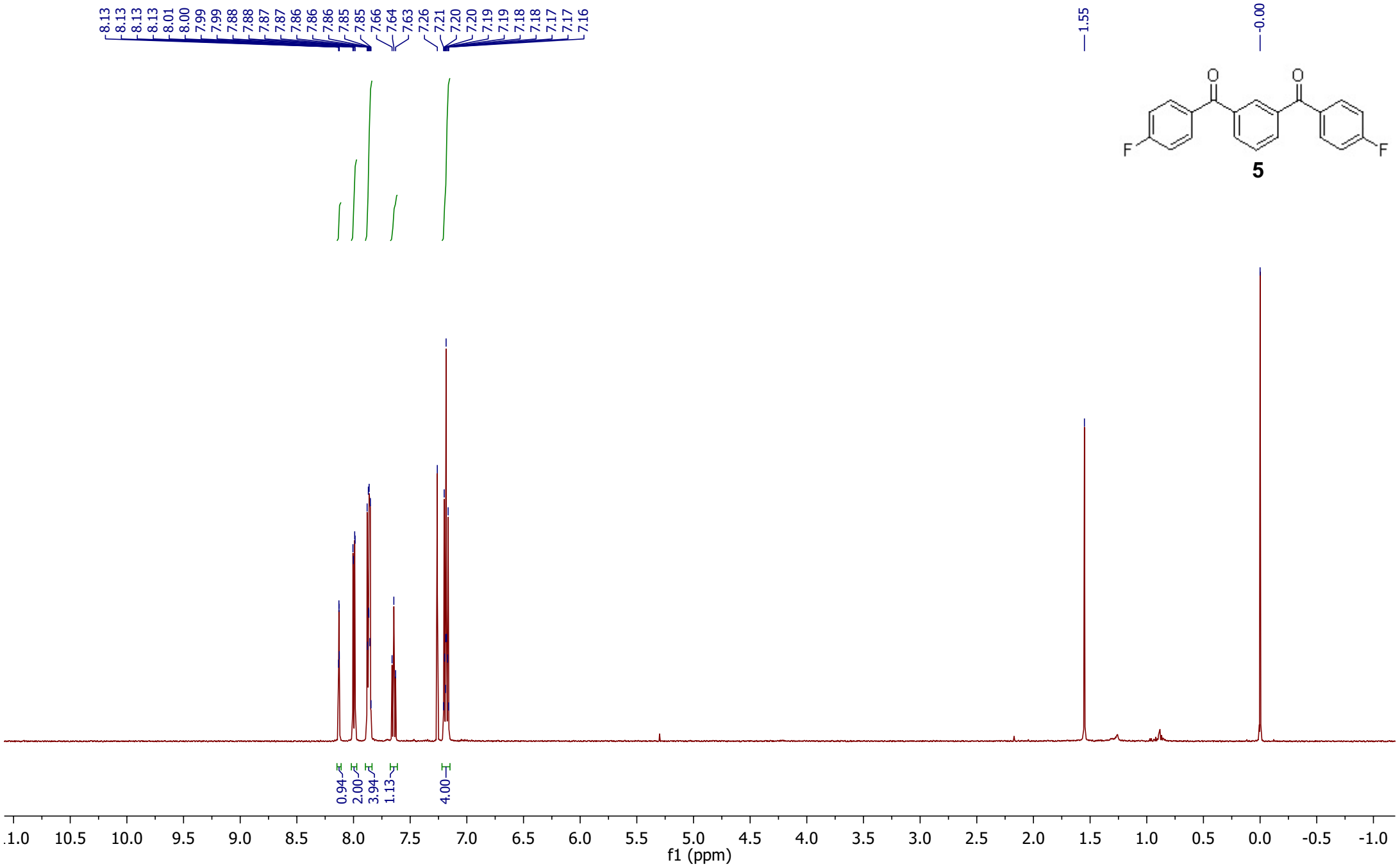
HRMS(ESI) for Compound **4**

C:\Xcalibur\...\ENP_II_21_Orbi+ESI 1/13/2015 11:19:57 PM

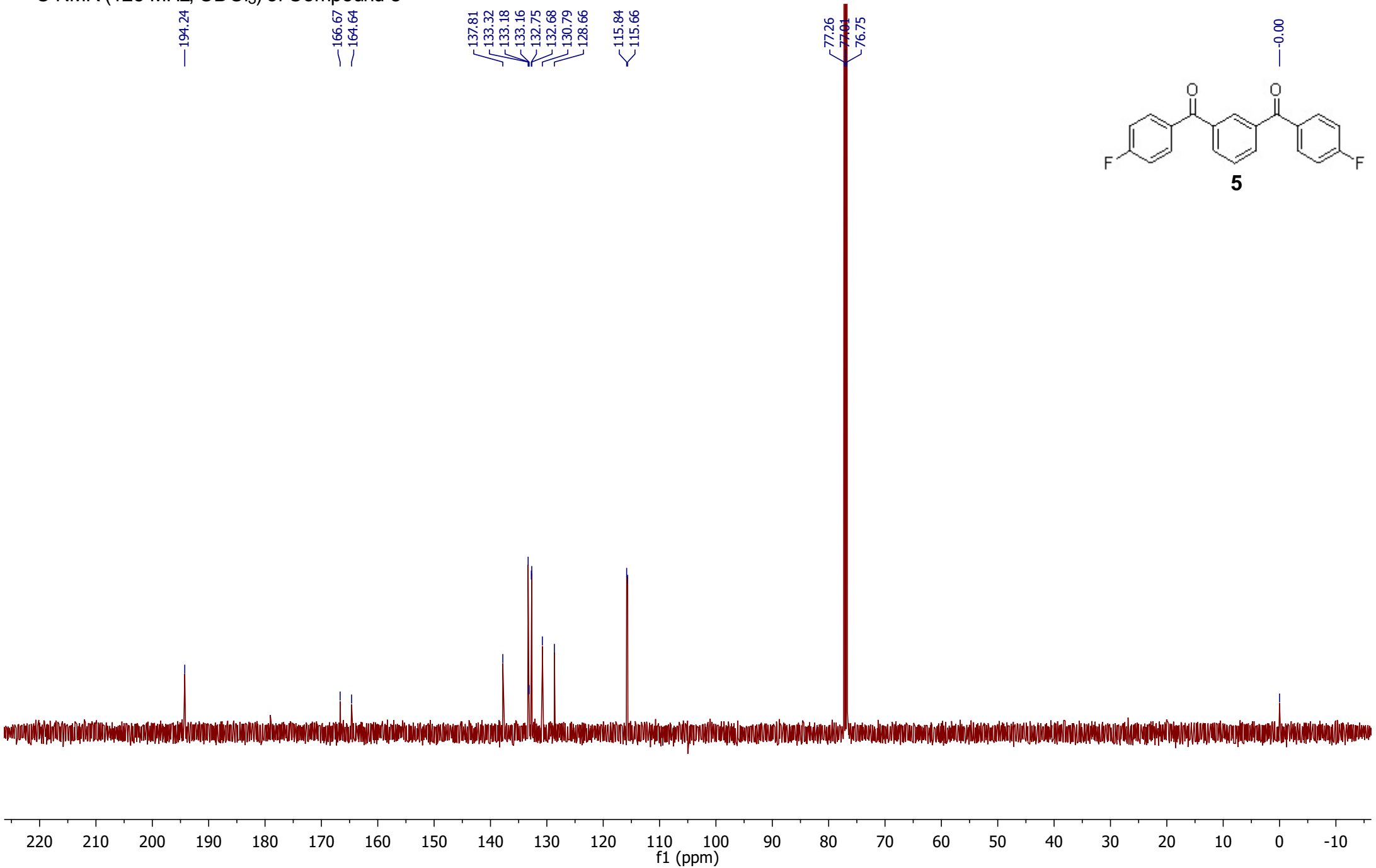




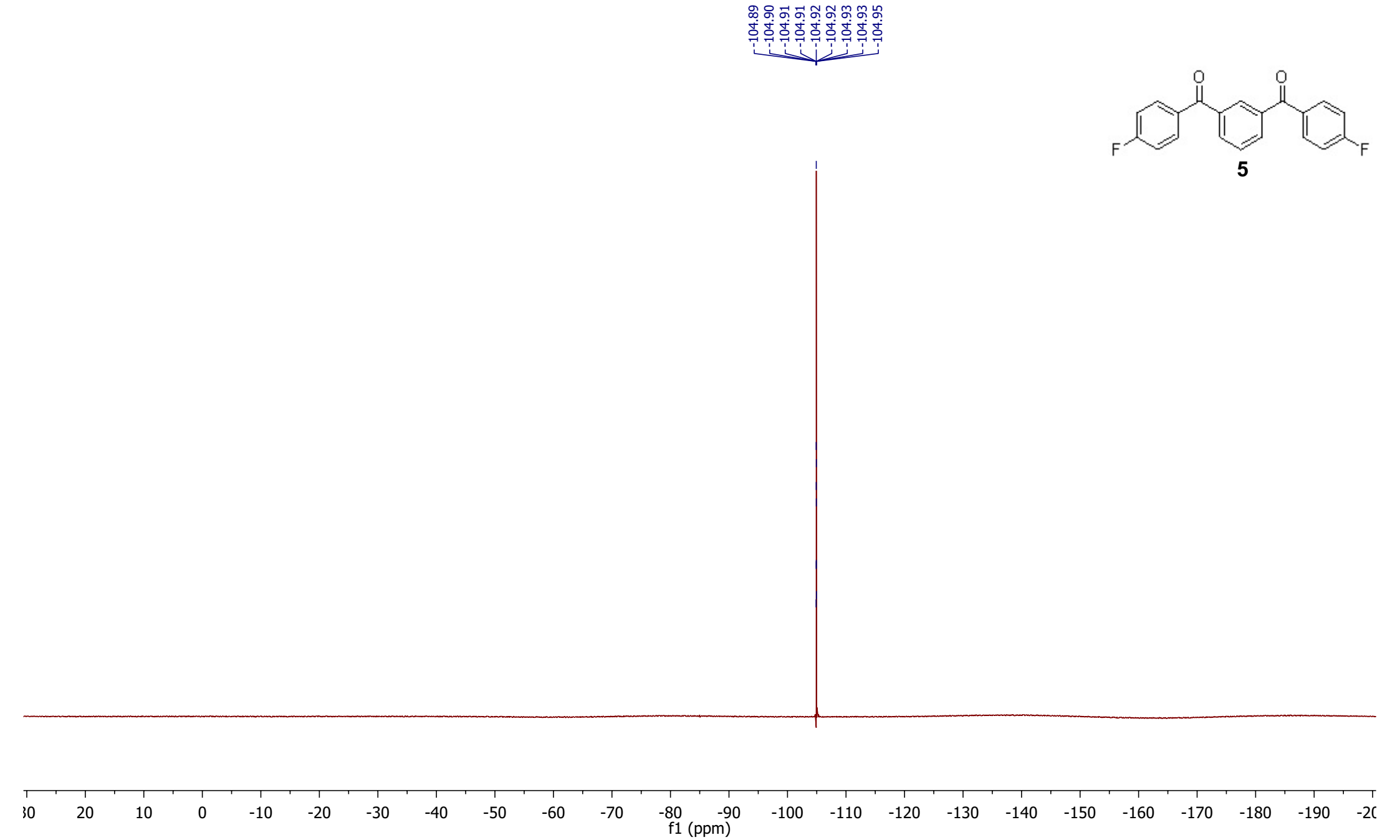
^{1}H NMR (500 MHz, $CDCl_3$) of Compound **5**



^{13}C NMR (125 MHz, $CDCl_3$) of Compound **5**

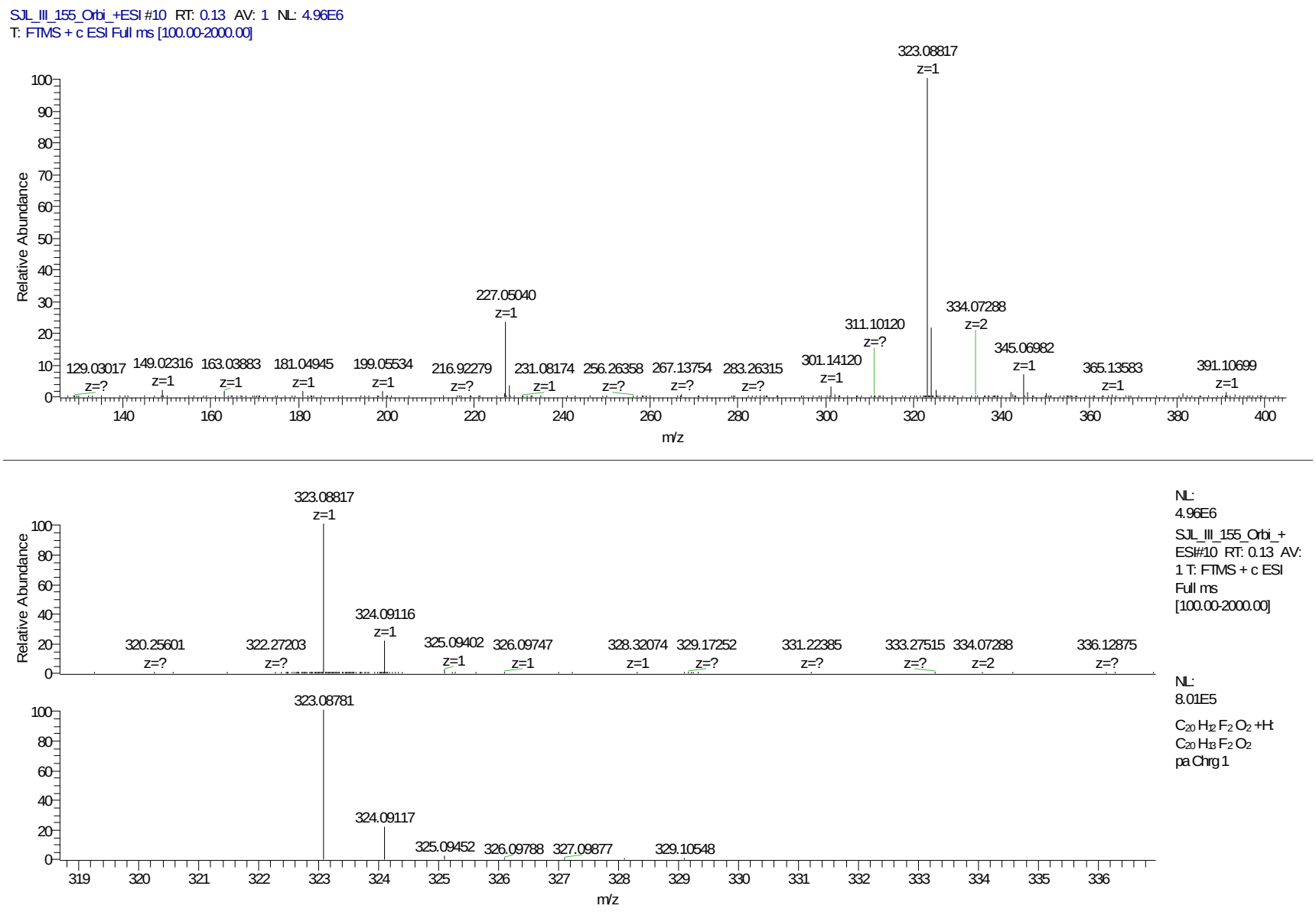


^{19}F NMR (470 MHz, $CDCl_3$) of Compound **5**

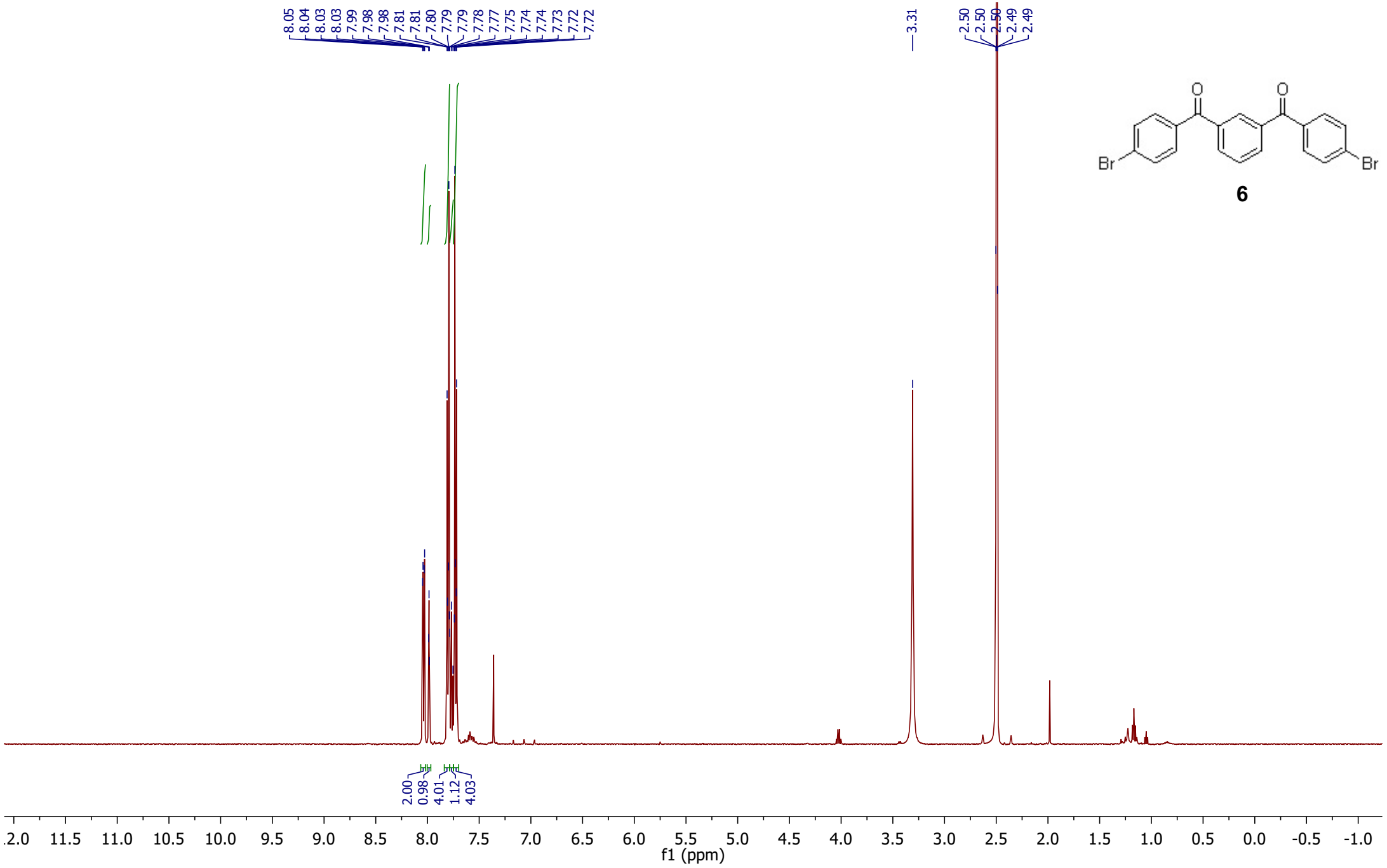


HRMS (ESI) for Compound **5**

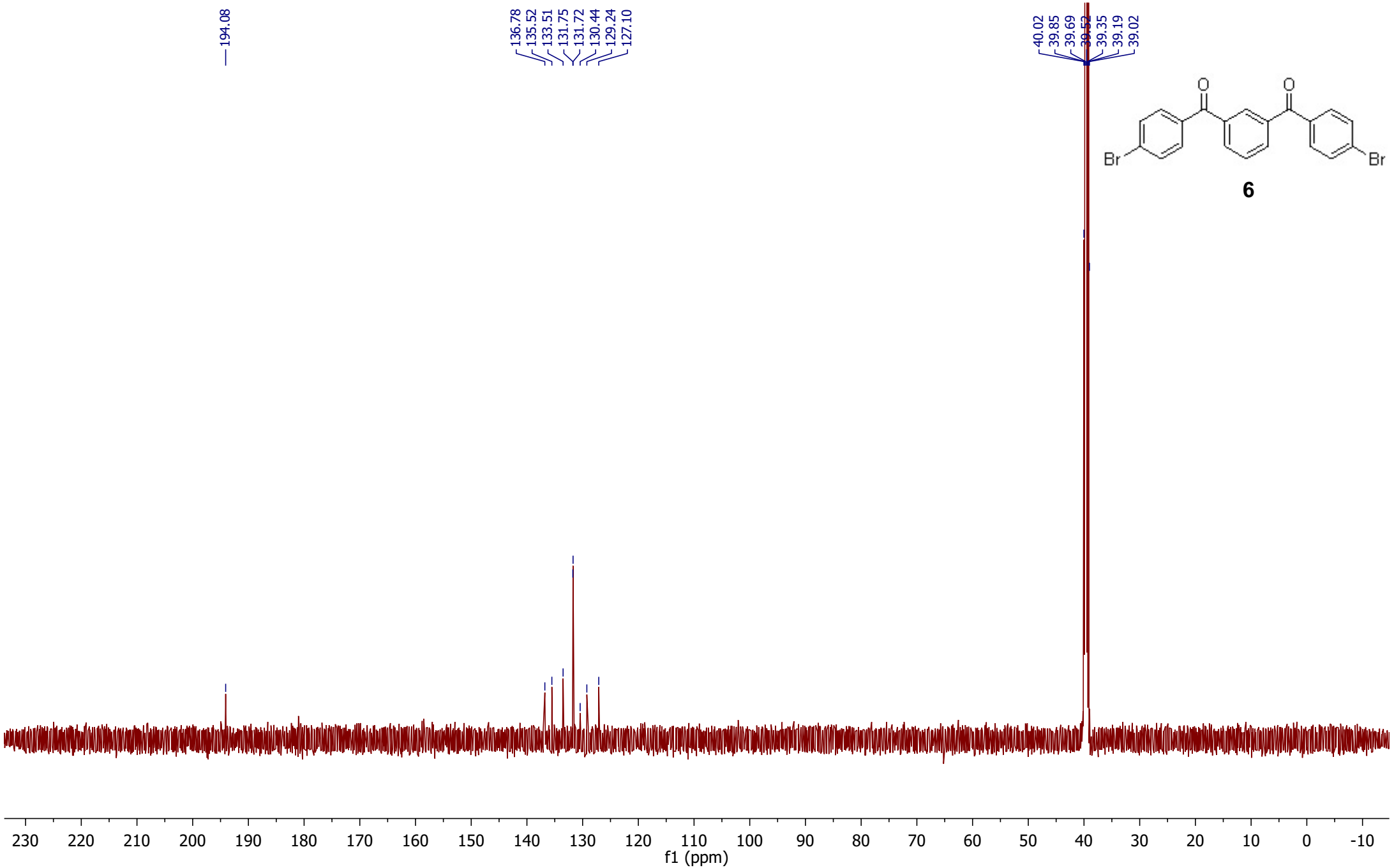
C:\Xcalibur\...\SJL_III_155_Orbi_+ESI 12/30/2014 9:09:59 PM



^{1}H NMR (500 MHz, DMSO-d_6) of Compound **6**

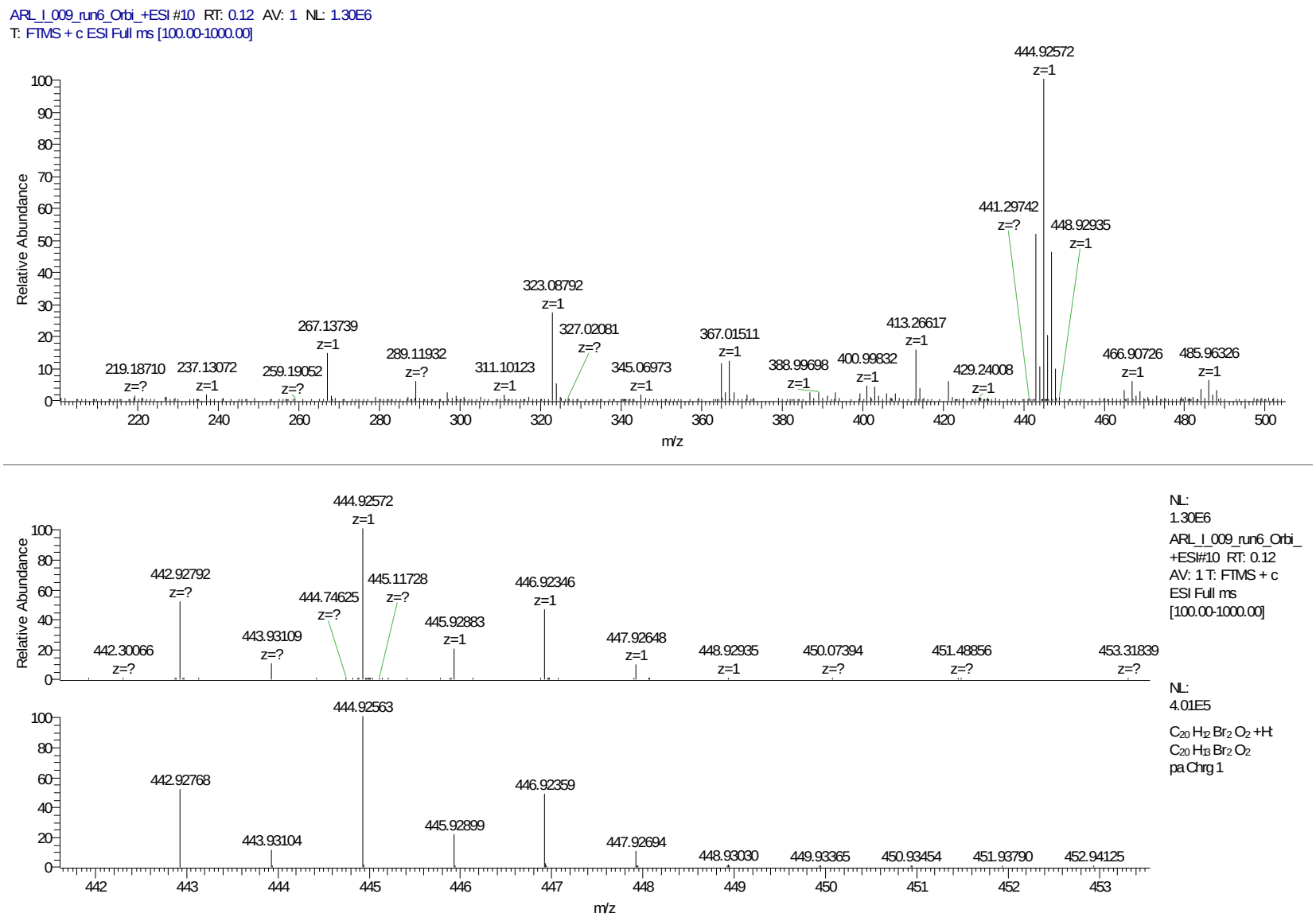


^{13}C NMR (125 MHz, DMSO-d_6) of Compound **6**

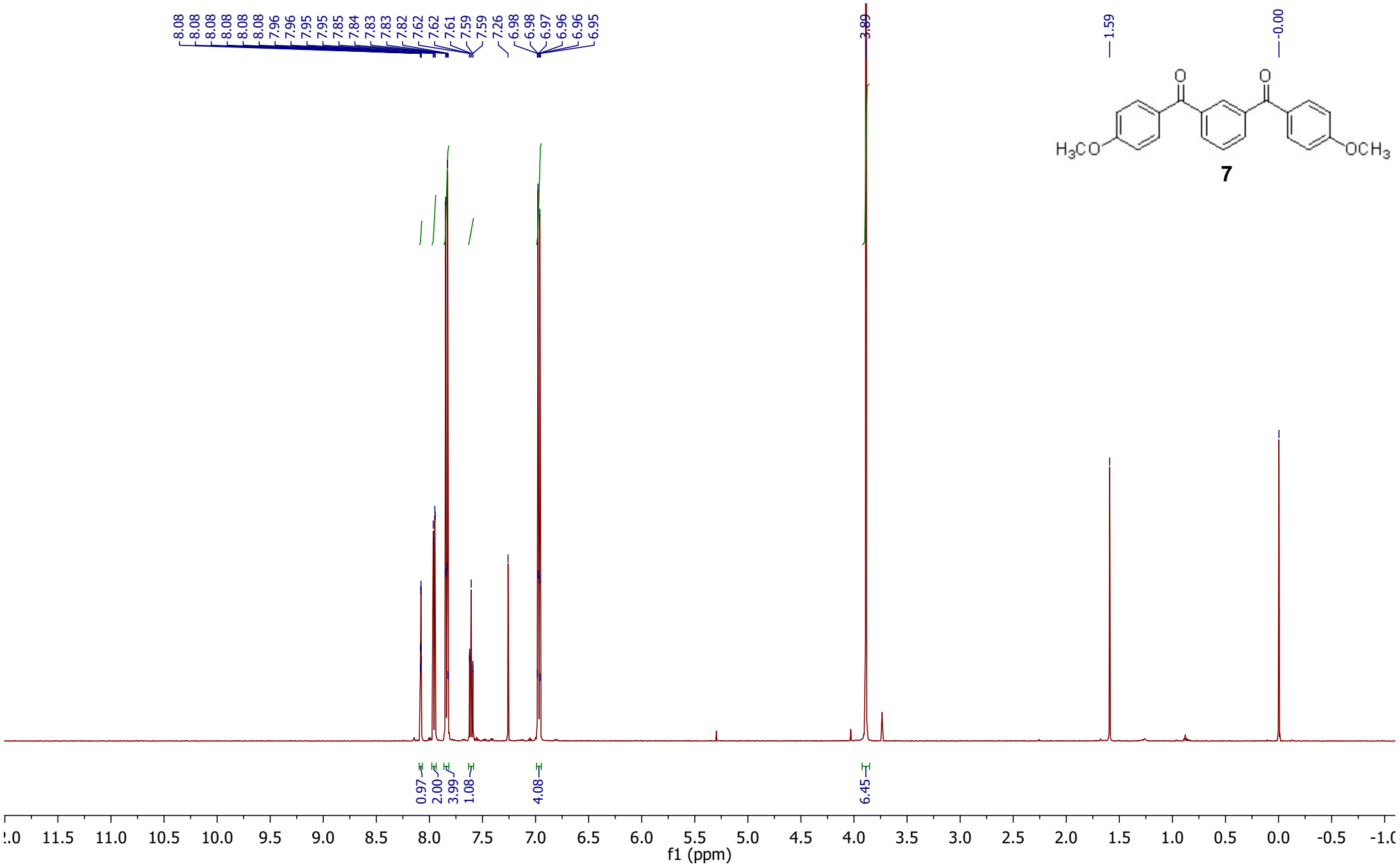


HRMS (ESI) for Compound **6**

C:\Xcalibur\...\ARL_I_009_run6_Orbi_+ESI 12/30/2014 11:54:26 PM

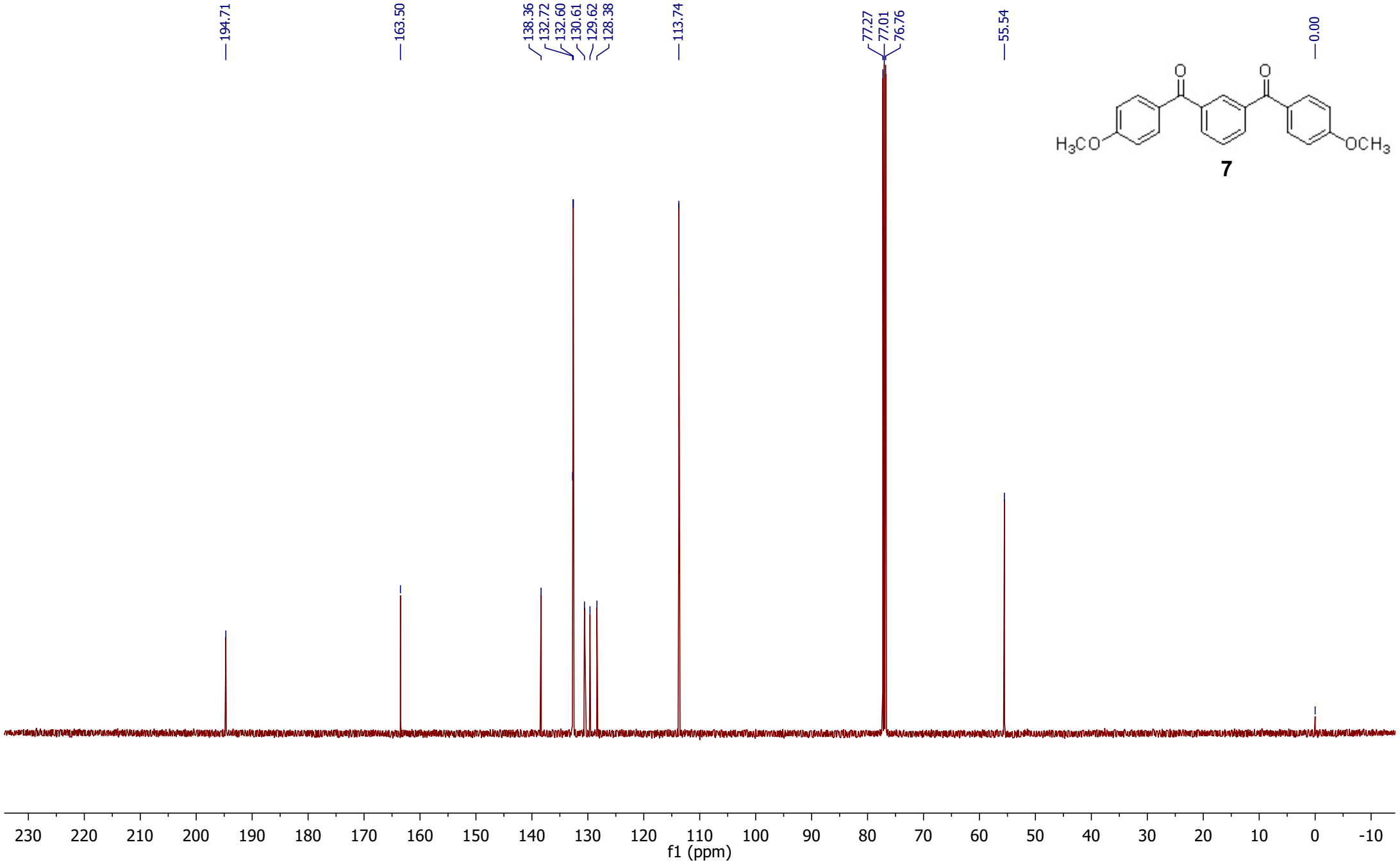


^{1}H NMR (500 MHz, $CDCl_3$) of Compound **7**



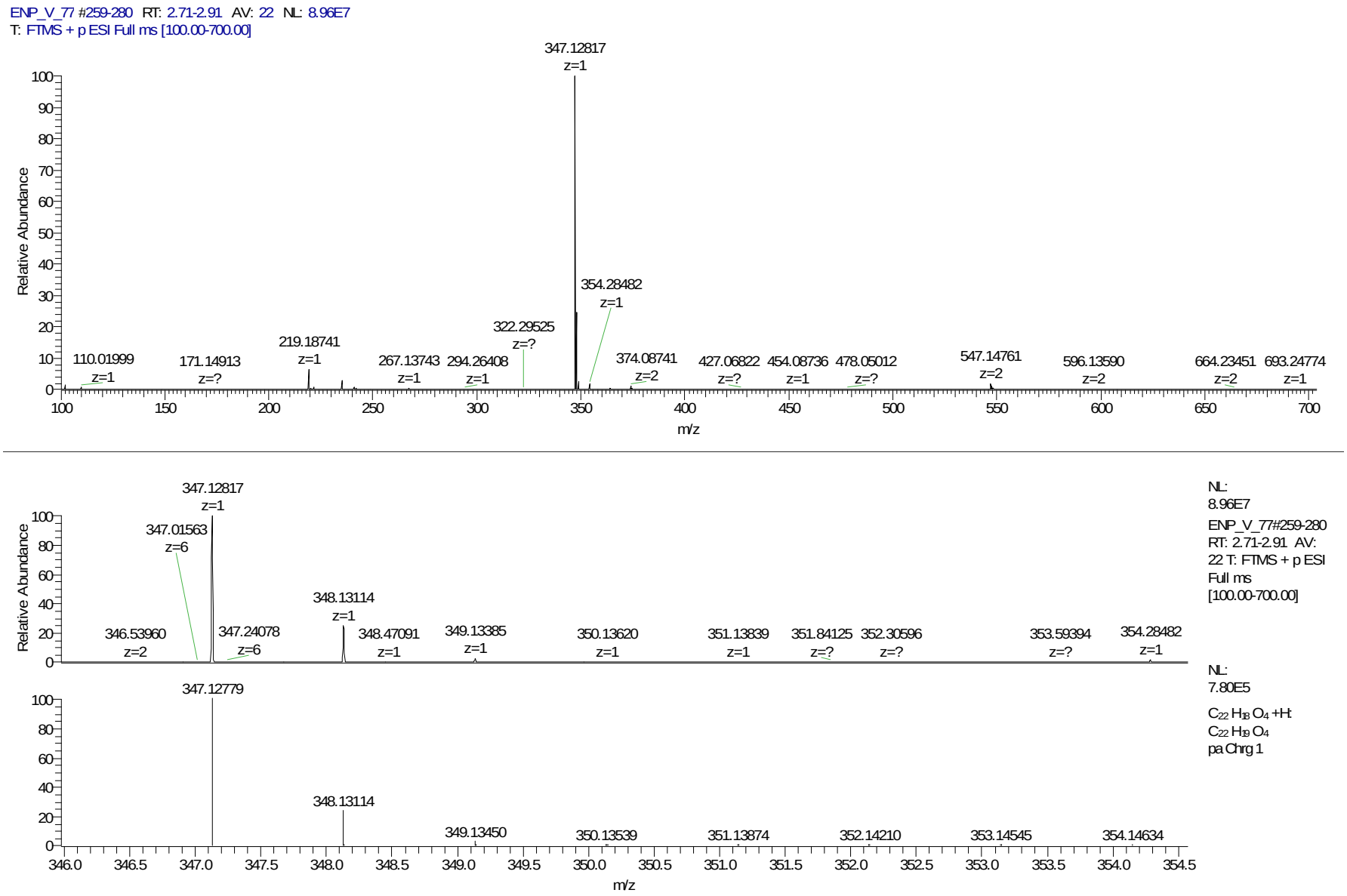
7

^{13}C NMR (125 MHz, $CDCl_3$) of Compound **7**

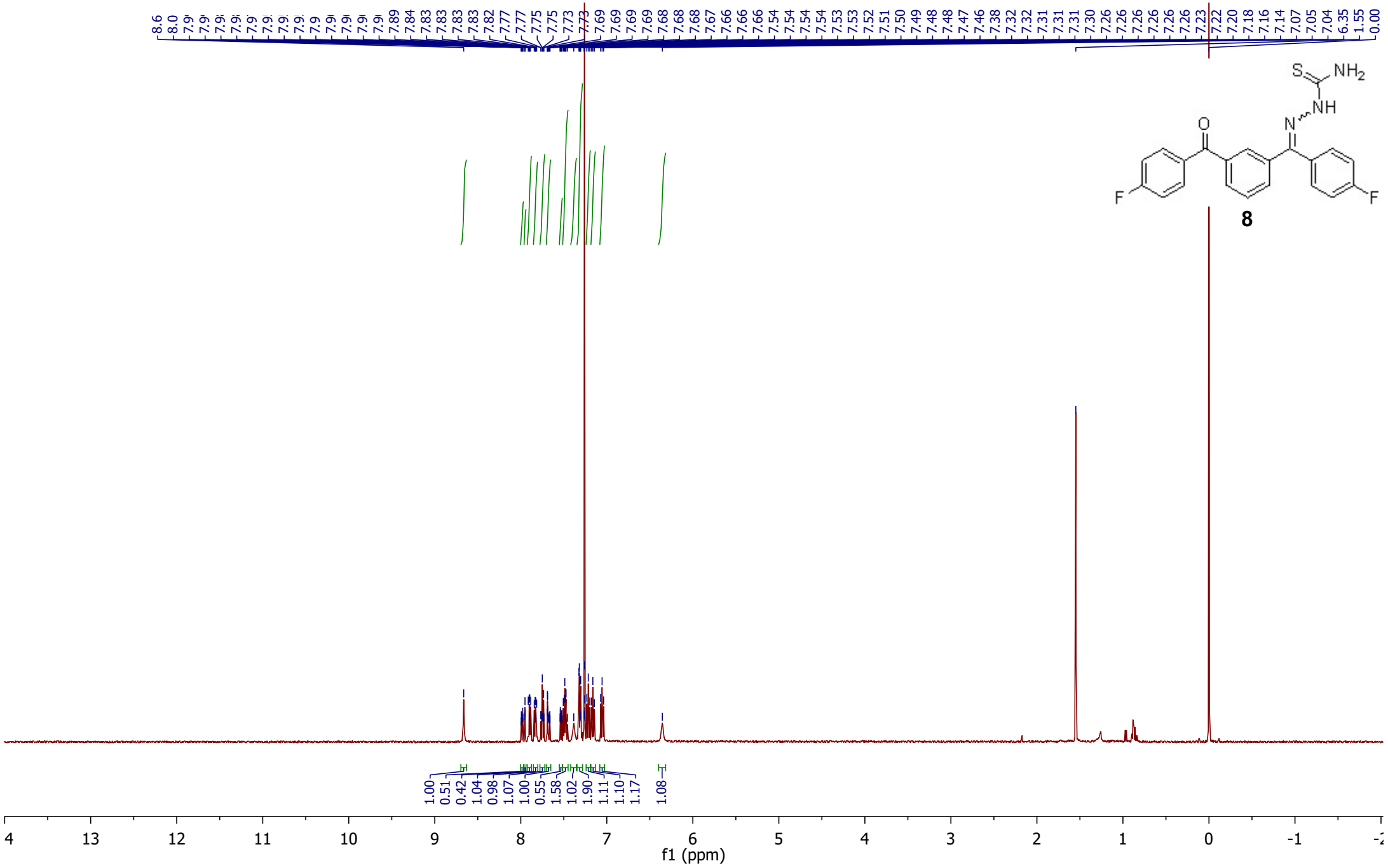


HRMS (ESI) for Compound **7**

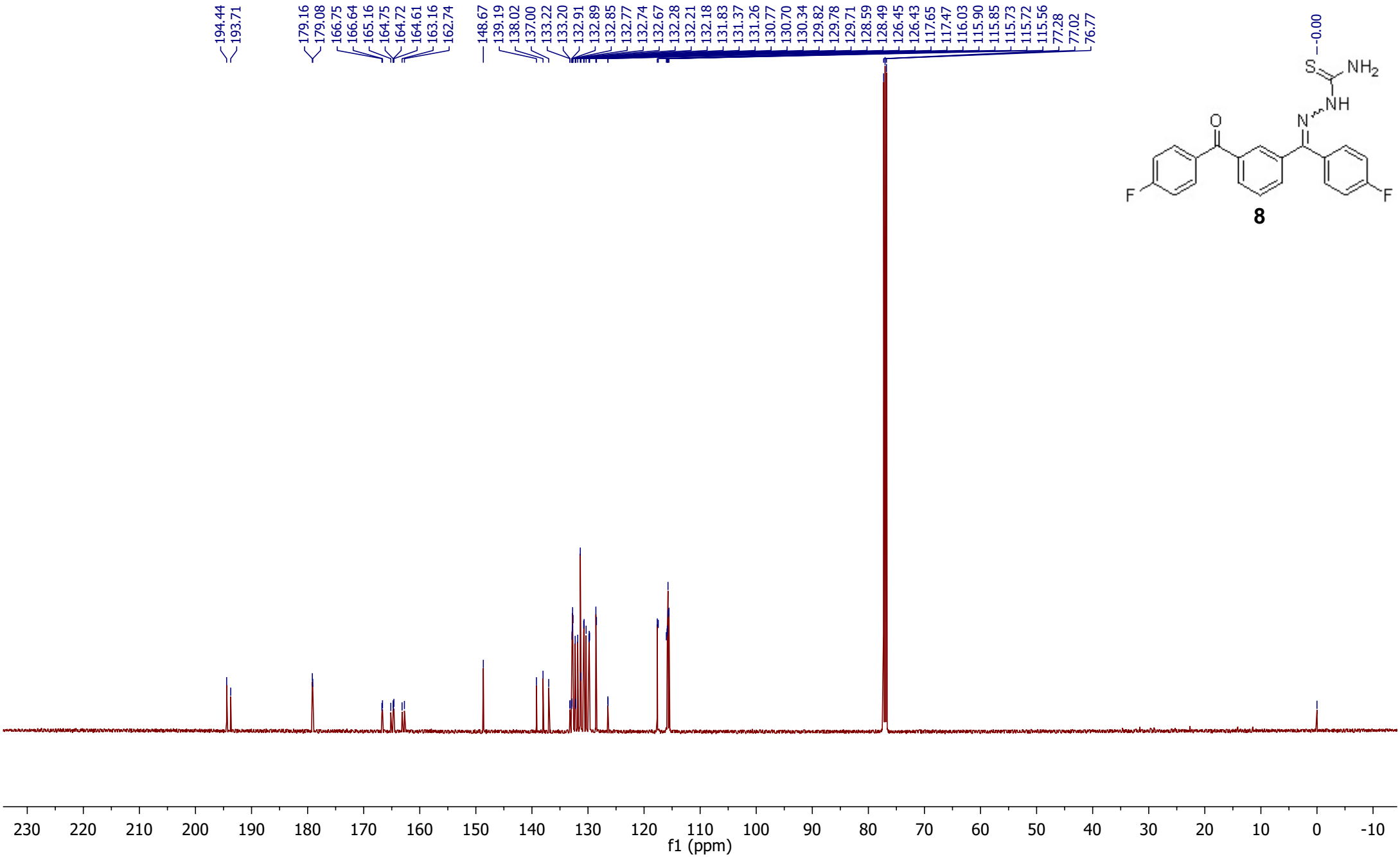
C:\Xcalibur\...\Erica\12-19-14\ENP_V_77 12/19/2014 10:06:00 AM



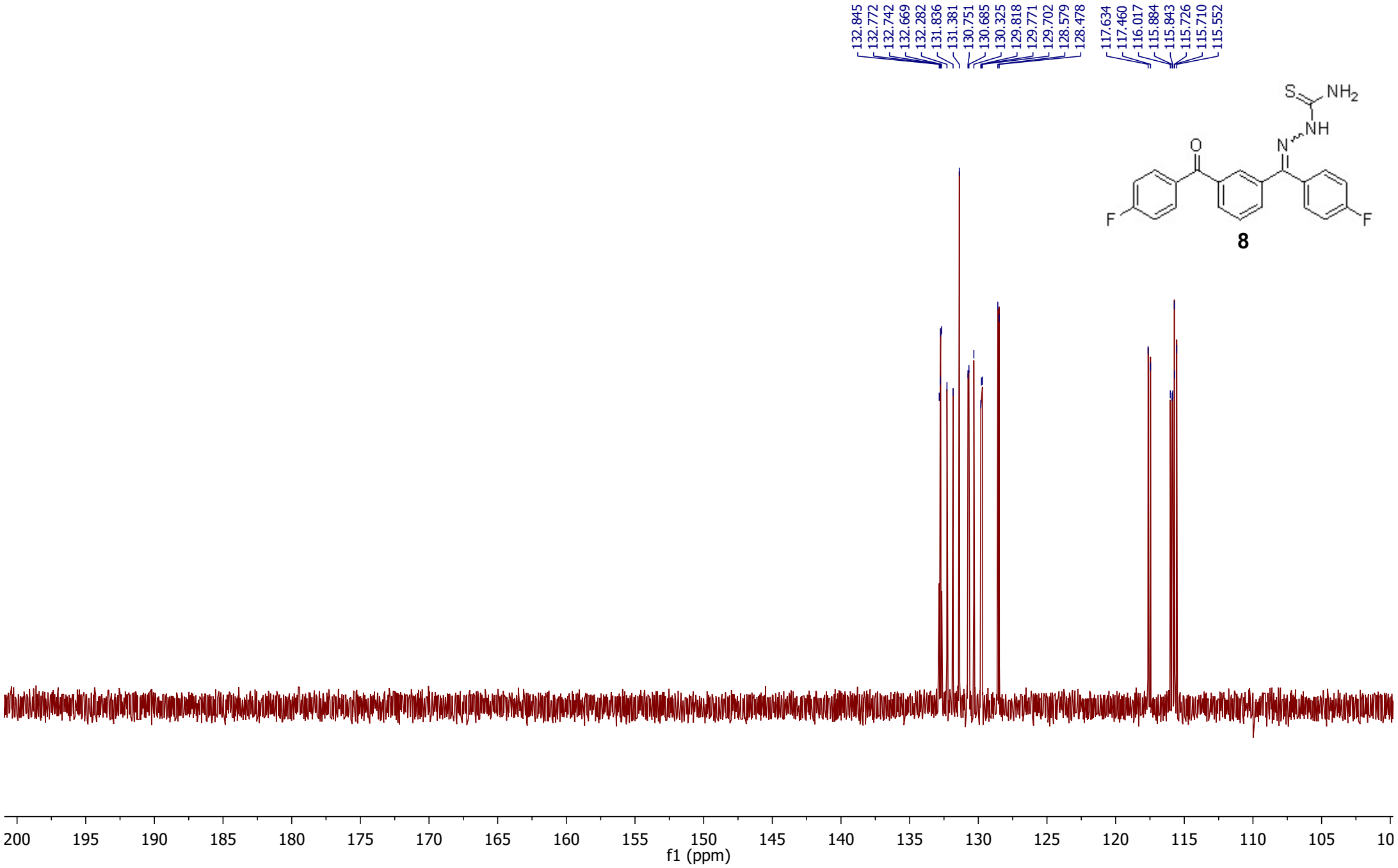
^{1}H NMR (500 MHz, $CDCl_3$) of Compound **8**



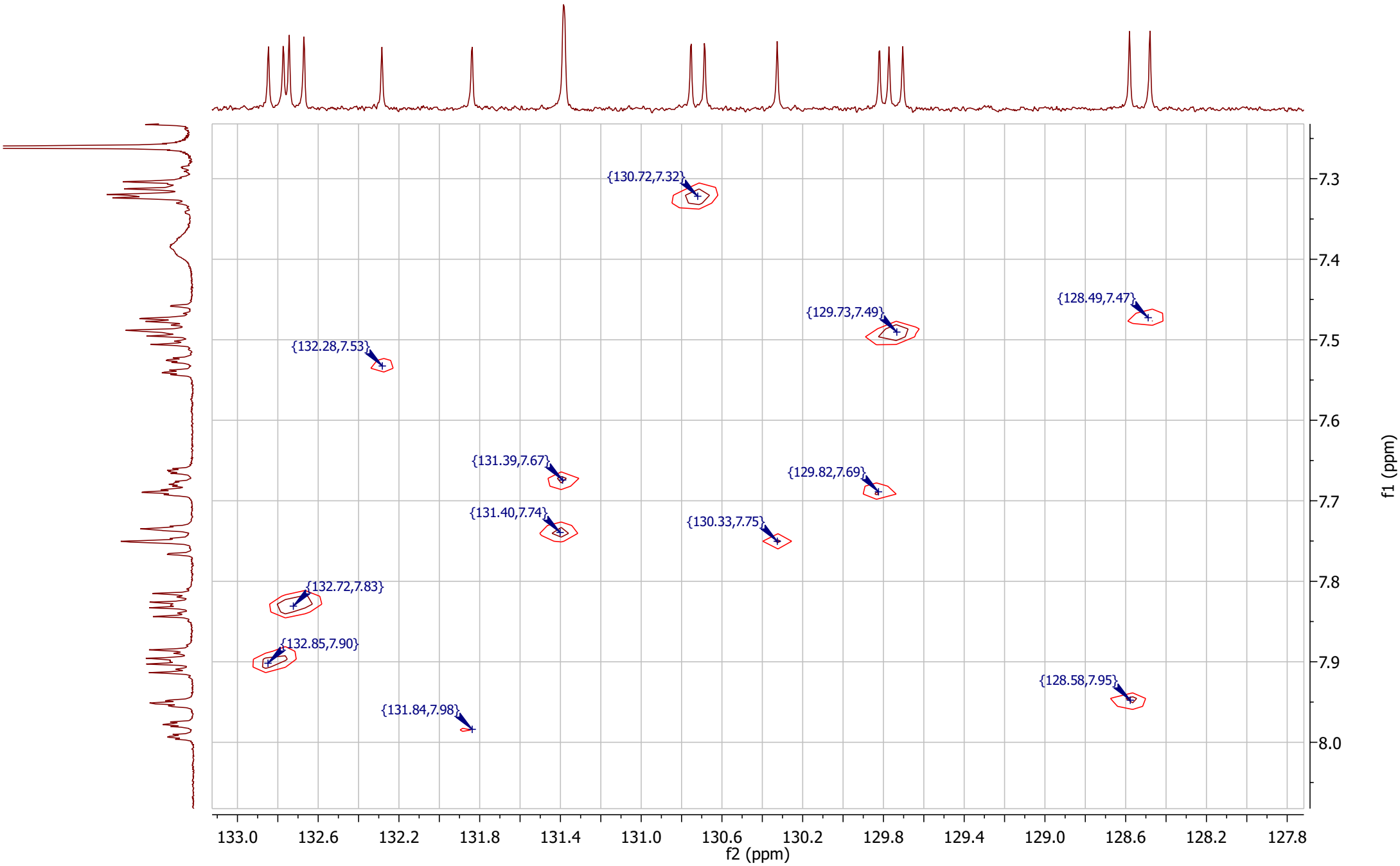
^{13}C NMR (125 MHz, $CDCl_3$) of Compound **8**



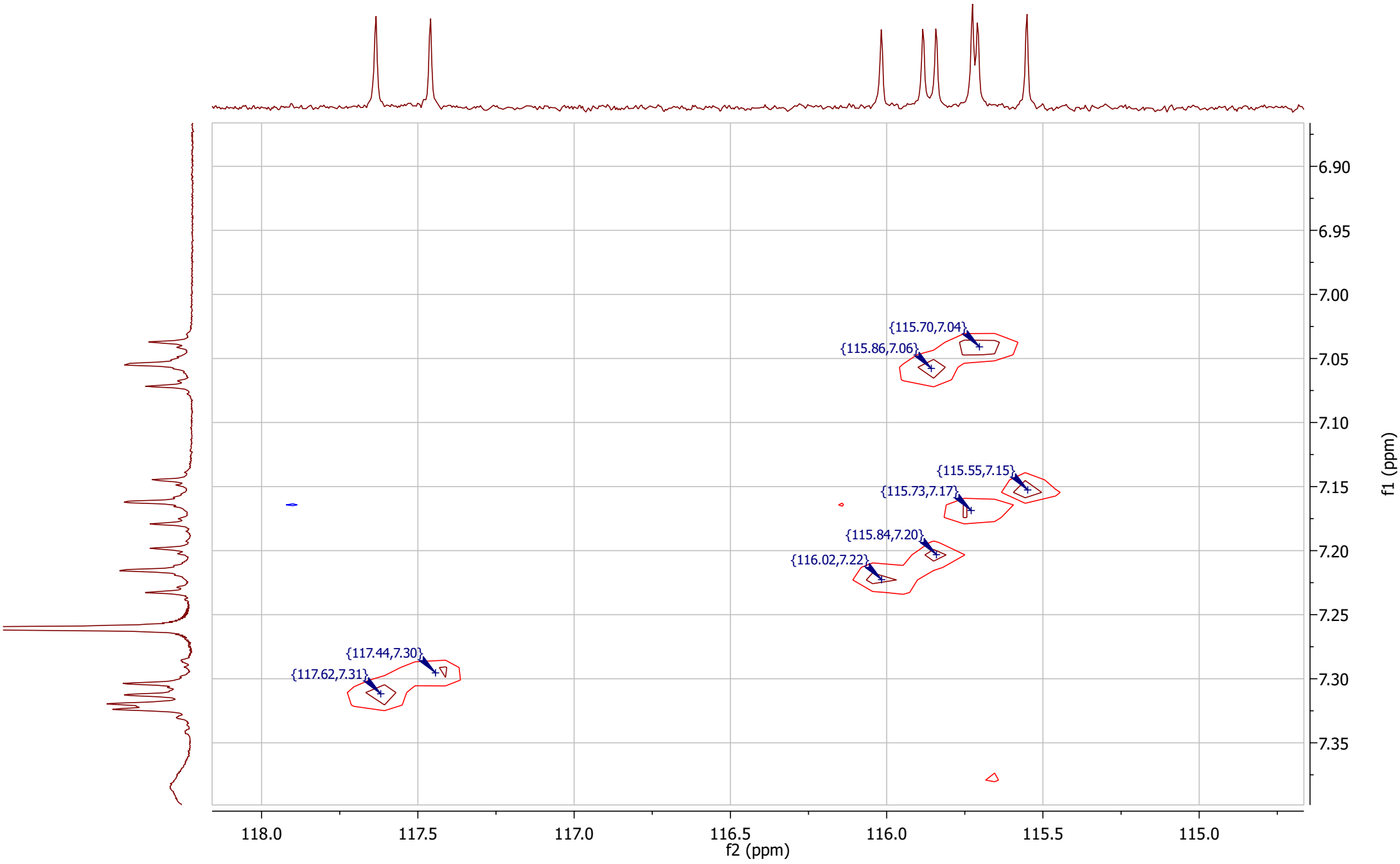
DEPT (CH only, 125 MHz, $CDCl_3$) for compound **8**



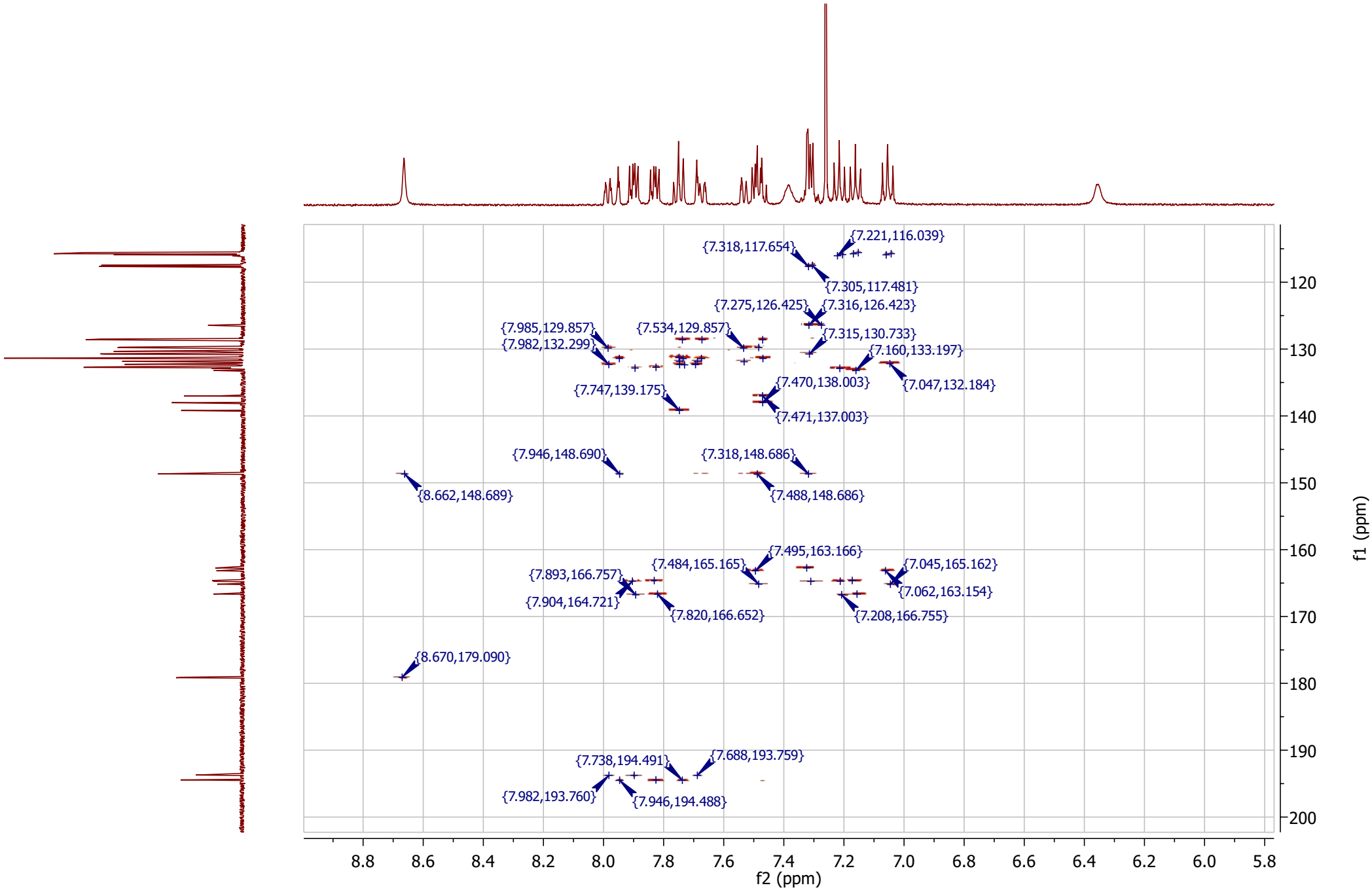
gHETCOR (125 MHz, $CDCl_3$) for compound **8**



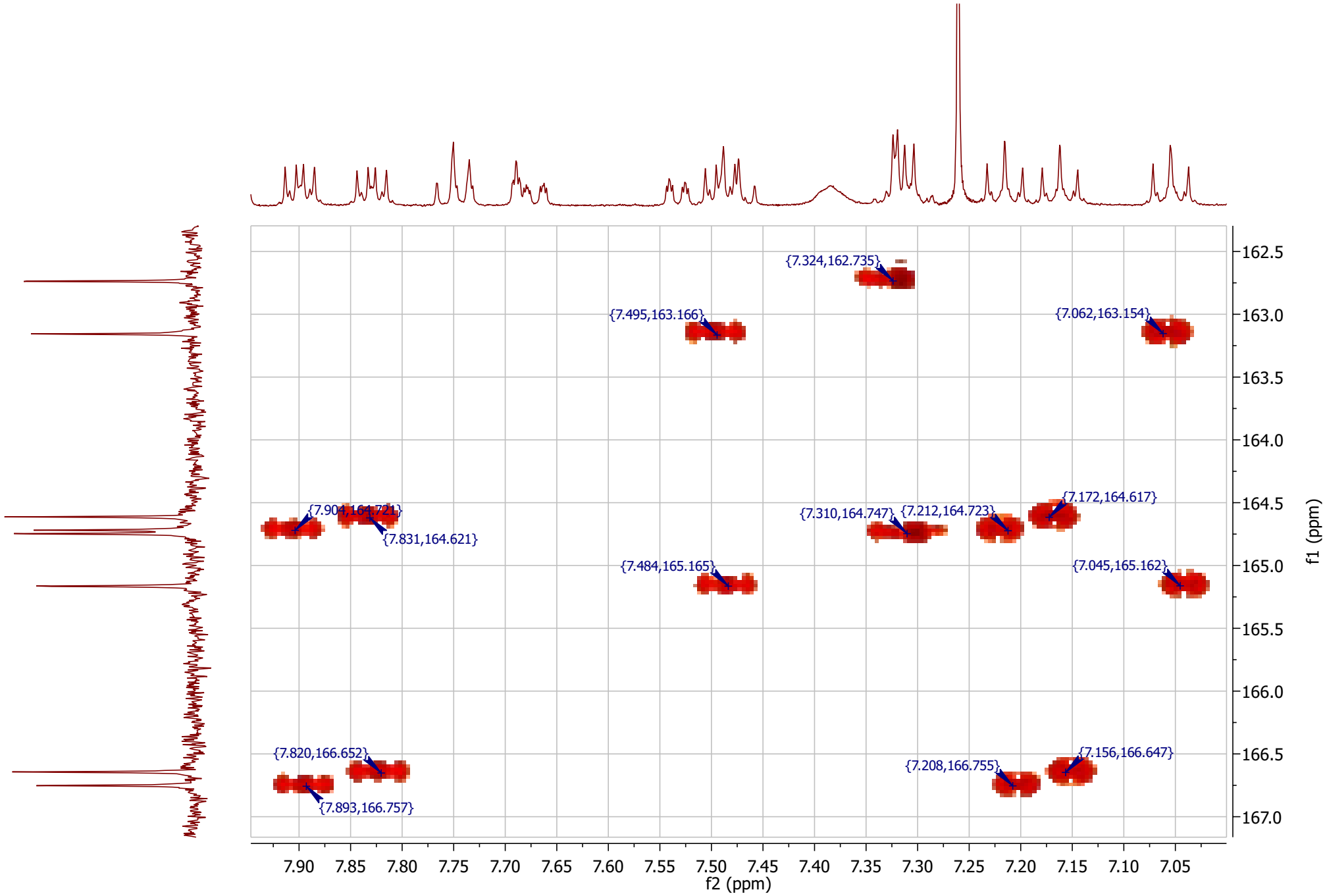
gHETCOR (125 MHz, $CDCl_3$) for compound **8**



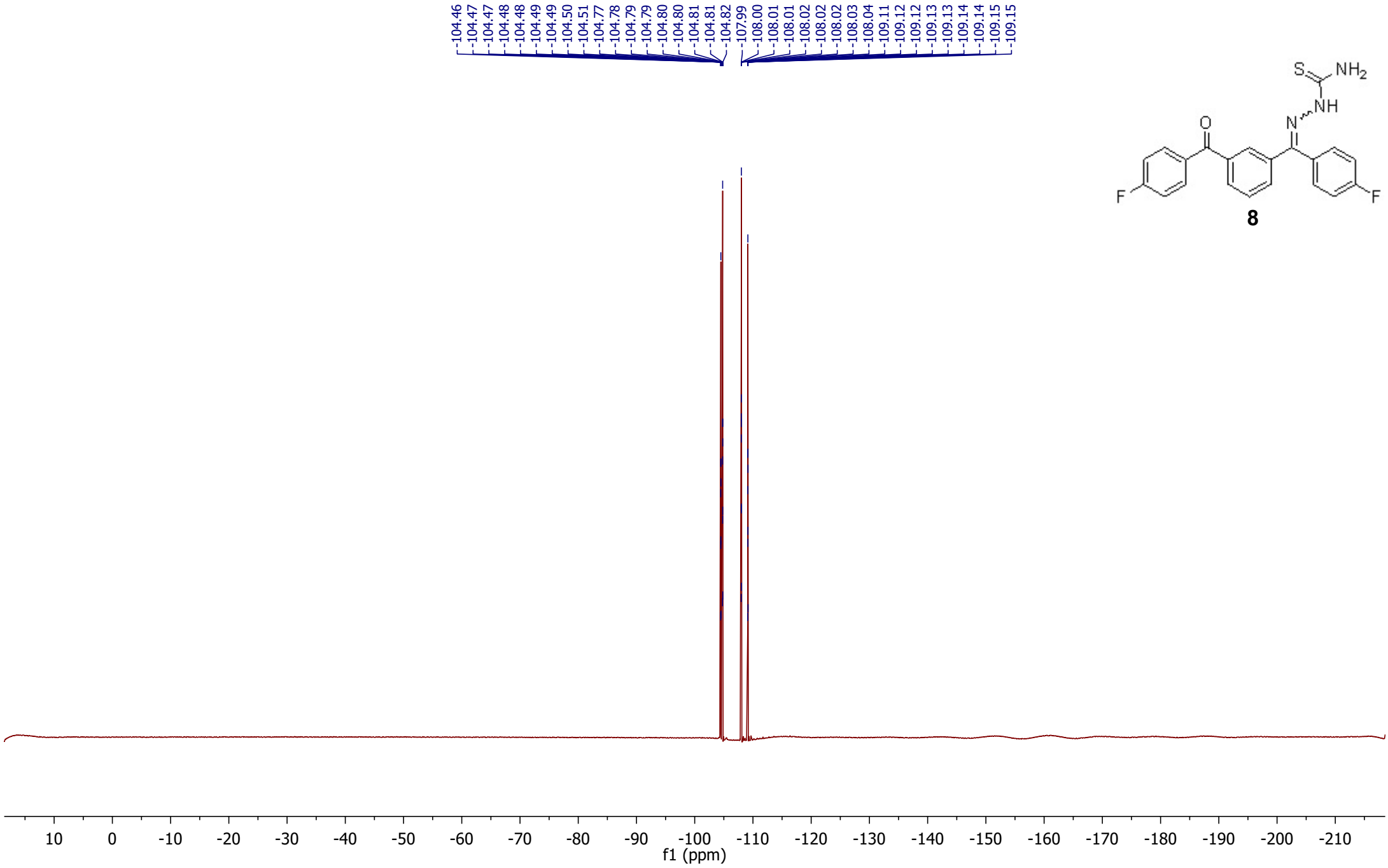
gHMBCAD ($CDCl_3$) for compound **8**



gHMBCAD ($CDCl_3$) for compound **8**



^{19}F NMR (565 MHz, $CDCl_3$) of Compound **8**



Data File C:\CHEM32\1\DATA\ERICAP\KGP244000031.D
Sample Name: KGP244

HPLC trace for Compound 8

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Acq. Operator   : ERICAP
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 4/30/2014 7:01:47 PM
Acq. Method     : C:\CHEM32\1\METHODS\GRAD 2 50-90 ACN.M
Last changed    : 4/30/2014 6:49:33 PM by ERICAP
Analysis Method : C:\CHEM32\1\DATA\ERICAP\KGP244000031.D\DA.M (GRAD 2 50-90 ACN.M)
Last changed    : 6/12/2014 9:58:06 PM by ERICAP
Sample Info     : KGP244

                  Method:

                  0-25 Min. 50:70 to 90:10 ACN:Water
                  25-30 min 90:10 ACN:Water
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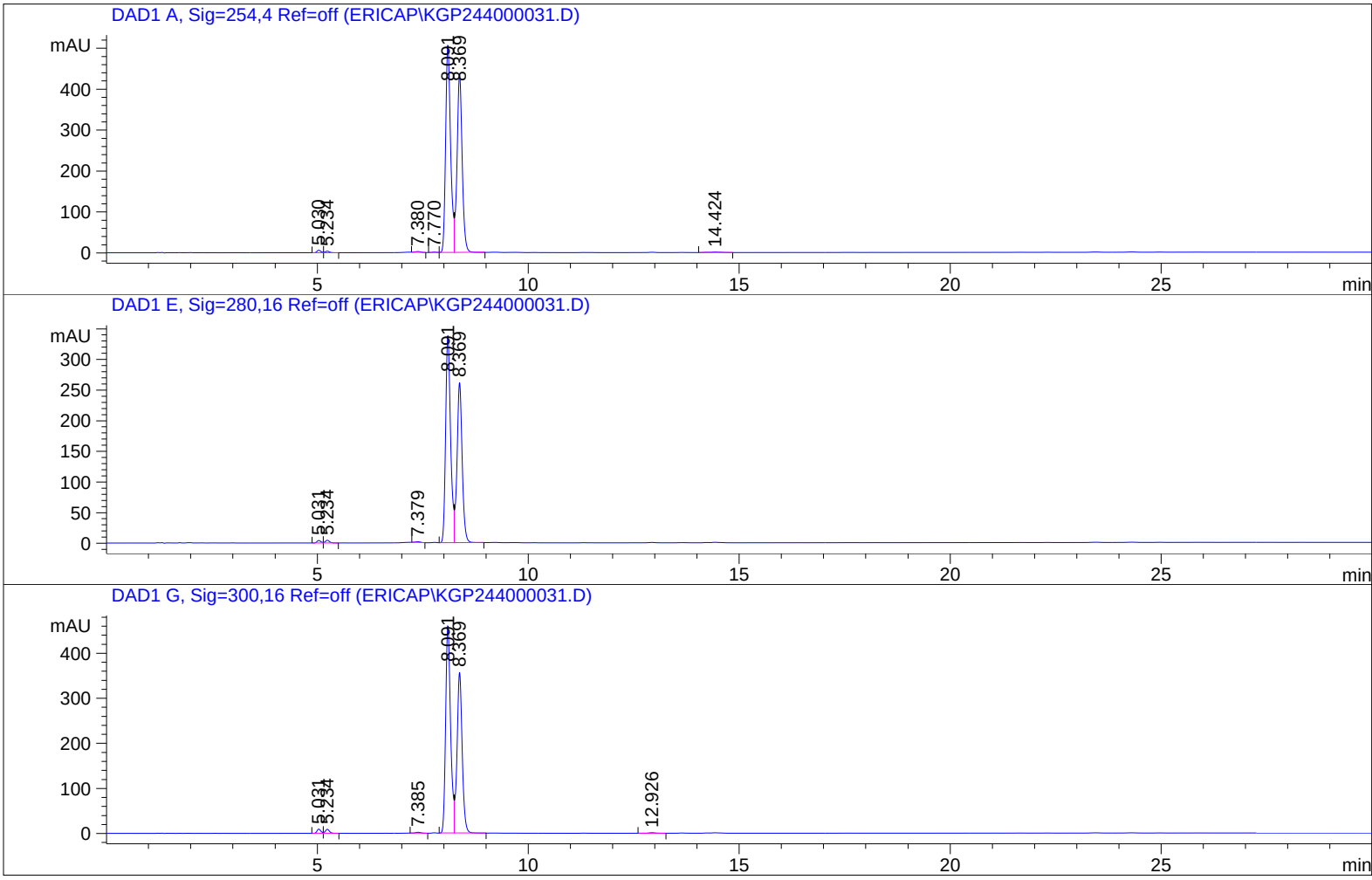
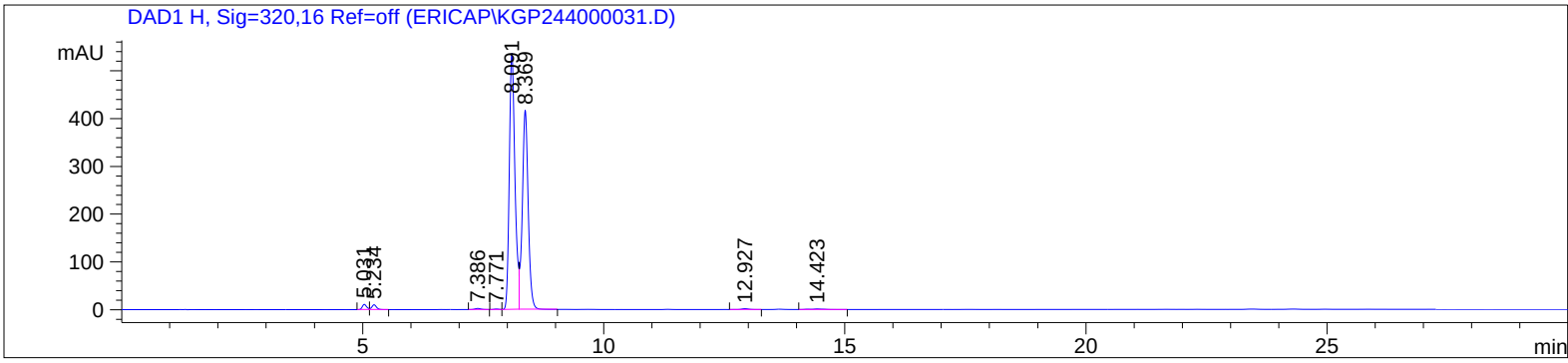
Two peaks observed in the HPLC traces are due to the presence of both E and Z geometrical isomers.



Data File C:\CHEM32\1\DATA\ERICAP\KGP244000031.D
Sample Name: KGP244

HPLC trace for Compound 8



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.030	BV	0.0973	39.87519	6.17963	0.5025
2	5.234	VB	0.1027	26.38915	3.81628	0.3326
3	7.380	BB	0.1266	14.92891	1.88135	0.1881
4	7.770	BV	0.1083	7.21967	1.04835	0.0910
5	8.091	VV	0.1233	4137.96680	506.67725	52.1481
6	8.369	VB	0.1284	3684.60937	436.77277	46.4348
7	14.424	BB	0.2493	24.03401	1.26687	0.3029

Totals : 7935.02311 957.64250

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.031	BV	0.0975	26.57289	4.10678	0.5277
2	5.234	VB	0.1015	30.19439	4.42914	0.5996
3	7.379	BB	0.1236	10.06317	1.28235	0.1998
4	8.091	VV	0.1231	2759.27563	338.43115	54.7979
5	8.369	VB	0.1286	2209.25806	261.37827	43.8748

Totals : 5035.36414 609.62768

Signal 3: DAD1 G, Sig=300,16 Ref=off

Data File C:\CHEM32\1\DATA\ERICAP\KGP244000031.D
Sample Name: KGP244

HPLC trace for Compound 8

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.031	BV	0.0969	60.33349	9.40099	0.8712
2	5.234	VB	0.1010	61.07416	9.01911	0.8819
3	7.385	BB	0.1292	15.99178	1.91966	0.2309
4	8.091	VV	0.1232	3757.75464	460.61365	54.2599
5	8.369	VB	0.1287	3018.68164	356.78674	43.5881
6	12.926	BB	0.1531	11.63206	1.13920	0.1680
Totals :				6925.46778	838.87935	

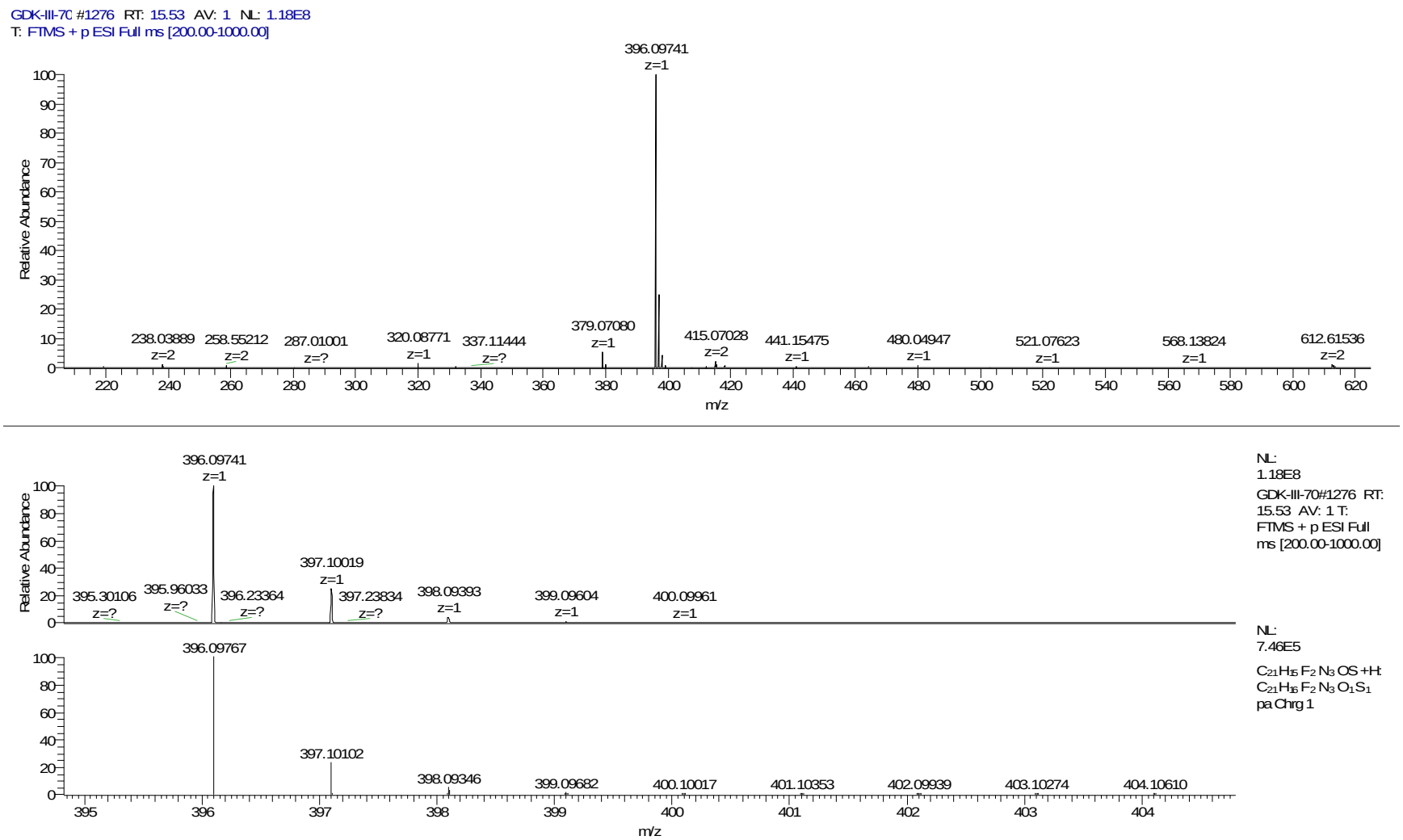
Signal 4: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.031	BV	0.0968	70.38661	10.97993	0.8671
2	5.234	VB	0.1010	68.74670	10.15010	0.8469
3	7.386	BB	0.1342	19.21360	2.23756	0.2367
4	7.771	BV	0.1095	7.10434	1.01688	0.0875
5	8.091	VV	0.1232	4382.60156	536.96875	53.9870
6	8.369	VB	0.1288	3529.76855	416.80865	43.4814
7	12.927	BB	0.1527	17.24854	1.72506	0.2125
8	14.423	BB	0.2519	22.81199	1.19943	0.2810
Totals :				8117.88189	981.08637	

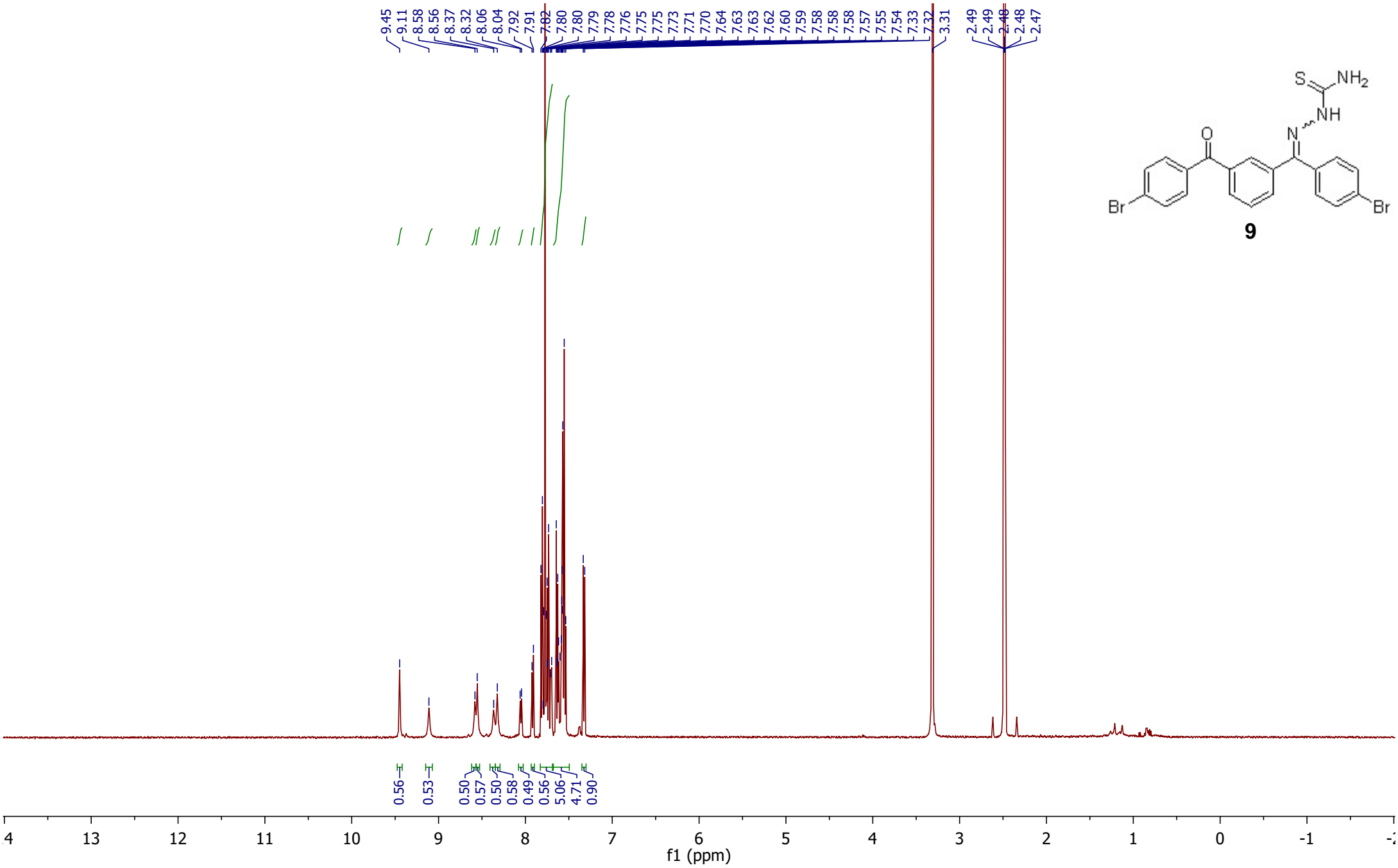
*** End of Report ***

HRMS (ESI) for Compound **8**

C:\Xcalibur\...\song\01-28-13\GDK-III-70 1/28/2013 8:31:55 PM

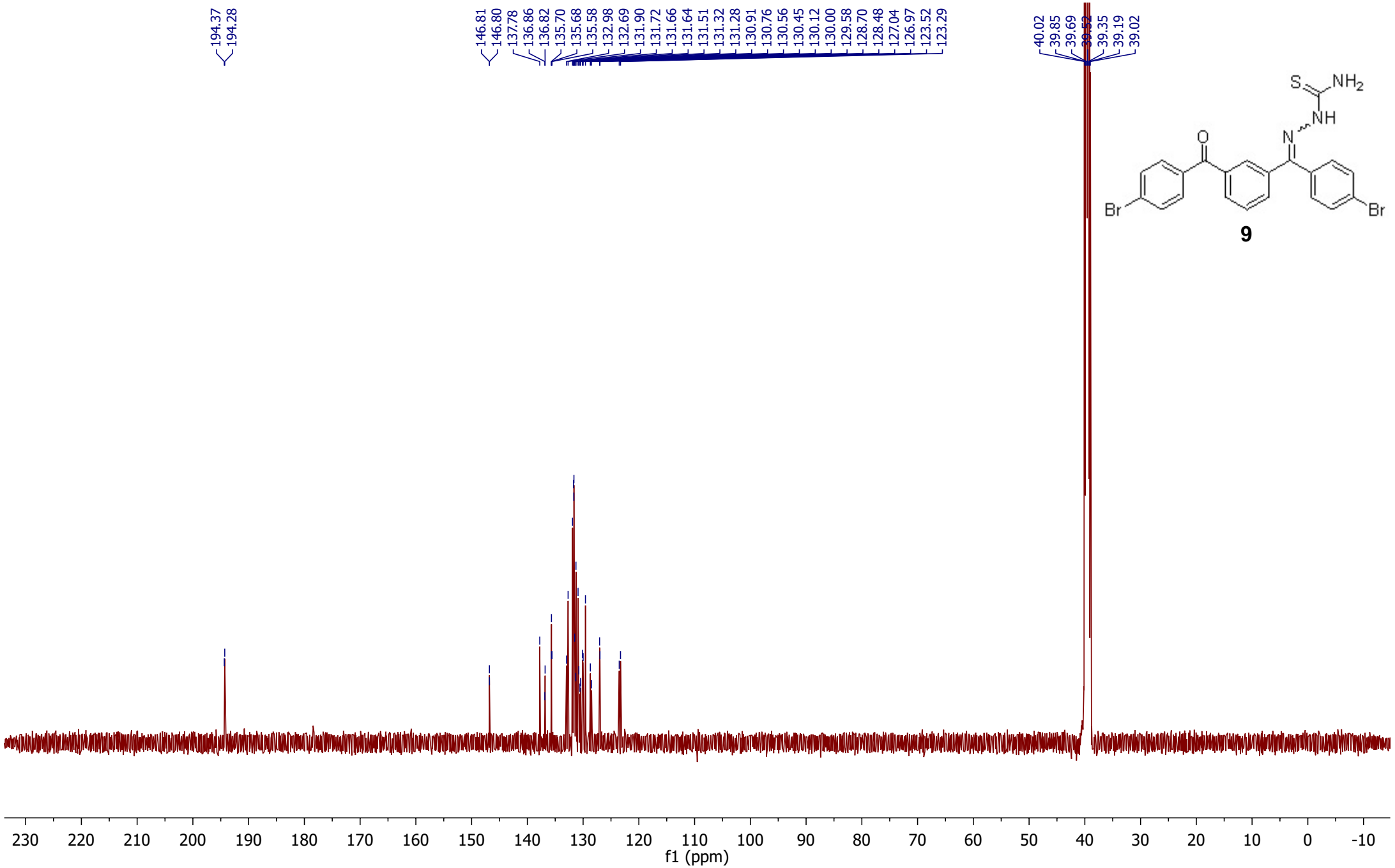


^{1}H NMR (500 MHz, DMSO-d_6) of Compound **9**



9

^{13}C NMR (125 MHz, DMSO-d_6) of Compound **9**



Data File C:\CHEM32\1\DATA\ERICAP\ENPIV59000030.D
Sample Name: ENPIV59

HPLC trace for Compound 9

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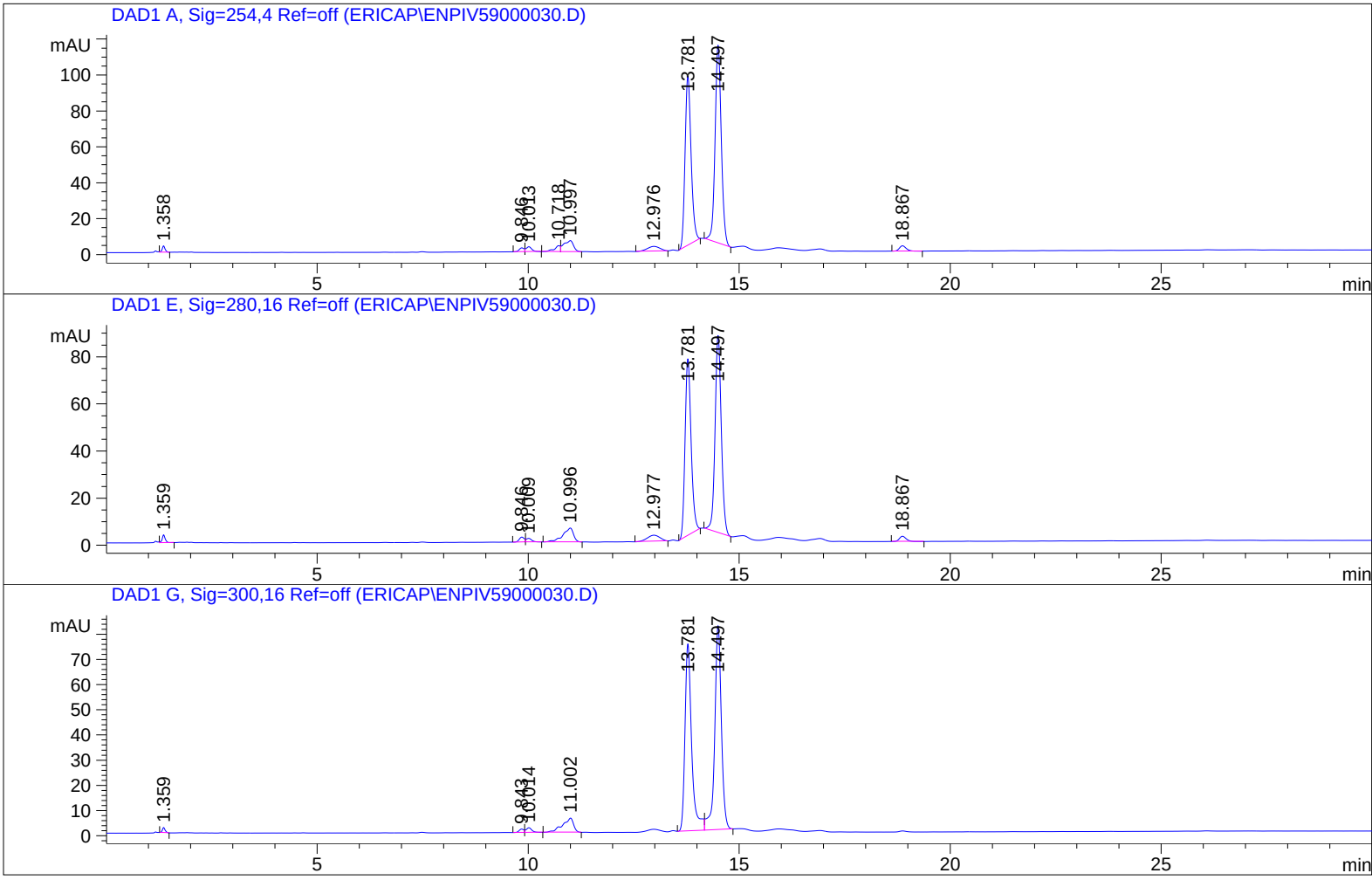
Acq. Operator   : ERICAP
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 5/6/2014 6:35:52 PM
Acq. Method     : C:\CHEM32\1\METHODS\GRAD 2 50-90 ACN.M
Last changed    : 5/6/2014 5:33:52 PM by ERICAP
Analysis Method : C:\CHEM32\1\DATA\ERICAP\ENPIV59000030.D\DA.M (GRAD 2 50-90 ACN.M)
Last changed    : 6/12/2014 9:28:34 PM by ERICAP
                  (modified after loading)
Sample Info     : ENP-IV-59

                  Method:

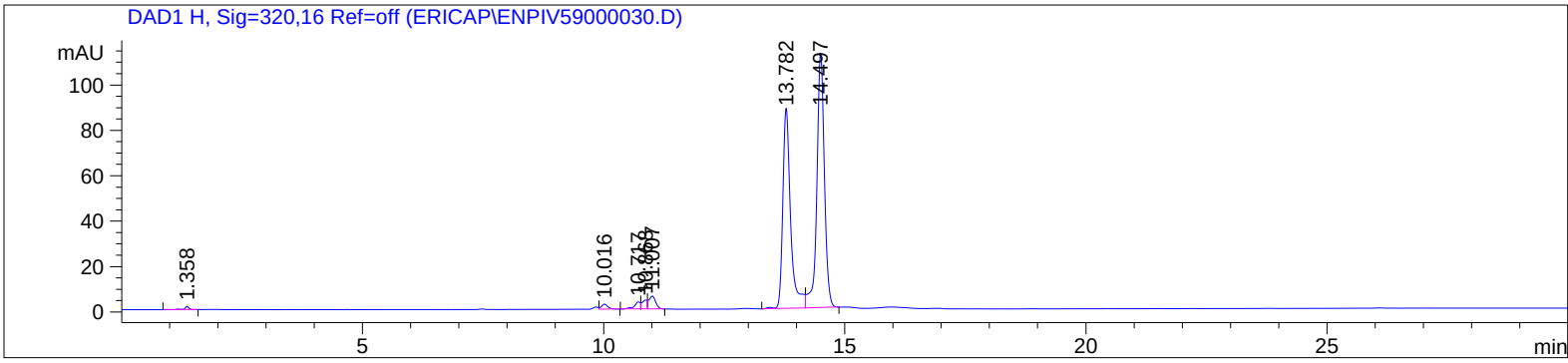
                  0-25 Min. 50:70 to 90:10 ACN:Water
                  25-30 min 90:10 ACN:Water
```

Two peaks observed in the HPLC traces are due to the presence of both E and Z geometrical isomers.



Data File C:\CHEM32\1\DATA\ERICAP\ENPIV59000030.D
Sample Name: ENPIV59

HPLC trace for Compound 9



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.358	VB	0.0737	17.79614	3.59831	0.7590
2	9.846	BV	0.1214	17.20547	2.14990	0.7338
3	10.013	VB	0.1370	25.15250	2.74306	1.0728
4	10.718	BV	0.1400	32.79762	3.29833	1.3988
5	10.997	VB	0.2147	95.89358	6.12182	4.0899
6	12.976	BB	0.3234	54.48132	2.63350	2.3236
7	13.781	BB	0.1541	939.08997	94.33542	40.0525
8	14.497	BB	0.1555	1129.07703	110.24906	48.1555
9	18.867	BB	0.1709	33.15601	2.95592	1.4141
Totals :				2344.64962	228.08533	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.359	VB	0.0720	16.53173	3.32318	0.9008
2	9.846	BV	0.1298	17.96309	2.10092	0.9788
3	10.009	VB	0.1283	13.53448	1.54282	0.7375
4	10.996	BB	0.2358	103.06053	5.90035	5.6157
5	12.977	BB	0.3234	54.22454	2.59896	2.9547
6	13.781	BB	0.1538	745.04364	75.03146	40.5972
7	14.497	BB	0.1558	860.08588	83.73415	46.8659
8	18.867	BB	0.1723	24.76358	2.21701	1.3494
Totals :				1835.20747	176.44885	

HPLC trace for Compound 9

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.359	BB	0.0673	9.28621	2.03340	0.5024
2	9.843	BV	0.1200	10.68927	1.35568	0.5783
3	10.014	VB	0.1362	16.94087	1.86086	0.9166
4	11.002	BB	0.2427	102.95238	5.64647	5.5701
5	13.781	BV	0.1664	817.20447	74.26231	44.2138
6	14.497	VB	0.1644	891.22760	80.97018	48.2188
Totals :				1848.30080	166.12891	

Signal 4: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.358	BB	0.0889	8.99925	1.43979	0.3819
2	10.016	VB	0.1354	19.91768	2.20501	0.8451
3	10.717	BV	0.1311	28.69333	3.12627	1.2175
4	10.868	VV	0.1065	28.48808	3.93471	1.2088
5	11.007	VB	0.1456	55.55571	5.70562	2.3573
6	13.782	BV	0.1695	994.26270	88.20777	42.1881
7	14.497	VB	0.1631	1220.81995	112.07932	51.8013
Totals :				2356.73668	216.69849	

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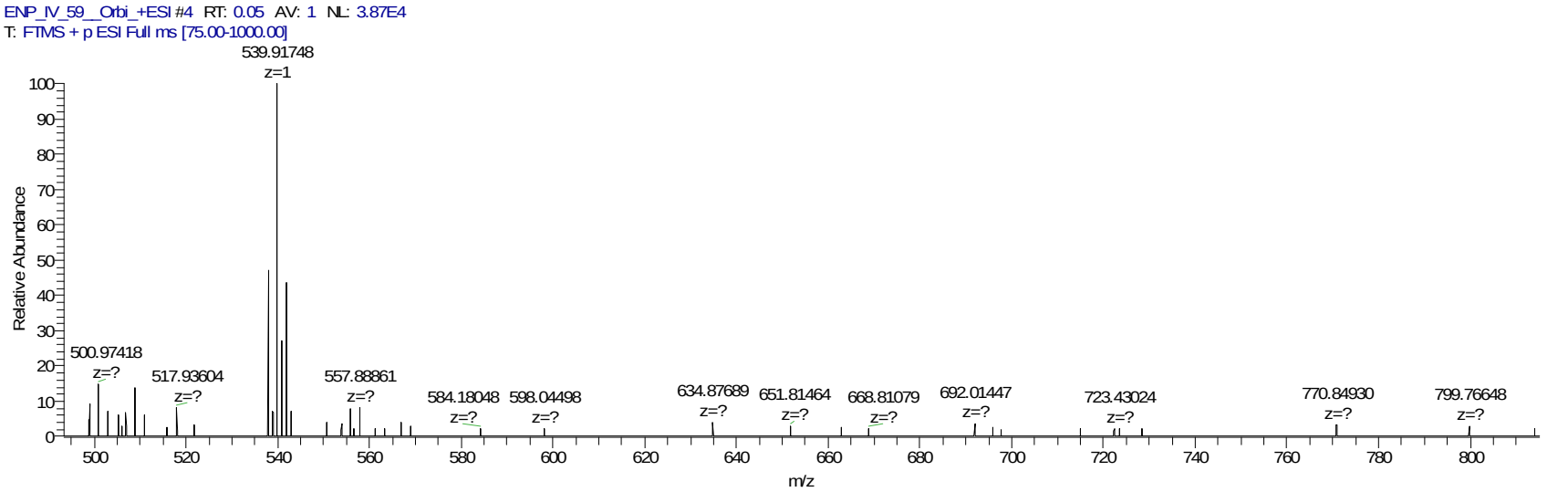
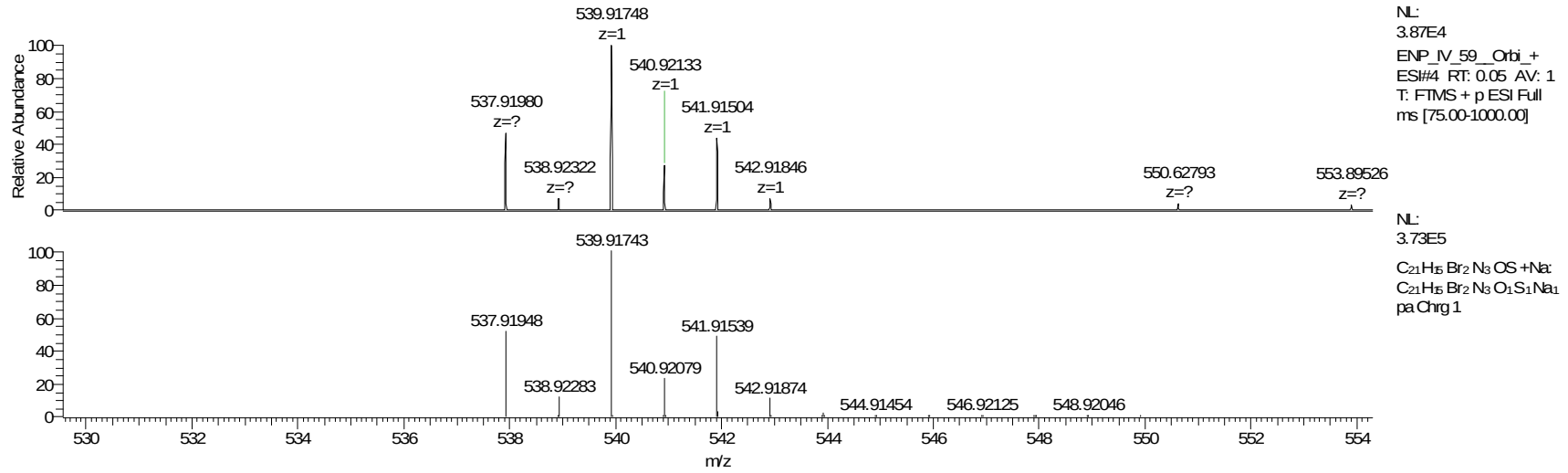
*** End of Report ***

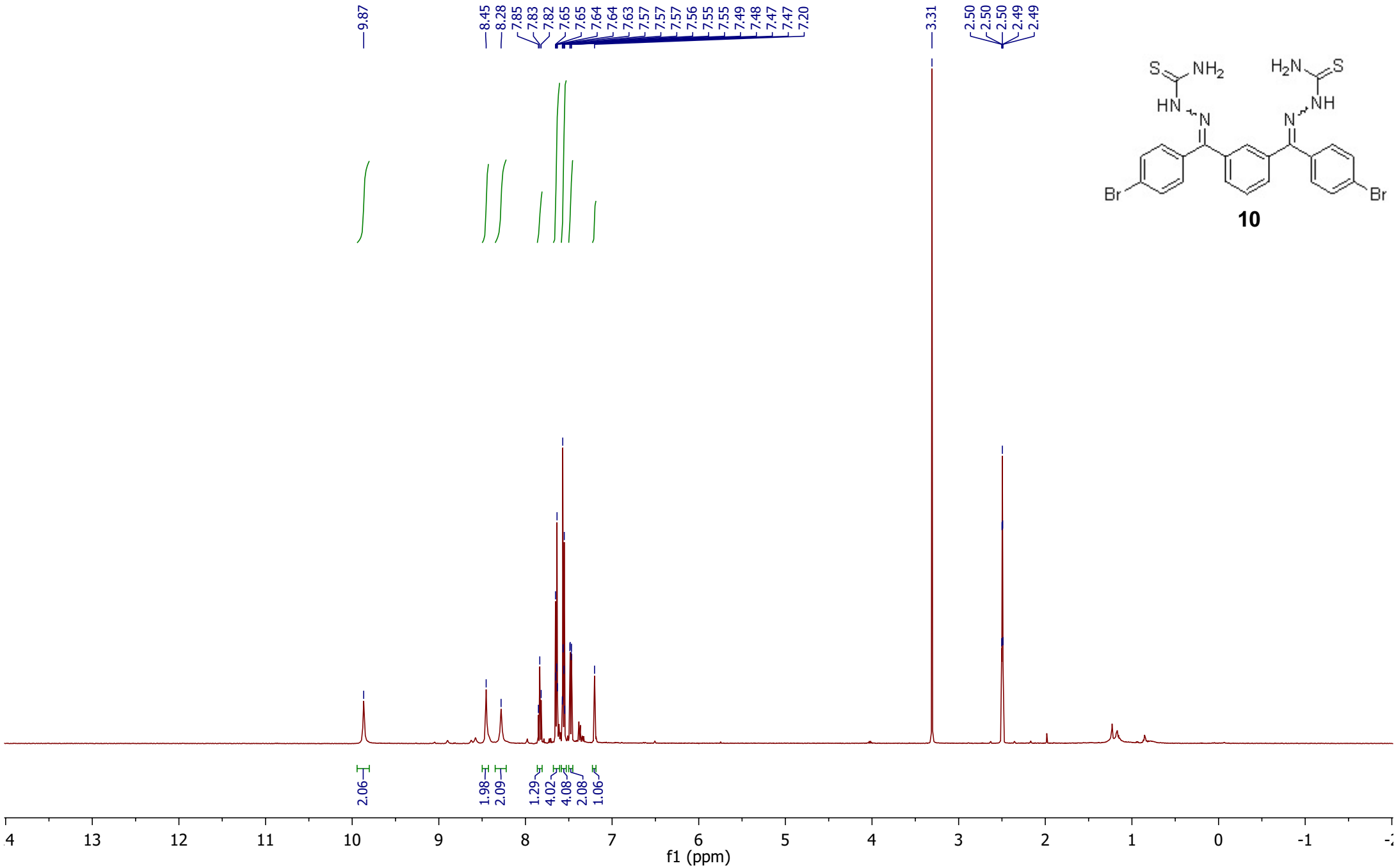
HRMS(ESI) for Compound **9**

C:\Xcalibur\...\ENP_IV_59__Orbi_+ESI 1/13/2015 4:48:56 PM



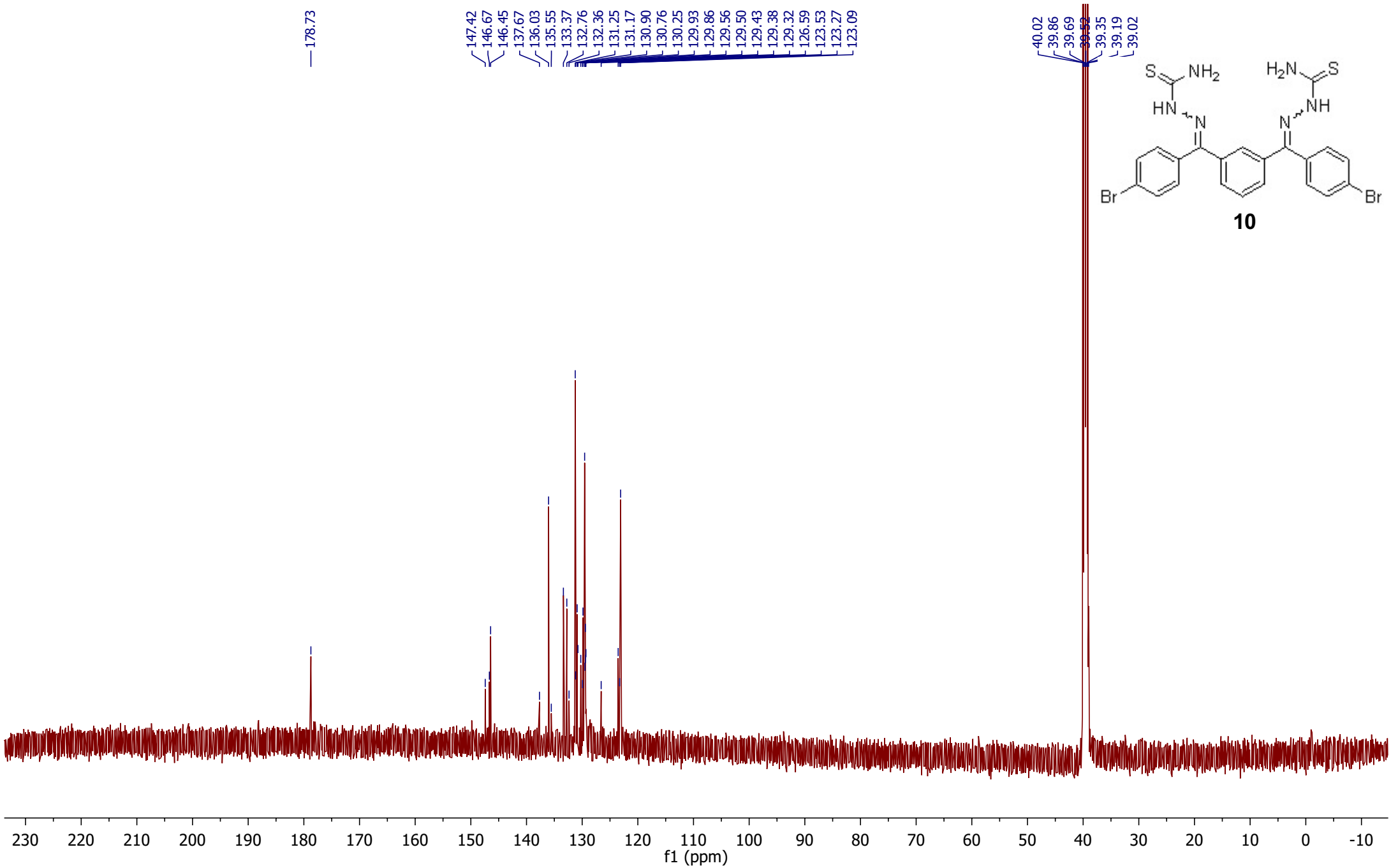


^{1}H NMR (500 MHz, DMSO-d_6) of Compound **10**



10

^{1}H NMR (500 MHz, DMSO-d_6) of Compound **10**



Data File C:\CHEM32\1\DATA\ERICAP_ARL_I_010R0103.D
Sample Name: _ARL_I_010R

HPLC trace for Compound 10

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Acq. Instrument : Instrument 1                    Location :   -
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Acq. Method     : C:\CHEM32\1\METHODS\GRAD 2 50-90 ACN.M
Last changed    : 2/5/2015 2:49:15 AM by ERICAP
Analysis Method : C:\CHEM32\1\DATA\ERICAP\_ARL_I_010R0103.D\DA.M (GRAD 2 50-90 ACN.M)
Last changed    : 2/5/2015 3:32:22 AM by ERICAP
                  (modified after loading)
Sample Info     : _ARL_I_010R
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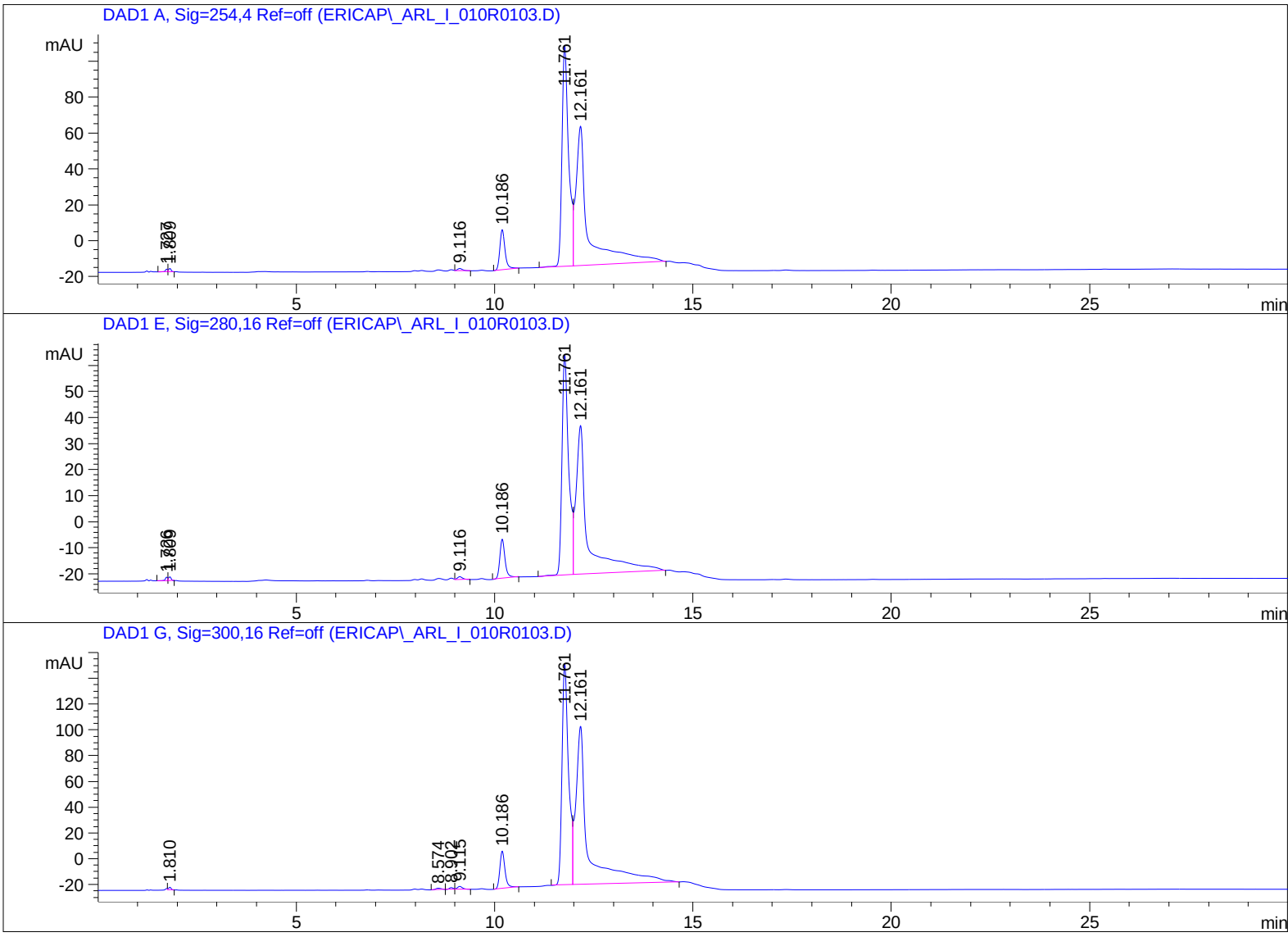
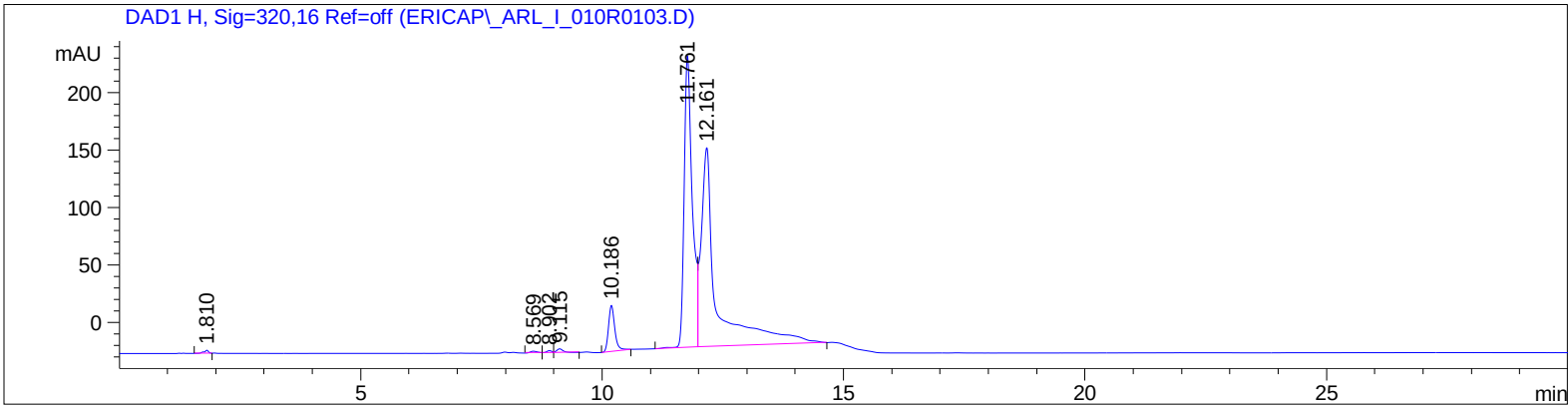
Three peaks observed in the HPLC traces are due to the presence of three E/Z geometrical isomers.



Data File C:\CHEM32\1\DATA\ERICAP_ARL_I_010R0103.D
Sample Name: _ARL_I_010R

HPLC trace for Compound 10



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.727	BV	0.0629	6.21257	1.48276	0.1843
2	1.809	VB	0.0680	8.21576	1.84343	0.2438
3	9.116	VB	0.1431	13.38051	1.38070	0.3970
4	10.186	BB	0.1378	202.40236	22.31227	6.0051
5	11.761	BV	0.1731	1442.30054	122.77618	42.7918
6	12.161	VB	0.2975	1697.99292	77.54384	50.3780
Totals :				3370.50466	227.33917	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.726	BV	0.0636	5.77921	1.35939	0.2432
2	1.809	VB	0.0678	6.50234	1.46422	0.2736
3	9.116	VB	0.1414	10.82703	1.13434	0.4556
4	10.186	BB	0.1387	138.05728	15.08823	5.8100
5	11.761	BV	0.1734	995.59772	84.54379	41.8990
6	12.161	VB	0.2911	1219.42065	57.10430	51.3184
Totals :				2376.18423	160.69428	

HPLC trace for Compound 10

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.810	VB	0.0700	10.04898	2.17284	0.2007
2	8.574	BV	0.1697	12.81582	1.20885	0.2560
3	8.902	VV	0.1208	11.98277	1.50651	0.2393
4	9.115	VB	0.1402	22.26705	2.35807	0.4447
5	10.186	BB	0.1376	262.58127	28.99889	5.2442
6	11.761	BV	0.1725	2008.22327	171.65239	40.1079
7	12.161	VB	0.2963	2679.13525	122.92649	53.5072
Totals :				5007.05441	330.82403	

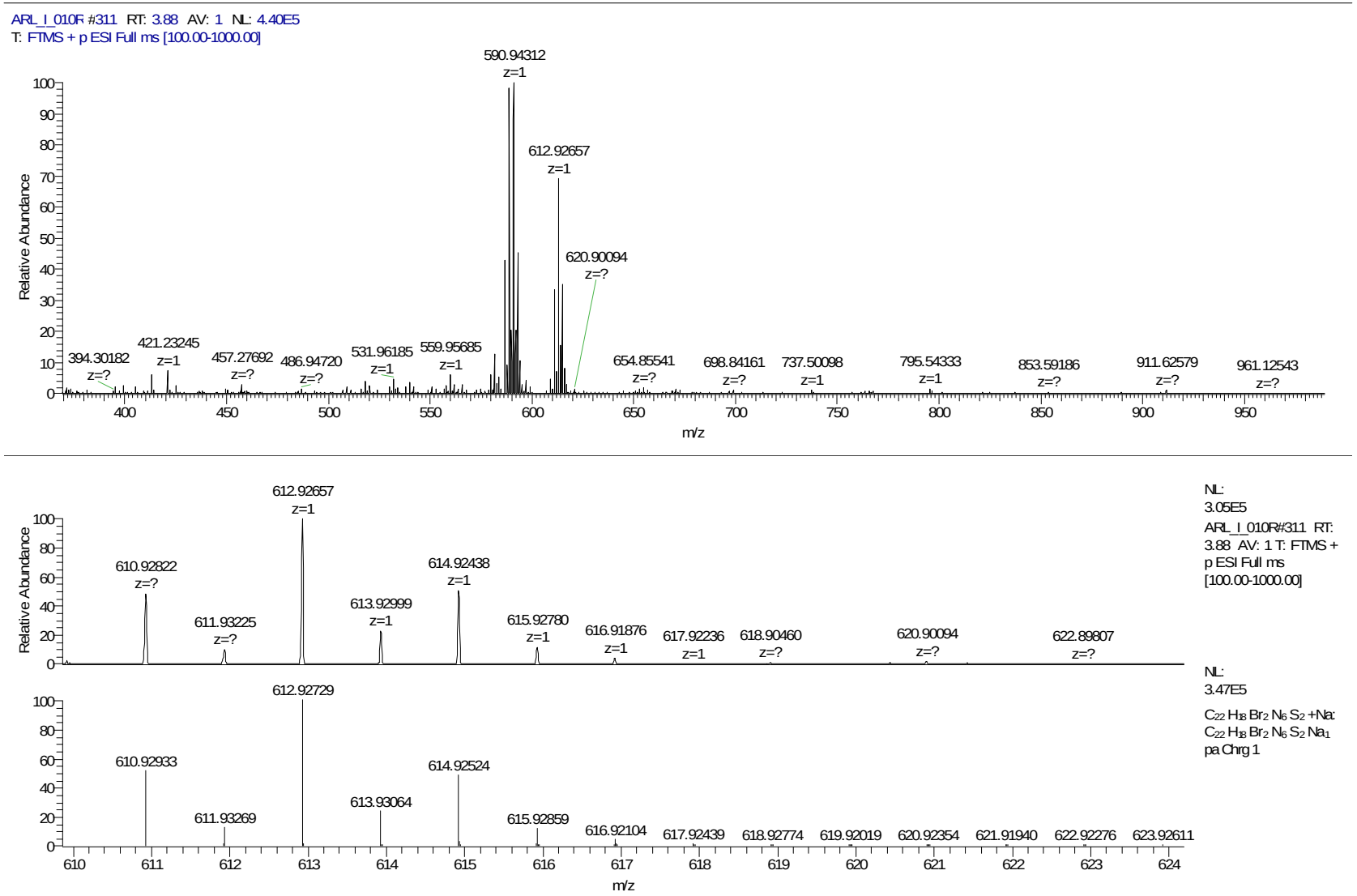
Signal 4: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.810	BB	0.0895	16.34881	2.59416	0.2232
2	8.569	BV	0.1562	15.61079	1.51521	0.2131
3	8.902	VV	0.1207	14.34423	1.80600	0.1959
4	9.115	VB	0.1421	31.51148	3.27852	0.4302
5	10.186	BB	0.1370	360.24457	40.02496	4.9187
6	11.761	BV	0.1734	2993.03223	254.07591	40.8661
7	12.161	VB	0.3038	3892.90820	173.50217	53.1528
Totals :				7324.00031	476.79692	

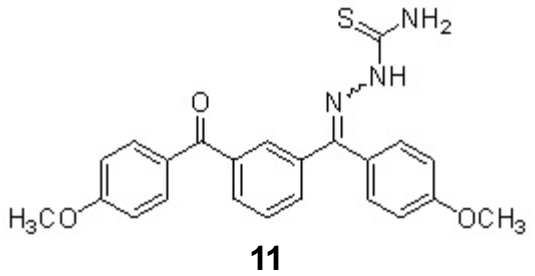
*** End of Report ***

HRMS(ESI) for Compound **10**

C:\Xcalibur\...\01-02-2015\ARL_I_010R 1/2/2015 10:39:16 PM

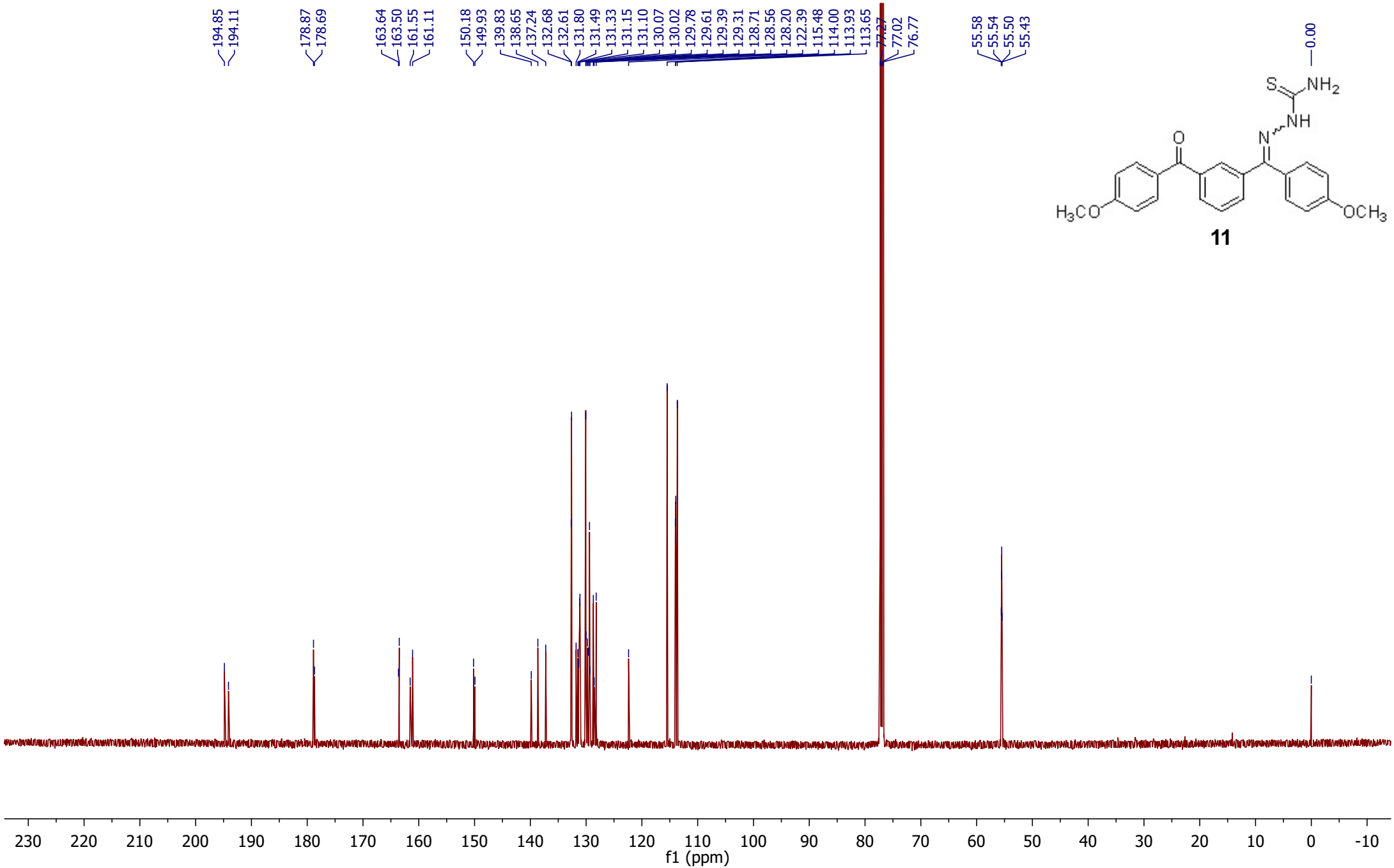


^{1}H NMR (500 MHz, $CDCl_3$) of Compound **11**



11

^{13}C NMR (125 MHz, $CDCl_3$) of Compound **11**



Data File C:\CHEM32\1\DATA\ERICAP\ENPV89000001.D
Sample Name: ENPV89

HPLC trace for Compound 11

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Acq. Operator   : ERICAP
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 8/12/2014 11:35:22 PM
Acq. Method     : C:\CHEM32\1\METHODS\GRAD 2 50-90 ACN.M
Last changed    : 8/12/2014 11:15:45 PM by ERICAP
Analysis Method : C:\CHEM32\1\DATA\ERICAP\ENPV89000001.D\DA.M (GRAD 2 50-90 ACN.M)
Last changed    : 12/22/2014 11:54:51 PM by ERICAP
                  (modified after loading)
Sample Info     : ENP-V-89

                  Method:

                  0-25 min. gradient 50:50 to 10:90 Water:ACN
                  25-30 min 10:90 Water:ACN
```
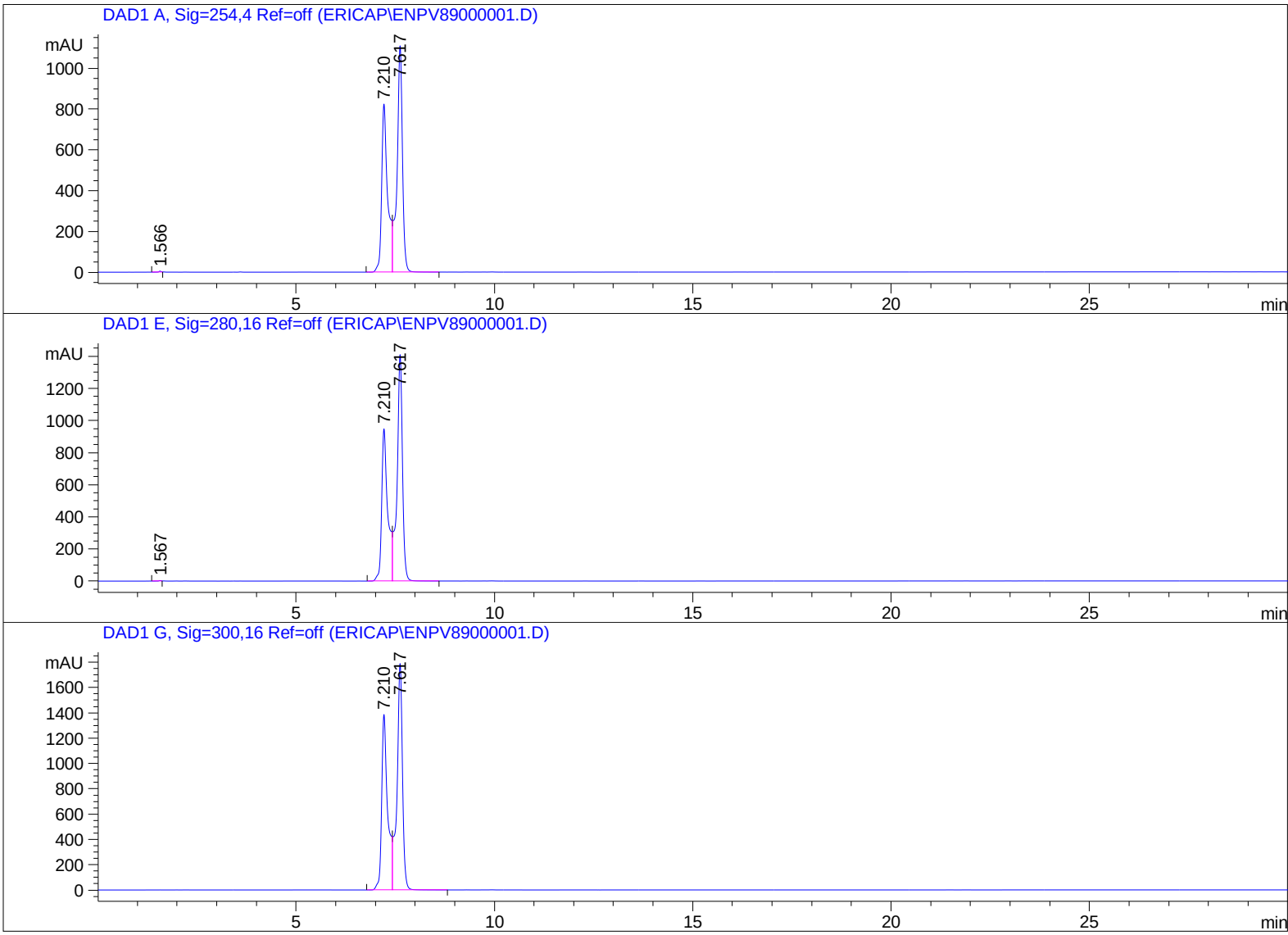
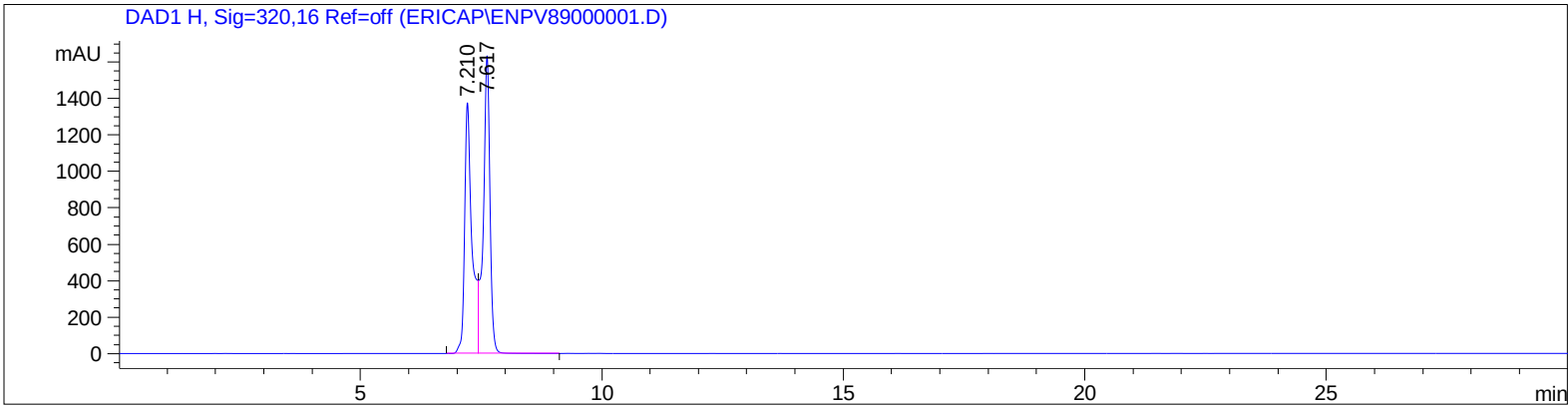

Two peaks observed in the HPLC traces are due to the presence of both E and Z geometrical isomers.



Data File C:\CHEM32\1\DATA\ERICAP\ENPV89000001.D
Sample Name: ENPV89

HPLC trace for Compound 11



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.566	BV	0.0609	20.04630	4.98794	0.1041
2	7.210	BV	0.1493	8726.91504	825.43494	45.3176
3	7.617	VB	0.1383	1.05103e4	1111.56714	54.5783
Totals :				1.92572e4	1941.99002	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.567	BV	0.0616	12.16926	2.98251	0.0520
2	7.210	BV	0.1515	1.00376e4	948.42145	42.8540
3	7.617	VB	0.1386	1.33730e4	1411.17322	57.0941
Totals :				2.34227e4	2362.57718	

HPLC trace for Compound 11

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.210	BV	0.1515	1.46958e4	1388.21680	46.2547
2	7.617	VB	0.1392	1.70757e4	1790.73413	53.7453
Totals :				3.17715e4	3178.95093	

Signal 4: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.210	BV	0.1534	1.45694e4	1377.45435	48.2465
2	7.617	VB	0.1395	1.56285e4	1635.54553	51.7535
Totals :				3.01979e4	3012.99988	

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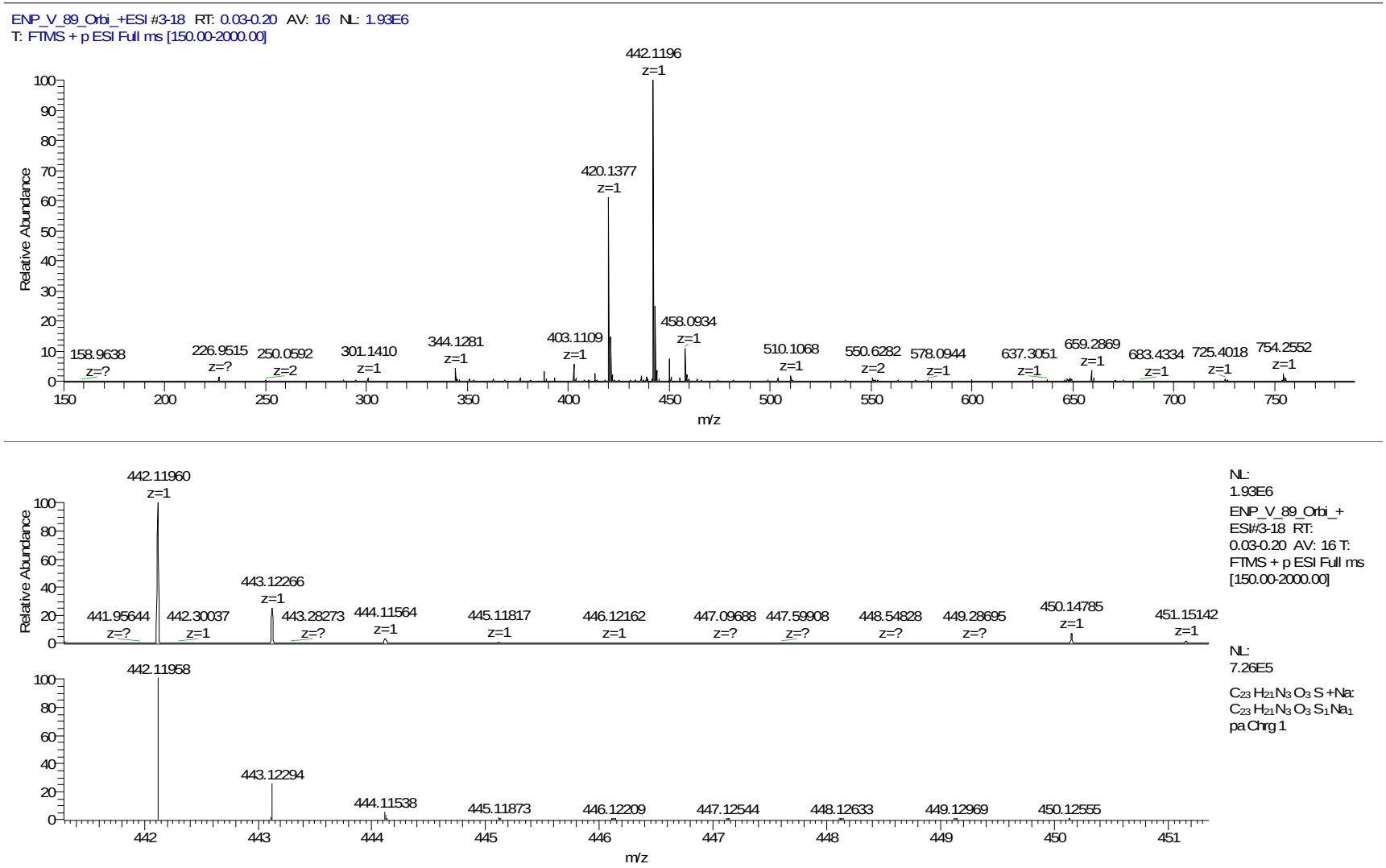
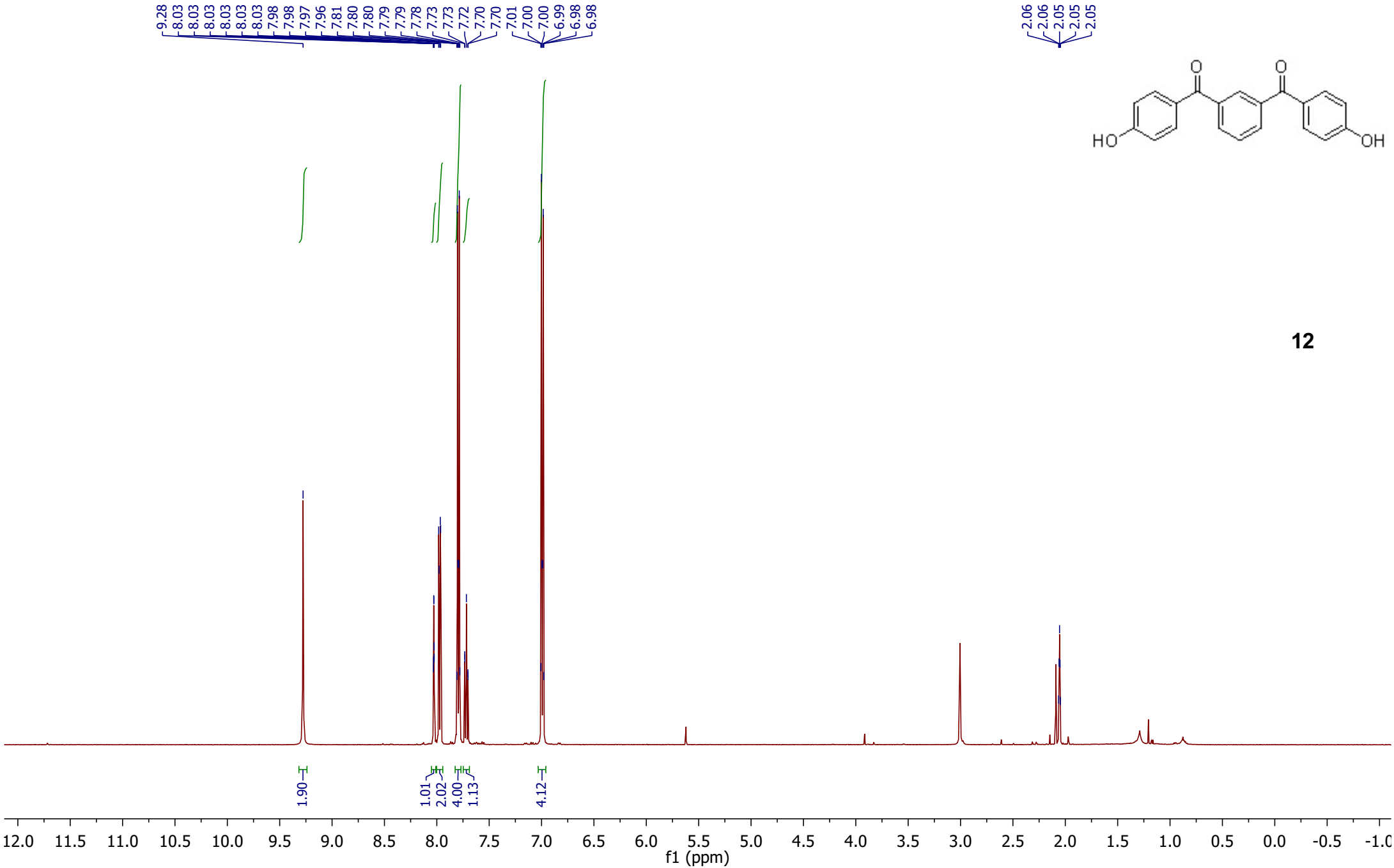
*** End of Report ***

HRMS (ESI) for Compound **11**

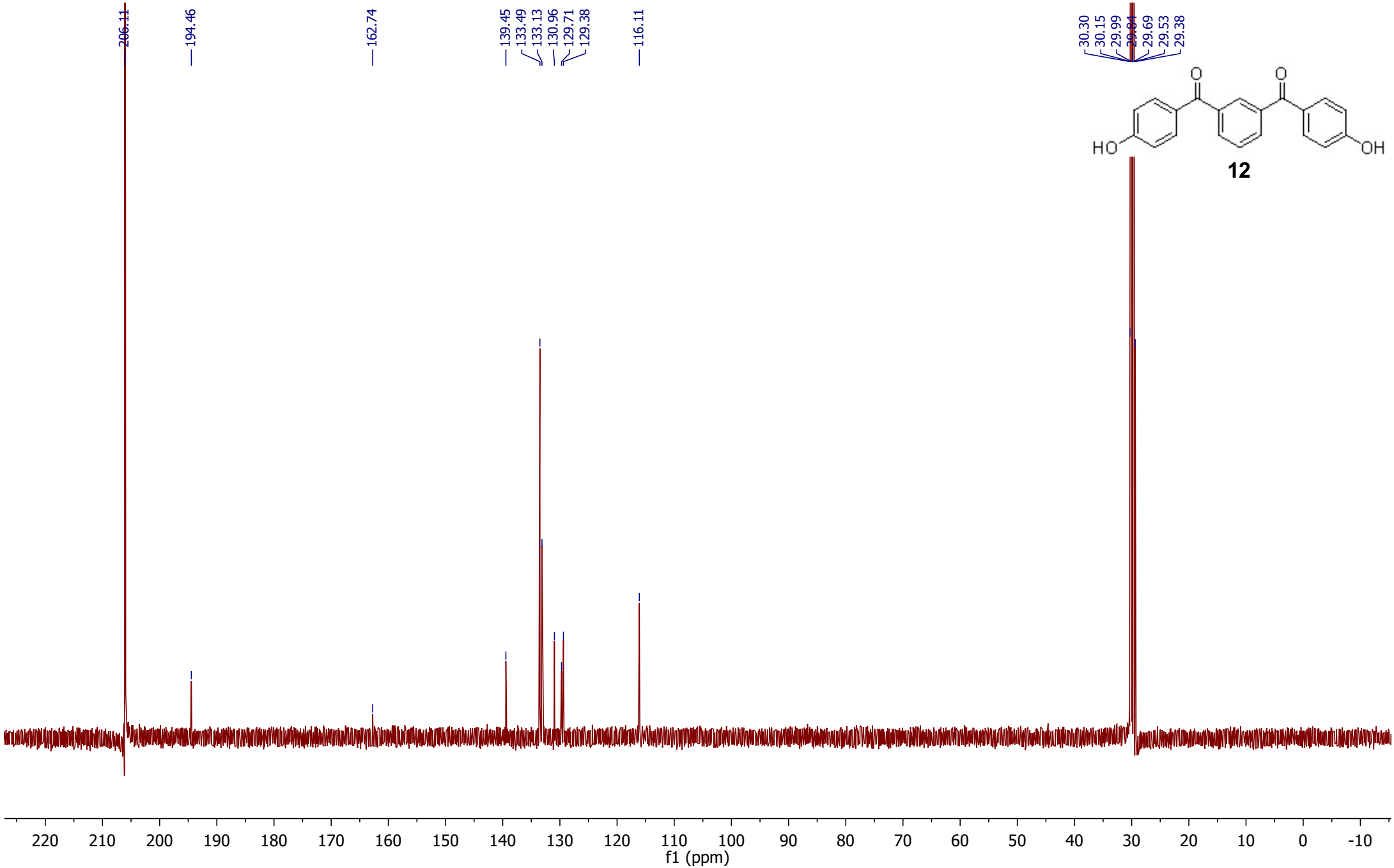
C:\Xcalibur\...\ENP_V_89_Orbi_+ESI 8/18/2014 3:17:46 PM



^{1}H NMR (500 MHz, Acetone-d_6) of Compound **12**

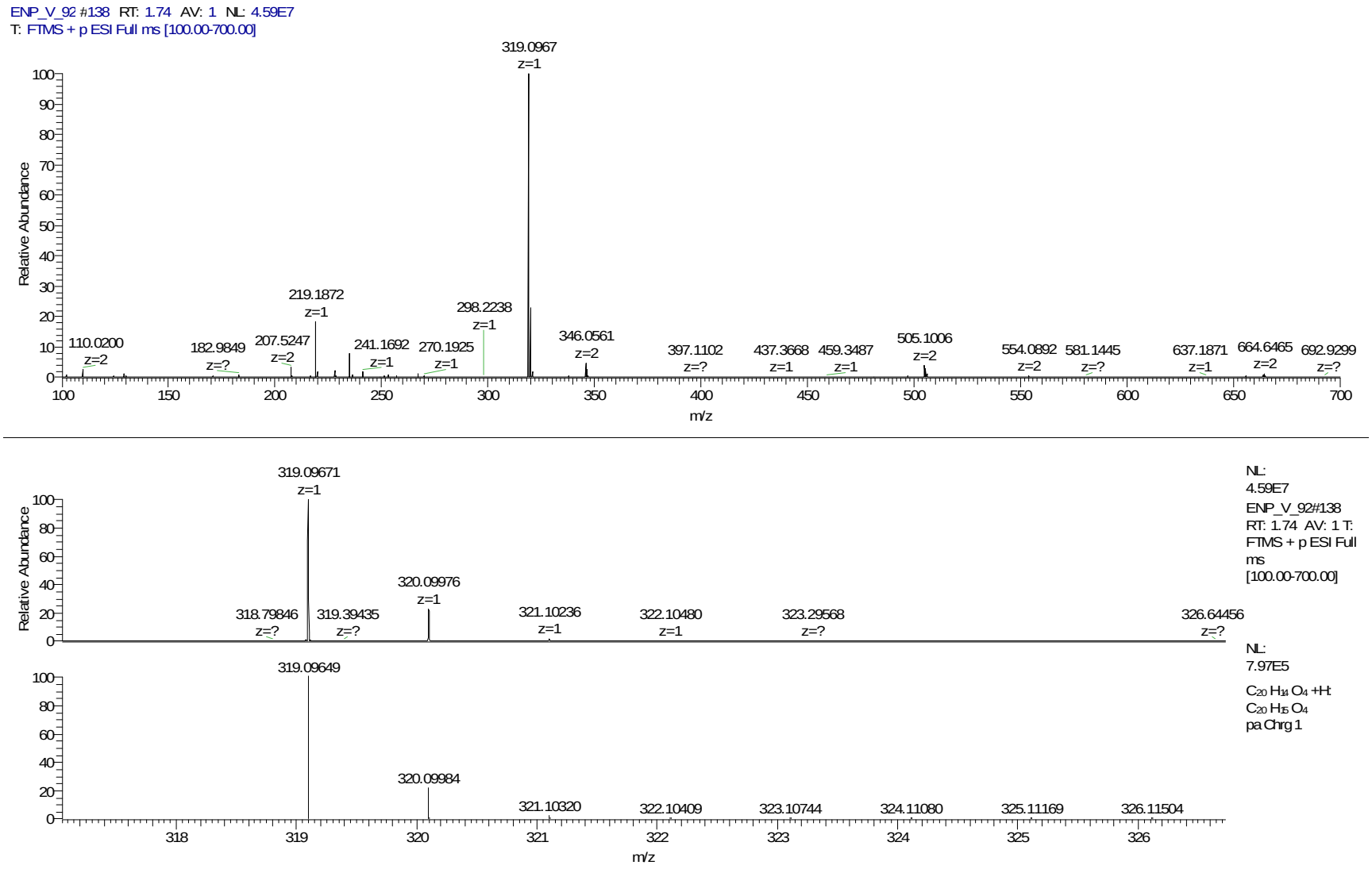


^{13}C NMR (125 MHz, Acetone-d_6) of Compound **12**

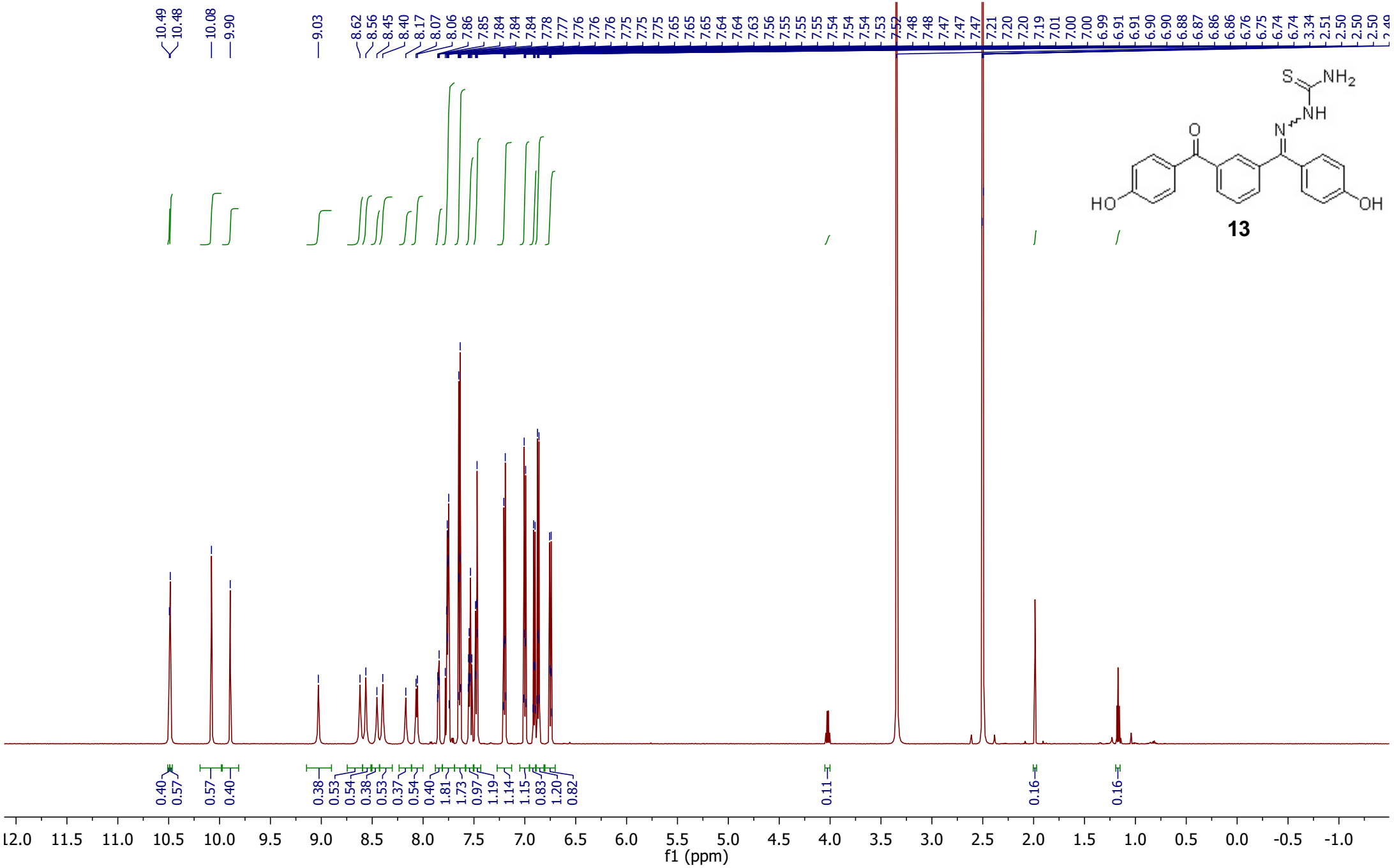


HRMS (ESI) for Compound **12**

C:\Xcalibur\...\Erica\12-19-14\ENP_V_92 12/19/2014 9:55:22 AM

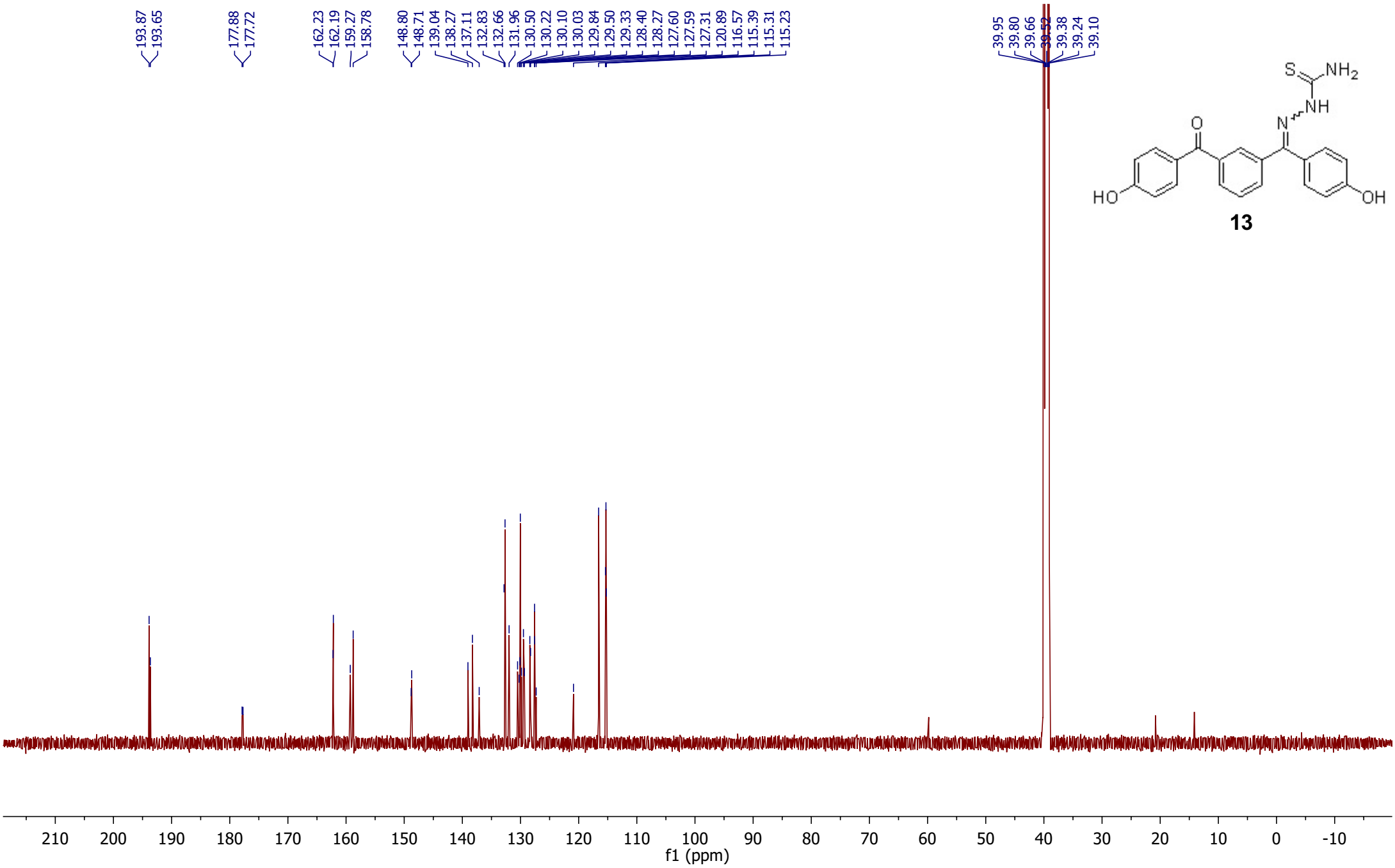


^{1}H NMR (600 MHz, DMSO-d$_6$) of Compound **13**



13

^{13}C NMR (150 MHz, DMSO-d_6) of Compound **13**



Data File C:\CHEM32\1\DATA\ERICA P\ENPV94NOLYO0002.D
Sample Name: ENPV94nolyo

HPLC trace for Compound 13

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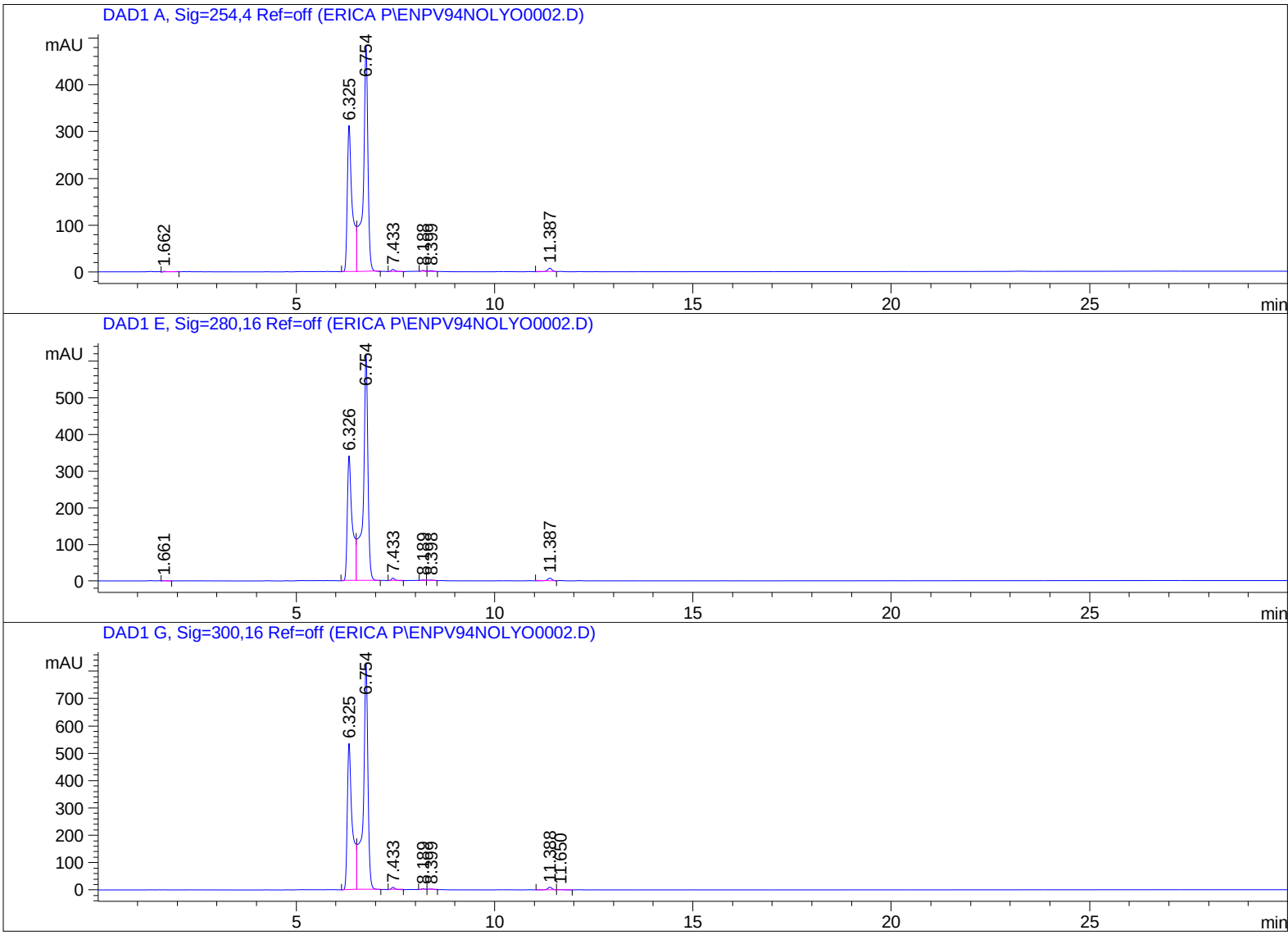
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 12/4/2014 4:20:38 PM
Acq. Method     : C:\CHEM32\1\METHODS\GRAD 2 30-90 ACN.M
Last changed    : 12/4/2014 3:31:16 PM by ERICA P
Analysis Method : C:\CHEM32\1\DATA\ERICA P\ENPV94NOLYO0002.D\DA.M (GRAD 2 30-90 ACN.M)
Last changed    : 12/23/2014 12:09:10 AM by ERICAP
                  (modified after loading)
Sample Info     : ENPV94 nolyo

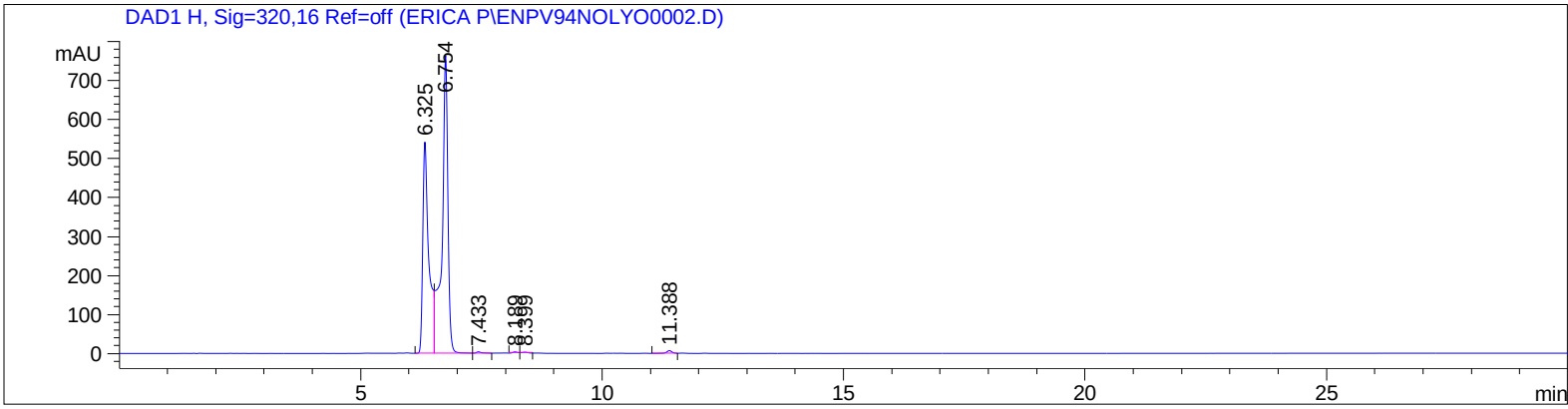
                  Method:

                  0-25 min gradient ACN:Water 30:70 to 90:10
                  25-30 min ACN:Water 90:10
```

Two peaks observed in the HPLC traces are due to the presence of both E and Z geometrical isomers.



HPLC trace for Compound 13



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.662	BB	0.1258	15.86365	1.71752	0.2278
2	6.325	BV	0.1255	2772.37378	312.63953	39.8080
3	6.754	VB	0.1202	4058.80469	482.32565	58.2796
4	7.433	BB	0.0965	29.68061	4.64805	0.4262
5	8.188	BV	0.0975	13.42526	2.07389	0.1928
6	8.399	VB	0.1220	13.41390	1.63097	0.1926
7	11.387	BV	0.1181	60.80157	7.69954	0.8730
Totals :				6964.36345	812.73515	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.661	BB	0.0896	6.79549	1.10736	0.0814
2	6.326	BV	0.1251	3019.75562	341.58194	36.1853
3	6.754	VV	0.1201	5190.49023	617.19513	62.1968
4	7.433	BB	0.0948	42.22719	6.76395	0.5060
5	8.189	BV	0.0945	11.95339	1.87082	0.1432
6	8.398	VB	0.1213	13.18598	1.61438	0.1580
7	11.387	BV	0.1192	60.85531	7.62100	0.7292

HPLC trace for Compound 13

Totals : 8345.26322 977.75458

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.325	BV	0.1255	4755.72754	535.93927	39.9371
2	6.754	VB	0.1203	6972.91406	827.21509	58.5563
3	7.433	BB	0.0962	53.62053	8.42650	0.4503
4	8.189	BV	0.1007	19.17342	2.91529	0.1610
5	8.399	VB	0.1228	19.43227	2.34274	0.1632
6	11.388	BV	0.1186	77.60942	9.78288	0.6517
7	11.650	VB	0.1436	9.57091	1.01840	0.0804

Totals : 1.19080e4 1387.64017

Signal 4: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.325	BV	0.1258	4831.85156	542.90118	42.3136
2	6.754	VV	0.1209	6468.16846	763.32953	56.6432
3	7.433	VB	0.1059	24.17973	3.36286	0.2117
4	8.189	BV	0.1030	20.42628	3.01716	0.1789
5	8.399	VB	0.1246	19.15187	2.26725	0.1677
6	11.388	BV	0.1186	55.37372	6.97799	0.4849

Totals : 1.14192e4 1321.85598

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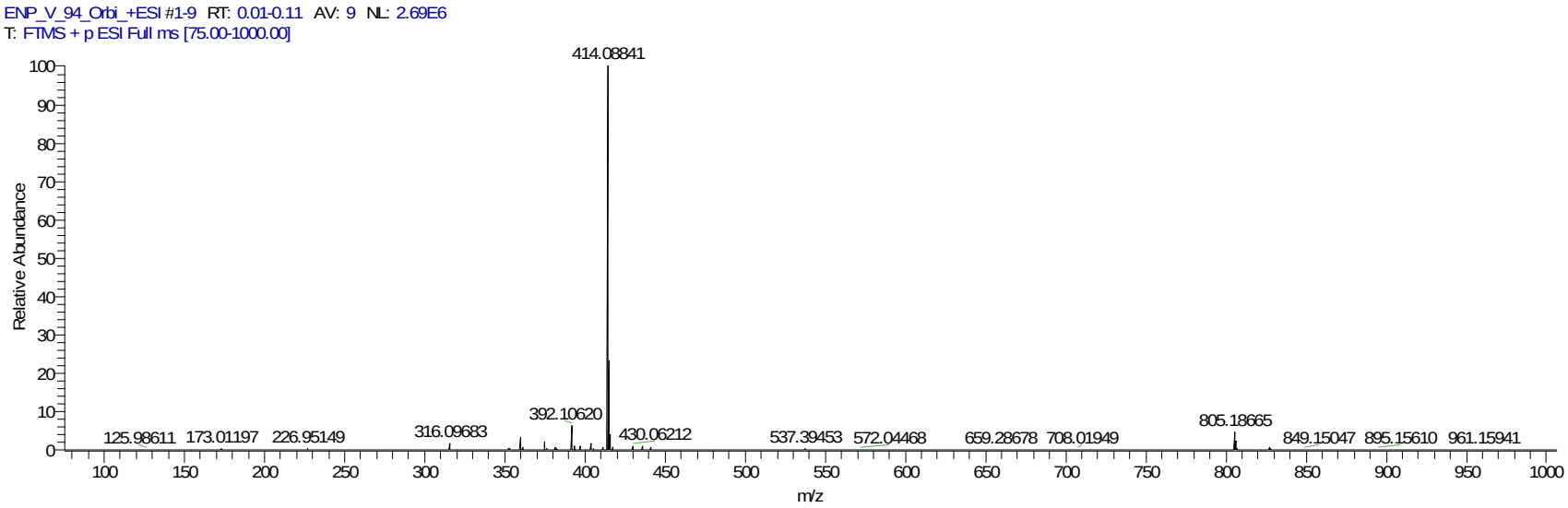
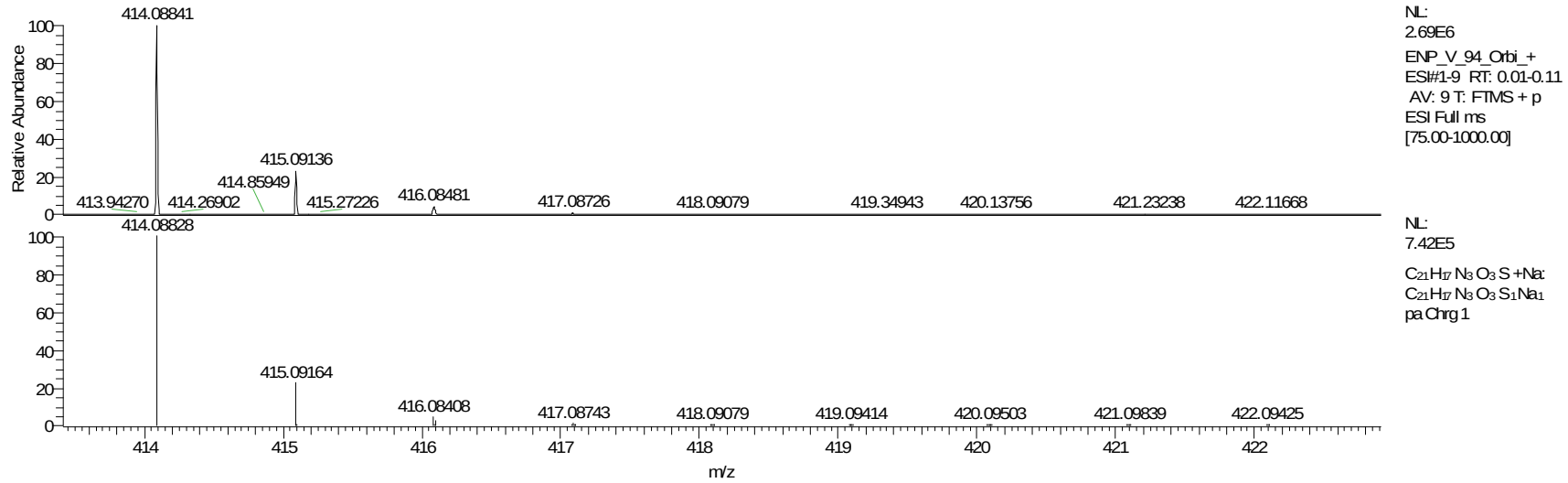
*** End of Report ***

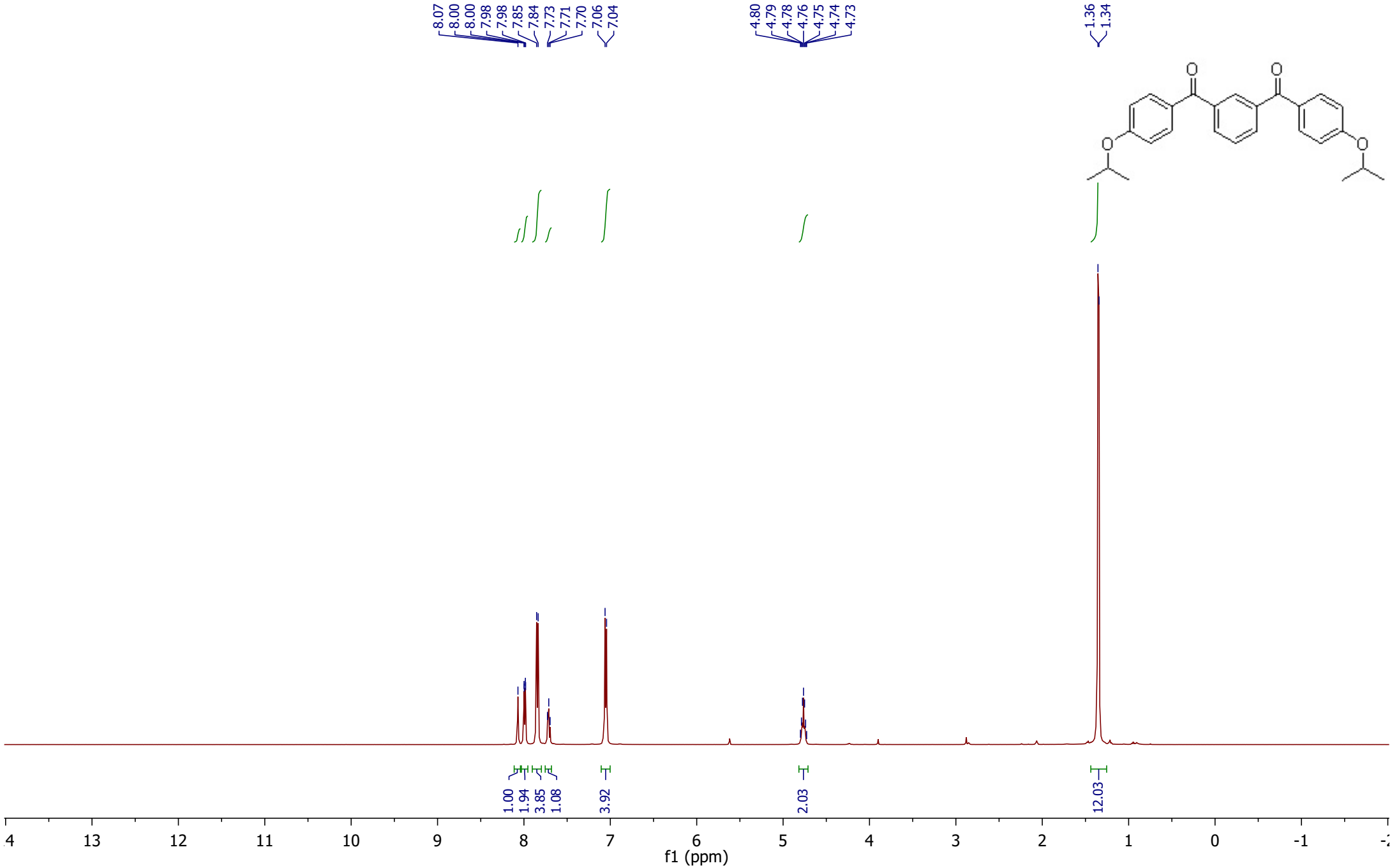
HRMS(ESI) for Compound **13**

C:\Xcalibur\...\ENP_V_94_Orbi_+ESI 1/13/2015 5:05:20 PM

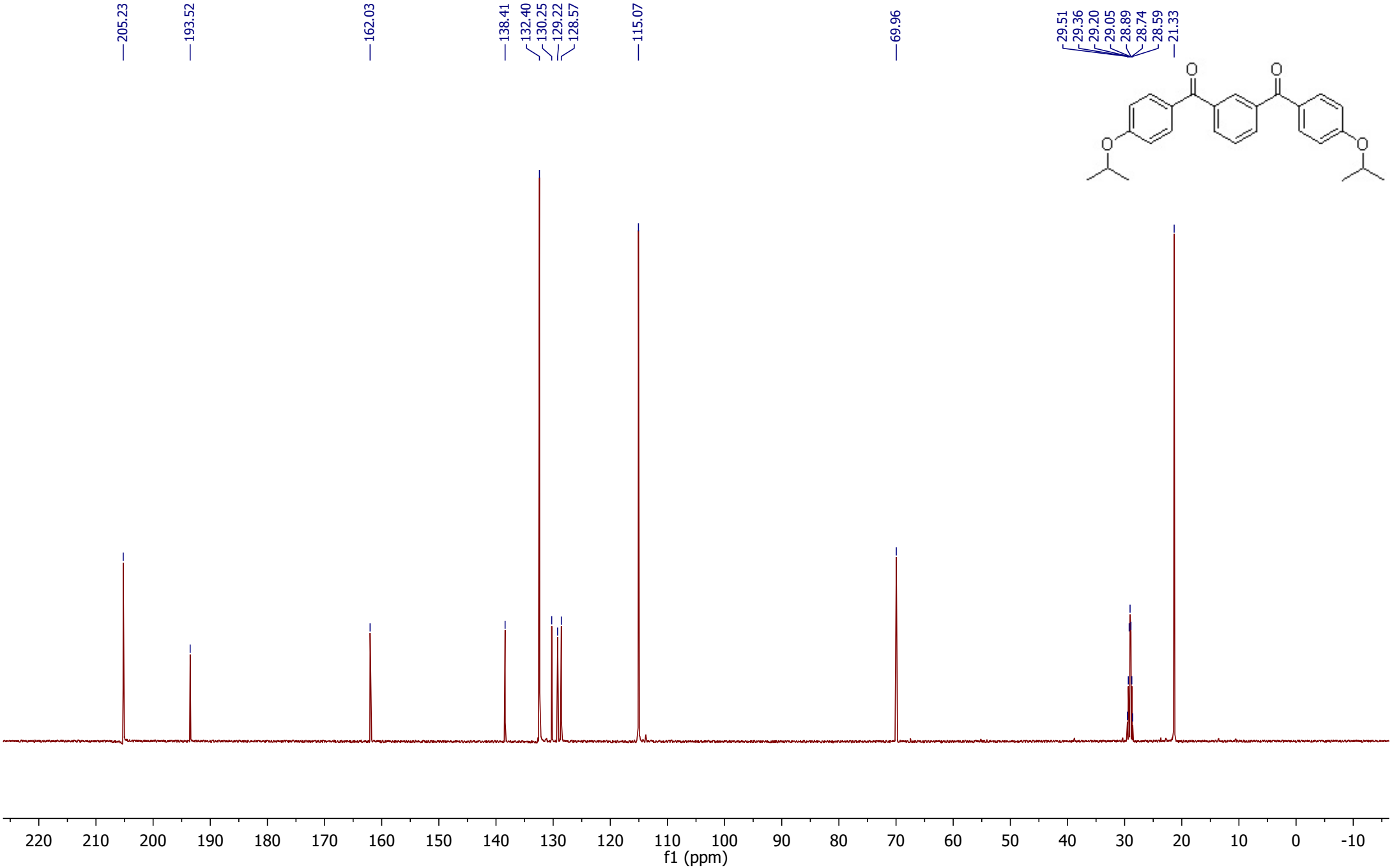




^{1}H NMR (500 MHz, Acetone-d_6) for intermediate between Compound **12** and Compound **14**

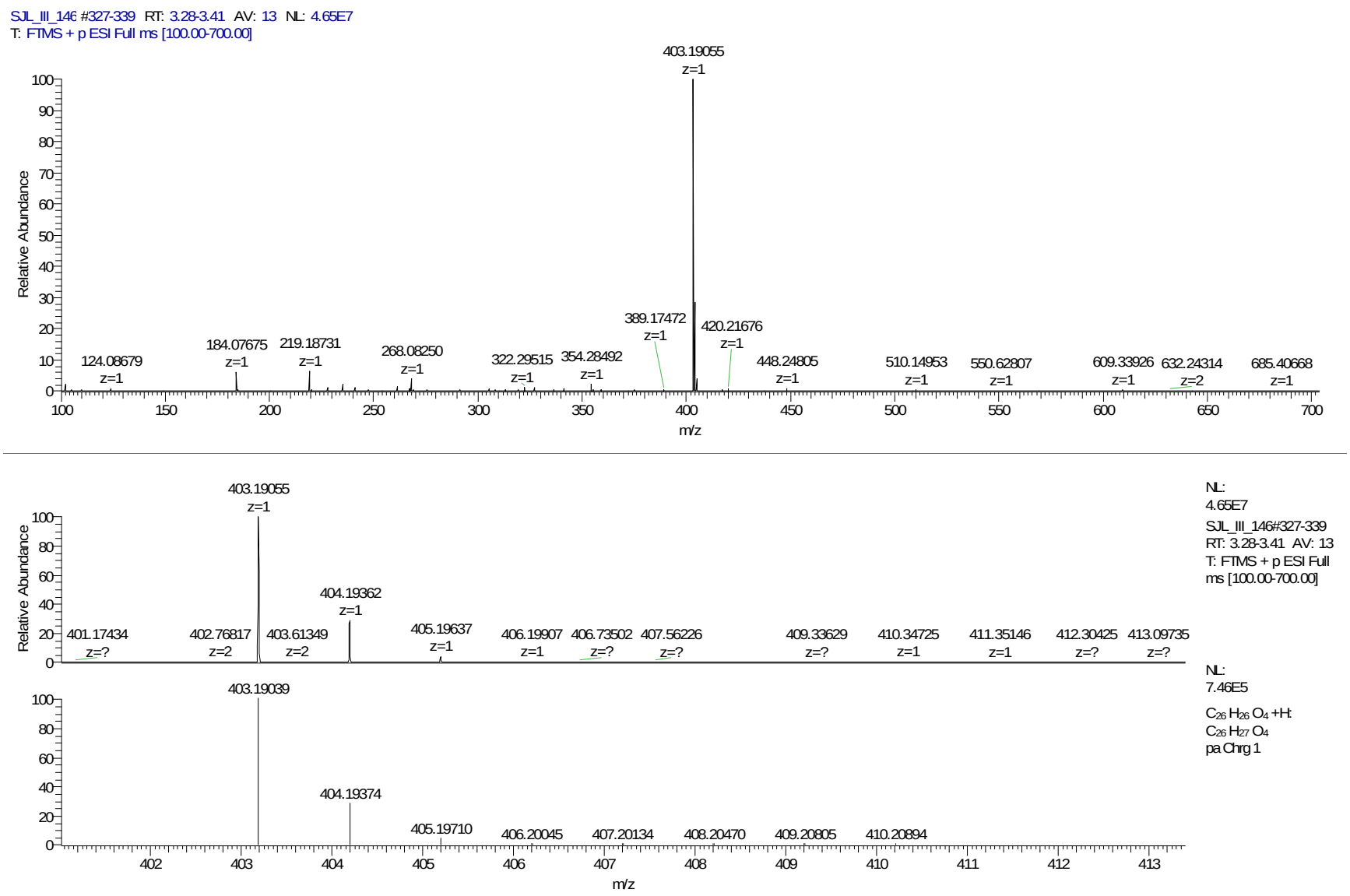


^{13}C NMR (125 MHz, Acetone-d_6) for intermediate between Compound **12** and Compound **14**

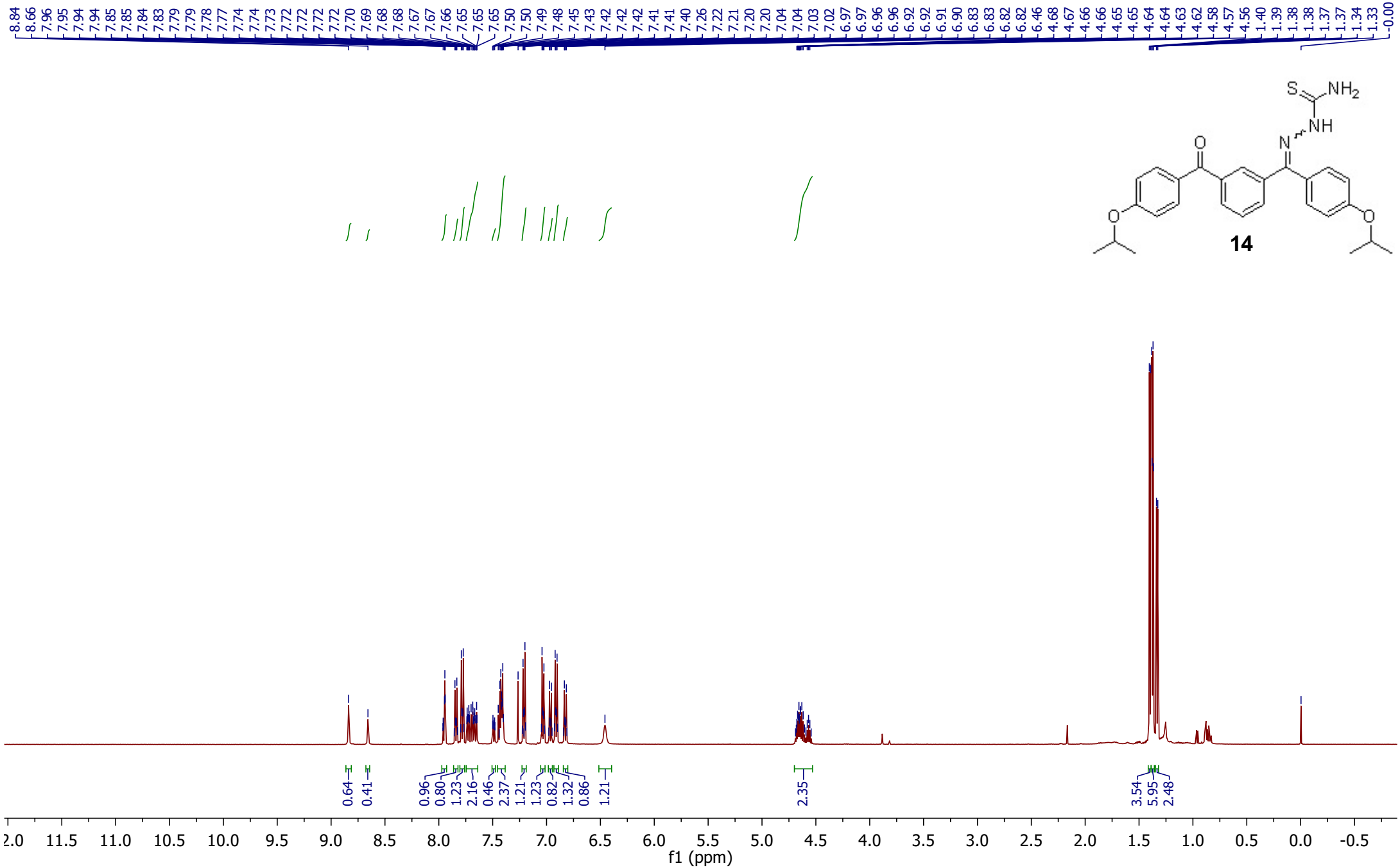


HRMS (ESI) for intermediate between Compound **12** and **14**

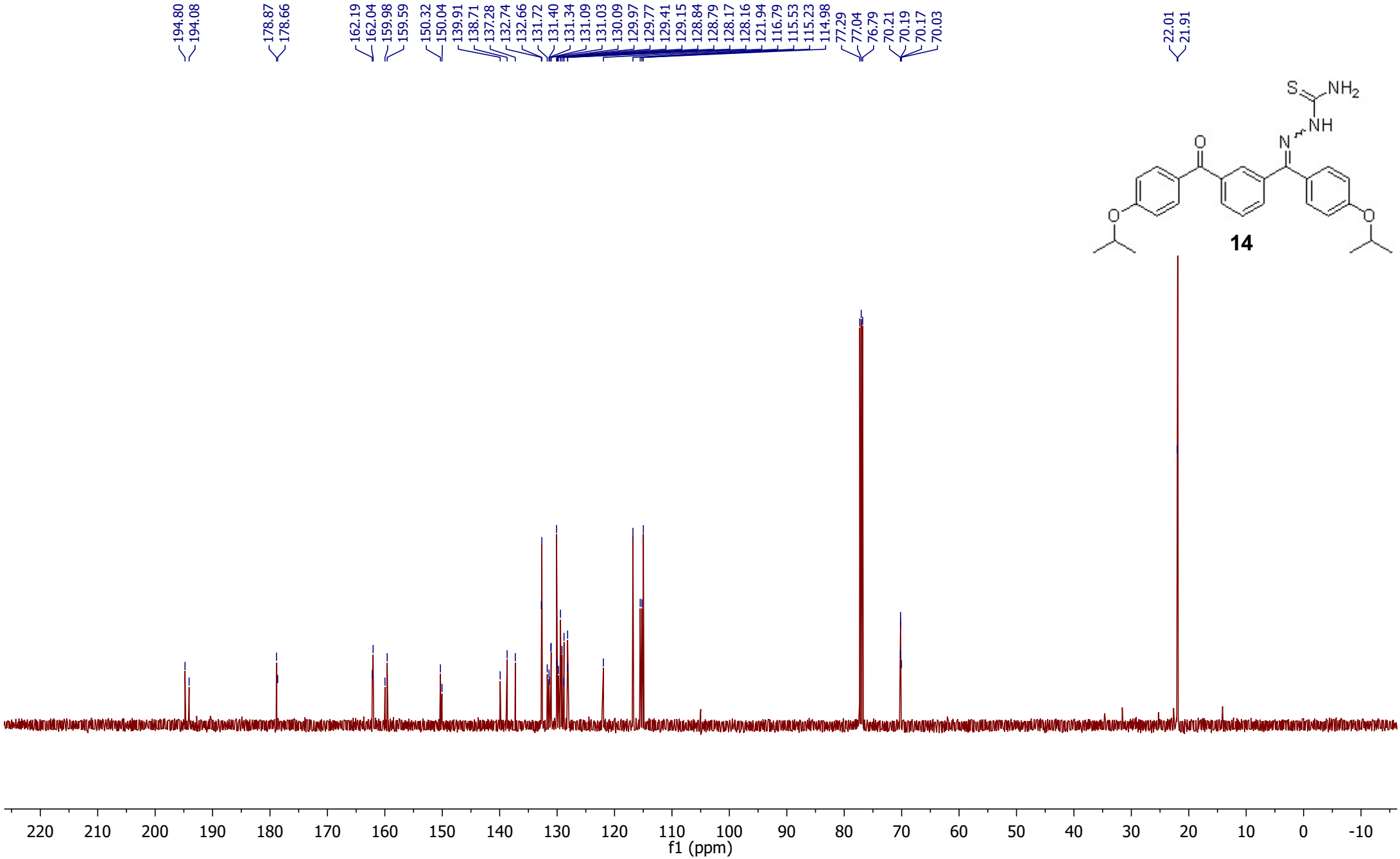
C:\Xcalibur\...\12-19-14\SJL_III_146 12/19/2014 10:48:28 AM



^{1}H NMR (500 MHz, $CDCl_3$) for Compound **14**



^{13}C NMR (125 MHz, $CDCl_3$) for Compound **14**



Data File C:\CHEM32\1\DATA\ERICAP\SJLIV029000003.D
Sample Name: SJLIV029

HPLC trace for Compound 14

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Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 8/13/2014 9:29:28 PM
Acq. Method     : C:\CHEM32\1\METHODS\GRAD 2 50-90 ACN.M
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Last changed    : 12/23/2014 12:02:20 AM by ERICAP
                  (modified after loading)
Sample Info     : SJL-IV-029

                  Method:

                  0-25 min. gradient 50:50 to 10:90 Water:ACN
                  25-30 min 10:90 Water:ACN
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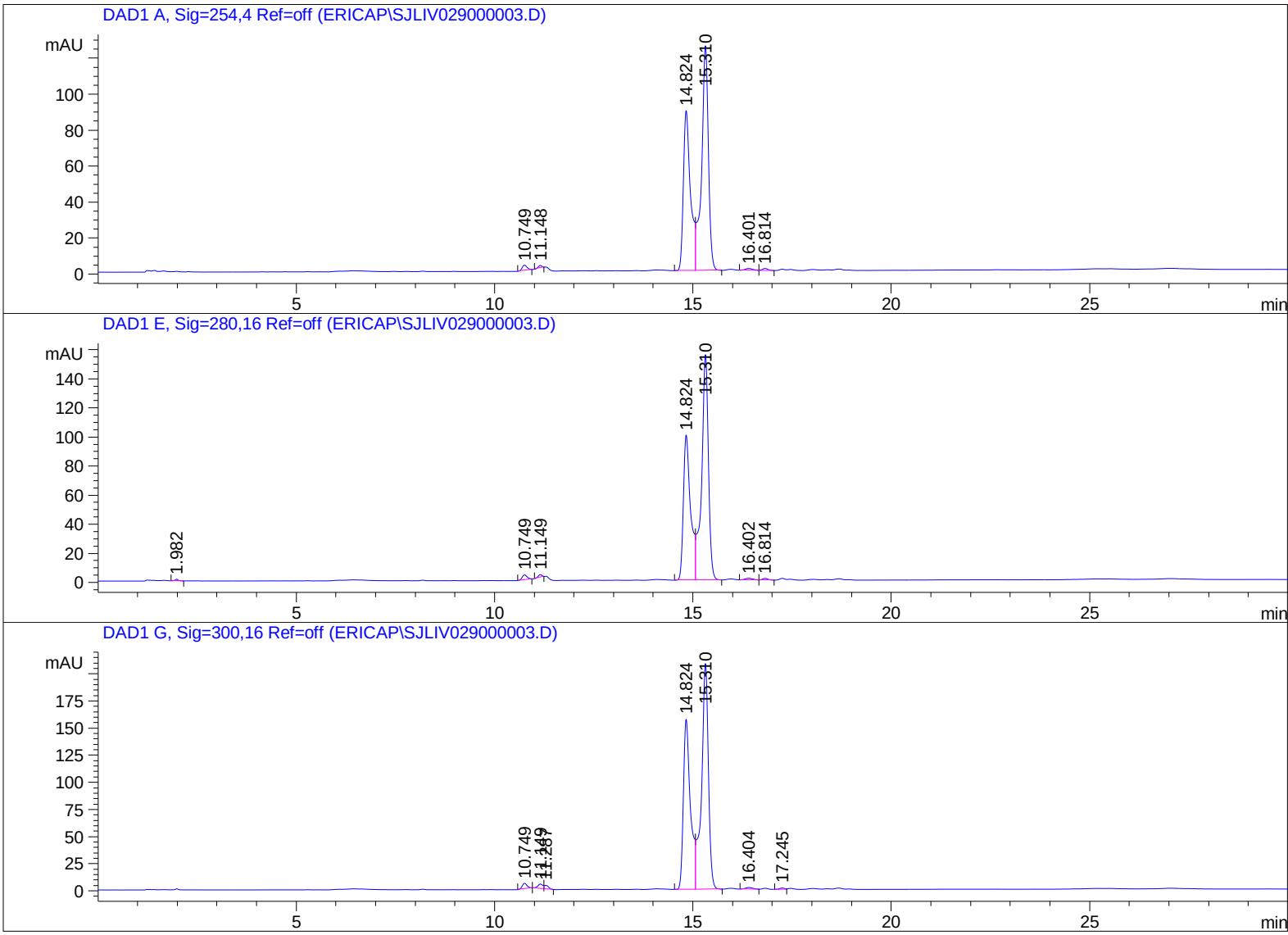
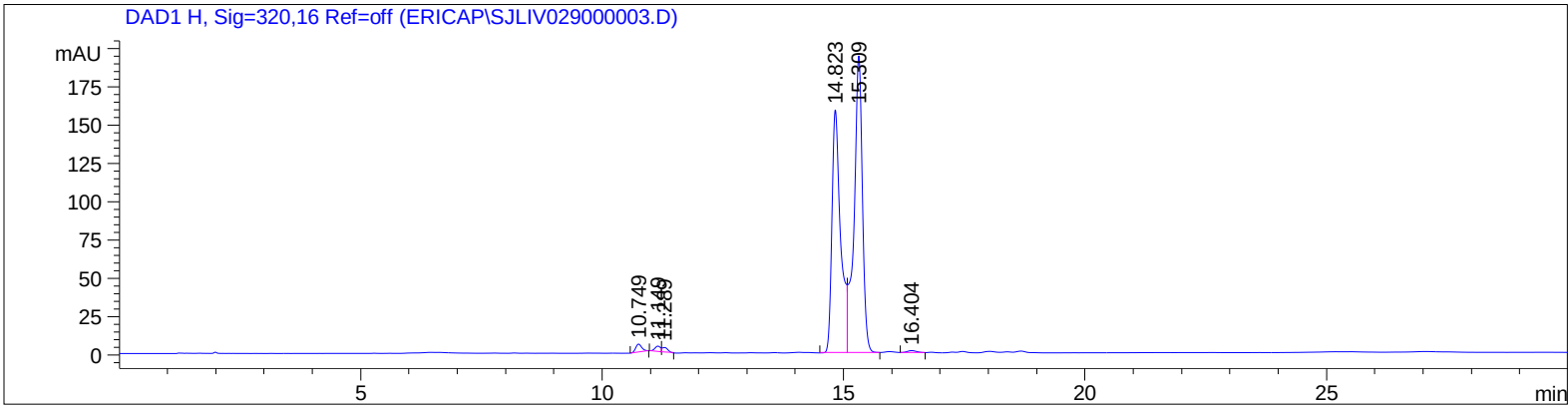
Two peaks observed in the HPLC traces are due to the presence of both E and Z geometrical isomers.



Data File C:\CHEM32\1\DATA\ERICAP\SJLIV029000003.D
Sample Name: SJLIV029

HPLC trace for Compound 14



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.749	BB	0.1332	25.58280	2.94847	0.9577
2	11.148	BB	0.1067	9.40060	1.42943	0.3519
3	14.824	BV	0.1824	1116.94592	89.00146	41.8115
4	15.310	VB	0.1756	1495.36731	124.98199	55.9772
5	16.401	BV	0.2082	13.79019	1.01703	0.5162
6	16.814	VB	0.1456	10.29943	1.09639	0.3855
Totals :				2671.38626	220.47478	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.982	BB	0.0699	5.45845	1.14002	0.1717
2	10.749	BB	0.1326	28.72618	3.33248	0.9037
3	11.149	BB	0.1070	12.14089	1.84059	0.3819
4	14.824	BV	0.1829	1256.60889	99.80403	39.5320
5	15.310	VB	0.1752	1849.91211	155.08711	58.1969
6	16.402	BV	0.2042	15.15580	1.14671	0.4768
7	16.814	VB	0.1440	10.70900	1.15686	0.3369
Totals :				3178.71131	263.50780	

HPLC trace for Compound 14

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.749	BB	0.1339	44.75120	5.12385	0.9734
2	11.149	BV	0.1350	36.41380	4.04440	0.7921
3	11.287	VB	0.1148	24.61936	3.23311	0.5355
4	14.824	BV	0.1822	1964.89246	156.75853	42.7406
5	15.310	VB	0.1759	2493.82300	207.99771	54.2460
6	16.404	BV	0.2044	20.89652	1.57921	0.4545
7	17.245	BV	0.1437	11.85075	1.26023	0.2578
Totals :				4597.24708	379.99703	

Signal 4: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.749	BB	0.1354	46.18006	5.21004	1.0421
2	11.149	BV	0.1310	30.41051	3.51175	0.6862
3	11.289	VB	0.1165	23.15547	2.98347	0.5225
4	14.823	BV	0.1819	1984.11694	158.67049	44.7719
5	15.309	VB	0.1763	2331.42114	193.81932	52.6088
6	16.404	BB	0.2011	16.33257	1.26118	0.3685
Totals :				4431.61670	365.45624	

*** End of Report ***

HRMS (ESI) for Compound **14**

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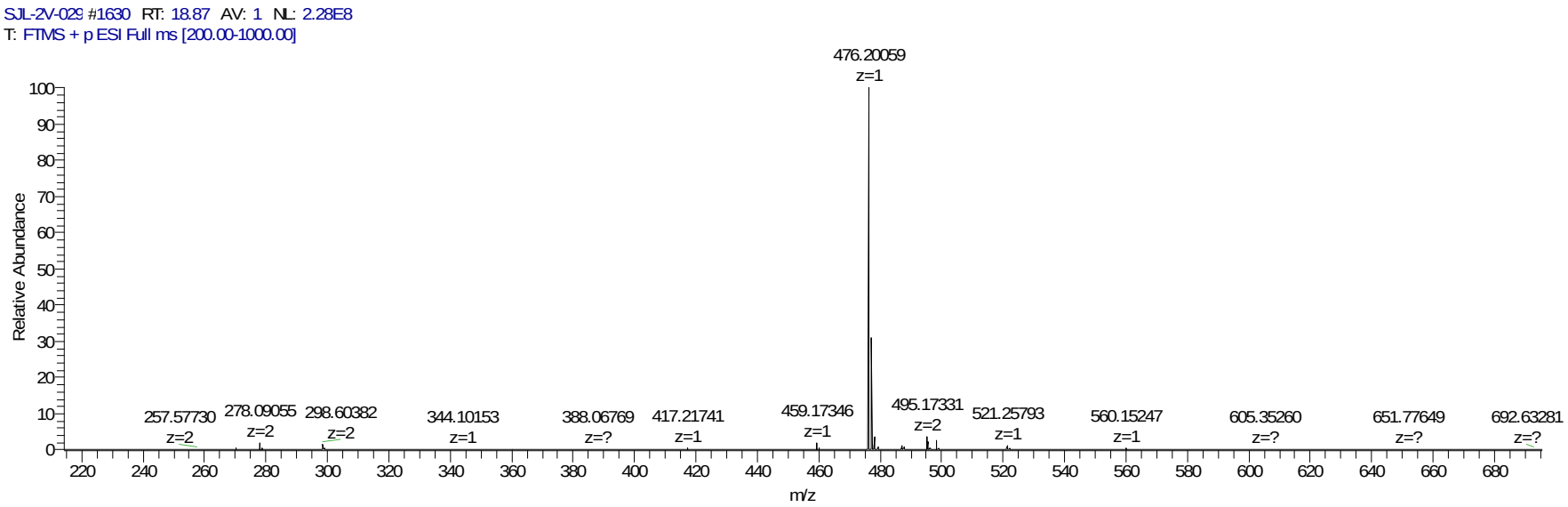
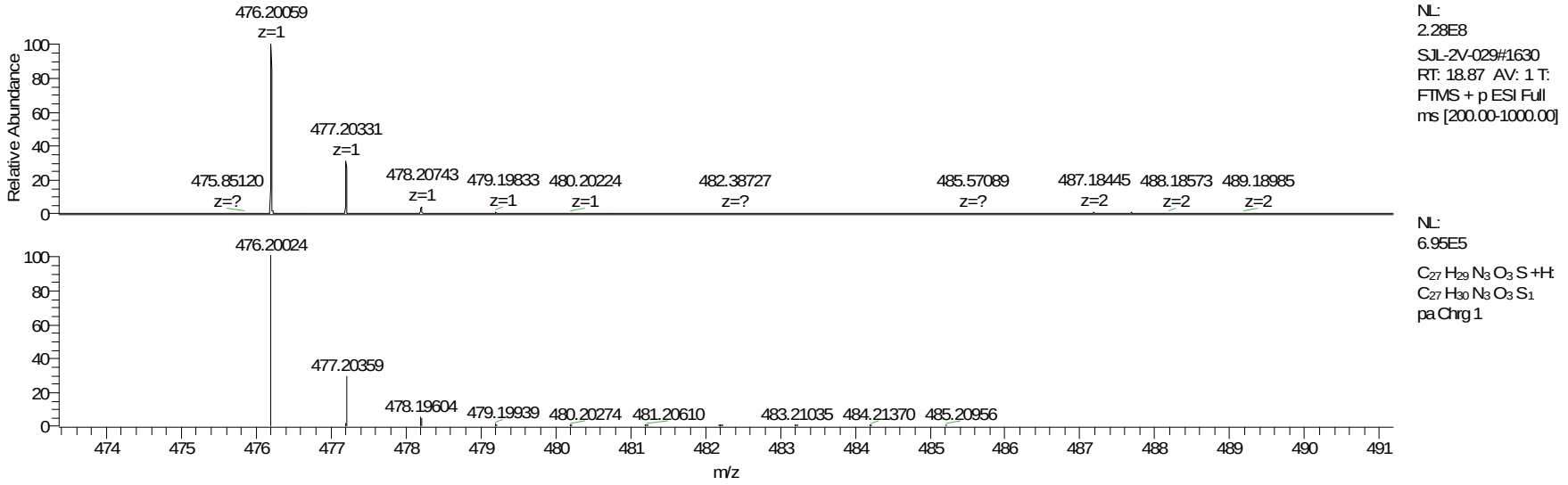
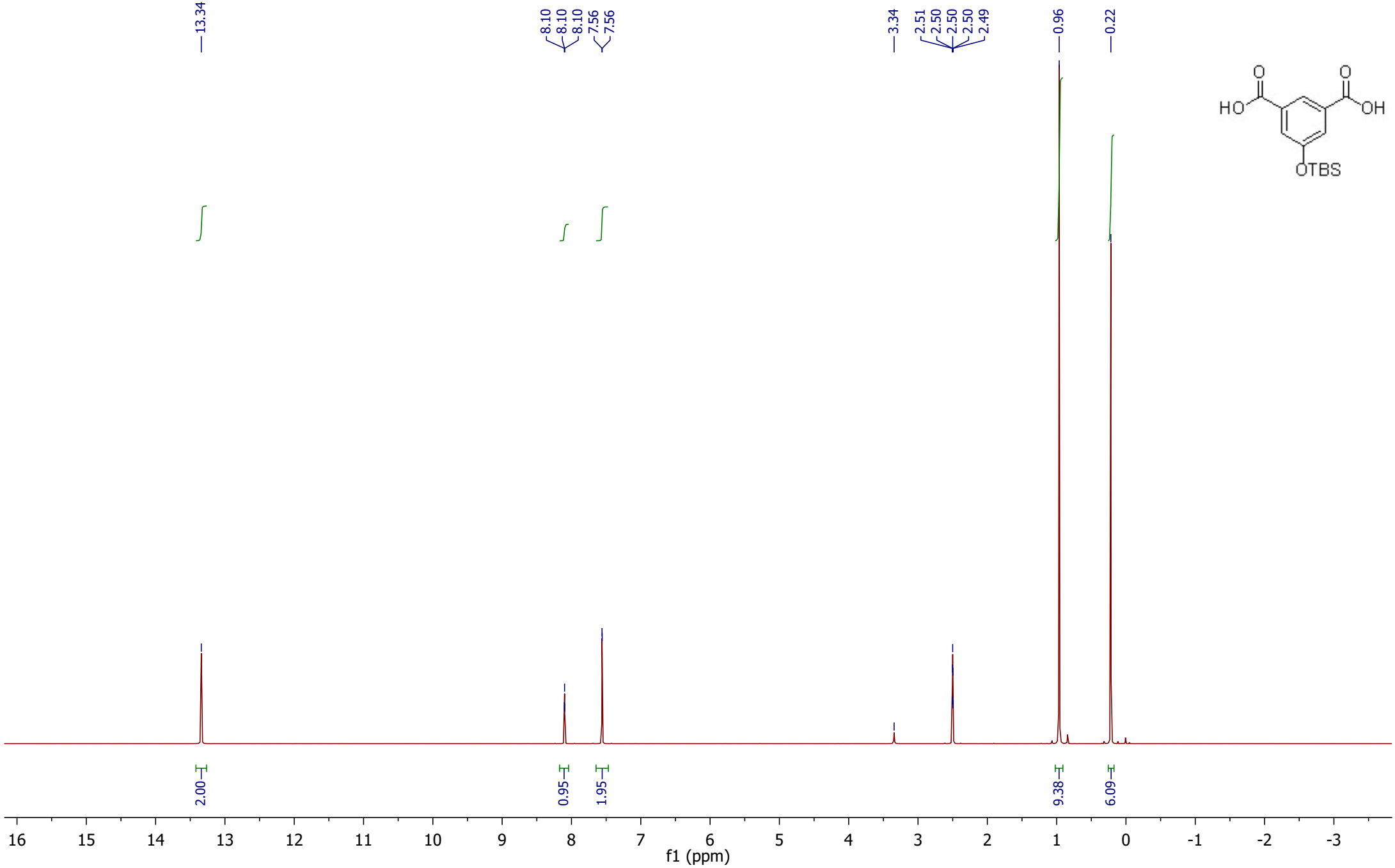
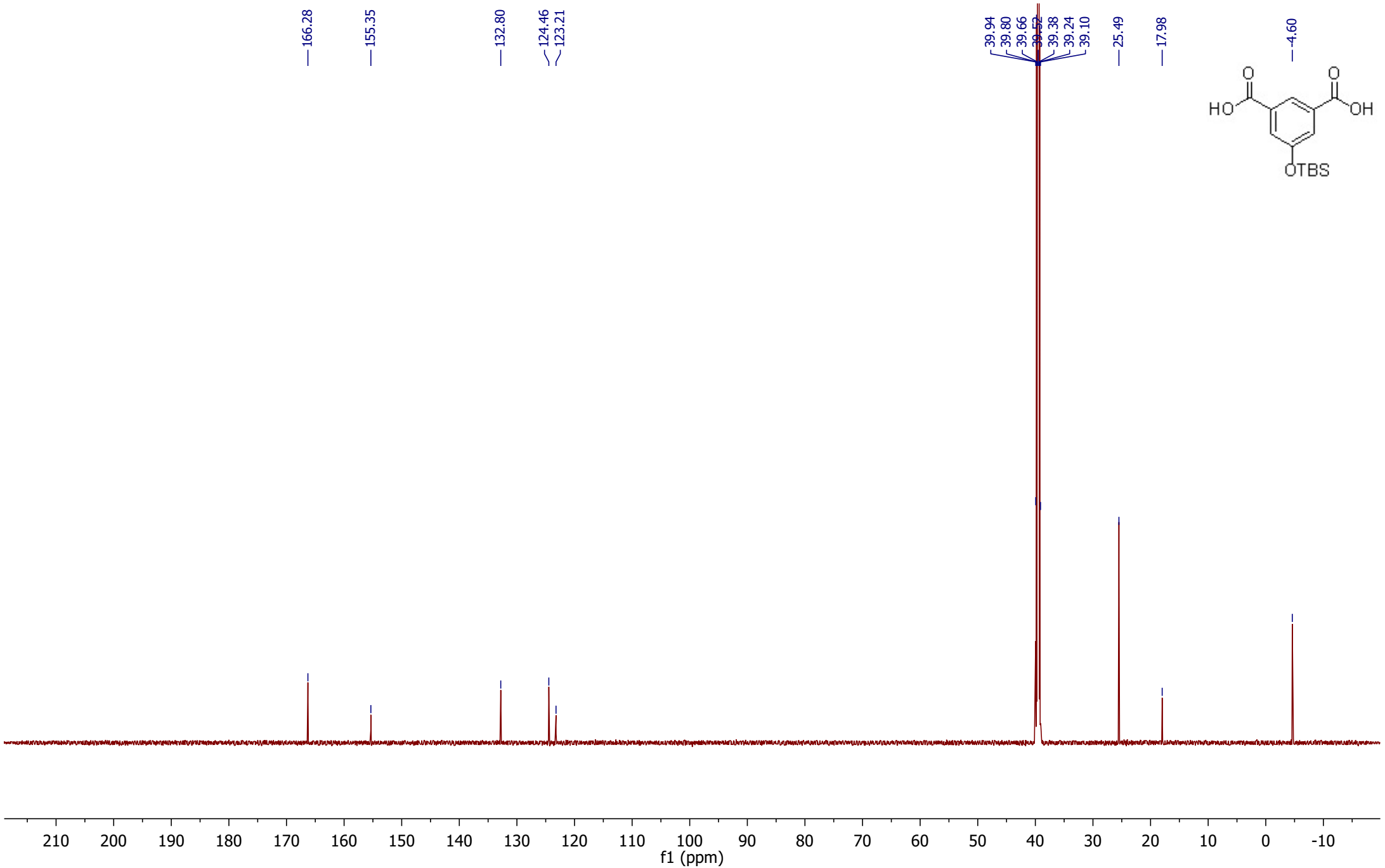




^{1}H NMR (600 MHz, DMSO-d_6) of intermediate for Compound **15**

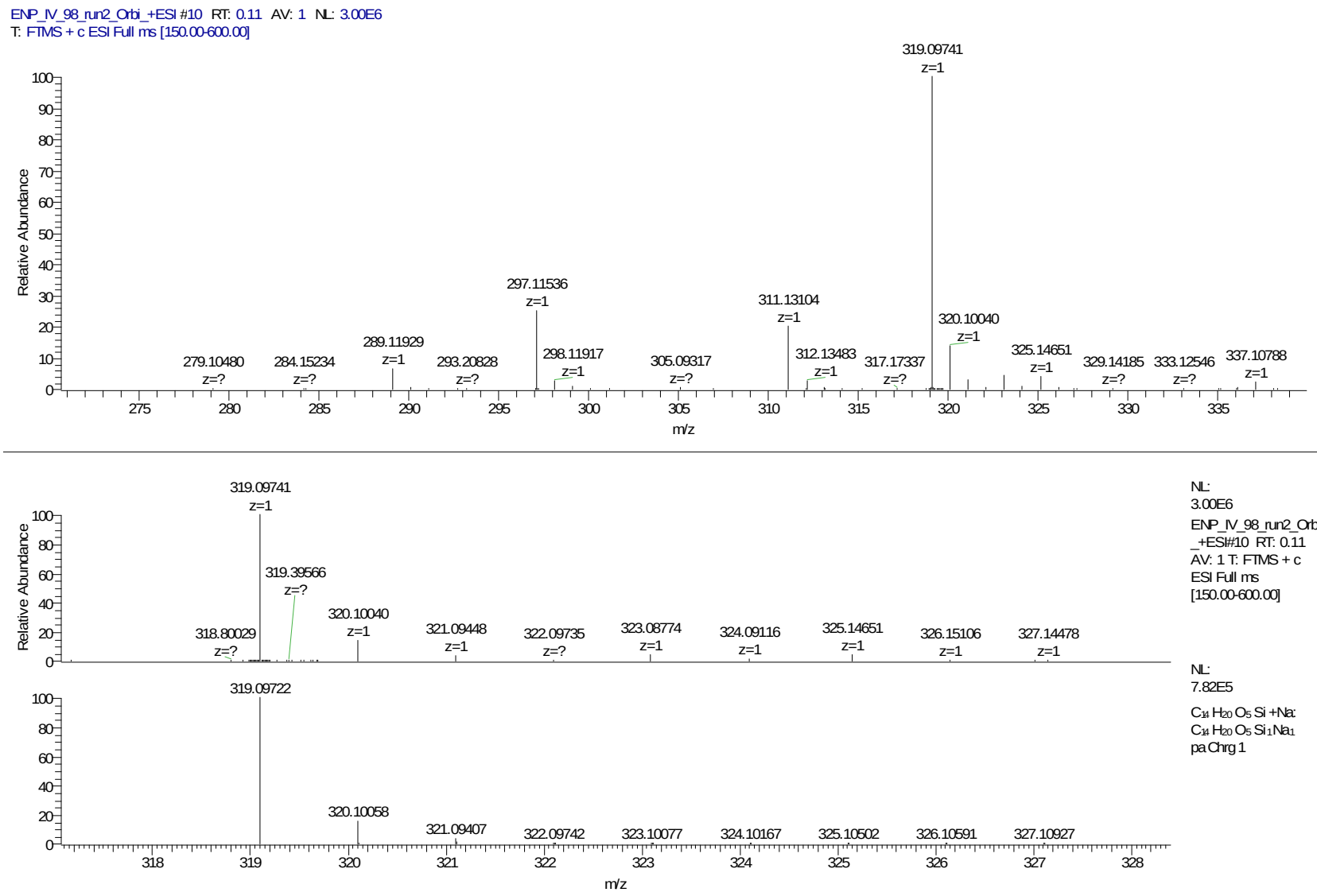


^{13}C NMR (150 MHz, DMSO-d_6) of intermediate for Compound **15**

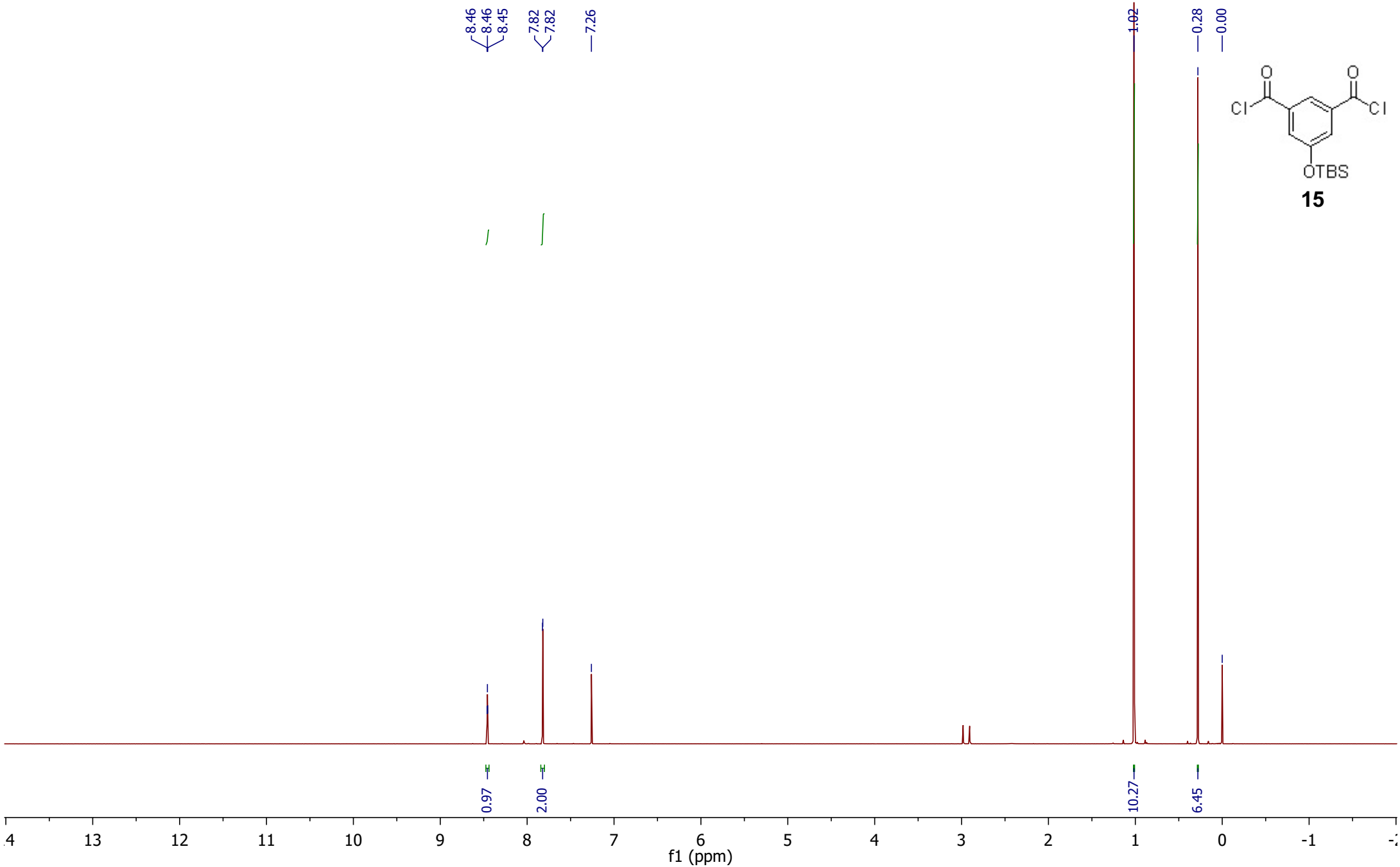


HRMS (ESI) for intermediate before Compound **15**

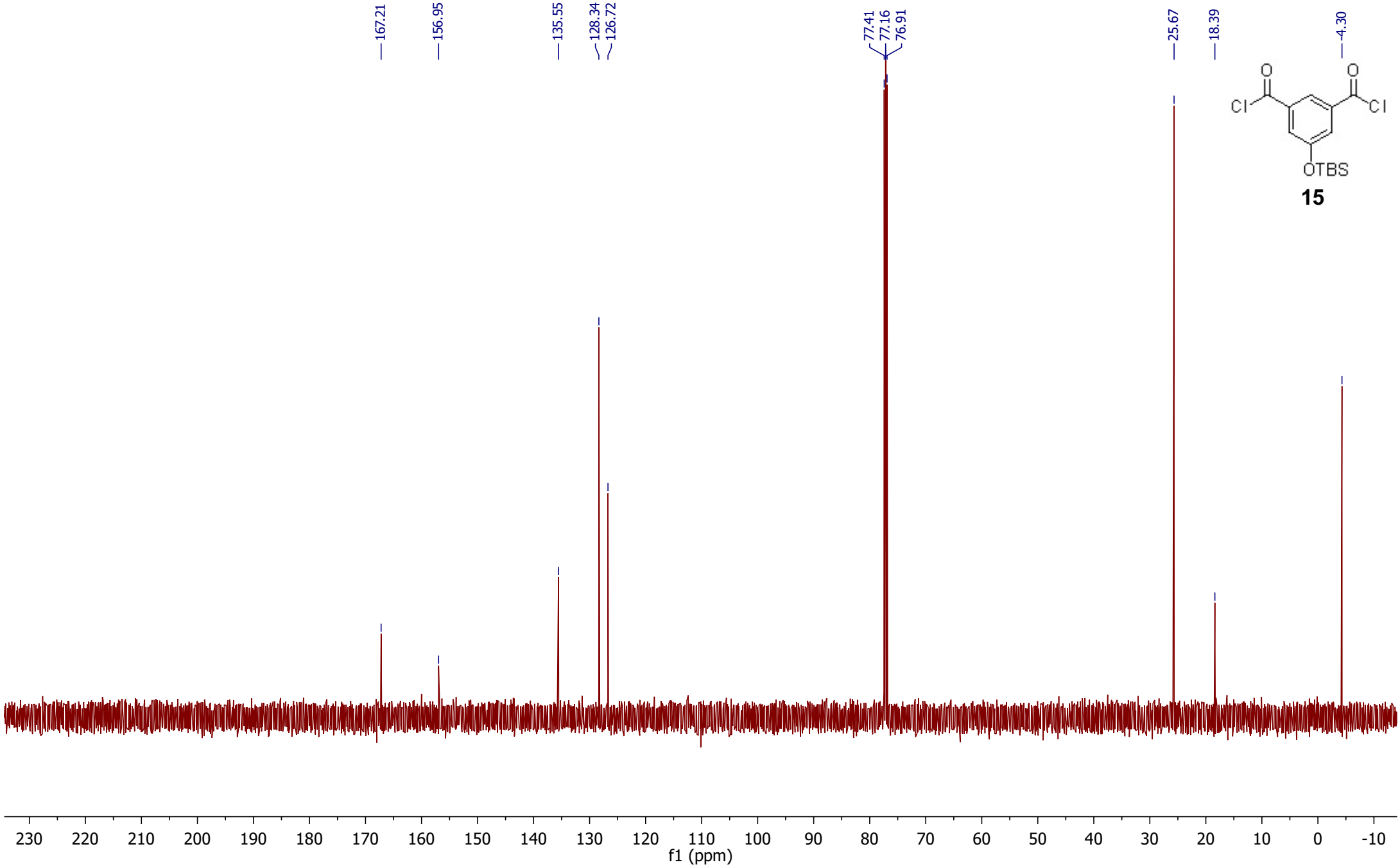
C:\Xcalibur\...\ENP_IV_98_run2_Orbi_+ESI 12/30/2014 4:26:22 PM



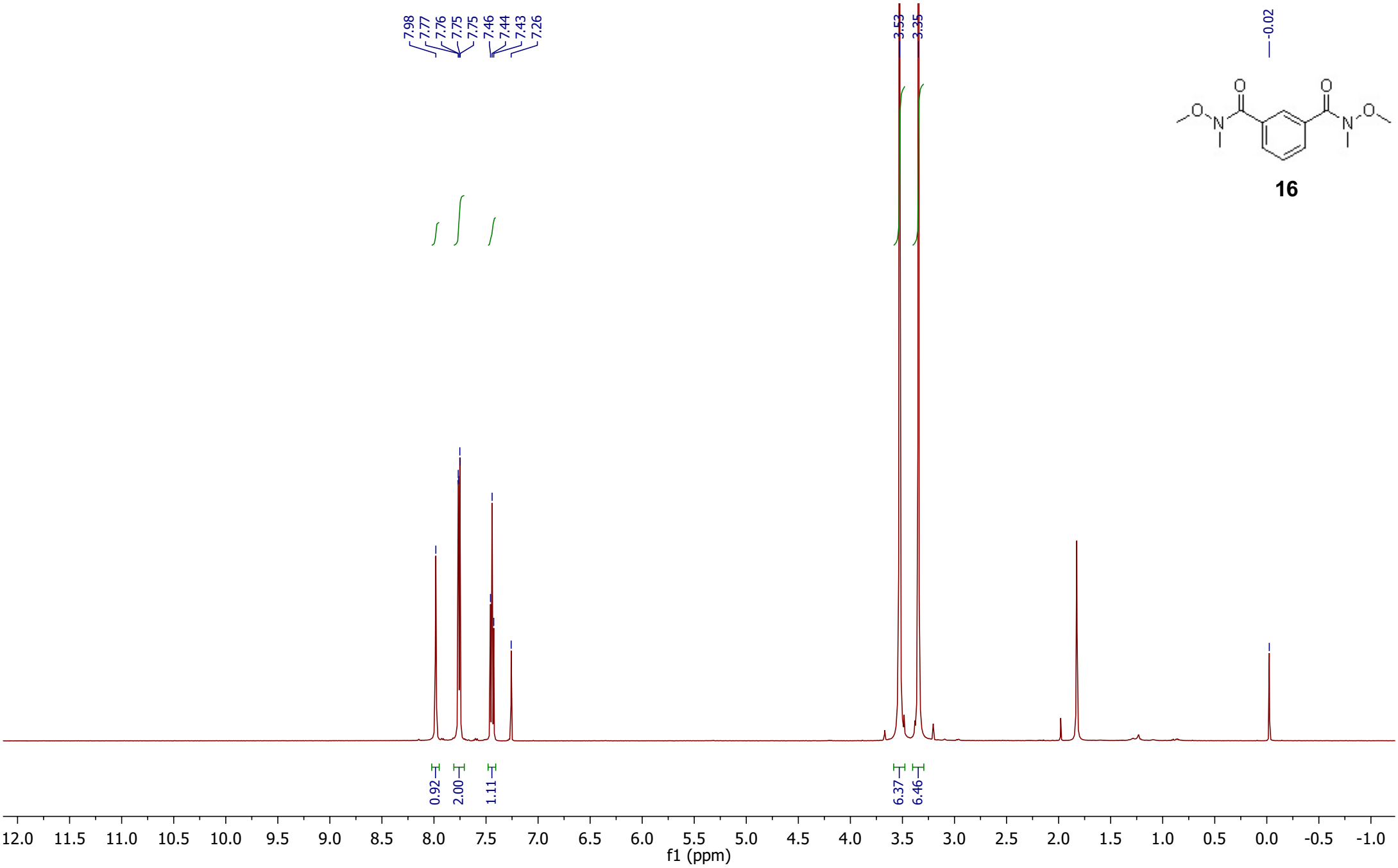
^{1}H NMR (500 MHz, $CDCl_3$) of Compound **15**



^{13}C NMR (125 MHz, $CDCl_3$) of Compound **15**

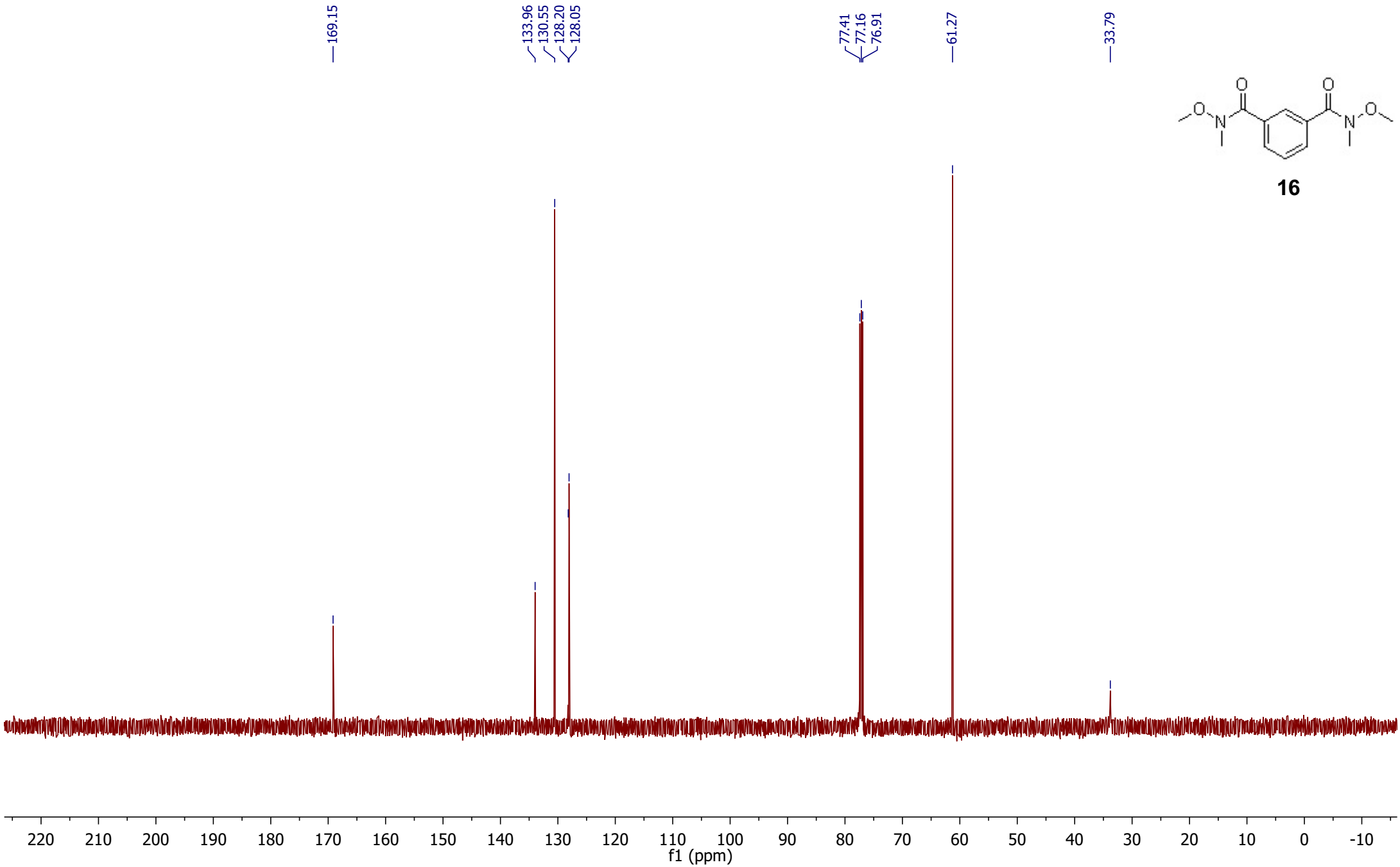


^{1}H NMR (500 MHz, $CDCl_3$) of Compound **16**



16

^{13}C NMR (125 MHz, $CDCl_3$) of Compound **16**



HRMS (ESI) for Compound **16**

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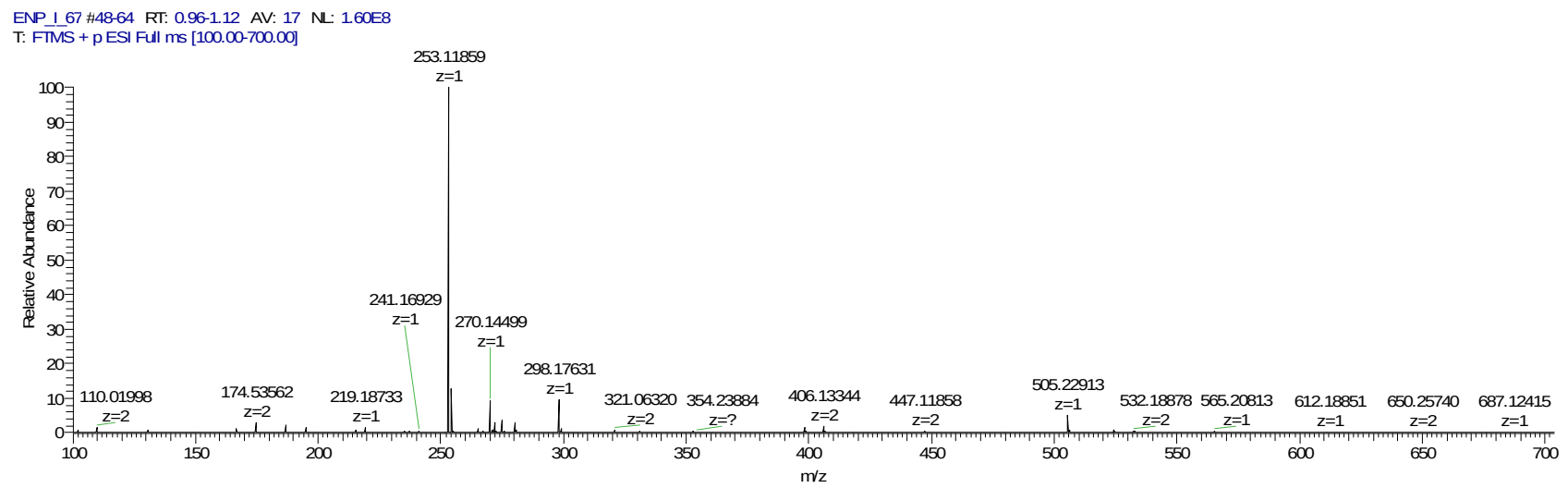
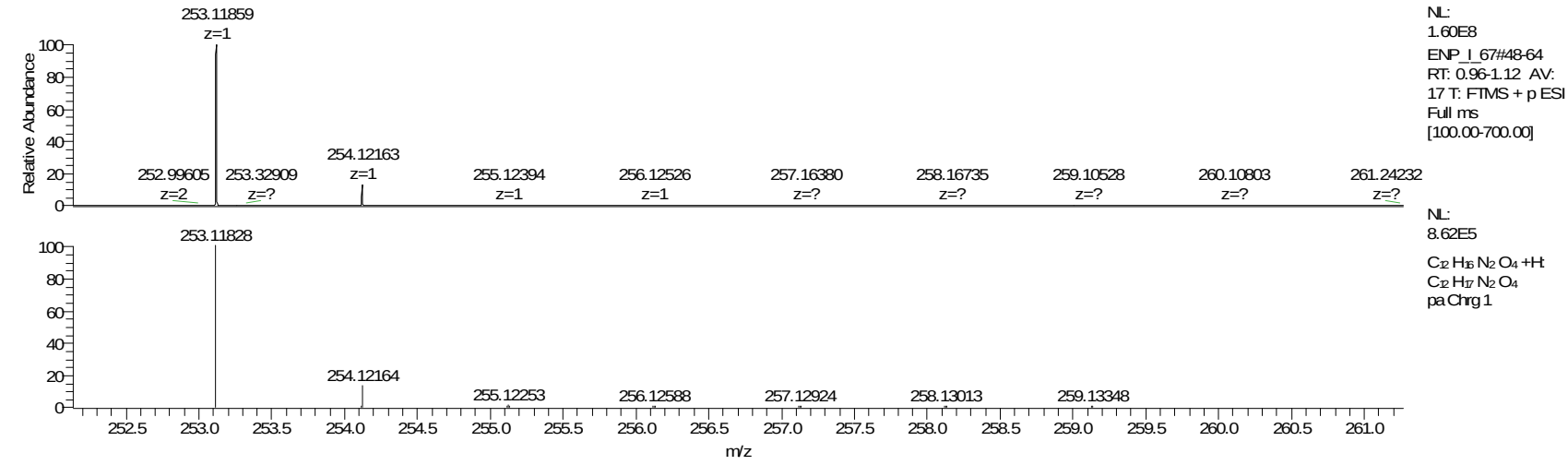
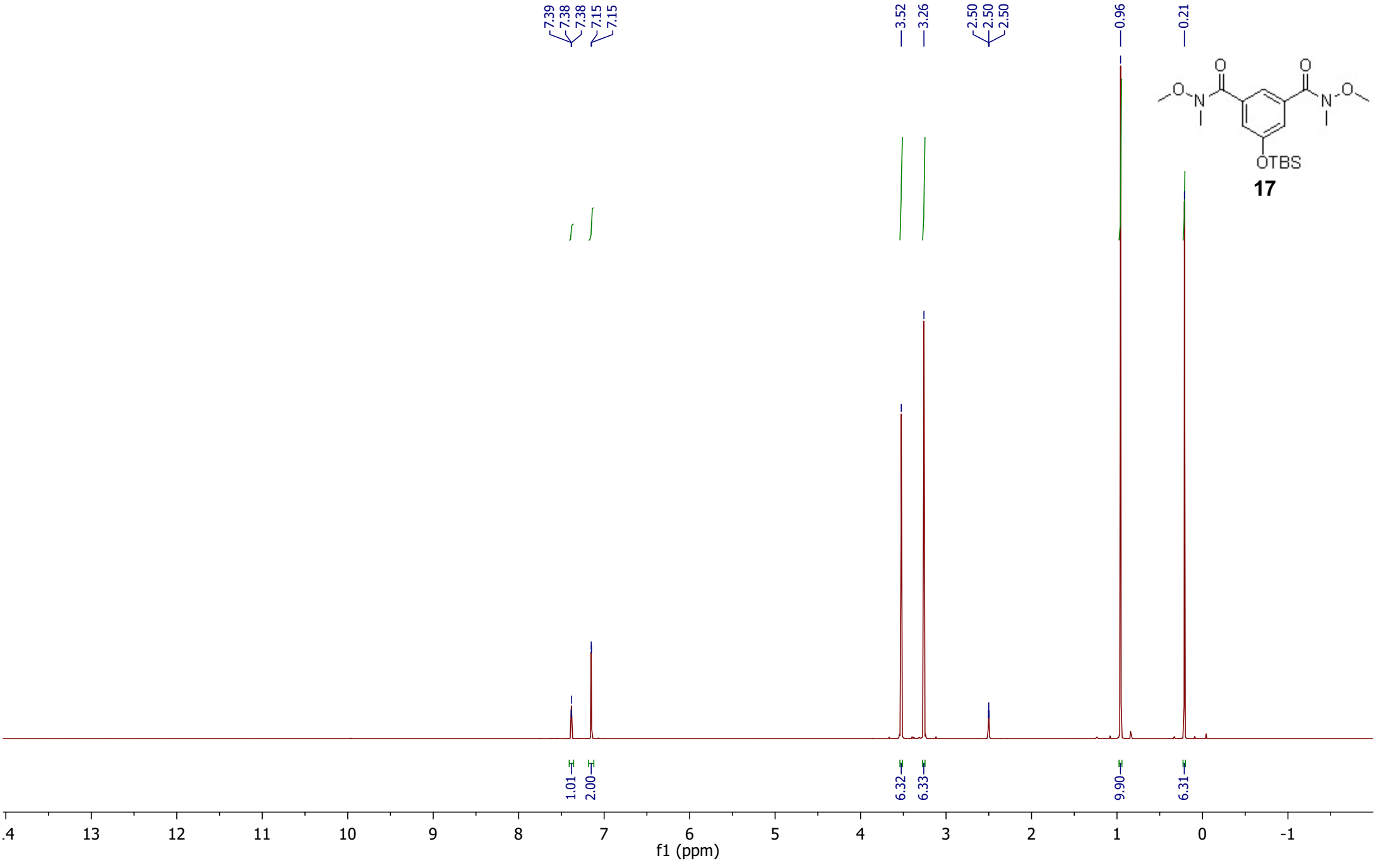
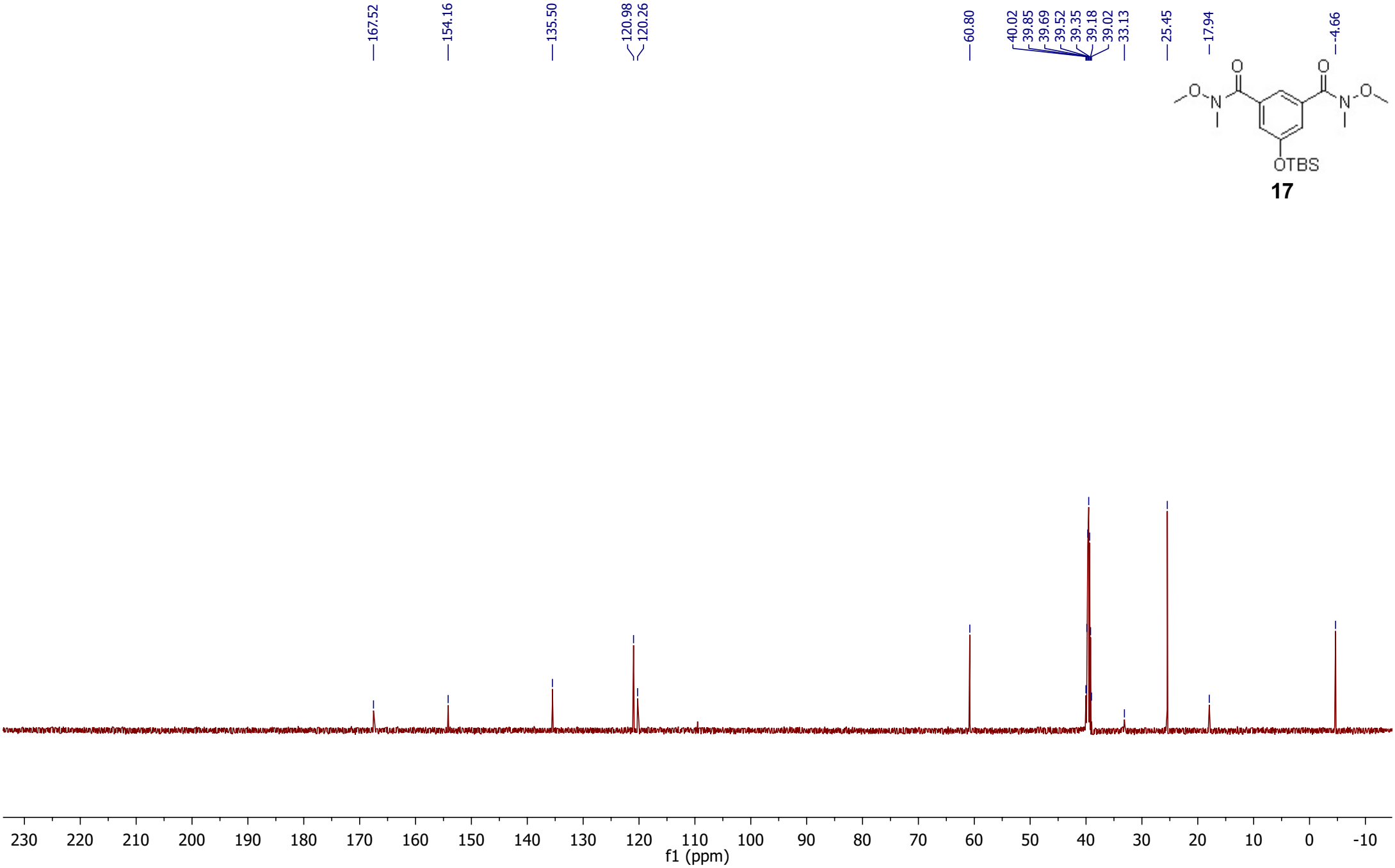




^{1}H NMR (500 MHz, DMSO-d_6) for Compound **17**



^{13}C NMR (125 MHz, DMSO-d_6) for Compound **17**



HRMS (ESI) for Compound **17**

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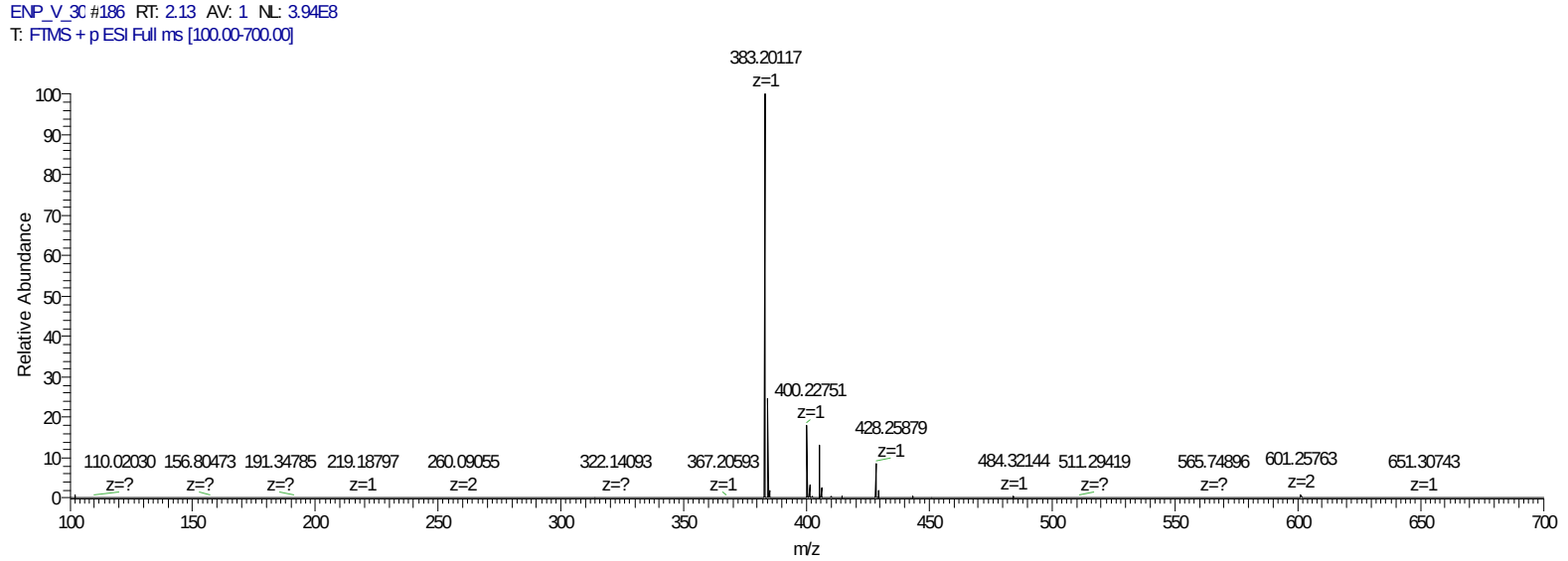
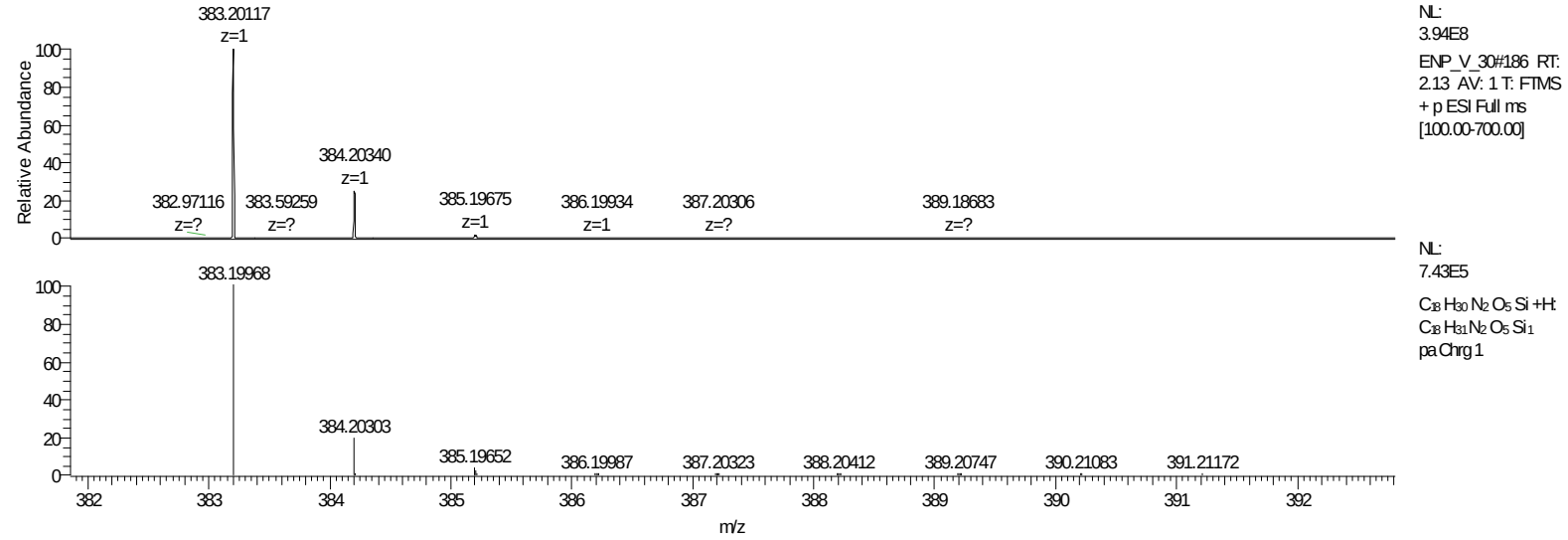
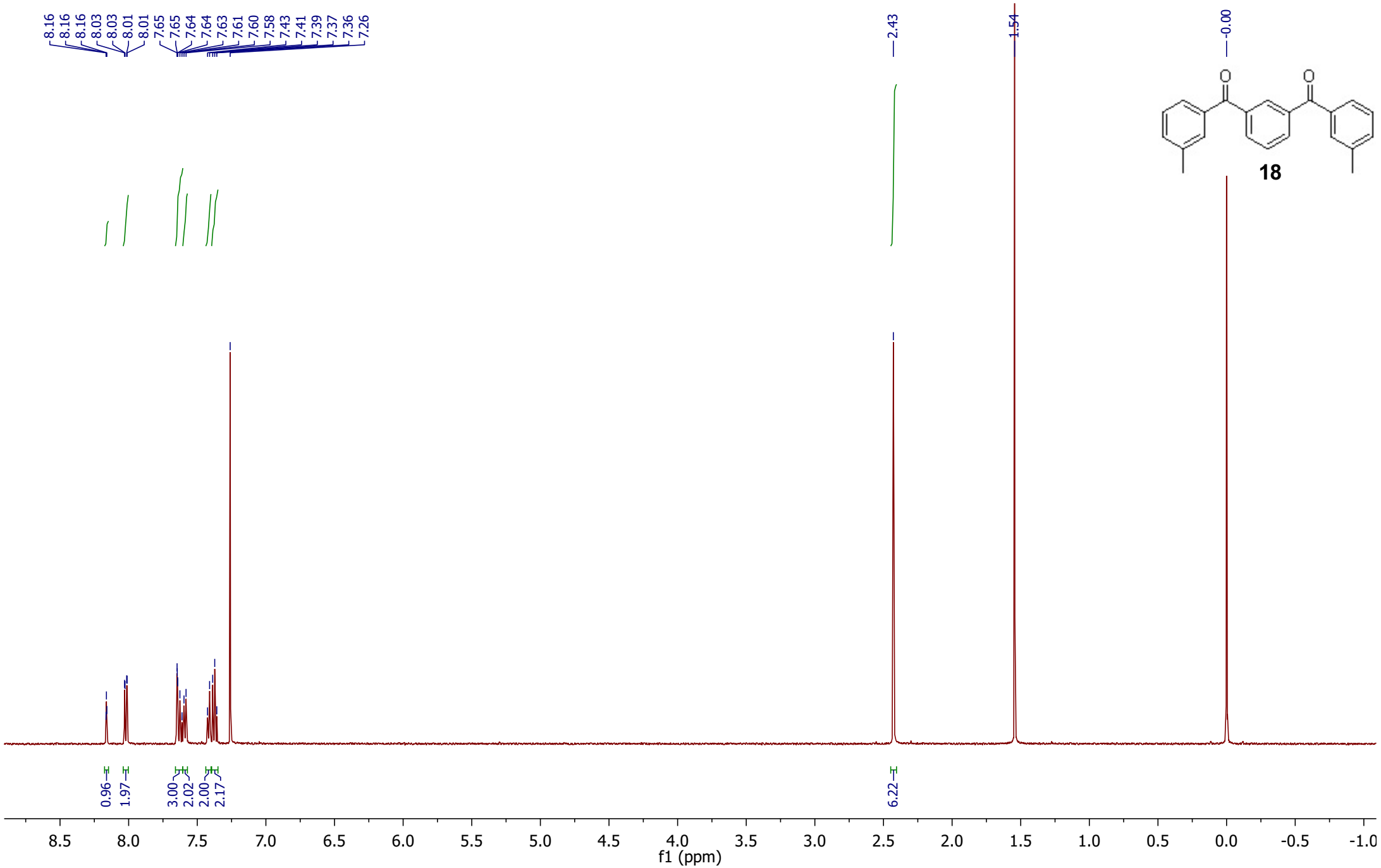
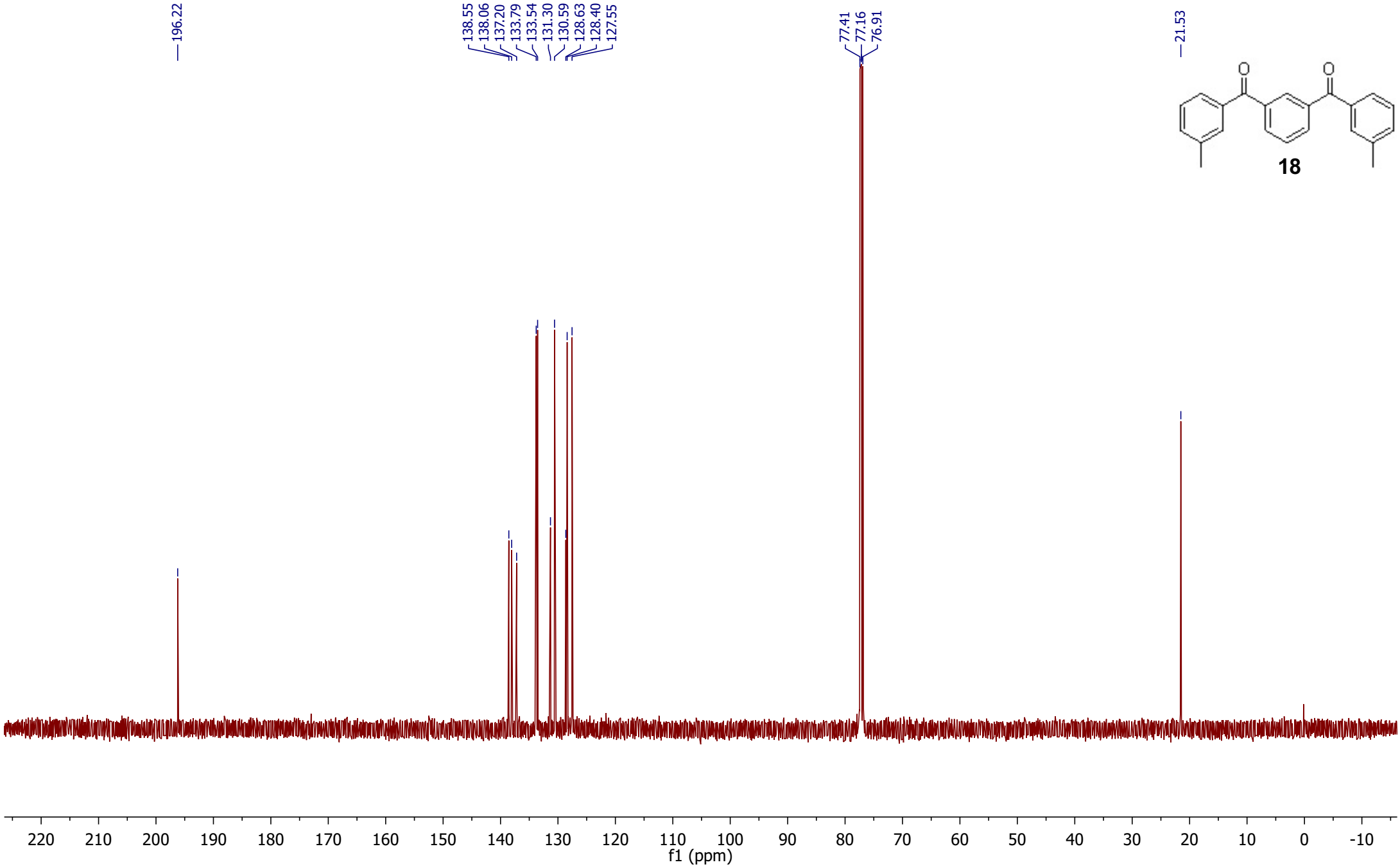




^{1}H NMR (500 MHz, $CDCl_3$) of Compound **18**



^{13}C NMR (125 MHz, $CDCl_3$) of Compound **18**



HRMS (ESI) for Compound **18**

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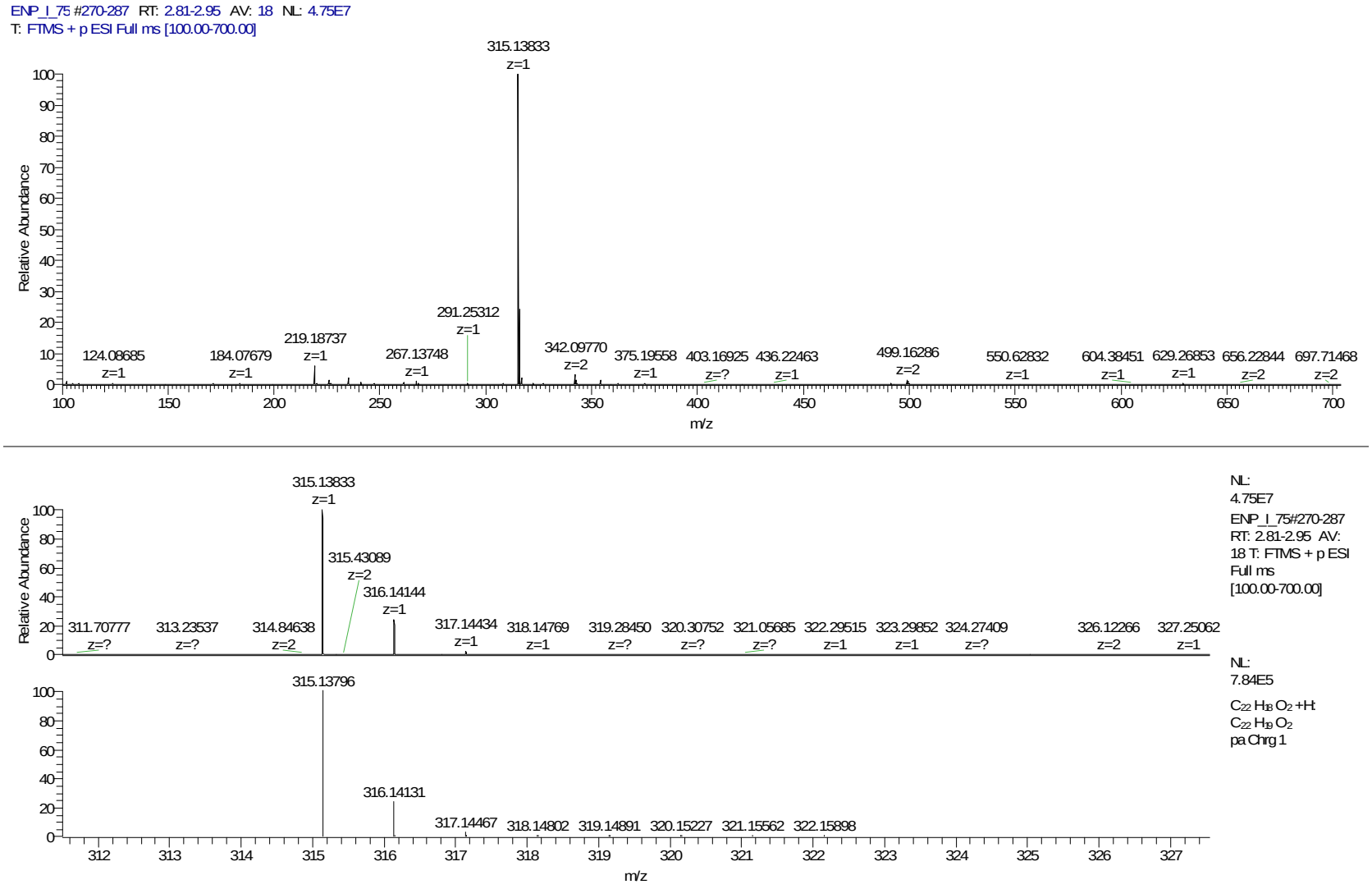
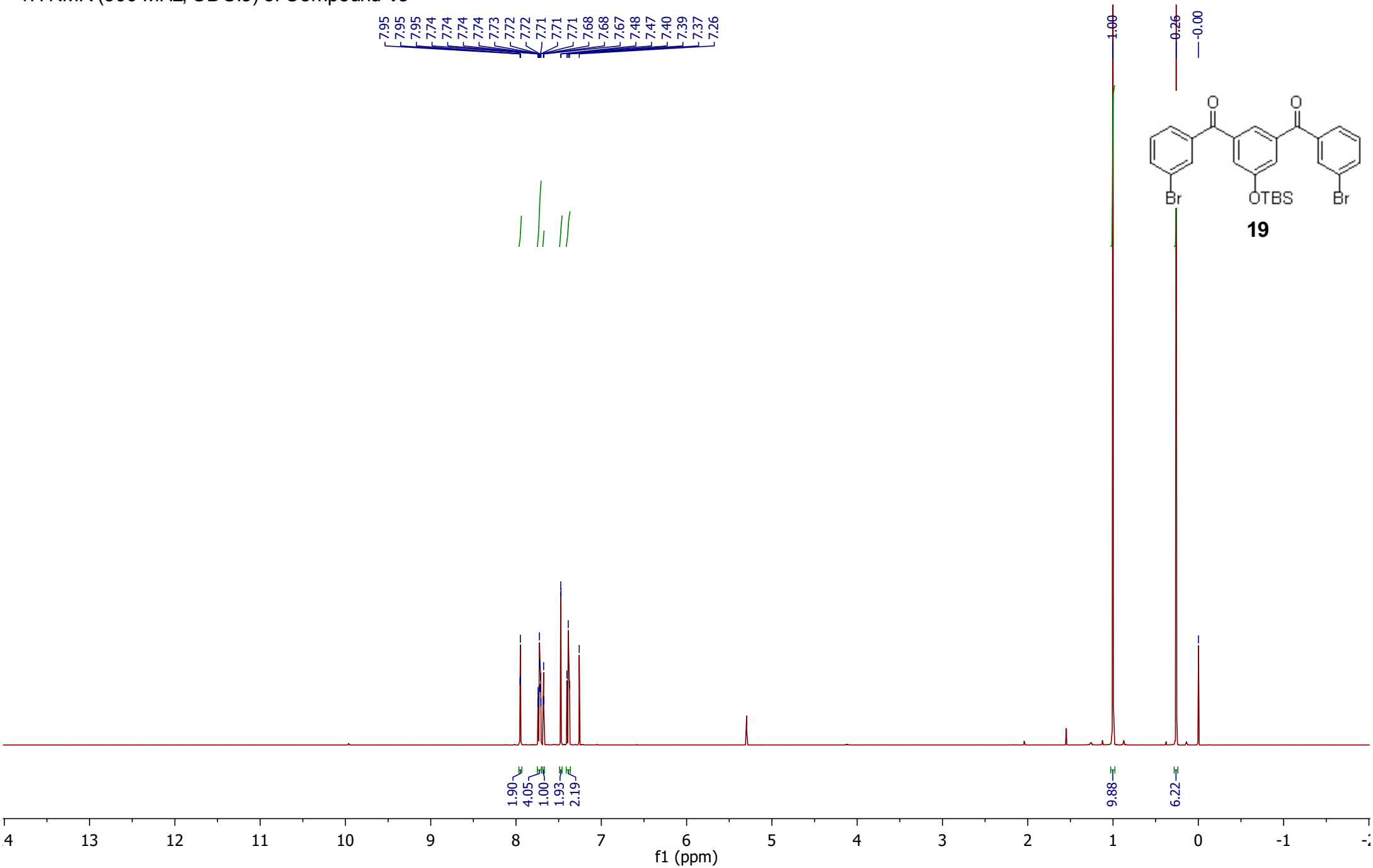
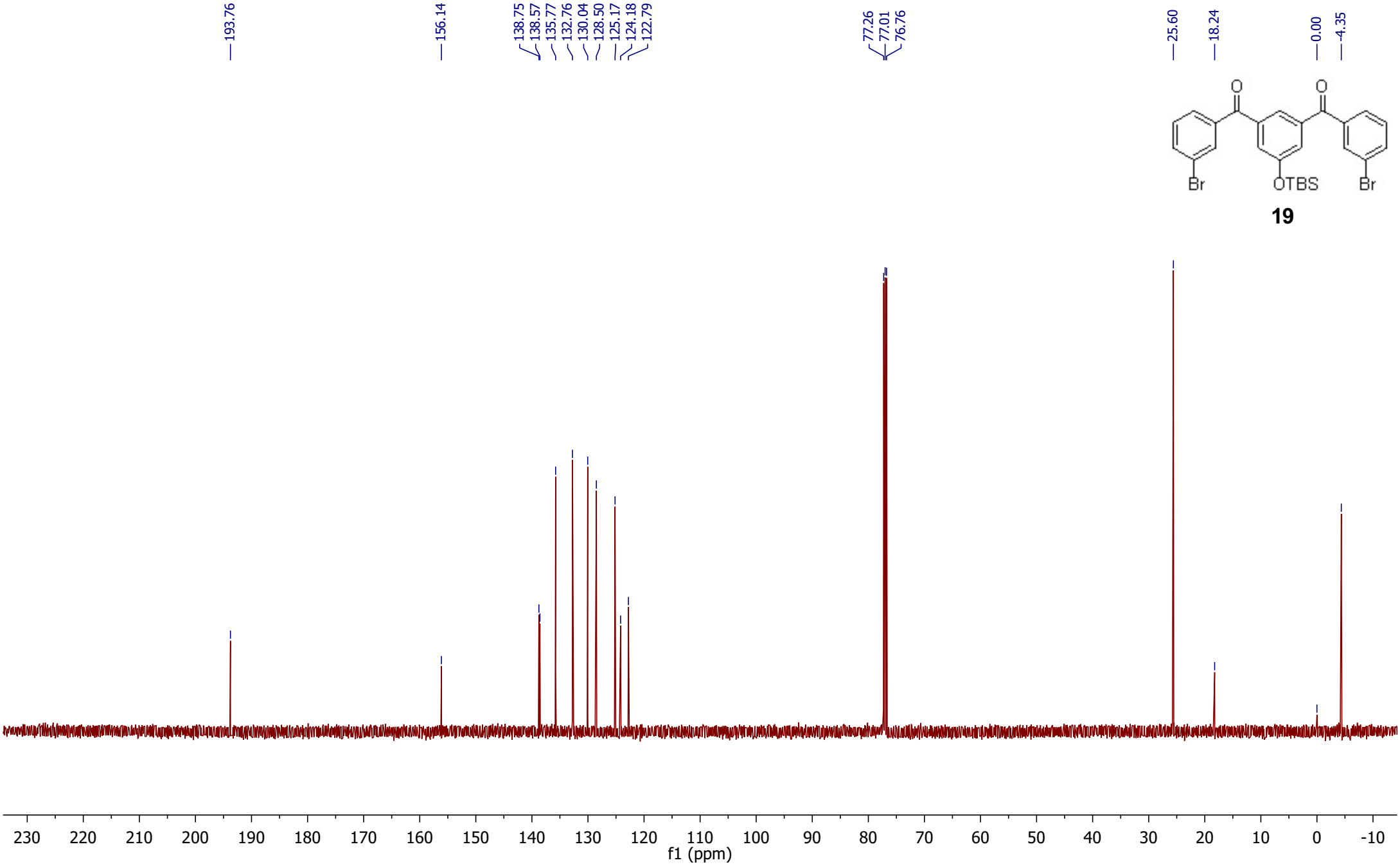


1H NMR (500 MHz, CDCl3) of Compound **19**



13C NMR (125 MHz, CDCl3) of Compound **19**



HRMS (ESI) for Compound **19**

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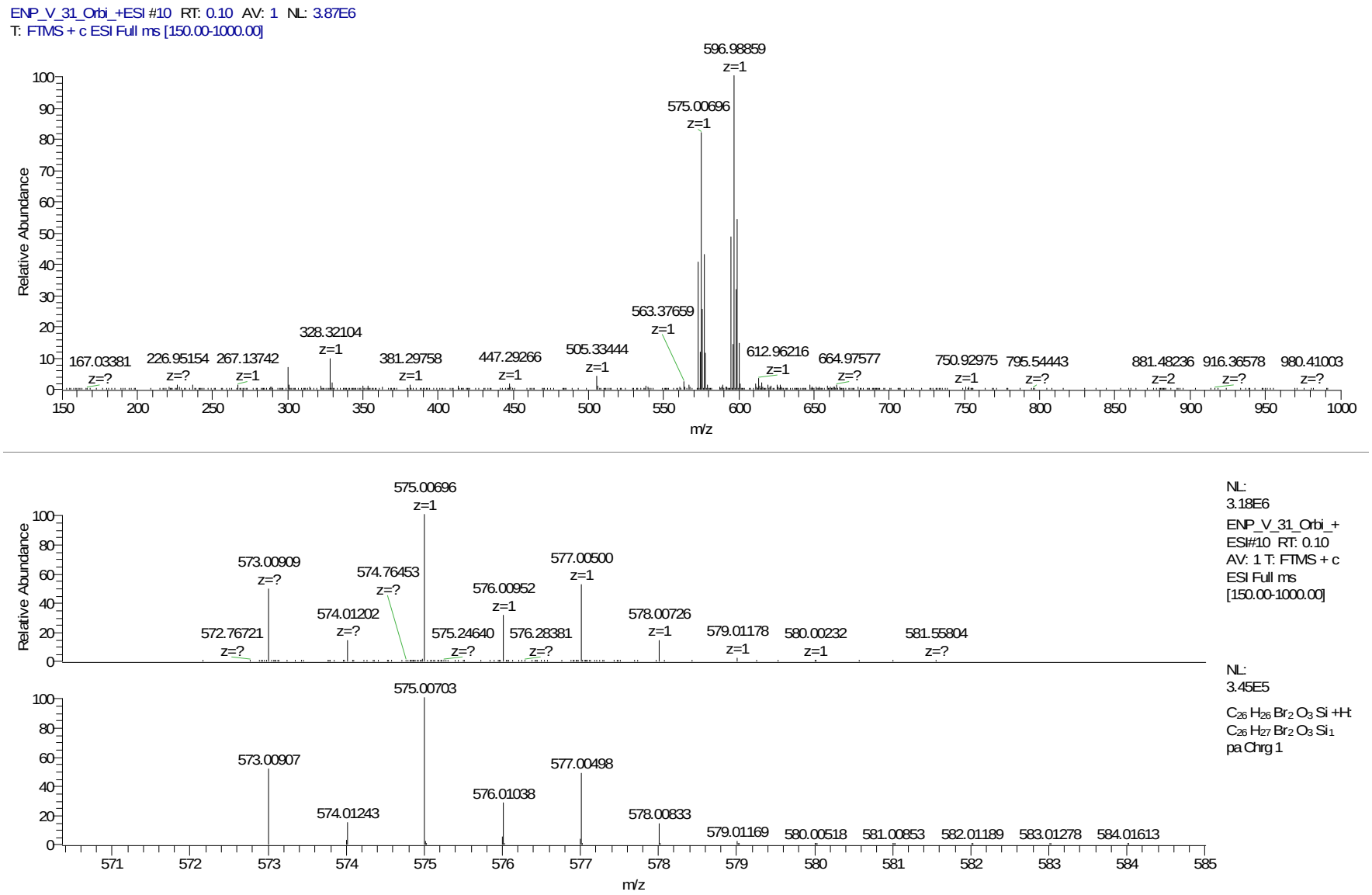
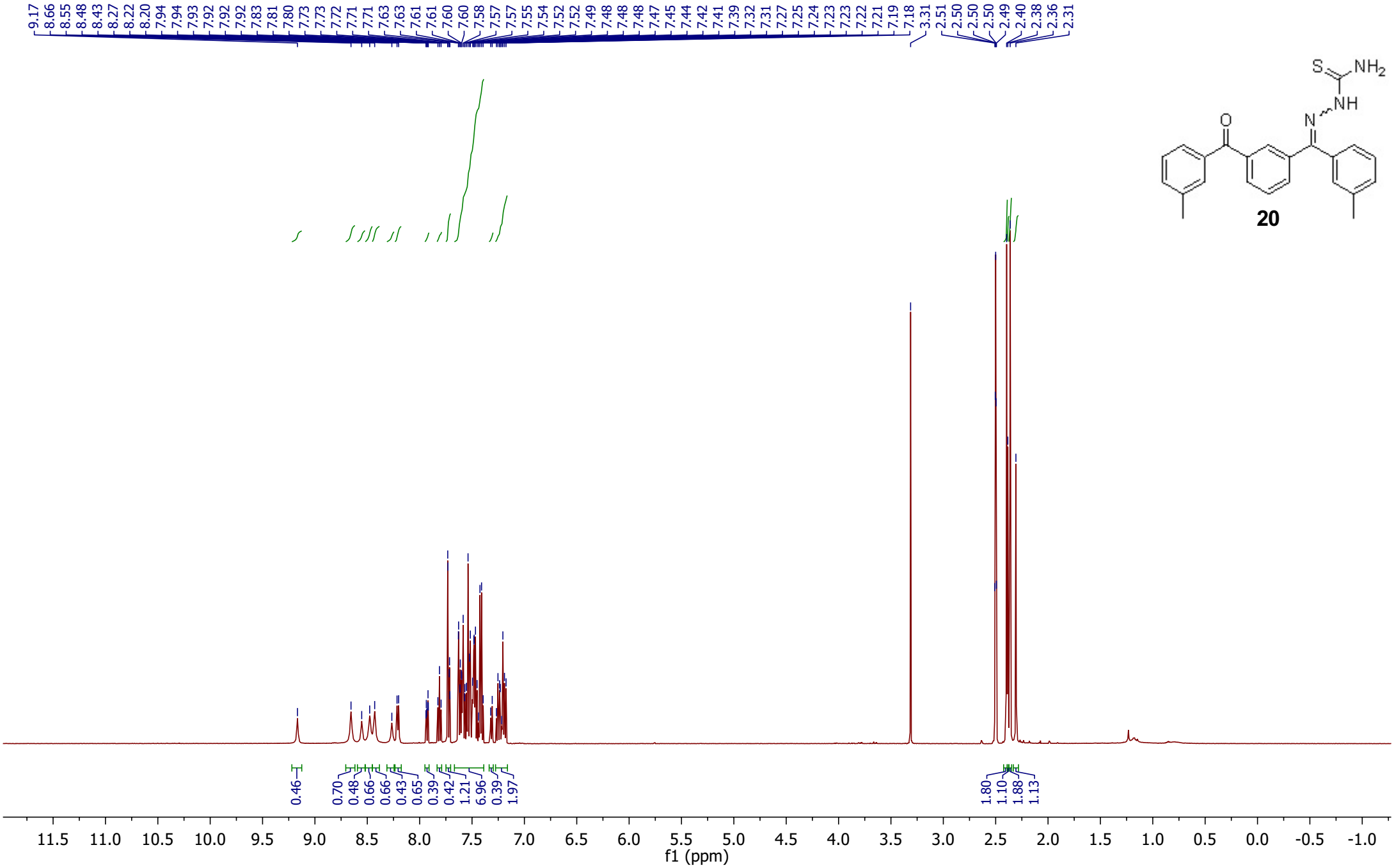
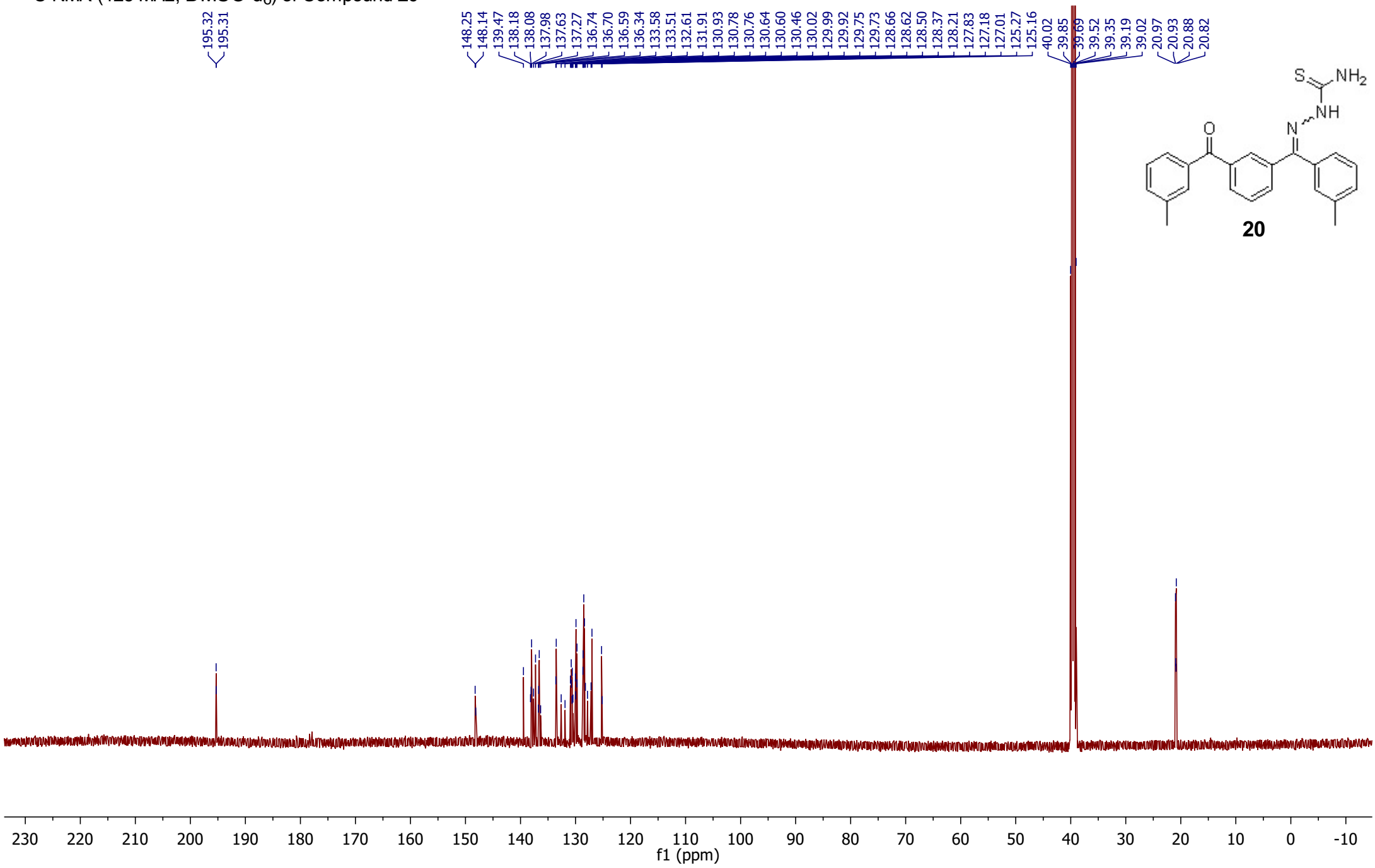


^{1}H NMR (500 MHz, DMSO-d_6) of Compound **20**



^{13}C NMR (125 MHz, DMSO-d_6) of Compound **20**



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Sample Name: ENPIV09

HPLC trace for Compound 20

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Last changed    : 4/30/2014 10:29:31 PM by ERICAP
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Last changed    : 6/12/2014 9:09:01 PM by ERICAP
                  (modified after loading)
Sample Info     : ENP-IV-09

                  Method:

                  0-25 Min. 50:70 to 90:10 ACN:Water
                  25-30 min 90:10 ACN:Water
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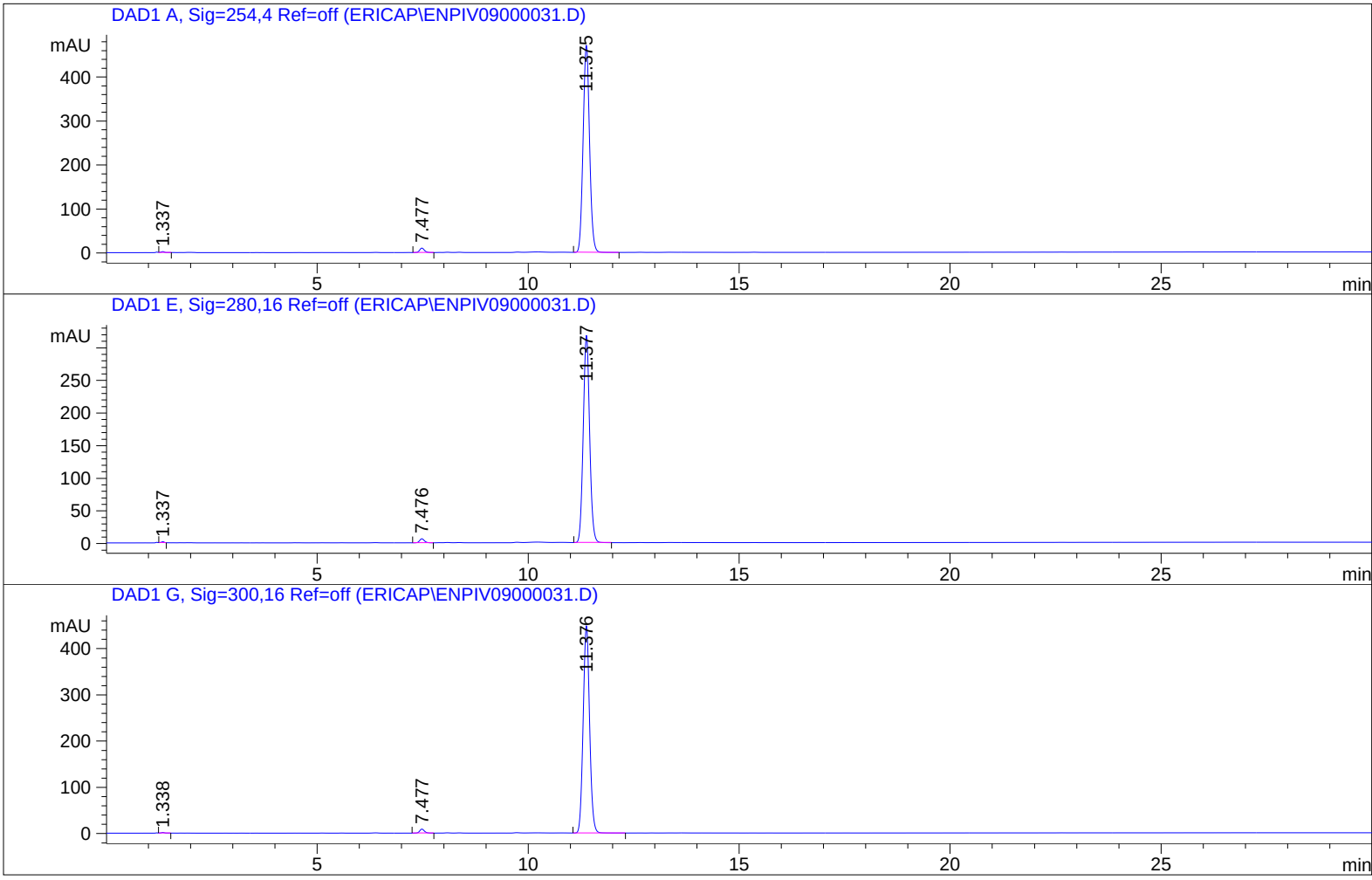
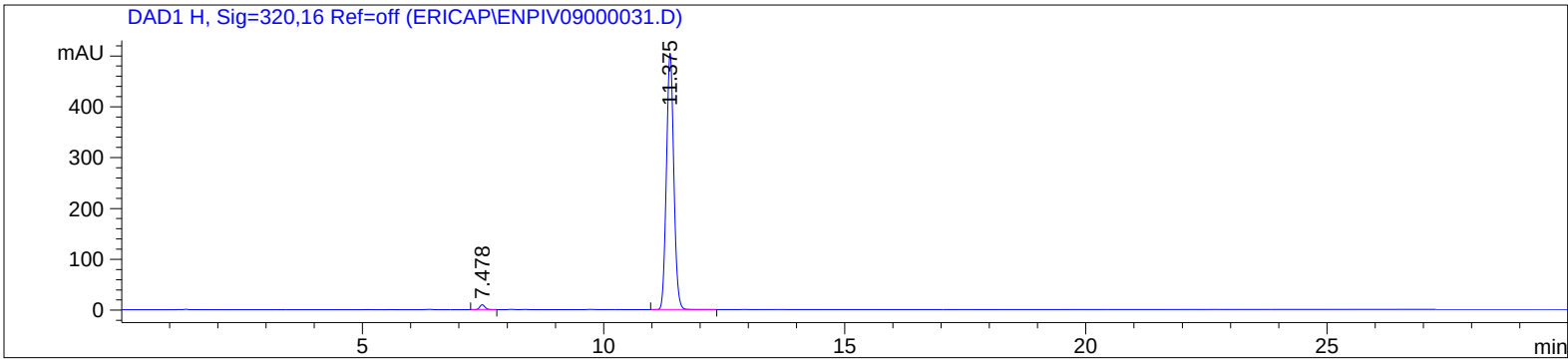
Exist as a mixture of E/Z geometrical isomers in solution as shown in H NMR spectra. One peak observed in HPLC trace.



HPLC trace for Compound 20



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.337	VB	0.0842	12.07581	2.19581	0.2375
2	7.477	BB	0.1215	79.19593	10.09940	1.5578
3	11.375	BB	0.1637	4992.60352	470.76309	98.2047
Totals :				5083.87525	483.05830	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.337	BB	0.0718	6.55098	1.47447	0.1934
2	7.476	BB	0.1222	48.78468	6.17627	1.4403
3	11.377	BB	0.1624	3331.74487	317.57977	98.3663
Totals :				3387.08054	325.23052	

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.338	VB	0.0853	7.19908	1.28711	0.1497
2	7.477	BB	0.1205	67.01131	8.63634	1.3932
3	11.376	BB	0.1632	4735.58984	448.44730	98.4571
Totals :				4809.80023	458.37075	

HPLC trace for Compound 20

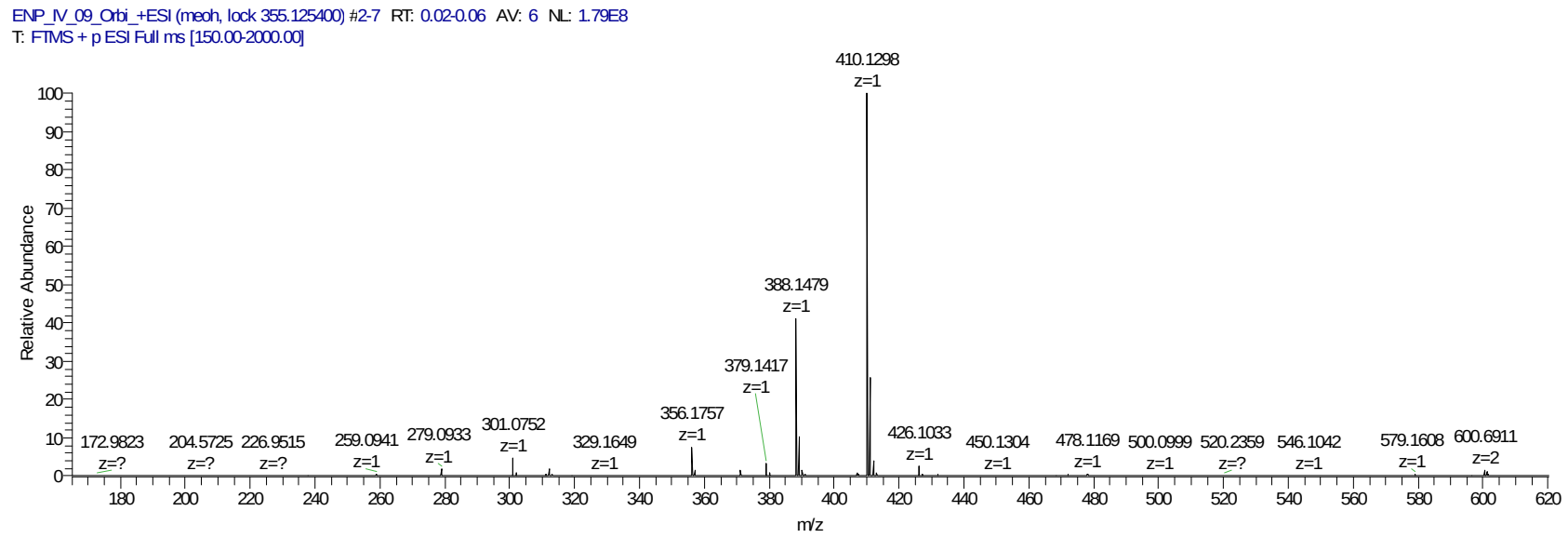
Signal 4: DAD1 H, Sig=320,16 Ref=off

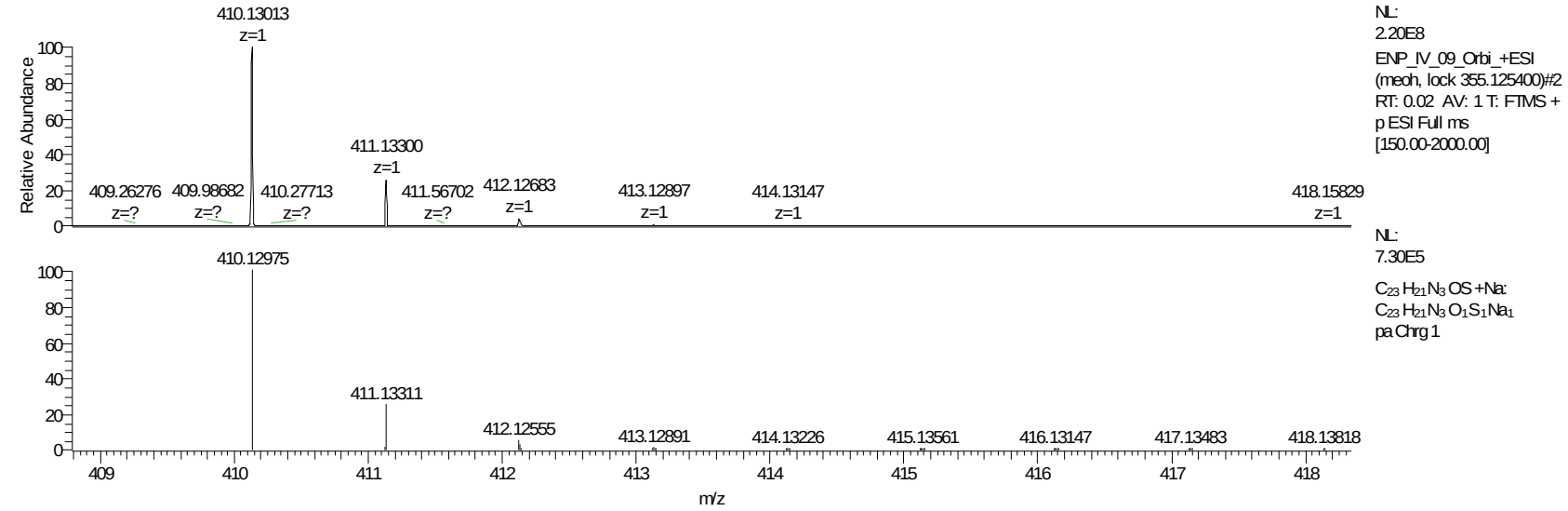
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.478	BB	0.1178	74.80412	9.71347	1.3800
2	11.375	BB	0.1637	5345.67920	504.13174	98.6200
Totals :				5420.48331	513.84521	

*** End of Report ***

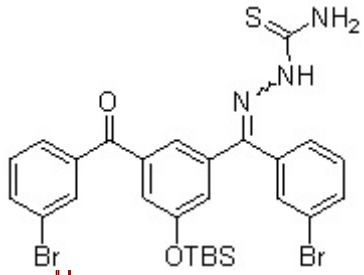
HRMS (ESI) for Compound **20**

ENP_IV_09_Orbi_+ESI (meoh, lock 355.1... 5/7/2014 11:01:35 PM





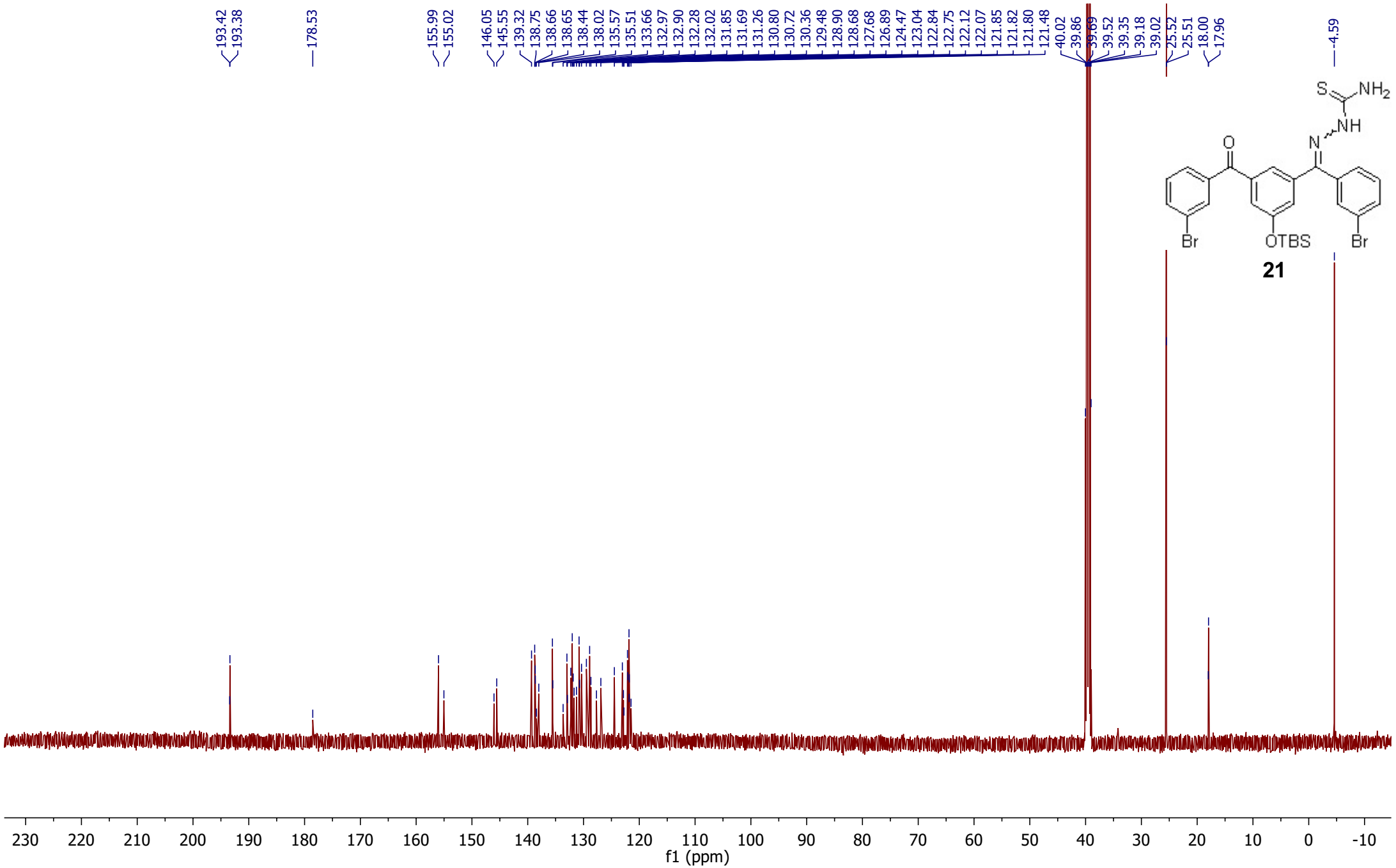
^{1}H NMR (500 MHz, DMSO-d_6) of Compound **21**



21

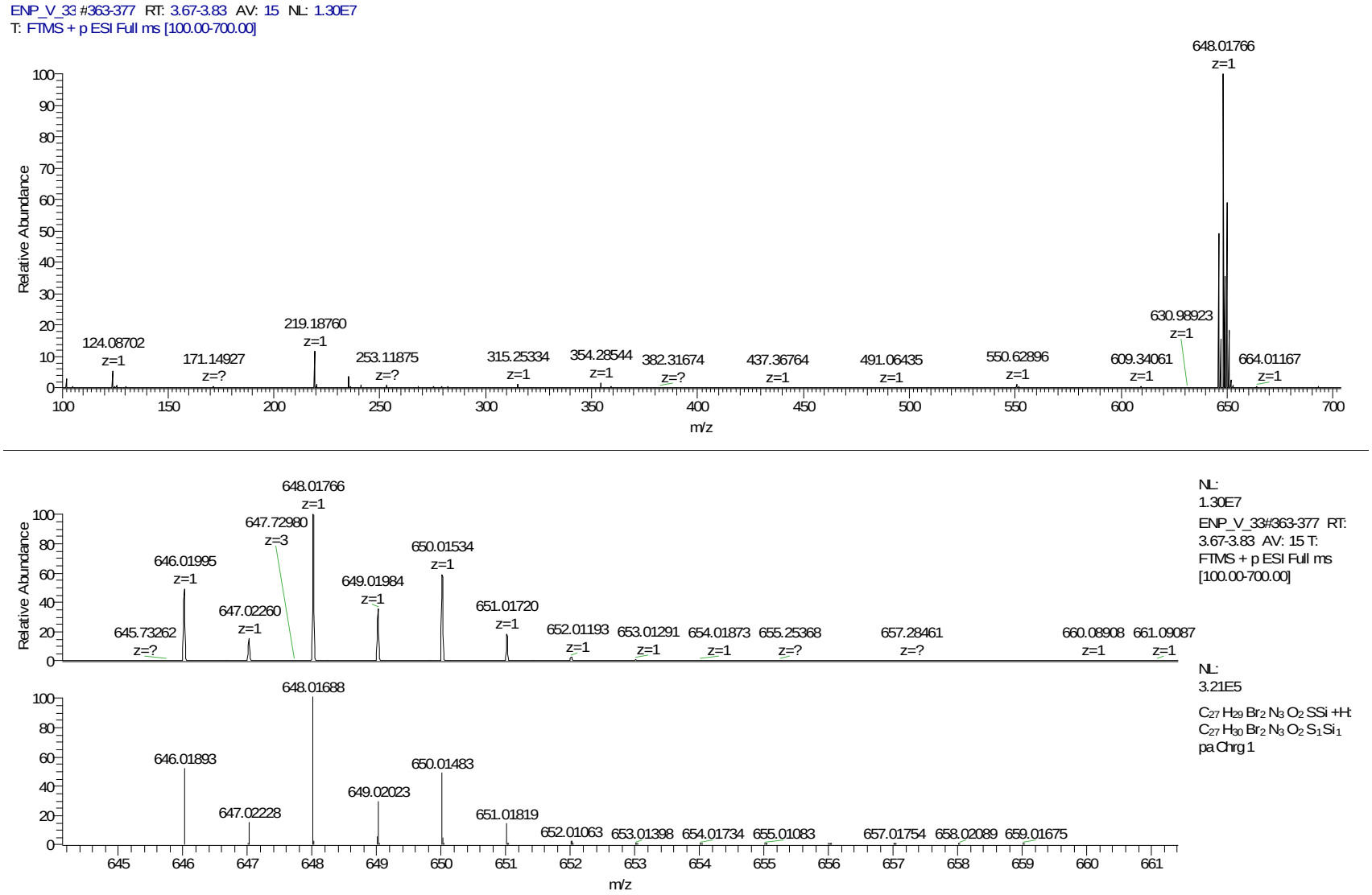
f1 (ppm)

^{13}C NMR (125 MHz, DMSO-d_6) of Compound **21**

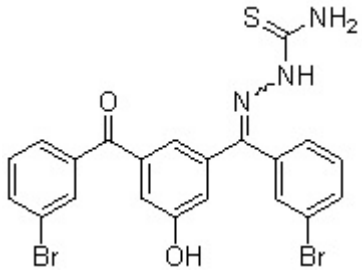


HRMS (ESI) for Compound **21**

C:\Xcalibur\...\Erica\12-19-14\ENP_V_33 12/19/2014 11:52:10 AM



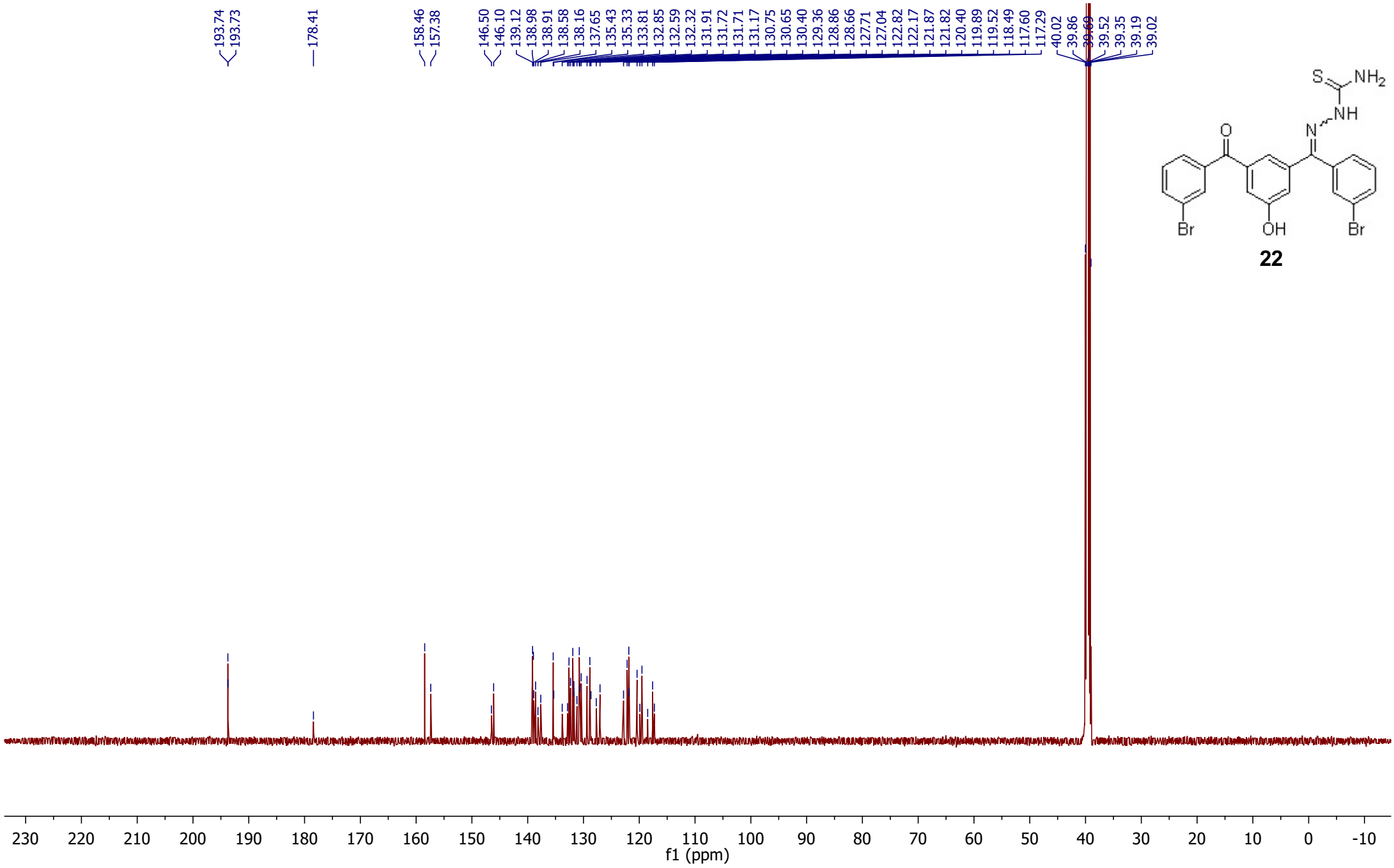
^{1}H NMR (500 MHz, DMSO-d_6) of Compound **22**



22

f1 (ppm)

^{1}H NMR (500 MHz, DMSO-d_6) of Compound **22**



Data File C:\CHEM32\1\DATA\ERICAP\ENPV34000032.D
Sample Name: ENPV34

HPLC trace for Compound 22

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Acq. Instrument : Instrument 1                    Location :   -
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Last changed    : 4/23/2014 9:43:22 PM by ERICAP
Analysis Method : C:\CHEM32\1\DATA\ERICAP\ENPV34000032.D\DA.M (GRAD 2 30-90 ACN.M)
Last changed    : 6/12/2014 11:25:01 PM by ERICAP
                  (modified after loading)
Sample Info     : ENP-V-34

                  Method:

                  0-25 Min. 30:70 to 90:10 ACN:Water
                  25-30 min 90:10 ACN:Water
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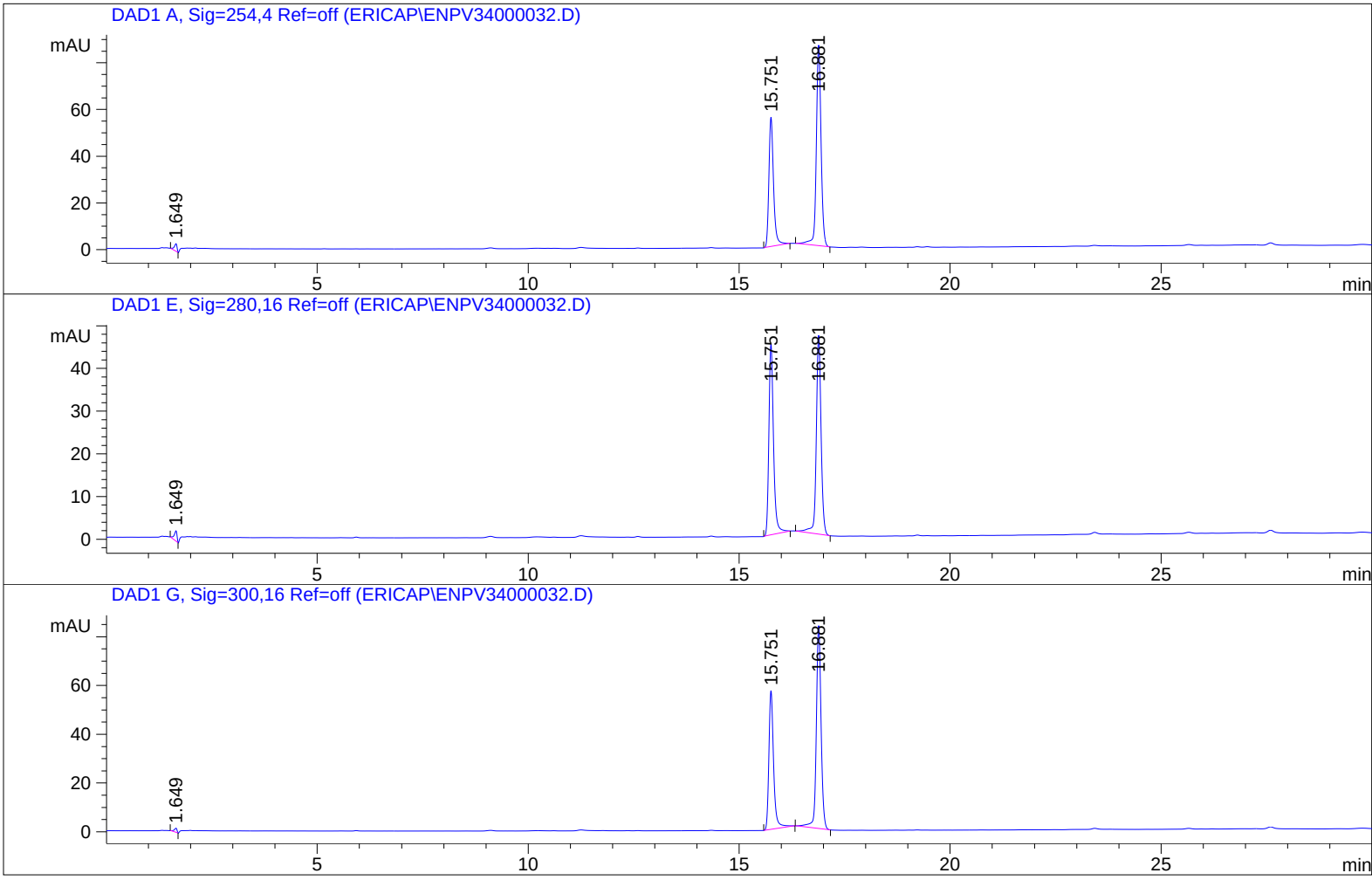
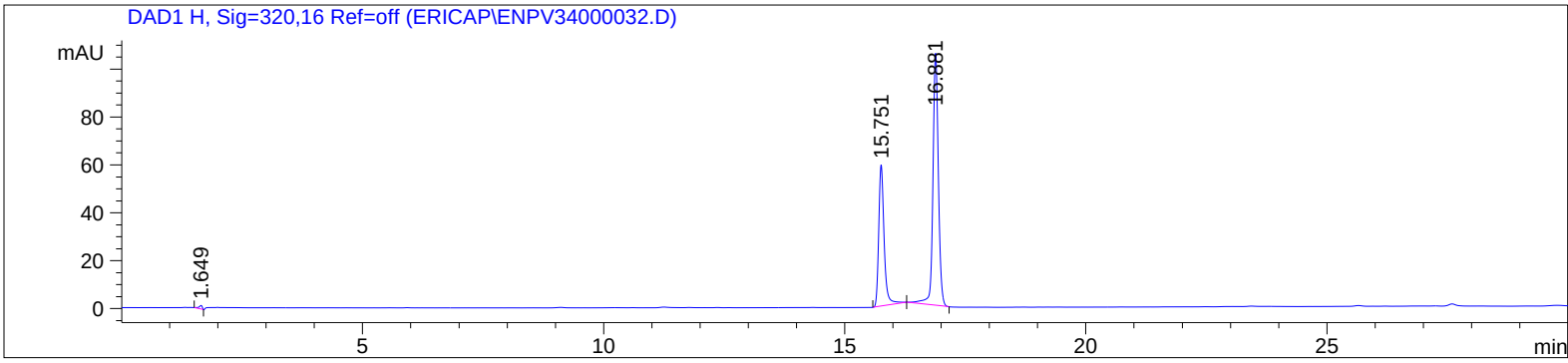
Two peaks observed in the HPLC traces are due to the presence of both E and Z geometrical isomers.



Data File C:\CHEM32\1\DATA\ERICAP\ENPV34000032.D
Sample Name: ENPV34

HPLC trace for Compound 22



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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.649	BB	0.0681	14.61391	3.27222	1.3158
2	15.751	BB	0.1150	422.91922	55.41271	38.0777
3	16.881	BB	0.1193	673.14227	85.99469	60.6066
Totals :				1110.67541	144.67962	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.649	BB	0.0712	11.05270	2.42217	1.5396
2	15.751	BB	0.1148	340.31268	44.72145	47.4036
3	16.881	BB	0.1198	366.53976	46.58216	51.0569
Totals :				717.90515	93.72577	

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.649	BB	0.0716	7.99208	1.74052	0.7262
2	15.751	BB	0.1163	440.12030	56.88736	39.9926
3	16.881	BB	0.1194	652.39142	83.24355	59.2812
Totals :				1100.50380	141.87144	

HPLC trace for Compound 22

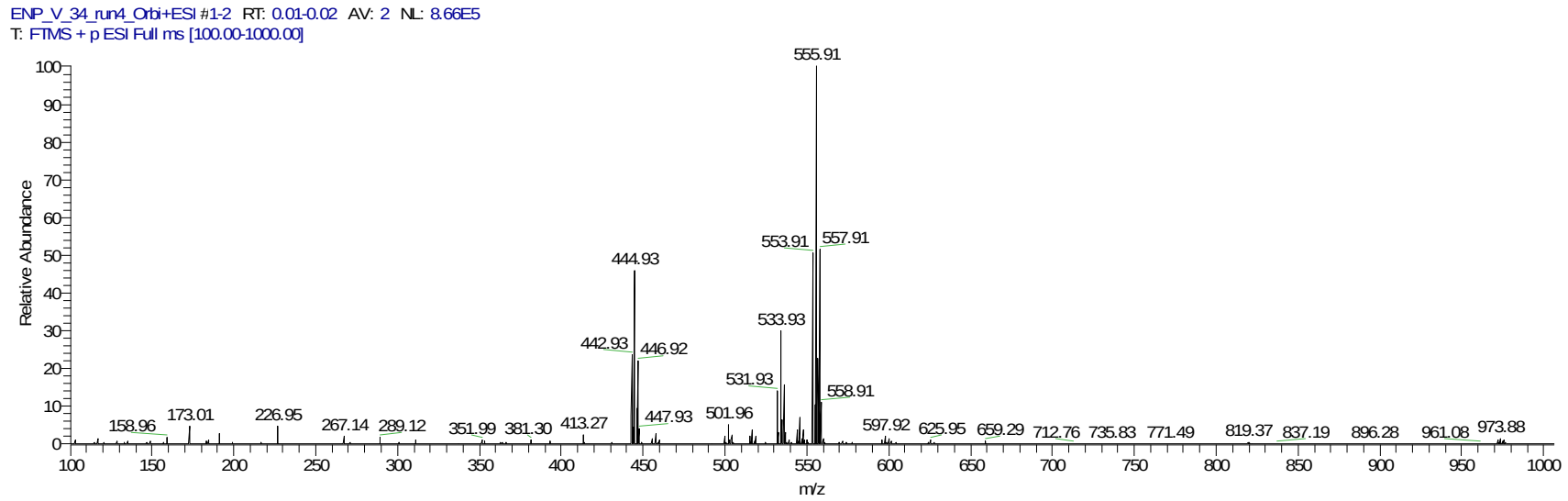
Signal 4: DAD1 H, Sig=320,16 Ref=off

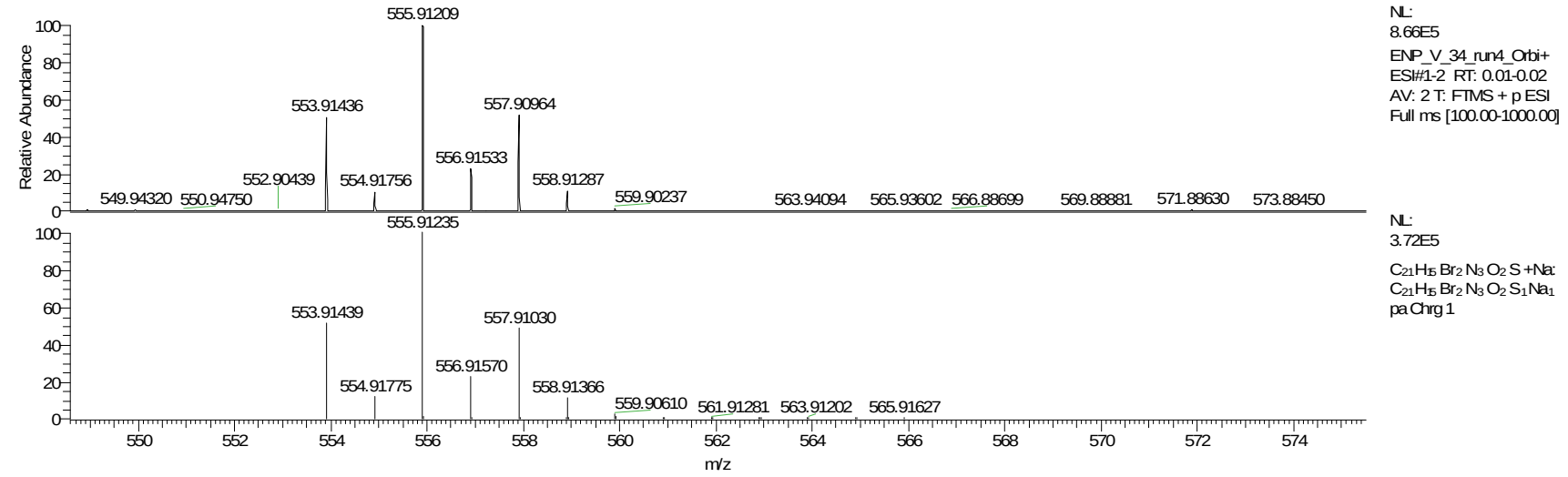
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.649	BB	0.0707	7.10945	1.51755	0.5515
2	15.751	BB	0.1161	455.21680	58.96165	35.3130
3	16.881	BB	0.1196	826.76489	105.30540	64.1355
Totals :				1289.09114	165.78460	

*** End of Report ***

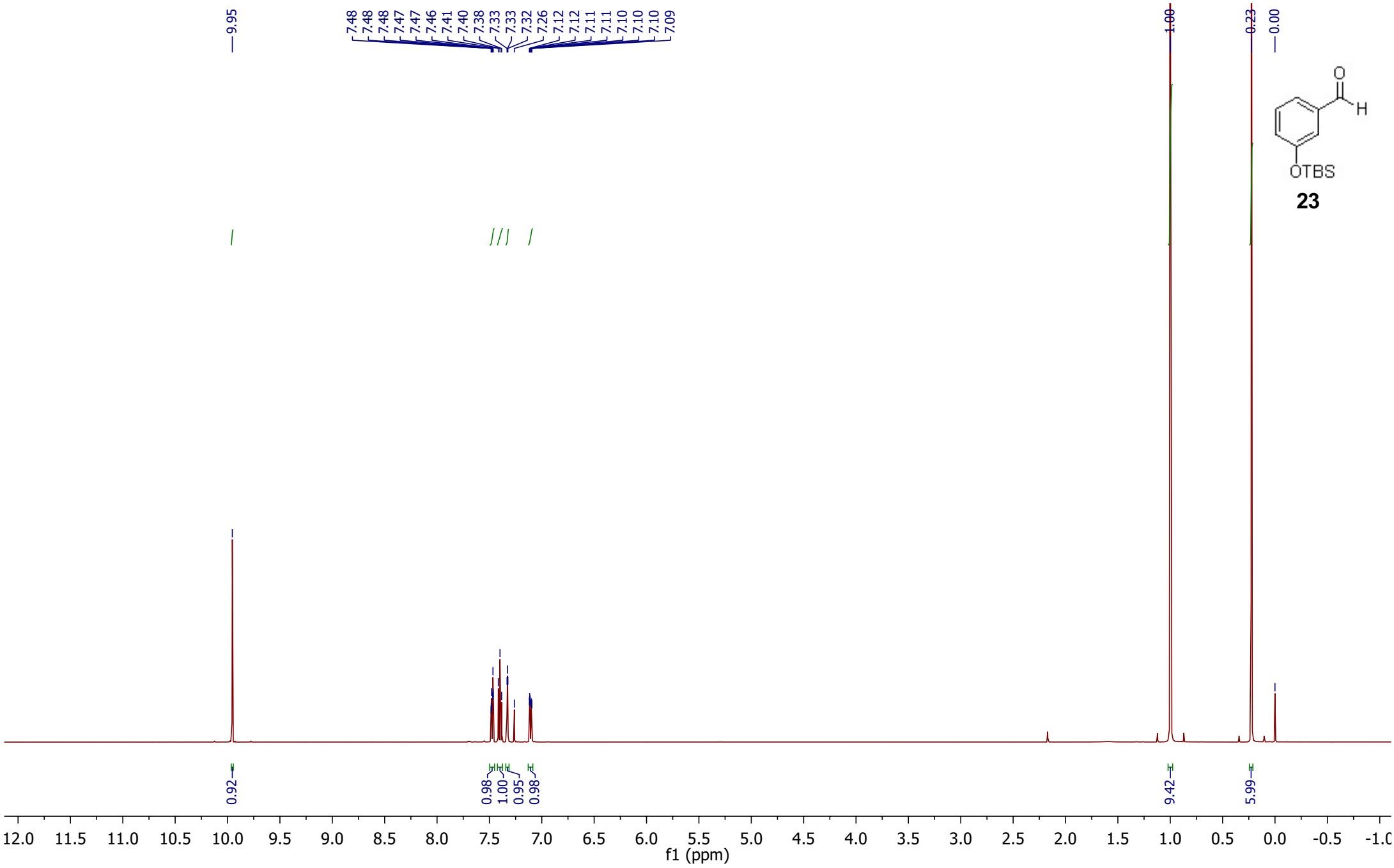
HRMS(ESI) for Compound **22**

C:\Xcalibur\...\ENP_V_34_run4_Orbi+ESI 1/13/2015 10:57:00 PM

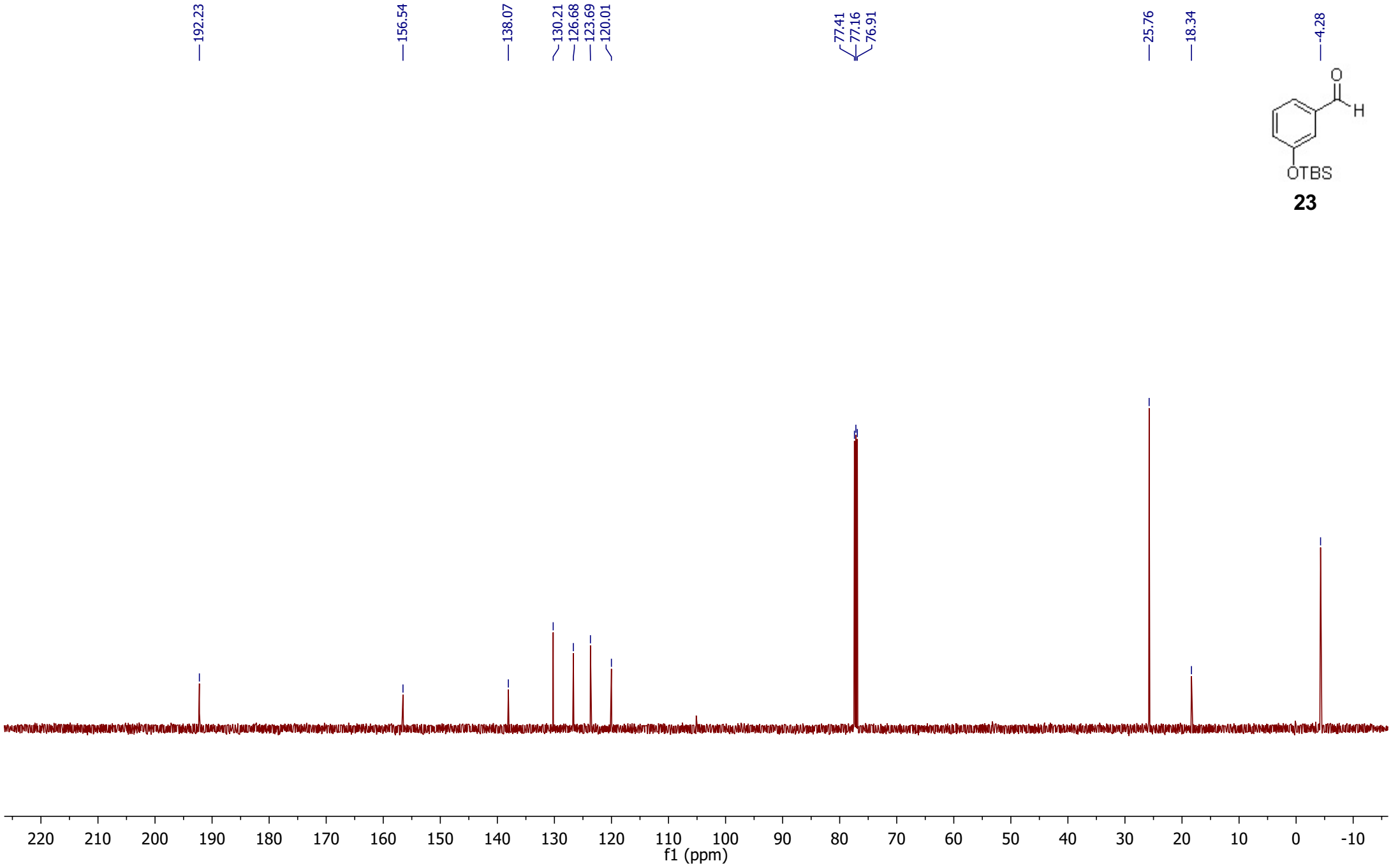




^{1}H NMR (500 MHz, $CDCl_3$) of Compound **23**



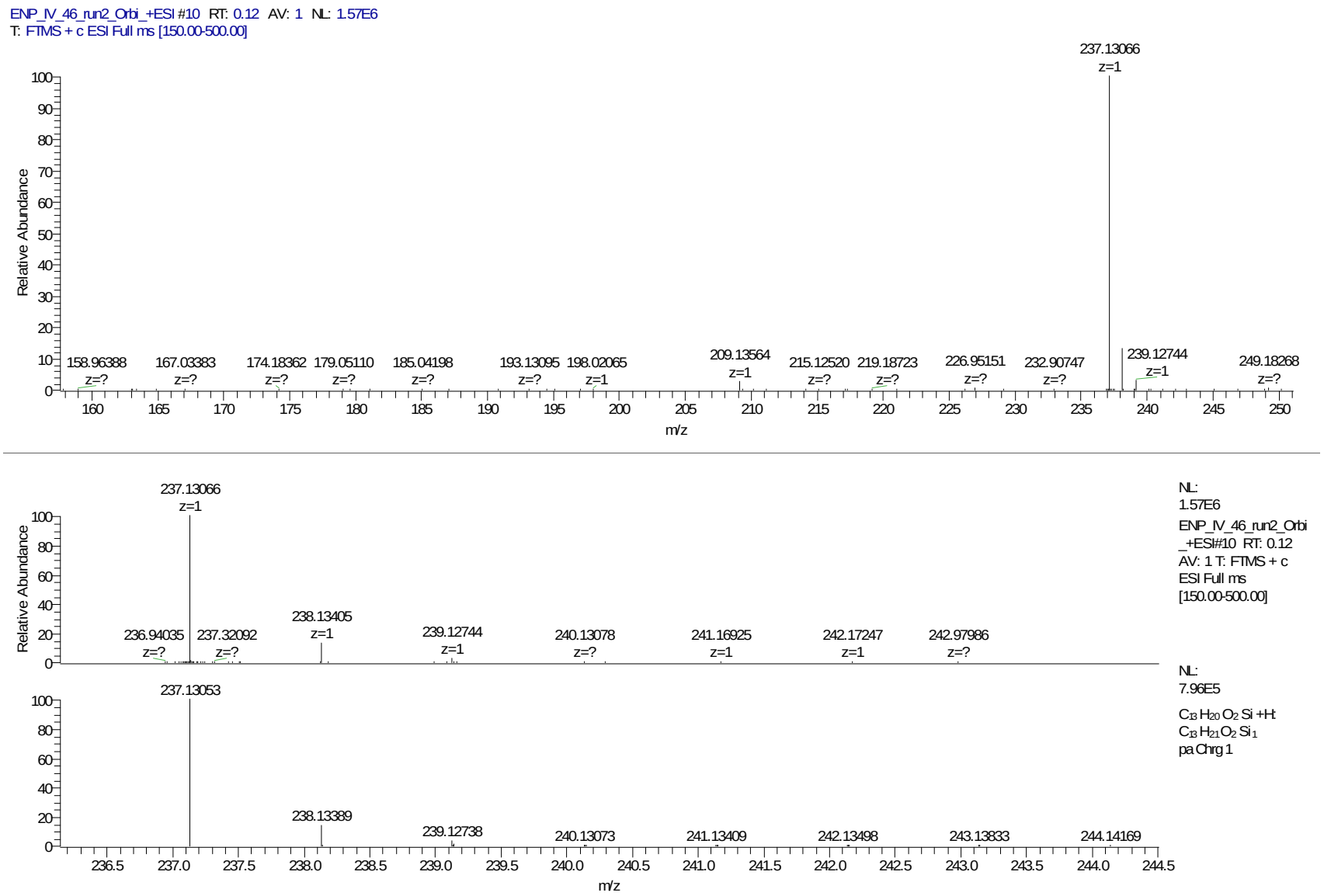
^{13}C NMR (125 MHz, $CDCl_3$) of Compound **23**



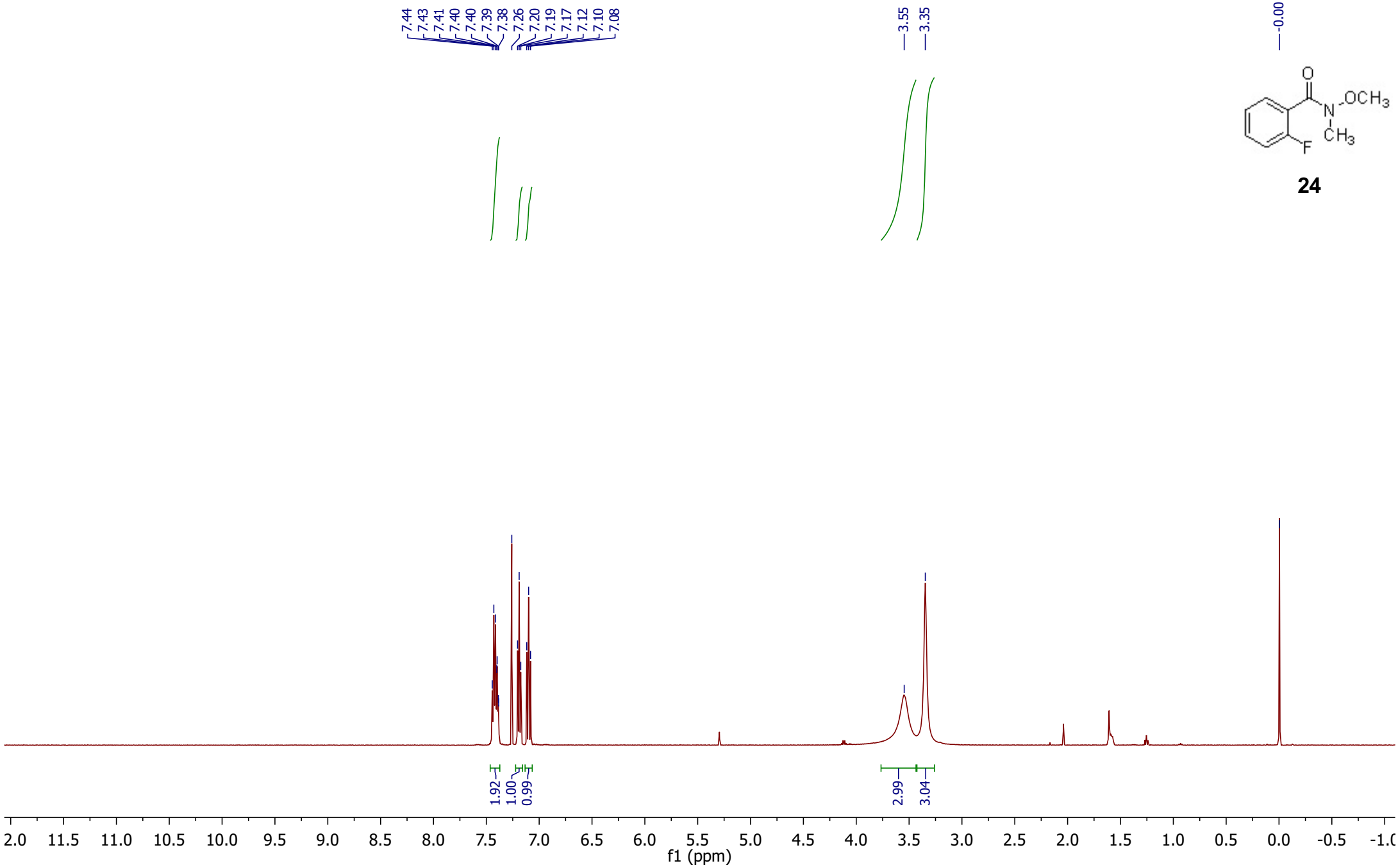
23

HRMS (ESI) for Compound **23**

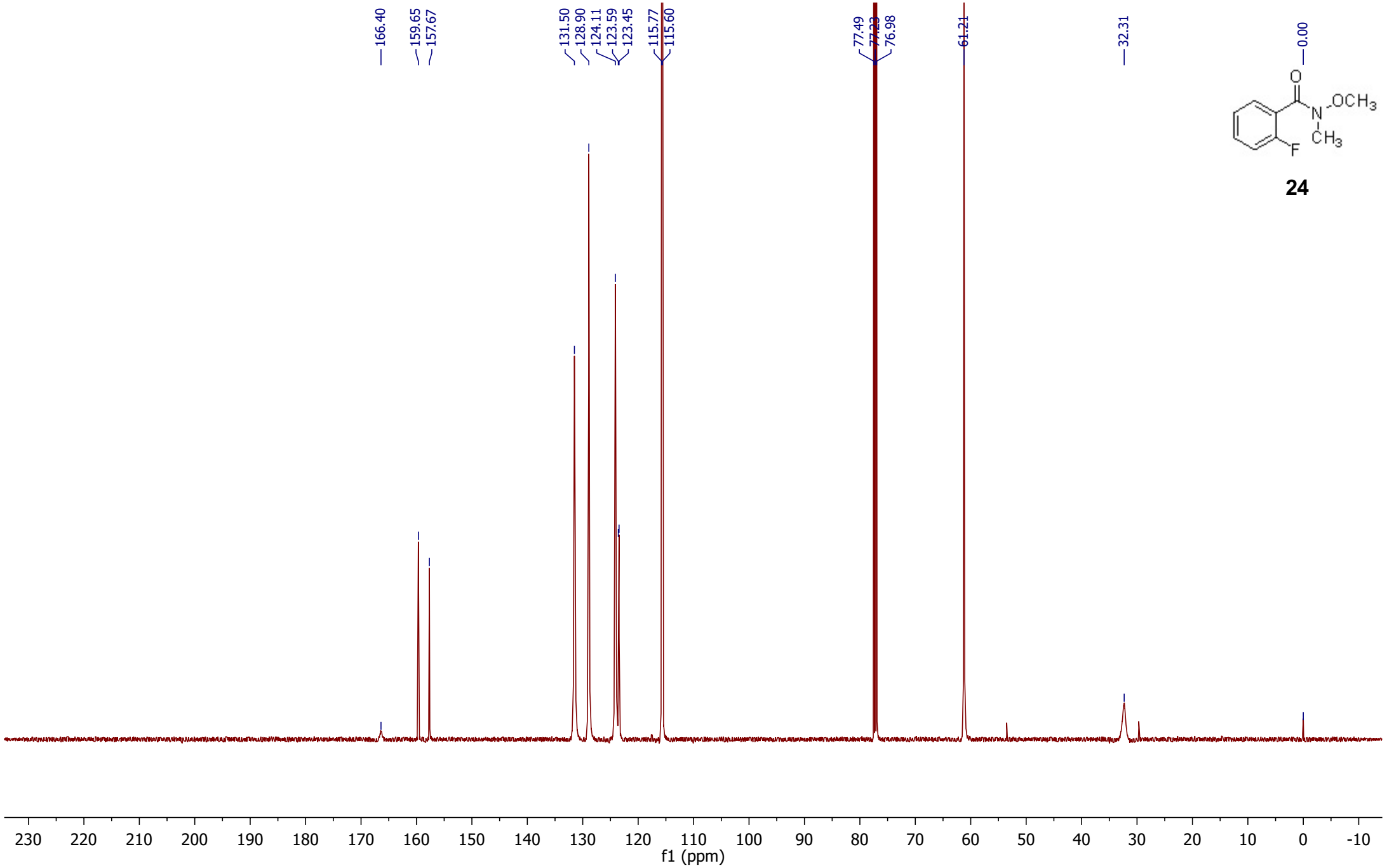
C:\Xcalibur\...\ENP_IV_46_run2_Orbi_+ESI 12/30/2014 7:22:33 PM



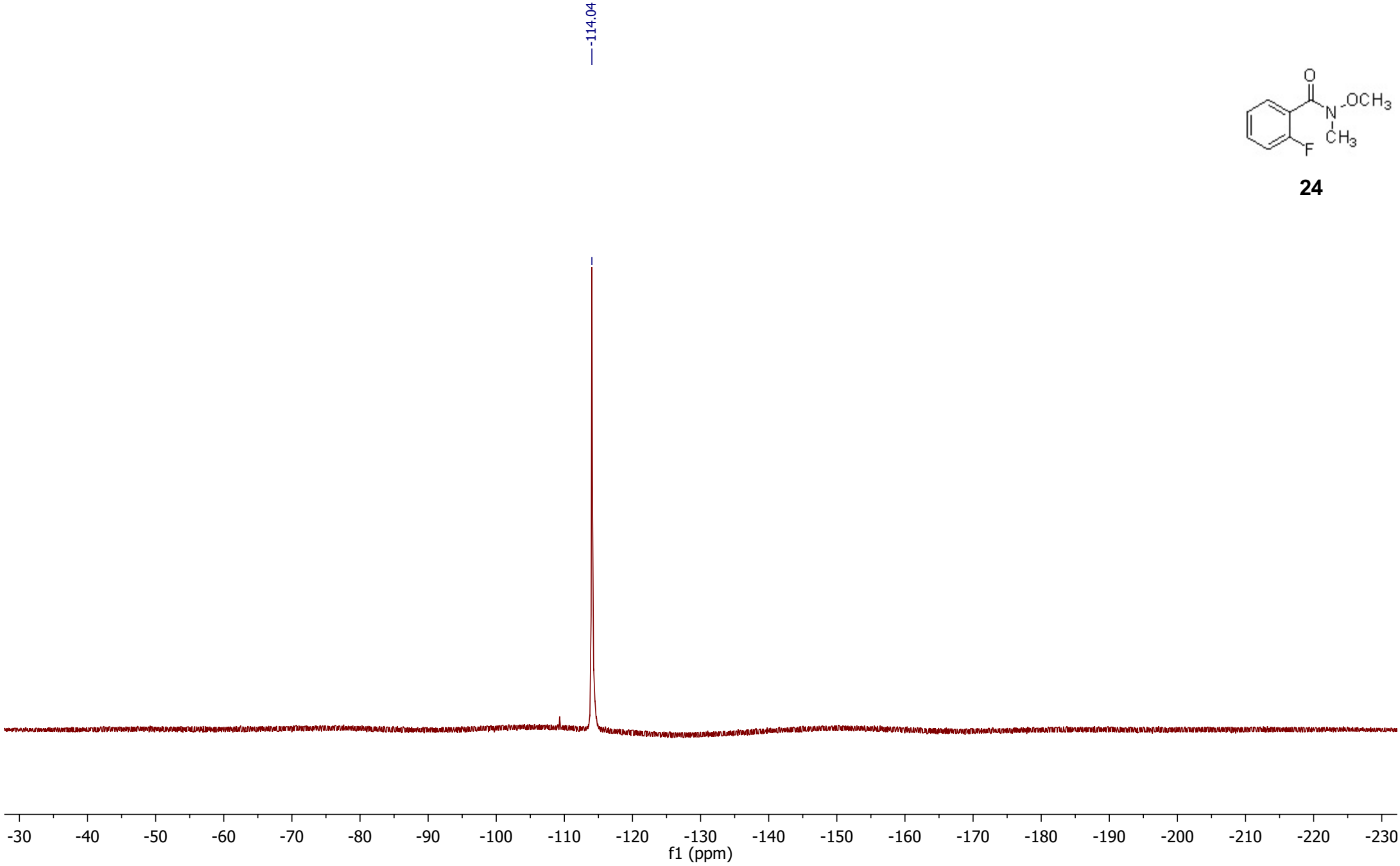
^{1}H NMR (500 MHz, $CDCl_3$) of Compound **24**



^{1}C NMR (125 MHz, $CDCl_3$) of Compound **24**



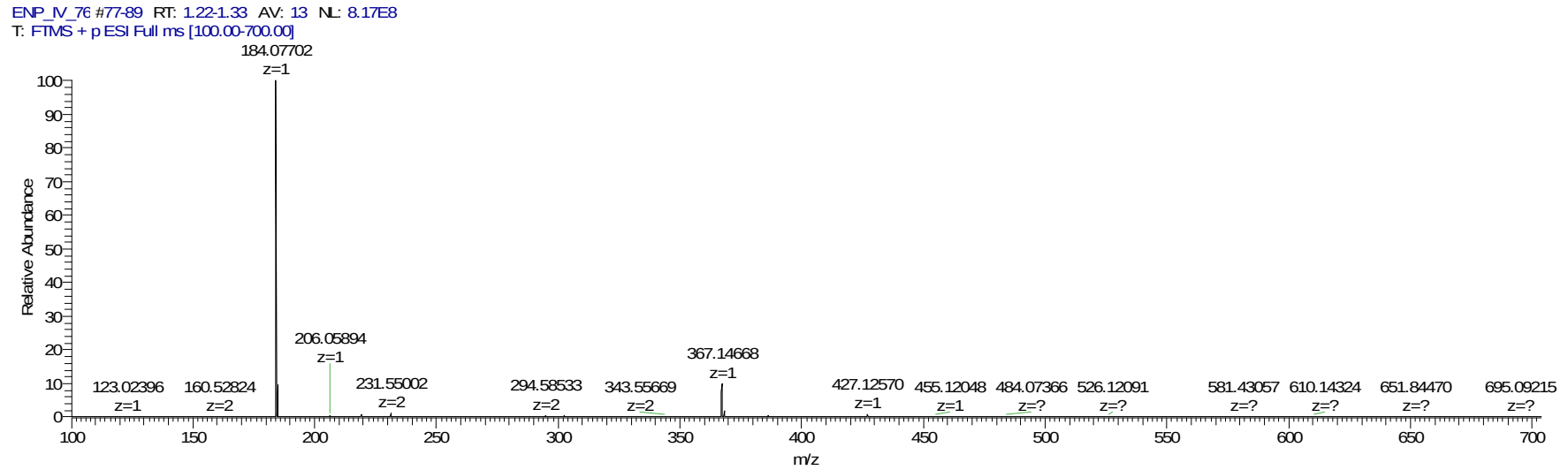
^{19}F NMR (470 MHz, $CDCl_3$) of Compound **24**

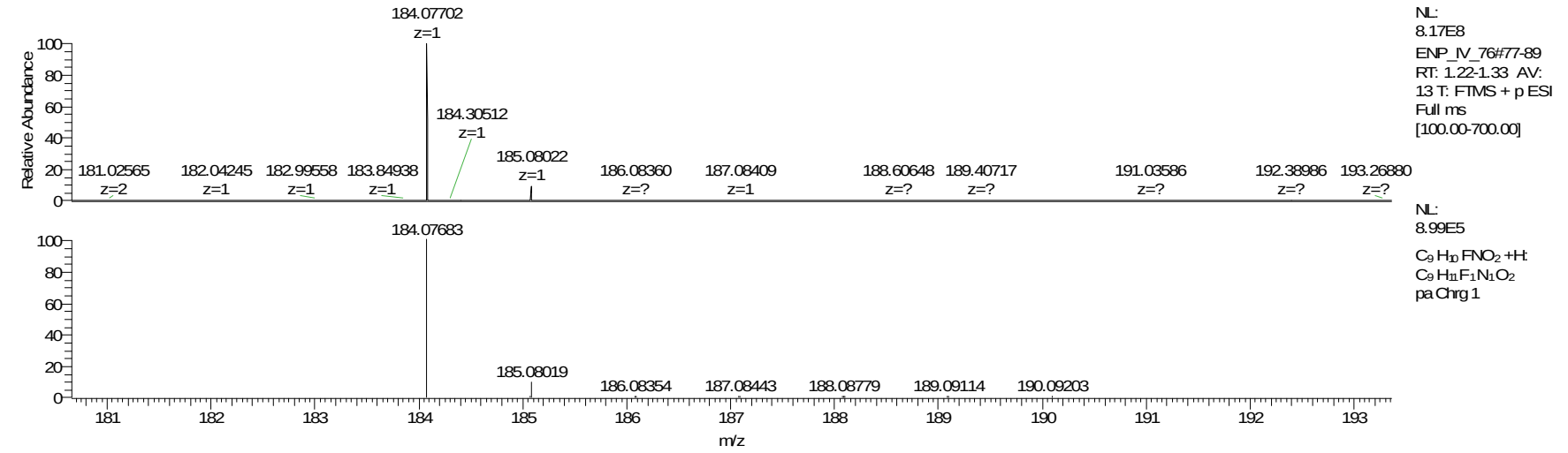


24

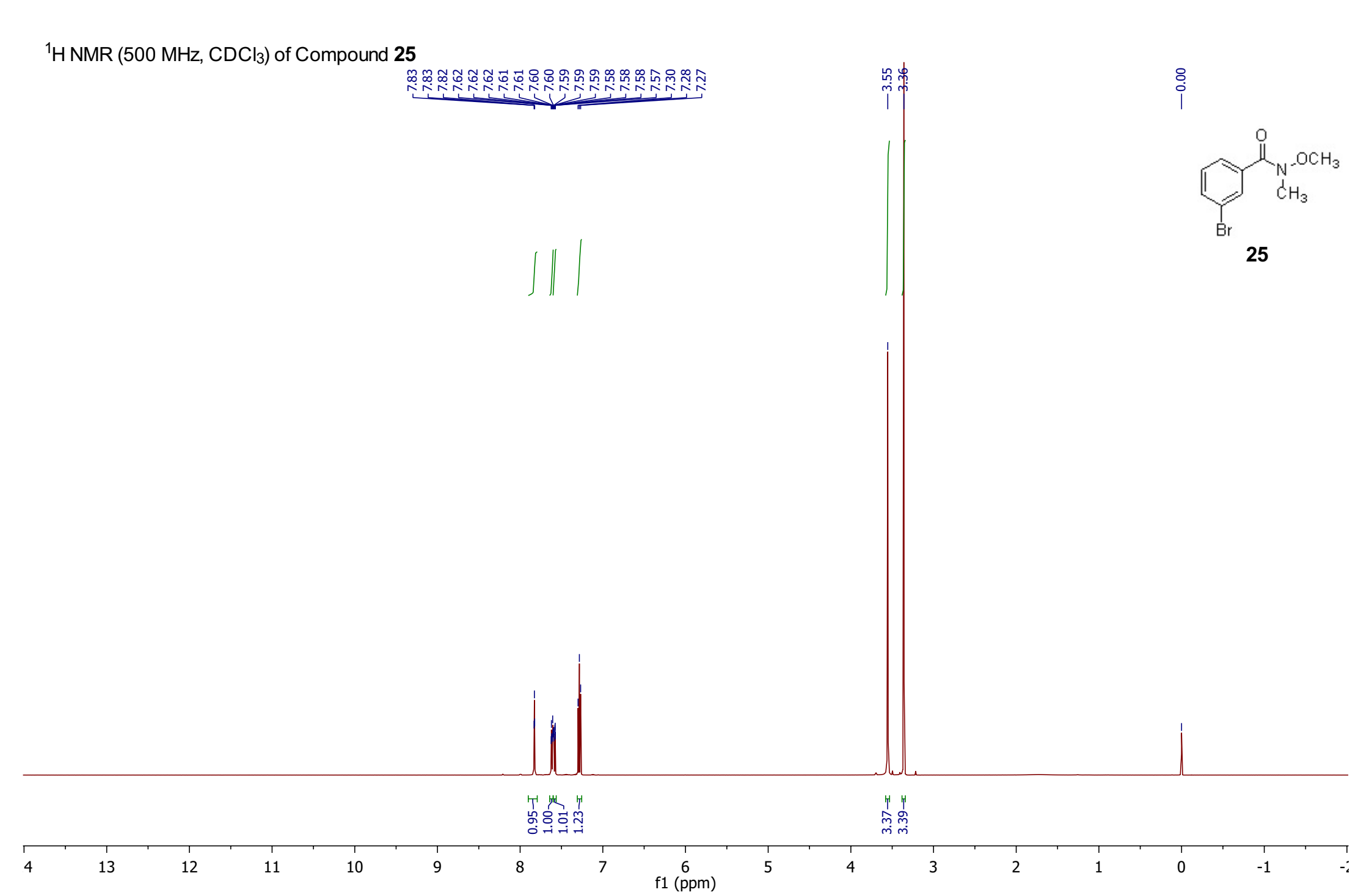
HRMS (ESI) for Compound **24**

C:\Xcalibur\...\Erica\12-19-14\ENP_IV_76 12/19/2014 10:37:50 AM

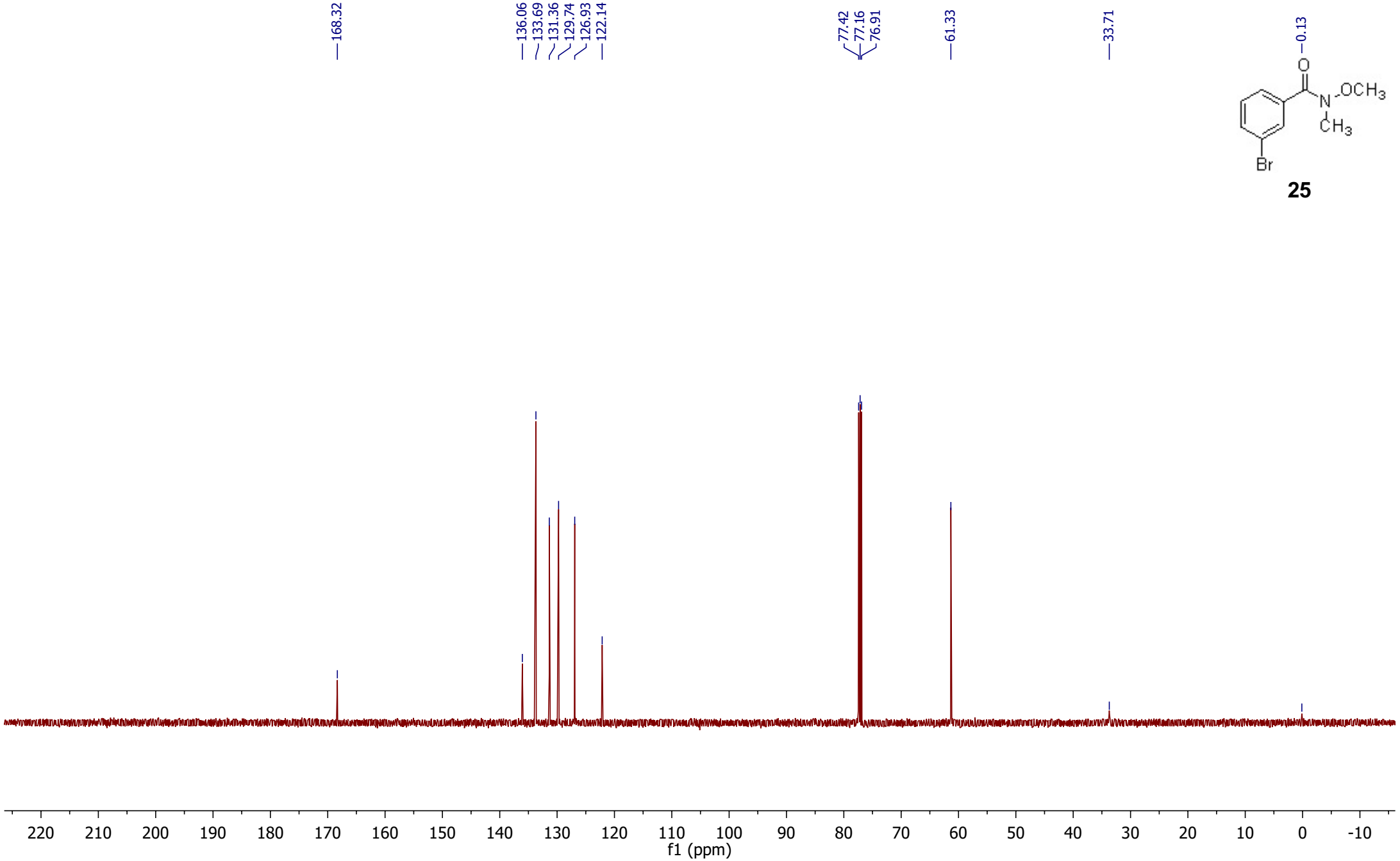




^{1}H NMR (500 MHz, $CDCl_3$) of Compound **25**

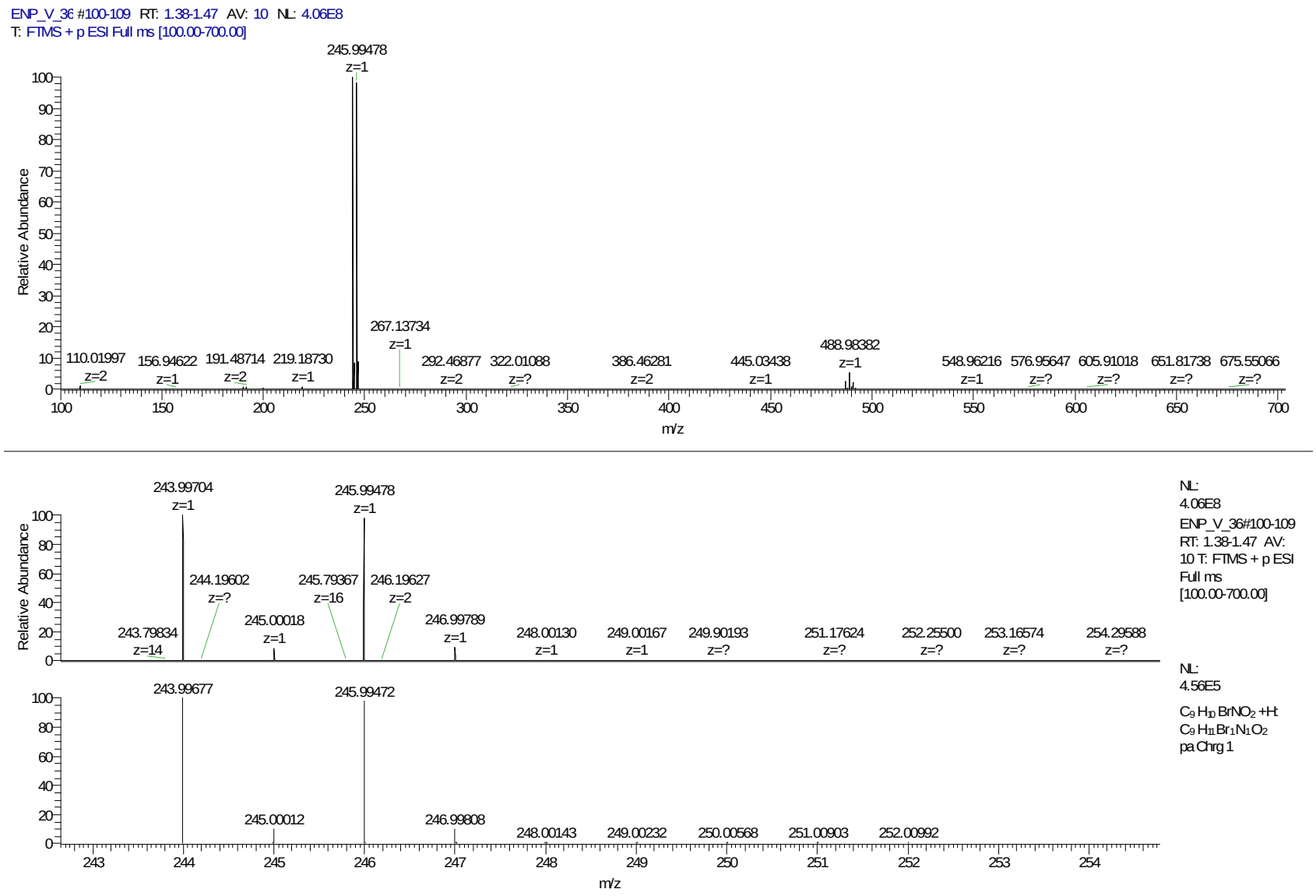


^{13}C NMR (125 MHz, $CDCl_3$) of Compound **25**

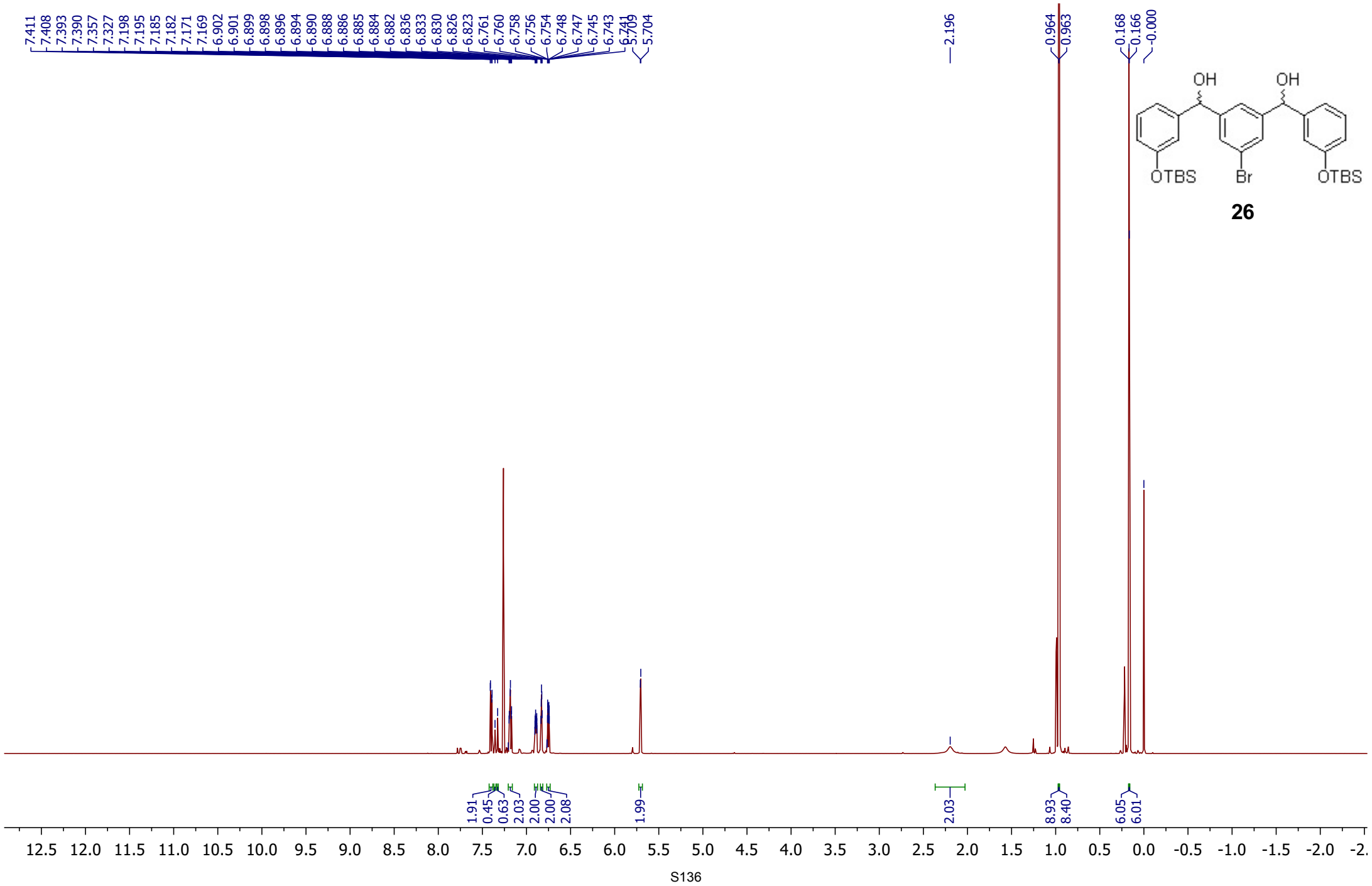


HRMS (ESI) for Compound **25**

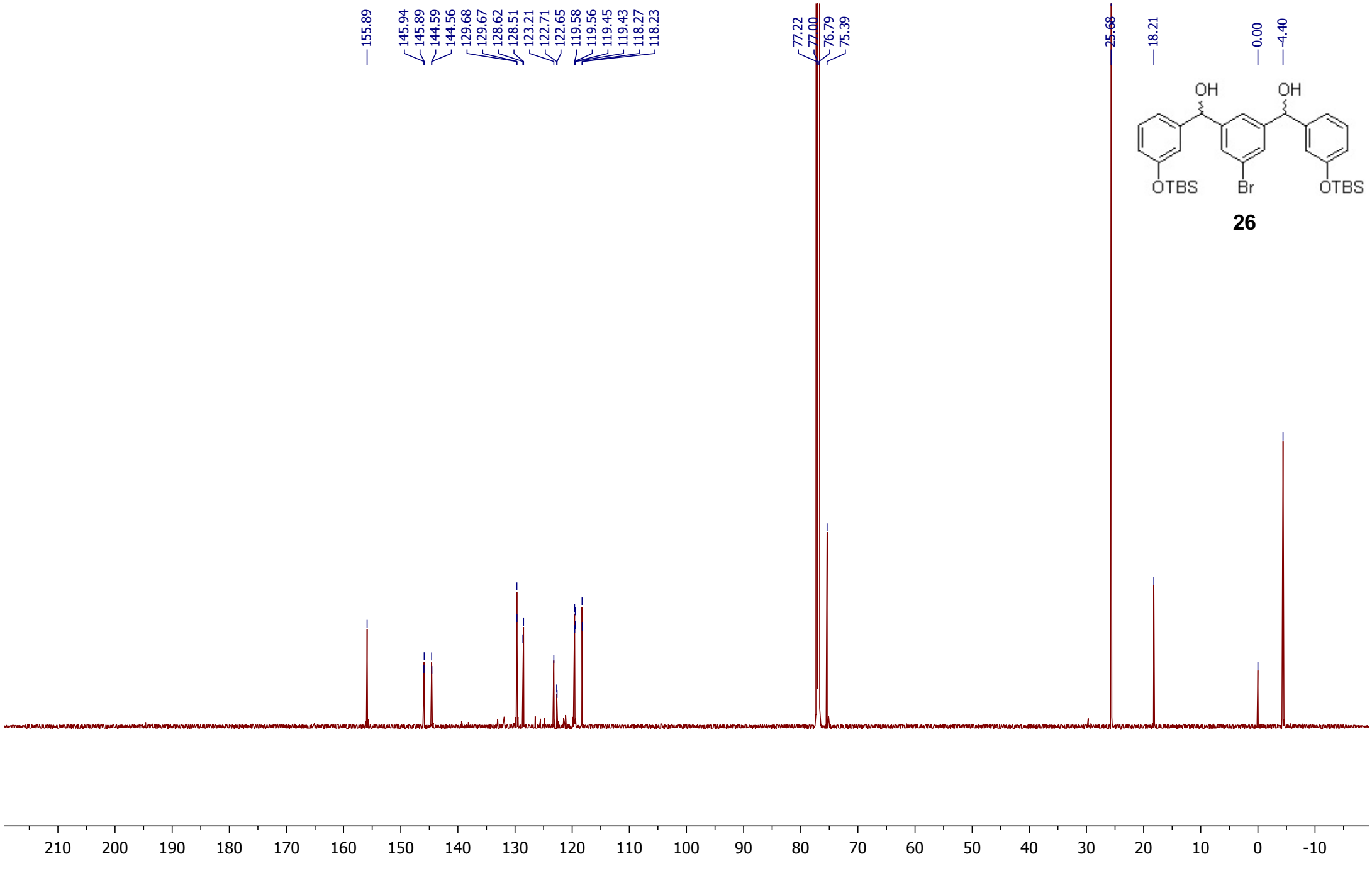
C:\Xcalibur\...\Erica\12-19-14\ENP_V_36 12/19/2014 12:45:21 PM



^{1}H NMR (600 MHz, $CDCl_3$) of Compound **26**



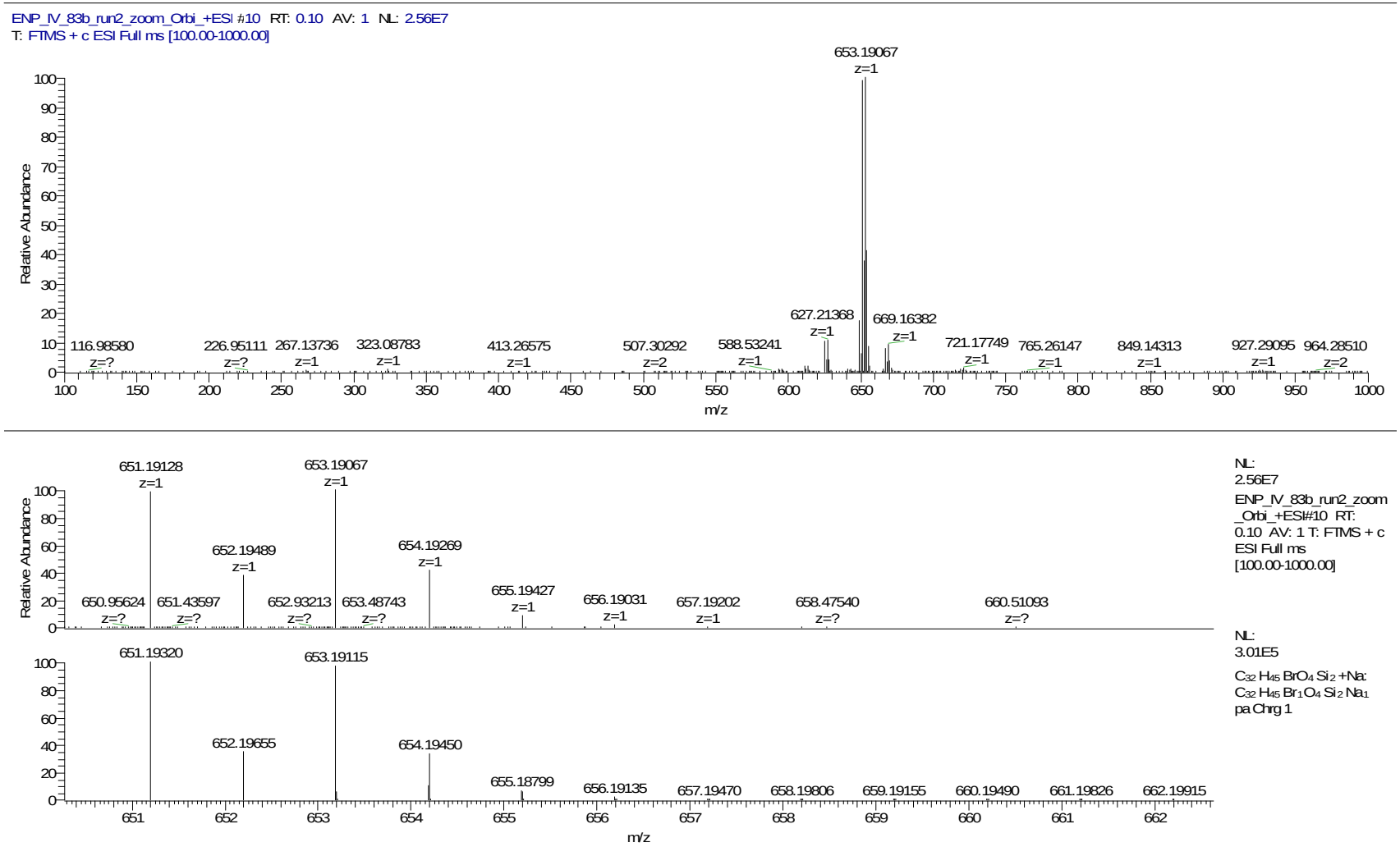
^{13}C NMR (150 MHz, $CDCl_3$) of Compound **26**



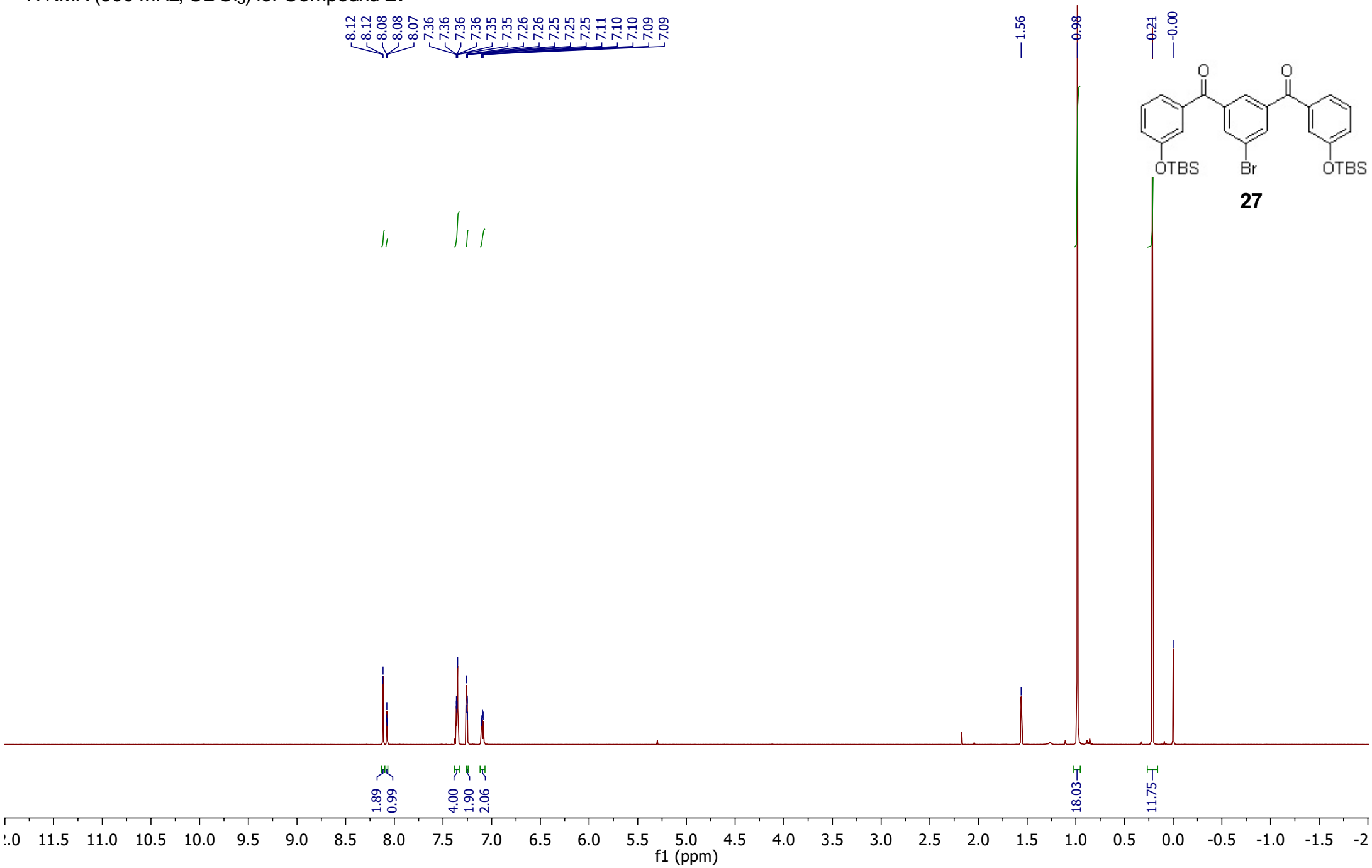
26

HRMS (ESI) for Compound **26**

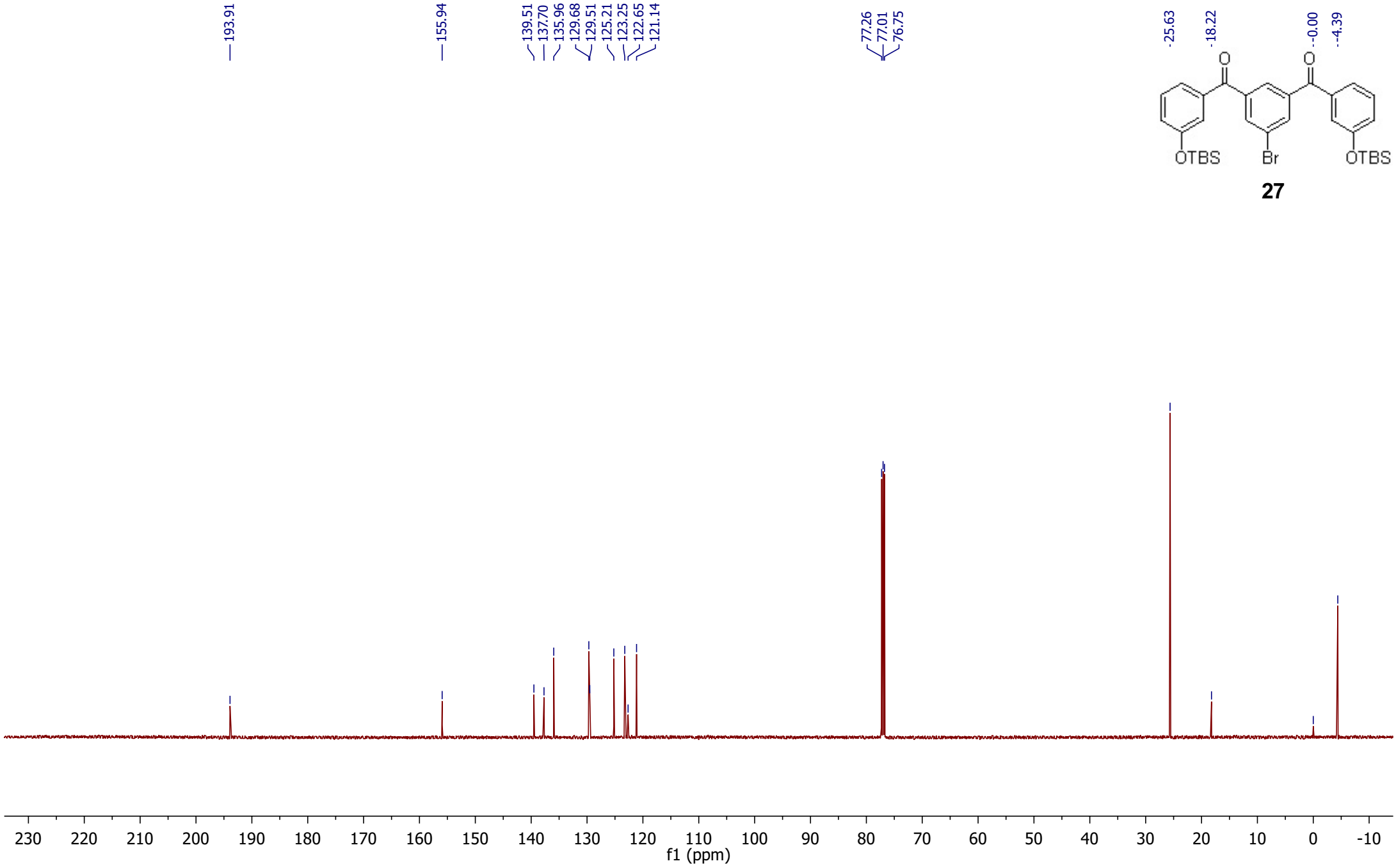
ENP_IV_83b_run2_zoom_Orbi_+ESI 12/30/2014 9:48:09 PM



^{1}H NMR (500 MHz, $CDCl_3$) for Compound **27**



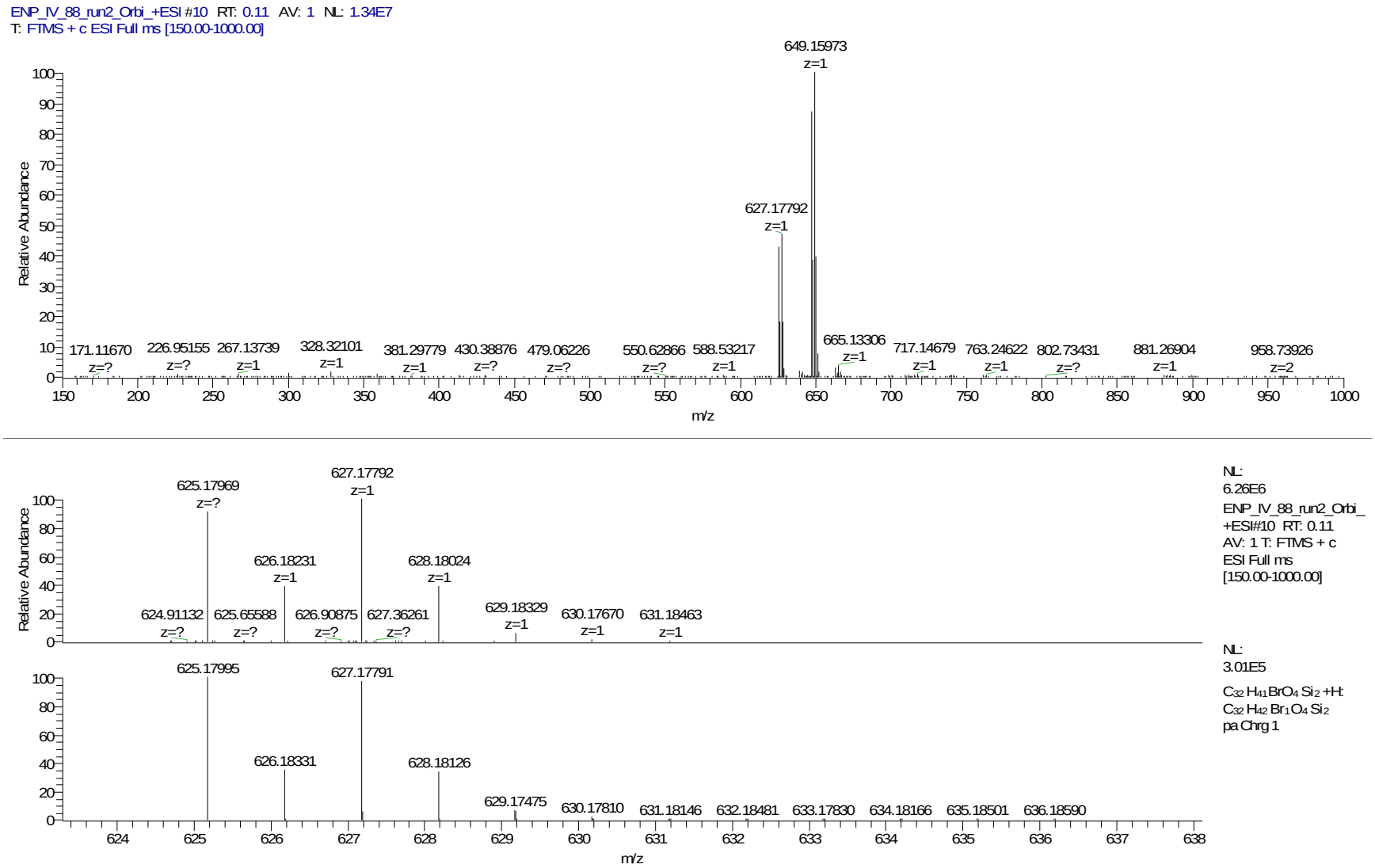
^{13}C NMR (125 MHz, $CDCl_3$) for Compound **27**



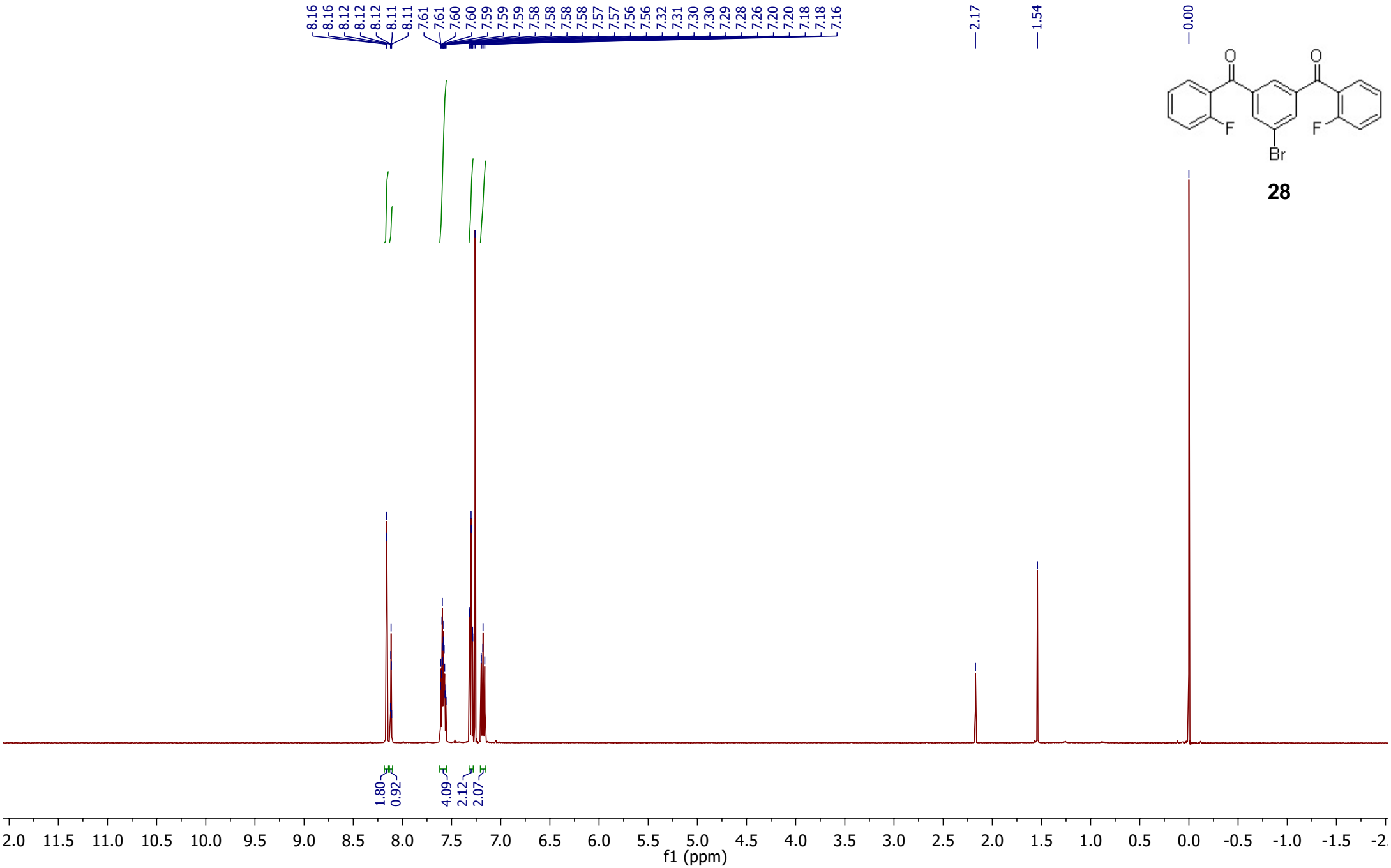
27

HRMS (ESI) for Compound **27**

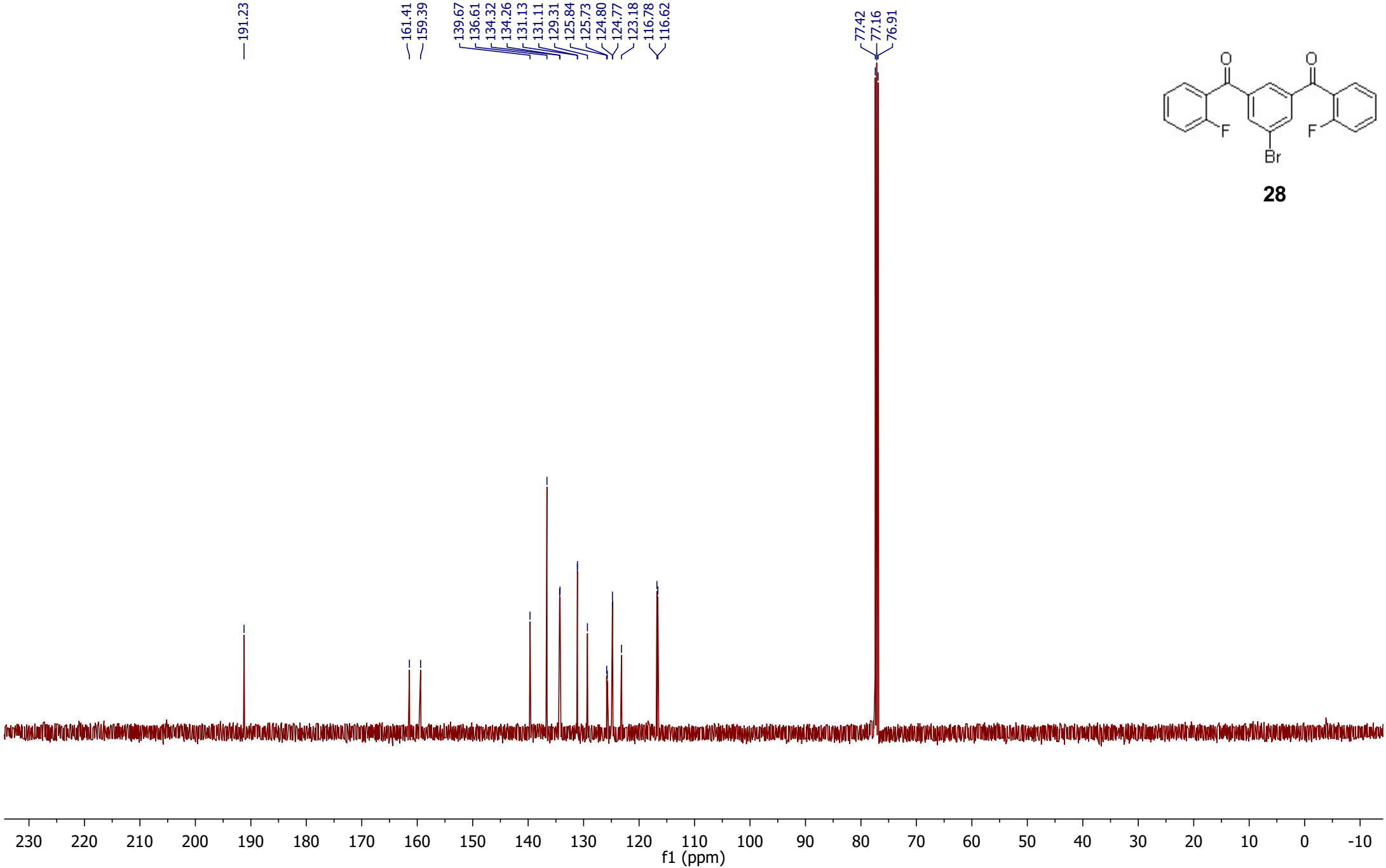
C:\Xcalibur\...\ENP_IV_88_run2_Orbi_+ESI 12/30/2014 6:52:36 PM



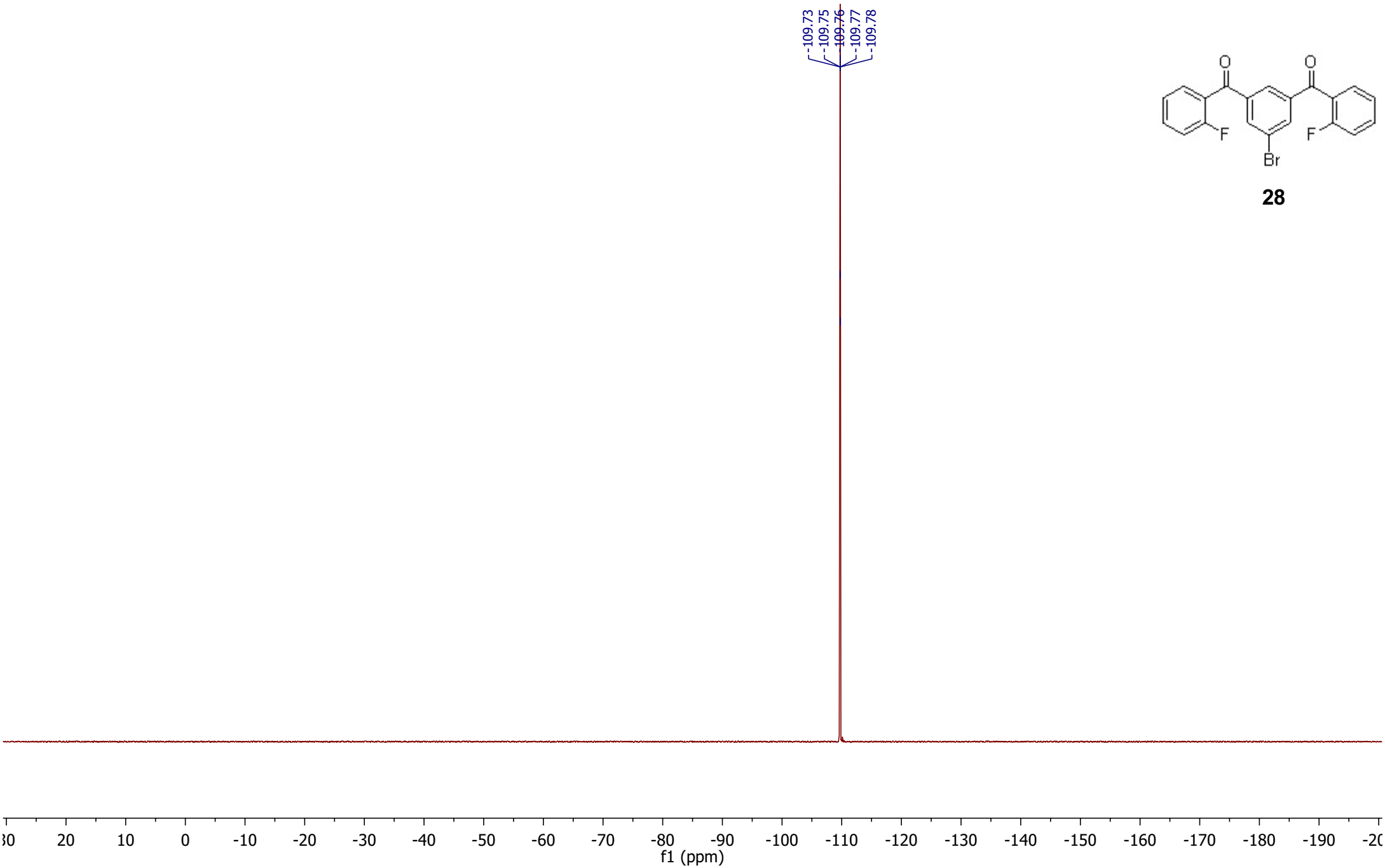
^{1}H NMR (500 MHz, $CDCl_3$) of Compound **28**



^{13}C NMR (125 MHz, $CDCl_3$) of Compound **28**

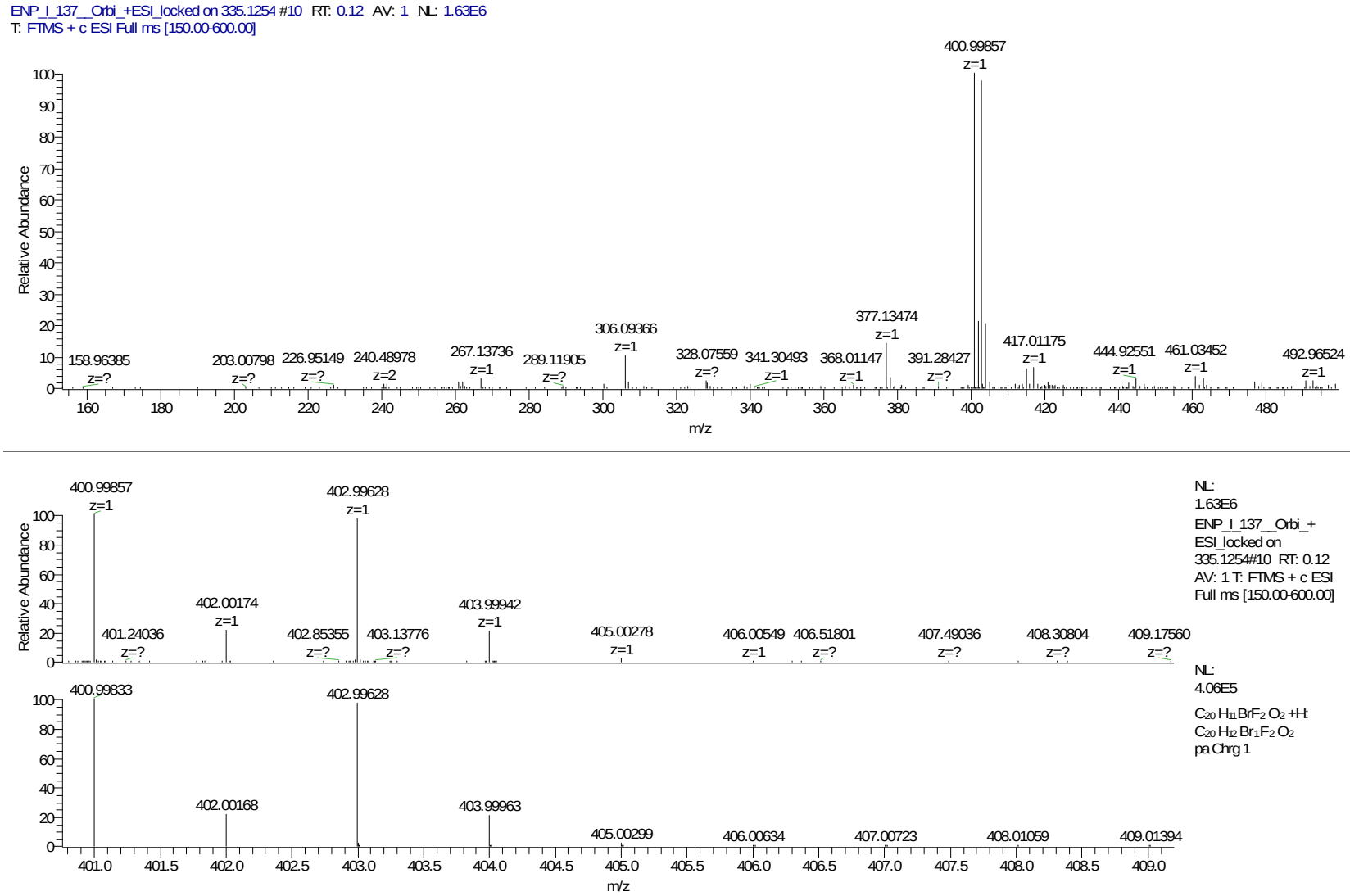


^{19}F NMR (470 MHz, $CDCl_3$) of Compound **28**

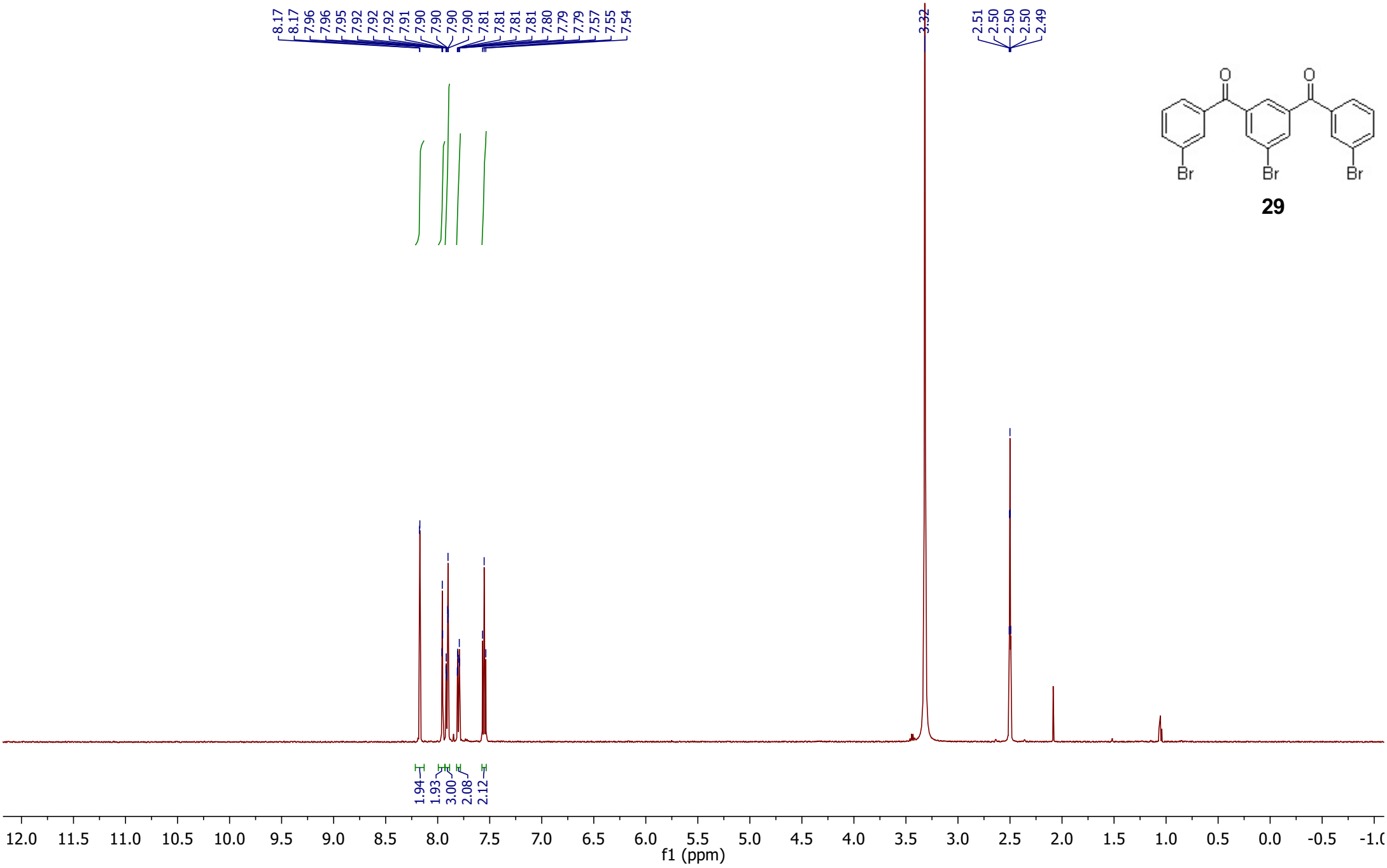


HRMS (ESI) for Compound **28**

ENP_I_137__Orbi_+ESI_locked on 335.1254 12/30/2014 3:25:47 PM

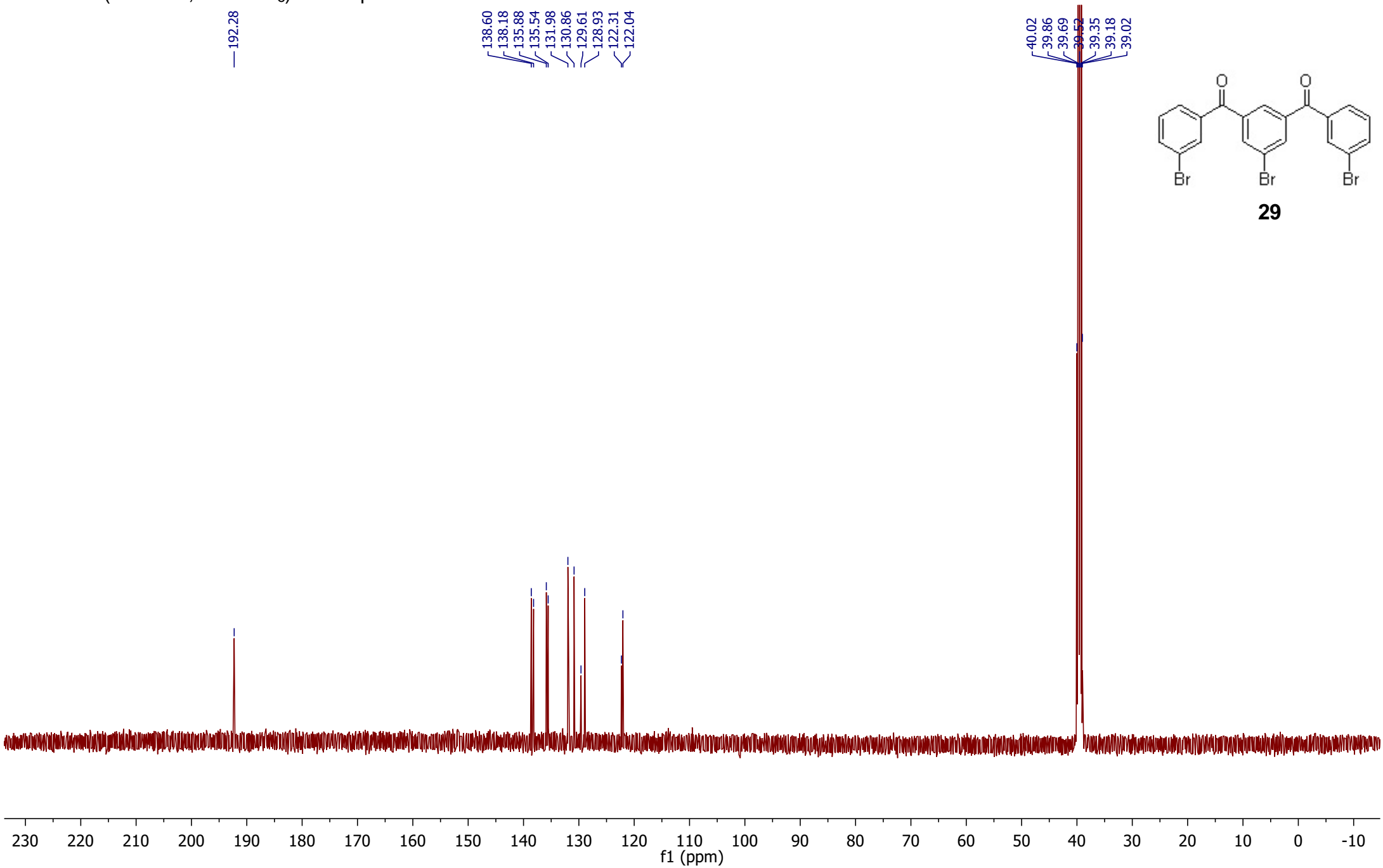


^{1}H NMR (500 MHz, DMSO-d_6) of Compound **29**



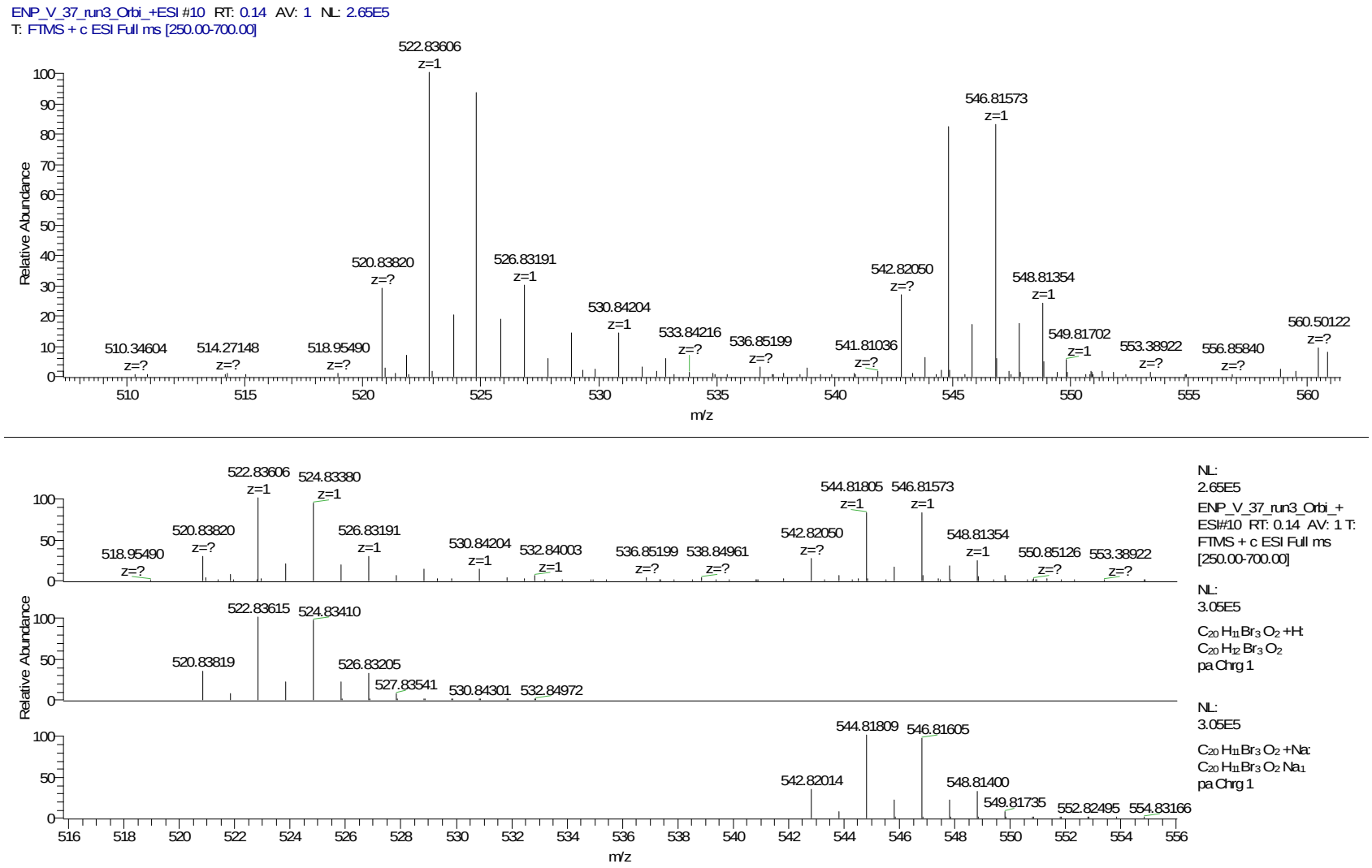
29

^{13}C NMR (125 MHz, DMSO-d_6) of Compound **29**

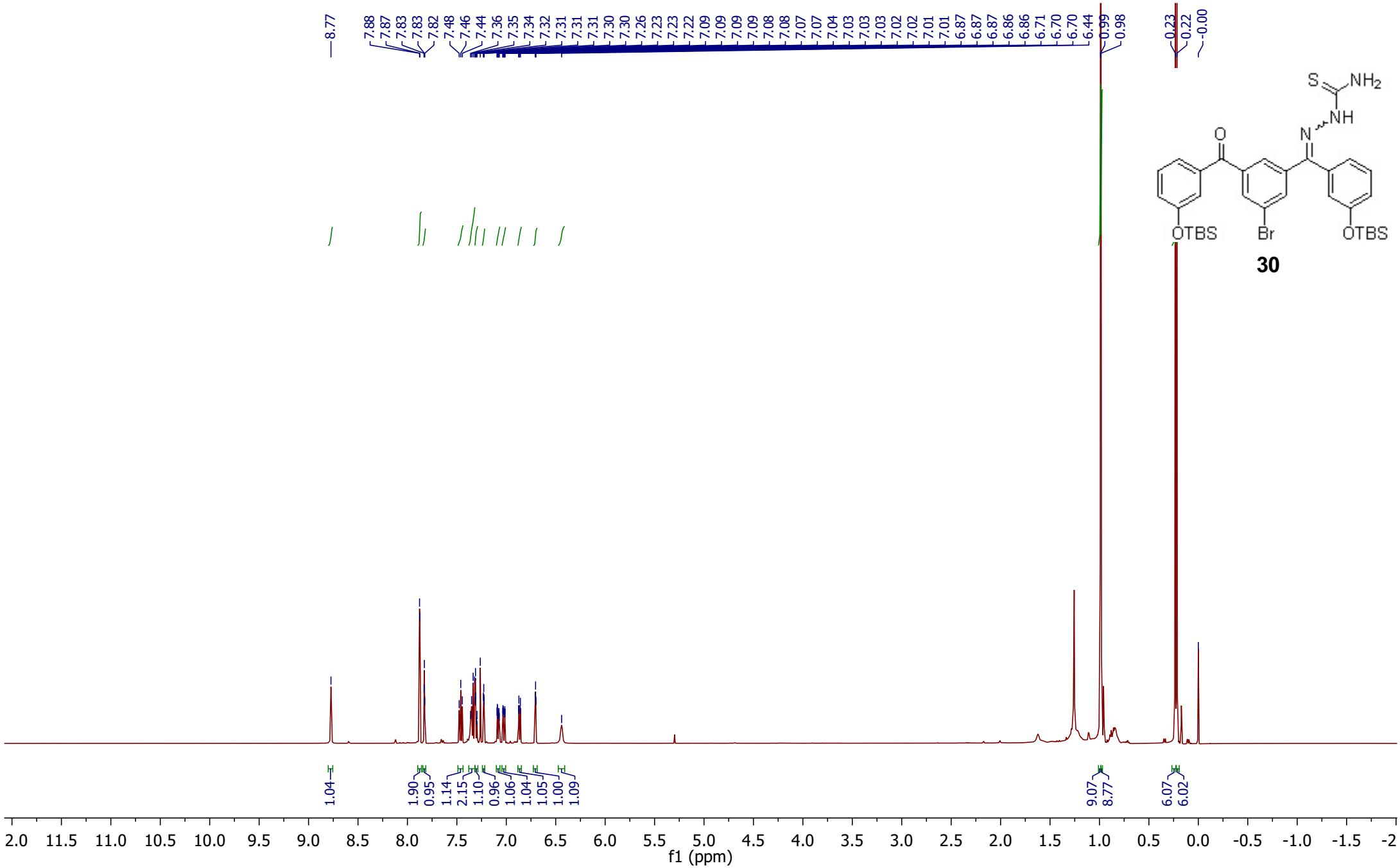


HRMS (ESI) for Compound **29**

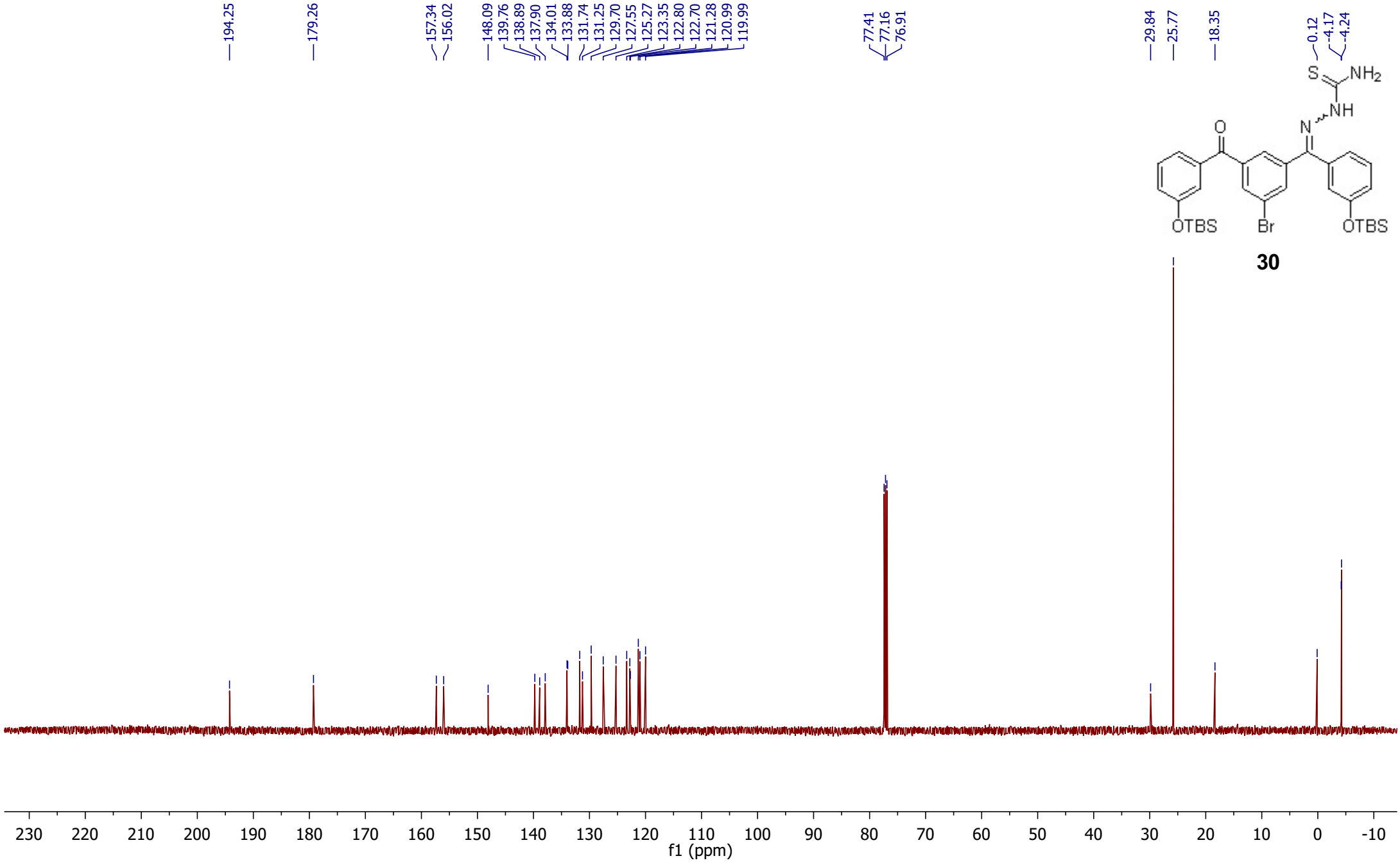
C:\Xcalibur\...\ENP_V_37_run3_Orbi_+ESI 12/30/2014 8:37:32 PM



^{1}H NMR (500 MHz, $CDCl_3$) of Compound **30**

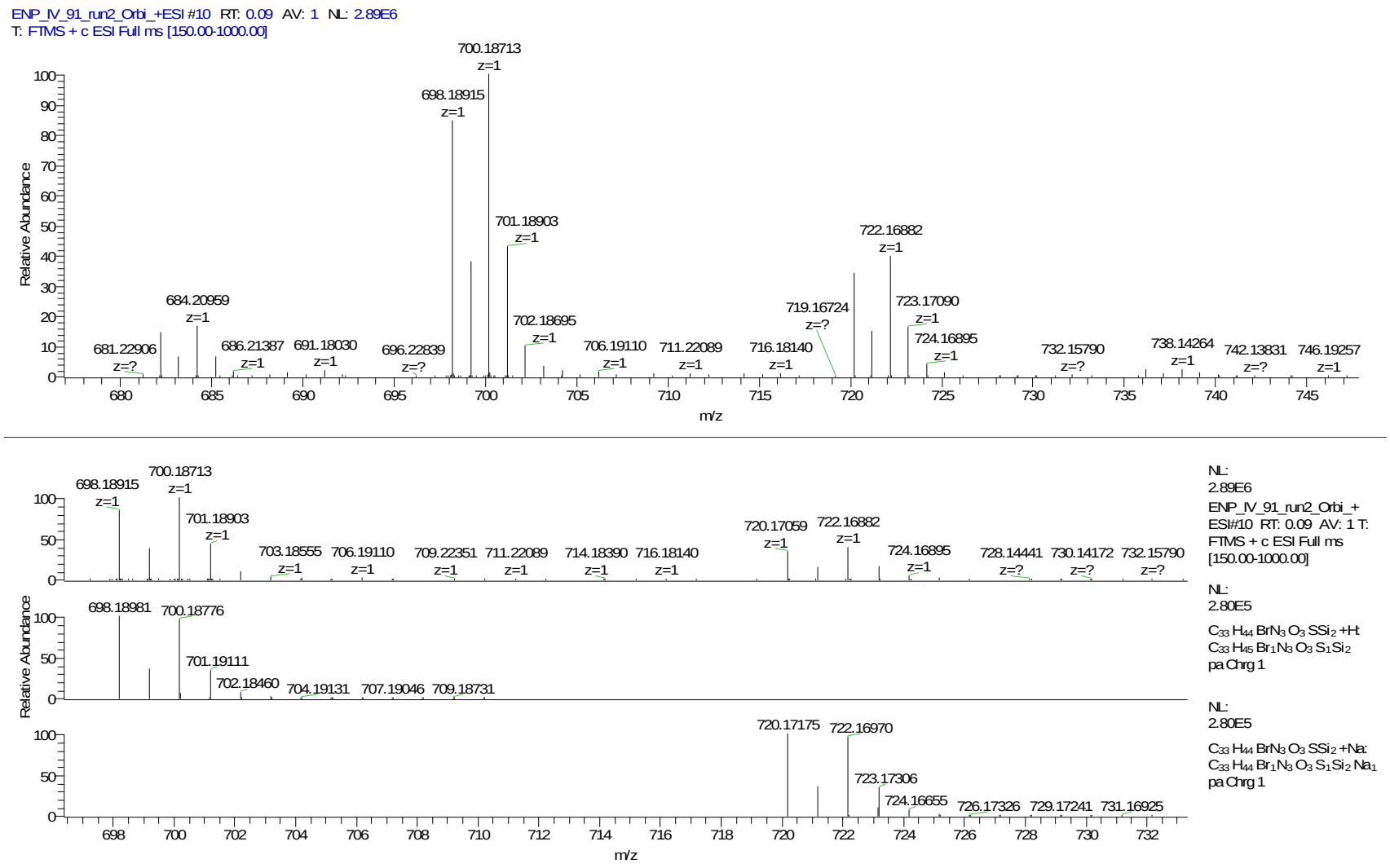


^{13}C NMR (125 MHz, $CDCl_3$) of Compound **30**

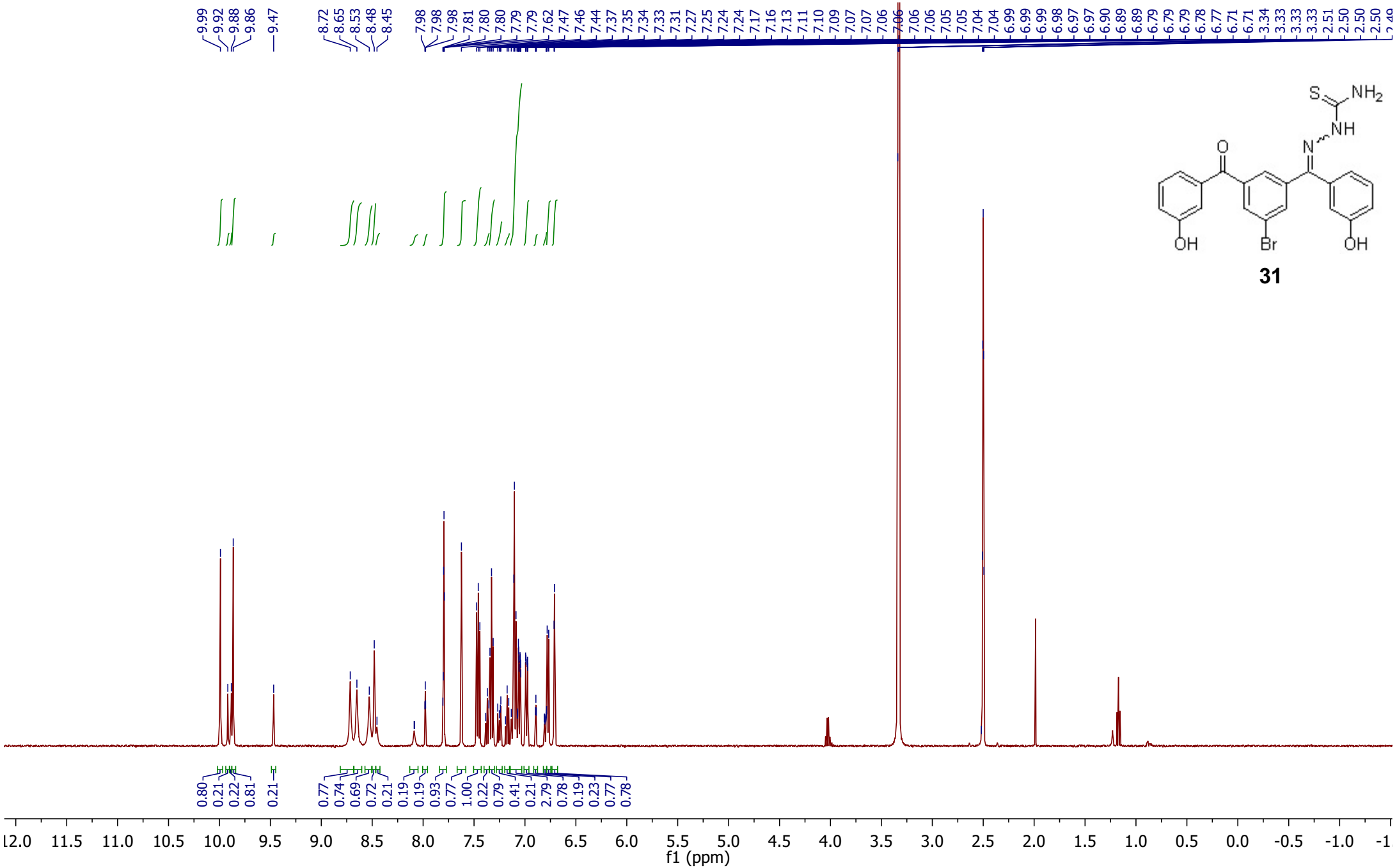


HRMS (ESI) for Compound **30**

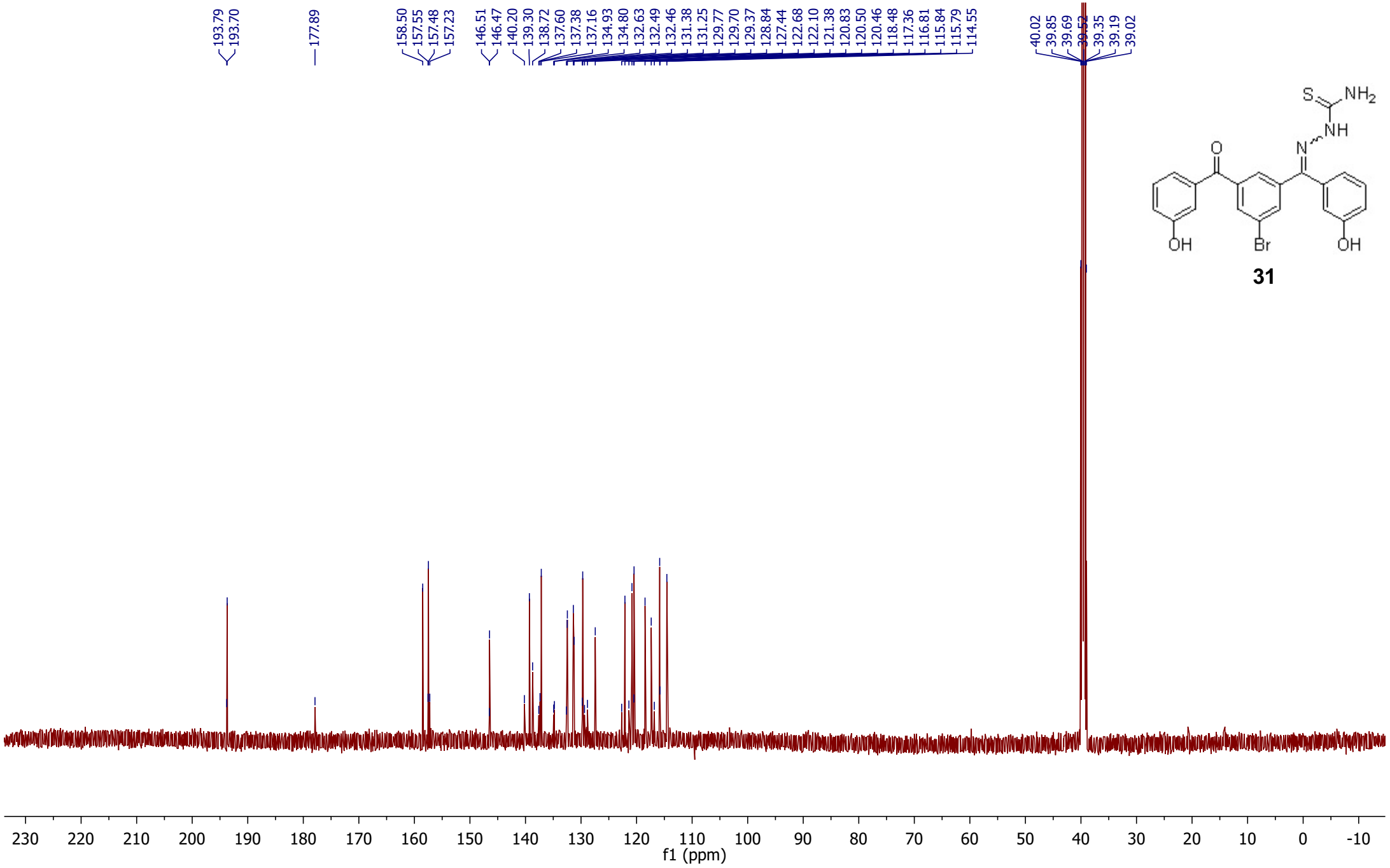
C:\Xcalibur\...\ENP_IV_91_run2_Orbi_+ESI 12/30/2014 6:32:30 PM



^{1}H NMR (500 MHz, DMSO-d_6) of Compound **31**



^{13}C NMR (125 MHz, DMSO-d_6) of Compound **31**



31

Data File C:\CHEM32\1\DATA\ERICAP\ENPIV95000030.D
Sample Name: ENPIV95

HPLC trace for Compound 31

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Acq. Instrument : Instrument 1                    Location :   -
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Acq. Method     : C:\CHEM32\1\METHODS\GRAD 2 30-90 ACN.M
Last changed    : 4/25/2014 11:52:20 AM by ERICAP
Analysis Method : C:\CHEM32\1\DATA\ERICAP\ENPIV95000030.D\DA.M (GRAD 2 30-90 ACN.M)
Last changed    : 6/12/2014 11:21:16 PM by ERICAP
                  (modified after loading)
Sample Info     : ENP-IV-95

                  Method:

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                  25-30 min 90:10 ACN:Water
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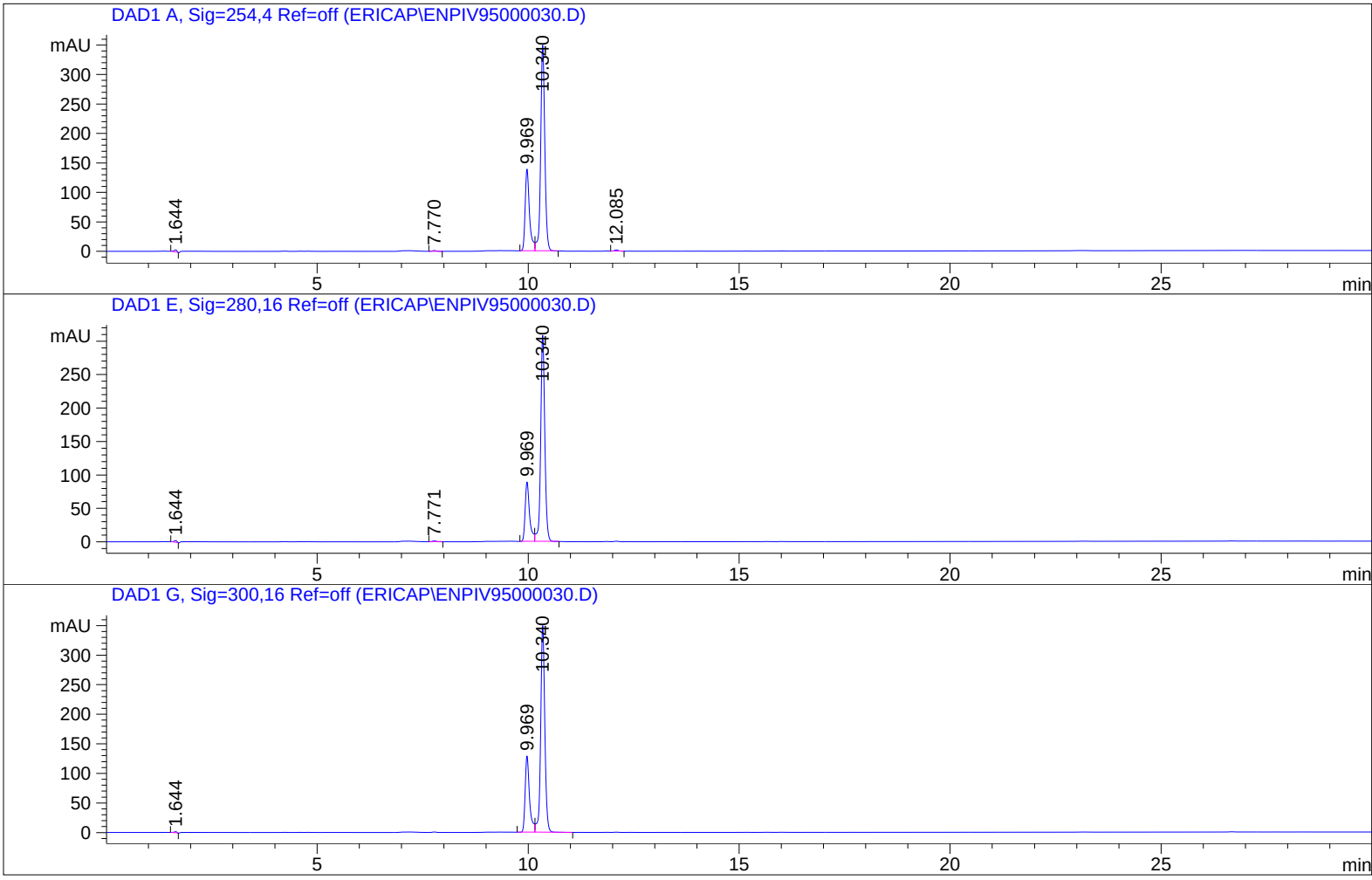
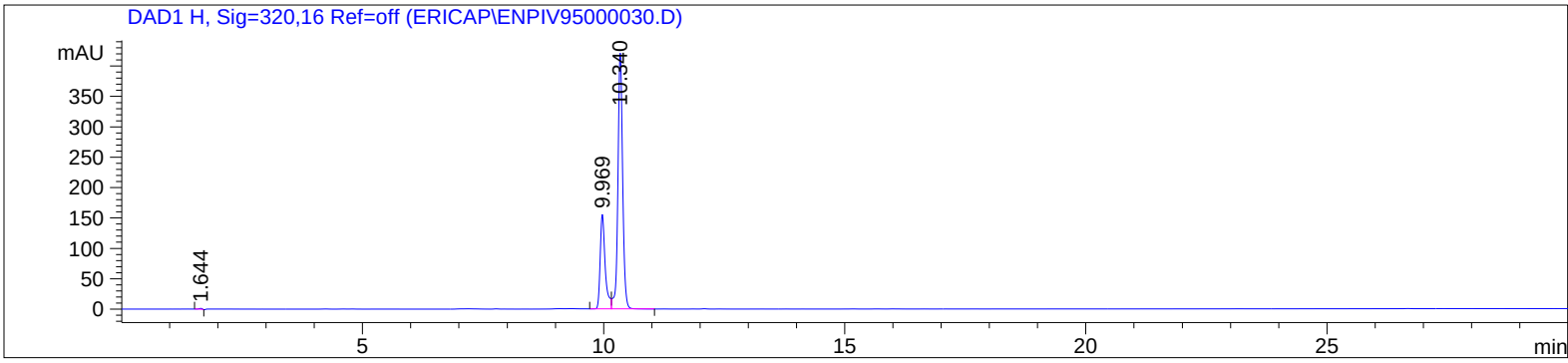
Two peaks observed in the HPLC traces are due to the presence of both E and Z geometrical isomers.



Data File C:\CHEM32\1\DATA\ERICAP\ENPIV95000030.D
Sample Name: ENPIV95

HPLC trace for Compound 31



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

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1	1.644	BB	0.0797	18.54496	3.74883	0.5430
2	7.770	BB	0.0945	8.02507	1.29170	0.2350
3	9.969	BV	0.1072	990.19165	138.85767	28.9947
4	10.340	VB	0.1035	2384.42212	349.75323	69.8204
5	12.085	VB	0.1052	13.89472	2.04570	0.4069
Totals :				3415.07852	495.69714	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.644	BB	0.0797	13.71861	2.77335	0.4962
2	7.771	BB	0.0939	7.99437	1.29687	0.2892
3	9.969	BV	0.1083	644.19257	89.12112	23.3016
4	10.340	VB	0.1033	2098.67676	308.57321	75.9130
Totals :				2764.58229	401.76455	

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.644	BB	0.0807	10.21376	2.02849	0.3066
2	9.969	BV	0.1077	926.89996	129.25491	27.8197
3	10.340	VB	0.1038	2394.69263	350.12573	71.8737

HPLC trace for Compound 31

Totals :	3331.80635	481.40913	

Signal 4: DAD1 H, Sig=320,16 Ref=off

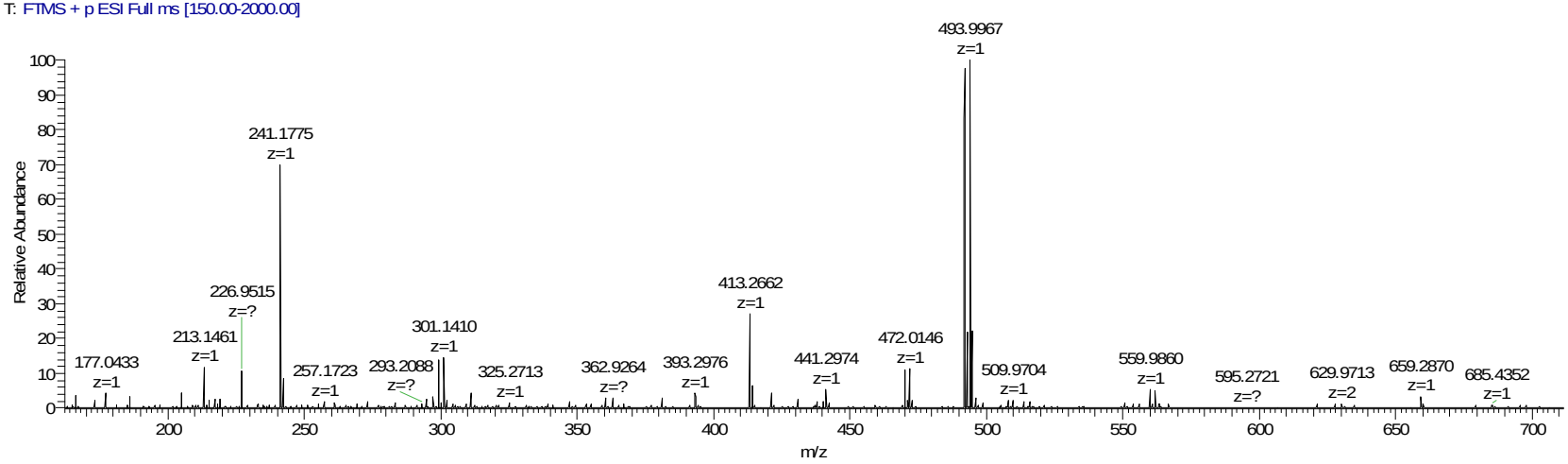
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.644	BB	0.0818	9.08203	1.77197	0.2265
2	9.969	BV	0.1078	1116.46643	155.51645	27.8403
3	10.340	VB	0.1038	2884.70776	421.56287	71.9333
Totals :				4010.25623	578.85129	

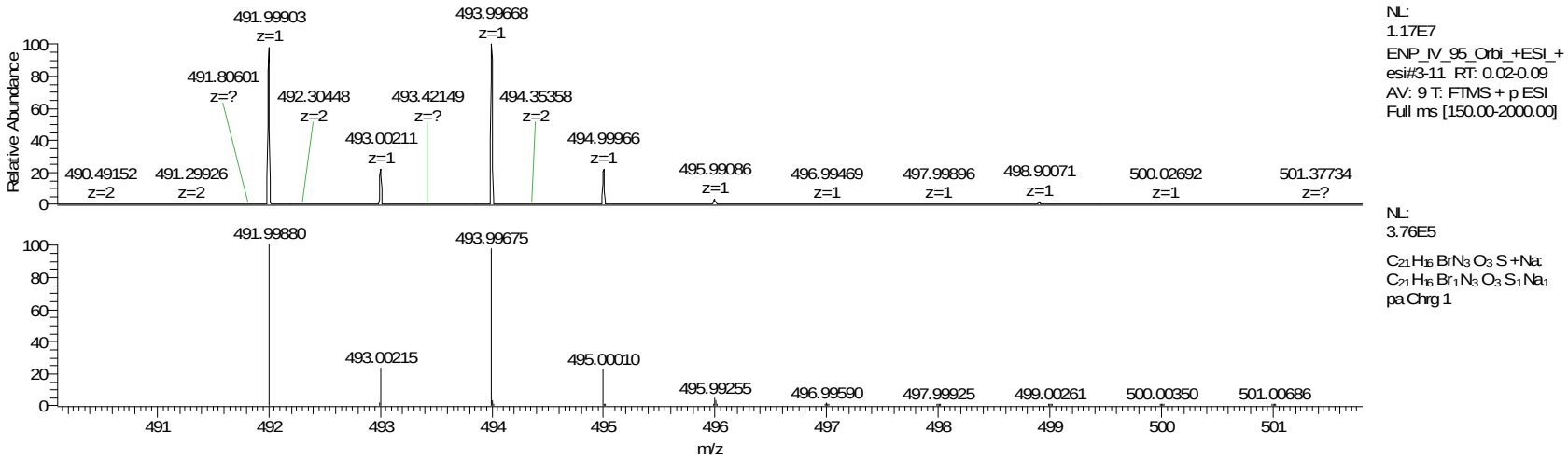
*** End of Report ***

HRMS (ESI) for Compound **31**

C:\Xcalibur\...\ENP_IV_95_Orbi_+ESI_+esi 3/7/2014 3:00:04 PM

ENP_IV_95_Orbi_+ESI_+esi #3-11 RT: 0.02-0.09 AV: 9 NL: 1.17E7
T: FTMS + p ESI Full ms [150.00-2000.00]



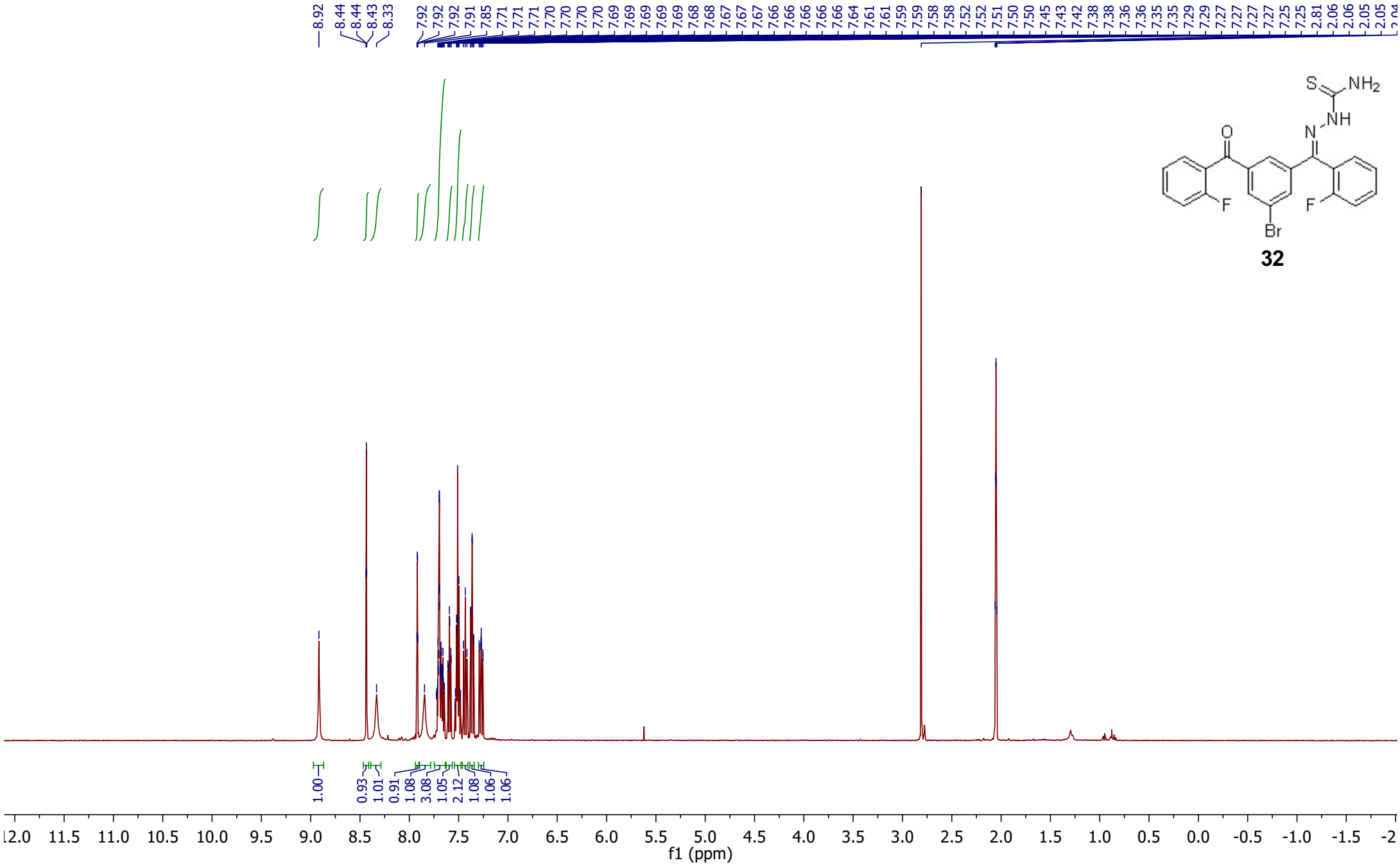


NL:
1.17E7
ENP_IV_95_Orbi_+ESI_+esi#3-11 RT: 0.02-0.09 AV: 9 T: FTMS + p ESI Full ms [150.00-2000.00]

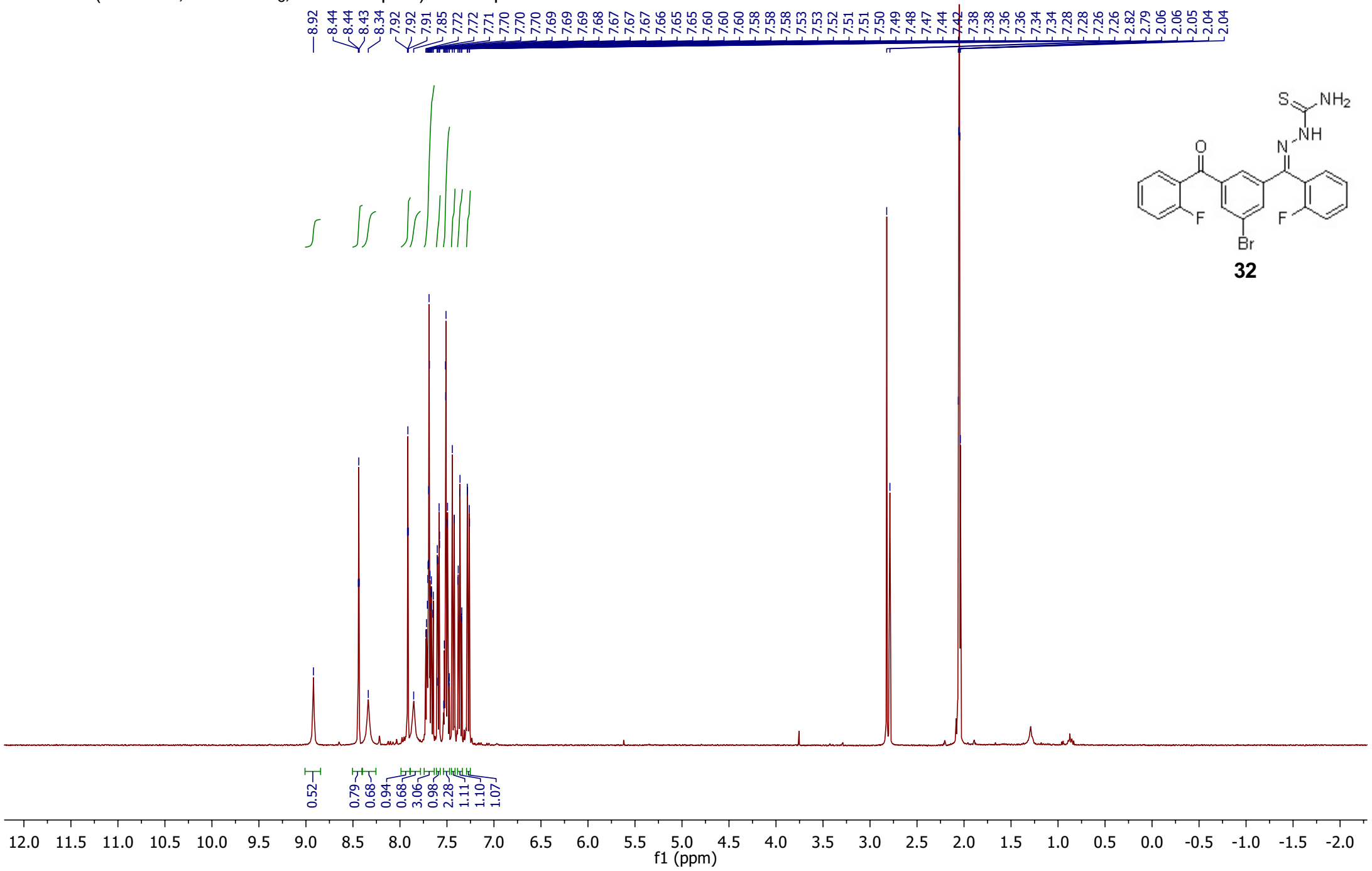
NL:
3.76E5

$C_{21}H_{16}BrN_3O_3S+Na$:
$C_{21}H_{16}Br_1N_3O_3S_1Na_1$
pa Chrg 1

^{1}H NMR (500 MHz, Acetone-d_6) of Compound **32**

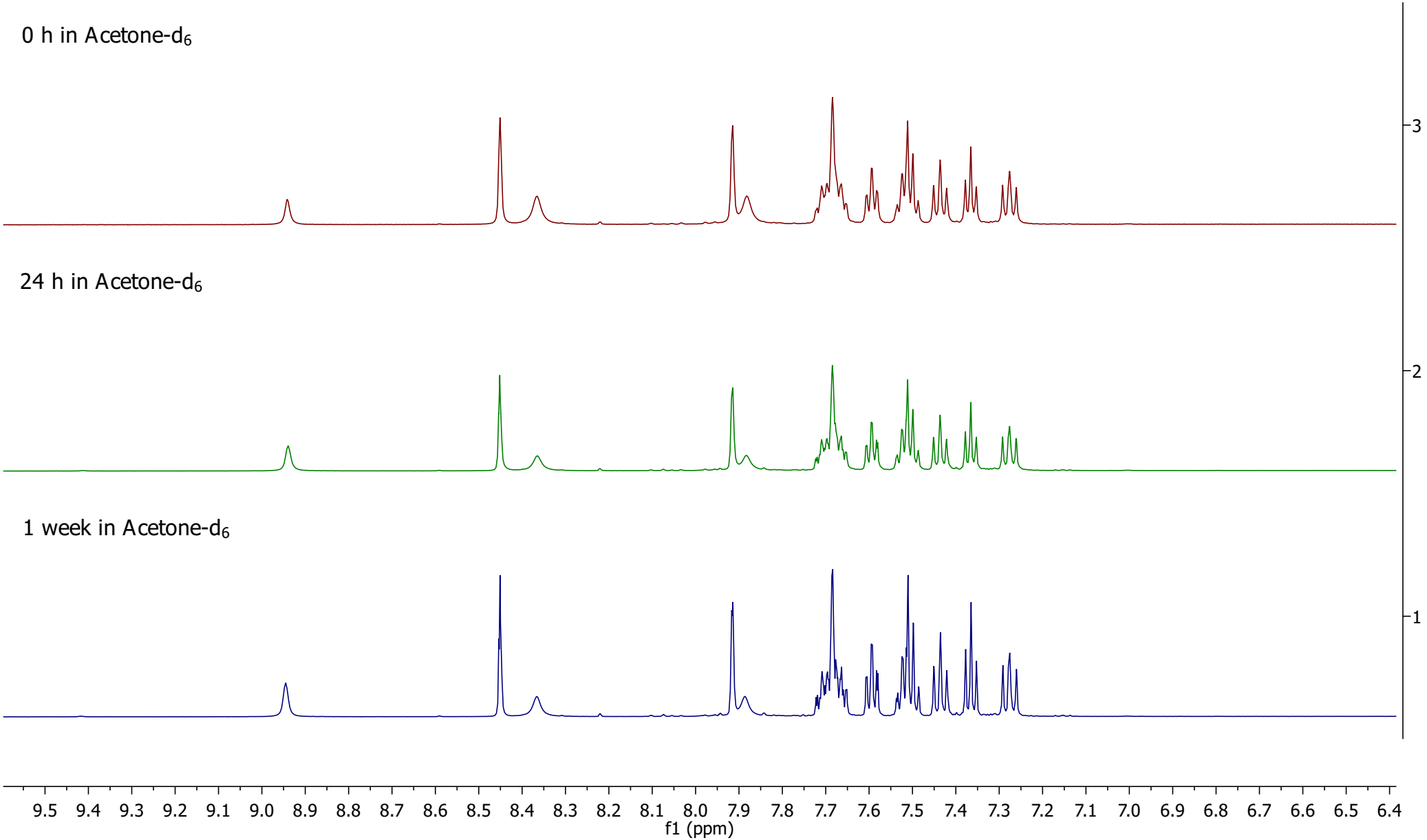


^{1}H NMR (400 MHz, Acetone-d$_6$, ^{19}F decoupled) of Compound **32**

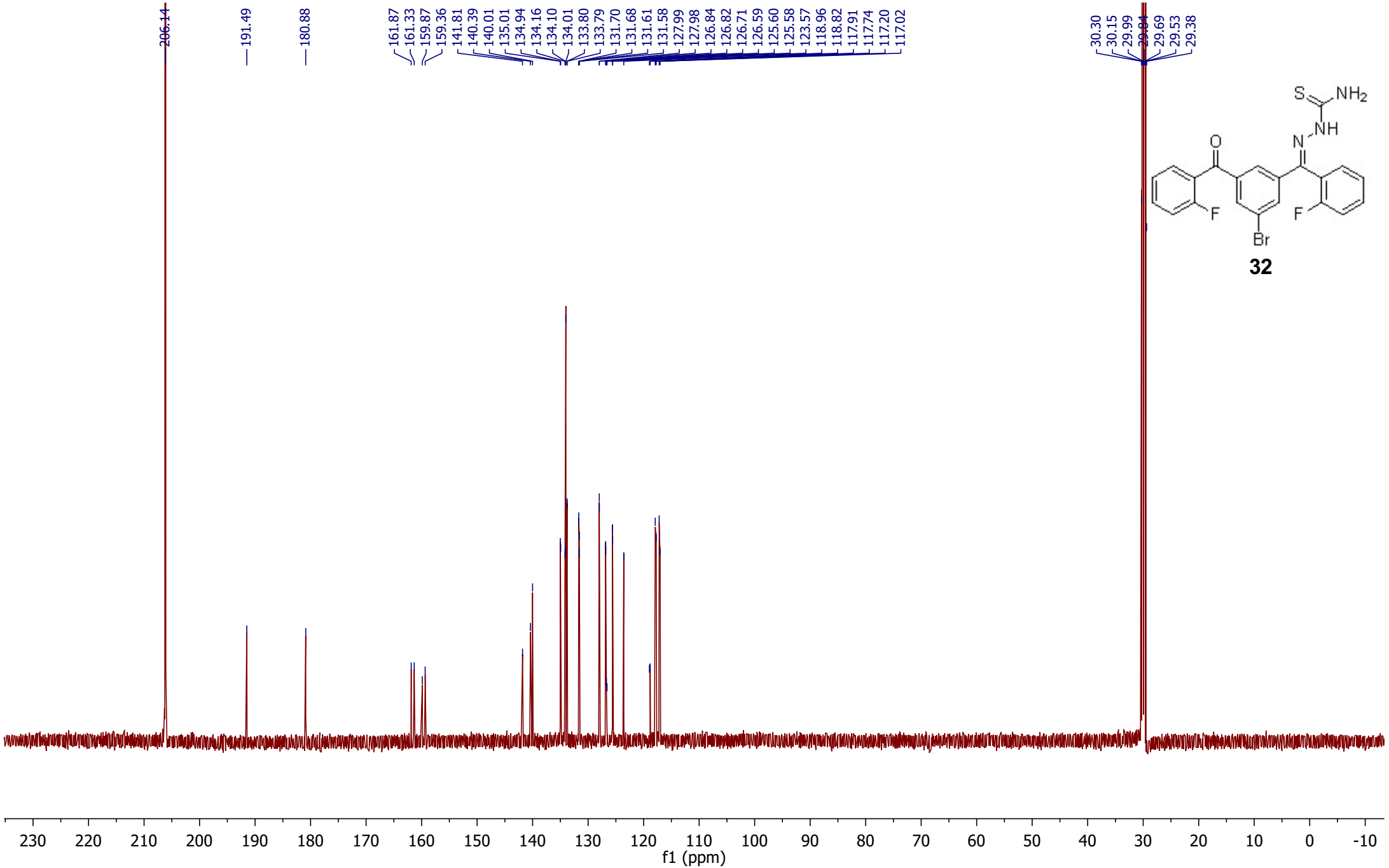


32

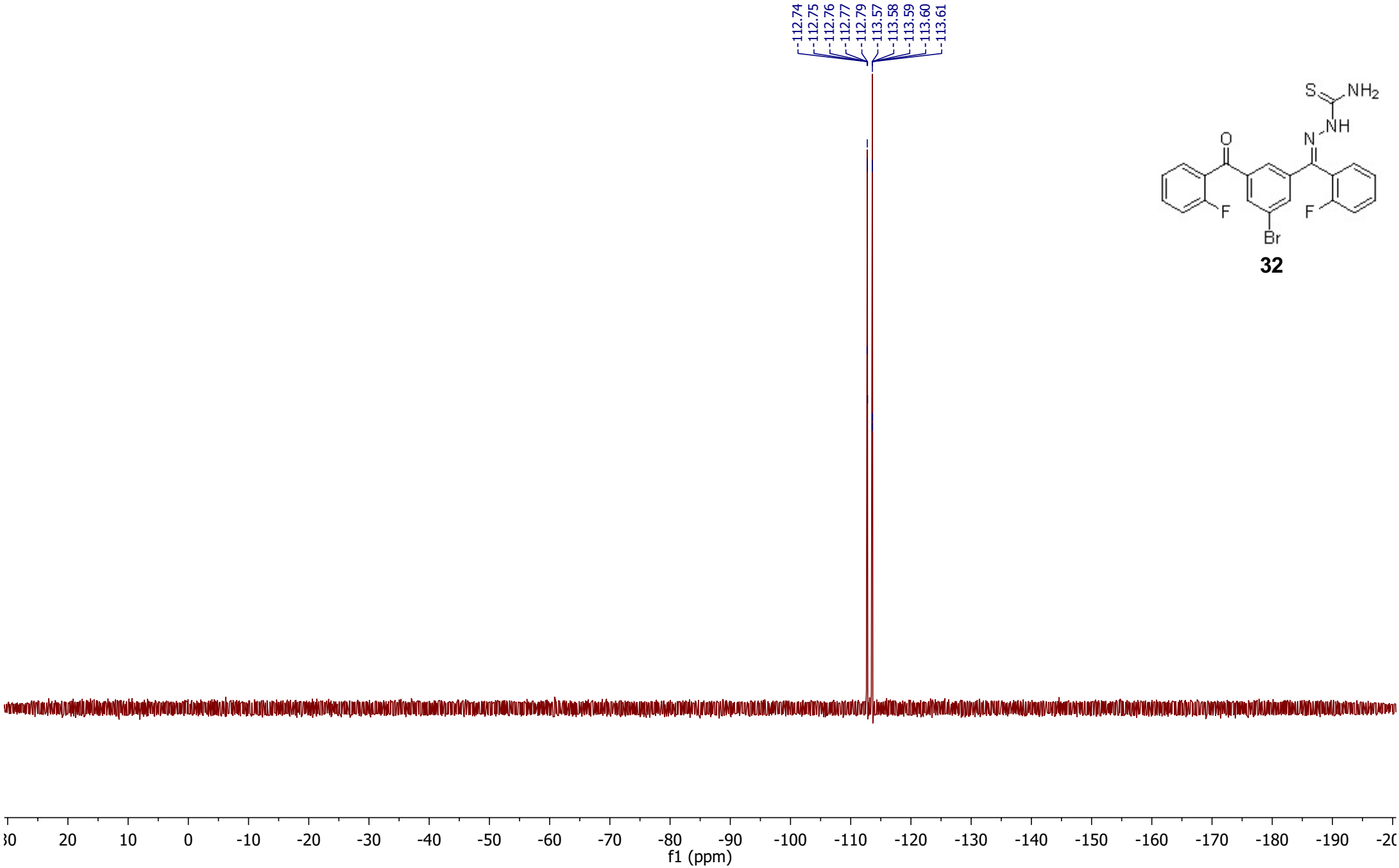
^{1}H NMR (600 MHz, Acetone-d_6) of Compound **32** at various time intervals



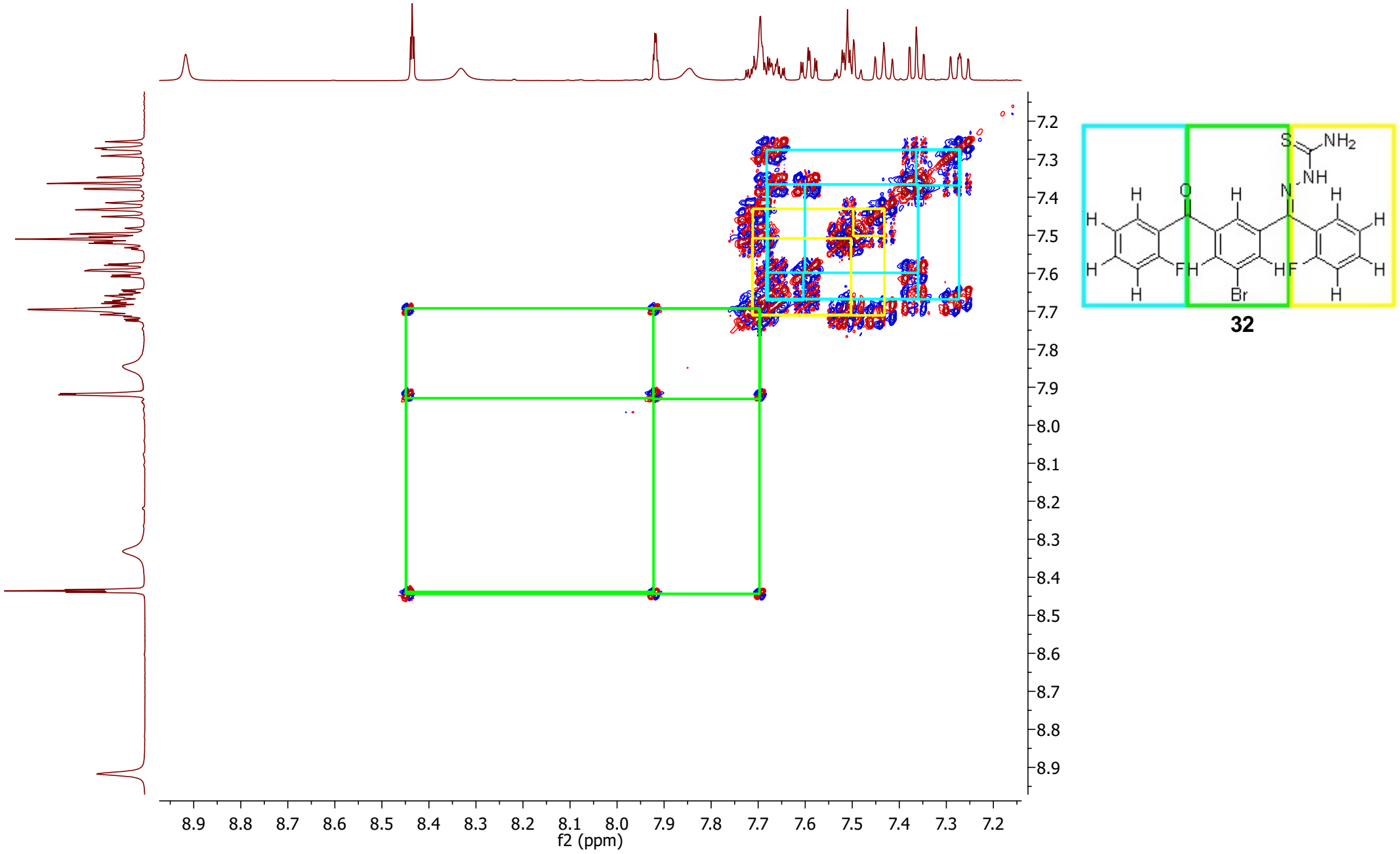
^{13}C NMR (125 MHz, Acetone-d_6) of Compound **32**



^{19}F NMR (470 MHz, Acetone-d_6) of Compound **32**

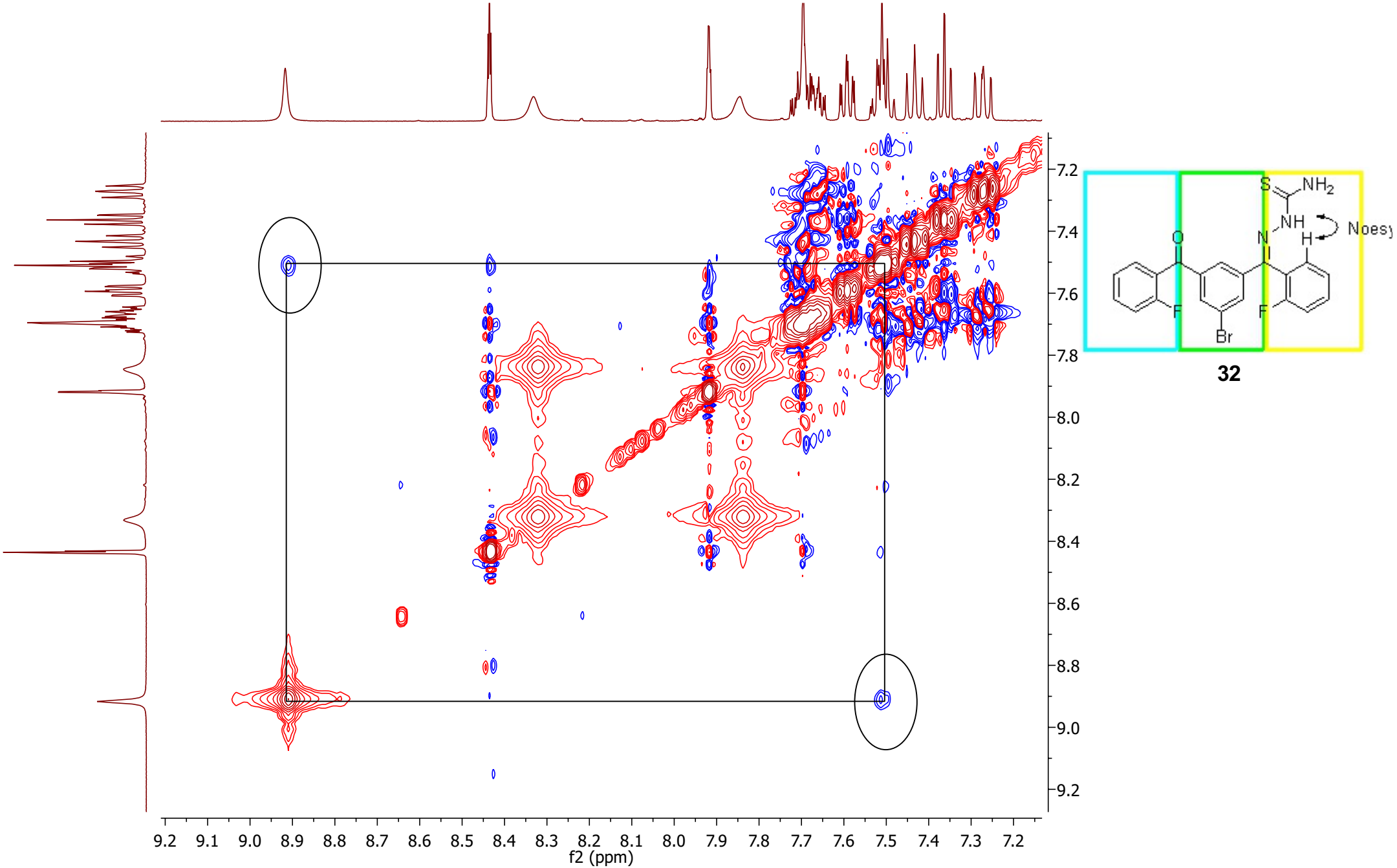


COSYGPSW (400 MHz, Acetone-d_6) of Compound **32**



32

NOESYPHSW (400 MHz, Acetone-d_6) of Compound **32**



32

Data File C:\CHEM32\1\DATA\ERICAP_ENP_1_15100002.D
Sample Name: _ENP_1_151

HPLC trace for Compound 32

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Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 1/19/2015 9:23:47 PM
Acq. Method     : C:\CHEM32\1\METHODS\GRAD 2 50-90 ACN.M
Last changed    : 1/19/2015 9:20:17 PM by ERICAP
Analysis Method : C:\CHEM32\1\DATA\ERICAP\_ENP_1_15100002.D\DA.M (GRAD 2 50-90 ACN.M)
Last changed    : 1/30/2015 12:11:43 AM by ERICAP
                  (modified after loading)
Sample Info     : ENP_1_151

                  Method:

                  0-25 min gradient 50:50 to 90:10 ACN:Water
                  25-30 min isocratic 90:10 ACN:Water
```
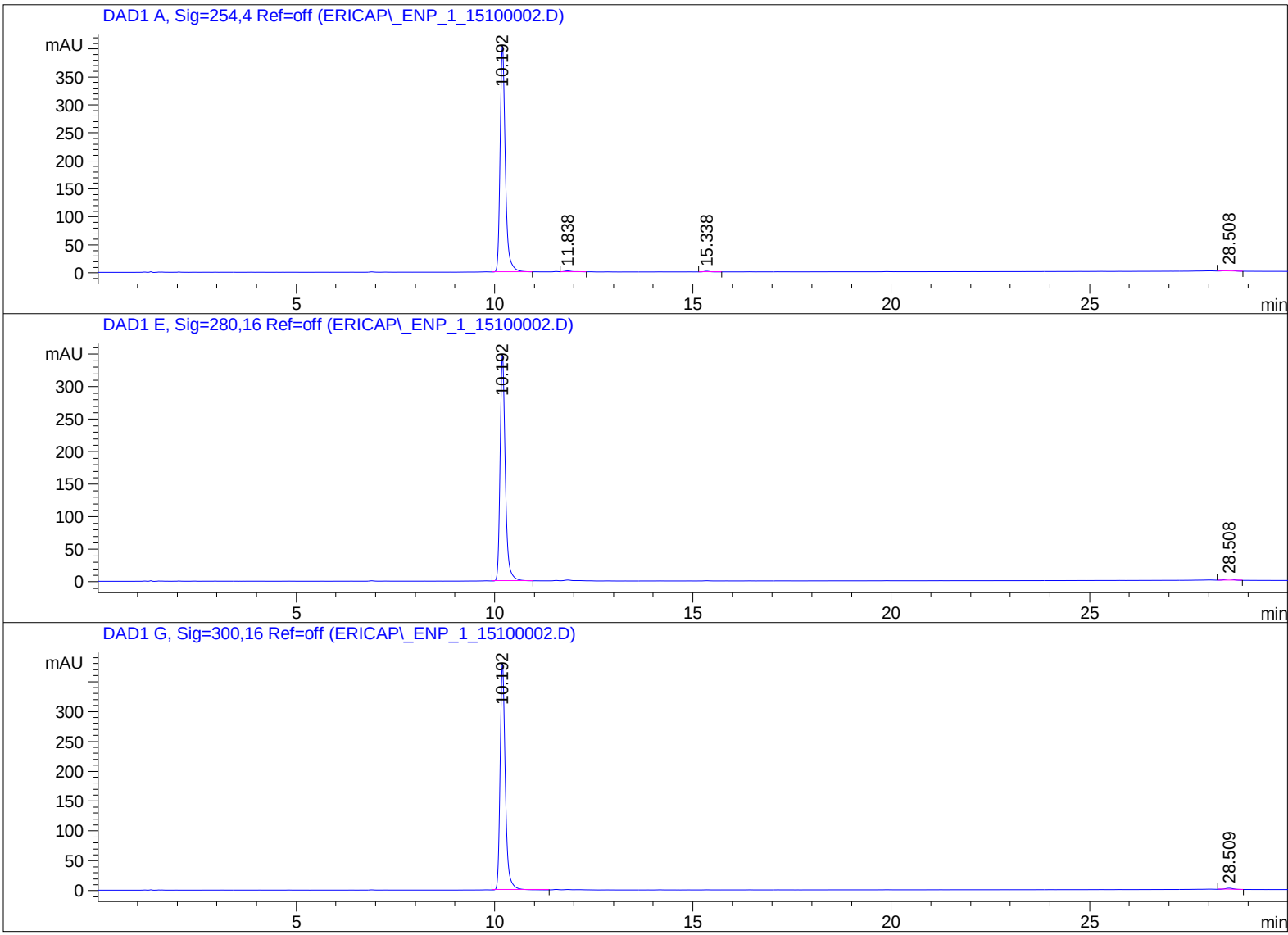
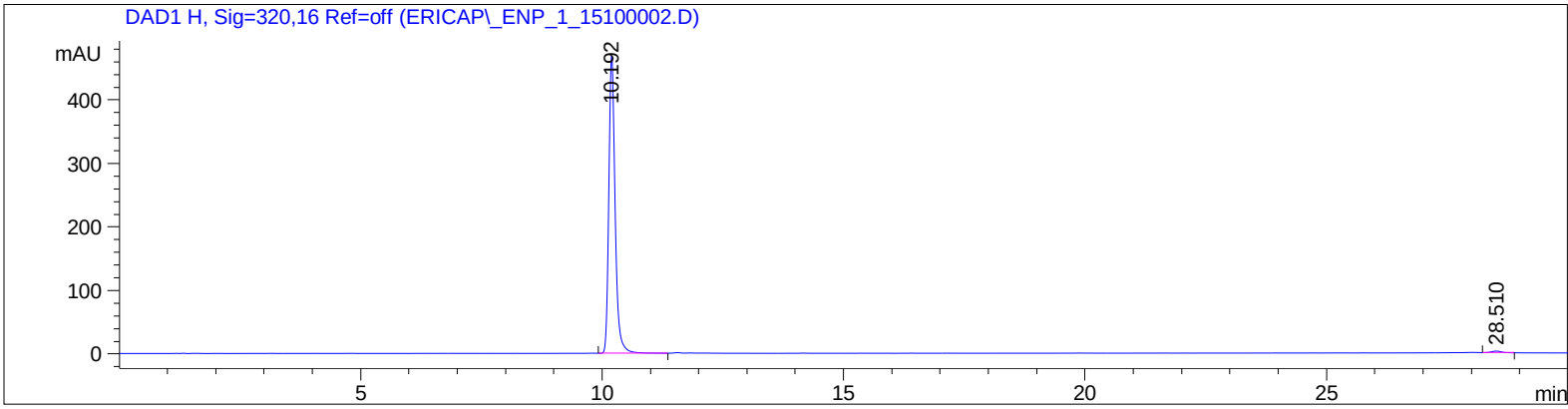

Isolated as the Z geometrical isomer as shown in the H NMR spectra. Only one peak observed in the HPLC trace.



Data File C:\CHEM32\1\DATA\ERICAP_ENP_1_15100002.D
Sample Name: _ENP_1_151

HPLC trace for Compound 32



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.192	BB	0.1385	3686.86572	404.02744	98.1430
2	11.838	VB	0.2041	23.26824	1.65460	0.6194
3	15.338	BB	0.1492	12.01820	1.23878	0.3199
4	28.508	BB	0.2201	34.47456	2.45158	0.9177
Totals :				3756.62673	409.37240	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.192	BB	0.1377	3154.12451	347.99039	99.1103
2	28.508	BB	0.2158	28.31306	2.01687	0.8897
Totals :				3182.43758	350.00725	

HPLC trace for Compound 32

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.192	BB	0.1383	3453.58618	379.02155	99.1981
2	28.509	BB	0.2169	27.91662	1.99900	0.8019
Totals :				3481.50280	381.02055	

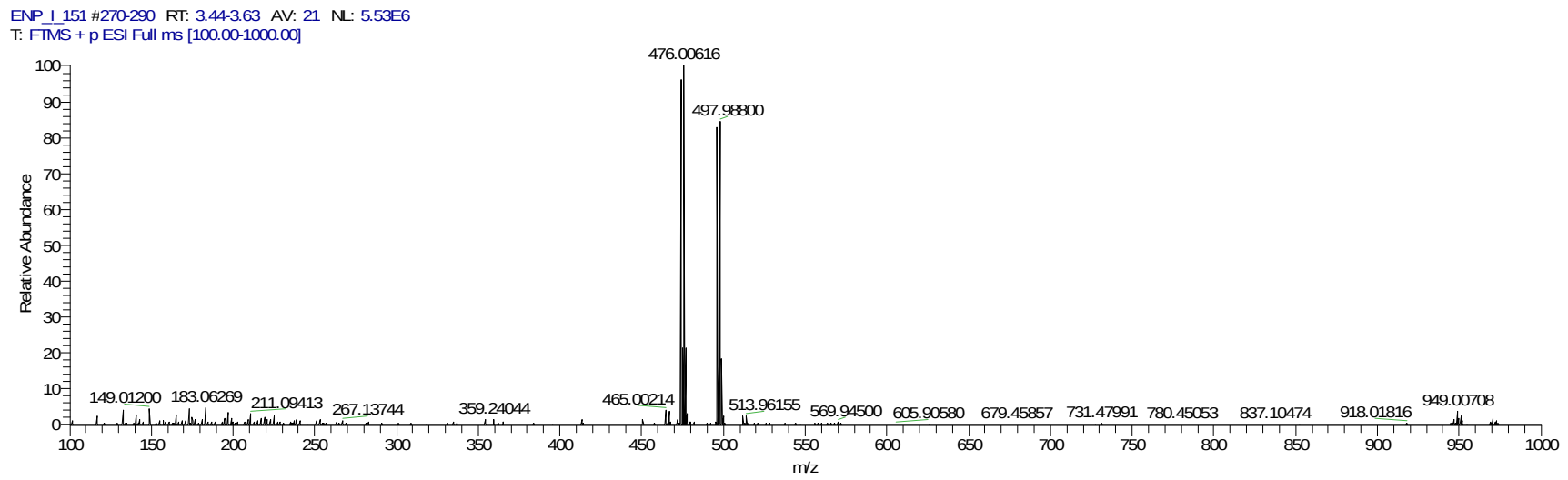
Signal 4: DAD1 H, Sig=320,16 Ref=off

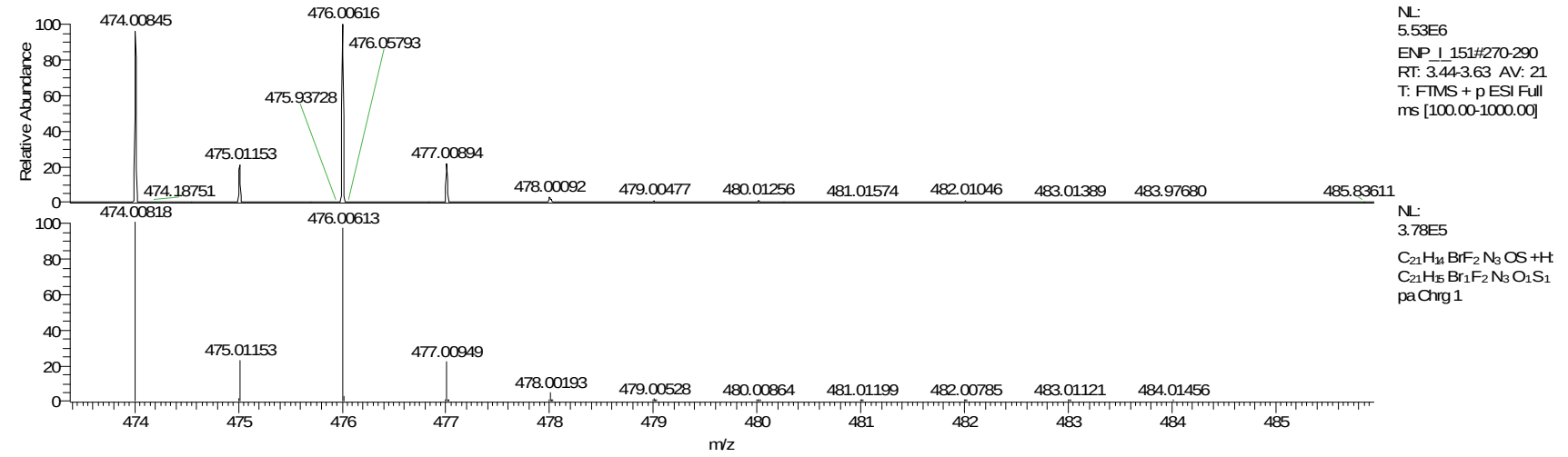
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.192	BB	0.1377	4249.60937	468.87698	99.1954
2	28.510	BB	0.2149	34.46865	2.46907	0.8046
Totals :				4284.07803	471.34605	

*** End of Report ***

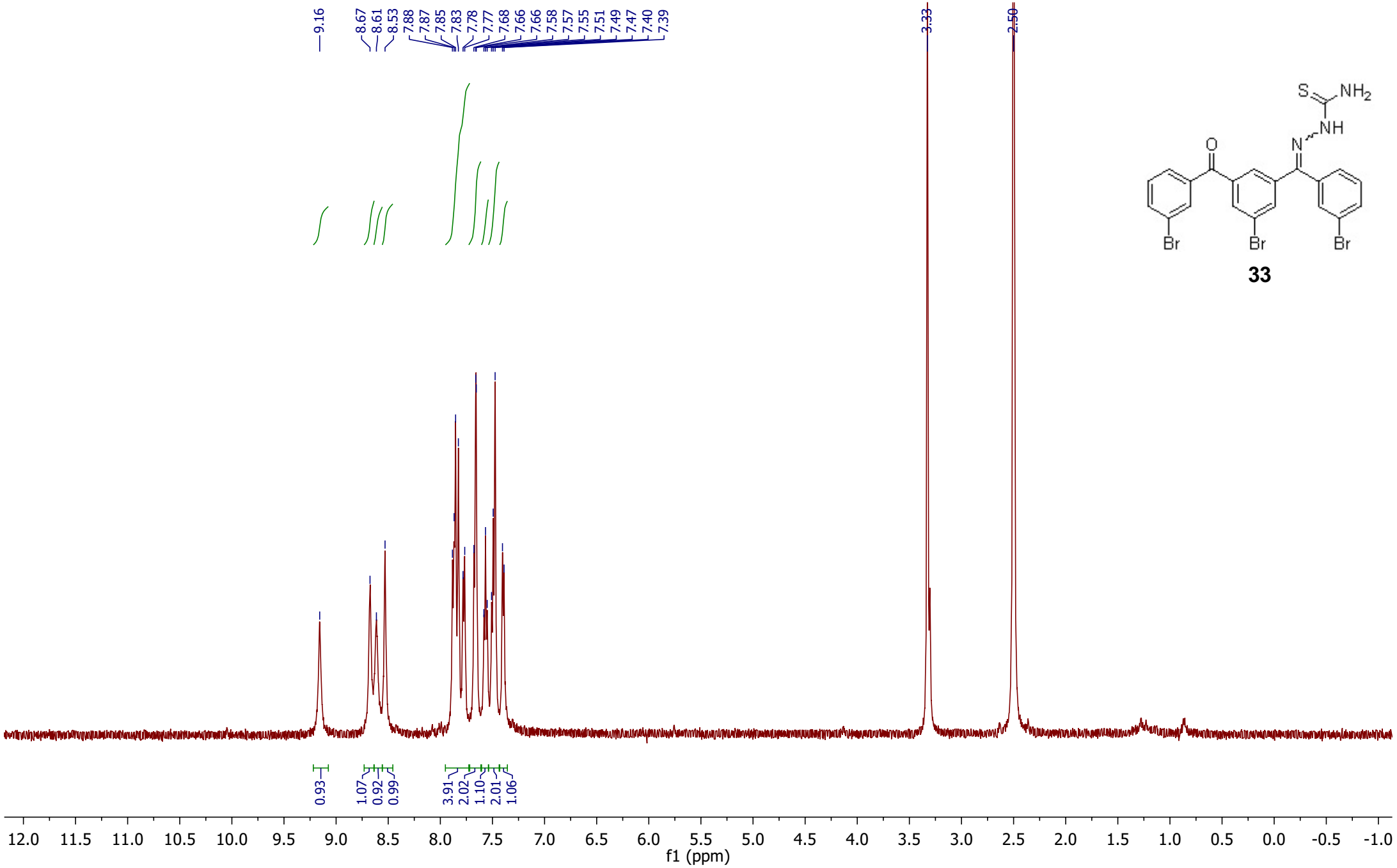
HRMS(ESI) for Compound **32**

C:\Xcalibur\...\01-02-2015\ENP_I_151 1/2/2015 10:18:02 PM



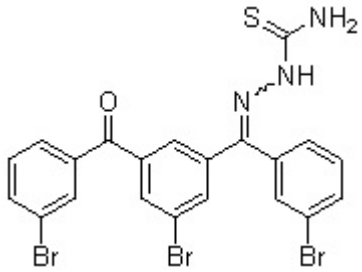


^{1}H NMR (500 MHz, DMSO-d_6) at 0 h for Compound **33**



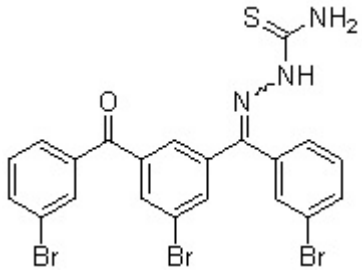
33

^{1}H NMR (500 MHz, DMSO-d_6) at 24 h for Compound **33**



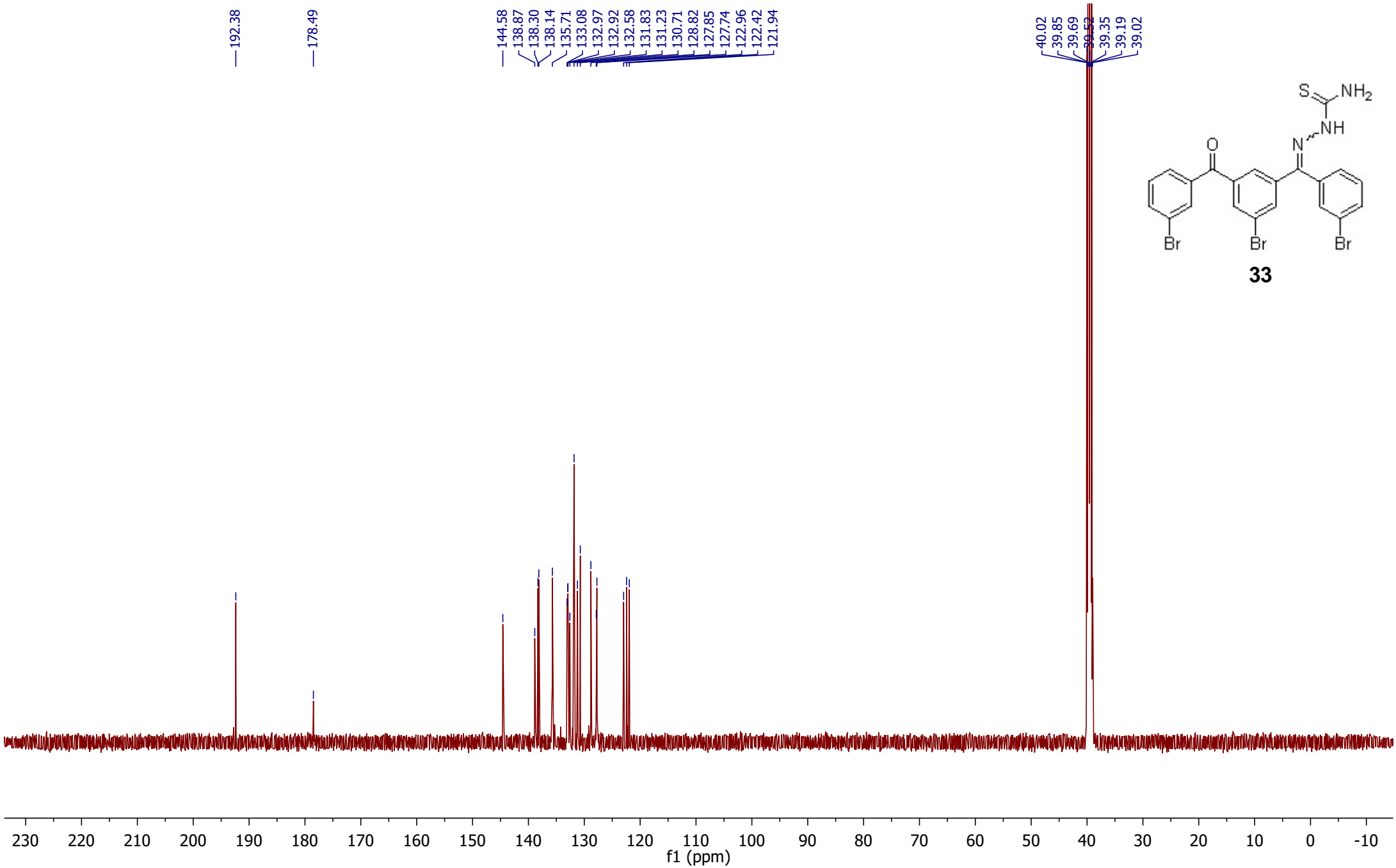
33

^{1}H NMR (500 MHz, DMSO-d_6) at 16 days for Compound **33**



33

^{13}C NMR (125 MHz, DMSO-d_6) for Compound **33**



Data File C:\CHEM32\1\DATA\ERICAP\ENPV54A000036.D
Sample Name: ENPV54A

HPLC trace for Compound 33

```
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Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 4/29/2014 9:53:23 PM
Acq. Method     : C:\CHEM32\1\METHODS\GRAD 2 50-90 ACN.M
Last changed    : 4/29/2014 9:52:15 PM by ERICAP
                  (modified after loading)
Analysis Method : C:\CHEM32\1\DATA\ERICAP\ENPV54A000036.D\DA.M (GRAD 2 50-90 ACN.M)
Last changed    : 6/12/2014 9:45:00 PM by ERICAP
                  (modified after loading)
Sample Info     : ENP-V-54A

                  Method:

                  0-25 Min. 50
                  :70 to 90:10 ACN:Water
                  25-30 min 90:10 ACN:Water
```
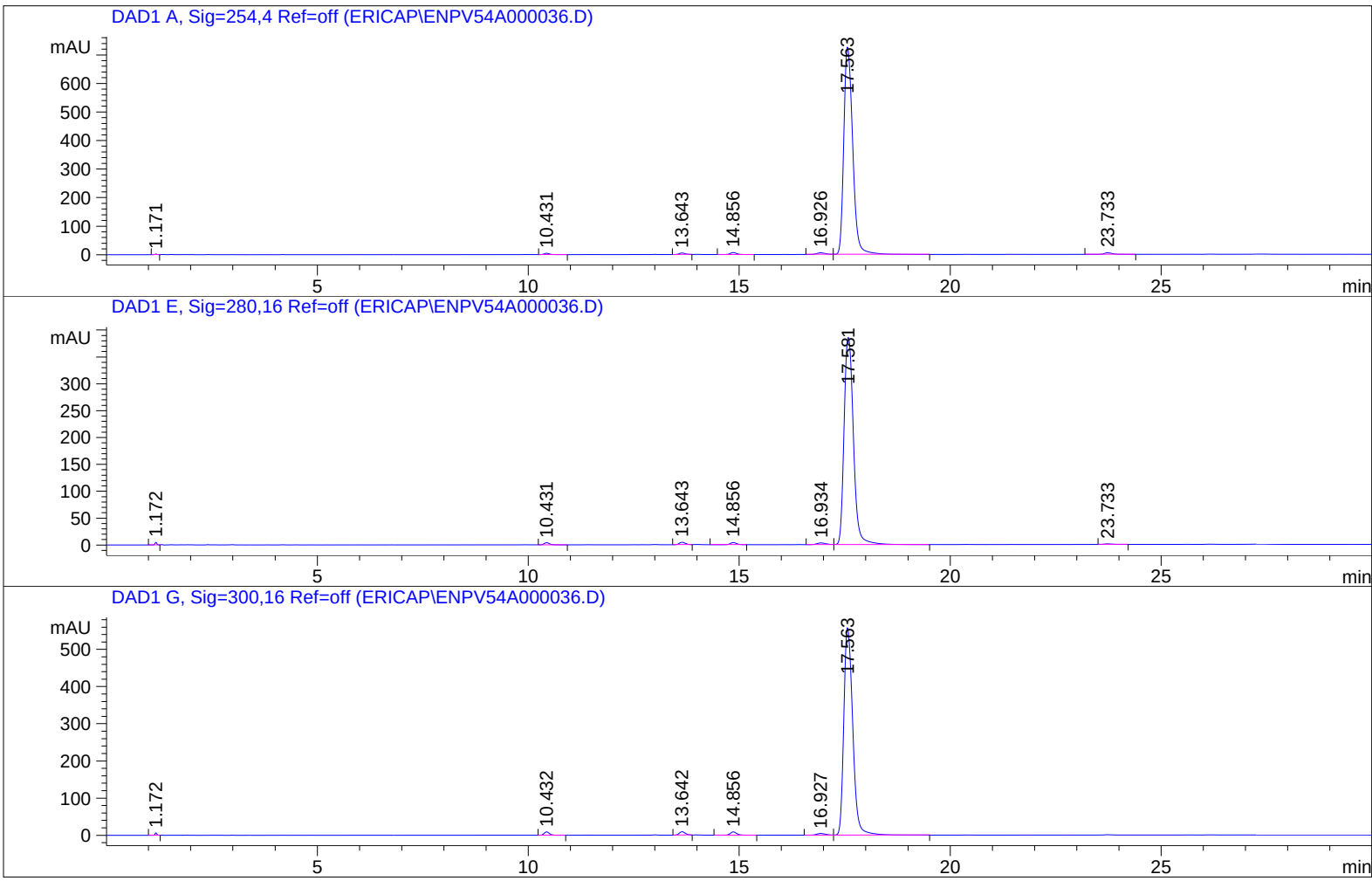
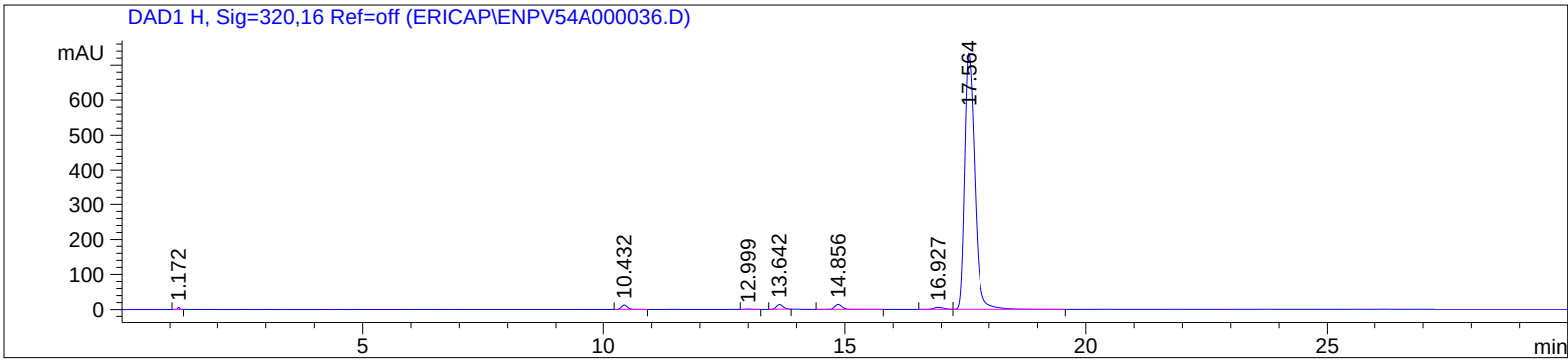

Isolated as a single geometrical isomer. Isomerizes to a mixture of E/Z geometrical isomers in solution.



HPLC trace for Compound 33



==========

Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.171	BV	0.0510	7.87582	2.35338	0.0716
2	10.431	BB	0.1342	40.63835	4.64135	0.3695
3	13.643	BB	0.1532	53.48111	5.41818	0.4862
4	14.856	BB	0.1593	71.34914	6.86153	0.6487
5	16.926	BV	0.2292	87.81870	5.91430	0.7984
6	17.563	VB	0.2314	1.06672e4	726.20331	96.9788
7	23.733	BB	0.1959	71.15097	5.53792	0.6469
Totals :				1.09995e4	756.92998	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.172	BV	0.0516	16.58449	4.89014	0.2704
2	10.431	BB	0.1345	35.12454	3.99845	0.5728
3	13.643	BB	0.1538	45.20145	4.55400	0.7371
4	14.856	BB	0.1589	41.56075	4.00905	0.6777
5	16.934	BV	0.2351	48.93949	3.22429	0.7980
6	17.581	VB	0.2435	5931.77734	385.45874	96.7274
7	23.733	BB	0.1895	13.28068	1.06473	0.2166
Totals :				6132.46873	407.19940	

HPLC trace for Compound 33

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.172	BV	0.0496	20.75646	6.43937	0.2428
2	10.432	BB	0.1335	78.86343	9.06844	0.9226
3	13.642	BB	0.1534	90.39398	9.14135	1.0575
4	14.856	BB	0.1594	91.44717	8.78706	1.0698
5	16.927	BV	0.2261	66.01421	4.52863	0.7723
6	17.563	VB	0.2335	8200.51074	557.71246	95.9350
Totals :				8547.98599	595.67731	

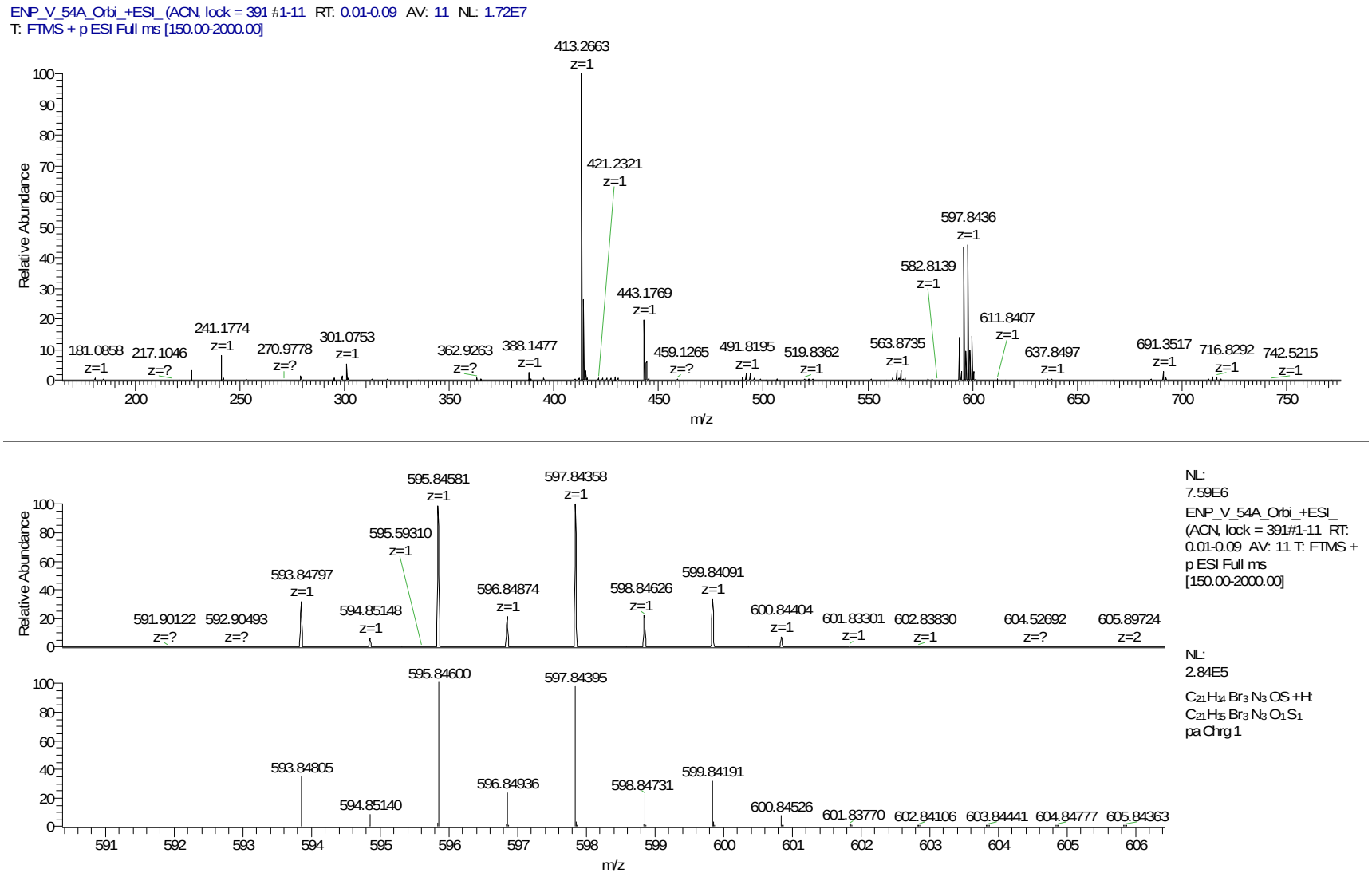
Signal 4: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.172	BV	0.0488	20.34552	6.45876	0.1800
2	10.432	BB	0.1333	111.17649	12.80841	0.9837
3	12.999	BB	0.1413	10.32658	1.14361	0.0914
4	13.642	BB	0.1529	135.37752	13.75121	1.1979
5	14.856	BB	0.1593	149.97922	14.42933	1.3271
6	16.927	BV	0.2257	85.89504	5.90670	0.7600
7	17.564	VB	0.2336	1.07885e4	733.43652	95.4599
Totals :				1.13016e4	787.93455	

*** End of Report ***

HRMS (ESI) for Compound **33**

ENP_V_54A_Orbi_+ESI_ (ACN, lock = 391 5/8/2014 12:09:40 AM



X-Ray crystallographic data obtained for 1,3,5-trisbenzoylbenzene thiosemicarbazone (Compound **2**) has been deposited in the Cambridge Crystallographic Data Centre and was assigned the deposition number CDCC 1042567.

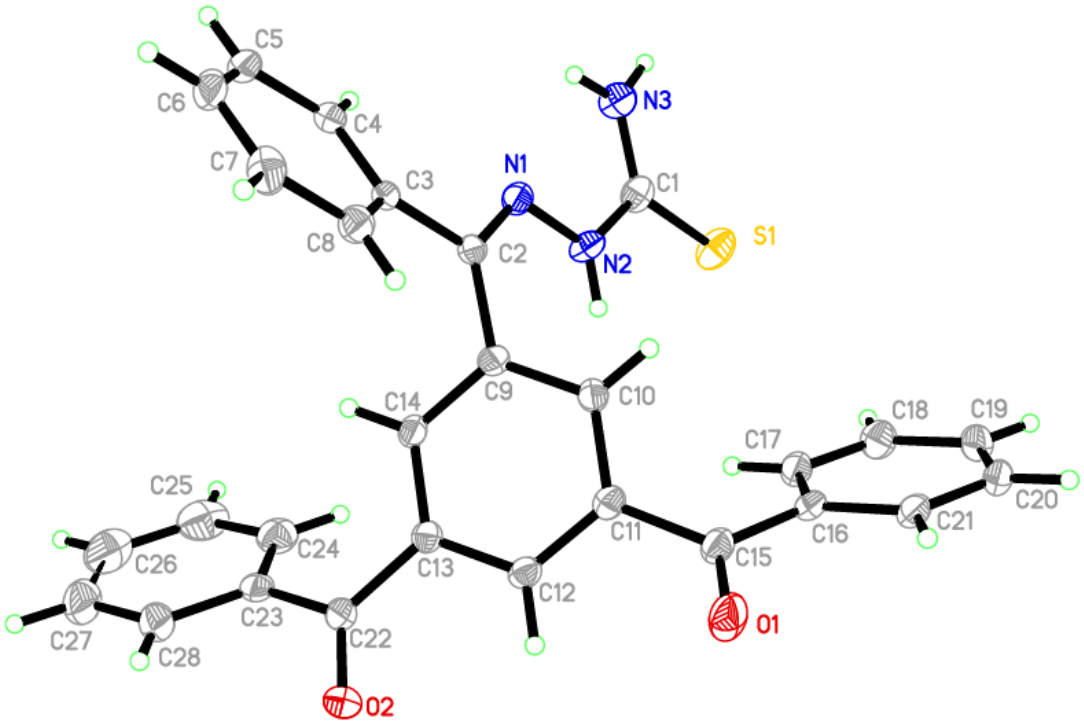


Figure S7. X-Ray Crystal Structure of Compound **2**

Table S2. Crystal data and structure refinement for Compound **2**.

Identification code	kp65	
Empirical formula	C28 H21 N3 O2 S	
Formula weight	463.54	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 11.354(2) Å	α= 90°.
	b = 10.1178(17) Å	β= 100.994(5)°.
	c = 20.493(4) Å	γ = 90°.
Volume	2311.1(7) $Å^3$	
Z	4	
Density (calculated)	1.332 Mg/m^3	
Absorption coefficient	0.172 mm^{-1}	
F(000)	968	
Crystal size	0.27 x 0.27 x 0.07 mm^3	
Theta range for data collection	1.91 to 27.94°.	

Index ranges	-14<=h<=14, -10<=k<=13, -26<=l<=27
Reflections collected	30934
Independent reflections	5493 [R(int) = 0.0644]
Completeness to theta = 27.94°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9881 and 0.9553
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5493 / 0 / 319
Goodness-of-fit on F^2	1.054
Final R indices [I>2sigma(I)]	R1 = 0.0450, wR2 = 0.1052
R indices (all data)	R1 = 0.0634, wR2 = 0.1182
Largest diff. peak and hole	0.448 and -0.386 e.$Å^{-3}$

Table S3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Compound **2**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	1905(1)	4504(1)	2459(1)	30(1)
O(1)	2110(1)	10212(1)	4828(1)	33(1)
O(2)	5832(1)	11865(1)	4047(1)	28(1)
N(1)	4820(1)	4973(1)	3795(1)	19(1)
N(2)	3782(1)	5227(2)	3348(1)	22(1)
N(3)	3649(2)	3015(2)	3146(1)	25(1)
C(1)	3176(2)	4208(2)	3008(1)	22(1)
C(2)	5324(1)	5931(2)	4158(1)	16(1)
C(3)	6485(1)	5645(2)	4601(1)	18(1)
C(4)	7241(2)	4665(2)	4436(1)	22(1)
C(5)	8337(2)	4426(2)	4848(1)	28(1)
C(6)	8684(2)	5140(2)	5429(1)	30(1)
C(7)	7937(2)	6104(2)	5598(1)	29(1)
C(8)	6841(2)	6362(2)	5184(1)	22(1)
C(9)	4860(1)	7309(2)	4143(1)	17(1)
C(10)	3734(1)	7602(2)	4284(1)	18(1)
C(11)	3367(1)	8917(2)	4298(1)	18(1)
C(12)	4120(1)	9924(2)	4174(1)	18(1)

C(13)	5220(1)	9637(2)	4001(1)	17(1)
C(14)	5590(1)	8329(2)	3997(1)	17(1)
C(15)	2177(2)	9276(2)	4463(1)	21(1)
C(16)	1097(1)	8490(2)	4168(1)	19(1)
C(17)	1022(2)	7838(2)	3562(1)	21(1)
C(18)	-14(2)	7161(2)	3286(1)	26(1)
C(19)	-974(2)	7124(2)	3615(1)	26(1)
C(20)	-901(2)	7765(2)	4218(1)	24(1)
C(21)	126(2)	8456(2)	4493(1)	21(1)
C(22)	5988(1)	10750(2)	3847(1)	21(1)
C(23)	6925(2)	10506(2)	3443(1)	23(1)
C(24)	6725(2)	9662(2)	2895(1)	29(1)
C(25)	7605(2)	9521(2)	2514(1)	41(1)
C(26)	8677(2)	10194(2)	2680(1)	48(1)
C(27)	8878(2)	11028(2)	3222(1)	46(1)
C(28)	8001(2)	11195(2)	3600(1)	33(1)

Table S4. Bond lengths [Å] and angles [°] for Compound **2**.

S(1)-C(1)	1.6795(18)
O(1)-C(15)	1.219(2)
O(2)-C(22)	1.225(2)
N(1)-C(2)	1.287(2)
N(1)-N(2)	1.372(2)
N(2)-C(1)	1.356(2)
N(3)-C(1)	1.329(2)
C(2)-C(3)	1.480(2)
C(2)-C(9)	1.488(2)
C(3)-C(8)	1.390(2)
C(3)-C(4)	1.396(2)
C(4)-C(5)	1.386(2)
C(5)-C(6)	1.386(3)
C(6)-C(7)	1.379(3)
C(7)-C(8)	1.391(2)
C(9)-C(14)	1.391(2)

C(9)-C(10)	1.396(2)
C(10)-C(11)	1.397(2)
C(11)-C(12)	1.385(2)
C(11)-C(15)	1.498(2)
C(12)-C(13)	1.393(2)
C(13)-C(14)	1.390(2)
C(13)-C(22)	1.495(2)
C(15)-C(16)	1.490(2)
C(16)-C(21)	1.392(2)
C(16)-C(17)	1.394(2)
C(17)-C(18)	1.385(2)
C(18)-C(19)	1.386(2)
C(19)-C(20)	1.383(3)
C(20)-C(21)	1.385(2)
C(22)-C(23)	1.488(2)
C(23)-C(28)	1.391(3)
C(23)-C(24)	1.393(3)
C(24)-C(25)	1.388(3)
C(25)-C(26)	1.380(4)
C(26)-C(27)	1.378(4)
C(27)-C(28)	1.384(3)

C(2)-N(1)-N(2)	118.39(14)
C(1)-N(2)-N(1)	119.20(15)
N(3)-C(1)-N(2)	115.90(16)
N(3)-C(1)-S(1)	124.37(14)
N(2)-C(1)-S(1)	119.73(14)
N(1)-C(2)-C(3)	116.94(14)
N(1)-C(2)-C(9)	125.22(15)
C(3)-C(2)-C(9)	117.77(14)
C(8)-C(3)-C(4)	119.22(15)
C(8)-C(3)-C(2)	120.29(15)
C(4)-C(3)-C(2)	120.48(15)
C(5)-C(4)-C(3)	119.91(17)
C(4)-C(5)-C(6)	120.54(17)
C(7)-C(6)-C(5)	119.82(17)

C(6)-C(7)-C(8)	120.08(18)
C(3)-C(8)-C(7)	120.43(17)
C(14)-C(9)-C(10)	119.62(15)
C(14)-C(9)-C(2)	118.46(14)
C(10)-C(9)-C(2)	121.91(14)
C(9)-C(10)-C(11)	119.70(15)
C(12)-C(11)-C(10)	120.03(15)
C(12)-C(11)-C(15)	118.52(15)
C(10)-C(11)-C(15)	121.43(15)
C(11)-C(12)-C(13)	120.53(15)
C(14)-C(13)-C(12)	119.21(15)
C(14)-C(13)-C(22)	121.79(15)
C(12)-C(13)-C(22)	118.97(15)
C(13)-C(14)-C(9)	120.76(15)
O(1)-C(15)-C(16)	121.38(15)
O(1)-C(15)-C(11)	119.43(15)
C(16)-C(15)-C(11)	119.18(14)
C(21)-C(16)-C(17)	119.59(15)
C(21)-C(16)-C(15)	119.05(15)
C(17)-C(16)-C(15)	121.30(14)
C(18)-C(17)-C(16)	120.05(15)
C(17)-C(18)-C(19)	119.99(17)
C(20)-C(19)-C(18)	120.16(17)
C(19)-C(20)-C(21)	120.16(16)
C(20)-C(21)-C(16)	120.04(16)
O(2)-C(22)-C(23)	120.28(15)
O(2)-C(22)-C(13)	119.69(15)
C(23)-C(22)-C(13)	120.01(15)
C(28)-C(23)-C(24)	119.63(17)
C(28)-C(23)-C(22)	118.52(17)
C(24)-C(23)-C(22)	121.77(16)
C(25)-C(24)-C(23)	119.6(2)
C(26)-C(25)-C(24)	120.4(2)
C(27)-C(26)-C(25)	120.3(2)
C(26)-C(27)-C(28)	120.0(2)
C(27)-C(28)-C(23)	120.2(2)

Symmetry transformations used to generate equivalent atoms:

Table S5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Compound **2**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	25(1)	37(1)	25(1)	-6(1)	-4(1)	7(1)
O(1)	24(1)	32(1)	46(1)	-18(1)	13(1)	-1(1)
O(2)	25(1)	16(1)	44(1)	-2(1)	6(1)	-1(1)
N(1)	17(1)	21(1)	20(1)	2(1)	4(1)	2(1)
N(2)	21(1)	21(1)	23(1)	0(1)	0(1)	6(1)
N(3)	26(1)	24(1)	24(1)	-5(1)	0(1)	1(1)
C(1)	22(1)	27(1)	18(1)	-3(1)	6(1)	3(1)
C(2)	16(1)	16(1)	19(1)	3(1)	7(1)	1(1)
C(3)	14(1)	16(1)	23(1)	6(1)	6(1)	0(1)
C(4)	19(1)	17(1)	32(1)	5(1)	8(1)	1(1)
C(5)	19(1)	24(1)	44(1)	12(1)	11(1)	5(1)
C(6)	17(1)	36(1)	36(1)	18(1)	2(1)	1(1)
C(7)	24(1)	39(1)	23(1)	7(1)	1(1)	-5(1)
C(8)	21(1)	24(1)	22(1)	4(1)	7(1)	1(1)
C(9)	17(1)	17(1)	16(1)	1(1)	2(1)	2(1)
C(10)	16(1)	19(1)	18(1)	1(1)	4(1)	-1(1)
C(11)	17(1)	20(1)	18(1)	-2(1)	3(1)	2(1)
C(12)	17(1)	17(1)	20(1)	-3(1)	1(1)	2(1)
C(13)	15(1)	18(1)	18(1)	0(1)	0(1)	0(1)
C(14)	14(1)	19(1)	18(1)	2(1)	3(1)	2(1)
C(15)	19(1)	22(1)	23(1)	0(1)	7(1)	4(1)
C(16)	16(1)	17(1)	24(1)	3(1)	4(1)	4(1)
C(17)	18(1)	23(1)	22(1)	2(1)	5(1)	2(1)
C(18)	23(1)	28(1)	25(1)	-1(1)	3(1)	0(1)
C(19)	18(1)	25(1)	34(1)	4(1)	2(1)	-1(1)
C(20)	17(1)	24(1)	32(1)	6(1)	9(1)	3(1)
C(21)	19(1)	21(1)	25(1)	3(1)	7(1)	6(1)
C(22)	16(1)	19(1)	26(1)	3(1)	0(1)	0(1)

C(23)	21(1)	18(1)	31(1)	11(1)	7(1)	3(1)
C(24)	33(1)	28(1)	29(1)	8(1)	9(1)	5(1)
C(25)	54(1)	39(1)	36(1)	12(1)	23(1)	11(1)
C(26)	44(1)	48(1)	60(2)	24(1)	34(1)	15(1)
C(27)	27(1)	43(1)	71(2)	23(1)	19(1)	2(1)
C(28)	23(1)	28(1)	47(1)	11(1)	8(1)	-1(1)

X-Ray crystallographic data obtained for 1,3,5-trisbenzoylbenzene thiosemicarbazone (Compound **10**) has been deposited in the Cambridge Crystallographic Data Centre and was assigned the deposition number CDCC 1046061.

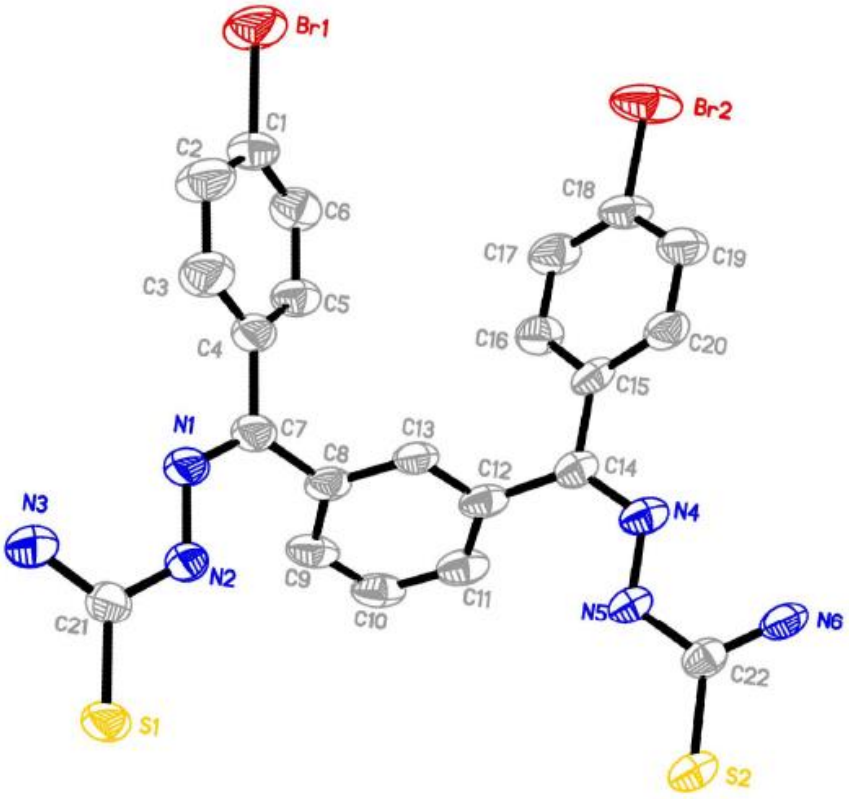


Figure S8. X-Ray Crystal Structure of Compound **10**

Table S6. Crystal data and structure refinement for Compound **10**.

Identification code	KK67	
Empirical formula	C22 H18 Br2 N6 S2	
Formula weight	590.36	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 29.008(3) Å	α= 90°.
	b = 17.6911(16) Å	β= 110.569(3)°.
	c = 12.7098(11) Å	γ = 90°.
Volume	6106.7(10) $Å^3$	
Z	8	
Density (calculated)	1.284 Mg/m^3	
Absorption coefficient	2.809 mm^{-1}	

F(000)	2352
Crystal size	0.140 x 0.077 x 0.049 mm^3
Theta range for data collection	5.103 to 25.682°.
Index ranges	-35<=h<=35, -21<=k<=21, -15<=l<=14
Reflections collected	29003
Independent reflections	5751 [R(int) = 0.0438]
Completeness to theta = 25.242°	99.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.732 and 0.581
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5751 / 0 / 289
Goodness-of-fit on F^2	1.029
Final R indices [I>2sigma(I)]	R1 = 0.1086, wR2 = 0.2988
R indices (all data)	R1 = 0.1422, wR2 = 0.3245
Extinction coefficient	n/a
Largest diff. peak and hole	2.812 and -1.618 e.$Å^{-3}$

Table S7. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Compound **10**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	1675(1)	4900(1)	1357(1)	80(1)
Br(2)	3621(1)	6759(1)	1718(1)	85(1)
S(1)	-705(1)	9682(1)	94(2)	53(1)
S(2)	1795(1)	12076(1)	-103(2)	45(1)
N(1)	299(3)	8101(4)	825(7)	53(2)
N(2)	76(3)	8806(4)	673(7)	53(2)
N(3)	-646(4)	8194(5)	311(12)	92(4)
N(4)	2330(3)	10044(4)	650(6)	43(2)
N(5)	2022(3)	10662(4)	496(6)	40(2)
N(6)	2599(3)	11311(4)	11(6)	47(2)
C(1)	1392(4)	5870(5)	1333(9)	55(2)
C(2)	923(4)	6019(6)	598(11)	68(3)
C(3)	726(4)	6733(6)	564(11)	65(3)
C(4)	992(3)	7295(5)	1273(8)	46(2)

C(5)	1455(4)	7125(5)	2023(8)	48(2)
C(6)	1660(4)	6413(5)	2064(8)	52(2)
C(7)	772(4)	8062(5)	1226(8)	47(2)
C(8)	1114(3)	8708(5)	1638(7)	44(2)
C(9)	1089(4)	9197(5)	2471(7)	51(2)
C(10)	1421(4)	9766(5)	2859(7)	51(2)
C(11)	1789(4)	9876(5)	2420(7)	47(2)
C(12)	1825(3)	9395(4)	1582(7)	42(2)
C(13)	1487(3)	8808(4)	1206(7)	40(2)
C(14)	2232(3)	9458(4)	1123(7)	38(2)
C(15)	2555(3)	8794(4)	1226(7)	41(2)
C(16)	2623(4)	8274(5)	2080(8)	49(2)
C(17)	2927(4)	7665(6)	2207(8)	57(3)
C(18)	3185(4)	7583(5)	1490(8)	52(2)
C(19)	3122(4)	8081(5)	619(8)	54(2)
C(20)	2809(3)	8681(5)	486(8)	46(2)
C(21)	-412(4)	8847(5)	373(10)	57(3)
C(22)	2164(3)	11310(4)	137(7)	38(2)

Table S8. Bond lengths [Å] and angles [°] for Compound **10**.

Br(1)-C(1)	1.897(9)
Br(2)-C(18)	1.885(9)
S(1)-C(21)	1.681(9)
S(2)-C(22)	1.687(8)
N(1)-C(7)	1.287(13)
N(1)-N(2)	1.386(10)
N(2)-C(21)	1.332(12)
N(3)-C(21)	1.327(13)
N(4)-C(14)	1.280(10)
N(4)-N(5)	1.384(10)
N(5)-C(22)	1.351(10)
N(6)-C(22)	1.326(12)
C(1)-C(6)	1.372(14)
C(1)-C(2)	1.379(14)

C(2)-C(3)	1.381(14)
C(3)-C(4)	1.382(15)
C(4)-C(5)	1.380(13)
C(4)-C(7)	1.492(11)
C(5)-C(6)	1.386(13)
C(7)-C(8)	1.483(13)
C(8)-C(13)	1.387(12)
C(8)-C(9)	1.389(12)
C(9)-C(10)	1.361(14)
C(10)-C(11)	1.380(14)
C(11)-C(12)	1.396(12)
C(12)-C(13)	1.391(12)
C(12)-C(14)	1.493(13)
C(14)-C(15)	1.481(12)
C(15)-C(16)	1.384(12)
C(15)-C(20)	1.398(13)
C(16)-C(17)	1.366(13)
C(17)-C(18)	1.373(14)
C(18)-C(19)	1.376(13)
C(19)-C(20)	1.367(13)

C(7)-N(1)-N(2)	118.8(8)
C(21)-N(2)-N(1)	118.9(8)
C(14)-N(4)-N(5)	117.7(7)
C(22)-N(5)-N(4)	117.3(7)
C(6)-C(1)-C(2)	120.9(9)
C(6)-C(1)-Br(1)	118.9(7)
C(2)-C(1)-Br(1)	120.2(8)
C(1)-C(2)-C(3)	119.7(10)
C(2)-C(3)-C(4)	120.5(10)
C(5)-C(4)-C(3)	118.6(8)
C(5)-C(4)-C(7)	121.6(9)
C(3)-C(4)-C(7)	119.7(9)
C(4)-C(5)-C(6)	121.6(9)
C(1)-C(6)-C(5)	118.6(9)
N(1)-C(7)-C(8)	125.9(8)

N(1)-C(7)-C(4)	116.5(8)
C(8)-C(7)-C(4)	117.6(8)
C(13)-C(8)-C(9)	118.7(9)
C(13)-C(8)-C(7)	118.5(8)
C(9)-C(8)-C(7)	122.8(8)
C(10)-C(9)-C(8)	121.1(9)
C(9)-C(10)-C(11)	120.6(8)
C(10)-C(11)-C(12)	119.8(9)
C(13)-C(12)-C(11)	119.0(8)
C(13)-C(12)-C(14)	118.7(7)
C(11)-C(12)-C(14)	122.2(8)
C(8)-C(13)-C(12)	120.8(8)
N(4)-C(14)-C(15)	116.3(8)
N(4)-C(14)-C(12)	125.7(7)
C(15)-C(14)-C(12)	118.0(7)
C(16)-C(15)-C(20)	118.0(8)
C(16)-C(15)-C(14)	120.5(8)
C(20)-C(15)-C(14)	121.5(7)
C(17)-C(16)-C(15)	121.7(9)
C(16)-C(17)-C(18)	118.9(8)
C(17)-C(18)-C(19)	121.2(8)
C(17)-C(18)-Br(2)	118.1(7)
C(19)-C(18)-Br(2)	120.7(7)
C(20)-C(19)-C(18)	119.4(9)
C(19)-C(20)-C(15)	120.8(8)
N(3)-C(21)-N(2)	116.1(8)
N(3)-C(21)-S(1)	122.8(8)
N(2)-C(21)-S(1)	121.1(7)
N(6)-C(22)-N(5)	117.3(7)
N(6)-C(22)-S(2)	123.2(6)
N(5)-C(22)-S(2)	119.5(6)

Symmetry transformations used to generate equivalent atoms:

Table S9. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Compound **10**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	71(1)	38(1)	123(1)	6(1)	22(1)	21(1)
Br(2)	135(1)	56(1)	65(1)	14(1)	36(1)	52(1)
S(1)	61(1)	40(1)	76(2)	26(1)	45(1)	20(1)
S(2)	58(1)	28(1)	48(1)	7(1)	16(1)	2(1)
N(1)	67(5)	32(4)	79(6)	14(4)	48(5)	11(3)
N(2)	56(5)	32(4)	85(6)	22(4)	44(4)	12(3)
N(3)	63(6)	35(5)	186(13)	23(6)	56(7)	14(4)
N(4)	57(4)	29(4)	40(4)	3(3)	13(3)	5(3)
N(5)	47(4)	27(3)	46(4)	5(3)	15(3)	1(3)
N(6)	64(5)	27(3)	50(4)	6(3)	22(4)	4(3)
C(1)	57(6)	36(5)	72(7)	5(5)	25(5)	14(4)
C(2)	51(6)	38(5)	98(8)	-6(5)	5(6)	7(4)
C(3)	49(6)	43(5)	95(8)	4(5)	14(6)	11(4)
C(4)	58(5)	33(4)	60(6)	13(4)	35(5)	11(4)
C(5)	66(6)	37(5)	43(5)	6(4)	23(4)	12(4)
C(6)	56(6)	48(5)	48(5)	12(4)	15(4)	17(5)
C(7)	61(6)	34(4)	60(6)	12(4)	37(5)	14(4)
C(8)	64(6)	28(4)	47(5)	15(4)	29(4)	15(4)
C(9)	79(7)	40(5)	45(5)	15(4)	37(5)	28(5)
C(10)	83(7)	39(5)	35(4)	4(4)	27(5)	23(5)
C(11)	71(6)	33(4)	35(4)	4(3)	15(4)	12(4)
C(12)	63(5)	27(4)	36(4)	7(3)	15(4)	11(4)
C(13)	62(5)	25(4)	42(4)	5(3)	29(4)	10(4)
C(14)	47(5)	30(4)	34(4)	3(3)	11(4)	1(3)
C(15)	60(5)	23(4)	38(4)	4(3)	16(4)	-3(4)
C(16)	71(6)	40(5)	40(5)	5(4)	26(4)	9(4)
C(17)	84(7)	41(5)	46(5)	14(4)	24(5)	13(5)
C(18)	79(6)	32(4)	43(5)	5(4)	20(5)	19(4)
C(19)	79(7)	38(5)	52(5)	7(4)	32(5)	16(5)
C(20)	63(6)	31(4)	47(5)	11(4)	23(4)	5(4)
C(21)	65(6)	41(5)	87(7)	23(5)	54(6)	14(4)
C(22)	49(5)	29(4)	33(4)	-4(3)	12(4)	-3(3)

X-Ray crystallographic data obtained for 1,3,5-trisbenzoylbenzene thiosemicarbazone (Compound **33**) has been deposited in the Cambridge Crystallographic Data Centre and was assigned the deposition number CDCC 1042568.

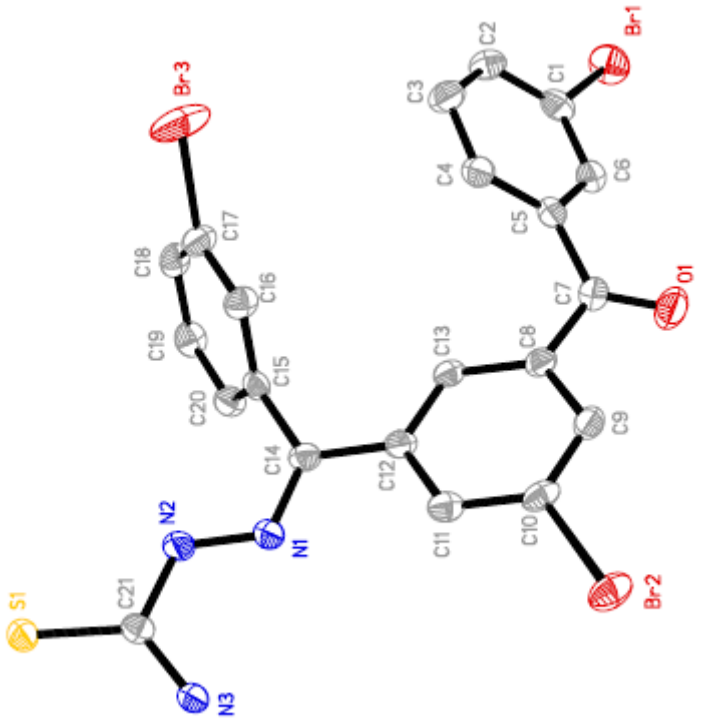


Figure S9. X-Ray Crystal Structure for Compound **33**

Table S10. Crystal data and structure refinement for Compound **33**.

Identification code	KP68	
Empirical formula	C21 H14 Br3 N3 O S	
Formula weight	596.14	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 9.8474(4) Å	α= 80.6333(12)°.
	b = 10.1192(4) Å	β= 86.6676(13)°.
	c = 10.9296(4) Å	γ = 85.3138(12)°.
Volume	1069.88(7) $Å^3$	
Z	2	
Density (calculated)	1.851 Mg/m^3	
Absorption coefficient	5.771 mm^{-1}	
F(000)	580	

Crystal size	0.296 x 0.138 x 0.042 mm^3
Theta range for data collection	5.116 to 25.680°.
Index ranges	-12<=h<=12, -12<=k<=12, -13<=l<=13
Reflections collected	23243
Independent reflections	4027 [R(int) = 0.0316]
Completeness to theta = 25.242°	99.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.543 and 0.191
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4027 / 0 / 262
Goodness-of-fit on F^2	1.052
Final R indices [I>2sigma(I)]	R1 = 0.0365, wR2 = 0.0867
R indices (all data)	R1 = 0.0399, wR2 = 0.0892
Extinction coefficient	n/a
Largest diff. peak and hole	2.962 and -2.202 e.$Å^{-3}$

Table S11. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Compound **33**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	3858(1)	9655(1)	3004(1)	42(1)
Br(2)	5680(1)	1690(1)	10380(1)	32(1)
Br(3)	11086(1)	8541(1)	6113(1)	55(1)
S(1)	11060(1)	6522(1)	13447(1)	25(1)
O(1)	3957(3)	5319(3)	6514(3)	44(1)
N(1)	8451(3)	5772(3)	11165(3)	24(1)
N(2)	9371(3)	6415(3)	11705(3)	26(1)
N(3)	8912(3)	5050(3)	13530(3)	26(1)
C(1)	5161(4)	8570(4)	4017(3)	28(1)
C(2)	6533(4)	8766(4)	3813(3)	31(1)
C(3)	7463(4)	7947(4)	4553(4)	31(1)
C(4)	7021(4)	6957(4)	5489(3)	25(1)
C(5)	5633(4)	6784(3)	5691(3)	23(1)
C(6)	4694(4)	7589(4)	4933(3)	27(1)
C(7)	5059(4)	5730(4)	6654(3)	26(1)

C(8)	5802(3)	5182(3)	7807(3)	22(1)
C(9)	5514(4)	3902(4)	8408(3)	24(1)
C(10)	6117(4)	3402(3)	9515(3)	24(1)
C(11)	6992(4)	4122(3)	10042(3)	24(1)
C(12)	7269(3)	5414(3)	9452(3)	22(1)
C(13)	6667(3)	5937(3)	8328(3)	20(1)
C(14)	8162(4)	6223(3)	10027(3)	22(1)
C(15)	8682(3)	7481(3)	9299(3)	21(1)
C(16)	9534(4)	7422(3)	8249(3)	25(1)
C(17)	9978(4)	8609(4)	7581(3)	28(1)
C(18)	9598(4)	9838(4)	7928(3)	27(1)
C(19)	8752(4)	9887(4)	8980(3)	28(1)
C(20)	8296(4)	8717(4)	9670(3)	25(1)
C(21)	9701(3)	5937(3)	12902(3)	21(1)

Table S12. Bond lengths [Å] and angles [°] for Compound **33**.

Br(1)-C(1)	1.902(4)
Br(2)-C(10)	1.903(3)
Br(3)-C(17)	1.895(4)
S(1)-C(21)	1.682(4)
O(1)-C(7)	1.220(4)
N(1)-C(14)	1.293(4)
N(1)-N(2)	1.369(4)
N(2)-C(21)	1.367(4)
N(3)-C(21)	1.316(5)
C(1)-C(6)	1.377(5)
C(1)-C(2)	1.382(6)
C(2)-C(3)	1.387(6)
C(3)-C(4)	1.388(5)
C(4)-C(5)	1.393(5)
C(5)-C(6)	1.397(5)
C(5)-C(7)	1.493(5)
C(7)-C(8)	1.498(5)
C(8)-C(13)	1.392(5)

C(8)-C(9)	1.396(5)
C(9)-C(10)	1.381(5)
C(10)-C(11)	1.380(5)
C(11)-C(12)	1.400(5)
C(12)-C(13)	1.402(5)
C(12)-C(14)	1.479(5)
C(14)-C(15)	1.498(5)
C(15)-C(16)	1.389(5)
C(15)-C(20)	1.393(5)
C(16)-C(17)	1.389(5)
C(17)-C(18)	1.376(5)
C(18)-C(19)	1.385(5)
C(19)-C(20)	1.389(5)

C(14)-N(1)-N(2)	118.3(3)
C(21)-N(2)-N(1)	118.9(3)
C(6)-C(1)-C(2)	121.9(3)
C(6)-C(1)-Br(1)	118.1(3)
C(2)-C(1)-Br(1)	120.0(3)
C(1)-C(2)-C(3)	118.8(3)
C(2)-C(3)-C(4)	120.6(4)
C(3)-C(4)-C(5)	119.8(3)
C(4)-C(5)-C(6)	119.9(3)
C(4)-C(5)-C(7)	123.9(3)
C(6)-C(5)-C(7)	116.2(3)
C(1)-C(6)-C(5)	119.0(3)
O(1)-C(7)-C(5)	119.7(3)
O(1)-C(7)-C(8)	119.1(3)
C(5)-C(7)-C(8)	121.2(3)
C(13)-C(8)-C(9)	120.3(3)
C(13)-C(8)-C(7)	122.3(3)
C(9)-C(8)-C(7)	117.2(3)
C(10)-C(9)-C(8)	118.7(3)
C(11)-C(10)-C(9)	122.2(3)
C(11)-C(10)-Br(2)	118.5(3)
C(9)-C(10)-Br(2)	119.2(3)

C(10)-C(11)-C(12)	119.4(3)
C(11)-C(12)-C(13)	119.2(3)
C(11)-C(12)-C(14)	120.2(3)
C(13)-C(12)-C(14)	120.6(3)
C(8)-C(13)-C(12)	120.3(3)
N(1)-C(14)-C(12)	116.0(3)
N(1)-C(14)-C(15)	123.6(3)
C(12)-C(14)-C(15)	120.4(3)
C(16)-C(15)-C(20)	119.9(3)
C(16)-C(15)-C(14)	120.2(3)
C(20)-C(15)-C(14)	119.9(3)
C(15)-C(16)-C(17)	118.8(3)
C(18)-C(17)-C(16)	122.0(3)
C(18)-C(17)-Br(3)	118.9(3)
C(16)-C(17)-Br(3)	119.0(3)
C(17)-C(18)-C(19)	118.7(3)
C(18)-C(19)-C(20)	120.6(3)
C(19)-C(20)-C(15)	119.9(3)
N(3)-C(21)-N(2)	116.2(3)
N(3)-C(21)-S(1)	125.7(3)
N(2)-C(21)-S(1)	118.1(3)

Symmetry transformations used to generate equivalent atoms:

Table S13. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Compound **33**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	44(1)	41(1)	37(1)	7(1)	-15(1)	2(1)
Br(2)	39(1)	18(1)	36(1)	1(1)	6(1)	-7(1)
Br(3)	73(1)	35(1)	54(1)	-8(1)	38(1)	-18(1)
S(1)	26(1)	25(1)	24(1)	0(1)	-5(1)	-6(1)
O(1)	35(2)	51(2)	44(2)	11(1)	-13(1)	-21(1)
N(1)	28(2)	25(2)	19(1)	-1(1)	-3(1)	-7(1)

N(2)	34(2)	25(2)	20(1)	3(1)	-5(1)	-11(1)
N(3)	31(2)	27(2)	19(1)	1(1)	-6(1)	-10(1)
C(1)	34(2)	29(2)	22(2)	-2(1)	-7(2)	1(2)
C(2)	35(2)	30(2)	25(2)	3(2)	2(2)	-6(2)
C(3)	26(2)	36(2)	29(2)	-1(2)	5(2)	-4(2)
C(4)	24(2)	29(2)	22(2)	-4(1)	-1(1)	0(1)
C(5)	26(2)	25(2)	21(2)	-5(1)	-3(1)	-4(1)
C(6)	24(2)	32(2)	25(2)	-6(2)	-4(1)	-4(2)
C(7)	25(2)	28(2)	26(2)	-6(2)	-1(1)	-7(2)
C(8)	21(2)	25(2)	21(2)	-3(1)	4(1)	-4(1)
C(9)	23(2)	25(2)	26(2)	-6(1)	3(1)	-8(1)
C(10)	28(2)	16(2)	26(2)	-2(1)	9(1)	-4(1)
C(11)	28(2)	22(2)	21(2)	-2(1)	2(1)	-2(1)
C(12)	25(2)	21(2)	18(2)	-3(1)	3(1)	-4(1)
C(13)	23(2)	18(2)	19(2)	-1(1)	3(1)	-4(1)
C(14)	25(2)	21(2)	19(2)	0(1)	0(1)	-4(1)
C(15)	23(2)	20(2)	19(2)	0(1)	-7(1)	-3(1)
C(16)	30(2)	18(2)	27(2)	-3(1)	1(1)	-5(1)
C(17)	28(2)	28(2)	27(2)	-2(2)	5(2)	-7(2)
C(18)	29(2)	20(2)	31(2)	2(1)	-5(2)	-7(1)
C(19)	32(2)	20(2)	32(2)	-6(1)	-5(2)	-1(1)
C(20)	28(2)	26(2)	23(2)	-4(1)	-2(1)	-2(1)
C(21)	25(2)	18(2)	20(2)	-2(1)	-2(1)	0(1)