Electronic Supplementary Material (ESI) for MedChemComm.

Design, Synthesis and Biological Evaluation of Novel 1,3-Diarylpyrazoles as Cyclooxygenase Inhibitors, Antiplatelet, and Anticancer Agents

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Figures **Page**

General procedure for the preparation of 3/4-[(1*E*)-1-(2-phenylhidraziniliden)ethyl] pyridine derivatives (2a, 7)

A solution of acetylpyridine derivative (0.052 mol), phenyl hydrazine (6.27 g, 0.058 mol) and acetic acid (2 ml, 0.035 mol) in ethanol was stirred for 2 hat reflux, and then evaporated. The precipitated was filtered off and dried.

***N*-Phenyl-*N'*-(1-pyridine-3-il-ethyliden)hydrazine 2a**

Yield %90, mp 138.8 – 140 ˚C [1]. IR (FTIR/FTNIR-ATR): 3169 cm^{-1} (N-H), 2993 cm^{-1} (aliphatic C-H). ^{1}H-NMR ($CDCl_3$) δ: 8.98 (1H, d, *J*=2.4 Hz), 8.53 (1H, dd, *J*=1.6 Hz, 4.8 Hz), 8.10 (1H, dt, *J*=2 Hz, 8 Hz), 7.47 (1H, s), 7.31-7.26 (3H, m), 7.18 (2H, d, *J*=7.2 Hz), 6.91 (1H, t, *J*=7.2 Hz), 2.26 (3H, s). HRMS $C_{13}H_{14}N_3$ $[M+H]^+$ *Calc.* 212.1188, Found m/z 212.1187. Anal. *Calc*. (%) for $C_{13}H_{13}N_3$ Calc. % C: 73.91 H: 6.20 N: 19.89, Found % C: 74.27 H: 6.08 N: 19.60.

4-(1-(2-phenylhydrazono)ethyl)pyridine 7

Yield 85%, mp 147℃ (Lit. Mp. [1, 2]: 148-149 ℃). IR (FTIR/FTNIR-ATR): 3227 cm^{-1} (N-H), 1941 cm^{-1} (C=N). ^{1}H-NMR ($CDCl_3$) δ: 8.58-8.60 (2H, d, *J*=6.4 Hz), 7.65 (2H, d, *J*=6 Hz), 7.59 (1H, s), 7.29-7.33 (2H, t, *J*=7.6 Hz), 7.19-7.22 (2H, d, *J*=7.6 Hz), 6.92-6.95 (1H, m, *J*=6.8 Hz, *J*=7.6 Hz), 2.22 (3H, s). HRMS $C_{13}H_{14}N_3$ $[M+H]^+$ *Calc*. 212.1188, Found m/z 212.1180. Anal. *Calc*. (%) for $C_{13}H_{13}N_3$. C: 73.91 H: 6.20 N: 19.89, Found C: 74.21 H: 6.22 N: 19.38.

General procedure for the preparation of 1-phenyl-3-(pyridine-3/4-yl)-1*H*-pyrazole-4-carbaldehyde derivatives (3a,8)

In a dry flask, phosphoroxy chloride ($POCl_3$) (0.124 mol) was added drop wise to an ice-cold stirred solution of hydrazon derivative (0.041 mol) in 80 ml DMF. The reaction mixture was allowed to attain room temperature, and then heated at 50 ℃ for 4 h. The resulting mixture was poured onto crushed ice, neutralized with dilute NaOH and left overnight. The yellow precipitate obtained was purified by crystallization in toluene.

1-Phenyl-3-(pyridine-3-yl)-1*H*-pyrazole-4-carbaldehyde 3a

Yield %85, mp 158.8–160 ˚C [1]. IR (FTIR/FTNIR-ATR): 1673 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 10.06 (1H, s), 9.12 (1H, d, *J*=2.4 Hz), 8.70 (1H, dd, J_a=1.6 Hz, J_b=4.8 Hz), 8.58 (1H, s), 8.47 (1H, dt, J_a=2 Hz, J_b=8 Hz), 7.81 (2H, d, *J*=7.6 Hz), 7.56-7.52 (2H, m), 7.46-7.41 (2H, m). HRMS $C_{15}H_{12}N_3O$ $[M+H]^+$ *Calc.* 250.0980, Found m/z 250.0979.

Anal. *Calc*. (%) for $C_{15}H_{12}N_3O$ Calc. % C: 72.28 H: 4.45 N: 16.86, Found % C: 72.06 H: 4.46 N: 16.77

1-Phenyl-3-(pyridine-4-yl)-1*H*-pyrazole-4-carbaldehyde 8

Yield 13.8 (92%), mp 147 – 149 ℃ [1]. IR (FTIR/FTNIR-ATR): 1669 cm^{-1} (C=O). ^{1}H-NMR (DMSO-d_6) δ: 10.04 (1H, s), 9.43 (1H, s), 8.73 (2H, d, *J*=1.6 Hz), 8.02-7.97 (4H, m), 7.62-7.58 (2H, m), 7.48-7.44 (1H, m). HRMS $C_{15}H_{12}N_3O$ $[M+H]^+$ *Calc*. 250.0980, Found m/z 250.0980. Anal. *Calc*. (%) for $C_{15}H_{11}N_3O$ C: 72.28 H: 4.45 N: 16.86, Found C: 72.20 H: 4.42 N: 17.07

General procedure for the preparation of (2*E*)-3-[1-Substituted phenyl-3-(pyridine-3/4-yl)-1*H*-pyrazole-4-yl]prop-2-enoic acid derivatives (4a, 9)

To a solution of 1-phenyl-3-(pyridin-3/4-yl)-1*H*-pyrazole-4-carbaldehyde (8.72 mmol) in pyridine (20 ml), malonic acid (0.035 mol), and piperidine (0.0131 mol) were added, and the reaction mixture was refluxed for 4 h. On cooling, the reaction mixture was poured onto a solution (100 ml) of crushed ice and concentrated HCl (50% by volume) mixture, then, pH was adjusted to 5. The resulting precipitated was filtered off, washed with acidified water and dried.

(2*E*)-3-[1-Phenyl-3-(pyridine-3-yl)-1*H*-pyrazole-4-yl)acrylic acid 4a

Yield %91, mp 240–242 ˚C [1]. IR (FTIR/FTNIR-ATR): 1668 cm^{-1} (C=O). ^{1}H-NMR (DMSO-d_6) δ: 12.38 (1H, s), 9.27 (1H, s), 8.84 (1H, d, *J*=1.6 Hz), 8.69 (1H, dd, *J*=1.6 Hz, *J*=5.2 Hz), 8.05 (1H, dt, *J*=2 Hz, 7.6 Hz), 7.94 (2H, d, *J*=7.6 Hz), 7.61-7.55 (2H, m), 7.48 (1H, d, *J*=15.6 Hz), 7.41 (2H, m), 6.48-6.44 (1H, d, *J*=16 Hz). HRMS $C_{17}H_{14}N_3O_2$ $[M+H]^+$ *Calc.* 292.1086, Found m/z 292.1095.

(2*E*)-3-[1-Phenyl-3-(pyridin-4-yl)-1*H*-pyrazol-4-yl]acrylic acid 9

Yield 78%, mp 287 – 288 ℃ [1]. IR (FTIR/FTNIR-ATR): 1681cm^{-1} (C=O), 2440 cm^{-1} (C=C). ^{1}H-NMR (DMSO-d_6) δ: 9.27 (1H, s), 8.75-8.73 (2H, d, *J*=6 Hz), 7.96-7.93 (2H, d, *J*=8.4 Hz), 7.67-7.65 (2H, d, *J*=6.4 Hz), 7.60-7.53 (3H, m), 7.43-7.40 (1H, t, *J*=7.6 Hz), 6.51-6.47 (1H, d, *J*=16 Hz). HRMS $C_{17}H_{14}N_3O$ $[M+H]^+$ *Calc*. 292.1086, Found m/z 292.1089. Anal. *Calc*. (%) for $C_{17}H_{13}N_3O$ C: 70.09 H: 4.50 N: 14.42, Found C: 69.92 H: 4.65 N: 14.34

Figure S1. Spectral data of Compound **2a**

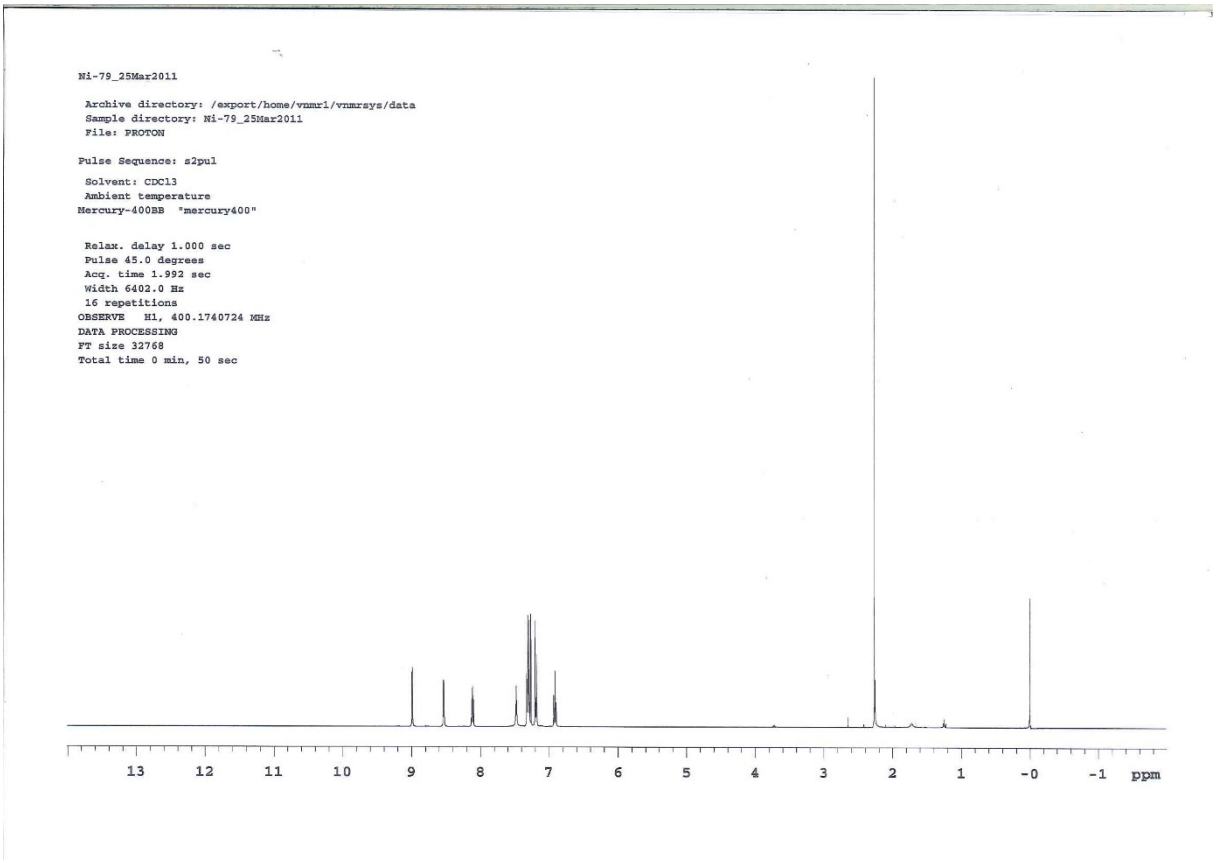


Figure S2. Spectral data of Compound **2b**

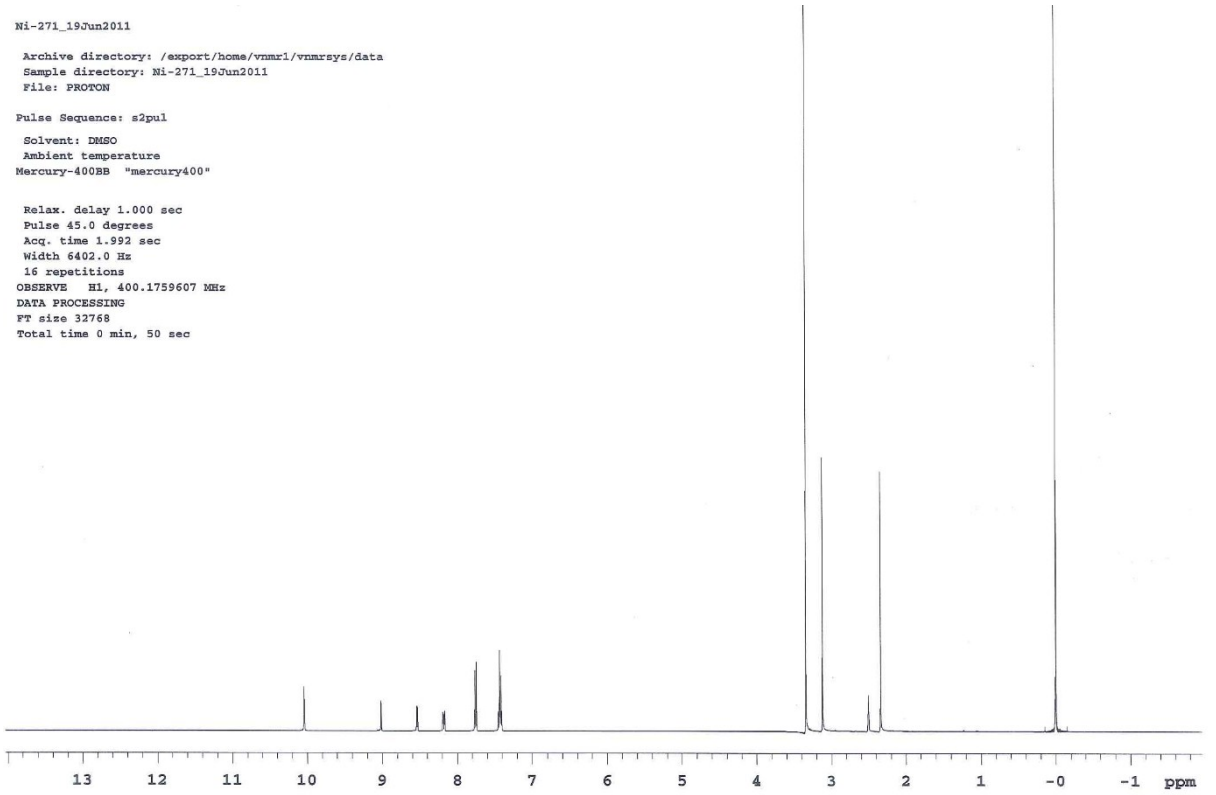


Figure S3. Spectral data of Compound **7**

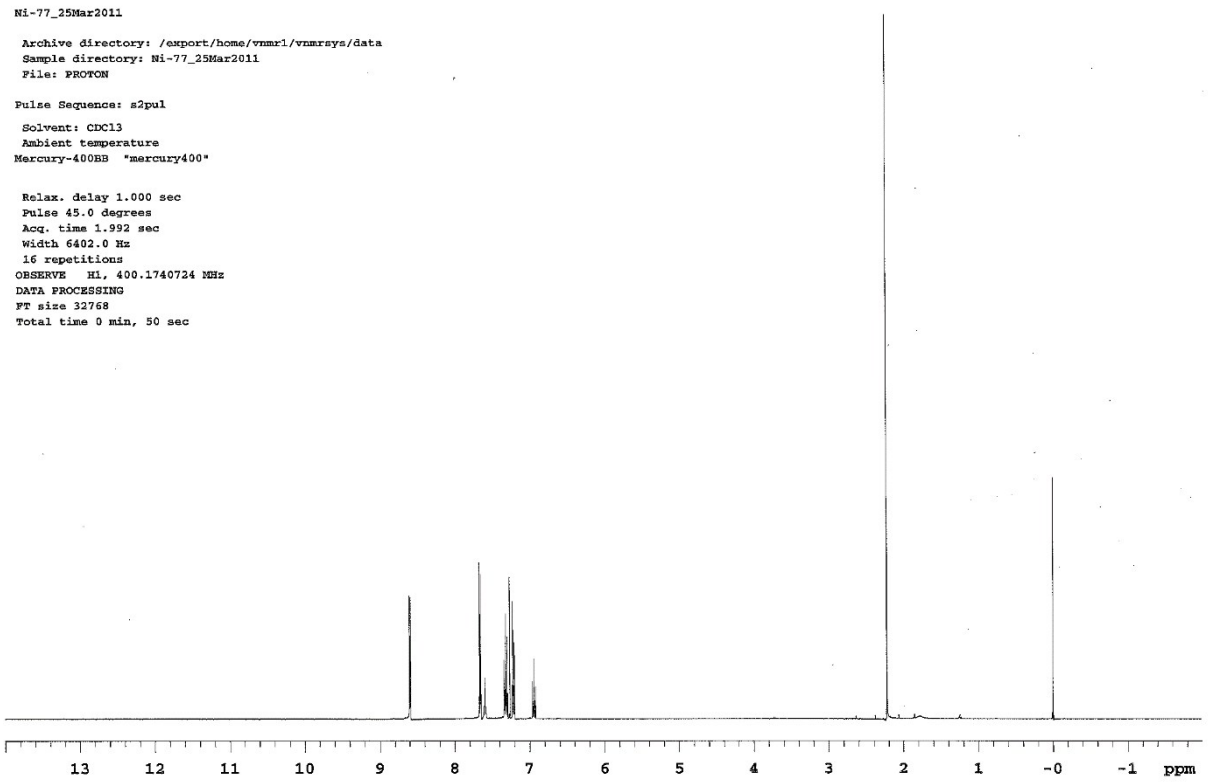


Figure S4. Spectral data of Compound **3a**

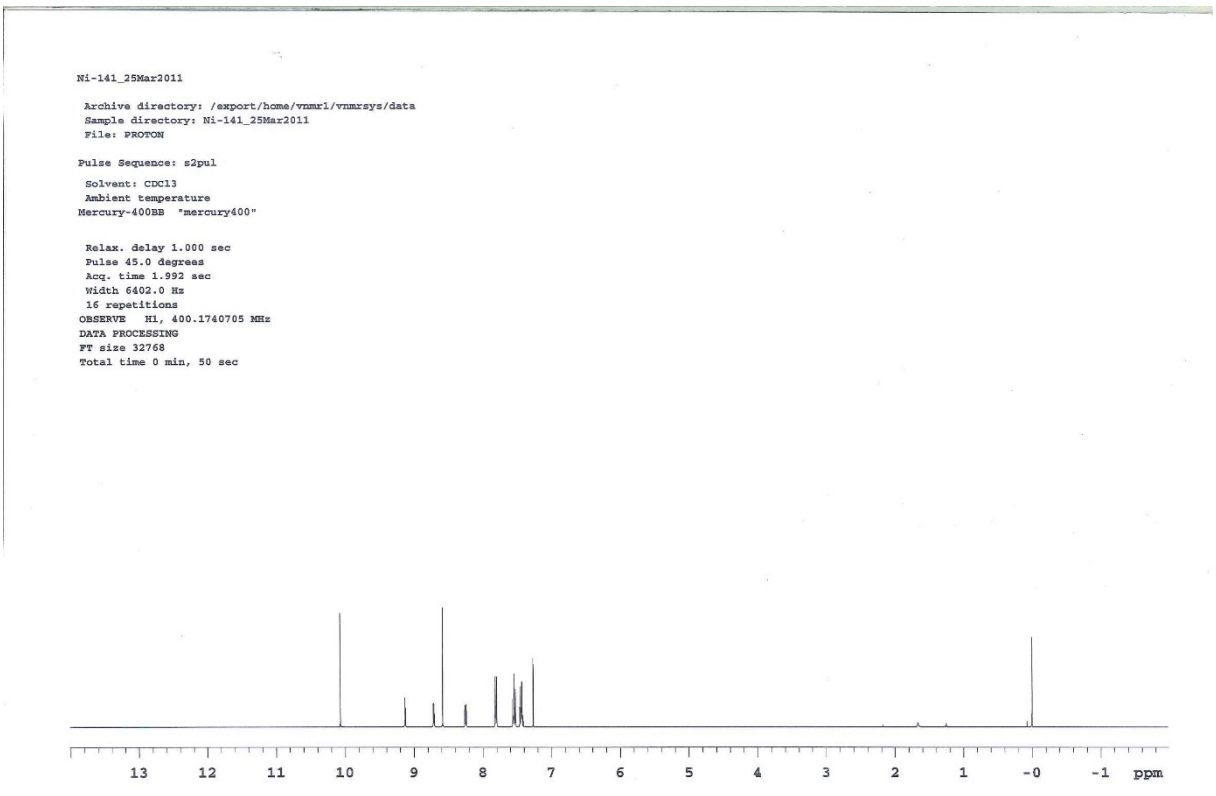
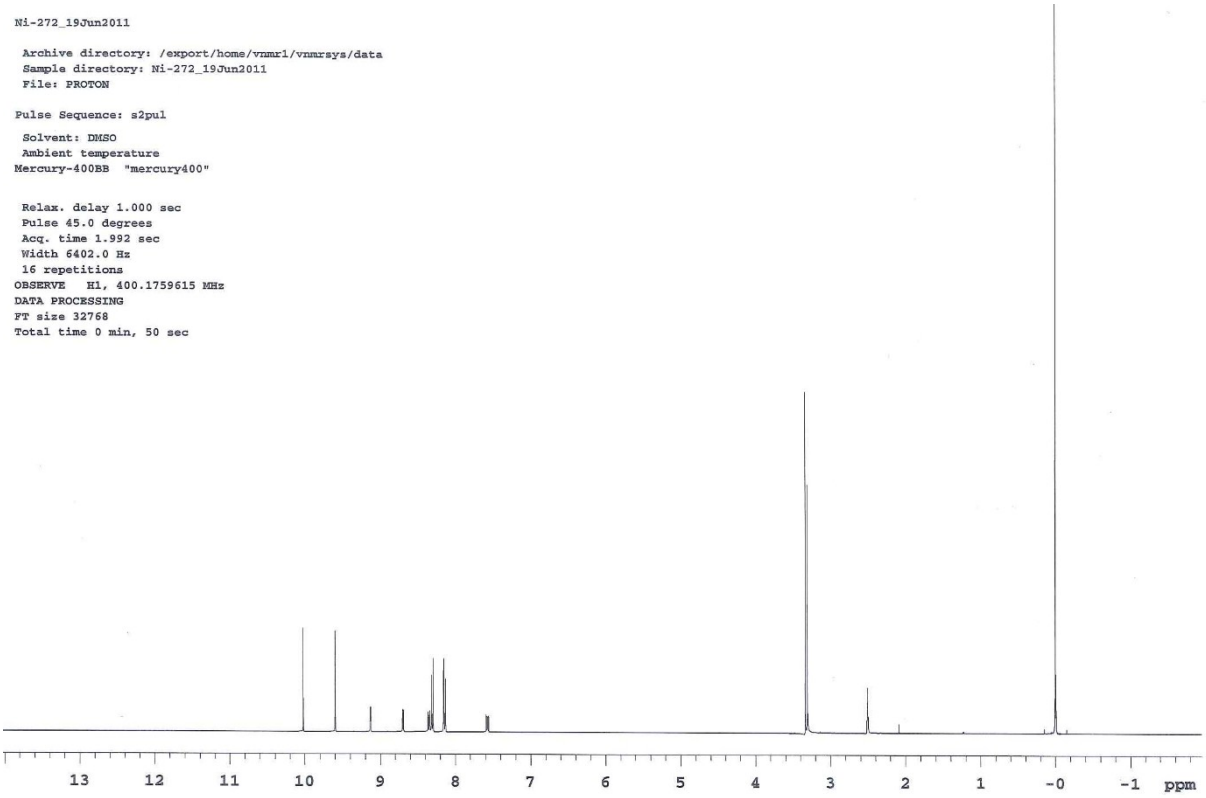
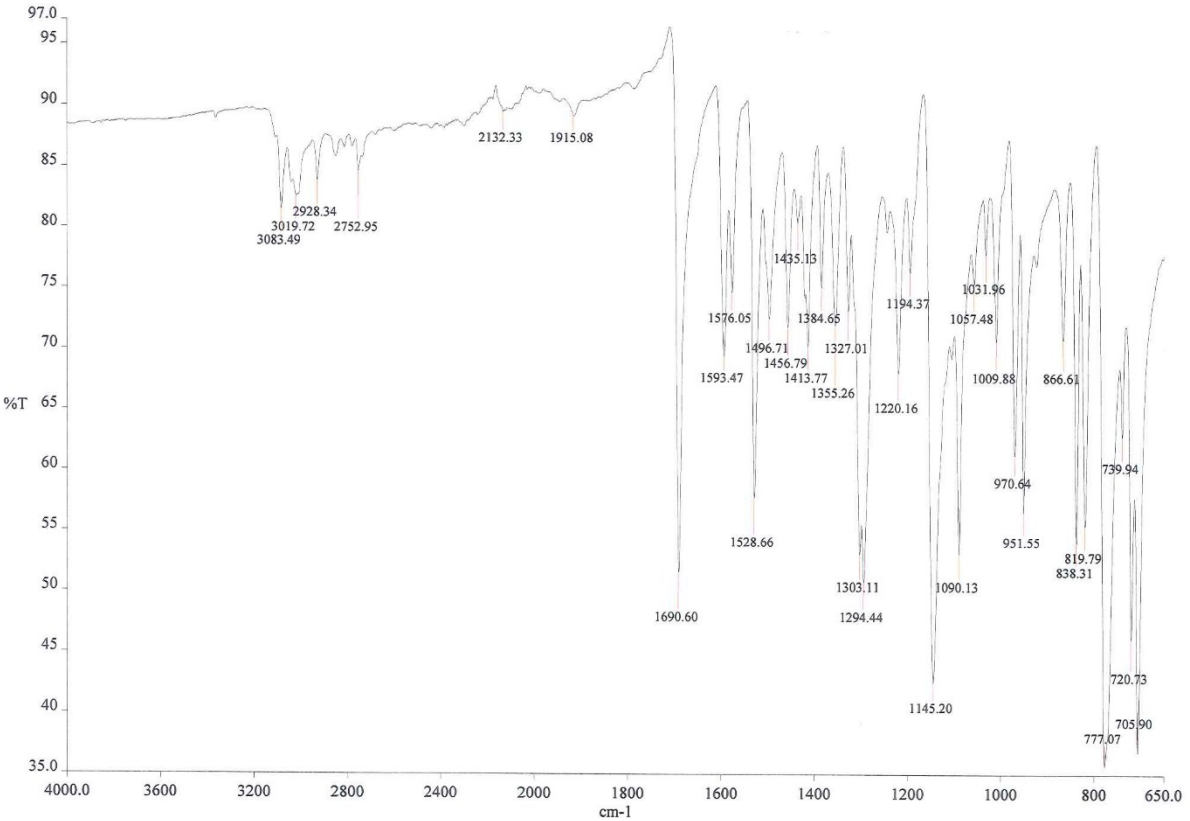


Figure S5. Spectral data of Compound **3b**

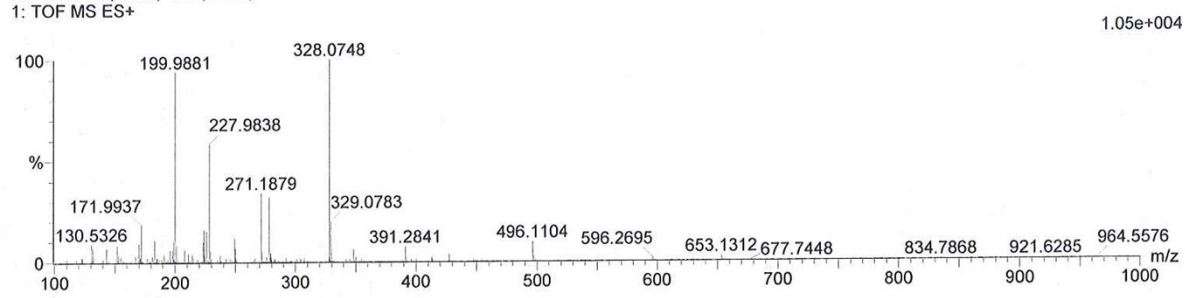




Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
125 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-40 H: 1-40 N: 1-8 O: 1-5 S: 1-1
NI-272-2 71 (2.763) Cm (69:71)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
328.0748	328.0756	-0.8	-2.4	11.5	238.7	0.0	C16 H14 N3 O3 S

Figure S6. Spectral data of Compound **8**

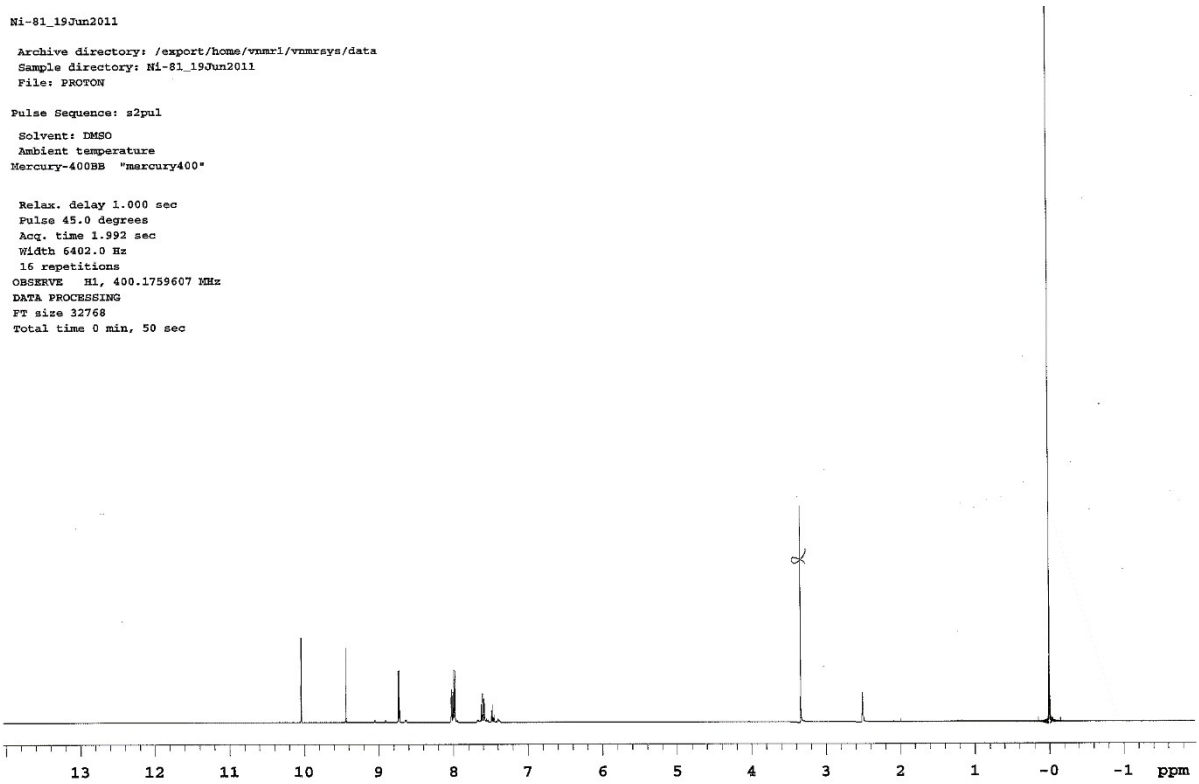


Figure S7. Spectral data of Compound **4a**

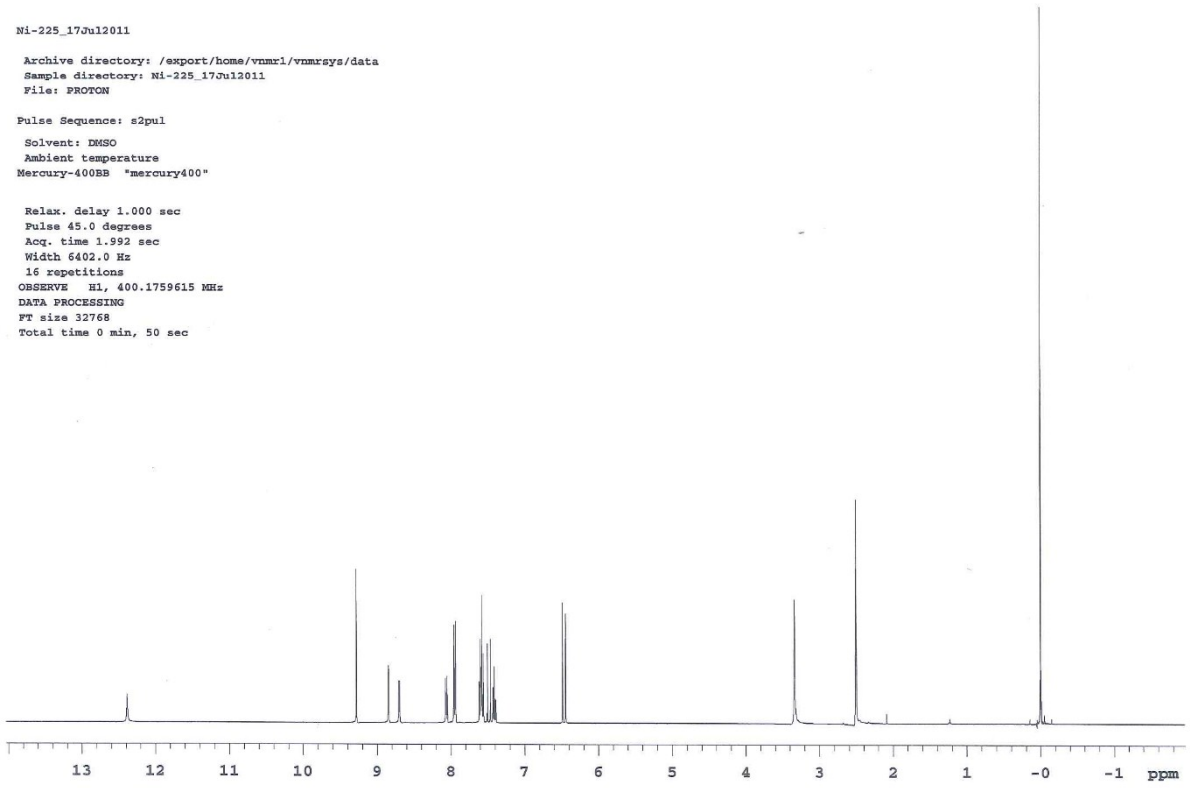
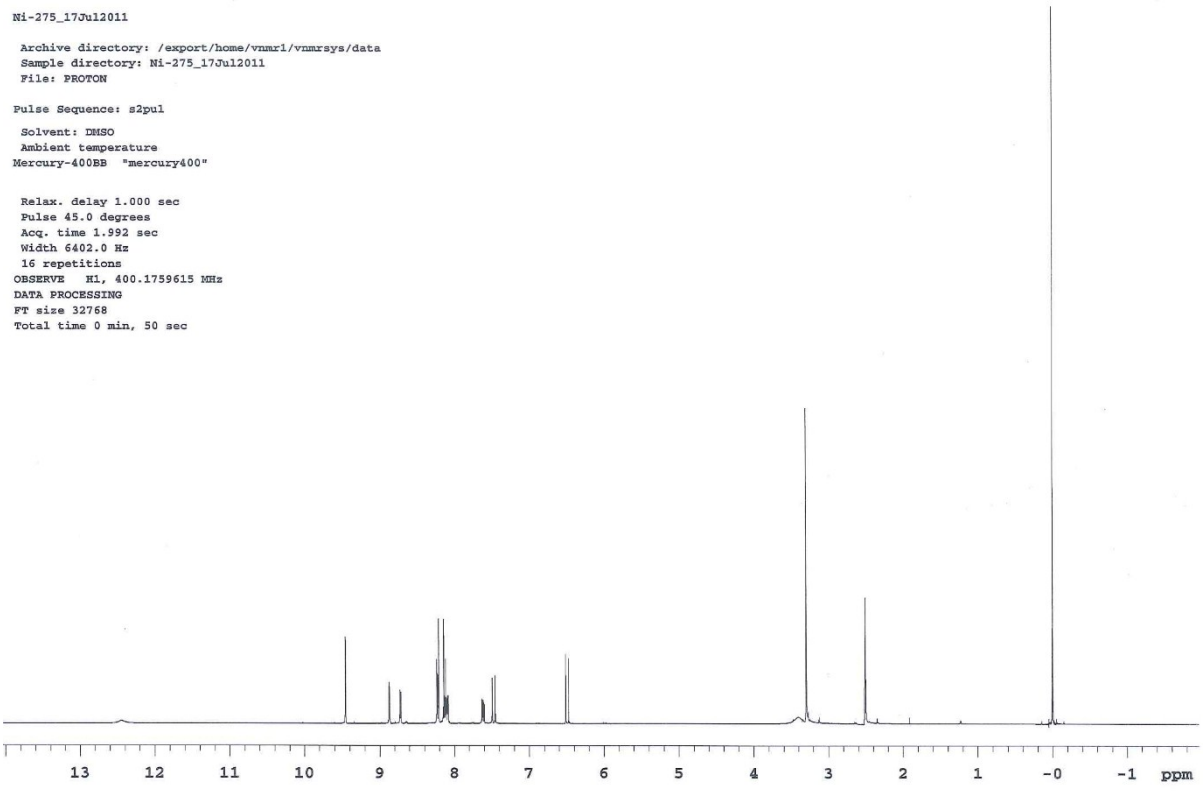
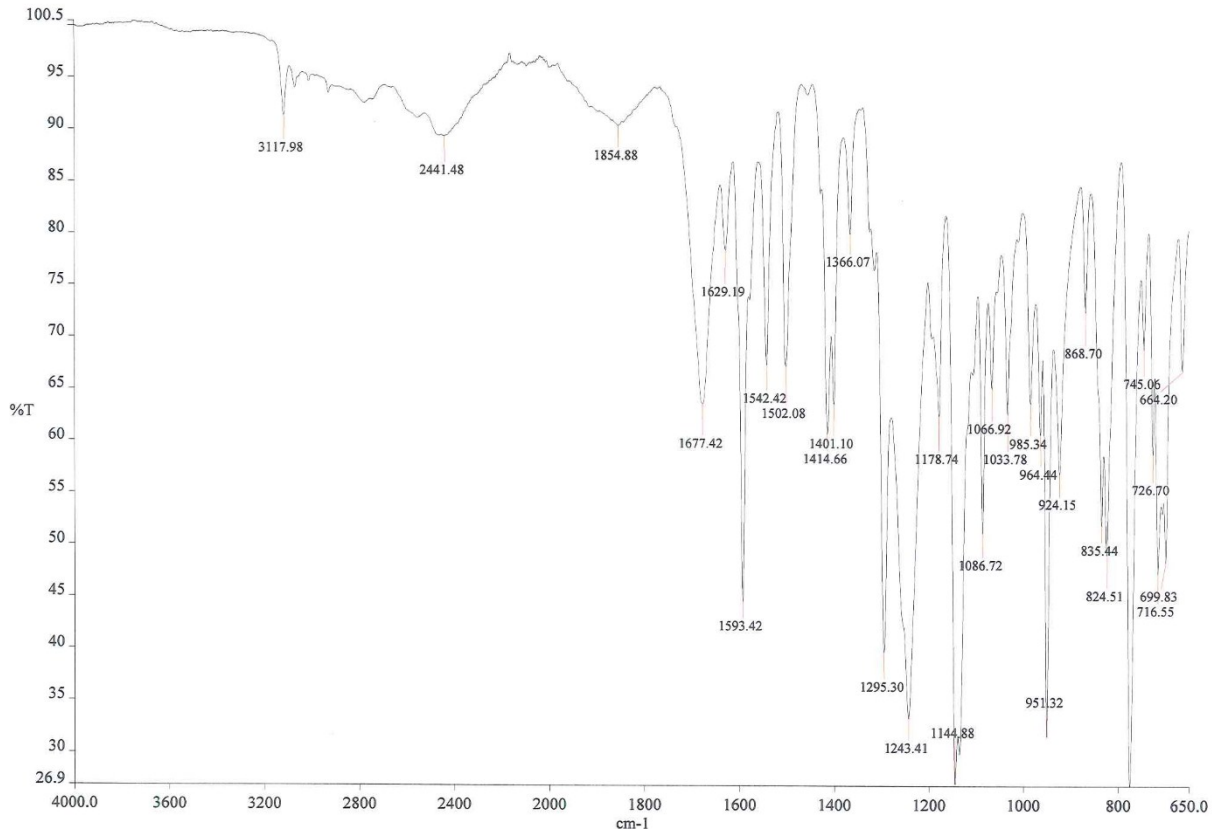


Figure S8. Spectral data of Compound **4b**





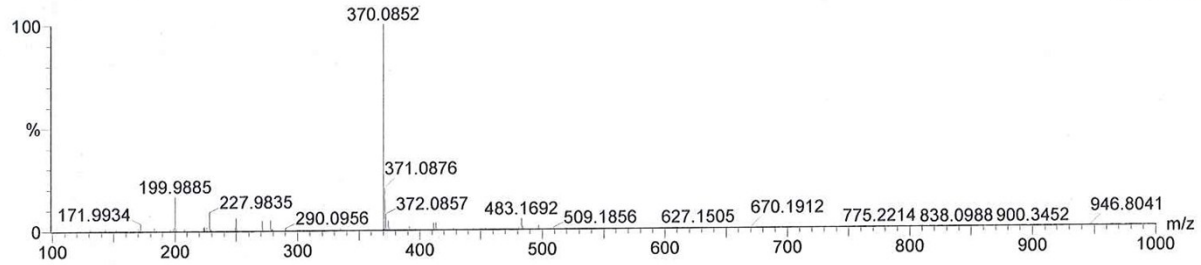
Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
158 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-40 H: 1-40 N: 1-8 O: 1-6 S: 1-1
NI-275 57 (2.233) Cm (57:60)
1: TOF MS ES+

9.33e+004



Minimum:				-1.5							
Maximum:		5.0	5.0	50.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula				
370.0852	370.0862	-1.0	-2.7	12.5	257.3	0.0	C18	H16	N3	O4	S

Figure S9. Spectral data of Compound **9**

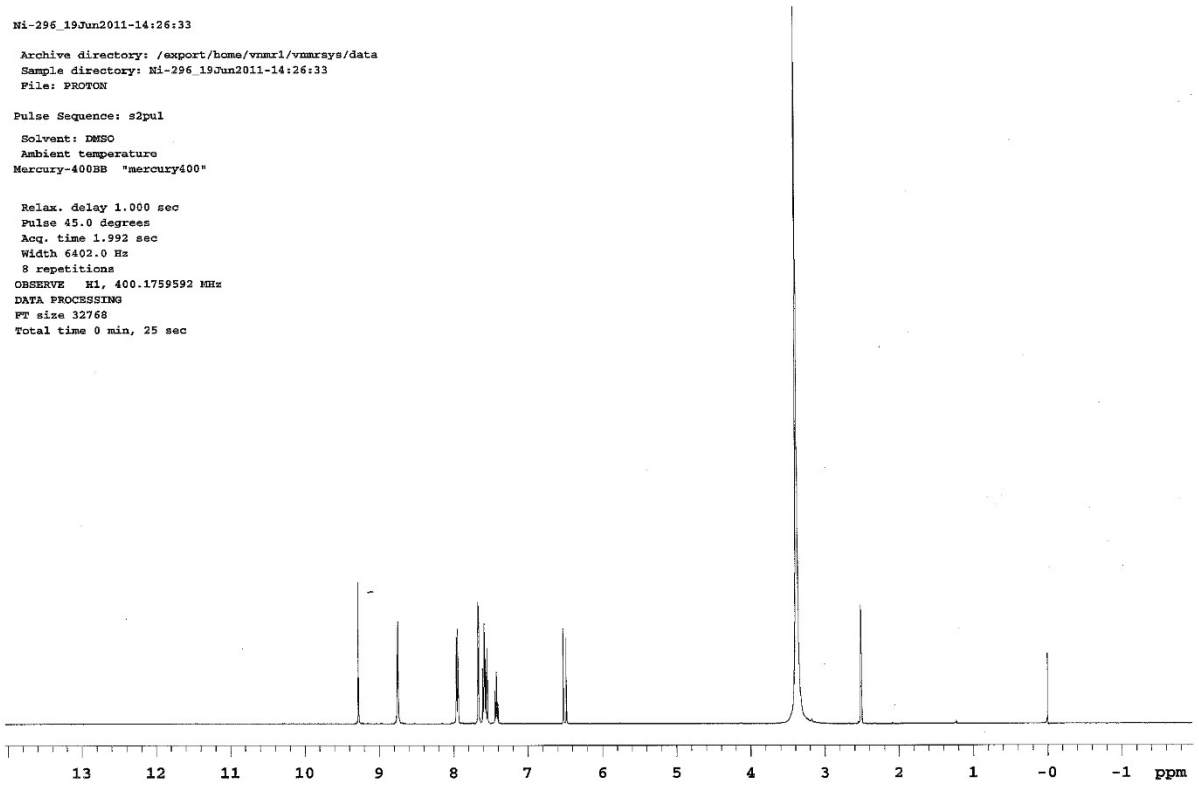
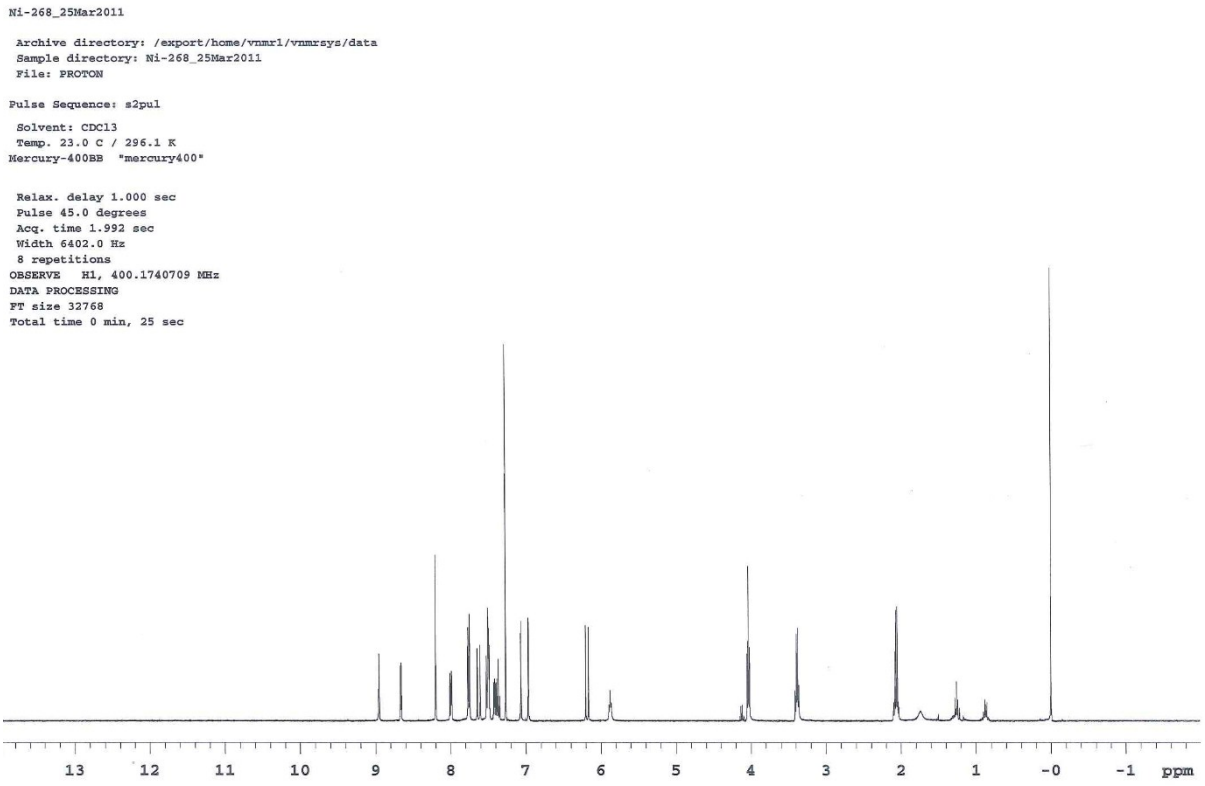
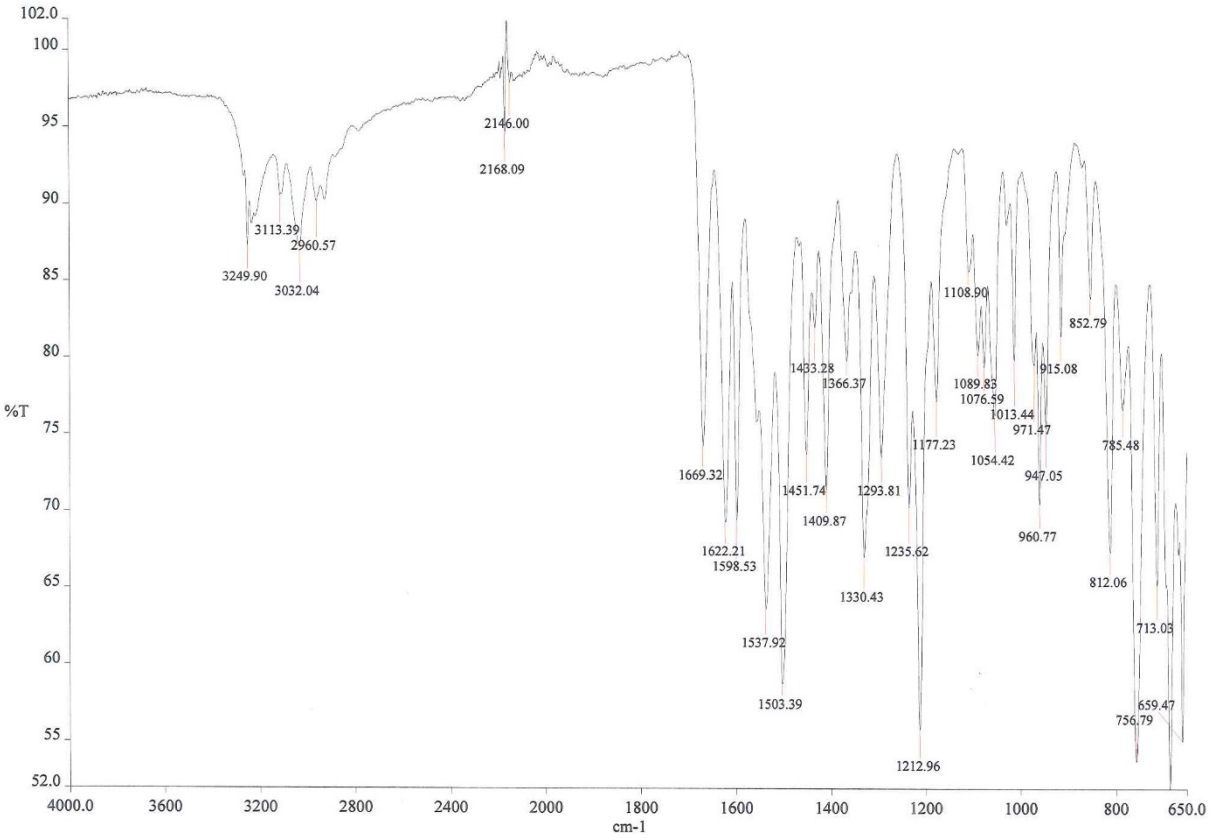


Figure S10. Spectral data of Compound **5a**



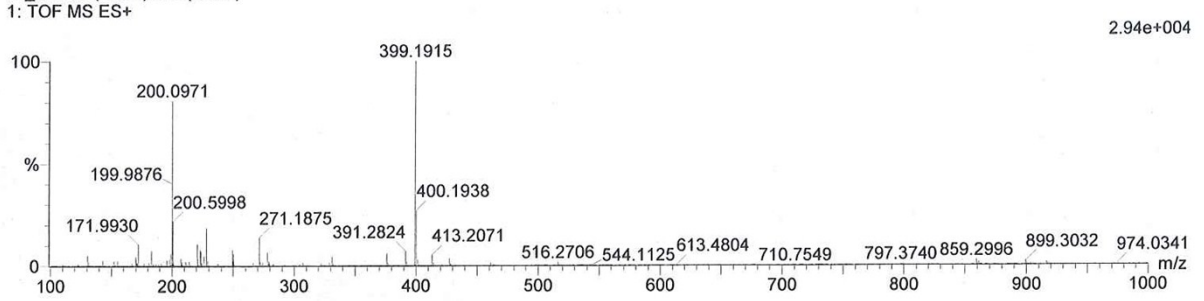


Elemental Composition Report

Single Mass Analysis

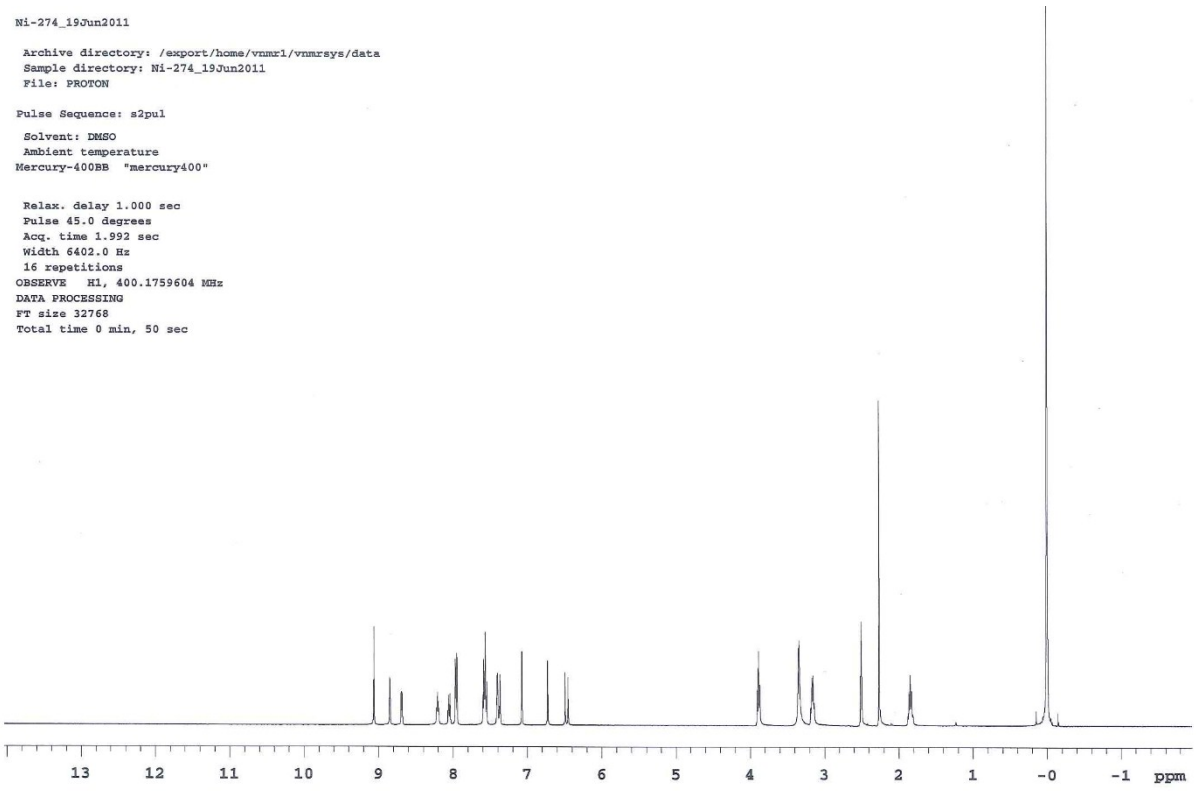
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

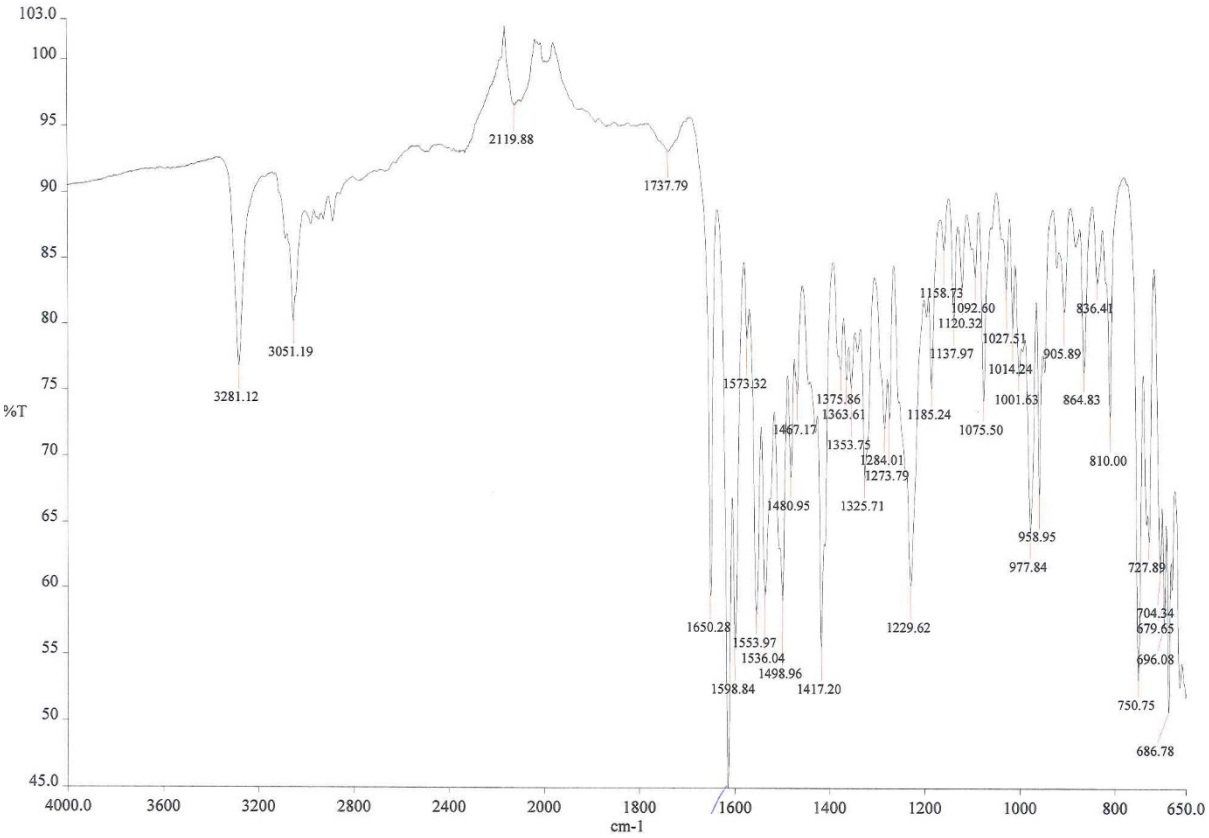
Monoisotopic Mass, Even Electron Ions
100 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-30 H: 1-30 N: 1-8 O: 1-5
NI_268 52 (2.012) Cm (52:55)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
399.1915	399.1920	-0.5	-1.3	10.5	141.2	0.8	C22 H27 N2 O5
	399.1933	-1.8	-4.5	15.5	141.0	0.6	C23 H23 N6 O

Figure S11. Spectral data of Compound **5b**

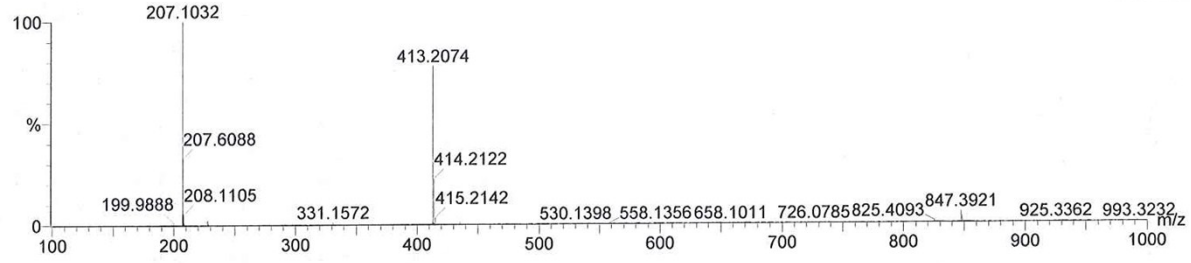




Elemental Composition Report

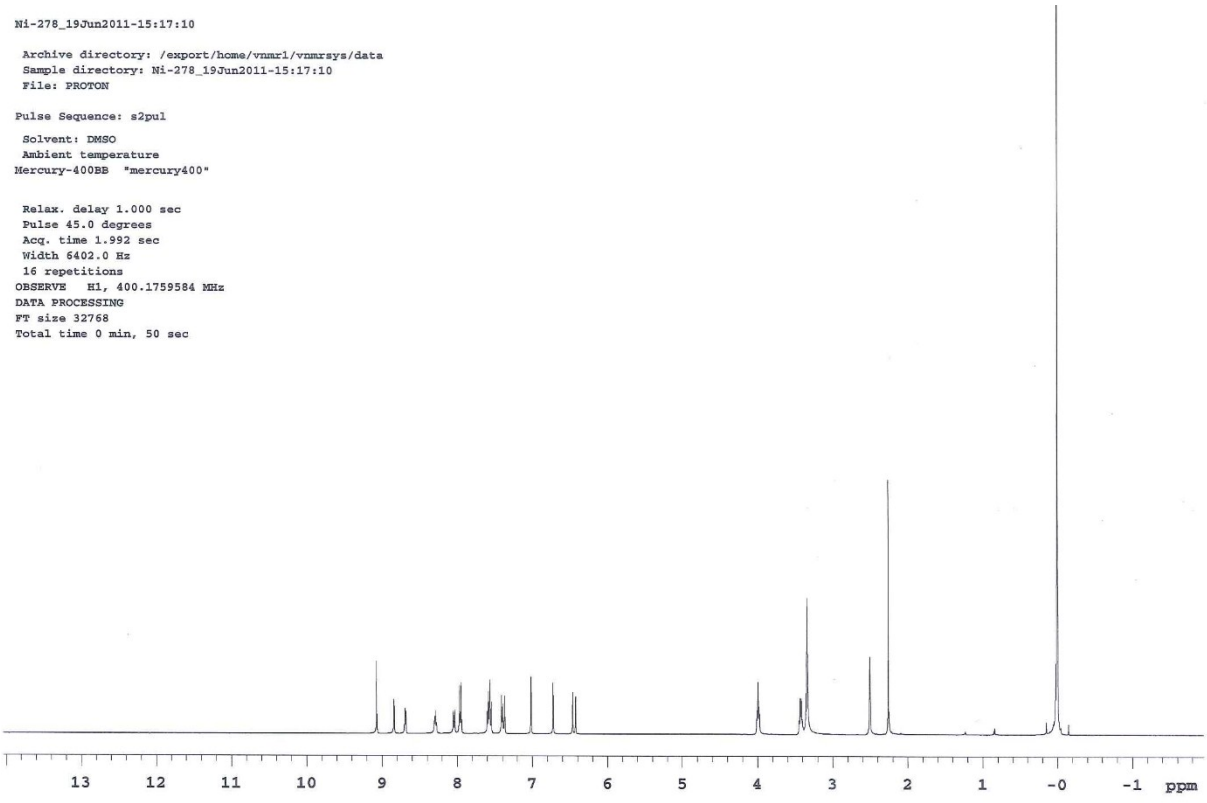
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

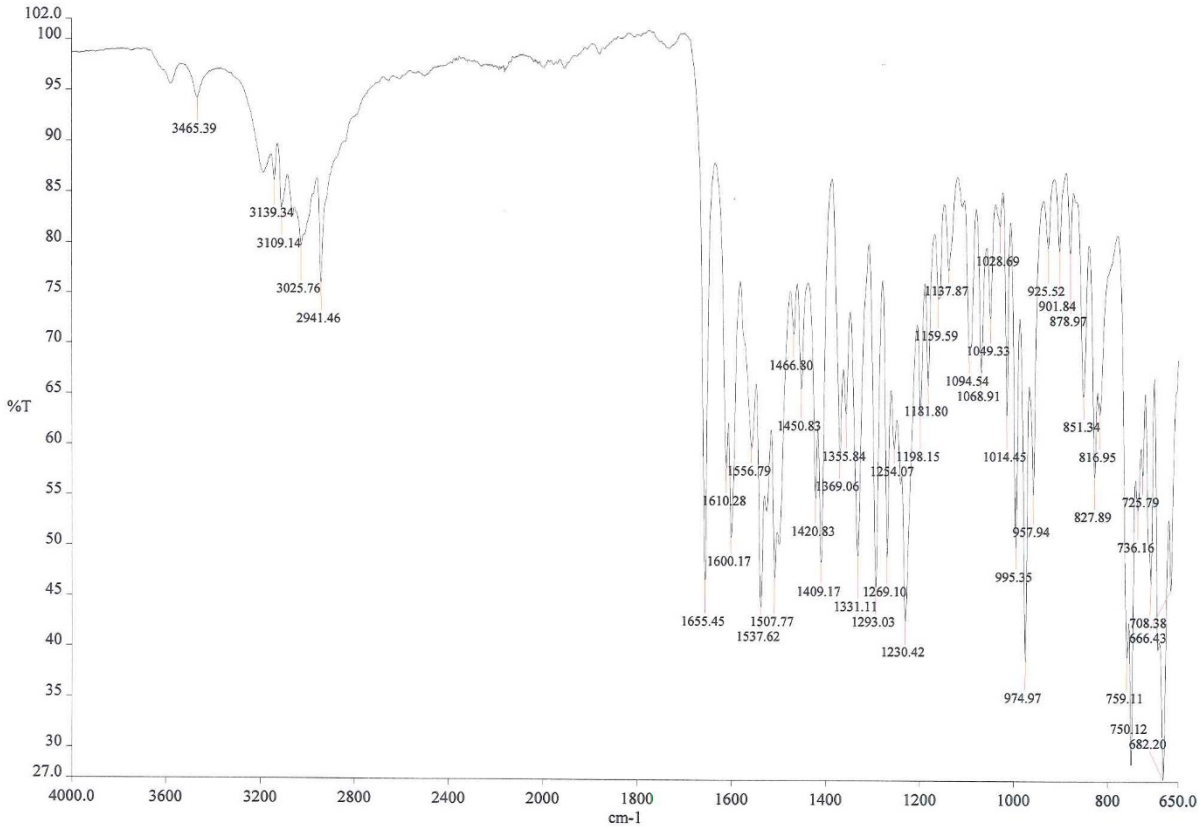
Monoisotopic Mass, Even Electron Ions
26 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-40 H: 1-40 N: 1-8 O: 1-1
NI-274 50 (1.949) Cm (49:52)
1: TOF MS ES+
5.75e+005



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
413.2074	413.2090	-1.6	-3.9	15.5	492.5	0.0	C24 H25 N6 O

Figure S12. Spectral data of Compound **5c**



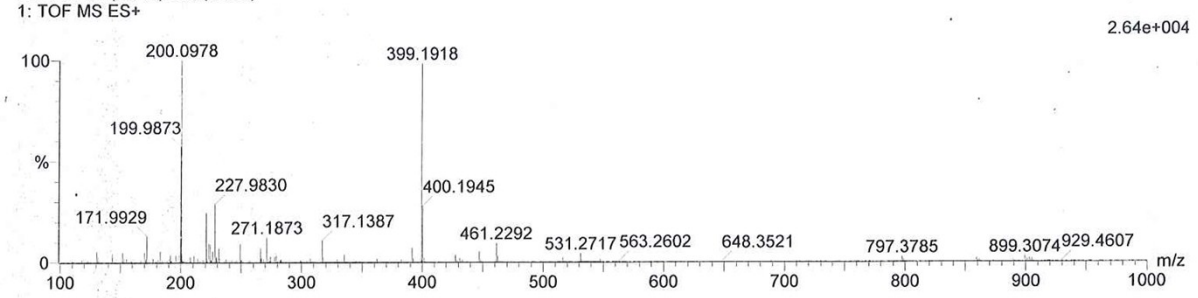


Elemental Composition Report

Single Mass Analysis

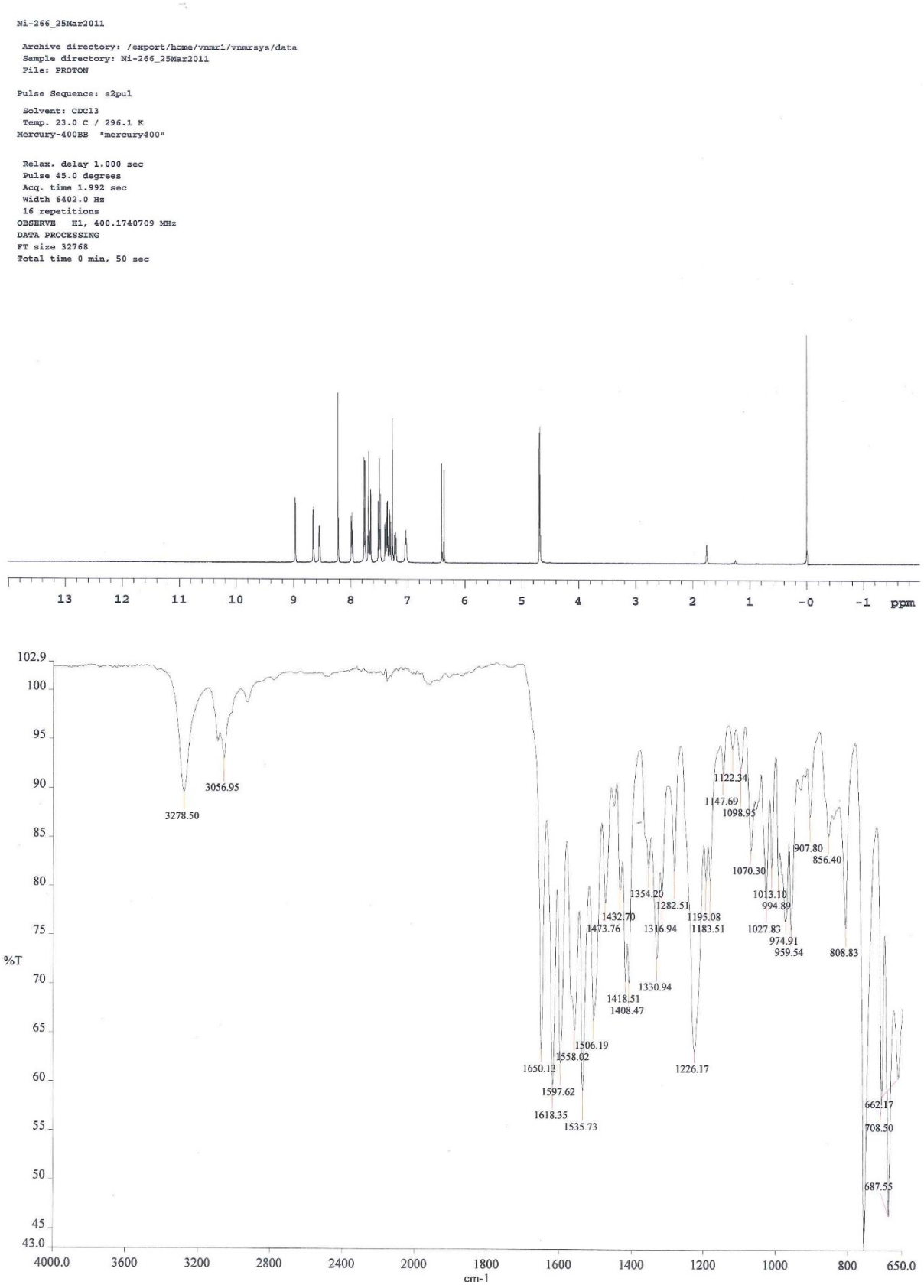
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
75 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-27 H: 1-33 N: 1-6 O: 1-5
NI-278X 52 (2.012) Cm (52:55)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
399.1918	399.1920	-0.2	-0.5	10.5	180.2	1.0	C22 H27 N2 O5
	399.1933	-1.5	-3.8	15.5	179.6	0.4	C23 H23 N6 O

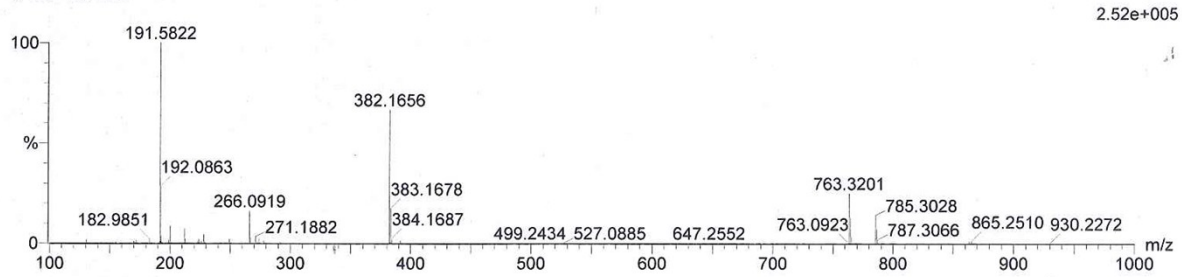
Figure S13. Spectral data of Compound **5d**



Elemental Composition Report **Page 1 of 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
21 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-30 H: 1-30 N: 1-8 O: 1-1
NI266 53 (2.078) Cm (51:60)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
382.1656	382.1668	-1.2	-3.1	16.5	449.7	0.0	C23 H20 N5 O

Figure S14. Spectral data of Compound **5e**

```
Ni-263_25Mar2011

 Archive directory: /export/home/vnmr1/vnmrsys/data
 Sample directory: Ni-263_25Mar2011
 File: PROTON

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
Mercury-400BB  "mercury400"

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.992 sec
 Width 6402.0 Hz
 32 repetitions
OBSERVE   H1, 400.1740701 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 40 sec
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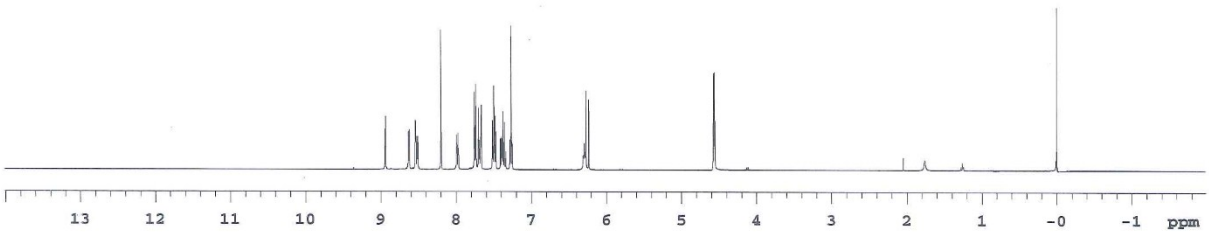
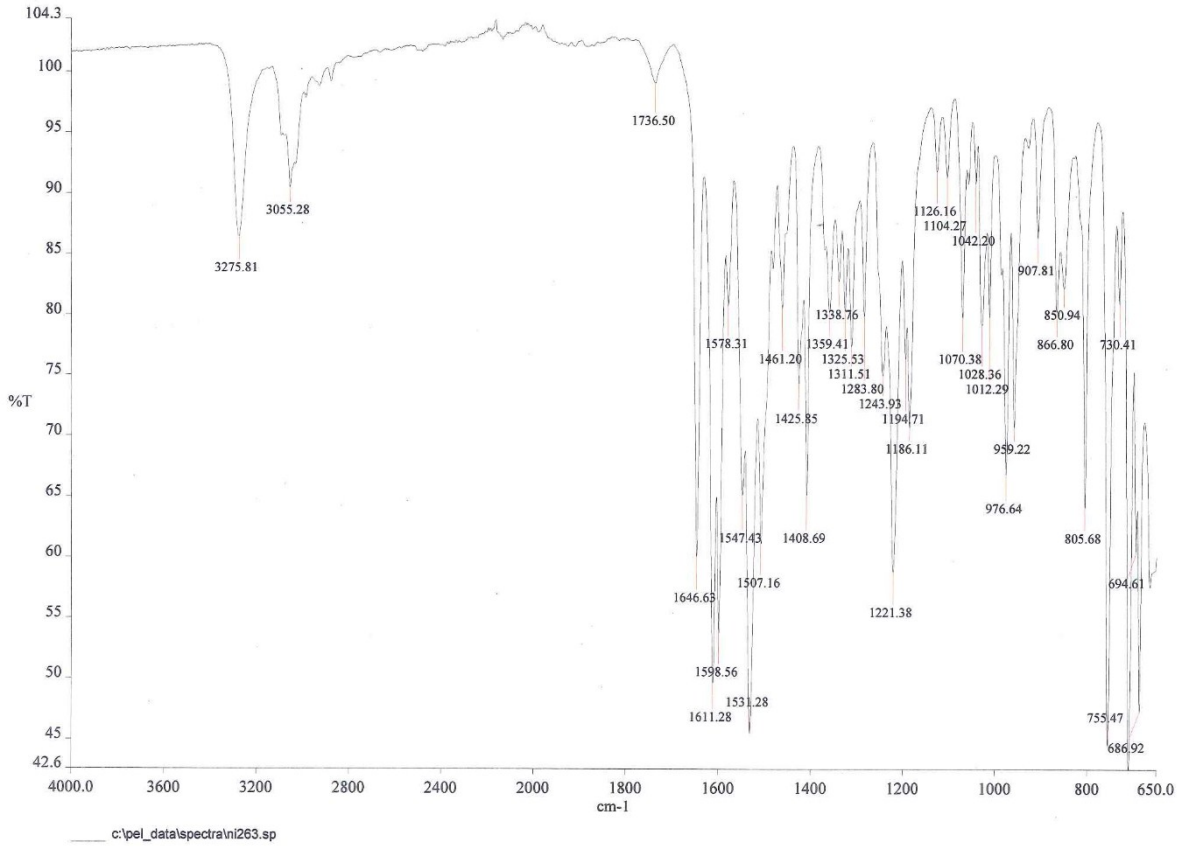


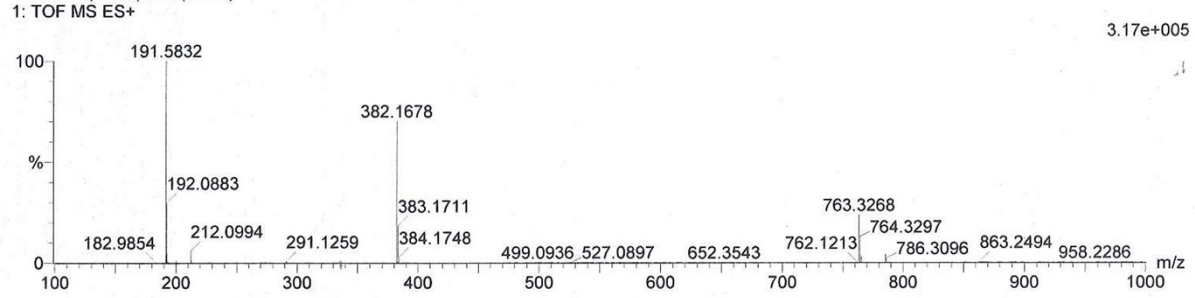


Elemental Composition Report

Single Mass Analysis

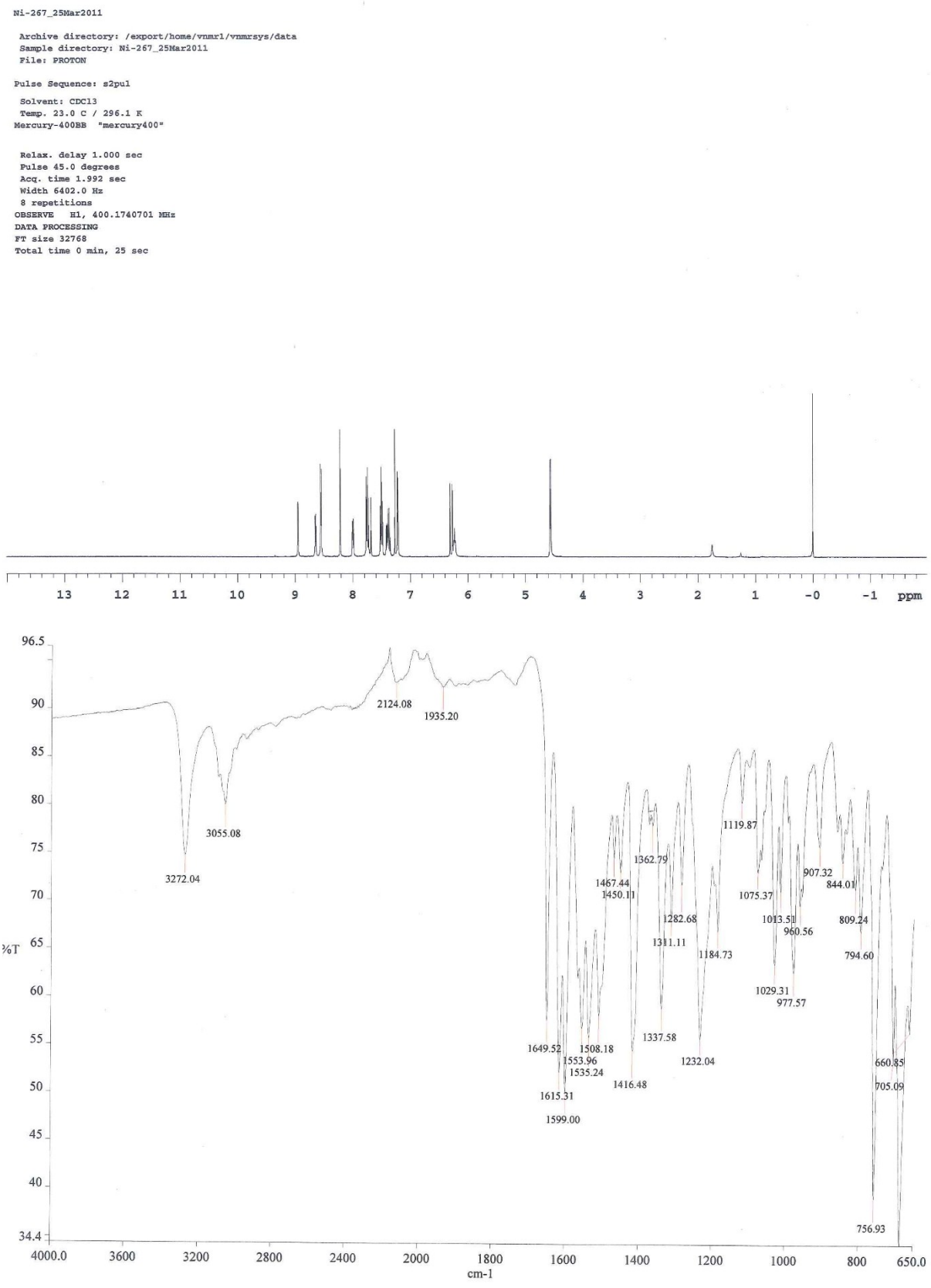
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
188 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-40 H: 1-40 N: 1-8 O: 1-7
NI263 49 (1.916) Cm (48:50)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
382.1678	382.1668	1.0	2.6	16.5	436.6	0.0	C23 H20 N5 O

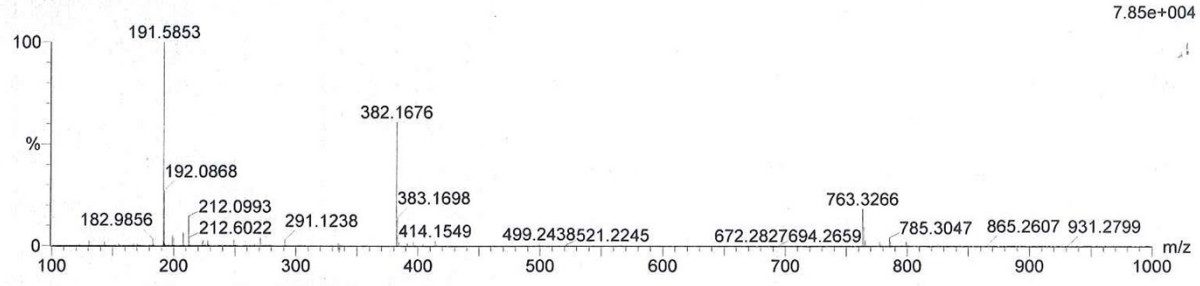
Figure S15. Spectral data of Compound **5f**



Elemental Composition Report **Page 1 of 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
21 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-30 H: 1-30 N: 1-8 O: 1-1
NI267 51 (1.981) Cm (51:54)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
382.1676	382.1668	0.8	2.1	16.5	151.5	0.0	C23 H20 N5 O

Figure S16. Spectral data of Compound **5g**

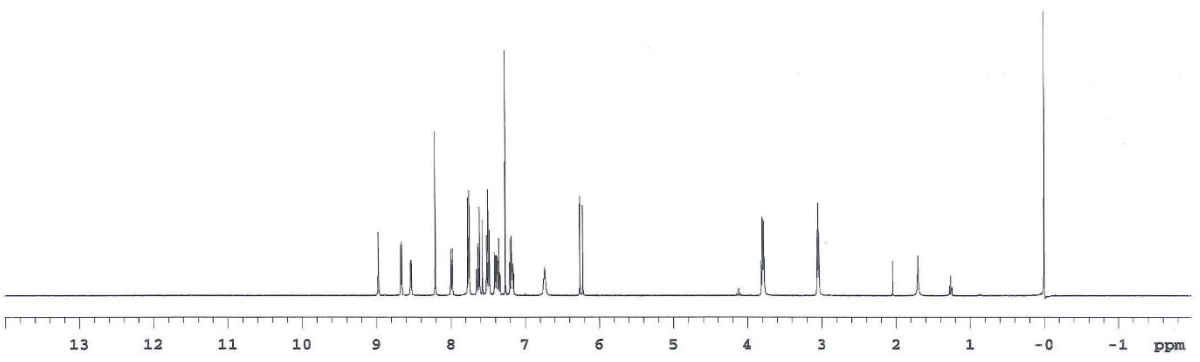
Ni-269_25Mar2011

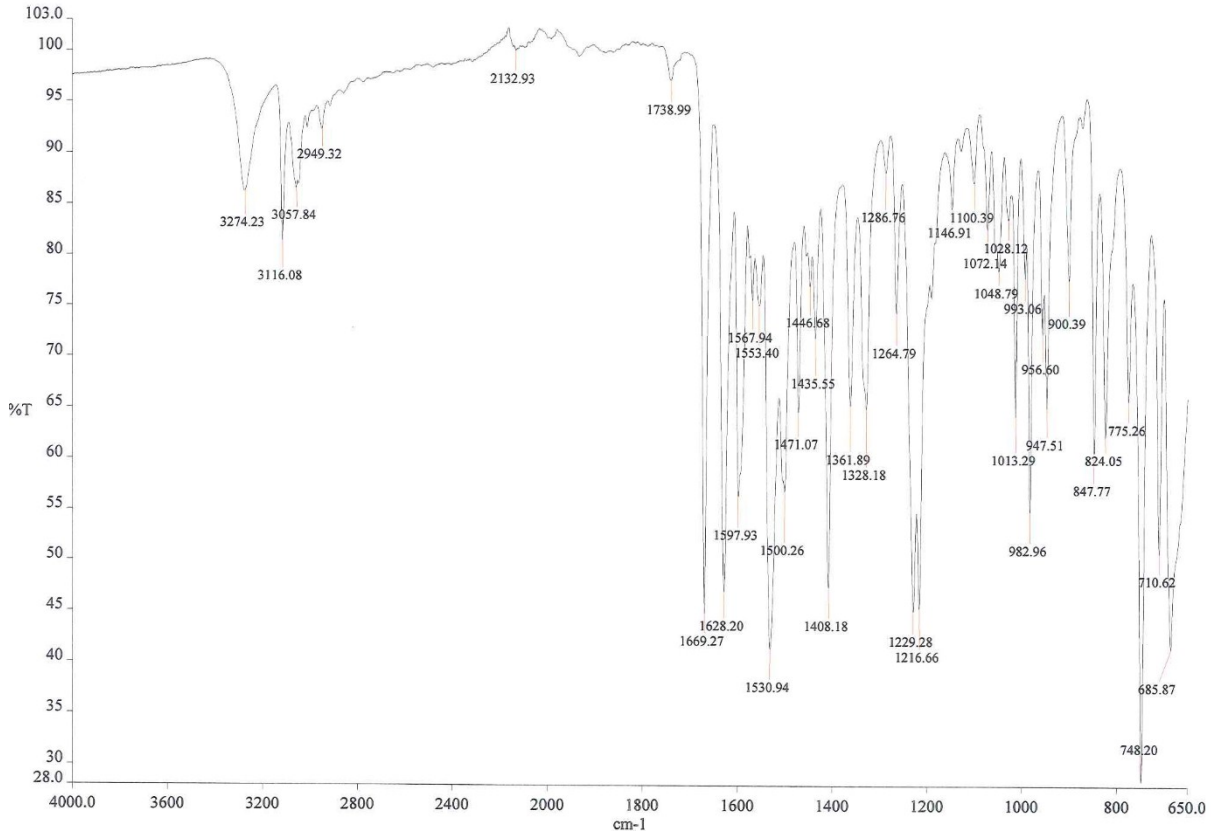
Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory: Ni-269_25Mar2011
File: PROTON

Pulse Sequence: s2pul

Solvent: CDCl3
Temp. 23.0 C / 296.1 K
Mercury-400BB "mercury400"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.992 sec
Width 6402.0 Hz
8 repetitions
OBSERVE H1, 400.1740709 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 25 sec





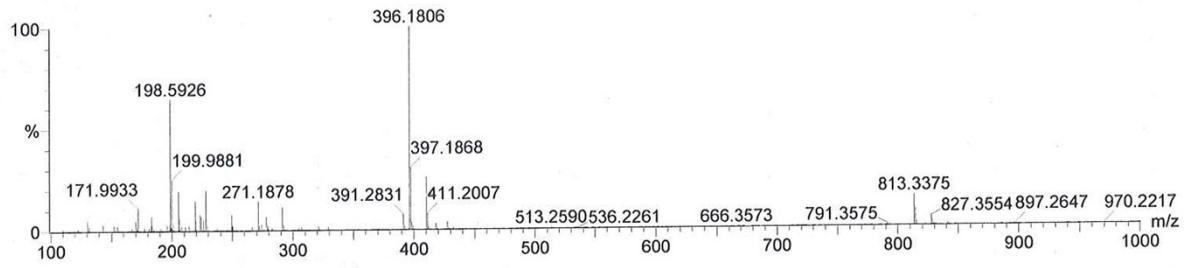
Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

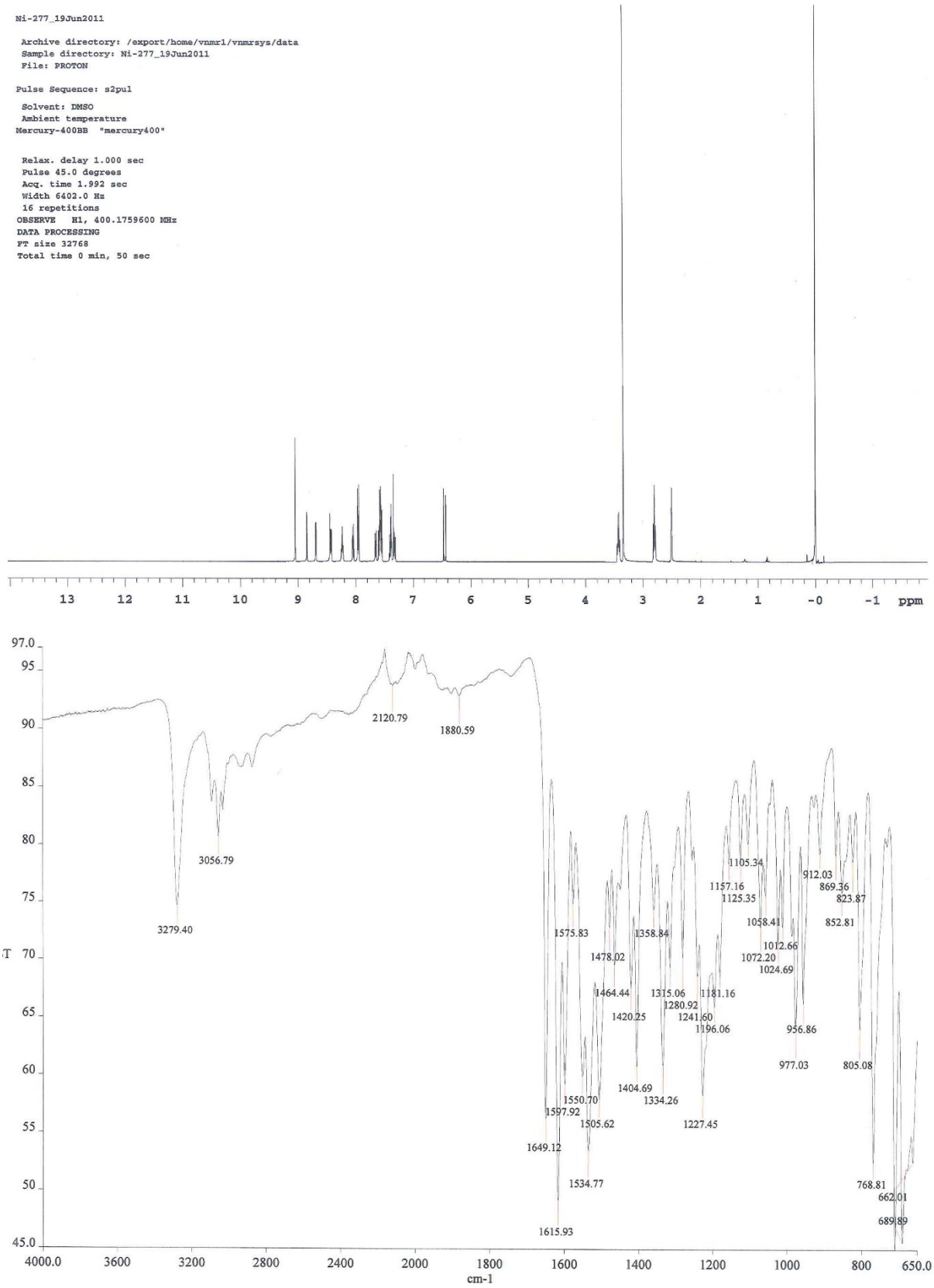
Monoisotopic Mass, Even Electron Ions
101 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-30 H: 1-30 N: 1-8 O: 1-5
NI_269 54 (2.104) Cm (54:56)
1: TOF MS ES+

2.17e+004



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
396.1806	396.1811	-0.5	-1.3	11.5	105.1	2.1	C23 H26 N O5
	396.1824	-1.8	-4.5	16.5	103.1	0.1	C24 H22 N5 O

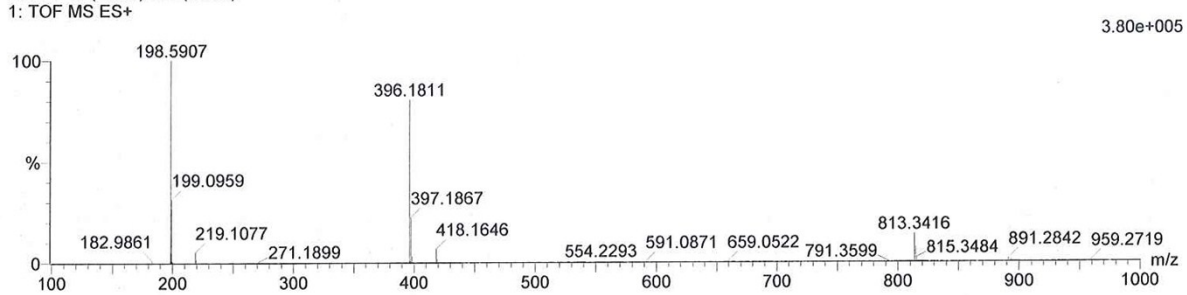
Figure S17. Spectral data of Compound **5h**



Elemental Composition Report

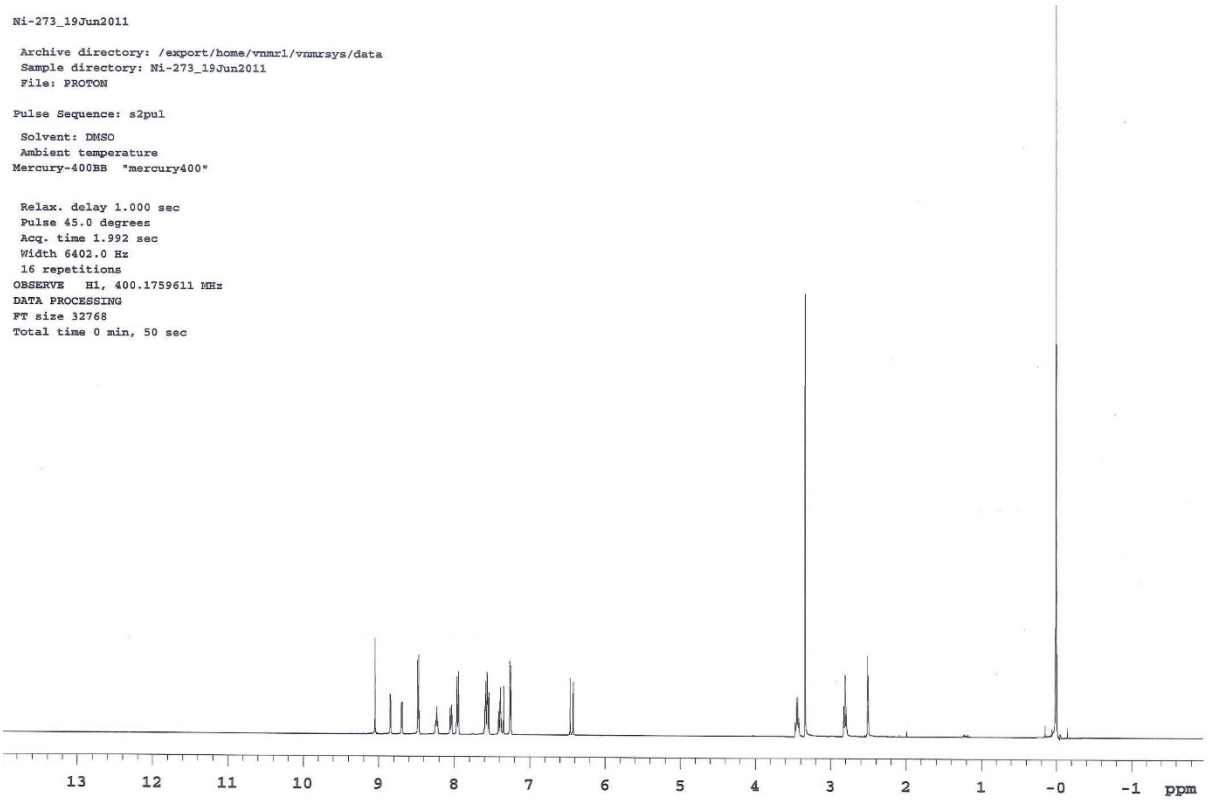
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

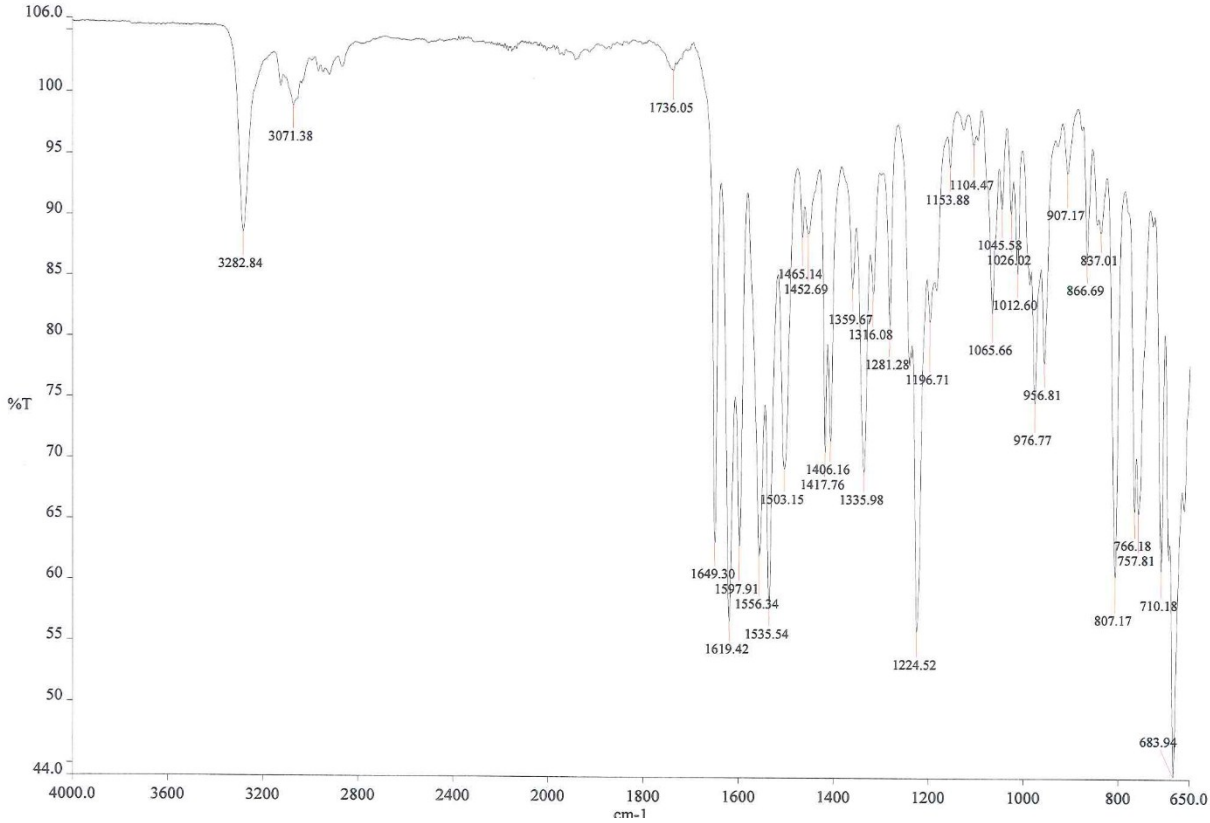
Monoisotopic Mass, Even Electron Ions
134 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-40 H: 1-40 N: 1-8 O: 1-5
NI-277 49 (1.917) Cm (49:52)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
396.1811	396.1811	0.0	0.0	11.5	405.9	1.2	C23 H26 N O5
	396.1824	-1.3	-3.3	16.5	405.1	0.4	C24 H22 N5 O

Figure S18. Spectral data of Compound **5i**





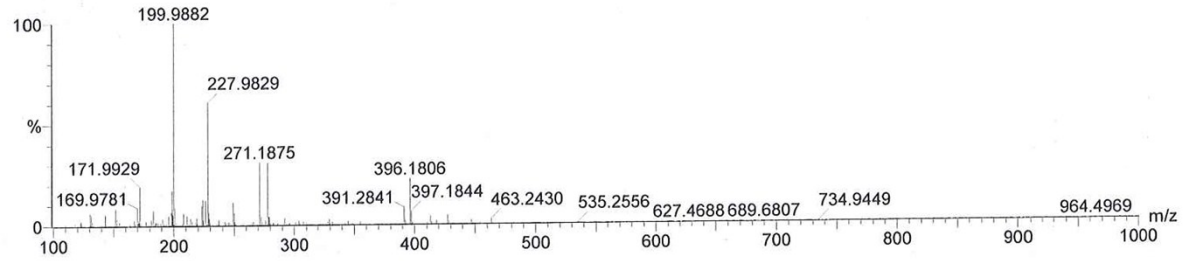
Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

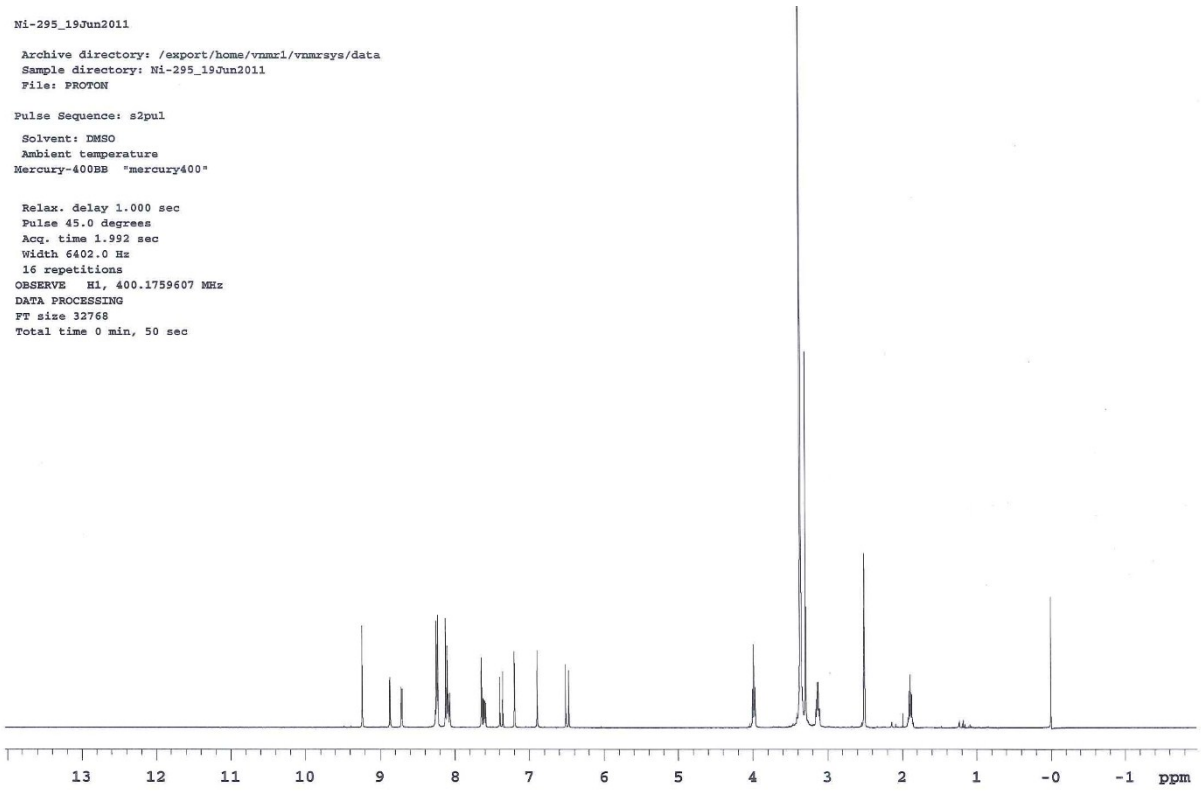
Monoisotopic Mass, Even Electron Ions
27 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-40 H: 1-40 N: 1-8 O: 1-1
NI-273 72 (2.794) Cm (71:73)
1: TOF MS ES+

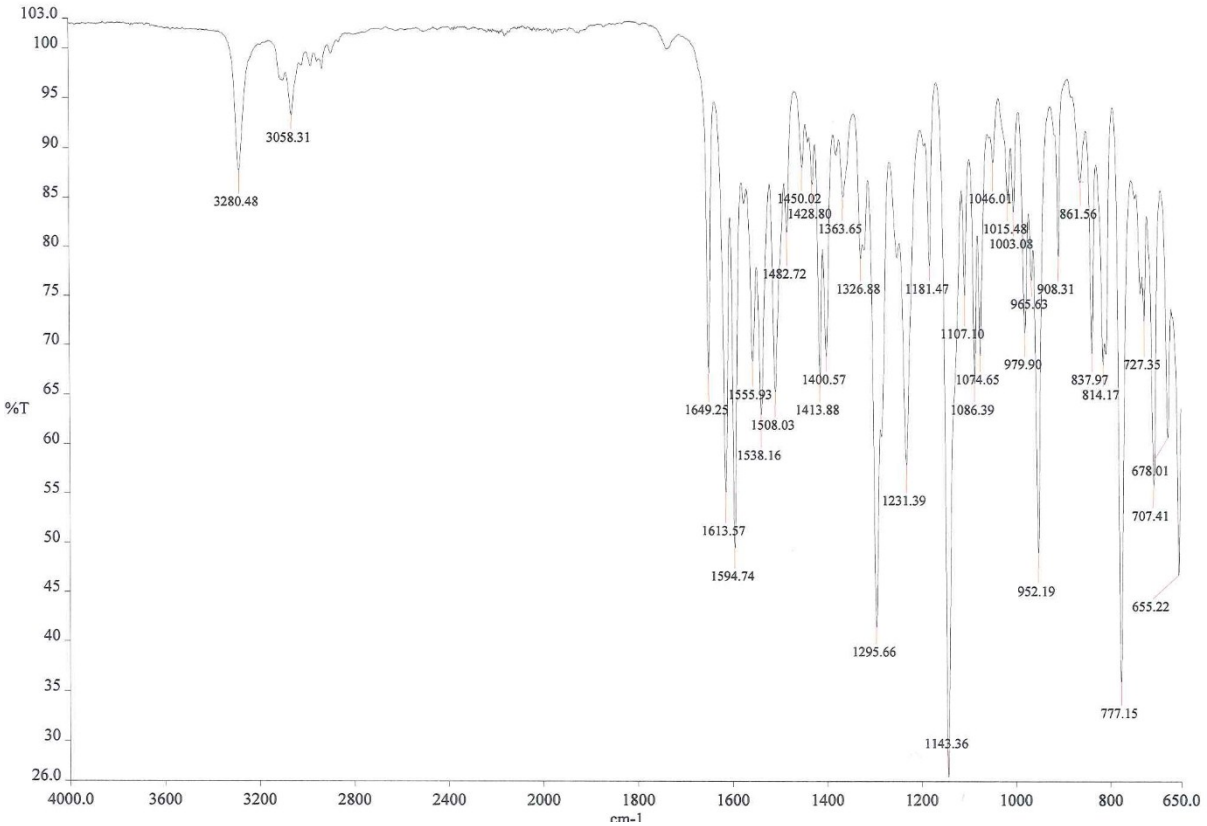
1.22e+004



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
396.1806	396.1824	-1.8	-4.5	16.5	115.8	0.0	C24 H22 N5 O

Figure S19. Spectral data of Compound **5j**

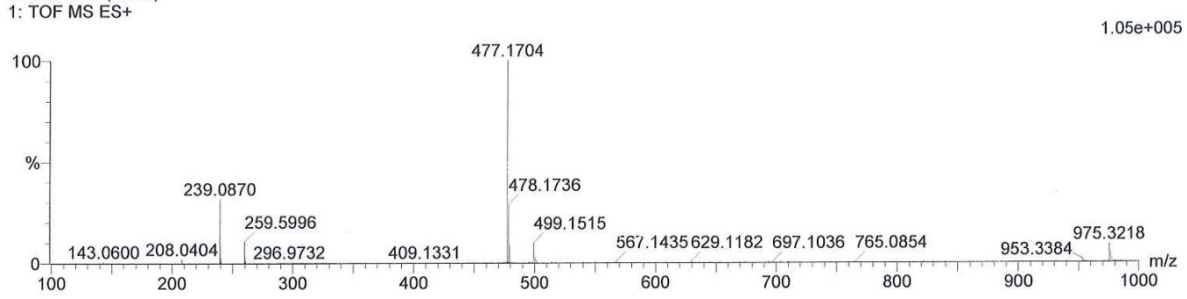




Elemental Composition Report

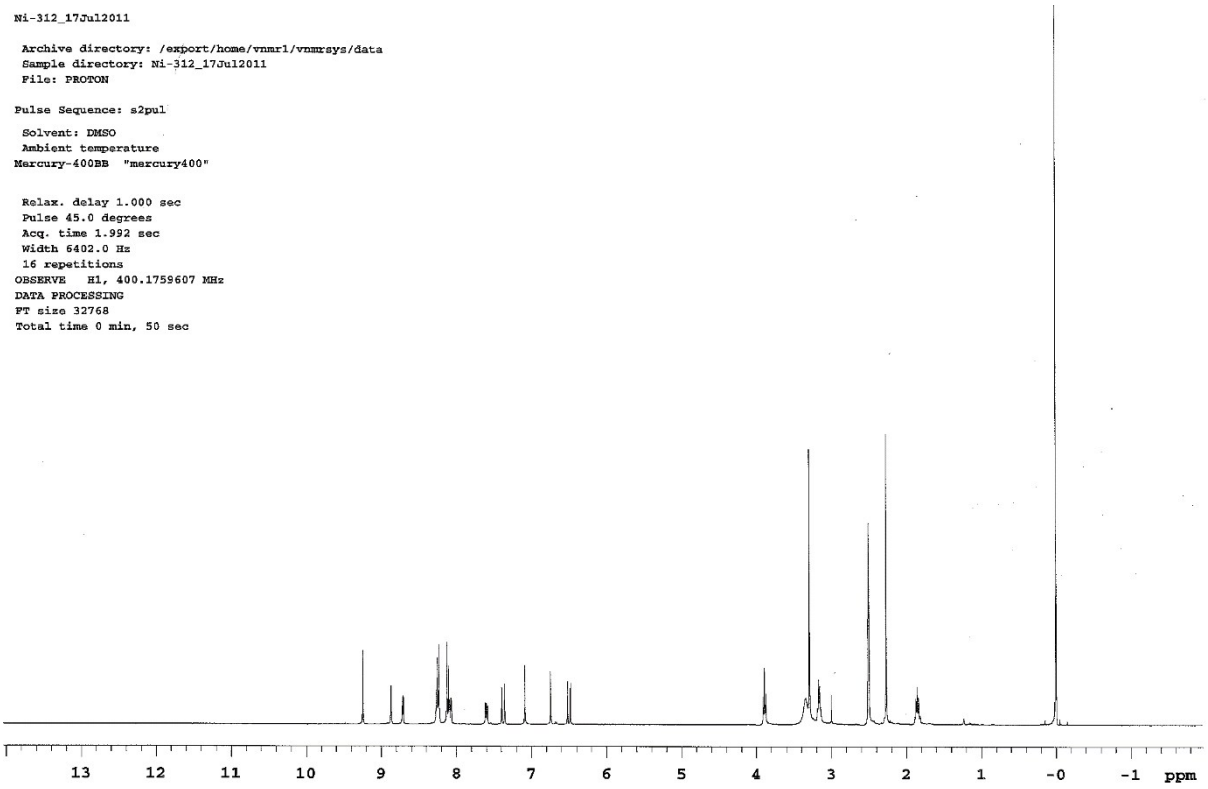
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

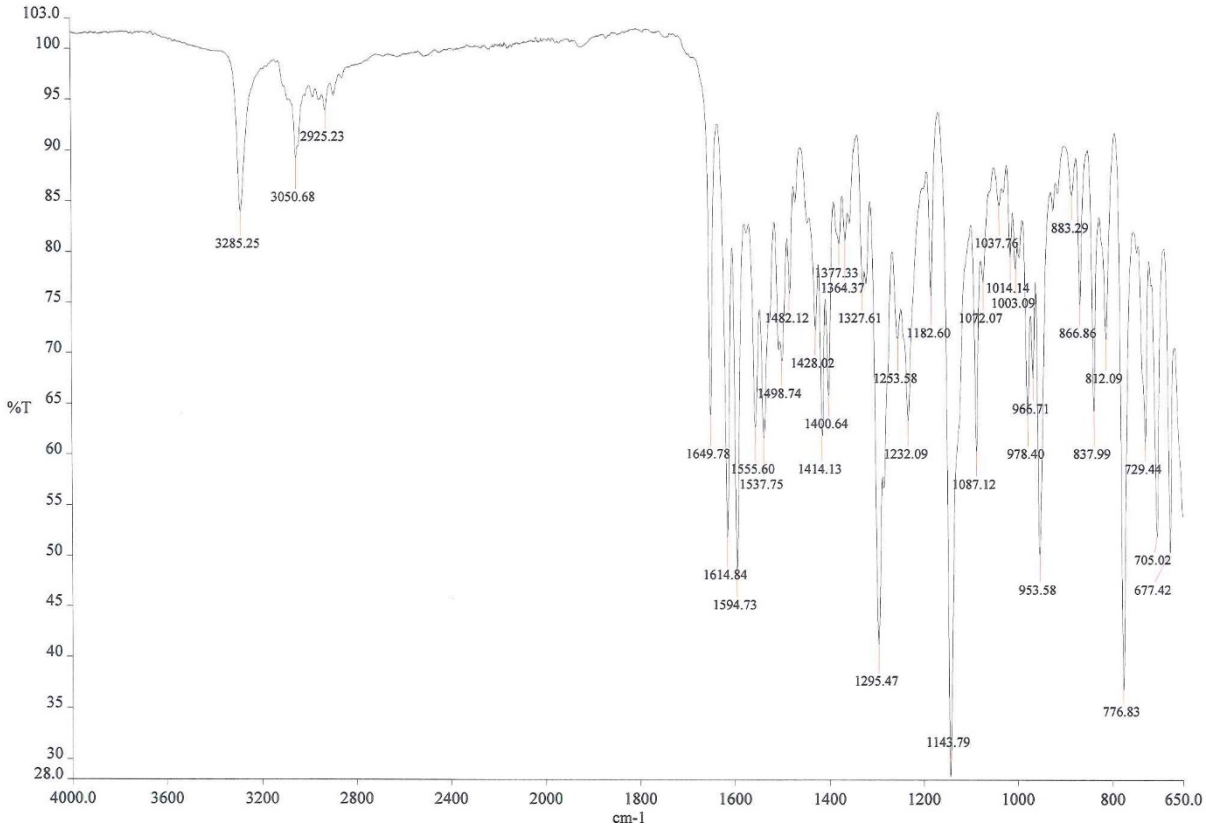
Monoisotopic Mass, Even Electron Ions
399 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-50 H: 1-50 N: 1-8 O: 1-6 S: 1-2
NI-295-2 41 (1.605)
1: TOF MS ES+



Minimum:				-1.5								
Maximum:		5.0	5.0	50.0								
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula					
477.1704	477.1702	0.2	0.4	6.5	240.9	10.6	C16	H29	N8	O5	S2	
	477.1709	-0.5	-1.0	15.5	230.3	0.0	C24	H25	N6	O3	S	

Figure S20. Spectral data of Compound **5k**





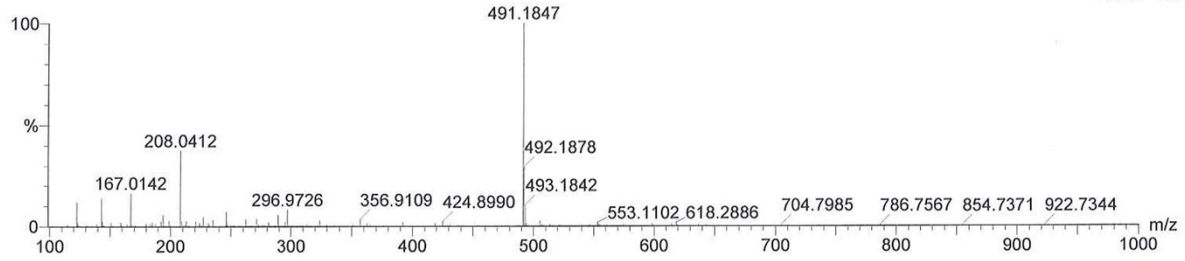
Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

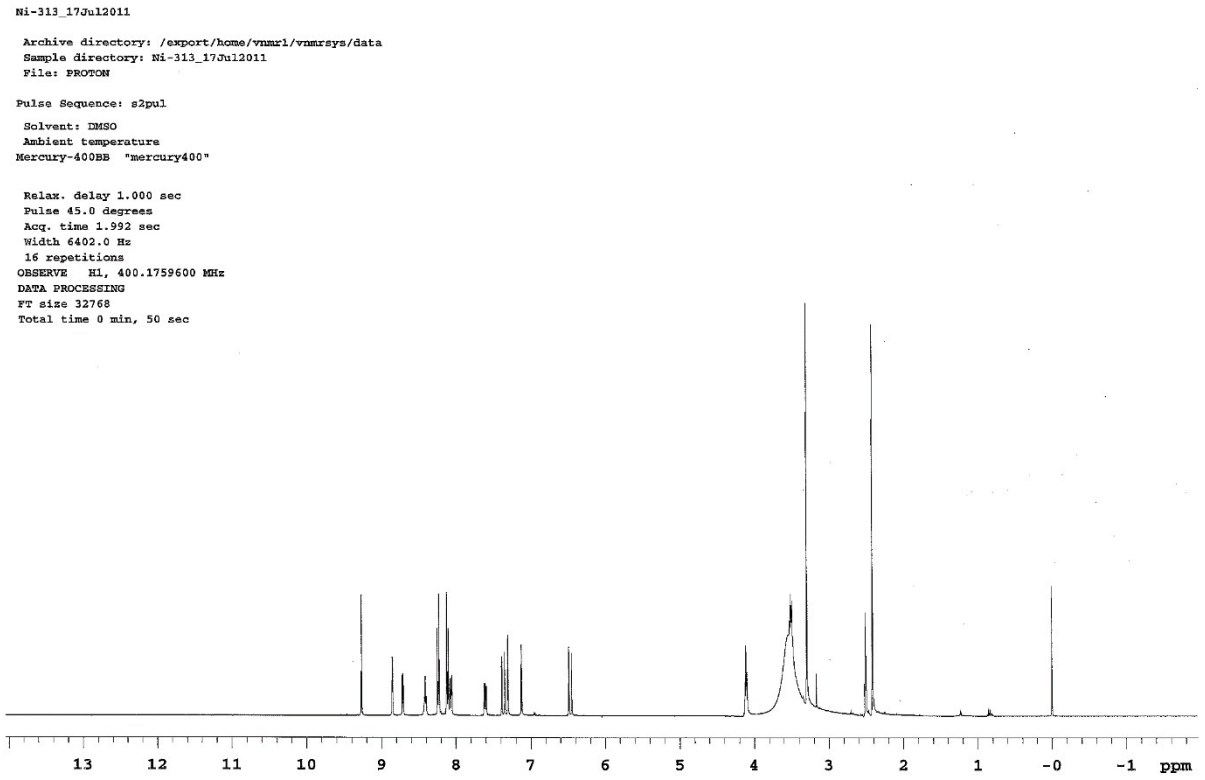
Monoisotopic Mass, Even Electron Ions
180 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-29 H: 1-50 N: 1-9 O: 1-3 S: 1-2
NI-312 47 (1.821) Cm (47:49)
1: TOF MS ES+

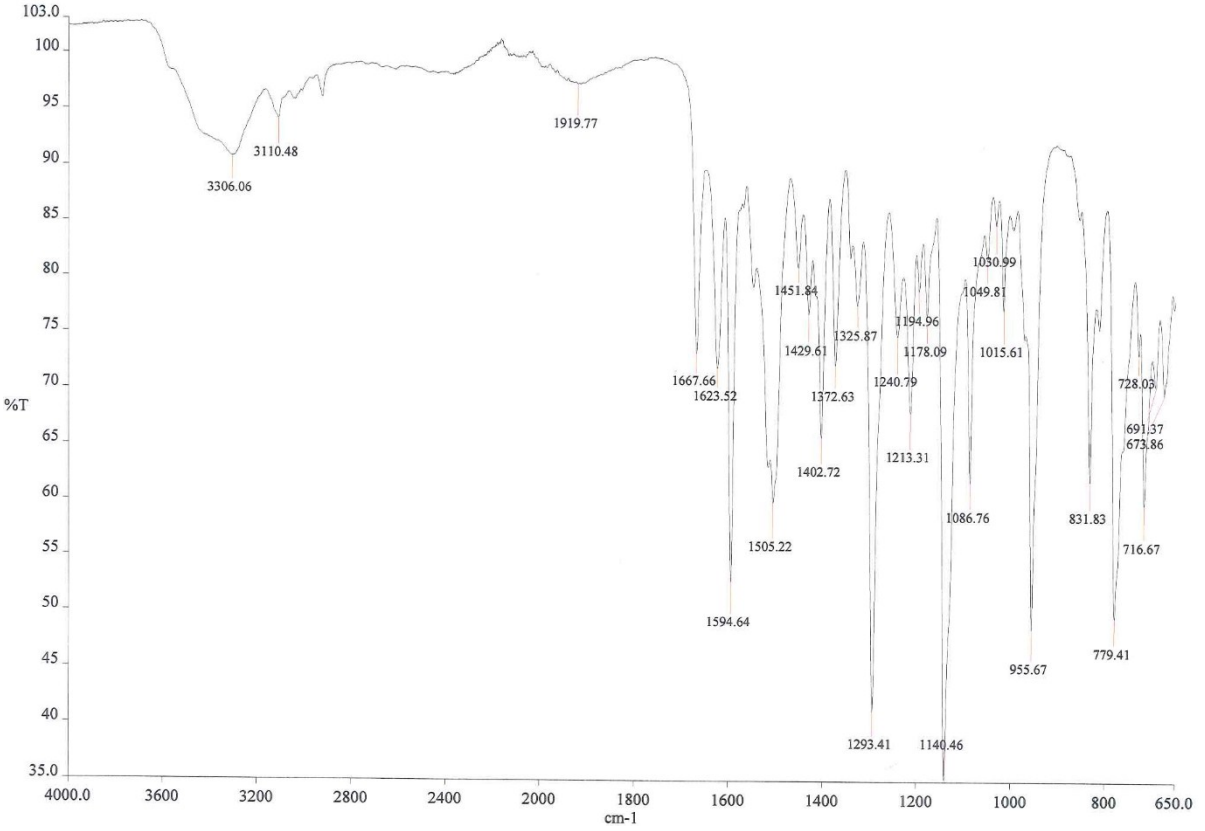
5.92e+004



Minimum:				-1.5								
Maximum:		5.0	5.0	50.0								
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula					
491.1847	491.1865	-1.8	-3.7	15.5	185.9	0.1	C25	H27	N6	O3	S	
	491.1827	2.0	4.1	14.5	188.8	2.9	C28	H31	N2	O2	S2	

Figure S21. Spectral data of Compound **5l**

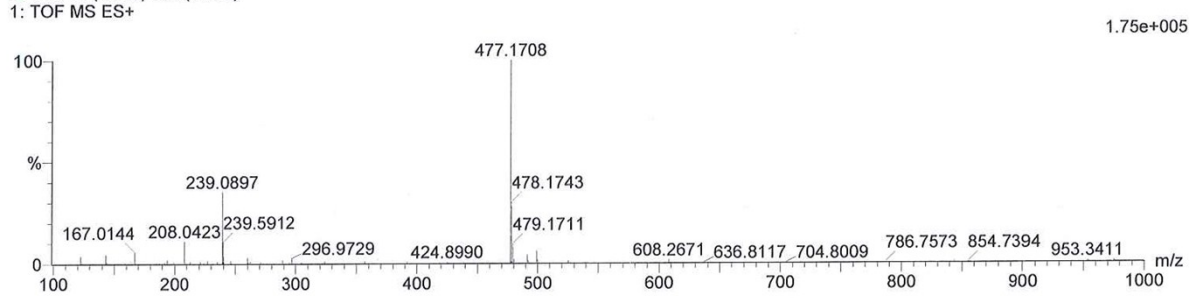




Elemental Composition Report **Page 1 of 1**

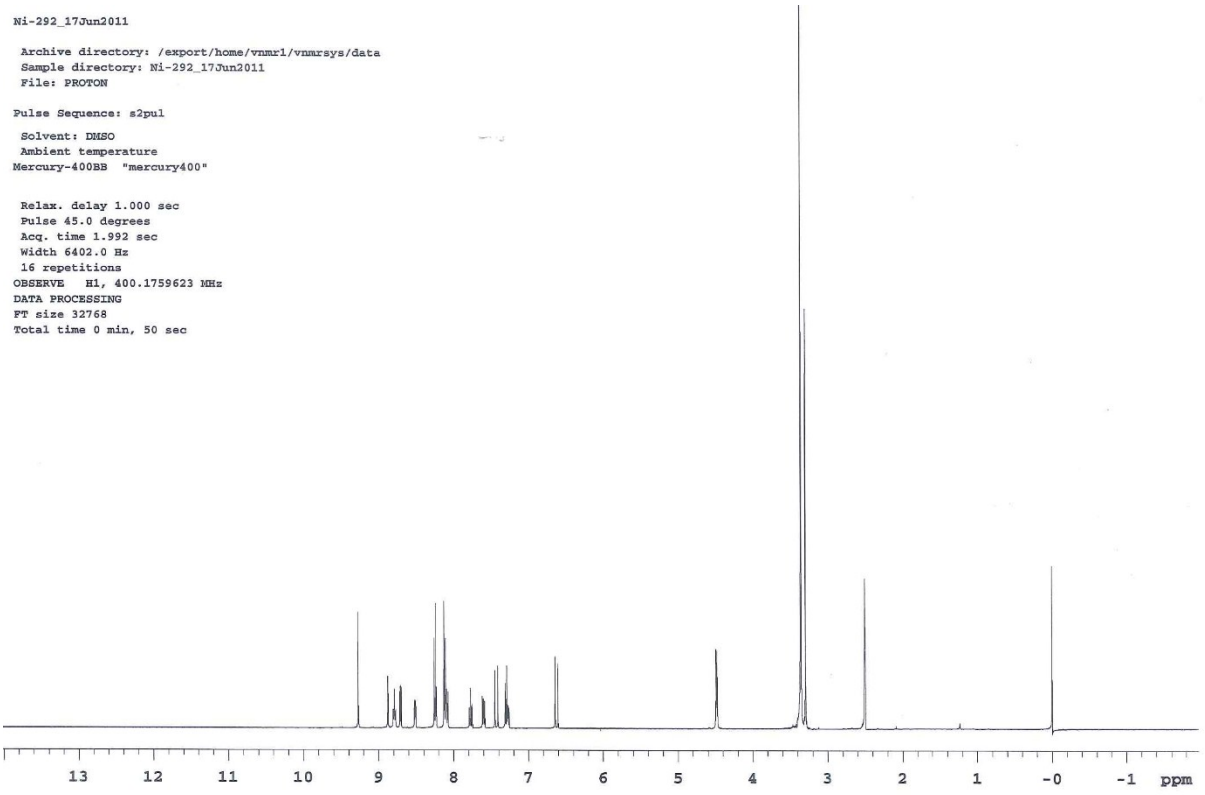
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

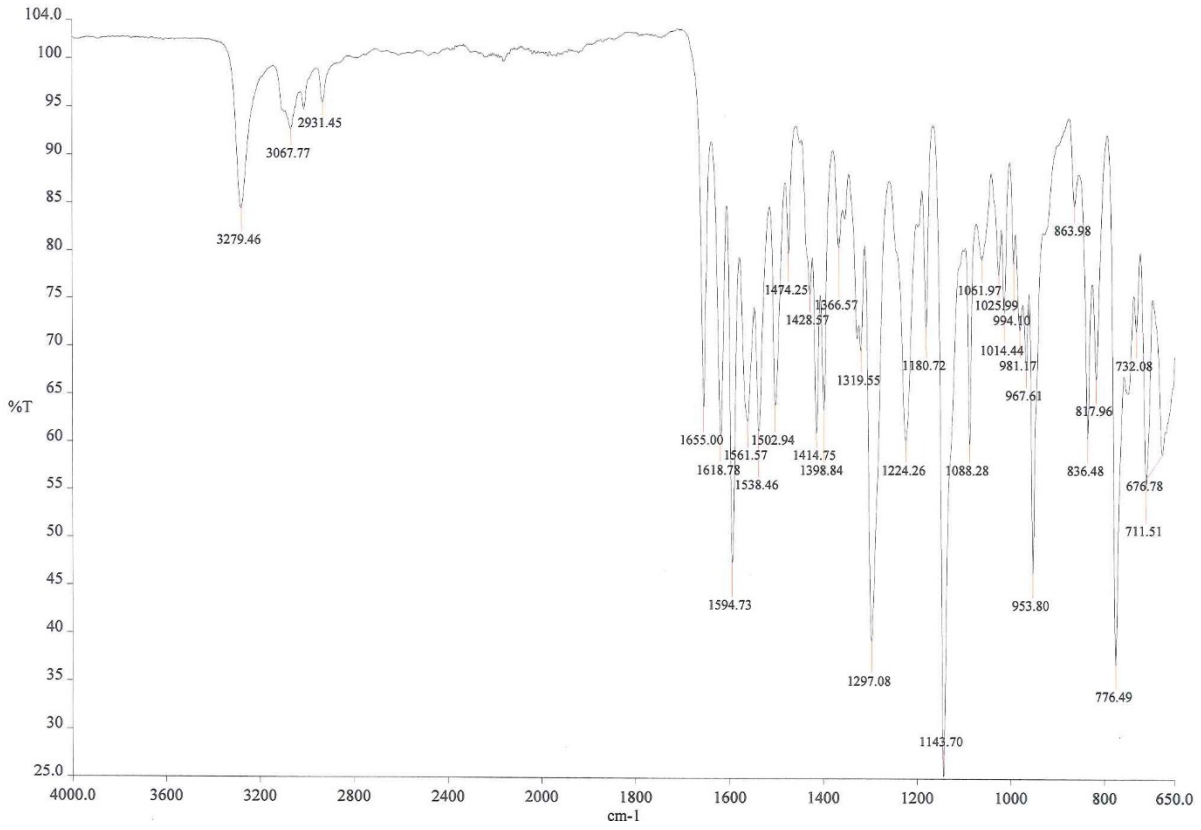
Monoisotopic Mass, Even Electron Ions
196 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-29 H: 1-50 N: 1-9 O: 1-3 S: 1-2
NI-313 44 (1.696) Cm (44:46)
1: TOF MS ES+



Minimum:				-1.5						
Maximum:		5.0	5.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
477.1708	477.1709	-0.1	-0.2	15.5	329.5	0.0	C24	H25	N6	O3 S

Figure S22. Spectral data of Compound **5m**



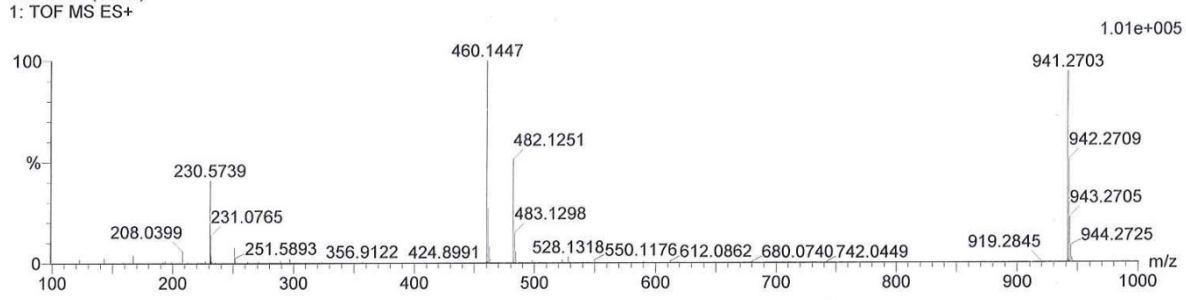


Elemental Composition Report

Single Mass Analysis

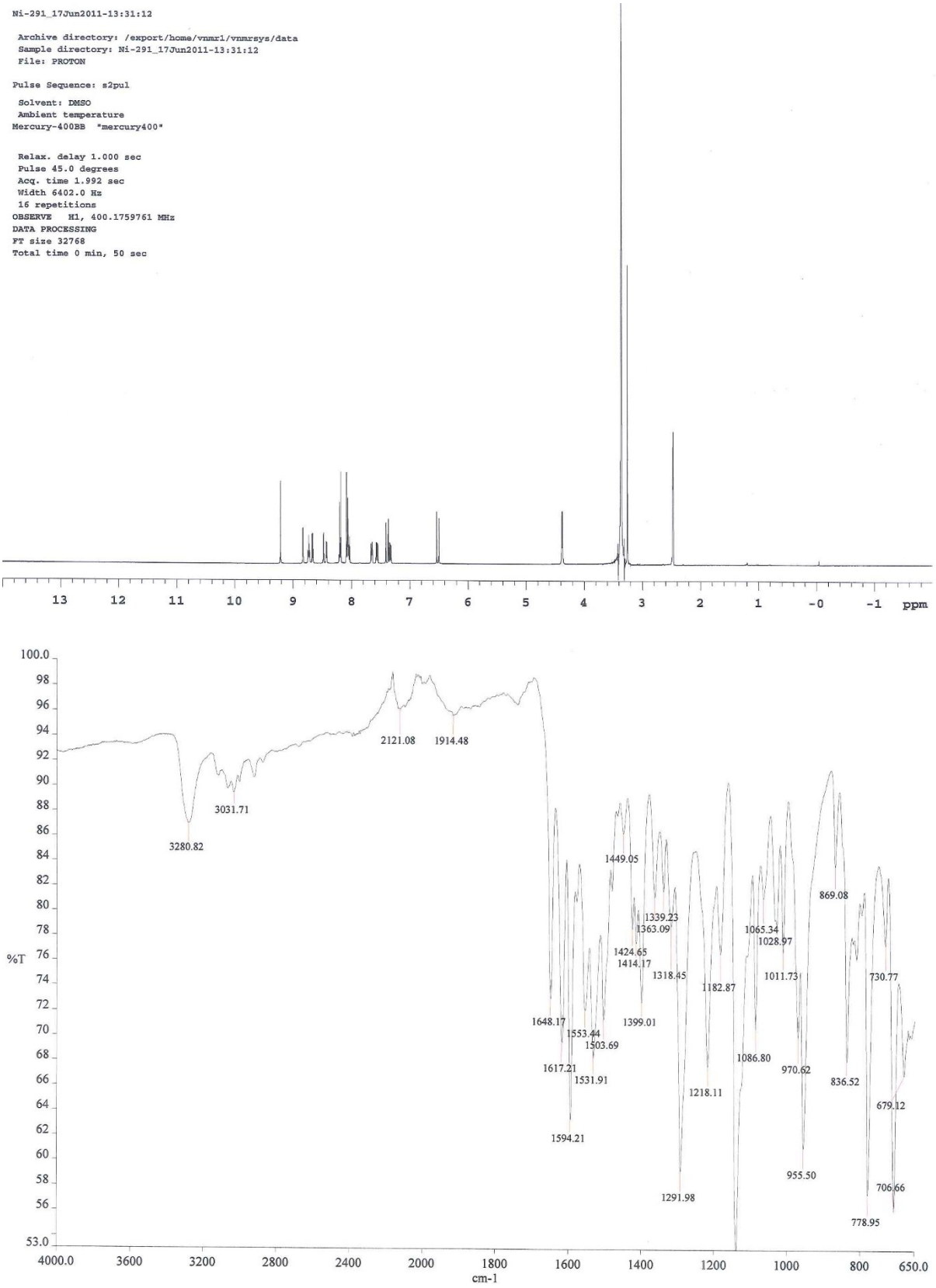
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
395 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-50 H: 1-50 N: 1-8 O: 1-6 S: 1-2
NI-292 36 (1.382)
1: TOF MS ES+



Minimum:				-1.5							
Maximum:		5.0	5.0	50.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula				
460.1447	460.1443	0.4	0.9	16.5	235.6	0.0	C24	H22	N5	O3	S
	460.1437	1.0	2.2	7.5	241.0	5.3	C16	H26	N7	O5	S2

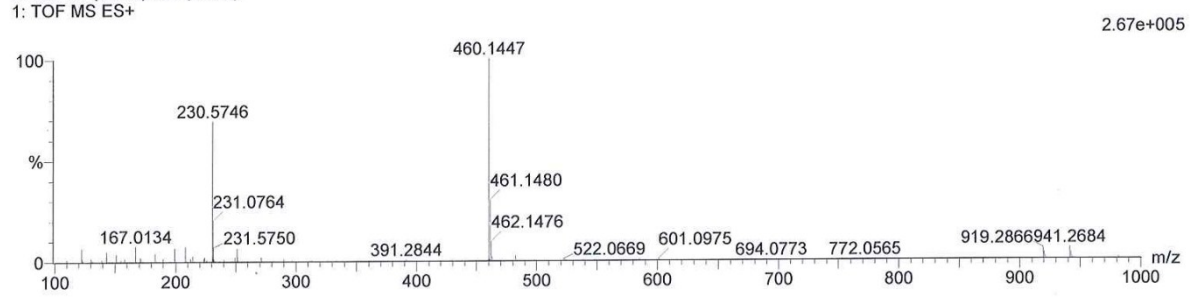
Figure S23. Spectral data of Compound **5n**



Elemental Composition Report **Page 1 of 1**

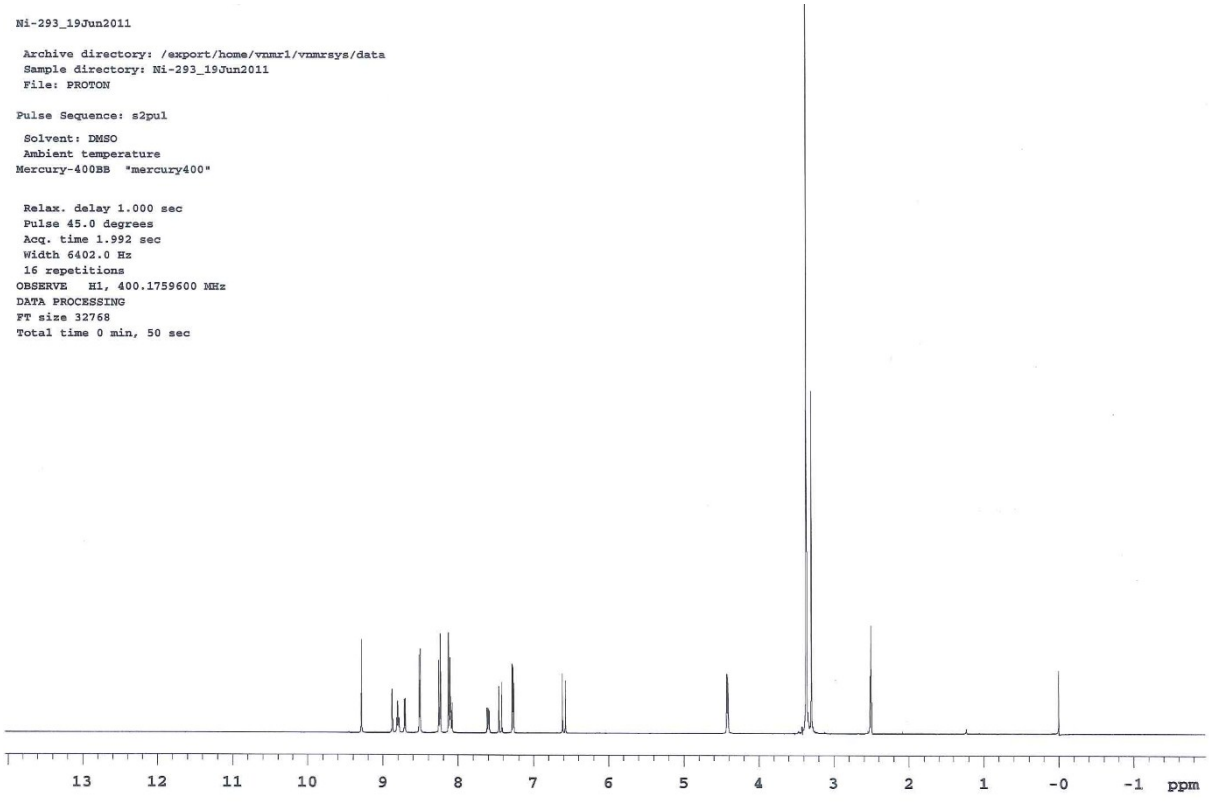
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

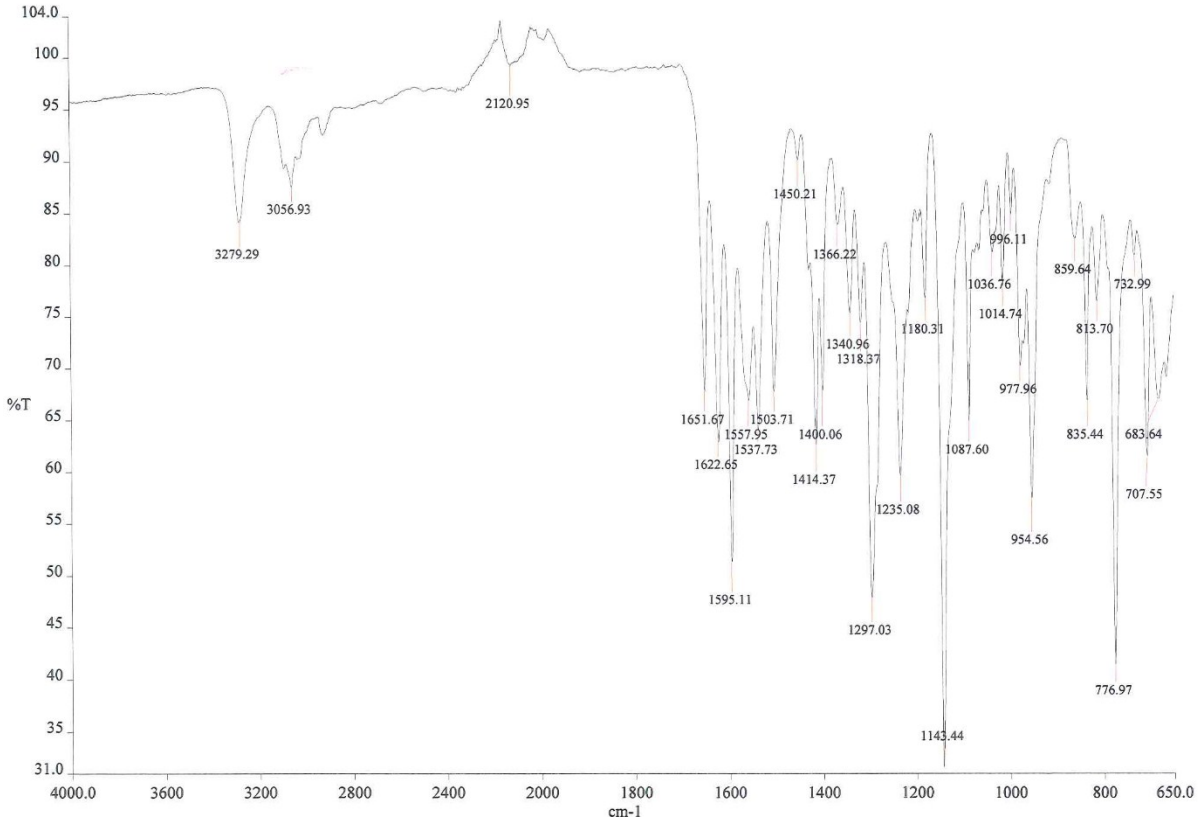
Monoisotopic Mass, Even Electron Ions
331 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-25 H: 1-25 N: 1-8 O: 1-6 S: 1-2 Ni: 0-1
NI-291 24 (0.912) Cm (21:26)
1: TOF MS ES+



Minimum:				-1.5						
Maximum:		5.0	5.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
460.1447	460.1443	0.4	0.9	16.5	485.1	0.0	C24	H22	N5	O3 S

Figure S24. Spectral data of Compound **5o**





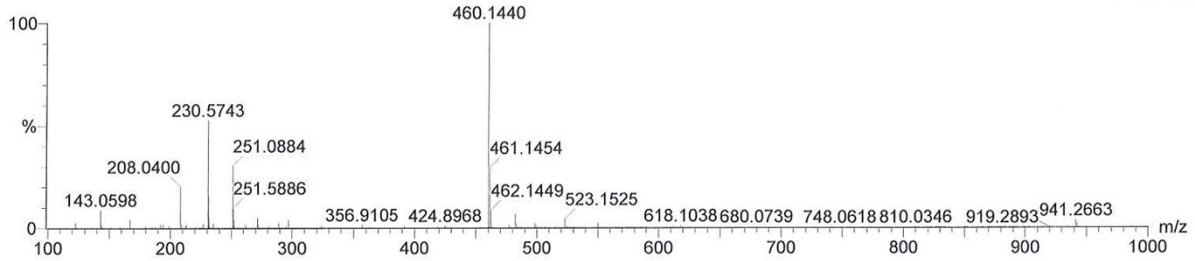
Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

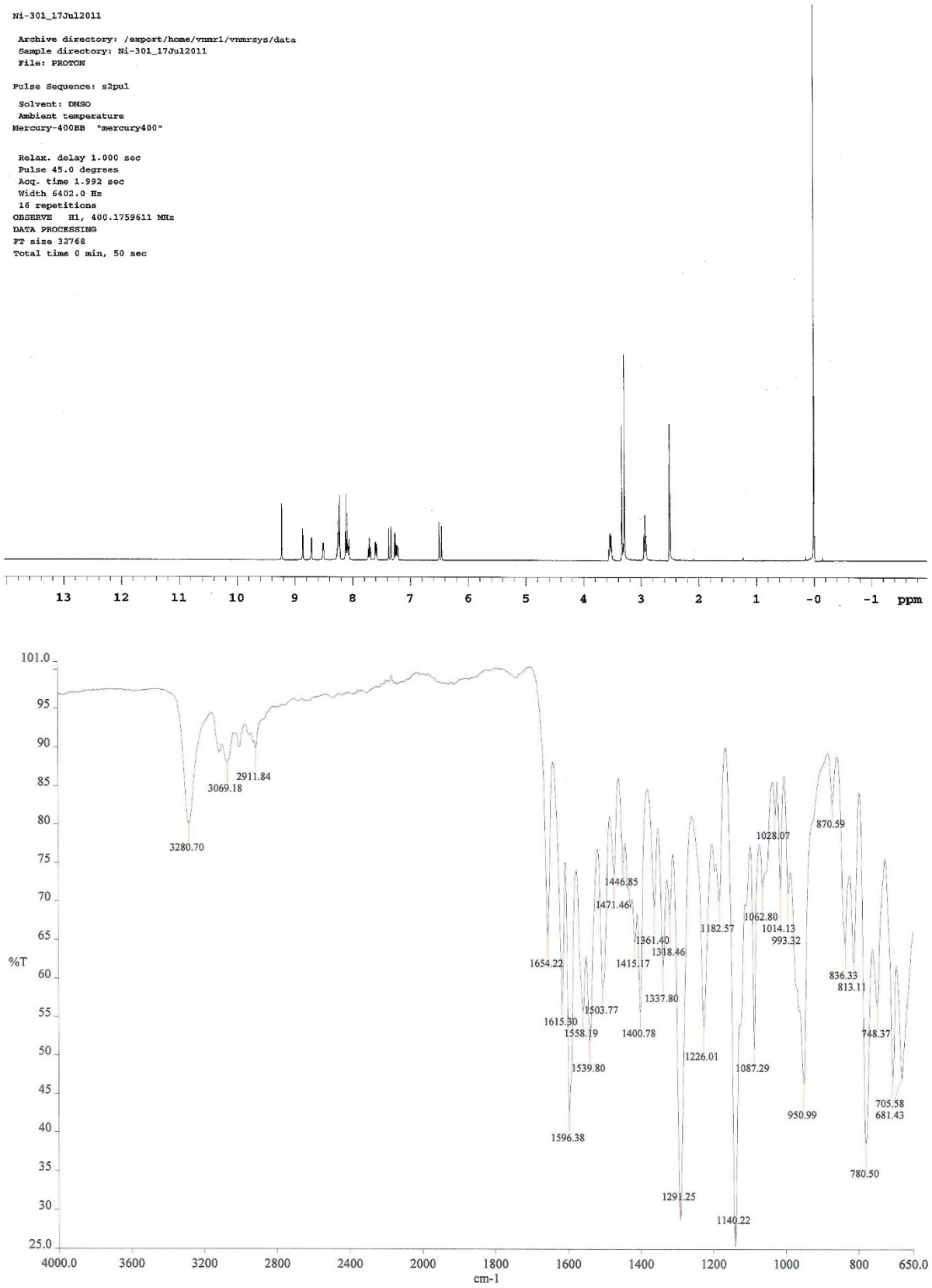
Monoisotopic Mass, Even Electron Ions
395 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-50 H: 1-50 N: 1-8 O: 1-6 S: 1-2
NI-293-2 42 (1.635) Cm (42:44)
1: TOF MS ES+

4.34e+004



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
460.1440	460.1443	-0.3	-0.7	16.5	118.9	0.0	C24 H22 N5 O3 S
	460.1437	0.3	0.7	7.5	129.1	10.3	C16 H26 N7 O5 S2

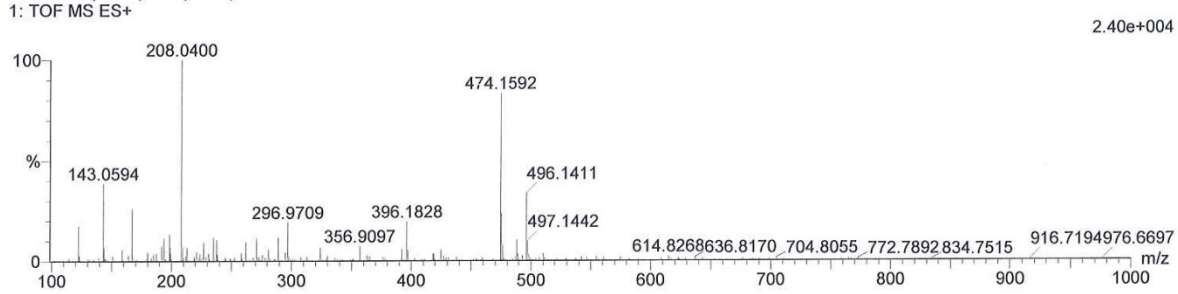
Figure S25. Spectral data of Compound **5p**



Elemental Composition Report Page 1 of 1

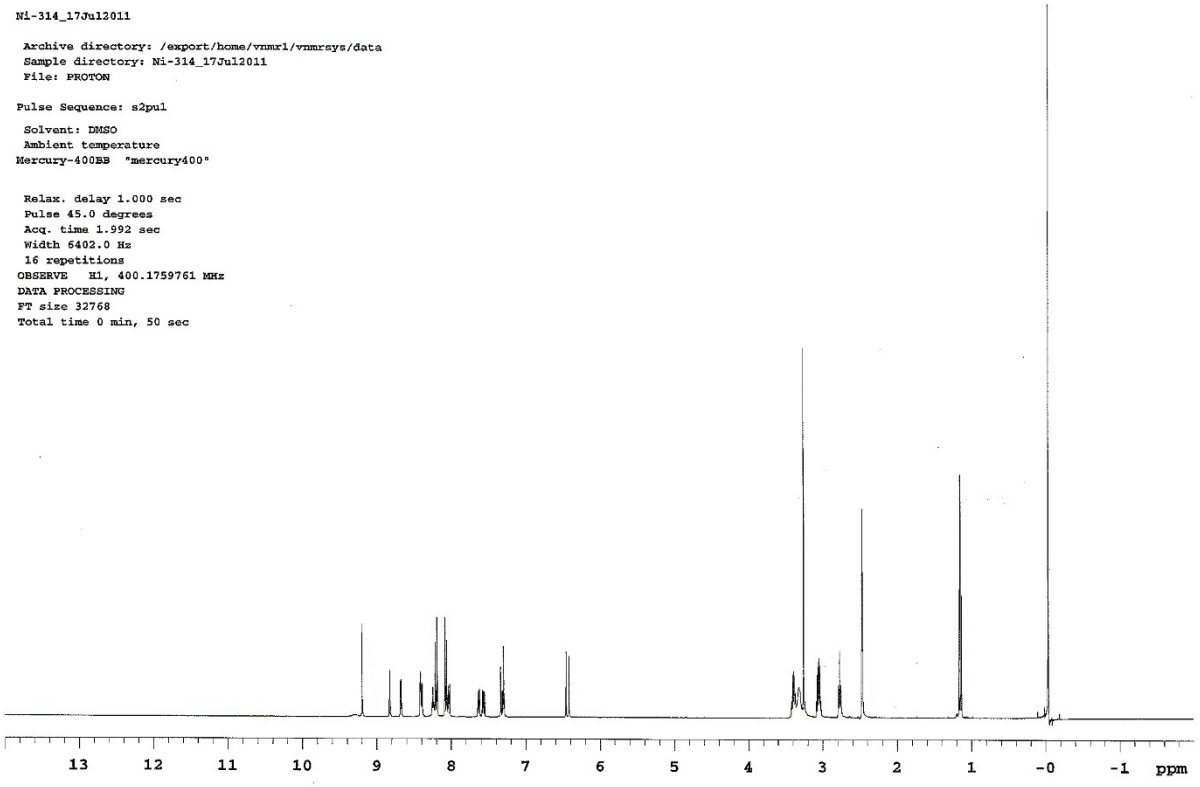
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

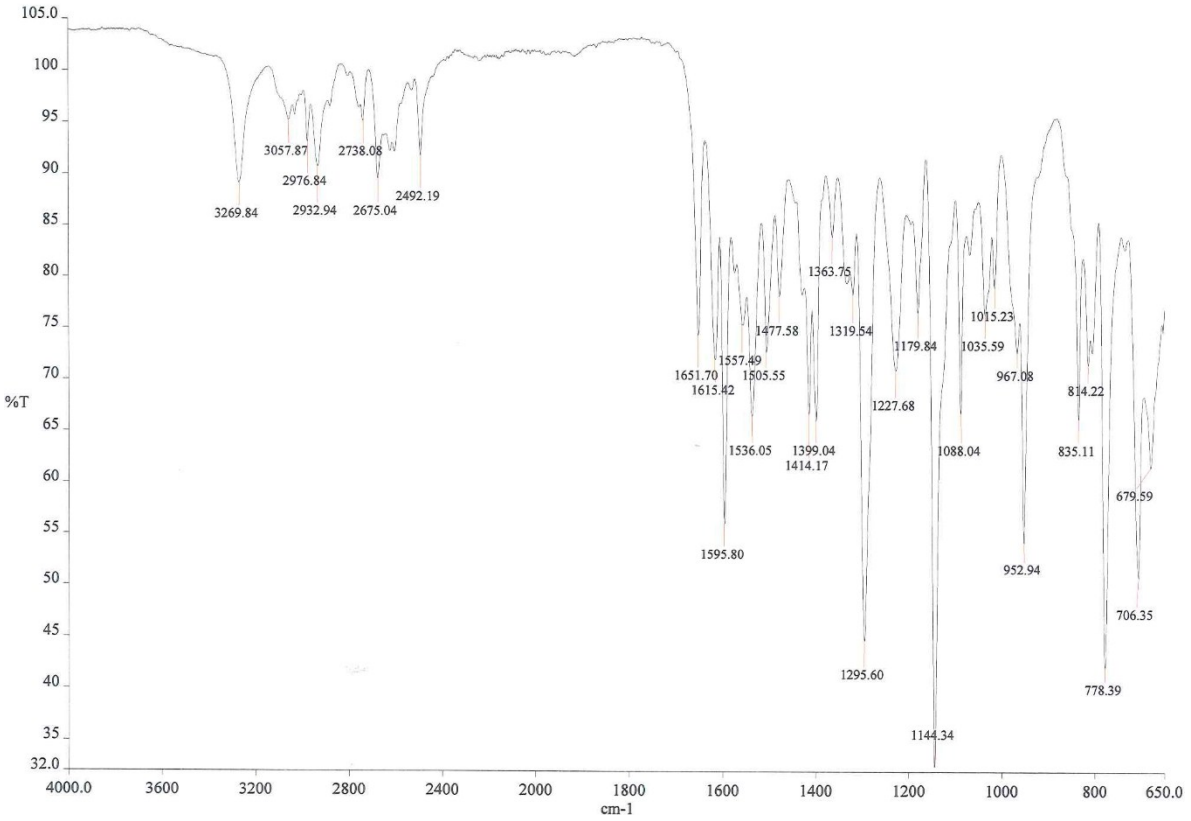
Monoisotopic Mass, Even Electron Ions
58 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-25 H: 1-33 N: 1-6 O: 1-4 S: 1-2
NI-301 48 (1.851) Cm (48:52)
1: TOF MS ES+



Minimum:				-1.5						
Maximum:		5.0	5.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
474.1592	474.1600	-0.8	-1.7	16.5	202.8	0.0	C25	H24	N5	O3 S

Figure S26. Spectral data of Compound **5r**





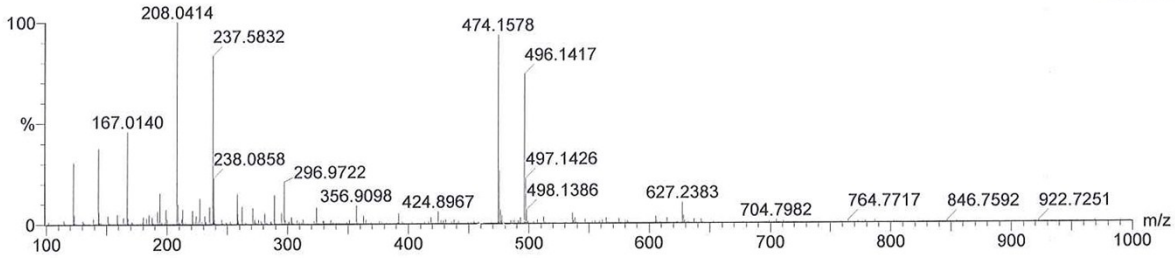
Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

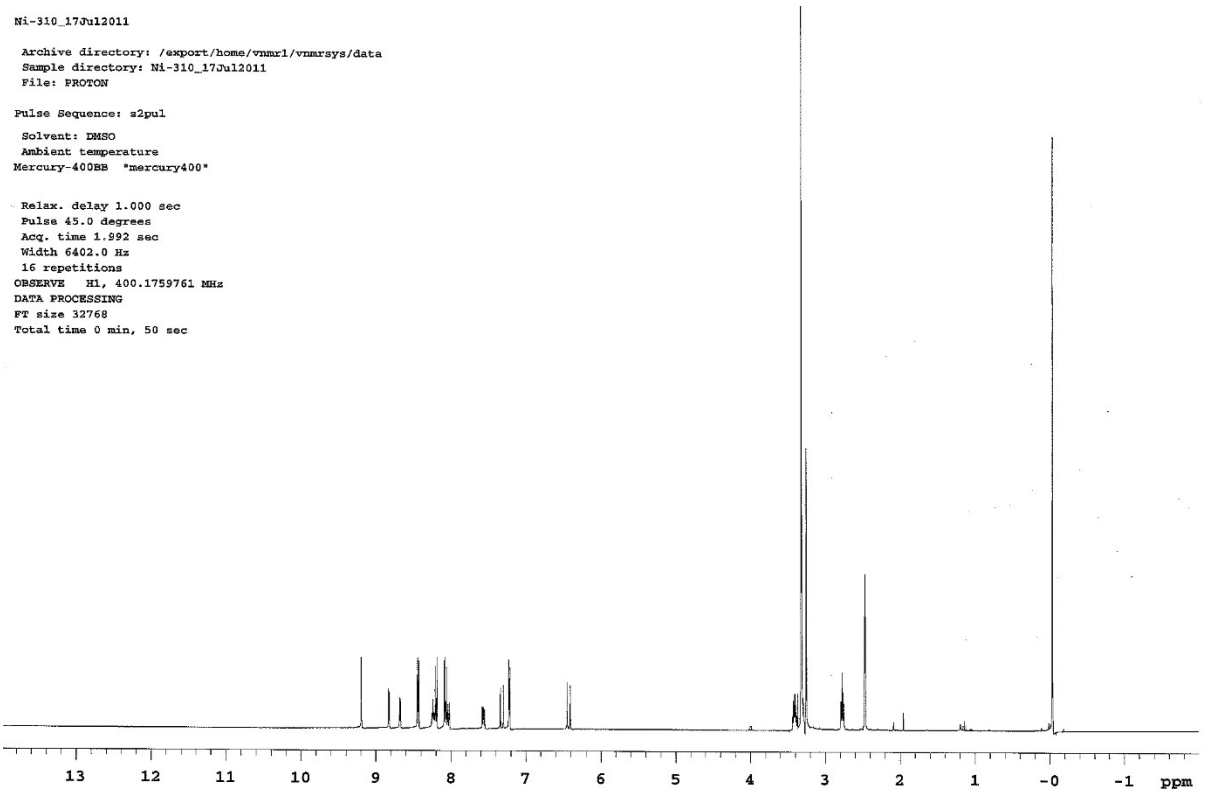
Monoisotopic Mass, Even Electron Ions
200 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-29 H: 1-50 N: 1-9 O: 1-3 S: 1-2
NI-314 45 (1.758) Cm (45:48)
1: TOF MS ES+

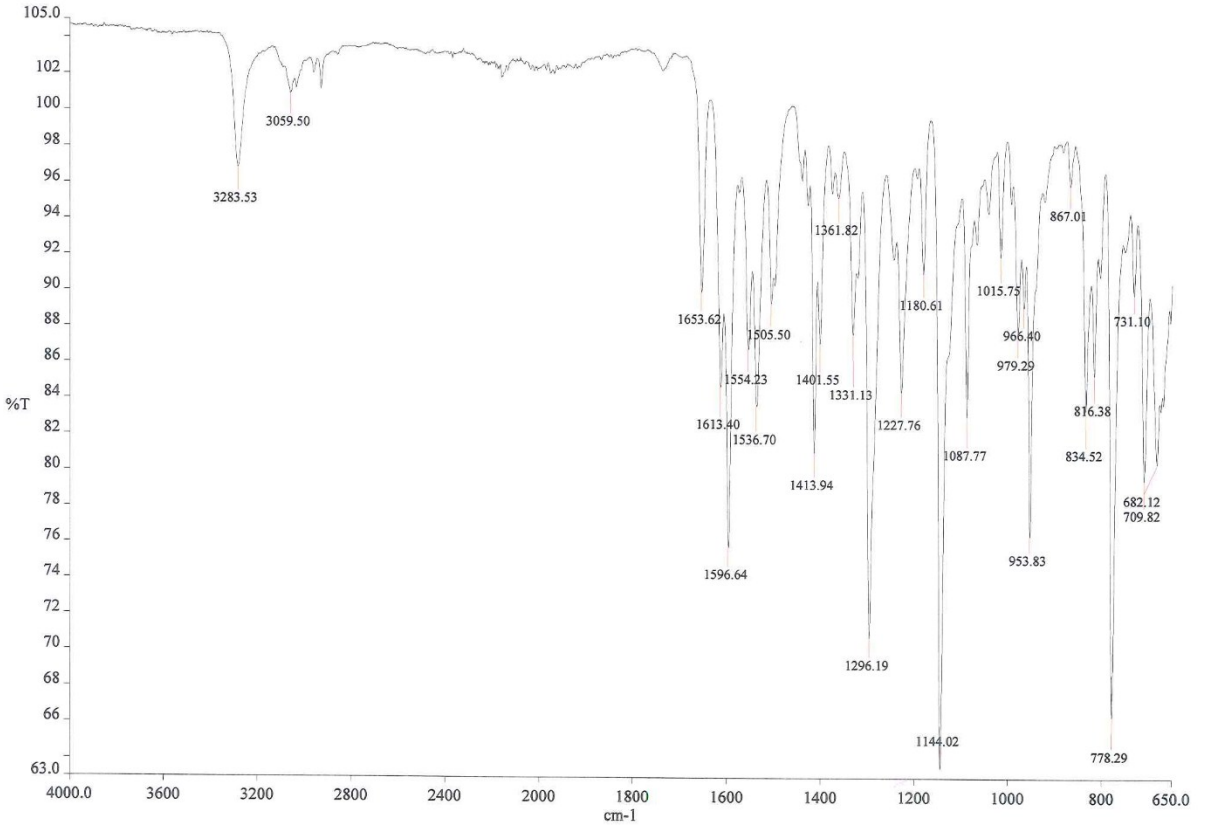
2.86e+004



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
474.1578	474.1561	1.7	3.6	15.5	208.7	3.4	C28 H28 N O2 S2
	474.1600	-2.2	-4.6	16.5	205.3	0.0	C25 H24 N5 O3 S

Figure S27. Spectral data of Compound **5s**

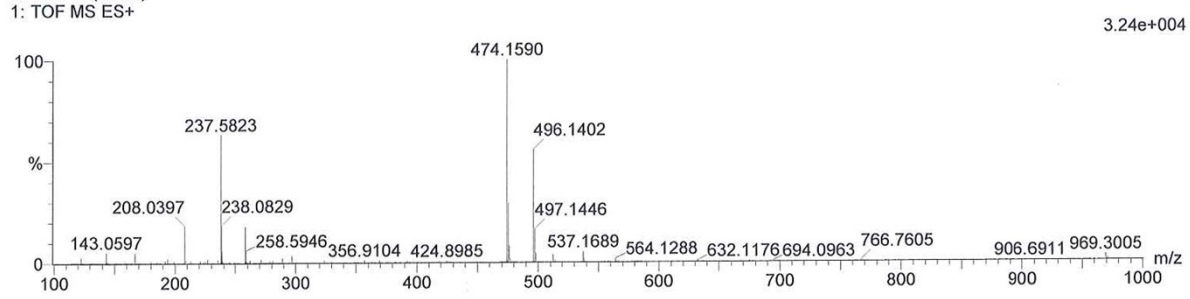




Elemental Composition Report

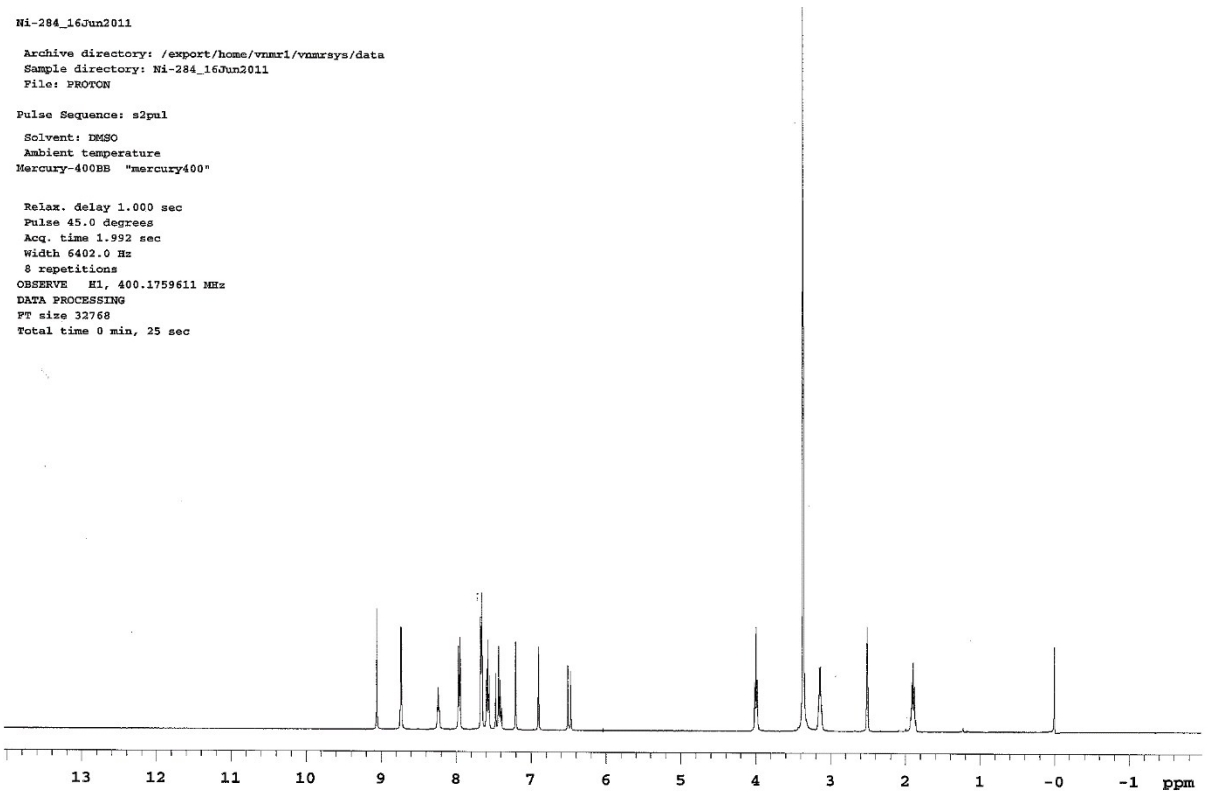
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

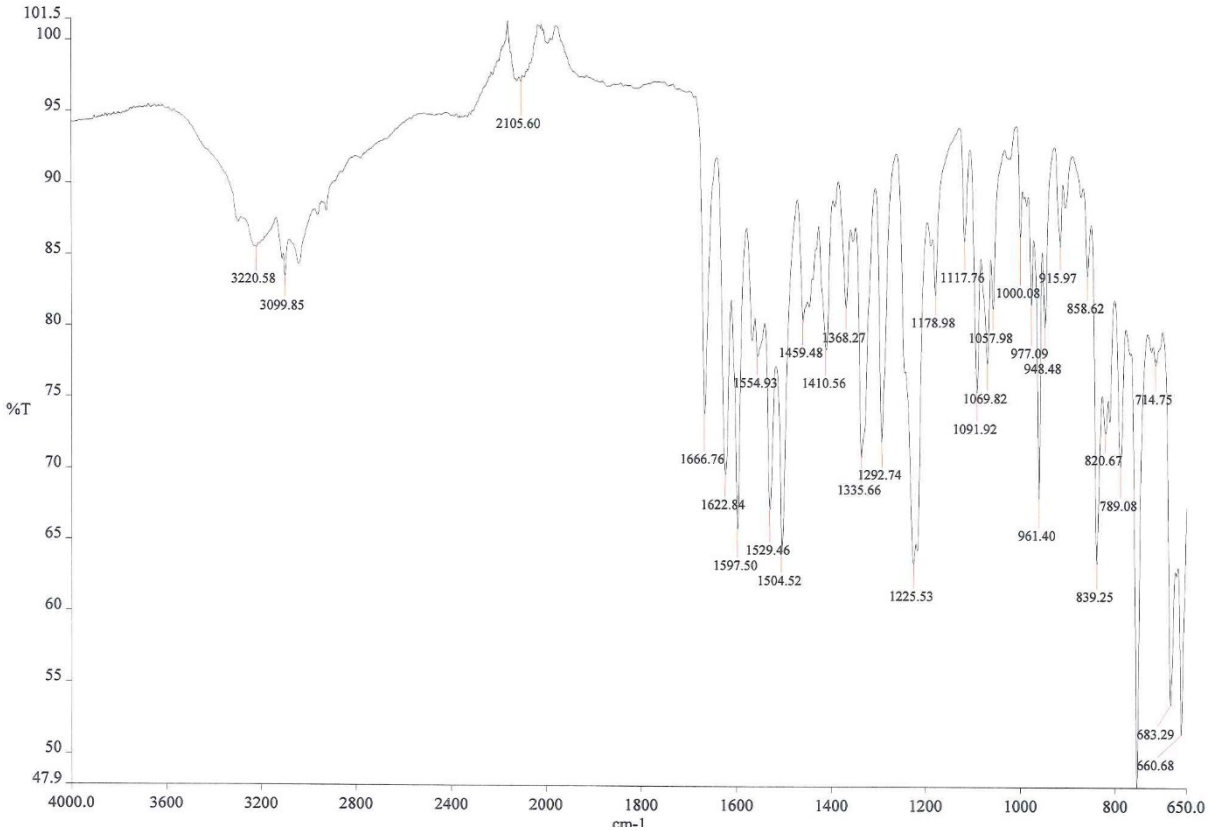
Monoisotopic Mass, Even Electron Ions
134 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-30 H: 1-25 N: 1-6 O: 1-6 S: 1-2
NI-310 44 (1.692)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
474.1590	474.1600	-1.0	-2.1	16.5	111.5	0.0	C25 H24 N5 O3 S

Figure S28. Spectral data of Compound **10a**





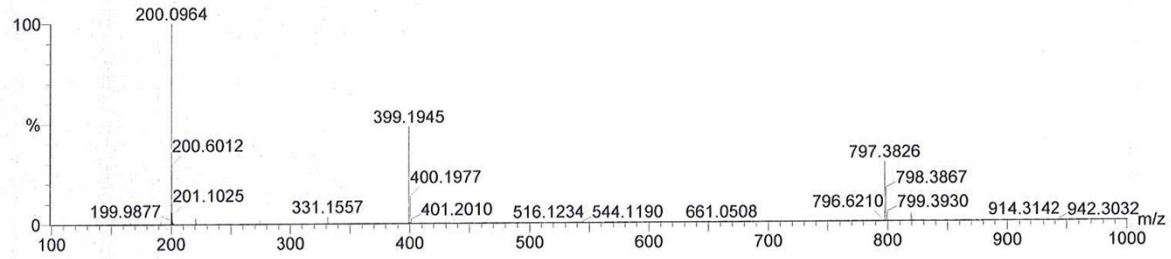
Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

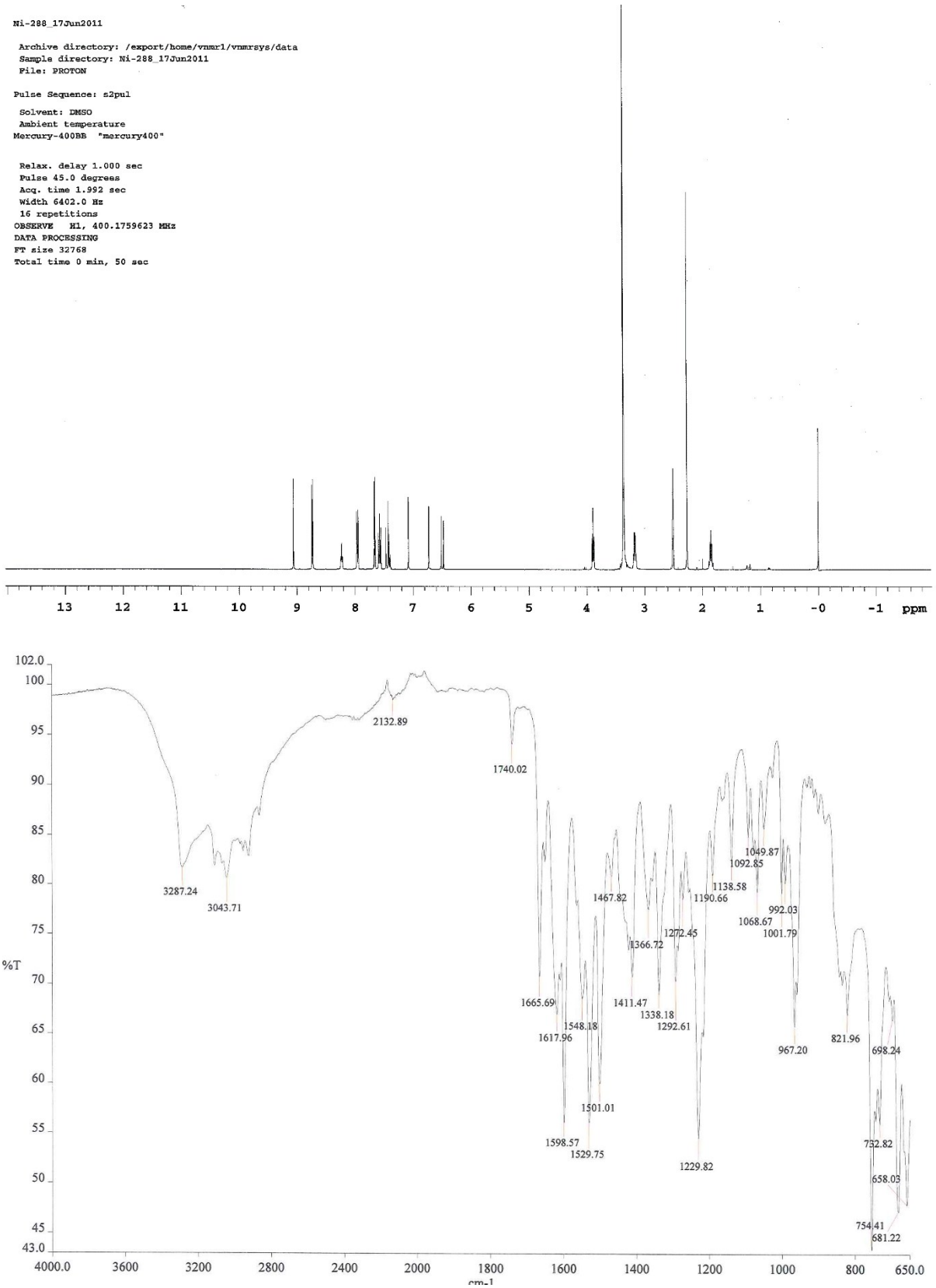
Monoisotopic Mass, Even Electron Ions
75 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-27 H: 1-33 N: 1-6 O: 1-5
NI-284 42 (1.636) Cm (41:44)
1: TOF MS ES+

4.04e+005



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
399.1945	399.1933	1.2	3.0	15.5	497.9	0.0	C23 H23 N6 O

Figure S29. Spectral data of Compound **10b**



Elemental Composition Report

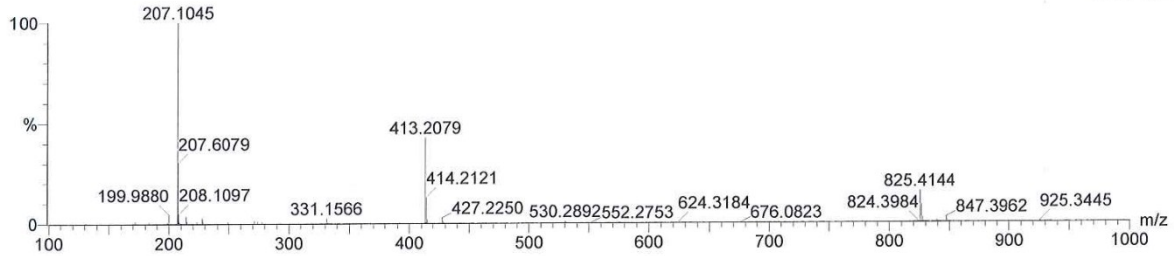
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
180 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-25 H: 1-25 N: 1-8 O: 1-6 Ni: 0-1

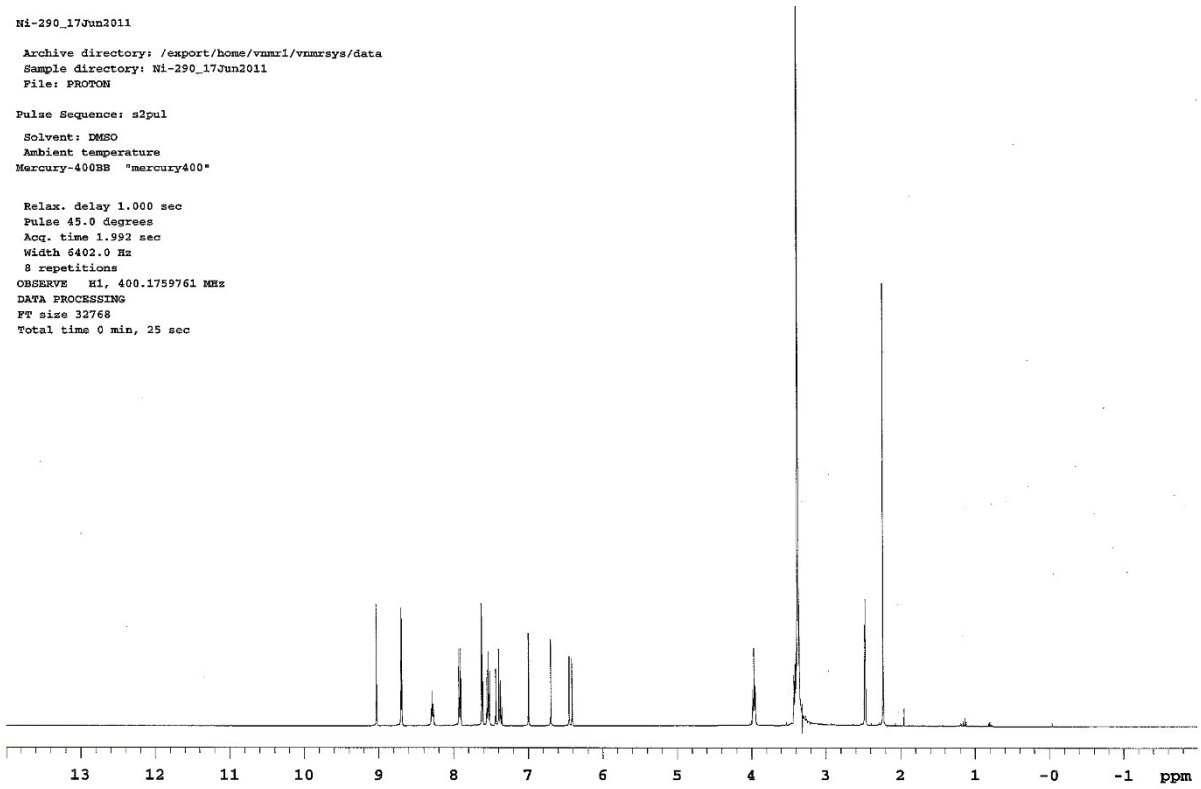
NI288 44 (1.696) Cm (44:46)
1: TOF MS ES+

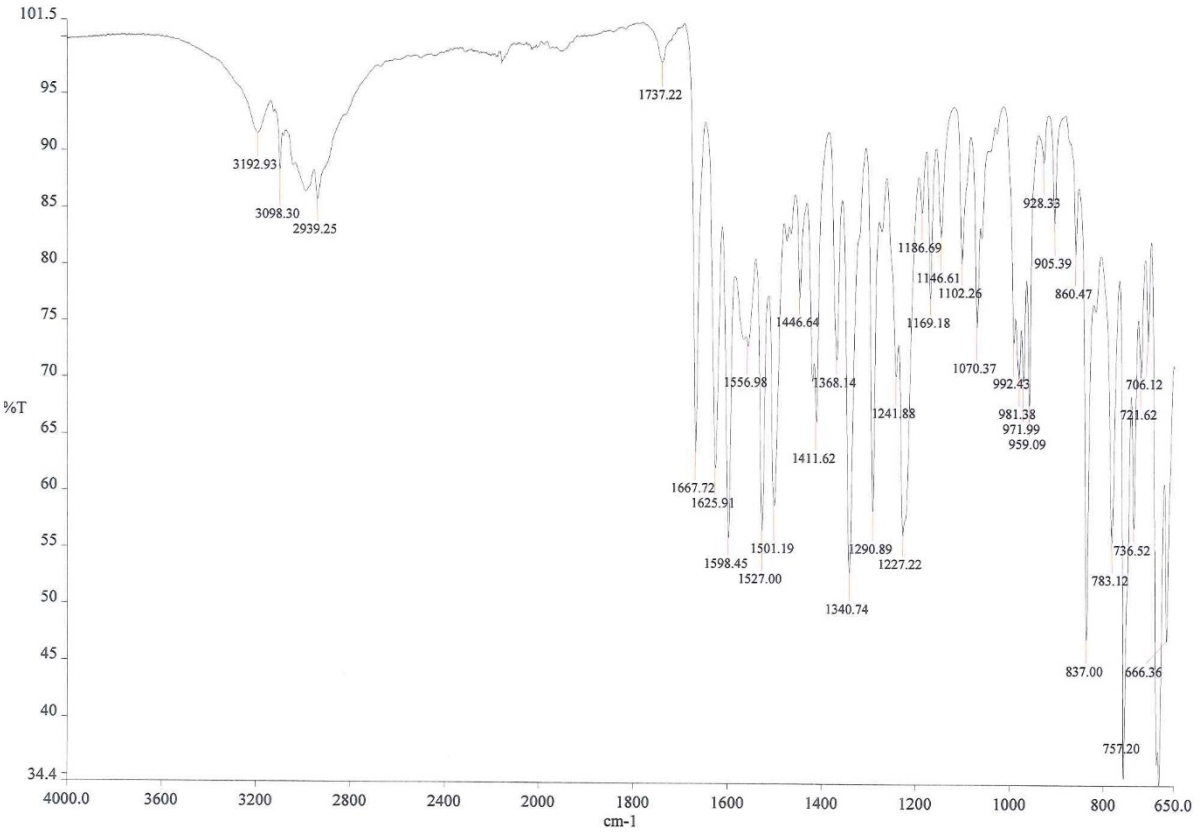
1.37e+005



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
413.2079	413.2090	-1.1	-2.7	15.5	283.8	0.0	C24 H25 N6 O

Figure S30. Spectral data of Compound **10c**

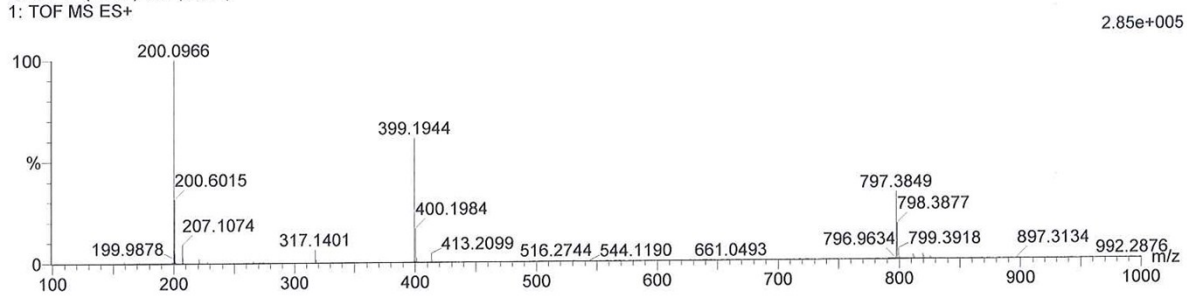




Elemental Composition Report

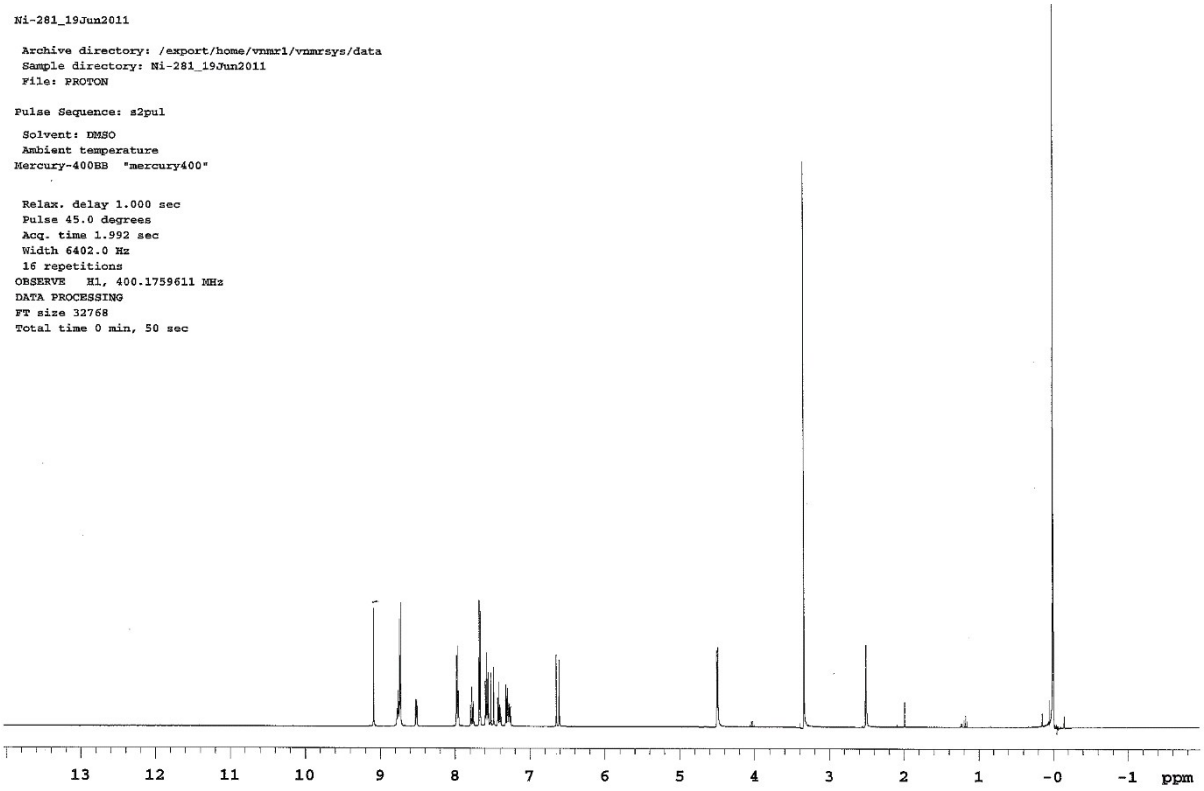
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

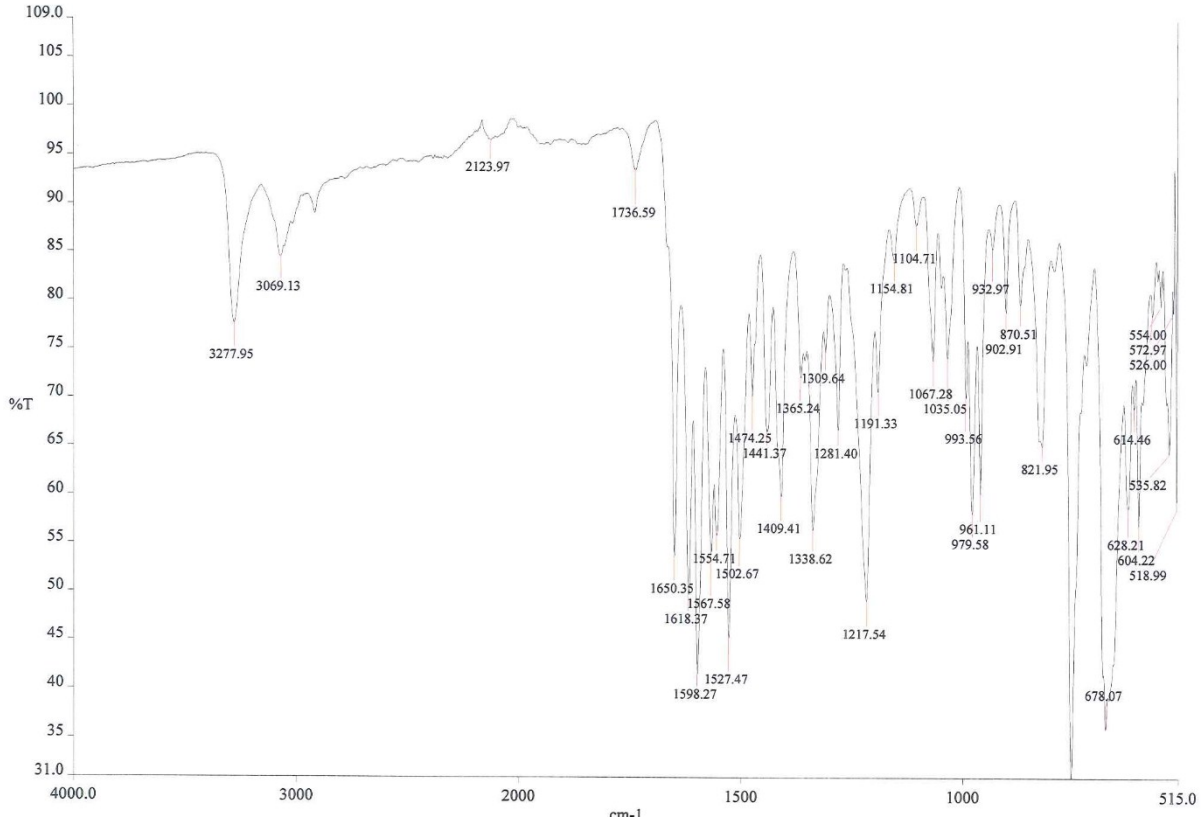
Monoisotopic Mass, Even Electron Ions
189 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-25 H: 1-25 N: 1-8 O: 1-6 Ni: 0-1
NI290 41 (1.602) Cm (41:44)
1: TOF MS ES+



Minimum:				-1.5					
Maximum:		5.0	5.0	50.0					
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula		
399.1944	399.1933	1.1	2.8	15.5	445.6	0.0	C23	H23	N6 O

Figure S31. Spectral data of Compound **10d**



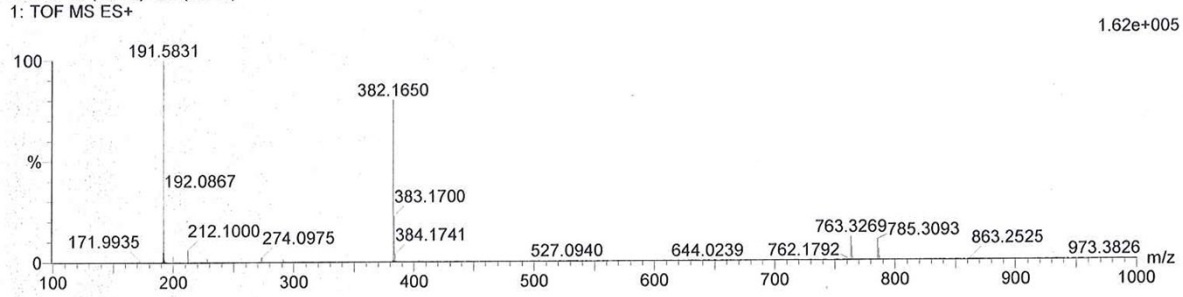


Elemental Composition Report

Single Mass Analysis

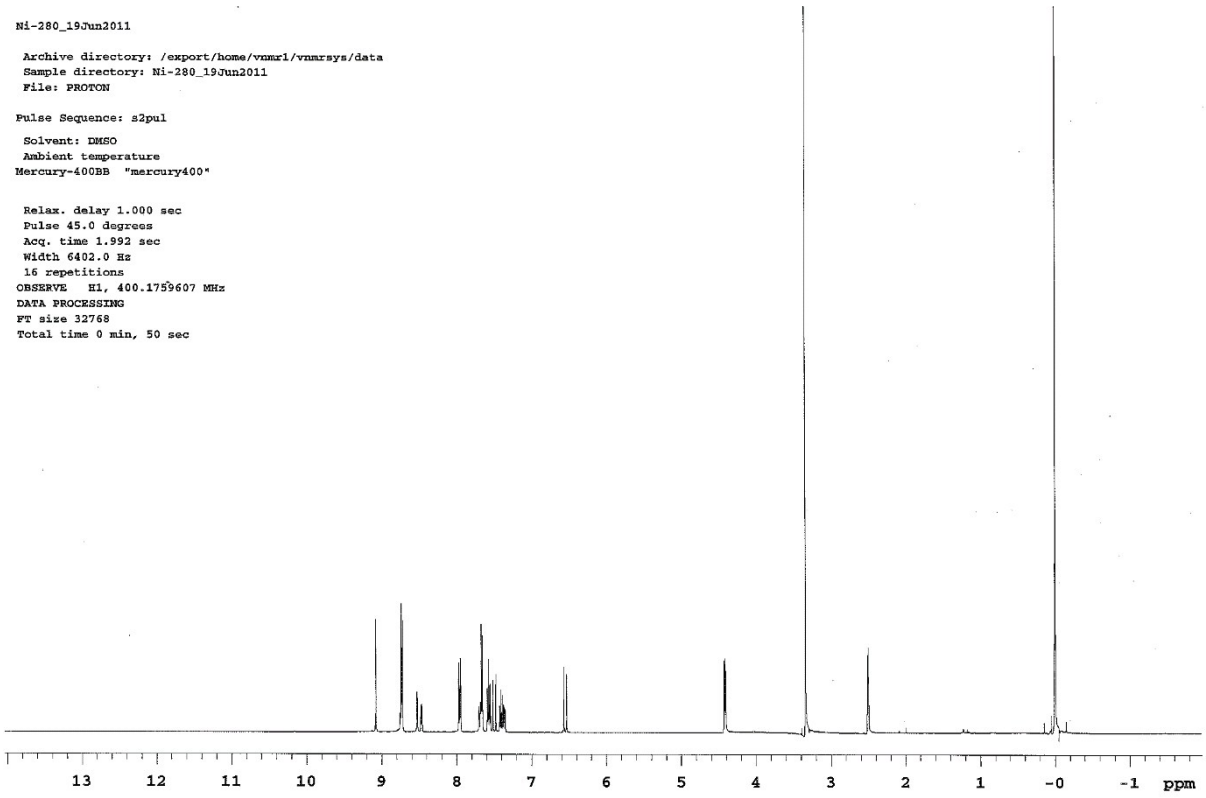
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

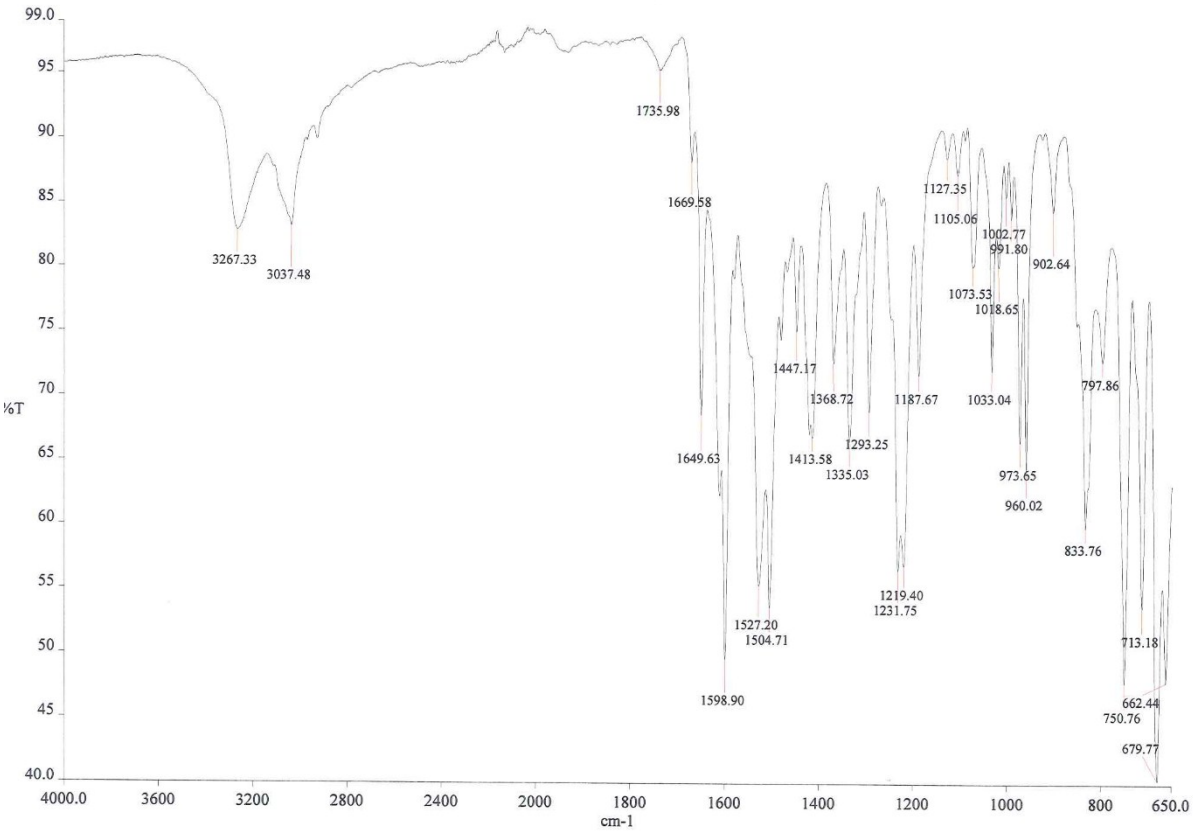
Monoisotopic Mass, Even Electron Ions
77 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-27 H: 1-33 N: 1-6 O: 1-5
NI-281 45 (1.762) Cm (43:45)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
382.1650	382.1654	-0.4	-1.0	11.5	387.1	2.0	C22 H24 N O5
	382.1668	-1.8	-4.7	16.5	385.2	0.1	C23 H20 N5 O

Figure S32. Spectral data of Compound **10e**

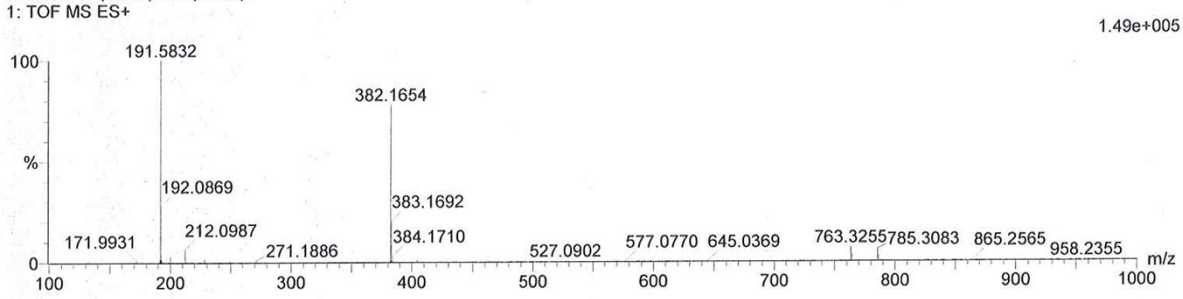




Elemental Composition Report Page 1 of 1

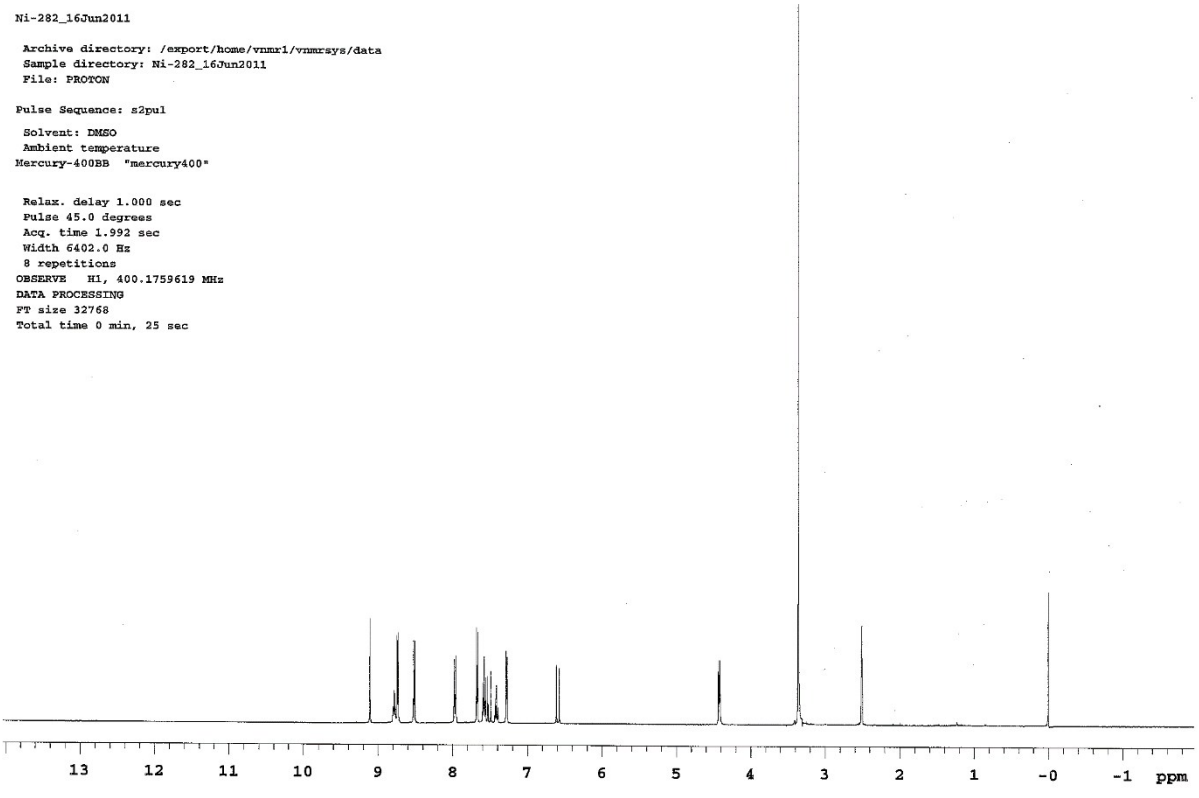
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

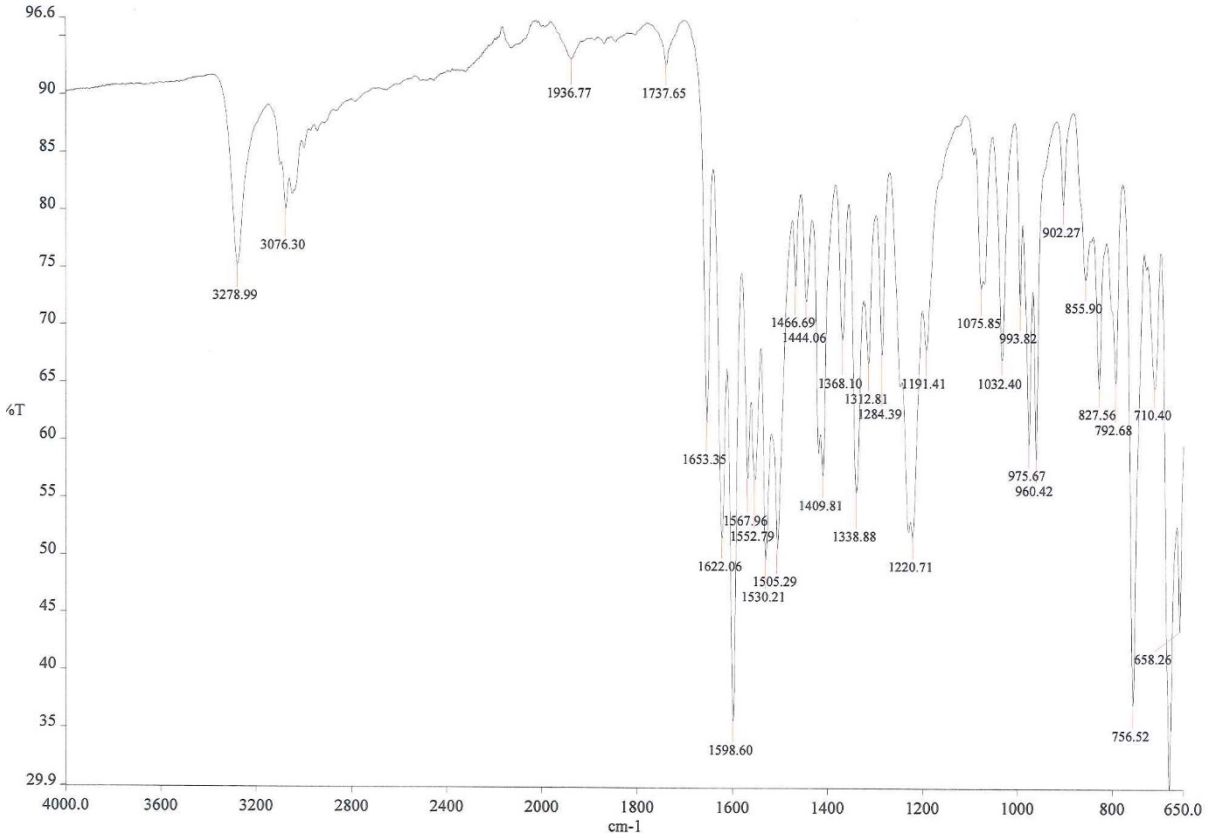
Monoisotopic Mass, Even Electron Ions
77 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-27 H: 1-33 N: 1-6 O: 1-5
NI-280X 44 (1.697) Cm (44:46)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
382.1654	382.1654	0.0	0.0	11.5	372.2	0.0	C22 H24 N O5
	382.1668	-1.4	-3.7	16.5	376.2	4.1	C23 H20 N5 O

Figure S33. Spectral data of Compound **10f**





Elemental Composition Report

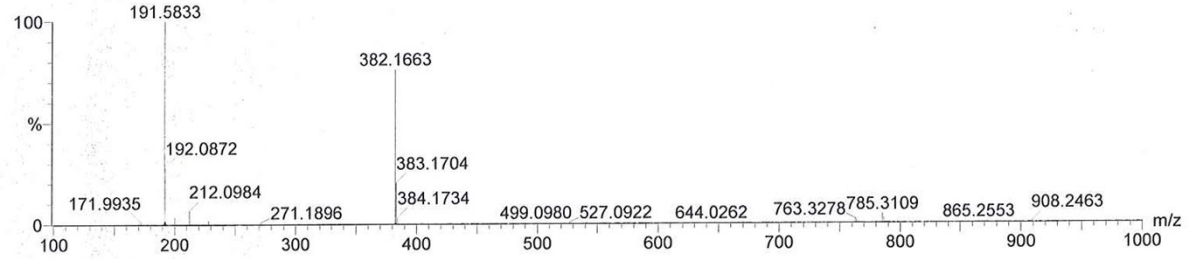
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
77 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-27 H: 1-33 N: 1-6 O: 1-5

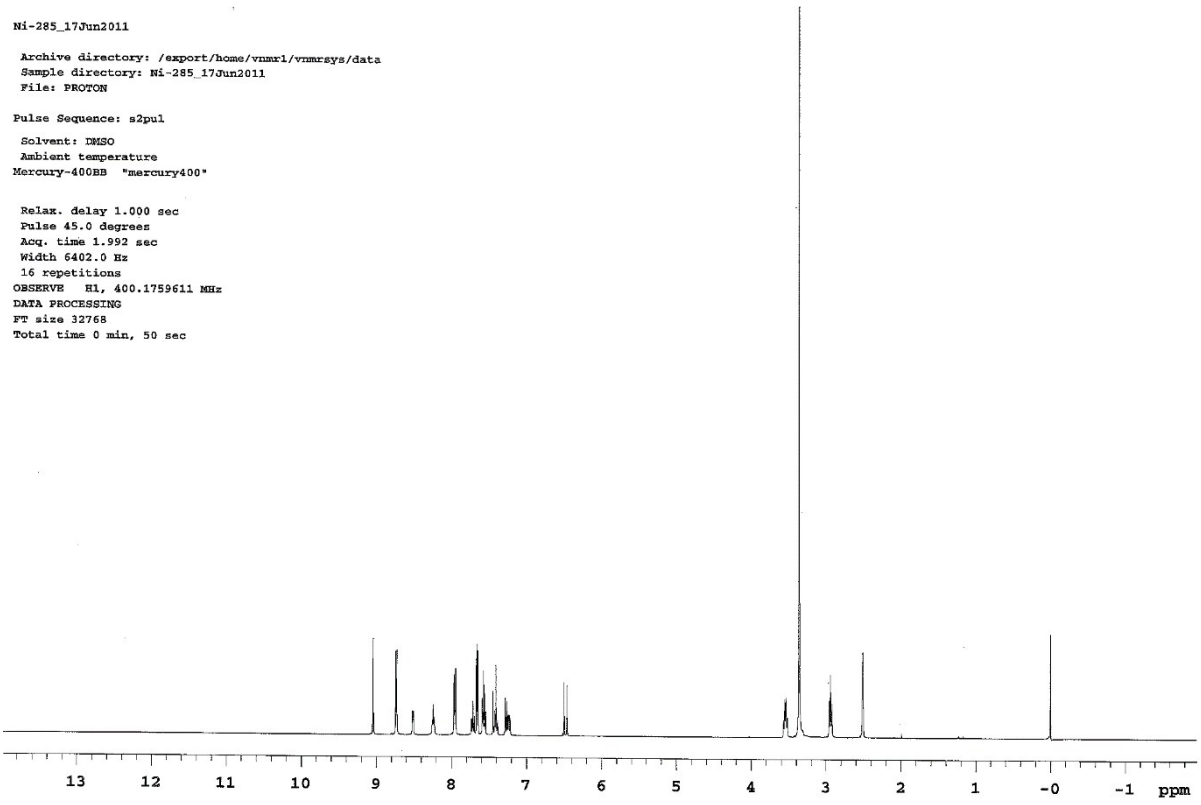
NI-282 43 (1.665) Cm (43:45)
1: TOF MS ES+

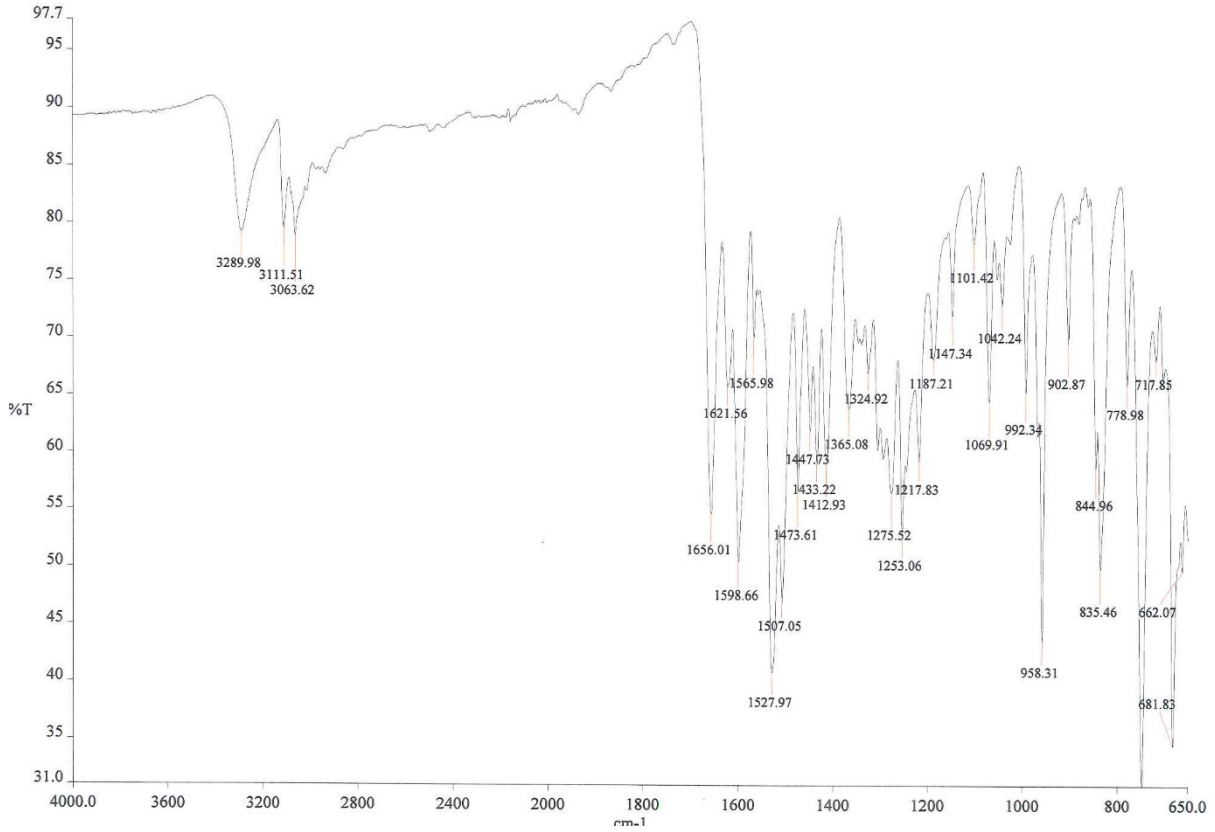
1.84e+005



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
382.1663	382.1668	-0.5	-1.3	16.5	456.6	0.7	C23 H20 N5 O
	382.1654	0.9	2.4	11.5	456.6	0.7	C22 H24 N O5

Figure S34. Spectral data of Compound **10g**

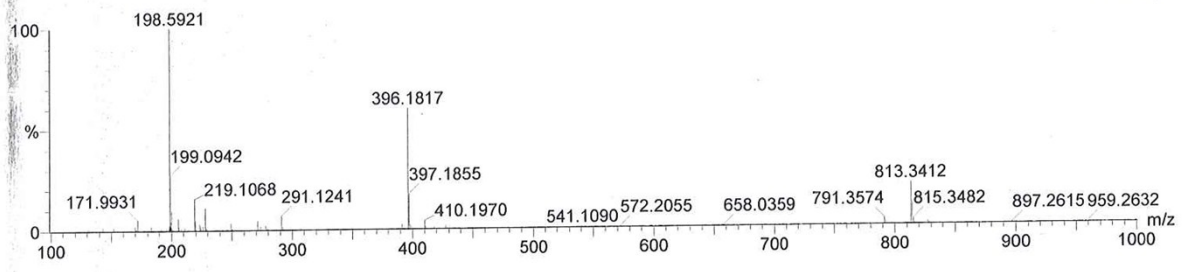




Elemental Composition Report Page 1 of 1

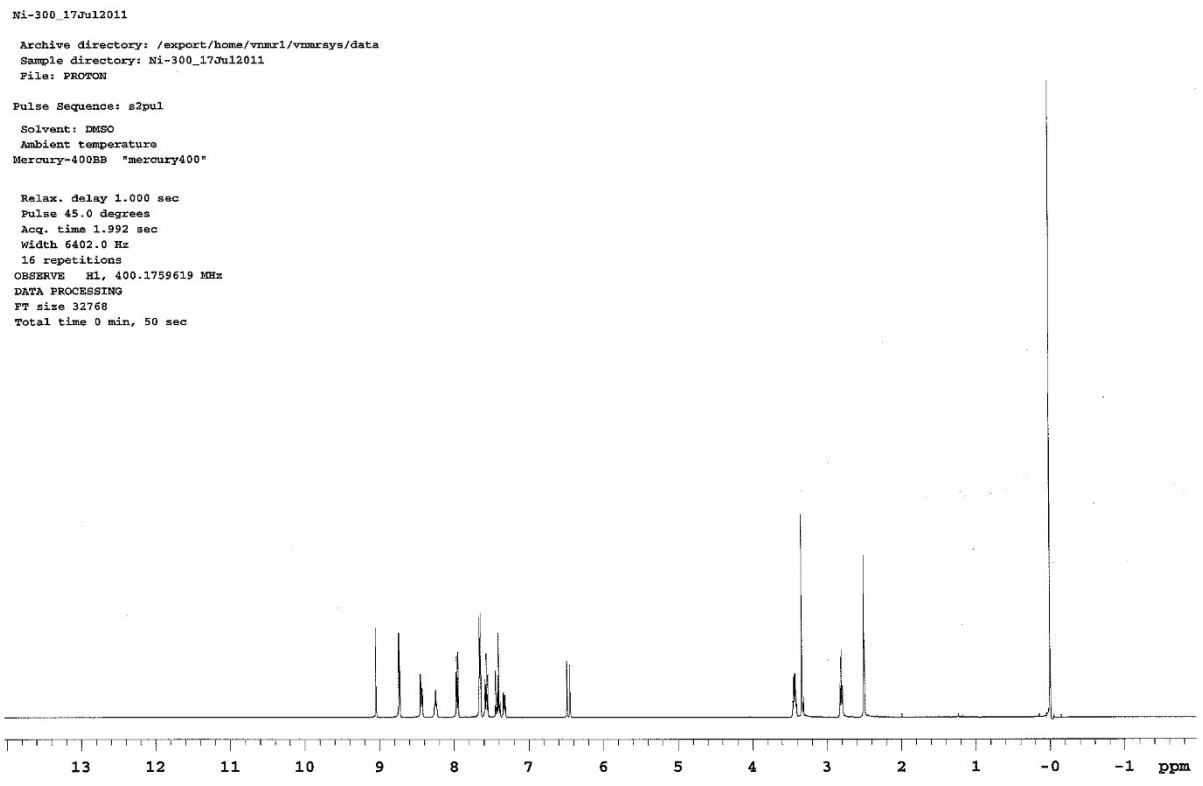
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

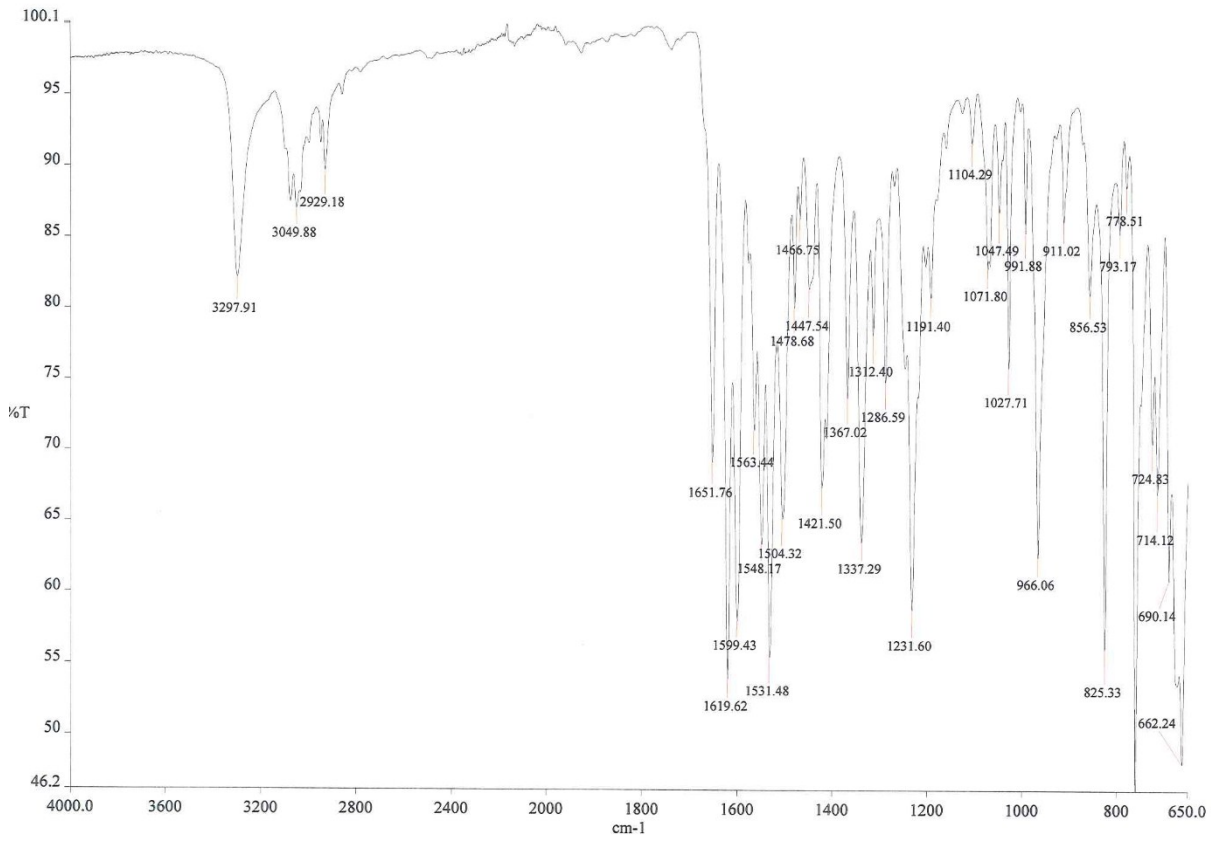
Monoisotopic Mass, Even Electron Ions
72 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-27 H: 1-33 N: 1-6 O: 1-5
NI-285 45 (1.765) Cm (45:49)
1: TOF MS ES+ 8.05e+004



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
396.1817	396.1811	0.6	1.5	11.5	266.1	1.7	C23 H26 N O5
	396.1824	-0.7	-1.8	16.5	264.6	0.2	C24 H22 N5 O

Figure S35. Spectral data of Compound **10h**





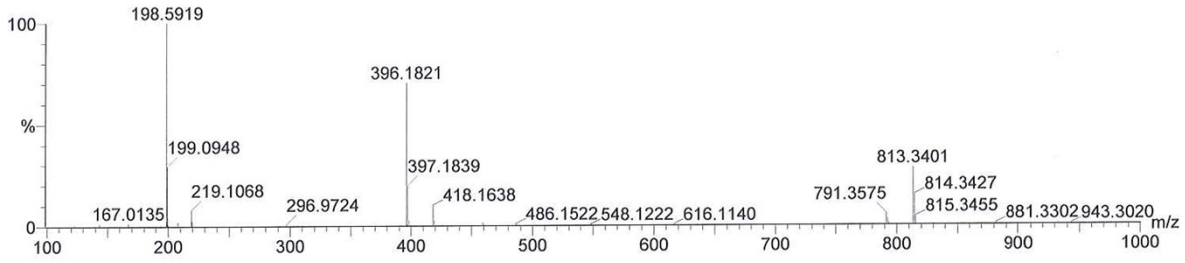
Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

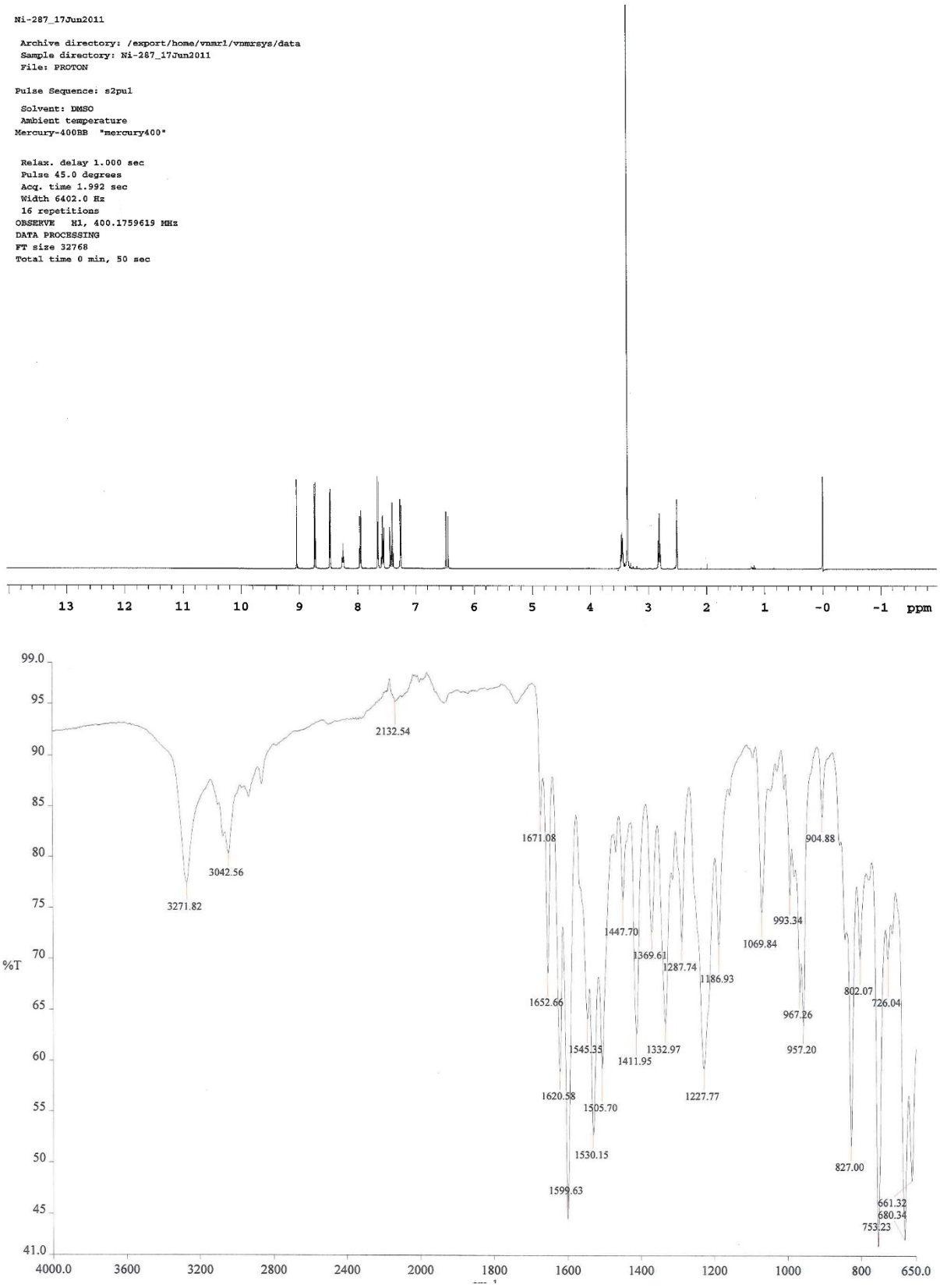
Monoisotopic Mass, Even Electron Ions
45 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-25 H: 1-33 N: 1-6 O: 1-4
NI-300 44 (1.693) Cm (44:46)
1: TOF MS ES+

3.45e+005



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
396.1821	396.1824	-0.3	-0.8	16.5	414.1	0.0	C24 H22 N5 O

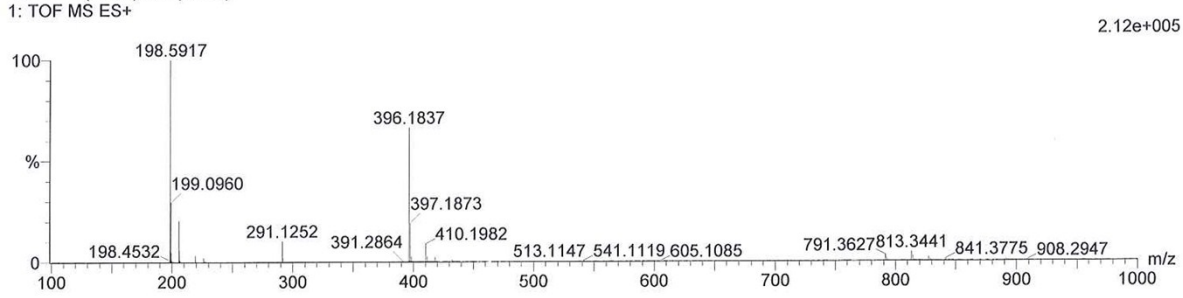
Figure S36. Spectral data of Compound **10i**



Elemental Composition Report **Page 1 of 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
177 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-25 H: 1-25 N: 1-8 O: 1-6 Ni: 0-1
NI287 42 (1.632) Cm (42:44)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
396.1837	396.1824	1.3	3.3	16.5	432.5	0.0	C24 H22 N5 O

References

[1] S.N.I. Baytas, N.; Yılmaz, A.; , Synthesis, cytotoxicity and molecular properties prediction of novel 1,3-diarylpyrazole derivatives, Med. Chem. Res., 22 (2013) 4893-4908
[2] C.C. Chu, Teague, P. C., 4-Pyridylhydantoins, J. Org. Chem., 23 (1958) 1578.