Triaryl benzimidazoles as a new class of antibacterial agents against resistant pathogenic microorganisms

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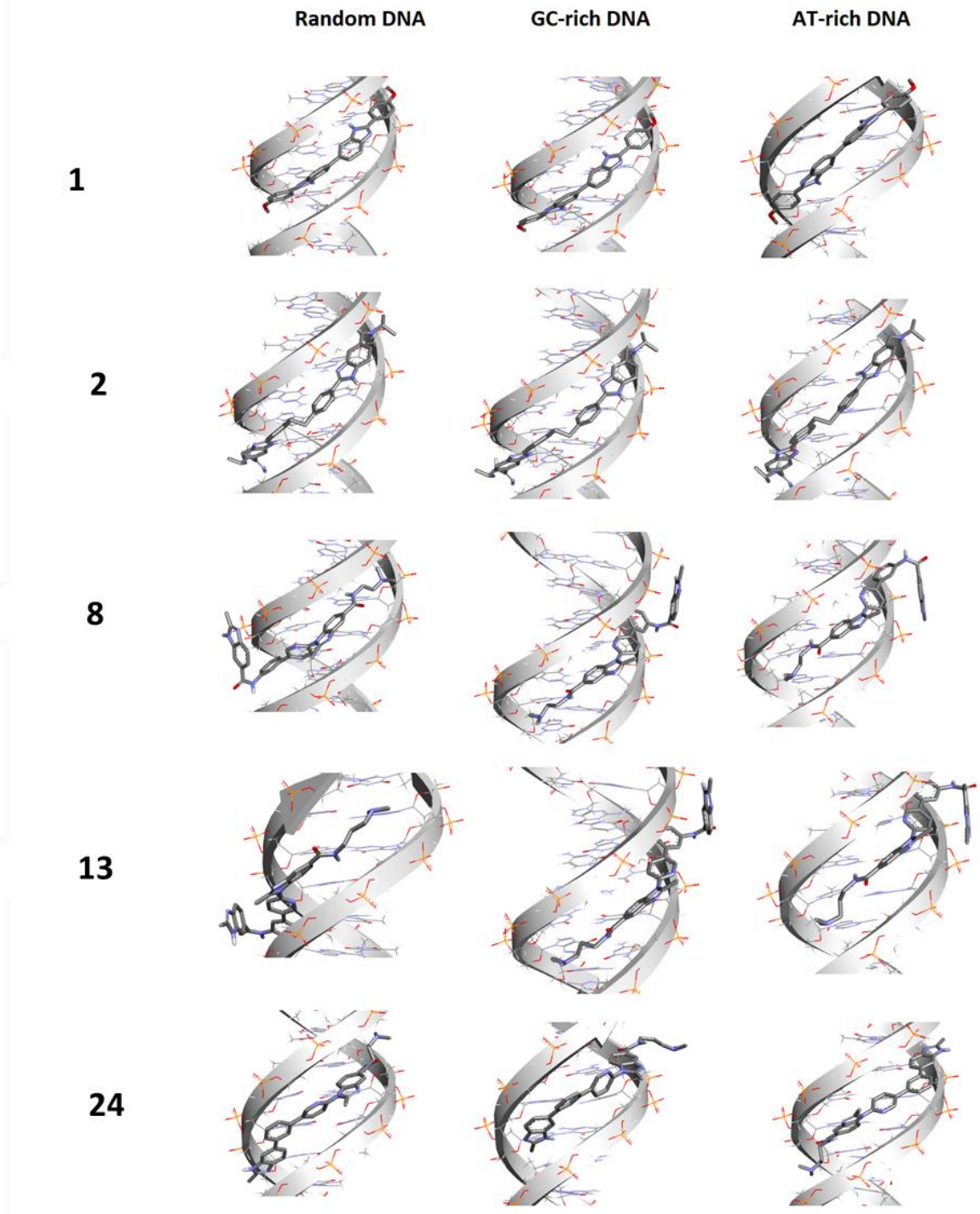
Supporting info:

- **S1. Molecular docking poses for selected compound against selected DNA sequences.**
- **S2. Molecular docking affinity for selected compound against selected DNA sequences.**
- **S3. Molecular docking affinity for compound 13 against DNA gyrase from *S. aureus***
- **S4. Key interactions between compound 13 and the subunit 1 of DNA gyrase**
- **S5. Key interactions between compound 13 and the subunit 2 of DNA gyrase**
- **S6. LC-MS method for purity determination**
- **S7. NMR spectra for key compounds**
- **S8. HRMS analysis for target compounds.**

S1. Molecular docking poses for selected compound against selected DNA sequences.



S2. Molecular docking affinity for selected compound against selected DNA sequences.

DNA sequences:

Random sequences: 5’-TAGCTAGCTAGCTAGCG- 3’

AT-rich sequences: 5’-TATATAAATATATATAT- 3’

GC-rich sequences: 5’-GCGCGCGCGCGGCGCGC- 3’

Molecular Docking	**Affinity (kcal/mol) to different DNA sequences**		
Ligand	**Random Seq.**	**AT-rich Seq.**	**GC-rich Seq.**
Compound 1	-11.0	-12.3	-10.5
Compound 2	-11.4	-11.9	-12.0
Compound 8	-10.2	-10.4	-10.0
Compound 13	-9.7	-10.3	-9.4
Compound 24	-10.9	-11.1	-8.3

- **S3. Molecular docking affinity for compound 13 against DNA gyrase from *S. aureus***

	S.a. GyrA subunit1		**S.a. GyrA subunit2**	
Compound 13	CHEM score	Affinity (kcal/mole)	CHEM score	Affinity (kcal/mole)
1	28.6538	-34.2763	26.5265	-32.5067
2	22.442	-26.8676	25.9537	-28.9776
3	22.12	-26.4111	24.7465	-29.9077
4	20.845	-27.3906	23.7392	-29.761
5	20.8319	-25.5703	23.5713	-31.9042
6	20.6561	-26.2499	22.9578	-32.2137
7	20.5713	-25.2211	22.0263	-26.5639
8	20.3774	-24.9868	20.8056	-24.4638
9	20.3053	-24.3578	20.3246	-29.7576
10	18.5813	-25.2827	20.2807	-28.122

- **S4. Key interactions between compound 13 and the subunit 1 of DNA gyrase**

S .aureus GyrA-Compound 13 atoms (Subunit1)	Distance	Category	Types
A:LYS43:HZ1 - TR4:N9	1.75967	Hydrogen Bond	Conventional Hydrogen Bond
A:ARG92:HH11 - TR4:O25	2.06515	Hydrogen Bond	Conventional Hydrogen Bond
TR4:H65 - A:PHE97:O	1.8968	Hydrogen Bond	Conventional Hydrogen Bond
TR4:H73 - A:ILE175:O	2.63965	Hydrogen Bond	Carbon Hydrogen Bond
A:PHE97 - TR4	5.21933	Hydrophobic	Pi-Pi T-shaped
TR4 - A:PHE97	5.00551	Hydrophobic	Pi-Pi T-shaped
A:ALA89 - TR4:C30	4.40196	Hydrophobic	Alkyl
A:HIS46 - TR4:C30	5.08122	Hydrophobic	Pi-Alkyl
TR4 - A:ARG92	4.5201	Hydrophobic	Pi-Alkyl
TR4 - A:ARG92	4.30607	Hydrophobic	Pi-Alkyl

Note: The laboratory code of compound 13 is TR4

- **S5. Key interactions between compound 13 and the subunit 2 of DNA gyrase**

***S. aureus* GyrA-Compound 13 (TR4) atoms (Subunit2)**	**Distance**	**Category**	**Types**
B:SER85:HG - TR4:O25	2.17997	Hydrogen Bond	Conventional Hydrogen Bond
B:ARG92:HH11 - TR4:O28	1.76771	Hydrogen Bond	Conventional Hydrogen Bond
B:SER98:HG - TR4:O28	2.52034	Hydrogen Bond	Conventional Hydrogen Bond
B:LYS43:HE1 - TR4:N36	2.58103	Hydrogen Bond	Carbon Hydrogen Bond
B:HIS46:HE1 - TR4:N36	2.69043	Hydrogen Bond	Carbon Hydrogen Bond
TR4:H48 - B:SER173:O	2.85213	Hydrogen Bond	Carbon Hydrogen Bond
TR4:H73 - B:SER112:O	2.96937	Hydrogen Bond	Carbon Hydrogen Bond
TR4:H75 - B:SER112:O	2.9033	Hydrogen Bond	Carbon Hydrogen Bond
TR4:H76 - B:VAL268:O	3.05128	Hydrogen Bond	Carbon Hydrogen Bond
TR4:H78 - B:VAL268:O	2.83848	Hydrogen Bond	Carbon Hydrogen Bond
B:LYS43:NZ - TR4	3.79377	Electrostatic	Pi-Cation
B:LYS43:NZ - TR4	4.07598	Electrostatic	Pi-Cation
B:LYS43:HZ1 - TR4	3.12671	Hydrogen Bond;Electrostatic	Pi-Cation;Pi-Donor Hydrogen Bond

Note: The laboratory code of compound 13 is TR4

S6. LC-MS method for purity determination

LC-MS analyses were performed on a Waters Alliance 2695 system, eluting in gradient with according to the condition reported herein:

1) 10 minutes method: flow 0.5 mL/min

Solvents: A) water + 0.1 % formic acid

B) acetonitrile + 0.1% formic acid

Time (min)	0	2	5	6	7.5	9	10
A (%)	95	95	50	50	5	95	95
B (%)	5	5	50	50	95	5	5

2) 5 minutes method: flow 1 mL/min

Solvents: A) water + 0.1 % formic acid

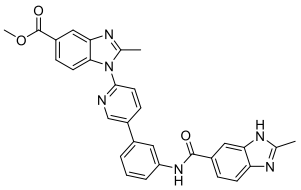
B) acetonitrile + 0.1% formic acid

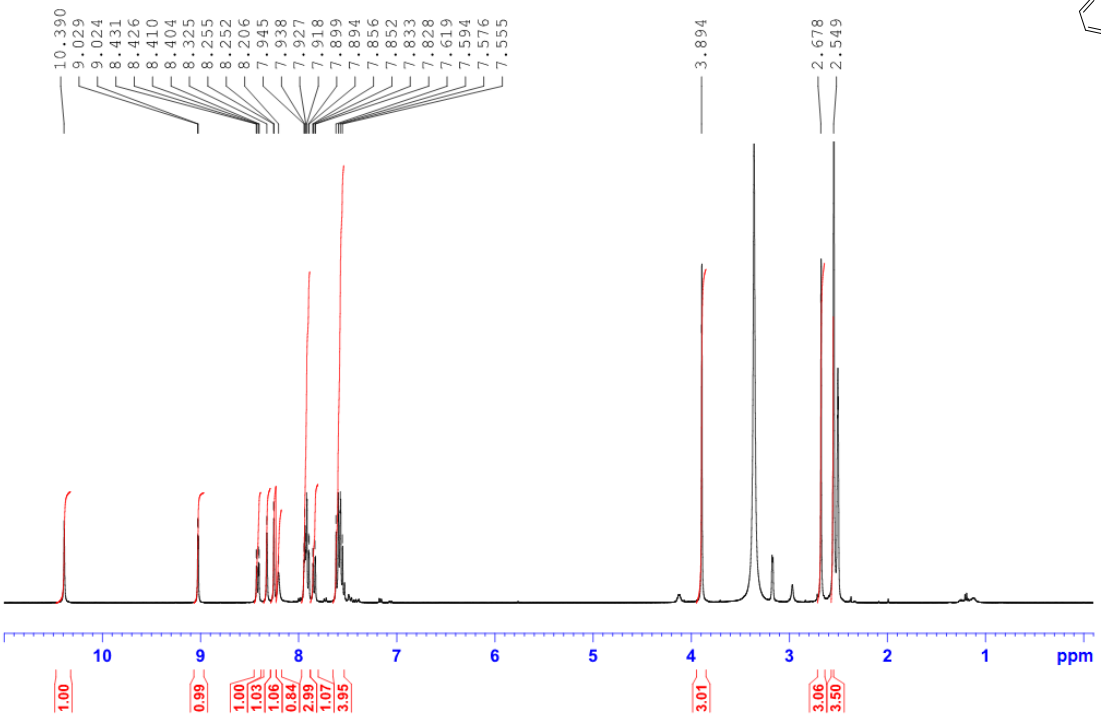
Time (min)	0	3	3.5	4.5	5
A (%)	95	10	5	5	95
B (%)	5	90	95	95	5

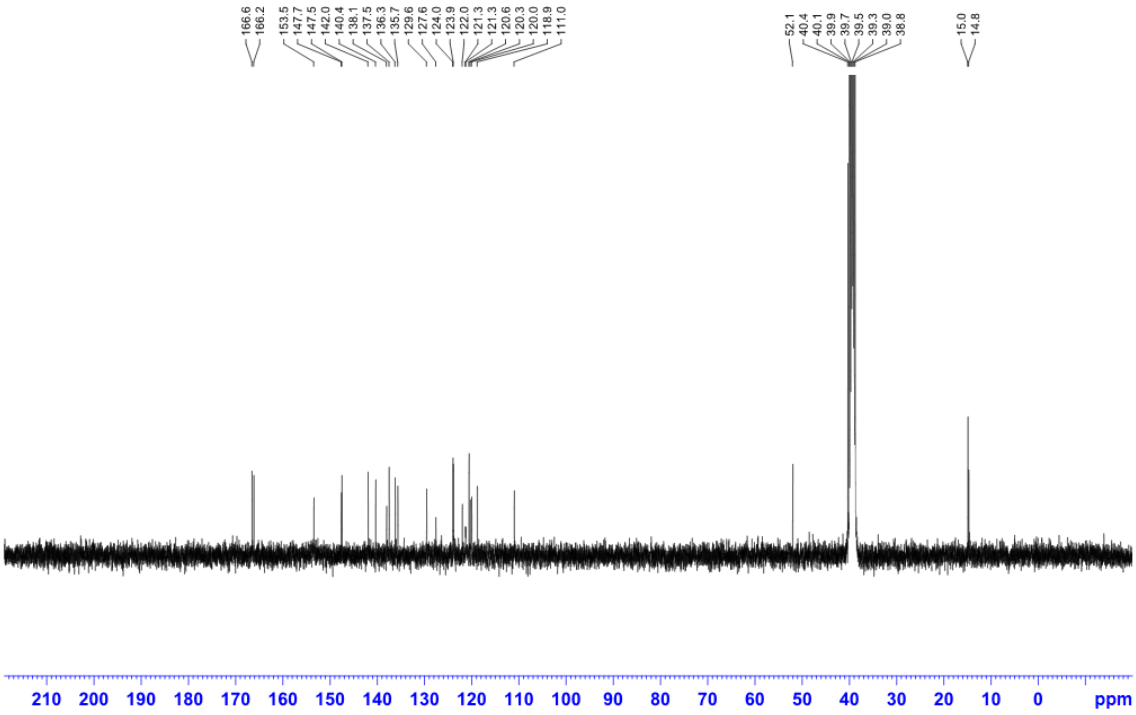
The analyses were performed on a Monolithic C18 50 X 4.60 mm column by Phenomenex. UV detection was performed on a Diode Array Detector. Mass spectra were registered in both ESI+ and ESI- mode.

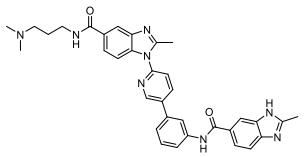
S7. NMR spectra for key compounds

Compound 7

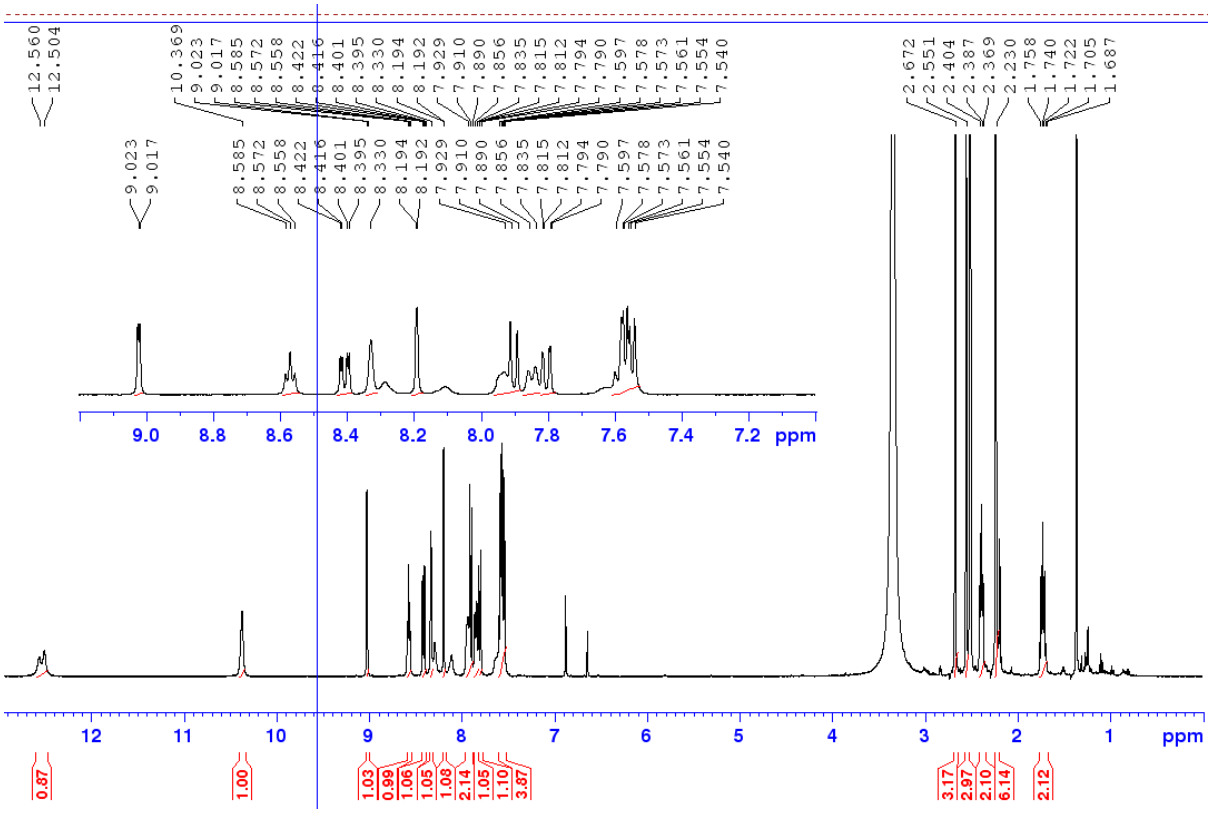








Compound 13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8.194
8.192
7.929
7.910
7.890
7.856
7.835
7.815
7.812
7.794
7.790
7.597
7.578
7.573
7.561
7.554
7.540
2.672
2.551
2.404
2.387
2.369
2.230
1.758
1.740
1.722
1.705
1.687
9.0
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
ppm
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.87
1.00
1.03
0.99
1.06
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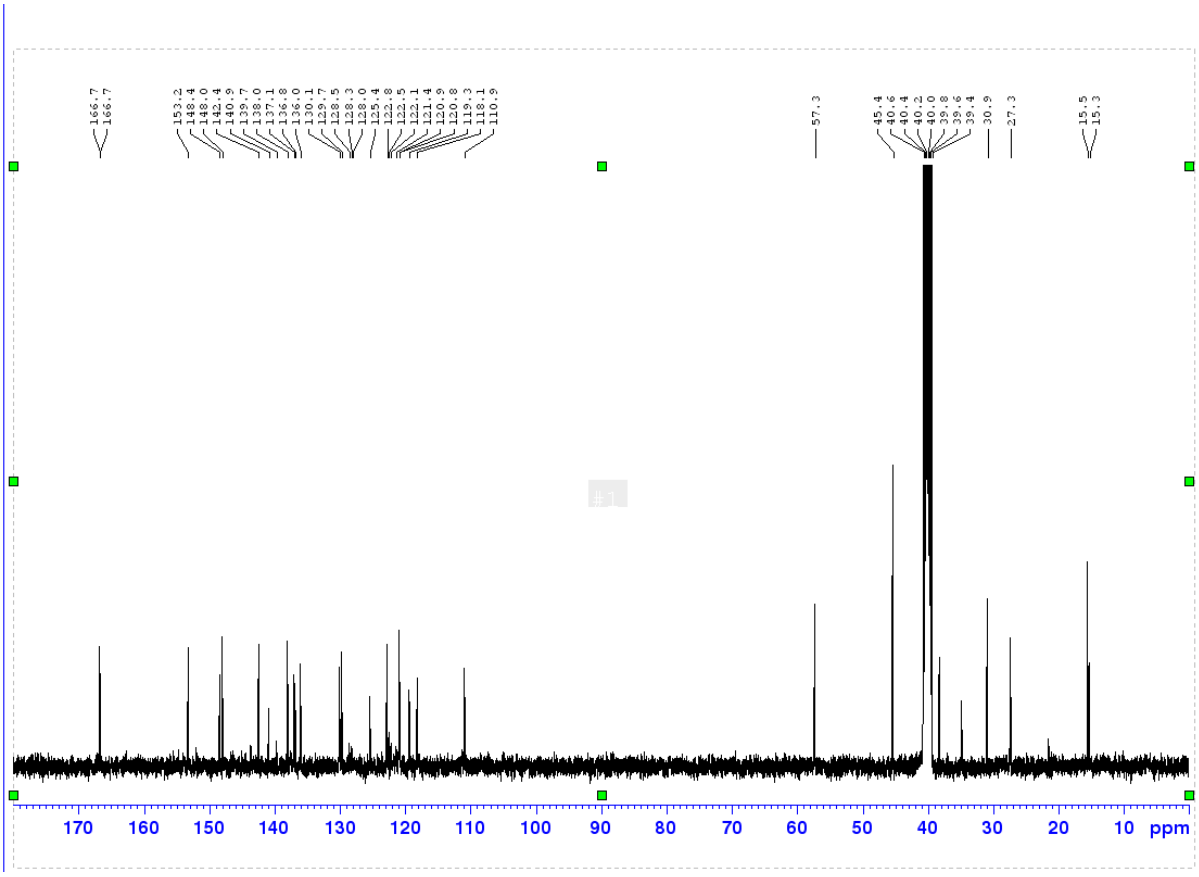
3.17
2.97
2.10
6.14
2.12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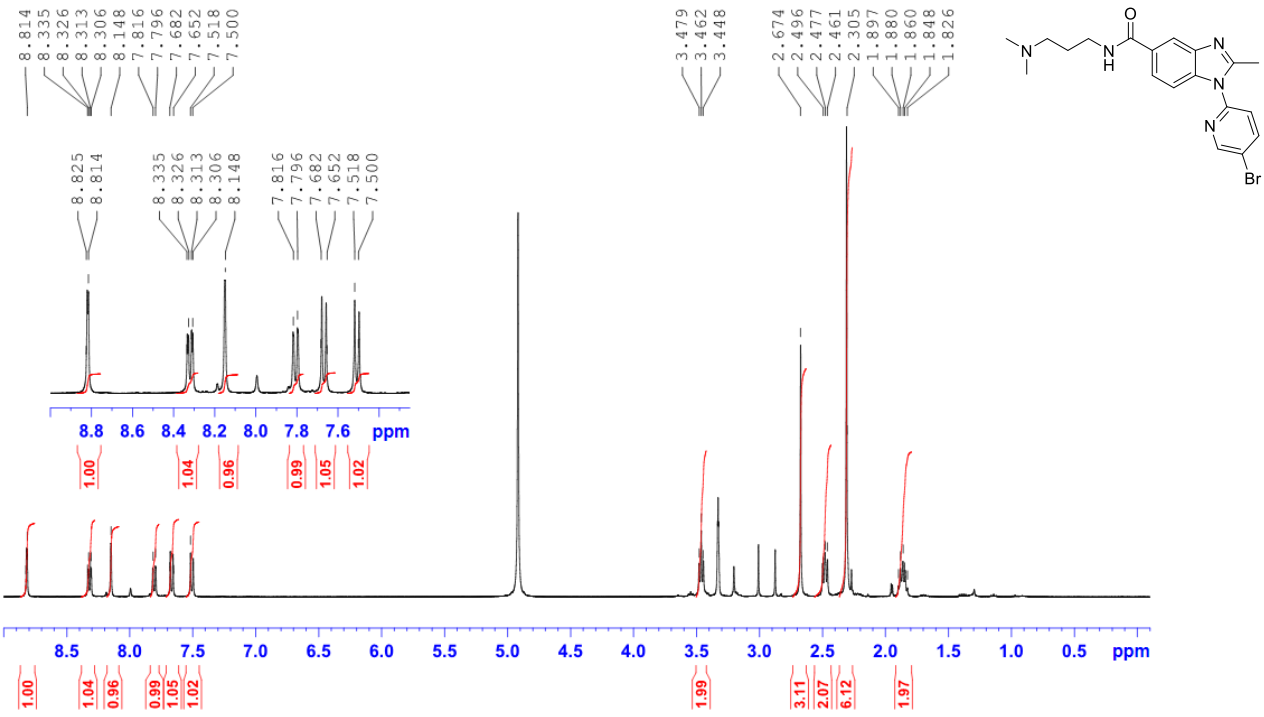
148.4
148.0
142.4
140.9
139.7
138.0
137.1
136.8
136.0
130.1
129.7
128.5
128.3
128.0
125.4
122.8
122.5
122.1
121.4
120.9
120.8
119.3
118.1
110.9
57.3
45.4
40.6
40.4
40.2
40.0
39.8
39.6
39.4
30.9
27.3
15.5
15.3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Compound 18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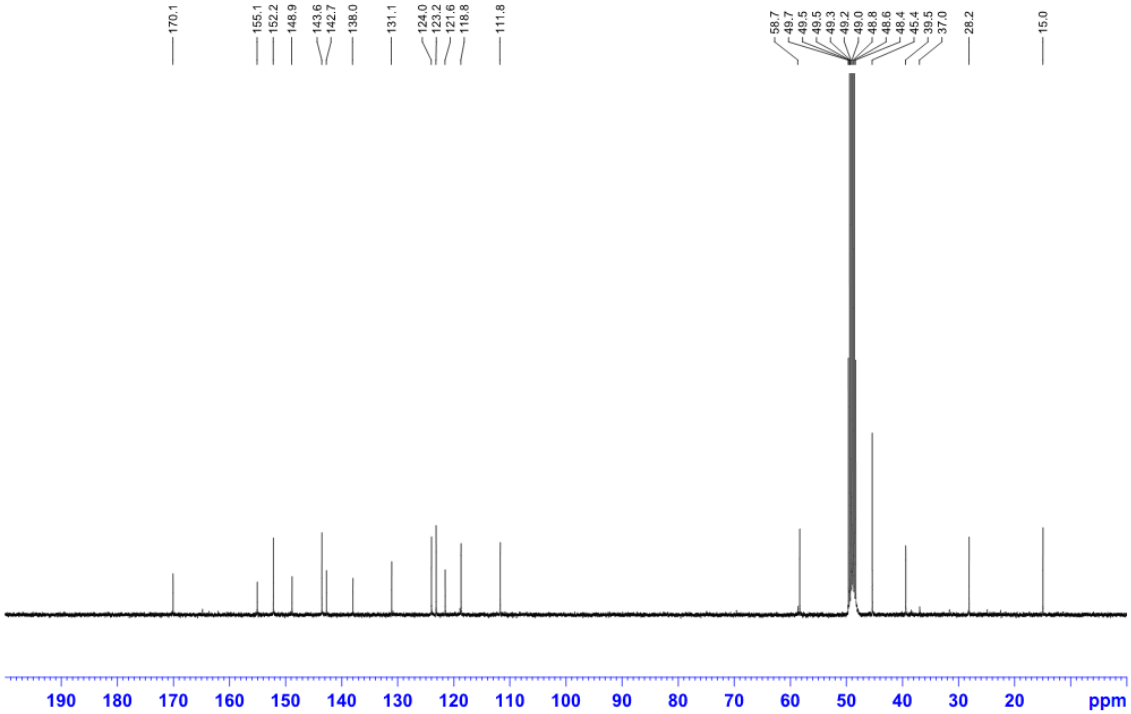
8.326
8.313
8.306
8.148
7.816
7.796
7.682
7.652
7.518
7.500
3.479
3.462
3.448
2.674
2.496
2.477
2.461
2.305
1.897
1.880
1.860
1.848
1.826
N
N
H
O
N
N
N
Br
8.8 8.6 8.4 8.2 8.0 7.8 7.6 ppm
1.00
1.04
0.96
0.99
1.05
1.02
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.04
0.96
0.99
1.05
1.02
1.99
3.11
2.07
6.12
1.97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152.2
148.9
143.6
142.7
138.0
131.1
124.0
123.2
121.6
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58.7
49.7
49.5
49.5
49.3
49.2
49.0
48.8
48.6
48.4
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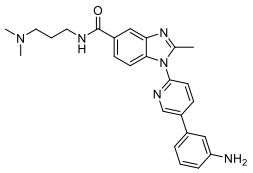
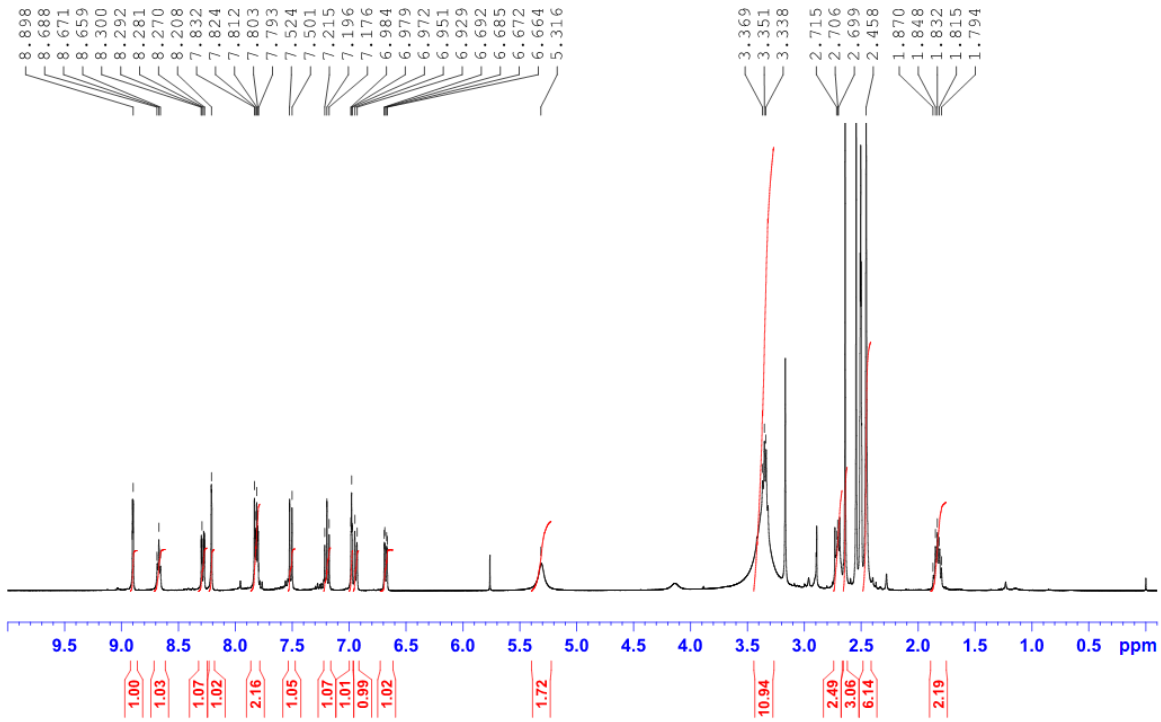
39.5
37.0
28.2
15.0
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

Compound 19


O
N
H
N
N
N
NH2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7.176
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6.972
6.951
6.929
6.692
6.685
6.672
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3.351
3.338
2.715
2.706
2.699
2.458
1.870
1.848
1.832
1.815
1.794
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.03
1.07
1.02
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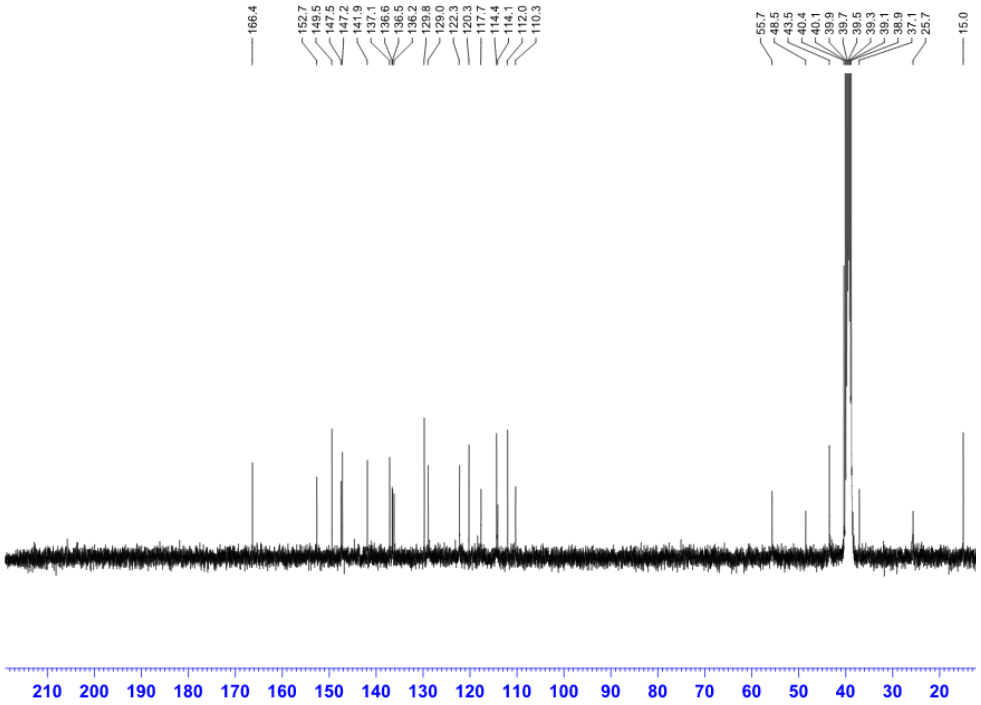
1.72
10.94
2.49
3.06
6.14
2.19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147.5
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141.9
137.1
136.6
136.5
136.2
129.8
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120.3
117.7
114.4
114.1
112.0
110.3
55.7
48.5
43.5
40.4
40.1
39.9
39.7
39.5
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39.1
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37.1
25.7
15.0
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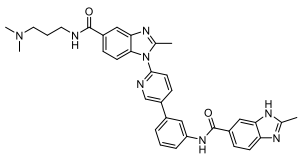
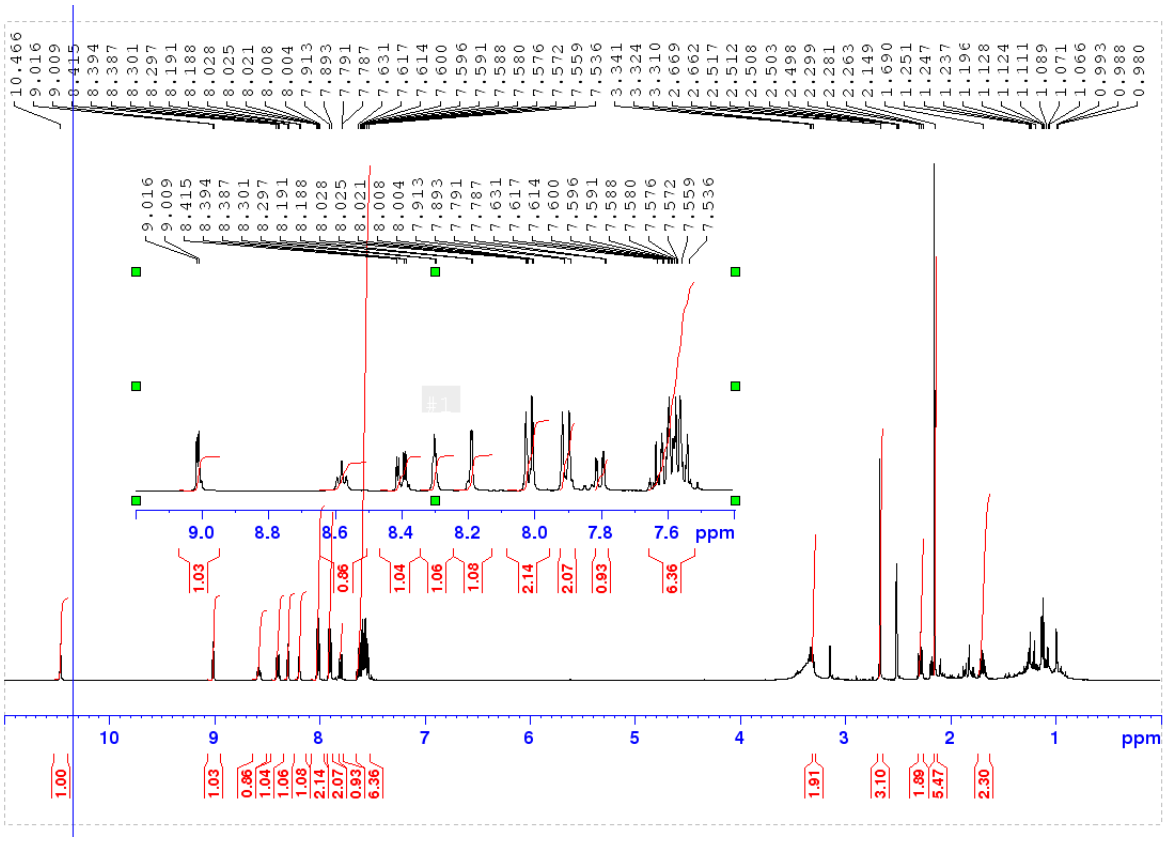


Compound 21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8.188
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8.021
8.008
8.004
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7.893
7.791
7.787
7.631
7.617
7.614
7.600
7.596
7.591
7.588
7.580
7.576
7.572
7.559
7.536
3.341
3.324
3.310
2.669
2.662
2.517
2.512
2.508
2.503
2.498
2.299
2.281
2.263
2.149
1.690
1.251
1.247
1.237
1.196
1.128
1.124
1.111
1.089
1.071
1.066
0.993
0.988
0.980
9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 ppm
1.03 0.86 1.04 1.06 1.08 2.14 2.07 0.93 6.36
10 9 8 7 6 5 4 3 2 1 ppm
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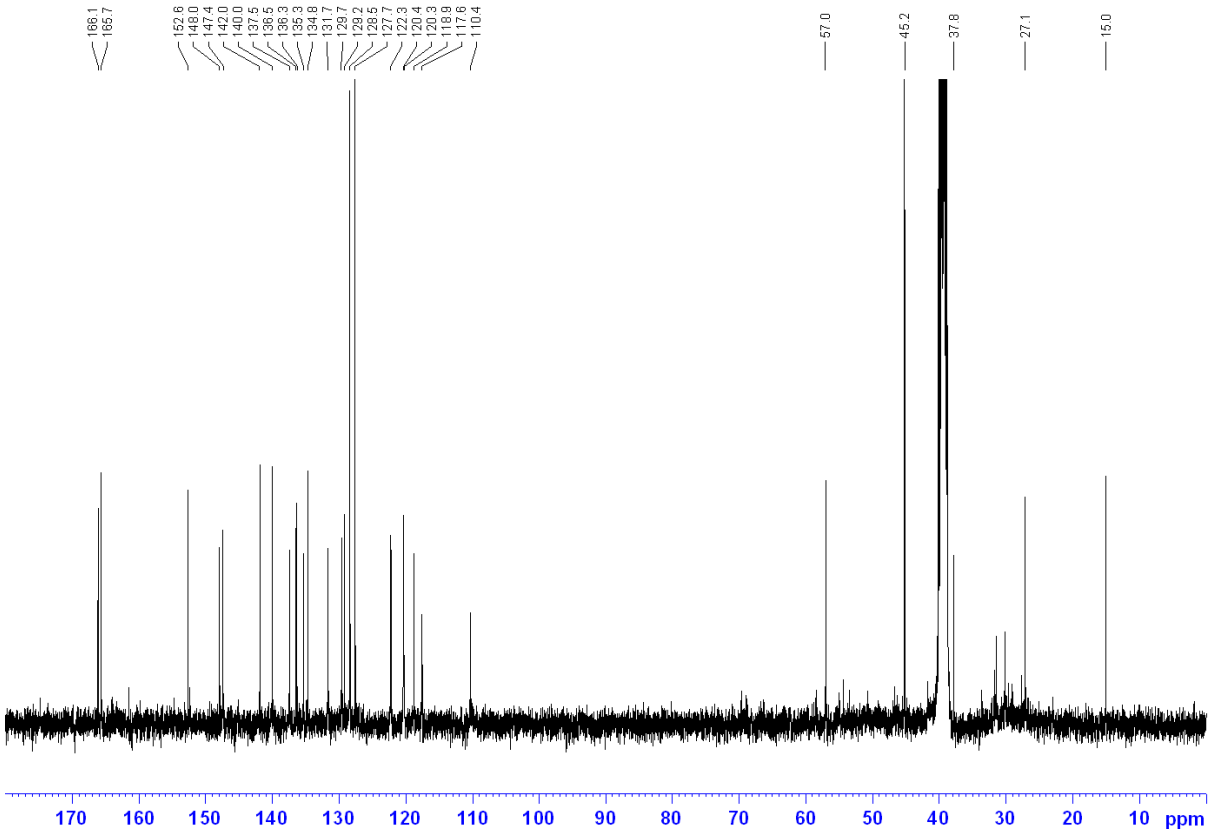
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147.4
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37.8
27.1
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30
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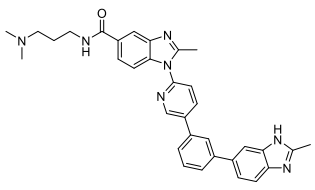
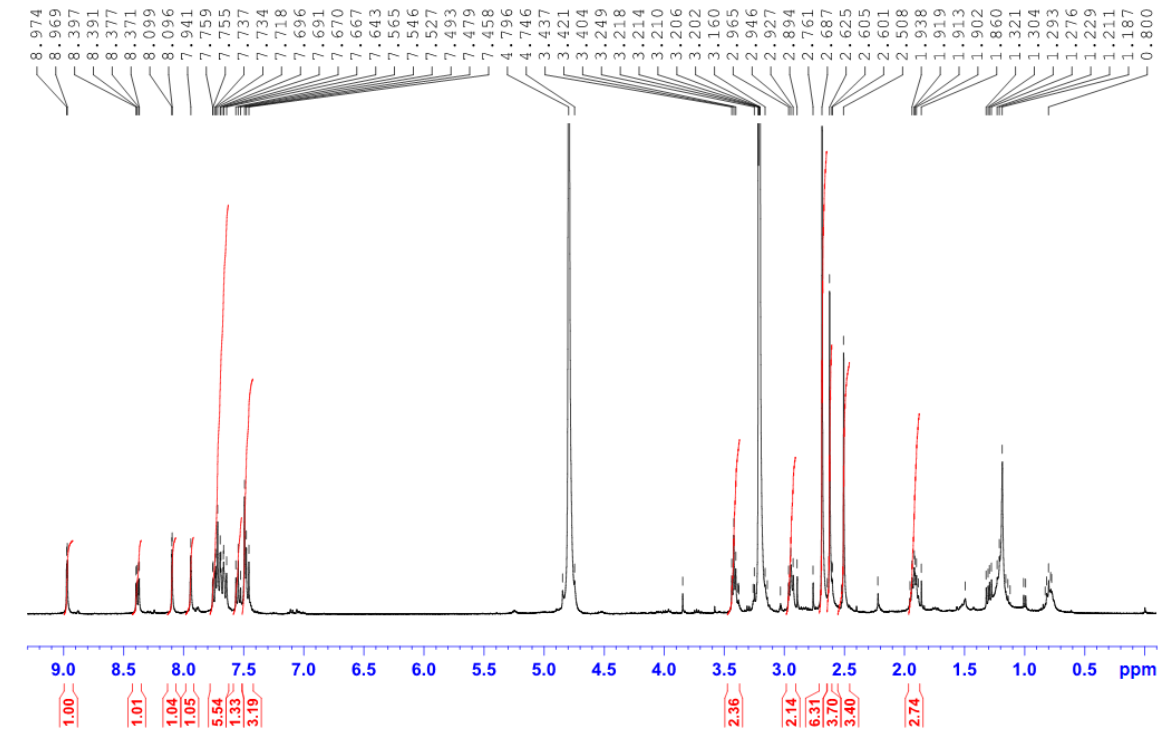
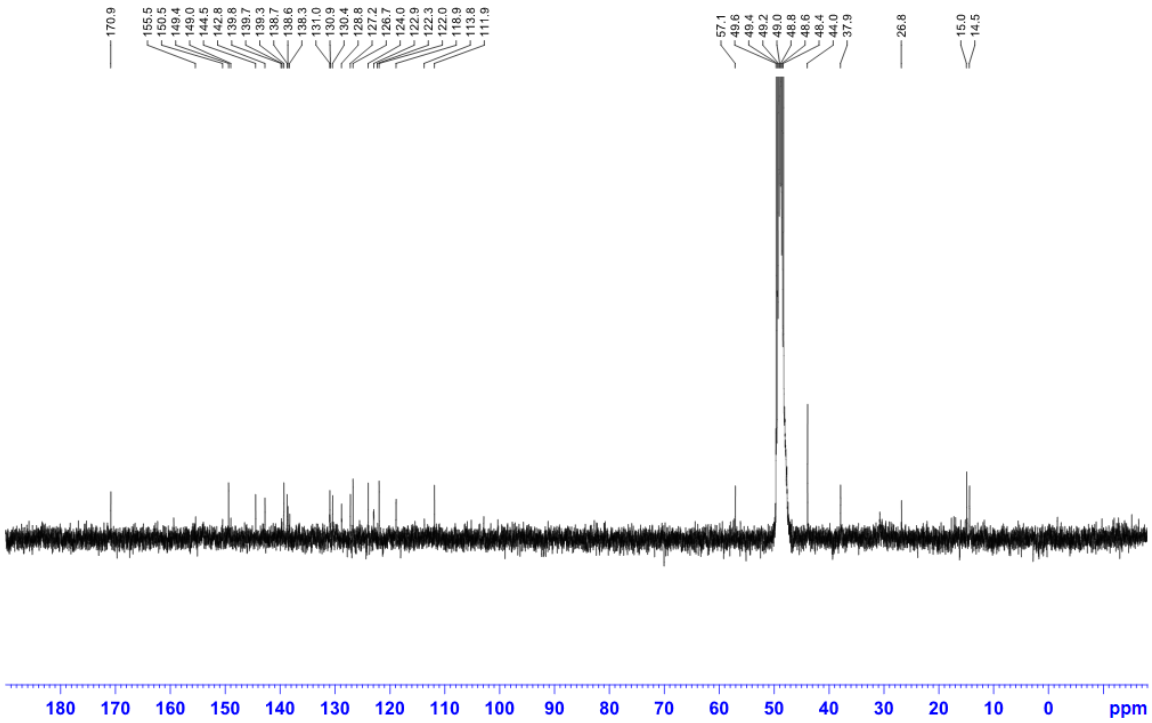


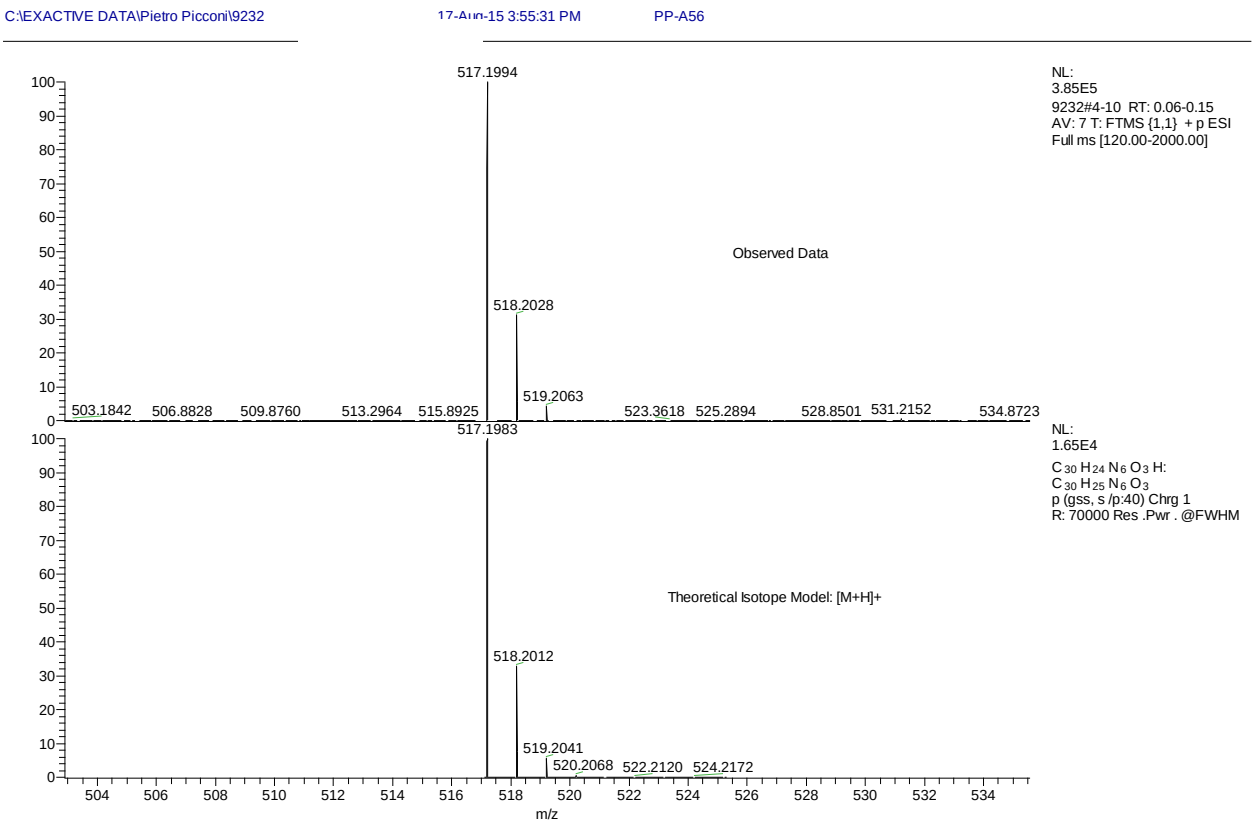
Compound 24



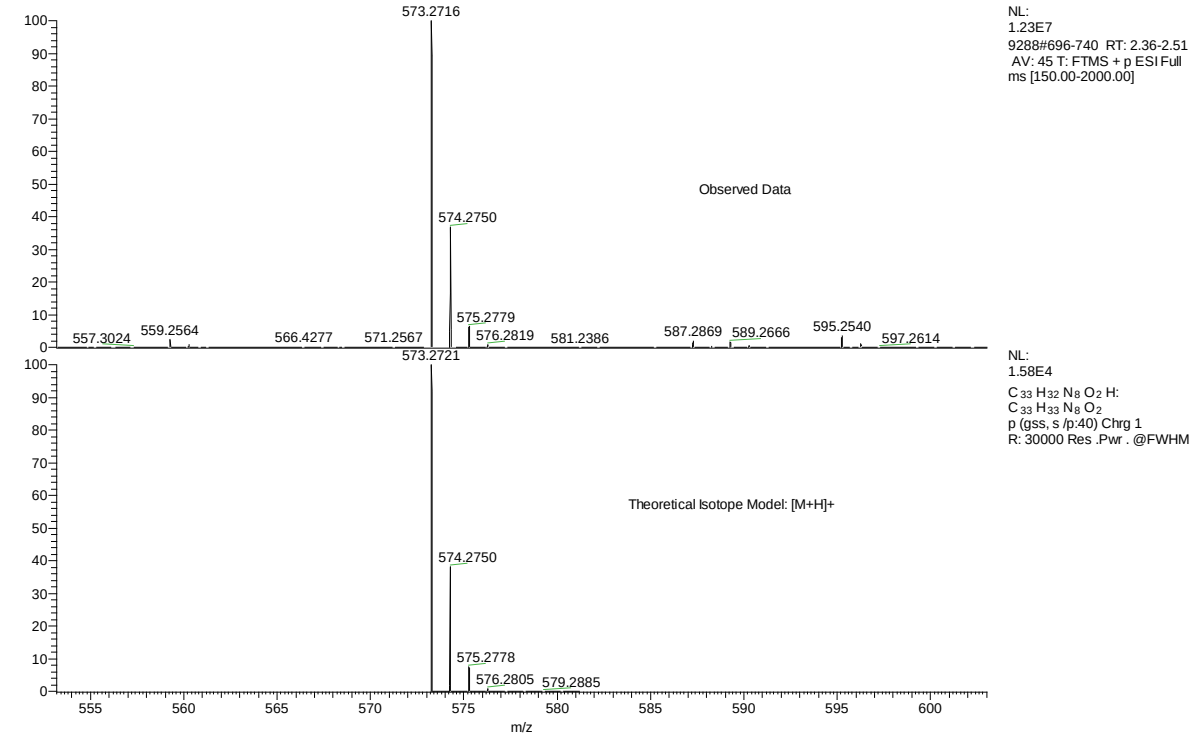


S8.HRMS analysis for target compounds.

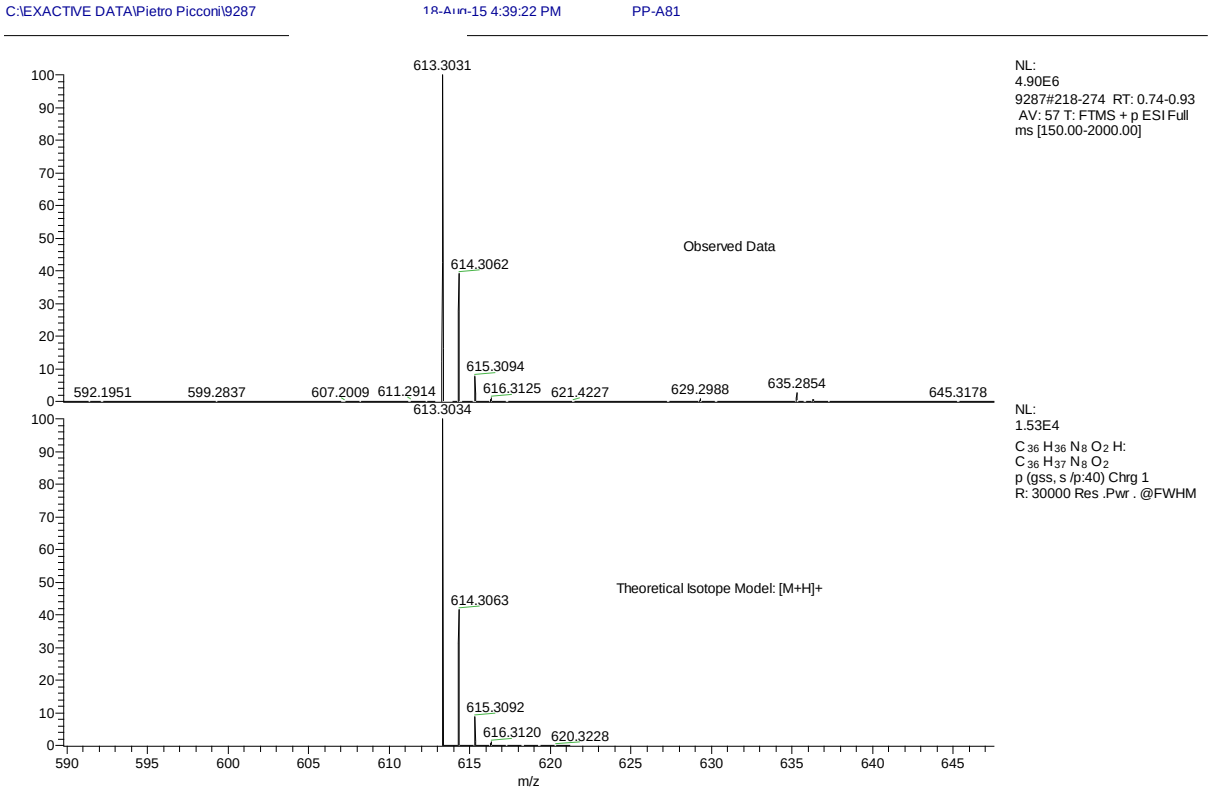
Compound 7



Compound 8



Compound 9



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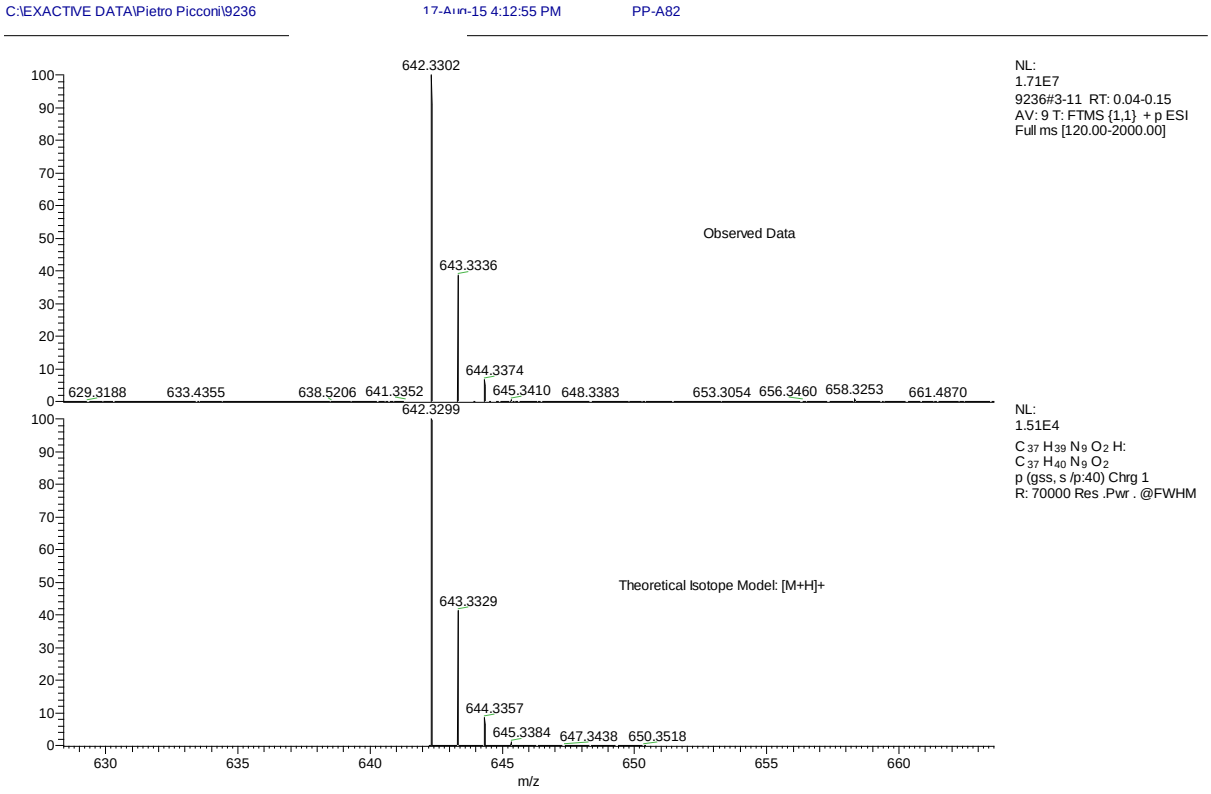

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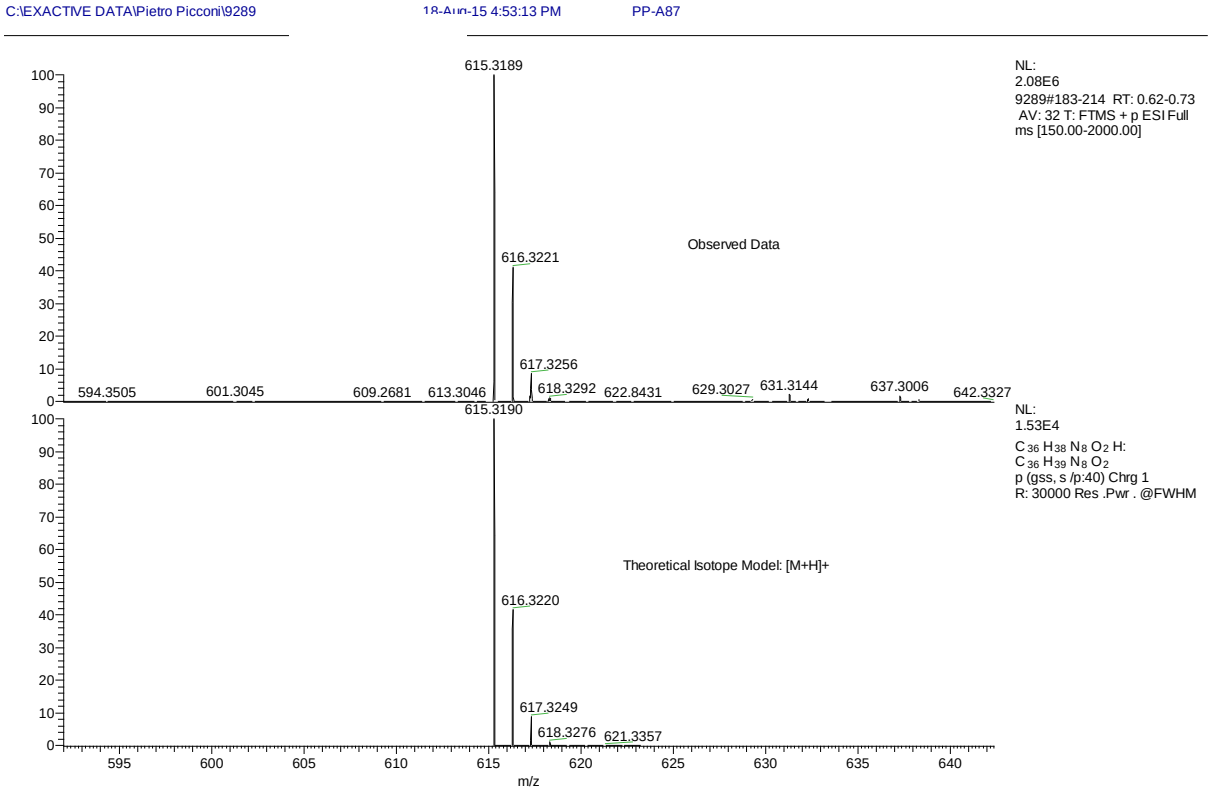

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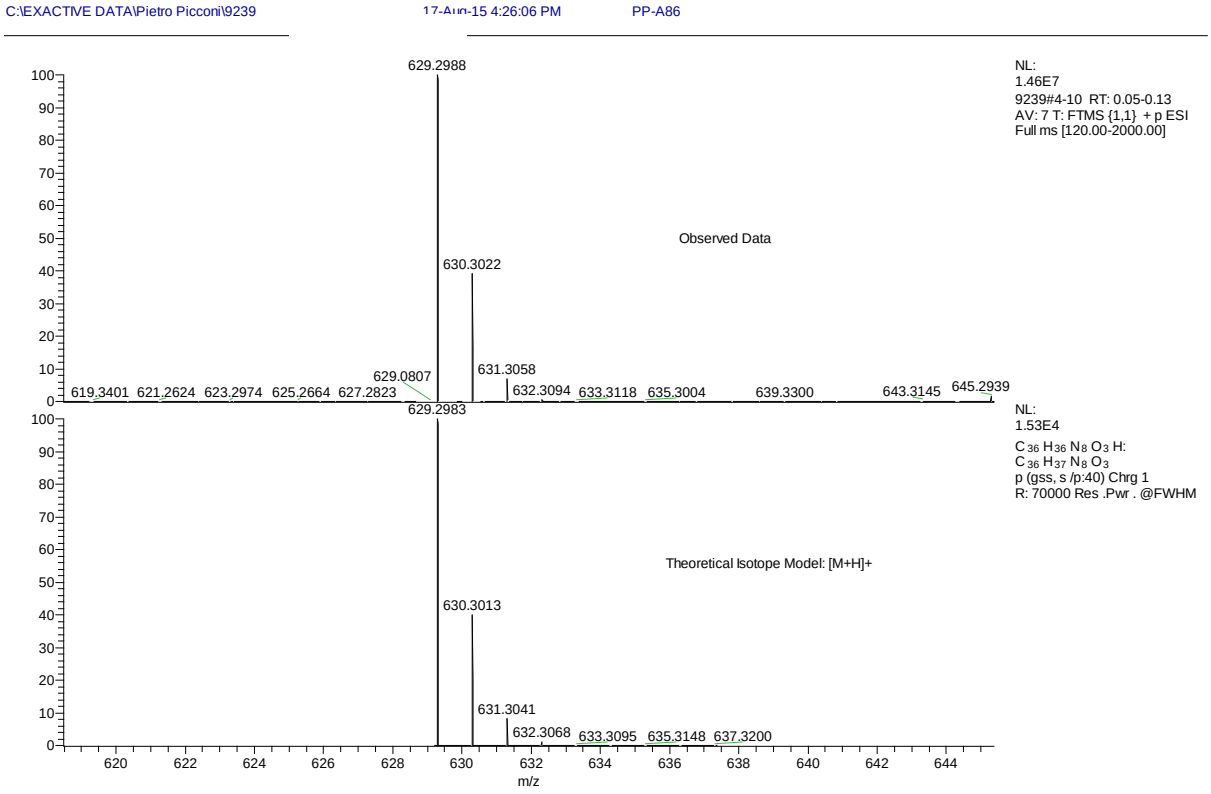
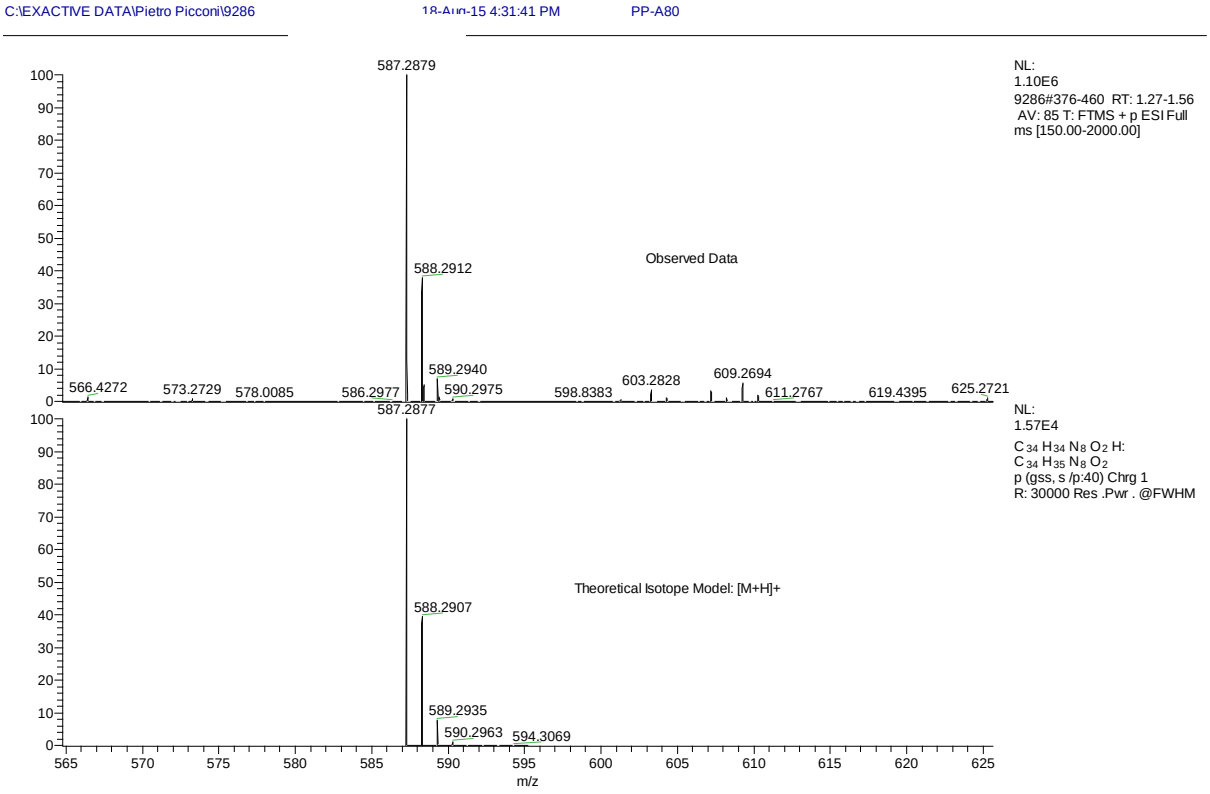
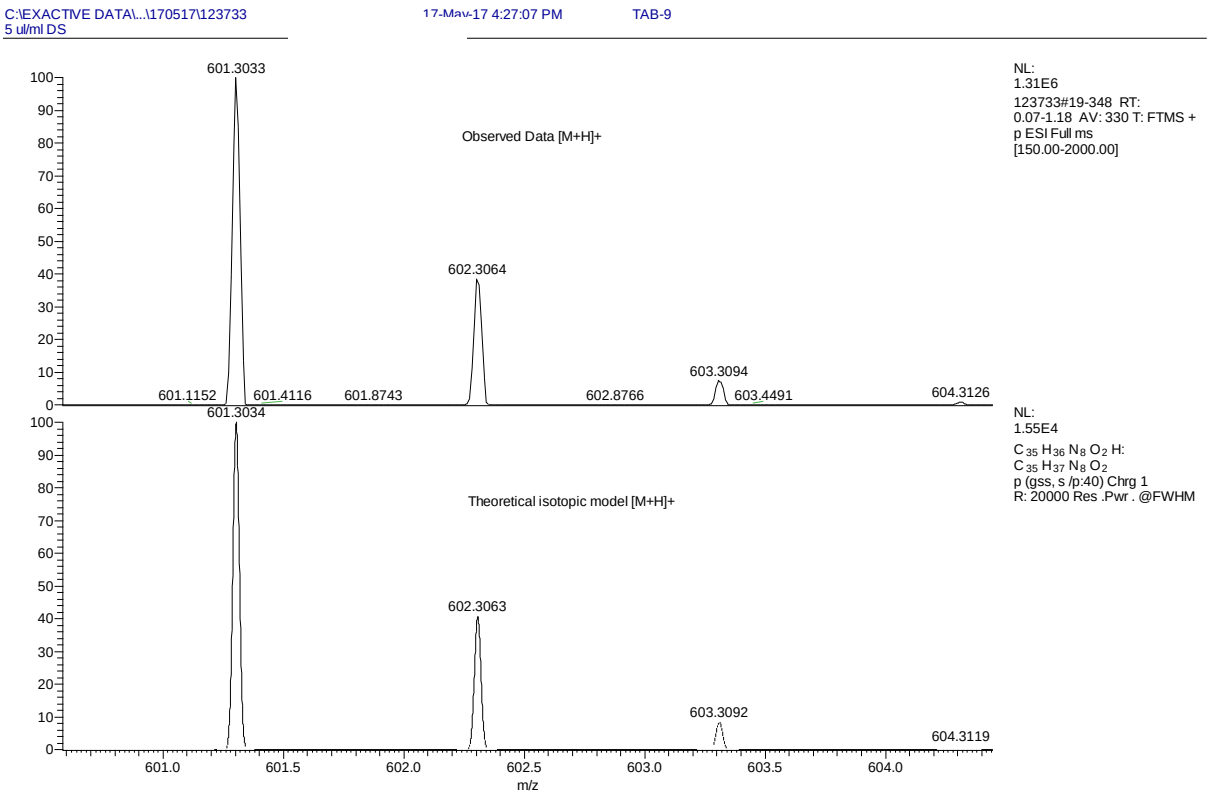


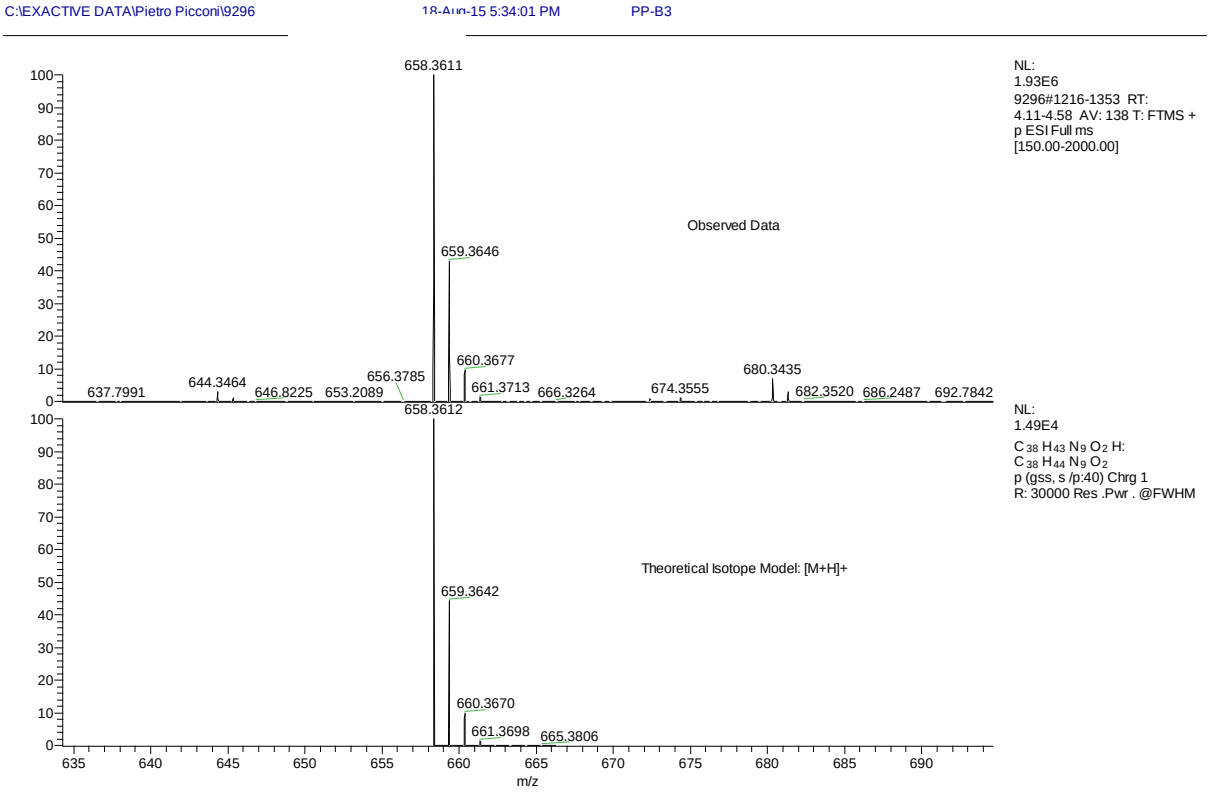
Compound 13



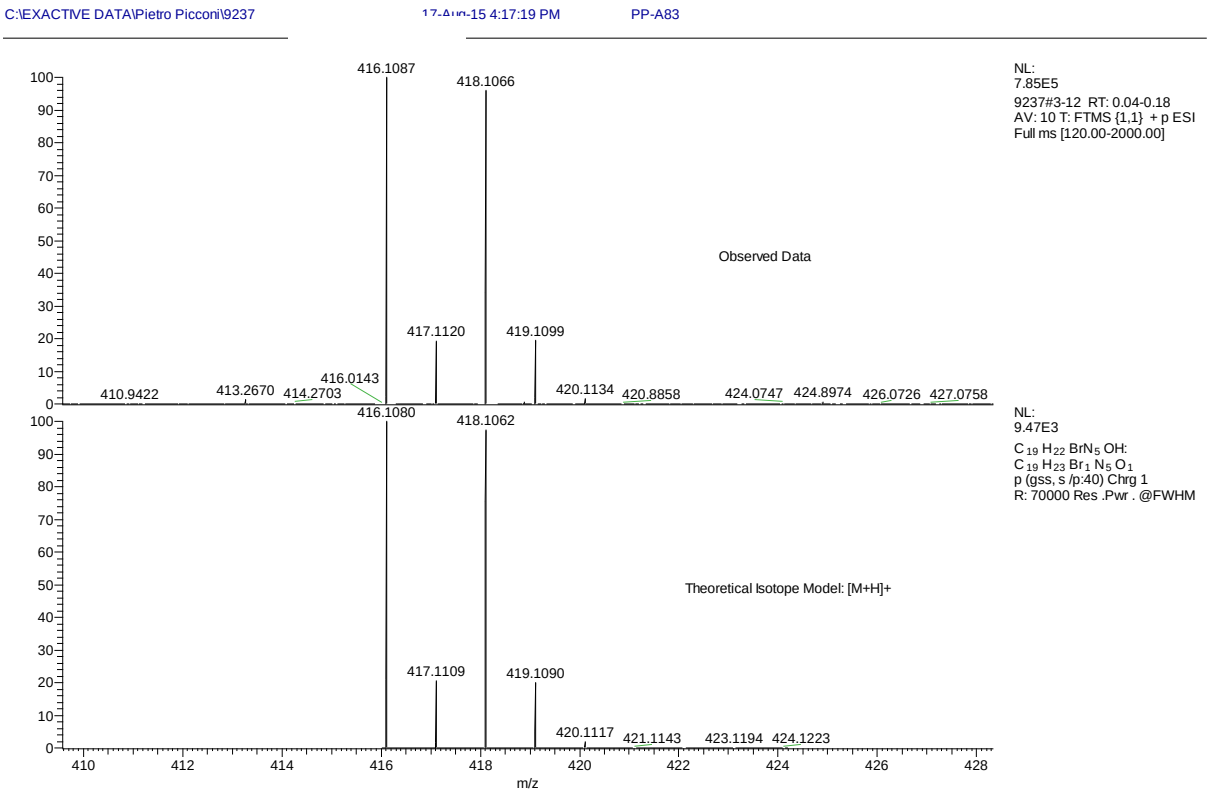
Compound 14



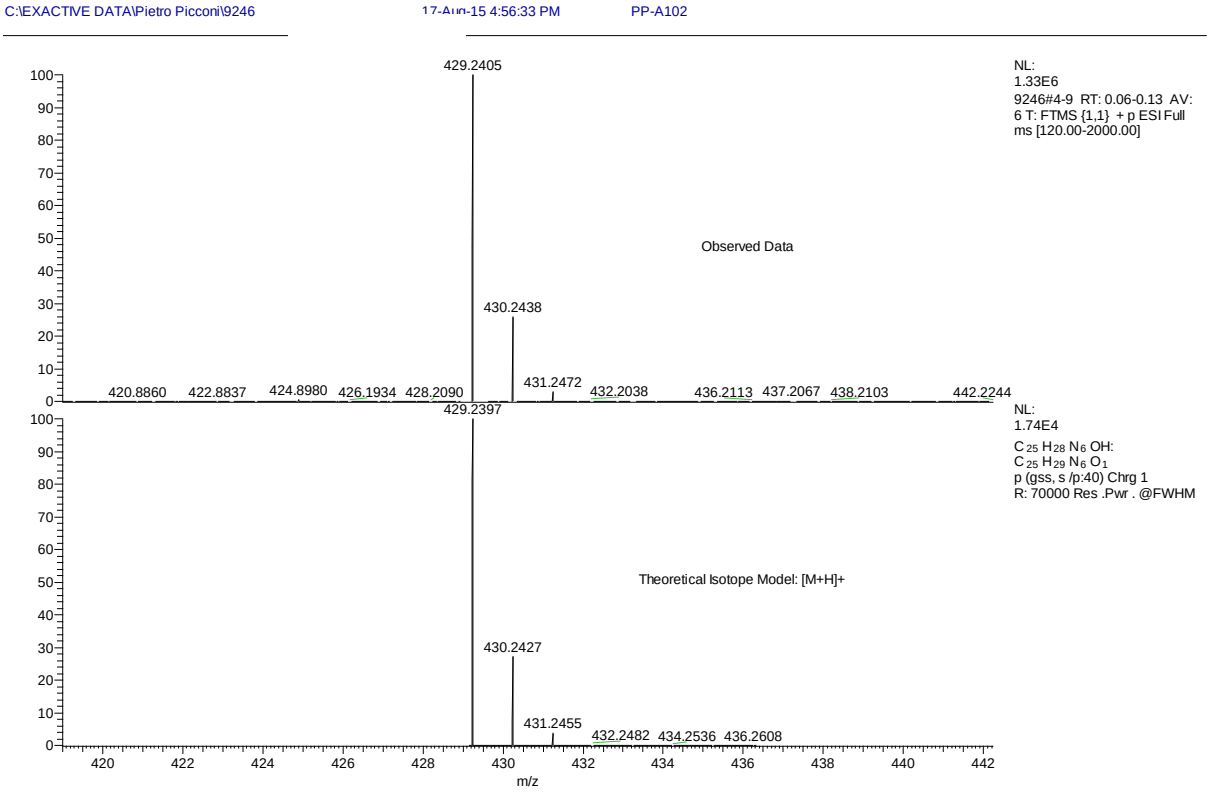
Compound 17



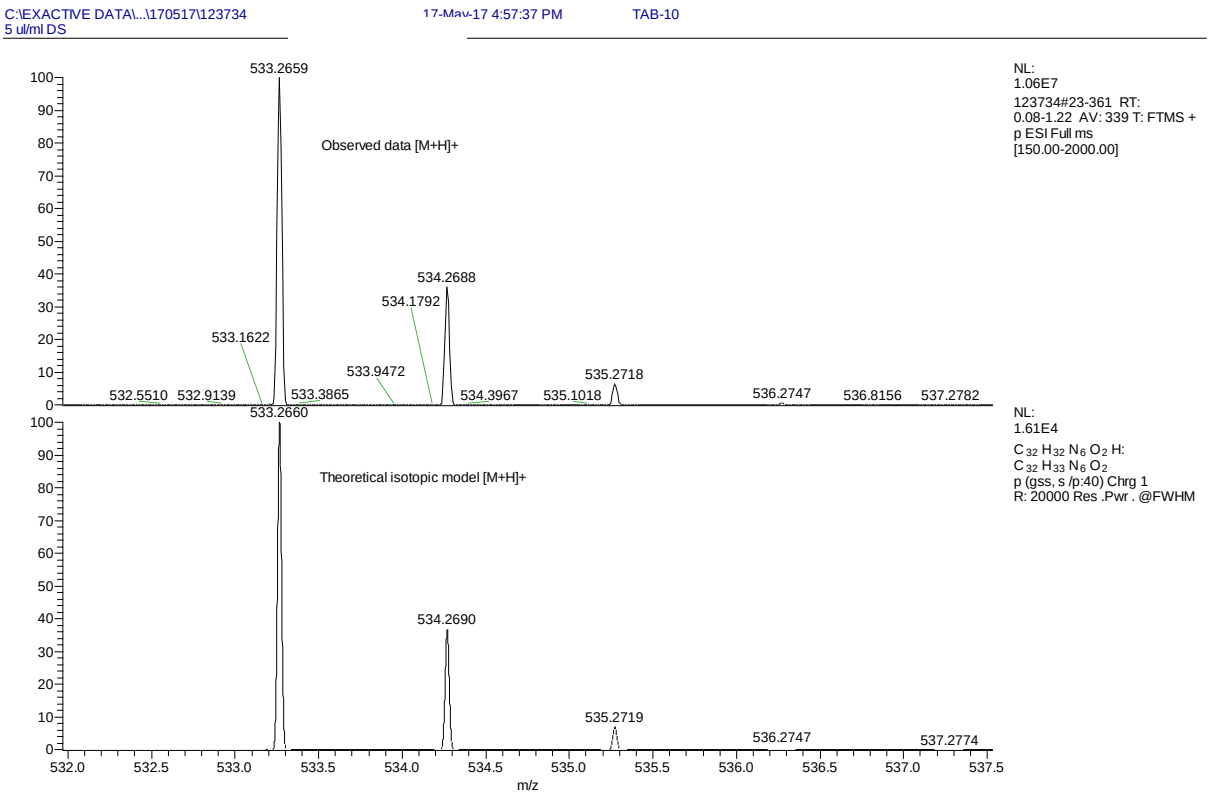
Compound 18



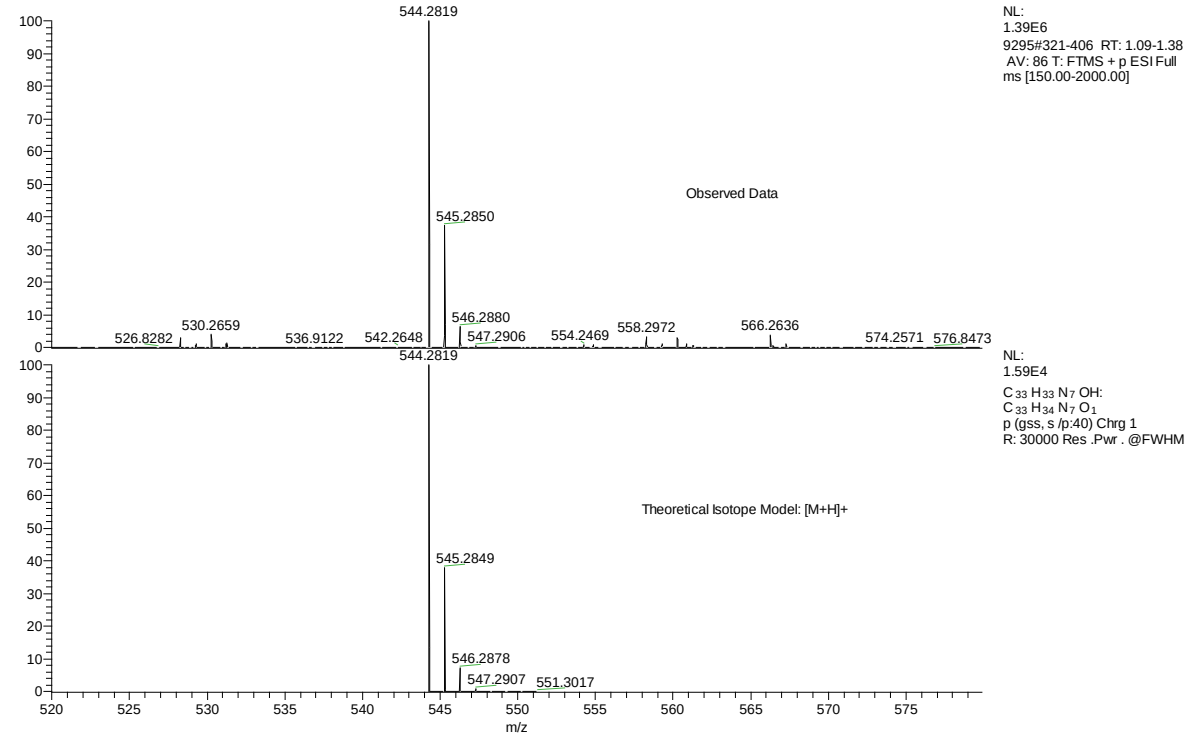
Compound 19



Compound 21



Compound 24


544.2819
NL:
1.39E6
9295#321-406 RT: 1.09-1.38
AV: 86 T: FTMS + p ESI Full
ms [150.00-2000.00]
Observed Data
545.2850
546.2880
547.2906
526.8282
530.2659
536.9122
542.2648
554.2469
558.2972
566.2636
574.2571
576.8473
544.2819
NL:
1.59E4
C33 H33 N7 OH:
C33 H34 N7 O1
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
545.2849
546.2878
547.2907
551.3017
m/z