

Supporting Information

Symmetric 4,6-Dialkylamine-5-Nitro/Aminopyrimidines: Theoretical Explanation of Why Aminolysis of Alkoxy Groups Is Favoured over That of Chlorine in Nitro-Activated Pyrimidines.

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1. DFT calculations

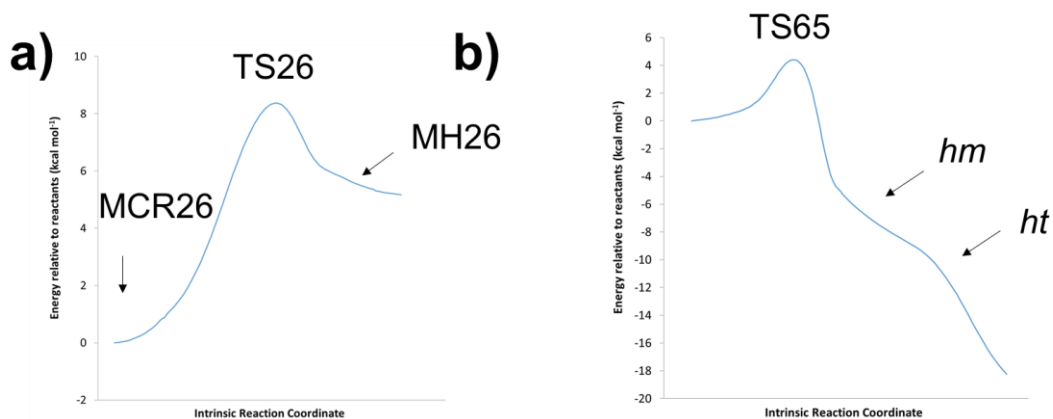


Figure S1. Computed IRC profiles for reactions from **2** to **6** (a) and **6** to **5** (b). Calculations were performed at the M06-2X/6-31G* level of theory including solvation effects (dichloromethane).

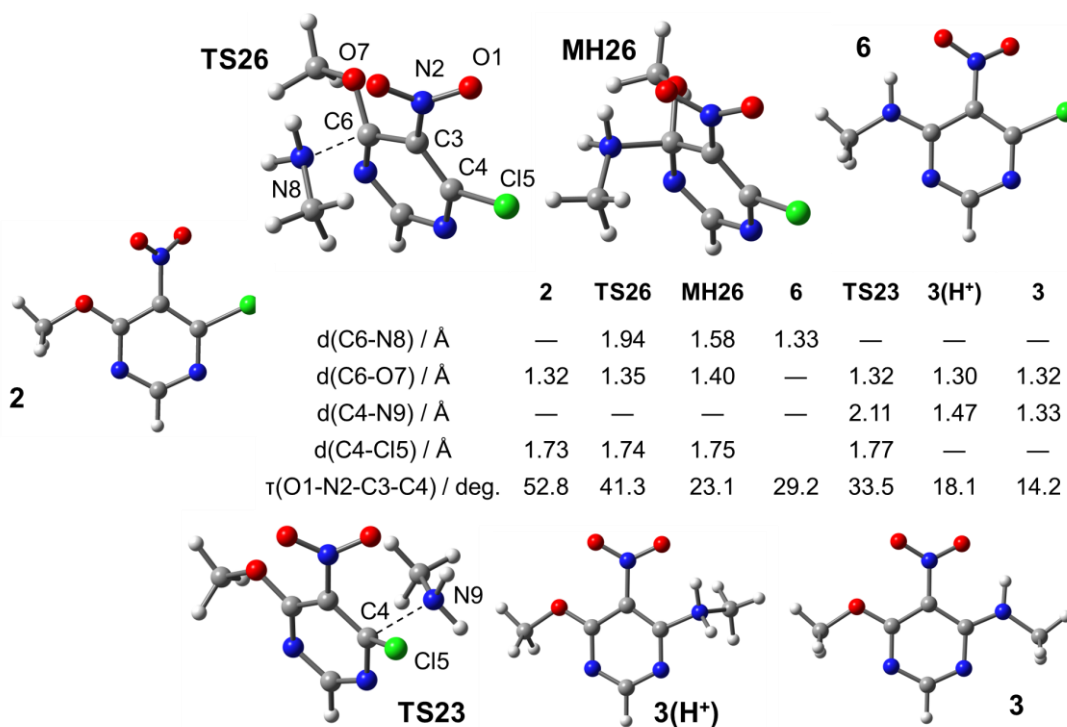
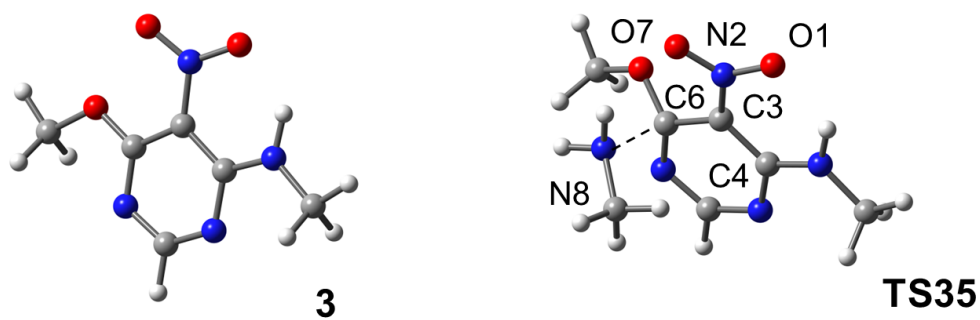


Figure S2. Molecular structure calculated for different species involved in reaction pathways 1 and 2 shown in reaction Scheme 3a. Calculations were performed at the M06-2X/6-31G* level of theory including solvation effects (dichloromethane).



	3	TS35	MH35	5
$d(\text{C6-N8}) / \text{\AA}$	—	1.94	1.57	1.33
$d(\text{C6-O7}) / \text{\AA}$	1.32	1.35	1.40	—
$\tau(\text{O1-N2-C3-C4}) / \text{deg.}$	14.1	15.7	2.57	0.00

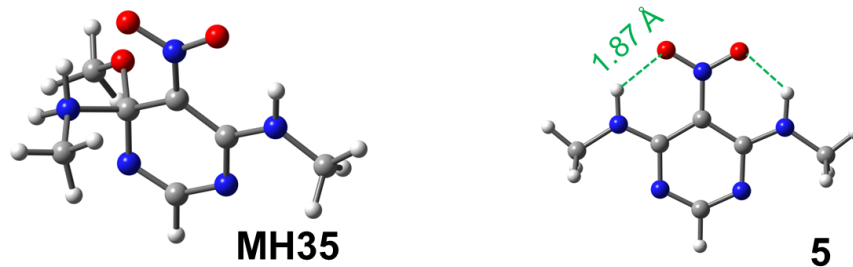
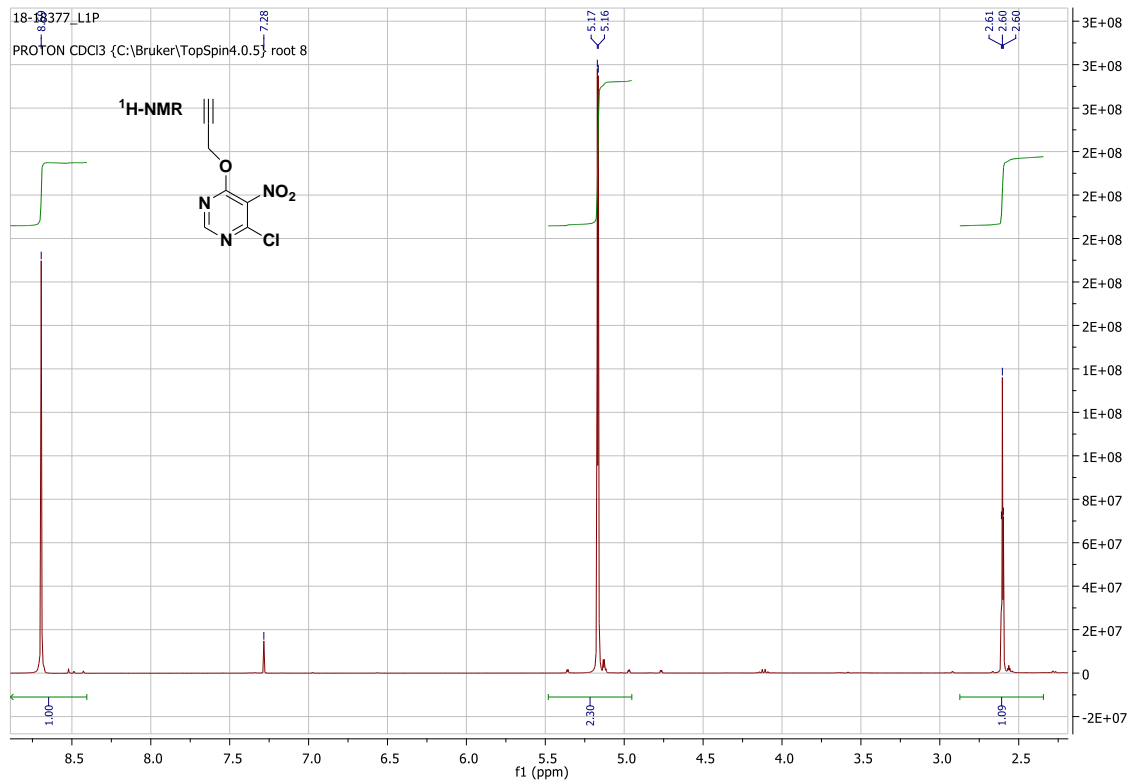
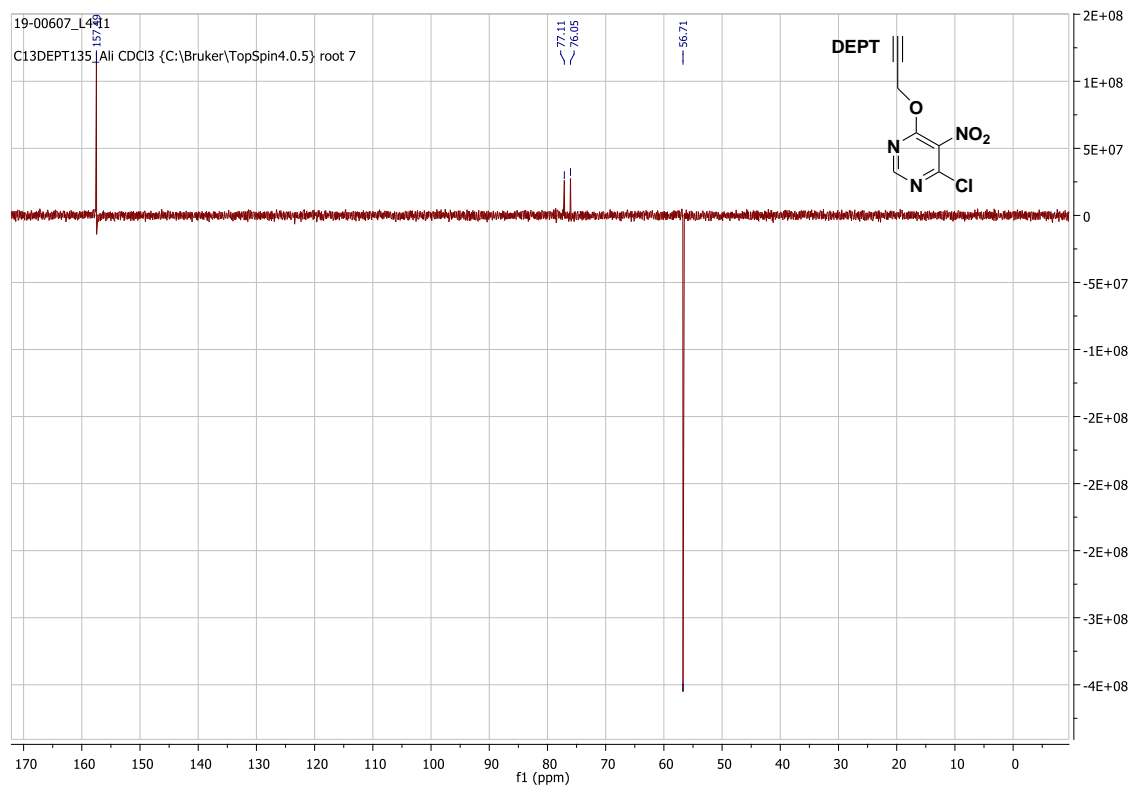
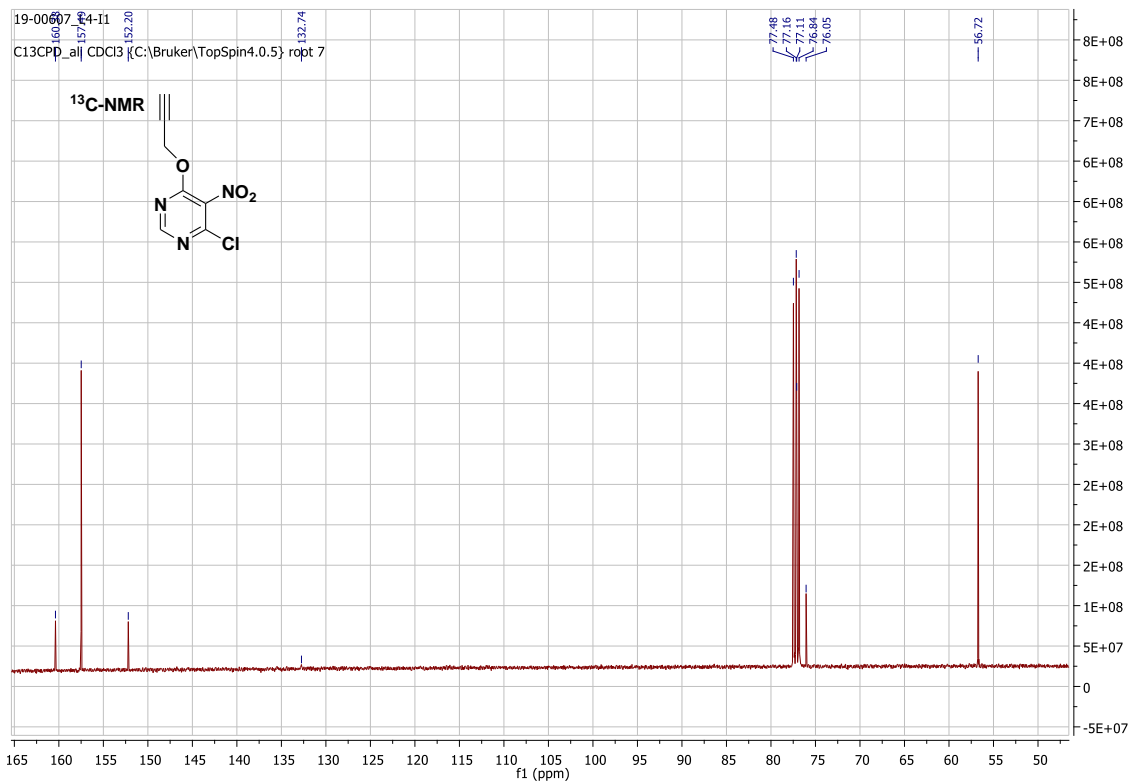


Figure S3. Molecular structure calculated for different species involved in reaction pathway 3 shown in reaction Scheme 3b. Calculations were performed at the M06-2X/6-31G* level of theory including solvation effects (dichloromethane).

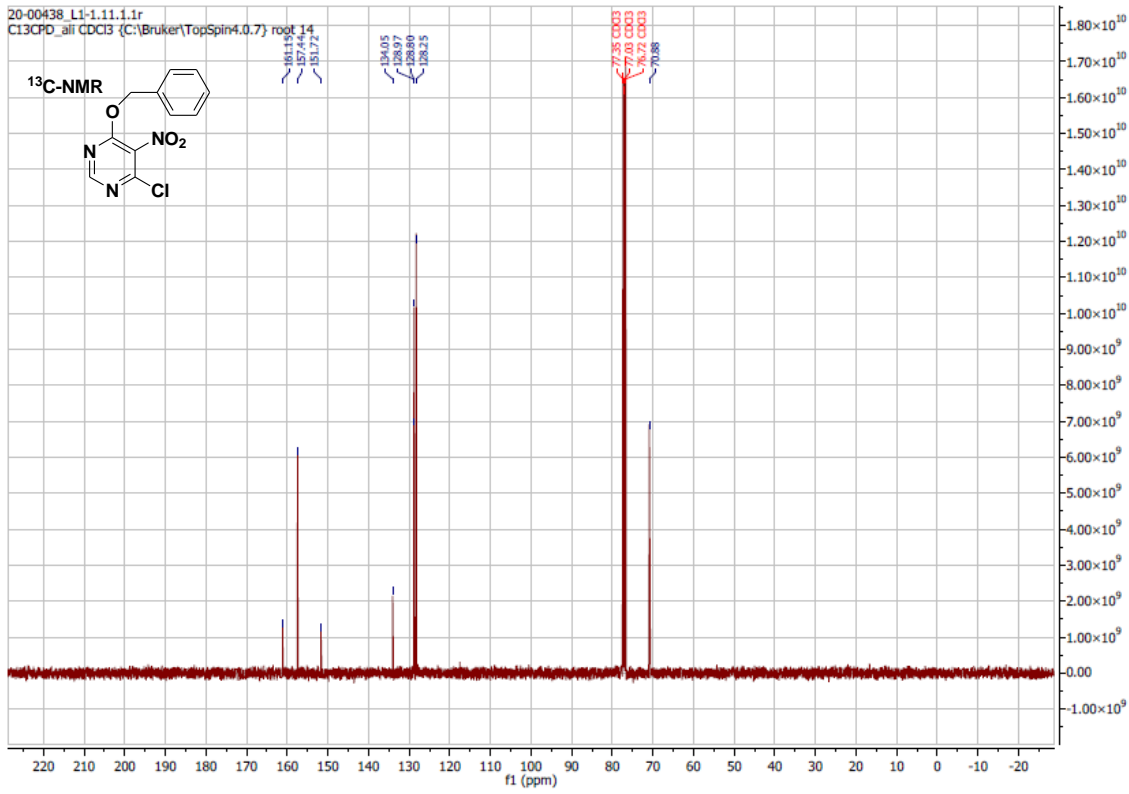
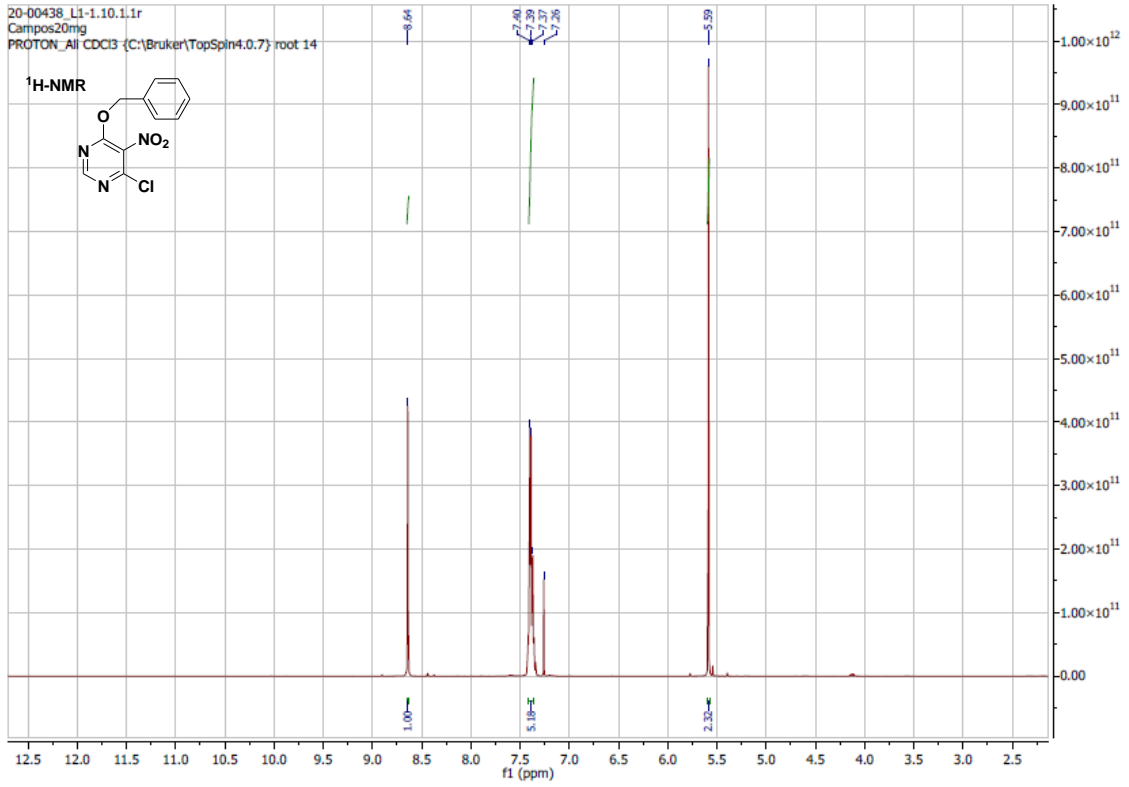
2. Synthesis

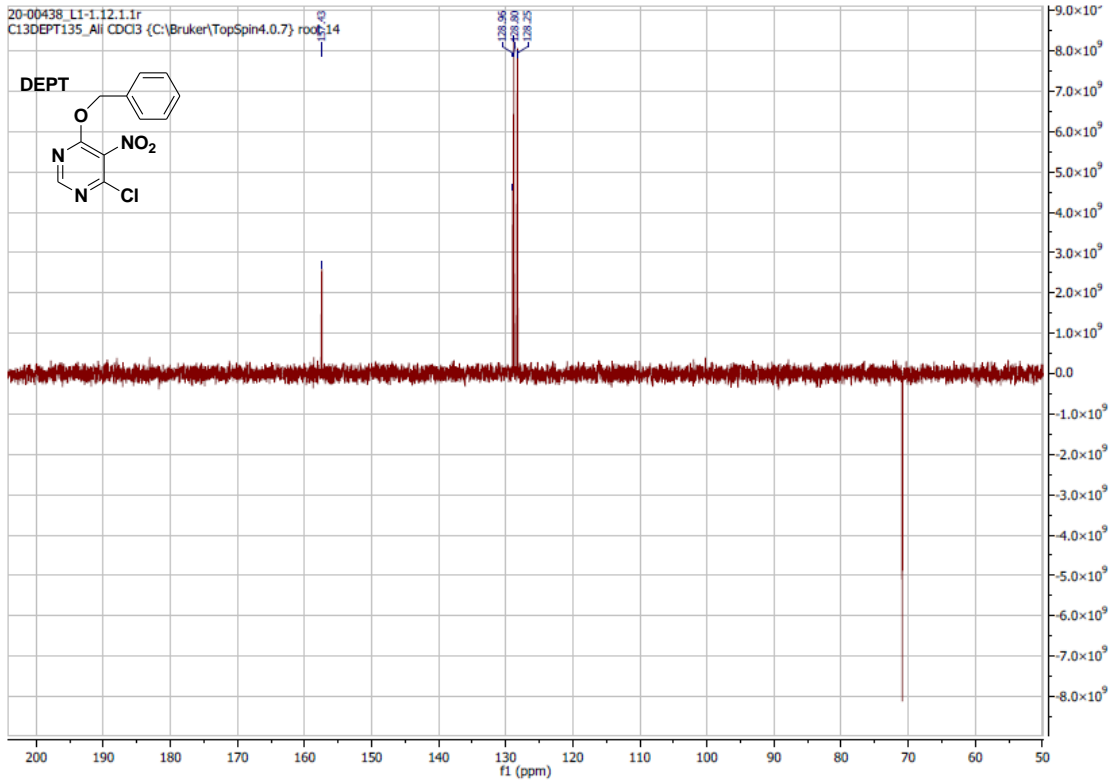
- 4-chloro-5-nitro-6-(prop-2-ynoxy)pyrimidine (2a):



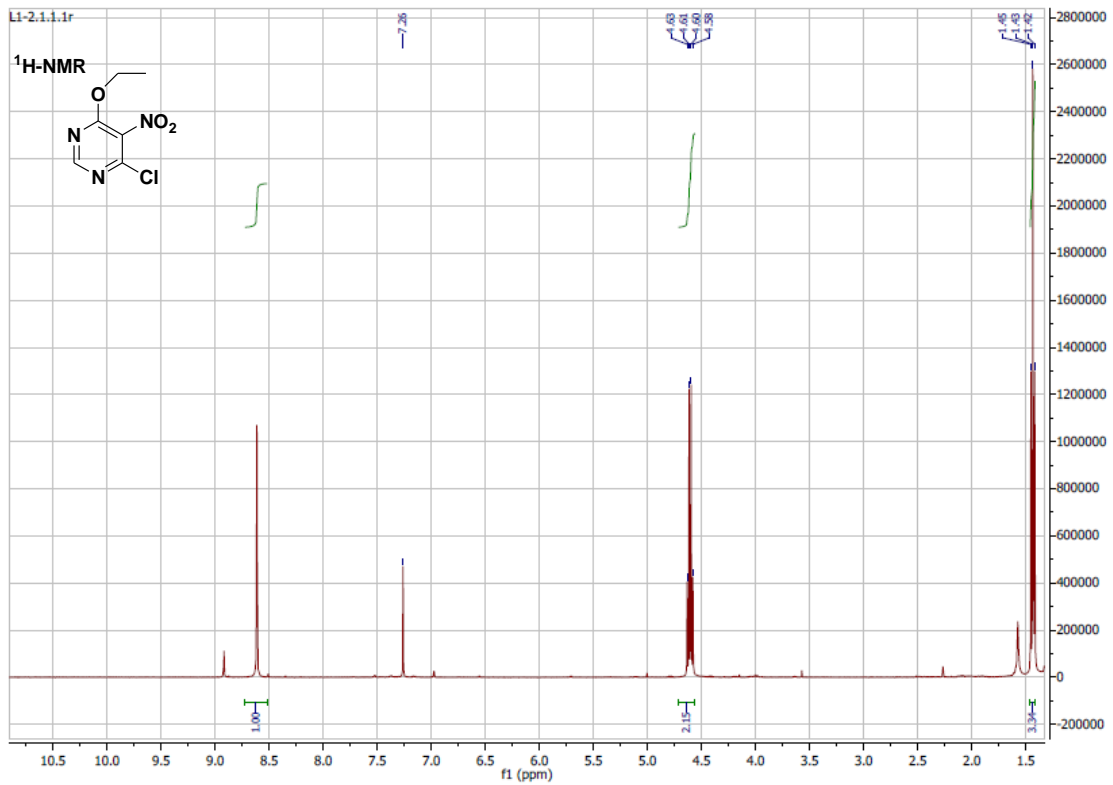


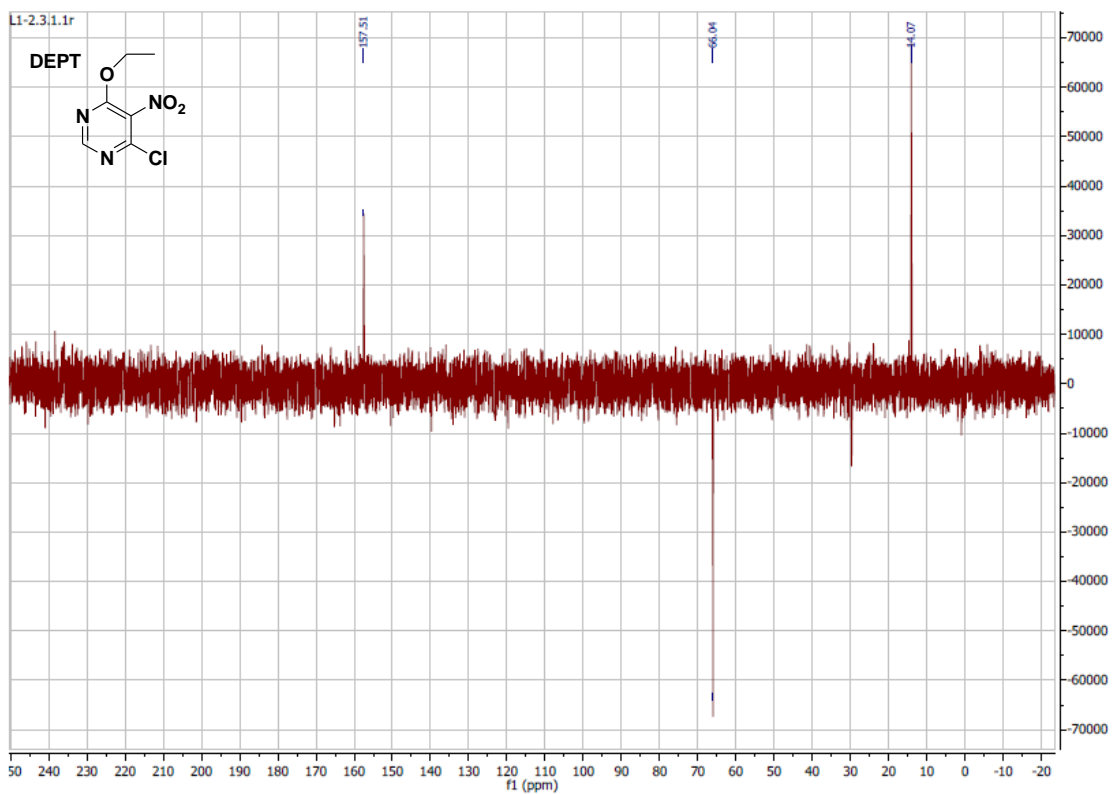
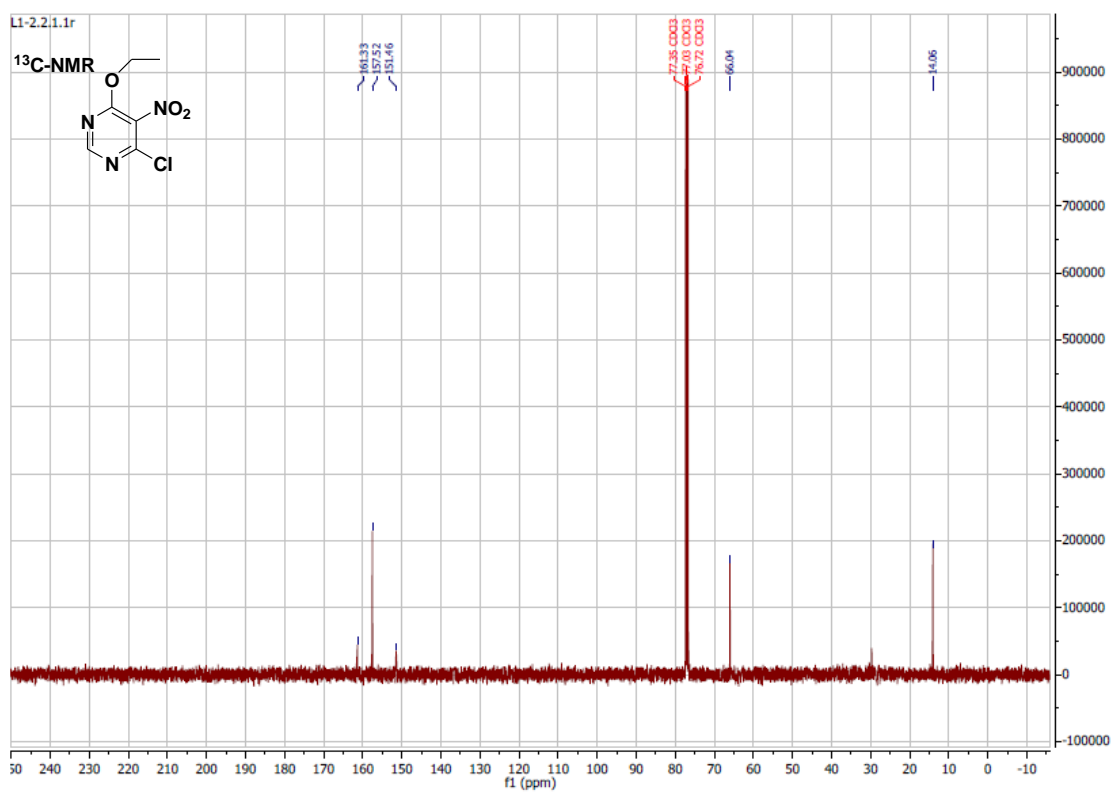
- **4-benzyloxy-6-chloro-5-nitropyrimidine (2b):**



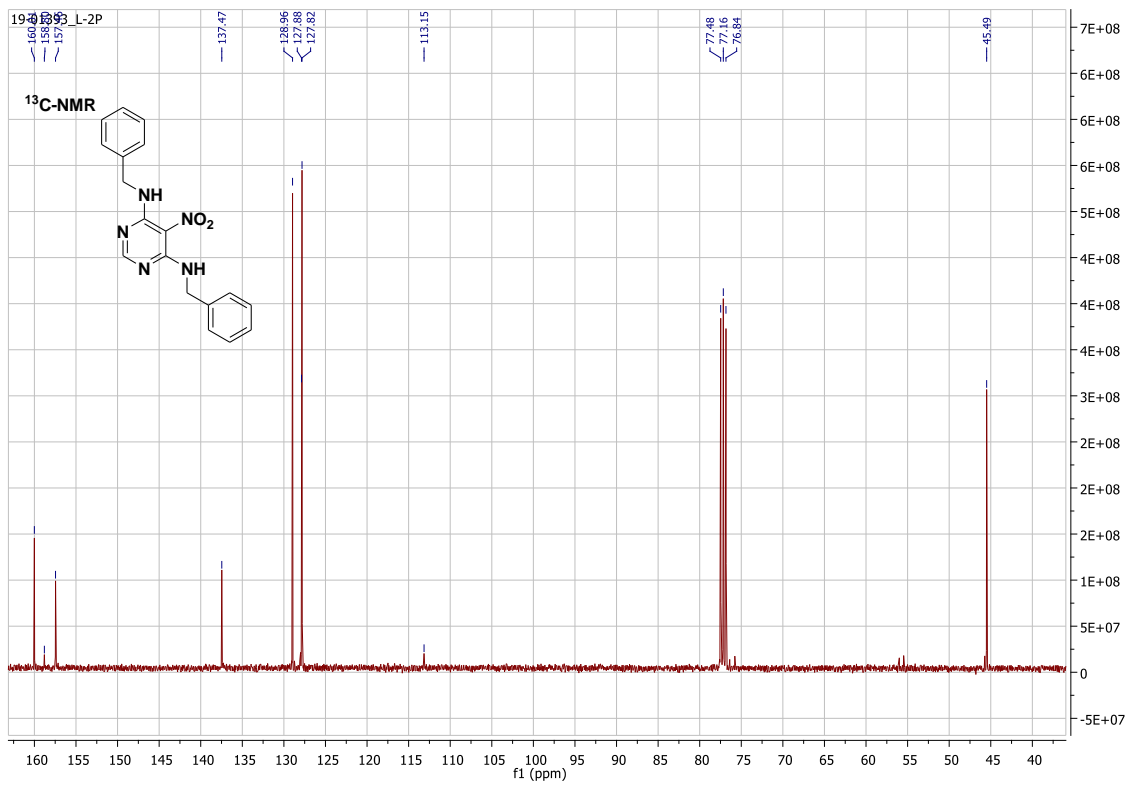
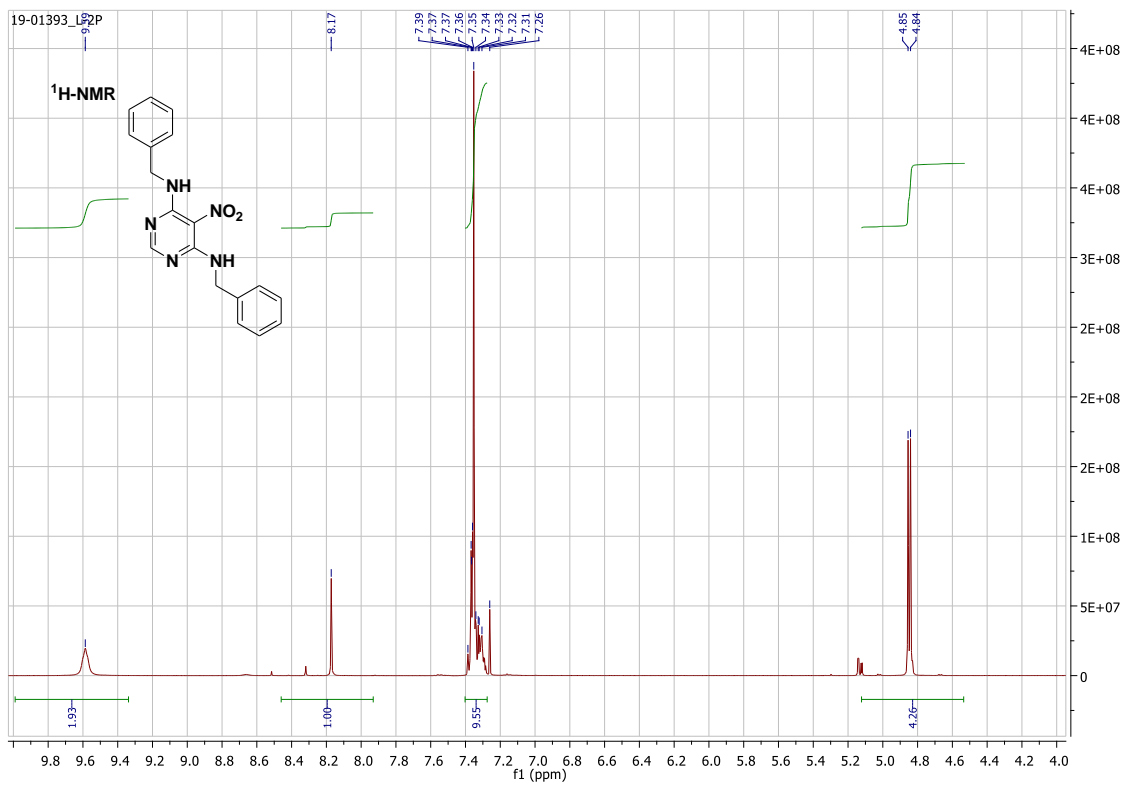


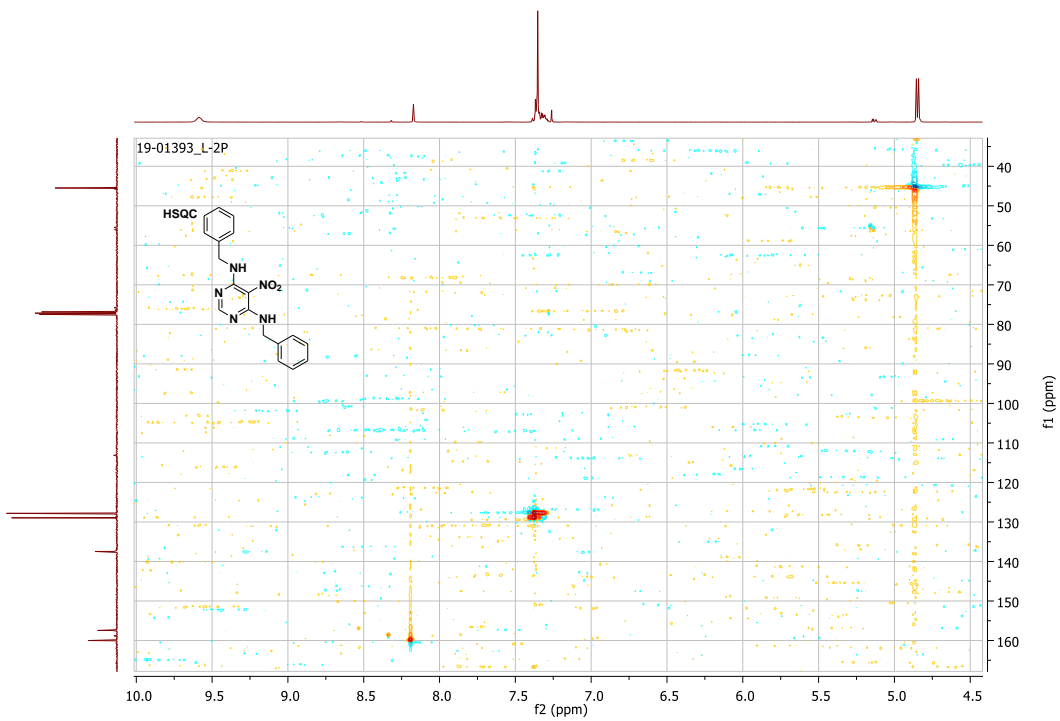
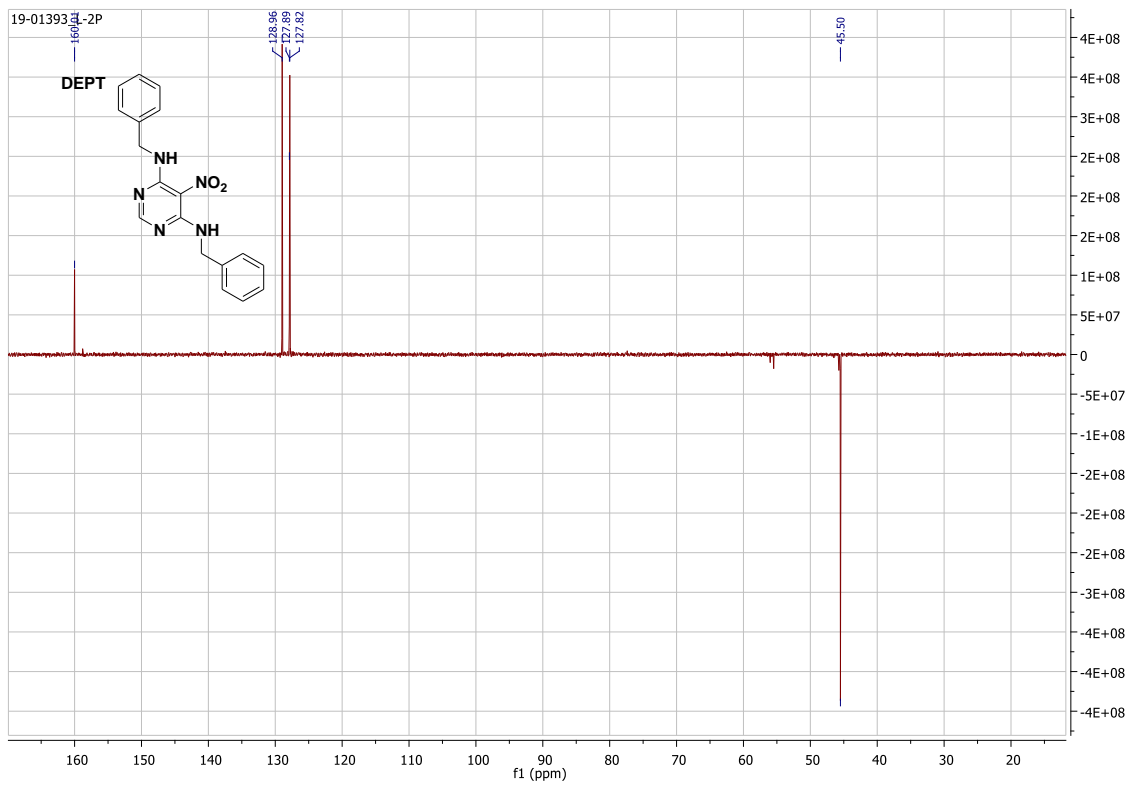
- 4- chloro-6-ethoxy-5-nitropyrimidine (2c):

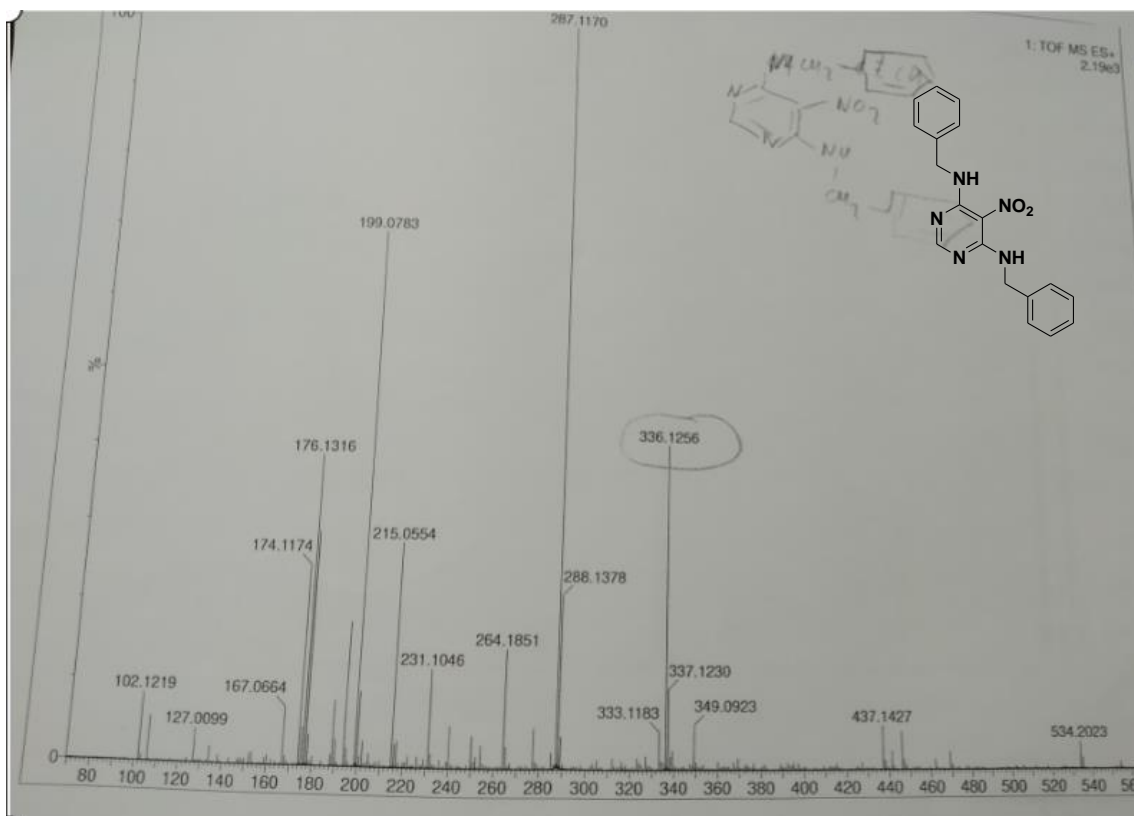




- **N⁴,N⁶-dibenzyl-5-nitropyrimidine-4,6-diamine (5a):**







Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 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

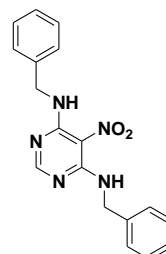
175 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)

Elements Used:

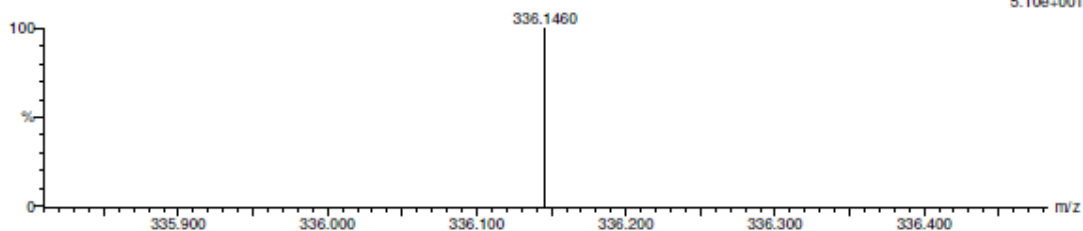
C: 0-19 H: 0-1000 N: 0-6 O: 0-4 Na: 0-1

13-02MariaJose 66 (1.428) AM (Top, 1, Ht, 5000.0, 0.00, 1.00)

1: TOF MS ES+



Page 1

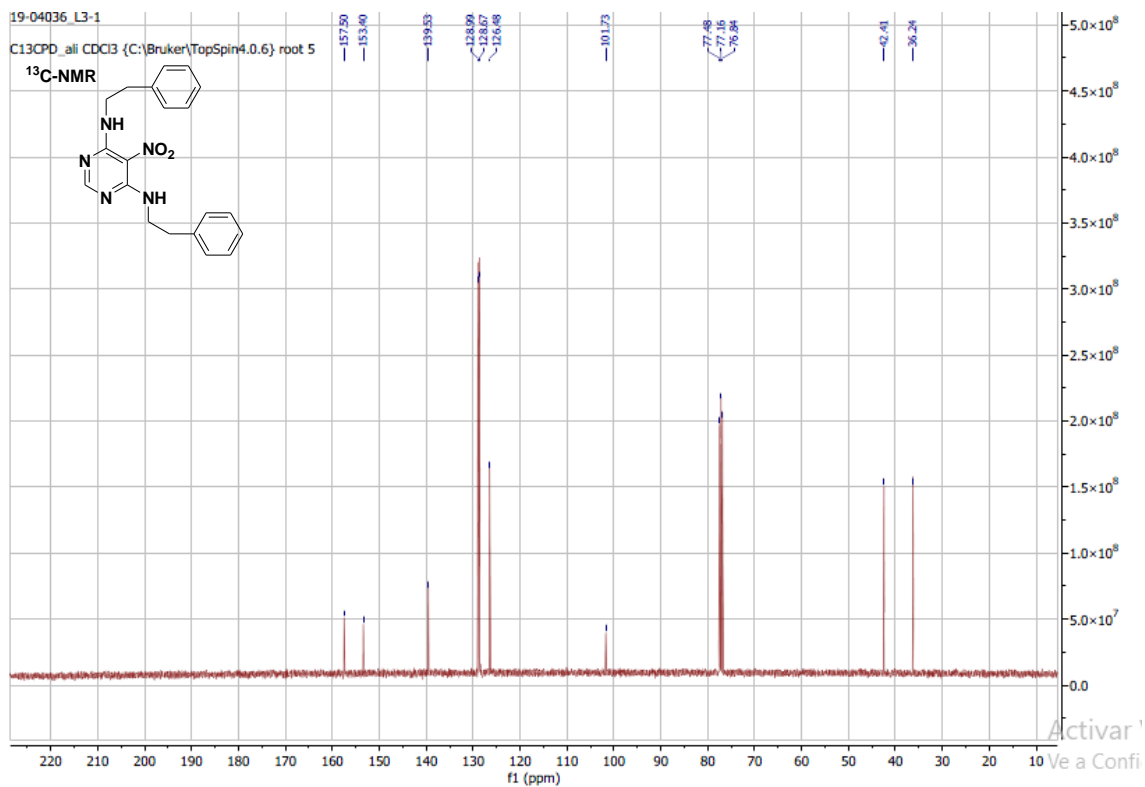
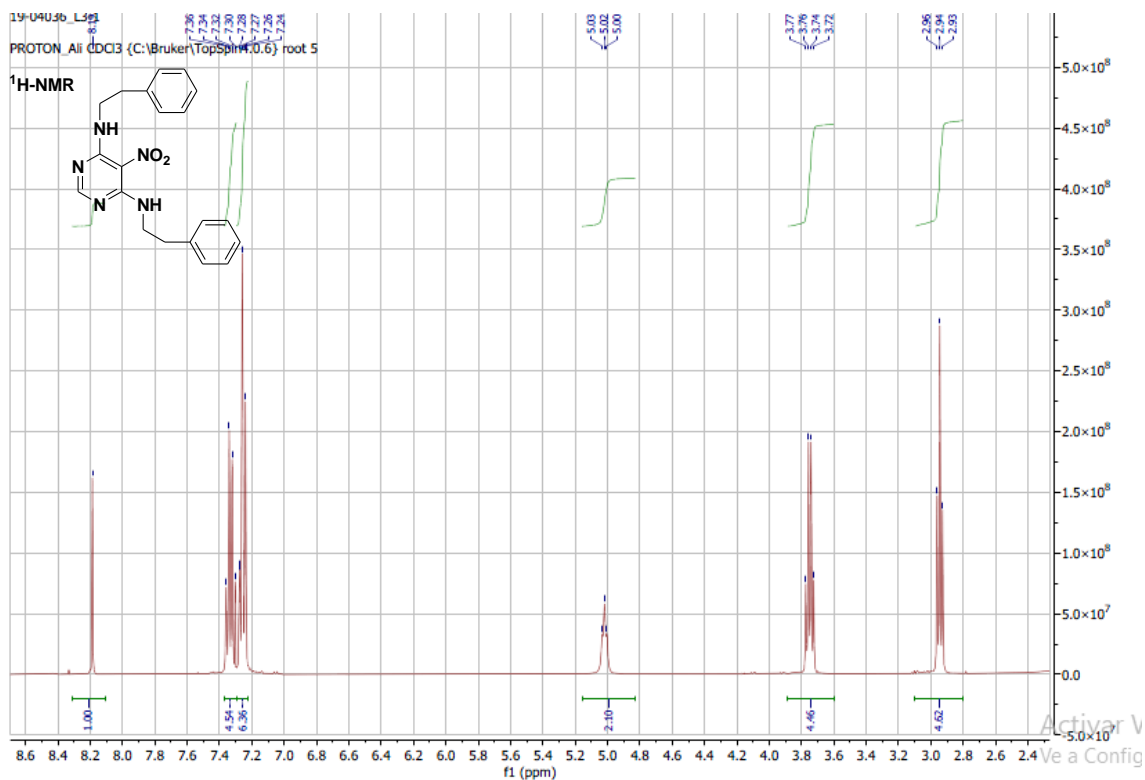


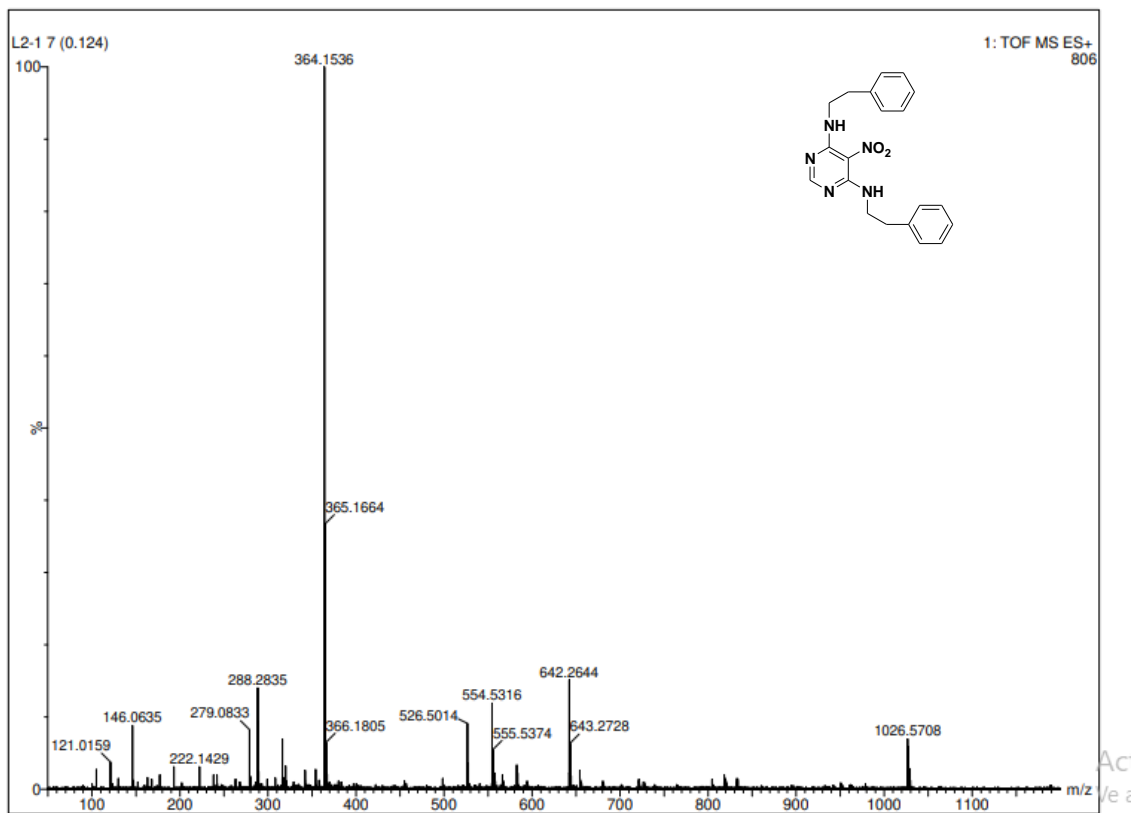
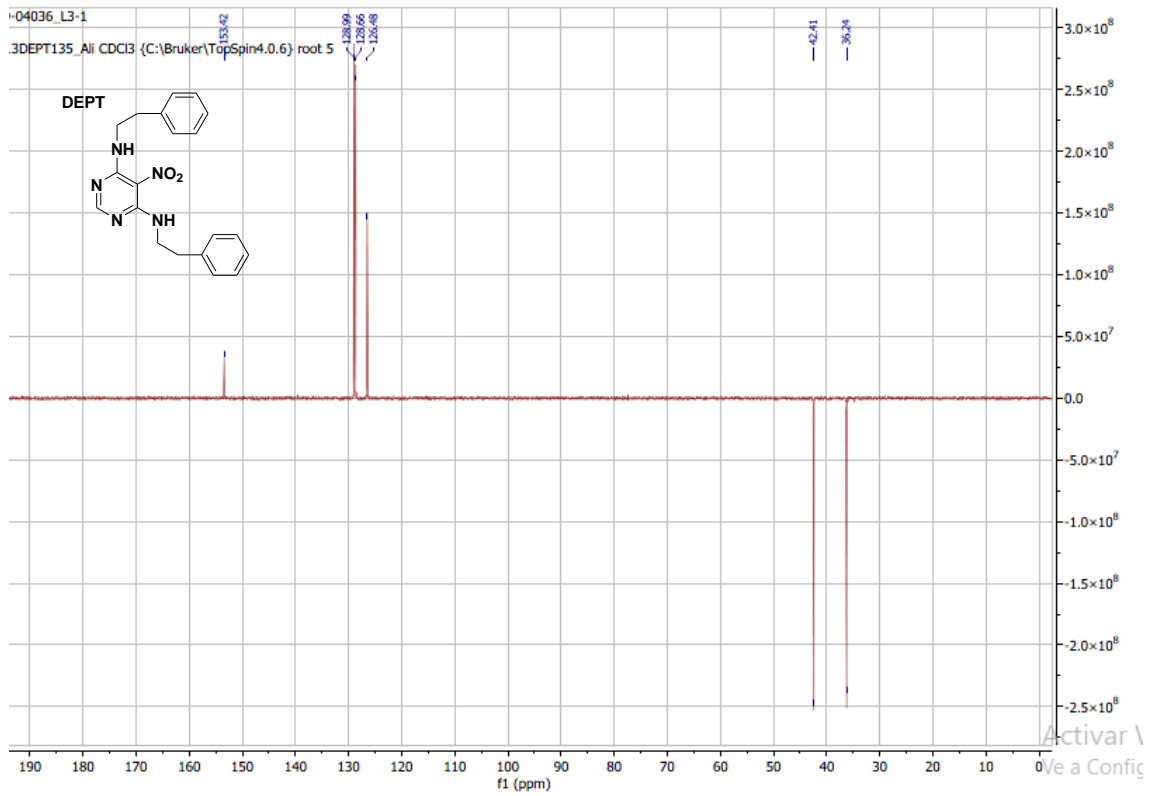
5.10e+001

Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
336.1460	336.1461	-0.1	-0.3	12.5	16.7	0.7	C18 H18 N5 O2
	336.1436	2.4	7.1	9.5	16.6	0.6	C16 H19 N5 O2 Na

- 5-nitro-N⁴,N⁶- diphenethylpyrimidine-4,6-diamine (5b):





Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 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

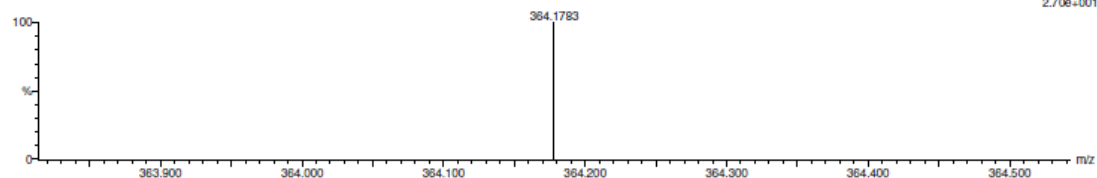
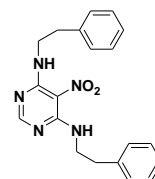
294 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-20 H: 0-1000 N: 0-8 O: 0-5 Na: 0-1

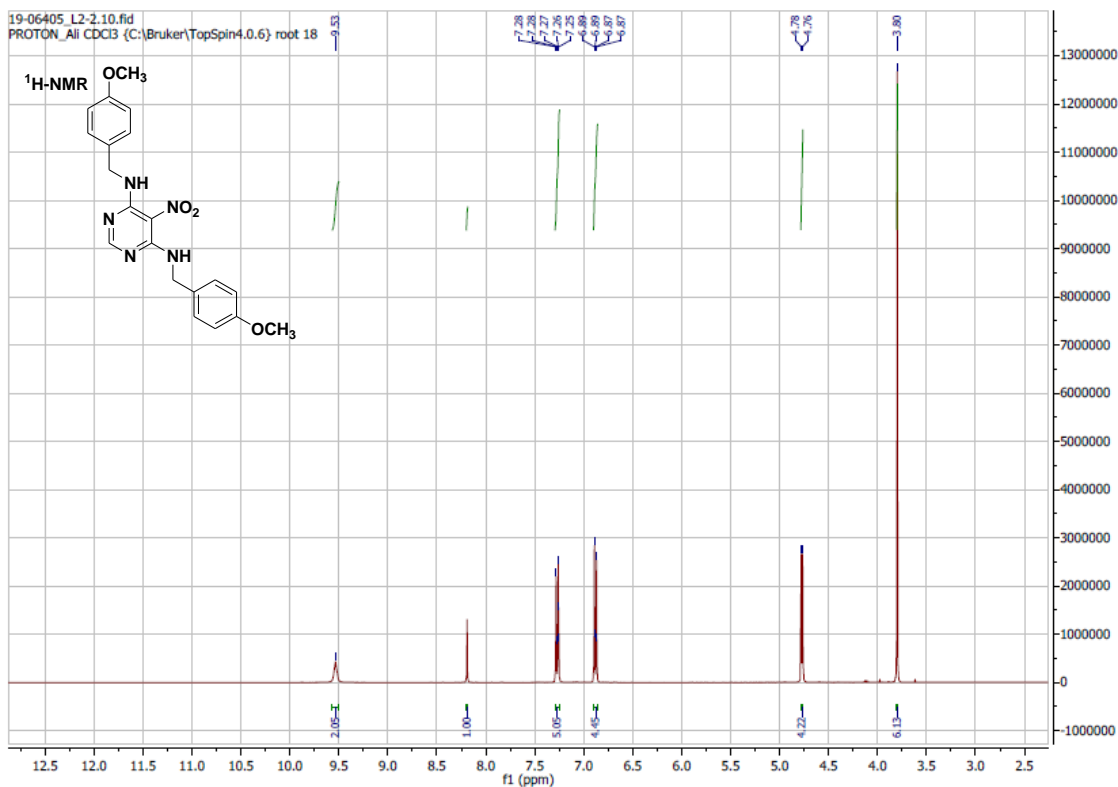
L2-1-27 (0.141)AM (Top,1, H1,5000.0,0.00,1.00)

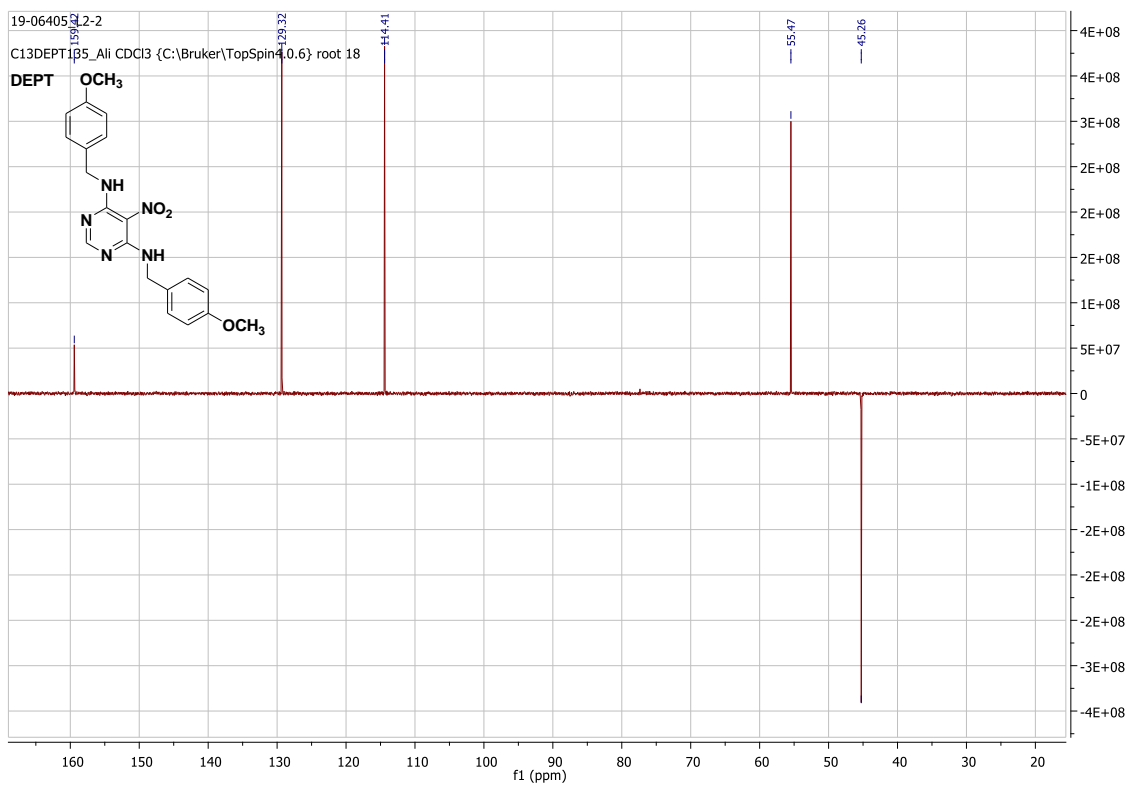
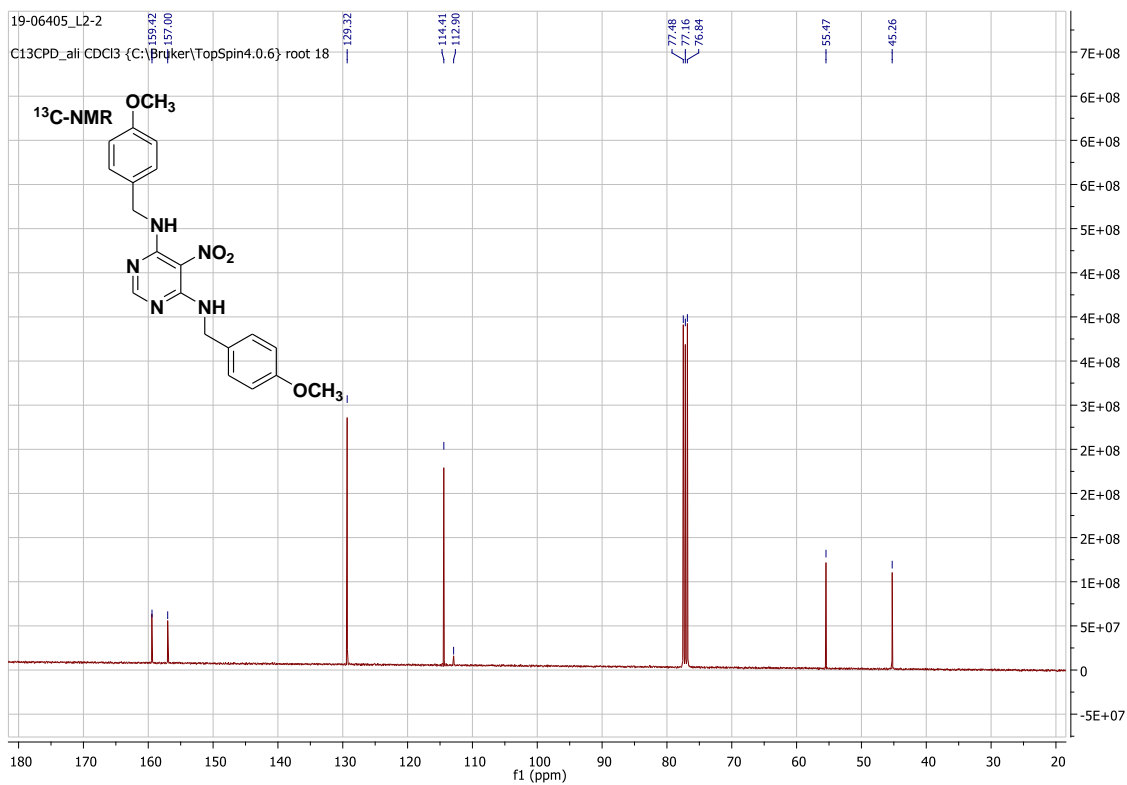
1: TOF MS ES+

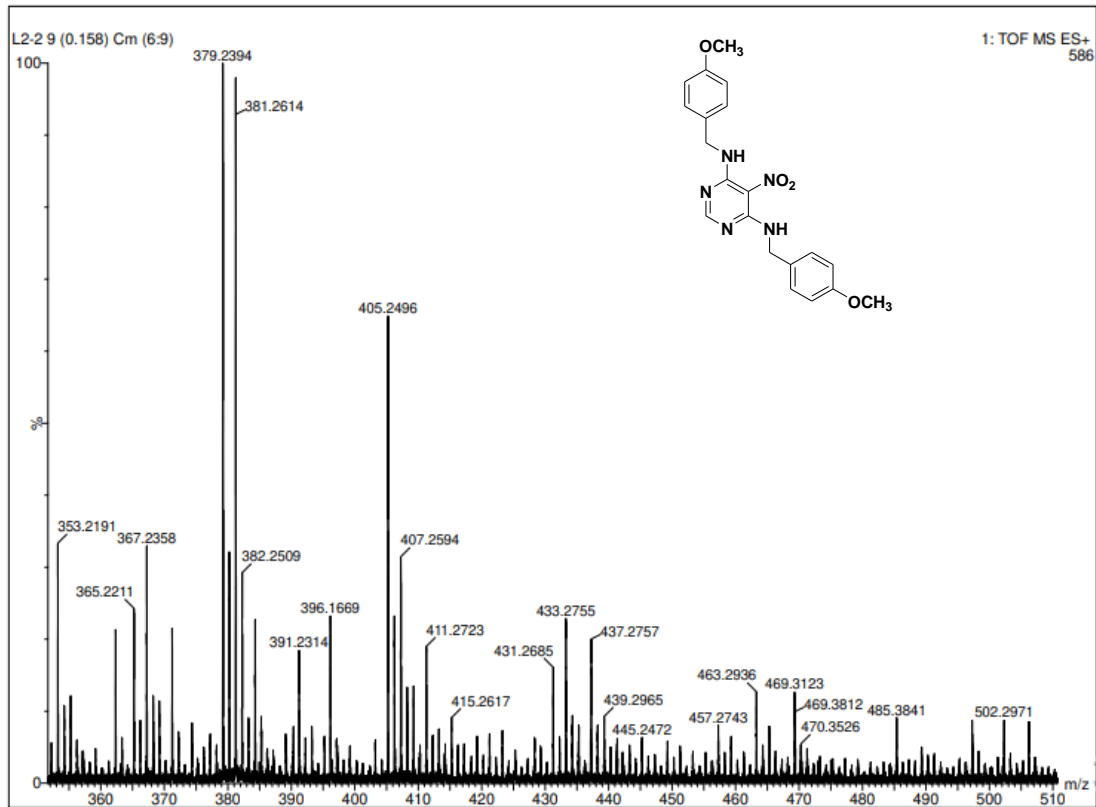


Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	1-FIT (Norm)	Formula
364.1783	364.1774	0.9	2.5	12.5	14.7	0.7	C20 H22 N5 O2
	364.1749	3.4	9.3	9.5	14.7	0.7	C18 H23 N5 O2 Na

- **N⁴,N⁶-bis (4-methoxybenzyl)-5-nitropyrimidine-4,6-diamine (5c):**







Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 10.0 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

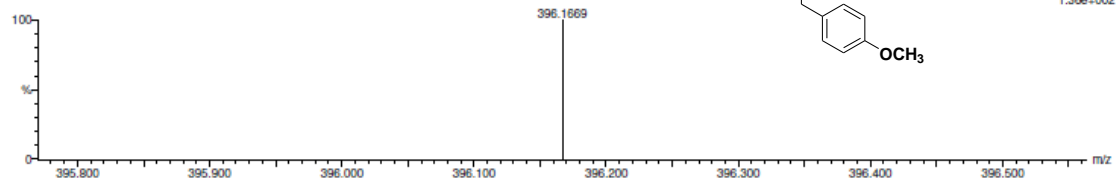
76 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-20 H: 0-1000 N: 0-5 O: 0-4 Na: 0-1

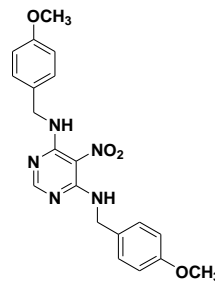
L2-2 9 (0.158) AM (Top, 6, Ht, 5000, 0.0, 0.0, 1.00); Cm (6.9)

1: TOF MS ES+

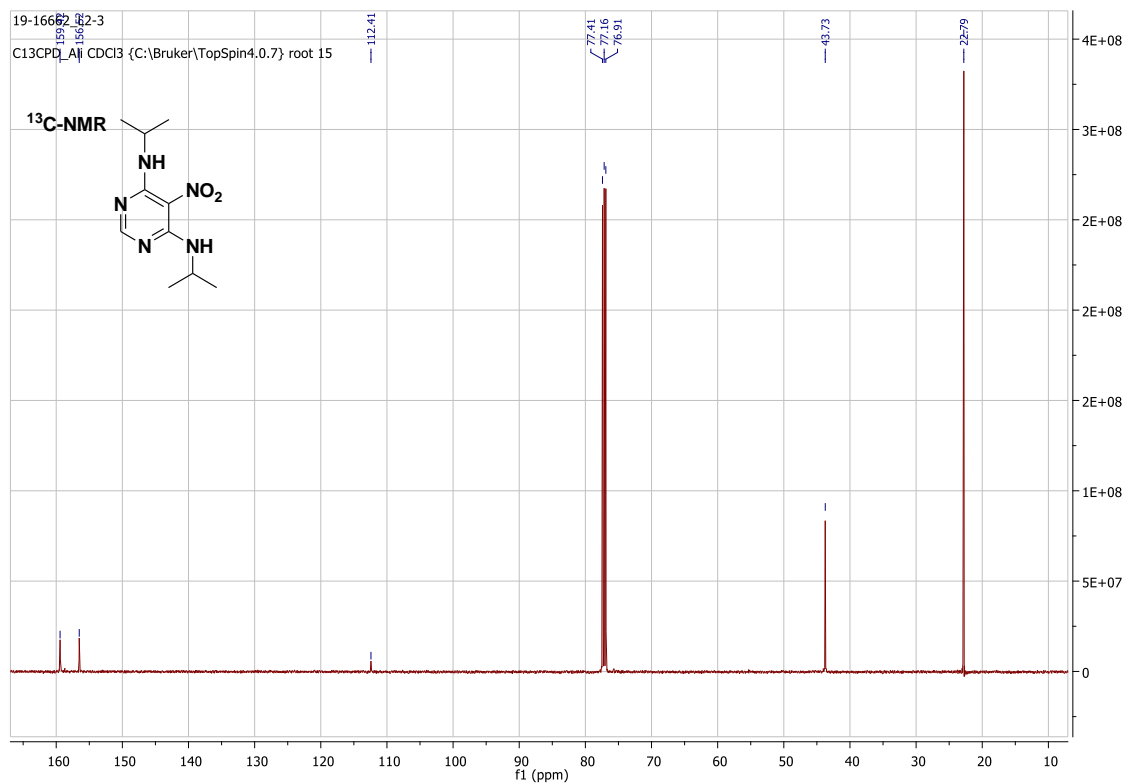
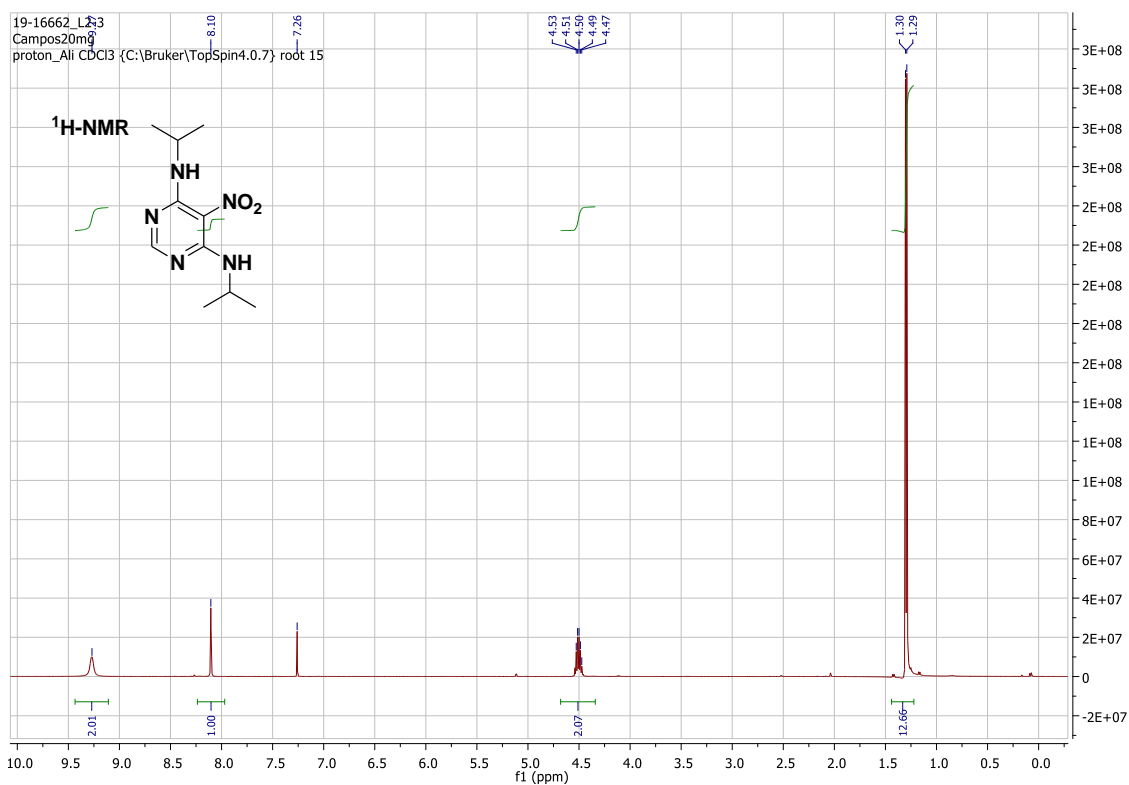


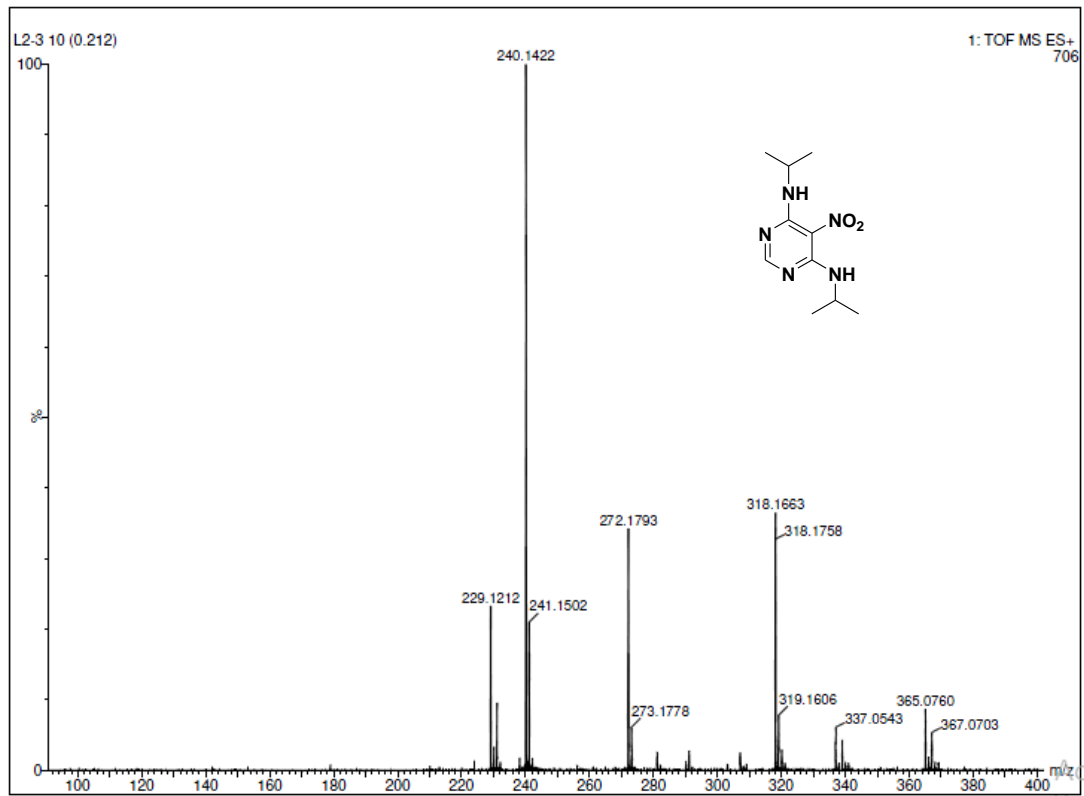
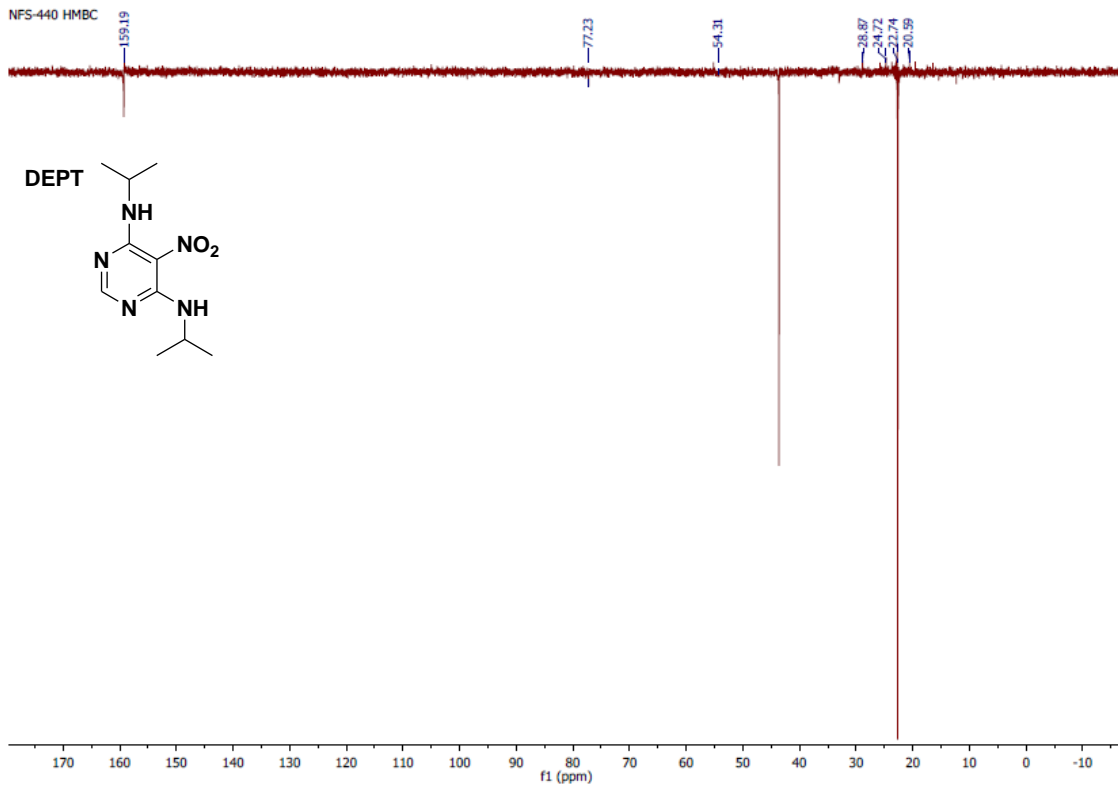
Minimum: 5.0 10.0 -1.5
Maximum: 396.1672 396.1648 2.1 5.3 9.5

Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	1-FIT (Norm)	Formula
396.1669	396.1672	-0.3	-0.8	12.5	19.2	0.6	C20 H22 N5 O4
	396.1648	2.1	5.3	9.5	19.4	0.8	C18 H23 N5 O4 Na



- **N⁴,N⁶-diisopropyl-5-nitropyrimidine-4,6-diamine (5d):**





Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

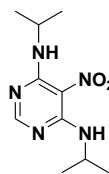
Monoisotopic Mass, Even Electron Ions
259 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)

Elements Used:

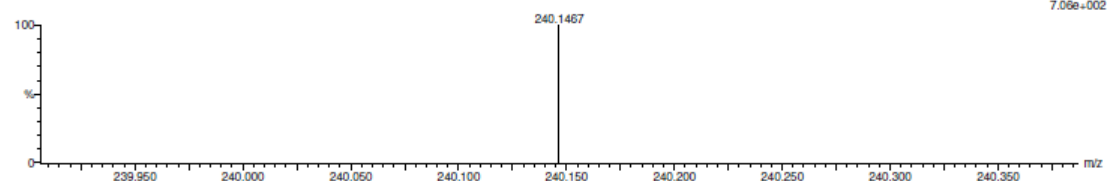
C: 0-31 H: 0-1000 N: 0-8 O: 0-20

L2-3 10 (0.212) AM (Cen,6, 5.00, HL5000.0,0.00,1.00)

1: TOF MS ES+

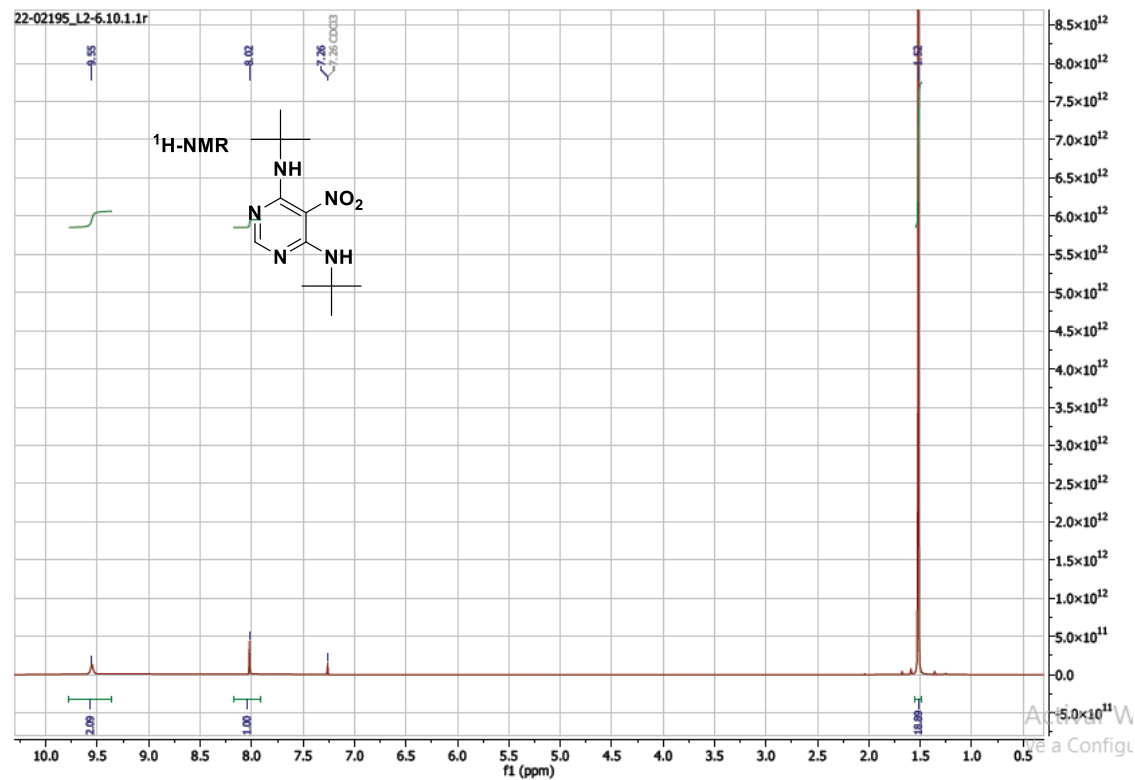


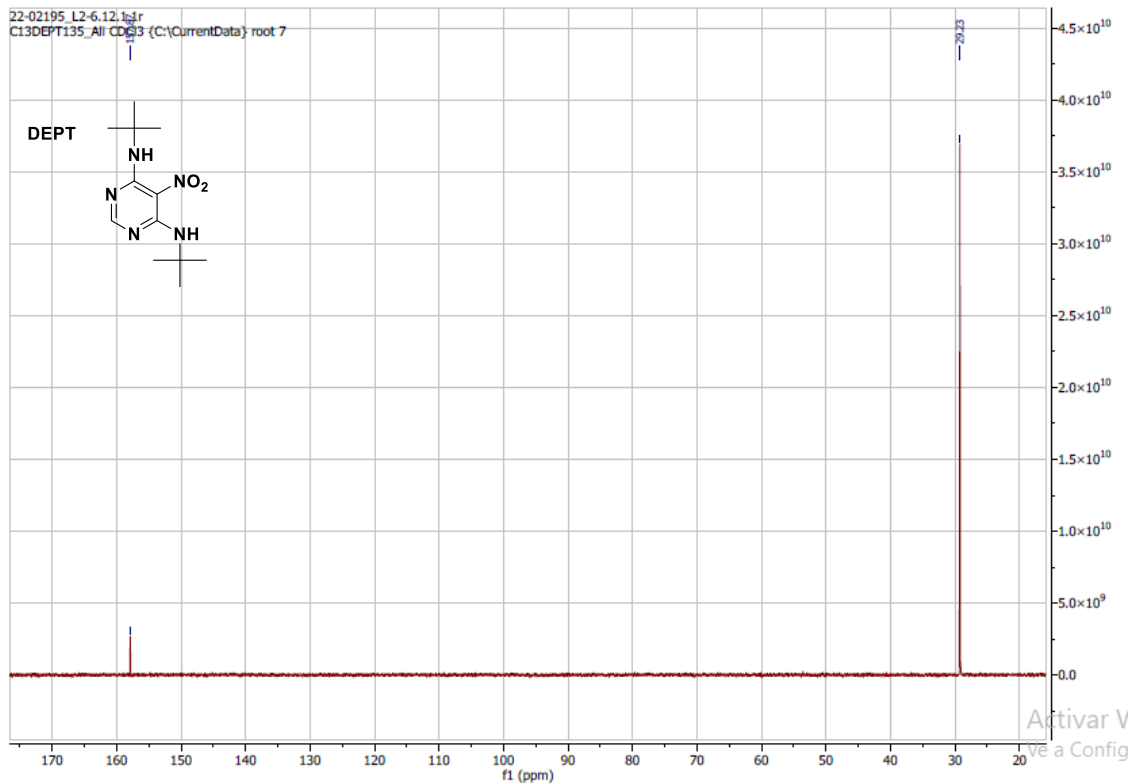
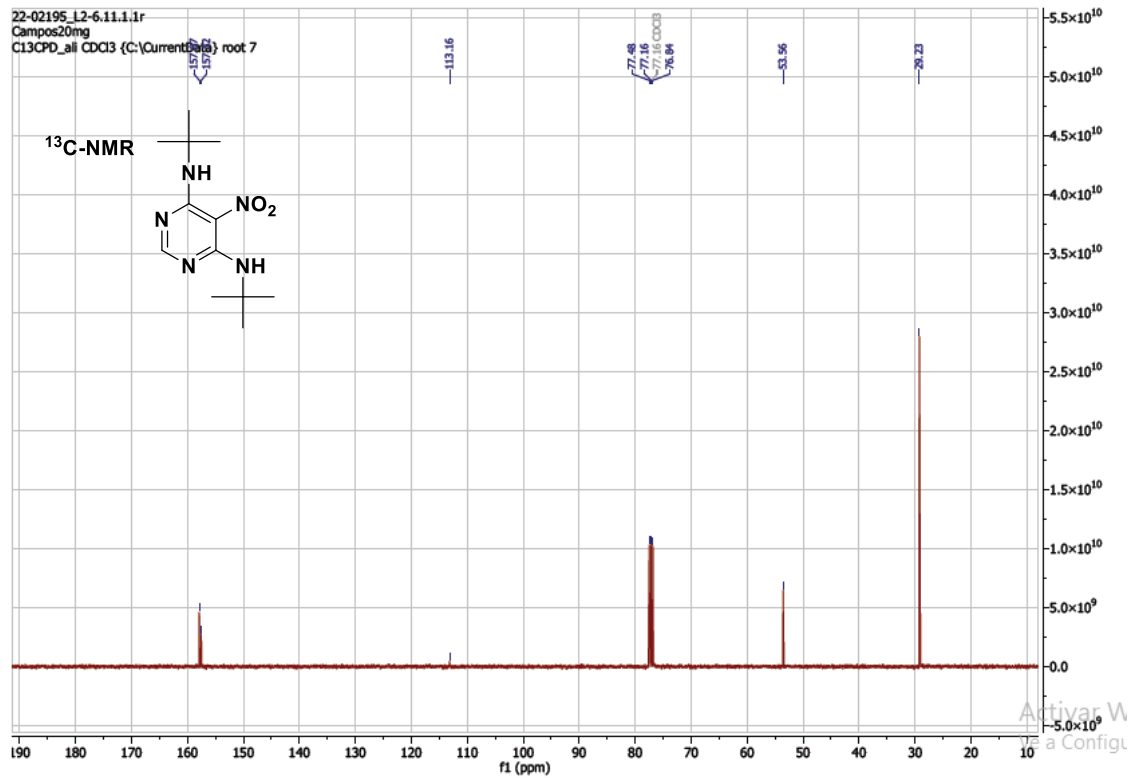
Page 1

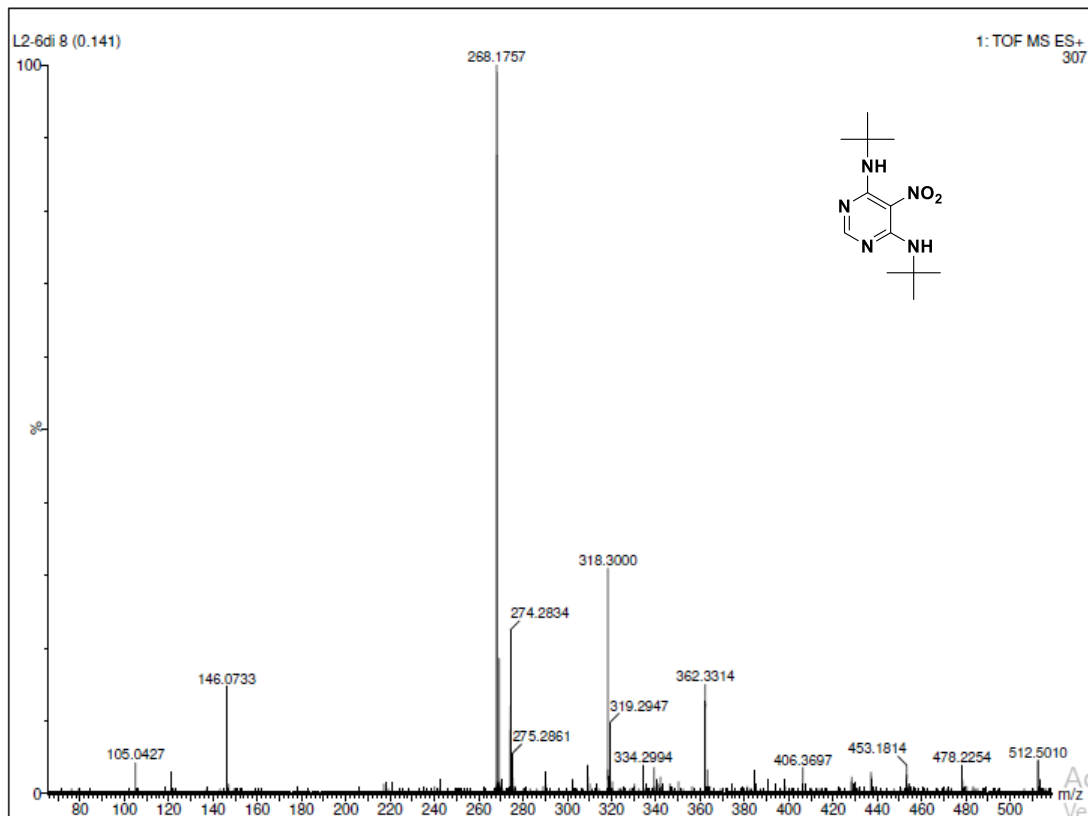


Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	1-FIT (Norm)	Formula
240.1467	240.1461	0.6	2.5	4.5	22.2	0.3	C10 H18 N5 O2
	240.1447	2.0	8.3	-0.5	23.2	1.2	C9 H22 N O6

- **N⁴,N⁶-di-tert-butyl-5-nitropyrimidine-4,6-diamine (5e):**





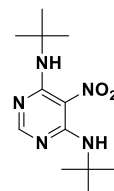


Elemental Composition Report

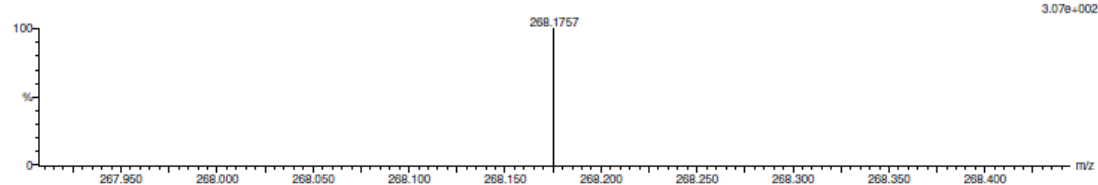
Single Mass Analysis

Tolerance = 10.0 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
 76 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)
 Elements Used:
 C: 0-12 H: 0-1000 N: 0-5 O: 0-7
 L2-6di 8 (0.141)AM (Top,6, Ht,5000.0,0.00,1.00)
 1: TOF MS ES+



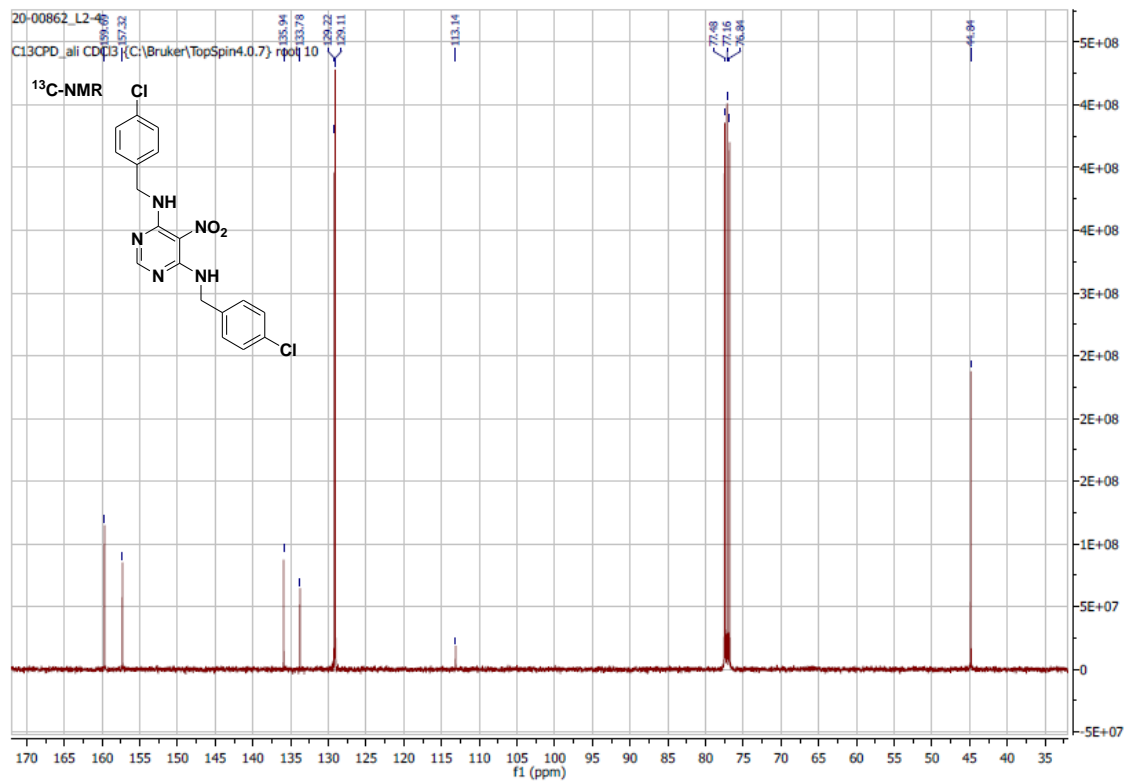
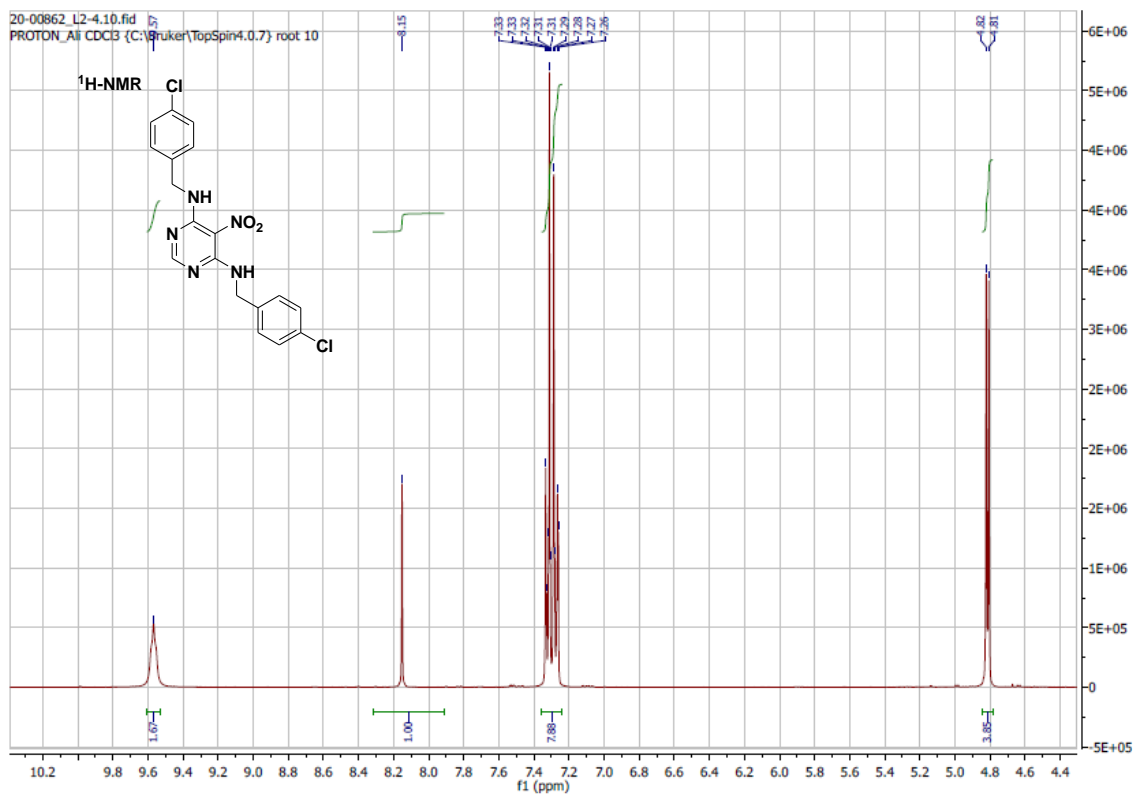
Page 1

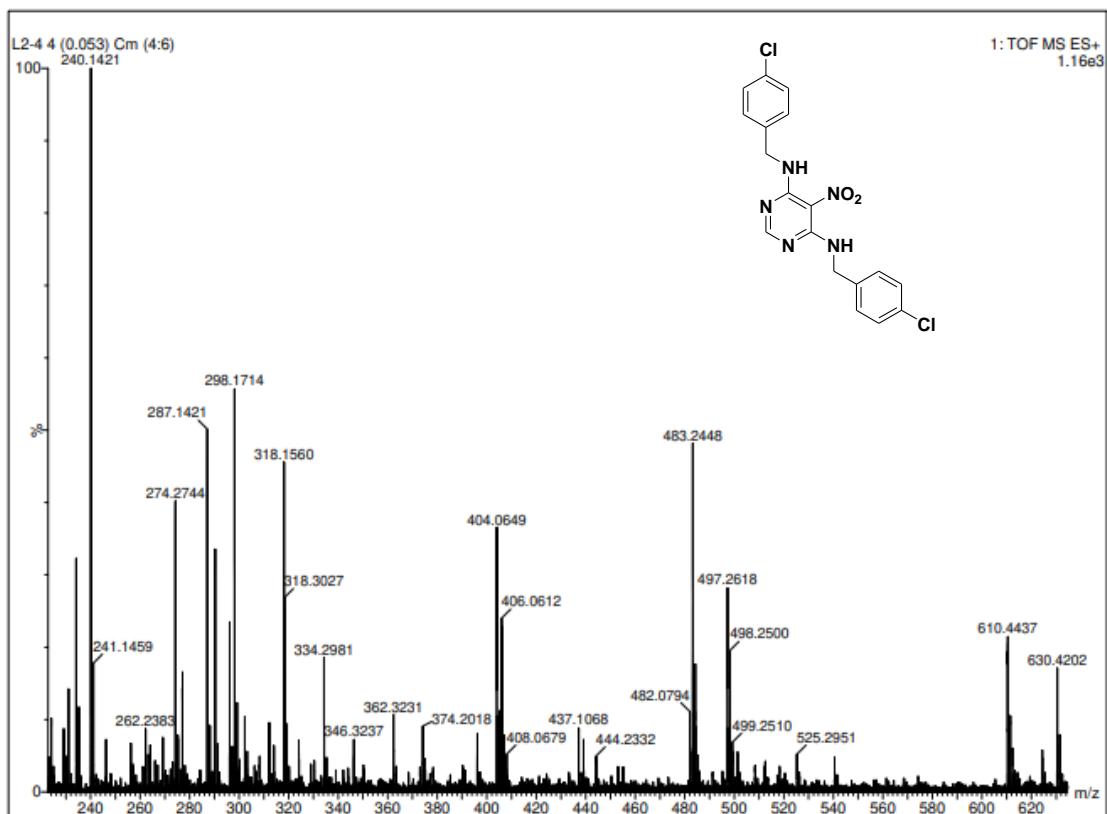
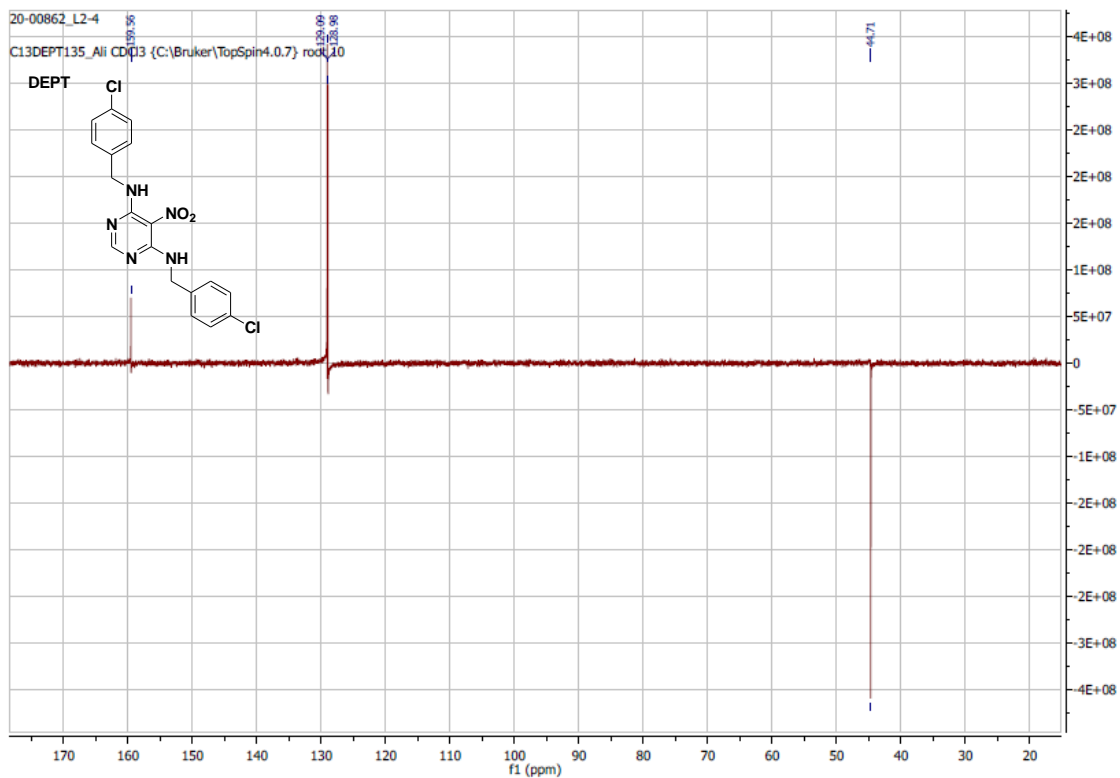


Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	1-FIT (Norm)	Formula
268.1757	268.1774	-1.7	-6.3	4.5	20.9	1.2	C12 H22 N5 O2
	268.1760	-0.3	-1.1	-0.5	20.1	0.4	C11 H26 N O6

3.078+002

- N^4,N^6 -bis(4-chlorobenzyl)-5-nitropyrimidine-4,6-diamine (5f):





Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

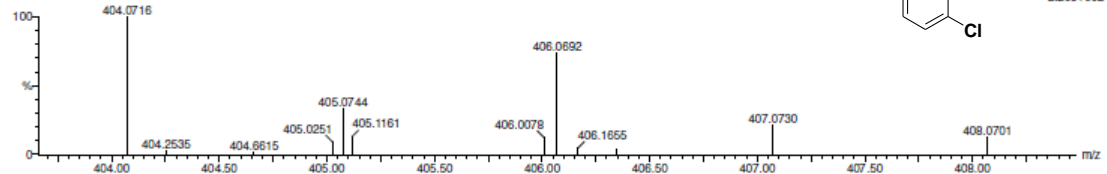
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
117 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:

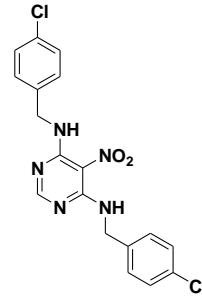
C: 0-18 H: 0-1000 N: 0-8 O: 0-2 Cl: 0-2

L2-4.4 (0.053)AM (Cen,6, 50.00, Ht,5000.0,0.00,1.00)

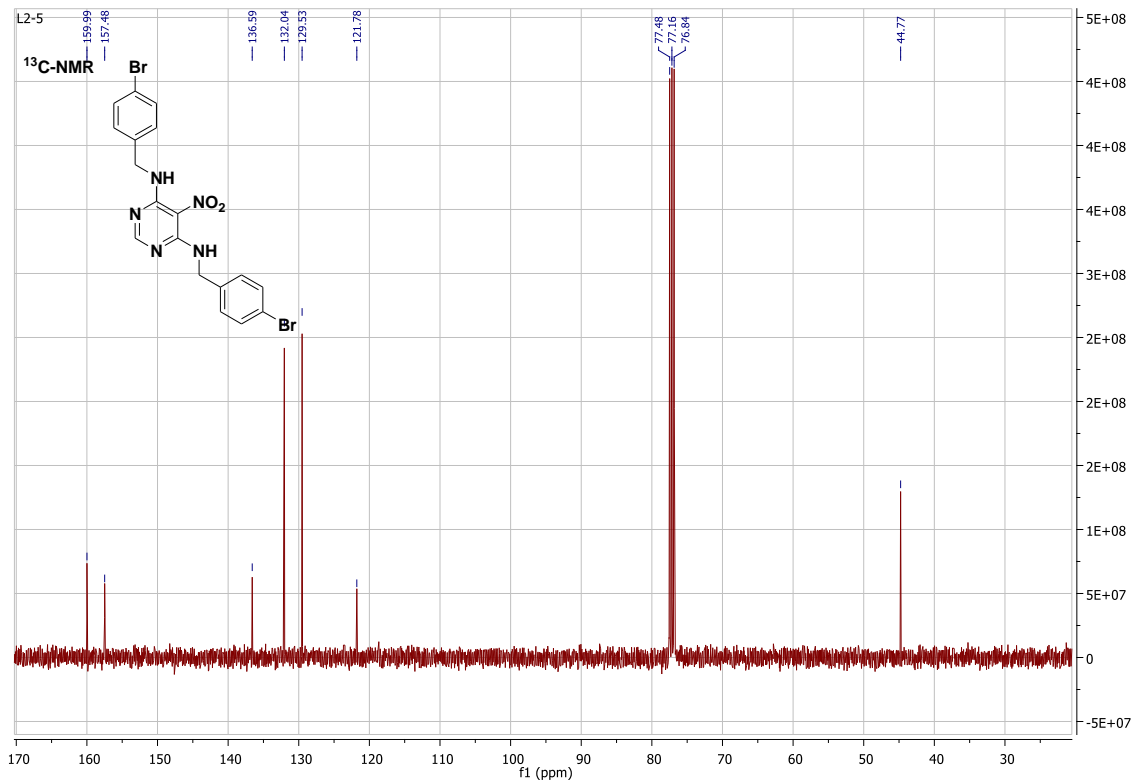
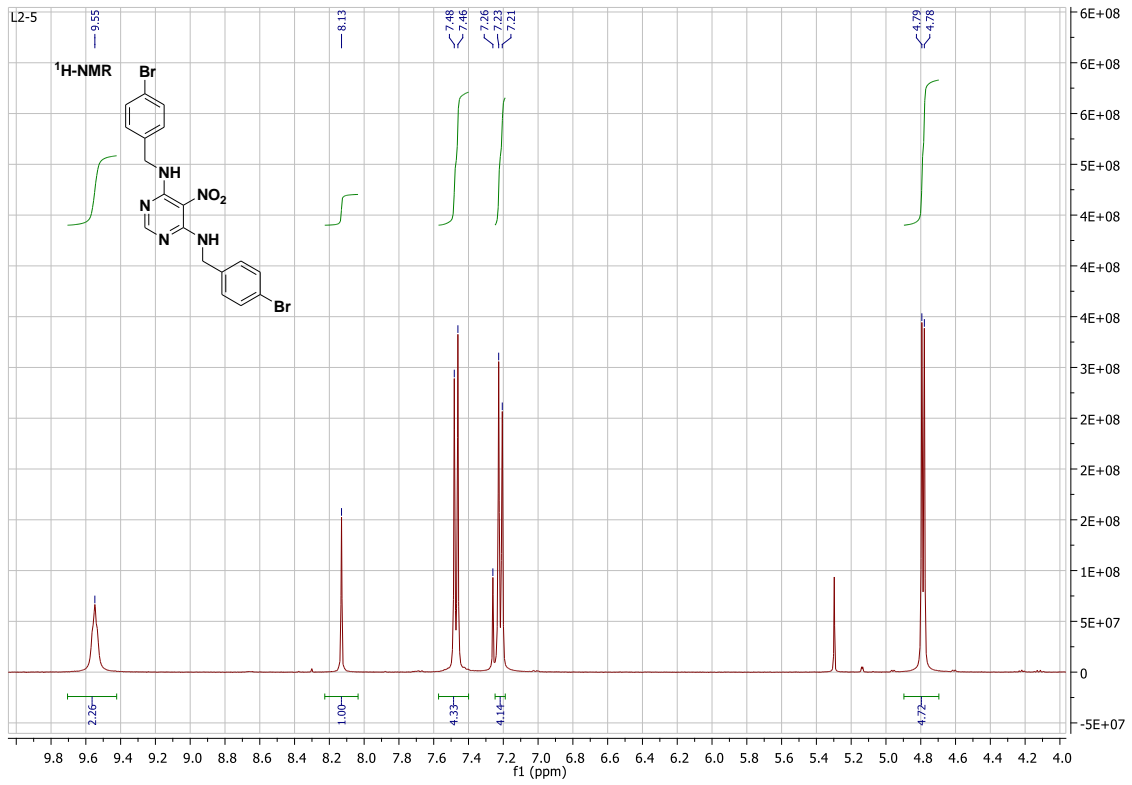
1: TOF MS ES+

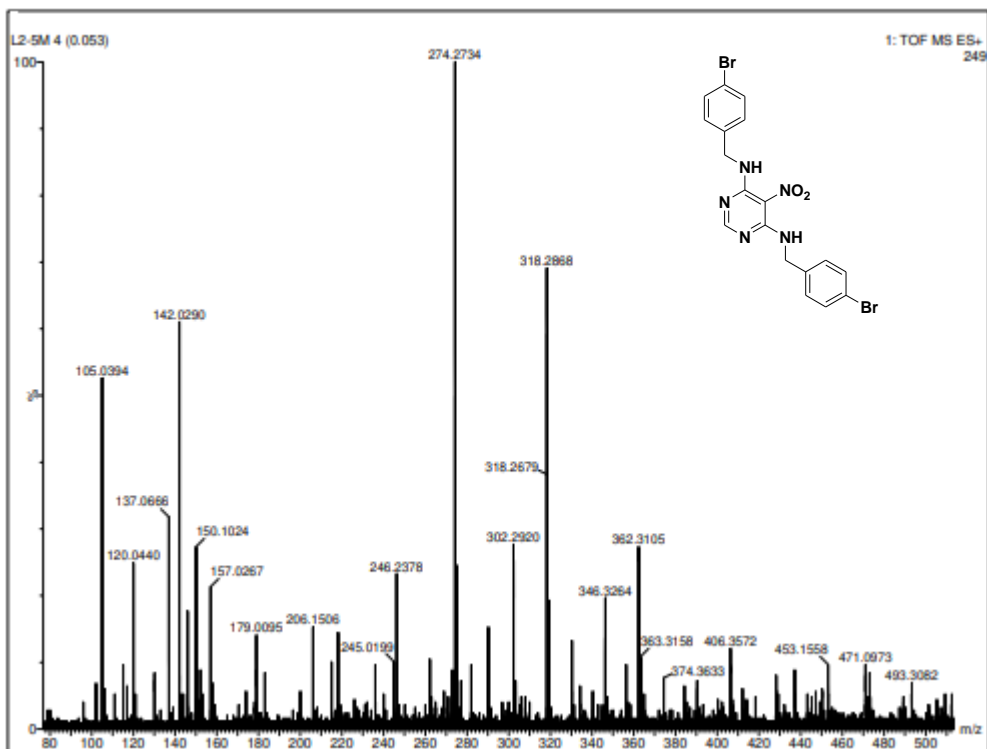
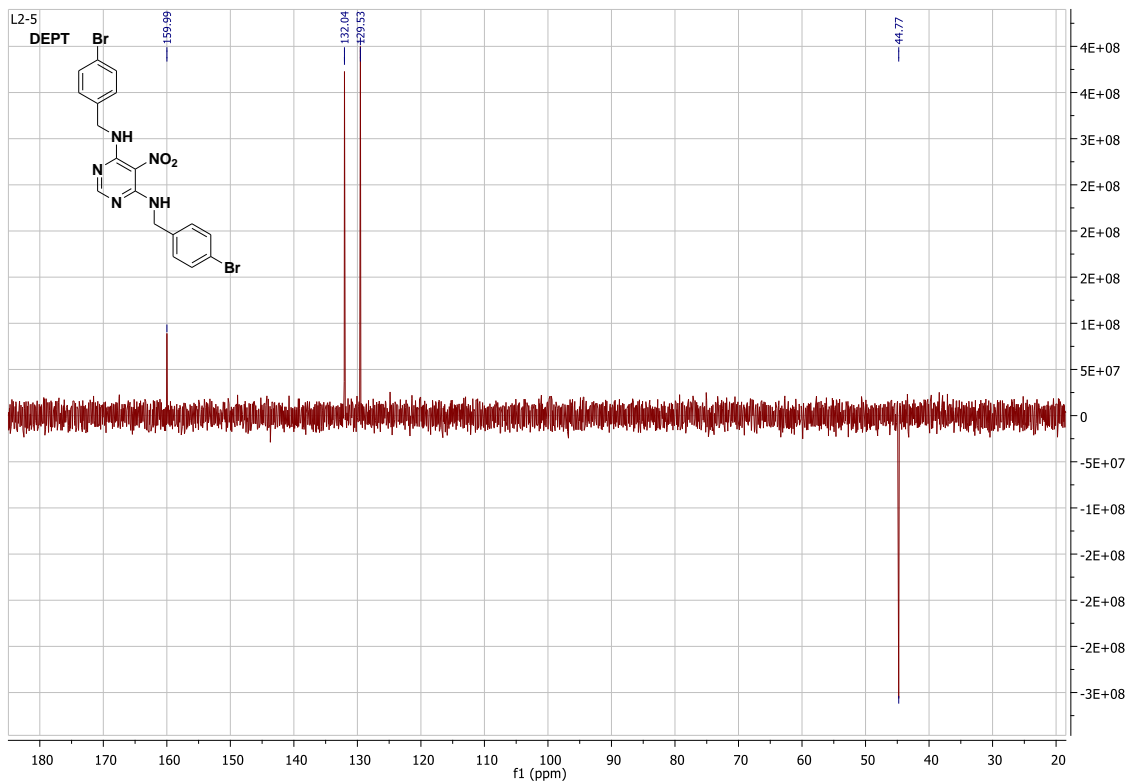


Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	1-FIT (Norm)	Formula
404.0716	404.0681	3.5	8.7	12.5	44.0	0.0	C18 H16 N5 O2 Cl2



- **N⁴,N⁶-bis(4-bromobenzyl)-5-nitropyrimidine-4,6-diamine (5g):**





Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 10.0 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

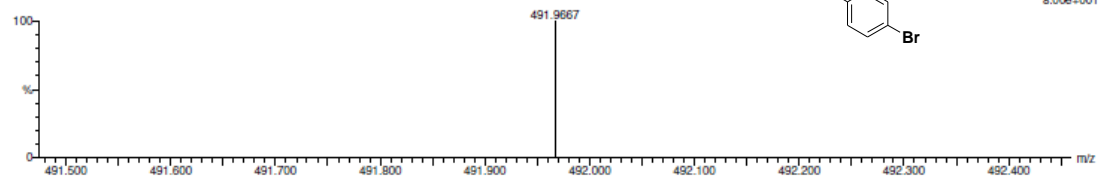
125 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-18 H: 0-1000 N: 0-9 O: 0-2 Br: 0-2

11032020-L2-5pos 168 (3.665) AM (Top,2, Ht,5000.0,0.00,1.00)

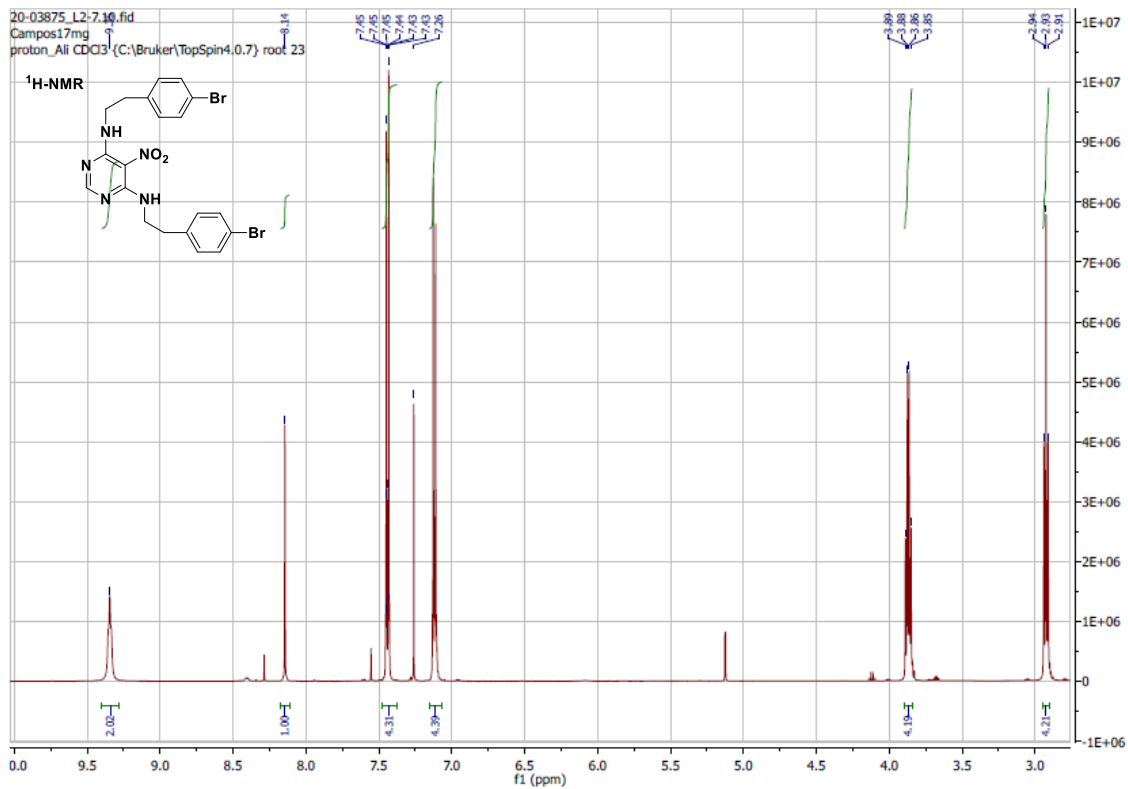
1: TOF MS ES+

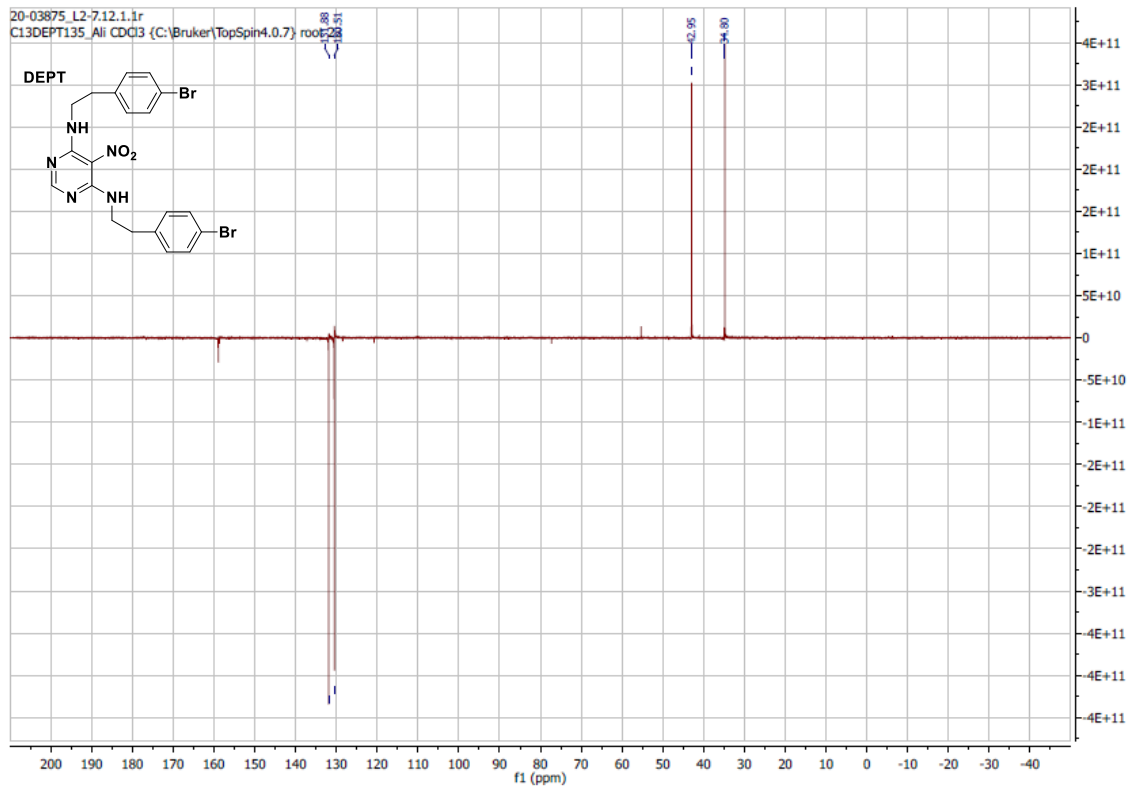
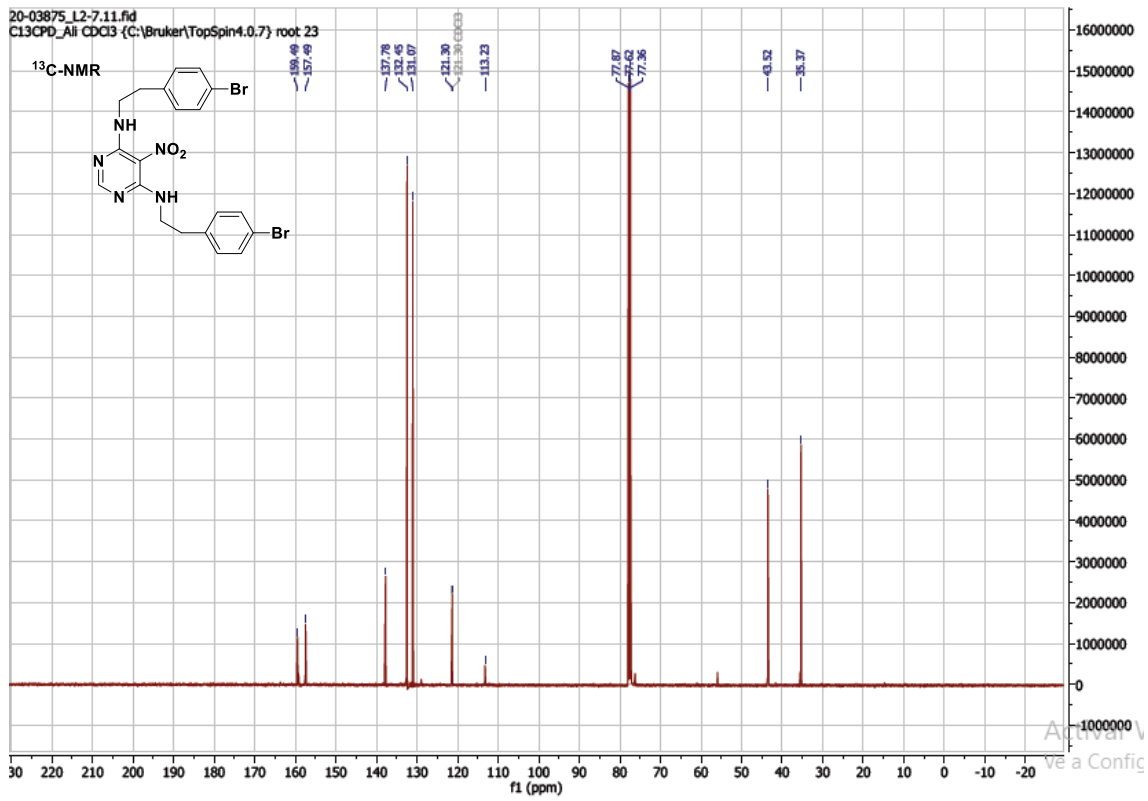


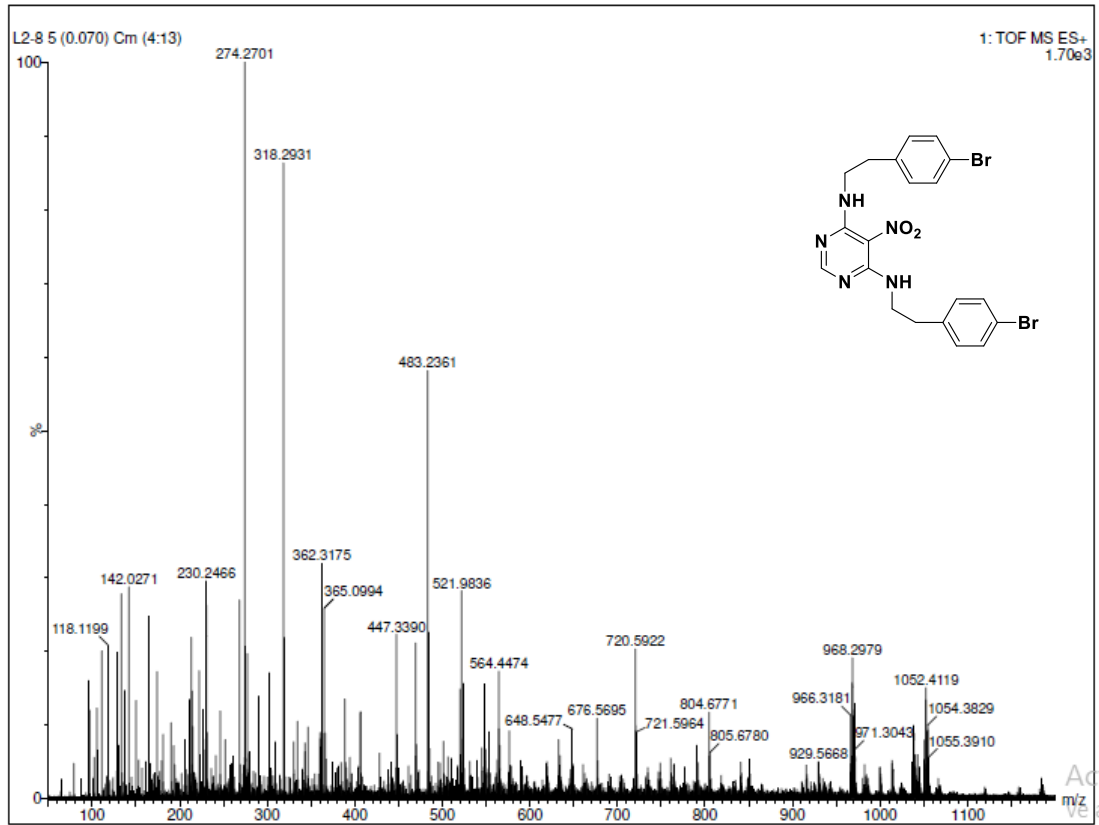
Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	1-FIT (Norm)	Formula
491.9667	491.9671	-0.4	-0.8	12.5	19.7	0.0	C18 H16 N5 O2 Br2

- **N⁴,N⁶-bis(4-bromophenethyl)-5-nitropyrimidine-4,6-diamine (5h):**







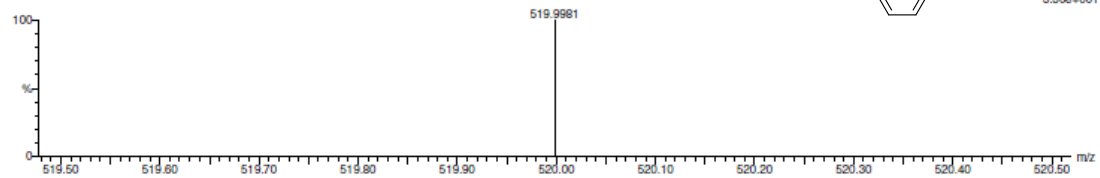
Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
 Element prediction: Off
 Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
 58 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
 Elements Used:
 C: 0-20 H: 0-1000 N: 0-5 O: 0-2 Br: 0-2

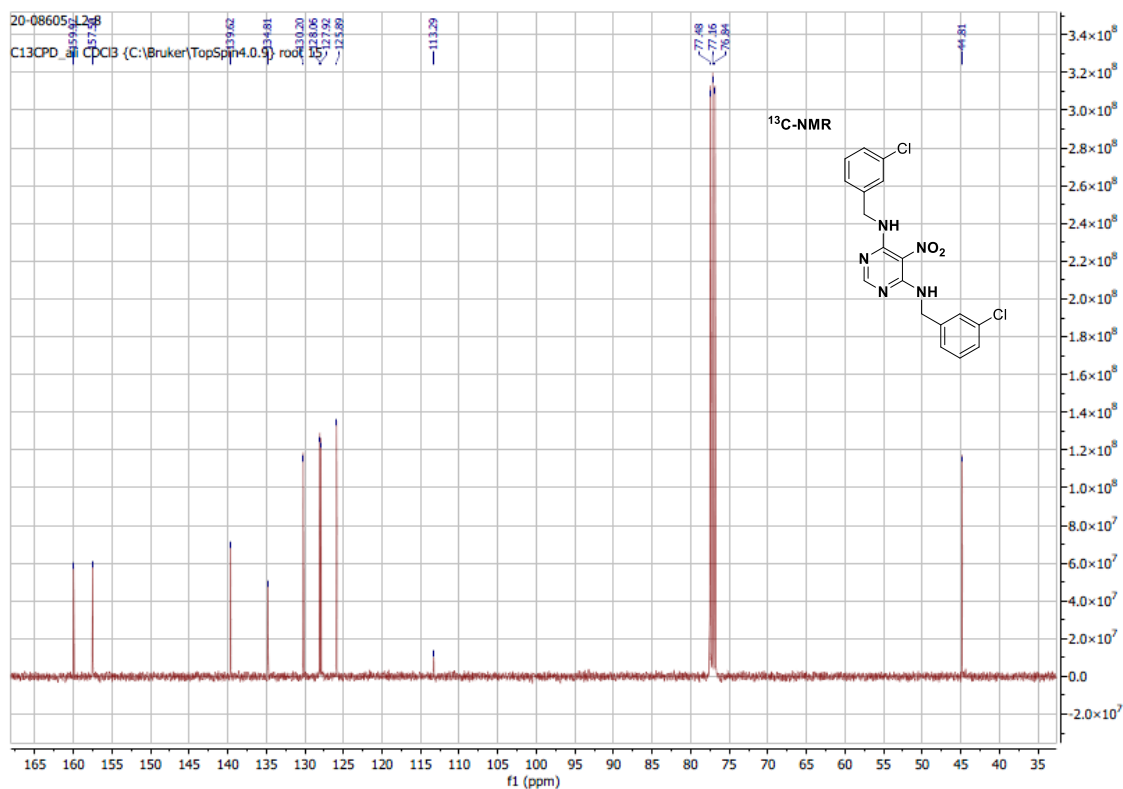
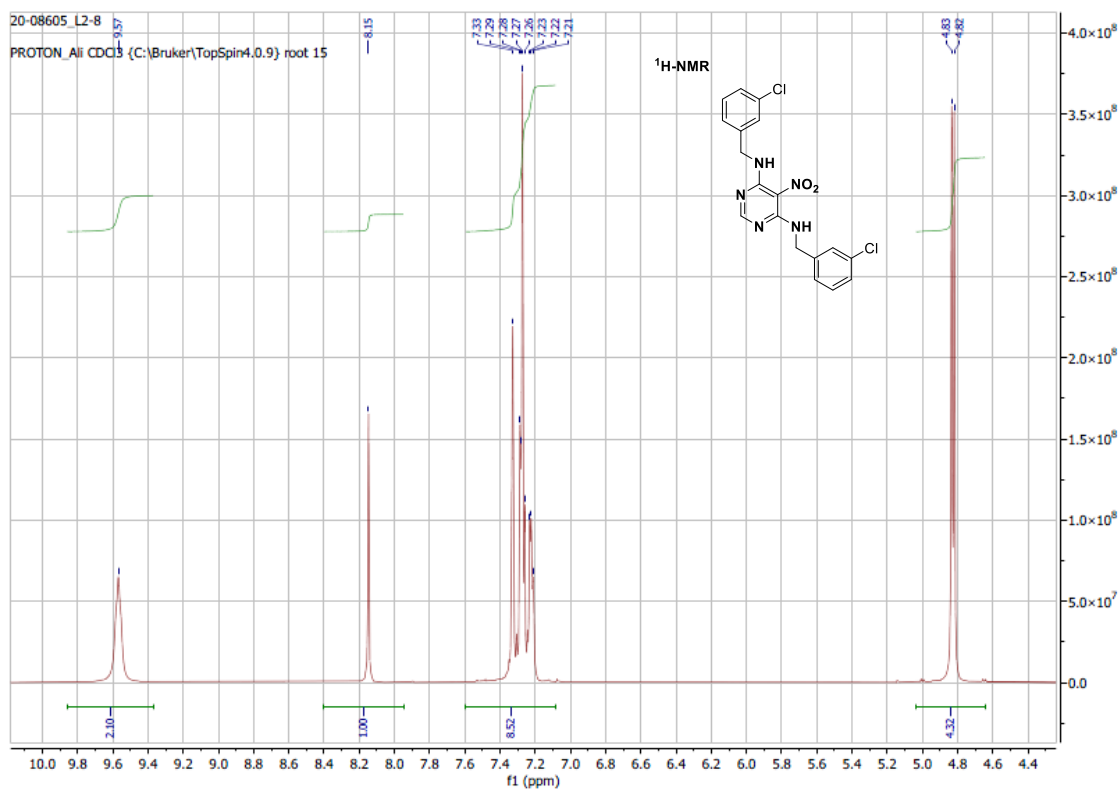
L2-8 21 (0.422) AM (Top, 1, H, 5000, 0, 0, 0, 1, 00)
 1: TOF MS ES+

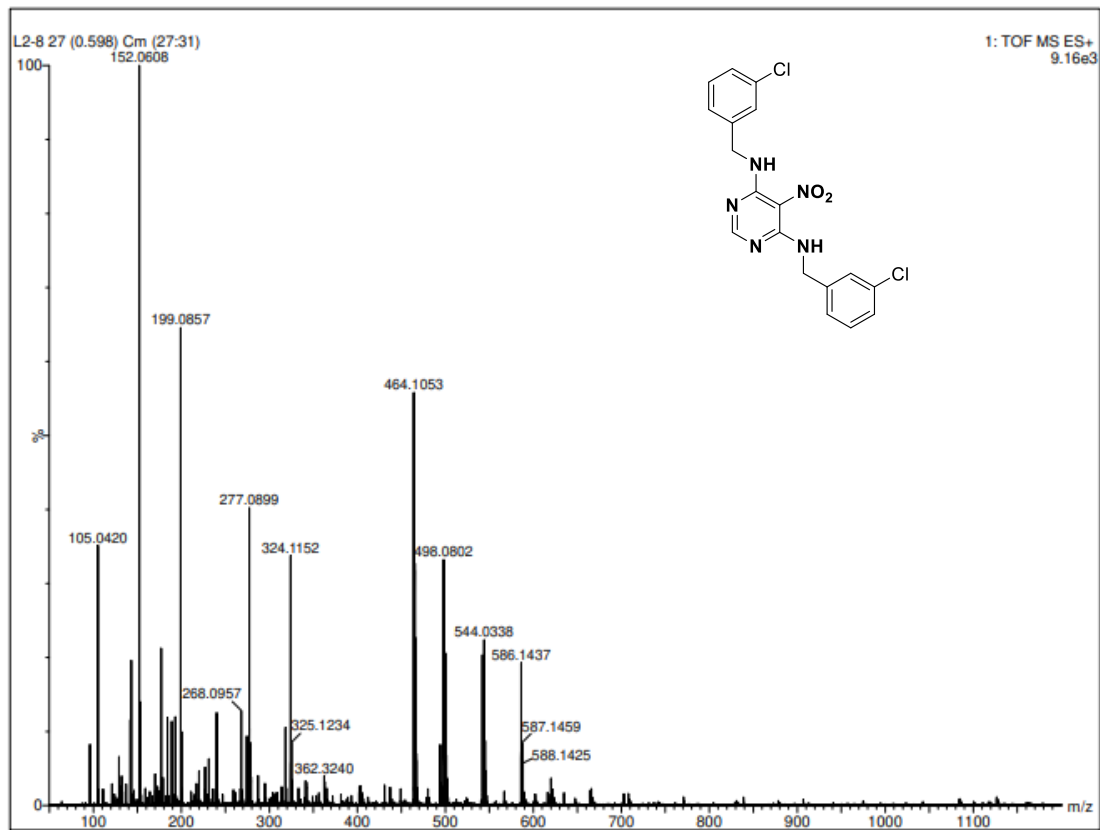
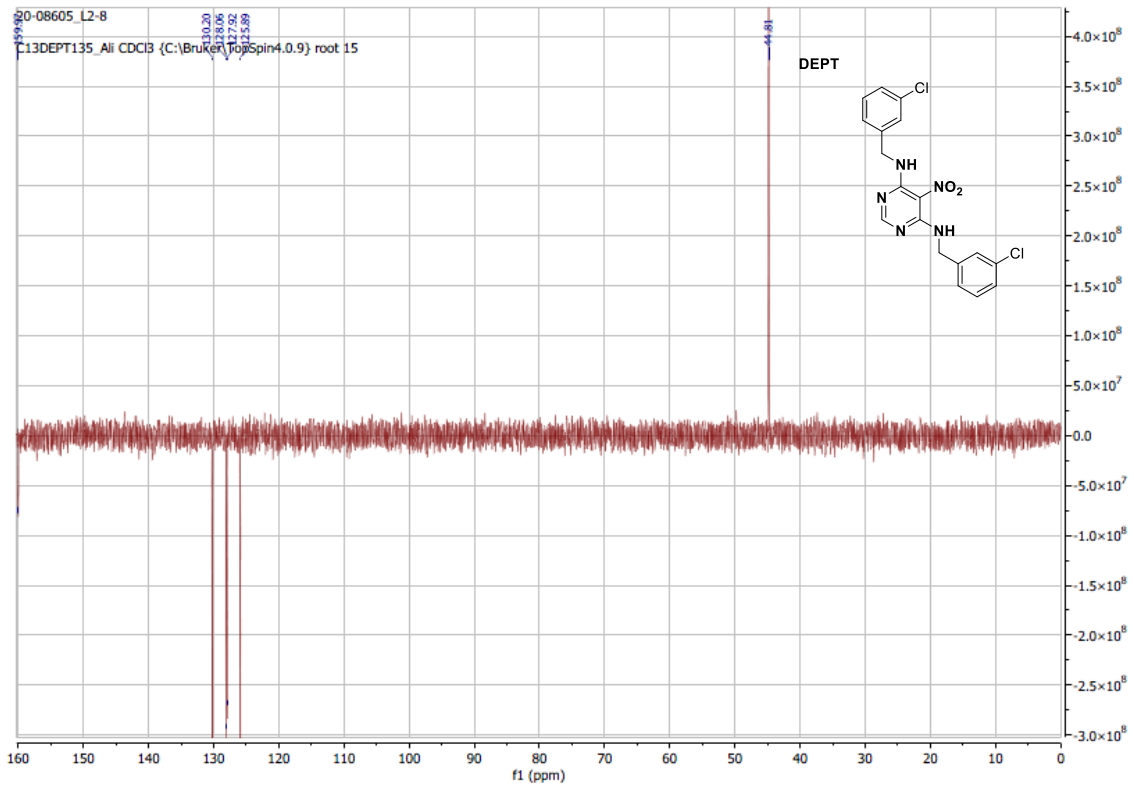


Minimum: 5.0 10.0 -1.5
 Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
519.9981	519.9984	-0.3	-0.6	12.5	17.9	0.0	C20 H20 N5 O2 Br2

• **N⁴,N⁶-bis(3-chlorobenzyl)-5-nitropyrimidine-4,6-diamine (5i):**





Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 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

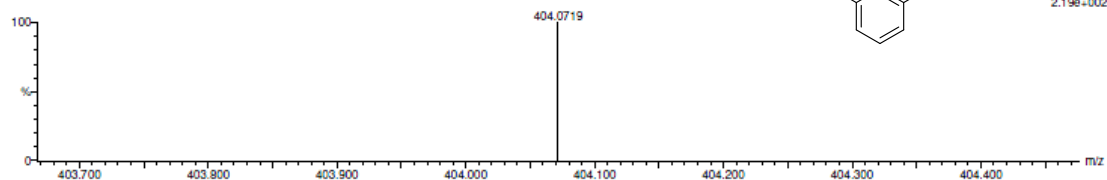
58 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

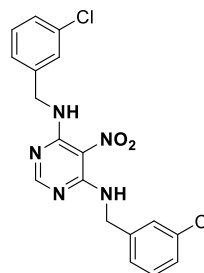
C: 0-18 H: 0-1000 N: 0-5 O: 0-2 Cl: 0-2

L2-6 27 (0.698) AM (Cen,6, 80.00, Ht,5000.0,0.00,1.00); Cm (27.31)

1: TOF MS ES+

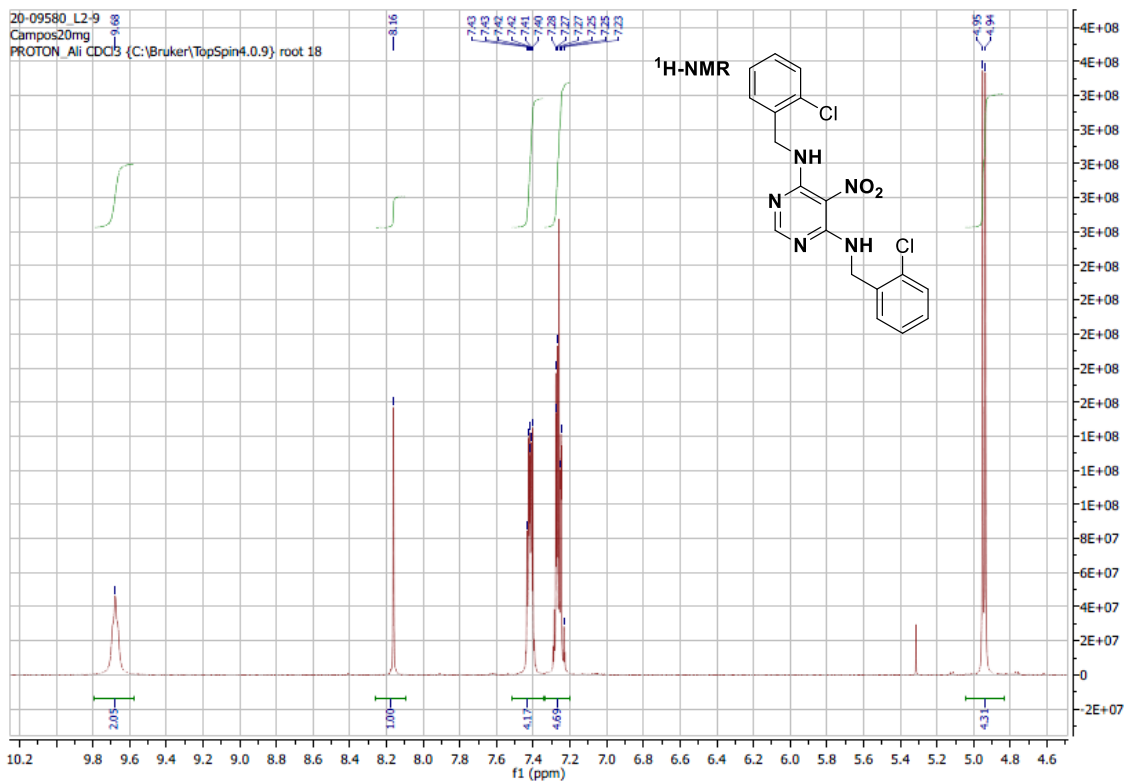


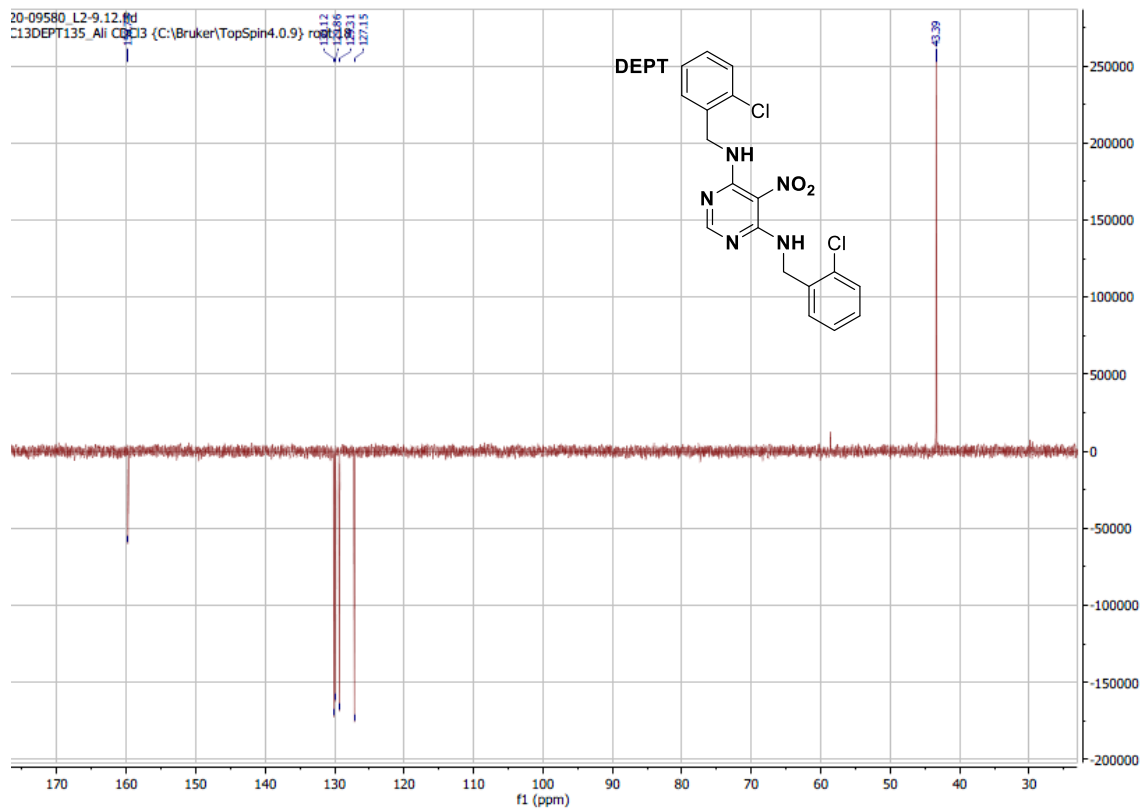
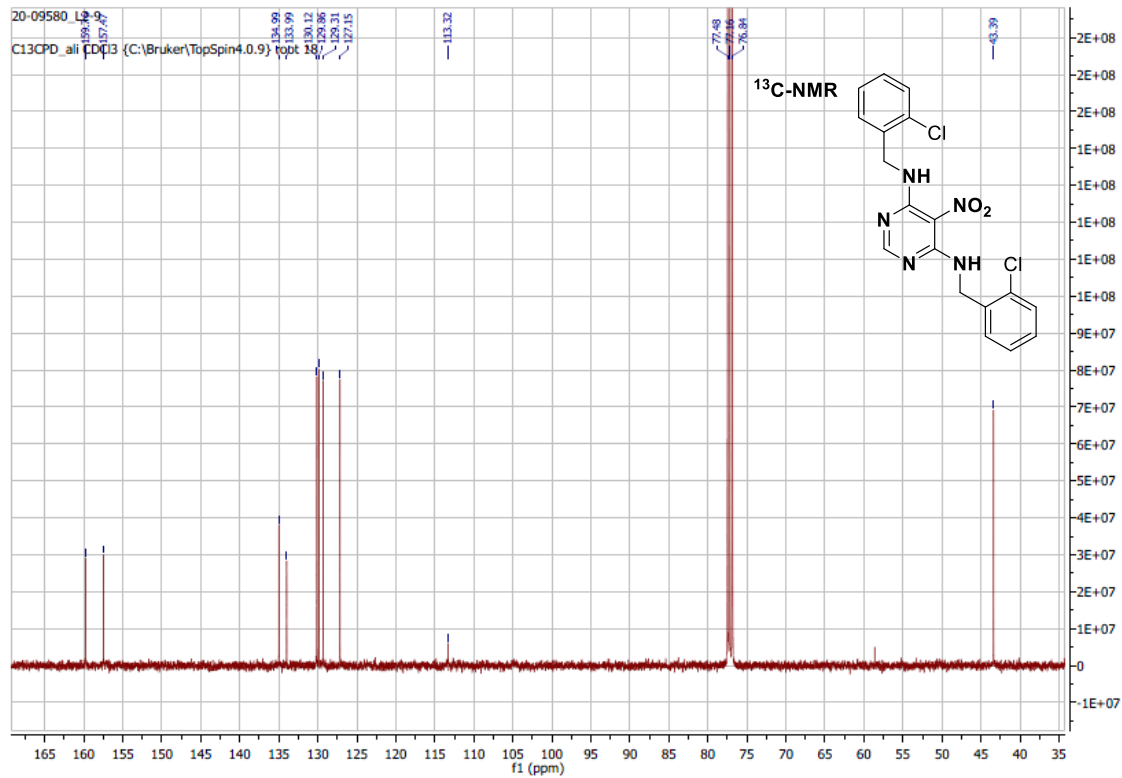
Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	1-FIT (Norm)	Formula
404.0719	404.0681	3.8	9.4	12.5	22.3	0.0	C18 H16 N5 O2 Cl2

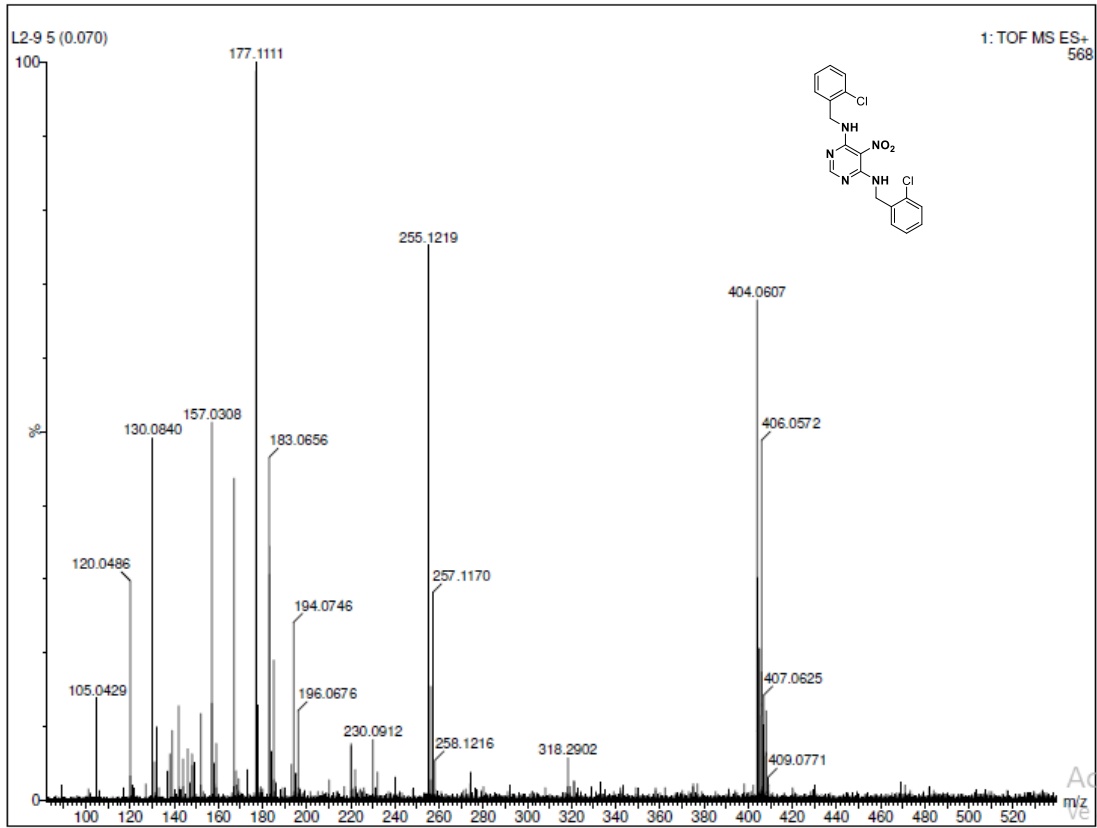


2.19e+002

- **N⁴,N⁶-bis(2-chlorobenzyl)-5-nitropyrimidine-4,6-diamine (5j):**







Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 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

145 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

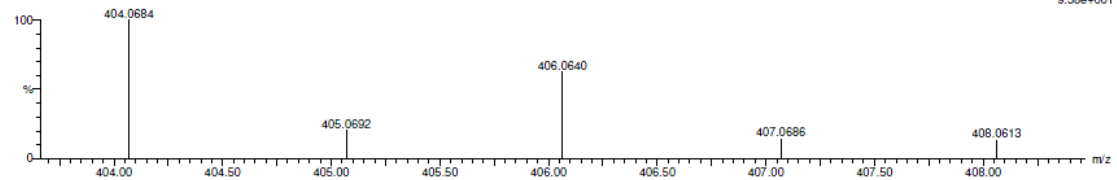
Elements Used:

C: 0-18 H: 0-1000 N: 0-5 O: 0-5 Cl: 0-2

L2-9 21 (0.422) AM (Cen.6, 100.00, Ht.5000.0,0.00,1.00)

1: TOF MS ES+

Page 1

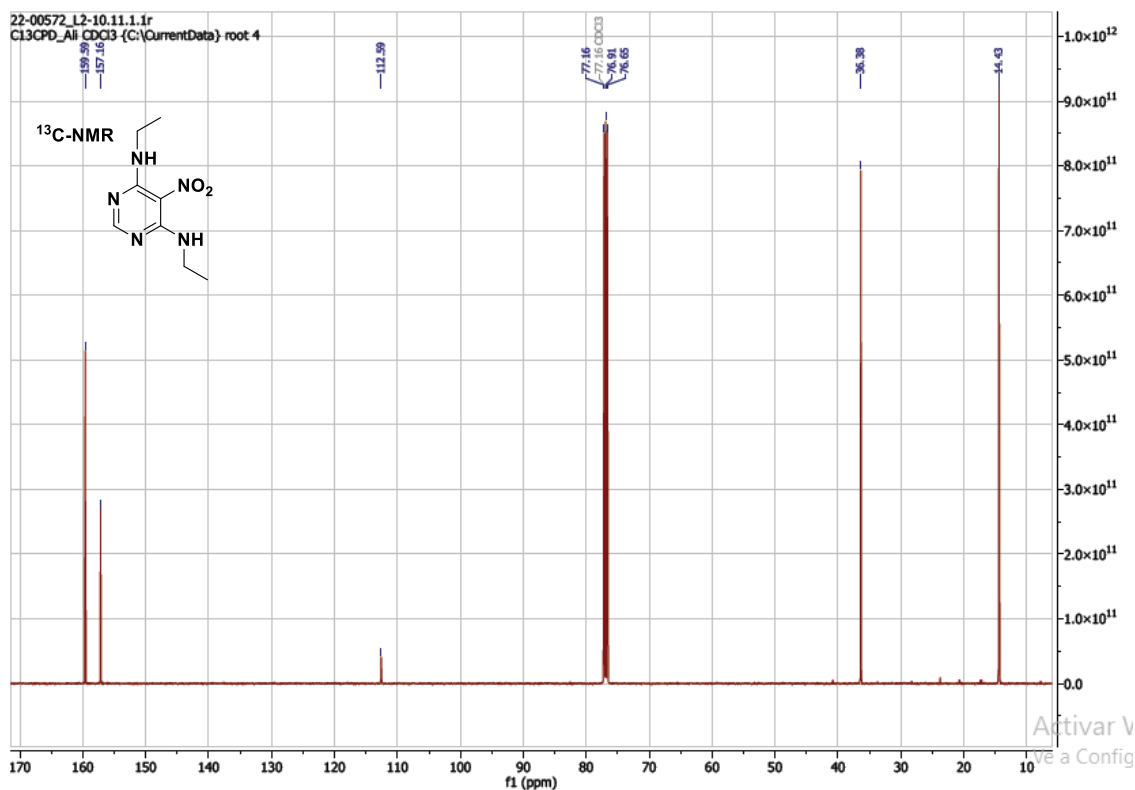
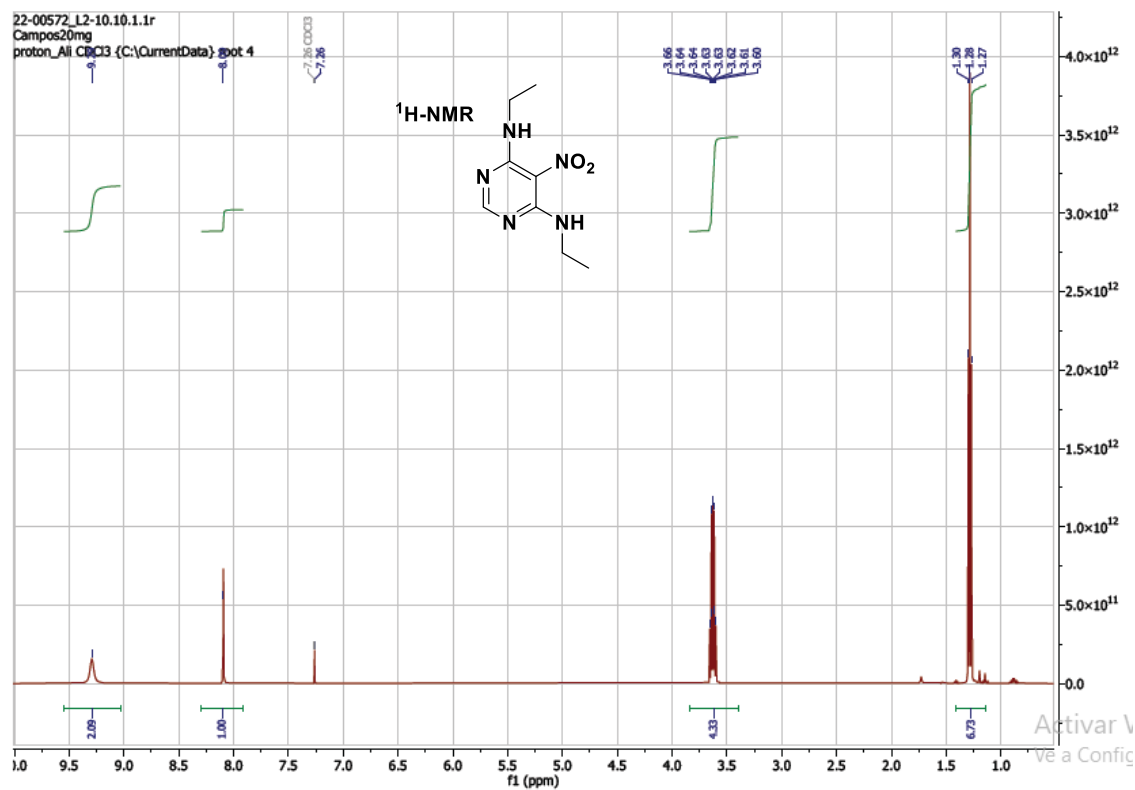


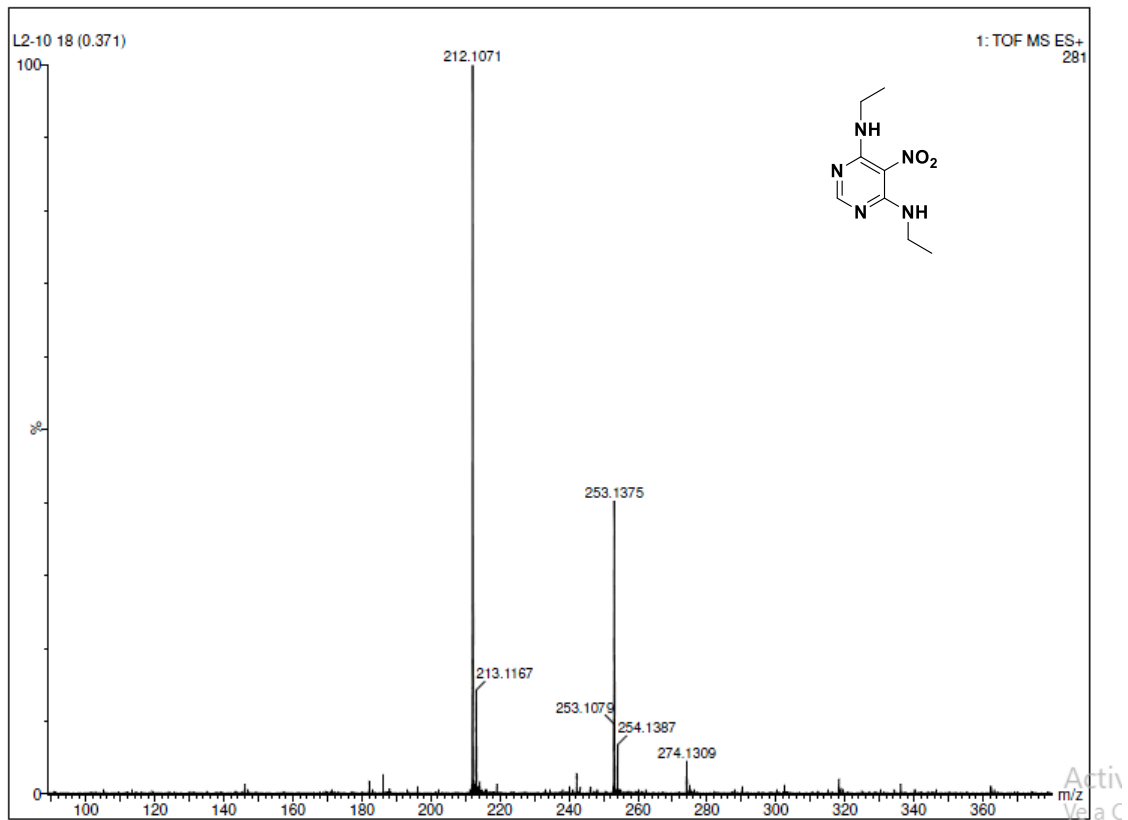
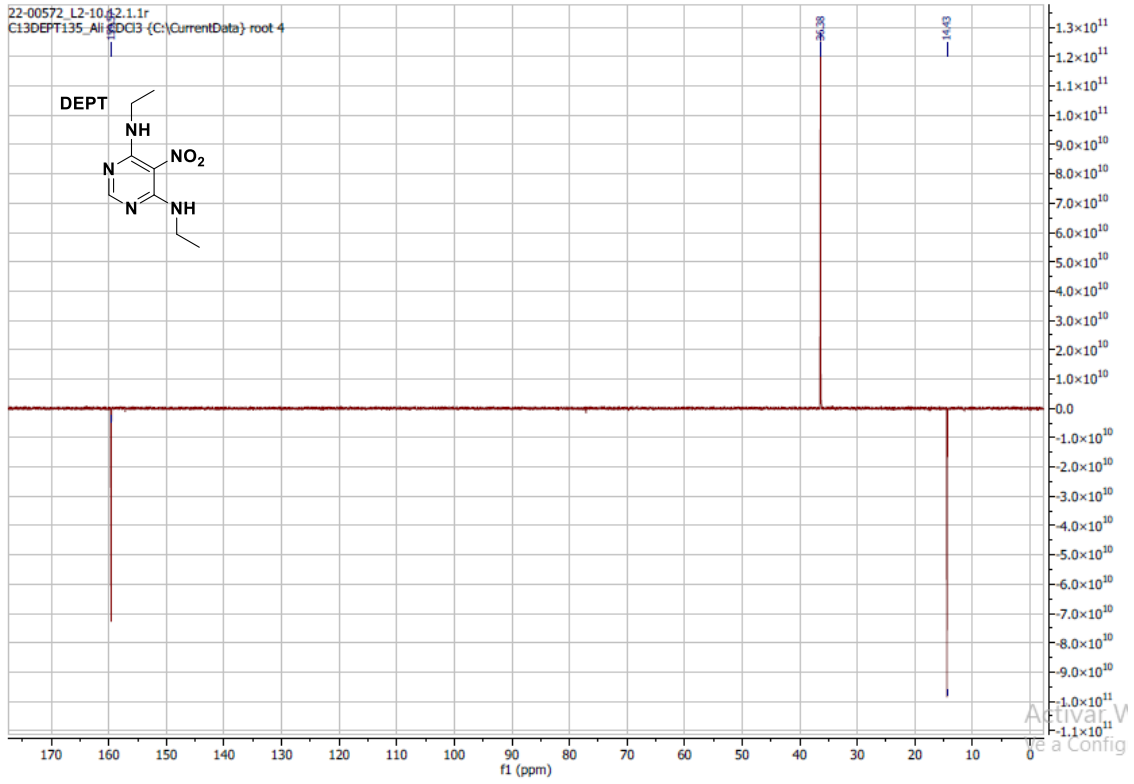
9.38e+001

Minimum: 5.0 10.0 -1.5
 Maximum: 5.0 50.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
404.0684	404.0681	0.3	0.7	12.5	5.6	0.0	C18 H16 N5 O2 Cl2

- N^4,N^6 -diethyl-5-nitropyrimidine-4,6-diamine (5k):

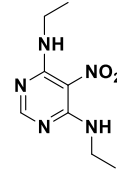




Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
 Element prediction: Off
 Number of isotope peaks used for i-FIT = 3

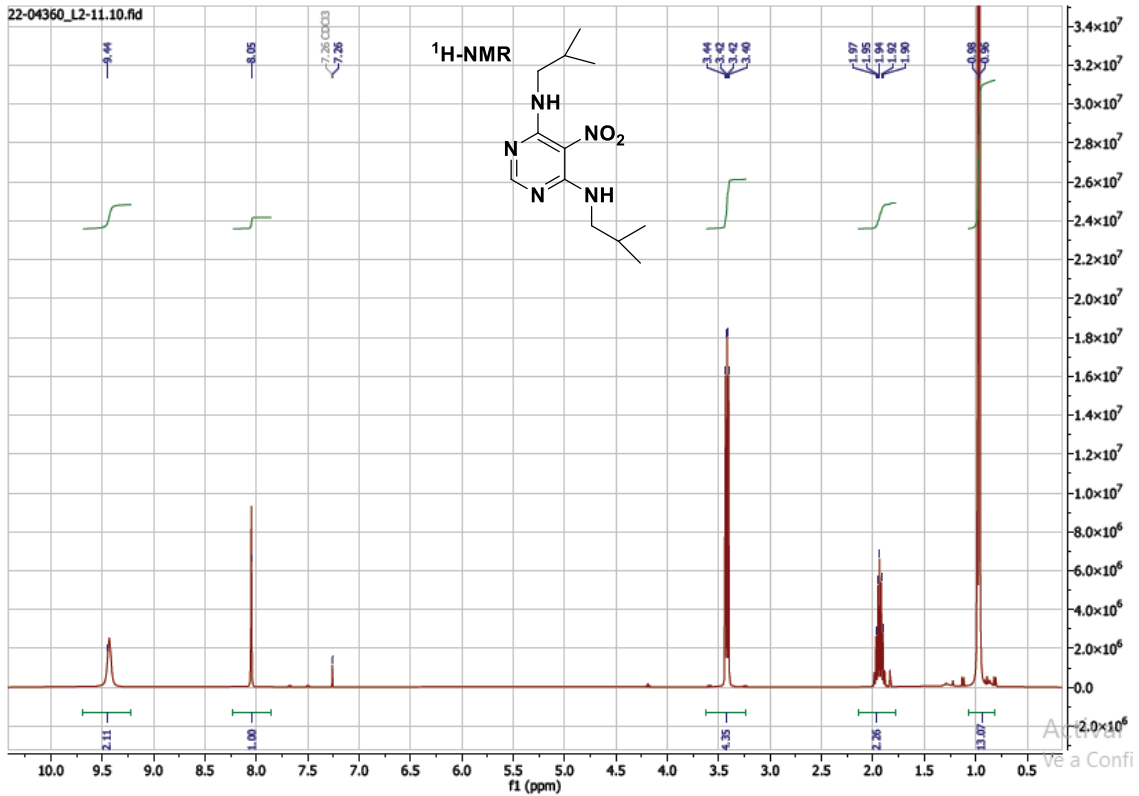


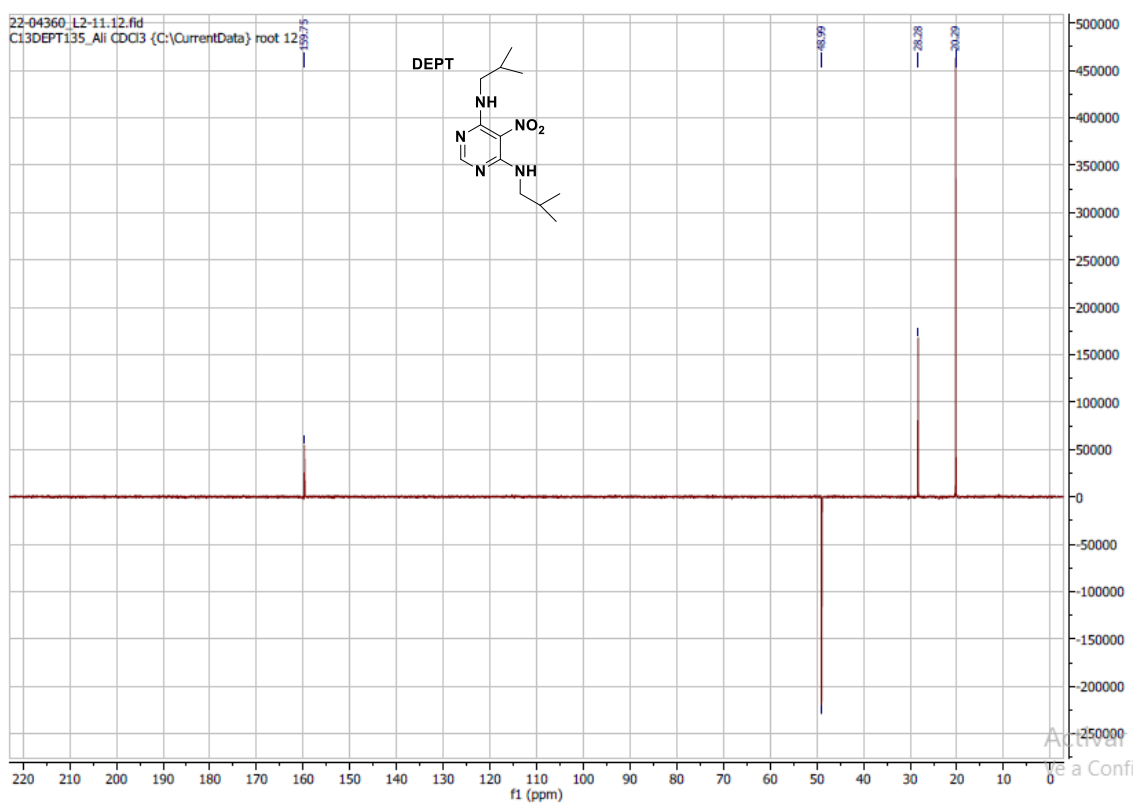
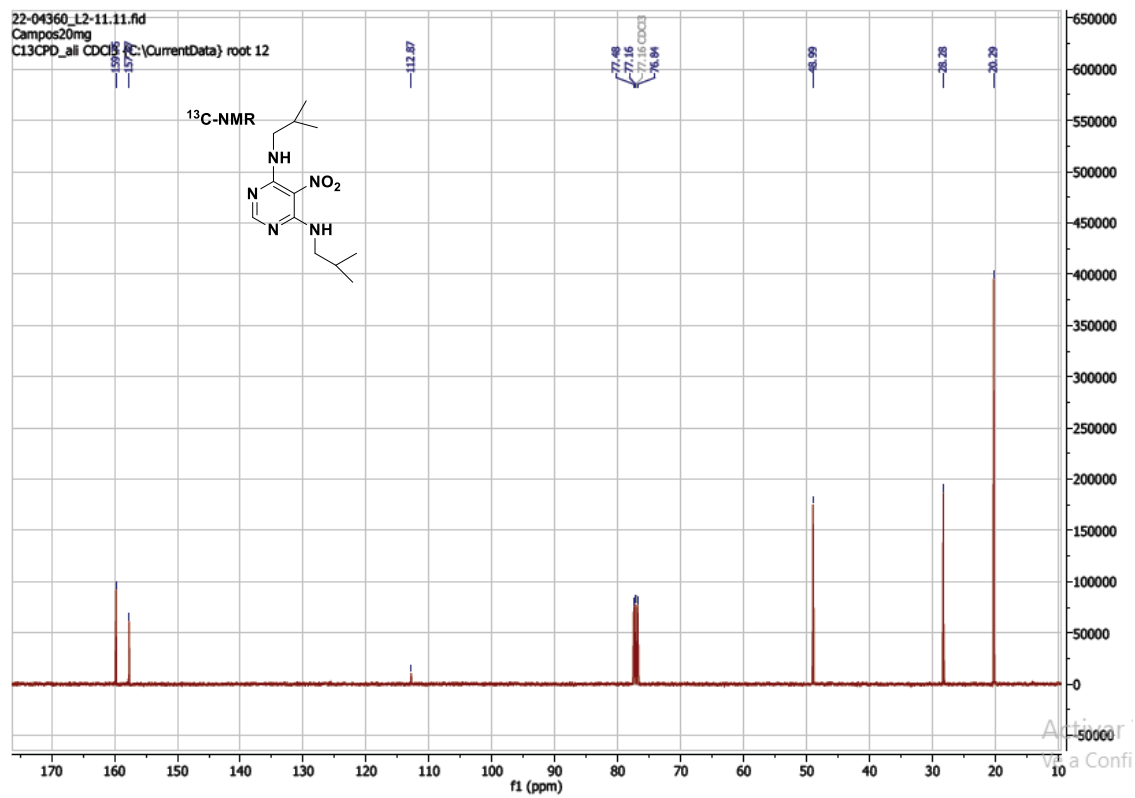
Monoisotopic Mass, Even Electron Ions
 144 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)
 Elements Used:
 C: 0-8 H: 0-1000 N: 0-8 O: 0-18
 L2:10.6 (0.145) AM (Top,6, Ht,5000.0,0.00,1.00)
 1: TOF MS ES+

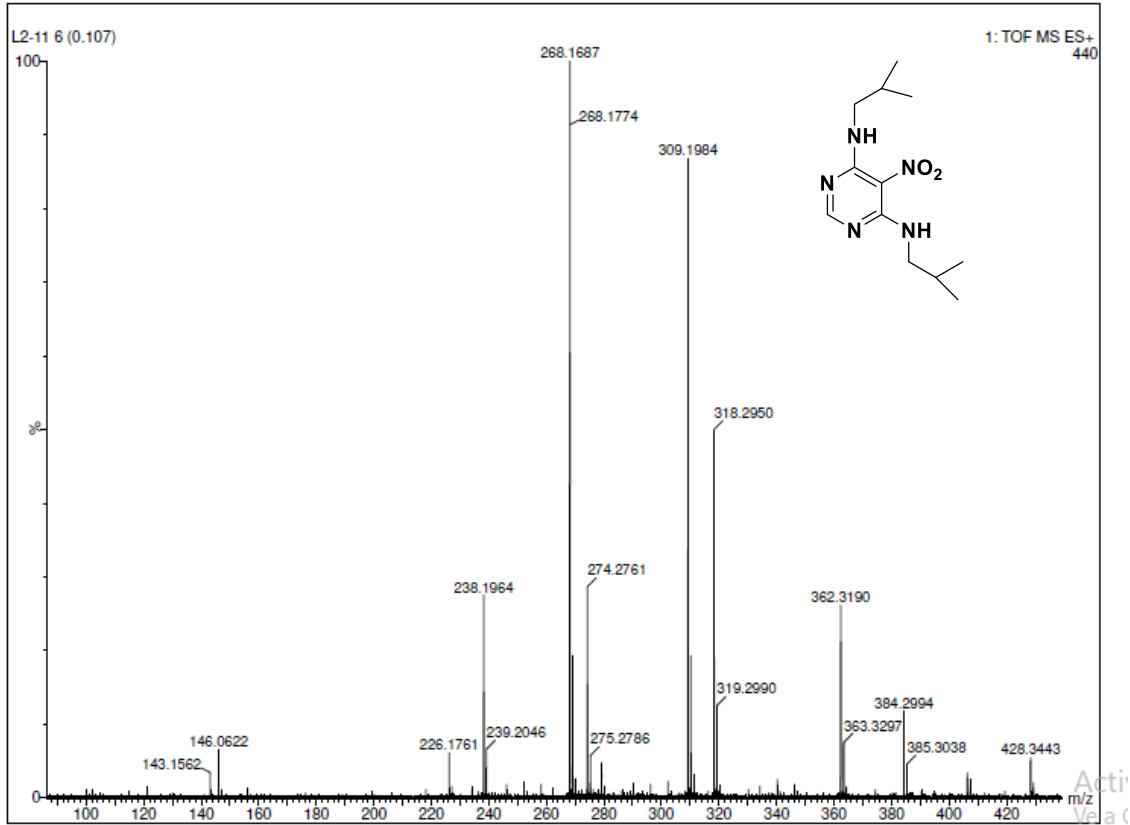


Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	1-FIT (Norm)	Formula
212.1143	212.1147	-0.4	-1.9	4.5	23.4	0.7	C8 H14 N5 O2
	212.1134	0.9	4.2	-0.5	23.5	0.7	C7 H18 N O6

- N⁴,N⁶-diisobutyl-5-nitropyrimidine-4,6-diamine (5I):







Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 10.0 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

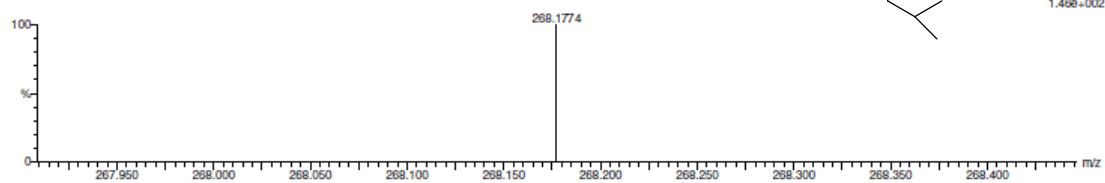
190 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 0-20 H: 0-1000 N: 0-5 O: 0-5 I: 0-1

L2-11 9 (0.158) AM (Top 6, Ht:5000.0,0.00,1.00)

1: TOF MS ES+

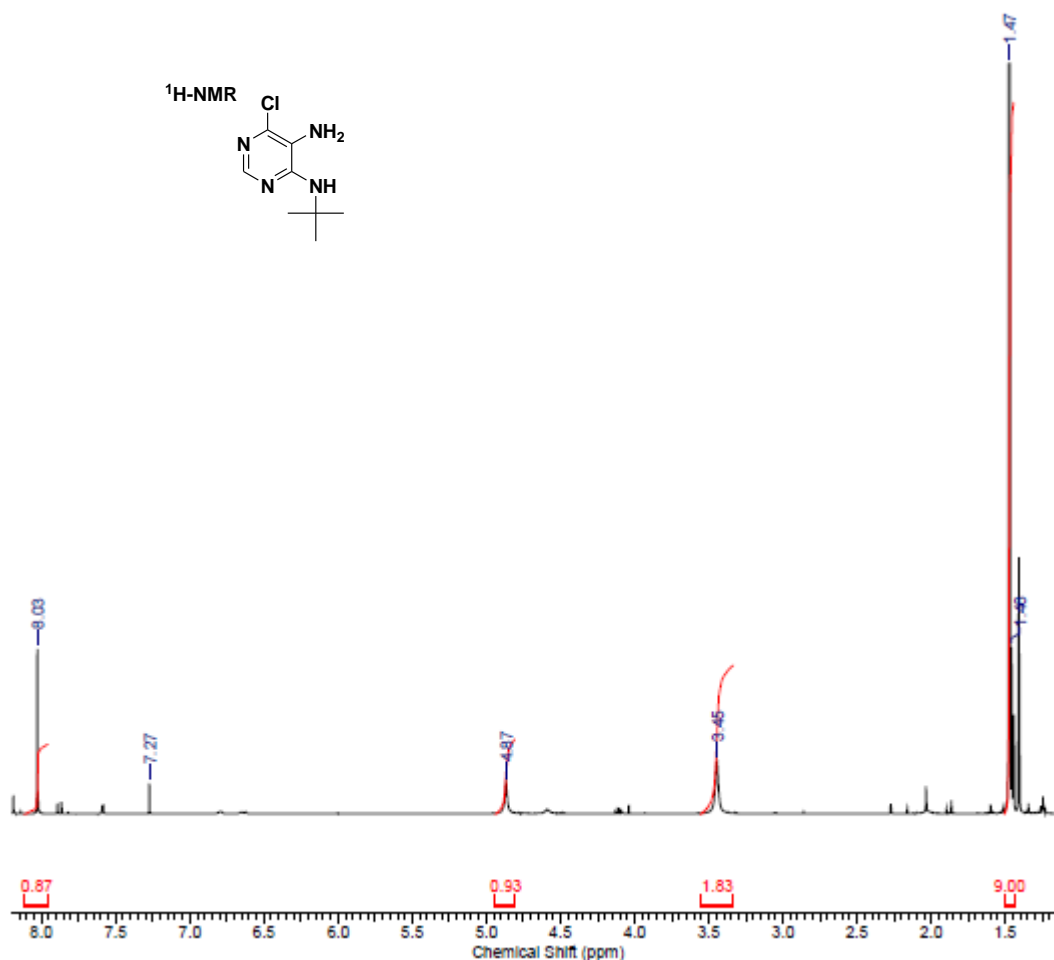


Minimum: -1.5

Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	1-FIT (Norm)	Formula
268.1774	268.1774	0.0	0.0	4.5	18.3	0.0	C12 H22 N5 O2

- 5-Amino-4-tert-butylamino-6-chloropyrimidine (6b):



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

960 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

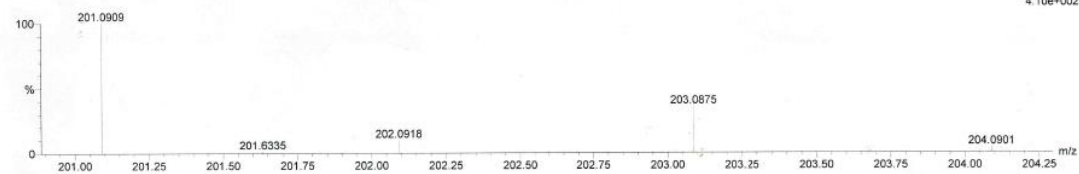
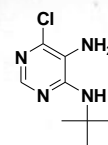
Elements Used:

C: 0-17 H: 0-1000 N: 0-10 O: 0-10 Na: 0-1 S: 0-1 Cl: 0-1

PRE-TB-F dilu 9 (0.217)

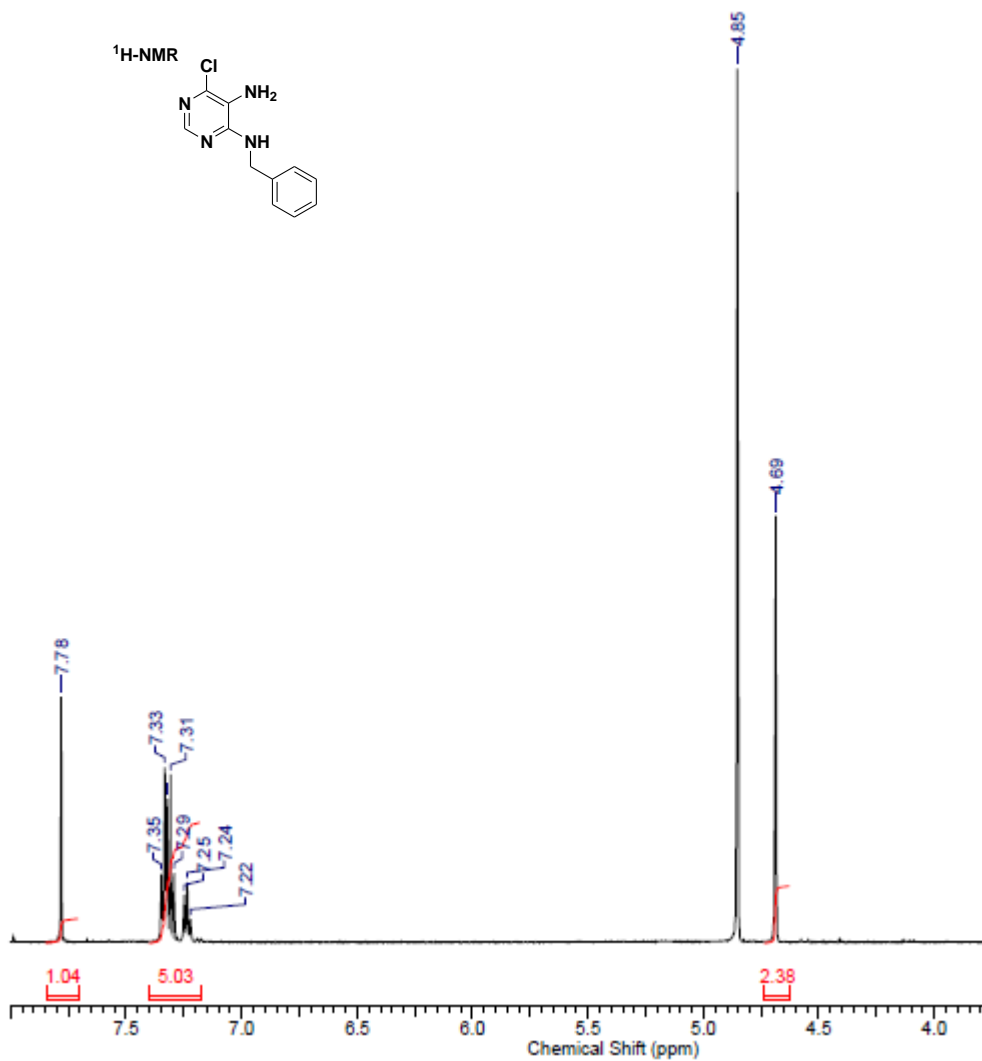
1: TOF MS ES+

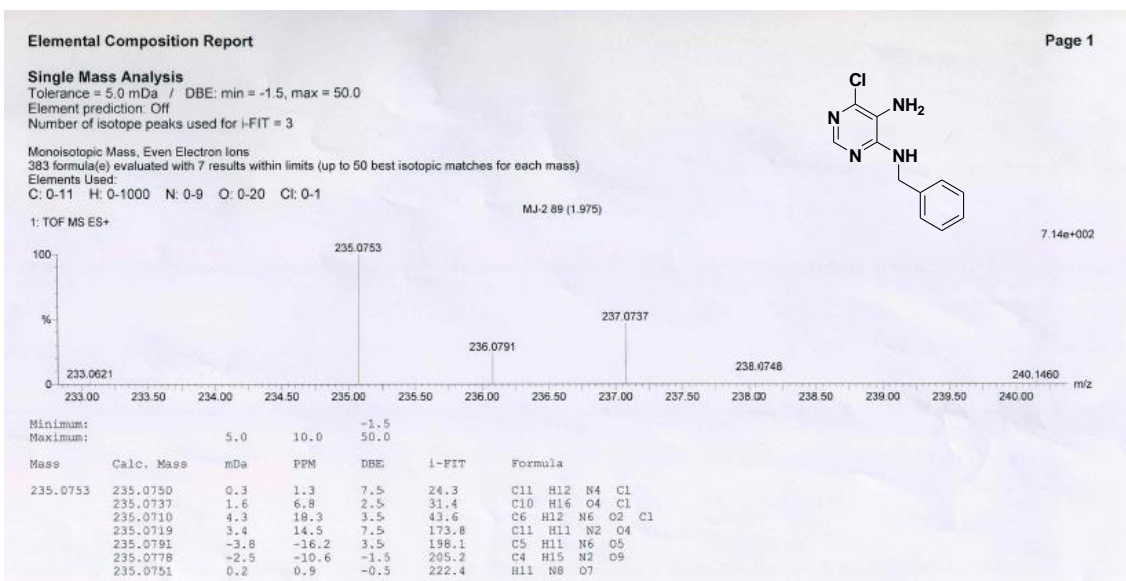
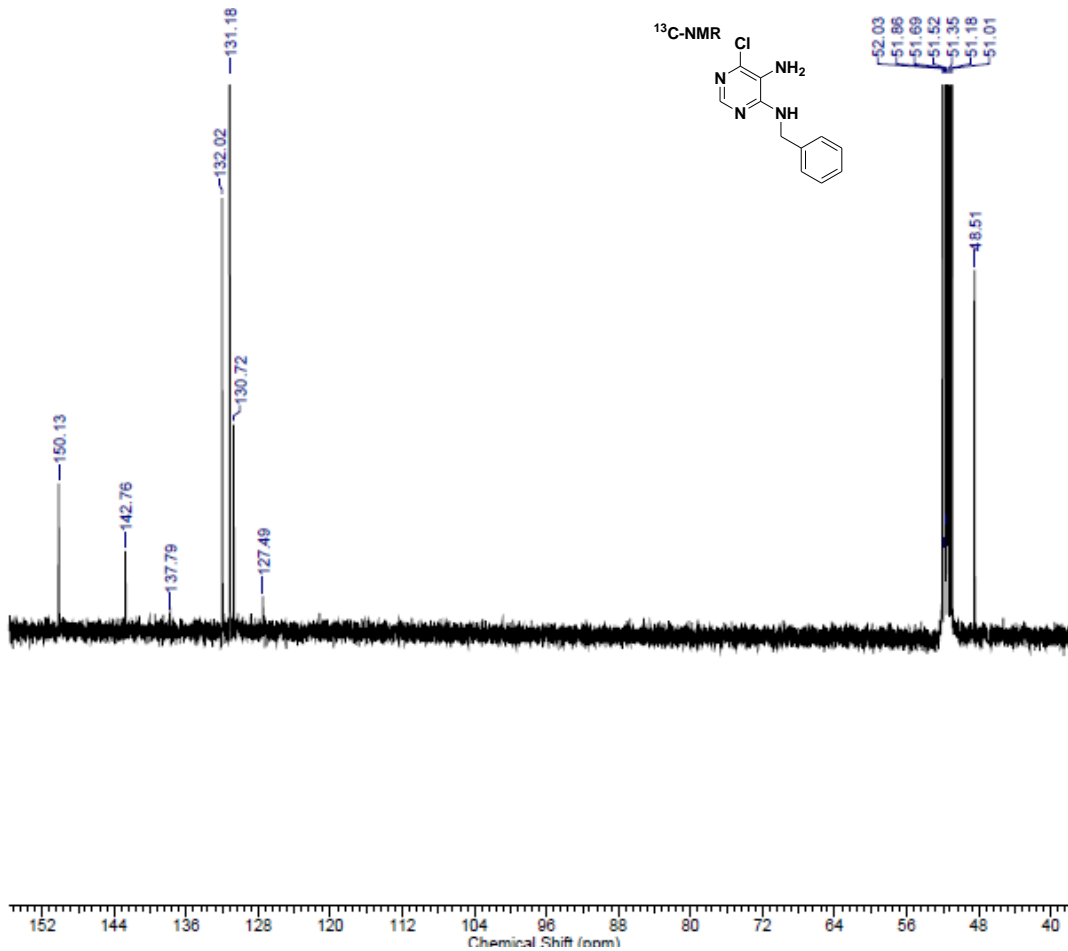
Page 1



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
201.0909	201.0907	0.2	1.0	3.5	0.6	C9 H14 N4 Cl
	201.0909	0.0	0.0	-1.5	92.4	C5 H17 N2 O4 S
	201.0916	-0.7	-3.5	7.5	72.7	C13 H13 O2

- 5-Amino-4-benzylamino-6-chloropyrimidine (6c):



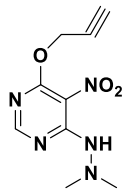


Elemental Composition Report

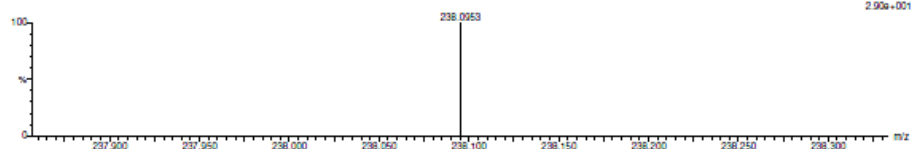
Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: CH
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
212 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-19 H: 0-1000 N: 0-6 O: 0-4 Na: 0-1
ALM-15 57 (1.252) AM (Top, 1, H: 5000 0.0, 0.0, 1.00)
1: TOF MS ES+



Page 1



Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	1-FIT (Norm)	Formula
238.0953	238.0940	1.3	5.5	6.5	12.7	0.5	C9 H12 N5 O3
	238.0956	-0.3	-1.3	7.5	13.1	0.9	C12 H13 N3 O Na

Ac