

Supplementary Materials

Development of Pleiotropic TrkB and 5-HT₄ Receptor Ligands as Neuroprotective Agents

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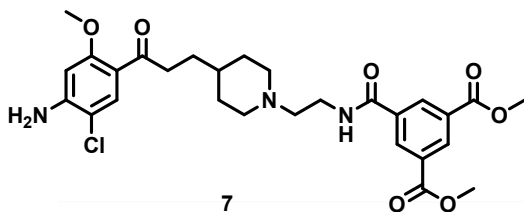
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Analytical spectrum of compounds 7 – 19

1,3-dimethyl-5-[(2-{4-[3-(4-amino-5-chloro-2-methoxyphenyl)-3-oxopropyl]piperidin-1-yl}ethyl)carbamoyl]benzene-1,3-dicarboxylate carbamate (7)



Elemental Composition Report

Page 6

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

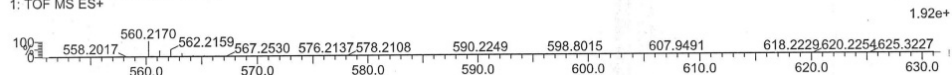
13720 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 28-28 H: 35-35 B: 0-1 N: 0-200 O: 0-200 Na: 0-1 Cl: 0-8

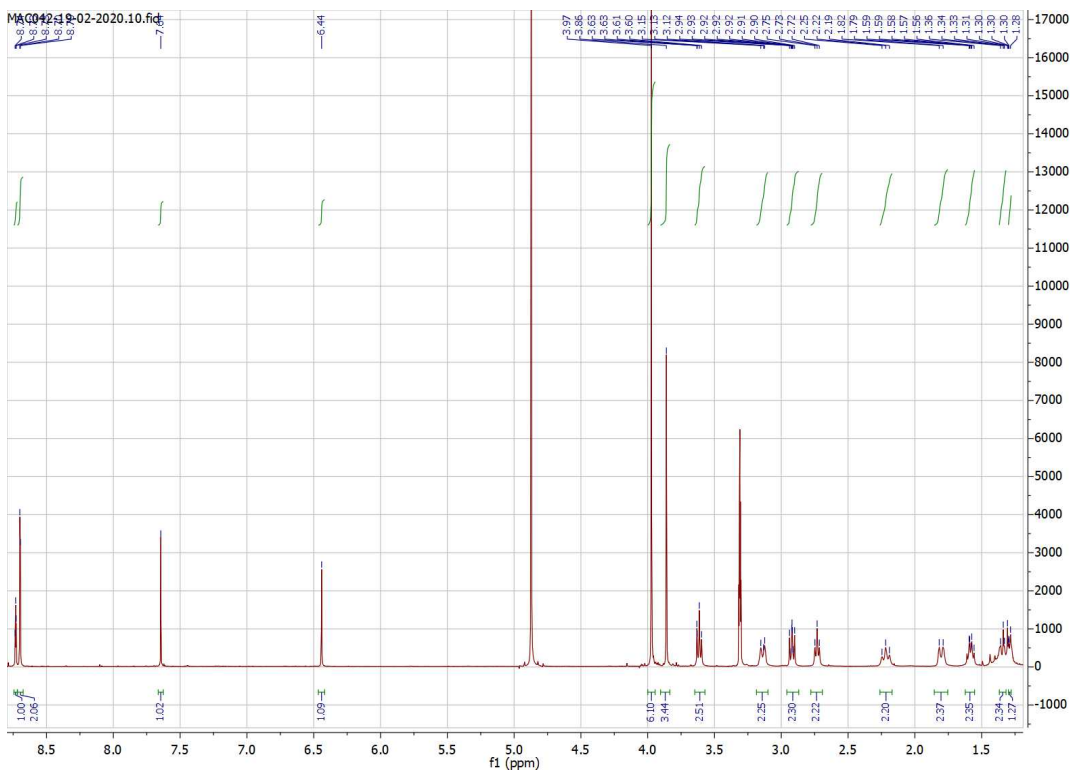
MAC042 187 (1.710) Cm (180:216)

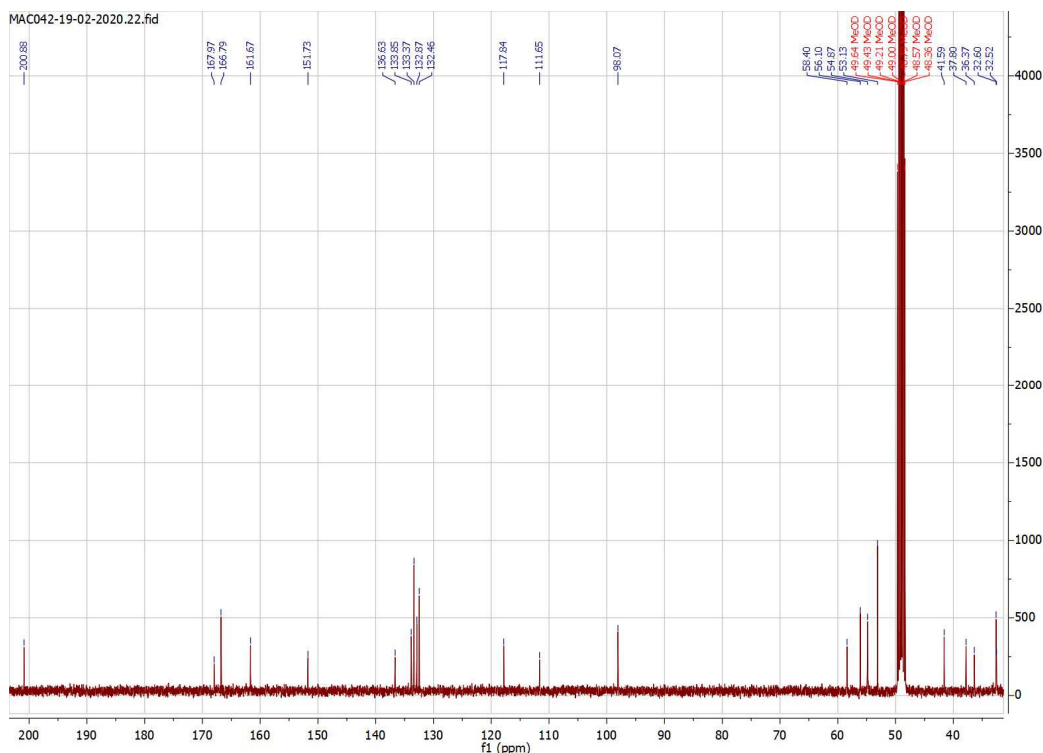
1: TOF MS ES+



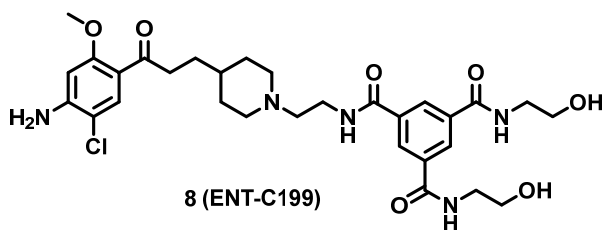
Minimum: -1.5
Maximum: 5.0 5.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
560.2170	560.2164	0.6	1.1	12.5	1604.2	n/a	n/a	C ₂₈ H ₃₅ N ₃ O ₇ Cl





*N*¹-(2-{4-[3-(4-amino-5-chloro-2-methoxyphenyl)-3-oxopropyl]piperidin-1-yl}ethyl)-*N*³,*N*⁵-bis(2-hydroxyethyl)benzene-1,3,5-tricarboxamide (**8**)



Elemental Composition Report

Page 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 = 5

Monoisotopic Mass, Even Electron Ions

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

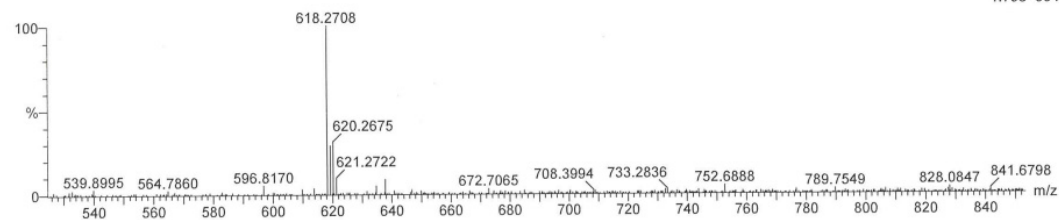
Elements Used:

C: 0-30 H: 0-1000 N: 0-6 O: 0-8 35Cl: 0-1

CERMN_MAC_D43 145 (1.364) Cm (144:145-(135:139+203:210))

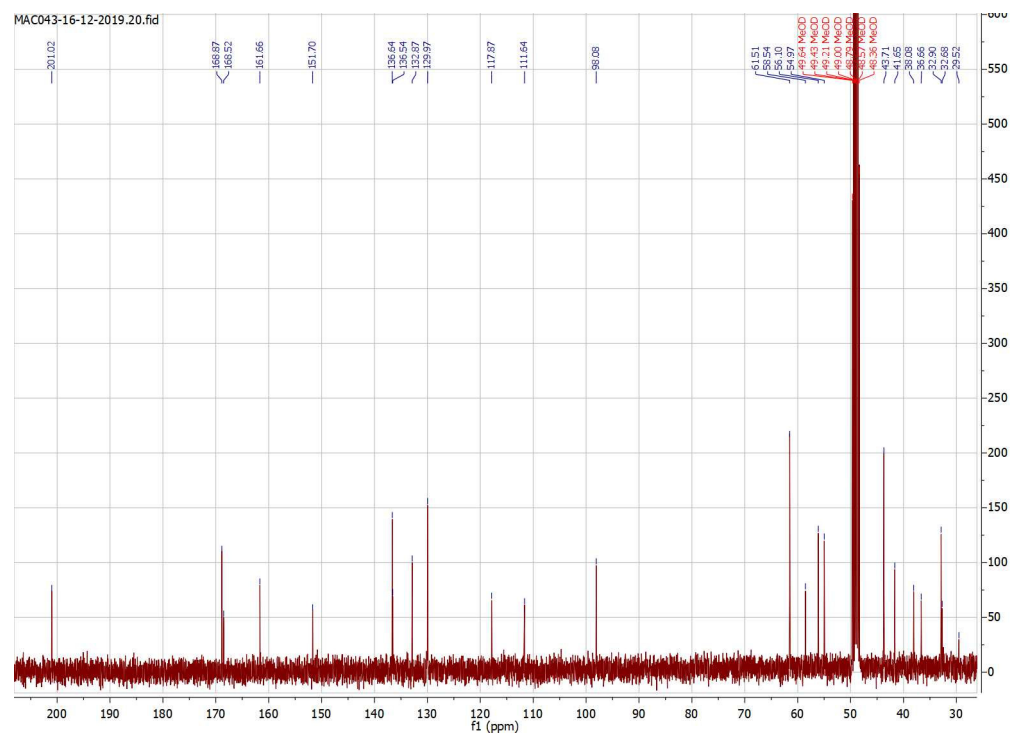
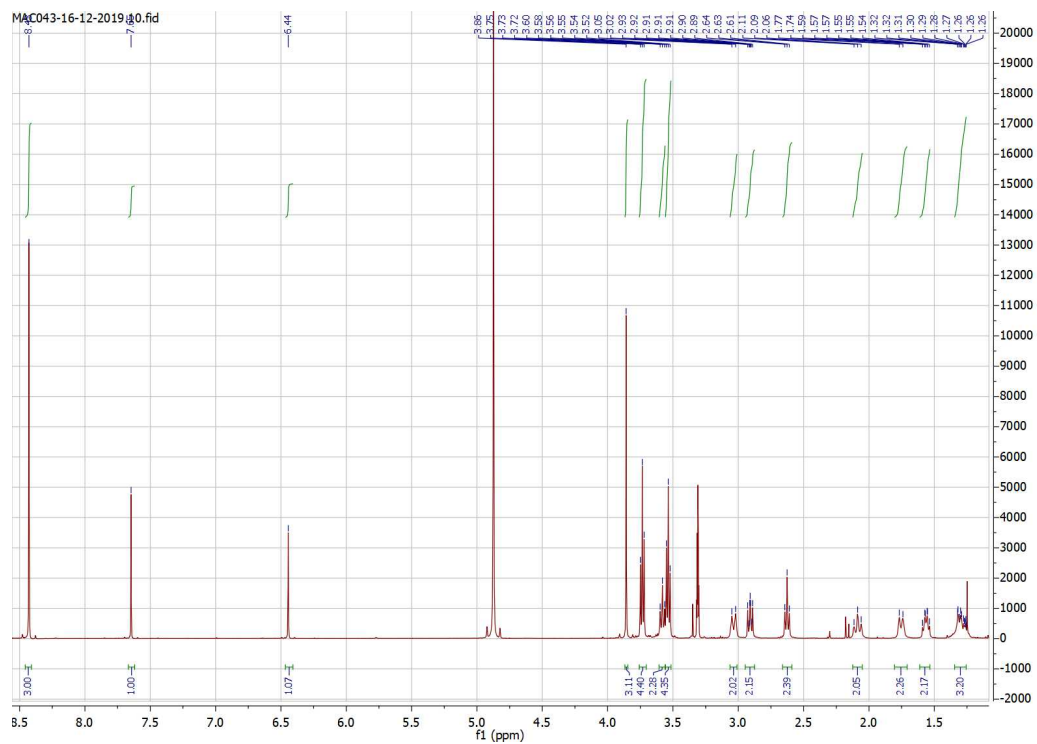
1: TOF MS ES⁺

1.79e+004

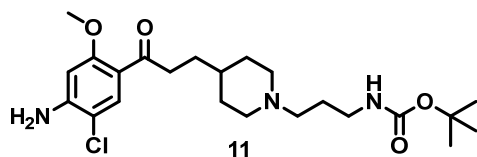


Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
618.2708	618.2695	1.3	2.1	12.5	72.1	n/a	n/a	C30 H41 N5 O7 35Cl



Tert-butyl-(3-(4-(3-(4-amino-5-chloro-2-methoxyphenyl)-3-oxopropyl)piperidin-1-yl)propyl)carbamate
(11)



Elemental Composition Report

Page 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

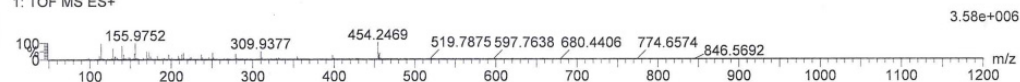
323 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-31 H: 0-100 N: 0-4 O: 0-6 Cl: 0-1

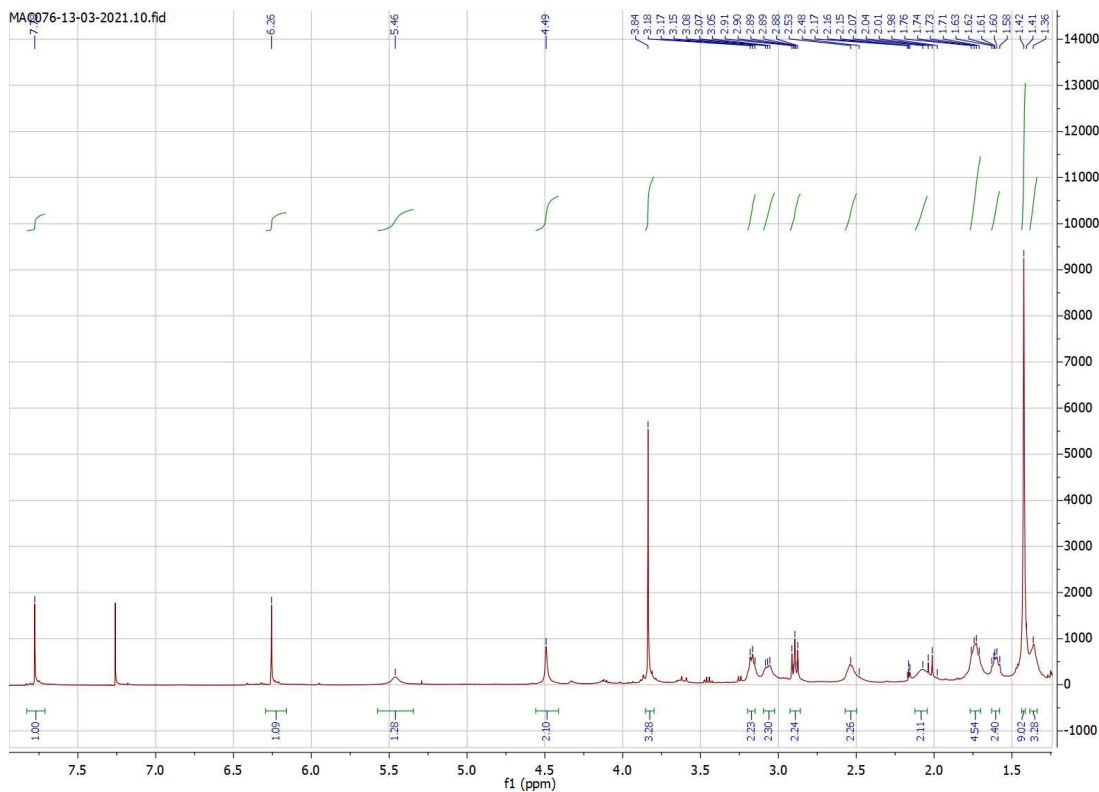
MAC076 181 (1.698) Cm (181:186)

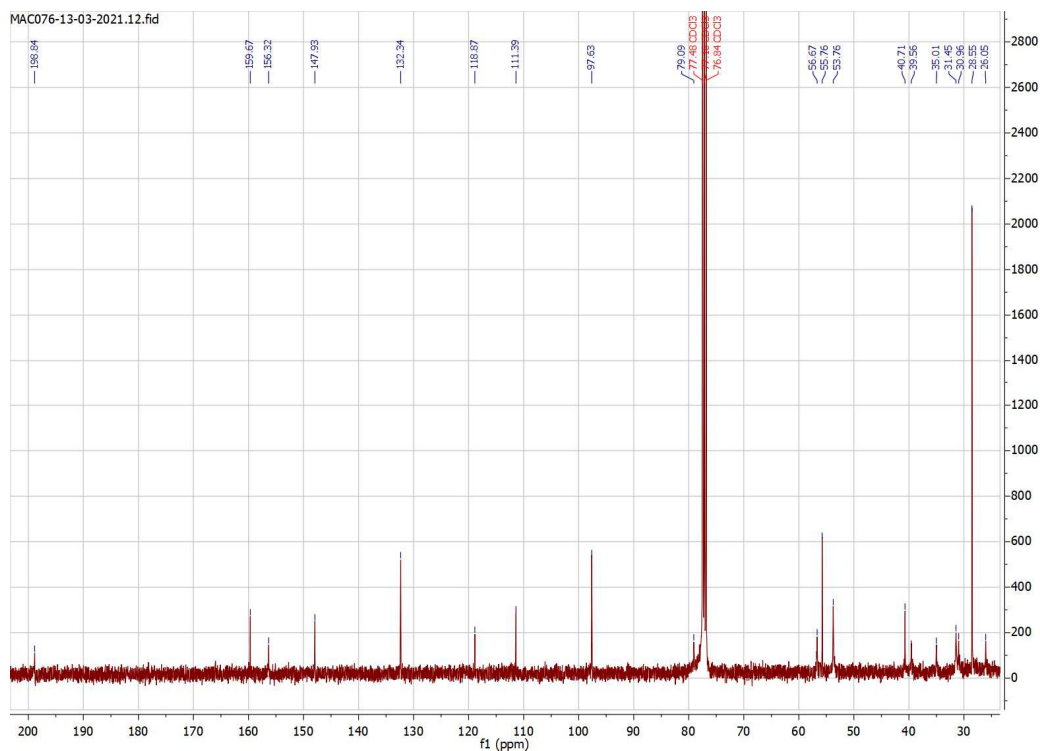
1: TOF MS ES+



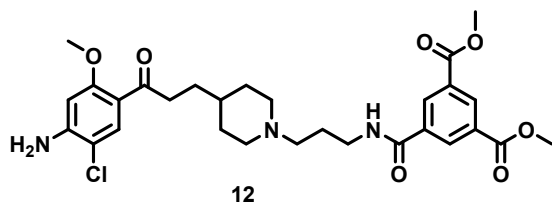
Minimum: -1.5
Maximum: 5.0 5.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
454.2469	454.2473	-0.4	-0.9	6.5	1716.8	n/a	n/a	C23 H37 N3 O4 Cl





1,3-dimethyl-5-[(2-{4-[3-(4-amino-5-chloro-2-methoxyphenyl)-3-oxopropyl]piperidin-1-yl}propyl)carbamoyl]benzene-1,3-dicarboxylate (12)



Elemental Composition Report

Page 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

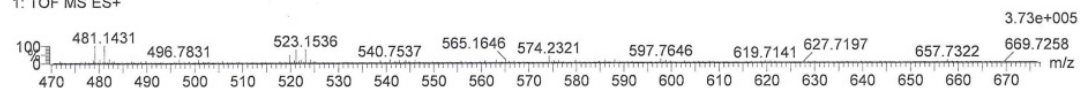
123 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-31 H: 0-100 N: 0-4 O: 0-7 Cl: 0-1

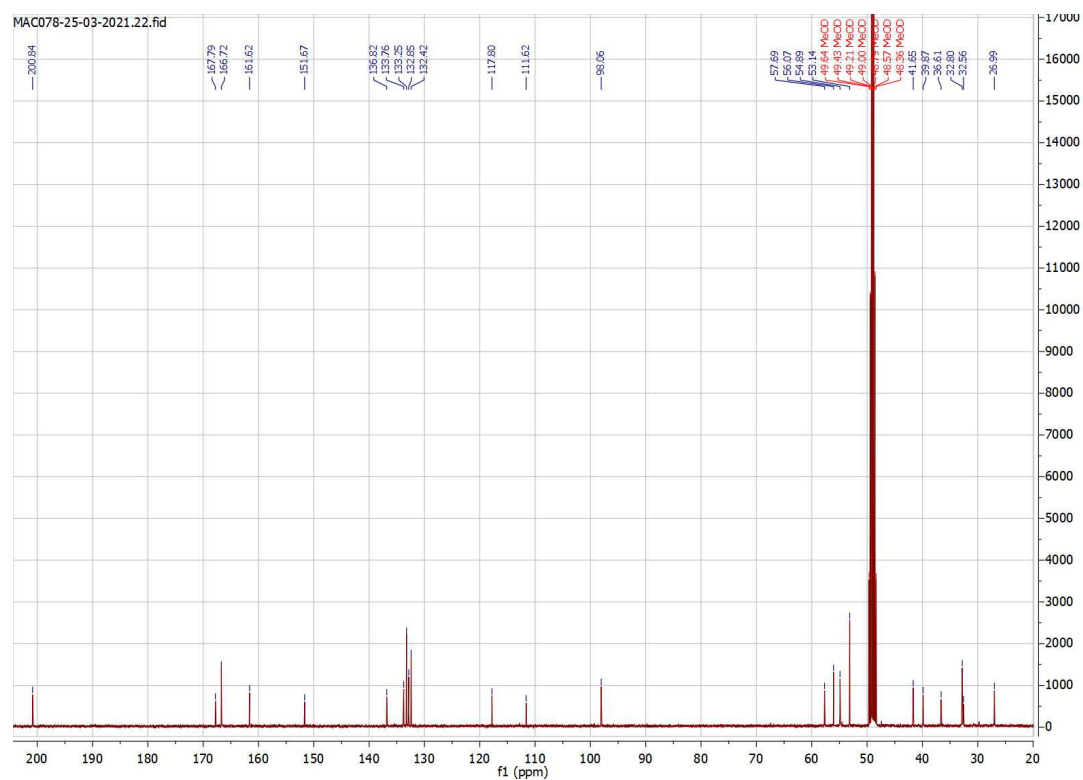
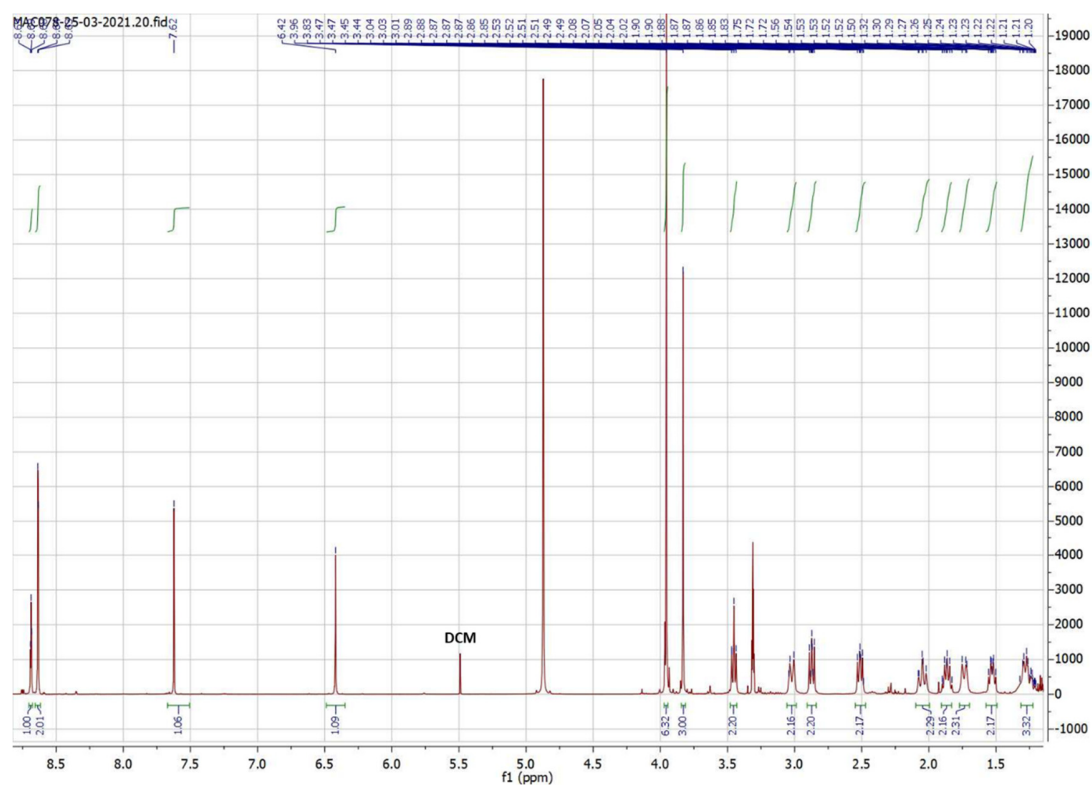
MAC078 230 (2.146) Cm (230:237)

1: TOF MS ES+

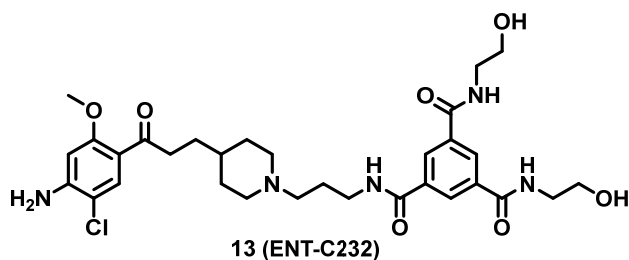


Minimum: -1.5
Maximum: 5.0 5.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
574.2321	574.2320	0.1	0.2	12.5	1562.9	n/a	n/a	C29 H37 N3 O7 Cl



*N*¹-(3-(4-(3-(4-amino-5-chloro-2-methoxyphenyl)-3-oxopropyl)piperidin-1-yl)propyl)-*N*³,*N*⁵-bis(2-hydroxyethyl)benzene-1,3,5-tricarboxamide (13)



Elemental Composition Report

Page 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

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

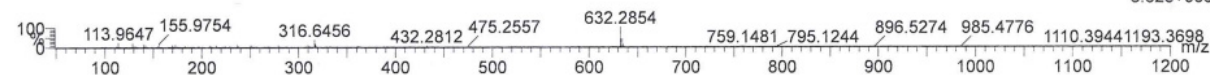
Elements Used:

C: 0-31 H: 0-100 N: 0-5 O: 0-7 Cl: 0-1

MAC079 148 (1.391) Cm (145:148)

1: TOF MS ES+

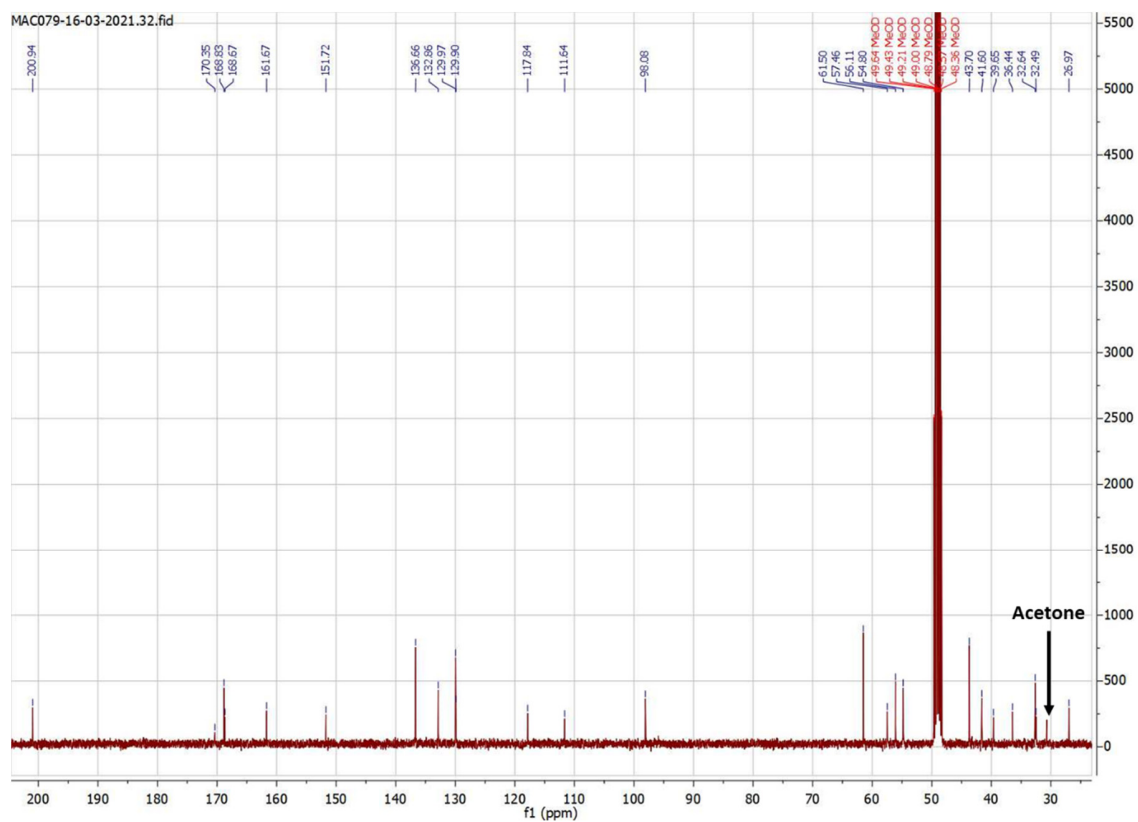
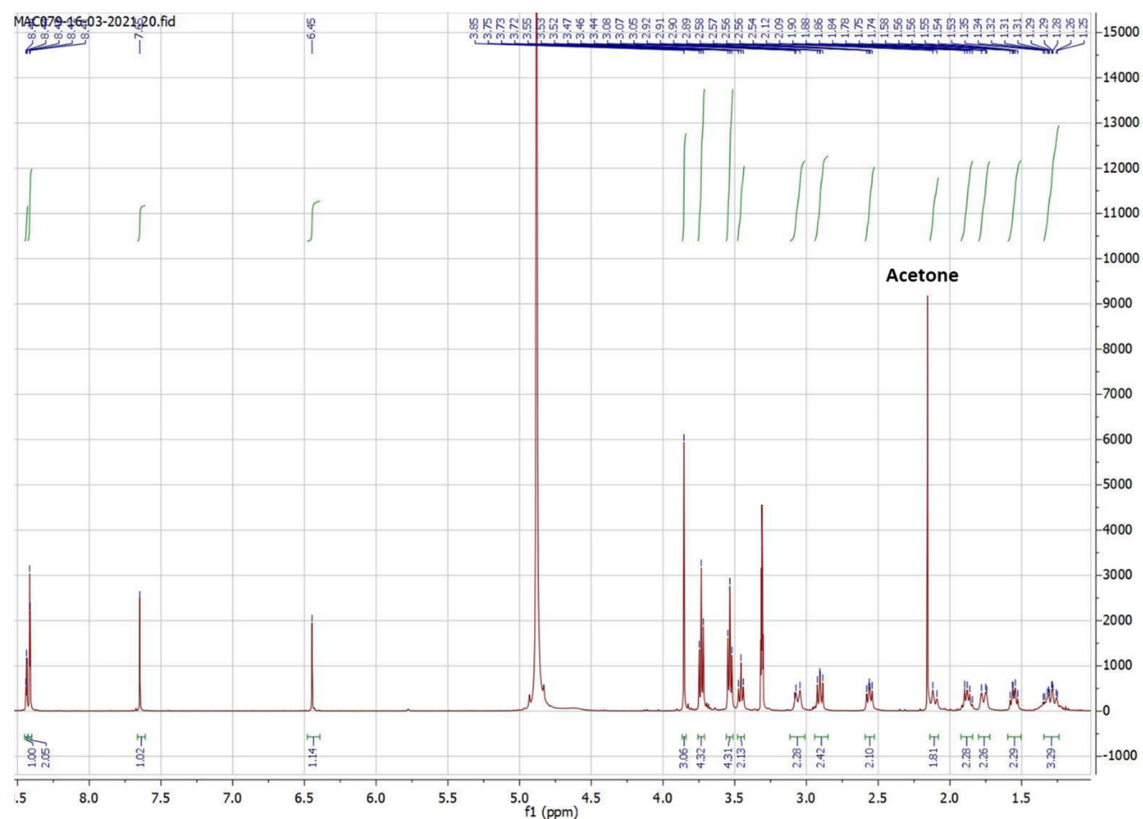
8.62e+006



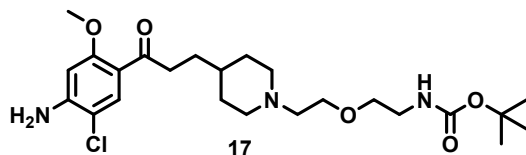
Minimum:

Maximum: 5.0 5.0 -1.5

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
632.2854	632.2851	0.3	0.5	12.5	1507.7	n/a	n/a	C31 H43 N5 O7 Cl



Tert-butyl-(2-(2-(4-(3-(4-amino-5-chloro-2-methoxyphenyl)-3-oxopropyl)piperidin-1-yl)ethoxy)ethyl)carbamate (17)



Elemental Composition Report

Page 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

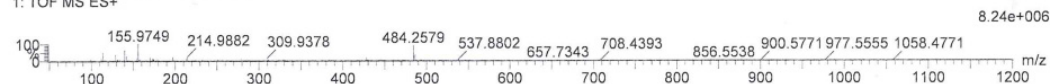
456 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-24 H: 0-100 N: 0-3 O: 0-5 Na: 0-1 Cl: 0-1 I: 0-1

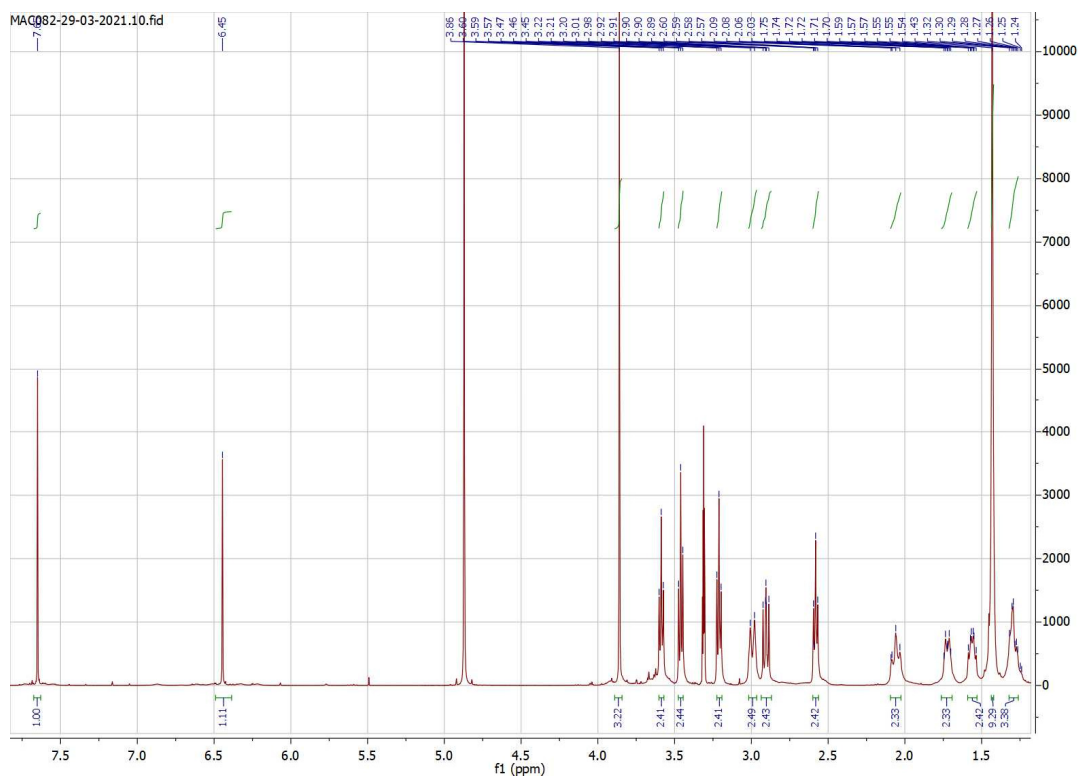
MAC082 183 (1.715) Cm (183:188)

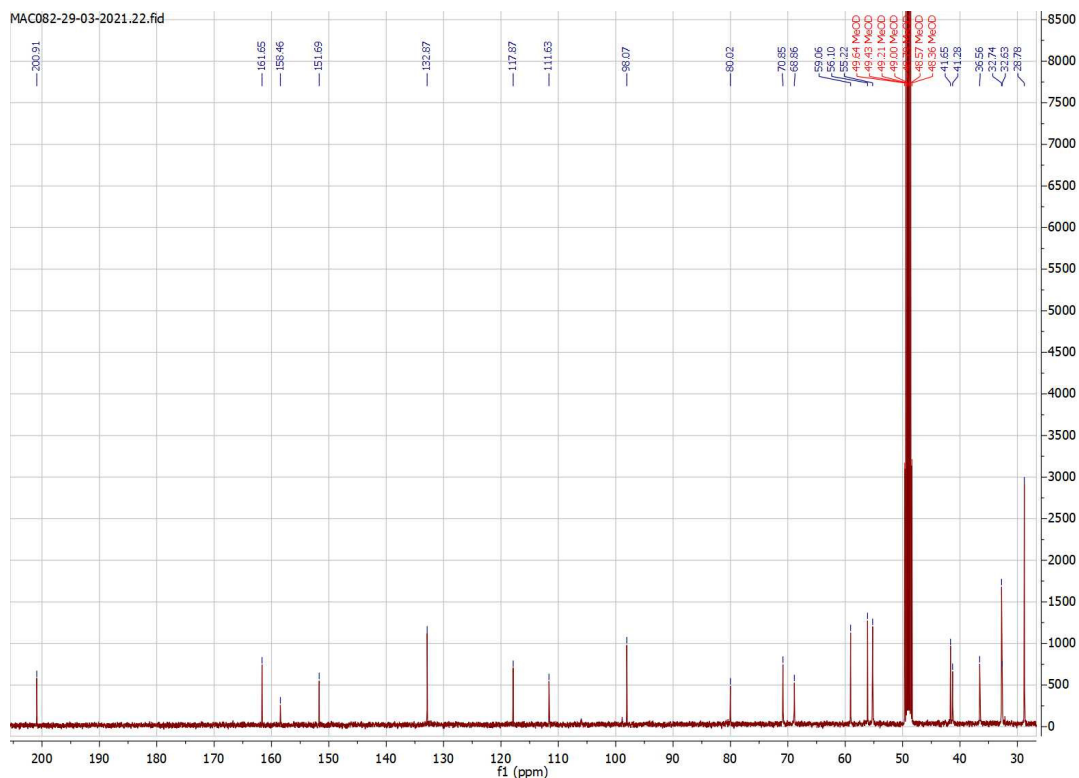
1: TOF MS ES+



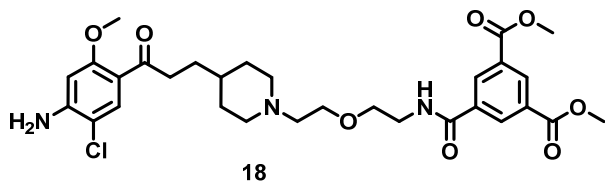
Minimum: -1.5
Maximum: 5.0 5.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
484.2579	484.2578	0.1	0.2	6.5	1974.3	n/a	n/a	C24 H39 N3 O5 Cl





1,3-dimethyl-5-[(2-{2-[4-[3-(4-amino-5-chloro-2-methoxyphenyl)-3-oxopropyl]piperidin-1-yl}ethoxy)ethyl]carbamoyl]benzene-1,3-dicarboxylate (18)



Elemental Composition Report

Page 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

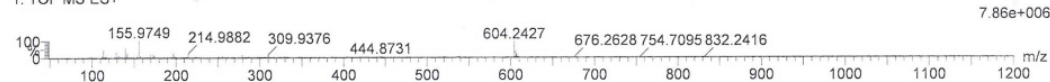
244 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 30-30 H: 0-40 N: 0-3 O: 0-8 Na: 0-1 Cl: 0-1 I: 0-1

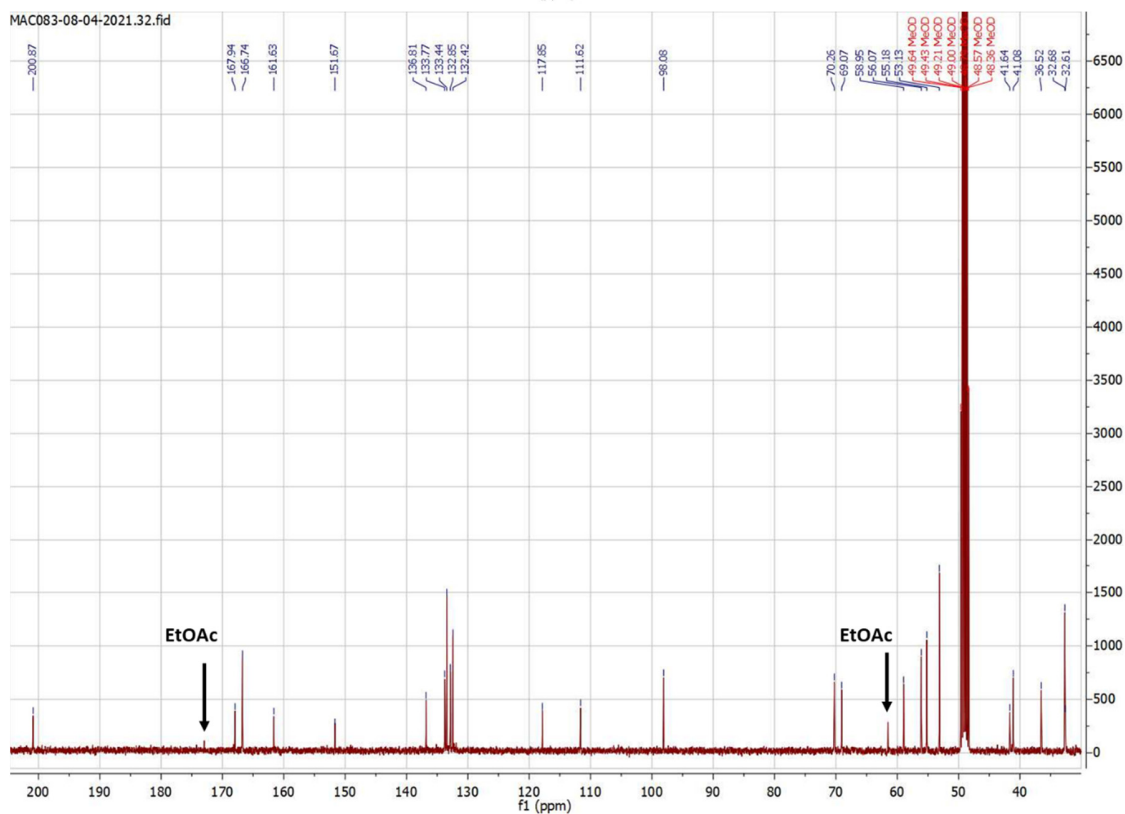
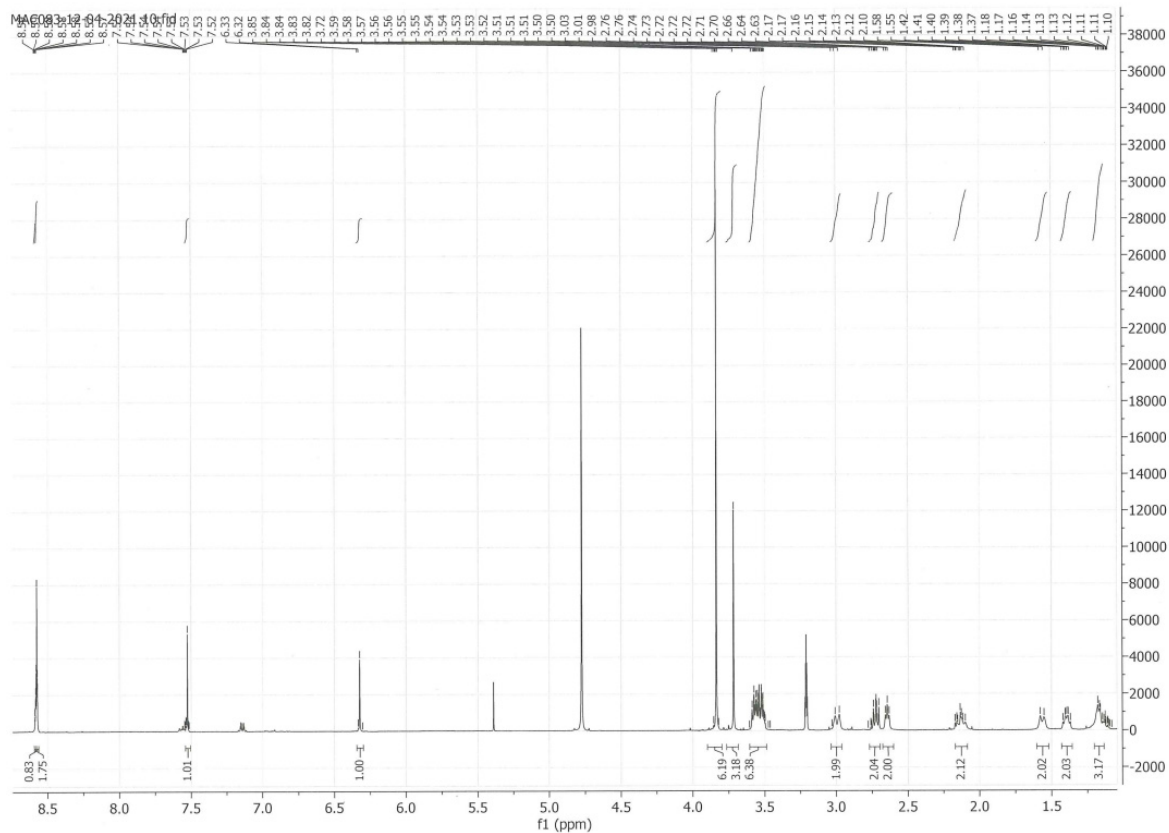
MAC083 189 (1.768) Cm (189:193)

1: TOF MS ES+

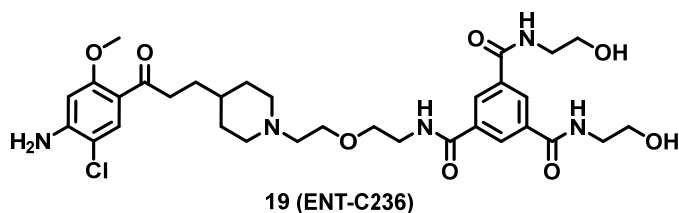


Minimum: -1.5
Maximum: 5.0 5.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
604.2427	604.2426	0.1	0.2	12.5	1739.7	n/a	n/a	C30 H39 N3 O8 Cl



*N*¹-(2-(2-(4-(3-(4-amino-5-chloro-2-methoxyphenyl)-3-oxopropyl)piperidin-1-yl)ethoxy)ethyl)-*N*³,*N*⁵-bis(2-hydroxyethyl)benzene-1,3,5-tricarboxamide (19)



Elemental Composition Report

Page 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

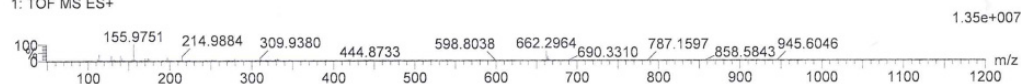
473 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 30-32 H: 0-45 N: 0-5 O: 0-8 Na: 0-1 Cl: 0-1 I: 0-1

MAC084 155 (1.452) Cm (155:161)

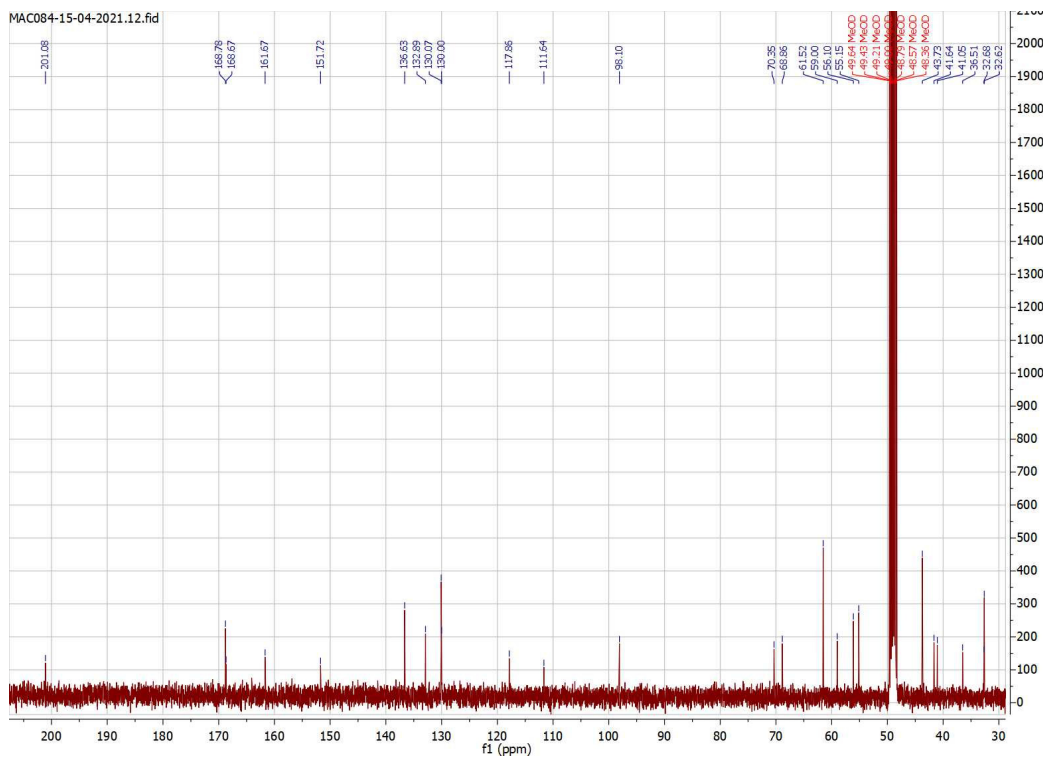
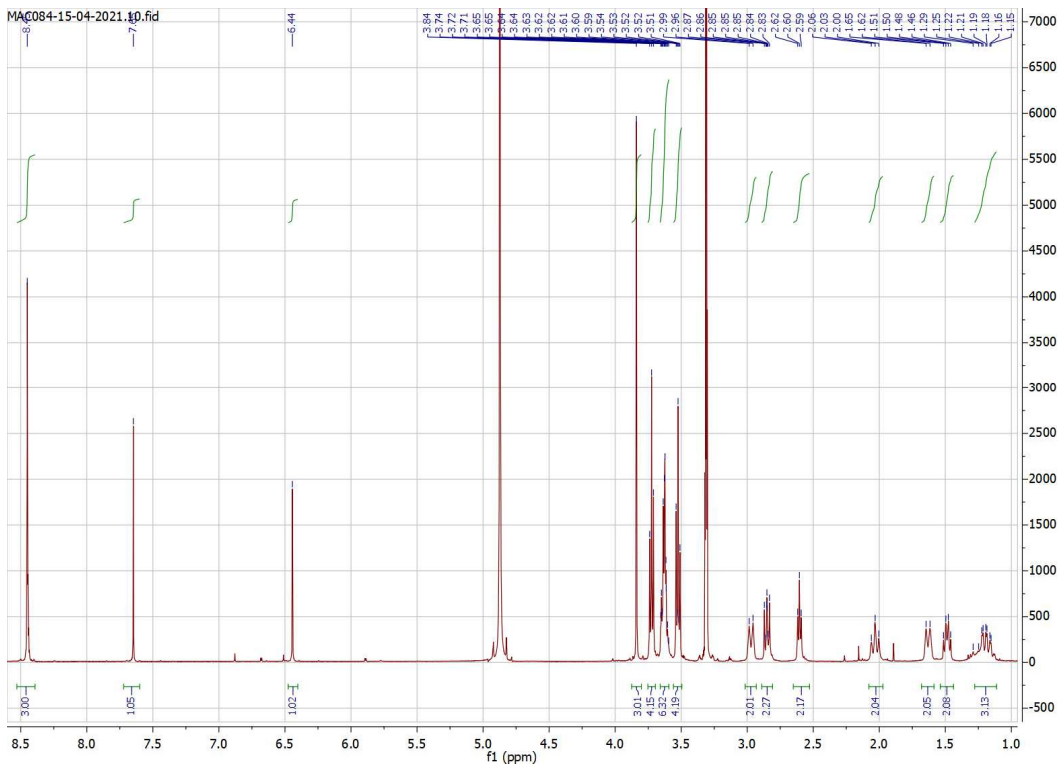
1: TOF MS ES+



Minimum: -1.5

Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
662.2964	662.2957	0.7	1.1	12.5	1891.7	n/a	n/a	C32 H45 N5 O8 Cl



Full images of Western blot of phosphorylation assay of NIH-3T3 TrkB cell line

In parallel with described compounds other derivatives (named compound) have been tested along the main one in the experiment.

In the main text, on the Figure 4., it is shown the part of the Western blot from the Image 2.

Image 1.

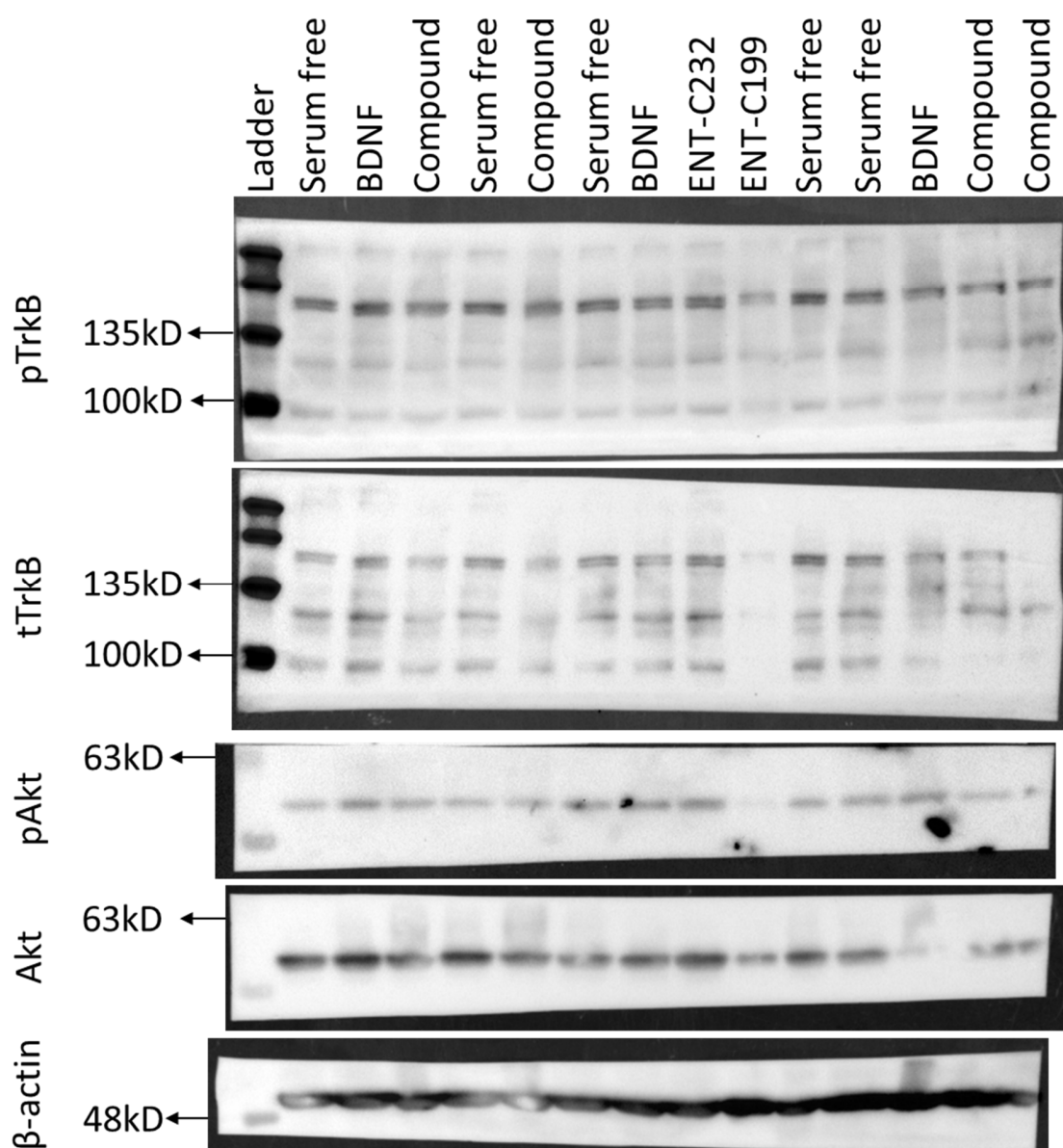


Image 2.

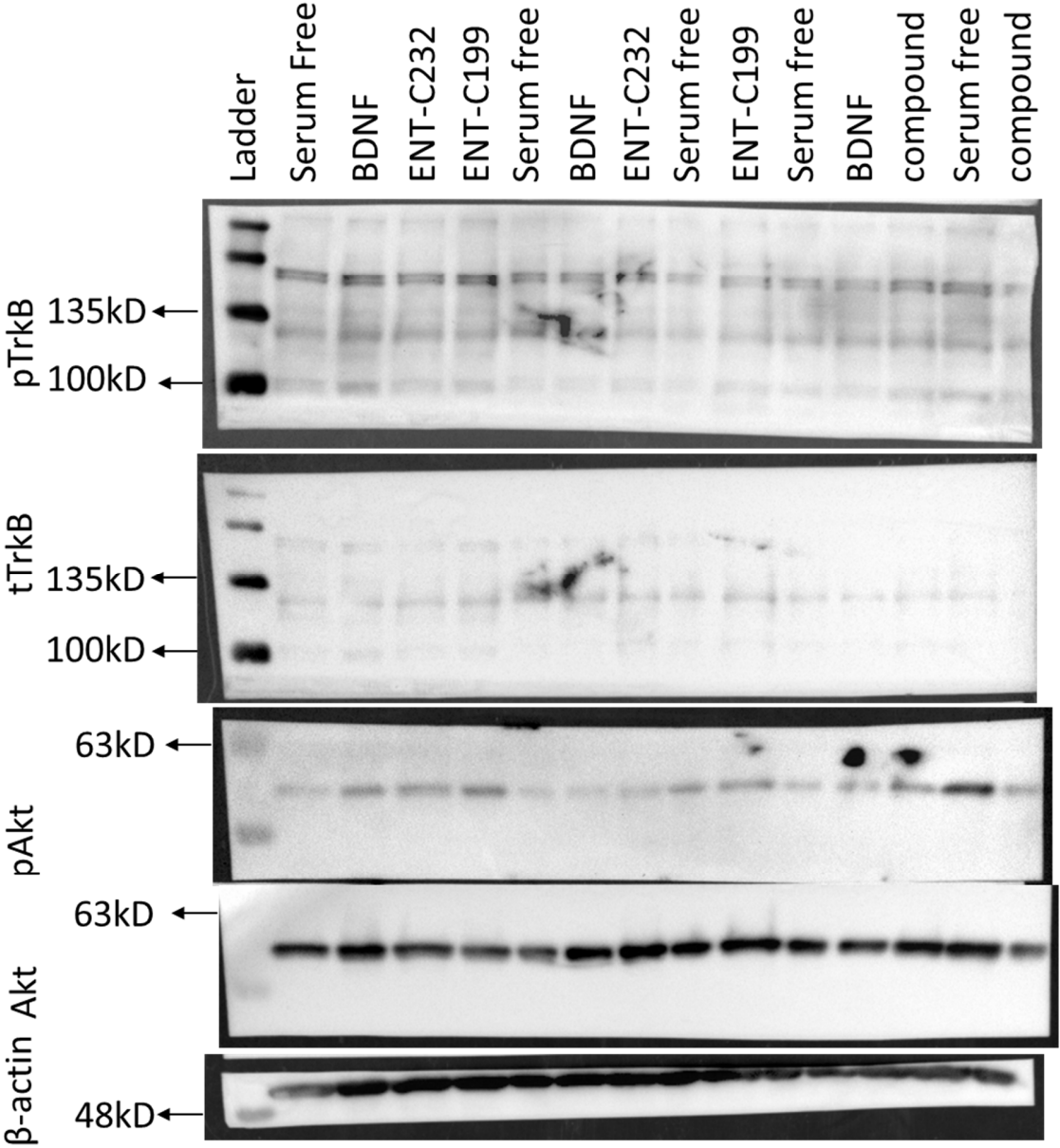


Image 3.

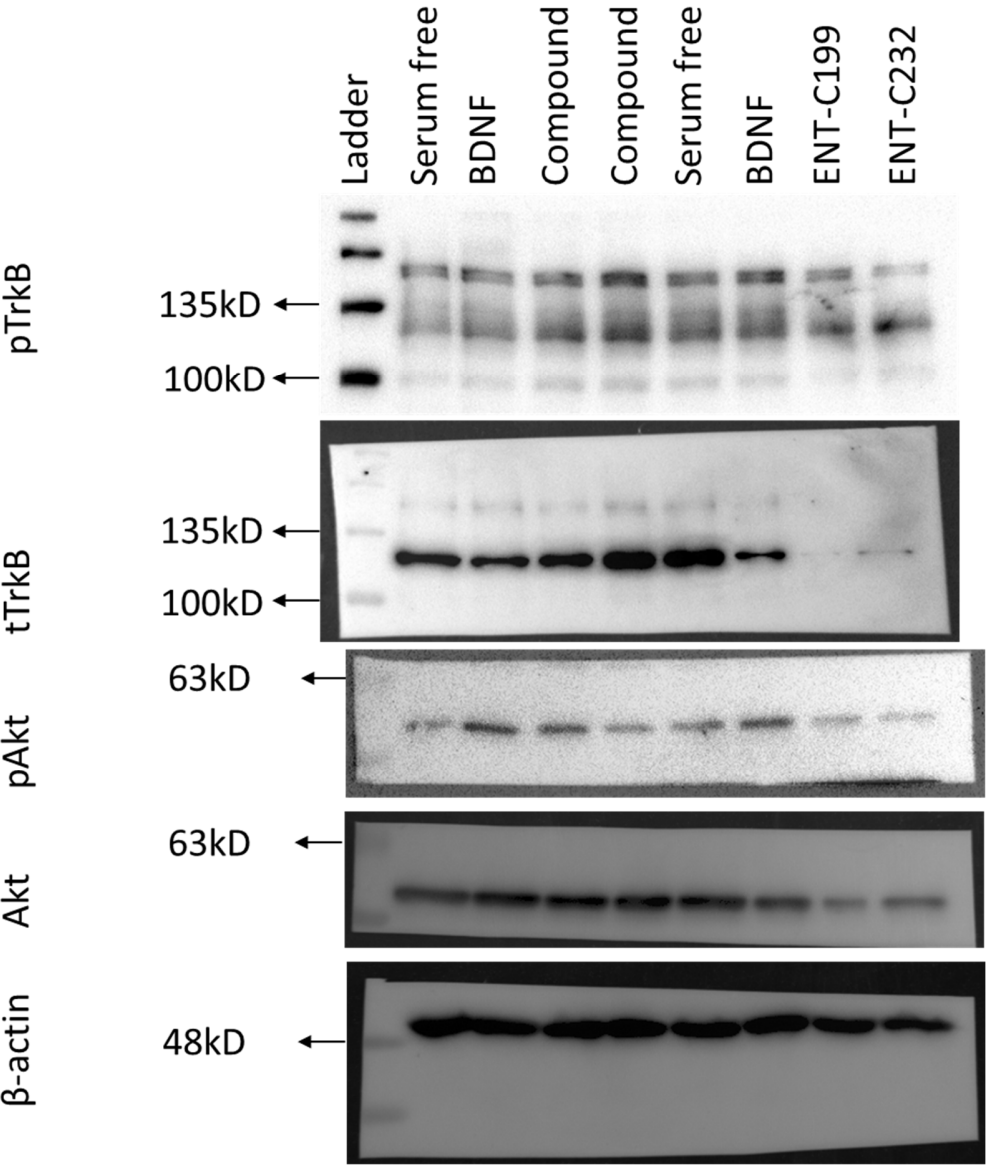
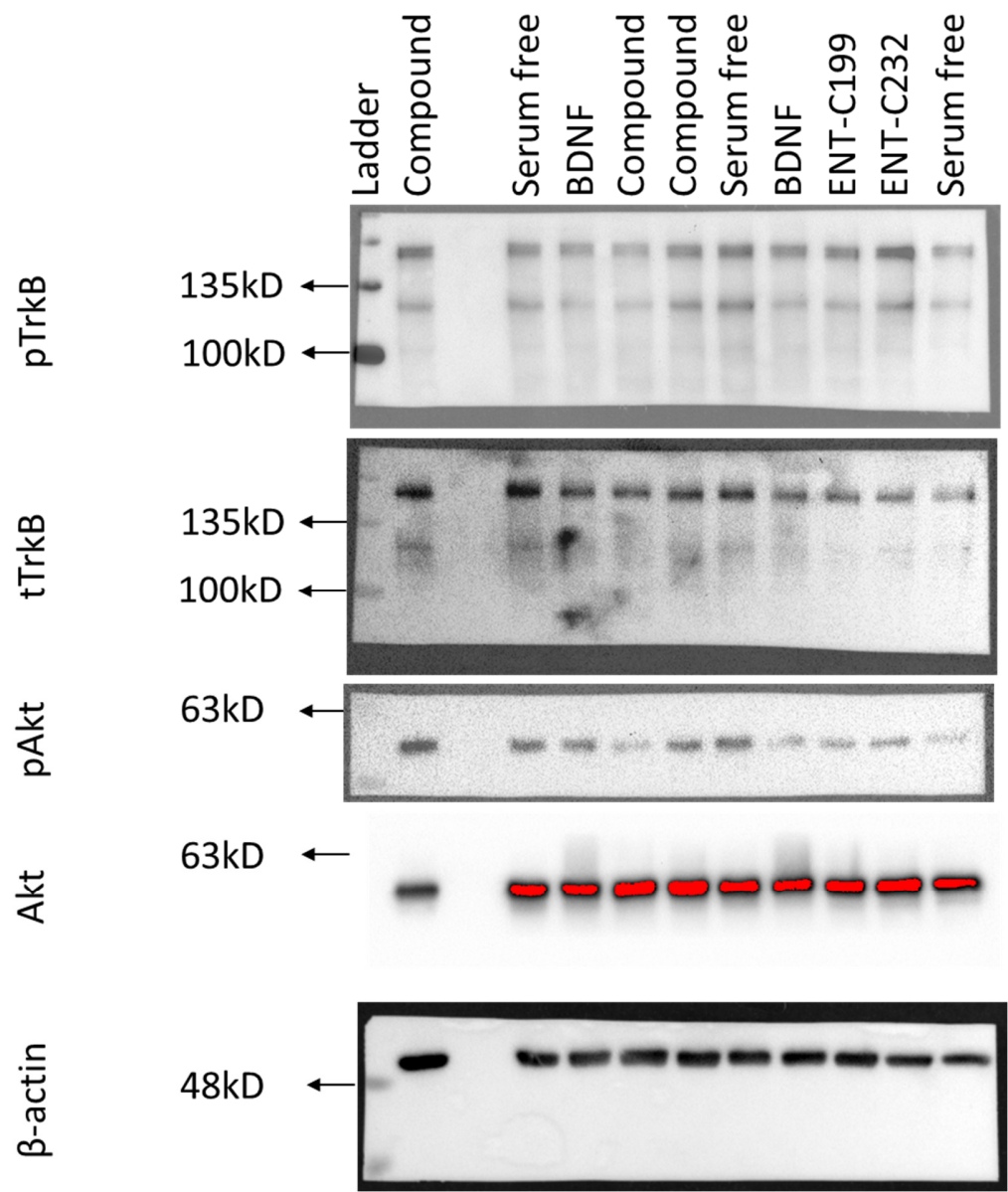


Image 4.



Determination of cAMP production

5-HT

	EC50	Log(EC50)	Top AMPc
TC27	2.20E-09	-8.7	100.00%
TC14	4.33E-09	-8.4	100.00%
TC15	3.70E-09	-8.4	100.00%
Moy.	3.41E-09	-8.5	100%
SEM	6.33E-10	0.1	0.00%

RS 67333

	EC50	Log(EC50)	Top AMPc
TC27	7.86E-10	-9.1	67.01%
TC14	1.54E-09	-8.8	60.01%
TC15	2.93E-10	-9.5	76.26%
Moy.	8.72E-10	-9.1	68%
SEM	3.62E-10	0.2	4.71%

ENT-C199

	EC50	Log(EC50)	Top AMPc
TC27	1.25E-09	-8.9	53.83%
TC14	3.96E-10	-9.4	46.75%
TC15	8.71E-10	-9.1	42.14%
Moy.	8.40E-10	-9.1	48%
SEM	2.48E-10	0.1	3.40%

