

May 1,2-dithiolane-4-carboxylic acid and its derivatives serve as a specific thioredoxin reductase 1 inhibitor?

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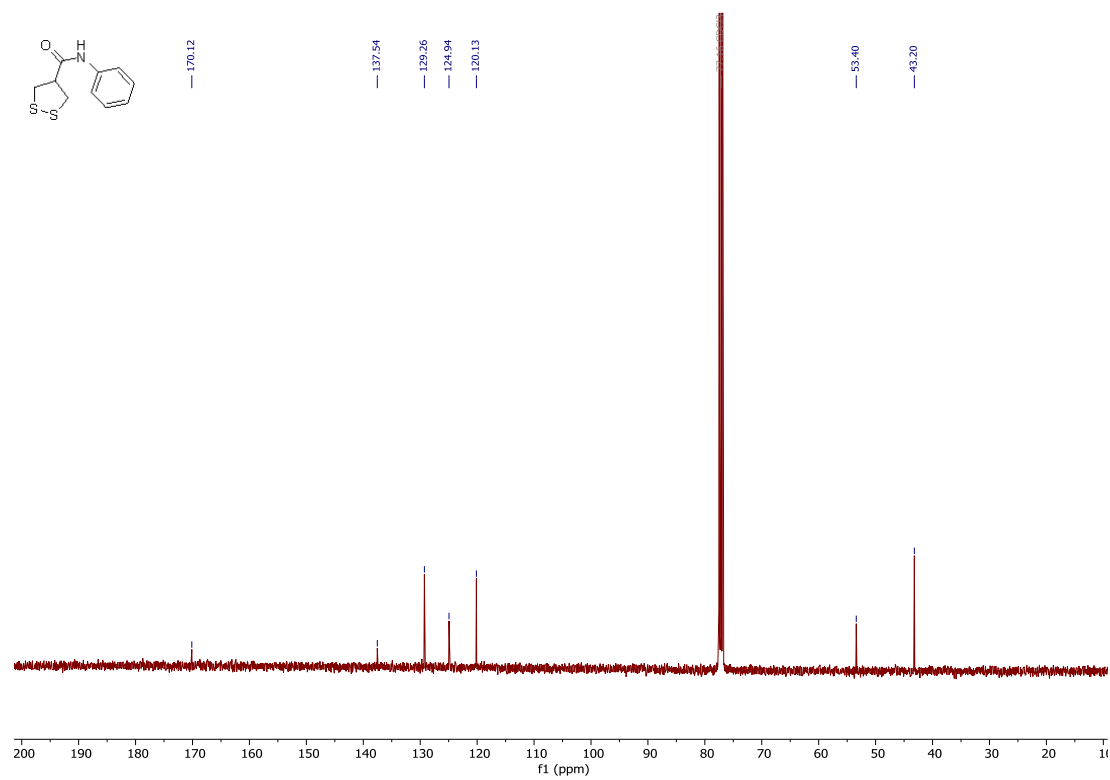
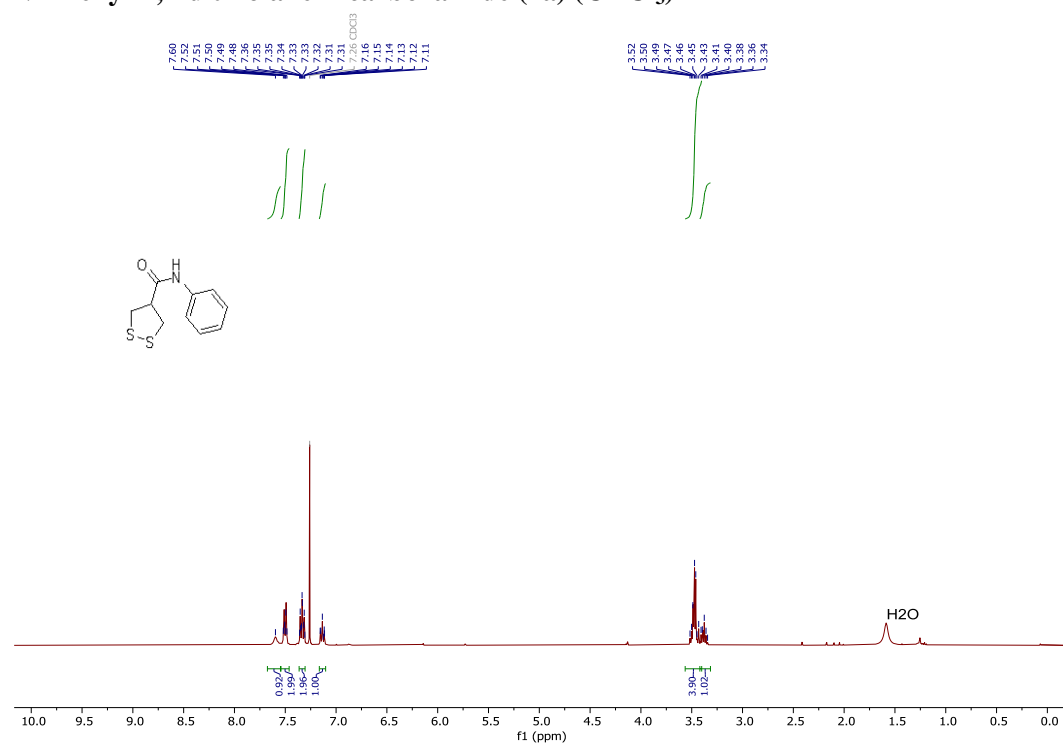
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***N*-Phenyl-1,2-dithiolane-4-carboxamide (2a) (CDCl₃)**



Elemental Composition Report

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

138 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

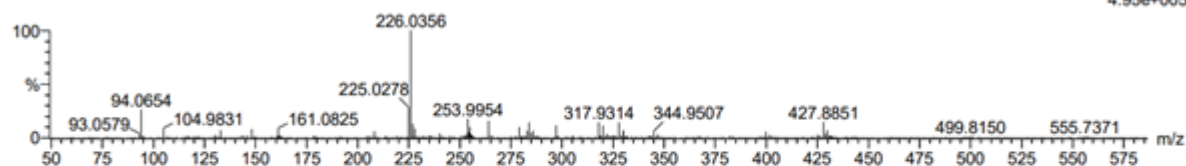
Elements Used:

C: 0-50 H: 0-100 N: 0-3 O: 0-3 S: 0-2

2883 Nikitjuka **2a**

HRMS_2022_04_528 689 (1.970) Cm (689:699-(663.675+723:729))

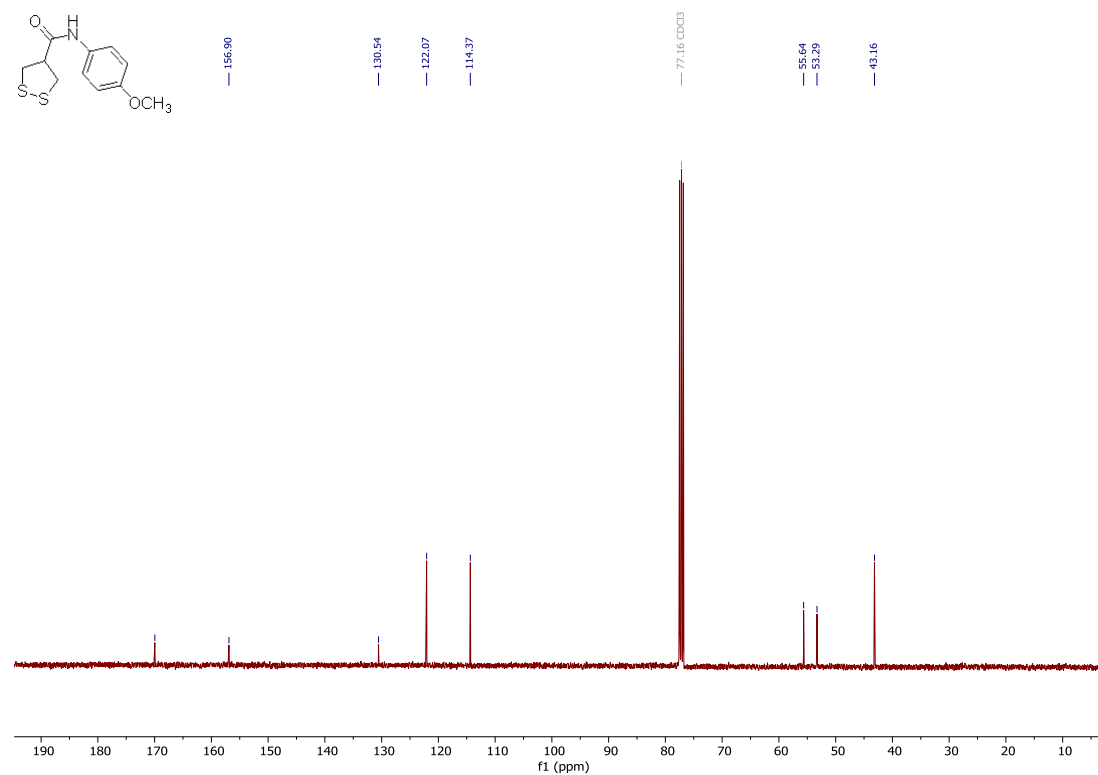
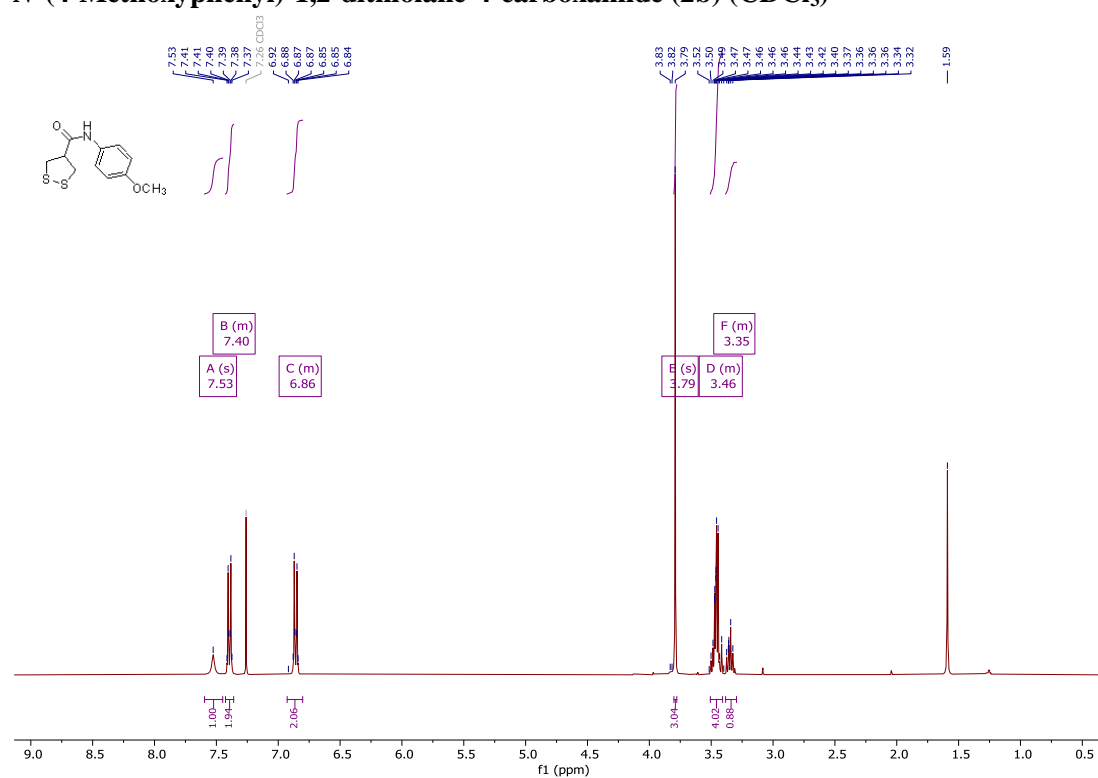
OSI/FOKL-MS
Synapt G2-Si
1: TOF MS ES+
4.95e+005



Minimum: 80.00
Maximum: 100.00

Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
226.0356	100.00	226.0360	-0.4	-1.8	5.5	295.0	n/a	n/a	C10 H12 N O S2

***N*-(4-Methoxyphenyl)-1,2-dithiolane-4-carboxamide (2b) (CDCl₃)**



Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

156 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-50 H: 0-100 N: 0-3 O: 0-3 S: 0-2

2882 Nikitjuka **2b**

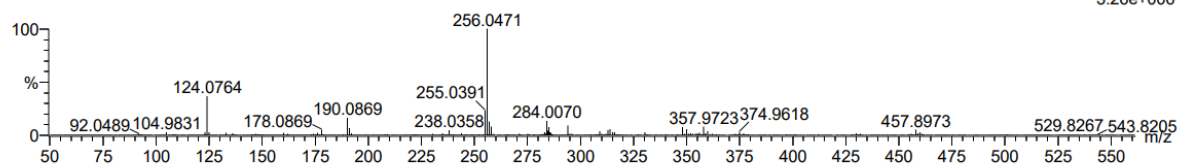
HRMS_2022_04_526 674 (1.929) Cm (673:683-(645:651+699:708))

OSI/FOKL-MS

Synapt G2-Si

1: TOF MS ES+

3.26e+006



Minimum: 80.00

-1.5

Maximum: 100.00

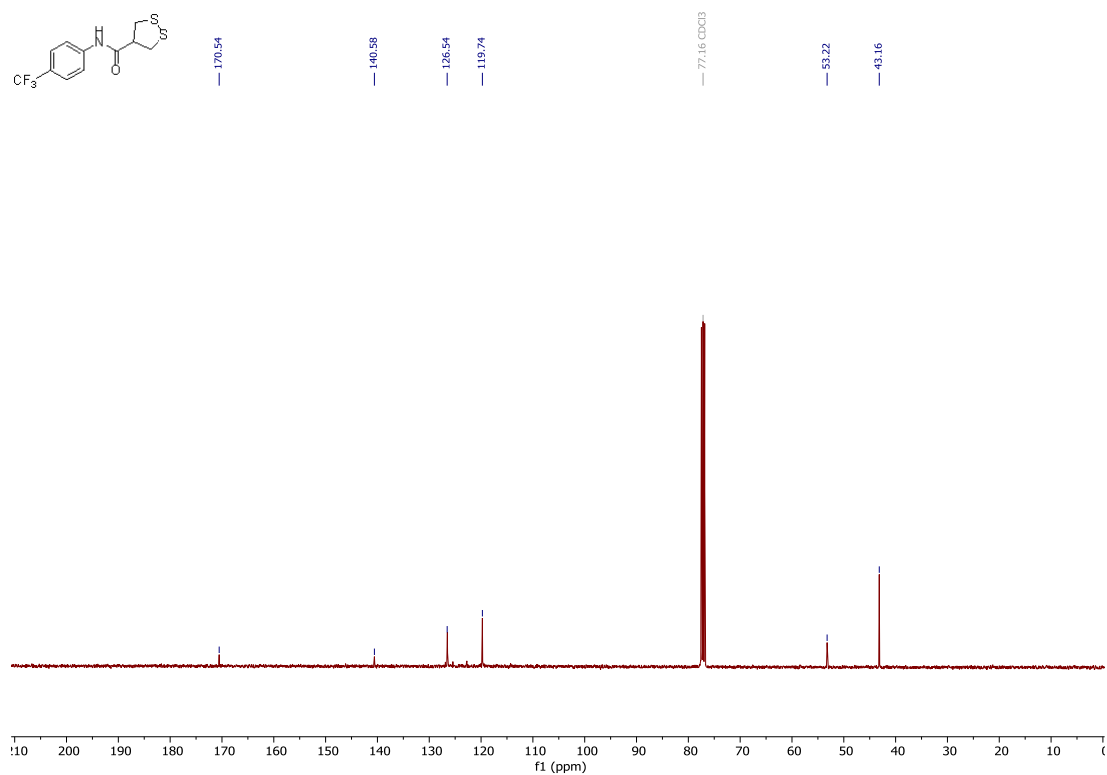
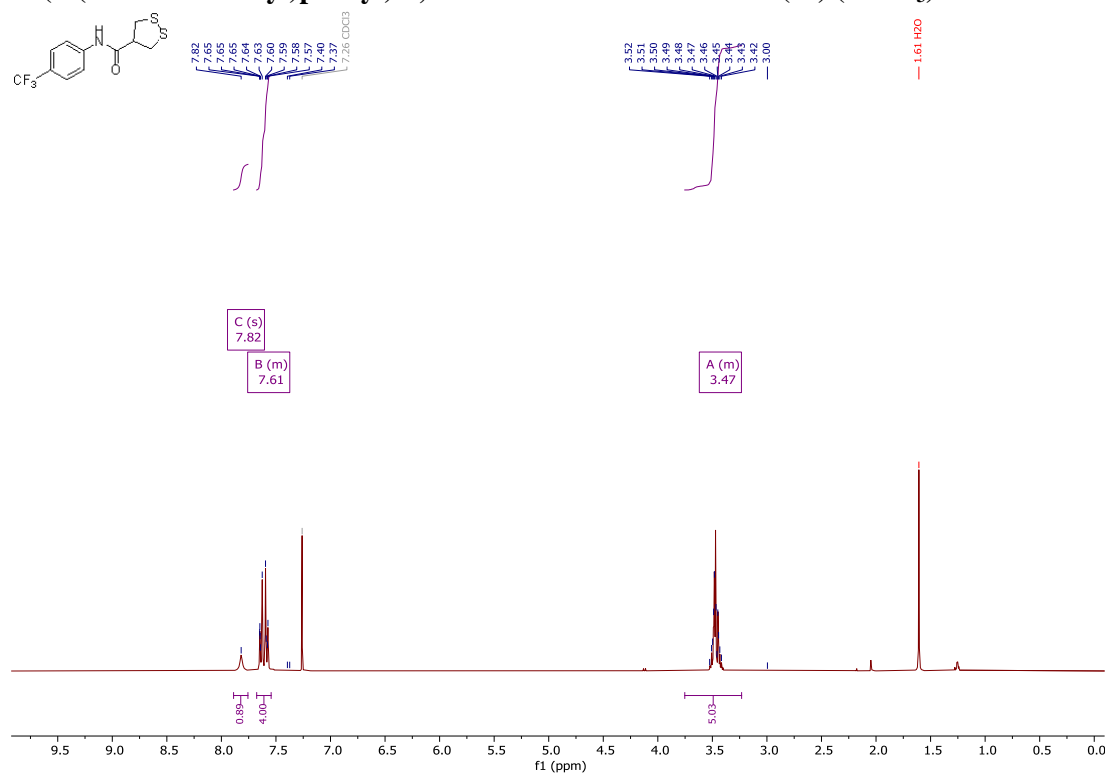
5.0

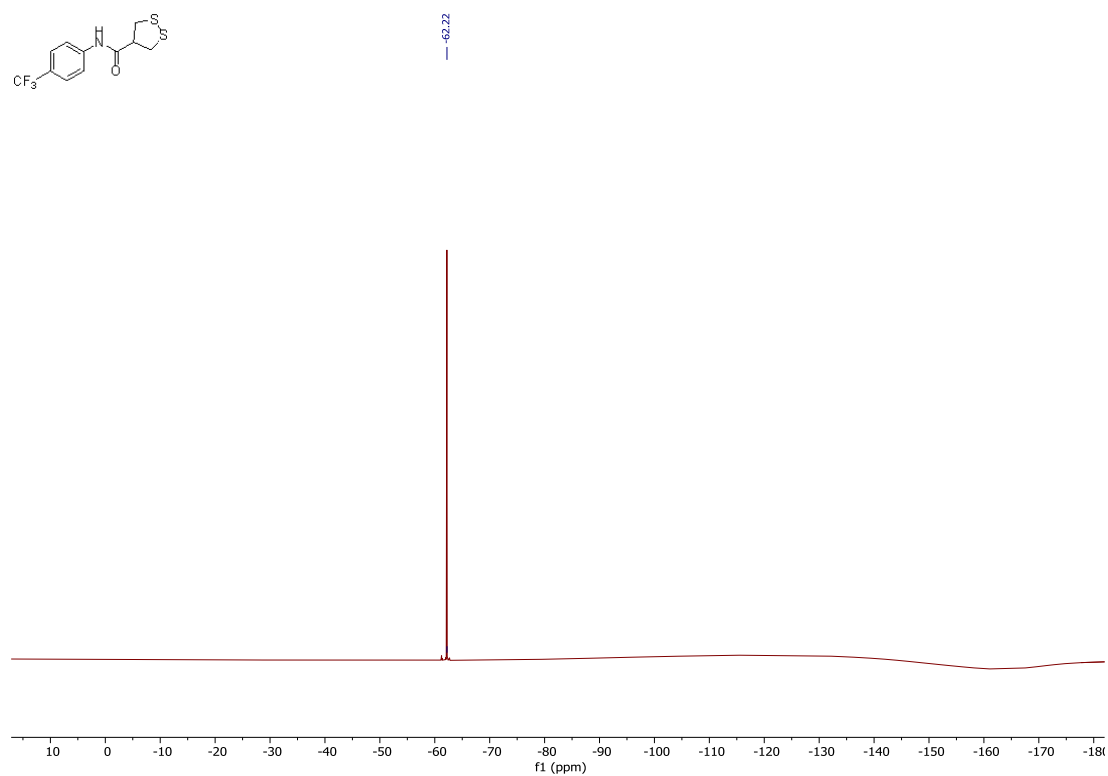
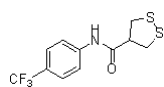
5.0

200.0

Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
256.0471	100.00	256.0466	0.5	2.0	5.5	633.4	n/a	n/a	C11 H14 N O2 S2

***N*-(4-(Trifluoromethyl)phenyl)-1,2-dithiolane-4-carboxamide (2c) (CDCl₃)**





Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

2c

Monoisotopic Mass, Even Electron Ions

370 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

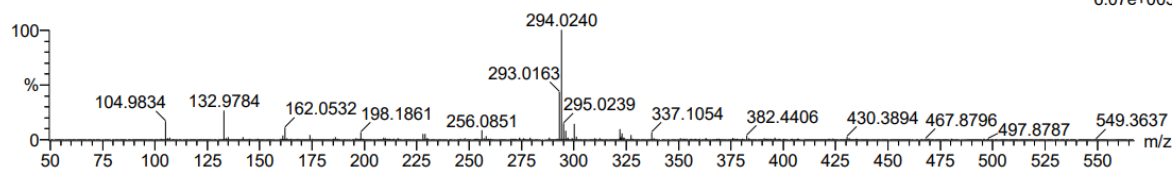
Elements Used:

C: 0-50 H: 0-100 N: 0-2 O: 0-2 F: 0-3 S: 0-2

2886 Nikitjuka

HRMS_2022_04_534 769 (2.200) Cm (768:775-740:750)

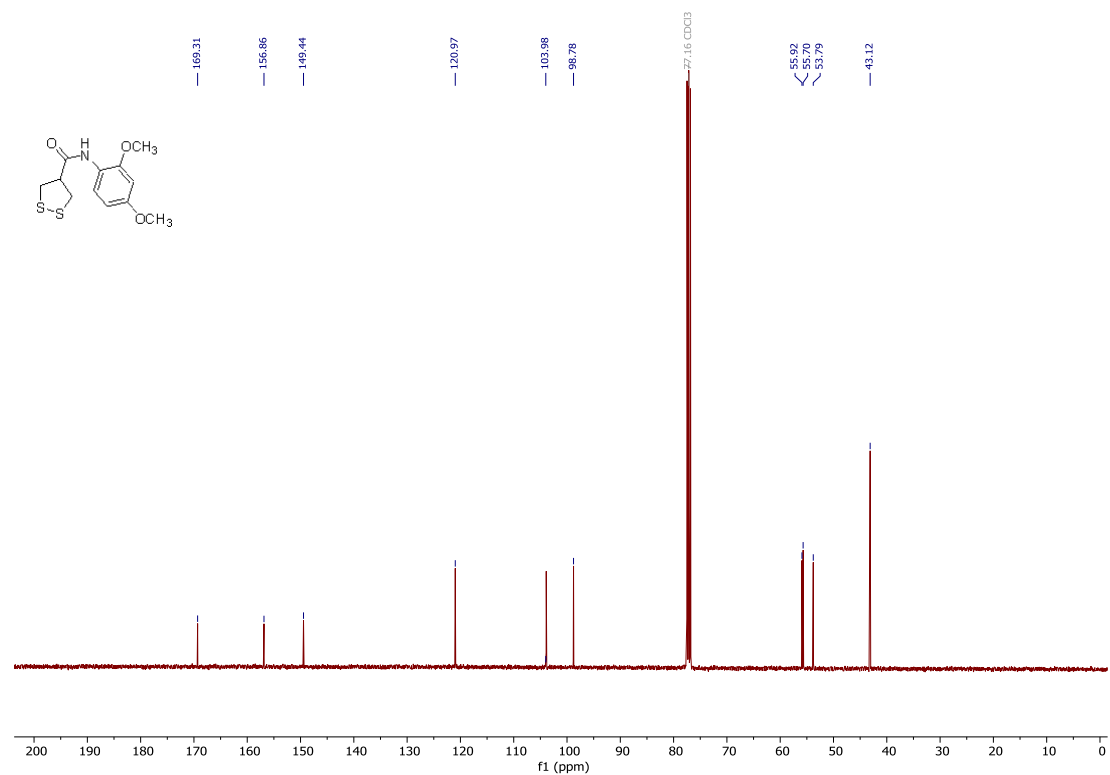
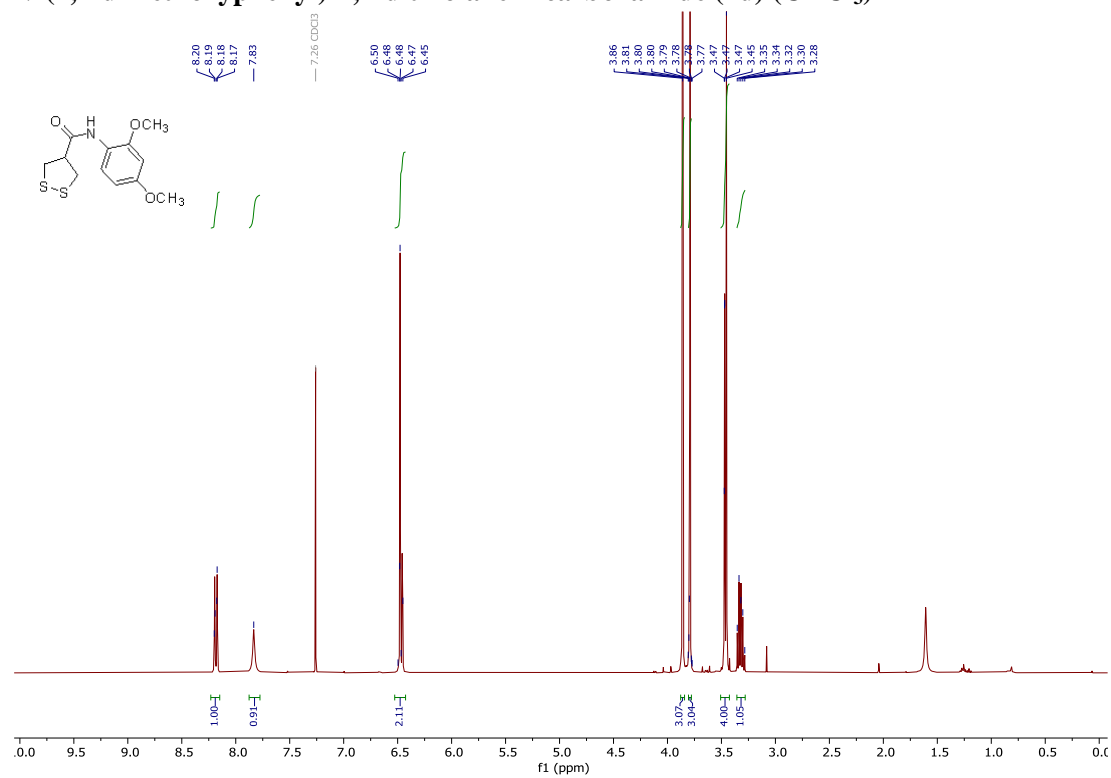
OSI/FOKL-MS
Synapt G2-Si
1: TOF MS ES+
6.07e+005



Minimum: 80.00
Maximum: 100.00

Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
294.0240	100.00	294.0234	0.6	2.0	5.5	513.4	n/a	n/a	C11 H11 N O F3 S2

***N*-(2,4-dimethoxyphenyl)-1,2-dithiolane-4-carboxamide (2d) (CDCl₃)**



Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0
 Element prediction: Off
 Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

172 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

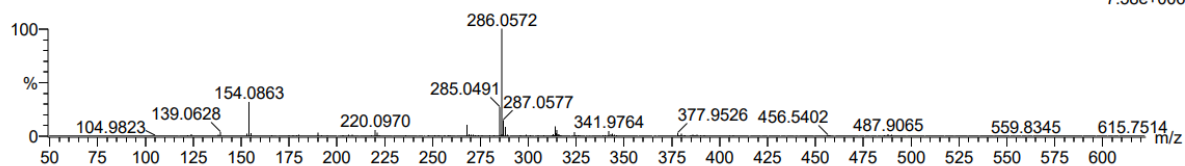
Elements Used:

C: 0-50 H: 0-100 N: 0-3 O: 0-3 S: 0-2

2887 Nikitjuka **2d**

HRMS_2022_04_536 706 (2.017) Cm (706:713-668:678)

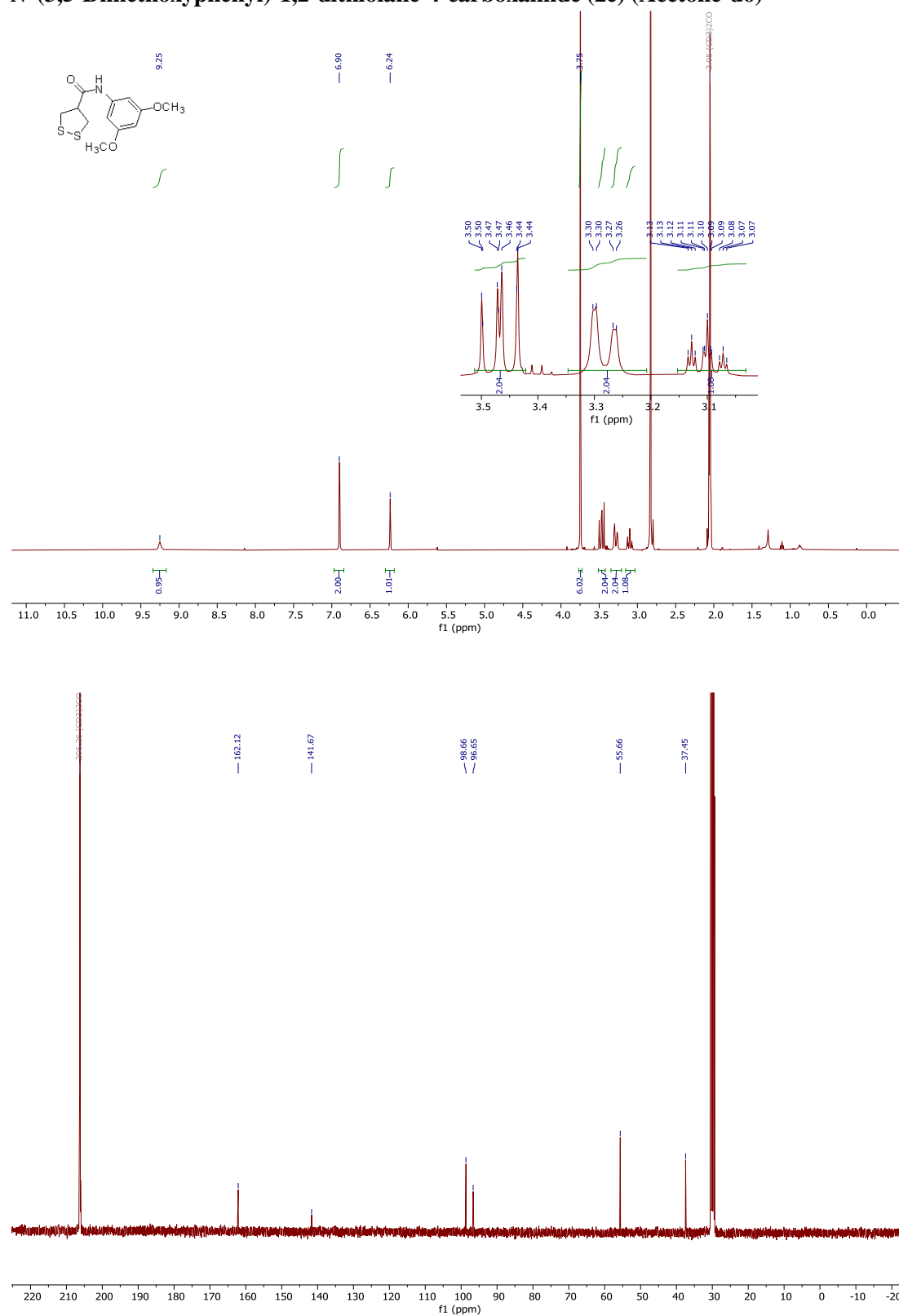
OSI/FOKL-MS
 Synapt G2-Si
 1: TOF MS ES+
 7.58e+006



Minimum: 80.00 -1.5
 Maximum: 100.00 2.0 5.0 200.0

Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
286.0572	100.00	286.0572	0.0	0.0	5.5	894.8	n/a	n/a	C12 H16 N O3 S2

***N*-(3,5-Dimethoxyphenyl)-1,2-dithiolane-4-carboxamide (2e) (Acetone-d₆)**



Single Mass Analysis

Tolerance = 3.0 PPM / DBE: min = -0.5, max = 200.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

552 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)

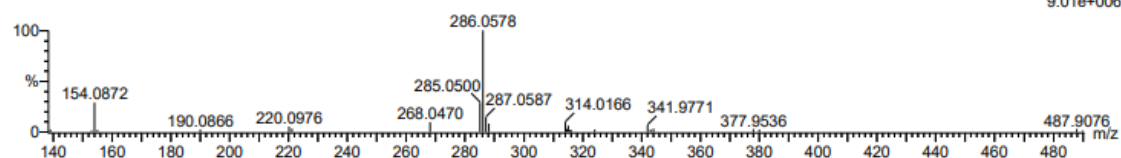
Elements Used:

C: 1-100 H: 1-150 N: 0-15 O: 0-15 S: 1-2

2576 Nikitjuka **2e**

HRMS_2023_08_080 692 (1.978) Cm (692:701-634:649)

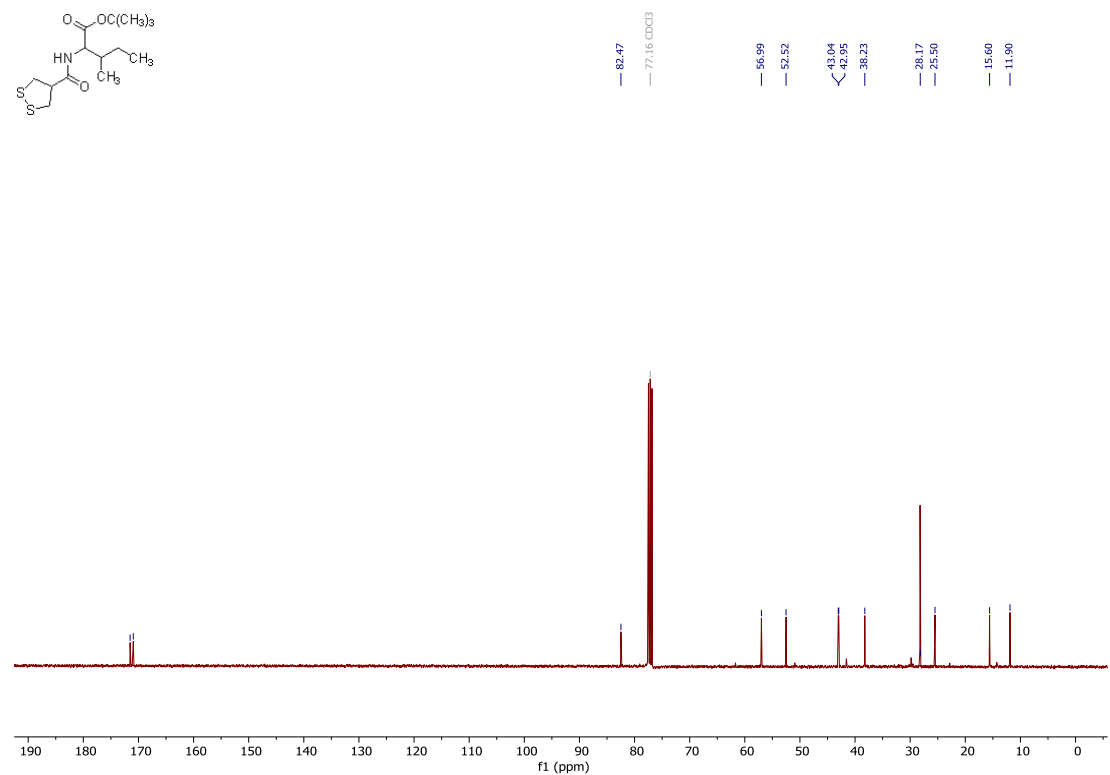
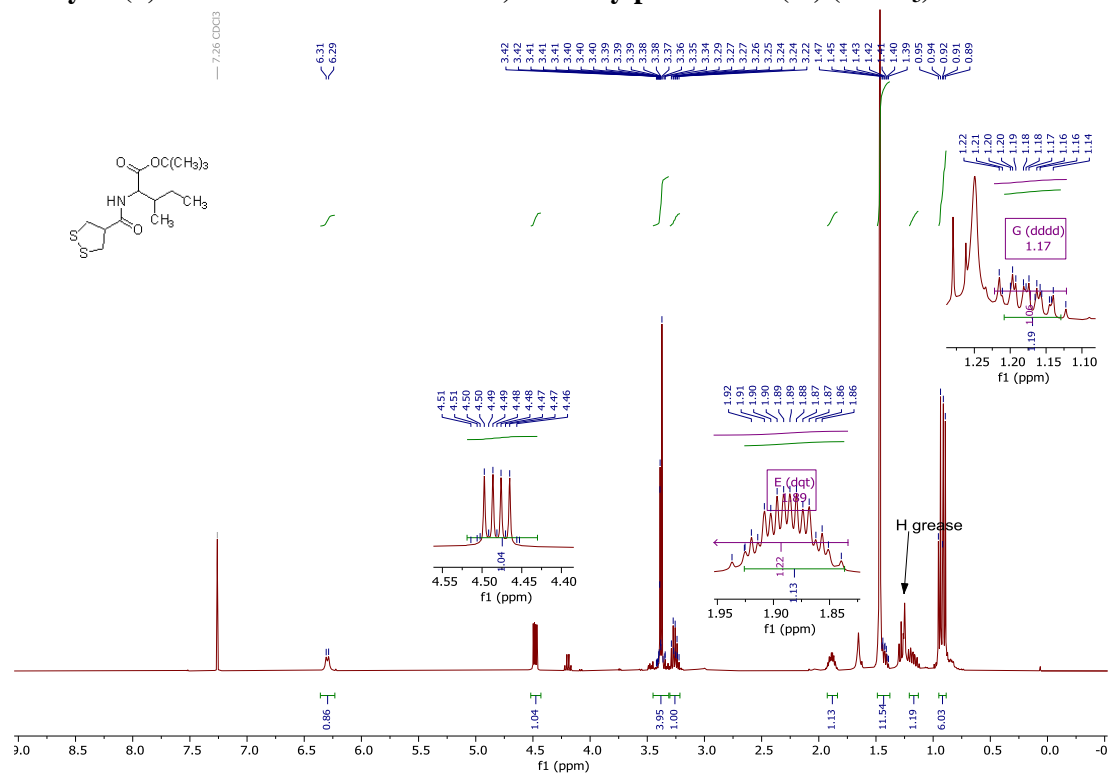
OSI/FOKL-MS
Synapt G2-Si
1: TOF MS ES+
9.01e+006



Minimum: -0.5
Maximum: 10.0 3.0 200.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
286.0578	286.0583	-0.5	-1.7	7.5	60.5	0.235	79.09	C5 H8 N11 O2 S
	286.0572	0.6	2.1	5.5	66.9	6.594	0.14	C12 H16 N O3 S2
	286.0570	0.8	2.8	2.5	61.9	1.572	20.77	C4 H12 N7 O6 S

***t*Butyl 2-(1,2-dithiolane-4-carboxamido)-3-methylpentanoate (2f) (CDCl₃)**



Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

188 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

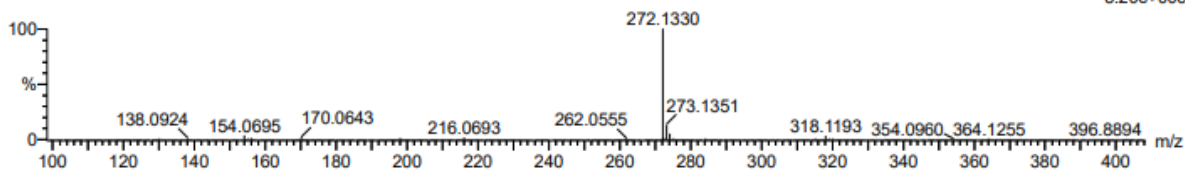
Elements Used:

C: 0-50 H: 0-100 N: 0-3 O: 0-3 S: 0-2

2888 Nikutjuka. **2f**

HRMS_2022_04_544 804 (2.257) Cm (802:811-777:789)

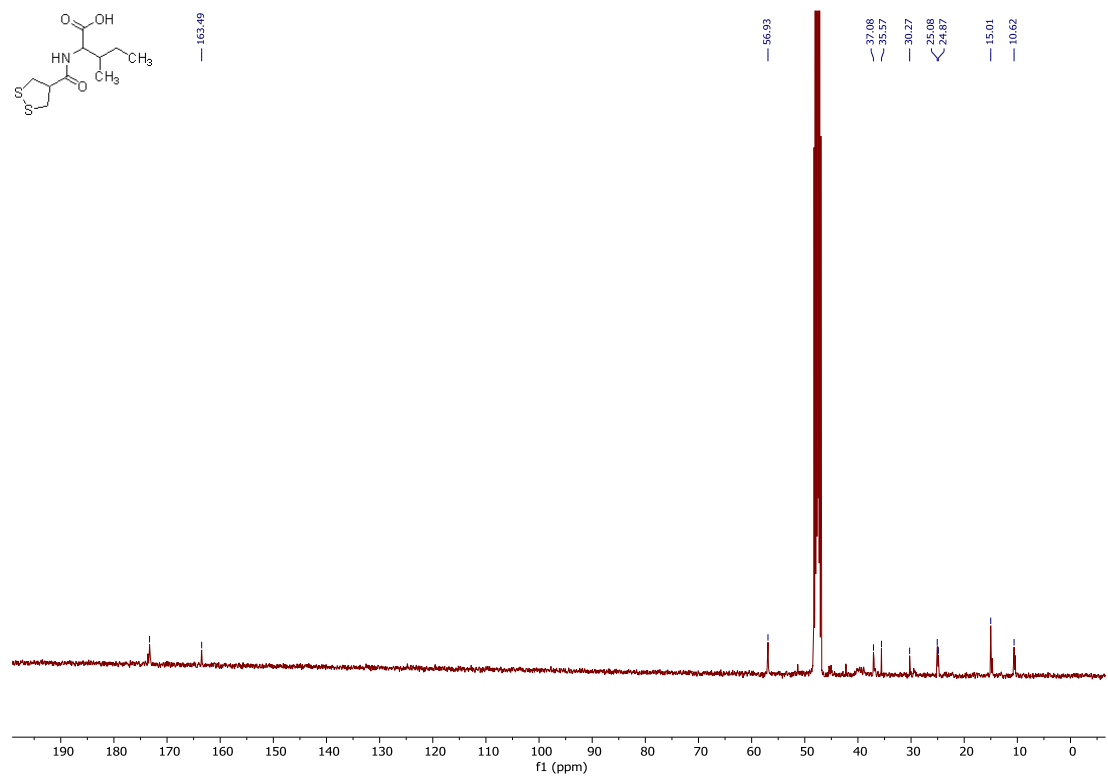
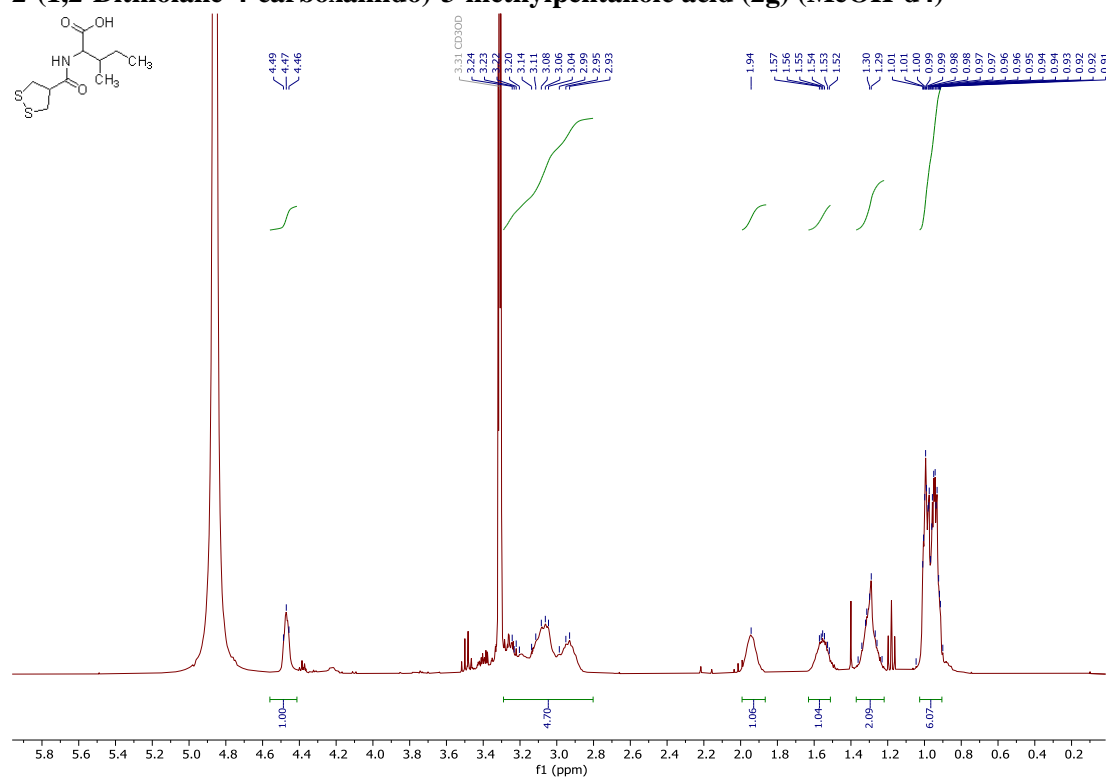
OSI/FOKL-MS
Synapt G2-Si
1: TOF MS ES-
5.20e+006



Minimum: -1.5
Maximum: 2.0 5.0 200.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
318.1193	318.1198	-0.5	-1.6	3.5	387.1	n/a	n/a	C14 H24 N O3 S2

2-(1,2-Dithiolane-4-carboxamido)-3-methylpentanoic acid (2g) (MeOH-d4)



Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

156 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

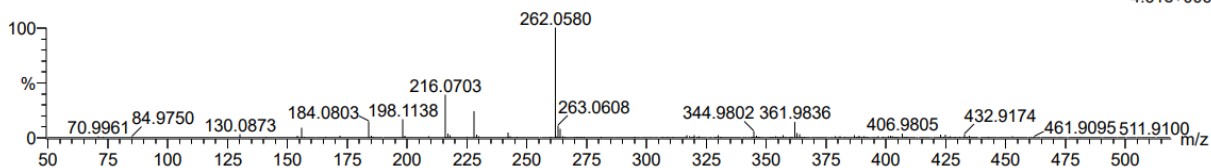
Elements Used:

C: 0-50 H: 0-100 N: 0-3 O: 0-3 S: 0-2

2889 Nikutjuka. **2g**

HRMS_2022_04_543 644 (1.814) Cm (642:651-(621:626+679:684))

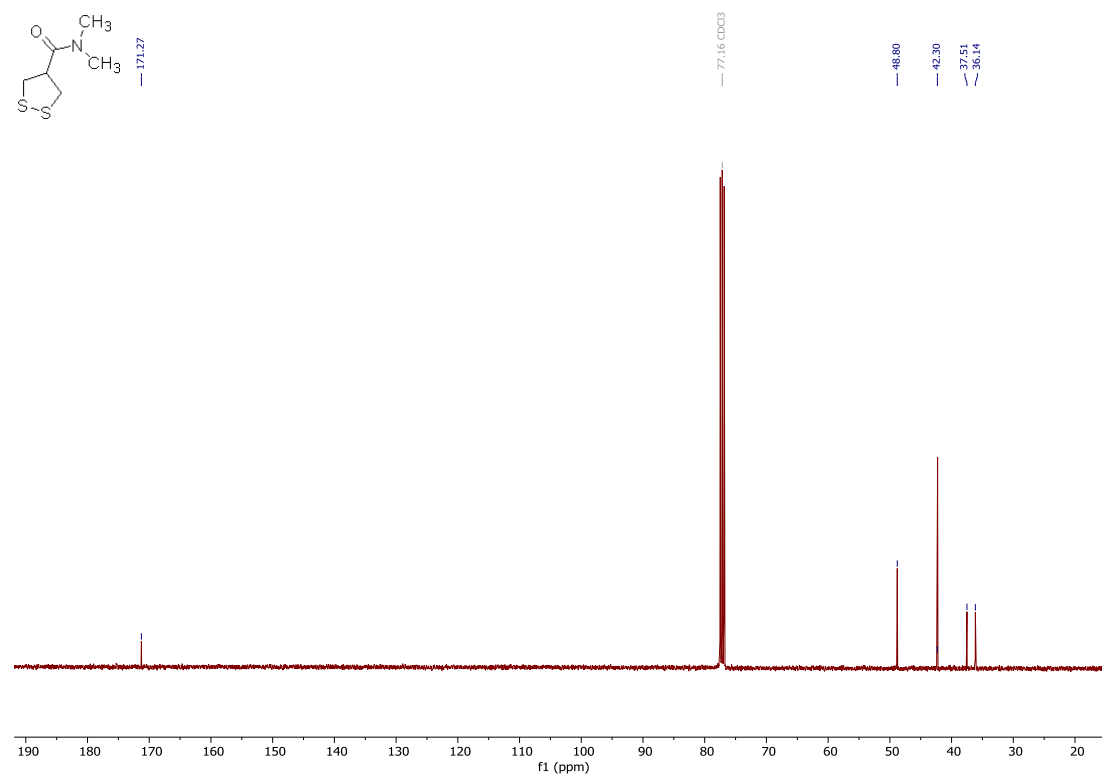
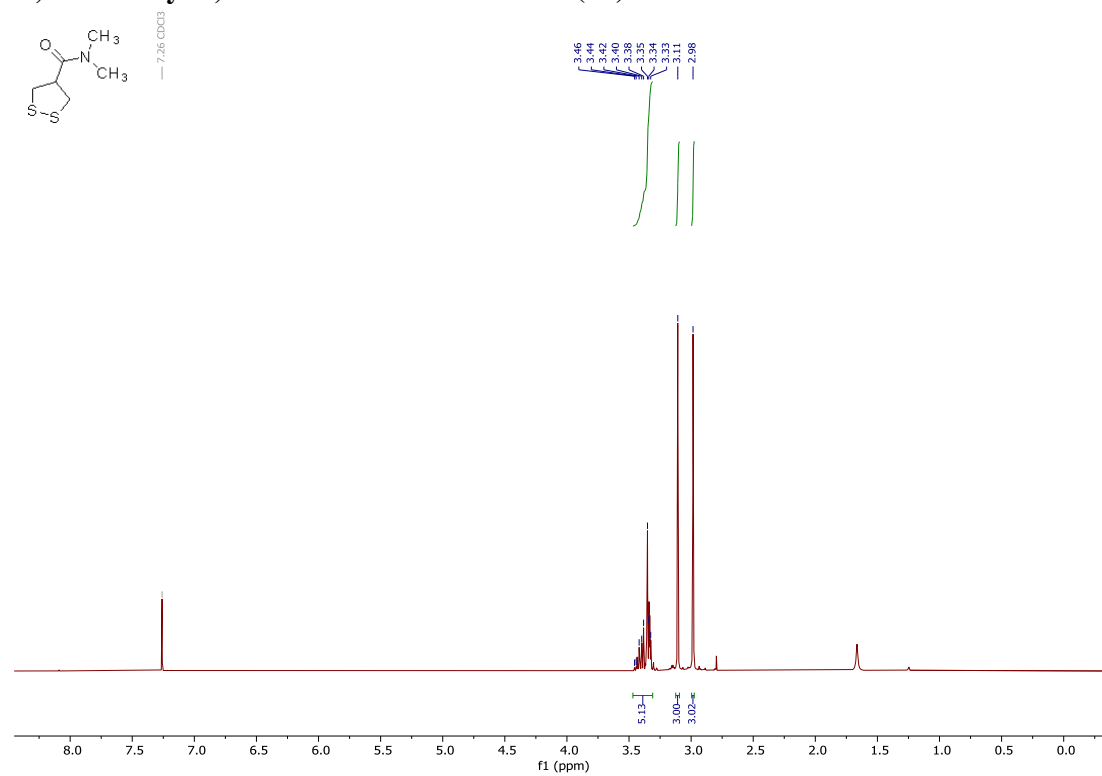
OSI/FOKL-MS
Synapt G2-Si
1: TOF MS ES-
4.61e+006



Minimum: 80.00 -1.5
Maximum: 100.00 2.0 5.0 200.0

Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
262.0580	100.00	262.0572	0.8	3.1	3.5	799.9	n/a	n/a	C10 H16 N O3 S2

***N,N*-Dimethyl-1,2-dithiolane-4-carboxamide (2h)**



Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

108 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

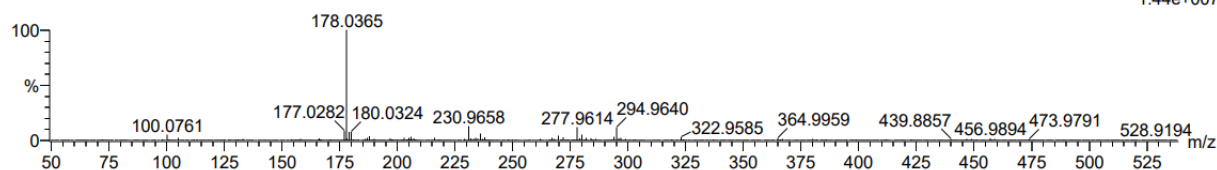
Elements Used:

C: 0-50 H: 0-100 N: 0-3 O: 0-3 S: 0-2

2885 Nikitjuka **2h**

HRMS_2022_04_532 557 (1.598) Cm (557:573-(487:503+603:616))

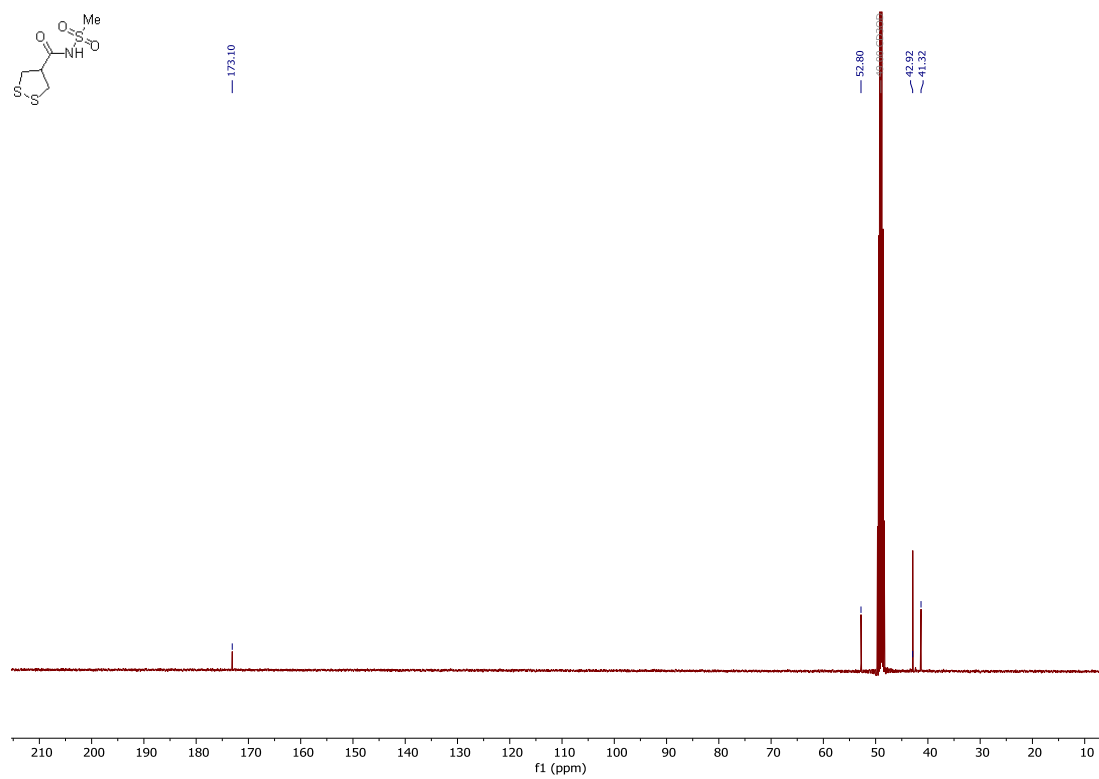
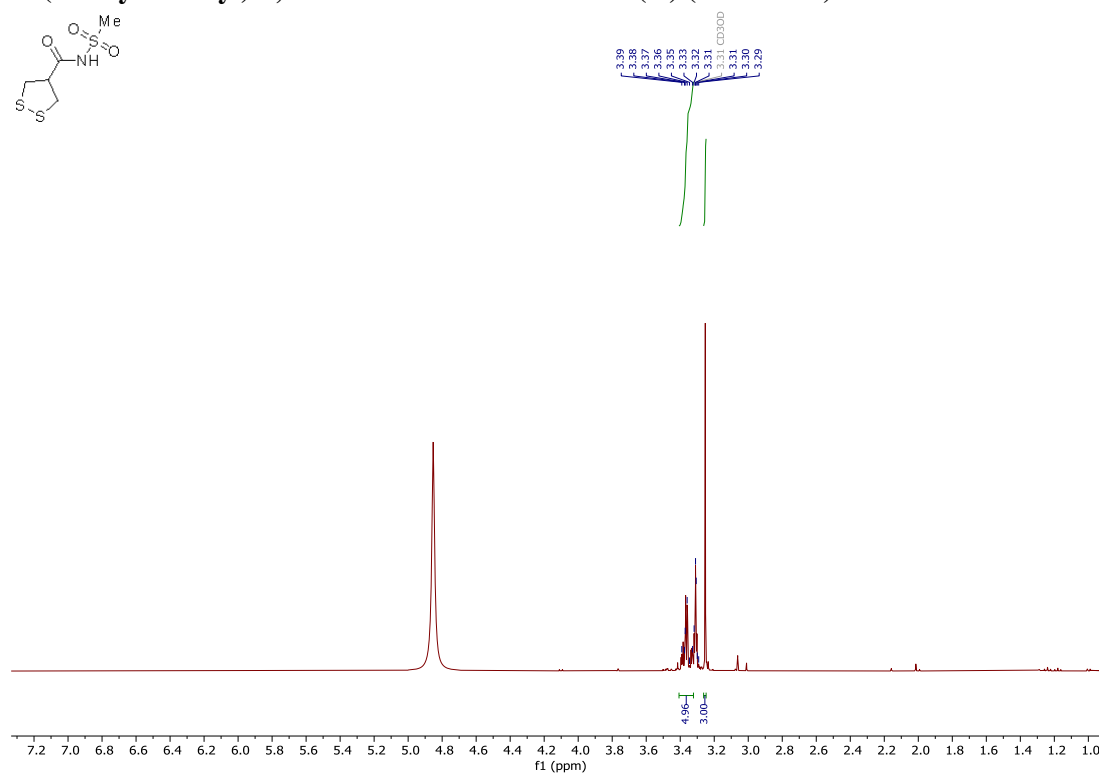
OSI/FOKL-MS
Synapt G2-Si
1: TOF MS ES+
1.44e+007



Minimum: 80.00
Maximum: 100.00

5.0 5.0 -1.5
200.0

Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
178.0365	100.00	178.0360	0.5	2.8	1.5	919.9	n/a	n/a	C6 H12 N O S2

COS(=O)(=O)NC(=O)C1CCSC1

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

181 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-50 H: 0-100 N: 0-2 O: 0-5 S: 0-3

2884 Nikutjuka **2i**

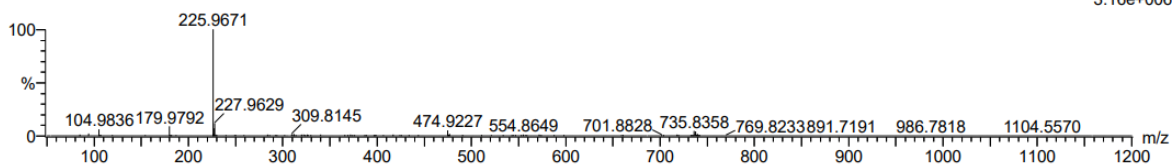
OSI/FOKL-MS

Synapt G2-Si

1: TOF MS ES-

3.16e+006

HRMS_2022_04_546 573 (1.614) Cm (573:580-(542:548+599:603))

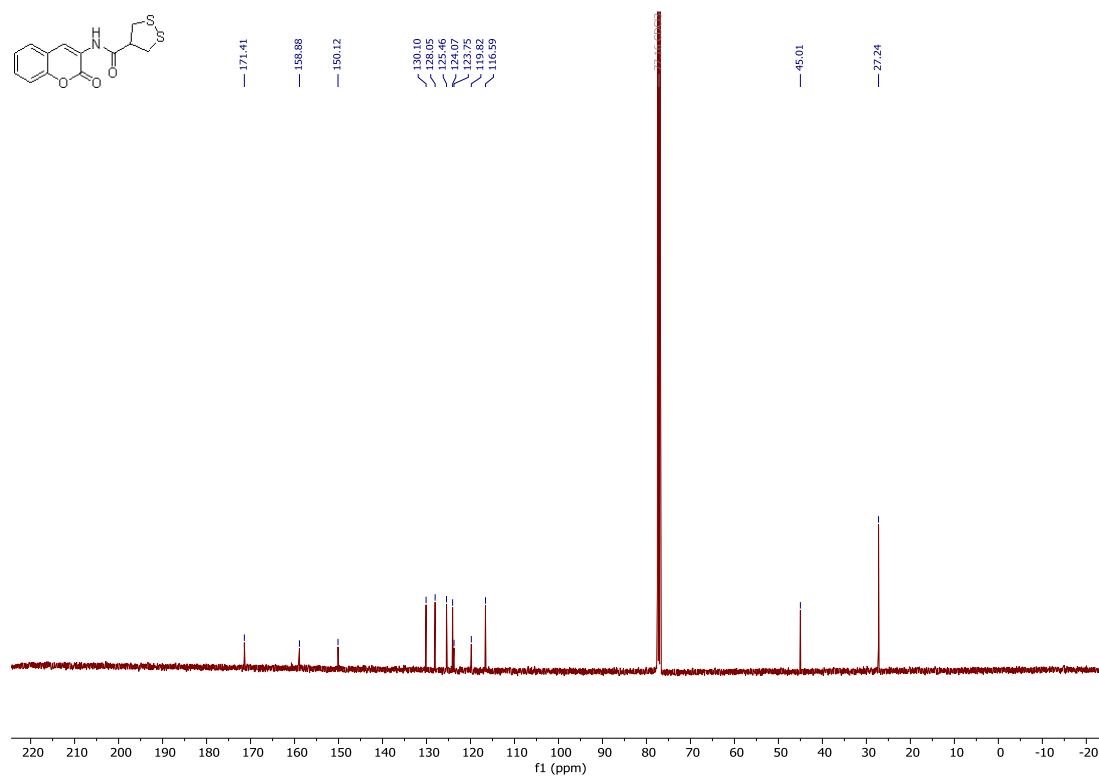
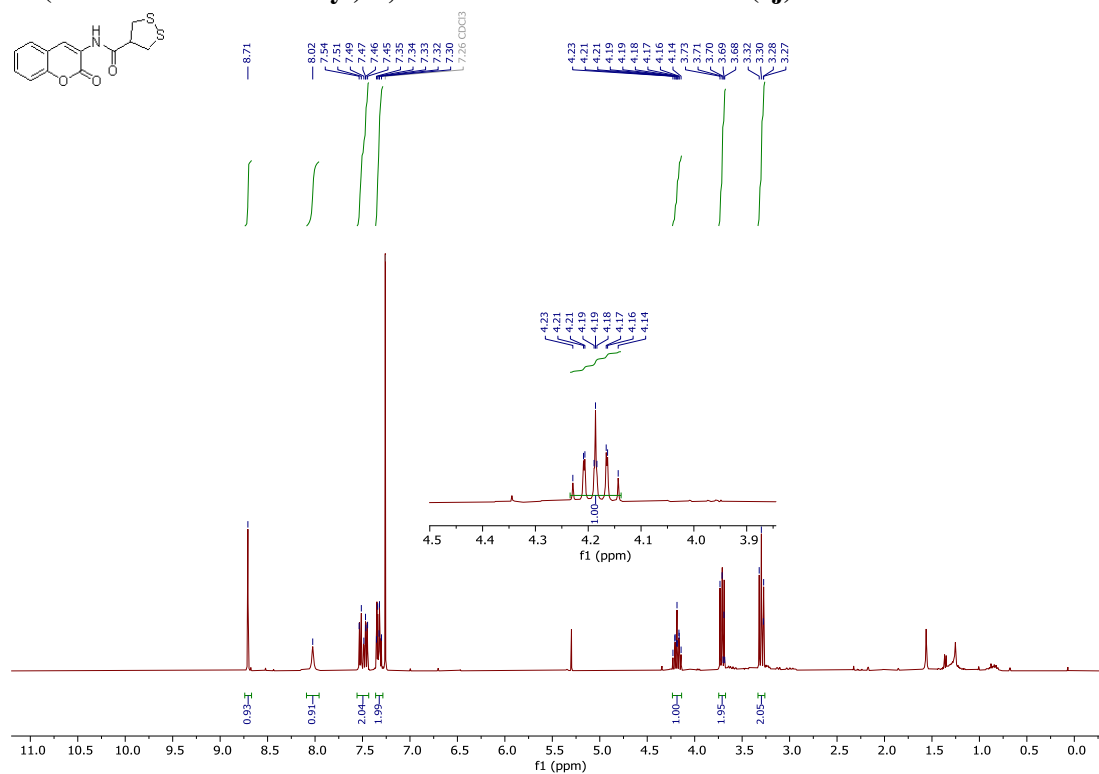


Minimum: 80.00
Maximum: 100.00

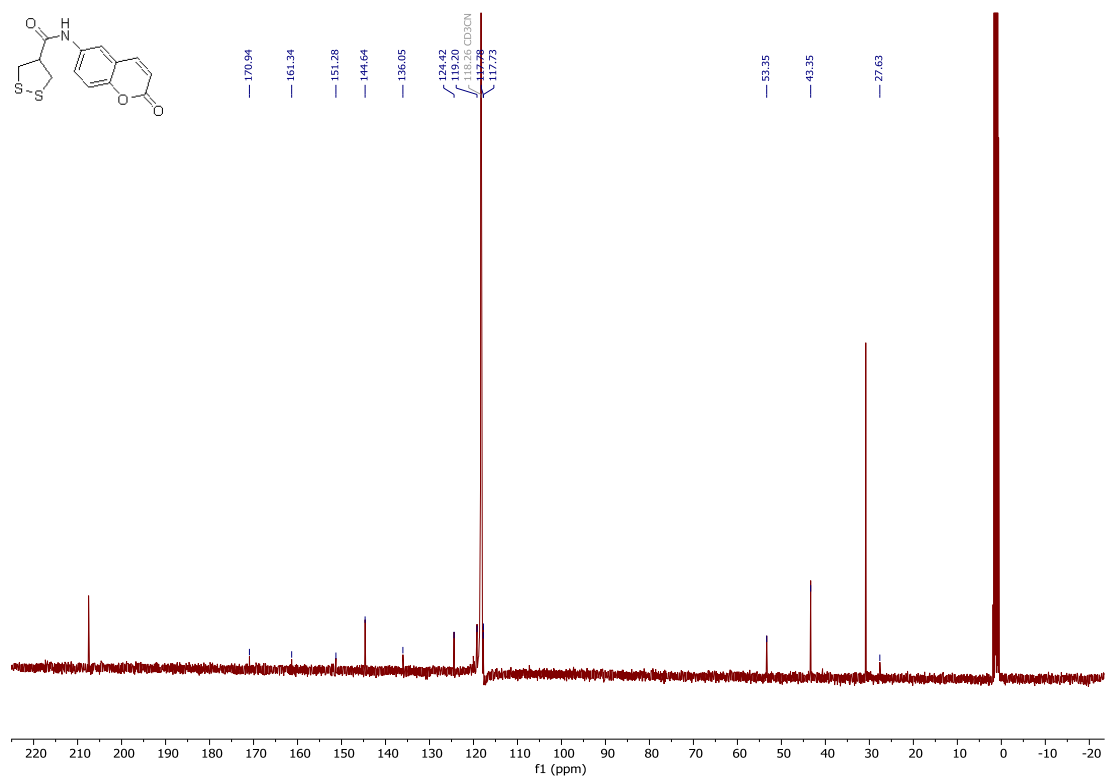
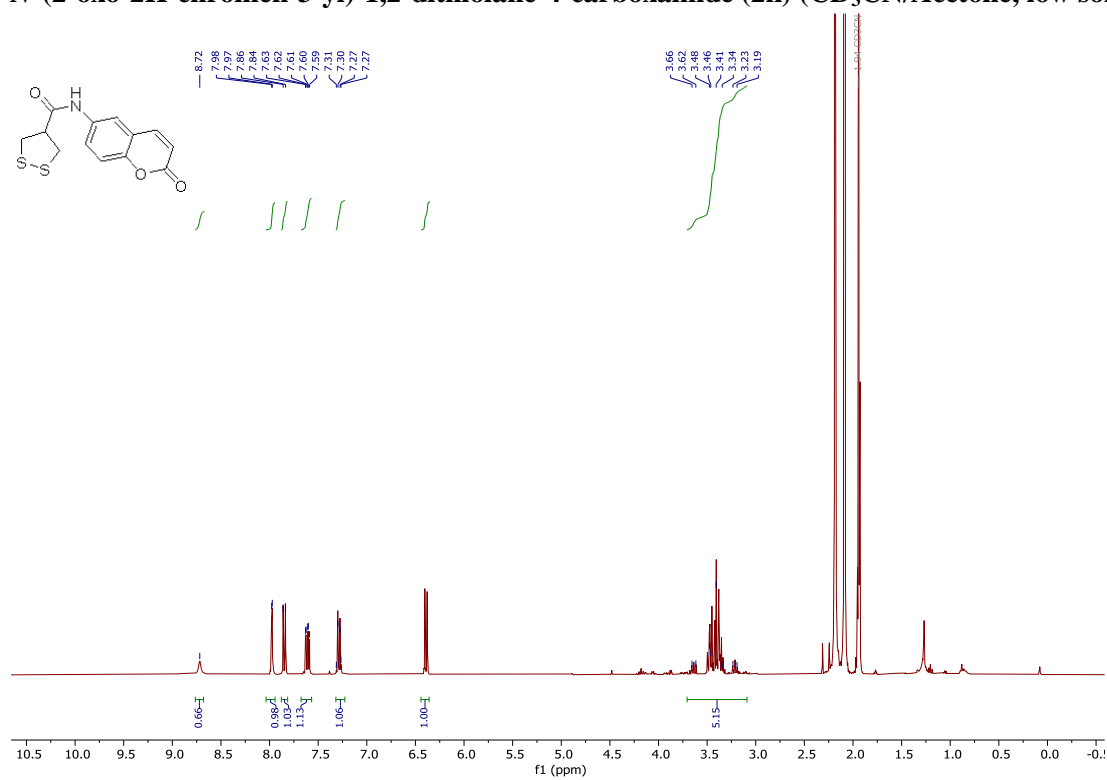
2.0 5.0 -1.5
200.0

Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
225.9671	100.00	225.9666	0.5	2.2	2.5	718.6	n/a	n/a	C5 H8 N O3 S3

***N*-(2-Oxo-2H-chromen-6-yl)-1,2-dithiolane-4-carboxamide (2j)**



***N*-(2-oxo-2H-chromen-3-yl)-1,2-dithiolane-4-carboxamide (2k) (CD₃CN/Acetone, low solubility)**



Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

248 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

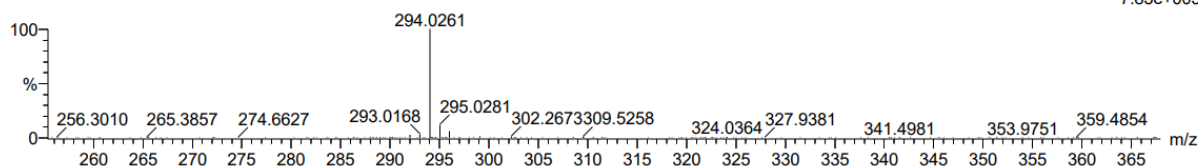
Elements Used:

C: 0-80 H: 0-150 N: 0-10 O: 0-10 S: 2-2

3118 Nikitjuka. 2k

HRMS_2022_05_322 658 (1.885) Cm (658:662-(672:677+629:640))

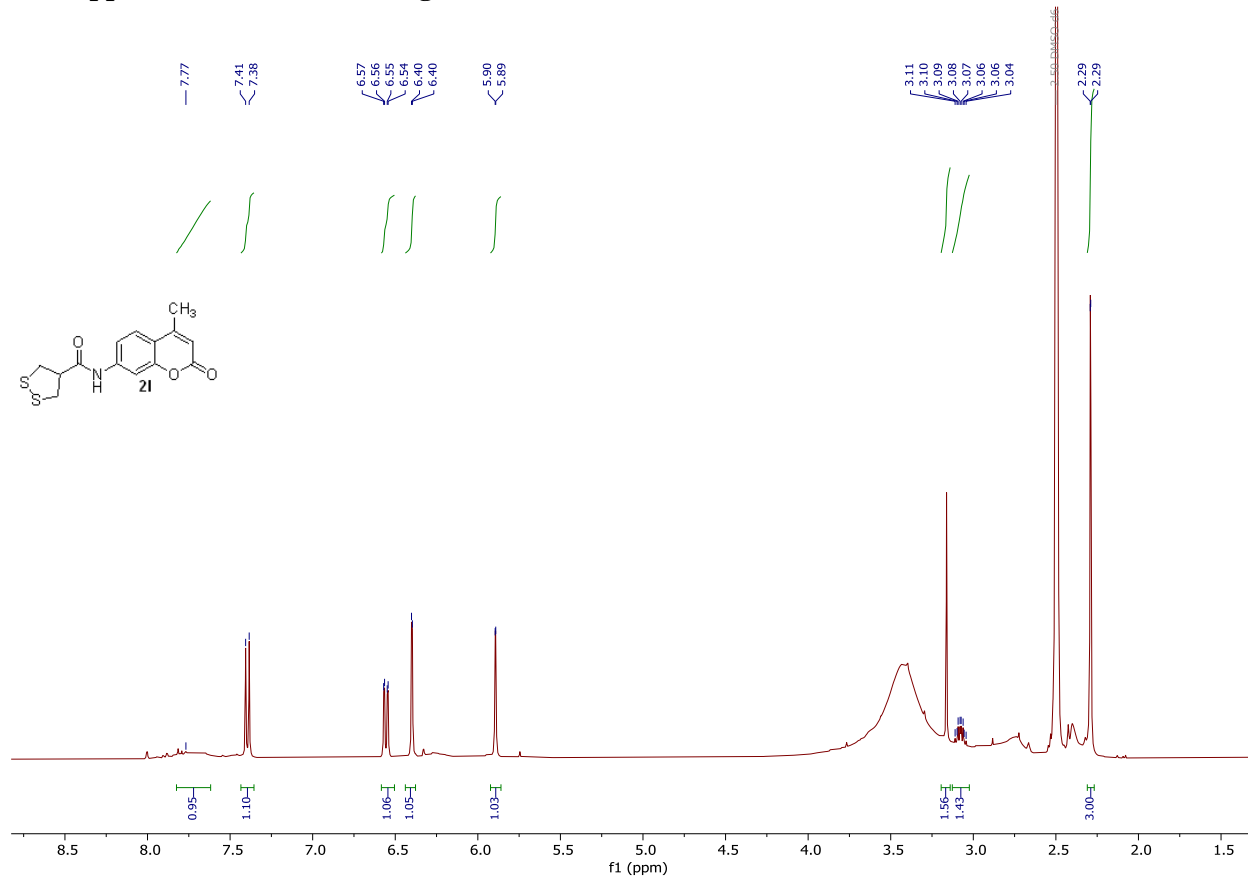
OSI/FOKL-MS
Synapt G2-Si
1: TOF MS ES+
7.83e+005

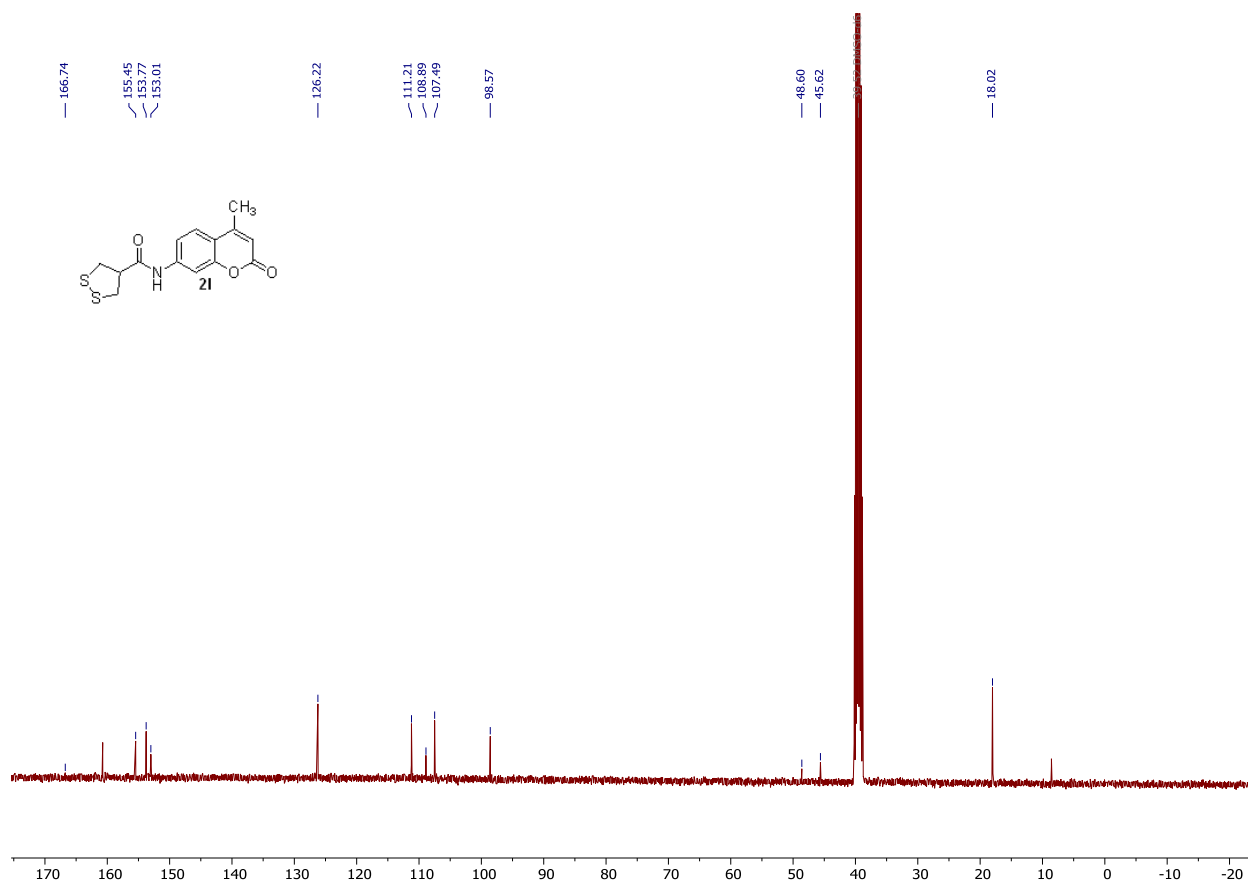


Minimum: -1.5
Maximum: 2.0 5.0 200.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
294.0261	294.0259	0.2	0.7	8.5	178.1	n/a	n/a	C13 H12 N O3 S2

***N*-(4-methyl-2-oxo-2H-chromen-7-yl)-1,2-dithiolane-4-carboxamide (21, 1,2-dithiolane signal is overlapped with residue water signal)**





Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

276 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

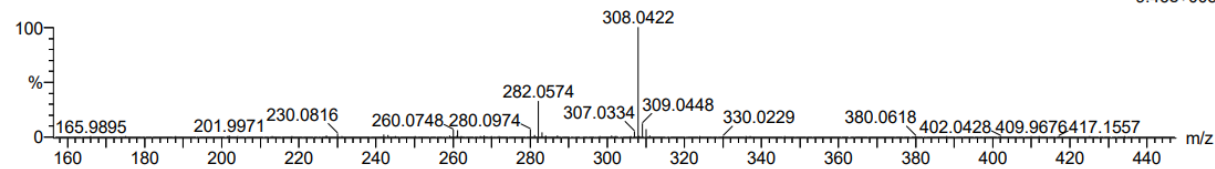
Elements Used:

C: 0-80 H: 0-150 N: 0-10 O: 0-10 S: 2-2

3119 Nikitjuka **2I**

HRMS_2022_05_324 673 (1.926) Cm (672:679-(654:660+700))

OSI/FOKL-MS
Synapt G2-Si
1: TOF MS ES+
9.46e+005



Minimum: -1.5
Maximum: 2.0 5.0 200.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
308.0422	308.0415	0.7	2.3	8.5	694.8	n/a	n/a	C14 H14 N O3 S2

Determination of the Reaction Rate and IC₅₀ of colorimetric TrxR1 enzymatic assays

IC₅₀ was obtained using Thioredoxin Reductase Colorimetric Assay Kit provided by Cayman Chemicals and the provided kit booklet was used for the IC₅₀ calculation ([Thioredoxin Reductase Colorimetric Assay Kit \(TrxR, TxnR\) | Cayman Chemical](#)). In brief, the reaction rate (ΔA) was determined and corrected:

$$\Delta A/\text{min}(\text{sample}) - [\Delta A/\text{min}(\text{sample}+\text{enzyme}) - \Delta A/\text{min}(\text{Background}+\text{enzyme})]$$

$$\text{TrxR activity} = \frac{\Delta A}{\text{min}(\text{sample}) - [\Delta A/\text{min}(\text{sample}+\text{enzyme}) - \Delta A/\text{min}(\text{Background}+\text{enzyme})]}$$

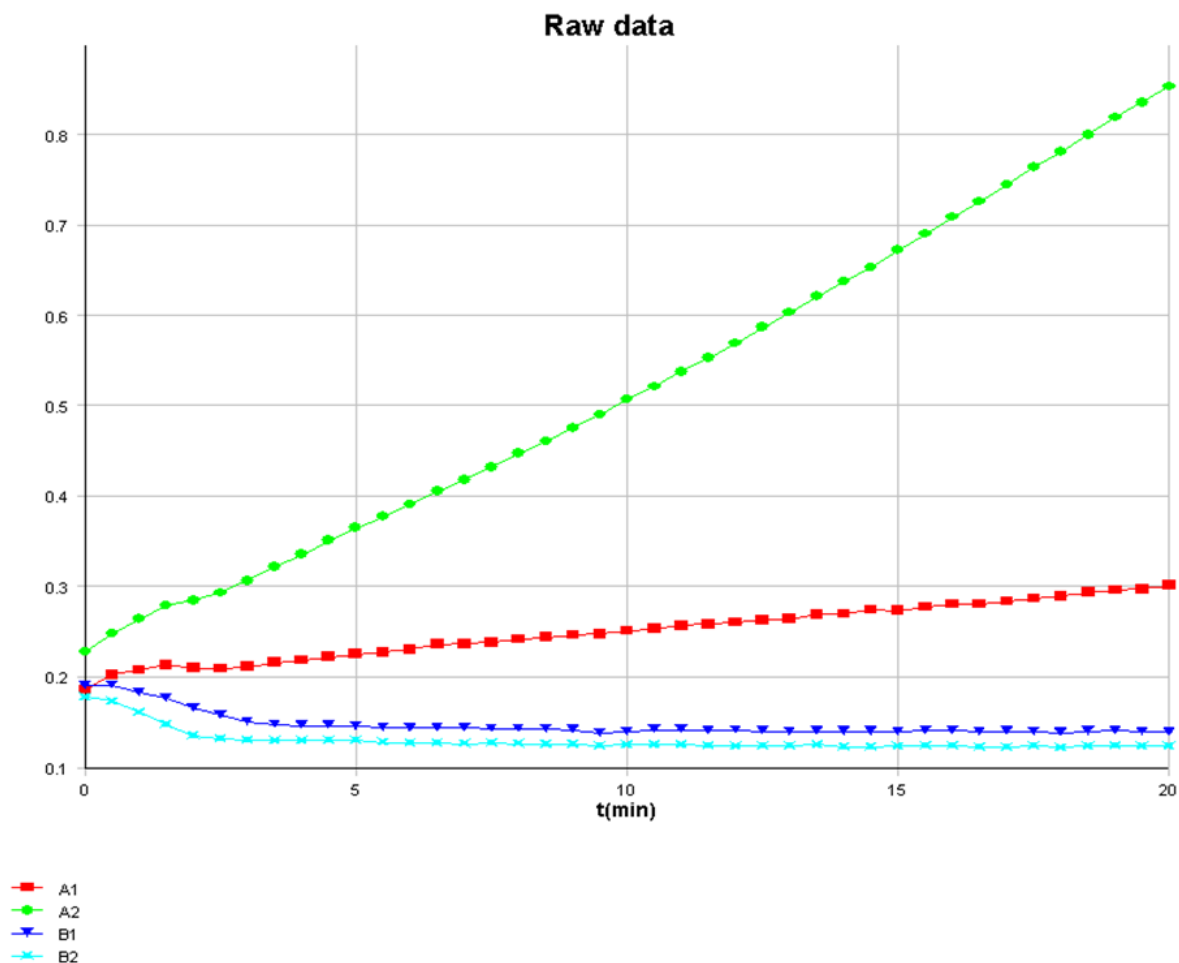


Figure S1. Representative example of activity plot of the rat liver TrxR1 (x = time (minutes); y = absorbance at 405 nm).