Article

N-Derivatives of (Z)-methyl 3-(4-oxo-2-thioxothiazolidin-5-ylidene) methyl)-1*H*-indole-2-carboxylates as antimicrobial agents. *In silico* and *in vitro* evaluation.

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Table S1. Prediction of organ toxicity and toxicity end points for compounds **1-17**.

Comp.	Organ toxicity		Toxicity end points				
	Cardiotoxicity	**Hepatotoxicity**	**Carcinogenicity**	**Immunotoxicity**	**Mutagenicity**	**Cytotoxicity**	**Phospholipidosis**
1	Inactive (0.79)	Inactive (0.68)	Inactive (0.62)	Inactive(0.55)	Inactive (0.74)	Inactive(0.64)	Inactive (0.99)
2	Inactive (0.75)	Active (0.56)	Inactive (0.63)	Inactive (0.97)	Inactive (0.55)	Inactive (0.64)	Inactive (0.89)
3	Inactive (0.93)	Active (0.59)	Inactive (0.61)	Active (0.61)	Inactive (0.54)	Inactive(0.61)	Inactive (0.89)
4	Inactive (0.93)	Active (0.60)	Inactive (0.60)	Active(0.72)	Inactive (0.53)	Inactive(0.64)	Inactive (0.89)
5	Inactive (0.60)	Inactive (0.66)	Inactive (0.57)	Active (0.88)	Inactive (0.69)	Inactive (0.65)	Inactive (0.81)
6	Inactive (0.93)	Active (0.52)	Inactive (0.56)	Inactive (0.76)	Inactive (0.58)	Inactive (0.65)	Inactive (0.93)
7	Inactive (0.84)	Inactive (0.50)	Inactive (0.58)	Inactive (0.76)	Inactive (0.61)	Inactive (0.62)	Inactive (0.89)
8	Inactive (0.84)	Active (0.55)	Inactive (0.66)	Active (0.64)	Inactive (0.64)	Inactive (0.70)	Inactive (0.99)
9	Inactive (0.84)	Active (0.51)	Inactive (0.62)	Active (0.77)	Inactive (0.71)	Inactive (0.63)	Inactive (0.99)
10	Inactive (0.93)	Active (0.59)	Inactive (0.62)	Active (0.84)	Inactive (0.58)	Inactive (0.67)	Inactive (0.89)
11	Inactive (0.84)	Inactive (0.53)	Inactive (0.63)	Inactive (0.82)	Inactive (0.69)	Inactive (0.64)	Inactive (0.99)
12	Inactive (0.84)	Inactive (0.54)	Inactive (0.68)	Inactive (0.88)	Inactive (0.63)	Inactive (0.67)	Inactive (0.99)
13	Inactive (0.93)	Active (0.57)	Inactive (0.60)	Active (0.98)	Inactive (0.59)	Inactive (0.70)	Inactive (0.81)
14	Inactive (0.84)	Inactive (0.52)	Inactive (0.63)	Active (0.78)	Inactive (0.70)	Inactive (0.63)	Inactive (0.99)
15	Inactive (0.93)	Active (0.56)	Inactive (0.63)	Inactive (0.54)	Inactive (0.58)	Inactive (0.73)	Inactive (0.89)
16	Inactive (0.93)	Active (0.51)	Inactive (0.59)	Active (0.81)	Inactive (0.57)	Inactive (0.65)	Inactive (0.93)
17	Inactive (0.79)	Active (0.59)	Inactive (0.63)	Active (0.79)	Inactive (0.71)	Inactive (0.63)	Inactive (0.99)

Number in brackets indicate possibilites. Cardiotoxicity is reffered to the probability of inhibition of the inward rectifying voltage gated potassium channel in the heart encoded by the human ether-a-go-go related gene (hERG).

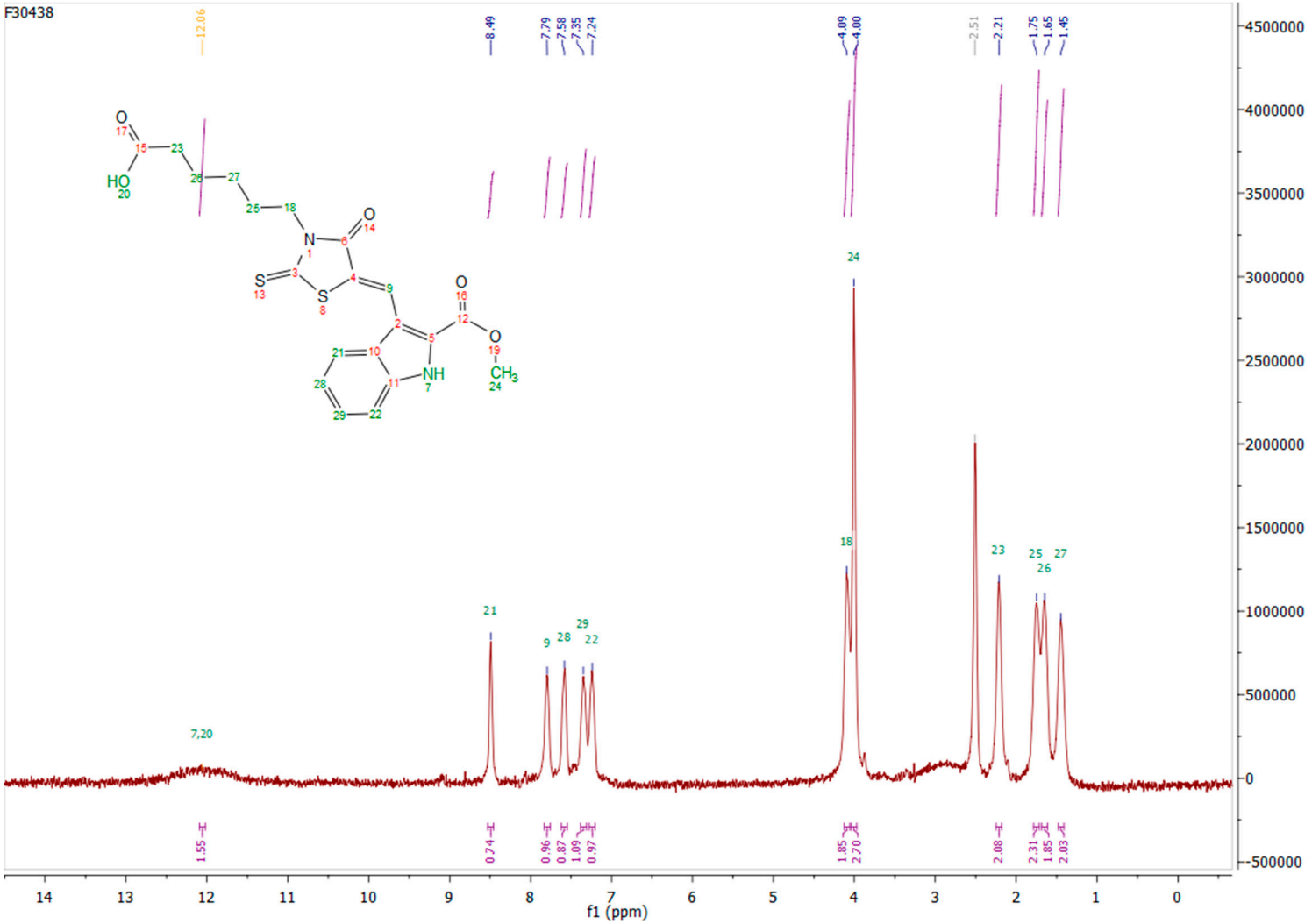
Table S2. Prediction of adverse outcomes according to TOX21 of compounds **1-17**.

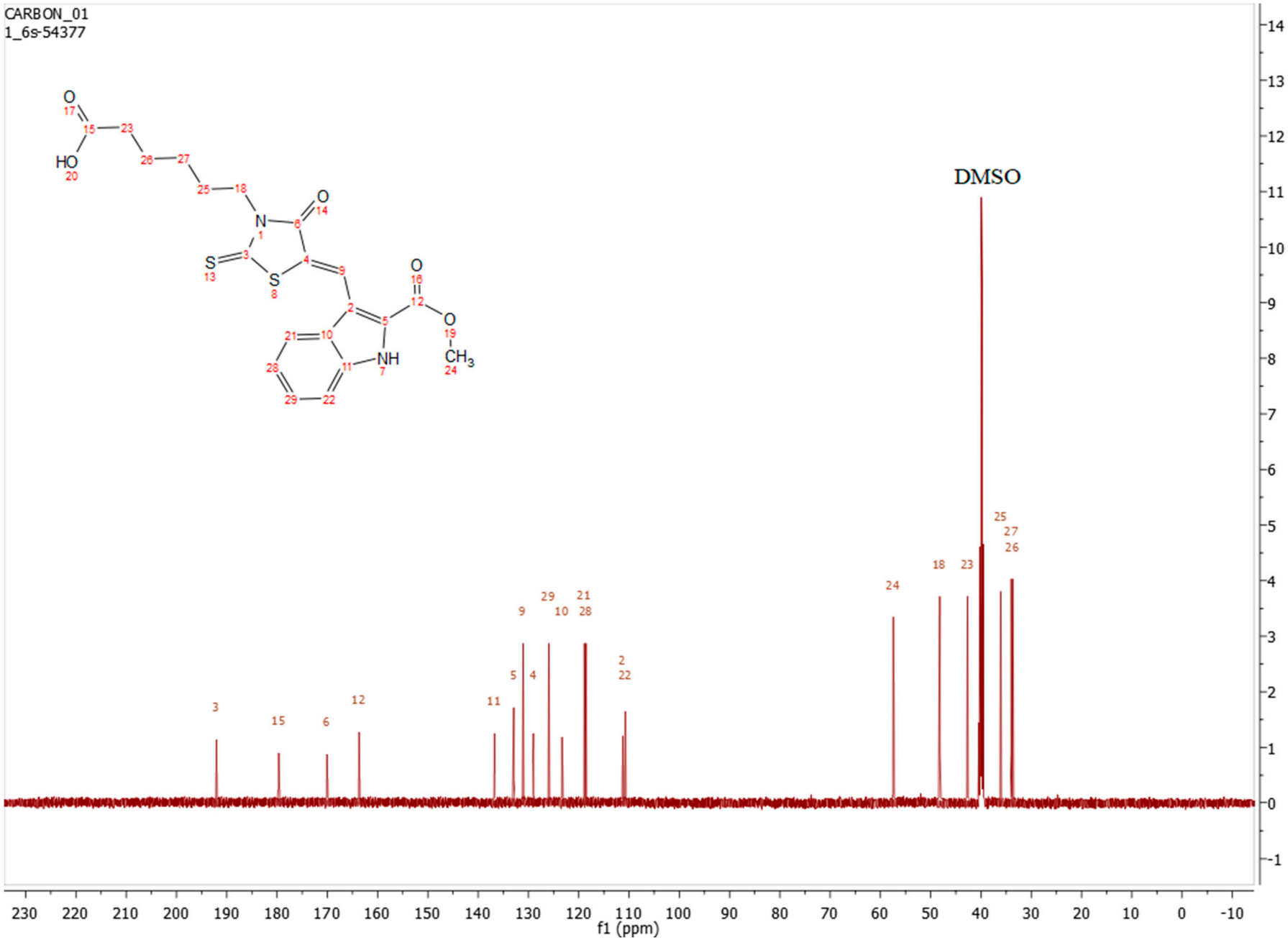
Comp.	Tox21-Nuclear receptor signalling pathways							Tox21-Stress response pathways				
	AhR	**AR**	**AR-LBD**	**ARO**	**ER**	**ER-LBD**	**PPARγ**	**NRF2/ARE**	**HSE**	**MMP**	**p53**	**ATAD5**
1	Inactive (0.77)	Inactive (0.98)	Inactive (0.97)	Inactive (0.93)	Inactive (0.87)	Inactive (0.95)	Inactive (0.81)	Inactive (0.85)	Inactive (0.85)	Inactive (0.85)	Inactive (0.81)	Inactive (0.90)
2	Inactive (0.61)	Inactive (0.95)	Inactive (0.97)	Inactive (0.81)	Inactive (0.76)	Inactive (0.92)	Inactive (0.81)	Inactive (0.90)	Inactive (0.90)	Inactive (0.54)	Inactive (0.75)	Inactive (0.71)
3	Inactive (0.60)	Inactive (0.92)	Inactive (0.97)	Inactive (0.84)	Inactive (0.73)	Inactive (0.92)	Inactive (0.82)	Inactive (0.89)	Inactive (0.89)	Inactive (0.51)	Inactive (0.71)	Inactive (0.75)
4	Inactive (0.63)	Inactive (0.94)	Inactive (0.97)	Inactive (0.83)	Inactive (0.72)	Inactive (0.90)	Inactive (0.81)	Inactive (0.91)	Inactive (0.91)	Inactive (0.51)	Inactive (0.70)	Inactive (0.75)
5	Inactive (0.78)	Inactive (0.95)	Inactive (0.93)	Inactive (0.91)	Inactive (0.87)	Inactive (0.94)	Inactive (0.82)	Inactive (0.91)	Inactive (0.91)	Inactive (0.75)	Inactive (0.82)	Inactive (0.94)
6	Inactive (0.82)	Inactive (0.95)	Inactive (0.95)	Inactive (0.90)	Inactive (0.87)	Inactive (0.94)	Inactive (0.88)	Inactive (0.92)	Inactive (0.92)	Inactive (0.69)	Inactive (0.89)	Inactive (0.94)
7	Inactive (0.65)	Inactive (0.98)	Inactive (0.96)	Inactive (0.93)	Inactive (0.84)	Inactive (0.95)	Inactive (0.84)	Inactive (0.91)	Inactive (0.91)	Inactive (0.79)	Inactive (0.81)	Inactive (0.83)
8	Inactive (0.63)	Inactive (0.97)	Inactive (0.97)	Inactive (0.87)	Inactive (0.79)	Inactive (0.88)	Inactive (0.87)	Inactive (0.89)	Inactive (0.89)	Inactive (0.65)	Inactive (0.79)	Inactive (0.91)
9	Inactive (0.78)	Inactive (0.98)	Inactive (0.97)	Inactive (0.90)	Inactive (0.84)	Inactive (0.90)	Inactive (0.79)	Inactive (0.85)	Inactive (0.85)	Inactive (0.82)	Inactive (0.82)	Inactive (0.87)
10	Inactive (0.65)	Inactive (0.96)	Inactive (0.96)	Inactive (0.87)	Inactive (0.71)	Inactive (0.83)	Inactive (0.78)	Inactive (0.89)	Inactive (0.89)	Inactive (0.54)	Inactive (0.73)	Inactive (0.82)
11	Inactive (0.72)	Inactive (0.98)	Inactive (0.97)	Inactive (0.93)	Inactive (0.89)	Inactive (0.95)	Inactive (0.80)	Inactive (0.86)	Inactive (0.86)	Inactive (0.83)	Inactive (0.84)	Inactive (0.79)
12	Inactive (0.64)	Inactive (0.97)	Inactive (0.97)	Inactive (0.91)	Inactive (0.82)	Inactive (0.92)	Inactive (0.88)	Inactive (0.90)	Inactive (0.90)	Inactive (0.67)	Inactive (0.79)	Inactive (0.89)
13	Inactive (0.63)	Inactive (0.95)	Inactive (0.95)	Inactive (0.88)	Inactive (0.72)	Inactive (0.88)	Inactive (0.86)	Inactive (0.89)	Inactive (0.89)	Inactive (0.53)	Inactive (0.75)	Inactive (0.84)
14	Inactive (0.78)	Inactive (0.98)	Inactive (0.96)	Inactive (0.89)	Inactive (0.84)	Inactive (0.89)	Inactive (0.81)	Inactive (0.86)	Inactive (0.86)	Inactive (0.82)	Inactive (0.83)	Inactive (0.86)
15	Inactive (0.58)	Inactive (0.97)	Inactive (0.96)	Inactive (0.89)	Inactive (0.80)	Inactive (0.93)	Inactive (0.89)	Inactive (0.91)	Inactive (0.91)	Inactive (0.65)	Inactive (0.77)	Inactive (0.88)
16	Inactive (0.84)	Inactive (0.97)	Inactive (0.93)	Inactive (0.91)	Inactive (0.80)	Inactive (0.90)	Inactive (0.90)	Inactive (0.91)	Inactive (0.91)	Inactive (0.73)	Inactive (0.89)	Inactive (0.93)
17	Inactive (0.79)	Inactive (0.98)	Inactive (0.96)	Inactive (0.94)	Inactive (0.89)	Inactive (0.95)	Inactive (0.80)	Inactive (0.89)	Inactive (0.89)	Inactive (0.85)	Inactive (0.81)	Inactive (0.84)

(1) Aryl hydrocarbon Receptor, (2) Androgen Receptor, (3) Androgen Receptor Ligand Binding Domain, (4) Aromatase, (5) Estrogen Receptor Alpha, (6) Estrogen Receptor Ligand Binding Domain, (7) Peroxisome Proliferator Activated Receptor Gamma, (8) Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element, (9) Heat shock factor response element, (10) Heat shock factor response element, (11) Phosphoprotein (Tumor Suppressor) p53, (12) ATPase family AAA domain-containing protein 5

^{1}H-NMR and ^{13}C-NMR of compounds

Compound 1

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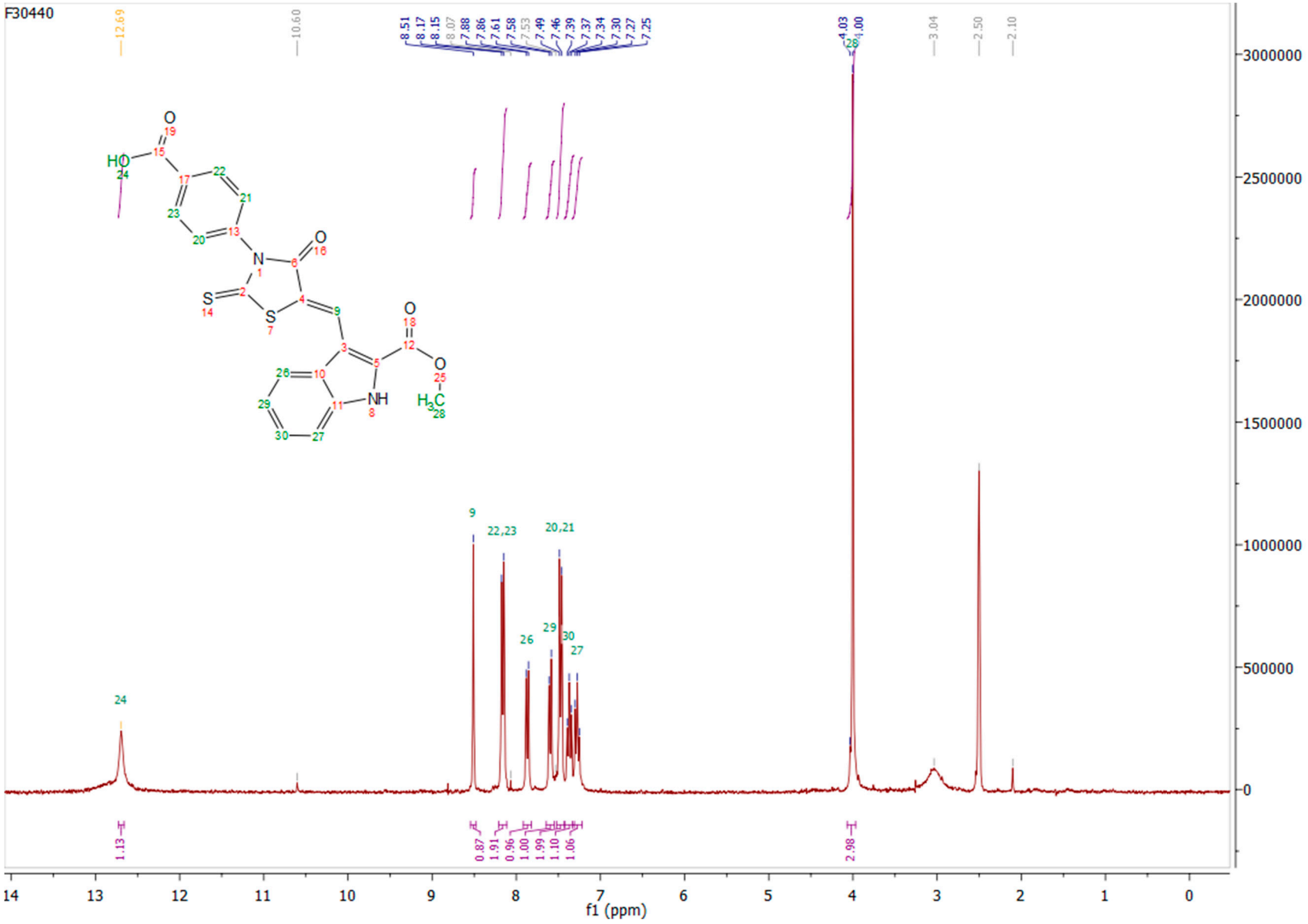
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7.49
7.46
7.39
7.37
7.34
7.30
7.27
7.25
4.03
4.00
3.04
2.50
2.10
9
22,23
20,21
26
29
30
27
24
1.13
0.87
1.91
0.96
1.00
1.99
1.10
1.06
2.98
3000000
2500000
2000000
1500000
1000000
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7
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5
4
3
2
1
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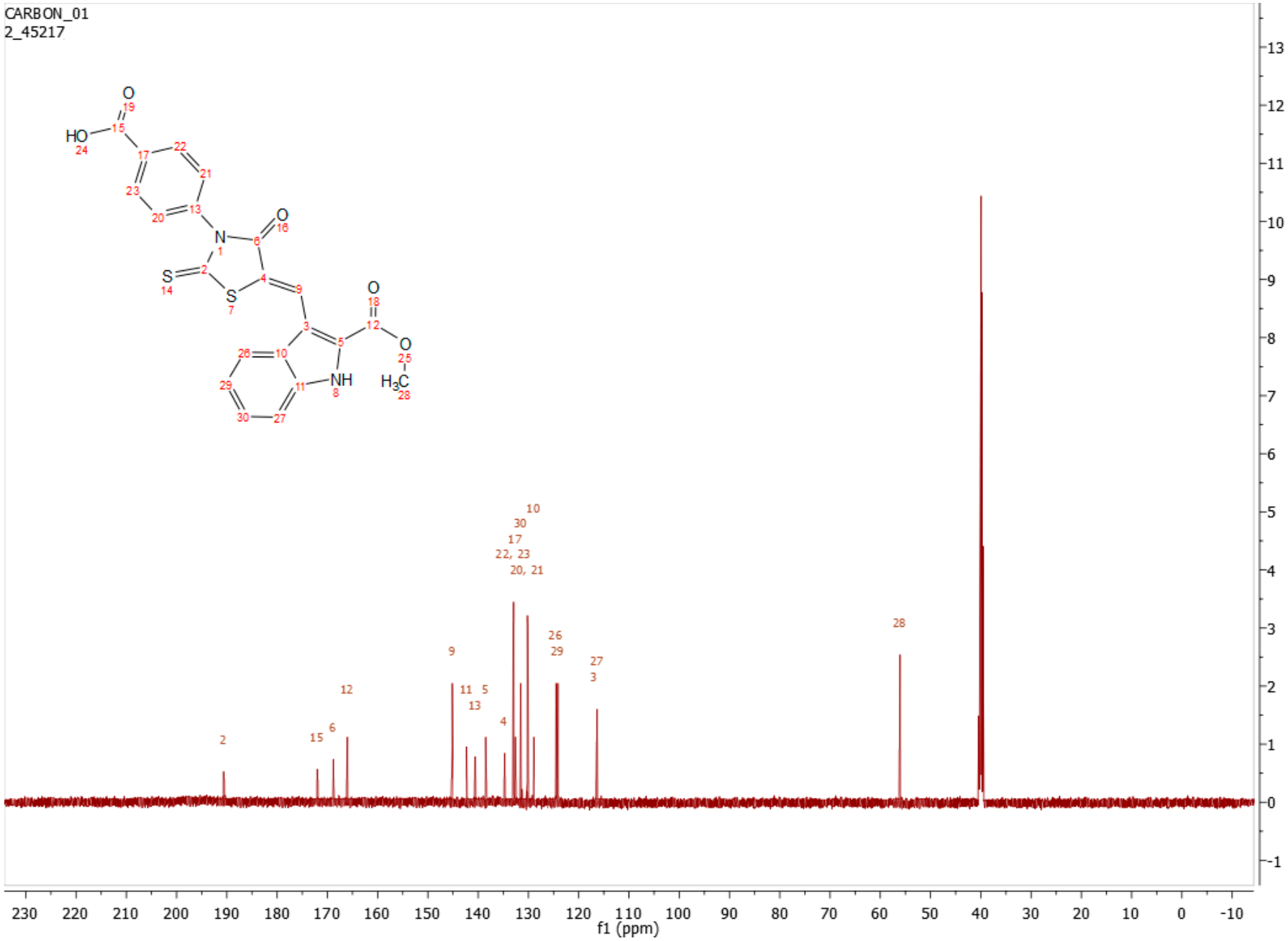
f1 (ppm)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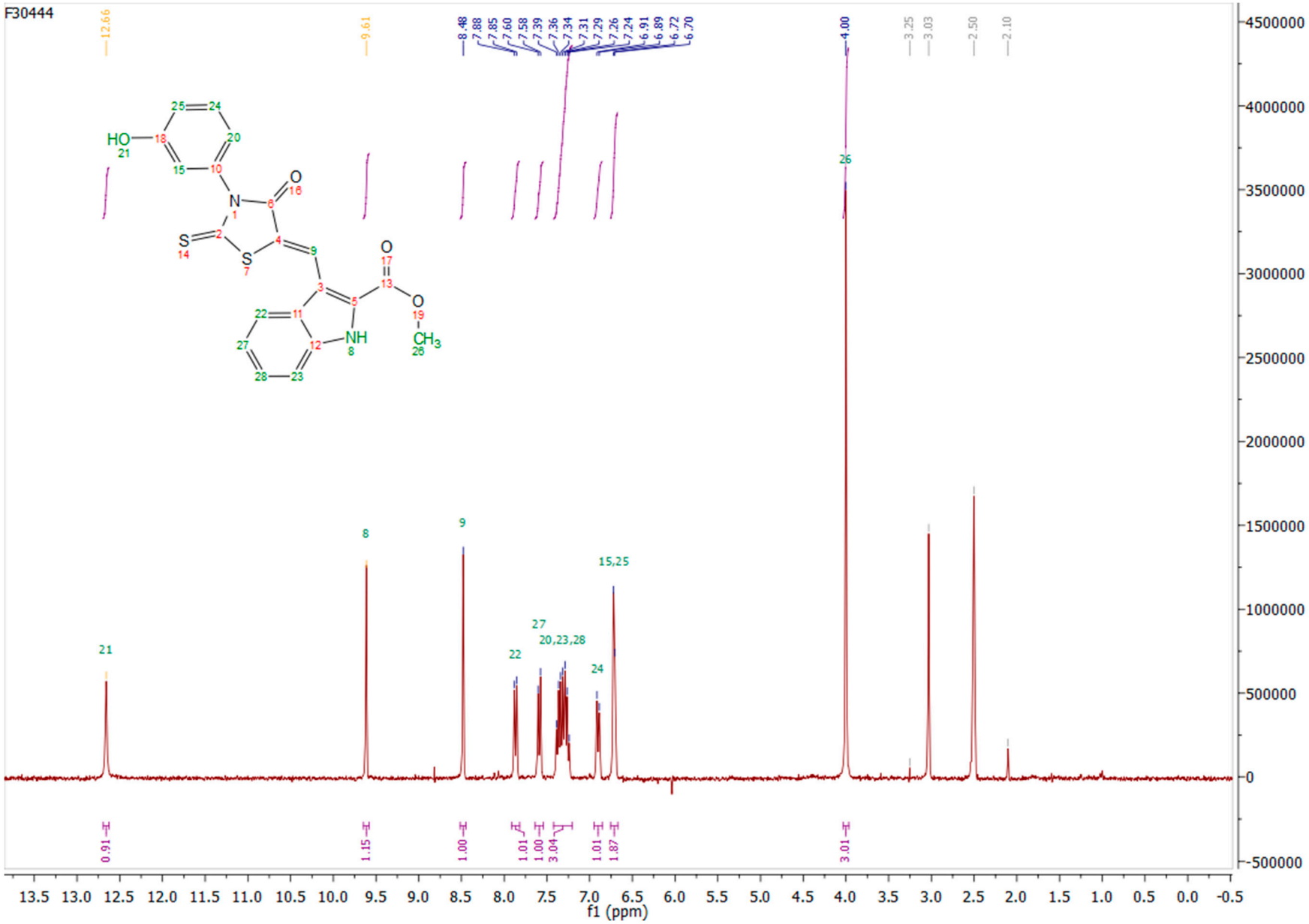
N
S
S
O
O
NH
H3C
f1 (ppm)

Compound 3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7.29
7.26
7.24
6.91
6.89
6.72
6.70
4.00
3.25
3.03
2.50
2.10
HO
N
S
S
O
NH
CH3
21
8
9
22
27
20,23,28
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1.01
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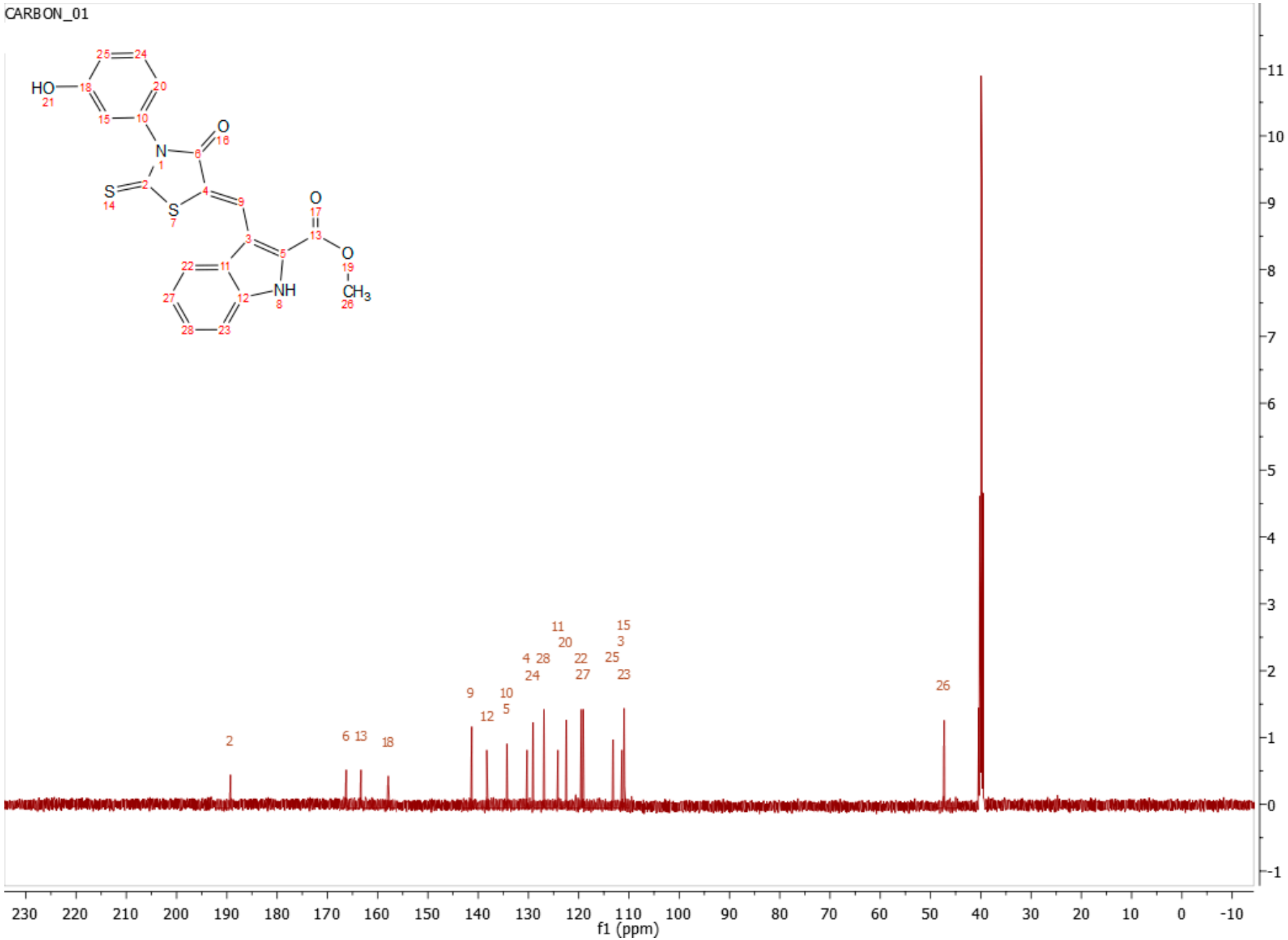
3.01
f1 (ppm)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O
17
13
O
19
CH3
26
22
11
27
12
NH
8
28
23
2
6 13
18
9
12
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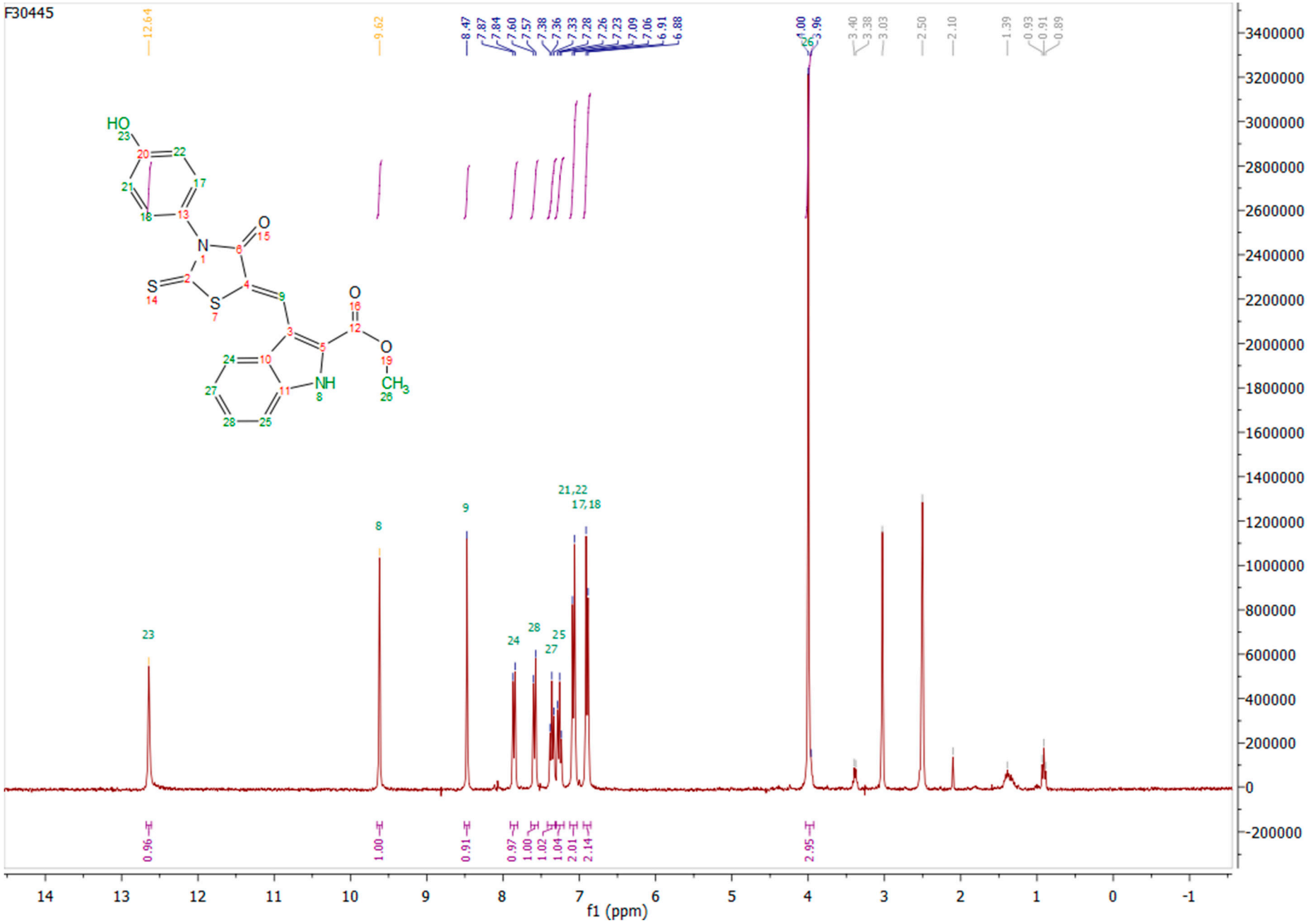
5
4 28
24
11
20
22
27
15
3
25
23
26
f1 (ppm)

Compound 4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7.26
7.23
7.09
7.06
6.91
6.88
4.00
3.96
3.40
3.38
3.03
2.50
2.10
1.39
0.93
0.91
0.89
HO
O
N
S
S
O
O
O
NH
CH3
23
8
9
24
28
25
27
21,22
17,18
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0.91
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2.01
2.14
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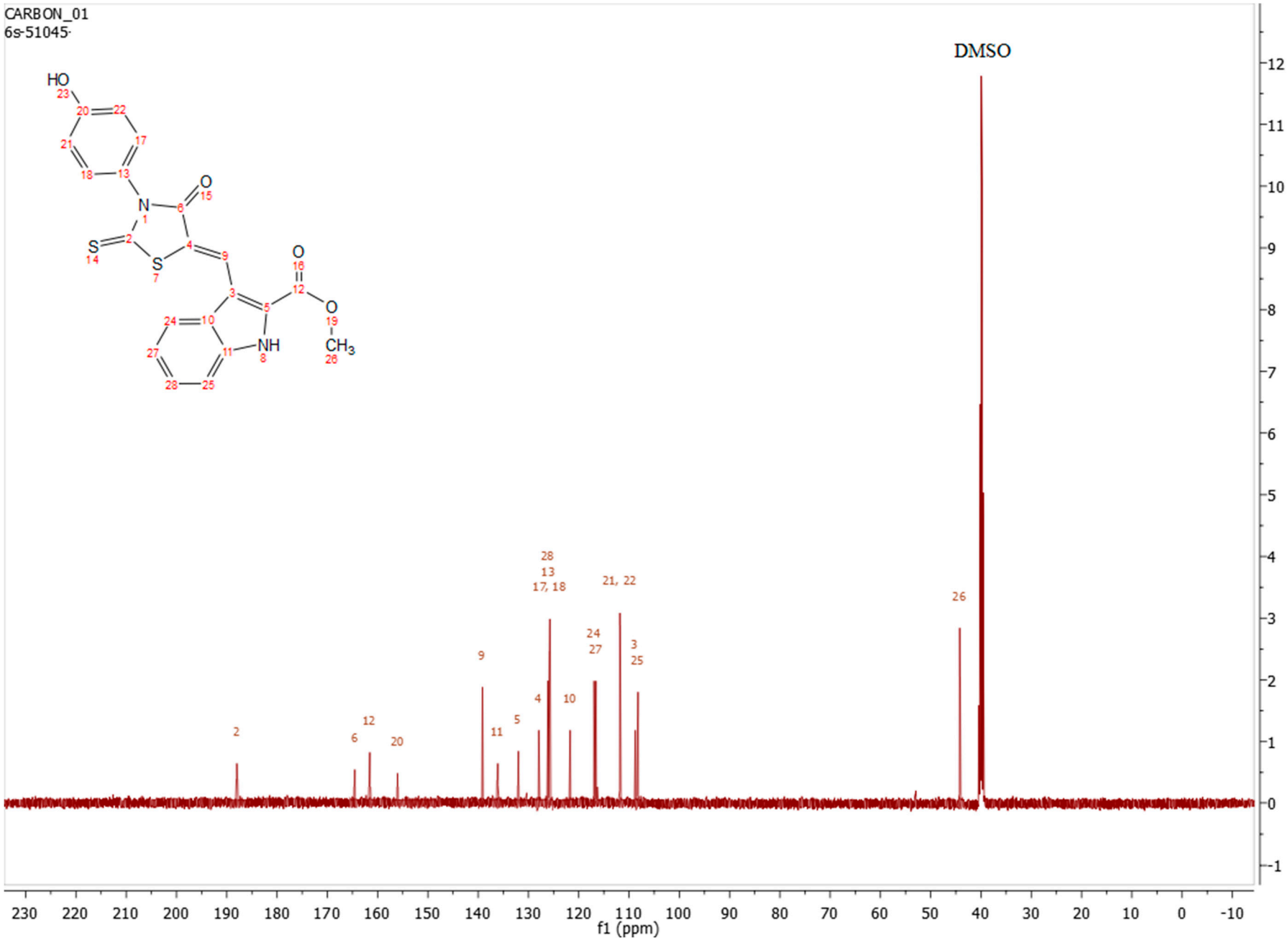
f1 (ppm)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23
20
22
21
17
18
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15
N
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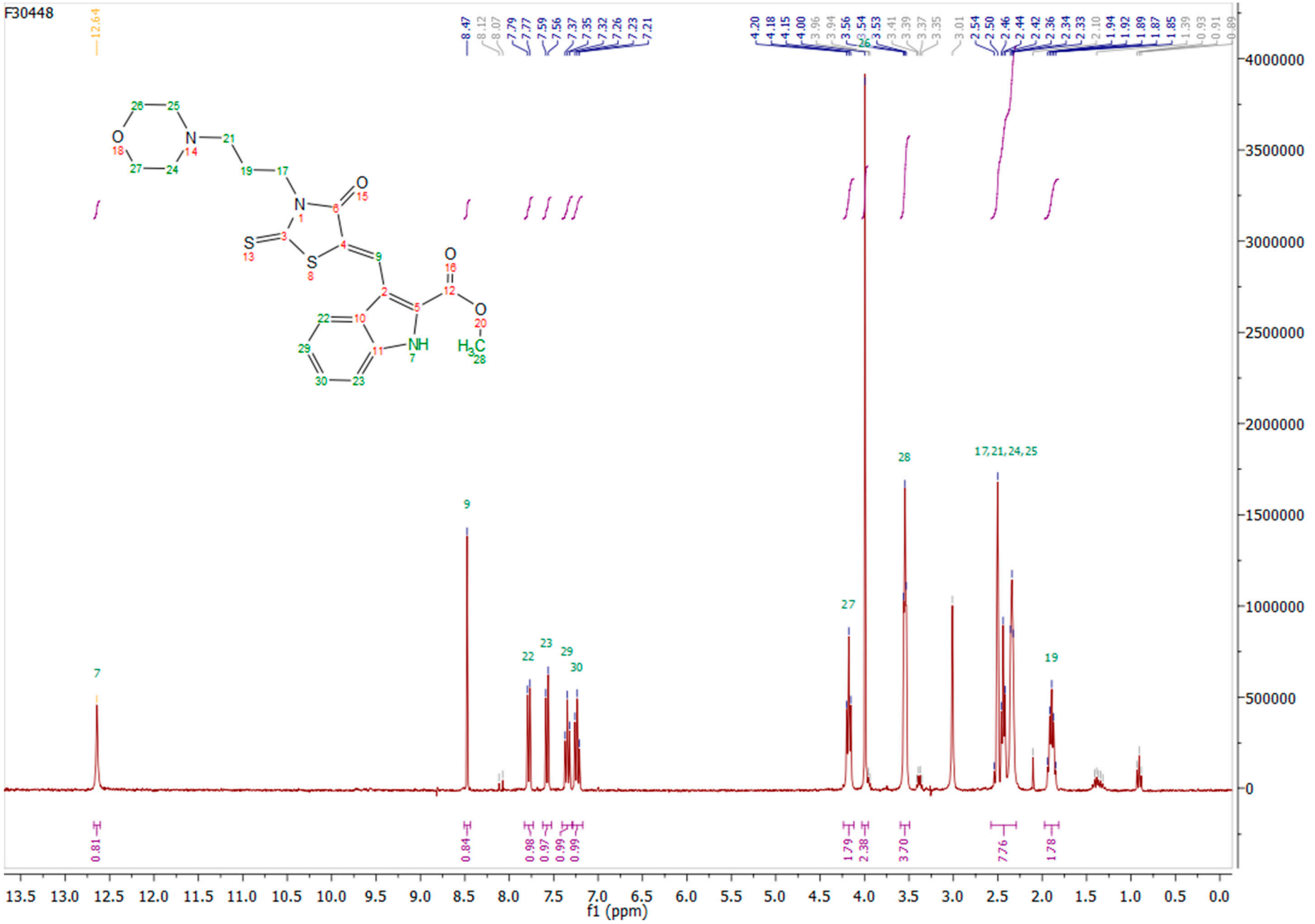
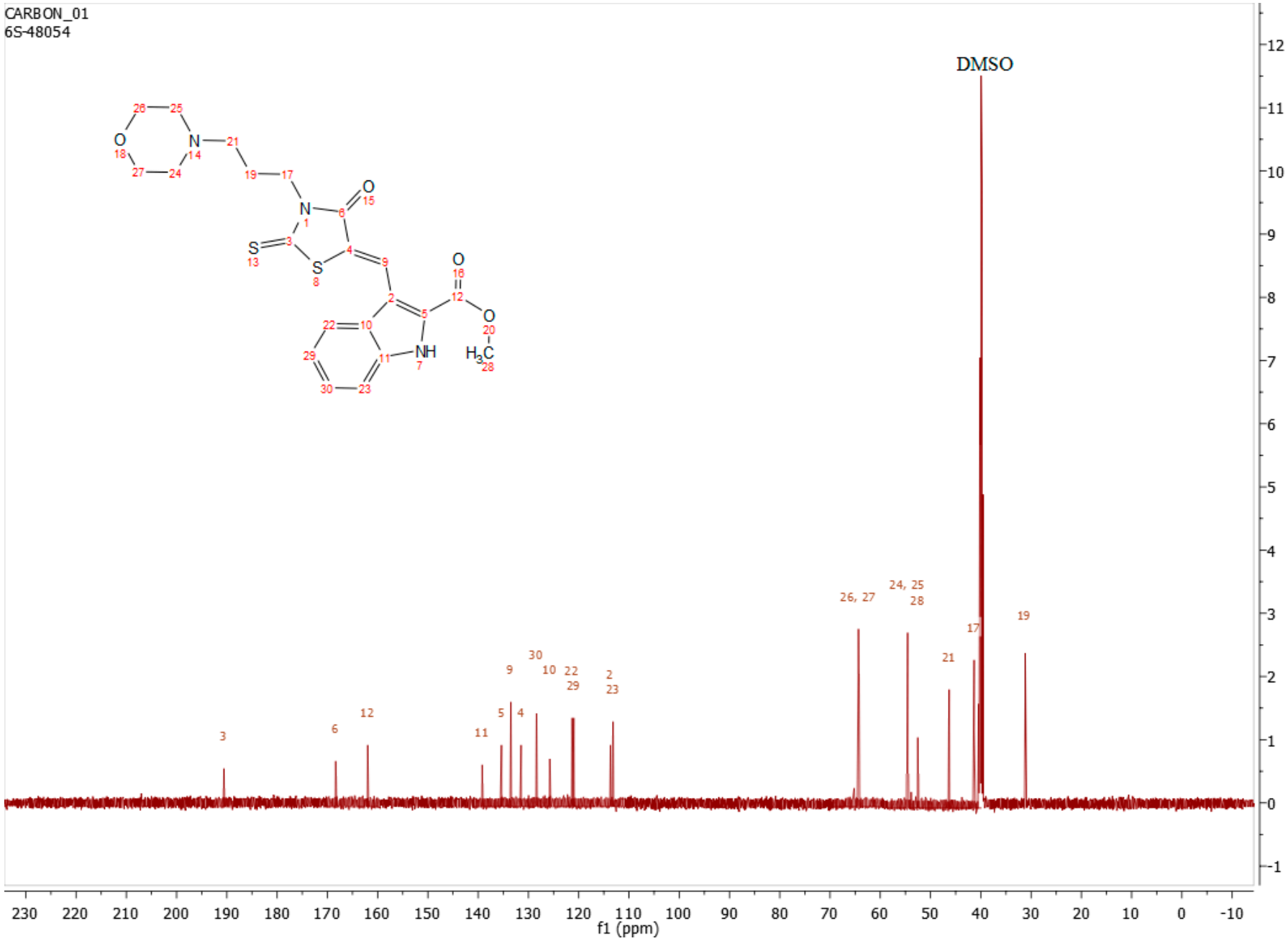
2
S
14
S
7
4
9
O
16
12
3
5
O
19
24
10
NH
8
CH3
26
27
11
28
25
28
13
17, 18
21, 22
26
24
27
3
25
9
4
10
11
5
2
6
12
20
f1 (ppm)

Compound 5

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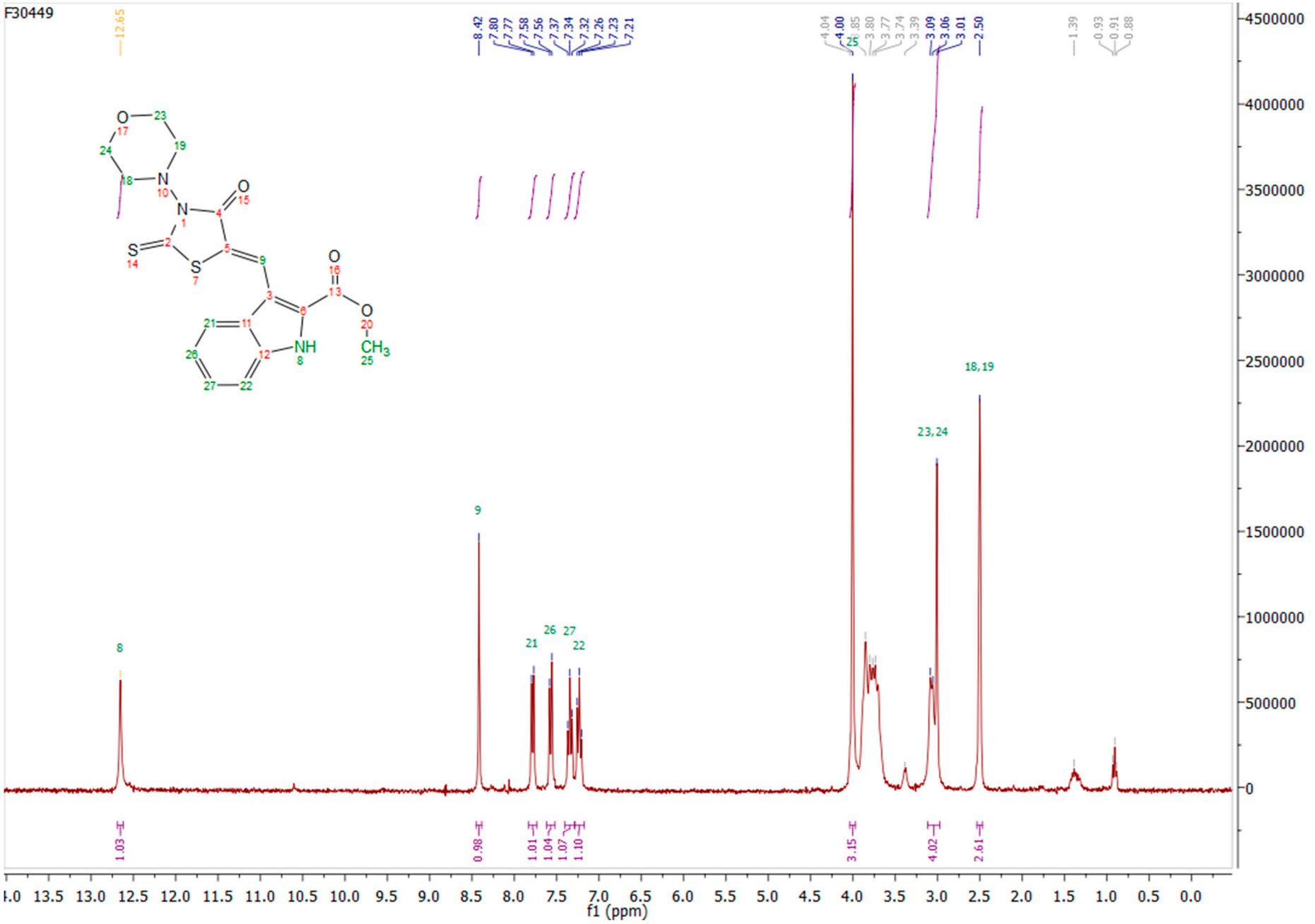
DMSO
26, 27
24, 25
28
19
17
21
30
9
10
22
29
2
23
5
4
12
6
11
3
f1 (ppm)

Compound 6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7.21
4.04
4.00
3.85
3.80
3.77
3.74
3.39
3.09
3.06
3.01
2.50
1.39
0.93
0.91
0.88
25
18,19
23,24
9
8
21
26
27
22
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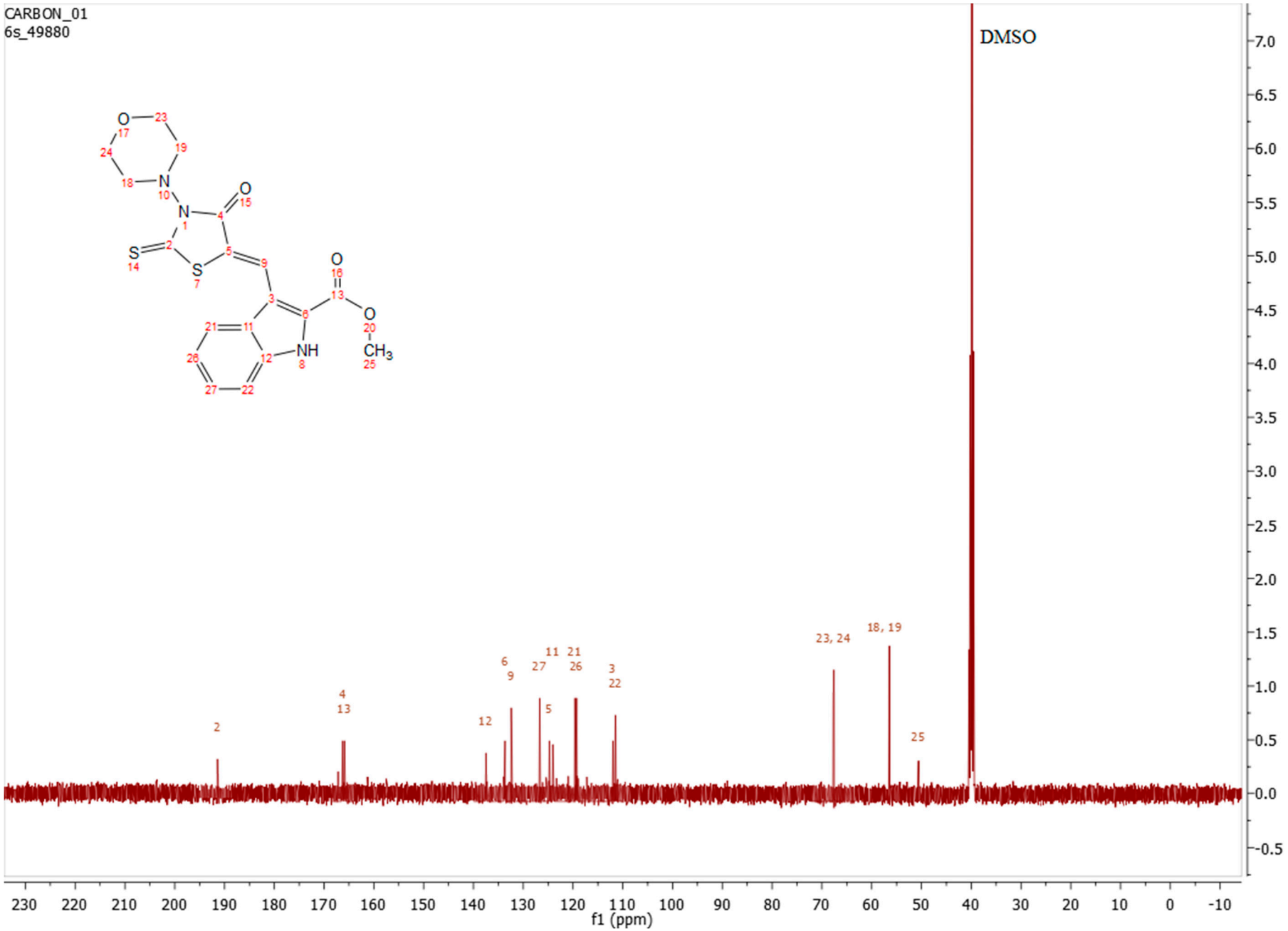
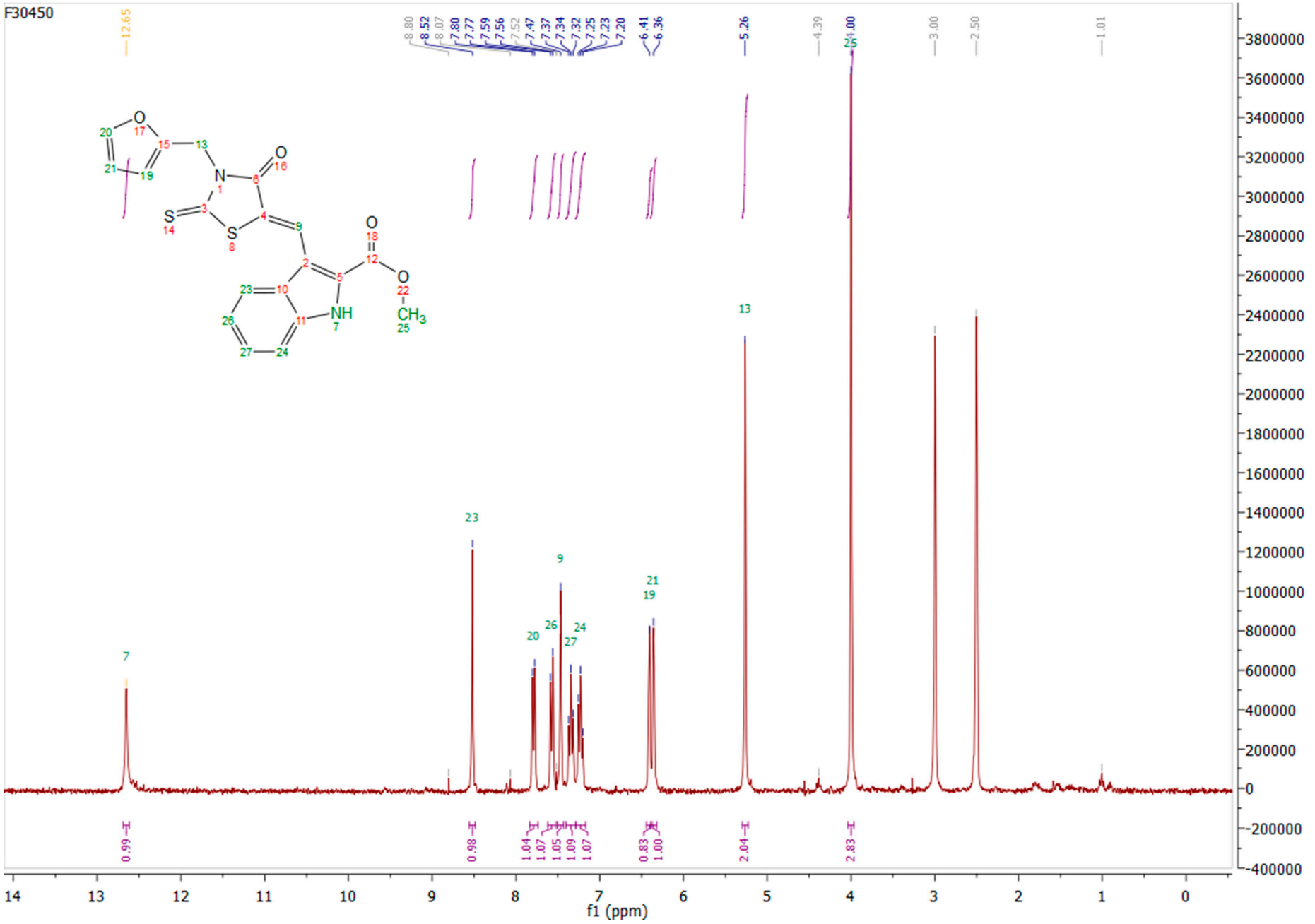
0.98
1.01
1.04
1.07
1.10
3.15
4.02
2.61
f1 (ppm)


CARBON_01
6s_49880
DMSO
2
4
13
12
6
9
27
11
5
21
26
3
22
23, 24
18, 19
25
f1 (ppm)

Compound 7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7.59
7.56
7.52
7.47
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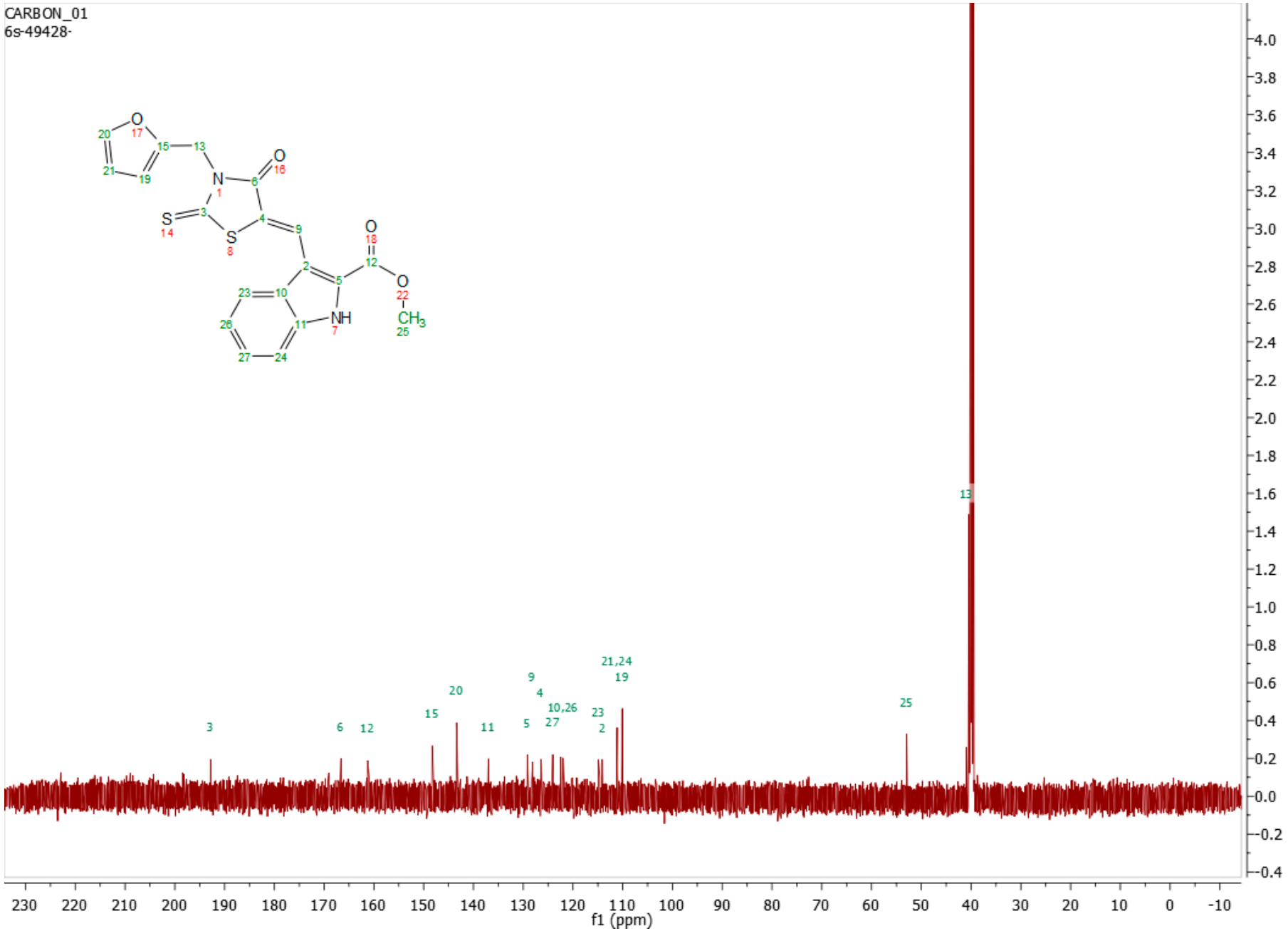
7.34
7.32
7.25
7.23
7.20
6.41
6.36
5.26
4.39
4.00
3.00
2.50
1.01
O
O
N
S
S
O
O
O
NH
CH3
f1 (ppm)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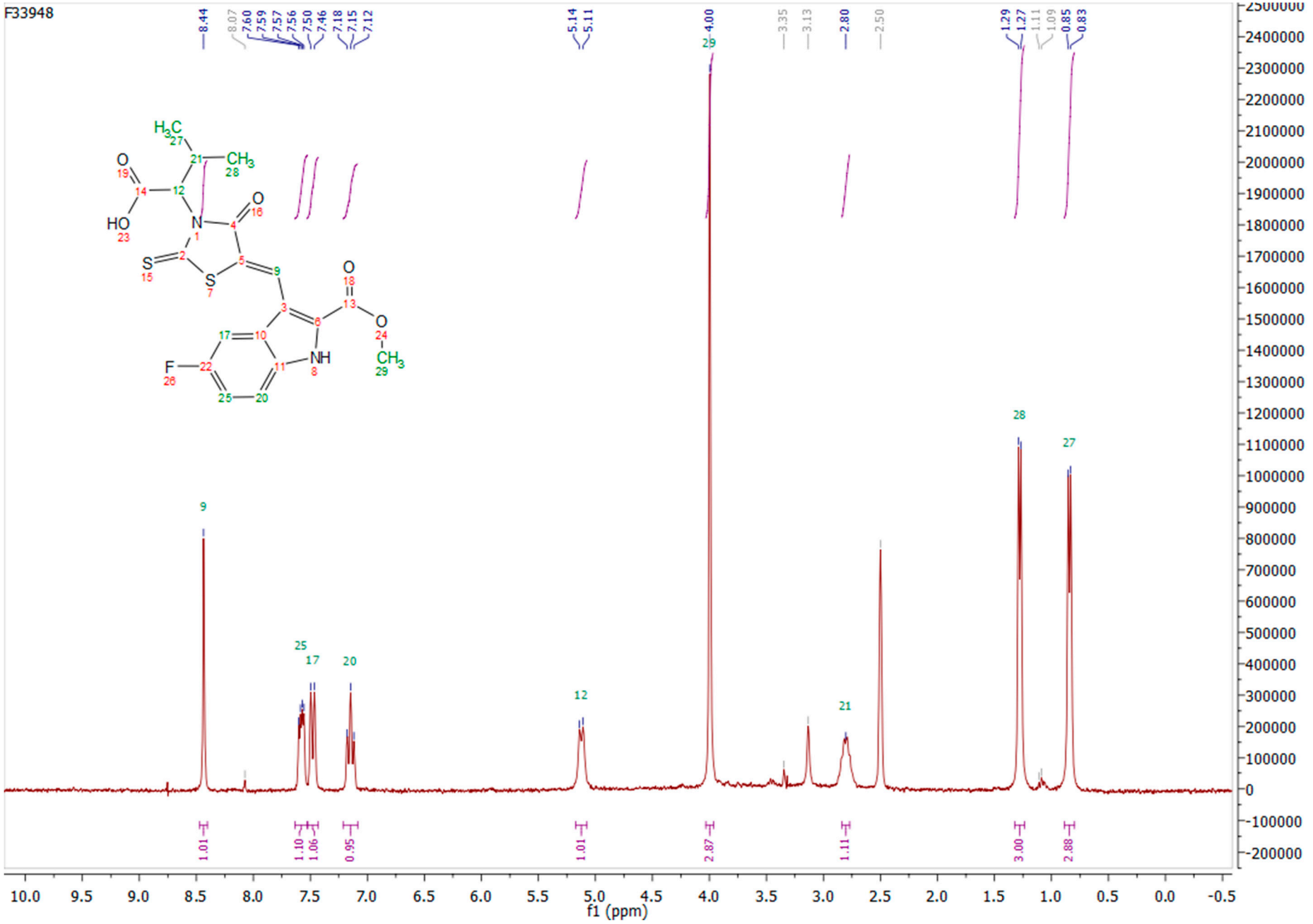
6s-49428-
f1 (ppm)

Compound 8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7.50
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7.12
5.14
5.11
4.00
3.35
3.13
2.80
2.50
1.29
1.27
1.11
1.09
0.85
0.83
9
25
17
20
12
21
28
27
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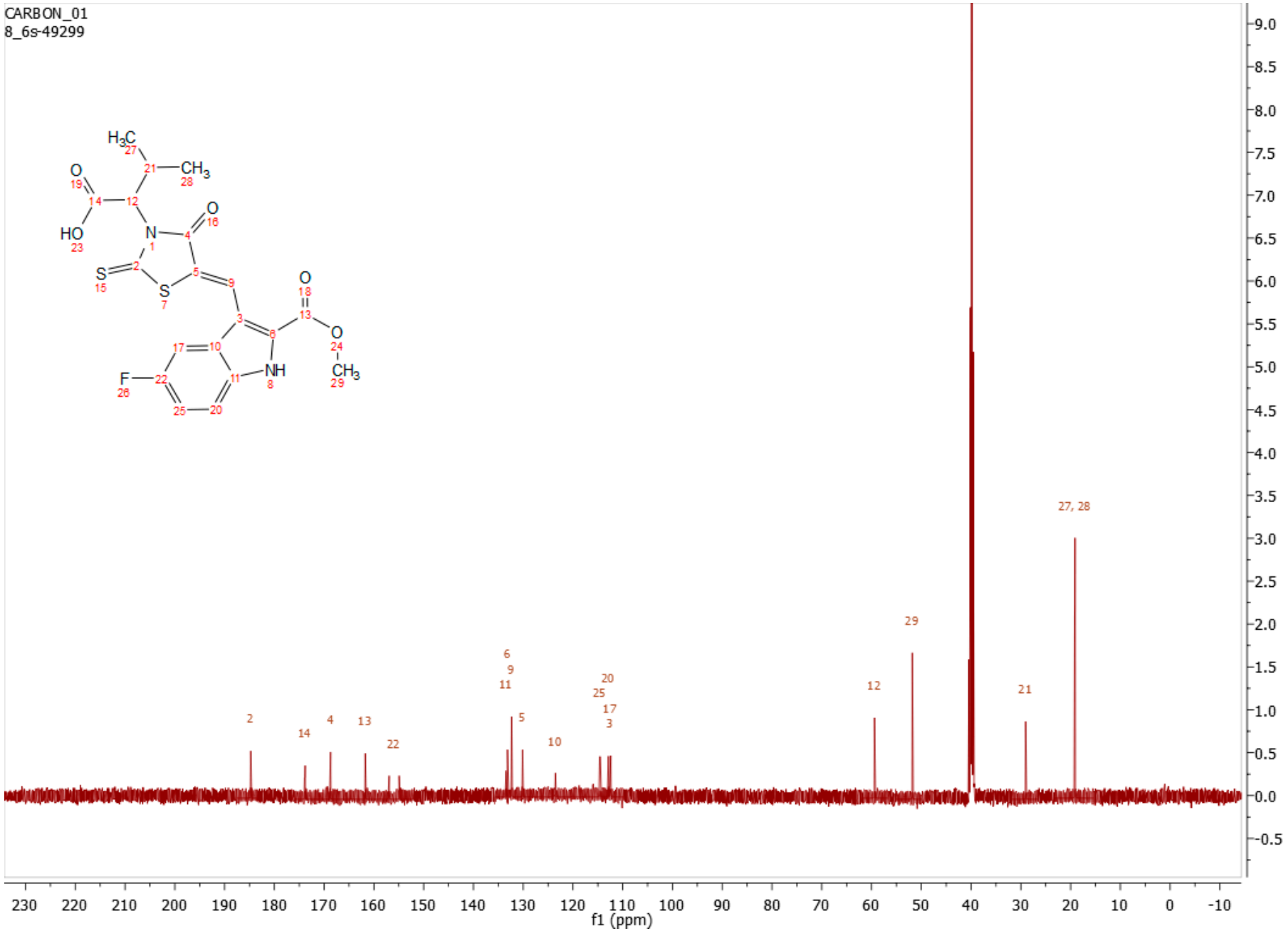
1.11
3.00
2.88
f1 (ppm)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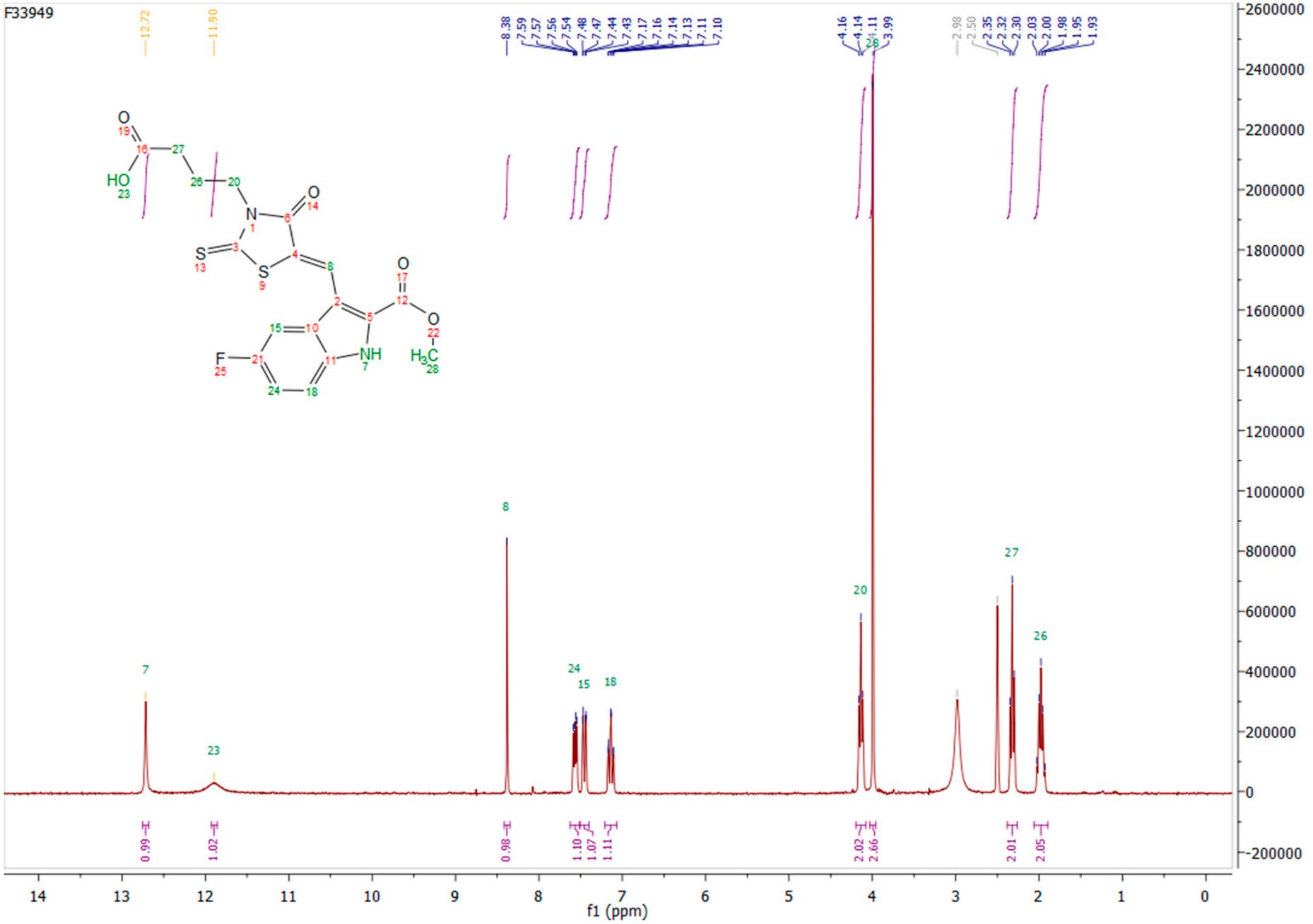
f1 (ppm)
2
14
4
13
22
6
9
11
5
10
20
25
17
3
12
29
21
27, 28

Compound 9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7.57
7.56
7.54
7.48
7.47
7.44
7.43
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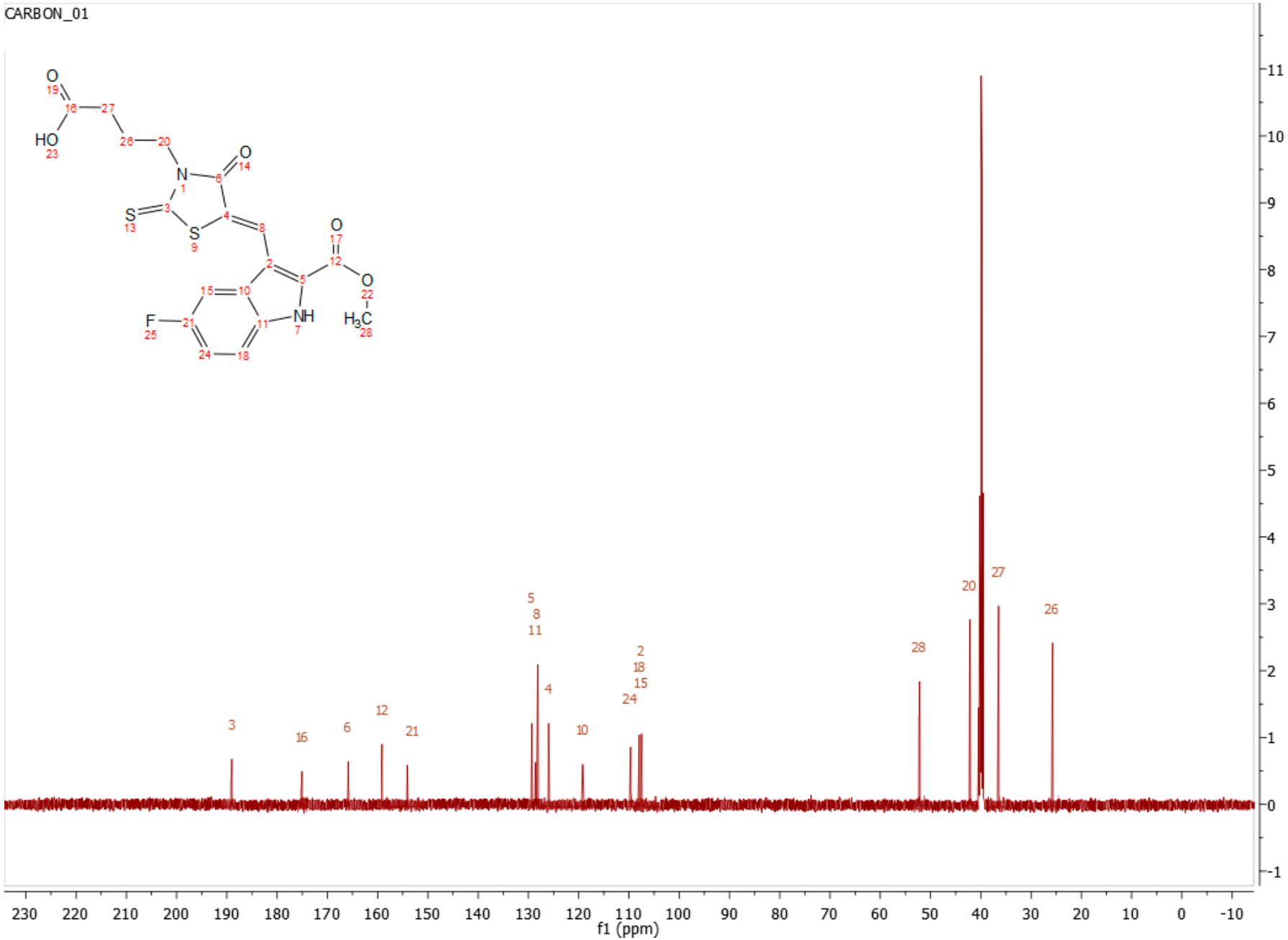
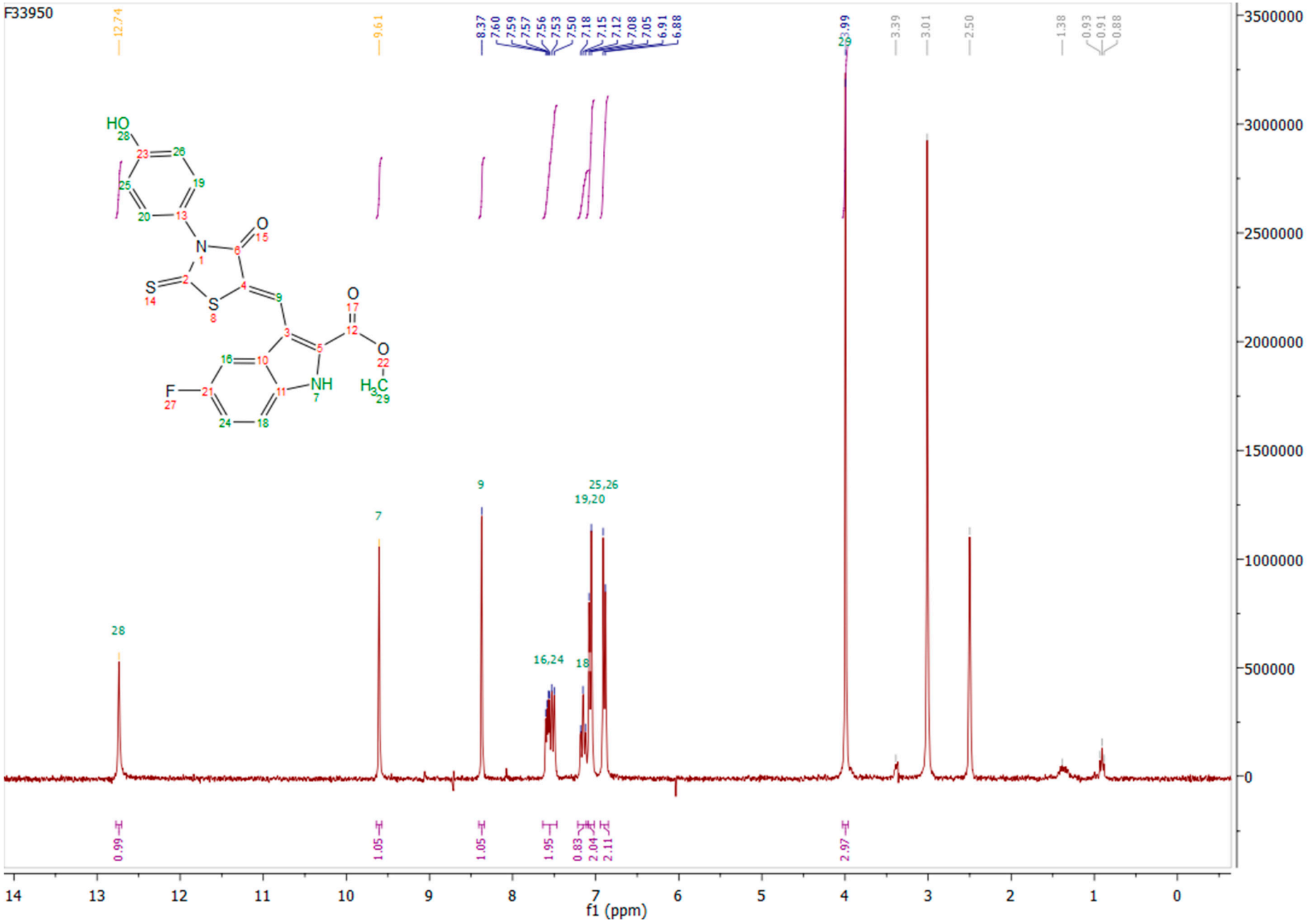
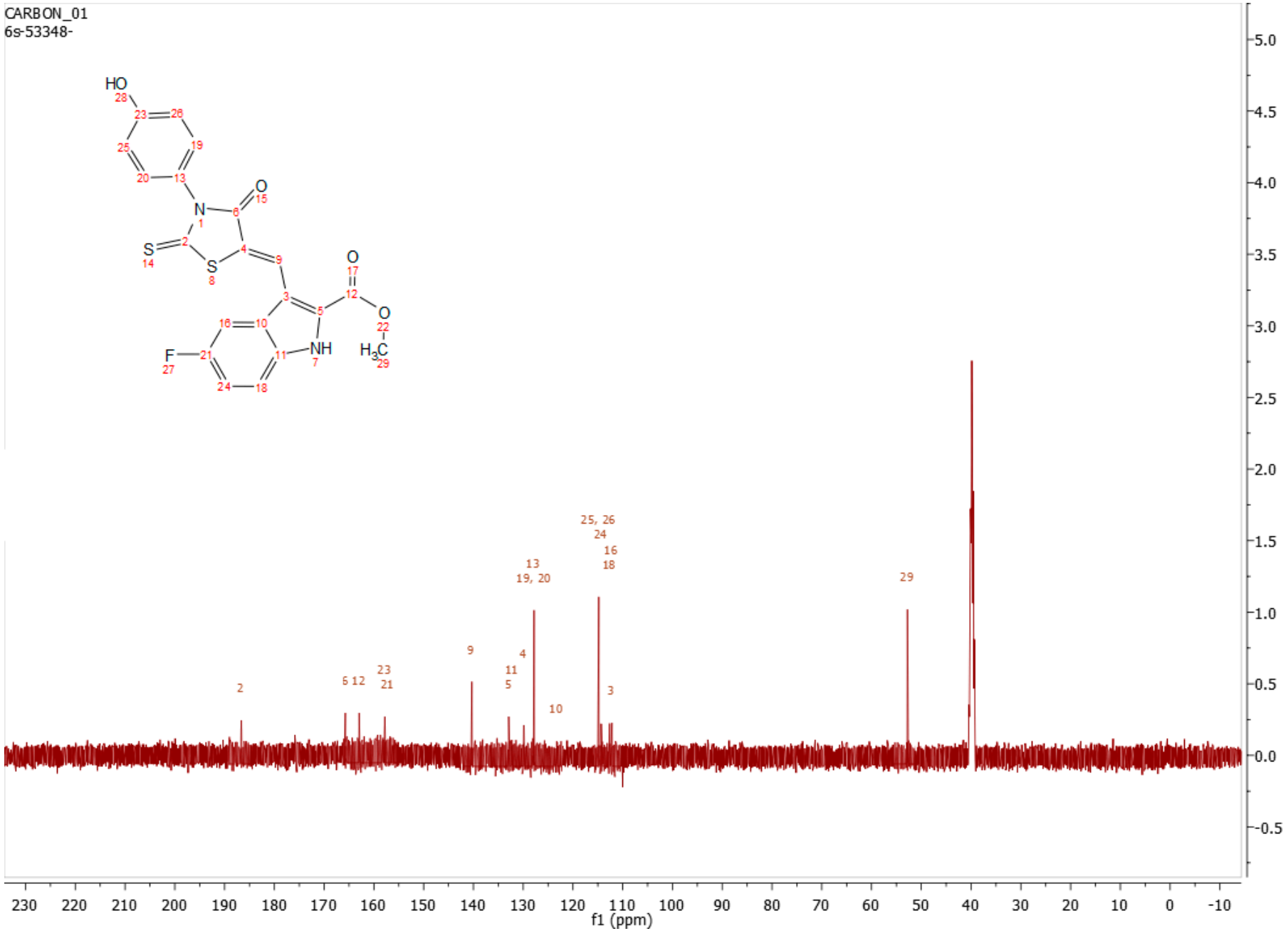
7.16
7.14
7.13
7.11
7.10
4.16
4.14
4.11
3.99
2.98
2.50
2.35
2.32
2.30
2.03
2.00
1.98
1.95
1.93
HO
O
N
S
S
NH
F
H3C
7
23
8
24
15
18
20
27
26
0.99
1.02
0.98
1.10
1.07
1.11
2.02
2.66
2.01
2.05
f1 (ppm)

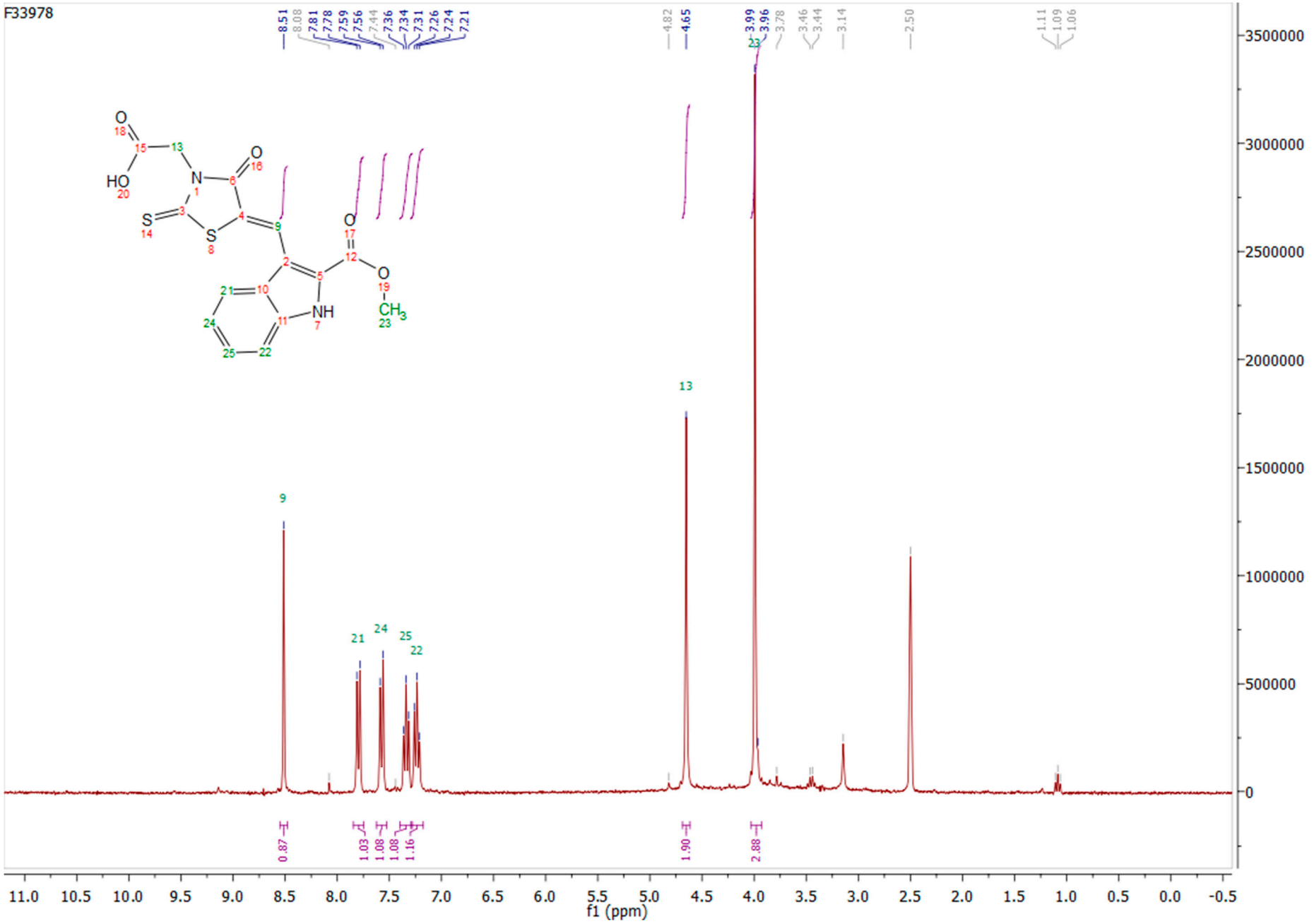

CARBON_01
f1 (ppm)

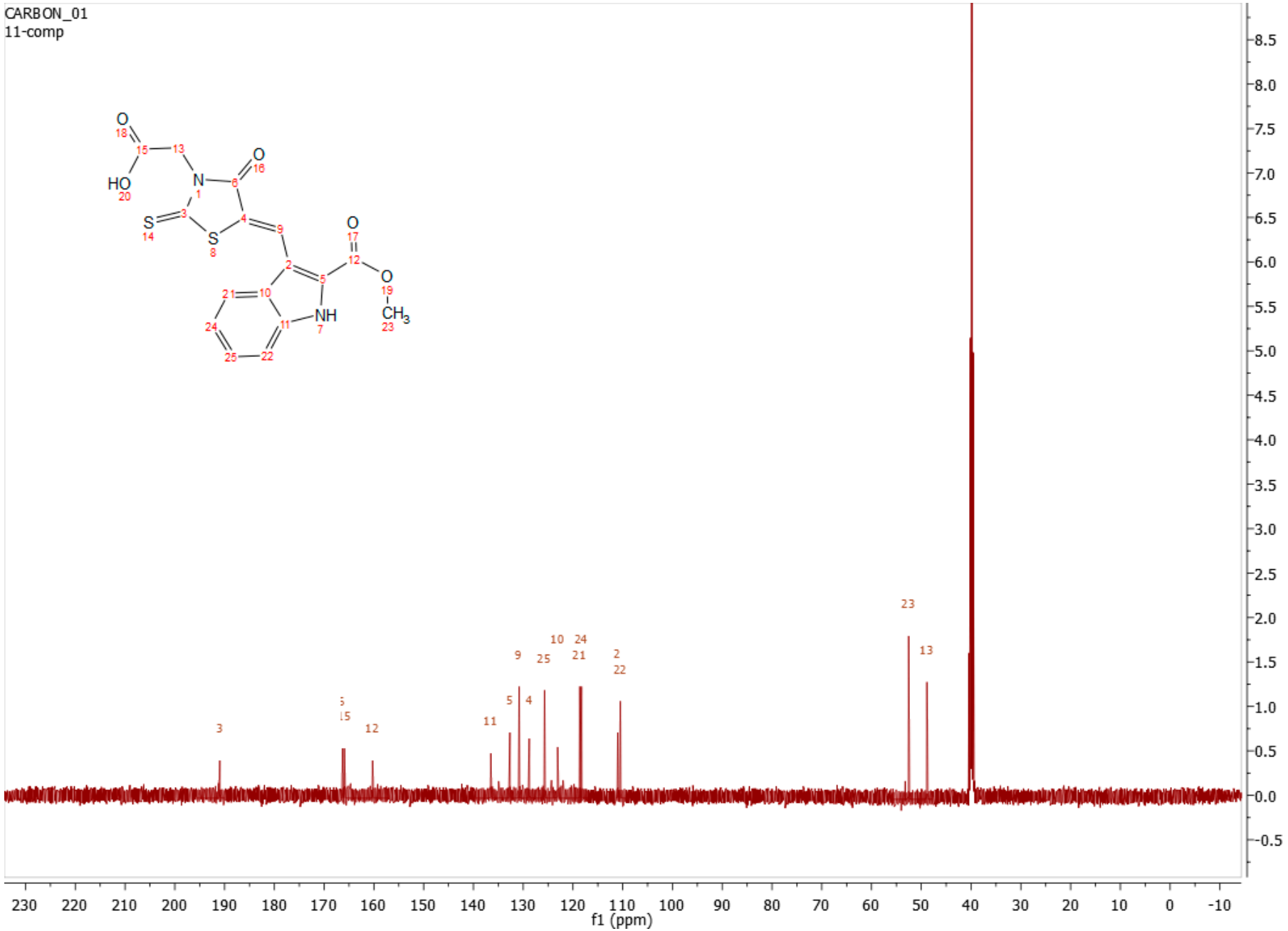
Compound 10


F33950
12.74
9.61
8.37
7.60
7.59
7.57
7.56
7.53
7.50
7.18
7.15
7.12
7.08
7.05
6.91
6.88
3.99
3.39
3.01
2.50
1.38
0.93
0.91
0.88
HO
O
N
S
S
O
O
O
F
NH
H3C
28
9
7
25,26
19,20
16,24
18
0.99
1.05
1.05
1.95
0.83
2.04
2.11
2.97
f1 (ppm)

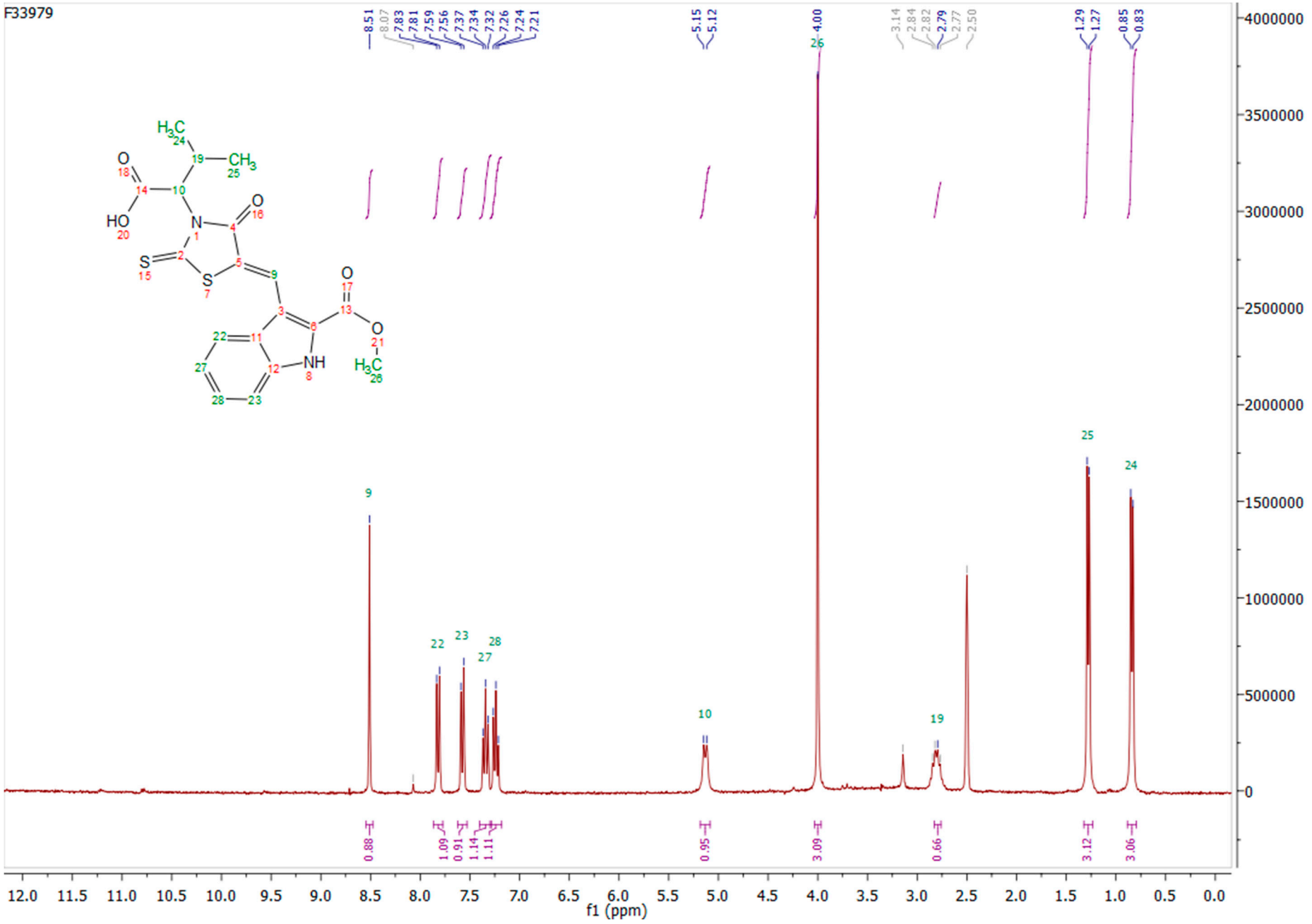

CARBON_01
6s-53348-
HO
28
23
26
25
19
20
13
O
15
N
1
6
S
14
2
4
9
S
8
O
17
12
3
5
O
22
16
10
NH
7
H3C
29
F
27
21
11
24
18
2
6 12
23
21
9
11
5
4
13
19, 20
10
25, 26
24
16
18
3
29
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

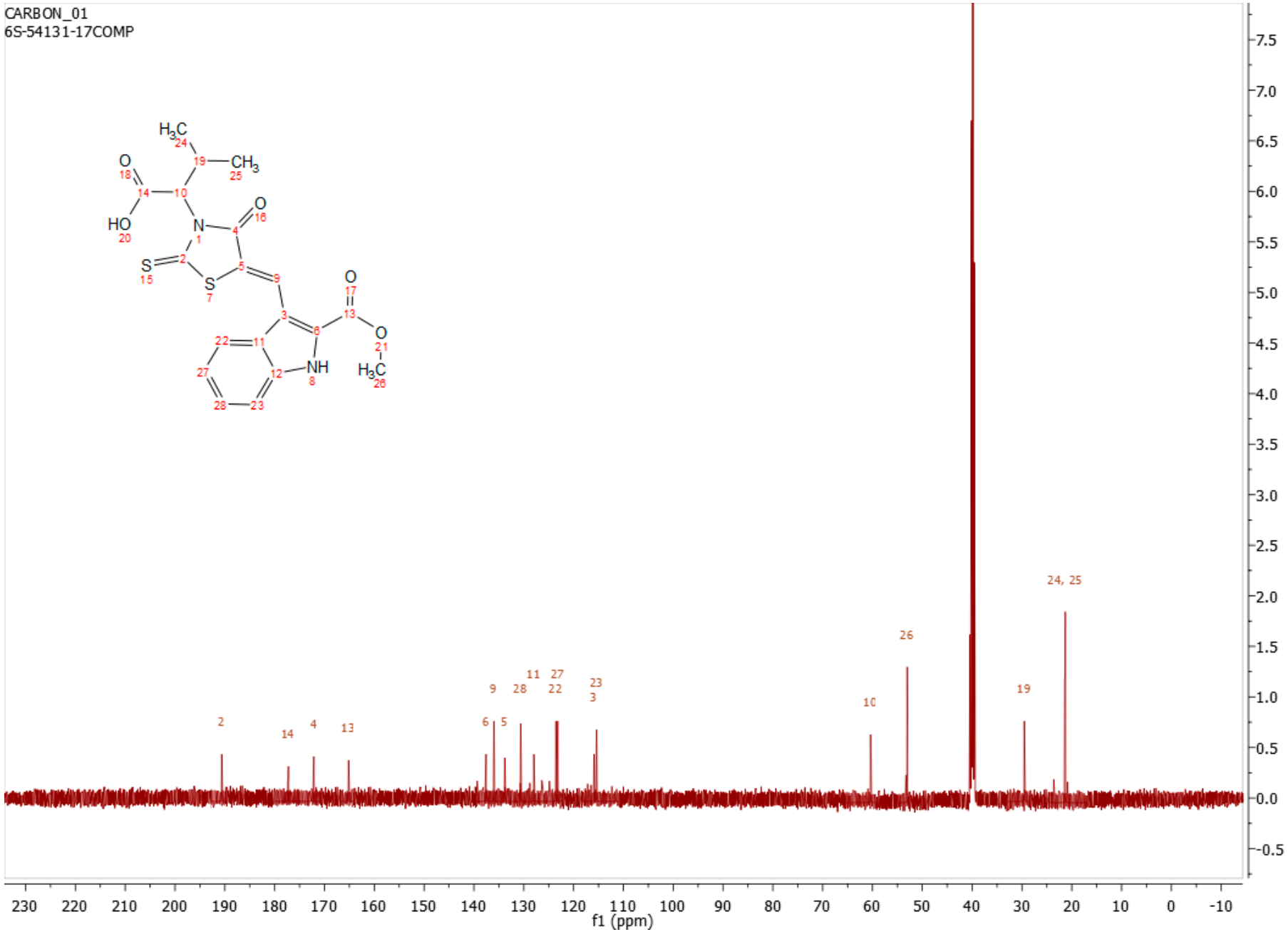
Compound 11


F33978
8.51
8.08
7.81
7.78
7.59
7.56
7.44
7.36
7.34
7.31
7.26
7.24
7.21
4.82
4.65
3.99
3.96
3.78
3.46
3.44
3.14
2.50
1.11
1.09
1.06
O
18
15
13
HO
20
N
1
6
O
16
S
14
3
4
S
8
9
2
5
O
17
12
O
19
21
10
NH
7
CH3
23
24
11
25
22
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
13
9
21
24
25
22
0.87
1.03
1.08
1.08
1.16
1.90
2.88
11.0
10.5
10.0
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
0.0
-0.5
f1 (ppm)

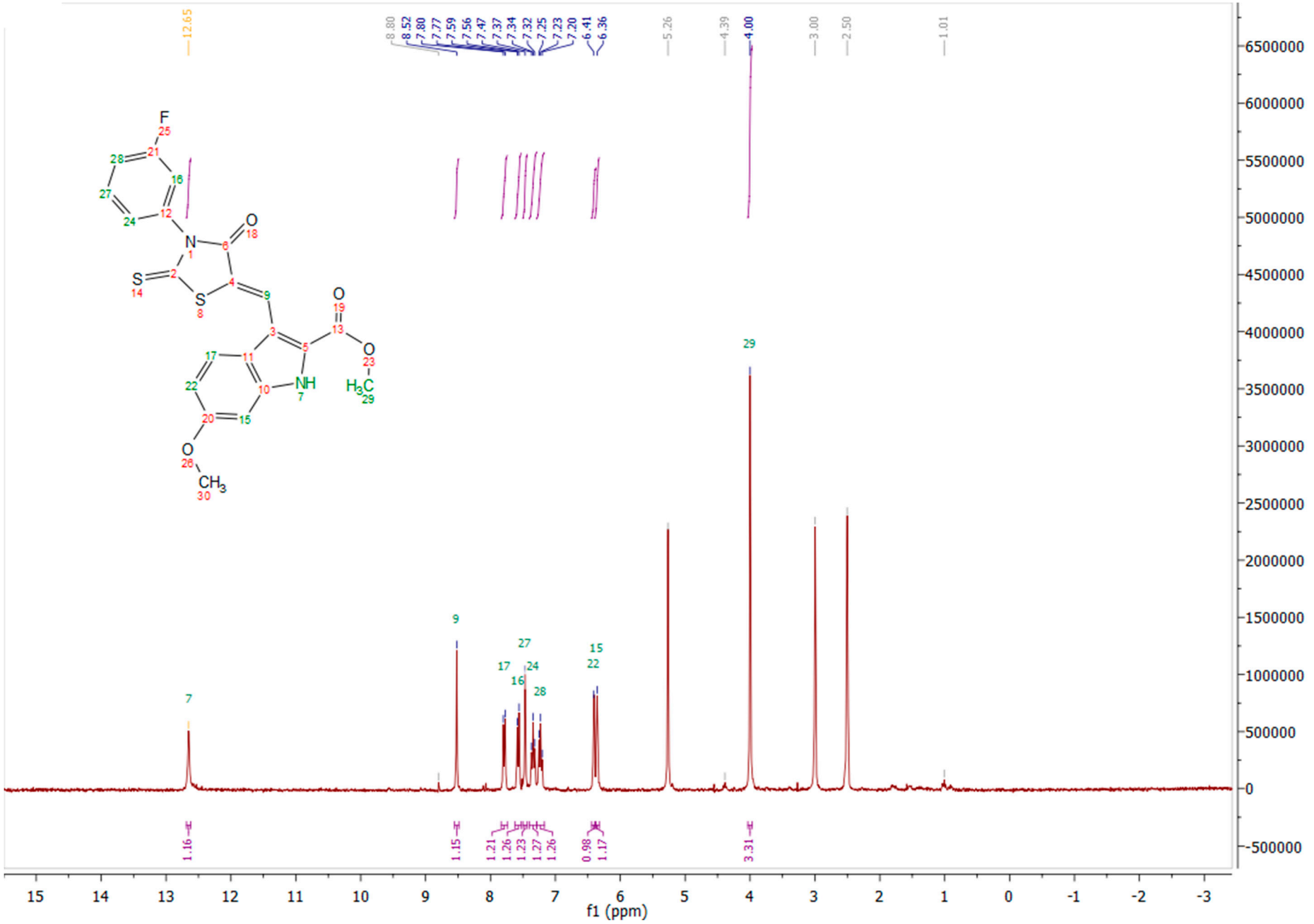

CARBON_01
11-comp
f1 (ppm)

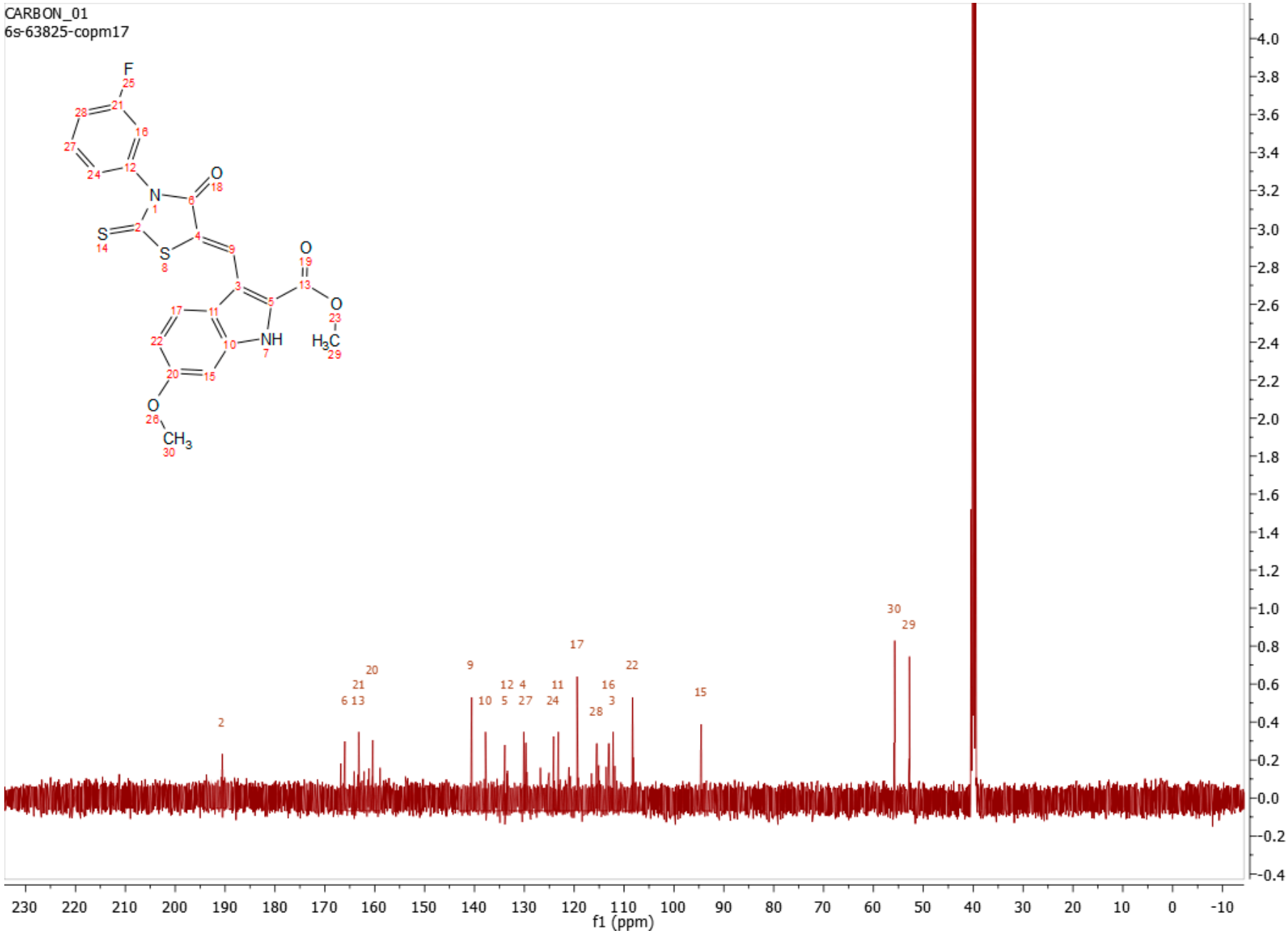
Compound 12


F33979
8.51
8.07
7.83
7.81
7.59
7.56
7.37
7.34
7.32
7.26
7.24
7.21
5.15
5.12
4.00
3.14
2.84
2.82
2.79
2.77
2.50
1.29
1.27
0.85
0.83
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
9
22
23
27
28
10
19
25
24
0.88
1.09
0.91
1.14
1.11
0.95
3.09
0.66
3.12
3.06
12.0
11.5
11.0
10.5
10.0
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
0.0
f1 (ppm)

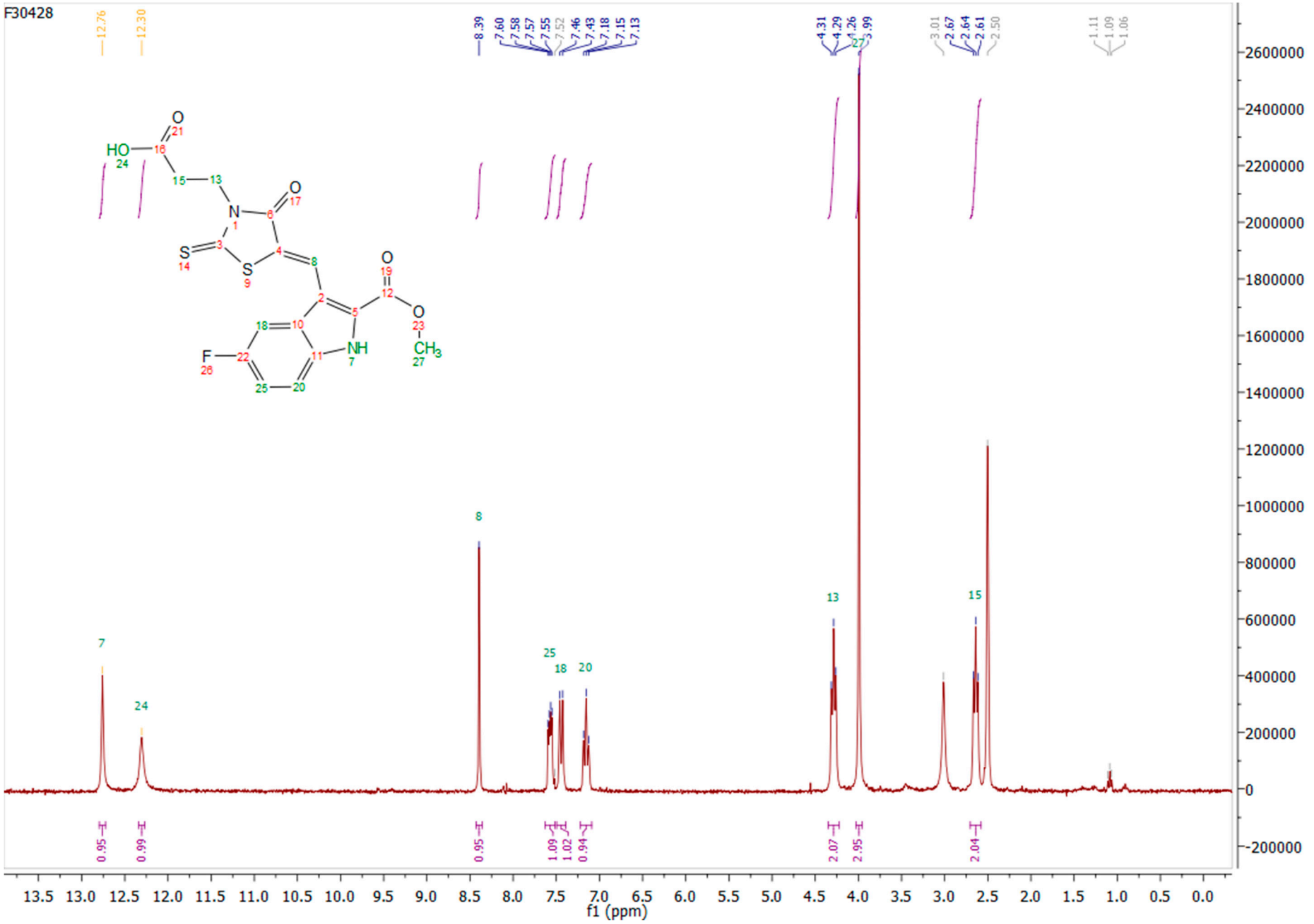

CARBON_01
6S-54131-17COMP
f1 (ppm)
2
14
4
13
9
6
5
28
11
27
22
23
3
10
26
19
24, 25

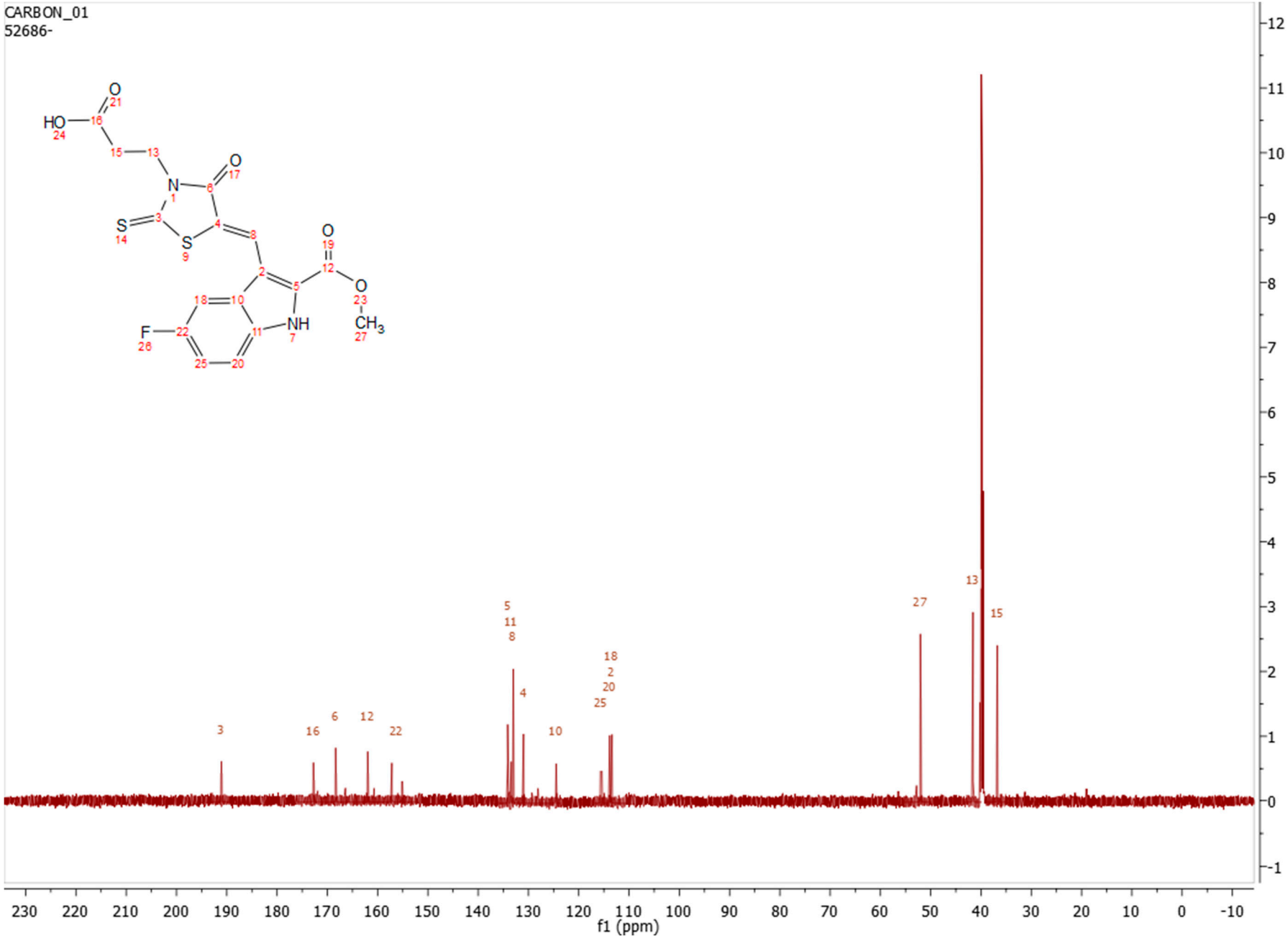
Compound 13


12.65
8.80
8.52
7.80
7.77
7.59
7.56
7.47
7.37
7.34
7.32
7.25
7.23
7.20
6.41
6.36
5.26
4.39
4.00
3.00
2.50
1.01
F
25
28
21
16
27
24
12
N
1
6
O
18
S
2
14
4
9
S
8
3
5
O
19
13
O
23
17
11
22
10
NH
7
H3C
29
20
15
O
26
CH3
30
29
9
27
17
24
16
28
15
22
7
1.16
1.15
1.21
1.26
1.23
1.27
1.26
0.98
1.17
3.31
6500000
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
f1 (ppm)

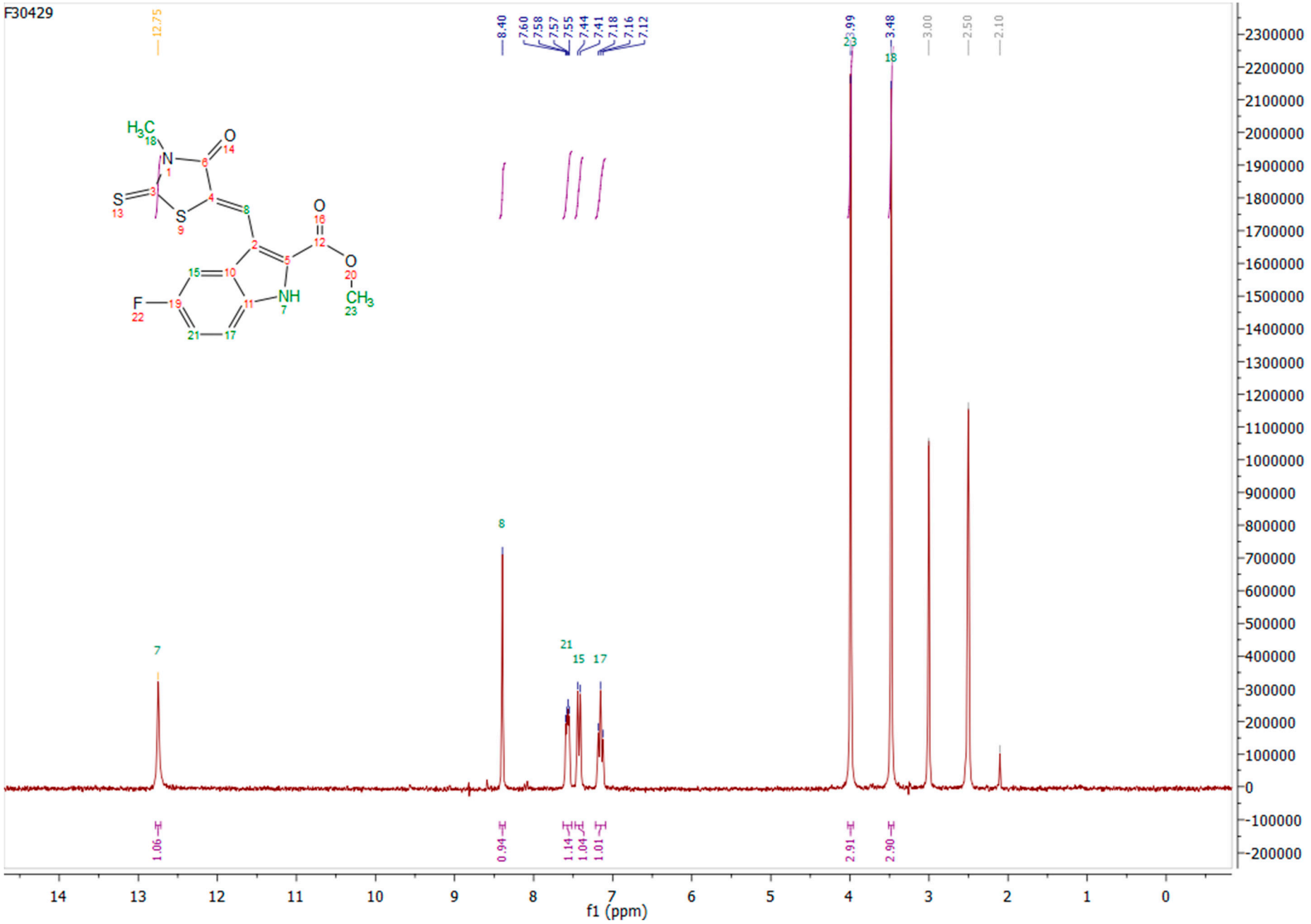

CARBON_01
6s-63825-copm17
F
25
28
21
16
27
24
12
O
18
N
1
6
S
2
14
4
9
S
8
O
19
13
3
5
O
23
17
11
22
10
NH
7
H3C
29
20
15
O
26
CH3
30
2
6 13
21
20
9
10
12 5
4
27
11
24
17
28
16
3
22
15
30
29
f1 (ppm)

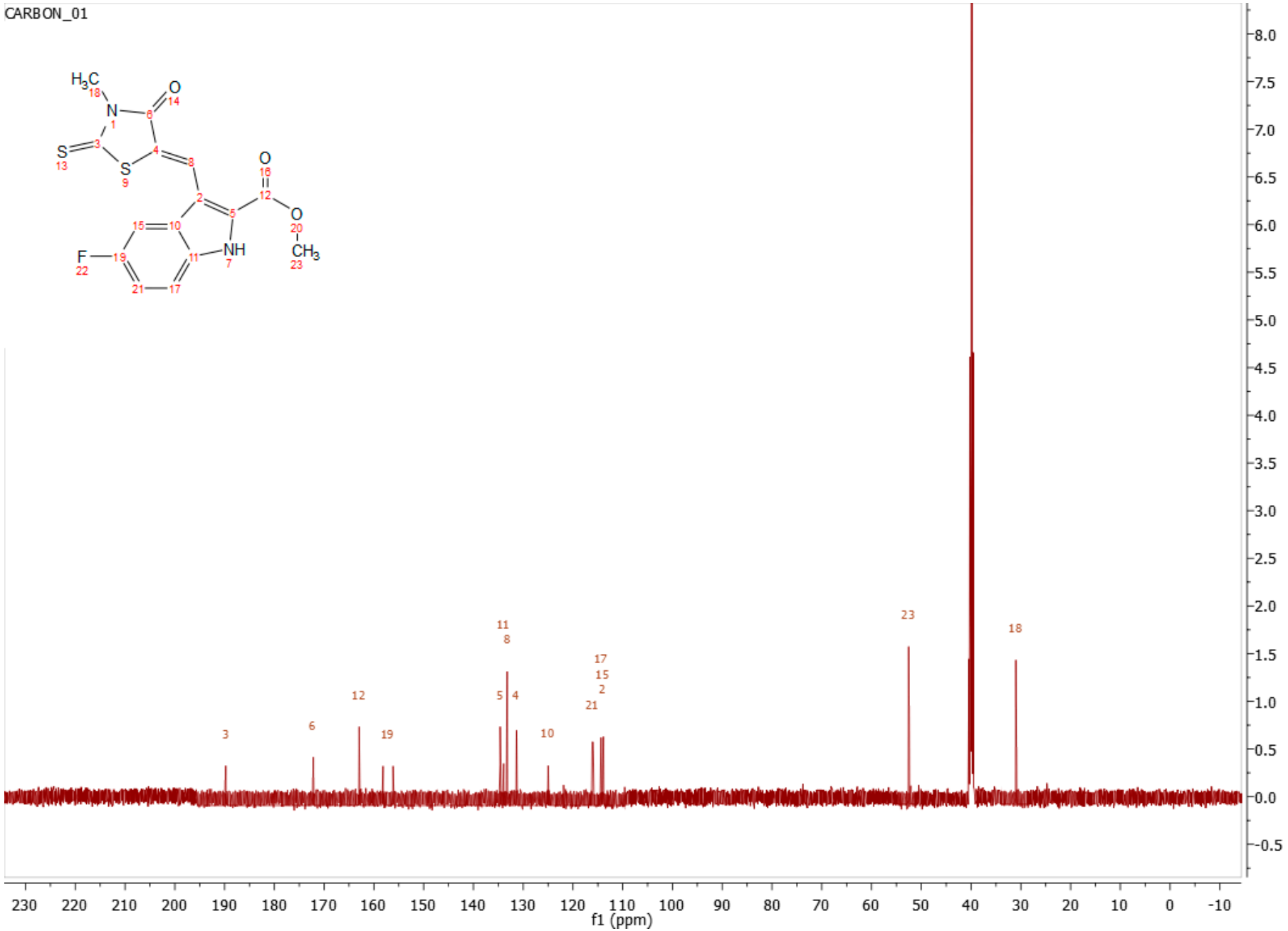
Compound 14


F30428
12.76
12.30
8.39
7.60
7.58
7.57
7.55
7.52
7.46
7.43
7.18
7.15
7.13
4.31
4.29
4.26
3.99
3.01
2.67
2.64
2.61
2.50
1.11
1.09
1.06
HO
O
N
S
S
NH
F
CH3
7
24
8
25
18
20
13
15
27
0.95
0.99
0.95
1.09
1.02
0.94
2.07
2.95
2.04
f1 (ppm)

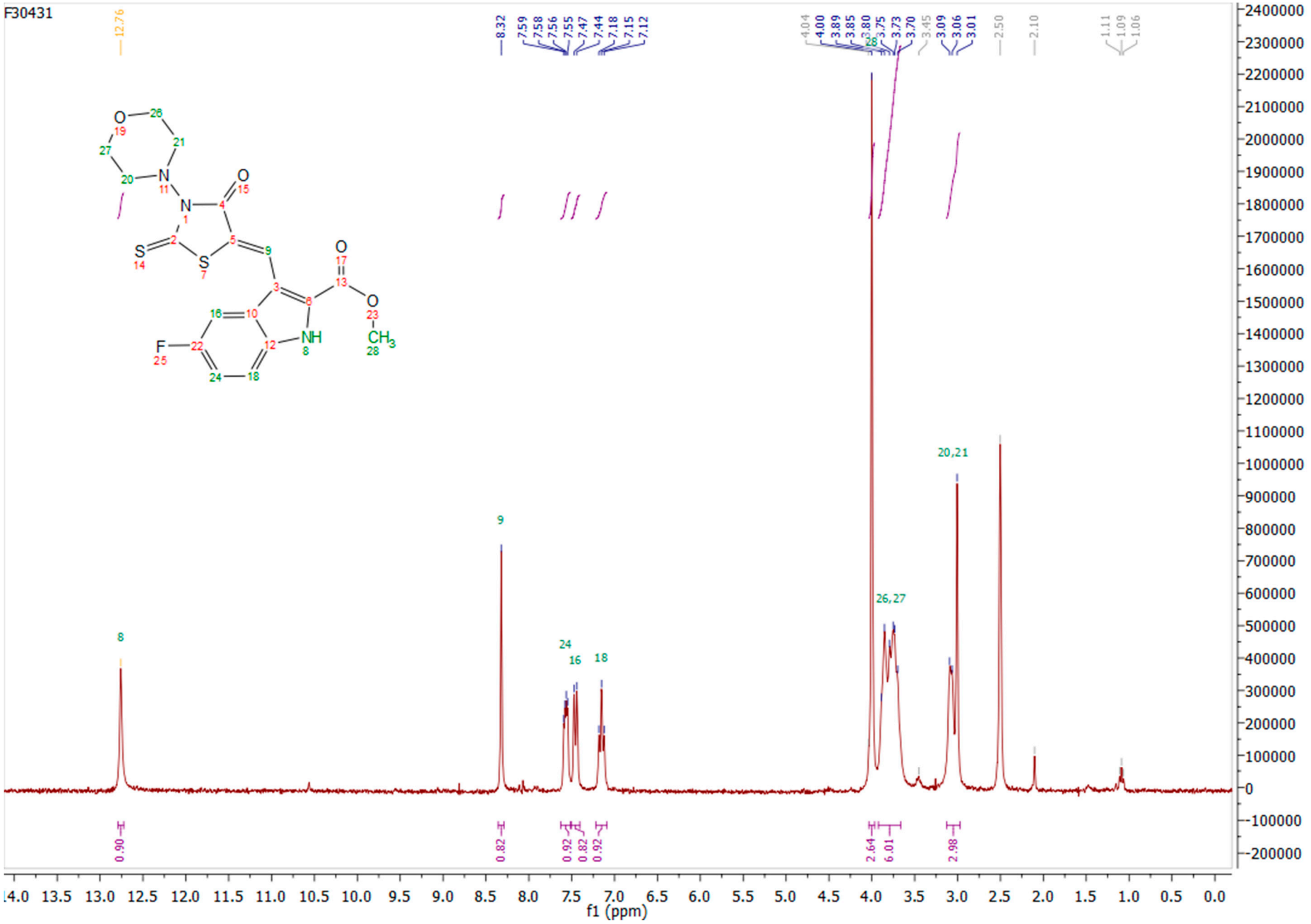

CARBON_01
52686-
HO
O
F
NH
CH3
S
N
f1 (ppm)

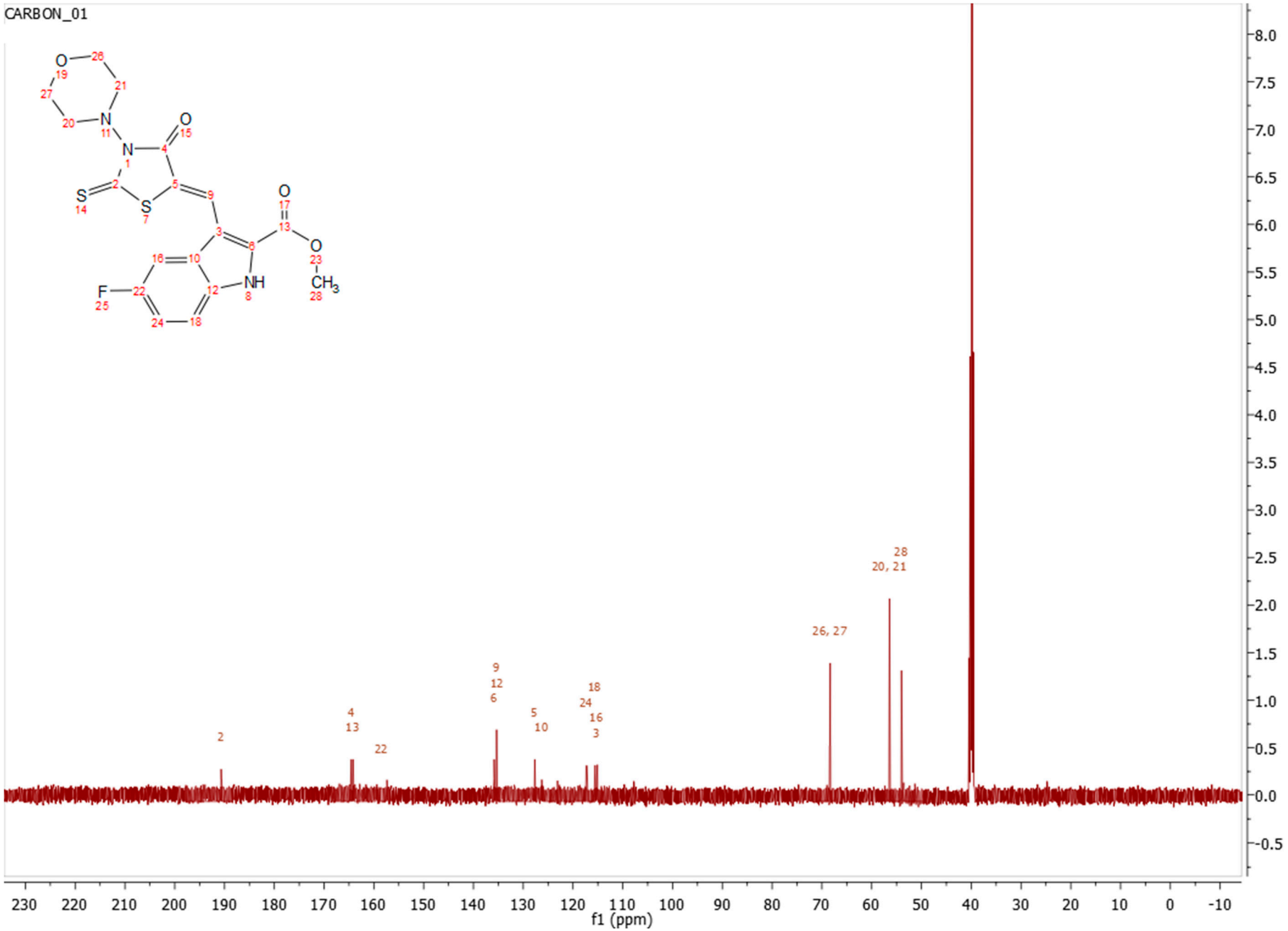
Compound 15


F30429
12.75
8.40
7.60
7.58
7.57
7.55
7.44
7.41
7.18
7.16
7.12
3.99
3.48
3.00
2.50
2.10
H3C
18
N
1
O
14
6
S
13
3
4
8
S
9
O
16
12
2
5
O
20
CH3
23
15
10
F
22
19
11
NH
7
21
17
7
8
21
15
17
1.06
0.94
1.14
1.04
1.01
2.91
2.90
f1 (ppm)

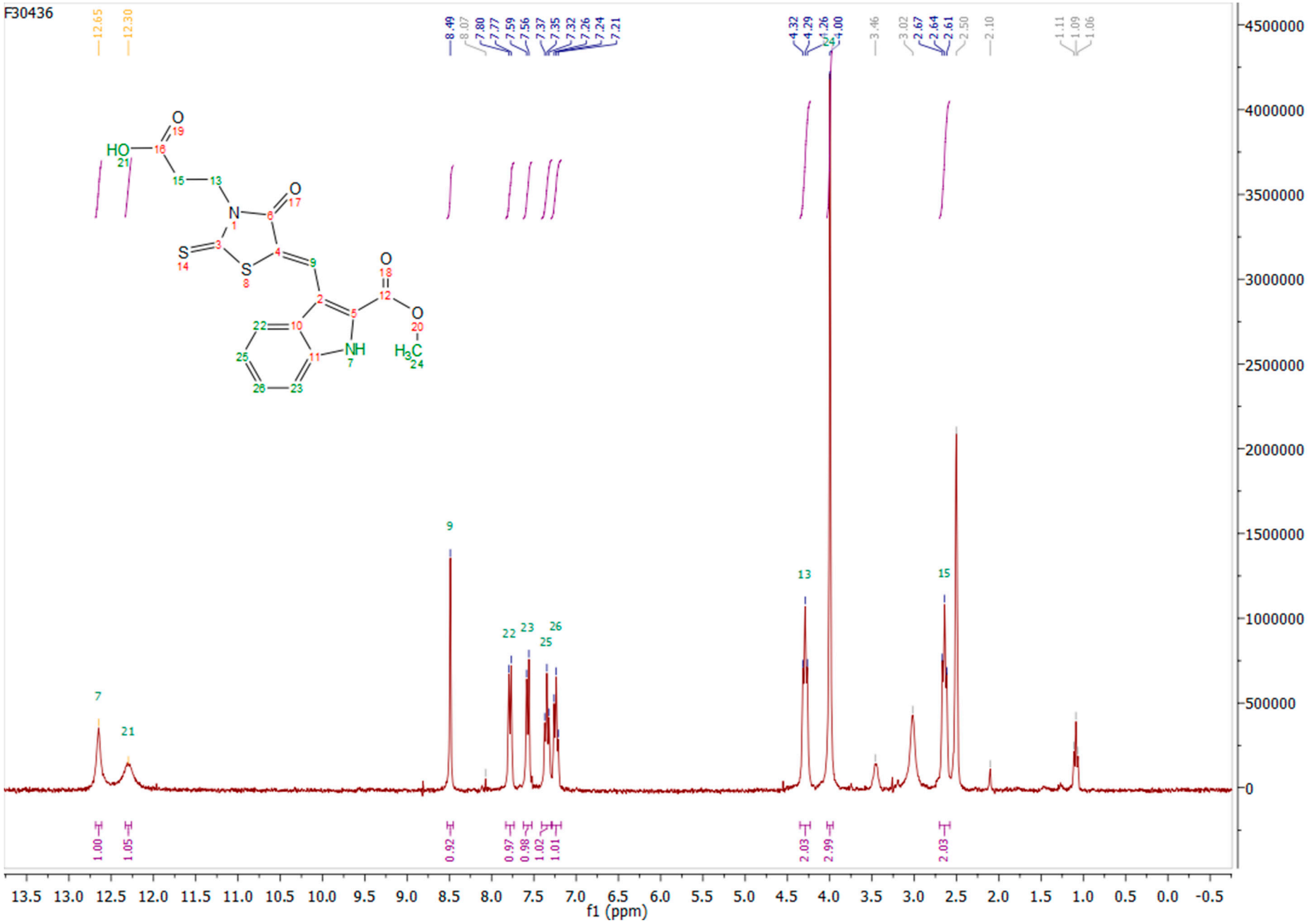

CARBON_01
f1 (ppm)

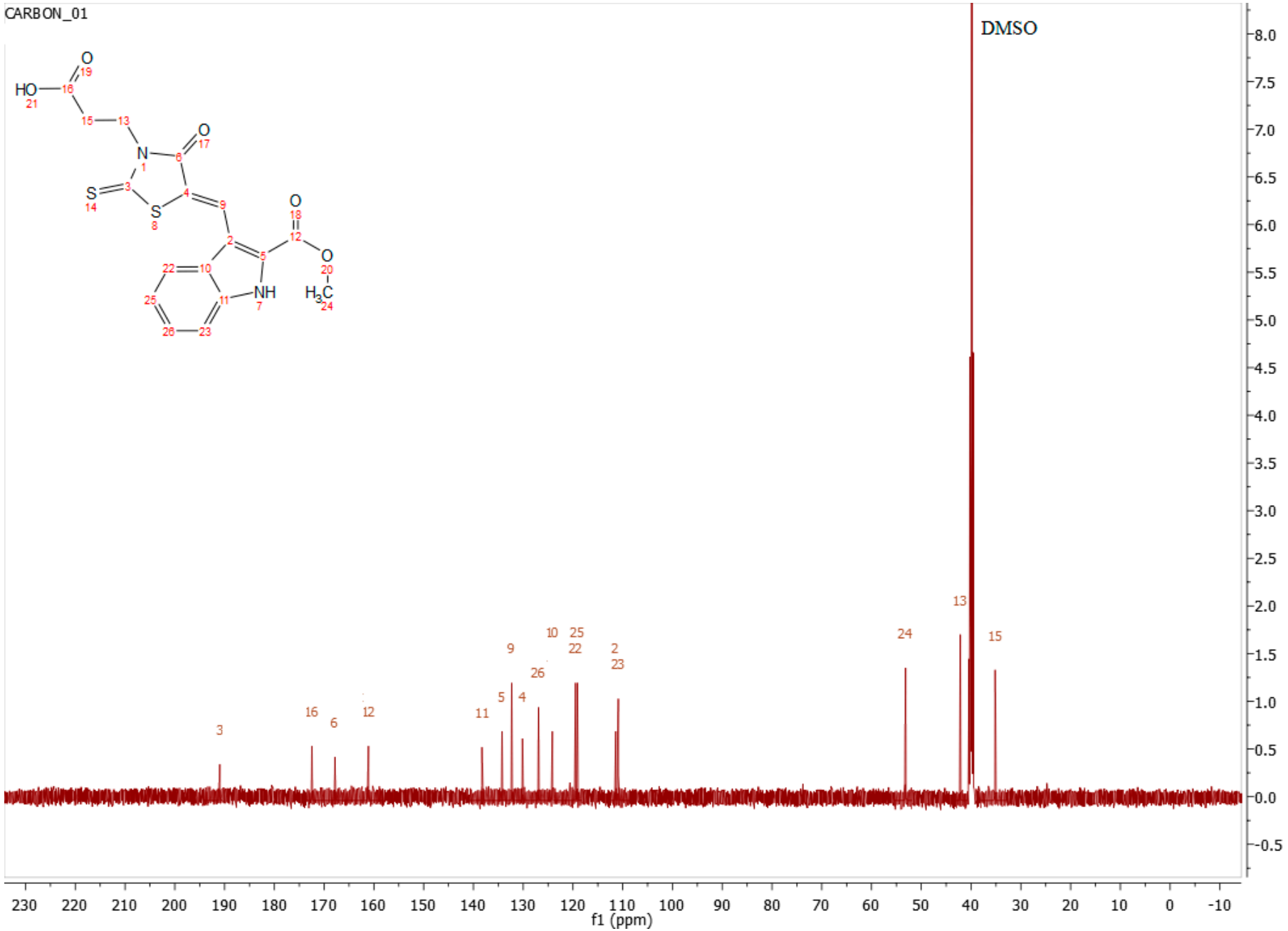
Compound 16


F30431
12.76
8.32
7.59
7.58
7.56
7.55
7.47
7.44
7.18
7.15
7.12
4.04
4.00
3.89
3.85
3.80
3.75
3.73
3.70
3.45
3.09
3.06
3.01
2.50
2.10
1.11
1.09
1.06
8
9
24
16
18
26,27
20,21
0.90
0.82
0.92
0.82
0.92
2.64
6.01
2.98
f1 (ppm)


CARBON_01
f1 (ppm)
2
4
13
22
9
12
6
5
10
18
24
16
3
26, 27
28
20, 21

Compound 17


F30436
12.65
12.30
8.49
8.07
7.80
7.77
7.59
7.56
7.37
7.35
7.32
7.26
7.24
7.21
4.32
4.29
4.26
4.00
3.46
3.02
2.67
2.64
2.61
2.50
2.10
1.11
1.09
1.06
HO
O
O
N
S
S
NH
O
O
H3C
7
21
9
22
23
26
25
13
15
1.00
1.05
0.92
0.97
0.98
1.02
1.01
2.03
2.99
2.03
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 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 0.0 -0.5
f1 (ppm)


CARBON_01
DMSO
HO
O
O
O
O
O
N
S
S
NH
H3C
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
3
16
6
12
11
5
9
4
26
10
25
22
2
23
24
13
15
f1 (ppm)