Supporting Information

for

Combined experimental and theoretical studies of regio- and stereoselectivity in reactions of β-isoxazolyl- and β-imidazolyl enamines with nitrile oxides

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NMR spectra of compounds 3a–c, 4a–p and X-ray study of isoxazoles 4a,o,p

Contents

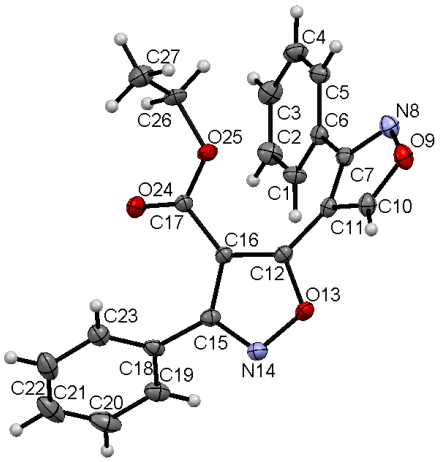
X-ray diffraction study

X-ray analyses were accomplished on an Xcalibur 3 diffractometer using the standard procedure (graphite-monochromated MoK-irradiation, ω-scanning with step 1o, T = 150.00(10) K) (**4o,p**) or 295(2) K (**4a**).

4a. $C_{13}H_{10}N_4O_3$, M = 270.25, orthorhombic, a = 6.5164(4) Å, b = 10.4597(4) Å, c = 17.7719(8) Å, V = 1211.33(10) Å^3, space group $P2_12_12_1$ (no. 19), Z = 4, μ(Mo Kα) = 0.109 mm^{-1}, D_{calc} = 1.4818 g/cm^3, 4294 reflections measured (4.52° ≤ 2Θ ≤ 61.22°), 3018 unique (R_{int} = 0.0169, R_{sigma} = 0.0324) which were used in all calculations. The final R_1 was R_1 = 0.0440, wR_2 = 0.1032 (I>=2σ(I)) and R_1 = 0.0565, wR_2 = 0.1112 (all data). Goodness-of-fit on F^2 1.055, largest diff. peak/hole 0.17/-0.25 ēÅ^{-3}.

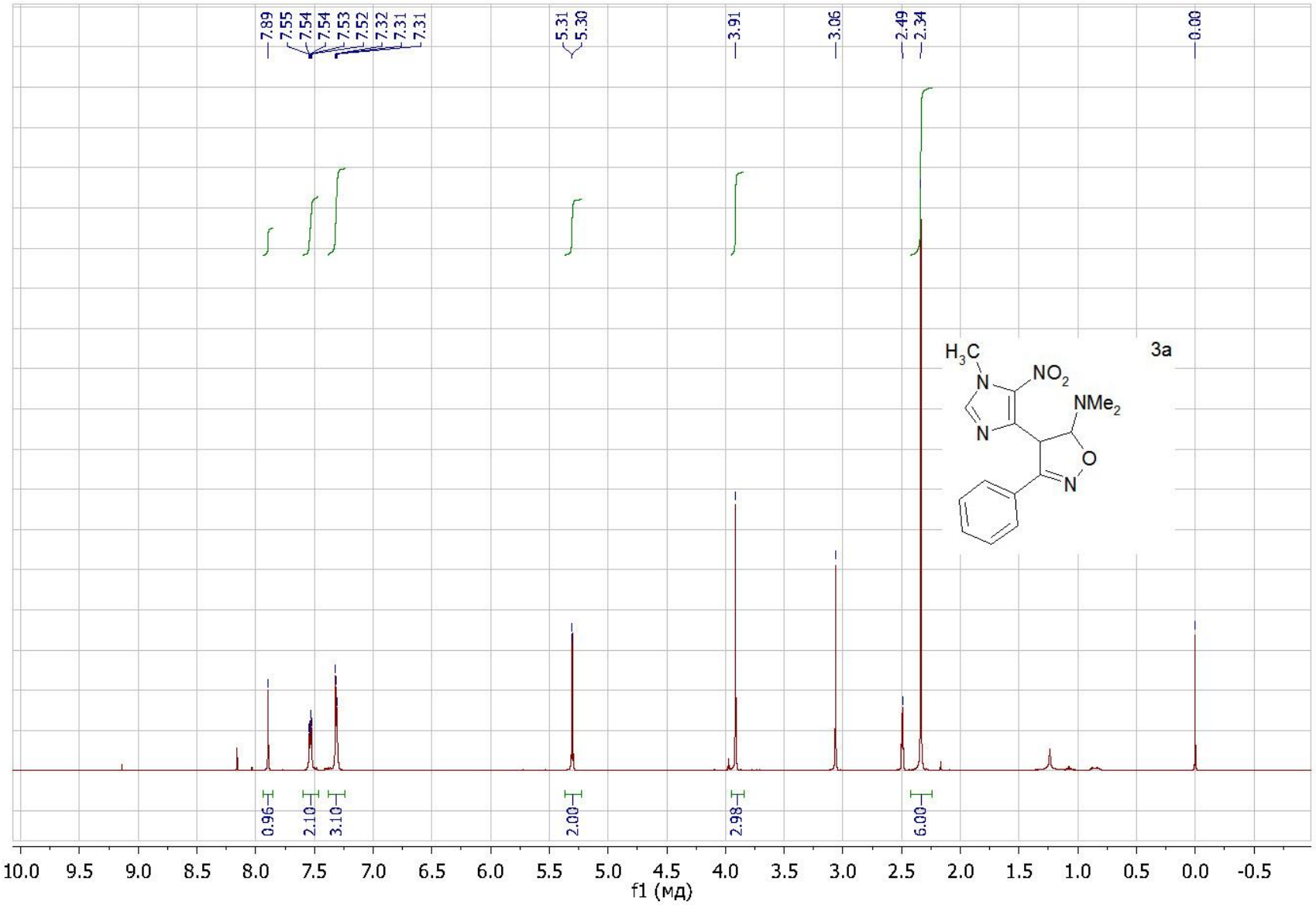
4o. $C_{20}H_{15}N_3O_4$, M =361.35, monoclinic, a = 8.9292(3) Å, b = 12.2608(4) Å, c = 15.9631(6) Å, β = 101.183(3)°, V = 1714.45(10) Å^3, T = 150.00(10), space group $P2_1/c$ (no. 14), Z = 4, μ(MoKα) = 0.100 mm^{-1}, 8807 reflections measured, 4683 unique (R_{int} = 0.0263) which were used in all calculations. The final wR_2 was 0.1333 (all data) and R_1 was 0.0453 (I>2σ(I)).

4p. $C_{21}H_{16}N_2O_4$, M =360.36, monoclinic, a = 8.9596(4) Å, b = 12.5516(3) Å, c = 15.7754(4) Å, β = 100.144(3)°, V = 1746.33(10) Å^3, T = 150.00(10), space group $P2_1/c$ (no. 14), Z = 4, μ(MoKα) = 0.096 mm^{-1}, 8512 reflections measured, 4626 unique (R_{int} = 0.0208) which were used in all calculations. The final wR_2 was 0.1379 (all data) and R_1 was 0.0438 (I>2σ(I)).



NMR Spectra of isoxazoles 4a–p description. The ^{1}H and ^{13}C NMR spectra for products **4a–p** demonstrate that all of the compounds belong to the same structural type. The ^{1}H NMR spectra of isoxazoles **4a–p** contain signals of C^5–H of isoxazole ring in the range of 9.42–9.85 ppm apart from 3-cyclohexyl isoxazoles **4e,h,m** and 2,6-dihalophenylisoxazoles **4d,g,l** which are out of this range and exhibit those signals at 9.19 and 10.04–10.32 ppm, respectively. ^{13}C NMR spectra of **4a–p** show the signals of the carbon atoms at the 3-, 4- and 5-positions of the new isoxazole ring at 159.4−161.4 ppm, 105.8–110.5 and 161.2–165.5 ppm, respectively. 2D NMR spectra show direct coupling of C^5 with H, that could be diagnostic for 3,4-disubstituted

isoxazoles **4a-p**. For the alternative 3,5-disubstituted isoxazoles **5** we would have expected to observe the direct coupling of H with the C^4–H carbon. One can conclude that, 3,4- and 3,5-disubstituted isoxazoles could be easily distinguished by NMR spectroscopy due to the structural features.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7.54
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3.06
2.49
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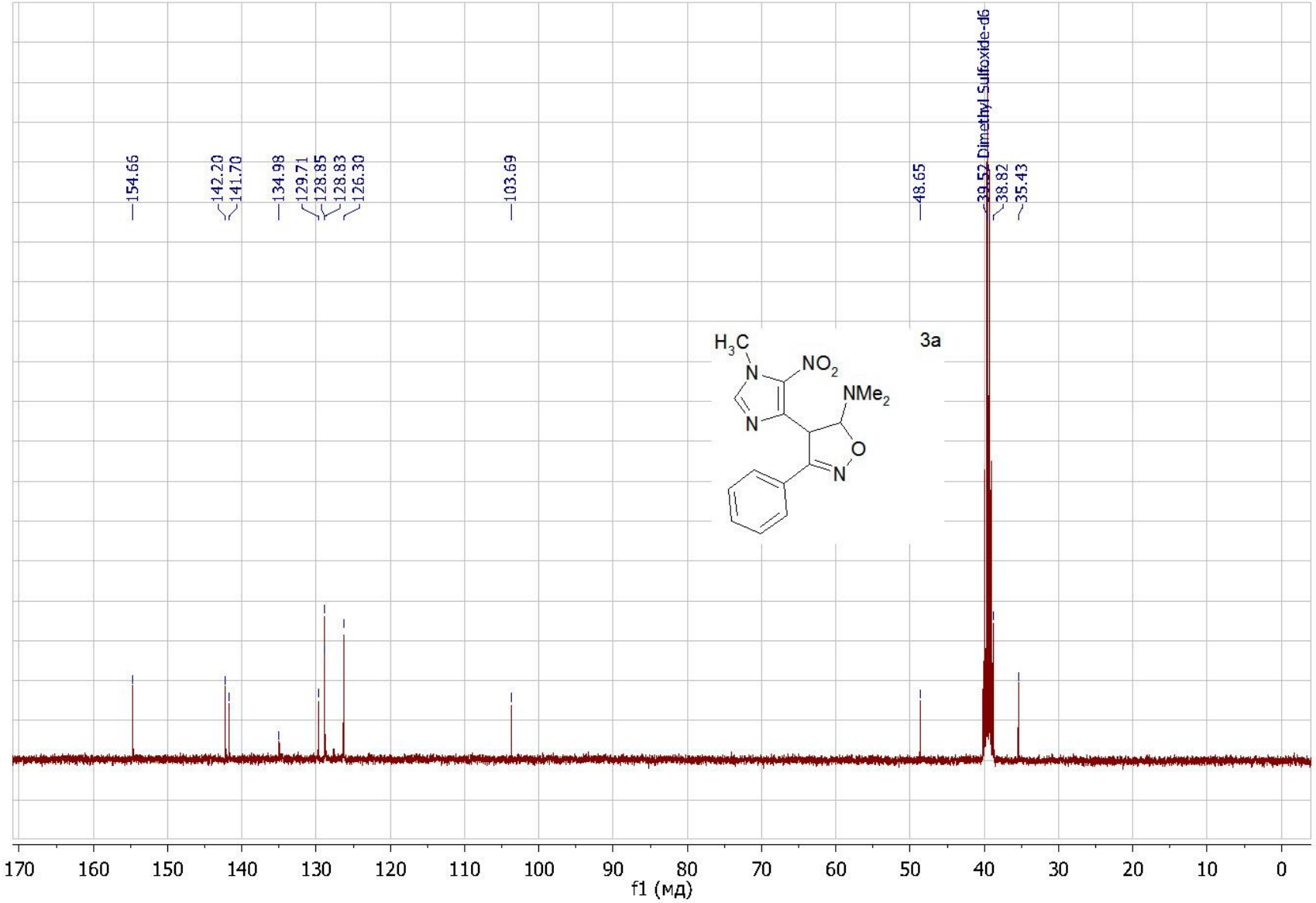
0.00
3a
0.96
2.10
3.10
2.00
2.98
6.00
f1 (мд)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103.69
48.65
39.52 Dimethyl Sulfoxide-d6
38.82
35.43
3a
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NMe_2
N
N
O
N
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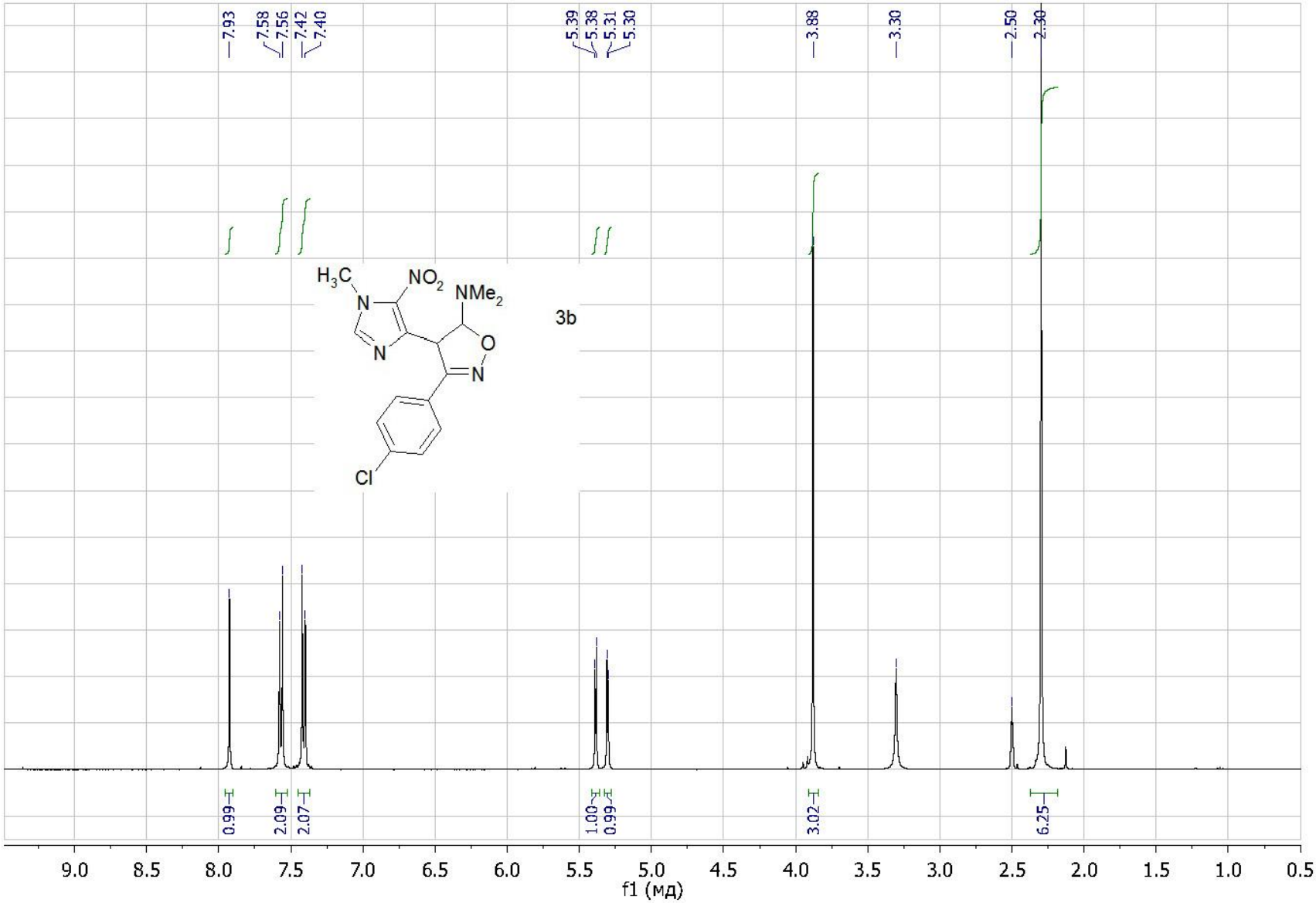
f1 (мд)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H3C
NO2
NMe2
N
N
O
N
Cl
3b
0.99
2.09
2.07
1.00
0.99
3.02
6.25
9.0
8.5
8.0
7.5
7.0
6.5
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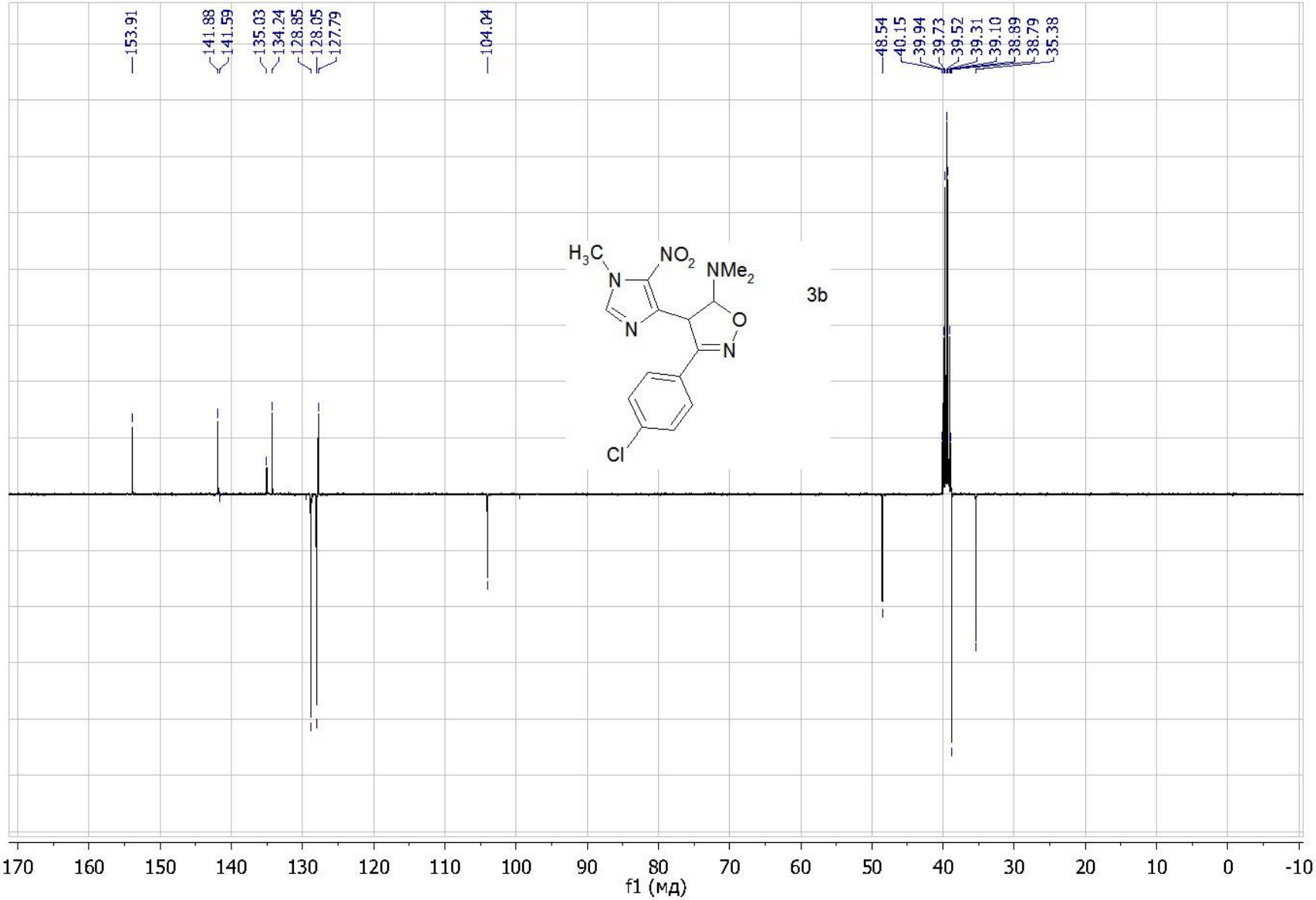
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134.24
128.85
128.05
127.79
104.04
48.54
40.15
39.94
39.73
39.52
39.31
39.10
38.89
38.79
35.38
H3C
NO2
NMe2
N
N
O
N
Cl
3b
170
160
150
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80
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20
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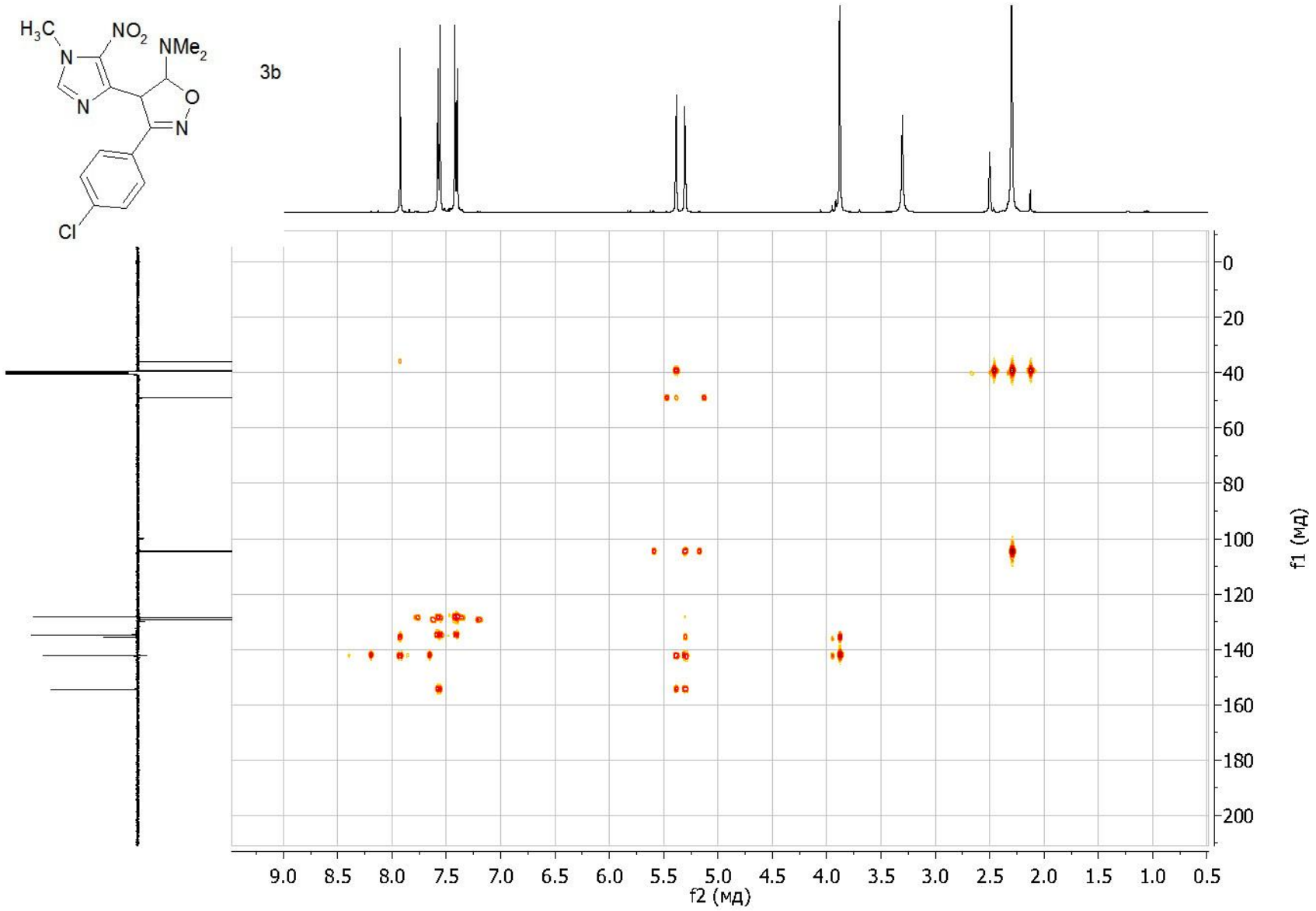
0
-10
f1 (мд)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N
O
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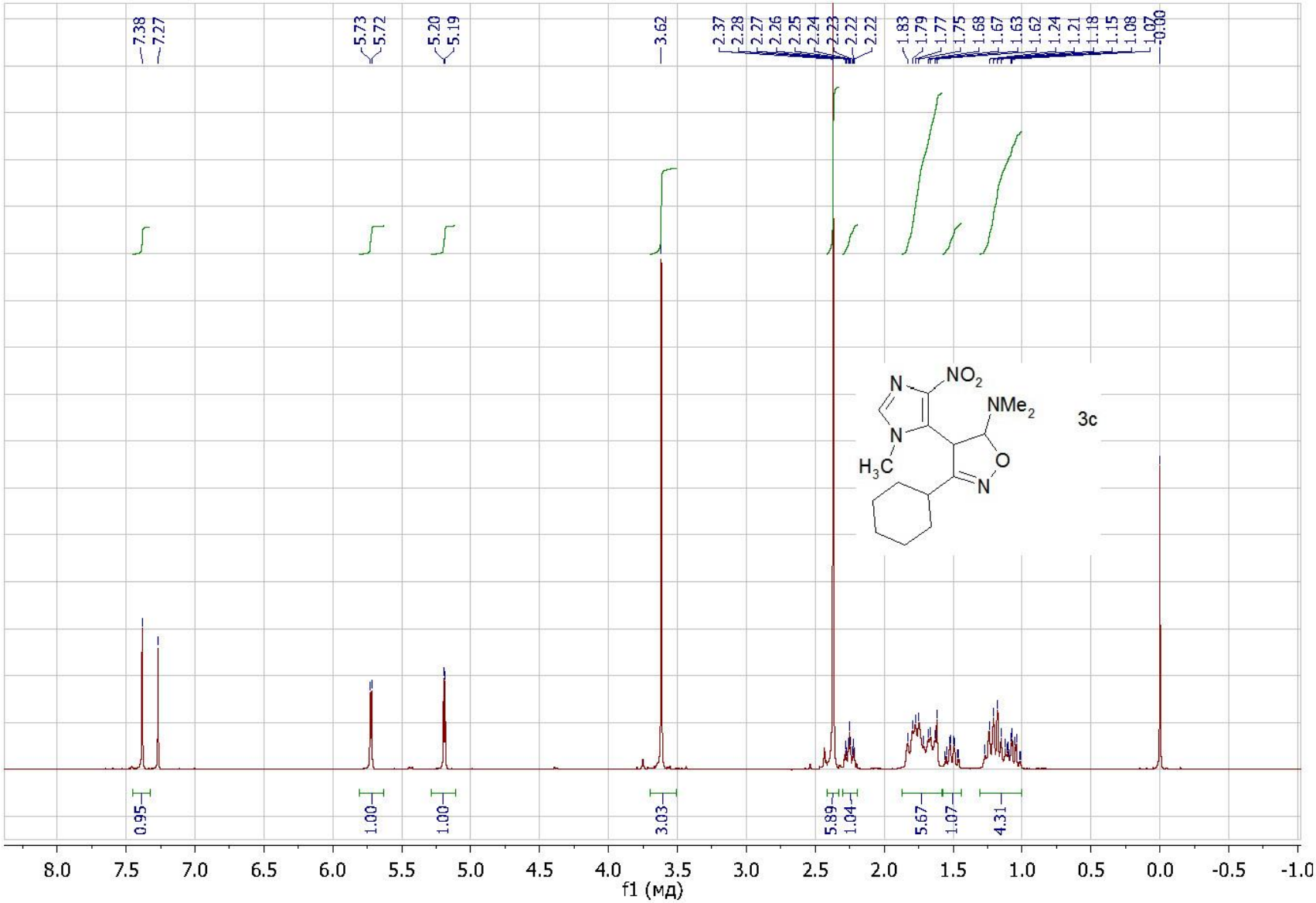
Cl
f2 (мд)
f1 (мд)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2.23
2.22
2.22
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1.77
1.75
1.68
1.67
1.63
1.62
1.24
1.21
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1.15
1.08
1.07
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NO2
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N
N
H3C
O
N
3c
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1.00
1.00
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1.04
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1.07
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5.0
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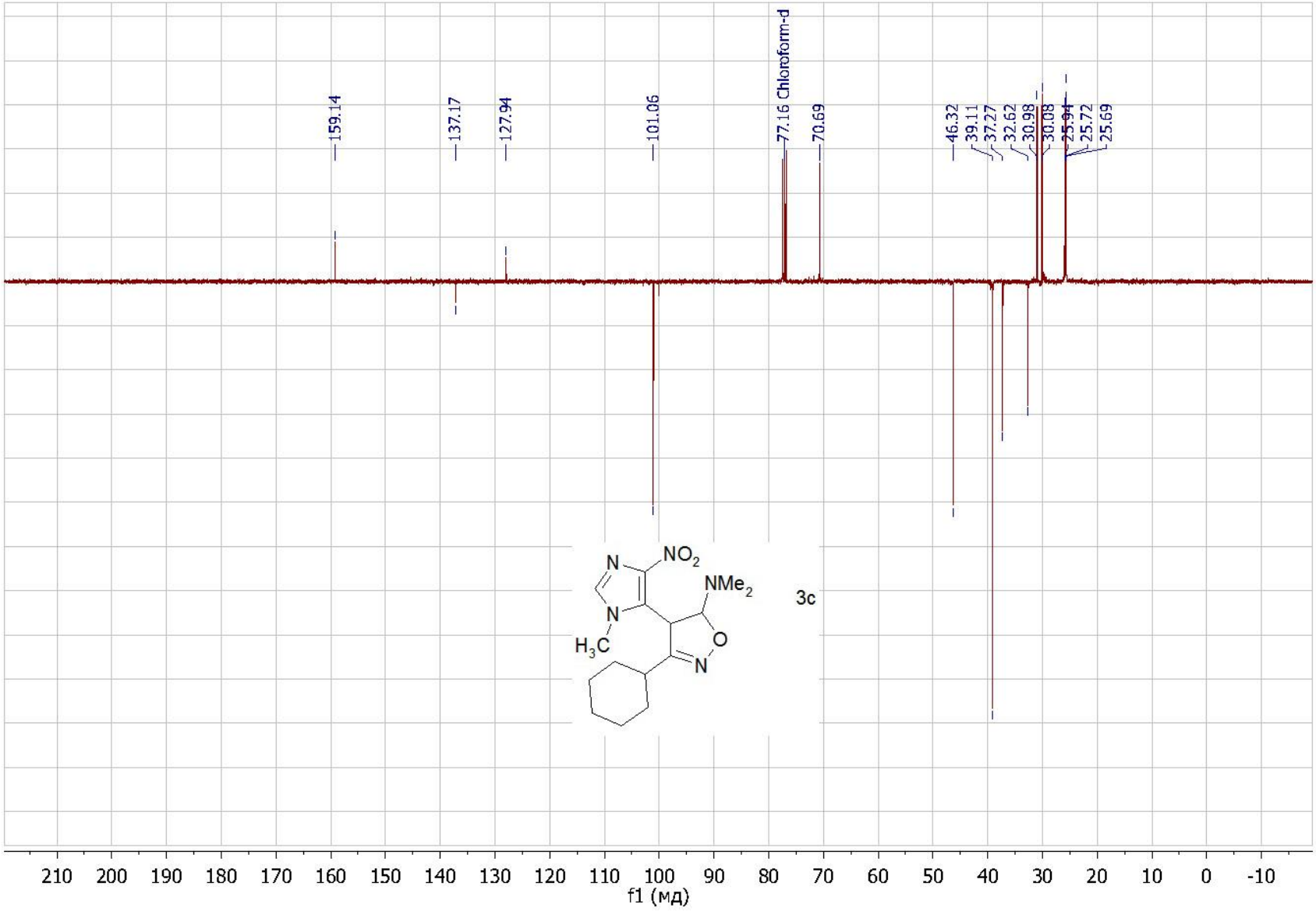
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30.08
25.94
25.72
25.69
NO2
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H3C
O
N
3c
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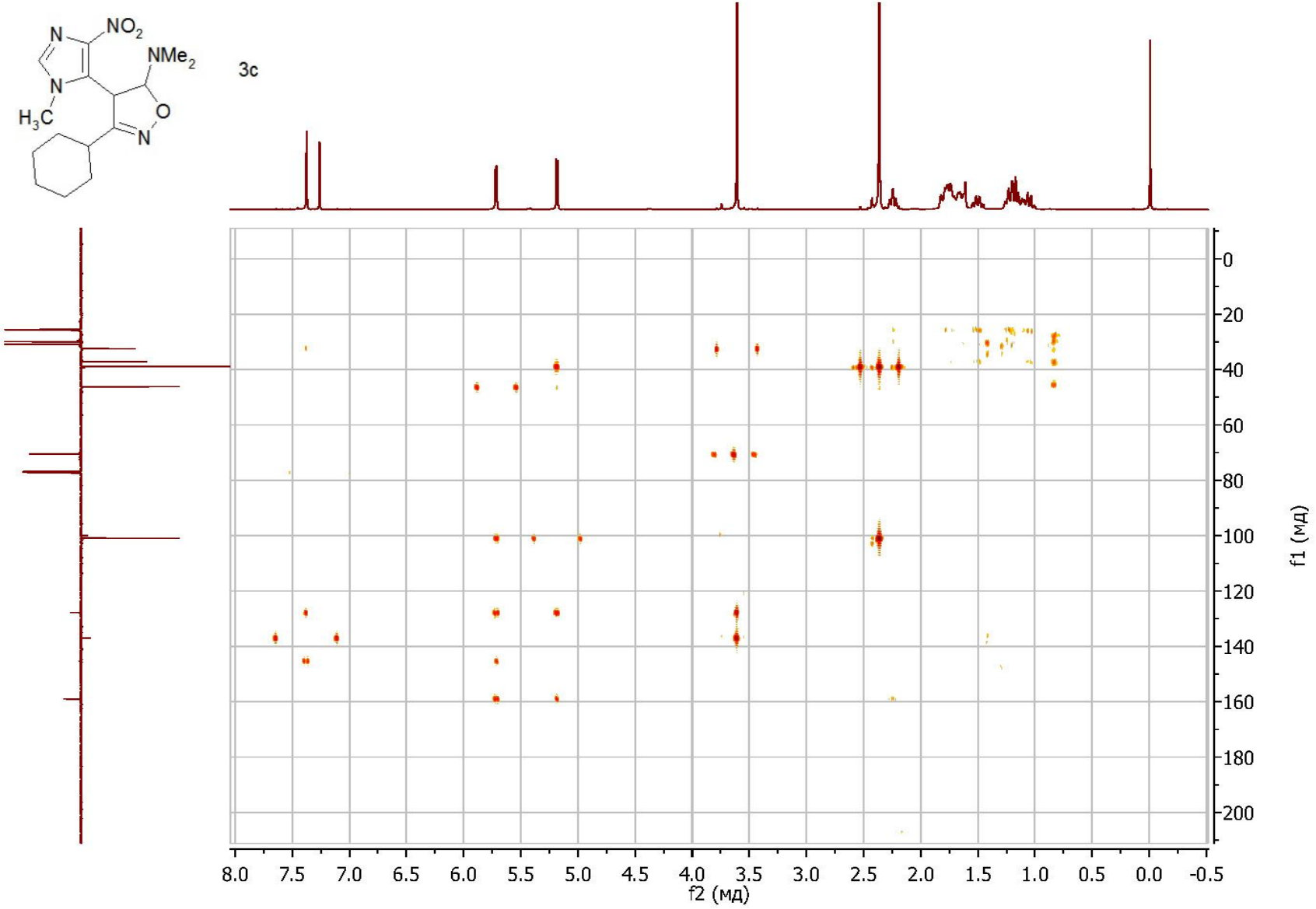
f1 (мд)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40
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100
120
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160
180
200
f1 (мд)
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7.5
7.0
6.5
6.0
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5.0
4.5
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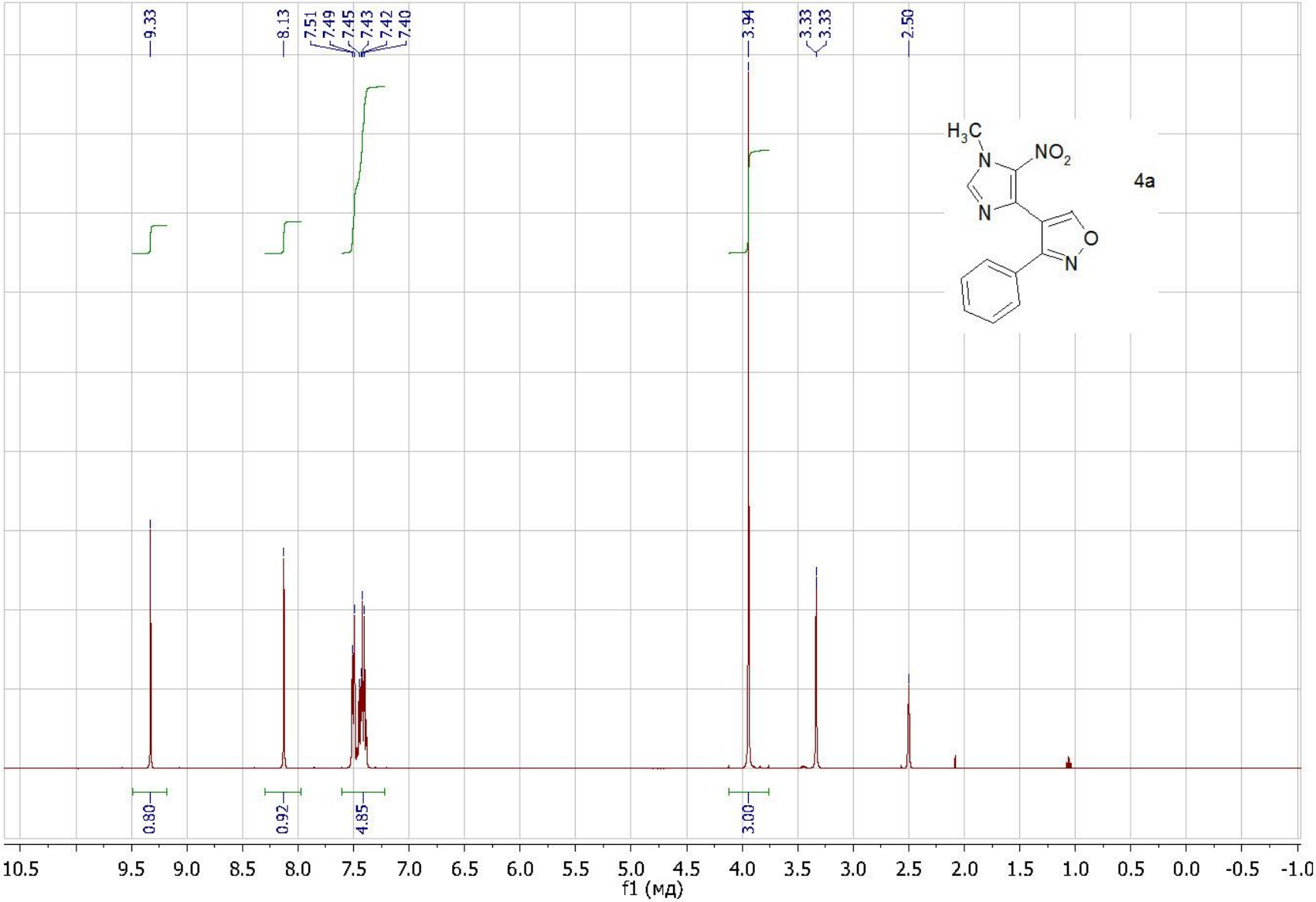
f2 (мд)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3.00
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8.5
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6.0
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5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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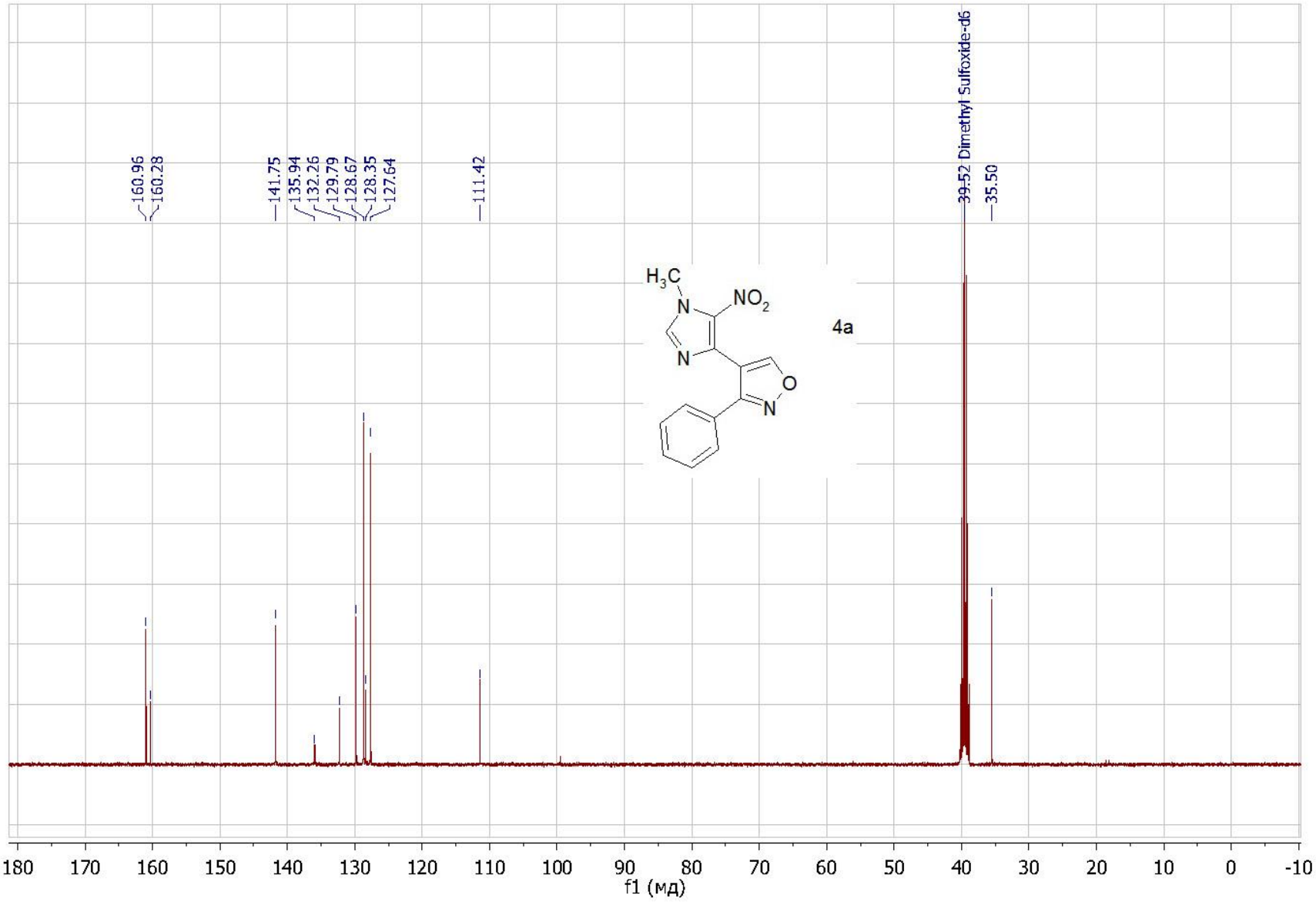
f1 (мд)
H3C
N
NO2
N
O
N
4a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111.42
39.52 Dimethyl Sulfoxide-d6
35.50
H3C
N
NO2
N
O
N
4a
180
170
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150
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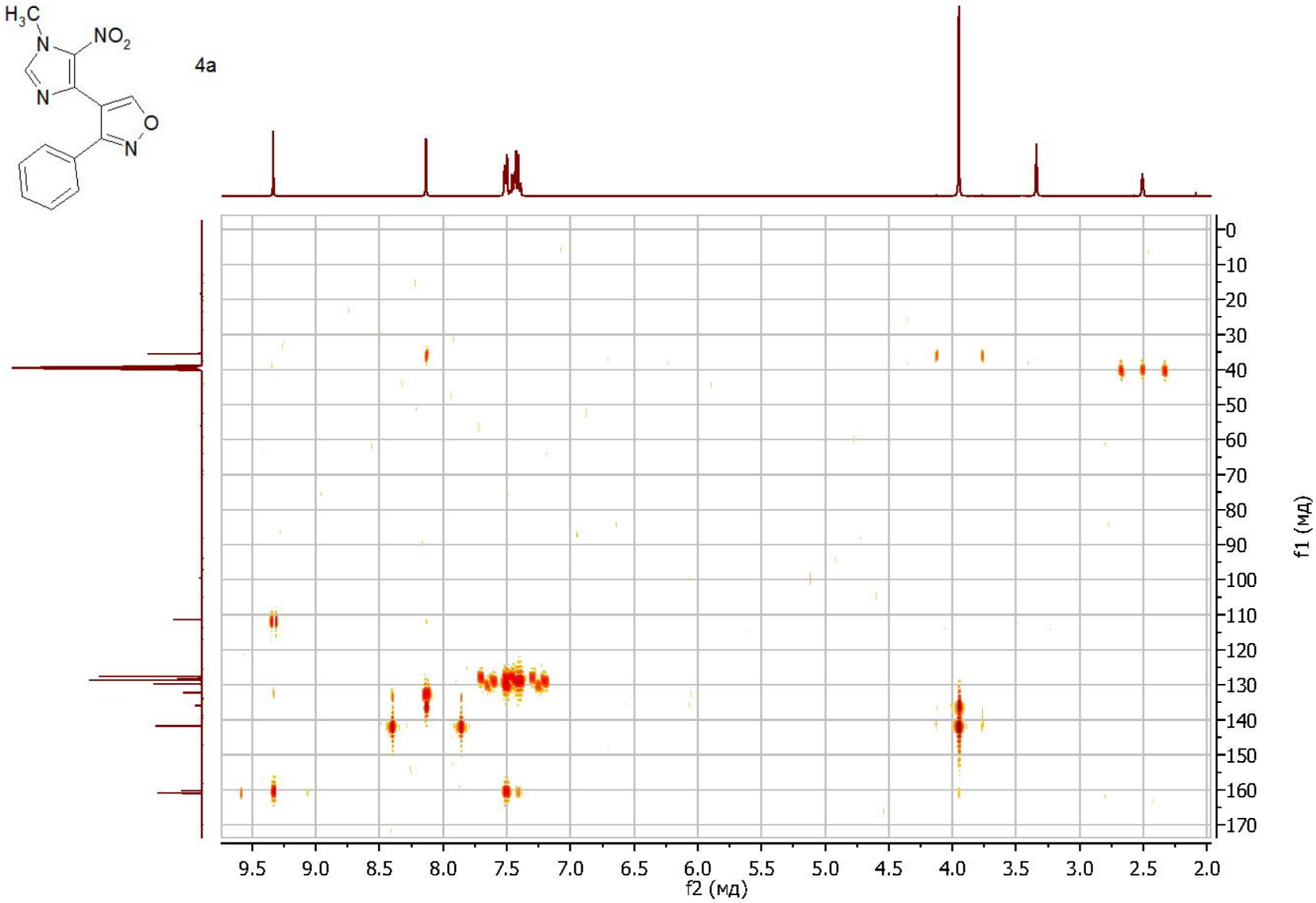
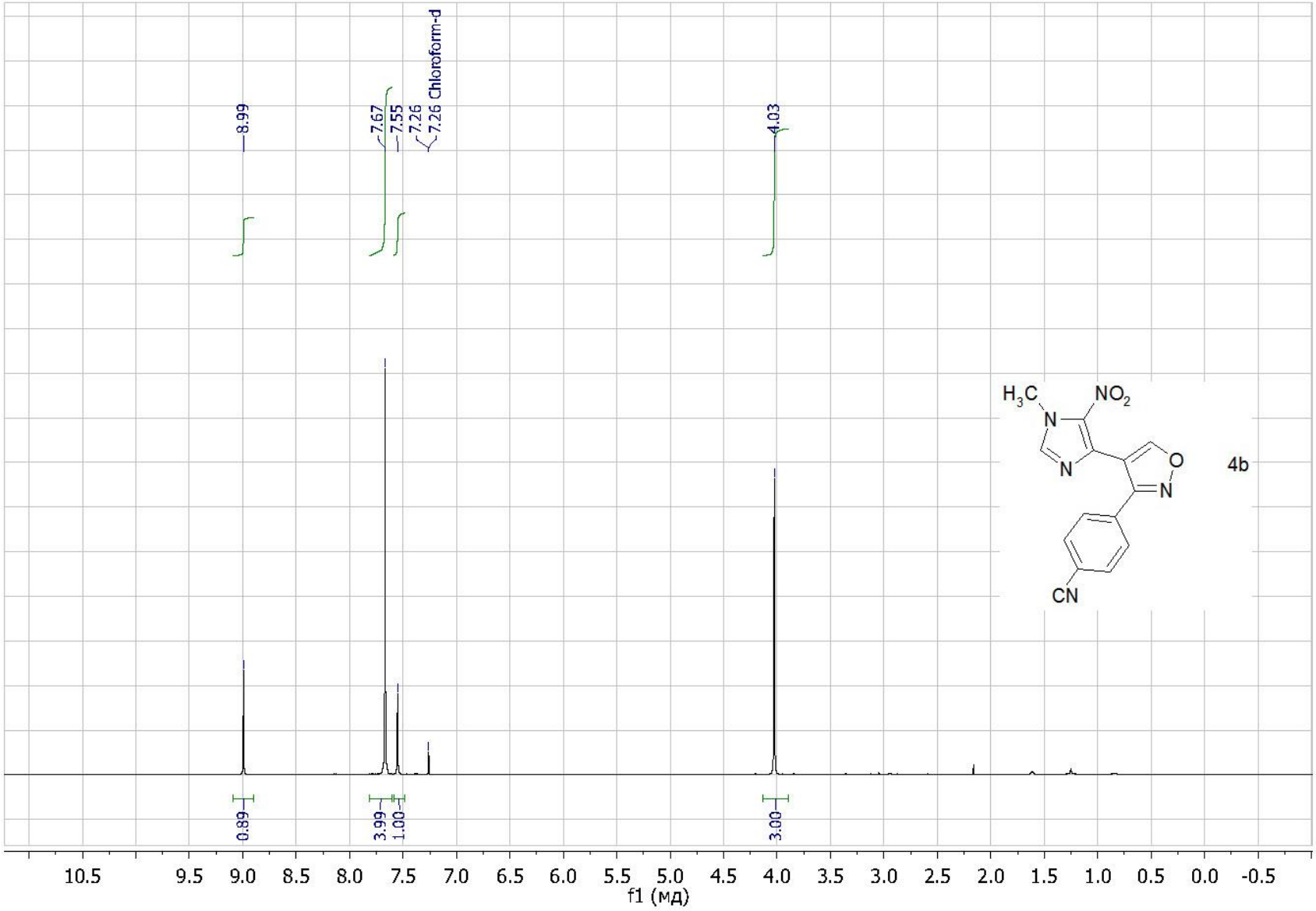

4a
f2 (мд)
f1 (мд)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9.5
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7.5
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3.5
3.0
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2.0
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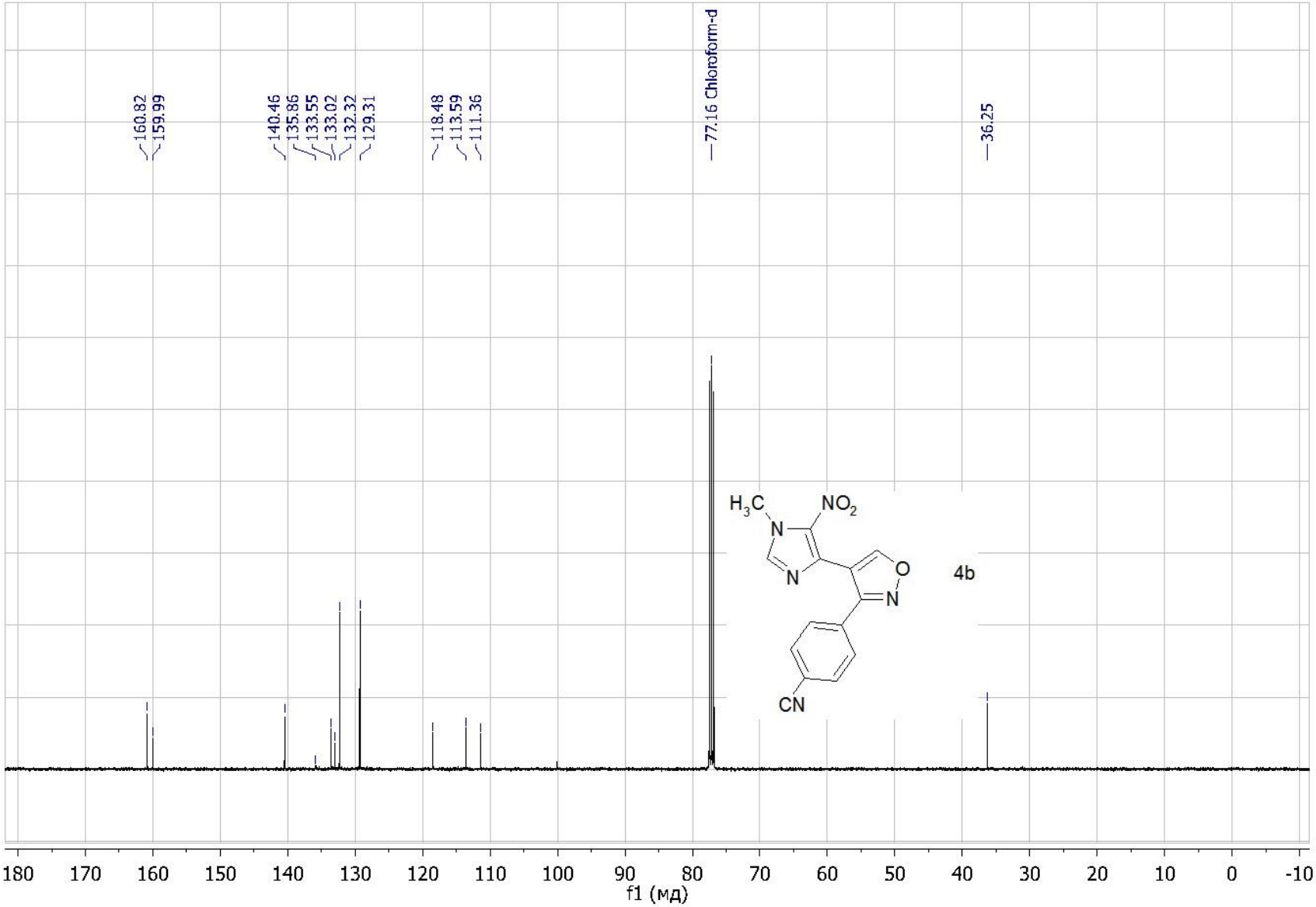
N
NO2
N
O
N
CN
4b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36.25
H3C
N
NO2
N
O
N
CN
4b
180
170
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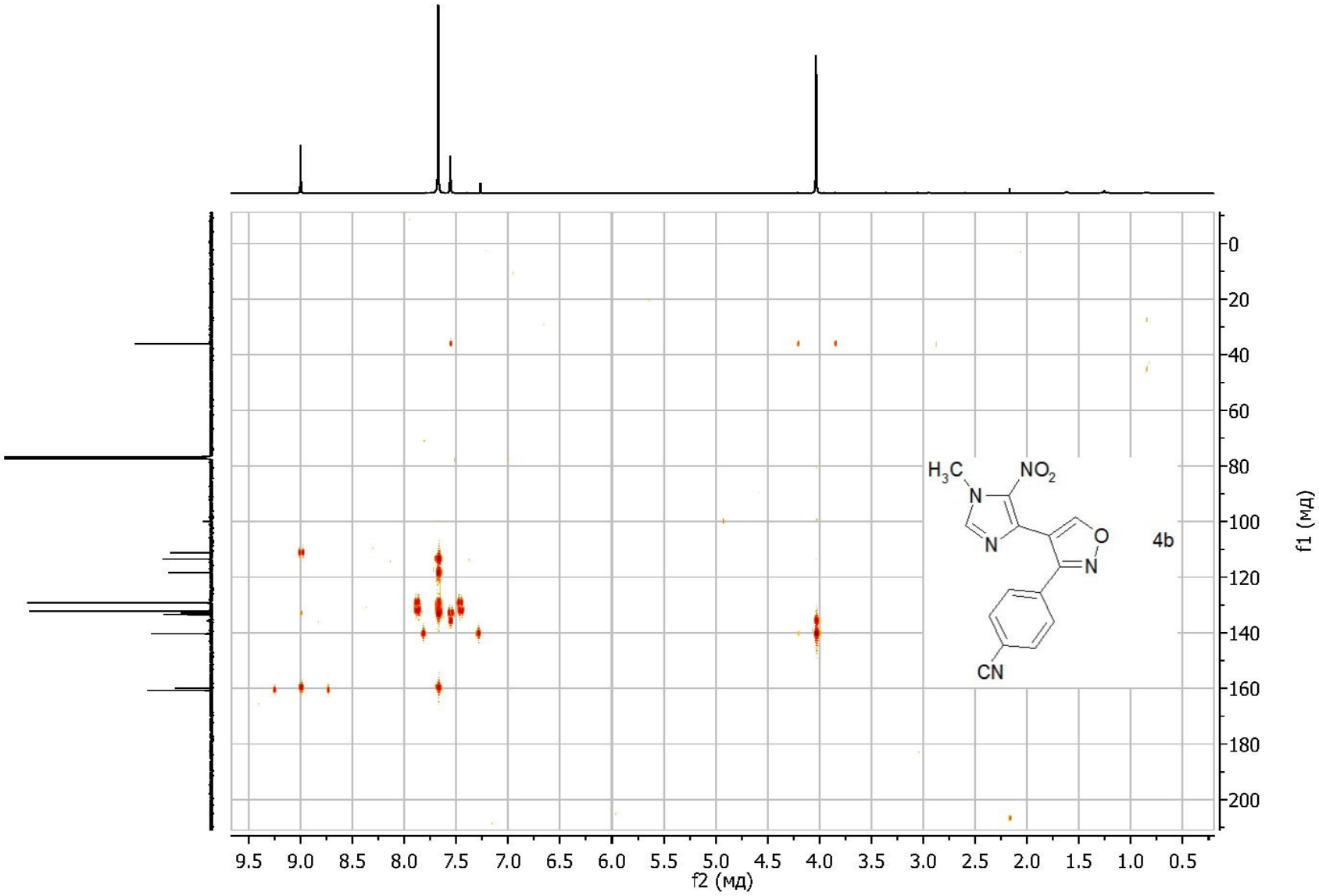
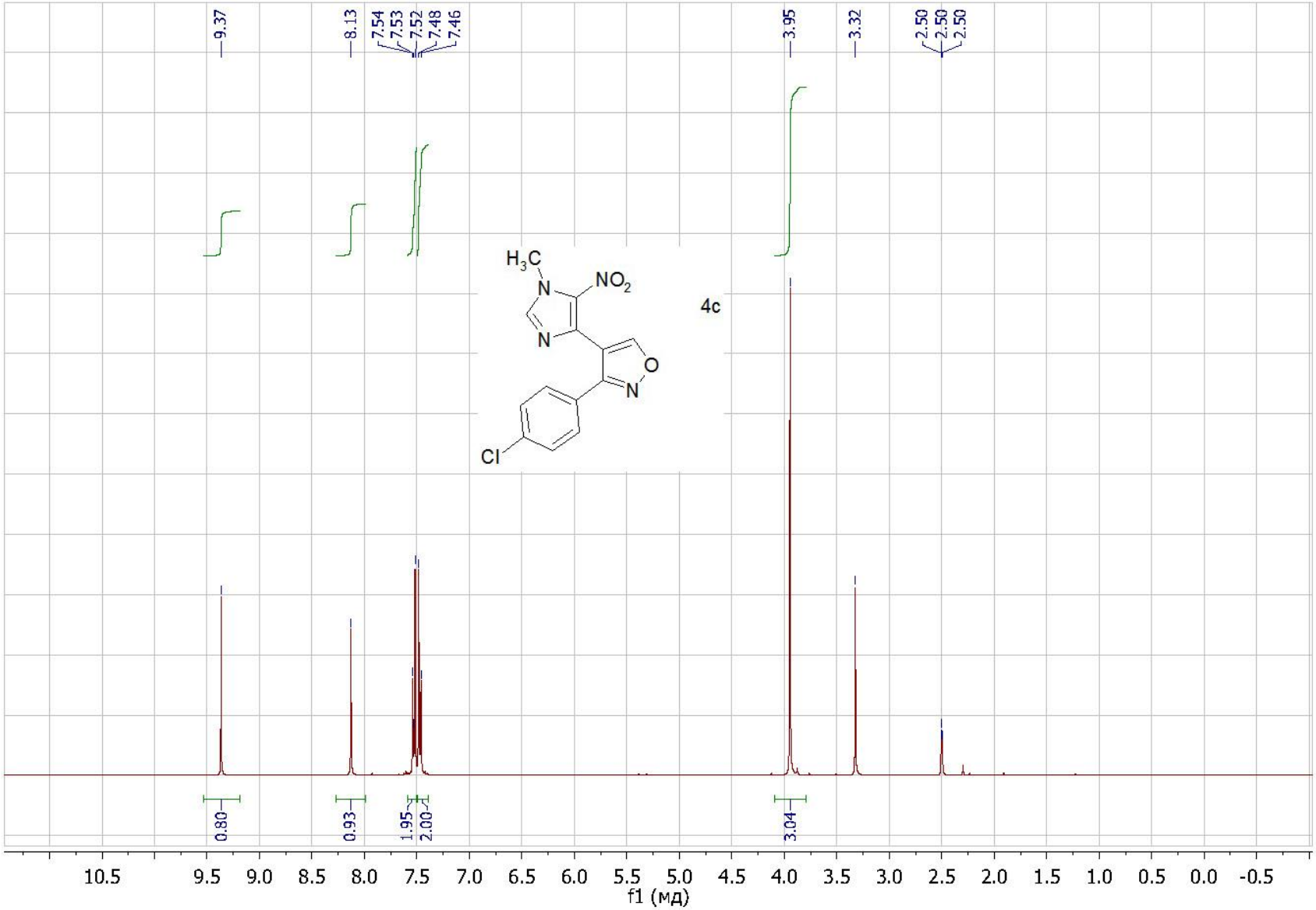
f1 (мд)


f2 (мд)
f1 (мд)
4b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Cl
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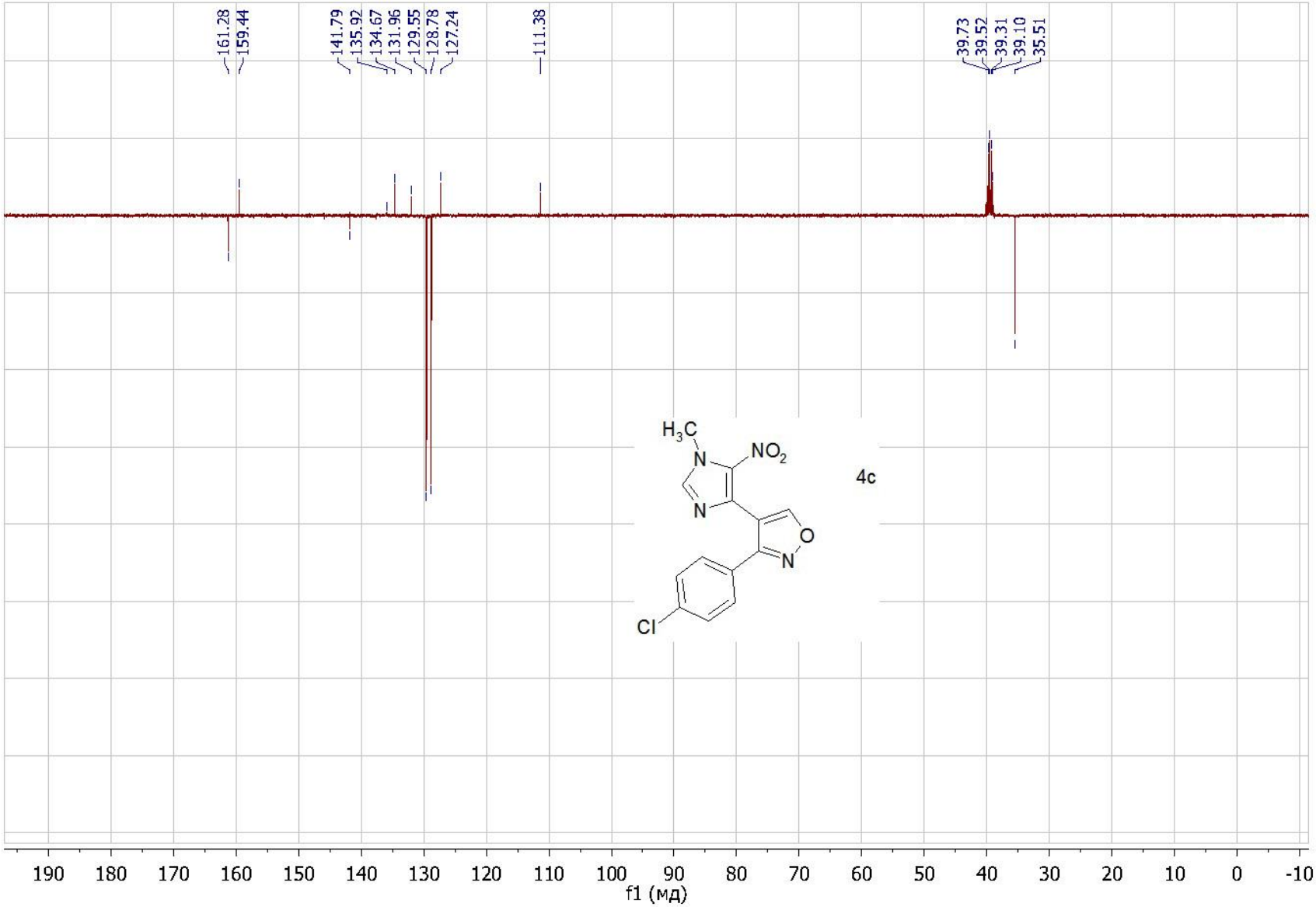
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N
O
N
Cl
4c
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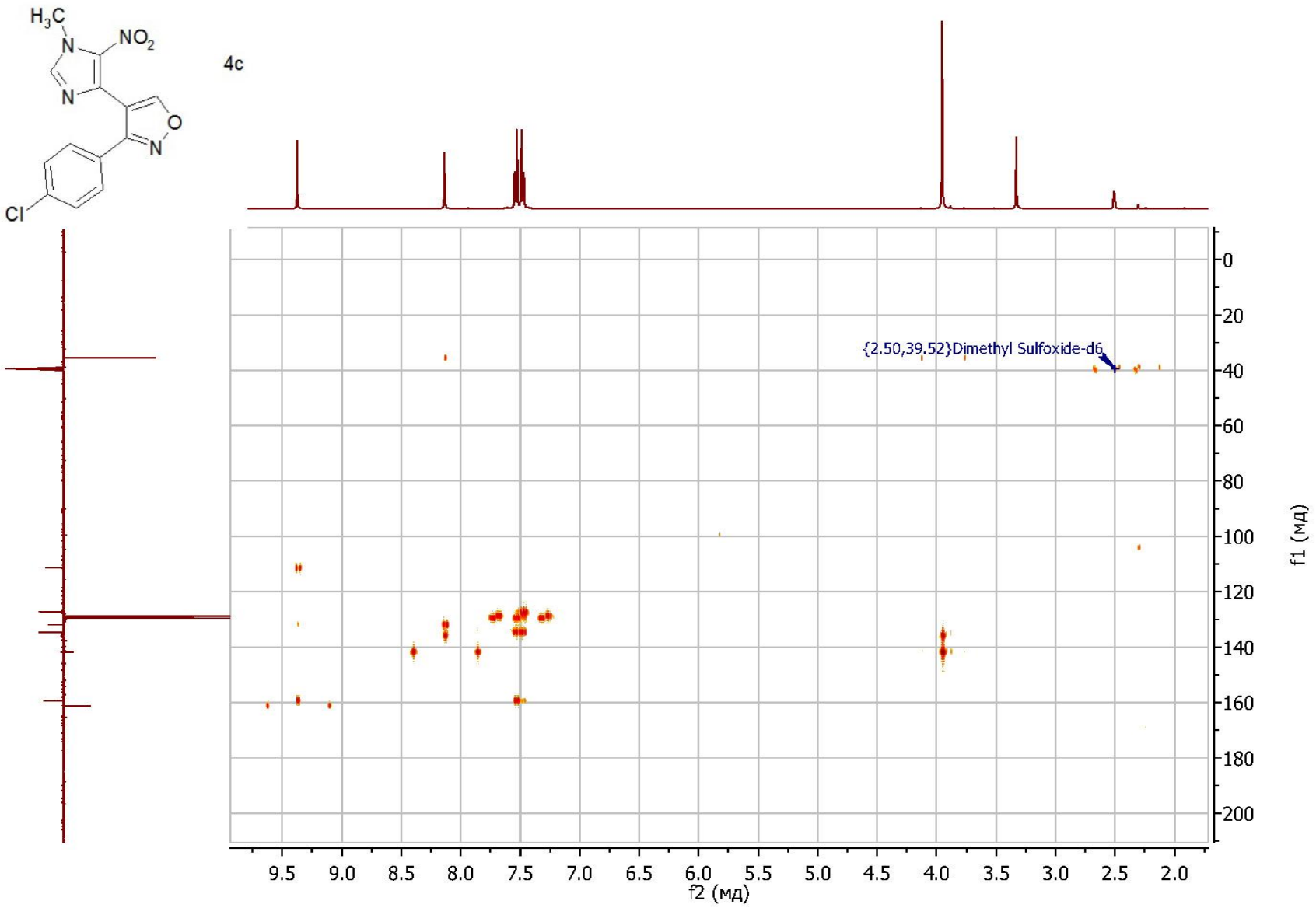
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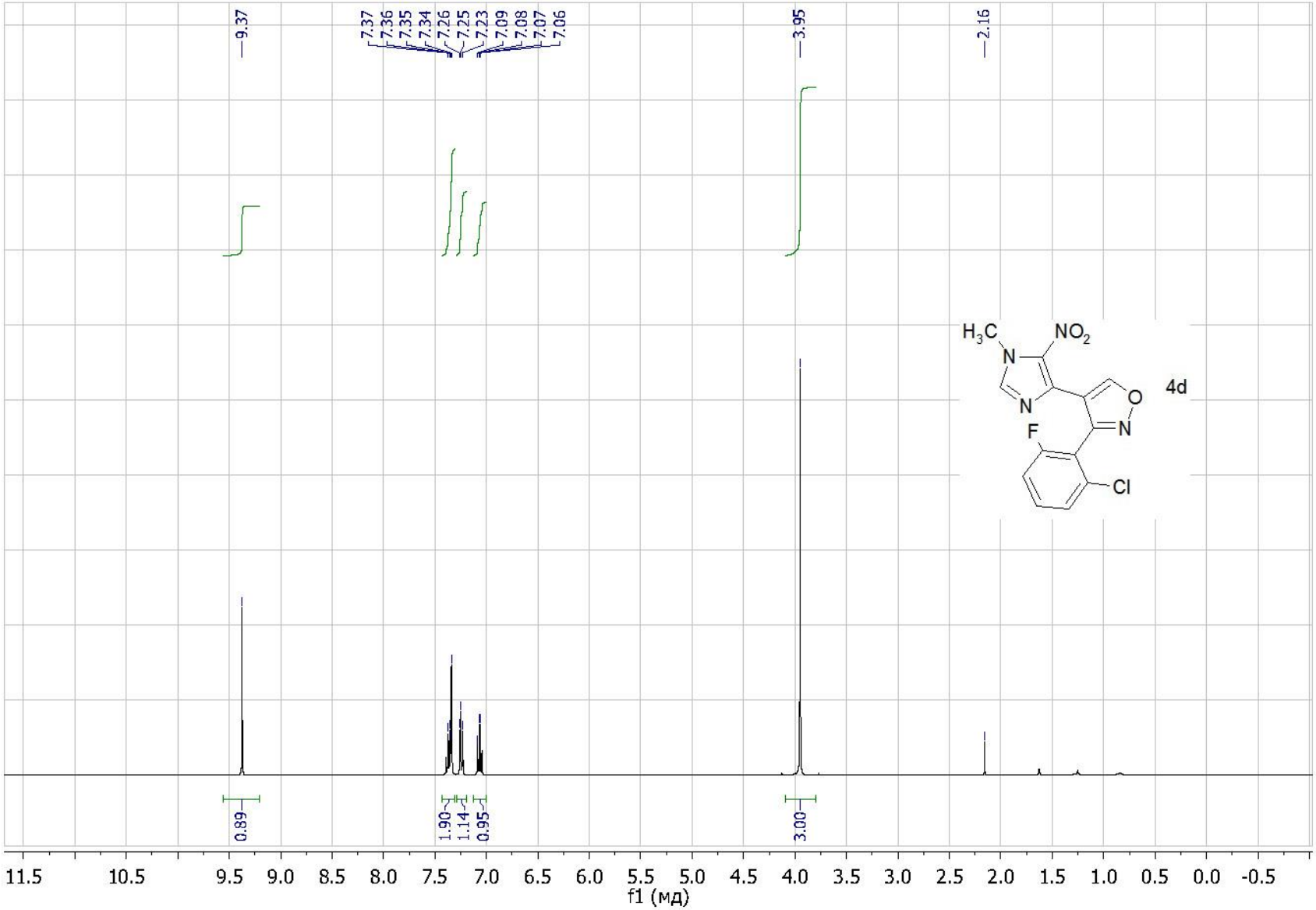
f1 (мд)
f2 (мд)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F
Cl
4d
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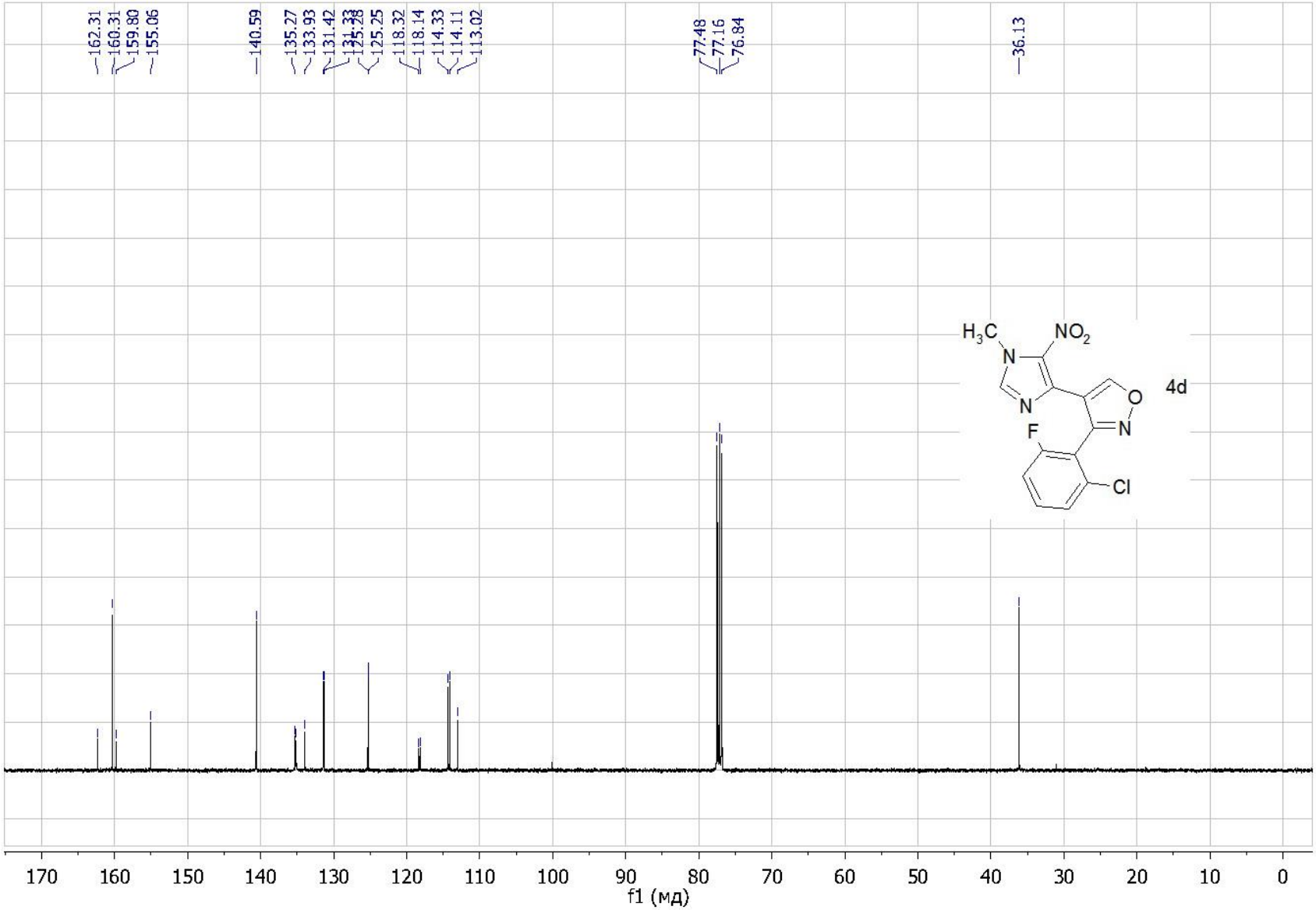
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F
Cl
4d
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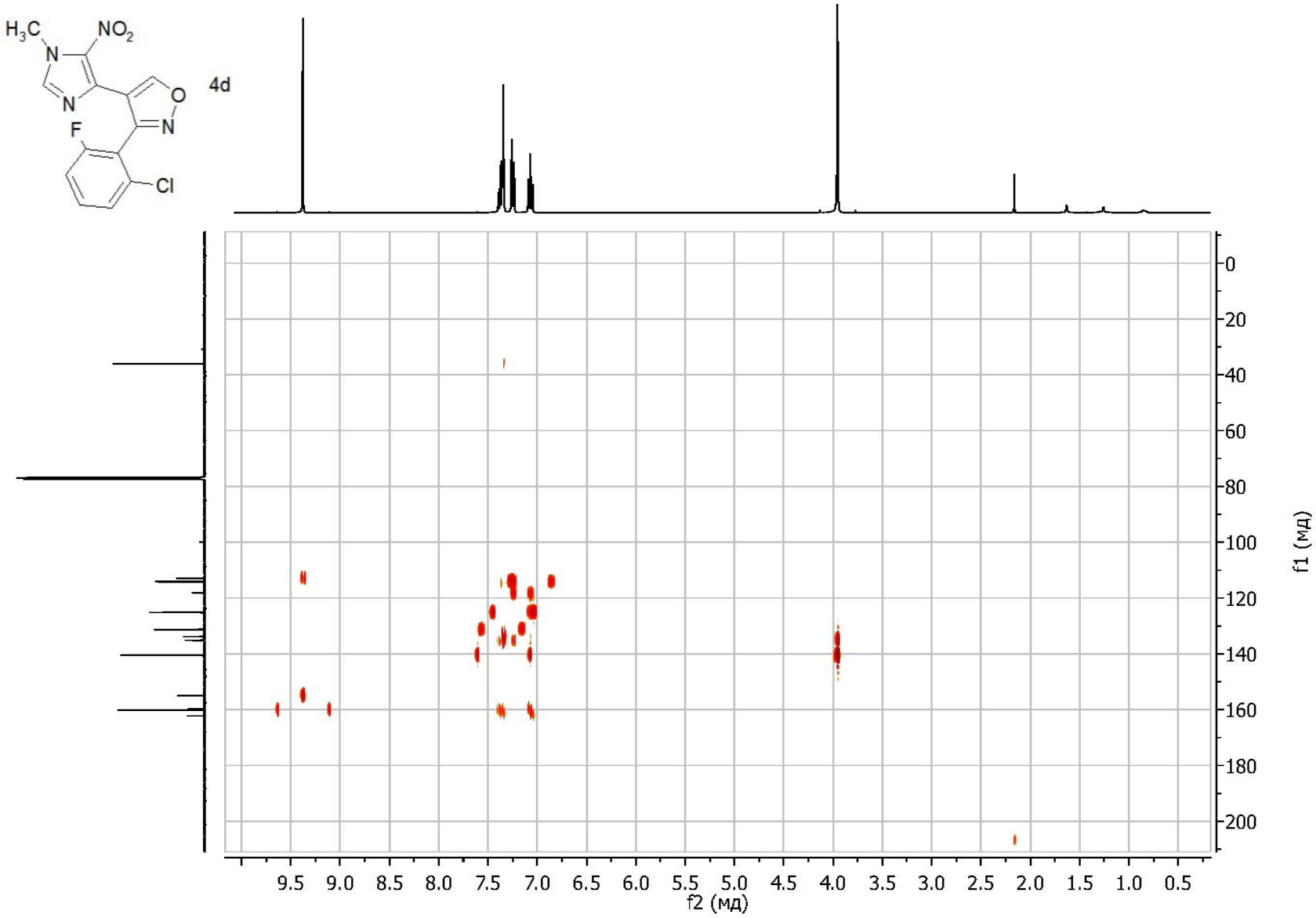
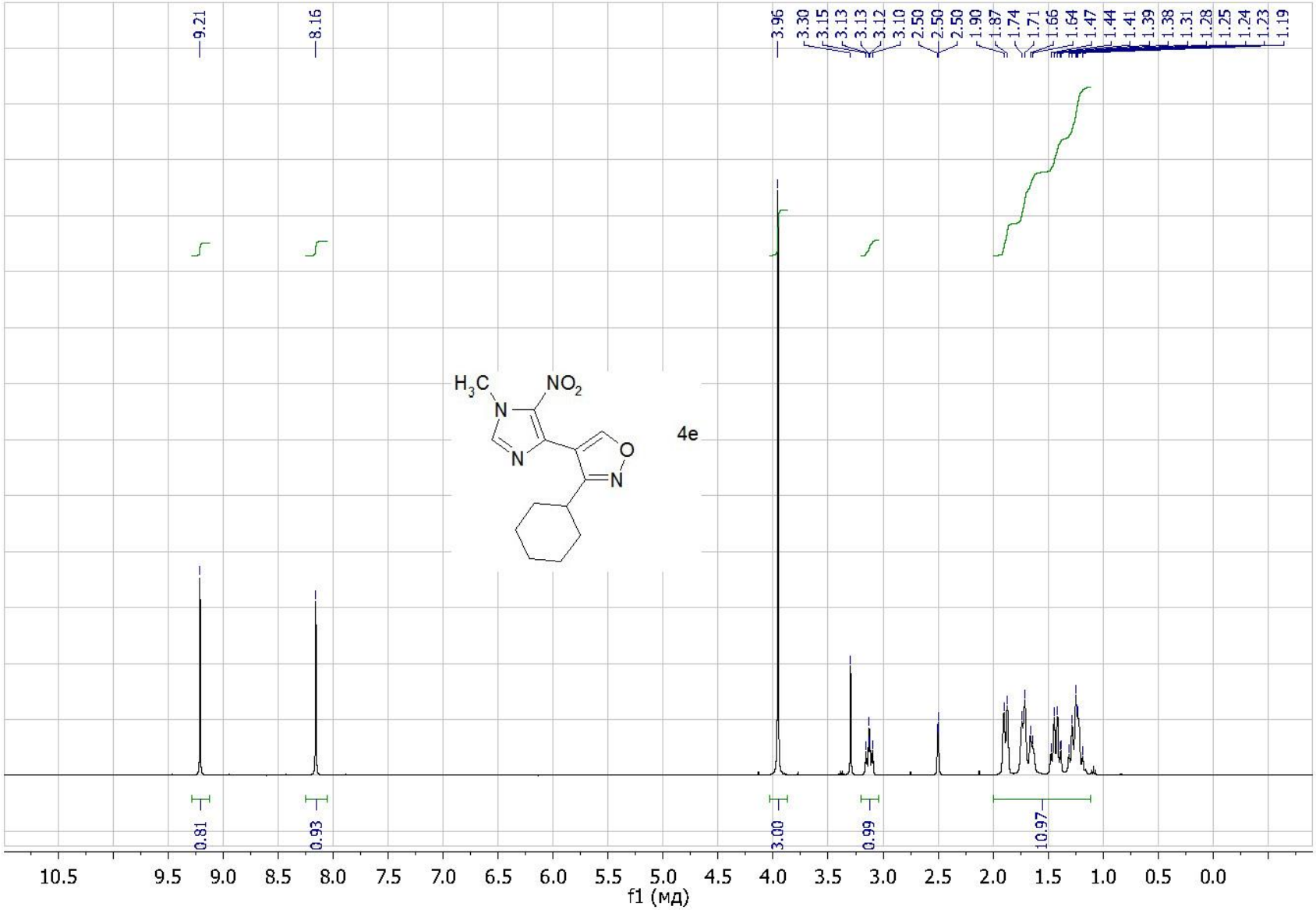

4d
f2 (мд)
f1 (мд)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1.39
1.38
1.31
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1.24
1.23
1.19
H3C
NO2
N
N
O
N
4e
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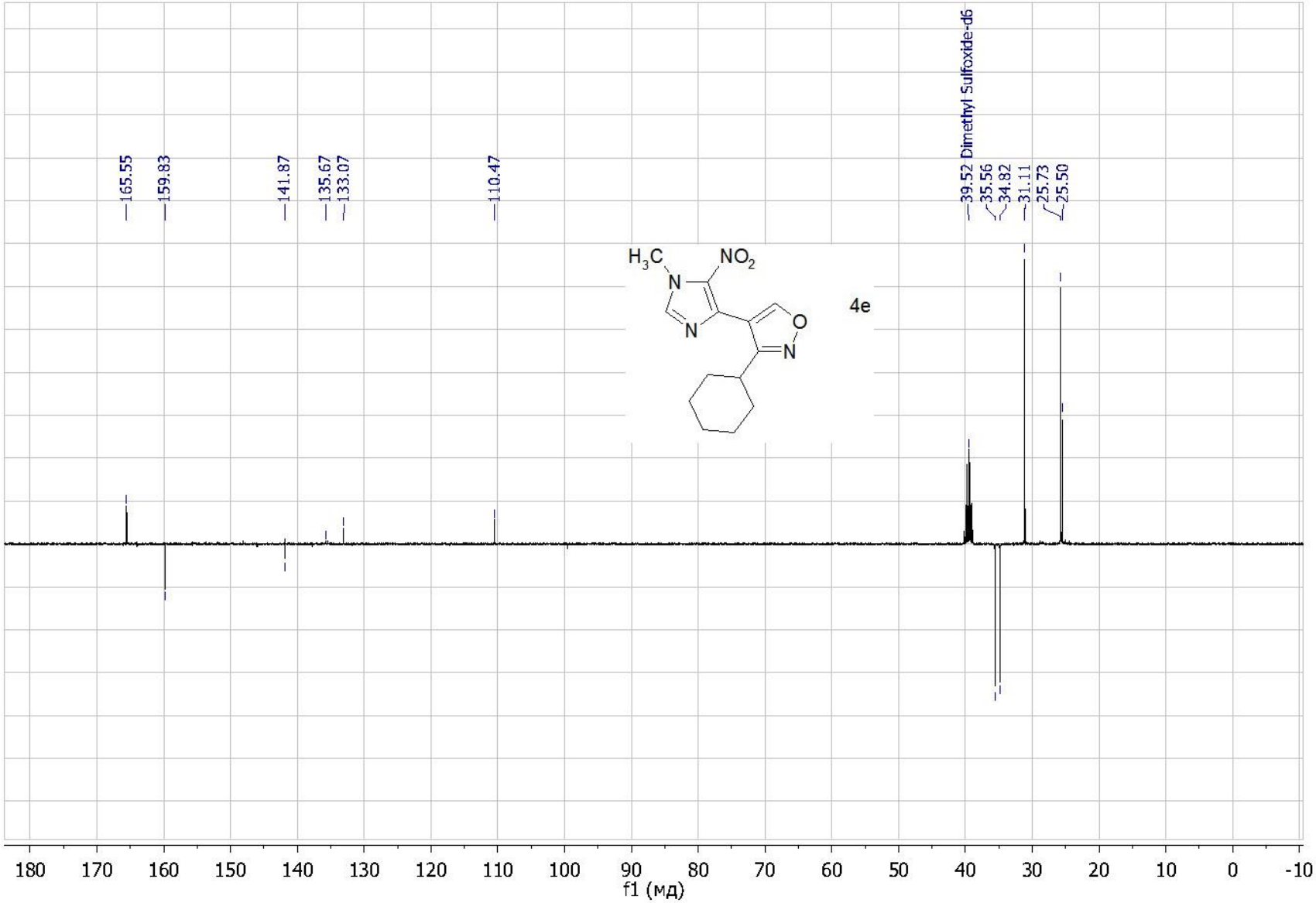
165.55
159.83
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110.47
39.52 Dimethyl Sulfoxide-d6
35.56
34.82
31.11
25.73
25.50
H3C
NO2
N
N
O
N
4e
180
170
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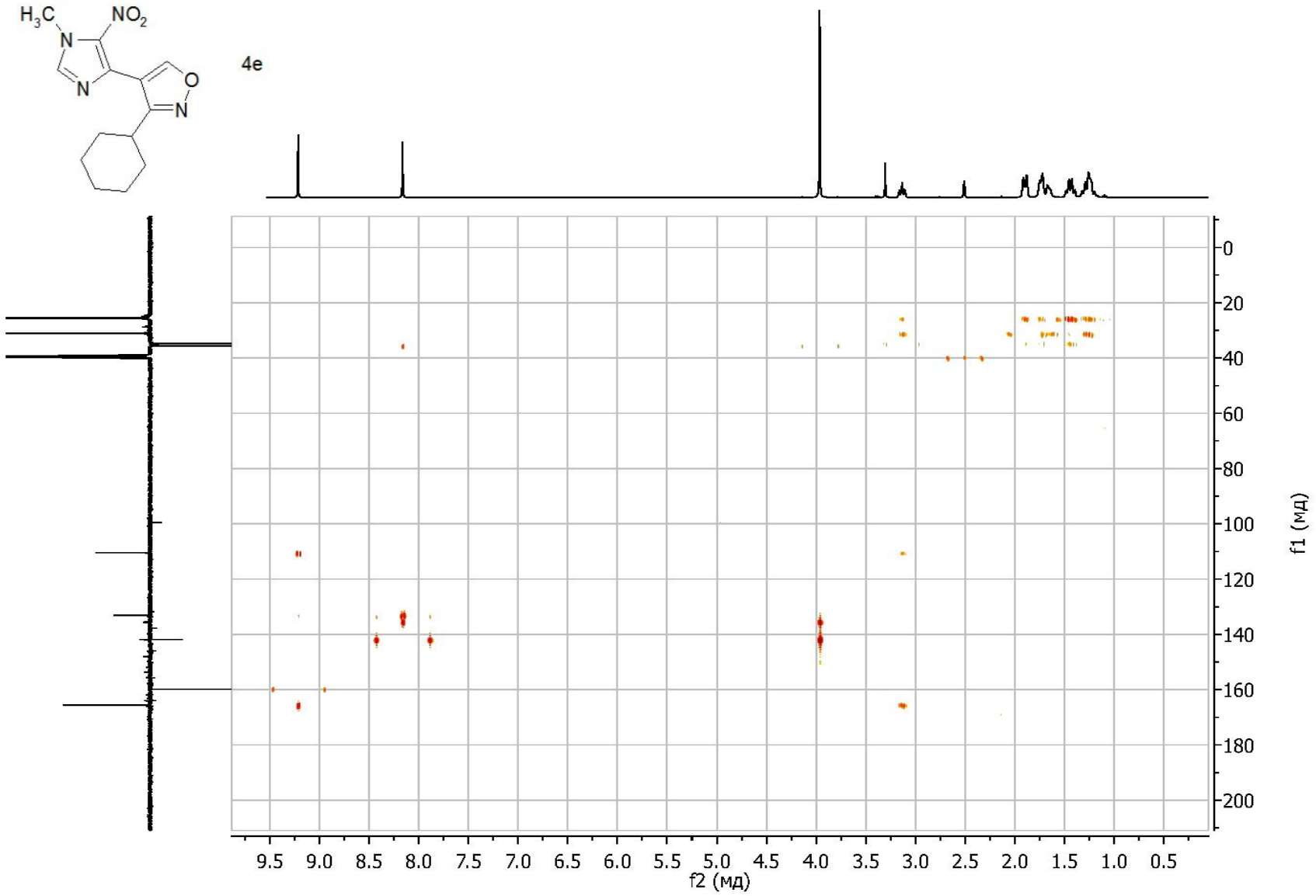
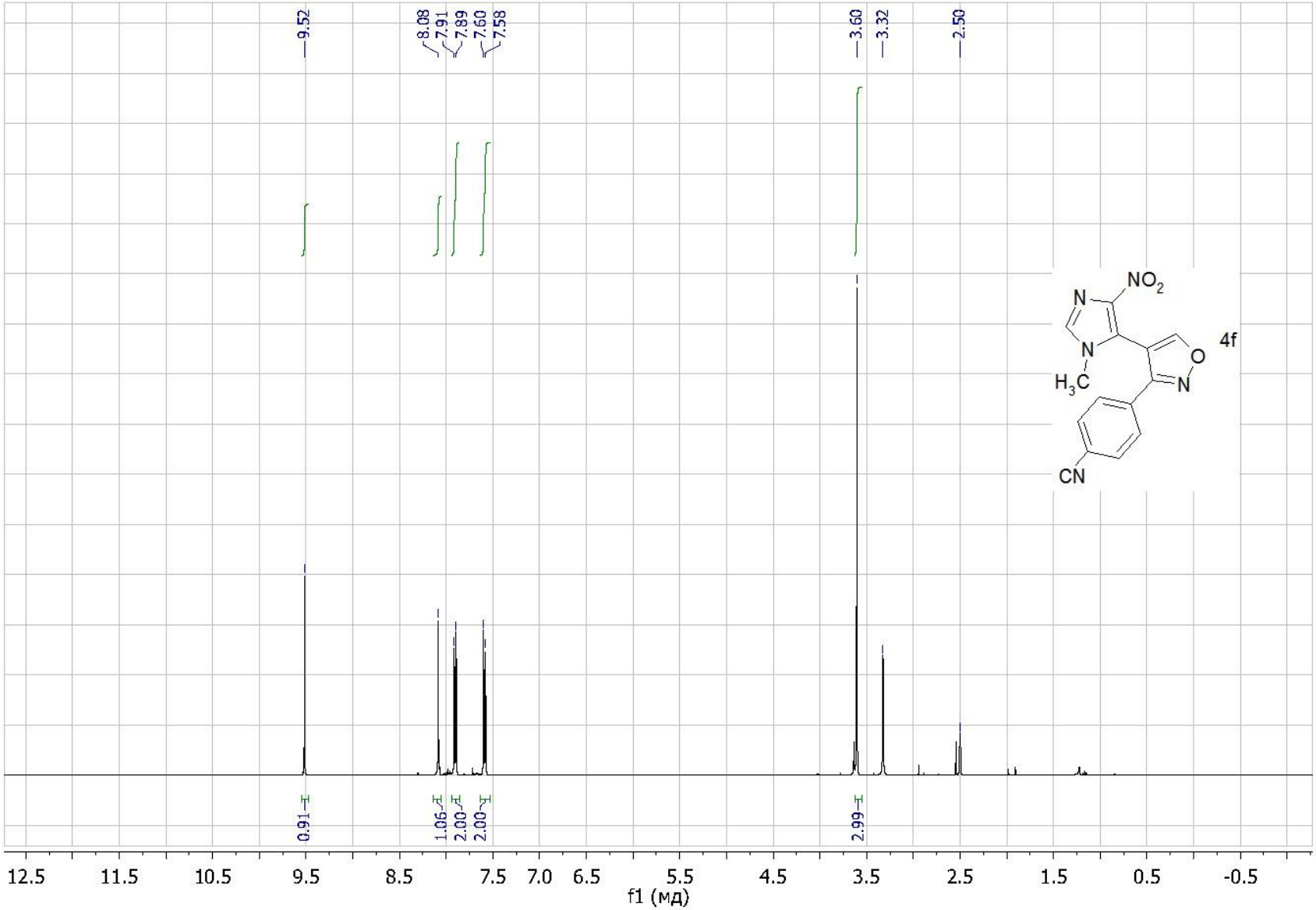
f1 (мд)


4e
f2 (мд)
f1 (мд)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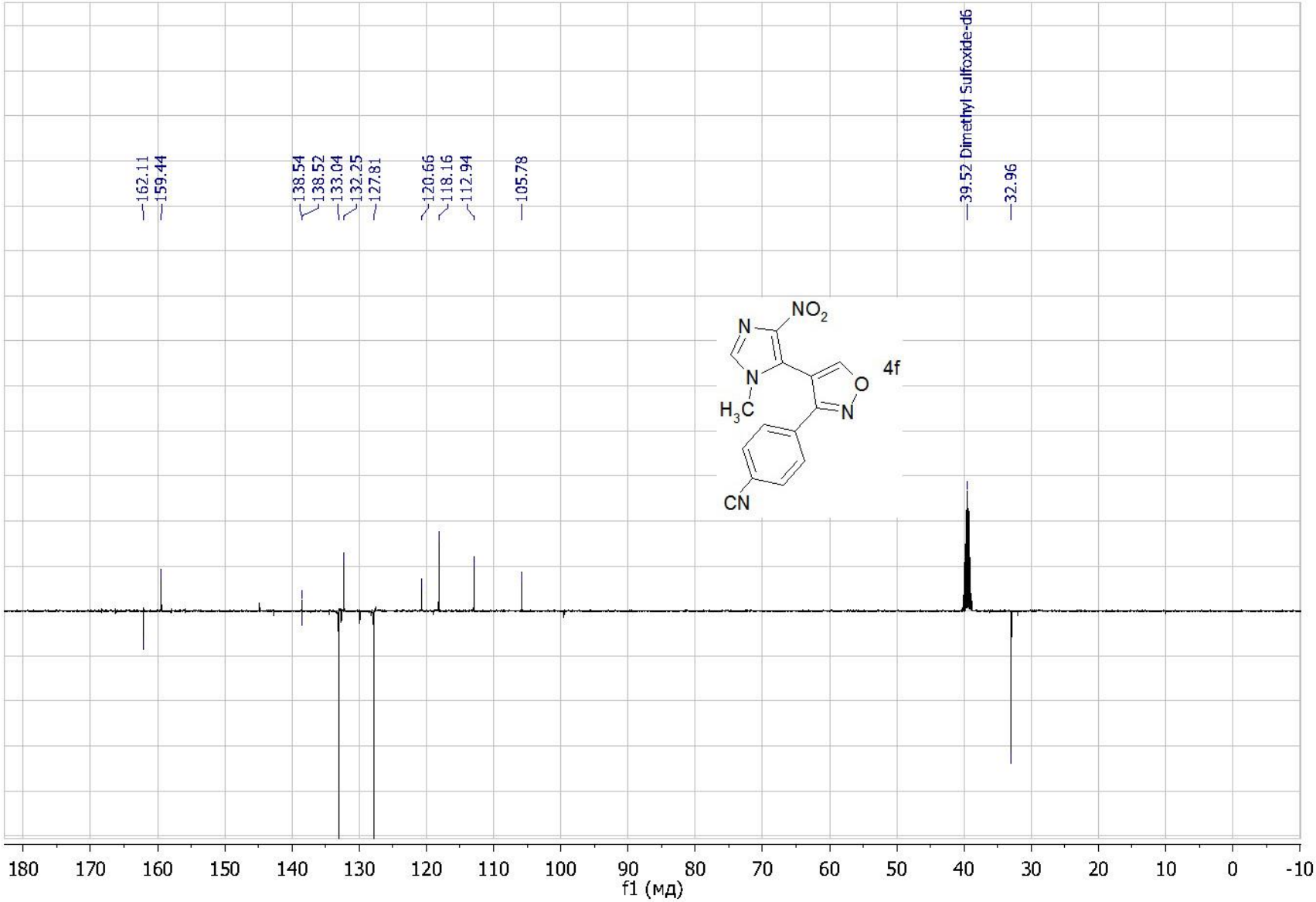
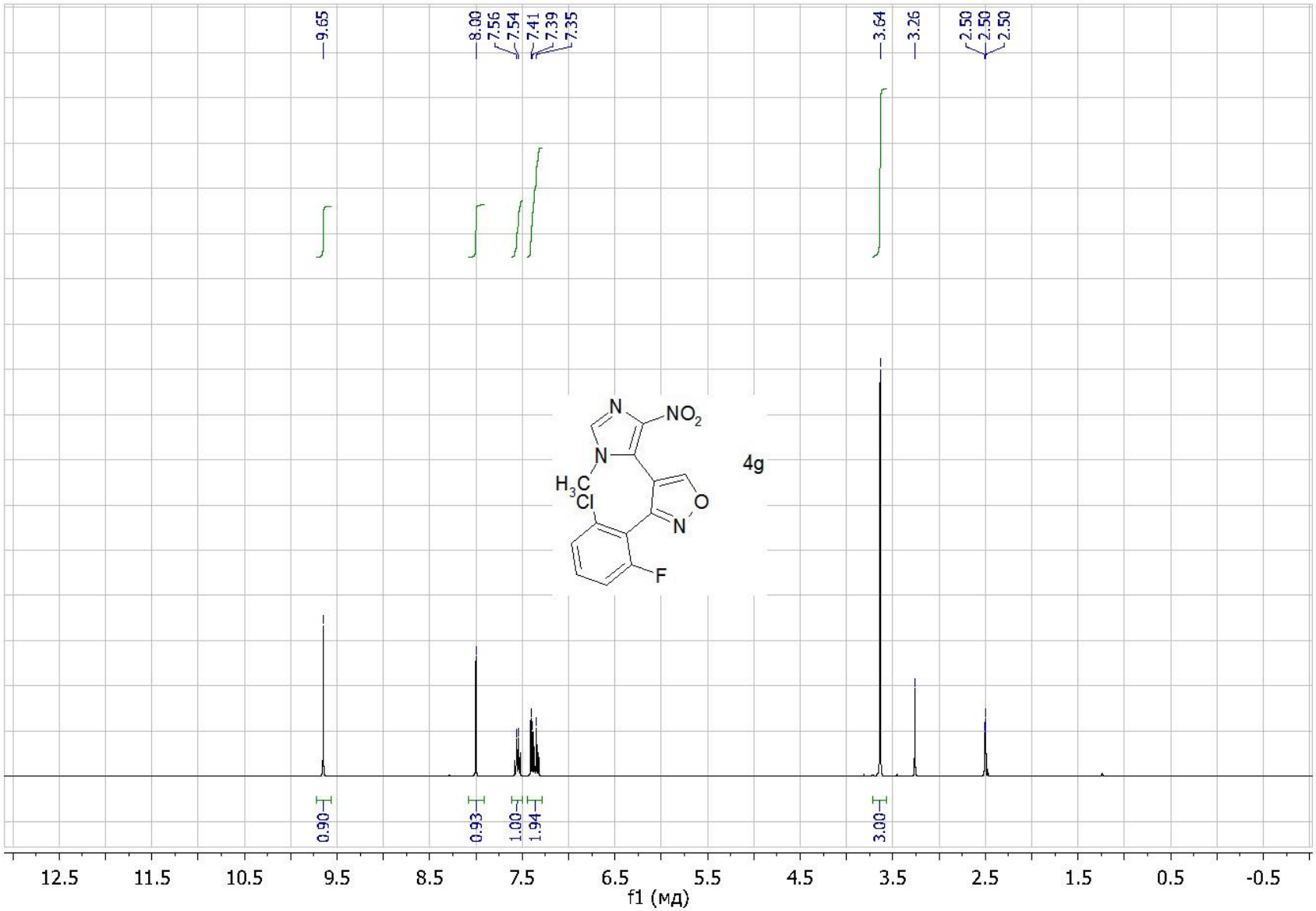
7.58
3.60
3.32
2.50
0.91
1.06
2.00
2.00
2.99
12.5
11.5
10.5
9.5
8.5
7.5
7.0
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (мд)
NO2
N
N
H3C
O
N
CN
4f


162.11
159.44
138.54
138.52
133.04
132.25
127.81
120.66
118.16
112.94
105.78
39.52 Dimethyl Sulfoxide-d6
32.96
NO2
N
N
H3C
O
N
CN
4f
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (мд)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7.39
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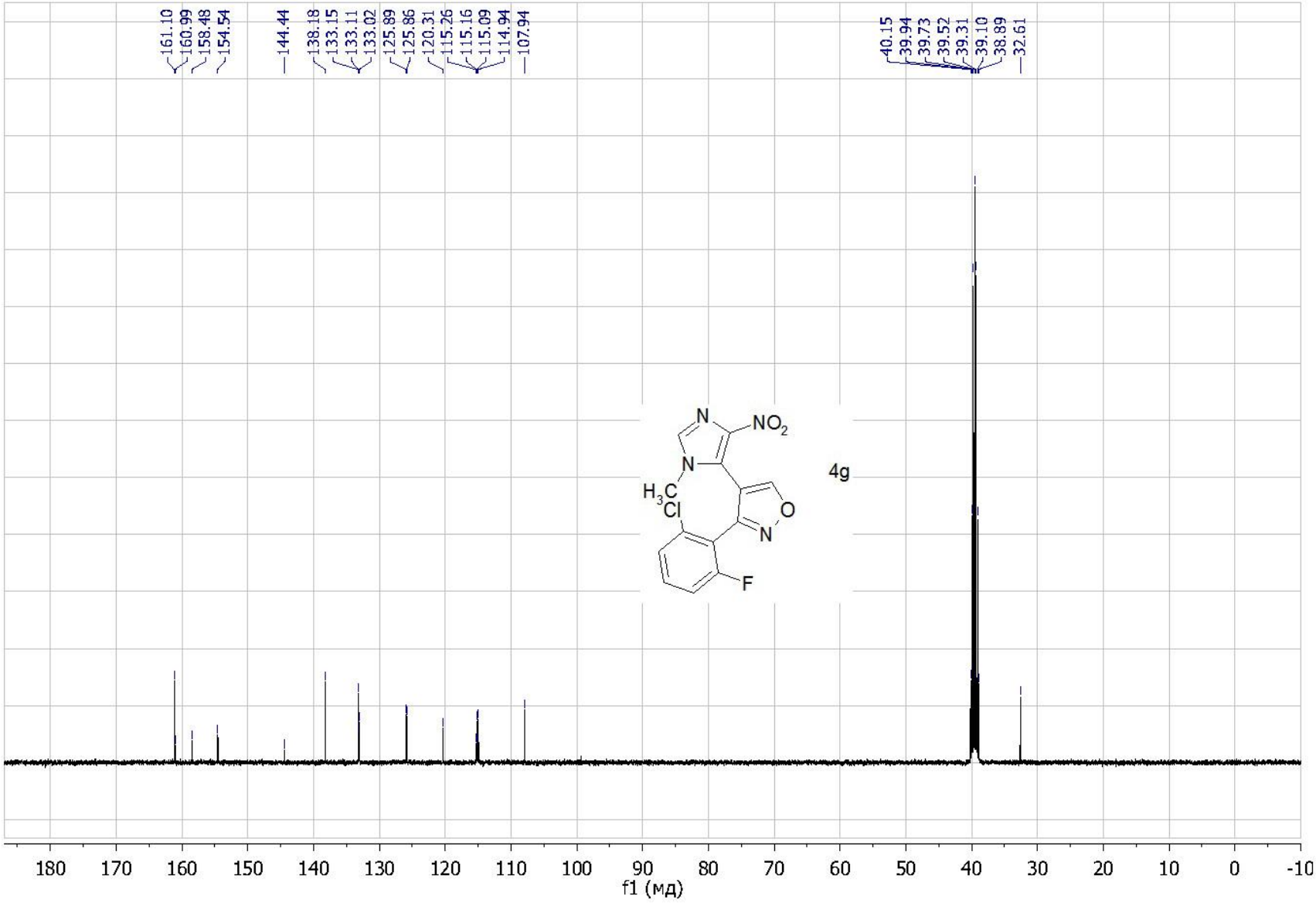
3.64
3.26
2.50
2.50
2.50
N
NO2
N
H3C
Cl
O
N
F
4g
0.90
0.93
1.00
1.94
3.00
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (мд)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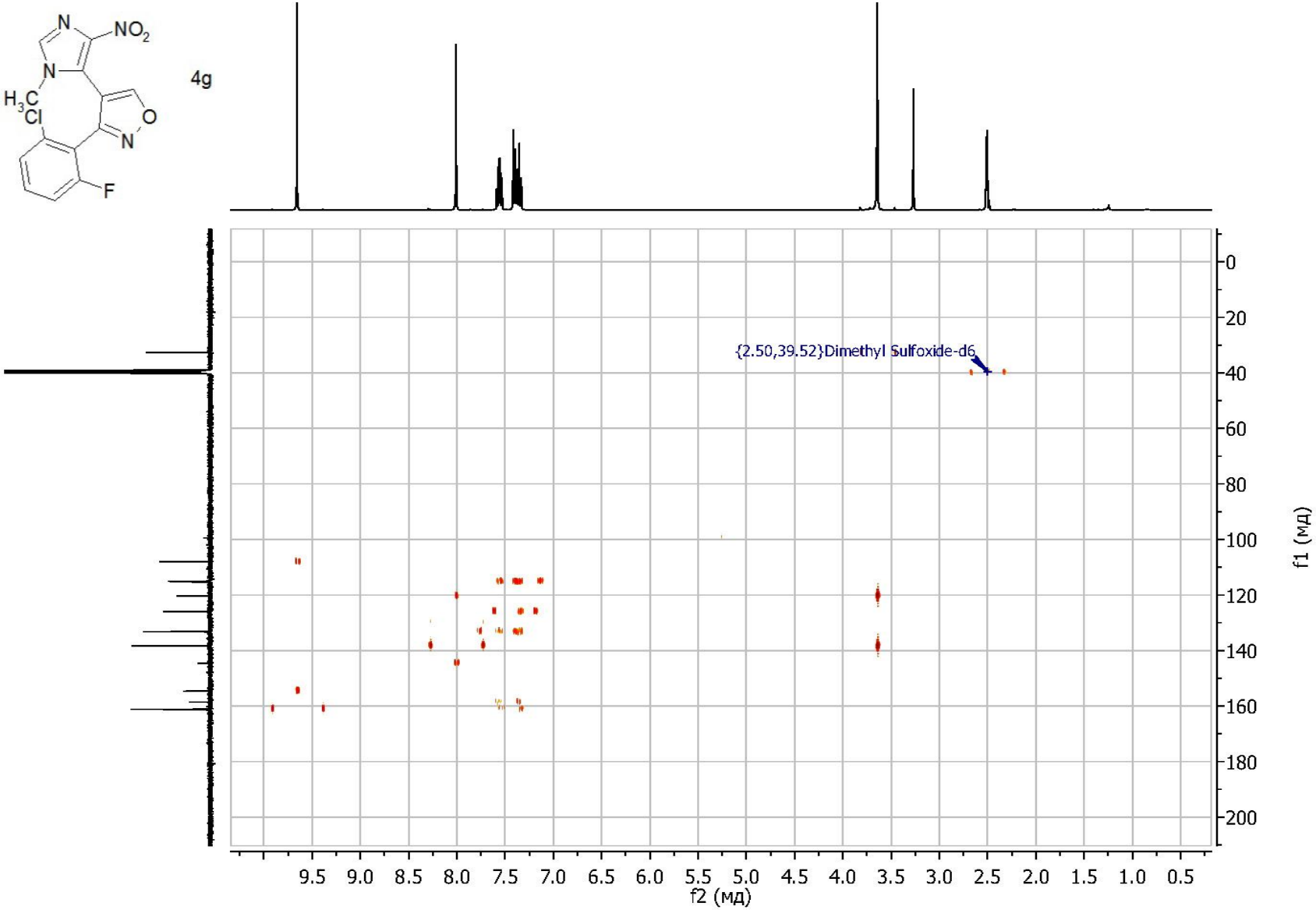
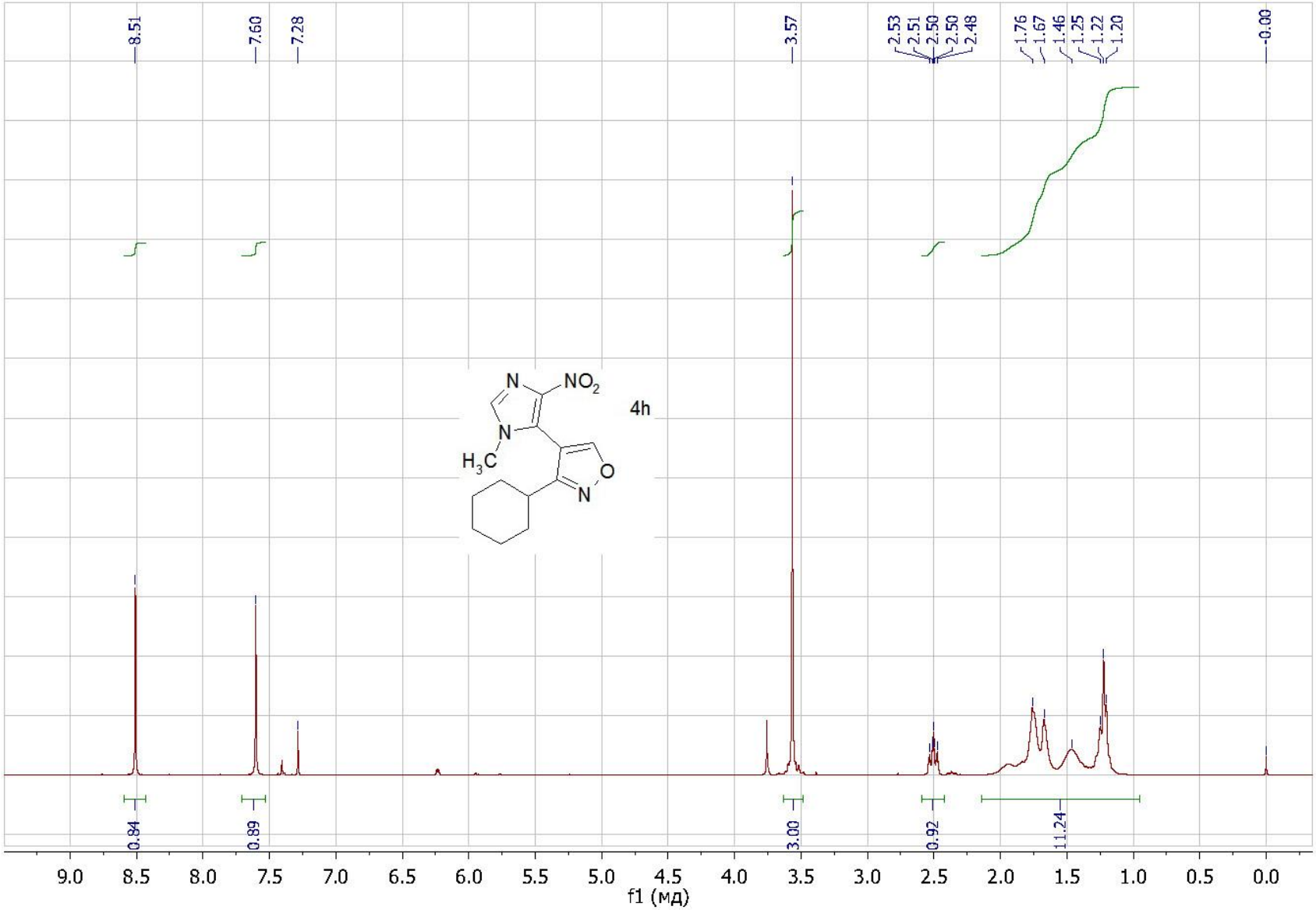
138.18
133.15
133.11
133.02
125.89
125.86
120.31
115.26
115.16
115.09
114.94
107.94
40.15
39.94
39.73
39.52
39.31
39.10
38.89
32.61
N
NO2
N
H3C
Cl
O
N
F
4g
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)


4g
{2.50,39.52}Dimethyl Sulfoxide-d6
f2 (мд)
f1 (мд)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7.28
3.57
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2.51
2.50
2.50
2.48
1.76
1.67
1.46
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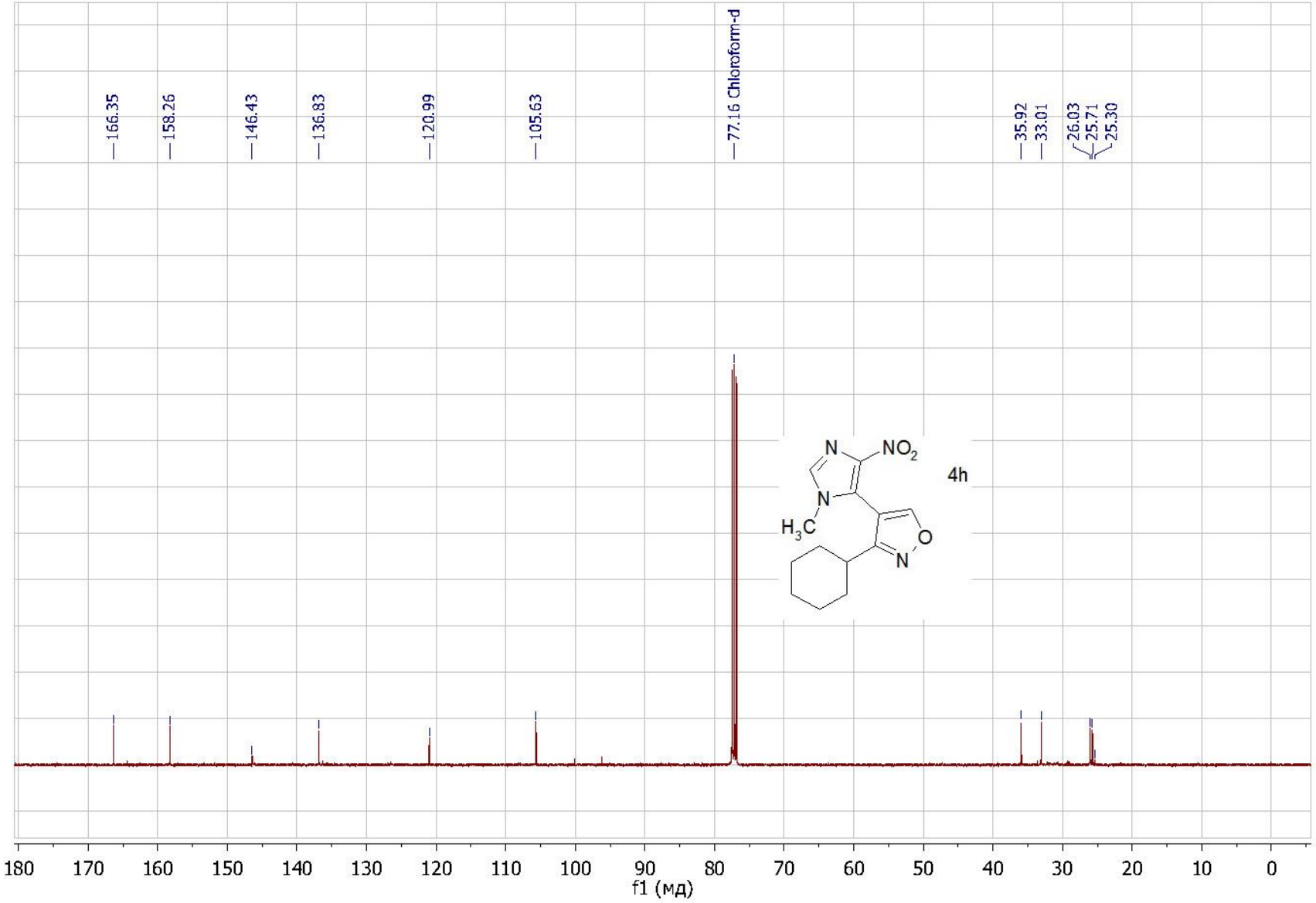
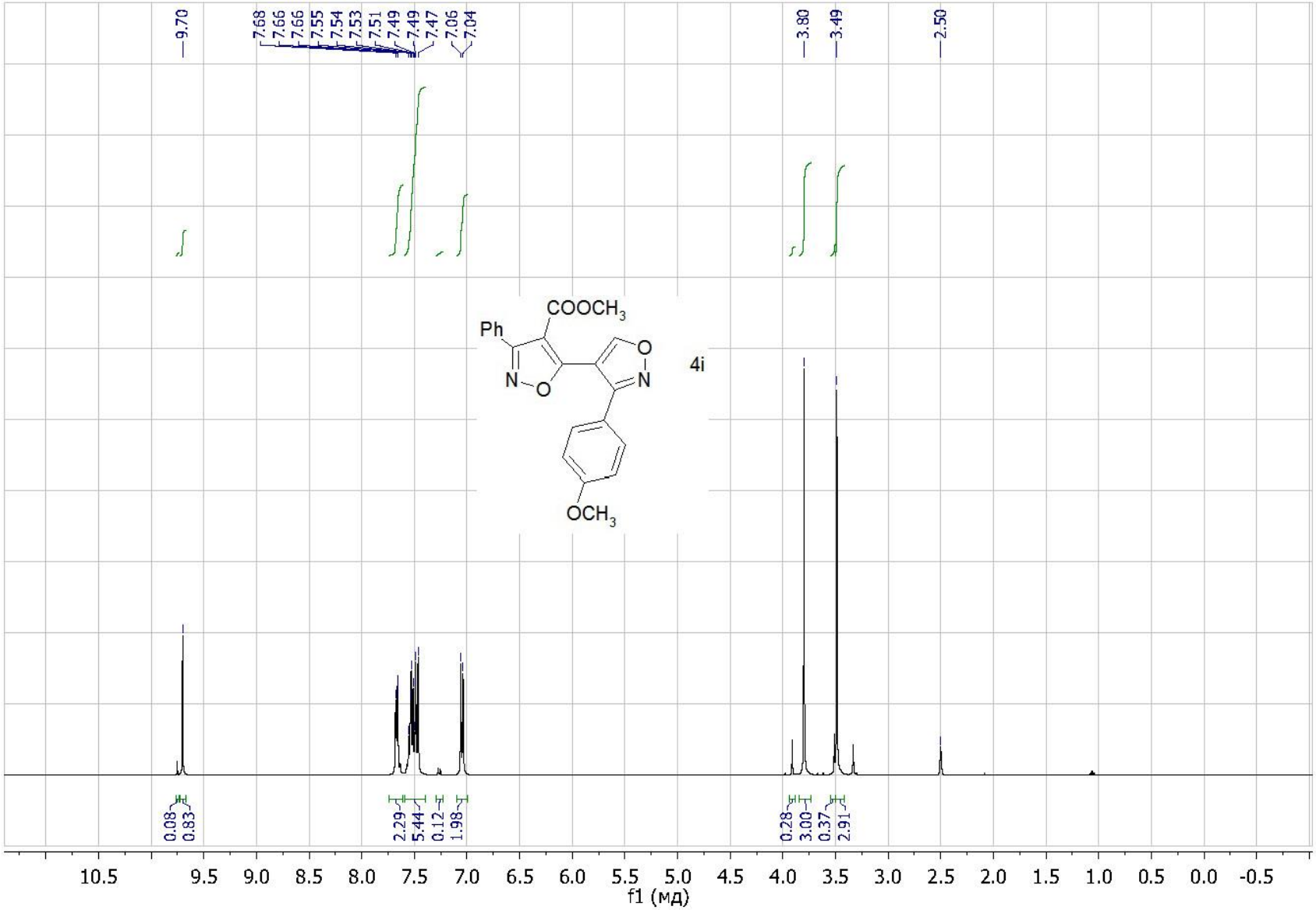
1.22
1.20
0.00
4h
0.84
0.89
3.00
0.92
11.24
f1 (мд)


166.35
158.26
146.43
136.83
120.99
105.63
77.16 Chloroform-d
35.92
33.01
26.03
25.71
25.30
N
NO2
N
H3C
O
N
4h
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)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7.49
7.47
7.06
7.04
3.80
3.49
2.50
COOCH3
Ph
O
N
N
O
OCH3
4i
0.08
0.83
2.29
5.44
0.12
1.98
0.28
3.00
0.37
2.91
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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2.0
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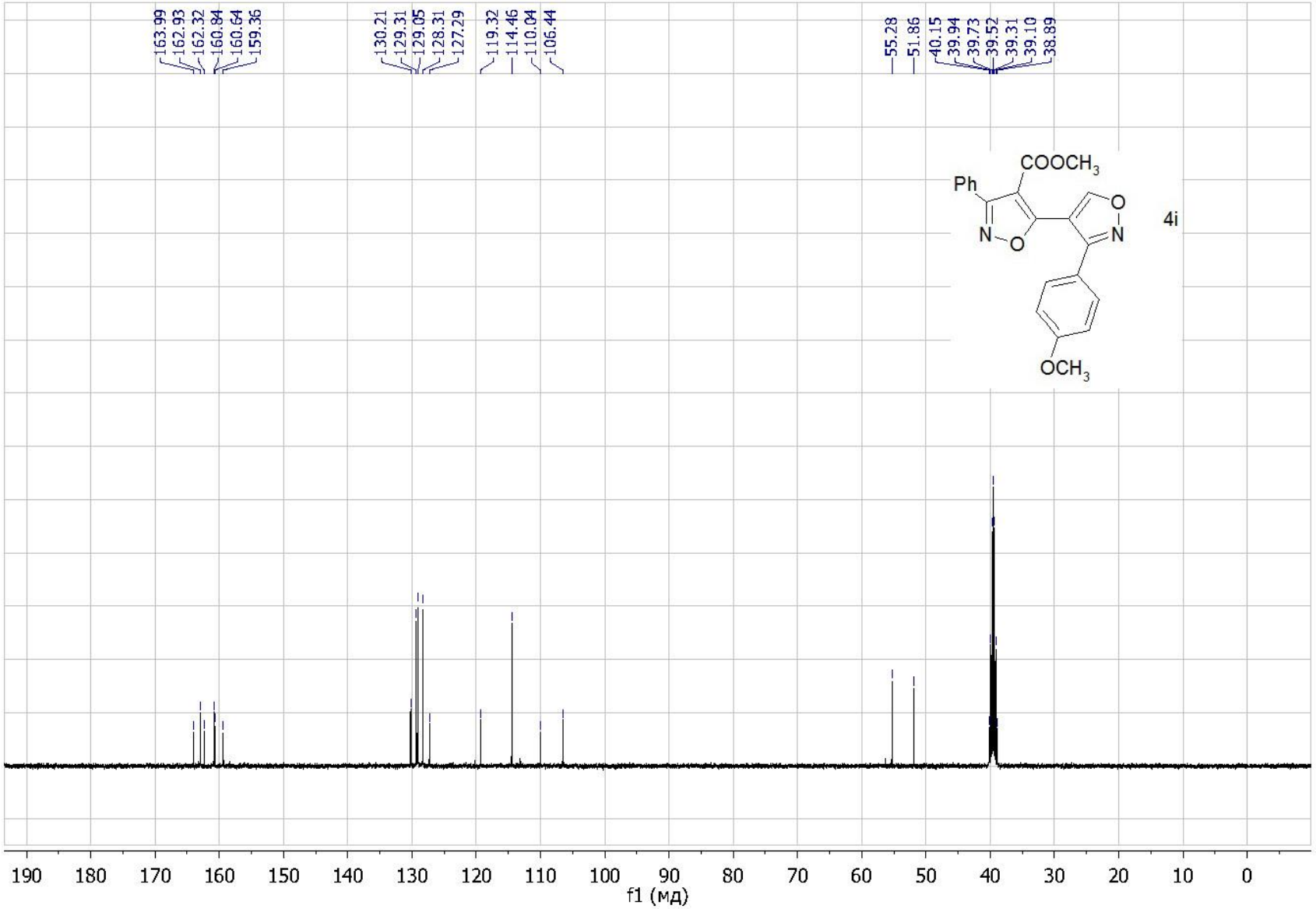
f1 (мд)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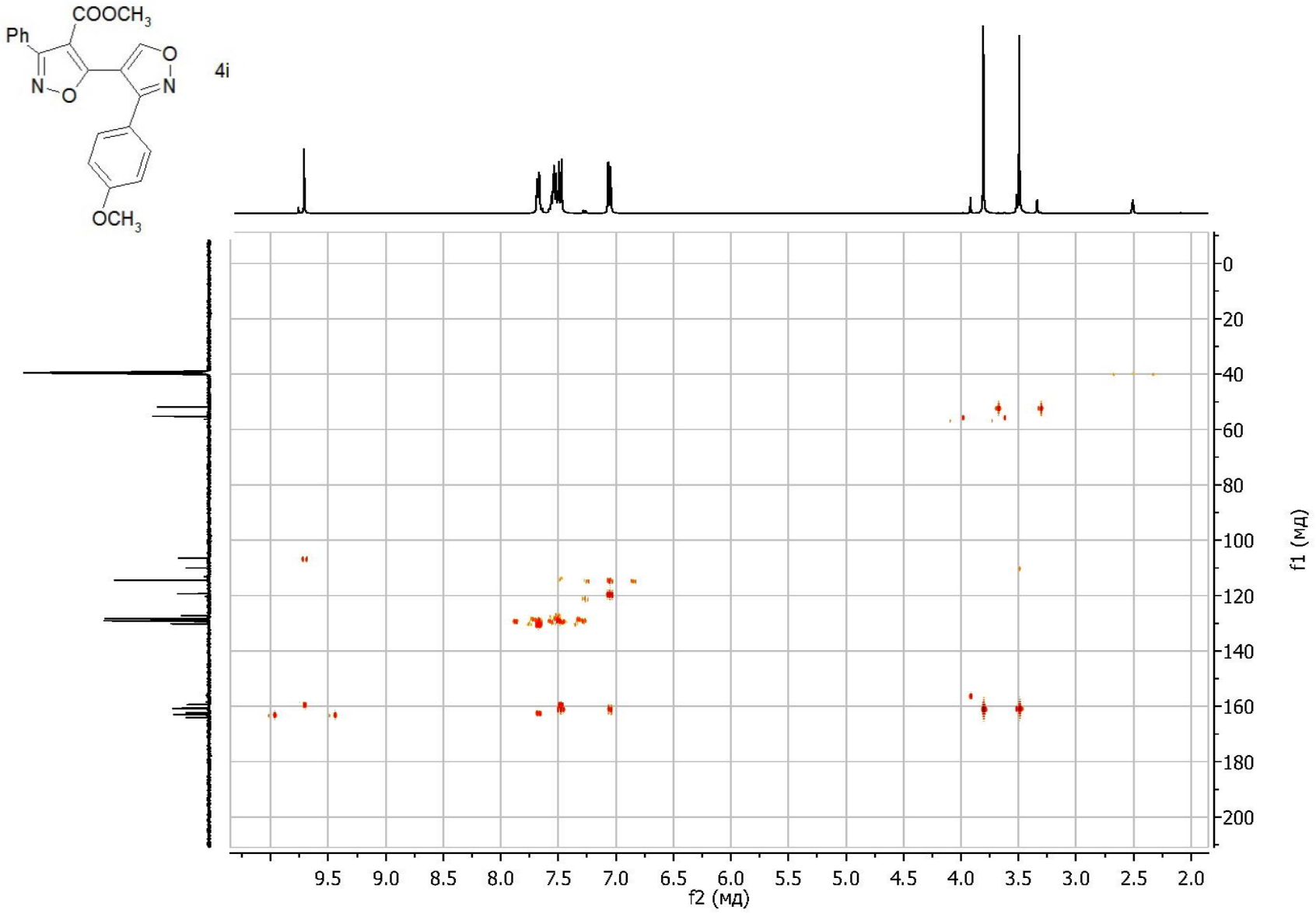
129.31
129.05
128.31
127.29
119.32
114.46
110.04
106.44
55.28
51.86
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOCH3
Ph
O
N
N
O
OCH3
4i
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)


COOCH3
Ph
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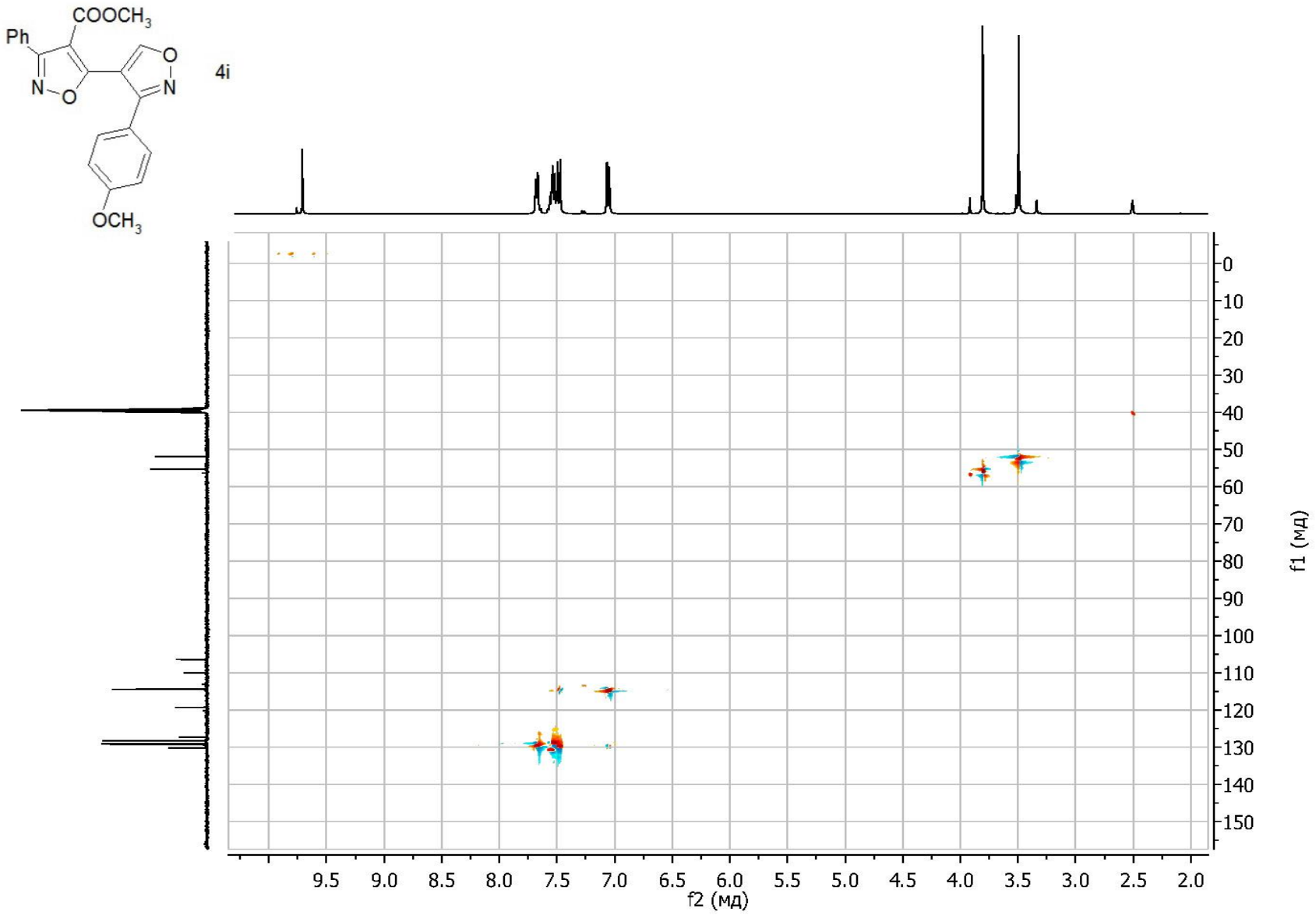
N
N
O
OCH3
4i
0
20
40
60
80
100
120
140
160
180
200
f1 (мд)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f2 (мд)


COOCH3
Ph
O
N
N
O
OCH3
4i
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
f1 (мд)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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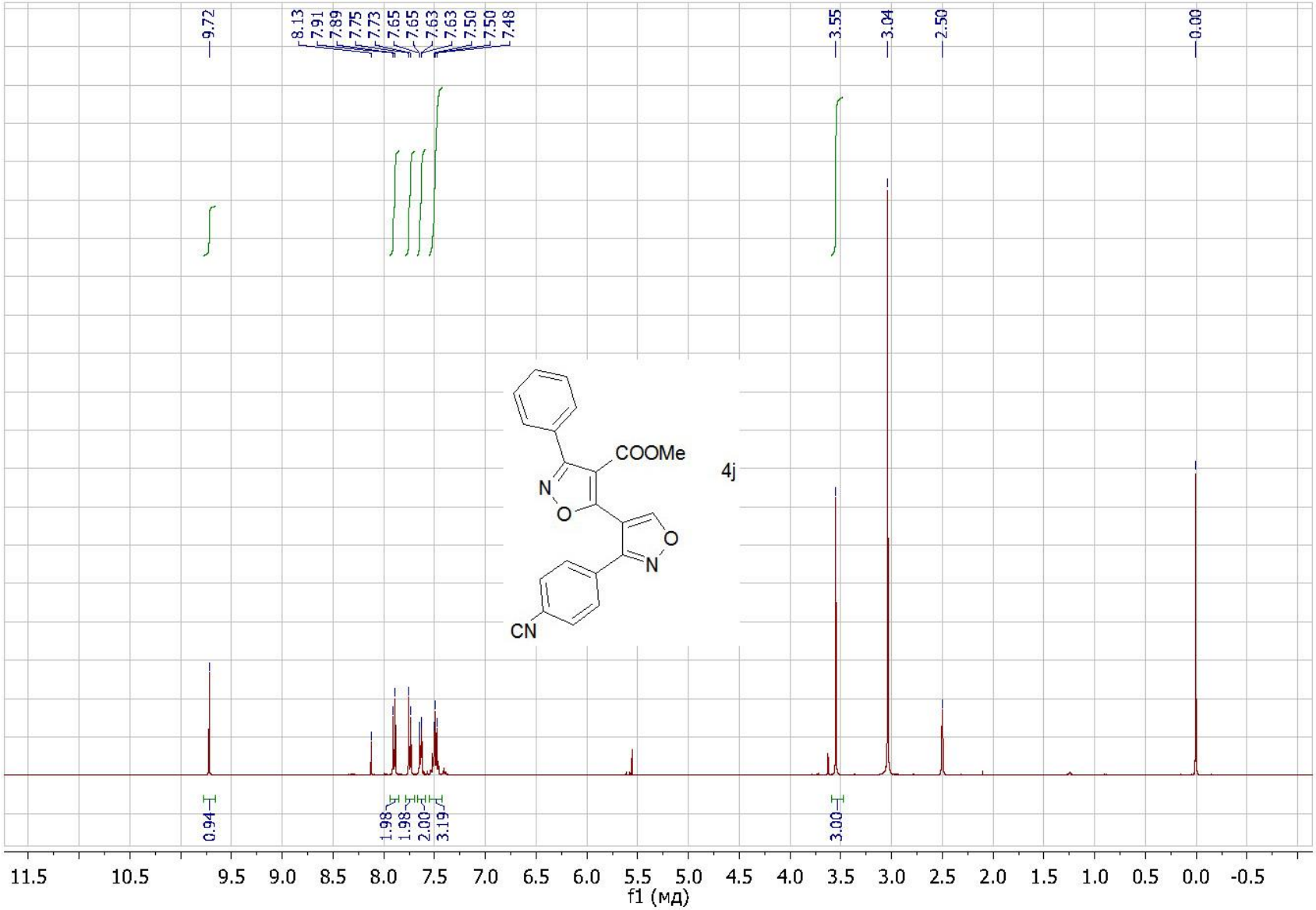
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f2 (мд)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7.63
7.63
7.50
7.50
7.48
3.55
3.04
2.50
0.00
COOMe
N
O
O
N
CN
4j
0.94
1.98
1.98
2.00
3.19
3.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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5.0
4.5
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1.5
1.0
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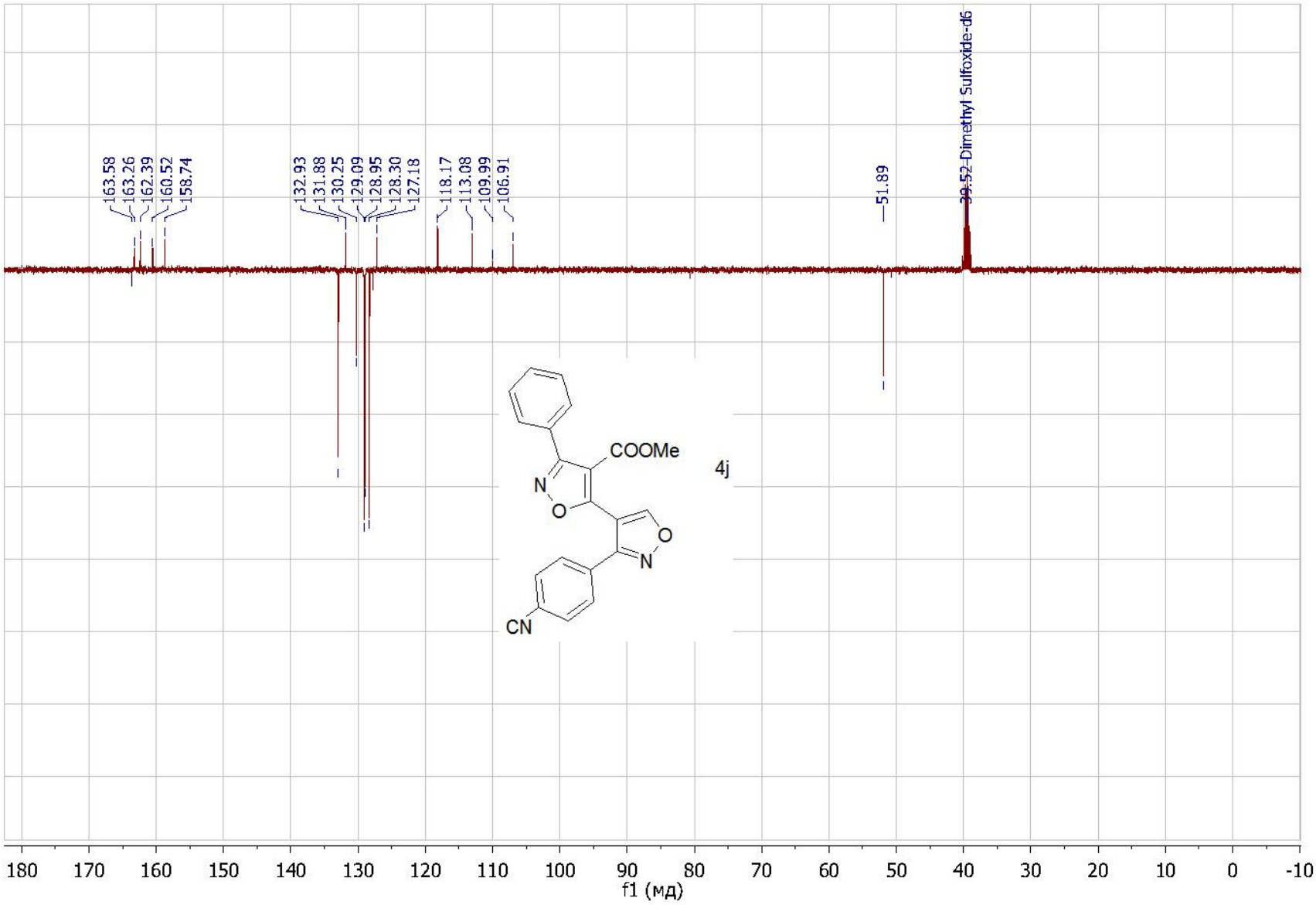
f1 (мд)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130.25
129.09
128.95
128.30
127.18
118.17
113.08
109.99
106.91
51.89
39.52-Dimethyl Sulfoxide-d6
COOMe
N
O
O
N
CN
4j
180
170
160
150
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130
120
110
100
90
80
70
60
50
40
30
20
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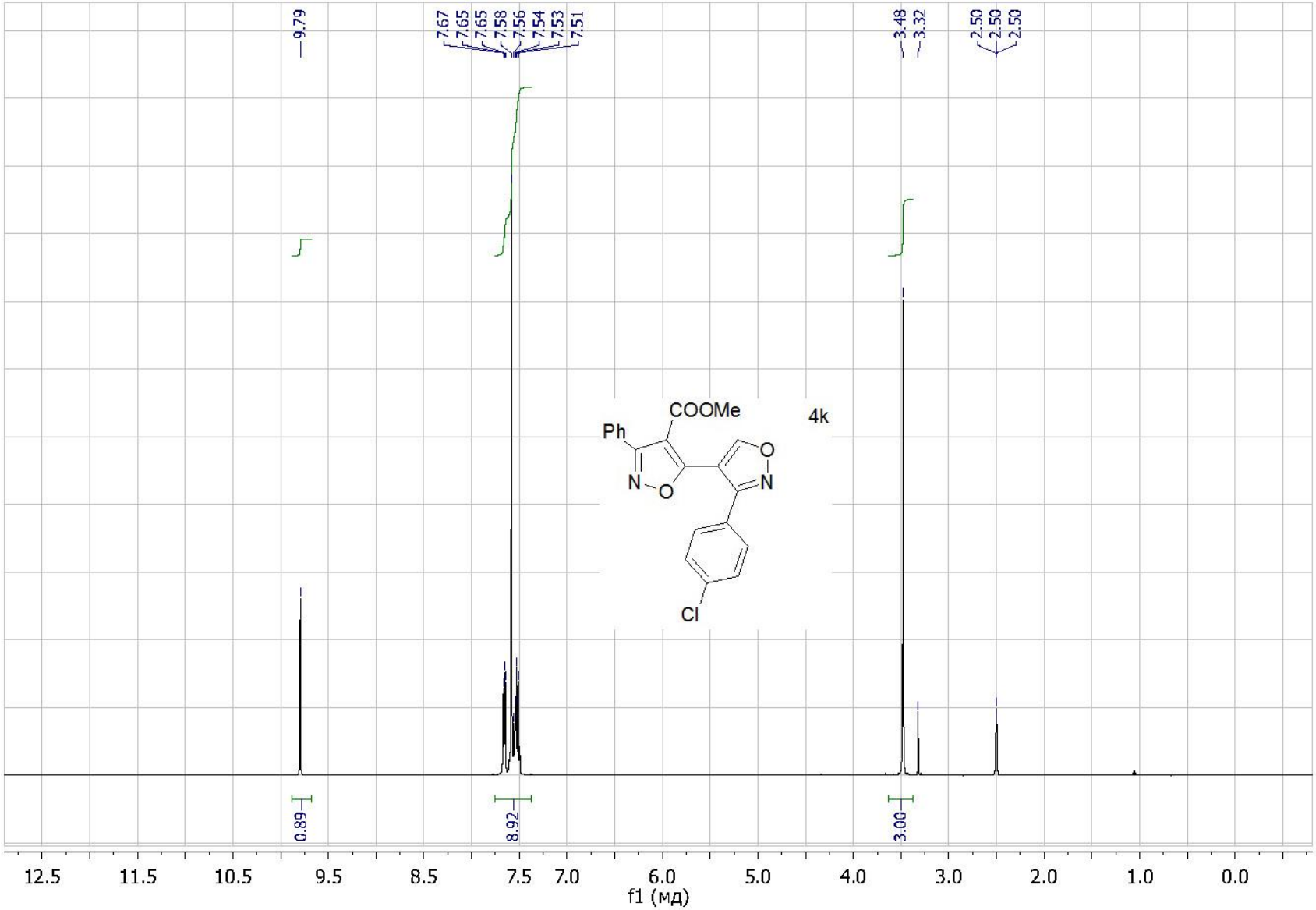
0
-10
f1 (мд)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7.65
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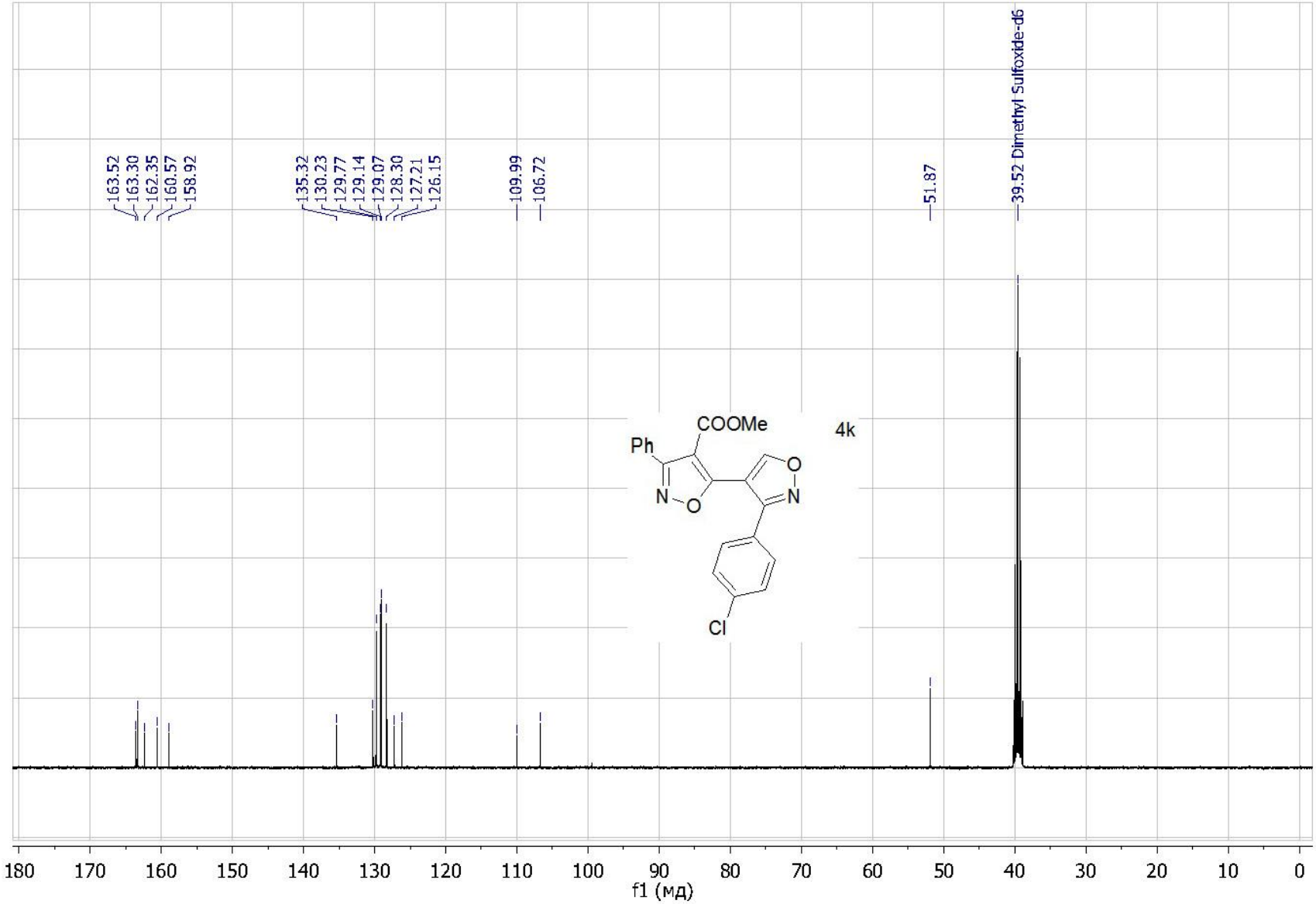
7.53
7.51
3.48
3.32
2.50
2.50
2.50
COOMe
Ph
N
O
O
N
Cl
4k
0.89
8.92
3.00
12.5
11.5
10.5
9.5
8.5
7.5
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (мд)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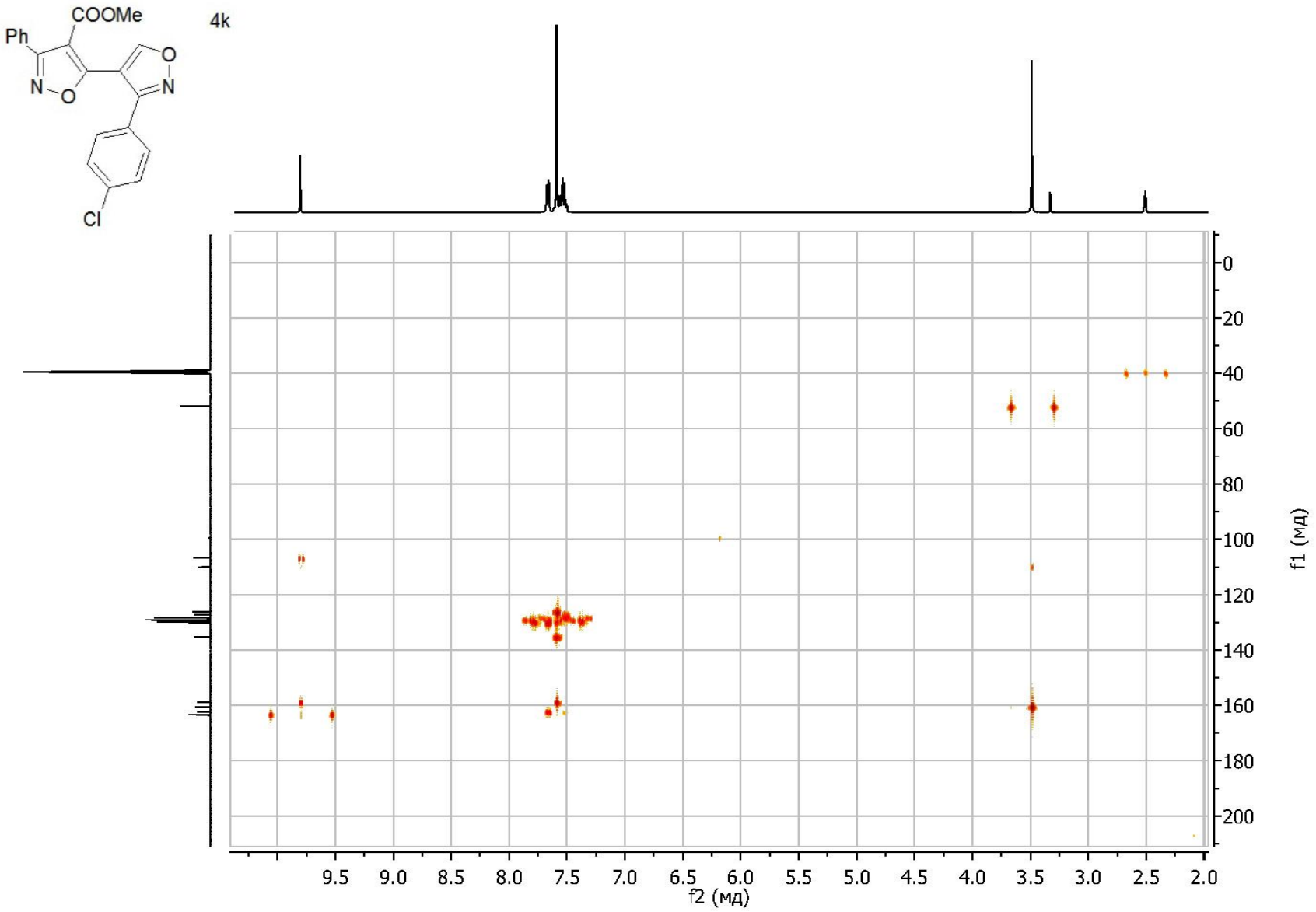
162.35
160.57
158.92
135.32
130.23
129.77
129.14
129.07
128.30
127.21
126.15
109.99
106.72
51.87
39.52 Dimethyl Sulfoxide-d6
COOMe
Ph
N
O
O
N
Cl
4k
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)


COOMe
Ph
N
O
O
N
Cl
4k
0
20
40
60
80
100
120
140
160
180
200
f1 (мд)
9.5
9.0
8.5
8.0
7.5
7.0
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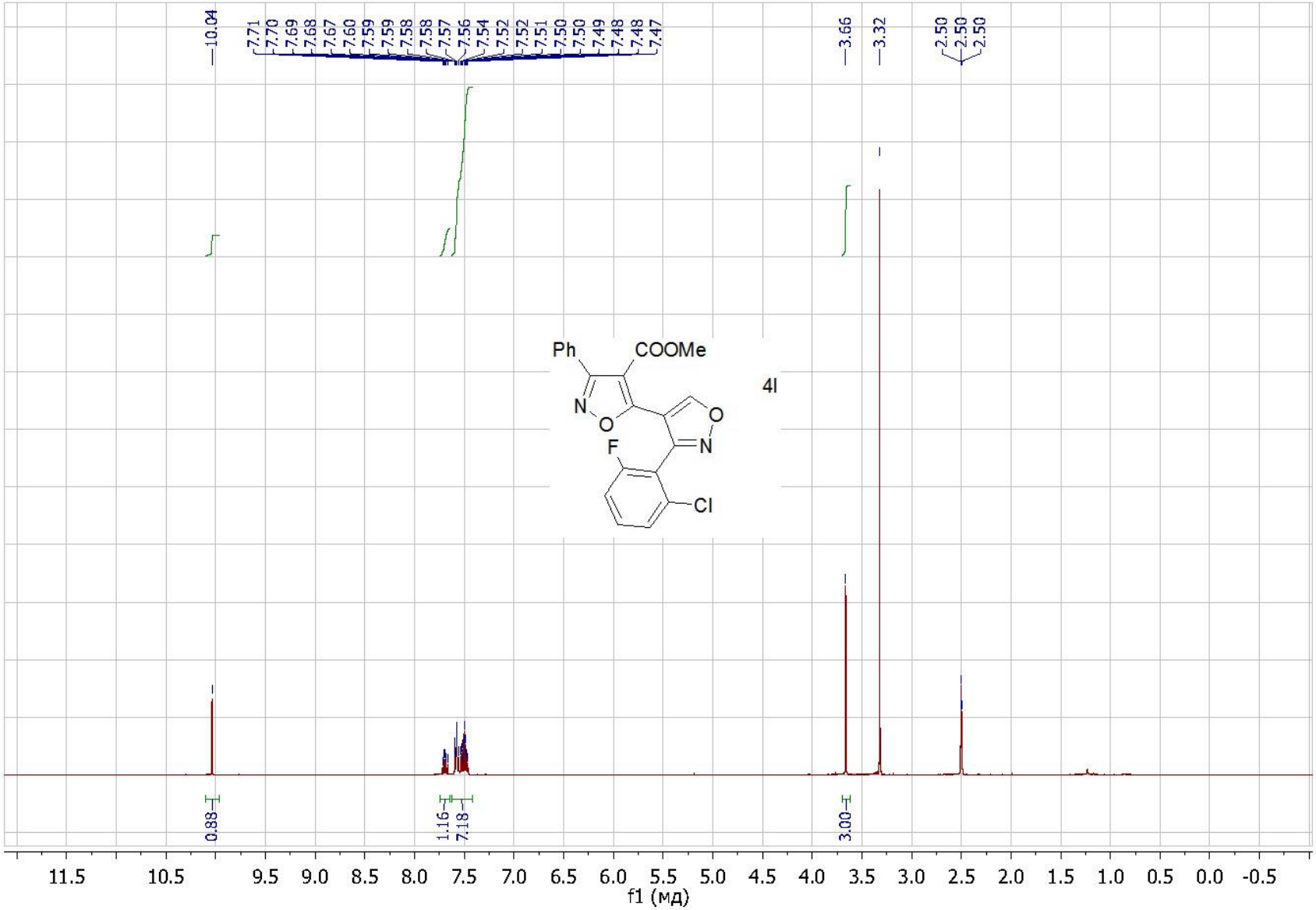
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f2 (мд)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7.58
7.57
7.56
7.54
7.52
7.52
7.51
7.50
7.50
7.49
7.48
7.48
7.47
3.66
3.32
2.50
2.50
2.50
Ph
COOMe
N
O
F
O
N
Cl
4l
0.88
1.16
7.18
3.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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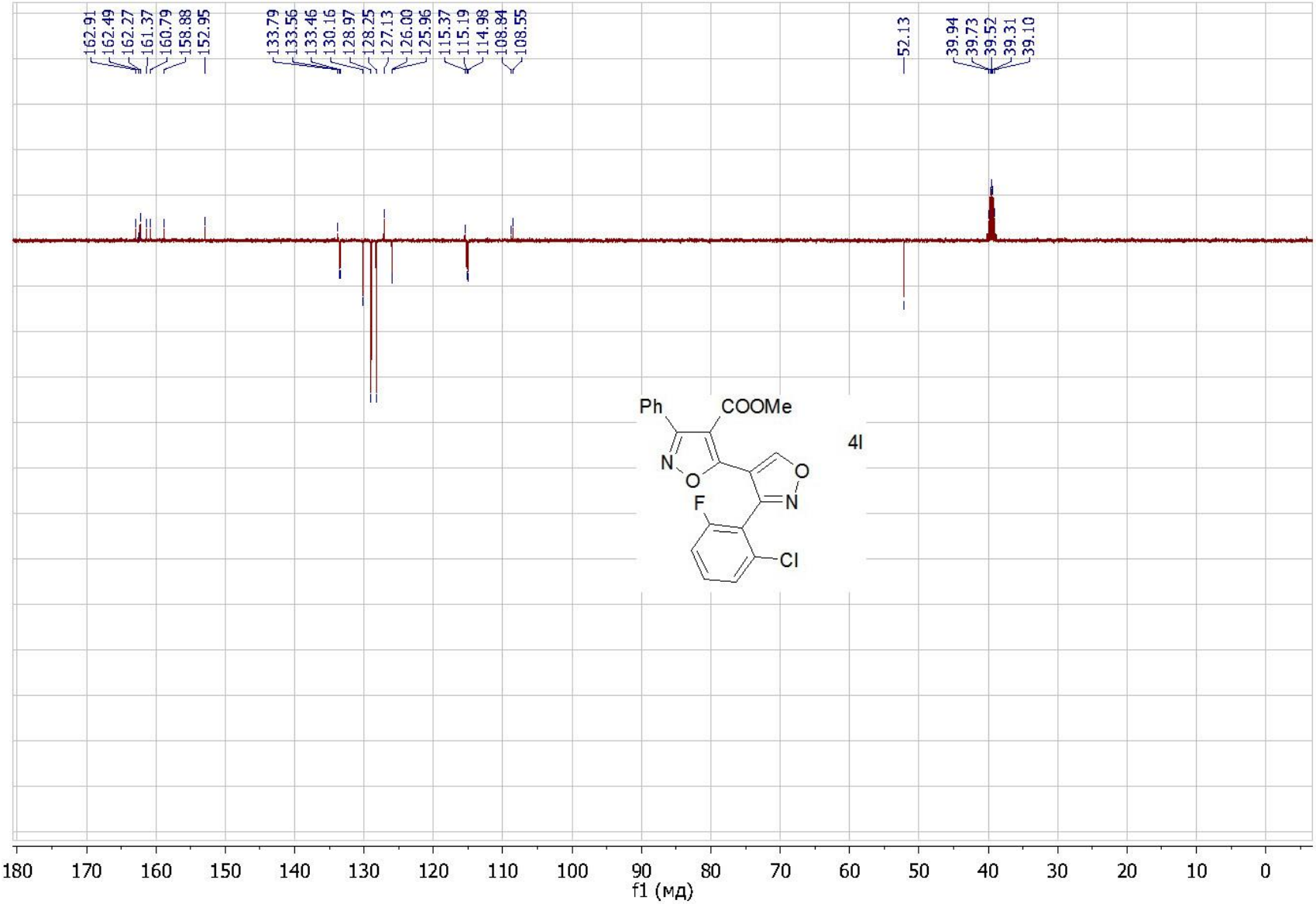
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (мд)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128.97
128.25
127.13
126.00
125.96
115.37
115.19
114.98
108.84
108.55
52.13
39.94
39.73
39.52
39.31
39.10
Ph
COOMe
N
O
O
N
F
Cl
4l
180
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160
150
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130
120
110
100
90
80
70
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50
40
30
20
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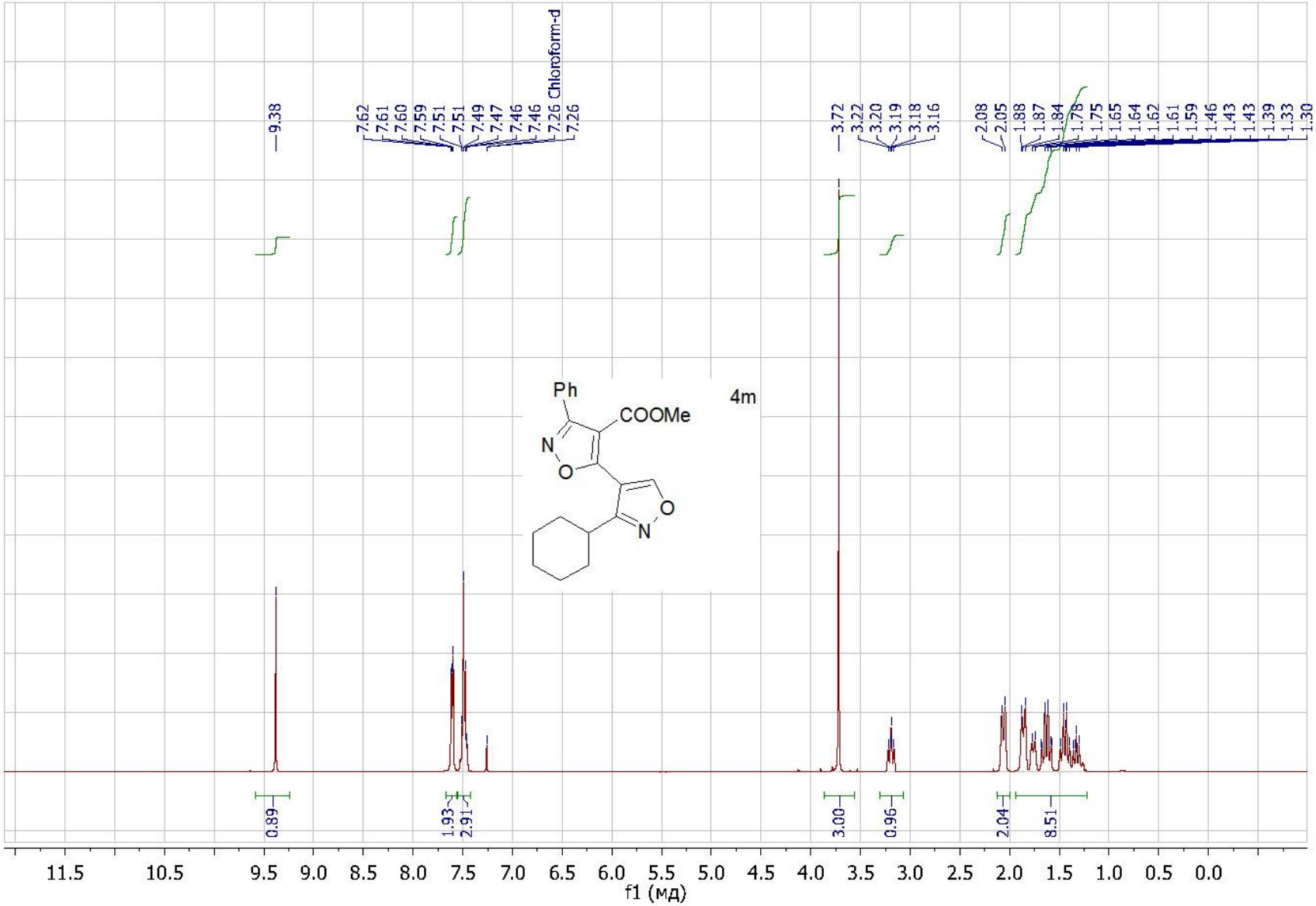
0
f1 (мд)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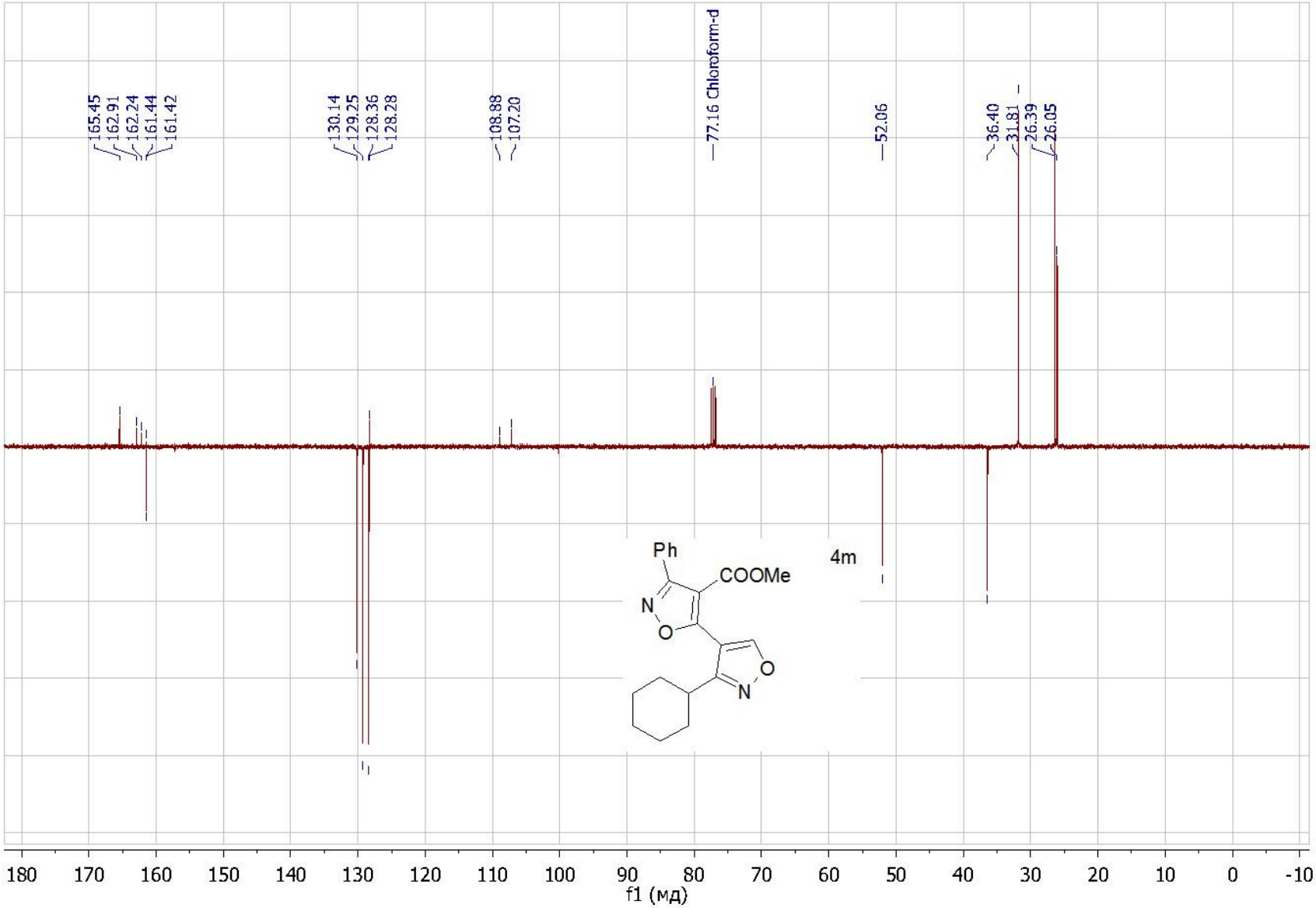
7.60
7.59
7.51
7.51
7.49
7.47
7.46
7.46
7.26 Chloroform-d
7.26
3.72
3.22
3.20
3.19
3.18
3.16
2.08
2.05
1.88
1.87
1.84
1.78
1.75
1.65
1.64
1.62
1.61
1.59
1.46
1.43
1.43
1.39
1.33
1.30
Ph
COOMe
N
O
O
N
4m
0.89
1.93
2.91
3.00
0.96
2.04
8.51
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (мд)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161.44
161.42
130.14
129.25
128.36
128.28
108.88
107.20
77.16 Chloroform-d
52.06
36.40
31.81
26.39
26.05
Ph
COOMe
N
O
O
N
4m
180
170
160
150
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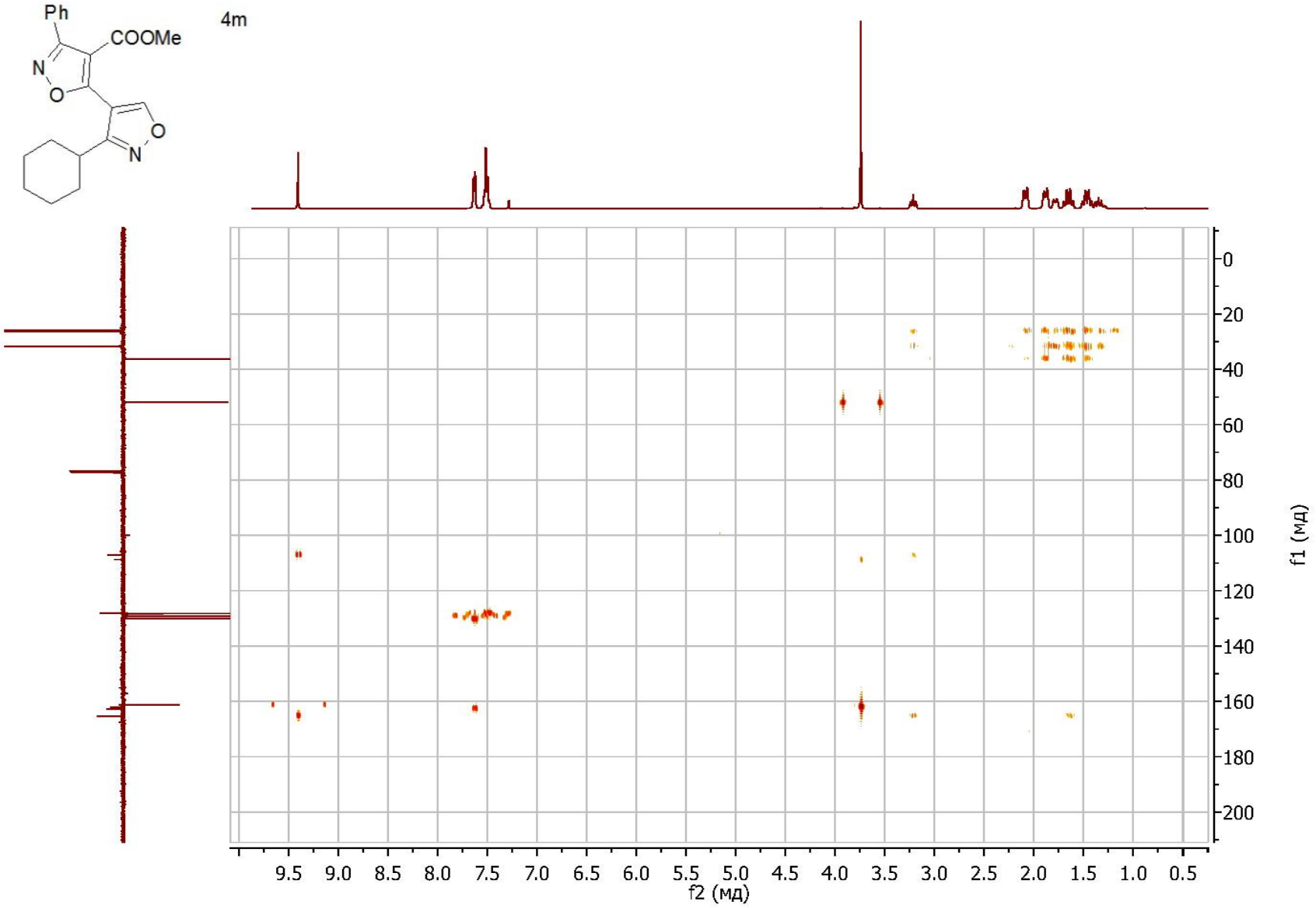
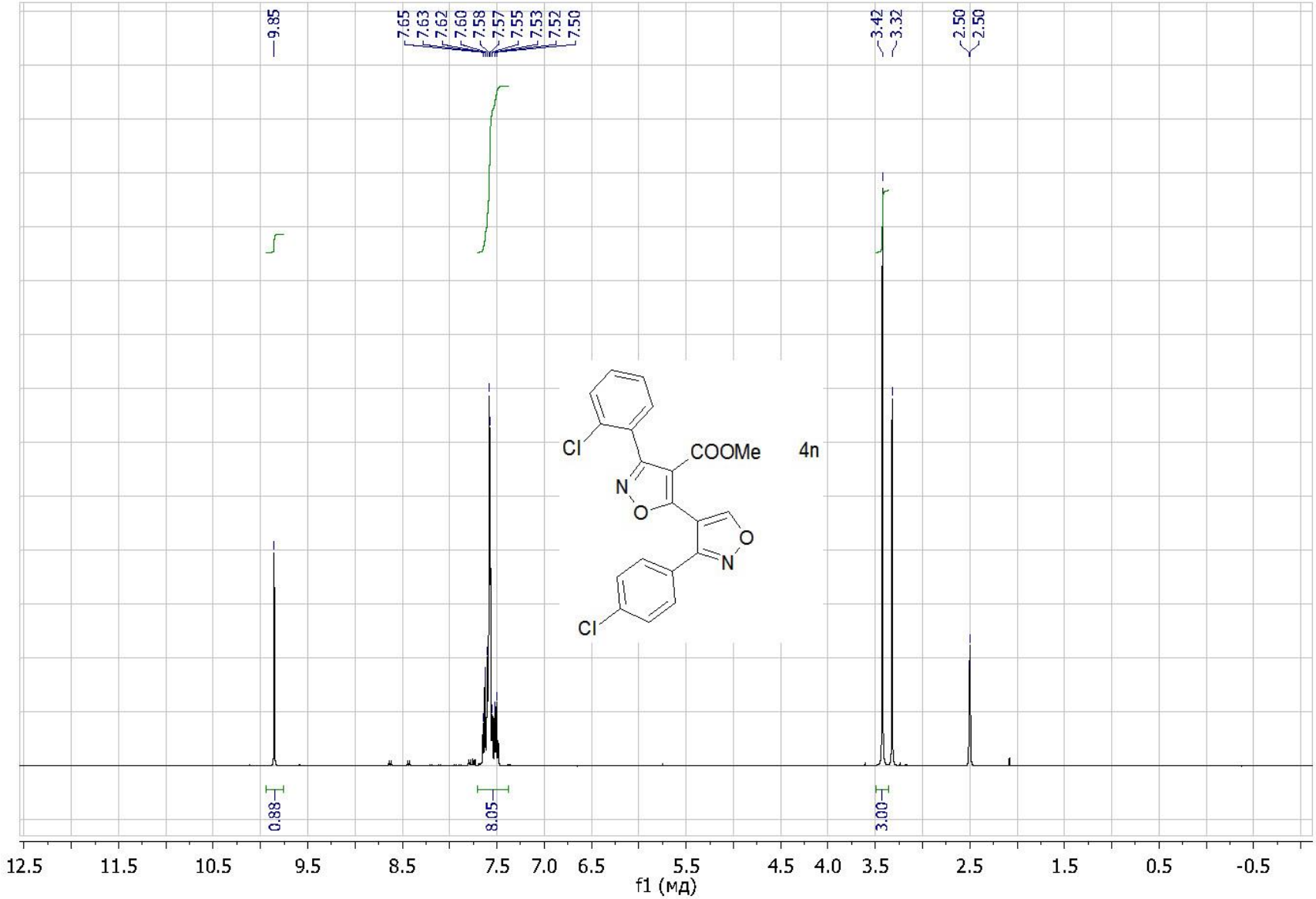
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)


Ph
COOMe
N
O
O
N
4m
0
20
40
60
80
100
120
140
160
180
200
f1 (мд)
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
f2 (мд)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7.62
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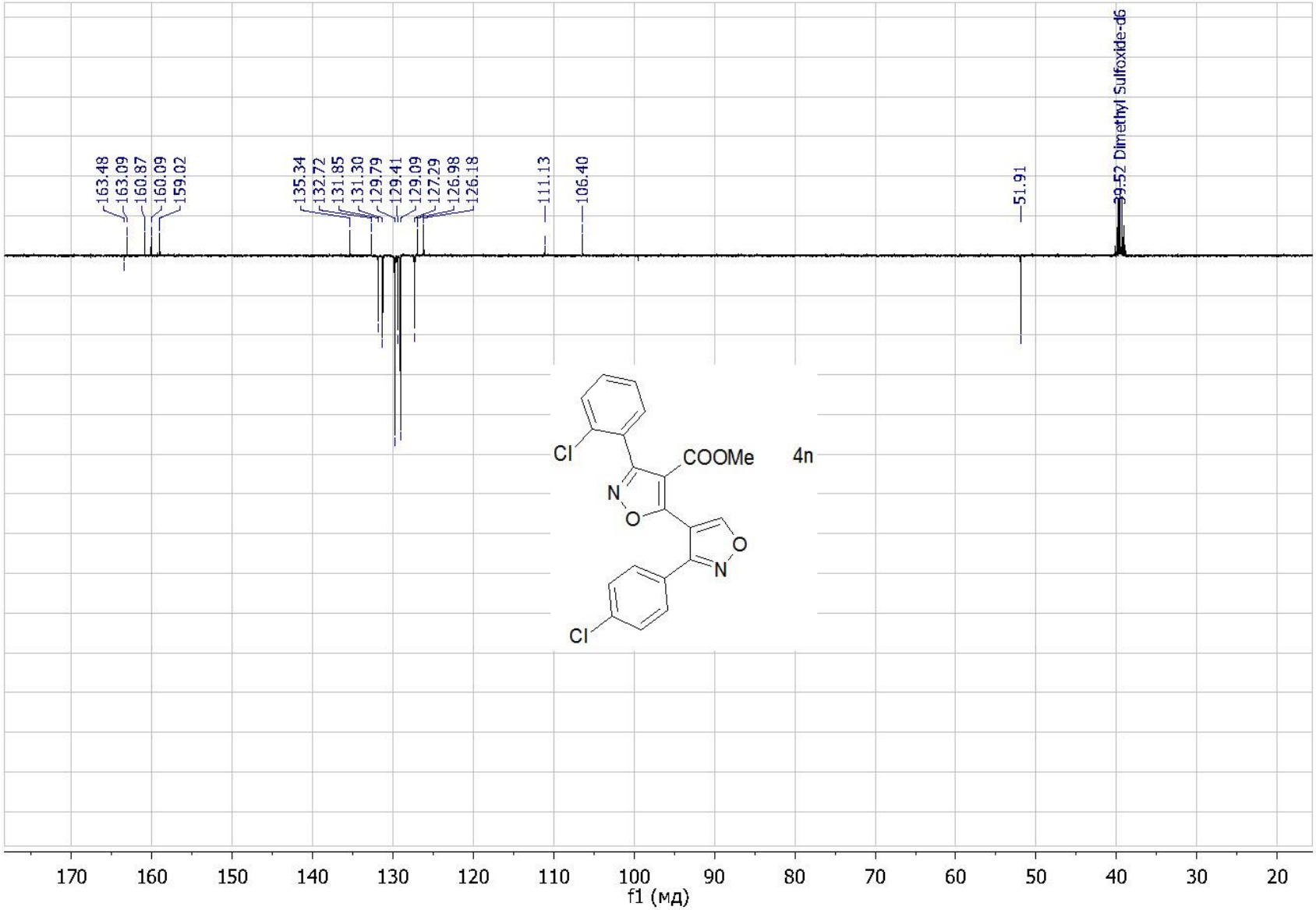
7.58
7.57
7.55
7.53
7.52
7.50
3.42
3.32
2.50
2.50
Cl
COOMe
4n
N
O
O
N
Cl
0.88
8.05
3.00
12.5
11.5
10.5
9.5
8.5
7.5
7.0
6.5
5.5
4.5
4.0
3.5
2.5
1.5
0.5
-0.5
f1 (мд)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160.09
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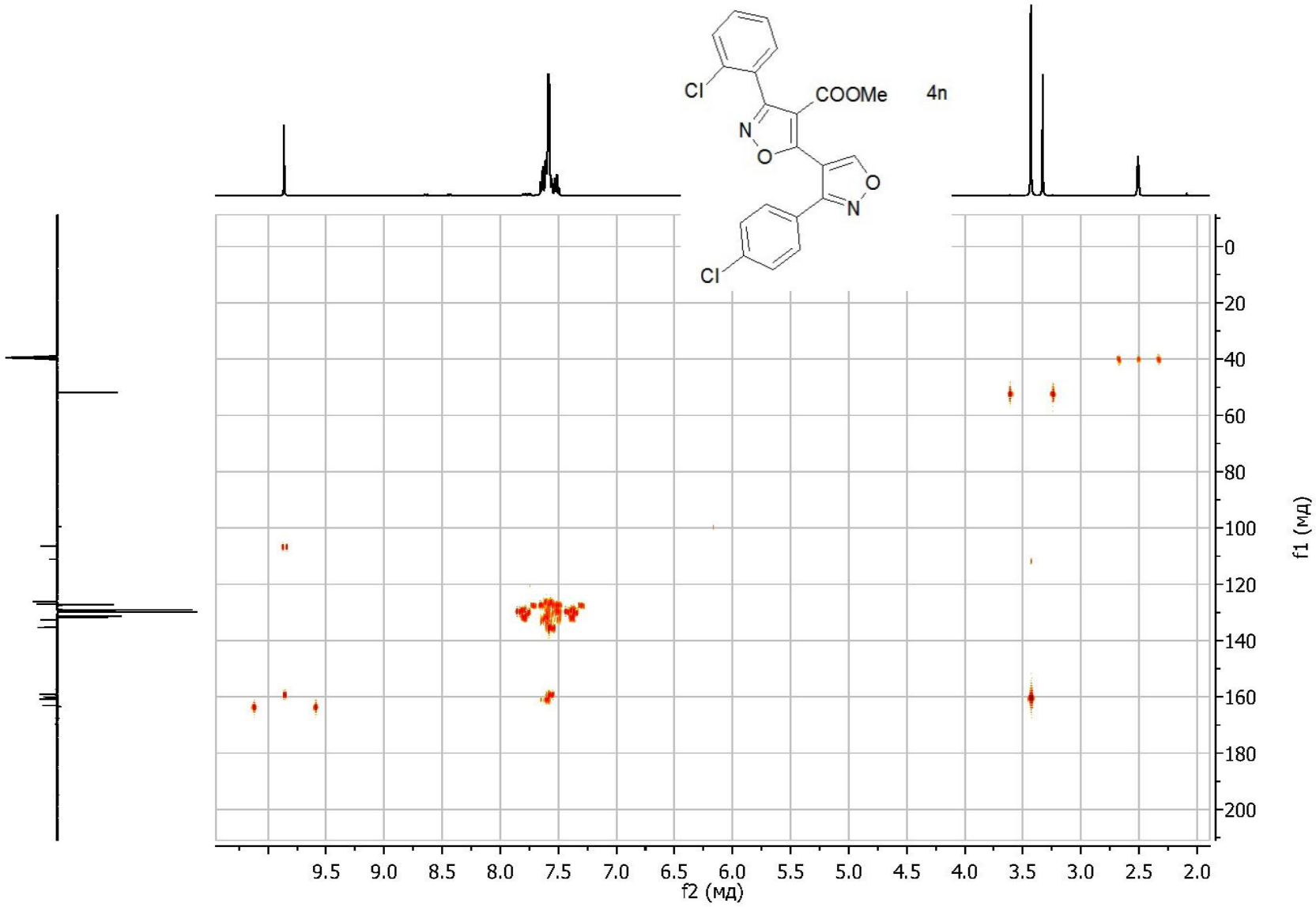
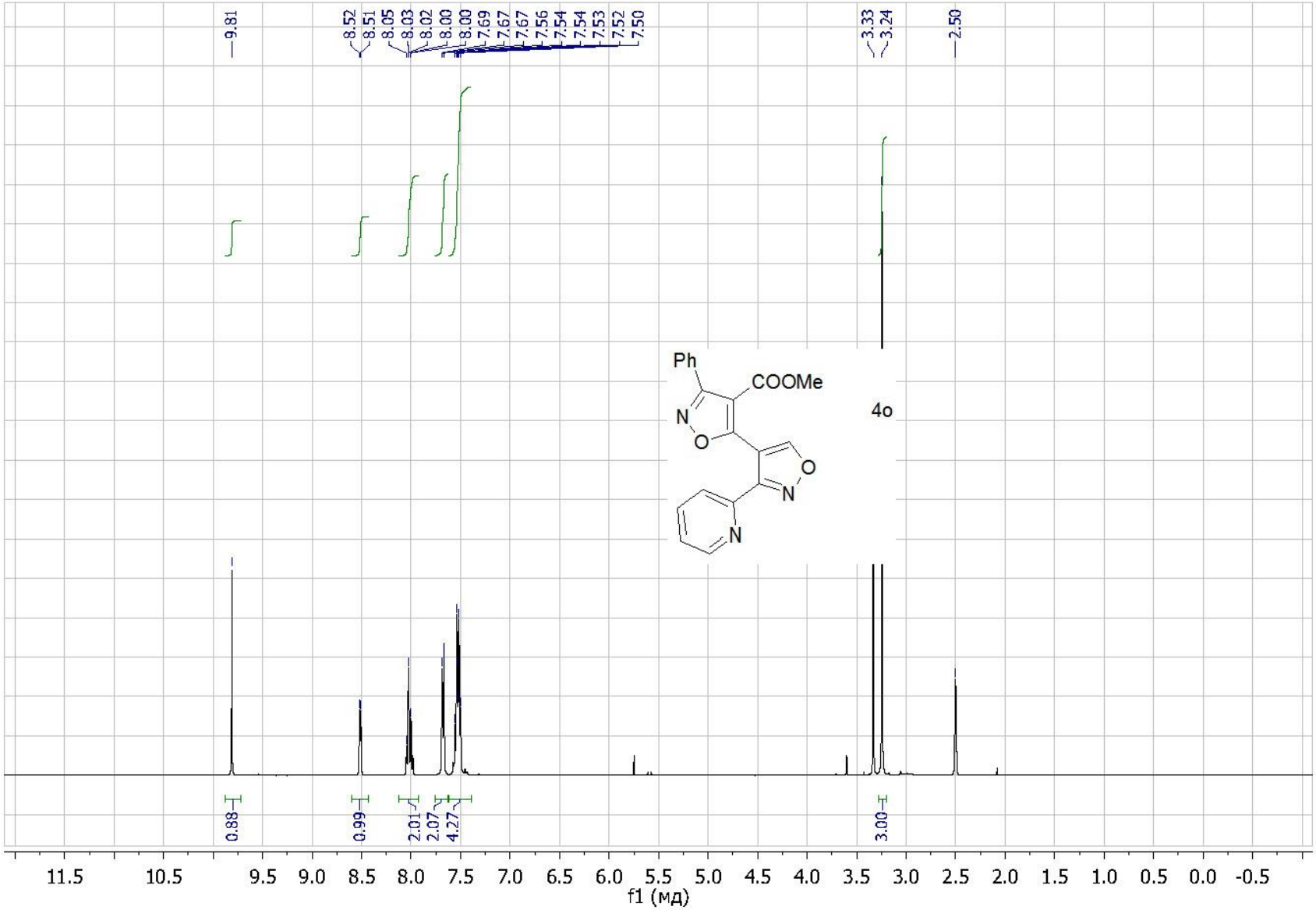
132.72
131.85
131.30
129.79
129.41
129.09
127.29
126.98
126.18
111.13
106.40
51.91
39.52 Dimethyl Sulfoxide-d6
Cl
COOMe
4n
N
O
O
N
Cl
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (мд)


Cl
COOMe
4n
N
O
O
N
Cl
0
20
40
60
80
100
120
140
160
180
200
f1 (мд)
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
f2 (мд)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8.00
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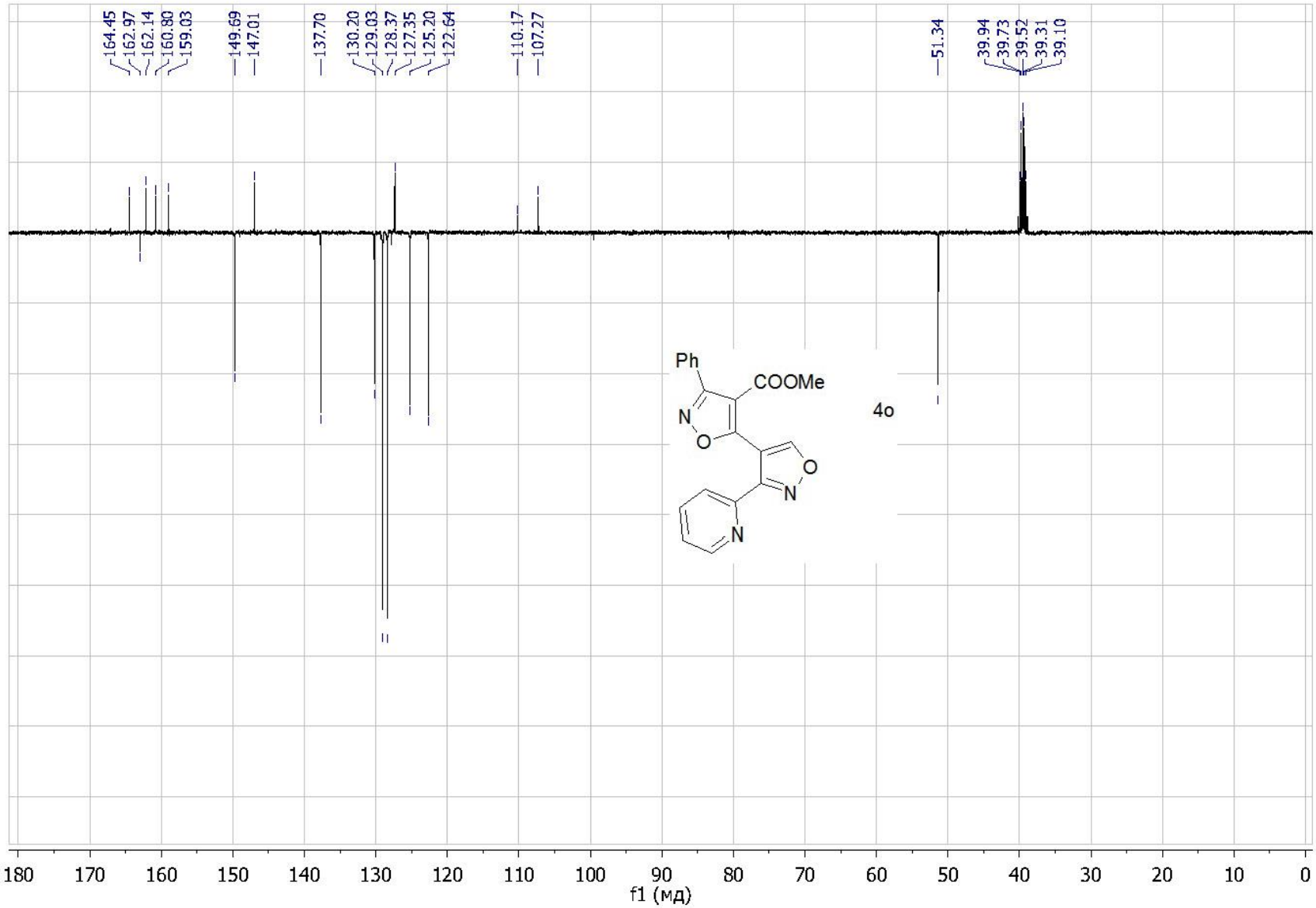
7.67
7.67
7.56
7.54
7.54
7.53
7.52
7.50
3.33
3.24
2.50
Ph
COOMe
N
O
O
N
N
4o
0.88
0.99
2.01
2.07
4.27
3.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (мд)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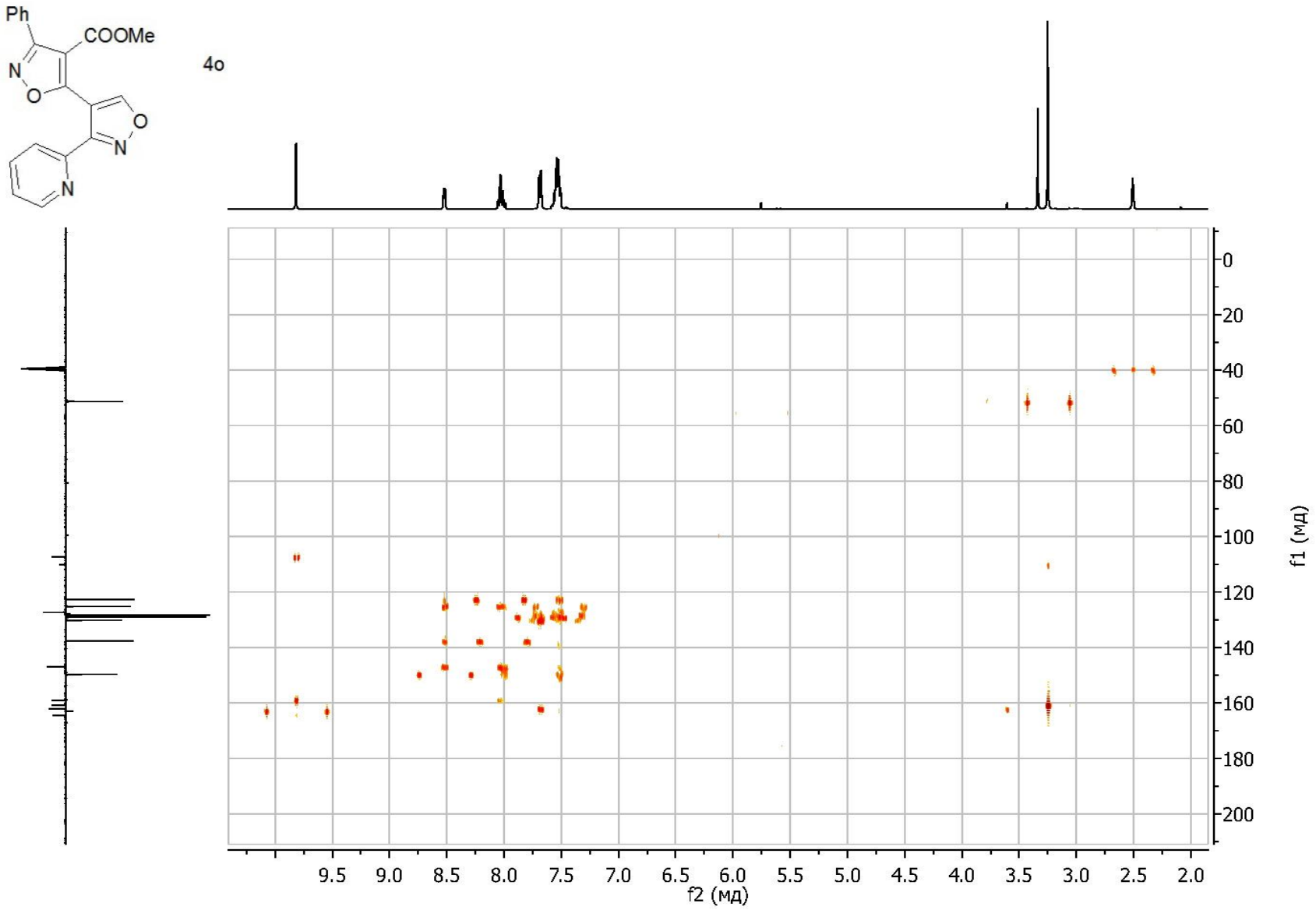
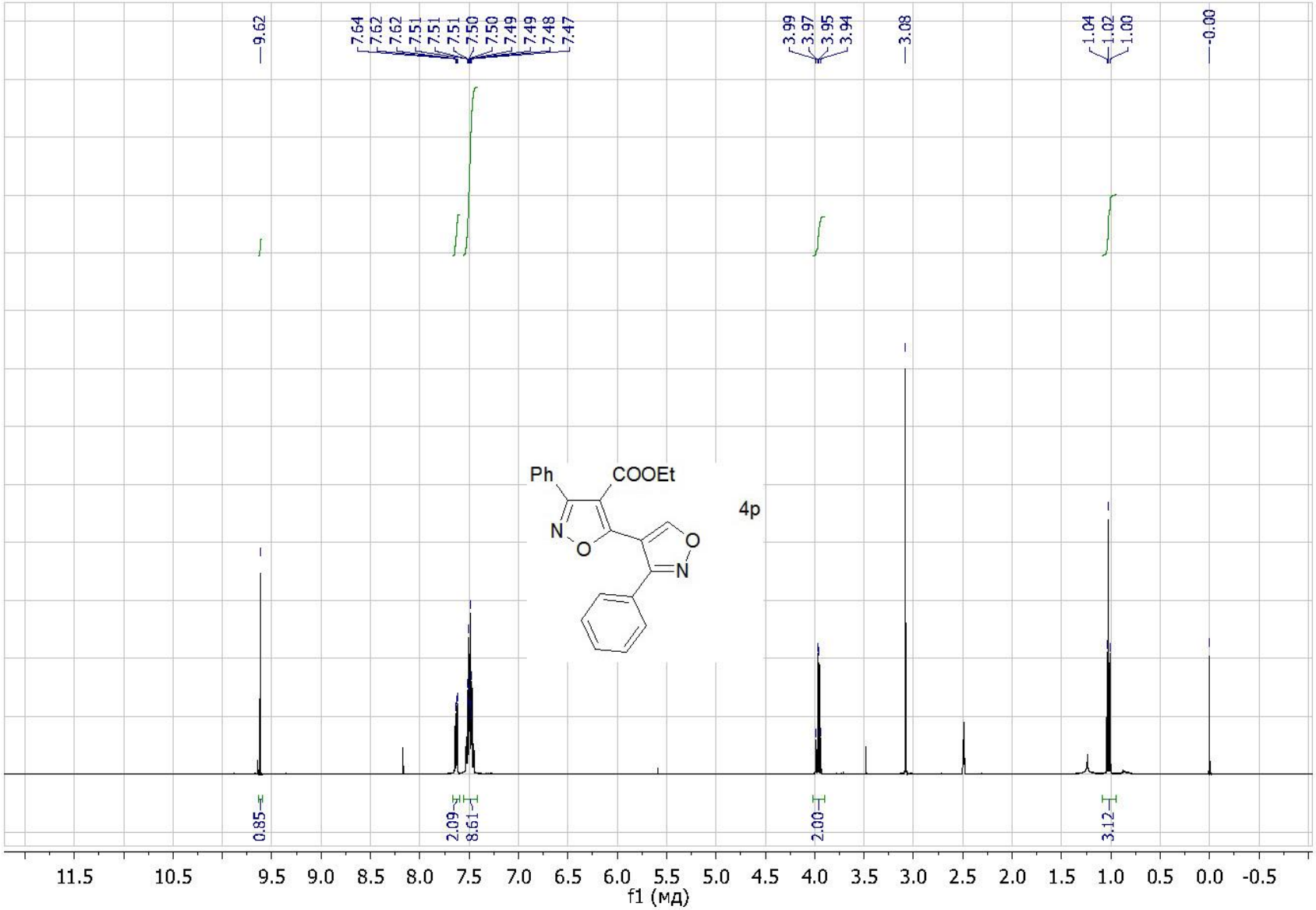
162.97
162.14
160.80
159.03
149.69
147.01
137.70
130.20
129.03
128.37
127.35
125.20
122.64
110.17
107.27
51.34
39.94
39.73
39.52
39.31
39.10
Ph
COOMe
N
O
O
N
N
4o
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)


Ph
COOMe
N
O
O
N
N
4o
0
20
40
60
80
100
120
140
160
180
200
f1 (мд)
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
f2 (мд)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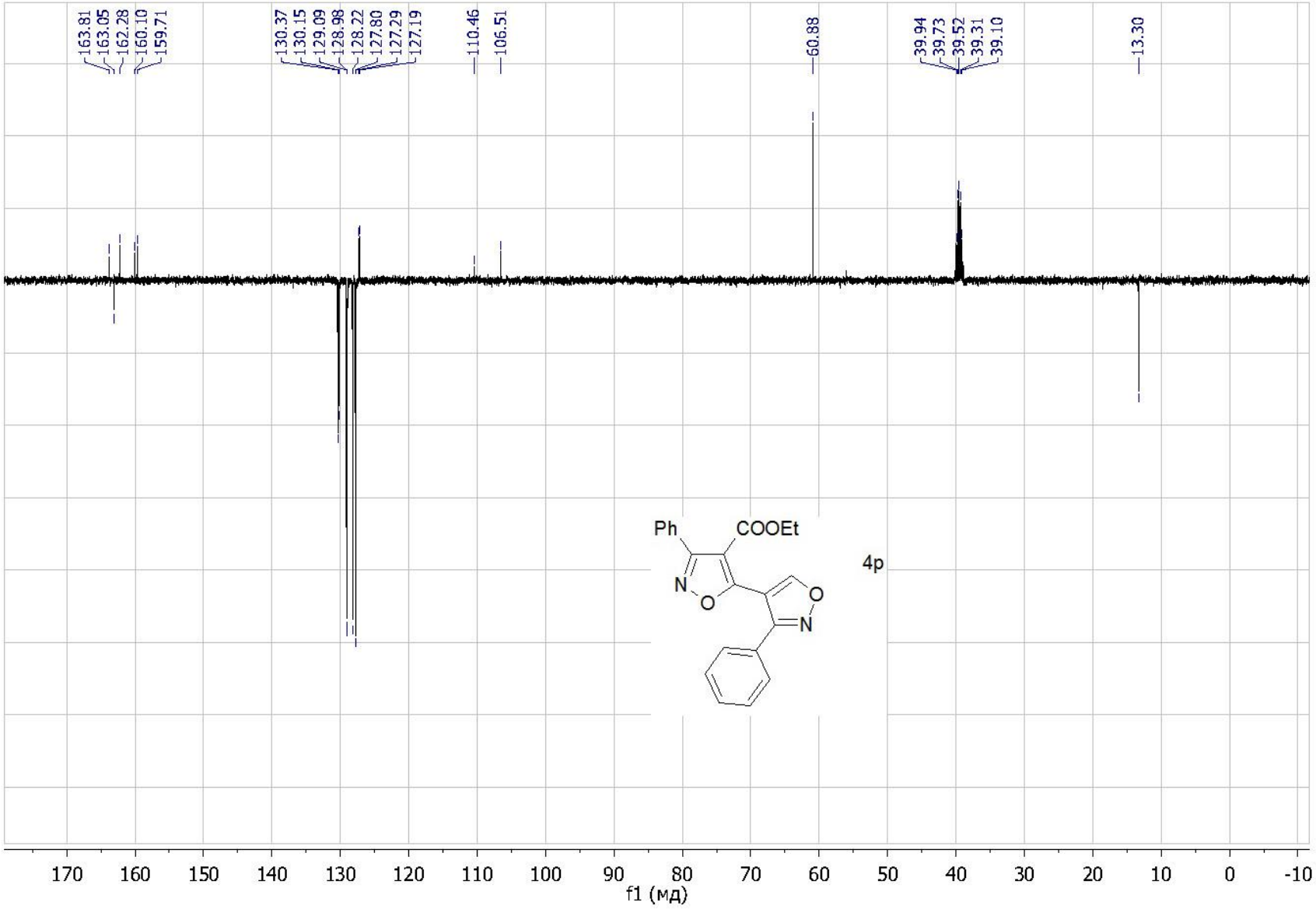
7.64
7.62
7.62
7.51
7.51
7.51
7.50
7.50
7.49
7.49
7.48
7.47
3.99
3.97
3.95
3.94
3.08
1.04
1.02
1.00
-0.00
Ph
COOEt
N
O
O
N
4p
0.85
2.09
8.61
2.00
3.12
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (мд)


163.81
163.05
162.28
160.10
159.71
130.37
130.15
129.09
128.98
128.22
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127.29
127.19
110.46
106.51
60.88
39.94
39.73
39.52
39.31
39.10
13.30
Ph
COOEt
N
O
O
N
4p
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)