Annulation of aliphatic nitro compounds with β-styryl sulfonium salts toward the synthesis of isoxazoline *N*-oxides

Pavel Yu. Ushakov, Stepan N. Chichulin, Alexey Yu. Sukhorukov and Andrey A. Tabolin

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1. General information.

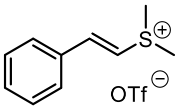
All reactions were carried out in oven-dried (150°C) glassware.

NMR spectra were recorded at 298K on Bruker AM300, Fourier 300HD and Avance NEO spectrometers with residual solvent peak as an internal standard. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). High resolution mass spectra were acquired on Bruker micrOTOF spectrometer using electrospray ionization (ESI).

Column chromatography was performed using Kieselgel 40–60 µm 60 A using ethyl acetate (EA) – petroleum ether (PE) mixture. Analytical thin layer chromatography was performed on silica gel plates with F 254 indicator. Visualization was accomplished with UV light and/or solution of anisaldehyde/H_2SO_4 in ethanol. Melting points were determined on a Koffler apparatus and are uncorrected.

Brine refers to a saturated aqueous solution of NaCl. Petroleum ether, ethyl acetate, MeCN, acetone and CH_2Cl_2 were distilled without drying agents. Et_3N and Tf_2O were distilled from CaH_2, DBU was distilled from CaH_2 under reduced pressure. Most of the chemicals were acquired from commercial sources and used as received.

2. Starting materials.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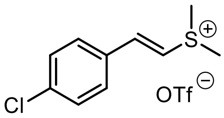
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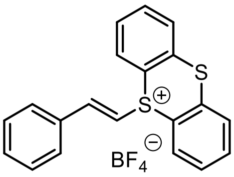
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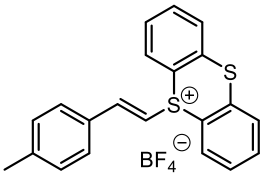
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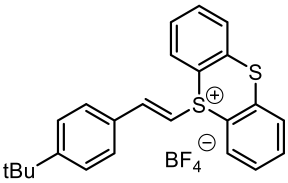
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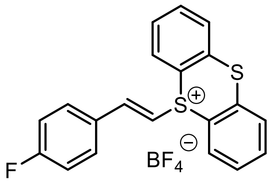
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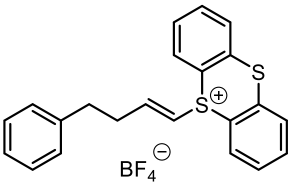
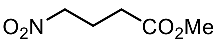

5e

Sulfonium salts **1a**[1] and **1b**[2] were prepared following literature methods.
Thianthrenium salts **5a**,[3] **5b**,[3] **5c**,[3] **5d**[3] and **5e**[4] were prepared following literature methods.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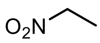
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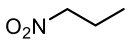
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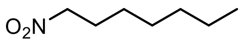
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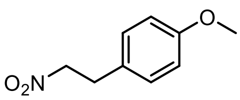
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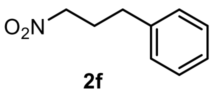
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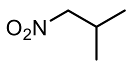
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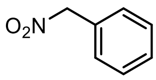
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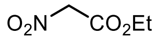
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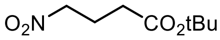
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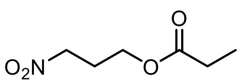
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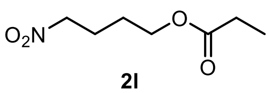
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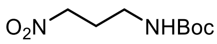
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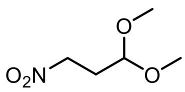

2n

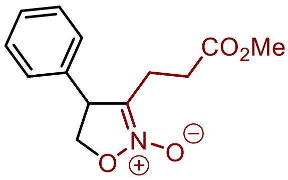
Nitro compounds **2b**, **2c**, **2h** and **2i** were received from commercial sources.
Nitro compounds **2a**,[5] **2d**,[6] **2e**,[7] **2f**,[6] **2g**,[8] **2j**,[9] **2k**,[6] **2l**,[10] **2m**[11] and **2n** [12] were prepared following literature methods.

3. Isoxazoline N-oxides 3.

General procedure 1 (GP-1) for the synthesis of isoxazoline N-oxides 3:

To the suspension of salt **1** or **5** (1.3 equiv., 0.65 mmol) in 1 mL of MeCN nitro compound **2** (1 equiv., 0,5 mmol) and DBU (1.5 equiv., 0.75 mmol, 114 mg, 112 µL) were added. The solution was stirred at room temperature for 1 h. After reaction mixture was co-evaporated with silica gel and purified by column chromatography with PE/EA (10:1 to 2:1) mixture as an eluent to give pure isoxazoline *N*-oxide **3**.

3-(3-Methoxy-3-oxopropyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3a)



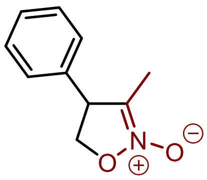
Isoxazoline *N*-oxide **3a** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and methyl 4-nitrobutyrate **2a** (74 mg, 0.5 mmol), yield – 112 mg (90%). This compound was also synthesized by **GP-1** from styryl thianthrenium salt **5a** (304 mg, 0.65 mmol) and methyl 4-nitrobutyrate **2a** (74 mg, 0.5 mmol), yield – 71% (88 mg). Colorless oil. R_f = 0.75 (PE/EA 1:1, anisaldehyde/H_2SO_4).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.24 (m, 5H, H_{Ph}), 4.77 (dd, *J* = 9.7, 7.6 Hz, 1H, $CH_{2a}O$), 4.55 (dd, *J* = 9.7, 6.2 Hz, 1H, CHPh), 4.33 (dd, *J* = 7.6, 6.2 Hz, 1H, $CH_{2b}O$), 3.65 (s, 3H, CH_3O), 2.79 – 2.55 (m, 2H, $CH_2CH_2CO_2Me$), 2.48 – 2.34 (m, 2H, $CH_2CH_2CO_2Me$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, DEPT135, HSQC) δ 172.6 (1C, C=O), 138.0 (1C, C_{Ph}), 129.5 (2C, CH_{Ph}), 128.6 (1C, CH_{Ph}), 127.7 (2C, CH_{Ph}), 117.2 (1C, C=NO), 71.3 (1C, CH_2O), 51.9 (2C, CHPh and OCH_3), 28.6 and 20.6 (2C, $CH_2CH_2CO_2Me$) ppm.

HRMS (ESI): m/z calcd for $C_{13}H_{16}NO_4^+$ $[M+H]^+$: 250.1074, found 250.1078.

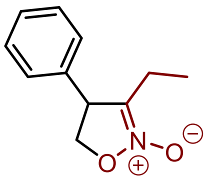
3-Methyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3b)



Isoxazoline *N*-oxide **3b** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and nitroethane **2b** (38 mg, 0.5 mmol), yield – 74 mg (84%). Colorless oil. R_f = 0.50 (PE/EA 1:1, anisaldehyde/H_2SO_4).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.23 (m, 5H, H_{Ph}), 4.78 (dd, *J* = 9.5, 7.5 Hz, 1H, $CH_{2a}O$), 4.43 (ddq, *J* = 9.5, 6.8, 1.6 Hz, 1H, CHPh), 4.35 – 4.28 (m, 1H, $CH_{2b}O$), 1.88 (d, *J* = 1.6 Hz, 3H, CH_3) ppm. NMR spectra were in agreement with literature data.[13]

3-Ethyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3c)



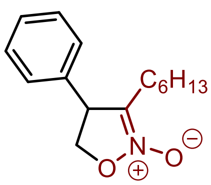
Isoxazoline *N*-oxide **3c** was synthesized by **GP-1** from styryl sulfonium salt **1a** (408 mg, 1.3 mmol) and 1-nitropropane **2c** (89 mg, 1 mmol), yield – 138 mg (72%). Colorless oil. R_f = 0.26 (PE/EA 2:1, anisaldehyde/H_2SO_4).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.22 (m, 5H, H_{Ph}), 4.75 (dd, *J* = 9.6, 7.5 Hz, 1H, $CH_{2a}O$), 4.46 (dd, *J* = 9.6, 6.1 Hz, 1H, CHPh), 4.29 (dd, *J* = 7.5, 6.1 Hz, 1H, $CH_{2b}O$), 2.46 (dq, *J* = 15.1, 7.6 Hz, 1H, CH_2CH_3), 2.15 (dq, *J* = 15.1, 7.6 Hz, 1H, CH_2CH_3), 0.99 (t, *J* = 7.6 Hz, 3H, CH_2CH_3) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 138.2 (1C, C_{Ph}), 129.4 (2C, CH_{Ph}), 128.4 (1C, CH_{Ph}), 127.5 (2C, CH_{Ph}), 119.2 (1C, C=NO), 71.0 (1C, CH_2O), 51.4 (1C, CHPh), 18.7 (1C, CH_2CH_3), 9.4 (1C, CH_2CH_3) ppm.

HRMS (ESI): m/z calcd for $C_{11}H_{14}NO_2^+$ $[M+H]^+$: 192.1019, found 192.1017.

3-Hexyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3d)

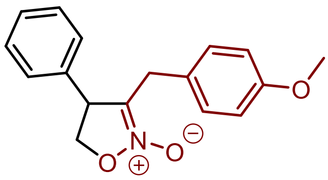


Isoxazoline *N*-oxide **3d** was synthesized by **GP-1** from styryl sulfonium salt **1a** (408 mg, 1.3 mmol) and 1-nitroheptane **2d** (145 mg, 1 mmol), yield – 206 mg (83%). Colorless oil. R_f = 0.47 (PE/EA 2:1, anisaldehyde/H_2SO_4).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.30 (m, 3H, H_{Ph}), 7.30 – 7.21 (m, 2H, H_{Ph}), 4.74 (dd, *J* = 9.4, 7.5 Hz, 1H, $CH_{2a}O$), 4.46 – 4.38 (m, 1H, CHPh), 4.30 (dd, *J* = 7.5, 6.2 Hz, 1H, $CH_{2b}O$), 2.52 – 2.36 (m, 1H, CH_2 of hexyl), 2.12 – 2.02 (m, 1H, CH_2 of hexyl), 1.50 – 1.32 (m, 2H, CH_2 of hexyl), 1.31 – 1.14 (m, 6H, CH_2 of hexyl), 0.90 – 0.79 (m, 3H, CH_3 of hexyl) ppm.

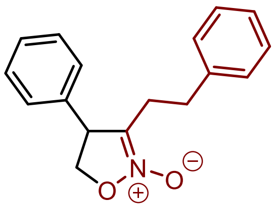
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 138.2 (1C, $\underline{C}_{Ph}$), 129.4 (2C, $\underline{C}H_{Ph}$), 128.5 (1C, $\underline{C}H_{Ph}$), 127.6 (2C, $\underline{C}H_{Ph}$), 118.6 (1C, $\underline{C}$=NO), 71.0 (1C, $\underline{C}H_2O$), 51.8 (1C, $\underline{C}$HPh), 31.4, 29.0, 25.2, 25.0 and 22.5 (5C, 5 × $\underline{C}H_2$ of hexyl), 14.1 (1C, $\underline{C}H_3$ of hexyl) ppm.
HRMS (ESI): m/z calcd for $C_{15}H_{22}NO_2^+$ [M+H]$^+$: 248.1645, found 248.1652.

3-(4-Methoxybenzyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3e)



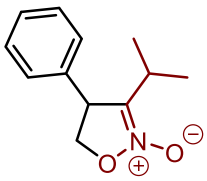
Isoxazoline *N*-oxide **3e** was synthesized by **GP-1** from styryl sulfonium salt **1a** (612 mg, 1.95 mmol) and 2-(4-methoxyphenyl)-1-nitroethane **2e** (272 mg, 1.5 mmol), yield – 408 mg (96%). Colorless oil. R_f = 0.43 (PE/EA 2:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.31 (m, 3H, $\underline{H}_{Ph}$), 7.19 – 7.16 (m, 2H, $\underline{H}_{Ph}$), 6.99 (d, *J* = 8.6 Hz, 2H, $\underline{H}_{Ar}$), 6.79 (d, *J* = 8.6 Hz, 2H, $\underline{H}_{Ar}$), 4.76 – 4.66 (m, 1H, $C\underline{H}_{2a}O$), 4.35 – 4.24 (m, 2H, $C\underline{H}_{2b}O$ and C$\underline{H}$Ph), 3.87 (d, *J* = 15.3 Hz, 1H, $C\underline{H}_{2a}Ar$), 3.79 (s, 3H, $C\underline{H}_3O$), 3.16 (d, *J* = 15.3 Hz, 1H, $C\underline{H}_{2b}Ar$) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 158.9 (1C, $\underline{C}_{Ar}$), 137.9 (1C, $\underline{C}_{Ph}$), 130.1, 129.4, 128.5 and 127.8 (7C, $\underline{C}H_{Ar}$ and $\underline{C}H_{Ph}$), 126.8 (1C, $\underline{C}_{Ar}$), 117.9 (1C, $\underline{C}$=NO), 114.2 (2C, $\underline{C}H_{Ar}$), 71.1 (1C, $\underline{C}H_2O$), 55.3 (1C, $C\underline{H}_3O$), 51.0 (1C, $\underline{C}$HPh), 30.4 (1C, $\underline{C}H_2Ar$) ppm.
HRMS (ESI): m/z calcd for $C_{17}H_{18}NO_3^+$ [M+H]$^+$: 284.1281, found 284.1284.

3-Phenethyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3f)



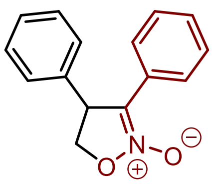
Isoxazoline *N*-oxide **3f** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and (3-nitropropyl)benzene **2f** (83 mg, 0.5 mmol), yield – 93 mg (69%). Colorless oil. R_f = 0.41 (PE/EA 2:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.06 (m, 10H, $\underline{H}_{Ph}$), 4.66 (dd, *J* = 9.6, 7.6 Hz, 1H, $C\underline{H}_{2a}O$), 4.29 – 4.25 (m, 1H, C$\underline{H}$Ph), 4.10 (dd, *J* = 9.5, 6.5 Hz, 1H, $C\underline{H}_{2b}O$), 2.96 – 2.70 (m, 3H, CH_2CH_2Ph), 2.45 – 2.28 (m, 1H, CH_2CH_2Ph) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 140.0 (1C, $\underline{C}_{Ph}$), 137.9 (1C, $\underline{C}_{Ph}$), 129.4 (2C, $\underline{C}H_{Ph}$), 128.7 (2C, $\underline{C}H_{Ph}$), 128.5 (1C, $\underline{C}H_{Ph}$), 128.3 (2C, $\underline{C}H_{Ph}$), 127.7 (2C, $\underline{C}H_{Ph}$), 126.6 (1C, $\underline{C}H_{Ph}$), 117.9 (1C, $\underline{C}$=NO), 71.0 (1C, $\underline{C}H_2O$), 51.9 (1C, $\underline{C}$HPh), 30.6 (1C, CH_2CH_2Ph), 26.7 (1C, CH_2CH_2Ph) ppm.
HRMS (ESI): m/z calcd for $C_{17}H_{18}NO_2^+$ [M+H]$^+$: 268.1332, found 268.1327.

3-Isopropyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3g)



Isoxazoline *N*-oxide **3g** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and 1-nitro-2-methylpropane **2g** (52 mg, 0.5 mmol), yield – 61 mg (60%). Colorless oil. R_f = 0.53 (PE/EA 2:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.25 (m, 5H, $\underline{H}_{Ph}$), 4.71 (dd, *J* = 9.1, 7.4 Hz, 1H, $C\underline{H}_{2a}O$), 4.38 (dd, *J* = 9.1, 4.4 Hz, 1H, C$\underline{H}$Ph), 4.31 (dd, *J* = 7.4, 4.4 Hz, 1H, $C\underline{H}_{2b}O$), 2.87 (hept, *J* = 7.0 Hz, 1H, $C\underline{H}Me_2$), 1.14 (d, *J* = 7.0 Hz, 3H, $C\underline{H}_3$), 0.88 (d, *J* = 7.0 Hz, 3H, $C\underline{H}_3$) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 139.4 (1C, $\underline{C}_{Ar}$), 129.3 (2C, $\underline{C}H_{Ph}$), 128.4 (1C, $\underline{C}H_{Ph}$), 127.6 (2C, $\underline{C}H_{Ph}$), 122.2 (1C, $\underline{C}$=NO), 71.4 (1C, $\underline{C}H_2O$), 50.9 (1C, $\underline{C}$HPh), 26.8 (1C, $\underline{C}HMe_2$), 18.7 (1C, $\underline{C}H_3$), 18.3 (1C, $\underline{C}H_3$) ppm.
HRMS (ESI): m/z calcd for $C_{12}H_{16}NO_2^+$ [M+H]$^+$: 206.1176, found 206.1175.

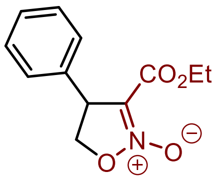
3,4-Diphenyl-4,5-dihydroisoxazole 2-oxide (3h)



Isoxazoline *N*-oxide **3h** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and phenylnitromethane **2h** (69 mg, 0.5 mmol), yield – 80 mg (67%). Colorless oil. R_f = 0.39 (PE/EA 2:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 2H, $\underline{H}_{Ph}$), 7.41 – 7.27 (m, 8H, $\underline{H}_{Ph}$), 4.94 – 4.83 (m, 2H, $C\underline{H}_{2a}O$ and C$\underline{H}$Ph), 4.45 – 4.30 (m, 1H, $C\underline{H}_{2b}O$) ppm.

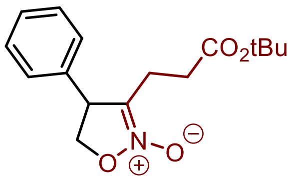
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 139.5 (1C, C_{Ph}), 129.5 (2C, CH_{Ph}), 129.3 (1C, CH_{Ph}), 128.7 (2C, CH_{Ph}), 128.3 (1C, CH_{Ph}), 127.3 (2C, CH_{Ph}), 126.7 (2C, CH_{Ph}), 126.3 (1C, C_{Ph}), 116.7 (1C, C=NO), 71.7 (1C, CH_2O), 51.1 (1C, CHPh) ppm.
HRMS (ESI): m/z calcd for $C_{15}H_{14}NO_2^+$ $[M+H]^+$: 240.1019, found 240.1020.

3-(Ethoxycarbonyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3i)



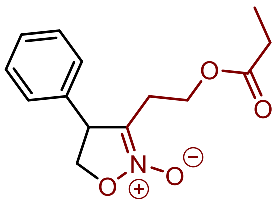
Isoxazoline *N*-oxide **3i** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and ethyl nitroacetate **2i** (67 mg, 0.5 mmol), yield – 35 mg (32%). Colorless oil. R_f = 0.75 (PE/EA 1:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.30 (m, 5H, H_{Ph}), 4.89 (dd, *J* = 9.4, 7.7 Hz, 1H, $CH_{2a}O$), 4.74 (dd, *J* = 9.4, 4.0 Hz, 1H, CHPh), 4.50 (dd, *J* = 7.7, 4.0 Hz, 1H, $CH_{2b}O$), 4.31 – 4.09 (m, 2H, OCH_2CH_3), 1.17 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 158.7 (1C, C=O), 139.2 (1C, C_{Ar}), 129.3 (2C, CH_{Ph}), 128.4 (1C, CH_{Ph}), 127.3 (2C, CH_{Ph}), 111.1 (1C, C=NO), 72.0 (1C, CH_2O), 61.8 (1C, OCH_2CH_3), 49.2 (1C, CHPh), 14.0 (1C, OCH_2CH_3) ppm.
HRMS (ESI): m/z calcd for $C_{12}H_{14}NO_4^+$ $[M+H]^+$: 236.0917, found 236.0926.

3-(3-(*Tert*-butoxy)-3-oxopropyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3j)



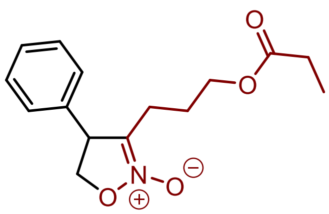
Isoxazoline *N*-oxide **3j** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and tert-butyl 4-nitrobutyrate **2j** (95 mg, 0.5 mmol), yield – 112 mg (77%). Colorless oil. R_f = 0.18 (PE/EA 3:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.23 (m, 5H, H_{Ph}), 4.76 (dd, *J* = 9.5, 7.5 Hz, 1H, $CH_{2a}O$), 4.55 (br s, 1H, CHPh), 4.37 – 4.27 (m, 1H, $CH_{2b}O$), 2.79 – 2.45 (m, 2H, $CH_2CH_2CO_2tBu$), 2.46 – 2.23 (m, 2H, $CH_2CH_2CO_2tBu$), 1.44 (s, 9H, CMe_3) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 171.3 (1C, C=O), 138.2 (1C, C_{Ph}), 129.5 (2C, CH_{Ph}), 128.6 (1C, CH_{Ph}), 127.7 (2C, CH_{Ph}), 81.1 (1C. CMe_3), 71.3 (1C, CH_2O), 51.9 (1C, CHPh), 30.2 and 20.8 (2C, $CH_2CH_2CO_2tBu$), 28.1 (3C, CMe_3) ppm. Signal of C=NO is absent due to broadening/low intensity.
HRMS (ESI): m/z calcd for $C_{16}H_{22}NO_4^+$ $[M+H]^+$: 292.1543, found 292.1540.

4-Phenyl-3-(2-(propionyloxy)ethyl)-4,5-dihydroisoxazole 2-oxide (3k)



Isoxazoline *N*-oxide **3k** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and 3-nitropropyl propionate **2k** (81 mg, 0.5 mmol), yield – 106 mg (80%). Colorless oil. R_f = 0.53 (PE/EA 1:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.31 (m, 3H, H_{Ph}), 7.32 – 7.21 (m, 2H, H_{Ph}), 4.78 (dd, *J* = 9.5, 7.6 Hz, 1H, $CH_{2a}O$ of isoxazoline *N*-oxide ring), 4.50 (dd, *J* = 9.5, 6.1 Hz, 1H, CHPh), 4.32 (dd, *J* = 7.6, 6.1 Hz, 1H, $CH_{2b}O$ of isoxazoline *N*-oxide ring), 4.24 – 4.05 (m, 2H, CH_2CH_2O), 2.88 – 2.71 (m, 1H, CH_2CH_2O), 2.49 – 2.33 (m, 1H, CH_2CH_2O), 2.27 (q, *J* = 7.5 Hz, 2H, CH_2CH_3), 1.10 (t, *J* = 7.5 Hz, 3H, CH_2CH_3) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 174.1 (1C, C=O), 137.9 (1C, C_{Ph}), 129.5 (2C, CH_{Ph}), 128.6 (1C, CH_{Ph}), 127.6 (2C, CH_{Ph}), 115.4 (1C, C=NO), 71.3 (1C, CH_2O), 59.4 (1C, CH_2CH_2O), 51.6 (1C, CHPh), 27.4 and 25.2 (2C, CH_2CH_2O and CH_2CH_3), 9.0 (1C, CH_2CH_3) ppm.
HRMS (ESI): m/z calcd for $C_{14}H_{18}NO_4^+$ $[M+H]^+$: 264.1230, found 264.1236.

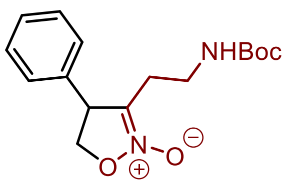
4-Phenyl-3-(3-(propionyloxy)propyl)-4,5-dihydroisoxazole 2-oxide (3l)



Isoxazoline *N*-oxide **3l** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and 4-nitrobutyl propionate **2l** (88 mg, 0.5 mmol), yield – 105 mg (76%). Colorless oil. R_f = 0.50 (PE/EA 1:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.23 (m, 5H, H_{Ph}), 4.78 (dd, *J* = 9.4, 7.5 Hz, 1H, $CH_{2a}O$ of isoxazoline *N*-oxide ring), 4.50 – 4.45 (m, 1H, CHPh), 4.35 – 4.30 (m, 1H, $CH_{2b}O$ of isoxazoline *N*-oxide ring), 4.11 – 3.92 (m, 2H, $CH_2CH_2CH_2O$), 2.59 – 2.42 (m,

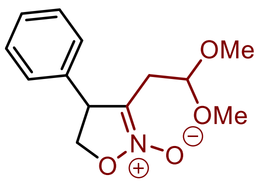
1H, $CH_{2a}CH_2CH_2O$), 2.27 (q, *J* = 7.6 Hz, 2H, CH_2CH_3), 2.24 – 2.10 (m, 1H, $CH_{2b}CH_2CH_2O$), 1.90 – 1.64 (m, 2H, $CH_2CH_2CH_2O$), 1.09 (t, *J* = 7.6 Hz, 3H, CH_2CH_3) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 174.3 (1C, C=O), 137.9 (1C, C_{Ph}), 129.5 (2C, CH_{Ph}), 128.6 (1C, CH_{Ph}), 127.6 (2C, CH_{Ph}), 117.4 (1C, C=NO), 71.1 (1C, CH_2O), 63.2 (1C, $CH_2CH_2CH_2O$), 51.7 (1C, CHPh), 27.5, 24.1 and 22.0 (3C, $CH_2CH_2CH_2O$, $CH_2CH_2CH_2O$ and CH_2CH_3), 9.1 (1C, CH_2CH_3) ppm.
HRMS (ESI): m/z calcd for $C_{15}H_{20}NO_4^+$ $[M+H]^+$: 278.1387, found 278.1388.

3-(2-((*Tert*-butoxycarbonyl)amino)ethyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3m)



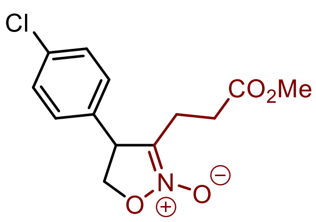
Isoxazoline *N*-oxide **3m** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and tert-butyl (3-nitropropyl)carbamate **2m** (102 mg, 0.5 mmol), yield – 136 mg (89%). Colorless oil. R_f = 0.48 (PE/EA 1:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.34 (m, 3H, H_{Ph}), 7.31 – 7.26 (m, 2H, H_{Ph}), 4.89 (br s, 1H, NHBoc), 4.78 (dd, *J* = 9.6, 7.5 Hz, 1H, $CH_{2a}O$), 4.62 – 4.53 (m, 1H, CHPh), 4.34 (dd, *J* = 7.5, 5.7 Hz, 1H, $CH_{2b}O$), 3.51 – 3.34 (m, 1H, CH_2CH_2NHBoc), 3.26 – 3.11 (m, 1H, CH_2CH_2NHBoc), 2.72 – 2.56 (m, 1H, CH_2CH_2NHBoc), 2.35 – 2.18 (m, 1H, CH_2CH_2NHBoc), 1.44 (s, 9H, NHBoc) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 156.1 (1C, C=O), 138.1 (1C, C_{Ph}), 129.6 (2C, CH_{Ph}), 128.6 (1C, CH_{Ph}), 127.7 (2C, CH_{Ph}), 117.1 (1C, C=NO), 79.6 (1C, CMe_3), 71.3 (1C, CH_2O), 51.5 (1C, CHPh), 36.8 and 26.3 (2C, CH_2CH_2NHBoc), 28.4 (3C, CMe_3) ppm.
HRMS (ESI): m/z calcd for $C_{16}H_{23}N_2O_4^+$ $[M+H]^+$: 307.1652, found 307.1649.

3-(2,2-Dimethoxyethyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3n)



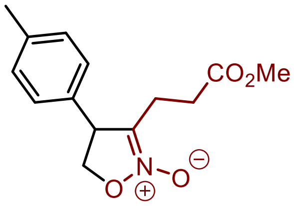
Isoxazoline *N*-oxide **3n** was synthesized by **GP-1** from styryl sulfonium salt **1a** (204 mg, 0.65 mmol) and 3-nitropropanal dimethyl acetal **2n** (75 mg, 0.5 mmol), yield – 64 mg (51%). Colorless oil. R_f = 0.44 (PE/EA 1:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.31 (m, 3H, H_{Ph}), 7.29 – 7.22 (m, 2H, H_{Ph}), 4.77 (dd, *J* = 9.7, 7.6 Hz, 1H, $CH_{2a}O$), 4.59 – 4.47 (m, 2H, CHPh and $CH_2CH(OMe)_2$), 4.32 (dd, *J* = 7.6, 6.1 Hz, 1H, $CH_{2b}O$), 3.30 (s, 3H, CH_3O), 3.26 (s, 3H, CH_3O), 2.82 (ddd, *J* = 14.8, 4.9, 1.1 Hz, 1H, $CH_{2a}CH(OMe)_2$), 2.31 (ddd, *J* = 14.8, 6.1, 1.2 Hz, 1H, $CH_{2b}CH(OMe)_2$) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 138.2 (1C, C_{Ph}), 129.4 (2C, CH_{Ph}), 128.4 (1C, CH_{Ph}), 127.7 (2C, CH_{Ph}), 115.2 (1C, C=NO), 100.8 (1C, $CH_2CH(OMe)_2$), 71.3 (1C, CH_2O), 53.9 (1C, CH_3O), 53.3 (1C, CH_3O), 51.8 (1C, CHPh), 29.1 (1C, $CH_2CH(OMe)_2$) ppm.
HRMS (ESI): m/z calcd for $C_{13}H_{18}NO_4^+$ $[M+H]^+$: 252.1230, found 252.1225.

4-(4-Chlorophenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3o)



Isoxazoline N-oxide **3o** was synthesized by **GP-1** from styryl sulfonium salt **1b** (226 mg, 0.65 mmol) and methyl 4-nitrobutyrate **2a** (74 mg, 0.5 mmol), yield – 110 mg (78%). Colorless oil. R_f = 0.40 (PE/EA 2:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.1 Hz, 2H, H_{Ar}), 7.24 (d, *J* = 8.2 Hz, 2H, H_{Ar}), 4.79 – 4.74 (br m, 1H, $CH_{2a}O$), 4.58 – 4.53 (br m, 1H, CHAr), 4.32 – 4.27 (br m, 1H, $CH_{2b}O$), 3.66 (s, 3H, CH_3O), 2.83 – 2.54 (m, 2H, $CH_2CH_2CO_2Me$), 2.51 – 2.30 (m, 2H, $CH_2CH_2CO_2Me$) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 172.6 (1C, C=O), 136.6 (1C, C_{Ar}), 134.5 (1C, C_{Ar}), 129.7 (2C, CH_{Ar}), 129.1 (2C, CH_{Ar}), 116.9 (1C, C=NO), 71.1 (1C, CH_2O), 52.0 and 51.4 (2C, CHAr and CH_3O), 28.7 and 20.5 (2C, $CH_2CH_2CO_2Me$) ppm.
HRMS (ESI): m/z calcd for $C_{13}H_{15}{}^{35}ClNO_4^+$ $[M+H]^+$: 284.0684, found 284.0686.

3-(3-Methoxy-3-oxopropyl)-4-(p-tolyl)-4,5-dihydroisoxazole 2-oxide (3p)



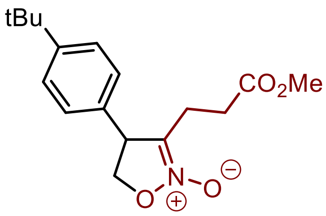
Isoxazoline *N*-oxide **3p** was synthesized by **GP-1** from styryl thianthrenium salt **5b** (313 mg, 0.65 mmol) and methyl 4-nitrobutyrate **2a** (74 mg, 0.5 mmol), yield – 89 mg (67%). Colorless oil. R_f = 0.16 (PE/EA 2:1, anisaldehyde/H_2SO_4).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 – 7.09 (m, 4H, $\underline{H}_{Ar}$), 4.73 (dd, *J* = 9.6, 7.5 Hz, 1H, $C\underline{H}_{2a}O$), 4.49 (dd, *J* = 9.5, 6.4 Hz, 1H, $C\underline{H}Ar$), 4.27 (dd, *J* = 7.6, 6.3 Hz, 1H, $C\underline{H}_{2b}O$), 3.63 (s, 3H, $C\underline{H}_3O$), 2.75 – 2.51 (m, 2H, $CH_2CH_2CO_2Me$), 2.45 – 2.35 (m, 2H, $CH_2CH_2CO_2Me$), 2.33 (s, 3H, $C\underline{H}_3$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 172.6 (1C, $\underline{C}$=O), 138.4 (1C, $\underline{C}_{Ar}$), 134.9 (1C, $\underline{C}_{Ar}$), 130.1 (2C, $\underline{C}H_{Ar}$), 127.6 (2C, $\underline{C}H_{Ar}$), 117.4 (1C, $\underline{C}$=NO), 71.4 (1C, $\underline{C}H_2O$), 51.9 and 51.6 (2C, $\underline{C}HAr$ and $\underline{C}H_3O$), 28.6 and 20.6 (2C, $\underline{C}H_2\underline{C}H_2CO_2Me$), 21.2 (1C, $\underline{C}H_3$) ppm.

HRMS (ESI): m/z calcd for $C_{14}H_{18}NO_4^+$ $[M+H]^+$: 264.1230, found 264.1225.

4-(4-(*Tert*-butyl)phenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3q)



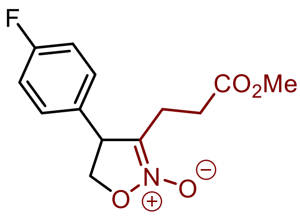
Isoxazoline *N*-oxide **3q** was synthesized by **GP-1** from styryl thianthrenium salt **5c** (341 mg, 0.65 mmol) and methyl 4-nitrobutyrate **2a** (74 mg, 0.5 mmol), yield – 100 mg (63%). Colorless oil. R_f = 0.19 (PE/EA 2:1, anisaldehyde/H_2SO_4).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.3 Hz, 2H, $\underline{H}_{Ar}$), 7.18 (d, *J* = 8.3 Hz, 2H, $\underline{H}_{Ar}$), 4.73 (dd, *J* = 9.7, 7.5 Hz, 1H, $C\underline{H}_{2a}O$), 4.51 (dd, *J* = 9.7, 6.4 Hz, 1H, $C\underline{H}Ar$), 4.30 (dd, *J* = 7.5, 6.5 Hz, 1H, $C\underline{H}_{2b}O$), 3.64 (s, 3H, $C\underline{H}_3O$), 2.78 – 2.56 (m, 2H, $CH_2CH_2CO_2Me$), 2.48 – 2.32 (m, 2H, $CH_2CH_2CO_2Me$), 1.31 (s, 9H, $C\underline{Me}_3$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 172.7 (1C, $\underline{C}$=O), 151.7 (1C, $\underline{C}_{Ar}$), 134.9 (1C, $\underline{C}_{Ar}$), 127.4 (2C, $\underline{C}H_{Ar}$), 126.4 (2C, $\underline{C}H_{Ar}$), 117.4 (1C, $\underline{C}$=NO), 71.5 (1C, $\underline{C}H_2O$), 51.9 and 51.6 (2C, $\underline{C}HAr$ and $\underline{C}H_3O$), 34.7 (1C, $\underline{C}Me_3$), 31.4 (1C, $C\underline{Me}_3$), 28.7 and 20.6 (2C, $\underline{C}H_2\underline{C}H_2CO_2Me$) ppm.

HRMS (ESI): m/z calcd for $C_{17}H_{23}NO_4^+$ $[M+H]^+$: 306.1700, found 306.1694.

4-(4-Fluorophenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3r)



Isoxazoline *N*-oxide **3r** was synthesized by **GP-1** from styryl thianthrenium salt **5d** (316 mg, 0.65 mmol) and methyl 4-nitrobutyrate **2a** (74 mg, 0.5 mmol), yield – 90 mg (67%). Colorless oil. R_f = 0.19 (PE/EA 2:1, anisaldehyde/H_2SO_4).

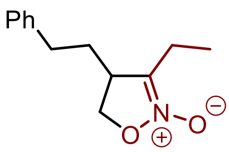
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 8.7, 5.2 Hz, 2H, $\underline{H}_{Ar}$), 7.09 (t, *J* = 8.7 Hz, 2H, $\underline{H}_{Ar}$), 4.76 (dd, *J* = 9.6, 7.7 Hz, 1H, $C\underline{H}_{2a}O$), 4.56 (dd, *J* = 9.6, 6.0 Hz, 1H, $C\underline{H}Ar$), 4.30 (dd, *J* = 7.6, 6.0 Hz, 1H, $C\underline{H}_{2b}O$), 3.66 (s, 3H, $C\underline{H}_3O$), 2.79 – 2.55 (m, 2H, $CH_2CH_2CO_2Me$), 2.48 – 2.32 (m, 2H, $CH_2CH_2CO_2Me$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 172.6 (1C, $\underline{C}$=O), 162.7 (d, *J* = 247.9 Hz, 1C, $\underline{C}_{Ar}$), 133.9 (d, *J* = 3.3 Hz, 1C, $\underline{C}_{Ar}$), 129.4 (d, *J* = 8.3 Hz, 2C, $\underline{C}H_{Ar}$), 117.1 (1C, $\underline{C}$=NO), 116.5 (d, *J* = 21.7 Hz, 2C, $\underline{C}H_{Ar}$), 71.3 (1C, $\underline{C}H_2O$), 52.0 and 51.3 (2C, $\underline{C}HAr$ and $\underline{C}H_3O$), 28.7 and 20.5 (2C, $\underline{C}H_2CH_2\underline{C}O_2Me$) ppm.

^{19}F{^{1}H} NMR (287 MHz, $CDCl_3$) δ -113.2

HRMS (ESI): m/z calcd for $C_{13}H_{15}FNO_4^+$ $[M+H]^+$: 268.0980, found 268.0980.

3-Ethyl-4-phenethyl-4,5-dihydroisoxazole 2-oxide (3s)



Isoxazoline *N*-oxide **3s** was synthesized by **GP-1** from styryl thianthrenium salt **5e** (322 mg, 0.65 mmol) and 1-nitropropane **2b** (45 mg, 0.5 mmol), yield – 33 mg (31%). Colorless oil. R_f = 0.25 (PE/EA 2:1, anisaldehyde/H_2SO_4).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.16 (m, 5H, $\underline{H}_{Ph}$), 4.46 (dd, *J* = 9.1, 7.7 Hz, 1H, $C\underline{H}_{2a}O$), 4.13 (dd, *J* = 7.7, 6.1 Hz, 1H, $C\underline{H}_{2b}O$), 3.41 – 3.28 (m, 1H, $C\underline{H}$), 2.79 – 2.57 (m, 2H, $C\underline{H}_2$), 2.56 – 2.40 (m, 1H, $C\underline{H}_2$), 2.35 – 2.19 (m, 1H, $C\underline{H}_2$), 2.12 – 1.94 (m, 1H, $C\underline{H}_2$), 1.97 – 1.77 (m, 1H, $C\underline{H}_2$), 1.13 (t, *J* = 7.6 Hz, 3H, $CH_2C\underline{H}_3$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 140.3 (1C, $\underline{C}_{Ph}$), 128.8 (2C, $\underline{C}H_{Ph}$), 128.3 (2C, $\underline{C}H_{Ph}$), 126.6 (1C, $\underline{C}H_{Ph}$), 119.6 (1C, $\underline{C}$=NO), 68.5 (1C, $\underline{C}H_2O$), 44.5 (1C, $\underline{C}H$), 32.7 and 32.6 (2C, $Ph\underline{C}H_2\underline{C}H_2$), 18.6 (1C, $\underline{C}H_2CH_3$), 9.6 (1C, $CH_2\underline{C}H_3$) ppm.

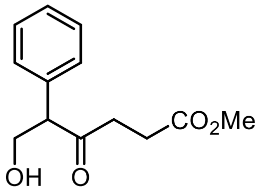
HRMS (ESI): m/z calcd for $C_{13}H_{18}NO_2^+$ [M+H]$^+$: 220.1332, found 220.1332.

4. Post-transformations of 3.

General procedure for reductive cleavage:

A solution of isoxazoline *N*-oxide **3** (1 mmol, 1 equiv) in 3 mL of EtOH was placed 25 mL-volume Schlenk tube. To this solution H_3BO_3 (62 mg, 1 mmol, 1 equiv) and 1 mL of water were added. After this a suspension of Ra-Ni (app. 100 mg, pre-washed with EtOH for 3 times) in 2 mL of EtOH (***Caution***: dry Ra-Ni is pyrophoric when exposed to air) was added to the solution. The main outlet was equipped with balloon with H_2 and the side outlet was equipped with a water jet pump. The Schlenk tube was **carefully** evacuated by a water jet pump and back-filled with H_2 from balloon. The action was repeated for 3 times. The mixture was hydrogenated with balloon of H_2 for 3h at rt with **vigorous** stirring. After that the solution was decanted from catalyst. The catalyst was washed with 5 ml of CH_2Cl_2 for 3 times. Combined solution was evaporated with silica gel and purified by column chromatography with a mixture of PE/EA as eluent to give pure hydroxy ketone.

Methyl 6-hydroxy-4-oxo-5-phenylhexanoate (6)



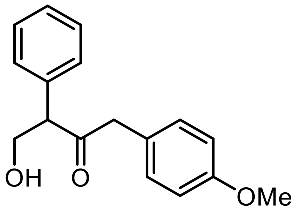
Hydroxy ketone **6** was obtained by hydrogenation of isoxazoline *N*-oxide **3a**, yield – 65% (61 mg). Colorless oil. R_f = 0.40 (PE/EA 1:1, anisaldehyde/H_2SO_4).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.20 (m, 5H, $\underline{H}_{Ph}$), 4.19 (dd, *J* = 11.2, 8.5 Hz, 1H, $C\underline{H}_{2a}OH$), 3.98 (dd, *J* = 8.5, 4.8 Hz, 1H, $C\underline{H}Ph$), 3.76 (dd, *J* = 11.2, 4.8 Hz, 1H, $C\underline{H}_{2b}OH$), 3.66 (s, 3H, $C\underline{H}_3O$), 2.80 – 2.43 (m, 5H, $C\underline{H}_2C\underline{H}_2CO_2Me$ and $CH_2O\underline{H}$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 209.5 (1C, C=O ketone), 173.2 (1C, C=O ester), 135.6 (1C, $\underline{C}_{Ph}$), 129.2 (2C, $\underline{C}H_{Ph}$), 128.7 (2C, $\underline{C}H_{Ph}$), 127.9 (1C, $\underline{C}H_{Ar}$), 64.3 (1C, $\underline{C}H_2OH$), 60.9 (1C, $\underline{C}HPh$), 51.9 (1C, $C\underline{H}_3O$), 36.9 and 27.9 (2C, $\underline{C}H_2\underline{C}H_2CO_2Me$) ppm.

HRMS (ESI): m/z calcd for $C_{13}H_{17}O_4^+$ $[M+H]^+$: 237.1121, found 237.1116.

4-Hydroxy-1-(4-methoxyphenyl)-3-phenylbutan-2-one (7)



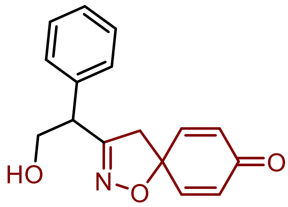
Hydroxy ketone **7** was obtained by hydrogenation of isoxazoline *N*-oxide **3e**, yield – 57% (54 mg). Colorless oil. R_f = 0.27 (PE/EA 1:1, anisaldehyde/H_2SO_4).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.30 (m, 3H, $\underline{H}_{Ph}$), 7.24 – 7.13 (m, 2H, $\underline{H}_{Ph}$), 6.98 (d, *J* = 8.6 Hz, 2H, $\underline{H}_{Ar}$), 6.84 (d, *J* = 8.6 Hz, 2H, $\underline{H}_{Ar}$), 4.15 (dd, *J* = 11.1, 8.5 Hz, 1H, $C\underline{H}_{2a}OH$), 4.02 (dd, *J* = 8.5, 4.7 Hz, 1H, $C\underline{H}Ph$), 3.80 (s, 3H, $C\underline{H}_3O$), 3.72 (dd, *J* = 11.1, 4.7 Hz, 1H, $C\underline{H}_{2b}OH$), 3.61 (br s, 2H, $C\underline{H}_2Ar$), 2.36 (br s, 1H, $CH_2O\underline{H}$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, DEPT135, HSQC) δ 209.0 (1C, C=O ketone), 158.8 (1C, $\underline{C}_{Ar}$), 135.4 (1C, $\underline{C}_{Ph}$), 130.6 (2C, $\underline{C}H_{Ar}$), 129.3 (2C, $\underline{C}H_{Ph}$), 128.9 (2C, $\underline{C}H_{Ph}$), 128.0 (1C, $\underline{C}H_{Ph}$), 125.8 (1C, $\underline{C}_{Ar}$), 114.2 (2C, $\underline{C}H_{Ar}$), 64.2 (1C, $\underline{C}H_2OH$), 59.9 (1C, $\underline{C}HPh$), 55.4 (1C, $\underline{C}H_3O$), 48.2 (1C, $\underline{C}H_2Ar$) ppm.

HRMS (ESI): m/z calcd for $C_{17}H_{19}O^+$ $[M+H]^+$: 271.1329, found 271.1323.

3-(2-Hydroxy-1-phenylethyl)-1-oxa-2-azaspiro[4.5]deca-2,6,9-trien-8-one (8)

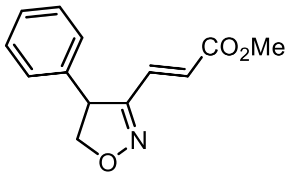


To a solution of isoxazoline *N*-oxide **3e** (1 equiv., 0.25 mmol, 71 mg) in 1 mL of THF TsOH·H_2O (1 equiv., 0.25 mmol, 48 mg) was added. Reaction mixture was stirred at room temperature overnight. After that solution was evaporated with silica gel and purified by column chromatography with a mixture of PE/EA (1:1 to 1:3) as eluent to give pure **8**. Yield – 75% (50 mg). Colorless oil. R_f = 0.54 (PE/EA 1:3, anisaldehyde/H_2SO_4).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.31 (m, 3H, $\underline{H}_{Ph}$), 7.32 – 7.22 (m, 2H, $\underline{H}_{Ph}$), 6.88 (dd, *J* = 10.0, 3.1 Hz, 1H, $C\underline{H}CHC{=}O$), 6.78 (dd, *J* = 10.0, 3.1 Hz, 1H, $C\underline{H}CHC{=}O$), 6.24 (dd, *J* = 10.0, 1.9 Hz, 1H, $CHC\underline{H}C{=}O$), 6.19 (dd, *J* = 10.0, 1.9 Hz, 1H, $CHC\underline{H}C{=}O$), 4.19 (dd, *J* = 11.2, 8.1 Hz, 1H, $C\underline{H}_{2a}OH$), 3.97 (dd, *J* = 11.3, 5.3 Hz, 1H, $C\underline{H}_{2b}OH$), 3.88 (dd, *J* = 8.2, 5.4 Hz, 1H, $C\underline{H}Ph$), 3.03 (d, *J* = 17.4 Hz, 1H, $C\underline{H}_{2a}$), 2.92 (d, *J* = 17.4 Hz, 1H, $C\underline{H}_{2b}$) ppm.

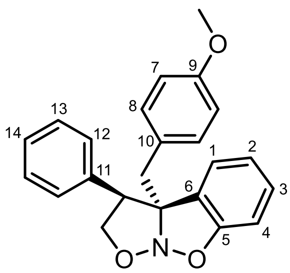
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 184.8 (1C, C=O), 159.6 (1C, C=N), 145.4 and 145.2 (2C, 2×CHCHC=O), 136.3 (1C, C_{Ph}), 129.44 (2C, CH_{Ph}), 129.2, 128.8 and 128.3 (3C, 2×CHCHC=O and CH_{Ph}), 128.1 (2C, CH_{Ph}), 79.6 (1C, C-O), 64.7 (1C, CH_2OH), 48.6 (1C, CHPh), 46.8 (1C, CH_2) ppm.
HRMS (ESI): m/z calcd for $C_{16}H_{16}NO_3^+$ $[M+H]^+$: 270.1125, found 270.1122.

Methyl (*E*)-3-(4-phenyl-4,5-dihydroisoxazol-3-yl)acrylate (10)



To a solution of isoxazoline *N*-oxide **3a** (1 equiv., 0.4 mmol, 100 mg) in 0.8 mL of freshly distilled CH_2Cl_2 TMSOTf (2.2 equiv., 0,88 mmol, 196 mg, 123 µL) and freshly distilled Et_3N (4 equiv., 1.6 mmol, 162 mg, 224 µL) were added at -78 °C under Ar atmosphere. Reaction mixture was stirred for 30 min at this temperature and then maintained overnight at 0 °C. After that the mixture was diluted with 20 mL of EA and washed with 20 mL of 0.25M aqueous solution of $NaHSO_4$. Organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and crude material was purified by column chromatography with a mixture of PE/EA (10:1 to 5:1) as eluent to give pure **10**. Yield – 75% (69 mg). Colorless oil. R_f = 0.76 (PE/EA 3:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 16.2 Hz, 1H, CH=CHCO$_2$Me), 7.44 – 7.28 (m, 3H, H_{Ph}), 7.22 – 7.16 (m, 2H, H_{Ph}), 5.92 (d, *J* = 16.2 Hz, 1H, CH=CHCO$_2$Me), 4.81 (dd, *J* = 10.6, 8.3 Hz, 1H, $CH_{2a}O$), 4.53 (dd, *J* = 10.6, 5.7 Hz, 1H, CHPh), 4.43 (dd, *J* = 8.3, 5.7 Hz, 1H, $CH_{2b}O$), 3.72 (s, 3H, CH_3O) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135) δ 166.1 (1C, C=O), 158.1 (1C, C=N), 138.6 (1C, C_{Ph}), 132.3, 128.2 and 125.7 (3C, CH=CHCO$_2$Me and CH_{Ph}), 129.5 (2C, CH_{Ph}), 127.4 (2C, CH_{Ph}), 79.6 (1C, CH_2O), 52.8 and 52.0 (2C, CH_3O and CHPh) ppm.
HRMS (ESI): m/z calcd for $C_{13}H_{14}NO_3^+$ $[M+H]^+$: 232.0968, found 232.0975.

3a-(4-Methoxybenzyl)-3-phenyl-3,3a-dihydro-2H-benzo[d]isoxazolo[2,3-b]isoxazole (12)



CsF (2 equiv., 0.7 mmol, 106 mg) was placed in a Schlenk tube and dried at ~250 °C (heat gun) in a vacuum (~ 1-2 torr) for 2 min. After cooling to rt, a solution of *N*-oxide **3e** (1 equiv., 0.35 mmol, 100 mg) in 3 mL of freshly distilled MeCN was added to a Schenk tube with CsF under Ar atmosphere. After dissolution of *N*-oxide, 2-(trimethylsilyl)phenyl triflate **10** (1 equiv., 0.35 mmol, 104 mg) was added to the solution and the mixture was stirred at rt overnight. After that the mixture was diluted with 20 mL of EA and washed with 20 mL of Brine. Organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and crude material was purified by column chromatography with a mixture of PE/EA (6:1 to 3:1) as eluent to give pure **12** as mixture of diastereomers (dr = 5.4:1). Yield – 65% (82 mg). Starting *N*-oxide **3d** was also isolated (30 mg, 30% recovery). Colorless oil. R_f = 0.72 (PE/EA 3:1, anisaldehyde/H_2SO_4).
^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY, *major diastereomer*) δ 7.33 – 7.22 (m, 5H, CH_{Ar}-8, CH_{Ar}-13 and CH_{Ar}-14), 7.14 – 7.07 (m, 1H, CH_{Ar}-3), 6.90 (dd, *J* = 7.8, 1.5 Hz, 2H, CH_{Ar}-12), 6.82 (d, *J* = 8.7 Hz, 2H, CH_{Ar}-7), 6.72 (d, *J* = 8.0 Hz, 1H, CH_{Ar}-4), 6.62 – 6.54 (m, 1H, CH_{Ar}-2), 5.98 – 5.91 (m, 1H, CH_{Ar}-1), 4.45 – 4.31 (m, 2H, CH_2O), 3.89 (dd, *J* = 11.2, 7.8 Hz, 1H, CHPh), 3.78 (s, 3H, CH_3O), 3.41 (d, *J* = 14.5 Hz, 1H, $CH_{2a}Ar$), 3.26 (d, *J* = 14.5 Hz, 1H, $CH_{2b}Ar$) ppm.
^{13}C NMR (75 MHz, $CDCl_3$, DEPT135, HSQC, HMBC, *major diastereomer*) δ 158.5 (1C, C_{Ar}-9), 157.1 (1C, C_{Ar}-5), 133.4 (1C, C_{Ar}-11), 131.9 (2C, CH_{Ar}-8), 129.19 (2C, CH_{Ar}-12), 129.13 (1C, CH_{Ar}-3), 128.3 (2C, CH_{Ar}-13), 127.9 (1C, CH_{Ar}-14), 127.5 (1C, C_{Ar}-10), 125.2 (1C, CH_{Ar}-1), 124.6 (1C, C_{Ar}-6), 120.2 (1C, CH_{Ar}-2), 113.6 (2C, CH_{Ar}-7), 106.2 (1C, CH_{Ar}-4), 86.9 (1C, C-N), 73.1 (1C, CH_2O), 55.6 (1C, CHPh), 55.1 (1C, CH_3O), 42.5 (1C, CH_2Ar) ppm.
^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY, *characteristic signals of minor diastereomer*) δ 7.57 – 7.51 (m, 2H, CH_{Ar}-12), 7.52 – 7.40 (m, 2H, CH_{Ar}-13), 7.19 – 7.13 (m, 2H, CH_{Ar}-1 and CH_{Ar}-3), 7.05 – 6.96 (app td, *J* = 7.4, 0.9 Hz, 1H CH_{Ar}-3), 6.72 – 6.62 (m, 1H, CH_{Ar}-4), 4.38 – 4.32 (m, 2H, CH_2O), 3.81 (dd, *J* = 3.5, 2.3 Hz, 1H, CHPh), 3.69 (s, 3H, CH_3O), 2.87 – 2.77 (m, 2H, CH_2Ar) ppm.

^{13}C NMR (75 MHz, $CDCl_3$, DEPT135, HSQC, HMBC, *characteristic signals of minor diastereomer*) δ 138.8 (1C, $\underline{C}_{Ar}$-11), 131.4, 128.9, 128.8, 127.8, 127.73, 122.9 (1C, $\underline{C}H_{Ar}$-1), 121.5 (1C, $\underline{C}H_{Ar}$-2), 112.9 (2C, $\underline{C}H_{Ar}$-7), 107.2 (1C, $\underline{C}H_{Ar}$-4), 88.0 (1C, $\underline{C}$-N), 59.7 (1C, $\underline{C}$HPh), 55.0 (1C, $\underline{C}H_3O$), 40.3 (1C, $\underline{C}H_2Ar$) ppm.

NOESY characteristic correlations (*major isomer*): C$\underline{H}$Ph/C$\underline{H}_2$Ar; C$\underline{H}_{Ar}$-12/C$\underline{H}_{Ar}$-1.

NOESY characteristic correlations (*minor isomer*): C$\underline{H}_{Ar}$-12/C$\underline{H}_2$Ar; C$\underline{H}_{Ar}$-1/ C$\underline{H}$Ph

HRMS (ESI): m/z calcd for $C_{23}H_{22}NO_3^+$ $[M+H]^+$: 360.1594, found 360.1581.

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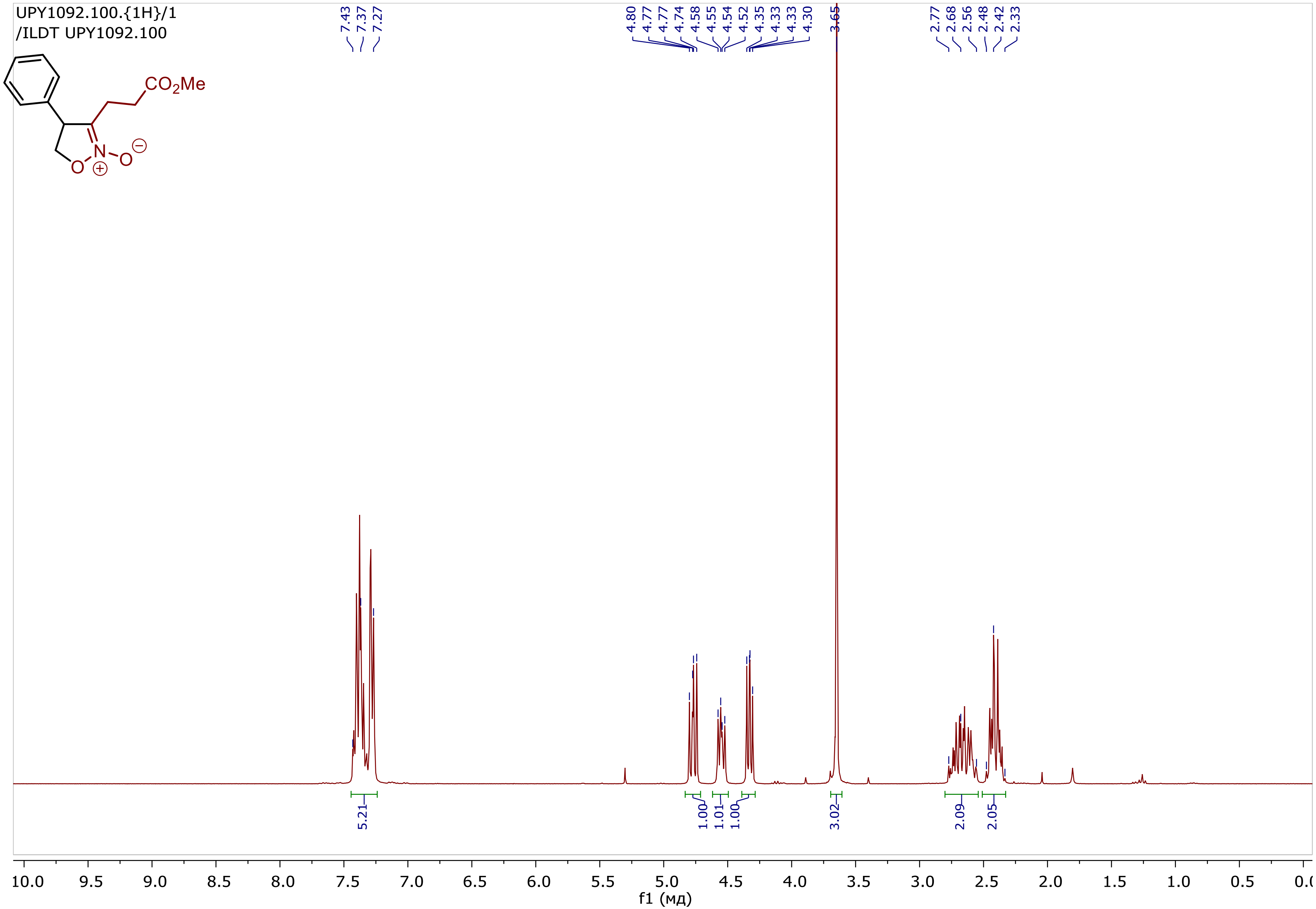
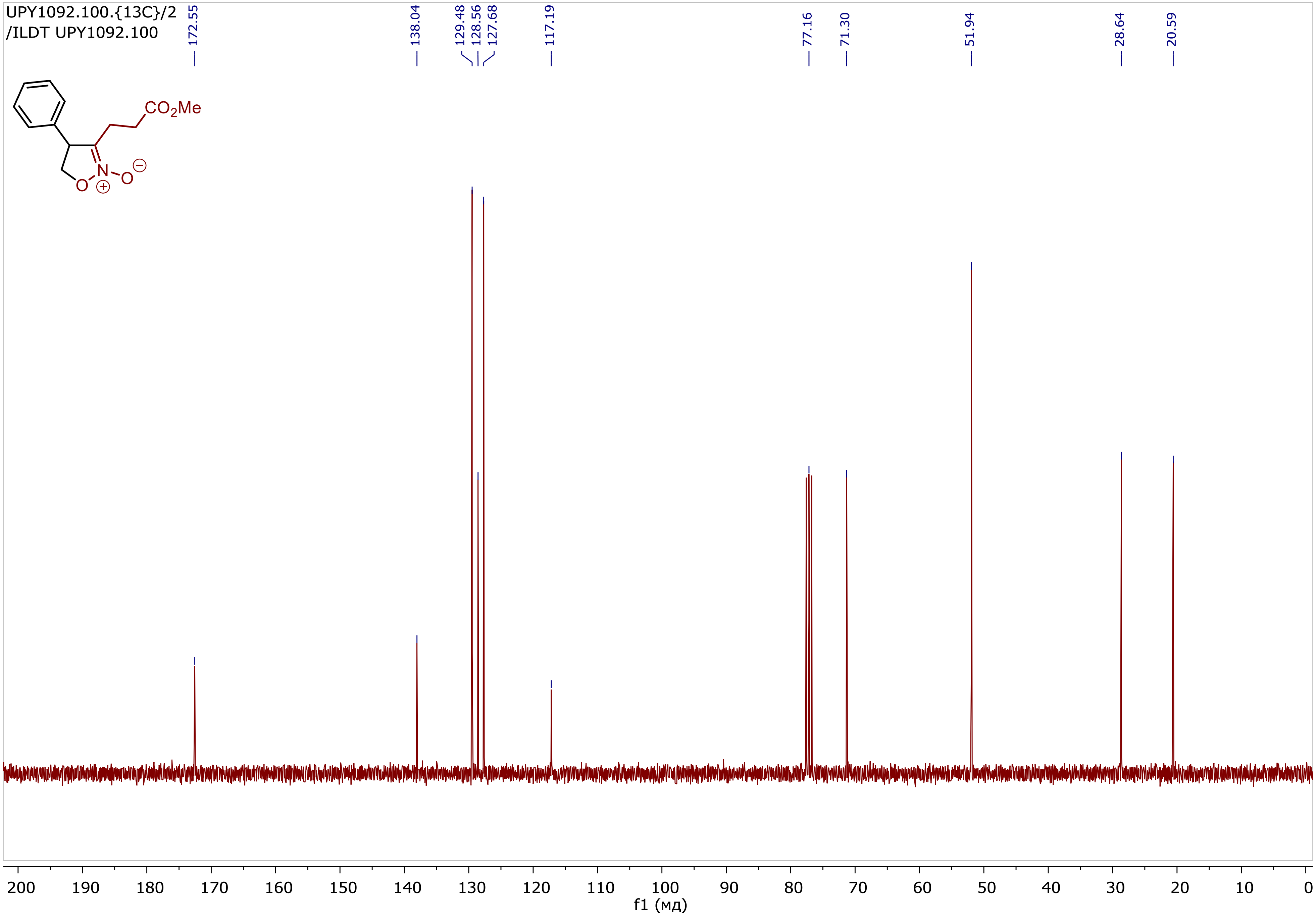
6. NMR spectra copies.

3-(3-Methoxy-3-oxopropyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3a)



3-(3-Methoxy-3-oxopropyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3a)



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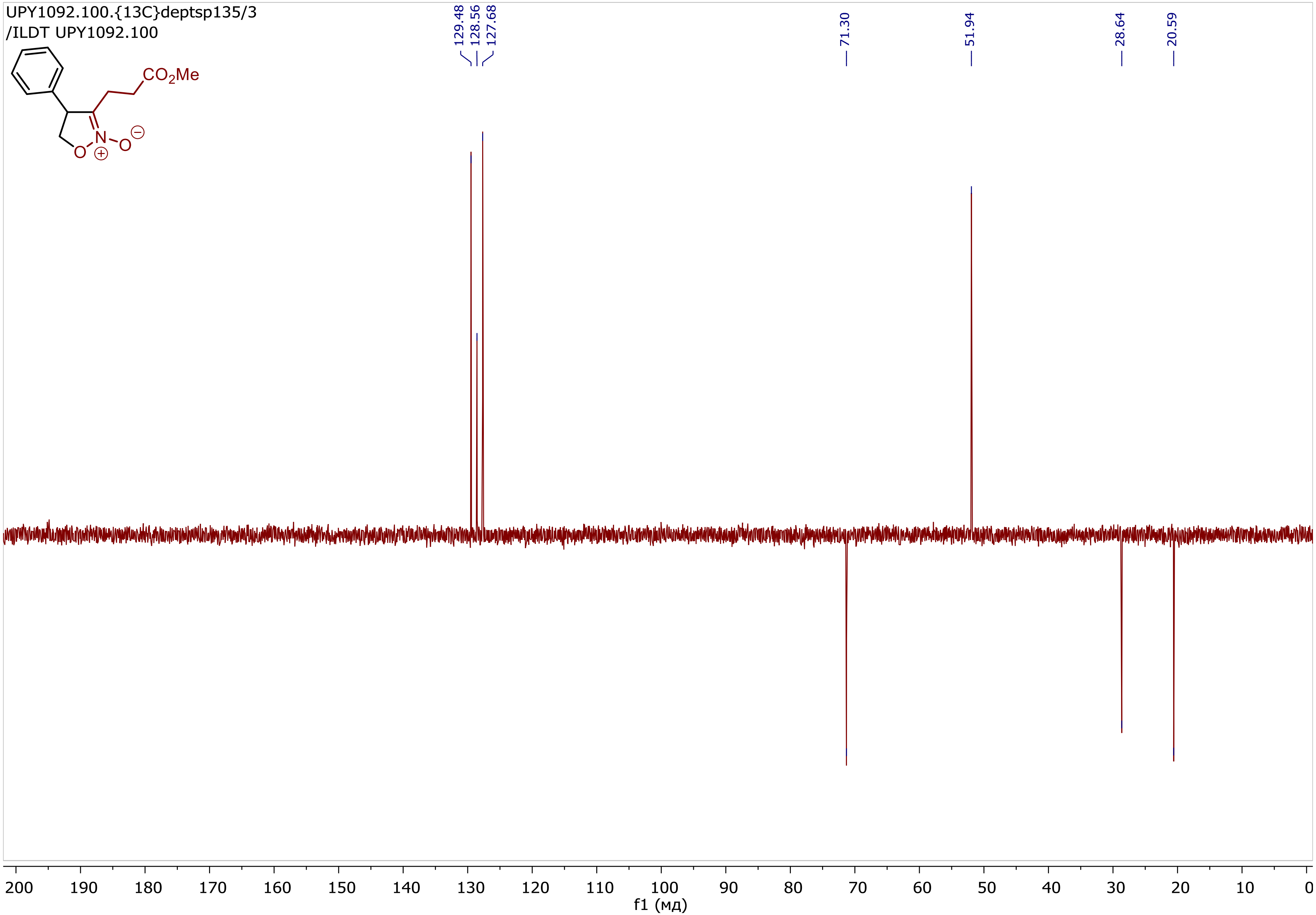

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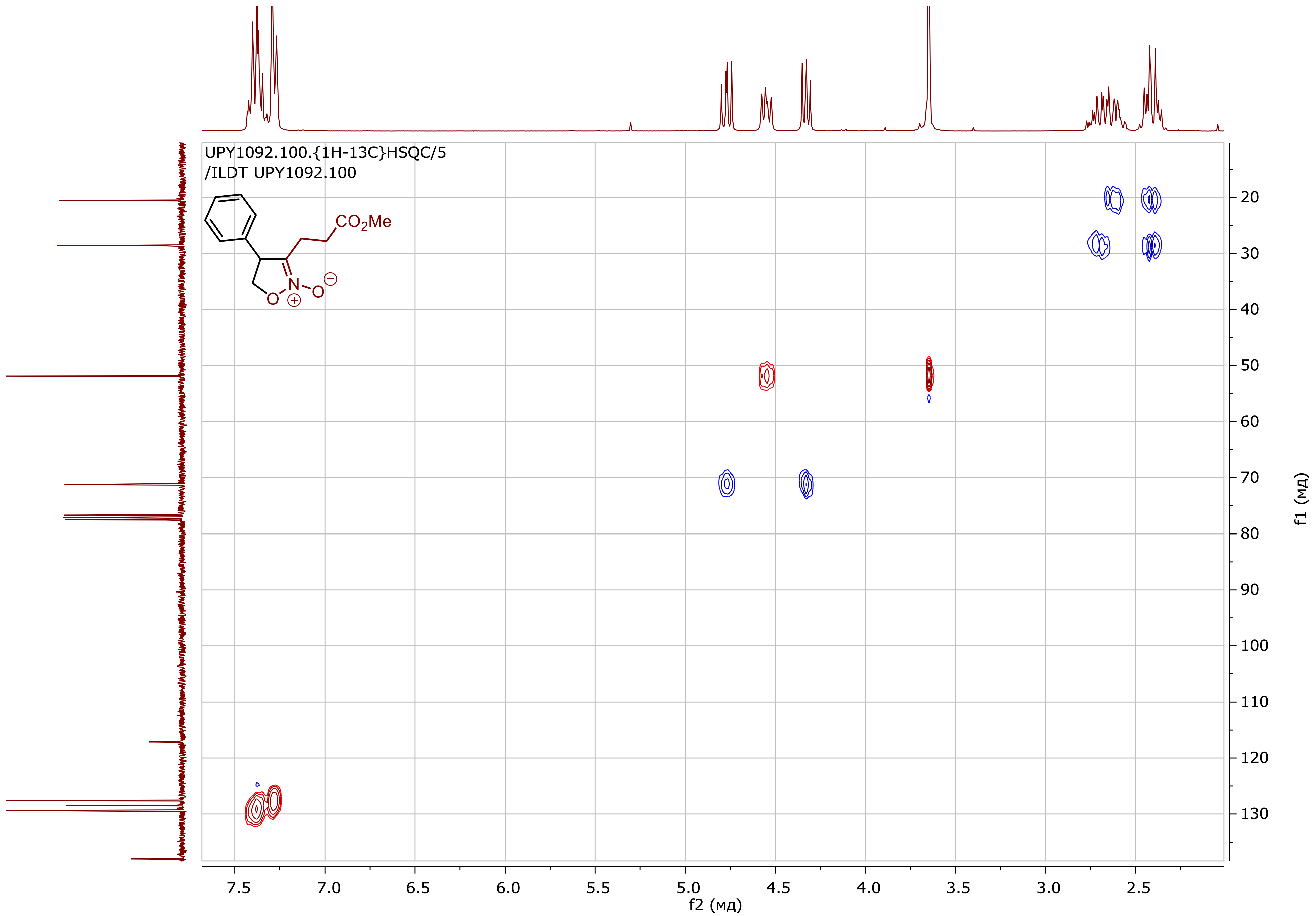
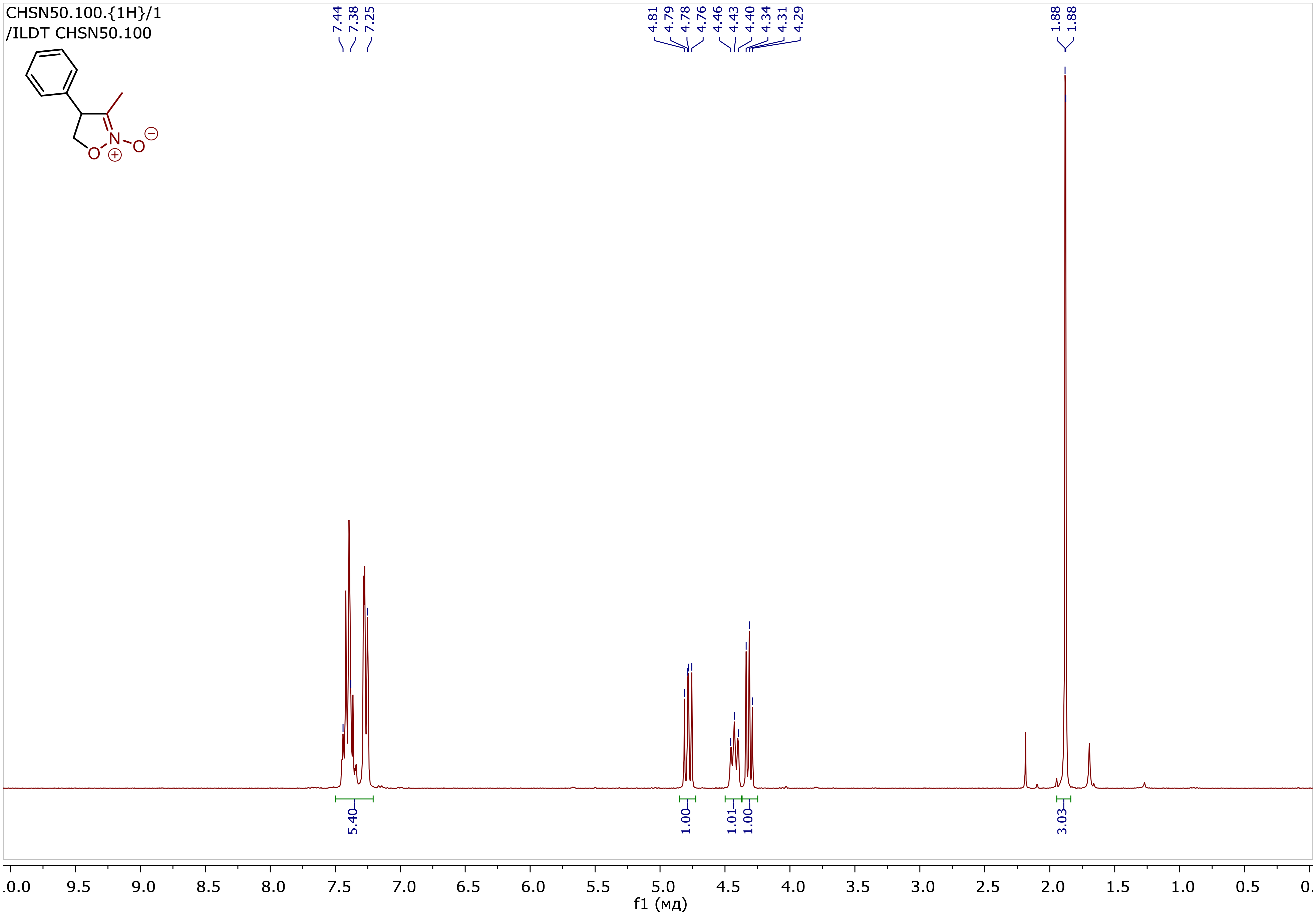
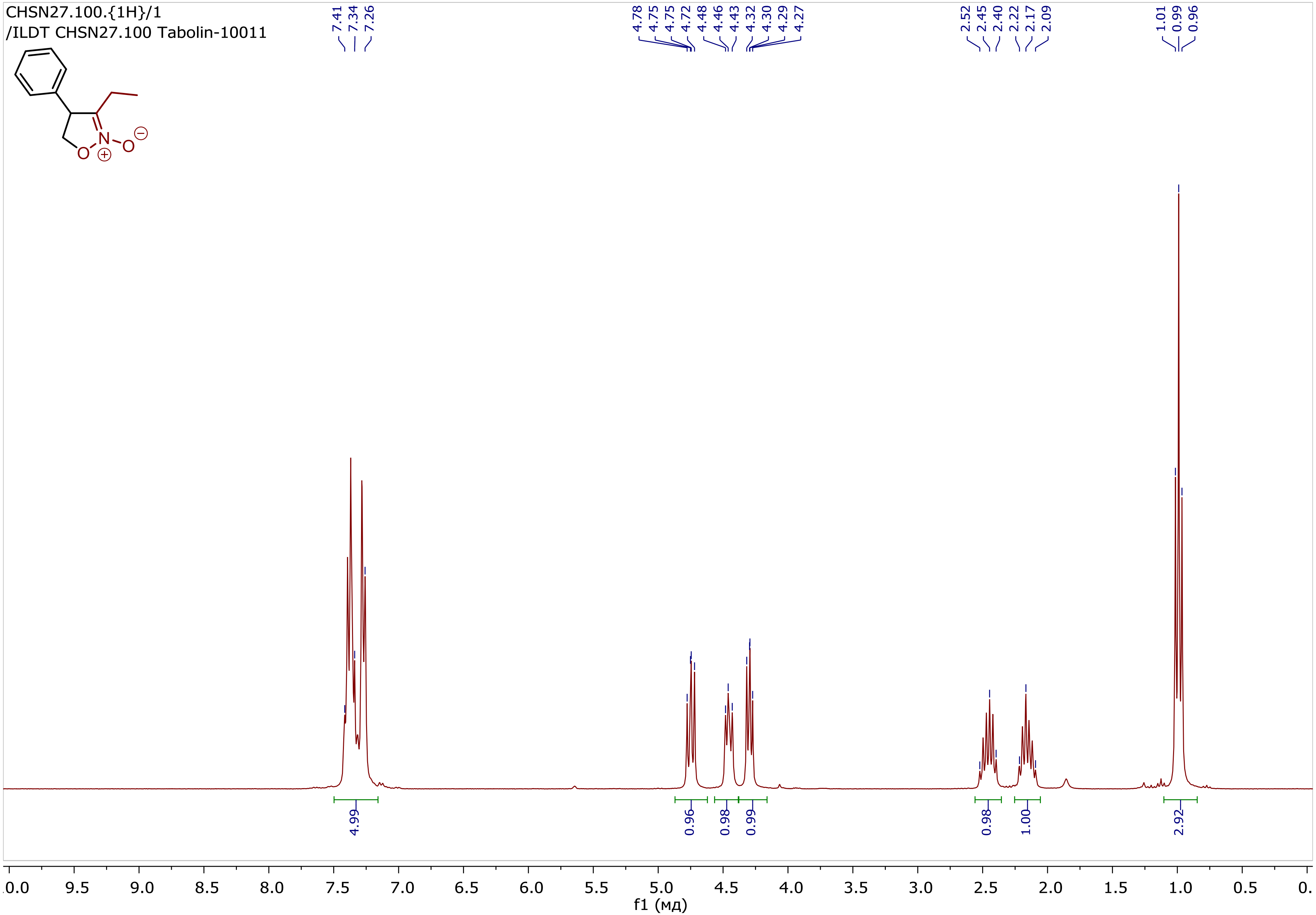


3-Methyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3b)



3-Ethyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3c)



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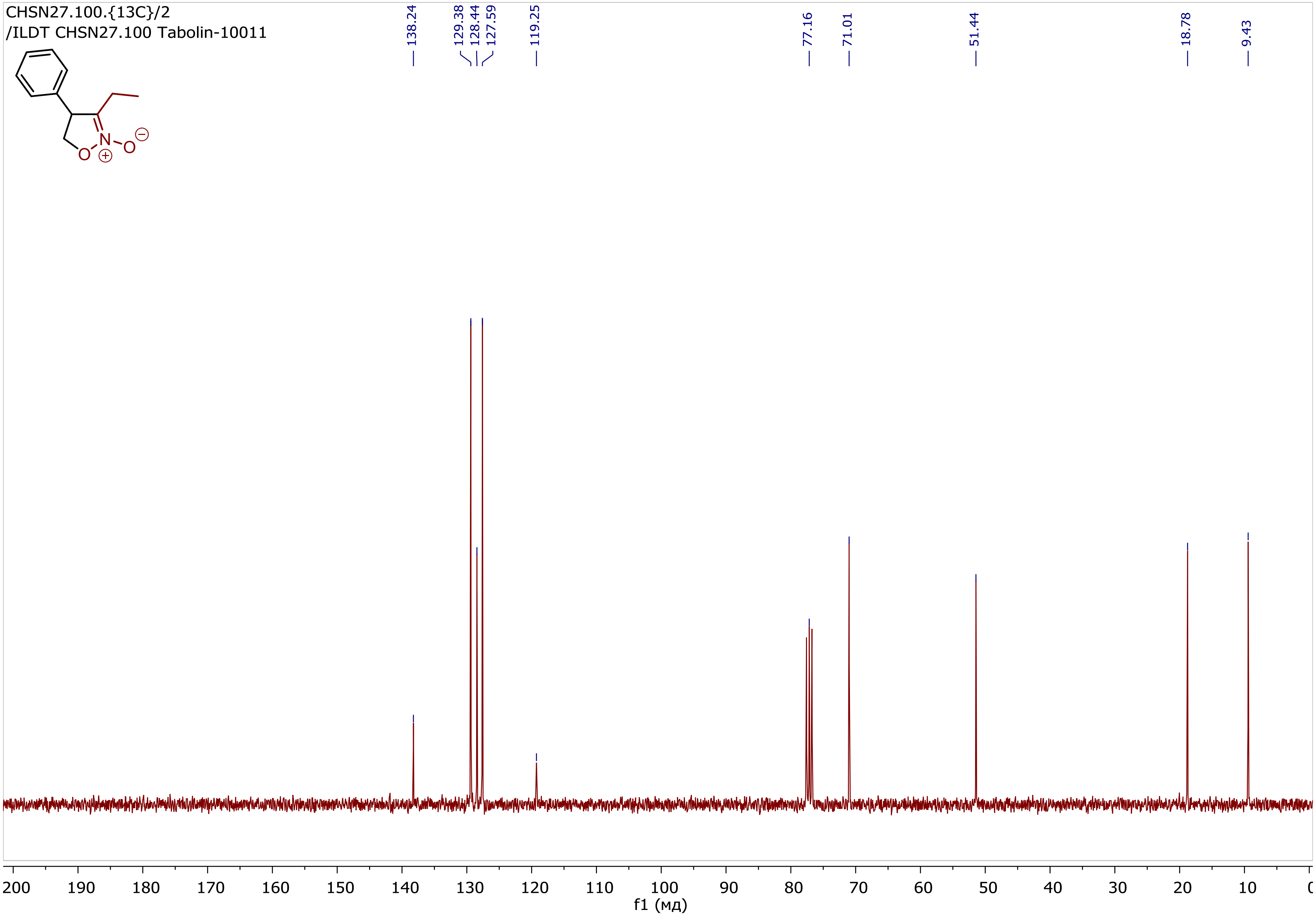

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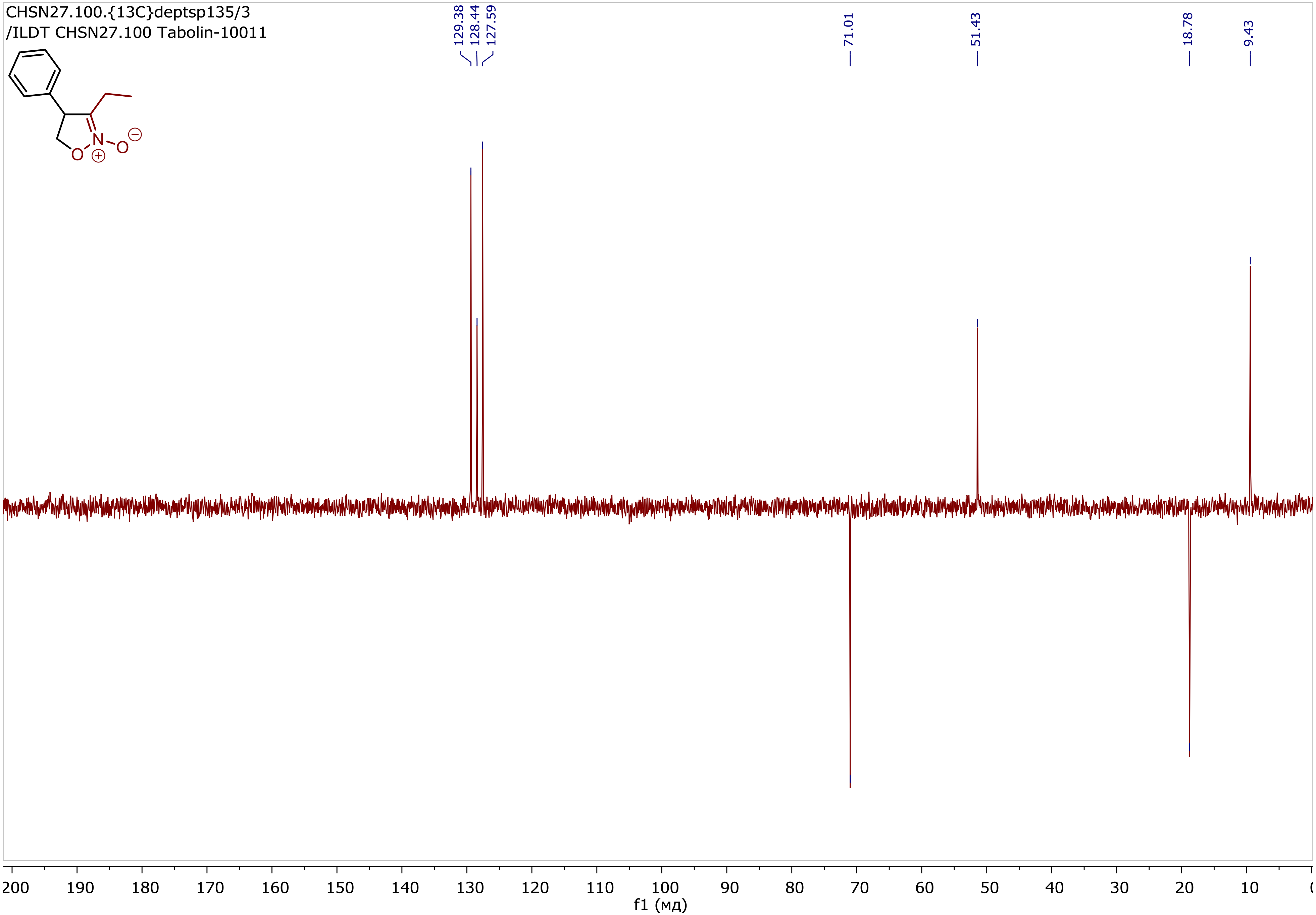

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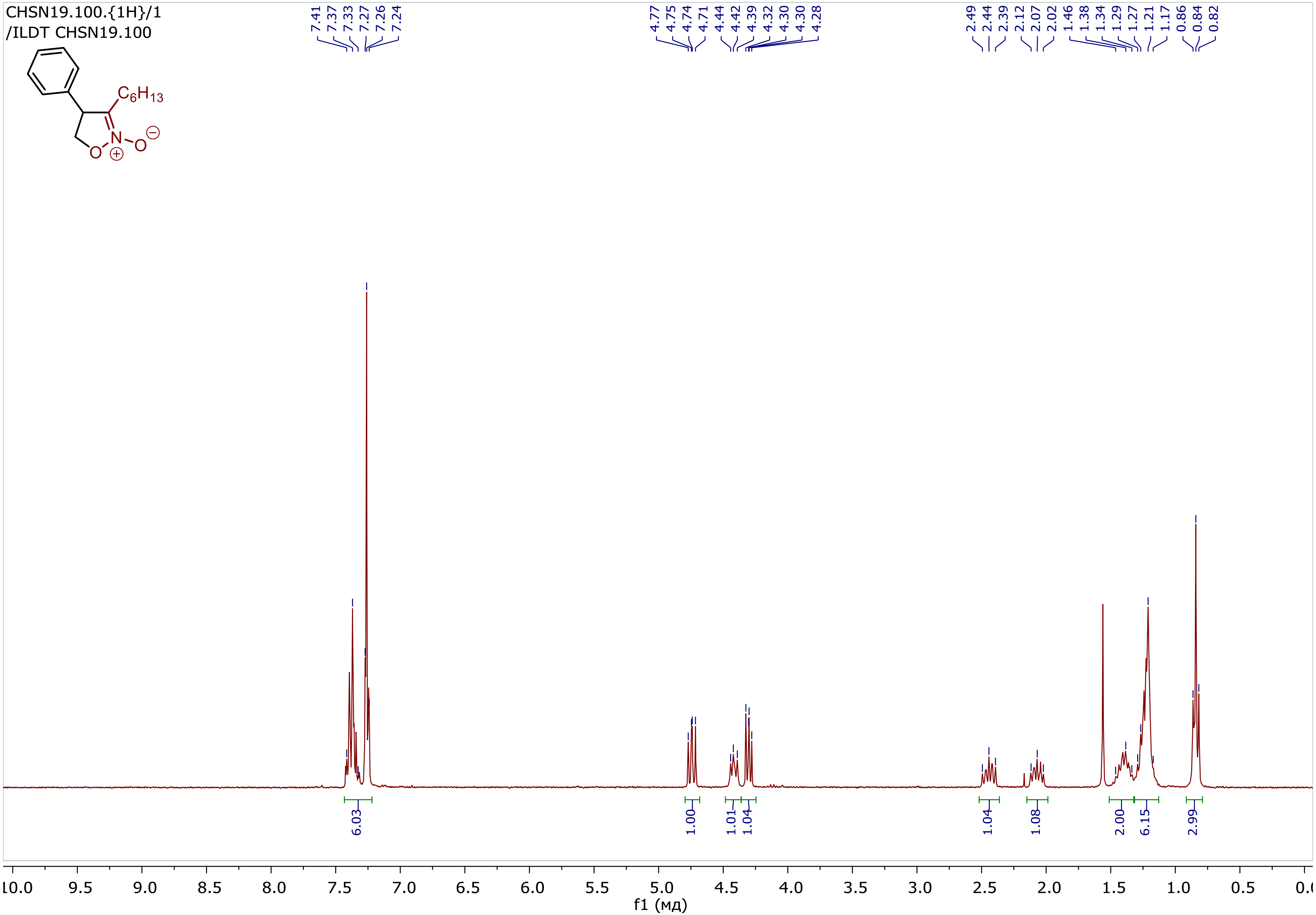
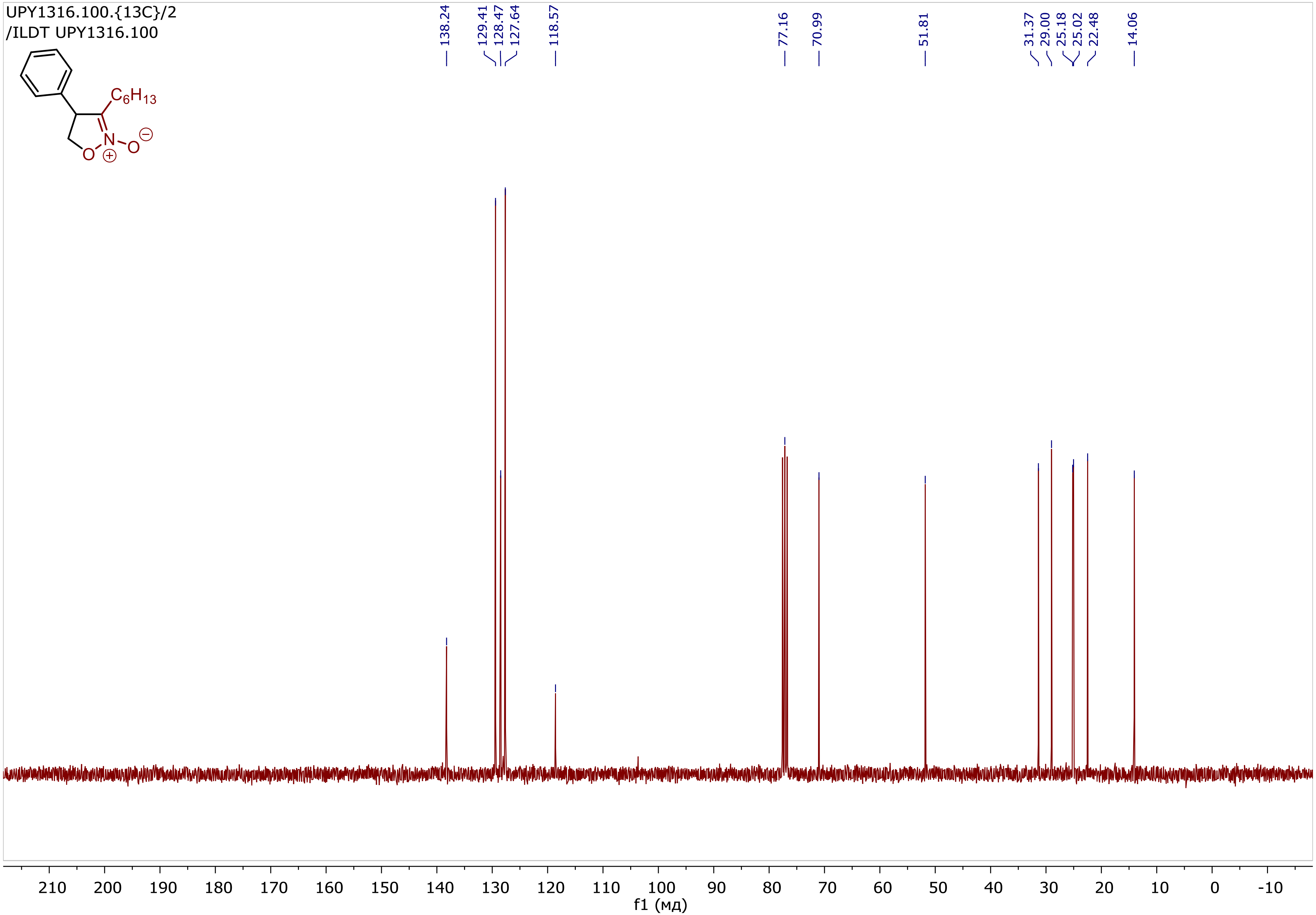
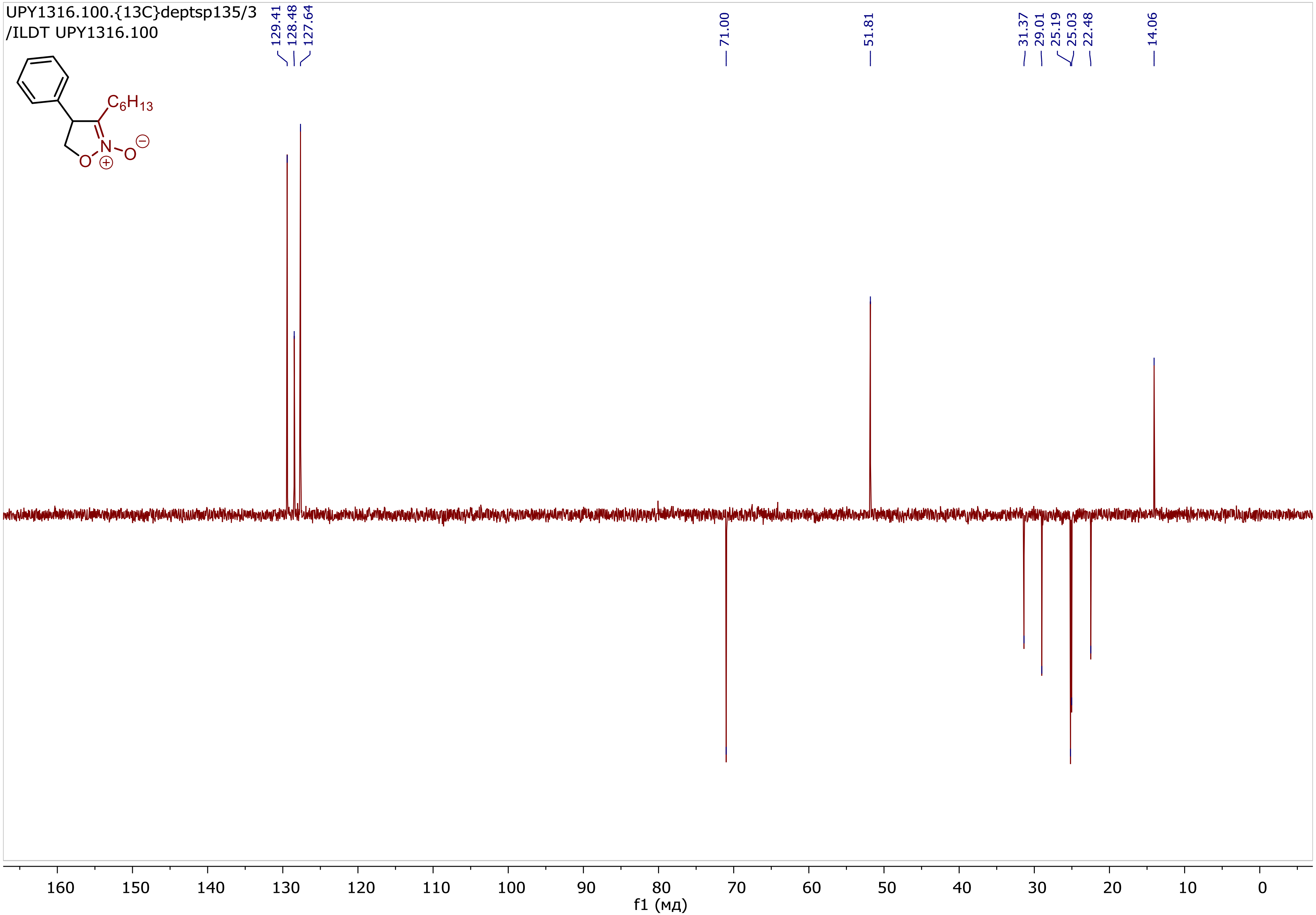


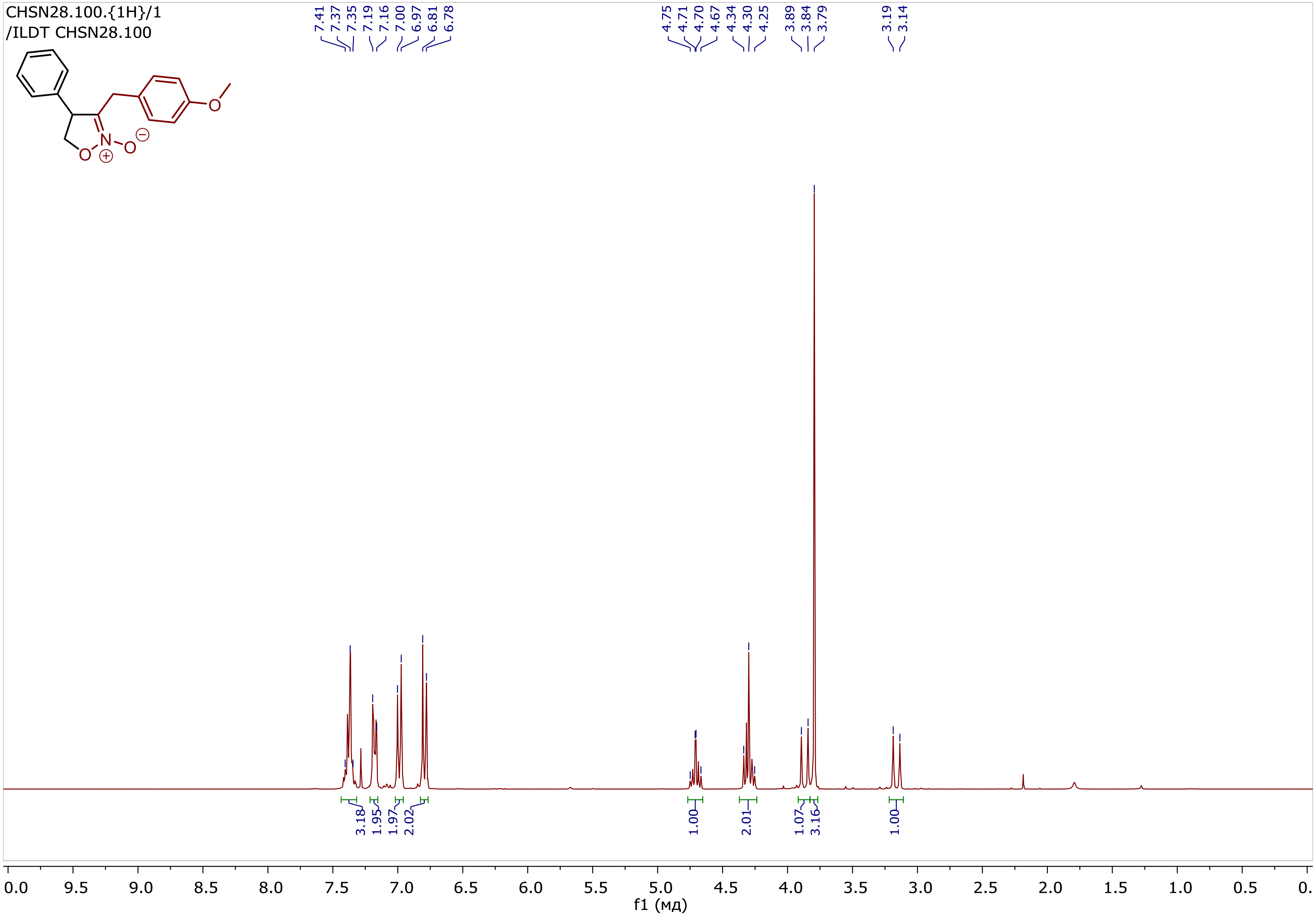
3-Hexyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3d)



3-Hexyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3d)



3-(4-Methoxybenzyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3e)



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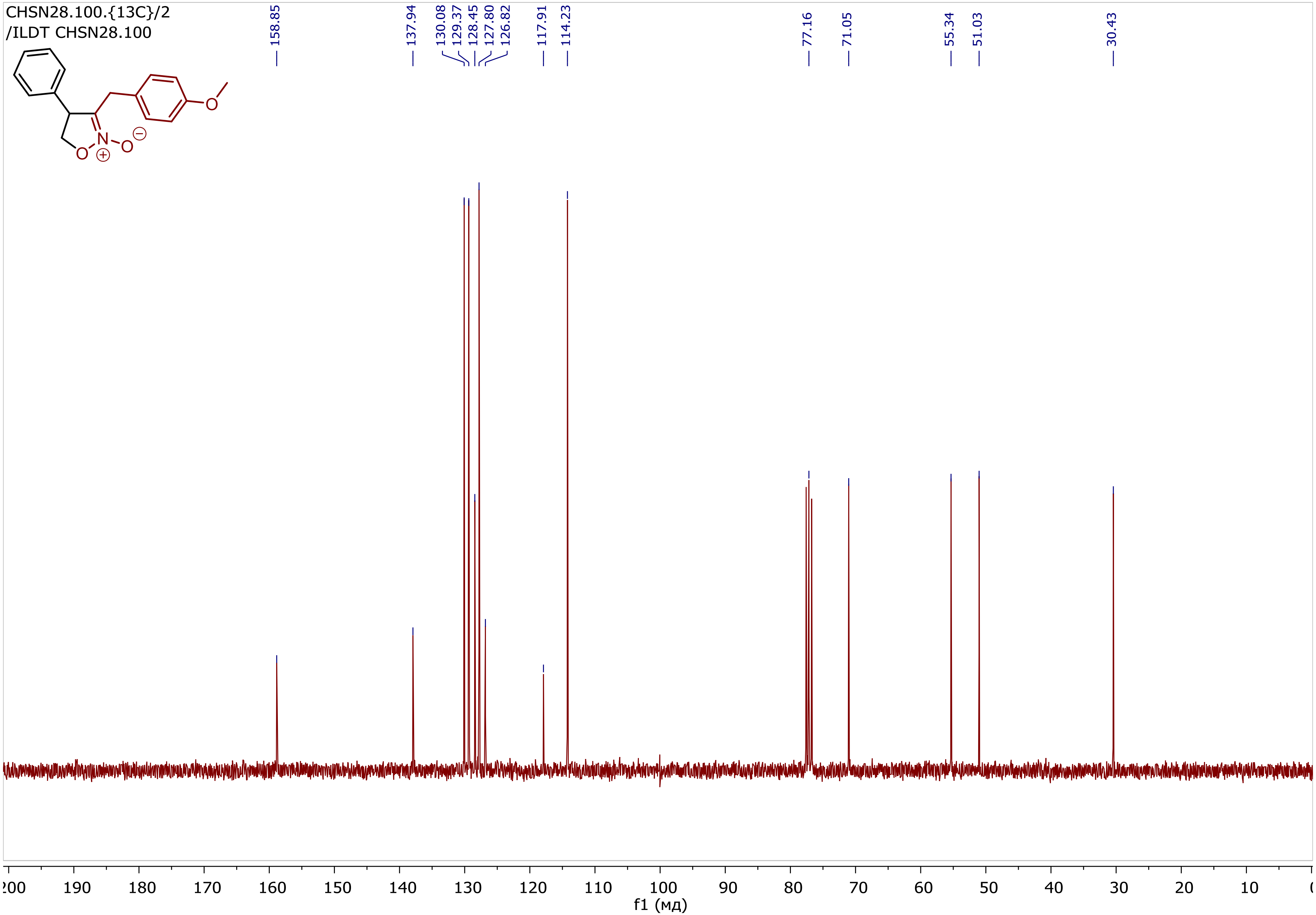

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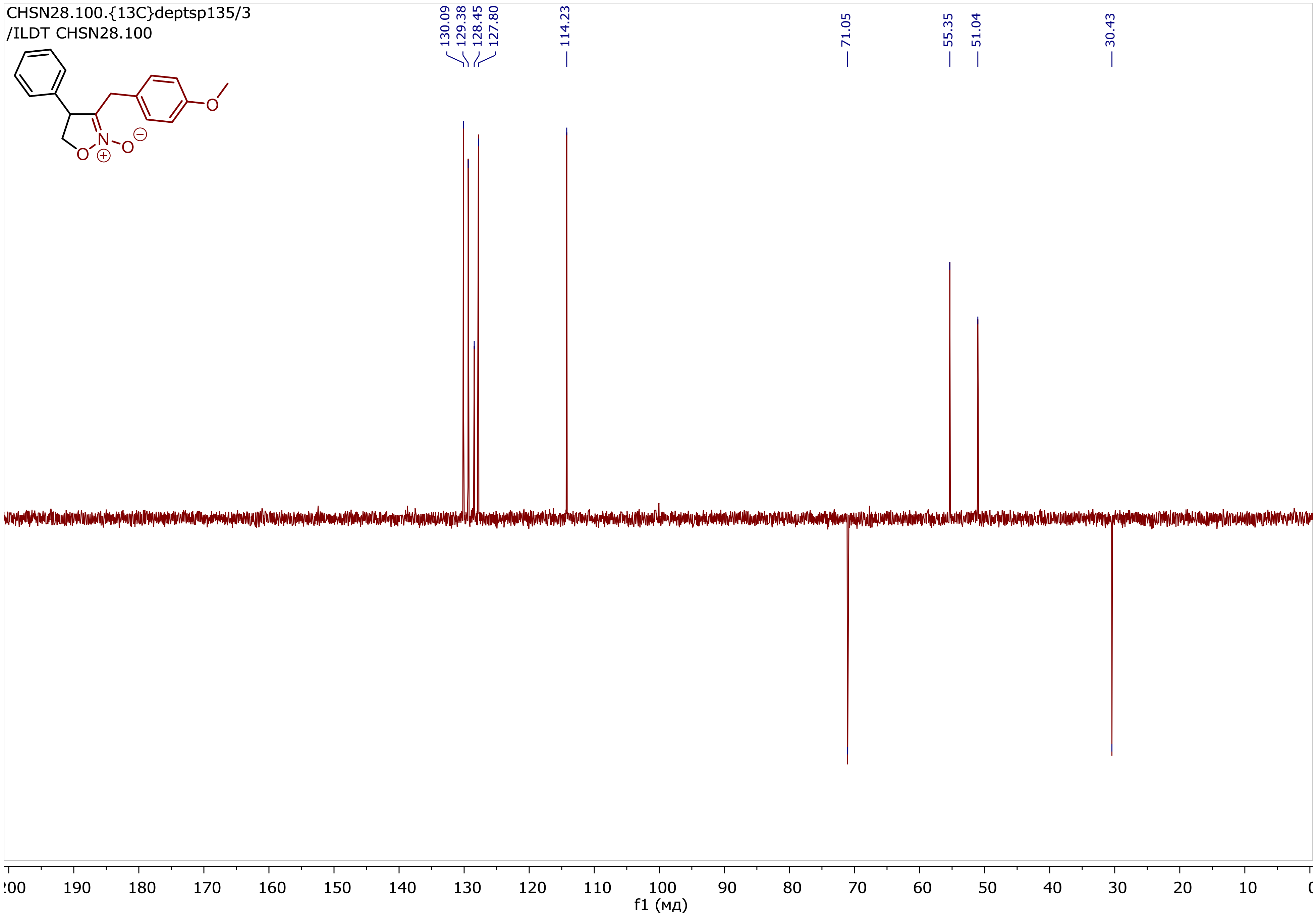
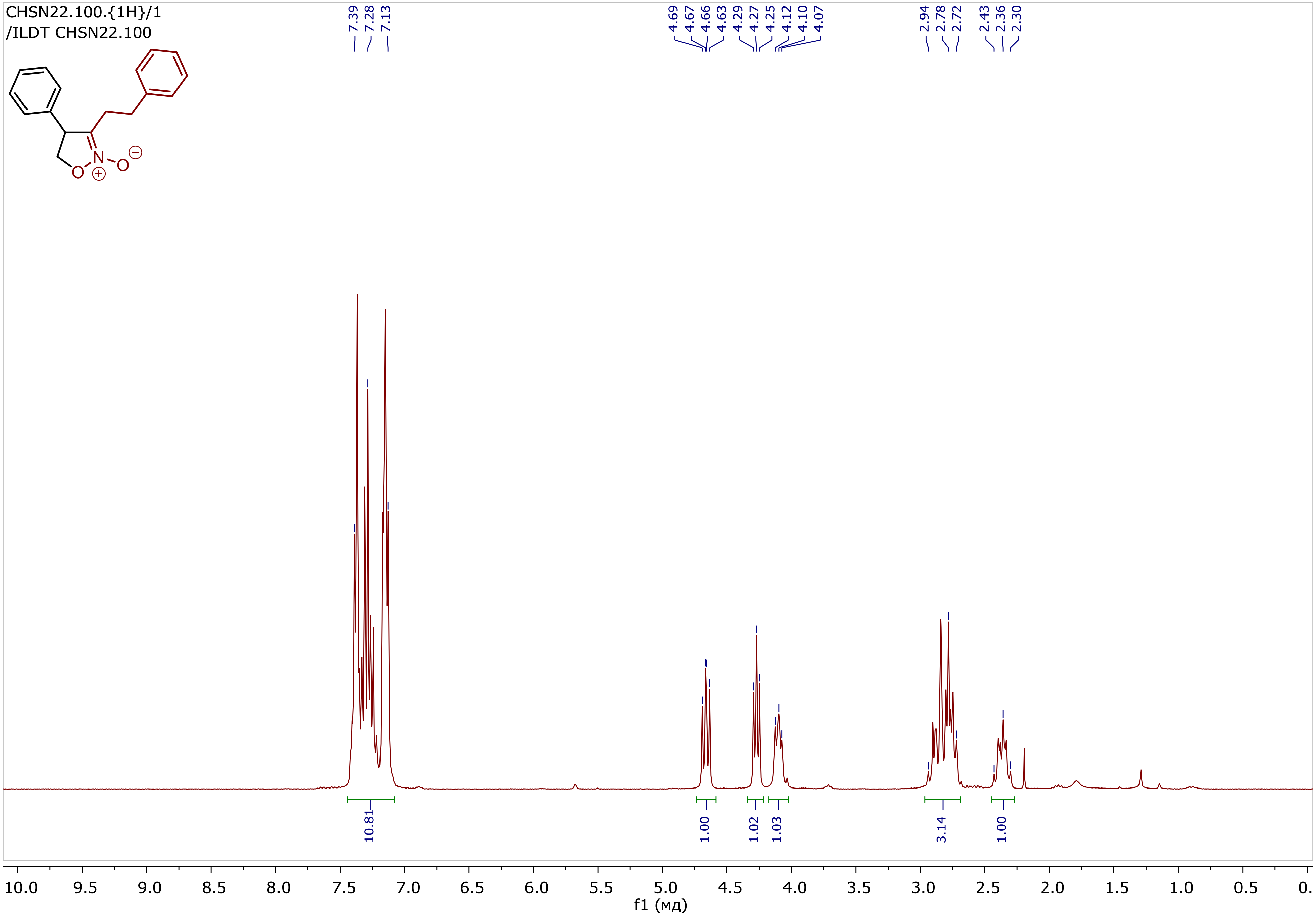
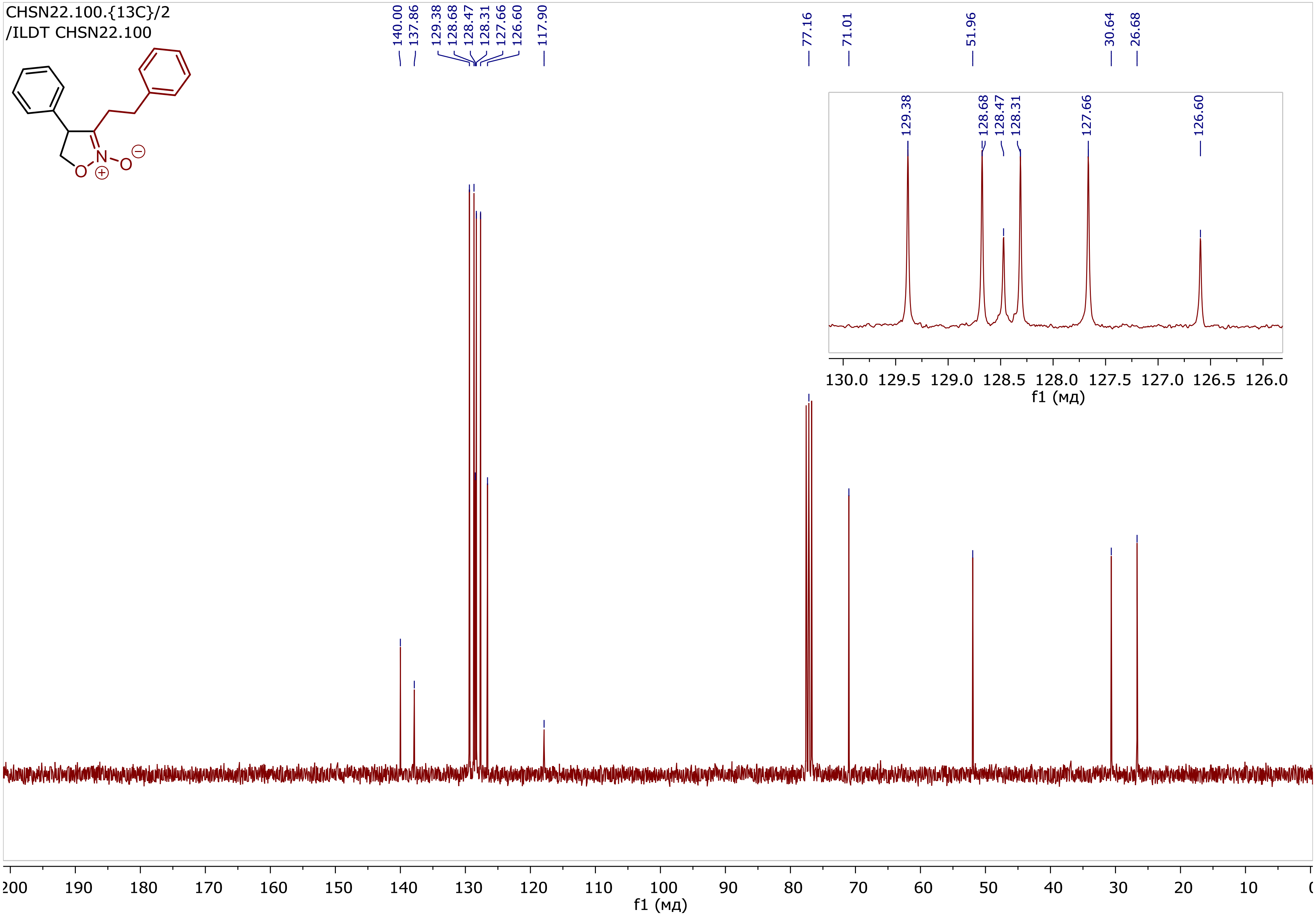


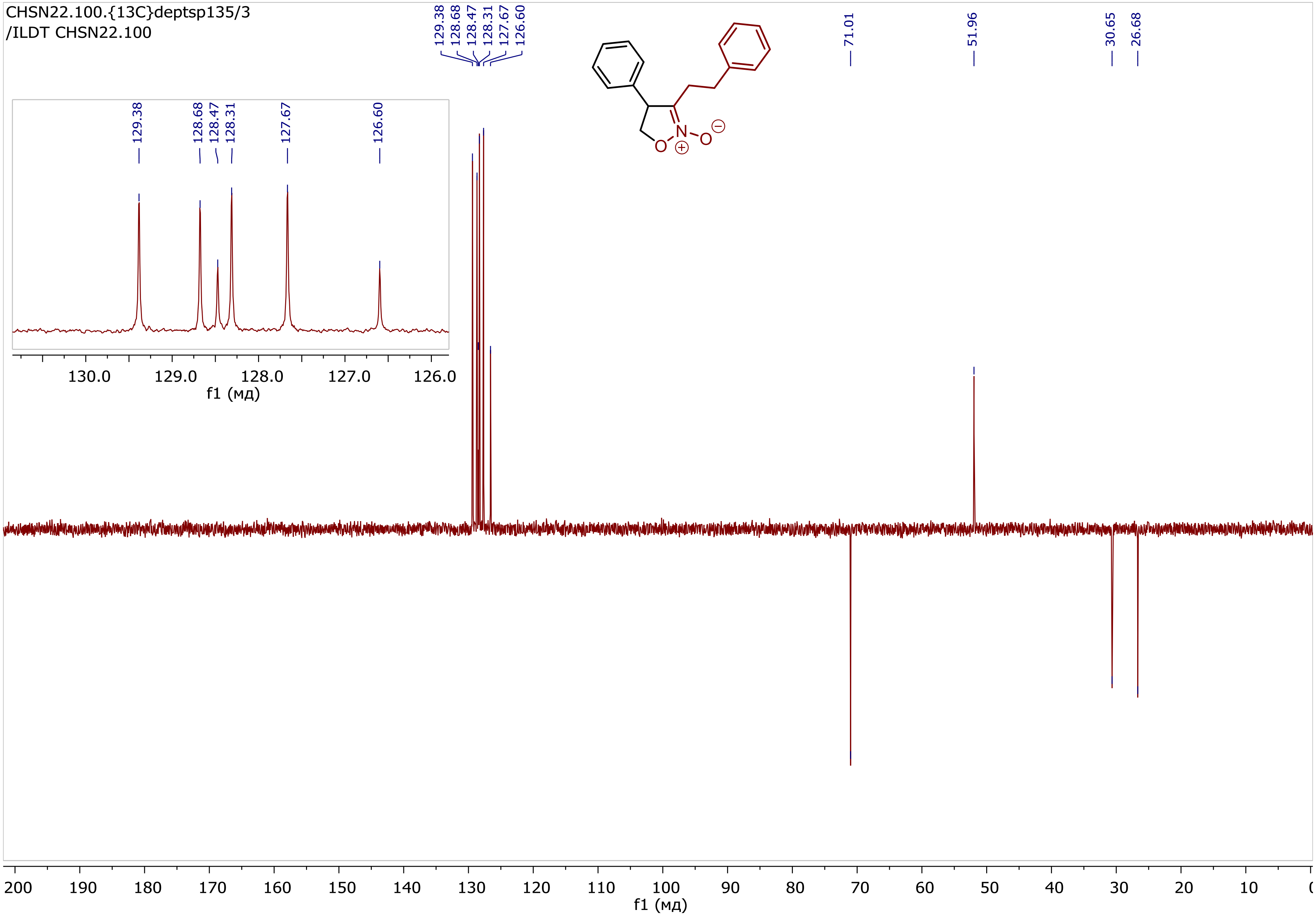
3-Phenethyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3f)



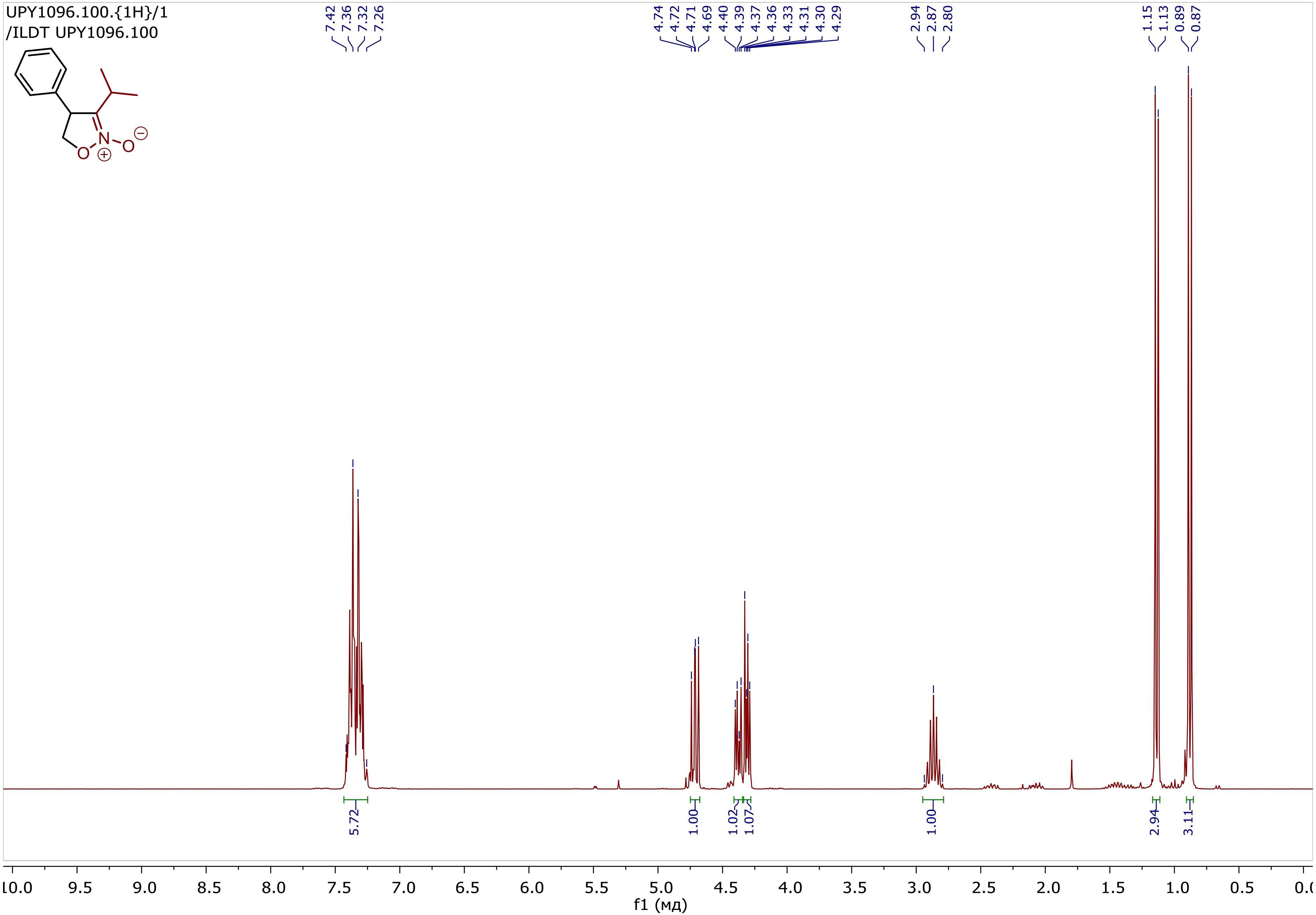
3-Phenethyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3f)



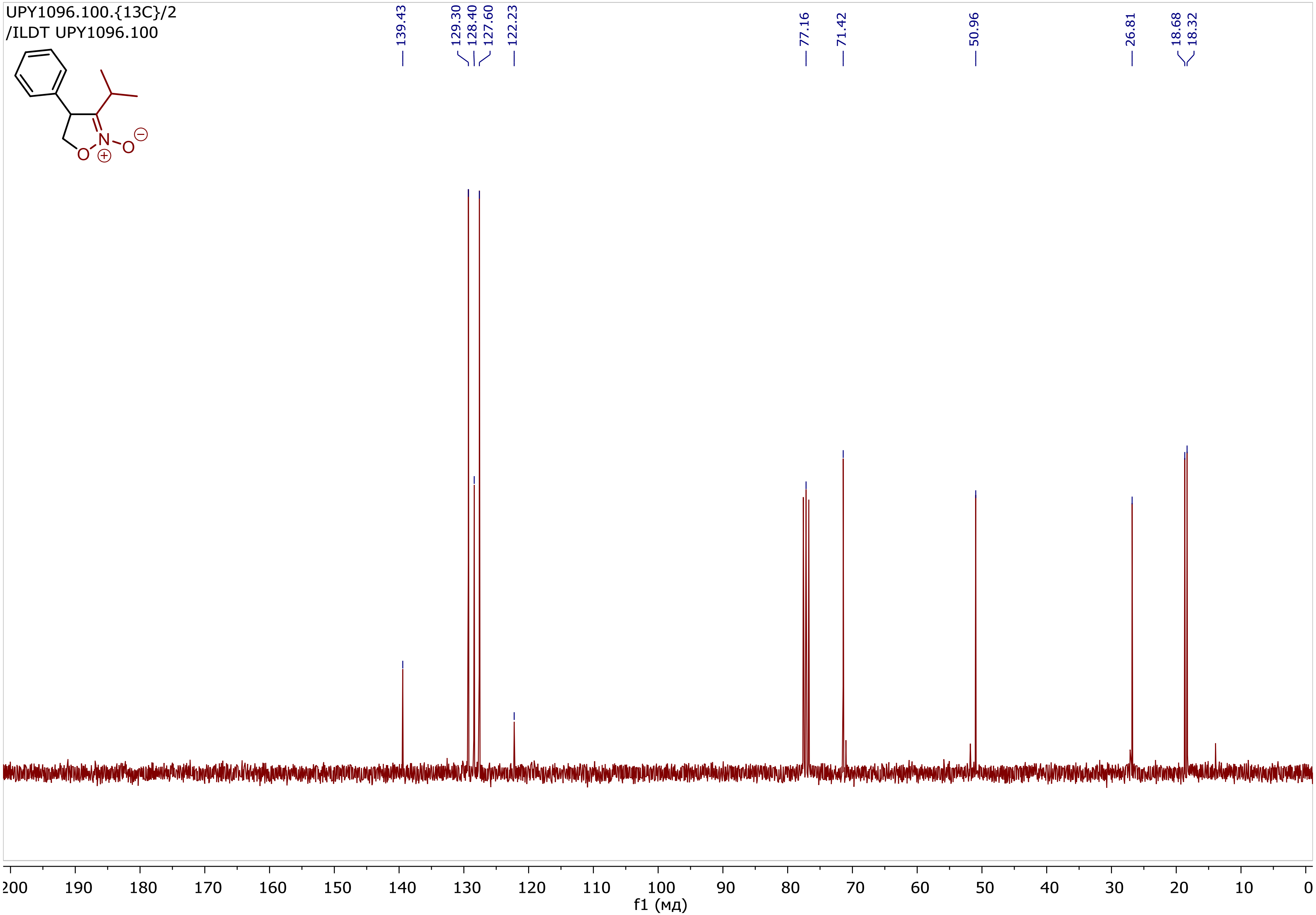
3-Phenethyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3f)



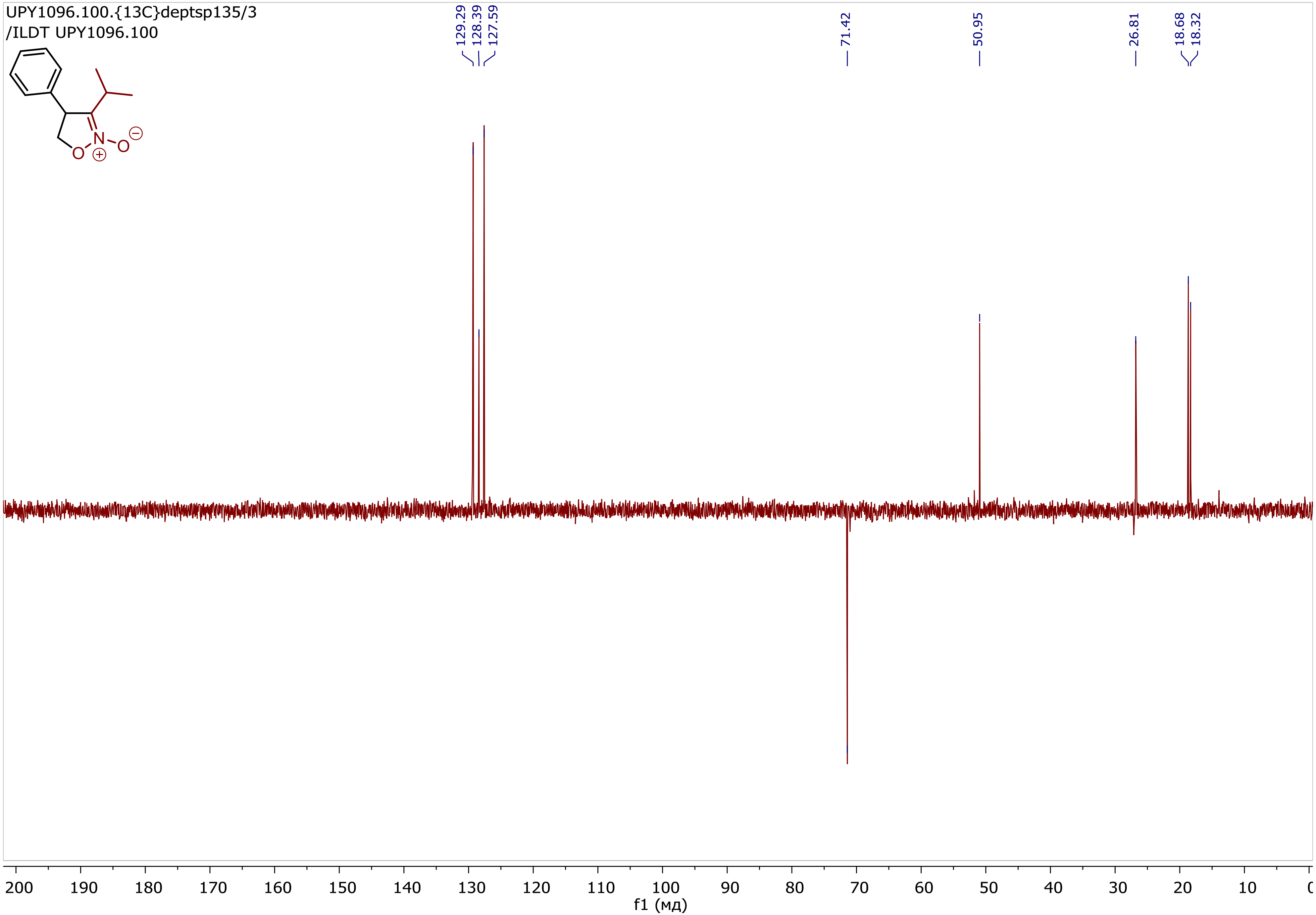
3-Isopropyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3g)



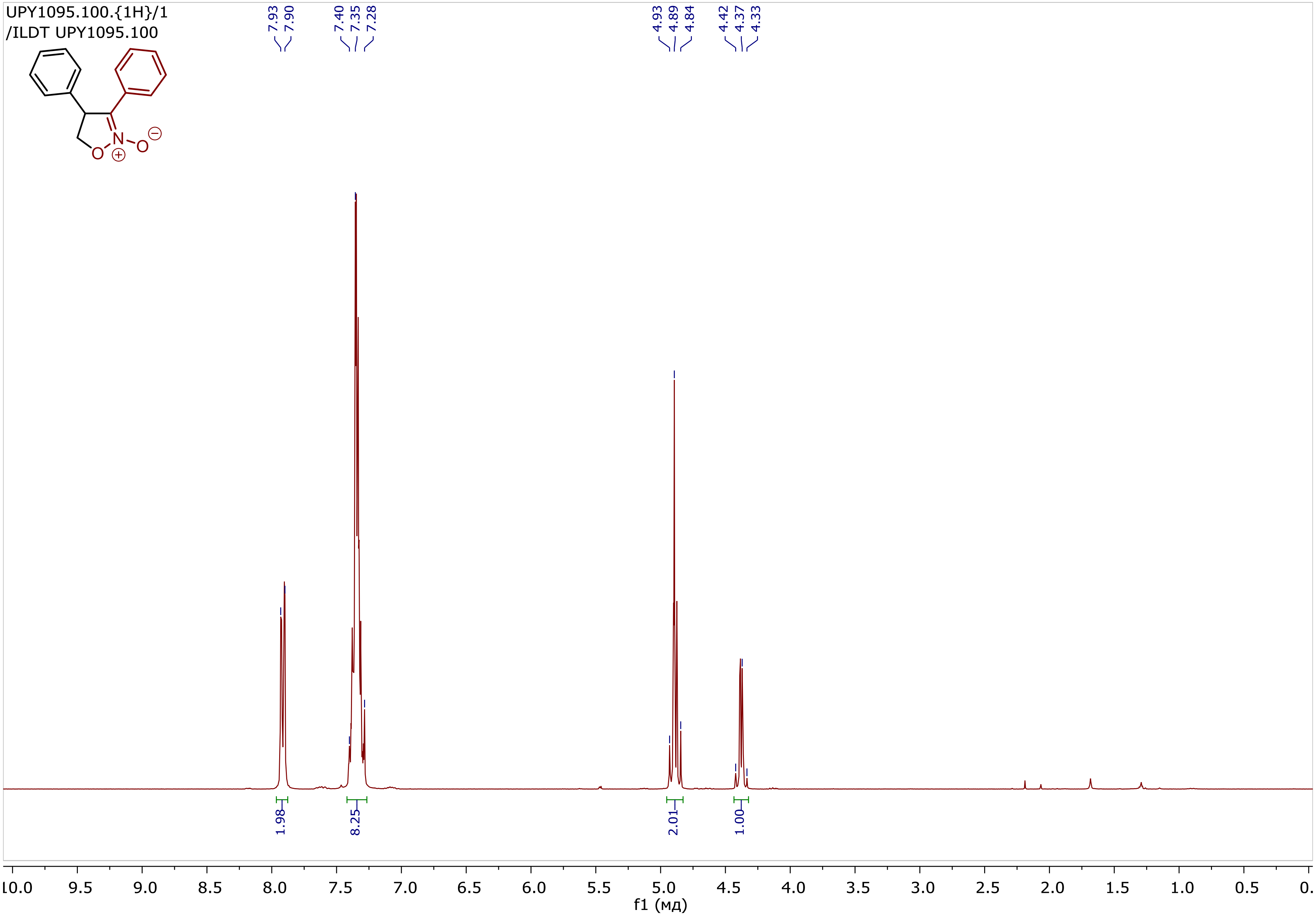
3-Isopropyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3g)



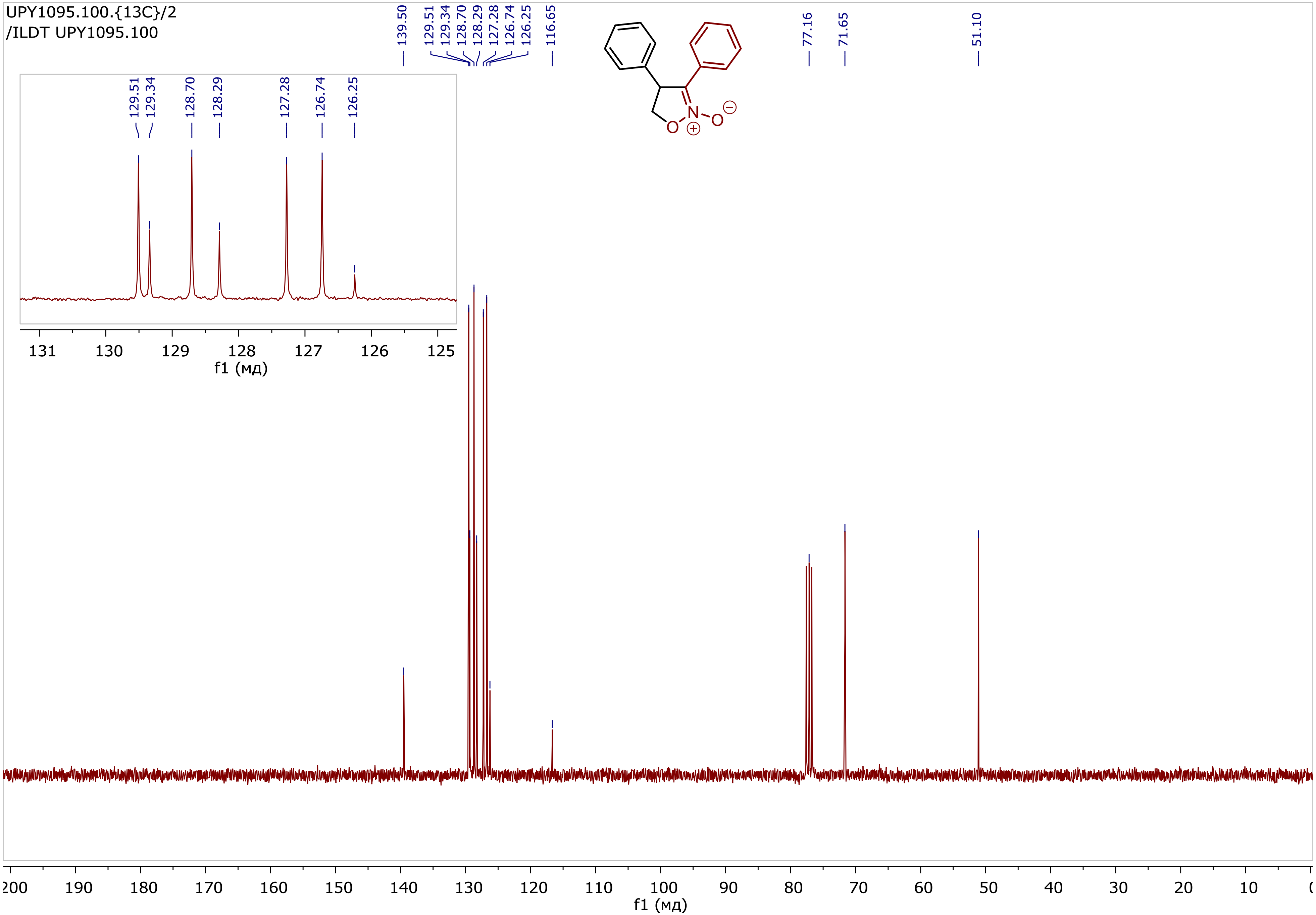
3-Isopropyl-4-phenyl-4,5-dihydroisoxazole 2-oxide (3g)



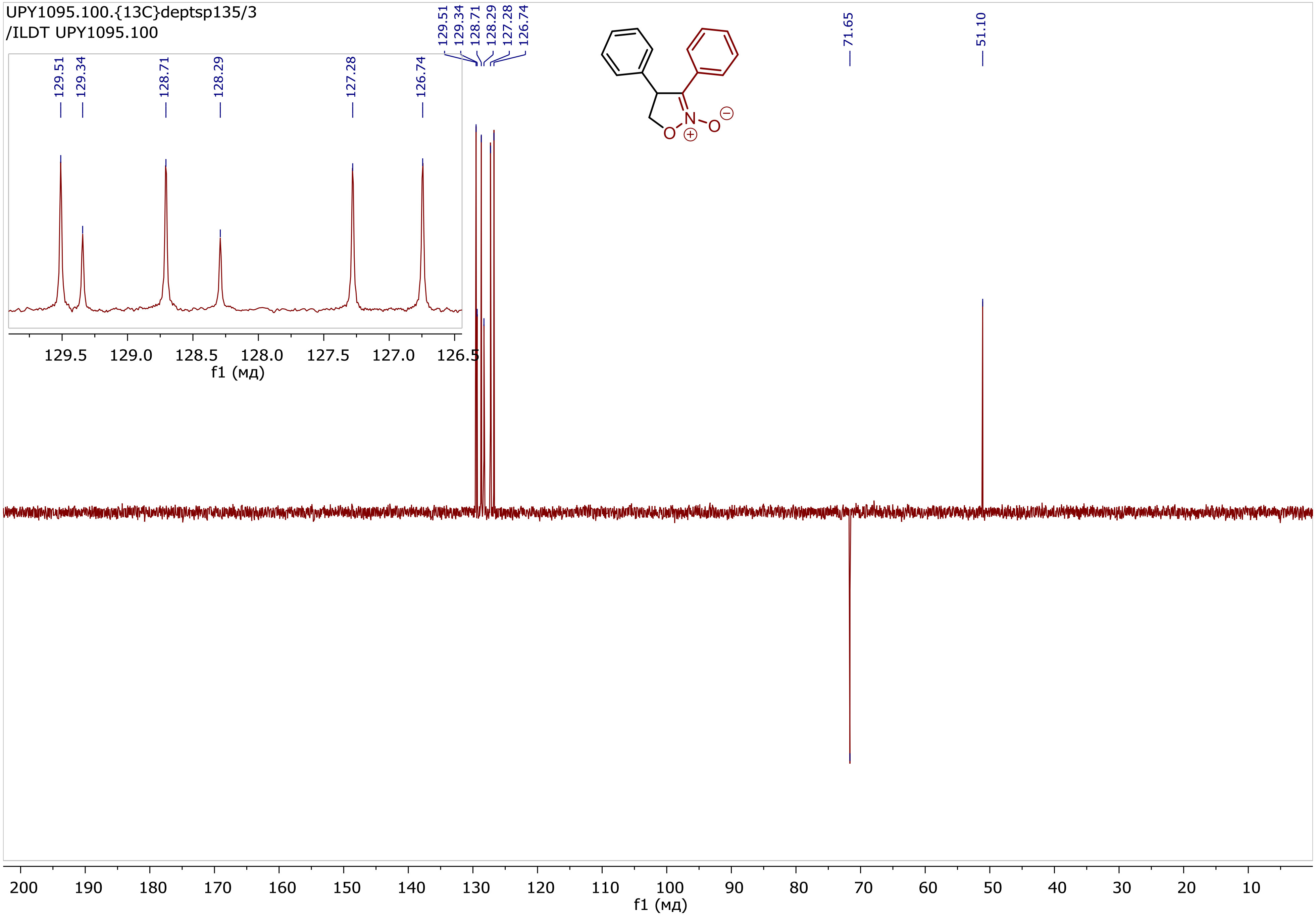
3,4-Diphenyl-4,5-dihydroisoxazole 2-oxide (3h)



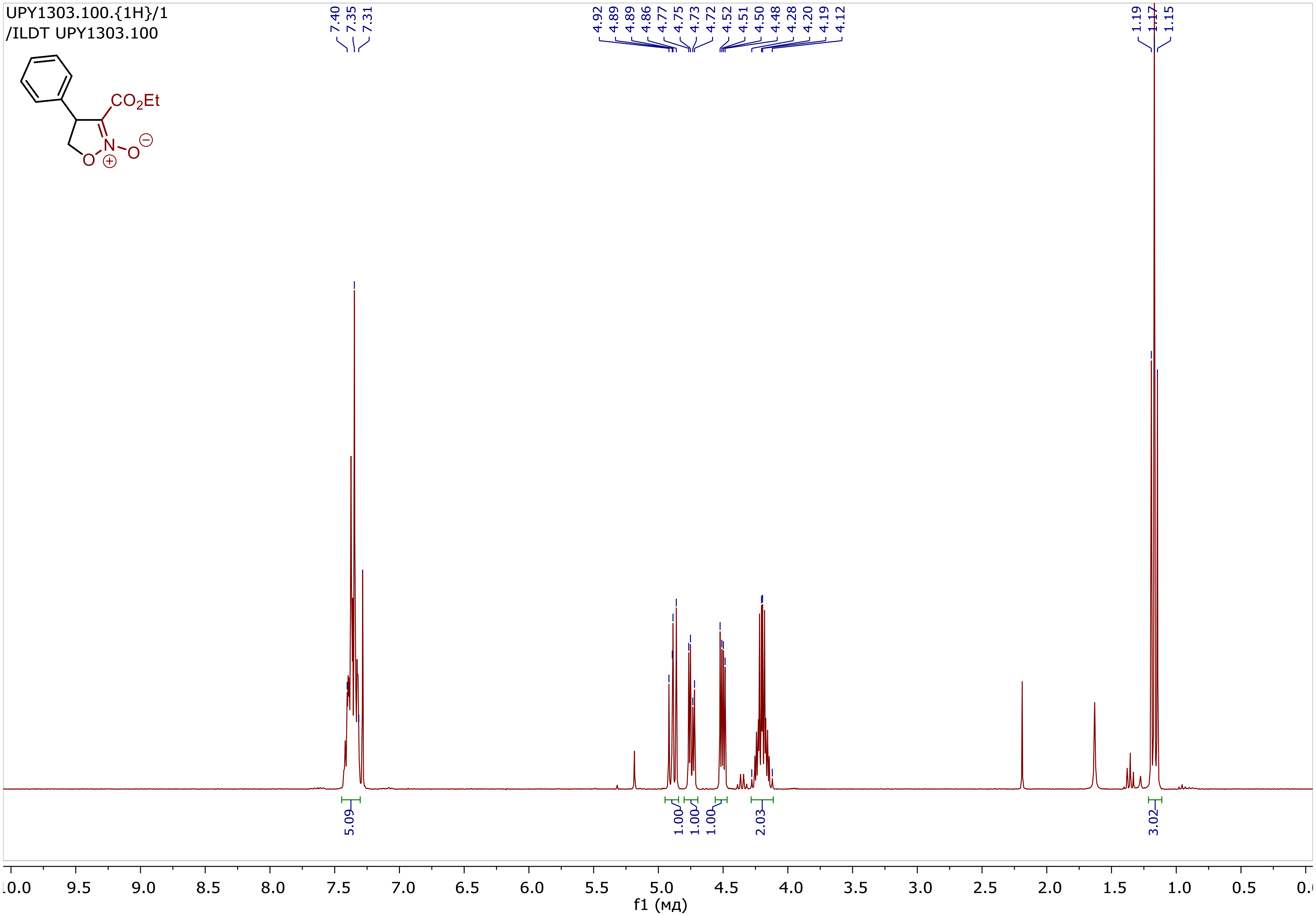
3,4-Diphenyl-4,5-dihydroisoxazole 2-oxide (3h)



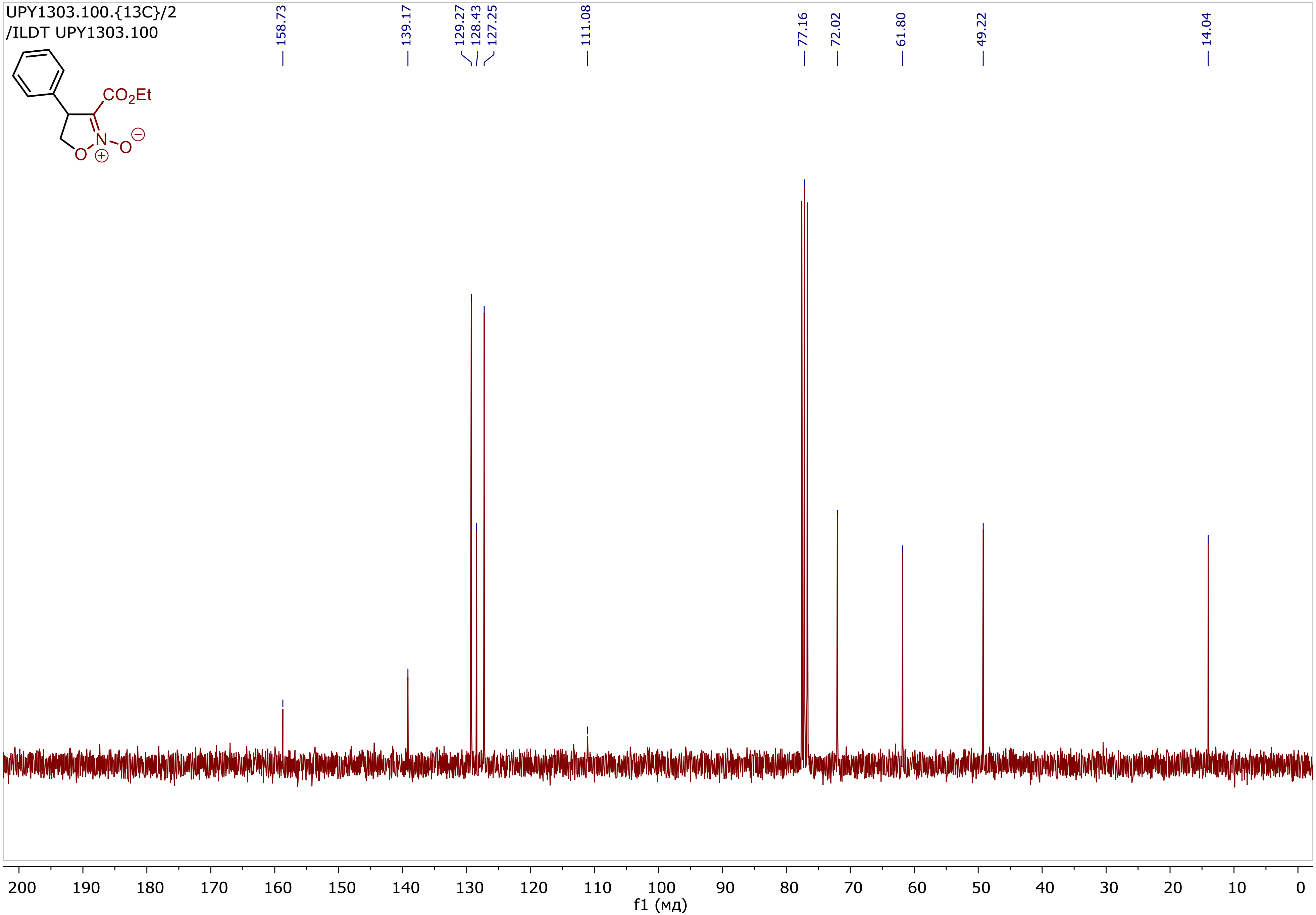
3,4-Diphenyl-4,5-dihydroisoxazole 2-oxide (3h)



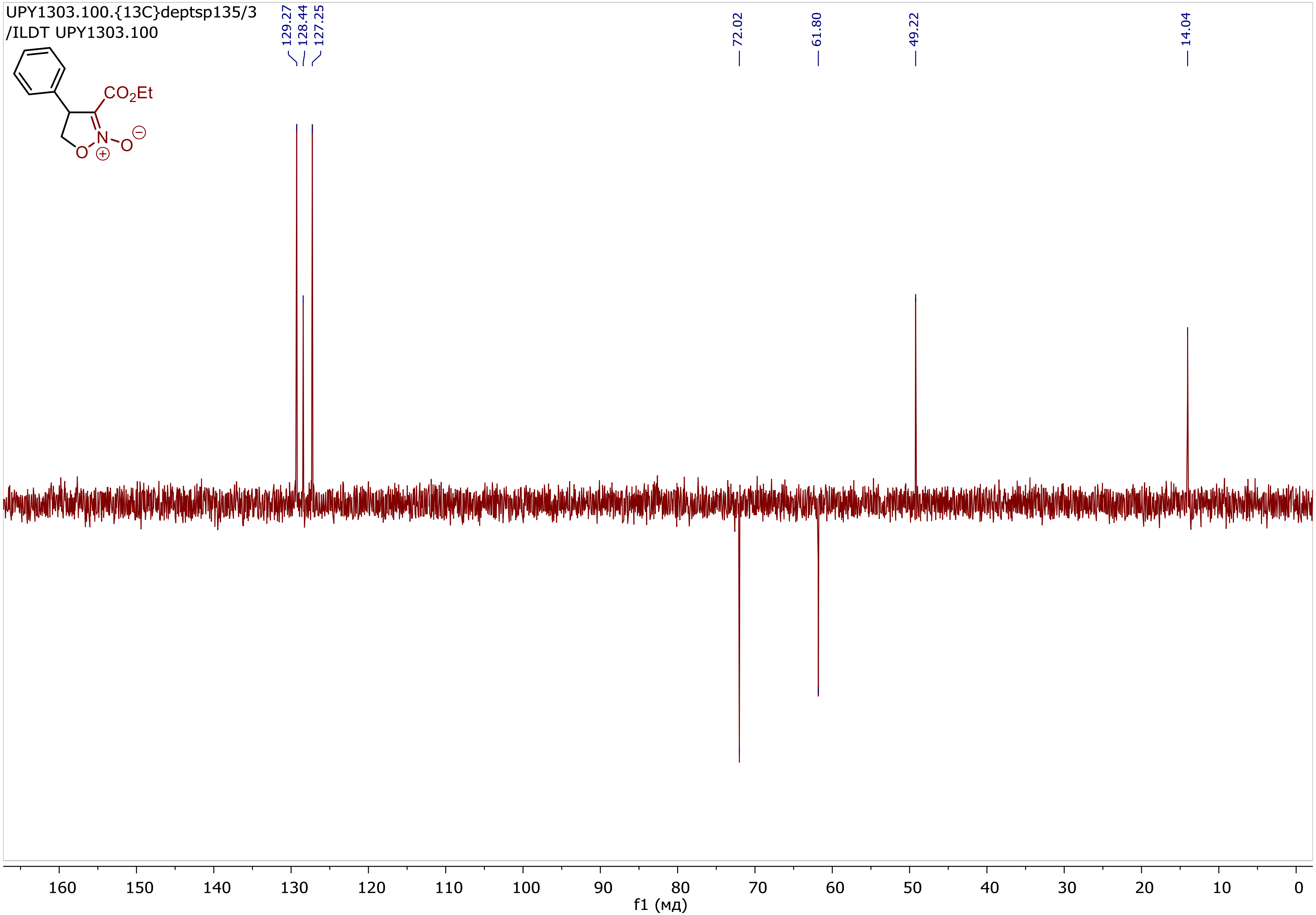
3-(Ethoxycarbonyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3i)



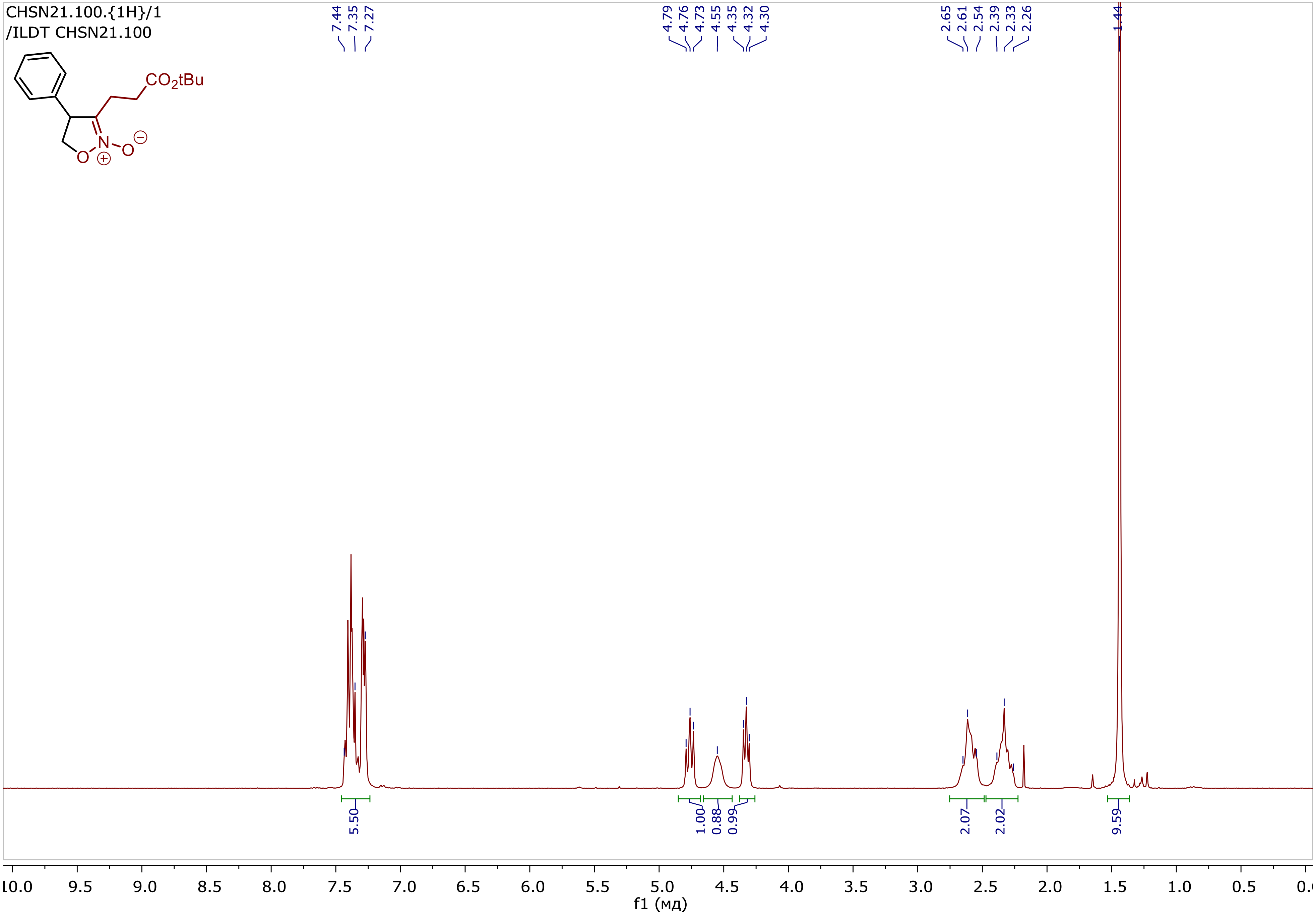
3-(Ethoxycarbonyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3i)



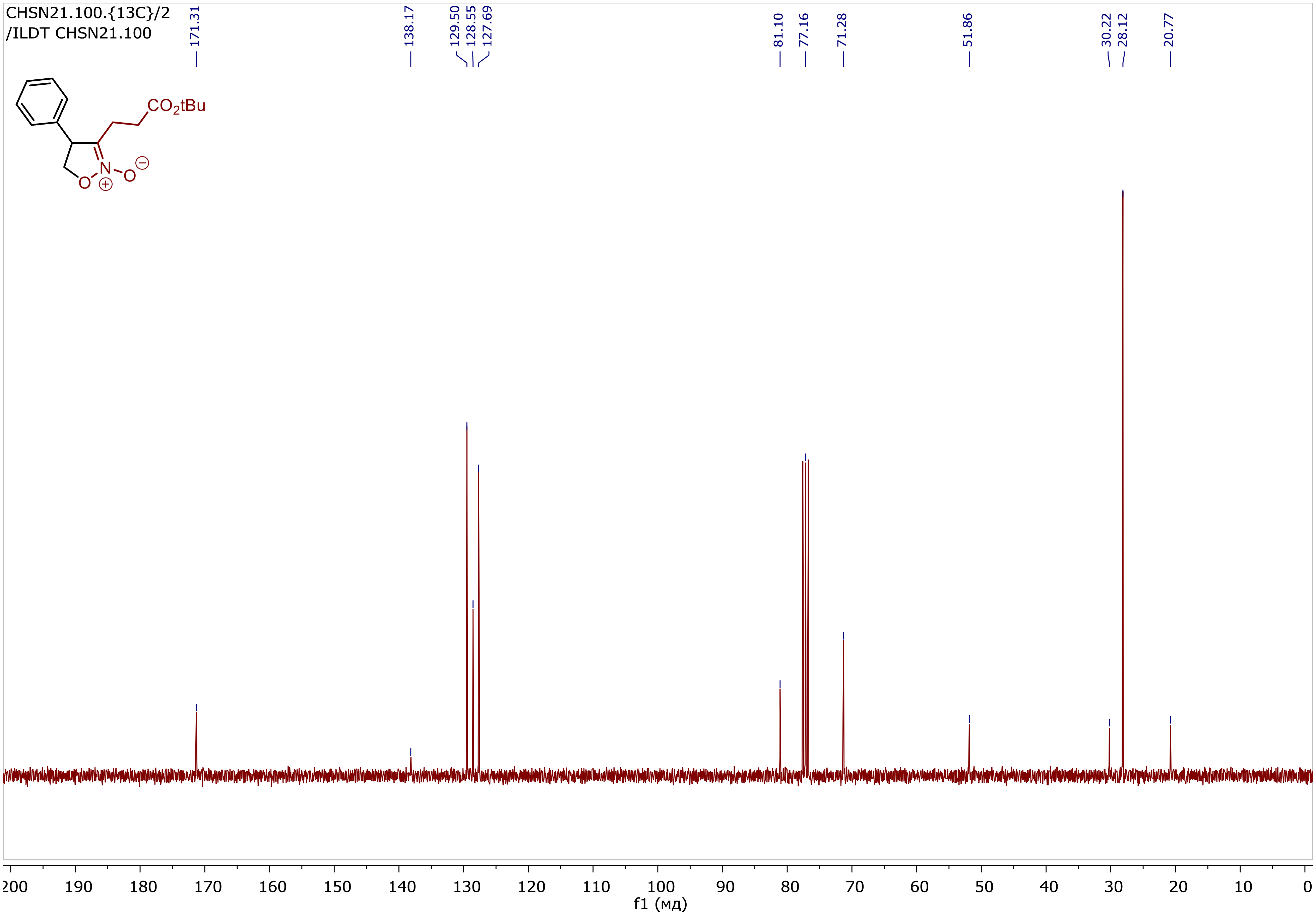
3-(Ethoxycarbonyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3i)



3-(3-(*Tert*-butoxy)-3-oxopropyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3j)



3-(3-(*Tert*-butoxy)-3-oxopropyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3j)



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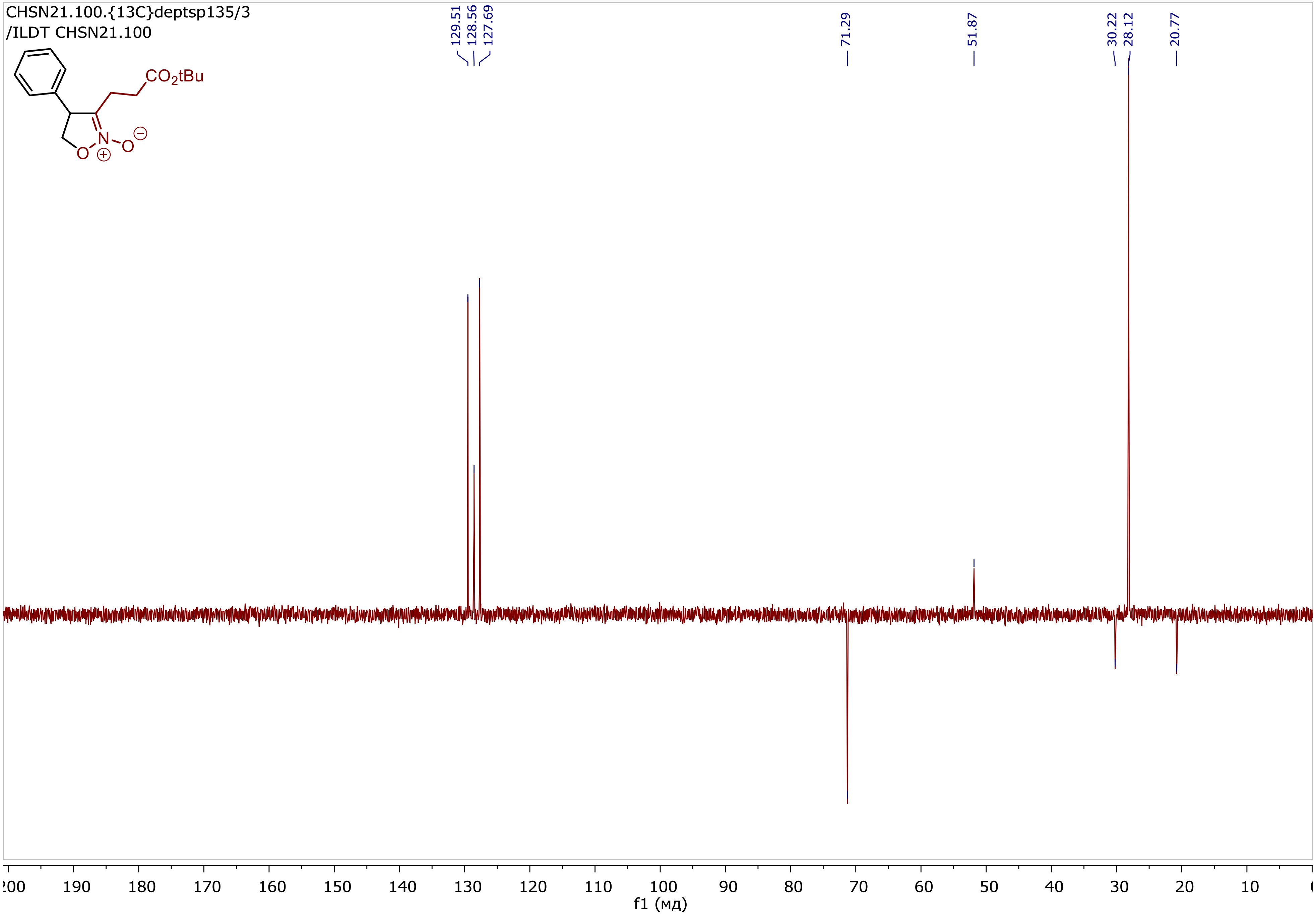
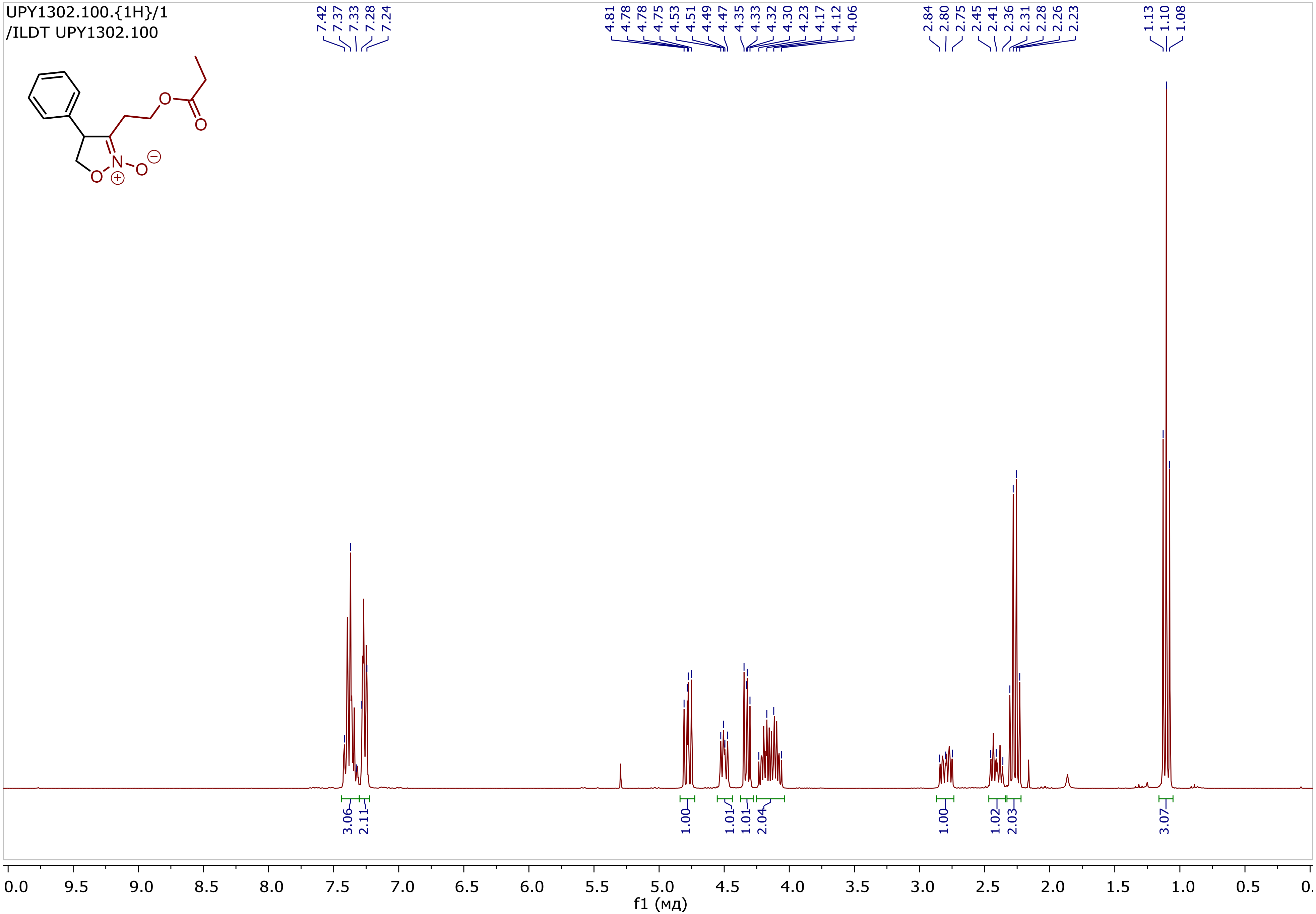
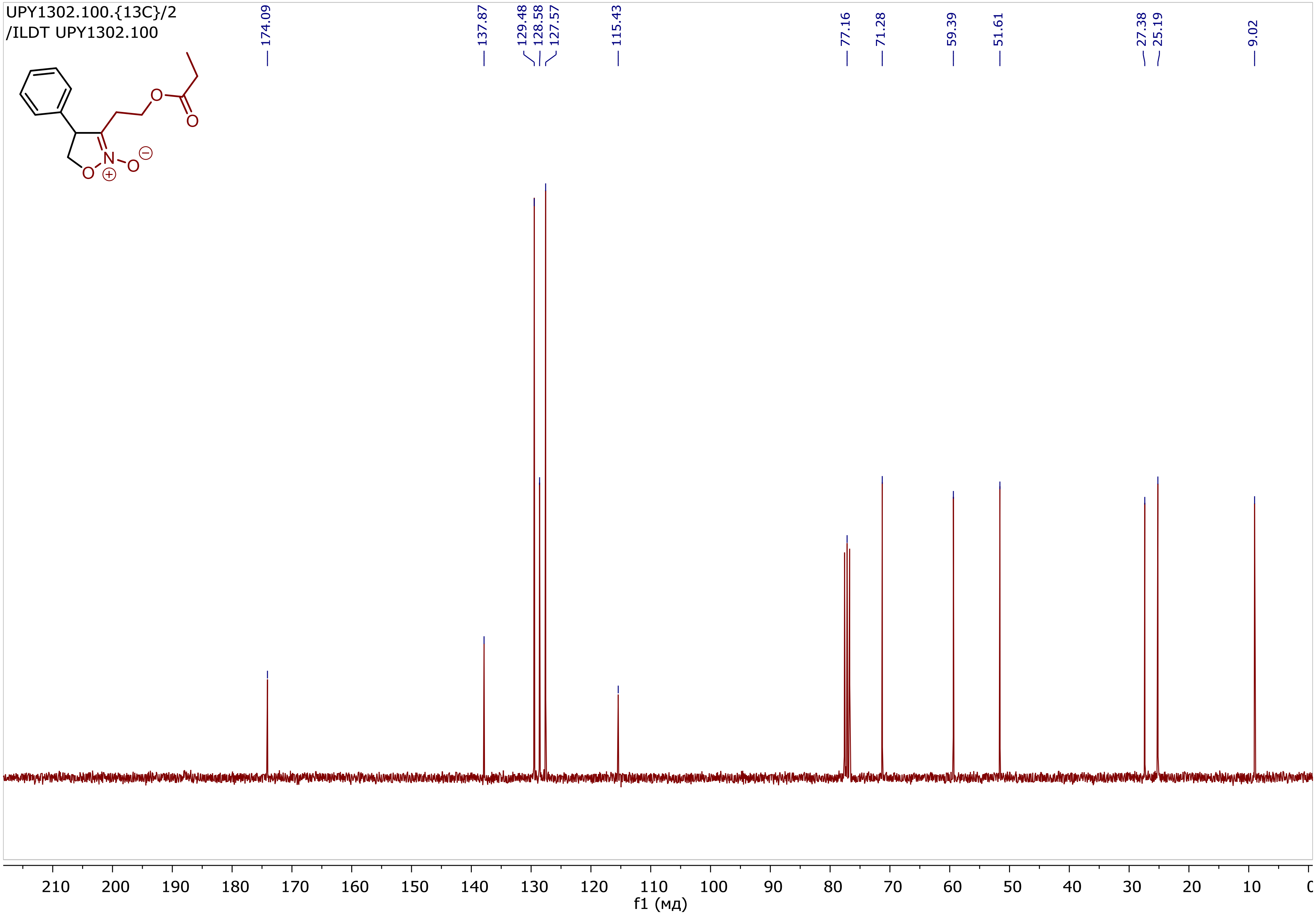


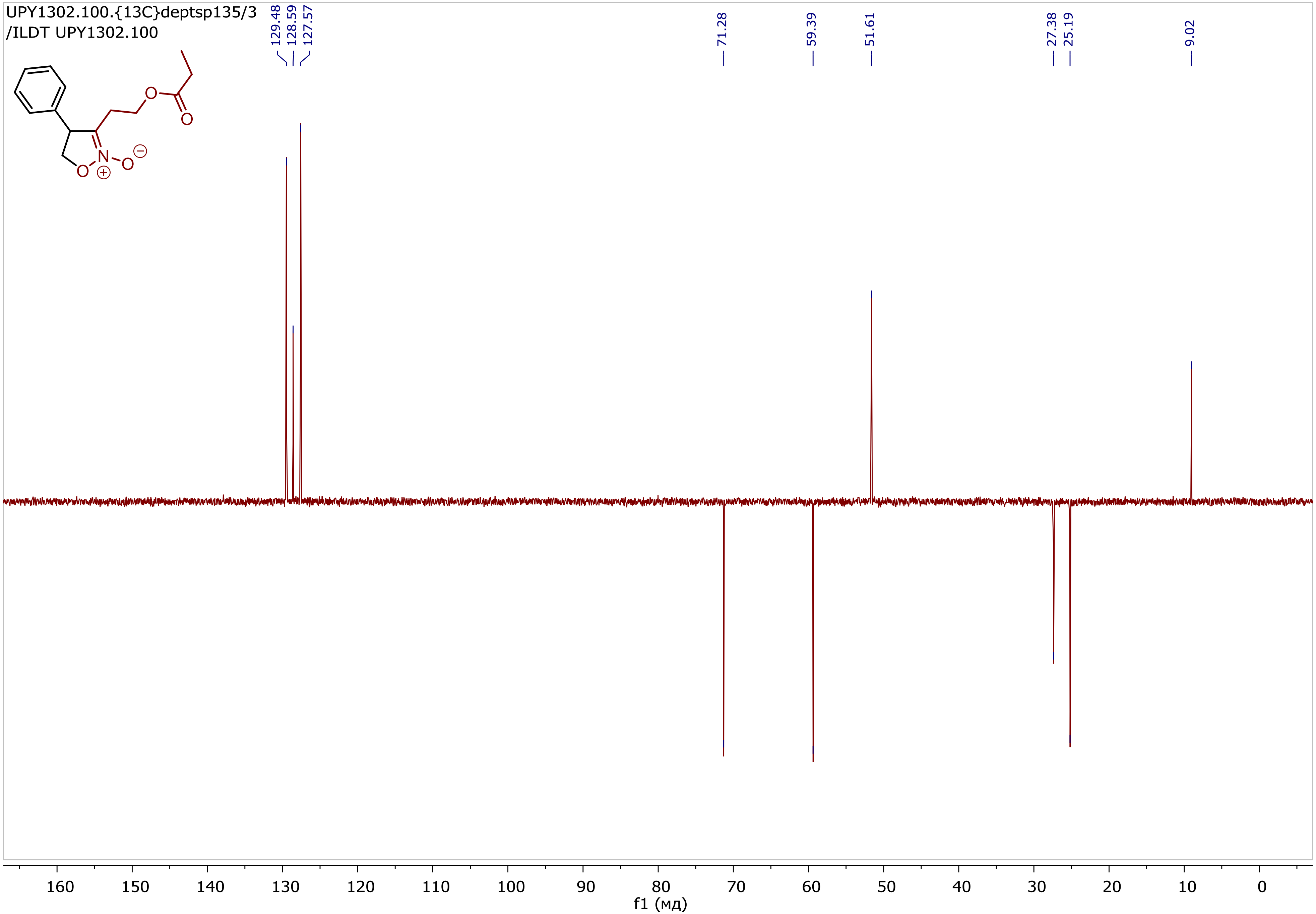
4-Phenyl-3-(2-(propionyloxy)ethyl)-4,5-dihydroisoxazole 2-oxide (3k)



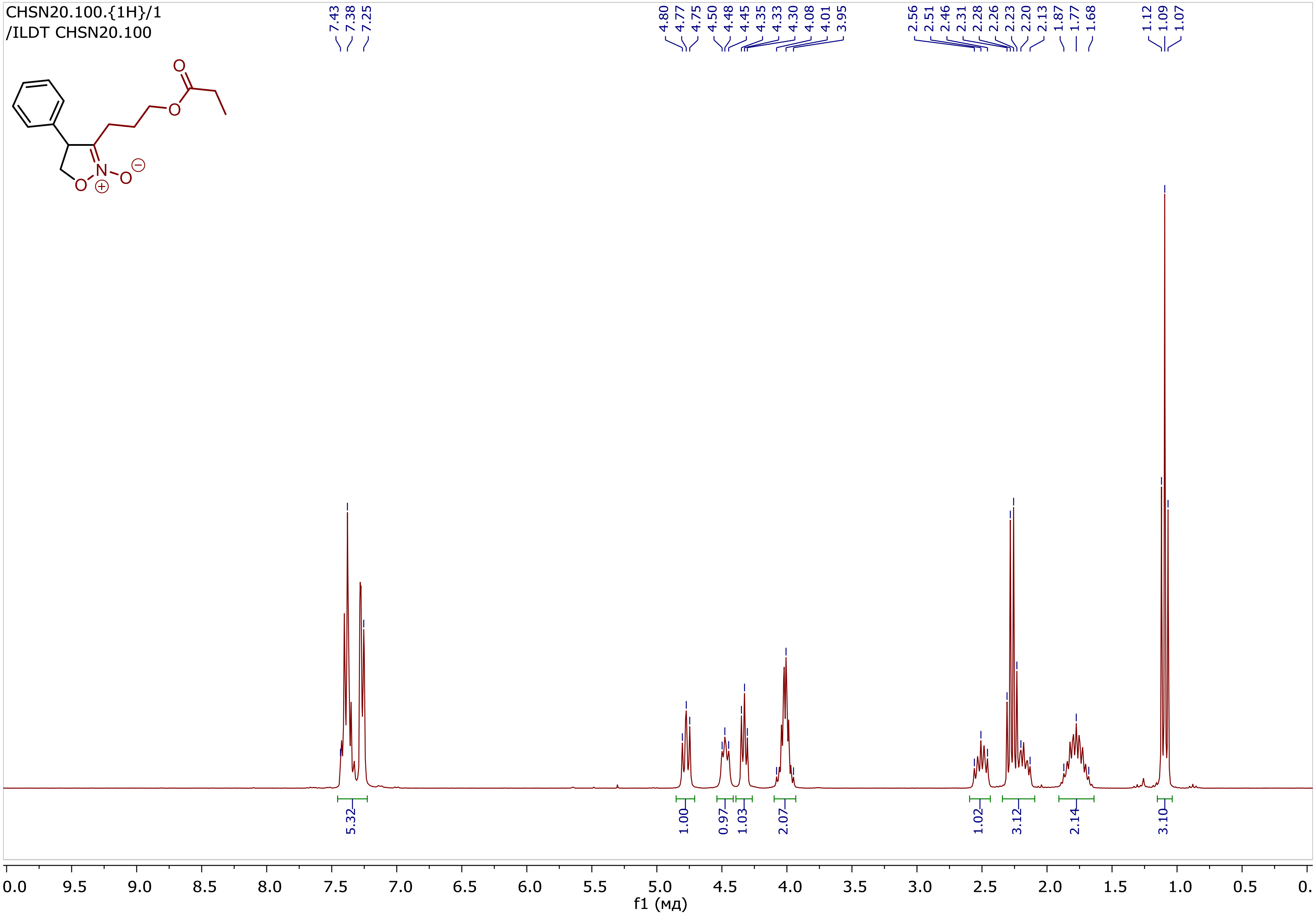
4-Phenyl-3-(2-(propionyloxy)ethyl)-4,5-dihydroisoxazole 2-oxide (3k)



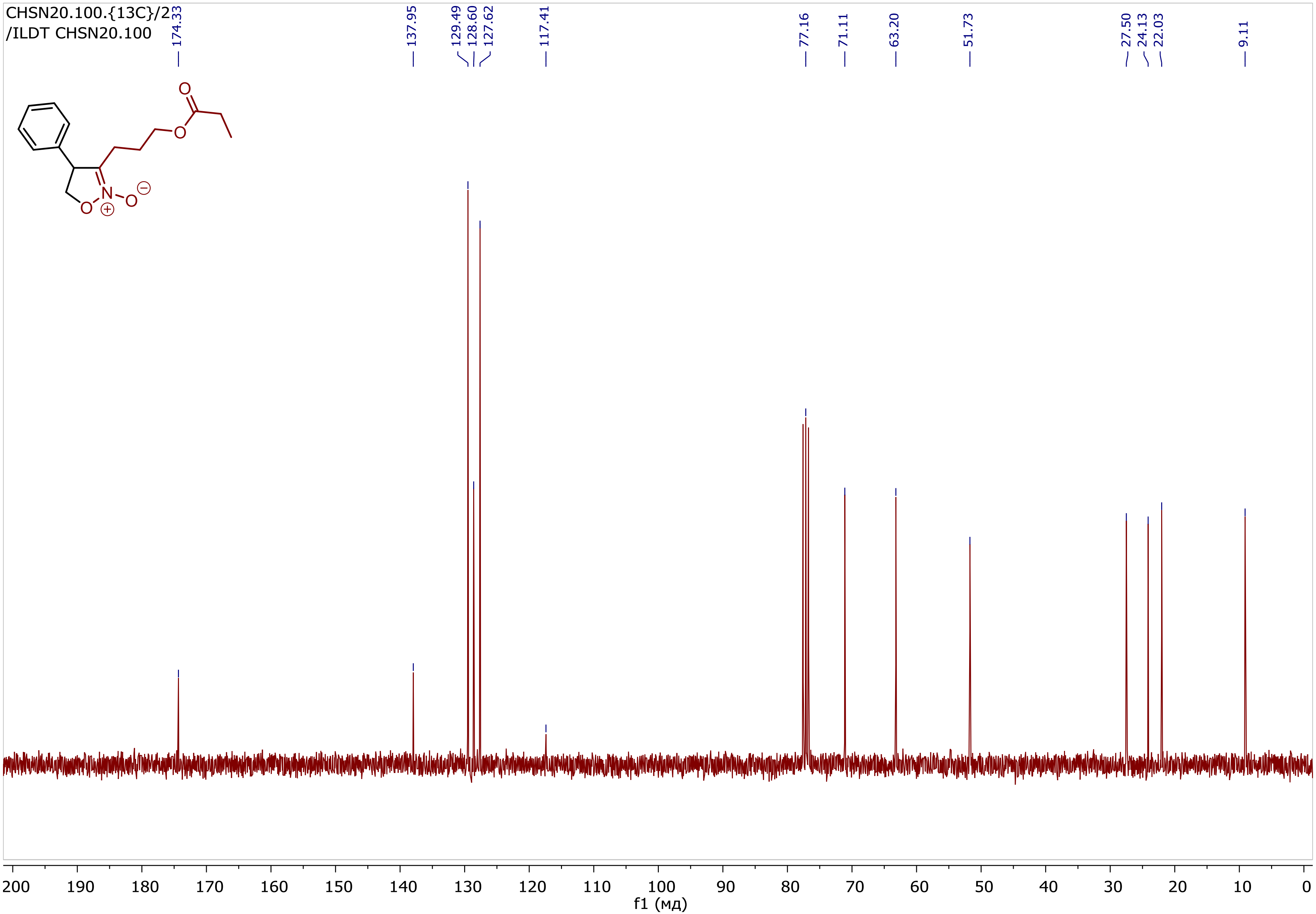
4-Phenyl-3-(2-(propionyloxy)ethyl)-4,5-dihydroisoxazole 2-oxide (3k)



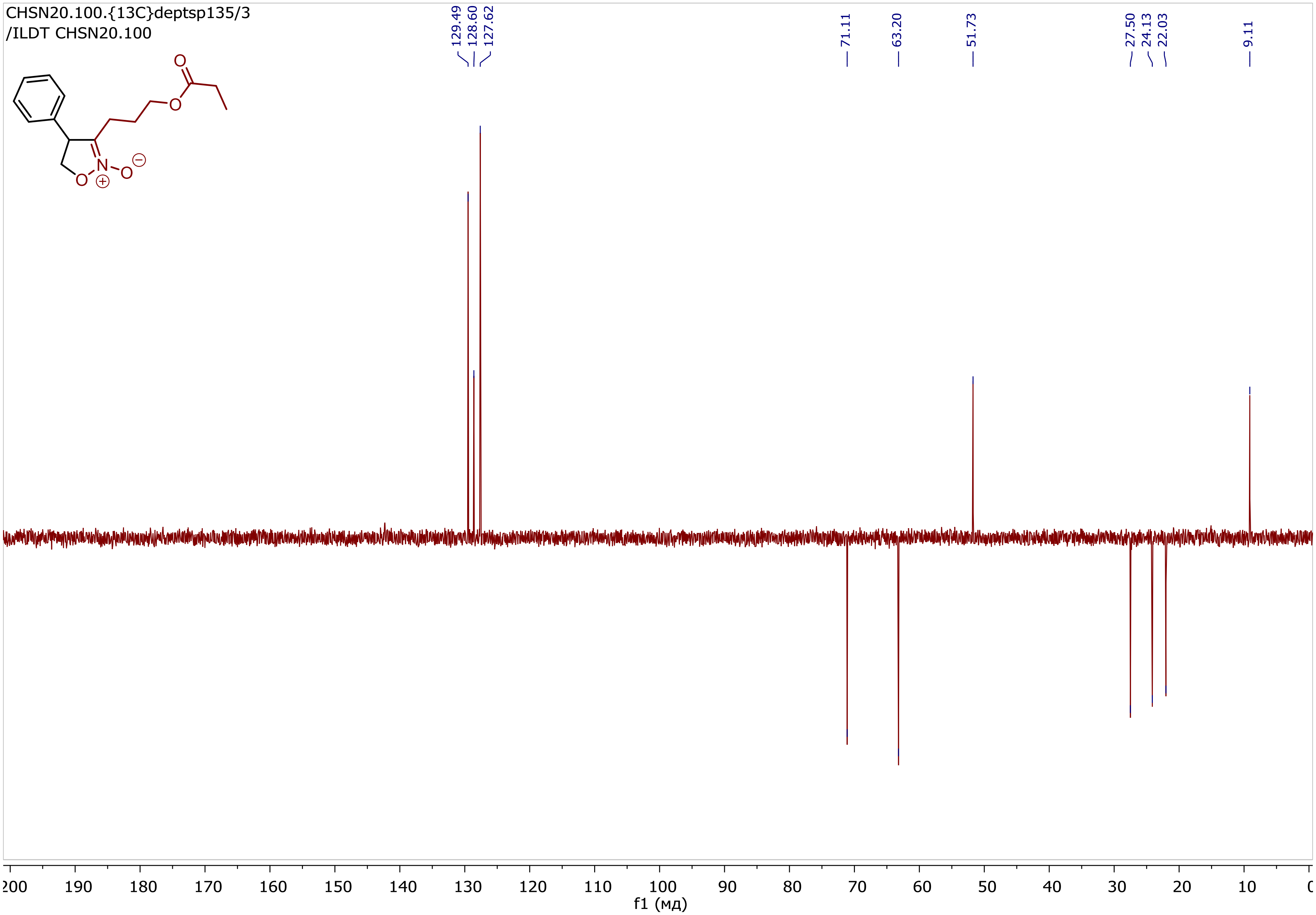
4-Phenyl-3-(3-(propionyloxy)propyl)-4,5-dihydroisoxazole 2-oxide (3l)



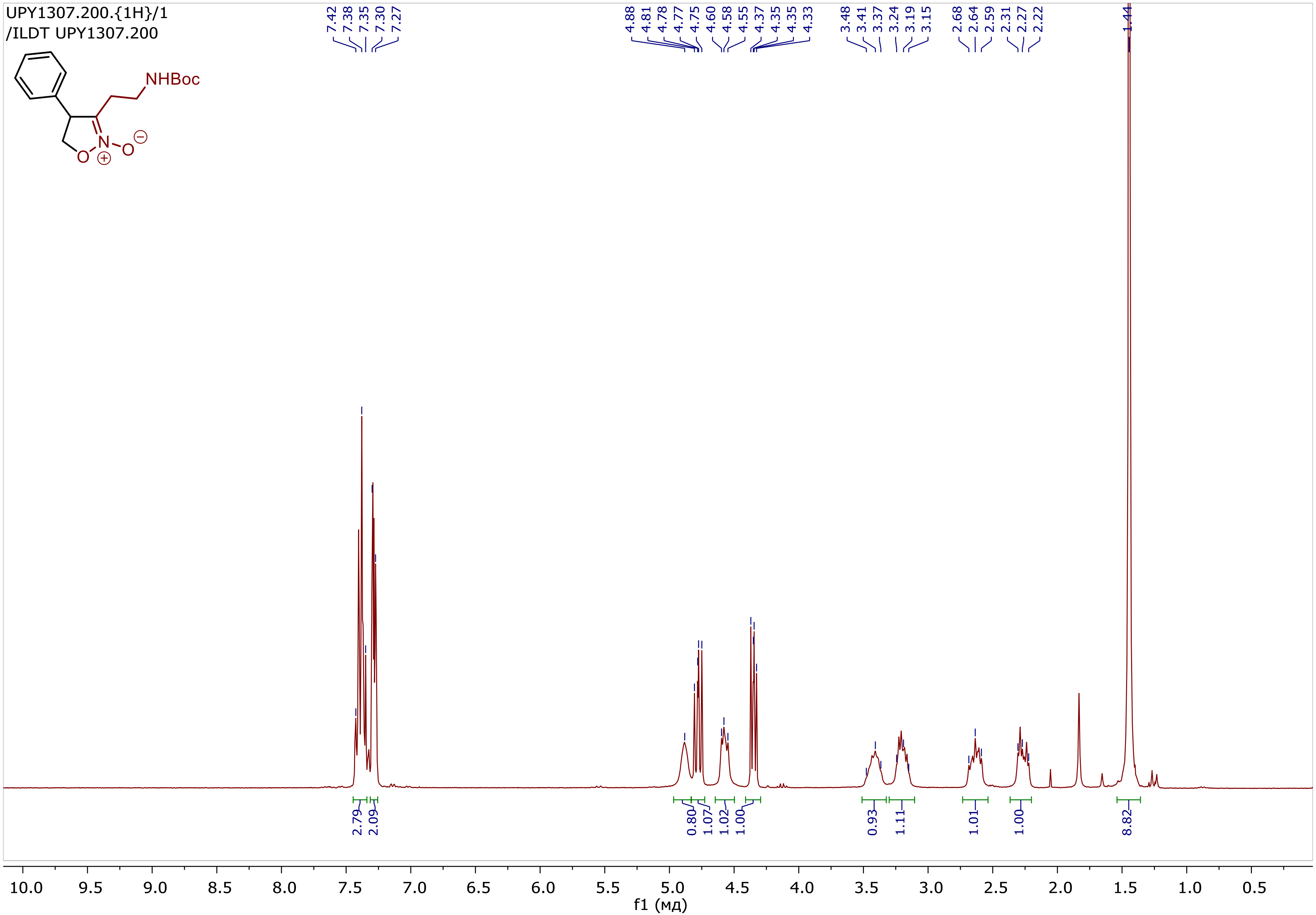
4-Phenyl-3-(3-(propionyloxy)propyl)-4,5-dihydroisoxazole 2-oxide (3l)



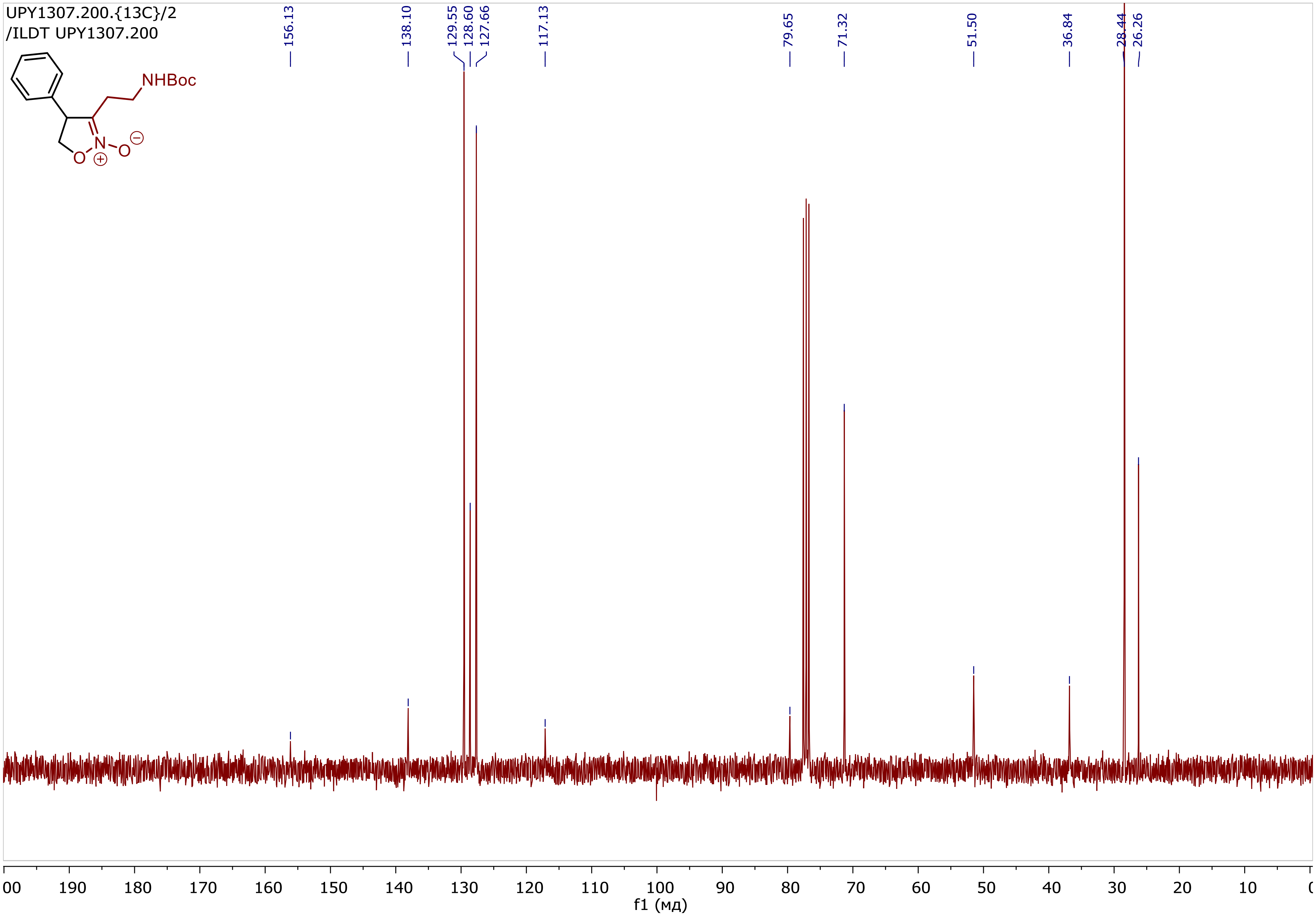
4-Phenyl-3-(3-(propionyloxy)propyl)-4,5-dihydroisoxazole 2-oxide (3l)



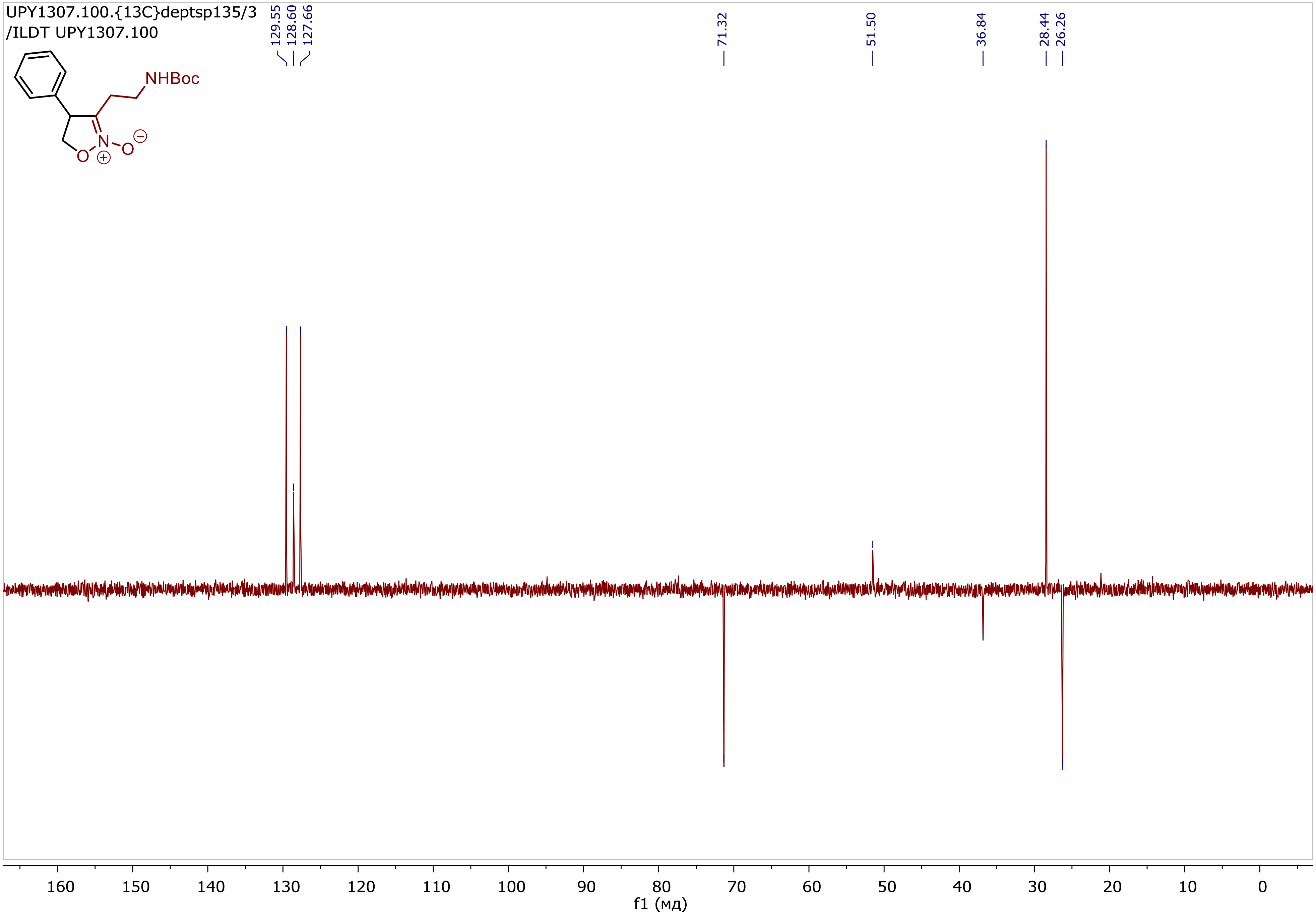
3-(2-((*Tert*-butoxycarbonyl)amino)ethyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3m)



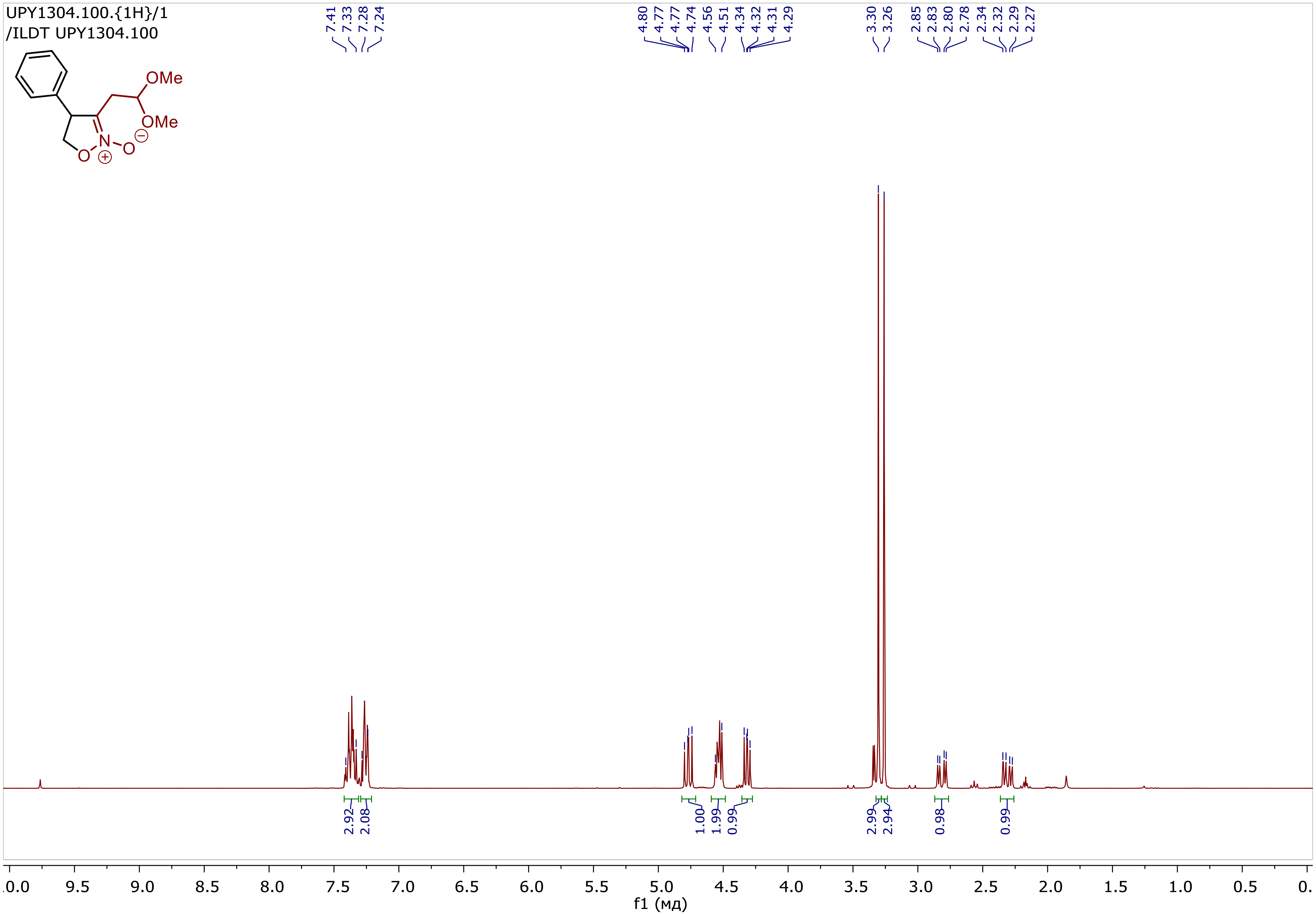
3-(2-((*Tert*-butoxycarbonyl)amino)ethyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3m)



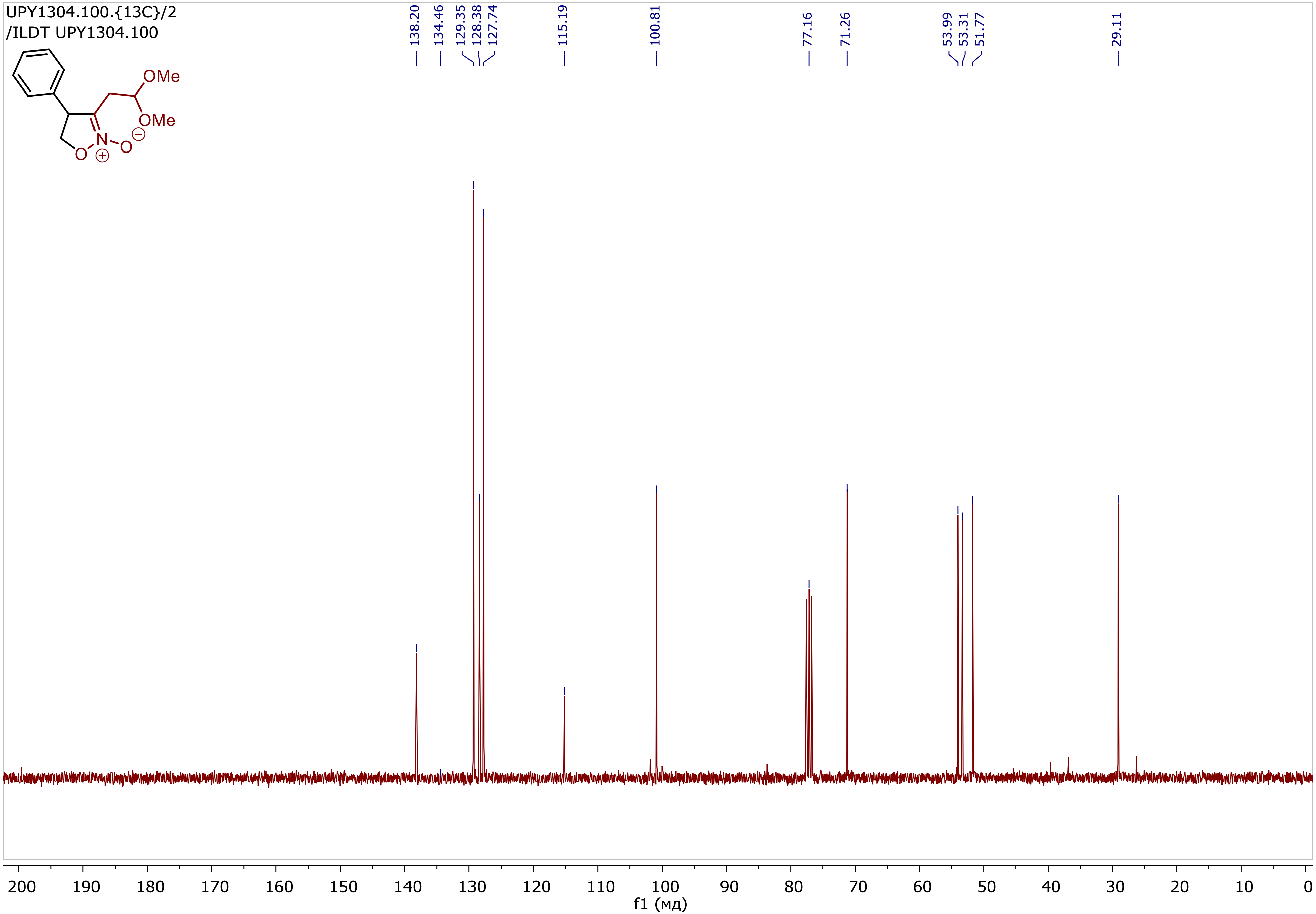
3-(2-((*Tert*-butoxycarbonyl)amino)ethyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3m)



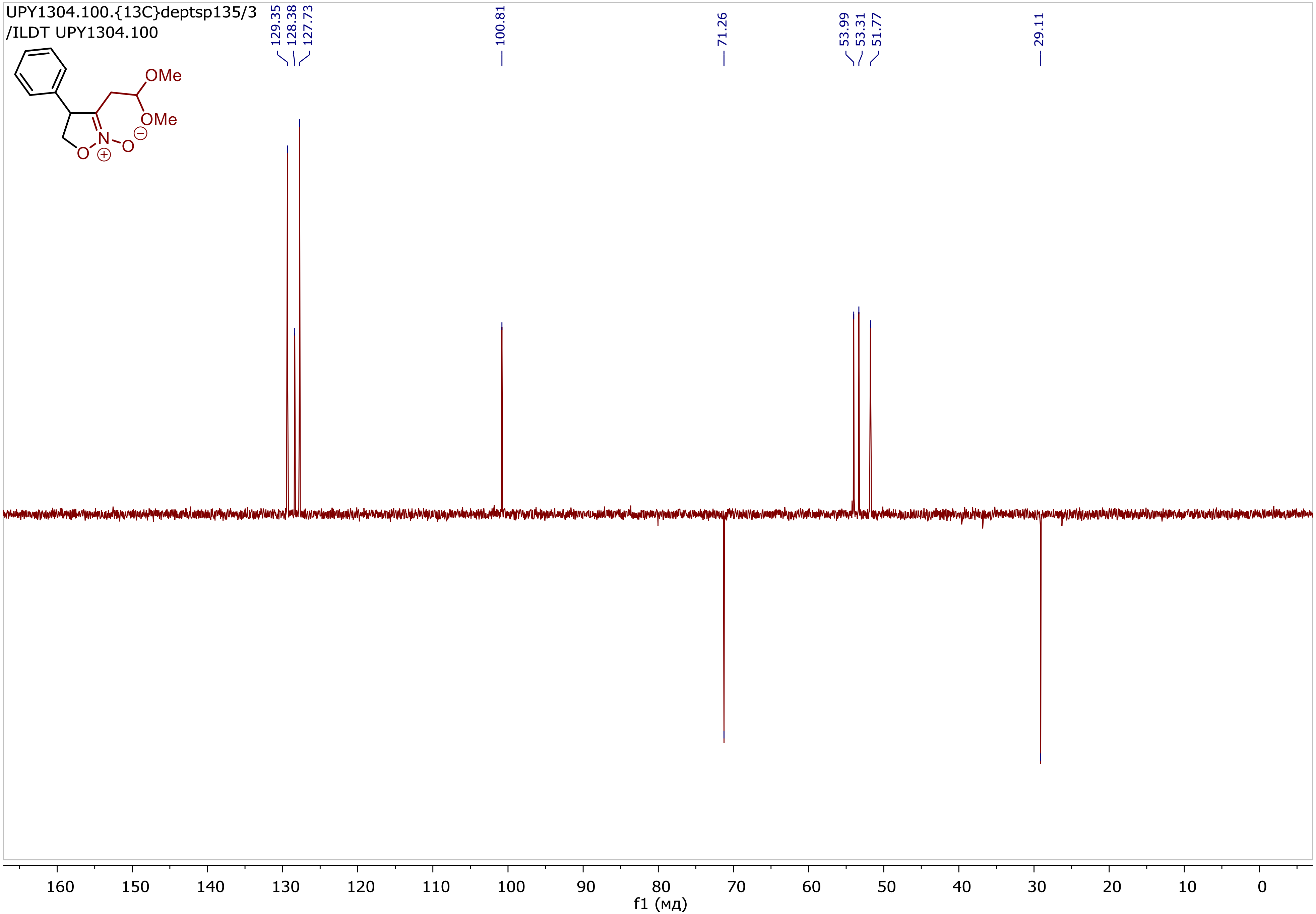
3-(2,2-Dimethoxyethyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3n)



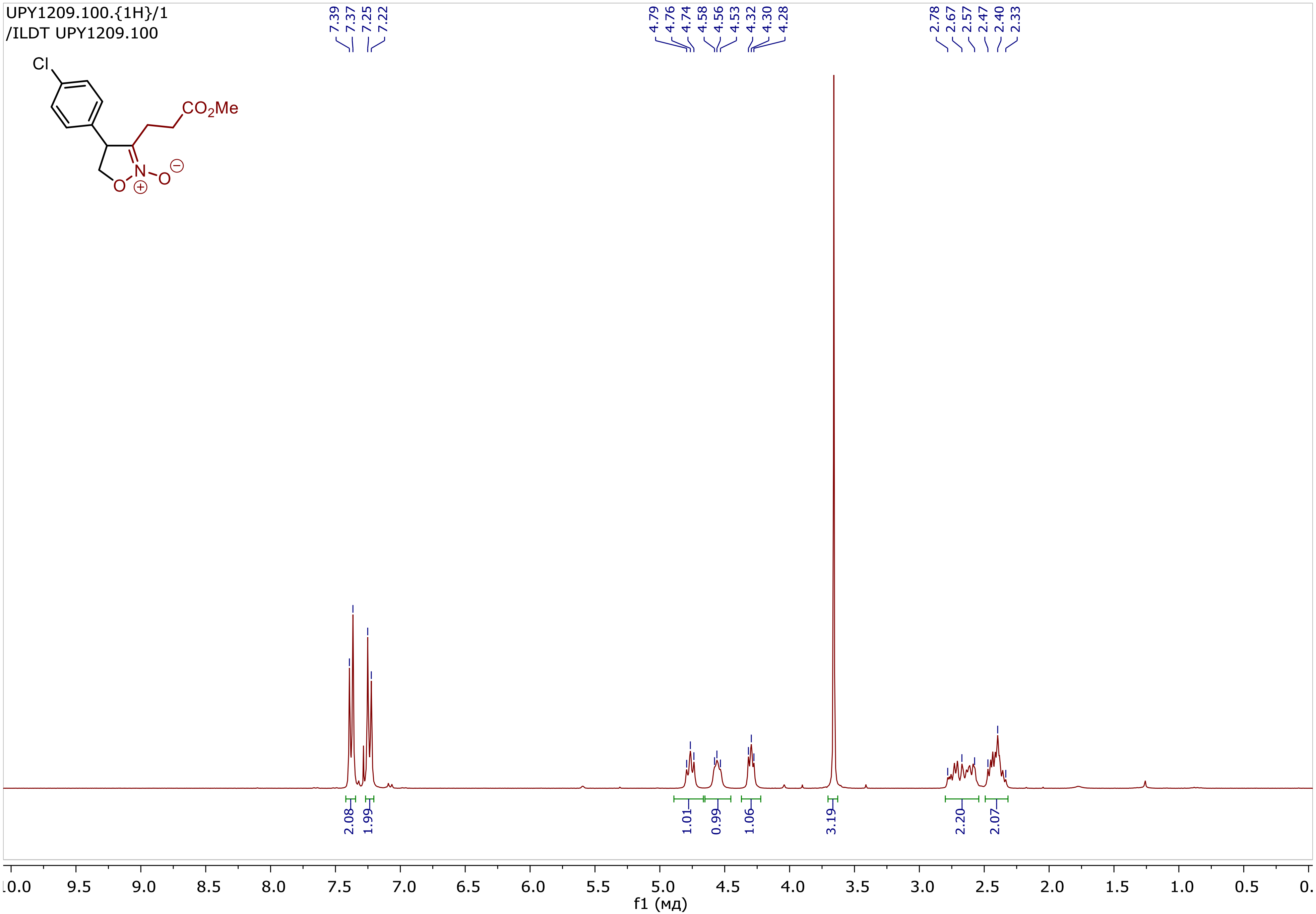
3-(2,2-Dimethoxyethyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3n)



3-(2,2-Dimethoxyethyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3n)



4-(4-Chlorophenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3o)



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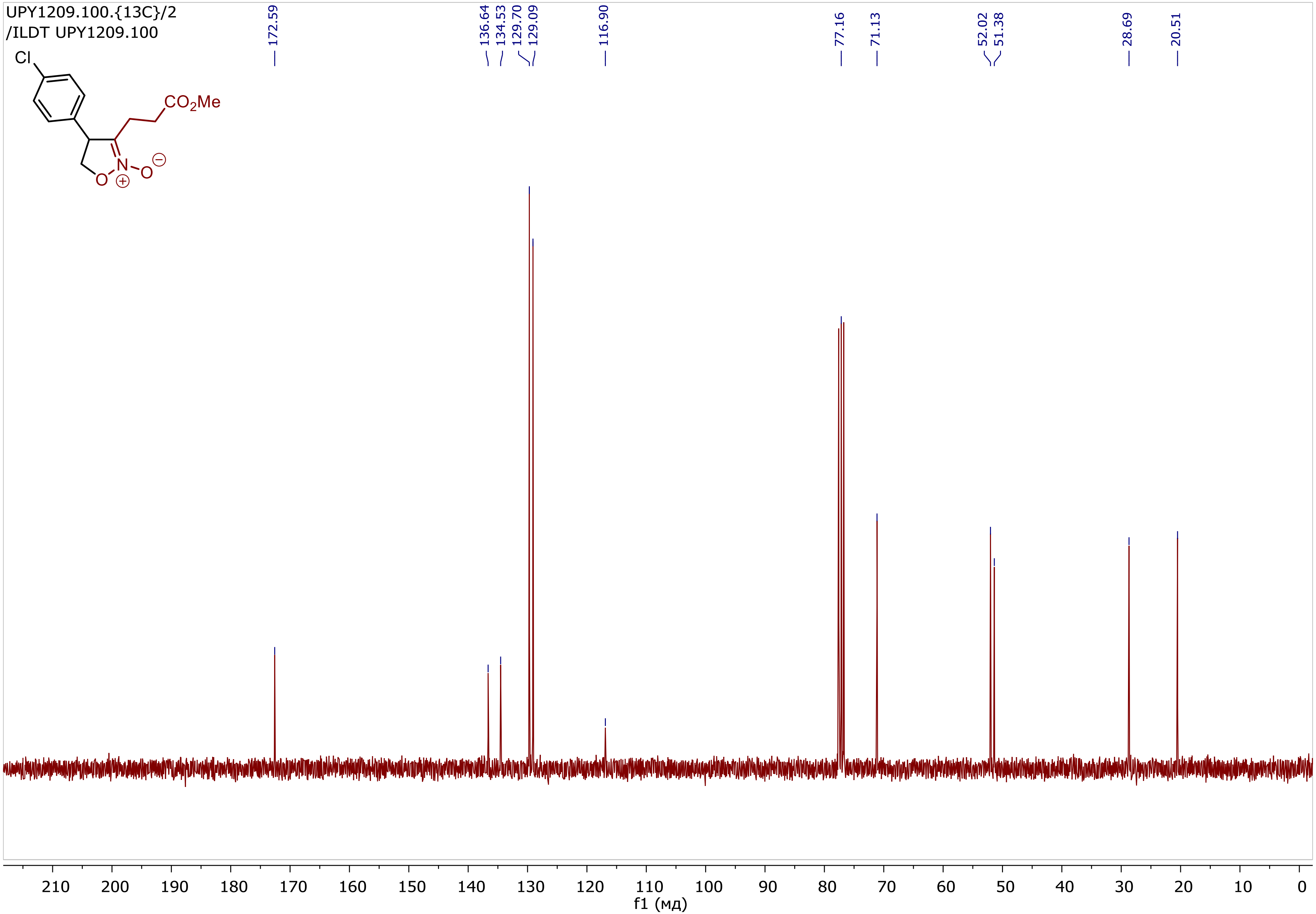
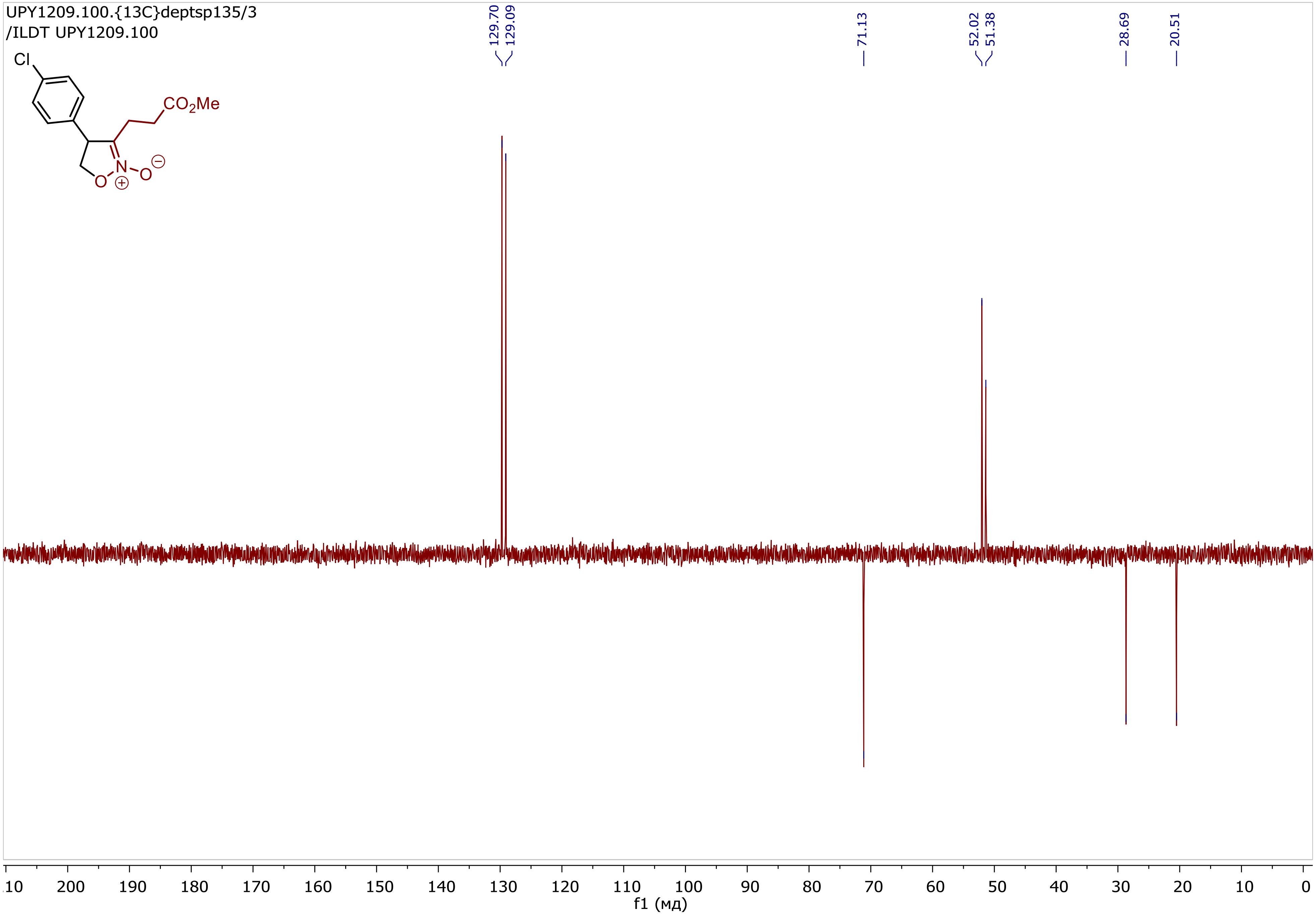
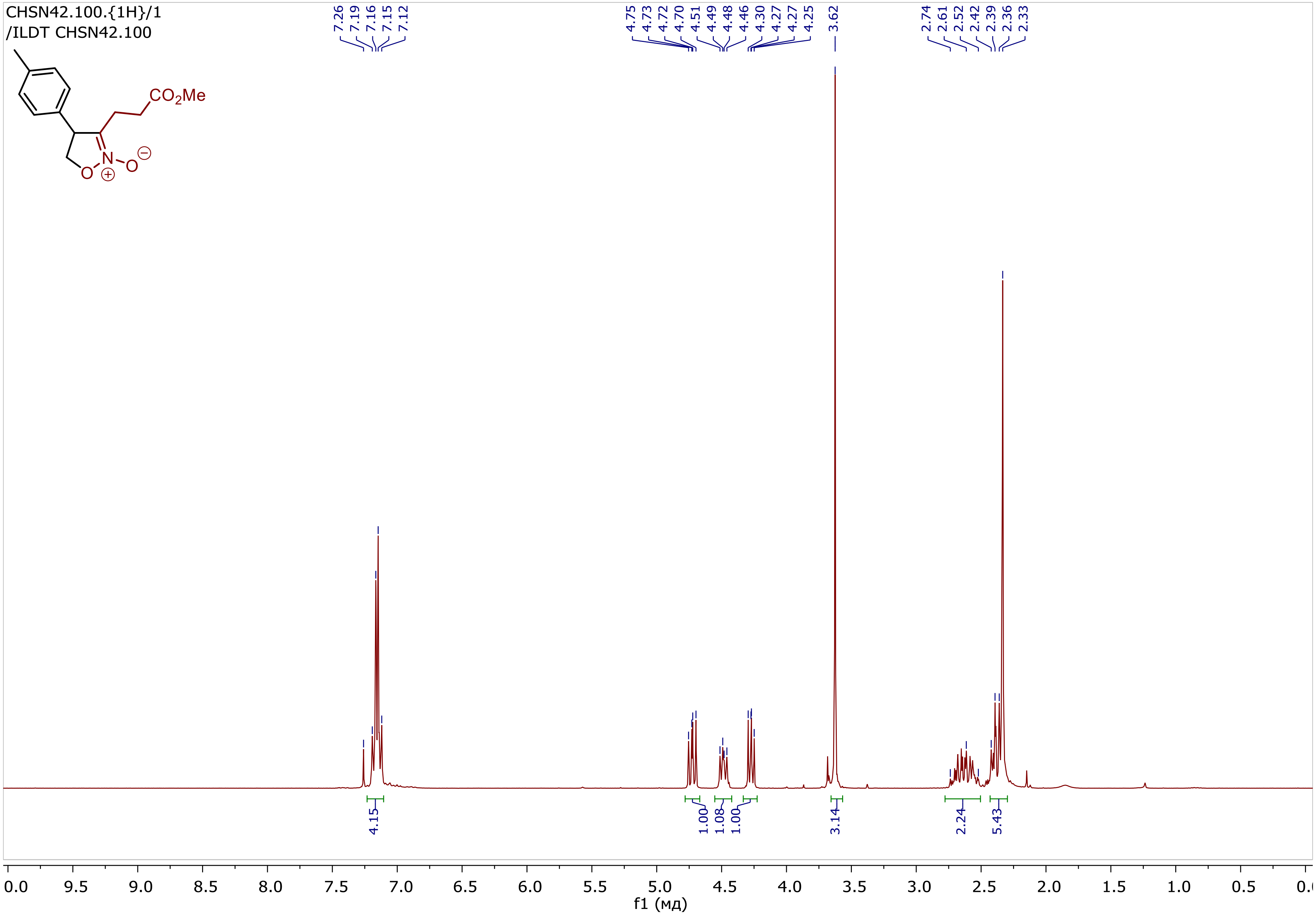


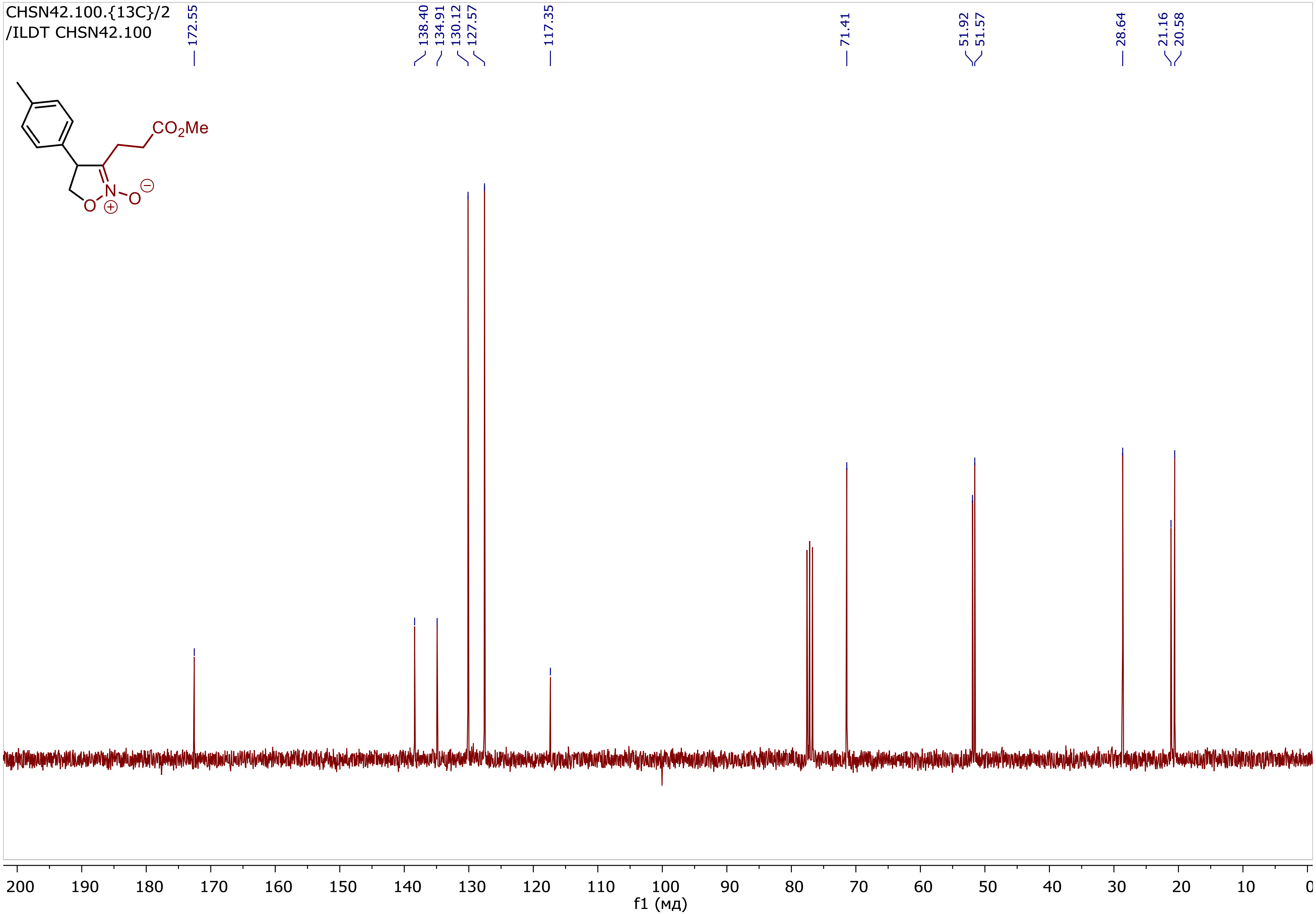
4-(4-Chlorophenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3o)



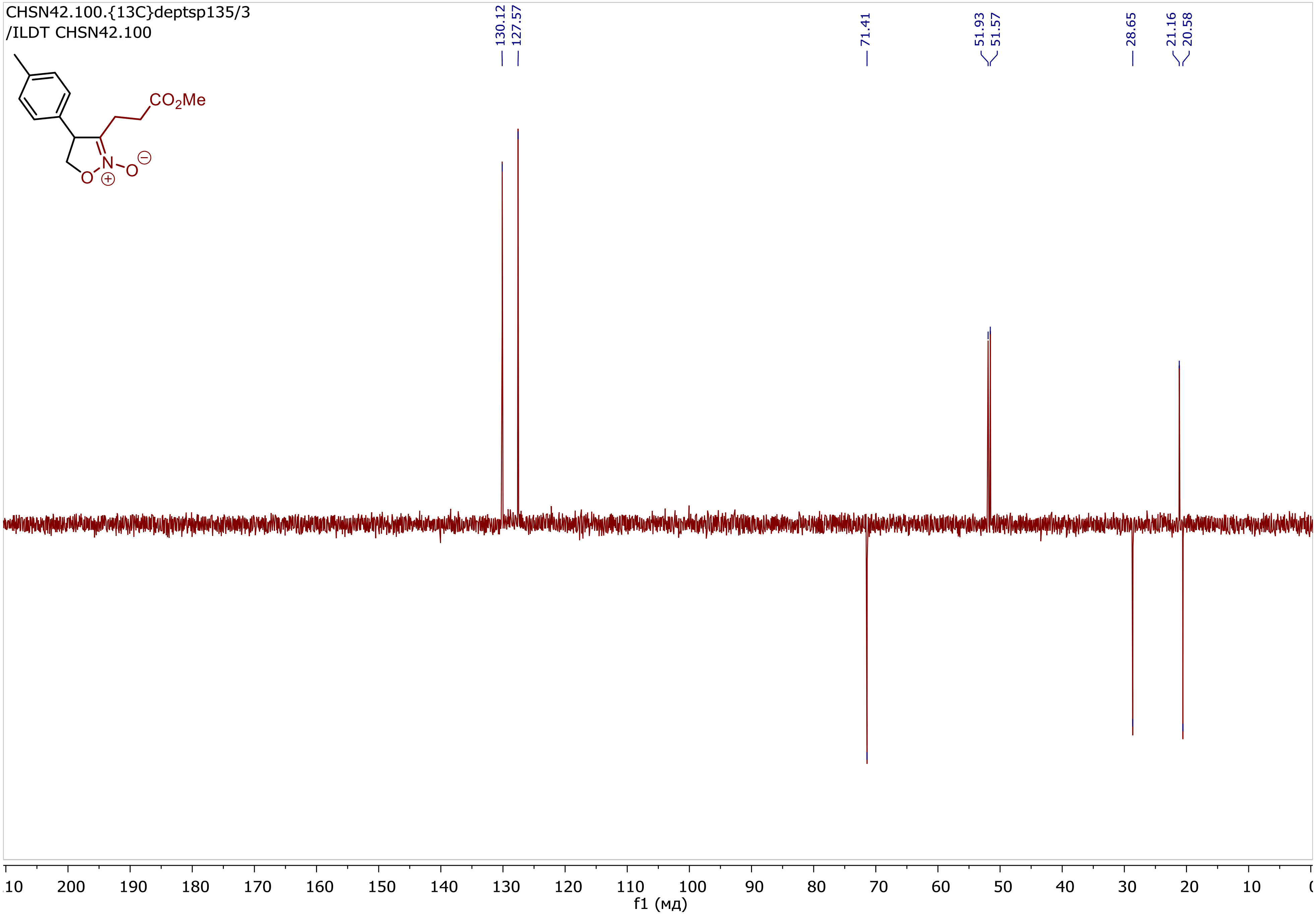
3-(3-Methoxy-3-oxopropyl)-4-(p-tolyl)-4,5-dihydroisoxazole 2-oxide (3p)



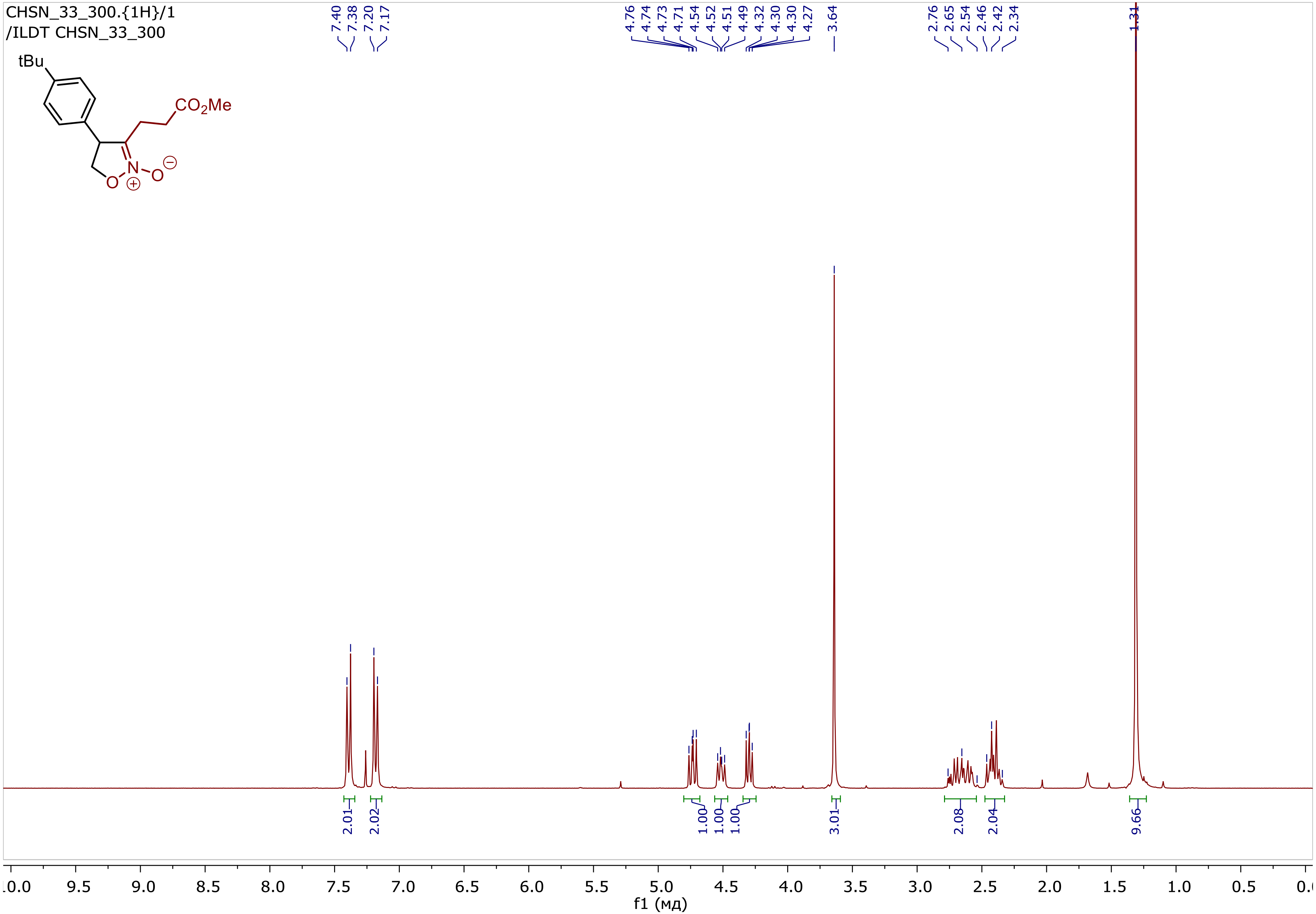
3-(3-Methoxy-3-oxopropyl)-4-(p-tolyl)-4,5-dihydroisoxazole 2-oxide (3p)



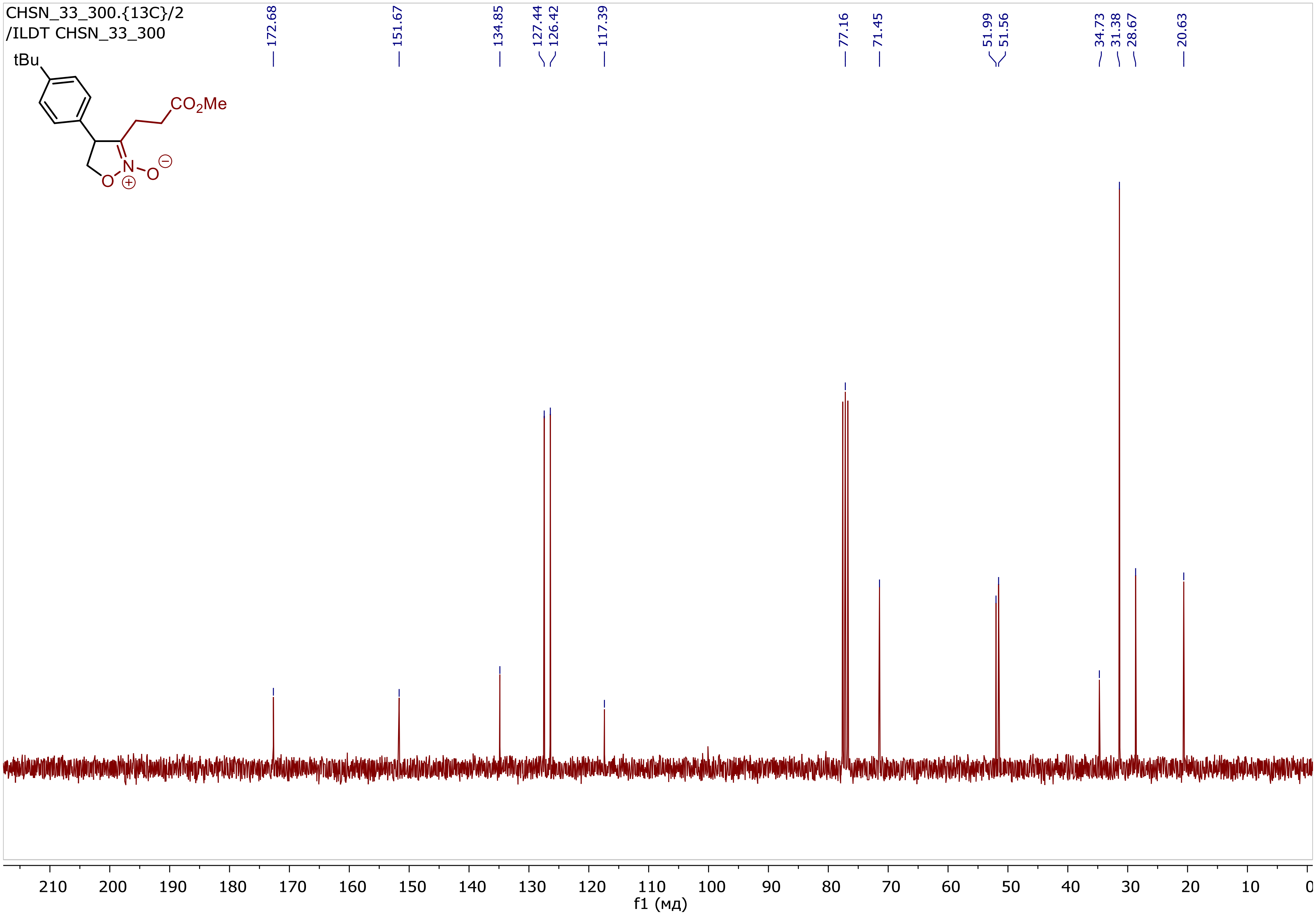
3-(3-Methoxy-3-oxopropyl)-4-(p-tolyl)-4,5-dihydroisoxazole 2-oxide (3p)



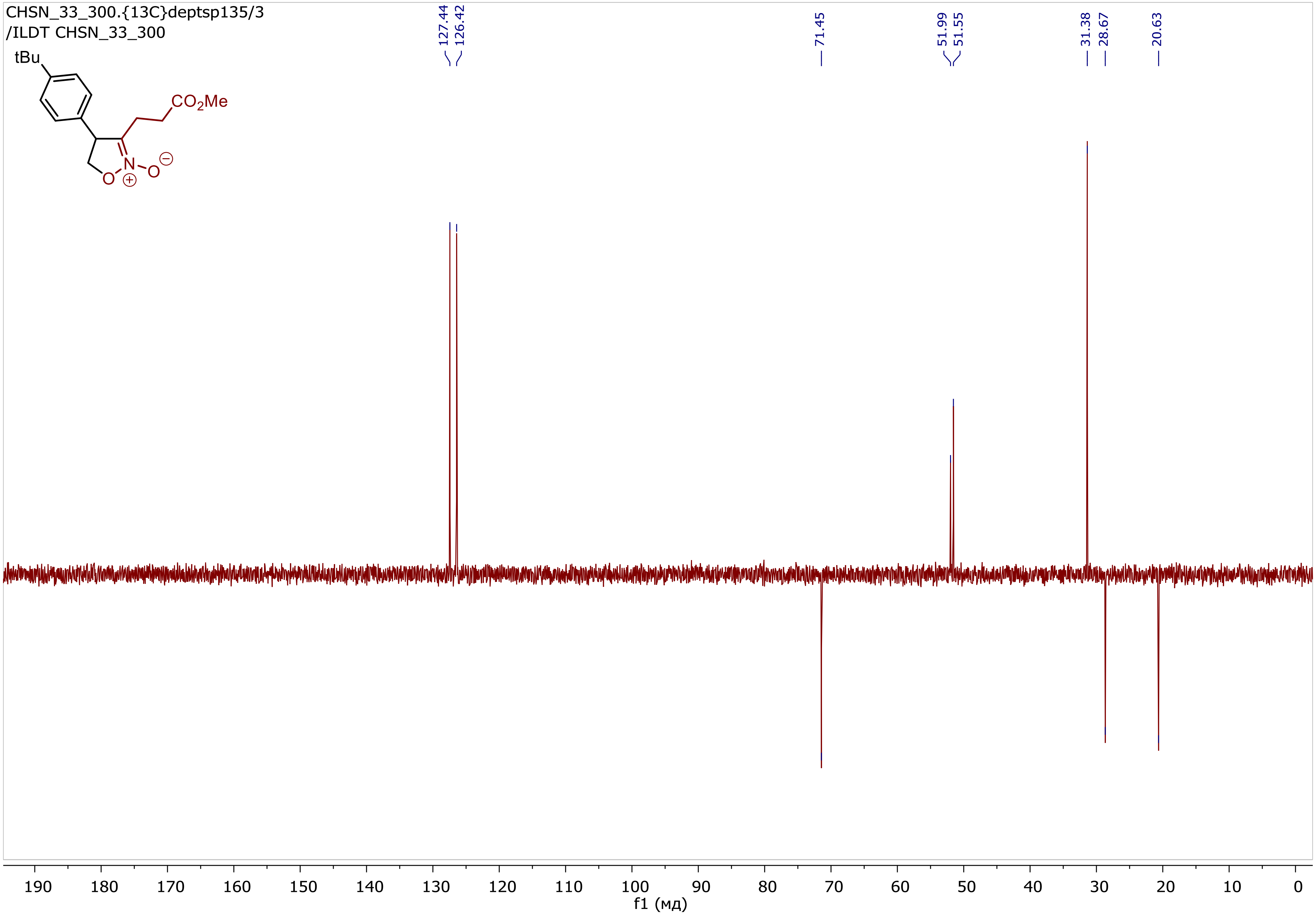
4-(4-(*Tert*-butyl)phenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3q)



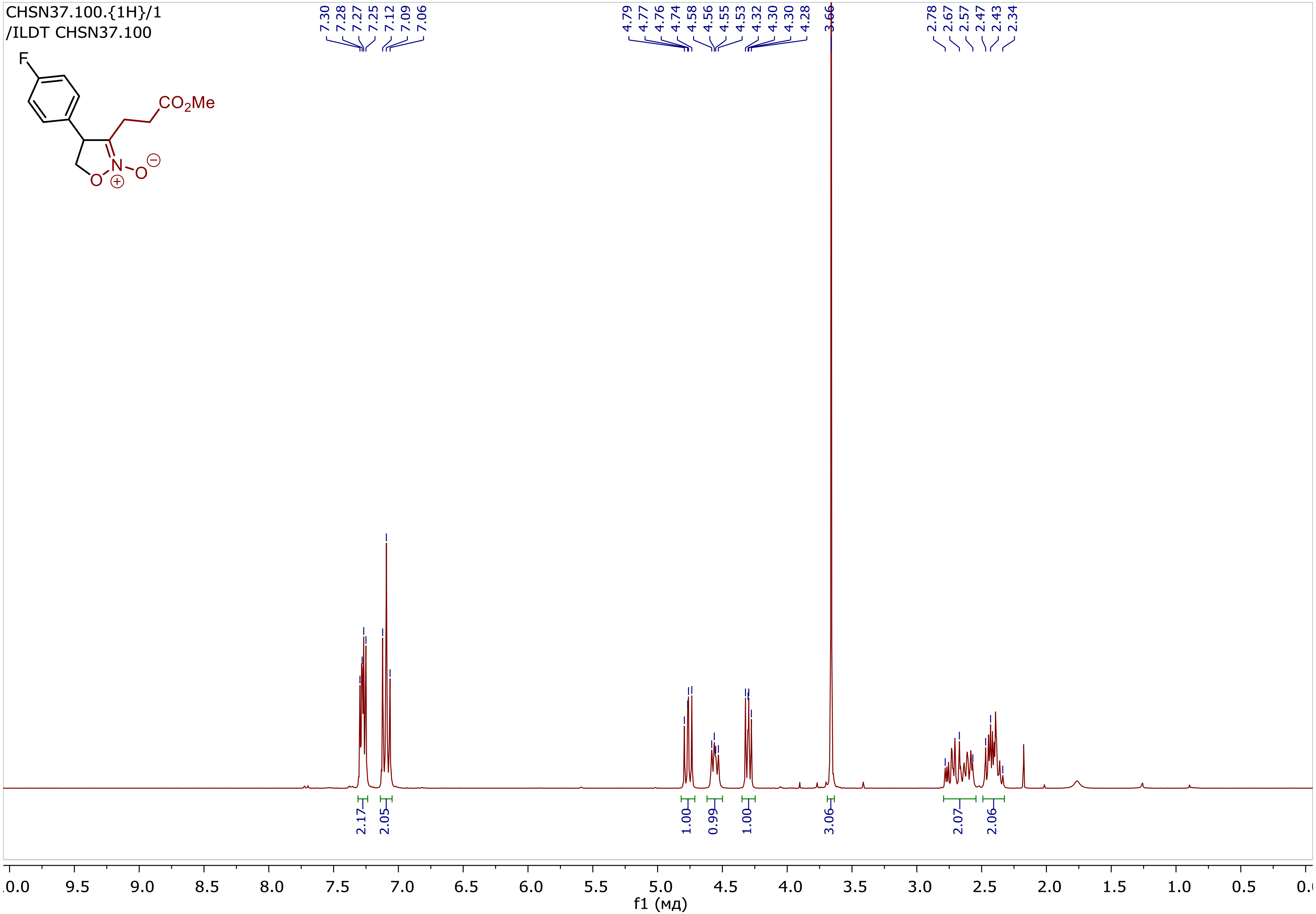
4-(4-(*Tert*-butyl)phenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3q)



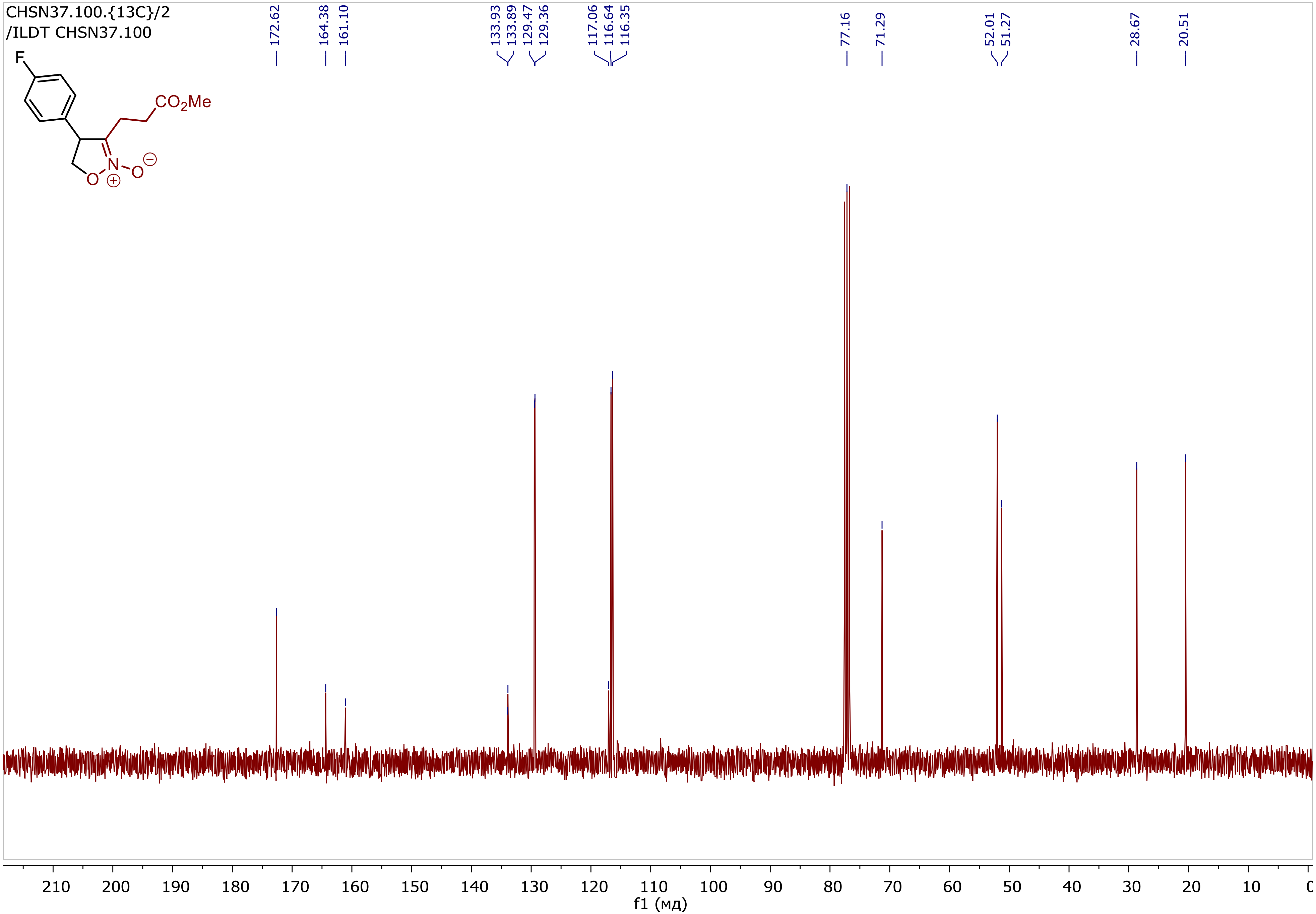
4-(4-(*Tert*-butyl)phenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3q)



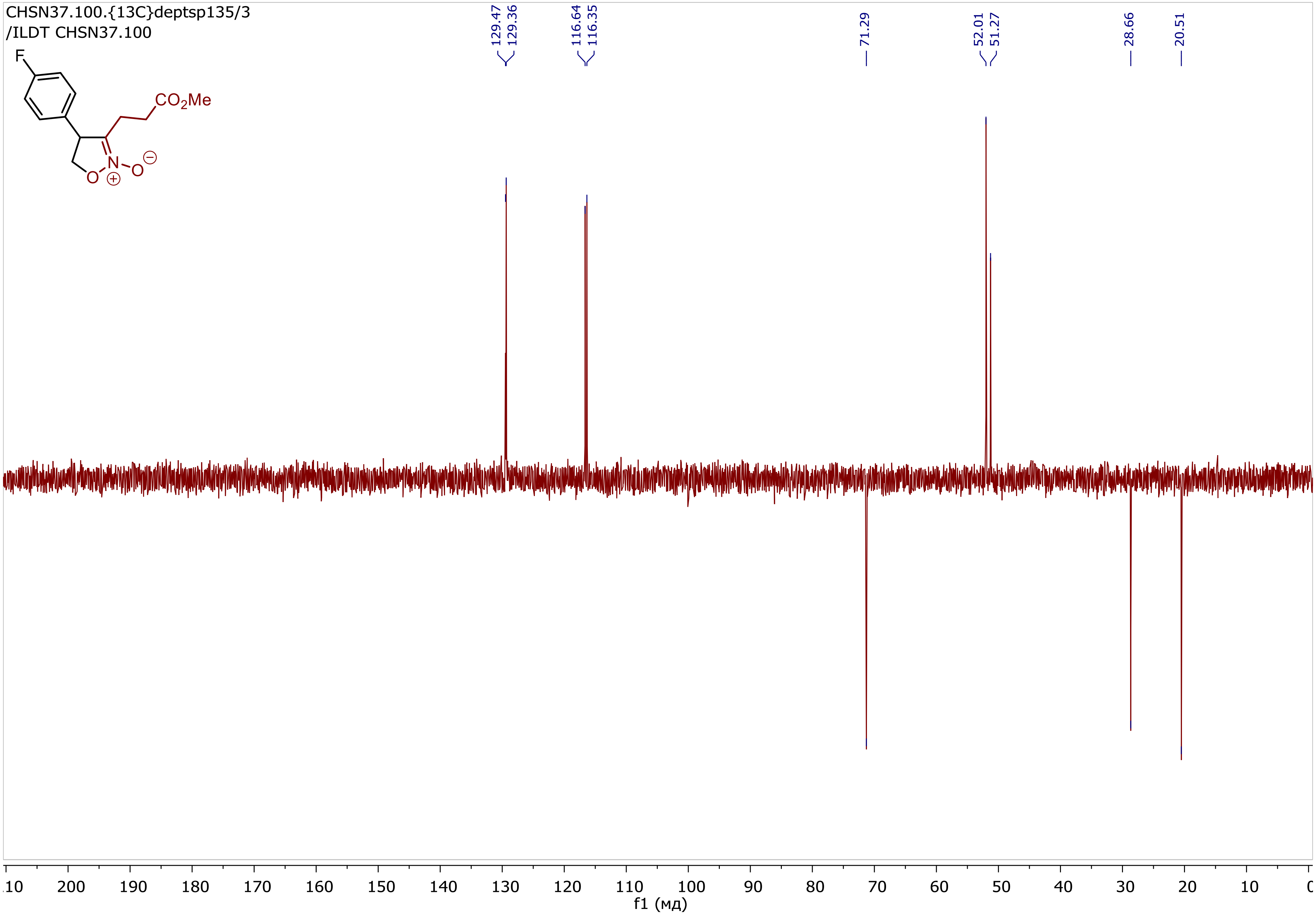
4-(4-Fluorophenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3r)



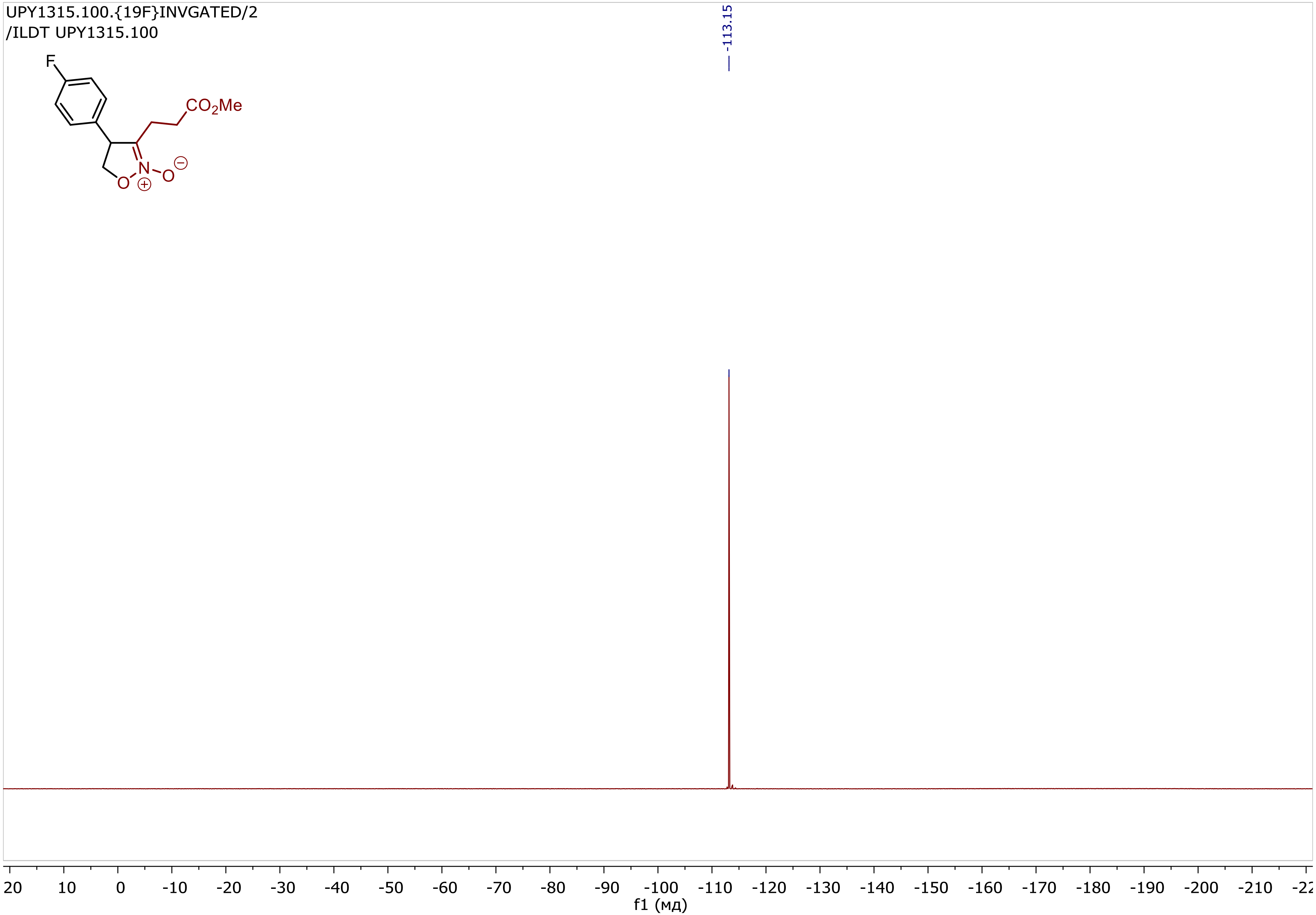
4-(4-Fluorophenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3r)



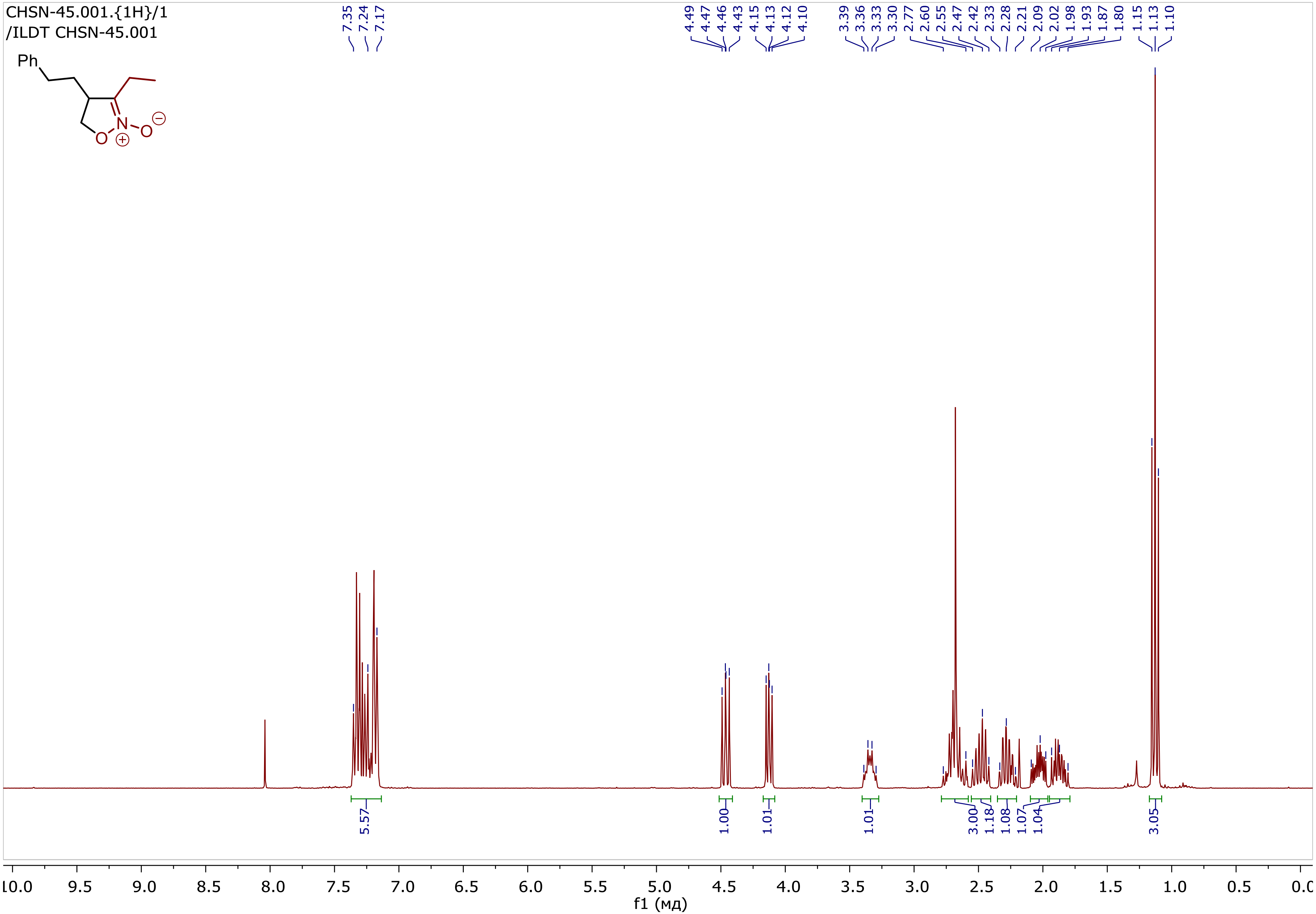
4-(4-Fluorophenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3r)



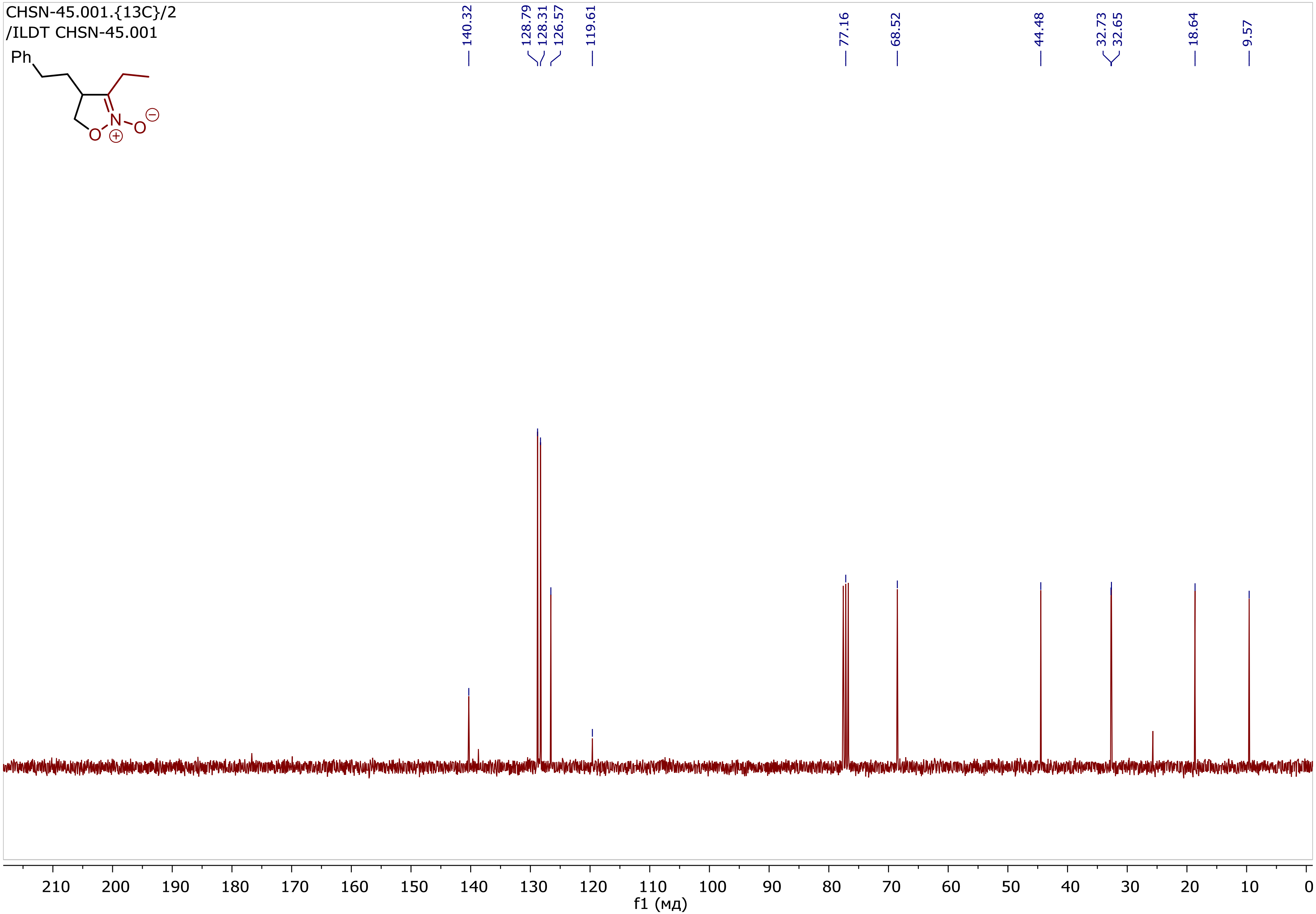
4-(4-Fluorophenyl)-3-(3-methoxy-3-oxopropyl)-4,5-dihydroisoxazole 2-oxide (3r)



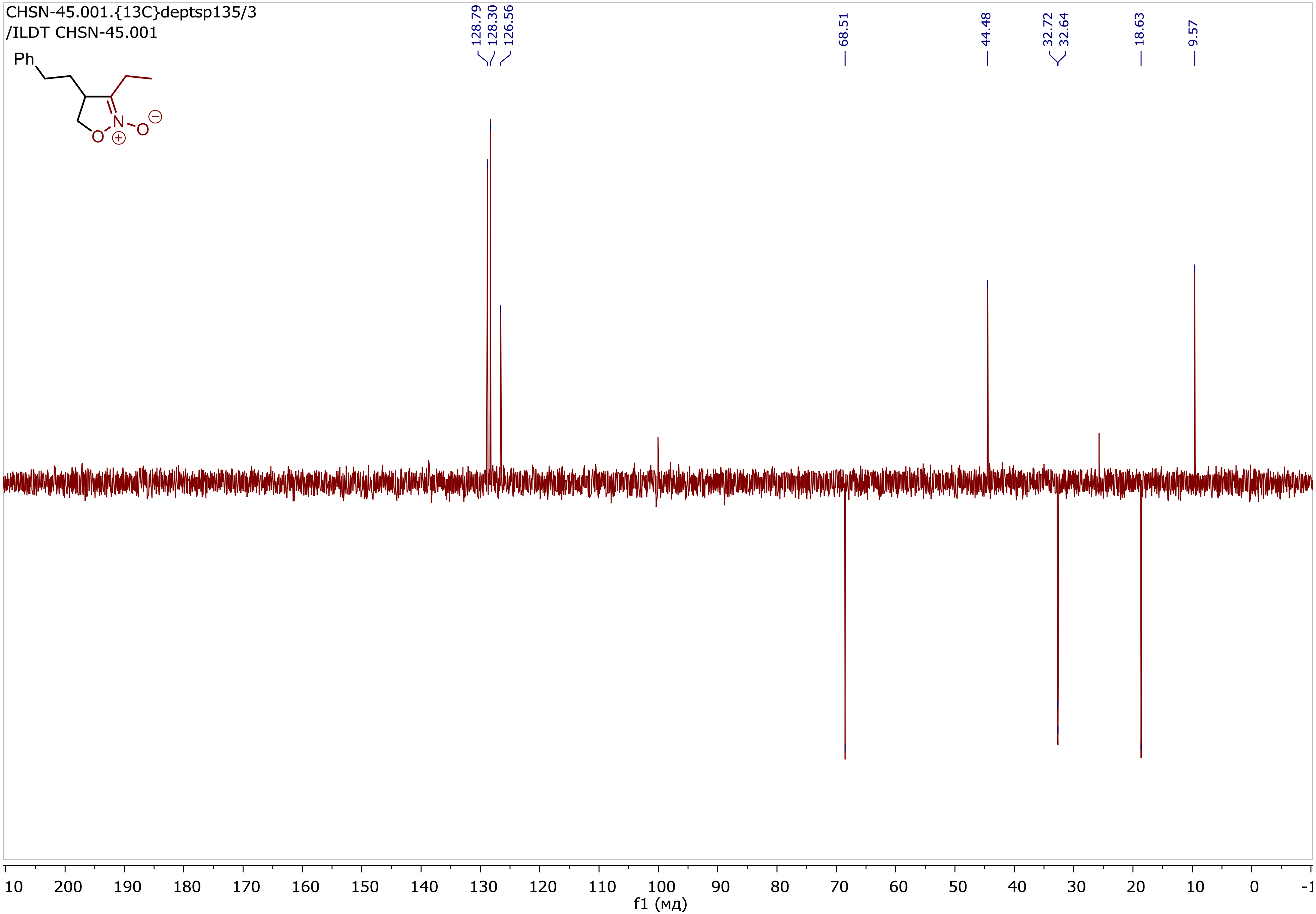
3-Ethyl-4-phenethyl-4,5-dihydroisoxazole 2-oxide (3s)



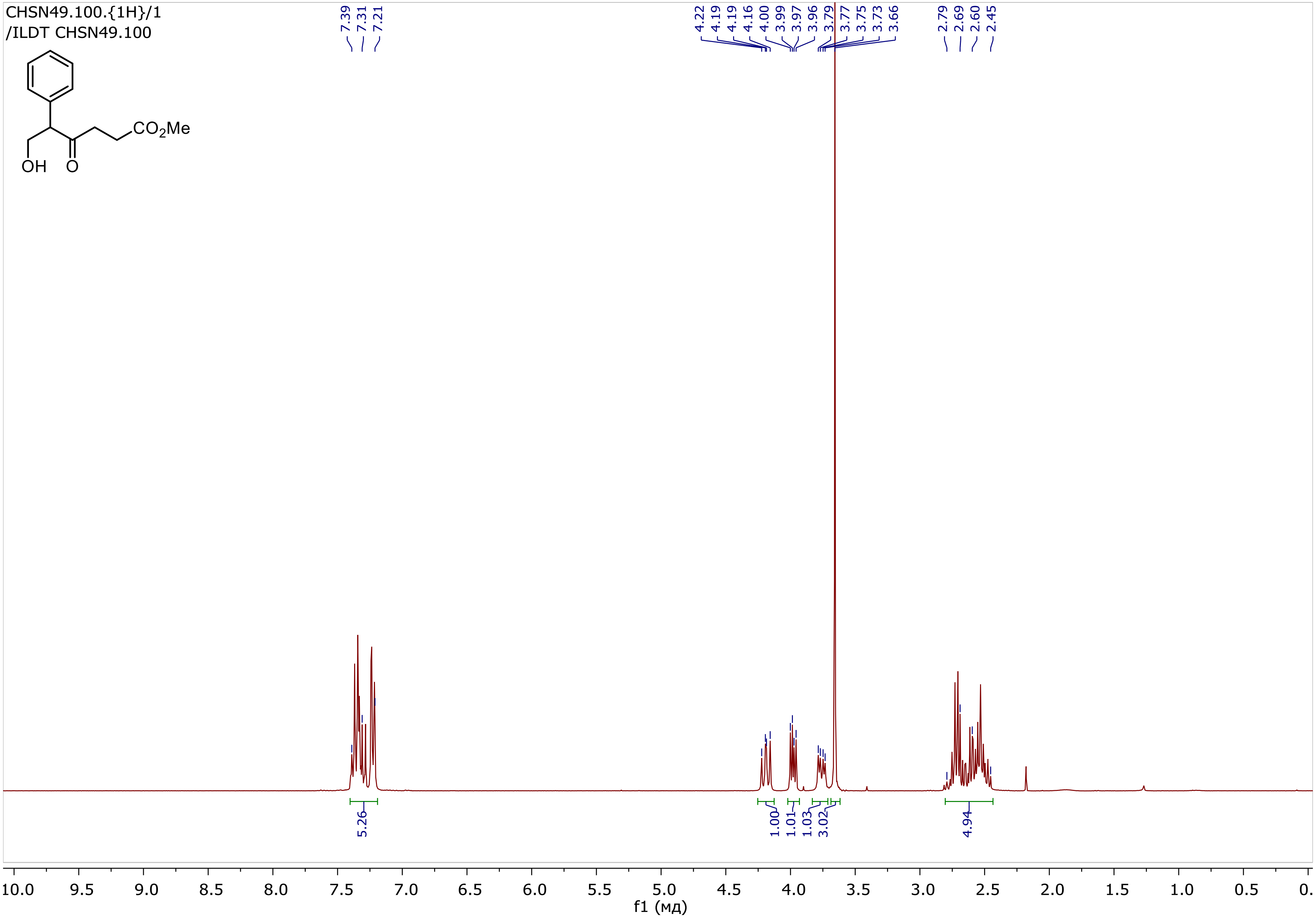
3-Ethyl-4-phenethyl-4,5-dihydroisoxazole 2-oxide (3s)



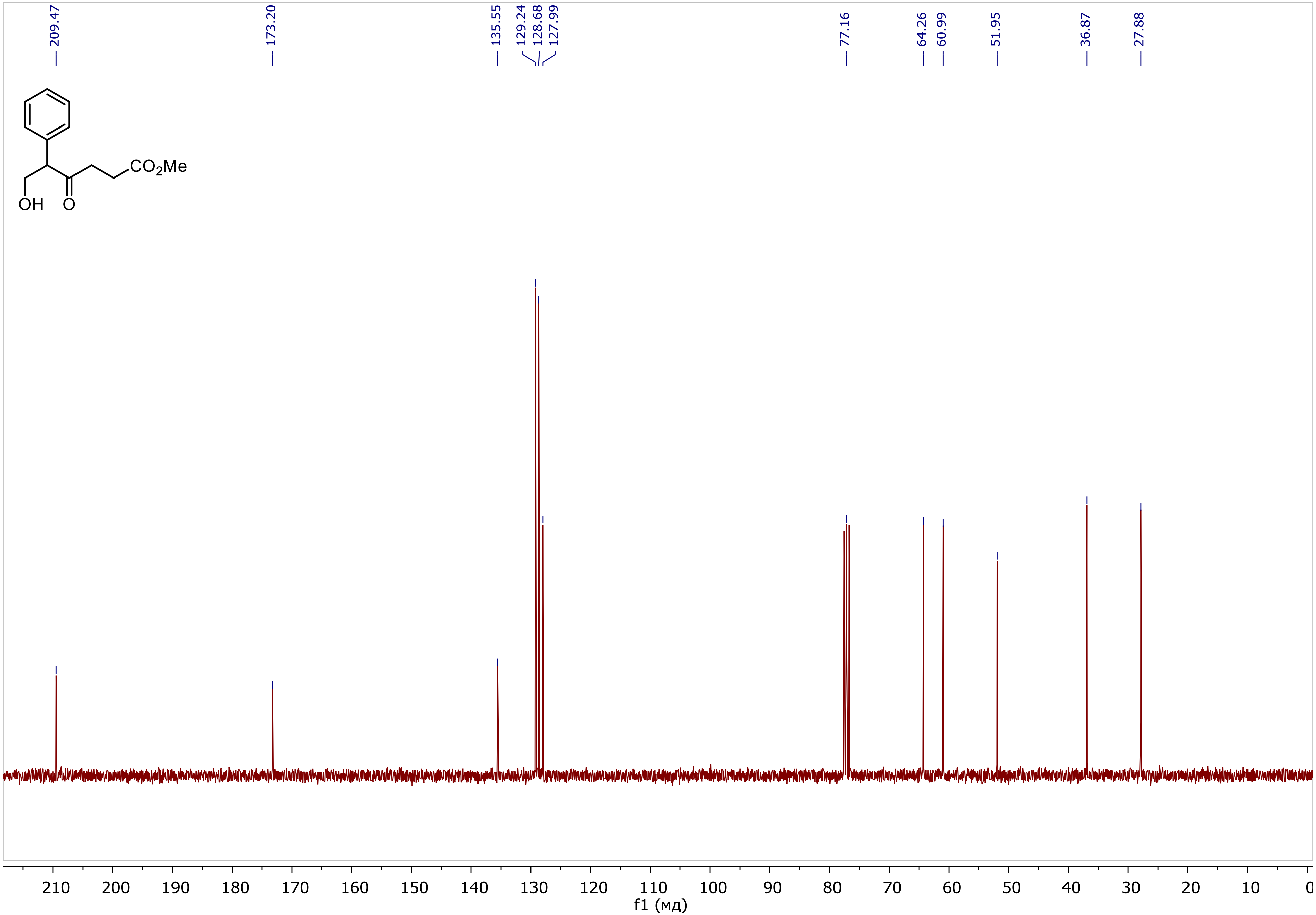
3-Ethyl-4-phenethyl-4,5-dihydroisoxazole 2-oxide (3s)



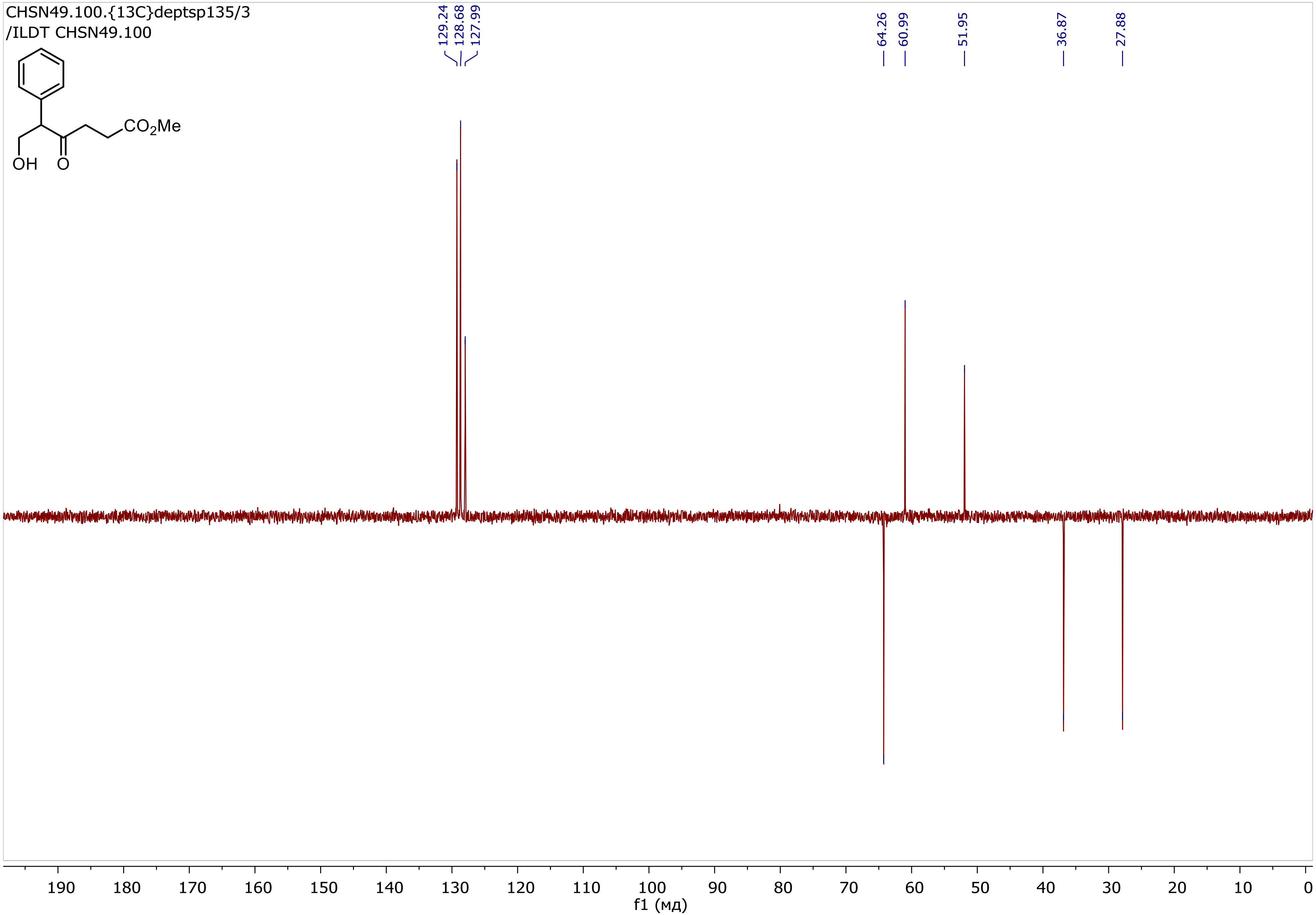
Methyl 6-hydroxy-4-oxo-5-phenylhexanoate (6)



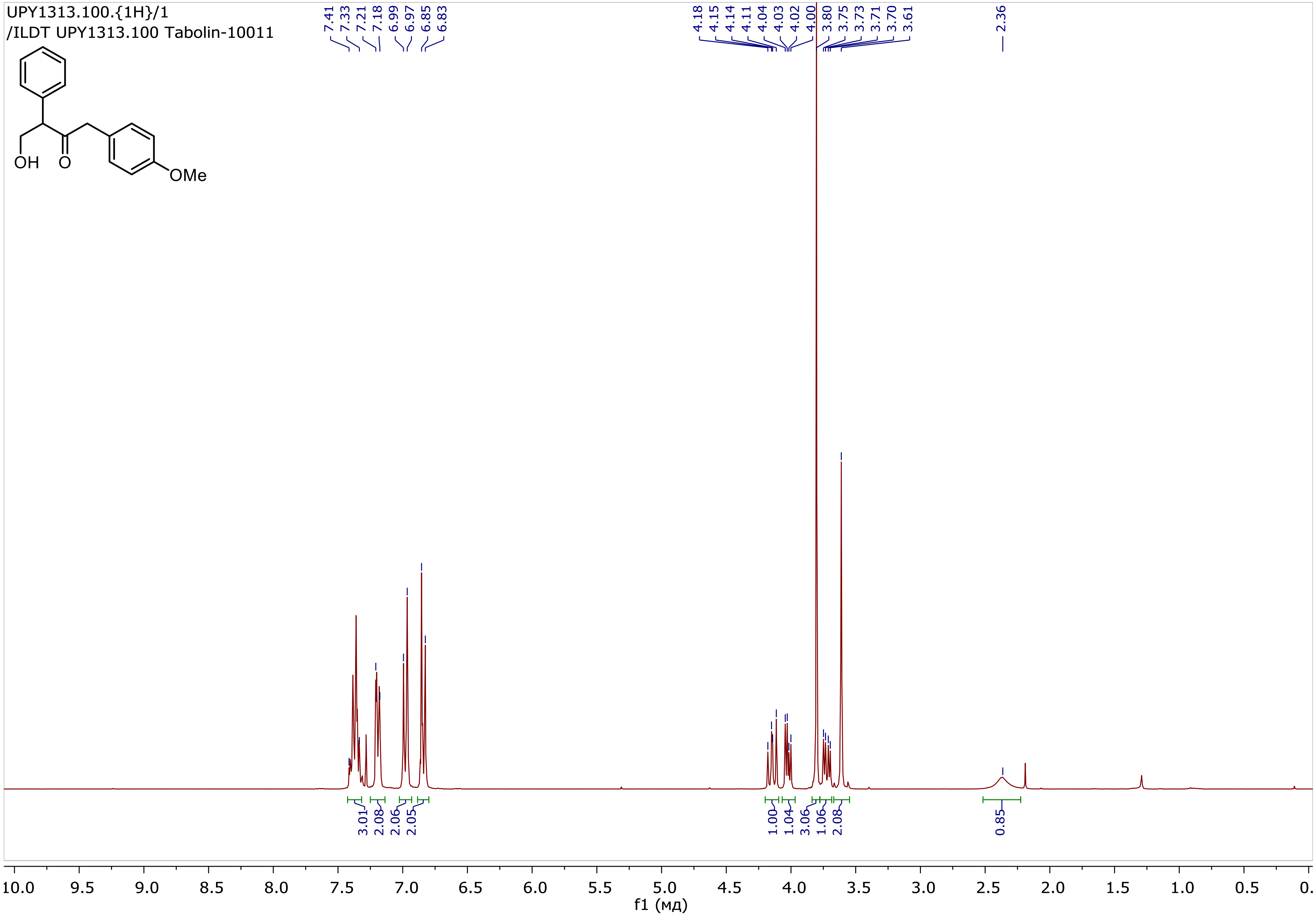
Methyl 6-hydroxy-4-oxo-5-phenylhexanoate (6)



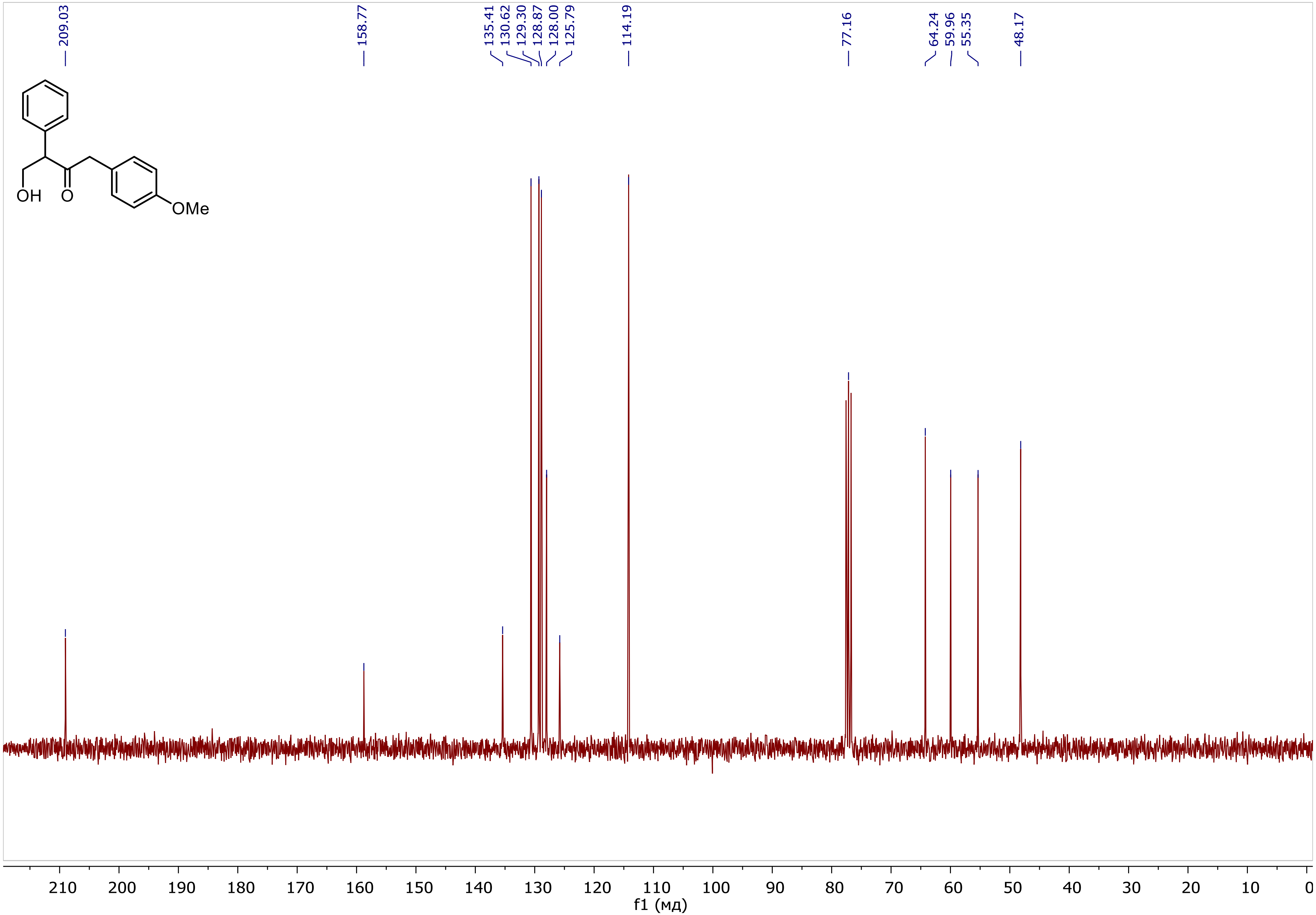
Methyl 6-hydroxy-4-oxo-5-phenylhexanoate (6)



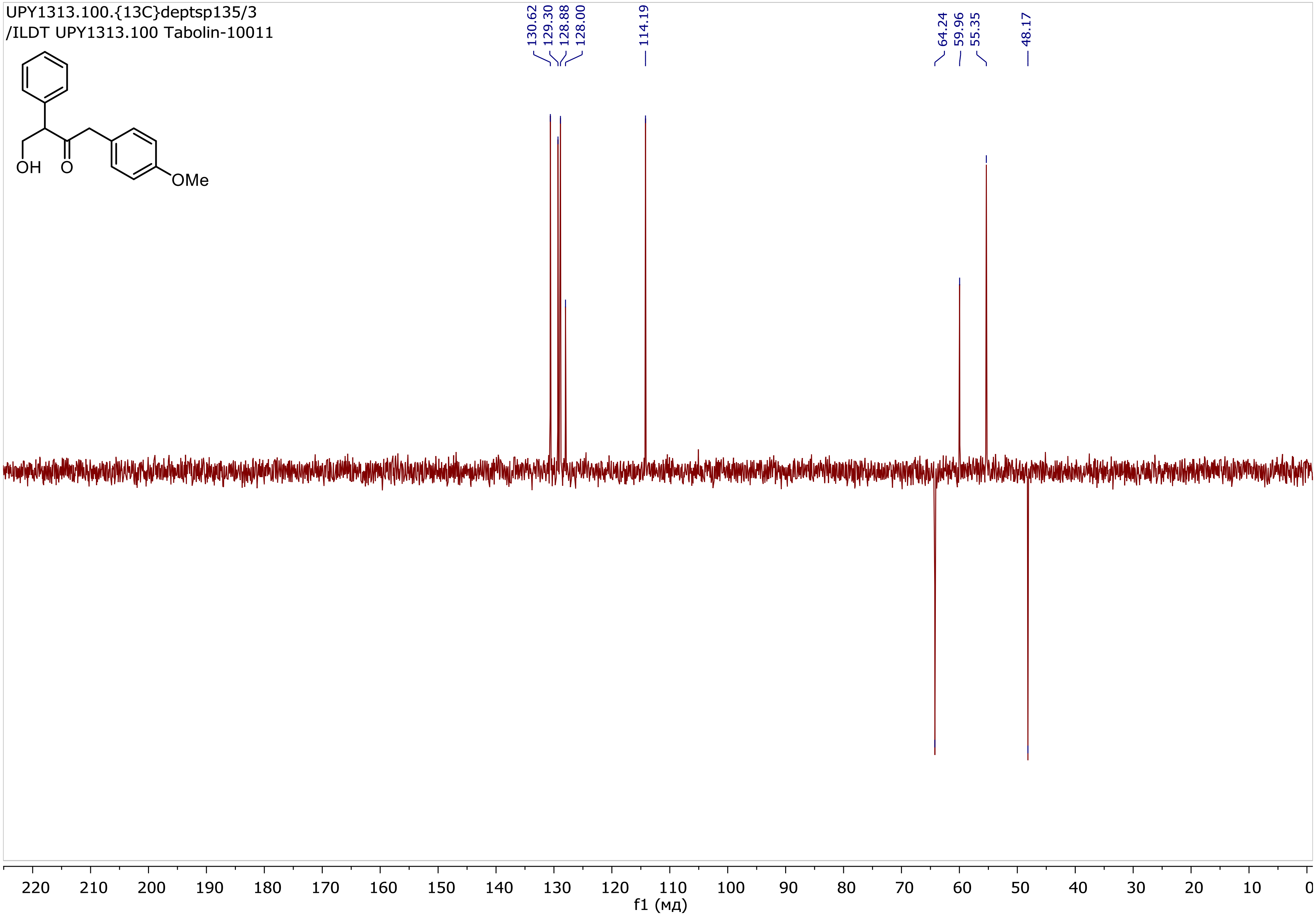
4-Hydroxy-1-(4-methoxyphenyl)-3-phenylbutan-2-one (7)



4-Hydroxy-1-(4-methoxyphenyl)-3-phenylbutan-2-one (7)



4-Hydroxy-1-(4-methoxyphenyl)-3-phenylbutan-2-one (7)



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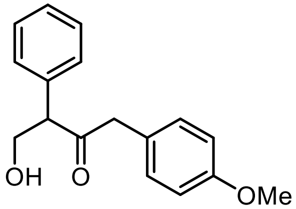
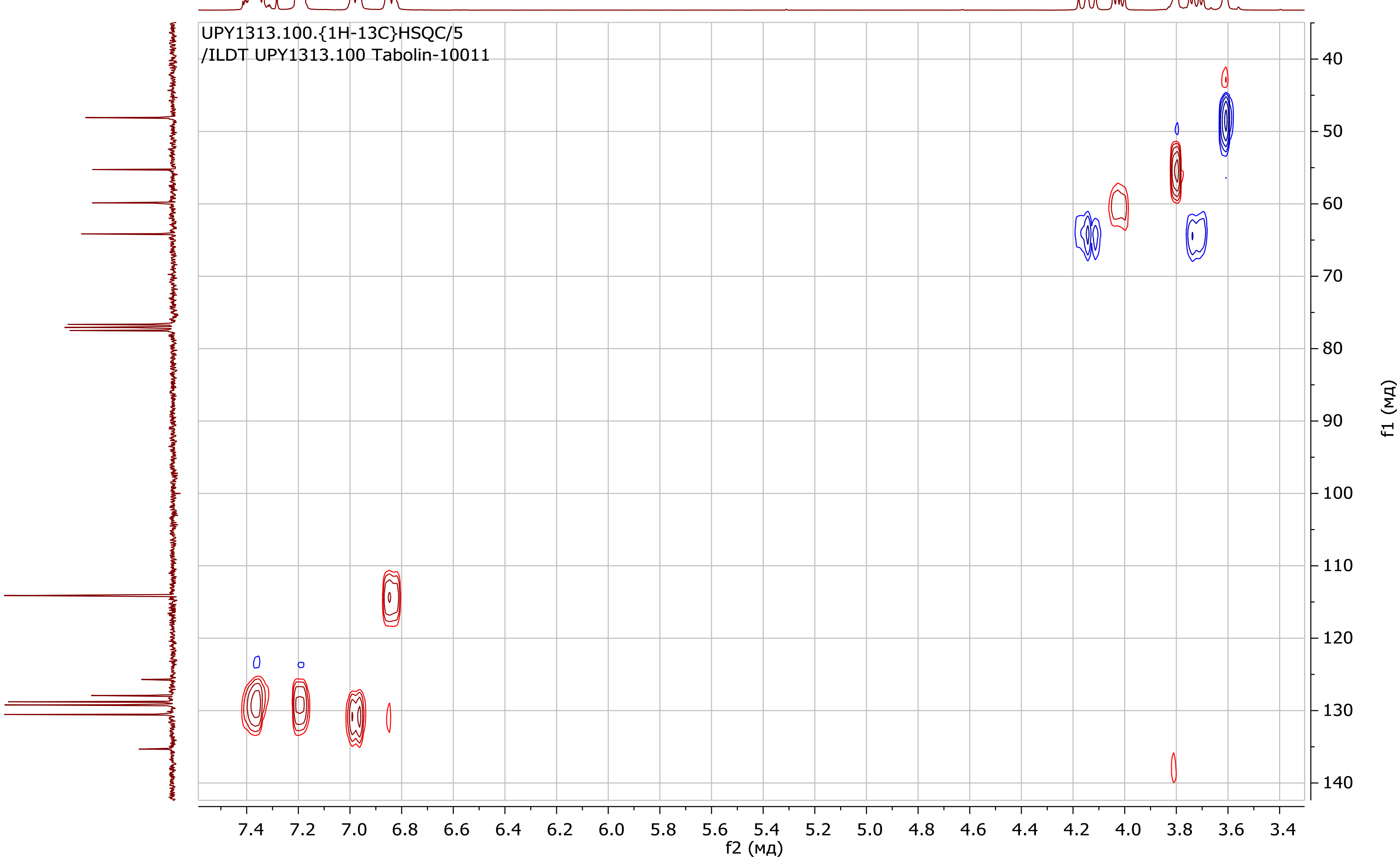
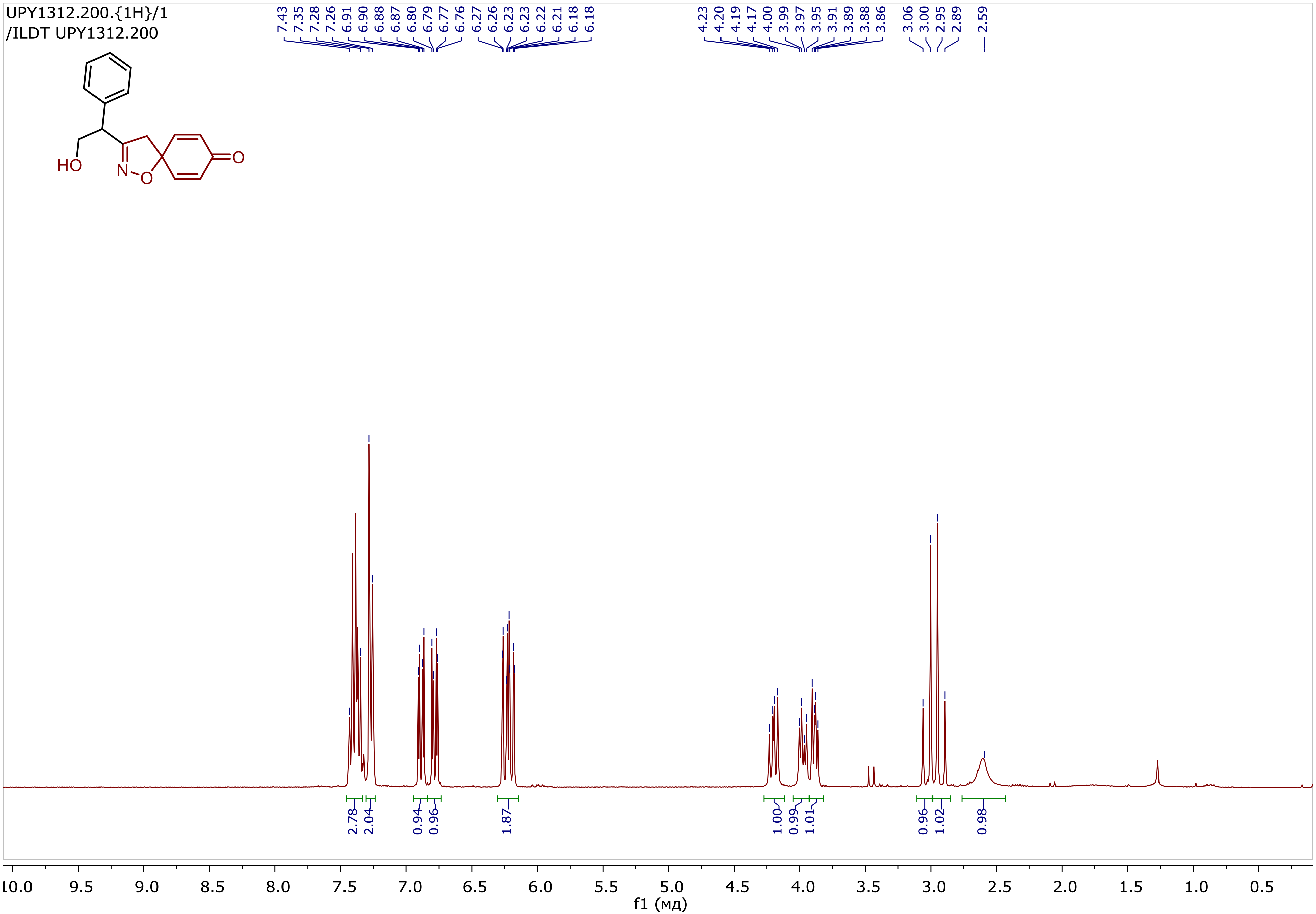




3-(2-Hydroxy-1-phenylethyl)-1-oxa-2-azaspiro[4.5]deca-2,6,9-trien-8-one (8)



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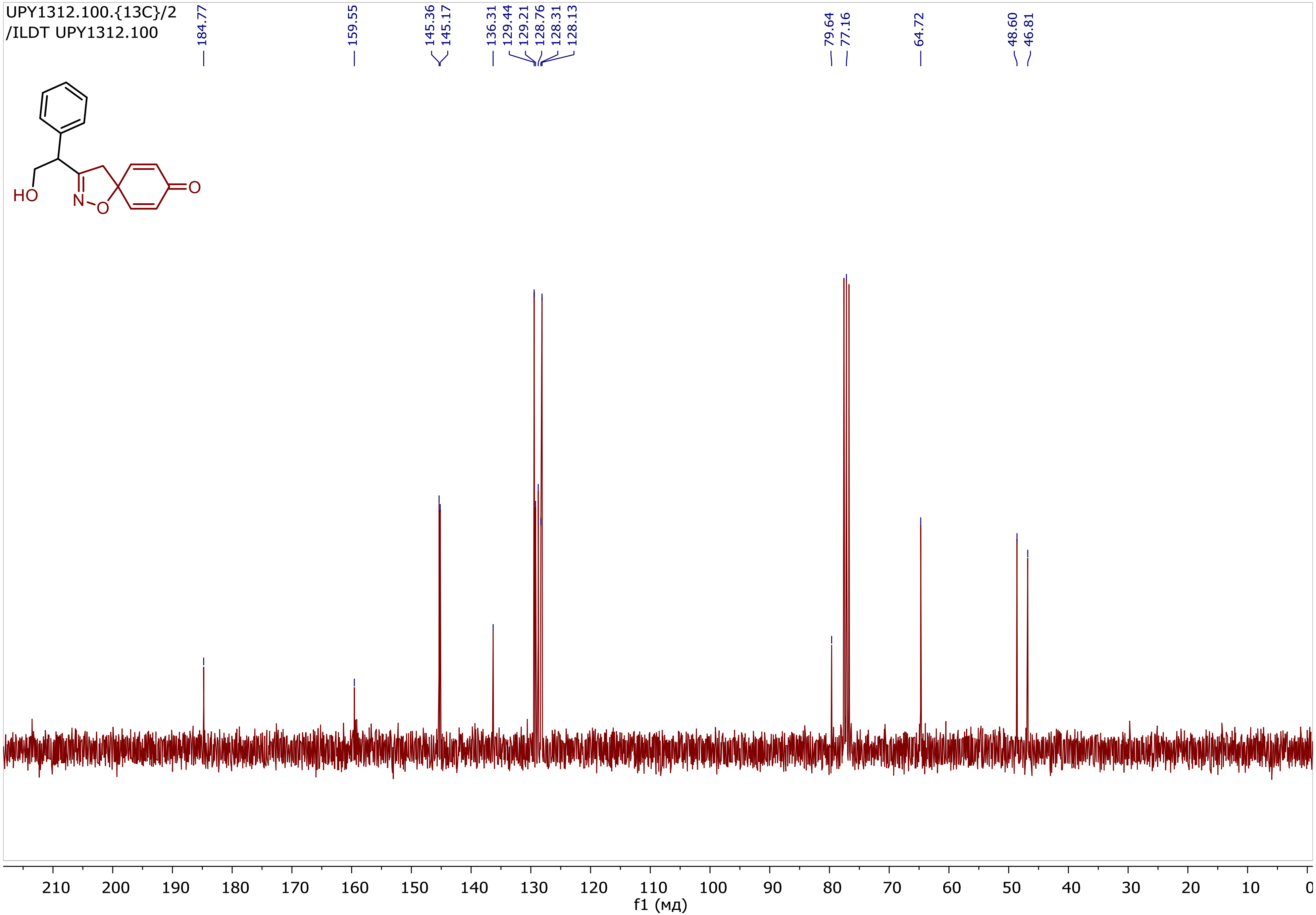
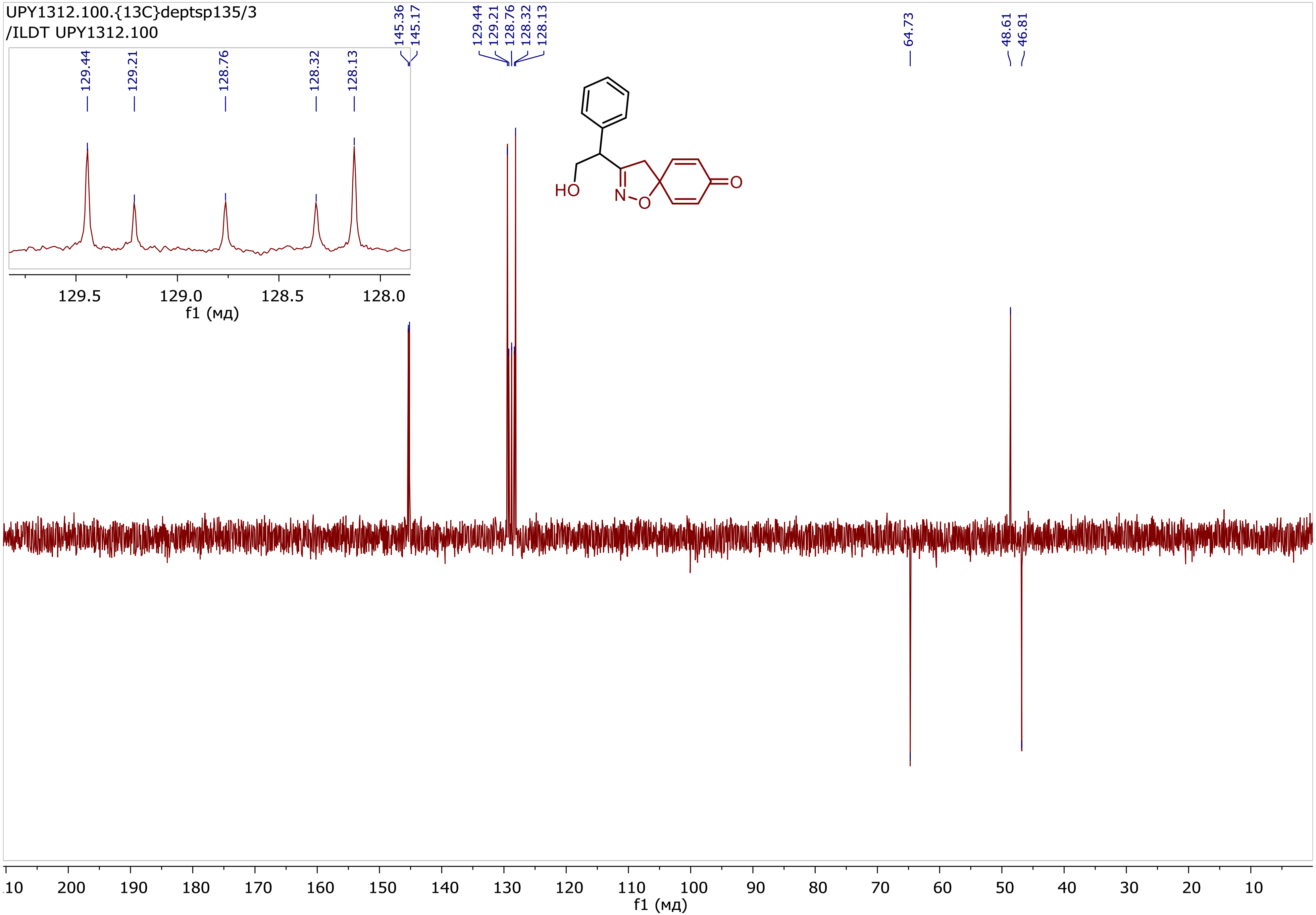
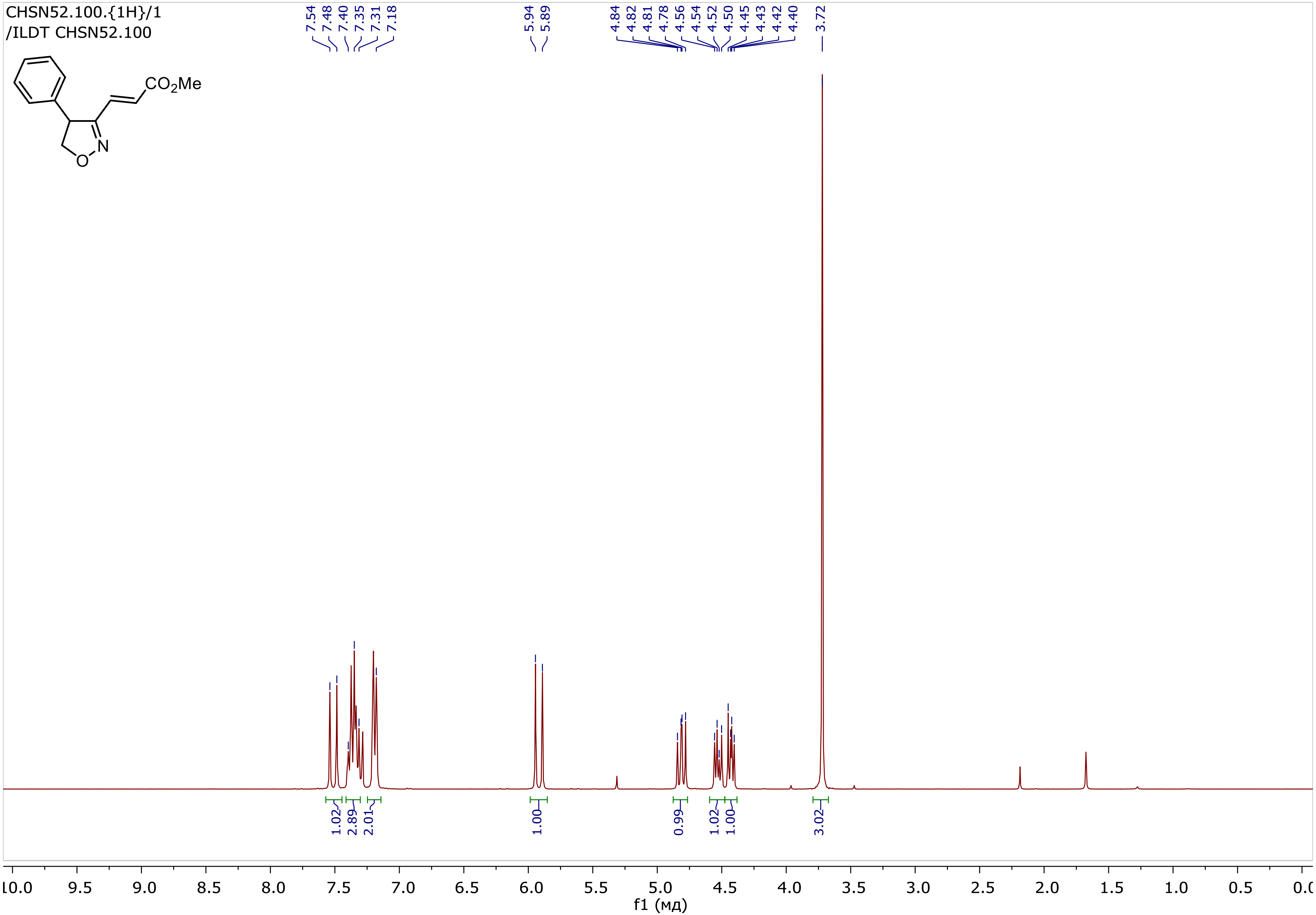


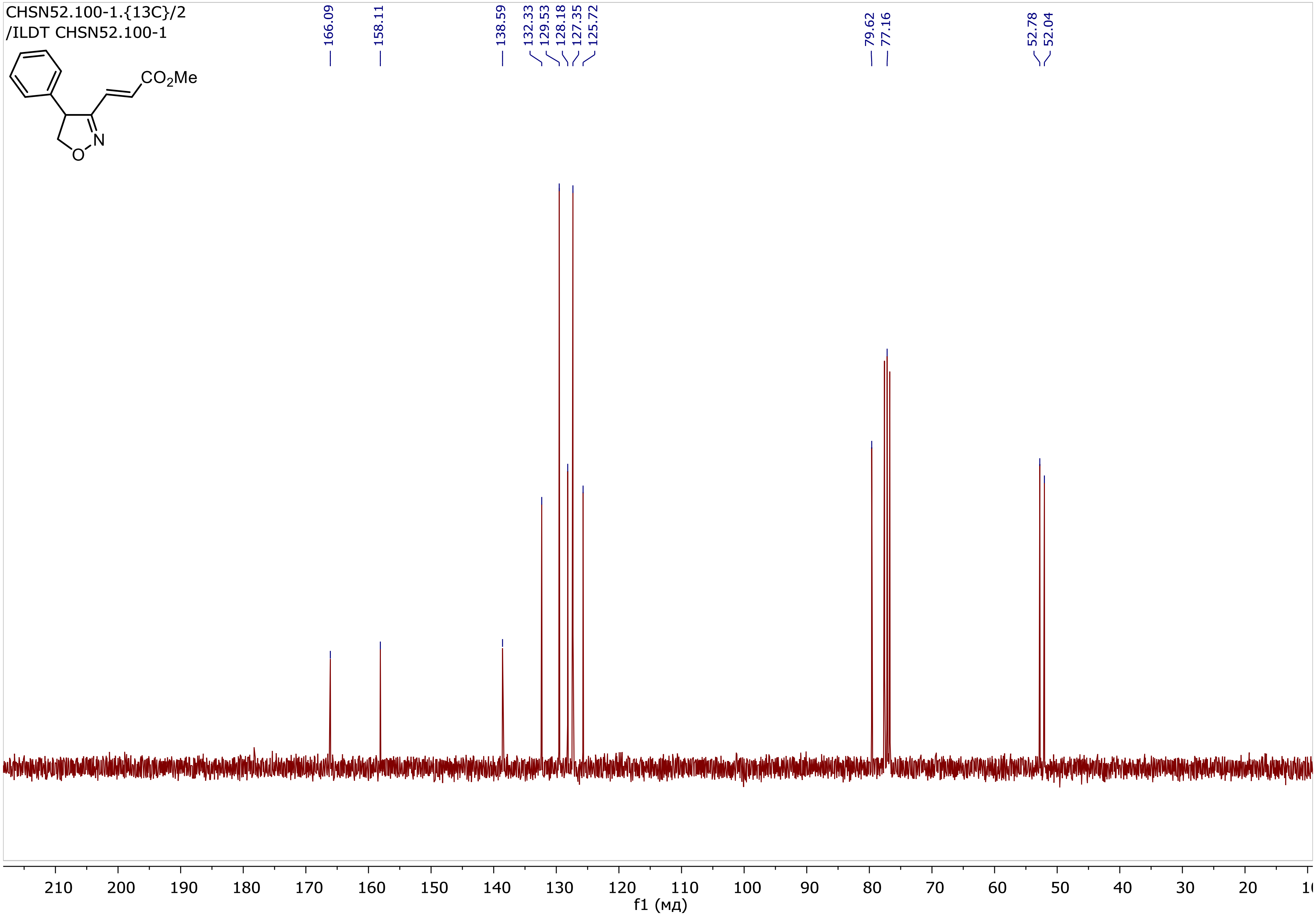
3-(2-Hydroxy-1-phenylethyl)-1-oxa-2-azaspiro[4.5]deca-2,6,9-trien-8-one (8)



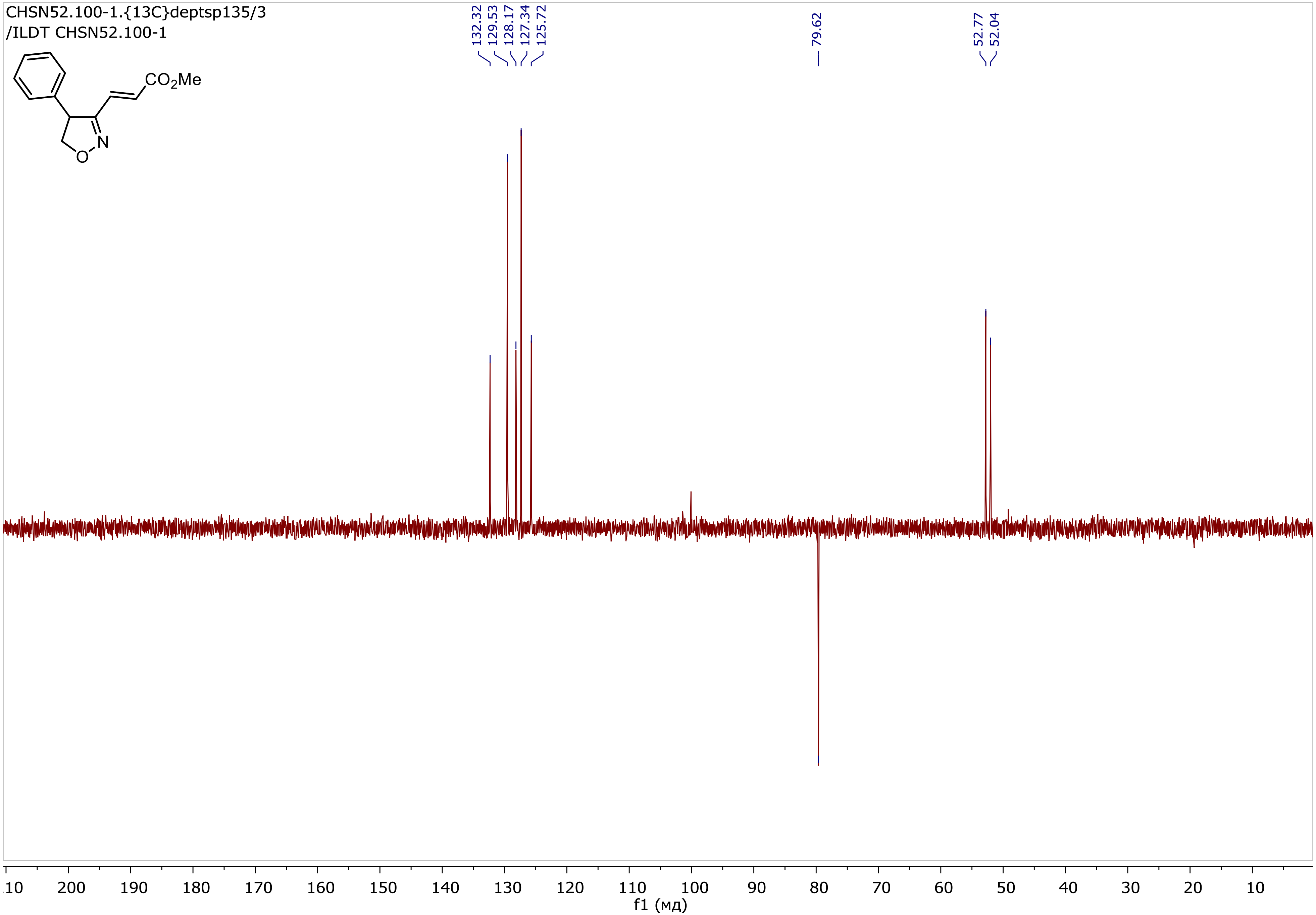
Methyl (*E*)-3-(4-phenyl-4,5-dihydroisoxazol-3-yl)acrylate (10)



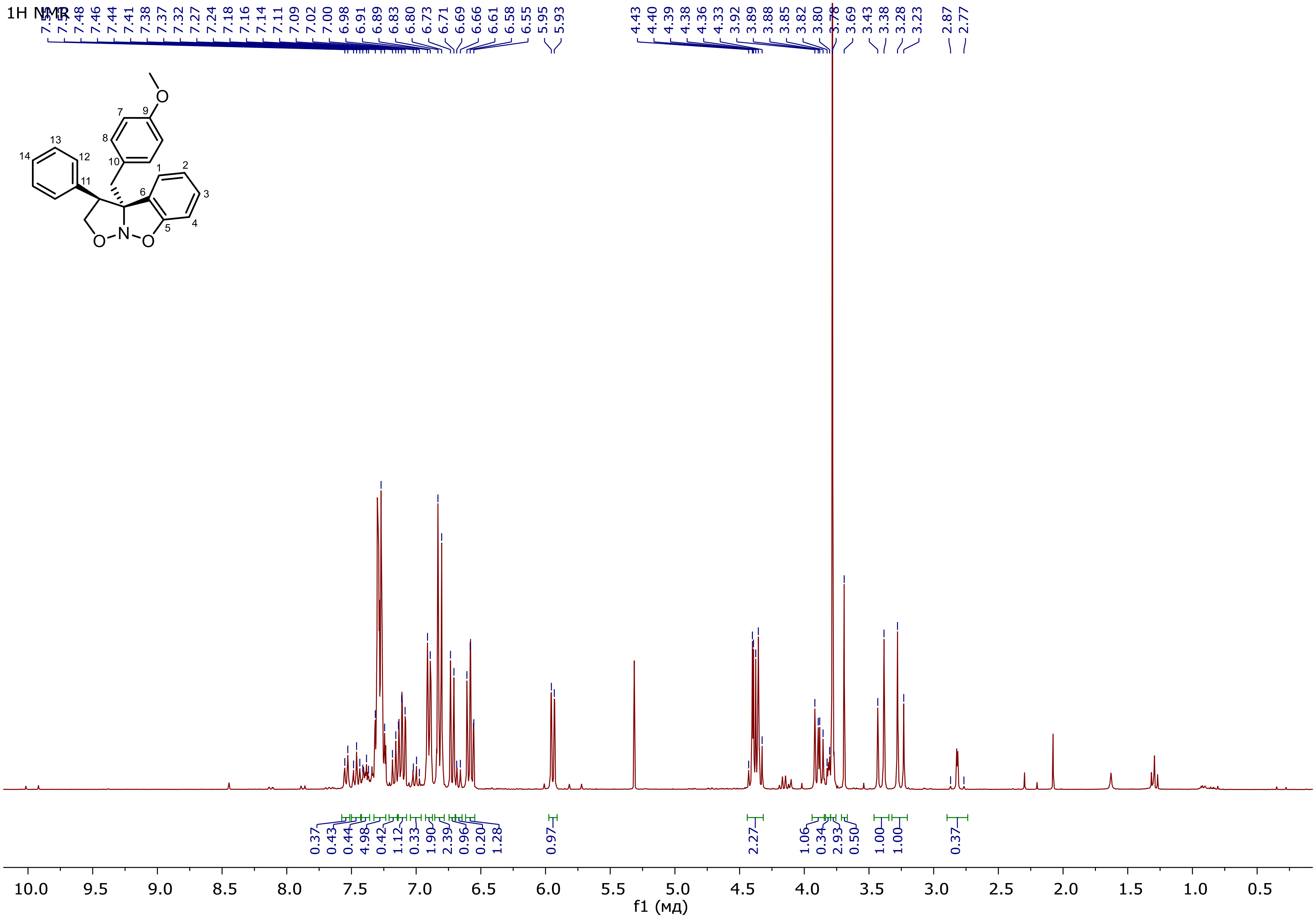
Methyl (*E*)-3-(4-phenyl-4,5-dihydroisoxazol-3-yl)acrylate (10)



Methyl (*E*)-3-(4-phenyl-4,5-dihydroisoxazol-3-yl)acrylate (10)

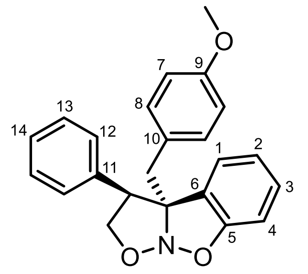


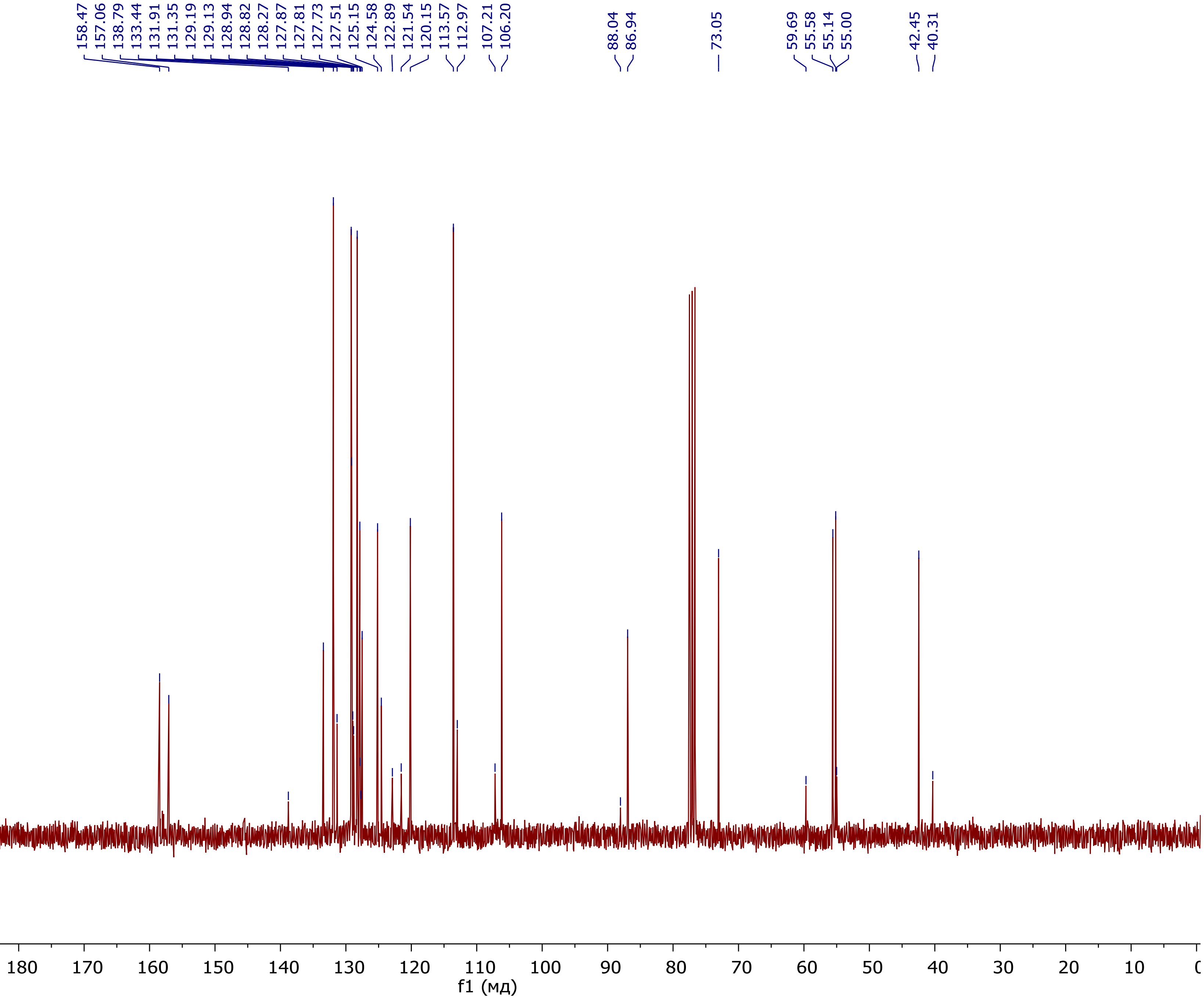
3a-(4-Methoxybenzyl)-3-phenyl-3,3a-dihydro-2H-benzo[d]isoxazolo[2,3-b]isoxazole (12)



3a-(4-Methoxybenzyl)-3-phenyl-3,3a-dihydro-2H-benzo[d]isoxazolo[2,3-b]isoxazole (12)

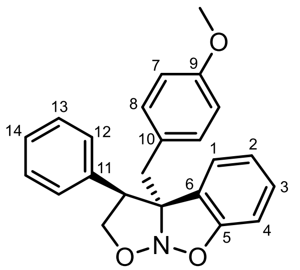
13C NMR

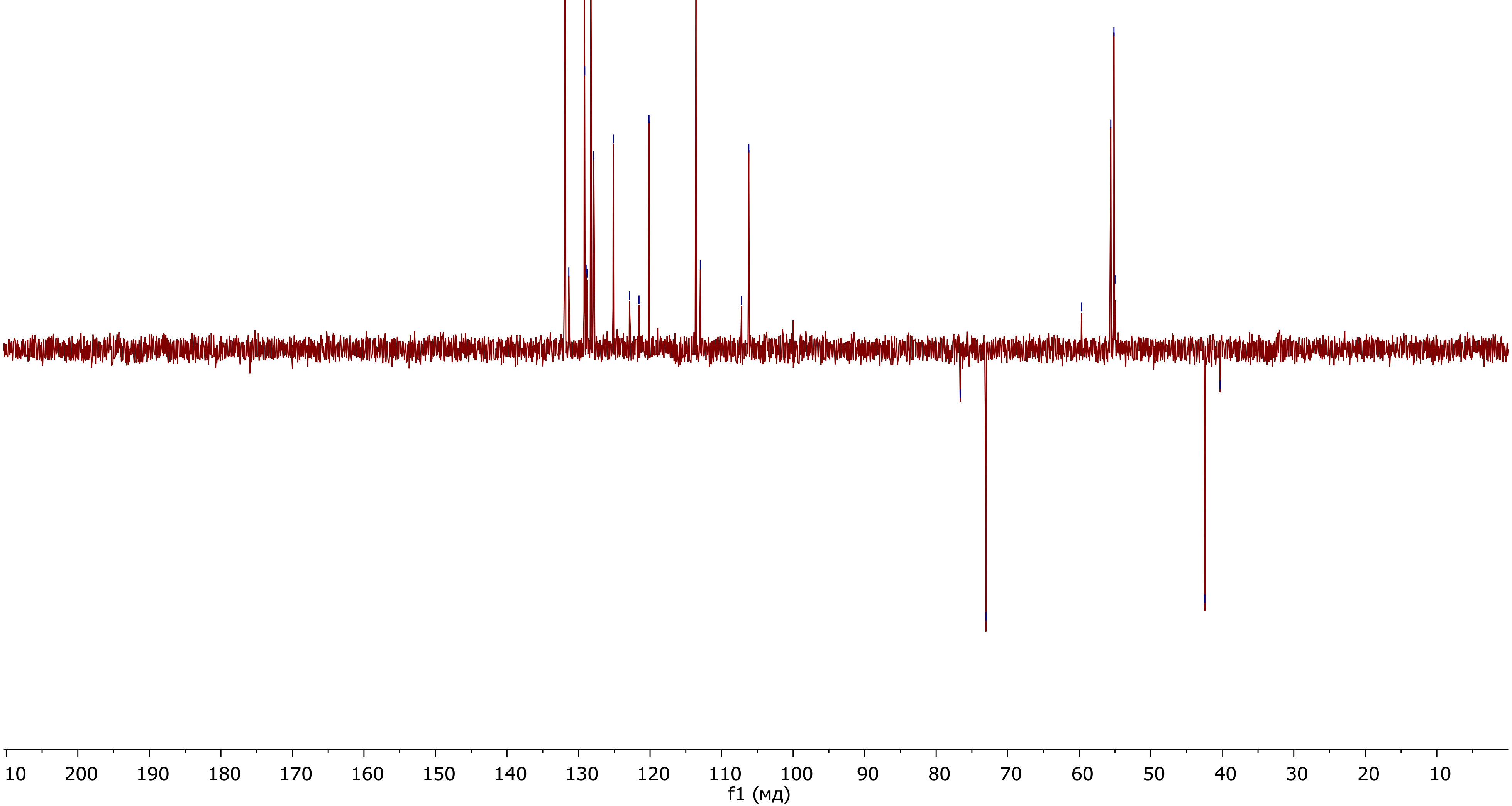




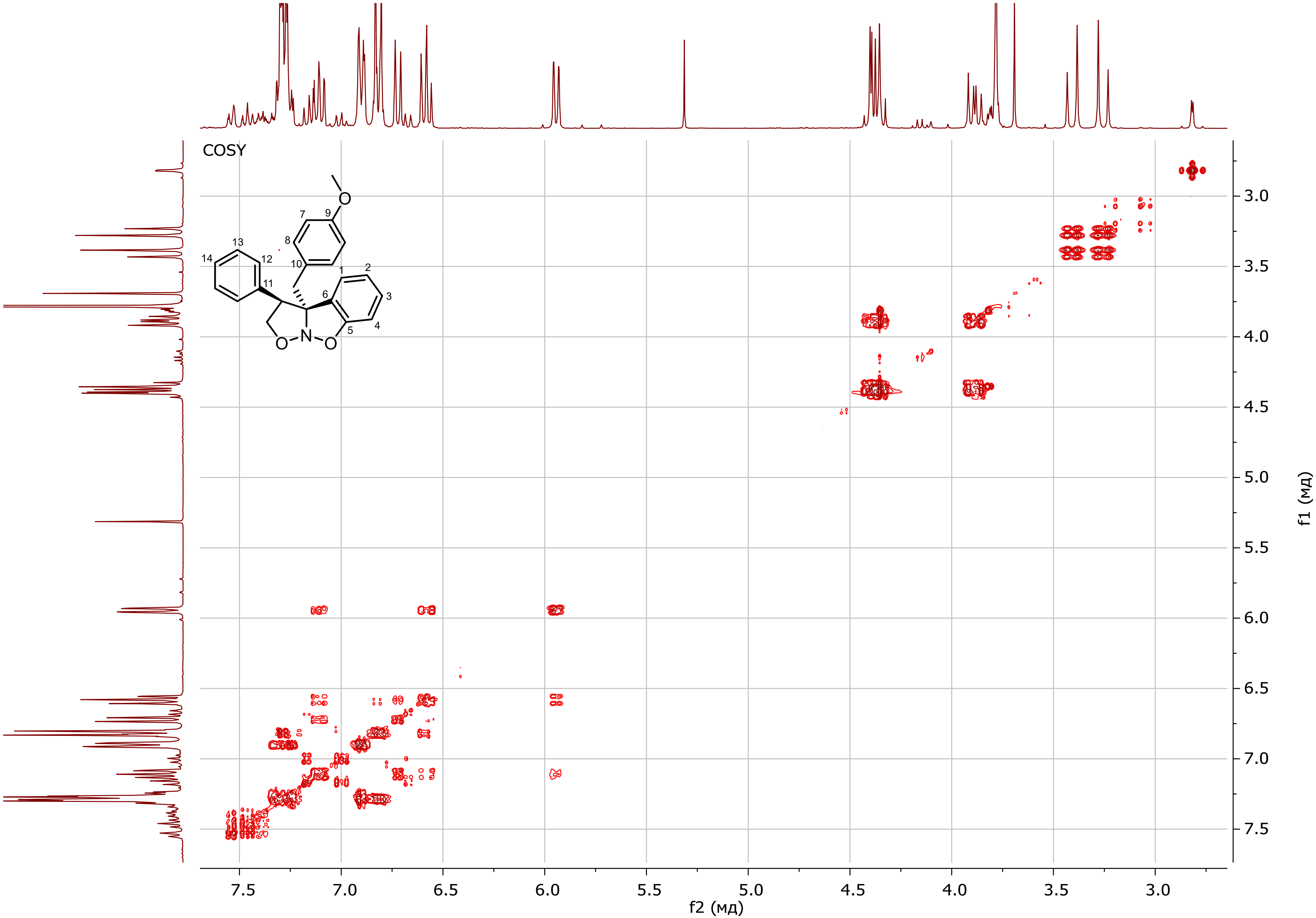
3a-(4-Methoxybenzyl)-3-phenyl-3,3a-dihydro-2H-benzo[d]isoxazolo[2,3-b]isoxazole (12)

DEPT 135

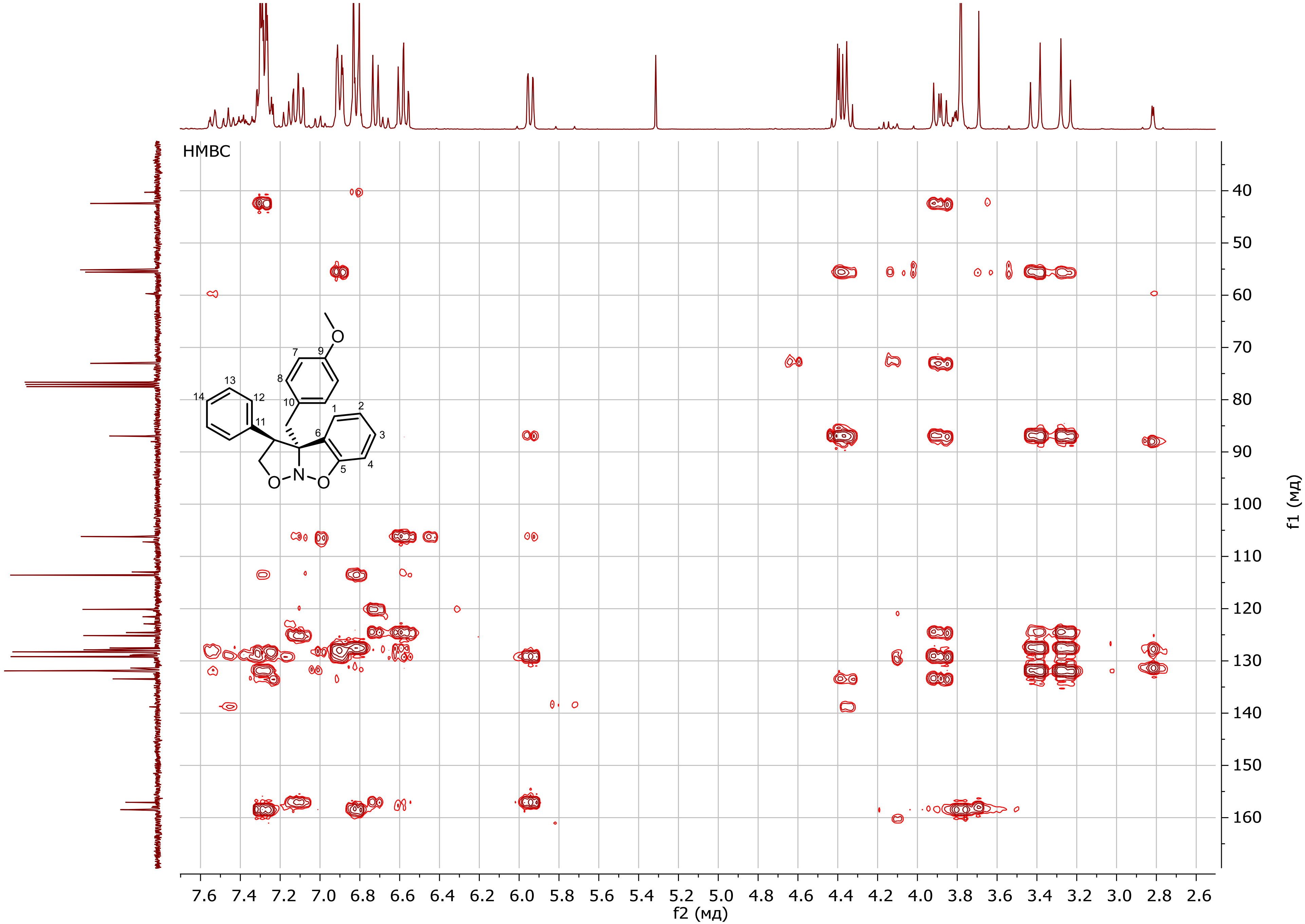




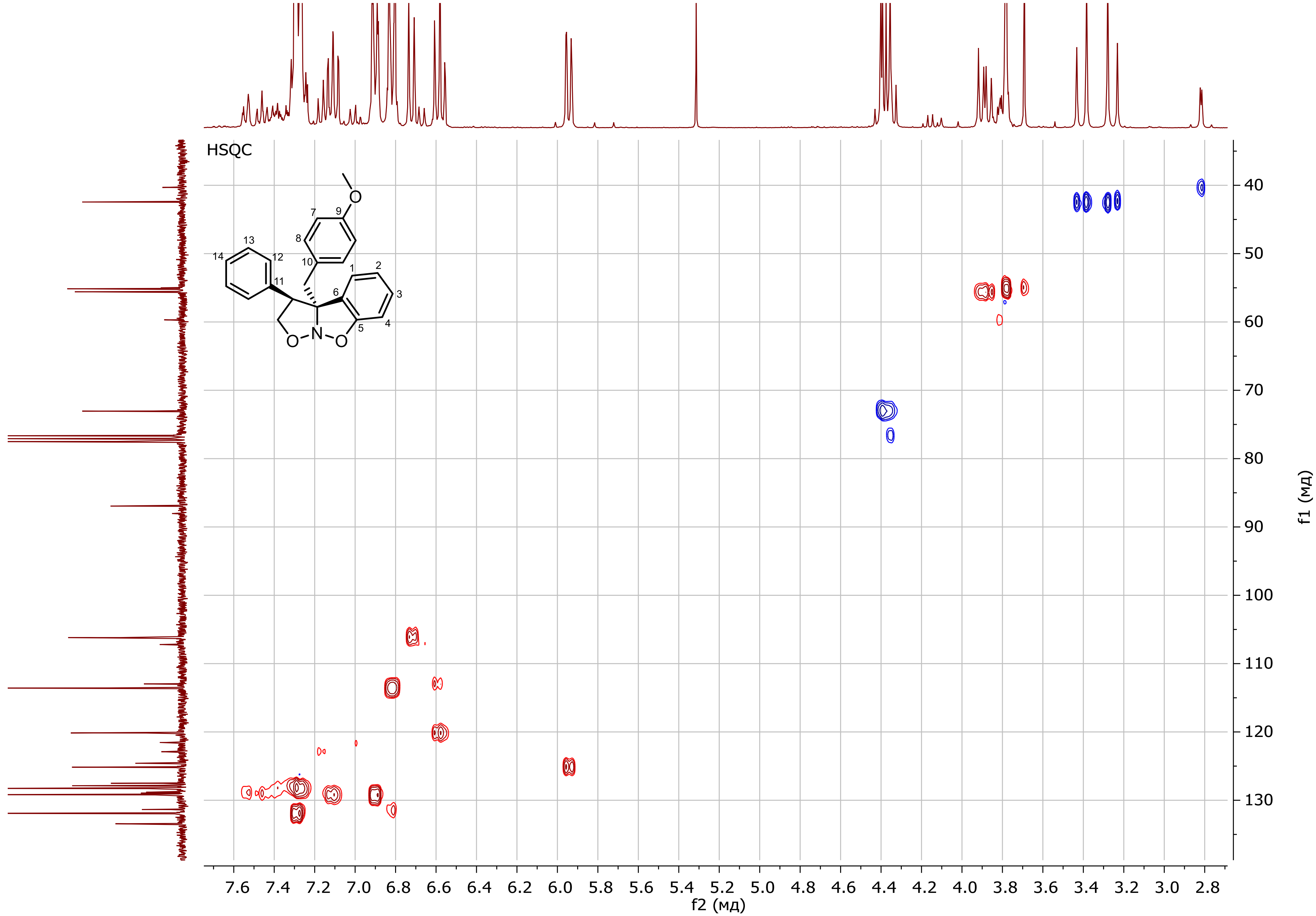
3a-(4-Methoxybenzyl)-3-phenyl-3,3a-dihydro-2H-benzo[d]isoxazolo[2,3-b]isoxazole (12)



3a-(4-Methoxybenzyl)-3-phenyl-3,3a-dihydro-2H-benzo[d]isoxazolo[2,3-b]isoxazole (12)



3a-(4-Methoxybenzyl)-3-phenyl-3,3a-dihydro-2H-benzo[d]isoxazolo[2,3-b]isoxazole (12)



3a-(4-Methoxybenzyl)-3-phenyl-3,3a-dihydro-2H-benzo[d]isoxazolo[2,3-b]isoxazole (12)