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Supporting information

Fluoronitroalkenes in tandem [4+1]/[3+2]-cycloaddition: one-pot three-component assembly of fluorinated bicyclic nitroso acetals

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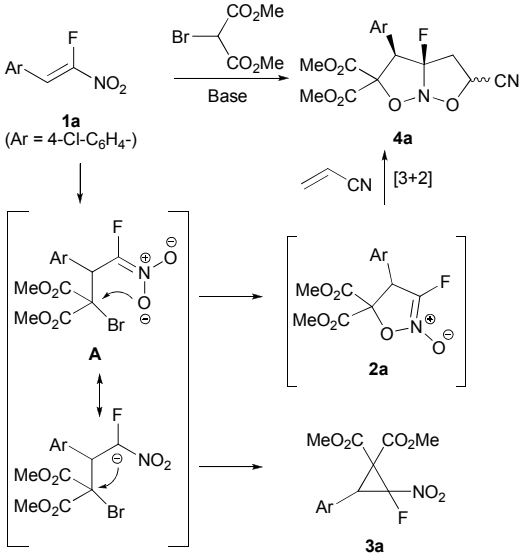
General experimental

All reactions were performed in oven-dried (150 °C) glassware. Most of the chemicals were acquired from commercial sources and used as received. TLC were performed on silica coated on aluminium with UV254 indicator. Visualization was generally accomplished with UV and anisaldehyde/H_2SO_4 stain. For visualisation of compound **10** UV and Ceric Ammonium Molybdate stain were used. Column chromatography was performed on silica (0.04–0.063 mm, 60 Å). NMR spectra were recorded at the following spectrometer frequencies: 300 MHz (^{1}H NMR), 75 MHz or 100 MHz (^{13}C NMR), 282 MHz (^{19}F NMR). Multiplicities are assigned as s (singlet), d (doublet), t (triplet), q (quadruplet), p (pentet), m (multiplet), br (broad), app (apparent). High resolution mass spectra were acquired at TOF spectrometer using electrospray ionization (ESI). Tandem HPLC-HRMS was made on Agilent Poroshell 120 EC-C18 column (3.0 × 50 mm; 2.7 µm). The column was eluted in a gradient of concentrations of solvent A (acetonitrile) and solvent B (water) with the flow rate of 400 µl/min in the following gradient parameters: 0-15% A for 6.0 min, then 15%-85% A for 1.5 min, then 85%-100% A for 0.1 min, 100% A for 2.4 min.

Starting compounds were prepared according to literature procedures: (*Z*)-1-chloro-4-(2-fluoro-2-nitrovinyl)benzene **1a**,[s1] (*Z*)-methyl 4-(2-fluoro-2-nitrovinyl)benzoate **1b**,[s1] (*Z*)-1-fluoro-4-(2-fluoro-2-nitrovinyl)benzene **1c**,[s1] (*Z*)-1-(2-fluoro-2-nitrovinyl)-4-methoxybenzene **1d**,[s1] (*Z*)-1-(2-fluoro-2-nitrovinyl)-3-methoxybenzene **1e**,[s2] (*Z*)-1-bromo-2-(2-fluoro-2-nitrovinyl)benzene **1f**,[s1] methyl 4-vinylbenzoate,[s3] 4-vinylbiphenyl,[s4] 1-vinylnaphthalene,[s5] *p*-methoxy-β-nitrostyrene **5**,[s6] *p*-methoxy-β-bromo-β-nitrostyrene **7b**,[s7] $PhICl_2$.[s8]

Optimizations of reaction conditions



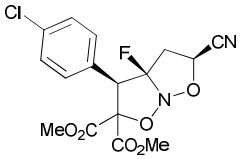
Entry	Conditions	Acrylonitrile, equiv.	Yield **2a**,% [a]	Yield **3a**,%[a]	Yield **4a**,%[a]
1	DBU, CH_2Cl_2 (0.1 M), rt	none	0	18	-
2	Et_3N, CH_2Cl_2 (0.1 M), rt	none	0	13	-
3	K_2CO_3, MeOH (0.1 M), rt	none	0	0	-
4	K_2CO_3, MeCN (0.1 M), rt	none	n.r.[c]	n.r.[c]	-
5	K_2CO_3, DMF (0.1 M), rt	none	16	10	-
6	K_2CO_3, DMF (0.1 M), rt	20		5	61 (58[b])
7	K_2CO_3, THF/H_2O (0.1 M), TBAC (1%), rt	20		5	7
8	K_2CO_3, DMF (0.1 M), 0°C-rt	20		4	65
9	K_2CO_3, DMF (0.1 M), 50°C	20		0	0
10	Cs_2CO_3, DMF (0.1 M), 0°C-rt	20		4	57
11	Na_2CO_3, DMF (0.1 M), 0°C-rt	20		4	60
12	**K_2CO_3, DMF (0.05 M), 0°C-rt**	**20**		**2**	**67 (65[b])**
13	K_2CO_3, DMF (0.5 M), 0°C-rt	20		13	46
14	Et_3N, DMF (0.1 M), 0°C-rt	20		5	37
15	DIPEA, DMF (0.1 M), 0°C-rt	20		2	43
16	DABCO, DMF (0.1 M), 0°C-rt	20		12	0
17	K_2CO_3, DMF (0.1 M), 0°C-rt	10		2	50
18	K_2CO_3, DMF (0.1 M), 0°C-rt	3		2	21

[a] ^{19}FNMR yields; [b] isolated yields in brackets; [c] n. r.= no reaction (**1a** was recovered);

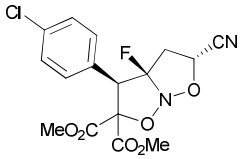
General procedure 1 for the one-pot synthesis of fluorinated 5,5-annulated nitrosoacetals 4a-4w.

The solution of α-fluoronitroalkene **1** (0.3 mmol), dimethyl bromomalonate (0.33 mmol, 1.1 equiv.) and dipolarophile (6 mmol, 20 equiv., unless otherwise mentioned) in dry DMF (6 ml) was cooled to 0°C using ice bath and finely powdered K_2CO_3 (0.45 mmol, 1.5 equiv.) was added. Mixture was stirred at 0°C for 10 min., then warmed to r. t. and stirring was continued for additional 2-6 hours. After the reaction was complete (TLC monitoring), mixture was poured into H_2O (15 ml), and product was extracted with t-BuOMe (3x20 ml). Organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. Crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 9:1 – 7:3) to afford fluorinated nitrosoacetals **4a-4w**.

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-5-cyano-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4a** (major isomer) and ***rel*-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-5-cyano-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'a** (minor isomer)



major isomer



minor isomer

Nitrosoacetals **4,4'a** was obtained from α-fluoronitroalkene **1a** (91 mg, 0.45 mmol) and acrylonitrile following the general procedure 1. Column chromatography (eluent: 9:1, then 5:1, then 7:3 PE/EtOAc) afforded **4a** (82 mg, 47%) and **4'a** (26 mg, 15%) as colorless oils.

Major isomer (**4a**):

R_f = 0.37 (PE/EtOAc, 1:1)

mp = 135-136 °C (EtOH).

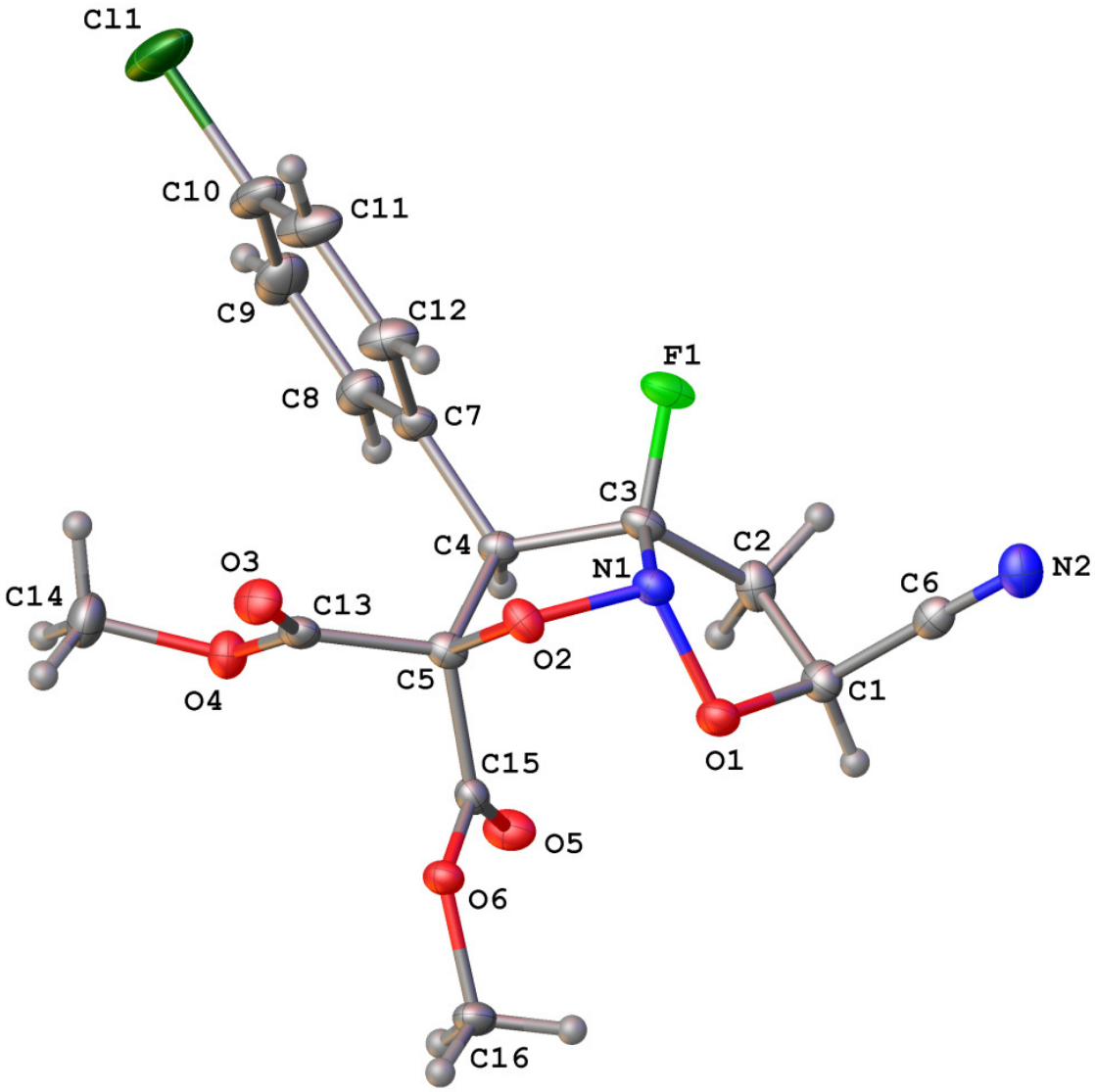
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.98 (ddd, *J* = 20.4, 14.2, 4.8 Hz, 1H, CH_{2a}), 3.31 (ddd, *J* = 23.7, 14.2, 9.4 Hz, 1H, CH_{2b}), 3.34 (s, 3H, CO_2Me), 3.87 (s, 3H, CO_2Me), 4.85 (d, *J* = 6.5 Hz, Ar-C**H**), 5.16 (ddd, *J* = 9.4, 4.7, 0.6 Hz, O-C**H**-CN), 7.29-7.38 (m, 4H, CH_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ 41.4 (d, $^2J_{CF}$ = 29.0 Hz, CH_2), 53.0 (-CO_2**Me**), 54.4 (-CO_2**Me**), 55.7 (d, $^2J_{CF}$ = 22.6 Hz, CH–Ar), 66.5 (**C**H–CN), 92.0 (C–O), 115.5 (CN), 118.8 (d, $^1J_{CF}$ = 222.5 Hz, C–F), 128.7 (CH_{Ar}), 128.8 (d, $^3J_{CF}$ = 3.7 Hz, C_{Ar}), 131.8 (d, $^4J_{CF}$ = 1.4 Hz, $CH_{Ar,}$), 135.2 (C_{Ar}), 164.4 (-**C**O_2Me), 167.0 (-**C**O_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -133.9 (td, *J* = 20.0, 4.9 Hz).

HRMS (ESI): m/z calcd. for [$C_{16}H_{14}ClFN_2O_6$ + H^+]: 385.0597, found: 385.0593.

X-ray data was deposited in the Cambridge Crystallographic Data Centre (CCDC 1849100).



General view of the compound **4a** in representation of atoms *via* thermal ellipsoids at 50% probability level.

Minor isomer (**4'a**):

R_f = 0.48 (PE/EtOAc, 1:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.12 (ddd, *J* = 24.0, 14.7, 9.5 Hz, 1H, CH_{2a}), 3.29 (ddd, *J* = 24.6, 14.7, 4.9 Hz, 1H, CH_{2b}), 3.32 (s, 3H, CO_2Me), 3.92 (s, 3H, CO_2Me), 5.00 (s, Ar-C**H**), 5.31 (dd, *J* = 9.5, 4.9 Hz, O-C**H**-CN), 7.31-7.37 (m, 4H, CH_{Ar}).

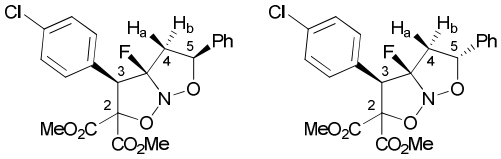
^{13}C NMR (75 MHz, $CDCl_3$): δ 42.0 (d, $^2J_{CF}$ = 30.4 Hz, CH_2), 52.8 (-CO_2**Me**), 53.8 (d, $^2J_{CF}$ = 21.9 Hz, CH–Ar), 54.6 (-CO_2**Me**), 68.6 (**C**H–CN), 89.0 (C–O), 116.7 (CN), 118.9 (d, $^1J_{CF}$ = 225.2 Hz, C–F), 128.6 (CH_{Ar}), 129.5 (d, $^3J_{CF}$ = 3.5 Hz, C_{Ar}), 132.0 ($CH_{Ar,}$), 135.0 (C_{Ar}), 165.3 (-**C**O_2Me), 166.3 (-**C**O_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -133.2 (t, *J* = 24.1 Hz).

HRMS (ESI): m/z calcd. for [$C_{16}H_{14}ClFN_2O_6$ + Na^+]: 407.0417, found: 407.0411.

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4b** (major) and ***rel*-(3R,3aR,5R)-Dimethyl 3-(4-**

chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'b (minor)



Nitrosoacetals **4,4'b** was obtained from α-fluoronitroalkene **1a** (60.4 mg, 0.3 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4b** (87.2 mg, 64%, dr (**4b**:**4'b**)= 10:1) as colorless solid. Pure major isomer was obtained by recrystallization from chloroform as colorless crystals. Mother liquor was evaporated to give mixture of **4b:4'b** = 2:1.

R_f = 0.61 (PE/EtOAc, 1:1)

mp = 142-146 °C ($CHCl_3$)

Major isomer (**4b**):

^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY): δ 2.66 (ddd, *J* = 24.6, 14.1, 7.7 Hz, 1H, CH_{2a}(4)), 3.20 (ddd, *J* = 20.1, 14.1, 8.4 Hz, 1H, CH_{2b}(4)), 3.36 (s, 3H, CO_2Me), 3.91 (s, 3H, CO_2Me), 4.95 (d, *J* = 3.9 Hz, 1H, CH(3)), 5.16 (app td, *J* = 8.2, 1.7 Hz, 1H, CH(5)), 7.33-7.45 (m, 9H, CH_{Ar}).

Characteristic NOESY interactions: CH(3)-CH_{2b}(4); CH_{2b}(4)-CH(5).

Characteristic HOESY interactions: F-CH_{2a}(4); CH_{Ar}-F.

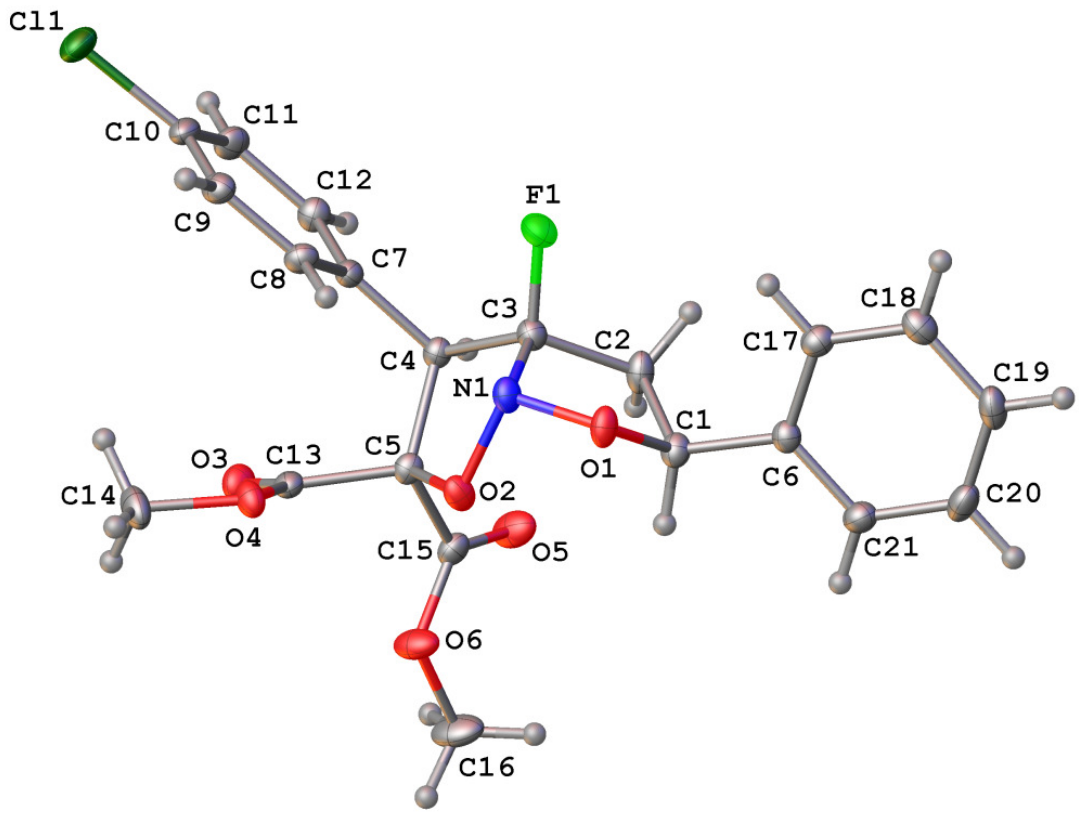
^{13}C NMR (75 MHz, $CDCl_3$): δ 44.7 (d, $^2J_{CF}$ = 28.0 Hz, CH_2(4)), 52.7 (-CO_2**Me**), 54.1 (-CO_2**Me**), 55.8 (d, $^2J_{CF}$ = 22.5 Hz, CH(3)), 85.2 (C(5)), 89.4 (C(2)), 119.1 (d, $^1J_{CF}$ = 221.7 Hz, C–F), 127.0 (CH_{Ar}), 128.4 (CH_{Ar}), 128.8 (CH_{Ar}), 129.0 (CH_{Ar}), 130.3 (d, $^3J_{CF}$ = 3.2 Hz, $C_{Ar,}$), 132.1 (d, *J* = 1.2 Hz, CH_{Ar}), 134.7 (C_{Ar}), 137.0 (C_{Ar}), 165.9 (-**C**O_2Me), 167.2 (-**C**O_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -131.4 (ddd, *J* = 24.6, 20.1, 3.9 Hz).

^{15}N NMR (30 MHz, $CDCl_3$, from ^{1}H-^{15}N HMBC): δ 288 (d, $^2J_{NF}$ = 36 Hz).

HRMS (ESI): m/z calcd. for [$C_{21}H_{19}ClFNO_6$ + H^+]: 436.0958, found: 436.0959.

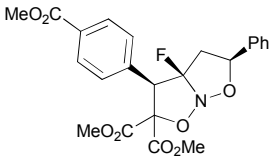
X-ray data was deposited in the Cambridge Crystallographic Data Centre (CCDC 1849099).



General view of the compound **4b** in representation of atoms *via* thermal ellipsoids at 50% probability level.

Minor isomer (**4'b**):
^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY): δ 2.85 (ddd, *J* = 26.6, 13.9, 9.5 Hz, 1H, CH_{2b}(4)), 2.90-3.03 (m, 1H, CH_{2a}(4)), 3.36 (s, 3H, CO_2Me), 3.77 (s, 3H, CO_2Me), 4.93-4.94 (m, 1H, CH(3)), 5.50 (dd, *J* = 9.5, 7.1 Hz, 1H, CH(5)), 7.33-7.45 (m, 9H, CH_{Ar}).
Characteristic NOESY interactions: CH(5)-CH_{2a}(4).
Characteristic HOESY interactions: F-CH(5); F-CH_{2a}(4); CH_{Ar}-F.
^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): 44.4 (d, $^{2}J_{CF}$ = 28.1 Hz, CH_2(4)), 52.7 (-CO_2**Me**), 53.8 (-CO_2**Me**), 56.6 (d, $^{2}J_{CF}$ = 23.3 Hz, CH(3)), 81.9 (C-3), 92.9 (C(5)), 120.1 (d, $^{1}J_{CF}$ = 222.6 Hz, C–F), 126.7 (CH_{Ar}), 128.6 (CH_{Ar}), 128.7 (CH_{Ar}), 129.0 (CH_{Ar}), 129.8 (d, $^{3}J_{CF}$ = 3.6 Hz, $C_{Ar,}$), 131.9 (d, *J* = 1.6 Hz, CH_{Ar}), 134.7 (C_{Ar}), 137.2 (C_{Ar}), 165.9 (-**C**O_2Me), 167.6 (-**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -134.1 (ddd, *J* = 27.0, 20.2, 6.6 Hz).
HRMS (ESI, from HPLC-HRMS): m/z calcd. for [$C_{21}H_{19}ClFNO_6$ + H^+]: 436.0958, found: 436.0955.

***rel*-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-(methoxycarbonyl)phenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4c** (major isomer)



major isomer

Nitrosoacetals **4,4'c** was obtained from α-fluoronitroalkene **1b** (30 mg, 0.13 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 2:1 PE/EtOAc) afforded **4,4'c** (31 mg, 56%, dr (**4c**:**4'c**) = 7:1, ^{1}H NMR) as colorless solid.

R_f = 0.59 (PE/EtOAc, 1:1)

mp = 151-152 °C (PE/EtOAc, 10:1)

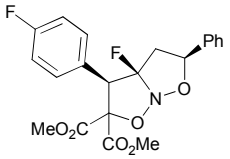
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.67 (ddd, J = 24.8, 14.1, 7.6 Hz, 1H, CH_{2a}(4)), 3.23 (ddd, J = 20.5, 14.1, 8.4 Hz, 1H, CH_{2b}(4)), 3.29 (s, 3H, CO_2Me), 3.91 (s, 3H, CO_2Me), 3.94 (s, 3H, CO_2Me), 5.03 (d, J = 3.9 Hz, 1H, Ar-C**H**), 5.63 (td, J = 8.4, 1.7 Hz, 1H, O-C**H**-Ph), 7.35-7.43 (m, 5H, CH_{Ph}), 7.54 (d, J = 8.2 Hz, 2H, CH_{Ar}), 8.04 (d, J = 8.2 Hz, 2H, CH_{Ar}). Minor isomer (characteristic signal): δ 5.50 (dd, J = 9.6, 7.0 Hz, 1H, O-C**H**-Ph).

^{13}C NMR (75 MHz, $CDCl_3$): δ 44.6 (d, $^2J_{CF}$ = 27.9 Hz, CH_2), 52.2 (CO_2**Me**), 52.7 (CO_2**Me**), 54.2 (CO_2**Me**), 56.2 (d, $^2J_{CF}$ = 22.4 Hz, CH–Ar), 85.3 (Ph**C**H–O), 89.3 (C–O), 119.2 (d, $^1J_{CF}$ = 222.2 Hz, C–F), 127.0 (CH_{Ar}), 128.8 (CH_{Ar}), 129.0 (CH_{Ar}), 129.3 (CH_{Ar}), 130.2 (C_{Ar}), 130.8 (CH_{Ar}), 136.8 (d, $^3J_{CF}$ = 3.0 Hz, $C_{Ar,}$), 137.0 (C_{Ar}), 165.8 (-**C**CO_2Me), 166.6 (-**C**CO_2Me), 167.0 (-**C**CO_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -131.3 (t, J_{HF} = 22.4 Hz). Minor isomer: δ -133.8 (t, J_{HF} = 25.8 Hz).

HRMS (ESI): m/z calcd. for [$C_{23}H_{22}FNO_8$+ Na^+]: 482.1222, found: 482.1219.

***rel*-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-fluorophenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4d** (major isomer)



major isomer

Nitrosoacetals **4,4'd** was obtained from α-fluoronitroalkene **1c** (62 mg, 0.33 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4,4'd** (105 mg, 72%, dr (**4d**:**4'd**) = 10:1) as colorless solid.

R_f = 0.50 (PE/EtOAc, 1:1)

mp = 134-135 °C (PE/EtOAc, 10:1)

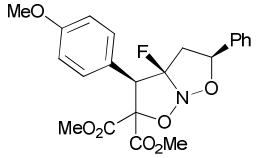
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.66 (ddd, J = 24.5, 14.1, 7.7 Hz, 1H, CH_{2a}(4)), 3.20 (ddd, J = 20.0, 14.1, 8.4 Hz, 1H, CH_{2b}(4)), 3.35 (s, 3H, CO_2Me), 3.91 (s, 3H, CO_2Me), 4.97 (d, J =4.4 Hz, 1H, Ar-C**H**), 5.60 (app td, J = 8.1, 1.7 Hz, 1H, O-C**H**-Ph), 7.07 (t, J = 8.7 Hz, 2H, CH_{Ar}), 7.36-7.47 (m, 7H, CH_{Ar}).

Minor isomer (characteristic signal): 5.50 (dd, J = 9.5, 7.0 Hz, 1H, O-C**H**-Ph),

^{13}C NMR (75 MHz, $CDCl_3$): δ 44.6 (d, $^2J_{CF}$ = 18.8 Hz, CH_2), 52.6 (CO_2**Me**), 54.0 (CO_2**Me**), 55.6 (d, $^2J_{CF}$ = 10.6 Hz, CH–Ar), 85.2 (Ph**C**H–O), 89.5 (C–O), 115.2 (d, $^2J_{CF}$ = 21.6 Hz, CH_{Ar}), 119.1 (d, $^1J_{CF}$ = 221.9 Hz, C–F), 127.0 (CH_{Ar}), 127.6 (t, J_{CF} = 3.5 Hz, C_{Ar}), 128.8 (CH_{Ar}), 129.0

(CH_{Ar}), 132.6 (d, $^{3}J_{CF}$ = 7.4 Hz, $CH_{Ar,}$), 137.1 (C_{Ar}), 162.7 (d, $^{1}J_{CF}$= 248.0 Hz, C_{Ar}), 166.0 (-**C**CO_2Me), 167.1 (-**C**CO_2Me).
^{19}F NMR (212 MHz, $CDCl_3$): δ -113.0 (s, Ar-F), -131.5 (t, *J* = 22.0 Hz, N–C–F). Minor isomer (characteristic signal): -134.2 (t, *J* = 23.4 Hz, N–C–F).
HRMS (ESI): m/z calcd. for [$C_{21}H_{19}F_2NO_6$+ H^+]: 420.1253, found: 420.1256.

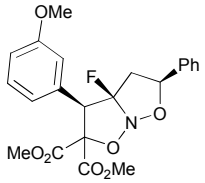
***rel*-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-methoxyphenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4e** (major isomer)



major isomer

Nitrosoacetals **4,4'e** was obtained from α-fluoronitroalkene **1d** (55.1 mg, 0.28 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4,4'e** (79 mg, 63%, dr (**4e**:**4'e**)= 10:1, ^{1}H NMR) as slightly yellow oil which solidifies upon storage in a refrigerator.
R_f = 0.51 (PE/EtOAc, 1:1)
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.64 (ddd, *J* = 24.1, 14.0, 7.8 Hz, 1H, CH_{2a}(4)), 3.19 (ddd, *J* = 19.0, 14.0, 8.3 Hz, 1H, CH_{2b}(4)), 3.35 (s, 3H, CO_2Me), 3.82 (s, 3H, OMe), 3.90 (s, 3H, CO_2Me), 4.92 (d, *J* =5.5 Hz, 1H, Ar-C**H**), 5.60 (td, *J* = 8.0, 1.5 Hz, 1H, O-C**H**-Ph), 6.89 (d, *J* = 8.8 Hz, 2H, CH_{Ar}), 7.36-7.43 (m, 7H, CH_{Ar}). Minor isomer (characteristic sigmal): 5.49 (dd, *J* = 9.5, 7.1 Hz, 1H, O-C**H**-Ph).
^{13}C NMR (75 MHz, $CDCl_3$): δ 44.8 (d, $^{2}J_{CF}$ = 28.1 Hz, CH_2), 52.6 (-CO_2**Me**), 54.0 (CO_2**Me**), 55.2 (OMe), 55.8 (d, $^{2}J_{CF}$ = 22.6 Hz, CH–Ar), 84.9 (Ph**C**H–O), 89.7 (C–O), 113.6 (CH_{Ar}), 119.2 (d, $^{1}J_{CF}$ = 221.2 Hz, C–F), 123.5 (d, $^{3}J_{CF}$ = 3.2 Hz, $C_{Ar,}$), 127.0 (CH_{Ar}), 128.8 (CH_{Ar}), 128.9 (CH_{Ar}), 131.9 (d, *J* = 0.6 Hz, CH_{Ar}), 137.3 (C_{Ar}), 159.7 (**C**$_{Ar}$-OMe), 166.2 (**C**O_2Me), 167.3 (**C**O_2Me).
^{19}F NMR (212 MHz, $CDCl_3$): δ -132.0 (t, *J* = 20.9 Hz). Minor isomer: δ -134.6 (br t, *J* = 22.6 Hz)
HRMS (ESI): m/z calcd. for [$C_{22}H_{22}FNO_7$ + H^+]: 432.1453, found: 432.1449.

***rel*-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(3-methoxyphenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4f** (major isomer)

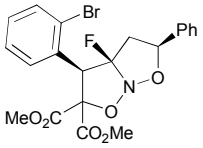


major isomer

Nitrosoacetals **4,4'f** was obtained from α-fluoronitroalkene **1e** (59 mg, 0.3 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4,4'f** (105 mg, 78%, dr (**4f**:**4'f**) = 16:1, ^{19}F NMR) as colorless solid.
R_f = 0.58 (PE/EtOAc, 1:1)
mp (decomp.) = 168-169 °C (PE/EtOAc, 3:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.66 (ddd, *J* = 24.5, 13.6, 7.9 Hz, 1H, CH_{2a}(4)), 3.21 (ddd, *J* = 20.1, 13.4, 8.5 Hz, 1H, CH_{2b}(4)), 3.33 (s, 3H, CO_2Me), 3.83 (s, 3H, OMe), 3.90 (s, 3H, CO_2Me), 4.93 (d, *J* =3.9 Hz, 1H, Ar-C**H**), 5.60 (app t, *J* = 7.5 Hz,1H, O-C**H**-Ph), 6.88 (d, *J* = 7.7 Hz, 1H, CH_{Ar}), 6.95-7.03 (m, 2H, CH_{Ar}), 7.25-7.31 (m, 1H, CH_{Ar}), 7.31-7.44 (m, 5H, CH_{Ph}).
^{13}C NMR (75 MHz, $CDCl_3$): δ 44.8 (d, $^2J_{CF}$ = 28.1 Hz, CH_2), 52.6 (-CO_2**Me**), 54.0 (CO_2**Me**), 55.3 (OMe), 56.4 (d, $^2J_{CF}$ = 22.7 Hz, CH–Ar), 85.0 (Ph**C**H–O), 89.7 (C–O), 114.5 (CH_{Ar}), 115.9 (CH_{Ar}), 119.3 (d, $^1J_{CF}$ = 222.2 Hz, C–F), 123.0 (CH_{Ar}), 127.0 (CH_{Ar}), 128.8 (CH_{Ar}), 128.9 (CH_{Ar}), 129.1 (CH_{Ar}), 133.1 (d, $^3J_{CF}$ = 3.1 Hz, $C_{Ar,}$), 137.3 (C_{Ar}), 159.4 (**C**$_{\mathbf{Ar}}$-OMe), 166.0 (-**C**O_2Me), 167.2 (-**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -132.3 (t, *J* = 21.5 Hz). Minor isomer: δ -135.0 (t, *J* = 23.3 Hz).
HRMS (ESI): m/z calcd. for [$C_{22}H_{22}FNO_7$ + Na^+]: 454.1273, found: 454.1270.

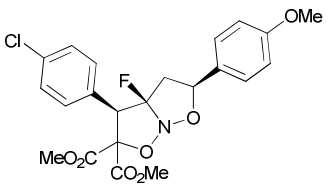
***rel*-(3R,3aR,5S)-Dimethyl 3-(2-bromophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4g** (major isomer)



major isomer

Nitrosoacetals **4,4'g** was obtained from α-fluoronitroalkene **1f** (42.5 mg, 0.17 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4,4'g** (61 mg, 70%, dr (**4g**:**4'g**) = 11:1) as colorless oil which solidifies upon storage in a refrigerator.
R_f = 0.55 (PE/EtOAc, 1:1)
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.69 (ddd, *J* = 25.2, 14.1, 7.5 Hz, 1H, CH_{2a}(4)), 3.29 (s, 3H, CO_2Me), 3.36 (ddd, *J* = 21.3, 14.1, 8.5 Hz, 1H, CH_{2b}(4)), 3.93 (s, 3H, CO_2Me), 5.61 (app td, *J* =8.0, 1.8 Hz, 1H, O-C**H**-Ph), 5.84 (d, *J* = 2.6 Hz, 1H, Ar-C**H**), 7.18 (td, 1H, *J* = 7.7, 1.6 Hz, CH_{Ar}), 7.33-7.44 (m, 6H, CH_{Ar}), 7.63 (dd, *J* = 8.0, 1.1 Hz, 1H, CH_{Ar}), 7.72 (ddd, *J* = 7.9, 2.4, 1.8 Hz, 1H, CH_{Ar}). Minor isomer (characteristic signals): δ 3.77 (s, 3H, -CO_2Me), 5.48 (dd, *J* = 8.7, 8.0 Hz, 1H, O-C**H**-Ar).
^{13}C NMR (75 MHz, $CDCl_3$): δ 44.7 (d, $^2J_{CF}$ = 28.0 Hz, CH_2), 52.5 (-CO_2**Me**), 54.0 (d, $^2J_{CF}$ = 21.7 Hz, CH–Ar), 54.1 (-CO_2**Me**), 86.2 (Ph**C**H–O), 89.4 (C–O), 119.2 (d, $^1J_{CF}$ = 222.8 Hz, C–F), 126.2 (C_{Ar}), 127.0 (CH_{Ar}), 127.2 (CH_{Ar}), 128.8 (CH_{Ar}), 128.9 (CH_{Ar}), 129.8 (CH_{Ar}), 131.8 (d, $^3J_{CF}$ = 3.2 Hz, $C_{Ar,}$), 132.7 (d, $^4J_{CF}$ = 3.2 Hz, $CH_{Ar,}$), 132.8 (CH_{Ar}), 137.1 (C_{Ar}), 165.8 (-**C**O_2Me), 167.8 (-**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -131.1 (t, *J* = 23.1 Hz). Minor isomer: δ -132.3 (t, *J* = 23.6 Hz).
HRMS (ESI): m/z calcd. for [$C_{21}H_{19}{}^{79}BrFNO_6$+ H^+]: 480.0453, found: 480.0444.

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4h** (major isomer)



major isomer

Nitrosoacetals **4,4'h** was obtained from α-fluoronitroalkene **1a** (70.4 mg, 0.35 mmol) and 4-vinylanisole following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4,4'h** (114 mg, 68%, dr (**4h**:**4'h**) = 19:1, ^{1}H NMR) as slightly yellow oil, which solidifies upon storage in a refrigerator.

R_f = 0.51 (PE/EtOAc, 1:1)

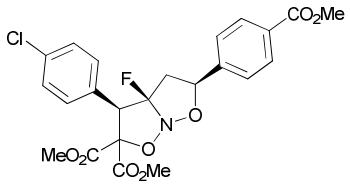
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.63 (ddd, *J* = 25.0, 14.2, 7.8 Hz, 1H, CH_{2a}(4)), 3.15 (ddd, *J* = 20.4, 14.2, 8.3 Hz, 1H, CH_{2b}(4)), 3.32 (s, 3H, CO_2Me), 3.81 (s, 3H, OMe), 3.89 (s, 3H, CO_2Me), 4.93 (d, *J* = 4.1 Hz, 1H, Ar-C**H**), 5.55 (td, *J* = 8.0, 1.5 Hz, 1H, O-C**H**-Ar), 6.91 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 7.31-7.41 (m, 6H, CH_{Ar}). Minor isomer (characteristic signal): δ 5.40 (dd, *J* = 9.1, 7.5 Hz, 1H, O-C**H**-Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ 44.5 (d, $^2J_{CF}$ = 28.0 Hz, CH_2), 52.6 (CO_2**Me**), 54.0 (CO_2**Me**), 55.2 (OMe), 55.7 (d, $^2J_{CF}$ = 22.5 Hz, CH–Ar), 85.2 (Ar**C**H–O), 89.1 (C–O), 114.1 (CH_{Ar}), 119.1 (d, $^1J_{CF}$ = 221.5 Hz, C–F), 128.3 (CH_{Ar}), 128.5 (C_{Ar}), 128.6 (CH_{Ar}), 130.3 (d, $^3J_{CF}$ = 3.3 Hz, C_{Ar}), 132.0 (CH_{Ar}), 134.5 (C_{Ar}), 160.1 (**C**-OMe), 165.9 (**C**O_2Me), 166.9 (**C**O_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -131.1 (t, *J* = 22.4 Hz). Minor isomer: δ -133.4 (t, *J* = 24.2 Hz).

HRMS (ESI): m/z calcd. for [$C_{22}H_{21}ClFNO_7$ + H^+]: 466.1063, found: 466.1066.

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4i**
(major isomer)



major isomer

Nitrosoacetals **4,4'i** was obtained from α-fluoronitroalkene **1a** (40.3 mg, 0.20 mmol) and methyl 4-vinylbenzoate (**10 equiv**.) following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4i,4'i** (59 mg, 58%, dr (**4i**:**4'i**) = 12:1, ^{1}H NMR) as colorless solid.

R_f = 0.46 (PE/EtOAc, 1:1)

mp = 133-135°C ($CHCl_3$)

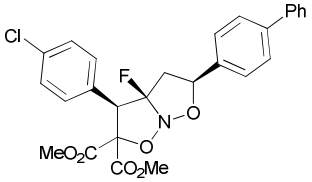
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.62 (ddd, *J* = 24.0, 14.1, 7.4 Hz, 1H, CH_{2a}), 3.25 (ddd, *J* = 20.2, 14.1, 8.6 Hz, 1H, CH_{2b}), 3.34 (s, 3H, CO_2Me), 3.89 (s, 3H, CO_2Me), 3.92 (s, 3H, CO_2Me), 4.95 (d, *J* = 4.7 Hz, 1H, Ar-C**H**), 5.65 (app t, *J* = 7.9 Hz, 1H, O-C**H**-Ar), 7.31-7.40 (m, 4 H, CH_{Ar}), 7.47 (d, *J* = 8.3 Hz, 2 H, CH_{Ar}), 8.05 (d, *J* = 8.3 Hz, 2 H, CH_{Ar}). Minor isomer (characteristic signal): δ 5.57 (dd, *J* = 9.2, 7.3 Hz, 1H, O-C**H**-Ar).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT, HMBC): δ 44.6 (d, $^2J_{CF}$ = 27.8 Hz, CH_2), 52.2 (-CO_2**Me**), 52.7 (-CO_2**Me**), 54.2 (-CO_2**Me**), 55.7 (d, $^2J_{CF}$ = 22.4 Hz, CH–Ar), 84.2 (Ar**C**H–O), 89.6 (C–O), 119.1 (d, $^1J_{CF}$ = 222.3 Hz, C–F), 126.7 (CH_{Ar}), 128.5 (CH_{Ar}), 130.1 (CH_{Ar}), 130.6 (C_{Ar}), 132.0 (C_{Ar}), 132.1 (CH_{Ar}), 134.7 (C_{Ar}), 142.3 (C_{Ar}), 165.8 (-**C**O_2Me), 166.5 (-**C**O_2Me), 167.0 (-**C**O_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -131.8 (app t, *J* = 20.7 Hz).

HRMS (ESI): m/z calcd. for [$C_{23}H_{21}ClFNO_8$ + Na^+]: 516.0832, found: 516.0827.

***rel*-(3R,3aR,5S)-Dimethyl 5-(biphenyl-4-yl)-3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4j** (major isomer)



major isomer

Nitrosoacetals **4j** was obtained from α-fluoronitroalkene **1a** (40.3 mg, 0.20 mmol) and 4-vinylbiphenyl (**10 equiv**.) following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4,4'j** (63 mg, 60%, dr (**4j**:**4'j**)= 14:1, ^{1}H NMR) as colorless oil which solidifies upon storage in a refrigerator.

R_f = 0.56 (PE/EtOAc, 1:1)

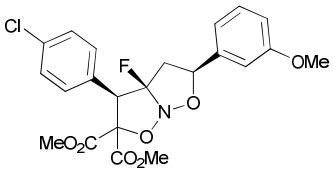
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.71 (ddd, *J* = 24.6, 14.1, 7.6 Hz, 1H, CH_{2a}), 3.24 (ddd, *J* = 20.3, 14.1, 8.4 Hz, 1H, CH_{2b}), 3.37 (s, 3H, CO_2Me), 3.93 (s, 3H, CO_2Me), 4.98 (d, *J* = 4.3 Hz, 1H, Ar-C**H**), 5.65 (app td, *J* = 8.3, 1.3 Hz, 1H, O-C**H**-Ar), 7.35-7.65 (m, 13 H, CH_{Ar}). Minor isomer (characteristic signal): δ 5.55 (dd, *J* = 9.4, 7.0 Hz, 1H, O-C**H**-Ar).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT): δ 44.7 (d, $^2J_{CF}$ = 27.7 Hz, CH_2), 52.7 (-CO_2**Me**), 54.2 (-CO_2**Me**), 55.8 (d, $^2J_{CF}$ = 22.6 Hz, CH–Ar), 85.1 (Ar**C**H–O), 89.4 (C–O), 119.2 (d, $^1J_{CF}$ = 222.4 Hz, C–F), 127.1 (CH_{Ar}), 127.5 (CH_{Ar}), 127.6 (2 × CH_{Ar}), 128.5 (CH_{Ar}), 128.8 (CH_{Ar}), 130.3 (d, *J* = 3.1 Hz, C_{Ar}), 132.1 (d, *J* = 0.6 Hz, CH_{Ar}), 134.7 (C_{Ar}), 135.9 (C_{Ar}), 140.4 (C_{Ar}), 142.0 (C_{Ar}), 166.0 (-**C**O_2Me), 167.1 (-**C**O_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -131.3 (app t, *J* = 21.6 Hz).

HRMS (ESI): m/z calcd. for [$C_{27}H_{23}ClFNO_6$ + H^+]: 512.1271, found: 512.1255.

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(3-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4k** (major isomer)



major isomer

Nitrosoacetals **4,4'k** was obtained from α-fluoronitroalkene **1a** (40.3 mg, 0.20 mmol) and 3-vinylanisole (**10 equiv**.) following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4,4'k** (53 mg, 55%, dr (**4k**:**4'k**)= 7:1, ^{1}H NMR) as colorless oil which solidifies upon storage in a refrigerator.

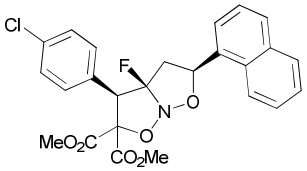
R_f = 0.56 (PE/EtOAc, 1:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.64 (ddd, *J* = 24.5, 14.1, 7.6 Hz, 1H, CH_{2a}), 3.19 (ddd, *J* = 20.1, 14.1, 8.4 Hz, 1H, CH_{2b}), 3.35 (s, 3H, CO_2Me), 3.81 (s, 3H, CO_2Me), 3.90 (s, 3H, OMe), 4.95 (d, *J* = 4.5 Hz, 1H, Ar-C**H**), 5.58 (app td, *J* = 7.9, 1.1 Hz, 1H, O-C**H**-Ar), 6.88-6.98 (m, 3 H, CH_{Ar}), 7.27-7.41 (m, 5 H, CH_{Ar}). Minor isomer (characteristic signal): δ 5.46 (dd, *J* = 9.4, 7.1 Hz, 1H, O-C**H**-Ar).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT): δ 44.7 (d, $^2J_{CF}$ = 27.9 Hz, CH_2), 52.7 (-CO_2**Me**), 54.2 (-CO_2**Me**), 55.3 (-O**Me**), 55.8 (d, $^2J_{CF}$ = 22.5 Hz, CH–Ar), 85.0 (Ar**C**H–O), 89.5 (C–O), 112.2 (CH_{Ar}), 114.7 (CH_{Ar}), 119.1 (d, $^1J_{CF}$ = 222.0 Hz, C–F), 119.1 (CH_{Ar}), 128.4 (CH_{Ar}), 129.8

(CH_{Ar}), 130.3 (d, J = 3.5 Hz, C_{Ar}), 132.1 (CH_{Ar}), 134.7 (C_{Ar}), 138.7 (C_{Ar}), 160.0 (C_{Ar}–O), 165.9 (-**C**O_2Me), 167.1 (-**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -131.7 (app t, J = 21.9 Hz). Minor isomer: δ -134.5 (app t, J = 20.2 Hz).
HRMS (ESI): m/z calcd. for [$C_{22}H_{21}ClFNO_7$ + Na^+]: 488.0883, found: 488.0883.

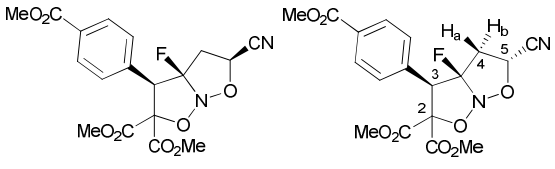
***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(naphthalen-1-yl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4l** (major isomer)



major isomer

Nitrosoacetals **4,4'l** was obtained from α-fluoronitroalkene **1a** (40.3 mg, 0.20 mmol) and 1-vinylnaphtalene (**10 equiv**.) following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4,4'l** (59 mg, 59%, dr (**4l**:**4'l**)= 16:1, ^{19}F NMR) as colorless oil which solidifies upon storage in a refrigerator.
R_f = 0.62 (PE/EtOAc, 1:1)
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.76 (ddd, J = 24.2, 13.9, 7.9 Hz, 1H, CH_{2a}), 3.39 (s, 3H, CO_2Me), 3.45 (ddd, J = 22.1, 13.9, 8.2 Hz, 1H, CH_{2b}), 3.96 (s, 3H, CO_2Me), 5.04 (d, J = 4.6 Hz, 1H, Ar-C**H**), 6.30 (app t, J = 7.9 Hz, 1H, O-C**H**-Ar), 7.36-7.61 (m, 7 H, CH_{Ar}), 7.77 (d, J = 7.2 Hz, 1H, CH_{Ar}), 7.86 (d, J = 8.3 Hz, 1H, CH_{Ar}), 7.90-7.93 (m, 2H, CH_{Ar}).
^{13}C NMR (75 MHz, $CDCl_3$, DEPT, HSQC): δ 44.1 (d, $^2J_{CF}$ = 27.8 Hz, CH_2), 52.8 (-CO_2**Me**), 54.2 (-CO_2**Me**), 56.4 (d, $^2J_{CF}$ = 22.8 Hz, CH–Ar), 81.8 (Ar**C**H–O), 90.1 (C–O), 119.3 (d, $^1J_{CF}$ = 222.7 Hz, C–F), 122.7 (CH_{Ar}), 123.4 (CH_{Ar}), 125.6 (CH_{Ar}), 126.0 (CH_{Ar}), 126.6 (CH_{Ar}), 128.5 (CH_{Ar}), 129.1 (CH_{Ar}), 130.2 (C_{Ar}), 130.2 (d, J = 3.5 Hz, C_{Ar}), 132.1 (2 × CH_{Ar}), 133.0 (C_{Ar}), 133.7 (C_{Ar}), 134.7 (C_{Ar}), 165.8 (-**C**O_2Me), 167.4 (-**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -131.6 (app t, J = 20.6 Hz). Minor isomer: δ -135.1-135.4 (m).
HRMS (ESI): m/z calcd. for [$C_{25}H_{21}ClFNO_6$ + Na^+]: 508.0934, found: 508.0947.

***rel*-(3R,3aR,5S)-Dimethyl 5-cyano-3a-fluoro-3-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4m** (major isomer) and ***rel*-(3R,3aR,5R)-Dimethyl 5-cyano-3a-fluoro-3-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'm** (minor isomer)



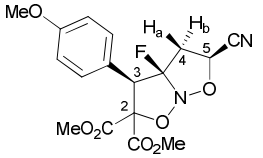
major isomer minor isomer

Nitrosoacetals **4,4'm** was obtained from α-fluoronitroalkene **1b** (67.5 mg, 0.2 mmol) and acrylonitrile following the general procedure 1. Column chromatography (eluent: 7:3 PE/EtOAc) afforded **4m** (69.6 mg of mixture **4m**:**4'm** = 15:1) and 24.3 mg of **4k**:**4'k** = 1:4.5, total yield 66%, total dr **4m**:**4'm** = 3:1, as colorless oils.
Major isomer (**4m**):
R_f = 0.27 (PE/EtOAc, 3:1).

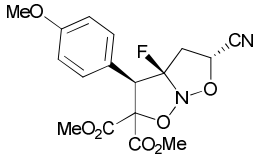
mp = 126-127 °C (PE/EtOAc, 3:1)
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.99 (ddd, *J* = 20.1, 14.2, 4.7 Hz, 1H, CH_{2a}), 3.28 (s, 3H, CO_2Me), 3.34 (ddd, *J* = 23.6, 14.2, 9.5 Hz, 1H, CH_{2b}), 3.87 (s, 3H, CO_2Me), 3.94 (s, 3H, CO_2Me), 4.94 (d, *J* = 6.1 Hz, 1H, Ar-C**H**), 5.18 (dd, *J* = 9.4, 4.7 Hz, 1H, O-C**H**-CN), 7.45 (d, *J* = 8.2 Hz, 2H, CH_{Ar}), 8.04 (d, *J* = 8.3 Hz, 2H, CH_{Ar}).
Characteristic NOESY interactions: CH(3)-CH_{2b}(4).
Characteristic HOESY interactions: F-CH_{2a}(4); CH_{Ar}-F.
^{13}C NMR (75 MHz, $CDCl_3$): δ 41.5 (d, $^2J_{CF}$ = 29.0 Hz, CH_2), 52.2 (-CO_2**Me**), 52.9 (-CO_2**Me**), 54.4 (-CO_2**Me**), 56.1 (d, $^2J_{CF}$ = 22.5 Hz, CH–Ar), 66.6 (**C**H–CN), 92.0 (C–O), 115.4 (CN), 118.9 (d, $^1J_{CF}$ = 226.5 Hz, C–F), 129.6 (CH_{Ar}), 130.6 (d, $^4J_{CF}$ = 1.3 Hz, CH_{Ar}), 130.7 (C_{Ar}), 135.3 (d, $^3J_{CF}$ = 3.2 Hz, $C_{Ar,}$), 164.3 (-**C**O_2Me), 166.3 (-**C**O_2Me), 166.9 (-**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -133.7 (app t, *J* = 18.9 Hz).
HRMS (ESI): m/z calcd. for [$C_{18}H_{17}FN_2O_8$ + Na^+]: 431.0861, found: 431.0866.

Minor isomer (**4'm**):
R_f = 0.38 (PE/EtOAc, 3:1).
^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY): δ 3.15 (ddd, *J* = 24.1, 14.7, 9.6 Hz, 1H, CH_{2a}), 3.26 (s, 3H, CO_2Me), 3.33 (ddd, *J* = 24.7, 14.7, 5.0 Hz, 1H, CH_{2b}), 3.92 (s, 3H, CO_2Me), 3.94 (s, 3H, CO_2Me), 5.10 (s, 1H, Ar-C**H**), 5.32 (dd, *J* = 9.5, 4.9 Hz, 1H, O-C**H**-CN), 7.48 (d, *J* = 8.3 Hz, 2H, CH_{Ar}), 8.04 (d, *J* = 8.3 Hz, 2H, CH_{Ar}).
Characteristic NOESY interactions: CH(3)-CH_{2b}(4).
Characteristic HOESY interactions: F-CH(5); F-CH_{2a}(4); CH_{Ar}-F.
^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): δ 42.0 (d, $^2J_{CF}$ = 30.4 Hz, CH_2(4)), 52.2 (-CO_2**Me**), 52.8 (CO_2**Me**), 54.2 (d, $^2J_{CF}$ = 21.9 Hz, CH(3)–Ar), 54.6 (CO_2**Me**), 68.6 (**C**H(5)–CN), 89.0 (C(2)–O), 116.7 (CN), 119.0 (d, $^1J_{CF}$ = 226 Hz, C–F), 129.5 (CH_{Ar}), 130.6 (C_{Ar}), 130.7 (C_{Ar}), 135.9 (d, J_{CF} = 3.3 Hz, $C_{Ar,}$), 135.2 (C_{Ar}), 165.2 (-**C**O_2Me), 166.3 (-**C**O_2Me), 166.4 (-**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -133.5 (t, *J* = 24.1 Hz).
^{15}N NMR (from ^{1}H-^{15}N HMBC): δ 285 (d, *J* = 40 Hz).
HRMS (ESI): m/z calcd. for [$C_{18}H_{17}FN_2O_8$ + Na^+]: 431.0861, found: 431.0857.

***rel*-(3R,3aR,5S)-Dimethyl 5-cyano-3a-fluoro-3-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4n** (major isomer) and ***rel*-(3R,3aR,5R)-Dimethyl 5-cyano-3a-fluoro-3-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'n**



major isomer

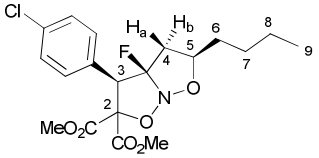


minor isomer

Nitrosoacetals **4,4'n** was obtained from α-fluoronitroalkene **1c** (32 mg, 0.16 mmol) and acrylonitrile following the general procedure 1. Column chromatography (eluent: 7:3 PE/EtOAc) afforded **4n** (31.2 mg) and **4'n** (12.2 mg) (total yield 71%) as colorless oils which solidifies upon storage in a refrigerator.
Major isomer (**4n**):
R_f = 0.37 (PE/EtOAc, 1:1).

^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY): δ 2.94 (ddd, *J* = 20.0, 14.2, 4.9 Hz, 1H, CH_{2a}(4)), 3.29 (ddd, *J* = 19.2, 14.2, 9.4 Hz, 1H, CH_{2b}(4)), 3.33 (s, 3H, CO_2Me), 3.81 (s, 3H, OMe), 3.85 (s, 3H, CO_2Me), 4.81 (d, *J* =7.7 Hz, 1H, CH(3)), 5.15 (ddd, *J* = 9.4, 4.9, 0.6 Hz, 1H, CH(5)), 6.88 (d, *J* = 8.9 Hz, 2H, CH_{Ar}), 7.27 (d, *J* = 8.9 Hz, 2H, CH_{Ar}).
Characteristic NOESY interactions: CH(3)-CH_{2b}(4).
Characteristic HOESY interactions: F-CH_{2a}(4).
^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): δ 41.4 (d, $^2J_{CF}$ = 29.0 Hz, CH_2(4)), 53.0 (-CO_2**Me**), 54.4 (-CO_2**Me**), 55.3 (OMe), 55.8 (d, $^2J_{CF}$ = 22.7 Hz, CH(3)), 66.2 (C(5)), 92.4 (C–O), 113.8 (CH_{Ar}), 115.6 (CN), 118.8 (d, $^1J_{CF}$ = 226 Hz, C–F), 121.9 (d, $^3J_{CF}$ = 3.3 Hz, C_{Ar}), 131.7 (d, $^4J_{CF}$ = 1.6 Hz, $CH_{Ar,}$), 159.9 (**C**$_{Ar}$–OMe), 164.4 (-**C**O_2Me), 167.2 (-**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -134.5 (td, *J* = 19.5, 7.8 Hz).
HRMS (ESI): m/z calcd. for [$C_{17}H_{17}FN_2O_7$+ H^+]: 381.1093, found: 381.1083.
Minor isomer (**4'n**):
R_f = 0.48 (PE/EtOAc, 1:1).
^{1}H NMR (300 MHz, $CDCl_3$): δ 3.11 (ddd, *J* = 24.0, 14.7, 9.5 Hz, 1H, CH_{2a}), 3.30 (ddd, *J* = 24.4, 14.7, 5.0 Hz, 1H, CH_{2b}), 3.31 (s, 3H, CO_2Me), 3.88 (s, 3H, OMe), 3.92 (s, 3H, CO_2Me), 4.98 (s, 1H, Ar-C**H**), 5.29 (dd, *J* = 9.5, 5.0 Hz, 1H, O-C**H**-CN), 6.89 (d, *J* = 8.8 Hz, 2H, CH_{Ar}), 7.30 (d, *J* = 8.8 Hz, 2H, CH_{Ar}).
^{13}C NMR (100 MHz, $CDCl_3$): δ 42.2 (d, $^2J_{CF}$ = 30.6 Hz, CH_2), 52.8 (CO_2**Me**), 53.9 (-CO_2**Me**), 53.9 (d, $^2J_{CF}$ = 22.1 Hz, CH–Ar), 54.5 (CO_2**Me**), 55.3 (CO_2**Me**), 68.5 (**C**H–CN), 89.6 (C–O), 116.7 (CN), 113.8 (CH_{Ar}), 116.8 (CN), 119.1 (d, $^1J_{CF}$ = 224.4 Hz, C–F), 122.9 (CH_{Ar}), 160.0 (-**C**$_{Ar}$–OMe), 165.7 (-**C**O_2Me), 166.7 (-**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -133.2 (t, *J* = 23.8 Hz).
HRMS (ESI): m/z calcd. for [$C_{17}H_{17}FN_2O_7$+ Na^+]: 403.0912, found: 403.0903.

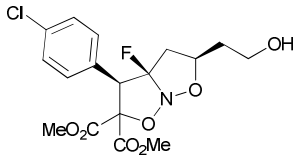
***rel*-(3R,3aR,5R)-Dimethyl 5-butyl-3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4o** (major isomer)



Nitrosoacetals **4,4'o** was obtained from α-fluoronitroalkene **1a** (60.4 mg, 0.3 mmol) and 1-hexene following the general procedure 1. Column chromatography (eluent: 4:1 PE/EtOAc) afforded **4,4'o** (86 mg, 66%, dr **4o**:**4'o** = 6:1) as colorless oil which solidifies upon storage in a refrigerator. Pure sample of **4o** was obtained by recrystallization (-20°C) from hexane (dr (**4o**:**4'o**) = 16:1, ^{1}H NMR)
R_f = 0.60 (PE/EtOAc, 1:1)
^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY): δ 0.91 (t, *J* = 7.0 Hz, CH_3(9)), 1.27-1.49 (m, 4H, CH_2(7,8)), 1.63-1.74 (m, 1H, CH_{2a}(6)), 1.78-1.90 (m, 1H, CH_{2b}(6)), 2.28 (ddd, *J* = 25.2, 13.7, 7.7 Hz, 1H, CH_{2a}(4)), 2.85 (ddd, *J* = 19.2, 13.7, 7.7 Hz, 1H, CH_{2b}(4)), 3.34 (s, 3H, CO_2Me), 3.86 (s, 3H, CO_2Me), 4.61 (pd, *J* = 7.7, 1.8 Hz, 1H, CH(5)), 4.84 (d, *J* = 4.3 Hz, 1H, CH(3)), 7.31-7.38 (m, 4H, CH_{Ar}). Minor isomer (characteristic signal): δ 4.39-4.49 (m, 1H, CH(5)).
Characteristic NOESY interactions: CH_{2b}(4)-CH(3); CH_{2b}(4)-CH(5); CH_{2a}(4)-CH_2(6).
Characteristic HOESY interactions: CH_{2a}(4)-F; CH(3)-F; CH_{Ar}-F.

^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): δ 13.9 (CH_3(9)), 22.4 and 27.8 (CH_2(7) and CH_2(8)), 33.3 (CH_2(6)), 42.4 (d, $^2J_{CF}$ = 27.6 Hz, CH_2(4)), 52.6 (CO_2**Me**), 54.0 (CO_2**Me**), 56.1 (d, $^2J_{CF}$ = 22.9 Hz, CH(3)), 83.9 (CH(5)), 89.4 (C(2)), 118.9 (d, $^1J_{CF}$ = 221.1 Hz, C–F), 128.4 (CH_{Ar}), 130.4 (d, $^3J_{CF}$ = 3.4 Hz, C_{Ar}), 132.1 (d, $^4J_{CF}$ = 1.3 Hz, $CH_{Ar,}$), 134.6 (C_{Ar}), 166.0 (**C**O_2Me), 167.1 (**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -131.3 (td, J_{HF} = 25.2, 19.2, 4.3 Hz). Minor isomer: δ -133.1 (ddd, J = 23.1, 21.5, 7.5 Hz).
^{15}N NMR (30 MHz,$CDCl_3$, from ^{1}H-^{15}N-HMBC): δ 288.
HRMS (ESI): m/z calcd. for [$C_{19}H_{23}ClFNO_6$+ H^+]: 416.1271, found: 416.1262.

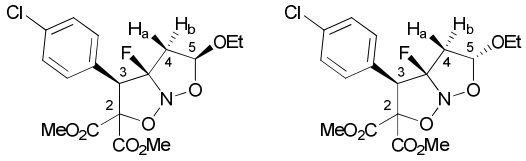
***rel*-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(2-hydroxyethyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4p** (major isomer)



major isomer

Nitrosoacetals **4,4'p** was obtained from α-fluoronitroalkene **1a** (50.4 mg, 0.25 mmol) and 3-buten-1-ol (**10 equiv.**) following the general procedure 1. Column chromatography (eluent: 1:2 PE/EtOAc) afforded **4,4'p** (49.6 mg, 47 %, dr (**4p**:**4'p**) = 5:1, ^{19}F NMR) as colorless solid.
R_f = 0.09 (PE/EtOAc, 1:1)
mp = 121-122 °C (PE/EtOAc, 1:1)
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.73 (br s, 1H, OH), 1.92-2.12 (m, 2H, HO-CH_2-**C**$\mathbf{H_2}$-), 2.39 (ddd, J = 24.9, 13.8, 7.5 Hz, 1H, CH_{2a}(4)), 2.92 (ddd, J = 19.4, 13.7, 7.8 Hz, 1H, CH_{2b}(4)), 3.33 (s, 3H, CO_2Me), 3.77-3.83 (m, 2H, **C**$\mathbf{H_2}$OH), 3.86 (s, 3H, CO_2Me), 4.78-4.85 (m, 1 H, CH–O), 4.84 (d, J = 5.1 Hz, 1H, Ar-C**H**), 7.29-7.34 (m, 4H, CH_{Ar}).
^{13}C NMR (75 MHz, $CDCl_3$, DEPT): δ 36.3 (-**C**$\mathbf{H_2}$-CH_2-OH), 42.4 (d, $^2J_{CF}$ = 27.6 Hz, CH_2(4)), 52.7 (CO_2**Me**), 54.0 (CO_2**Me**), 56.0 (d, $^2J_{CF}$ = 22.6 Hz, CH–Ar), 59.4 (-**C**$\mathbf{H_2}$OH), 81.5 (C-3), 89.6 (C–O), 119.0 (d, $^1J_{CF}$ = 221.5 Hz, C–F), 128.4 (CH_{Ar}), 130.1 (d, $^3J_{CF}$ = 1.4 Hz, $C_{Ar,}$), 132.0 (d, J = 0.9 Hz, CH_{Ar}), 134.7 (C_{Ar}), 165.8 (CO_2Me), 167.0 (CO_2Me).
^{19}F NMR (212 MHz, $CDCl_3$): δ -131.6 (t, J = 21.6 Hz). Minor isomer: δ -133.3 (t, J = 22.9 Hz).
HRMS (ESI): m/z calcd. for [$C_{17}H_{19}ClFNO_7$ + H^+]: 426.0726, found: 426.0728.

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-5-ethoxy-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4q** (major isomer)



major isomer minor isomer

Nitrosoacetals **4,4'q** was obtained from α-fluoronitroalkene **1a** (34 mg, 0.17 mmol) and ethyl vinyl etherfollowing the general procedure 1. Column chromatography (eluent: 7:3 PE/EtOAc) afforded mixture of isomers **4q**,**4'q** (59 mg, 83%, dr (**4q**:**4'q**) = 5:1) as colorless oil, which solidifies upon storage in a refrigerator.
R_f = 0.46 (PE/EtOAc, 1:1)

^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY): δ 1.24 (t, *J* = 7.1 Hz, CH_3), 2.60 (ddd, *J* = 19.5, 14.1, 2.6 Hz, 1H, CH_{2a}(4)), 3.08 (td, *J* = 14.1, 6.6 Hz, 1H, CH_{2b}(4)), 3.36 (s, 3H, CO_2Me), 3.51 (dq, *J* = 9.6, 7.1 Hz, 1H, -O-C**H**$_{2a}$-Me), 3.84 (s, 3H, CO_2Me), 3.87-3.95 (m, 1H, -O-C**H**$_{2b}$-Me), 4.78 (d, *J* =13.1 Hz, 1H, CH(2)), 5.32 (ddd, *J* = 6.6, 2.6, 0.8 Hz,1H, CH(5)), 7.30-7.33 (m, 4H, CH_{Ar}). Minor isomer (characteristic signals): δ 2.71-2.92 (m, 2H, CH_2(4)), 3.39 (s, 3H, CO_2Me), 3.51-3.62 (m, 1H, -O-C**H**$_{2a}$-Me), 5.07 (d, *J* = 10.3 Hz, 1H, CH(2)), 5.63 (ddd, *J* = 5.8, 2.4 Hz,1H, CH(5)).

Characteristic NOESY interactions (major isomer): CH_{2b}(4)-CH(3); CH_{2b}(4)-CH(5); CH(3)-CH(5).

Characteristic HOESY interactions (major isomer): F-CH_{Ar}; F-CH_{2a}(4).

Characteristic HOESY interactions (minor isomer): F-CH_{Ar}.

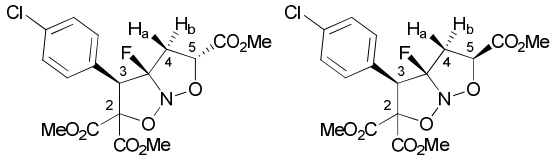
^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): δ 14.9 (CH_3), 42.7 (d, $^{2}J_{CF}$ = 26.4 Hz, CH2), 52.8 (CO_2**Me**), 53.9 (CO_2**Me**), 58.3 (d, $^{2}J_{CF}$ = 23.8 Hz, CH(2)), 64.4 (-O**C**H_2Me), 94.3 (C(2)), 102.5 (d, $^{3}J_{CF}$ = 3.4 Hz, C(5)), 119.3 (d, $^{1}J_{CF}$ = 224.4 Hz, C–F), 128.5 (CH_{Ar}), 129.2 (d, $^{3}J_{CF}$ = 3.2 Hz, C_{Ar}), 131.9 (d, $^{4}J_{CF}$ = 2.7 Hz, $CH_{Ar,}$), 134.8 (C_{Ar}), 164.4 (CO_2Me), 167.9 (CO_2Me). Minor isomer: δ 14.8 (CH_3), 43.5 (d, $^{2}J_{CF}$ = 28.7 Hz, CH_2(4)), 52.7 (CO_2**Me**), 53.7 (CO_2**Me**), 55.8 (d, $^{2}J_{CF}$ = 22.4 Hz, CH(2)), 64.7 (-O**C**H_2Me), 90.2 (C(2)), 109.0 (d, $^{3}J_{CF}$ = 1.6 Hz, C(5)), 118.8 (d, $^{1}J_{CF}$ = 220.2 Hz, C–F), 128.4 (CH_{Ar}), 129.7 (d, $^{3}J_{CF}$ = 2.1 Hz, C_{Ar}), 132.3 (d, $^{4}J_{CF}$ = 2.1 Hz, $CH_{Ar,}$), 134.7 (C_{Ar}), 166.3 (CO_2Me), 166.9 (CO_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -136.9 (dt, *J* = 19.5, 13.3 Hz). Minor isomer: -134.0 (ddd, *J* = 22.2, 17.2, 10.3 Hz).

^{15}N NMR (30 MHz, from ^{1}H-^{15}N HMBC): δ 282 (d, $^{2}J_{NF}$ = 44 Hz). Minor isomer: δ 287 (d, $^{2}J_{NF}$ = 42 Hz)

HRMS (ESI): m/z calcd. for [$C_{17}H_{19}ClFNO_7$ + Na^+]: 426.0726, found: 426.0727.

***rel*-(3R,3aR,5R)-Trimethyl 3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2,5-tricarboxylate 4'r** (major isomer) and ***rel*-(3R,3aR,5S)-Trimethyl 3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2,5-tricarboxylate 4r** (minor isomer)



Nitrosoacetals **4r**,**4'r** were obtained from α-fluoronitroalkene **1a** (89 mg, 0.44 mmol) and methyl acrylate following the general procedure 1. Column chromatography (eluent: 7:3 PE/EtOAc) afforded **4r** (125 mg, 65%, dr (**4r**:**4'r**)= 1:1.1) as colorless which solidifies upon storage in a reftigerator. Enriched major isomer (dr = 4:1) was obtained by recrystallization (-20°C) from PE/EtOAc (10:1).

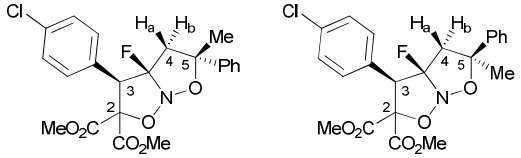
R_f = 0.31; 0.27 (PE/EtOAc, 1:1)

Major isomer (**4'r**):

^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY): δ 2.83 (ddd, *J* = 23.7, 14.5, 9.3 Hz, 1H, CH_{2a}(4)), 3.26 (ddd, *J* = 25.3, 14.5, 5.2 Hz, 1H, CH_{2b}(4)), 3.29 (s, 3H, CO_2Me), 3.81 (s, 3H, CO_2Me), 3.87 (s, 3H, CO_2Me), 5.01 (d, *J* =2.4 Hz,1H, CH(3)), 5.04 (dd, *J* = 9.3, 5.2 Hz, 1H, CH(5)), 7.31-7.38 (m, 4H, CH_{Ar}).

Characteristic NOESY interactions: CH_{2a}(4)-CH(5); CH_{2b}(4)-CH(2).
Characteristic HOESY interactions: F-CH_{2a}(4); F-CH_{Ar}; F-CH(5).
^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): δ 38.2 (d, $^2J_{CF}$ = 28.6 Hz, CH2), 52.7 (CO_2**Me**), 52.9 (CO_2**Me**), 54.0 (CO_2**Me**), 54.3 (d, $^2J_{CF}$ = 21.9 Hz, CH(2)), 79.8 (C(5)), 89.4 (C(2)), 118.6 (d, $^1J_{CF}$ = 223.9 Hz, C–F), 128.4 (CH_{Ar}), 130.0 (d, $^3J_{CF}$ = 3.2 Hz, $C_{Ar,}$), 132.1 (d, $^4J_{CF}$ = 1.3 Hz, $CH_{Ar,}$), 134.7 (C_{Ar}), 165.6 (CO_2Me), 166.2 (CO_2Me), 169.6 (CO_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -134.1 (td, *J* = 24.6, 2.3 Hz).
^{15}N NMR (30 MHz, from ^{1}H-^{15}N HMBC): δ 284 (d, $^2J_{NF}$ = 50 Hz).
Minor isomer (**4r**):
^{1}H NMR (300 MHz, $CDCl_3$ COSY, NOESY): δ 2.91 (ddd, *J* = 21.3, 14.1, 5.9 Hz, 1H, CH_{2a}(4)), 3.11 (ddd, *J* = 18.2, 14.1, 9.7 Hz, 1H, CH_{2b}(4)), 3.34 (s, 3H, CO_2Me), 3.84 (s, 3H, CO_2Me), 3.86 (s, 3H, CO_2Me), 4.89 (d, *J* = 8.0 Hz, 1H, CH(3)), 4.96 (dd, *J* = 9.7, 5.9 Hz, 1H, CH(5)), 7.25-7.36 (m, 4H, CH_{Ar}).
Characteristic NOESY interactions: CH_{2a}(4)-CH(5); CH_{2b}(4)-CH(5); CH_{2b}(4)-CH(2).
Characteristic HOESY interactions: F-CH_{2a}(4); F-CH_{Ar}.
^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): δ 39.1 (d, $^2J_{CF}$ = 28.4 Hz, CH_2(4)), 52.7 (CO_2**Me**), 53.0 (CO_2**Me**), 54.0 (CO_2**Me**), 56.0 (d, $^2J_{CF}$ = 22.7 Hz, CH(3)), 78.0 (C(5)), 91.7 (C(2)), 118.7 (d, $^1J_{CF}$ = 224.4 Hz, C–F), 128.6 (CH_{Ar}), 129.4 (d, $^3J_{CF}$ = 3.1 Hz, $C_{Ar,}$), 132.0 (d, $^4J_{CF}$ = 1.9 Hz, $CH_{Ar,}$), 134.9 (C_{Ar}), 165.0 (**C**CO_2Me), 167.3 (**C**CO_2Me), 169.0 (-**C**CO_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -136.0 (ddd, *J* = 21.3, 18.2, 8.3 Hz).
^{15}N NMR (30 MHz, from ^{1}H-^{15}N HMBC): δ 284 (d, $^2J_{NF}$ = 38 Hz).
HRMS (ESI): m/z calcd. for [$C_{17}H_{17}ClFNO_8$+ Na^+]: 440.0519, found: 440.0523.

***rel*-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methyl-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4s** (major isomer) and ***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methyl-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4's** (minor isomer)



Nitrosoacetals **4,4's** was obtained from α-fluoronitroalkene **1a** (70.4 mg, 0.35 mmol) and α-methylstyrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded mixture of diastereomers **4s,4's** (101 mg, 62%, dr (**4s**:**4's**)= 1.1:1) as colorless oil.
R_f = 0.60 (PE/EtOAc, 1:1)
Major isomer (**4s**):
^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY): δ 1.74 (s, 3H, Me), 2.90 (dd, *J* = 22.6, 14.1 Hz, 1H, CH_{2a}(4)), 3.13 (dd, *J* = 27.1, 14.1 Hz, 1H, CH_{2b}(4)), 3.29 (s, 3H, CO_2Me), 3.42 (s, 3H, CO_2Me), 4.78 (d, *J* = 4.7 Hz, 1H, Ar-C**H**), 7.26-7.49 (m, 9H, CH_{Ar}).
Characteristic NOESY interactions: Me-CH_{2a}(4); CH(3)-CH_{2b}(4).
Characteristic HOESY interactions: F-CH_{2a}(4); F-Me; F-CH_{Ar}; F-CH(3).
^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): δ 30.8 (Me), 48.8 (d, $^2J_{CF}$ = 25.8 Hz, CH_2(4)), 52.6 (CO_2**Me**), 53.6 (CO_2**Me**), 55.3 (d, $^2J_{CF}$ = 22.9 Hz, CH(3)), 90.1 (C(2)), 91.3 (CH(5)); 119.7 (d,

$^{1}J_{CF}$ = 221.7 Hz, C–F), 124.3 (CH_{Ar}), 127.1 (CH_{Ar}), 128.1 (CH_{Ar}), 128.4 (CH_{Ar}), 130.1 (d, $^{3}J_{CF}$ = 3.3 Hz, C_{Ar}), 132.1 (d, $^{4}J_{CF}$ = 1.1 Hz, $CH_{Ar,}$), 134.6 (C_{Ar}), 145.6 (C_{Ar}), 165.8 (**C**O_2Me), 166.7 (**C**O_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -134.1 (ddd, *J* = 27.1, 22.6, 4.7 Hz).

^{15}N NMR (30 MHz, from ^{1}H-^{15}N HMBC): δ 285 (d, $^{2}J_{NF}$ = 47 Hz).

Minor isomer (**4's**):

^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY): δ 1.67 (s, 3H, Me), 2.97-3.14 (m, CH_2(4)), 3.37 (s, 3H, CO_2Me), 3.90 (s, 3H, CO_2Me), 4.92 (d, $^{2}J_{HF}$ = 8.6 Hz, 1H, Ar-C**H**), 7.26-7.49 (m, 9H, CH_{Ar}).

Characteristic HOESY interactions: F-Ar; F-CH(3); F-Ph.

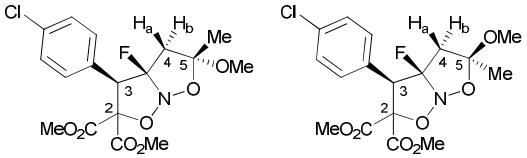
^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): δ 29.4 (Me), 49.8 (d, $^{2}J_{CF}$ = 25.3 Hz, CH_2(4)), 52.8 (CO_2**Me**), 53.9 (CO_2**Me**), 58.2 (d, $^{2}J_{CF}$ = 24.0 Hz, CH(3)), 86.3 (CH(5)), 93.7 (C(2)), 120.7 (d, $^{1}J_{CF}$ = 223.2 Hz, C–F), 124.4 (CH_{Ar}), 127.3 (CH_{Ar}), 128.2 (C_{Ar}), 128.4 (CH_{Ar}), 129.7 (d, $^{3}J_{CF}$ = 3.6 Hz, C_{Ar}), 131.9 (d, $^{4}J_{CF}$ = 2.0 Hz, $CH_{Ar,}$), 134.6 (C_{Ar}), 144.6 (C_{Ar}), 164.6 (**C**O_2Me), 167.9 (-**C**O_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -131.5 (td, *J* = 21.2, 8.7 Hz).

^{15}N NMR (30 MHz, from ^{1}H-^{15}N HMBC): δ 283 (d, $^{2}J_{NF}$ = 42 Hz).

HRMS (ESI): m/z calcd. for [$C_{22}H_{21}ClFNO_6$+ H^+]: 450.1114, found: 450.1112.

***rel*-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methoxy-5-methyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4t** (major isomer) and ***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methoxy-5-methyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4't** (minor isomer)



major isomer minor isomer

Nitrosoacetals **4,4't** was obtained from α-fluoronitroalkene **1a** (60.4 mg, 0.3 mmol) and 2-methoxypropene following the general procedure 1. Column chromatography (eluent: 2:1 PE/EtOAc) afforded mixture of diastereomers **4t,4't** (61 mg, 48%, dr (**4t**:**4't**) = 1.5:1) as slightly yellow oil, which solidifies upon storage in a refrigerator.

Major isomer (**4t**):

R_f = 0.47 (PE/EtOAc, 1:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.60 (Me), 2.63 (dd, *J* = 23.5, 14.2, 1H, CH_{2a}(4)), 2.96 (dd, *J* = 15.3, 14.2, 1H, CH_{2b}(4)), 3.33 (s, 3H, OMe), 3.41 (s, 3H, CO_2Me), 3.83 (s, 3H, CO_2Me), 5.05 (d, *J* = 10.7 Hz, 1H, CH(3)), 7.27-7.39 (m, 4H, CH_{Ar}).

Characteristic NOESY interactions: Me-CH_{2a}(4); CH(3)-CH_{2b}(4).

Characteristic HOESY interactions: F-CH_{Ar}; F-CH(3); F-CH_{2a}(4).

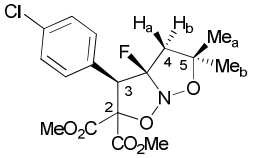
^{13}C NMR (75 MHz, $CDCl_3$): δ 21.2 (Me), 49.4 (d, $^{2}J_{CF}$ = 28.7 Hz, CH_2(4)), 50.0 (OMe), 52.7 (CO_2**Me**), 53.6 (CO_2**Me**), 56.5 (d, $^{2}J_{CF}$ = 22.7 Hz, CH(3)), 90.2 (C(2)), 115.5 (d, $^{3}J_{CF}$ = 1.7 Hz, C(5)), 119.8 (d, $^{1}J_{CF}$ = 219.4 Hz, C–F), 128.4 (CH_{Ar}), 129.7 (d, $^{3}J_{CF}$ = 2.4 Hz, $C_{Ar,}$), 132.3 (d, $^{4}J_{CF}$ = 2.2 Hz, CH_{Ar}), 134.7 (C_{Ar}), 166.4 (-**C**O_2Me), 167.1 (-**C**O_2Me).

^{19}F NMR (282 MHz, $CDCl_3$): δ -130.7 (ddd, *J* = 23.5, 15.3, 10.7 Hz).

^{15}N NMR (30 MHz, from ^{1}H-^{15}N HMBC): δ 289 (d, $^{2}J_{NF}$ = 48 Hz).

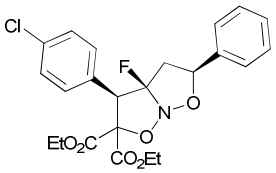
Minor isomer (**4't**):
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.46 (Me), 2.76 (dd, *J* = 20.6, 14.2, 1H, CH_{2a}(4)), 2.93 (dd, *J* = 17.4, 14.2, 1H, CH_{2b}(4)), 3.37 (s, 3H, CO_2Me), 3.38 (s, 3H, OMe), 3.84 (s, 3H, CO_2Me), 4.77 (d, *J* = 10.1 Hz, 1H, CH(3)), 7.27-7.39 (m, 4H, CH_{Ar}).
Characteristic NOESY interactions: Me-CH_{2b}(4); CH(3)-CH_{2b}(4).
Characteristic HOESY interactions: F-CH_{Ar}; F-CH(3); F-CH_{2a}(4).
^{13}C NMR (75 MHz, $CDCl_3$): δ 20.2 (Me), 48.9 (d, $^{2}J_{CF}$ = 25.8 Hz, CH_2(4)), 49.6 (OMe), 52.9 (CO_2**Me**), 53.8 (CO_2**Me**), 59.5 (d, $^{2}J_{CF}$ = 25.0 Hz, CH(3)), 95.3 (C(2)), 106.4 (d, $^{3}J_{HF}$ = 2.4 Hz, C(5)), 120.6 (d, $^{1}J_{CF}$ = 224.4 Hz, C–F), 128.4 (CH_{Ar}), 129.3 (d, $^{3}J_{CF}$ = 4.0 Hz, $C_{Ar,}$), 131.8 (d, $^{4}J_{CF}$ = 2.3 Hz, CH_{Ar}), 134.7 (C_{Ar}), 163.9 (**C**O_2Me), 167.9 (**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -130.2 (ddd, *J* = 20.6, 17.4, 10.1 Hz).
^{15}N NMR (30 MHz, from ^{1}H-^{15}N HMBC): δ 284 (d, $^{2}J_{NF}$ = 46 Hz).
HRMS (ESI): m/z calcd. for [$C_{17}H_{19}ClFNO_7$ + Na^+]: 426.0726, found: 426.0718.

***rel*-(3R,3aR)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5,5-dimethyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4u**



Nitrosoacetal **4u** was obtained from α-fluoronitroalkene **1a** (60.4 mg, 0.3 mmol) and isobutylene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4u** (67 mg, 55%, single diastereomer) as colorless solid.
R_f = 0.62 (PE/EtOAc, 1:1)
mp = 98-100 °C (PE/EtOAc, 1:1)
^{1}H NMR (300 MHz, $CDCl_3$, COSY, NOESY): δ 1.45 (s, 3H, Me_b), 1.47 (s, 3H, Me_a), 2.48 (dd, *J* = 21.7, 13.8 Hz, 1H, CH_{2a}(4)), 2.68 (dd, *J* = 25.3, 13.8 Hz, 1H, CH_{2b}(4)), 3.32 (s, 3H, CO_2Me), 3.84 (s, 3H, CO_2Me), 4.83 (d, *J* = 6.7 Hz, 1H, CH(3)), 7.31 (s, 4H, CH_{Ar}).
Characteristic NOESY interactions: Me_a-CH_{2a}(4); Me_b-CH_{2b}(4).
Characteristic HOESY interactions: F-CH_{2a}(4); F-CH_{Ar}; F-CH(3), F-Me_a.
^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): δ 28.1 (2 × Me), 48.3 (d, $^{2}J_{CF}$ = 25.1 Hz, CH_2(4)), 52.6 (CO_2**Me**), 53.8 (CO_2**Me**), 56.8 (d, $^{2}J_{CF}$ = 23.1 Hz, CH(3)), 86.0 (C(5)), 91.6 (C(2)), 120.1 (d, $^{1}J_{CF}$ = 221.8 Hz, C–F), 128.3 (CH_{Ar}), 130.1 (d, J_{CF} = 3.7 Hz, C_{Ar}), 132.0 (d, J_{CF} = 1.7 Hz, $CH_{Ar,}$), 134.5 (C_{Ar}), 165.3 (**C**O_2Me), 167.7 (**C**O_2Me).
^{19}F NMR (282 MHz, $CDCl_3$): δ -132.8 (ddd, *J* = 25.3, 21.7, 6.7 Hz).
^{15}N NMR (30 MHz, from ^{1}H-^{15}N HMBC): δ 285 (d, $^{2}J_{NF}$ = 44 Hz).
HRMS (ESI): m/z calcd. for [$C_{17}H_{19}ClFNO_6$+ H^+]: 388.0958, found: 388.0958.

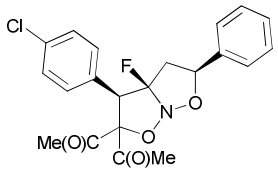
***rel*-(3R,3aR,5S)-diethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4v** (major isomer)



major isomer

Nitrosoacetals **4,4'v** was obtained from α-fluoronitroalkene **1a** (75 mg, 0.37 mmol) and styrene following the general procedure 1 with diethyl bromomalonate (92 mg, 0.41 mmol, 1.1 equiv.) instead of diethyl bromomalonate. Column chromatography (eluent: 9:1, then 3:1, then 7:3 PE/EtOAc) afforded **4,4'v** (126 mg, 75%, dr = 7:1, ^{1}H NMR) as slightly yellow oil.
R_f = 0.63 (PE/EtOAc, 1:1).
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (t, *J* = 7.1 Hz, 3 H, Me), 1.32 (t, *J* = 7.1 Hz, 3 H, Me), 2.64 (ddd, *J* = 24.9, 14.1, 7.7 Hz, 1H, CH_{2a}(4)), 3.22 (ddd, *J* = 20.0, 14.1, 8.4 Hz, 1H, CH_{2b}(4)), 3.67-3.77 (m, 1H, C**H**$_{2a}$O), 3.81-3.92 (m, 1H, C**H**$_{2b}$O), 4.27-4.44 (m, 2H, C**H**$_{2cd}$O),4.96 (d, *J* = 3.7 Hz, 1H, Ar-C**H**), 5.59 (td, *J* = 8.0, 1.2 Hz, 1H, O-C**H**-Ar), 7.32-7.43 (m, 9H, CH_{Ar}). Minor isomer (characteristic signal): δ 5.49 (dd, *J* = 9.3, 7.2 Hz, 1H, O-C**H**-Ar).
^{13}C NMR (75 MHz, $CDCl_3$, DEPT): δ 13.5 (Me), 13.9 (Me), 44.8 (d, $^2J_{CF}$ = 28.1 Hz, CH_2), 55.6 (d, $^2J_{CF}$ = 22.6 Hz, CH–Ar), 62.2 (CH_2O), 63.4 (CH_2O), 85.1 (Ar**C**H–O), 89.3 (C–O), 119.3 (d, $^1J_{CF}$ = 221.5 Hz, C–F), 127.0 (CH_{Ar}), 128.4 (CH_{Ar}), 128.8 (CH_{Ar}), 128.9 (CH_{Ar}), 130.5 (d, $^3J_{CF}$ = 3.3 Hz, C_{Ar}), 132.3 (CH_{Ar}), 134.6 (C_{Ar}), 137.1 (C_{Ar}), 165.4 (**C**O_2Et), 166.6 (**C**O_2Et).
^{19}F NMR (282 MHz, $CDCl_3$): δ -131.2 (t, *J* = 22.3 Hz). Minor isomer: δ -134.5 (t, *J* = 21.4 Hz).
HRMS (ESI): m/z calcd. for [$C_{23}H_{23}ClFNO_6$ + Na^+]: 486.1090, found: 486.1086.

***rel*-1,1'-((3R,3aR,5S)-3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-diyl)diethanone 4w** (major isomer)

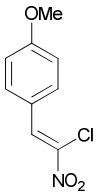


major isomer

Nitrosoacetals **4,4'w** was obtained from α-fluoronitroalkene **1a** (75 mg, 0.37 mmol) and styrene following the general procedure 1 with 3-chloro-2,4-pentandione (55 mg, 0.41 mmol, 1.1 equiv.) instead of dimethylbromomalonate. Column chromatography (eluent: 9:1, then 3:1, then 7:3 PE/EtOAc) afforded **4,4'w** (36 mg, 24%, dr = 8:1, ^{1}H NMR) as slightly yellow oil.
R_f = 0.55 (PE/EtOAc, 1:1).
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.16 (Me), 2.27 (Me), 2.65 (ddd, *J* = 22.7, 14.1, 7.7 Hz, 1H, CH_{2a}(4)), 2.94 (ddd, *J* = 17.0, 14.1, 8.3 Hz, 1H, CH_{2b}(4)), 4.92 (d, *J* = 7.3 Hz, 1H, Ar-C**H**), 5.45 (td, *J* = 8.1, 1.1 Hz, 1H, O-C**H**-Ar), 7.33-7.43 (m, 9H, CH_{Ar}). Minor isomer (characteristic signal): δ 5.35 (dd, *J* = 9.8, 6.4 Hz, 1H, O-C**H**-Ar).
^{13}C NMR (75 MHz, $CDCl_3$, HMBC): δ 25.6 (Me), 27.8 (Me), 44.3 (d, $^2J_{CF}$ = 27.3 Hz, CH_2), 54.0 (d, $^2J_{CF}$ = 21.9 Hz, CH–Ar), 84.1 (Ar**C**H–O), 89.1 (C–O), 100.0 (C–O), 119.6 (d, $^1J_{CF}$ = 234 Hz, C–F), 126.8 (CH_{Ar}), 128.8 (CH_{Ar}), 128.9 (CH_{Ar}), 129.0 (CH_{Ar}), 129.8 (d, $^3J_{CF}$ = 3.0 Hz, $C_{Ar,}$), 132.1 (d, $^4J_{CF}$ = 1.9 Hz, CH_{Ar}), 134.7 (C_{Ar}), 137.4 (C_{Ar}), 198.8 (C=O), 203.8 (C=O).
^{19}F NMR (282 MHz, $CDCl_3$): δ -133.1 (app t, *J* = 17.4 Hz).
HRMS (ESI): m/z calcd. for [$C_{21}H_{19}ClFNO_4$ + H^+]: 426.0879, found: 426.0870.

Reaction of bromo-malonate, styrene and β-nitrostyrene 5.
Application of the general procedure 1 for *p*-methoxy-β-nitrostyrene **5** led to the formation of nitrocyclopropane **6** (Yield 57%, according to ^{1}H NMR with 1,4-dinitrobenzene as standard). The spectral characteristics match previously reported data.[s9]

1-[(*Z*)-2-chloro-2-nitroethenyl]-4-(methyloxy)benzene 7a



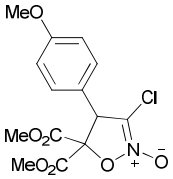
Obtained by modified literature procedure.[s10] To the stirring solution of *p*-methoxy-β-nitrostyrene **5** (0.20 g, 1.1 mmol) and pyridine (0.18 mL, 2.2 mmol, 2 equiv.) in THF (2.2 mL) $PhICl_2$ (0.46 g, 1.7 mmol, 1.5 equiv.) was added. The reaction mixture was stirred overnight and poured into EtOAc (40 mL)/ H_2O (30 mL) mixture. Organic layer was washed with $NaHSO_4$ (0.5 M in H_2O, 20 mL), brine (20 mL), dried over Na_2SO_4 and evaporated. Crude product was purified by column chromatography on silica gel (eluent: PE, then PE/EtOAc = 9:1) to afford **7a** (0.13 g, 54%) as a yellow solid. ^{1}H NMR matched previously reported data.[s11]

R_f = 0.29 (PE/EtOAc, 9:1).

^{1}H NMR (300 MHz, $CDCl_3$): 3.91 (s, 3H, OMe), 7.02 (d, *J* = 8.9 Hz, 2H, CH_{Ar}), 7.87 (d, *J* = 8.9 Hz, 2H, CH_{Ar}), 8.36 (s, 1H, =CH)..

^{13}C NMR (75 MHz, $CDCl_3$): δ 55.6 (O**Me**), 114.7 (CH_{Ar}), 122.1 (C_{Ar}), 131.7 (=CH), 133.6 (CH_{Ar}), 162.7 (**C**$_{Ar}$-OMe). C–NO_2 could not be unambiguously identified due to broadening/low intensity.

3-Chloro-5,5-bis(methoxycarbonyl)-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide 8a



To the solution of *p*-methoxy-β-chloro-β-nitrostyrene **7a** (26.5 mg, 0.12 mmol), dimethyl bromomalonate (29 mg, 0.14 mmol, 1.1 equiv.) and acrylonitrile (127 mg, 2.4 mmol, 20 equiv.) in dry DMF (2.4 ml) finely powdered K_2CO_3 (25 mg, 0.18 mmol, 1.5 equiv.) was added at 0 °C. Mixture was stirred for 20 min, warmed to r.t. and stirred for additional 1 hour (TLC monitoring). After that the reaction mixture was poured into t-BuOMe (40 mL) / H_2O (30 mL). Organic layer was washed with H_2O (20 mL), brine (20 mL), dried over Na_2SO_4 and evaporated. Crude product was purified by column chromatography on silica gel (eluent: PE/EtOAc = 5:1, then 1:1) to afford **8a** (38.9 mg, 91%) as a colorless oil.

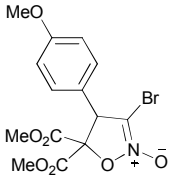
R_f = 0.20 (PE/EtOAc, 1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.35 (s, 3H, CO_2Me), 3.82 (s, 3H, OMe), 3.92 (s, 3H, CO_2Me), 5.39 (s, 1H, Ar-C**H**), 6.91 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 7.18 (d, *J* = 8.7 Hz, 2H, CH_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT, HMBC): δ 53.1 (CO_2**Me**), 54.3 (CO_2**Me**), 54.8 (CH(4)), 55.3 (O**Me**), 84.8 (C(5)), 109.2 (C(3)), 114.4 (CH_{Ar}), 123.0 (C_{Ar}), 130.3 (CH_{Ar}), 160.5 (**C**$_{Ar}$-OMe), 163.5 (-**C**O_2Me), 165.9 (-**C**O_2Me).

HRMS (ESI): m/z calcd. for [$C_{14}H_{14}{}^{35}ClNO_7 + NH_4^+$]: 361.0797, found: 361.0798.

3-Bromo-5,5-bis(methoxycarbonyl)-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide 8b



To the solution of *p*-methoxy-β-bromo-β-nitrostyrene **7b** (26.2 mg, 0.1 mmol), dimethyl bromomalonate (25 mg, 0.11 mmol, 1.1 equiv.) and acrylonitrile (106 mg, 2 mmol, 20 equiv.) in dry DMF (1 ml) finely powdered K_2CO_3 (21 mg, 0.15 mmol, 1.5 equiv.) was added. Mixture was stirred at r. t. for 1 hour (TLC monitoring). After that the reaction mixture was poured into H_2O, and product was extracted with t-BuOMe (3 x 30 ml). Organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. Crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 2:1) to afford **8b** (31.0 mg, 76%) as a colorless oil.

R_f = 0.45 (PE/EtOAc, 1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.34 (s, 3H, CO_2Me), 3.81 (s, 3H, OMe), 3.91 (s, 3H, CO_2Me), 5.39 (s, 1H, Ar-C**H**), 6.90 (d, *J* = 8.8 Hz, 2H, CH_{Ar}), 7.15 (d, *J* = 8.8 Hz, 2H, CH_{Ar}).

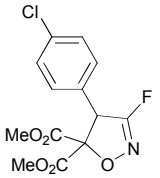
^{13}C NMR (75 MHz, $CDCl_3$): δ 53.1 (CO_2**Me**), 54.2 (CO_2**Me**), 55.3 (O**Me**), 56.6 (CH(4)), 85.2 (C(5)), 97.1 (C(3)), 114.3 (CH_{Ar}), 123.5 (C_{Ar}), 130.3 (CH_{Ar}), 160.4 (**C**$_{Ar}$-OMe), 164.3 (-**C**O_2Me), 166.0 (-**C**O_2Me).

HRMS (ESI): m/z calcd. for [$C_{14}H_{14}{}^{79}BrNO_7$ + Na^+]: 409.9846, found: 409.9841.

Synthesis of 3-fluoroisoxazolines 9a-9b.

To the solution of 3-cyano-substituted fluorinated nitrosoacetal **4** (0.05 mmol) in CH_2Cl_2 (0.5 ml) Et_3N (0.10mmol, 10 mg, 2 equiv.) was added. Mixture was stirred at r.t. for 48 hours, then evaporated on silica gel and purified by column chromatography (PE/EtOAc, 3:1) to afford isoxazolines **9** as colorless oils.

Dimethyl 4-(4-chlorophenyl)-3-fluoroisoxazole-5,5(4H)-dicarboxylate 9a



Yield 13.2 mg (64%). R_f = 0.48 (PE/EtOAc, 1:1).

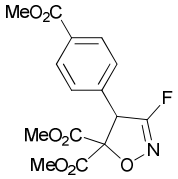
^{1}H NMR (300 MHz, $CDCl_3$): δ 3.39 (s, 3H, CO_2Me), 3.93 (s, 3H, CO_2Me), 5.37 (d, $^2J_{HF}$ = 4.5 Hz, 1H, Ar-C**H**), 7.21 (d, *J* = 8.4 Hz, 2H, CH_{Ar}), 7.40 (d, *J* = 8.4 Hz, 2H, CH_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ 52.6 (d, $^2J_{HF}$ = 24.4 Hz, C(4)), 52.9 (CO_2**Me**), 54.2 (CO_2**Me**), 93.7 (d, $^3J_{CF}$ = 3.5 Hz, C(5)), 128.3 (d, $^3J_{CF}$= 3.7 Hz, C_{Ar}), 129.4 (CH_{Ar}), 130.3 (CH_{Ar}), 135.7 (C_{Ar}), 163.9 (-**C**O_2Me), 166.2 (-**C**O_2Me), 166.8 (d, $^1J_{CF}$ = 286.5 Hz, C(3)).

^{19}F NMR (282 MHz, $CDCl_3$): δ -120.5 (s).

HRMS (ESI): m/z calcd. for [$C_{13}H_{11}ClFNO_5$ + Na^+]: 338.0202, found: 338.0202.

Dimethyl 3-fluoro-4-(4-(methoxycarbonyl)phenyl)isoxazole-5,5(4H)-dicarboxylate 9m



Yield 15.0 mg (68%). R_f = 0.45 (PE/EtOAc, 1:1).

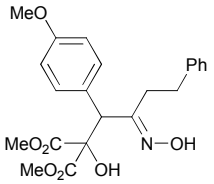
^{1}H NMR (300 MHz, $CDCl_3$): δ 3.31 (s, 3H, CO_2Me), 3.95 (s, 3H, CO_2Me), 3.96 (s, 3H, CO_2Me), 5.45 (d, $^2J_{HF}$ = 4.5 Hz, 1H, Ar-C**H**), 7.35 (d, *J* = 7.8 Hz, 2H, CH_{Ar}), 8.09 (d, *J* = 7.8 Hz, 2H, CH_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ 52.3 (-CO_2**Me**), 52.9 (CO_2**Me**), 53.0 (d, $^2J_{CF}$ = 24.4 Hz, Ar-**C**H), 54.2 (CO_2**Me**), 93.8 (d, $^3J_{CF}$ = 3.6 Hz, C–O), 129.0 (CH_{Ar}), 130.2 (CH_{Ar}), 131.3 (C_{Ar}), 134.7 (d, $^3J_{CF}$ = 3.6 Hz, C_{Ar}), 163.8 (C=O), 166.1 (C=O), 166.8 (d, $^1J_{CF}$ = 286.8 Hz, C=N).

^{19}F NMR (282 MHz, $CDCl_3$): δ -120.1 (s).

HRMS (ESI): m/z calcd. for [$C_{15}H_{14}FNO_7$ + Na^+]: 362.0647, found: 362.0648.

Dimethyl 2-hydroxy-2-(2-(hydroxyimino)-1-(4-methoxyphenyl)-4-phenylbutyl)malonate 10



To the solution of nitroso acetal **4e** (57.6 mg, 0.13 mmol) in MeOH (0.53 mL) over 10% Pd/C (23 mg) was added. The mixture was hydrogenated with stirring at 30 atm of H_2 for 14 hours. After that it was filtered through Celite®, Celite® was washed with MeOH (20 mL) and combined filtrate was evaporated. Column chromatography (PE/EtOAc, 3:1 then 1:1) afforded oxime **10** (24.3 mg, 44%) as colorless oil.

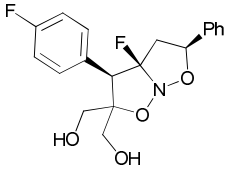
R_f = 0.22 (PE/EtOAc, 1:1).

^{1}H NMR (300 MHz, $CDCl_3$, COSY): δ 2.13-2.21 (m, 1H) and 2.66-2.89 (m, 3H) (2×CH_2), 3.65 (s, 3H, CO_2Me), 3.80 (s, 3H, OMe), 3.84 (s, 3H, CO_2Me), 4.65 (s, 1H, Ar-C**H**), 5.26 (br s, 1 H, OH), 6.86 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 7.12-7.15 (m, 2H, CH_{Ar}), 7.17-7.21 (m, 1H, CH_{Ar}), 7.24-7.30 (m, 4H, CH_{Ar}), 8.10 (br s, 1H, OH).

^{13}C NMR (75 MHz, $CDCl_3$, HSQC, HMBC): δ 30.2 (CH_2), 31.3 (CH_2), 53.18 (**C**H–Ar), 53.23 (-CO_2**Me**), 53.5 (CO_2**Me**), 55.2 (OMe), 82.5 (C–O), 113.9 (CH_{Ar}), 125.6 (C_{Ar}), 126.1 (CH_{Ph}), 128.2 (CH_{Ar}), 128.4 (CH_{Ar}), 131.4 (CH_{Ar}), 141.2 (C_{Ph}), 159.5 (C_{Ar}–OMe), 160.8 (C=N), 168.2 (C=O), 170.4 (C=O).

HRMS (ESI): m/z calcd. for [$C_{22}H_{25}NO_7$+ H^+]: 416.1704, found: 416.1703.

***rel*-((3R,3aR,5S)-3a-Fluoro-3-(4-fluorophenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-diyl)dimethanol 13**



To the stirred solution of nitrosoacetal **4d** (40 mg, 0.09 mmol) in THF (0.9 mL) lithium aluminium hydride was added in small portions for 5 min. The mixture was stitted at room

temperature for 4 hours, then poured into EtOAc/aqueous KOH (5% solution). Water layer was extracted with EtOAc (4×20 ml), combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and evaporated. Column chromatography (2:3 PE/EtOAc) afforded **13** (21 mg, 54%) as colorless solid.

R_f = 0.15 (PE/EtOAc, 1:1)

mp = 141-143 °C ($CHCl_3$)

^{1}H NMR (300 MHz, acetone-d_6): δ 2.47 (ddd, *J* = 22.2, 12.8, 10.3 Hz, 1H, CH_{2a}(4)), 3.14-3.25 (m, 2H, CH_{2b}(4) and $CH_{2a}O$), 3.48 (dd, *J* = 12.5, 7.7 Hz, 1H, $CH_{2b}O$), 3.57 (br dd, *J* = 6.7, 5.6 Hz, 1H, OH), 3.89 (dd, *J* = 11.9, 4.8 Hz, 1H, $CH_{2c}O$), 3.96 (dd, *J* = 12.5, 4.7 Hz, 1H, $CH_{2d}O$), 4.21 (dd, *J* = 7.7, 4.7 Hz, 1H, OH), 4.45 (d, *J* = 21.9 Hz, 1H, Ar-C**H**), 5.91 (dd, *J* = 10.2, 5.8 Hz, 1H, O-C**H**-Ph), 7.14 (t, *J* = 8.8 Hz, 2H, CH_{Ar}), 7.37-7.57 (m, 7H, CH_{Ar}).

^{1}H NMR (300 MHz, acetone-d_6, after H/D-exchange:10 d storage): δ 2.47 (ddd, *J* = 22.2, 12.8, 10.3 Hz, 1H, CH_{2a}(4)), 3.08-3.17 (m, 1H, CH_{2b}(4)), 3.18 (d, *J* = 12.0 Hz, $CH_{2a}O$), 3.44 (d, *J* = 12.5 Hz, 1H, $CH_{2b}O$), 3.88 (d, *J* = 12.0 Hz, 1H, $CH_{2c}O$), 3.93 (d, *J* = 12.5 Hz, 1H, $CH_{2d}O$), 4.40 (d, *J* = 21.9 Hz, 1H, Ar-C**H**), 5.89 (dd, *J* = 10.2, 5.8 Hz, 1H, O-C**H**-Ph), 7.10 (t, *J* = 8.8 Hz, 2H, CH_{Ar}), 7.37-7.57 (m, 7H, CH_{Ar}).

^{13}C NMR (75 MHz, acetone-d_6, DEPT, HMBC): δ 47.4 (d, $^2J_{CF}$ = 29.0 Hz, **C**H(3)-Ar), 54.1 (d, $^2J_{CF}$ = 20.1 Hz, CH_2(4)), 62.1 (CH_2OH), 63.1 (CH_2OH), 85.6 (**C**H–Ph), 87.6 (C(2)), 115.6 (d, $^2J_{CF}$ = 21.3 Hz, CH_{Ar}), 122.1 (d, $^1J_{CF}$ = 218.6 Hz, C–F), 128.0 (CH_{Ph}), 129.4 (br s, C_{Ar}), 129.5 ($CH_{Ph,}$), 129.6 (CH_{Ph}), 134.3 (dd, J_{CF} = 8.1, 3.6 Hz, $CH_{Ar,}$), 137.9 (C_{Ph}), 162.4 (d, $^1J_{CF}$= 245.1 Hz, C_{Ar}).

^{19}F NMR (282 MHz, acetone-d_6): δ -115.6 (br s, 1F, Ar-F), -129.0-129.3 (m, 1F, N–C–F).

HRMS (ESI): m/z calcd. for [$C_{19}H_{19}F_2NO_4$+ H^+]: 386.1174, found: 386.1164.

References:

(s1) Nitration of bromofluorostyrenes with $Fe(NO)_3 \cdot 9H_2O$ in 1,4-dioxane: V. A. Motornov, V. M. Muzalevskiy, A. A. Tabolin, R. A. Novikov, Yu. V. Nelyubina, V. G. Nenajdenko and S. L. Ioffe, *J. Org. Chem.*, 2017, **82**, 5274.

(s2) V. A. Motornov, A. A. Tabolin, R. A. Novikov, Yu. V. Nelyubina, S. L. Ioffe, I. V. Smolyar and V. G. Nenajdenko, *Eur. J. Org. Chem.*, 2017, 6851.

(s3) N. S. Y. Loy, S. Kim, C.-M. Park, *Org. Lett.*, 2015, **17**, 395.

(s4) M. Brambilla, M. Tredwell, *Angew. Chem. Int. Ed.*, 2017, **56**, 11981.

(s5) A. L. Casalnuovo, T. V. RajanBabu, T. A. Ayers, T. H. Warren, *J. Am. Chem. Soc.*, 1994, **116**, 9869.

(s6) X. Ji, H. Tong and Y. Yuan, *Synth. Commun.*, 2011, **41**, 372.

(s7) L. V. Romashov, Yu. A. Khomutova, V. M. Danilenko, S. L. Ioffe and A. V. Lesiv, *Synthesis*, 2010, 407.

(s8) X.-F. Zhao, C. Zhang, *Synthesis*, 2007, 551.

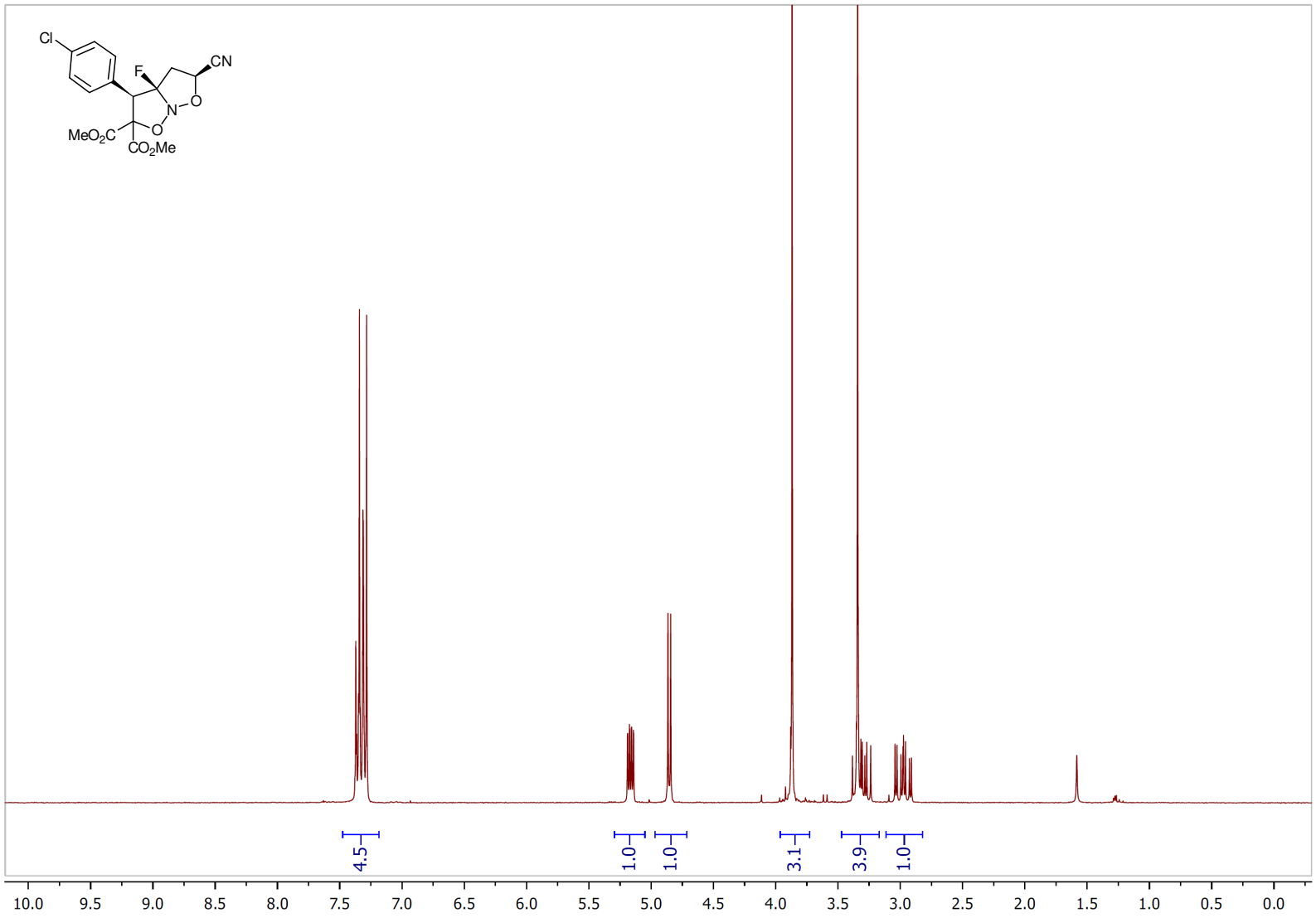
(s9) Y.-N. Xuan, S.-Z. Nie, L.-T. Dong, J.-M. Zhang, M. Yan, *Org. Lett.,* 2009, **11**, 1583.

(s10) L. Liu, D. Zhang-Negrerie, Y. Du, K. Zhao, *Org. Lett.*, 2014, **16**, 436.

(s11) D. Dauzonne, P. Demerseman, *Synthesis*, 1990, 66.

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-5-cyano-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4a** (major isomer)

^{1}H NMR



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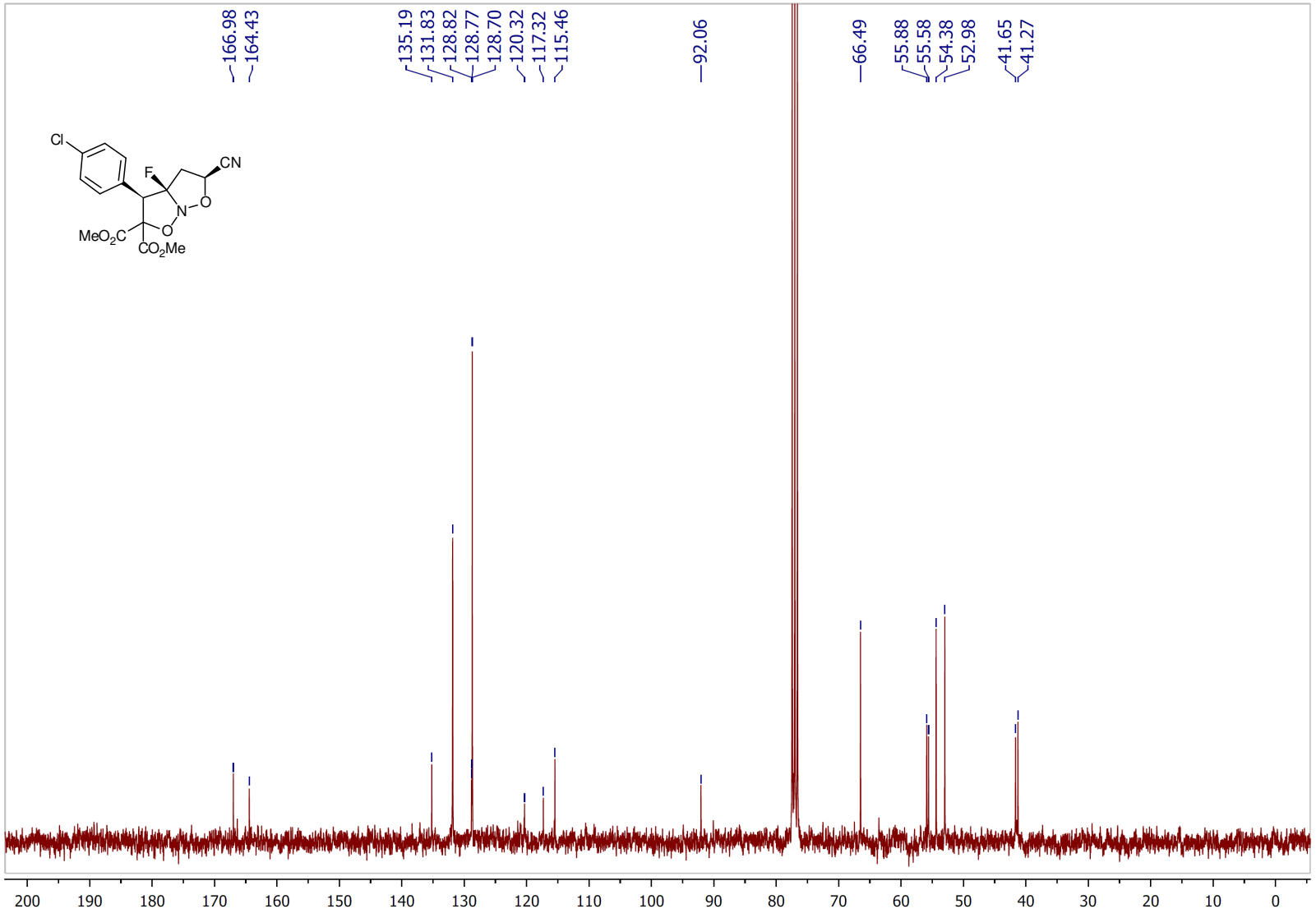
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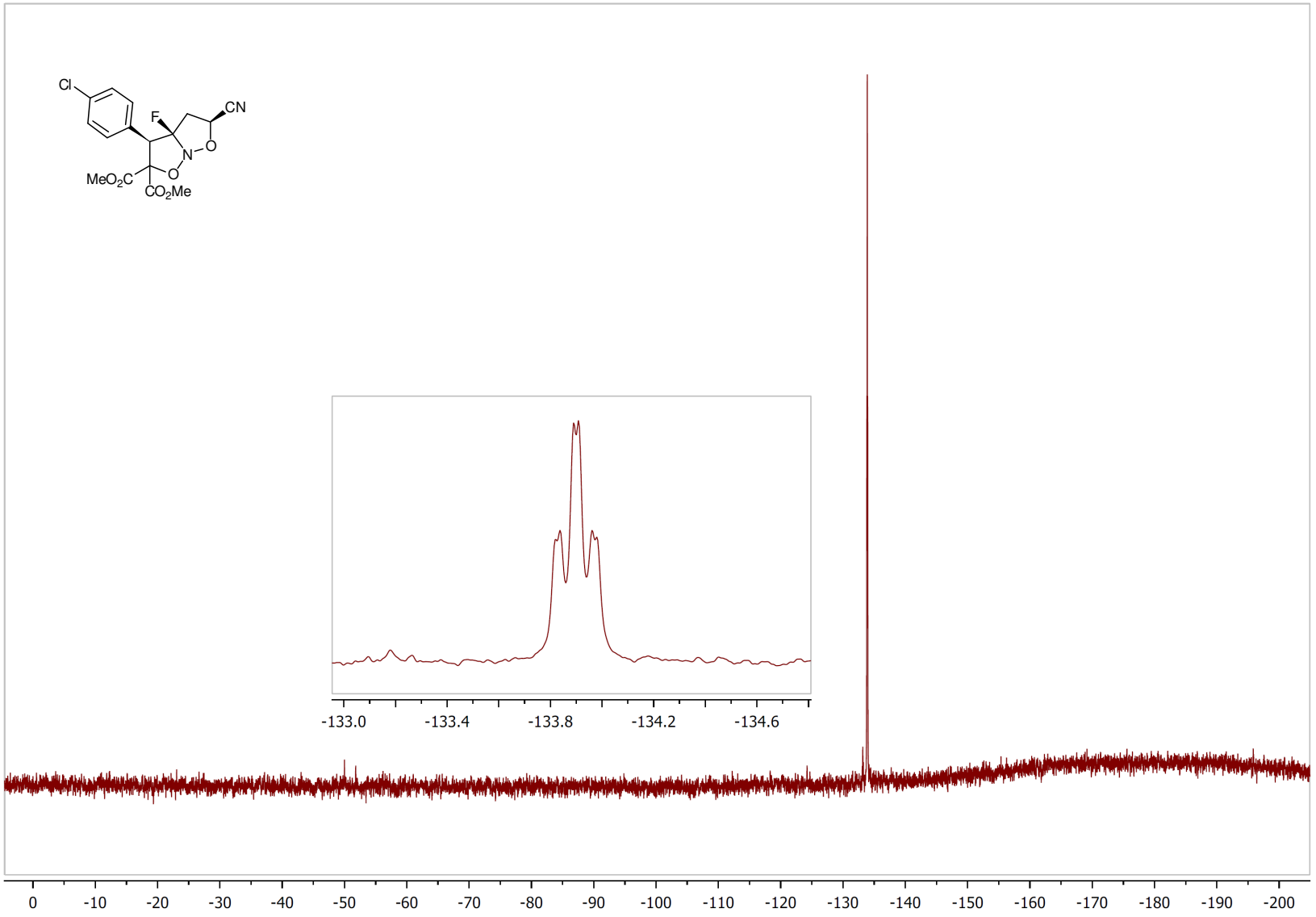
^{19}F NMR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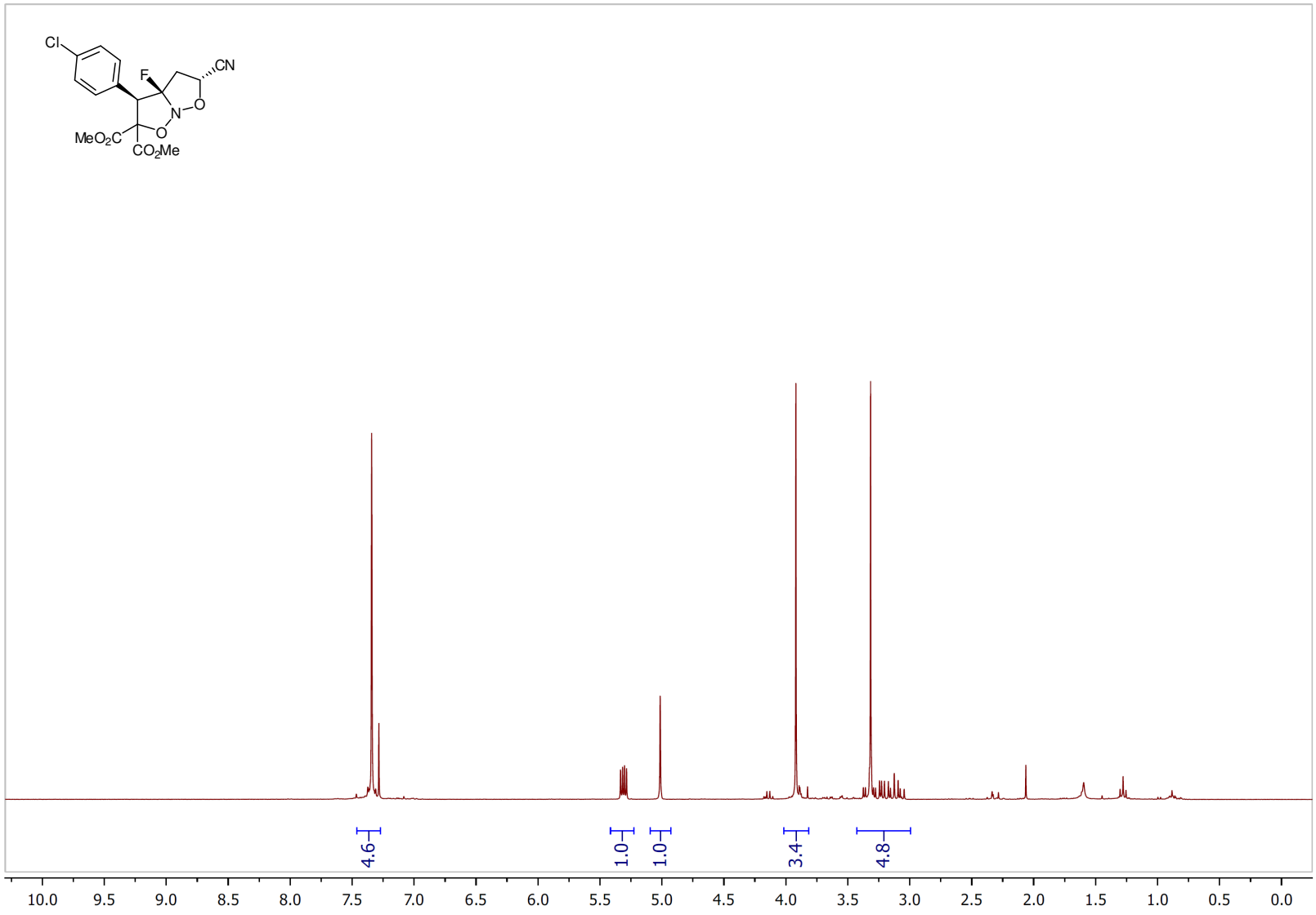
-200

***rel*-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-5-cyano-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'a** (minor isomer)

^{1}H NMR



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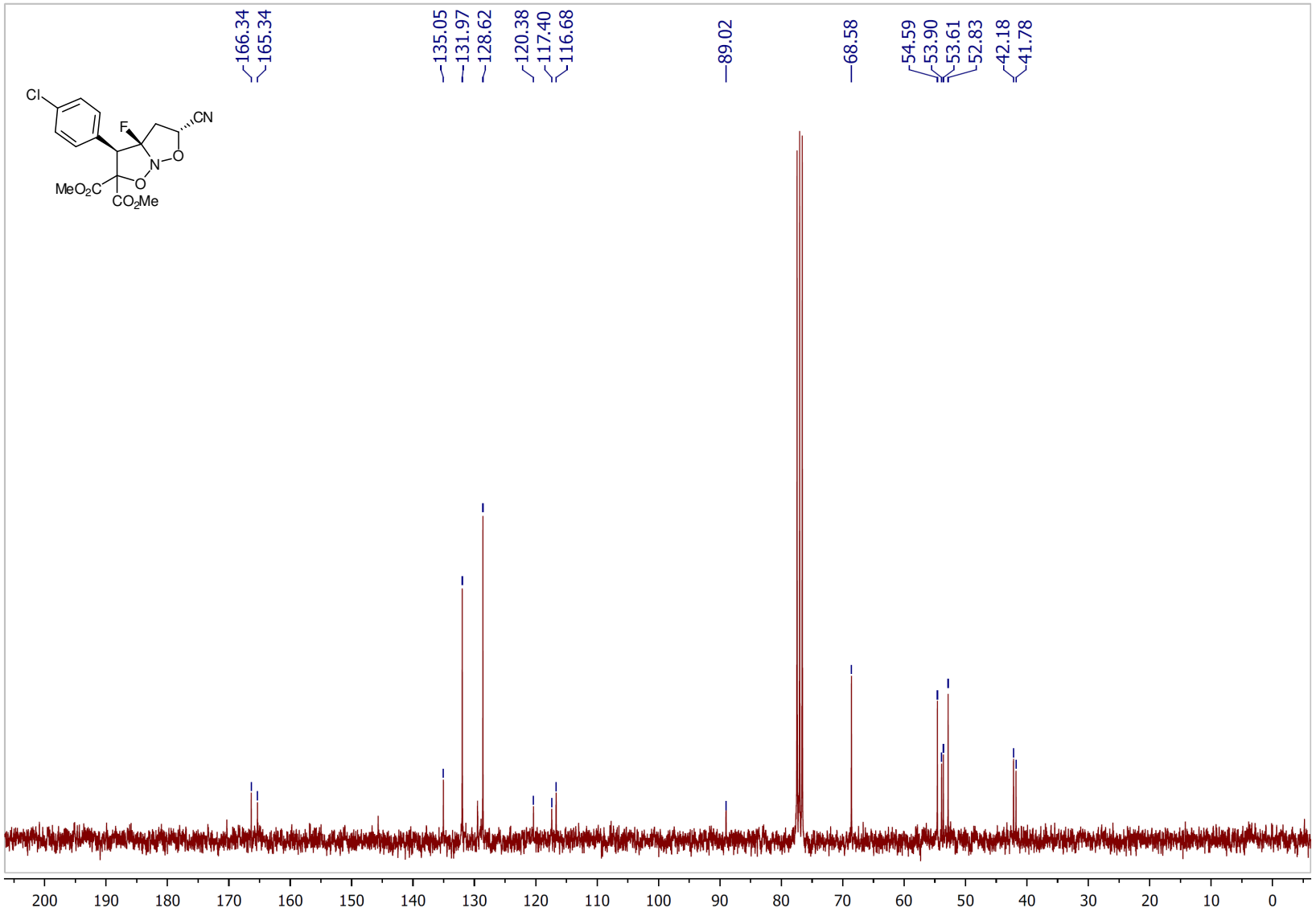
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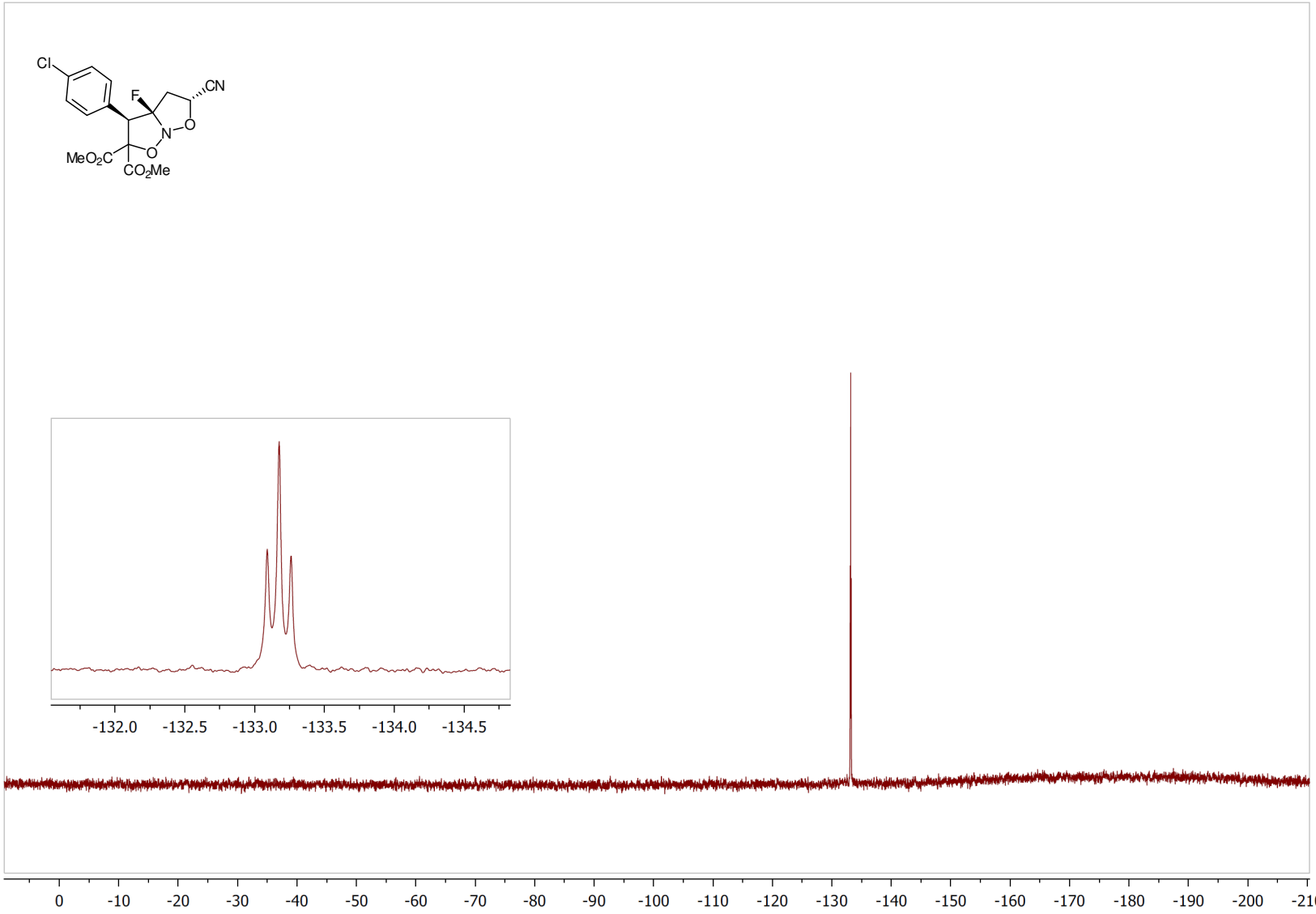
^{19}F NMR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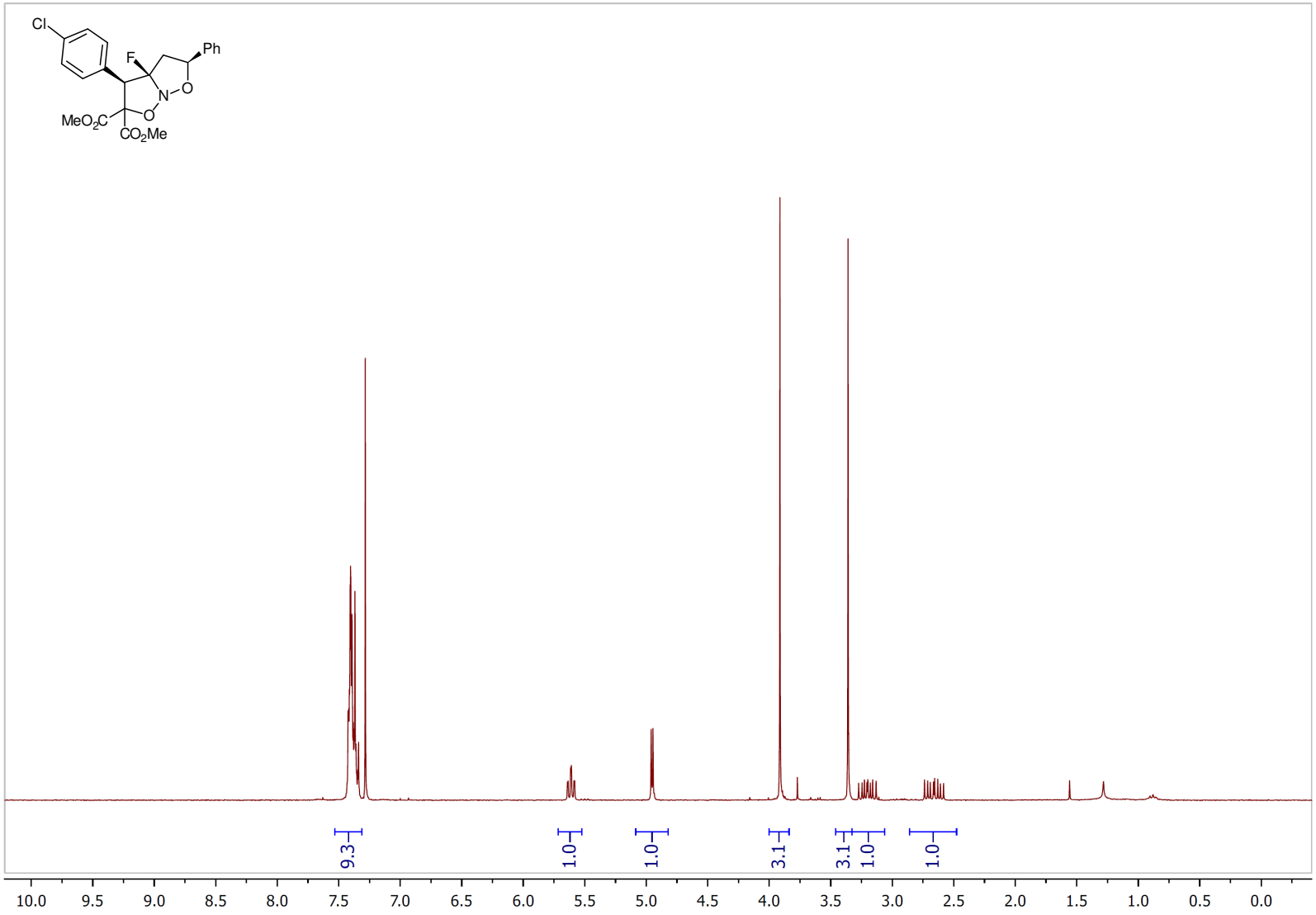
-200
-210

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4b** (major)

^{1}H NMR



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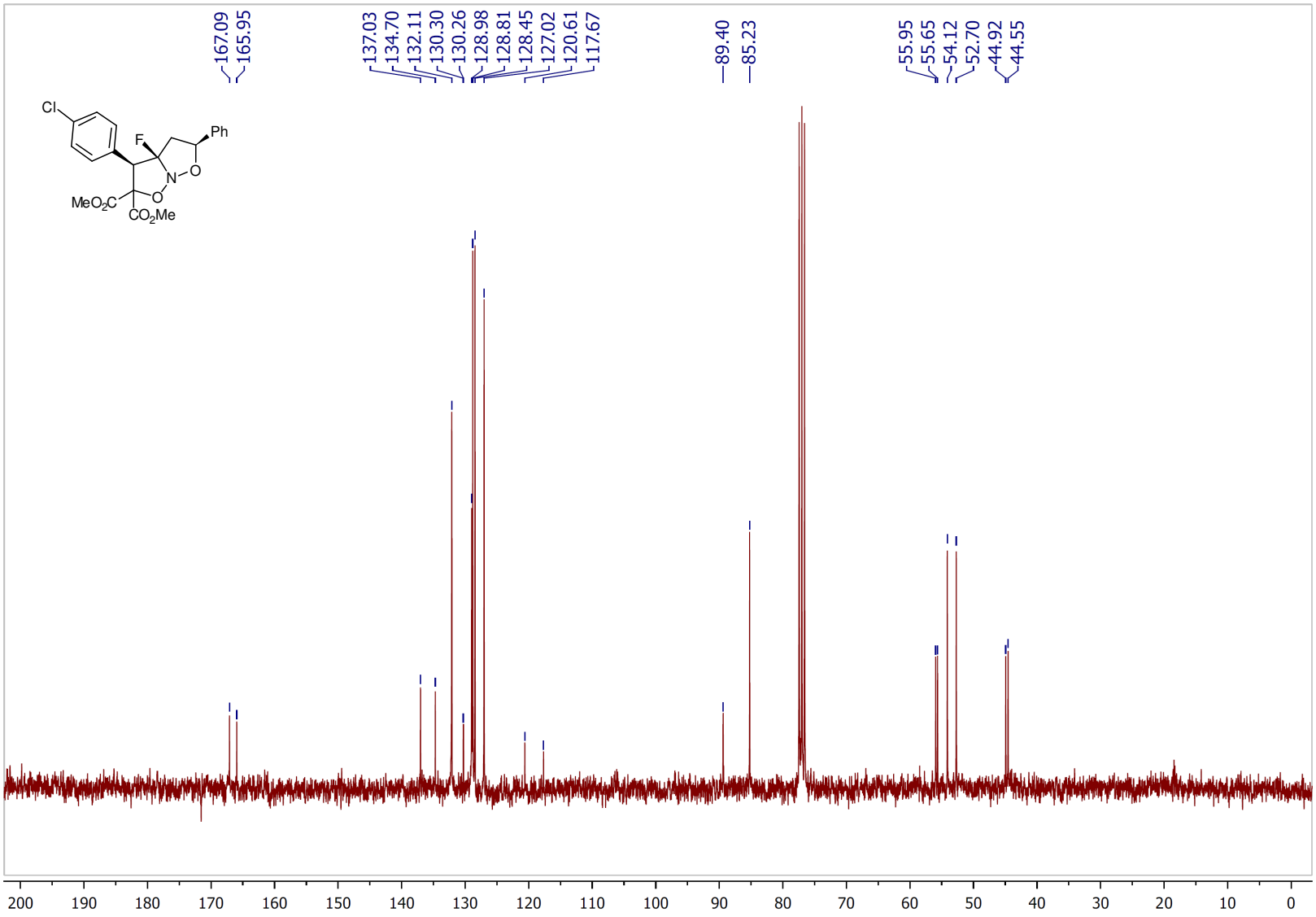
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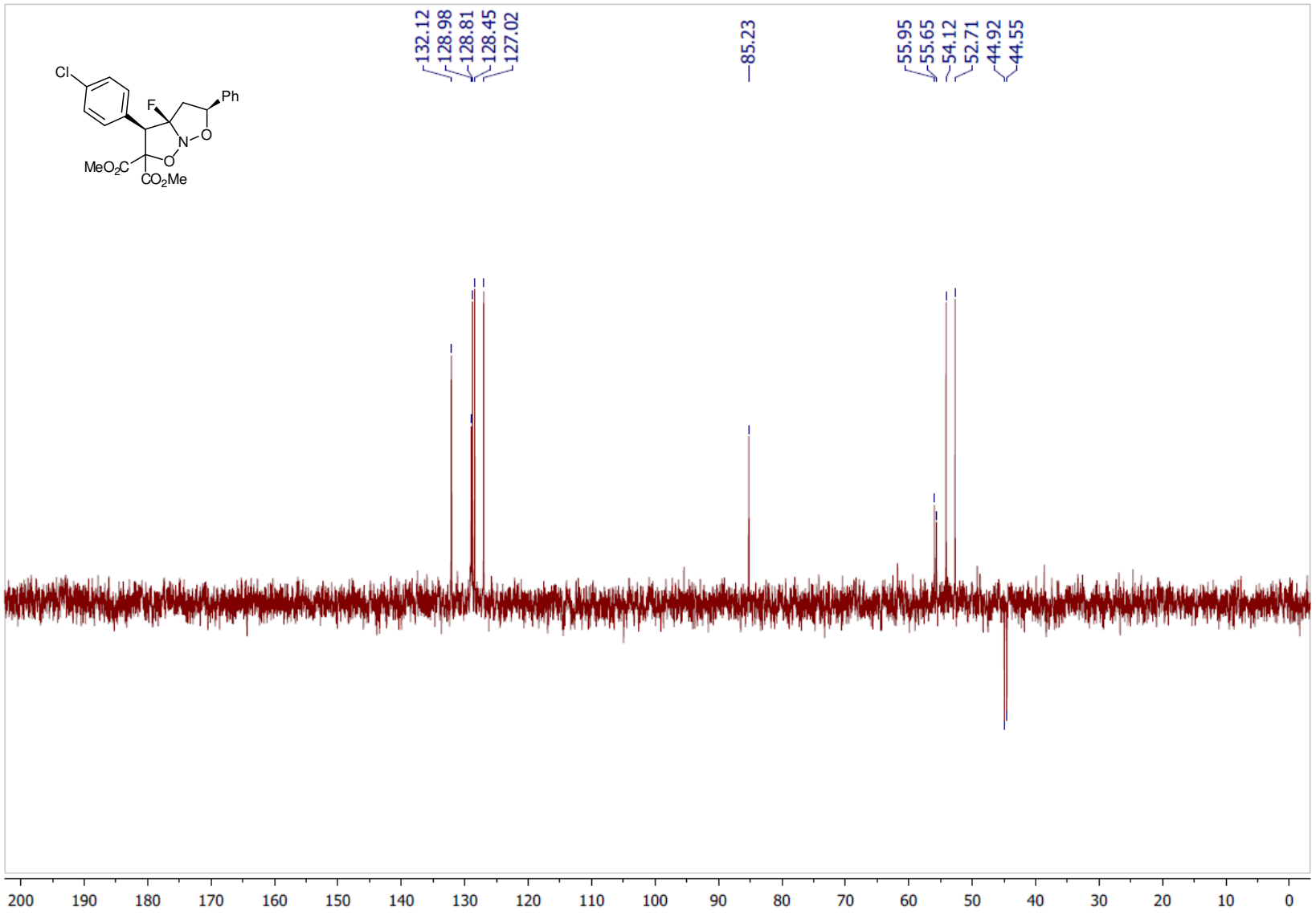
^{13}C NMR (DEPT)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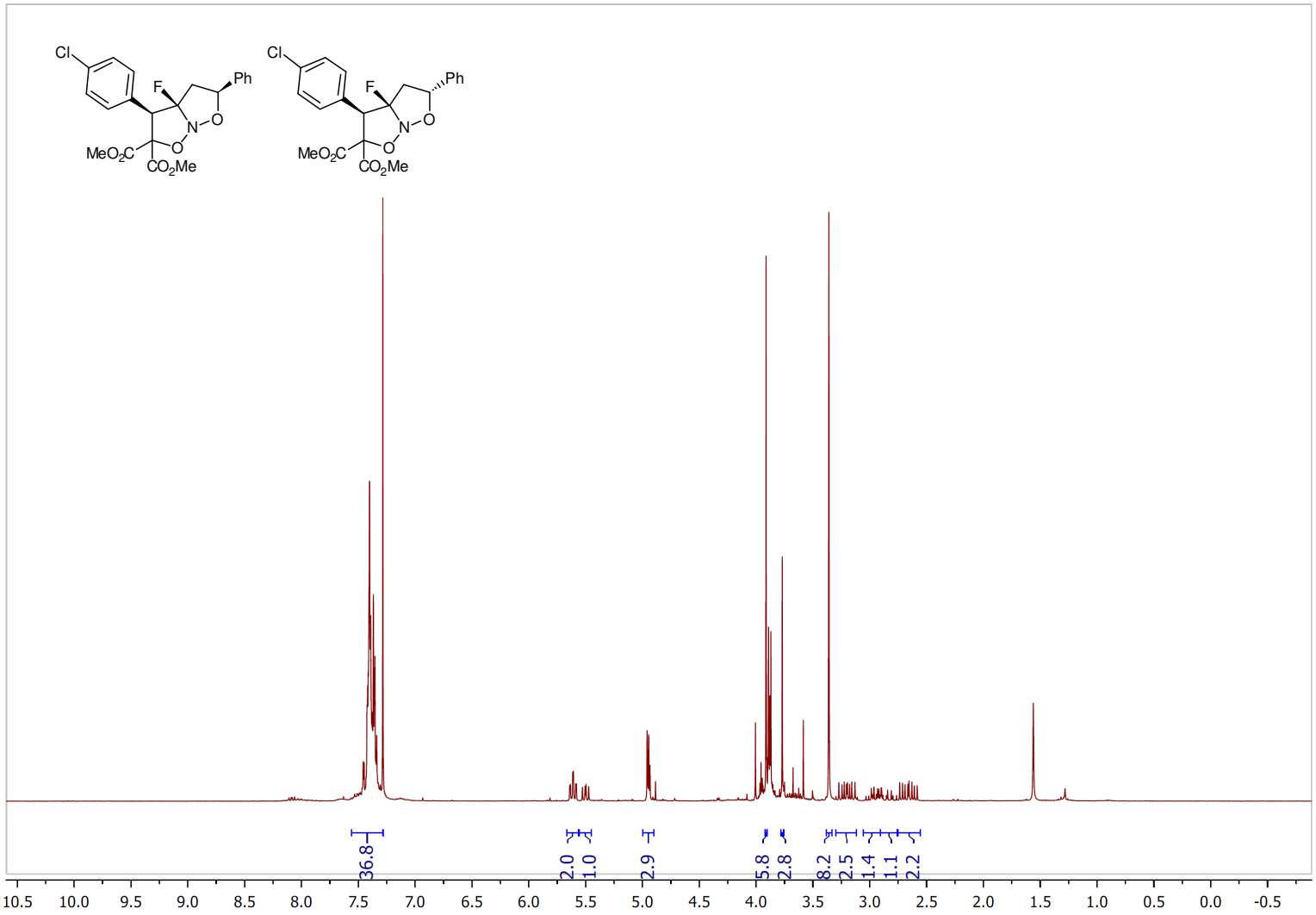
***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4b** (major) and ***rel*-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'b** (minor)

^{1}H NMR



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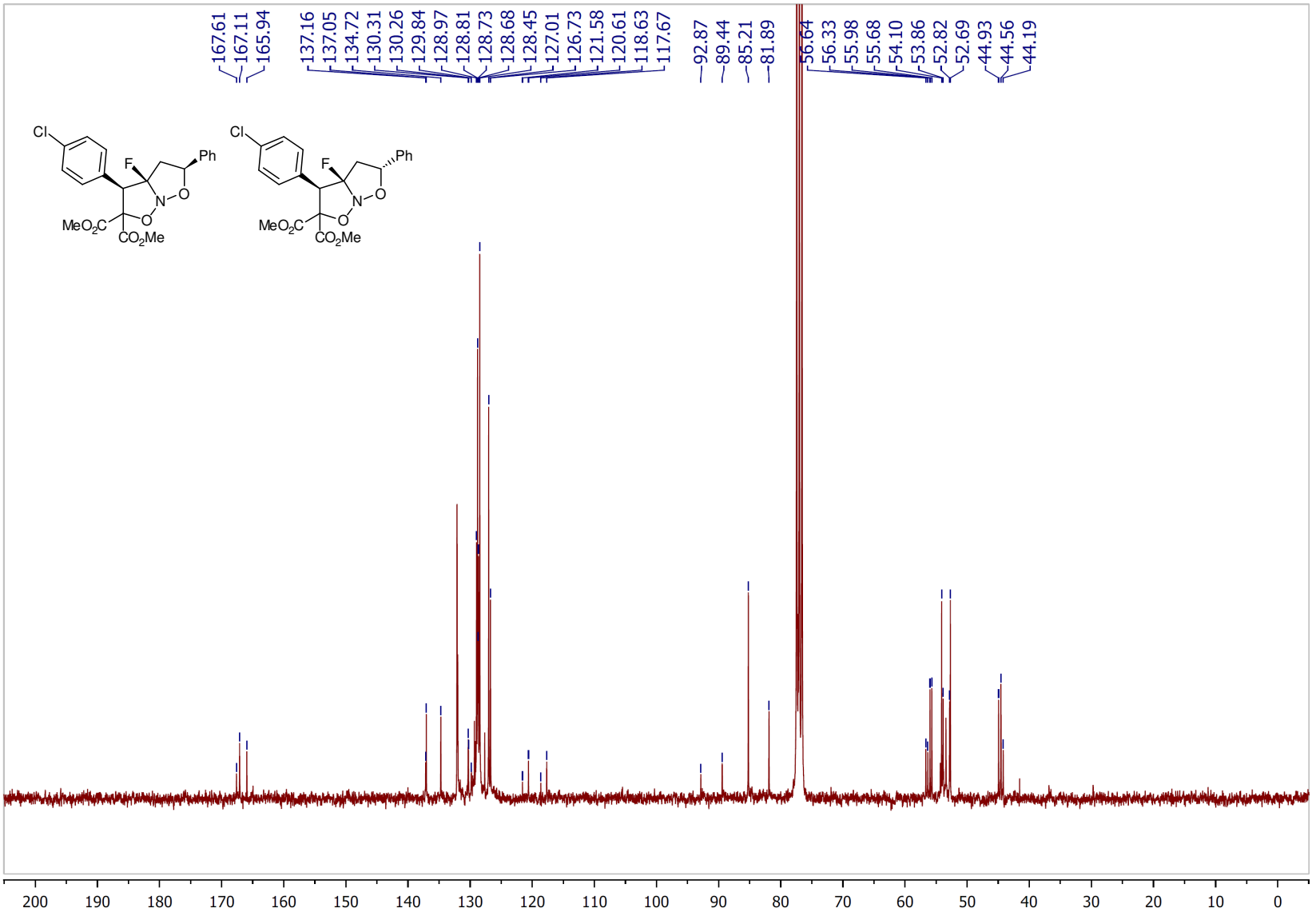
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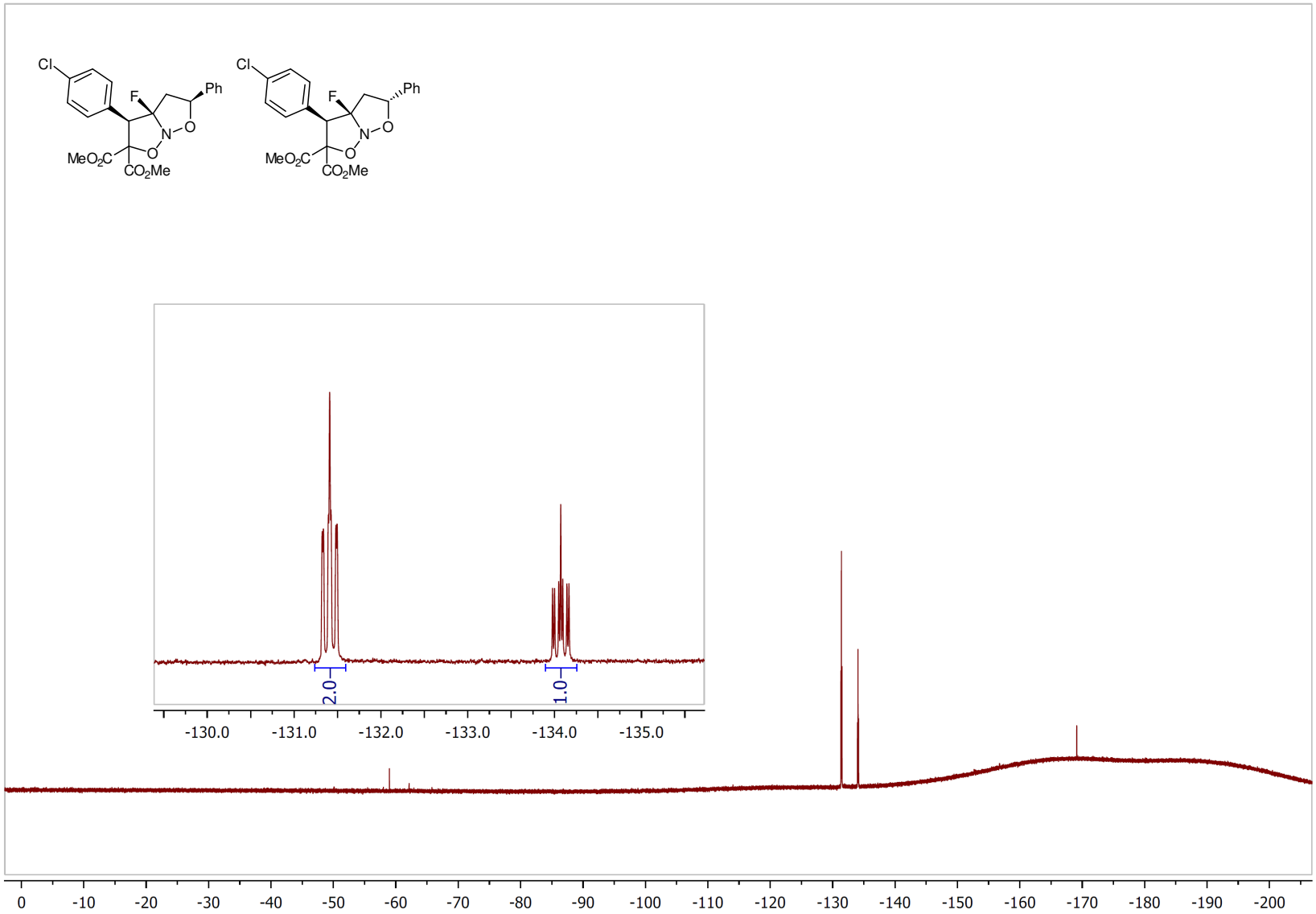
^{19}F NMR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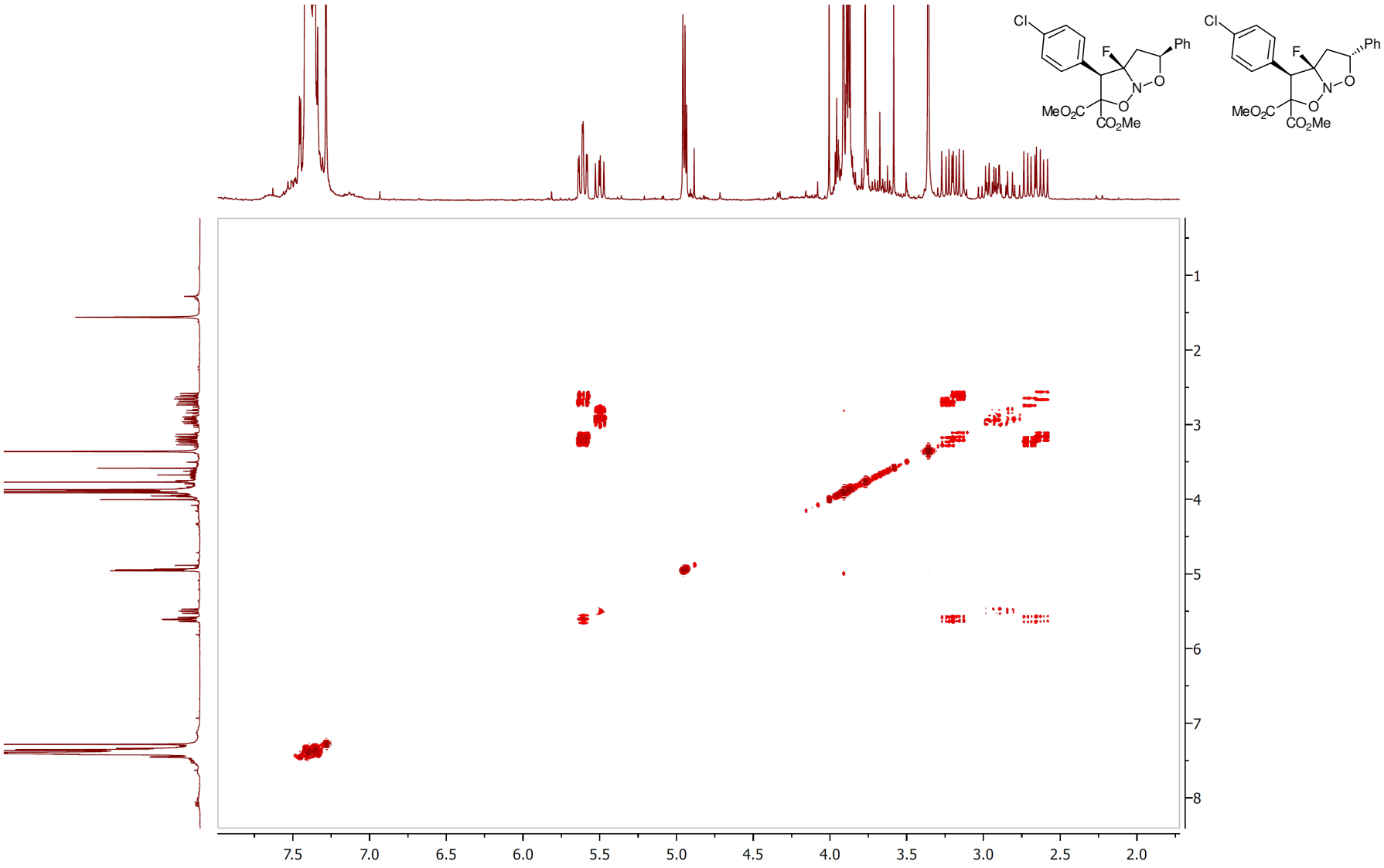
^{1}H-^{1}H COSY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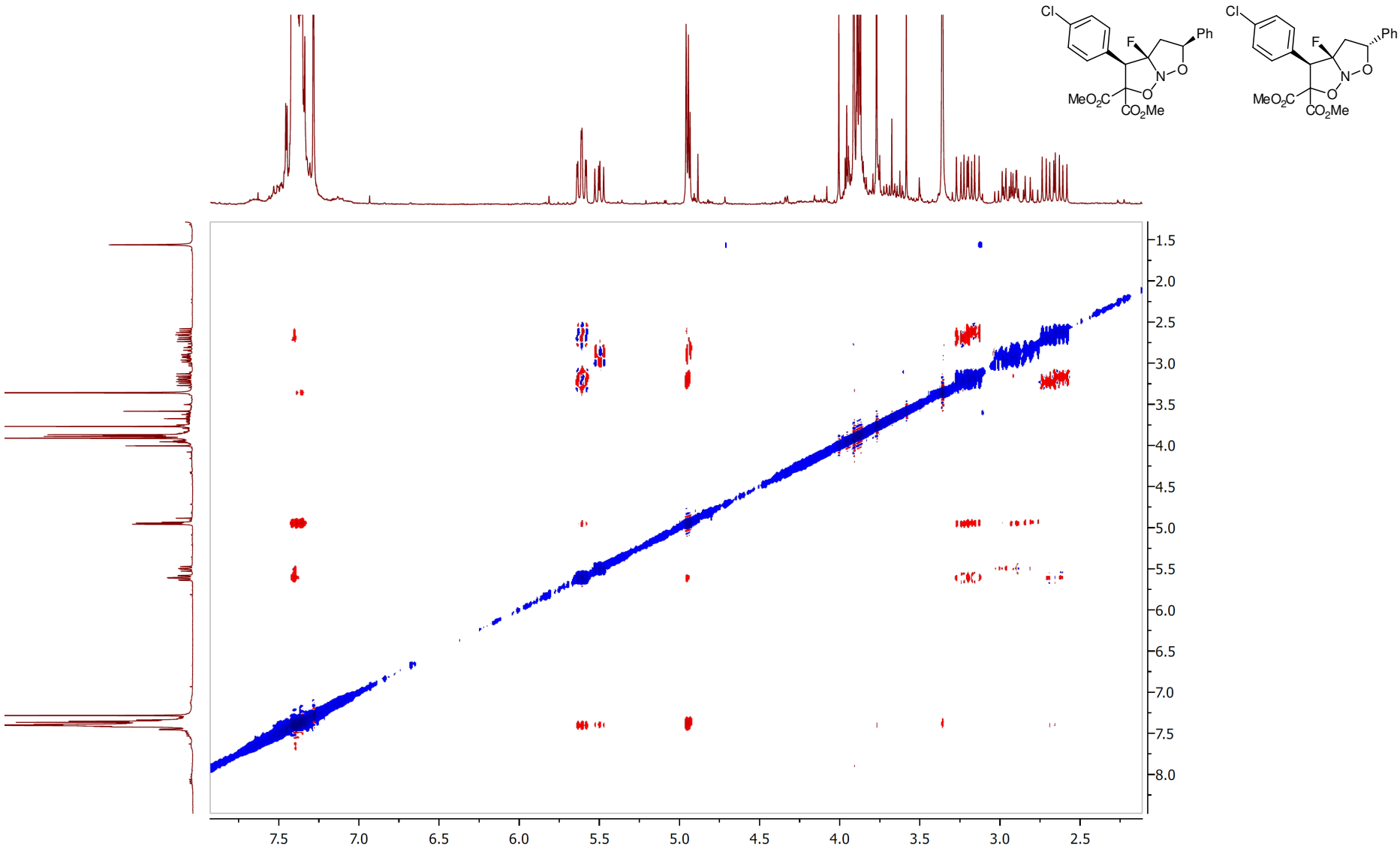
6
7
8

^{1}H-^{1}H NOESY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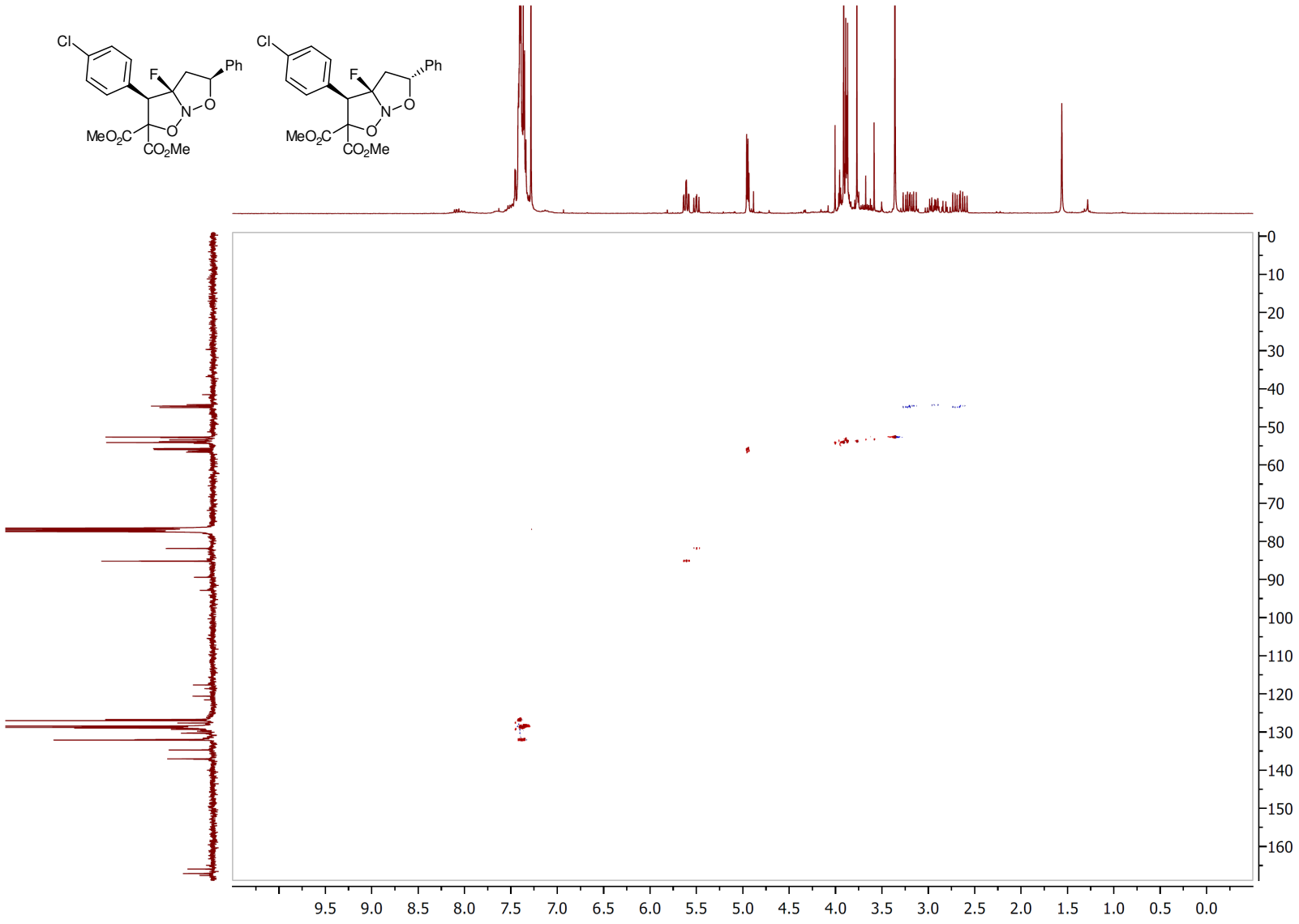
^{1}H-^{13}C HSQC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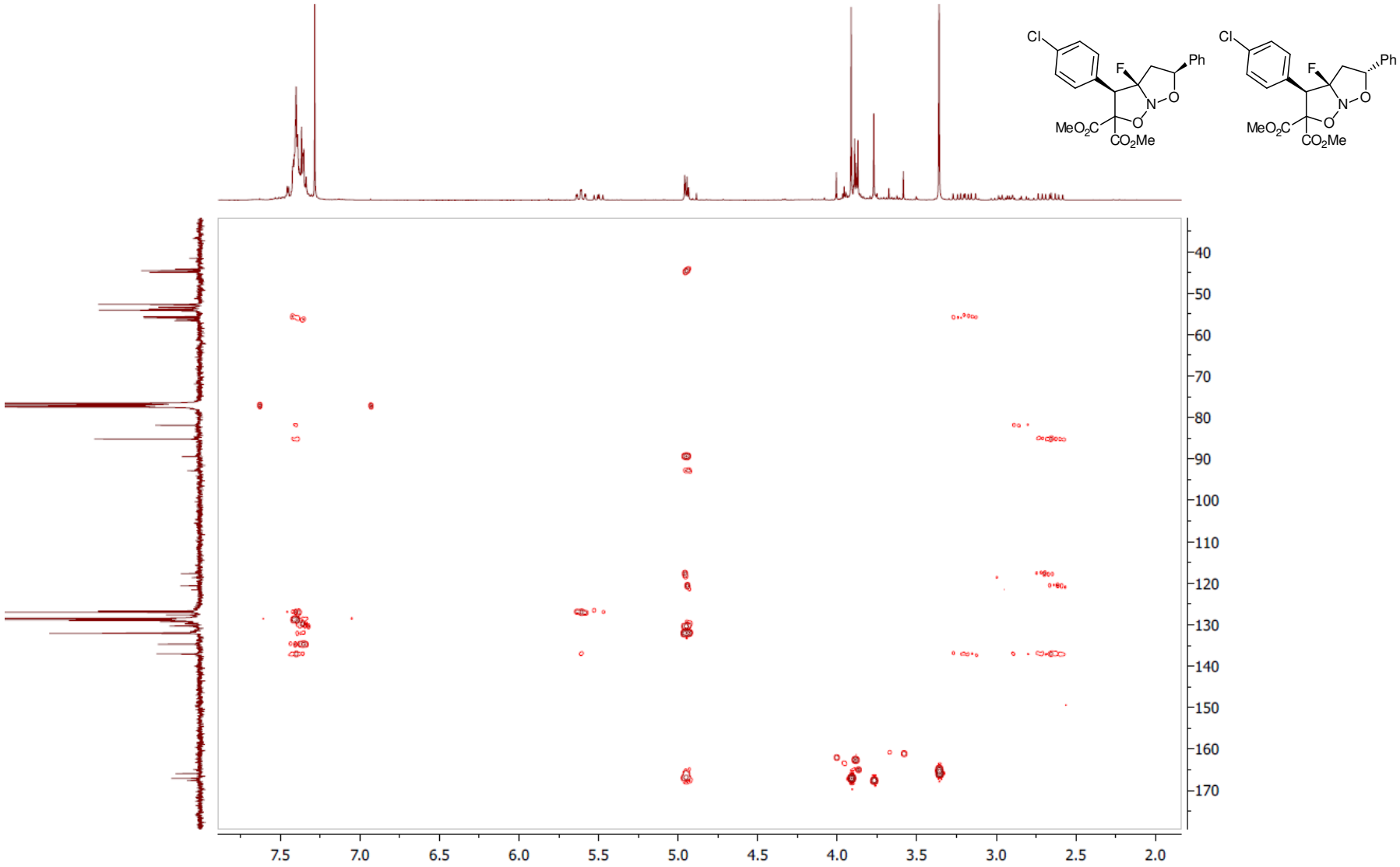
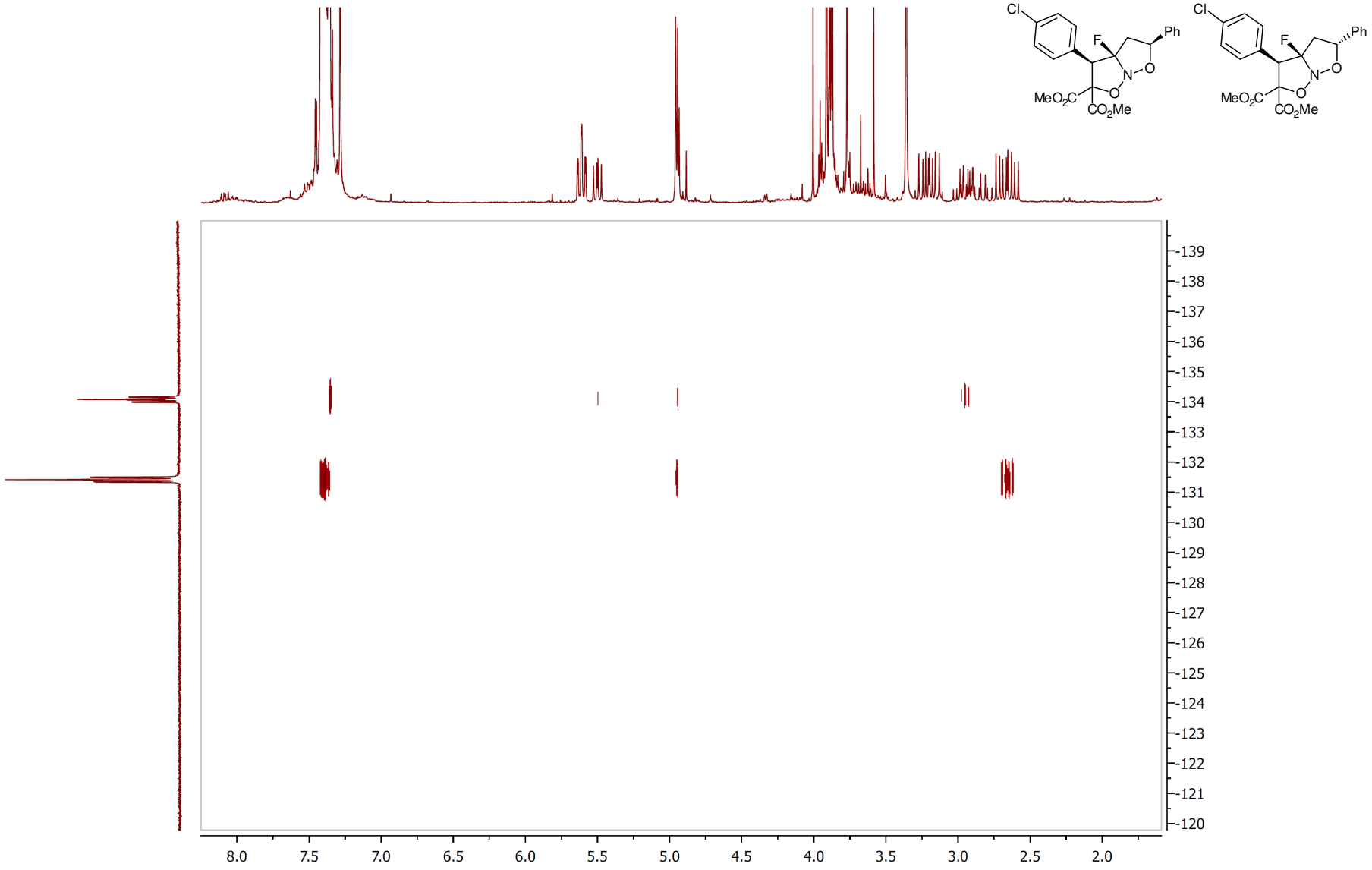
0.0

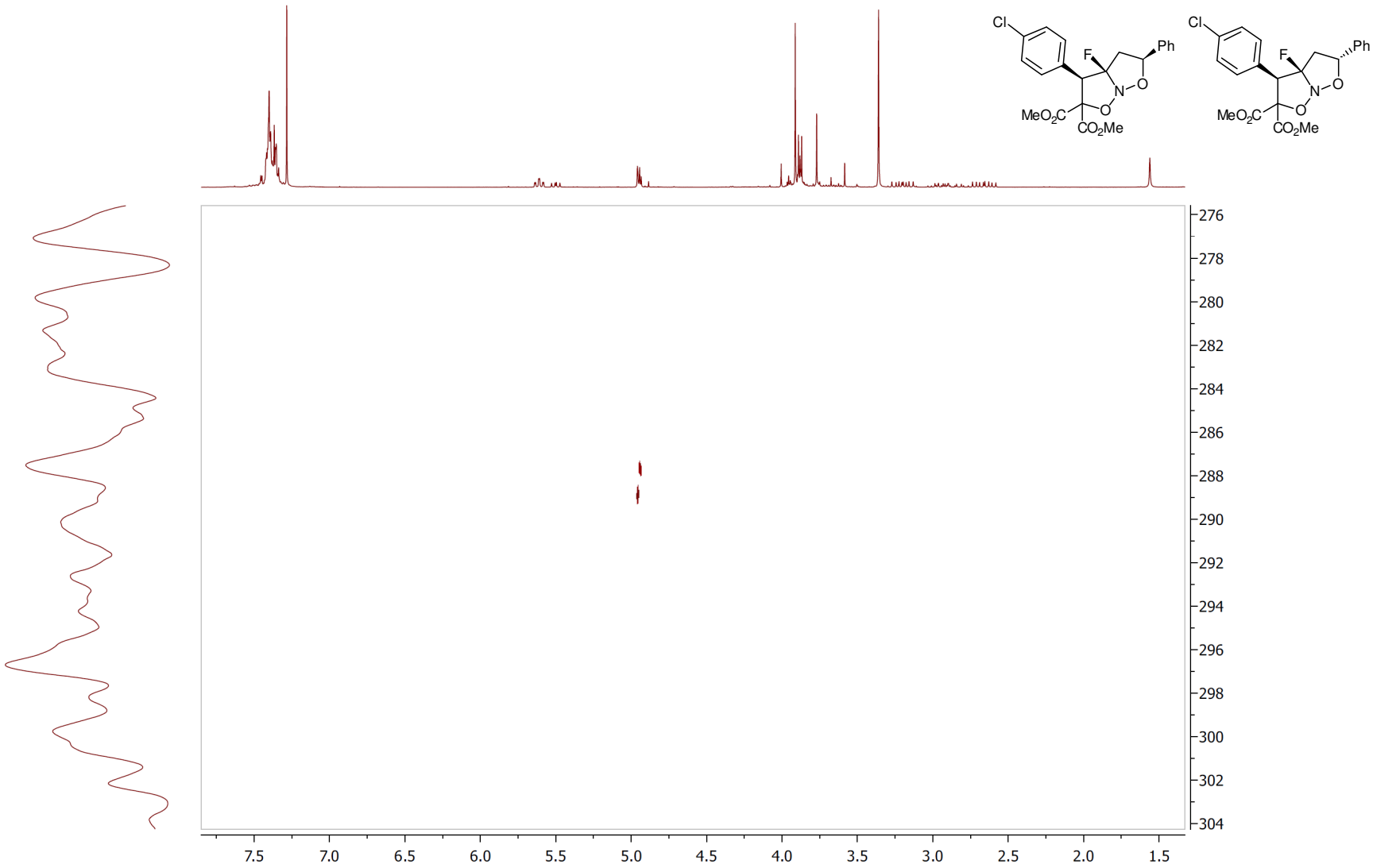
^{1}H-^{13}C HMBC


Cl
F
Ph
N
O
O
MeO2C
CO2Me
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
40
50
60
70
80
90
100
110
120
130
140
150
160
170

^{1}H-^{19}F HOESY

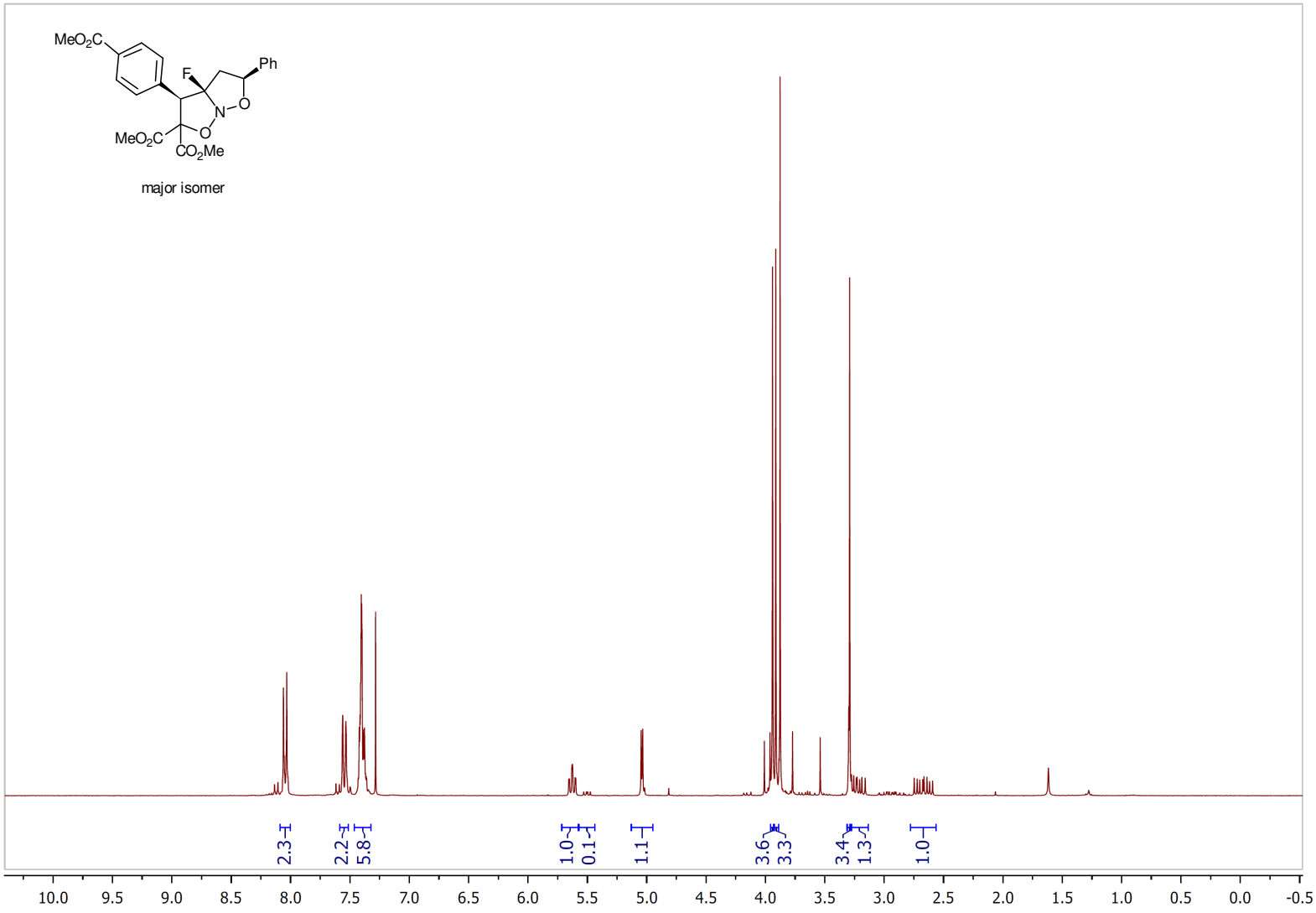

Cl
F
Ph
N
O
MeO2C
CO2Me
-139
-138
-137
-136
-135
-134
-133
-132
-131
-130
-129
-128
-127
-126
-125
-124
-123
-122
-121
-120
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0

^{1}H-^{15}N HMBC

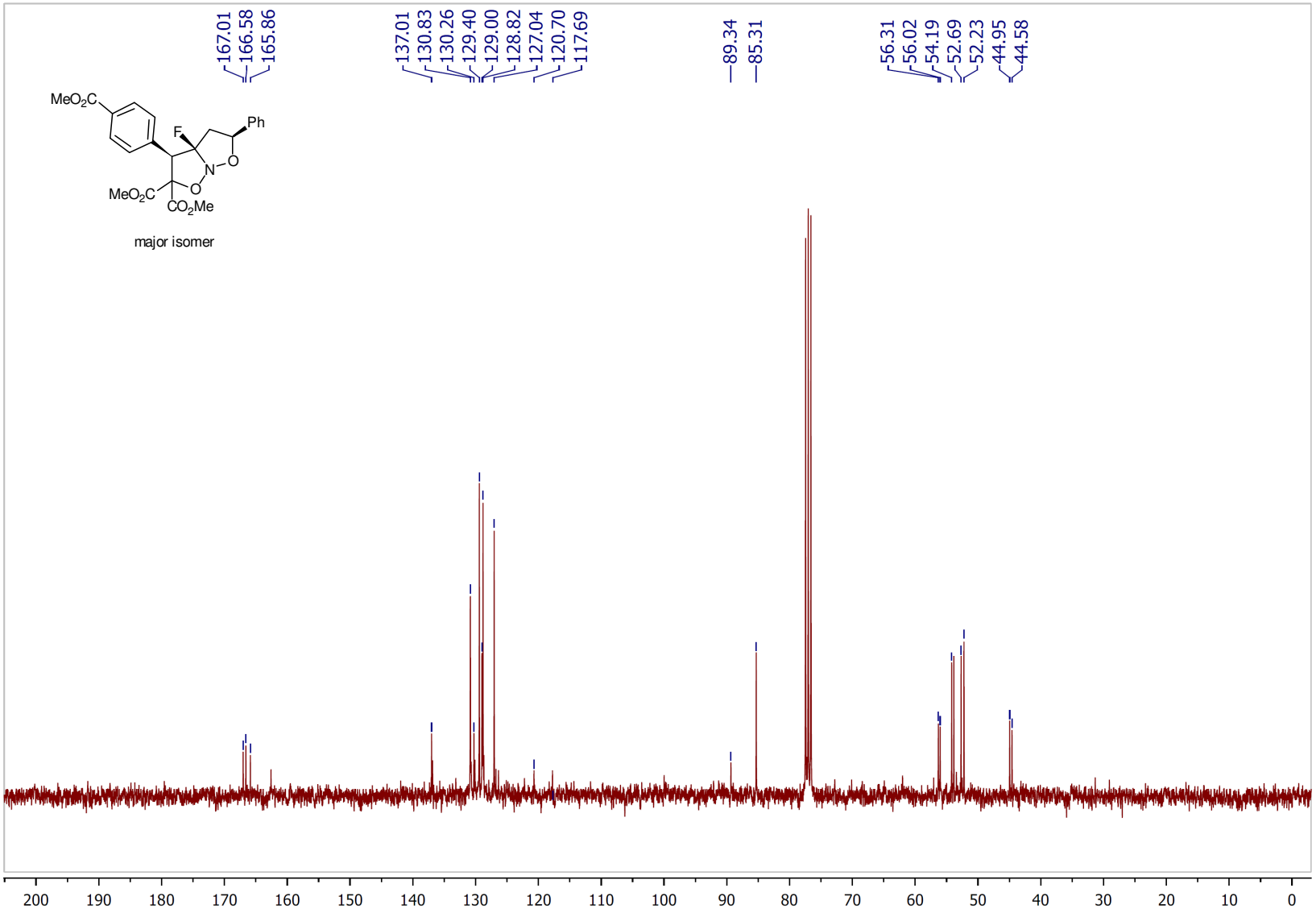

Cl
F
Ph
N
O
MeO2C
CO2Me
276
278
280
282
284
286
288
290
292
294
296
298
300
302
304
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

***rel*-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-(methoxycarbonyl)phenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4c** (major isomer)

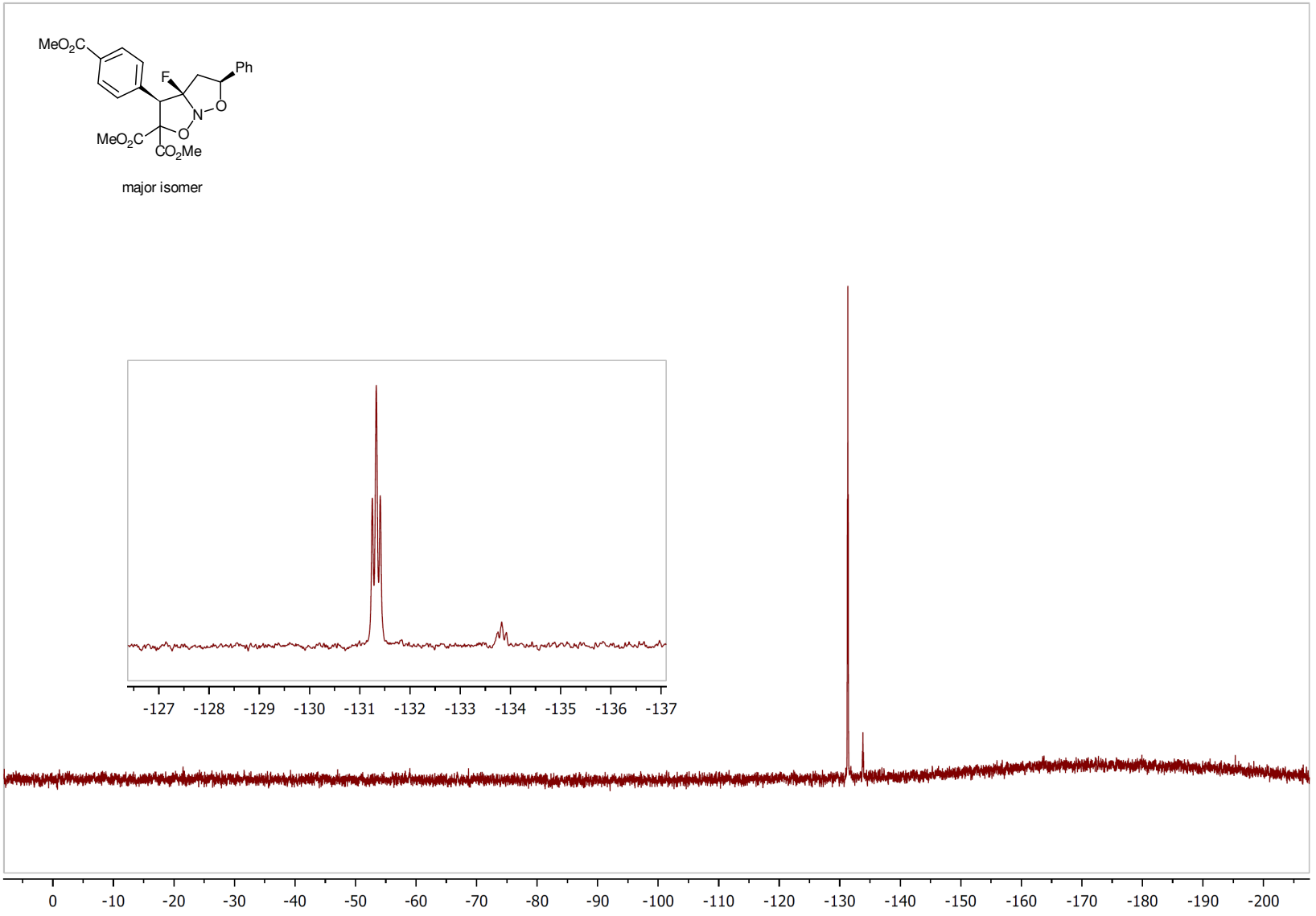
^{1}H NMR



^{13}C NMR

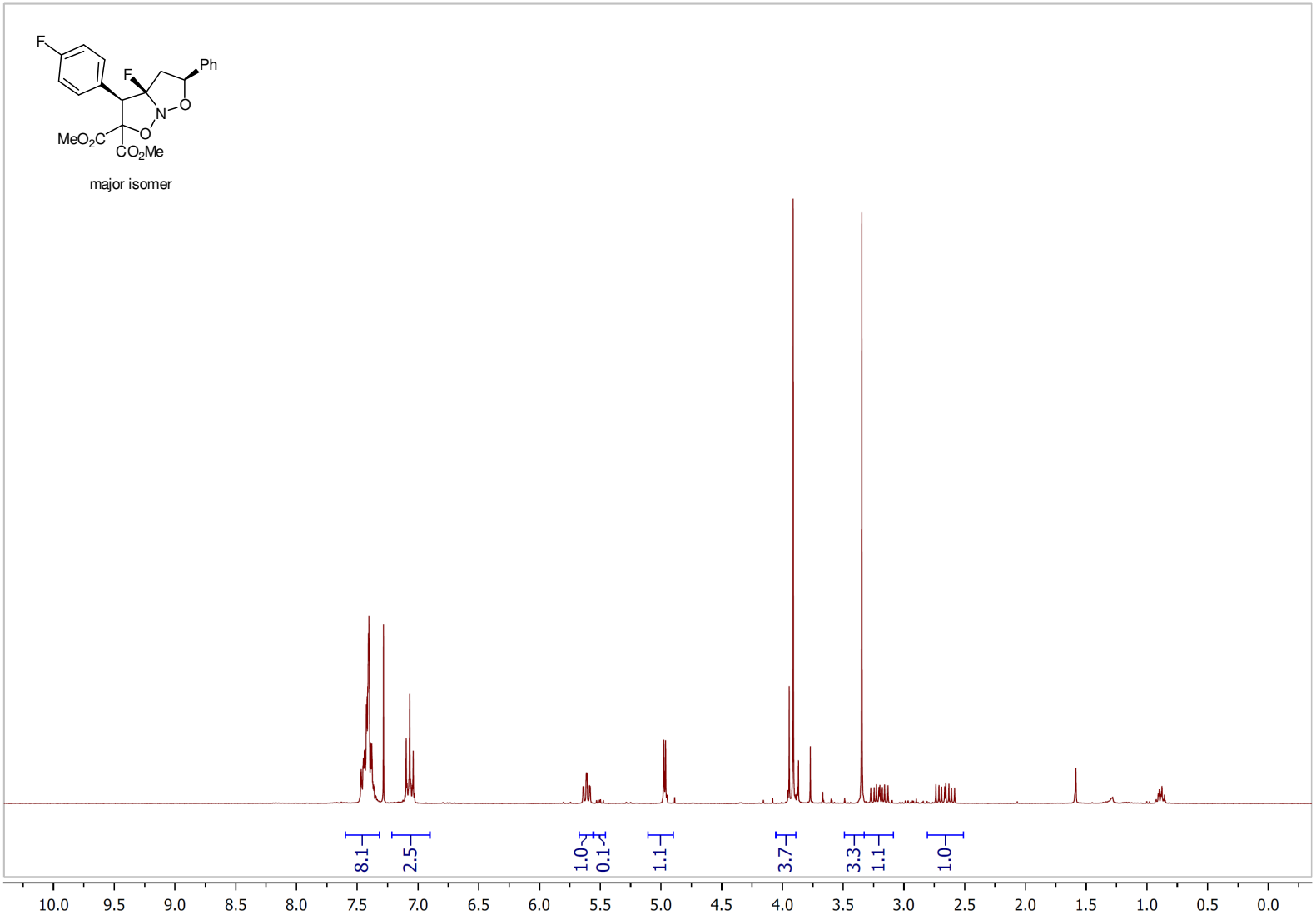

167.01
166.58
165.86
137.01
130.83
130.26
129.40
129.00
128.82
127.04
120.70
117.69
89.34
85.31
56.31
56.02
54.19
52.69
52.23
44.95
44.58
MeO2C
F
Ph
N
O
MeO2C
O
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

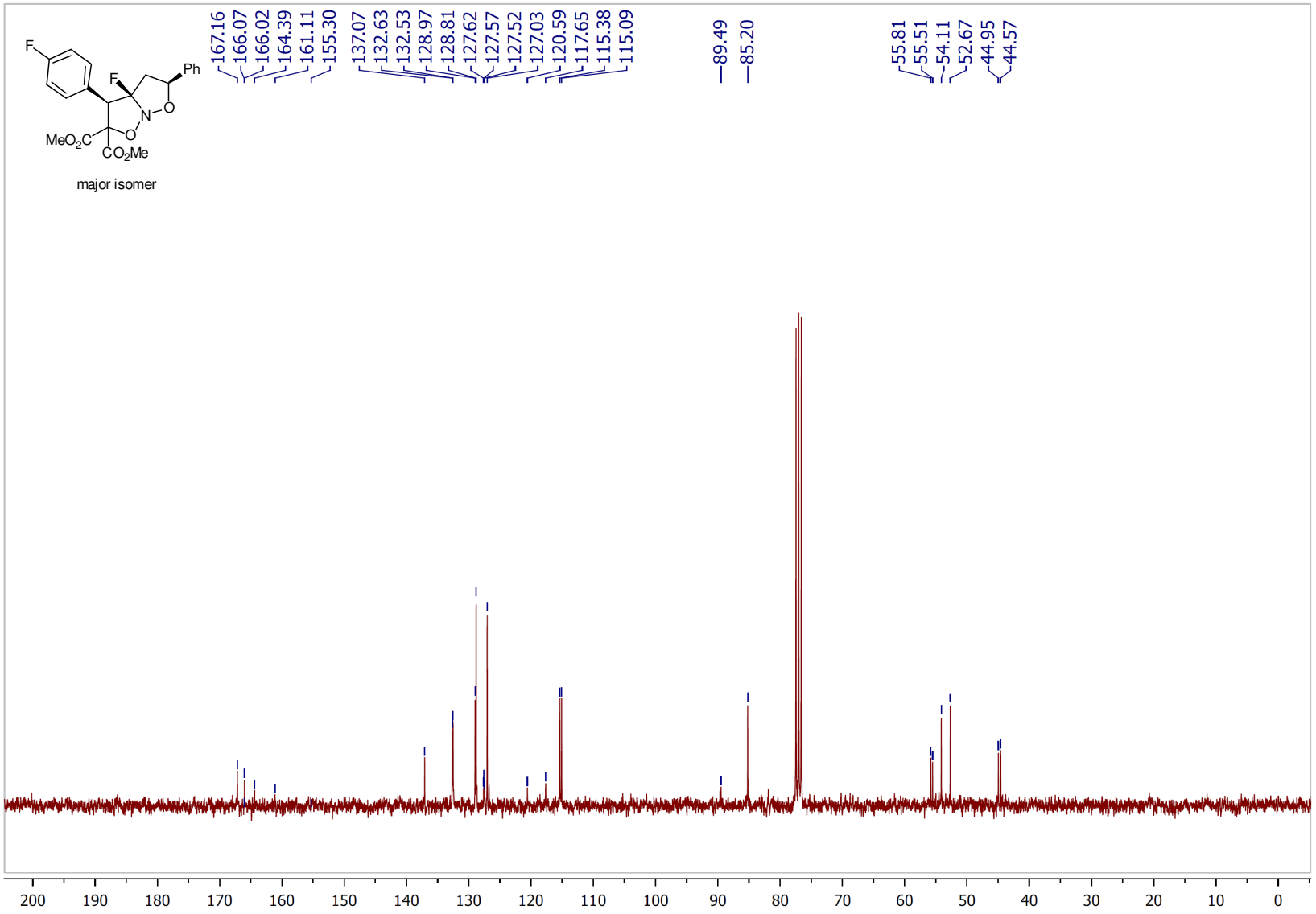

MeO2C
F
Ph
N
O
MeO2C
O
CO2Me
major isomer
-127 -128 -129 -130 -131 -132 -133 -134 -135 -136 -137
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200

***rel*-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-fluorophenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4d** (major isomer)

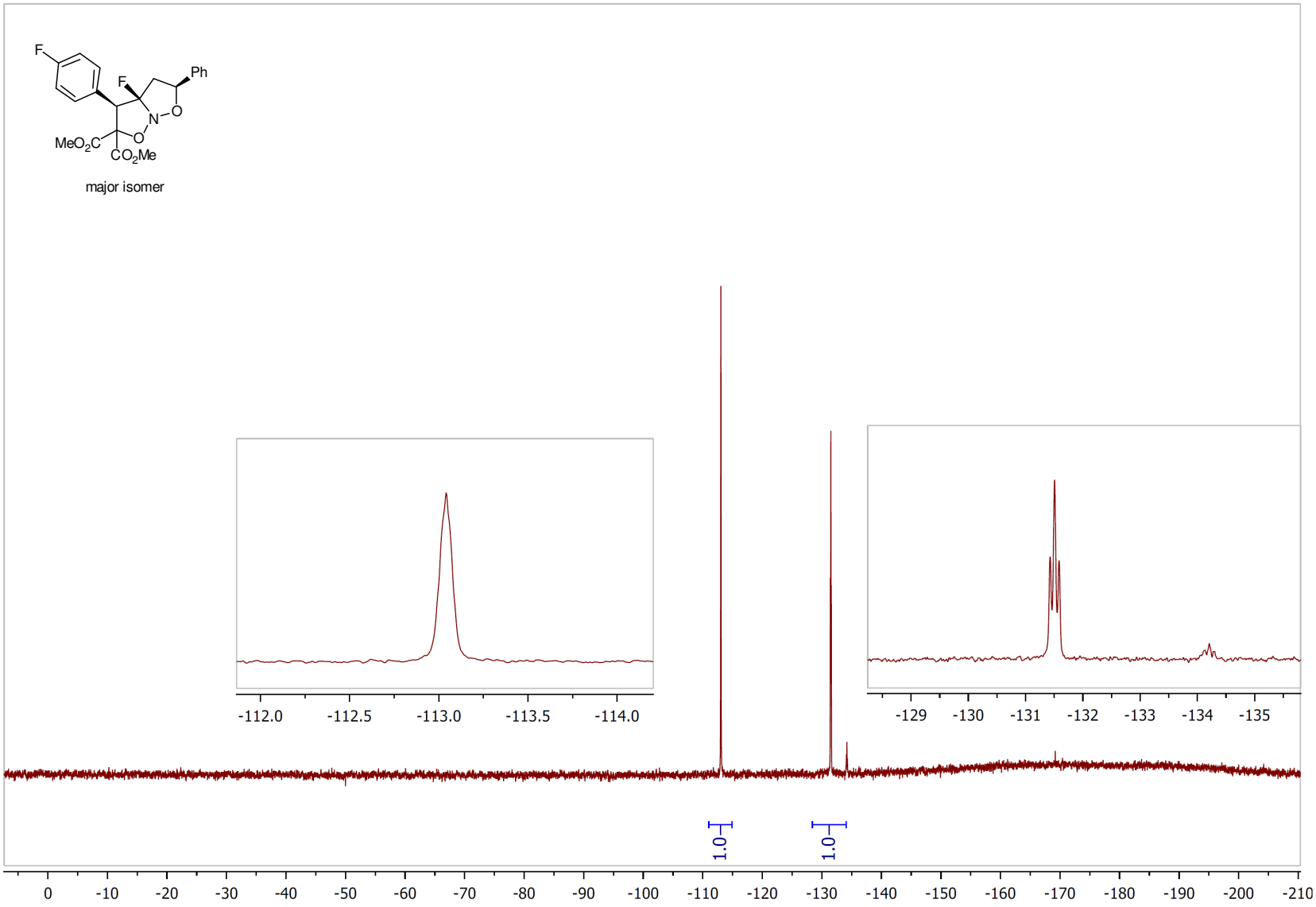
^{1}H NMR



^{13}C NMR

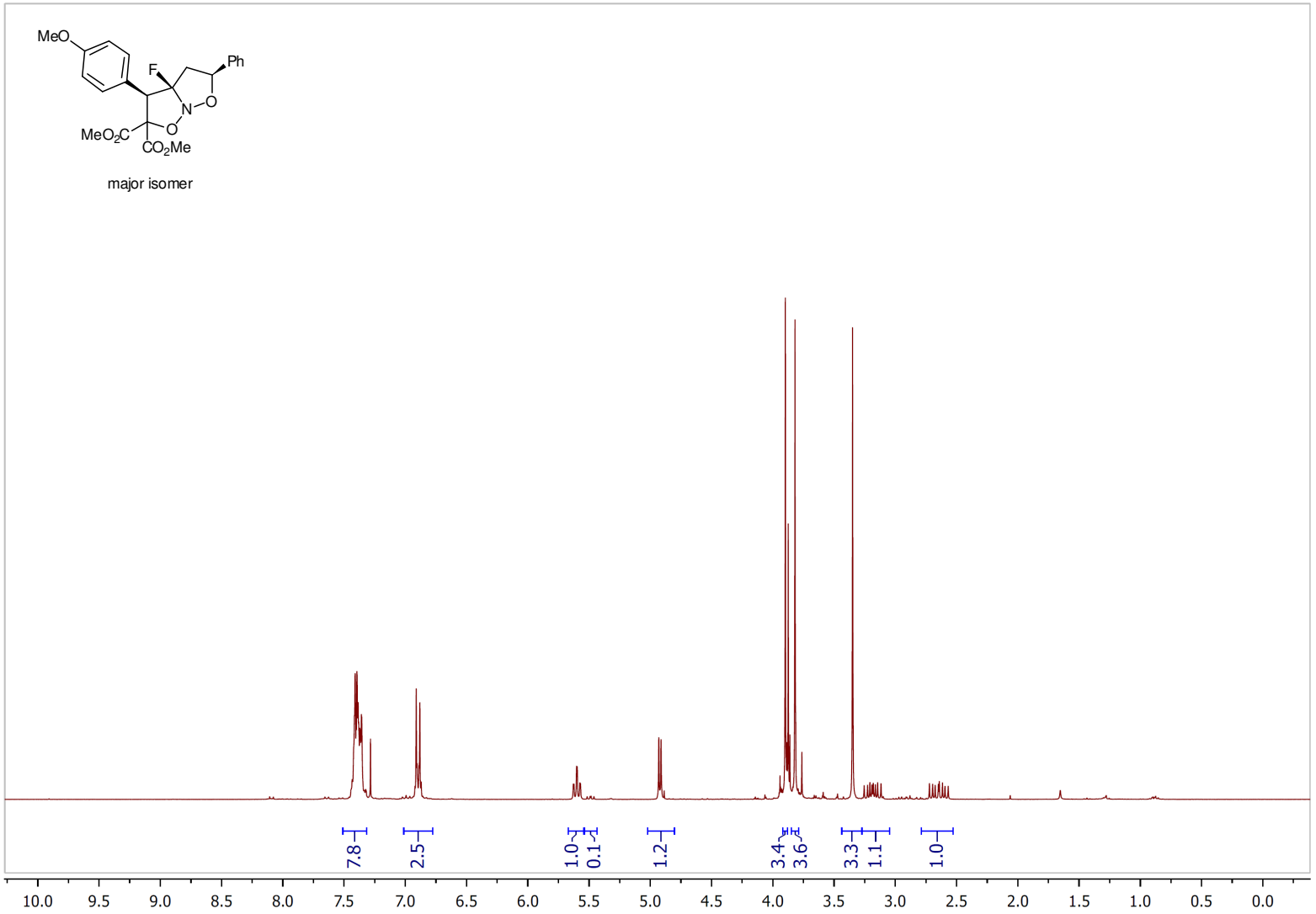

F
Ph
F
N
O
O
MeO2C
CO2Me
major isomer
167.16
166.07
166.02
164.39
161.11
155.30
137.07
132.63
132.53
128.97
128.81
127.62
127.57
127.52
127.03
120.59
117.65
115.38
115.09
89.49
85.20
55.81
55.51
54.11
52.67
44.95
44.57
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

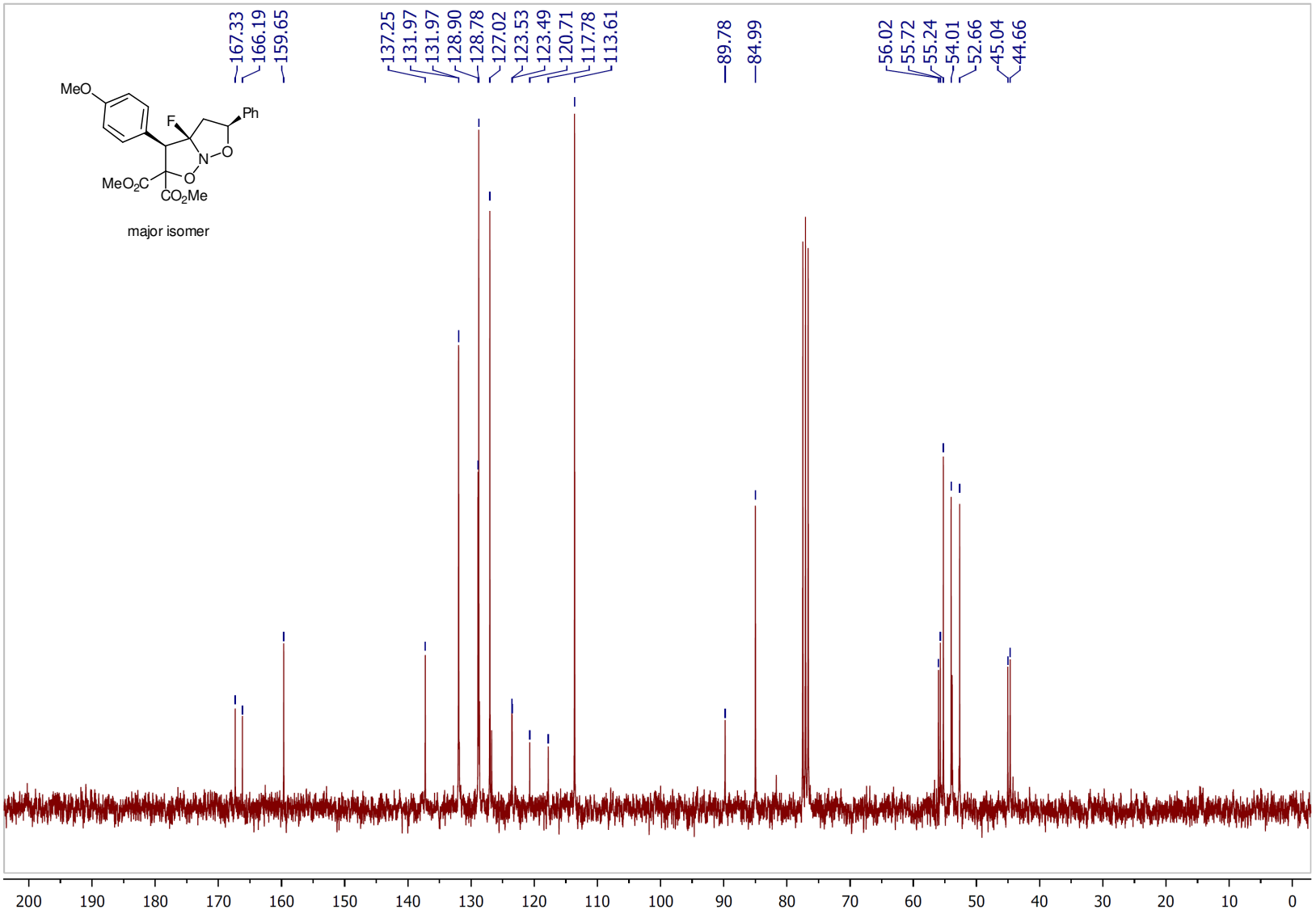

F
F
Ph
N
O
O
MeO2C
CO2Me
major isomer
-112.0
-112.5
-113.0
-113.5
-114.0
-129
-130
-131
-132
-133
-134
-135
1.0
1.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210

***rel*-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-methoxyphenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4e** (major isomer)

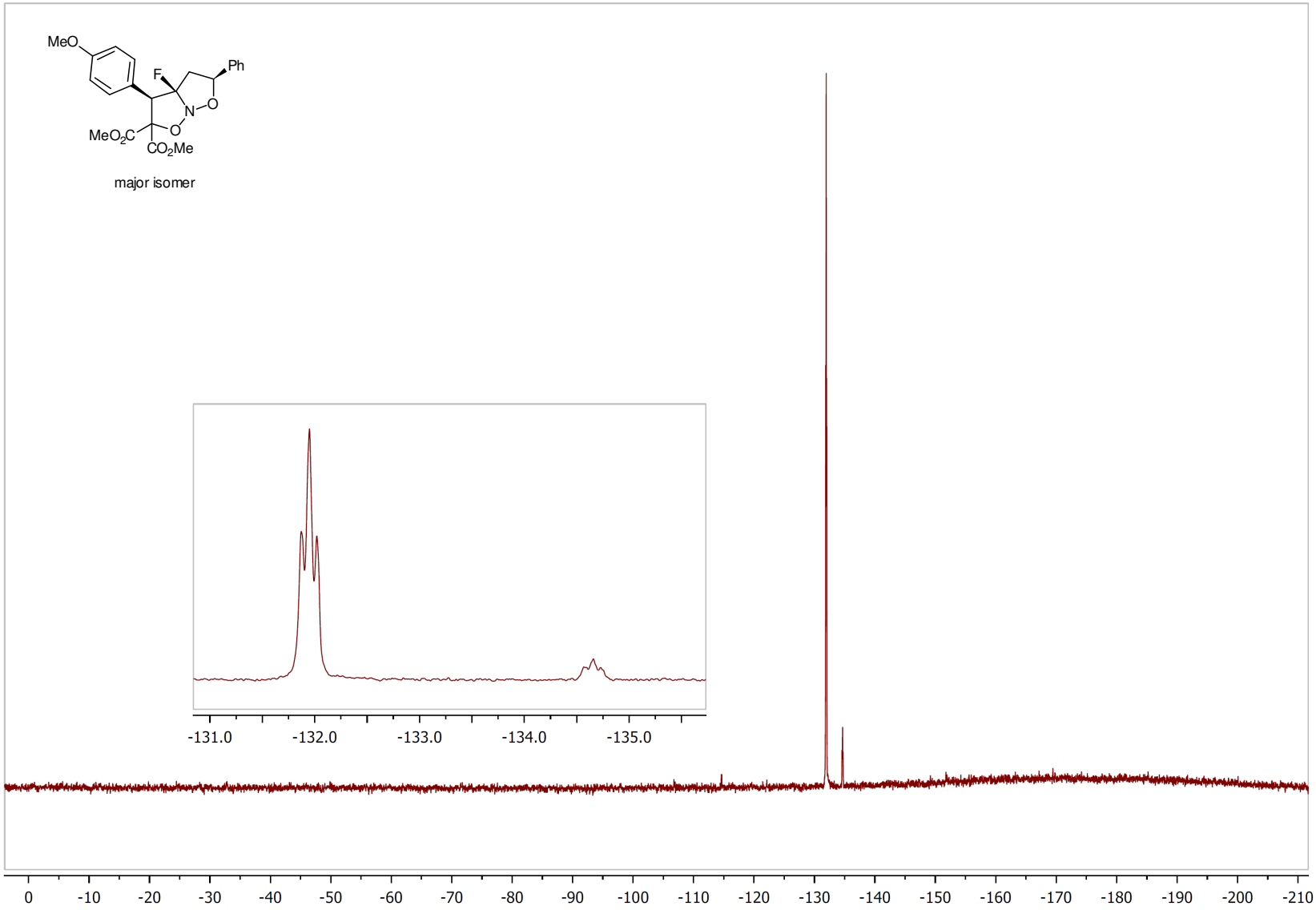
^{1}H NMR



^{13}C NMR

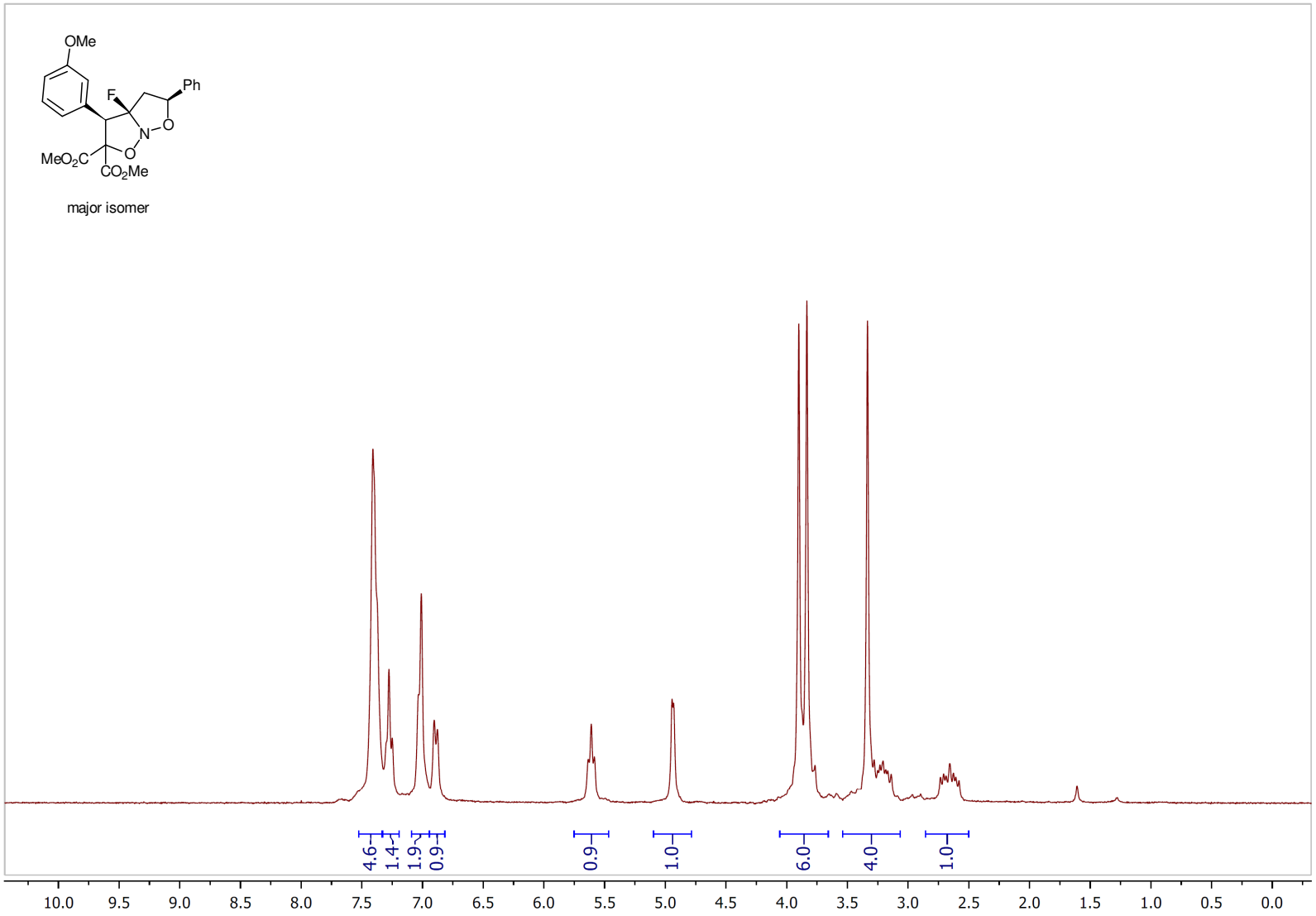

167.33
166.19
159.65
137.25
131.97
131.97
128.90
128.78
127.02
123.53
123.49
120.71
117.78
113.61
89.78
84.99
56.02
55.72
55.24
54.01
52.66
45.04
44.66
MeO
F
Ph
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

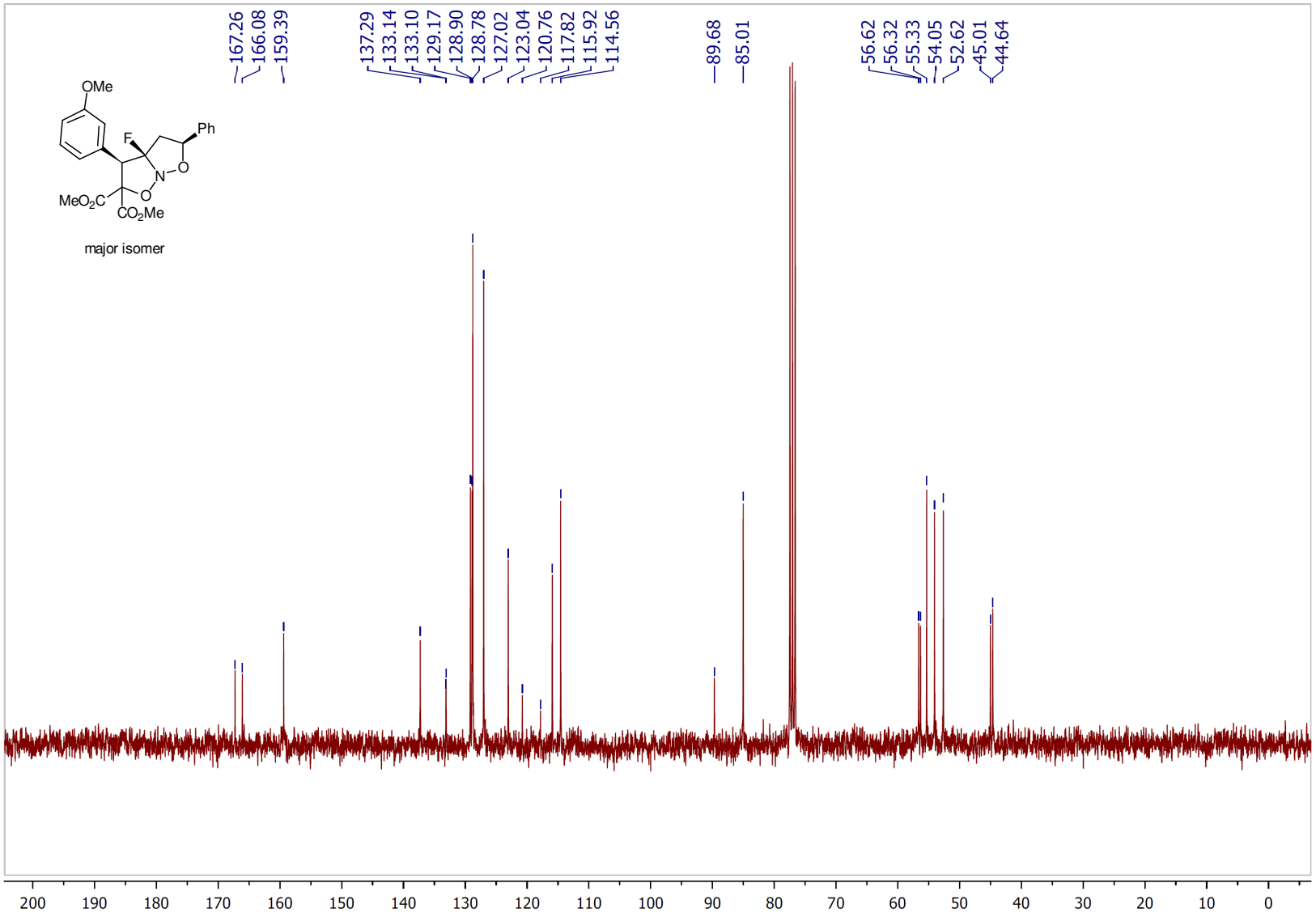

MeO
F
Ph
N
O
O
MeO2C
CO2Me
major isomer
-131.0
-132.0
-133.0
-134.0
-135.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210

***rel*-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(3-methoxyphenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4f** (major isomer)

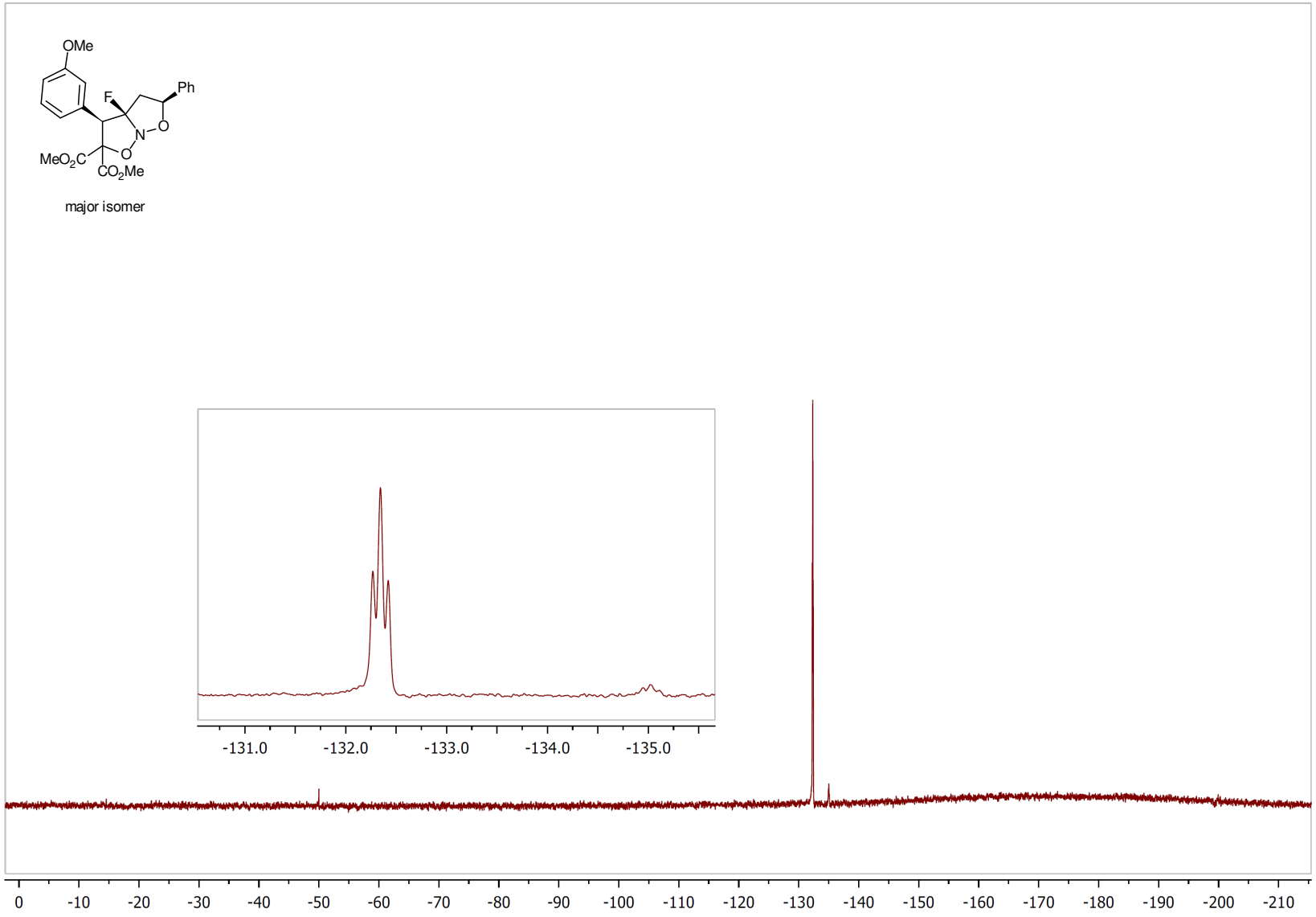
^{1}H NMR



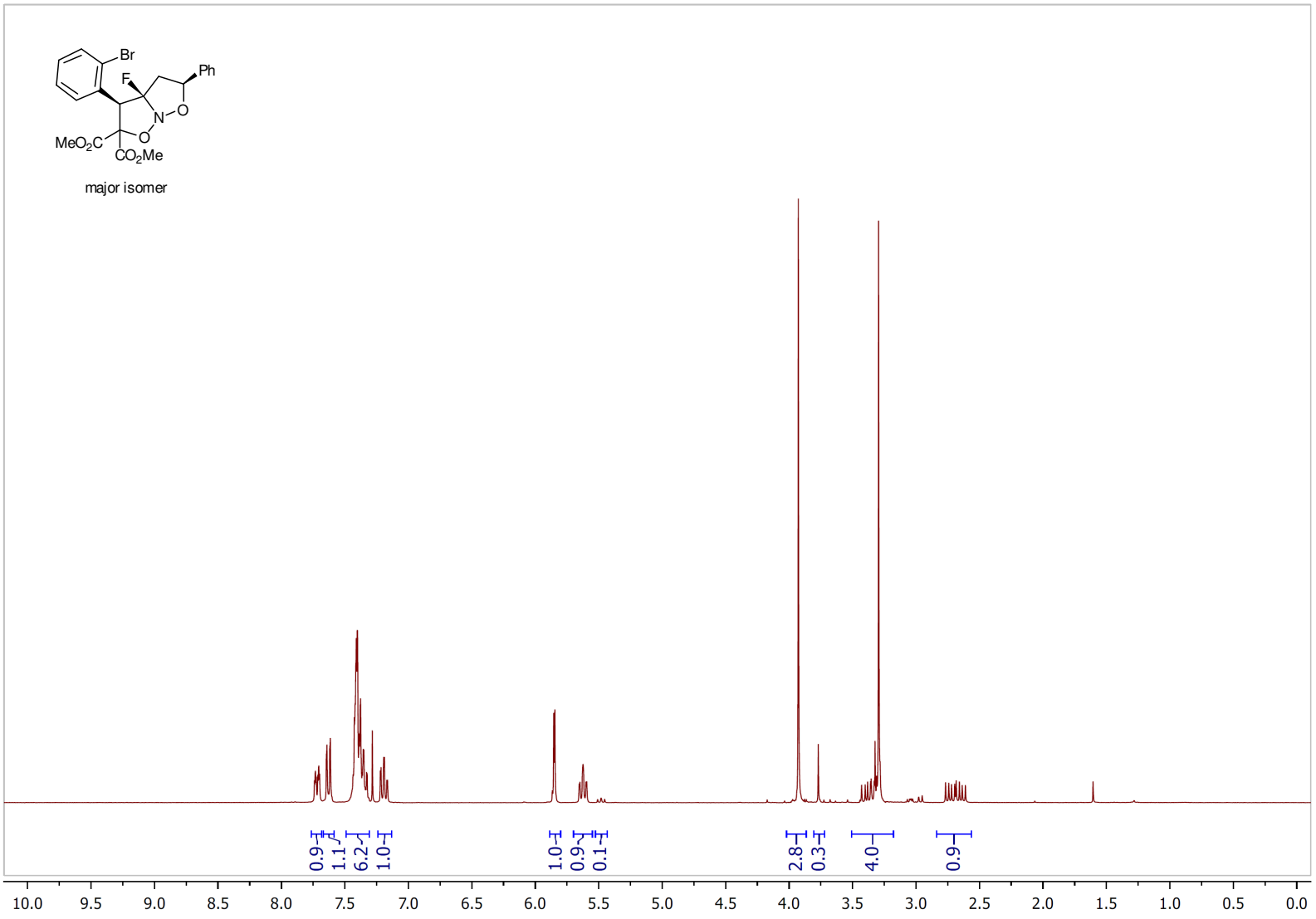
^{13}C NMR


167.26
166.08
159.39
137.29
133.14
133.10
129.17
128.90
128.78
127.02
123.04
120.76
117.82
115.92
114.56
89.68
85.01
56.62
56.32
55.33
54.05
52.62
45.01
44.64
OMe
Ph
F
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

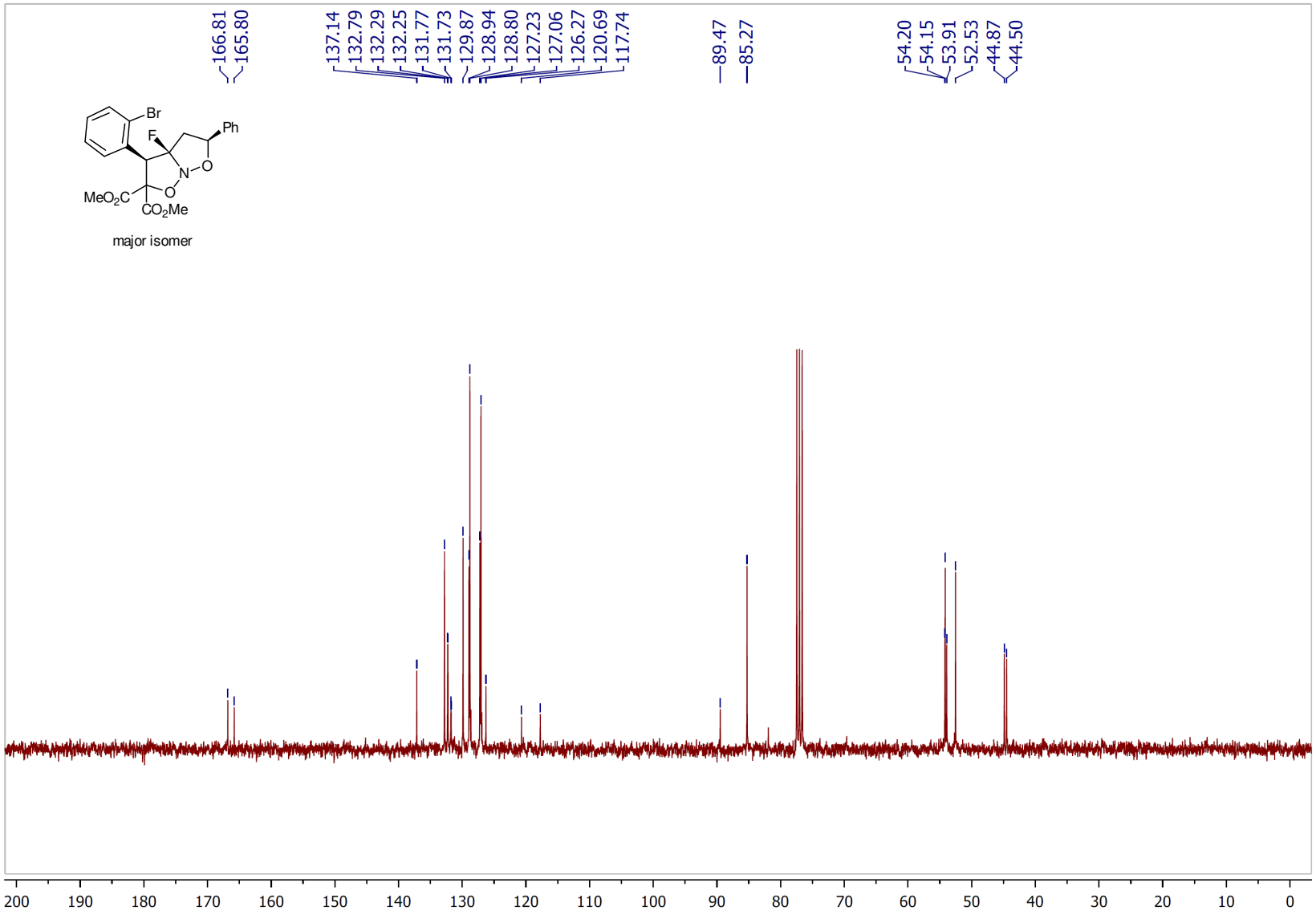
^{19}F NMR


OMe
F
Ph
N
O
O
MeO2C
CO2Me
major isomer
-131.0
-132.0
-133.0
-134.0
-135.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210

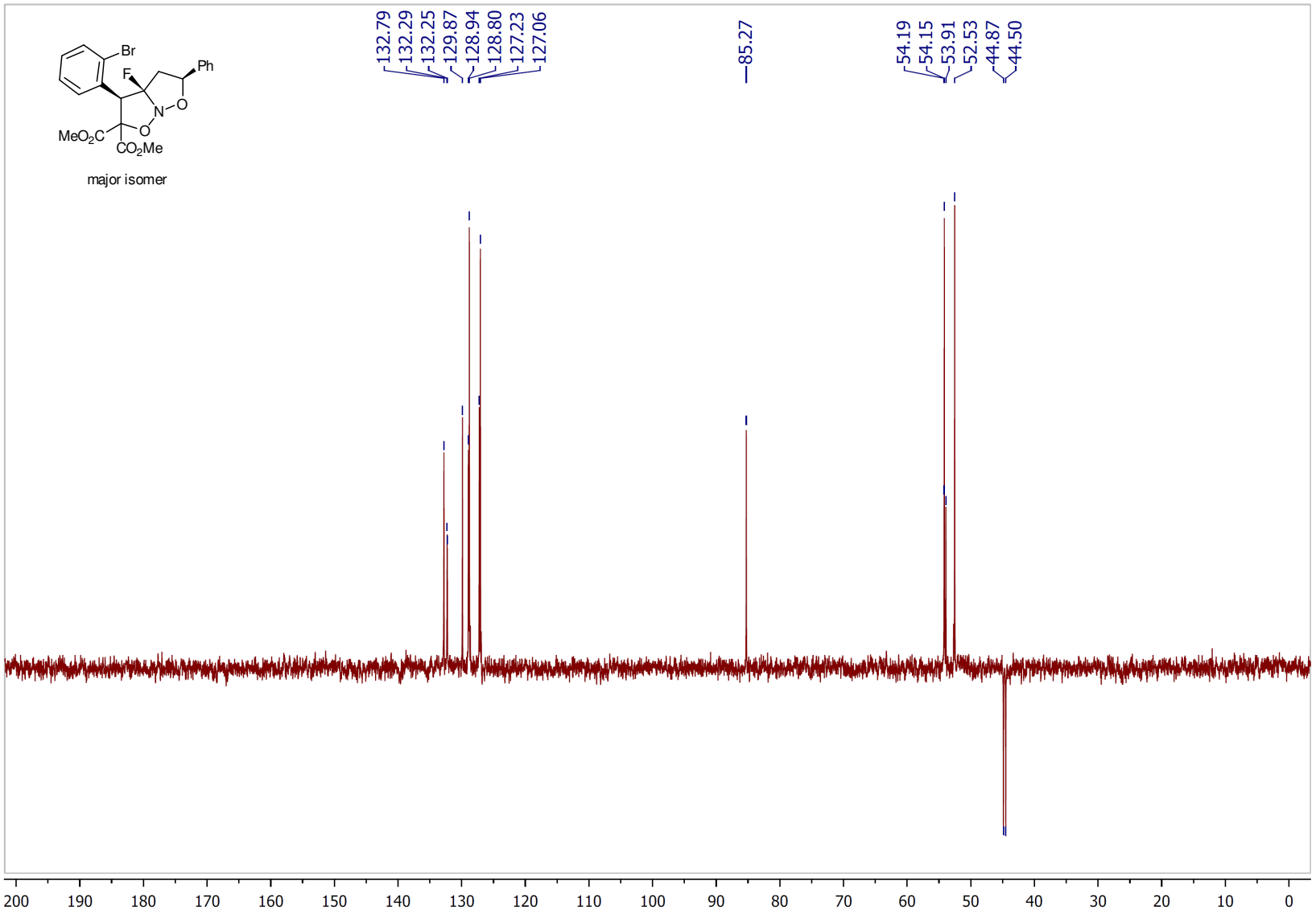
***rel*-(3R,3aR,5S)-Dimethyl 3-(2-bromophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4g** (major isomer)
^{1}H NMR



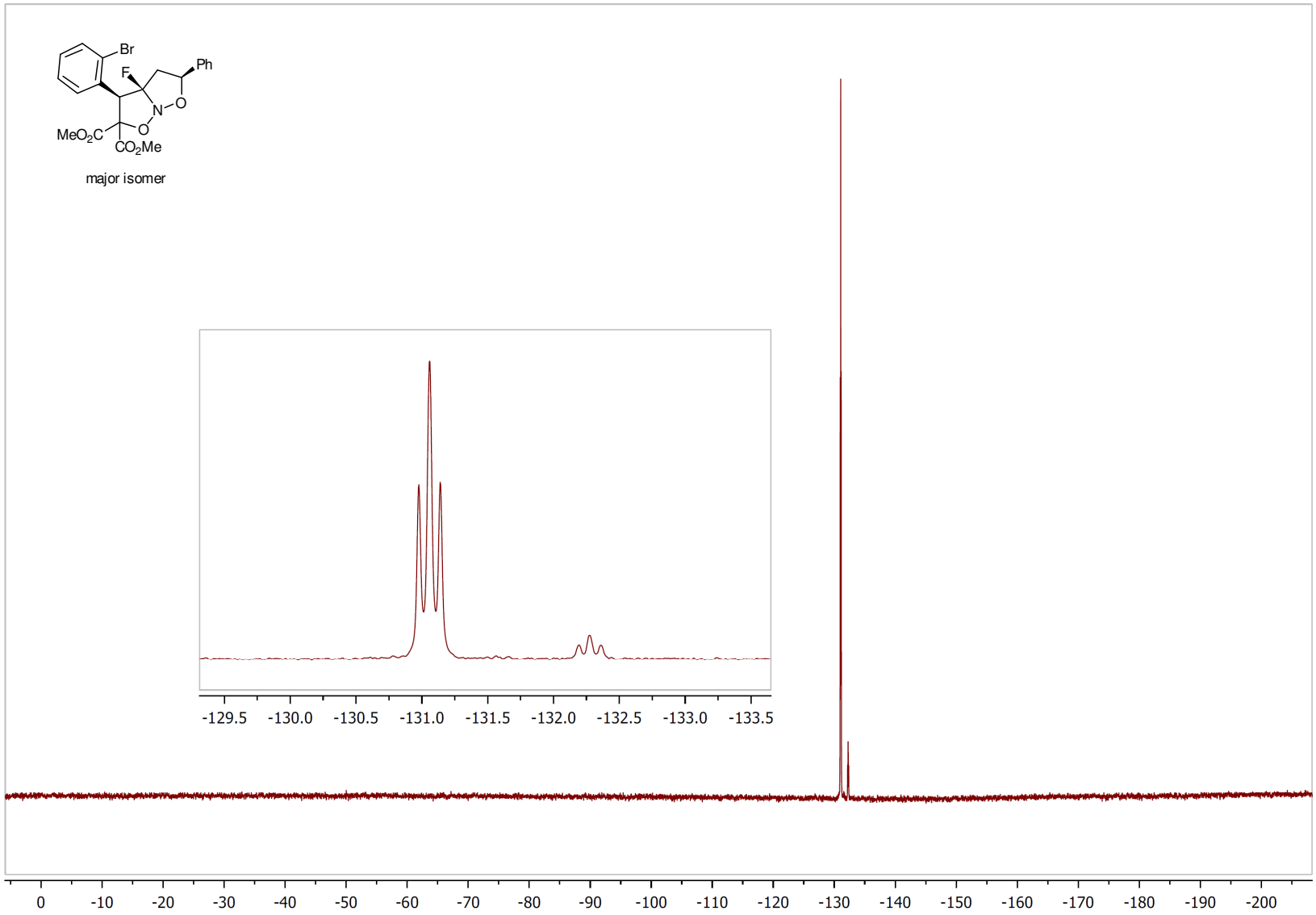
^{13}C NMR


166.81
165.80
137.14
132.79
132.29
132.25
131.77
131.73
129.87
128.94
128.80
127.23
127.06
126.27
120.69
117.74
89.47
85.27
54.20
54.15
53.91
52.53
44.87
44.50
Br
F
Ph
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{13}C NMR (DEPT)

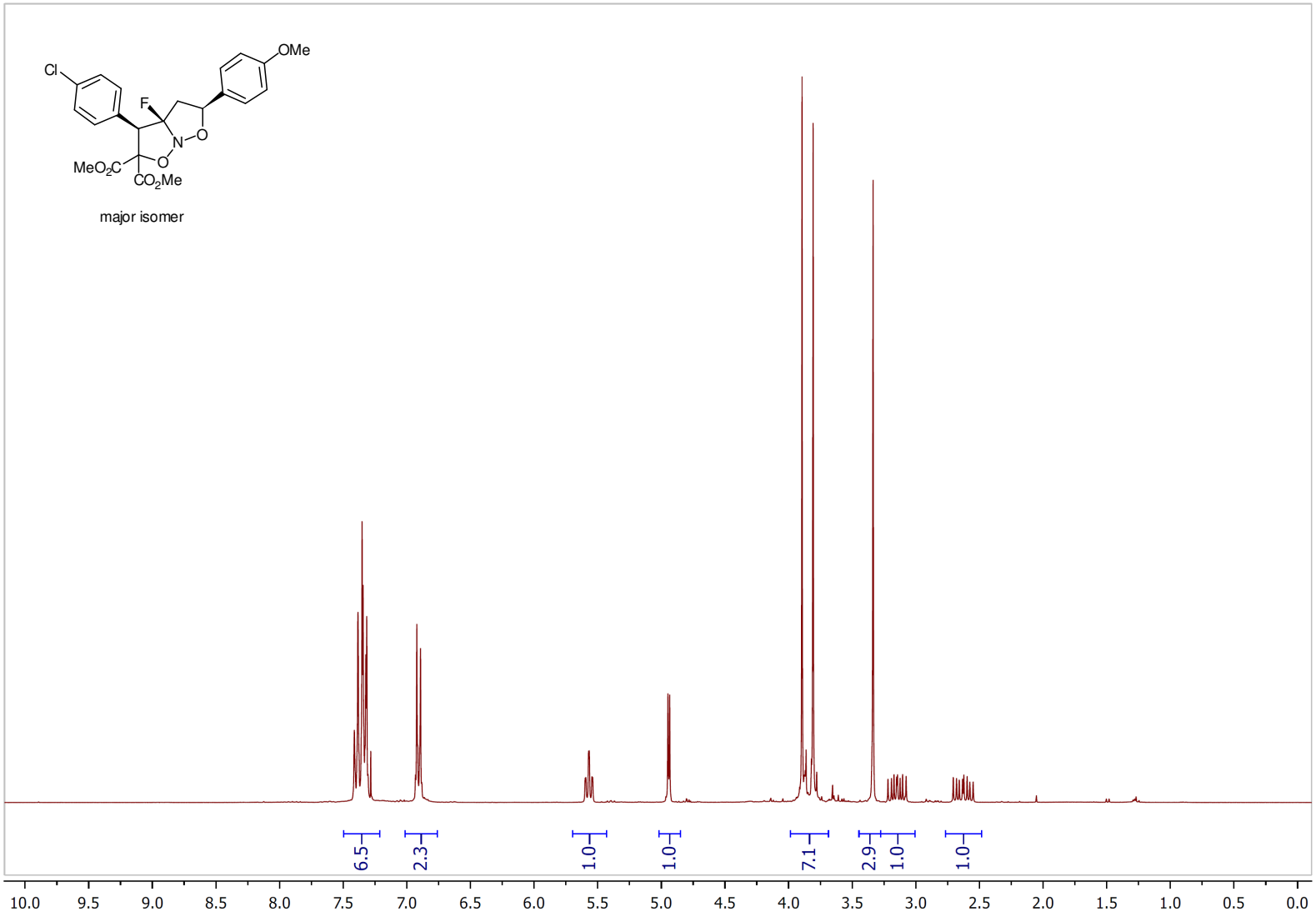

132.79
132.29
132.25
129.87
128.94
128.80
127.23
127.06
85.27
54.19
54.15
53.91
52.53
44.87
44.50
Br
F
Ph
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

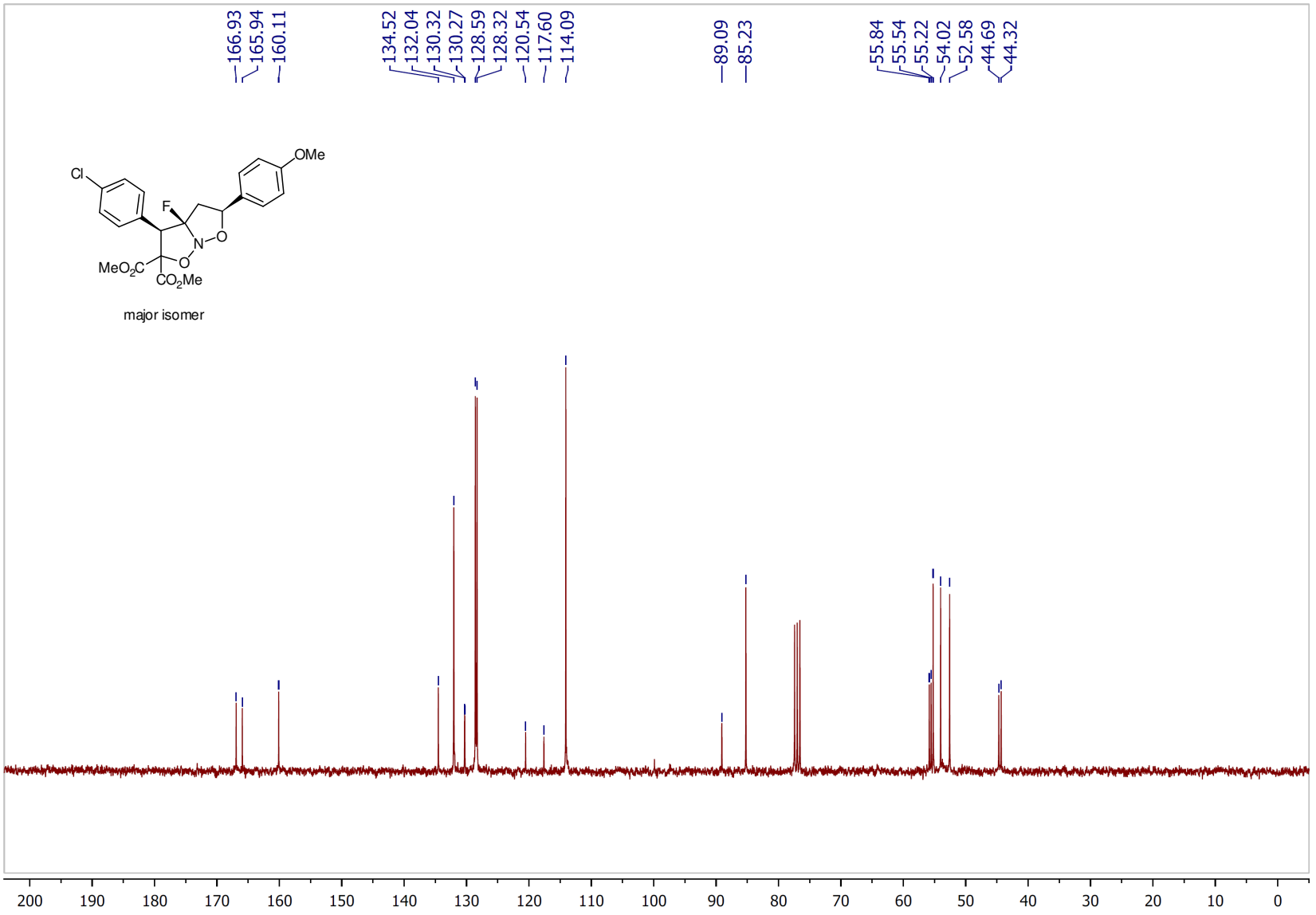

Br
F
Ph
N
O
O
MeO2C
CO2Me
major isomer
-129.5
-130.0
-130.5
-131.0
-131.5
-132.0
-132.5
-133.0
-133.5
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4h** (major isomer)

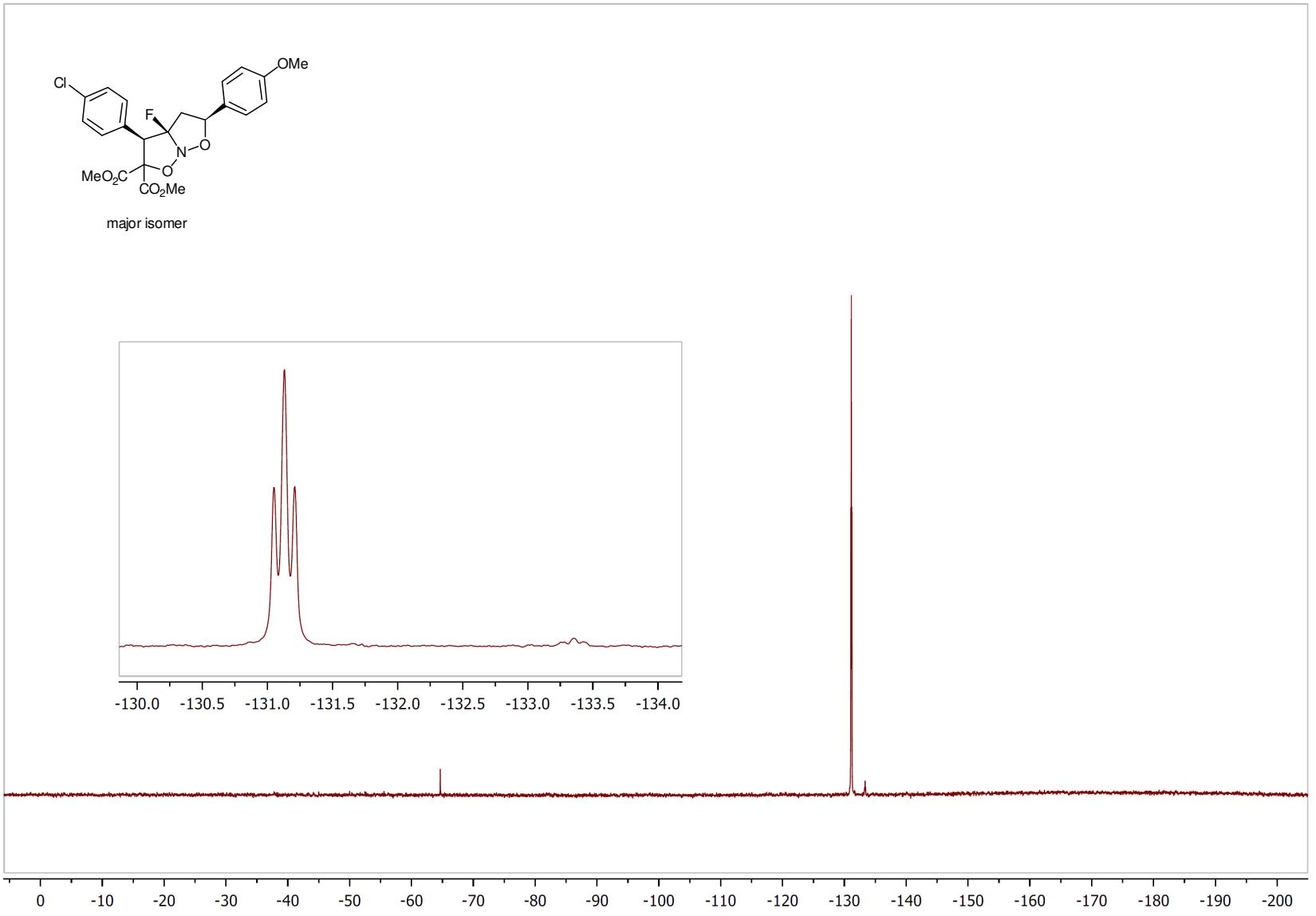
^{1}H NMR



^{13}C NMR

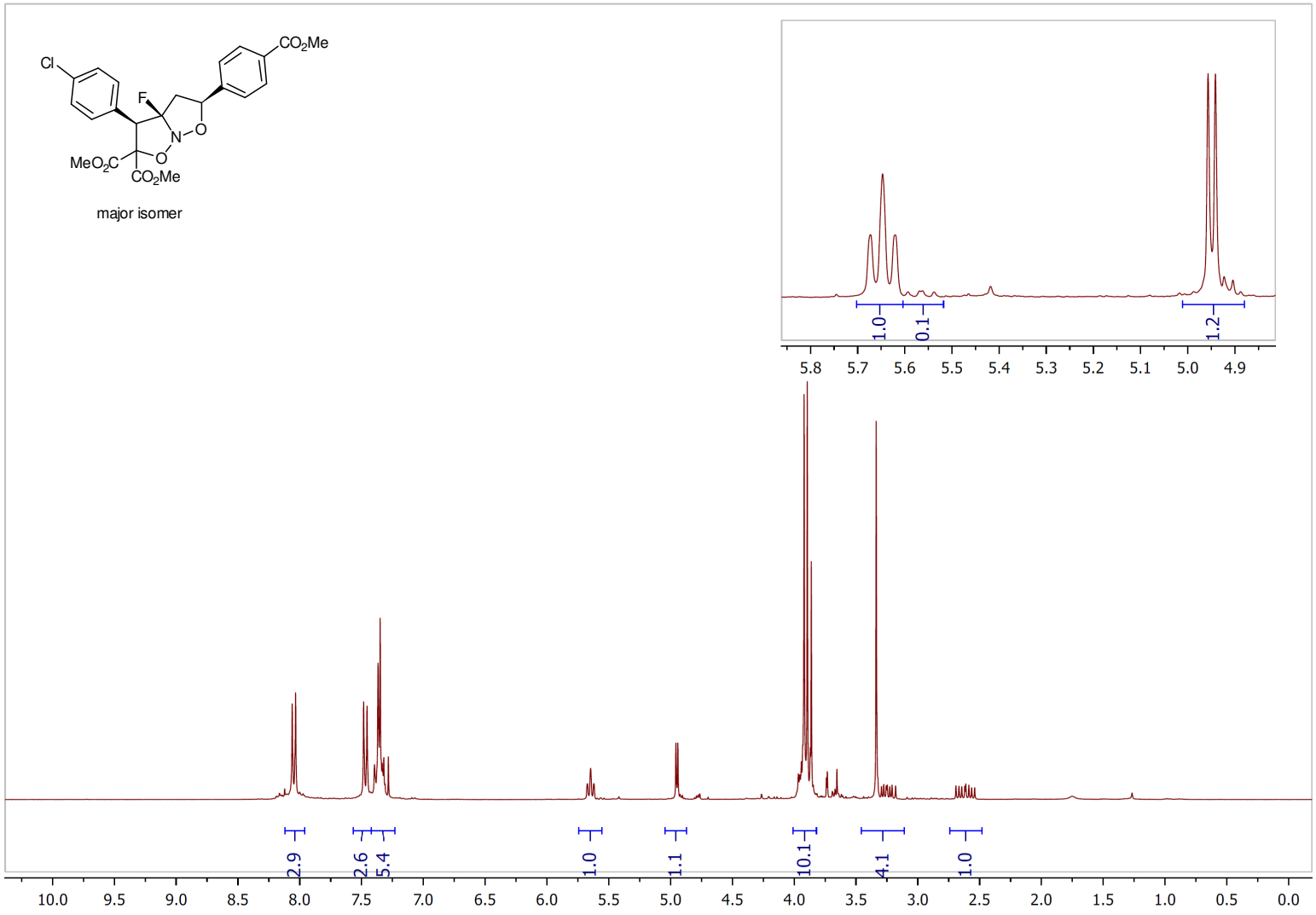

166.93
165.94
160.11
134.52
132.04
130.32
130.27
128.59
128.32
120.54
117.60
114.09
89.09
85.23
55.84
55.54
55.22
54.02
52.58
44.69
44.32
Cl
F
OMe
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

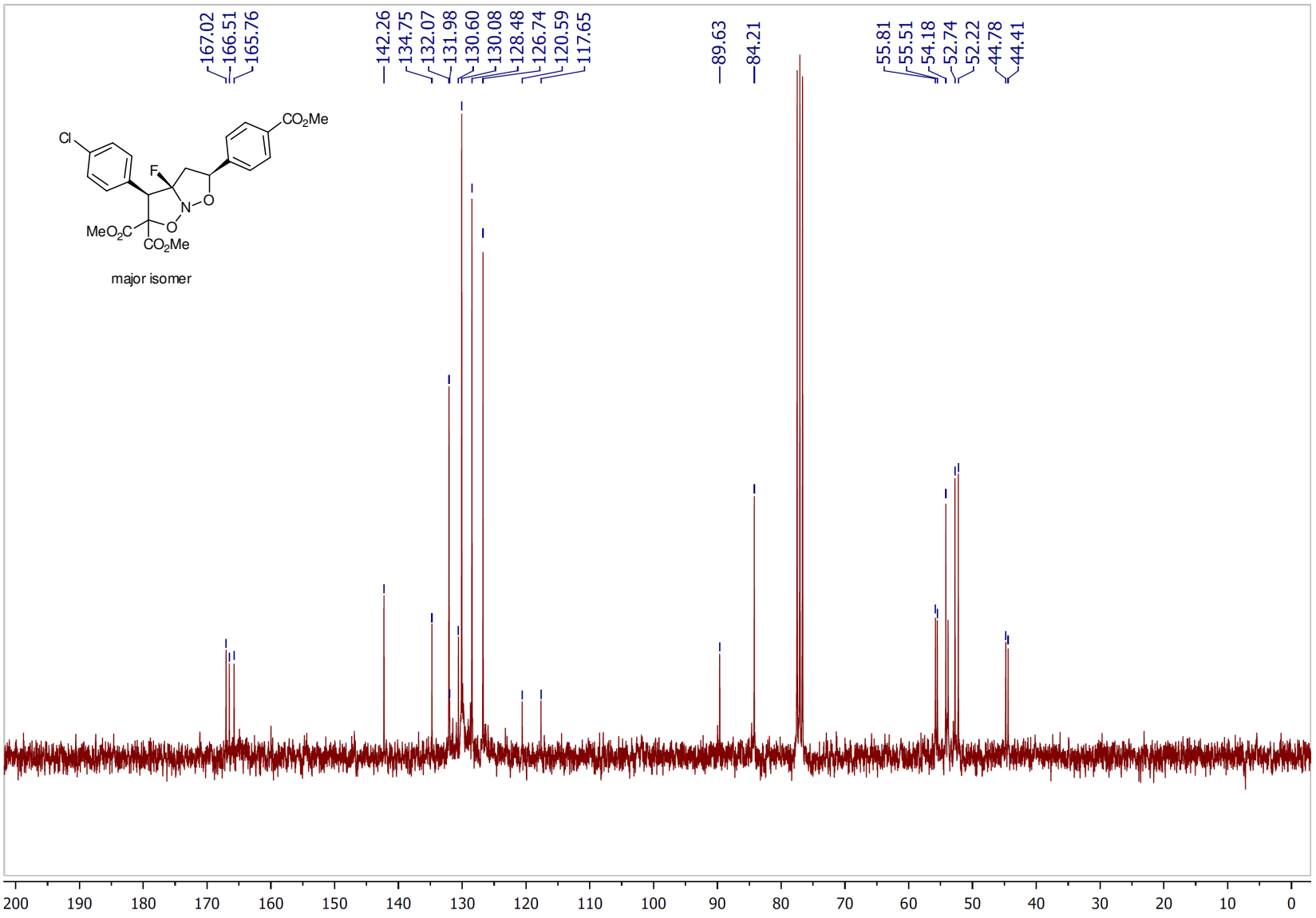

Cl
OMe
F
N
O
O
MeO2C
CO2Me
major isomer
-130.0
-130.5
-131.0
-131.5
-132.0
-132.5
-133.0
-133.5
-134.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4i** (major isomer)

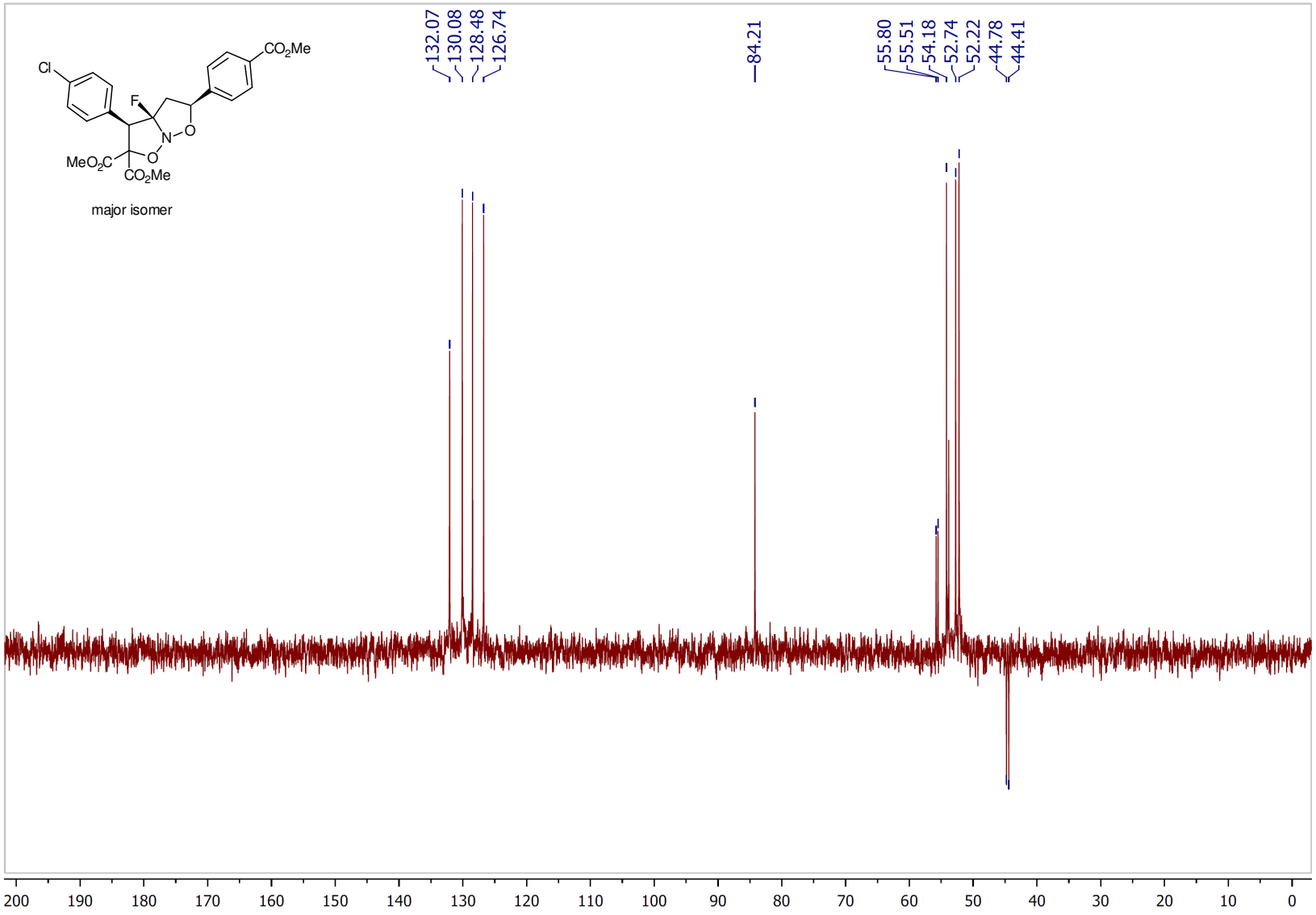
^{1}H NMR



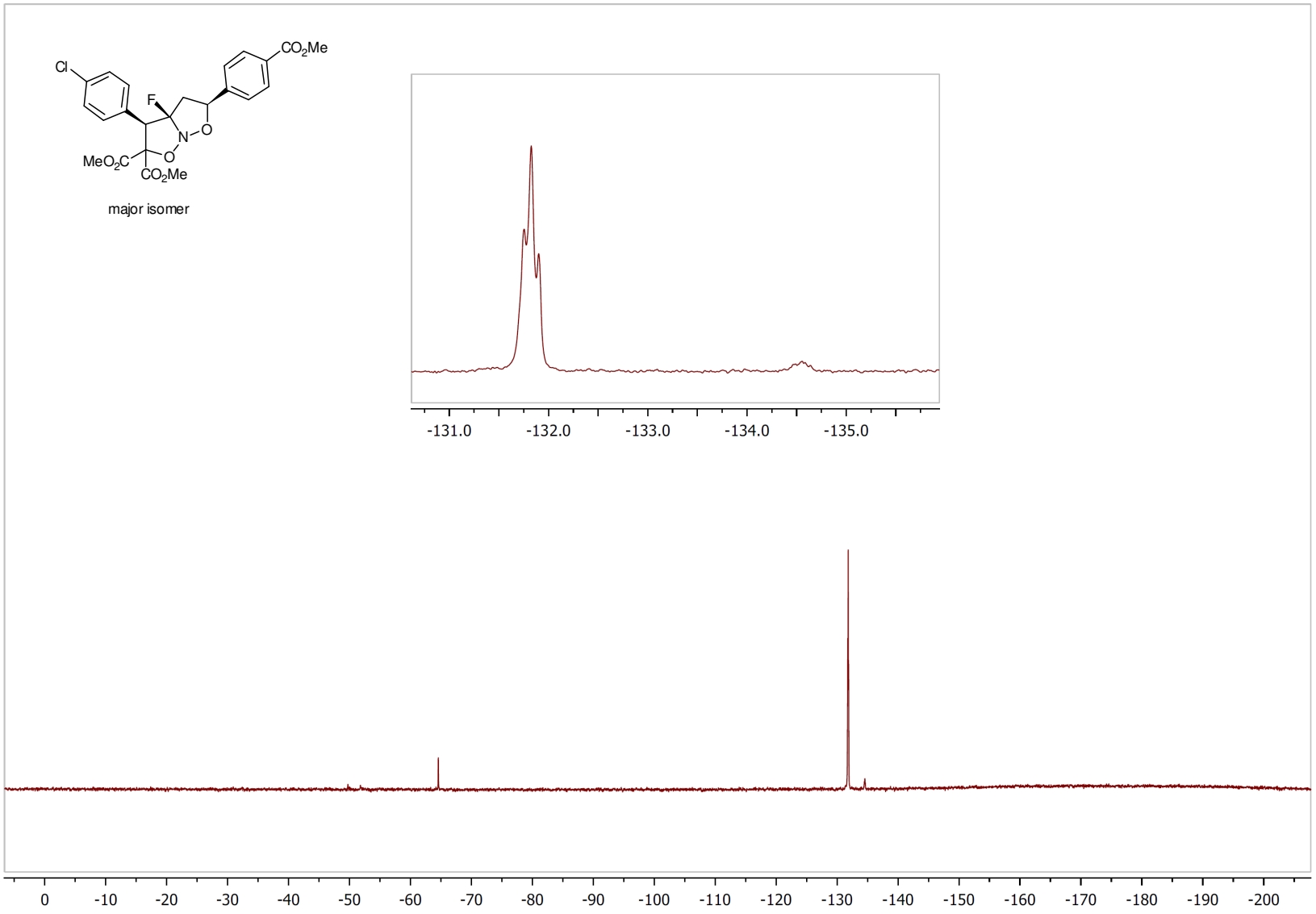
^{13}C NMR


167.02
166.51
165.76
142.26
134.75
132.07
131.98
130.60
130.08
128.48
126.74
120.59
117.65
89.63
84.21
55.81
55.51
54.18
52.74
52.22
44.78
44.41
Cl
F
N
O
O
MeO2C
CO2Me
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

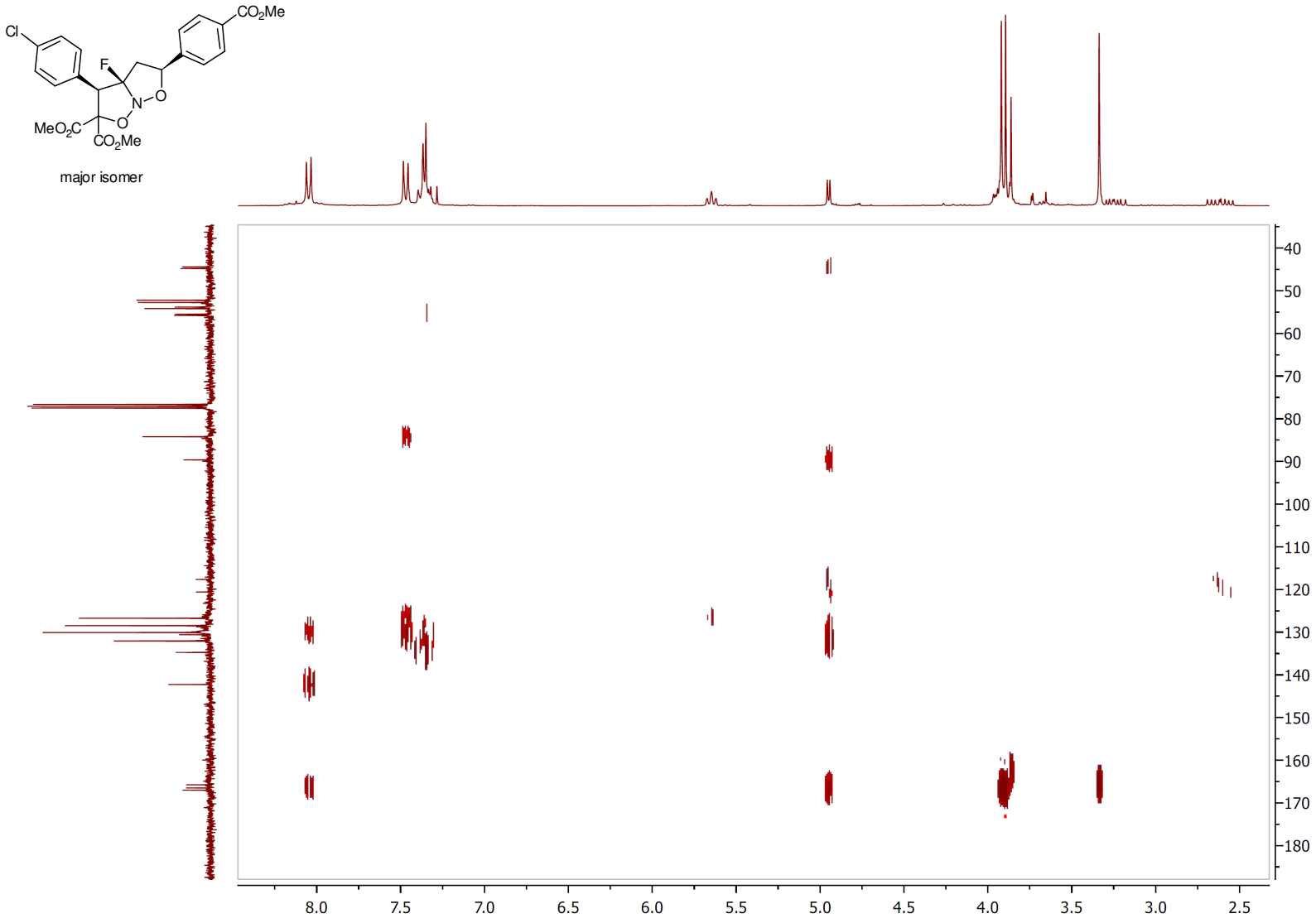
^{13}C NMR (DEPT)


Cl
F
N
O
O
CO_2Me
MeO_2C
CO_2Me
major isomer
132.07
130.08
128.48
126.74
84.21
55.80
55.51
54.18
52.74
52.22
44.78
44.41
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

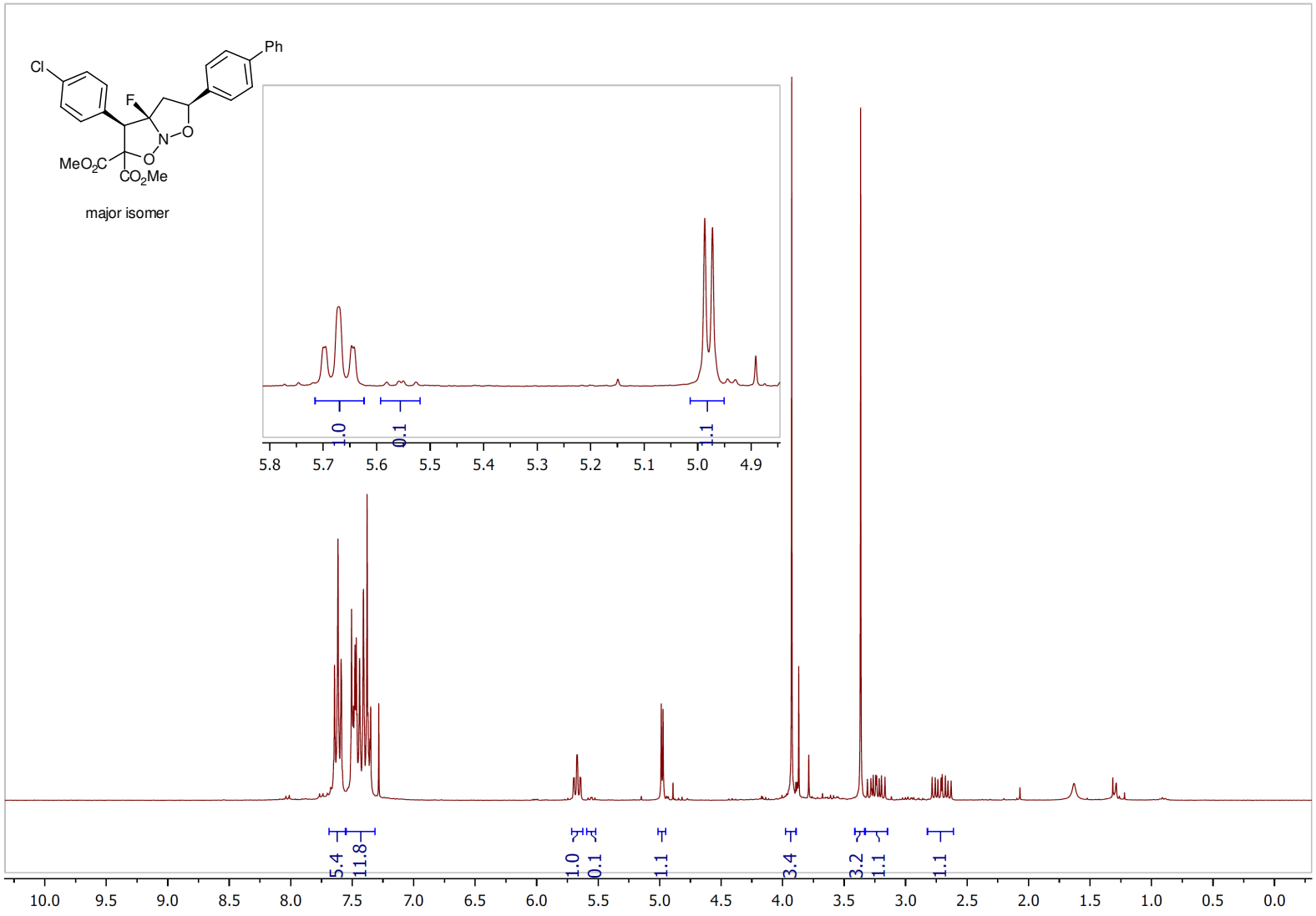

Cl
F
N
O
O
MeO2C
CO2Me
CO2Me
major isomer
-131.0
-132.0
-133.0
-134.0
-135.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

^{1}H-^{13}C HMBC

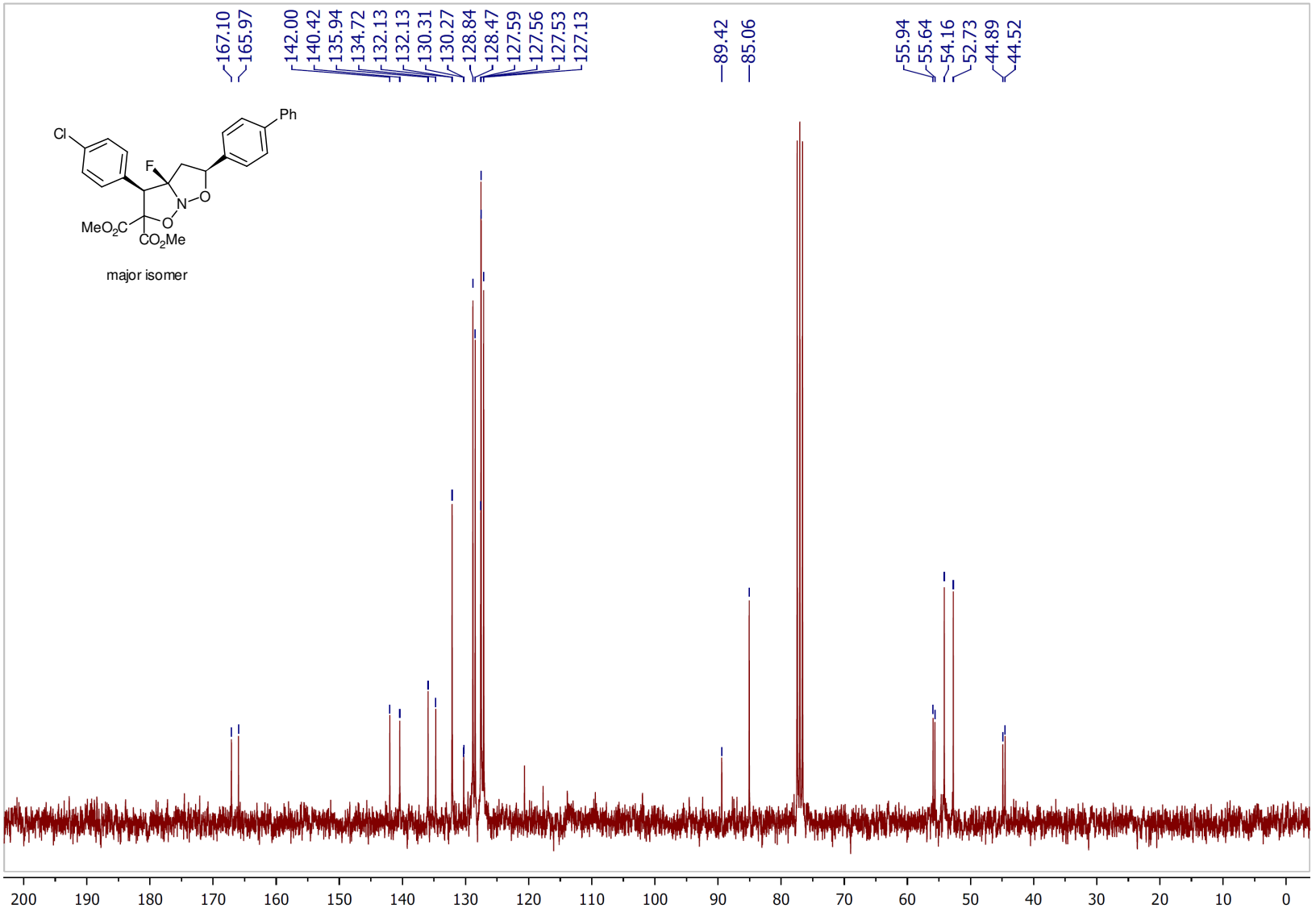

Cl
F
N
O
O
MeO_2C
CO_2Me
CO_2Me
major isomer
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5

***rel*-(3R,3aR,5S)-Dimethyl 5-(biphenyl-4-yl)-3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4j** (major isomer)

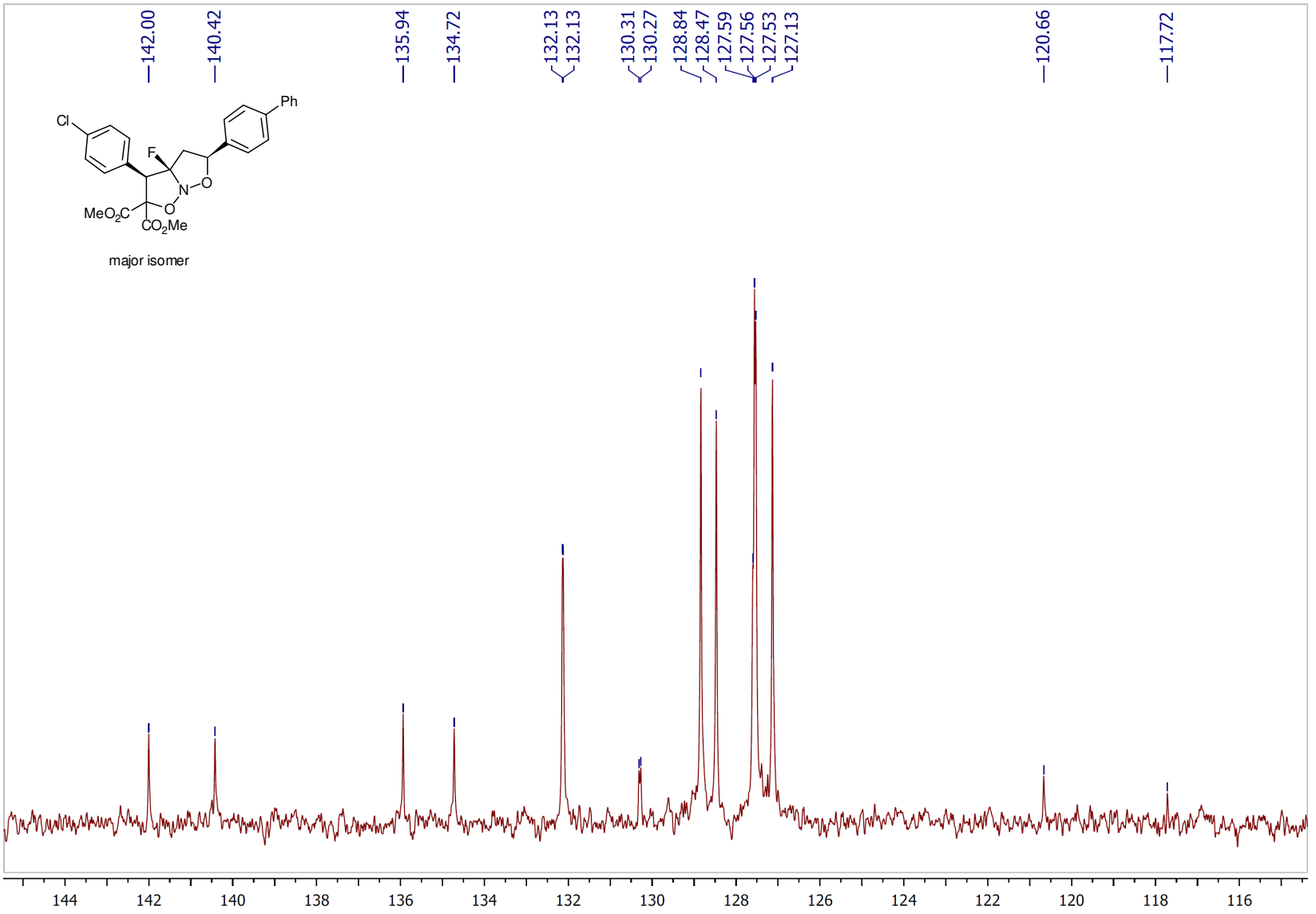
^{1}H NMR



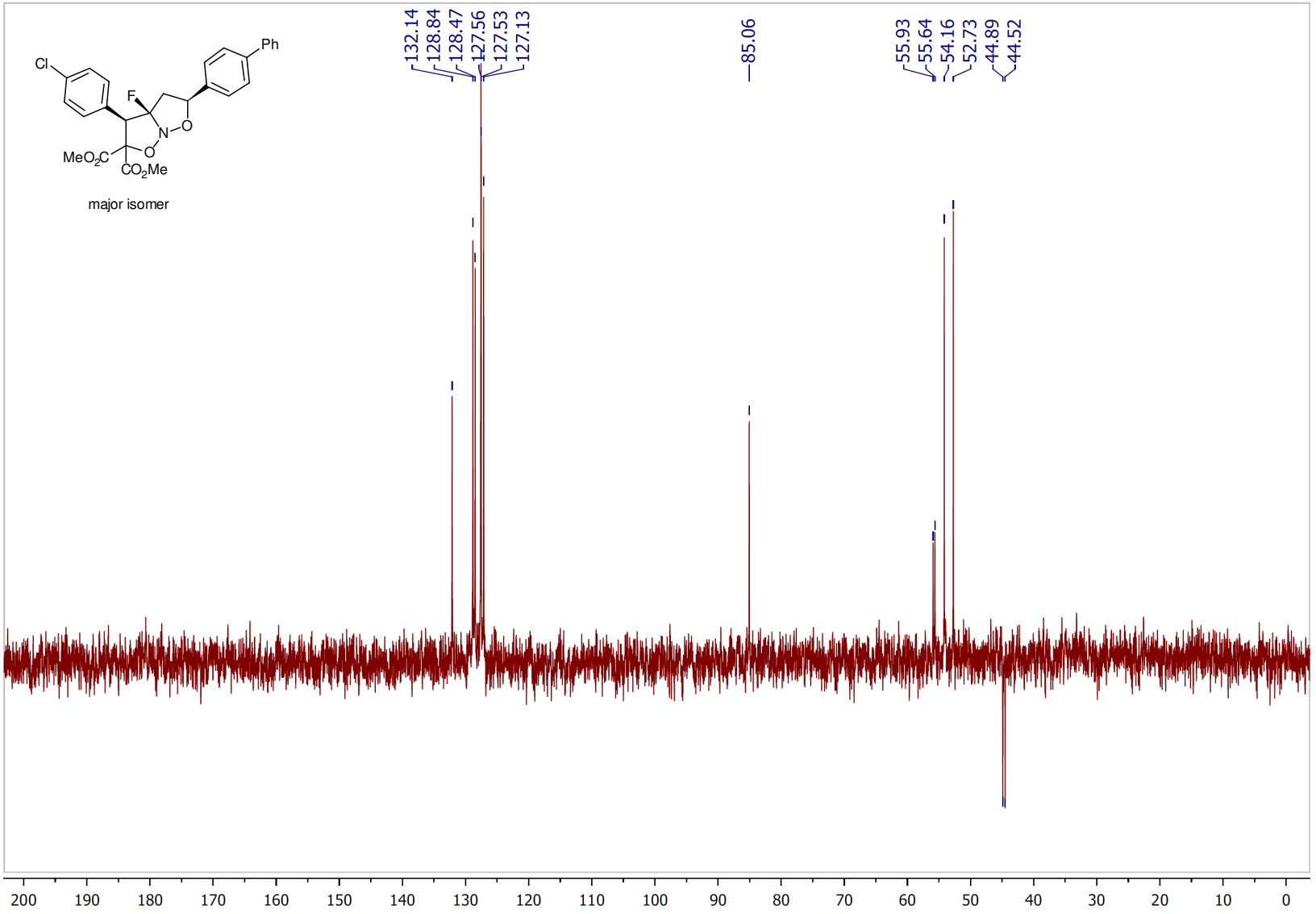
^{13}C NMR


167.10
165.97
142.00
140.42
135.94
134.72
132.13
132.13
130.31
130.27
128.84
128.47
127.59
127.56
127.53
127.13
89.42
85.06
55.94
55.64
54.16
52.73
44.89
44.52
Cl
F
Ph
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

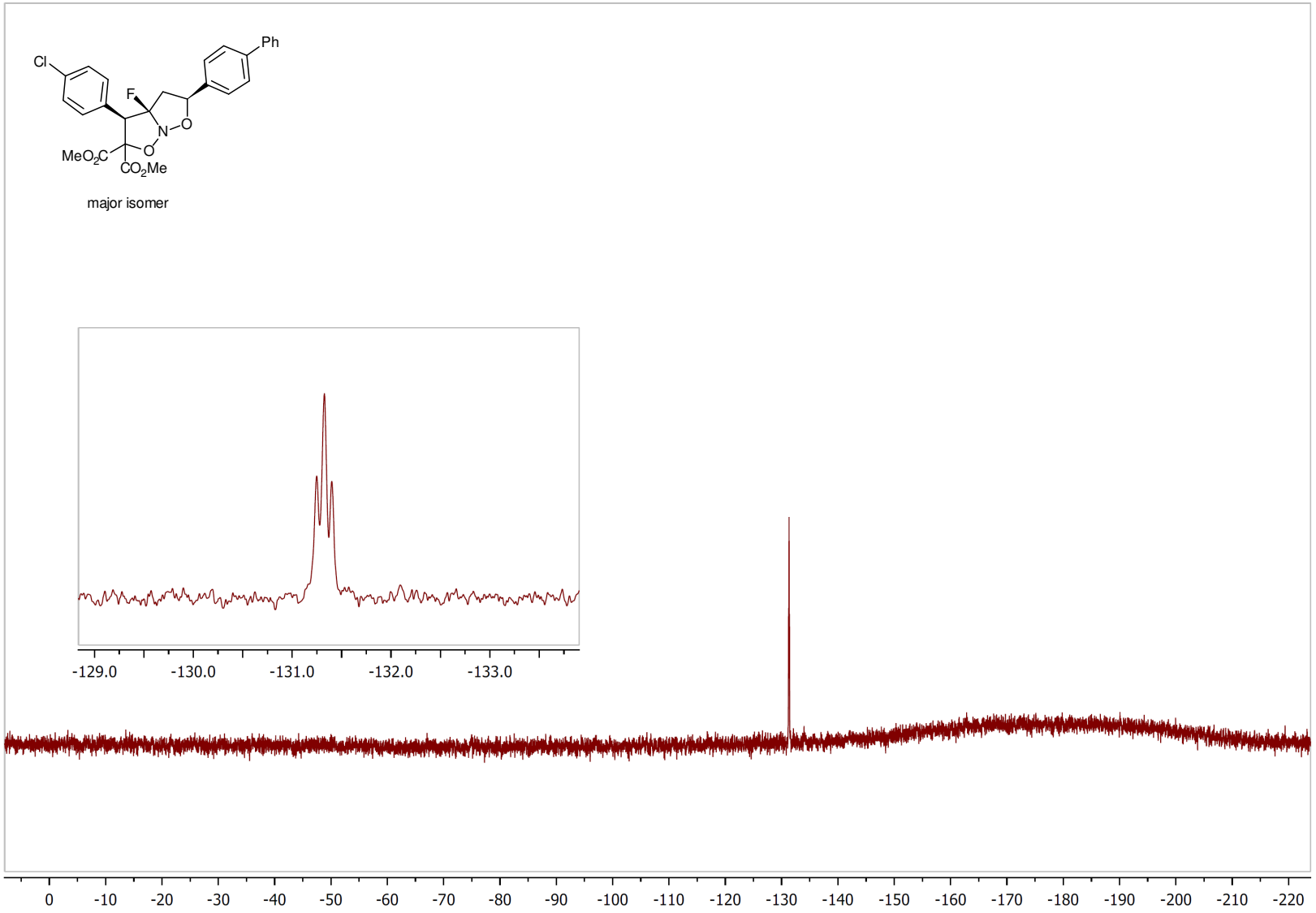
^{13}C NMR (expanded region 114-146 ppm)



^{13}C NMR (DEPT)

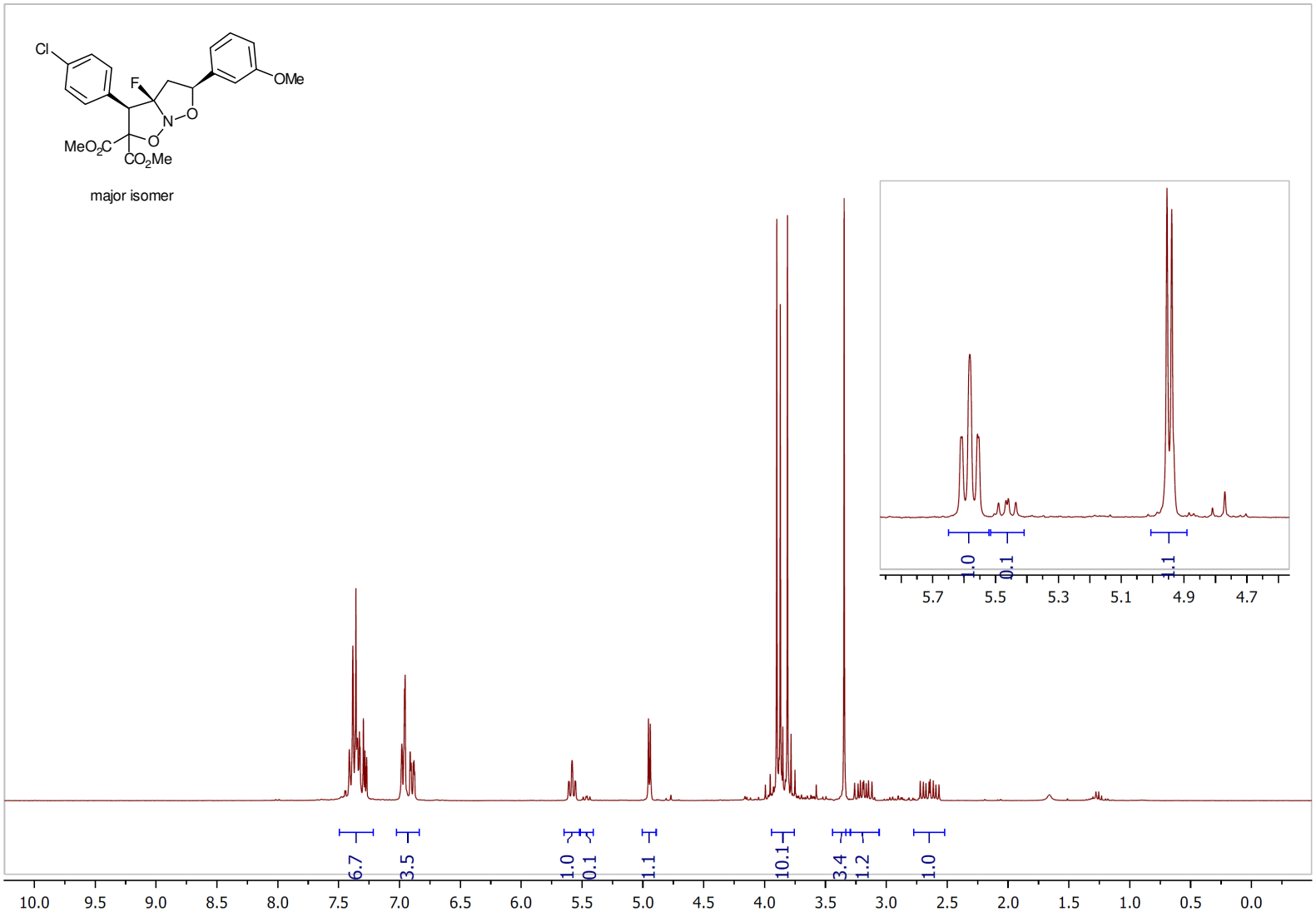

Cl
Ph
F
N
O
MeO2C
CO2Me
major isomer
132.14
128.84
128.47
127.56
127.53
127.13
85.06
55.93
55.64
54.16
52.73
44.89
44.52
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

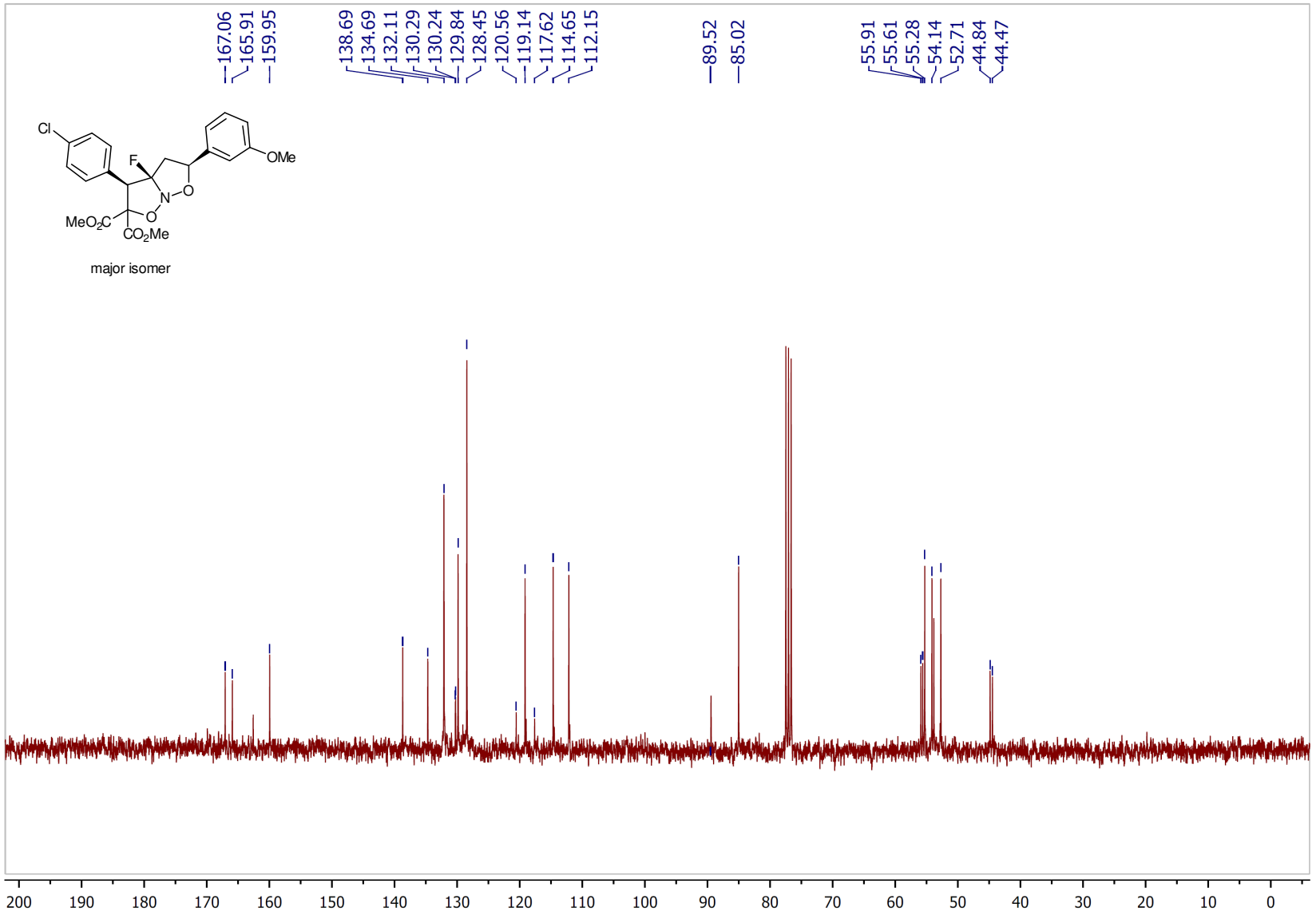

Cl
Ph
F
N
O
MeO2C
CO2Me
major isomer
-129.0
-130.0
-131.0
-132.0
-133.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(3-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4k** (major isomer)

^{1}H NMR



^{13}C NMR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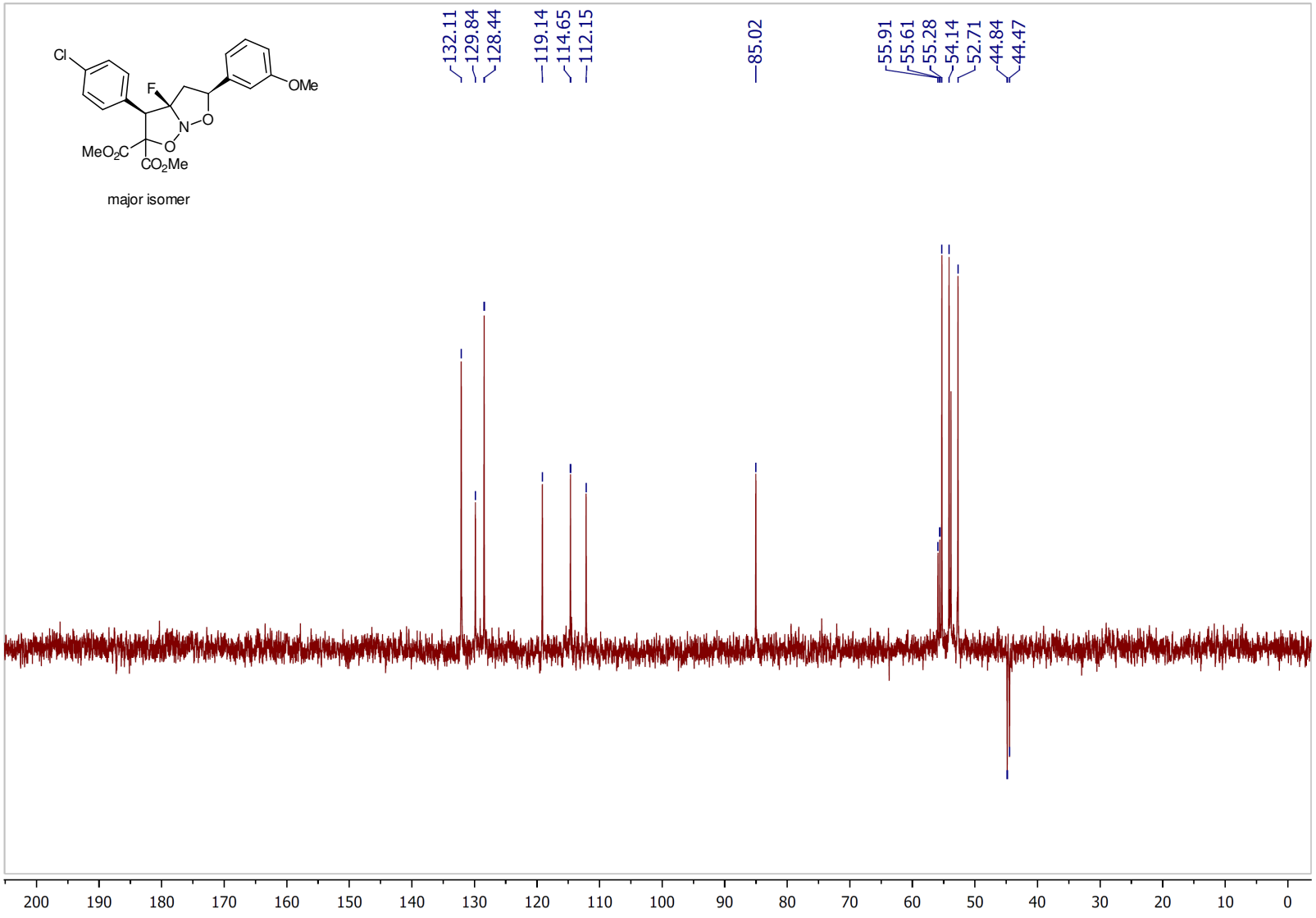
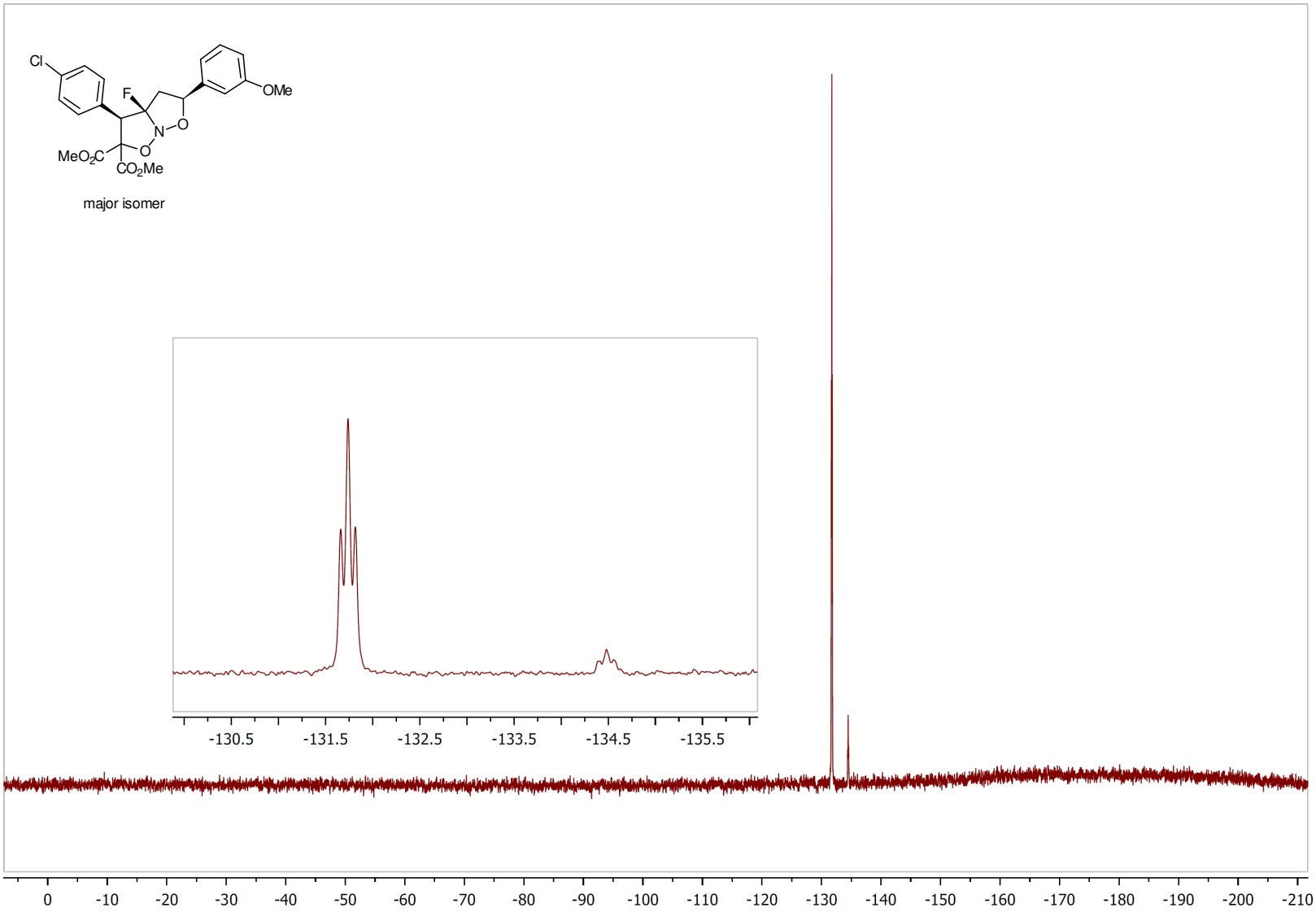
165.91
159.95
138.69
134.69
132.11
130.29
130.24
129.84
128.45
120.56
119.14
117.62
114.65
112.15
89.52
85.02
55.91
55.61
55.28
54.14
52.71
44.84
44.47
Cl
F
OMe
N
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{13}C NMR (DEPT)

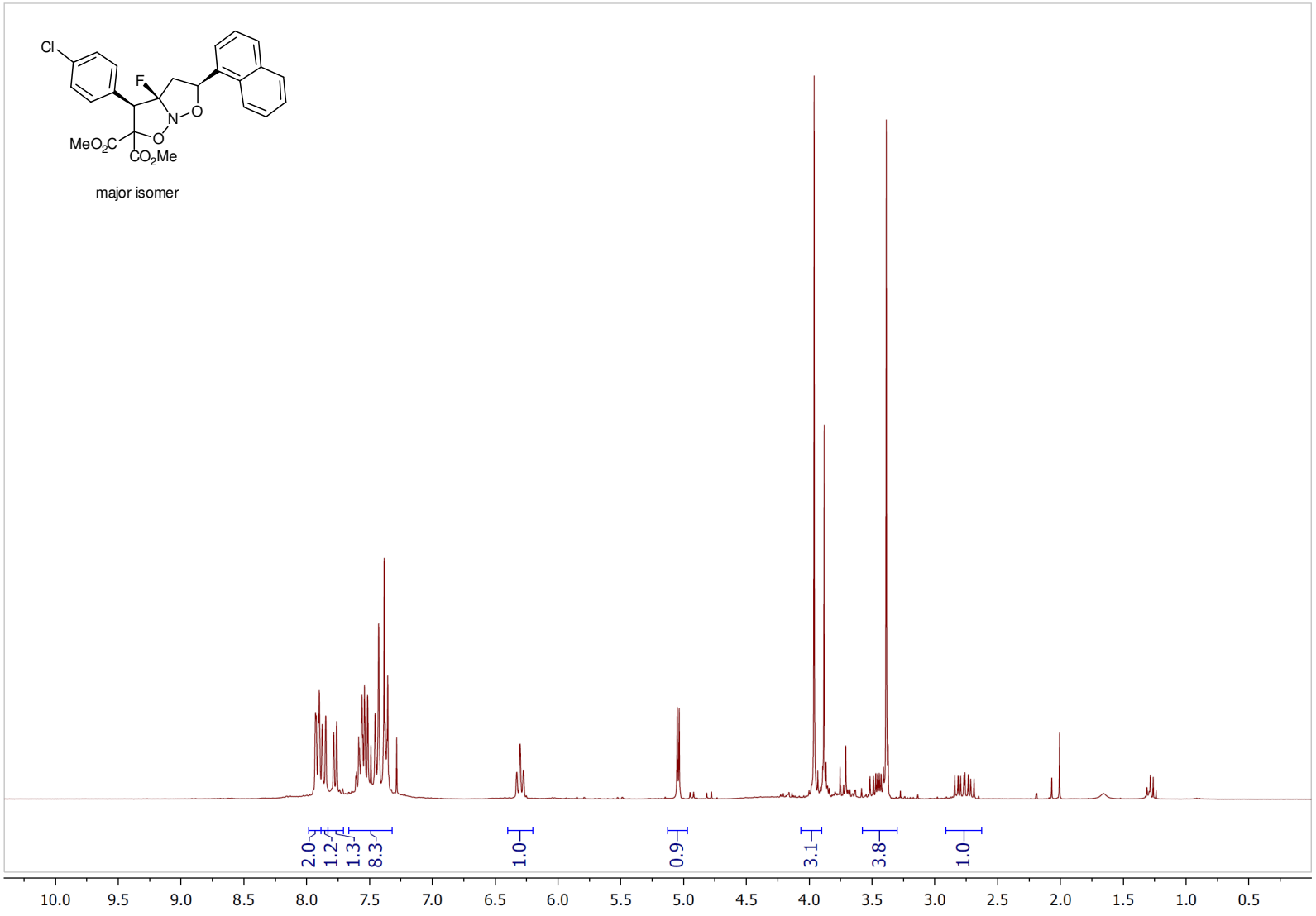

Cl
F
OMe
N
O
O
MeO2C
CO2Me
major isomer
132.11
129.84
128.44
119.14
114.65
112.15
85.02
55.91
55.61
55.28
54.14
52.71
44.84
44.47
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

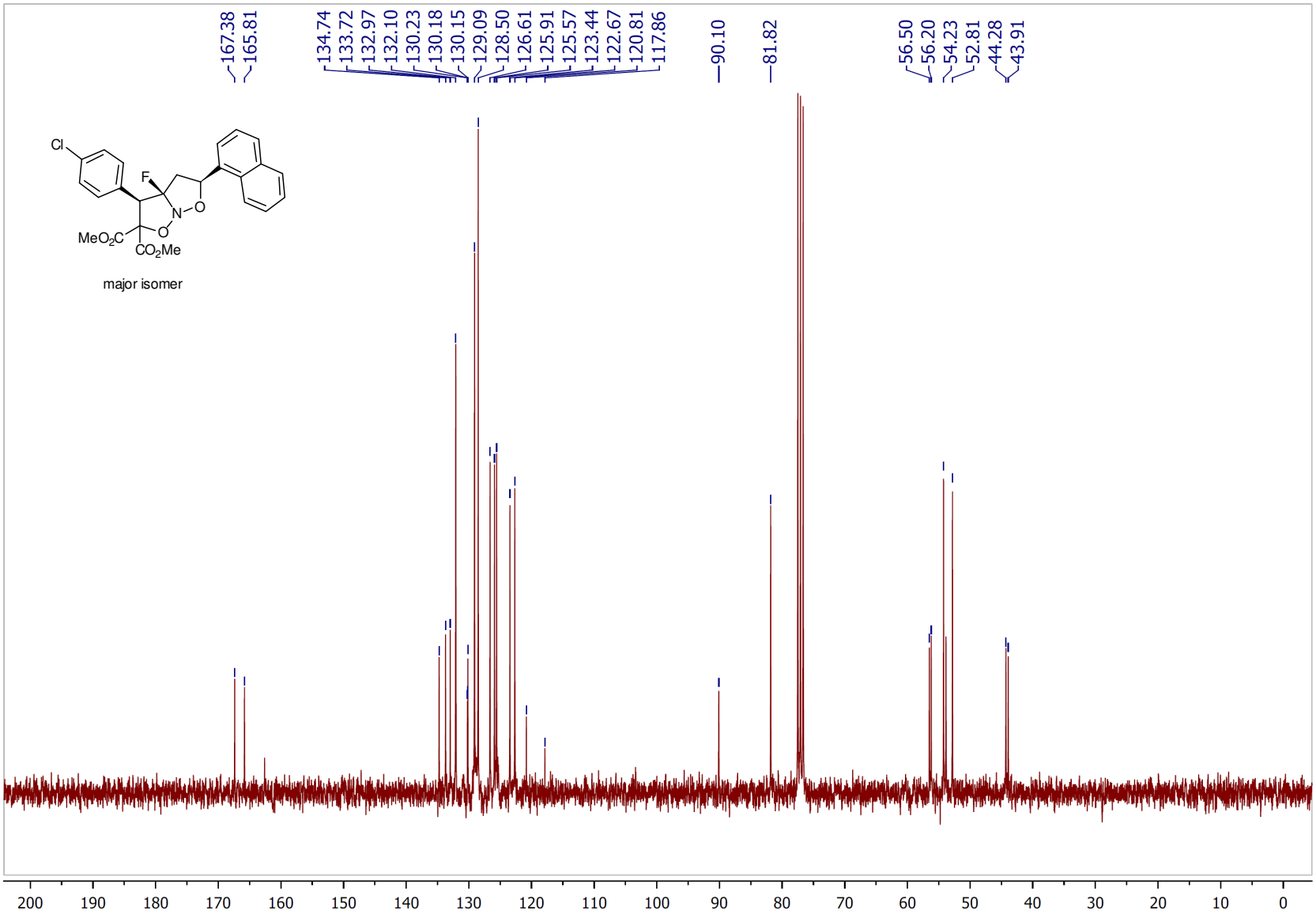

Cl
F
OMe
N
O
O
MeO2C
CO2Me
major isomer
-130.5
-131.5
-132.5
-133.5
-134.5
-135.5
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(naphthalen-1-yl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4l** (major isomer)

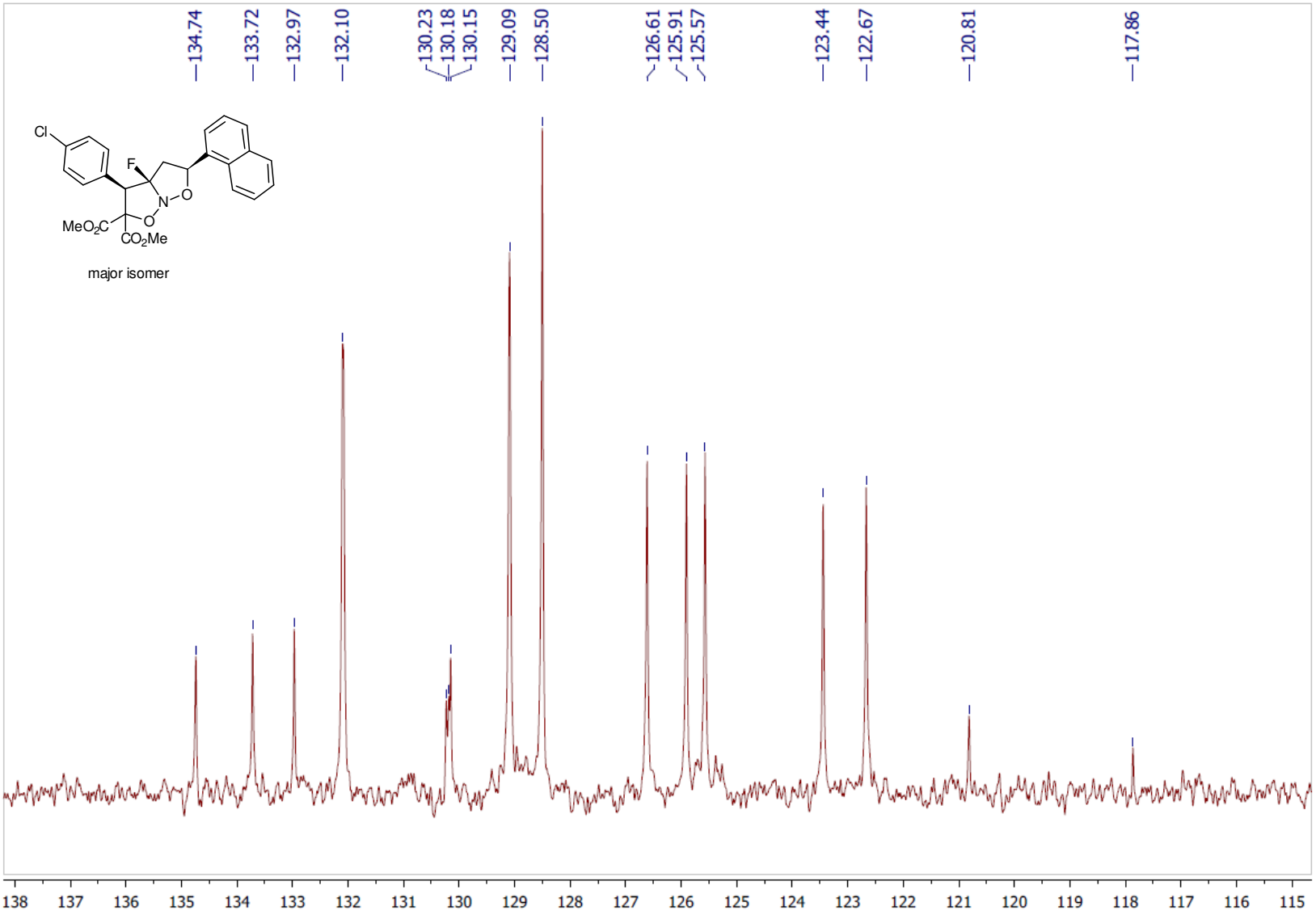
^{1}H NMR



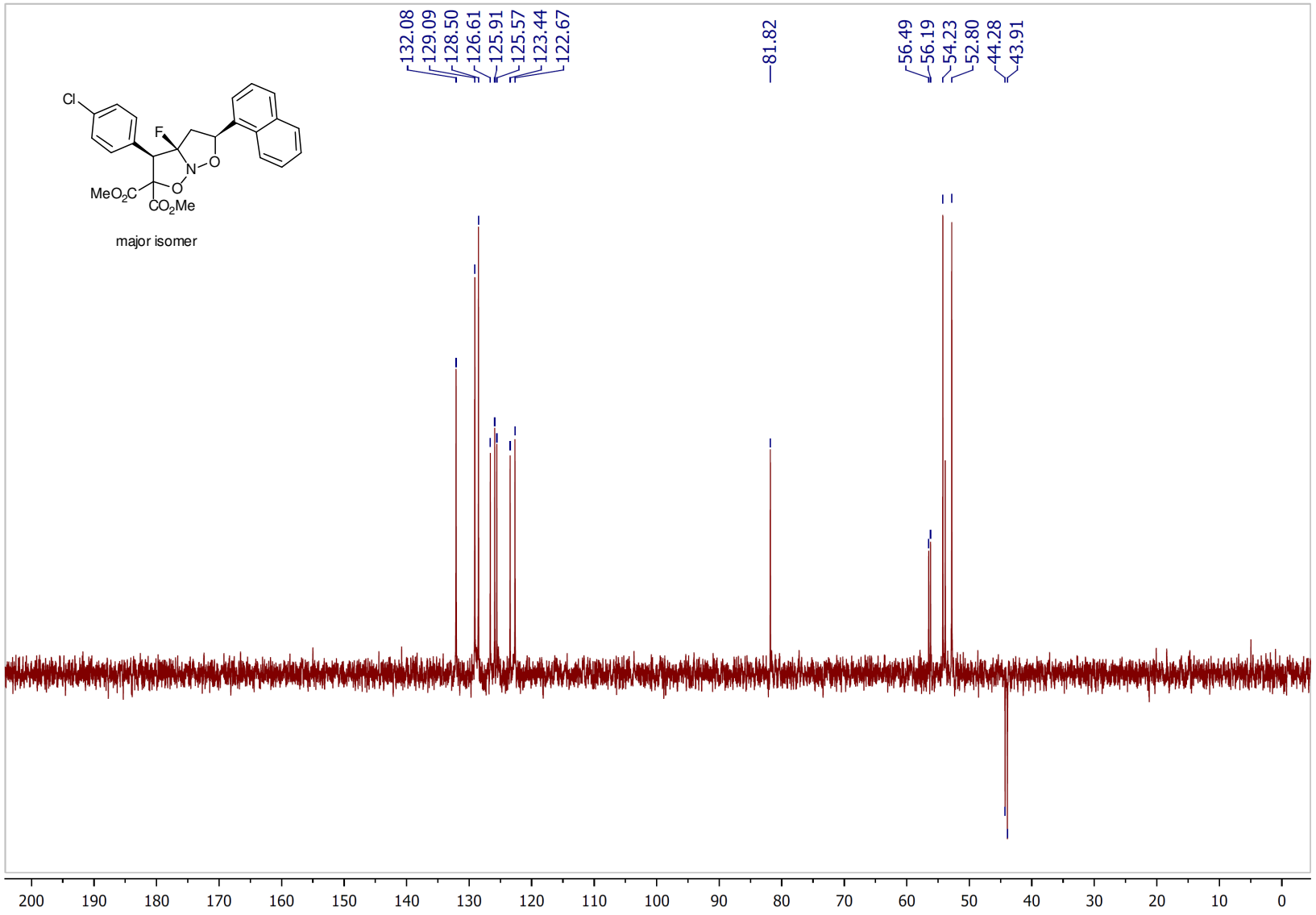
^{13}C NMR


167.38
165.81
134.74
133.72
132.97
132.10
130.23
130.18
130.15
129.09
128.50
126.61
125.91
125.57
123.44
122.67
120.81
117.86
90.10
81.82
56.50
56.20
54.23
52.81
44.28
43.91
Cl
F
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

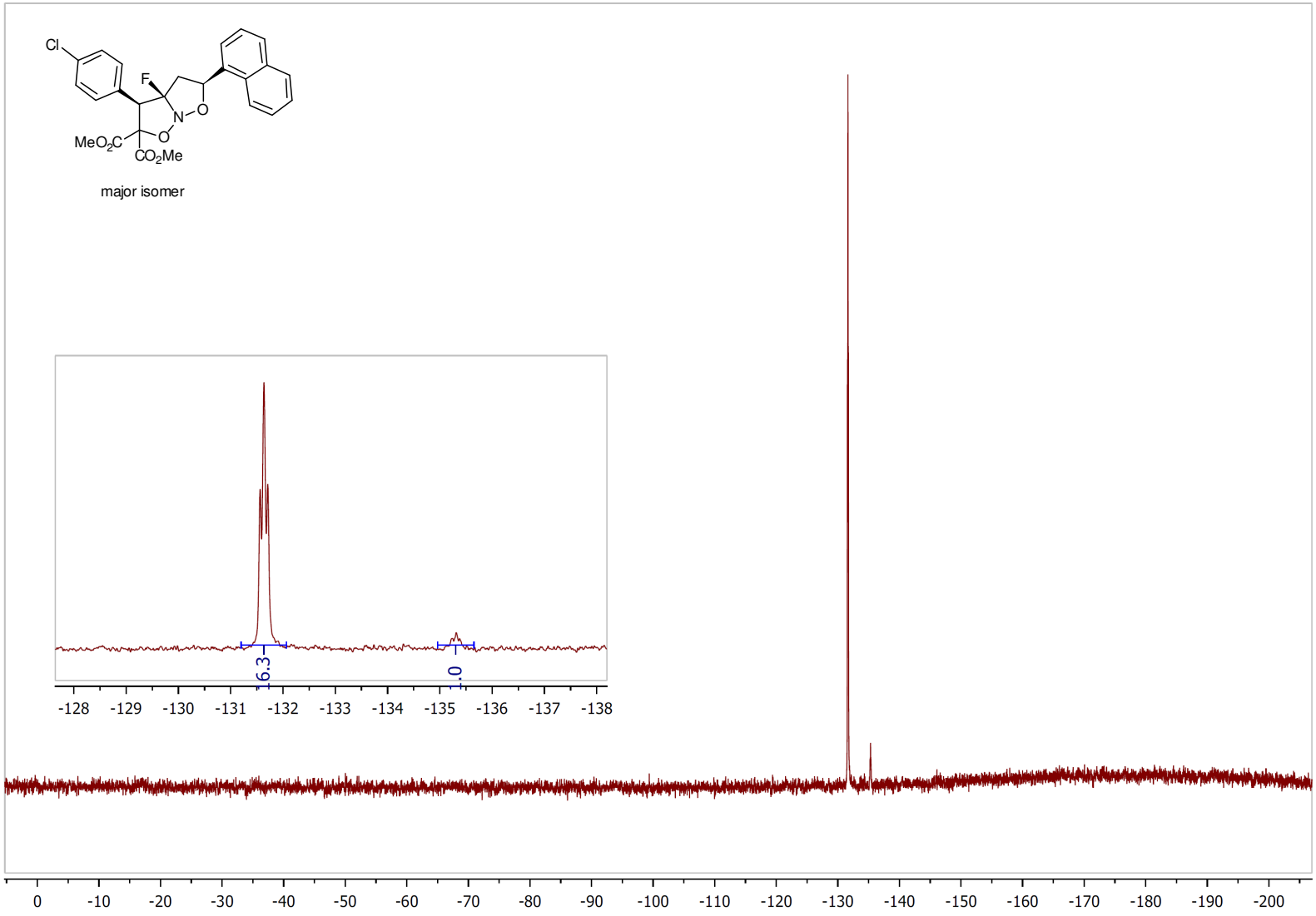
^{13}C NMR (expanded region 115-138 ppm)



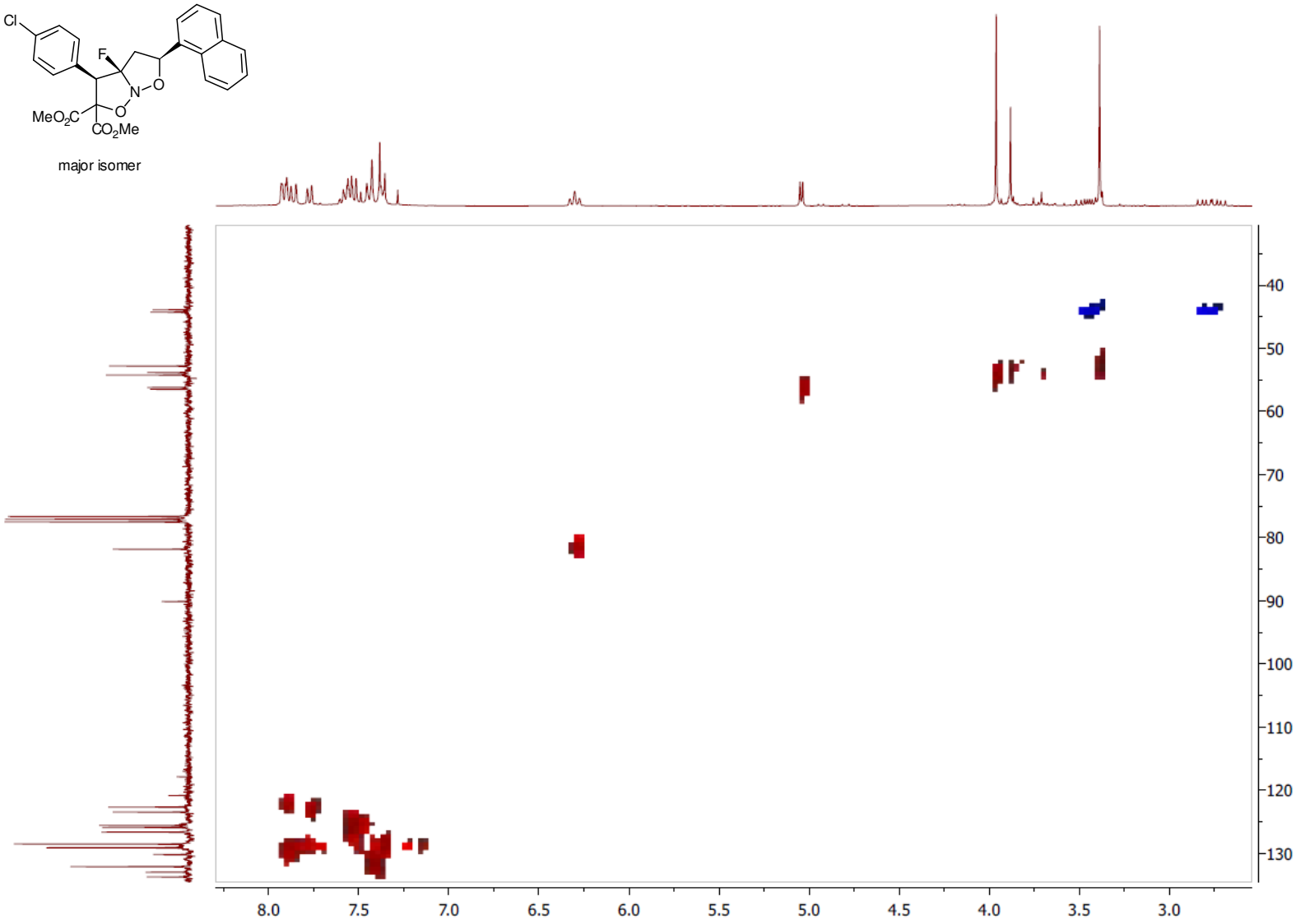
^{13}C NMR (DEPT)


132.08
129.09
128.50
126.61
125.91
125.57
123.44
122.67
81.82
56.49
56.19
54.23
52.80
44.28
43.91
Cl
F
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

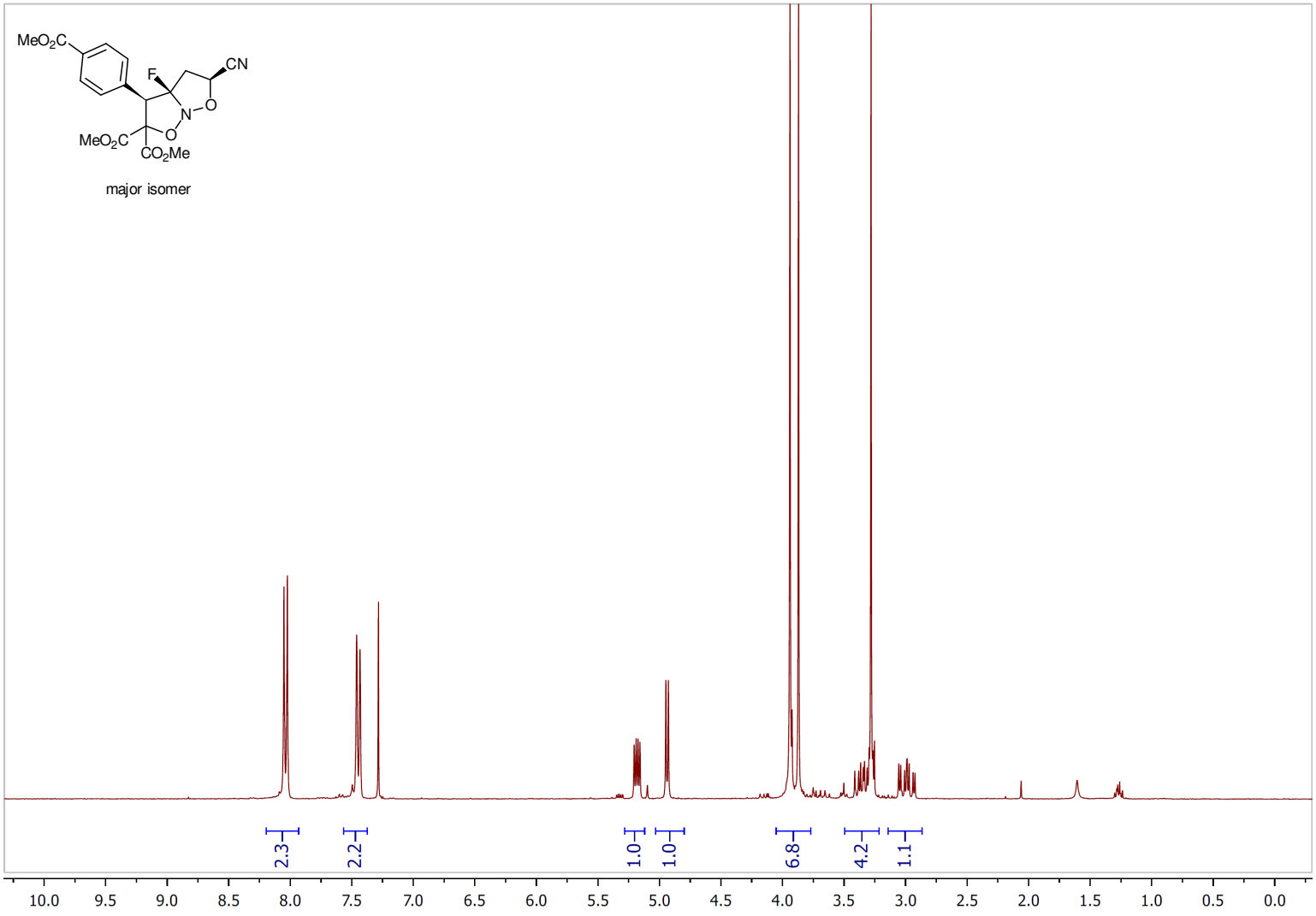

Cl
F
N
O
O
MeO2C
CO2Me
major isomer
16.3
1.0
-128 -129 -130 -131 -132 -133 -134 -135 -136 -137 -138
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200

^{1}H-^{13}C HSQC

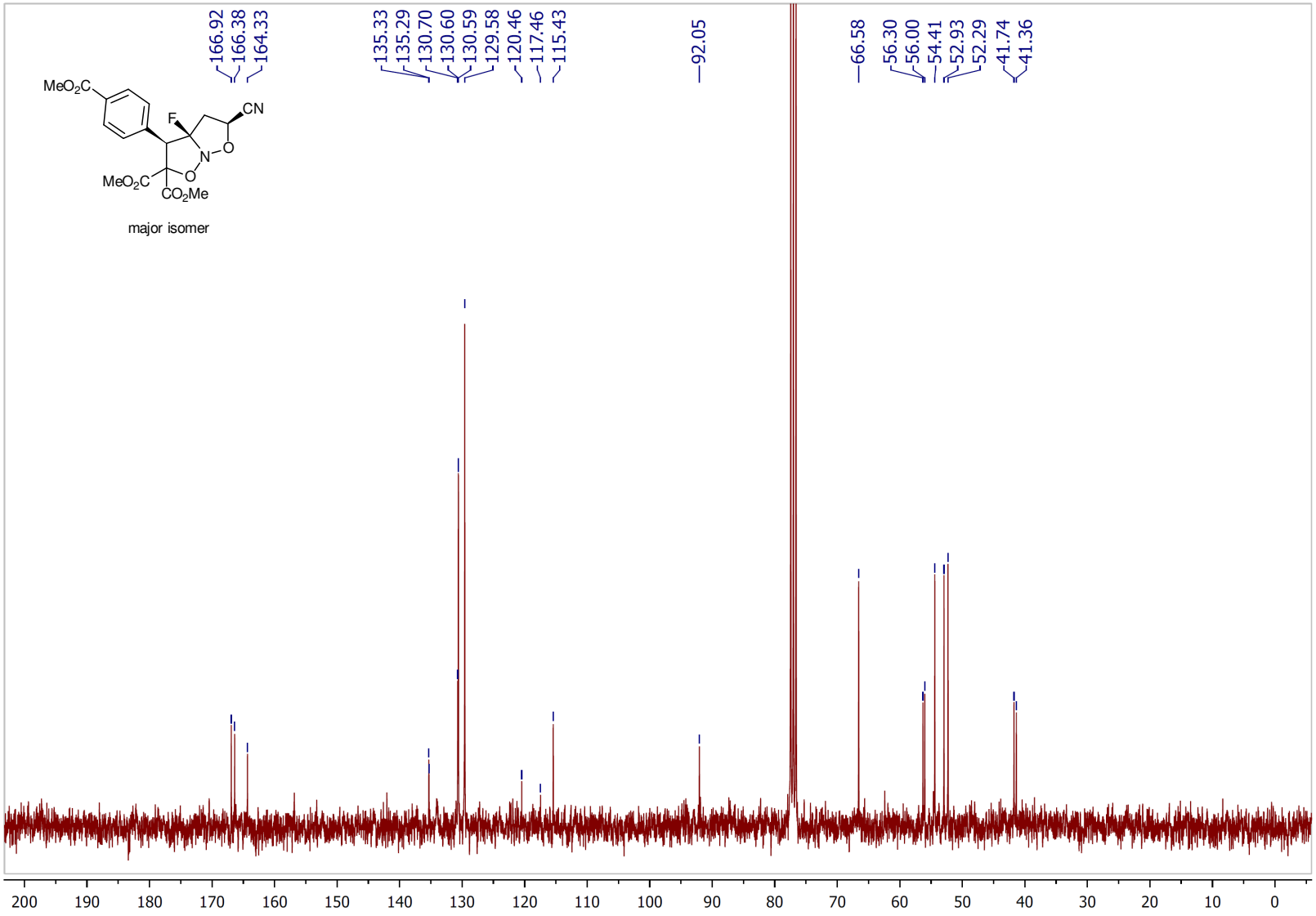

Cl
F
N
O
O
MeO2C
CO2Me
major isomer
40
50
60
70
80
90
100
110
120
130
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0

***rel*-(3R,3aR,5S)-Dimethyl 5-cyano-3a-fluoro-3-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4m** (enriched major isomer)

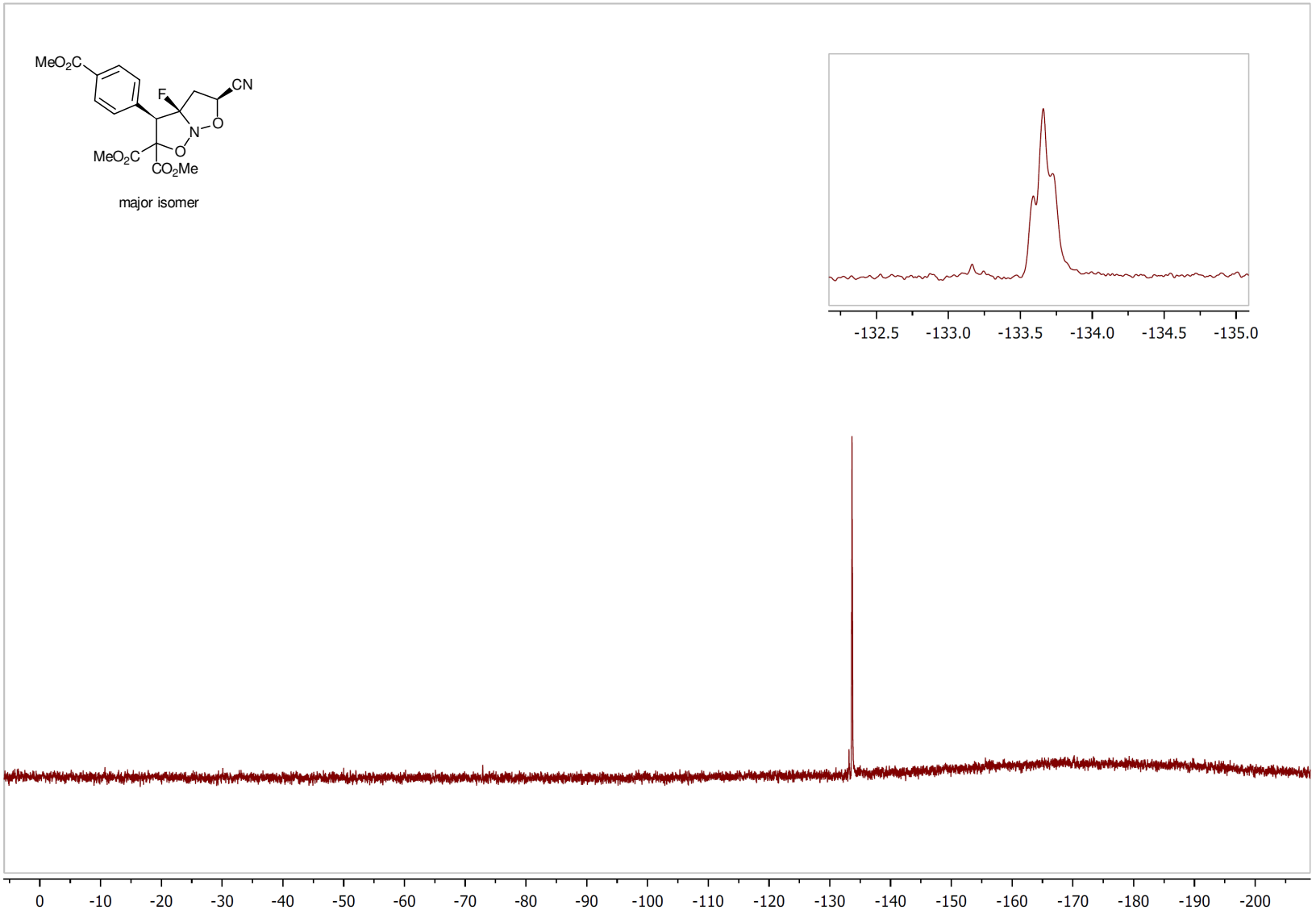
^{1}H NMR



^{13}C NMR

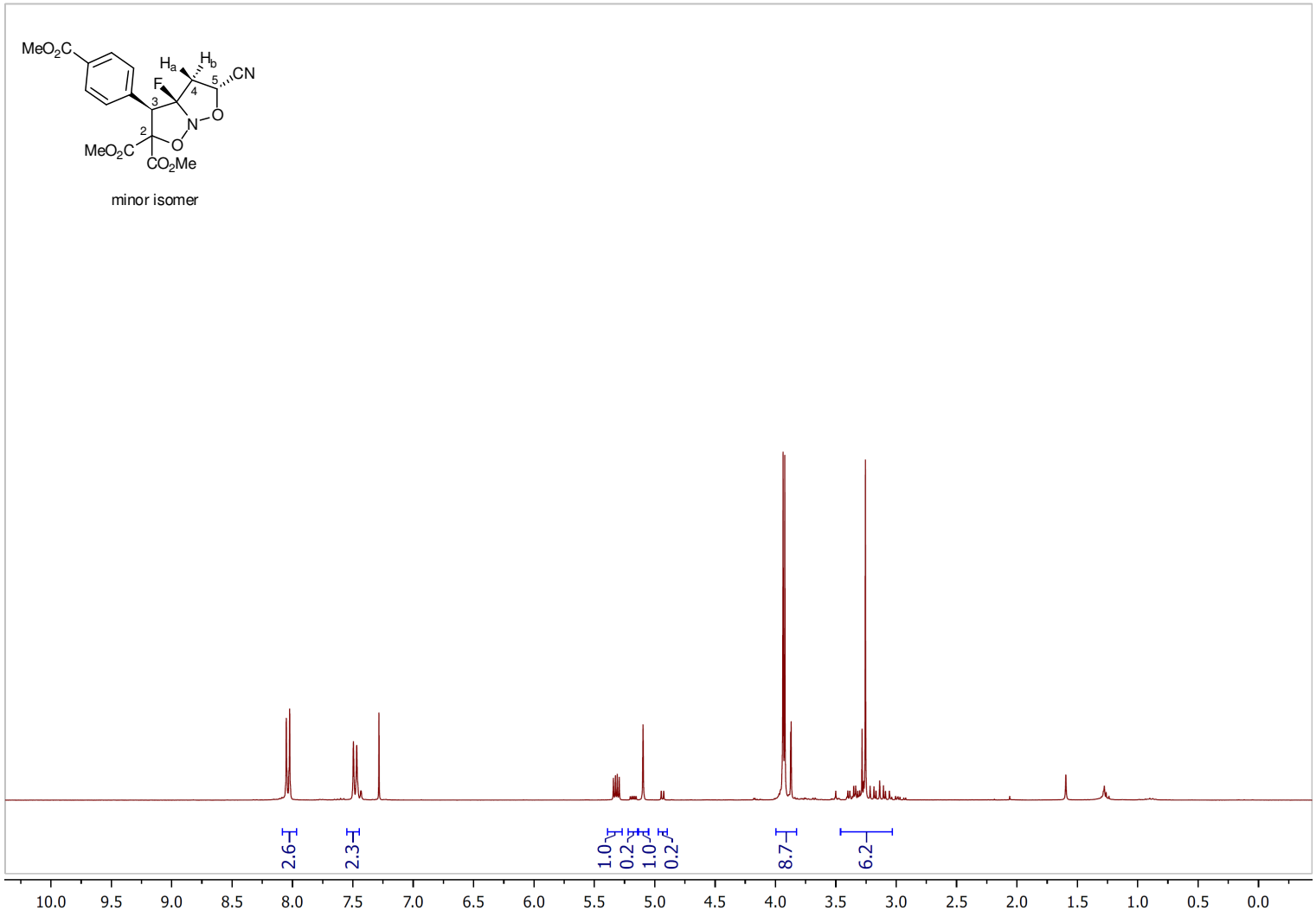

166.92
166.38
164.33
135.33
135.29
130.70
130.60
130.59
129.58
120.46
117.46
115.43
92.05
66.58
56.30
56.00
54.41
52.93
52.29
41.74
41.36
MeO2C
F
CN
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

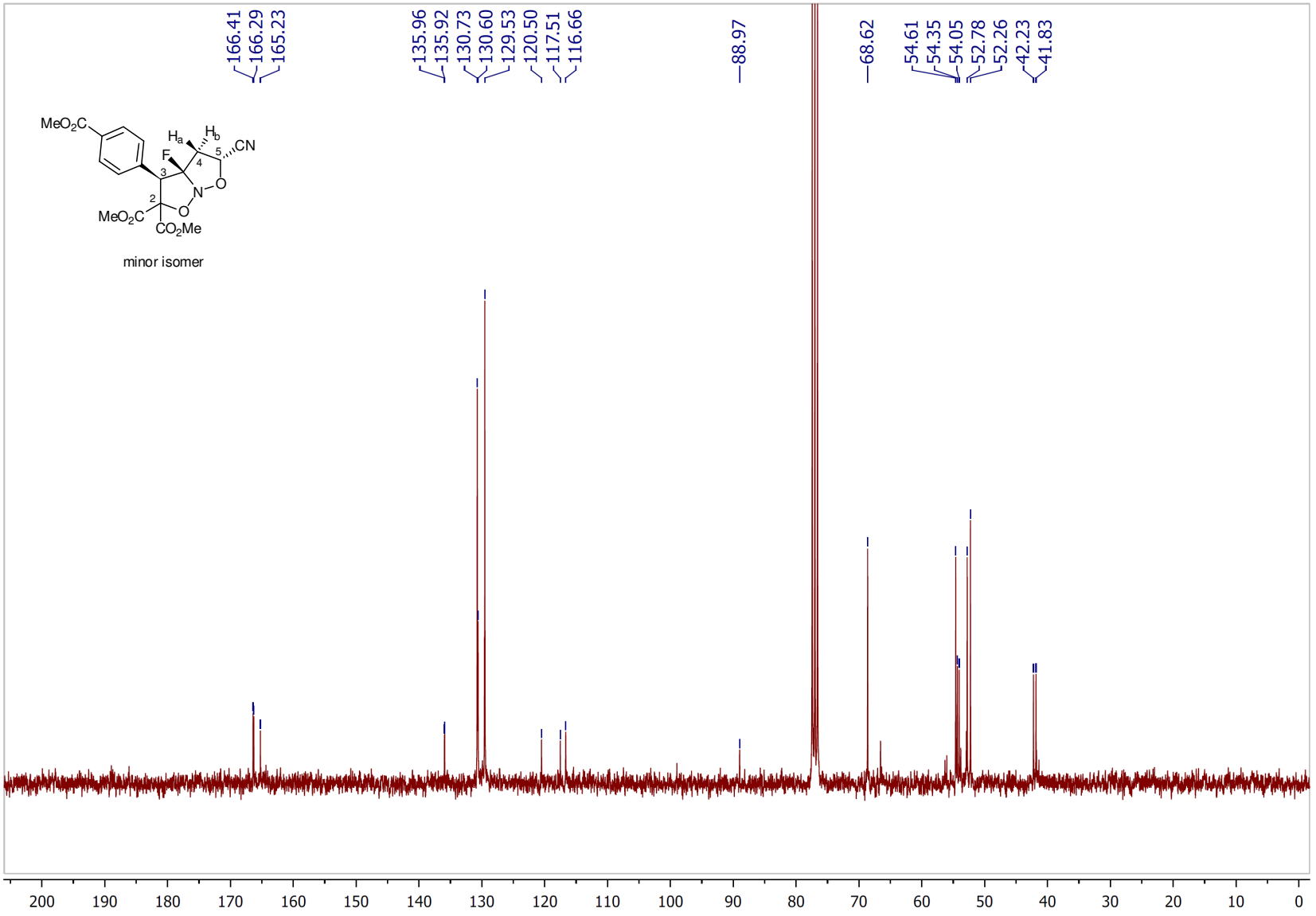

MeO2C
F
CN
N
O
MeO2C
O
CO2Me
major isomer
-132.5
-133.0
-133.5
-134.0
-134.5
-135.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

***rel*-(3R,3aR,5R)-Dimethyl 5-cyano-3a-fluoro-3-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'm** (enriched minor isomer)

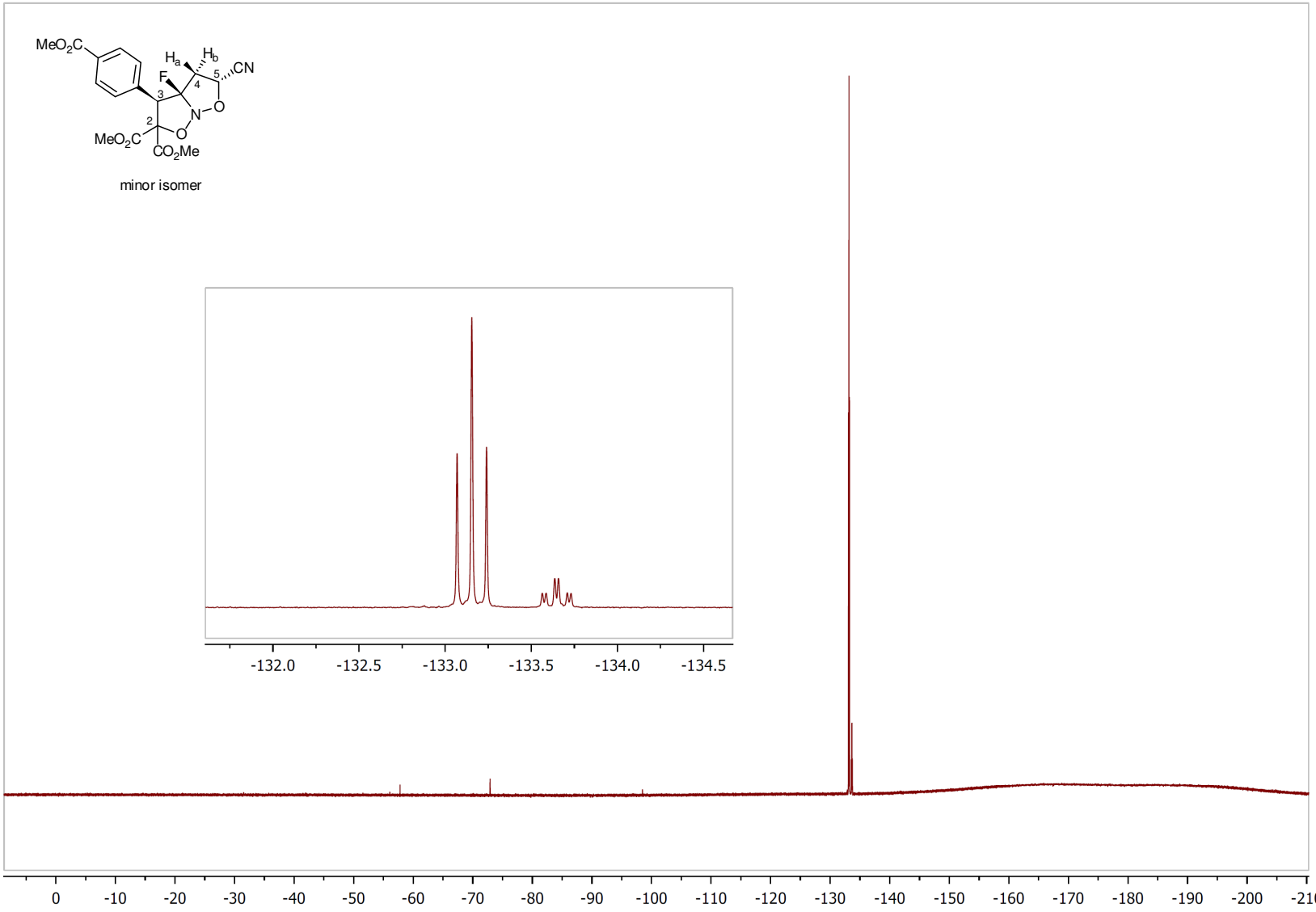
^{1}H NMR



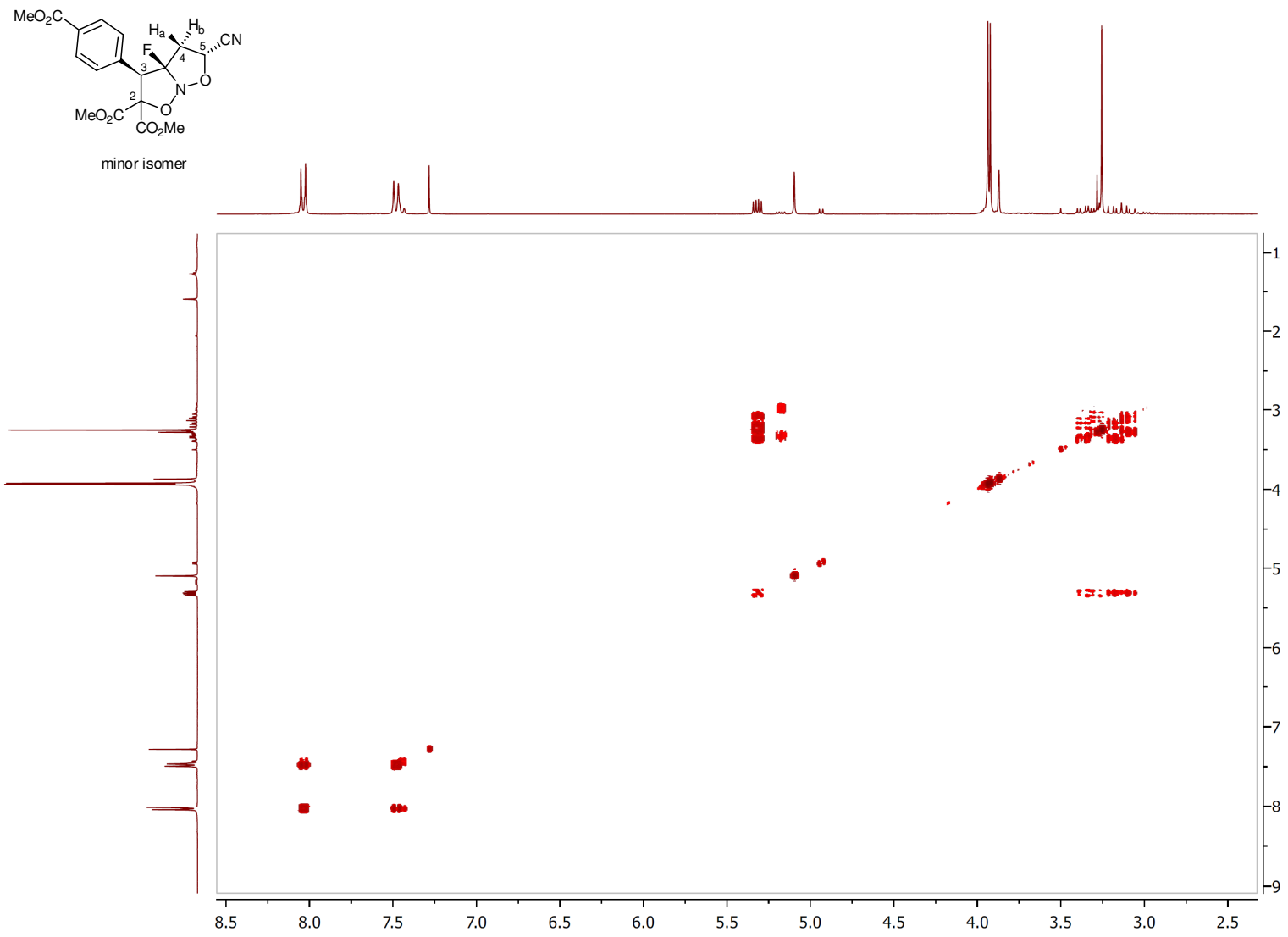
^{13}C NMR


166.41
166.29
165.23
135.96
135.92
130.73
130.60
129.53
120.50
117.51
116.66
88.97
68.62
54.61
54.35
54.05
52.78
52.26
42.23
41.83
MeO2C
Ha
Hb
F
CN
3
4
5
2
N
O
MeO2C
CO2Me
minor isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

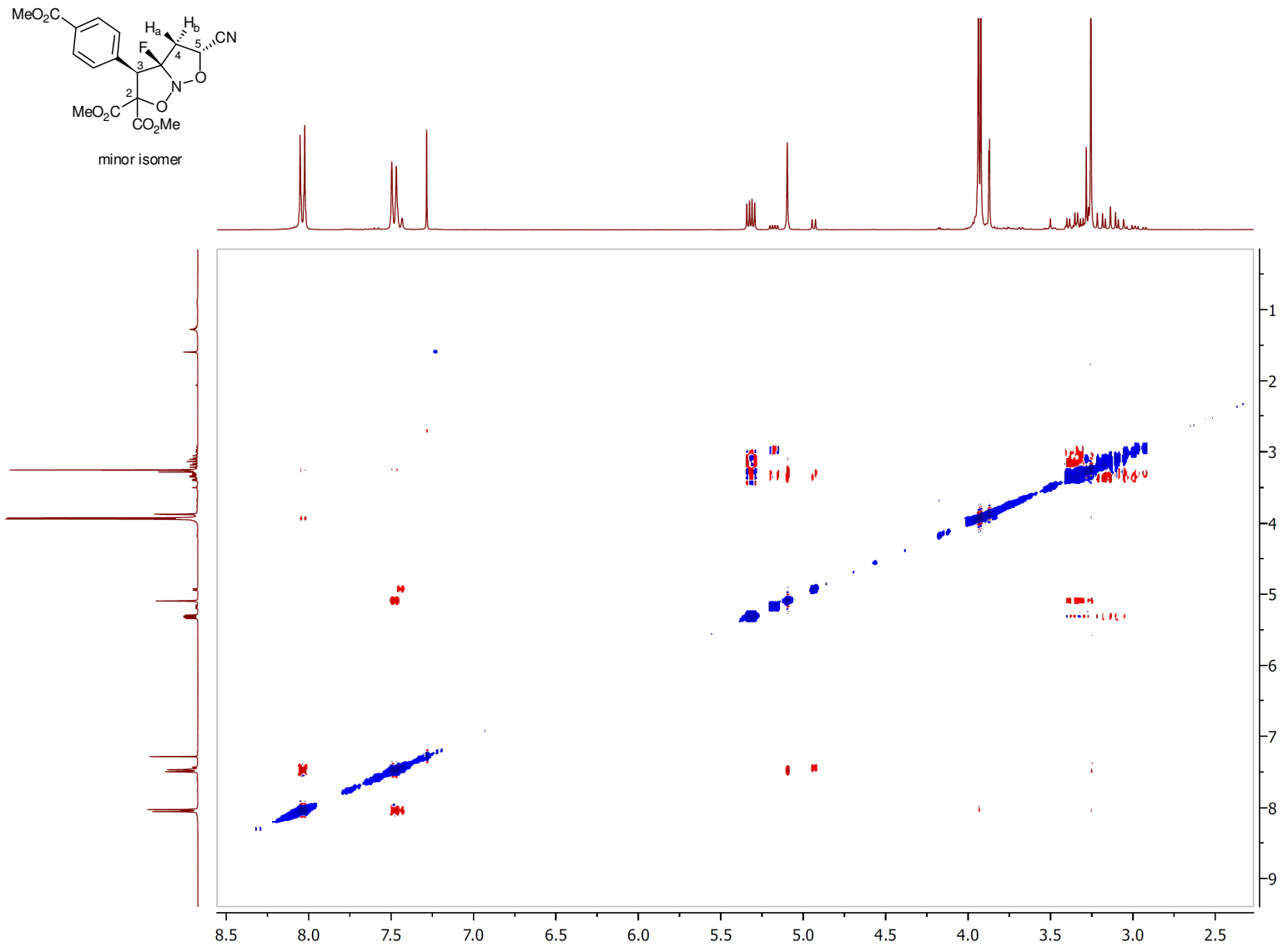
^{19}F NMR


MeO2C
Ha
Hb
F
3
4
5
CN
2
N
O
MeO2C
O
CO2Me
minor isomer
-132.0
-132.5
-133.0
-133.5
-134.0
-134.5
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210

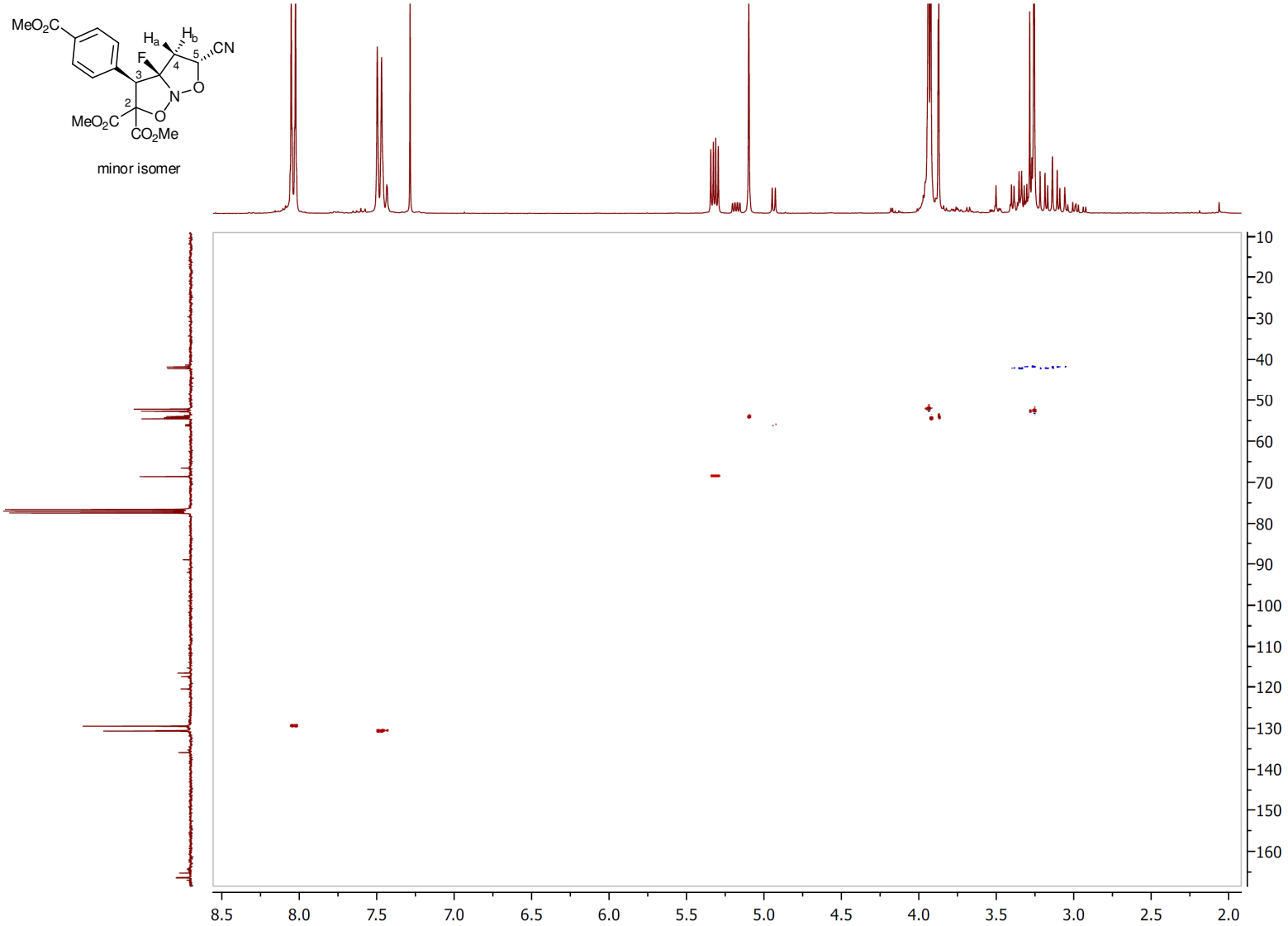
^{1}H-^{1}H COSY


MeO2C
Ha
Hb
F
3
4
5
CN
N
O
2
MeO2C
O
CO2Me
minor isomer
1
2
3
4
5
6
7
8
9
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

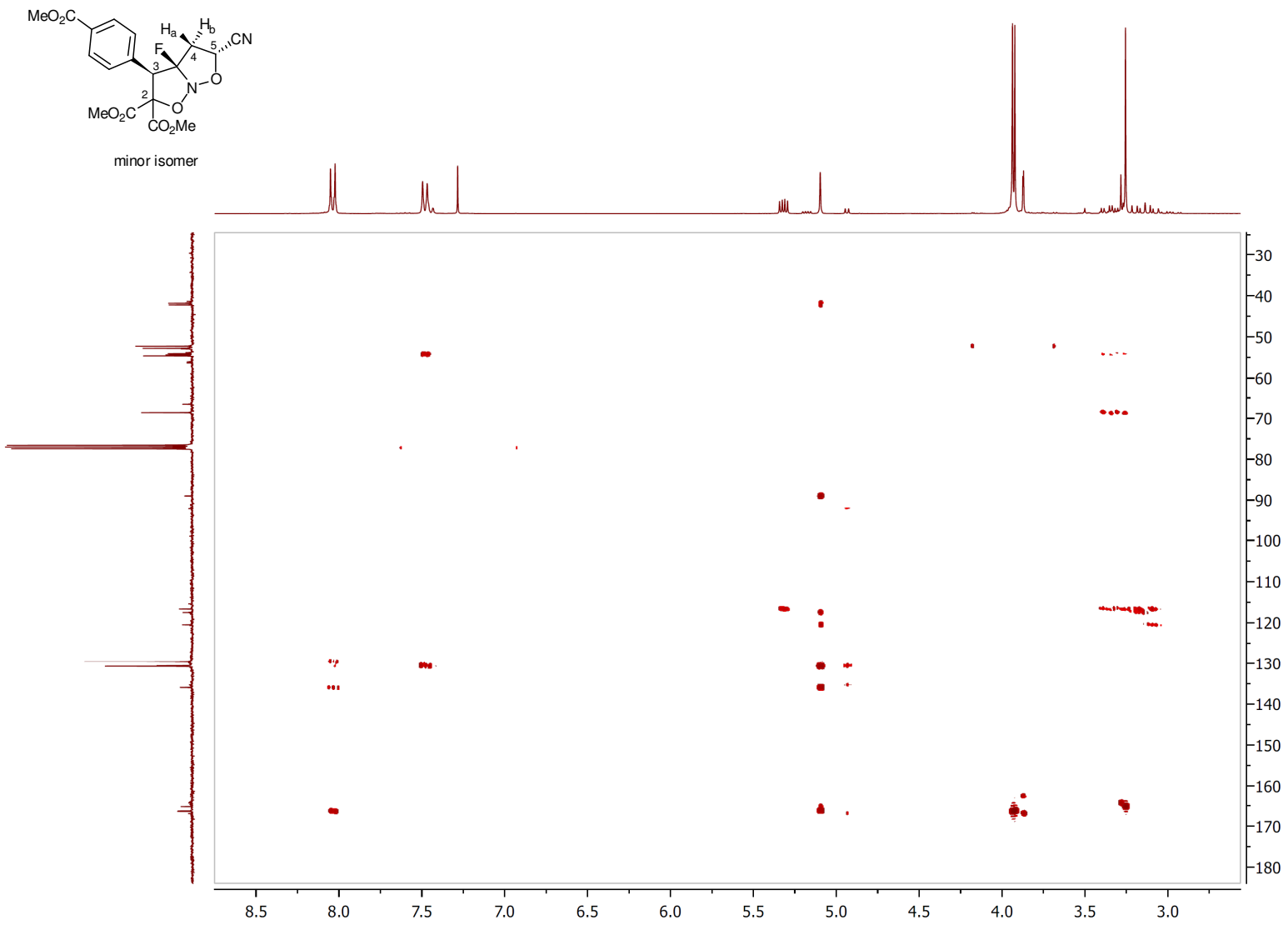
^{1}H-^{1}H NOESY


MeO2C
Ha
Hb
F
CN
3
4
5
2
N
O
MeO2C
CO2Me
minor isomer
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
1
2
3
4
5
6
7
8
9

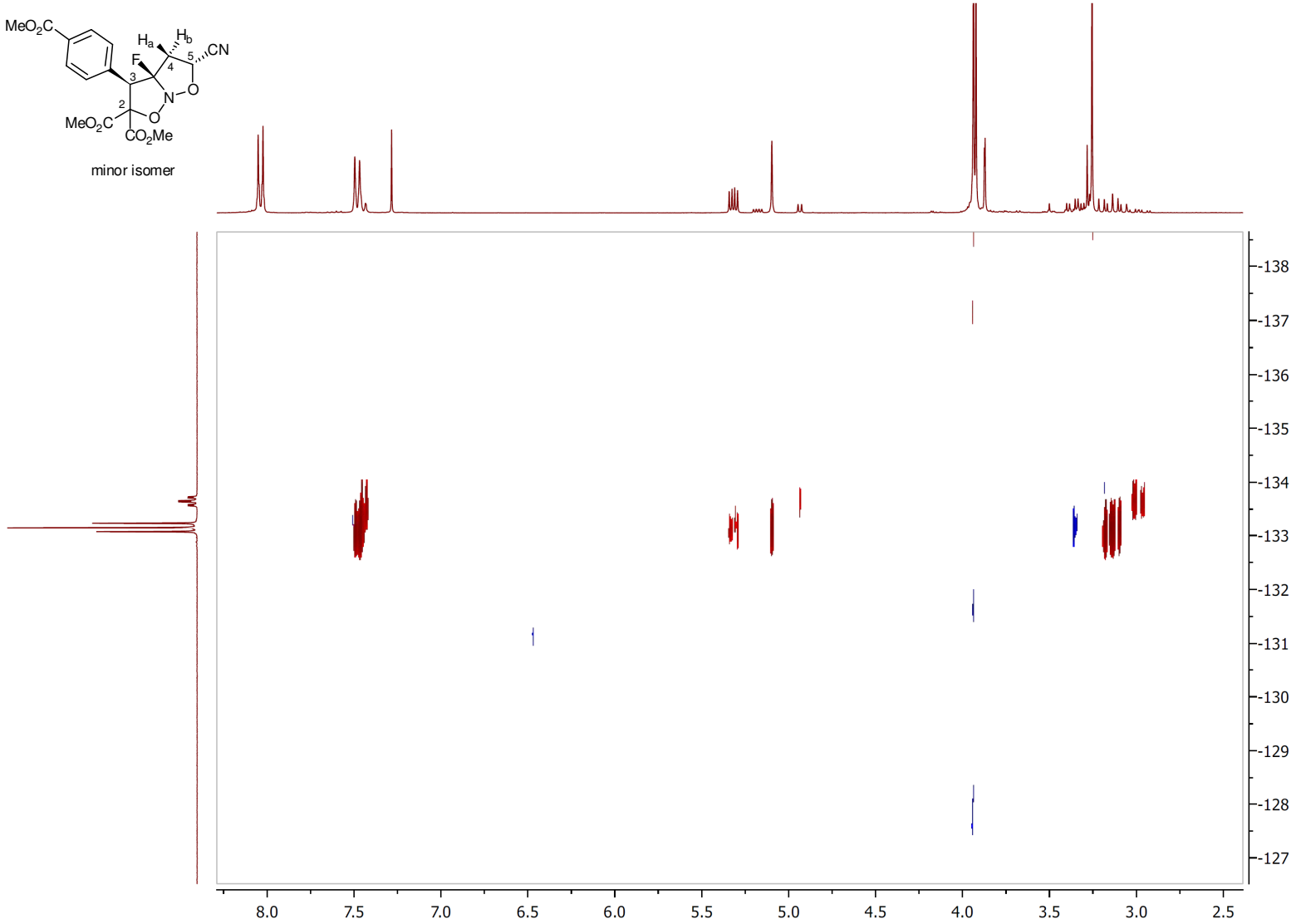
^{1}H-^{13}C HSQC


MeO2C
Ha
Hb
F
CN
3
4
5
2
N
O
MeO2C
CO2Me
minor isomer
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
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

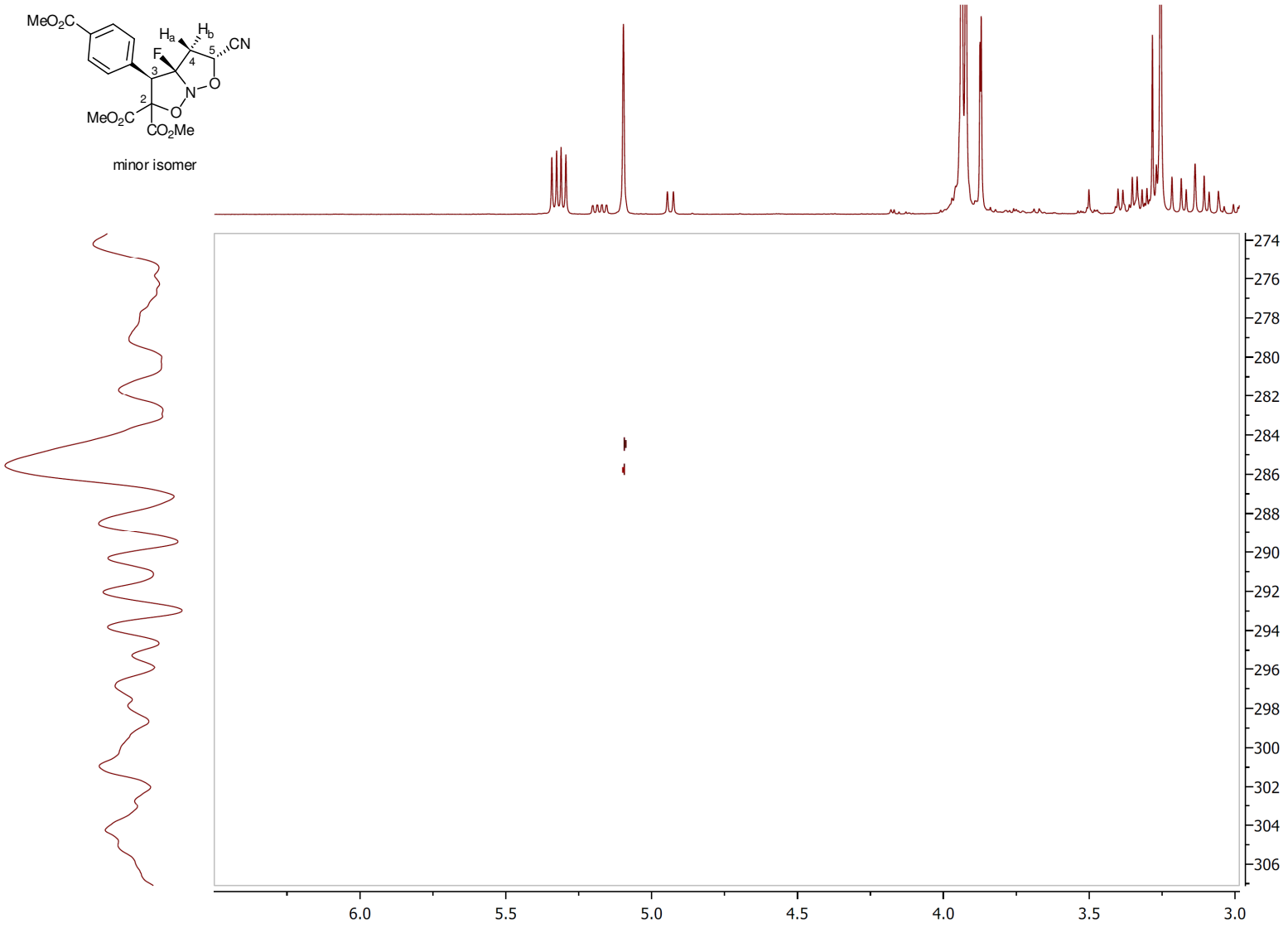
^{1}H-^{13}C HMBC


MeO2C
Ha
Hb
F
CN
3
4
5
2
N
O
MeO2C
CO2Me
minor isomer
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0

^{1}H-^{19}F HOESY

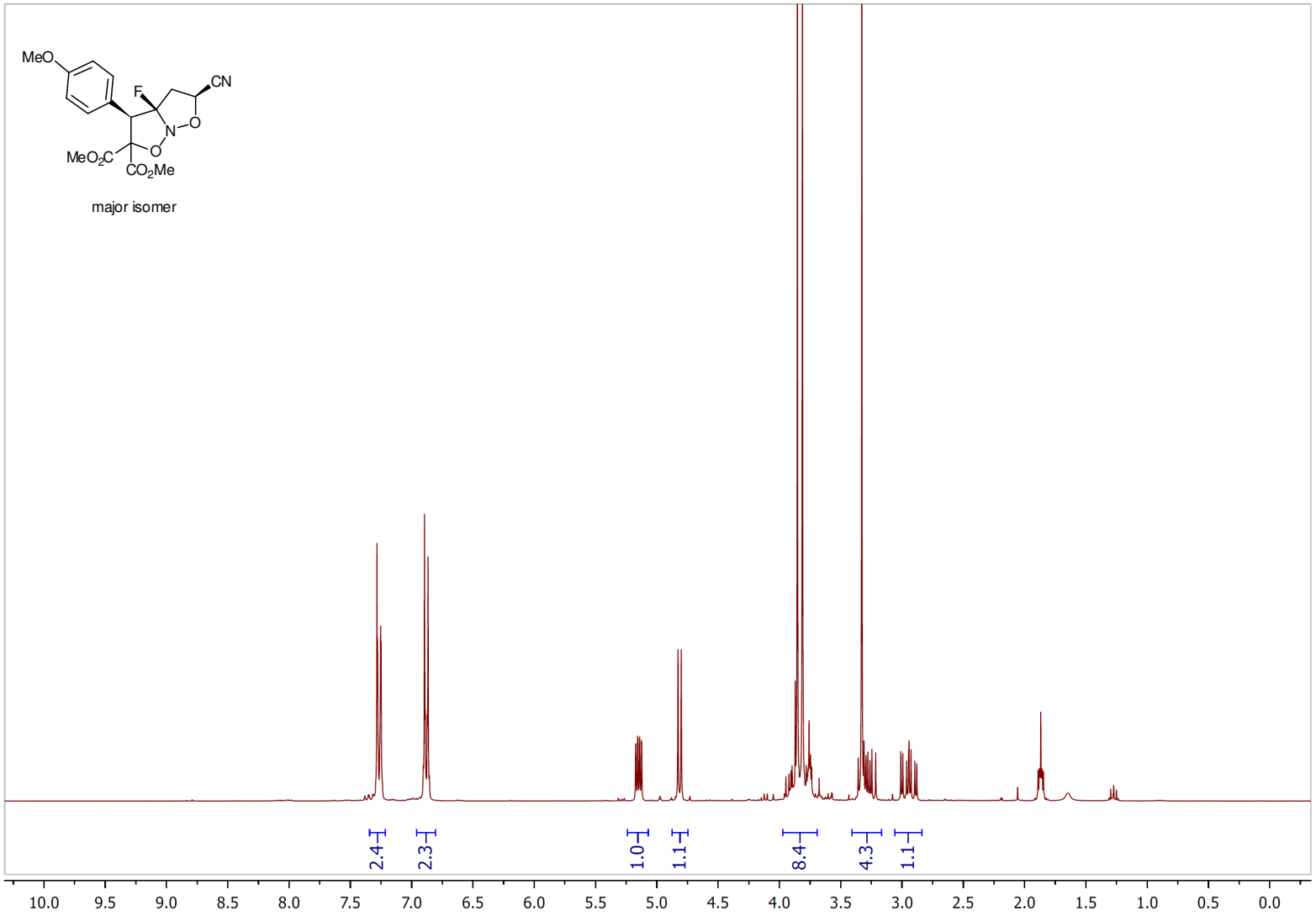

MeO2C
Ha
Hb
F
3
4
5
CN
2
N
O
MeO2C
CO2Me
minor isomer
-138
-137
-136
-135
-134
-133
-132
-131
-130
-129
-128
-127
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5

^{1}H-^{15}N HMBC

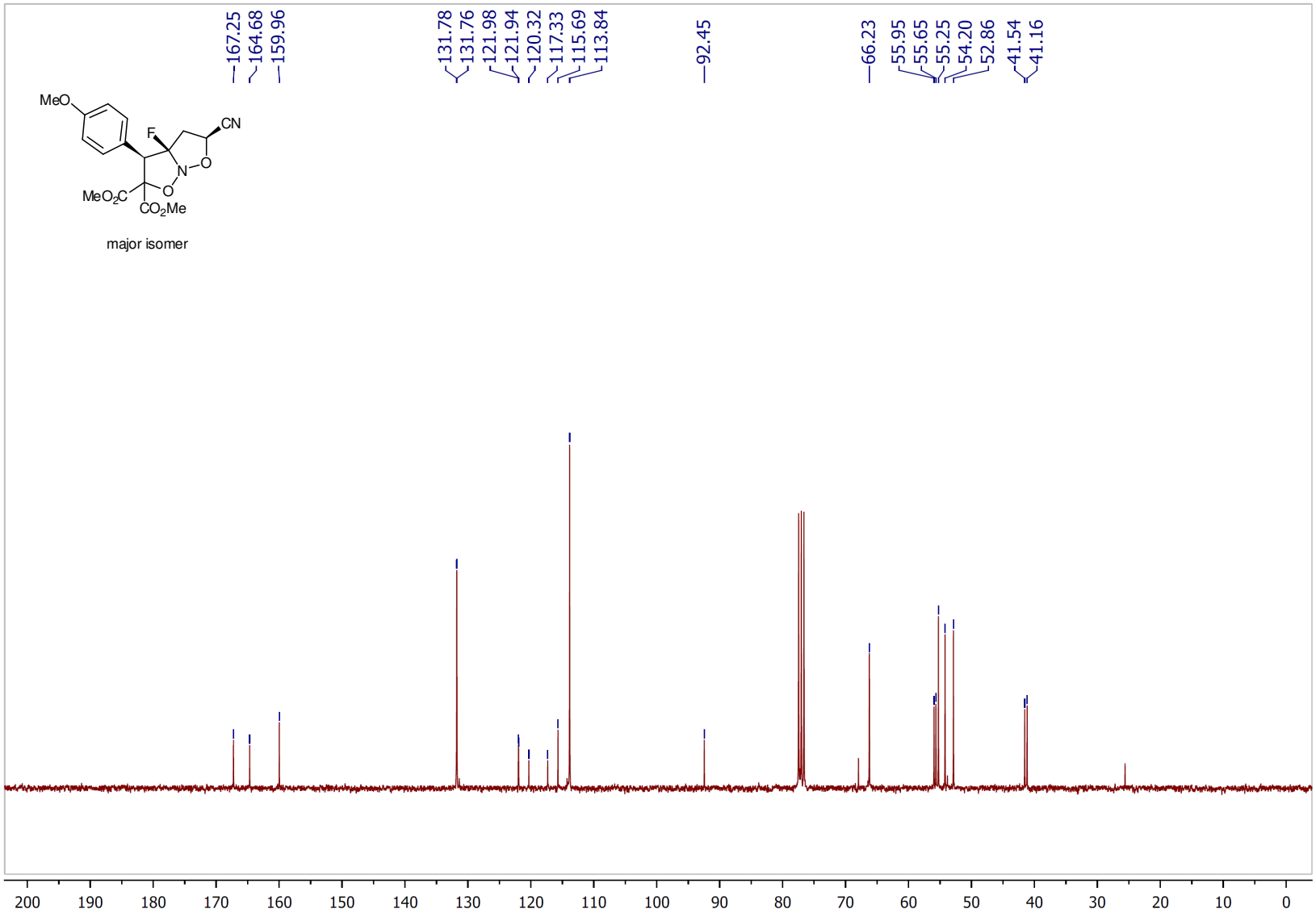

MeO2C
Ha
Hb
F
CN
3
4
5
2
N
O
MeO2C
O
CO2Me
minor isomer
274
276
278
280
282
284
286
288
290
292
294
296
298
300
302
304
306
6.0
5.5
5.0
4.5
4.0
3.5
3.0

***rel*-(3R,3aR,5S)-Dimethyl 5-cyano-3a-fluoro-3-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4n** (major isomer)

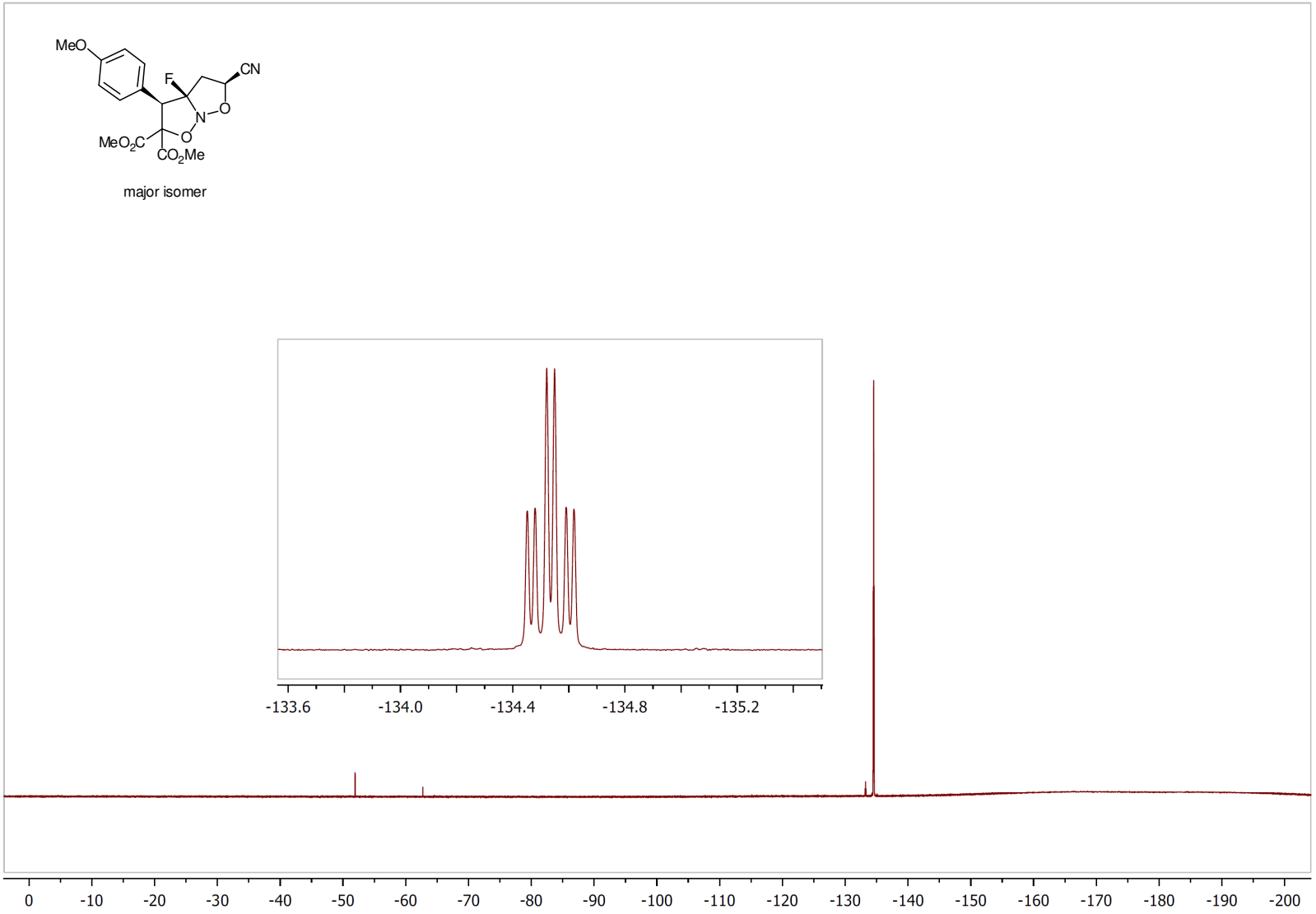
^{1}H NMR



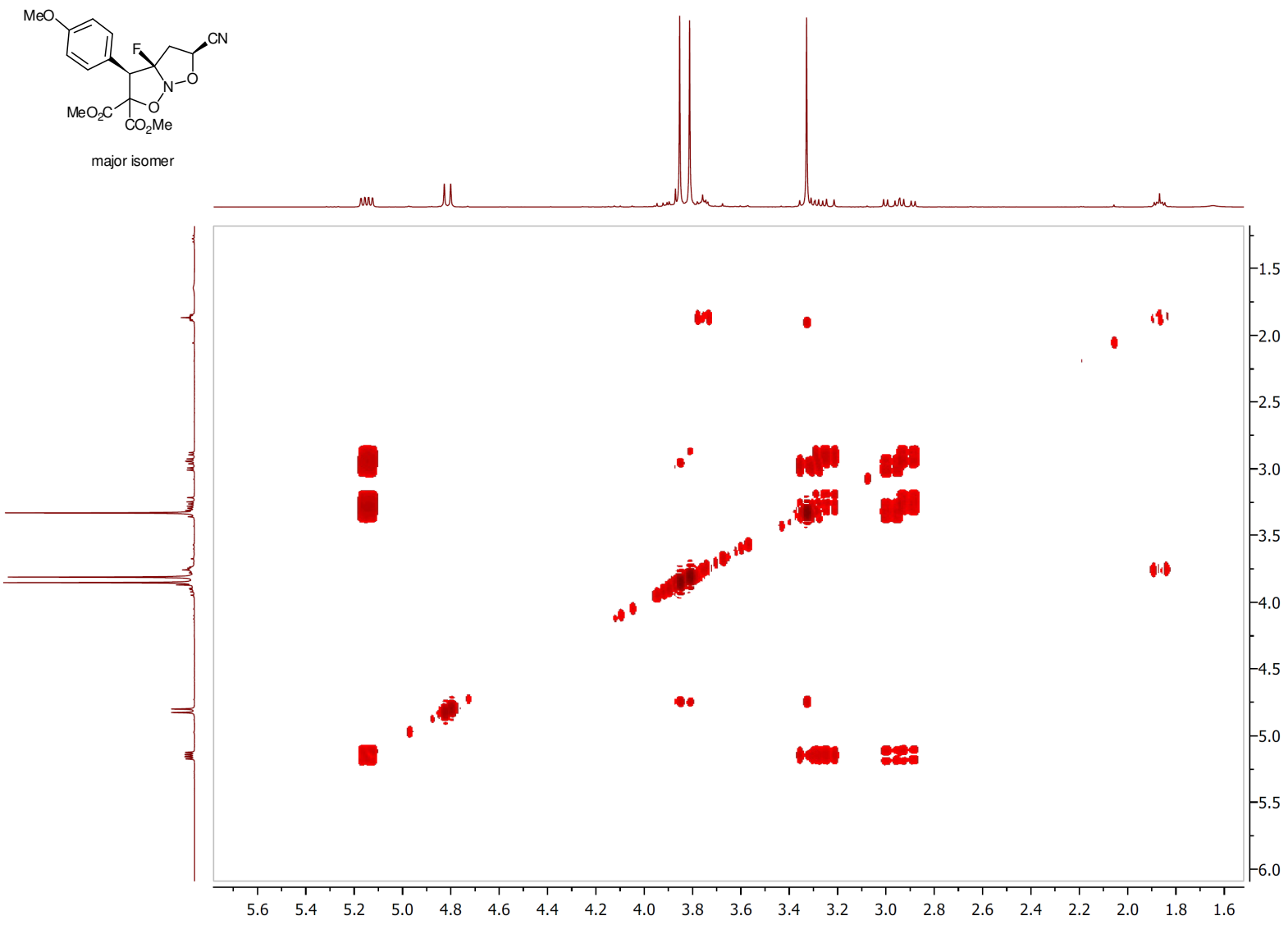
^{13}C NMR


167.25
164.68
159.96
131.78
131.76
121.98
121.94
120.32
117.33
115.69
113.84
92.45
66.23
55.95
55.65
55.25
54.20
52.86
41.54
41.16
MeO
F
CN
N
O
MeO2C
O
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

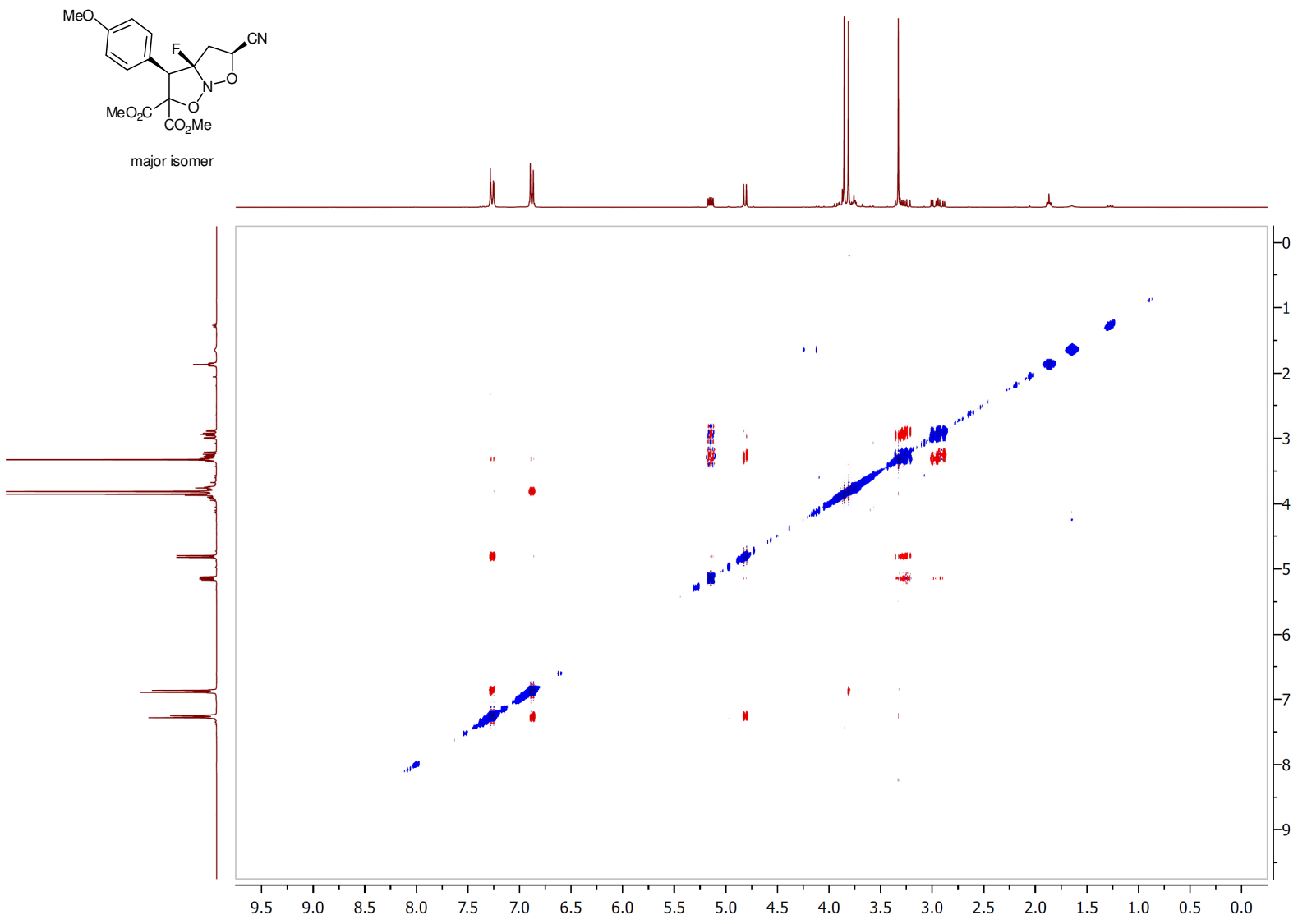
^{19}F NMR


MeO
F
CN
N
O
O
MeO2C
CO2Me
major isomer
-133.6
-134.0
-134.4
-134.8
-135.2
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

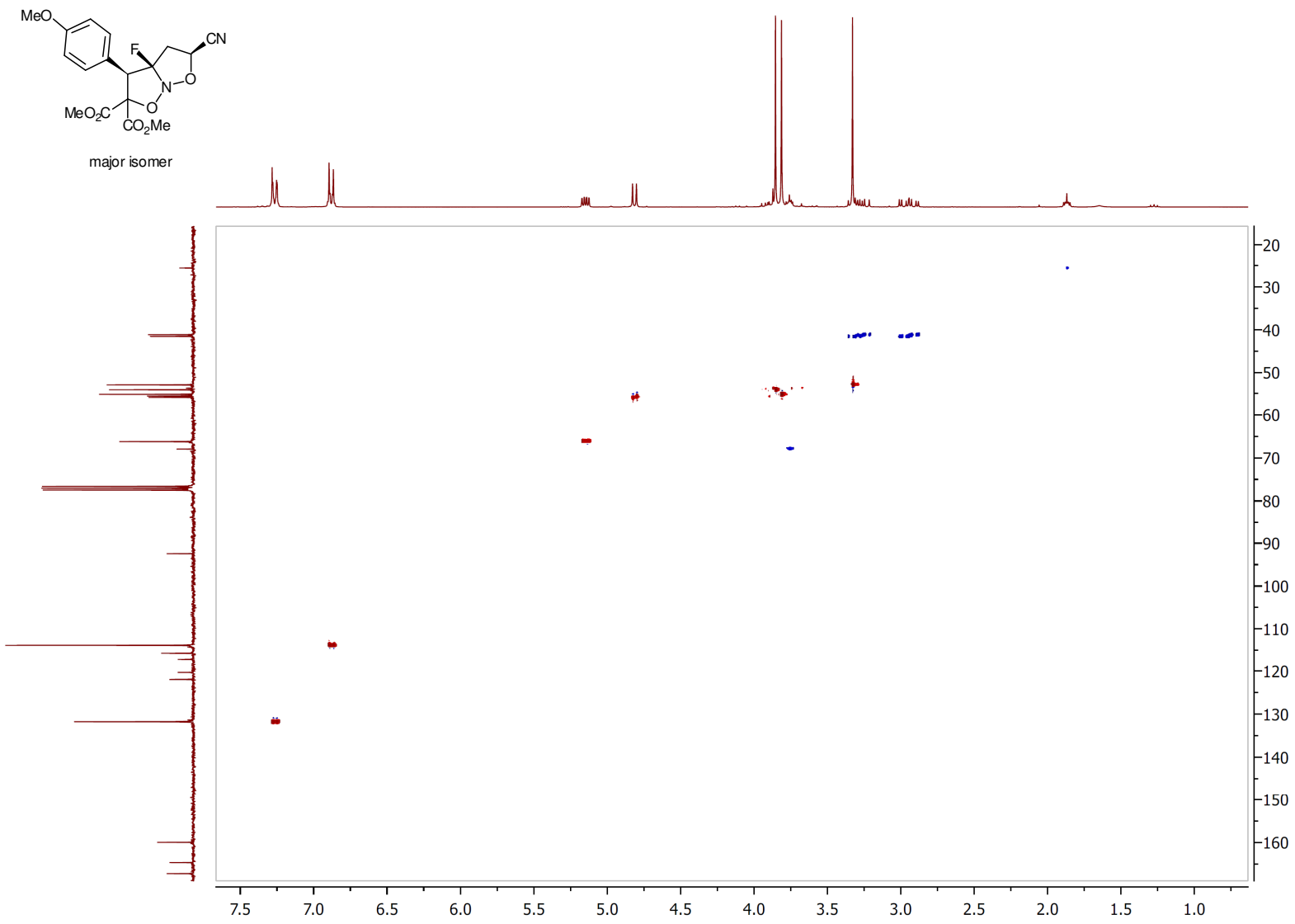
^{1}H-^{1}H COSY


MeO
F
CN
N
O
O
MeO2C
CO2Me
major isomer
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6

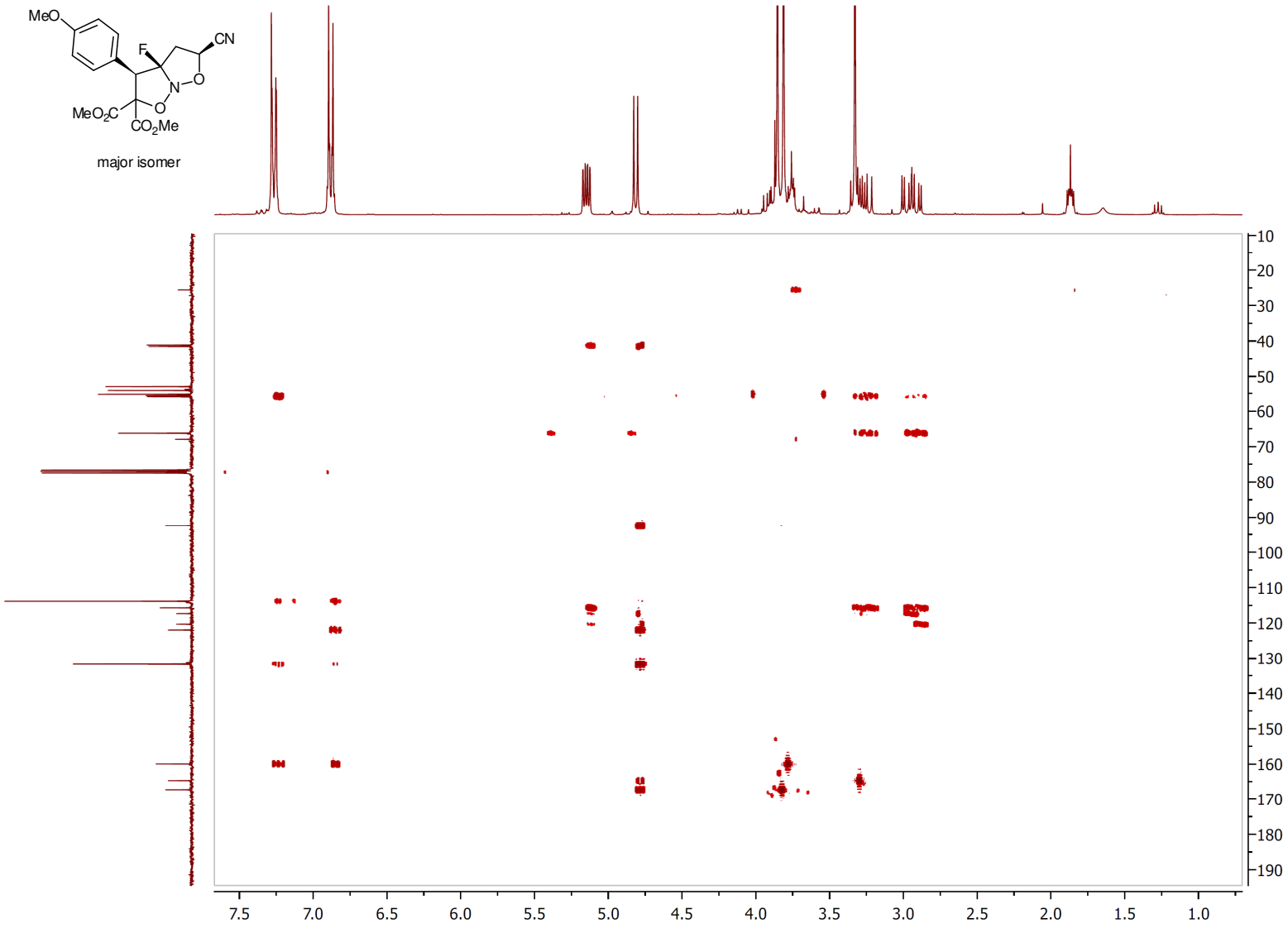
^{1}H-^{1}H NOESY


MeO
F
CN
N
O
O
MeO2C
CO2Me
major isomer
0
1
2
3
4
5
6
7
8
9
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

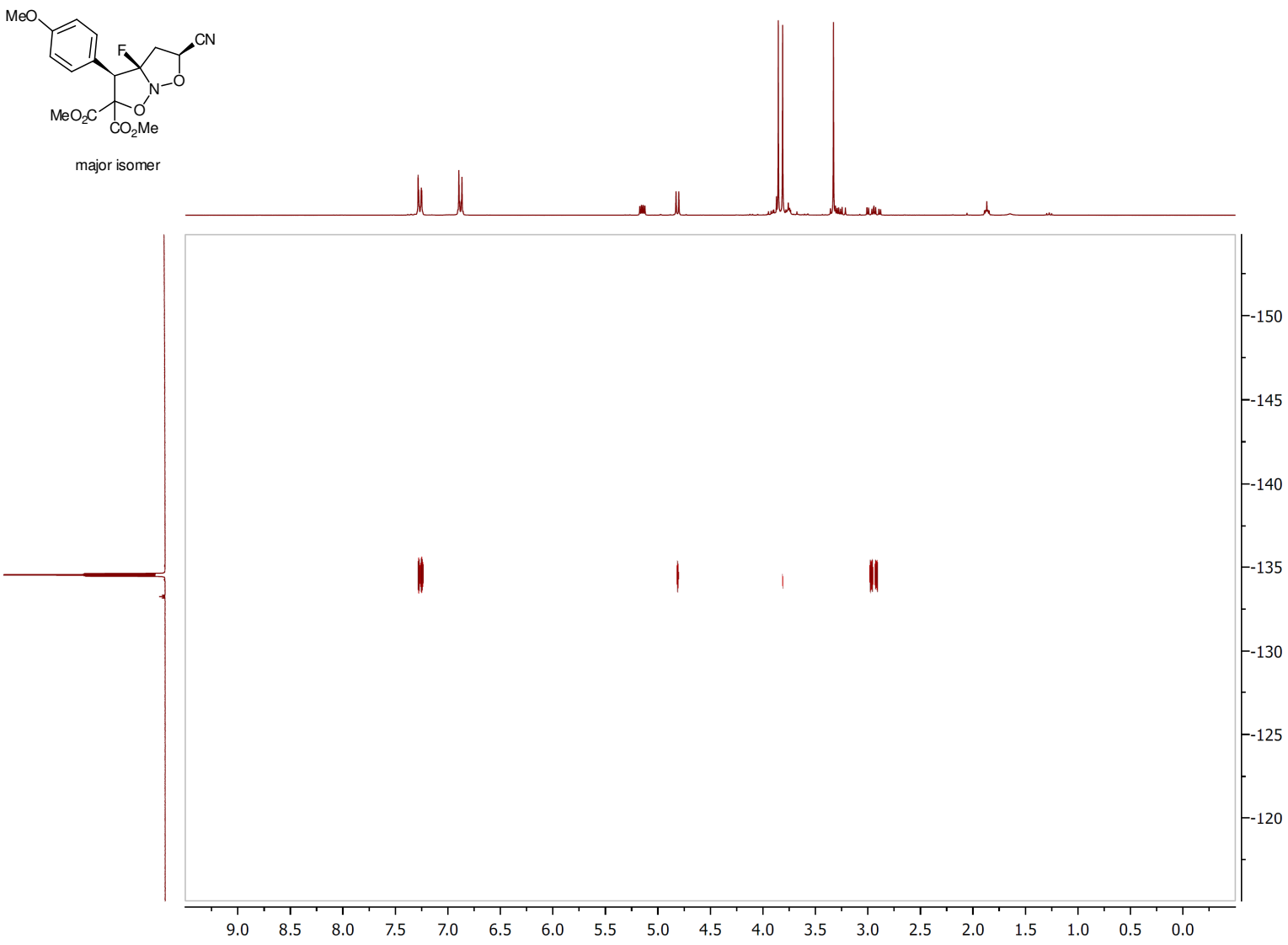
^{1}H-^{13}C HSQC


MeO
F
CN
N
O
O
MeO2C
CO2Me
major isomer
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
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

^{1}H-^{13}C HMBC

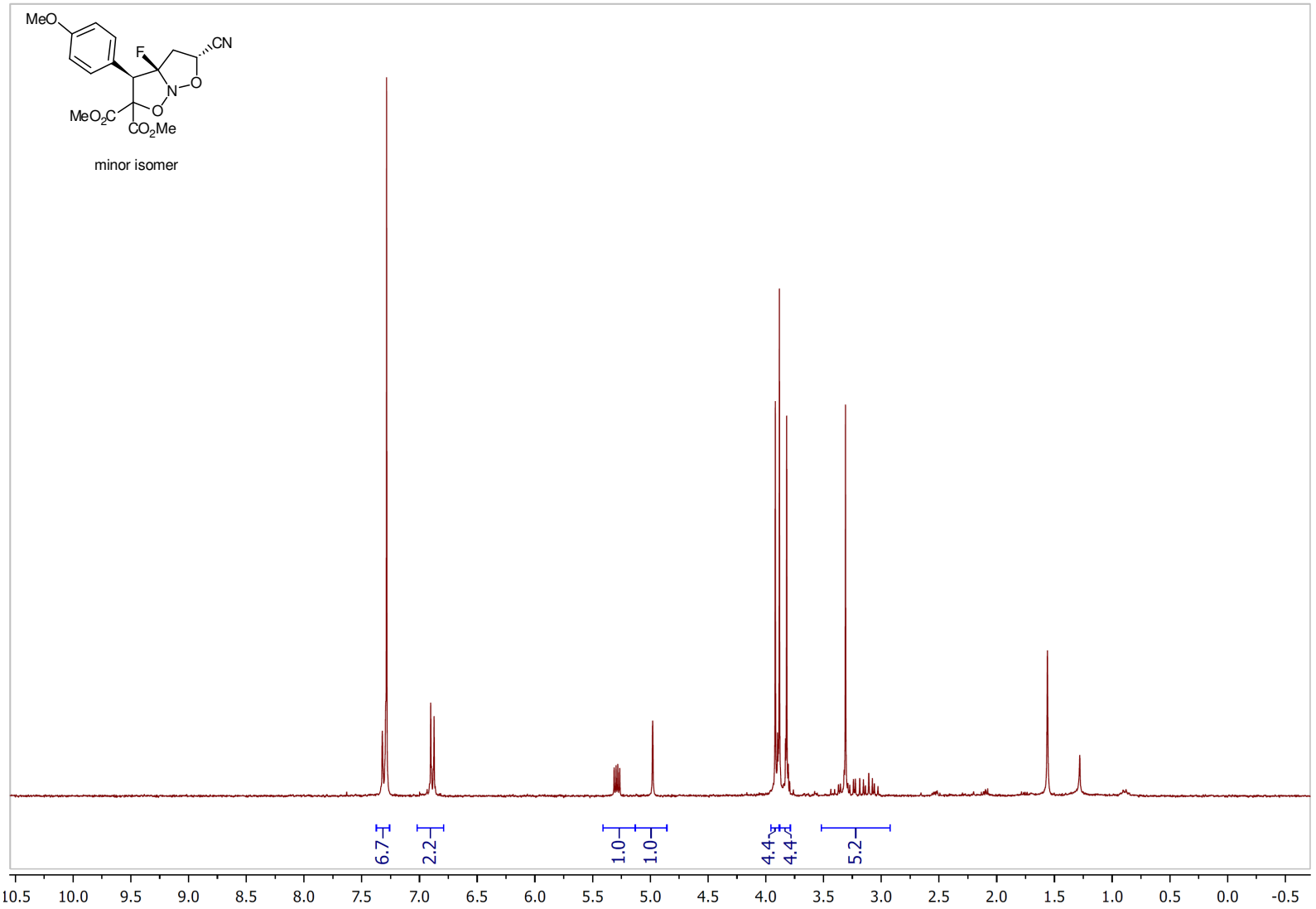

MeO
F
CN
N
O
O
MeO2C
CO2Me
major isomer
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

^{1}H-^{19}F HOESY

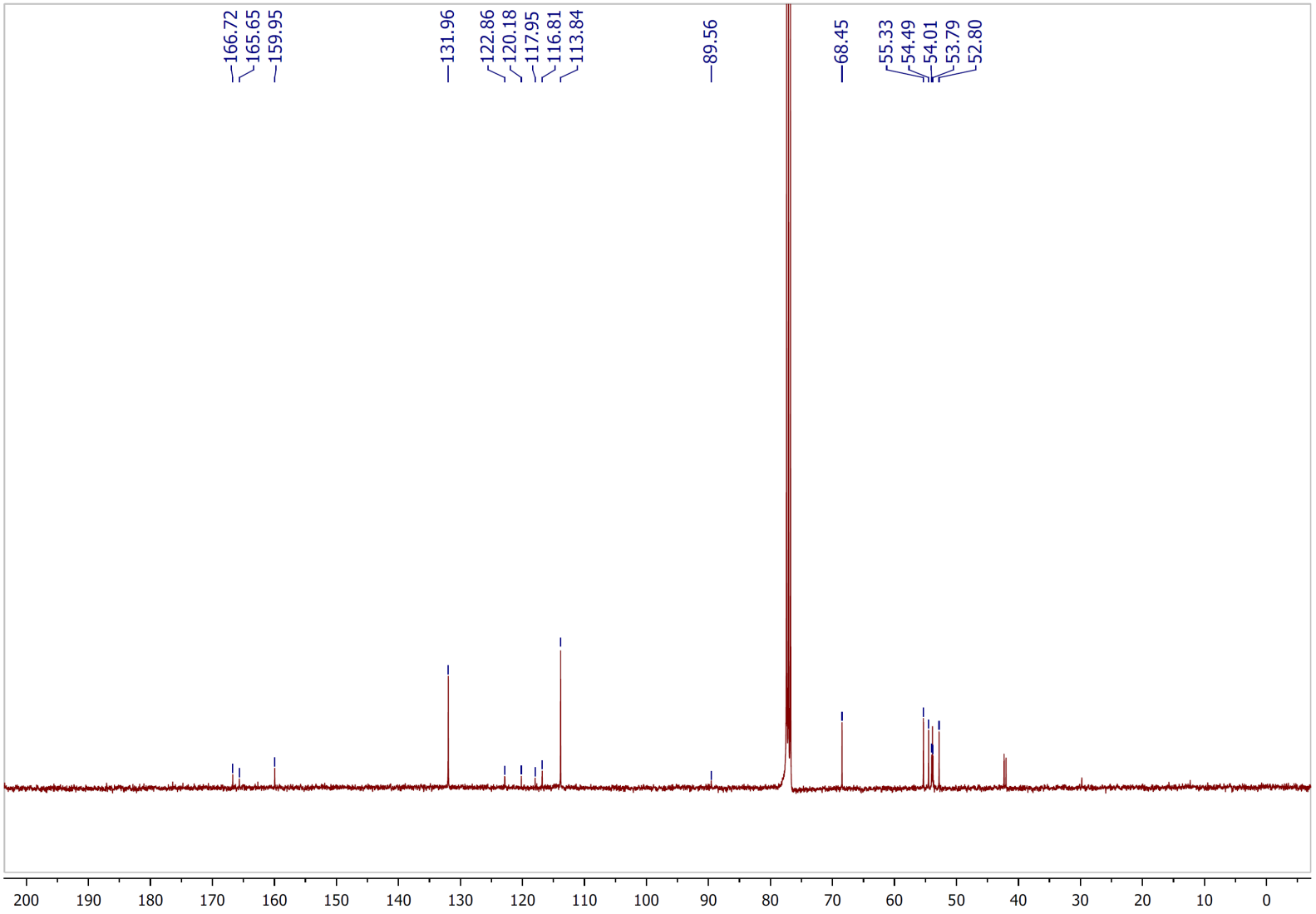

MeO
F
CN
N
O
O
MeO2C
CO2Me
major isomer
-150
-145
-140
-135
-130
-125
-120
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

***rel*-(3R,3aR,5R)-Dimethyl 5-cyano-3a-fluoro-3-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'n**

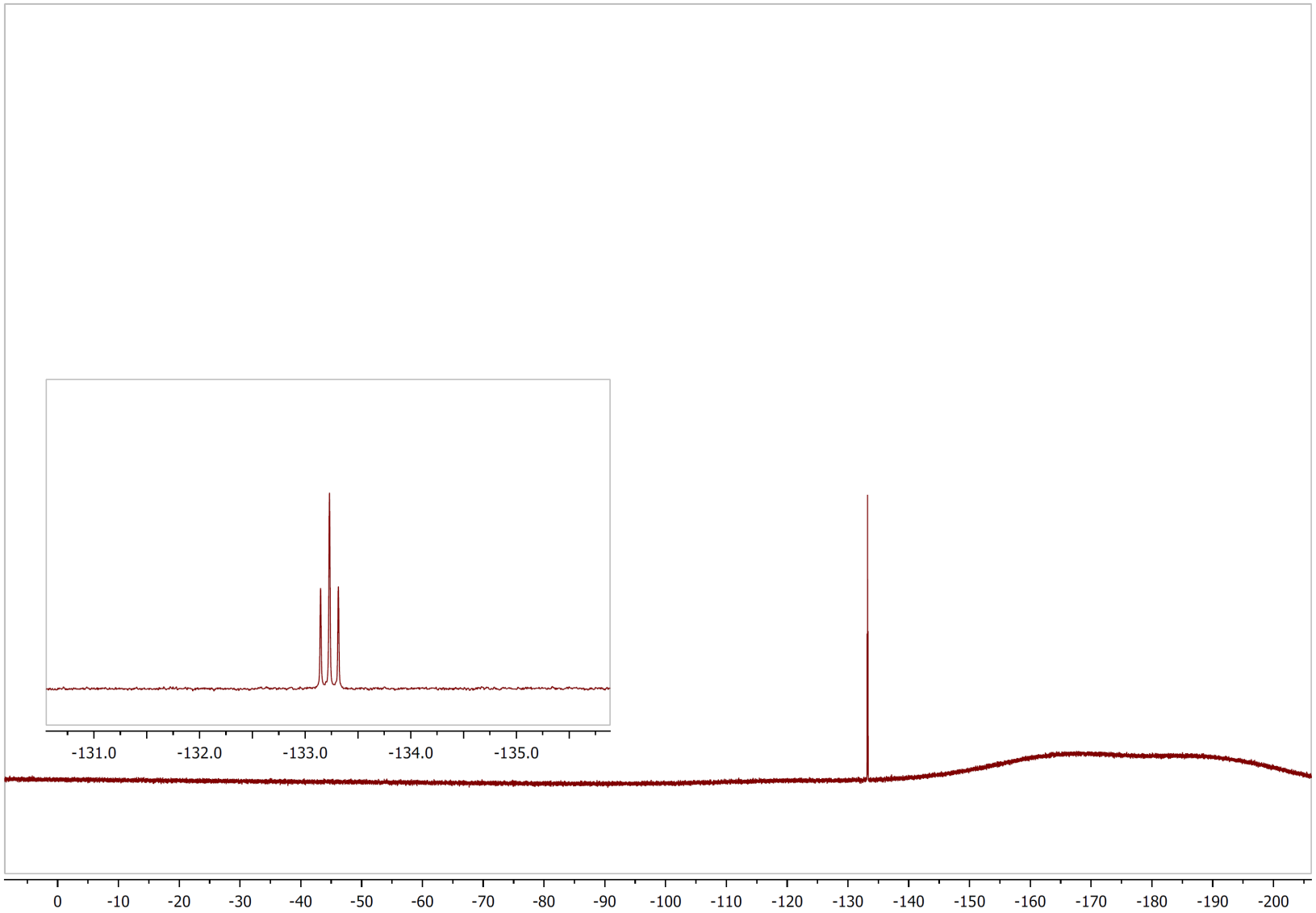
^{1}H NMR



^{13}C NMR

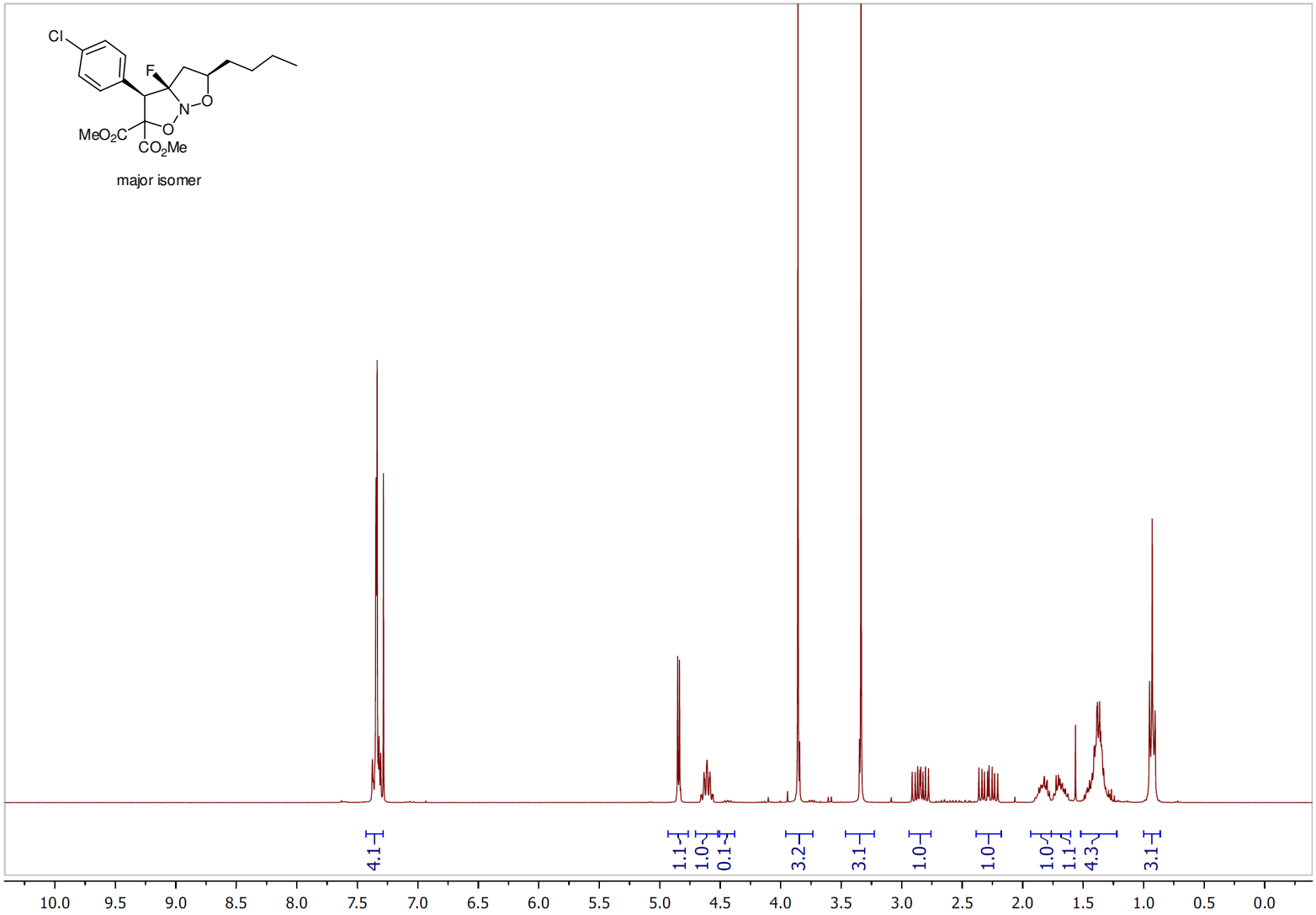

166.72
165.65
159.95
131.96
122.86
120.18
117.95
116.81
113.84
89.56
68.45
55.33
54.49
54.01
53.79
52.80
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

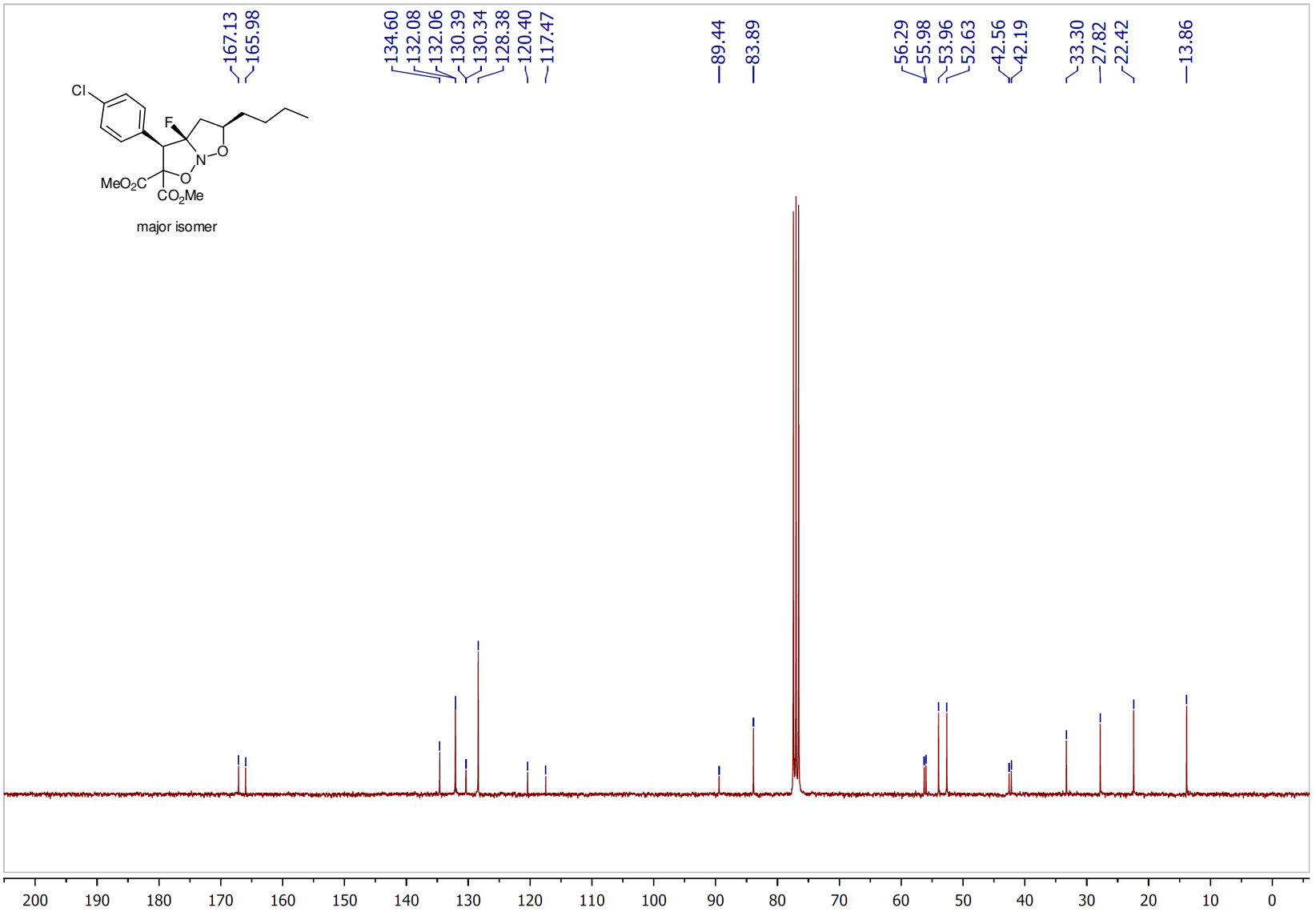

-131.0
-132.0
-133.0
-134.0
-135.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

***rel*-(3R,3aR,5R)-Dimethyl 5-butyl-3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4o** (major isomer)

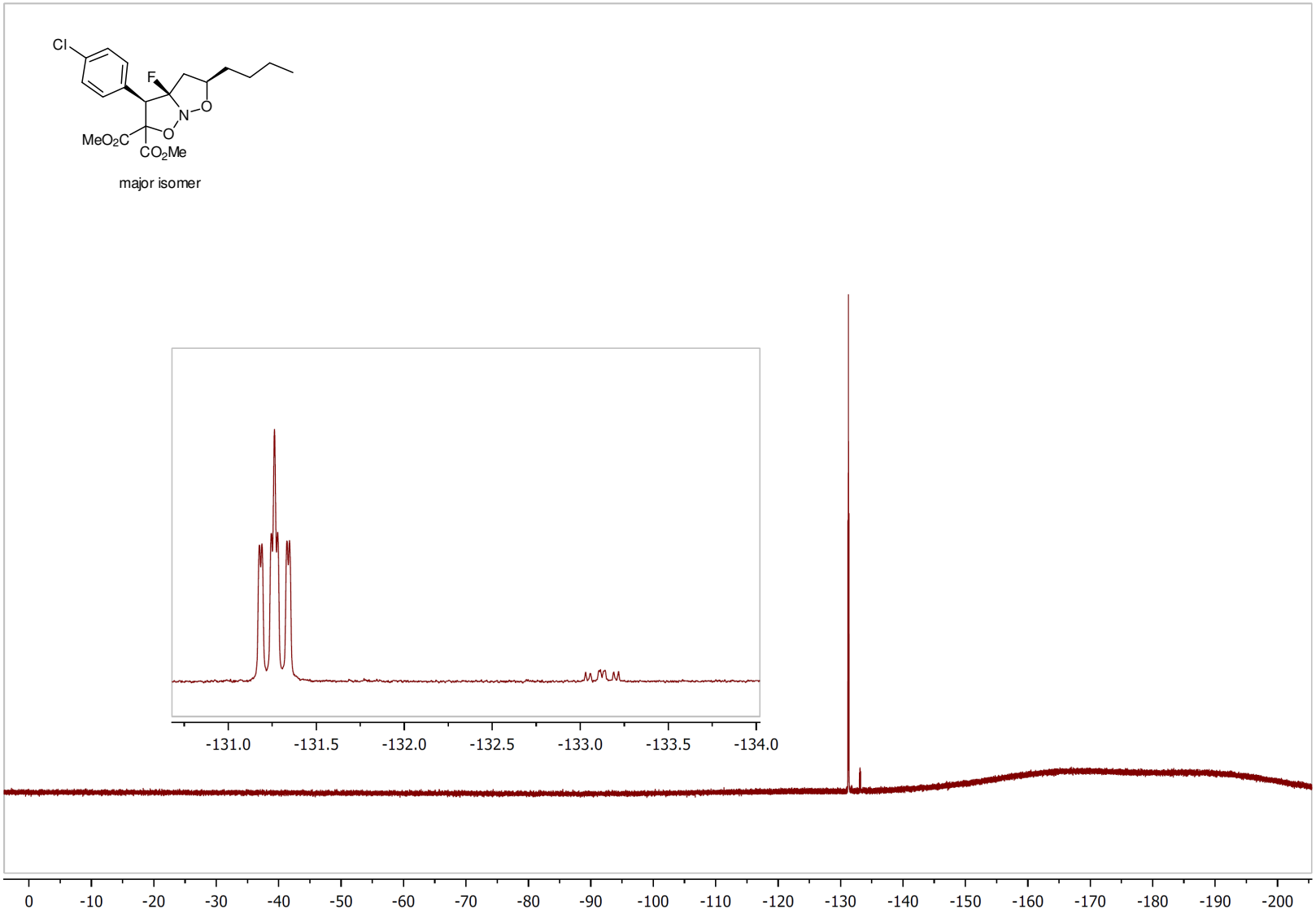
^{1}H NMR



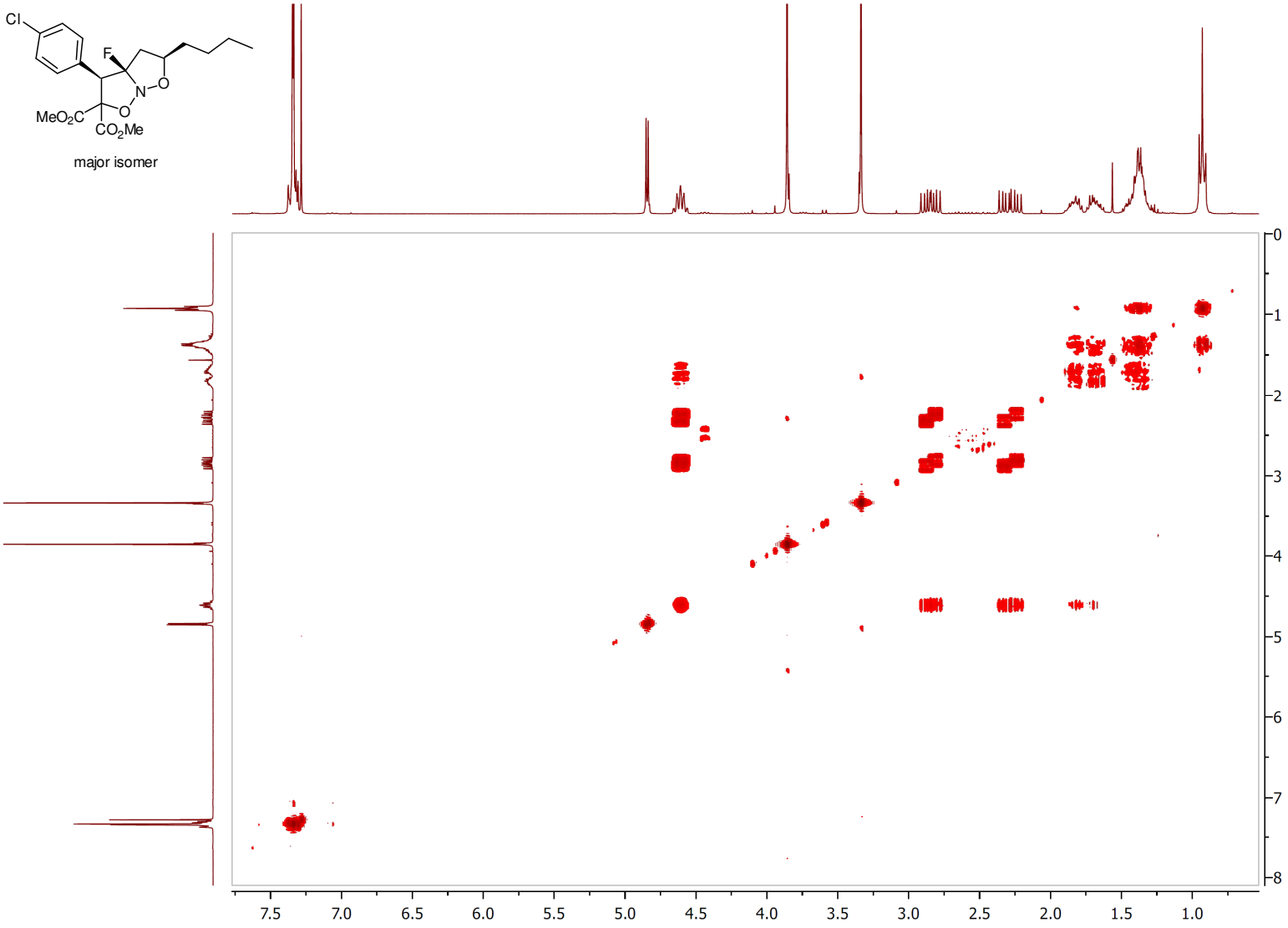
^{13}C NMR


167.13
165.98
134.60
132.08
132.06
130.39
130.34
128.38
120.40
117.47
89.44
83.89
56.29
55.98
53.96
52.63
42.56
42.19
33.30
27.82
22.42
13.86
Cl
F
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

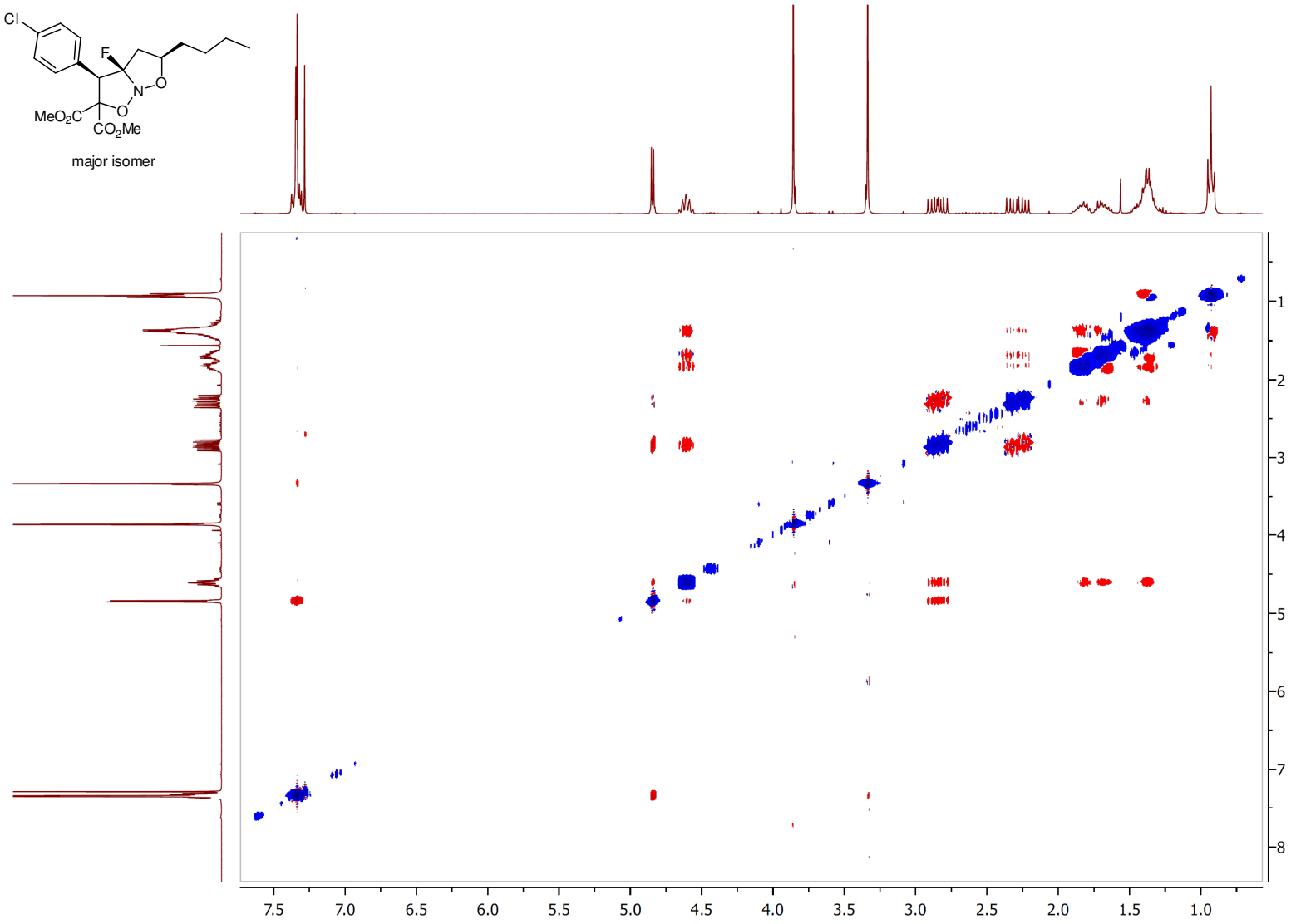
^{19}F NMR


Cl
F
N
O
O
MeO2C
CO2Me
major isomer
-131.0
-131.5
-132.0
-132.5
-133.0
-133.5
-134.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

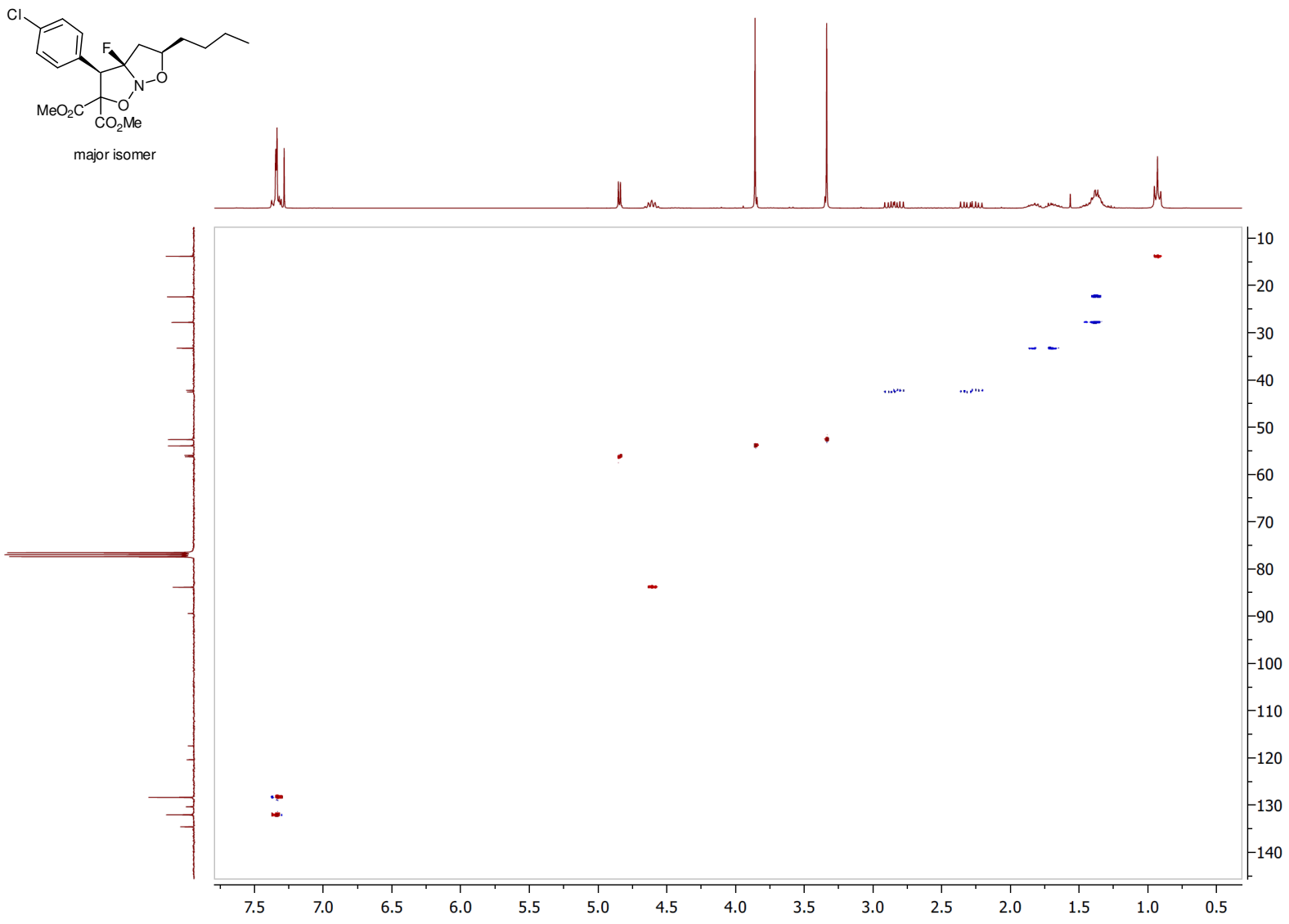
^{1}H-^{1}H COSY


Cl
F
N
O
O
MeO2C
CO2Me
major isomer
0
1
2
3
4
5
6
7
8
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

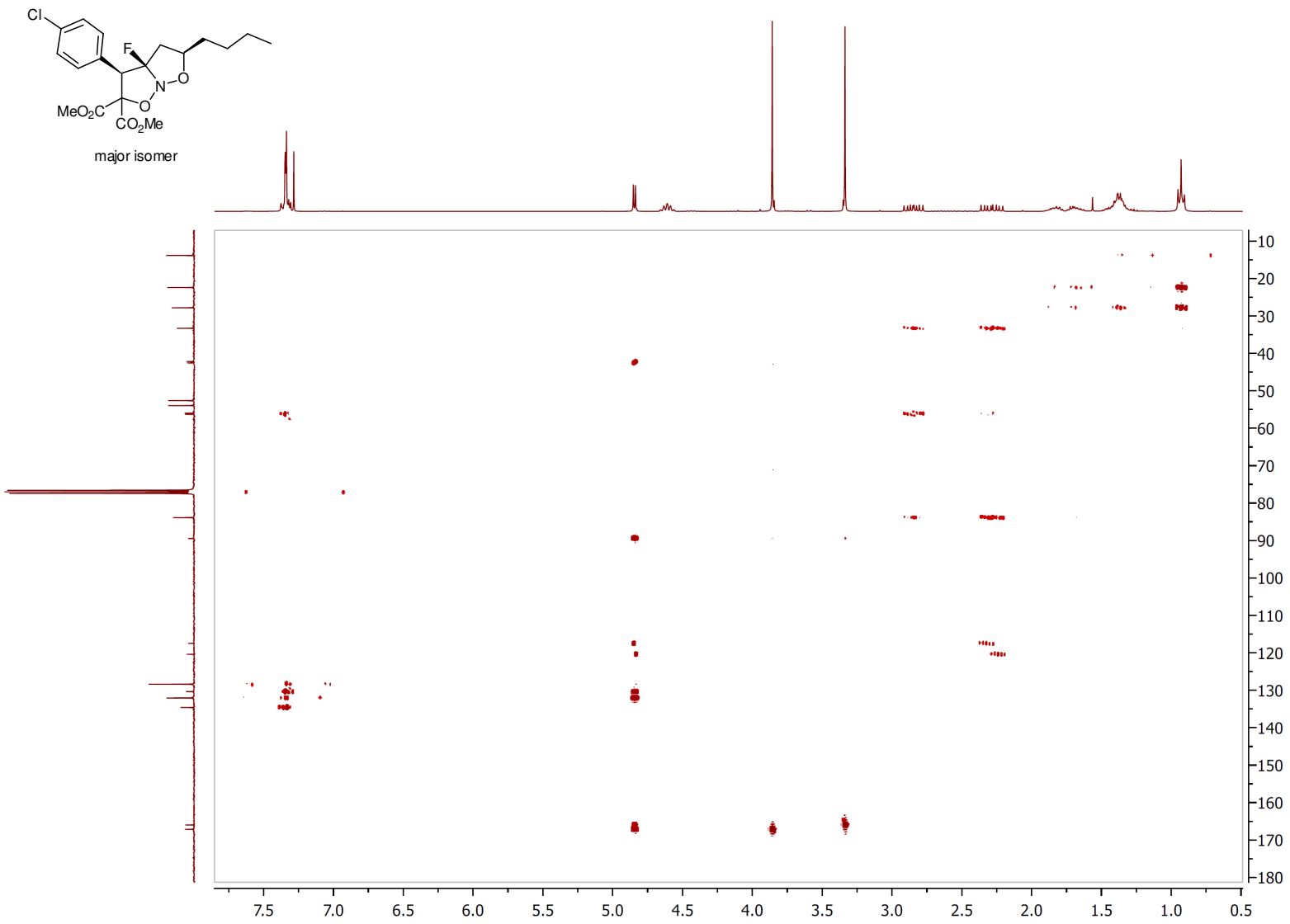
^{1}H-^{1}H NOESY


Cl
F
N
O
O
MeO2C
CO2Me
major isomer
1
2
3
4
5
6
7
8
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

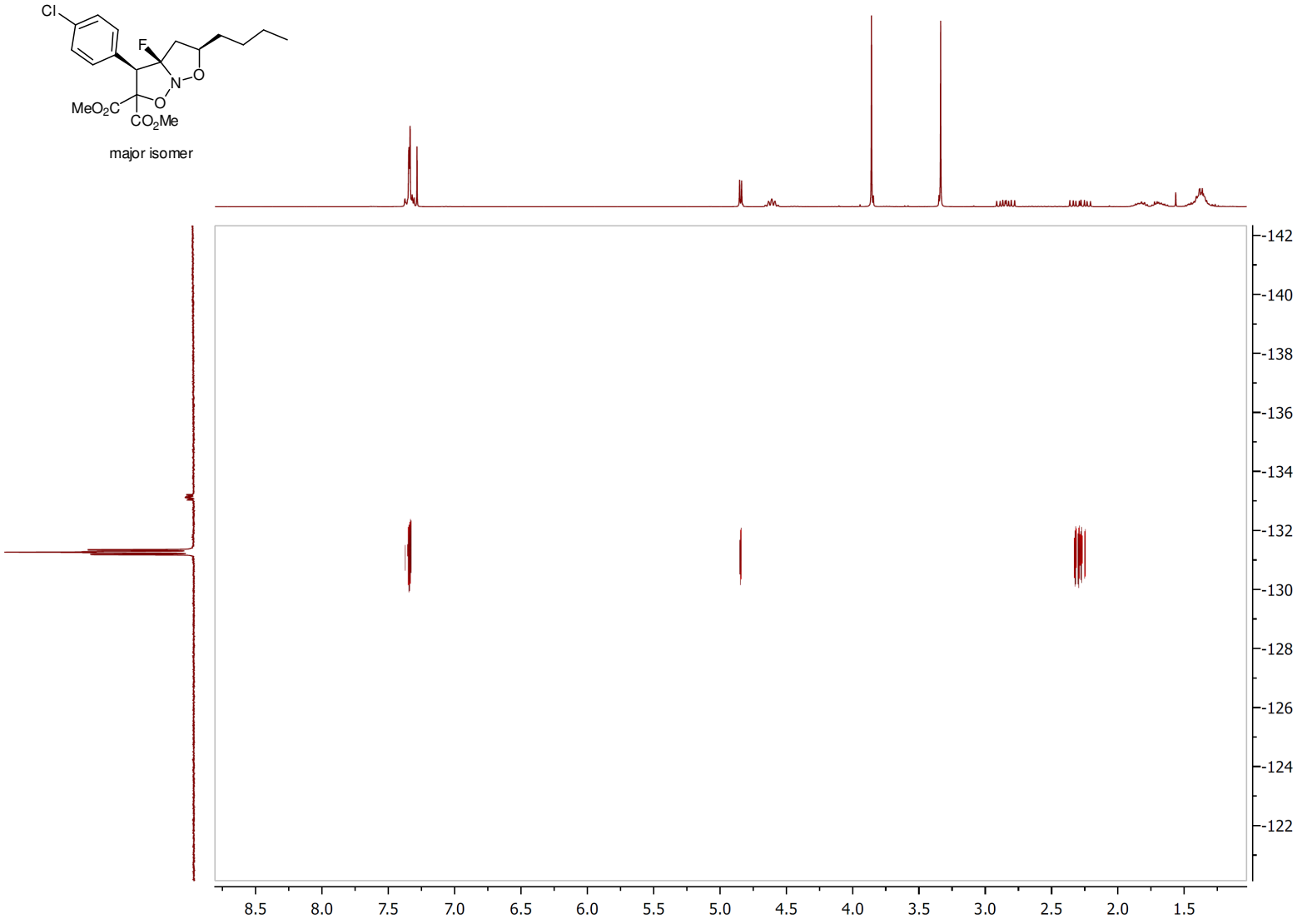
^{1}H-^{13}C HSQC


Cl
F
N
O
O
MeO2C
CO2Me
major isomer
10
20
30
40
50
60
70
80
90
100
110
120
130
140
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

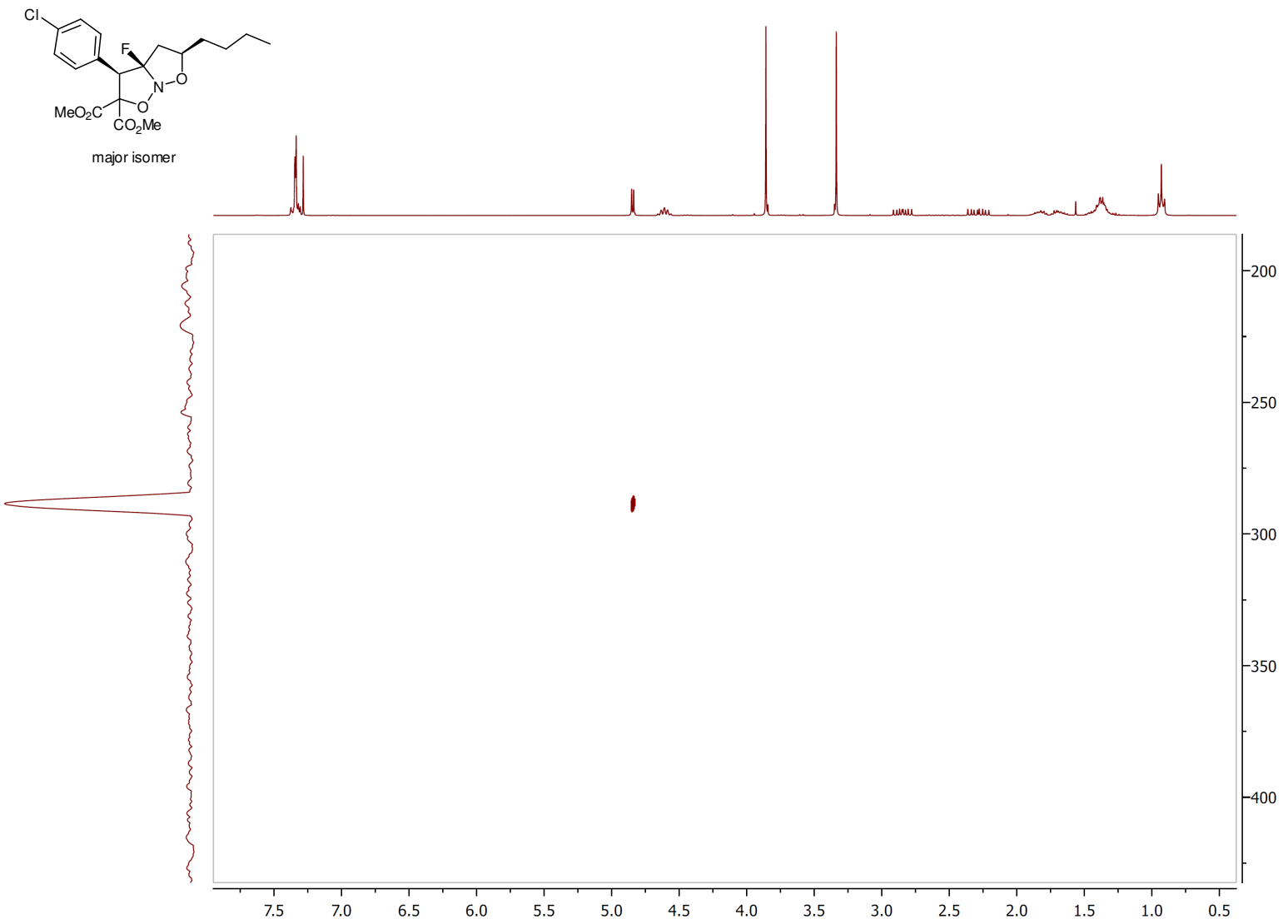
^{1}H-^{13}C HMBC


Cl
F
N
O
O
MeO2C
CO2Me
major isomer
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
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

^{1}H-^{19}F HOESY

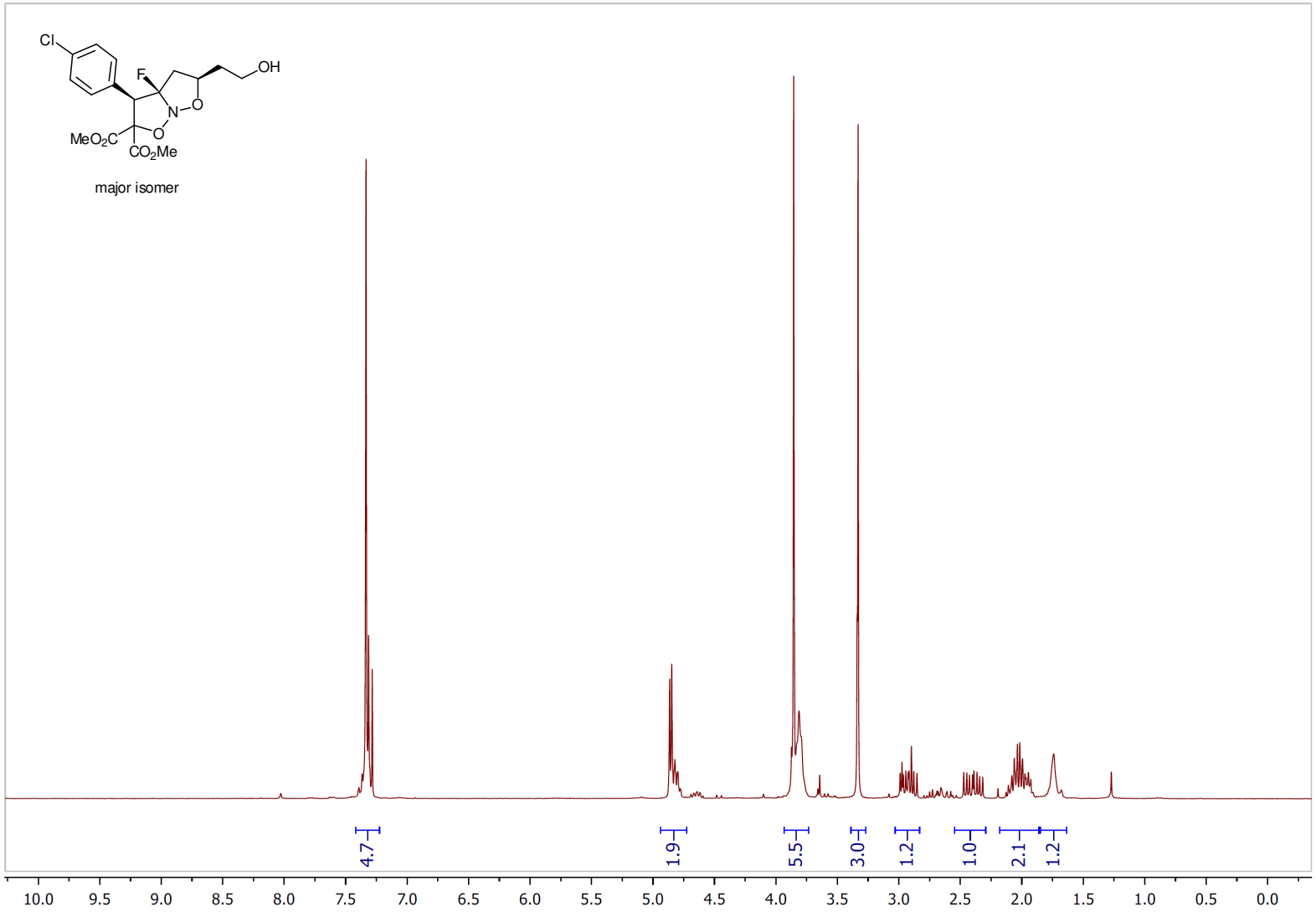

Cl
F
N
O
O
MeO2C
CO2Me
major isomer
-142
-140
-138
-136
-134
-132
-130
-128
-126
-124
-122
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

^{1}H-^{15}N HMBC

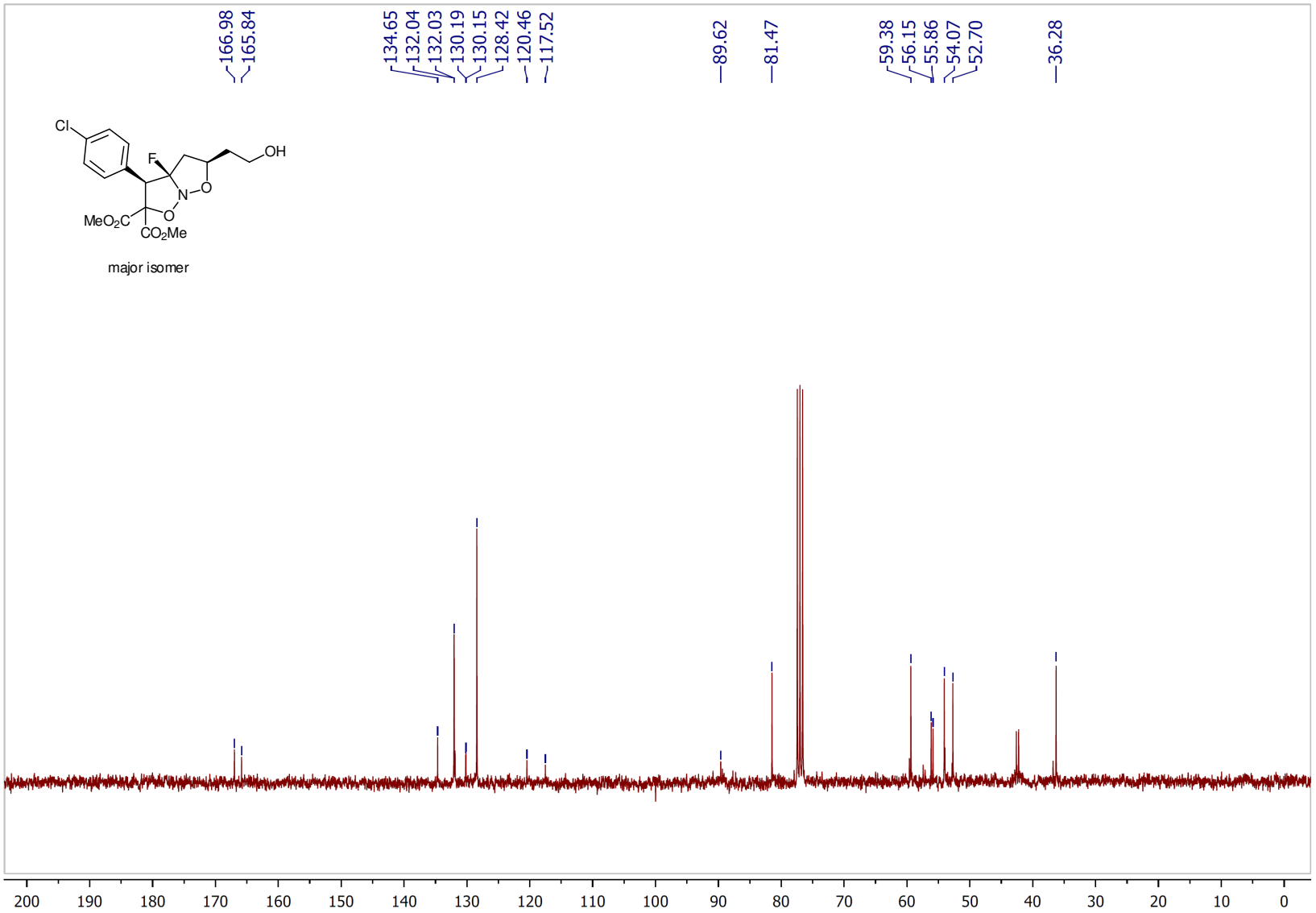

Cl
F
N
O
O
MeO2C
CO2Me
major isomer
200
250
300
350
400
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

***rel*-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(2-hydroxyethyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4p** (major isomer)

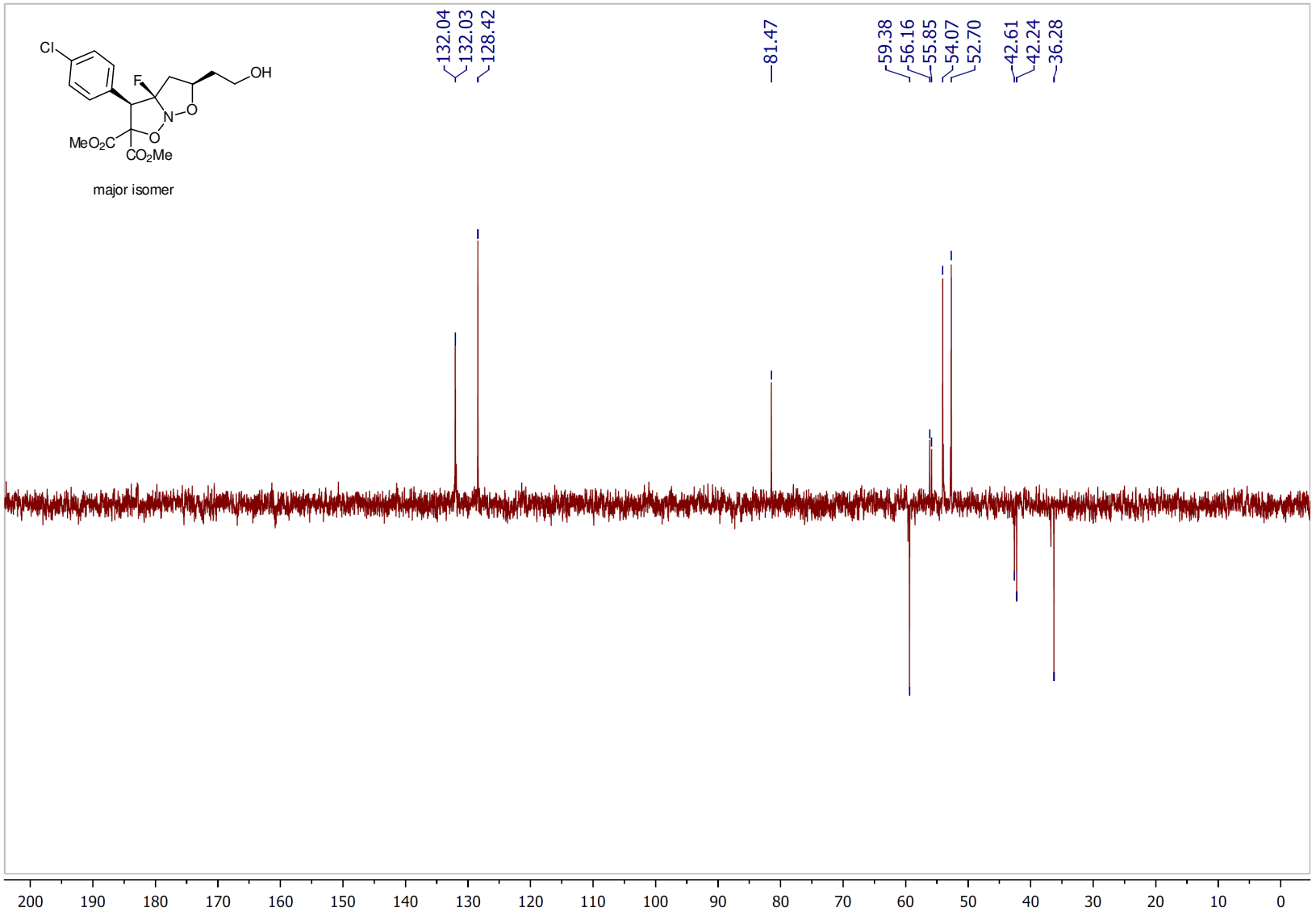
^{1}H NMR



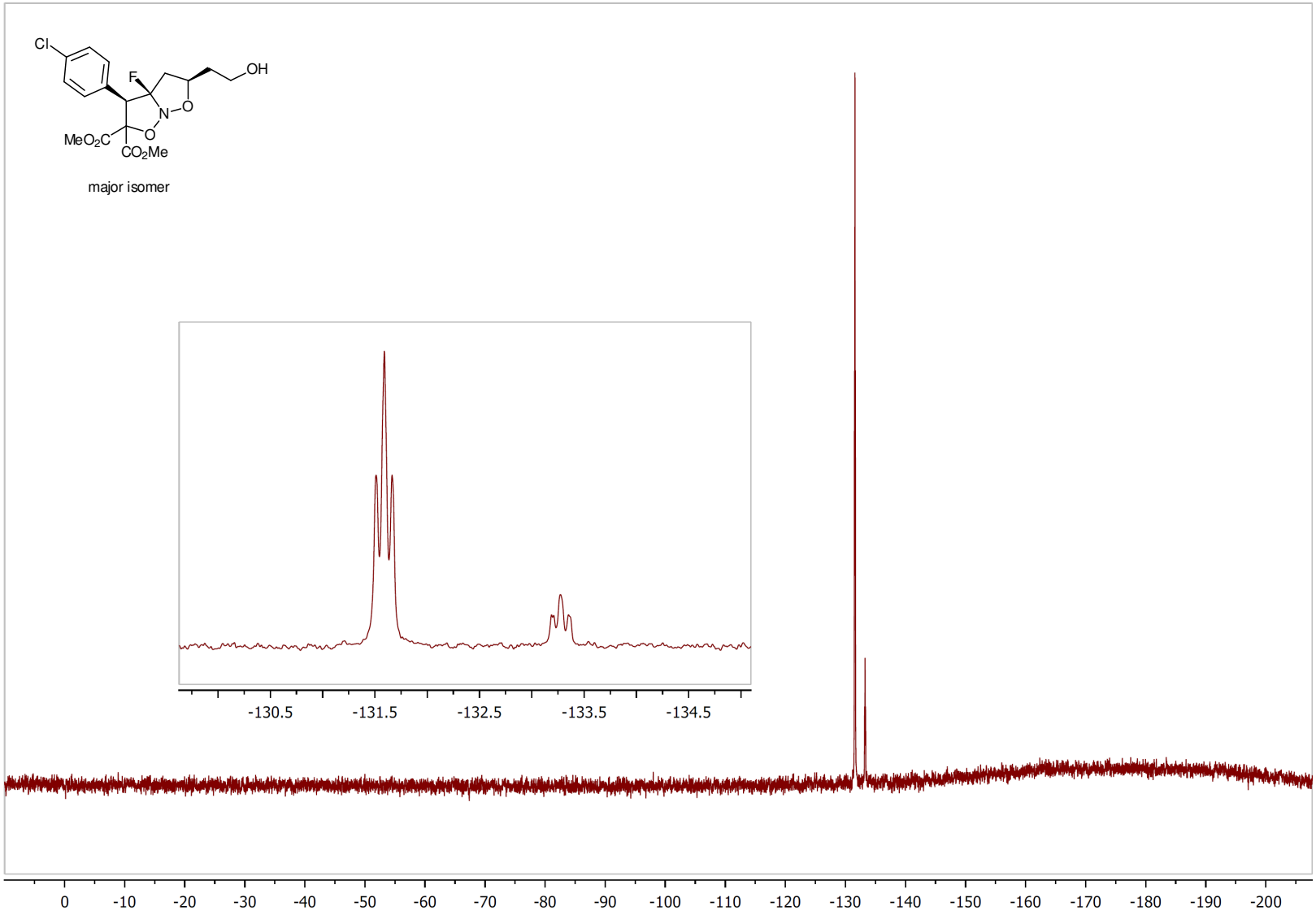
^{13}C NMR


166.98
165.84
134.65
132.04
132.03
130.19
130.15
128.42
120.46
117.52
89.62
81.47
59.38
56.15
55.86
54.07
52.70
36.28
Cl
F
OH
N
O
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{13}C NMR (DEPT)

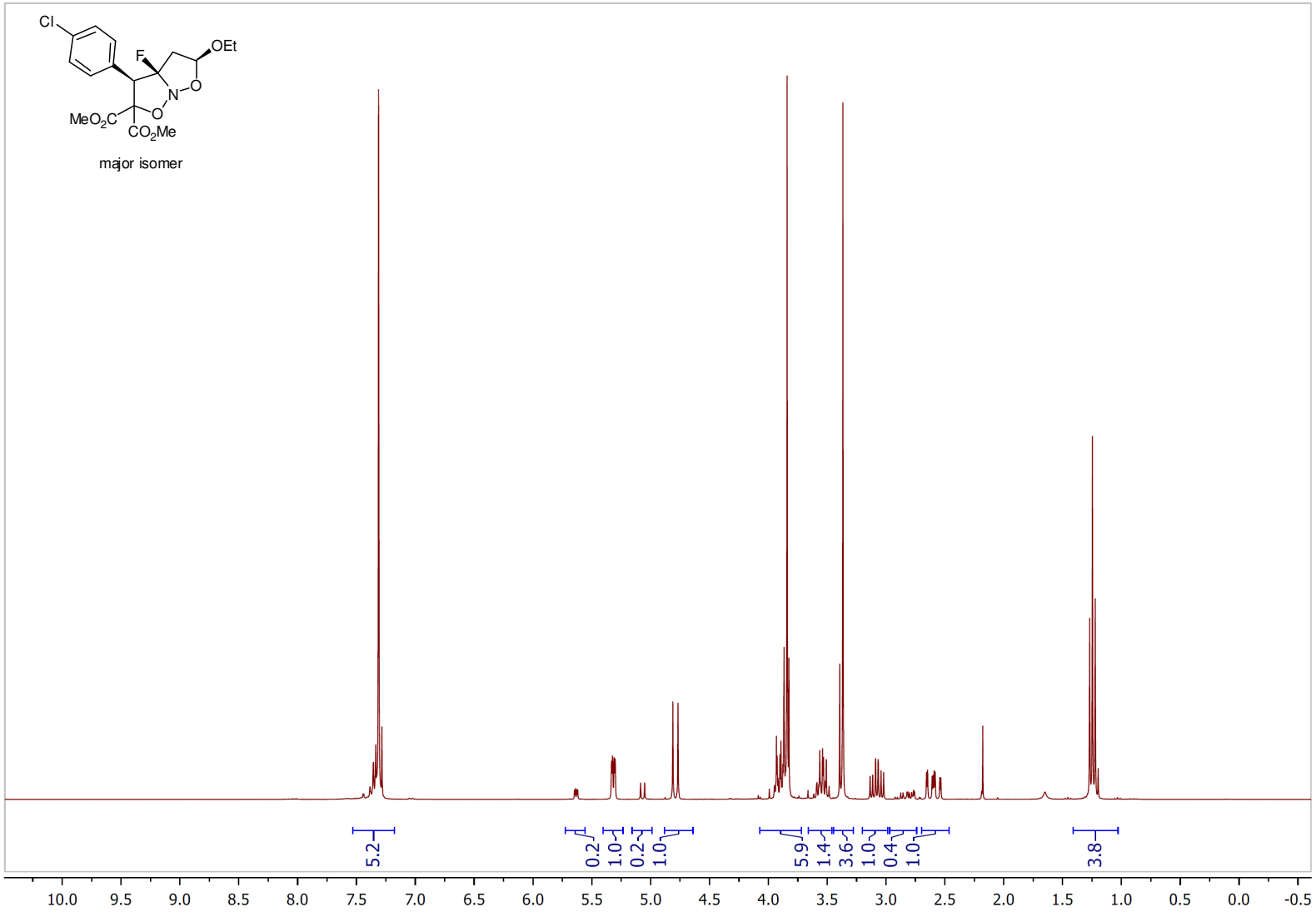

Cl
F
OH
N
O
O
MeO2C
CO2Me
major isomer
132.04
132.03
128.42
81.47
59.38
56.16
55.85
54.07
52.70
42.61
42.24
36.28
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

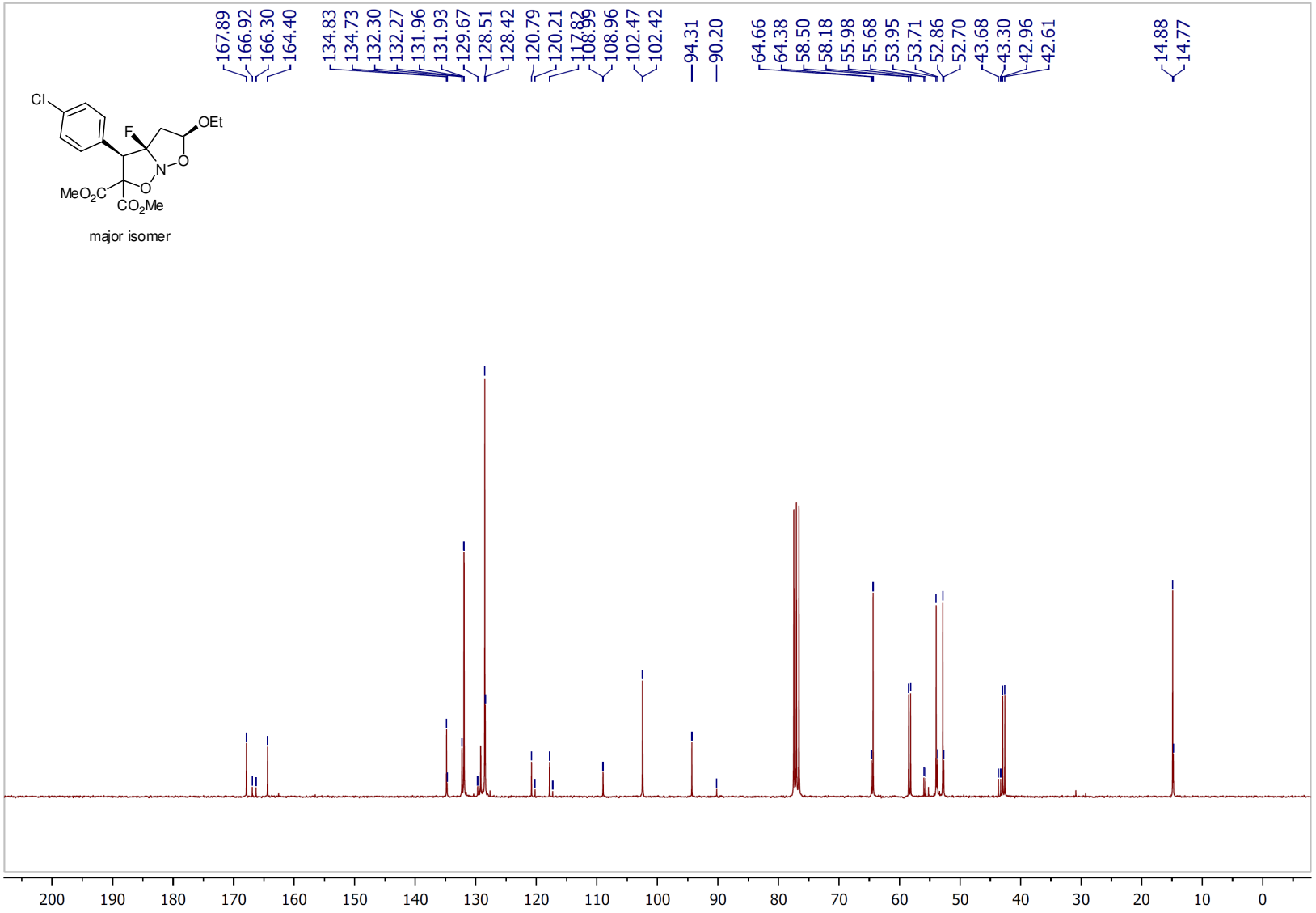

Cl
F
OH
N
O
O
MeO2C
CO2Me
major isomer
-130.5
-131.5
-132.5
-133.5
-134.5
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-5-ethoxy-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4q** (major isomer)

^{1}H NMR



^{13}C NMR


167.89
166.92
166.30
164.40
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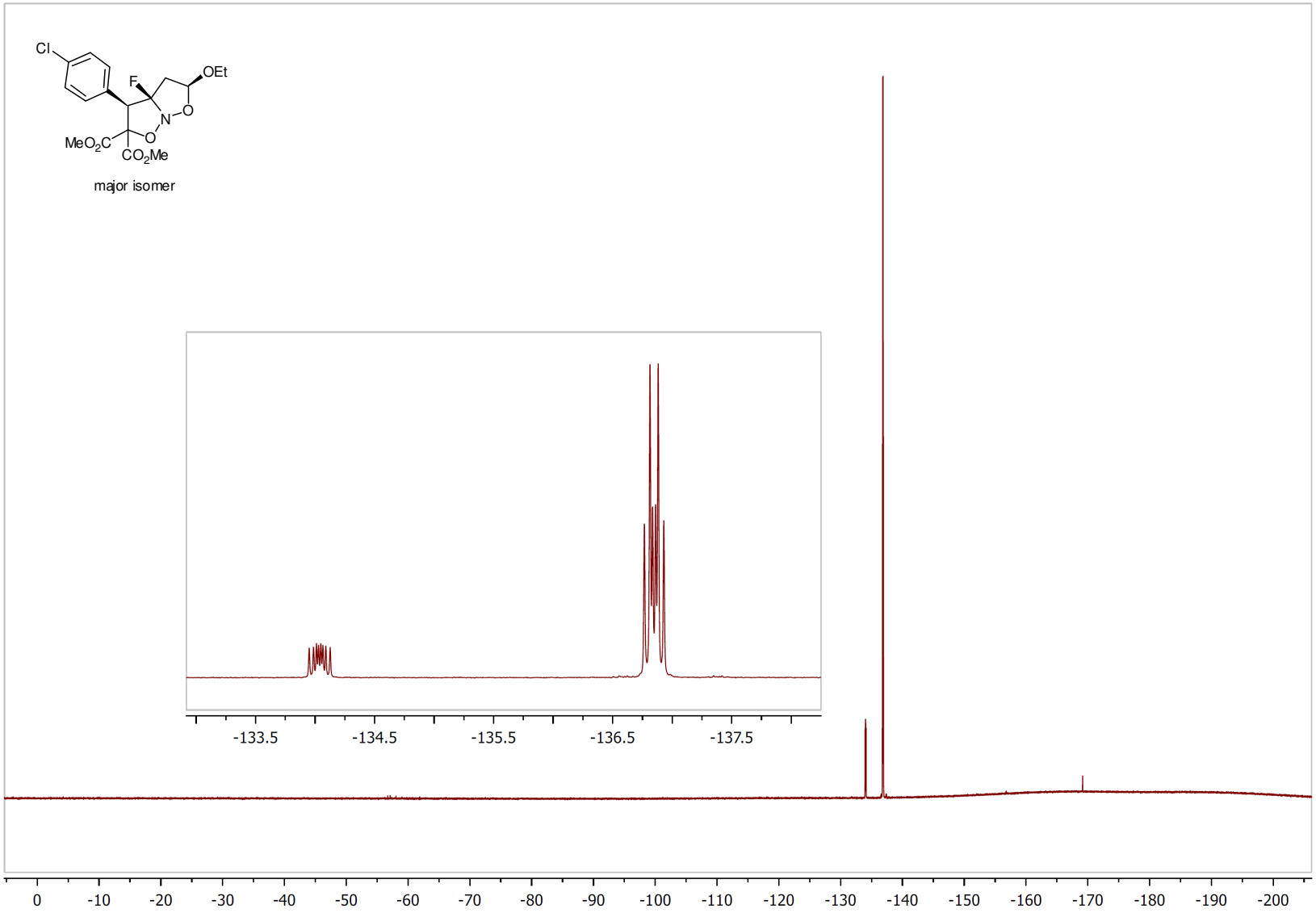
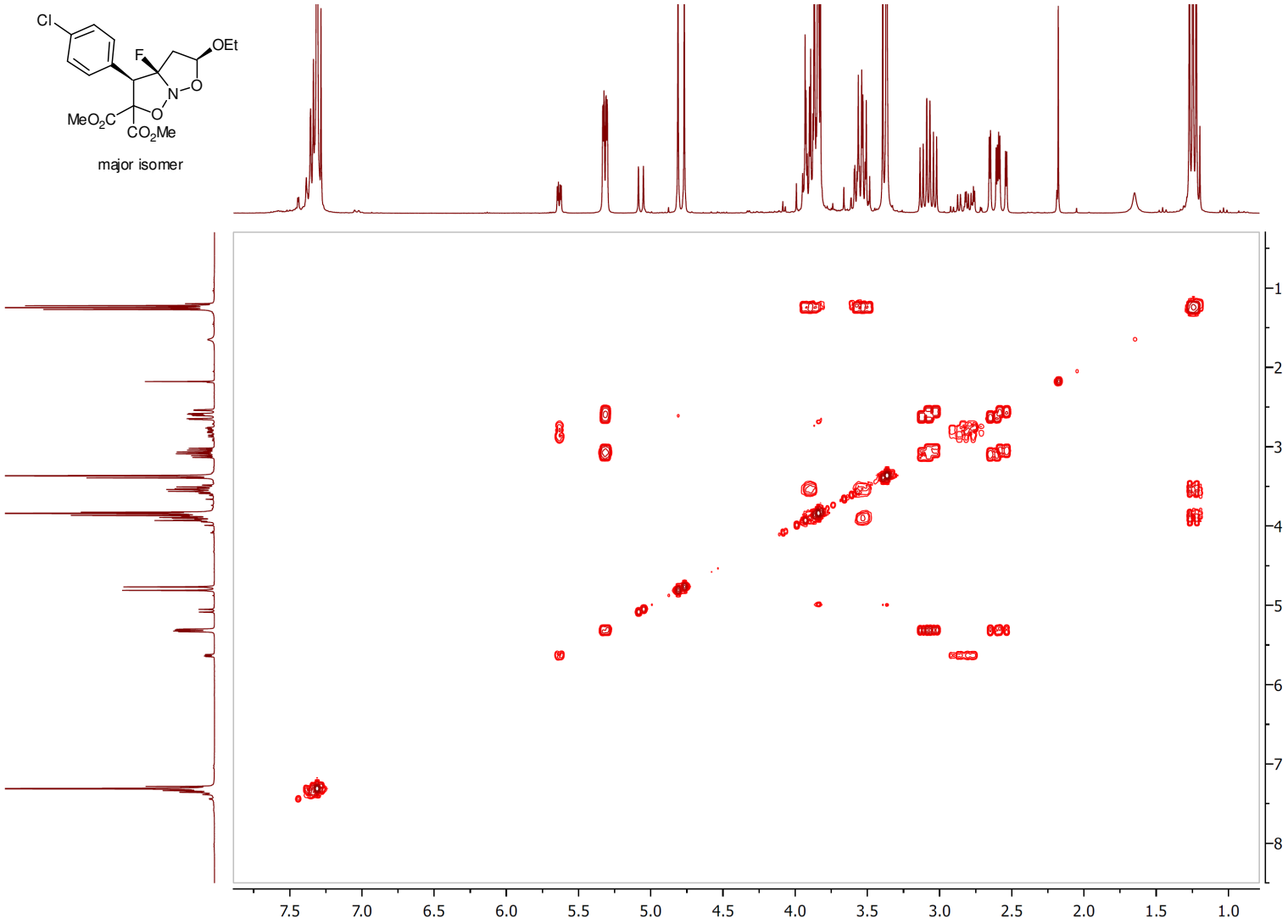
134.73
132.30
132.27
131.96
131.93
129.67
128.51
128.42
120.79
120.21
117.82
108.99
108.96
102.47
102.42
94.31
90.20
64.66
64.38
58.50
58.18
55.98
55.68
53.95
53.71
52.86
52.70
43.68
43.30
42.96
42.61
14.88
14.77
Cl
F
OEt
N
O
MeO2C
CO2Me
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

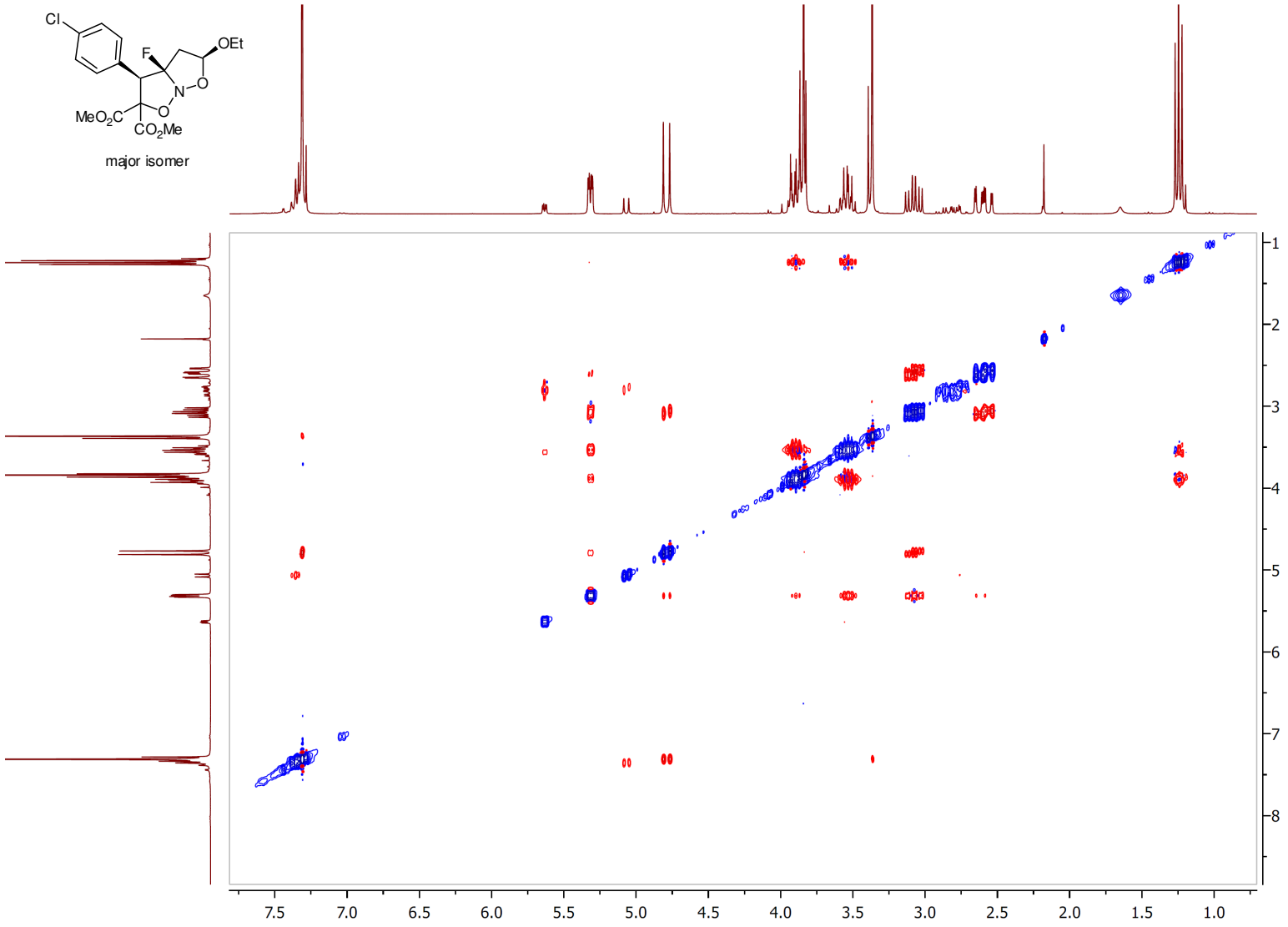
^{19}F NMR


Cl
F
OEt
N
O
O
MeO2C
CO2Me
major isomer
-133.5
-134.5
-135.5
-136.5
-137.5
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

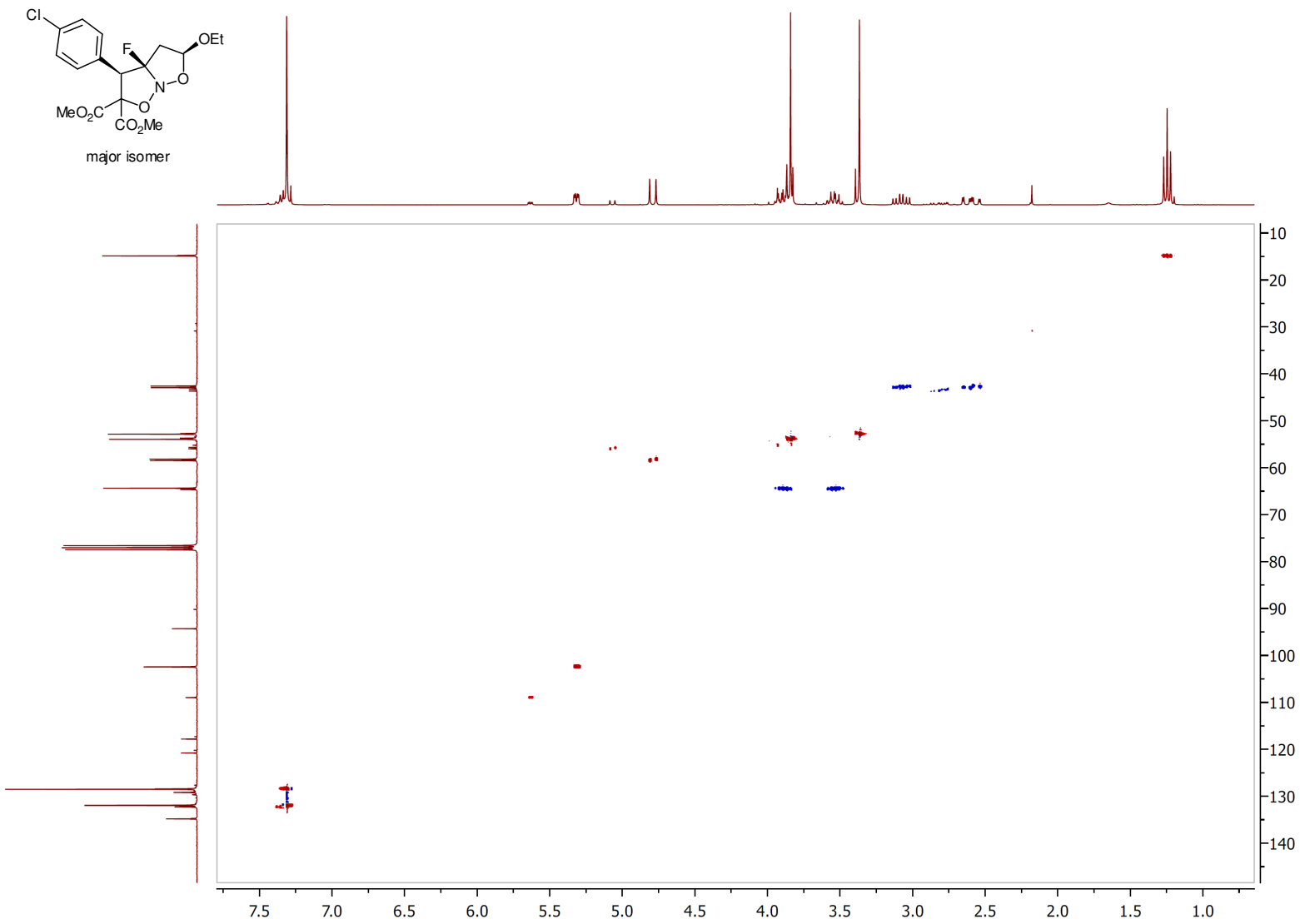
^{1}H-^{1}H COSY


Cl
F
OEt
N
O
O
MeO2C
CO2Me
major isomer
1
2
3
4
5
6
7
8
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

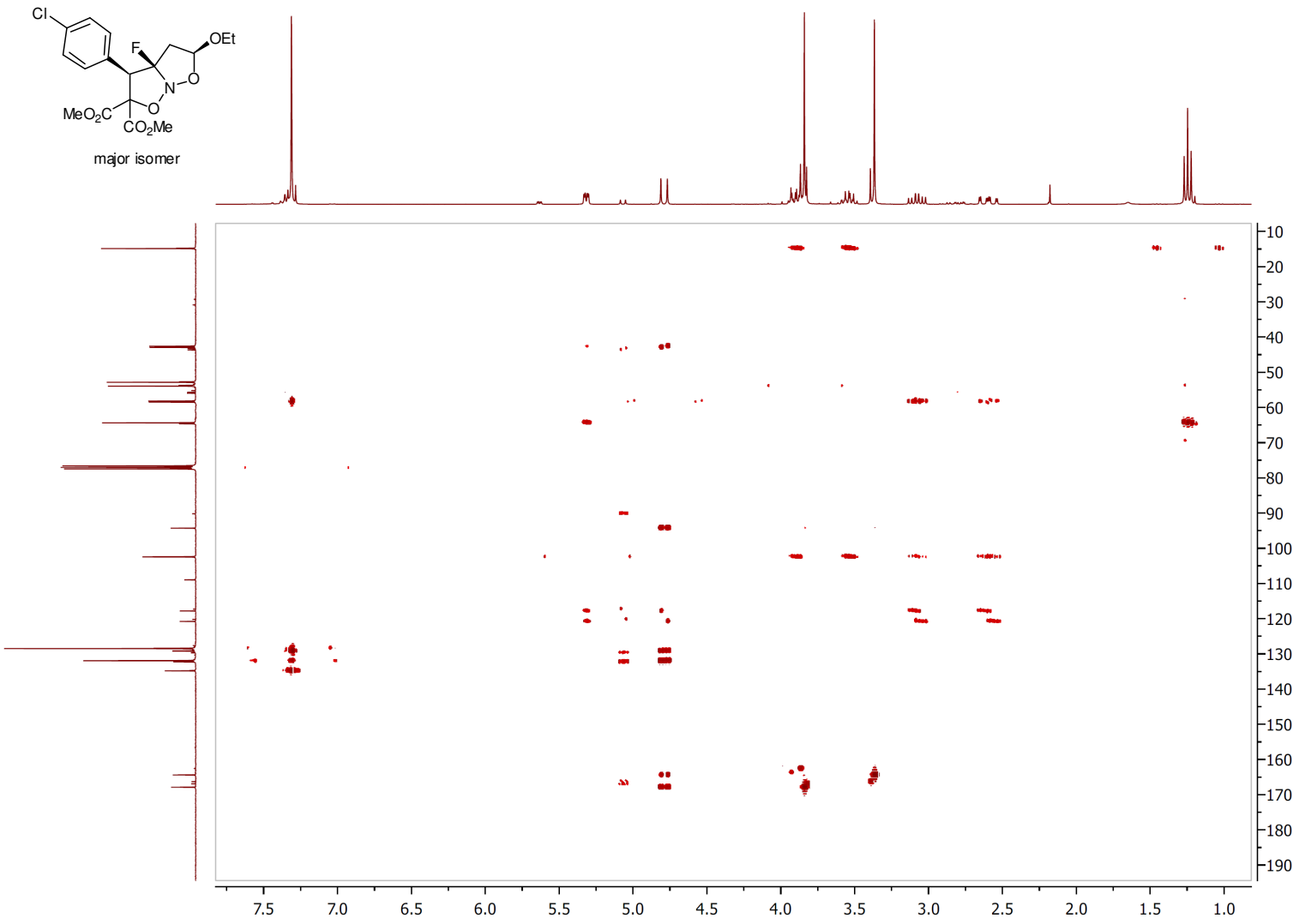
^{1}H-^{1}H NOESY


Cl
F
OEt
N
O
O
MeO2C
CO2Me
major isomer
1
2
3
4
5
6
7
8
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

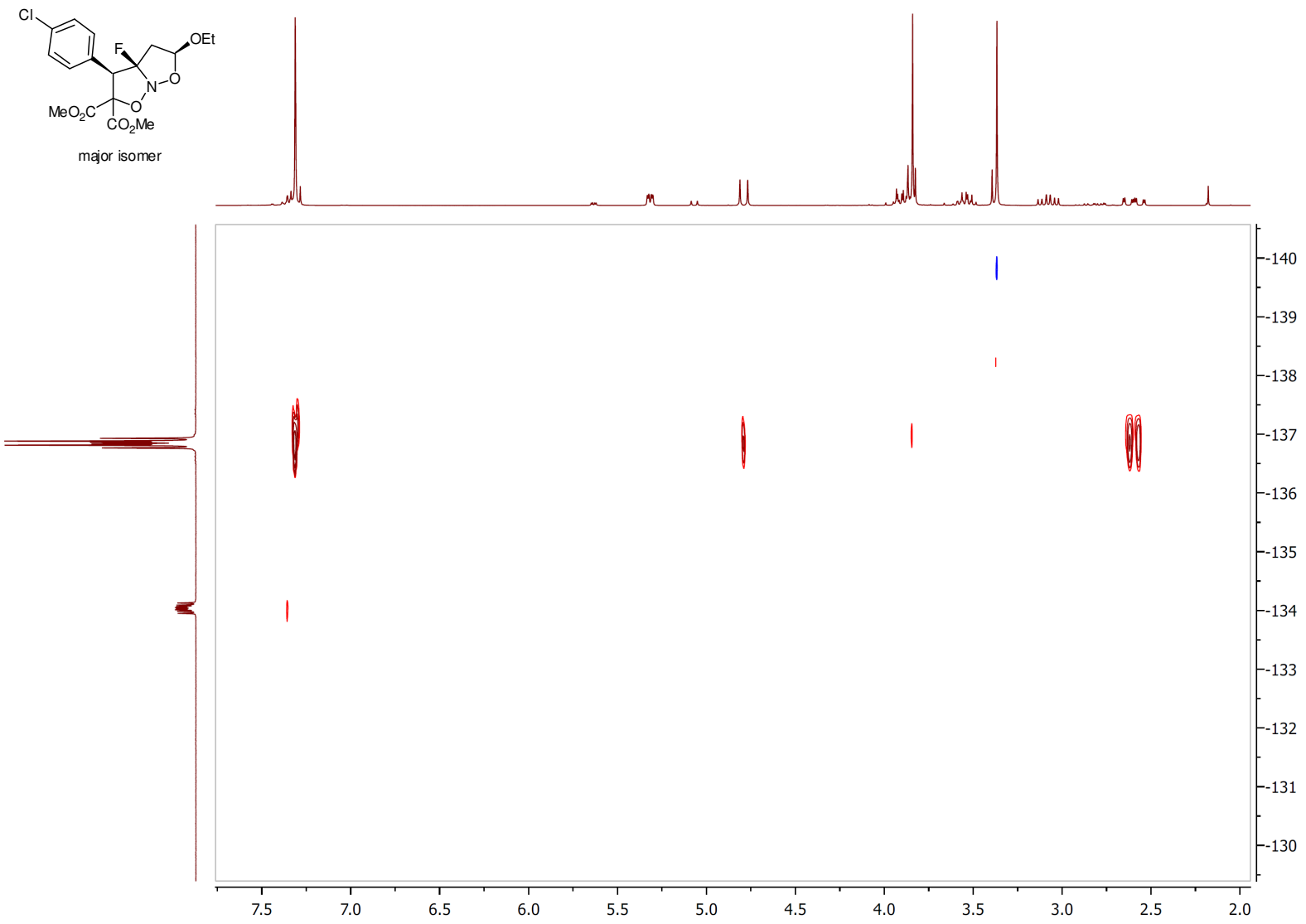
^{1}H-^{13}C HSQC


Cl
F
OEt
N
O
O
MeO2C
CO2Me
major isomer
10
20
30
40
50
60
70
80
90
100
110
120
130
140
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

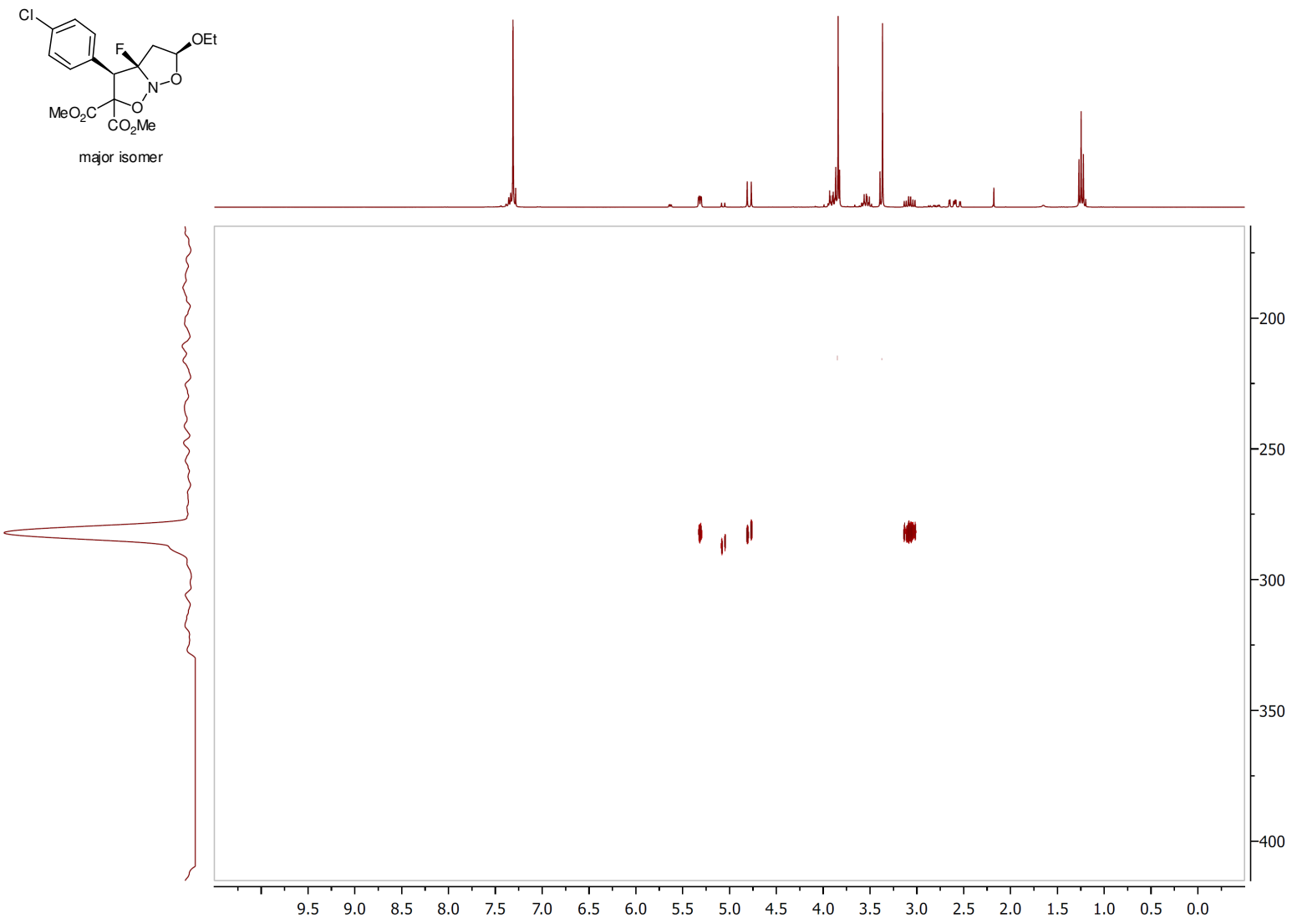
^{1}H-^{13}C HMBC


Cl
F
OEt
N
O
MeO2C
CO2Me
major isomer
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
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

^{1}H-^{19}F HOESY

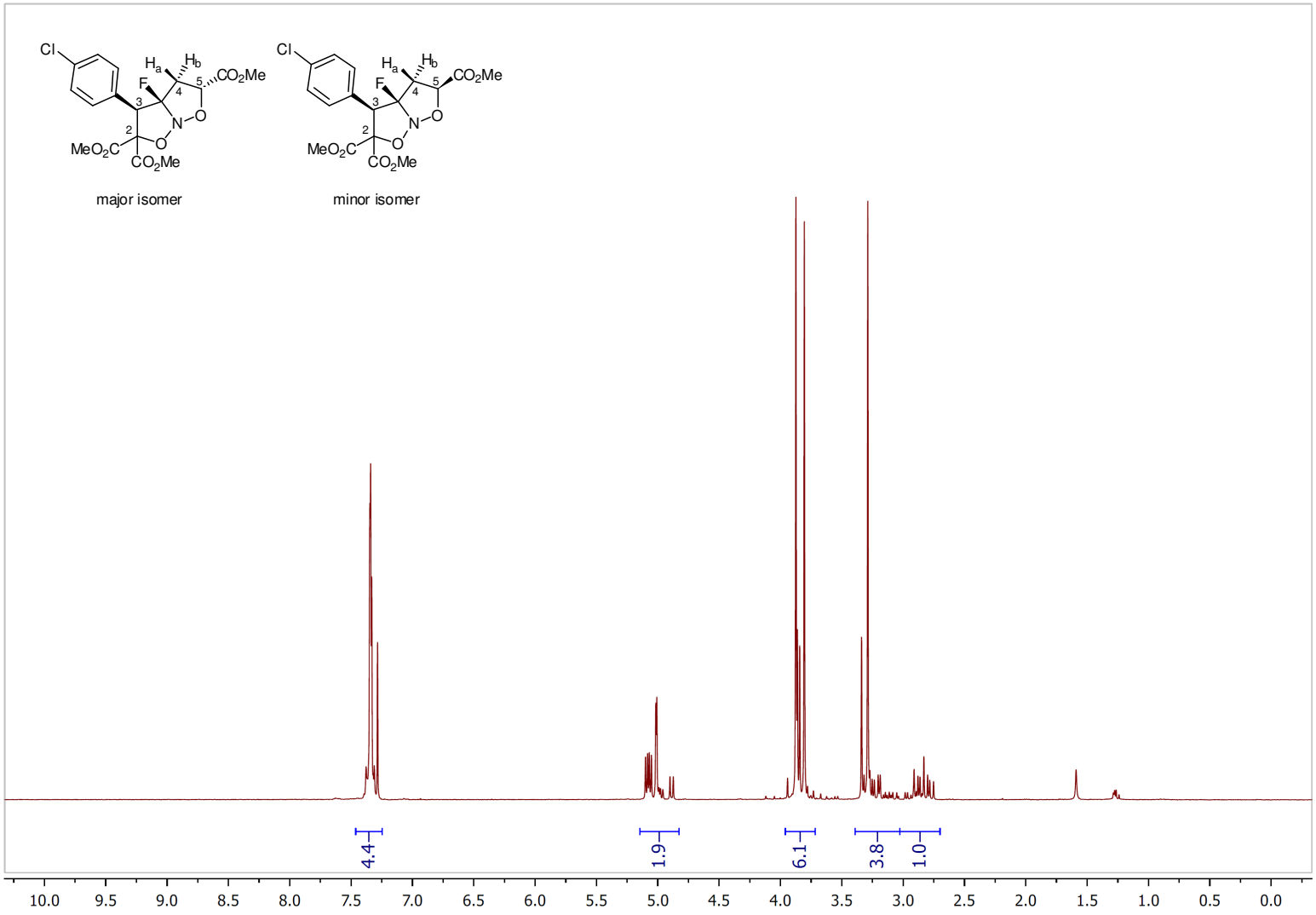

Cl
F
OEt
N
O
O
MeO2C
CO2Me
major isomer
-140
-139
-138
-137
-136
-135
-134
-133
-132
-131
-130
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0

^{1}H-^{15}N HMBC

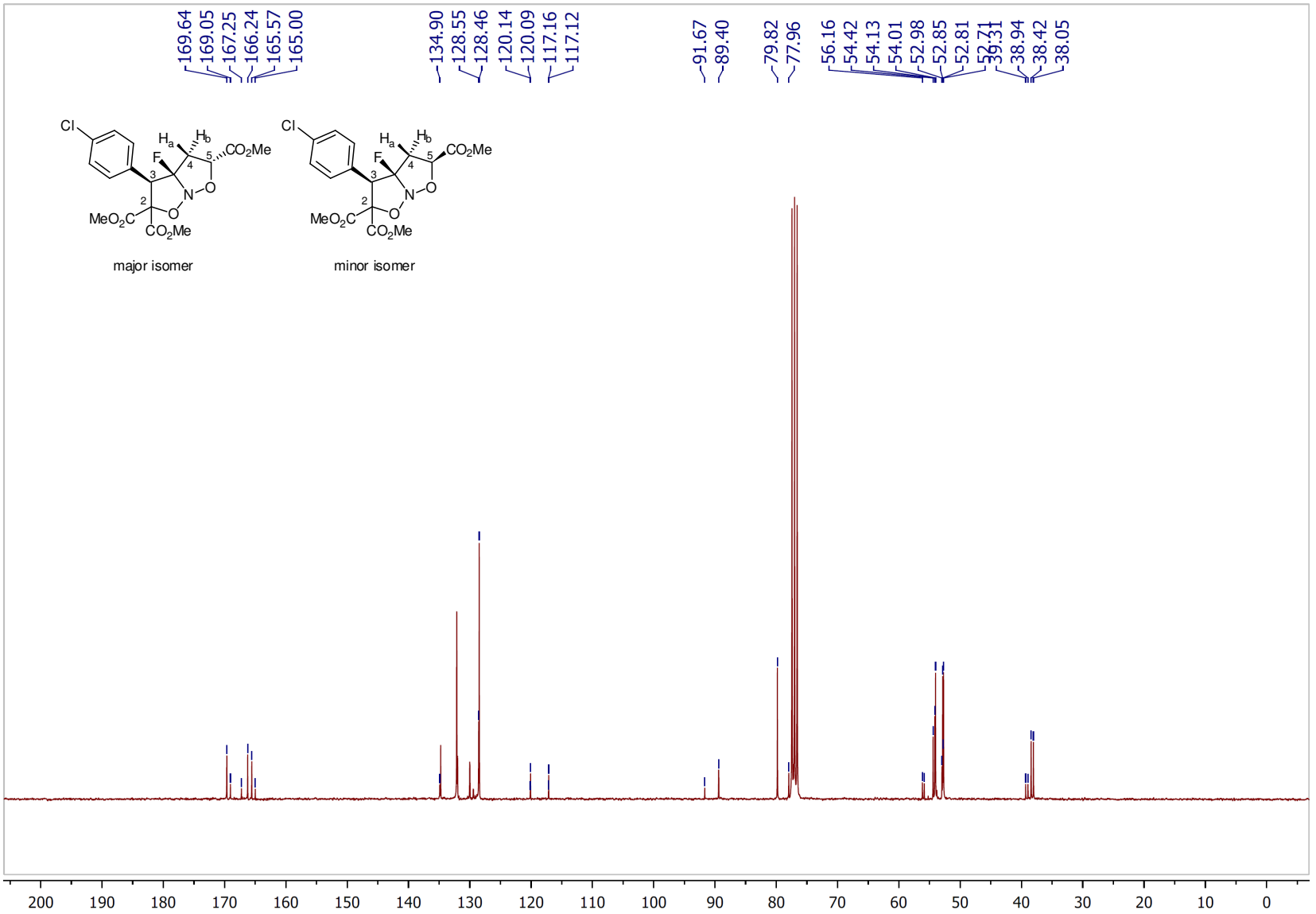

Cl
F
OEt
N
O
O
MeO2C
CO2Me
major isomer
200
250
300
350
400
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

***rel*-(3R,3aR,5R)-Trimethyl 3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2,5-tricarboxylate 4'r** (major isomer) and ***rel*-(3R,3aR,5S)-Trimethyl 3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2,5-tricarboxylate 4r** (minor isomer)

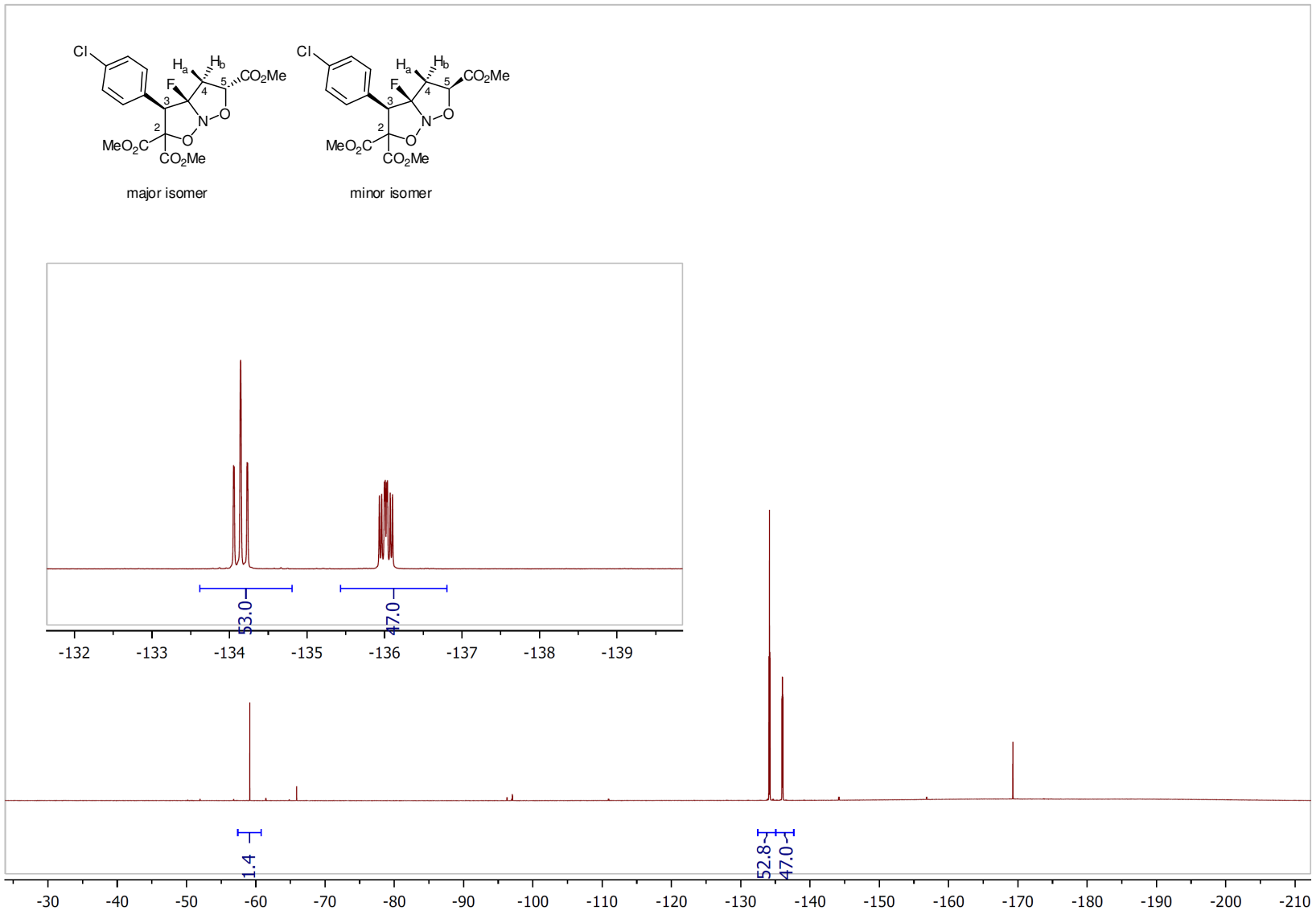
^{1}H NMR



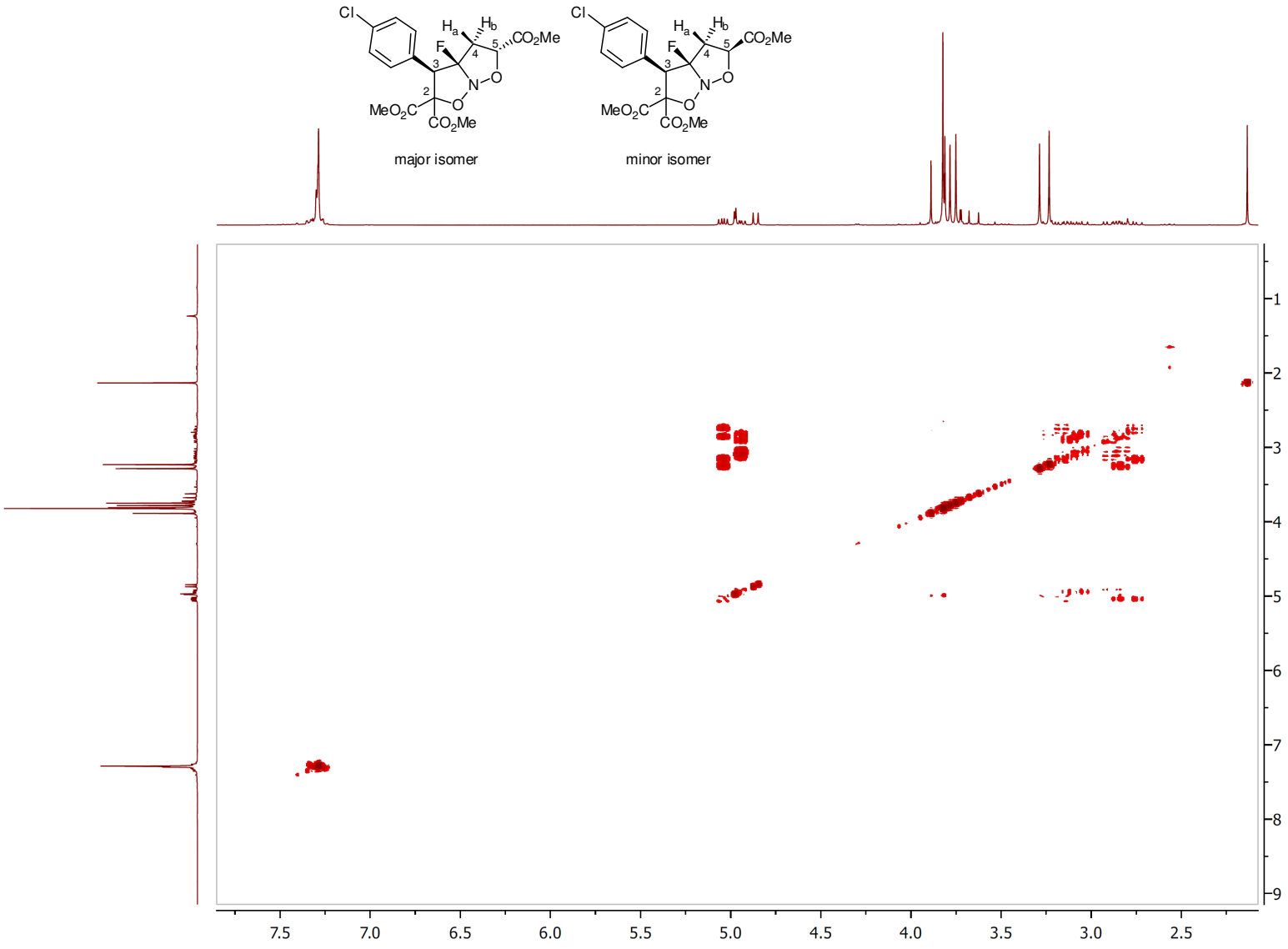
^{13}C NMR


169.64
169.05
167.25
166.24
165.57
165.00
134.90
128.55
128.46
120.14
120.09
117.16
117.12
91.67
89.40
79.82
77.96
56.16
54.42
54.13
54.01
52.98
52.85
52.81
52.71
39.31
38.94
38.42
38.05
major isomer
minor isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

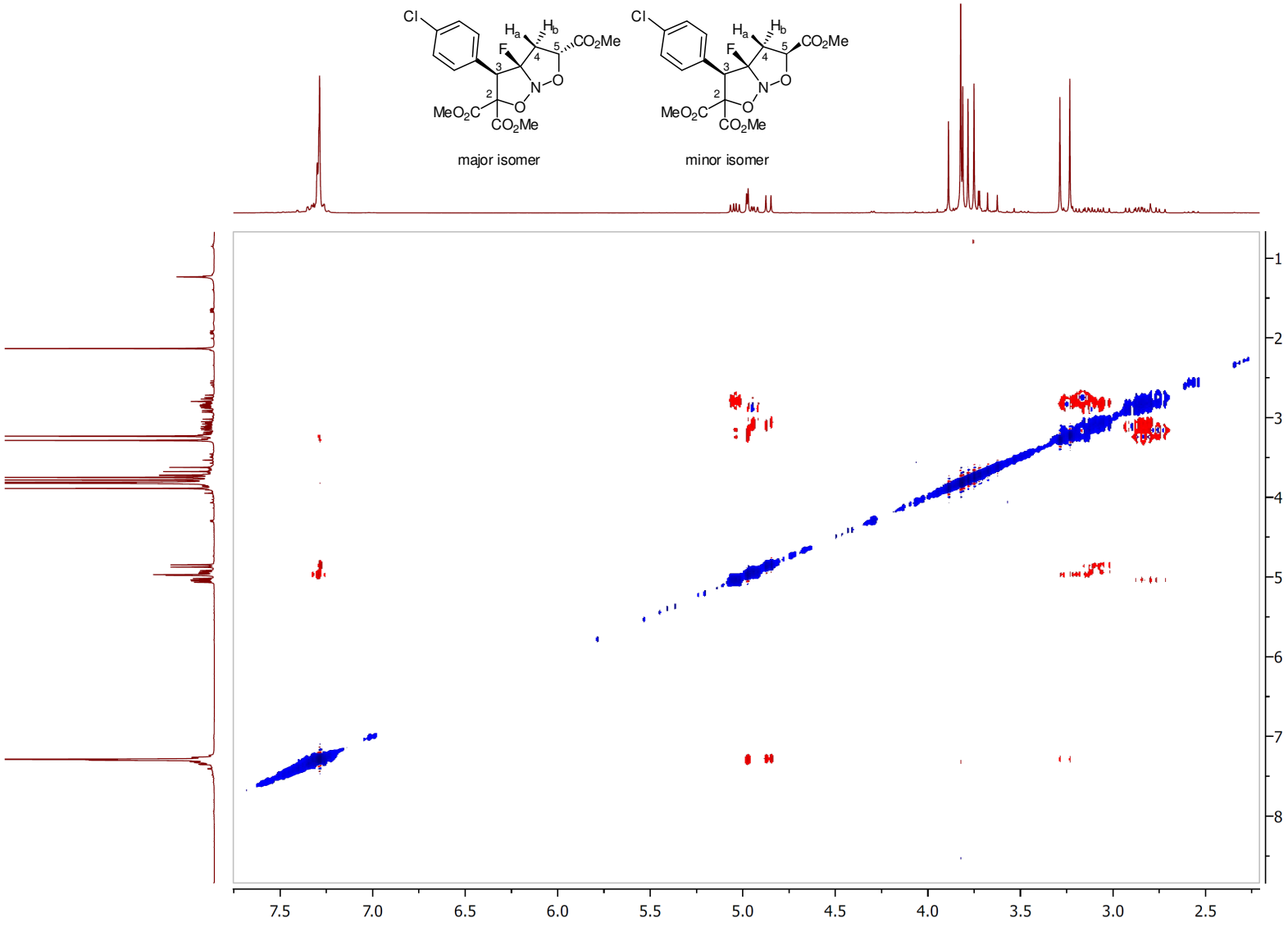
^{19}F NMR



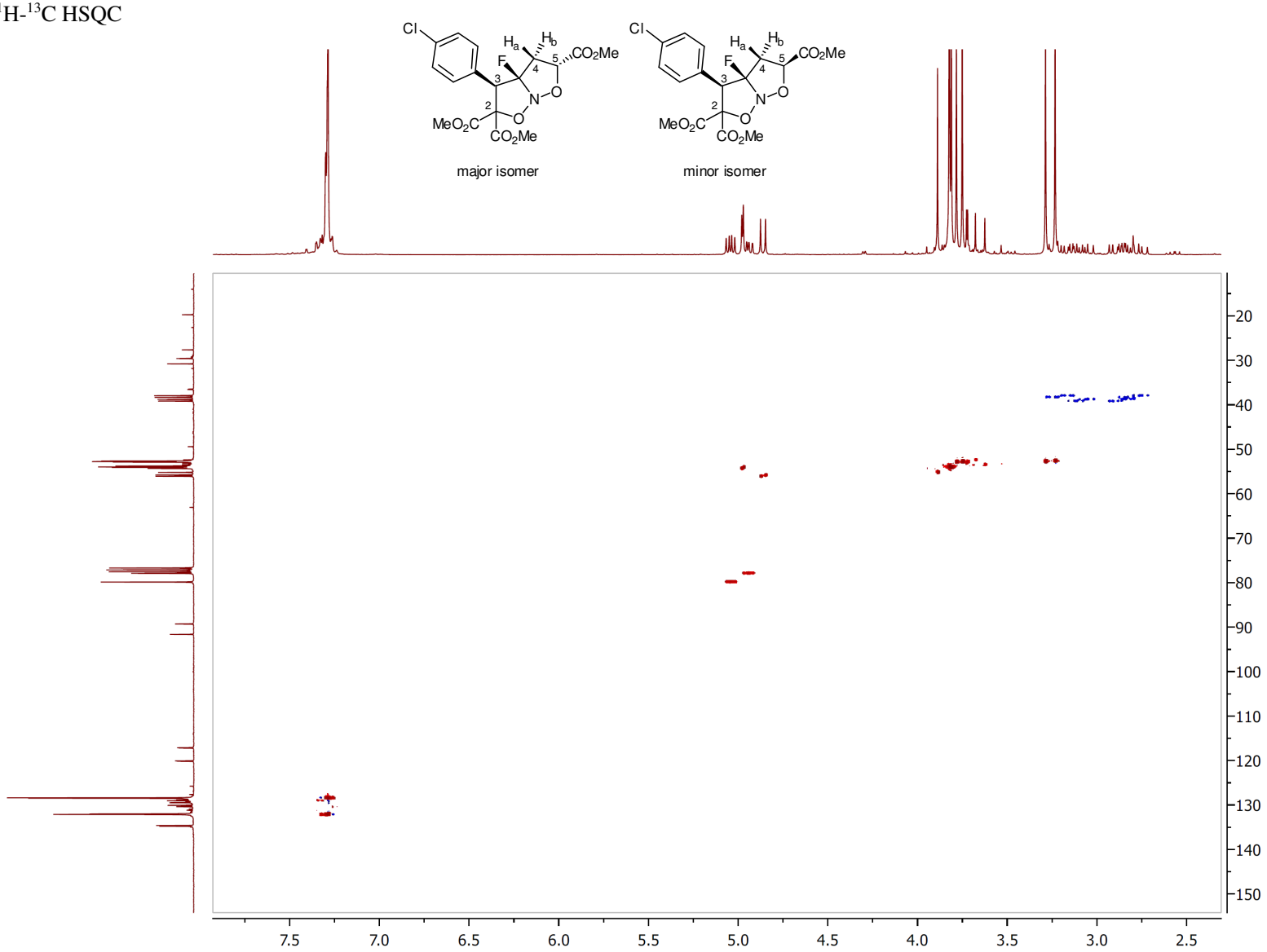
^{1}H-^{1}H COSY


major isomer
minor isomer
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
1
2
3
4
5
6
7
8
9

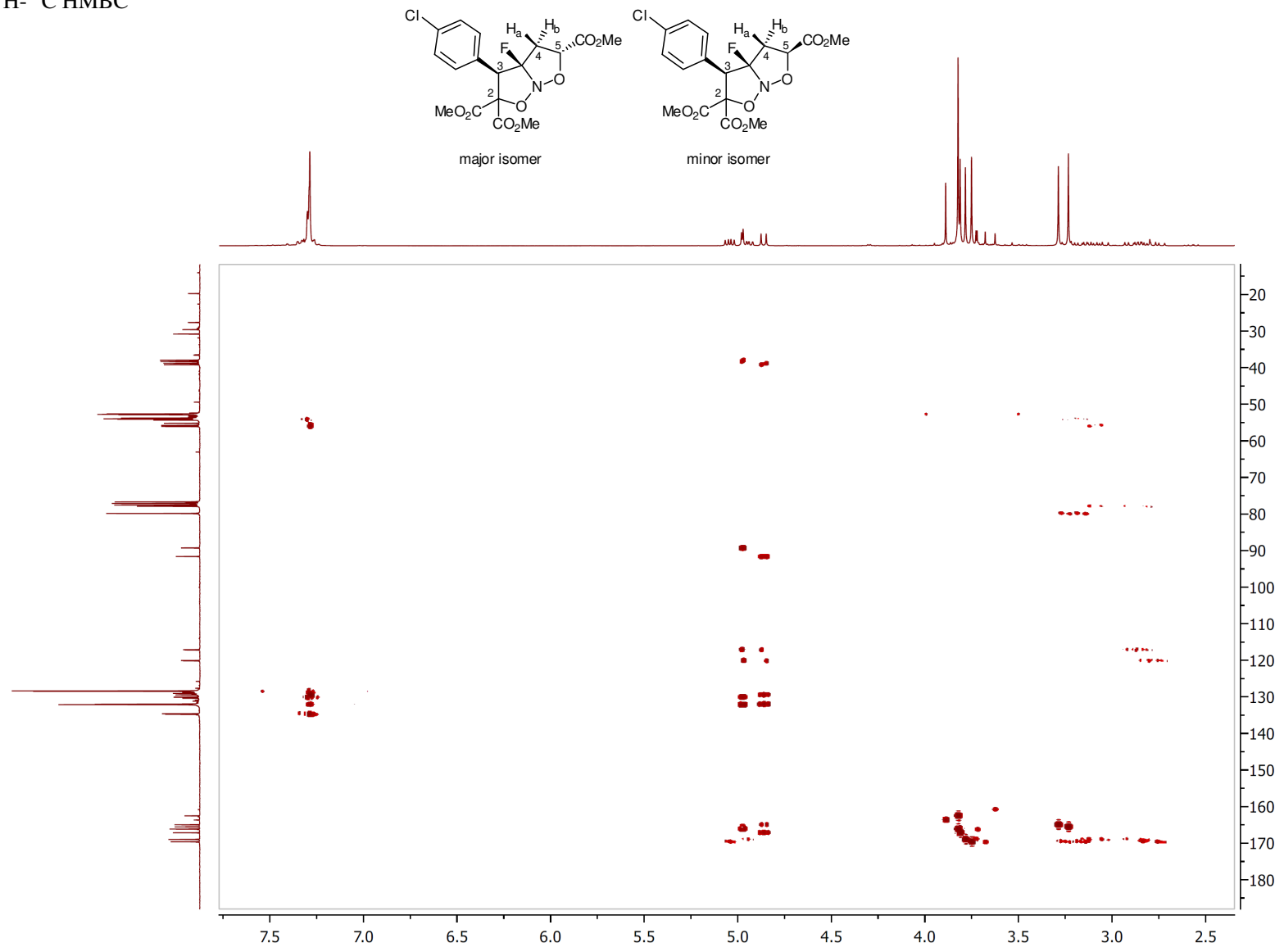
^{1}H-^{1}H NOESY



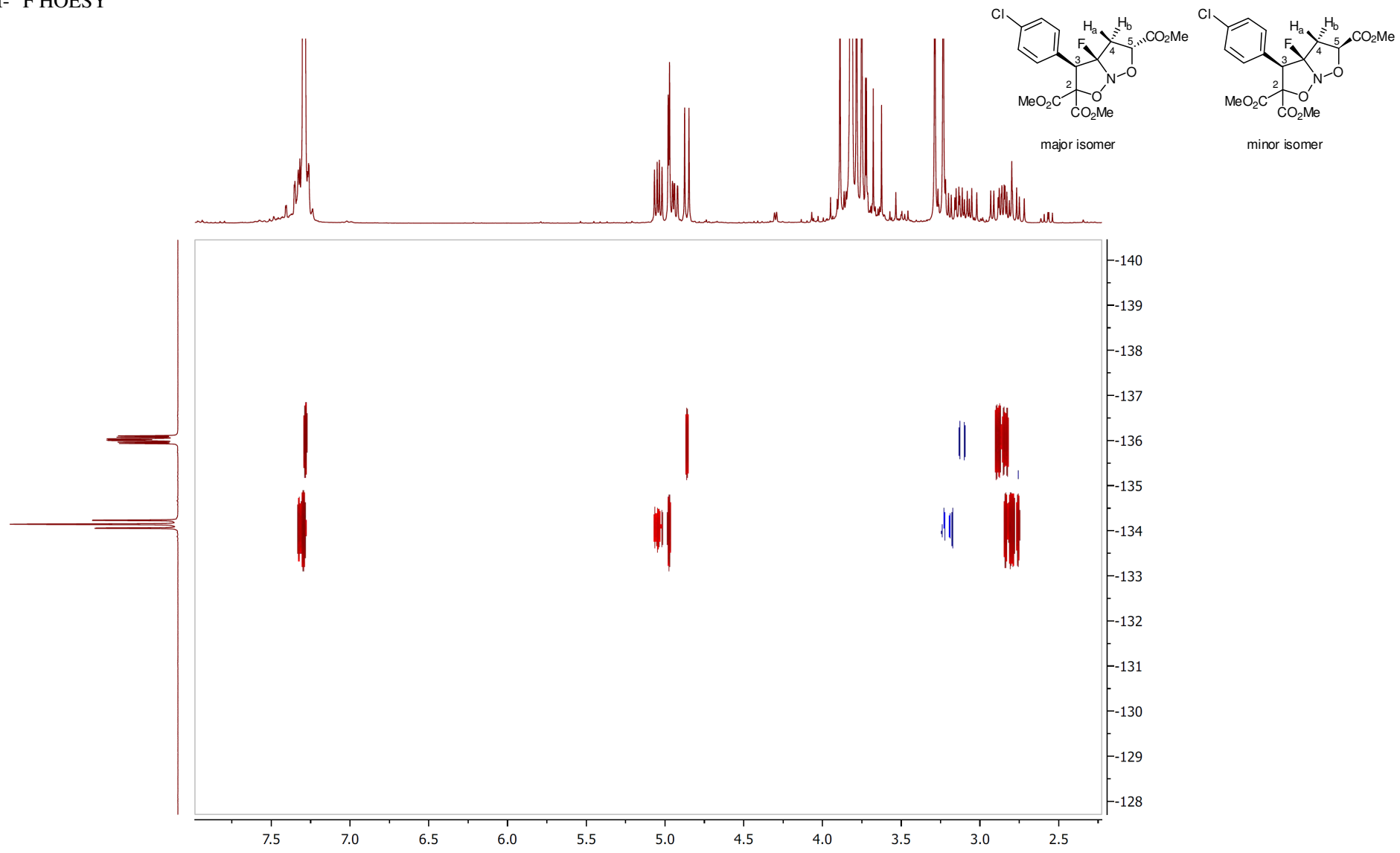
^{1}H-^{13}C HSQC


major isomer
minor isomer
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
20
30
40
50
60
70
80
90
100
110
120
130
140
150

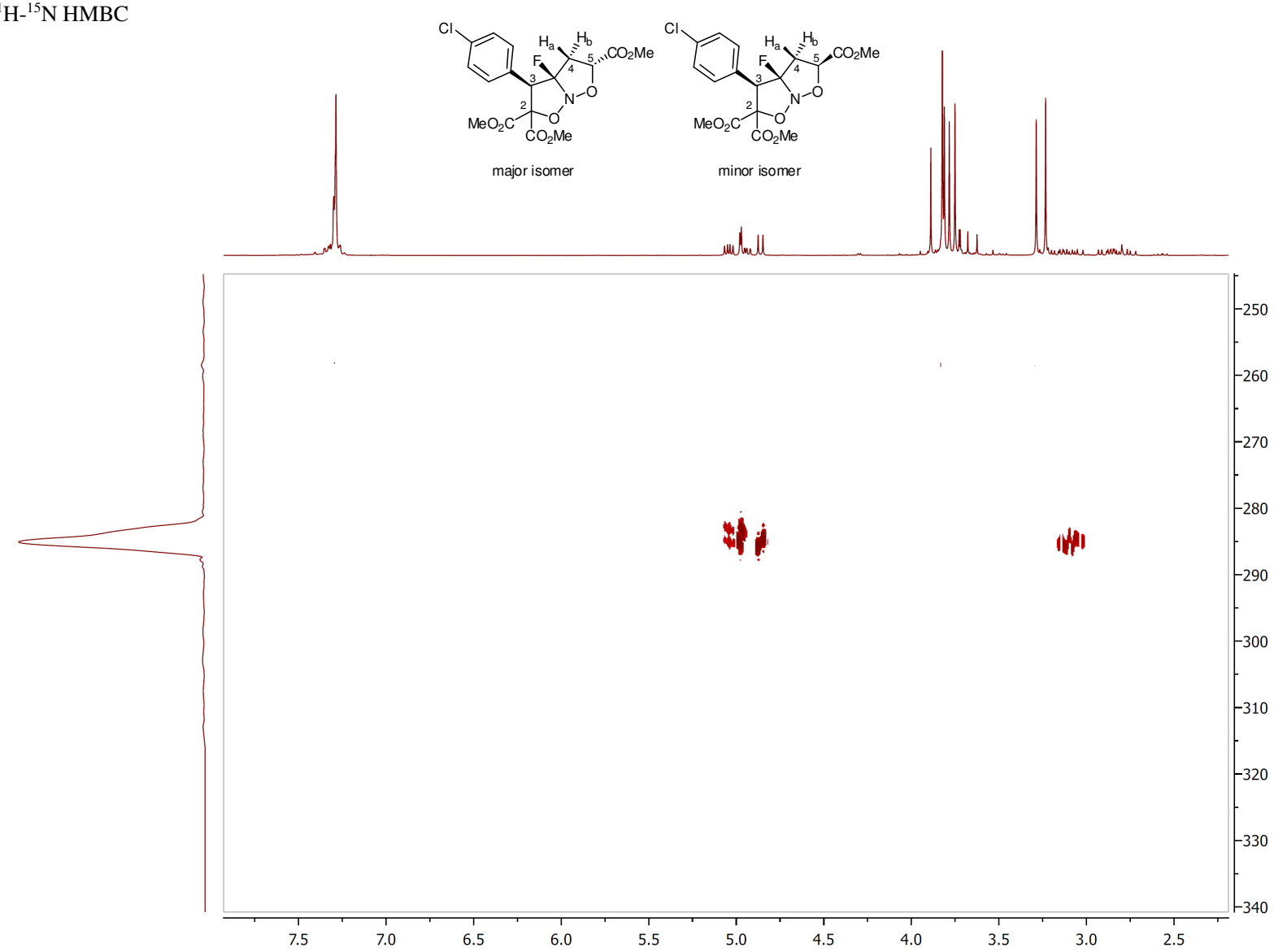
^{1}H-^{13}C HMBC


major isomer
minor isomer
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180

^{1}H-^{19}F HOESY

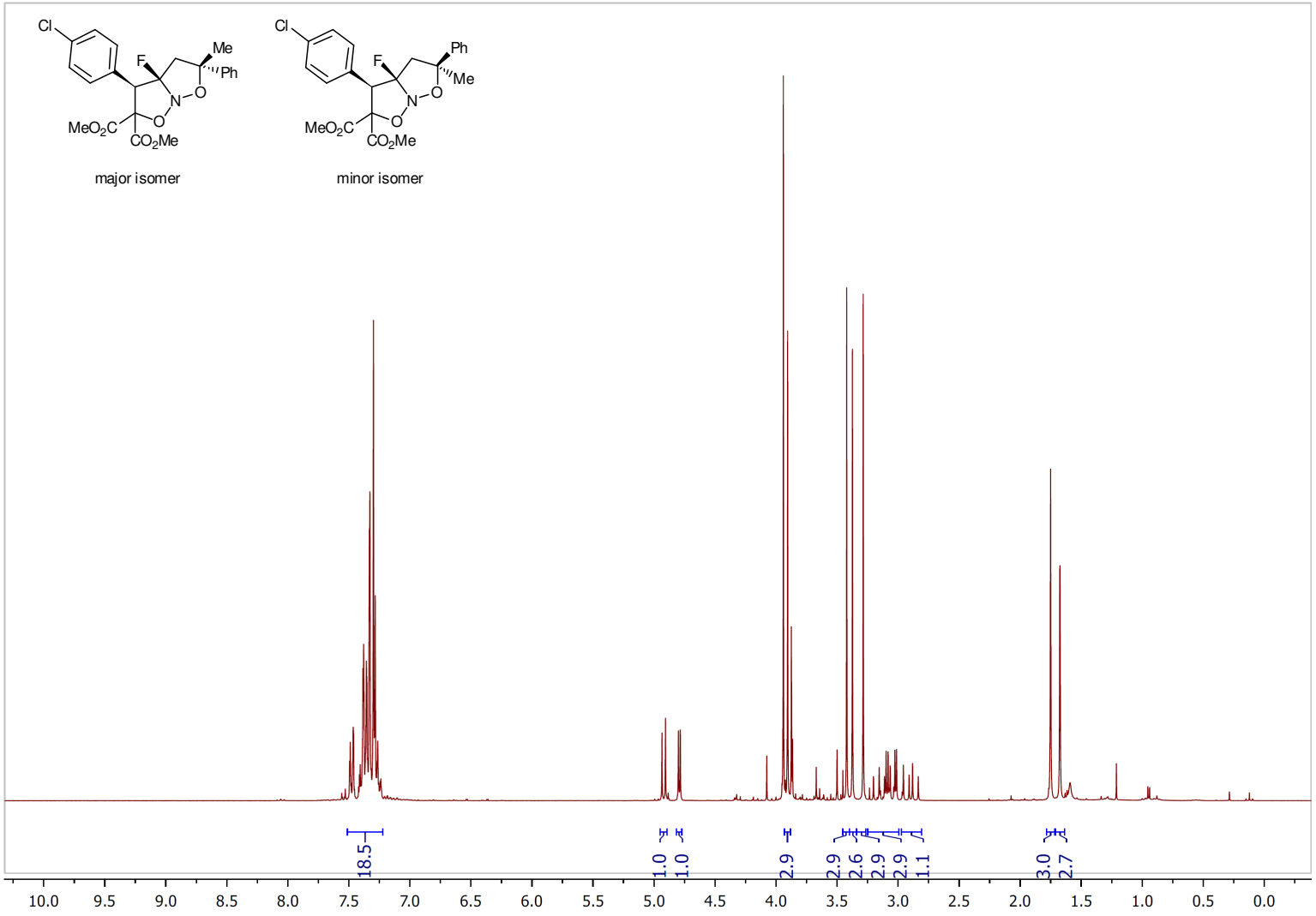

major isomer
minor isomer
-140
-139
-138
-137
-136
-135
-134
-133
-132
-131
-130
-129
-128
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5

^{1}H-^{15}N HMBC

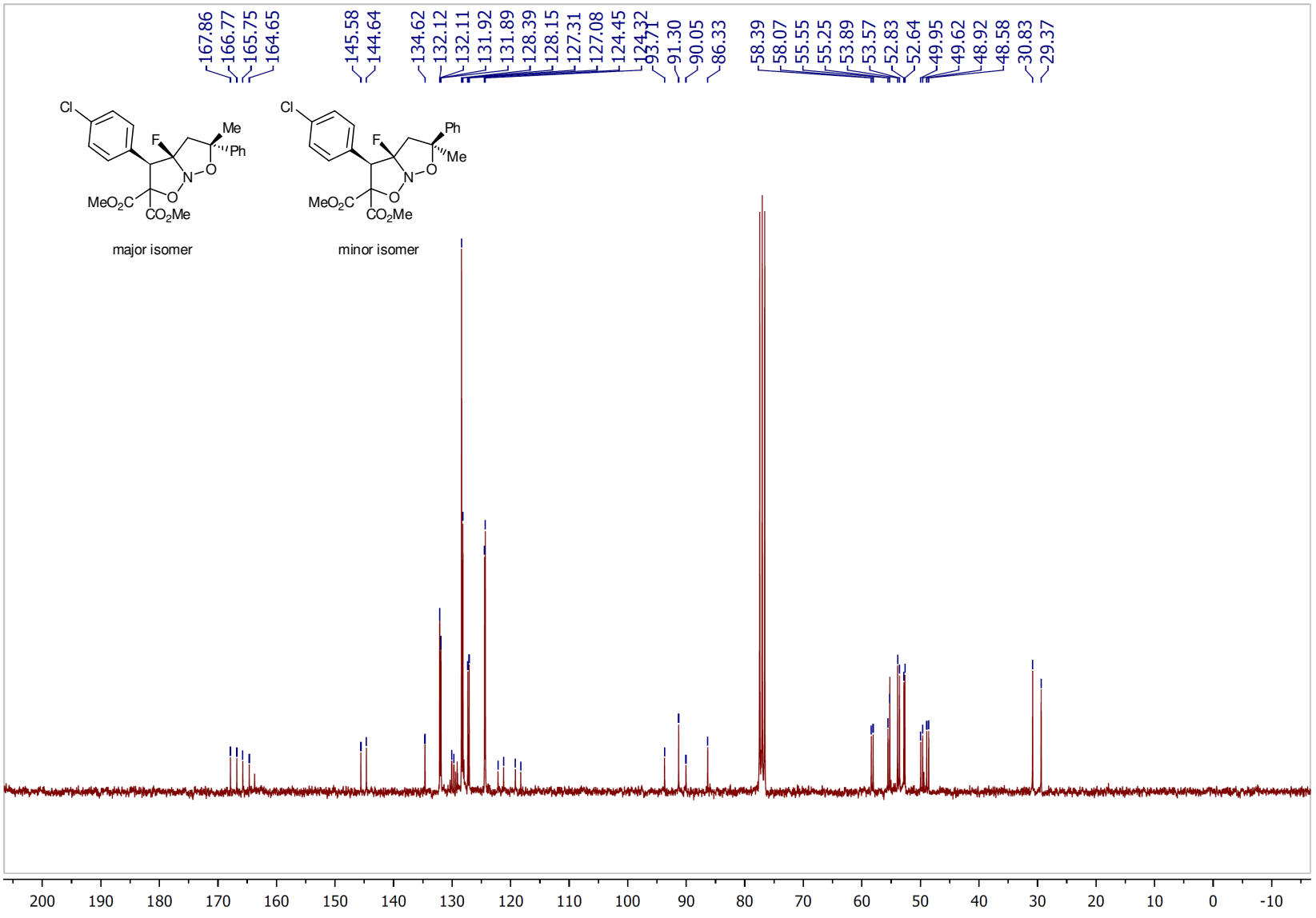

major isomer
minor isomer
250
260
270
280
290
300
310
320
330
340
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5

***rel*-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methyl-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4s** (major isomer) and ***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methyl-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4's** (minor isomer)

^{1}H NMR



^{13}C NMR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166.77
165.75
164.65
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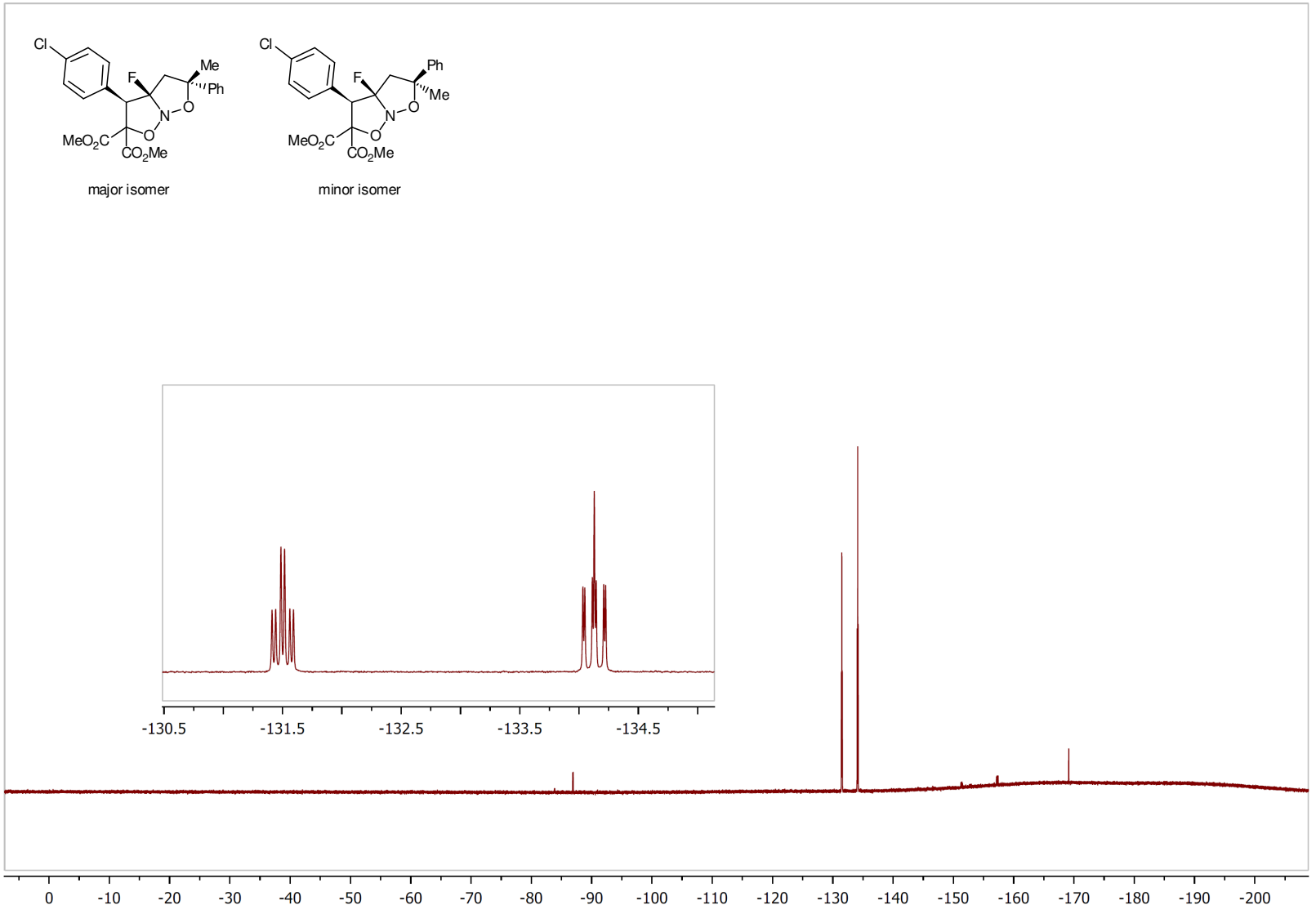
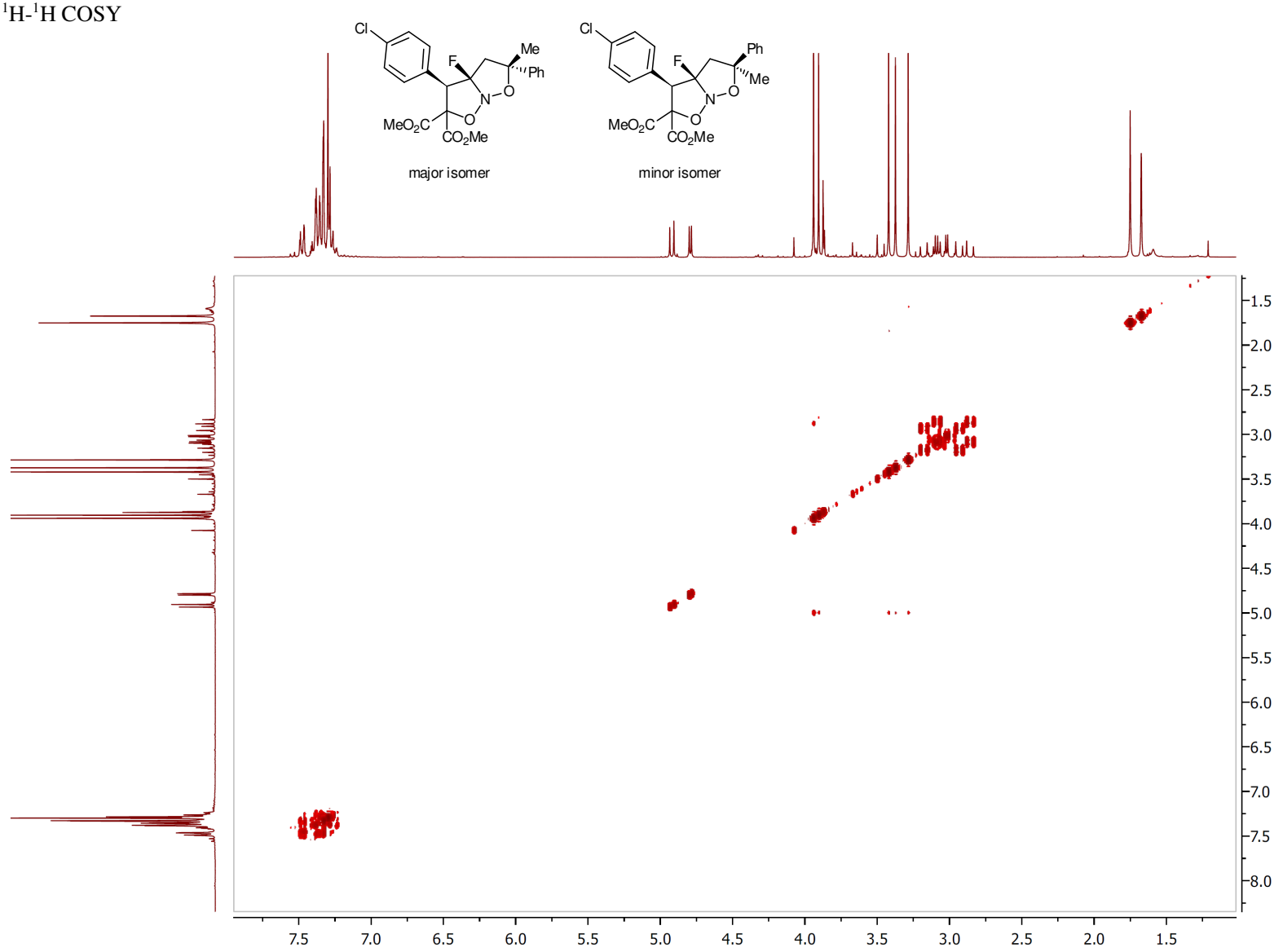
144.64
134.62
132.12
132.11
131.92
131.89
128.39
128.15
127.31
127.08
124.45
124.32
93.71
91.30
90.05
86.33
58.39
58.07
55.55
55.25
53.89
53.57
52.83
52.64
49.95
49.62
48.92
48.58
30.83
29.37
Cl
F
Me
Ph
N
O
MeO2C
CO2Me
major isomer
Cl
F
Ph
Me
N
O
MeO2C
CO2Me
minor isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

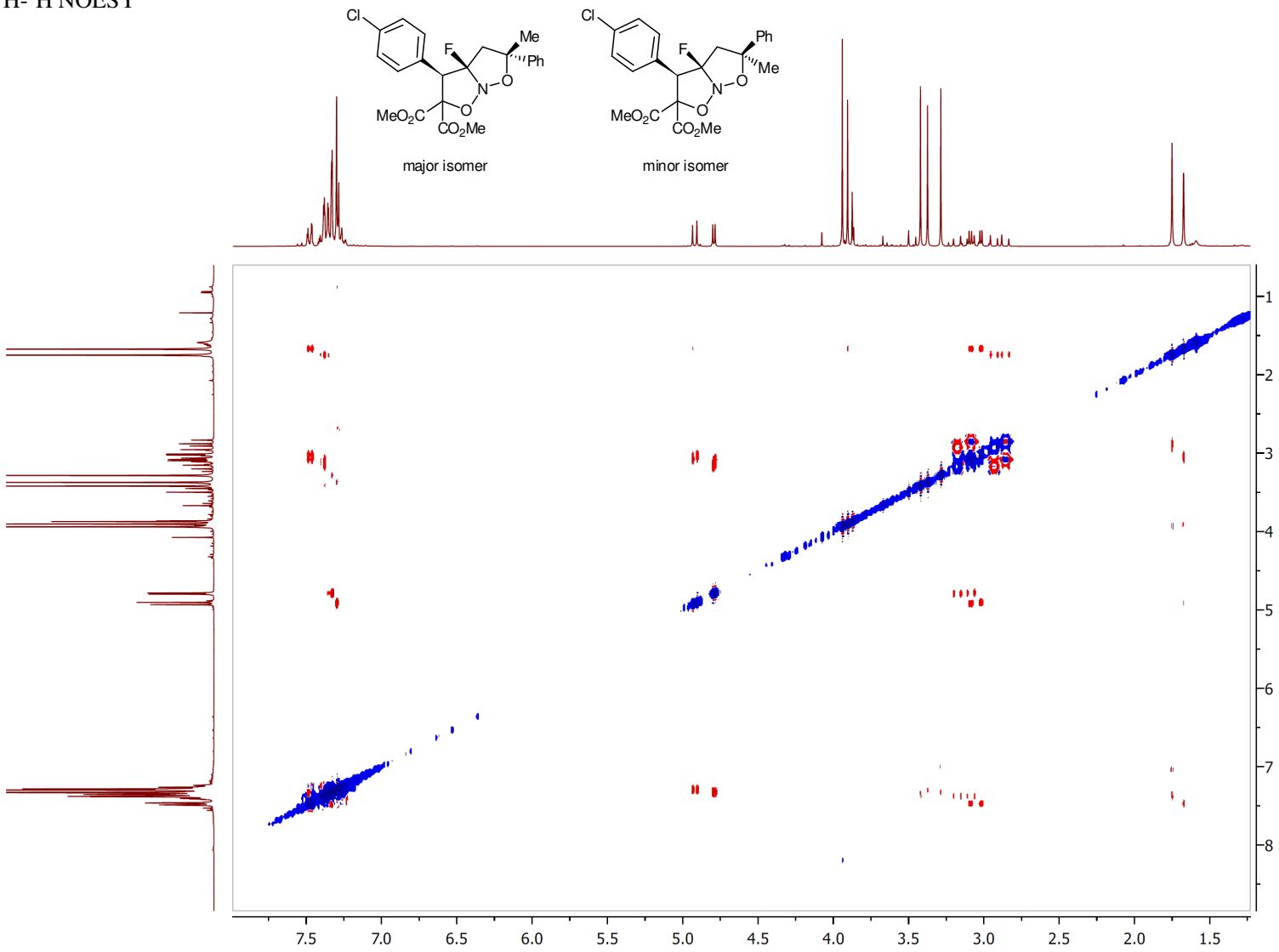
^{19}F NMR


major isomer
minor isomer
-130.5
-131.5
-132.5
-133.5
-134.5
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

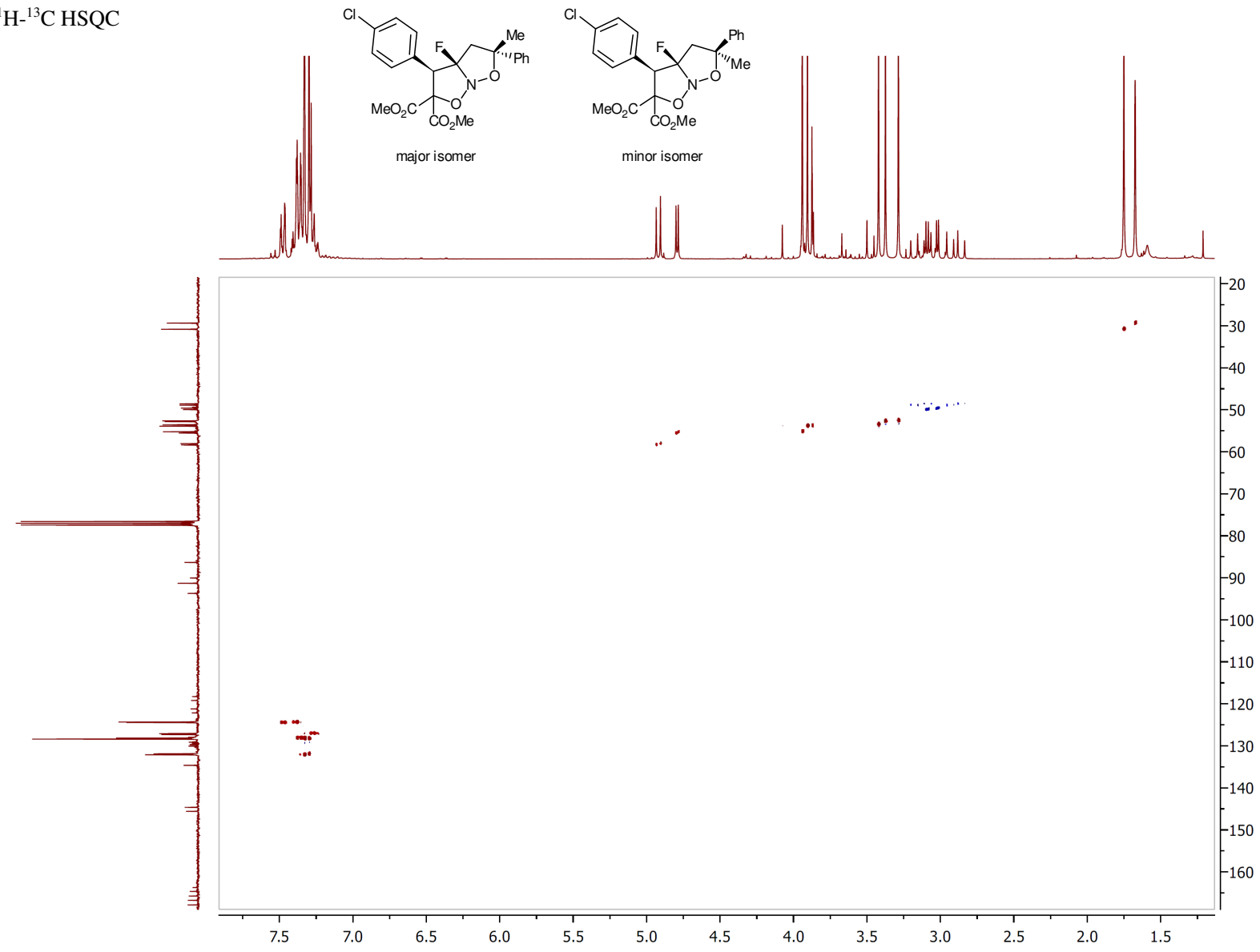
^{1}H-^{1}H COSY


Cl
F
Me
Ph
N
O
MeO2C
CO2Me
major isomer
Cl
F
Ph
Me
N
O
MeO2C
CO2Me
minor isomer
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
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

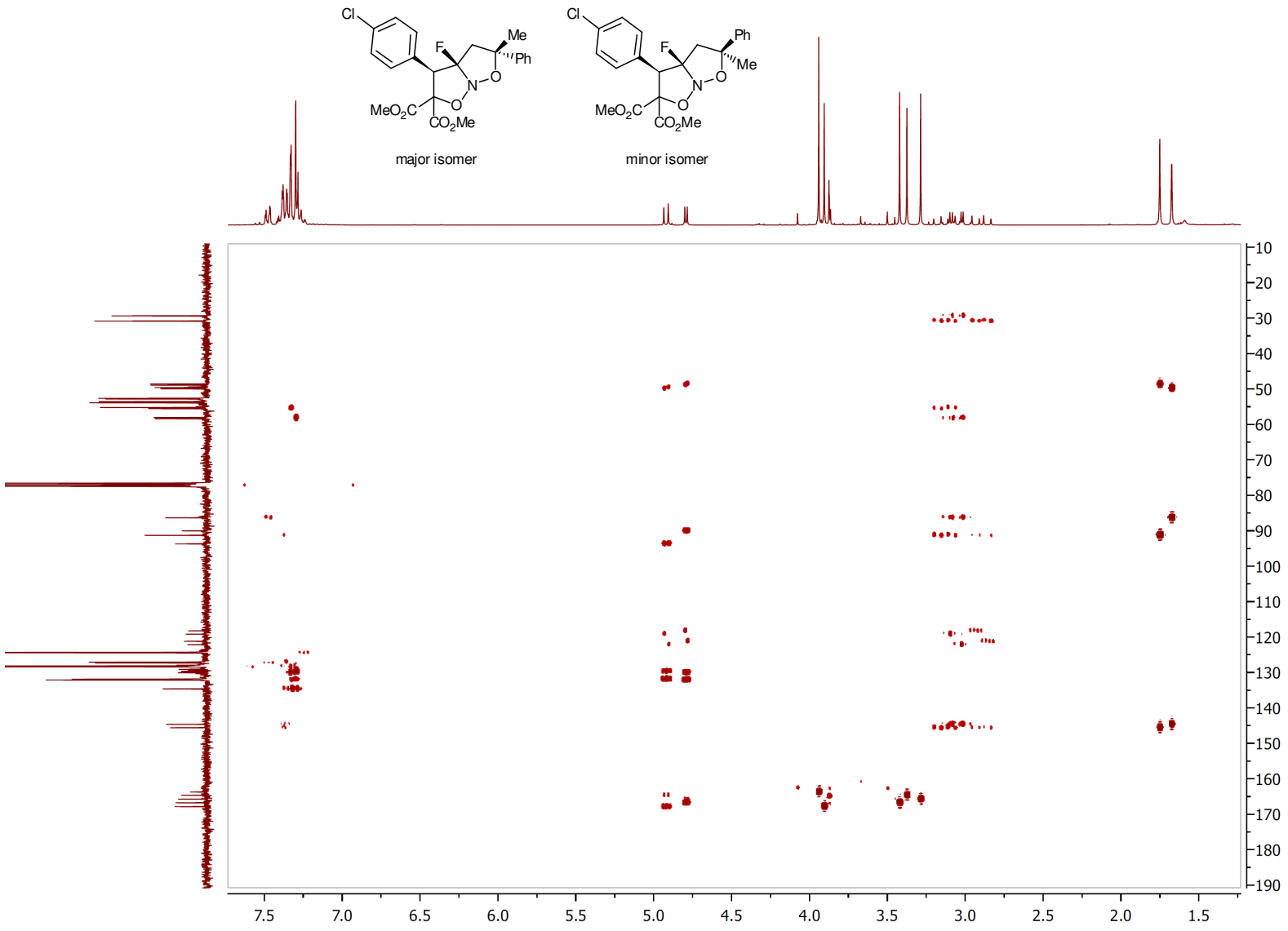
^{1}H-^{1}H NOESY


Cl
F
Me
Ph
N
O
MeO2C
CO2Me
major isomer
Cl
F
Ph
Me
N
O
MeO2C
CO2Me
minor isomer
1
2
3
4
5
6
7
8
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

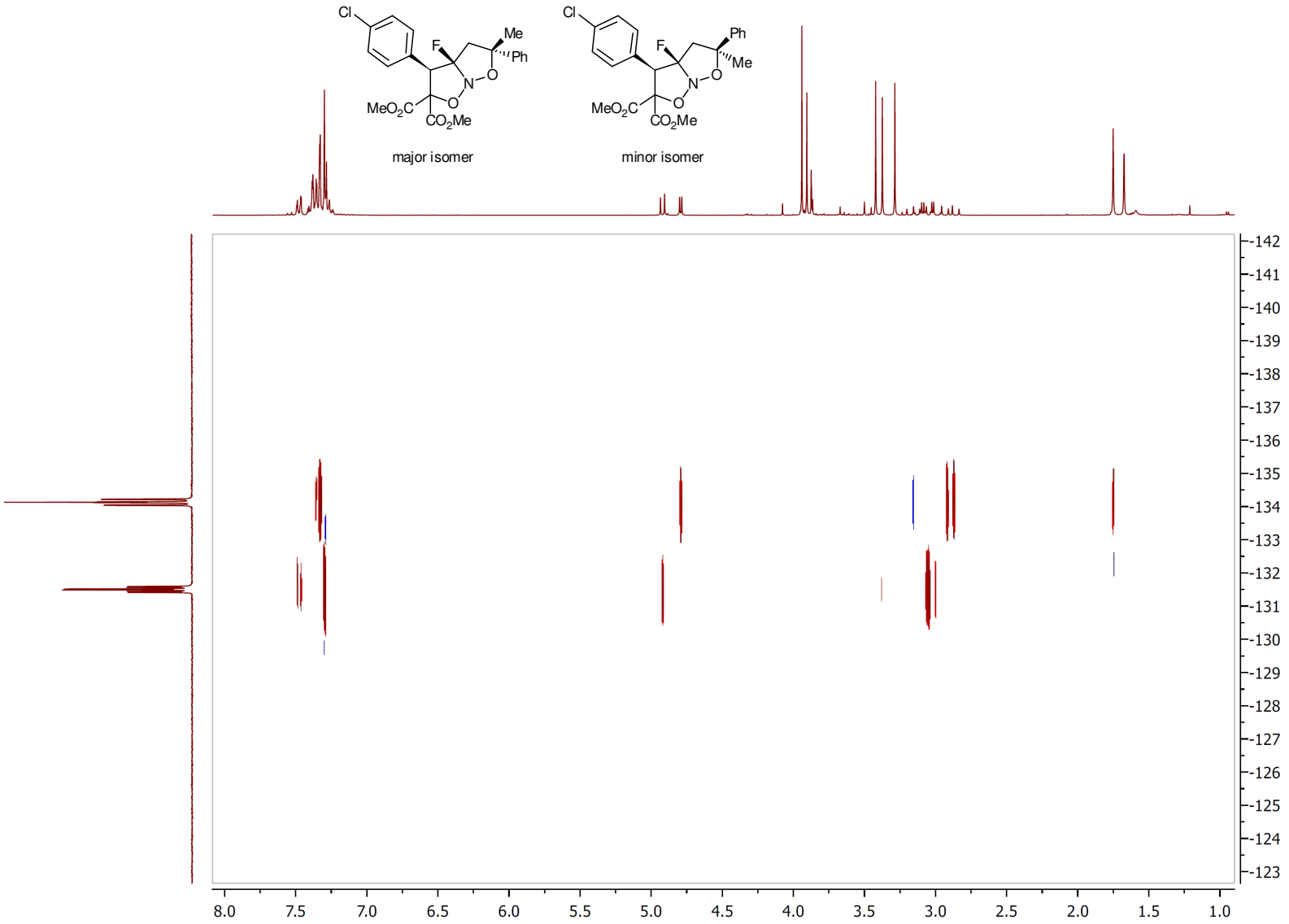
^{1}H-^{13}C HSQC


Cl
F
Me
Ph
N
O
MeO2C
CO2Me
major isomer
Cl
F
Ph
Me
N
O
MeO2C
CO2Me
minor isomer
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
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

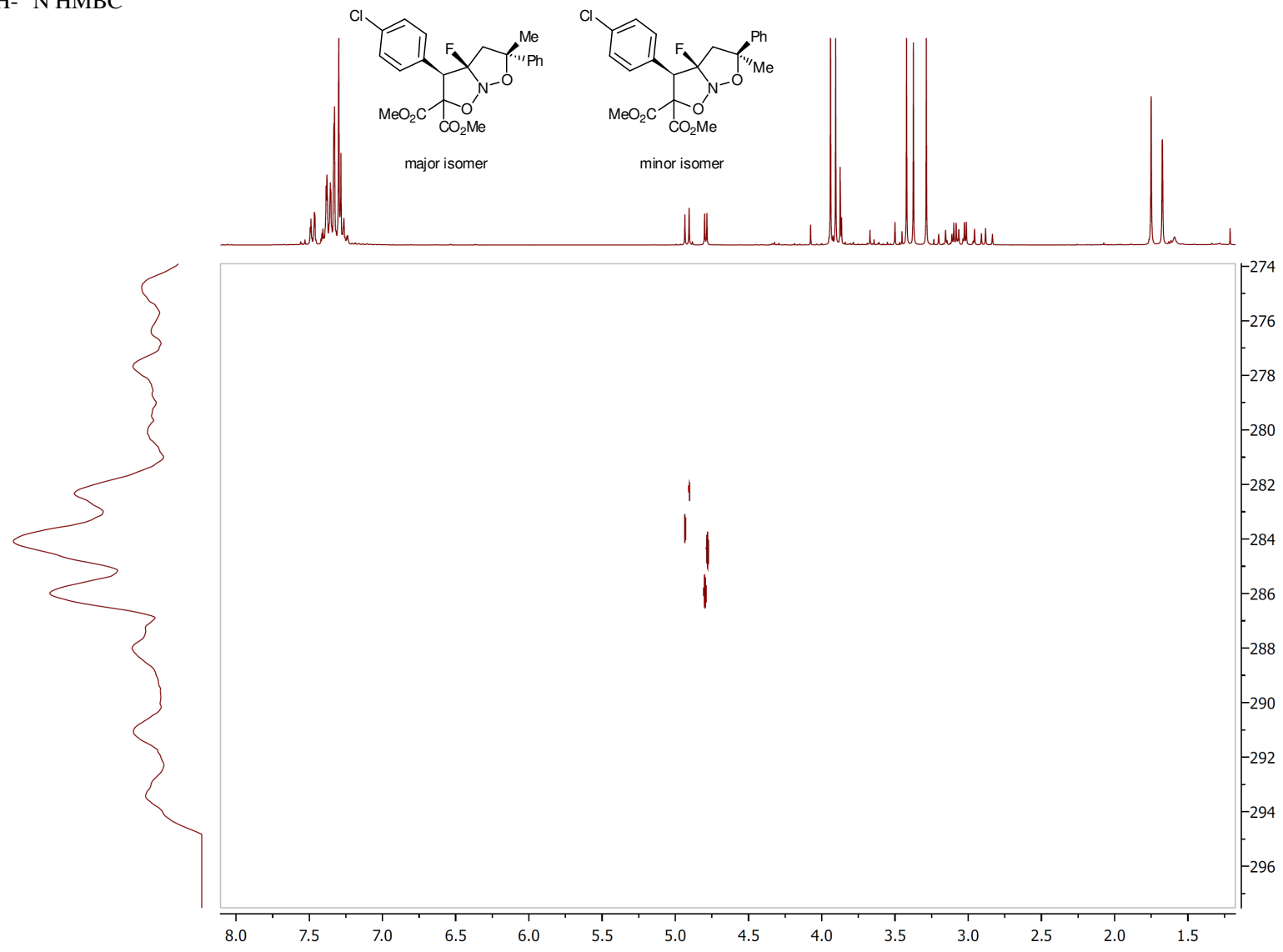
^{1}H-^{13}C HMBC


Cl
F
Me
Ph
N
O
MeO2C
CO2Me
major isomer
Cl
F
Ph
Me
N
O
MeO2C
CO2Me
minor isomer
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
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

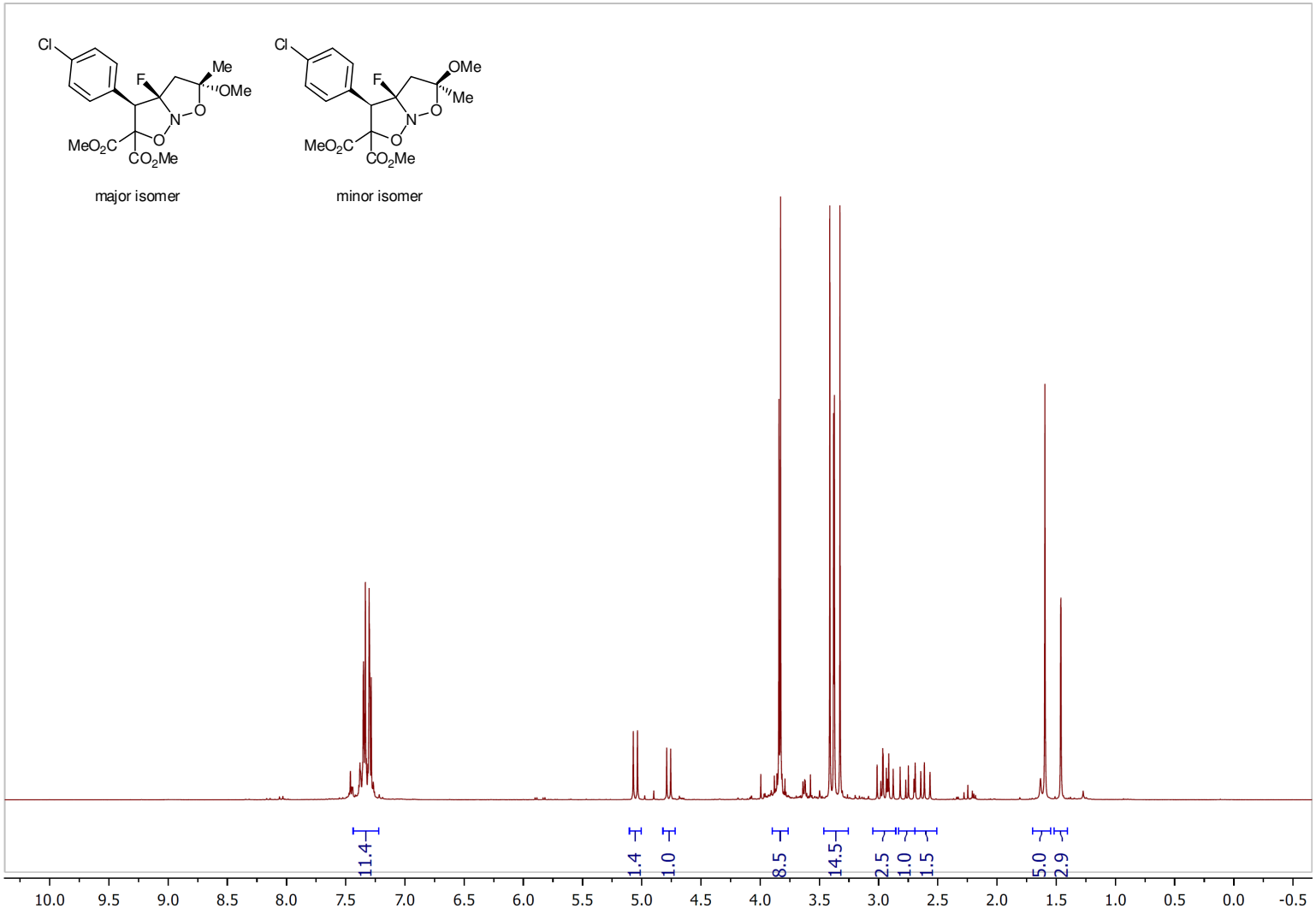
^{1}H-^{19}F HOESY


Cl
F
Me
Ph
N
O
MeO2C
CO2Me
major isomer
Cl
F
Ph
Me
N
O
MeO2C
CO2Me
minor isomer
-142
-141
-140
-139
-138
-137
-136
-135
-134
-133
-132
-131
-130
-129
-128
-127
-126
-125
-124
-123
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

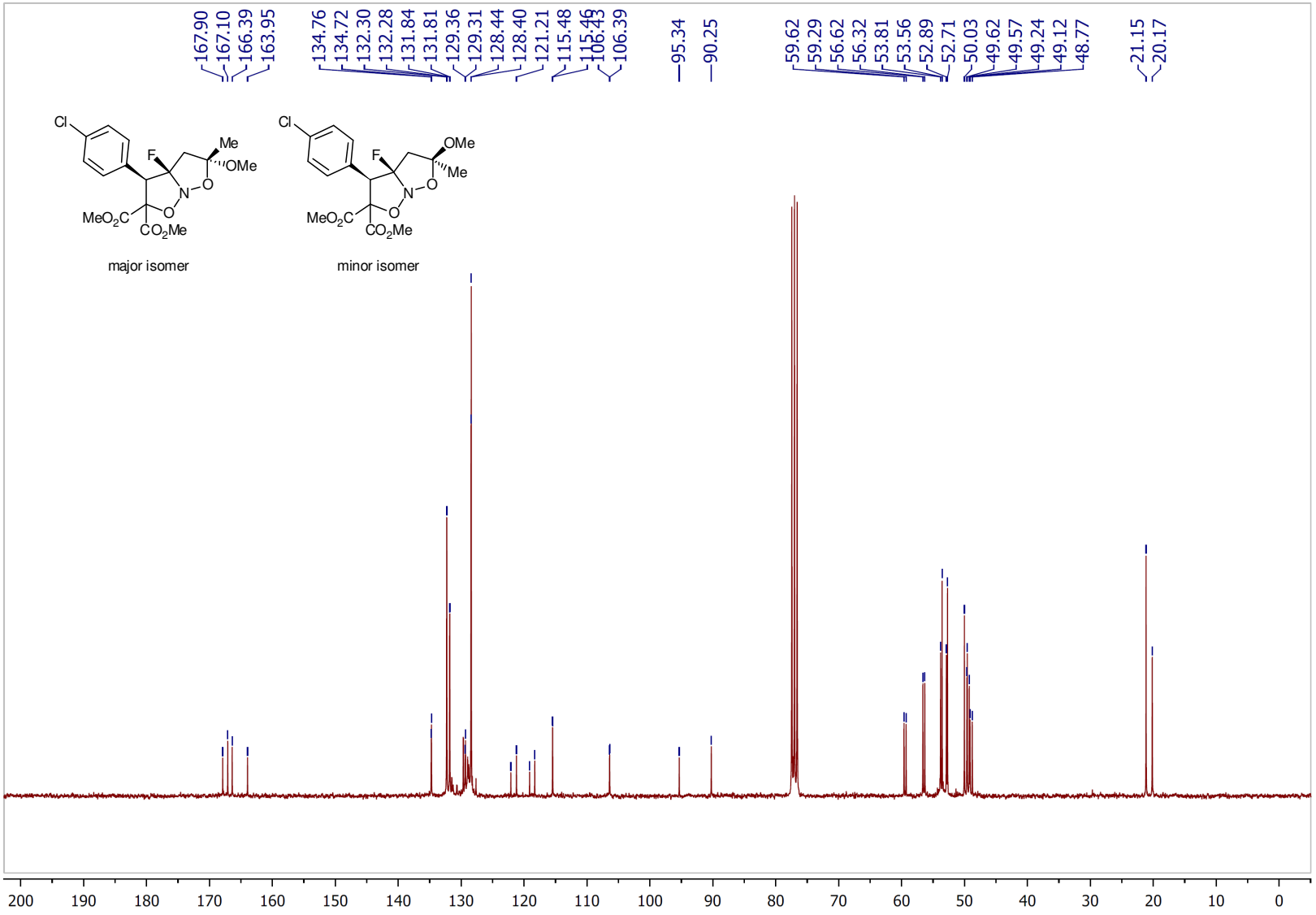
^{1}H-^{15}N HMBC


Cl
F
Me
Ph
N
O
MeO2C
CO2Me
major isomer
Cl
F
Ph
Me
N
O
MeO2C
CO2Me
minor isomer
274
276
278
280
282
284
286
288
290
292
294
296
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

***rel*-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methoxy-5-methyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4t** (major isomer) and ***rel*-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methoxy-5-methyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4't** (minor isomer)
^{1}H NMR



^{13}C NMR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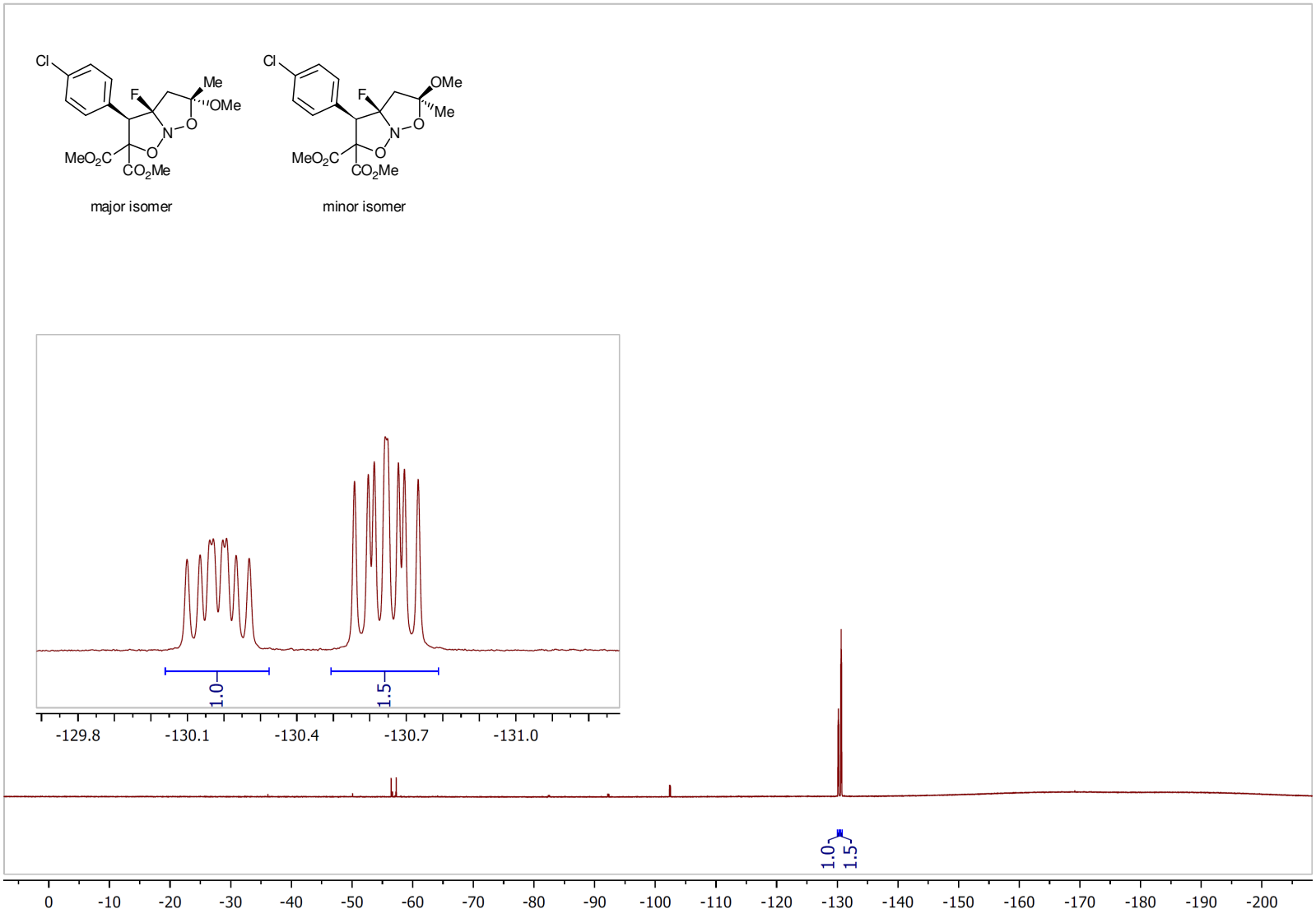
167.10
166.39
163.95
134.76
134.72
132.30
132.28
131.84
131.81
129.36
129.31
128.44
128.40
121.21
115.48
115.46
106.43
106.39
95.34
90.25
59.62
59.29
56.62
56.32
53.81
53.56
52.89
52.71
50.03
49.62
49.57
49.24
49.12
48.77
21.15
20.17
Cl
F
Me
OMe
N
O
MeO2C
CO2Me
major isomer
Cl
F
OMe
Me
N
O
MeO2C
CO2Me
minor isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR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F
Me
OMe
N
O
MeO2C
CO2Me
major isomer
Cl
F
OMe
Me
N
O
MeO2C
CO2Me
minor isomer
1.0
1.5
-129.8
-130.1
-130.4
-130.7
-131.0
1.0
1.5
0
-10
-20
-30
-40
-50
-60
-70
-80
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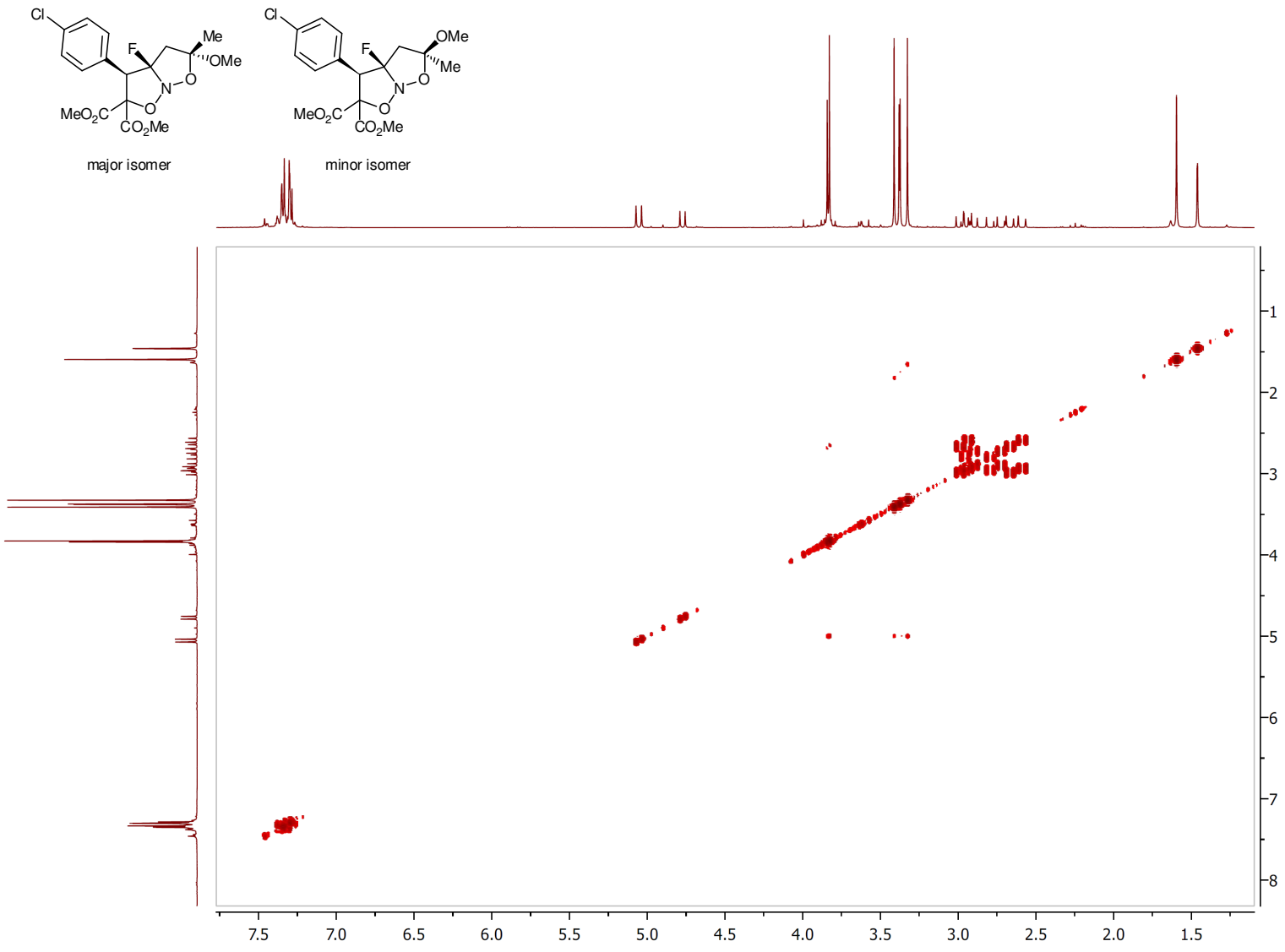
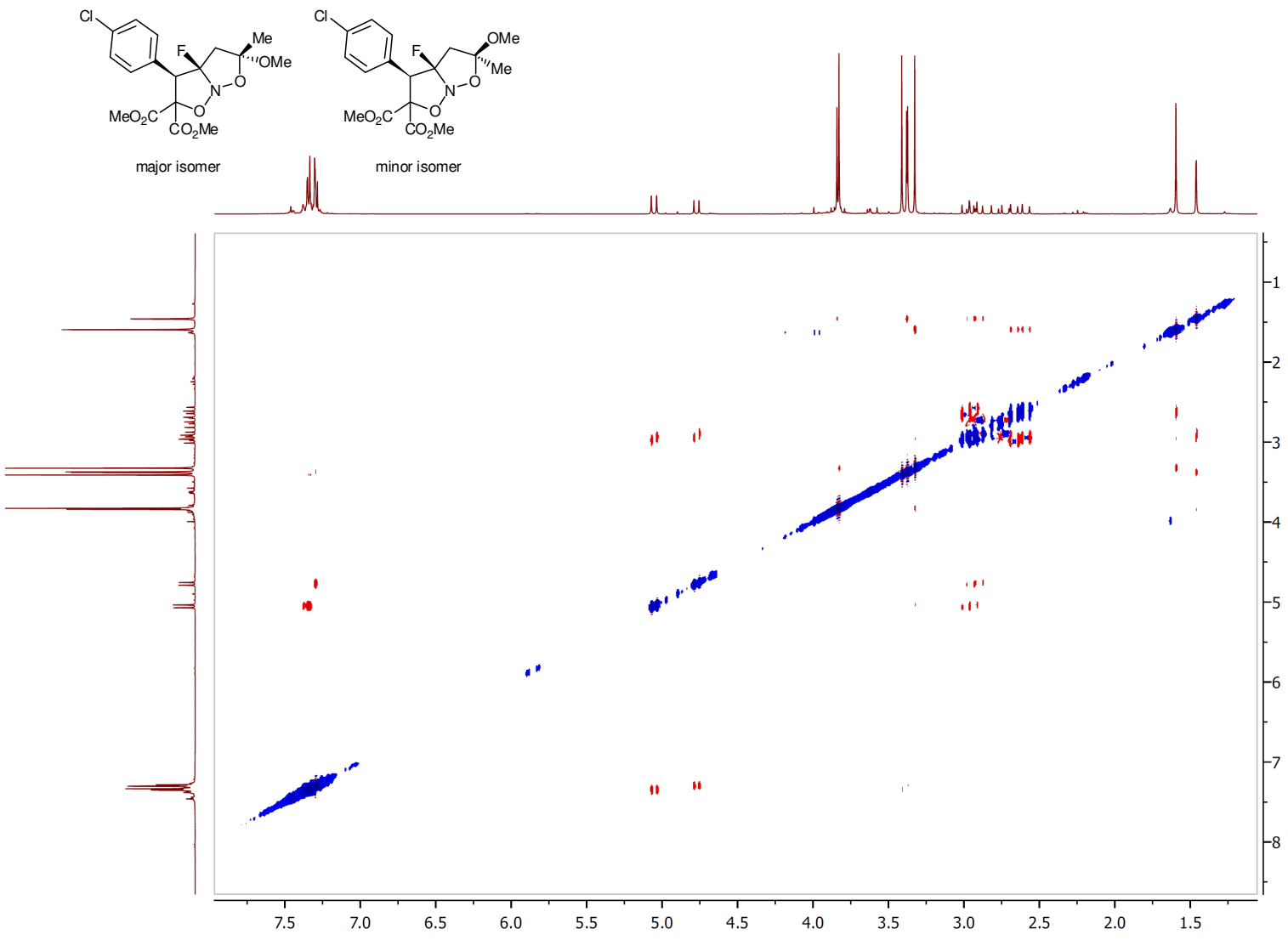
-130
-140
-150
-160
-170
-180
-190
-200

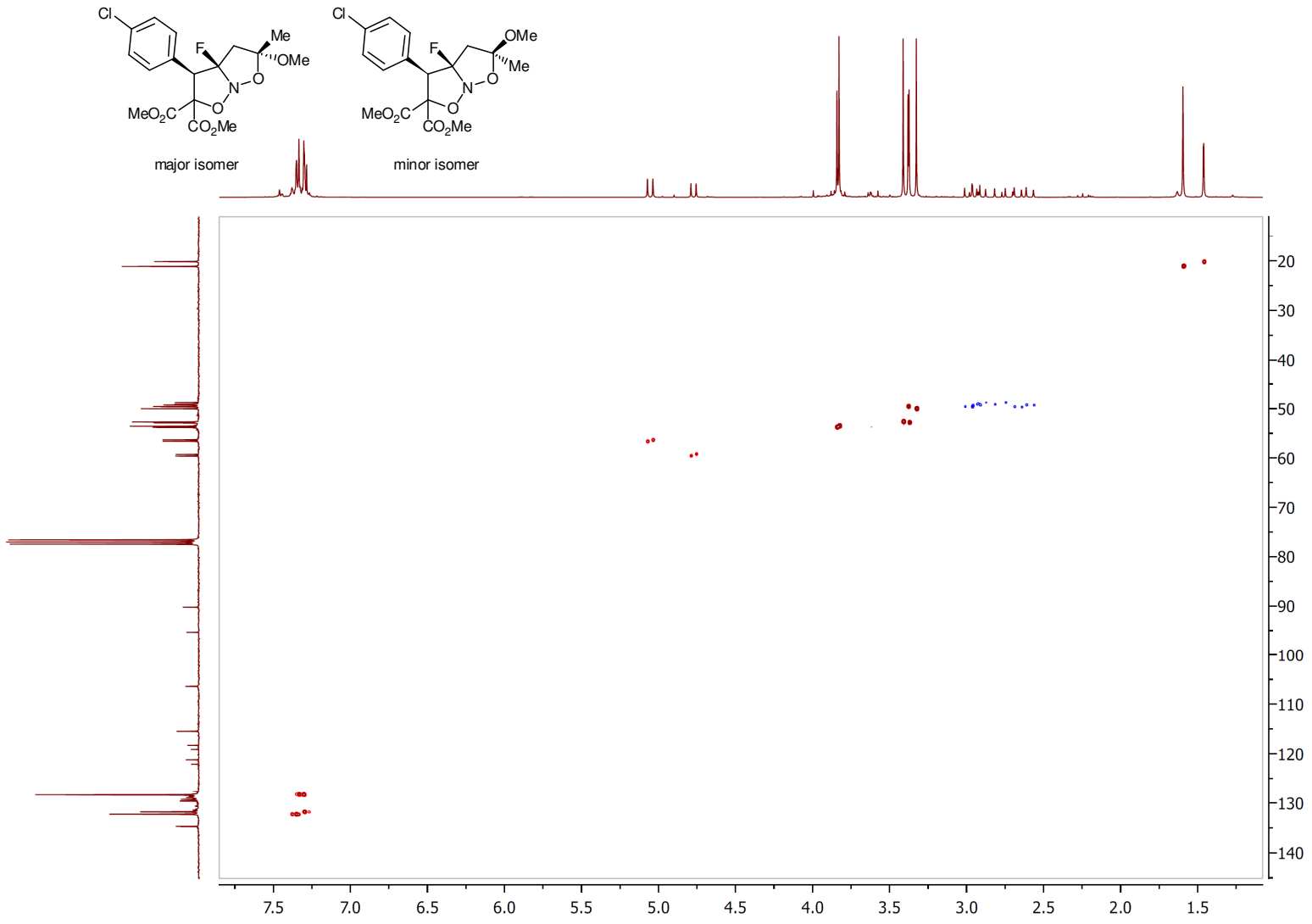
^{1}H-^{1}H COSY


Cl
F
Me
OMe
N
O
MeO2C
CO2Me
major isomer
Cl
F
OMe
Me
N
O
MeO2C
CO2Me
minor isomer
1
2
3
4
5
6
7
8
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}H-^{1}H NOESY


Cl
F
Me
OMe
N
O
MeO2C
CO2Me
major isomer
Cl
F
OMe
Me
N
O
MeO2C
CO2Me
minor isomer
1
2
3
4
5
6
7
8
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}H-^{13}C HSQC


Cl
F
Me
OMe
N
O
MeO2C
CO2Me
major isomer
Cl
F
OMe
Me
N
O
MeO2C
CO2Me
minor isomer
20
30
40
50
60
70
80
90
100
110
120
130
140
7.5
7.0
6.5
6.0
5.5
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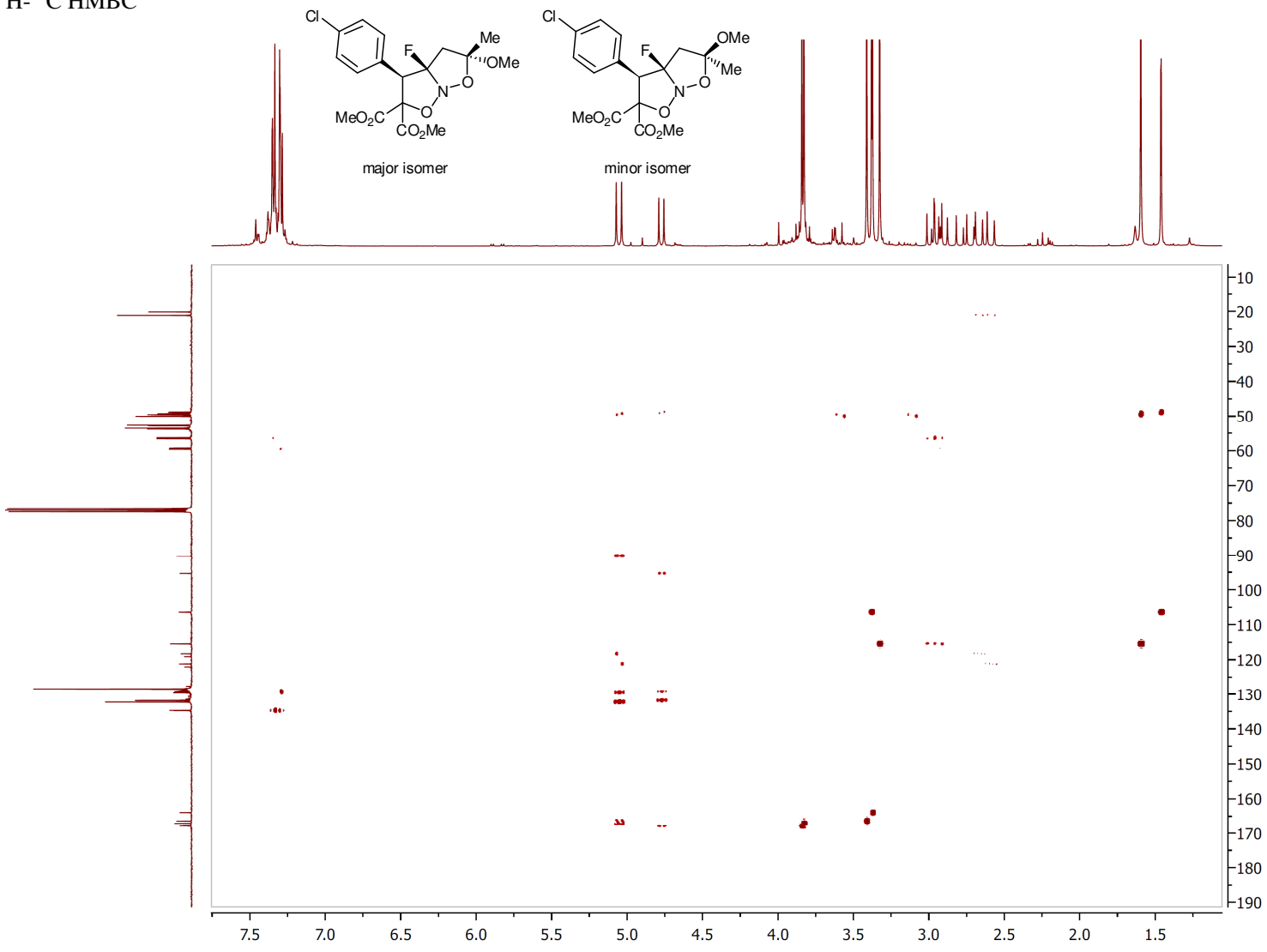
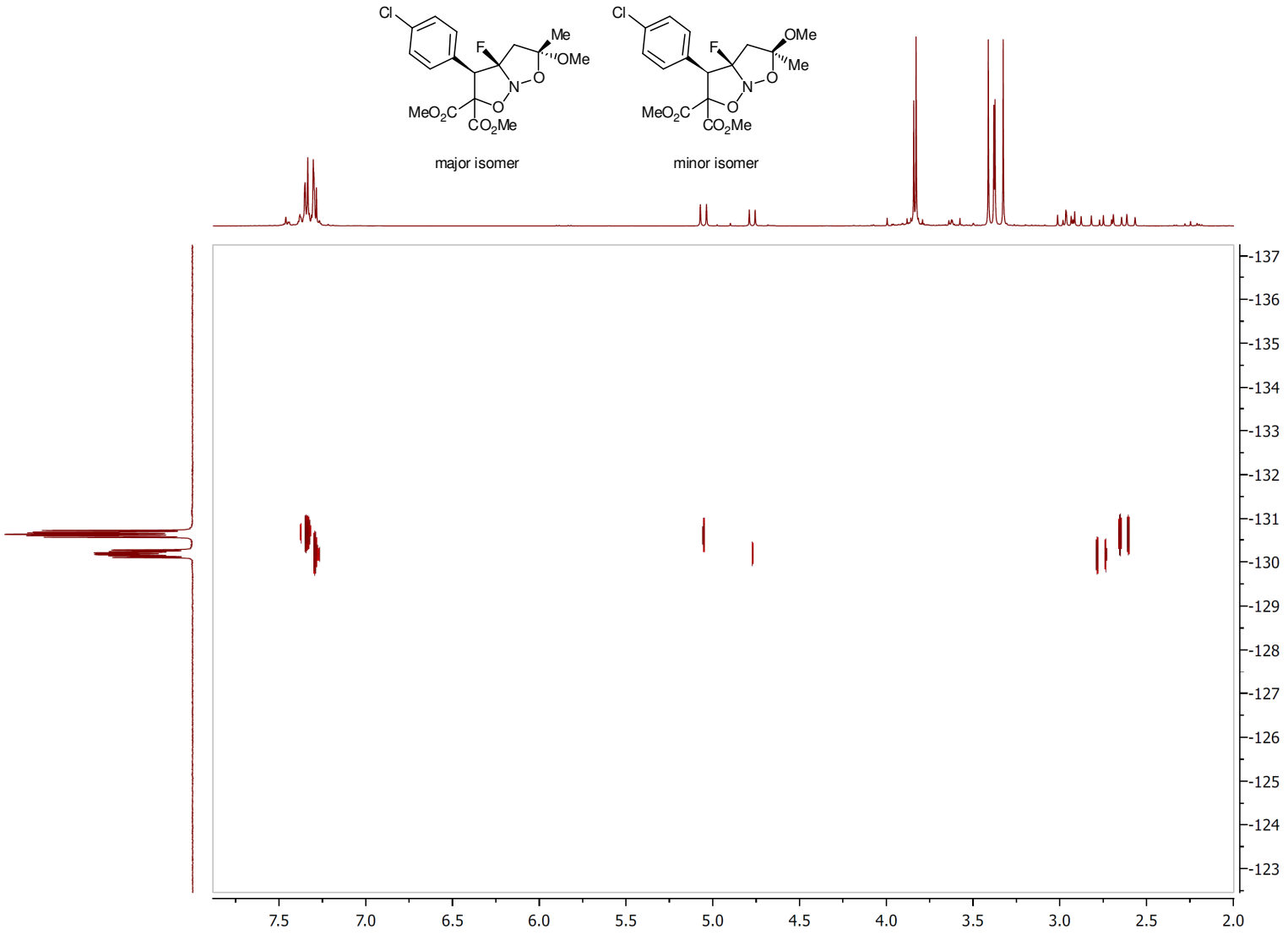
4.5
4.0
3.5
3.0
2.5
2.0
1.5

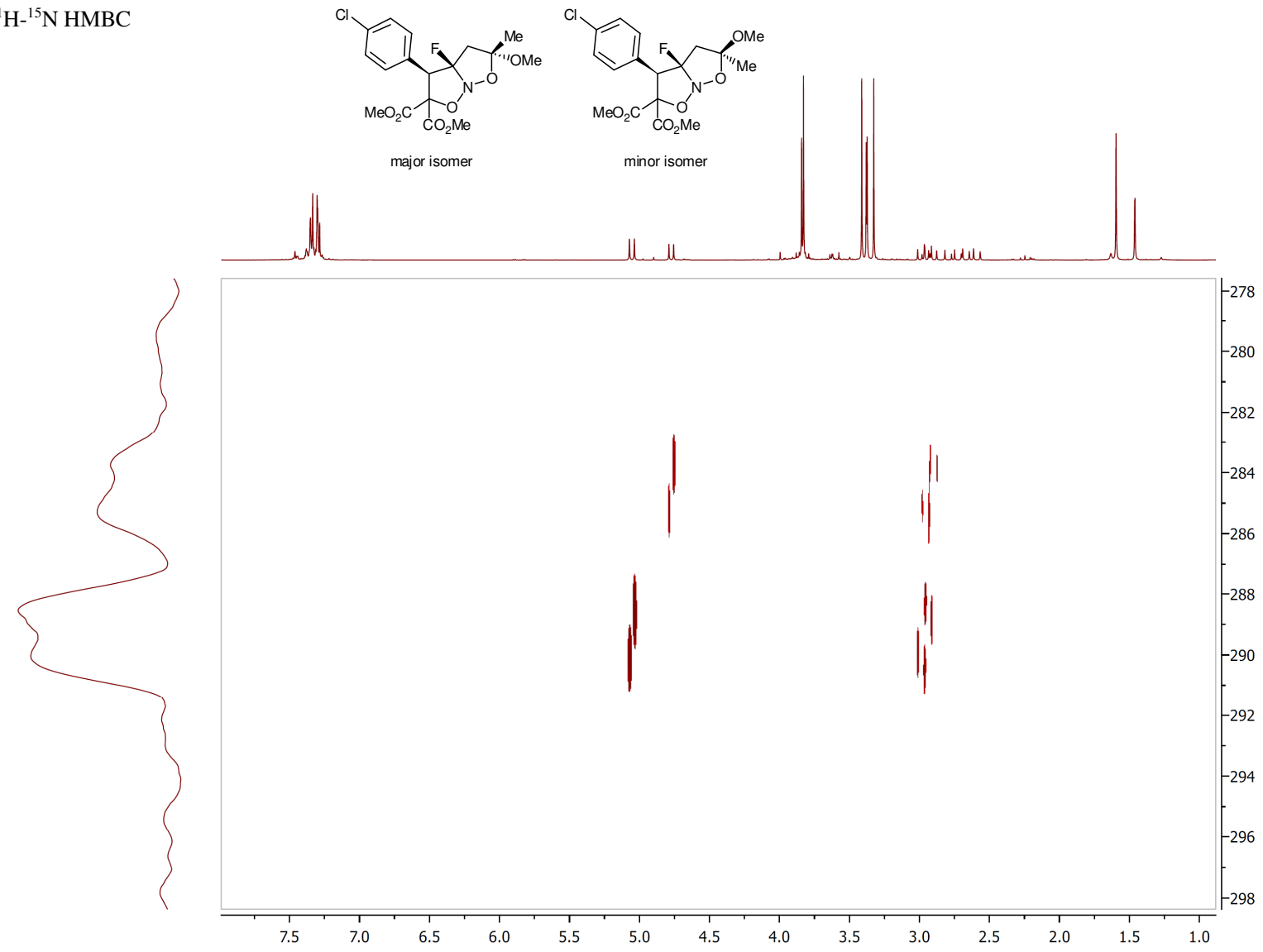
^{1}H-^{13}C HMBC


Cl
F
Me
OMe
N
O
MeO2C
CO2Me
major isomer
Cl
F
OMe
Me
N
O
MeO2C
CO2Me
minor isomer
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
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}H-^{19}F HOESY

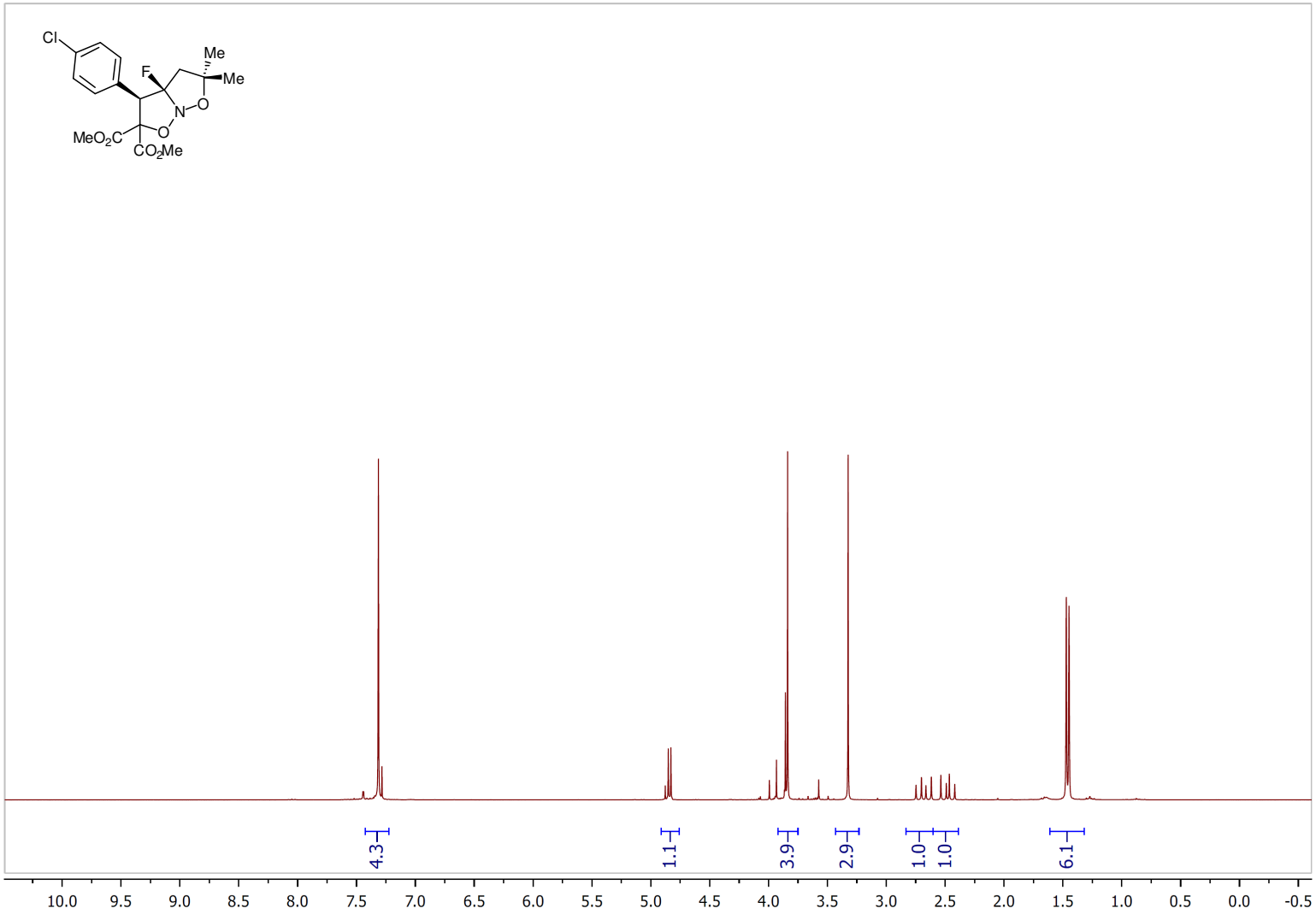

Cl
F
Me
OMe
N
O
MeO2C
CO2Me
major isomer
Cl
F
OMe
Me
N
O
MeO2C
CO2Me
minor isomer
-137
-136
-135
-134
-133
-132
-131
-130
-129
-128
-127
-126
-125
-124
-123
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0

^{1}H-^{15}N HMBC

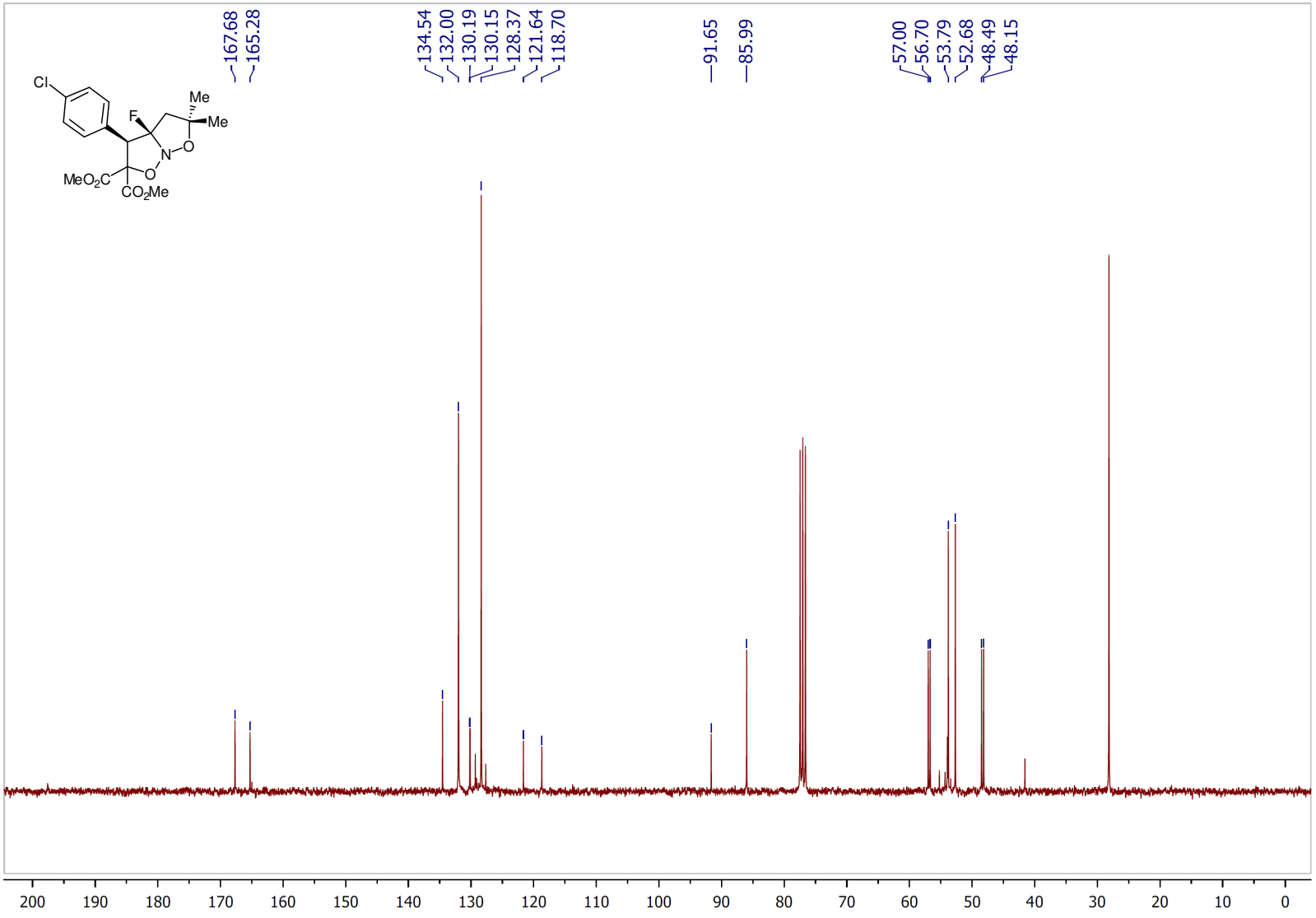

Cl
F
Me
OMe
N
O
MeO2C
CO2Me
major isomer
Cl
F
OMe
Me
N
O
MeO2C
CO2Me
minor isomer
278
280
282
284
286
288
290
292
294
296
298
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

***rel*-(3R,3aR)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5,5-dimethyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4u**

^{1}H NMR



^{13}C NMR


167.68
165.28
134.54
132.00
130.19
130.15
128.37
121.64
118.70
91.65
85.99
57.00
56.70
53.79
52.68
48.49
48.15
Cl
F
Me
Me
N
O
O
MeO2C
CO2Me
200
190
180
170
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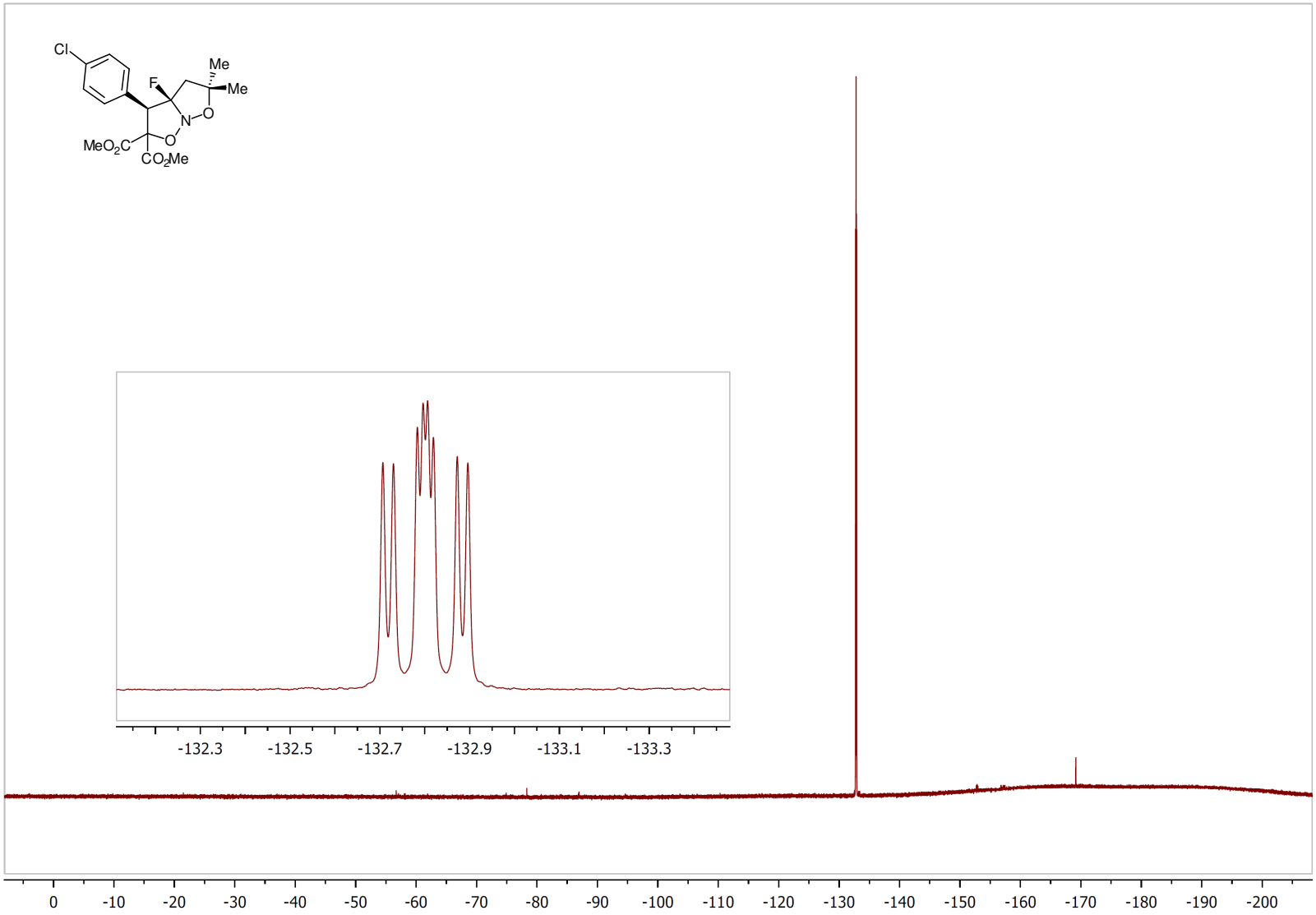
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR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N
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O
MeO2C
CO2Me
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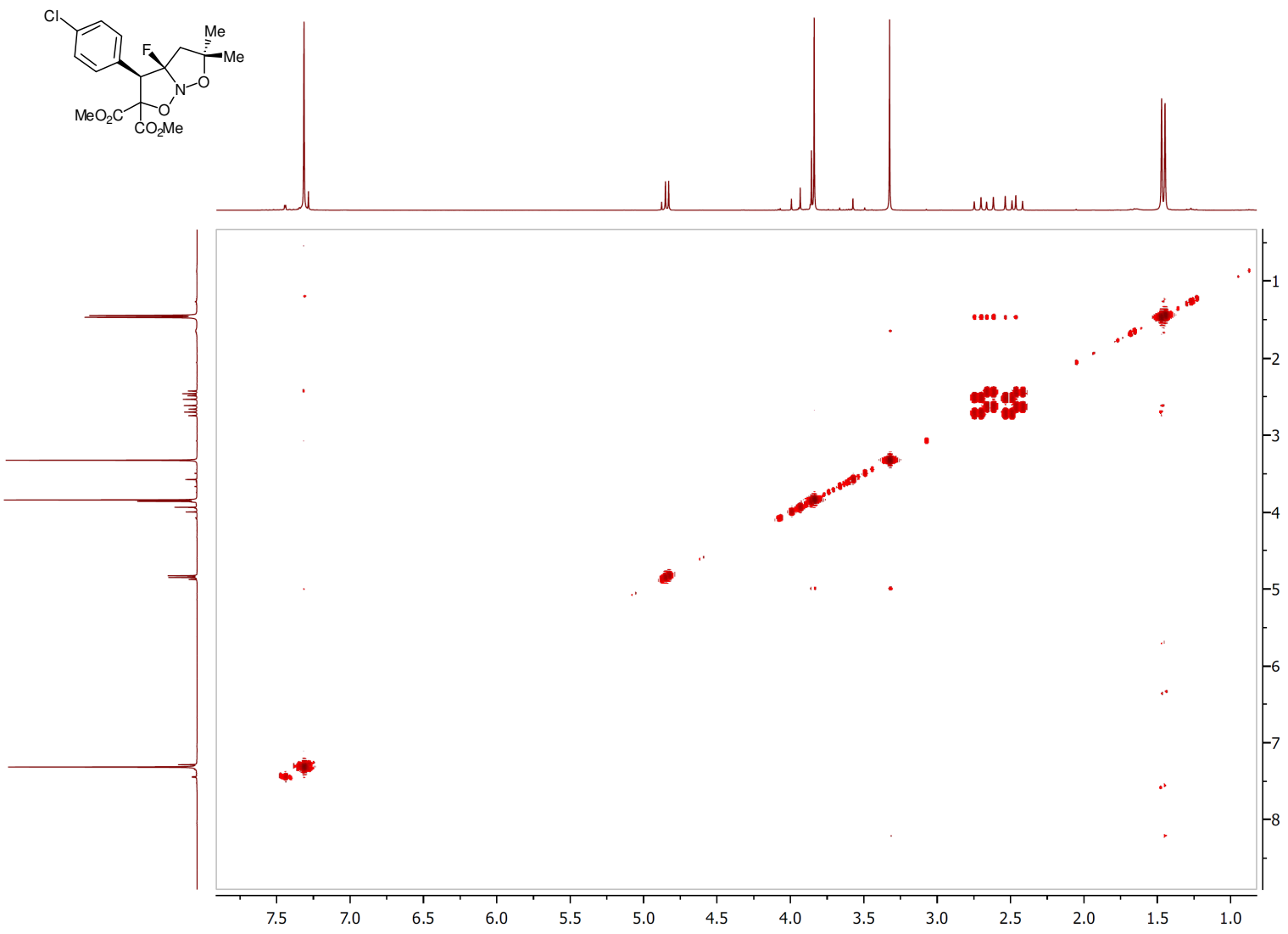
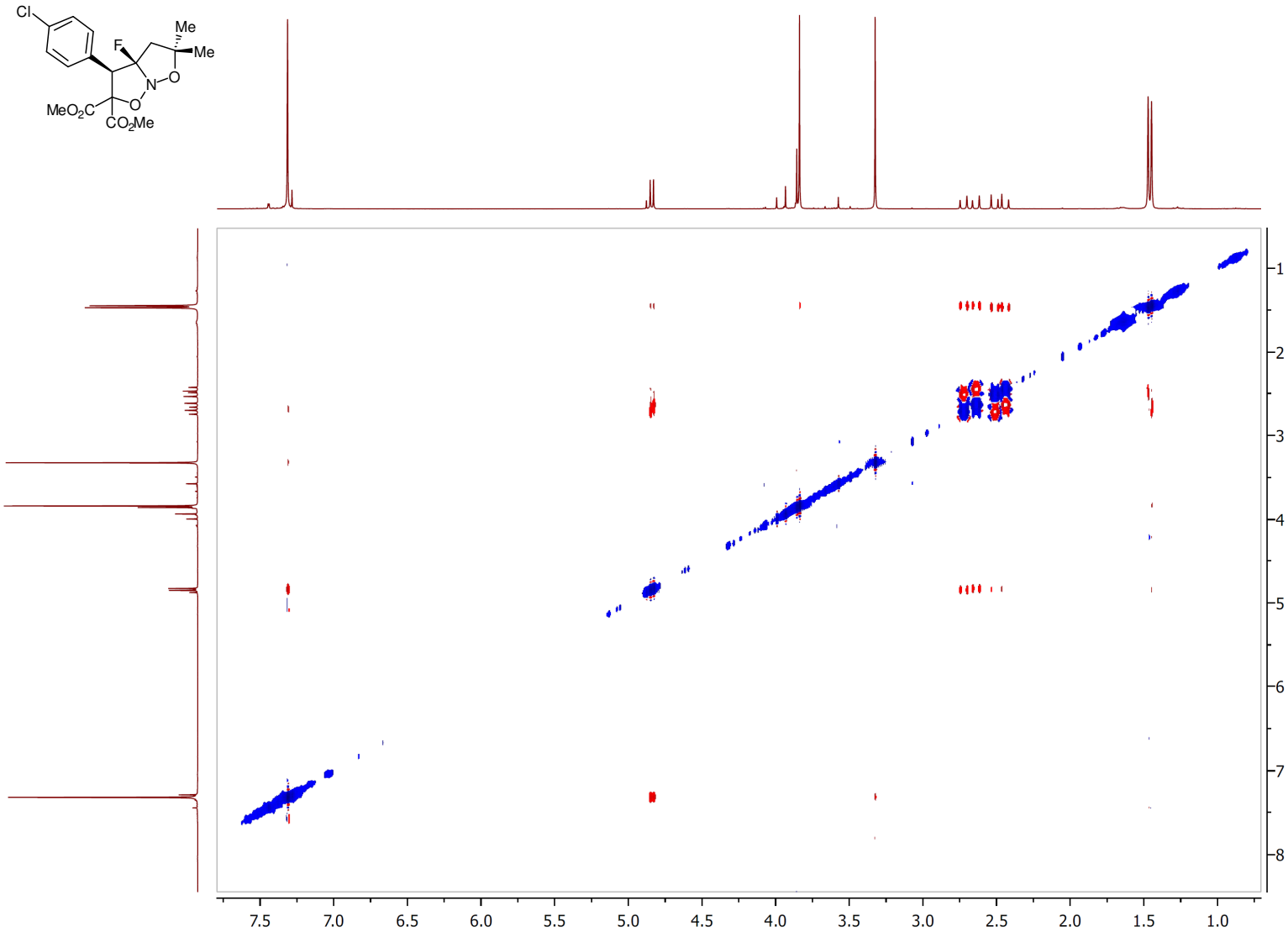
-132.5
-132.7
-132.9
-133.1
-133.3
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

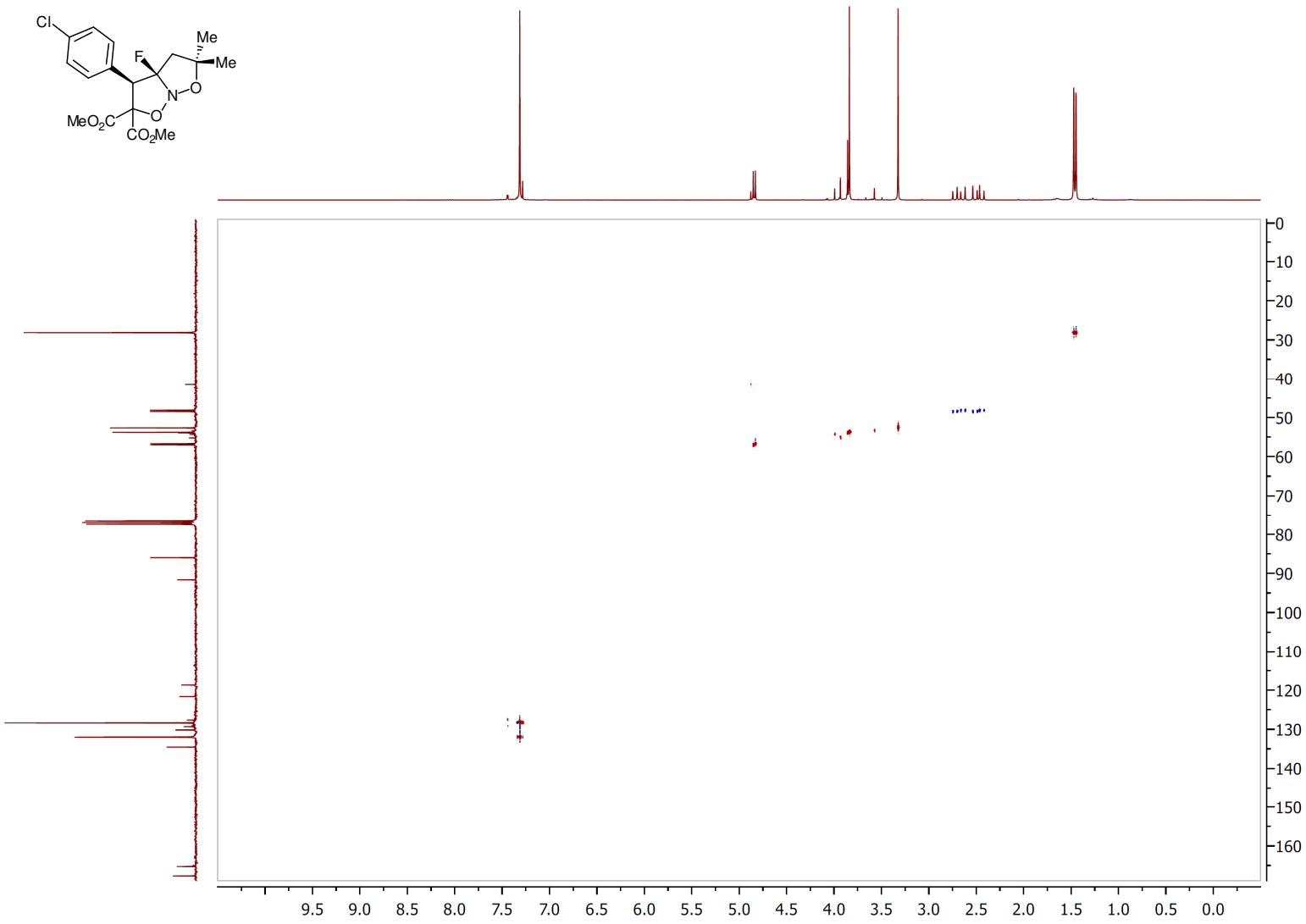
^{1}H-^{1}H COSY


Cl
F
Me
Me
N
O
O
MeO2C
CO2Me
1
2
3
4
5
6
7
8
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

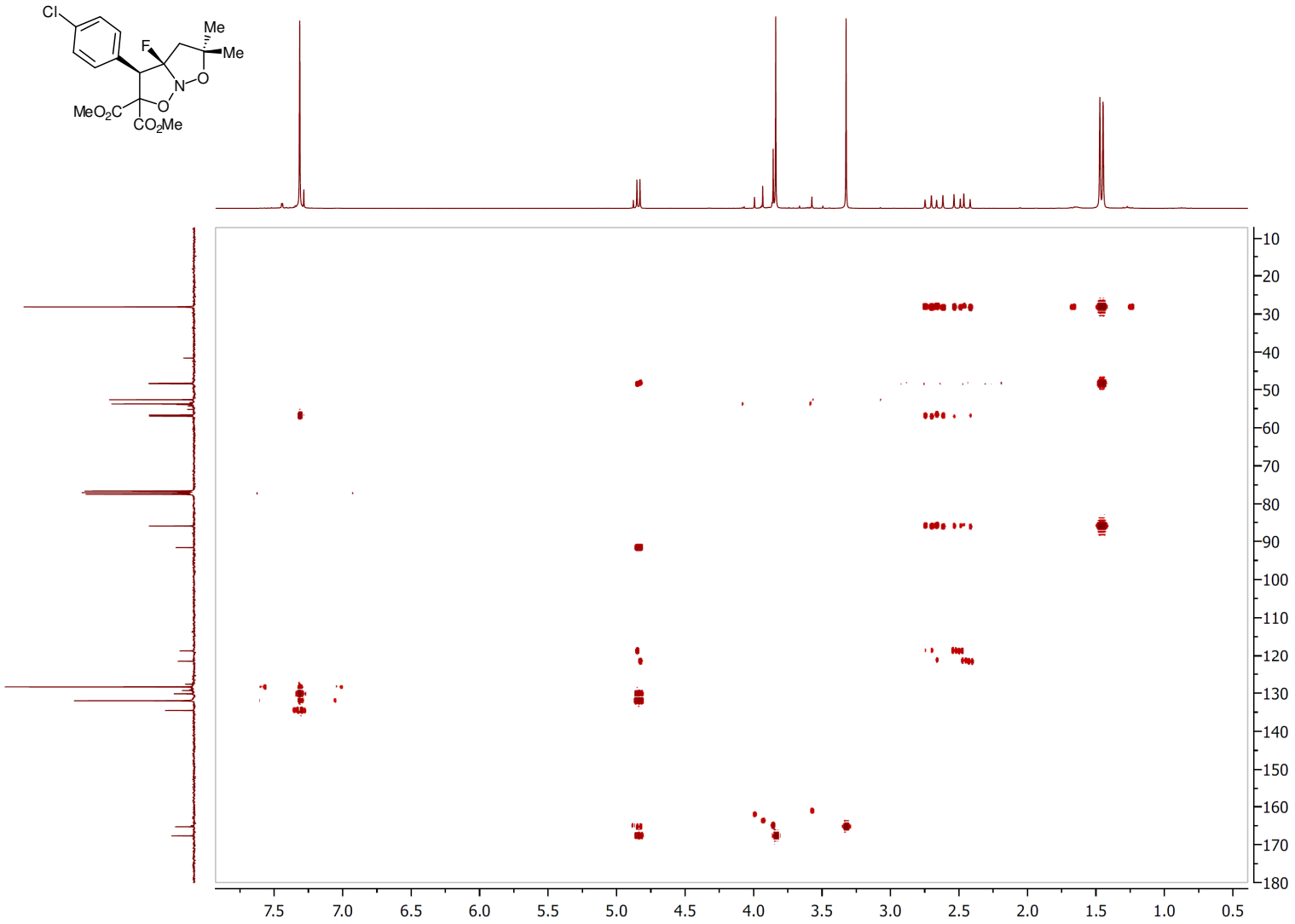
^{1}H-^{1}H NOESY


Cl
F
Me
Me
N
O
O
MeO2C
CO2Me
1
2
3
4
5
6
7
8
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

^{1}H-^{13}C HSQC


Cl
F
Me
Me
N
O
O
MeO2C
CO2Me
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
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

^{1}H-^{13}C HMBC


Cl
F
Me
Me
N
O
O
MeO2C
CO2Me
10
20
30
40
50
60
70
80
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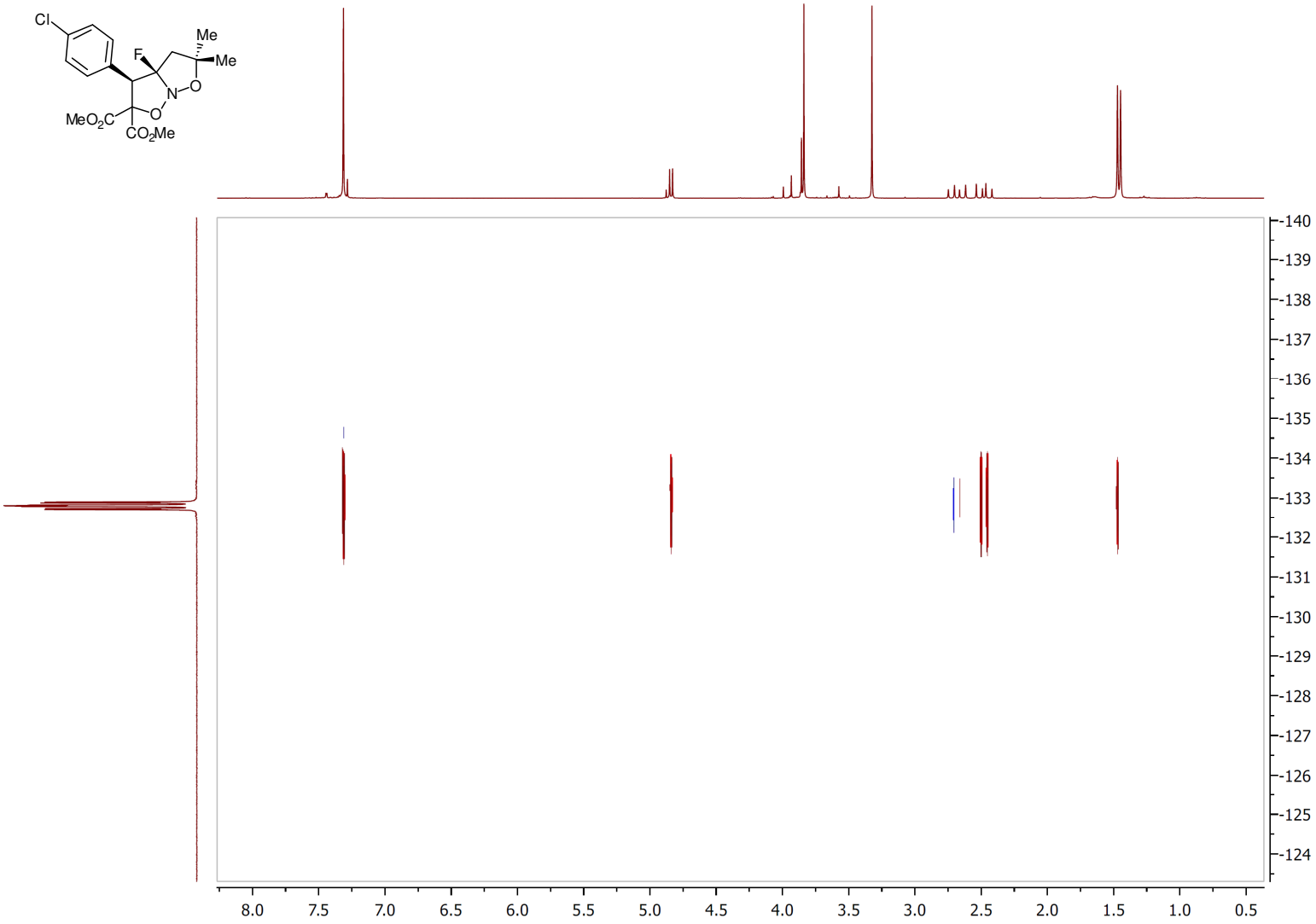
100
110
120
130
140
150
160
170
180
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

^{1}H-^{19}F HOESY


Cl
F
Me
Me
N
O
O
MeO2C
CO2Me
-140
-139
-138
-137
-136
-135
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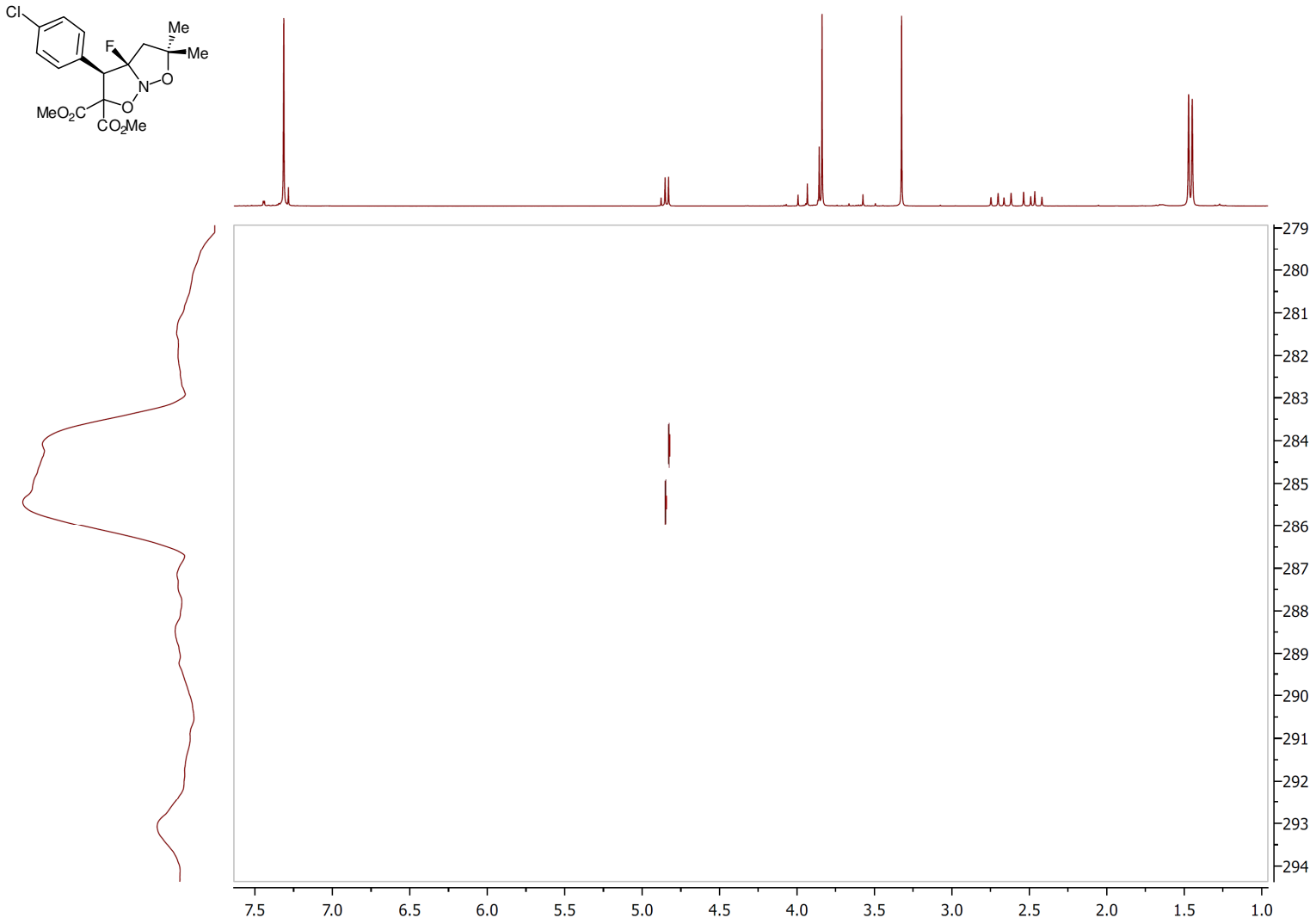
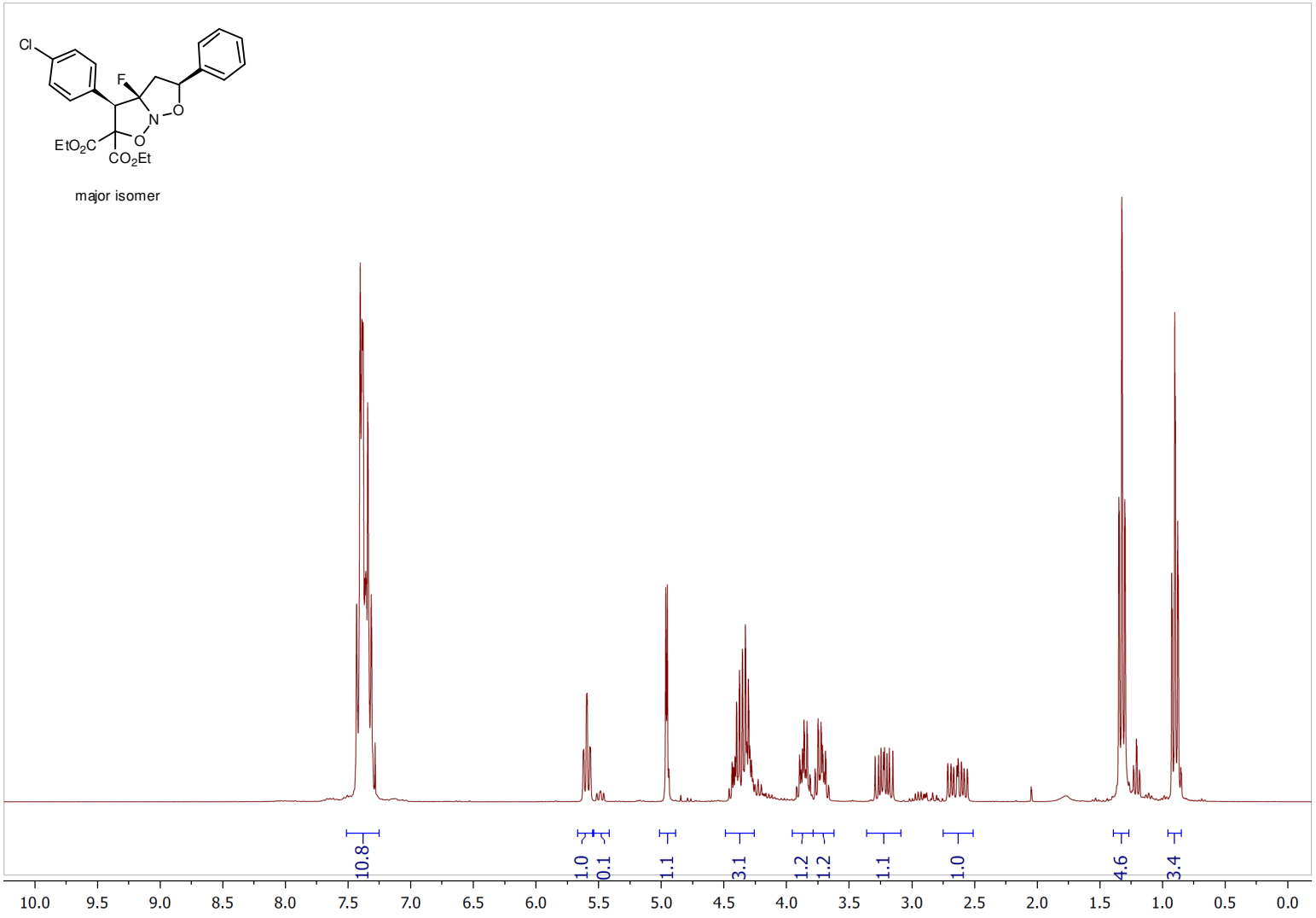
-133
-132
-131
-130
-129
-128
-127
-126
-125
-124
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

^{1}H-^{15}N HMBC

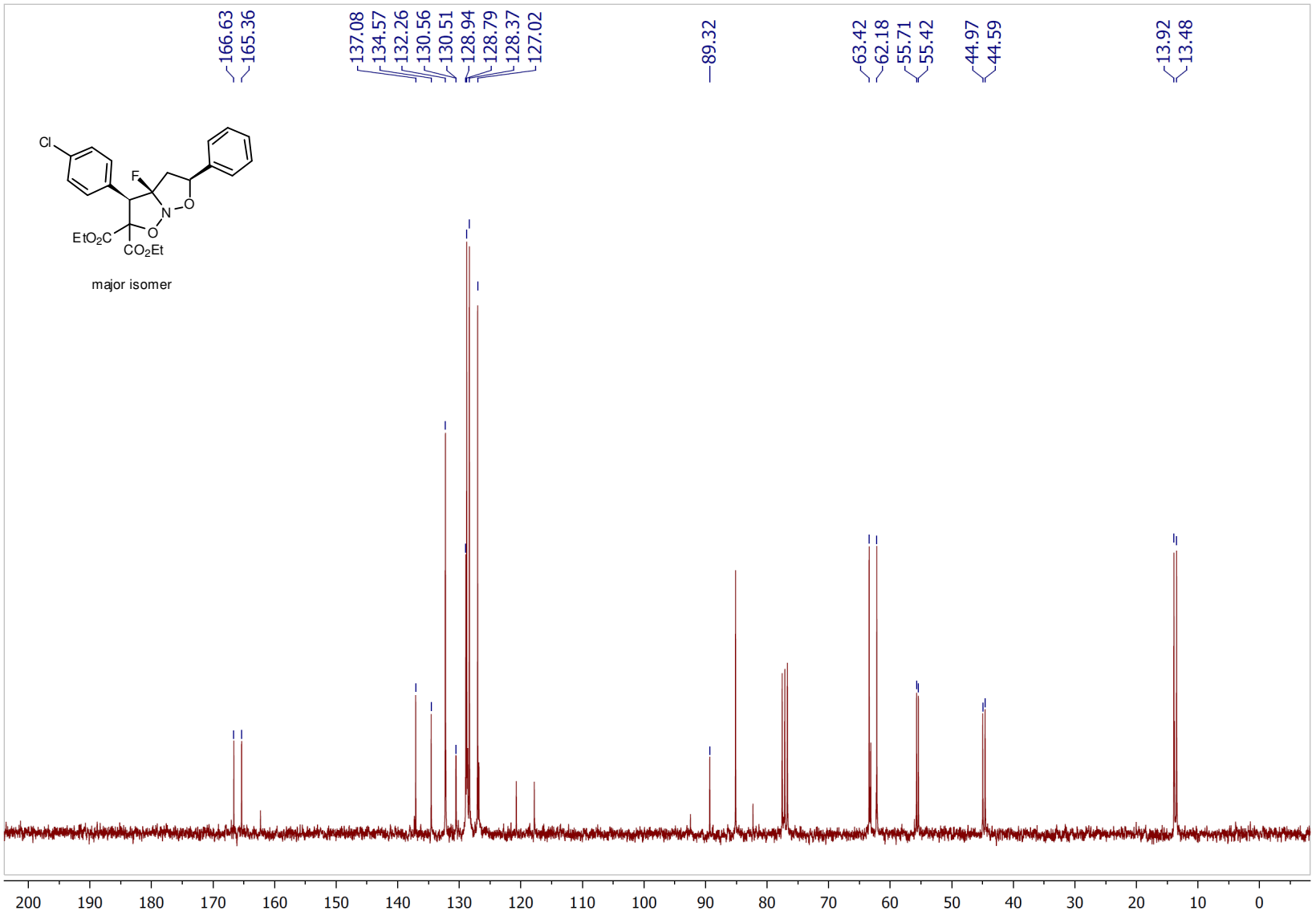

Cl
Me
F
Me
N
O
O
MeO2C
CO2Me
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

***rel*-(3R,3aR,5S)-diethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4v** (major isomer)

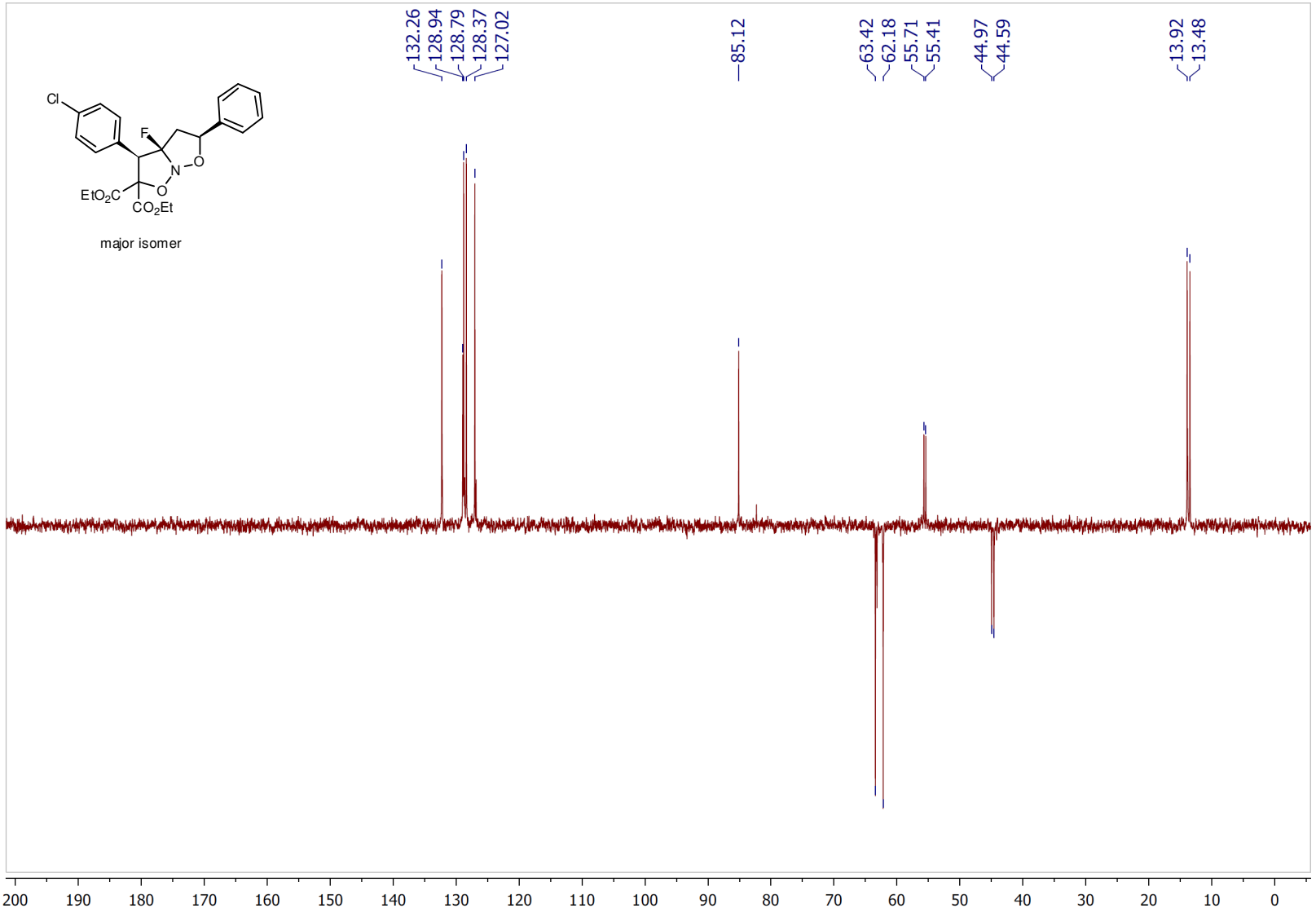
^{1}H NMR



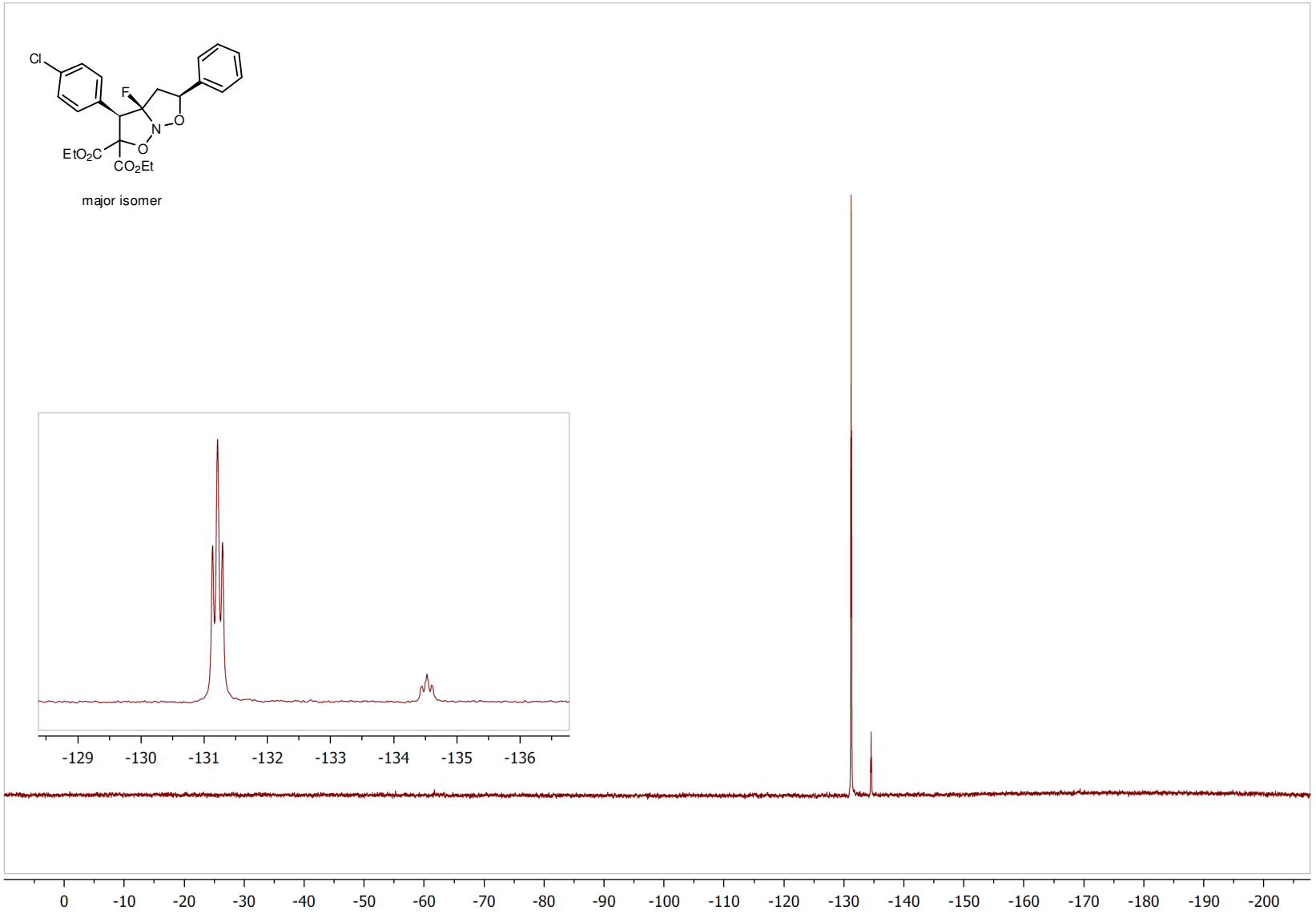
^{13}C NMR


166.63
165.36
137.08
134.57
132.26
130.56
130.51
128.94
128.79
128.37
127.02
89.32
63.42
62.18
55.71
55.42
44.97
44.59
13.92
13.48
Cl
F
N
O
O
EtO2C
CO2Et
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{13}C NMR (DEPT)

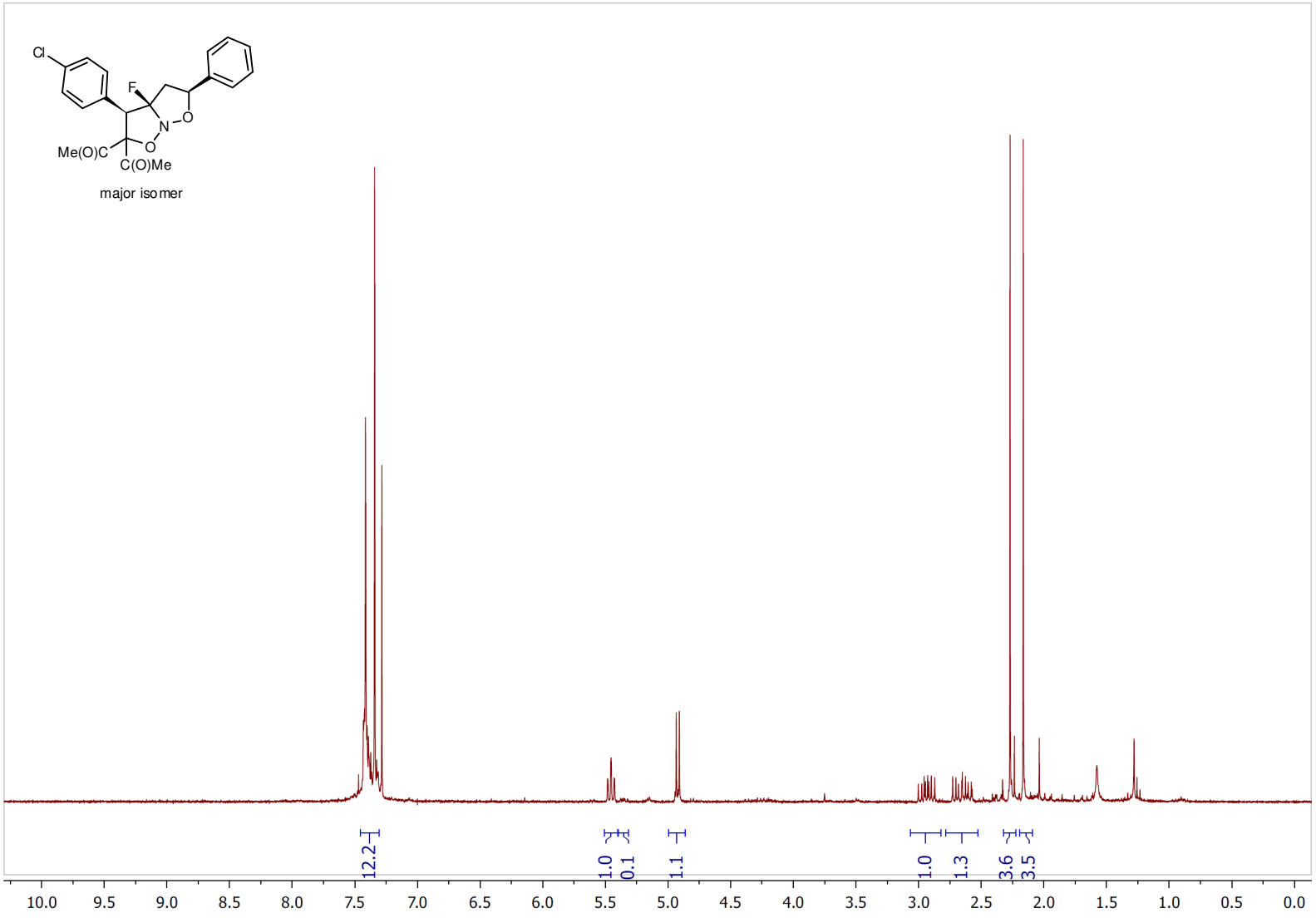

132.26
128.94
128.79
128.37
127.02
85.12
63.42
62.18
55.71
55.41
44.97
44.59
13.92
13.48
Cl
F
N
O
O
EtO2C
CO2Et
major isomer
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{19}F NMR

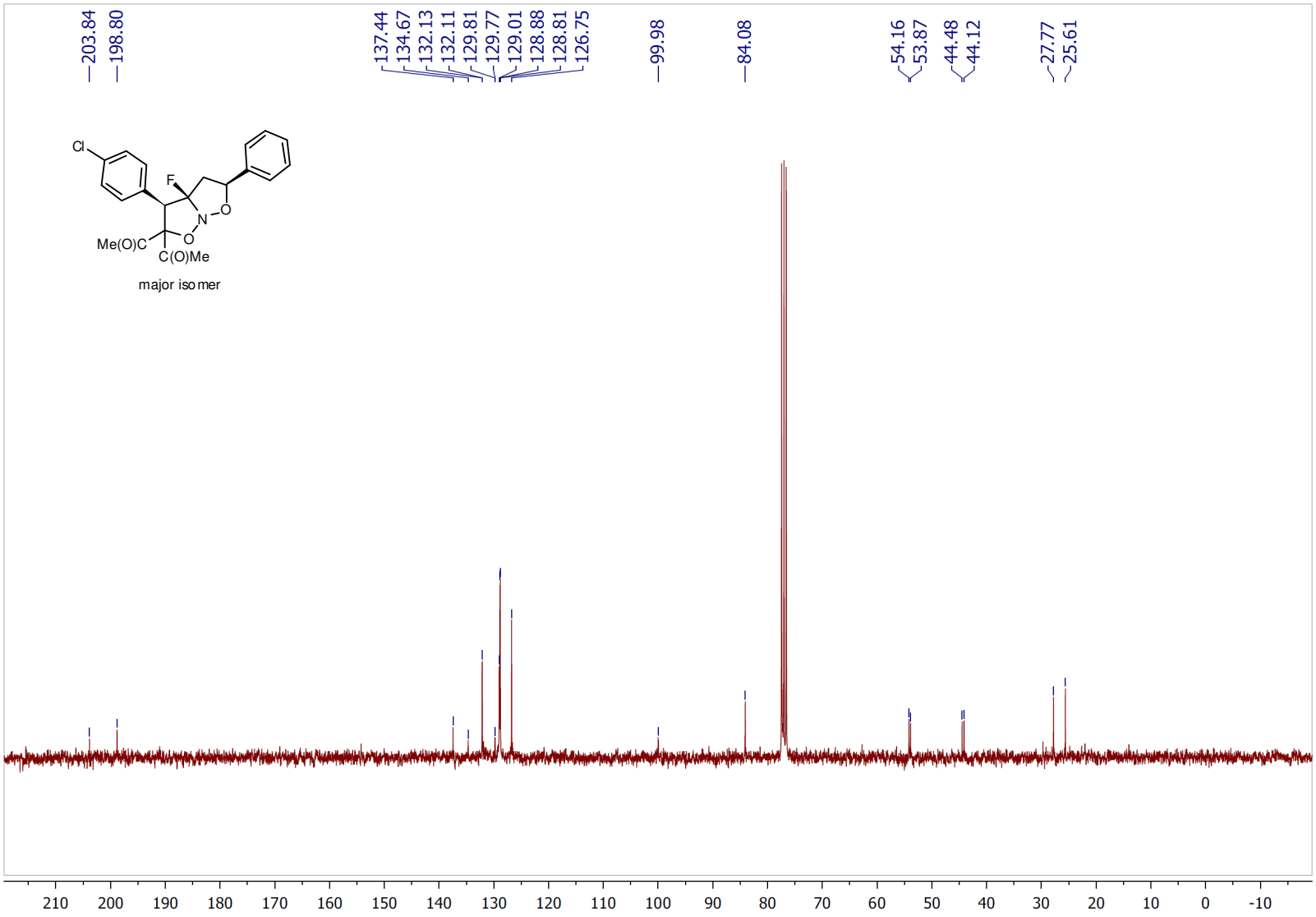

Cl
F
N
O
O
EtO2C
CO2Et
major isomer
-129
-130
-131
-132
-133
-134
-135
-136
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

***rel*-1,1'-((3R,3aR,5S)-3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-diyl)diethanone 4w** (major isomer)

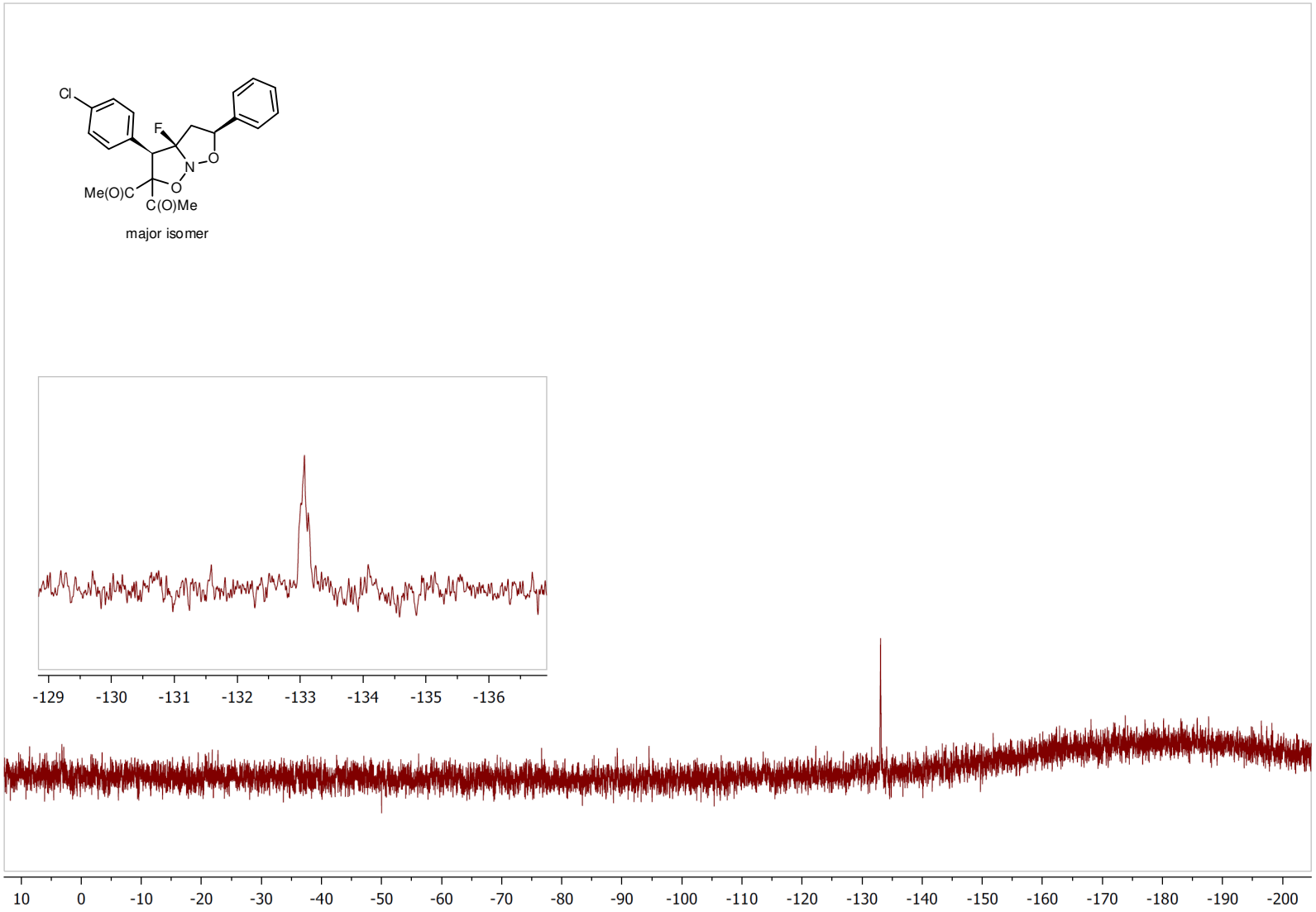
^{1}H NMR



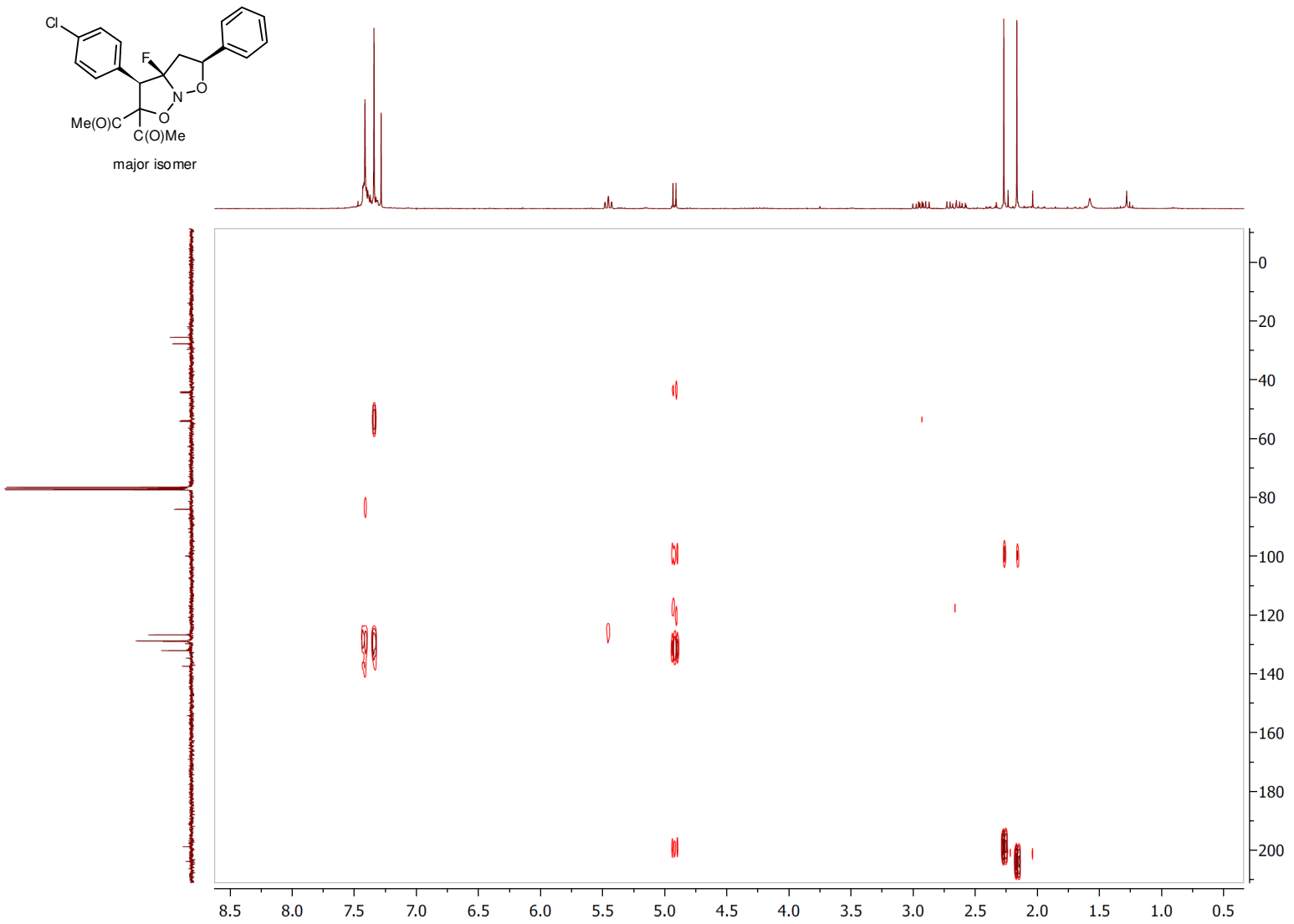
^{13}C NMR


203.84
198.80
137.44
134.67
132.13
132.11
129.81
129.77
129.01
128.88
128.81
126.75
99.98
84.08
54.16
53.87
44.48
44.12
27.77
25.61
Cl
F
N
O
O
Me(O)C
C(O)Me
major isomer
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

^{19}F NMR

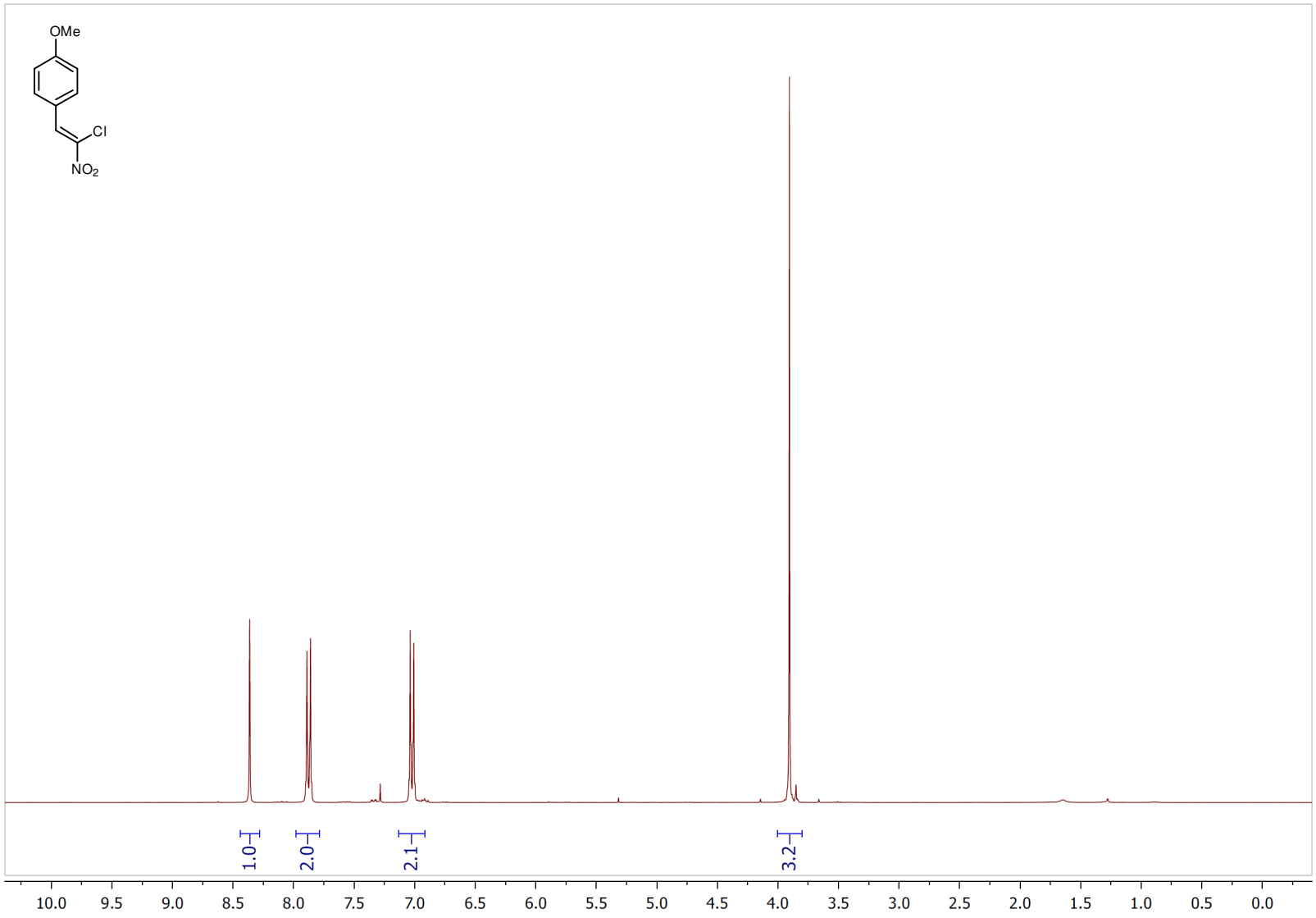

Cl
F
N
O
O
Me(O)C
C(O)Me
major isomer
-129
-130
-131
-132
-133
-134
-135
-136
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

^{1}H-^{13}C HMBC

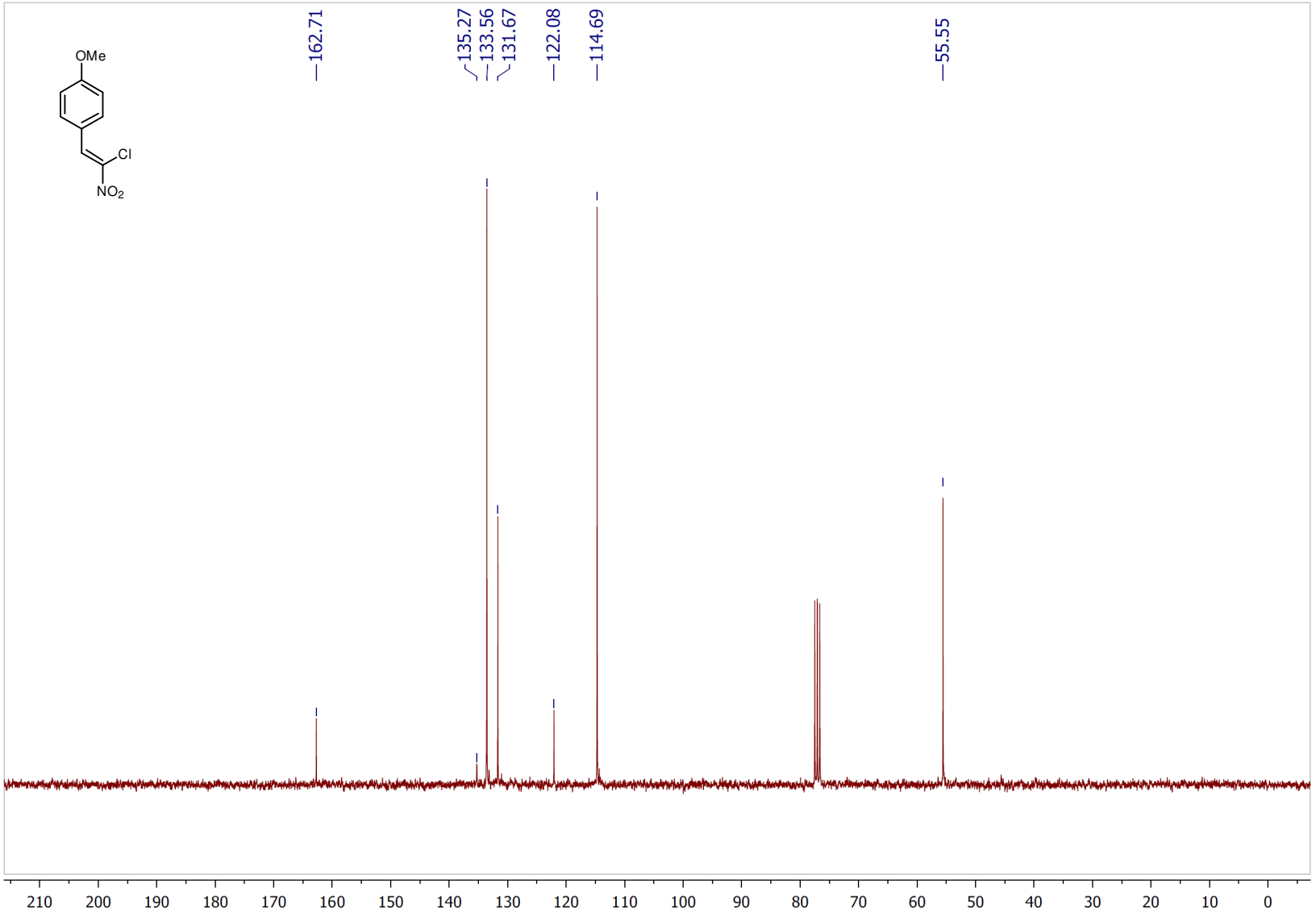

Cl
F
N
O
Me(O)C
O
C(O)Me
major isomer
0
20
40
60
80
100
120
140
160
180
200
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

1-[(*Z*)-2-chloro-2-nitroethenyl]-4-(methyloxy)benzene 7a

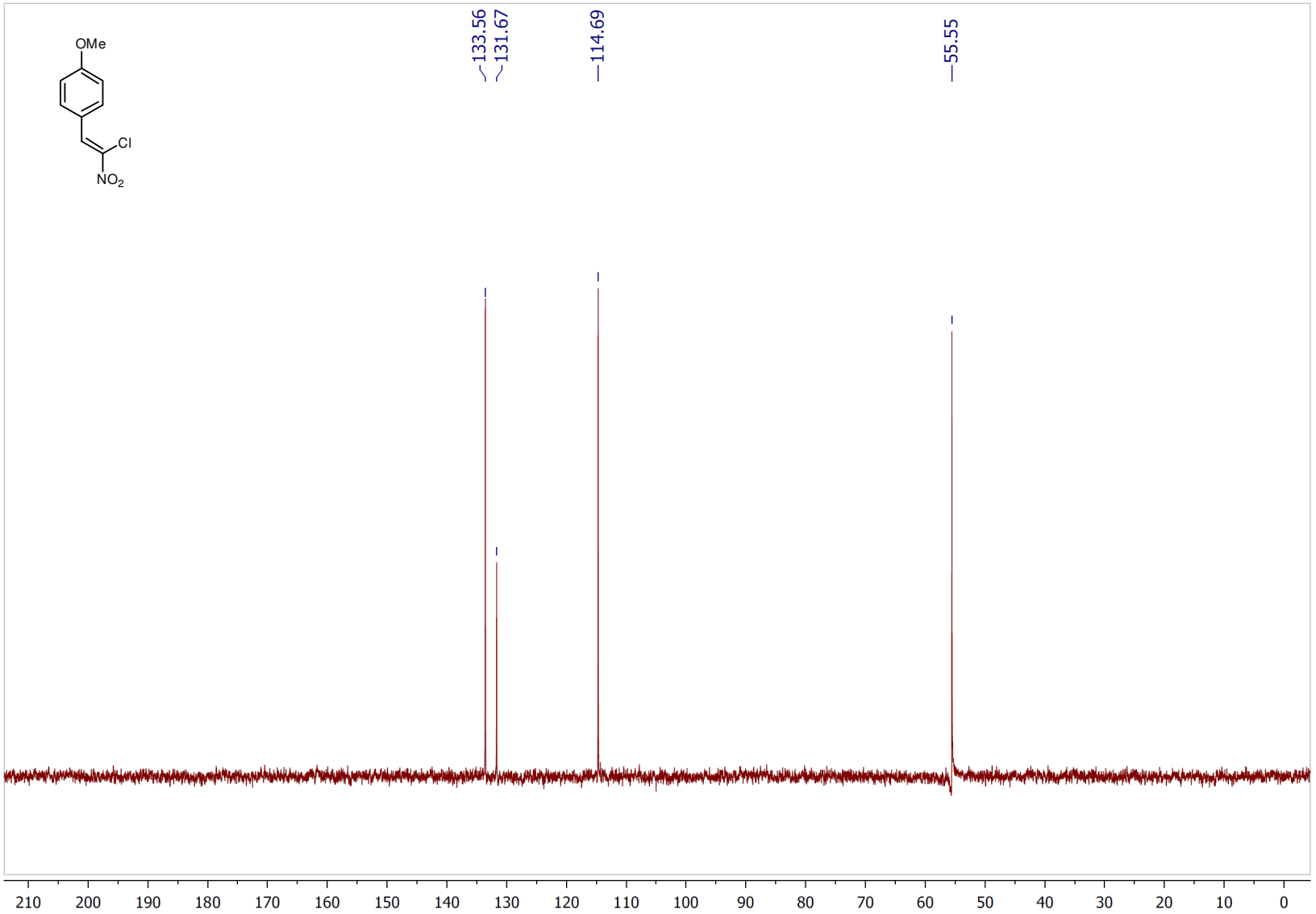
^{1}H NMR



^{13}C NMR

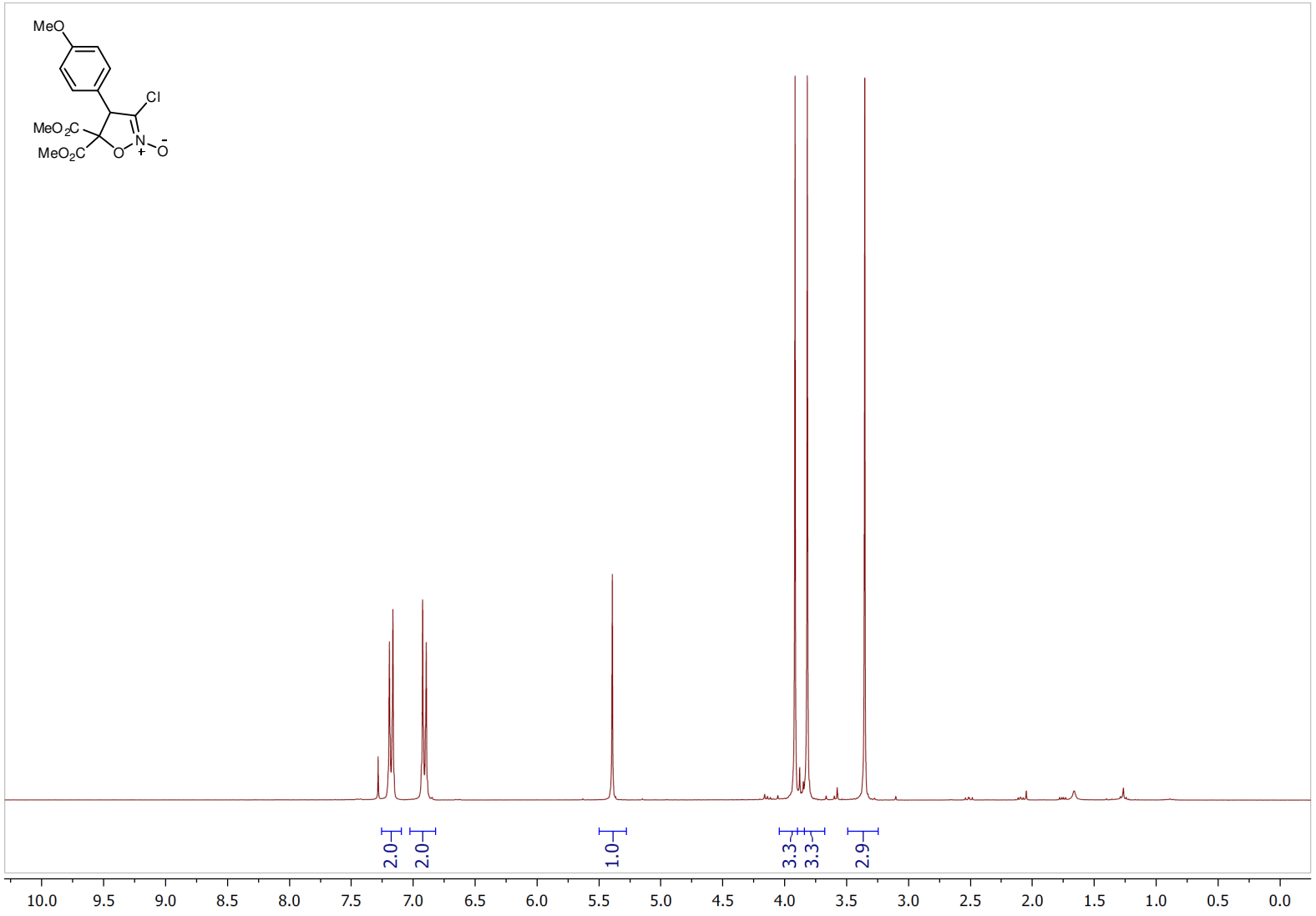

OMe
Cl
NO2
162.71
135.27
133.56
131.67
122.08
114.69
55.55
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{13}C NMR (DEPT)

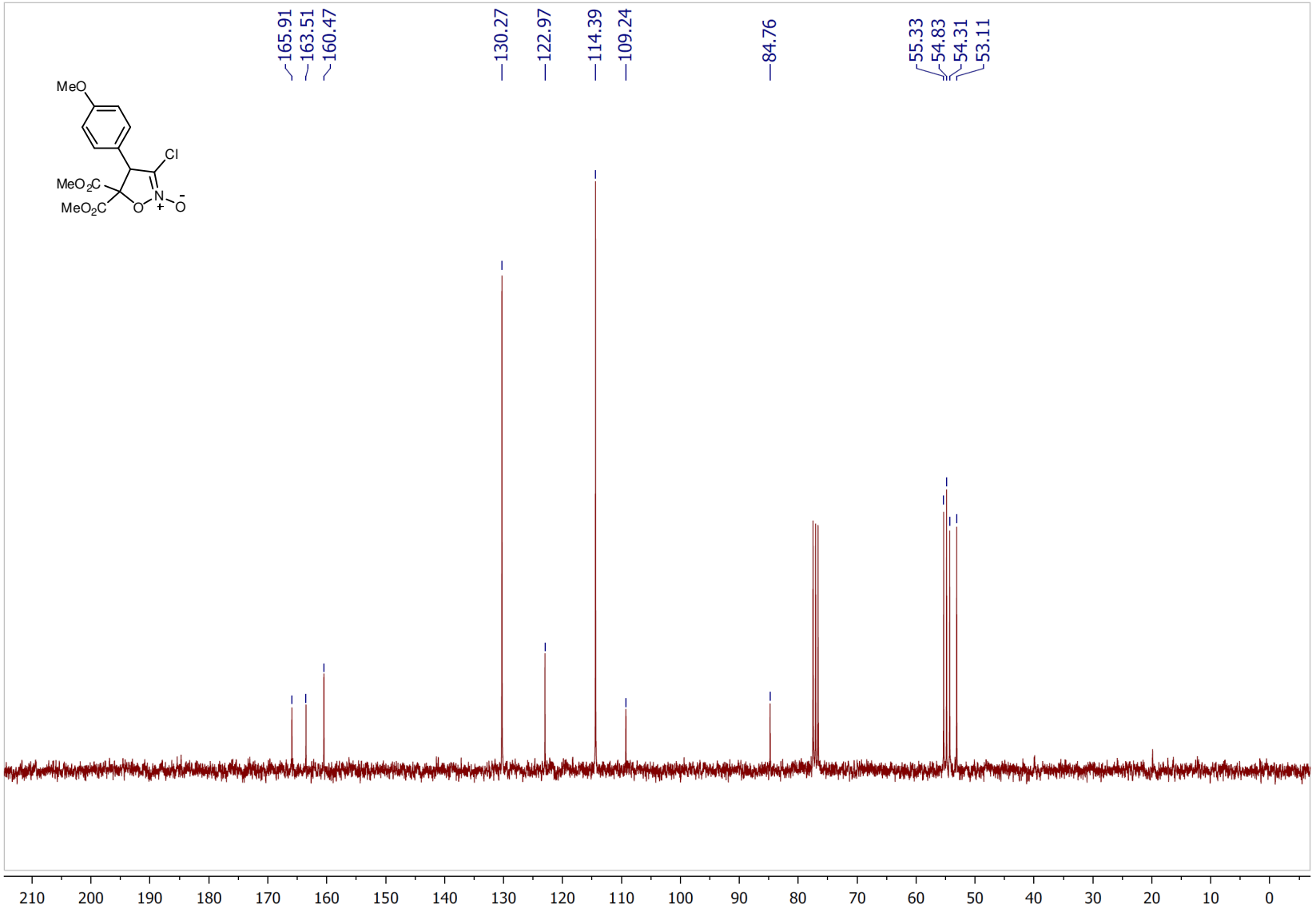

OMe
Cl
NO2
133.56
131.67
114.69
55.55
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

3-Chloro-5,5-bis(methoxycarbonyl)-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide 8a

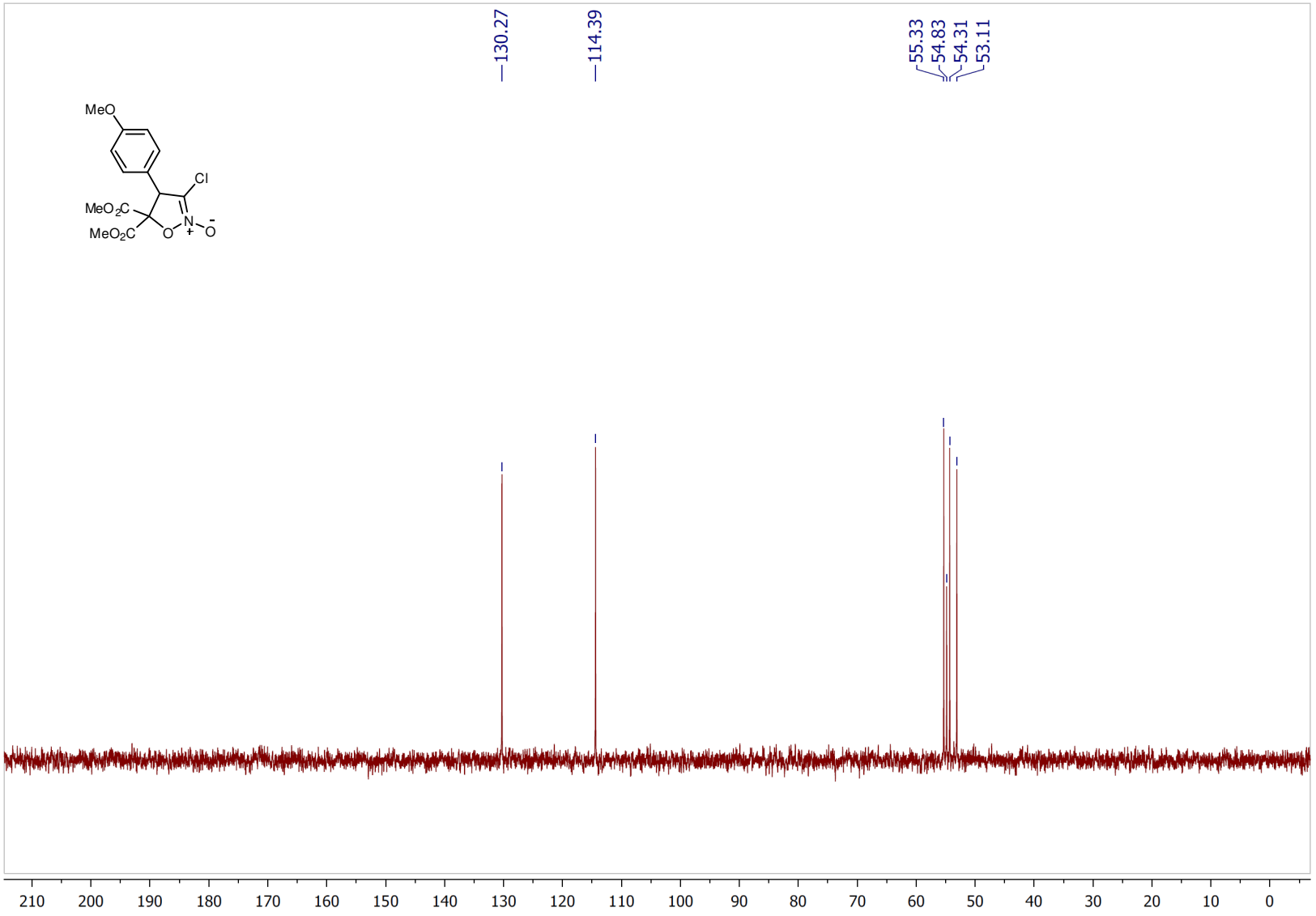
^{1}H NMR



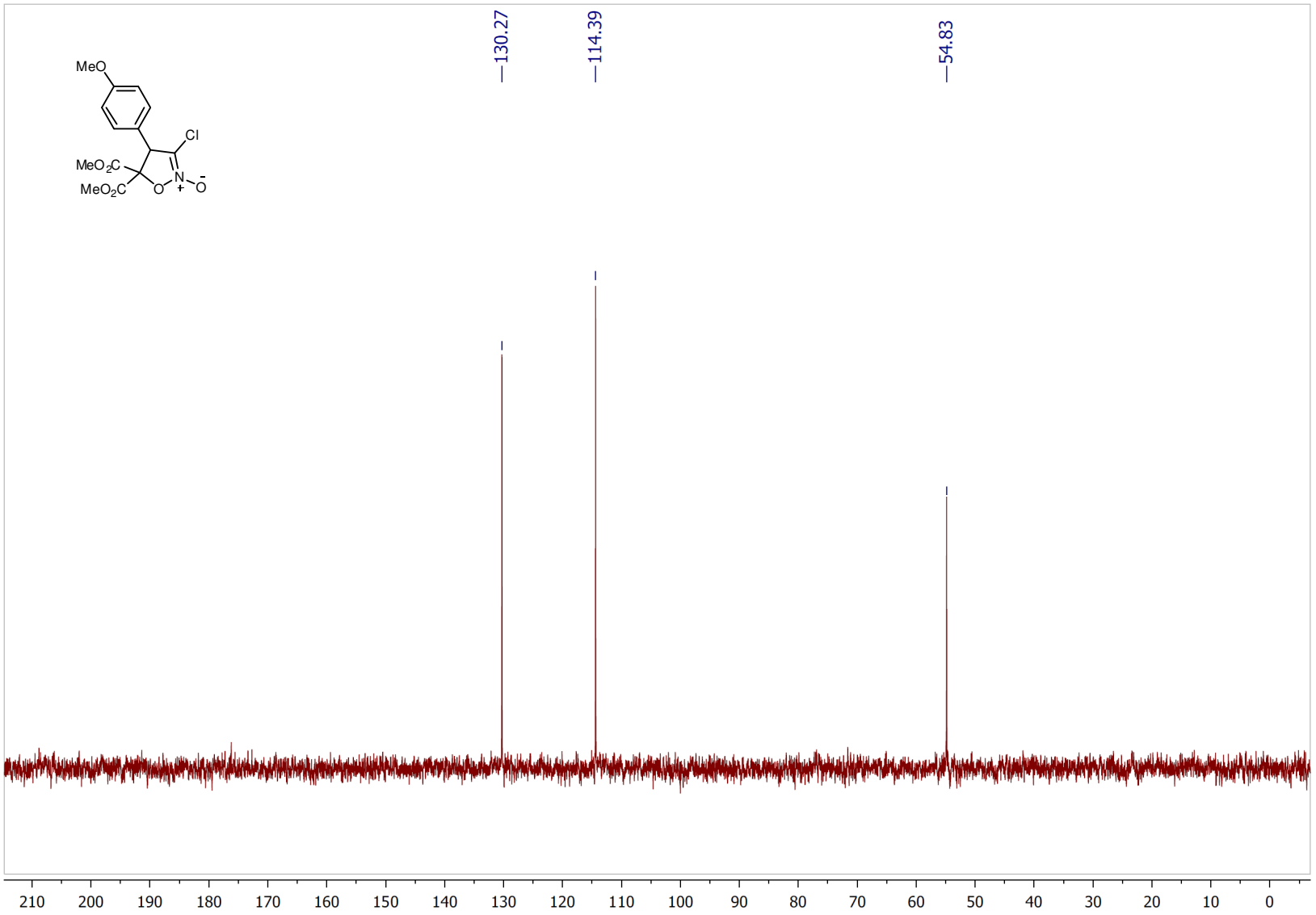
^{13}C NMR


165.91
163.51
160.47
130.27
122.97
114.39
109.24
84.76
55.33
54.83
54.31
53.11
MeO
Cl
MeO2C
MeO2C
O
N
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

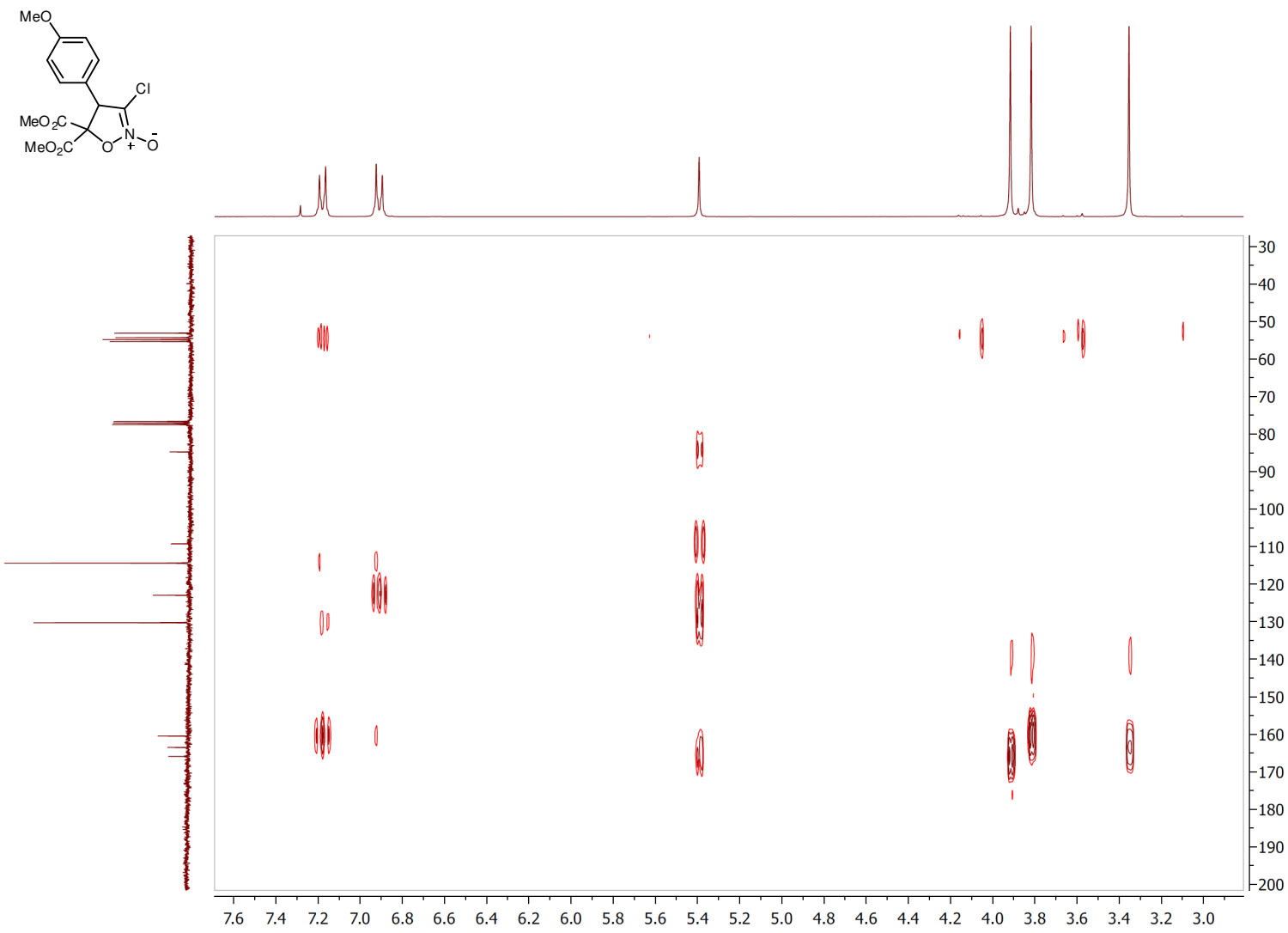
^{13}C NMR (DEPT)


130.27
114.39
55.33
54.83
54.31
53.11
MeO
Cl
MeO2C
MeO2C
O
N
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{13}C NMR (DEPT-90)

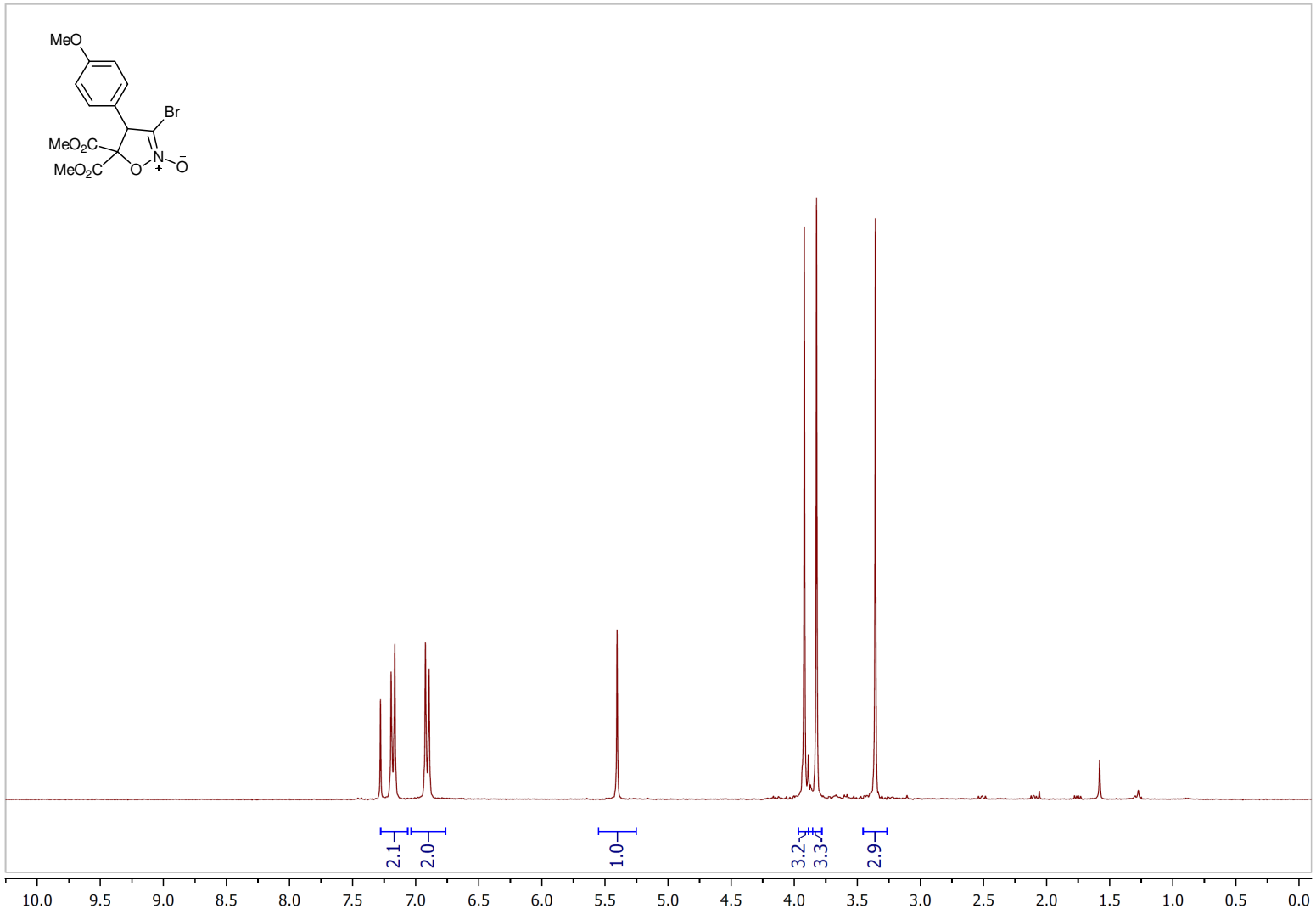


^{1}H-^{13}C HMBC

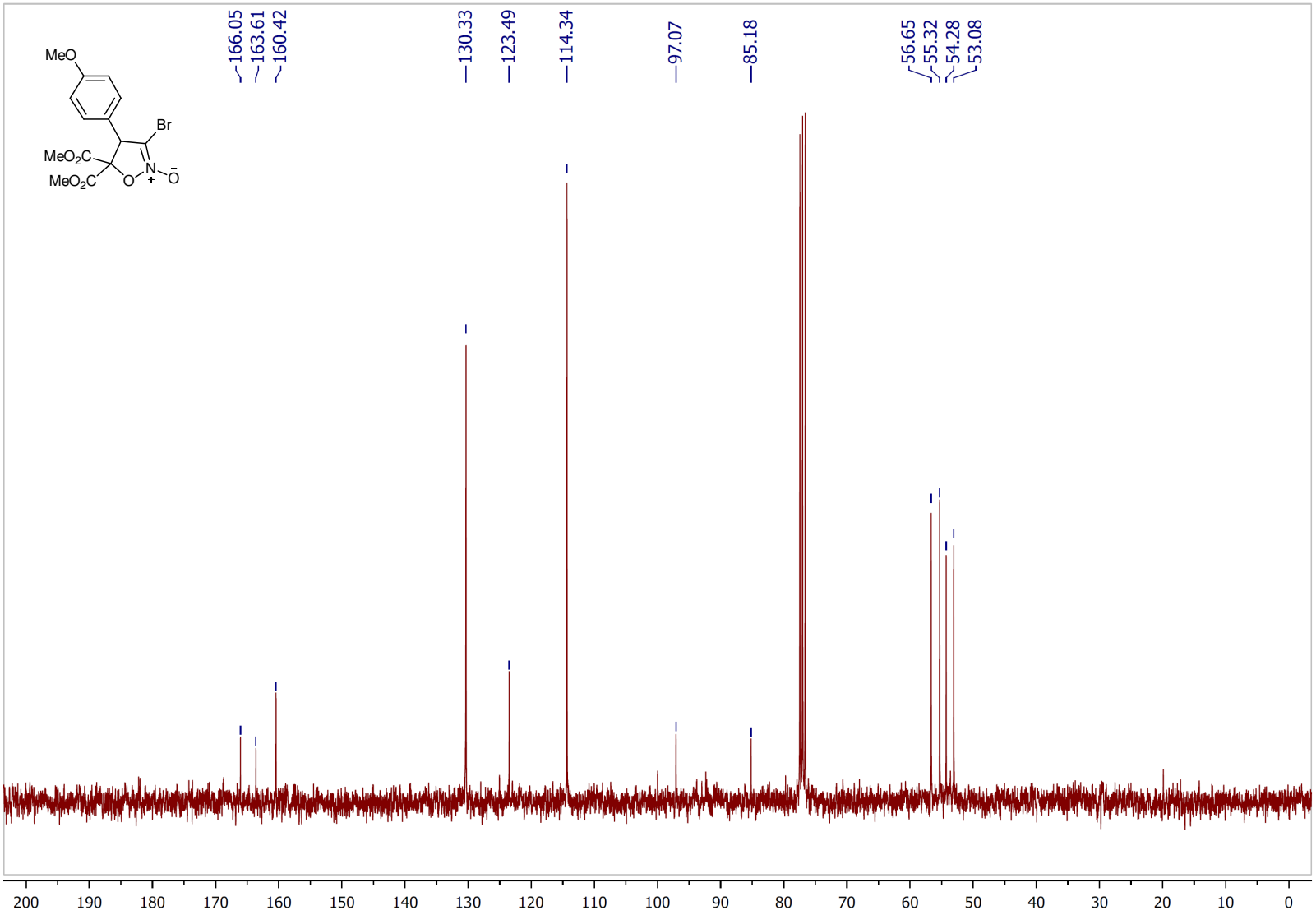

MeO
Cl
MeO2C
MeO2C
N
O
O
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0

3-Bromo-5,5-bis(methoxycarbonyl)-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide 8b

^{1}H NMR

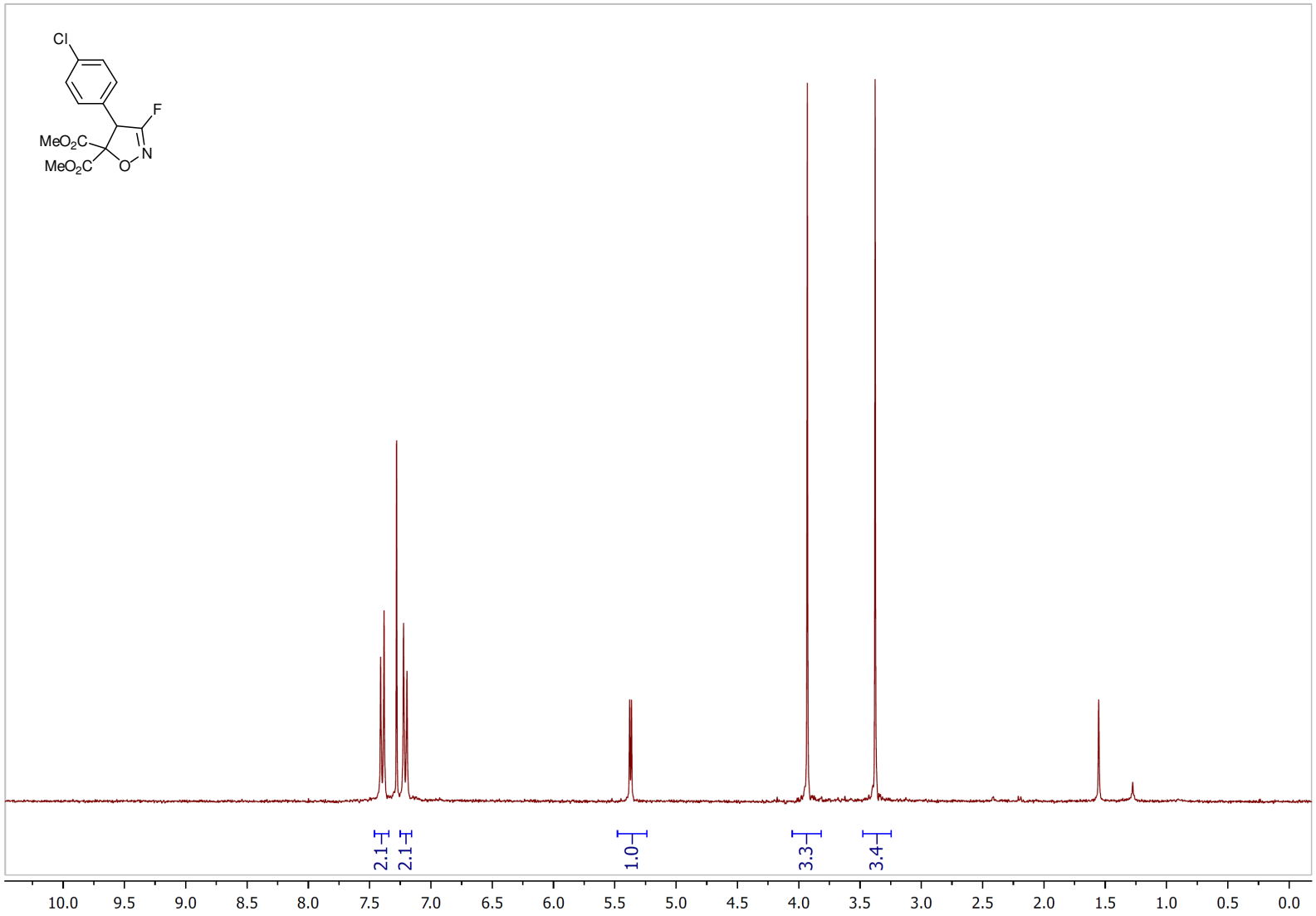


^{13}C NMR

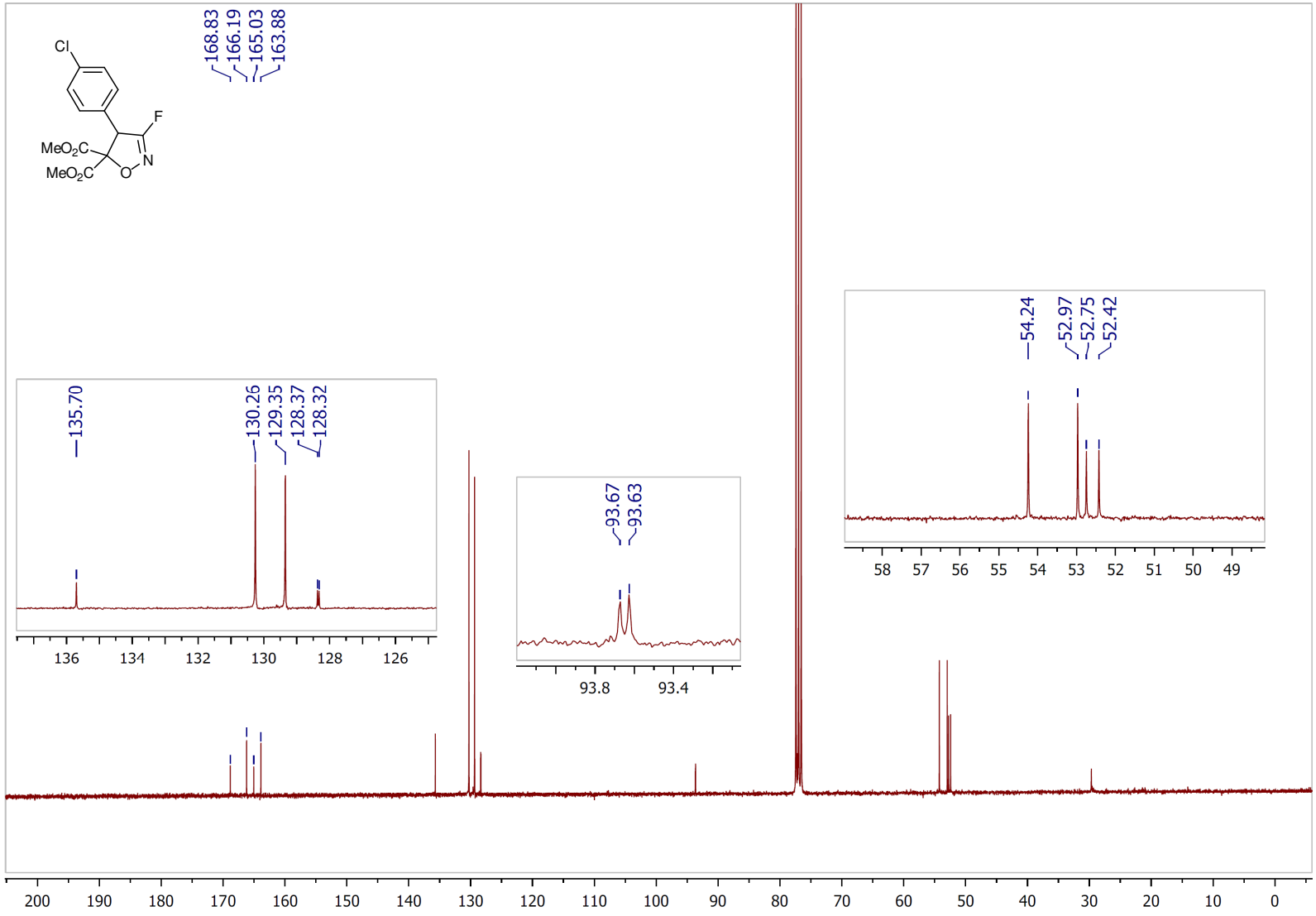

MeO
Br
MeO2C
MeO2C
N
O
166.05
163.61
160.42
130.33
123.49
114.34
97.07
85.18
56.65
55.32
54.28
53.08
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

Dimethyl 4-(4-chlorophenyl)-3-fluoroisoxazole-5,5(4H)-dicarboxylate 9a

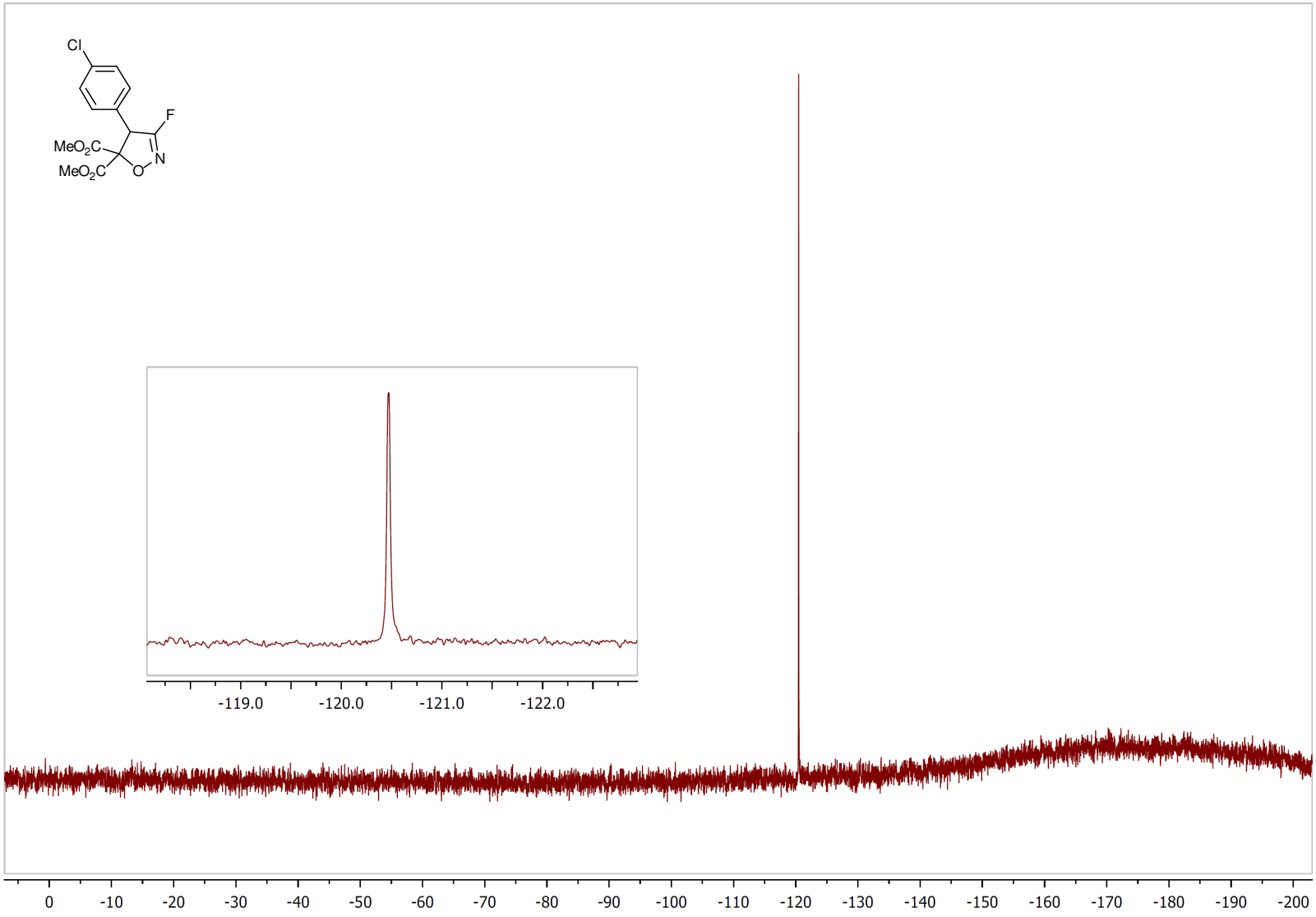
^{1}H NMR



^{13}C NMR

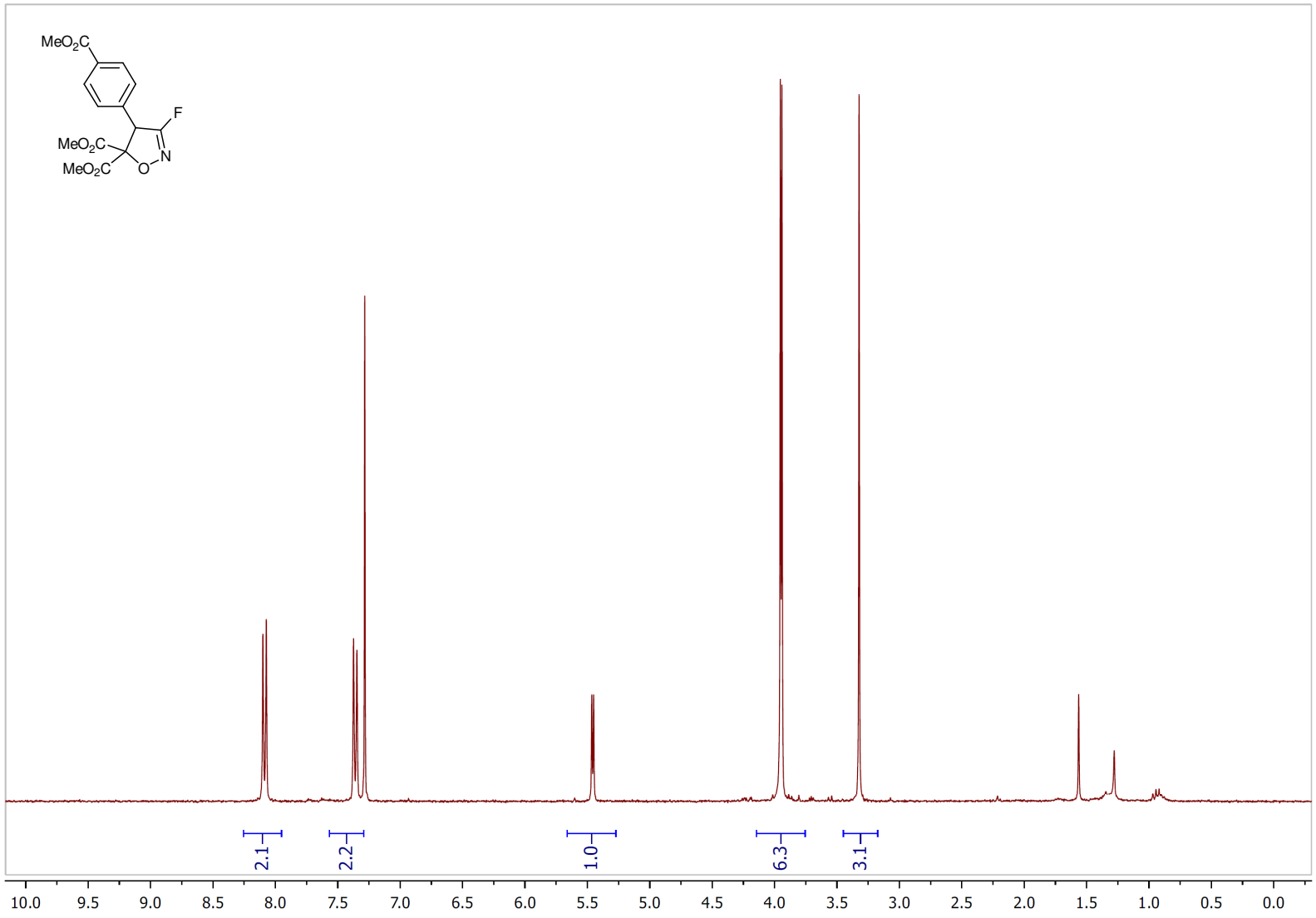

Cl
F
MeO2C
MeO2C
O
N
168.83
166.19
165.03
163.88
135.70
130.26
129.35
128.37
128.32
93.67
93.63
54.24
52.97
52.75
52.42
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
136 134 132 130 128 126
93.8 93.4
58 57 56 55 54 53 52 51 50 49

^{19}F NMR

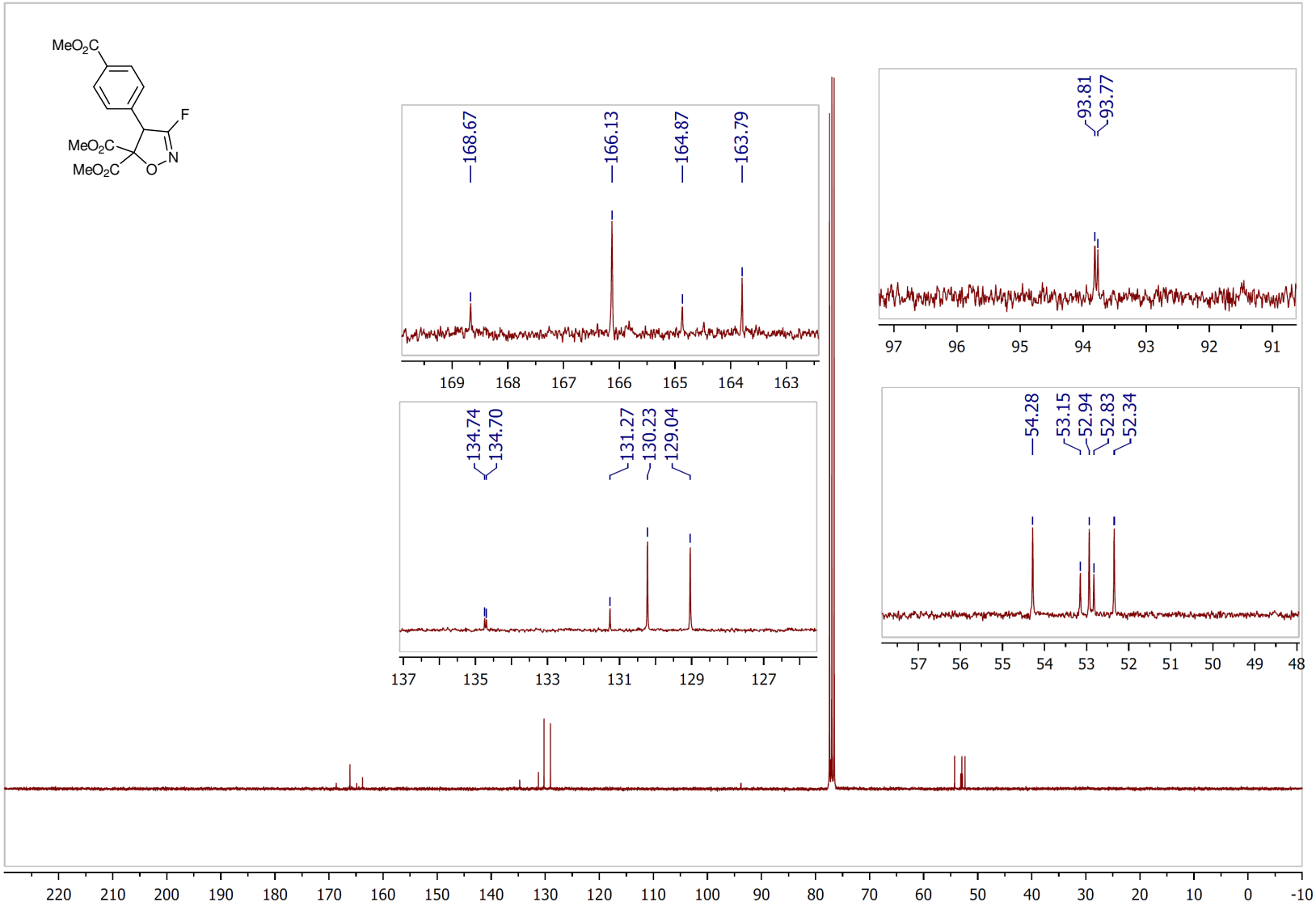

Cl
F
MeO2C
MeO2C
N
O
-119.0
-120.0
-121.0
-122.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

Dimethyl 3-fluoro-4-(4-(methoxycarbonyl)phenyl)isoxazole-5,5(4H)-dicarboxylate 9m

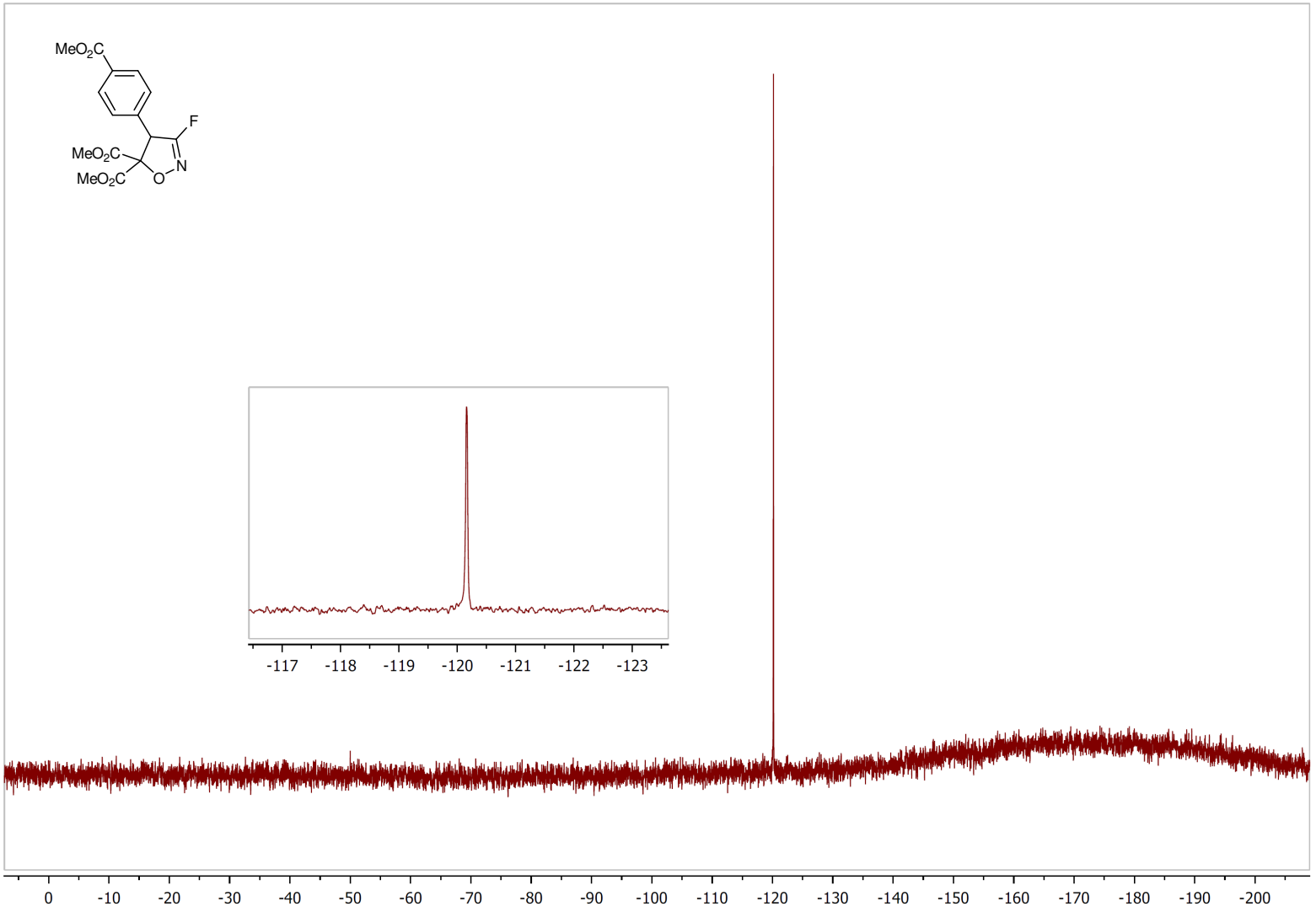
^{1}H NMR



^{13}C NMR

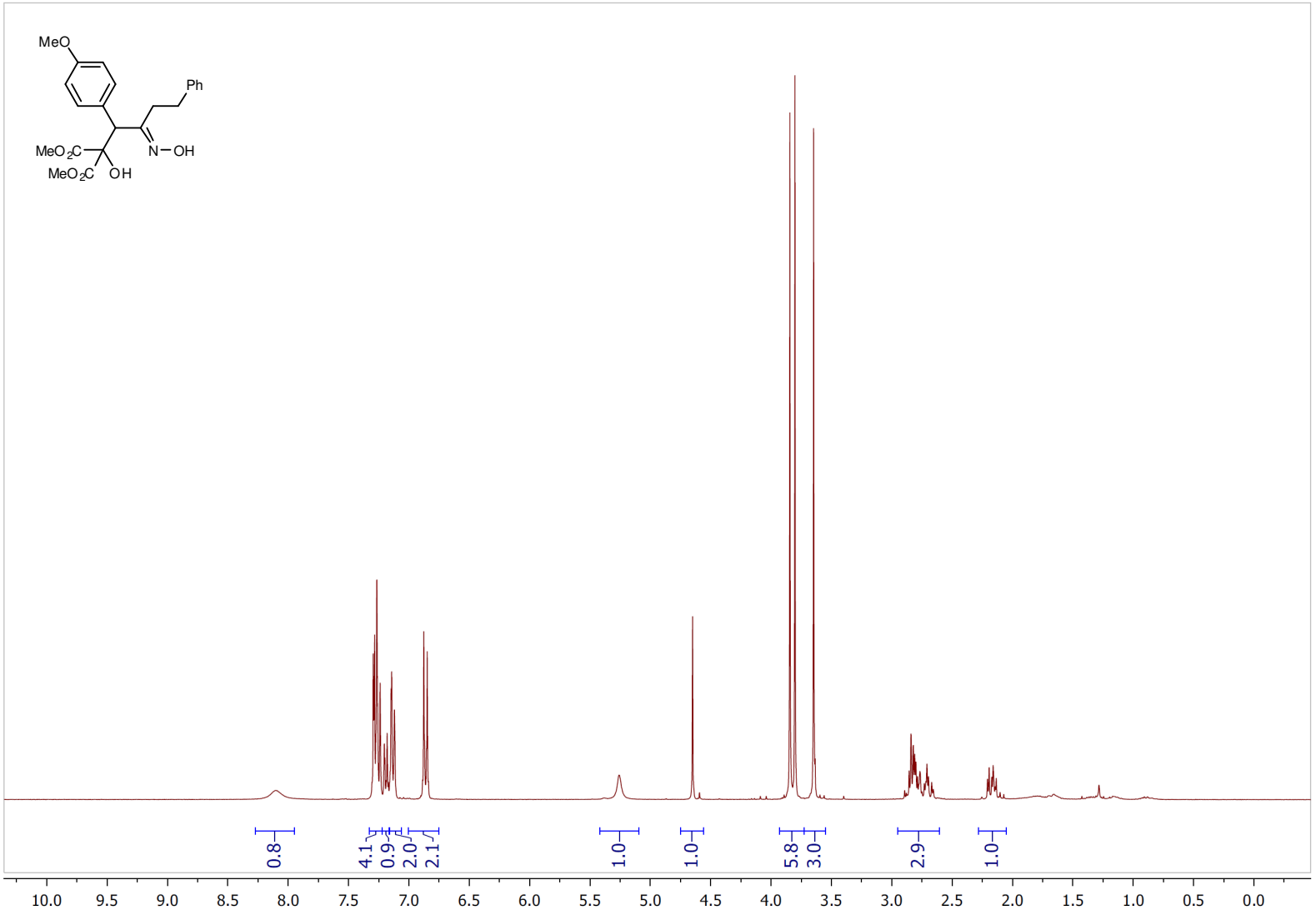

MeO2C
F
MeO2C
MeO2C
O
N
168.67
166.13
164.87
163.79
93.81
93.77
134.74
134.70
131.27
130.23
129.04
54.28
53.15
52.94
52.83
52.34

^{19}F NMR

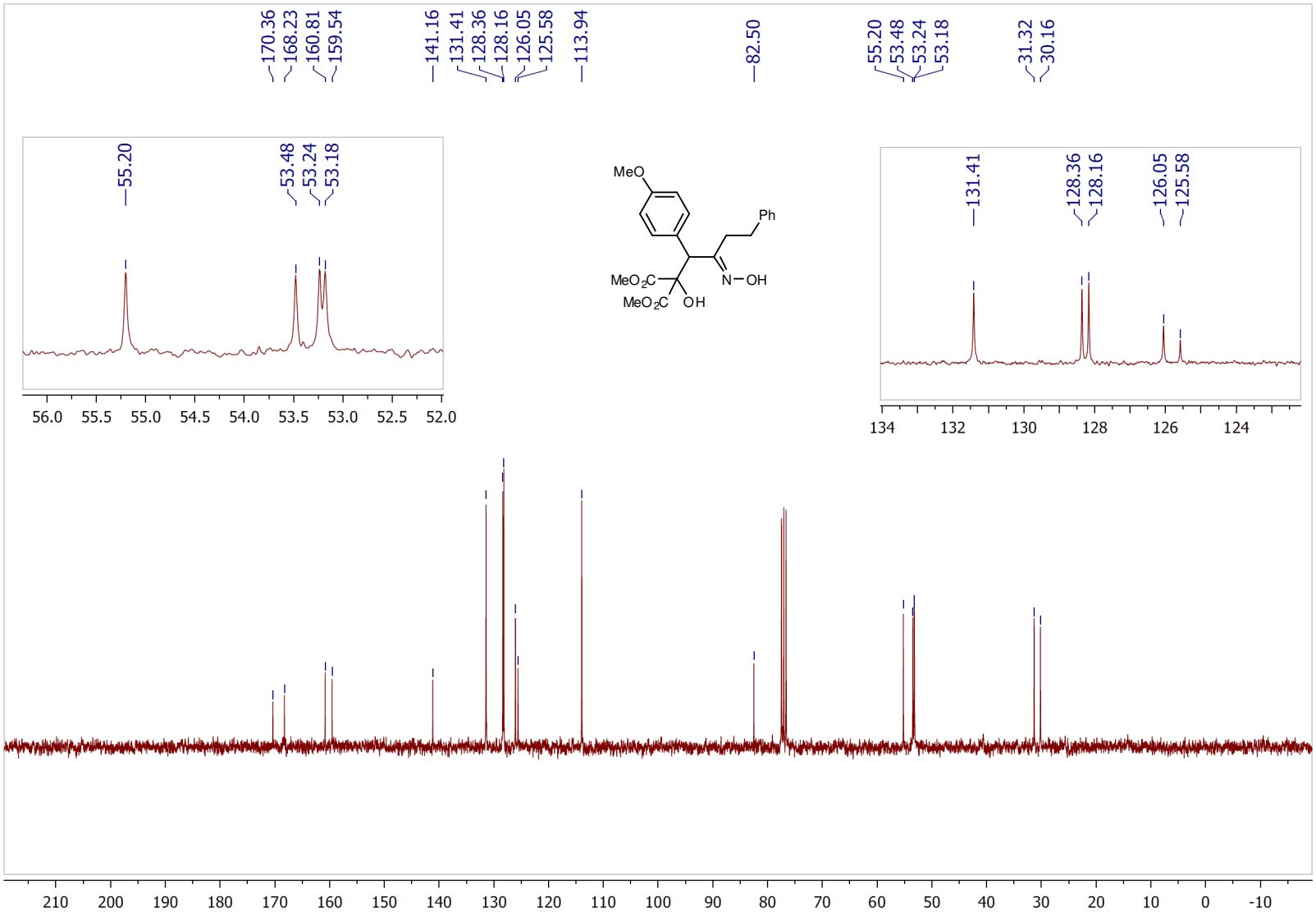

MeO2C
F
MeO2C
MeO2C
O
N
-117
-118
-119
-120
-121
-122
-123
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

Dimethyl 2-hydroxy-2-(2-(hydroxyimino)-1-(4-methoxyphenyl)-4-phenylbutyl)malonate 10

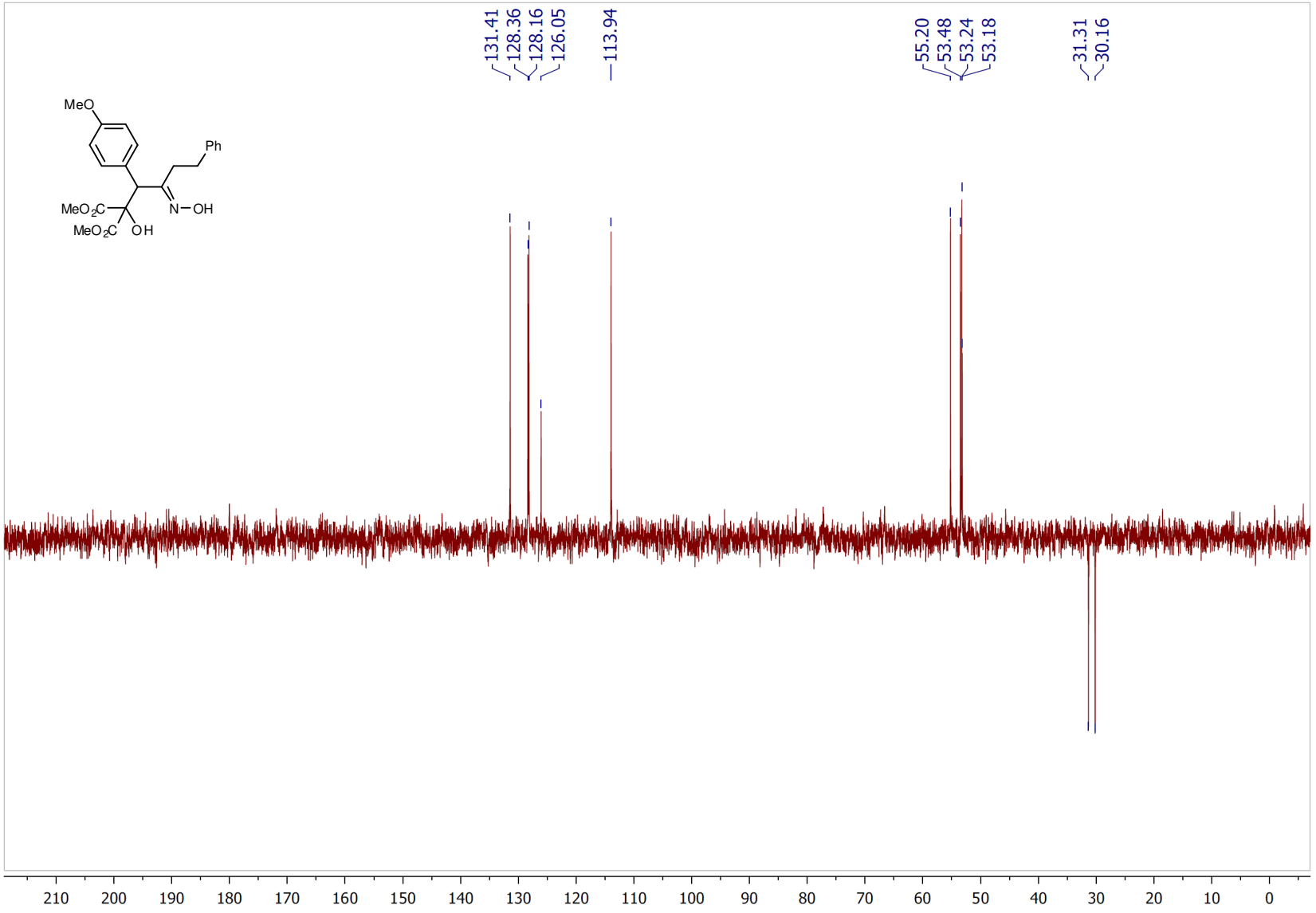
^{1}H NMR



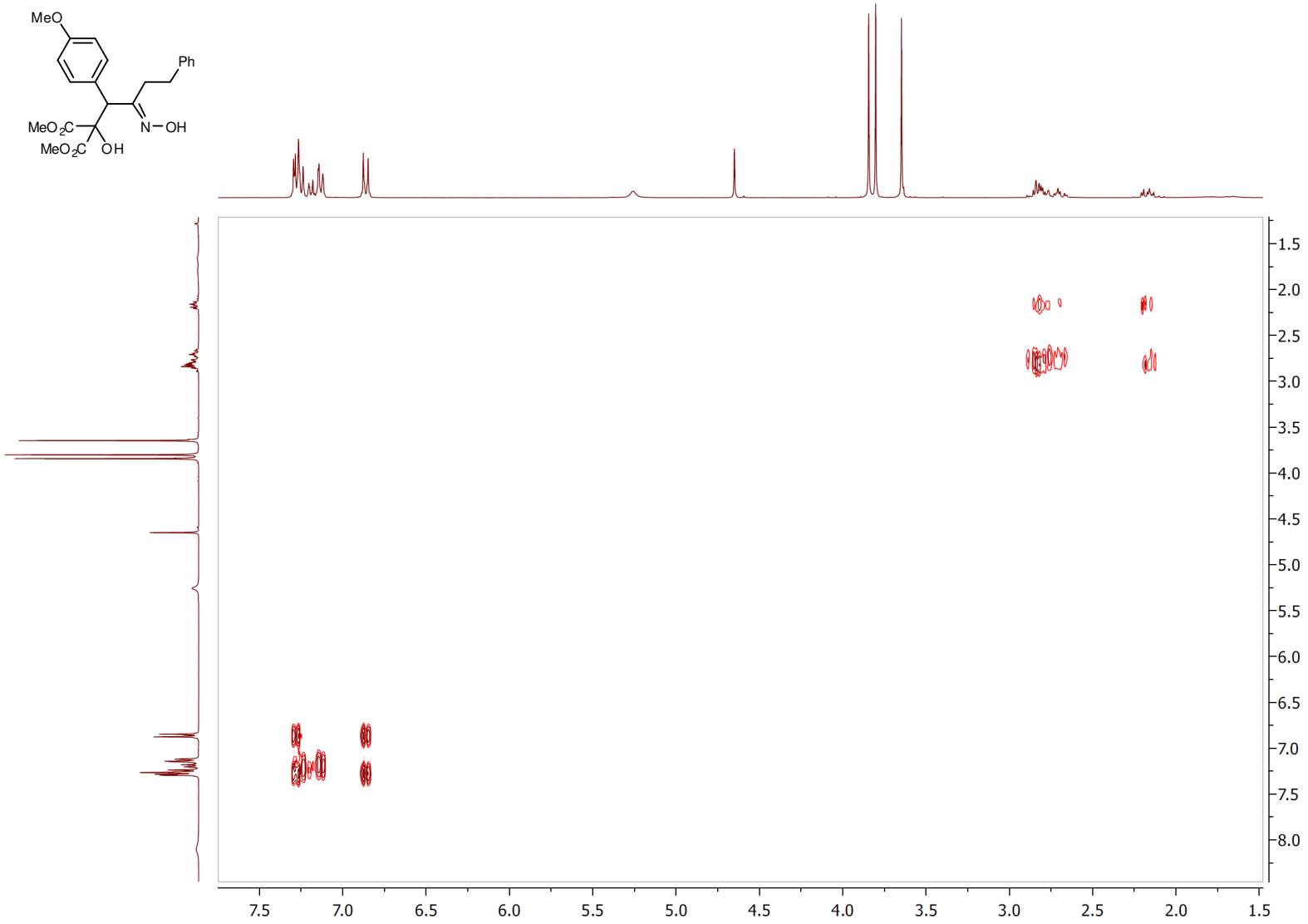
^{13}C NMR


170.36
168.23
160.81
159.54
141.16
131.41
128.36
128.16
126.05
125.58
113.94
82.50
55.20
53.48
53.24
53.18
31.32
30.16
MeO
Ph
MeO2C
N–OH
MeO2C
OH
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

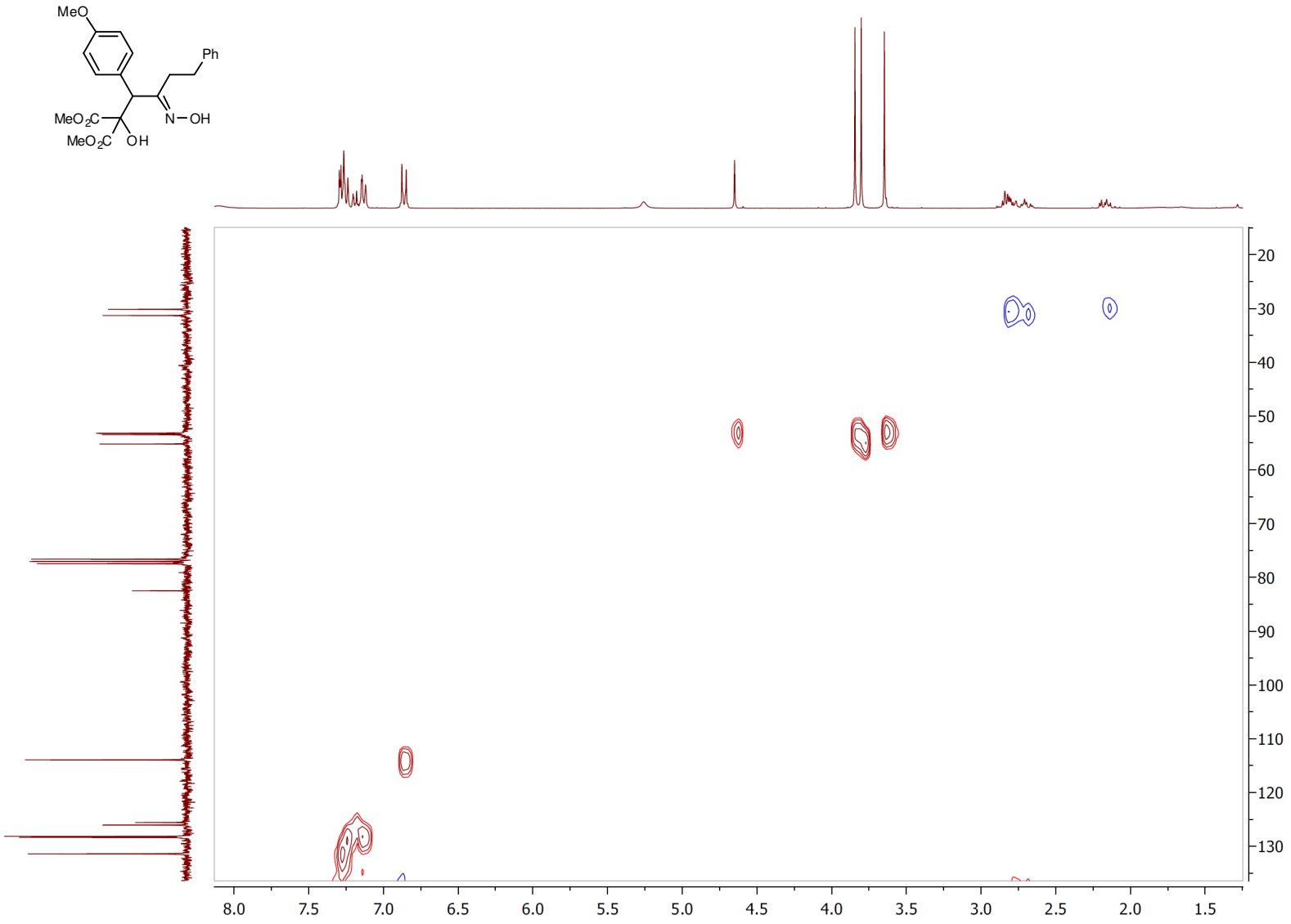
^{13}C NMR (DEPT)


131.41
128.36
128.16
126.05
113.94
55.20
53.48
53.24
53.18
31.31
30.16
MeO
Ph
MeO2C
N–OH
MeO2C
OH
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

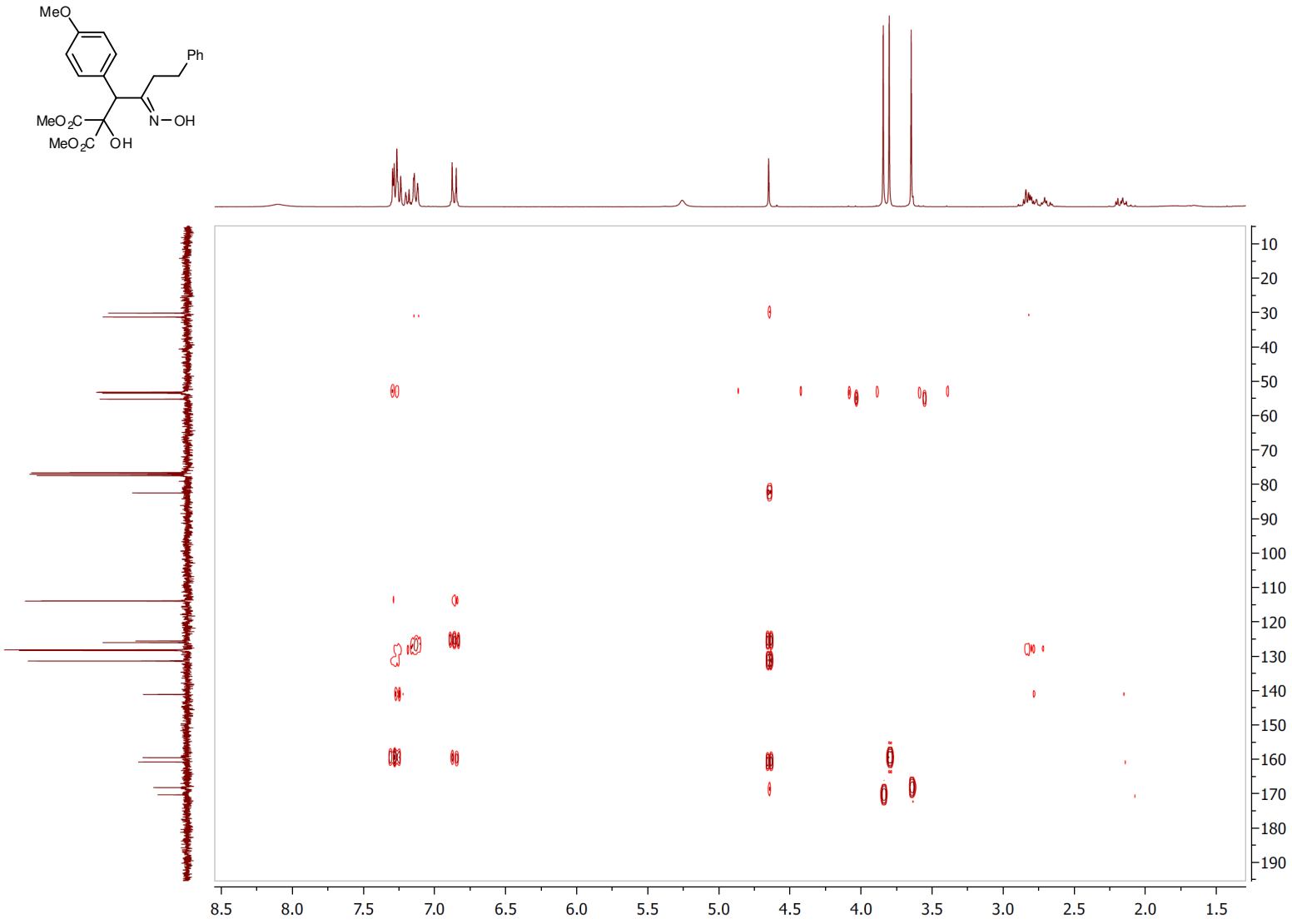
^{1}H-^{1}H COSY


MeO
Ph
MeO2C
N–OH
MeO2C
OH
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
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}H-^{13}C HSQC

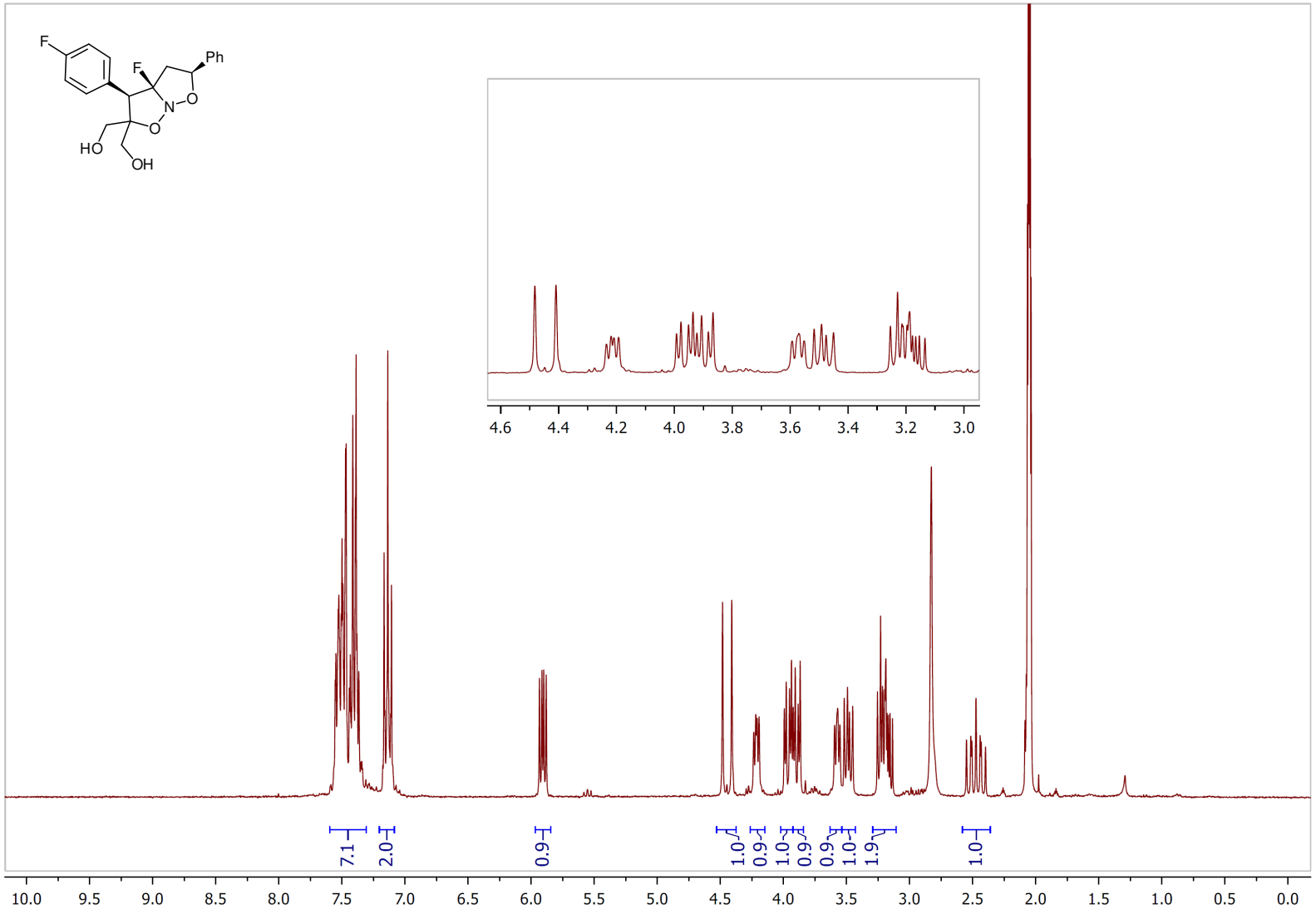

MeO
Ph
MeO2C
N–OH
MeO2C
OH
20
30
40
50
60
70
80
90
100
110
120
130
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

^{1}H-^{13}C HMBC

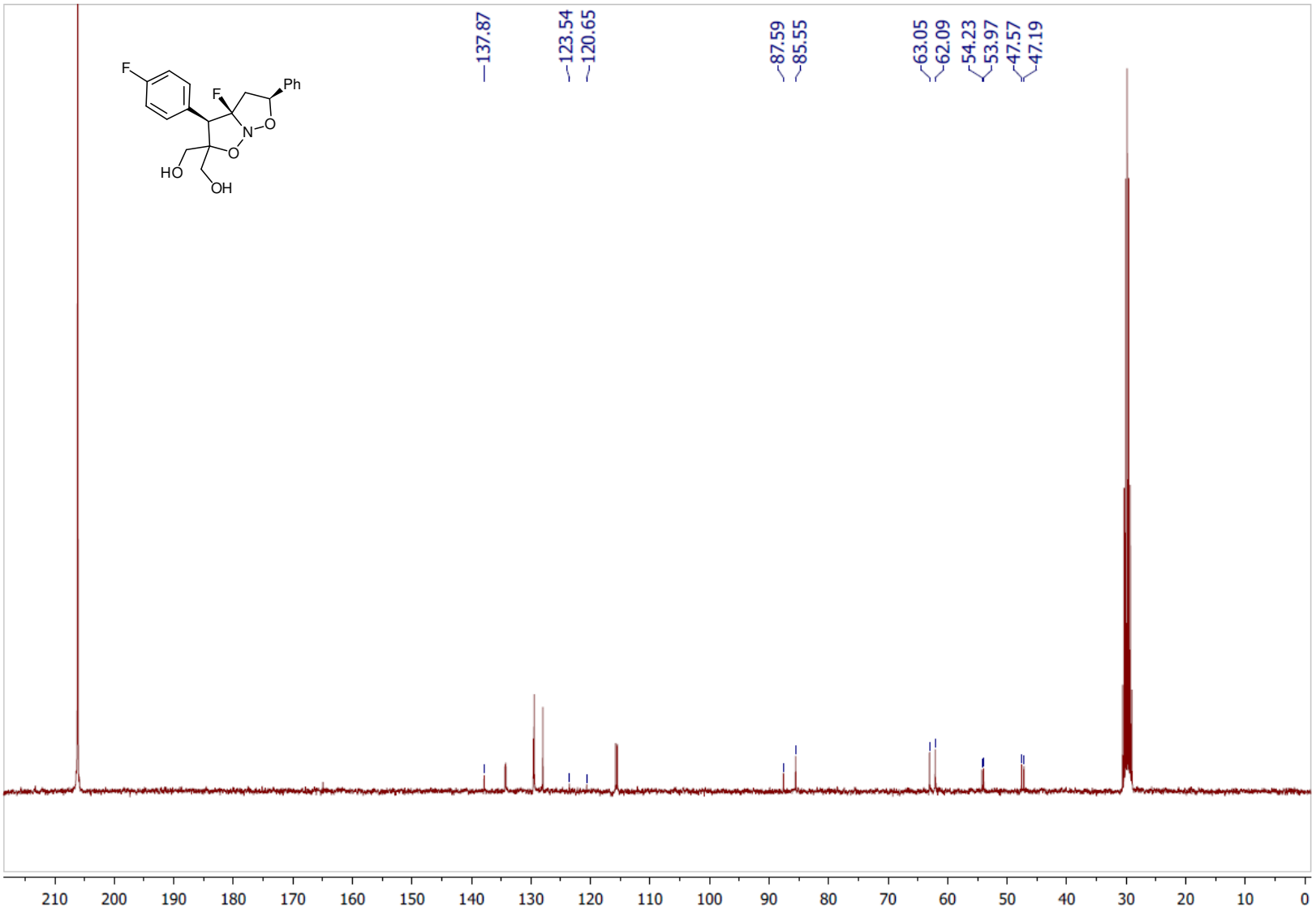

MeO
Ph
MeO2C
N–OH
MeO2C
OH
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

***rel*-((3R,3aR,5S)-3a-Fluoro-3-(4-fluorophenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-diyl)dimethanol 13**

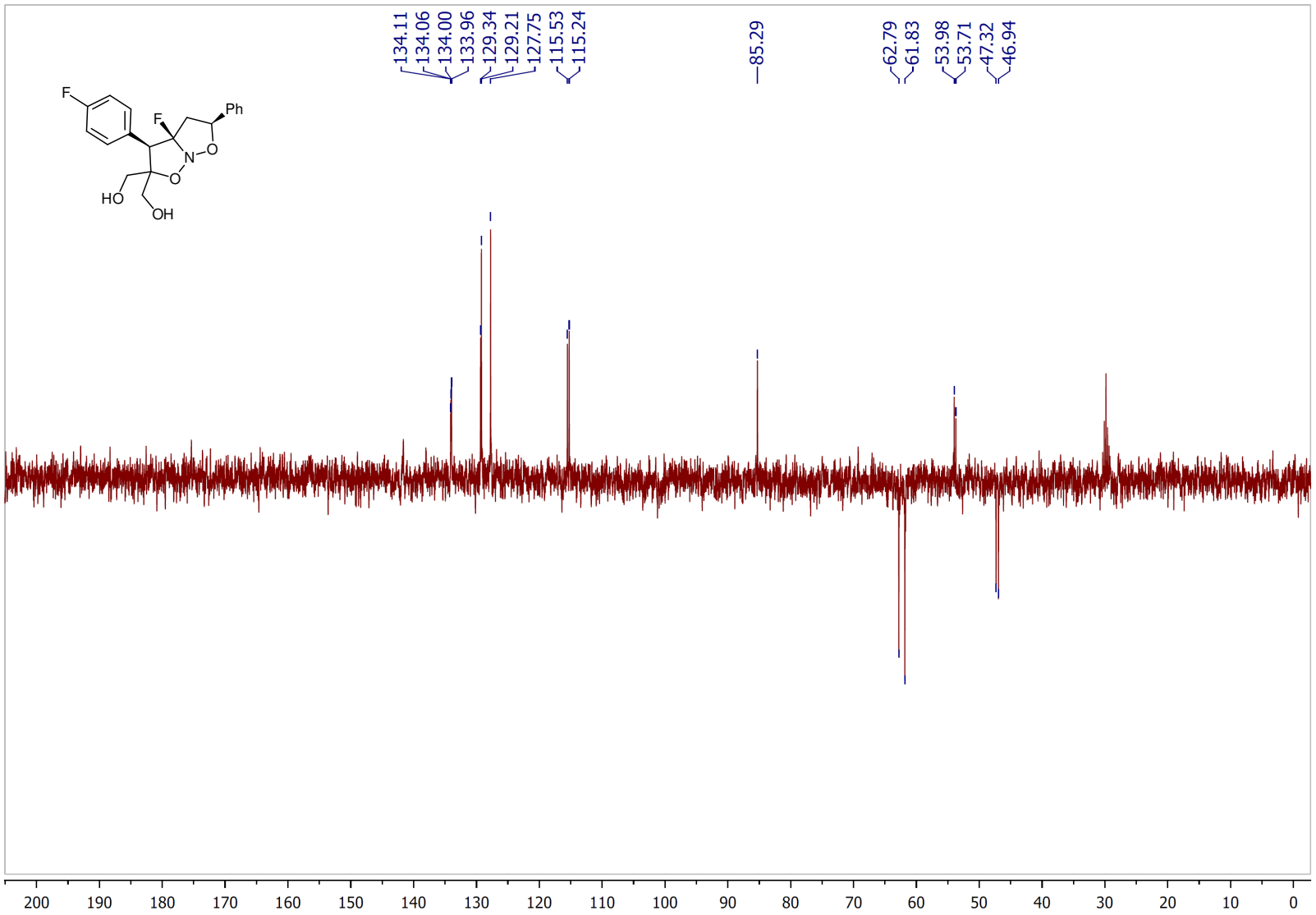
^{1}H NMR



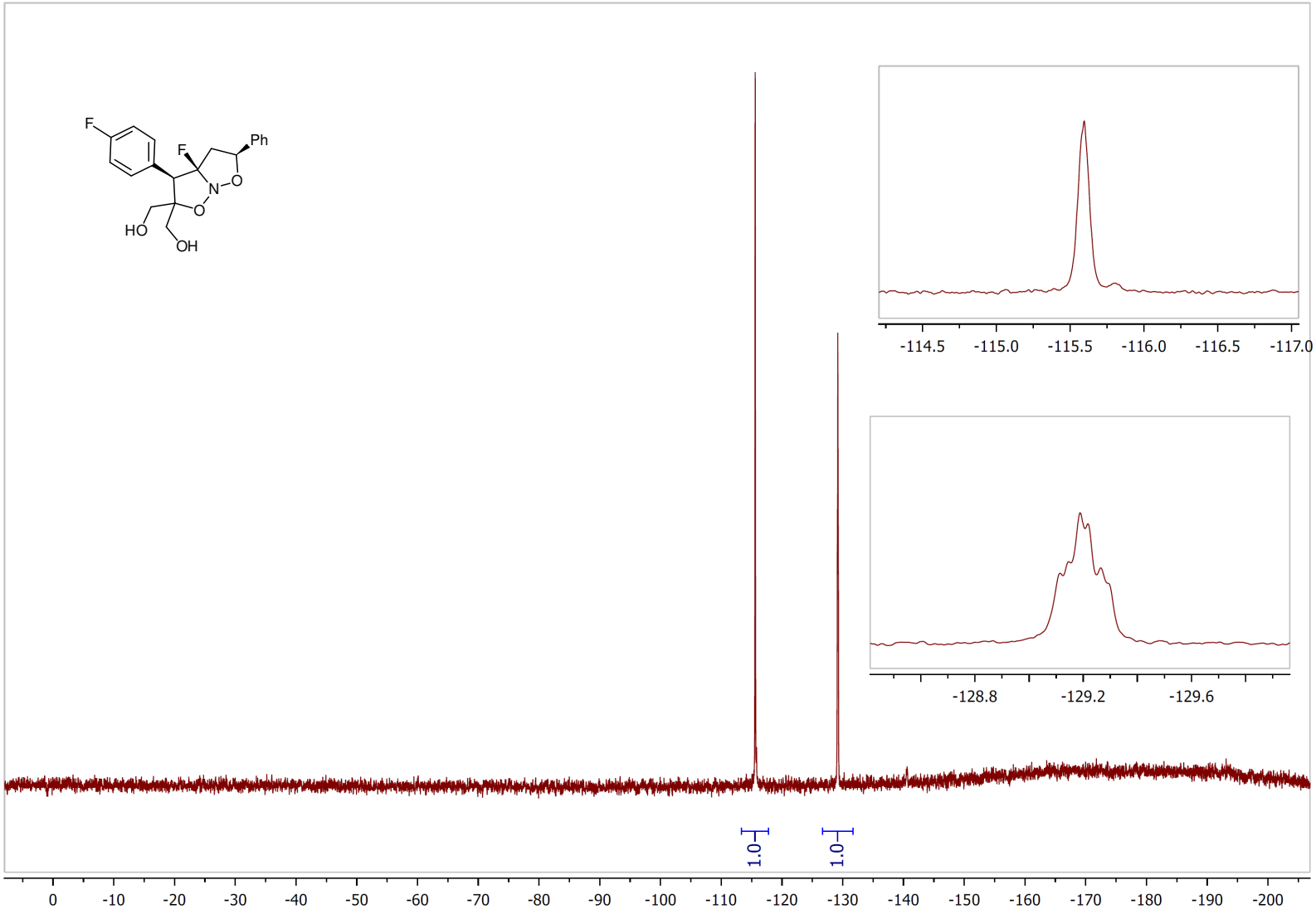
^{13}C NMR


137.87
123.54
120.65
87.59
85.55
63.05
62.09
54.23
53.97
47.57
47.19
F
F
Ph
N
O
O
HO
OH
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

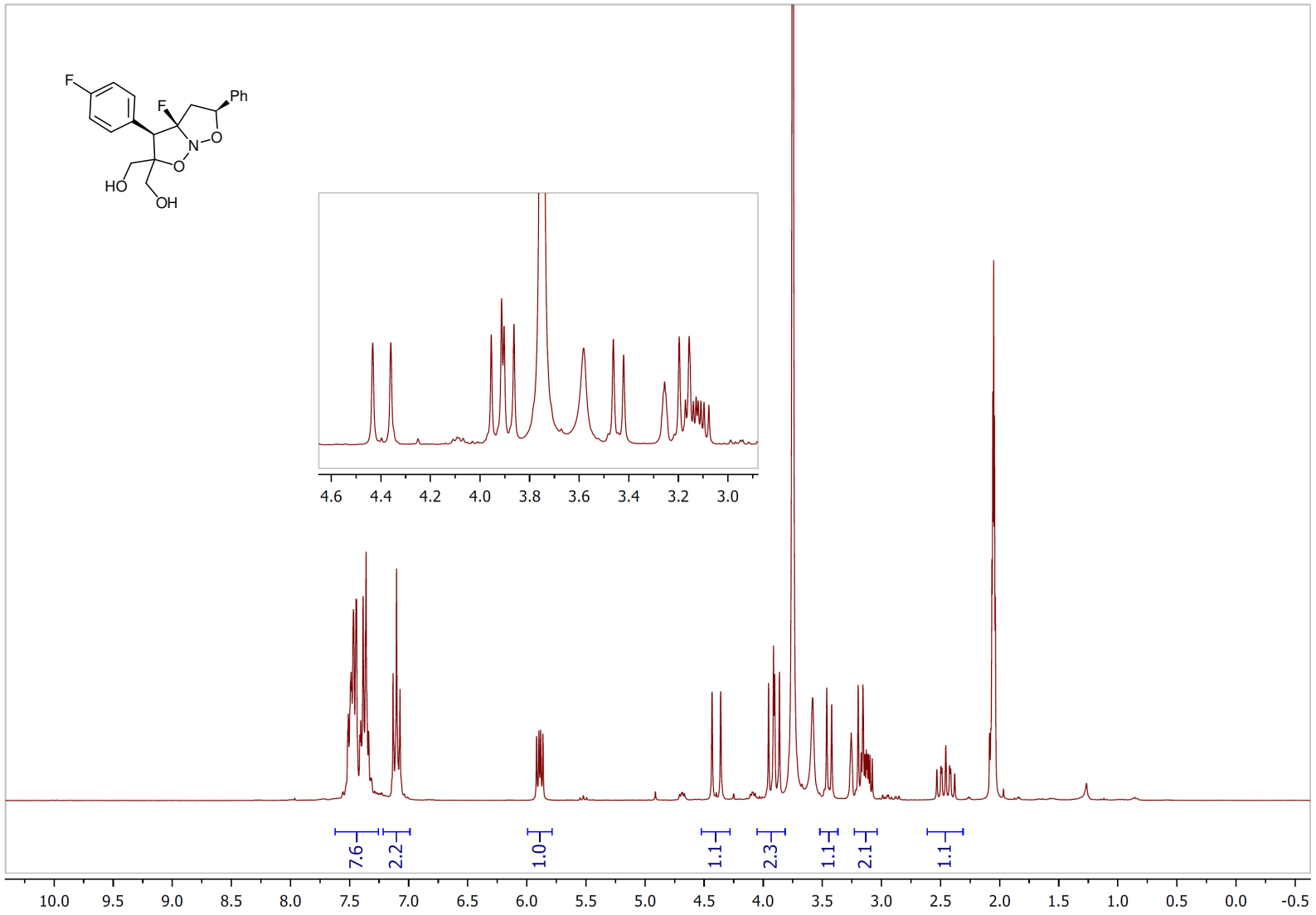
^{13}C NMR (DEPT)


134.11
134.06
134.00
133.96
129.34
129.21
127.75
115.53
115.24
85.29
62.79
61.83
53.98
53.71
47.32
46.94
F
F
Ph
N
O
O
HO
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

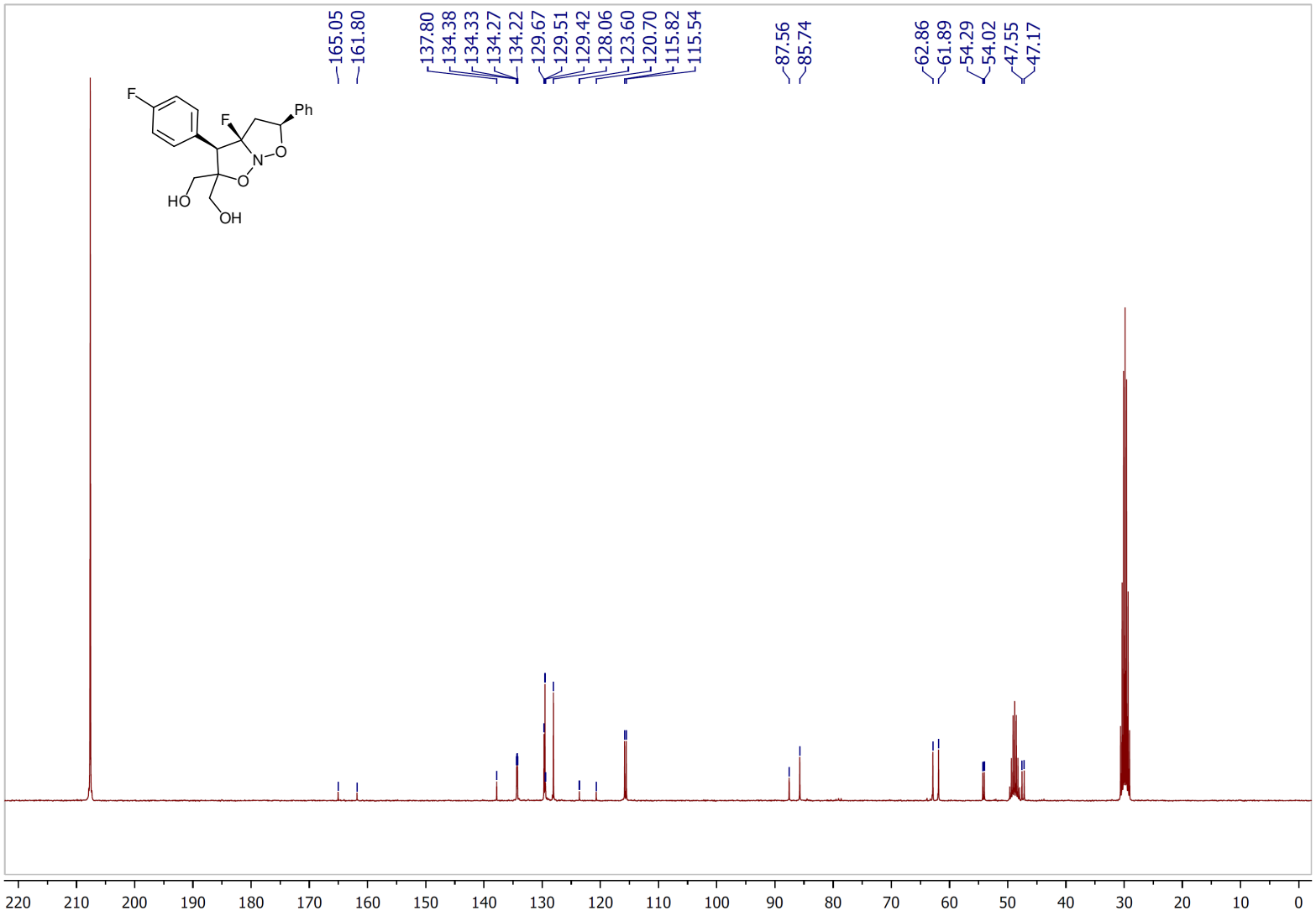
^{19}F NMR


F
F
Ph
N
O
O
HO
OH
-114.5
-115.0
-115.5
-116.0
-116.5
-117.0
-128.8
-129.2
-129.6
1.0
1.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

^{1}H NMR after H/D exchange



^{13}C NMR after H/D-exchange



^{1}H-^{13}C HMBC after H/D-exchange