Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

SUPPORTING INFORMATION

Intramolecular cyclopropylmethylation *via* non-classical carbenium ion

Marija Skvorcova, Aigars Jirgensons*

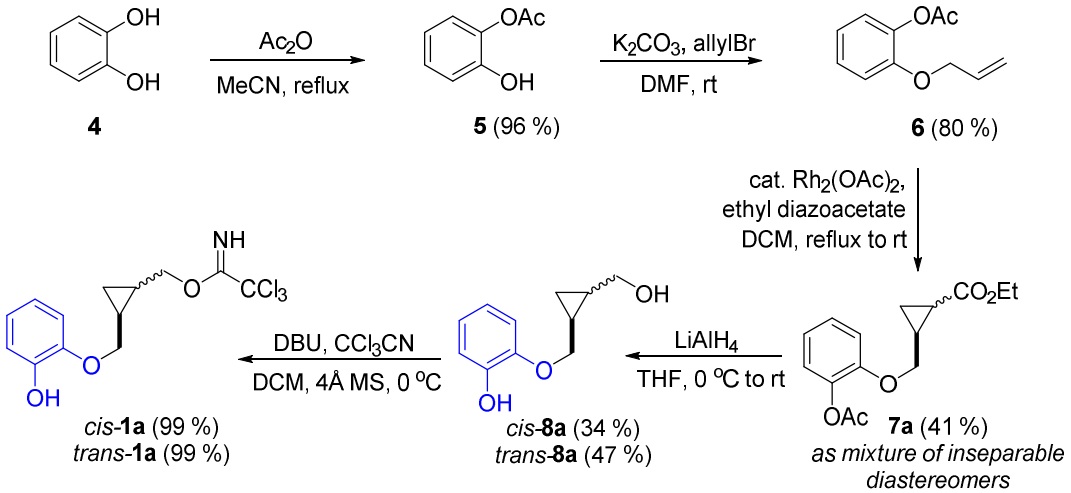
Latvian Institute of Organic Synthesis, Aizkraukles 21, Riga, LV-1006

1. General considerations

All procedures were performed under argon atmosphere unless noted otherwise. Reagents and starting materials were obtained from commercial sources and used as received. The solvents were purified and dried by standard procedures prior to use. Flash column chromatography was carried out using silica gel (230−400 mesh). Thin layer chromatography (TLC) was performed on silica gel and was visualized by UV lamp or staining with $KMnO_4$. NMR spectra were recorded on 300, 400 and 600 MHz spectrometers with chemical shift values (δ) in parts per million using the residual chloroform, dimethylsulfoxide or methanol signal as an internal standard. Gas chromatographic (GC) analysis was performed on Agilent Technologies gas chromatographer with triple-axis detector, heating range 80-280 °C, column 30 m × 0.25 mm, 0.25 μm, 7 inch cage. HRMS analyses were performed on a hybrid quadrupole time-of-flight mass spectrometer equipped with an electrospray ion source.

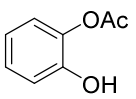
2. Substrate 1 synthesis

Trichloroacetimidates *cis/trans*-**1a** were synthesized in five steps from commercially available 1,2-dihydoxybenzene (**4**) (Scheme 1). Acylation and subsequent allylation of hydroxy groups gave alkene **6**. Separately racemic *trans*- and *cis*-isomers of **7a** were obtained in cyclopropanation reaction from alkene **6** and ethyl diazoacetate in the presence of Rh catalyst. Reduction of ester gave alcohol *cis*/*trans*-**8a**, which was converted to corresponding imidate *cis/trans*-**9a** in the presence of DBU and CCl_3CN.



Scheme 1

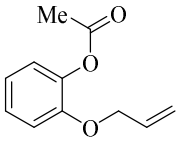
2-Hydroxyphenyl acetate (5)



To a stirred solution of 1,2-dihydoxybenzene (**4**) (1.54 g, 13.97 mmol, 1.0 equiv) in MeCN (12 mL) was added acetic acid anhydride (1.3 mL, 13.97 mmol, 1.0 equiv). The mixture was refluxed until the starting material disappeared (TLC). Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 2:1) afforded 2.02 g (96 %) of 2-hydroxyphenyl acetate **(5)** as a yellowish oil. This compound is known in the literature.[1]

^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.18 – 7.06 (m, 1H), 7.00 (dd, *J* = 8.1 and 1.6 Hz, 1H), 6.93 (ddd, *J* = 8.8, 7.2 and 1.6 Hz, 1H), 6.89 – 6.78 (m, 1H), 5.30 (bs, 1H), 2.36 (s, 3H).

2-(Allyloxy)phenyl acetate (6)

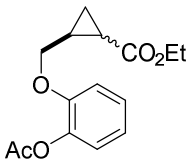


Allyl bromide (1.0 mL, 11.90 mmol, 1.05 equiv) was added dropwise to a cooled (0 °C) solution of phenol **5** (1.72 g, 11.30 mmol, 1.0 equiv) and anhydrous K_2CO_3 (4.60 g, 34.00 mmol, 3.0 equiv) in DMF (10 mL). After the addition was complete, the mixture was allowed to warm to room temperature and stirred until the starting material disappeared (TLC), then the reaction mixture was diluted with water and extracted with ethyl acetate (2 × 10 mL). The organic layers were combined, washed with brine (2 × 15 mL) and dried over $MgSO_4$. Filtration and concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 6:1) afforded 1.74 g (80 %) of 2-(allyloxy)phenyl acetate **(6)** as a colorless oil. This compound is known in the literature.[2]

^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.17 (td, *J* = 8.4, 7.8 and 2.0 Hz, 1H), 7.04 (dd, *J* = 7.7 and 1.9 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 2H), 6.01 (ddt, *J* = 17.1, 10.0 and 5.0 Hz, 1H), 5.38 (dt, *J* = 17.4 and 1.8 Hz, 1H), 5.26 (dt, *J* = 10.7 and 1.7 Hz, 1H), 4.56 (dt, *J* = 5.0 and 1.7 Hz, 2H), 2.31 (s, 3H).

[1] Liu, J. et al. *Tetrahedron* **2016**, 72, 4103.
[2] Combes, S.; Finet, J. P. *Tetrahedron* **1999**, 55, 3377.

Ethyl 2-((2-acetoxyphenoxy)methyl)cyclopropane-1-carboxylate (7a)

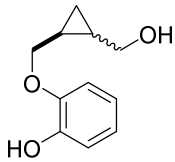


To a solution alkene **6** (466.9 mg, 2.43 mmol, 1.0 equiv) and rhodium (II) acetate dimer (10.7 mg, 2.40 μmol, 1 mol%) in DCM (20 mL) ethyl diazoacetate (831.5 mg, 7.29 mmol, 3.0 equiv) was added *via* syringe pump over 4 hours. The resulting mixture was stirred at room temperature for 12 hours. Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 6:1) afforded 277.9 mg (41 %) of ethyl 2-((2-acetoxyphenoxy)methyl)cyclopropane-1-carboxylate **(7a)** as an inseparable mixture of diastereomers.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.18 – 7.10 (m, 2H), 7.05 – 6.96 (m, 2H), 6.98 – 6.86 (m, 4H), 4.31 (dd, *J* = 10.2, 5.9 Hz, 1H), 4.18 – 3.98 (m, 6H), 3.83 (dd, *J* = 9.9, 6.5 Hz, 1H), 2.29 (dd, *J* = 1.4, 0.4 Hz, 6H), 1.89 – 1.79 (m, 2H), 1.78 – 1.64 (m, 2H), 1.31 – 1.10 (m, 9H), 0.96 (ddd, *J* = 8.4, 6.3, 4.4 Hz, 1H).

HR-MS (ESI-TOF) m/z: calcd. for $C_{15}H_{18}O_5Na$ 301.1052 ; found: 301.1066 $[M+Na]^+$.

2-((2-(Hydroxymethyl)cyclopropyl)methoxy)phenol (*cis*- and *trans*-8a)



A solution of ester **7a** (674.0 mg, 2.42 mmol, 1.0 equiv) in THF (24 mL) was cooled to 0 °C and $LiAlH_4$ (372.2 mg, 9.81 mmol, 4.05 equiv) was added in several portions. After the addition was complete, the mixture was allowed to warm to room temperature and then refluxed until the starting material disappeared (TLC). Reaction mixture was quenched with water (4.1 equiv) and filtered (to remove inorganic solids). A mixture of racemic *trans*- and *cis*-isomers *trans*-**8a** and *cis*-**8a** were obtained and their separation was done by column chromatography on silica gel (eluent hexanes/EtOAc 1:1.5). After purification 159 mg (34 %) of *cis*-**8a** and 220 mg (47 %) of *trans*-**8a** were obtained, both as colorless oils.

<u>*Cis-isomer:*</u> ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.00 – 6.85 (m, 4H), 6.82 (ddd, *J* = 7.9, 6.8, 2.4 Hz, 1H), 4.49 (dd, *J* = 10.7, 5.6 Hz, 1H), 4.09 (dd, *J* = 11.5, 4.5 Hz, 1H), 3.68 (t, *J* = 10.5 Hz, 1H), 3.44 – 3.32 (m, 1H), 2.24 (1H, bs), 1.58 – 1.44 (m, 1H), 1.41 (dddd, *J* = 13.8, 10.6, 8.5, 5.6 Hz, 1H), 0.91 (td, *J* = 8.4, 5.2 Hz, 1H), 0.30 (q, *J* = 5.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 147.4, 145.8, 122.8, 119.9, 115.69, 115.1, 70.9, 62.7, 18.1, 14.9, 7.9.

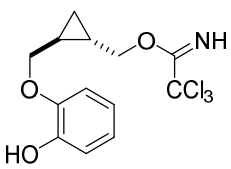
HR-MS (ESI-TOF) m/z: calcd. for $C_{11}H_{14}O_3Na$ 217.0841; found: 217.0832 $[M+Na]^+$.

Trans-isomer: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.96 – 6.74 (m, 4H), 6.17 (s, 1H), 4.02 (dd, *J* = 10.2, 6.3 Hz, 1H), 3.80 – 3.70 (m, 1H), 3.67 (dd, *J* = 11.2, 6.1 Hz, 1H), 3.36 (dd, *J* = 11.2, 7.6 Hz, 1H), 2.01 (s, 1H), 1.28 – 1.07 (m, 2H), 0.64 – 0.53 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 225.8, 146.2, 145.9, 121.8, 120.1, 114.9, 112.7, 72.9, 65.9, 19.9, 16.4, 8.0.

HR-MS (ESI-TOF) m/z: calcd. for $C_{11}H_{14}O_3Na$ 217.0841; found: 217.0842 $[M+Na]^+$.

((1*S,2*S**)-2-((2-Hydroxyphenoxy)methyl)cyclopropyl)methyl 2,2,2-trichloro-acetimidate (*trans*-1a)**

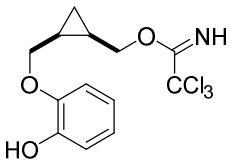


To a solution of alcohol *trans*-**8a** (16.9 mg, 0.087 mmol, 1.0 equiv) in CH_2Cl_2 (3 mL) 4 Å molecular sieves were added. Reaction mixture was cooled to 0 °C and then DBU (13 μL, 0.087 mmol, 1.0 equiv) was added. Solution was stirred at 0 °C for 30 minutes. Then trichloroacetonitrile (18 μL, 0.174 mmol, 2.0 equiv) was added, and the reaction mixture was stirred until TLC showed complete conversion. Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 8:1) afforded 29.3 mg (99 %) of ((1*S**,2*S**)-2-((2-hydroxyphenoxy)methyl)cyclopropyl)-methyl 2,2,2-trichloroacetimidate as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.21 (s, 1H), 6.86 (dt, *J* = 7.8, 1.2 Hz, 1H), 6.85 – 6.70 (m, 3H), 5.66 (s, 1H), 4.29 (dd, *J* = 11.3, 6.0 Hz, 1H), 4.10 – 3.91 (m, 2H), 3.75 (dd, *J* = 10.1, 7.2 Hz, 1H), 1.40 – 1.12 (m, 2H), 0.69 (ddt, *J* = 17.7, 8.3, 5.3 Hz, 2H).

Unstable under the conditions of HRMS.

((1*R,2*S**)-2-((2-Hydroxyphenoxy)methyl)cyclopropyl)methyl 2,2,2-trichloro-acetimidate (*cis*-1a)**



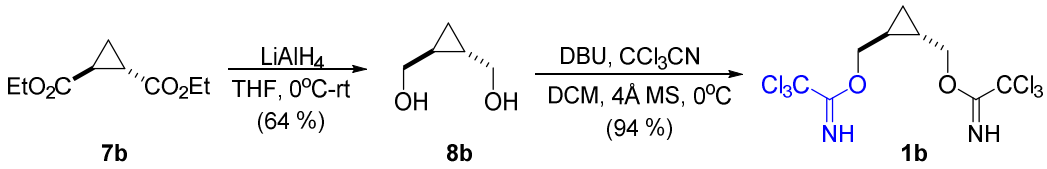
Prepared by analogy to compound *trans*-**1a** from *cis*-**8a** (17.4 mg, 0.090 mmol, 1.0 equiv), DBU (13 μL, 0.090 mmol, 1.0 equiv), trichloroacetonitrile (18 μL, 0.179 mmol, 2.0 equiv), and DCM (3 mL). Yield: 32.0 mg (99 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.29 (bs, 1H), 6.97 – 6.76 (m, 4H), 5.86 (s, 1H), 4.61 (dd, *J* = 11.8, 6.4 Hz, 1H), 4.26 – 4.05 (m, 3H), 1.67 – 1.47 (m, 2H), 1.04 (td, *J* = 8.5, 5.3 Hz, 1H), 0.55 (q, *J* = 5.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.9, 146.0, 145.7, 121.8, 120.0, 114.7, 112.2, 91.4, 69.5, 68.9, 15.4, 14.3, 8.5.

Unstable under the conditions of HRMS.

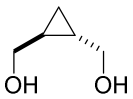
Bis-trichloroacetimidate **1b** was synthesized in two steps according to Scheme 2 from commercially available diethyl *trans*-1,2-cyclopropanedicarboxylate (**7b**). Reduction of diester gave diol **8b**, which was converted to corresponding *bis*-trichloroacetimidate **1b** in the presence of DBU and CCl_3CN.



7b **8b** **1b**

Scheme 2

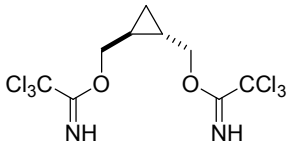
((1*S,2*S**)-Cyclopropane-1,2-diyl)dimethanol (8b)**



Prepared by analogy to compound **8a** from diester **7b** (510.0 mg, 2.74 mmol, 1.0 equiv), $LiAlH_4$ (416.0 mg, 10.96 mmol, 4.0 equiv), and THF (6 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded 178 mg (64 %) of ((1*S**,2*S**)-cyclopropane-1,2-diyl)dimethanol as a colorless oil. This compound is known in the literature.[3]

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 4.63 (bs, 2H), 3.77 (dd, *J* = 11.3, 4.6 Hz, 2H), 2.99 (dd, *J* = 11.3, 8.7 Hz, 2H), 1.02 – 0.87 (m, 2H), 0.42 – 0.30 (m, 2H).

((1*S,2*S**)-Cyclopropane-1,2-diyl)bis(methylene) bis(2,2,2-trichloroacetimidate) (1b)**



Prepared by analogy to compound **1a** from diol **8b** (170.0 mg, 1.66 mmol, 1.0 equiv), DBU (25 μL, 0.017 mmol, 0.1 equiv), trichloroacetonitrile (0.5 mL, 4.980 mmol, 3.0 equiv), and DCM (17 mL). Yield: 613.0 mg (94 %).

[3] Chanthamath, S.; Takaki, S.; Shibatomi, K.; Iwasa, S. *Angew. Chem. Int. Ed.* **2013**, 52, 5818.

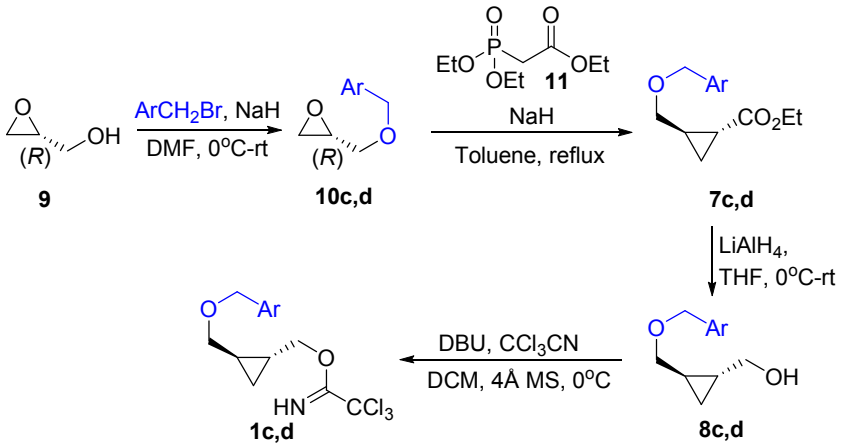
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.25 (bs, 2H), 4.27 – 4.18 (m, 2H), 4.18 – 4.07 (m, 2H), 1.38 (tt, J = 7.6, 5.0 Hz, 2H), 0.73 (dt, J = 11.5, 7.0 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.8, 162.8, 91.5, 72.1, 72.1, 15.7, 8.6.

Unstable under the conditions of HRMS.

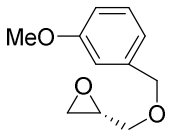
Trichloroacetimidates **1c,d** were synthesized in four steps according to Scheme 3 from commercially available (*R*)-(–)-glycidol (**9**). Cyclopropanes **7c,d** were obtained in *Horner-Wadsworth-Emmons* reaction from stabylized phosphonate **11** and epoxides **10c,d**. Reduction of ester groups gave alcohols **8c,d**, which were transformed to the corresponding trichloroacetimidates **1c,d** in the reaction with CCl_3CN using DBU as a base.

Note: Oxirane **10c** (Ar = Ph) was commercially available.



Scheme 3

(*S*)-2-(((3-Methoxybenzyl)oxy)methyl)oxirane (10d)

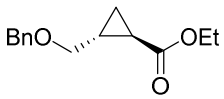


(*R*)-Glycidol (**9)** (0.4 mL, 6.03 mmol, 1.0 equiv) was added slowly to a suspension of NaH (313.3 mg, 7.83 mmol, 1.3 equiv) in anhydrous DMF (10 mL) at 0 °C. After 20 min, 3-metoxybenzyl bromide (1.1 mL, 7.83 mmol, 1.3 equiv) was added dropwise at 0 °C. The reaction mixture was stirred at room temperature. After completion (monitored by TLC), the reaction mixture was quenched with ice-cooled water (10 mL) and diluted with ethyl acetate (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried with Na_2SO_4, concentrated under reduced pressure, and purified by silica gel column chromatography (eluant EtOAc/hexane 1 : 6). Compound **10d** (505 mg, 43%) was obtained as a colorless liquid. This compound is known in the literature.[4]

^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.35 – 7.22 (m, 1H), 7.01 – 6.80 (m, 3H), 4.68 – 4.50 (m, 2H), 3.89 – 3.74 (m, 4H), 3.47 (dd, *J* = 11.4 and 5.8 Hz, 1H), 3.22 (ddt, *J* = 5.8, 4.2 and 2.9 Hz, 1H), 2.84 (dd, *J* = 5.1 and 4.1 Hz, 1H), 2.65 (dd, *J* = 5.0 and 2.7 Hz, 1H).

$[\alpha]_D^{20}$ = -2.0 (c = 1.0, $CHCl_3$).

Ethyl (1*R*,2*R*)-2-((benzyloxy)methyl)cyclopropane-1-carboxylate (7c)

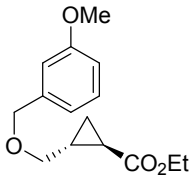


To a suspension of sodium hydride (385.6 mg, 9.64 mmol, 2.1 equiv, 60% in mineral oil) in toluene (24 mL) was added triethylphosphonoacetate (**11**) (1.82 mL, 9.18 mmol) dropwise over 30 min. After stirring at room temperature for 10 minutes ether **10c** (0.7 mL, 4.59 mmol, 1.0 equiv) was added dropwise, followed by heating at reflux for 14 hours. The solution was cooled to room temperature, diluted with ethyl acetate (30 mL), then washed with saturated aqueous ammonium chloride (2 x 15 mL). After drying over magnesium sulfate and concentration in vacuo, the crude material was purified via flash column chromatography (6:1 petrol:ether eluant), to yield ethyl (1*R*,2*R*)-2-((benzyloxy)methyl)cyclopropane-1-carboxylate (532 mg, 50 %) as a colourless oil. This compound is known in the literature.[5]

[4] Fu, H.; Newcomb, M.; Wong, C. H. *J. Am. Chem. Soc.* **1991**, 113 (*15*), 5878.
[5] Armstrong A.; Scutt J. N. *Org. Lett.* **2003**, 5 (*13*), 2331.

^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.38 – 7.27 (m, 5H), 4.52 (s, 2H), 4.12 (qd, *J* = 7.2 and 1.1 Hz, 2H), 3.51 – 3.29 (m, 2H), 1.74 (dqd, *J* = 8.8, 6.2 and 4.0 Hz, 1H), 1.62 – 1.51 (m, 1H), 1.31 – 1.15 (m, 4H), 0.86 (ddd, *J* = 8.4, 6.3 and 4.3 Hz, 1H).
$[\alpha]_D^{20}$ = -77 (c = 1.0, $CHCl_3$).

Ethyl (1*R*,2*R*)-2-(((3-methoxybenzyl)oxy)methyl)cyclopropane-1-carboxylate (7d)



Prepared by analogy to compound **7c** from ether **10d** (480.8 mg, 2.48 mmol, 1.0 equiv), triethylphosphonoacetate **11** (0.98 mL, 4.95 mmol, 2.0 equiv), sodium hydride (207.9 mg, 5.20 mmol, 2.1 equiv, 60 % in mineral oil), and toluene (24 mL), Yield: 385 mg (59 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.22 (t, *J* = 8.1 Hz, 1H), 6.91 – 6.84 (m, 2H), 6.84 – 6.76 (m, 1H), 4.47 (s, 2H), 4.16 – 4.04 (m, 2H), 3.78 (s, 3H), 3.42 (dd, *J* = 10.4 and 6.0 Hz, 1H), 3.32 (dd, *J* = 10.4 and 6.7 Hz, 1H), 1.71 (dddd, *J* = 12.8, 8.9, 6.3 and 4.1 Hz, 1H), 1.54 (ddd, *J* = 8.8, 4.9, 4.1 Hz, 1H), 1.27 – 1.13 (m, 4H), 0.83 (ddd, *J* = 8.3, 6.3, 4.2 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.6, 159.6, 139.7, 129.3, 119.7, 113.2, 112.7, 72.4, 71.4, 60.4, 55.0, 21.5, 18.4, 14.1, 12.8.
HR-MS (ESI-TOF) m/z: calcd. for $C_{15}H_{20}O_4Na$ 287.1259; found: 287.1251 $[M+Na]^+$.
$[\alpha]_D^{20}$ = -74 (c = 1.0, $CHCl_3$).

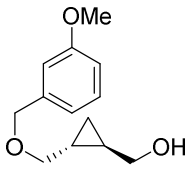
((1*R*,2*R*)-2-((Benzyloxy)methyl)cyclopropyl)methanol (8c)

Prepared by analogy to compound **8a** from ester **7c** (214.61 mg, 0.916 mmol, 1.0 equiv), $LiAlH_4$ (76.48 mg, 2.015 mmol, 2.2 equiv), and THF (22 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded ((1*R*,2*R*)-2-((benzyloxy)methyl)cyclopropyl)methanol (**8c**) (136 mg, 77 %) as a colorless oil. This compound is known in the literature.[6]

^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.32 – 7.14 (m, 5H), 4.45 (s, 2H), 3.47 – 3.10 (m, 4H), 2.52 (bs, 1H), 1.01 – 0.82 (m, 2H), 0.46 – 0.31 (m, 2H).
$[\alpha]_D^{20}$ = -11.6 (c = 1.0, $CHCl_3$).

[6] Fournier, J.; A. Charette, A. *Eur. J. Org. Chem.* **2004**, *7*, 1401.

((1*R*,2*R*)-2-(((3-Methoxybenzyl)oxy)methyl)cyclopropyl)methanol (8d)



Prepared by analogy to compound **8a** from ester **7d** (346.39 mg, 1.31 mmol, 1.0 equiv), $LiAlH_4$ (109.43 mg, 2.88 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded ((1*R*,2*R*)-2-(((3-methoxybenzyl)oxy)methyl) cyclopropyl)methanol (**8d**) **(**234 mg, 80 %) as a colorless oil.

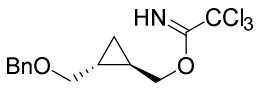
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.22 (t, *J* = 8.1 Hz, 1H), 6.88 (dd, *J* = 7.4 and 1.3 Hz, 2H), 6.83 – 6.75 (m, 1H), 4.47 (s, 2H), 3.77 (s, 3H), 3.45 (dd, *J* = 11.2 and 6.1 Hz, 1H), 3.43 – 3.27 (m, 2H), 3.23 (dd, *J* = 10.2 and 6.9 Hz, 1H), 2.57 (bs, 1H), 1.04 – 0.85 (m, 2H), 0.49 – 0.36 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 159.6, 139.8, 129.3, 119.8, 113.1, 112.9, 73.4, 72.4, 65.9, 55.1, 19.7, 16.7, 7.9.

HR-MS (ESI-TOF) m/z: calcd. for $C_{13}H_{17}O_2$ 205.1229; found: 205.1239 [M-H_2O+H]$^+$.

$[\alpha]_D^{20}$ = -22.2 (c = 1.0, $CHCl_3$).

((1*R*,2*R*)-2-((Benzyloxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1c)



Prepared by analogy to compound **1a** from alcohol **8c** (122.2 mg, 0.636 mmol, 1.0 equiv), DBU (19 μL, 0.127 mmol, 0.2 equiv), trichloroacetonitrile (0.13 mL, 1.335 mmol, 2.1 equiv), and DCM (12 mL). Yield: 209 mg (98 %).

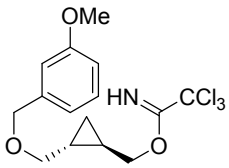
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.24 (bs, 1H), 7.38 – 7.21 (m, 5H), 4.54 (dd, *J* = 16.1 and 11.9 Hz, 2H), 4.26 – 4.12 (m, 2H), 3.38 (d, *J* = 6.5 Hz, 2H), 1.30 – 1.12 (m, 2H), 0.66 (dt, *J* = 8.5 and 5.1 Hz, 1H), 0.59 (dt, *J* = 8.4 and 5.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.8, 138.4, 128.3, 127.6, 127.5, 91.5, 72.9, 72.6, 72.3, 16.9, 15.4, 8.5.

Unstable under the conditions of HRMS.

$[\alpha]_D^{20}$ = -5.1 (c = 1.0, $CHCl_3$).

((1*R*,2*R*)-2-(((3-Methoxybenzyl)oxy)methyl)cyclopropyl)methyl 2,2,2-trichloro-acetimidate (1d)



Prepared by analogy to compound **1a** from alcohol **8d** (170.0 mg, 0.765 mmol, 1.0 equiv), DBU (23 μL, 0.153 mmol, 0.2 equiv), trichloroacetonitrile (0.16 mL, 1.606 mmol, 2.1 equiv), and DCM (12 mL). Yield: 256 mg (91 %).

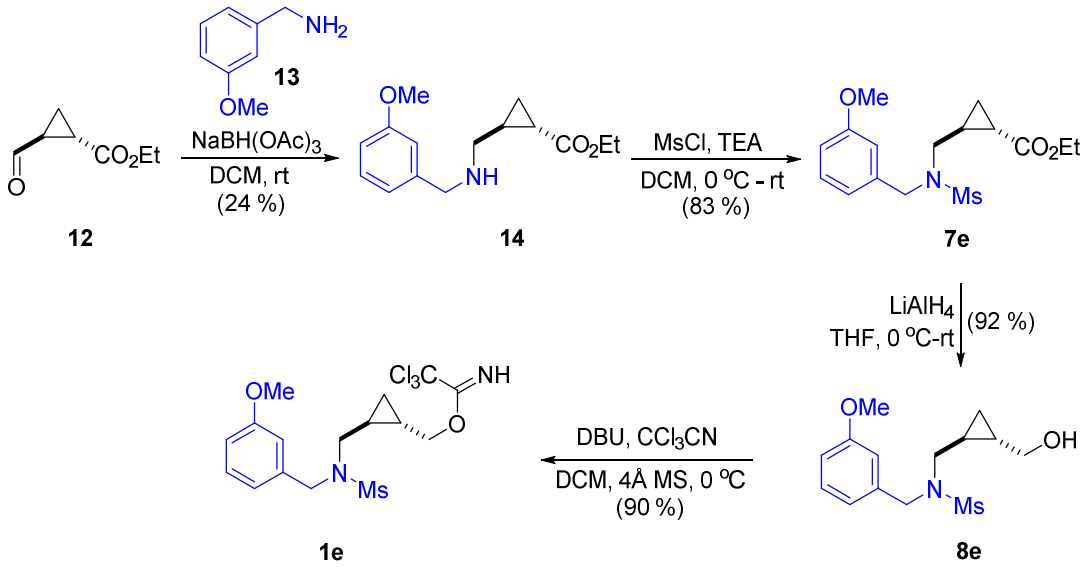
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.25 (s, 1H), 7.25 (t, J = 7.8 Hz, 1H), 6.95 – 6.87 (m, 2H), 6.86 – 6.78 (m, 1H), 4.59 – 4.47 (m, 2H), 4.27 – 4.13 (m, 2H), 3.81 (s, 3H), 3.39 (d, J = 6.5 Hz, 2H), 1.31 – 1.13 (m, 2H), 0.67 (dt, J = 8.5 and 5.1 Hz, 1H), 0.60 (dt, J = 8.4 and 5.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.8, 159.7, 140.0, 129.3, 119.8, 113.1, 112.8, 91.5, 72.9, 72.6, 72.1, 55.2, 16.9, 15.4, 8.5.

Unstable under the conditions of HRMS.

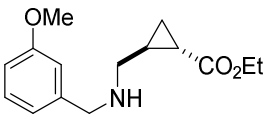
$[\alpha]_D^{20}$ = -22.8 (c = 1.0, $CHCl_3$).

Trichloroacetimidate **1e** was synthesized in four steps according to Scheme 4 from commercially available ethyl 2-formyl-1-cyclopropanecarboxylate (**12**). Reductive amination of aldehyde **12** with amine **13** gave ester **14**. Mesylation of amine **14** and subsequent reduction of ester group gave alcohol **8e**, which was converted to corresponding trichloroacetimidate **1e** in the presence of DBU and CCl_3CN.



Scheme 4

Ethyl (1*S,2*S**)-2-(((3-methoxybenzyl)amino)methyl)cyclopropane-1-carboxylate (14)**



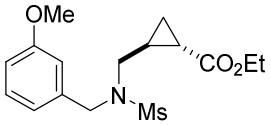
A solution of amine **13** (0.97 mL, 7.555 mmol, 1.0 equiv), and cyclopropanecarboxaldehyde **12** (1.0 mL, 7.555 mmol, 1.0 equiv) in methylene chloride (12 mL) was stirred at room temperature under an argon atmosphere for 1 h. Sodium triacetoxyborohydride (2.4 g, 11.333 mmol, 1.5 equiv) was added portionwise to the reaction mixture, and the mixture was stirred at room temperature under an argon atmosphere overnight. After 19 h of the reaction time, saturated aq. $NaHCO_3$ solution (10 mL) was added to the reaction mixture, and the resulting mixure was stirred vigorously for 1 h. The layers were separated, and the aqueous layer was washed with CH_2Cl_2 (3 × 10 mL). The combined CH_2Cl_2 extract was washed with water (20 mL), dried over $MgSO_4$, and concentrated in vacuo to give a crude product. The isolated crude was purified by flash column chromatography using an ethyl acetate/ methanol solvent gradient (from 1:0 to 0:1). The free base **14** (475 mg, 24% yield) was obtained as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.27 – 7.16 (m, 1H), 6.91 – 6.84 (m, 2H), 6.81 – 6.73 (m, 1H), 4.08 (qd, *J* = 7.1, 1.5 Hz, 2H), 3.81 – 3.73 (m, 5H), 2.73 (bs, 1H), 2.63 – 2.48 (m, 2H), 1.69 – 1.55 (m, 1H), 1.43 (dt, *J* = 8.7, 4.4 Hz, 1H), 1.27 – 1.12 (m, 4H), 0.75 (ddd, *J* = 8.3, 6.3, 4.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.7, 159.8, 140.9, 129.4, 120.4, 113.6, 112.7, 60.5, 55.2, 53.2, 51.6, 22.1, 19.2, 14.2, 13.8.

HR-MS (ESI-TOF) m/z: calcd. for $C_{15}H_{22}NO_3$ 264.1600; found: 264.1609 $[M+H]^+$.

Ethyl (1*S,2*S**)-2-((*N*-(3-methoxybenzyl)methylsulfonamido)methyl)cyclopropane-1-carboxylate (7e)**



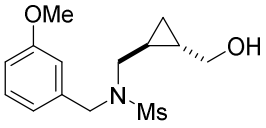
Mesyl chloride (61 μL, 0.78 1mmol, 1.05 equiv) was added dropwise to a cooled (0 °C) solution of ethyl (1*S**,2*S**)-2-(((3-methoxybenzyl)amino)methyl)cyclopropane-1-carboxylate **(14)** (196 mg, 0.744 mmol, 1.0 equiv) and Et_3N (0.22 mL, 1.563 mmol, 2.0 equiv) in DCM (12 mL) and reaction mixture was stirred at room temperature overnight. Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 1:1) afforded 212 mg (83 %) of *N*-(((1*S**,2*S**)-2-(hydroxymethyl)cyclopropyl)methyl)-*N*-(3-methoxybenzyl)-methanesulfonamide as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.28 – 7.19 (m, 1H), 6.94 – 6.85 (m, 2H), 6.81 (dd, *J* = 8.3, 2.6 Hz, 1H), 4.50 – 4.32 (m, 2H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 3.21 – 3.04 (m, 2H), 2.91 (s, 3H), 1.58 – 1.50 (m, 1H), 1.47 (td, *J* = 8.5, 3.6 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.16 (dt, *J* = 9.3, 4.7 Hz, 1H), 0.75 (ddd, *J* = 8.5, 6.2, 4.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.1, 159.9, 137.3, 129.8, 120.3, 113.5, 113.5, 60.7, 55.2, 50.7, 49.4, 39.7, 20.0, 19.5, 14.2, 13.9.

HR-MS (ESI-TOF) m/z: calcd. for $C_{16}H_{24}NO_5S$ 342.1375; found: 342.1369 $[M+H]^+$.

_N_-(((1_S_*,2_S_*)-2-(Hydroxymethyl)cyclopropyl)methyl)-_N_-(3-methoxybenzyl)-methanesulfonamide (8e)



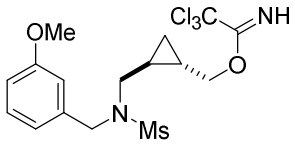
Prepared by analogy to compound **8a** from ester **7e** (207.79 mg, 0.609 mmol, 1.0 equiv), $LiAlH_4$ (50.82 mg, 1.339 mmol, 2.2 equiv), and THF (12 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded *N*-(((1*S**,2*S**)-2-(hydroxymethyl)cyclopropyl)methyl)-*N*-(3-methoxybenzyl)-methanesulfonamide (**8e**) (167 mg, 92 %) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.30 – 7.18 (m, 1H), 6.94 – 6.86 (m, 2H), 6.80 (ddd, *J* = 8.3, 2.6, 1.0 Hz, 1H), 4.44 (s, 2H), 3.77 (s, 3H), 3.50 (dd, *J* = 11.2, 6.0 Hz, 1H), 3.26 – 3.13 (m, 2H), 2.98 (dd, *J* = 15.0, 7.4 Hz, 1H), 2.90 (s, 3H), 2.03 (bs, 1H), 0.98 – 0.80 (m, 2H), 0.41 (dt, *J* = 8.4, 5.1 Hz, 1H), 0.35 (dt, *J* = 8.5, 5.1 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 159.9, 137.8, 129.7, 120.3, 113.7, 113.2, 65.8, 55.2, 50.8, 50.7, 39.4, 20.5, 15.4, 8.8.

Unstable under the conditions of HRMS.

((1_S_*,2_S_*)-2-((_N_-(3-Methoxybenzyl)methylsulfonamido)methyl)cyclopropyl)-methyl 2,2,2-trichloroacetimidate (1e)



Prepared by analogy to compound **1a** from alcohol **8e** (226.47 mg, 0.756 mmol, 1.0 equiv), DBU (23 μL, 0.151 mmol, 0.2 equiv), trichloroacetonitrile (0.17 mL, 1.664 mmol, 2.2 equiv), and DCM (10 mL). Yield: 303 mg (90 %).

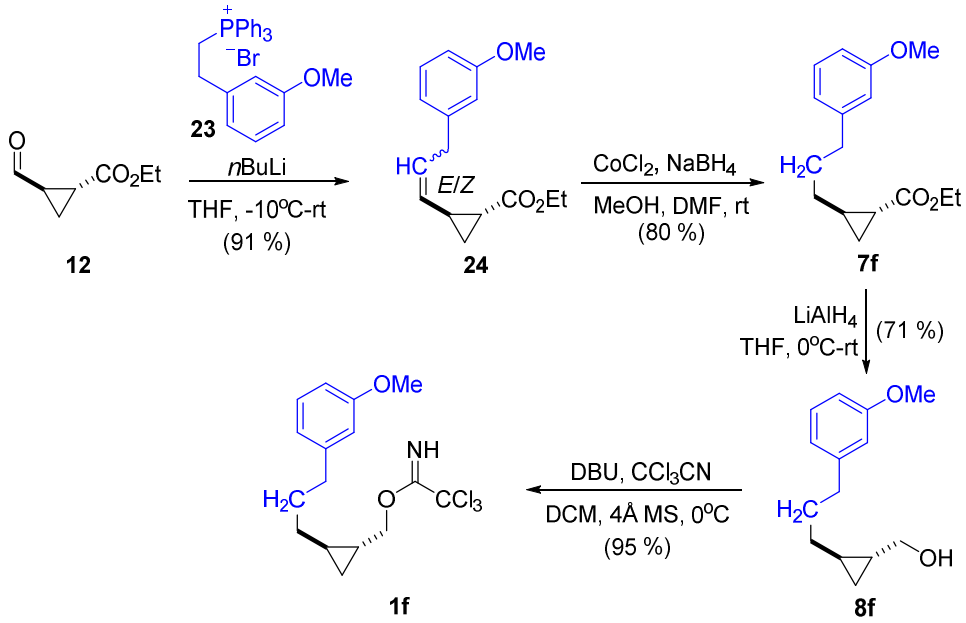
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.27 (bs, 1H), 7.27 – 7.20 (m, 1H), 6.96 – 6.86 (m, 2H), 6.85 – 6.77 (m, 1H), 4.50 (s, 2H), 4.30 (dd, *J* = 11.4, 5.9 Hz, 1H), 3.88 (dd, *J* = 11.4, 8.2 Hz, 1H), 3.78 (s, 3H), 3.34 (dd, *J* = 15.1, 5.8 Hz, 1H), 2.95 – 2.83 (m, 4H),

1.24 – 1.10 (m, 1H), 1.09 – 0.96 (m, 1H), 0.57 (dt, J = 8.5, 5.1 Hz, 1H), 0.48 (dt, J = 8.6, 5.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.7, 159.9, 137.6, 129.7, 120.4, 113.8, 113.2, 91.4, 72.6, 55.2, 50.1, 49.7, 39.9, 16.7, 15.7, 8.8.

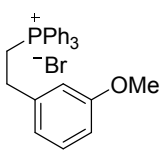
HR-MS (ESI-TOF) m/z: calcd. for $C_{16}H_{21}N_2O_4Cl_3SNa$ 465.0185; found: 465.0189 $[M+Na]^+$.

Trichloroacetimidate **1f** was synthesized in four steps according to Scheme 5 from commercially available ethyl 2-formyl-1-cyclopropanecarboxylate (**12**). Alkene **24** was obtained in *Wittig* reaction from aldehyde **12** and triphenyl phosphonium salt **23** as mixture of inseparable *E*/*Z*-isomers. Ester **7f** was obtained by reduction of double bond with $CoCl_2$ and $NaBH_4$. Finally, reduction of ester group gave alcohol **8f**, which was transformed to corresponding trichloroacetimidate **1f** in the presence of DBU and CCl_3CN.



Scheme 5

(3-Methoxyphenethyl)triphenylphosphonium bromide (23)



Triphenylphosphine (599.95 mg, 2.287 mmol) and 3-methoxyphenethyl bromide (491.99 mg, 2.287 mmol) was dissolved in 4 mL of dry toluene and refluxed under nitrogen for 12 h. After cooling to room temperature, the white precipitate was filtered off, washed with diethyl ether, and dryed under vacuum. Yield: 897 mg (82 %).

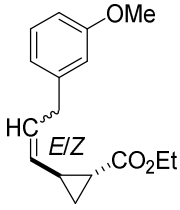
^{1}H NMR (400 MHz, Methanol-d_4) δ 7.93 – 7.69 (m, 15H), 7.19 (dd, J = 9.2, 7.1 Hz, 1H), 6.82 – 6.74 (m, 3H), 3.79 – 3.65 (m, 5H), 3.02 – 2.89 (m, 2H).

^{13}C NMR (101 MHz, Methanol-d_4) δ 160.1, 140.1 (d, J = 15.2 Hz), 134.92 (d, J = 3.0 Hz), 133.5 (d, J = 10.0 Hz), 130.1 (d, J = 12.5 Hz), 129.6, 120.1, 118.7, 117.9, 113.7, 112.2, 54.3, 27.9 (d, J = 3.6 Hz), 23.1 (d, J = 49.8 Hz).

EA: Calcd for $C_{27}H_{26}BrOP$: C, 67.93%; H, 5.49%; found: C,67.91%; H, 5.47%.

Mp (Hexane): 215.1 – 216.4 °C.

Ethyl (1*R,2*S**)-2-(3-(3-methoxyphenyl)prop-1-en-1-yl)cyclopropane-1-carboxylate (24)**



*n*BuLi (4.94 mL, 4.445 mmol, 1.1 equiv, 1 M in THF) was added dropwise to a suspension of triphenyl phosphonium salt **23** (1.929 g, 4.040 mmol, 1.0 equiv) in THF (100 mL) at 0 °C, and the mixture was stirred for 15 min at 0 °C. Then aldehyde **12** (0.59 mL, 4.445 mmol, 1.1 equiv) was added dropwise to resulting mixture and after the addition was complete, the mixture was allowed to warm to room temperature and stirred at room temperature overnight. The mixture was then quenched with sat. aq. NH_4Cl (10 mL) and diethyl ether (10 mL) was added. The phases were separated, aqueous layer was extracted with diethyl ether (2 × 10 mL), and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification by flash column chromatography (eluent hexanes/EtOAc 6:1) afforded ethyl (1*R**,2*S**)-2-(3-(3-methoxyphenyl)prop-1-en-1-yl)cyclopropane-1-carboxylate (**24**) (624.0 mg; 91 %) as a mixture of inseparable *Z*/*E*-isomers (ratio of *Z*/*E*-**24** was 2.6/1).

Z-isomer: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.30 – 7.11 (m, 2H), 6.85 – 6.68 (m, 2H), 5.62 (dtt, J = 10.0, 7.5, 1.2 Hz, 1H), 4.94 (ddq, J = 11.0, 9.5, 1.5 Hz, 1H), 4.18 – 4.09 (m, 2H), 3.79 (s, 3H), 3.56 – 3.46 (m, 2H), 2.32 – 2.23 (m, 1H), 1.68 – 1.61 (m, 1H), 1.47 – 1.41 (m, 1H), 1.30 – 1.21 (m, 3H), 0.98 – 0.90 (m, 1H).

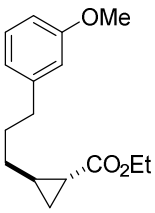
E-isomer: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.32 – 7.10 (m, 2H), 6.82 – 6.68 (m, 2H), 5.82 – 5.68 (m, 1H), 5.10 (ddt, J = 15.3, 8.4, 1.5 Hz, 1H), 4.20 – 4.06 (m, 2H), 3.79 (d, J = 1.4 Hz, 3H), 3.30 (dd, J = 6.8, 1.6 Hz, 2H), 2.05 – 1.91 (m, 1H), 1.63 – 1.55 (m, 1H), 1.37 – 1.31 (m, 1H), 1.30 – 1.21 (m, 3H), 0.99 – 0.86 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.5 and171.9, 159.8 and 159.7, 142.2 and 141.9, 131.2and 130.7, 129.4 and 129.4, 129.0 and 128.2, 120.9 and 120.7, 114.3 and

114.0, 111.4 and 111.3, 60.6 and 60.5, 55.1 and 55.1, 39.1 and 38.8, 33.9 and 33.8, 24.7 and 22.1, 20.9 and 19.2, 16.1 and 15.5, 14.5 and 14.3.

HR-MS (ESI-TOF) m/z: calcd. for $C_{16}H_{21}O_3$ 261.1491; found: 261.1489 $[M+H]^+$

Ethyl (1*R,2*R**)-2-(3-(3-methoxyphenyl)propyl)cyclopropane-1-carboxylate (7f)**



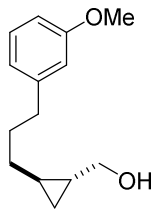
Prepared by analogy to the literature procedure.[7] A solution of alkene **24** (274.9 mg, 1.056 mmol, 1.0 equiv) in MeOH (5 mL) and anhydrous $CoCl_2$ (27.42 mg, 0.211 mmol, 0.2 equiv) was stirred for 30 min under argon atmosphere. Then, $NaBH_4$ (159.8 mg, 4.224 mmol, 4.0 equiv) in DMF (3 mL) was added at room temperature and stirred for additional 0.5 h. Then the reaction was quenched by water (10 mL) and the mixture was extracted with CH_2Cl_2 (2 × 10 mL). The organic phase was washed with water (3 × 15 mL) to remove DMF, dried over $MgSO_4$ and concentrated. The residues were chromatographed on silica gel (elution with hexanes/ethyl acetate 20:1) to afford the ester **7f** (222.0 mg, 80 %) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.25 – 7.14 (m, 1H), 6.81 – 6.70 (m, 3H), 4.17 – 4.06 (m, 2H), 3.80 (s, 3H), 2.69 – 2.52 (m, 2H), 2.39 – 2.24 (m, 1H), 1.74 (p, *J* = 7.5 Hz, 1H), 1.70 – 1.55 (m, 1H), 1.44 – 1.28 (m, 3H), 1.30 – 1.21 (m, 3H), 1.16 (dt, *J* = 8.8, 4.7 Hz, 1H), 0.68 (ddd, *J* = 7.6, 5.9, 4.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 174.4, 159.6, 143.9, 129.2, 120.8, 114.1, 110.9, 60.3, 55.1, 35.5, 32.5, 30.7, 22.6, 20.2, 15.4, 14.3.

HR-MS (ESI-TOF) m/z: calcd. for $C_{16}H_{23}O_3$ 263.1647; found: 263.1649 $[M+H]^+$

((1*R,2*R**)-2-(3-(3-Methoxyphenyl)propyl)cyclopropyl)methanol (8f)**



Prepared by analogy to compound **8a** from ester **7f** (215.5 mg, 0.821 mmol, 1.0 equiv), $LiAlH_4$ (68.59 mg, 1.807 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded 129 mg (71 %) of ((1*R**,2*R**)-2-(3-(3-methoxyphenyl)propyl)cyclopropyl)methanol as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.20 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 6.81 – 6.70 (m, 3H), 3.80 (d, *J* = 1.0 Hz, 3H), 3.50 – 3.38 (m, 2H), 2.61 (h, *J* = 7.9 Hz, 2H), 1.85

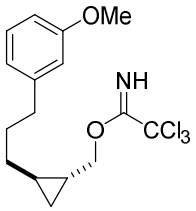
[7] He, R.; Deng, M. Z. *Tetrahedron* **2002**, 58, 7613.

– 1.66 (m, 3H), 1.30 (q, *J* = 7.0 Hz, 2H), 0.84 (qt, *J* = 7.0, 4.5 Hz, 1H), 0.69 – 0.55 (m, 1H), 0.38 (dt, *J* = 8.3, 4.7 Hz, 1H), 0.31 (dt, *J* = 8.1, 4.9 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 159.6, 144.3, 129.2, 120.8, 114.2, 110.8, 67.0, 55.1, 35.7, 33.2, 31.2, 21.1, 16.9, 9.9.

HR-MS (ESI-TOF) m/z: calcd. for $C_{14}H_{19}O$ 203.1436; found: 203.1433 $[M\text{-}H_2O+H]^+$

((1*R,2*R**)-2-(3-(3-Methoxyphenyl)propyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1f)**



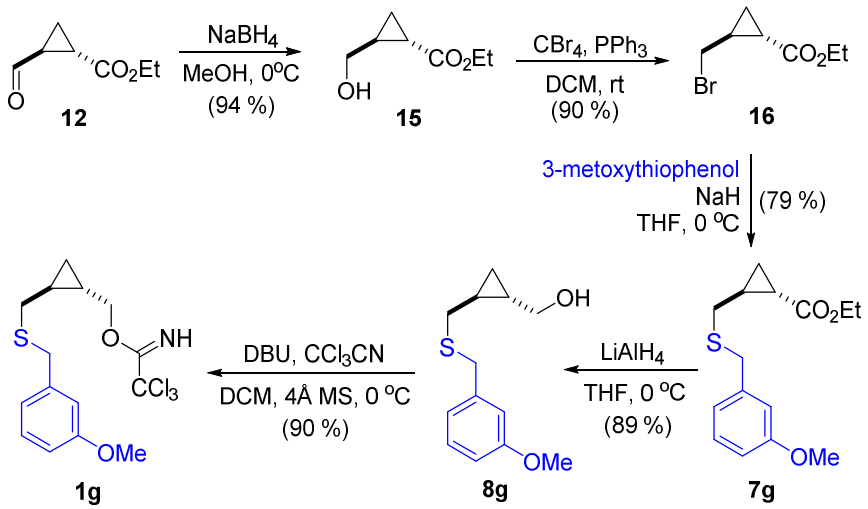
Prepared by analogy to compound **1a** from alcohol **8f** (122 mg, 0.554 mmol, 1.0 equiv), DBU (17 μL, 0.111 mmol, 0.2 equiv), trichloroacetonitrile (0.12 mL, 1.218 mmol, 2.2 equiv), and DCM (8 mL). Yield: 191 mg (90 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.20 (bs, 1H), 7.22 – 7.14 (m, 1H), 6.80 – 6.67 (m, 3H), 4.23 (dd, *J* = 11.2, 6.7 Hz, 1H), 4.04 (dd, *J* = 11.2, 7.8 Hz, 1H), 3.78 (s, 3H), 2.66 – 2.57 (m, 2H), 1.78 – 1.67 (m, 2H), 1.46 – 1.31 (m, 1H), 1.19 (dd, *J* = 13.7, 7.5 Hz, 1H), 1.02 (dtd, *J* = 12.5, 8.1, 4.5 Hz, 1H), 0.85 – 0.72 (m, 1H), 0.56 – 0.47 (m, 1H), 0.40 (dt, *J* = 8.3, 5.1 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 163.0, 159.6, 144.2, 129.1, 120.8, 114.1, 110.9, 91.7, 73.7, 55.1, 35.5, 32.9, 30.9, 17.6, 16.8, 10.3.

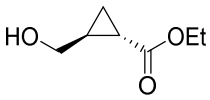
HR-MS (ESI-TOF) m/z: calcd. for $C_{16}H_{21}NO_2Cl_3$ 364.0638; found: 364.0630 $[M+H]^+$

Trichloroacetimidate **1g** was synthesized in five steps according to Scheme 6 from commercially available ethyl 2-formyl-1-cyclopropanecarboxylate (**12**). Reduction of aldehyde **12** gave alcohol **15**, which under *Appel* reaction conditions was transformed to bromide **16**. Alkylation of 3-metoxythiophenol with bromide **16** and subsequent reduction of ester group gave alcohol **8g**, which was converted to corresponding trichloroacetimidate **1g** in the presence of DBU and CCl_3CN.



Scheme 6

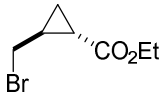
Ethyl (1*S,2*S**)-2-(hydroxymethyl)cyclopropane-1-carboxylate (15)**



$NaBH_4$ (1.57 g, 41.55 mmol, 1.1 equiv) was added portionwise to a cooled (0 °C) solution of aldehyde **12** (5.0 mL, 37.77 mmol, 1.0 equiv) in MeOH (25 mL) and reaction mixture was stirred at 0 °C for 1 hour. Then solvent was evaporated and dry crude mixture quenched with water (10 mL) and extracted with EtOAc (2 × 15 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Alcohol **15** (5.1 g, 94 %) was used for the next step without further purification. This compound is known in the literature.[8]

^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 4.20 – 4.05 (m, 2H), 3.63 (dd, *J* = 11.5 and 6.1 Hz, 1H), 3.49 (dd, *J* = 11.5 and 6.8 Hz, 1H), 1.80 – 1.64 (m, 1H), 1.57 (dt, *J* = 8.8 and 4.5 Hz, 1H), 1.41 (bs, 1H), 1.34 – 1.16 (m, 4H), 0.86 (ddd, *J* = 8.5, 6.3 and 4.3 Hz, 1H).

Ethyl (1*S,2*S**)-2-(bromomethyl)cyclopropane-1-carboxylate (16)**



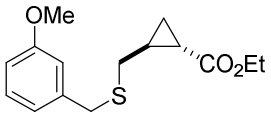
To a solution of alcohol **15** (4.0 g, 27.7 mmol, 1.0 equiv) and carbon tetrabromide (18.4 g, 55.5 mmol, 2.0 equiv) in DCM (50 mL) triphenylphosphine (14.6 g, 55.5 mmol, 2.0 equiv) was added. The reaction mixture was stirred at room temperature for 16 h. Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 10:1) afforded ethyl (1*S**,2*S**)-2-(bromomethyl)cyclopropane-1-carboxylate (**16**).

[8] Jeffrey, J. L.; Terrett, J. A.; MacMillan, D. W. *Science* **2015**, 349 (*6255*), 1532.

(5.2 g, 90 %) as a yellowish oil. This compound is known in the literature.[9]

^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 4.14 (q, *J* = 7.0 Hz, 2H), 3.34 (qd, *J* = 10.4, 7.4 Hz, 2H), 1.91 (dtdd, *J* = 8.8, 7.4, 6.1, 4.0 Hz, 1H), 1.65 (ddd, *J* = 8.9, 5.1, 4.0 Hz, 1H), 1.39 (dt, *J* = 8.3, 4.7 Hz, 1H), 1.27 (t, *J* = 7.2 Hz, 3H), 0.95 (ddd, *J* = 8.7, 6.1, 4.7 Hz, 1H).

Ethyl (1*S,2*S**)-2-(((3-methoxybenzyl)thio)methyl)cyclopropane-1-carboxylate (7g)**



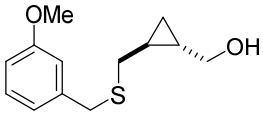
Prepared by analogy to compound **7i** from 3-metoxythiophenol (472.6 mg, 3.064 mmol, 1.0 equiv), NaH (122.56 mg, 3.064 mmol, 1.0 equiv, 60 % dispersion in mineral oil), bromide **16** (634.5 mg, 3.064 mmol, 1.0 equiv), and DMF (2 mL). Yield: 675 mg (79 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.24 – 7.18 (m, 1H), 6.93 – 6.87 (m, 2H), 6.78 (ddd, *J* = 8.3, 3.1, 1.3 Hz, 1H), 4.12 (qd, *J* = 7.1, 1.3 Hz, 2H), 3.80 (d, *J* = 1.3 Hz, 3H), 3.73 (s, 2H), 2.46 (ddd, *J* = 13.5, 6.7, 1.4 Hz, 1H), 2.36 (ddd, *J* = 13.5, 7.1, 1.4 Hz, 1H), 1.68 – 1.54 (m, 1H), 1.52 – 1.43 (m, 1H), 1.25 (td, *J* = 7.2, 1.2 Hz, 4H), 0.78 (dddd, *J* = 8.4, 6.2, 4.4, 1.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.5, 159.7, 139.7, 129.4, 121.1, 114.2, 112.6, 60.5, 55.2, 36.2, 34.3, 21.9, 20.7, 15.5, 14.2.

HR-MS (ESI-TOF) m/z: calcd. for $C_{15}H_{20}O_3SNa$ 303.1031; found: 303.1035 $[M+Na]^+$.

((1*S,2*S**)-2-(((3-Methoxybenzyl)thio)methyl)cyclopropyl)methanol (8g)**



Prepared by analogy to compound **8a** from ester **7g** (491.2 mg, 1.752 mmol, 1.0 equiv), $LiAlH_4$ (146.28 mg, 3.854 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded ((1*S**,2*S**)-2-(((3-methoxybenzyl)thio)methyl)cyclopropyl)methanol (**8g**) (373 mg; 89%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.22 – 7.16 (m, 1H), 6.90 – 6.85 (m, 2H), 6.78 – 6.72 (m, 1H), 3.78 (s, 3H), 3.72 (s, 2H), 3.47 (ddd, *J* = 11.2, 6.7, 2.0 Hz, 1H), 3.34

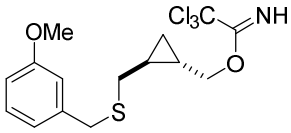
[9] Li, Z.; Zheng, Z.; Chen, H. *Tetrahedron: Asym*. **2000**, 11(5), 1157.

(dd, *J* = 11.2, 7.2 Hz, 1H), 2.45 (ddd, *J* = 13.1, 6.6, 1.7 Hz, 1H), 2.30 (dd, *J* = 13.1, 7.4 Hz, 1H), 1.76 (bs, 1H), 0.99 – 0.86 (m, 1H), 0.90 – 0.77 (m, 1H), 0.49 (dt, *J* = 8.3, 5.1 Hz, 1H), 0.43 (dtd, *J* = 8.4, 5.0, 1.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 159.7, 140.1, 129.4, 121.2, 114.3, 112.5, 66.3, 55.2, 36.3, 35.6, 21.9, 17.0, 10.8.

HR-MS (ESI-TOF) m/z: calcd. for $C_{13}H_{17}OS$ 221.1000; found: 221.1003 $[M-H_2O+H]^+$.

((1*S,2*S**)-2-(((3-Methoxybenzyl)thio)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1g)**



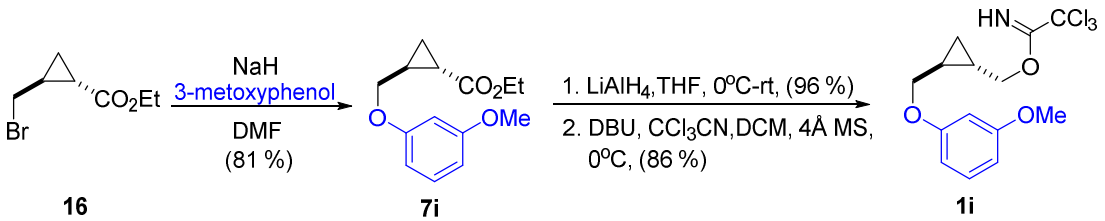
Prepared by analogy to compound **1a** from alcohol **8g** (329.99 mg, 1.385 mmol, 1.0 equiv), DBU (41 μL, 0.277 mmol, 0.2 equiv), trichloroacetonitrile (0.31 mL, 3.046 mmol, 2.2 equiv), and DCM (22 mL). Yield: 479 mg (90 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.25 (bs, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 6.95 – 6.87 (m, 2H), 6.82 – 6.74 (m, 1H), 4.21 (dd, *J* = 11.2, 6.7 Hz, 1H), 4.09 (dd, *J* = 11.3, 7.4 Hz, 1H), 3.80 (s, 3H), 3.76 (d, *J* = 3.7 Hz, 2H), 2.40 (qd, *J* = 13.4, 6.9 Hz, 2H), 1.25 – 1.12 (m, 1H), 1.12 – 0.98 (m, 1H), 0.65 (dt, *J* = 8.4, 5.1 Hz, 1H), 0.53 (dt, *J* = 8.5, 5.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.9, 159.7, 140.0, 129.4, 121.2, 114.3, 112.4, 91.5, 72.7, 55.2, 36.0, 35.1, 17.6, 17.3, 10.9.

HR-MS (ESI-TOF) m/z: calcd. for $C_{15}H_{18}NO_2Cl_3SNa$ 404.0022; found: 404.0016 $[M+Na]^+$.

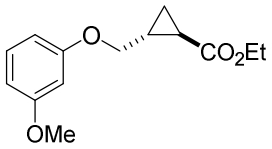
Trichloroacetimidate **1i** was synthesized in three steps according to Scheme 7 from building block **16**. Alkylation of 3-metoxyphenol with bromide **16** and subsequent reduction of ester **7i** gave alcohol **8i**, which was converted to corresponding trichloroacetimidate **1i** in the presence of DBU and CCl_3CN.



16 **7i** **1i**

Scheme 7

Ethyl (1*R,2*R**)-2-((3-methoxyphenoxy)methyl)cyclopropane-1-carboxylate (7i)**



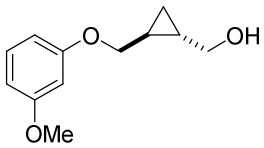
A solution of 3-metoxyphenol (177.86 mg, 1.433 mmol, 1.0 equiv) in DMF (3 mL) was cooled to 0 ºC and NaH (60.17 mg, 1.504, 1.05 equiv, 60% dispersion in mineral oil) was added in several portions. Reaction mixture was stirred at 0 ºC for 10 min, then solution of bromide **16** (296.67 mg, 1.433 mmol, 1.0 equiv) in DMF (2 mL) was added. After addition was complete, the mixture was allowed to warm to room temperature and stirred at room temperature overnight. The reaction was quenched with sat. NH_4Cl aq. (10 mL), extracted with diethyl ether (3 x 10 mL), washed with brine (3 ×10 mL), dried over $MgSO_4$, filtered. Concentration under reduced pressure gave crude product. After purification by column chromatography on silica gel (eluting with hexanes/EtOAc 6:1) 292 mg (81%) of the desired compound was obtained as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.16 (td, *J* = 8.1 and 0.5 Hz, 1H), 6.55 – 6.41 (m, 3H), 4.15 (qd, *J* = 7.1 and 1.0 Hz, 2H), 3.95 – 3.81 (m, 2H), 3.78 (s, 3H), 1.89 (dtd, *J* = 15.0, 6.3, 4.1 Hz, 1H), 1.74 – 1.65 (m, 1H), 1.34 – 1.22 (m, 4H), 0.99 (ddd, *J* = 8.4, 6.3 and 4.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.5, 160.8, 159.8, 129.8, 106.6, 101.1, 69.3, 60.6, 55.2, 20.9, 18.5, 14.2, 12.8.

Unstable under the conditions of HRMS.

((1*R,2*R**)-2-((3-Methoxyphenoxy)methyl)cyclopropyl)methanol (8i)**



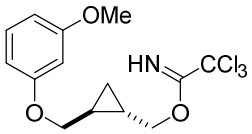
Prepared by analogy to compound **8a** from ester **7i** (282.8 mg, 1.13 mmol, 1.0 equiv), $LiAlH_4$ (94.34 mg, 2.49 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded 226 mg (96 %) of ((1*R**,2*R**)-2-((3-methoxyphenoxy)methyl)cyclopropyl) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.16 (t, *J* = 8.2 Hz, 1H), 6.54 – 6.42 (m, 3H), 3.86 (dd, *J* = 9.9 and 6.4 Hz, 1H), 3.77 (s, 4H), 3.56 (dd, *J* = 11.2 and 6.5 Hz, 1H), 3.48 (dd, *J* = 11.2 and 6.9 Hz, 1H), 2.02 (bs, 1H), 1.25 – 1.08 (m, 2H), 0.61 (tt, *J* = 8.7 and 5.1 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 160.7, 159.9, 129.8, 106.7, 106.3, 101.1, 71.2, 65.9, 55.2, 19.8, 16.1, 8.2.

HR-MS (ESI-TOF) m/z: calcd. for $C_{12}H_{15}O_2$ 191.1072; found: 191.1069 [M-H_2O+H]$^+$.

((1*S,2*S**)-2-((3-Methoxyphenoxy)methyl)cyclopropyl)methyl 2,2,2-trichloro-acetimidate (1i)**



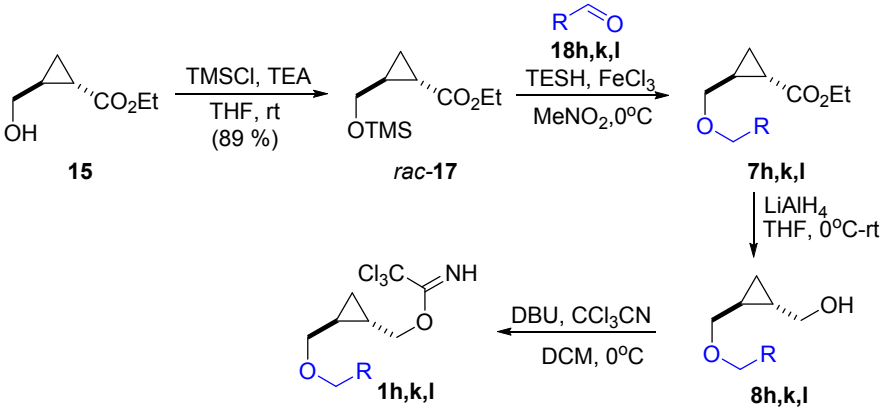
Prepared by analogy to compound **1a** from alcohol **8i** (116.2 mg, 0.56 mmol, 1.0 equiv), DBU (17 μL, 0.11 mmol, 0.2 equiv), trichloroacetonitrile (0.1 mL, 1.17 mmol, 2.1 equiv), and DCM (17 mL). Yield: 169.0 mg (86%).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.26 (bs, 1H), 7.16 (t, *J* = 8.2 Hz, 1H), 6.54 – 6.42 (m, 3H), 4.31 – 4.18 (m, 2H), 3.85 (ddd, *J* = 26.3, 16.1 and 6.2 Hz, 2H), 3.78 (s, 3H), 1.44 – 1.30 (m, 2H), 0.82 – 0.69 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.9, 160.8, 160.0, 129.8, 106.6, 106.4, 101.0, 91.6, 72.3, 70.8, 55.2, 16.5, 15.4, 8.8.

Unstable under the conditions of HRMS.

Trichloroacetimidates **1k,h,l** were synthesized in four steps according to Scheme 8 from alcohol **15**. Silylation of alcohol and subsequental reductive etherification of aldehydes **18h,k,l** gave ethers **7k,h,l**. Reduction of ester groups gave alcohols **8h,k,l**, which were transformed to corresponding trichloroacetimidates **1k,h,l** in the presence of DBU and CCl_3CN.



Scheme 8

Ethyl (1*S,2*S**)-2-(((trimethylsilyl)oxy)methyl)cyclopropane-1-carboxylate (*rac*-17)**

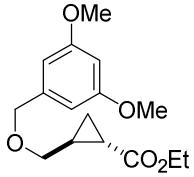
TMSCl (0.85 mL, 6.722 mmol, 1.2 equiv) was added dropwise to a cooled (0 °C) solution of alcohol **15** (807.6 mg, 5.602 mmol, 1.0 equiv) and Et_3N (0.94 mL, 6.722 mmol, 1.2 equiv) in THF (10 mL) and reaction mixture was stirred at room temperature overnight. The reaction solvent was evaporated to dryness. The crude mixture was diluted with dist. water (15 mL) and extracted with diethyl ether (2 × 15 mL). Combined organic phase was dried over $MgSO_4$ and filtered. Alcohol **17 (**1.1 g, 89%) was used for the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 4.09 (q, *J* = 7.0 Hz, 2H), 3.52 (qd, *J* = 11.0 and 5.7 Hz, 2H), 1.69 – 1.54 (m, 1H), 1.54 – 1.47 (m, 1H), 1.28 – 1.17 (m, 3H), 1.13 (dtd, *J* = 8.9, 4.5 and 1.9 Hz, 1H), 0.87 – 0.76 (m, 1H), 0.08 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.9, 63.6, 60.3, 23.9, 18.0, 14.2, 12.6, -0.5.

Unstable under the conditions of HRMS.

Ethyl (1*S,2*S**)-2-(((3,5-dimethoxybenzyl)oxy)methyl)cyclopropane-1-carboxylate (7h)**



Prepared according to literature procedure.[10,11] To a suspension of anhydrous $FeCl_3$ (19.47 mg, 0.12 mmol, 5 mol%) and aldehyde **18h** (399.02 mg, 2.401 mmol, 1.0 equiv) in nitromethane (4 mL) was added silyl ether *rac*-**17** (519.5 mg, 2.401 mmol, 1.0 equiv) and triethylsilane (0.46 mL, 2.905 mmol, 1.2 equiv) successively at 0 °C under atmosphere of argon. After 20 h of stirring, the reaction mixture was poured into sat. $NaHCO_3$ aq. solution and extracted with EtOAc. The combined extracts were washed with brine. After being dried over Na_2SO_4 the extracts were concentrated in vacuo.[12] After purification by column chromatography on silica gel (eluting with hexanes/EtOAc 4:1) of the desired compound **7h** (401 mg, 57 %) was obtained as a colorless liquid.

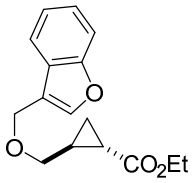
[10] Iwanami, K.; Yano, K.; Oriyama, T. *Synthesis* **2005**, 16, 2669.
[11] Chiba, J.; Muro, F.; Setoguchi, M.; Machinaga, N. *Chem. Pharm. Bull.* **2012**, 60(7), 882.
[12] In some of the cases, to remove unreacted aldehyde **18**, the crude reaction mixture were dissolved in MeOH and $NaBH_4$ (2.0 equiv) were added. After 5 min acetone (5 mL) was added and the reaction mixture were concentrated in vacuo and purificated by column chromatography on silica gel.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.47 – 6.46 (m, 2H), 6.38 – 6.36 (m, 1H), 4.44 (s, 2H), 4.10 (qdd, *J* = 7.1, 2.1, 0.8 Hz, 2H), 3.77 (s, 6H), 3.42 (dd, *J* = 10.4, 6.0 Hz, 1H), 3.32 (dd, *J* = 10.4, 6.7 Hz, 1H), 1.79 – 1.65 (m, 1H), 1.62 – 1.49 (m, 1H), 1.29 – 1.14 (m, 4H), 0.88 – 0.78 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.7, 160.9, 140.6, 105.3, 99.7, 72.5, 71.5, 60.5, 55.3, 21.6, 18.6, 14.2, 12.9.

HR-MS (ESI-TOF) m/z: calcd. for $C_{16}H_{22}O_5Na$ 317.1365; found: 317.1374 $[M+Na]^+$.

Ethyl (1*S,2*S**)-2-((benzofuran-3-ylmethoxy)methyl)cyclopropane-1-carboxylate (7k)**



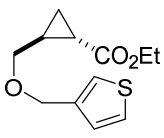
Prepared by analogy to compound **7h** from aldehyde **18k** (211.63 mg, 1.448 mmol, 1.0 equiv), silyl ether *rac*-**17** (313.3 mg, 1.448 mmol, 1.0 equiv), anhydrous $FeCl_3$ (11.7 mg, 0.072 mmol, 5mol%), triethylsilane (0.28 mL, 1.752 mmol, 1.2 equiv), and $MeNO_2$ (6 mL). Yield: 236 mg (59 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.65 (ddd, *J* = 7.5, 1.7, 0.8 Hz, 1H), 7.57 (s, 1H), 7.47 (dq, *J* = 8.1, 1.0 Hz, 1H), 7.34 – 7.20 (m, 2H), 4.65 (s, 2H), 4.10 (qd, *J* = 7.1, 1.6 Hz, 2H), 3.46 (dd, *J* = 10.3, 6.1 Hz, 1H), 3.37 (dd, *J* = 10.4, 6.7 Hz, 1H), 1.73 (dqd, *J* = 8.9, 6.3, 4.1 Hz, 1H), 1.54 (dt, *J* = 8.4, 4.5 Hz, 1H), 1.28 – 1.15 (m, 4H), 0.83 (ddd, *J* = 8.4, 6.3, 4.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.6, 1555, 142.8, 126.9, 124.5, 122.7, 120.1, 117.6, 111.4, 71.4, 63.0, 60.5, 21.4, 18.5, 14.2, 12.8.

Unstable under the conditions of HRMS.

Ethyl (1*S,2*S**)-2-((thiophen-3-ylmethoxy)methyl)cyclopropane-1-carboxylate (7l)**



Prepared by analogy to compound **7h** from aldehyde **18l** (0.4 mL, 4.565 mmol, 1.0 equiv), silyl ether *rac*-**17** (987.71 mg, 4.565 mmol, 1.0 equiv), anhydrous $FeCl_3$ (37.0 mg, 0.228 mmol, 5 mol%), triethylsilane (0.88 mL, 5.52 mmol, 1.2 equiv), and $MeNO_2$ (10 mL). Yield: 803.0 mg (73 %).

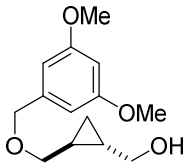
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.30 (ddd, *J* = 5.0, 2.9 and 0.5 Hz, 1H), 7.20 (ddq, *J* = 2.8, 1.4 and 0.8 Hz, 1H), 7.06 (ddd, *J* = 5.0, 1.3 and 0.5 Hz, 1H), 4.53 (s, 2H), 4.12 (qdd, *J* = 7.0, 2.0 and 0.6 Hz, 2H), 3.43 (dd, *J* = 10.4 and 6.1 Hz, 1H), 3.35

(dd, *J* = 10.4 and 6.6 Hz, 1H), 1.79 – 1.66 (m, 1H), 1.55 (dt, *J* = 8.4 and 4.3 Hz, 1H), 1.30 – 1.21 (m, 3H), 1.20 (dt, *J* = 9.1, 4.5 Hz, 1H), 0.84 (ddd, *J* = 8.4, 6.3, 4.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.7, 139.3, 127.2, 126.0, 122.7, 71.5, 67.9, 60.5, 21.5, 18.6, 14.2, 12.9.

Unstable under the conditions of HRMS.

((1*S,2*S**)-2-(((3,5-Dimethoxybenzyl)oxy)methyl)cyclopropyl)methanol (8h)**



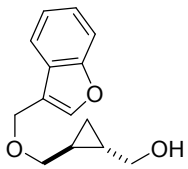
Prepared by analogy to compound **8a** from ester **7h** (346.9 mg, 1.179 mmol, 1.0 equiv), $LiAlH_4$ (98.41 mg, 2.593 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded ((1*S**,2*S**)-2-(((3,5-dimethoxybenzyl)oxy)methyl)cyclopropyl)methanol (**8h**) (283 mg, 95 %) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.51 – 6.48 (m, 2H), 6.37 (td, *J* = 2.4, 1.1 Hz, 1H), 4.46 (s, 2H), 3.78 (d, *J* = 1.4 Hz, 6H), 3.54 – 3.44 (m, 1H), 3.45 – 3.33 (m, 2H), 3.26 (ddd, *J* = 10.2, 6.9, 1.7 Hz, 1H), 2.14 (bs, 1H), 1.08 – 0.94 (m, 2H), 0.53 – 0.41 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 160.8, 140.8, 105.3, 99.6, 73.4, 72.5, 66.2, 55.3, 19.8, 16.7, 8.0.

HR-MS (ESI-TOF) m/z: calcd. for $C_{14}H_{20}O_4Na$ 275.1259; found: 275.1259 [M-H_2O+H]$^+$.

((1*S,2*S**)-2-((Benzofuran-3-ylmethoxy)methyl)cyclopropyl)methanol (8k)**



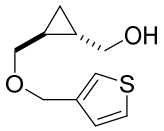
Prepared by analogy to compound **8a** from ester **7k** (228.7 mg, 0.834 mmol, 1.0 equiv), $LiAlH_4$ (69.61 mg, 1.834 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded ((1*S**,2*S**)-2-((benzofuran-3-ylmethoxy)methyl)cyclopropyl)methanol (**8k**) (175 mg, 90 %), as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.65 (ddd, *J* = 7.5, 1.6, 0.8 Hz, 1H), 7.57 (s, 1H), 7.49 – 7.43 (m, 1H), 7.33 – 7.19 (m, 2H), 4.65 (s, 2H), 3.43 (ddd, *J* = 18.0, 10.7, 6.2 Hz, 2H), 3.36 – 3.22 (m, 2H), 2.37 (bs, 1H), 1.06 – 0.86 (m, 1H), 0.49 – 0.38 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 155.5, 142.9, 127.0, 124.5, 122.7, 120.1, 117.7, 111.4, 73.3, 66.0, 62.9, 19.7, 16.6, 7.9.

Unstable under the conditions of HRMS.

((1*S,2*S**)-2-((Thiophen-3-ylmethoxy)methyl)cyclopropyl)methanol (8l)**



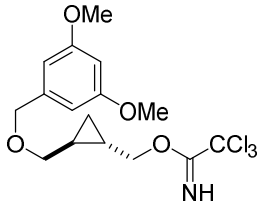
Prepared by analogy to compound **8a** from ester **7l** (256.9 mg, 1.069 mmol, 1.0 equiv), $LiAlH_4$ (89.26 mg, 2.352 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded ((1*S**,2*S**)-2-((thiophen-3-ylmethoxy)methyl)-cyclopropyl) methanol (**8l**) (186 mg, 88 %) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.28 (dd, *J* = 4.9 and 2.9 Hz, 1H), 7.19 (ddq, *J* = 3.0, 1.5 and 0.8 Hz, 1H), 7.06 (dd, *J* = 5.0 and 1.3 Hz, 1H), 4.52 (s, 1H), 3.48 (dd, *J* = 11.2 and 6.1 Hz, 1H), 3.45 – 3.29 (m, 2H), 3.24 (dd, *J* = 10.2 and 7.0 Hz, 1H), 2.37 (s, 1H), 1.05 – 0.92 (m, 1H), 0.51 – 0.40 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 139.4, 127.8, 125.9, 122.7, 73.4, 67.7, 66.1, 19.8, 16.7, 7.9.

HR-MS (ESI-TOF) m/z: calcd. for $C_{10}H_{13}OS$ 181.0687; found: 181.0685 $[M-H_2O+H]^+$.

((1*S,2*S**)-2-(((3,5-Dimethoxybenzyl)oxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1h)**



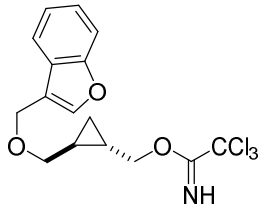
Prepared by analogy to compound **1a** from alcohol **8h** (197.4 mg, 0.782 mmol, 1.0 equiv), DBU (23 μL, 0.157 mmol, 0.2 equiv), trichloroacetonitrile (0.17 mL, 1.722 mmol, 2.2 equiv), and DCM (12 mL). Yield: 287 mg (93 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.24 (bs, 1H), 6.50 (dt, *J* = 2.3, 0.8 Hz, 2H), 6.37 (t, *J* = 2.4 Hz, 1H), 4.55 – 4.43 (m,2), 4.20 (dd, *J* = 6.9, 1.8 Hz, 2H), 3.78 (s, 6H), 3.38 (d, *J* = 6.6 Hz, 2H), 1.32 – 1.12 (m, 2H), 0.67 (dt, *J* = 8.4, 5.1 Hz, 1H), 0.59 (dt, *J* = 8.4, 5.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.8, 160.8, 140.8, 105.2, 99.6, 91.5, 72.9, 72.6, 72.2, 55.3, 16.9, 15.4, 8.5.

HR-MS (ESI-TOF) m/z: calcd. for $C_{16}H_{20}NO_4Cl_3Na$ 418.0356; found: 418.0351 $[M+Na]^+$.

((1*S,2*S**)-2-((Benzofuran-3-ylmethoxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1k)**



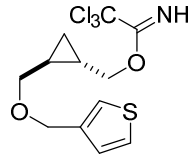
Prepared by analogy to compound **1a** from alcohol **8k** (161.3 mg, 0.694 mmol, 1.0 equiv), DBU (21 μL, 0.139 mmol, 0.2 equiv), trichloroacetonitrile (0.15 mL, 1.528 mmol, 2.2 equiv), and DCM (15 mL). Yield: 249 mg (95 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.23 (bs, 1H), 7.65 (ddt, *J* = 7.5, 1.6, 0.8 Hz, 1H), 7.58 (s, 1H), 7.49 – 7.43 (m, 1H), 7.34 – 7.18 (m, 2H), 4.75 – 4.63 (m, 2H), 4.18 (qd, *J* = 11.3, 6.9 Hz, 2H), 3.41 (d, *J* = 6.5 Hz, 2H), 1.29 – 1.11 (m, 2H), 0.65 (dt, *J* = 8.5, 5.1 Hz, 1H), 0.57 (dt, *J* = 8.4, 5.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.9, 155.5, 142.8, 127.1, 124.5, 122.7, 120.2, 117.8, 111.4, 91.5, 72.8, 72.6, 62.8, 16.9, 15.5, 8.5.

HR-MS (ESI-TOF) m/z: calcd. for $C_{16}H_{16}NO_3Cl_3Na$ 398.0093; found: 398.0098 $[M+Na]^+$.

((1*S,2*S**)-2-((Thiophen-3-ylmethoxy)methyl)cyclopropyl)methyl 2,2,2-trichloro-acetimidate (1l)**



Prepared by analogy to compound **1a** from alcohol **8l** (173.99 mg, 0.877 mmol, 1.0 equiv), DBU (26 μL, 0.175 mmol, 0.2 equiv), trichloroacetonitrile (0.19 mL, 1.843 mmol, 2.2 equiv), and DCM (10 mL). Yield: 276 mg (92 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.24 (bs, 1H), 7.29 (dd, *J* = 5.0, 2.9 Hz, 1H), 7.20 (ddd, *J* = 3.0, 1.3, 0.8 Hz, 1H), 7.08 – 7.06 (m, 1H), 4.62 – 4.50 (m, 2H), 4.27 – 4.12 (m, 2H), 3.38 (d, *J* = 6.7 Hz, 2H), 1.30 – 1.11 (m, 2H), 0.66 (dt, *J* = 8.6, 5.1 Hz, 1H), 0.59 (dt, *J* = 8.4, 5.2 Hz, 1H).

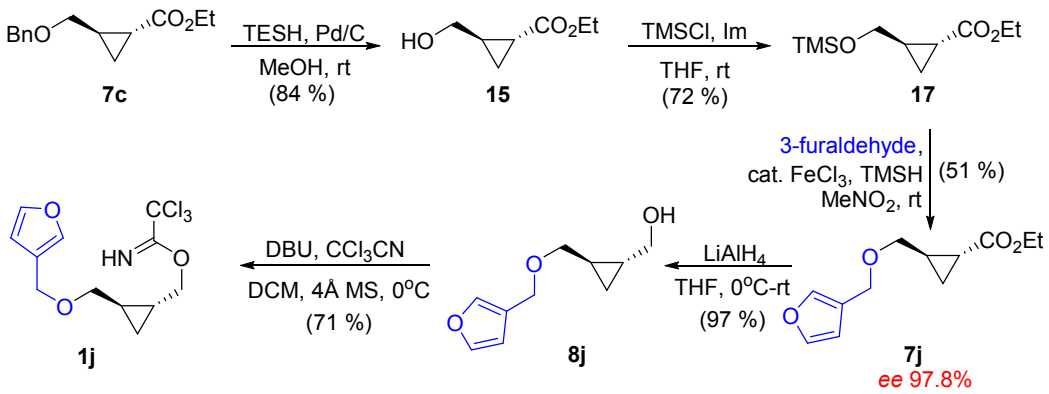
^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.9, 139.6, 127.3, 125.9, 122.6, 91.5, 72.9, 72.6, 67.56, 16.9, 15.5, 8.5.

HR-MS (ESI-TOF) m/z: calcd. for $C_{12}H_{14}NO_2Cl_3SNa$ 363.9709; found: 363.9711 $[M+Na]^+$.

Enantioenriched trichloroacetimidate **1j** (*ee* 97.8 %) was synthesized in five steps according to Scheme 9 from previously obtained benzyl ether **7c**. Removal of protecting group and subsequental silylation of alcohol gave silyl ether **17**. Reductive

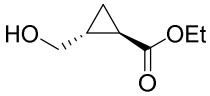
etherification of 3-furaldehyde gave ether **7j**, which further was reduced and transformed to corresponding trichloroacetimidate **1j**.

Enantiomeric excess of ester **7j** (97.8 %) was determined by SFC analysis on chiral phase (Chiralpak IC-2; 4.6x250 mm; 10 % IPA + 90 % Hex; F=1 mL/min; T=25 °C; t_r (major) 8.7 min, t_r (minor) 9.3 min).



Scheme 9

Ethyl (1*R*,2*R*)-2-(hydroxymethyl)cyclopropane-1-carboxylate (15)



To suspension of benzylether **7c** (408.3 mg, 1.743 mmol, 1.0 equiv) and Pd/C (40.8 mg, 10 wt%) in MeOH (5 mL) triethylsilane (2.8 mL, 17.426 mmol, 10 equiv) was added. The mixture was stirred at room temperature for 6 h, then filtered through a short pad of celite and concentrated under reduced pressure. Purification by column chromatography on silica gel (eluent: EtOAc) afforded ethyl (1*R*,2*R*)-2-(hydroxymethyl)cyclopropane-1-carboxylate **(15)** (210 mg, 84 %) as a colorless oil. This compound is known in the literature.[13]

^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 4.20 – 4.05 (m, 2H), 3.63 (dd, *J* = 11.5 and 6.1 Hz, 1H), 3.49 (dd, *J* = 11.5 and 6.8 Hz, 1H), 1.80 – 1.64 (m, 1H), 1.57 (dt, *J* = 8.8 and 4.5 Hz, 1H), 1.41 (bs, 1H), 1.34 – 1.16 (m, 4H), 0.86 (ddd, *J* = 8.5, 6.3 and 4.3 Hz, 1H).

$[\alpha]_D^{20}$ = -69.5 (c = 1.0, $CHCl_3$).

Ethyl (1*R*,2*R*)-2-(((trimethylsilyl)oxy)methyl)cyclopropane-1-carboxylate (17)

Prepared by analogy to *rac*-**17** from enantioenriched alcohol **15** (168 mg, 1.165 mmol, 1.0 equiv), TMSCl (0.18 mL, 1.398 mmol,

[13] Jeffrey, J. L.; Terrett, J. A.; MacMillan, D. W. *Science* **2015**, 349 (*6255*), 1532.

1.2 equiv), Et_3N (0.2 mL, 1.398 mmol, 1.2 equiv) and THF (6 mL). Yield: 215 mg (72 %)

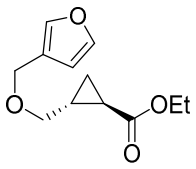
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 4.09 (q, *J* = 7.0 Hz, 2H), 3.52 (qd, *J* = 11.0 and 5.7 Hz, 2H), 1.69 – 1.54 (m, 1H), 1.54 – 1.47 (m, 1H), 1.28 – 1.17 (m, 3H), 1.13 (dtd, *J* = 8.9, 4.5 and 1.9 Hz, 1H), 0.87 – 0.76 (m, 1H), 0.08 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.9, 63.6, 60.3, 23.9, 18.0, 14.2, 12.6, -0.5.

Unstable under the conditions of HRMS.

$[\alpha]_D^{20}$ = -59.5 (c = 1.0, $CHCl_3$).

Ethyl (1*R*,2*R*)-2-((furan-3-ylmethoxy)methyl)cyclopropane-1-carboxylate (7j)



Prepared by analogy to compound **7h** from aldehyde 3-furaldehyde (97 μL, 1.159 mmol, 1.2 equiv), enantioenriched silyl ether **17** (209.0 mg, 0.966 mmol, 1.0 equiv), anhydrous $FeCl_3$ (7.8 mg, 0.048 mmol, 5mol%), triethylsilane (0.19 mL, 1.169 mmol, 1.21 equiv), and $MeNO_2$ (10 mL). Yield: 110 mg (51 %).

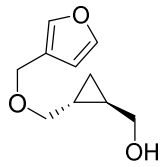
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.40 – 7.39 (m, 2H), 6.45 – 6.36 (m, 1H), 4.38 (s, 2H), 4.20 – 4.03 (m, 2H), 3.41 (dd, *J* = 10.4 and 6.1 Hz, 1H), 3.33 (dd, *J* = 10.4 and 6.6 Hz, 1H), 1.78 – 1.64 (m, 1H), 1.59 – 1.49 (m, 1H), 1.25 (td, *J* = 7.1 and 0.4 Hz, 3H), 1.25 – 1.15 (m, 1H), 0.83 (ddd, *J* = 8.3, 6.3 and 4.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.7, 143.4, 140.6, 122.1, 110.3, 71.3, 63.8, 60.5, 21.5, 18.6, 14.2, 12.9.

HR-MS (ESI-TOF) m/z: calcd. for $C_{12}H_{16}O_4Na$ 247.0946; found: 247.0945 $[M+Na]^+$.

$[\alpha]_D^{20}$ = -40.3 (c = 1.0, $CHCl_3$).

((1*R*,2*R*)-2-((Furan-3-ylmethoxy)methyl)cyclopropyl)methanol (8j)



Prepared by analogy to compound **8a** from enantioenriched ester **7j** (107.7 mg, 0.480 mmol, 1.0 equiv), $LiAlH_4$ (40.1 mg, 1.057 mmol, 2.2 equiv), and THF (20 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded 85.1 mg (97 %) of ((1*R*,2*R*)-2-((furan-3-ylmethoxy)methyl)cyclopropyl) as a colorless oil.

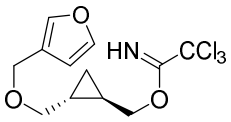
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.42 – 7.34 (m, 2H), 6.43 – 6.36 (m, 1H), 4.38 (s, 2H), 3.48 (dd, *J* = 11.2 and 6.3 Hz, 1H), 3.37 (ddd, *J* = 8.6, 6.2 and 3.0 Hz, 2H), 3.23 (ddt, *J* = 10.2, 6.9 and 2.0 Hz, 1H), 2.39 (bs, 1H), 1.05 – 0.90 (m, 2H), 0.52 – 0.39 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 143.3, 140.6, 122.2, 110.3, 73.2, 66.1, 63.7, 19.7, 16.6, 7.9.

HR-MS (ESI-TOF) m/z: calcd. for $C_{10}H_{14}O_3Na$ 205.0841; found: 205.0842 $[M+Na]^+$.

$[\alpha]_D^{20}$ = -38.7 (c = 1.0, $CHCl_3$).

((1*R*,2*R*)-2-((Furan-3-ylmethoxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1j)



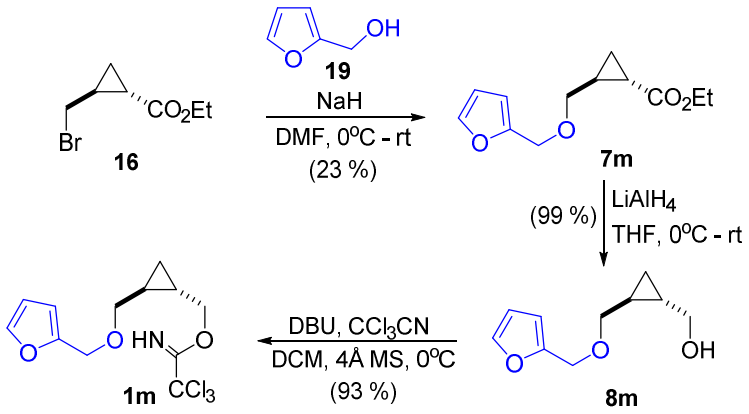
Prepared by analogy to compound **1a** from enantioenriched alcohol **8j** (80.8 mg, 0.575 mmol, 1.0 equiv), DBU (17 μL, 0.115 mmol, 0.2 equiv), trichloroacetonitrile (0.12 mL, 1.207 mmol, 2.1 equiv), and DCM (12 mL). Yield: 133 mg (71 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.24 (bs, 1H), 7.43 – 7.35 (m, 2H), 6.41 (dq, *J* = 1.3 and 0.5 Hz, 1H), 4.48 – 4.35 (m, 2H), 4.26 – 4.12 (m, 2H), 3.36 (d, *J* = 6.7 Hz, 2H), 1.29 – 1.10 (m, 2H), 0.66 (dt, *J* = 8.5, 5.1 Hz and 1H), 0.58 (dt, *J* = 8.4, 5.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.9, 143.3, 140.5, 122.3, 110.3, 91.5, 72.7, 72.6, 63.5, 16.9, 15.5, 8.5.

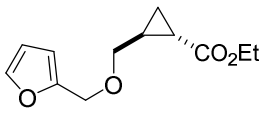
Unstable under the conditions of HRMS.

Trichloroacetimidate **1m** was synthesized in three steps according to Scheme 10 from building block **16**. Alkylation of furan-2-ylmethanol (**19**) with bromide **16** and subsequent reduction of ester group gave alcohol **8m**, which was converted to corresponding trichloroacetimidate **1m** in the presence of DBU and CCl_3CN.



Scheme 10

Ethyl (1*S,2*S**)-2-((furan-2-ylmethoxy)methyl)cyclopropane-1-carboxylate (7m)**



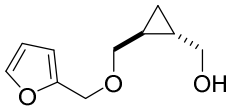
Prepared by analogy to compound **7i** from furfuryl alcohol (**19**) (158.0 mg, 1.610 mmol, 1.0 equiv), NaH (67.6 mg, 1.691 mmol, 1.05 equiv, 60% dispersion in mineral oil), bromide **16** (504.5.5 mg, 1.691 mmol, 1.05 equiv), and DMF (5 mL). Yield: 85 mg (23%).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.40 (dt, *J* = 1.5, 0.8 Hz, 1H), 6.34 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.31 (dt, *J* = 3.2, 0.7 Hz, 1H), 4.46 (s, 2H), 4.17 – 4.06 (m, 2H), 3.46 – 3.32 (m, 2H), 1.76 – 1.65 (m, 1H), 1.58 – 1.51 (m, 1H), 1.25 (td, *J* = 7.2, 0.7 Hz, 3H), 1.23 – 1.17 (m, 1H), 0.84 (ddd, *J* = 8.4, 6.3, 4.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 173.7, 151.6, 142.8, 110.2, 109.3, 71.5, 64.5, 60.5, 21.4, 18.6, 14.2, 12.9.

HR-MS (ESI-TOF) m/z: calcd. for $C_{12}H_{16}O_4Na$ 247.0946; found: 247.0947 $[M+Na]^+$.

((1*S,2*S**)-2-((Furan-2-ylmethoxy)methyl)cyclopropyl)methanol (8m)**



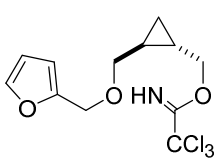
Prepared by analogy to compound **8a** from ester **7m** (78.0 mg, 0.348 mmol, 1.0 equiv), $LiAlH_4$ (27.06 mg, 0.713 mmol, 2.05 equiv), and THF (10 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded of ((1*S**,2*S**)-2-((furan-2-ylmethoxy)methyl)cyclopropyl)methanol (**8m**) (62.5 mg, 99 %) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.40 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.37 – 6.27 (m, 2H), 4.47 (s, 2H), 3.55 – 3.35 (m, 3H), 3.29 (dd, *J* = 10.2, 7.0 Hz, 1H), 1.68 (bs, 1H), 1.09 – 0.93 (m,1), 0.55 – 0.43 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 149.3, 140.1, 107.6, 106.5, 74.1, 63.7, 61.8, 17.2, 14.0, 5.5.

HR-MS (ESI-TOF) m/z: calcd. for $C_{10}H_{13}O_2$ 165.0916; found: 165.0913 $[M-H_2O+H]^+$.

((1*S,2*S**)-2-((Furan-2-ylmethoxy)methyl)cyclopropyl)methyl 2,2,2-trichloro-acetimidate (1m)**



Prepared by analogy to compound **1a** from alcohol **8m** (62.1 mg, 0.341 mmol, 1.0 equiv), DBU (10 μL, 0.068 mmol, 0.2 equiv),

trichloroacetonitrile (72 μL, 0.716 mmol, 2.1 equiv), and DCM (5 mL). Yield: 103.1 mg (93 %).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.24 (bs, 1H), 7.40 (dd, *J* = 1.8, 0.9 Hz, 1H), 6.33 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.32 – 6.29 (m, 1H), 4.54 – 4.44 (m, 2H), 4.19 (dd, *J* = 6.9, 0.9 Hz, 2H), 3.39 (dd, *J* = 6.7, 2.2 Hz, 2H), 1.29 – 1.12 (m, 2H), 0.67 (dt, *J* = 8.5, 5.1 Hz, 2H), 0.59 (dt, *J* = 8.5, 5.2 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.9, 151.8, 142.7, 110.2, 109.1, 91.5, 72.9, 72.5, 64.1, 16.7, 15.5, 8.6.

Unstable under the conditions of HRMS.

3. Optimization of conditions for the cyclopropylmethylation reaction

Several Lewis acids and solvents have been screened using imidate **1a** as starting material (see Table S1). These studies revealed $B(C_6F_5)_3$ as optimal catalyst and CH_3NO_2 as reaction media in room temperature to achieve the best yield of product **2a**. The configuration of the substrate *E*-**1a** or *Z*-**1a** had practically no impact on the product **2a** yield (table S1, entry 1-3). Since *E*-configuration disubstituted cyclopropanes were easier to access, the substrate scope investigation was performed with *E*-configured substrates **1**.

Table S1. LA promoted rearrangement of 1a

Z- or *E*-**1a** **2a**

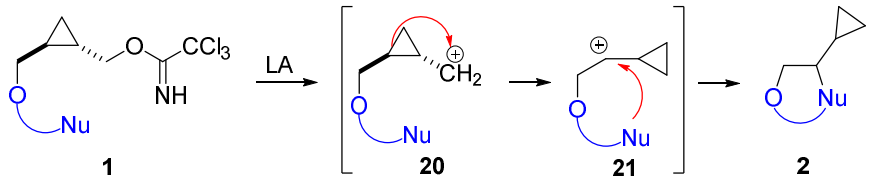
entry	starting material	LA (10 mol%)	solvent	time	NMR yield of 2a[a], %
1	*Z*-**1a**	$Cu(OTf)_2$	DCM	1d	40
2	*Z*-**1a**	$BF_3{\cdot}OEt_2$		10 min	40
3	*E*-**1a**	$Cu(OTf)_2$		4h	40
4	*E*-**1a**	$(CuOTf)_2{\cdot}C_6H_6$	DCM	7d	60
5		$(C_6F_5)_3B$		2h	50
6		$(C_6F_5)_3B$		2h	65 (58)[b]
7		$Fe(OTf)_3$		4h	55
8		$(C_6F_5)_3B$	CH_3NO_2	2h	80 (80)[b]
9			EtOAc	2h	60
10			MeCN	2h	30
11			THF	7d	*no reaction*
12			Toluene	2h	60
13			AcOH	7d	*slow decomposition of starting material*

[a] using 1,4-*b*is(trichloromethyl)benzene as internal standard; [b] isolated yield.

4. Cyclopropylmethylation reaction and characterization of the products

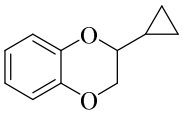
General procedure for rearrangement/cyclization

Molecular sieves (4 Å) and Lewis acid catalyst (0.05 mmol, 10 mol%) were added to a stirred solution of trichloroacetimidate **1** (0.50 mmol) in nitromethane (5 mL) at rt. After reaction was complete (TLC control in the first minute of the reaction), TEA (50 mol%) was added to the reaction mixture, then reaction solvent was removed under reduced pressure. The residue was purified by chromatography on a short silica gel column eluting with a mixture of light petroleum ether and ethyl acetate to afford desired products **2**.



Scheme 11

2-Cyclopropyl-2,3-dihydrobenzo[b][1,4]dioxine (2a)



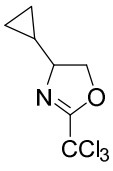
Prepared according to general procedure: from trichloroacetimidate **1a** (72.0 mg, 0.213 mmol), $(C_6F_5)_3B$ (10.9 mg, 0.021 mmol, 10 mol%) and $MeNO_2$ (4 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 10:1) afforded 2-cyclopropyl-2,3-dihydro-benzo[b][1,4]dioxine (**2a**) (30 mg, 80 %) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.94 – 6.77 (m, 4H), 4.33 (ddd, *J* = 11.3, 2.3, 0.7 Hz, 1H), 4.01 (ddd, *J* = 11.2, 8.2, 0.7 Hz, 1H), 3.47 – 3.37 (m, 1H), 1.08 – 0.94 (m, 1H), 0.78 – 0.66 (m, 1H), 0.69 – 0.52 (m, 2H), 0.45 – 0.34 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 143.5, 143.2, 121.4, 121.1, 117.3, 116.9, 77.5, 67.9, 11.3, 2.9, 1.7.

Unstable under the conditions of HRMS.

4-Cyclopropyl-2-(trichloromethyl)-4,5-dihydrooxazole (2b)



Prepared according to general procedure: from trichloroacetimidate **1b** (330.0 mg, 0.844 mmol), $BF_3{\cdot}OEt_2$ (11 μL, 0.084 mmol, 10 mol%) and DCM (10 mL). Purification by column chromatography on silica gel

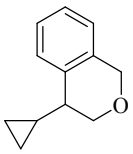
(eluent hexanes/EtOAc 8:1) afforded 4-cyclopropyl-2-(trichloromethyl)-4,5-dihydrooxazole (**2b**) (165 mg, 85 %) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 4.68 (dd, *J* = 9.6, 8.4 Hz, 1H), 4.36 (t, *J* = 8.3 Hz, 1H), 3.87 (dt, *J* = 9.6, 8.0 Hz, 1H), 0.98 (qt, *J* = 8.1, 4.9 Hz, 1H), 0.63 (dddd, *J* = 9.0, 8.1, 5.7, 4.5 Hz, 1H), 0.59 – 0.51 (m, 1H), 0.50 – 0.39 (m, 1H), 0.38 – 0.27 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.7, 86.7, 76.0, 70.8, 15.1, 2.9, 2.1.

Unstable under the conditions of HRMS.

4-Cyclopropylisochromane (2c)

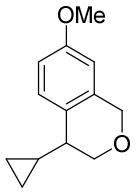


Prepared according to general procedure: From trichloroacetimidate **1c** (34.1 mg, 0.101 mmol), $(C_6F_5)_3B$ (5.19 mg, 0.010 mmol, 10 mol%) and $MeNO_2$ (1 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 10:1) afforded 4-cyclopropylisochromane (**2c**) (5.6 mg, 32 %) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.32 – 7.12 (m, 5H), 4.47 (d, *J* = 9.0 Hz, 2H), 3.53 (d, *J* = 5.8 Hz, 2H), 3.11 (ddt, *J* = 10.3, 8.2, 5.1 Hz, 1H), 0.85 (qt, *J* = 8.2, 5.2 Hz, 1H), 0.55 – 0.23 (m, 3H), 0.22 – 0.08 (m, 1H).

HR-MS (ESI-TOF) m/z: calcd. for $C_{12}H_{15}O$ 175.1123; found: 175.1122 $[M+H]^+$.

4-Cyclopropyl-7-methoxyisochromane (2d)



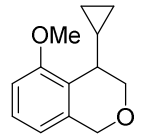
Prepared according to general procedure: From trichloroacetimidate **1d** (155.3 mg, 0.424 mmol), $(C_6F_5)_3B$ (21.68 mg, 0.042 mmol, 10 mol%) and $MeNO_2$ (4.3 mL). Two regioisomers **2d** and **2d'** were obtained and their separation was done by column chromatography on silica gel (eluent hexanes/EtOAc 4:1). After purification isomer **2d** (61.2 mg, 71%) and isomer **2d'** (14.5 mg, 17%) were both obtained as colorless oils.

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.41 (d, *J* = 8.5 Hz, 1H), 6.78 (ddt, *J* = 8.5, 2.7 and 0.8 Hz, 1H), 6.52 (d, *J* = 2.7 Hz, 1H), 4.75 (dd, *J* = 24.5 and 15.1 Hz, 1H), 3.98 (dd, *J* = 11.1 and 4.4 Hz, 1H), 3.84 (dd, *J* = 11.2 and 6.0 Hz, 1H), 3.79 (s, 3H), 1.94 (dt, *J* = 10.4 and 5.2 Hz, 1H), 0.98 – 0.82 (m, 1H), 0.75 – 0.66 (m, 1H), 0.56 – 0.43 (m, 2H), 0.30 – 0.18 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 157.9, 135.4, 129.6, 128.9, 112.7, 108.6, 70.5, 68.4, 55.2, 41.7, 15.1, 5.2, 2.5.

HR-MS (ESI-TOF) m/z: calcd. for $C_{13}H_{17}O_2$ 205.1229; found: 205.1226 $[M+H]^+$.

4-Cyclopropyl-5-methoxyisochromane (2d')

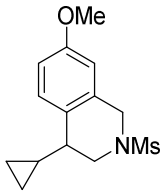


Isolated as a minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.15 (t, *J* = 7.9 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.64 – 6.56 (m, 1H), 4.87 (d, *J* = 15.4 Hz, 1H), 4.74 (dq, *J* = 15.2 and 0.9 Hz, 1H), 4.15 (dd, *J* = 10.9 and 1.5 Hz, 1H), 3.82 (s, 3H), 3.72 (dd, *J* = 10.8 and 2.8 Hz, 1H), 2.34 – 2.25 (m, 1H), 1.14 (dtt, *J* = 8.8, 8.1 and 5.0 Hz, 1H), 0.74 – 0.67 (m, 1H), 0.57 – 0.39 (m, 2H), 0.25 – 0.14 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 157.3, 135.6, 126.9, 126.0, 116.4, 108.0, 70.0, 67.6, 55.1, 36.4, 15.8, 5.2, 3.1.

Unstable under the conditions of HRMS.

4-Cyclopropyl-7-methoxy-2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinoline (2e)



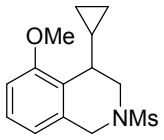
Prepared according to general procedure: From trichloroacetimidate **1e** (215.58 mg, 0.486 mmol), $(C_6F_5)_3B$ (24.87 mg, 0.049 mmol, 10 mol%) and $MeNO_2$ (5 mL). Two regioisomers **2e** and **2e'** were obtained and their separation was done by column chromatography on silica gel (eluent hexanes/EtOAc 2:1). After purification isomer **2d** (84 mg, 61 %) and isomer **2d'** (29 mg, 21 %) were both obtained as colorless oils.

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.48 – 7.38 (m, 1H), 6.78 (ddt, *J* = 8.6, 2.8, 0.7 Hz, 1H), 6.59 (d, *J* = 2.7 Hz, 1H), 4.47 – 4.30 (m, 2H), 3.76 (s, 3H), 3.60 – 3.50 (m, 1H), 3.36 (ddd, *J* = 11.9, 6.8, 2.2 Hz, 1H), 2.82 (s, 3H), 2.12 – 2.02 (m, 1H), 0.96 – 0.81 (m, 1H), 0.77 – 0.64 (m, 1H), 0.60 – 0.42 (m, 2H), 0.33 – 0.21 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 158.3, 132.4, 129.5, 129.0, 113.3, 110.7, 55.3, 48.9, 47.6, 42.7, 35.3, 15.6, 5.7, 2.8.

HR-MS (ESI-TOF) m/z: calcd. for $C_{14}H_{20}NO_3S$ 282.1164; found: 282.1164 $[M+H]^+$.

4-Cyclopropyl-5-methoxy-2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinoline (2e')



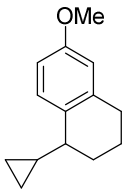
Isolated as a minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.18 (t, *J* = 8.0 Hz, 1H), 6.74 (dd, *J* = 13.3, 7.9 Hz, 2H), 4.71 (d, *J* = 15.4 Hz, 1H), 4.21 (d, *J* = 15.4 Hz, 1H), 3.99 (ddd, *J* = 11.5, 2.1, 1.1 Hz, 1H), 3.81 (s, 3H), 3.02 (dd, *J* = 11.5, 3.1 Hz, 1H), 2.88 (s, 3H), 2.63 (dt, *J* = 8.9, 2.3 Hz, 1H), 1.05 (qt, *J* = 8.8, 5.0 Hz, 1H), 0.69 (dddd, *J* = 9.3, 5.1, 3.1,

1.6 Hz, 1H), 0.49 (ddd, *J* = 8.0, 3.0, 1.6 Hz, 2H), 0.21 (dddd, *J* = 9.6, 4.9, 3.1, 1.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 157.2, 132.4, 127.4, 126.1, 118.5, 108.5, 55.2, 48.6, 46.8, 37.2, 35.2, 15.9, 5.2, 3.4.

HR-MS (ESI-TOF) m/z: calcd. for $C_{14}H_{20}NO_3S$ 282.1164; found: 282.1166 $[M+H]^+$.

1-Cyclopropyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (2f)



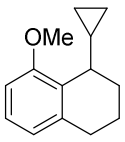
Prepared according to general procedure: from trichloroacetimidate **1f** (187.0 mg, 0.513 mmol), $(C_6F_5)_3B$ (26.25 mg, 0.051 mmol, 10 mol%) and $MeNO_2$ (5 mL). Two regioisomers **2f** and **2f'** were obtained which were separated by column chromatography on silica gel (eluent hexanes/EtOAc 2:1). After purification isomer **2f** (35 mg, 34%) and isomer **2f'** (23 mg, 22%) were both obtained as colorless oils.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.47 (d, *J* = 8.6 Hz, 1H), 6.72 (ddd, *J* = 8.5, 2.8, 0.7 Hz, 1H), 6.65 – 6.58 (m, 1H), 3.79 (d, *J* = 0.8 Hz, 3H), 2.85 – 2.67 (m, 2H), 2.00 – 1.89 (m, 2H), 1.91 – 1.81 (m, 1H), 1.77 – 1.63 (m, 2H), 0.92 – 0.78 (m, 1H), 0.76 – 0.63 (m, 1H), 0.53 – 0.40 (m, 2H), 0.26 – 0.13 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 157.5, 138.1, 133.2, 128.9, 113.4, 111.6, 55.2, 42.7, 30.1, 30.0, 21.2, 18.0, 6.4, 2.6.

No ionization in HRMS.

1-Cyclopropyl-8-methoxy-1,2,3,4-tetrahydronaphthalene (2f')

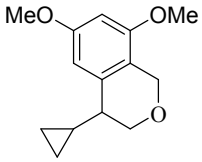


Isolated as a minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.08 (t, *J* = 7.9 Hz, 1H), 6.70 (dd, *J* = 12.2, 7.9 Hz, 2H), 3.79 (s, 3H), 2.92 – 2.68 (m, 2H), 2.57 (ddd, *J* = 8.1, 5.1, 2.3 Hz, 1H), 2.15 – 1.91 (m, 2H), 1.77 (ddt, *J* = 13.0, 7.3, 3.7 Hz, 1H), 1.67 (tq, *J* = 13.2, 5.0, 4.2 Hz, 1H), 0.91 – 0.81 (m, 1H), 0.67 – 0.56 (m, 1H), 0.52 – 0.40 (m, 1H), 0.43 – 0.30 (m, 1H), 0.18 – 0.07 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 157.5, 138.1, 129.4, 126.0, 121.5, 107.2, 54.9, 35.1, 29.0, 28.7, 18.3, 16.9, 5.9, 2.8.

No ionization in HRMS.

4-Cyclopropyl-6,8-dimethoxyisochromane (2h)



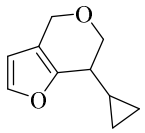
Prepared according to general procedure: From trichloroacetimidate **1h** (99.0 mg, 0.250 mmol), $(C_6F_5)_3B$ (9.03 mg, 0.025 mmol, 10 mol%) and $MeNO_2$ (2.5 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 8:1) afforded 4-cyclopropyl-6,8-dimethoxyisochromane (**2h**) (54 mg, 92%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.34 (d, *J* = 2.5 Hz, 1H), 6.12 (d, *J* = 2.4 Hz, 1H), 4.82 (d, *J* = 15.3 Hz, 1H), 4.70 (d, *J* = 15.2 Hz, 1H), 4.14 (dd, *J* = 10.8, 1.5 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.70 (dd, *J* = 10.8, 2.9 Hz, 1H), 2.27 – 2.16 (m, 1H), 1.11 (qt, *J* = 8.2, 5.0 Hz, 1H), 0.67 (td, *J* = 9.4, 5.4 Hz, 1H), 0.56 – 0.37 (m, 2H), 0.22 – 0.11 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 158.9, 158.4, 136.1, 118.5, 99.3, 96.7, 70.3, 67.9, 55.3, 55.1, 36.1, 15.9, 4.9, 3.0.

HR-MS (ESI-TOF) m/z: calcd. for $C_{14}H_{19}O_3$ 235.1334; found: 235.1335 $[M+H]^+$.

7-Cyclopropyl-6,7-dihydro-4*H*-furo[3,2-c]pyran (2j)



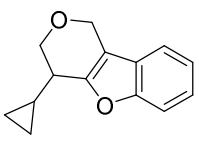
Prepared according to general procedure: from racemic and enantioenriched trichloroacetimidate **1j** (200.0 mg, 0.612 mmol), $(C_6F_5)_3B$ (31.4 mg, 0.061 mmol, 10 mol%) and $MeNO_2$ (6 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 15:1) afforded 7-cyclopropyl-6,7-dihydro-4*H*-furo[3,2-c]pyran (**2j**) (76 mg, 76 %) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.31 (dd, *J* = 2.0, 0.8 Hz, 1H), 6.20 (d, *J* = 2.0 Hz, 1H), 4.66 – 4.52 (m, 2H), 3.97 (dd, *J* = 11.2, 4.7 Hz, 1H), 3.80 (dd, *J* = 11.2, 5.5 Hz, 1H), 2.20 – 2.11 (m, 1H), 0.92 – 0.81 (m, 1H), 0.67 – 0.55 (m, 1H), 0.53 – 0.39 (m, 2H), 0.28 – 0.17 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 150.7, 141.3, 115.6, 106.9, 70.2, 64.5, 40.4, 12.2, 3.4, 2.4.

Unstable under the conditions of HRMS.

4-Cyclopropyl-3,4-dihydro-1*H*-pyrano[4,3-b]benzofuran (2k)



Prepared according to general procedure: from trichloroacetimidate **1k** (64.3 mg, 0.171 mmol), $(C_6F_5)_3B$ (8.74 mg, 0.017 mmol, 10

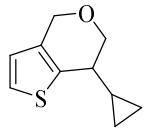
mol%) and $MeNO_2$ (1.7 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 10:1) afforded 4-cyclopropyl-3,4-dihydro-1*H*-pyrano[4,3-b]benzofuran **(2k)** (33.4 mg, 91 %) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.48 (dq, *J* = 8.0, 0.8 Hz, 1H), 7.35 (ddd, *J* = 7.4, 1.7, 0.8 Hz, 1H), 7.29 – 7.15 (m, 2H), 4.89 – 4.73 (m, 2H), 4.06 (dd, *J* = 11.2, 4.6 Hz, 1H), 3.92 (dd, *J* = 11.2, 5.2 Hz, 1H), 2.28 (ddd, *J* = 7.1, 6.0, 4.0 Hz, 1H), 1.02 – 0.89 (m, 1H), 0.74 – 0.62 (m, 1H), 0.63 – 0.46 (m, 2H), 0.34 – 0.23 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 154.4, 153.8, 125.8, 123.6, 122.5, 118.5, 111.7, 111.3, 70.1, 63.6, 40.5, 12.2, 3.8, 2.7.

Unstable under the conditions of HRMS.

7-Cyclopropyl-6,7-dihydro-4*H*-thieno[3,2-c]pyran (2l)



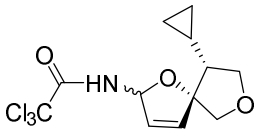
Prepared according to general procedure: from trichloroacetimidate **1l** (49.31 mg, 0.144 mmol), $(C_6F_5)_3B$ (5.2 mg, 0.014 mmol, 10 mol%) and $MeNO_2$ (1.4 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 10:1) afforded 7-cyclopropyl-6,7-dihydro-4*H*-thieno[3,2-c]pyran benzofuran **(2l)** (25.5 mg, 98 %) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.13 (d, *J* = 5.2 Hz, 1H), 6.72 (d, *J* = 5.2 Hz, 1H), 4.71 (d, *J* = 2.2 Hz, 2H), 4.08 (dd, *J* = 11.2, 4.8 Hz, 1H), 3.68 (dd, *J* = 10.8, 7.4 Hz, 1H), 2.13 (tdd, *J* = 9.3, 3.9, 2.3 Hz, 1H), 0.87 (dtt, *J* = 10.0, 8.0, 5.0 Hz, 1H), 0.71 – 0.59 (m, 1H), 0.60 – 0.48 (m, 1H), 0.42 (dq, *J* = 9.2, 4.9 Hz, 1H), 0.30 (td, *J* = 9.3, 4.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 137.9, 133.5, 123.2, 123.2, 70.0, 66.7, 41.9, 14.8, 3.9, 3.7.

Unstable under the conditions of HRMS.

2,2,2-Trichloro-*N*-(9-cyclopropyl-1,7-dioxaspiro[4.4]non-3-en-2-yl)acetamide (2m)



Prepared according to general procedure: from trichloroacetimidate **1m** (64.2 mg, 0.197 mmol), $(C_6F_5)_3B$ (10.1 mg, 0.020 mmol, 10 mol%) and $MeNO_2$ (3 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 4:1) afforded of 2,2,2-trichloro-*N*-(9-cyclopropyl-1,7-dioxaspiro[4.4]non-3-en-2-yl)acetamide (**2m**) (51 mg, 85 %) as a mixture of inseperable diastereomers (*dr* 2:1).

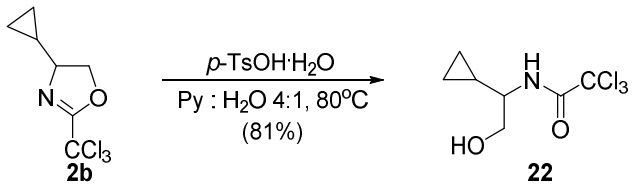
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.96 (d, *J* = 9.5 Hz, 0.3H, minor diastereomer) and 6.82 (d, *J* = 7.7 Hz, 0.7H, major diastereomer), 6.59 (dt, *J* = 9.3, 1.5 Hz, 0.3H, minor diastereomer) and 6.51 (dt, *J* = 8.7, 1.6 Hz, 0.7H, major diastereomer), 6.02 (dd, *J* = 5.8, 1.7 Hz, 0.7H, major diastereomer) and 5.99 (dd, *J* = 5.8, 1.6 Hz, 0.3H, minor diastereomer)), 5.94 (dd, *J* = 5.8, 1.3 Hz, 0.7H, major diastereomer) and 5.91 (dd, *J* = 5.8, 1.4 Hz, 0.3H, minor diastereomer), 4.11 – 3.74 (m, total 4H, both diastereomers), 1.44 (dddd, *J* = 11.2, 9.7, 7.9, 1.7 Hz, total 1H, both diastereomers), 0.90 – 0.76 (m, total 1H, both diastereomers), 0.59 – 0.39 (m, total 2H, both diastereomers), 0.21 – 0.10 (m, 0.6H, minor diastereomer), 0.10 – -0.02 (m, 1.4H, major diastereomer).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 160.9, 160.7, 134.7, 134.6, 127.2, 126.6, 98.1, 97.7, 92.2, 92.2, 87.9, 87.4, 77.9, 77.5, 72.9, 72.8, 54.2, 53.4, 6.3, 5.4, 3.2, 3.1, 2.7, 1.7.

Unstable under the conditions of HRMS.

5. Structure determination of oxazoline 2b by X-ray of trichloroacetamide 22

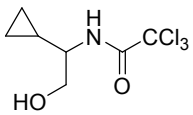
To approve structure of oxazoline **2b** it was hydrolyzed to trichloroacetamide **22** in the presence of *p*-TsOH·H_2O (Scheme 12). Product **22** was obtained as a white crystalline compound. Product configuration was determined by X-ray diffraction. Crystal of **22** was grown in system hexane/methylene chloride 1/1.



Scheme 12

*Derivatization procedure of **2b** and characterization of product **22***

2,2,2-Trichloro-*N*-(1-cyclopropyl-2-hydroxyethyl)acetamide (22)



Oxazoline **2b** (92.9 mg, 0.407 mmol) was dissolved in mixture of pyridine and water (4:1, 4 mL), then *p*-TsOH·H_2O (77.3 mg, 0.407, 1.0 equiv) was added. The mixture was heated at 80 °C for 4 h, then EtOAc (4 mL) was added. The layers were separated and the organic layer was washed with 5 % $KHSO_4$ aq. (4 × 5 mL) and sat. $CuSO_4$ aq. (1 × 5 mL). Organic

phase was dried over $MgSO_4$ and filtered. Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 2:1) afforded 2,2,2-trichloro-*N*-(1-cyclopropyl-2-hydroxyethyl)acetamide (**22**) (81.0 mg, 81%) as a white crystalline compound.

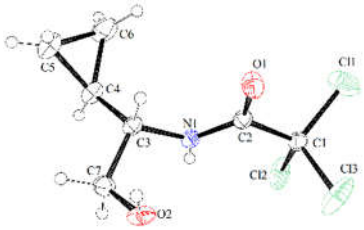
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.04 (bs, 1H), 3.86 (qd, J = 11.1, 4.0 Hz, 2H), 3.28 (ddt, J = 9.5, 7.9, 4.0 Hz, 1H), 2.03 (bs, 1H), 1.09 (dtt, J = 9.6, 8.0, 4.9 Hz, 1H), 0.66 – 0.58 (m, 2H), 0.53 – 0.45 (m, 1H), 0.39 – 0.32 (m, 1H).

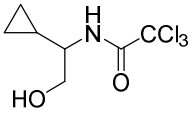
^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 162.1, 92.7, 64.6, 58.3, 12.4, 3.3, 3.1.

EA: Calcd for $C_7H_{10}Cl_3NO_2$: C, 34.11%; H, 4.09%; N, 5.68%; found: C, 34.13%; H, 4.11%; N, 5.70%.

Mp (Hexane): 78.1 – 79.7 °C.

X-ray structure of trichloroacetamide ***22***

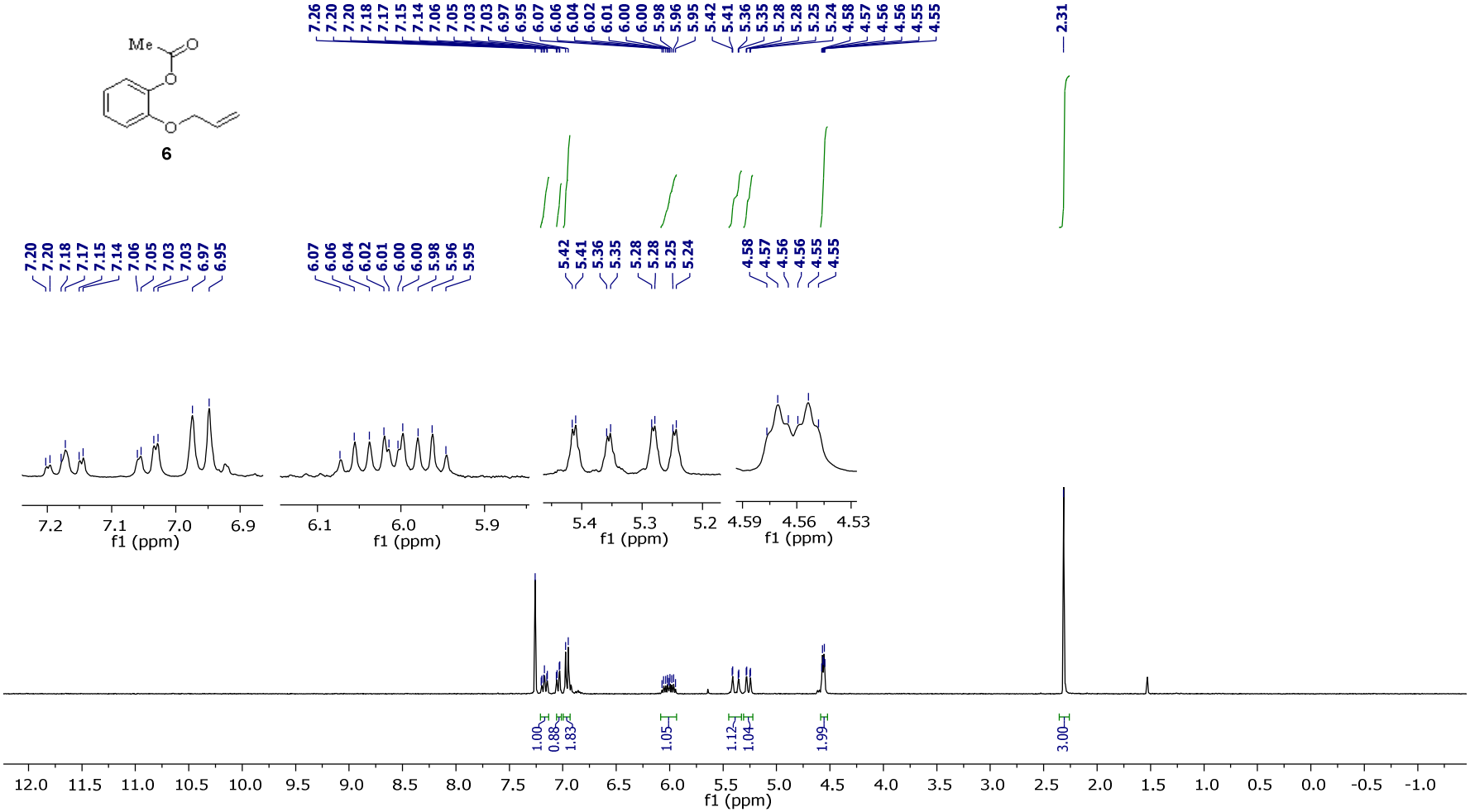


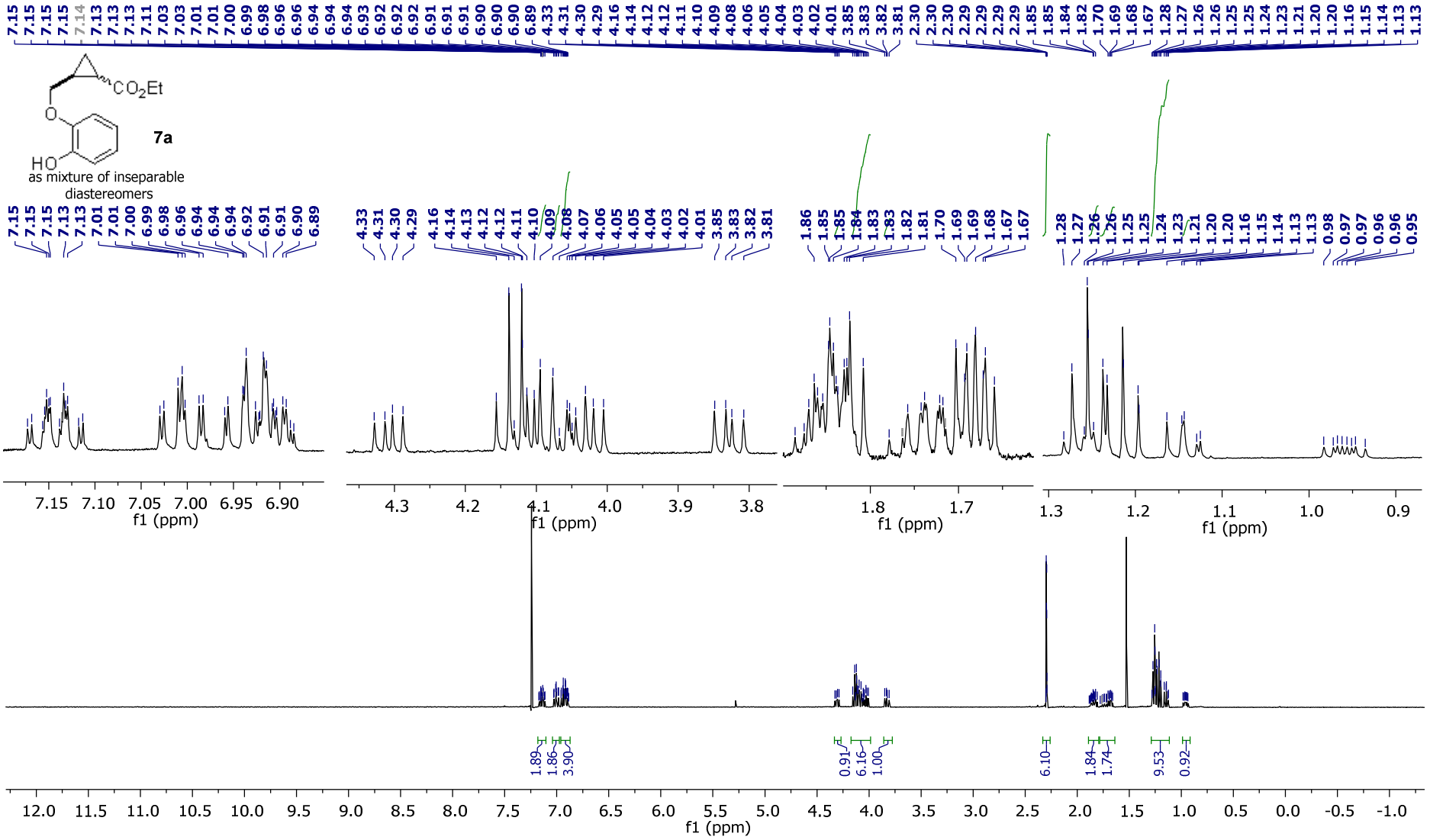


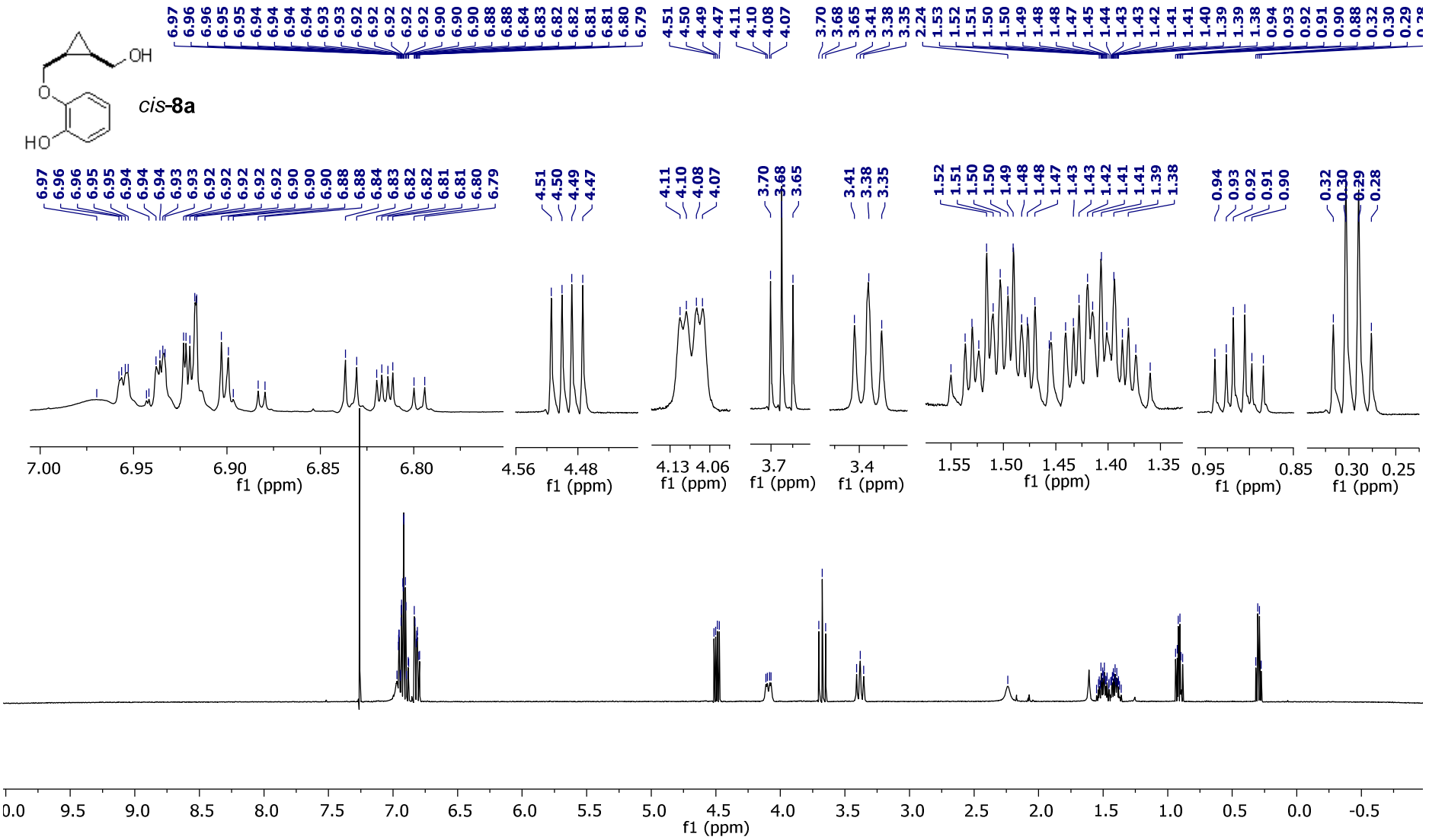
22

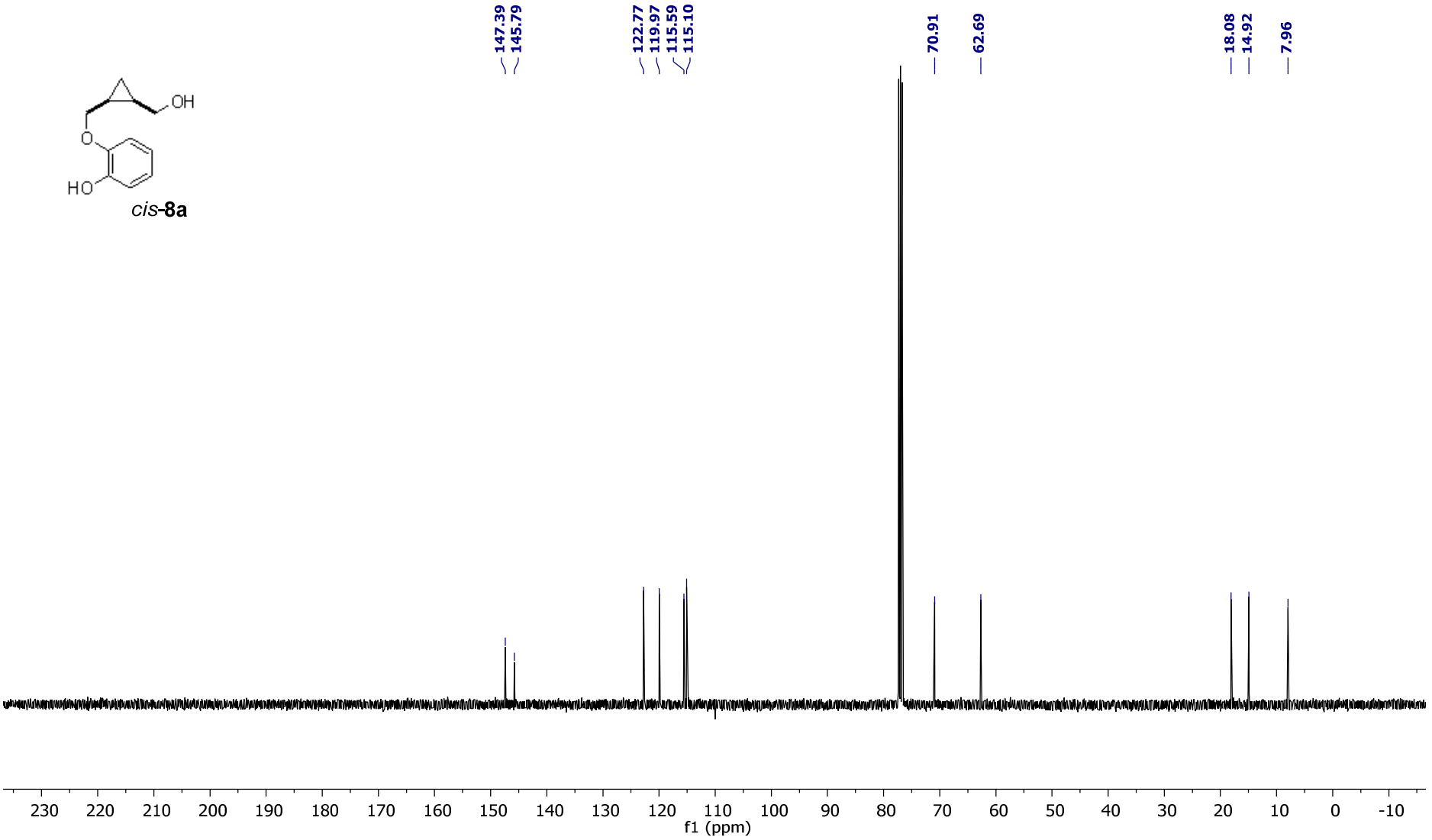
Figure S1 ORTEP diagram of derivatization product **22** (Displacement ellipsoid are drawn at 50% probability level)

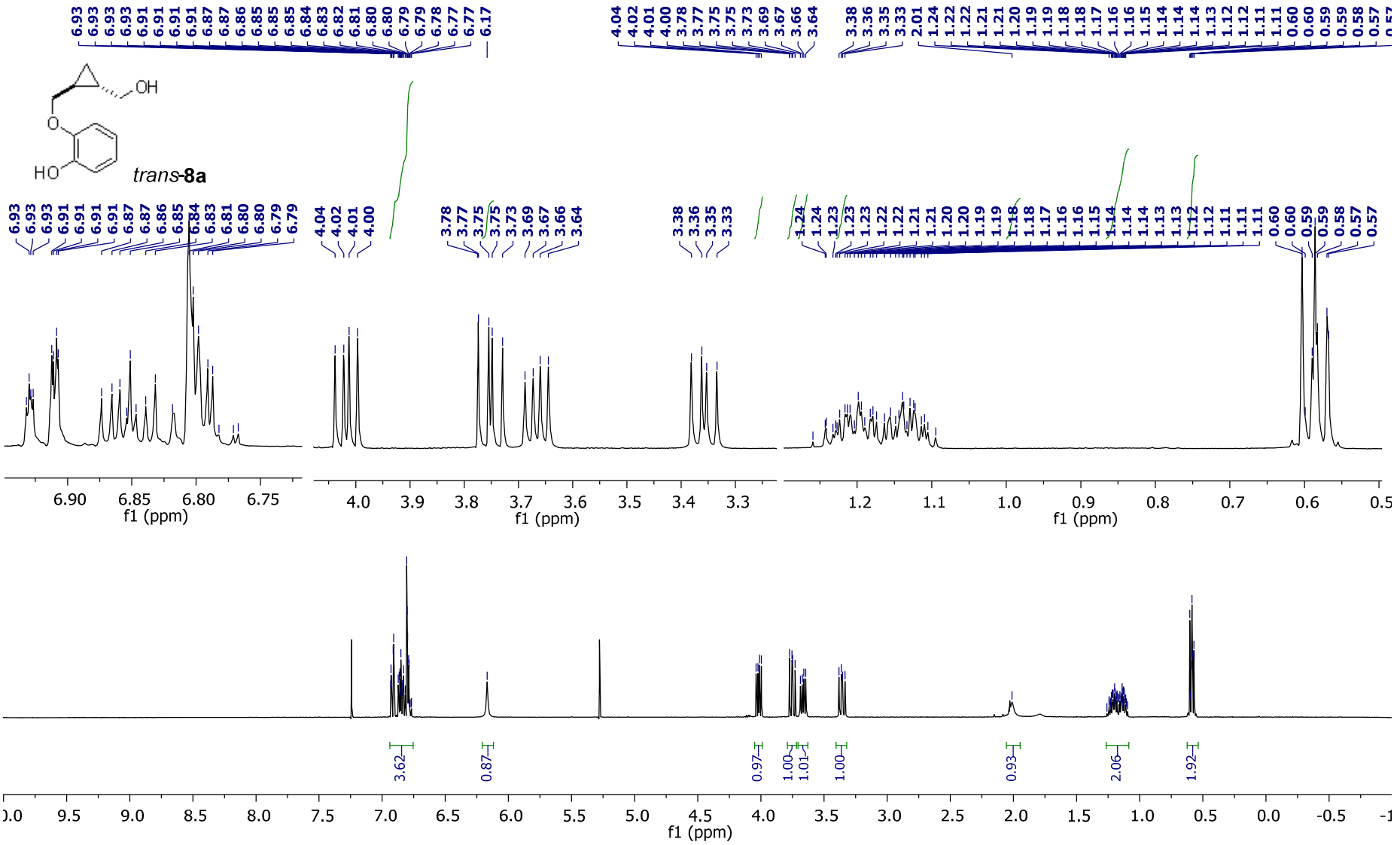
5. NMR data

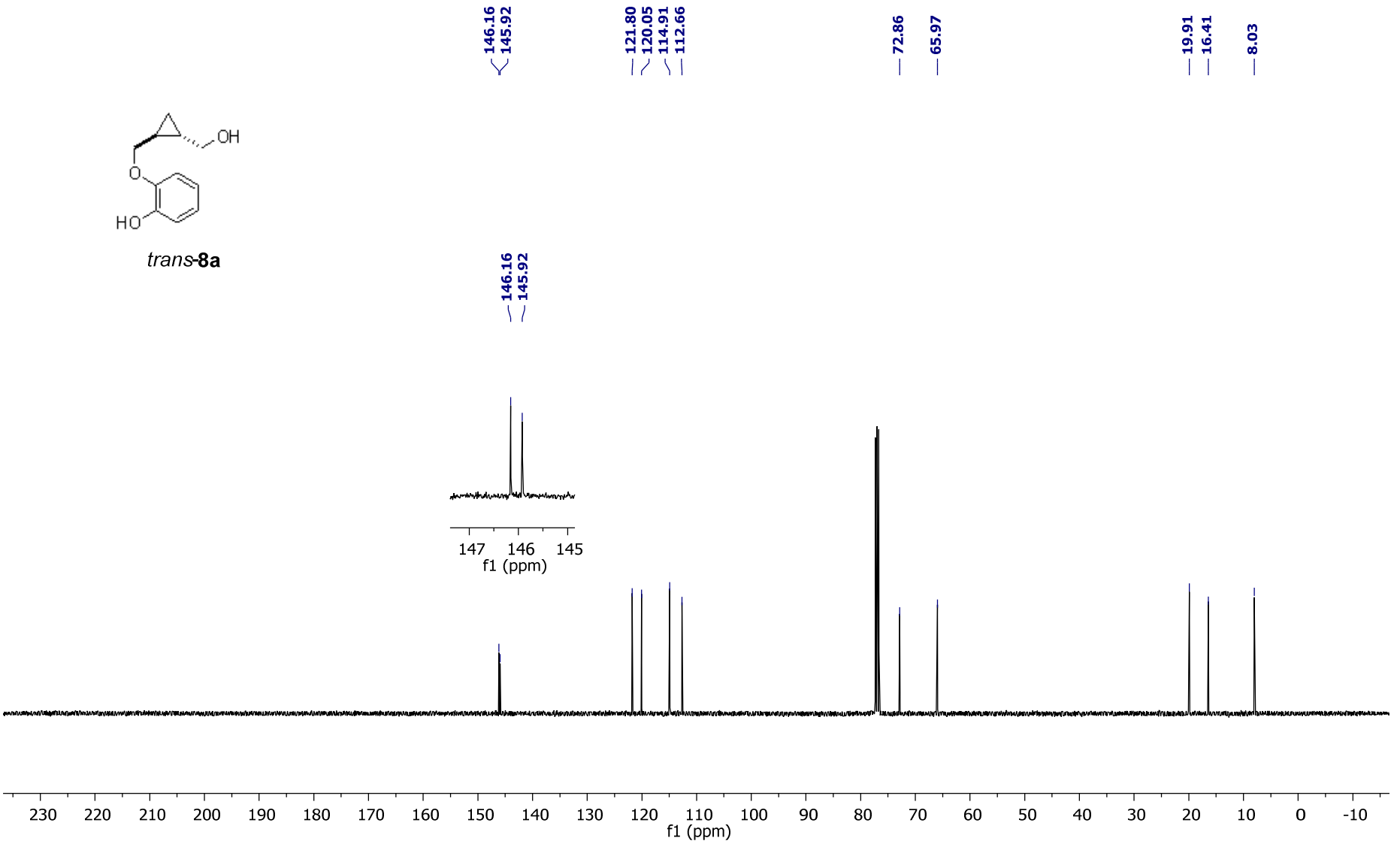

Me
O
O
O
6
7.26 7.20 7.20 7.18 7.17 7.15 7.14 7.06 7.05 7.03 7.03 6.97 6.95 6.07 6.06 6.04 6.02 6.01 6.00 6.00 5.98 5.96 5.95 5.42 5.41 5.36 5.35 5.28 5.28 5.25 5.24 4.58 4.57 4.56 4.56 4.55 4.55 2.31
f1 (ppm)
1.00 0.88 1.83 1.05 1.12 1.04 1.99 3.00

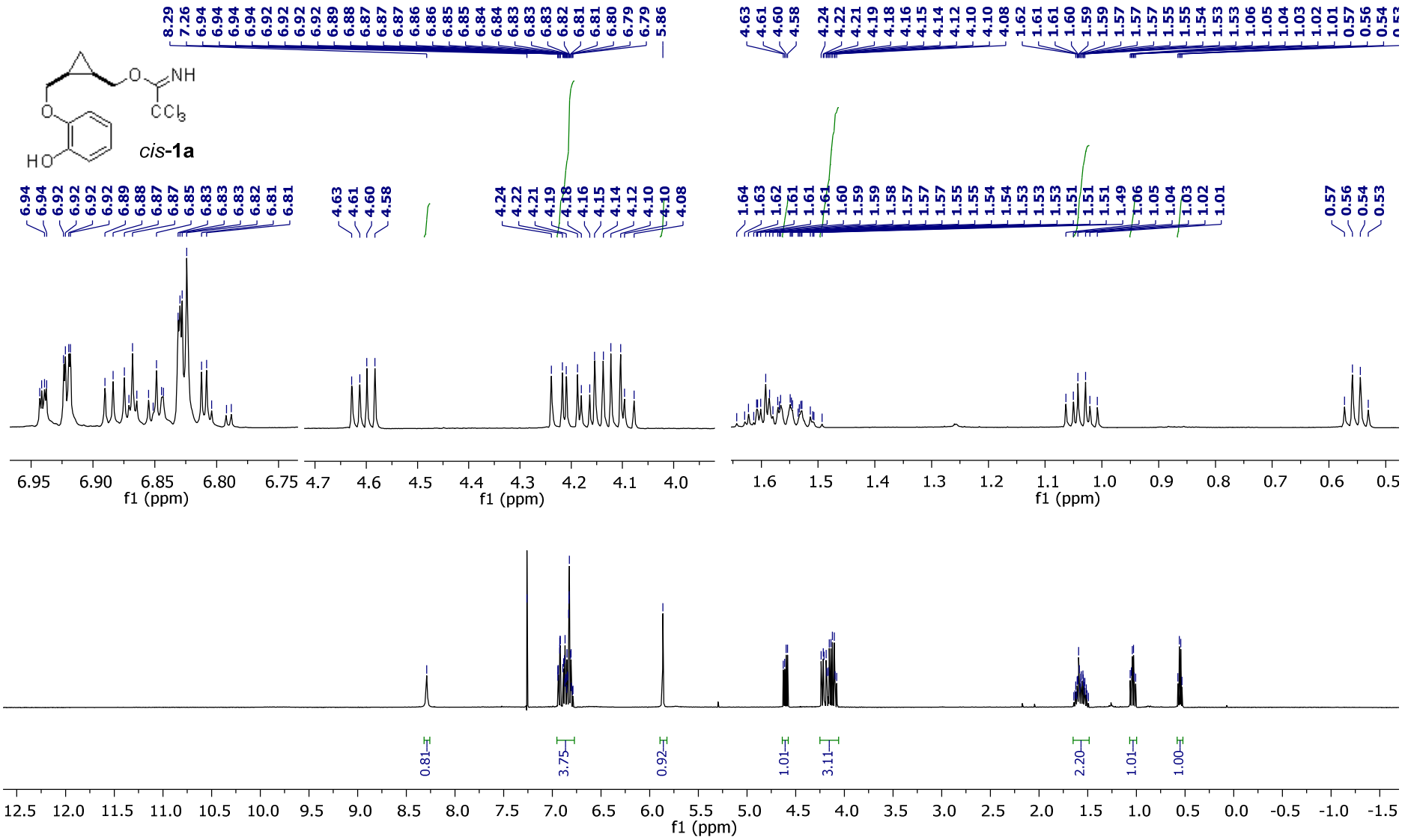

CO2Et
O
HO
7a
as mixture of inseparable
diastereomers
f1 (ppm)

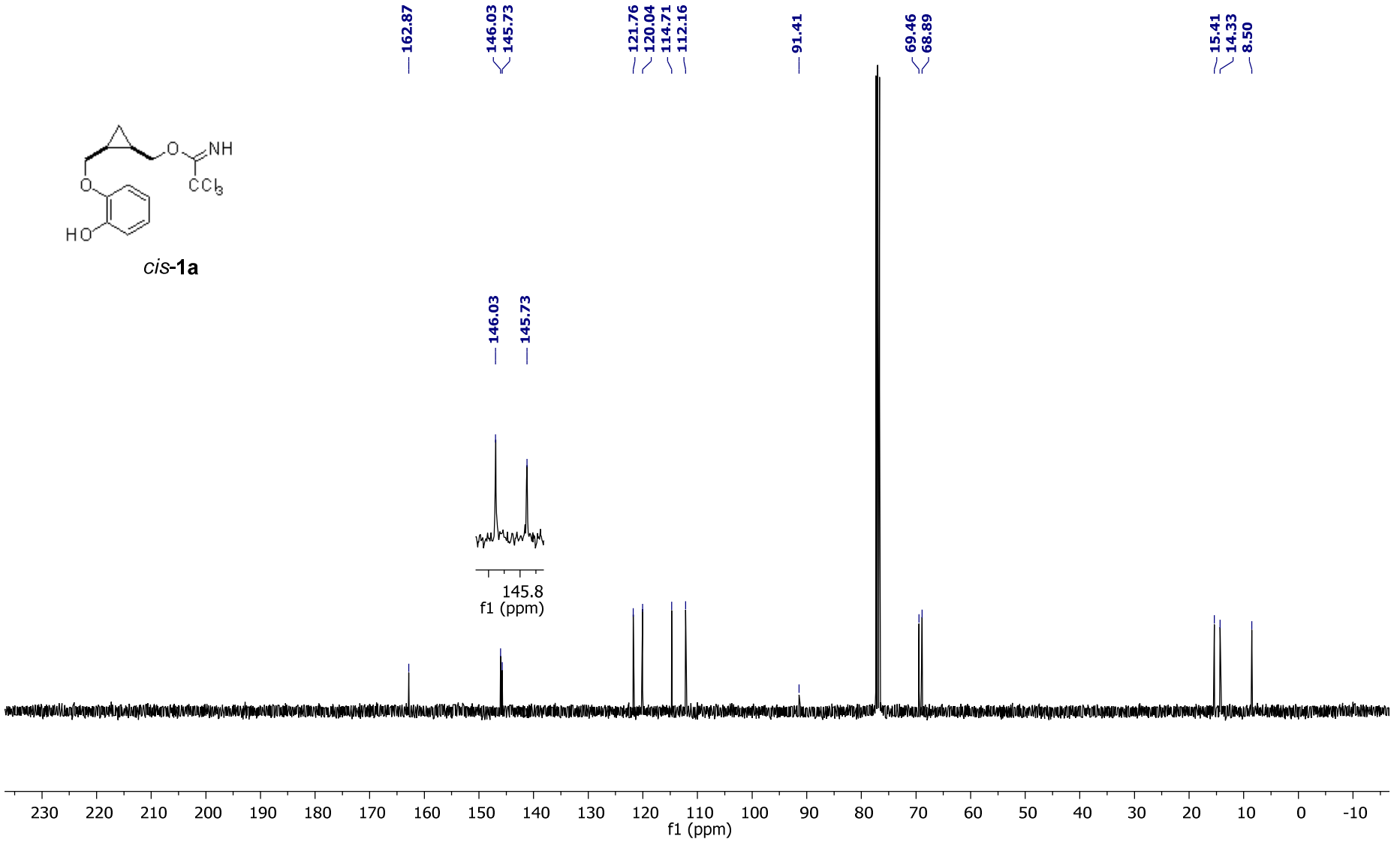

OH
O
HO
cis-8a
f1 (ppm)

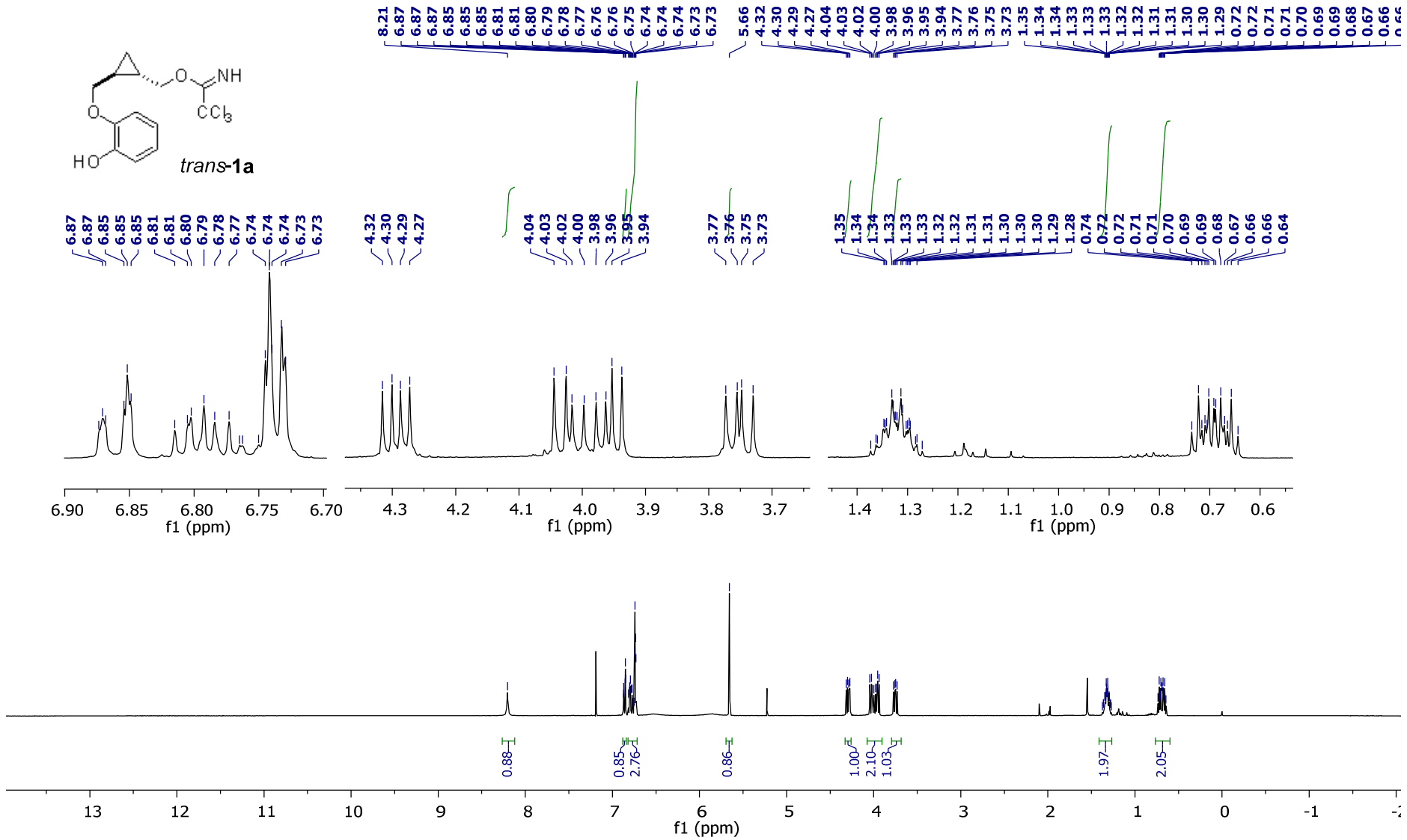

147.39
145.79
122.77
119.97
115.59
115.10
70.91
62.69
18.08
14.92
7.96
OH
O
HO
cis-8a
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

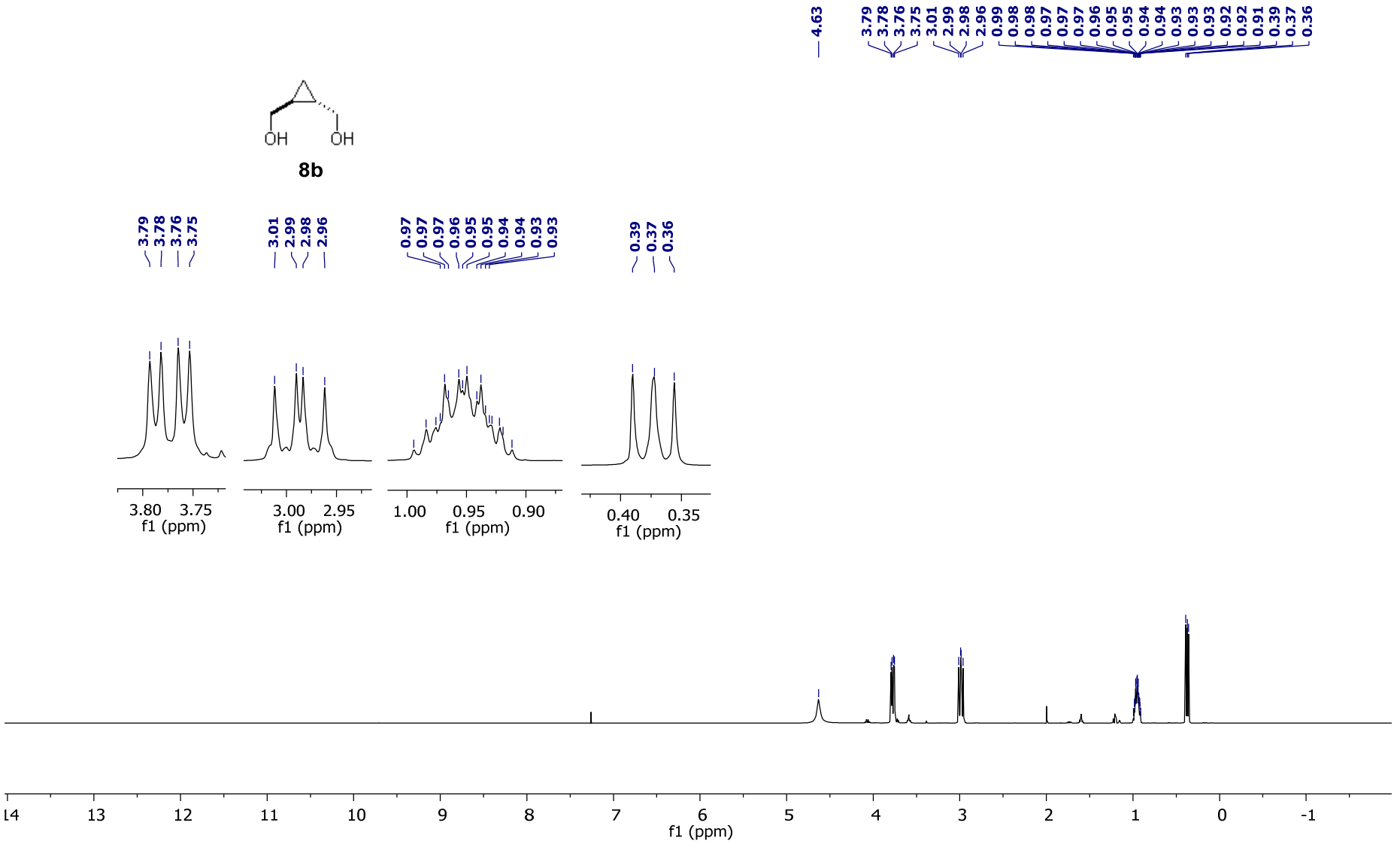

OH
O
HO
trans-8a
f1 (ppm)
3.62
0.87
0.97
1.00
1.01
1.00
0.93
2.06
1.92

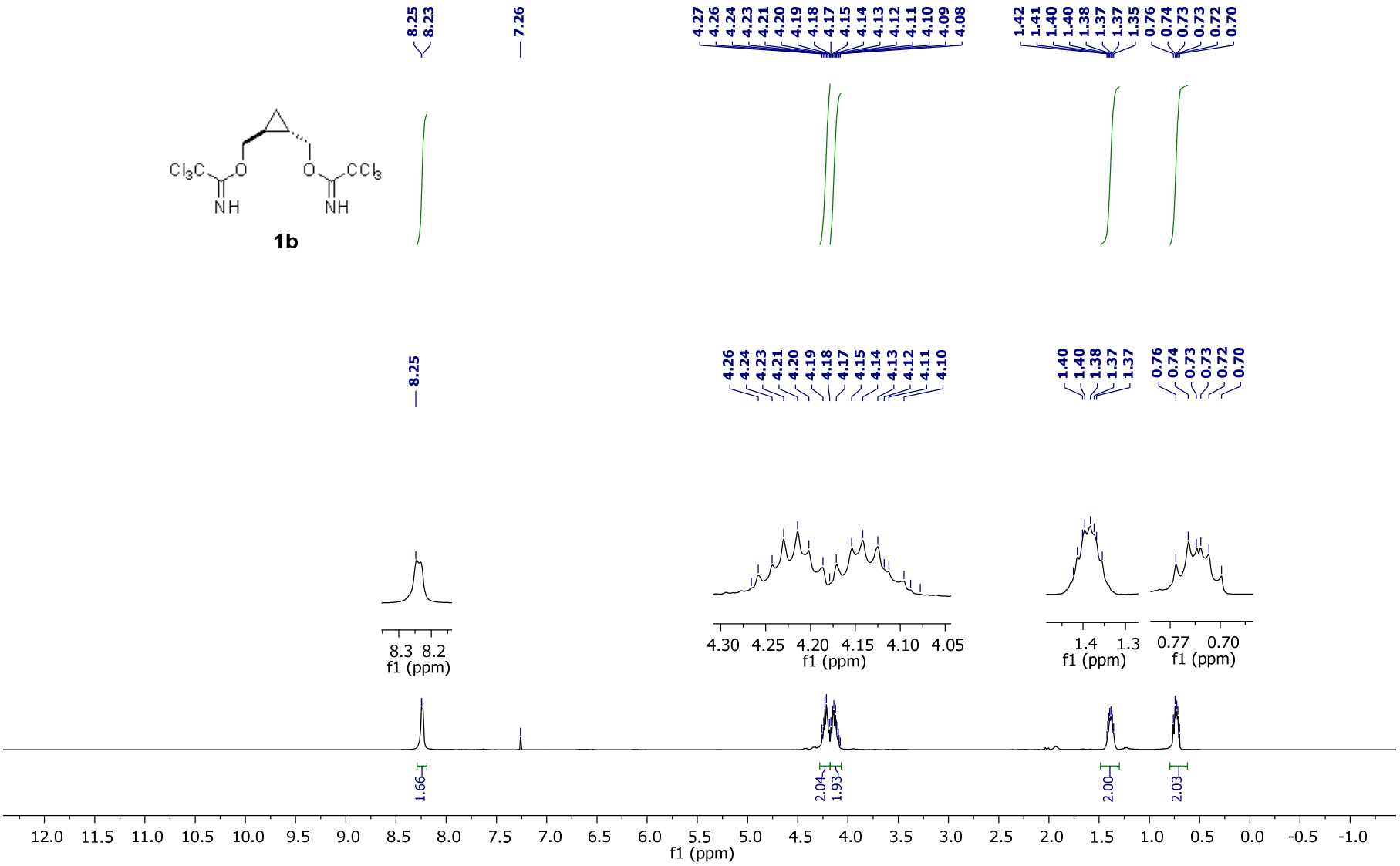

146.16
145.92
121.80
120.05
114.91
112.66
72.86
65.97
19.91
16.41
8.03
OH
O
HO
trans-8a
146.16
145.92
147
146
145
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

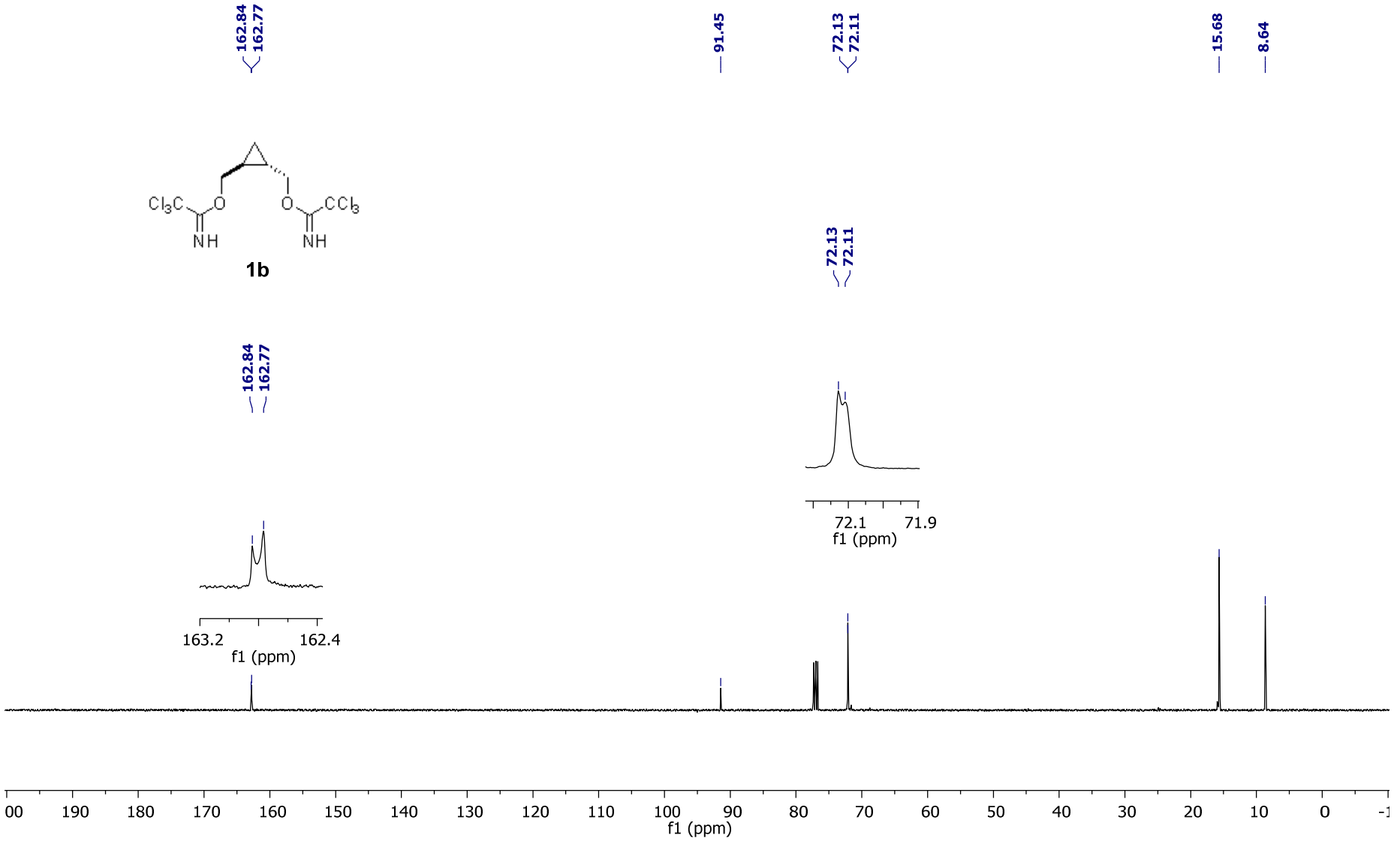

cis-1a
f1 (ppm)

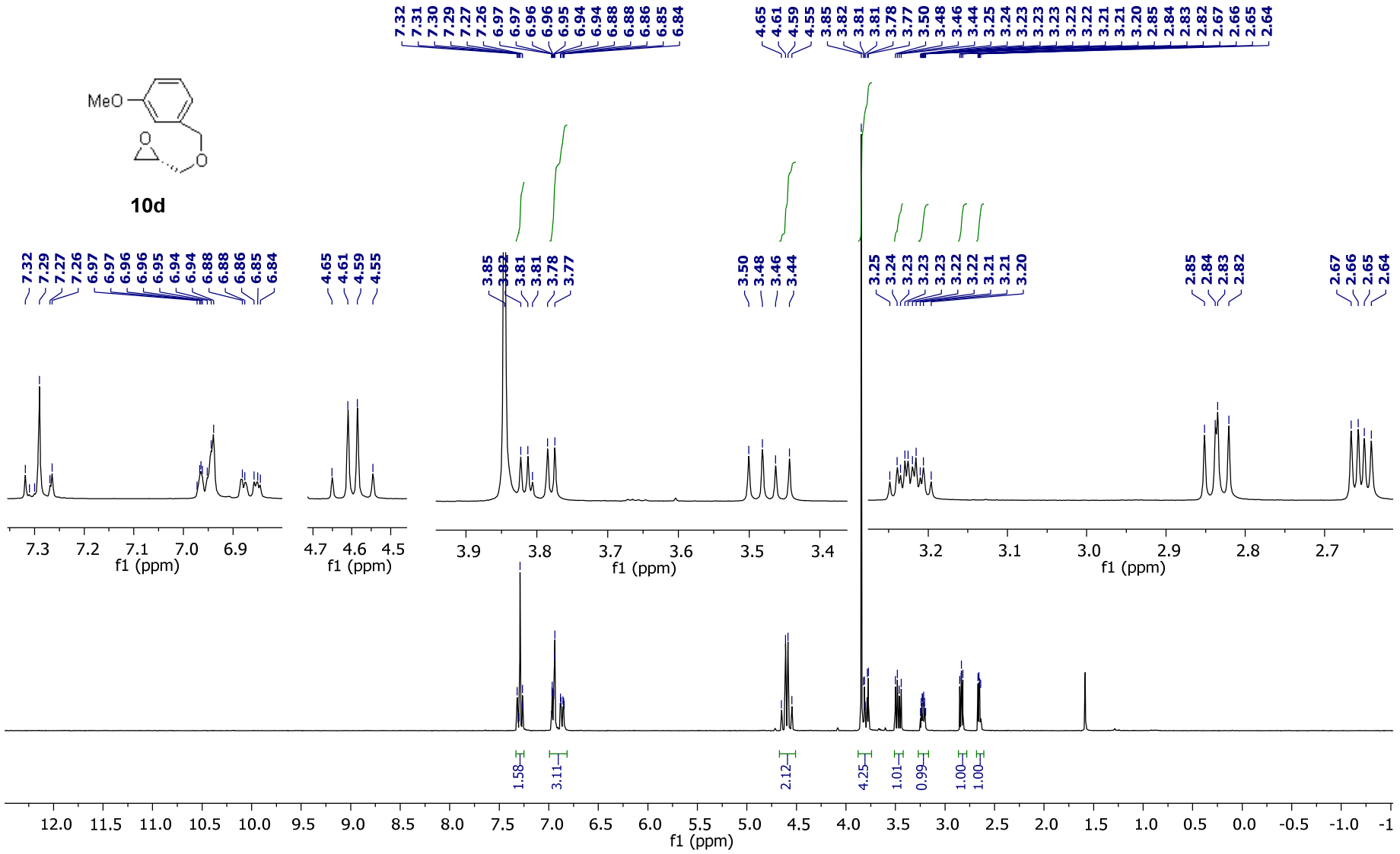

162.87
146.03
145.73
121.76
120.04
114.71
112.16
91.41
69.46
68.89
15.41
14.33
8.50
O
NH
CCl3
O
HO
cis-1a
146.03
145.73
145.8
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

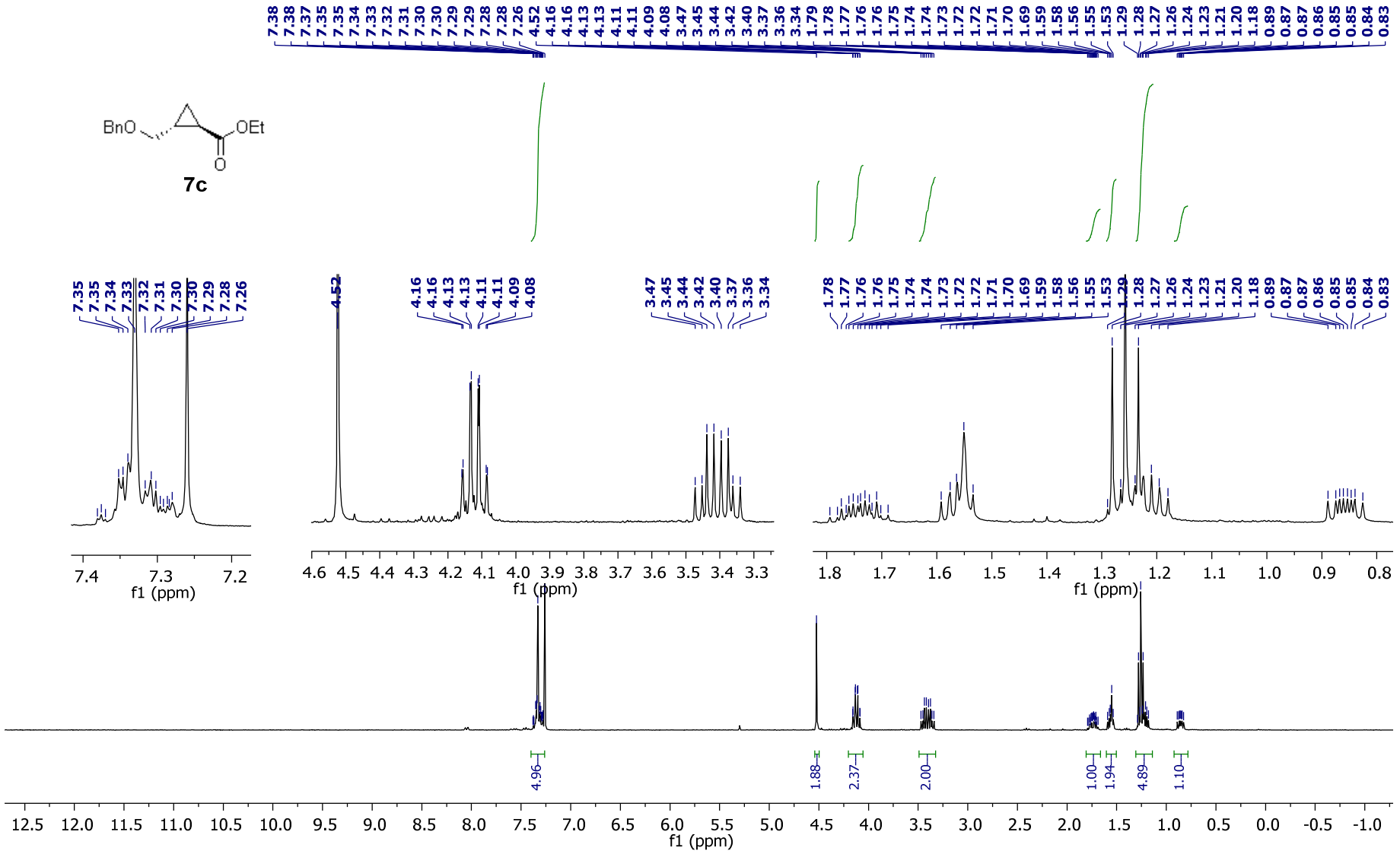

trans-1a
f1 (ppm)

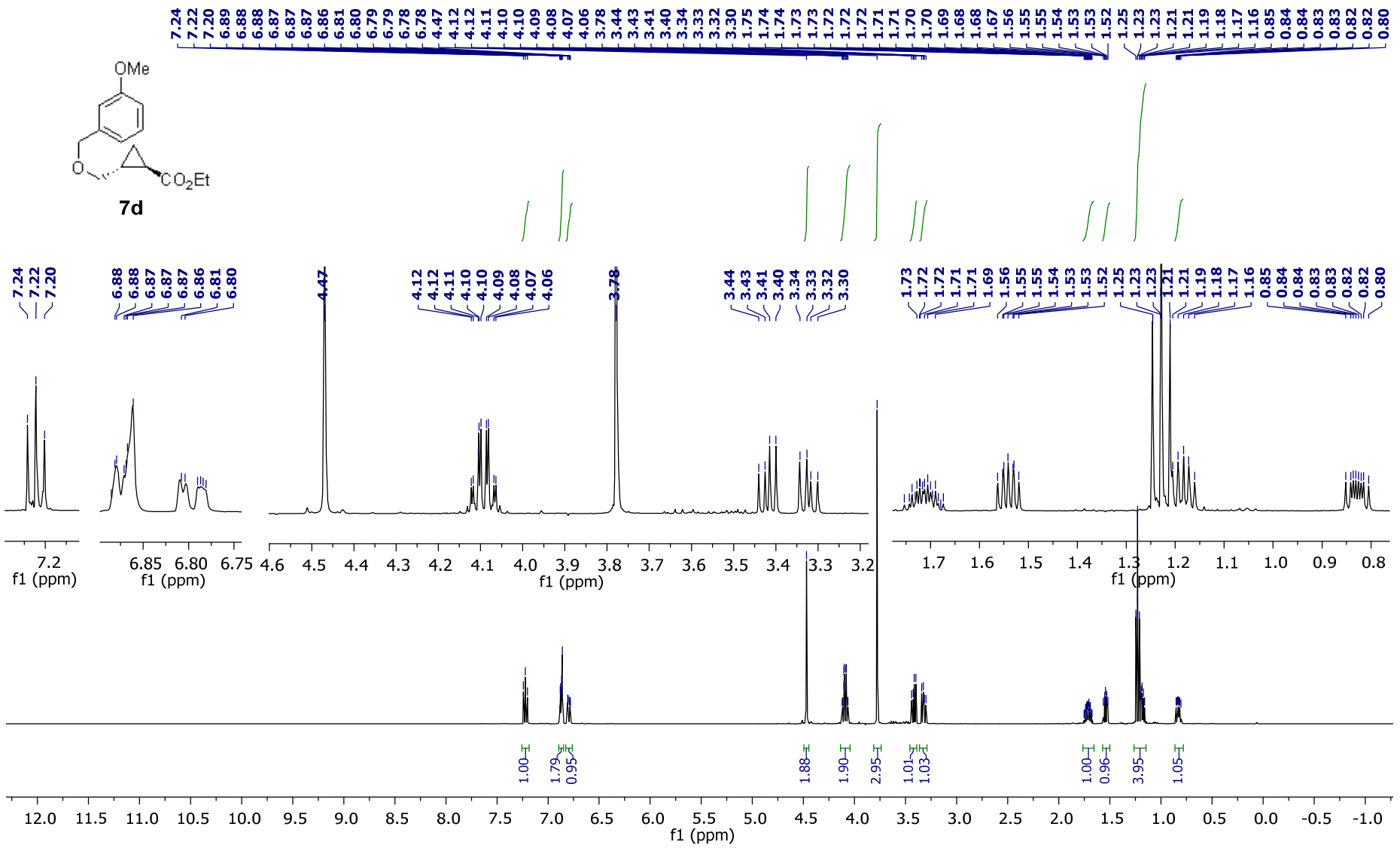

4.63
3.79
3.78
3.76
3.75
3.01
2.99
2.98
2.96
0.99
0.98
0.98
0.97
0.97
0.97
0.96
0.95
0.95
0.94
0.94
0.93
0.93
0.92
0.92
0.91
0.39
0.37
0.36
OH
OH
8b
3.80 3.75
f1 (ppm)
3.00 2.95
f1 (ppm)
1.00 0.95 0.90
f1 (ppm)
0.40 0.35
f1 (ppm)
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

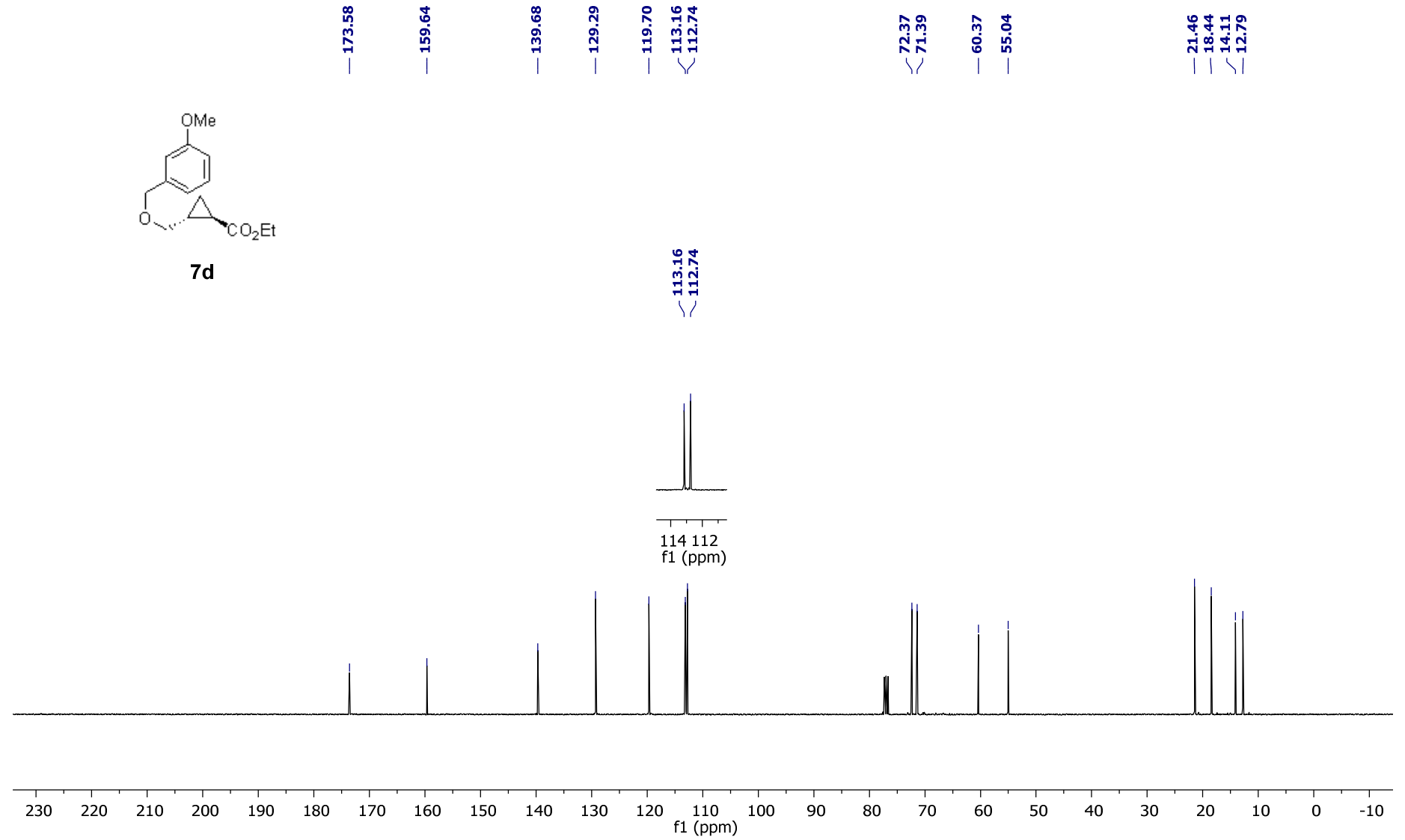

8.25
8.23
7.26
4.27
4.26
4.24
4.23
4.21
4.20
4.19
4.18
4.17
4.15
4.14
4.13
4.12
4.11
4.10
4.09
4.08
1.42
1.41
1.40
1.40
1.38
1.37
1.37
1.35
0.76
0.74
0.73
0.73
0.72
0.70
Cl3C
O
O
CCl3
NH
NH
1b
8.3 8.2
f1 (ppm)
4.30 4.25 4.20 4.15 4.10 4.05
f1 (ppm)
1.4 1.3
f1 (ppm)
0.77 0.70
f1 (ppm)
1.66
2.04
1.93
2.00
2.03
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

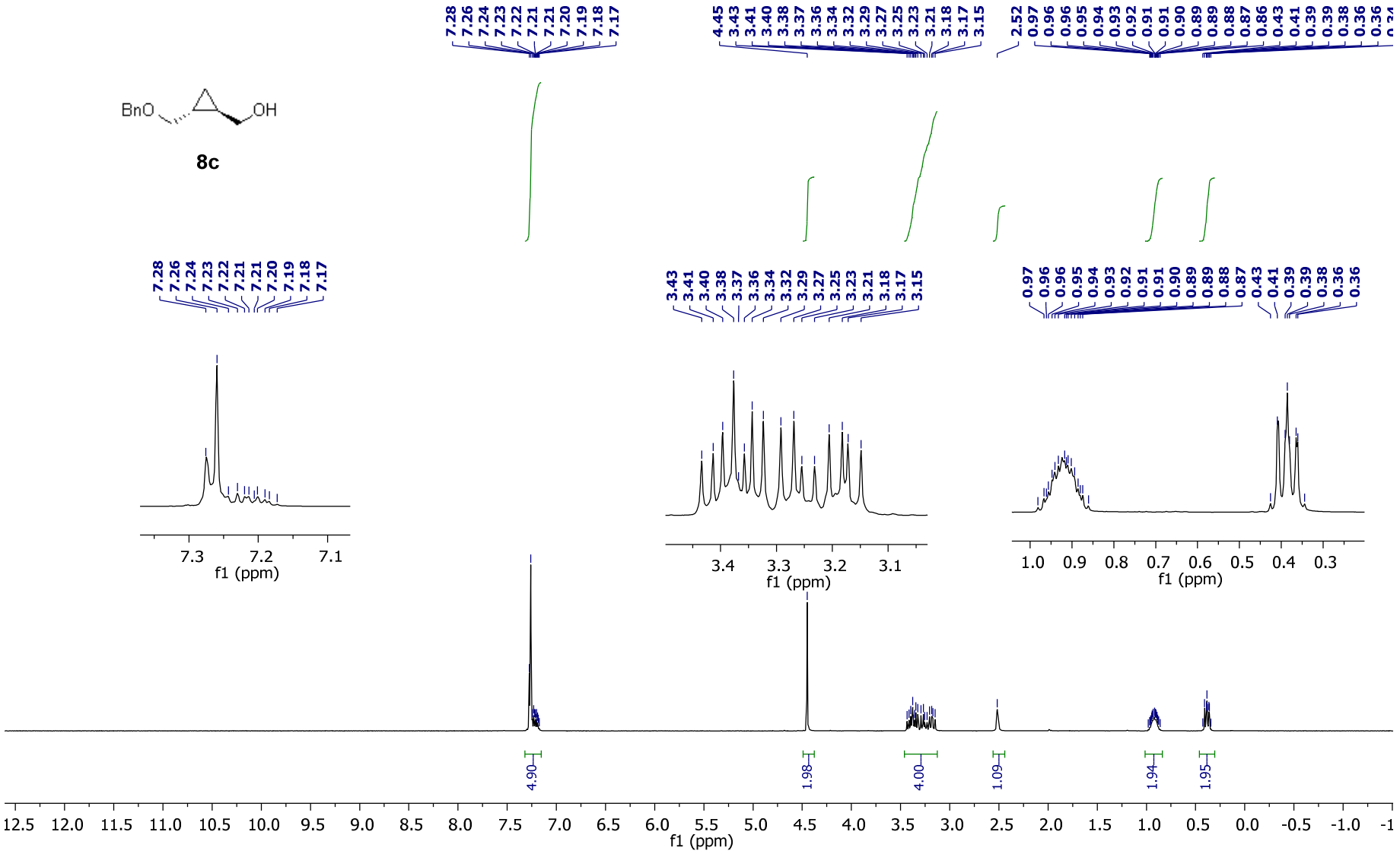

162.84
162.77
91.45
72.13
72.11
15.68
8.64
Cl3C
O
NH
O
CCl3
NH
1b
72.13
72.11
72.1
71.9
f1 (ppm)
162.84
162.77
163.2
162.4
f1 (ppm)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

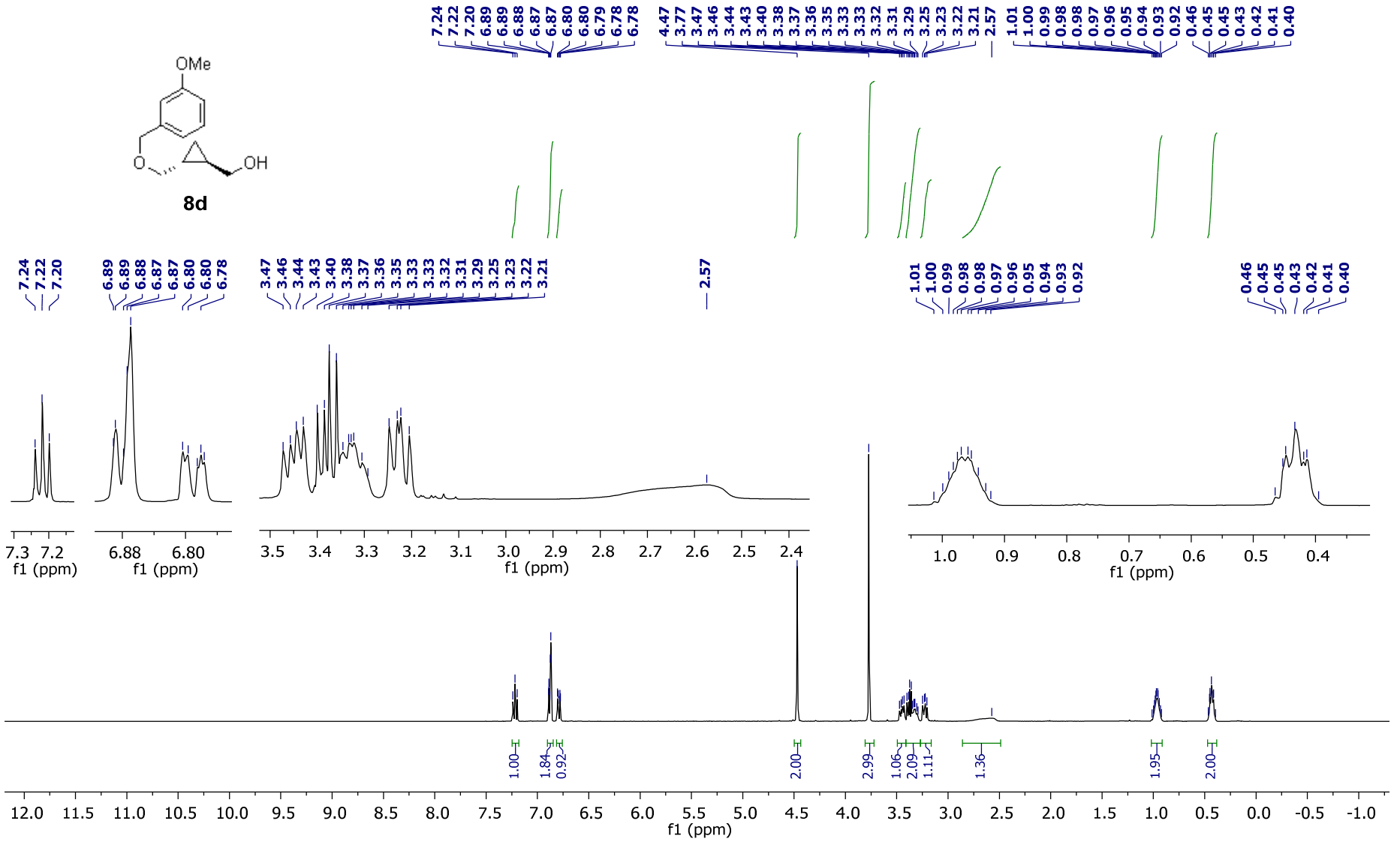

MeO
O
O
10d
7.32 7.31 7.30 7.29 7.27 7.26 6.97 6.97 6.96 6.96 6.95 6.94 6.94 6.88 6.88 6.86 6.85 6.84
4.65 4.61 4.59 4.55 3.85 3.82 3.81 3.81 3.78 3.77 3.50 3.48 3.46 3.44 3.25 3.24 3.23 3.23 3.22 3.22 3.21 3.21 3.20 2.85 2.84 2.83 2.82 2.67 2.66 2.65 2.64
f1 (ppm)
1.58 3.11 2.12 4.25 1.01 0.99 1.00 1.00

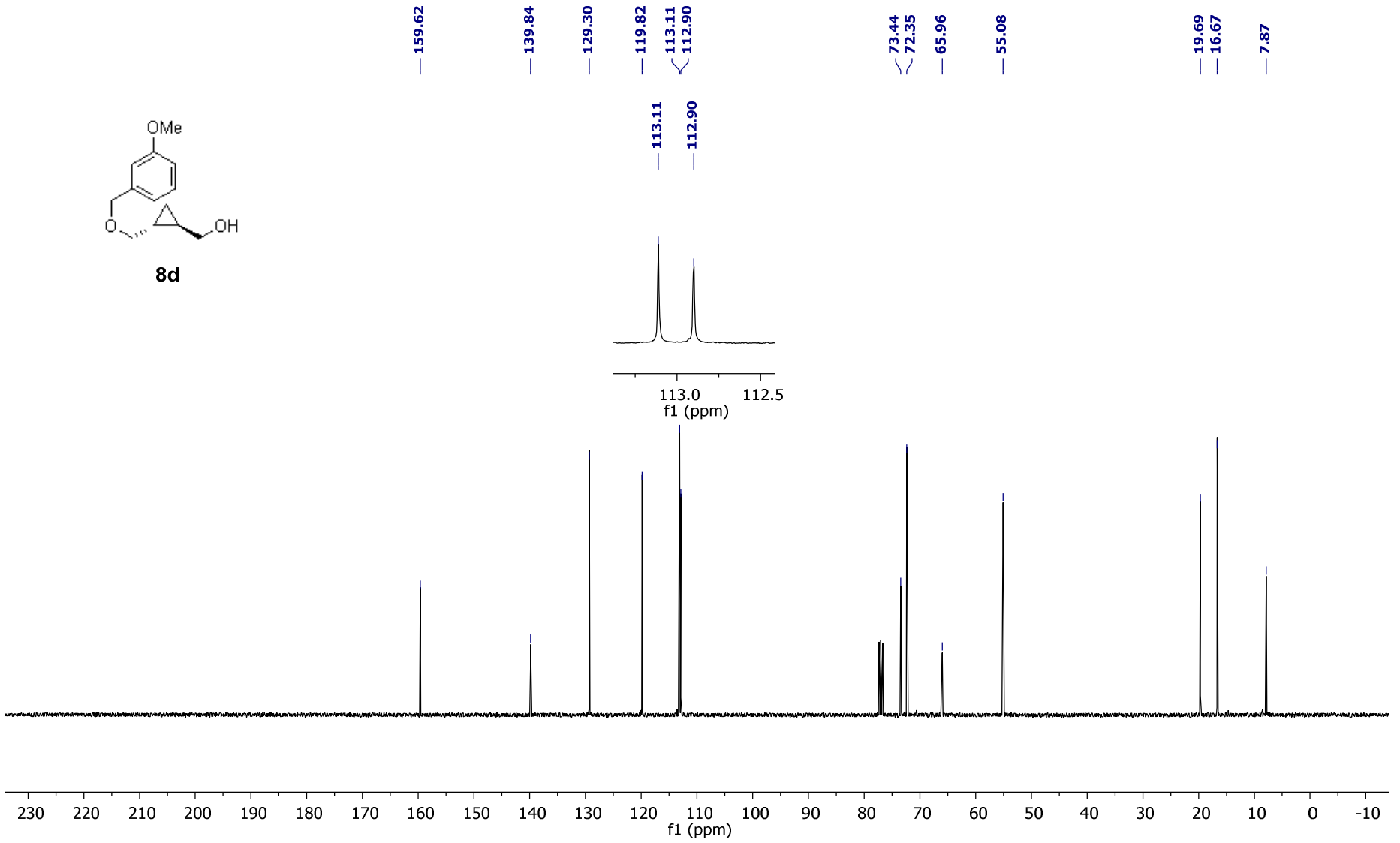

BnO
OEt
O
7c
f1 (ppm)

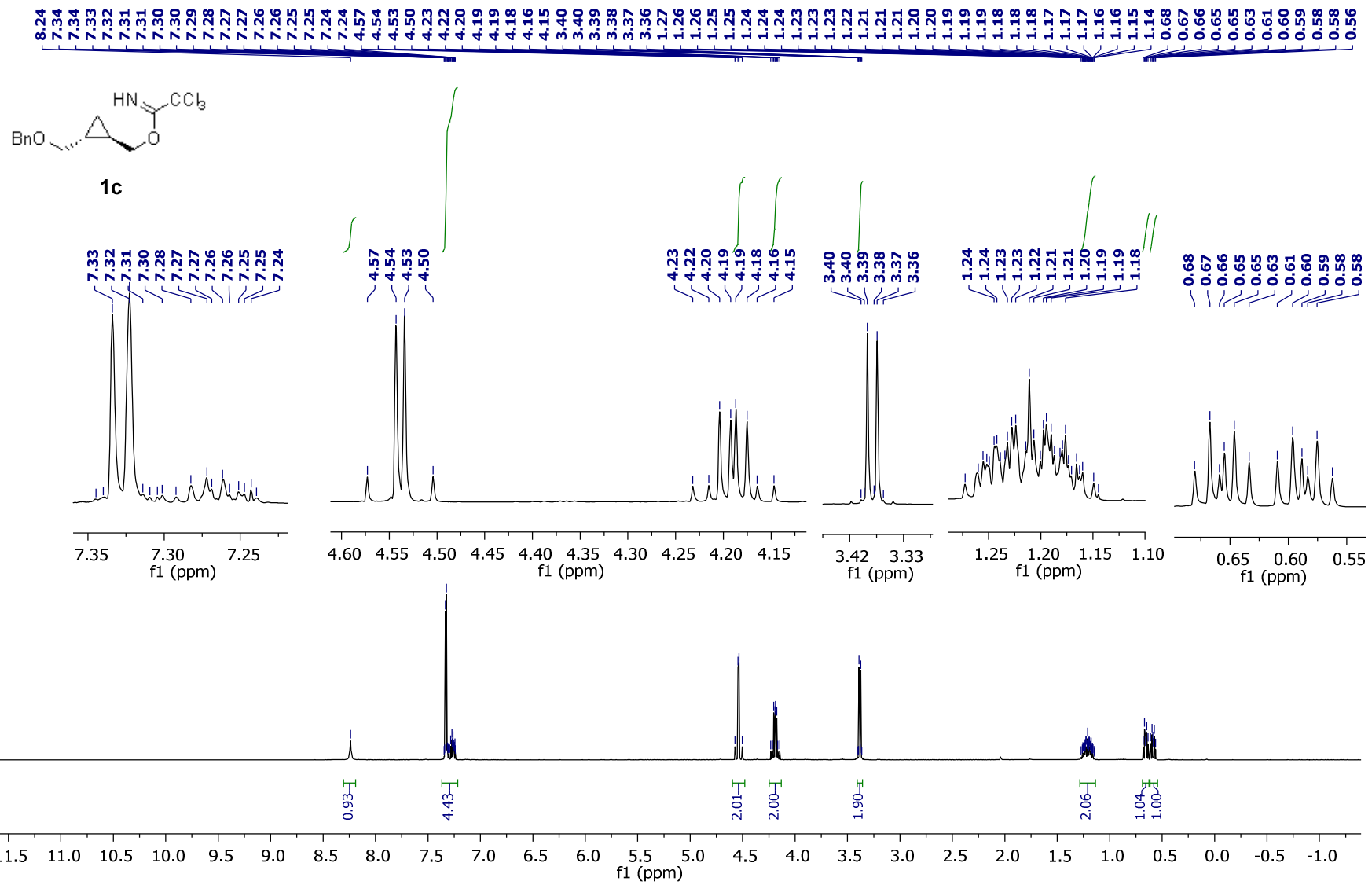

OMe
O
CO2Et
7d
f1 (ppm)

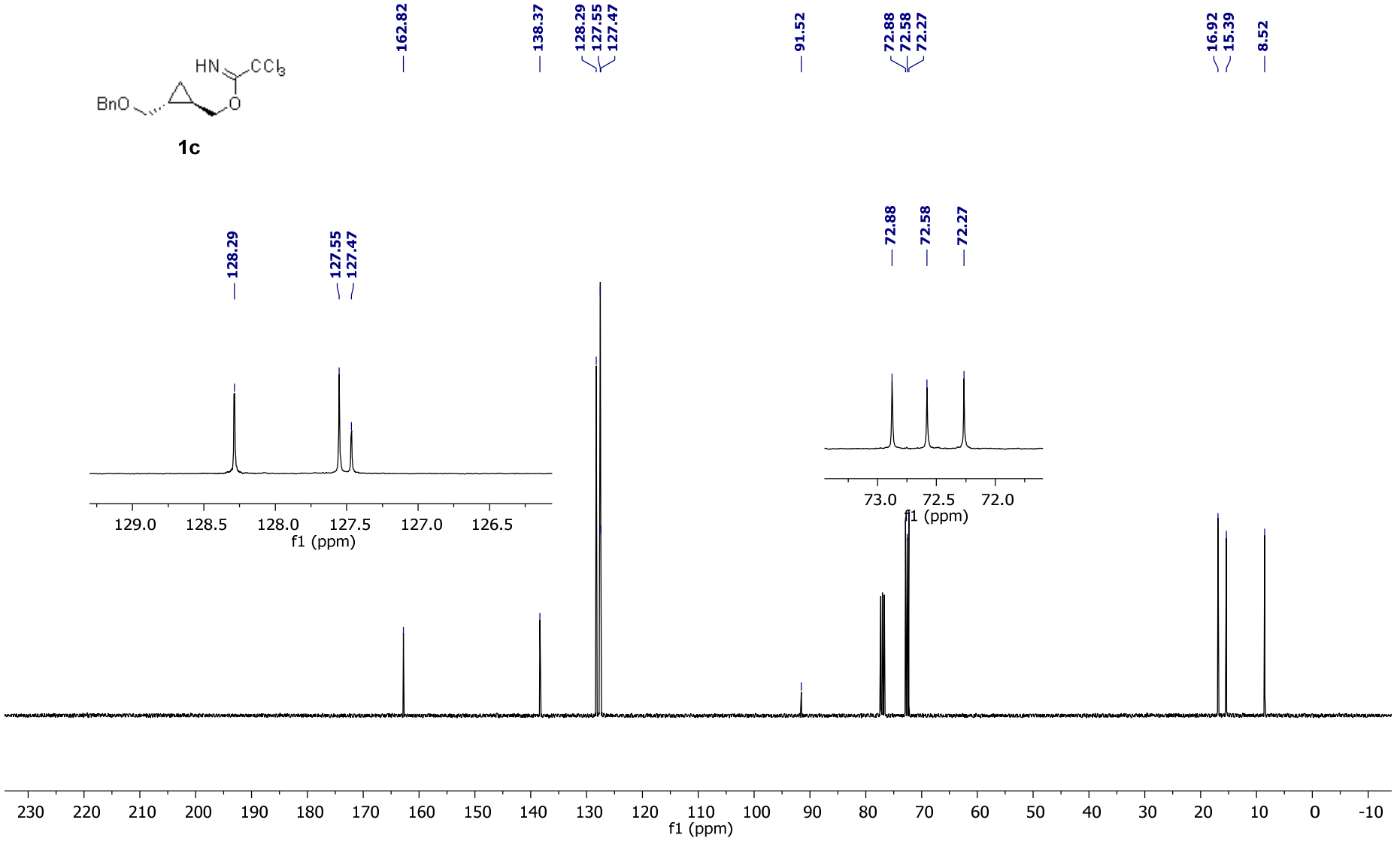

173.58
159.64
139.68
129.29
119.70
113.16
112.74
72.37
71.39
60.37
55.04
21.46
18.44
14.11
12.79
OMe
O
CO2Et
7d
113.16
112.74
114 112
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

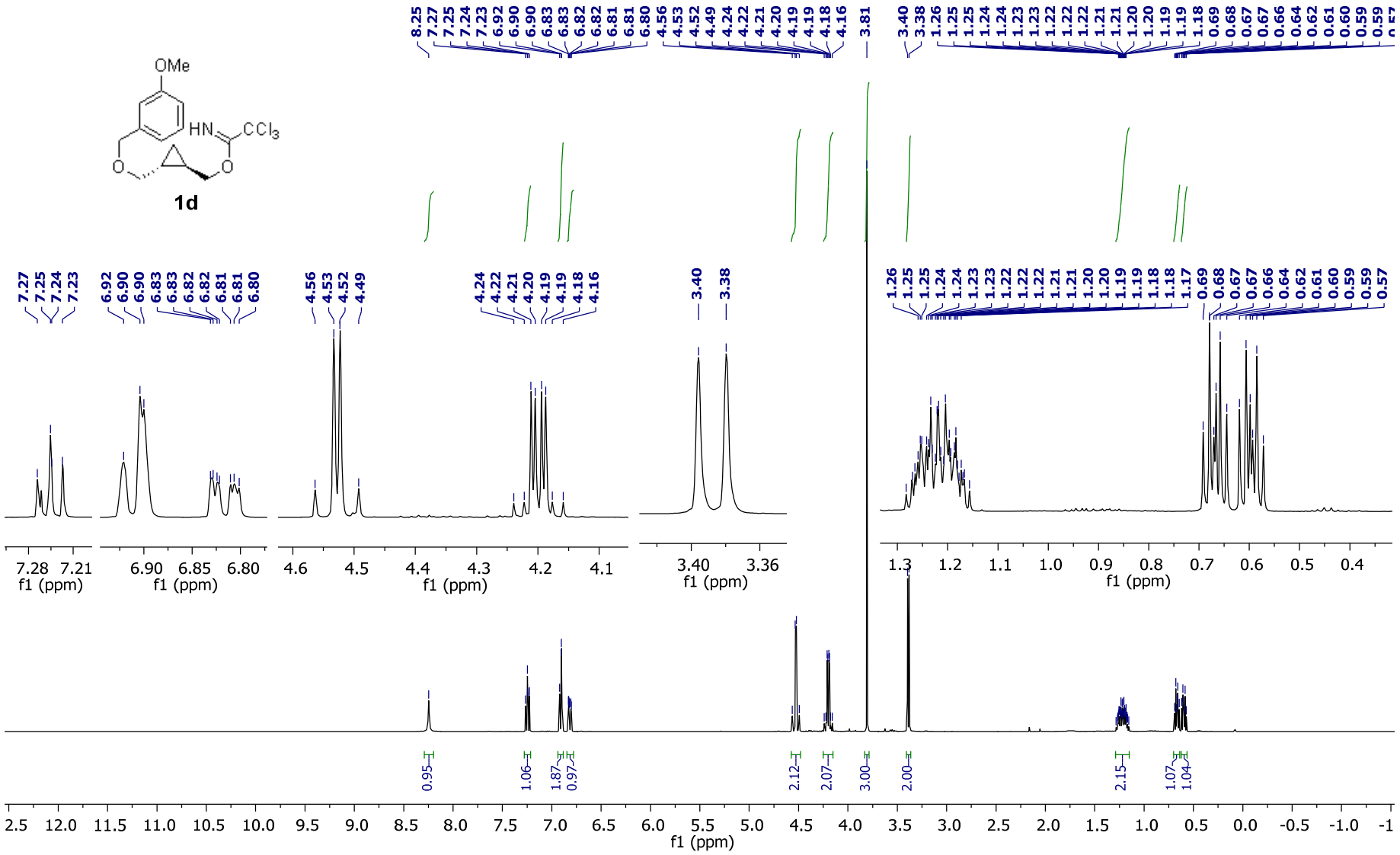

BnO
OH
8c
f1 (ppm)

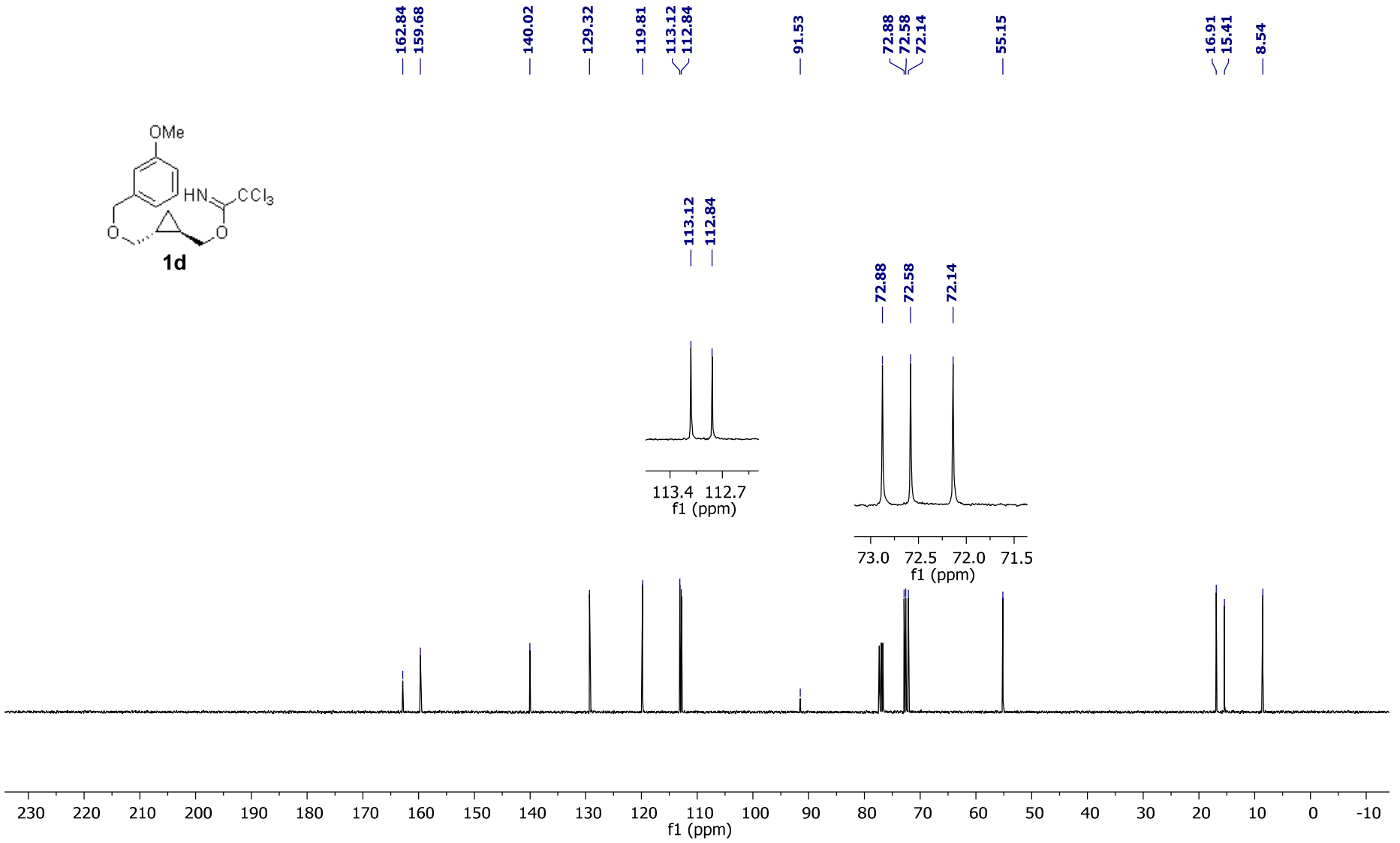

OMe
O
OH
8d
7.24 7.22 7.20 6.89 6.89 6.88 6.87 6.87 6.80 6.80 6.79 6.78 6.78
4.47 3.77 3.47 3.46 3.44 3.43 3.40 3.38 3.37 3.36 3.35 3.33 3.33 3.32 3.31 3.29 3.25 3.23 3.22 3.21
2.57
1.01 1.00 0.99 0.98 0.98 0.97 0.96 0.95 0.94 0.93 0.92
0.46 0.45 0.45 0.43 0.42 0.41 0.40
7.3 7.2 f1 (ppm)
6.88 6.80 f1 (ppm)
3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 f1 (ppm)
1.0 0.9 0.8 0.7 0.6 0.5 0.4 f1 (ppm)
1.00 1.84 0.92 2.00 2.99 1.06 2.09 1.11 1.36 1.95 2.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

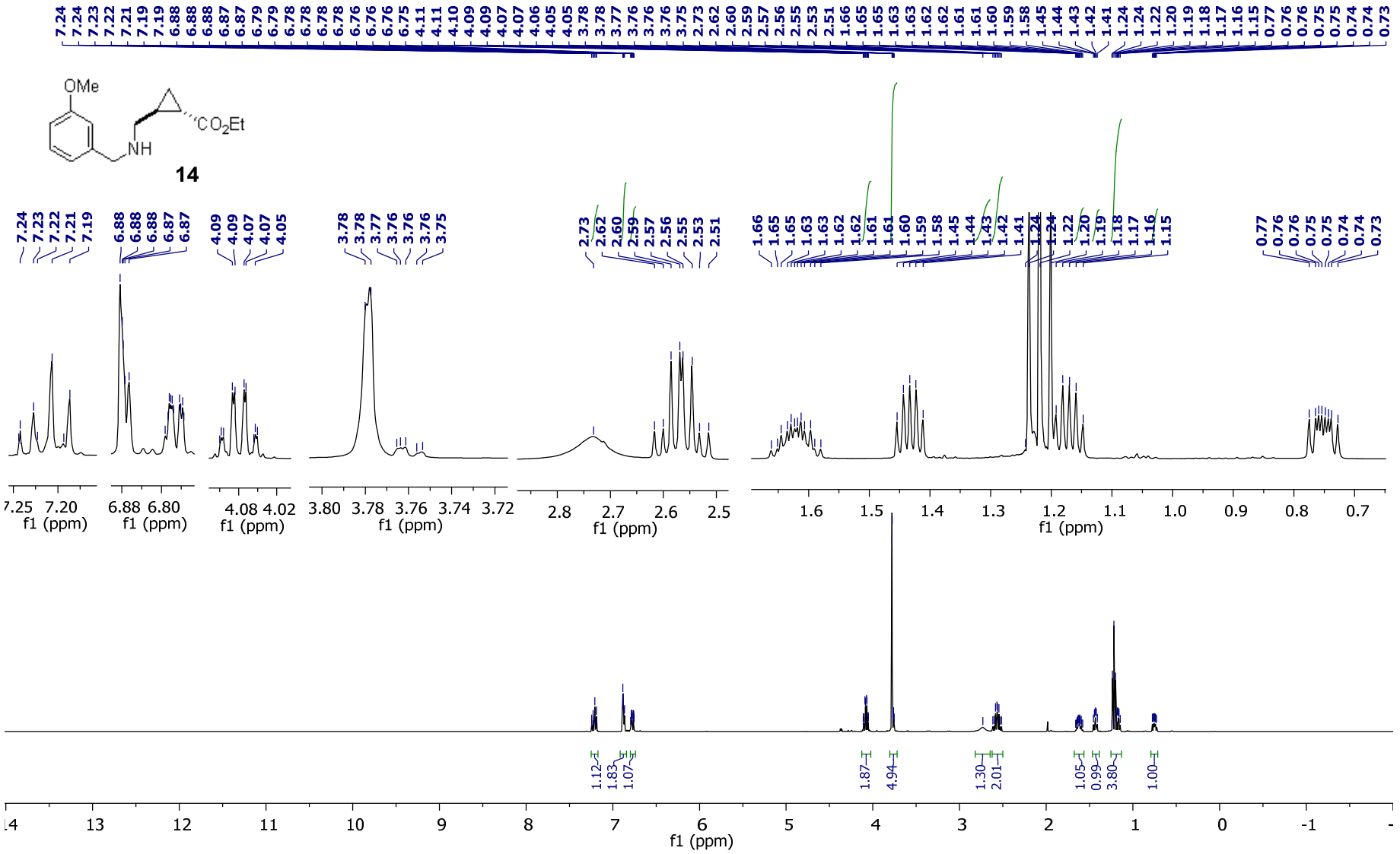

159.62
139.84
129.30
119.82
113.11
112.90
73.44
72.35
65.96
55.08
19.69
16.67
7.87
OMe
O
OH
8d
113.11
112.90
113.0
112.5
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

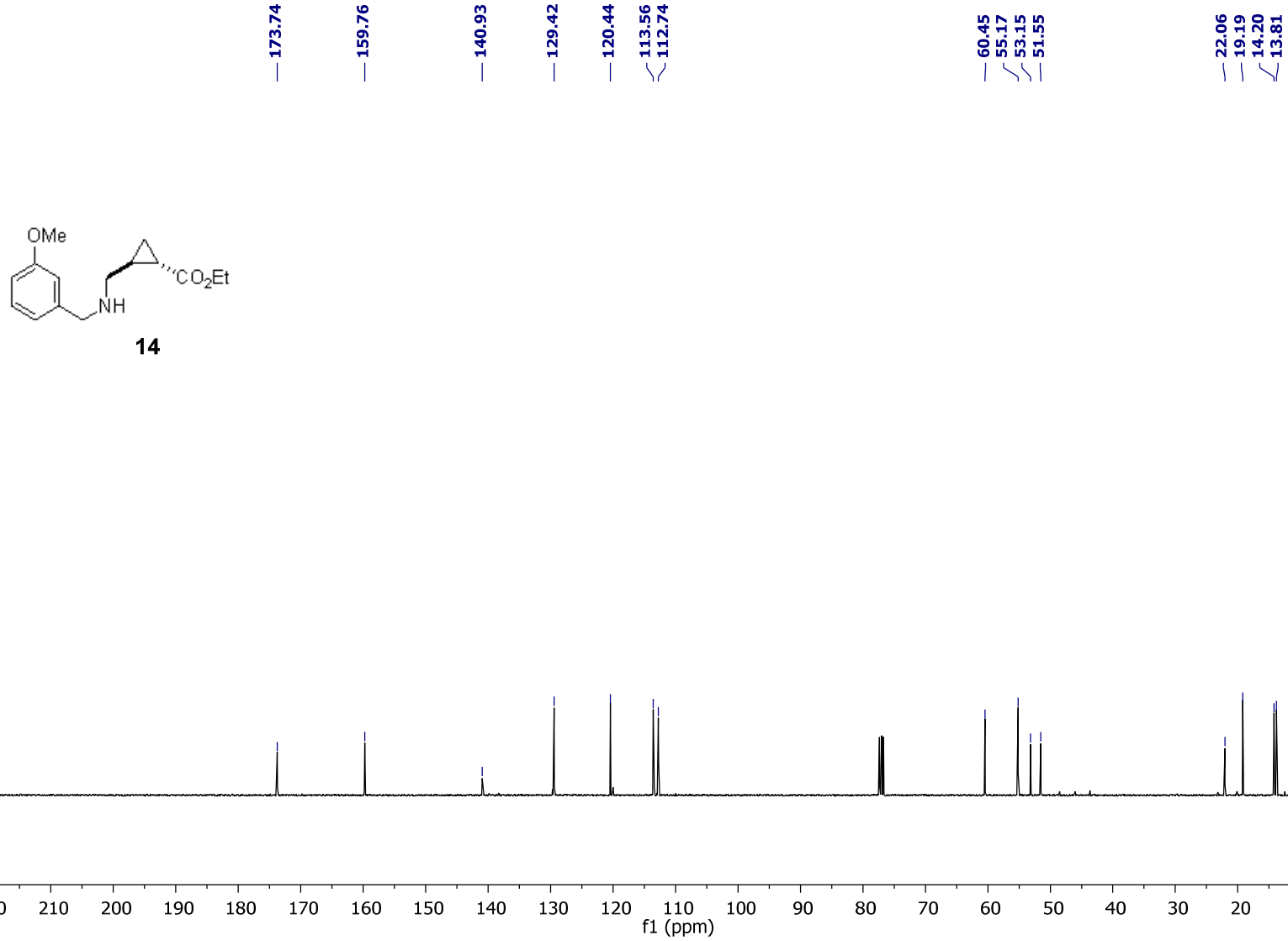

HN
CCl3
BnO
O
1c
f1 (ppm)

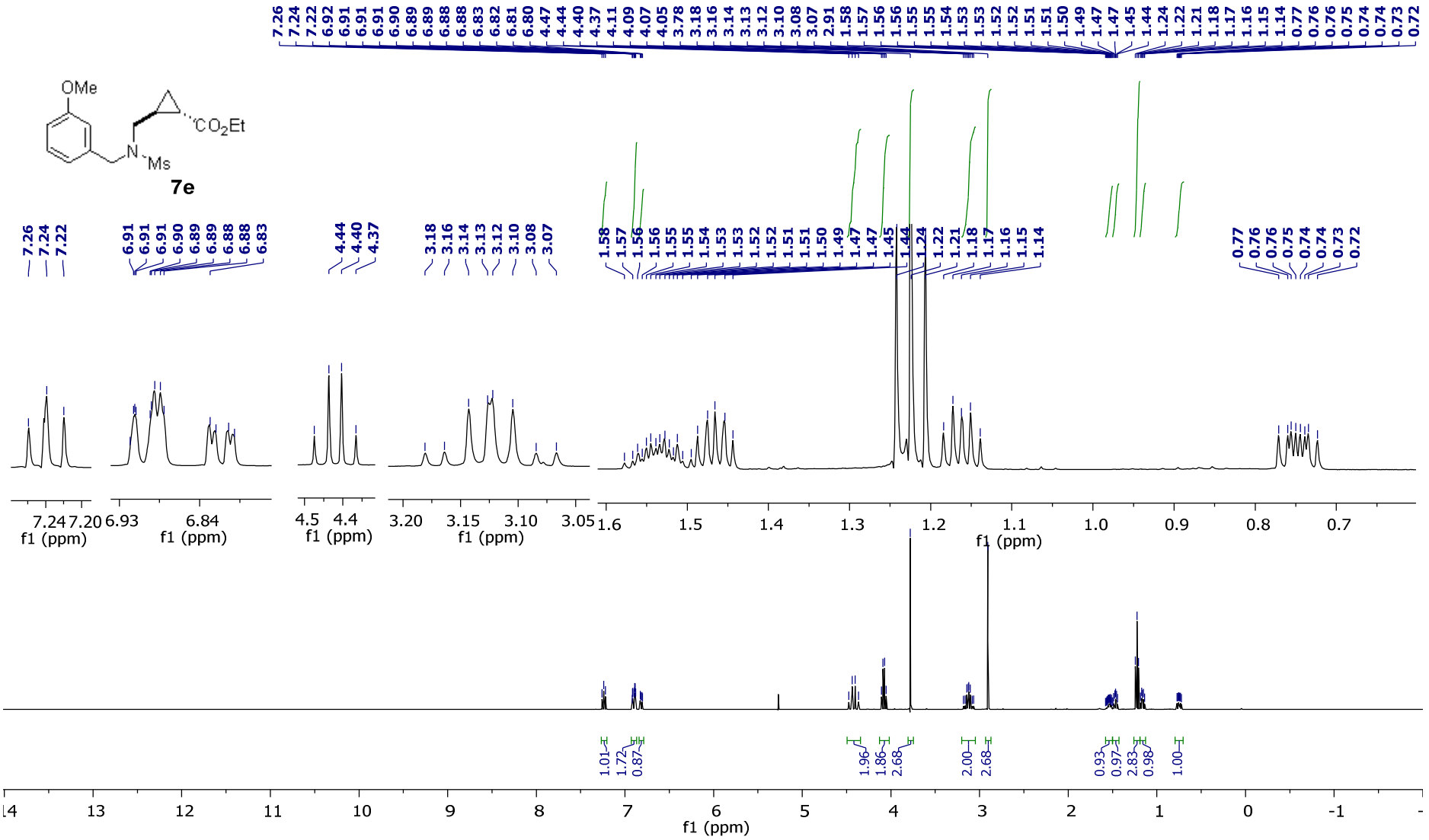

HN
CCl3
BnO
O
1c
162.82
138.37
128.29
127.55
127.47
91.52
72.88
72.58
72.27
16.92
15.39
8.52
129.0
128.5
128.0
127.5
127.0
126.5
f1 (ppm)
73.0
72.5
72.0
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

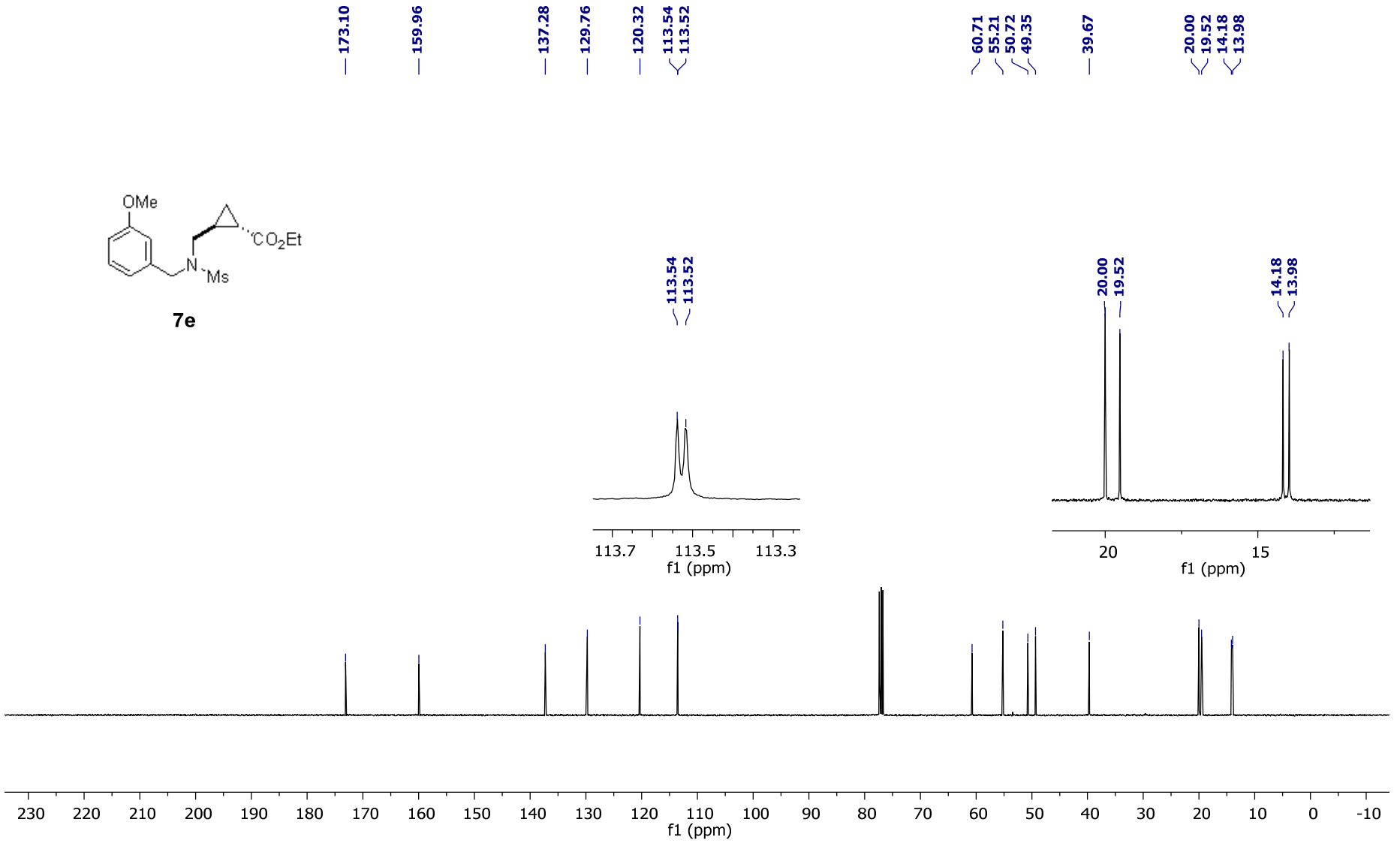

OMe
HN
CCl3
O
O
1d
f1 (ppm)

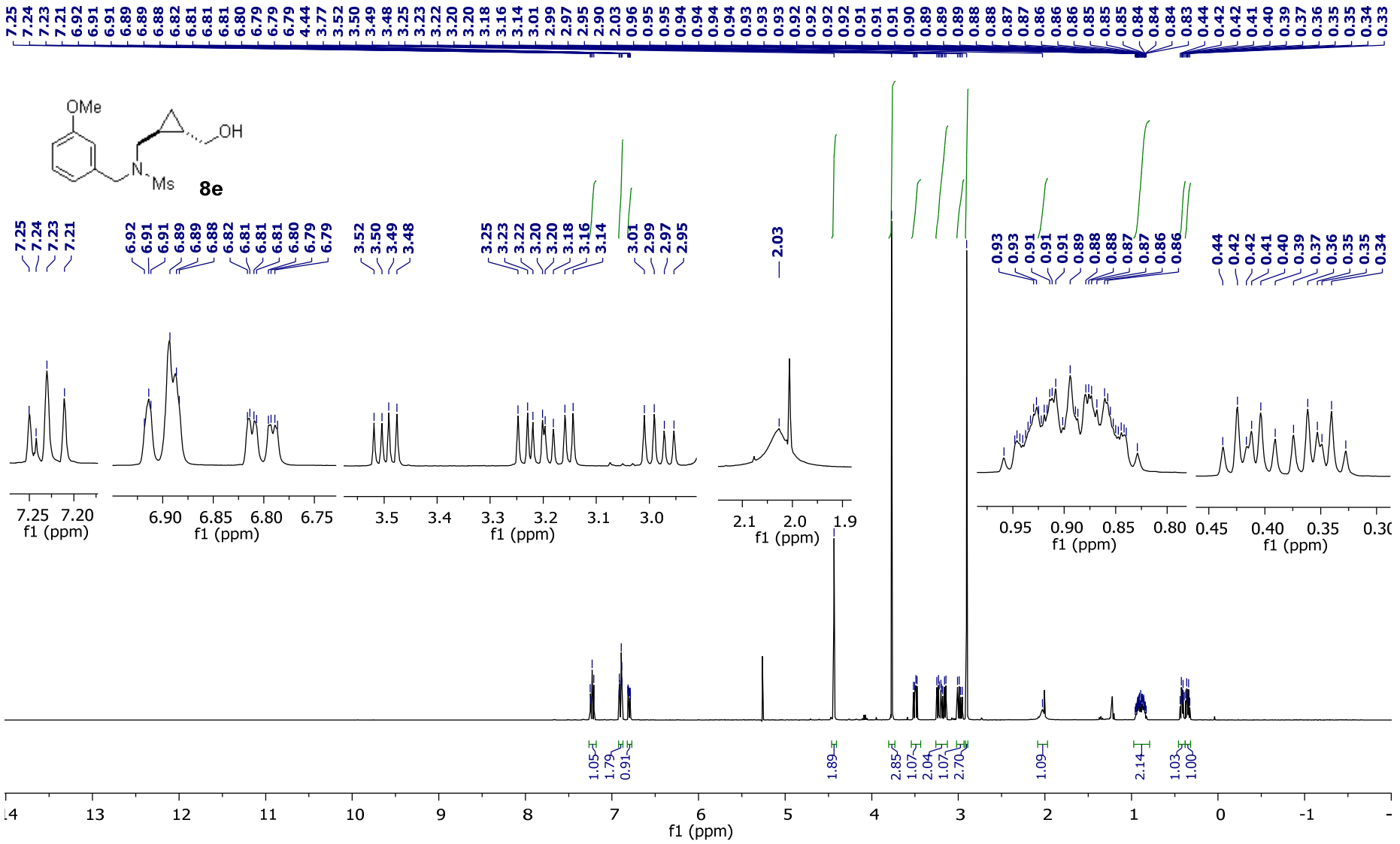

162.84
159.68
140.02
129.32
119.81
113.12
112.84
91.53
72.88
72.58
72.14
55.15
16.91
15.41
8.54
OMe
HN
CCl3
O
O
1d
113.12
112.84
113.4 112.7
f1 (ppm)
72.88
72.58
72.14
73.0 72.5 72.0 71.5
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

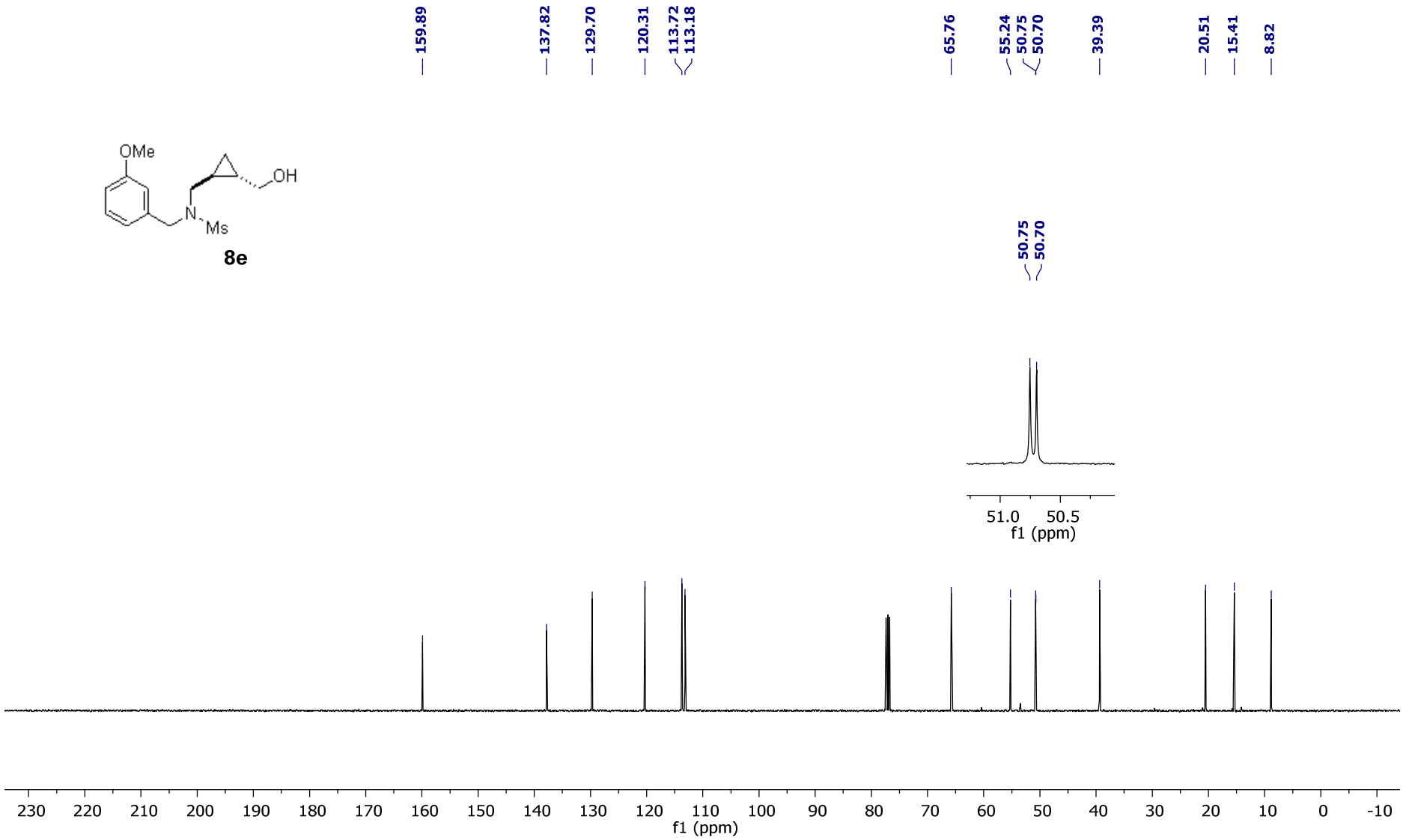

OMe
CO2Et
NH
14
f1 (ppm)

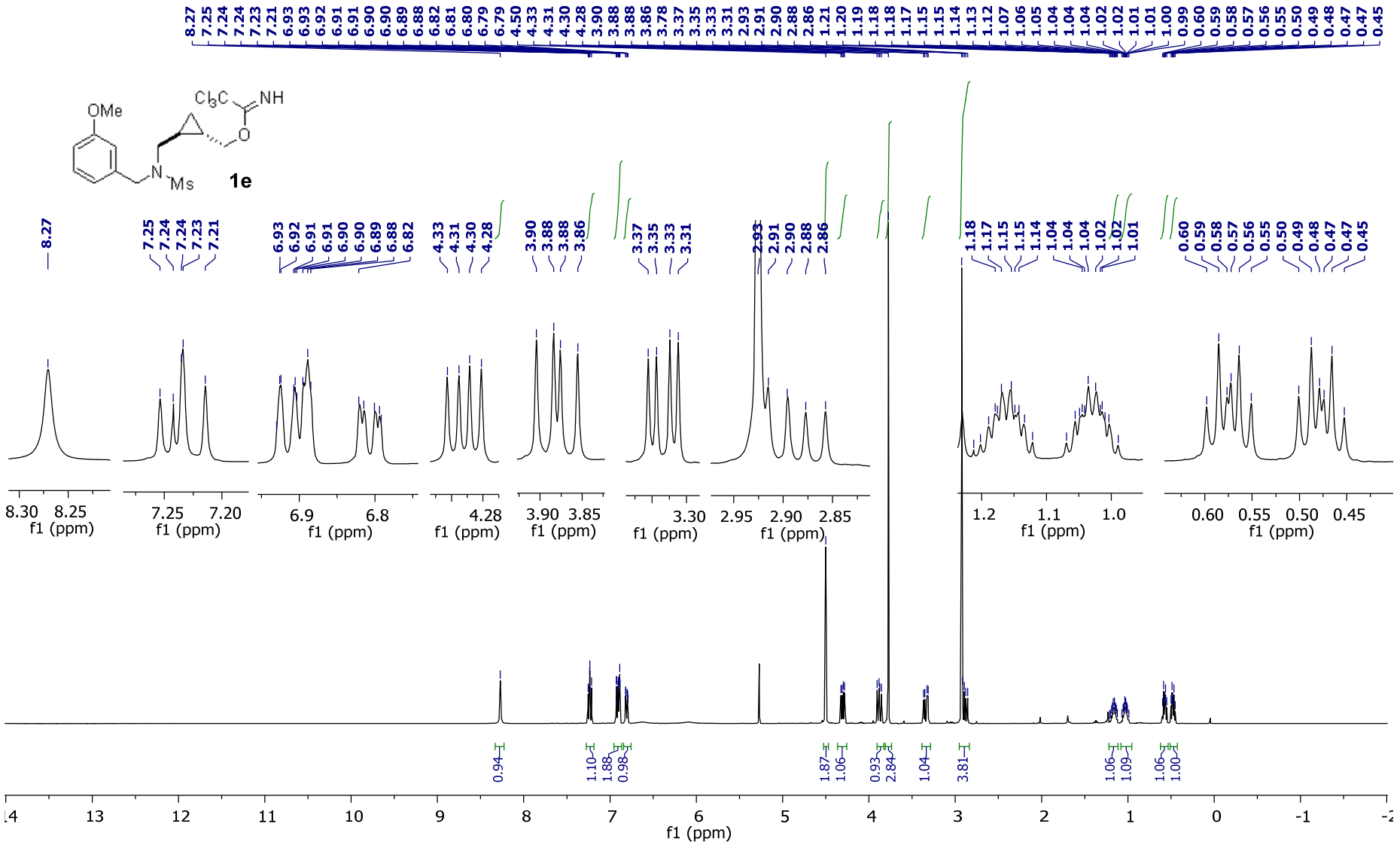

173.74
159.76
140.93
129.42
120.44
113.56
112.74
60.45
55.17
53.15
51.55
22.06
19.19
14.20
13.81
OMe
CO2Et
NH
14
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

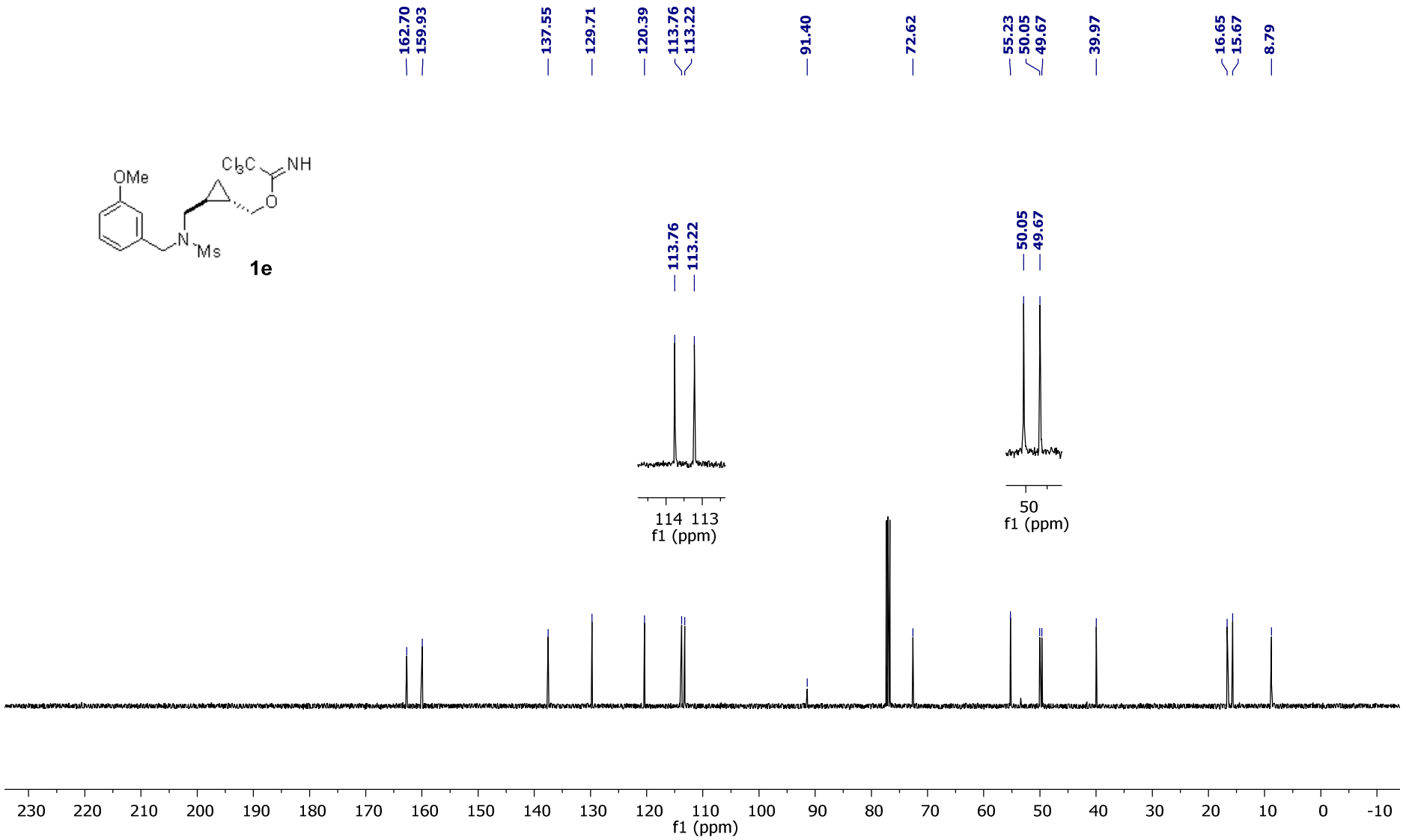

OMe
CO2Et
N
Ms
7e
f1 (ppm)

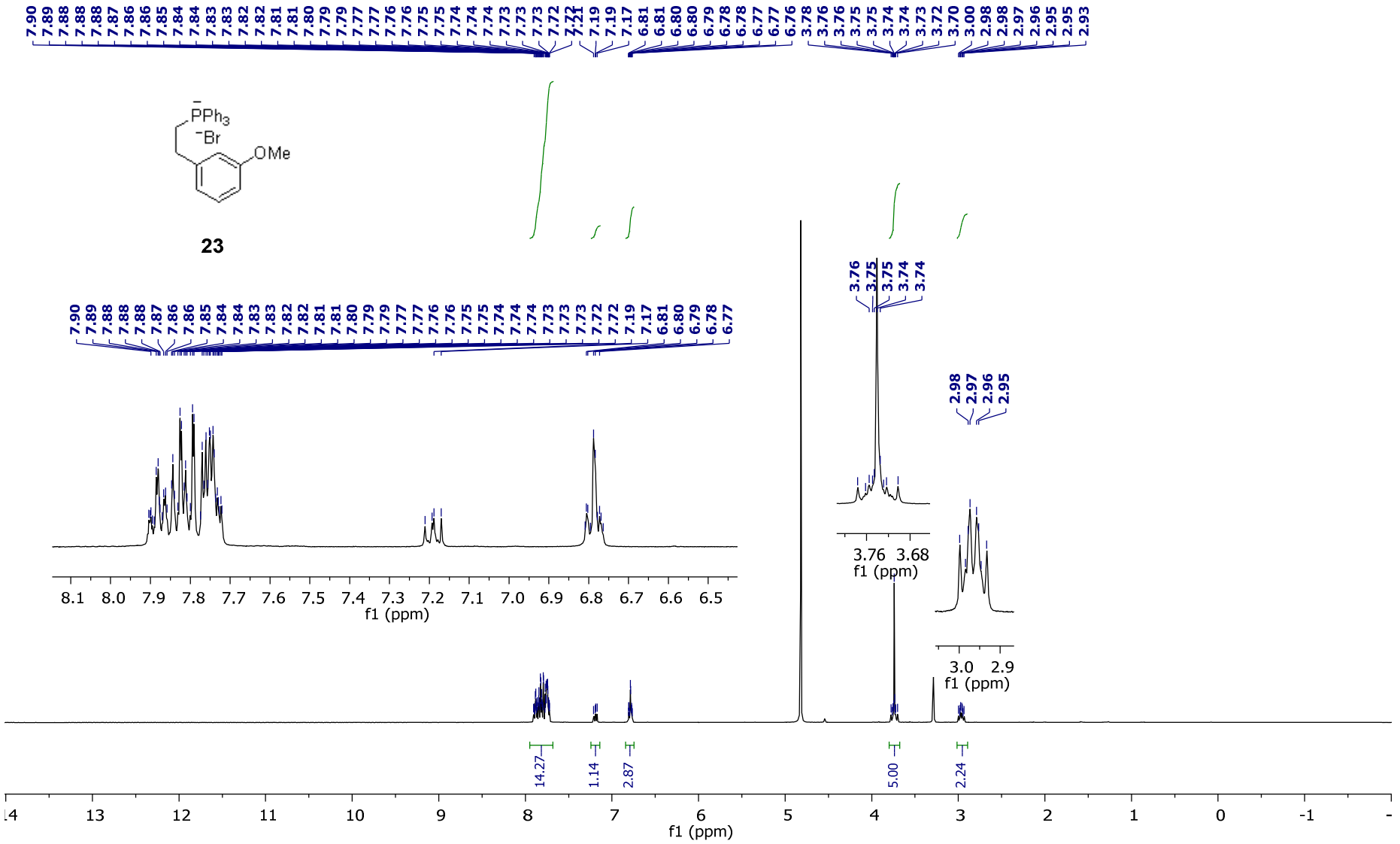

173.10
159.96
137.28
129.76
120.32
113.54
113.52
60.71
55.21
50.72
49.35
39.67
20.00
19.52
14.18
13.98
OMe
CO2Et
N
Ms
7e
113.7
113.5
113.3
f1 (ppm)
20
15
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

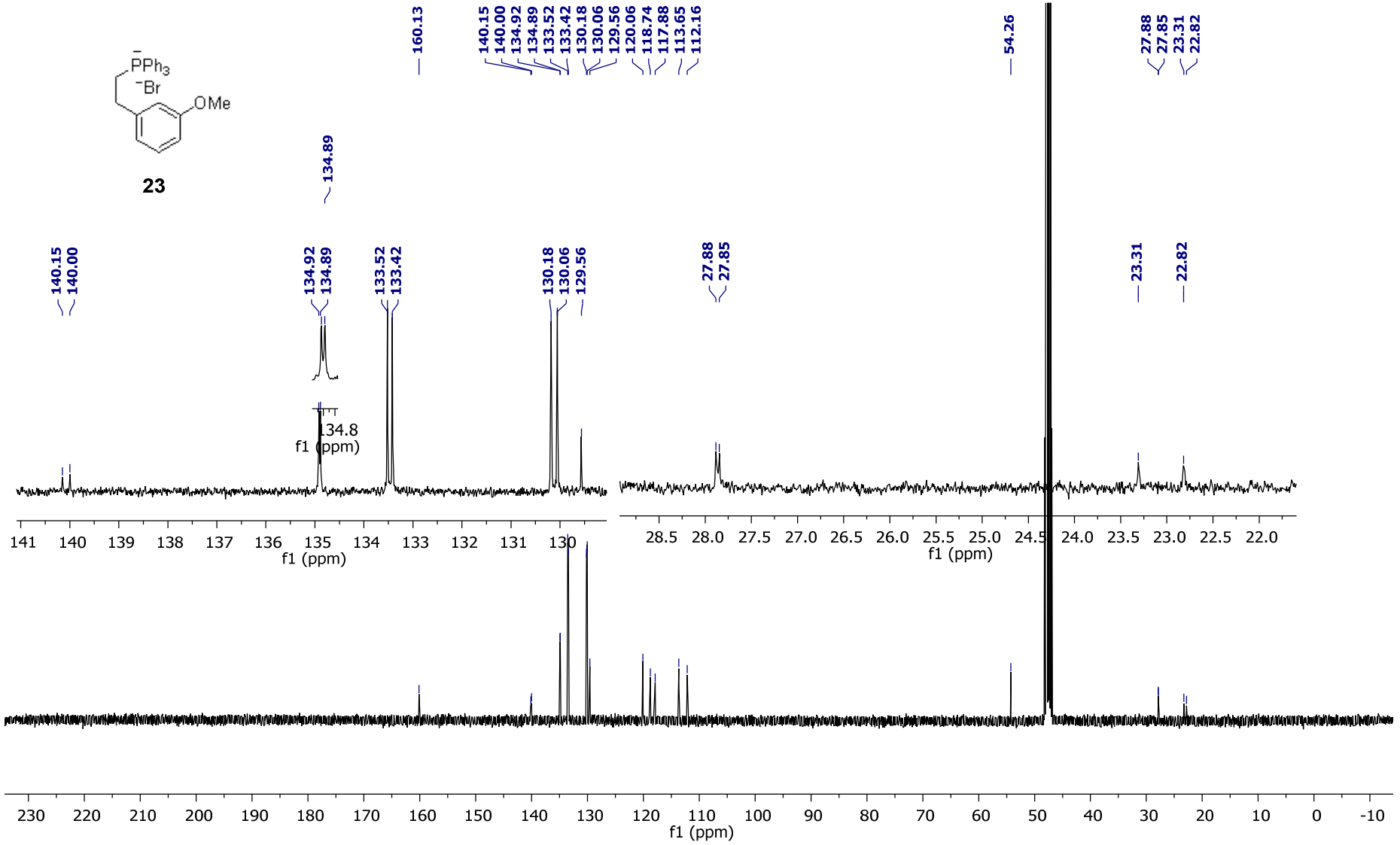

OMe
OH
N
Ms
8e
f1 (ppm)

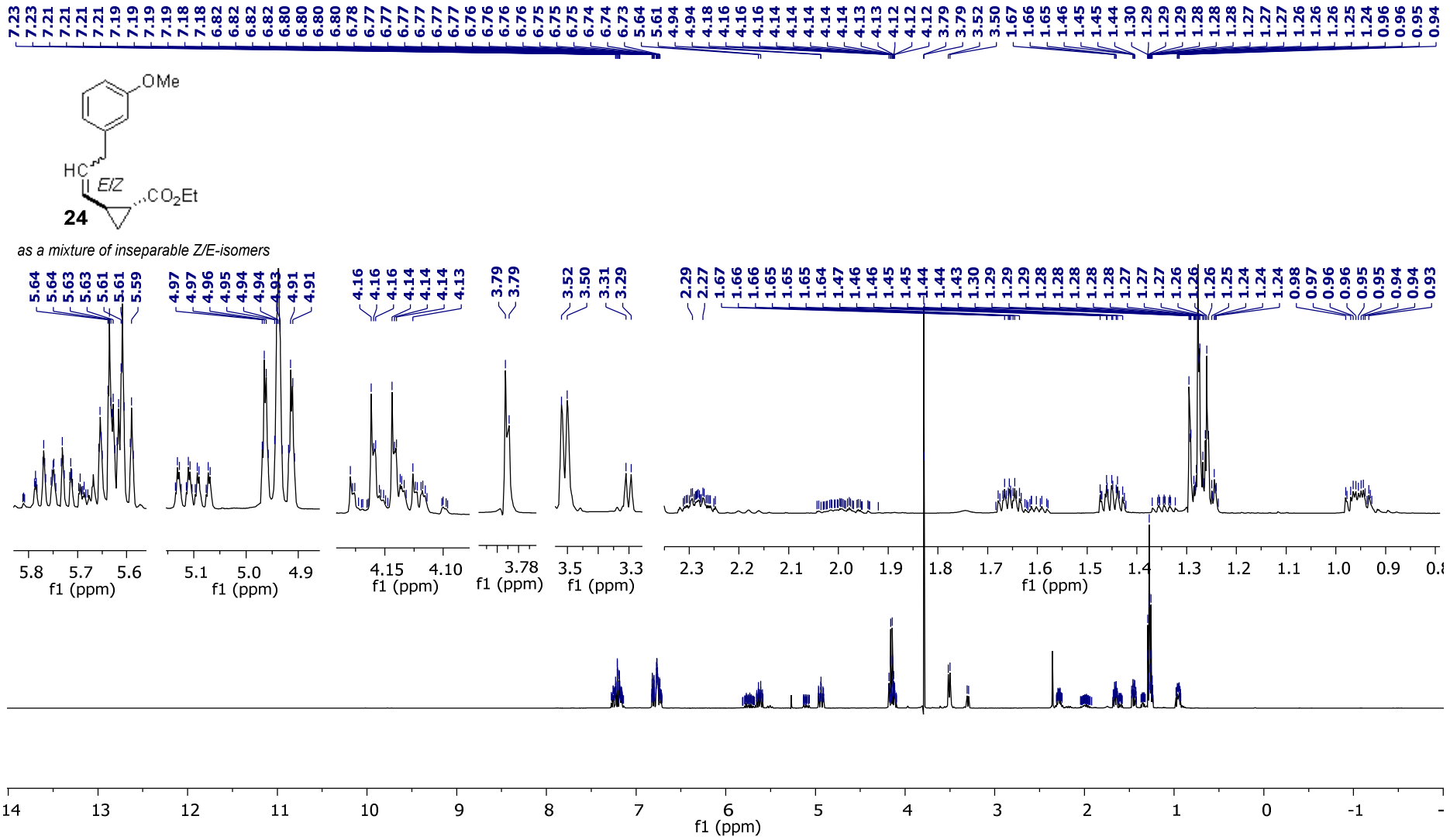

159.89
137.82
129.70
120.31
113.72
113.18
65.76
55.24
50.75
50.70
39.39
20.51
15.41
8.82
OMe
OH
N
Ms
8e
50.75
50.70
51.0
50.5
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

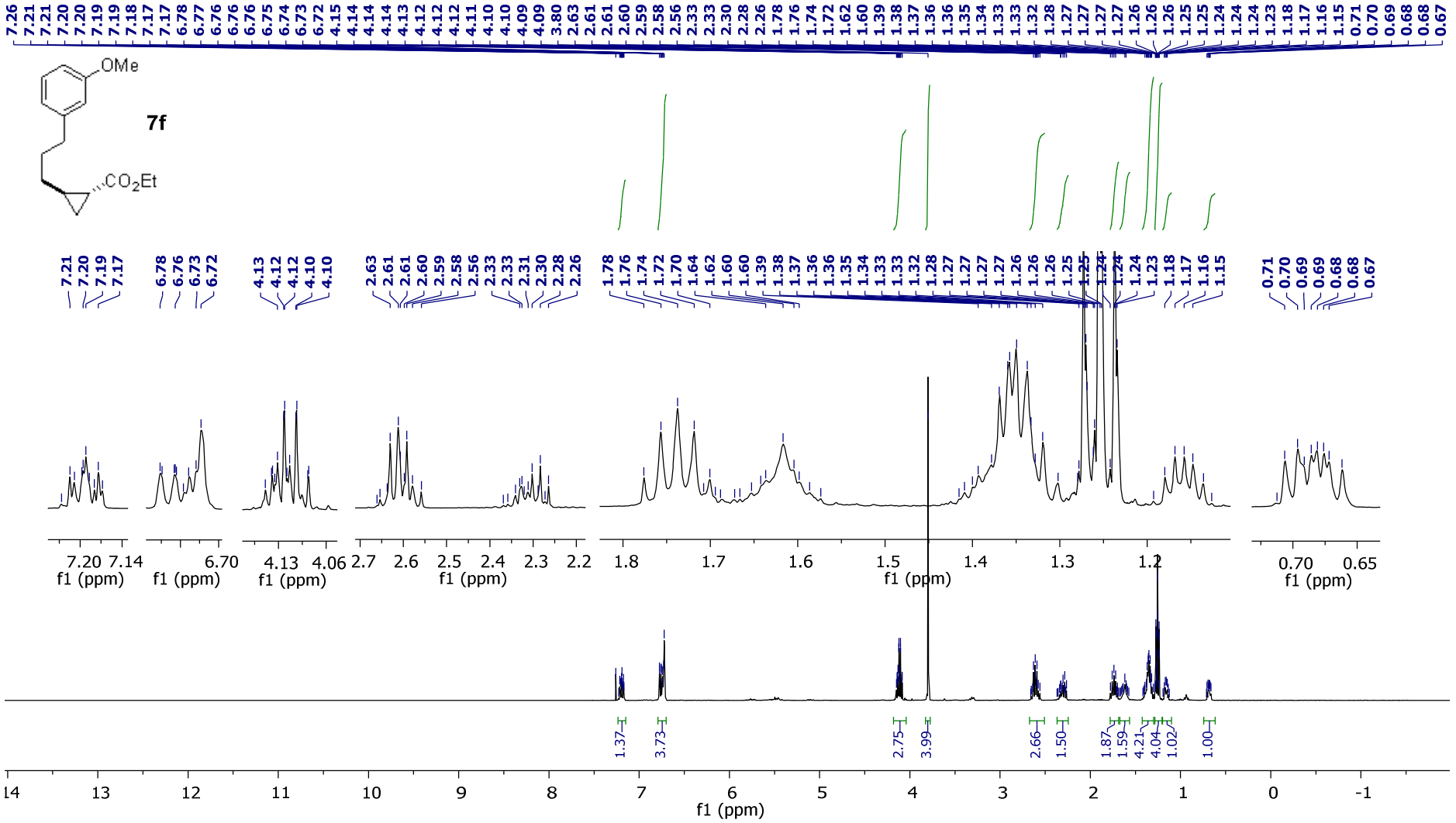

OMe
Cl3C
NH
O
N
Ms
1e
f1 (ppm)

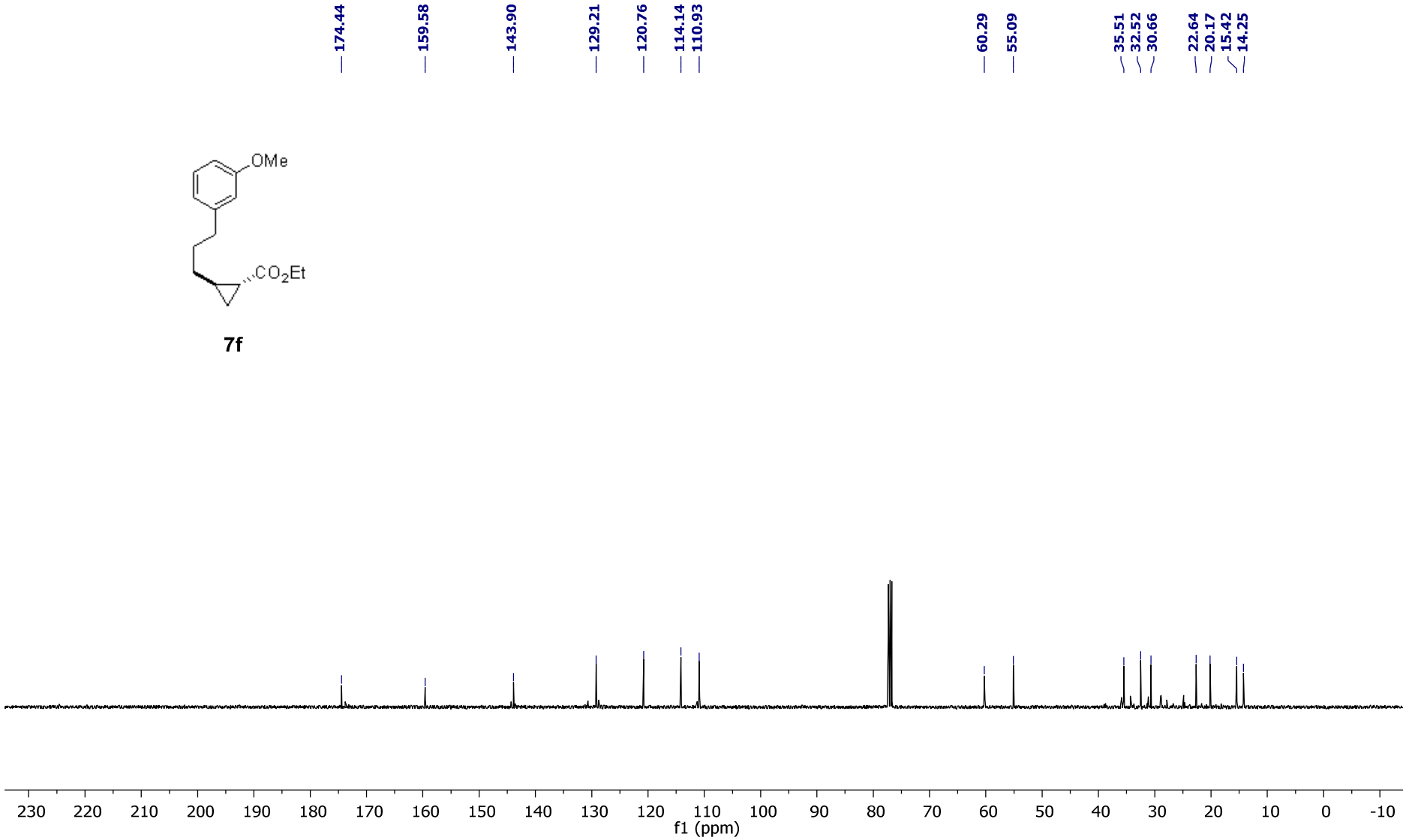

162.70
159.93
137.55
129.71
120.39
113.76
113.22
91.40
72.62
55.23
50.05
49.67
39.97
16.65
15.67
8.79
OMe
Cl3C
NH
O
N
Ms
1e
113.76
113.22
114 113
f1 (ppm)
50.05
49.67
50
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


PPh3
Br
OMe
23
f1 (ppm)

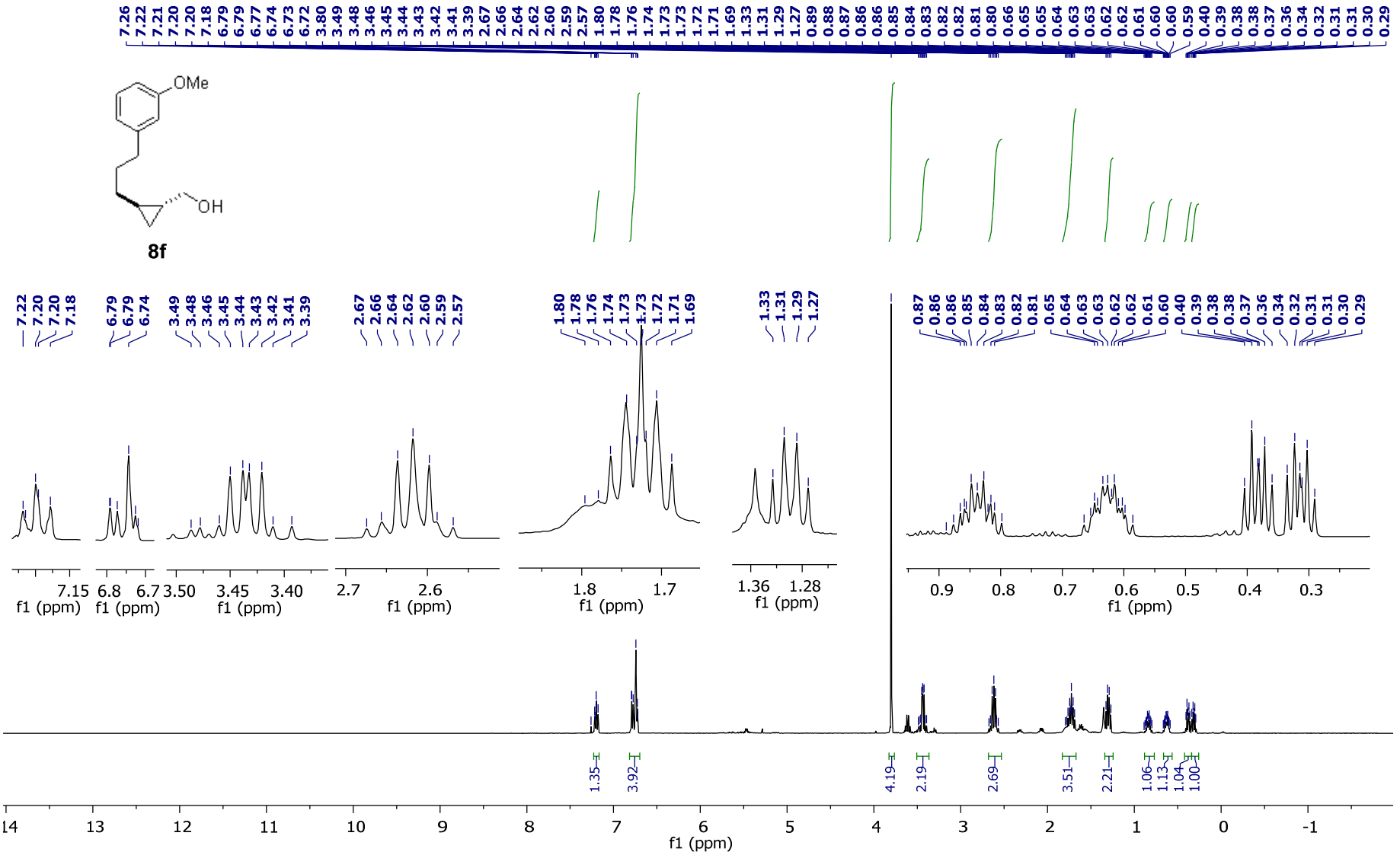

PPh3
Br
OMe
23
160.13
140.15
140.00
134.92
134.89
133.52
133.42
130.18
130.06
129.56
120.06
118.74
117.88
113.65
112.16
54.26
27.88
27.85
23.31
22.82
134.8
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

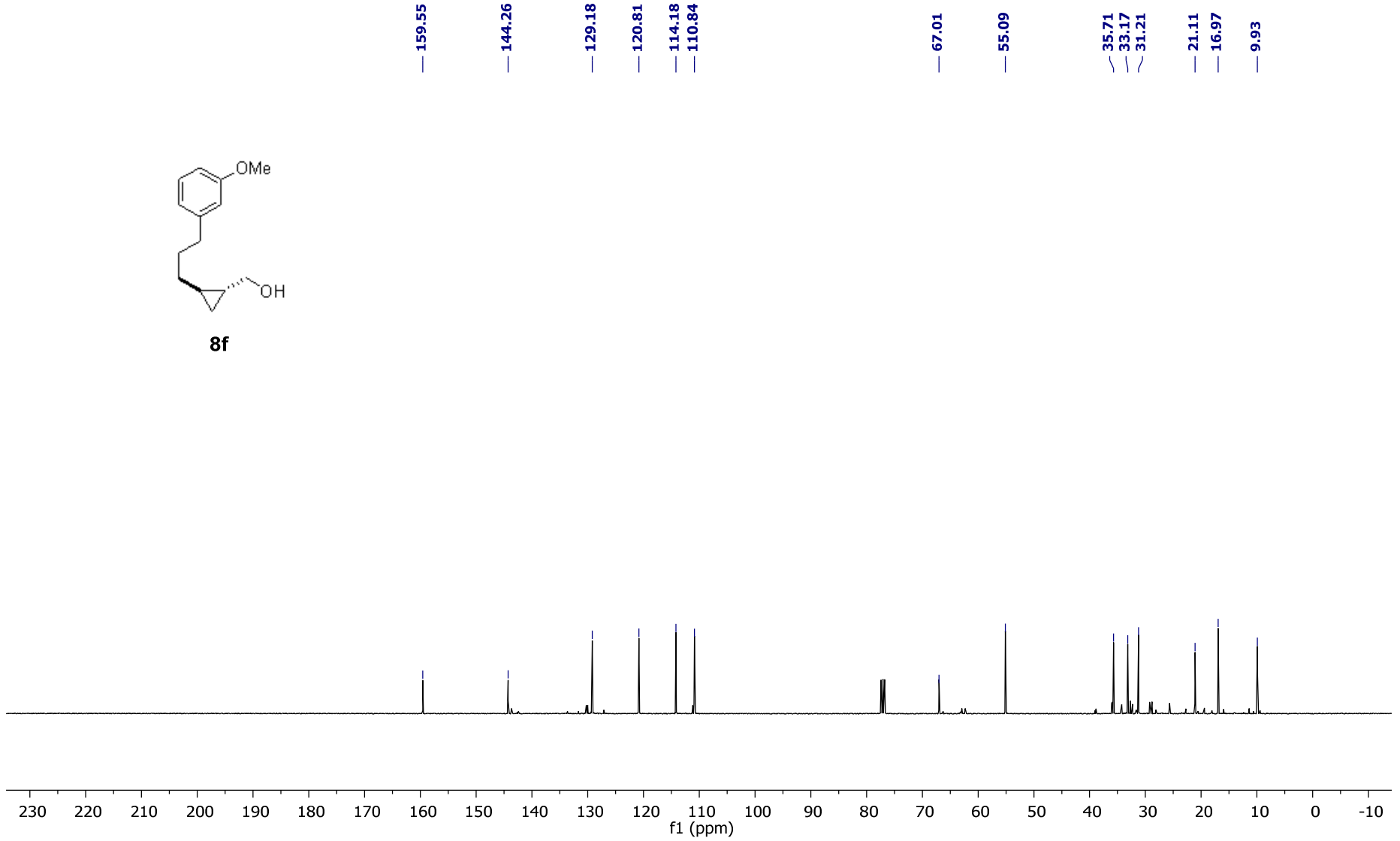

OMe
HC
E/Z
CO2Et
24
as a mixture of inseparable Z/E-isomers
f1 (ppm)


OMe
7f
CO2Et
f1 (ppm)

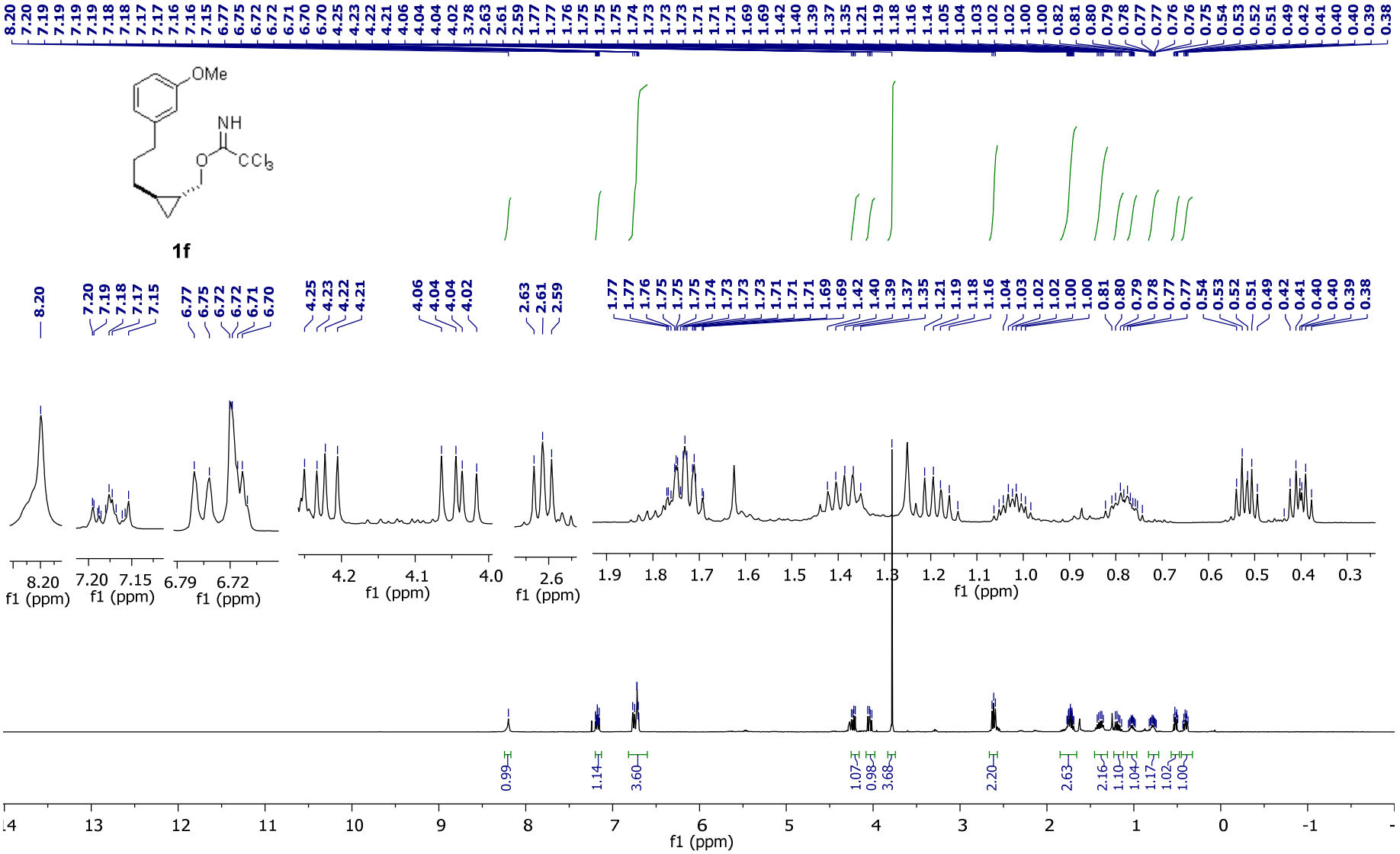

174.44
159.58
143.90
129.21
120.76
114.14
110.93
60.29
55.09
35.51
32.52
30.66
22.64
20.17
15.42
14.25
OMe
CO2Et
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

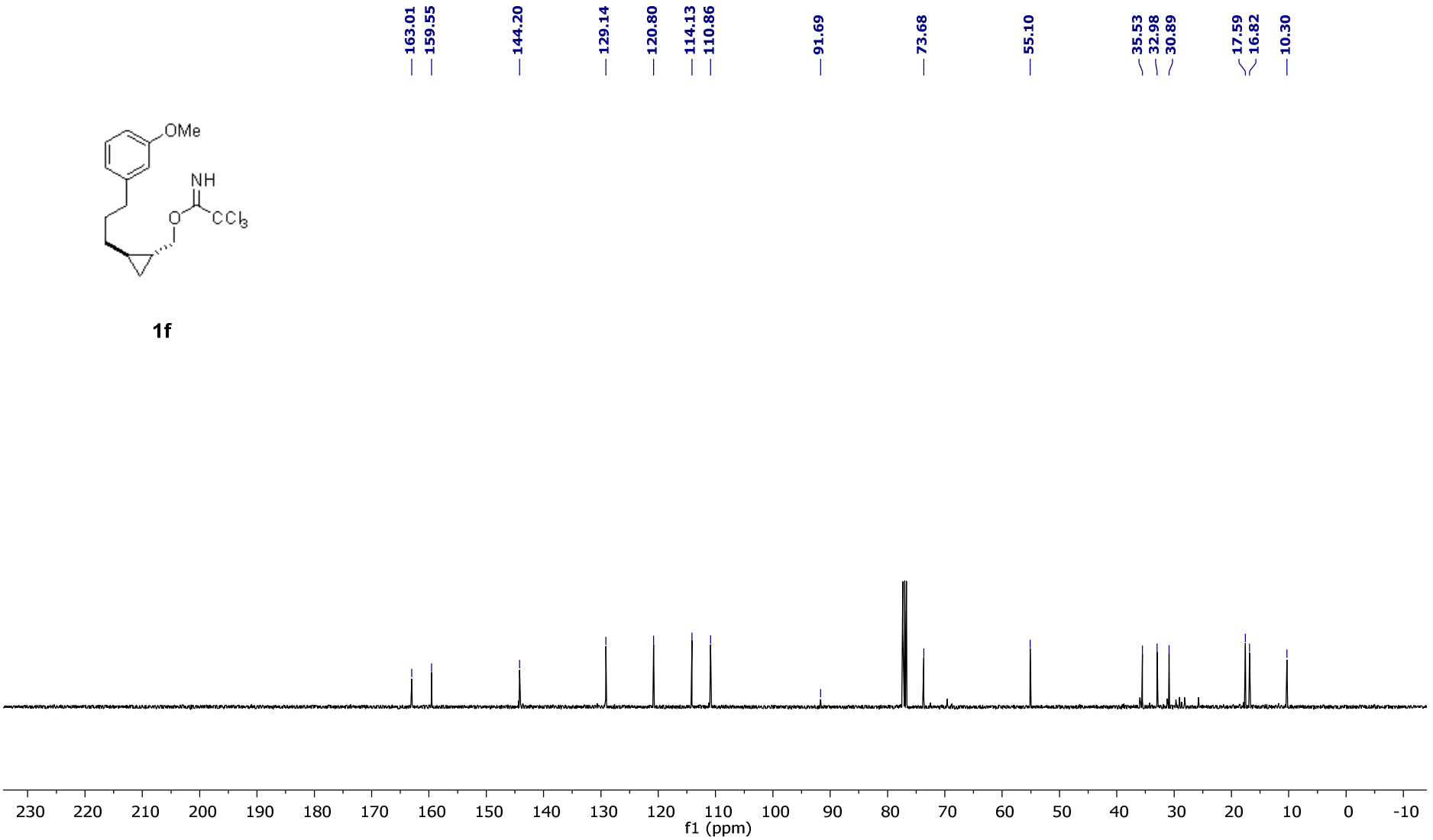
7f


OMe
OH
8f
f1 (ppm)

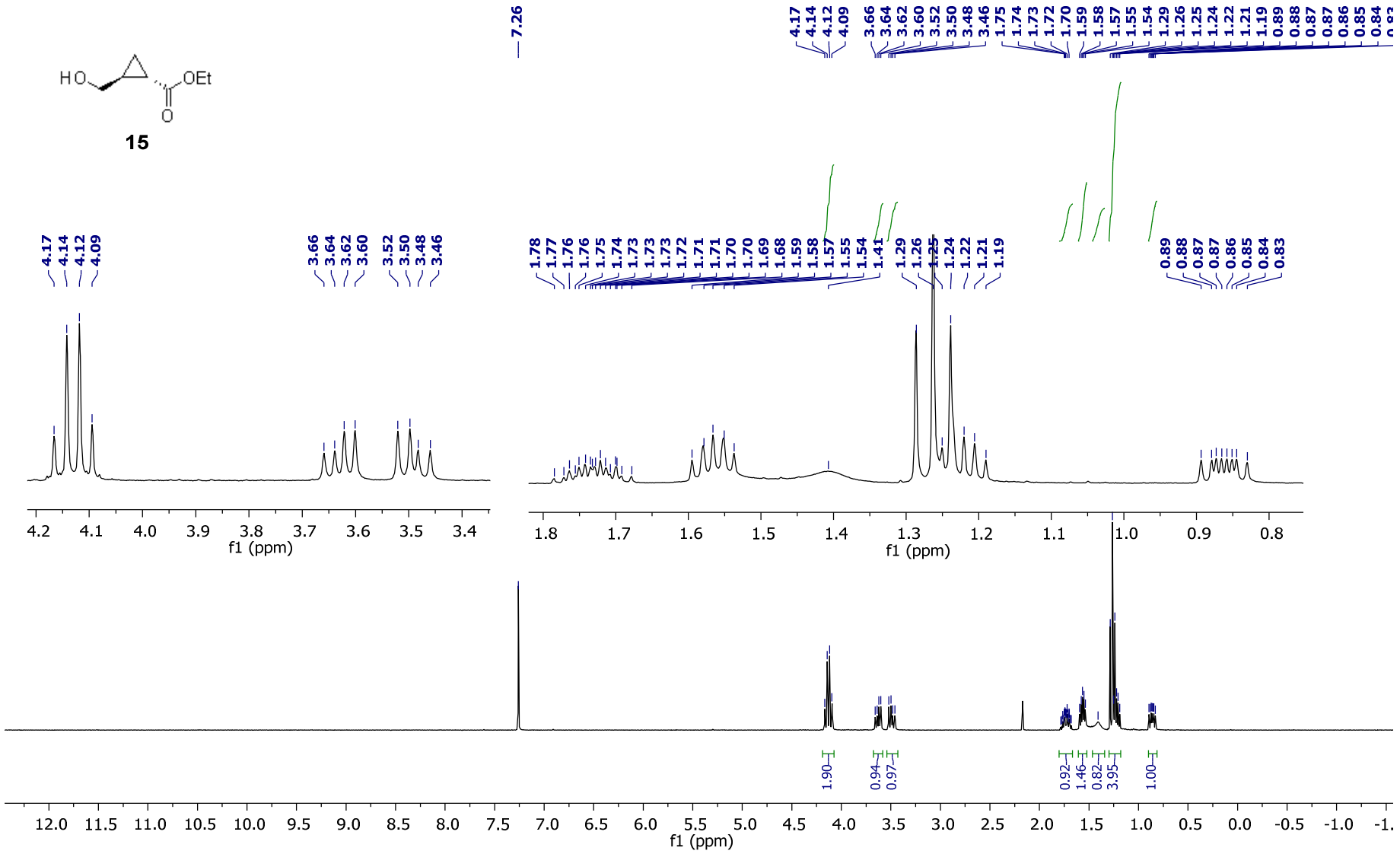

159.55
144.26
129.18
120.81
114.18
110.84
67.01
55.09
35.71
33.17
31.21
21.11
16.97
9.93
OMe
OH
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

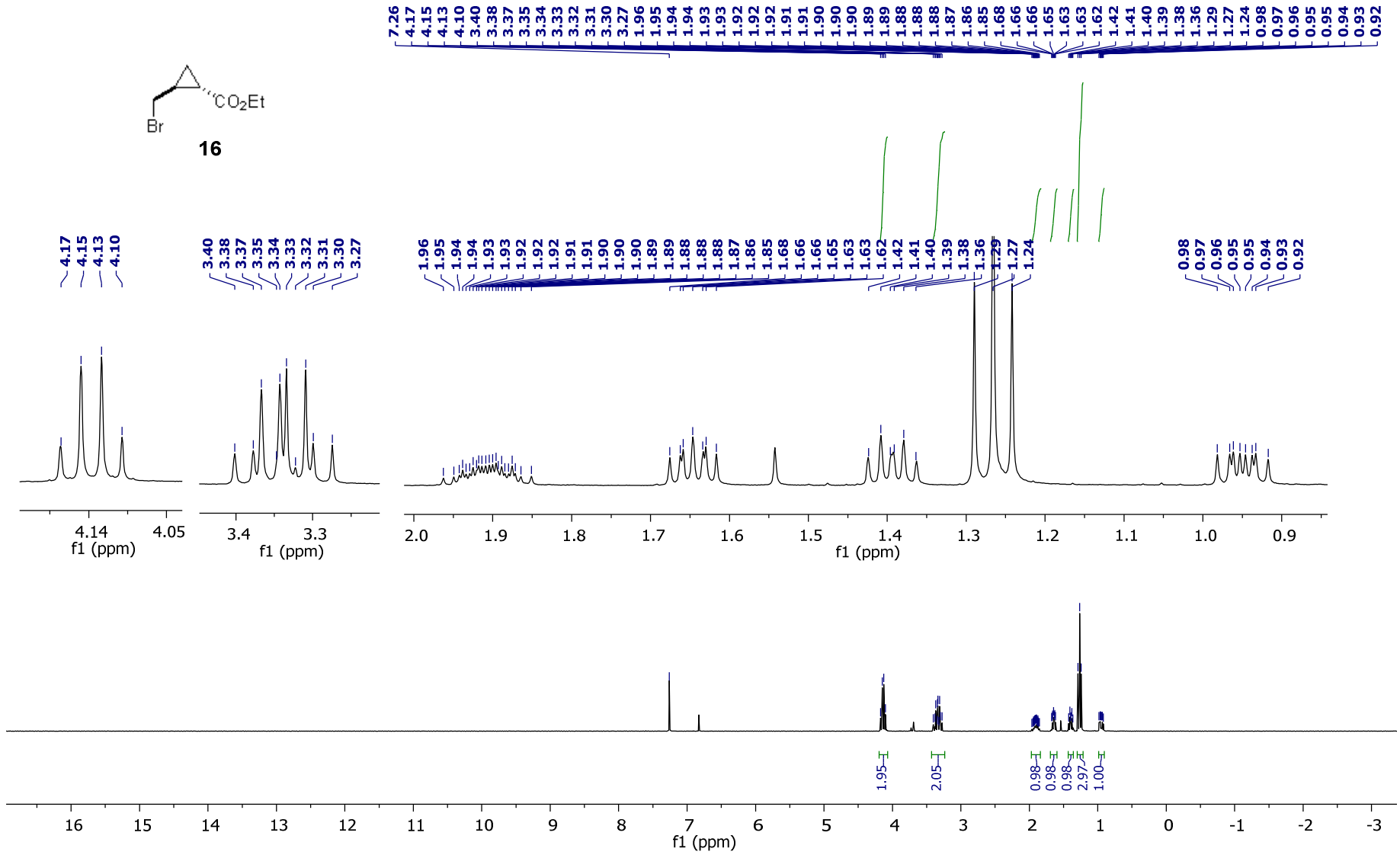
8f

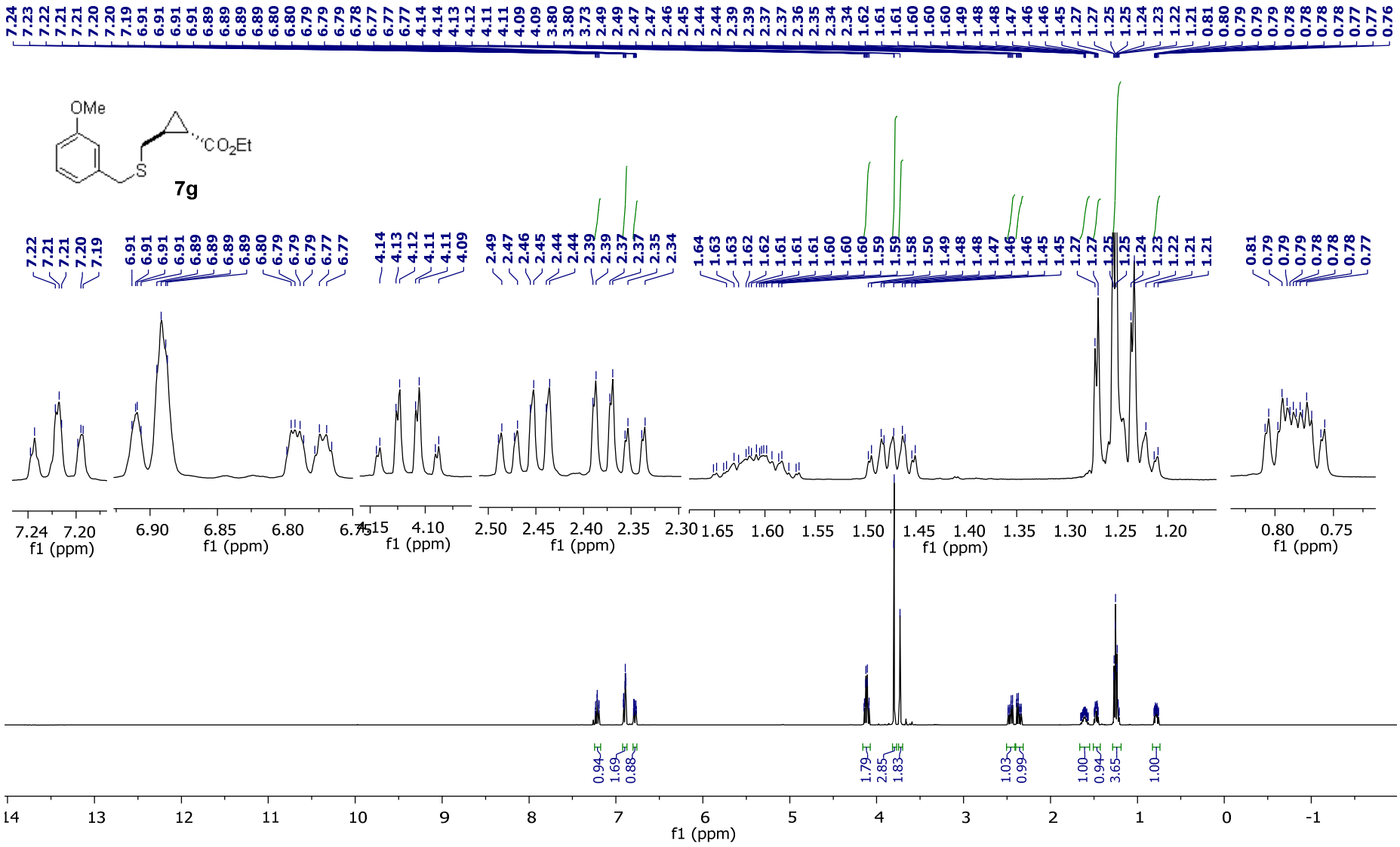

OMe
NH
O
CCl3
1f
f1 (ppm)

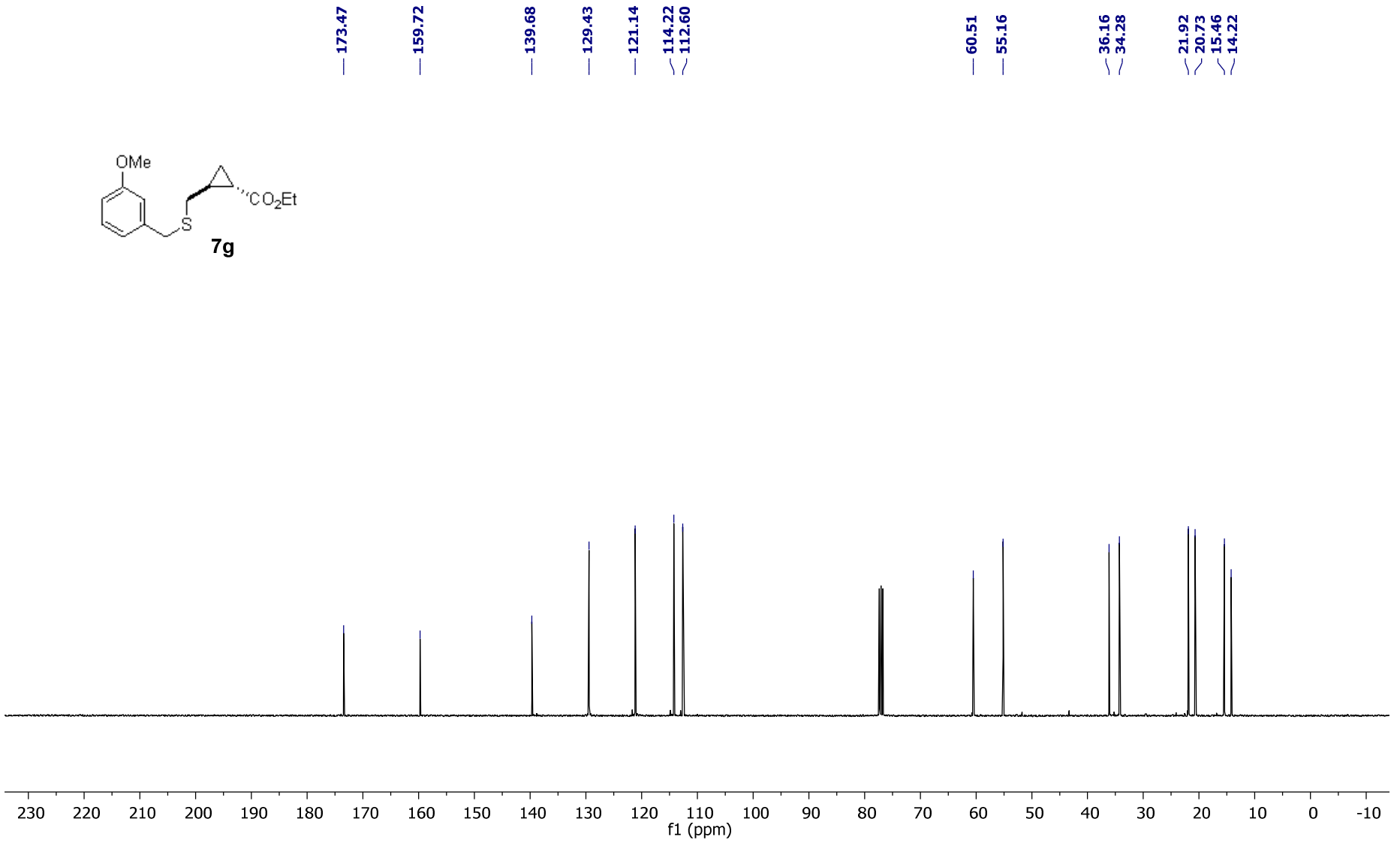

163.01
159.55
144.20
129.14
120.80
114.13
110.86
91.69
73.68
55.10
35.53
32.98
30.89
17.59
16.82
10.30
OMe
NH
O
CCl3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

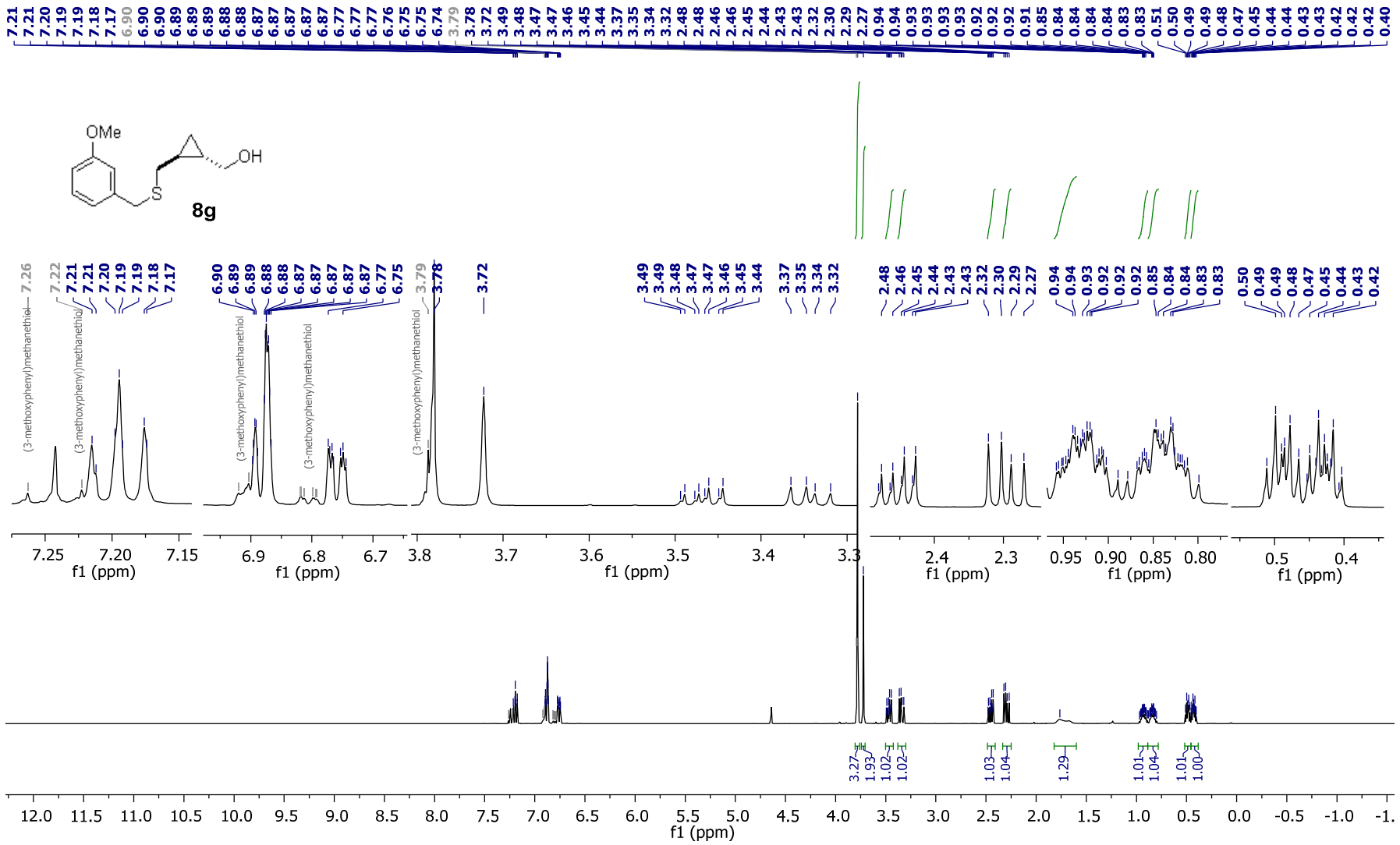
1f

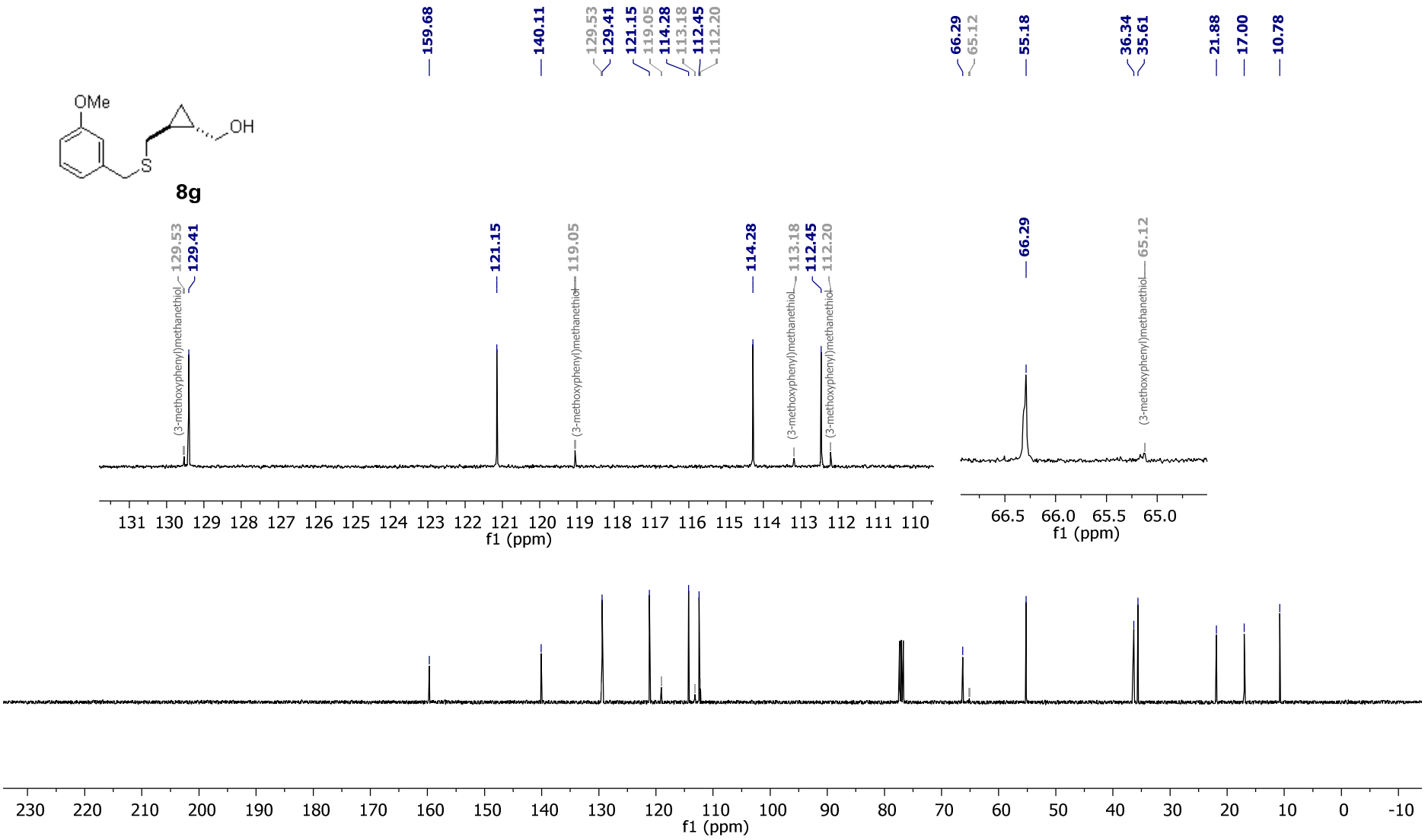

HO
OEt
O
15
7.26
4.17
4.14
4.12
4.09
3.66
3.64
3.62
3.60
3.52
3.50
3.48
3.46
1.78
1.77
1.76
1.75
1.74
1.73
1.72
1.71
1.70
1.69
1.68
1.59
1.58
1.57
1.55
1.54
1.41
1.29
1.26
1.25
1.24
1.22
1.21
1.19
0.89
0.88
0.87
0.86
0.85
0.84
0.83
f1 (ppm)
1.90
0.94
0.97
0.92
1.46
0.82
3.95
1.00

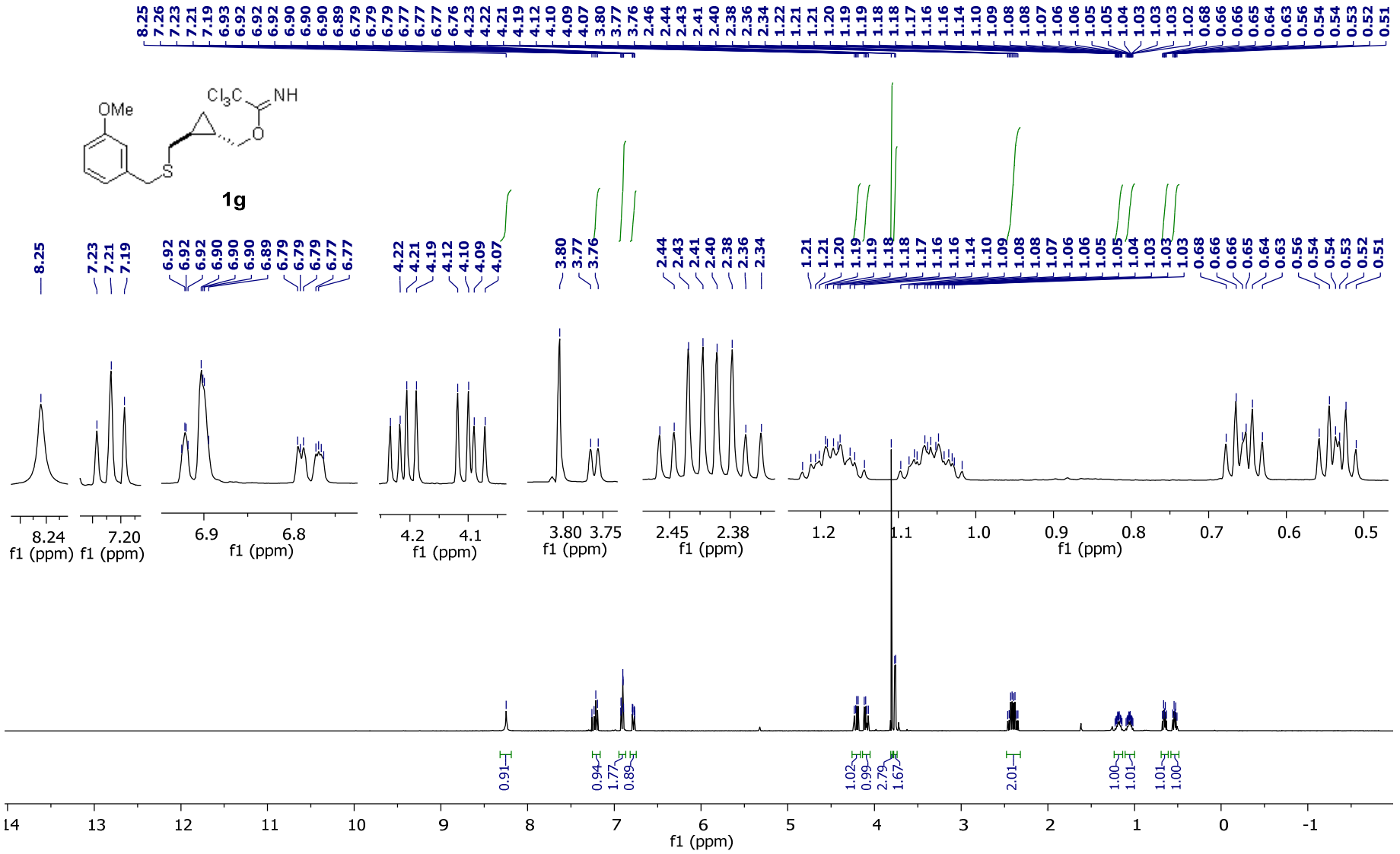

7.26
4.17
4.15
4.13
4.10
3.40
3.38
3.37
3.35
3.34
3.33
3.32
3.31
3.30
3.27
1.96
1.95
1.94
1.94
1.93
1.93
1.92
1.92
1.92
1.91
1.91
1.90
1.90
1.90
1.89
1.89
1.88
1.88
1.88
1.87
1.86
1.85
1.68
1.66
1.66
1.65
1.63
1.63
1.62
1.42
1.41
1.40
1.39
1.38
1.36
1.29
1.27
1.24
0.98
0.97
0.96
0.95
0.95
0.94
0.93
0.92
CO2Et
Br
16
4.14
4.05
f1 (ppm)
3.4
3.3
f1 (ppm)
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
f1 (ppm)
1.95
2.05
0.98
0.98
0.98
2.97
1.00
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
f1 (ppm)

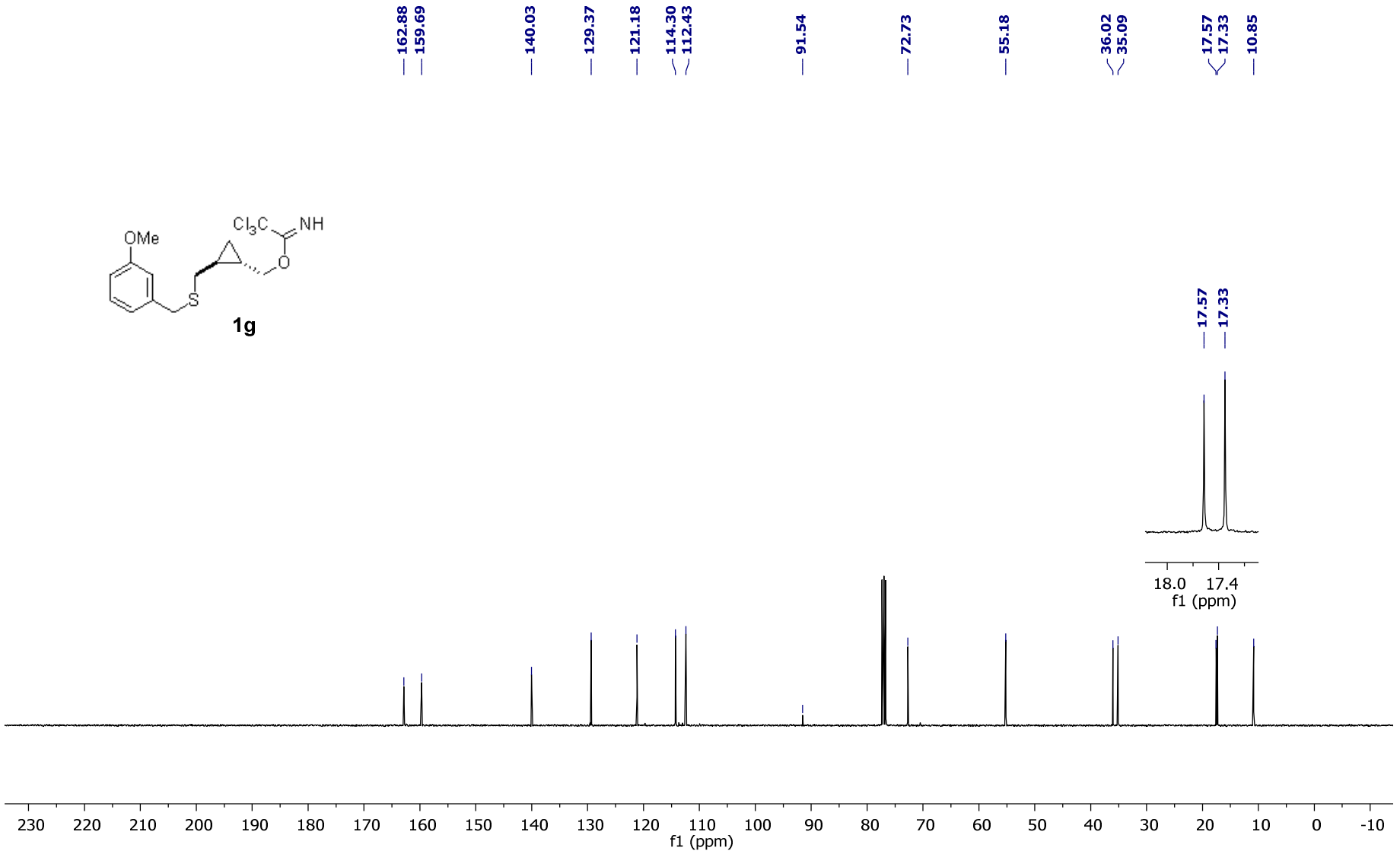

OMe
CO2Et
S
7g
f1 (ppm)

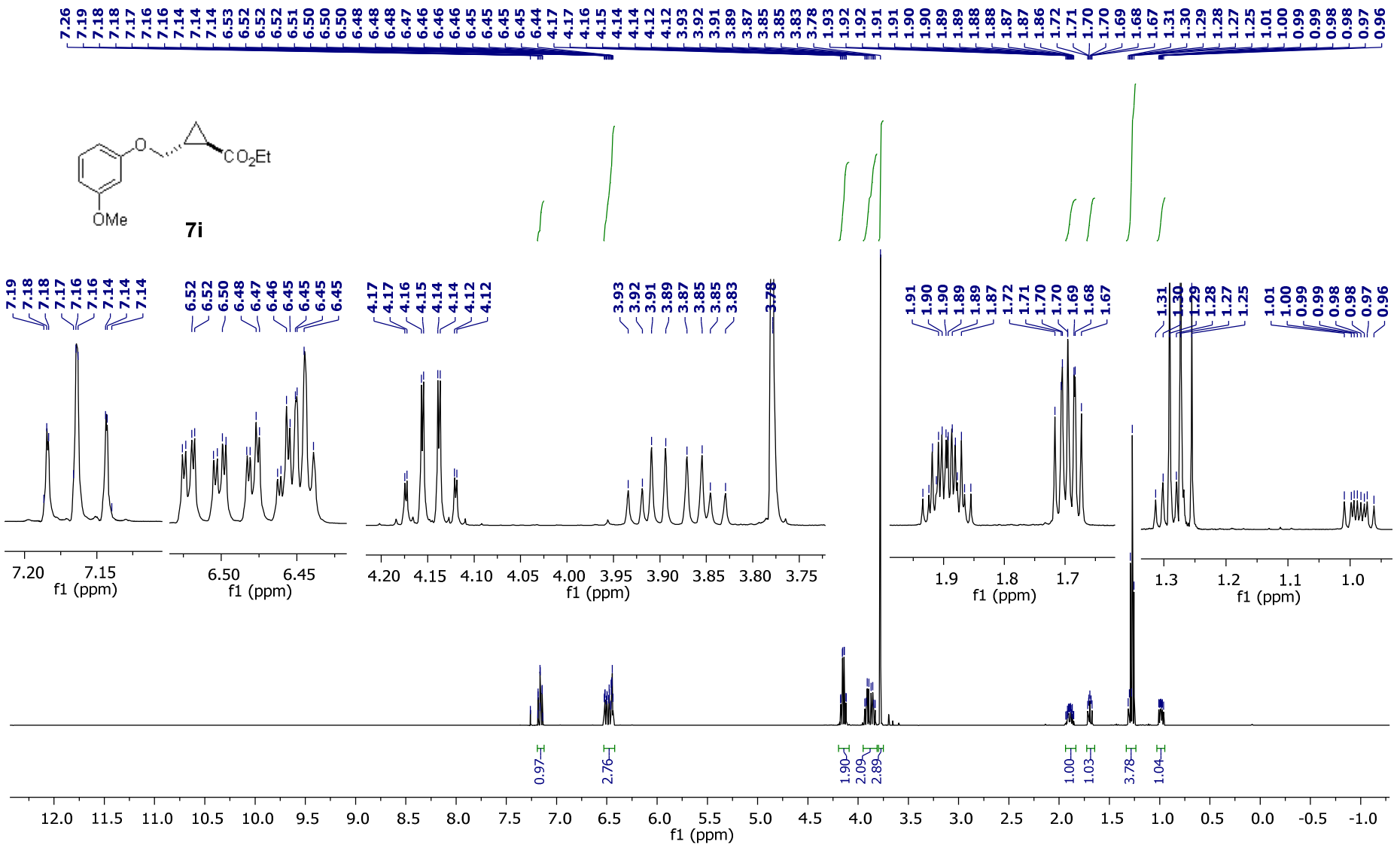

173.47
159.72
139.68
129.43
121.14
114.22
112.60
60.51
55.16
36.16
34.28
21.92
20.73
15.46
14.22
OMe
CO2Et
S
7g
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

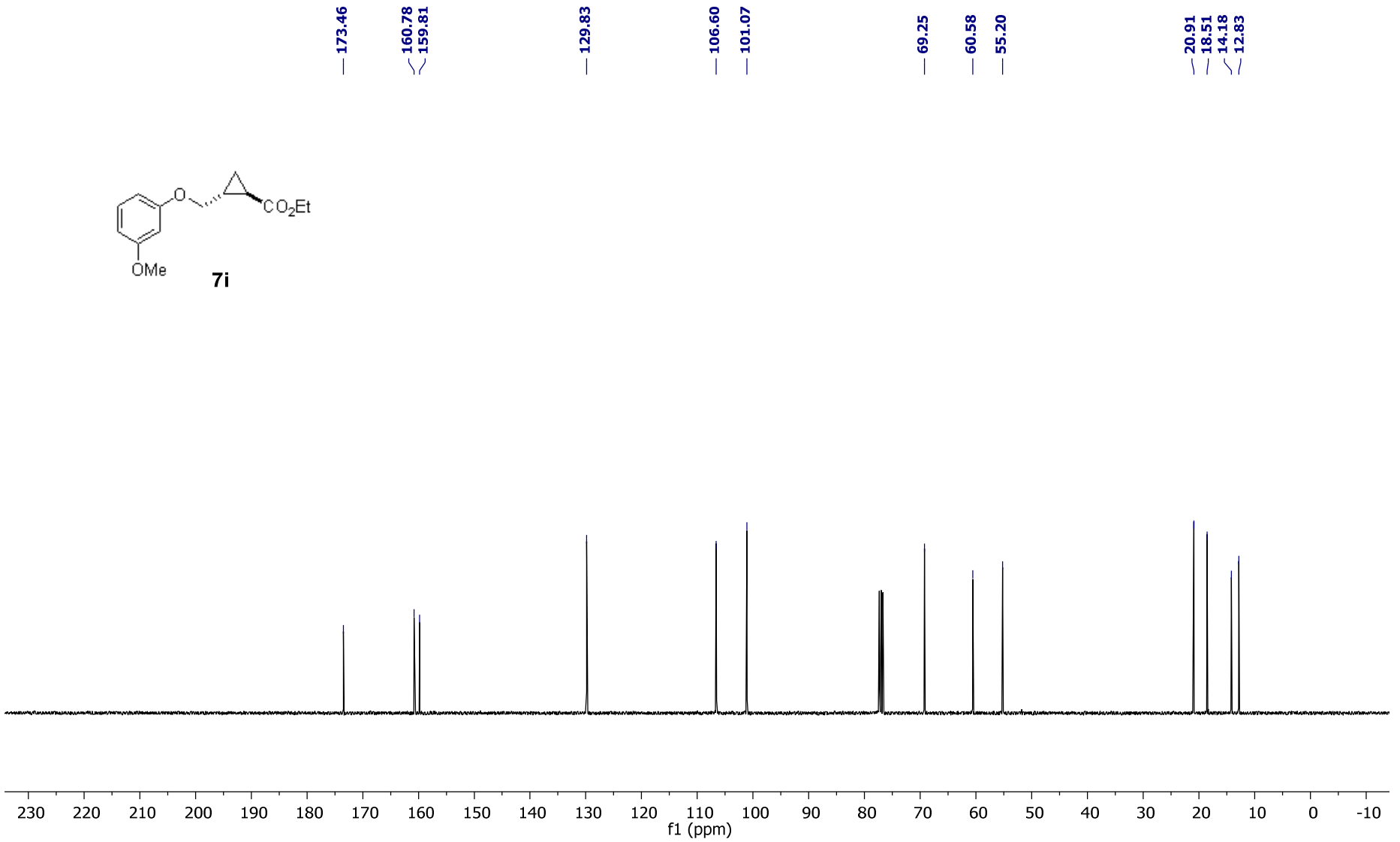

OMe
OH
S
8g
f1 (ppm)

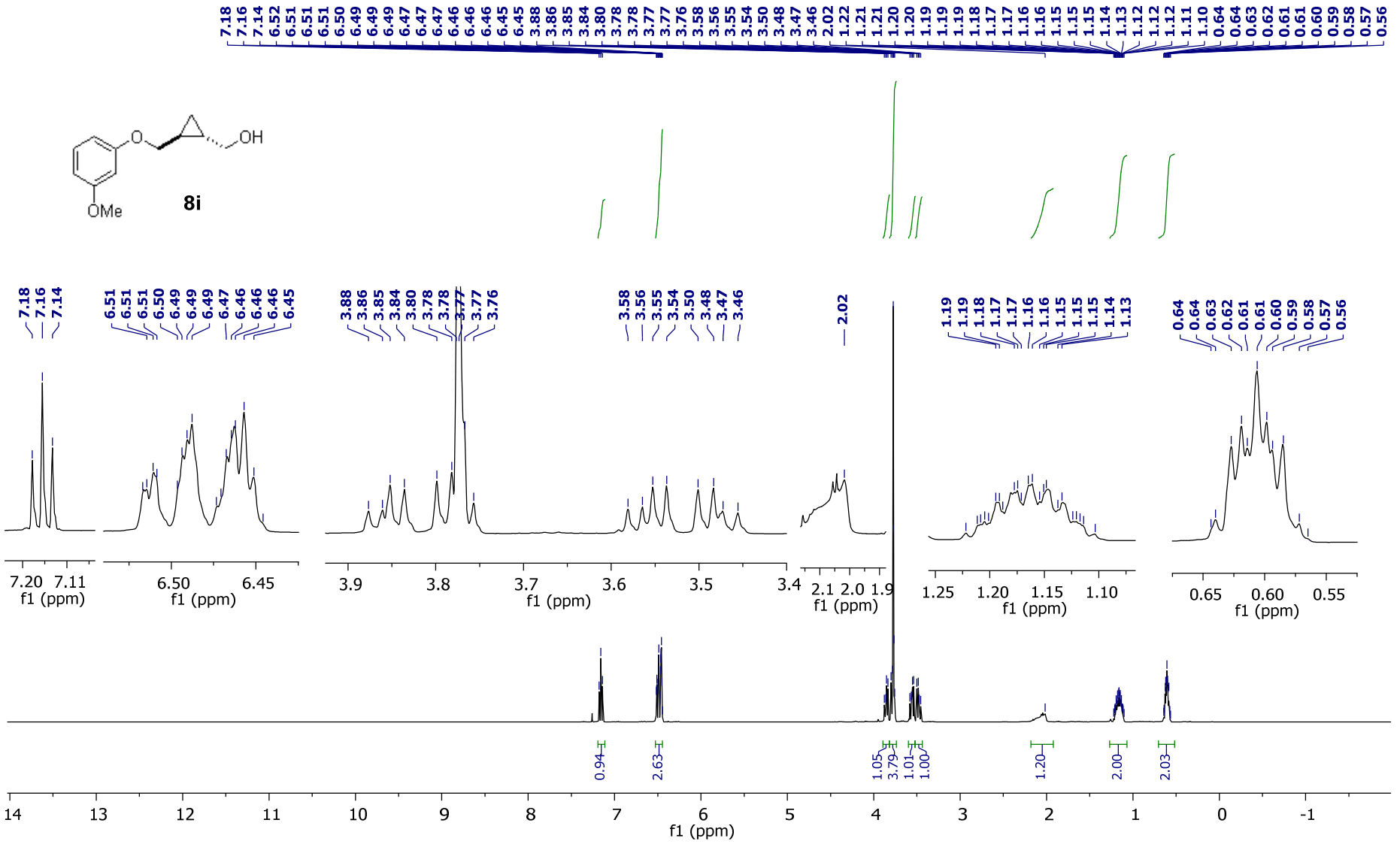

159.68
140.11
129.53
129.41
121.15
119.05
114.28
113.18
112.45
112.20
66.29
65.12
55.18
36.34
35.61
21.88
17.00
10.78
OMe
OH
S
8g
(3-methoxyphenyl)methanethiol
f1 (ppm)
f1 (ppm)
f1 (ppm)

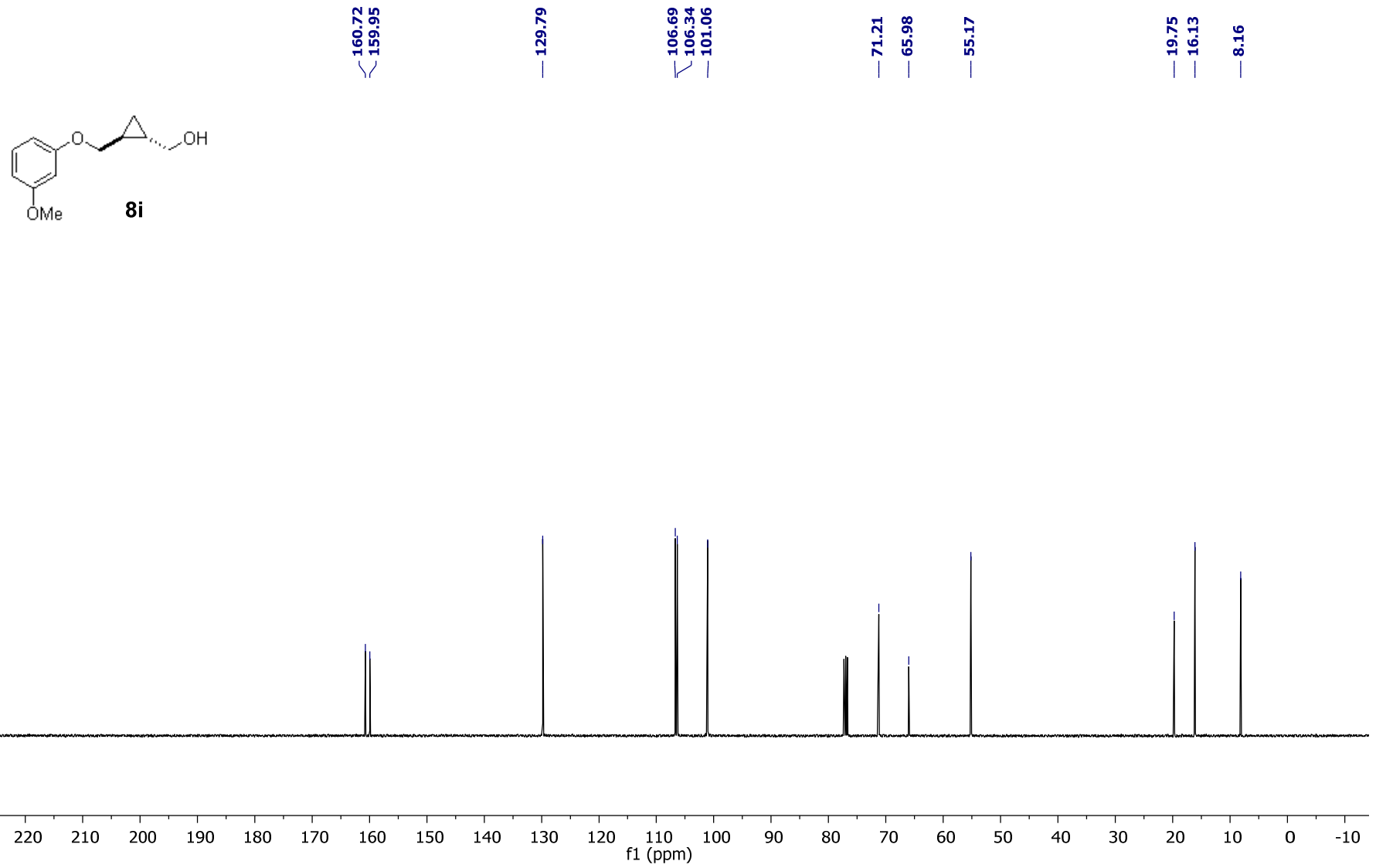

8.25 7.26 7.23 7.21 7.19 6.93 6.92 6.92 6.92 6.90 6.90 6.90 6.89 6.79 6.79 6.79 6.77 6.77 6.76 4.23 4.22 4.21 4.19 4.12 4.10 4.09 4.07 3.80 3.77 3.76 2.46 2.44 2.43 2.41 2.40 2.38 2.36 2.34 1.22 1.21 1.21 1.20 1.19 1.19 1.18 1.18 1.17 1.16 1.16 1.14 1.10 1.09 1.08 1.08 1.07 1.06 1.06 1.05 1.05 1.04 1.03 1.03 1.03 1.02 0.68 0.66 0.66 0.65 0.64 0.63 0.56 0.54 0.54 0.53 0.52 0.51
OMe
Cl3C
NH
O
S
1g
f1 (ppm)
0.91 0.94 1.77 0.89 1.02 0.99 2.79 1.67 2.01 1.00 1.01 1.01 1.00

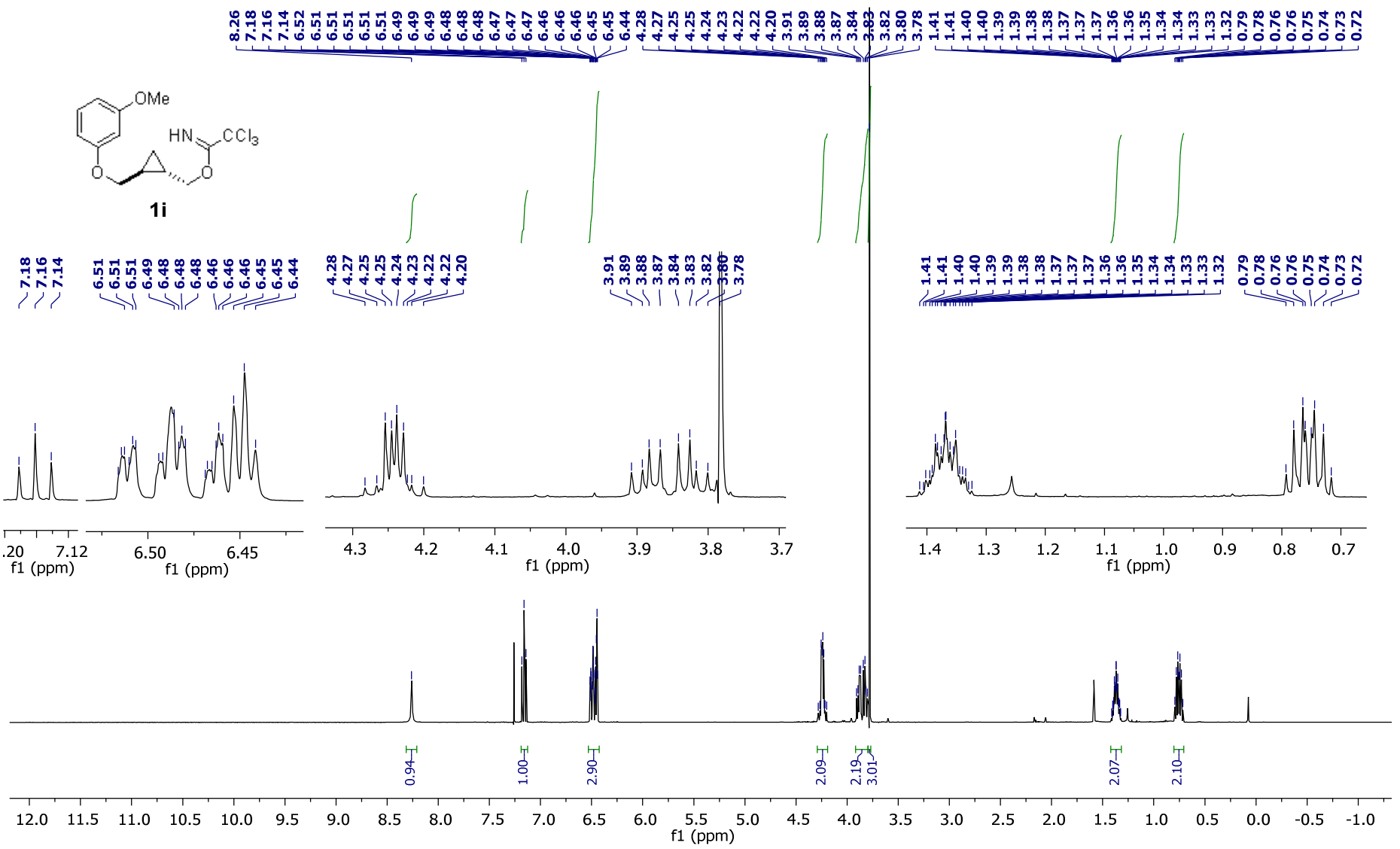

162.88
159.69
140.03
129.37
121.18
114.30
112.43
91.54
72.73
55.18
36.02
35.09
17.57
17.33
10.85
OMe
Cl3C
NH
O
S
1g
17.57
17.33
18.0
17.4
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

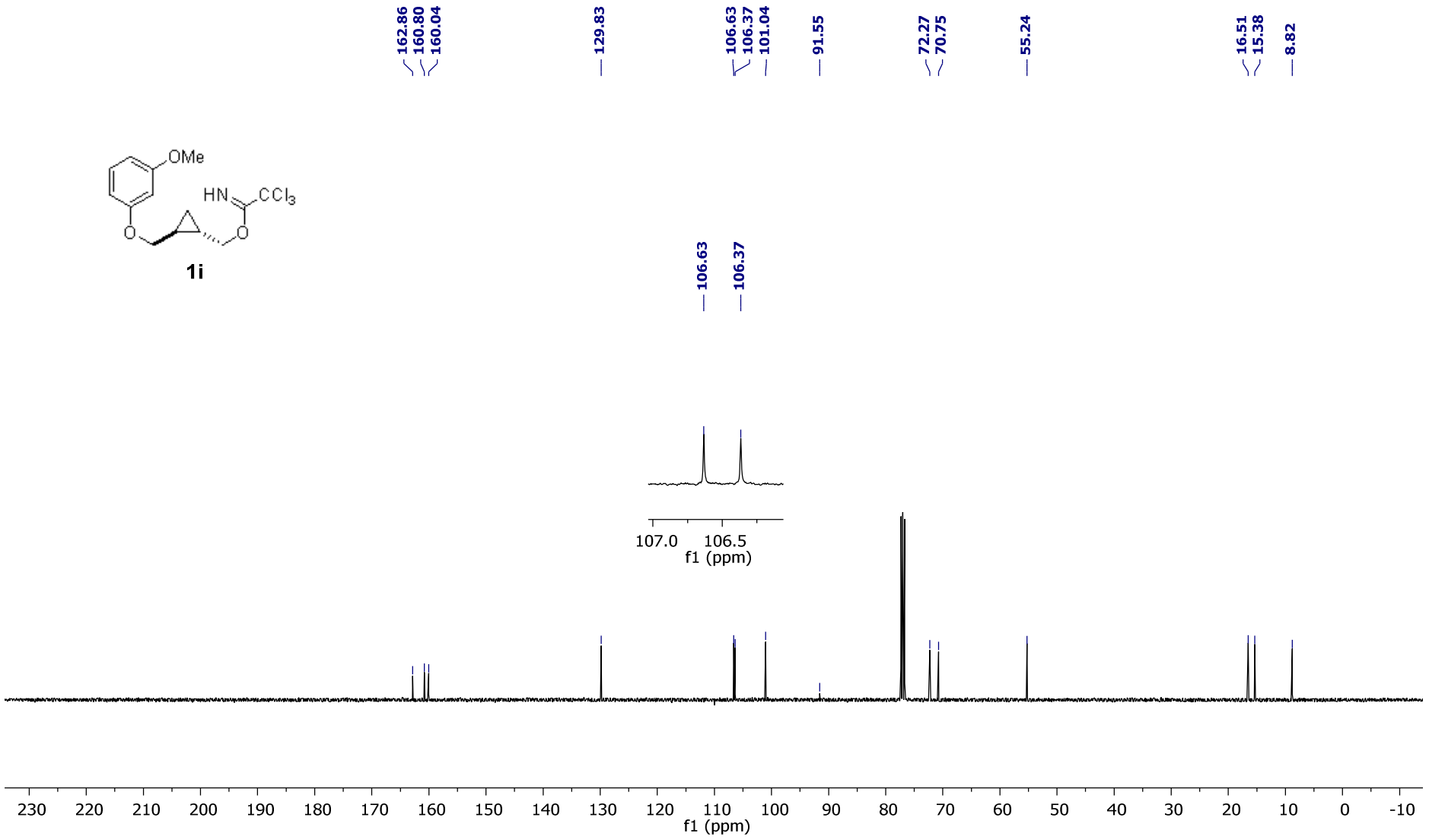

7.26 7.19 7.18 7.18 7.17 7.16 7.16 7.14 7.14 7.14 6.53 6.52 6.52 6.52 6.51 6.50 6.50 6.50 6.48 6.48 6.48 6.47 6.46 6.46 6.46 6.45 6.45 6.45 6.45 6.44 4.17 4.17 4.16 4.15 4.14 4.14 4.12 3.93 3.92 3.91 3.89 3.87 3.85 3.85 3.83 3.78 1.93 1.92 1.92 1.91 1.91 1.90 1.90 1.89 1.89 1.88 1.88 1.87 1.87 1.86 1.72 1.71 1.70 1.70 1.69 1.68 1.67 1.31 1.30 1.29 1.28 1.27 1.25 1.01 1.00 0.99 0.99 0.98 0.98 0.97 0.96
O
CO2Et
OMe
7i
f1 (ppm)
0.97
2.76
1.90
2.09
2.89
1.00
1.03
3.78
1.04

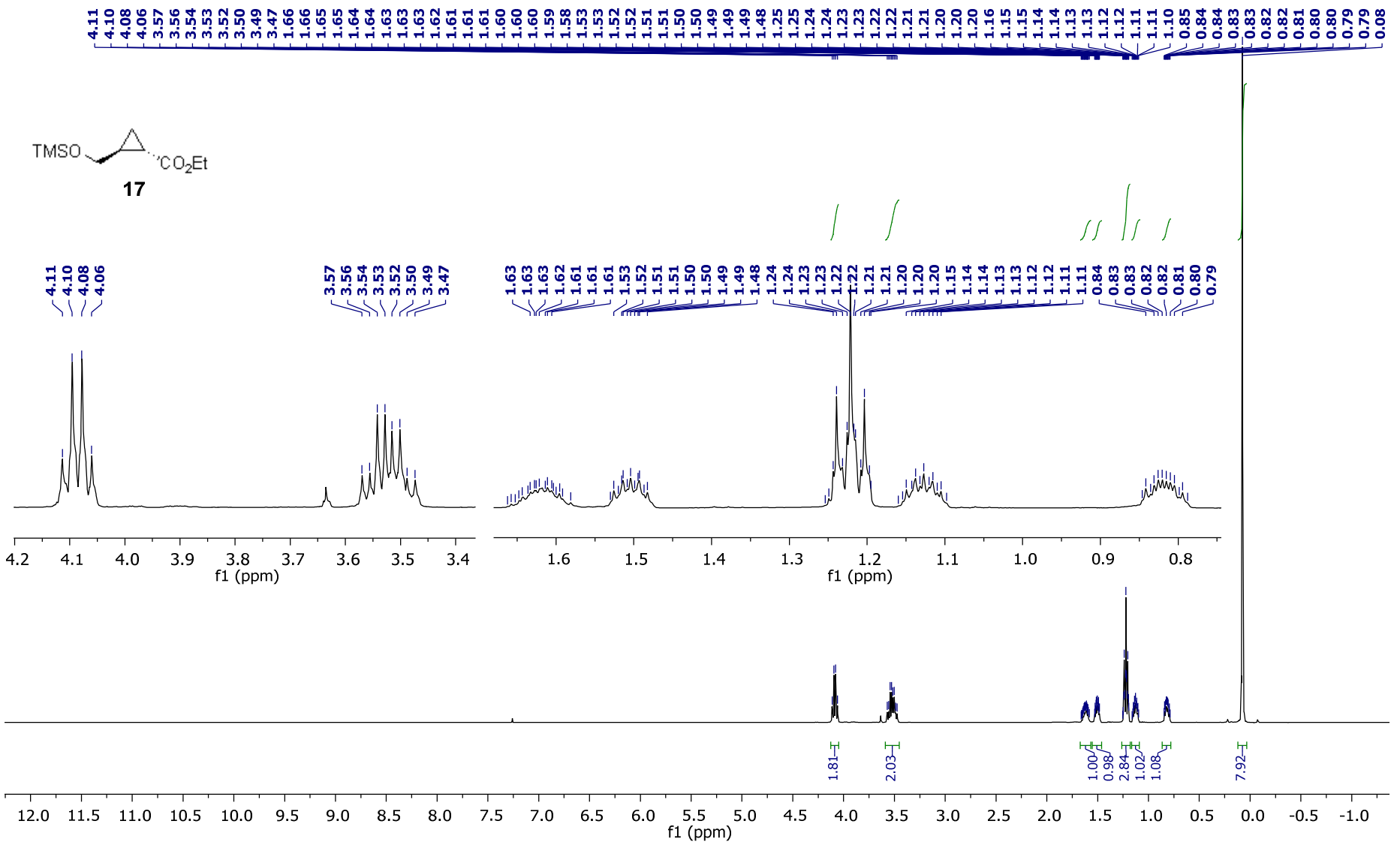

173.46
160.78
159.81
129.83
106.60
101.07
69.25
60.58
55.20
20.91
18.51
14.18
12.83
CO2Et
O
OMe
7i
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

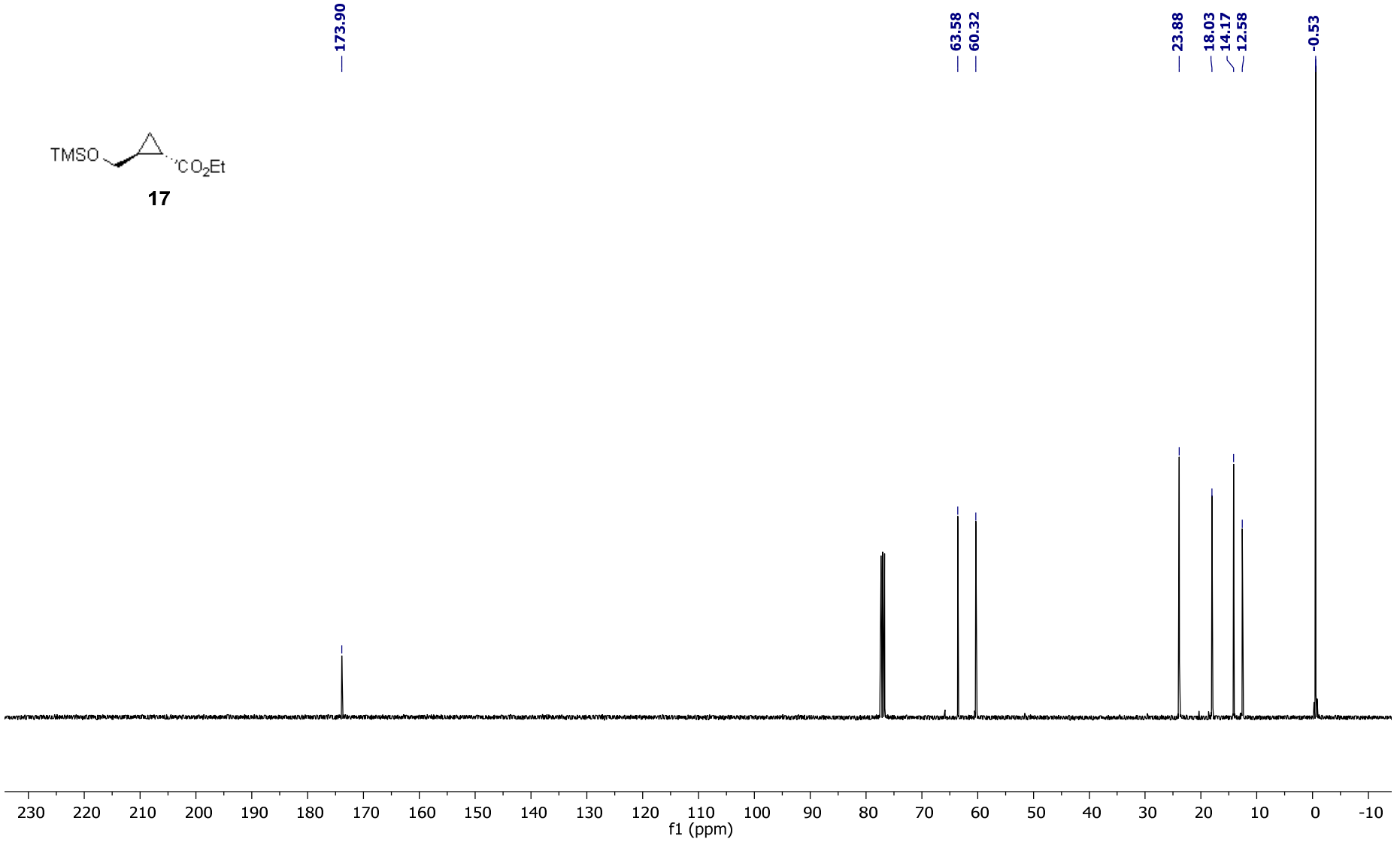

OH
O
OMe
8i
f1 (ppm)

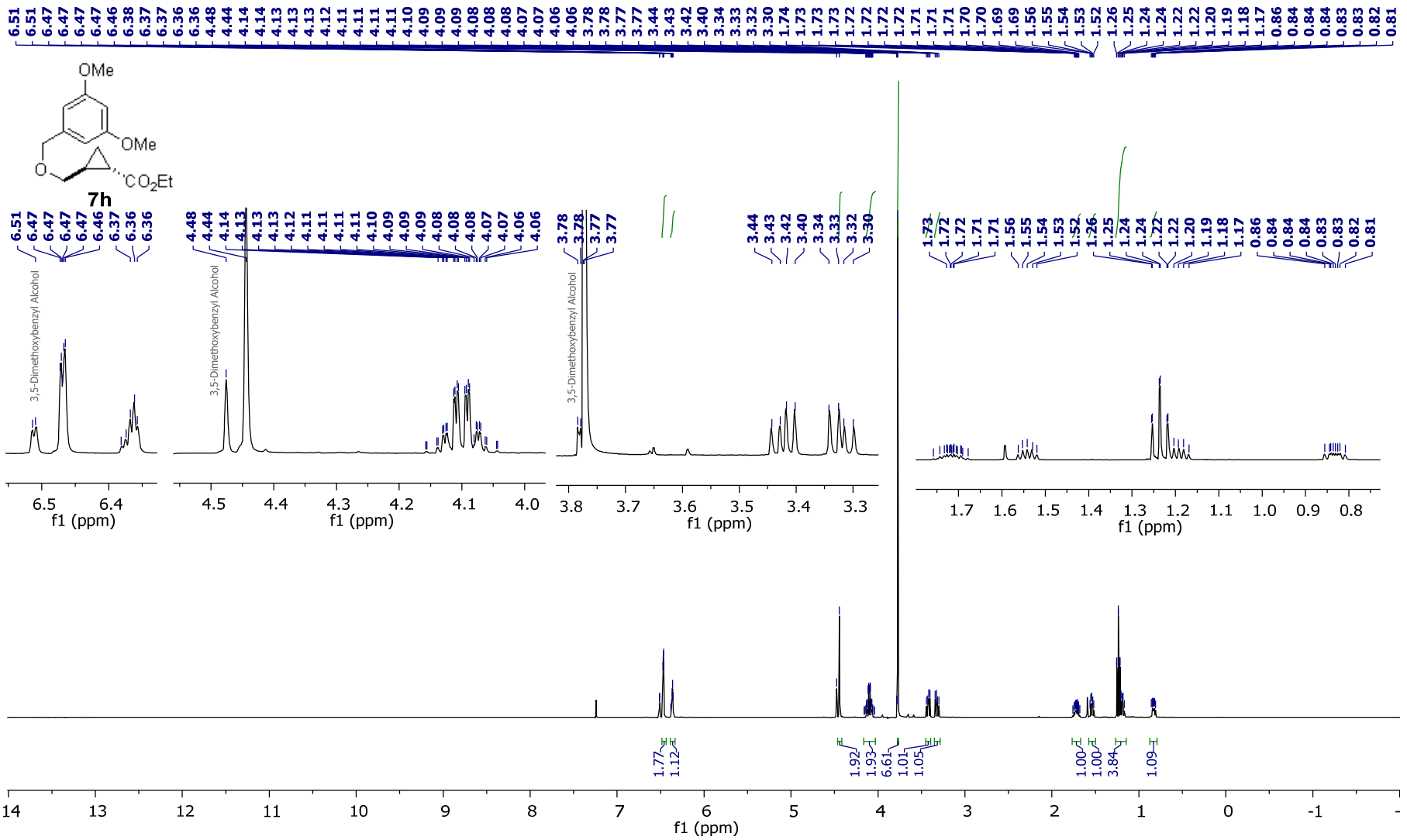

160.72
159.95
129.79
106.69
106.34
101.06
71.21
65.98
55.17
19.75
16.13
8.16
O
OH
OMe
8i
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

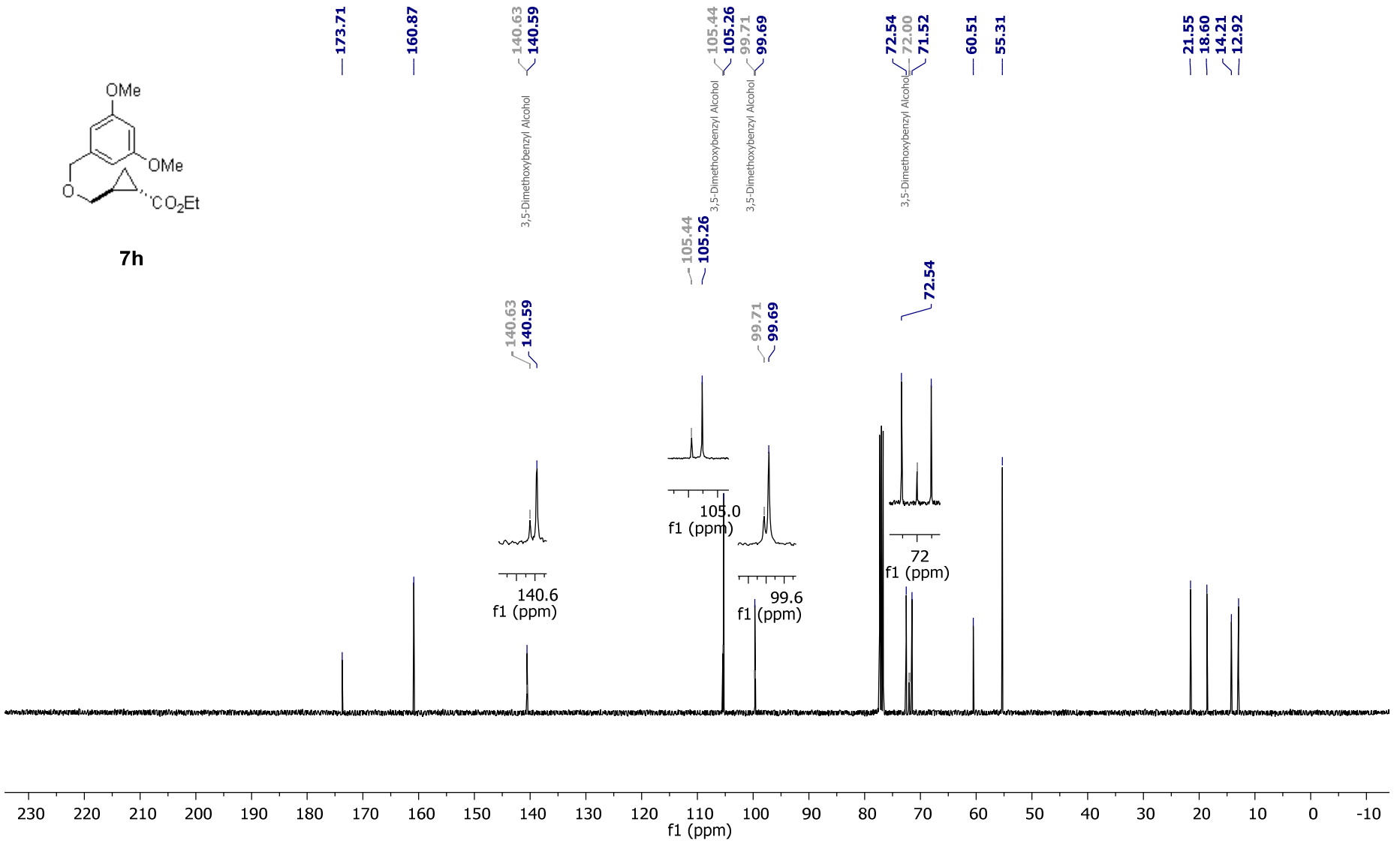

OMe
HN
CCl3
O
O
1i
8.26 7.18 7.16 7.14 6.52 6.51 6.51 6.51 6.51 6.49 6.49 6.48 6.48 6.48 6.47 6.47 6.47 6.46 6.46 6.46 6.45 6.45 6.44 4.28 4.27 4.25 4.25 4.24 4.23 4.22 4.22 4.20 3.91 3.89 3.88 3.87 3.84 3.83 3.82 3.80 3.78 1.41 1.41 1.40 1.40 1.39 1.39 1.38 1.38 1.37 1.37 1.37 1.36 1.36 1.35 1.34 1.34 1.33 1.33 1.32 0.79 0.78 0.76 0.76 0.75 0.74 0.73 0.72
f1 (ppm)
0.94
1.00
2.90
2.09
2.19
3.01
2.07
2.10

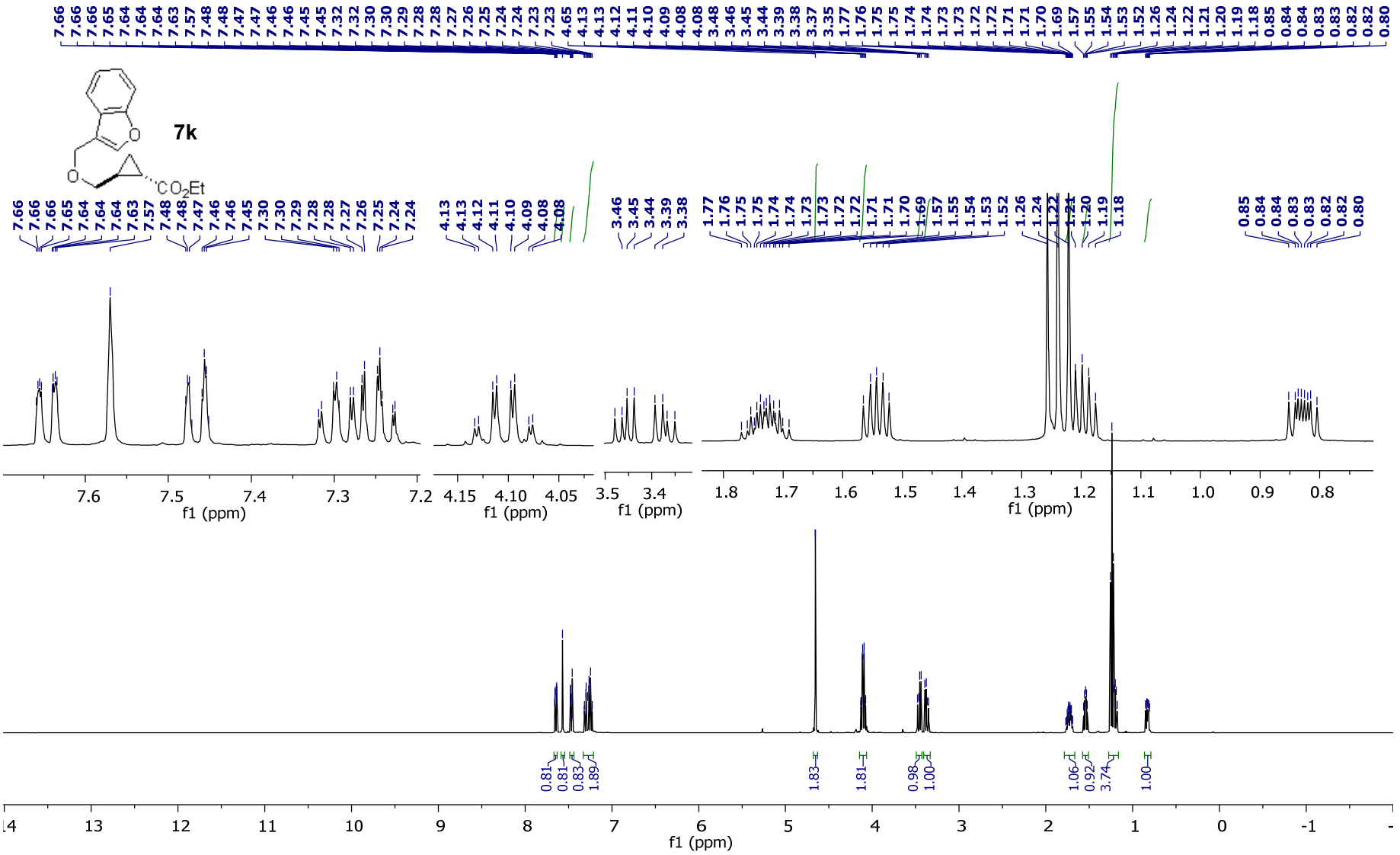

162.86
160.80
160.04
129.83
106.63
106.37
101.04
91.55
72.27
70.75
55.24
16.51
15.38
8.82
OMe
HN
CCl3
O
O
1i
106.63
106.37
107.0
106.5
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

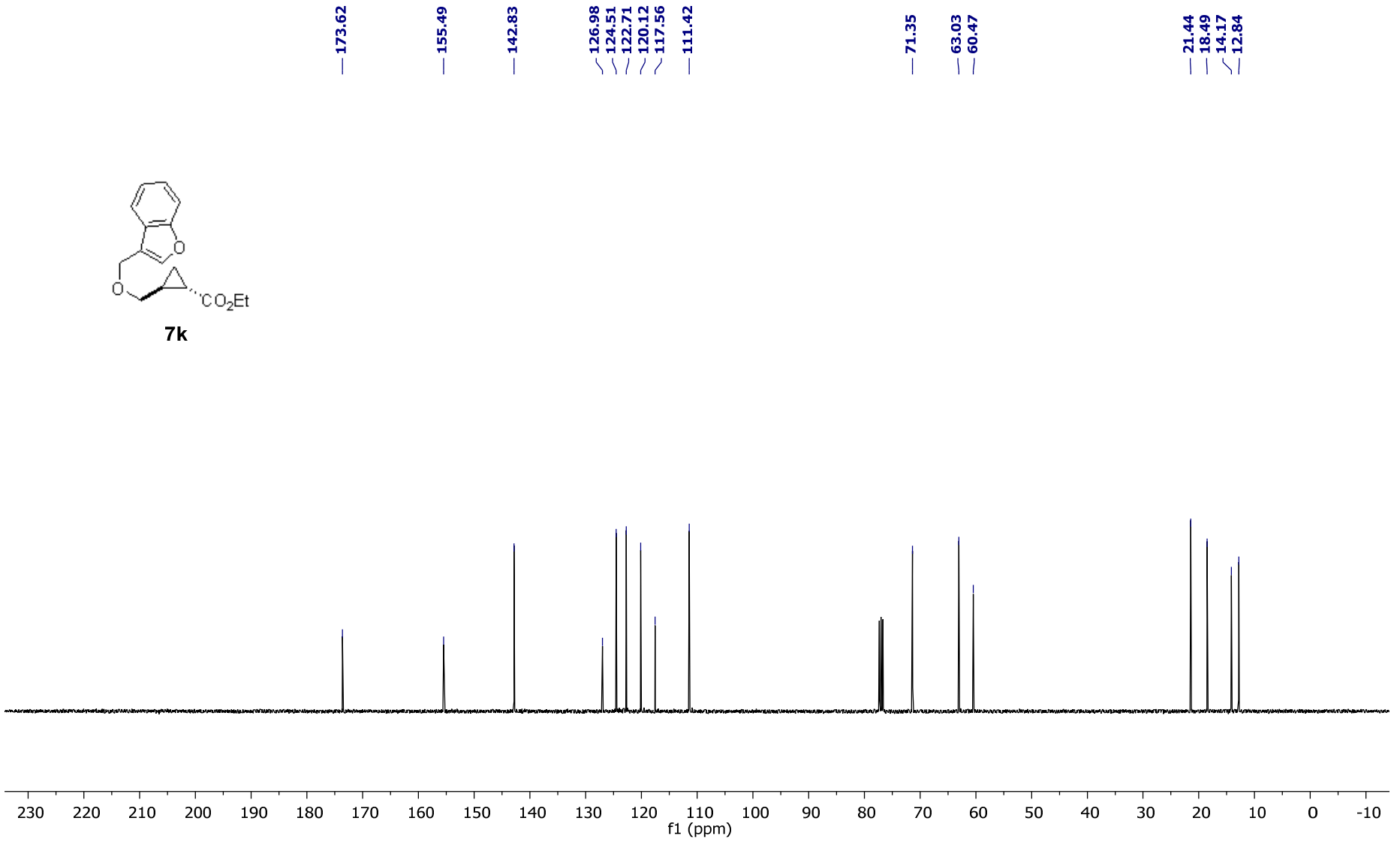

TMSO
CO2Et
17
f1 (ppm)
f1 (ppm)
f1 (ppm)


173.90
63.58
60.32
23.88
18.03
14.17
12.58
-0.53
TMSO
CO2Et
17
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

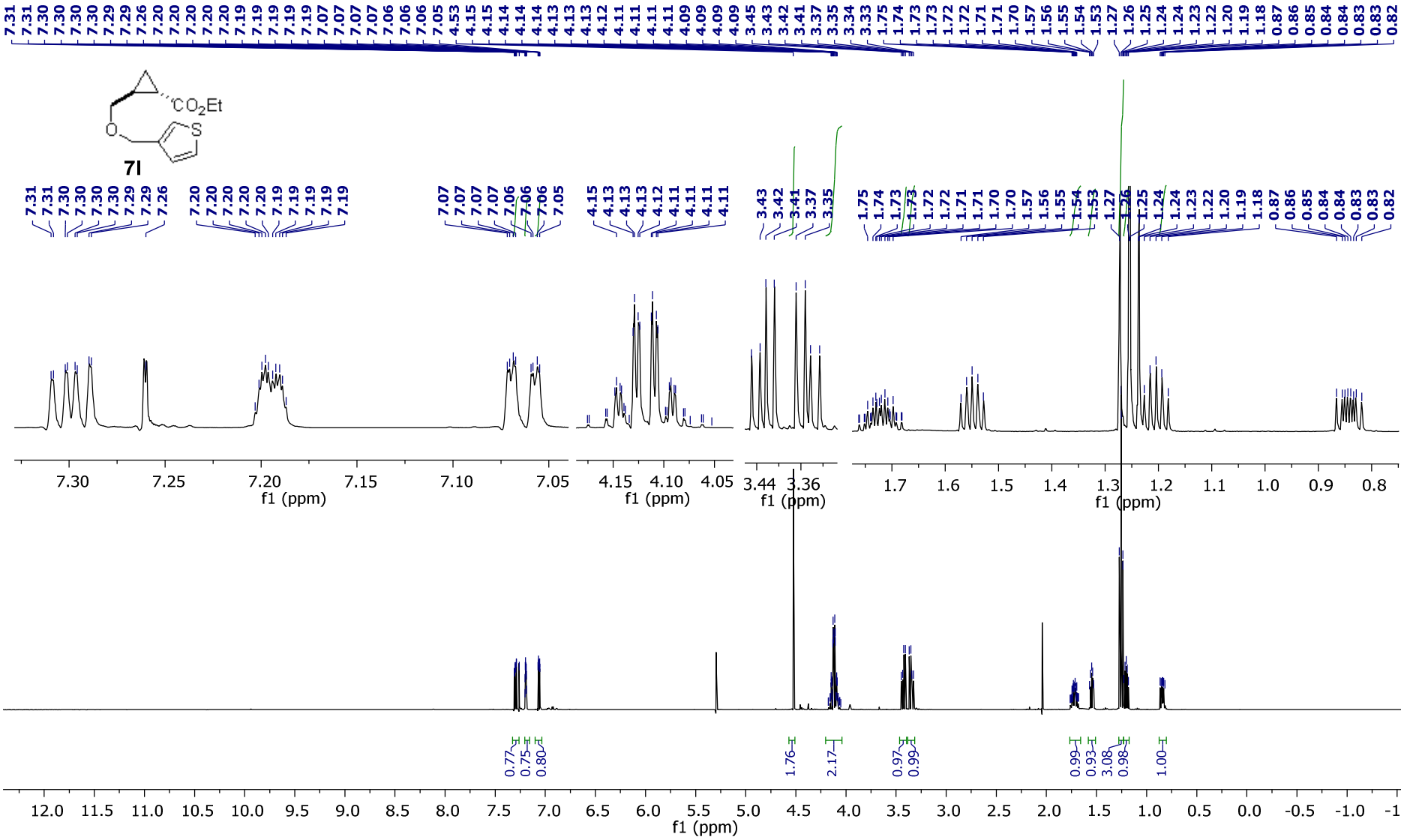

OMe
OMe
O
CO2Et
7h
3,5-Dimethoxybenzyl Alcohol
f1 (ppm)

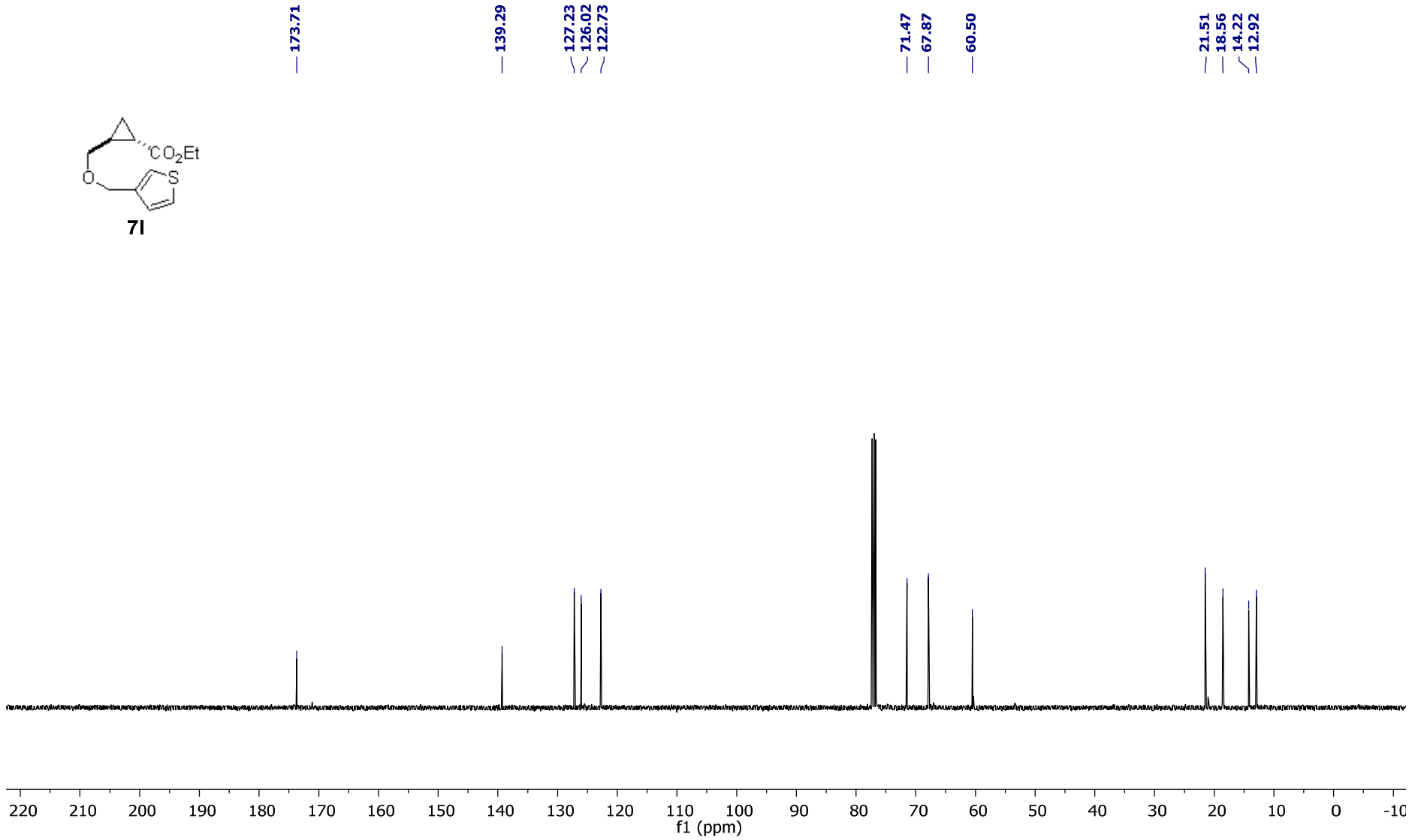

OMe
OMe
O
CO2Et
7h
173.71
160.87
140.63
140.59
105.44
105.26
99.71
99.69
72.54
72.00
71.52
60.51
55.31
21.55
18.60
14.21
12.92
3,5-Dimethoxybenzyl Alcohol
140.6
f1 (ppm)
105.0
f1 (ppm)
99.6
f1 (ppm)
72
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

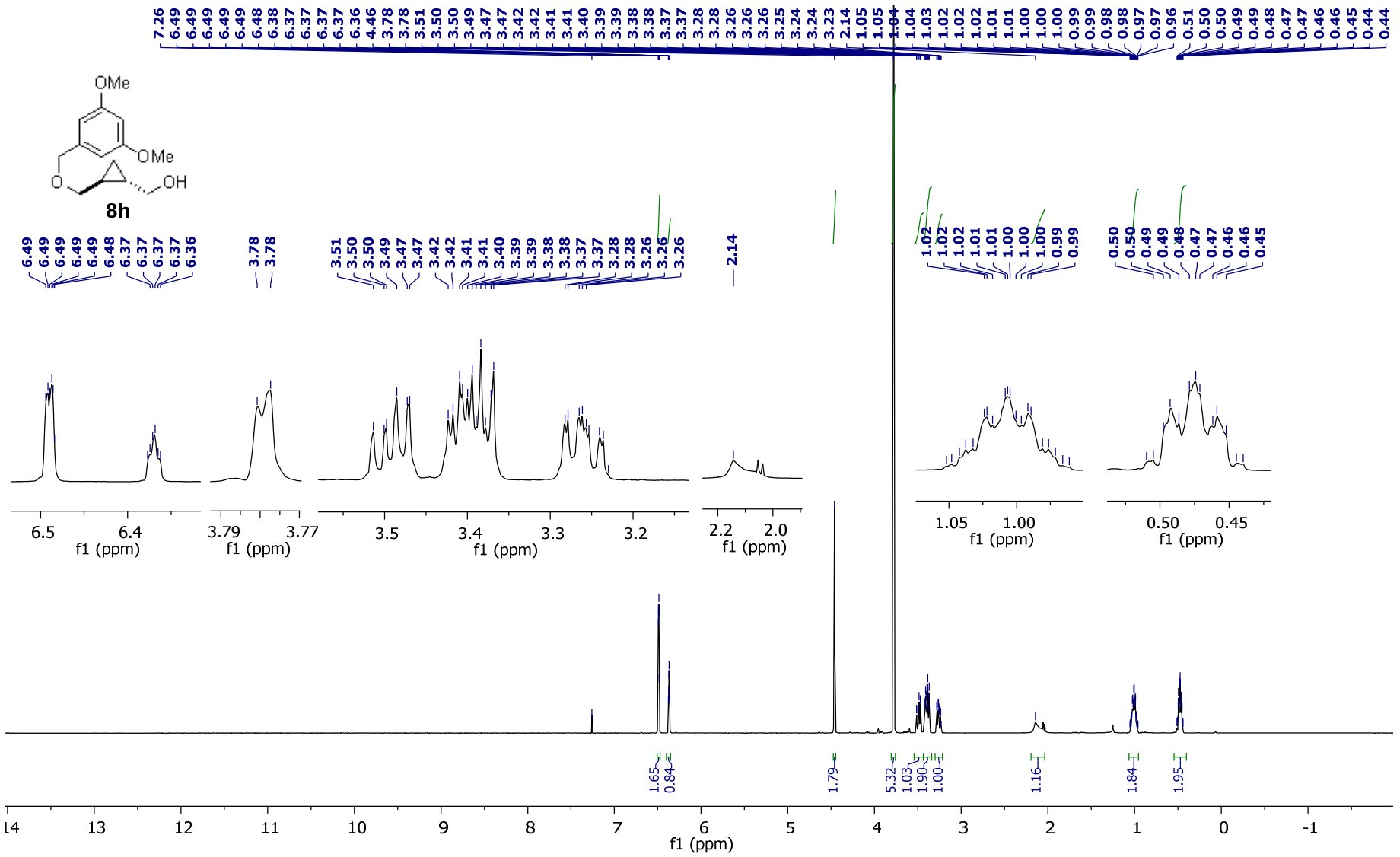

7k
CO2Et
f1 (ppm)

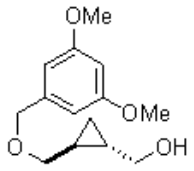

173.62
155.49
142.83
126.98
124.51
122.71
120.12
117.56
111.42
71.35
63.03
60.47
21.44
18.49
14.17
12.84
O
O
CO2Et
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

7k


CO2Et
O
S
7l
f1 (ppm)

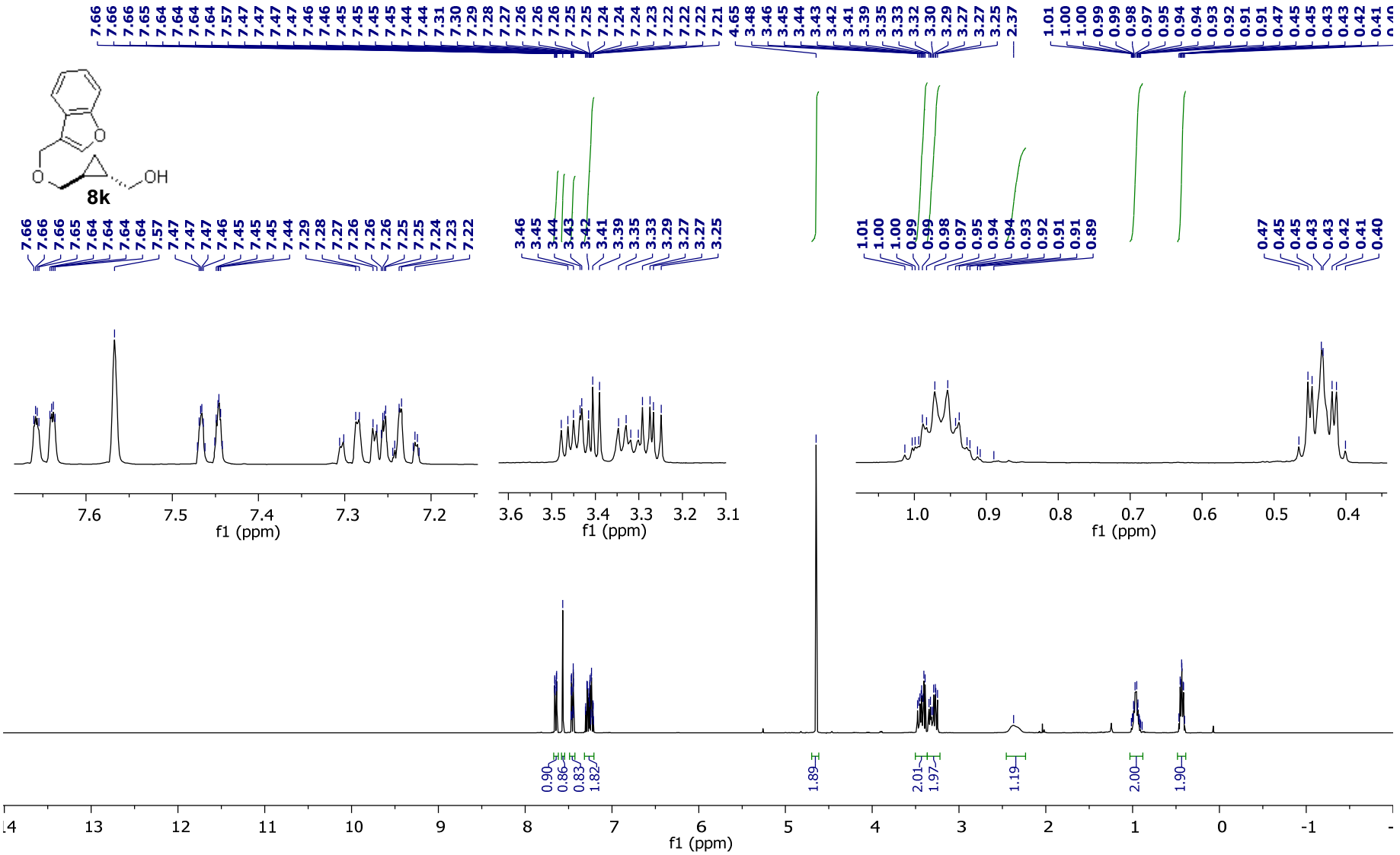

173.71
139.29
127.23
126.02
122.73
71.47
67.87
60.50
21.51
18.56
14.22
12.92
CO2Et
O
S
7l
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

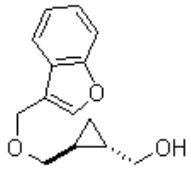

OMe
OMe
O
OH
8h
f1 (ppm)


OMe
OMe
O
OH

8h

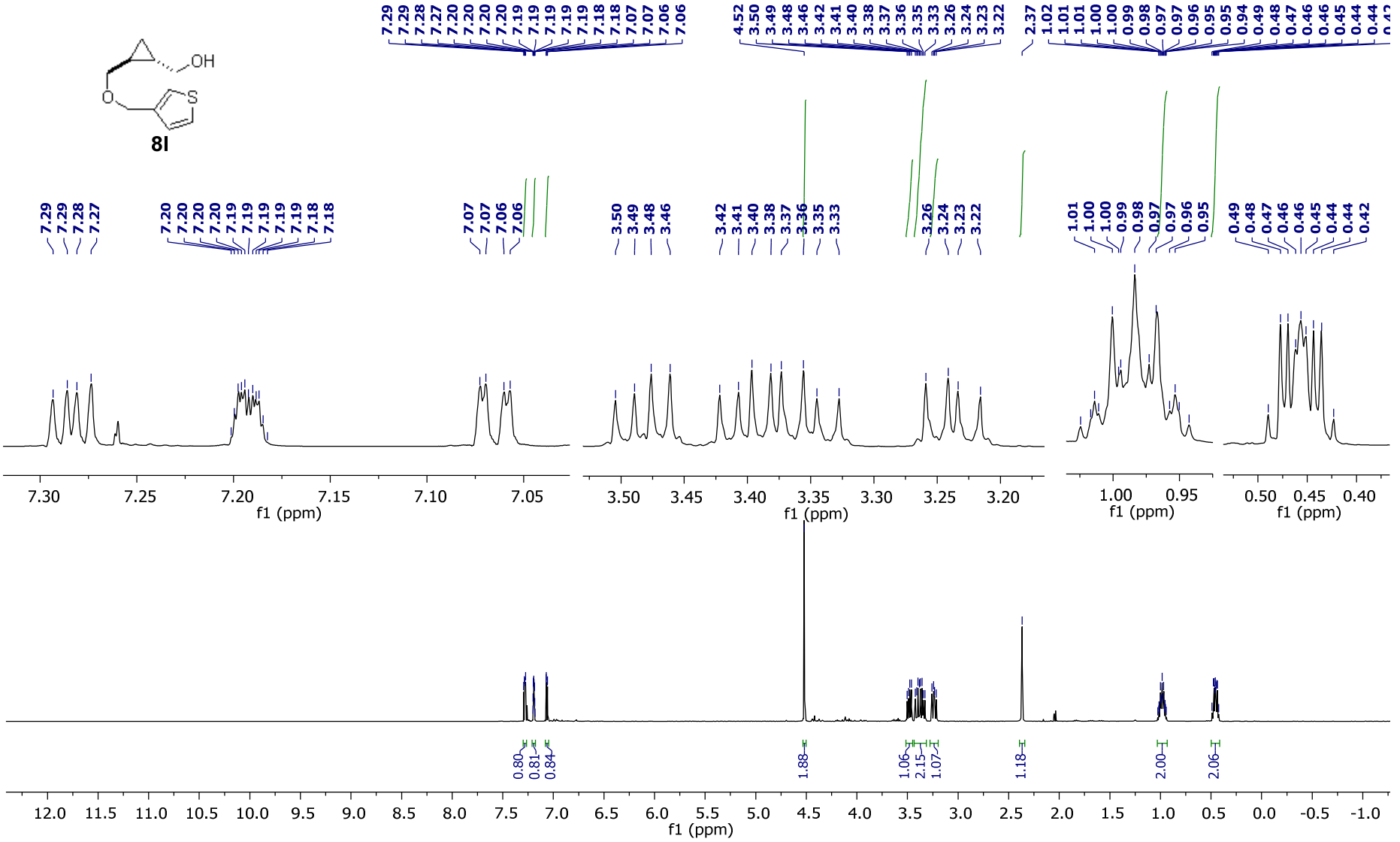
160.82
140.77
105.30
99.57
73.40
72.45
66.16
55.27
19.77
16.71
8.01
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

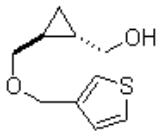

8k
f1 (ppm)


O
O
OH

8k

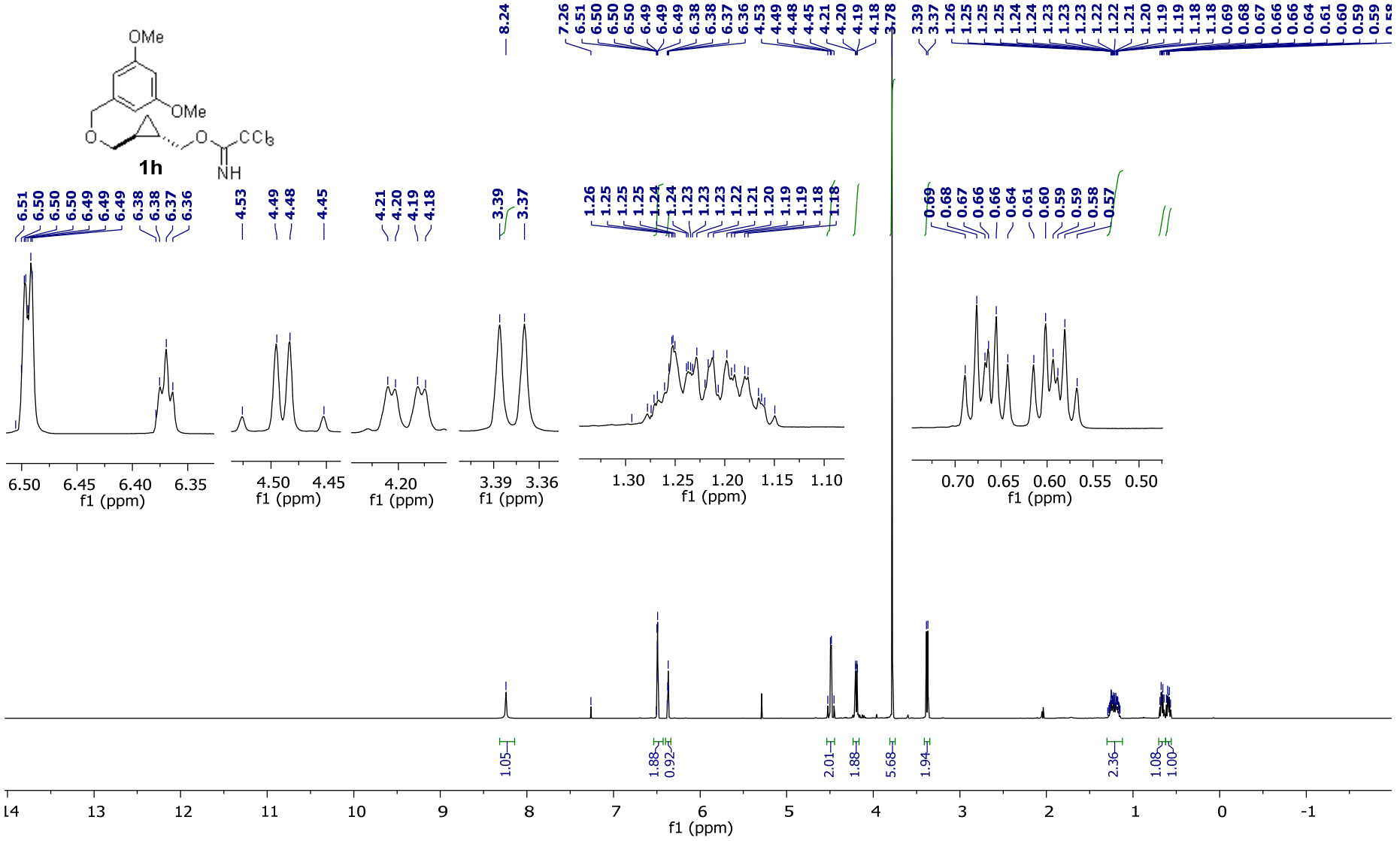
155.46
142.85
127.03
124.48
122.68
120.11
117.69
111.40
73.33
66.00
62.89
19.69
16.63
7.88
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

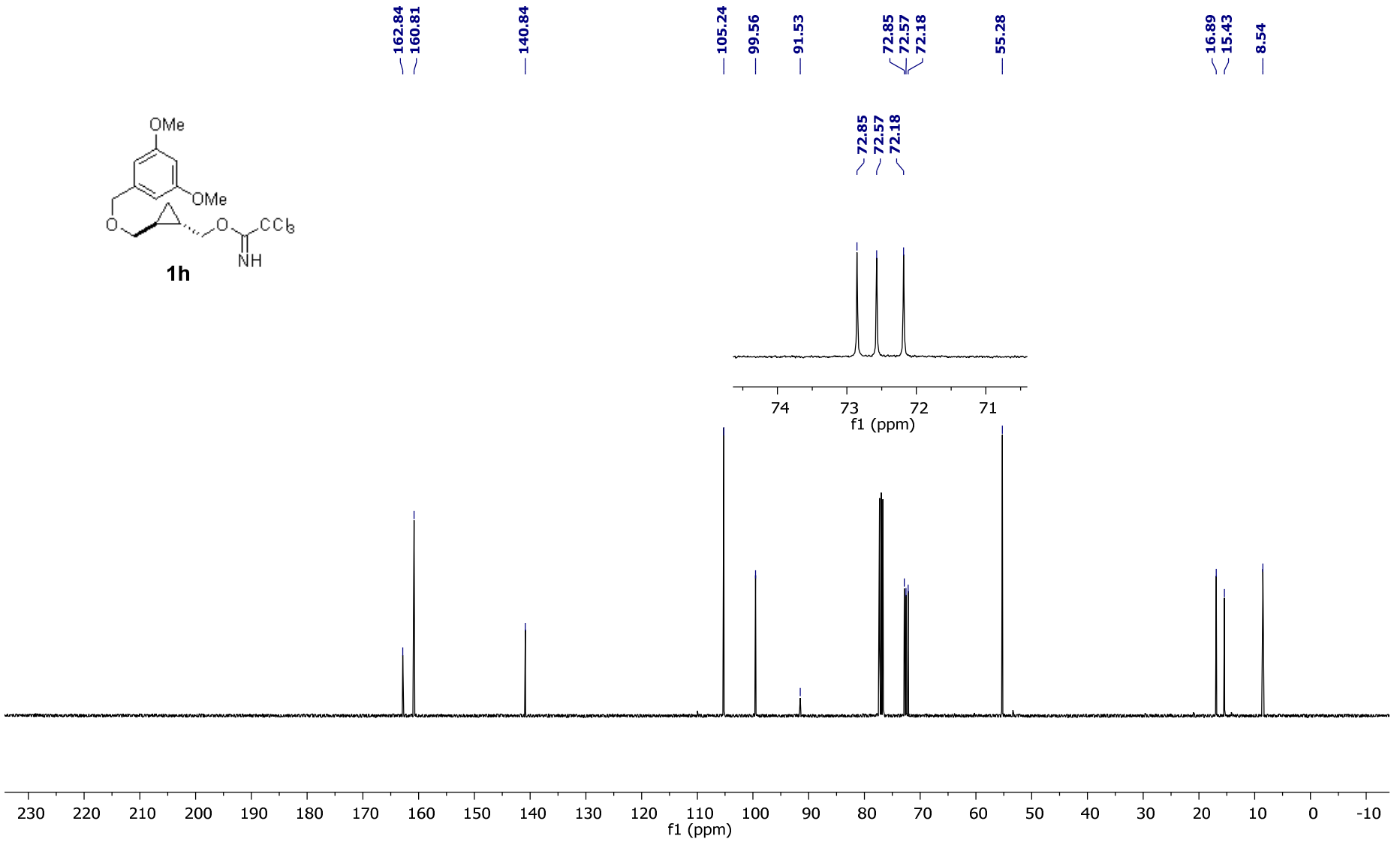

OH
O
S
8l
f1 (ppm)

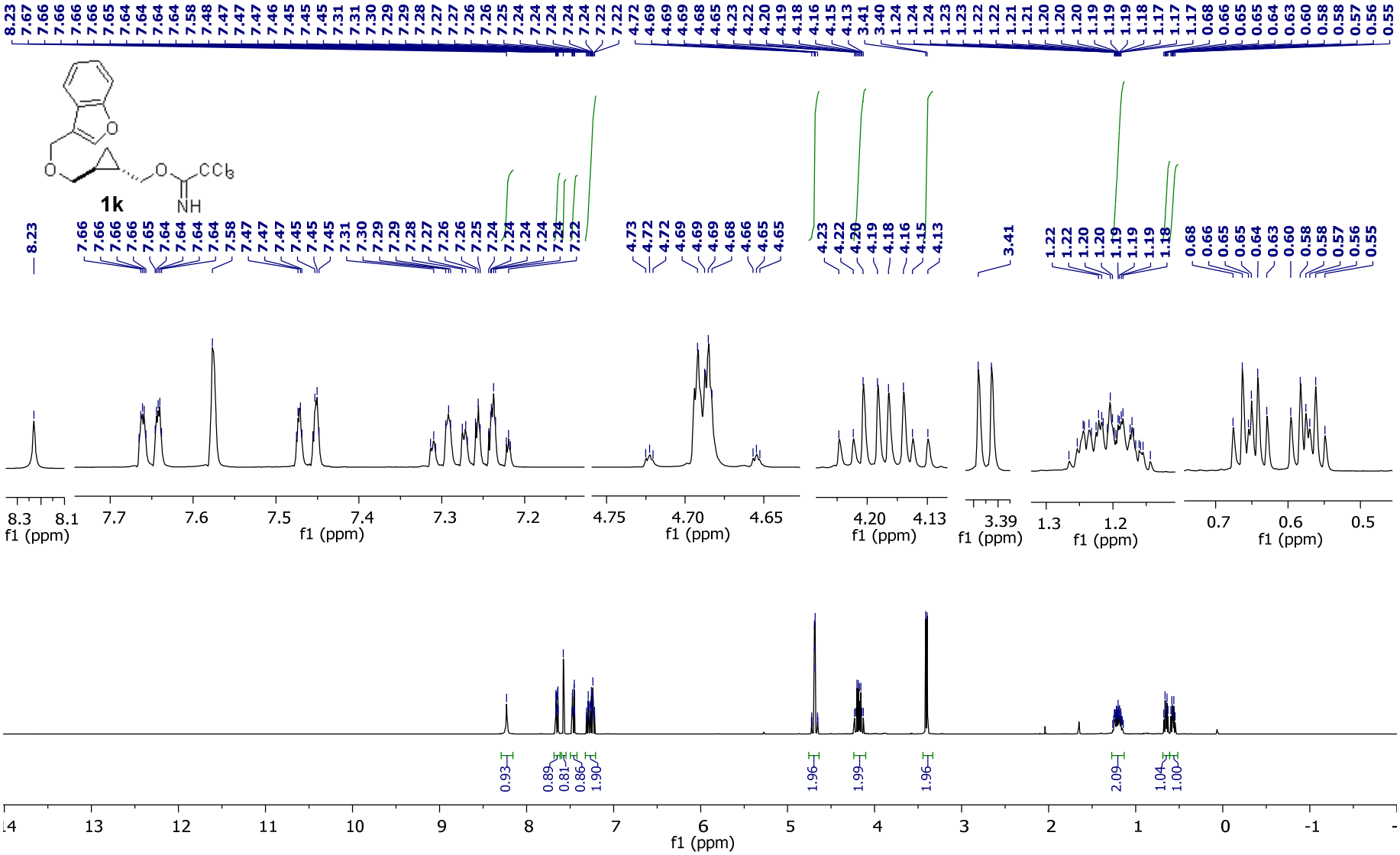

OH
O
S

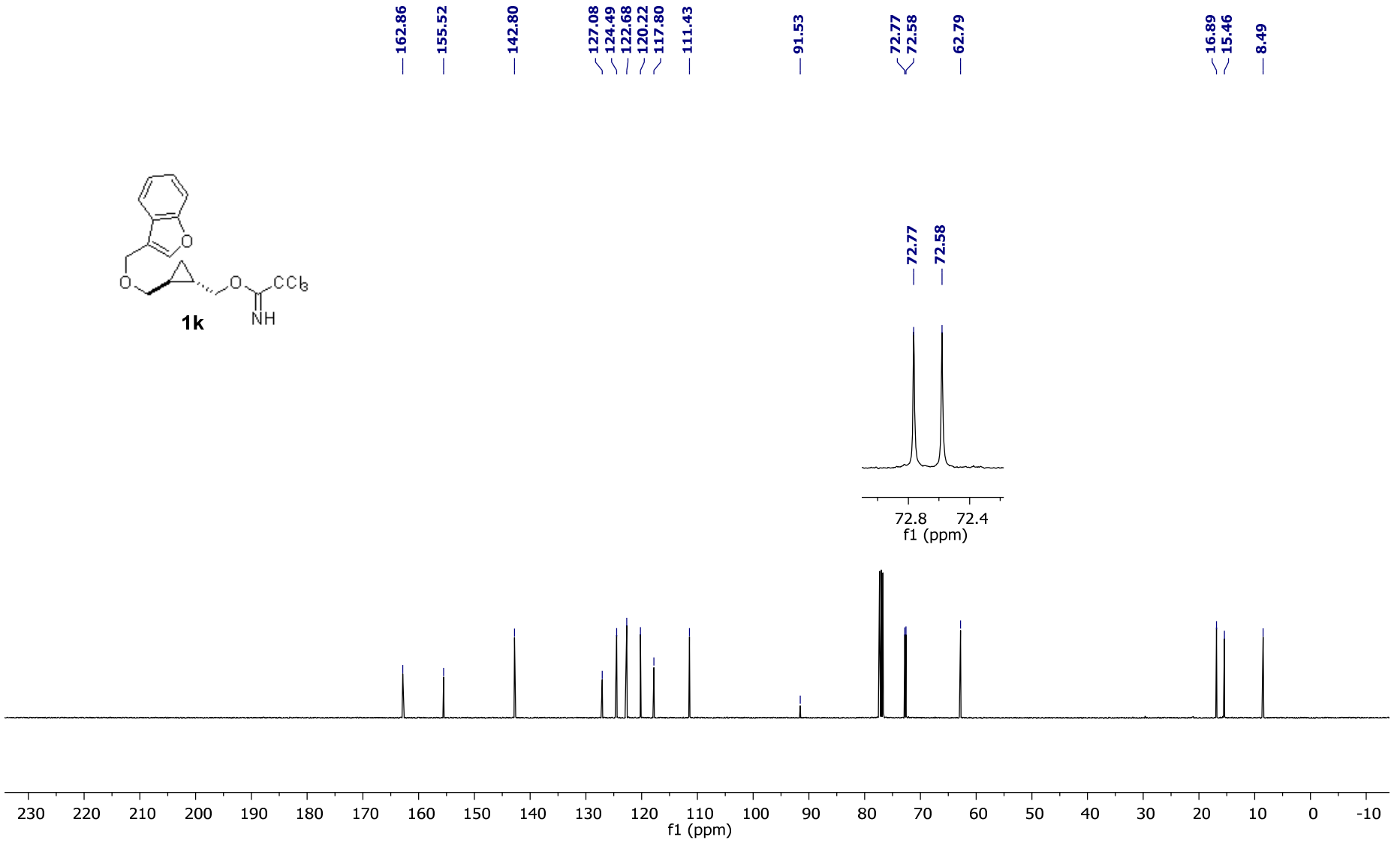
8l

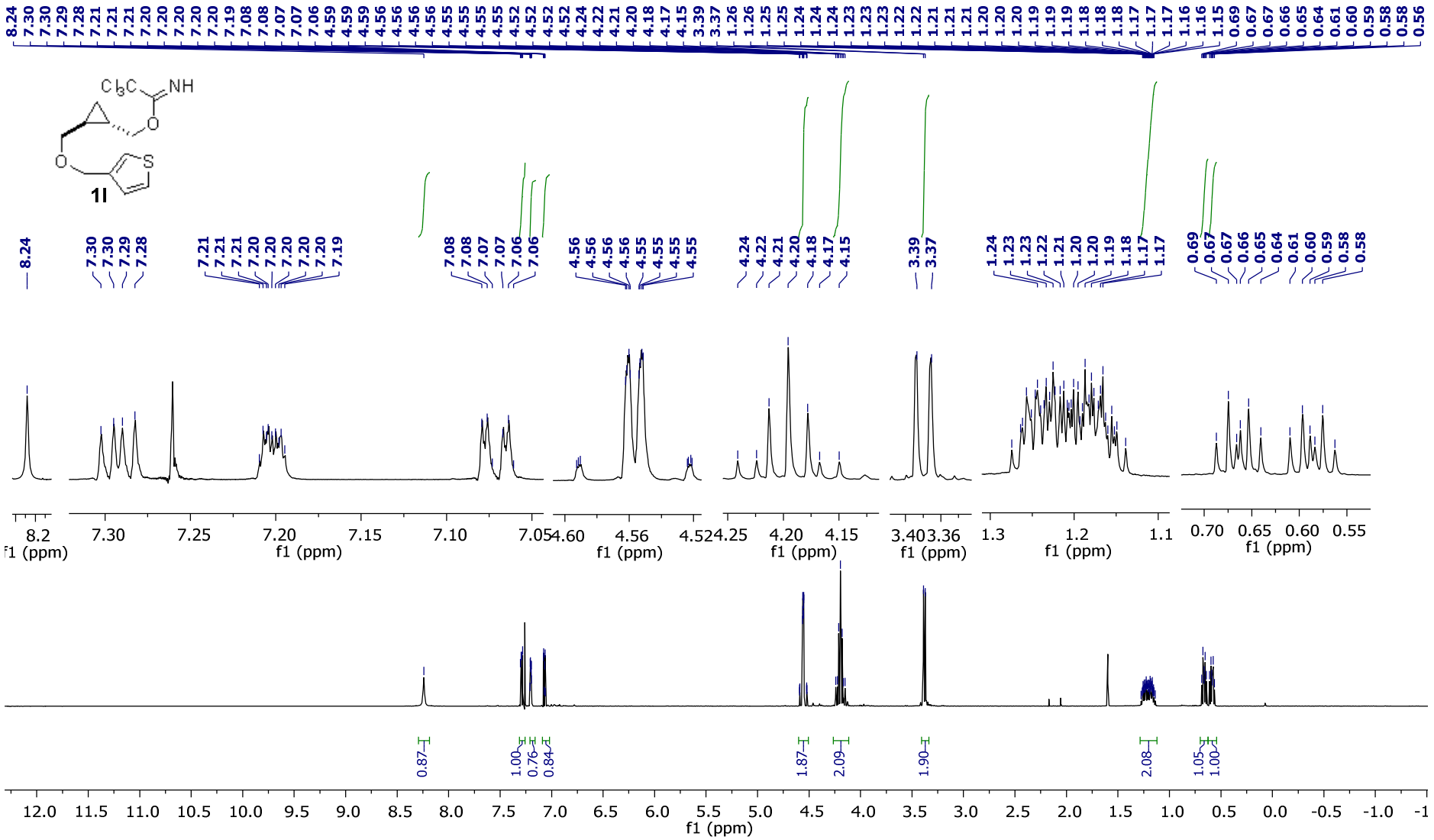
139.39
127.27
125.93
122.73
73.38
67.73
66.07
19.75
16.69
7.92
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

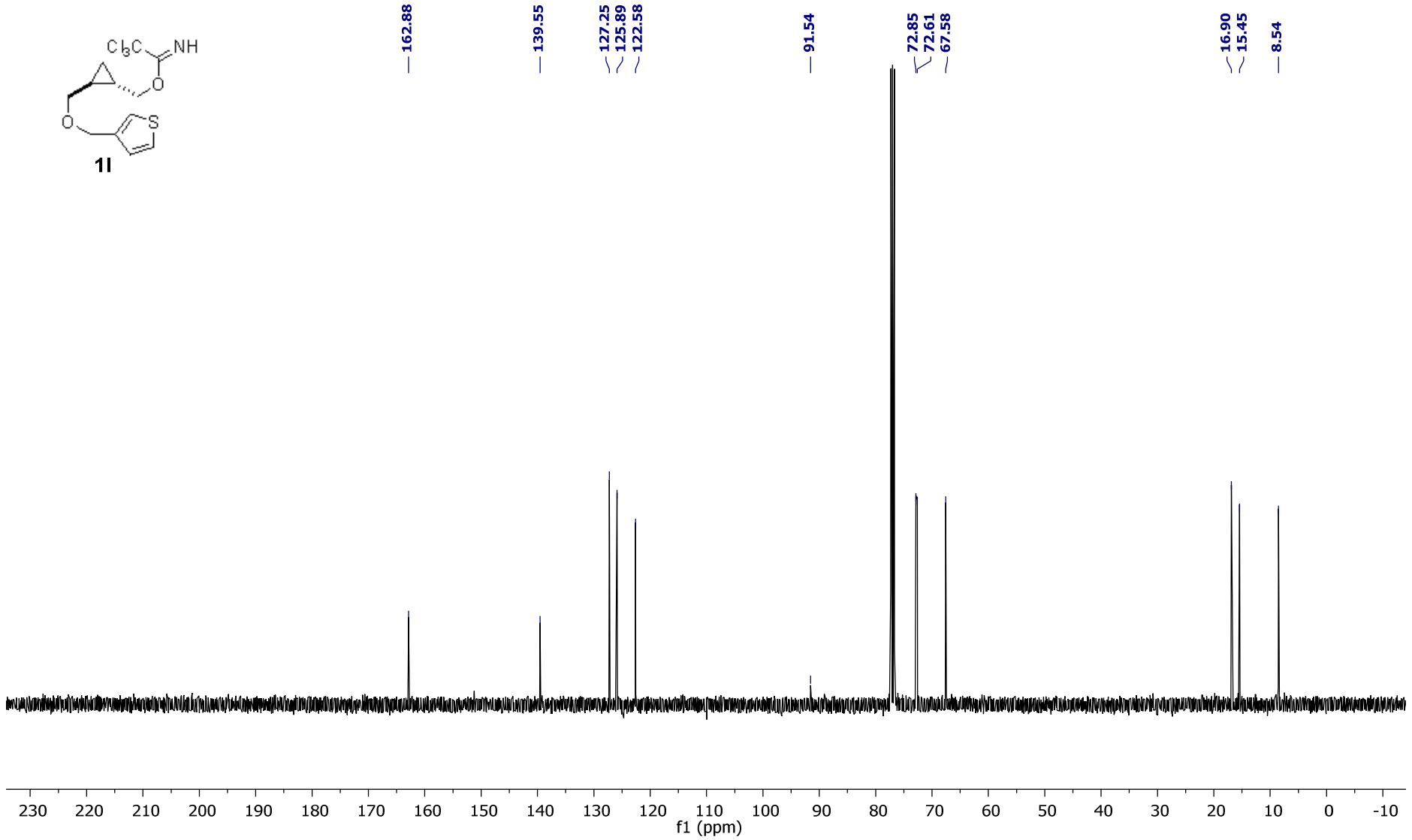

OMe
OMe
O
O
CCl3
NH
1h
f1 (ppm)

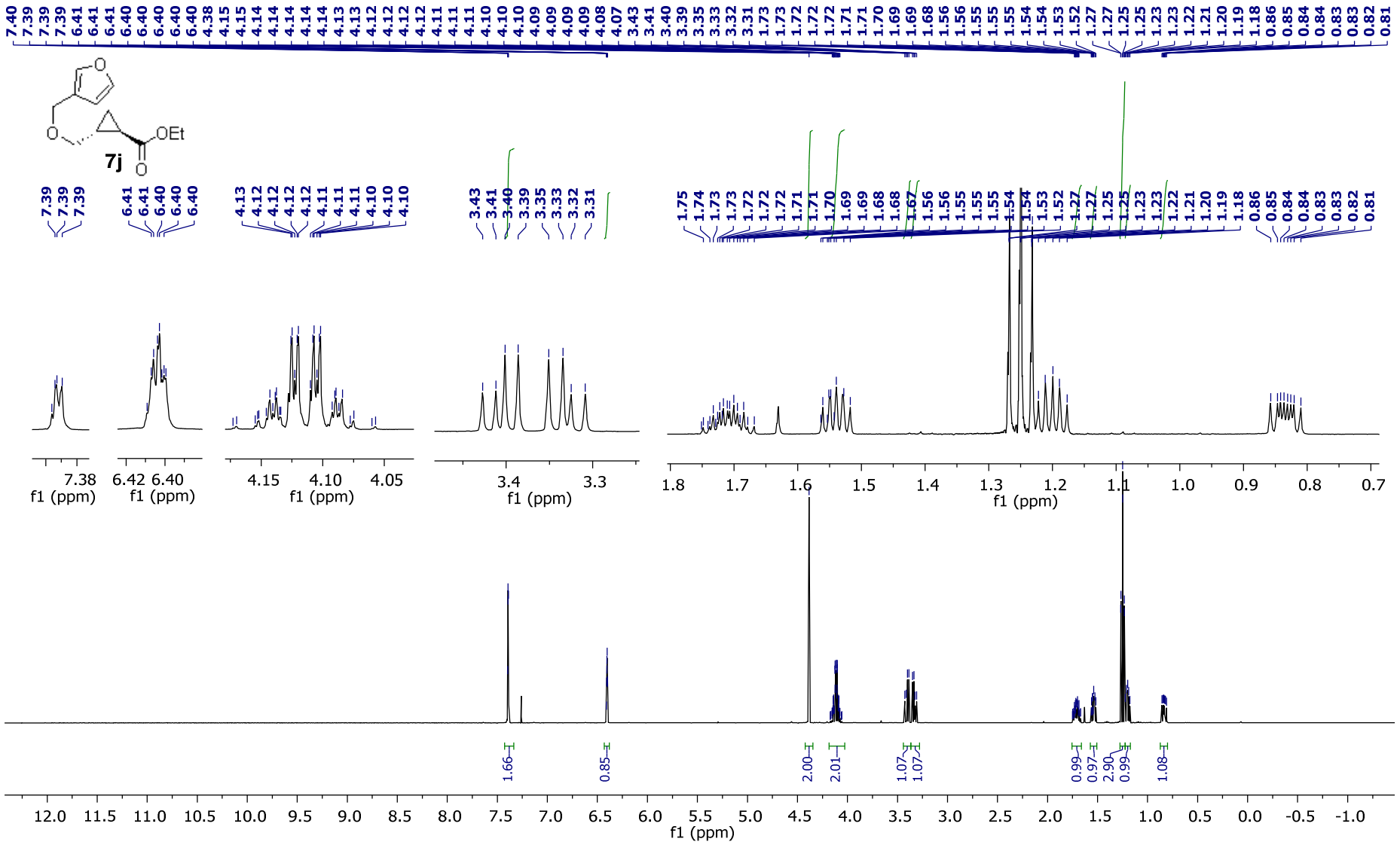

162.84
160.81
140.84
105.24
99.56
91.53
72.85
72.57
72.18
55.28
16.89
15.43
8.54
OMe
OMe
O
O
CCl3
NH
1h
f1 (ppm)
f1 (ppm)

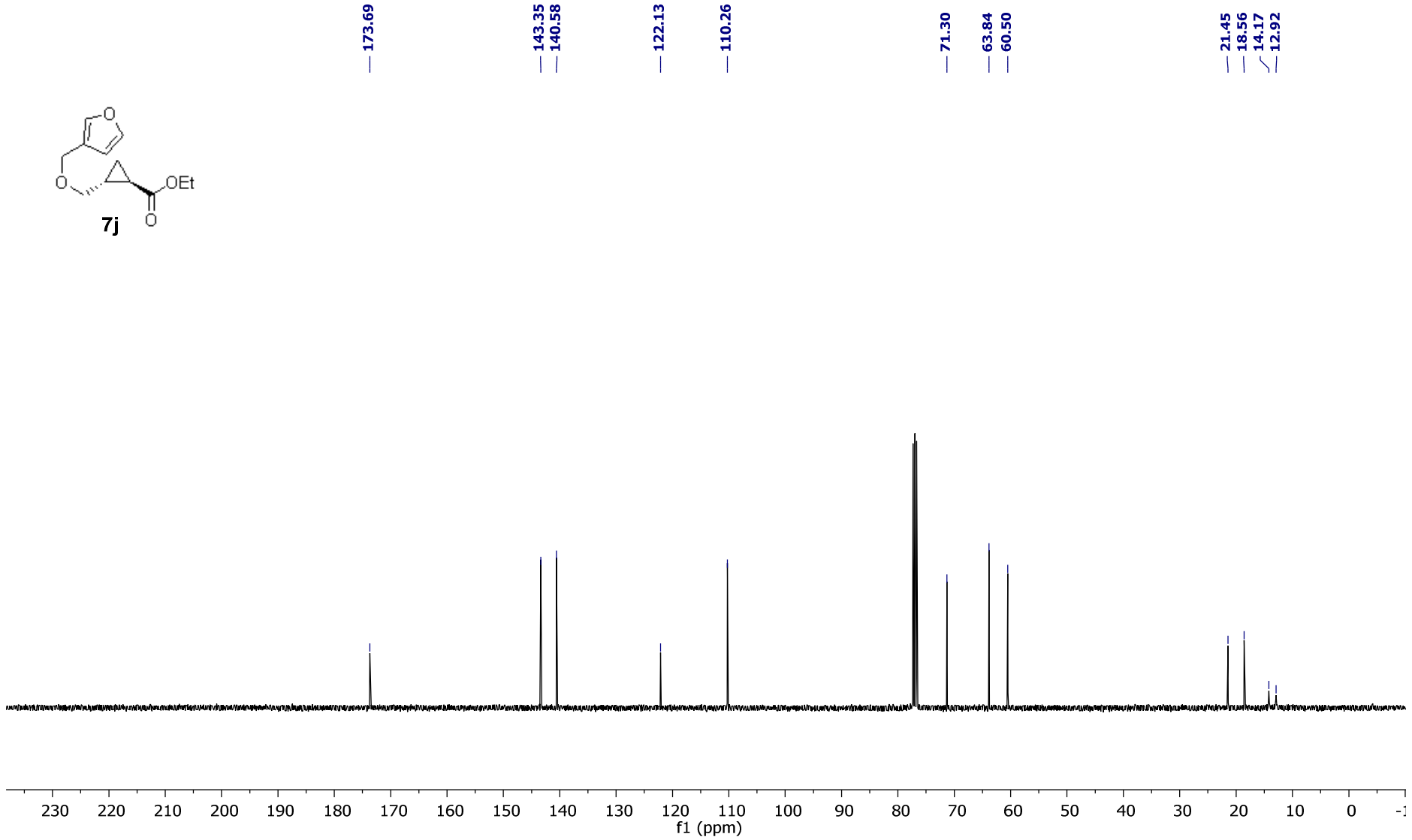

1k
NH
f1 (ppm)

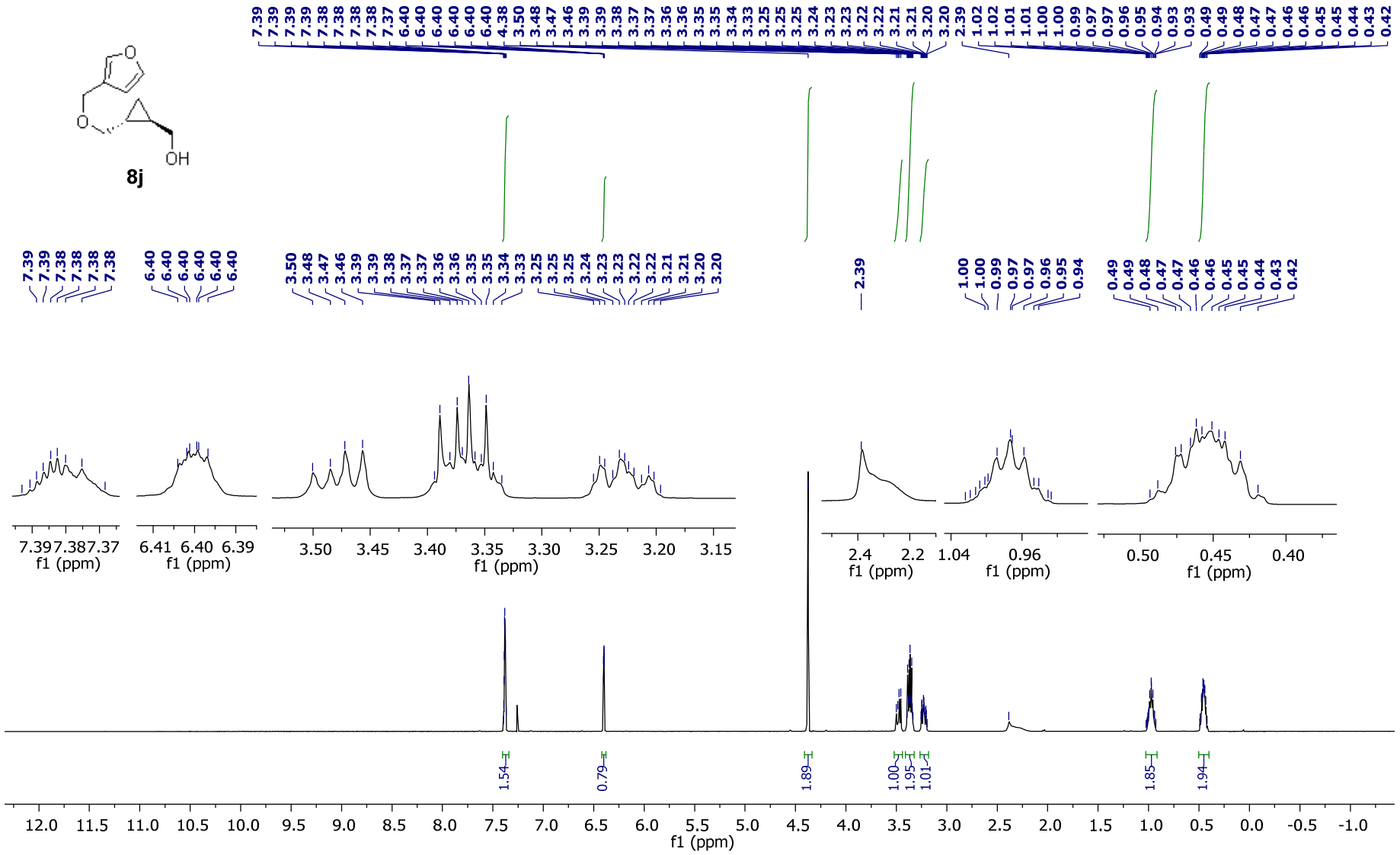

162.86
155.52
142.80
127.08
124.49
122.68
120.22
117.80
111.43
91.53
72.77
72.58
62.79
16.89
15.46
8.49
O
O
O
CCl3
NH
1k
72.77
72.58
72.8
72.4
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

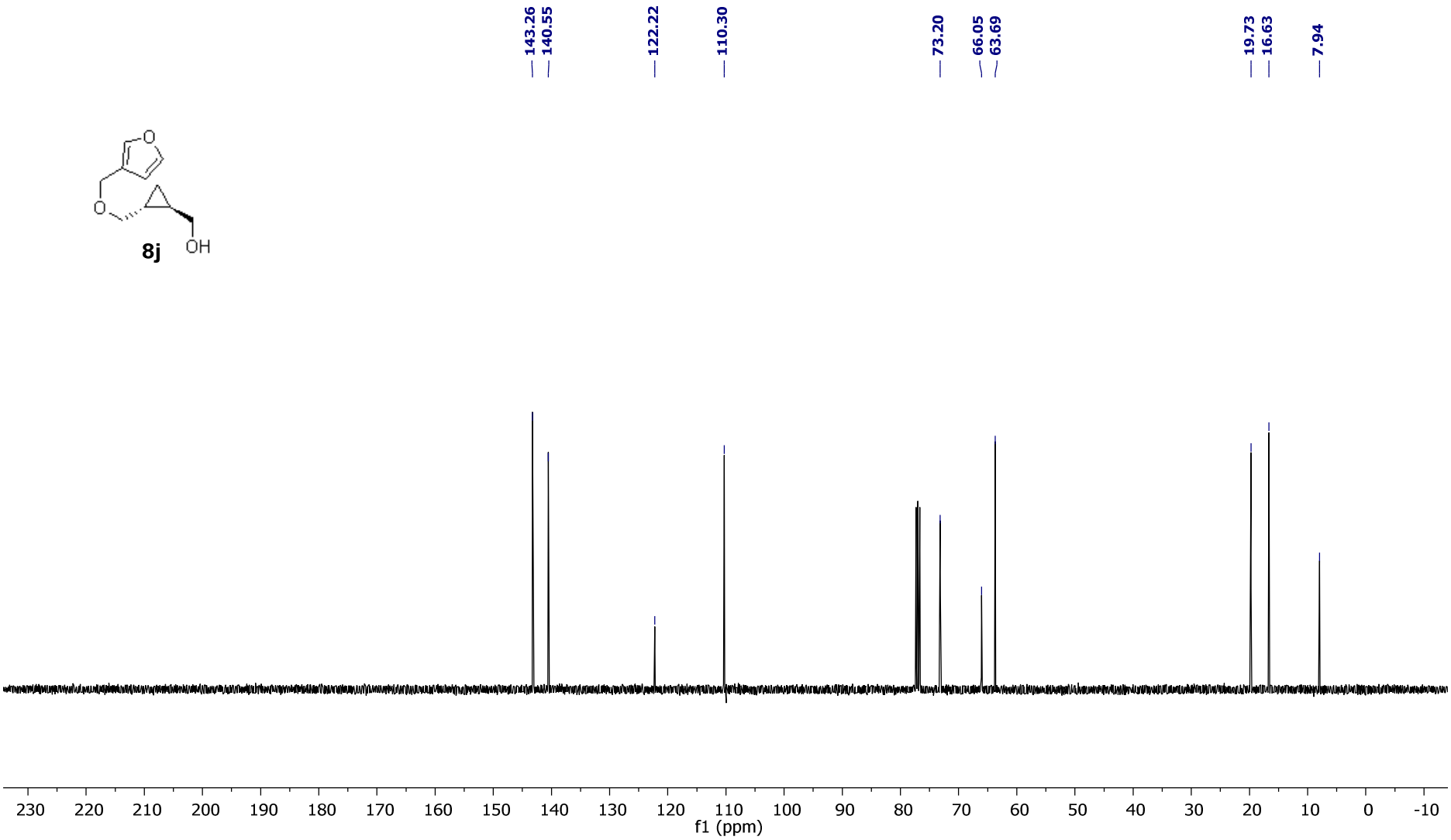

1l
f1 (ppm)

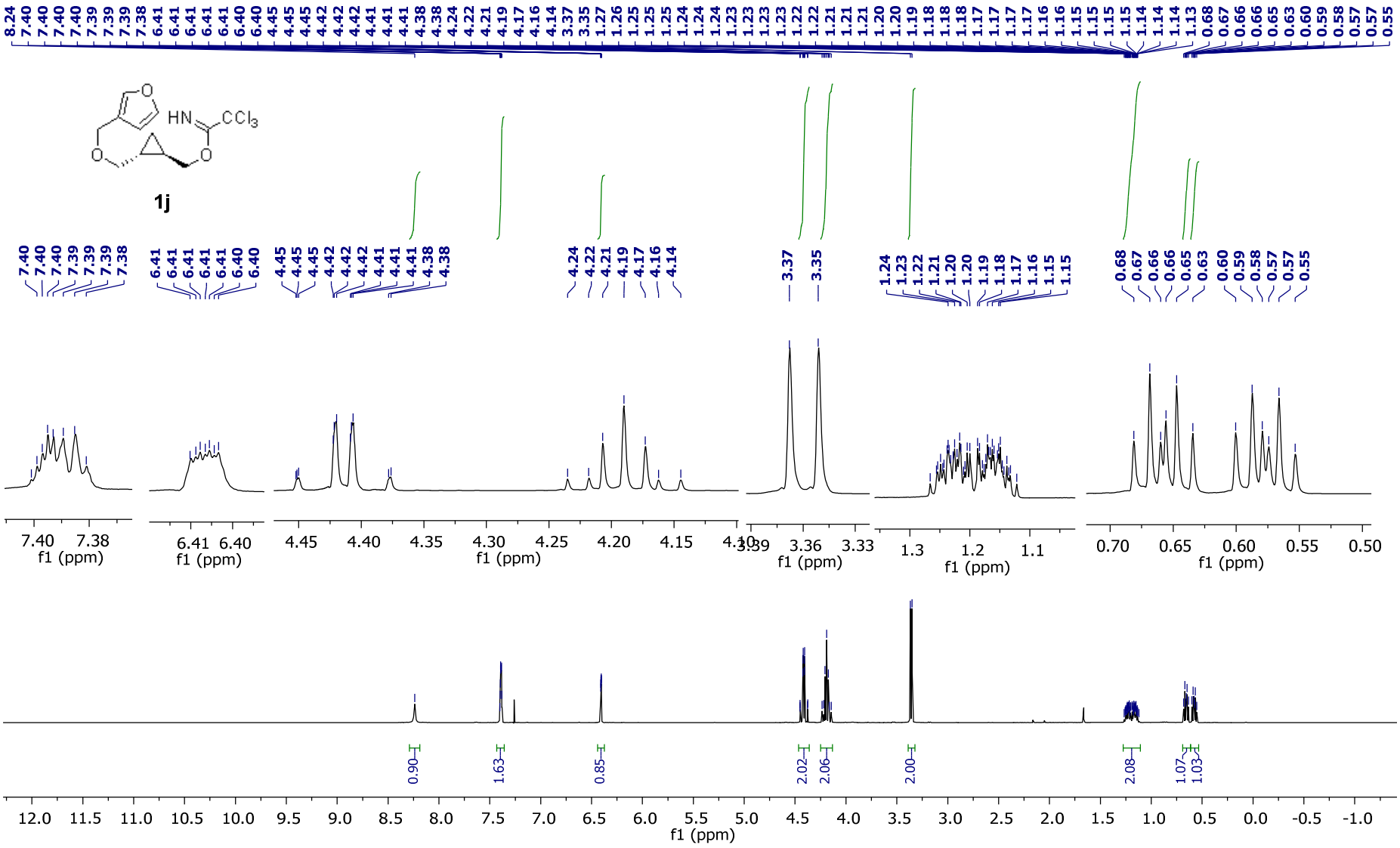

1l
162.88
139.55
127.25
125.89
122.58
91.54
72.85
72.61
67.58
16.90
15.45
8.54
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

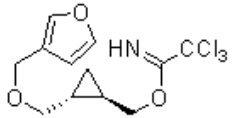

7j
OEt
f1 (ppm)


173.69
143.35
140.58
122.13
110.26
71.30
63.84
60.50
21.45
18.56
14.17
12.92
O
O
OEt
O
7j
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8j
OH
f1 (ppm)

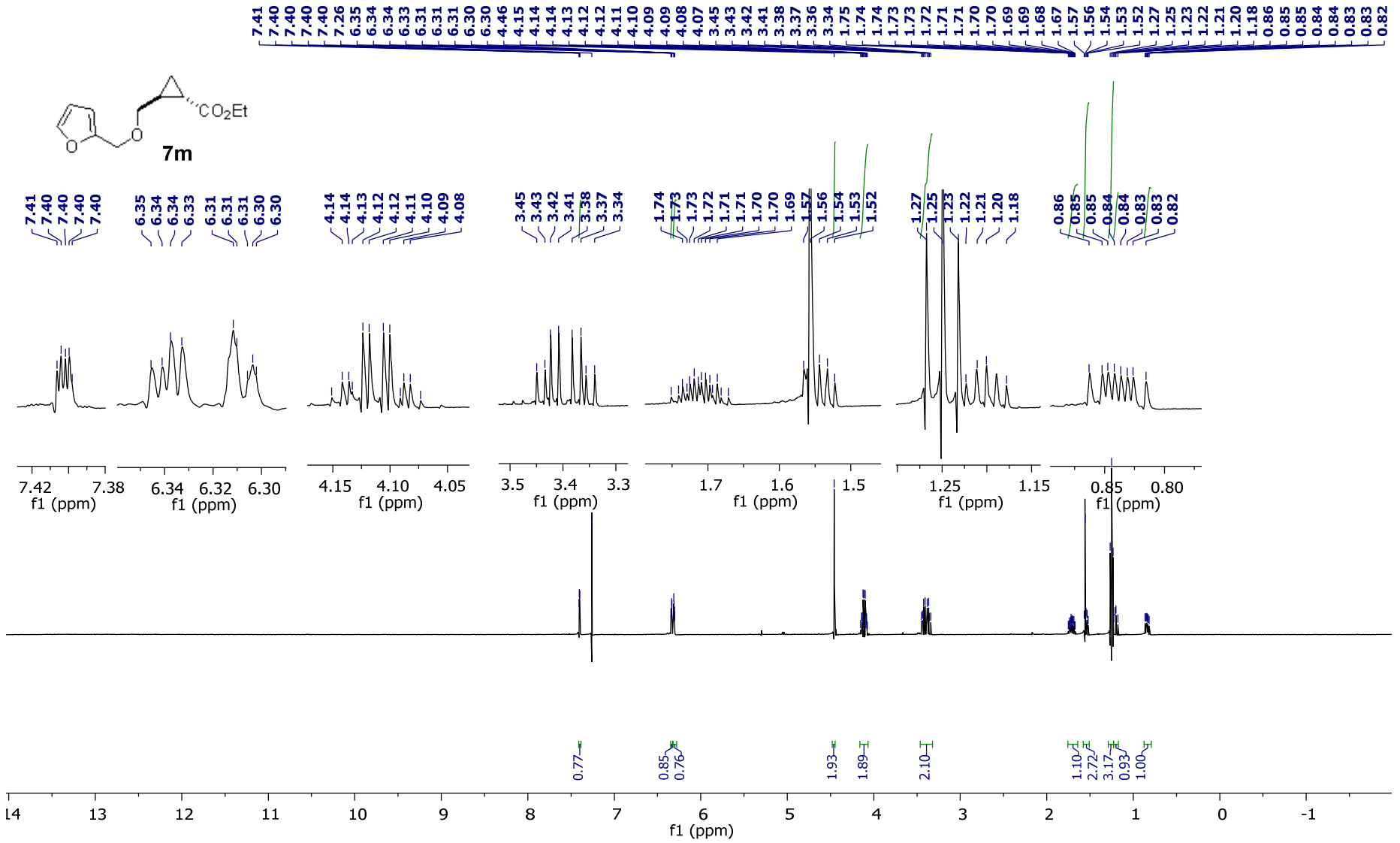

143.26
140.55
122.22
110.30
73.20
66.05
63.69
19.73
16.63
7.94
O
O
OH
8j
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

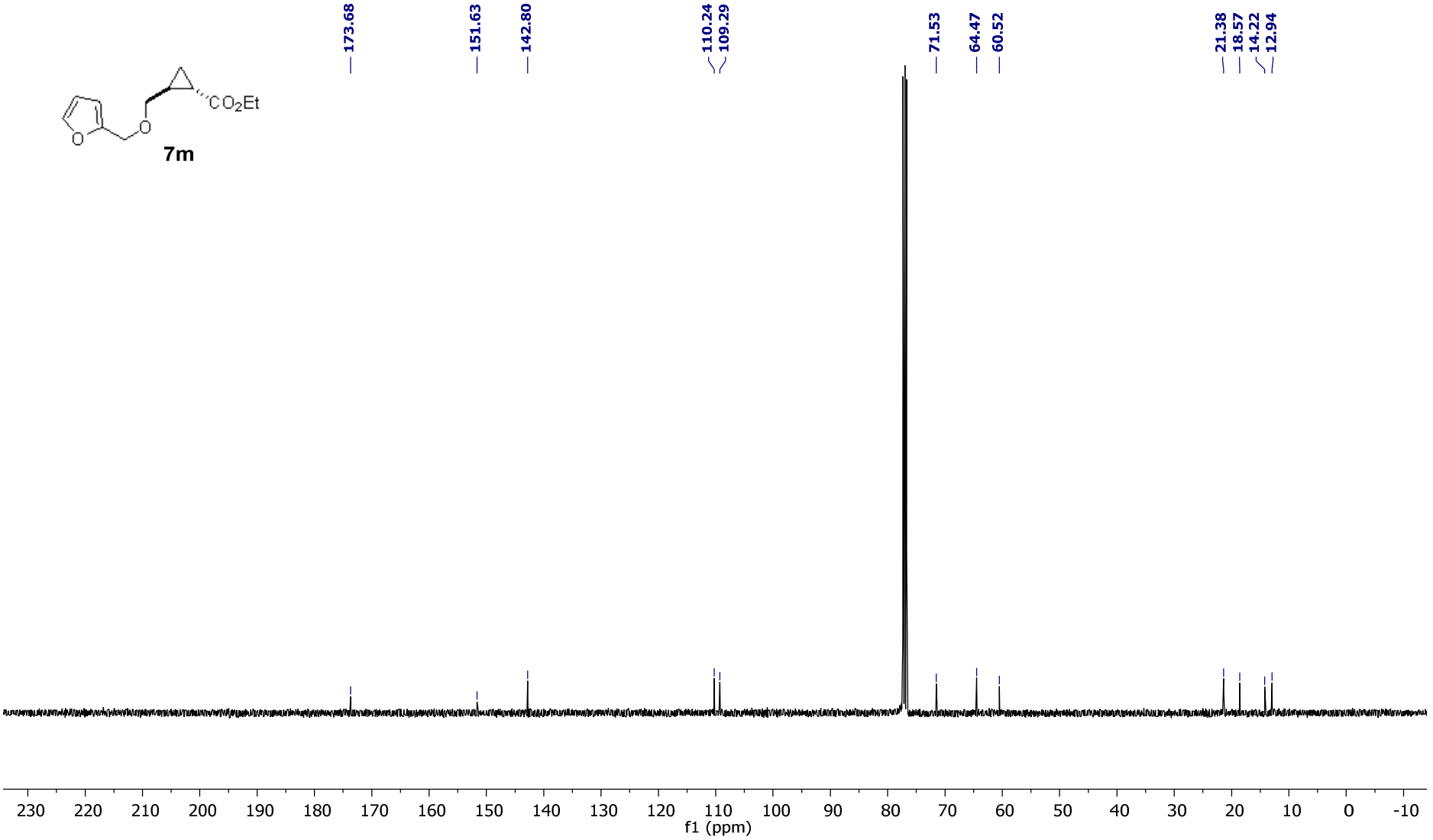

HN
CCl3
O
O
O
1j
f1 (ppm)

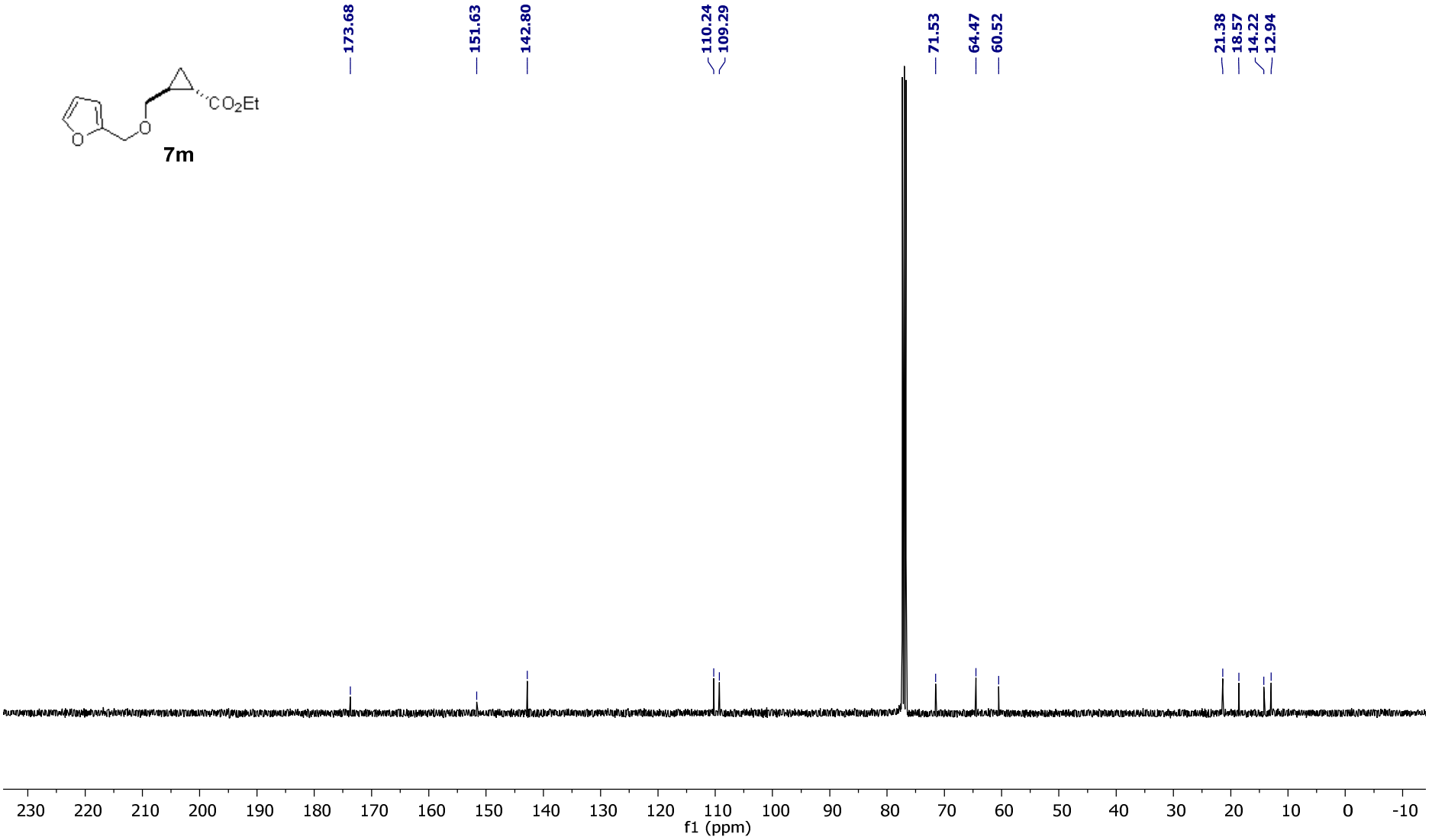

O
HN
CCl3
O
O

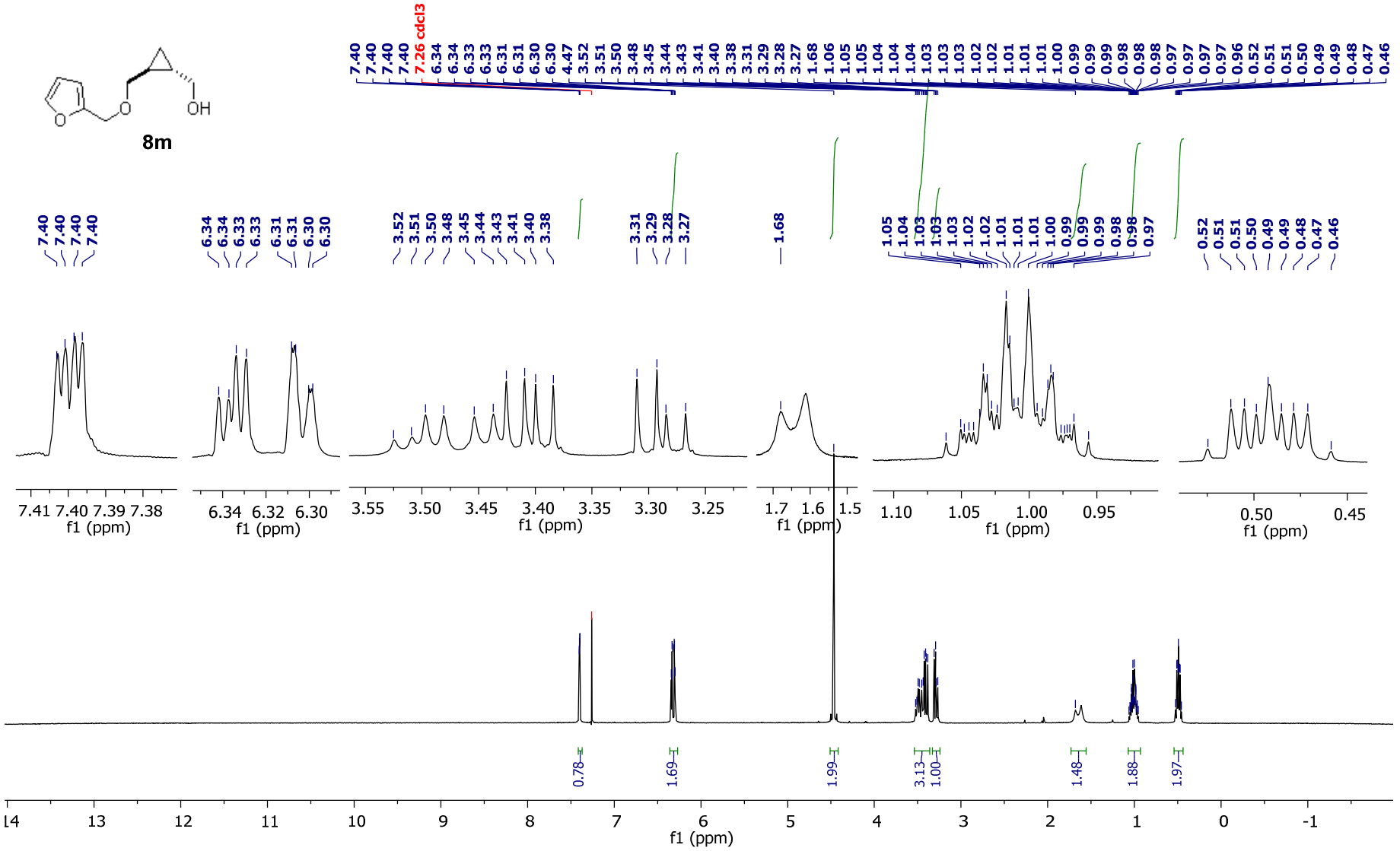
1j

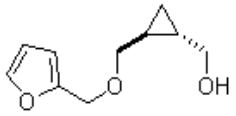
162.86
143.26
140.51
122.34
110.29
91.54
72.68
72.60
63.53
16.85
15.45
8.53
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.41 7.40 7.40 7.40 7.40 7.26 6.35 6.34 6.34 6.33 6.31 6.31 6.31 6.30 6.30 4.46 4.15 4.14 4.14 4.13 4.12 4.12 4.11 4.10 4.09 4.08 4.07 3.45 3.43 3.42 3.41 3.38 3.37 3.36 3.34 1.75 1.74 1.74 1.73 1.73 1.72 1.71 1.70 1.70 1.69 1.68 1.67 1.57 1.56 1.54 1.53 1.52 1.27 1.25 1.23 1.22 1.21 1.20 1.18 0.86 0.85 0.85 0.84 0.84 0.83 0.83 0.82
CO2Et
O
O
7m
f1 (ppm)
0.77
0.85
0.76
1.93
1.89
2.10
1.10
2.72
3.17
0.93
1.00


173.68
151.63
142.80
110.24
109.29
71.53
64.47
60.52
21.38
18.57
14.22
12.94
CO2Et
O
O
7m
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

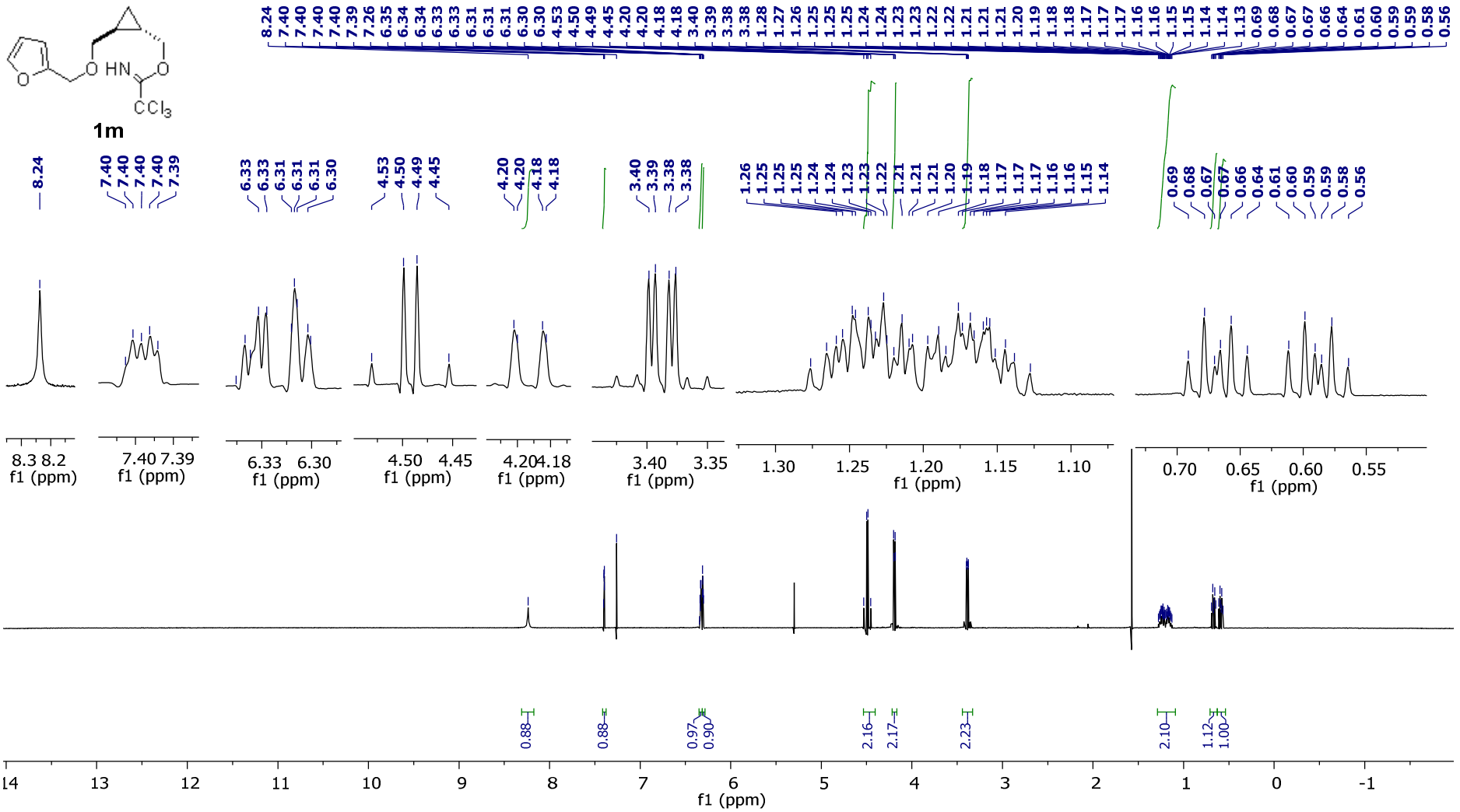

173.68
151.63
142.80
110.24
109.29
71.53
64.47
60.52
21.38
18.57
14.22
12.94
CO2Et
O
O
7m
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

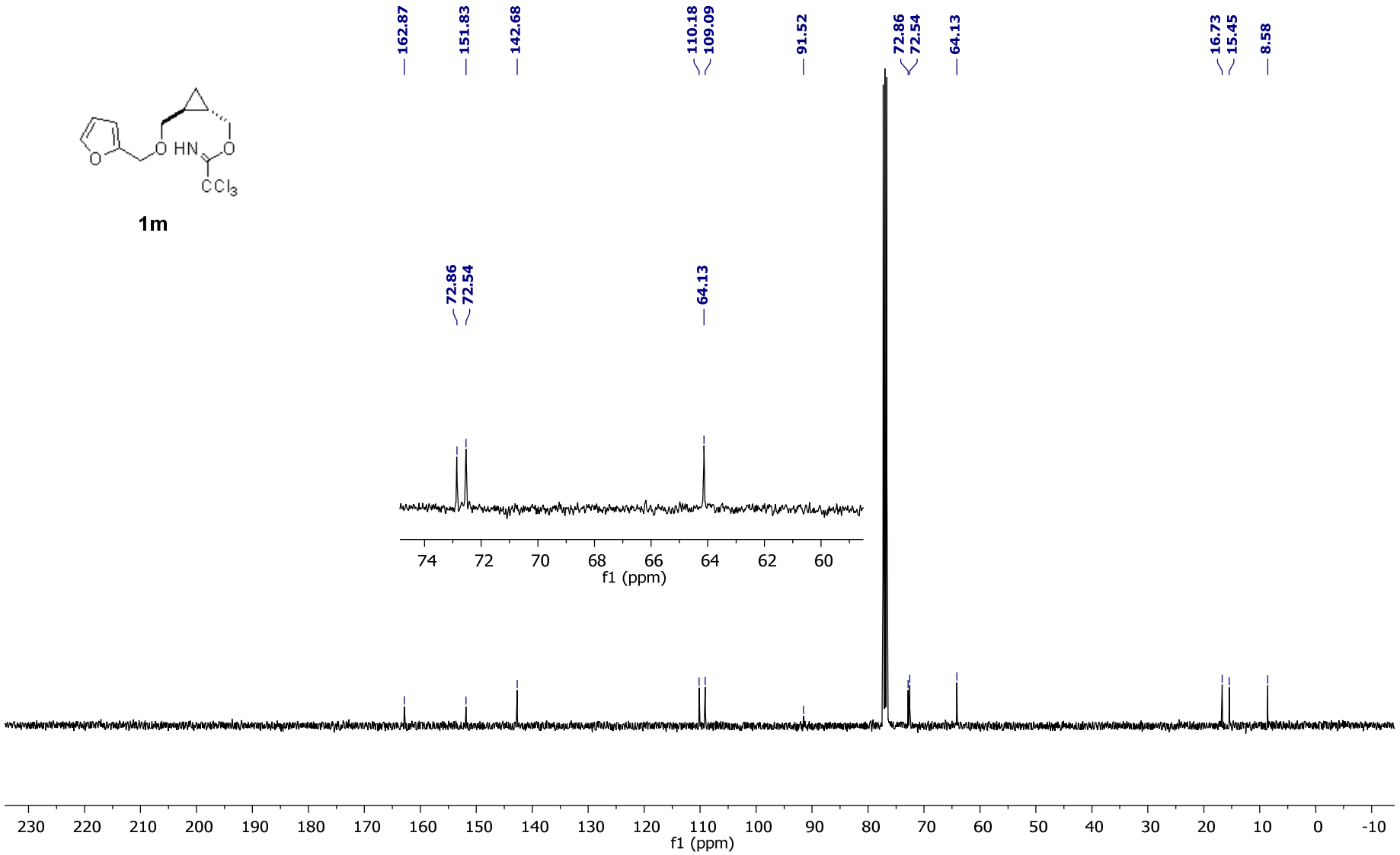

8m
O
OH
7.40 7.40 7.40 7.40 7.26 cdcl3 6.34 6.34 6.33 6.33 6.31 6.31 6.30 6.30 4.47 3.52 3.51 3.50 3.48 3.45 3.44 3.43 3.41 3.40 3.38 3.31 3.29 3.28 3.27 1.68 1.06 1.05 1.05 1.04 1.04 1.04 1.03 1.03 1.03 1.02 1.02 1.01 1.01 1.01 1.01 1.00 0.99 0.99 0.99 0.98 0.98 0.98 0.97 0.97 0.97 0.96 0.52 0.51 0.51 0.50 0.49 0.49 0.48 0.47 0.46
7.41 7.40 7.39 7.38 f1 (ppm)
6.34 6.32 6.30 f1 (ppm)
3.55 3.50 3.45 3.40 3.35 3.30 3.25 f1 (ppm)
1.7 1.6 1.5 f1 (ppm)
1.10 1.05 1.00 0.95 f1 (ppm)
0.50 0.45 f1 (ppm)
0.78 1.69 1.99 3.13 1.00 1.48 1.88 1.97
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 f1 (ppm)

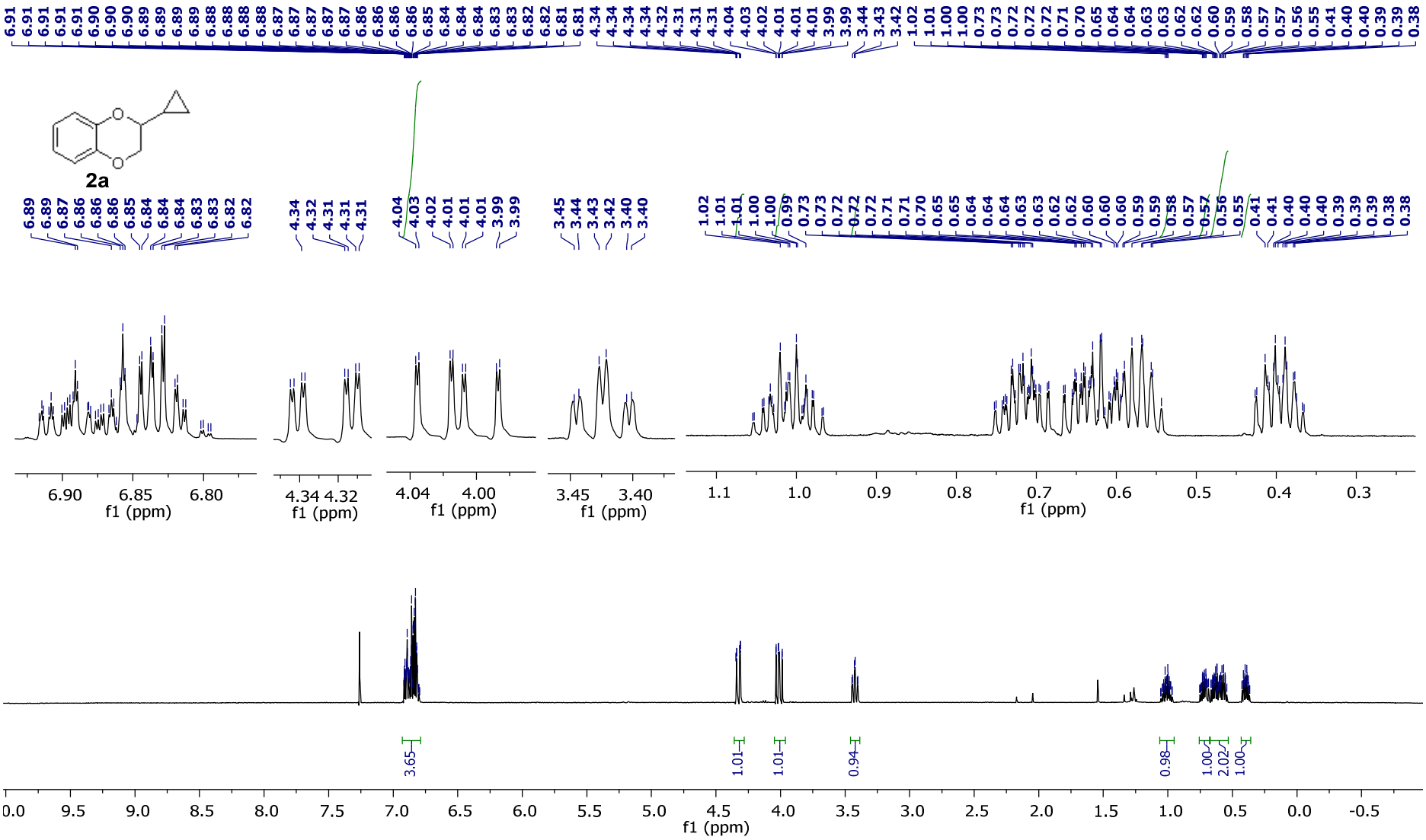

O
O
OH

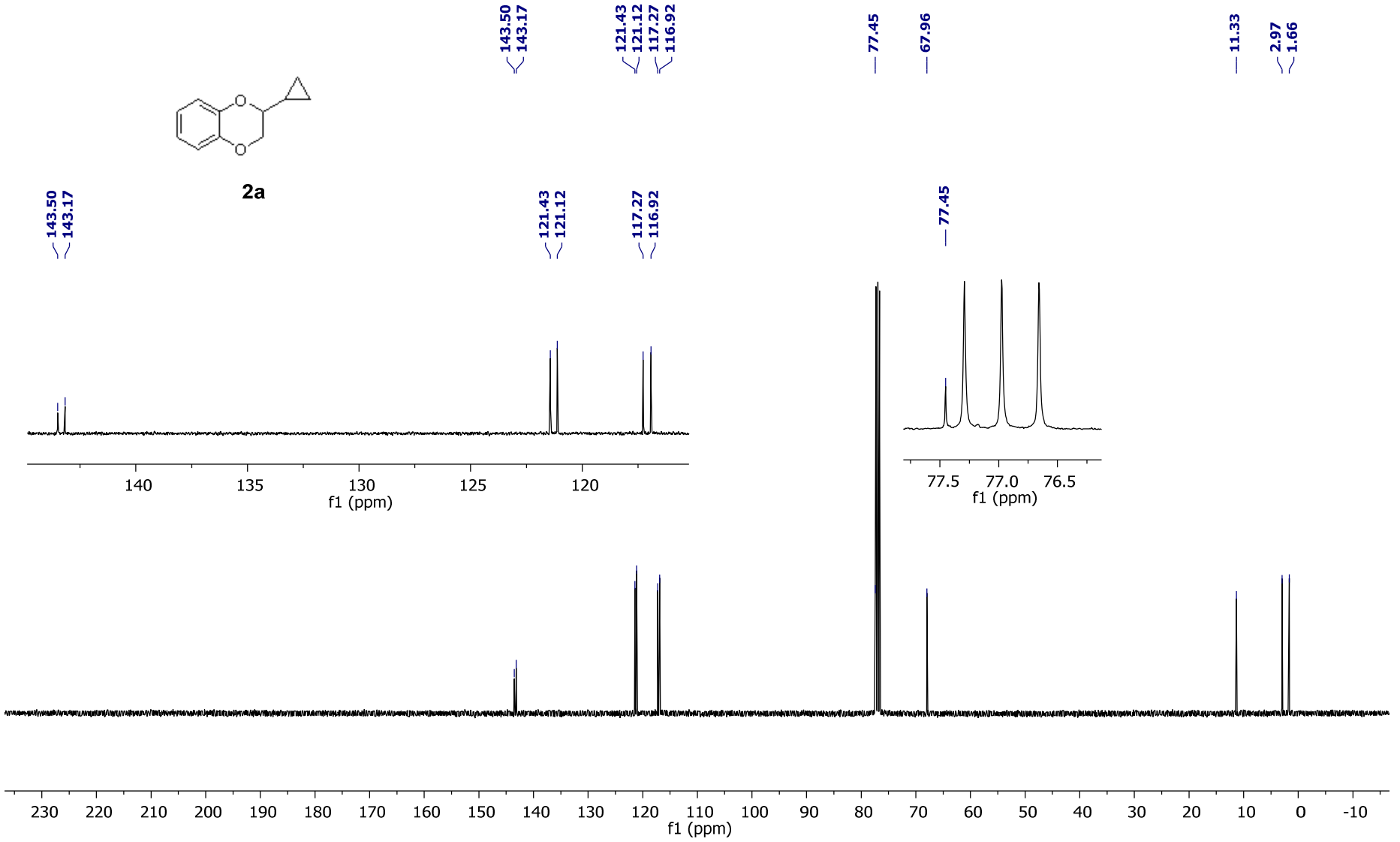
8m

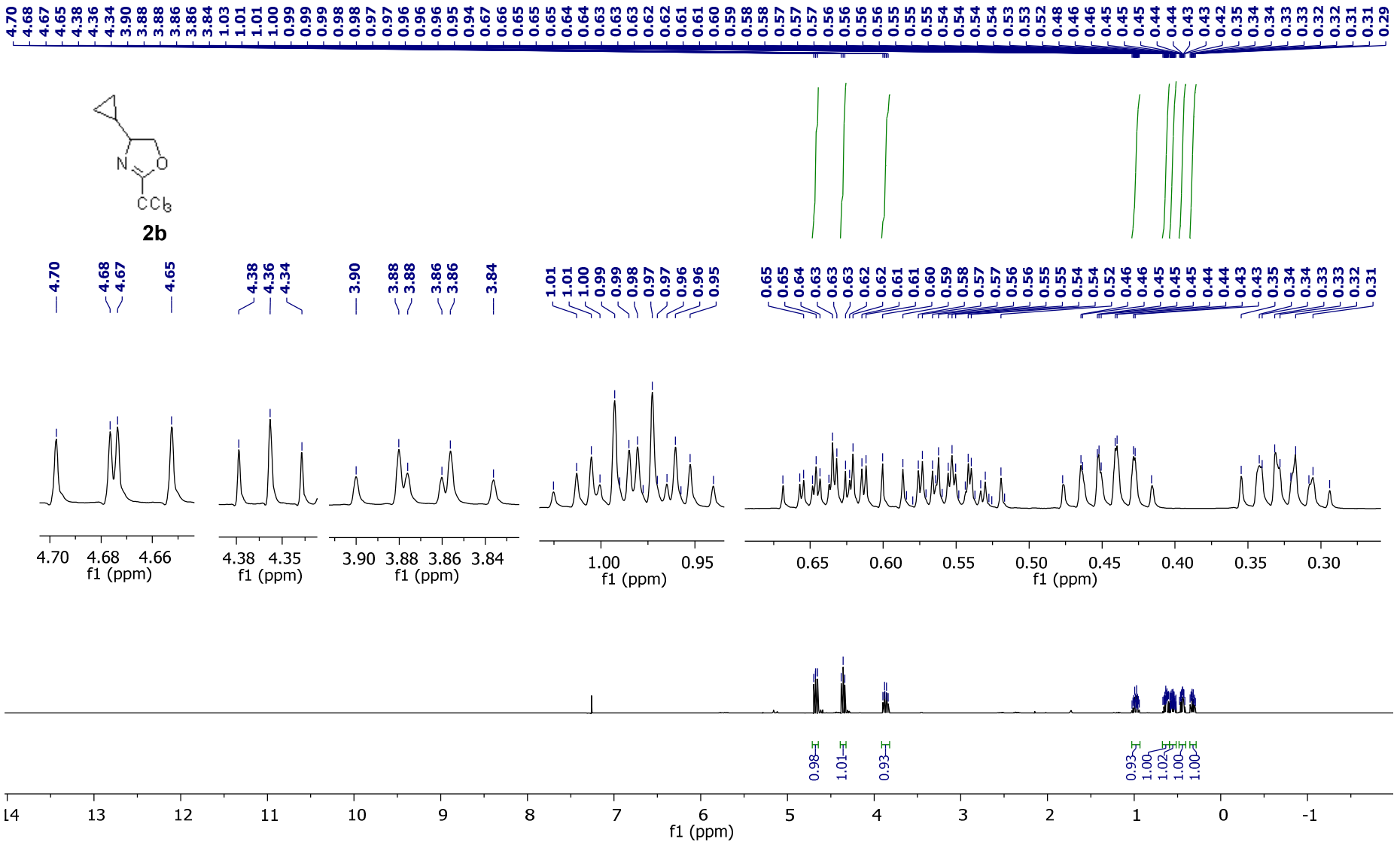
149.28
140.11
107.64
106.54
74.09
63.72
61.78
17.22
14.01
5.53
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

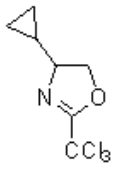

1m
f1 (ppm)


162.87
151.83
142.68
110.18
109.09
91.52
72.86
72.54
64.13
16.73
15.45
8.58
O
HN
O
O
CCl3
1m
f1 (ppm)
f1 (ppm)


2a
f1 (ppm)
3.65
1.01
1.01
0.94
0.98
1.00
2.02
1.00

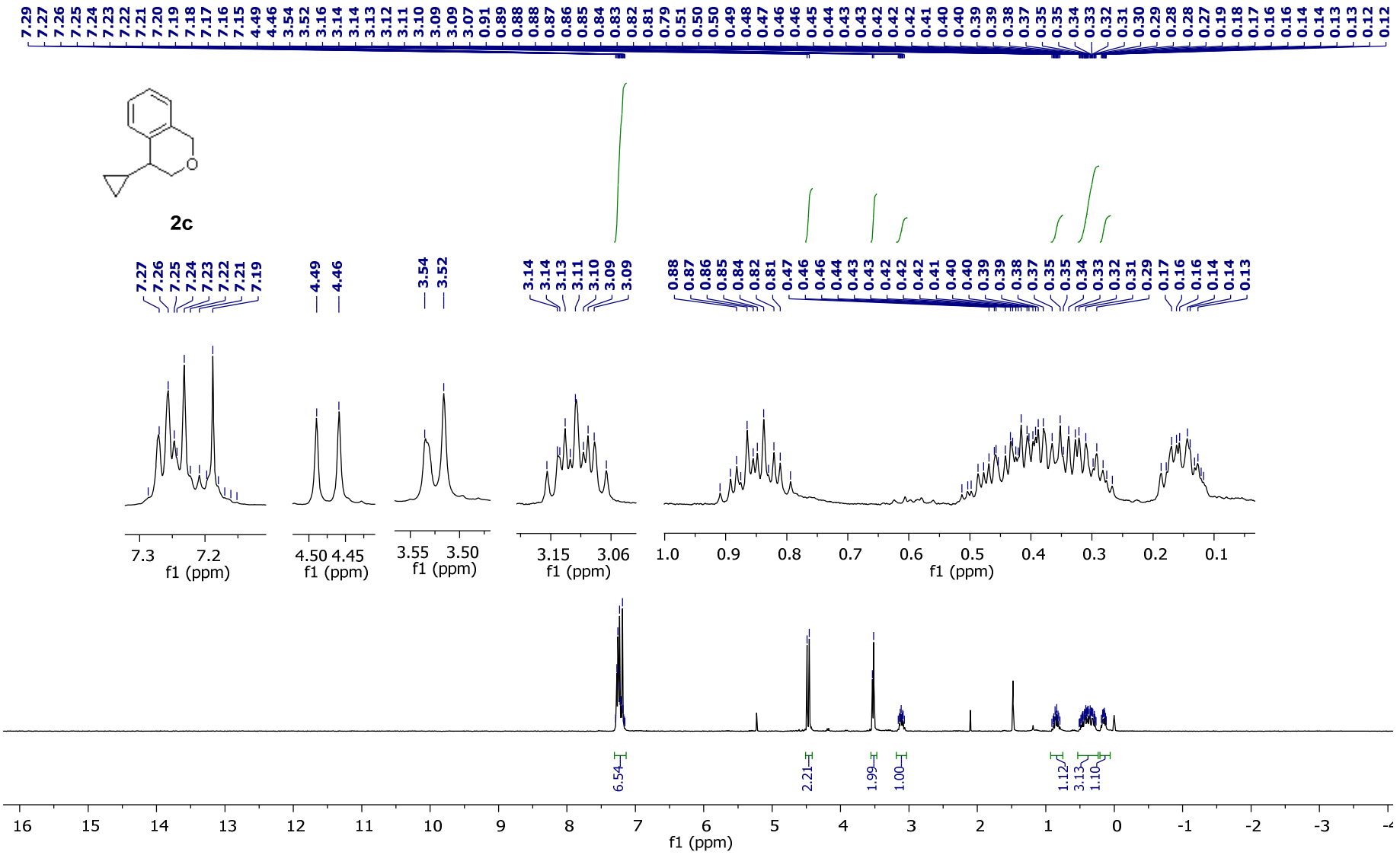

143.50
143.17
121.43
121.12
117.27
116.92
77.45
67.96
11.33
2.97
1.66
2a
140
135
130
125
120
f1 (ppm)
77.5
77.0
76.5
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

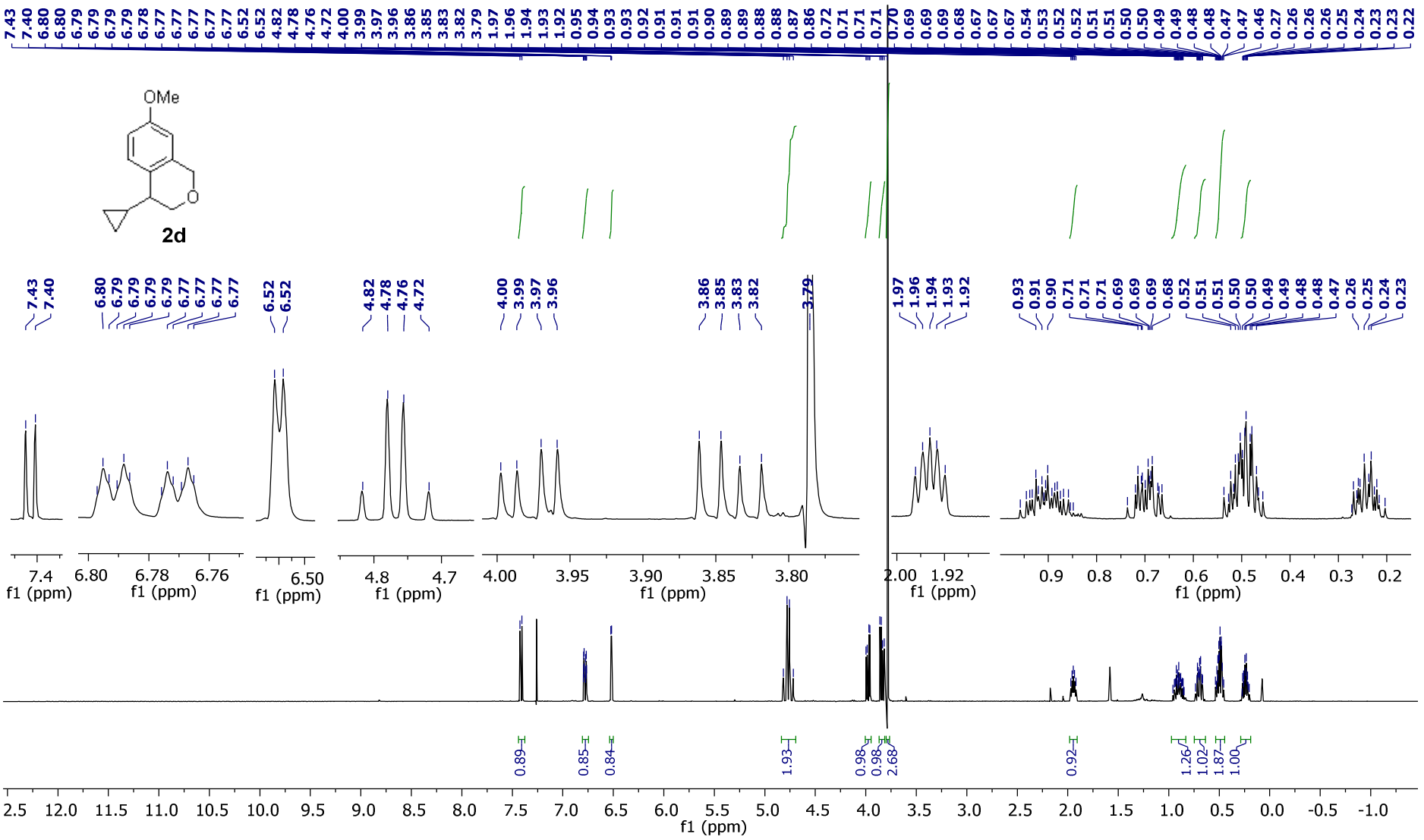

4.70 4.68 4.67 4.65 4.38 4.36 4.34 3.90 3.88 3.88 3.86 3.86 3.84 1.03 1.01 1.01 1.00 0.99 0.99 0.99 0.98 0.98 0.97 0.97 0.96 0.96 0.96 0.95 0.94 0.67 0.66 0.65 0.65 0.65 0.64 0.64 0.63 0.63 0.63 0.62 0.62 0.61 0.61 0.60 0.59 0.58 0.58 0.57 0.57 0.57 0.56 0.56 0.56 0.56 0.55 0.55 0.55 0.54 0.54 0.54 0.54 0.53 0.53 0.52 0.48 0.46 0.46 0.45 0.45 0.45 0.44 0.44 0.43 0.43 0.42 0.35 0.34 0.34 0.33 0.33 0.32 0.32 0.31 0.31 0.29
N
O
CCl3
2b
4.70 4.68 4.67 4.65 4.38 4.36 4.34 3.90 3.88 3.88 3.86 3.86 3.84 1.01 1.01 1.00 0.99 0.99 0.98 0.97 0.97 0.96 0.96 0.95 0.65 0.65 0.64 0.63 0.63 0.63 0.62 0.62 0.61 0.61 0.60 0.59 0.58 0.57 0.57 0.56 0.56 0.55 0.55 0.54 0.54 0.52 0.46 0.46 0.45 0.45 0.45 0.44 0.44 0.43 0.43 0.35 0.34 0.34 0.33 0.33 0.32 0.31
4.70 4.68 4.66
f1 (ppm)
4.38 4.35
f1 (ppm)
3.90 3.88 3.86 3.84
f1 (ppm)
1.00 0.95
f1 (ppm)
0.65 0.60 0.55 0.50 0.45 0.40 0.35 0.30
f1 (ppm)
0.98 1.01 0.93 0.93 1.00 1.02 1.00 1.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

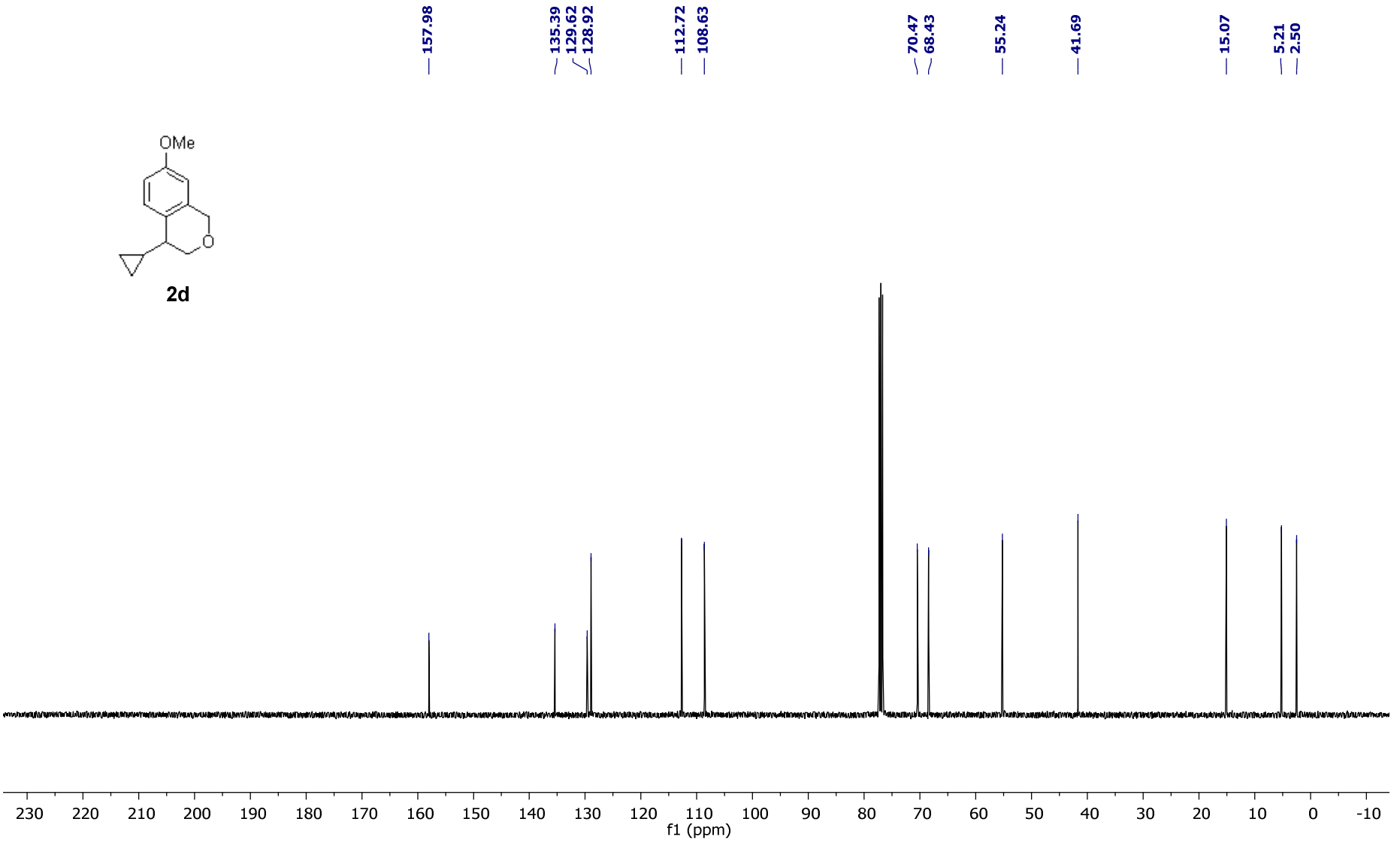

N
O
CCl3

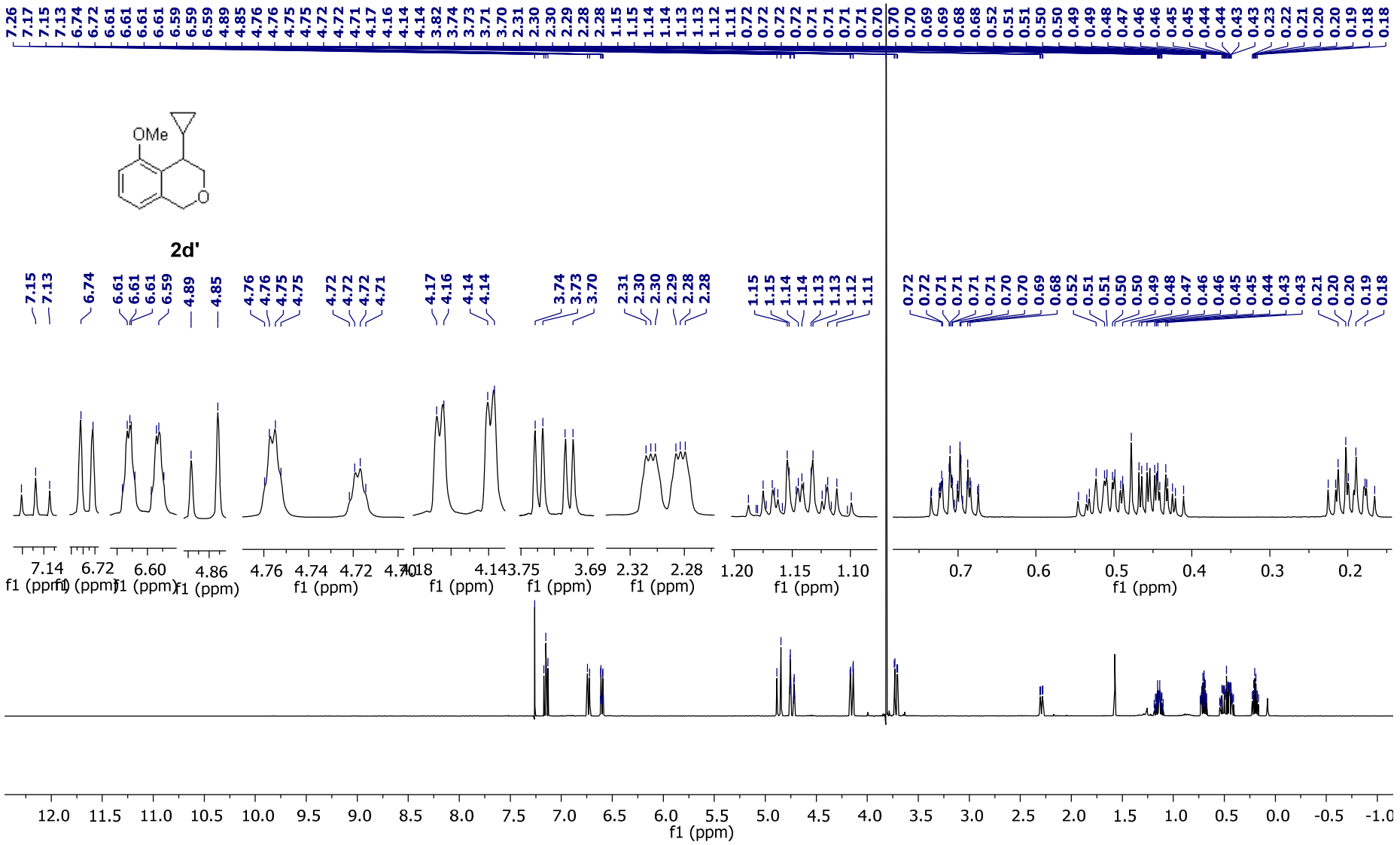
2b

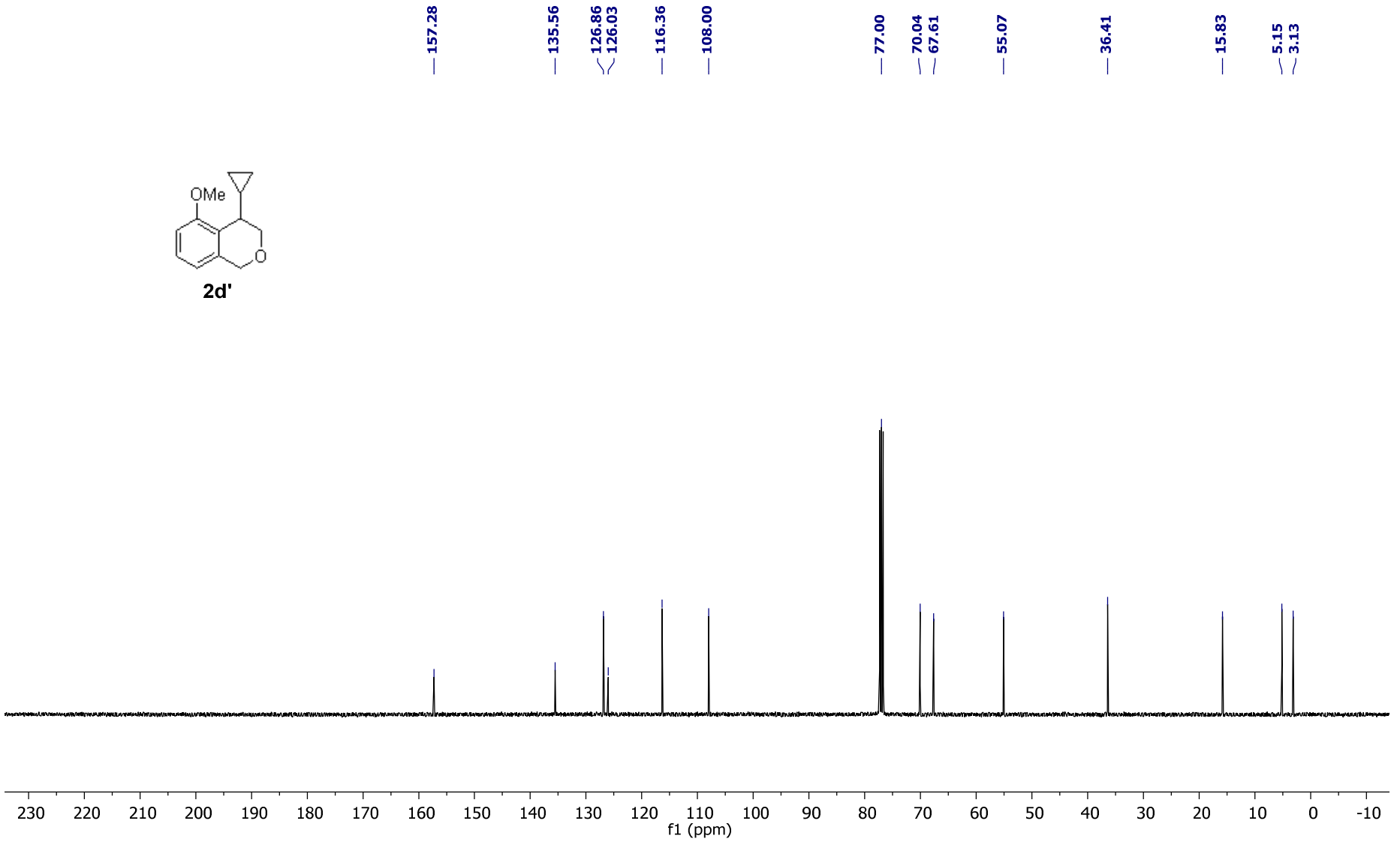
162.67
86.66
76.00
70.84
15.14
2.98
2.11
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

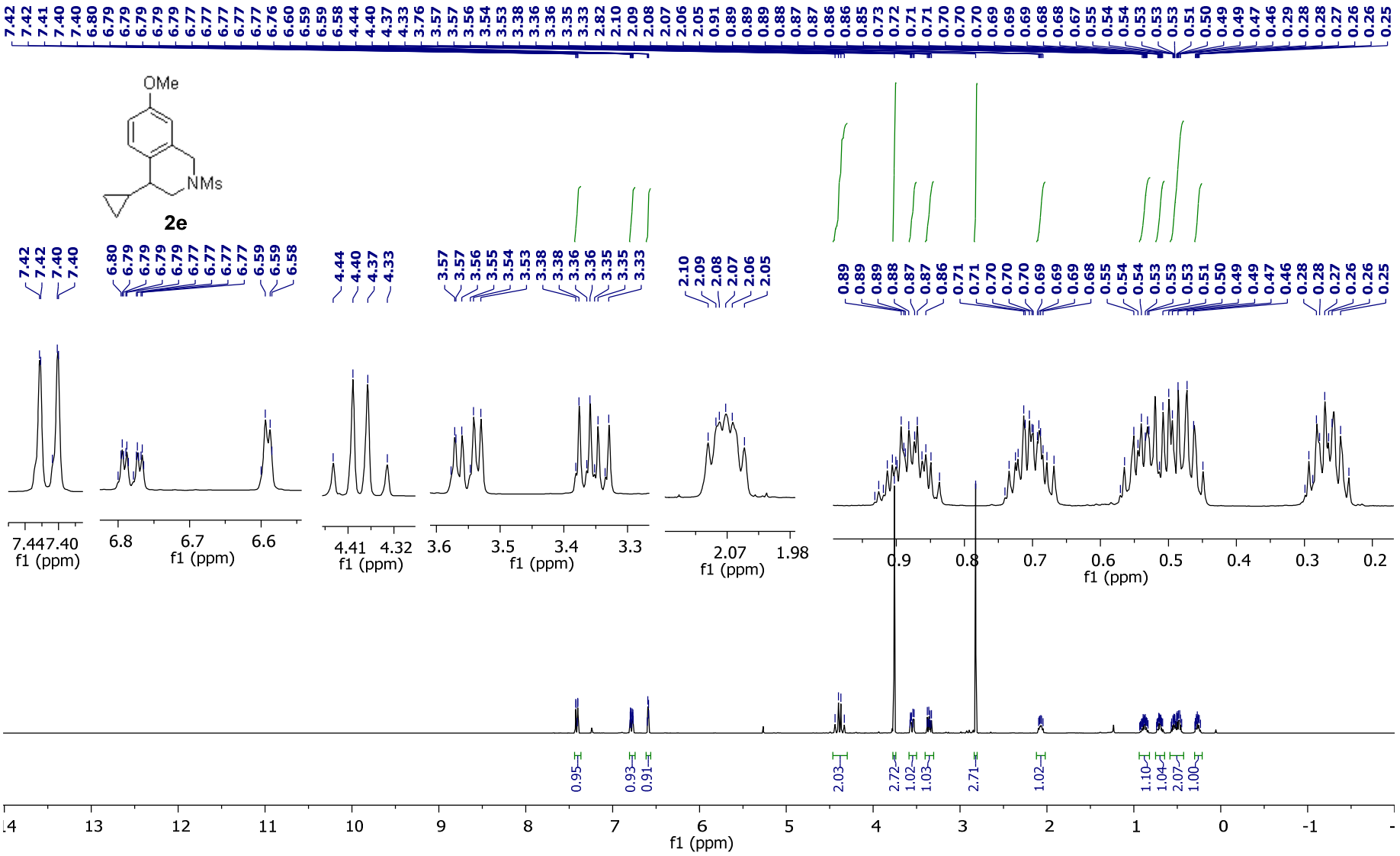

2c
f1 (ppm)

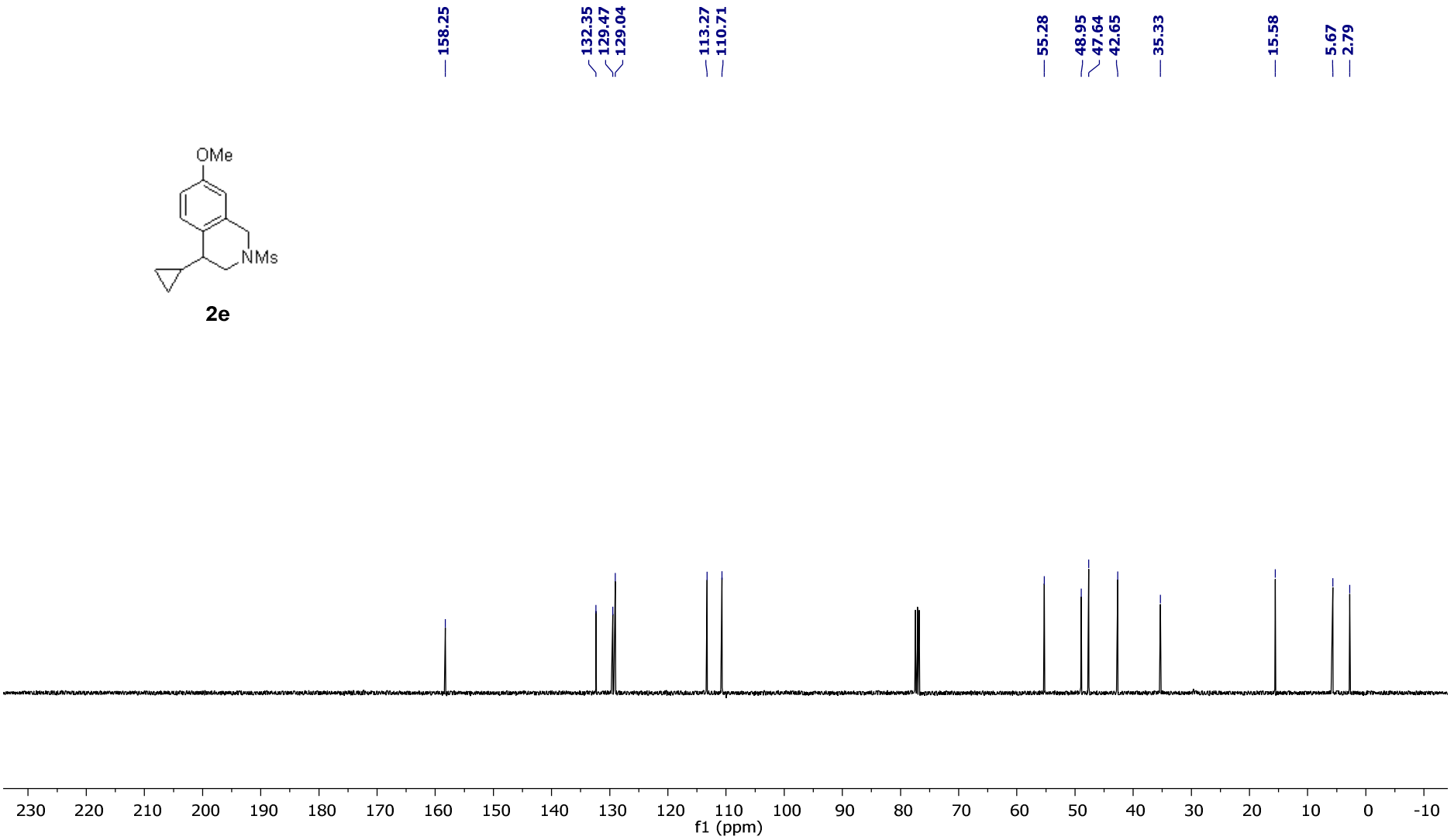

OMe
O
2d
f1 (ppm)

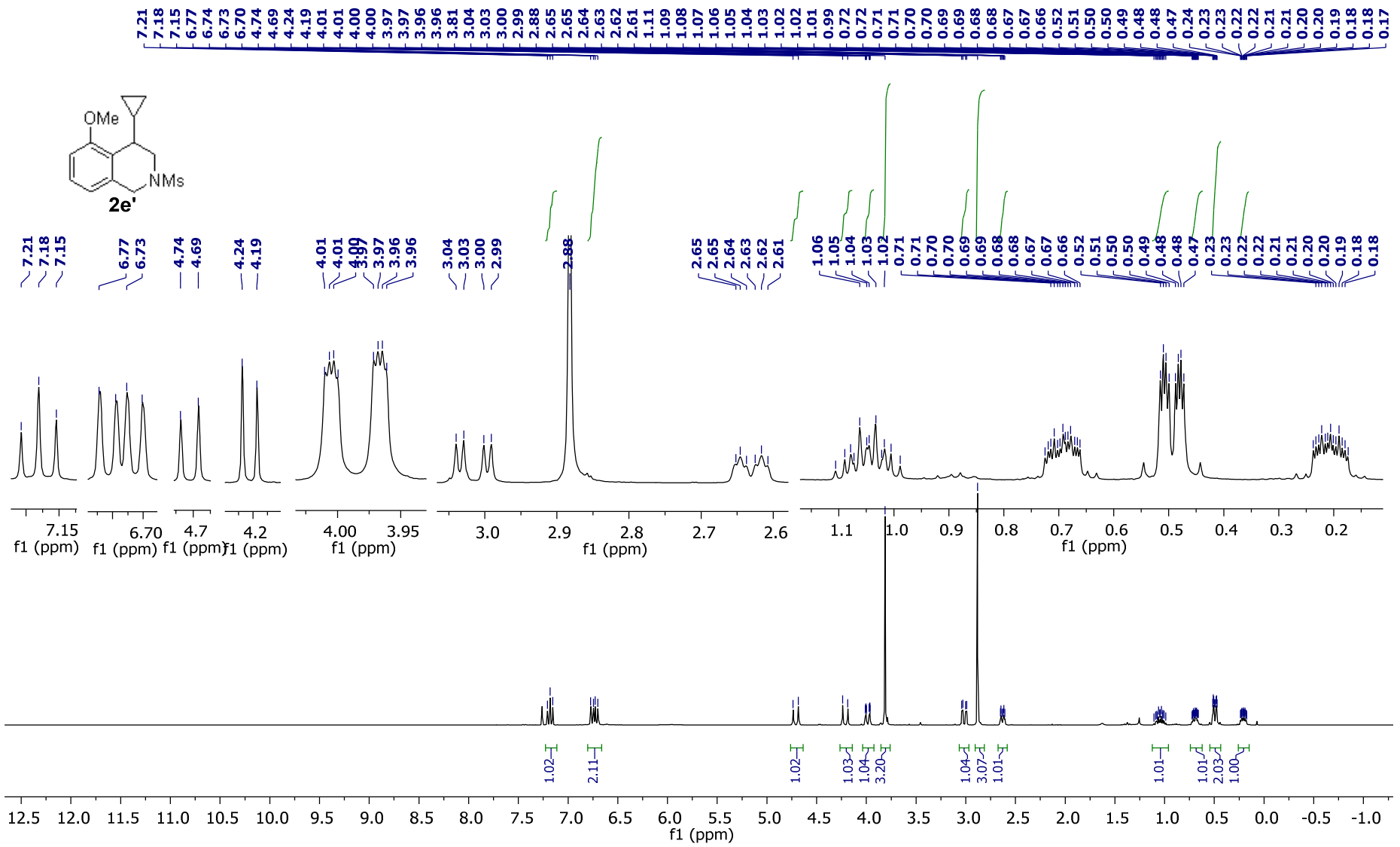

157.98
135.39
129.62
128.92
112.72
108.63
70.47
68.43
55.24
41.69
15.07
5.21
2.50
OMe
O
2d
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

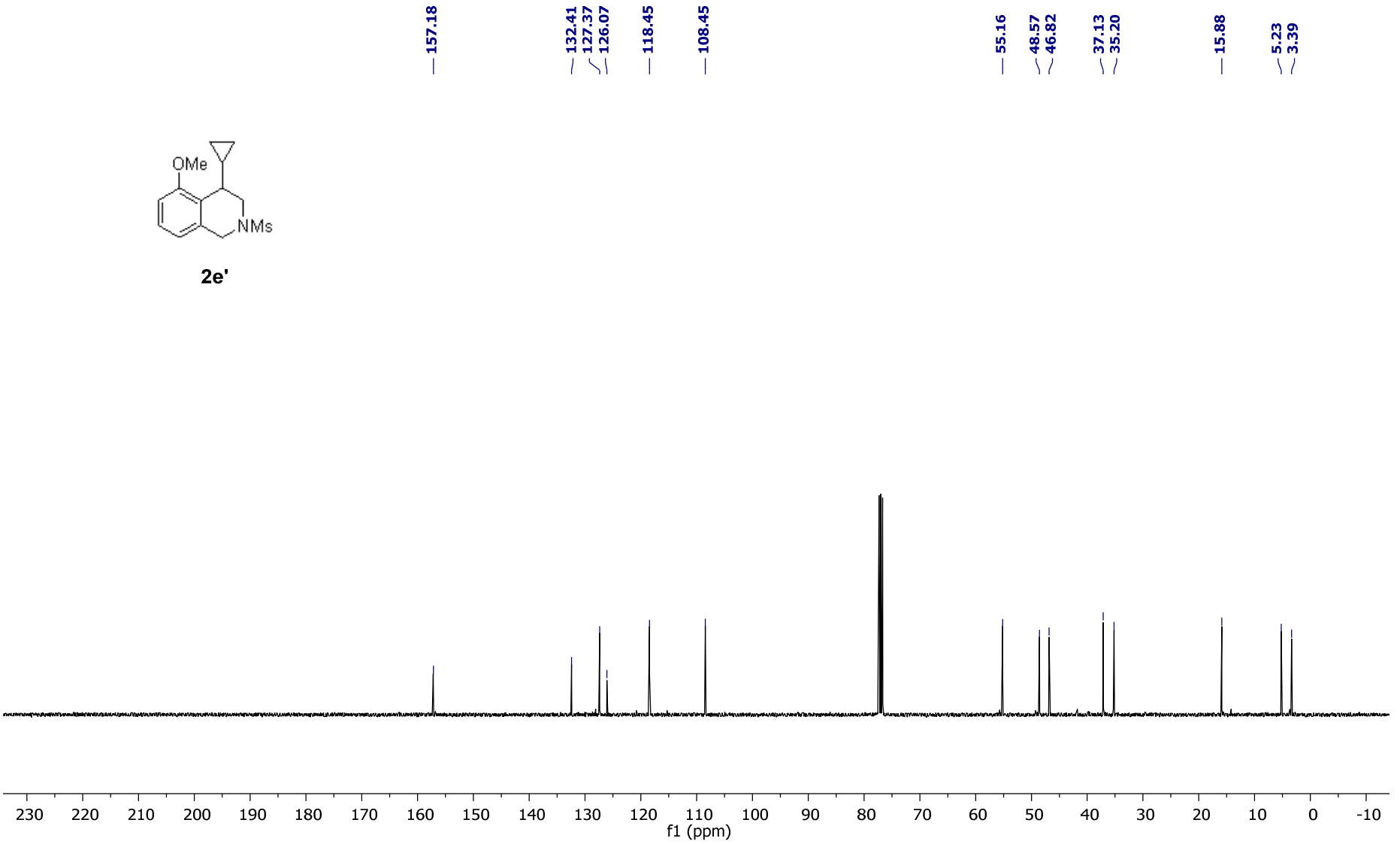

OMe
O
2d'
f1 (ppm)

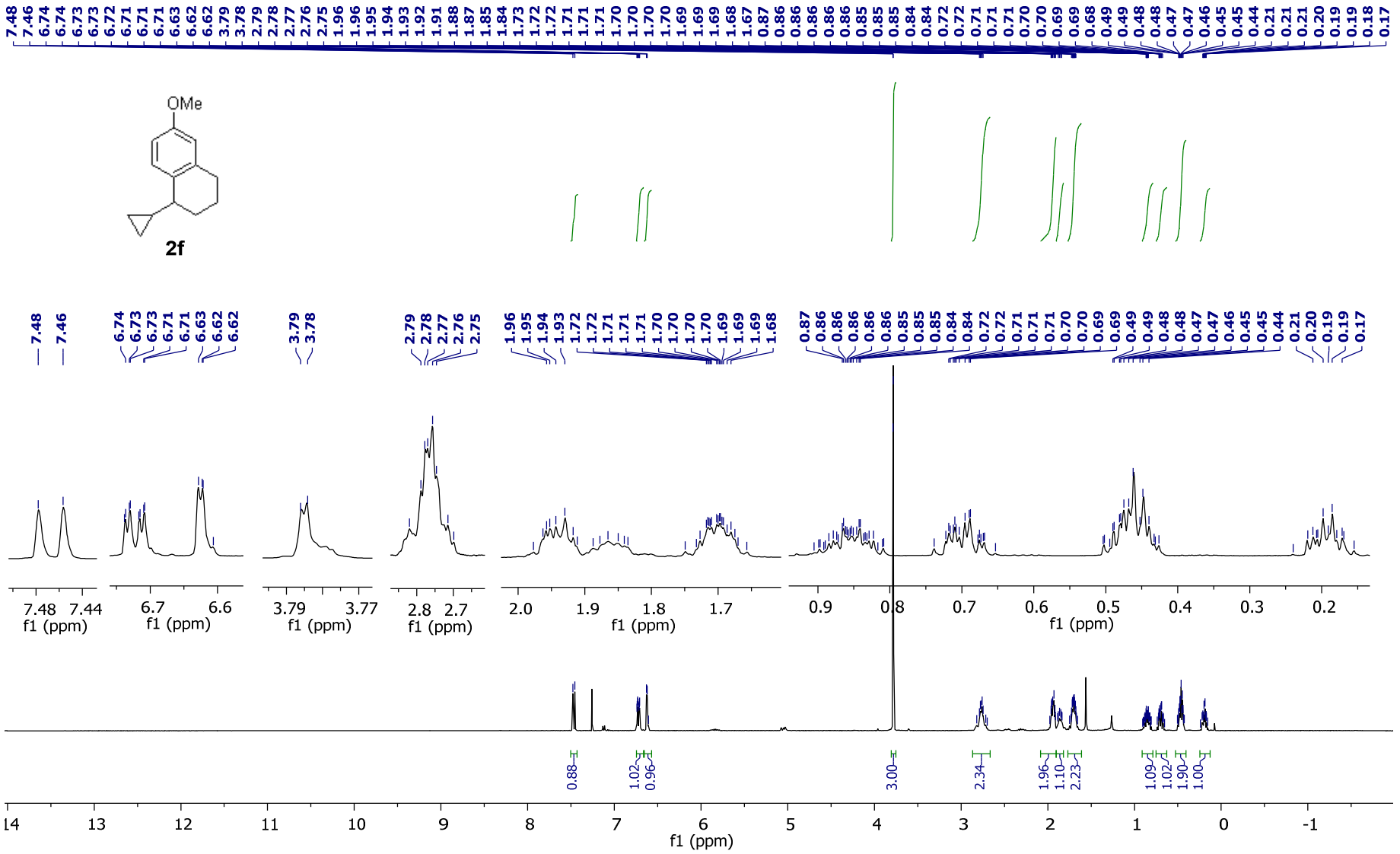

157.28
135.56
126.86
126.03
116.36
108.00
77.00
70.04
67.61
55.07
36.41
15.83
5.15
3.13
OMe
O
2d'
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

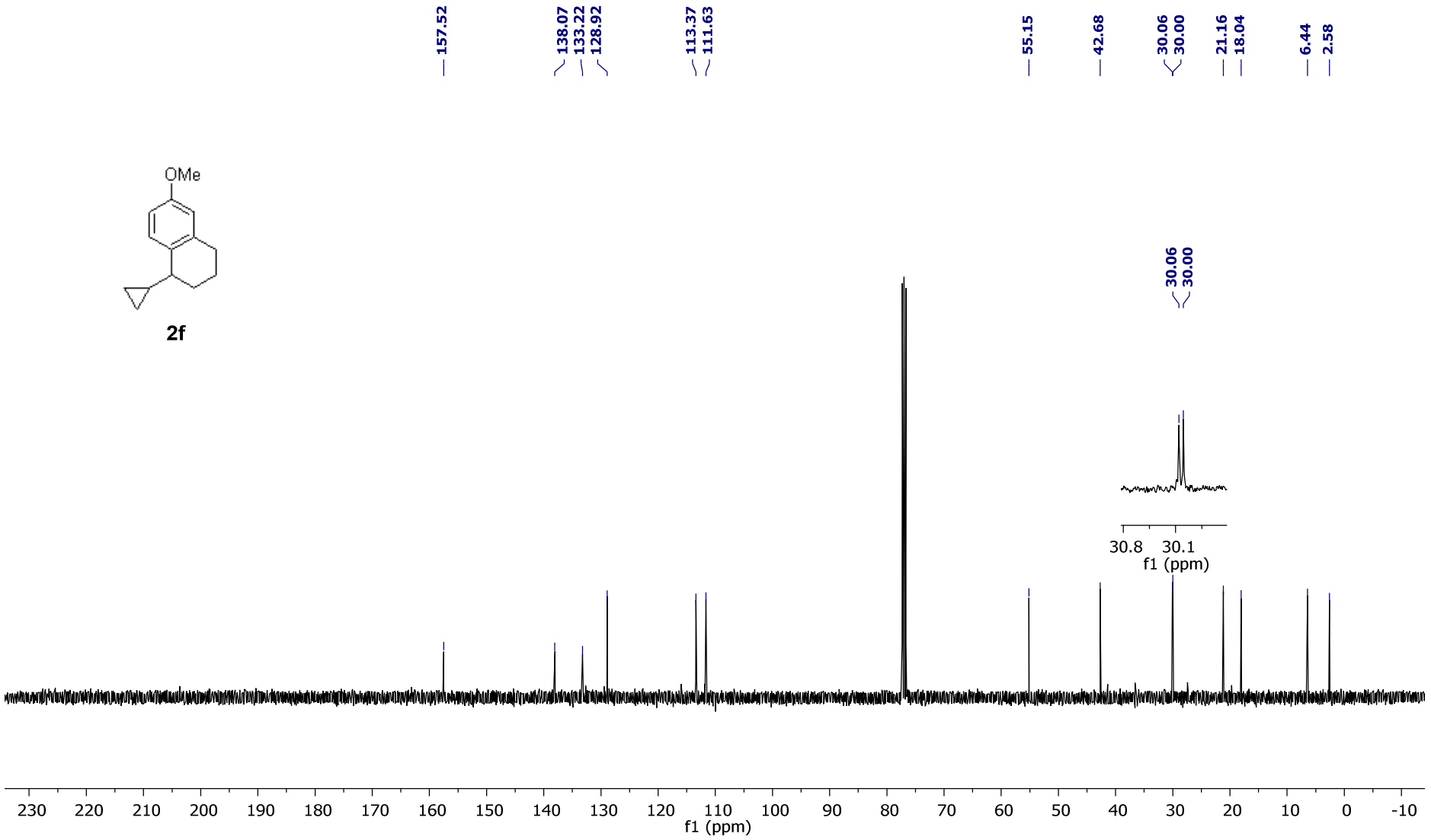

OMe
NMs
2e
f1 (ppm)

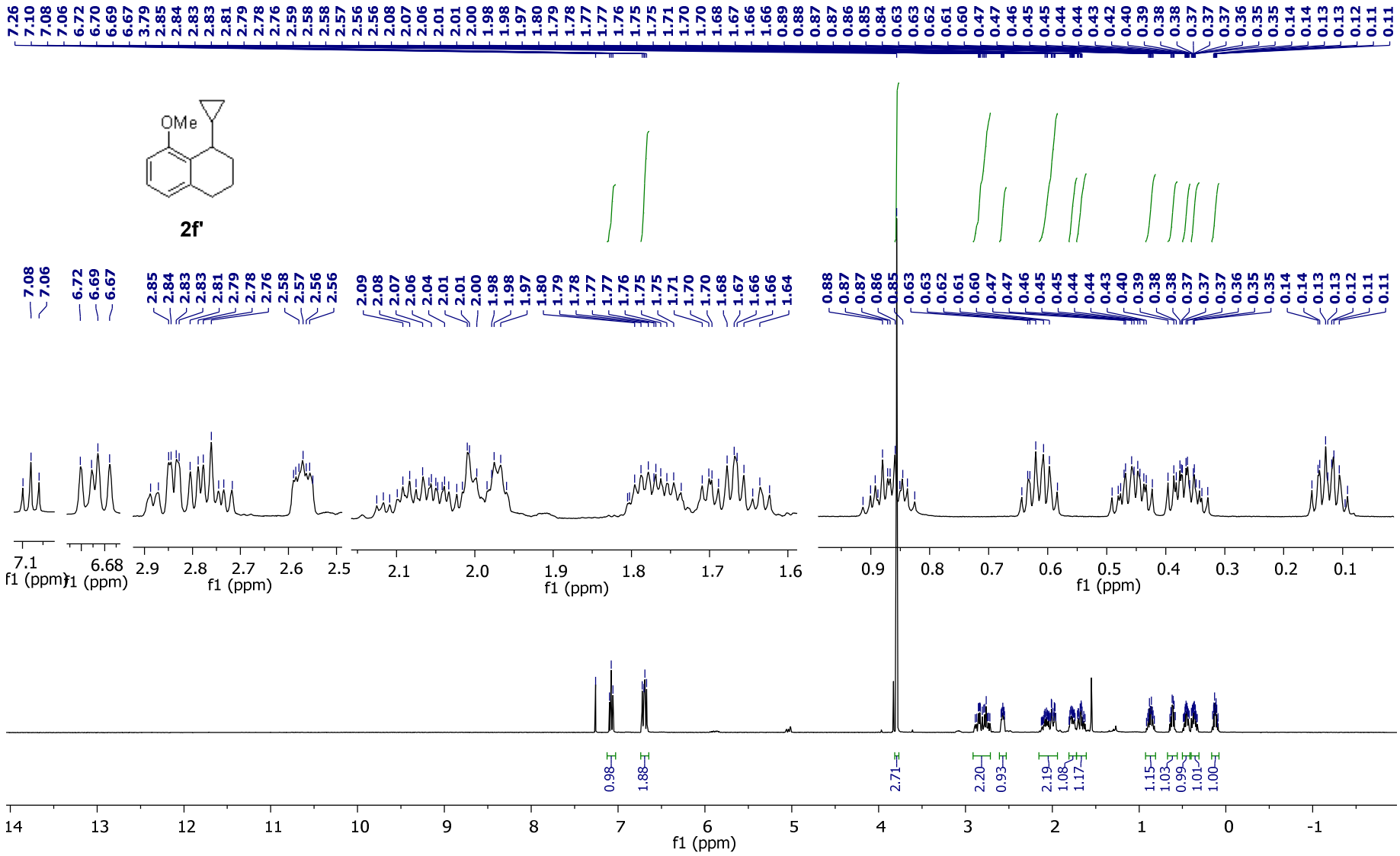

158.25
132.35
129.47
129.04
113.27
110.71
55.28
48.95
47.64
42.65
35.33
15.58
5.67
2.79
OMe
NMs
2e
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

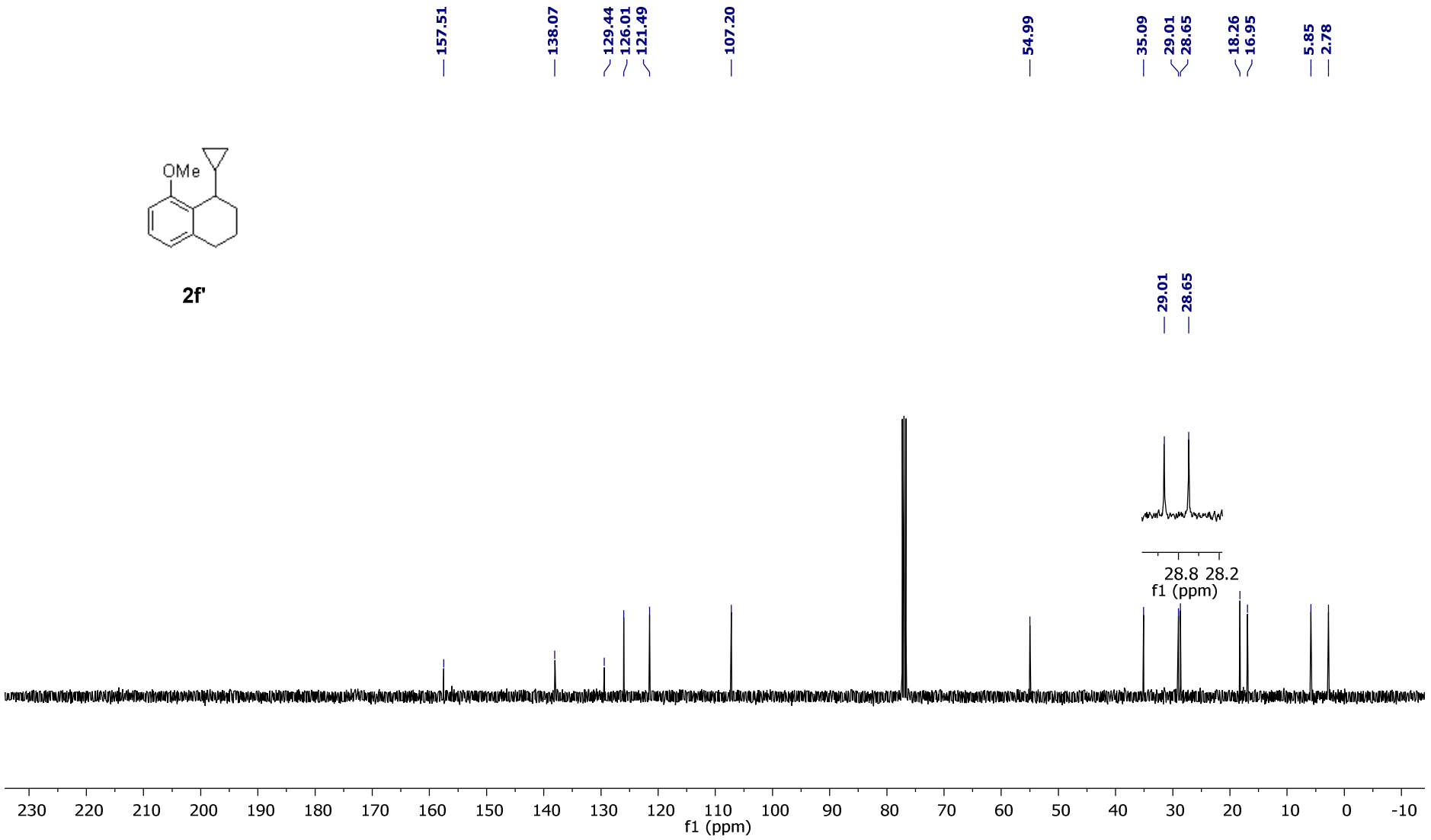

OMe
NMs
2e'
f1 (ppm)

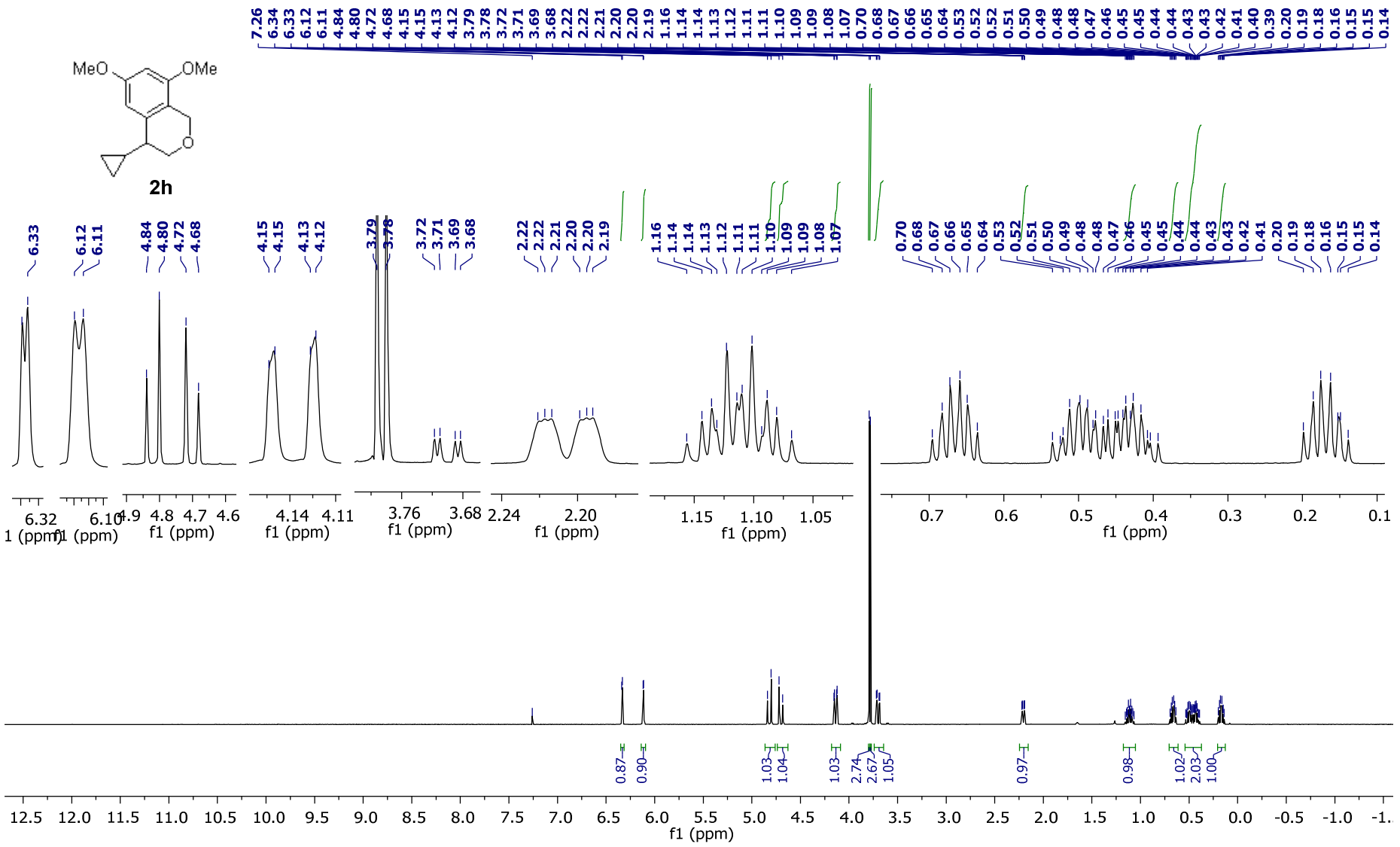

157.18
132.41
127.37
126.07
118.45
108.45
55.16
48.57
46.82
37.13
35.20
15.88
5.23
3.39
OMe
NMs
2e'
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

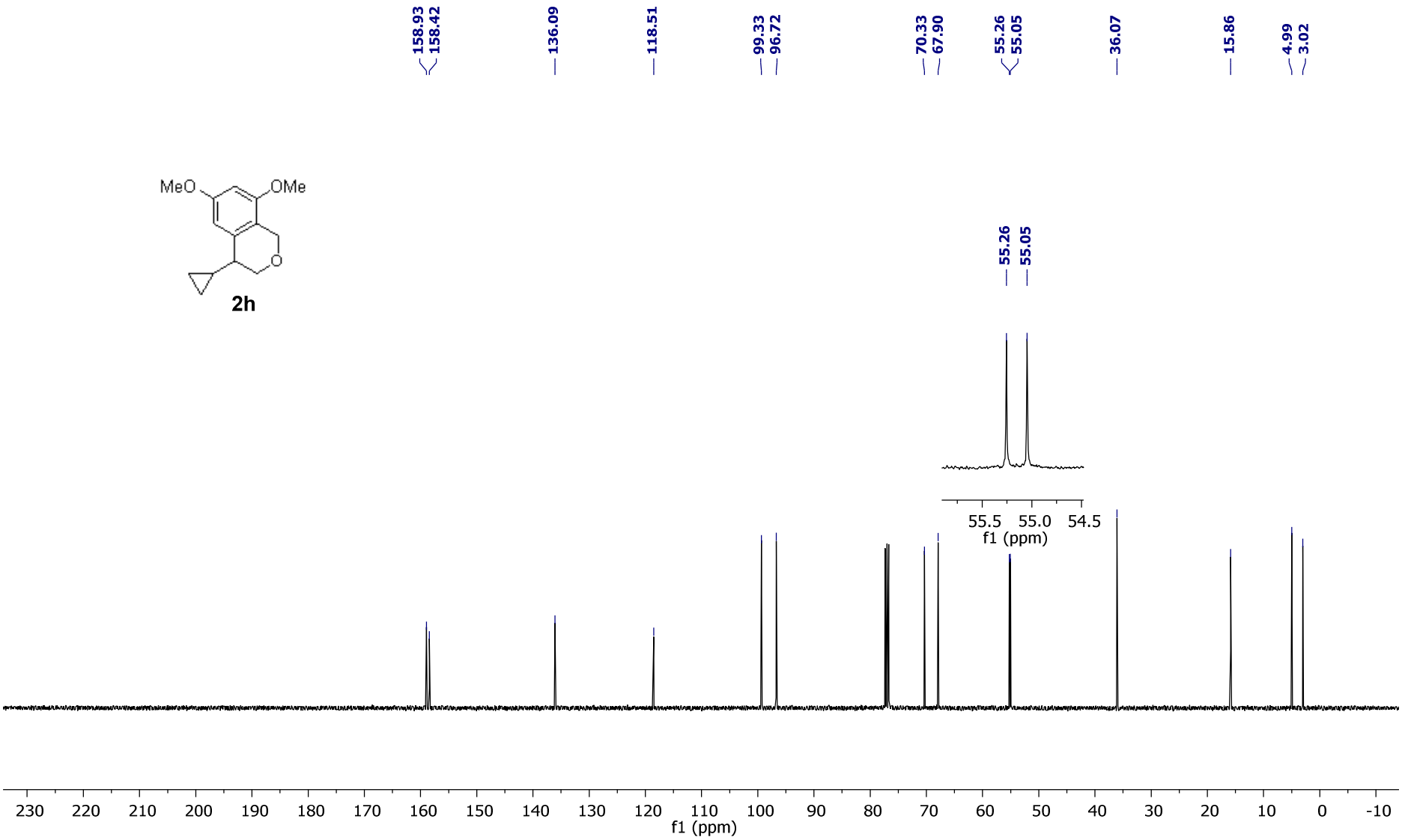

OMe
2f
f1 (ppm)

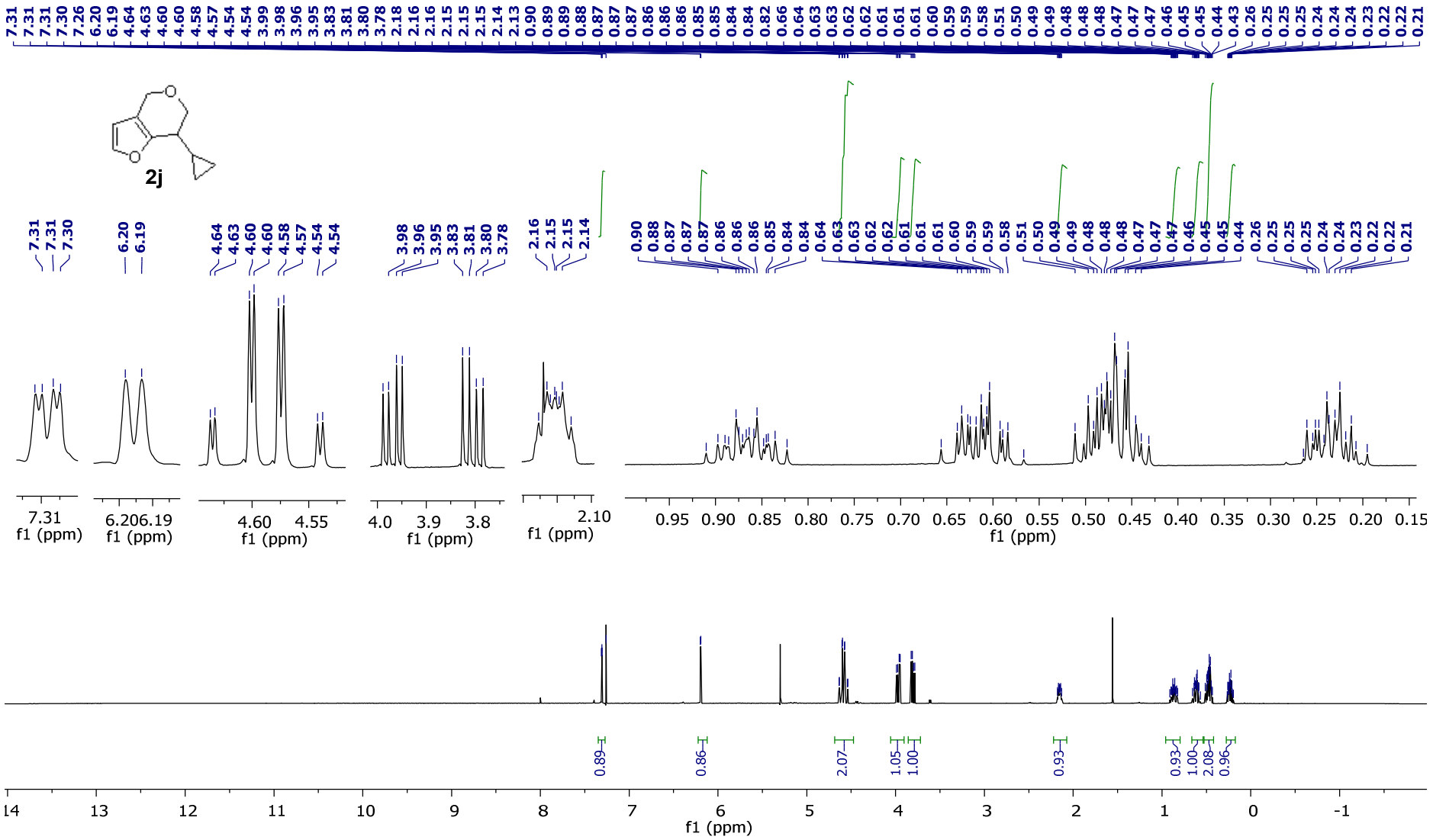

157.52
138.07
133.22
128.92
113.37
111.63
55.15
42.68
30.06
30.00
21.16
18.04
6.44
2.58
OMe
2f
30.06
30.00
30.8
30.1
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

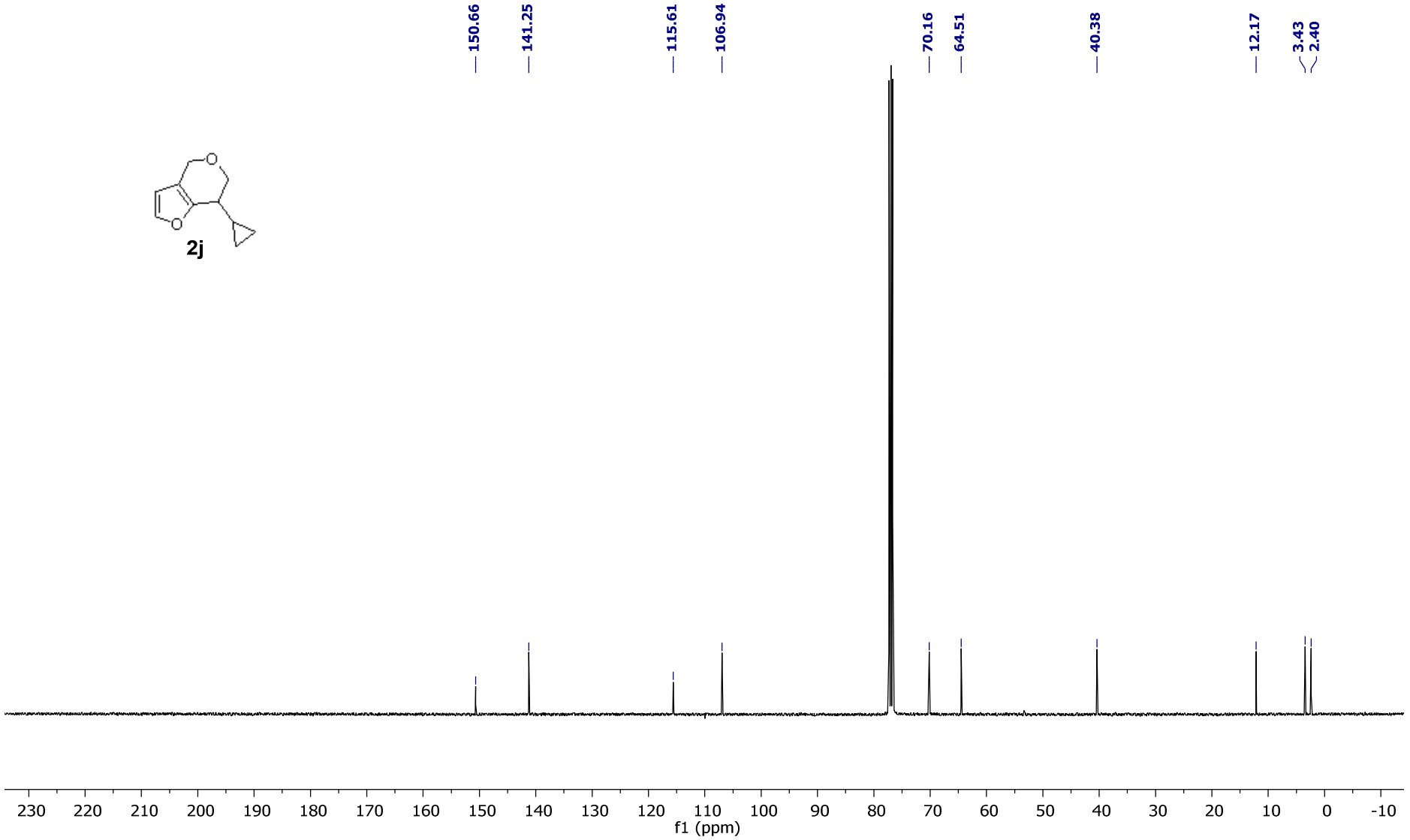

OMe
2f'
f1 (ppm)

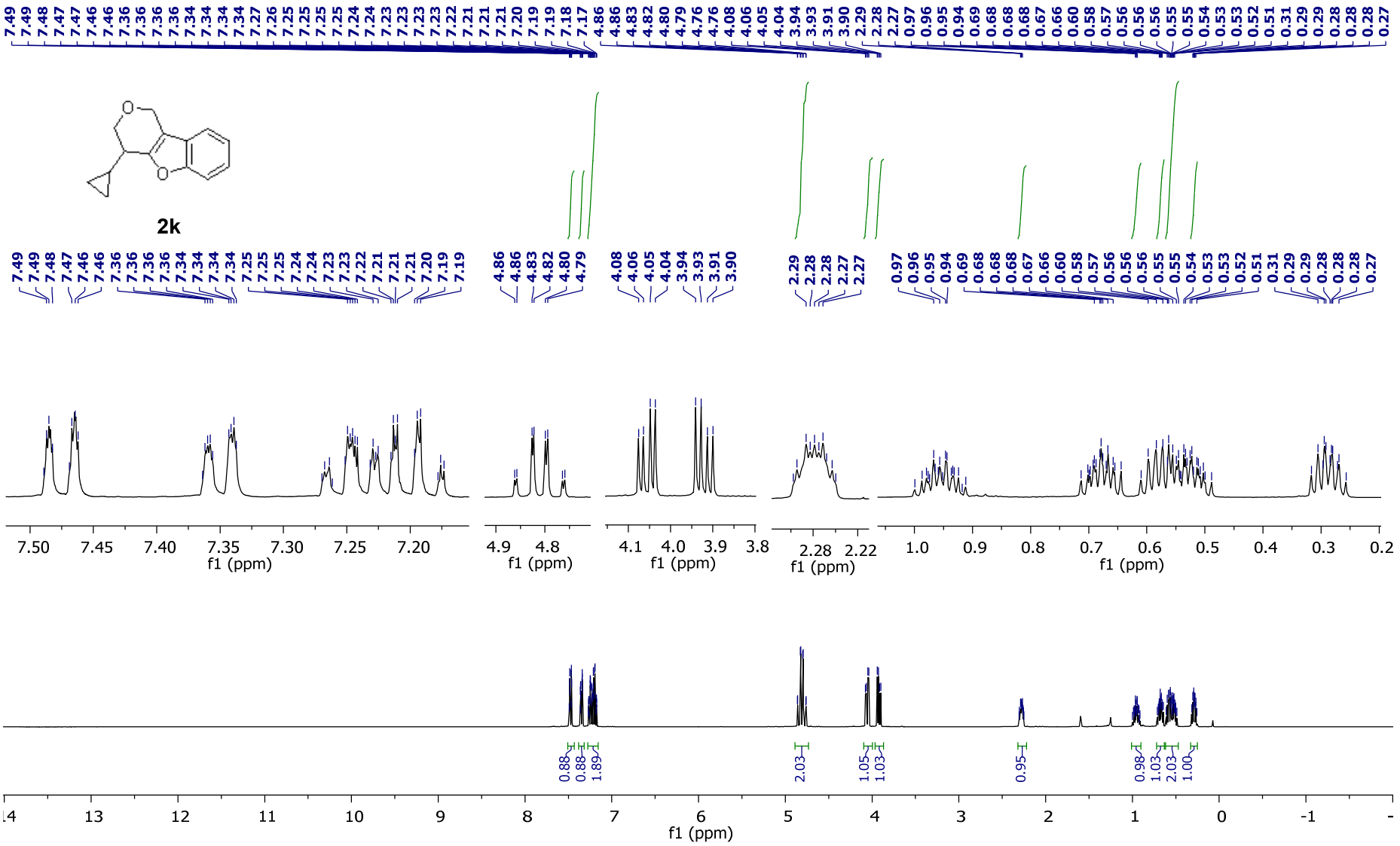

157.51
138.07
129.44
126.01
121.49
107.20
54.99
35.09
29.01
28.65
18.26
16.95
5.85
2.78
OMe
2f'
29.01
28.65
28.8 28.2
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

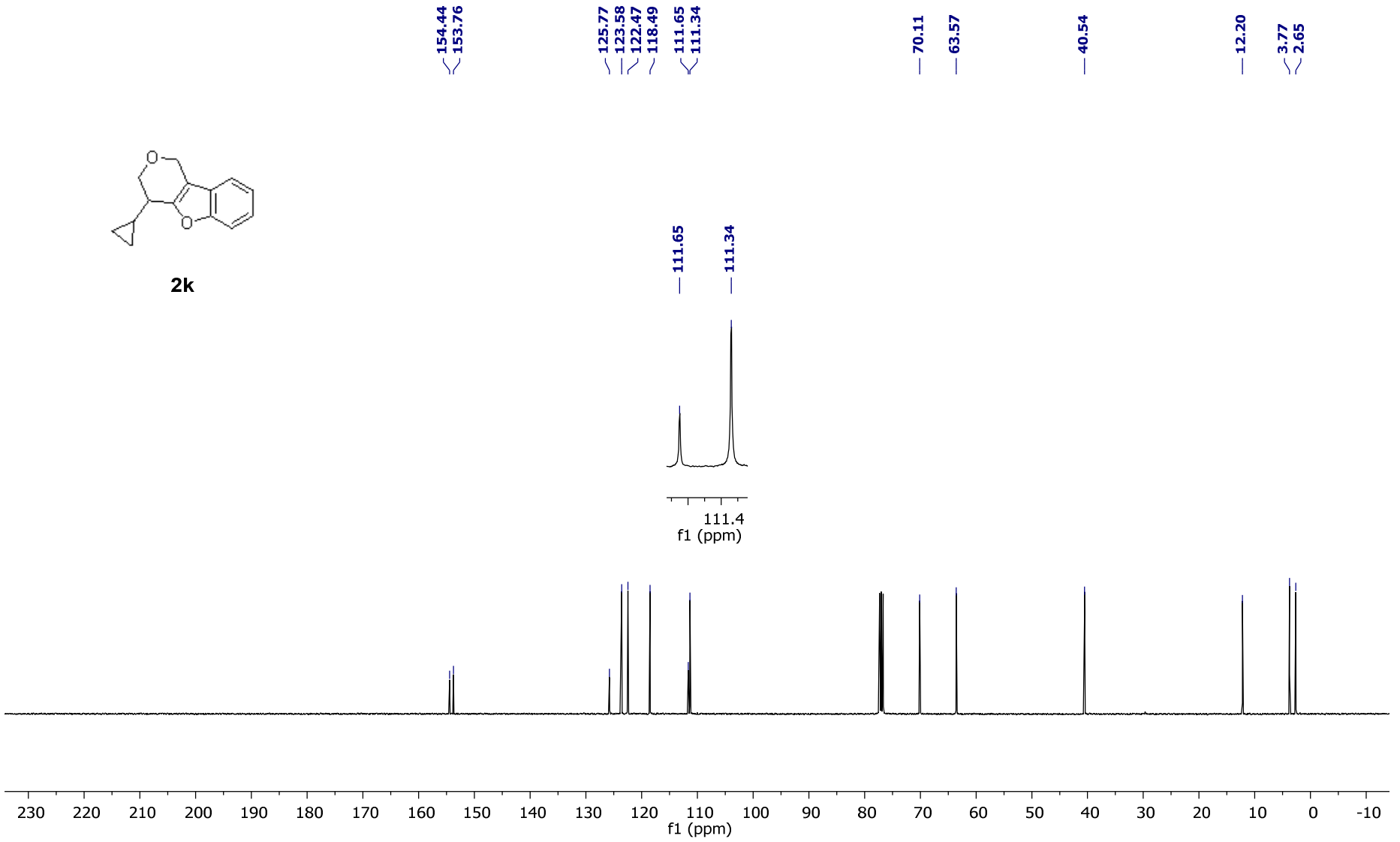

MeO
OMe
O
2h
7.26 6.34 6.33 6.12 6.11 4.84 4.80 4.72 4.68 4.15 4.15 4.13 4.12 3.79 3.78 3.72 3.71 3.69 3.68 2.22 2.22 2.21 2.20 2.20 2.19 1.16 1.14 1.14 1.13 1.12 1.11 1.11 1.10 1.09 1.09 1.08 1.07 0.70 0.68 0.67 0.66 0.65 0.64 0.53 0.52 0.51 0.50 0.49 0.48 0.48 0.47 0.46 0.45 0.45 0.44 0.44 0.43 0.43 0.42 0.41 0.40 0.39 0.20 0.19 0.18 0.16 0.15 0.15 0.14
6.33 6.12 6.11 4.84 4.80 4.72 4.68 4.15 4.15 4.13 4.12 3.79 3.78 3.72 3.71 3.69 3.68 2.22 2.22 2.21 2.20 2.20 2.19 1.16 1.14 1.14 1.13 1.12 1.11 1.11 1.10 1.09 1.09 1.08 1.07 0.70 0.68 0.67 0.66 0.65 0.64 0.53 0.52 0.51 0.50 0.49 0.48 0.48 0.47 0.46 0.45 0.45 0.44 0.44 0.43 0.43 0.42 0.41 0.20 0.19 0.18 0.16 0.15 0.15 0.14
6.32 6.10 f1 (ppm)
4.9 4.8 4.7 4.6 f1 (ppm)
4.14 4.11 f1 (ppm)
3.76 3.68 f1 (ppm)
2.24 2.20 f1 (ppm)
1.15 1.10 1.05 f1 (ppm)
0.7 0.6 0.5 0.4 0.3 0.2 0.1 f1 (ppm)
0.87 0.90 1.03 1.04 1.03 2.74 2.67 1.05 0.97 0.98 1.02 2.03 1.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.
f1 (ppm)

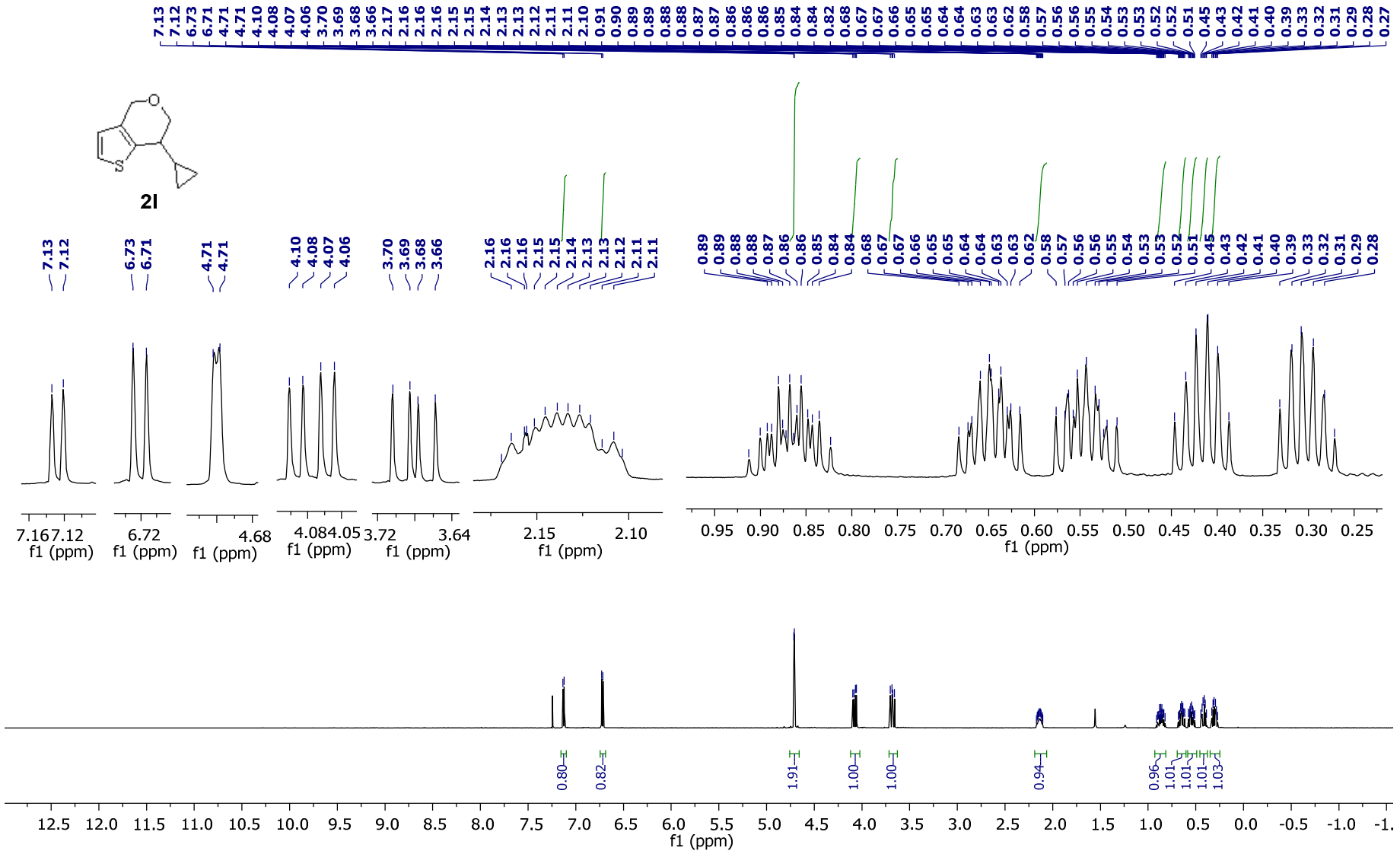

158.93
158.42
136.09
118.51
99.33
96.72
70.33
67.90
55.26
55.05
36.07
15.86
4.99
3.02
MeO
OMe
O
2h
55.26
55.05
55.5
55.0
54.5
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

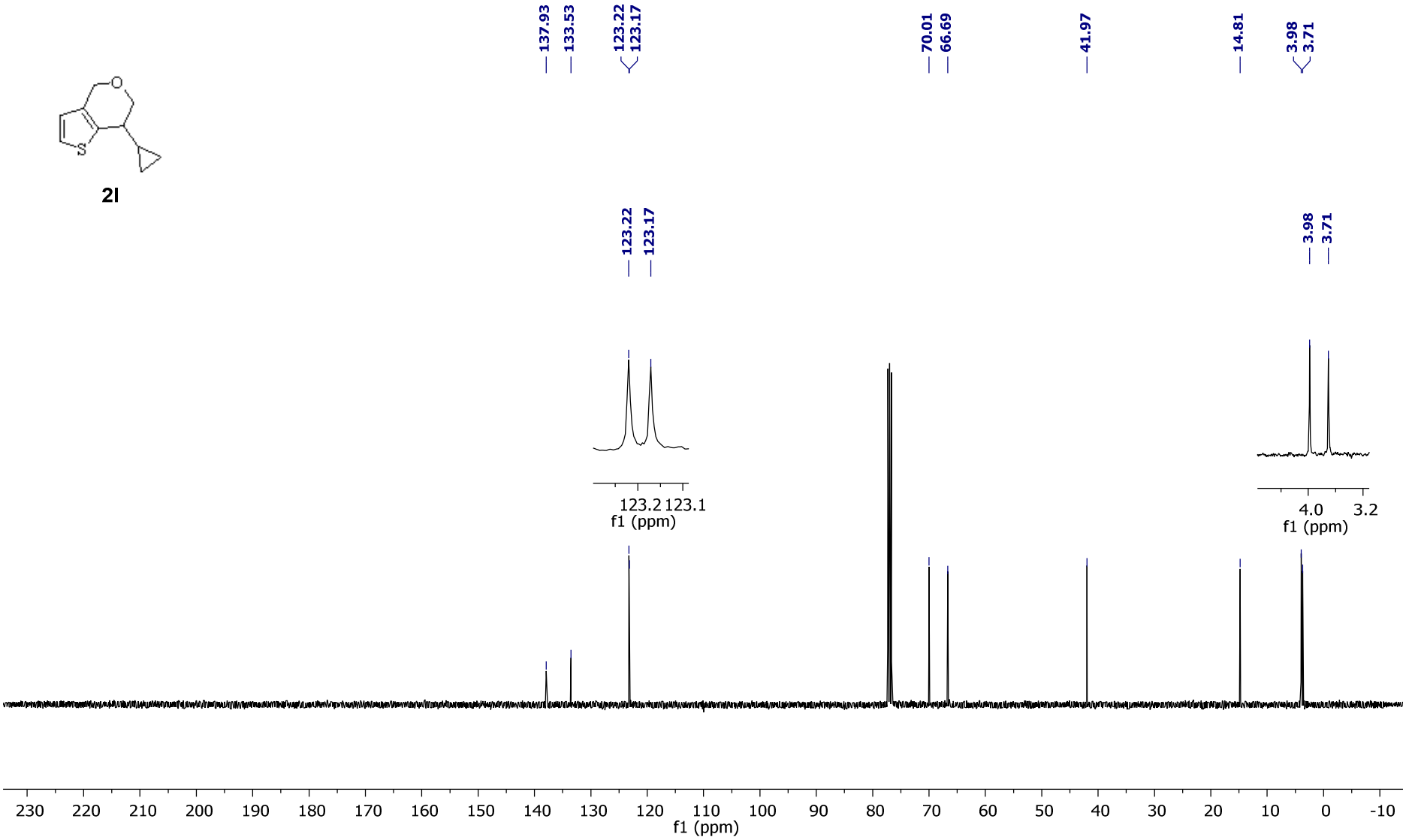

2j
f1 (ppm)

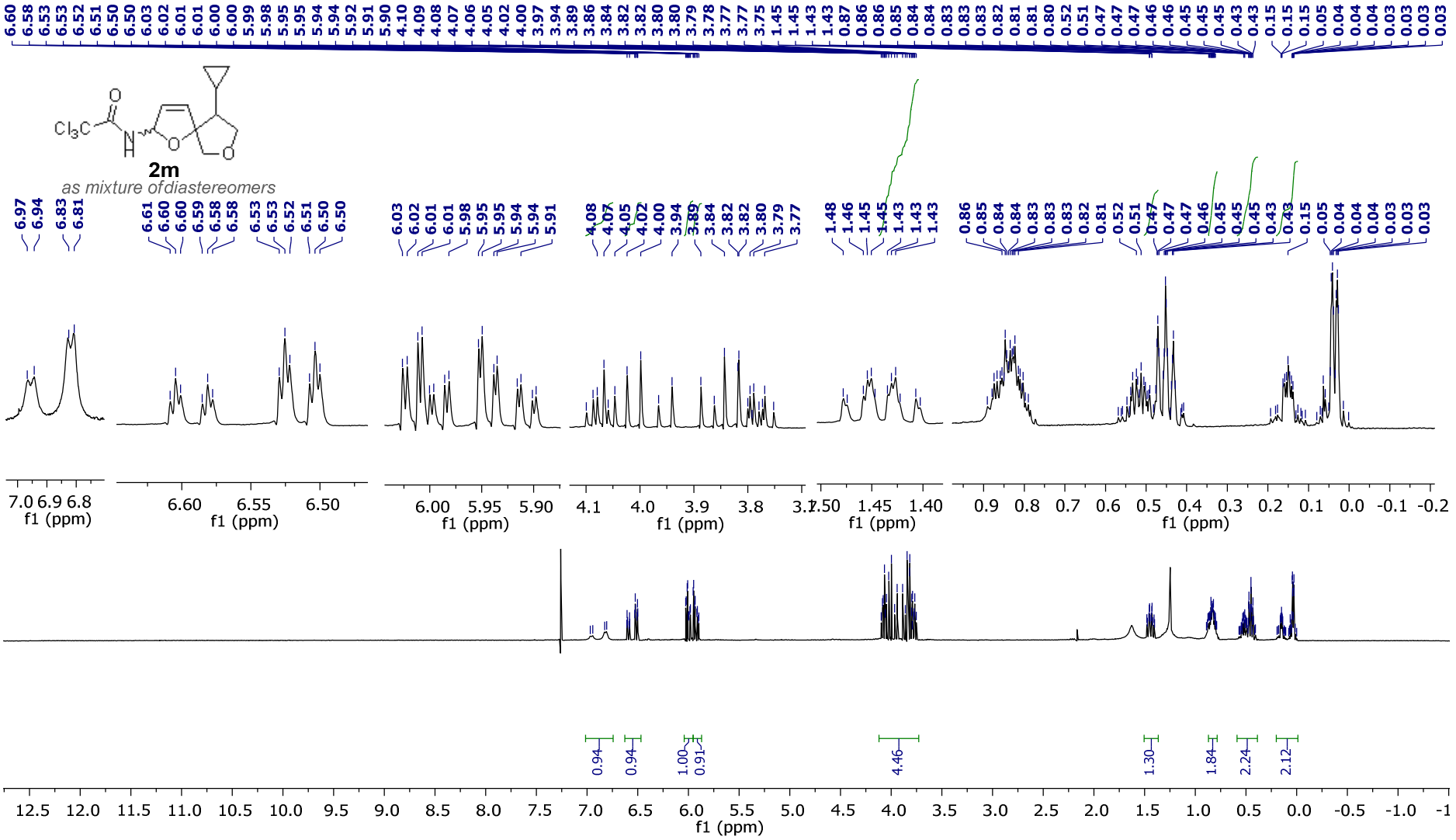

150.66
141.25
115.61
106.94
70.16
64.51
40.38
12.17
3.43
2.40
2j
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

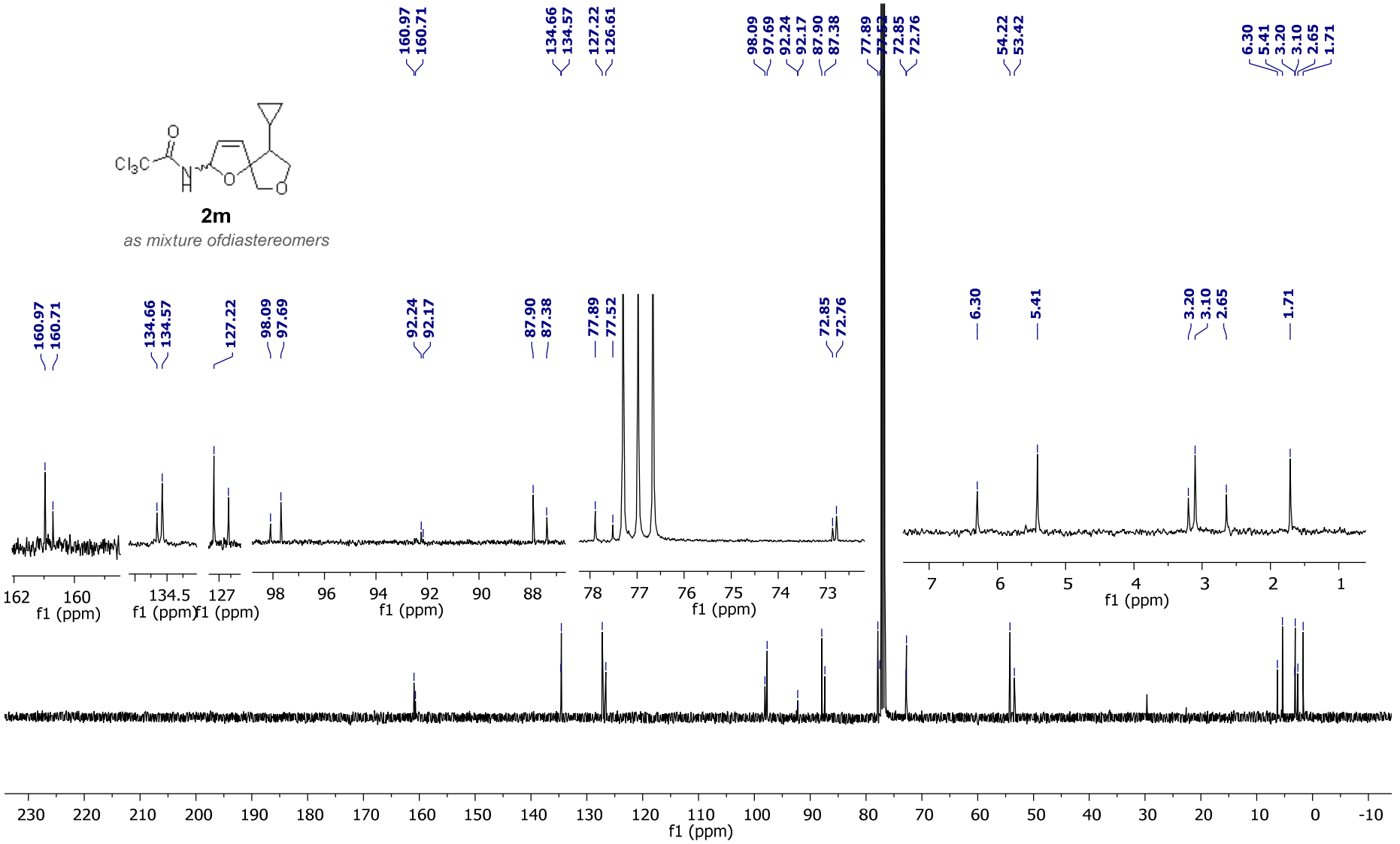

2k
f1 (ppm)

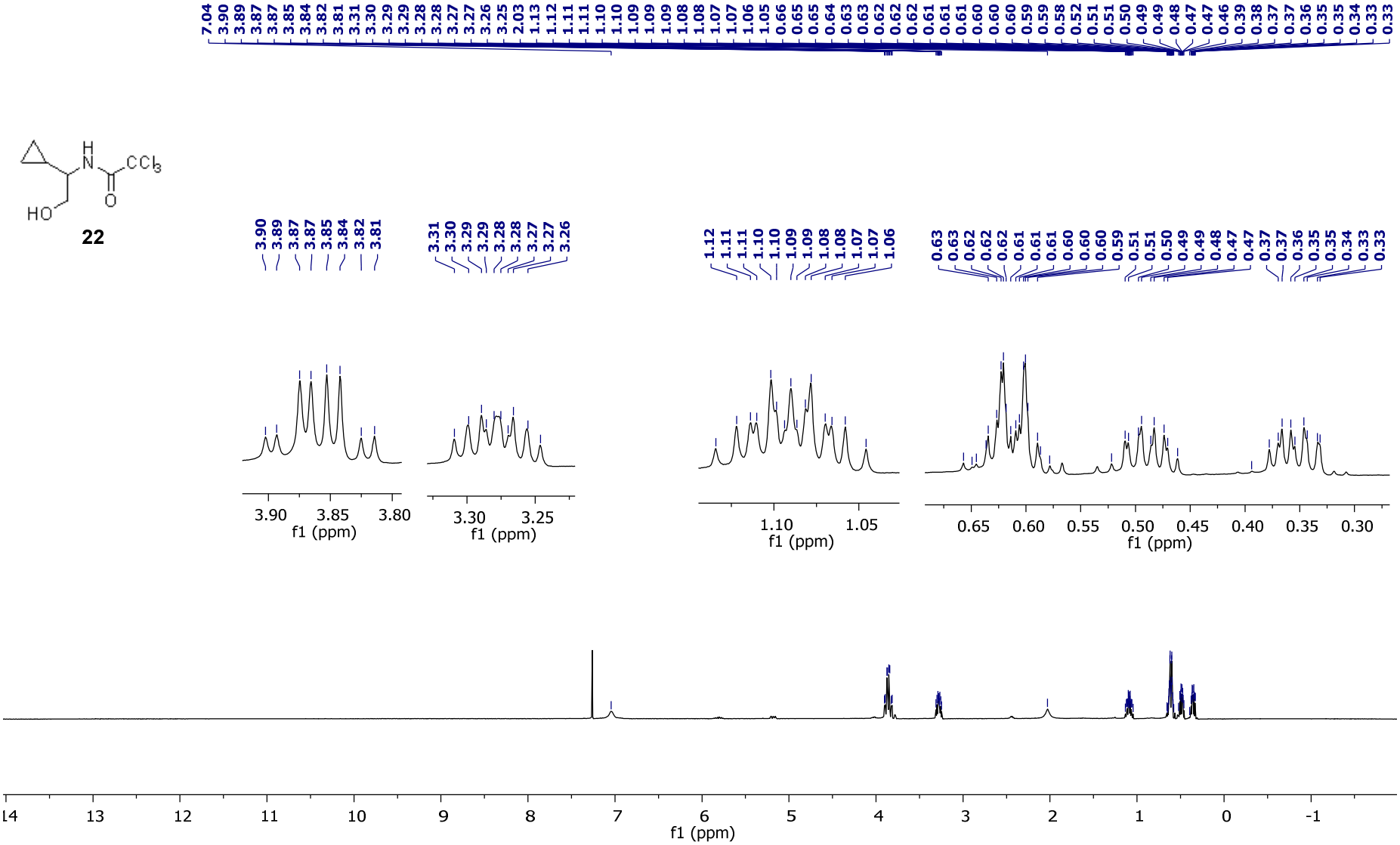

154.44
153.76
125.77
123.58
122.47
118.49
111.65
111.34
70.11
63.57
40.54
12.20
3.77
2.65
2k
111.65
111.34
111.4
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

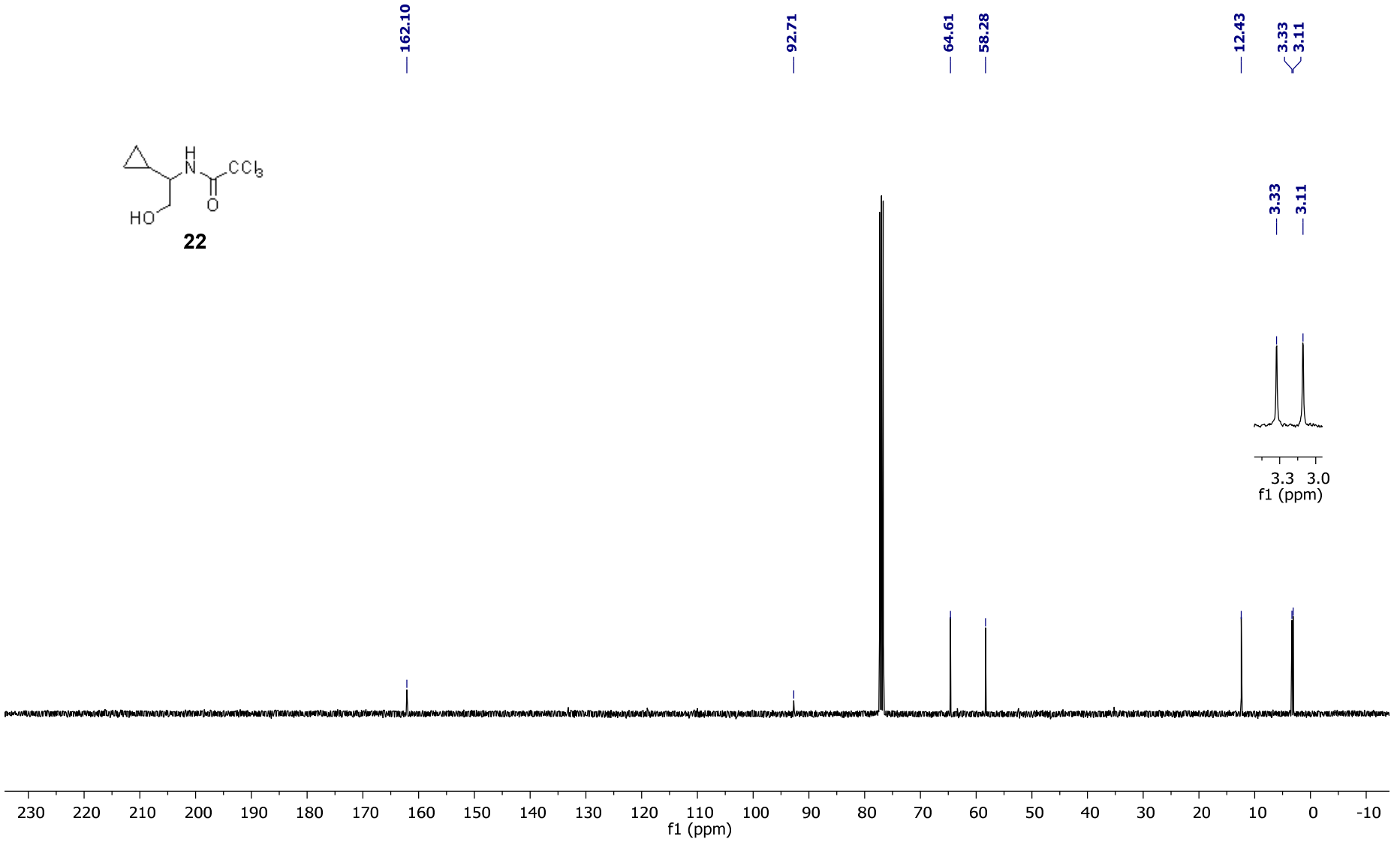

2l
7.13 7.12 6.73 6.71 4.71 4.71 4.10 4.08 4.07 4.06 3.70 3.69 3.68 3.66 2.17 2.16 2.16 2.15 2.15 2.14 2.13 2.13 2.12 2.11 2.11 2.10 0.91 0.90 0.89 0.89 0.88 0.88 0.87 0.87 0.86 0.86 0.86 0.85 0.84 0.84 0.82 0.68 0.67 0.67 0.66 0.65 0.65 0.64 0.64 0.63 0.62 0.58 0.57 0.56 0.56 0.55 0.54 0.53 0.53 0.52 0.52 0.51 0.45 0.43 0.42 0.41 0.40 0.39 0.33 0.32 0.31 0.29 0.28 0.27
7.16 7.12 f1 (ppm)
6.72 f1 (ppm)
4.68 f1 (ppm)
4.08 4.05 f1 (ppm)
3.72 3.64 f1 (ppm)
2.15 2.10 f1 (ppm)
0.95 0.90 0.85 0.80 0.75 0.70 0.65 0.60 0.55 0.50 0.45 0.40 0.35 0.30 0.25 f1 (ppm)
0.80 0.82 1.91 1.00 1.00 0.94 0.96 1.01 1.01 1.01 1.03
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.
f1 (ppm)


137.93
133.53
123.22
123.17
70.01
66.69
41.97
14.81
3.98
3.71
2I
123.2 123.1
f1 (ppm)
4.0 3.2
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


2m
as mixture ofdiastereomers
f1 (ppm)


160.97
160.71
134.66
134.57
127.22
126.61
98.09
97.69
92.24
92.17
87.90
87.38
77.89
77.52
72.85
72.76
54.22
53.42
6.30
5.41
3.20
3.10
2.65
1.71
Cl3C
O
N
H
O
O
2m
as mixture ofdiastereomers
f1 (ppm)


7.04 3.90 3.89 3.87 3.87 3.85 3.84 3.82 3.81 3.31 3.30 3.29 3.29 3.28 3.28 3.27 3.27 3.26 3.25 2.03 1.13 1.12 1.11 1.11 1.10 1.10 1.09 1.09 1.09 1.08 1.08 1.07 1.07 1.06 1.05 0.66 0.65 0.65 0.64 0.63 0.63 0.62 0.62 0.62 0.61 0.61 0.61 0.60 0.60 0.60 0.59 0.59 0.58 0.52 0.51 0.51 0.50 0.49 0.49 0.48 0.47 0.47 0.46 0.39 0.38 0.37 0.37 0.36 0.35 0.35 0.34 0.33 0.33
HO
N
H
CCl3
O
22
3.90 3.89 3.87 3.87 3.85 3.84 3.82 3.81
3.31 3.30 3.29 3.29 3.28 3.28 3.27 3.27 3.26
1.12 1.11 1.11 1.10 1.10 1.09 1.09 1.08 1.08 1.07 1.07 1.06
0.63 0.63 0.62 0.62 0.62 0.61 0.61 0.61 0.60 0.60 0.60 0.59 0.51 0.51 0.50 0.49 0.49 0.48 0.47 0.47 0.37 0.37 0.36 0.35 0.35 0.34 0.33 0.33
3.90 3.85 3.80
f1 (ppm)
3.30 3.25
f1 (ppm)
1.10 1.05
f1 (ppm)
0.65 0.60 0.55 0.50 0.45 0.40 0.35 0.30
f1 (ppm)
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)


162.10
92.71
64.61
58.28
12.43
3.33
3.11
HO
H
N
O
CCl3
22
3.33
3.11
3.3 3.0
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

6. Chiral HPLC of compound 7j

Racemic **7j**

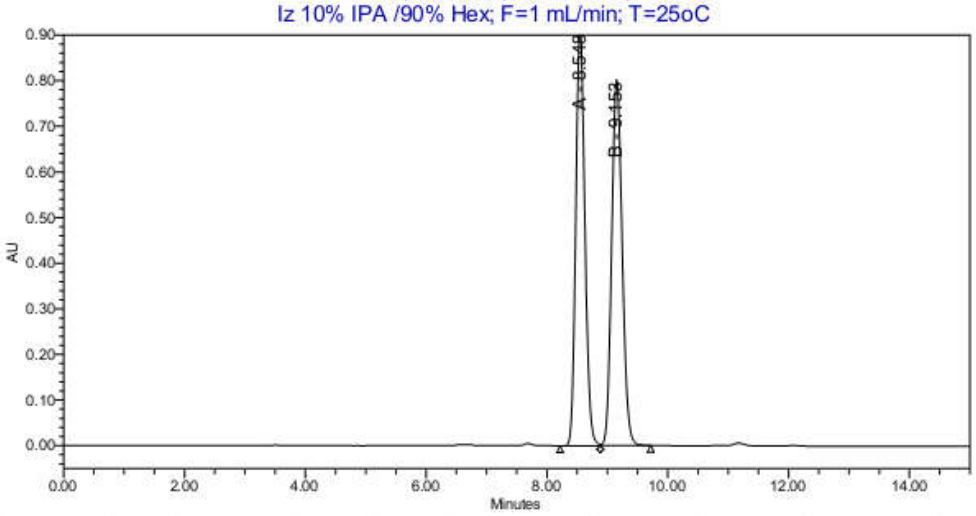
Empower 2 software

IC2_Ch 151

SAMPLE INFORMATION

Sample Name:	#585_Ch151_MS-1506-rac		
Sample Type:	Unknown	Sample Set Name:	Ch_151_051115
Vial:	33	Acq. Method Set:	Iz_210_254_F1_100A
Injection #:	1	Processing Method	Ch151_IC2_10%IPA
Injection Volume:	10.00 ul	Channel Name:	W2489 ChA
Run Time:	30.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 210nm
Date Acquired:	11/5/2015 11:58:34 AM EET	Acquired By:	System
Date Processed:	11/5/2015 12:26:33 PM EET		

Chiralpak IC -2 (4.6x250 mm)
Iz 10% IPA /90% Hex; F=1 mL/min; T=25oC



	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	A	8.548	9537601	49.60	921120	15816			0.160	1.514
2	B	9.153	9690707	50.40	803153	13181	2.056	1.118	0.188	1.692
Sum			19228308.4							

1 c~1,35 mg/mL (KF)

Reported by User: System
Report Method: IC2_Ch 151
Report Method ID6500
Page: 1 of 1

Project Name: Alliance-4_2015
Date Printed:
11/5/2015
12:27:30 PM Europe/Riga

Enantioenriched **7j**

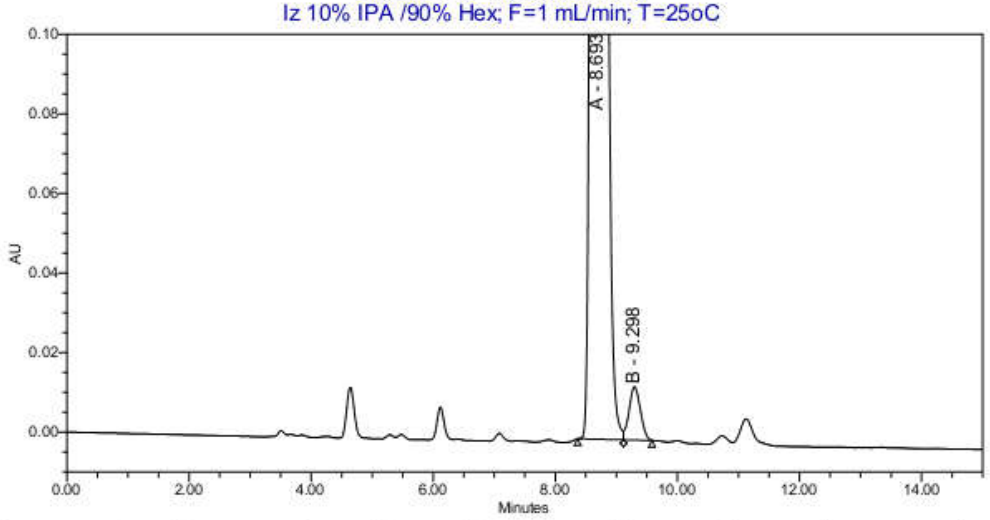
Empower2 software

IC2_Ch 151

SAMPLE INFORMATION

Sample Name:	#585_Ch151_MS-1506-hir		
Sample Type:	Unknown	Sample Set Name:	Ch_151_051115
Vial:	34	Acq. Method Set:	Iz_210_254_F1_100A
Injection #:	1	Processing Method	Ch151_IC2_10%IPA
Injection Volume:	10.00 ul	Channel Name:	W2489 ChA
Run Time:	30.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 210nm
Date Acquired:	11/5/2015 12:19:33 PM EET	Acquired By:	System
Date Processed:	11/5/2015 12:31:52 PM EET		

Chiralpak IC -2 (4.6x250 mm)
Iz 10% IPA /90% Hex; F=1 mL/min; T=25oC



	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	A	8.693	15476406	98.90	1437418	15045			0.167	1.557
2	B	9.298	172838	1.10	13413	11664	1.932	1.114	0.203	1.735
Sum			15649243.8							

1 c~1 mg/mL (KF)

Reported by User: System
Report Method: IC2_Ch 151
Report Method ID6503
Page: 1 of 1

Project Name: Alliance-4_2015
Date Printed:
11/5/2015
12:34:40 PM Europe/Riga