Stereoselective synthesis of chiral α-SCF_3-β-ketoesters featuring a quaternary stereocenter

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ELECTRONIC SUPPLEMENTARY INFORMATION

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General Methods and Materials

Commercial grade reagents and solvents were used without further purifications. Ethyl 2-methylacetoacetate (CAS 609-14-3), Ethyl 2-acetyl-3-phenylpropionate (CAS 620-79-1), Ethyl 2-oxocyclopentanecarboxylate (CAS 611-10-9), Ethyl cyclohexanone-2-carboxylate (CAS 1655-07-8) were purchased by Sigma Aldrich and they were used without further purifications.

$AgSCF_3$ (CAS 811-68-7) was purchased by TCI and it was used without further purifications.

NMR spectra: ^{1}H-NMR, ^{19}F-NMR and ^{13}C-NMR spectra were recorded with instruments at 300 MHz (Bruker AV 300). Proton chemical shifts are reported in ppm (δ) with the solvent reference relative to tetramethylsilane (TMS) employed as the internal standard ($CDCl_3$ δ = 7.26 ppm). ^{13}C NMR spectra were recorded operating at 75 MHz, with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ = 77.0 ppm). ^{19}F NMR spectra were recorded operating at 282 MHz. Fluorine chemical shifts are reported in ppm (δ) relative to CF_3Cl.

HPLC: For HPLC analyses on chiral stationary phase, to determine enantiomeric excesses, it was used an Agilent Instrument Series 1100. The specific operative conditions for each product are reported from time to time

Mass spectra: Mass spectra and accurate mass analysis were carried out on a VG AUTOSPEC-M246 spectrometer (double-focusing magnetic sector instrument with EBE geometry) equipped with EI source or with LCQ Fleet ion trap mass spectrometer, ESI source, with acquisition in positive ionization mode in the mass range of 50–2000 m/z.

TLC: Reactions and chromatographic purifications were monitored by analytical thin-layer chromatography (TLC) using silica gel 60 F_{254} pre-coated glass plates and visualized using UV light, vanillin or $KMnO_4$.

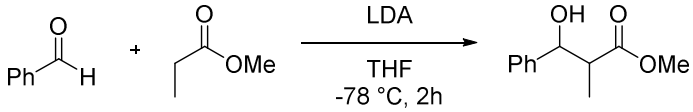
Chromatographic purification: Purification of the products was performed by column chromatography with flash technique (according to the Still method) using as stationary phase silica gel 230-400 mesh (SIGMA ALDRICH) or Aluminium oxide, neutral, Brockmann I 50-200 μm 60A previously deactivated with 6% of H_2O.

Dry solvents: The other dry solvents used are commercially available and they are stored under nitrogen over molecular sieves (bottles with crown cap).

Synthesis of Substrates

Methyl 2-methyl-3-oxo-3-phenylpropanoate

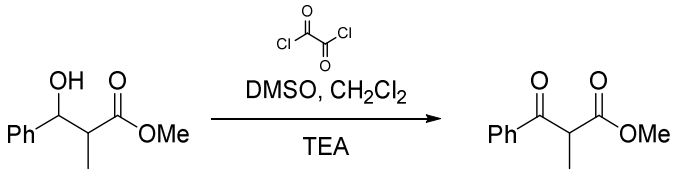
The compound was prepared in two-step from the corresponding freshly distilled benzaldehyde and the methyl propionate according to a published procedure[1].



The β-hydroxyester intermediate was obtained adding to a tree-necked-round bottom flask dry THF (0.17M) and fresh distilled diisopropylamine (6.12 mmol, 1.2 eq) and cooling down to -78°C. Then, a solution 2.5M of *n*BuLi in Hex (6.12 mmol, 1.2 eq) were added dropwise. After 5 minutes at -78°C, the solution was placed in an ice bath at 0°C and stirred for 20 minutes to favour the LDA formation. Next, a solution 2M of methyl propionate (5.1 mmol, 1 eq) was added at -78°C and the stirring was kept for 50 minutes. In the end, a solution 2.25M of benzaldehyde (5.6 mmol, 1.1 eq) was added dropwise and the reaction mixture was stirred 5 minutes at -78°C and 30 minutes at 0°C. The reaction was quenched with 2.5 mL of a saturated solution of NH_4Cl and the crude was purified by a flash column chromatography (Hex-AcOEt 8:2) giving the desired product as a mixture of diastereoisomers in 76% yield. The intermediate was isolated as a yellow liquid. All analytical data are in agreement with the literature.

^{1}H NMR (300 MHz, CDCl3) δ 7.44 – 7.12 (m, 5H), 5.13 (d, *J* = 4.0 Hz, 1H), 3.70 (s, 3H), 2.81 (qd, *J* = 7.2, 4.0 Hz, 1H), 1.14 (d, *J* = 7.2 Hz, 3H) ppm.

^{1}H NMR (300 MHz, CDCl3) δ 7.50 – 7.29 (m, 5H), 4.80 – 4.70 (m, 1H), 3.75 (s, 3H), 2.84 (dq, J = 14.4, 7.2 Hz, 1H), 1.03 (d, J = 7.2 Hz, 3H) ppm.

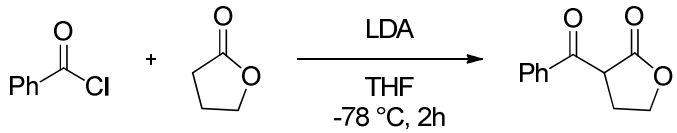


In a tree-necked flask, dry CH_2Cl_2 and oxalyl chloride were added and the solution was stirred at -60°C for 5 minutes. Firstly, a solution 4M of DMSO (6.63 mmol, 2.24 eq) in dry CH_2Cl_2 was added dropwise and, secondly, a solution 0.74M of the β-hydroxyester (2.96 mmol, 1 eq) was added dropwise at -70°C and the resulting slurry was stirred at -70°C for 45 minutes. After this time, trimethylamine (14.8 mmol, 5 eq) was added and the slurry stirred for other 10 minutes at -60°C. the reaction mixtures was warmed up to room temperature and quenched with 10 ml of water. The mixture was extracted with CH_2Cl_2 (2x60 mL) and the organic phase was washed with 15 mL of HCl 1% and 15 mL of $NaCO_3$ 5%. The solvent was removed under vacuum and the crude product was used with further purification. Yield: 90%.

^{1}H NMR (300 MHz, CDCl3) δ 8.00 (d, J = 7.4 Hz, 2H), 7.65 – 7.55 (m, 1H), 7.50 (t, J = 7.6 Hz, 2H), 4.43 (q, J = 7.1 Hz, 1H), 3.71 (s, 3H), 1.52 (d, J = 7.1 Hz, 3H) ppm.

[1] A. B. Smith, P.A. Levenberg, *Synthesis*, **1981**, *7*, 567-570.

3-benzoyldihydrofuran-2(3H)-one



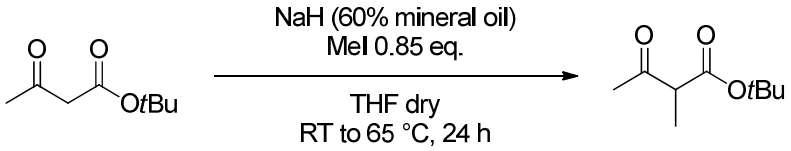
The compound was prepared from the corresponding acyl chloride and γ-buryrolactone according to a published procedure[2].

In a tree-necked flask, THF dry (7.5 mL) and fresh distilled diisopropylamine (7.5 mml, 2.5 eq) were cooled down to -78°C, then a solution 2.3M of nBuLi (7.5 mmol, 2.5 eq) was added dropwise. After 5 minutes at -78°C, the solution was placed in an ice bath at 0°C and stirred for 20 minutes to favour the LDA formation. Next, solution 0.5M of γ-buryrolactone (2.99 mmol, 1 eq) in THF dry was added slowly and the reaction mixture was stirred for 1 hour at that temperature. Then, benzoyl chloride (3.3 mmol, 1.1 eq.) was added at −78 °C and stirring was continued for 15 min. The reaction was subsequently quenched by the addition of 1 M HCl and this mixture was extracted with EtOAc (3 × 30 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated under vacuum. Purification by flash column chromatography (Hex-EtOAc = 6:4) gave the desired product as a white solid in 36% yield. All analytical data are in agreement with the literature.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10 (d, J = 7.8 Hz, 2H), 7.65 (t, J = 7.3 Hz, 1H), 7.53 (t, J = 7.7 Hz, 2H), 4.63 – 4.53 (m, 2H), 4.52 – 4.40 (m, 2H), 2.89 (tdd, J = 13.2, 5.5, 1.4 Hz, 1H), 2.53 (ddd, J = 16.1, 12.9, 8.2 Hz, 1H) ppm.

[2] L. Catti, K. Tiefenbacher, *Angew.Chem. Int .Ed.,* **2018***, 57,* 14589 –14592.

Tert-butyl 2-methyl-3-oxobutanoate

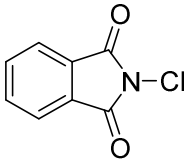


The compound was prepared from the corresponding *t*-butyl acetoacetone according to a published procedure[3].

A solution of *t*-butyl acetoacetone (10 mmol, 1 eq) in dry THF (3 mL) was added dropwise to a suspension of NaH 60 wt% (10 mmol, 1 eq) in THF (3 mL) at room temperature. The mixture was stirred for 1 hour at rt. A solution of methyl iodide (7 mmol, 0.7 eq) in THF (3 mL) was added dropwise and then the mixture was heated at 65 °C for 18 h. The reaction mixture was quenched with a saturated NH_4Cl aqueous solution (10 mL) and the aqueous phase was extracted with CH_2Cl_2 (10 mL x 3). The combined organic layer was washed with water (10 mL x 3) and dried over Na_2SO_4. After the solvent was removed by evaporation, the resulting crude material was purified with flash column chromatography (Hex-EtOAc = 99:1) to afford a colourless oil in 75% yield. All analytical data are in agreement with the literature.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.42 (q, *J* = 7.1 Hz, 1H), 2.24 (s, 3H), 1.48 (s, 12H), 1.31 (d, *J* = 7.1 Hz, 5H) ppm.

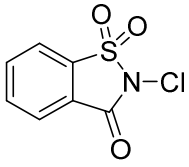
Synthesis of *N*-chlorophthalimide



$AlCl_3$ (10 mmol, 1 eq) was added to a solution of $Pb(OAc)_4$ (10 mmol, 1 eq) in dry CH_3CN (100 mL). The mixture was stirred at RT for 5 min, and then phthalimide (10 mmol, 1 eq) was added. The resulting mixture was gently refluxed under nitrogen for 20h, and then cooled to RT. The solvent was removed by rotary evaporation, and the crude was purified by filtration on a silica gel flash column with pure CH_2Cl_2 as eluent. Yield: 71%. All analytical data are in agreement with literature[4].

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.94-7.91 (m, 2H), 7.82-7.79 (m, 2H) ppm.

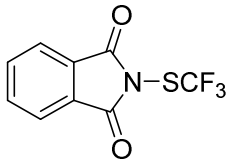
Synthesis of *N*-chlorosaccharin



To a suspension of saccharin (16.4 mmol, 1 eq) in MeOH (60 mL) was quickly added tBuOCl (2.5 mL). The suspension turned to clear solution with a formation of a large amount of white solid. The mixture was stirred for 10 min and standing for 5 min. The precipitate was recovered by filtration and dried under high vacuum. Yield: 71%. All analytical data are in agreement with literature[5].

[3] T. Osako, D. Panichakul, Y. Uozumi *Org. Lett.* **2012**, *14*, 1, 194–197.
[4] J-J. Kima, D-H. Kweona, S-D. Cho, H-K. Kima, S-G. Leeb, Y-J. Yoon, *Synlett*, **2006**, *2*, 194-200
[5] Q. Xiao, Q. He, J. Li, J. Wang, *Org. Lett.*, **2015** , *17*, 6090-6093

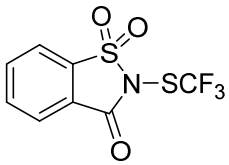
Synthesis of *N*-(trifluoromethylthio)phthalimide



$AgSCF_3$ (2.4 mmol, 1.3 eq) was added to a solution of *N*-chlorophthalimide (1.8 mmol, 1 eq) in CH_3CN (8 mL) under N_2 atmosphere. The mixture was stirred for 3h at RT, and then the solvent was removed by rotary evaporation. The crude obtained was dissolved in CH_2Cl_2, filtered through a HPLC filter in PTFE 0.45 µm and the solvent was removed by rotary evaporation to give a white solid. Yield: 89%. All analytical data are in agreement with literature[6].

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (dd, 2H, J = 6Hz, J = 3Hz), 7.88 (dd, 2H, J = 6Hz, J = 3Hz) ppm. **^{13}C NMR** ($CDCl_3$): δ 165.7, 135.4, 131.4, 127.9 (q, J = 322.5 Hz), 124.7 ppm. **^{19}F NMR** ($CDCl_3$): δ -49.32 ppm.

Synthesis of *N*-(trifluoromethylthio)saccharin



N-chlorosaccharin (1.15 mmol, 1 eq) and $AgSCF_3$ (1.38 mmol, 1.2 eq) were dissolved in CH_3CN (4 mL) under N_2 atmosphere. The mixture was stirred vigorously at room temperature for 10 min. The CH_3CN was then drained under reduced pressure. Furthermore, the residue was extracted with CH_2Cl_2 (3mL x 3) and filtered through a HPLC filter in PTFE 0.45 µm. The solvent was evaporated under vacuum to give the desired compound as a white solid. Yield: 77%. All analytical data are in agreement with literature[7].

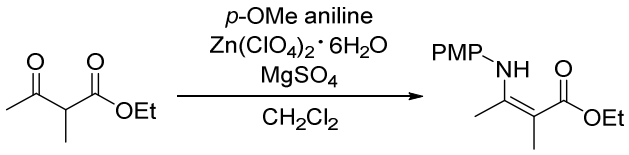
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (d, 1H J = 7.5 Hz), 8.08-7.99 (m, 2H), 7.98-7.91 (m, 1H) **^{13}C NMR** ($CDCl_3$): δ 158.4, 137.9, 136.4, 135.0, 127.8 (q, J = 315 Hz), 126.5, 126.1, 122.0 ppm **^{19}F NMR** ($CDCl_3$): δ -47.73 ppm.

[6] C. Xu, Q. Shen, *Org. Lett*, **2014**, *16*, 2046-2049

[7] C. Xu, B. Ma, Q. Shen, *Angew. Chem. Int. Ed.*, **2014**, 53, 9316-9320

Synthesis of achiral enamines

Ethyl 3-((4-methoxyphenyl)amino)-2-methylbut-2-enoate **2b**

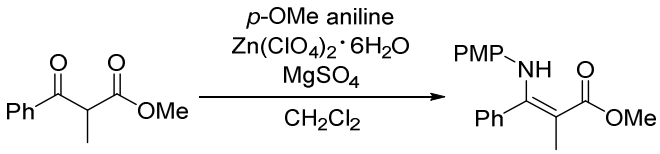


The compound was prepared from the corresponding β-ketoester and the *p*-Anisidine according to a published procedure[8].

Ethyl 2-methylacetoacetate (2.12 mmol, 1 eq) was dissolved in 850 µL of CH_2Cl_2 (2.5 M) and $Zn(ClO_4)_2{\cdot}6H_2O$ (0.11 mmol, 0.05 eq), $MgSO_4$ (0.64 mmol, 0.3 eq) and the *p*-OMe aniline (3.18 mmol, 1.5 eq) were added. The reaction mixture was stirred under nitrogen atmosphere at r.t. for 24 h. After this time, the reaction was quenched with the addition of 7.5 mL of CH_2Cl_2, the catalyst was filtered off and the solution was concentrated under vacuum. The crude was purified by filtration on a silica gel flash column (Hex-AcOEt 8:2 + 2% di NEt_3) and the desired product was isolated as a yellow oil in 83% yield. All analytical data are in agreement with the literature.[9]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.76 (bs, 1H), 6.97 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 8.9 Hz, 2H), 4.17 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 1.93 (s, 3H), 1.84 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H) ppm.

Methyl 3-((4-methoxyphenyl)amino)-2-methyl-3-phenylacrylate **2c**



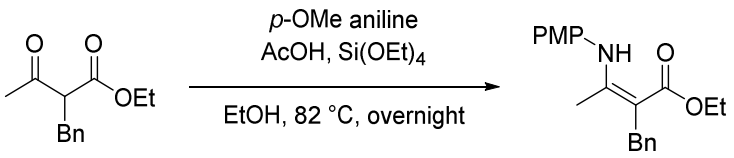
The compound was prepared from the corresponding β-ketoester and the *p*-Anisidine according to a published procedure[4].

Methyl 2-methyl-3-oxo-3-phenylpropanoate (1.12 mmol, 1 eq) was dissolved in 500 µL of CH_2Cl_2 (2.14 M) and $Zn(ClO_4)_2{\cdot}6H_2O$ (0.06 mmol, 0.05 eq), $MgSO_4$ (0.34 mmol, 0.3 eq) and *p*-OMe aniline (1.69 mmol, 1.5 eq) were added. The reaction mixture was stirred at r.t. for 24 h under nitrogen atmosphere. After this time, the reaction was quenched with addition of 5 mL of CH_2Cl_2, the catalyst was filtered off and the solution was concentrated under vacuum. The crude was purified by filtration on a silica gel flash column (Hex-AcOEt 9:1 + 2% di NEt_3) and the desired product was isolated as a pale-yellow solid in 41% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.79 (bs, 1H), 7.48 – 7.08 (m, 4H), 6.56 (s, 5H), 3.80 (s, 3H), 3.69 (s, 3H), 1.67 (s, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.88, 157.64, 155.42, 135.43, 134.03, 129.46, 128.36, 128.23, 124.25, 113.68, 92.38, 55.27, 50.96, 14.11 ppm. **MS (ESI+)** $C_{18}H_{19}NO_3$: 297.137150 (Calc. Mass 297.136494)

[8] G. Bartoli, M. Bosco, M. Locatelli, E. Marcantoni, P. Melchiorre, L. Sambri, *Synlett*, **2004**, *2*, 239–242.
[9] W. Werner, *Tetrahedron Letters*, **1971**, *9*, 1755-1760.

Ethyl 2-benzyl-3-((4-methoxyphenyl)amino)but-2-enoate **2d**

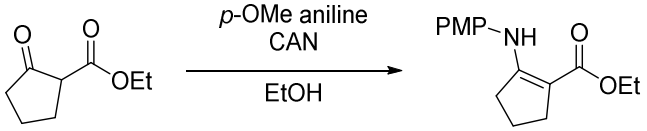


The compound was prepared from the corresponding β-ketoester and the *p*-Anisidine according to a published procedure[10].

Ethyl 2-acetyl-3-phenylpropionate (1 mmol, 1 eq) was dissolved in 5 mL of absolute ethanol (0.2 M) and tetraethyl orthosilicate (2 mmol, 2 eq), acetic adic (1.2 mmol, 1.2 eq) and the *p*-OMe aniline (1.2 mmol, 1.2 eq) were added. The reaction mixture was stirred at reflux (82 °C) with Dean-Stark for 24 hours under nitrogen atmosphere. After this time, the solvent was removed under vacuum and the crude was purified by filtration on a silica gel flash column (Hex-AcOEt 8:2 + 2% di NEt_3) and the desired product was isolated as a yellow solid in 75% yield. All analytical data are in agreement with the literature.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 11.00 (bs, 1H), 7.36 – 7.10 (m, 5H), 6.99 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 4.15 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 3.71 (s, 3H), 1.91 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H) ppm.

Ethyl 2-((4-methoxyphenyl)amino)cyclopent-1-enecarboxylate **2f**



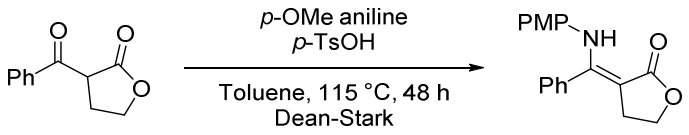
The compound was prepared from the corresponding β-ketoester and the *p*-Anisidine according to a published procedure[11].

Ethyl 2-oxocyclopentanecarboxylate (2 mmol, 1 eq) was dissolved in 2 mL of EtOH (1 M) and the *p*-OMe aniline (2 mmol, 1 eq) and CAN (0.1 mmo, 0.05 eq) were added. The mixture was stirred at r.t. for 5 hours under nitrogen atmosphere. After this time, the reaction was quenched with addition of 5 mL of CH_2Cl_2 and washed with H_2O then the organic phase was dried over Na_2SO_4 and evaporated under vacuum. The crude was purified by filtration on a silica gel flash column (Hex–EtOAc 8:2 + 2% di NEt_3) and the desired product was isolated as a pale-yellow liquid in 90% yield. All analytical data are in agreement with the literature.[12]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.29 (bs, 1H), 6.99 (d, J = 8.9 Hz, 2H), 6.83 (d, J = 8.9 Hz, 2H), 4.19 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 2.64 (t, J = 7.5 Hz, 2H), 2.56 (t, J = 7.5 Hz, 2H), 1.89 – 1.77 (p, J = 7.5, 2H), 1.30 (t, J = 7.1 Hz, 3H) ppm.

[10] Y. Zhao, J. Zhao, Y. Zhou, Z. Lei, L. Lia, H. Zhang, *New J. Chem*., **2005**, *29*, 769-772.
[11] V. Sridharan, C. Avendaño, J. C. Menéndez, *Synlett*, **2007**, *6*, 881–884.
[12] S. Z. Zhanga, L. Song, *Journal of Chemical Research*, **2005**, *12*, 817–820.

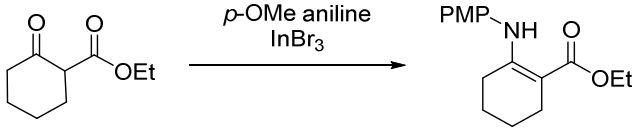
3-(((4-methoxyphenyl)amino)(phenyl)methylene)dihydrofuran-2(3H)-one **2e**



3-benzoyldihydrofuran-2(3H)-one (0.79 mmol, 1 eq) was dissolved in 4 mL of toluene (0.2 M) and the *p*-OMe aniline (0.95 mmol, 1.2 eq) and *p*-toluensolfonic acid (0.08 mmol, 0.1 eq) were added. The reaction mixture was stirred at reflux (110 °C) with Dean-Stark for 48 h. After this time, the solvent was evaporated and the crude was purified by filtration on a silica gel flash column (Hex–EtOAc 7:3 + 2% di NEt_3) and the desired product was isolated as a solid in 78% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.96 (bs, 1H), 7.32 (m, 2H), 7.25 (m, 2H), 6.60 (s, 5H), 4.30 (t, J = 7.8 Hz, 2H), 2.80 (t, J = 7.8 Hz, 2H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.41, 155.84, 154.96, 134.66, 133.13, 129.08, 128.62, 128.58, 124.18, 113.88, 90.88, 65.79, 55.32, 27.01 ppm. **MS(ESI+)** $C_{18}H_{17}NO_3$: 295.120450 (Calc. Mass 295.120844).

Ethyl 2-((4-methoxyphenyl)amino)cyclohex-1-enecarboxylate **2g**



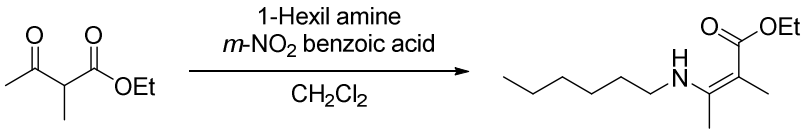
The compound was prepared from the corresponding β-ketoester and the *p*-Anisidine according to a published procedure[13].

Ethyl cyclohexanone-2-carboxylate (1.1 mmol, 1.1 eq), the aniline (1 mmol, 1.1 eq) and InBr3 (0.1 mmol, 1 eq) was stirred at room temperature for 24 hours under nitrogen atmosphere. After this time, the reaction mixture was washed with H_2O (2 mL) and extracted with EtOAc (2 mL). The combined organic layers were dried over Na_2SO_4, concentrated under vacuum, and the crude was purified by filtration on a silica gel flash column (Hex-EtOAc 9:1+ 2% di NEt_3). The desired product was isolated as white solid in 88% yield. All analytical data are in agreement with the literature.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.53 (s, 1H), 7.01 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 4.19 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 2.36 (t, J = 5.5 Hz, 2H), 2.23 (t, J = 5.5 Hz, 2H), 1.59 (m, 4H), 1.31 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.86, 157.56, 157.10, 132.66, 127.30, 114.03, 91.88, 58.93, 55.38, 27.97, 23.83, 22.77, 22.31, 14.62 ppm.

[13] Z. Zhang, L. Yin, Y. Wang, *Adv. Synth. Catal.* **2006***, 348,* 184 – 190.

Ethyl 3-(hexylamino)-2-methylbut-2-enoate **2a**



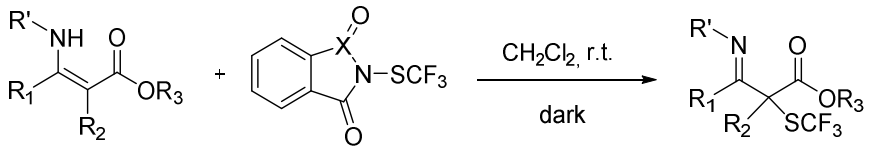
The compound was prepared from the corresponding β-ketoester and the hexilamine according to a published procedure[14].

Ethyl 2-methylacetoacetate (0.2 mmol, 1 eq) was dissolved in 500 µL of CH_2Cl_2, then the primary amine (0.21 mmol, 1.1 eq) was added. A solution of *m*-nitrobenzoic acid (0.04mmol, 0.2 eq) in 2 mL of CH_2Cl_2 was added to the first one. The reaction mixture was stirred at r. t. for 6 hours. After that time, the crude was purified quickly by filtration on an aluminum oxide basic flash column (Brockmann I 50-200µm 58Å) (Hex-EtOAc 9:1). The desired product was isolated as a colorless oil in 63% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.23 (s, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.18 (td, J = 7.1, 5.5 Hz, 2H), 1.95 (s, 3H), 1.78 (s, 3H), 1.55 (p, J = 7.1 Hz, 2H), 1.44 – 1.30 (m, 6H), 1.27 (t, J = 7.1 Hz, 3H), 1.06 – 0.84 (m, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.08, 159.76, 86.09, 58.59, 43.50, 31.54, 30.53, 26.63, 22.53, 15.26, 14.71, 14.00, 12.61. **MS(ESI+)** $C_{13}H_{25}NO_2$: 277.188270 (Calc. Mass 277.188529).

[14] C. Xu, L. Zhang, S. Luo, *J. Org. Chem.* **2014**, *79*, 23, 11517–11526.

General synthesis of α-SCF3 substituted β-imino esters

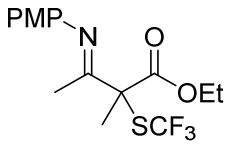


A: X= S=O
B: X= C

The achiral enamine (0.14 mmol, 1 eq) was dissolved in 1.4 mL of dry CH_2Cl_2 (0.1 M) and the trifluorometylatiolation agent (0.16 mmol, 1.2 eq) was added. The reaction was stirred at dark at r.t. for 18 hours under static nitrogen atmosphere. After this time, the reaction mixture was quenched with 2 mL x2 of NH_4Cl and extracted with 2 mL x2 of CH_2Cl_2: the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by filtration on an aluminum oxide basic flash column (Brockmann I 50-200µm 58Å).

Products characterization

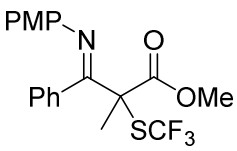
Ethyl 3-((4-methoxyphenyl)imino)-2-methyl-2-((trifluoromethyl)thio)butanoate **3b**



Prepared according to the general procedure. The crude mixture was purified by column chromatography an aluminum oxide basic flash column (Brockmann I 50-200µm 58Å) (Pentane-CH_2Cl_2 7:3) afford the desired product as a colourless oil in 65% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88 (d, *J* = 8.8 Hz, 2H), 6.67 (d, *J* = 8.8 Hz, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 3.80 (s, 3H), 2.01 (s, 3H), 1.87 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.18, 166.14, 156.69, 142.50, 130.61 (q, *J* = 309.2 Hz), 120.40, 114.48, 64.57, 63.01, 55.62, 23.51, 16.08, 14.04 ppm. **^{19}F NMR** (282 MHz, CDCl3): δ -37.28 ppm. **MS (ESI+)** $C_{15}H_{18}NO_3F_3S$: 349.096590 (Calc. Mass 349.095950).

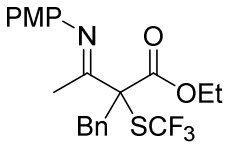
Methyl 3-((4-methoxyphenyl)imino)-2-methyl-3-phenyl-2-((trifluoromethyl)thio)propanoate **3c**



Prepared according to the general procedure. The crude mixture was purified by column chromatography an aluminum oxide basic flash column (Brockmann I 50-200µm 58Å) (Hexane-CH_2Cl_2-Et_2O 80:15:5) afford the desired product as a colourless oil in 78% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.19 (m, 2H), 7.09 – 6.95 (m, 2H), 6.65 (d, *J* = 1.4 Hz, 5H), 3.81 (s, 3H), 3.71 (s, 3H), 2.00 (s, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.42, 166.10, 156.97, 141.01, 133.82, 130.73 (q, J = 309.8 Hz), 129.34, 128.64, 128.35, 122.89, 113.82, 64.55, 55.40, 53.55, 23.91 ppm. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -37.68 ppm. **MS (ESI+)** $C_{19}H_{18}NO_3F_3S$: 397.095520 (Calc. Mass 397.095950).

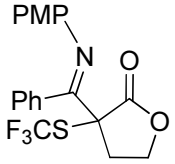
Ethyl 2-benzyl-3-((4-methoxyphenyl)imino)-2-((trifluoromethyl)thio)butanoate **3d**



Prepared according to the general procedure. The crude mixture was purified by column chromatography an aluminum oxide basic flash column (Brockmann I 50-200µm 58Å) (Hexane-CH_2Cl_2 8:2) afford the desired product as a colourless oil in 61% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.14 (m, 5H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.49 (d, *J* = 8.8 Hz, 2H), 4.27 (q, *J* = 7.2 Hz, 2H), 3,79 (s, 3H), 3.79 (d, *J* = 14.8 Hz, 1H), 3.69 (d, *J* = 15.1 Hz, 1H), 1.89 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.24, 165.04, 156.54, 142.46, 135.17, 130.91, 130.44 (q, *J* = 309.6 Hz) 128.18, 127.47, 120.09, 114.40, 69.55, 63.06, 55.57, 39.88, 17.38, 13.97 ppm. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -37.04 ppm. **MS (ESI+)** $C_{21}H_{22}NO_3F_3S$: 425.126790 (Calc. Mass 425.127250).

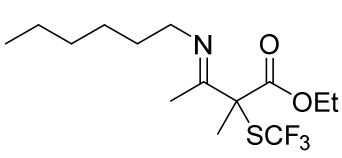
(E)-3-(((4-methoxyphenyl)imino)(phenyl)methyl)-3-((trifluoromethyl)thio)dihydrofuran-2(3H)-one **3e**



Prepared according to the general procedure. The crude mixture was purified by column chromatography a basic aluminum oxide flash column (Brockmann I 50-200µm 58+) (Hexane-CH_2Cl_2 8:2) afford the desired product as a colourless oil in 86% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.30 (m, 3H), 7.13 (m, 2H), 6.62 (m, 4H), 4.48 (td, 1H, J = 8.9Hz, J = 3.3Hz), 4.21 (m, 1H), 3.70 (s, 3H), 3.50 (m, 1H), 3.00 (m, 1H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 172.30, 162.59, 157.00, 140.87, 133.24, 131.03 (q, *J* = 309.6 Hz), 129.43, 128.72, 128.50,
122.75, 113.76, 66.88, 63.03, 55.28, 34.71 ppm. **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -36.87 (s, 3F) ppm. **MS (ESI+)** $C_{19}H_{16}NO_3F_3SH$: 396.0877 (Calc. Mass 396,0881).

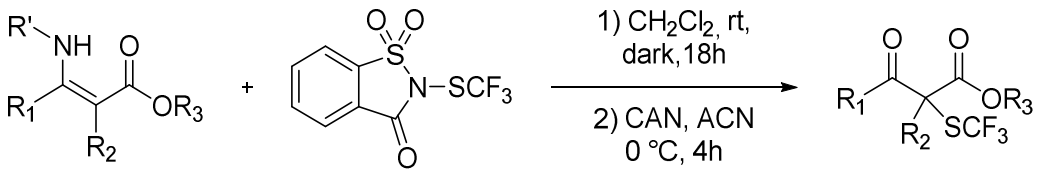
Ethyl 3-(hexylimino)-2-methyl-2-((trifluoromethyl)thio)butanoate **3a**



Prepared according to the general procedure using the N-SCF_3 ftalimide as trifluorometilating agent. The crude mixture was purified by column chromatography an aluminum oxide basic flash column (Brockmann I 50-200µm 58Å) (Pentane-CH_2Cl_2 8:2) afford the desired product as a colourless oil in 70% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.24 (q, *J* = 7.1 Hz, 2H), 3.30 (td, *J* = 7.4, 2.1 Hz, 2H), 1.86 (s, 3H), 1.82 (s, 3H), 1.70 – 1.53 (m, 2H), 1.41 – 1.21 (m, 9H), 0.94 – 0.83 (m, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.68, 163.34, 130.91 (q, *J* = 309.1 Hz), 65.06, 62.65, 51.61, 31.76, 30.14, 29.84, 27.16, 23.28, 22.75, 14.18, 13.98 ppm. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -37.77 ppm. **MS (ESI+)** $C_{12}H_{19}NOF_3S$: 282.113910 (Calc. Mass 282.113946).

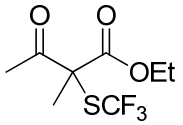
General synthesis of achiral α-SCF3 substituted β-ketoesters



The achiral enamine (0.14 mmol, 1 eq) was dissolved in 1.4 mL of dry CH_2Cl_2 (0.1 M) and the trifluorometylatiolation agent (0.16 mmol, 1.2 eq) was added. The reaction was stirred at dark at r.t. for 18 hours under static nitrogen atmosphere. After this time, the reaction mixture was quenched with 2 mL x2 of H_2O and extracted with 2 mL x2 of CH_2Cl_2: the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude was dissolved in 5.4 mL of acetonitrile (0.025 M), a solution of CAN (4.2 mmol, 3 eq) in 1.5 mL of H2O was added at 0 °C, and the stirring was continued at 0 °C for 4 hours. Then, after this time, the reaction mixture was quenched with 5 mL of H_2O and extracted with 5 mL of CH_2Cl_2: the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by filtration on silica gel flash column.

Products characterization

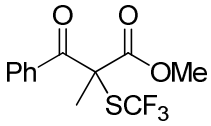
Ethyl 2-methyl-3-oxo-2-((trifluoromethyl)thio)butanoate **4**



Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hexane-CH_2Cl_2 7:3) afford the desired product as a colourless oil in 68% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 4.31 (q, J = 7.1 Hz, 2H), 2.35 (s, 3H), 1.90 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 198.17, 167.99, 129.58 (q, J = 308.6 Hz), 65.76, 63.41, 24.89, 21.52, 13.75 ppm. **^{19}F NMR** (282 MHz, CDCl3) δ -36.75 ppm. **MS (ESI+)** $C_8H_{11}O_3F_3SNa$: 267.0283 (Calc. Mass 267.0279).

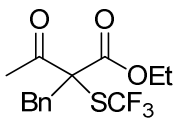
Methyl 2-methyl-3-oxo-3-phenyl-2-((trifluoromethyl)thio)propanoate **5**



Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hexane-CH_2Cl_2 7:3) afford the desired product as a colorless oil in 68% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.92 (d, *J* = 7.5 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 3.73 (s, 3H), 2.11 (s, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 190.76, 170.00, 133.78, 133.23, 129.70 (q, J = 308.8 Hz), 129.07, 128.79, 63.83, 53.91, 24.33 ppm. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -36.70 ppm. **MS (EI+)** $C_{12}H_{11}F_3O_3SH$ 293.0463 (Calc. Mass 293.0459).

Ethyl 2-benzyl-3-oxo-2-((trifluoromethyl)thio)butanoate **6**

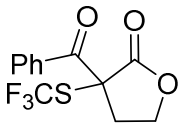


Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hexane-CH_2Cl_2 7:3) afford the desired

product as a colorless oil in 41% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.40 – 7.23 (m, 3H), 7.19 (dd, *J* = 7.0, 2.5 Hz, 2H), 4.19 (qq, *J* = 10.7, 7.2 Hz, 2H), 3.55 (dd, *J* = 55.1, 14.9 Hz, 2H), 2.36 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 197.57, 166.66, 134.27, 130.42, 129.36 (q, *J* = 309.3 Hz), 128.30, 127.56, 71.13, 63.41, 38.91, 29.69, 25.88, 13.68 ppm. **^{19}F NMR** (282 MHz, CDCl3) δ -36.39 ppm. **MS (ESI+)** $C_{14}H_{15}F_3O_3SH$: 321.0770 (Calc. Mass: 321,0772) **HPLC** (OJ-H 10µm, Hex-IPA 99-1, 0.8 mL/min, 31 bar) isomer 1: 8.177 min, isomer 2: 8.790 min.

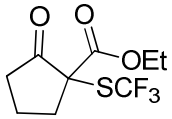
3-benzoyl-3-((trifluoromethyl)thio)dihydrofuran-2(3H)-one **7**



Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hexane-AcOEt 9:1-> 8:2) afford the desired product as a colourless oil in 45% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.31 (d, J = 8.2 Hz, 2H), 7.75 – 7.53 (m, 1H), 7.47 (t, J = 7.7 Hz, 2H), 4.55 (td, J = 8.8, 1.8 Hz, 1H), 4.41 (ddd, J = 10.1, 8.9, 5.8 Hz, 1H), 3.62 (dd, J = 13.1, 5.9 Hz, 1H), 2.95 – 2.78 (m, 1H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 188.58, 170.03, 134.09, 133.29, 130.73, 129.12 (q, *J* = 309.6 Hz), 128.37, 68.22, 62.08, 36.88 ppm. **^{19}F NMR** (282 MHz, CDCl3) δ -37.28 ppm. **MS (ESI+)** $C_{12}H_9O_3F_3SNa$: 313.0124 (Calc. Mass 313.0122). **HPLC** (Phenomenex Lux 3µm Amylose-1, Hex-IPA 98-2, 0.8 mL/min, 63 bar) isomer 1: 10.195 min, isomer 2: 10.847 min.

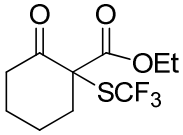
Ethyl 2-oxo-1-((trifluoromethyl)thio)cyclopentanecarboxylate **8**



Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Pentane-CH_2Cl_2 6:4) afford the desired product as a pale-yellow oil in 39% yield. All analytical data are in agreement with literature.[15]

^{1}H-NMR (300 MHz, $CDCl_3$): 4.44 – 4.14 (m, 2H), 3.07 – 2.86 (m, 1H), 2.56 – 2.46 (m, 2H), 2.44 – 2.32 (m, 1H), 2.28 – 2.06 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 206.56, 166.93, 129.56 (q, *J* = 309.2 Hz), 63.67, 63.27, 36.01, 35.75, 19.73, 13.83 ppm. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -36.78 ppm. **MS (ESI+)** $C_9H_{11}O_3F_3SNa$: 279.0277 (Calc. Mass 279.0279). **HPLC** (OD-H 10µm, Hex-IPA 98-2, 0.8 mL/min, 32 bar) isomer 1: 7.431 min, isomer 2: 8.781 min.

Ethyl 2-oxo-1-((trifluoromethyl)thio)cyclohexanecarboxylate **9**



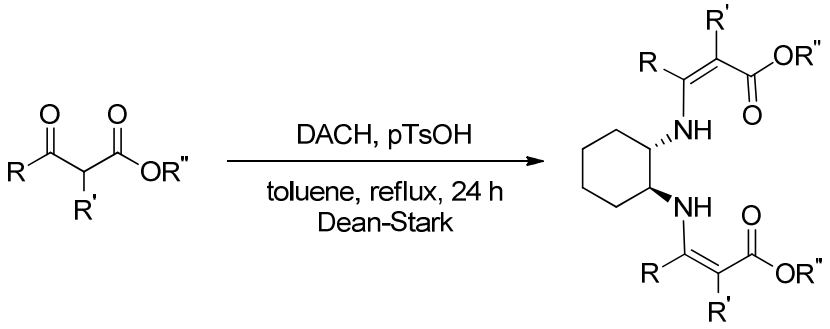
Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hexane-CH_2Cl_2 7:3) afford the desired product as a colourless oil in 77% yield. All analytical data are in agreement with literature.[16]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 4.45 – 4.19 (m, 2H), 3.09 (d, *J* = 13.8 Hz, 1H), 2.72 – 2.59 (m, 1H), 2.45 (td, *J* = 13.8, 5.9 Hz, 1H), 2.19 – 1.98 (m, 2H), 1.97 – 1.66 (m, 3H), 1.32 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 201.12, 167.09, 130.05 (q, *J* = 308.7 Hz), 67.48, 62.96, 40.28, 38.39, 27.13,

[15] X. Yang, K. Zheng, C. Zhang, *Org. Lett.* **2020***, 22,* 5, 2026–2031.
[16] X. Yang, K. Zheng, C. Zhang, *Org. Lett.* **2020***, 22,* 5, 2026–2031.

22.89, 13.73 ppm. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -36.21 ppm. **HPLC** (Phenomenex Lux 3µm Cellulose-1, Hex-IPA 98-2, 0.8 mL/min, 63 bar) isomer 1: 10.287 min, isomer 2: 10.749 min.

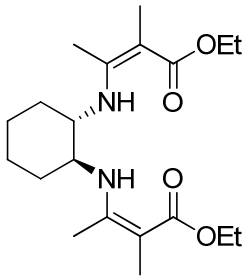
General procedure for the synthesis of chiral enamines



The β-keto ester (2.8 mmol, 2.2 eq) was dissolved in 12 mL of toluene (0.24 M) and 1,2-*trans*-diaminocyclohexane (1.3 mmol, 1 eq) and *p*-toluensulfonic acid (0.13 mmol, 0.1 eq) were added. The reaction mixture was stirred at reflux (110 °C) with Dean-Stark equipped with molecular sieves for 48 h. After this time, the reaction mixture was filtered over a plug of celite and washed with AcOEt, then the solvent was evaporated and the crude was purified by filtration on a silica gel flash column deactivated with NEt_3.

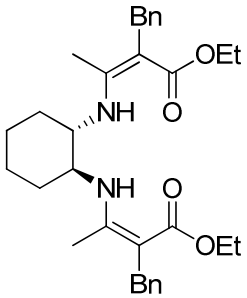
Products characterization

Diethyl 3,3'-((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(2-methylbut-2-enoate) **13**



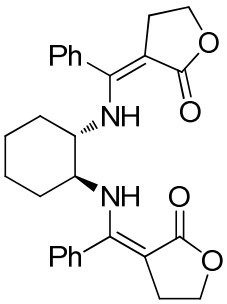
Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hex-EtOAc 9:1+ 2% di NEt_3) afford the desired product as a pale-yellow oil in 58 % yield.
^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.35 (d, J = 8.2 Hz, 2H), 4.09 (q, J = 7.1 Hz, 4H), 3.19 (m, 2H), 2.03 – 1.87 (m, 2H), 1.85 (s, 6H), 1.76 (m, 2H), 1.72 (s, 6H), 1.44 – 1.31 (m, 2H), 1.26 (t, J = 7.1 Hz, 6H), 1.20 (m, 2H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 171.19, 159.50, 86.75, 58.64, 58.11, 33.40, 24.69, 15.36, 14.67, 12.51 ppm. **MS (ESI+)** $C_{20}H_{34}N_2O_4$: 366.252830 (Calc. Mass 366.251858).

Diethyl 3,3'-((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(2-benzylbut-2-enoate) **16**



Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hex-EtOAc 8:2+ 2% di NEt_3) afford the desired product as a pale-yellow oil in 37 % yield.
^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.68 (d, *J* = 9.0 Hz, 2H), 7.22 (d, *J* = 7.1 Hz, 4H), 7.17 – 7.09 (m, 6H), 4.05 (q, *J* = 7.1 Hz, 4H), 3.60 (dd, *J* = 57.8, 16.9 Hz, 4H), 3.32 – 3.15 (m, 2H), 2.02 (d, *J* = 12.8 Hz, 2H), 1.89 (s, 6H), 1.79 (d, *J* = 8.1 Hz, 2H), 1.51 – 1.25 (m, 4H), 1.17 (t, *J* = 7.1 Hz, 6H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 171.22, 160.79, 143.07, 127.98, 127.65, 125.14, 90.51, 58.64, 58.03, 33.59, 32.67, 24.71, 15.37, 14.46 ppm. **MS (ESI+)** $C_{32}H_{42}N_2O_4$: 518.314640 (Calc. Mass 518.314458).

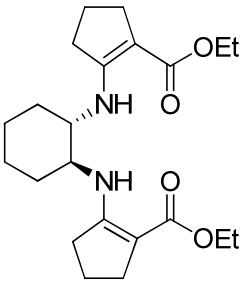
(3Z,3'Z)-3,3'-(((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(phenylmethanylylidene))bis(dihydrofuran-2(3H)-one) **17**



Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hex-EtOAc 8:2+ 2% di NEt_3) afford the desired product as a yellow solid in 16% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.96 (d, *J* = 9.3 Hz, 2H), 7.56 – 7.38 (m, 8H), 7.34 (bs, 2H), 4.22 (t, *J* = 8.0 Hz, 4H), 2.91 – 2.72 (m, 2H), 2.56 (td, *J* = 7.6, 2.5 Hz, 4H), 1.76 (d, *J* = 13.6 Hz, 2H), 1.49 (d, *J* = 9.4 Hz, 2H), 1.15 (m, 4H), 0.90 (m, 4H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 174.27, 159.38, 134.52, 129.16, 127.74, 87.39, 65.72, 58.07, 34.46, 26.92, 24.31 ppm. **MS (EI+)** $C_{28}H_{30}N_2O_4Na$: 481.2109 (Calc. 481.2103).

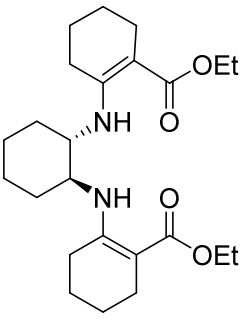
Diethyl 2,2'-((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(cyclopent-1-enecarboxylate) **18**



Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hex-EtOAc 9:1+ 2% di NEt_3) afford the desired product as a pale yellow oil in 53% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.39 (d, *J* = 5.9 Hz, 2H), 4.18 – 3.97 (m, 4H), 2.87 (bs, 2H), 2.52 (dt, *J* = 15.3, 7.5 Hz, 2H), 2.42 – 2.26 (m, 6H), 2.05 – 1.93 (m, 2H), 1.80 – 1.53 (m, 6H), 1.26 (d, *J* = 1.5 Hz, 4H), 1.22 (td, *J* = 7.1, 2.7 Hz, 6H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 168.76, 164.79, 92.77, 60.43, 58.32, 33.36, 32.37, 28.82, 24.85, 21.14, 14.75 ppm. **MS (ESI+)** $C_{22}H_{34}N_2O_4Na$: 413.2414 (Calc. 413.2416).

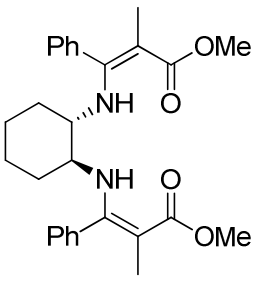
Diethyl 2,2'-(((1S,2S)-cyclohexane-1,2-diyl)bis(azanediyl))bis(cyclohex-1-ene-1-carboxylate) **19**



Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hex-EtOAc 97:3+ 2% di NEt_3) afford the desired product as a pale yellow oil in 88% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.99 (d, *J* = 9.4 Hz, 2H), 4.05 (qq, *J* = 10.7, 7.1 Hz, 4H), 3.07 (m, 2H), 2.38 – 1.62 (m, 16H), 1.53 – 1.38 (m, 6H), 1.31 (m 4H), 1.20 (t, *J* = 7.1 Hz, 6H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 171.07, 159.62, 89.24, 58.49, 57.34, 33.58, 26.55, 25.04, 23.92, 22.49, 22.32, 14.67 ppm. **MS (ESI+)** $C_{24}H_{38}N_2O_4Na$: 441.2731 (Calc. 441.2729).

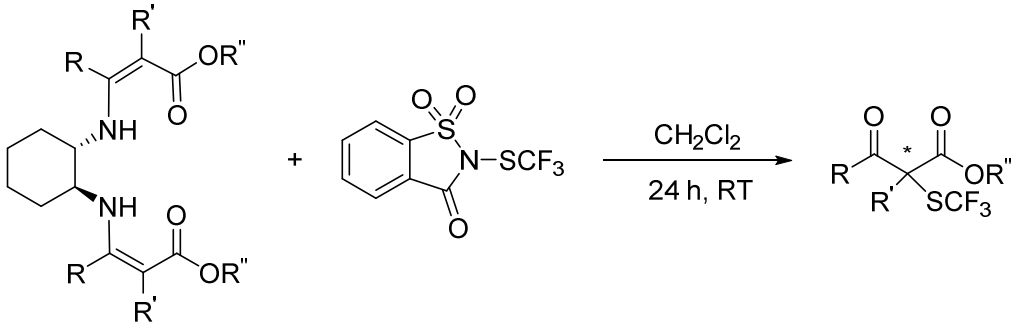
Dimethyl 3,3'-((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(2-methyl-3-phenylacrylate)



Prepared according to the general procedure. The crude mixture was purified by column chromatography on silica gel (Hex-EtOAc 8:2+ 2% di NEt_3) afford the desired product as a yellow solid in 18% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.98 (d, *J* = 9.4 Hz, 2H), 7.55 – 7.35 (m, 6H), 7.24 – 7.07 (m, 4H), 3.75 (s, 6H), 2.76 – 2.51 (m, 2H), 1.72 (d, *J* = 13.4 Hz, 2H), 1.45 (s, 6H), 0.96 (m, 6H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ 171.56, 161.84, 135.64, 129.02, 128.93, 128.40, 128.25, 127.65, 88.29, 57.43, 50.51, 33.61, 23.82, 13.97 ppm. **MS (EI+)**: $C_{28}H_{34}N_2O_4$: 463.28 (Calc. 462.25).

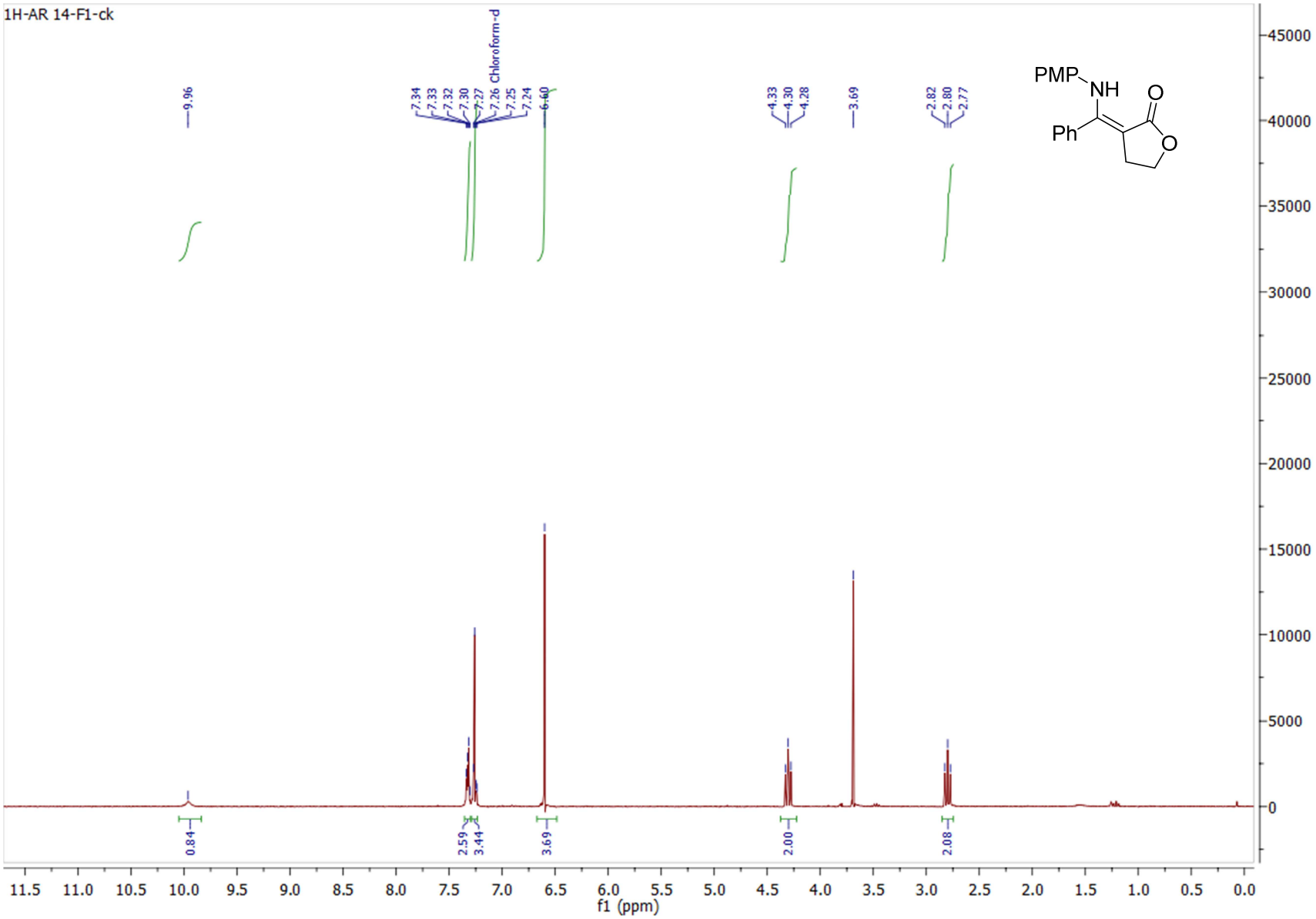
General procedure for the synthesis of chiral β-ketoesters



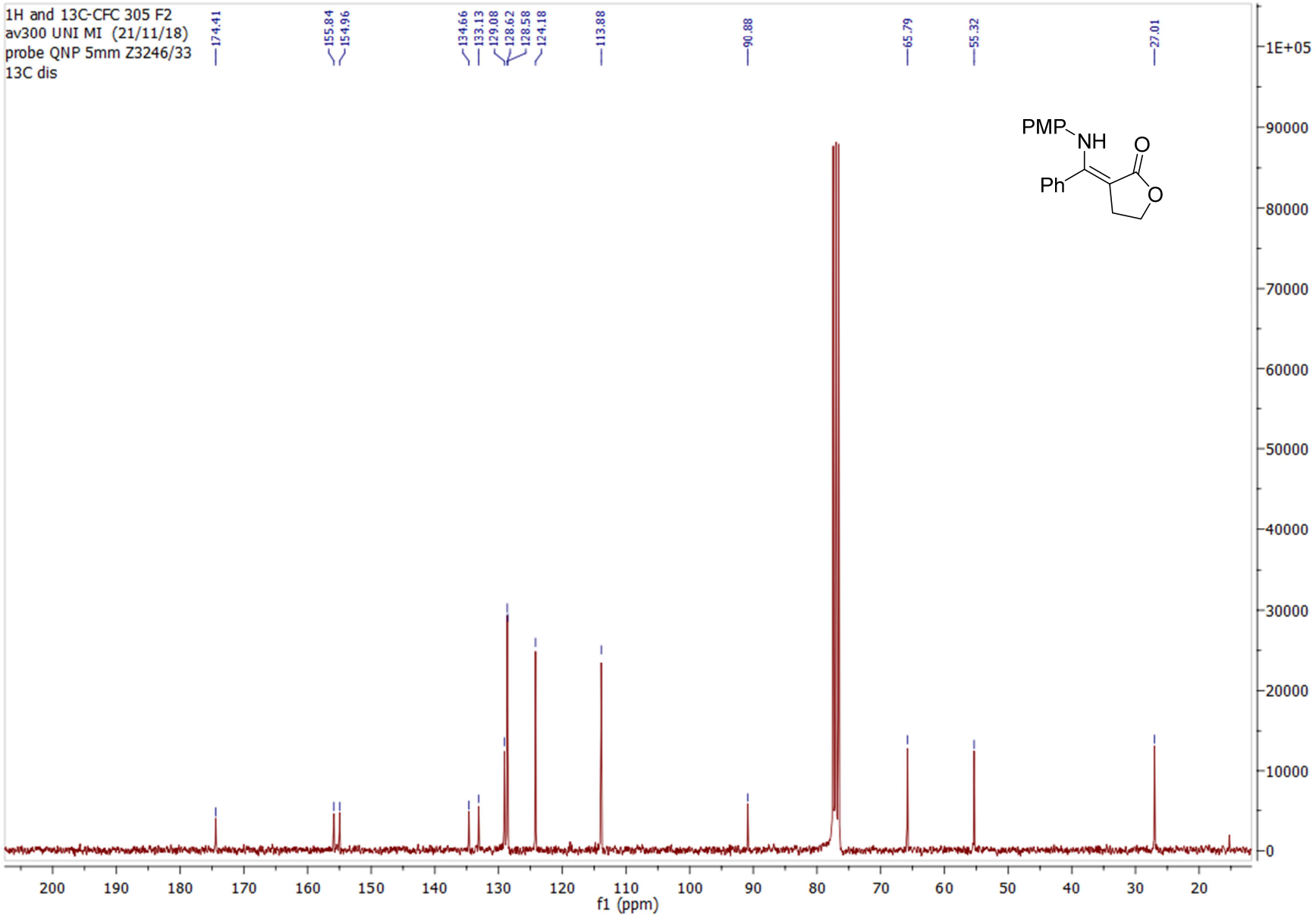
The chiral enamine (0.14 mmol, 1 eq), was dissolved in 1.4 mL of dry CH_2Cl_2 (0.1 M) and *N*-trifluoromethylthio saccharin (0.16 mmol, 1.2 eq) was added. The reaction mixture was stirred at dark at r.t. for 18 hours under static nitrogen atmosphere. After this time, the reaction mixture was quenched with 2 mL x2 of H_2O and extracted with 2 mL x2 of CH_2Cl_2: the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by filtration on silica gel flash column.

NMR Spectra

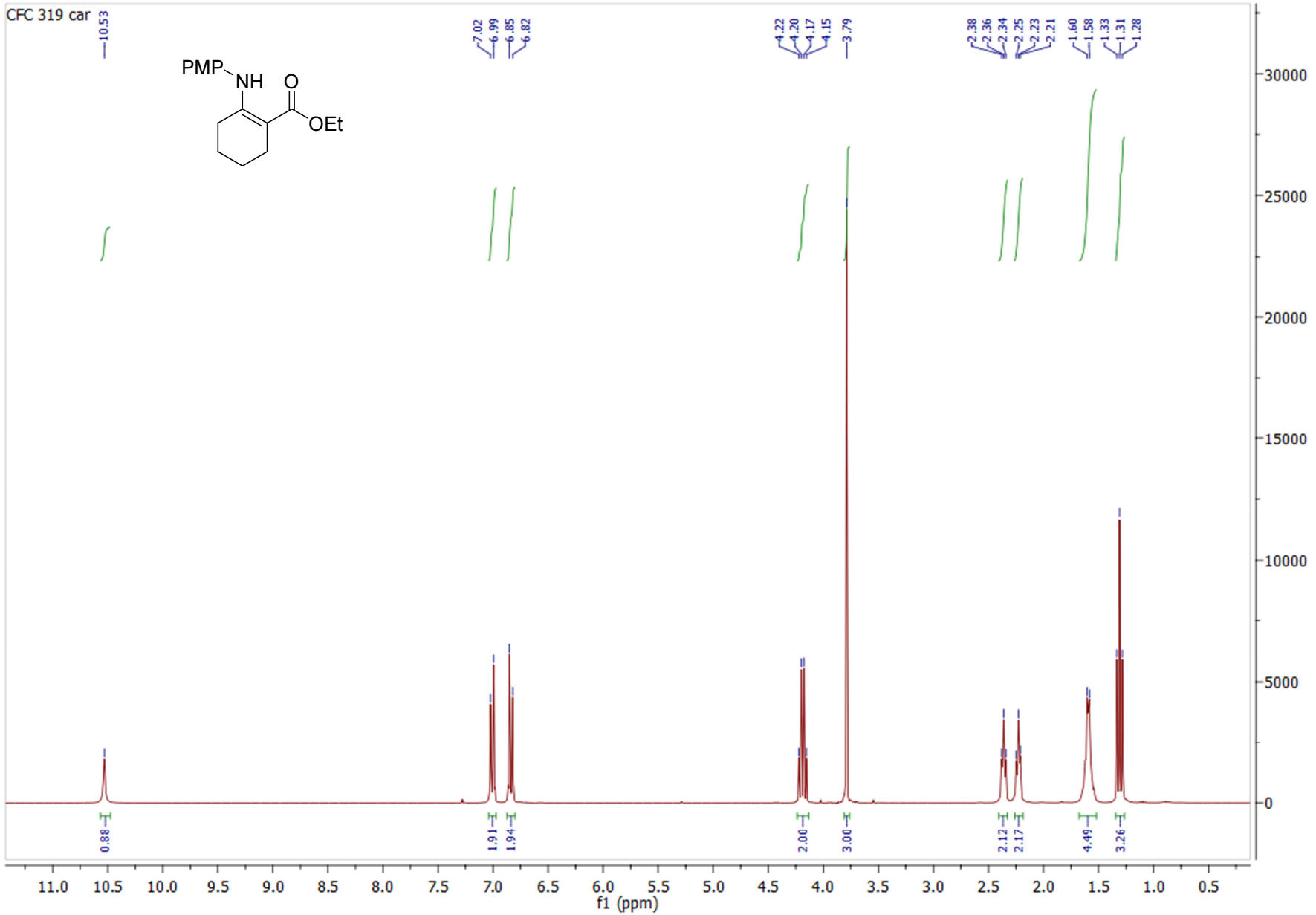
3-(((4-methoxyphenyl)amino)(phenyl)methylene)dihydrofuran-2(3H)-one – ^{1}H NMR



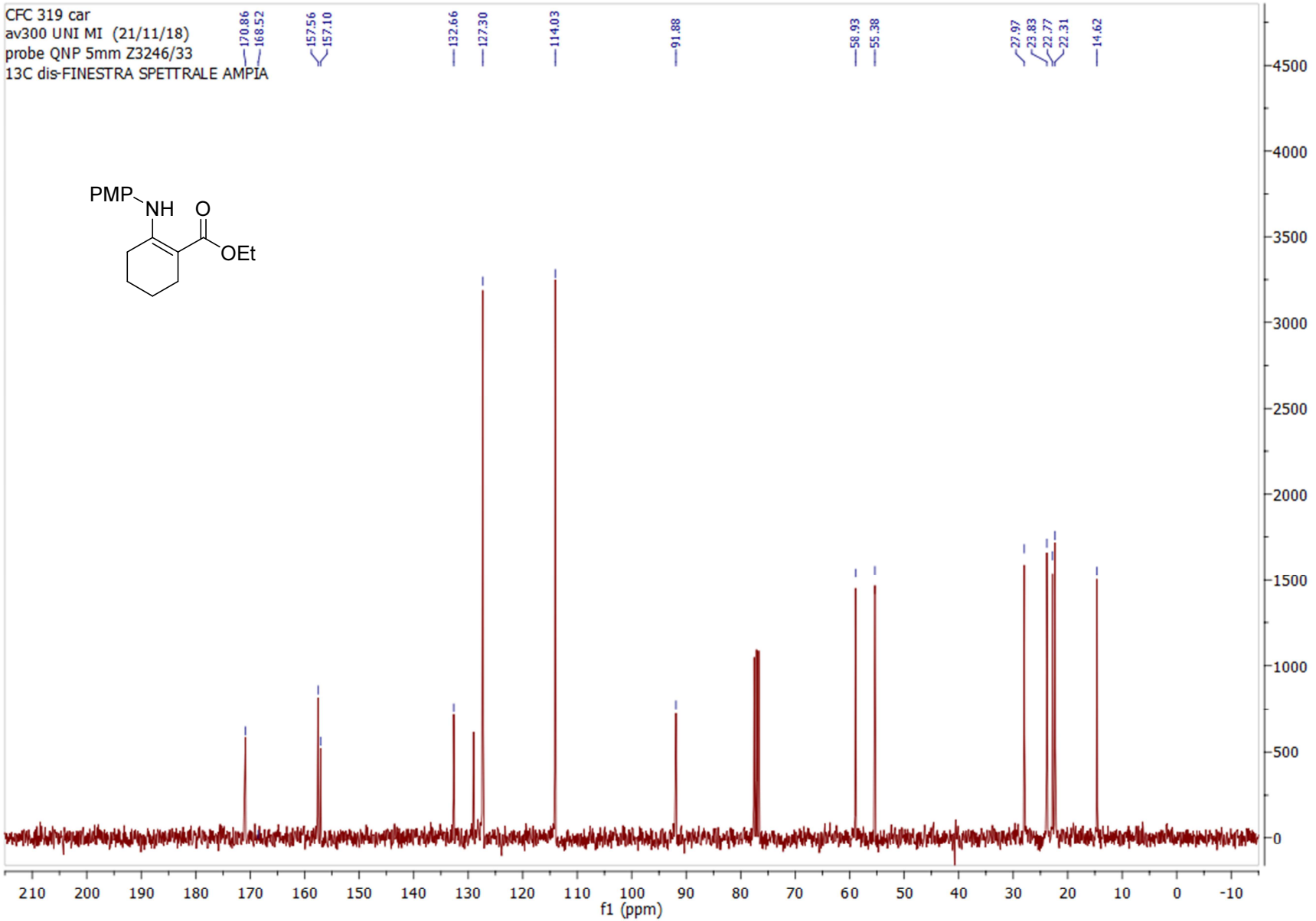
3-(((4-methoxyphenyl)amino)(phenyl)methylene)dihydrofuran-2(3H)-one – ^{13}C NMR



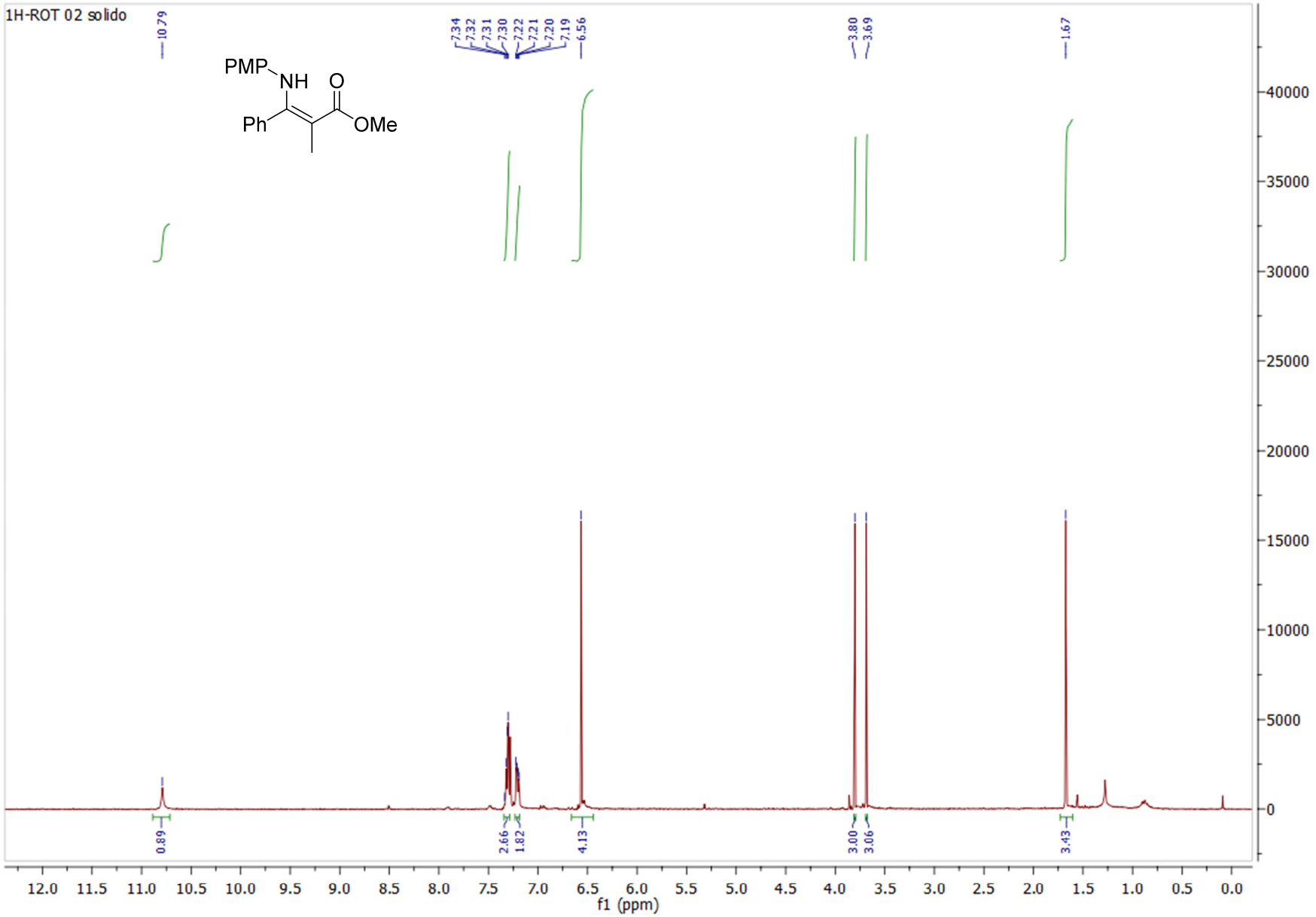
Ethyl 2-((4-methoxyphenyl)amino)cyclohex-1-enecarboxylate–^{1}H NMR



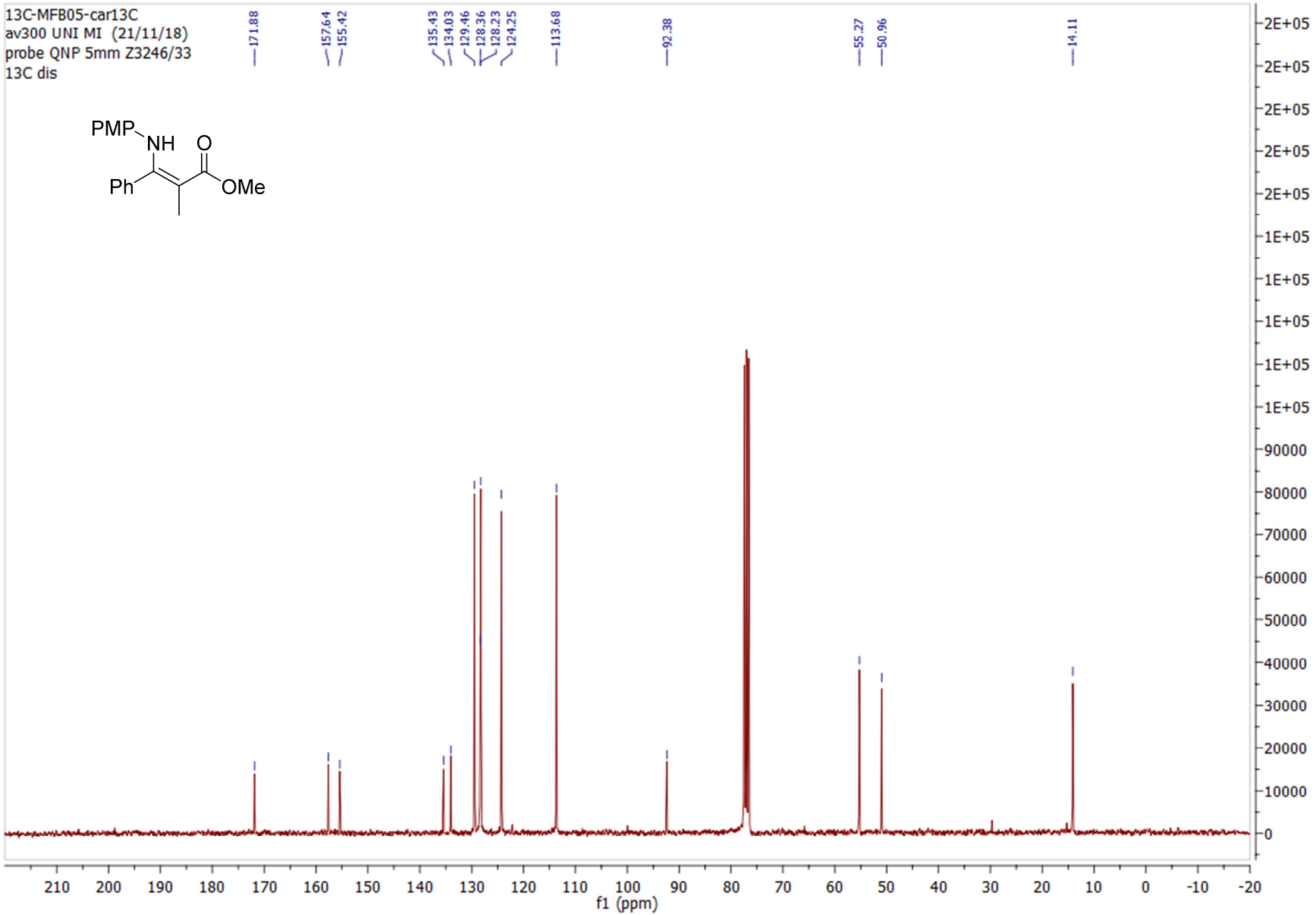
Ethyl 2-((4-methoxyphenyl)amino)cyclohex-1-enecarboxylate–^{13}C NMR



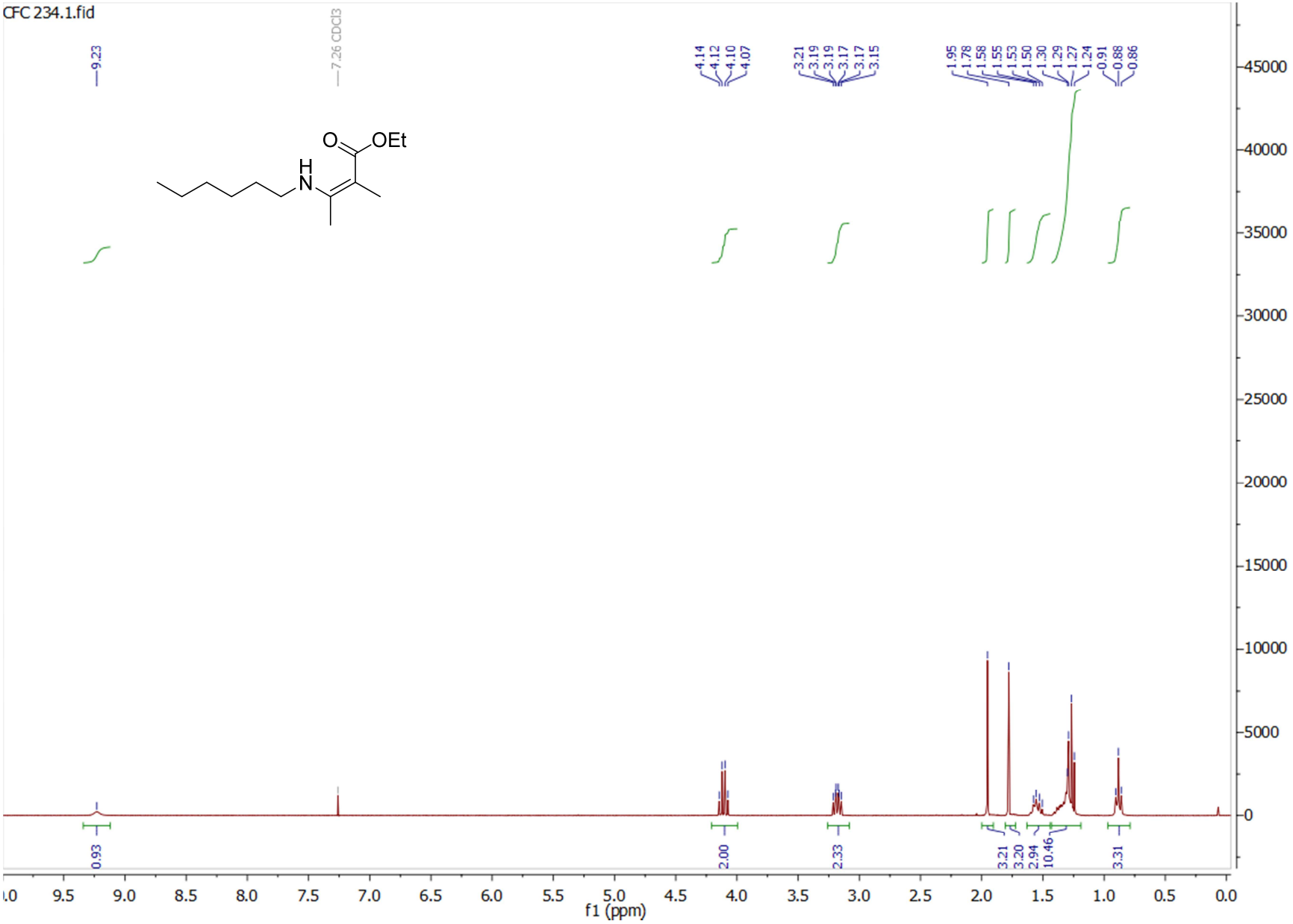
Methyl 3-((4-methoxyphenyl)amino)-2-methyl-3-phenylacrylate– ^{1}H NMR



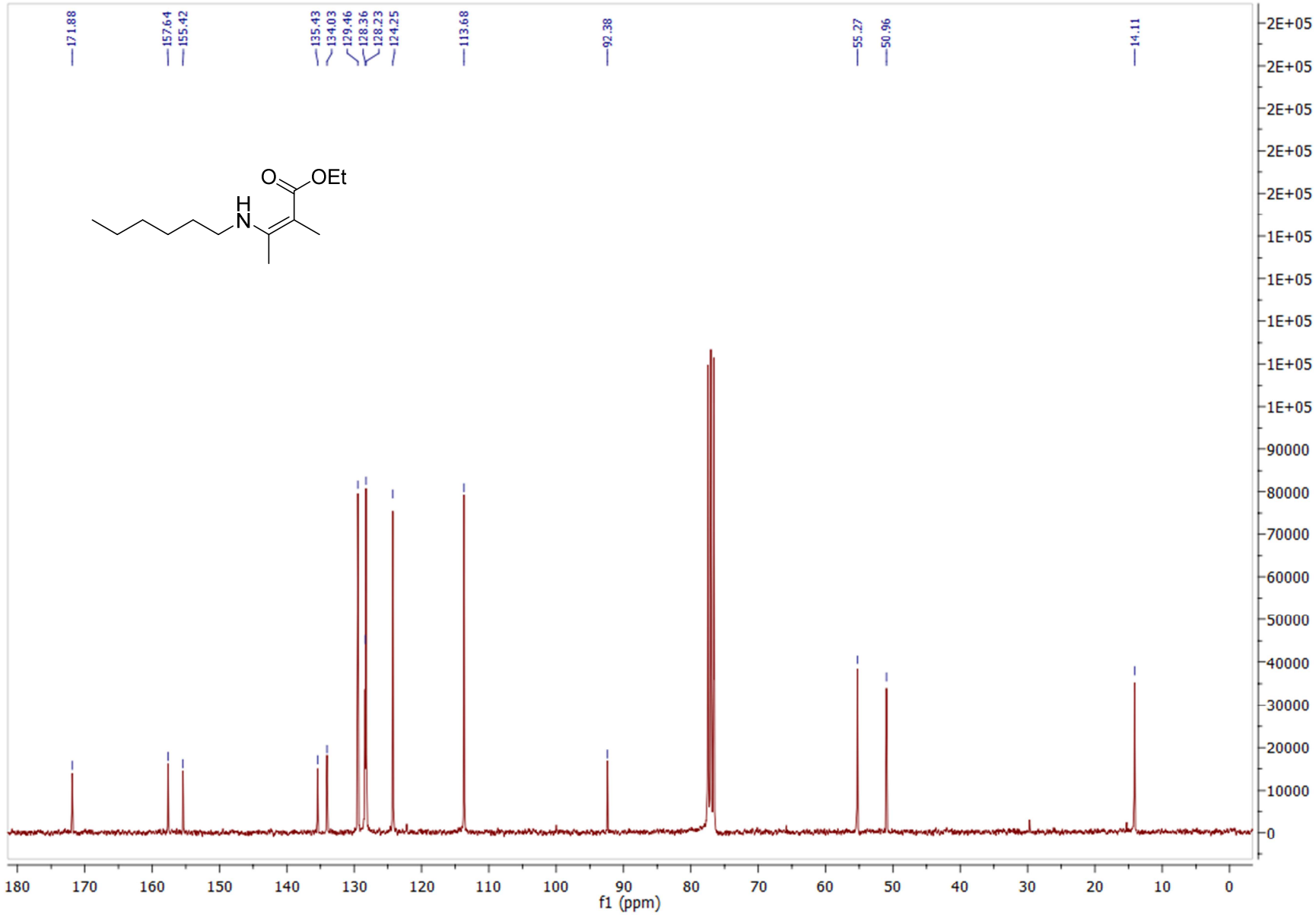
Methyl 3-((4-methoxyphenyl)amino)-2-methyl-3-phenylacrylate - ^{13}C NMR



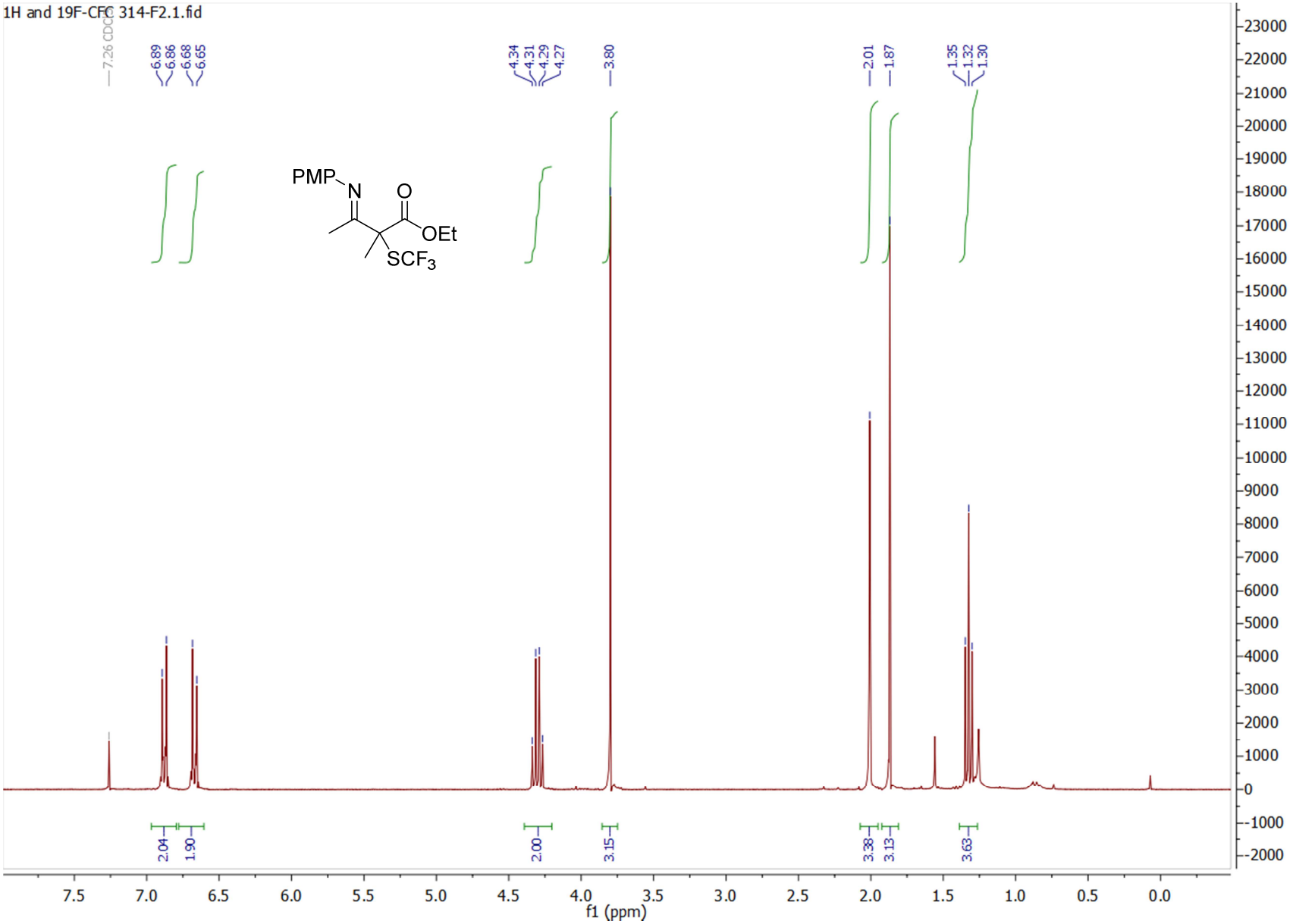
Ethyl 3-(hexylamino)-2-methylbut-2-enoate- ^{1}H NMR



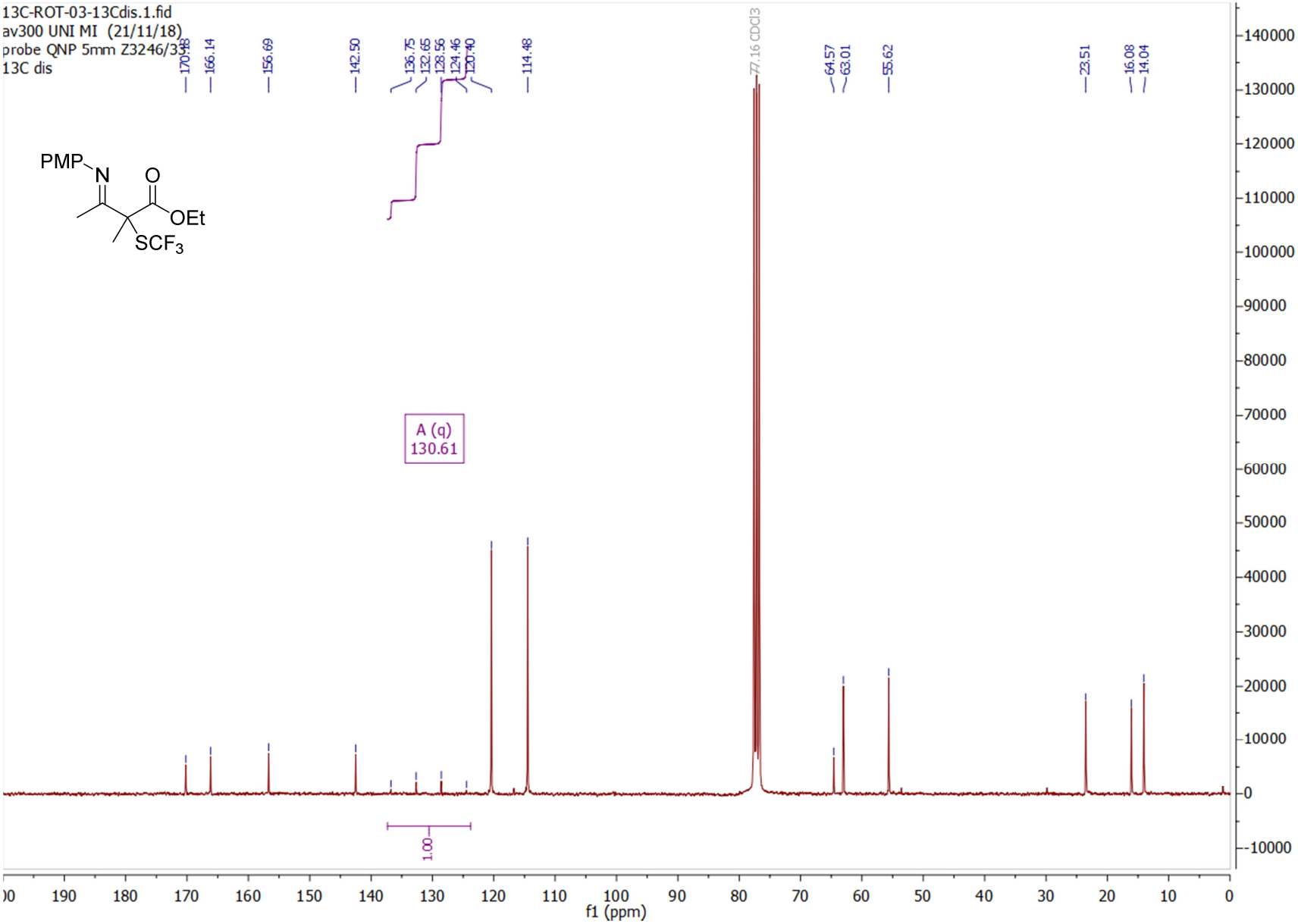
Ethyl 3-(hexylamino)-2-methylbut-2-enoate- ^{13}C NMR



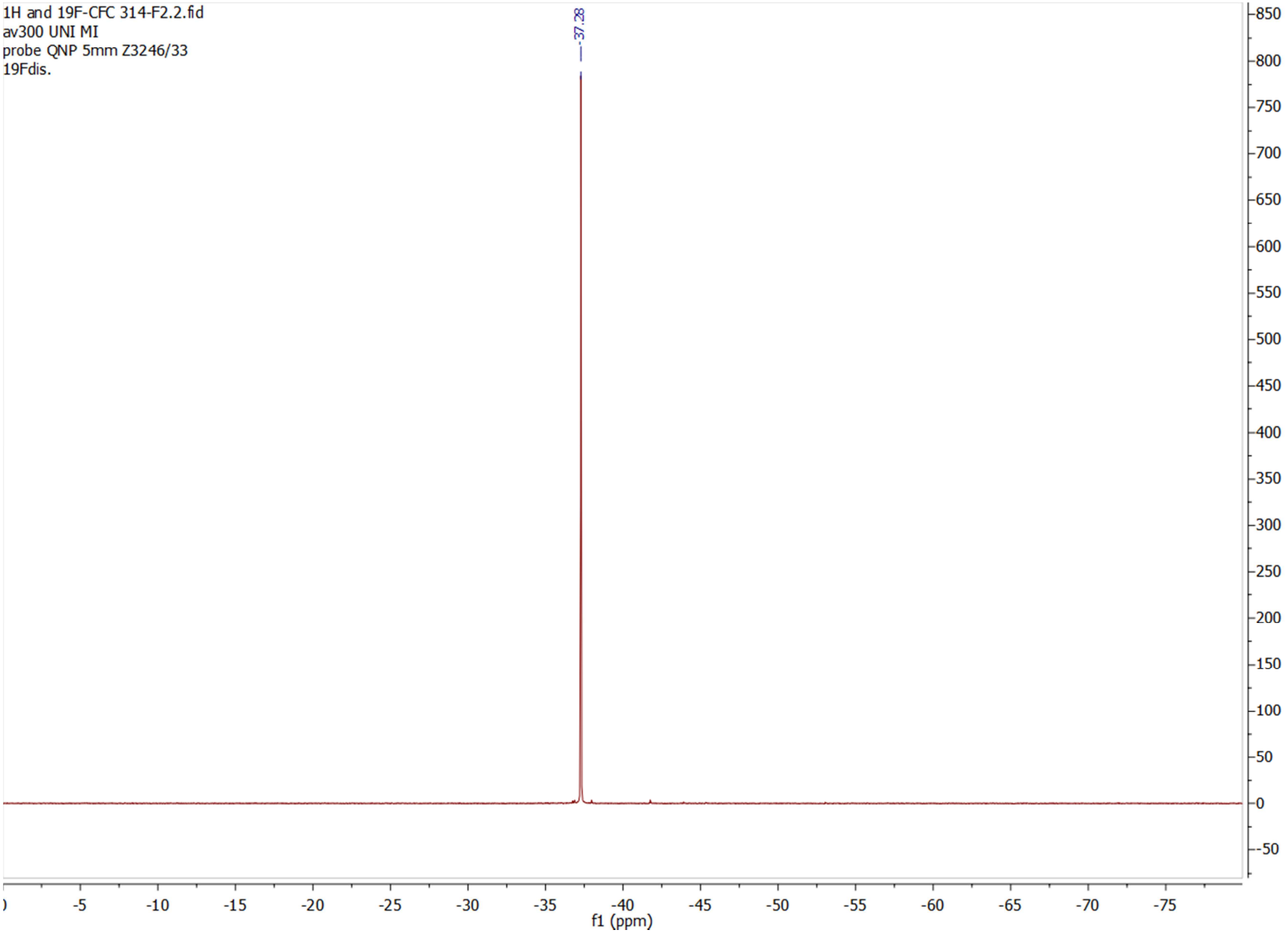
Ethyl 3-((4-methoxyphenyl)imino)-2-methyl-2-((trifluoromethyl)thio)butanoate-^{1}H NMR



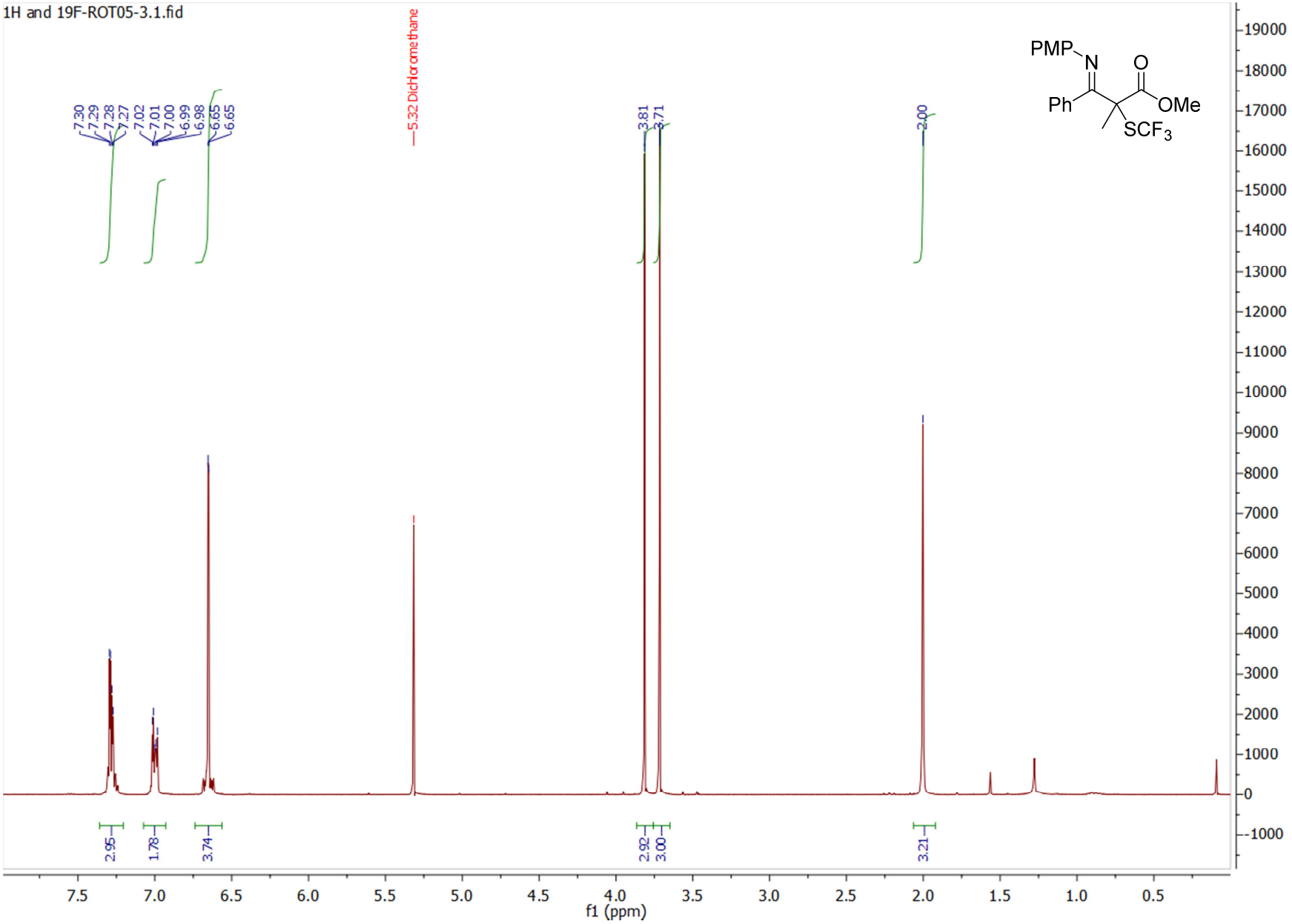
Ethyl 3-((4-methoxyphenyl)imino)-2-methyl-2-((trifluoromethyl)thio)butanoate-^{13}C NMR



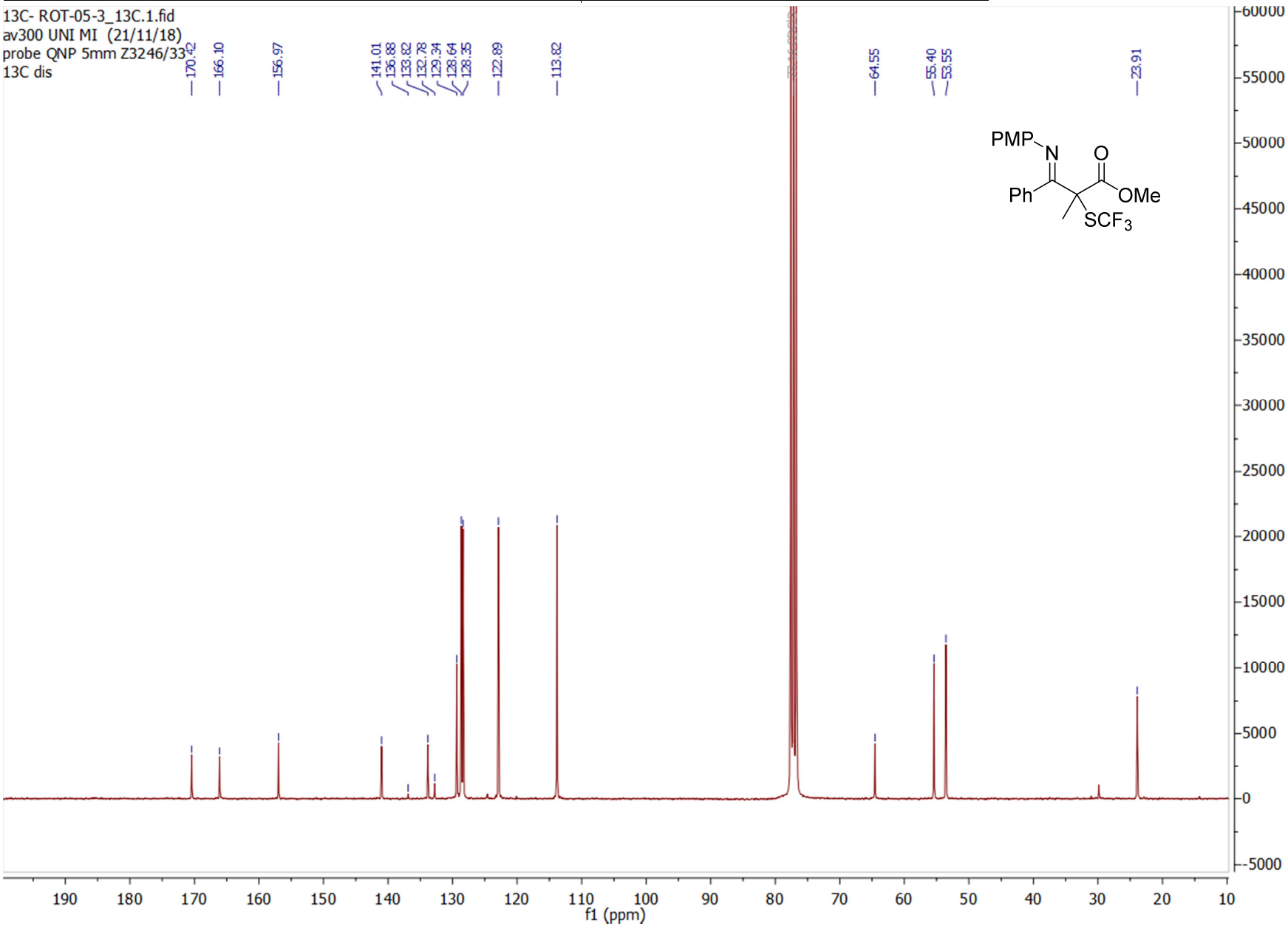
Ethyl 3-((4-methoxyphenyl)imino)-2-methyl-2-((trifluoromethyl)thio)butanoate-^{19}F NMR



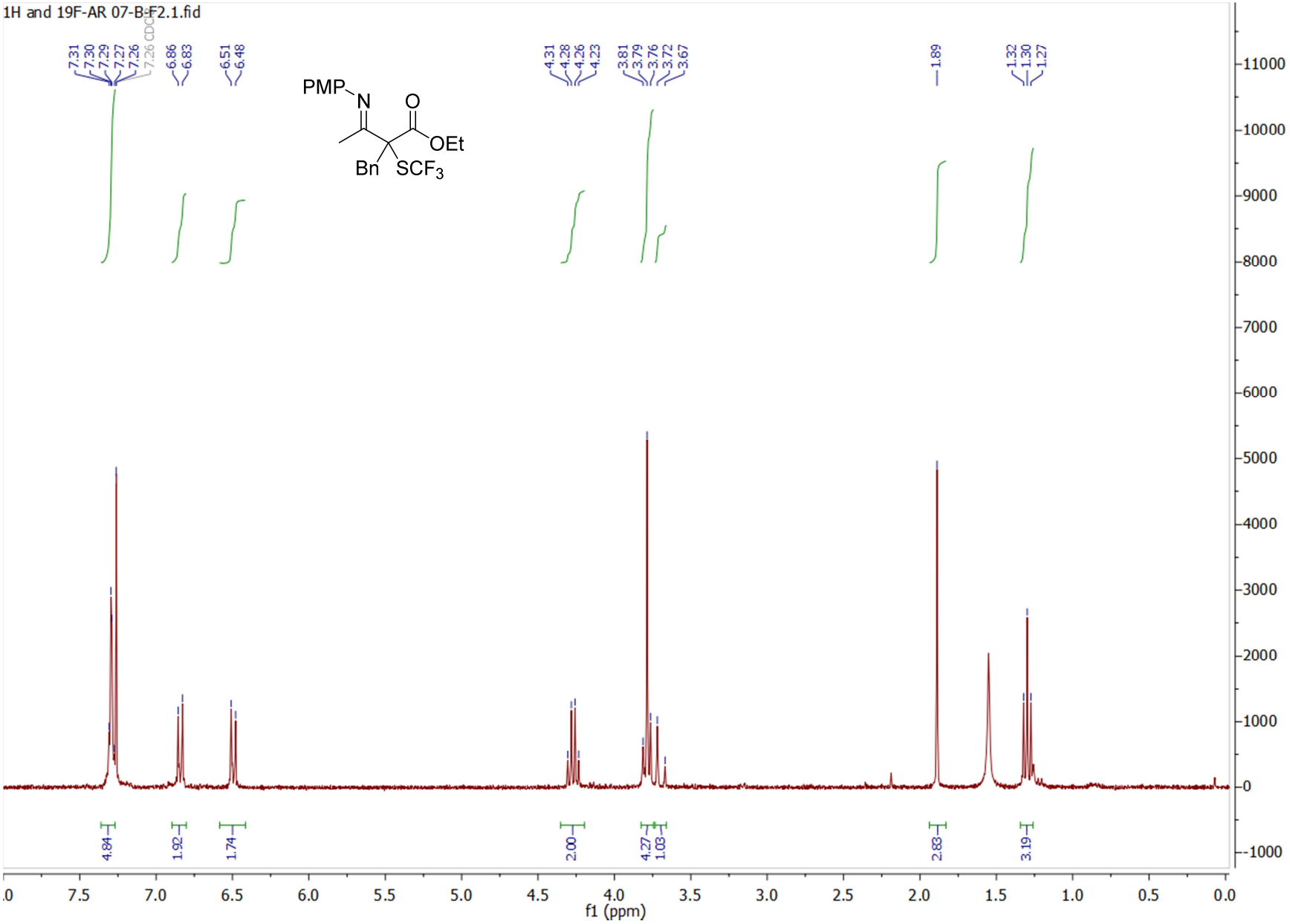
Methyl 3-((4-m ethoxyphenyl)imino)-2-methyl-3-phenyl-2-((trifluoromethyl)thio)propanoate-^{1}H NMR



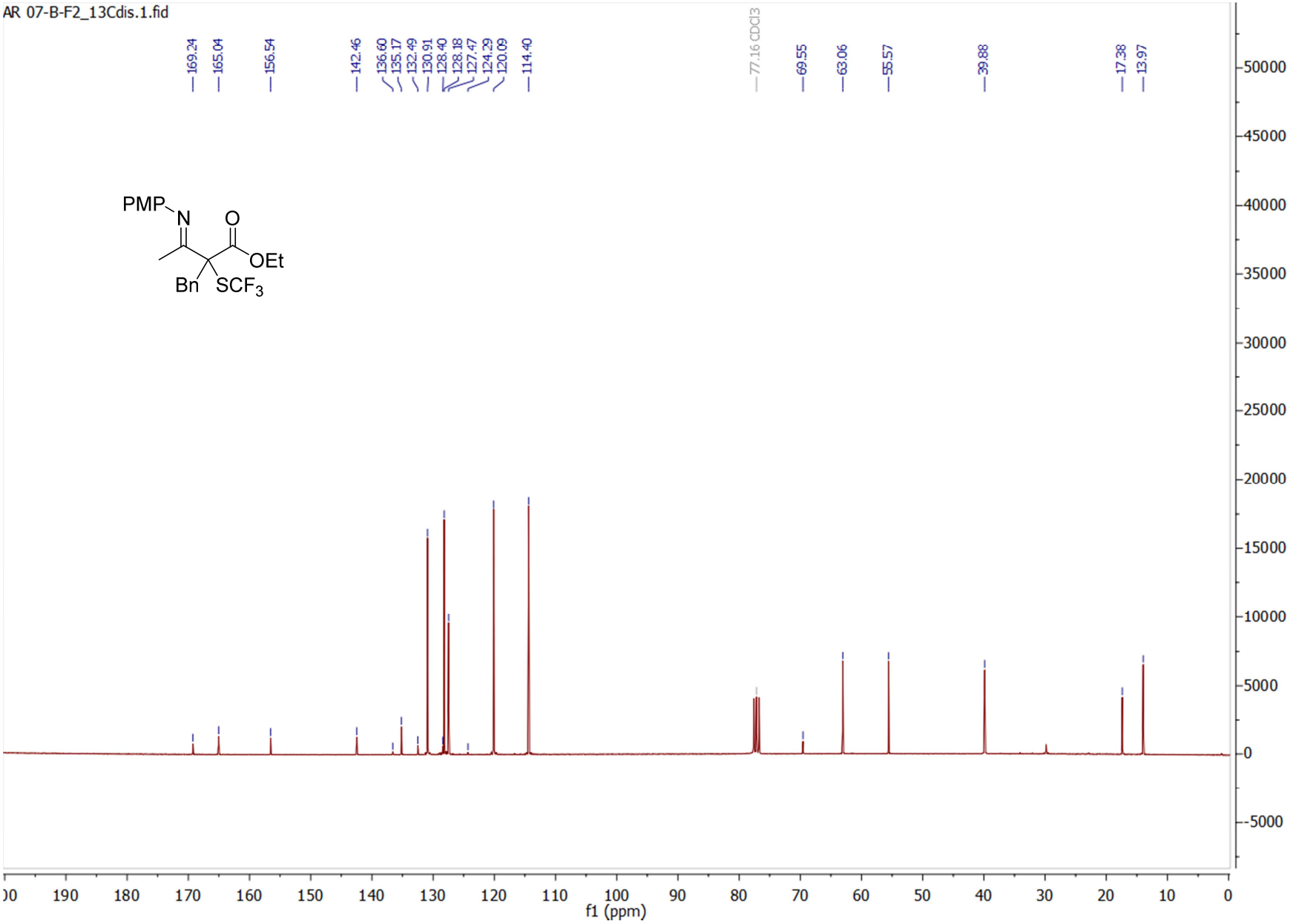
Methyl 3-((4-m ethoxyphenyl)imino)-2-methyl-3-phenyl-2-((trifluoromethyl)thio)propanoate-^{13}C NMR



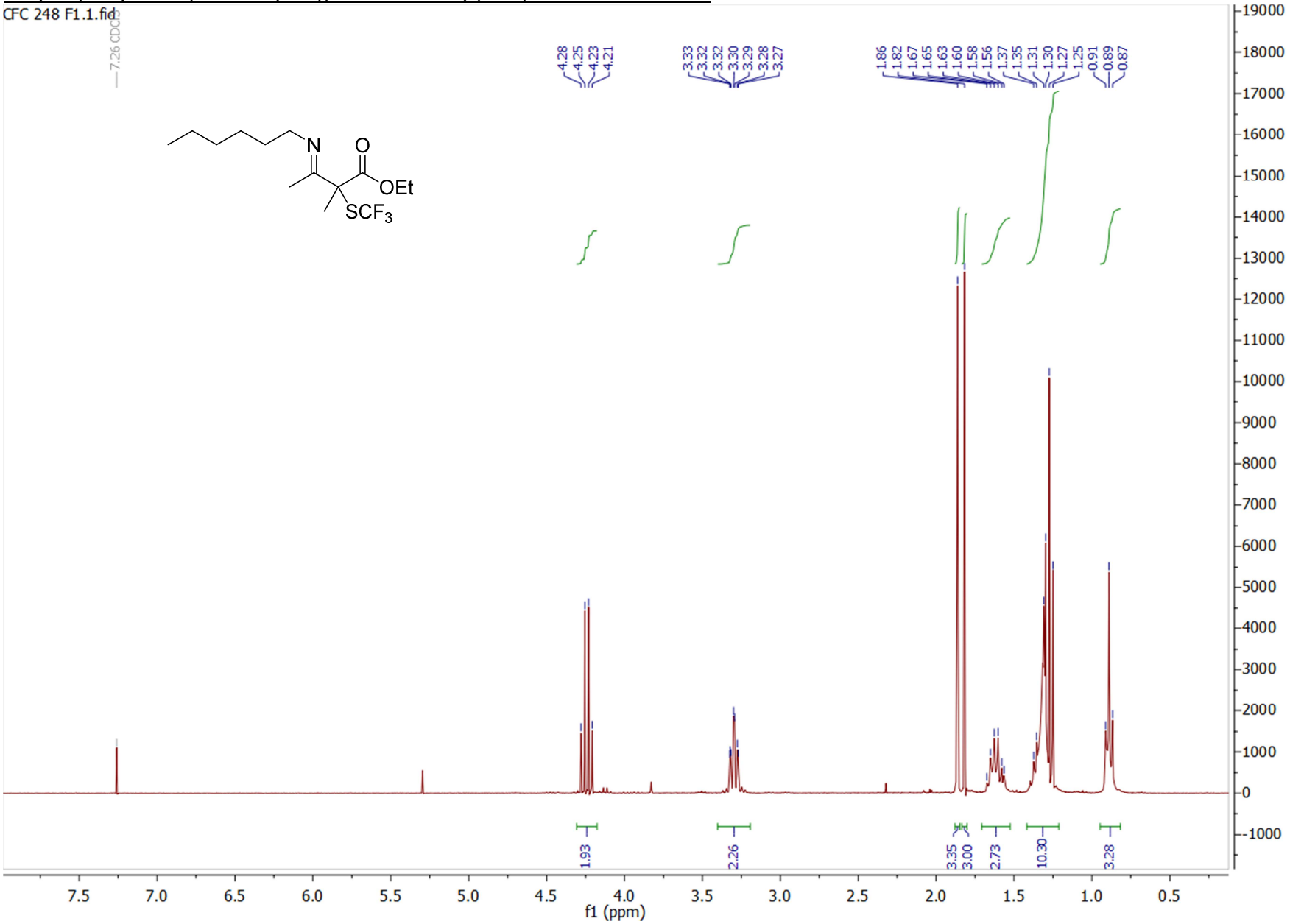
Ethyl 2-benzyl-3-((4-methoxyphenyl)imino)-2-((trifluoromethyl)thio)butanoate ^{1}H NMR



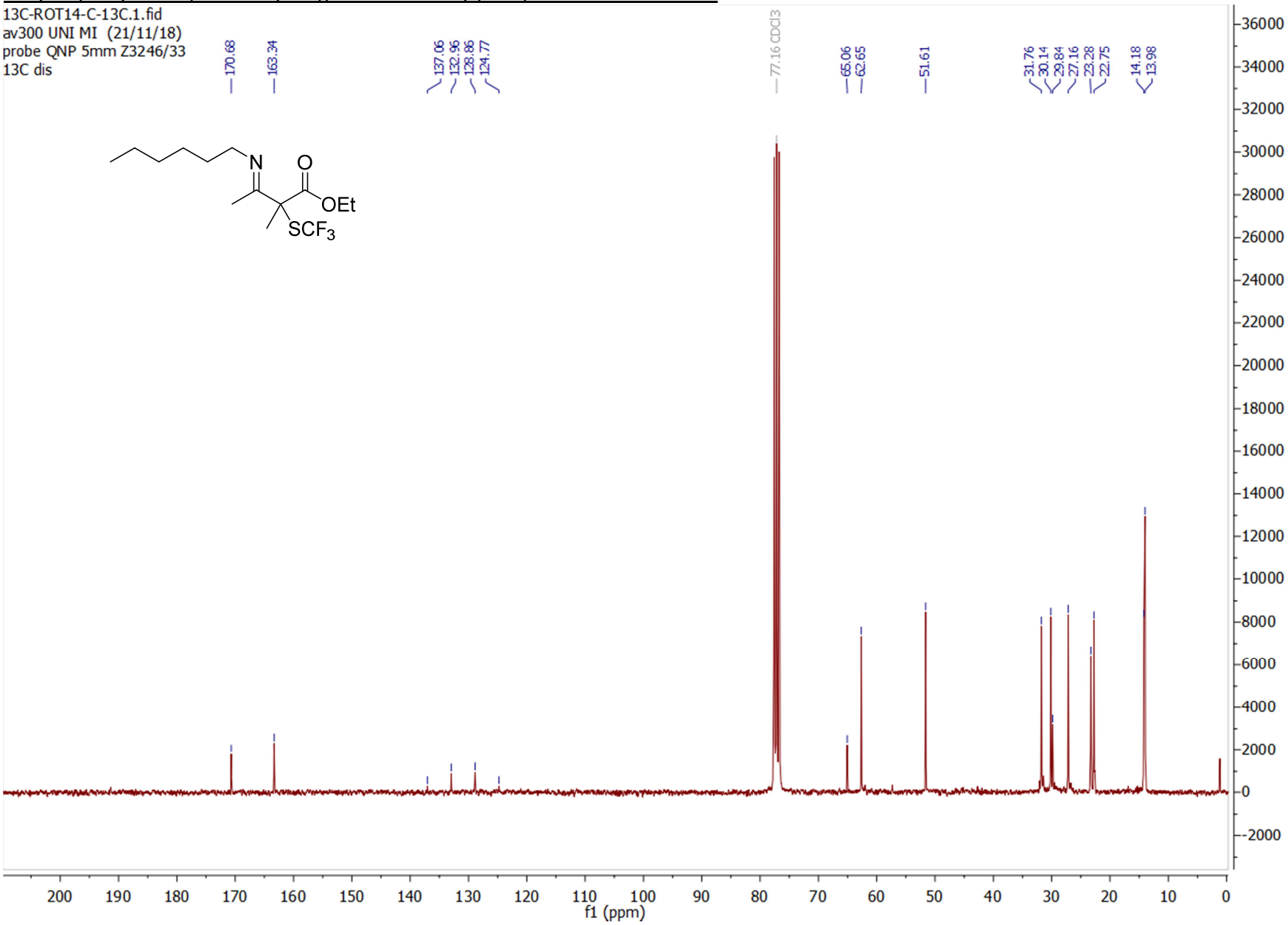
Ethyl 2-benzyl-3 -((4-methoxyphenyl)imino)-2-((trifluoromethyl)thio)butanoate^{13}C NMR



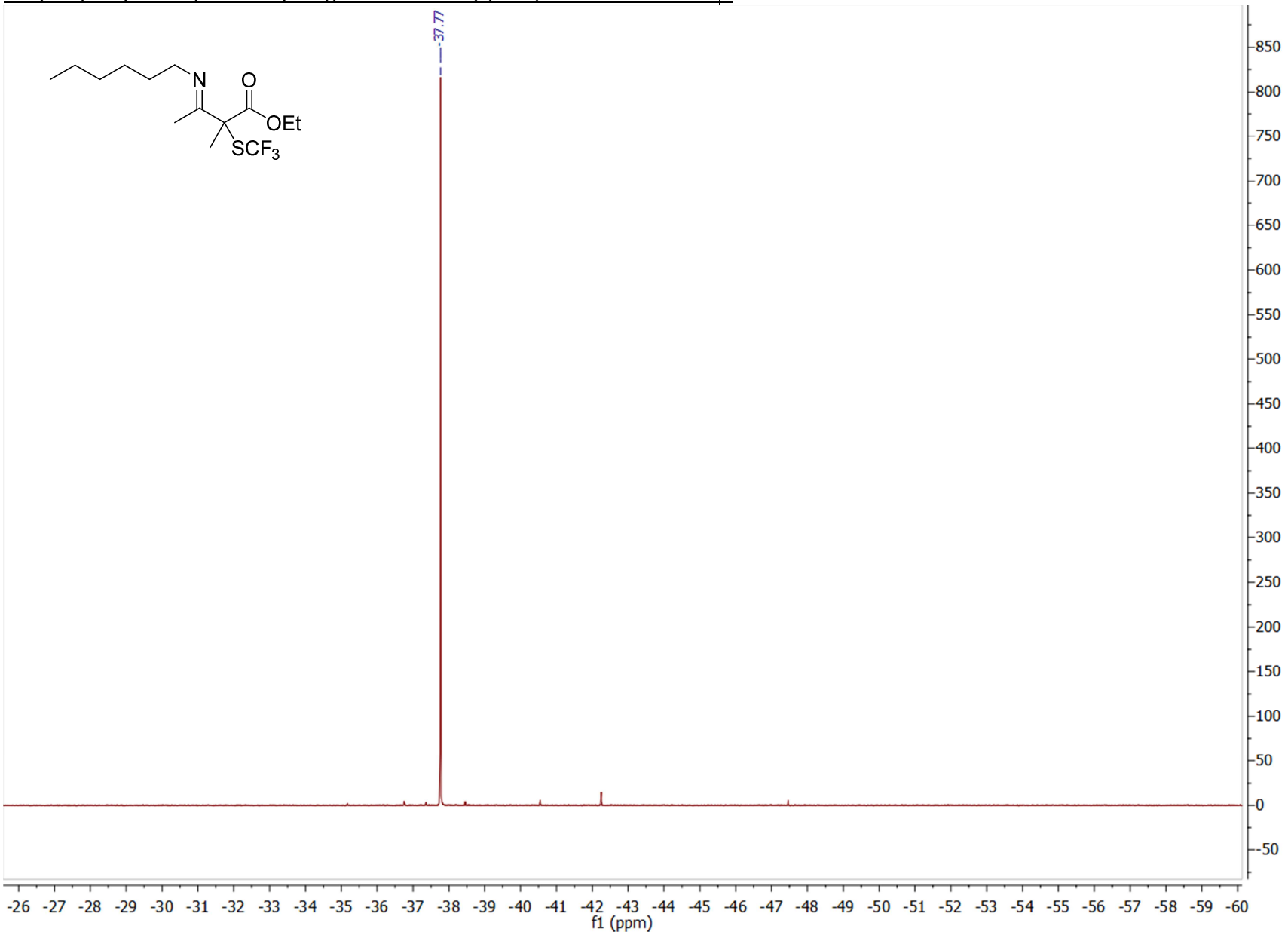
Ethyl 3-(hexylimino)-2-methyl-2-((trifluoromethyl)thio)butanoate-^{1}H NMR



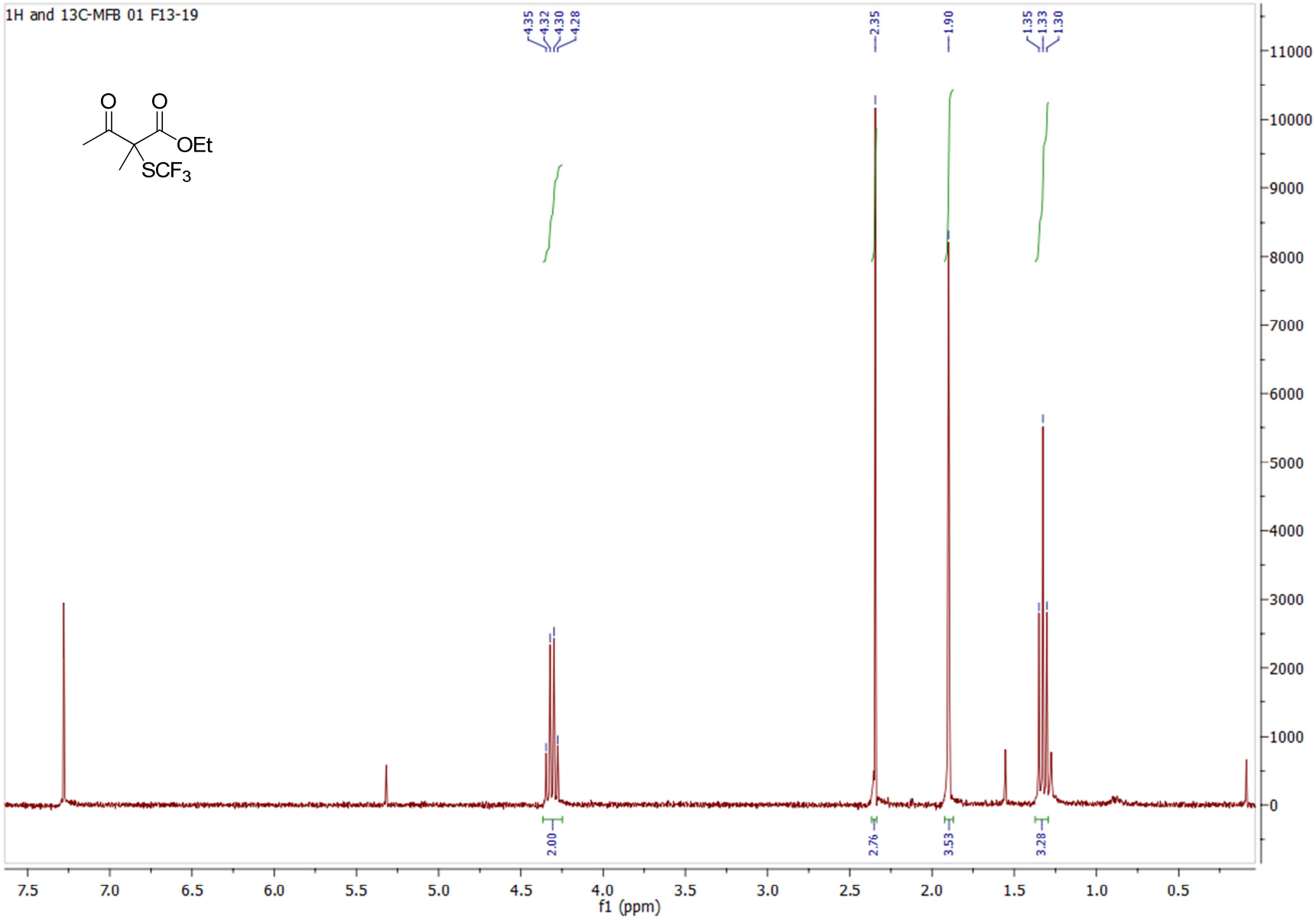
Ethyl 3-(hexylimino)-2-methyl-2-((trifluoromethyl)thio)butanoate-^{13}C NMR



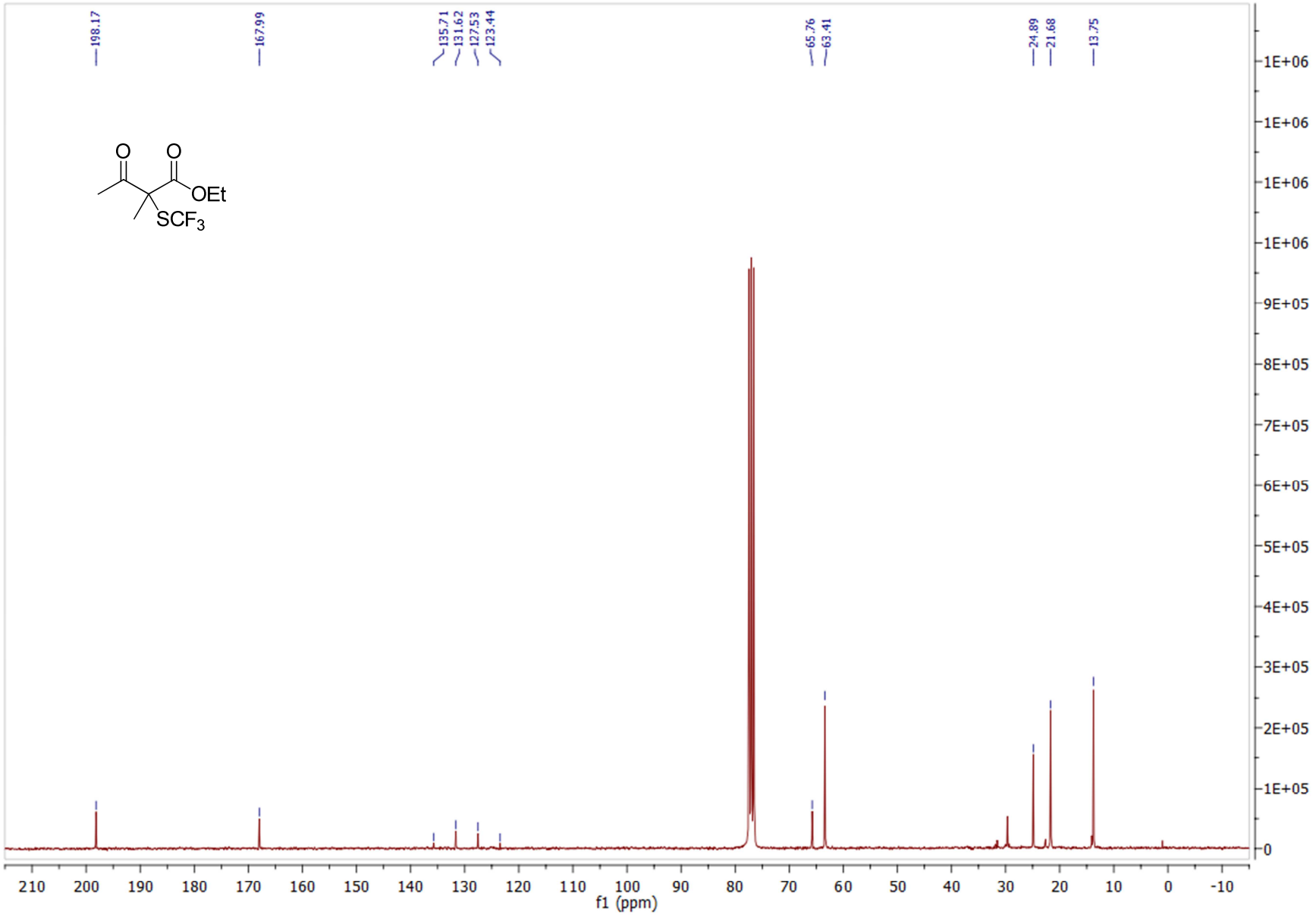
Ethyl 3-(hexylimino)-2-methyl-2-((trifluoromethyl)thio)butanoate-^{19}F NMR



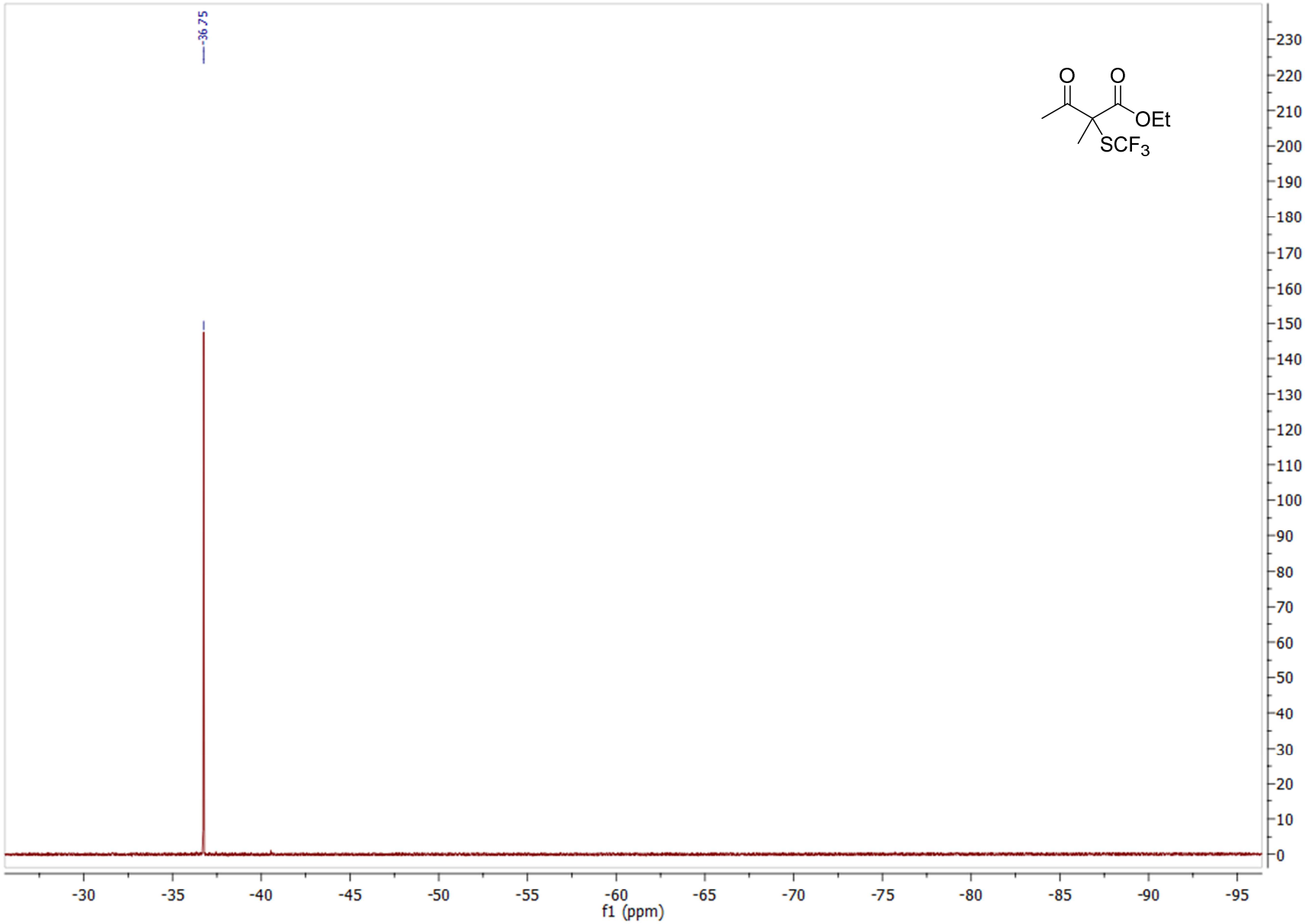
Ethyl 2-methyl-3-oxo-2-((trifluoromethyl)thio)butanoate -^{1}H NMR



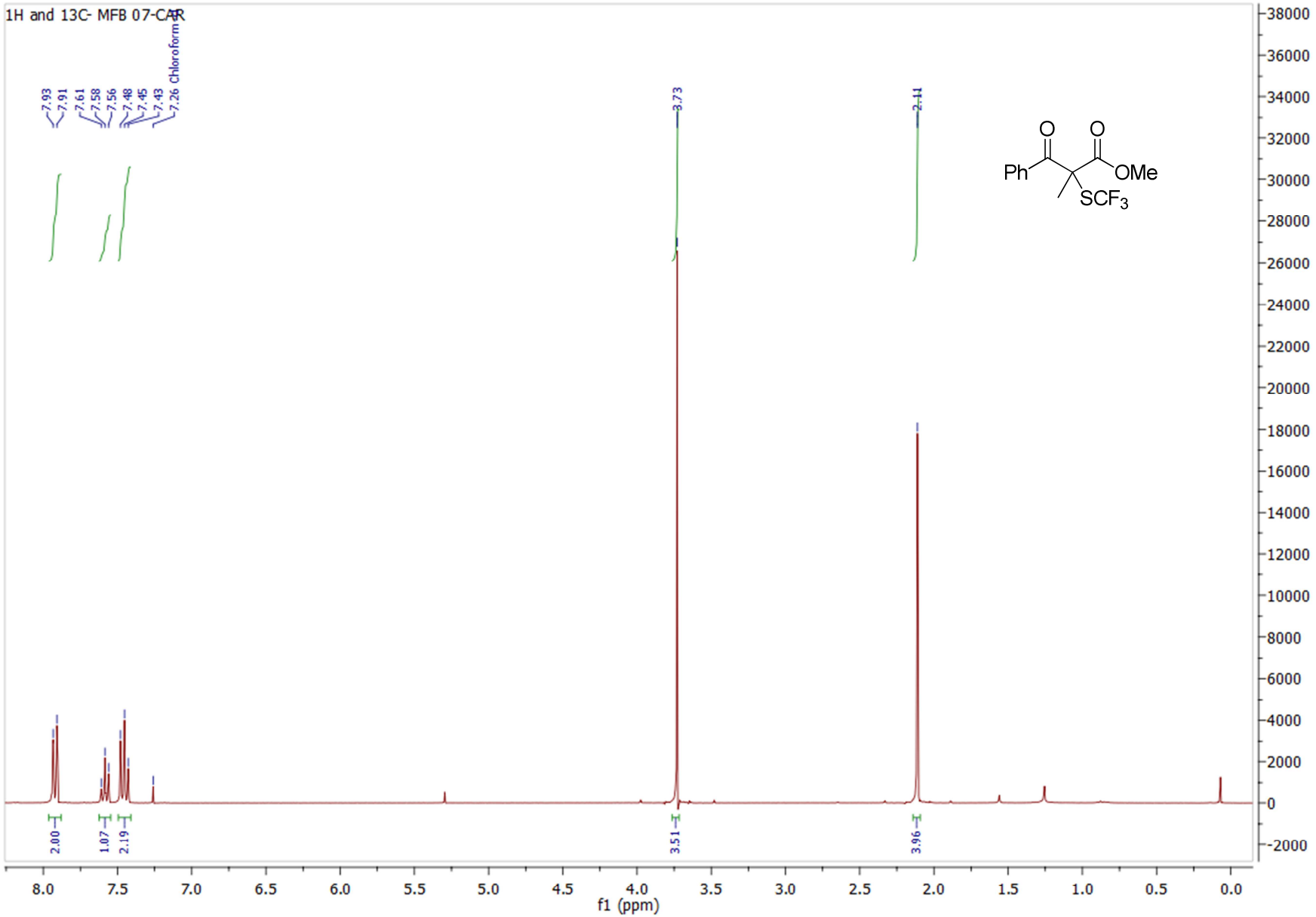
Ethyl 2-methyl-3-oxo-2-((trifluoromethyl)thio)butanoate -^{13}C NMR



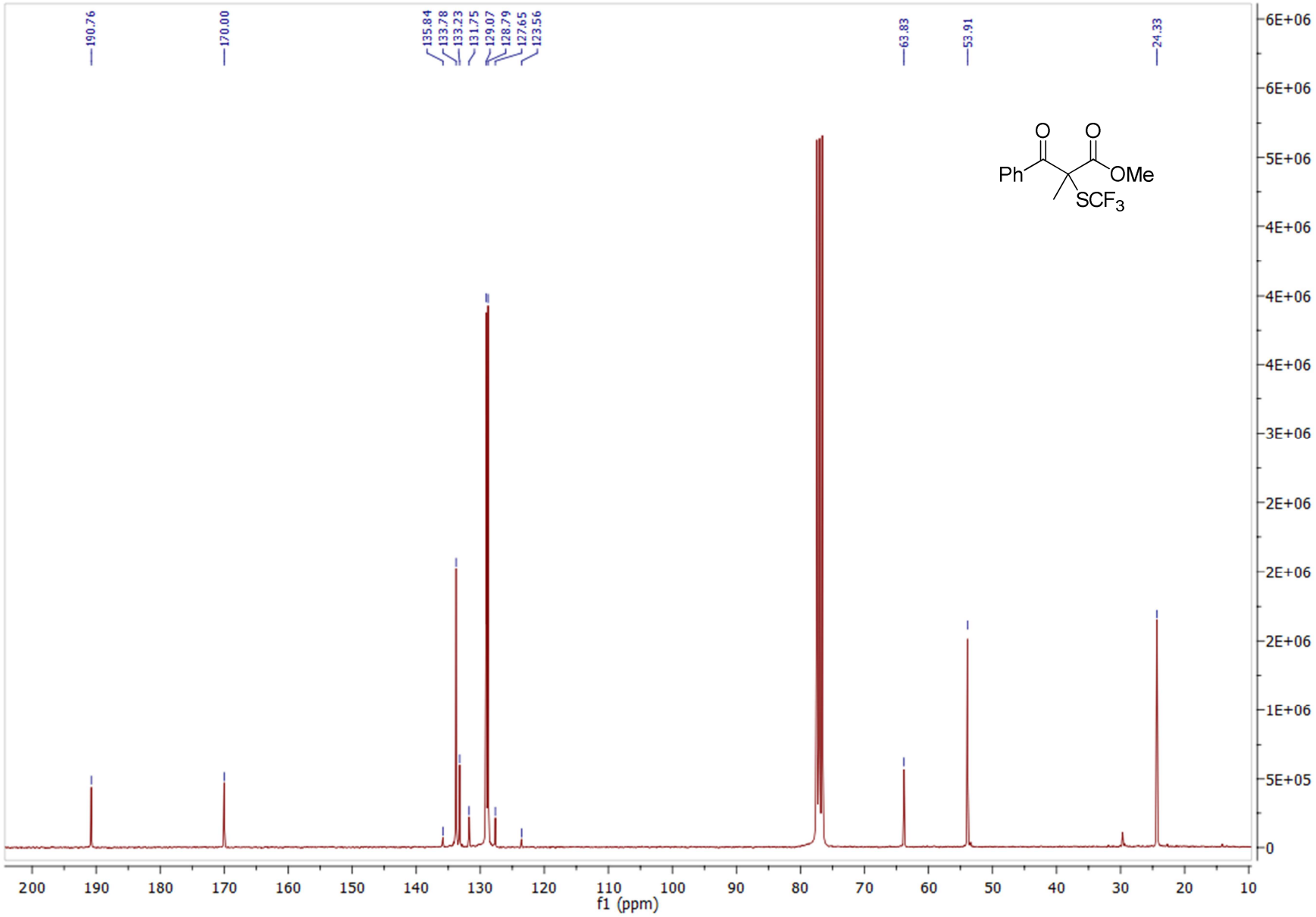
Ethyl 2-methyl-3-oxo-2-((trifluoromethyl)thio)butanoate -^{19}F NMR



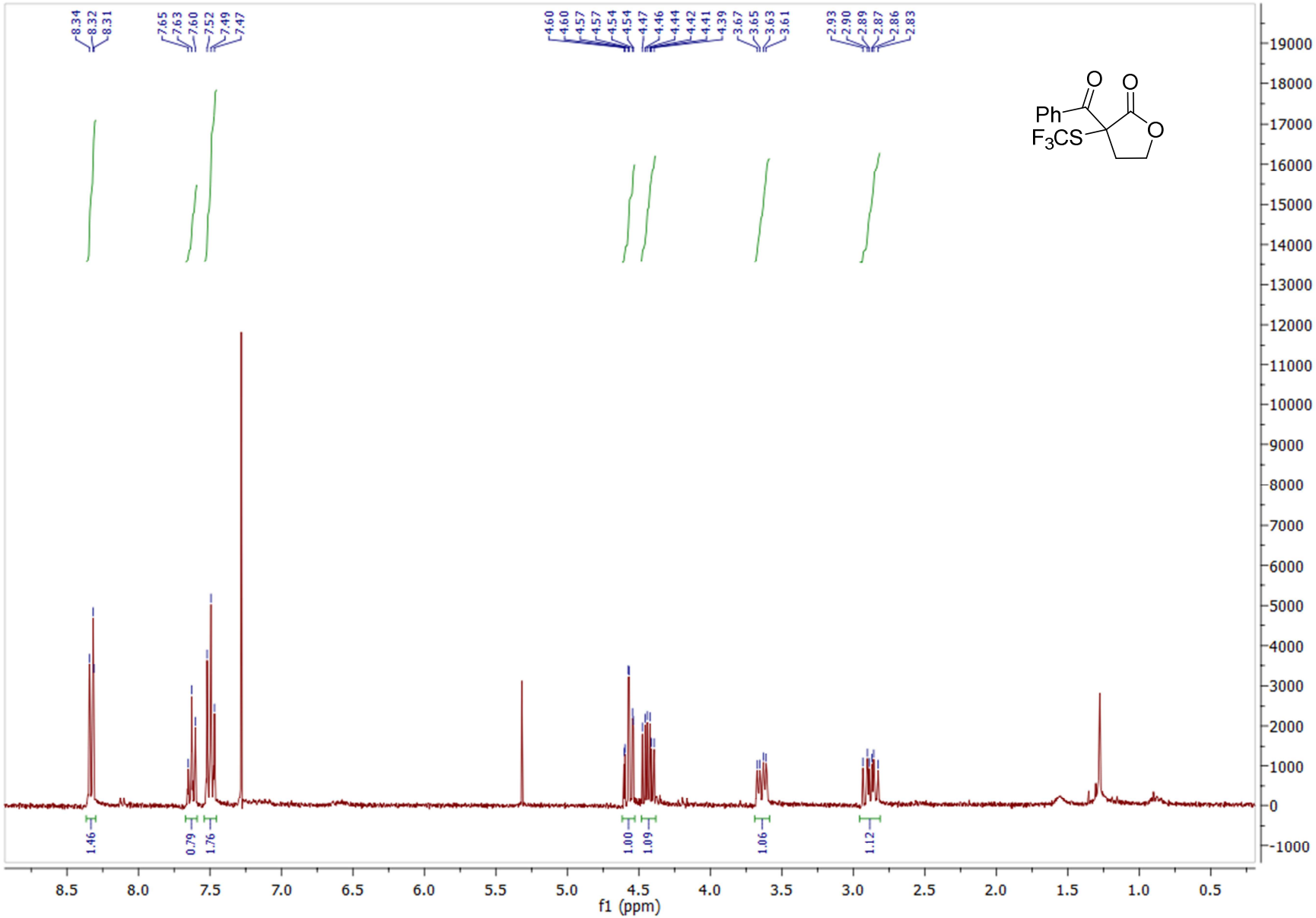
Methyl 2-methyl-3-oxo-3-phenyl-2-((trifluoromethyl)thio)propanoate-^{1}H NMR



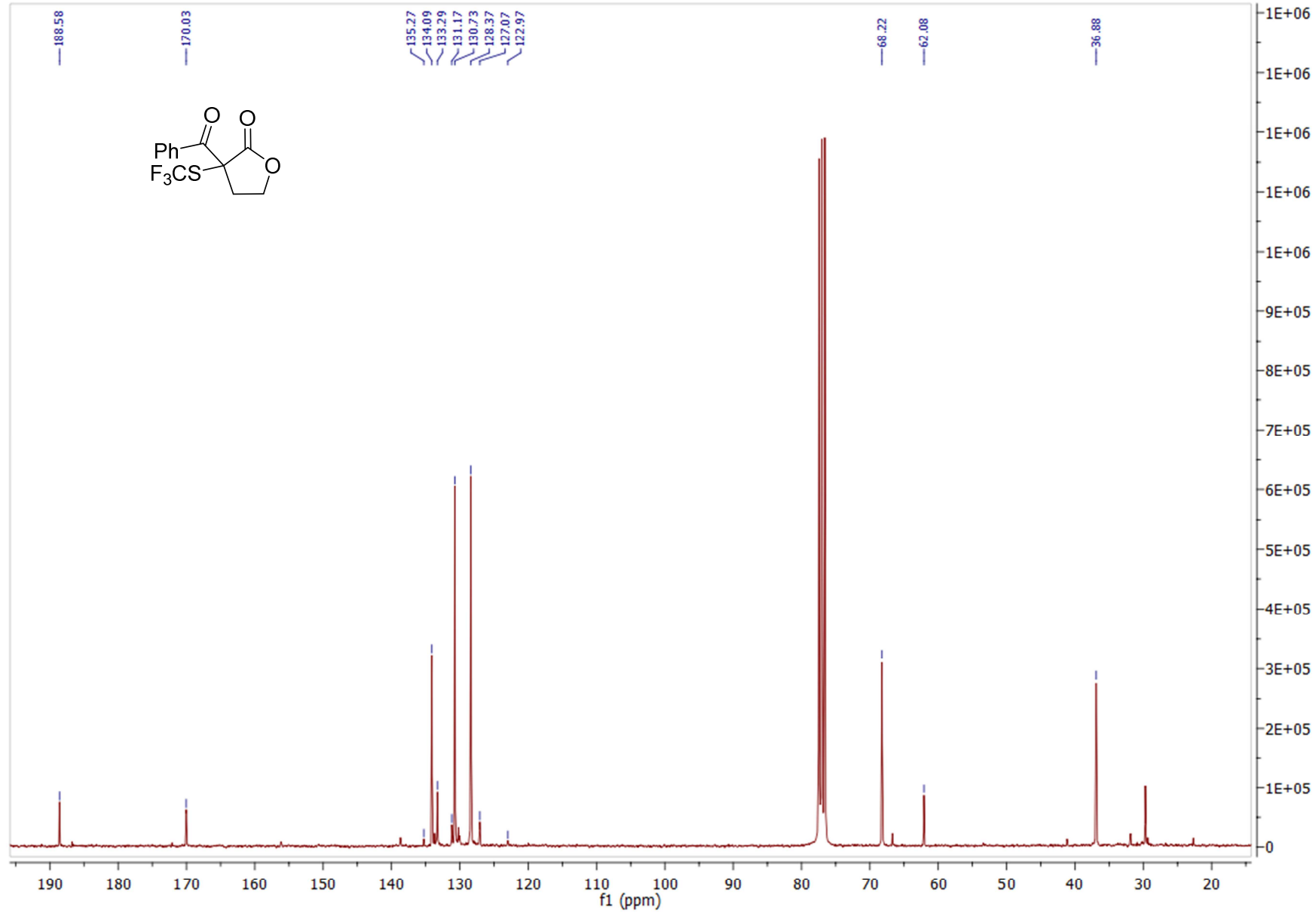
Methyl 2-methyl-3-oxo-3-phenyl-2-((trifluoromethyl)thio)propanoate-^{13}C NMR



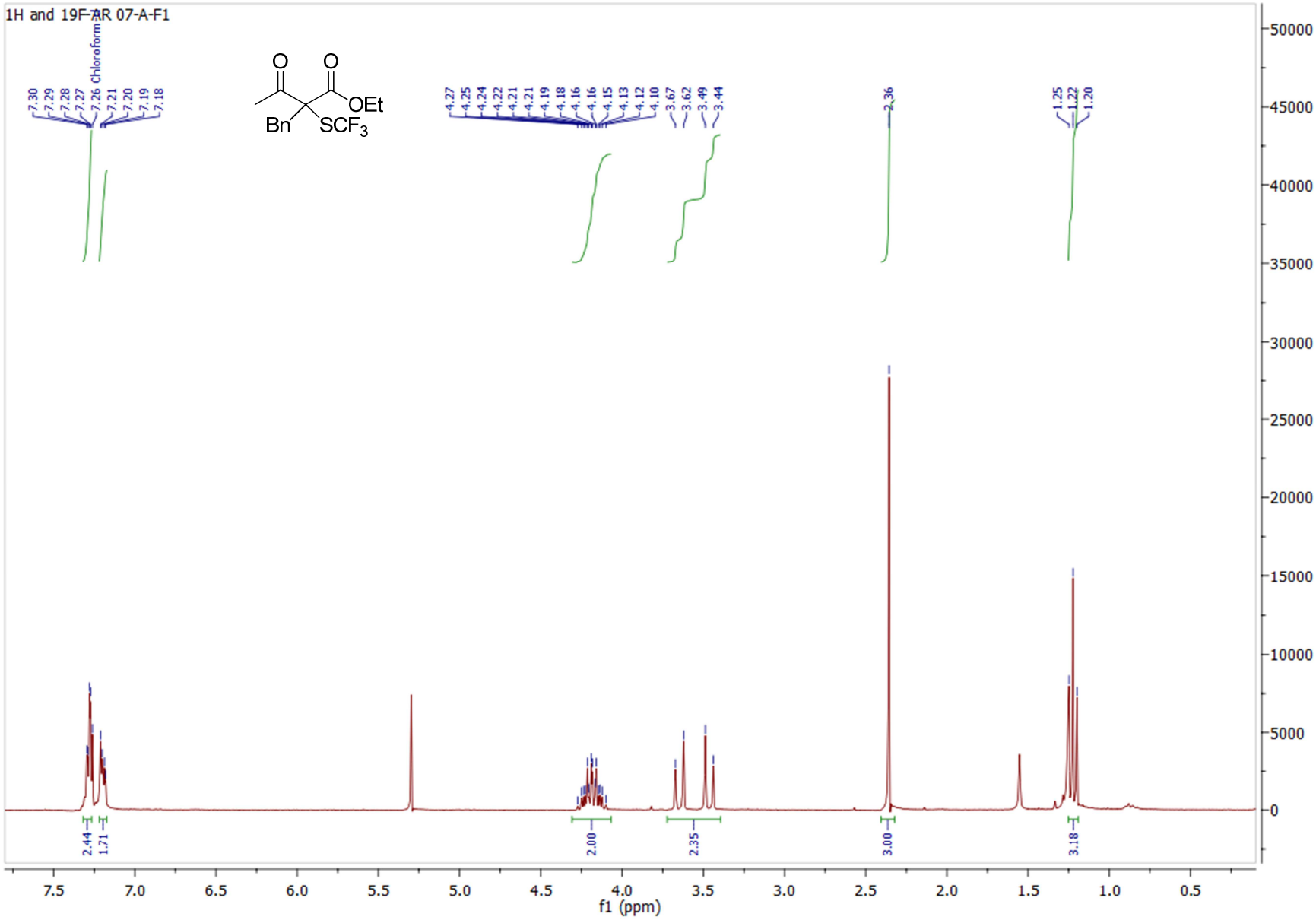
3-benzoyl-3-((trifluoromethyl)thio)dihydrofuran-2(3H)-one-^{1}H NMR



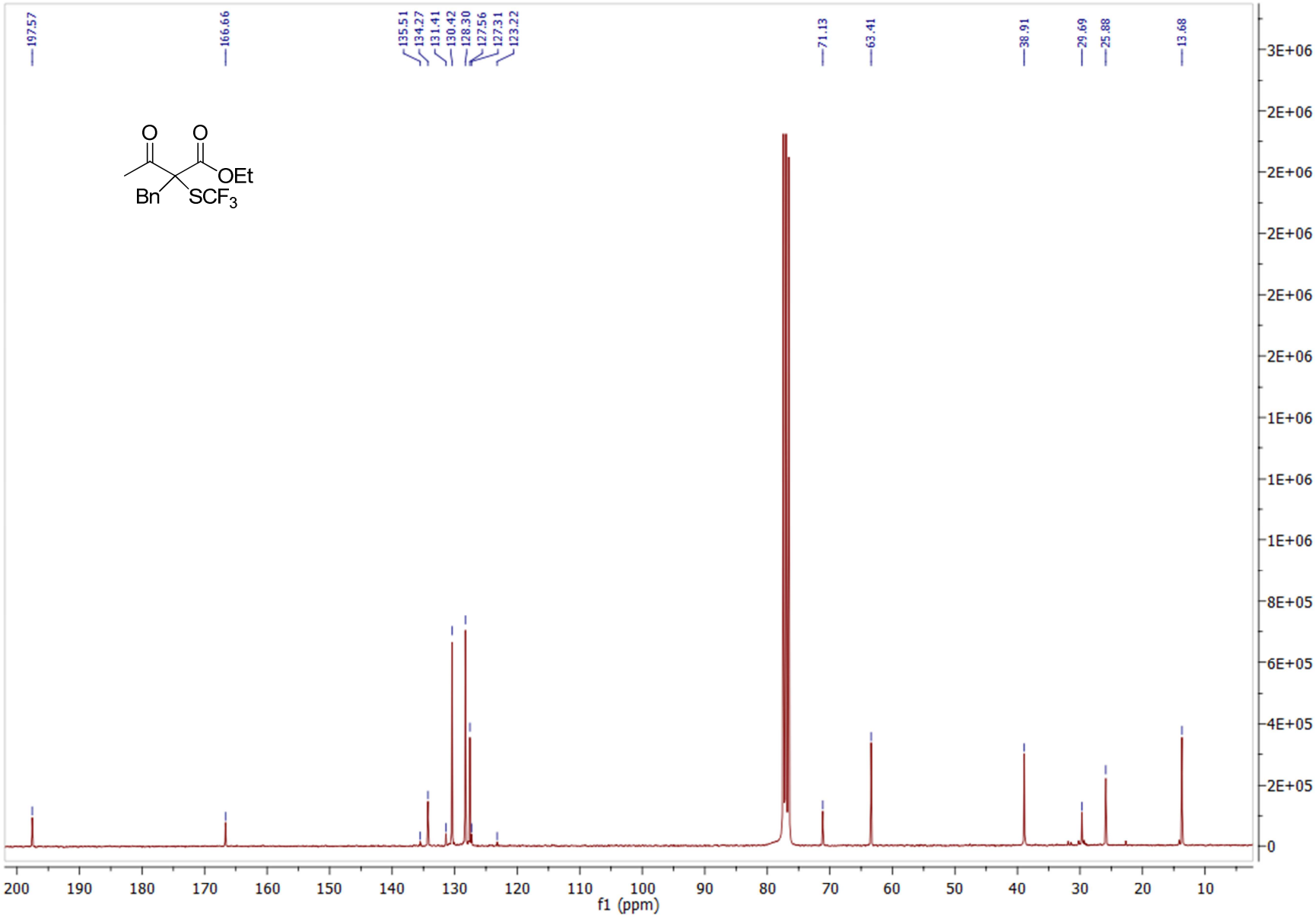
3-benzoyl-3-((trifluoromethyl)thio)dihydrofuran-2(3H)-one-^{13}C NMR



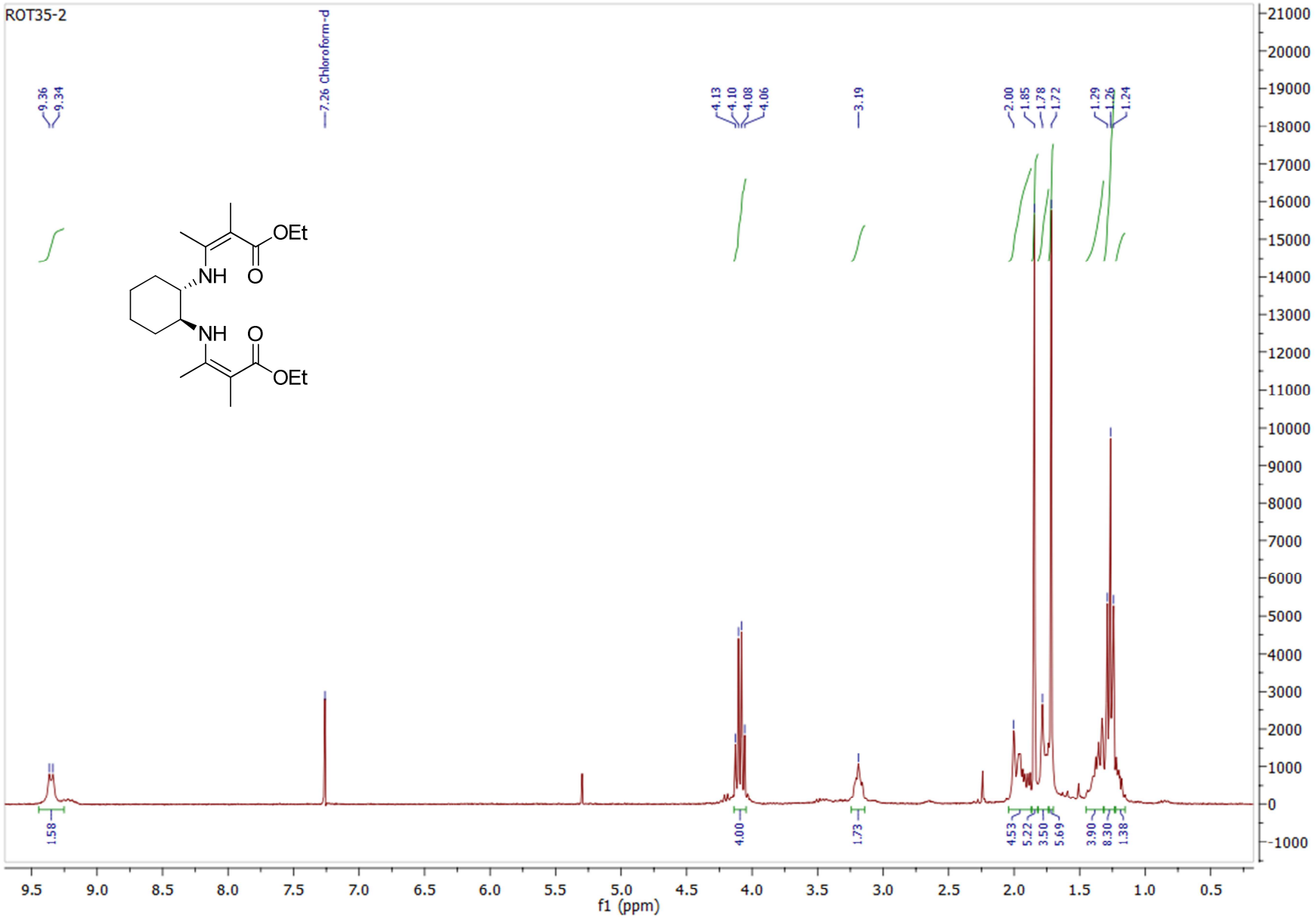
Ethyl 2-benzyl-3-oxo-2-((trifluoromethyl)thio)butanoate-^{1}H NMR



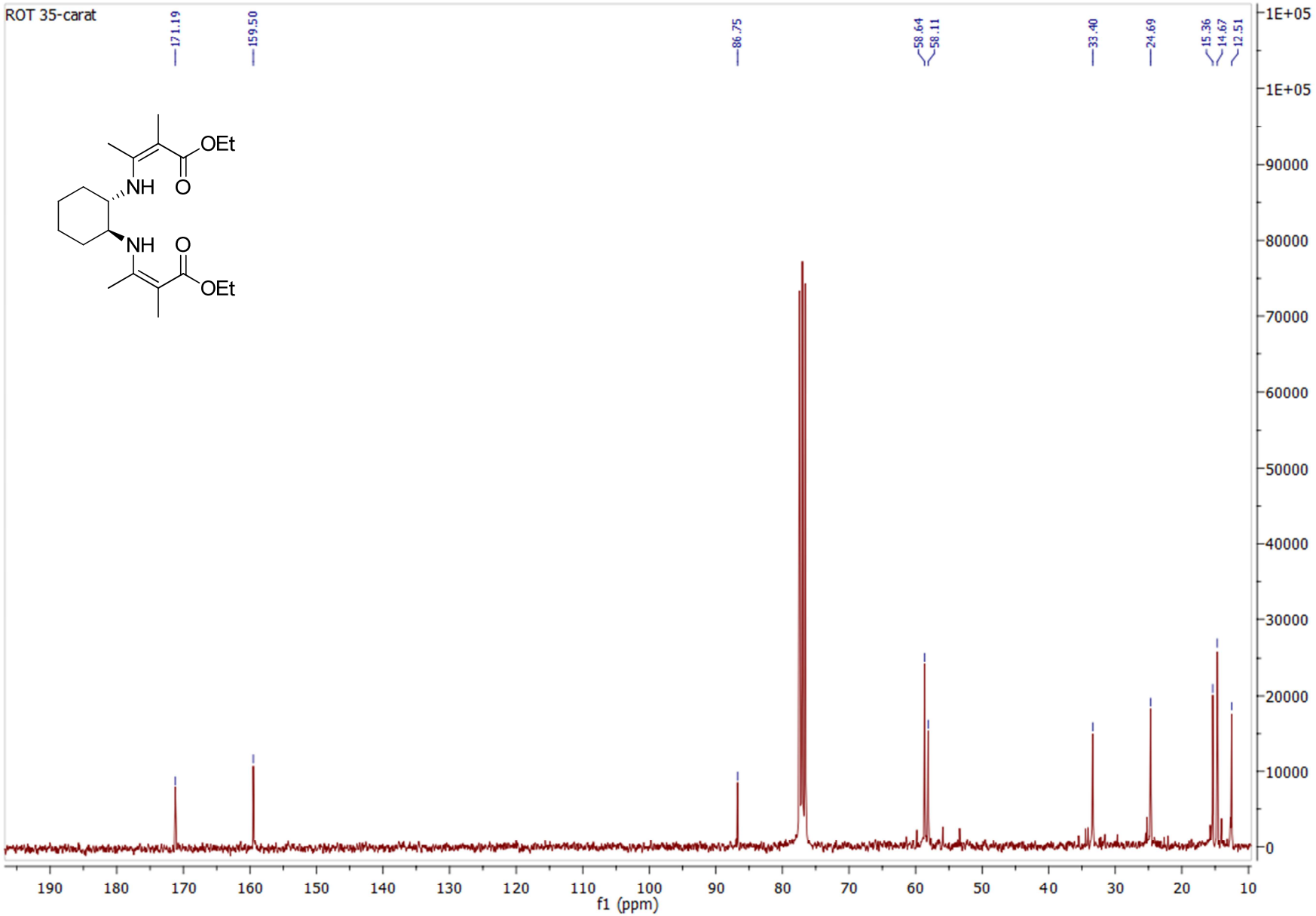
Ethyl 2-benzyl-3-oxo-2-((trifluoromethyl)thio)butanoate-^{13}C NMR



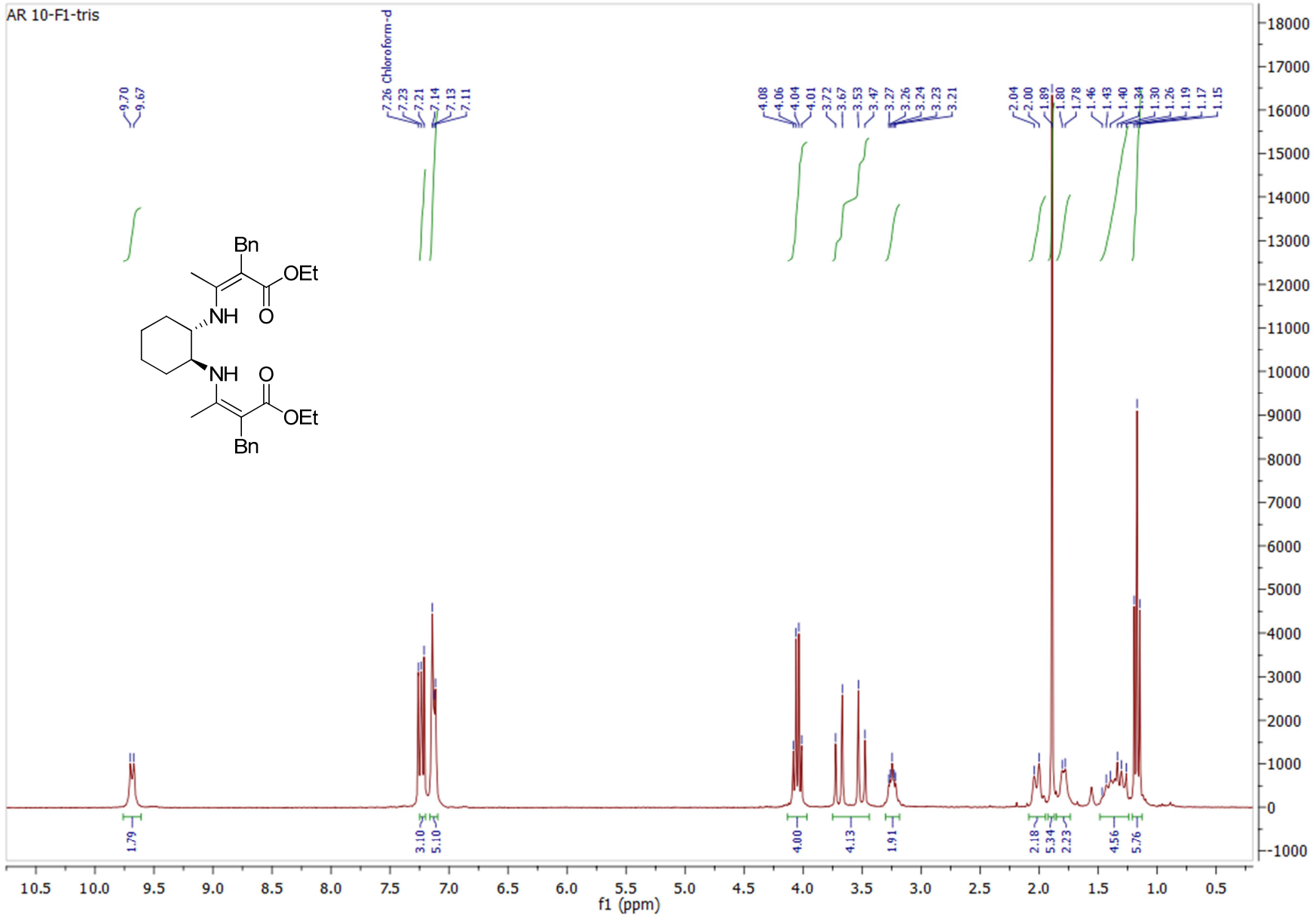
Diethyl 3,3'-((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(2-methylbut-2-enoate) -^{1}H NMR



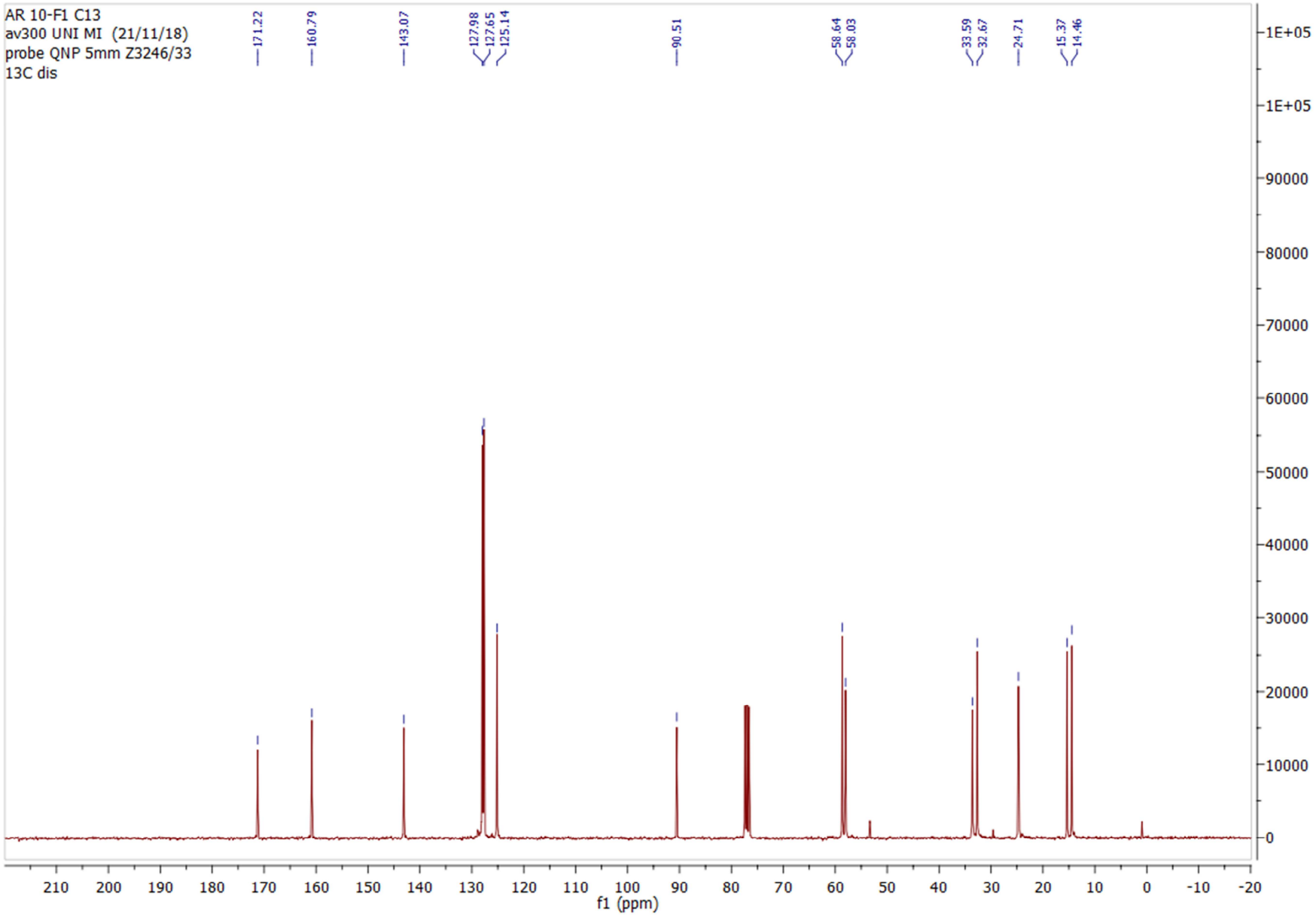
Diethyl 3,3'-((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(2-methylbut-2-enoate) -^{13}C NMR



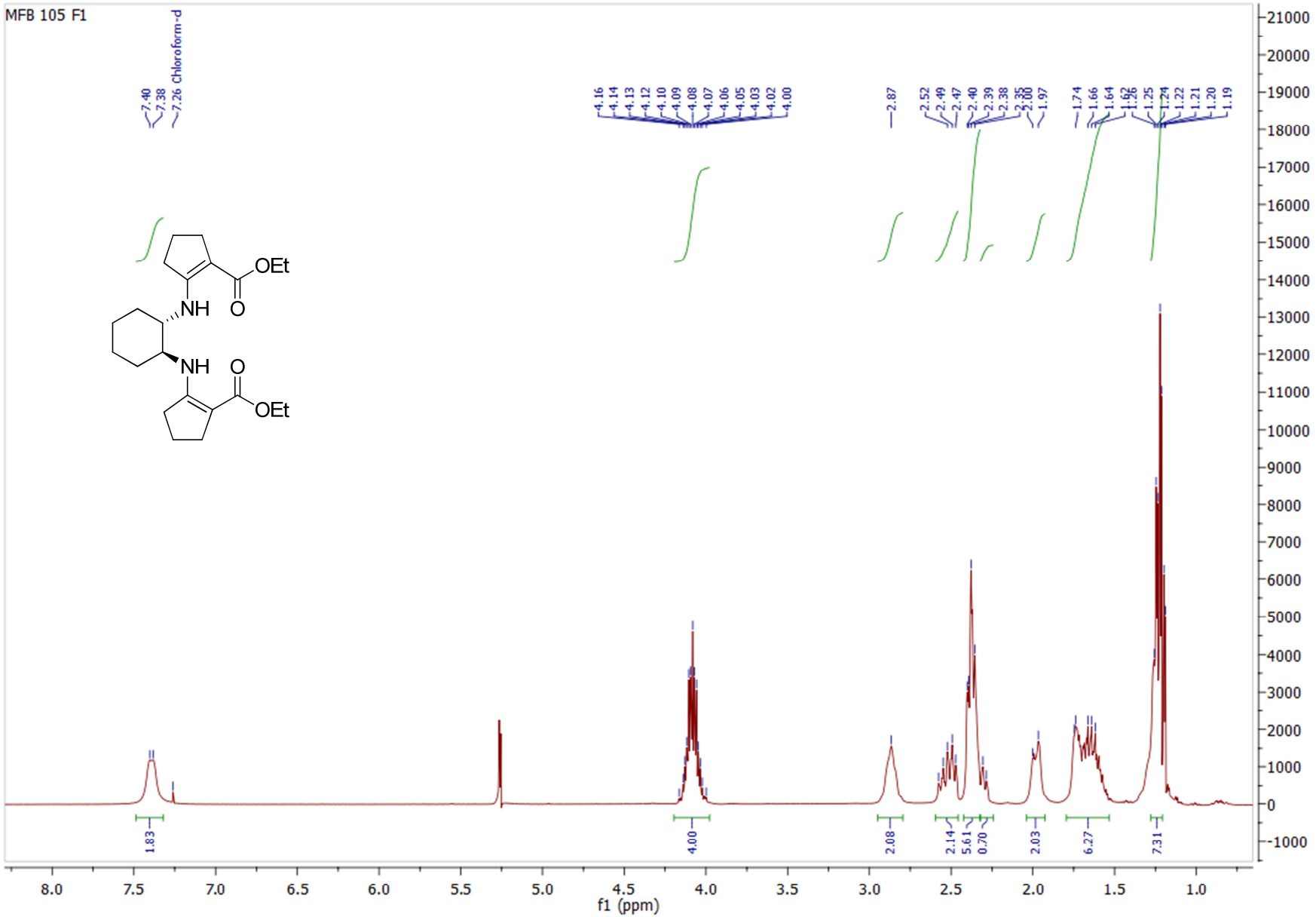
Diethyl 3,3'-((1S,2S)-cyclohexane-1,2 -diylbis(azanediyl))bis(2-benzylbut-2-enoate)- ^{1}H NMR



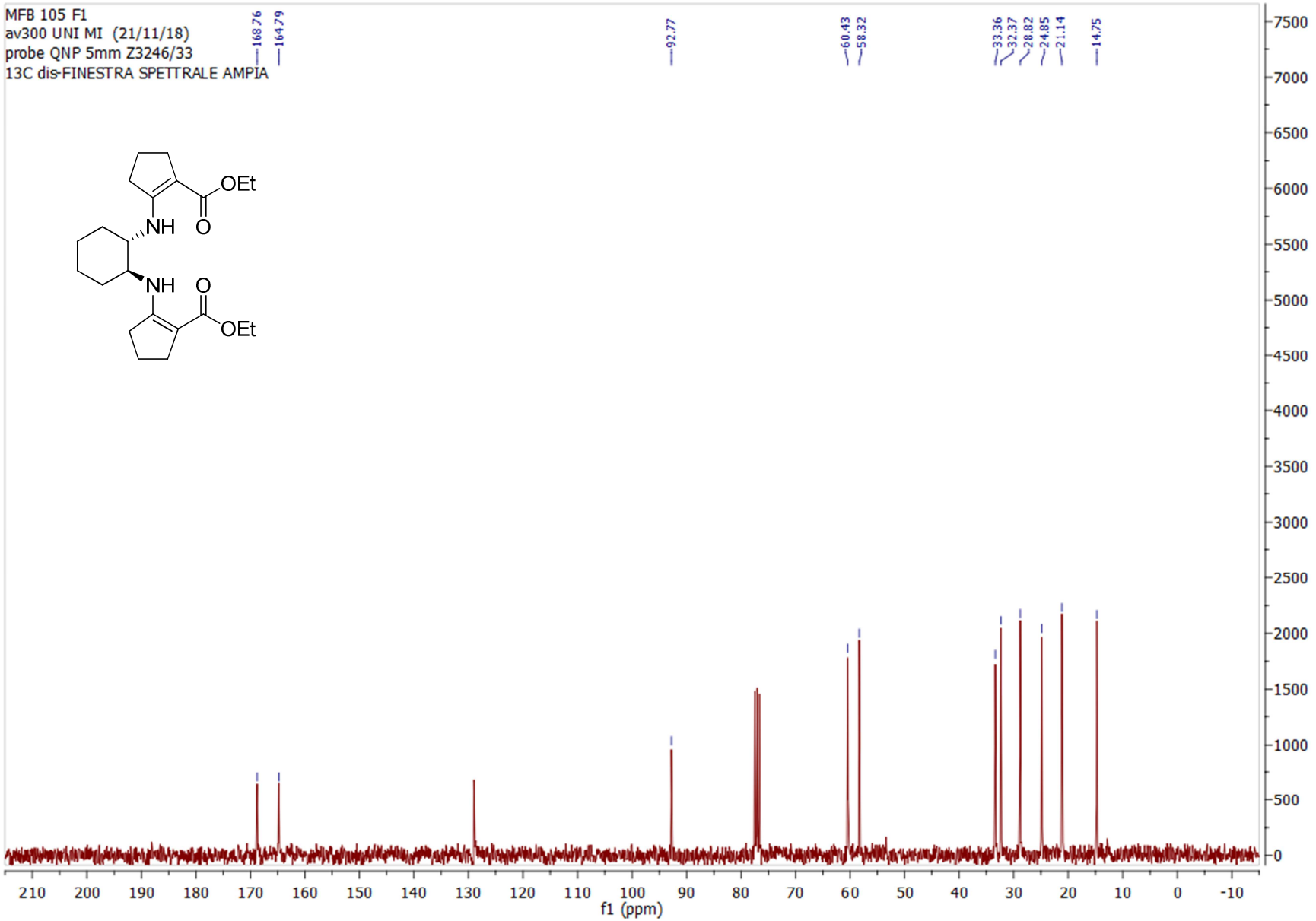
Diethyl 3,3'-((1S,2S)-cyclohexane-1,2 -diylbis(azanediyl))bis(2-benzylbut-2-enoate)- ^{13}C NMR



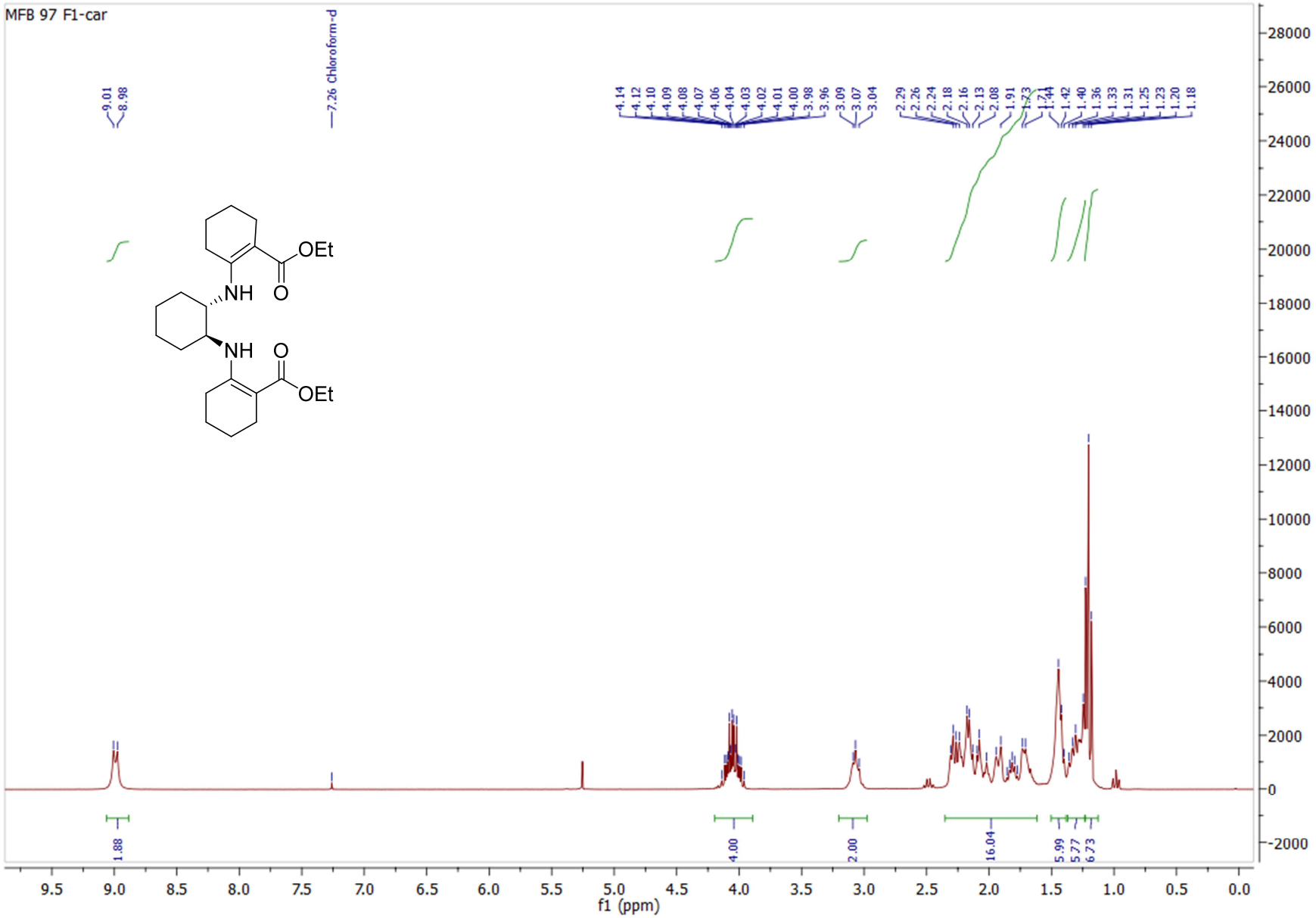
Diethyl 2,2'-((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(cyclopent-1-enecarboxylate)- ^{1}H NMR



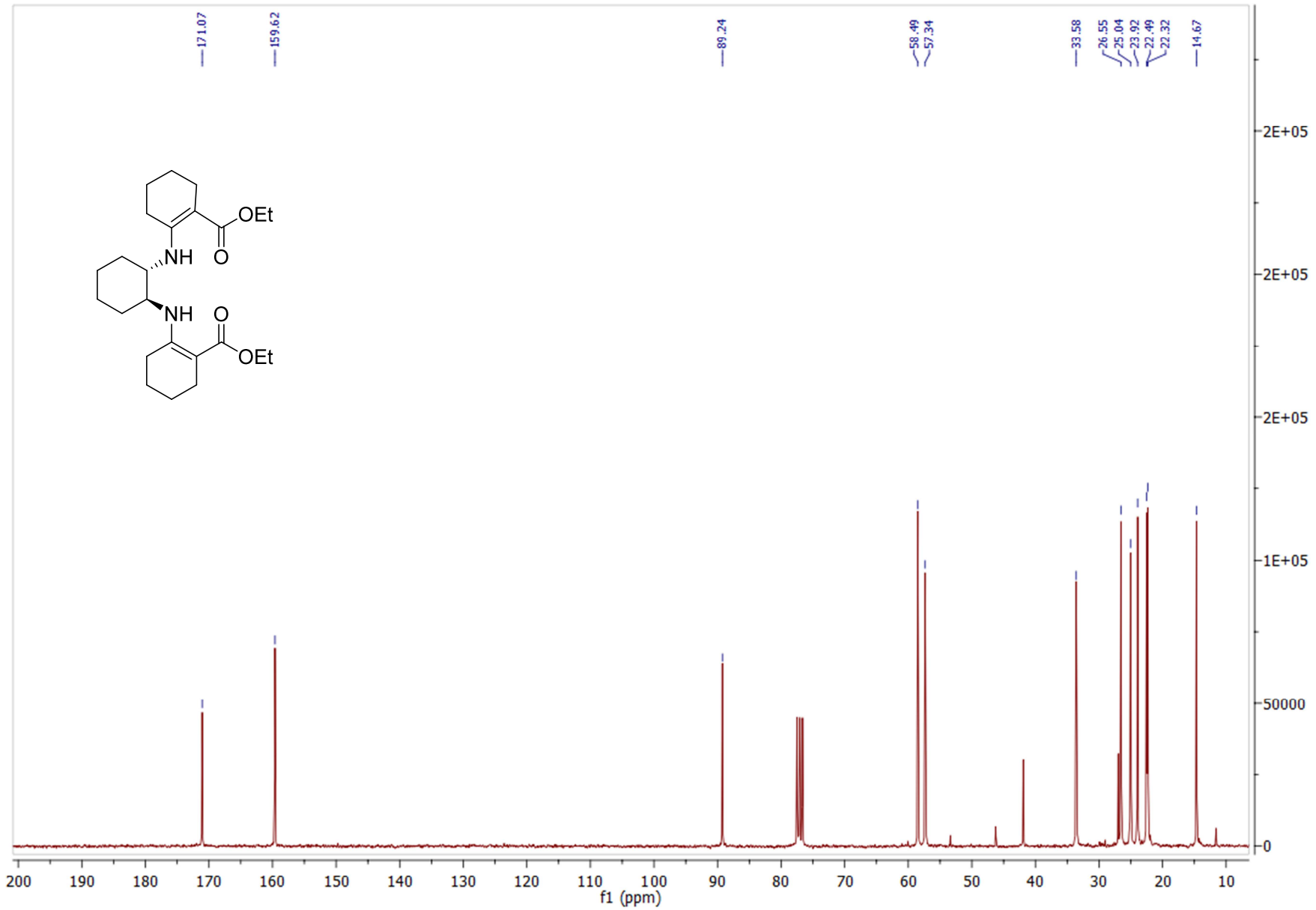
Diethyl 2,2'-((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(cyclopent-1-enecarboxylate)- ^{13}C NMR



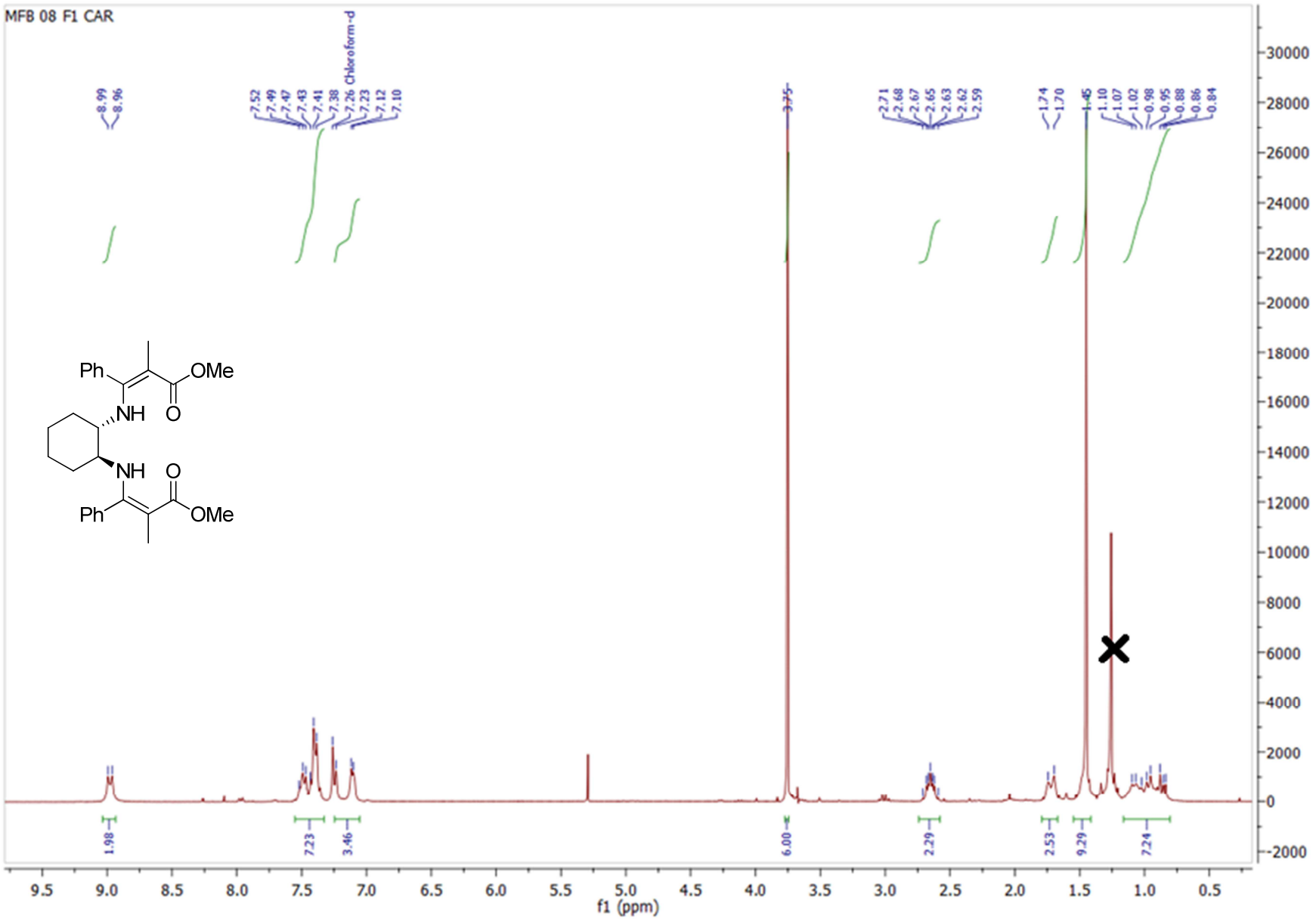
Diethyl 2,2'-(((1S,2S)-cyclohexane-1,2-diyl)bis(azanediyl))bis(cyclohex-1-ene-1-carboxylate) - ^{1}H NMR



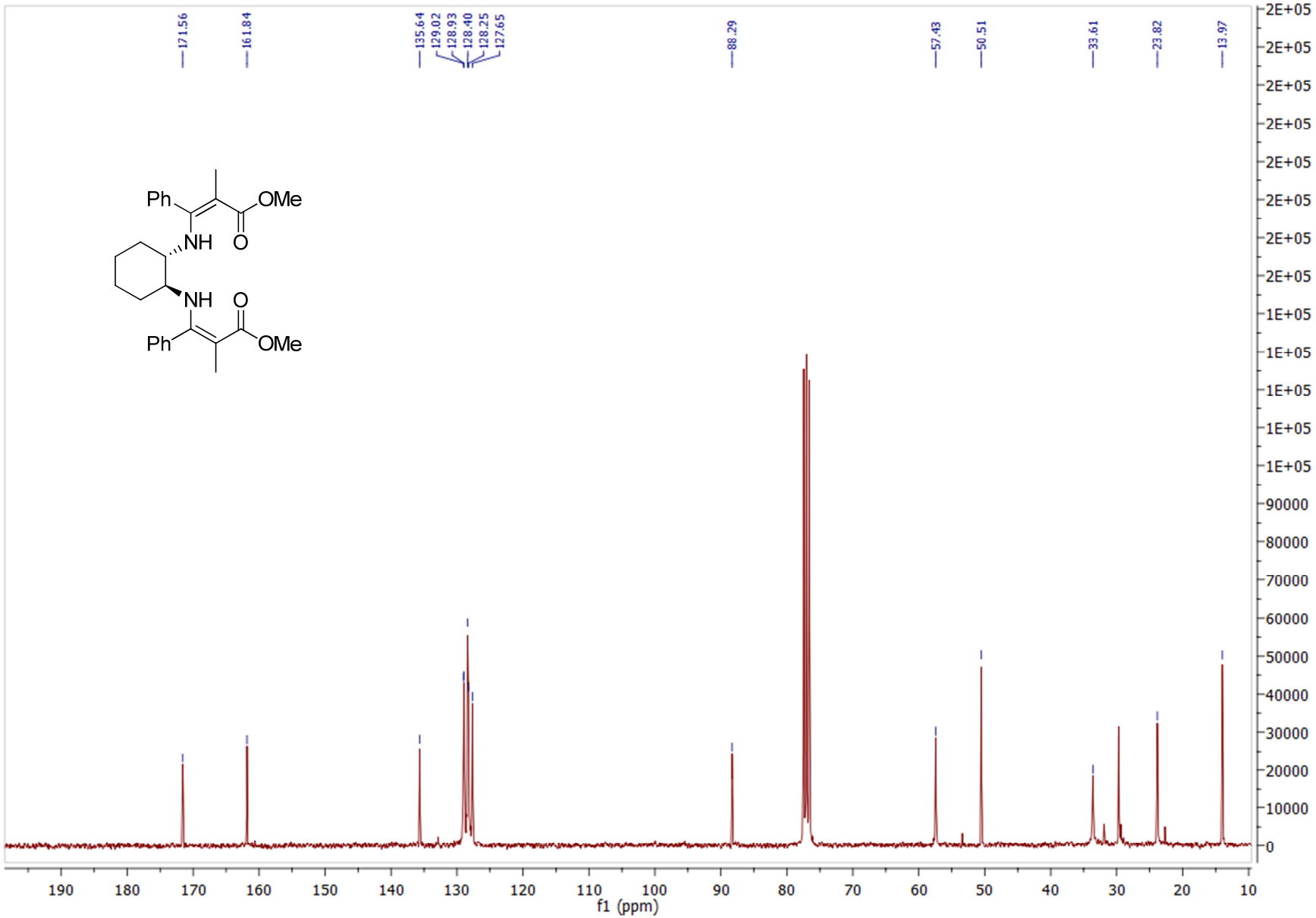
Diethyl 2,2'-(((1S,2S)-cyclohexane-1,2-diyl)bis(azanediyl))bis(cyclohex-1-ene-1-carboxylate) – ^{13}C NMR



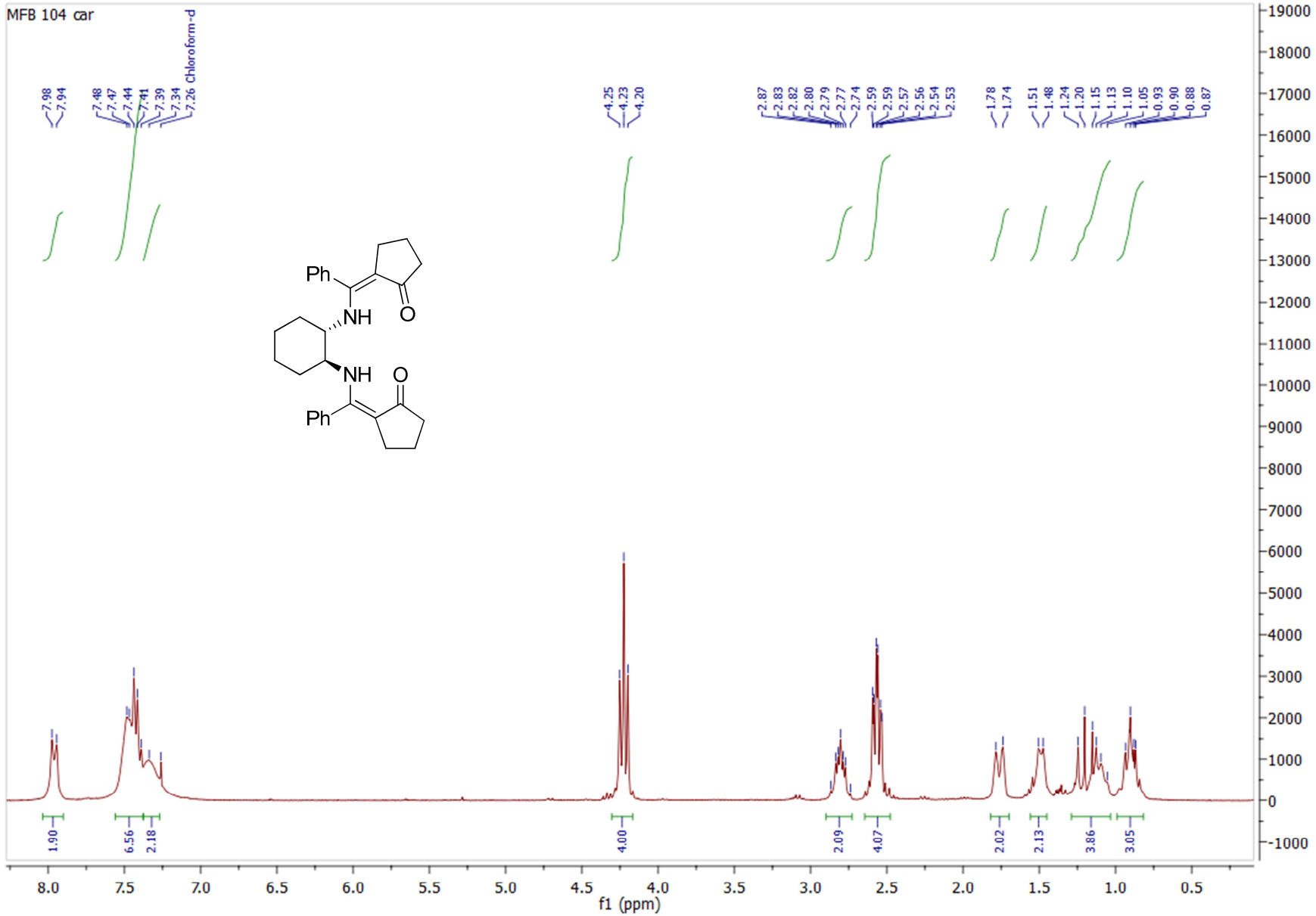
Dimethyl 3,3'-((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(2-methyl -3-phenylacrylate)- ^{1}H NMR



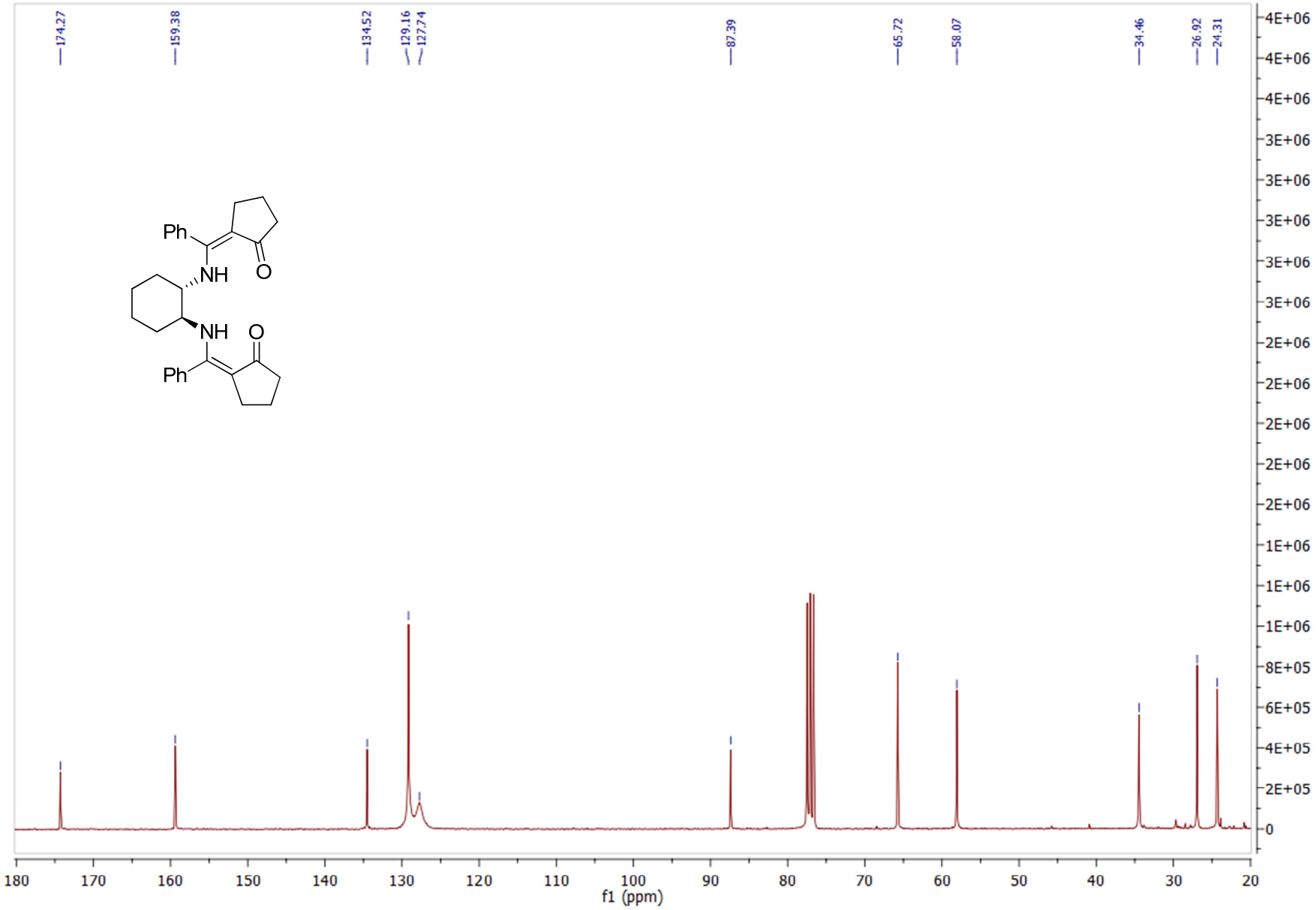
Dimethyl 3,3'-((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(2-methyl -3-phenylacrylate)- ^{13}C NMR



2,2'-(((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(phenylmethanylylidene))dicyclopentanone- ^{1}H NMR

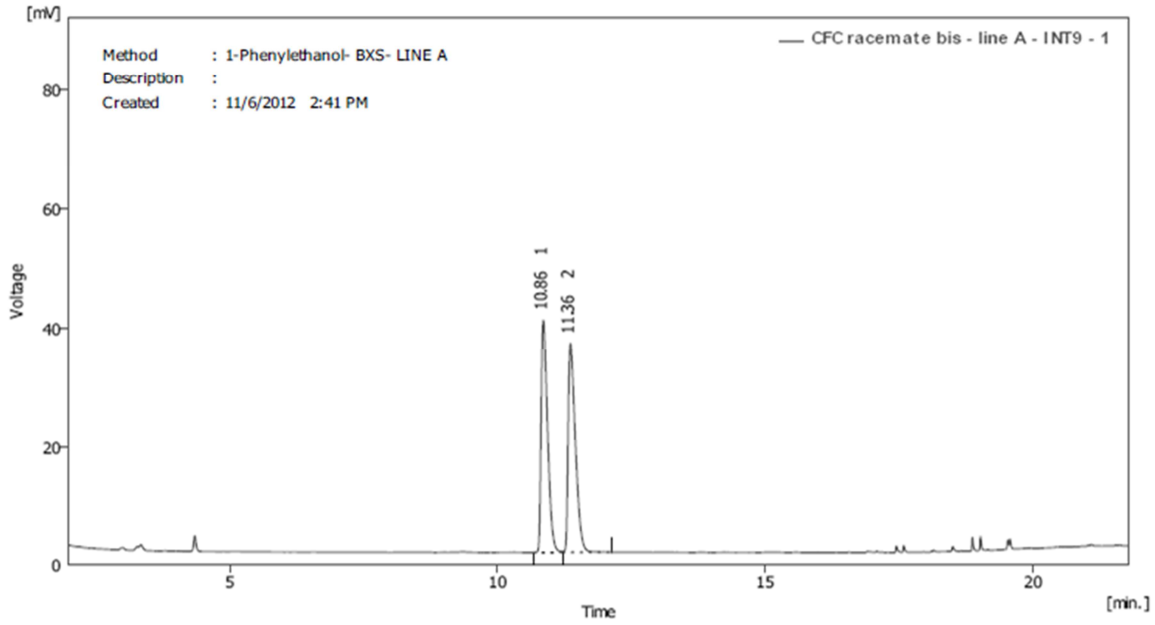


2,2'-(((1S,2S)-cyclohexane-1,2-diylbis(azanediyl))bis(phenylmethanylylidene))dicyclopentanon e- ^{13}C NMR



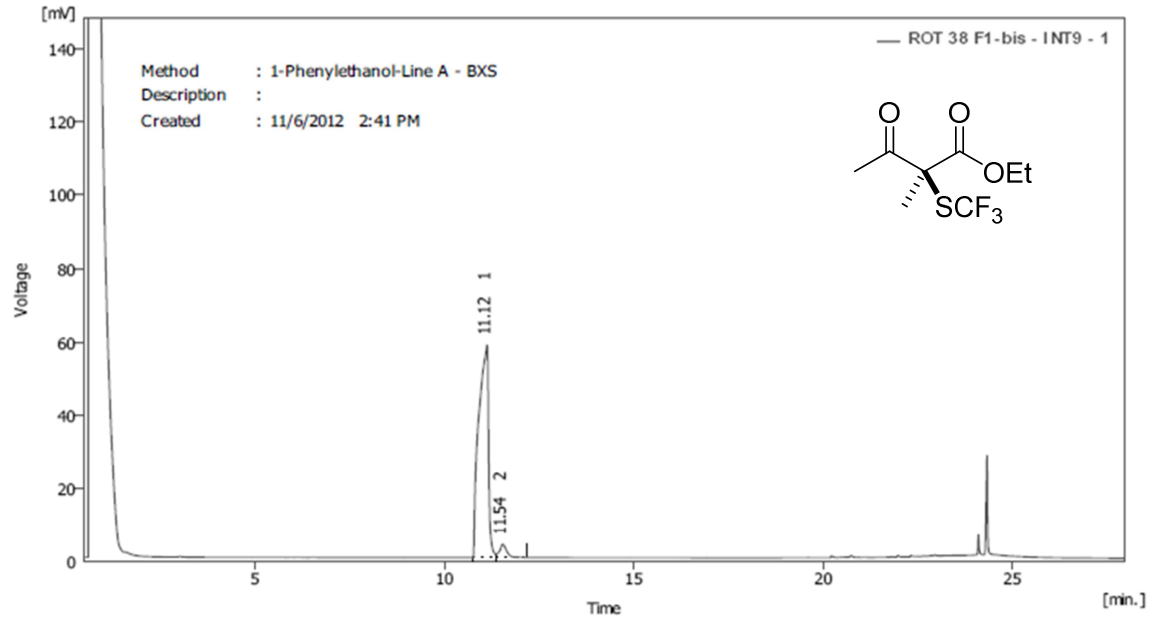
GC traces

Ethyl 2-methyl-3-oxo-2-((trifluoromethyl)thio)butanoate



Result Table (Uncal - CFC racemate bis - line A - INT9 - 1)

	Reten. Time [min]	Area [mV.s]	Area [%]	W05 [min]	Compound Name
1	10.856	330.583	49.78	0.14	
2	11.364	333.480	50.22	0.15	
	Total	664.062	100.00		



Result Table (Uncal - ROT 38 F1-bis - INT9 - 1)

	Reten. Time [min]	Area [mV.s]	Area [%]	W05 [min]	Compound Name
1	11.124	1037.726	95.63	0.32	
2	11.540	47.406	4.37	0.19	
	Total	1085.132	100.00		