Electronic Supplementary Information

Cu-Catalysed Three-Component C–H Trifluoroalkylation of Glycine Derivatives: Access to Diverse CF_3-Containing Amino Acids

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I. General Information

General procedures. All reactions were performed in oven-dried or flame-dried round-bottom flasks and vials. Solvents were dried and freshly distilled before use. Reactions were monitored with thin layer chromatography (TLC) using silica gel 60 F-254 plates. TLC plates were normally visualized by UV irradiation (254 nm or 365 nm), stained with basic $KMnO_4$ or phosphomolybdic acid. Flash chromatography was performed using silica gel 60 (200−300 mesh).

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra, carbon nuclear magnetic resonance ($^{13}C\{^1H\}$ NMR) spectra and fluorine nuclear magnetic resonance (^{19}F NMR) spectra were recorded on Bruker Ascend 400 MHz and 600 MHz. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to the NMR solvent residual peak ($CHCl_3$: δ 7.26). Chemical shifts for carbons are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$: δ 77.0). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants in Hertz (Hz), and integration. When ^{19}F NMR is used for quantitative purpose (yield and *dr* determination), a 30-degree pulse and extended delay time (d1 = 5 s) were employed and the receiver gain was manually set as 32. IR spectra were recorded on a Bruker FT-IR spectrometer. HRMS was measured on a TOF-Q mass spectrometer equipped with an ESI source.

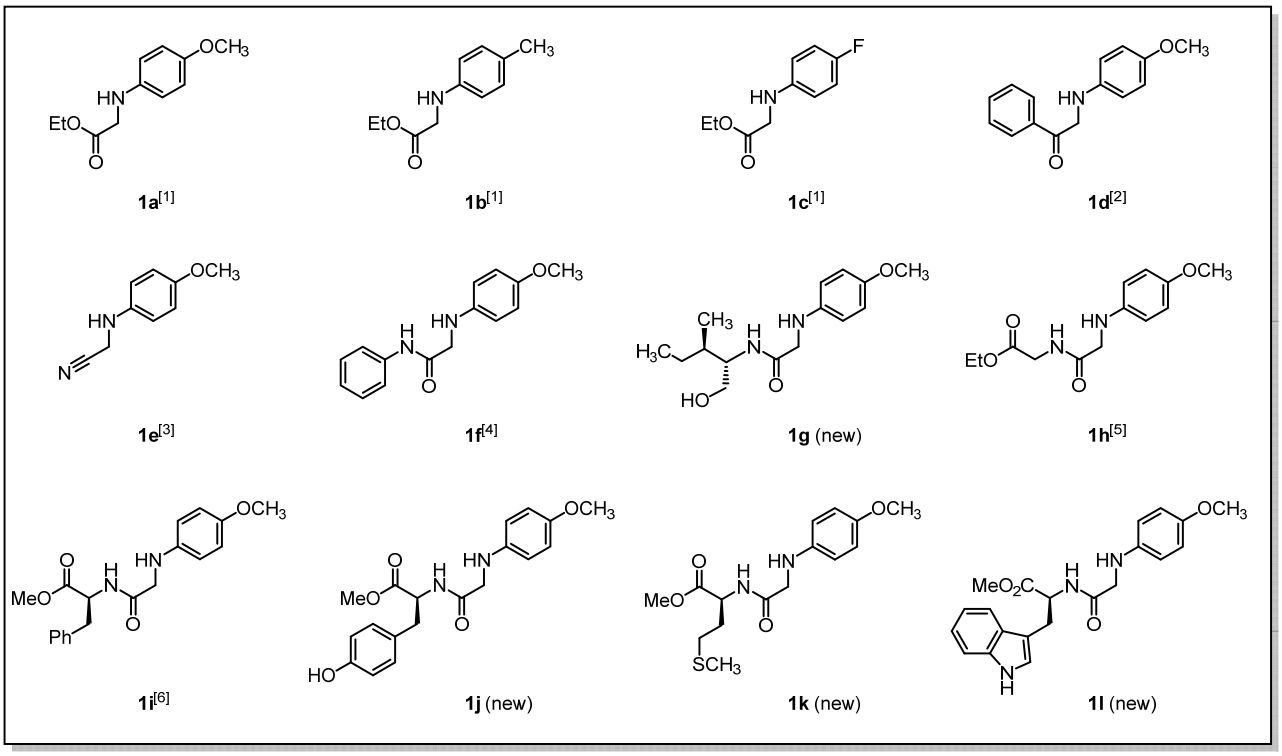
Abbreviations:

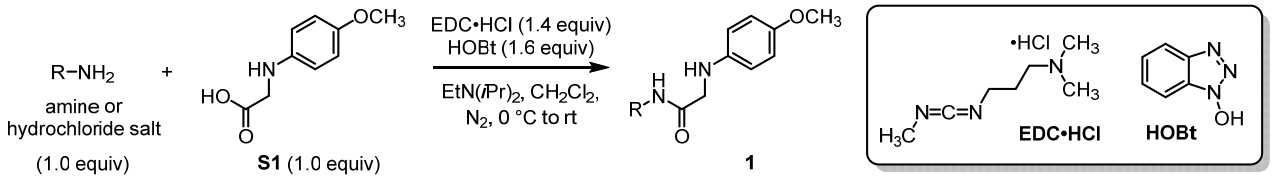
TLC–thin layer chromatography; PE–Petroleum Ethers (60–90 ˚C); THF–tetrahydrofuran; DMSO–dimethyl sulfoxide; DMF–*N*,*N*-dimethylformamide; DMA–*N*,*N*-dimethylacetamide; DCE–1,2-dichloroethane; EDC–1-ethyl-3-(3-dimethylaminopropyl)carbodiimide; HOBt–Hydroxybenzotriazole; TEMPO–(2,2,6,6-tetramethylpiperidin-1-yl)oxyl; DMPO–5,5-Dimethyl-1-pyrroline N-oxide; CAN–ceric ammonium nitrate.

II. The Preparation and Characterization of New Substrates

a) Glycine derivatives

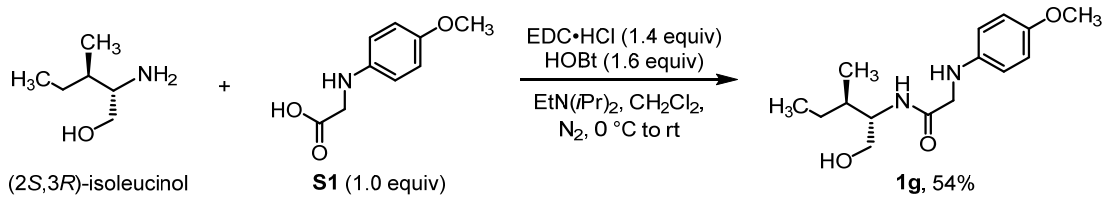
The glycine derivatives **1a**-**1l** used in this work are listed below. Among them, **1a**-**1f**, **1h**, and **1i** were prepared according to literature procedures,[1-6] while **1g**, **1j**, **1k**, and **1l** are new compounds and characterized for the first time.



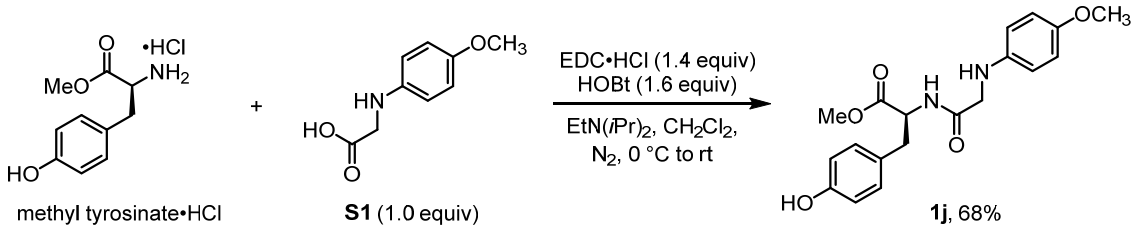


General procedure for the condensation of dipeptides: To a 100 mL round-bottom flask, *N*-PMP glycine **S1** (10 mmol, 1.81 g), EDC•HCl (14 mmol, 2.68 g) and HOBt (16 mmol, 2.16 g) were dissolved in CH_2Cl_2 (30 mL) under N_2 atmosphere, and the mixture was stirred at room temperature for 30 mins. Next, the reaction was cooled in an ice-water bath. At 0 °C, an amine or amino ester hydrochloride (10 mmol) was added into the flask, followed by the addition of EtN(*i*Pr)$_2$ (1.74 mL, 10 mmol for free amine; 20 mmol for amino ester hydrochloride) under N_2. After 30 mins, the reaction mixture was warmed up to room temperature and stirred overnight. After the reaction was

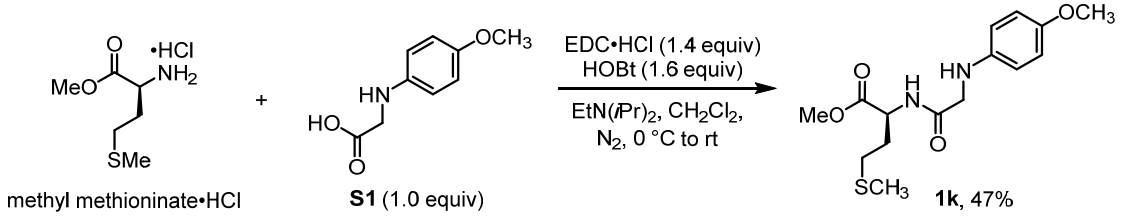
quenched with water (30 mL), the resulting mixture was separated and extracted with CH_2Cl_2 (30 mL × 3). The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo*, and purified through a silica gel flash column.



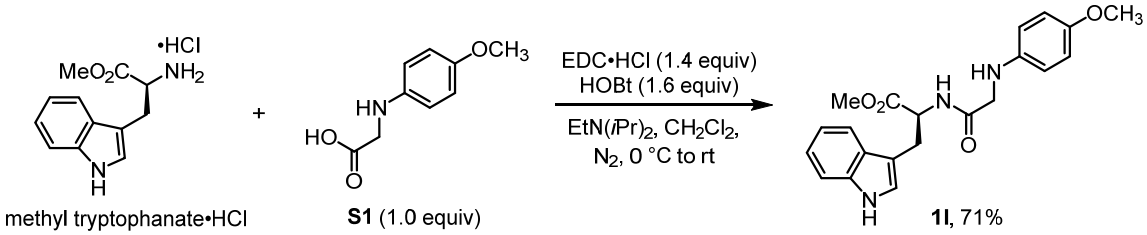
N-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-2-((4-methoxyphenyl)amino)acetamide (**1g**): Following the general procedure, compound **1g** was prepared from isoleucinol as a white foam (54% yield) after a flash column purification (CH_2Cl_2/MeOH = 20:1). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.07 (d, *J* = 8.4 Hz, 1H), 6.81 – 6.68 (m, 2H), 6.62 – 6.49 (m, 2H), 4.28 – 3.91 (m, 2H), 3.83 – 3.61 (m, 4H), 3,71 (s, 3H), 3.55 (dd, *J* = 11.4, 6.7 Hz, 1H), 1.64 – 1.47 (m, 1H), 1.41 – 1.28 (m, 1H), 1.04 – 0.91 (m, 1H), 0.82 (d, *J* = 6.7 Hz, 3H), 0.79 (t, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.0, 153.1, 141.0, 114.9, 114.6, 63.3, 55.9, 55.7, 49.7, 35.5, 25.3, 15.6, 11.2; IR ν_{max} (neat) cm^{-1}: 3290, 2984, 1644, 1562, 1174, 1065, 825, 578; HRMS (ESI, m/z): calcd for $C_{15}H_{25}N_2O_3^+$ $[M + H]^+$ 281.1860, found 281.1862.



Methyl (4-methoxyphenyl)glycyl-L-tyrosinate (**1j**): Following the general procedure, compound **1j** was prepared from methyl tyrosinate hydrochloride as a brownish oil (68% yield) after a flash column purification (PE/EtOAc = 2:1). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 8.8 Hz, 1H), 7.16 (brs, 1H), 6.84 – 6.68 (m, 4H), 6.66 – 6.54 (m, 2H), 6.51 – 6.37 (m, 2H), 4.99 – 4.84 (m, 1H), 4.36 – 3.85 (br, 1H), 3.74 (s, 3H), 3.72 – 3.67 (m, 4H), 3.63 (d, *J* = 17.6 Hz, 1H), 3.02 (dd, *J* = 14.1, 5.2 Hz, 1H), 2.92 (dd, *J* = 14.1, 7.1 Hz, 1H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.0, 171.4, 155.5, 153.1, 140.9, 130.2, 126.7, 115.6, 115.0, 114.5, 55.8, 52.8, 52.5, 49.3, 37.1; IR ν_{max} (neat) cm^{-1}: 3348, 2981, 1751, 1688, 1514, 1400, 1221, 1014, 904, 821, 731; HRMS (ESI, m/z): calcd for $C_{19}H_{23}N_2O_5^+$ $[M + H]^+$ 359.1601, found 359.1600.



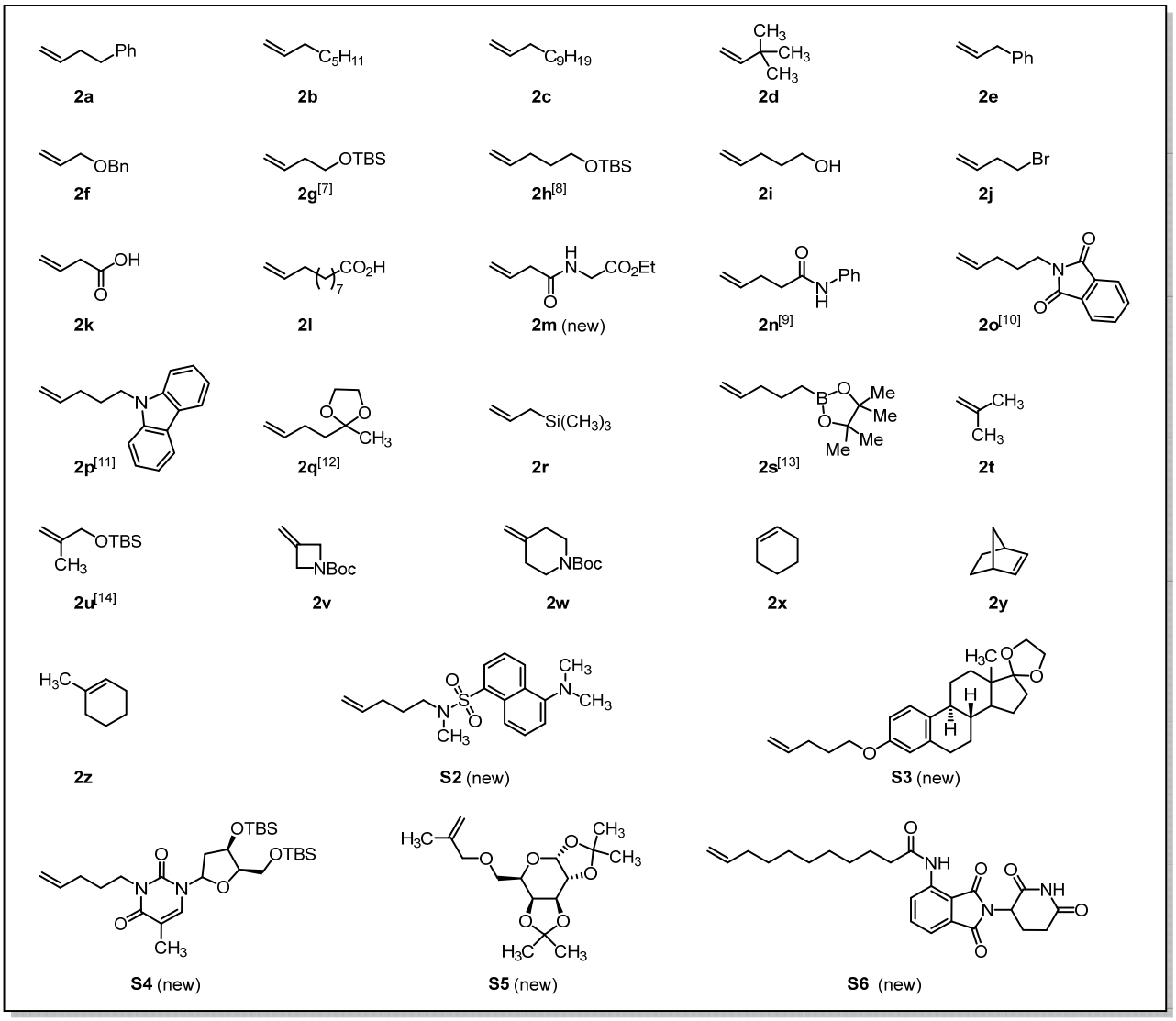
Methyl (4-methoxyphenyl)glycyl-L-methioninate (**1k**): Following the general procedure, compound **1k** was prepared from methyl methioninate hydrochloride as a colorless oil (47% yield) after a flash column purification (PE/EtOAc = 1:1). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 8.5 Hz, 1H), 6.83 – 6.70 (m, 2H), 6.63 – 6.50 (m, 2H), 4.74 (td, *J* = 8.0, 4.8 Hz, 1H), 4.42 – 3.91 (br, 1H), 3.76 (d, *J* = 5.9 Hz, 2H), 3.73 (s, 3H), 3.70 (s, 3H), 2.38 (t, *J* = 7.5 Hz, 2H), 2.21 – 2.05 (m, 1H), 1.99 (s, 3H), 1.97 – 1.86 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.1, 171.0, 153.2, 141.1, 114.9, 114.5, 55.7, 52.5, 51.1, 49.6, 31.4, 29.9, 15.4; IR ν_{max} (neat) cm^{-1}: 3371, 2961, 1741, 1652, 1544, 1137, 1104, 904, 832, 744; HRMS (ESI, m/z): calcd for $C_{15}H_{23}N_2O_4S^+$ $[M + H]^+$ 327.1373, found 327.1376.

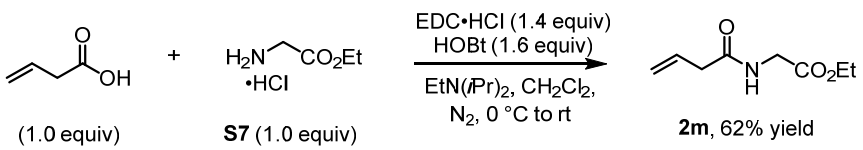


Methyl (4-methoxyphenyl)glycyl-L-tryptophanate (**1l**)**:** Following the general procedure, compound **1l** was prepared from methyl tryptophanate hydrochloride as a beige foam (71% yield) after a flash column purification (PE/EtOAc = 2:1).^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 (s, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.76 – 6.66 (m, 2H), 6.62 (s, 1H), 6.44 – 6.30 (m, 2H), 4.95 (dt, *J* = 8.4, 5.6 Hz, 1H), 3.91 – 3.77 (m, 1H), 3.73 (s, 3H), 3.66 (s, 3H), 3.54 (s, 2H), 3.31 (dd, *J* = 14.9, 5.8 Hz, 1H), 3.23 (dd, *J* = 14.9, 5.3 Hz, 1H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-d) δ 172.3, 171.2, 152.9, 141.2, 136.2, 127.4, 123.2, 122.1, 119.6, 118.4, 114.8, 114.3, 111.4, 109.3, 55.8, 52.4, 52.4, 49.3, 27.5; IR ν_{max} (neat) cm^{-1}: 3351, 2977, 1721, 1666, 1510, 1321, 1252, 1011, 909, 871, 711; HRMS (ESI, m/z): calcd for $C_{21}H_{24}N_3O_4^+$ $[M + H]^+$ 382.1761, found 382.1762.

b) Alkenes

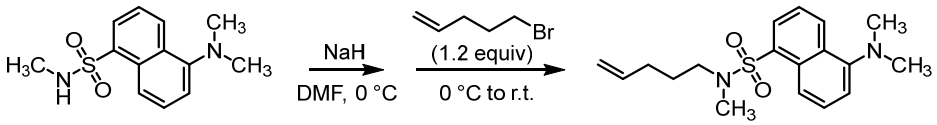
The alkenes used in this work are listed below. Among them, **2g**-**2h**, **2n**-**2q**, **2s**, and **2u** were prepared according to literature procedures,[7-14] while **2m** and **S2-S6** are new compounds and characterized for the first time. The rest of the alkenes listed below are all commercially available and distilled before use.





Ethyl but-3-enoylglycinate (**2m**): In a 100 mL round-bottom flask, but-3-enoic acid (10 mmol, 0.85 mL), EDC•HCl (14 mmol, 2.68 g) and HOBt (16 mmol, 2.16 g) were dissolved in CH_2Cl_2 (30 mL) under N_2 atmosphere, and the mixture was stirred at room temperature for 30 mins. Next, the reaction was cooled in an ice-water bath. At 0 ºC, ethyl glycinate hydrochloride **S7** (10 mmol) was

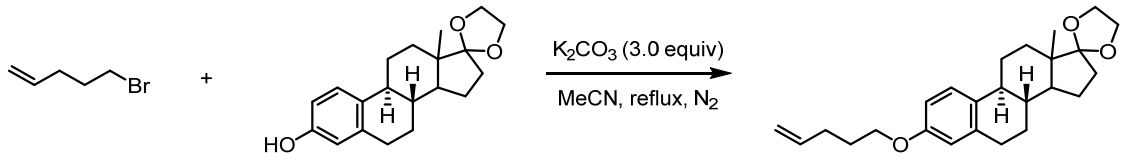
added into the flask, followed by the addition of EtN(*i*Pr)$_2$ (20 mmol, 3.48 mL) under N_2. After 30 min, the reaction mixture was warmed to room temperature and stirred overnight. After the reaction was quenched with water (30 mL), the resulting mixture was separated and extracted with CH_2Cl_2 (30 mL × 3). The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo*, and purified through a silica gel flash column (PE/EtOAc = 5:1) to give **2m** as a colorless oil (62% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.26 (brs, 1H), 5.92 (ddt, *J* = 16.0, 10.8, 7.1 Hz, 1H), 5.23 (d, *J* = 10.8 Hz, 1H), 5.22 (d, *J* = 16.0 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.99 (d, *J* = 5.2 Hz, 2H), 3.03 (d, *J* = 7.1 Hz, 2H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-d) δ 170.8, 169.9, 130.9, 120.0, 61.5, 41.4, 41.2, 14.1; IR ν_{max} (neat) cm^{-1}: 3077, 1770, 1452, 1321, 1254, 1159, 876; HRMS (ESI, m/z): calcd for $C_8H_{14}NO_3^+$ [M + H]$^+$ 172.0968, found 172.0968.



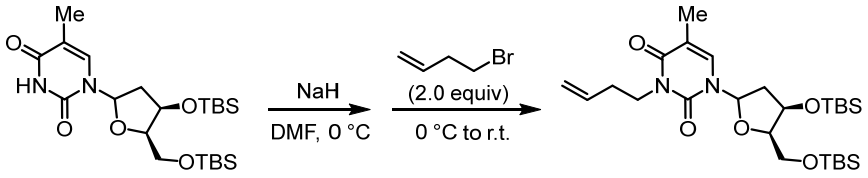
N-methyl dansyl amide (1.0 equiv)

S2, 74% yield

5-(Dimethylamino)-N-methyl-N-(pent-4-en-1-yl)naphthalene-1-sulfonamide (**S2**): In a 50 mL round-bottom flask, *N*-methyl dansyl amide (1.32 g, 5 mmol) was dissolved in dry DMF (10 mL), and the flask was cooled in an ice water bath. NaH (327 mg, 7.5 mmol, 55% in mineral oil) was added to the mixture under N_2, and the mixture was let stirred for 30 mins. Then, 5-bromopent-1-ene (6 mmol, 1.2 equiv) was added to the above solution. The mixture was warmed to room temperature and stirred for 1.5 h. After the reaction was quenched with water (30 mL), the resulting mixture was extracted with Et_2O (30 mL × 3). The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo*, and the residue was purified through a silica gel flash column (PE/EtOAc = 15:1) to afford compound **S2** as a light yellow oil (74% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 – 8.42 (m, 1H), 8.40 – 8.32 (m, 1H), 8.17 – 8.04 (m, 1H), 7.55 – 7.40 (m, 2H), 7.17 – 7.03 (m, 1H), 5.67 (ddt, *J* = 16.9, 10.3, 6.6 Hz, 1H), 4.99 – 4.80 (m, 2H), 3.18 (t, *J* = 7.3 Hz, 2H), 2.80 (s, 6H), 2.79 (s, 3H), 2.02 - 1.90 (m, 2H), 1.69 – 1.49 (m, 2H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 151.7, 137.4, 134.4, 130.3, 130.2, 130.1, 129.6, 127.9, 123.1, 119.7, 115.2, 49.1, 45.4, 34.1, 30.5, 26.8; IR ν_{max} (neat) cm^{-1}: 2940, 2870, 1570, 1453, 1325, 1140, 909, 789, 730, 624; HRMS (ESI, m/z): calcd for $C_{18}H_{25}N_2O_2S^+$ [M + H]$^+$ 333.1631, found 333.1634.

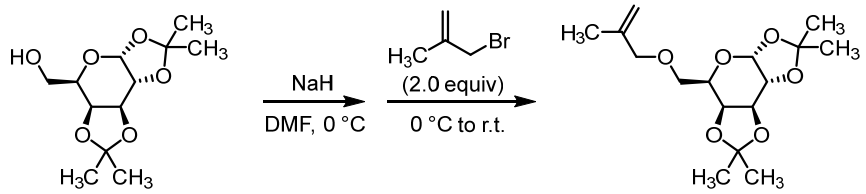


(8R,9S)-13-Methyl-3-(pent-4-en-1-yloxy)-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[a] phenanthrene-17,2'-[1,3]dioxolane] (**S3**). To a solution of estrone 17-ethylene ketal (597 mg, 1.90 mmol) in MeCN (5 mL) were added K_2CO_3 (787 mg, 5.70 mmol) and 4-bromo-1-butene (385 μL, 3.80 mmol, 2 equiv) under N_2. The reaction mixture was heated under reflux overnight before it was cooled to room temperature and concentrated *in vacuo*. The residue was suspended in water (20 mL) and extracted with ethyl acetate (10 mL × 3). The combined organic phase was then washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was then purified through a silica gel flash column (PE/EtOAc = 50:1) to give compound **S3** as a colorless oil (74% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.19 (m, 1H), 6.81 – 6.71 (m, 1H), 6.71 – 6.63 (m, 1H), 5.91 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.21 – 5.09 (m, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 4.07 – 3.88 (m, 6H), 2.98 – 2.82 (m, 2H), 2.43 – 2.34 (m, 1H), 2.34 – 2.20 (m, 3H), 2.16 – 2.02 (m, 1H), 2.01 – 1.78 (m, 6H), 1.76 – 1.64 (m, 1H), 1.64 – 1.56 (m, 1H), 1.56 – 1.32 (m, 4H), 0.95 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 157.0, 138.0, 137.9, 132.6, 126.3, 119.5, 115.2, 114.5, 112.1, 67.0, 65.3, 64.7, 49.4, 46.2, 43.7, 39.2, 34.3, 30.8, 30.3, 29.9, 28.6, 27.1, 26.3, 22.5, 14.4; IR ν_{max} (neat) cm^{-1}: 2975, 1680, 1511, 1234, 1181, 1160, 1034, 982, 816, 726, 654; HRMS (ESI, m/z): calcd for $C_{25}H_{35}O_3^+$ [M + H]$^+$ 383.2581, found 383.2584.



3-(But-3-en-1-yl)-1-((4R,5R)-4-((tert-butyldimethylsilyl)oxy)-5-(((tert-butyldimethylsilyl)oxy) methyl-z)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione (**S4**): In a 15 mL round-bottom flask, diO-TBS thymidine (940 mg, 2.0 mmol) was dissolved in dry DMF (4 mL), and the flask was cooled in an ice water bath. NaH (96 mg, 2.2 mmol, 55% in mineral oil) was added in portions into the mixture under N_2, and the mixture was let stirred for 30 min. Then, 4-bromo-1-butene (405 μL, 4 mmol) was added at 0 °C, and the reaction mixture was warmed to

room temperature and stirred overnight. After the reaction was quenched with water (15 mL), the resulting mixture was extracted with Et_2O (10 mL × 3). The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo*, and the residue was purified through a silica gel flash column (PE/EtOAc = 50:1) to afford compound **S4** as a colorless oil (79% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 (s, 1H), 6.33 (dd, *J* = 8.0, 5.8 Hz, 1H), 5.78 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.03 (d, *J* = 17.2 Hz, 1H), 4.97 (d, *J* = 10.2 Hz, 1H), 4.37 (dt, *J* = 5.7, 2.6 Hz, 1H), 4.06 – 3.93 (m, 2H), 3.93 – 3.87 (m, 1H), 3.83 (dd, *J* = 11.5, 2.7 Hz, 1H), 3.73 (dd, *J* = 11.4, 2.5 Hz, 1H), 2.35 (q, *J* = 7.3 Hz, 2H), 2.23 (ddd, *J* = 13.0, 5.8, 2.6 Hz, 1H), 1.96 (ddd, *J* = 13.6, 8.0, 6.0 Hz, 1H), 1.89 (s, 3H), 0.89 (s, 9H), 0.86 (s, 9H), 0.08 (s, 6H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 163.3, 150.8, 134.9, 133.3, 116.8, 109.9, 87.7, 85.4, 72.3, 63.0, 41.4, 40.5, 32.0, 25.9, 25.7, 18.4, 18.0, 13.3, -4.7, -4.9, -5.4, -5.5; IR ν_{max} (neat) cm^{-1}: 2968, 1734, 1679, 1517, 1434, 1151, 1023, 908, 841, 763; HRMS (ESI, m/z): calcd for $C_{26}H_{49}N_2O_5Si_2^+$ $[M + H]^+$ 525.3175, found 525.3179.

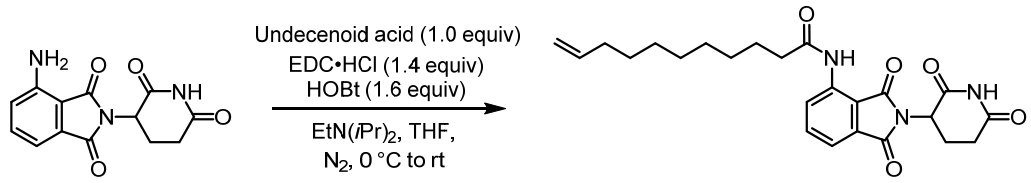


D-galactopyranose diacetalide (1.0 equiv)

S5, 84% yield

(3aR,5R,5aS,8aS,8bR)-2,2,7,7-Tetramethyl-5-(((2-methylallyl)oxy)methyl)tetrahydro-5H-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran (**S5**). In a 15 mL round-bottom flask, D-galactopyranose diacetalide (560 mg, 2.0 mmol) was dissolved in dry DMF (4 mL), and the flask was cooled in an ice water bath. NaH (96 mg, 2.2 mmol, 55% in mineral oil) was added in portions into the mixture under N_2, and the mixture was let stirred for 30 min. Then, 3-bromo-2-methylpropene (202 μL, 4 mmol) was added at 0 °C, and the reaction mixture was warmed to room temperature and stirred overnight. After the reaction was quenched with water (15 mL), the resulting mixture was extracted with Et_2O (10 mL × 3). The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo*, and the residue was purified through a silica gel flash column (PE/EtOAc = 20:1) to afford compound **S5** as a colorless oil (84% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.48 (d, *J* = 5.0 Hz, 1H), 4.91 (s, 1H), 4.83 (s, 1H), 4.55 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.26 (dd, *J* = 5.0, 2.4 Hz, 1H), 4.22 (dd, *J* = 7.9, 1.9 Hz, 1H), 3.96 – 3.90 (m, 1H), 3.92 (d, *J* = 12.7 Hz, 1H), 3.86 (d, *J* = 12.7 Hz, 1H), 3.58 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.50 (dd, *J* = 10.0, 6.7 Hz, 1H), 1.68 (s, 3H), 1.49 (s, 3H), 1.39 (s, 3H), 1.29 (s, 3H), 1.28 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 142.1, 112.1, 109.1, 108.4, 96.3, 75.1, 71.1, 70.61, 70.59,

68.5, 66.8, 26.0, 25.9, 24.9, 24.4, 19.3; IR ν_{max} (neat) cm^{-1}: 2983, 1675, 1523, 1245, 1108, 953, 706, 645; HRMS (ESI, m/z): calcd for $C_{16}H_{27}O_6^+$ $[M + H]^+$ 315.1802, found 315.1800.



N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)undec-10-enamide (**S6**): In a 100 mL round-bottom flask, undercenoic acid (10 mmol, 1.84 g), EDC•HCl (14 mmol, 2.68 g) and HOBt (16 mmol, 2.16 g) were dissolved in THF (30 mL) under N_2 atmosphere, and the mixture was stirred at room temperature for 30 mins. Next, the reaction was cooled in an ice-water bath. At 0 °C, pomalidomide (2.73 g, 10 mmol) was added into the flask, followed by the addition of EtN(*i*Pr)$_2$ (10 mmol, 1.74 mL) under N_2. After 30 min, the reaction mixture was warmed to room temperature and stirred overnight. After the reaction was quenched with water (30 mL), the resulting mixture was separated and the aqueous phase was extracted with EtOAc (30 mL × 3). The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo*, and purified through a silica gel flash column (PE/Acetone = 3:1) to afford compound **S6** as a white foam (61% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.40 (s, 1H), 8.81 (d, *J* = 8.9 Hz, 1H), 8.78 (s, 1H), 7.69 (t, *J* = 7.9 Hz, 1H), 7.52 (d, *J* = 7.2 Hz, 1H), 5.86 – 5.70 (m, 1H), 5.04 – 4.82 (m, 3H), 2.97 – 2.82 (m, 1H), 2.82 – 2.67 (m, 2H), 2.44 (t, *J* = 7.6 Hz, 2H), 2.20 – 2.08 (m, 1H), 2.01 (q, *J* = 7.1 Hz, 2H), 1.72 (p, *J* = 7.4 Hz, 2H), 1.43 – 1.20 (m, 10H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.5, 171.3, 169.2, 168.2, 166.8, 139.2, 137.9, 136.4, 131.1, 125.3, 118.4, 115.2, 114.2, 49.2, 38.0, 33.8, 31.4, 29.3, 29.2, 29.1, 29.0, 28.9, 25.2, 22.7; IR ν_{max} (neat) cm^{-1}: 3362, 1776, 1712, 1617, 1523, 1452, 1395, 1264, 1110, 1031, 928, 874, 643; HRMS (ESI, m/z): calcd for $C_{24}H_{30}N_3O_5^+$ $[M + H]^+$ 440.2180, found 440.2188.

III. The Discovery of Catalysts and Ligands

a) General procedure for a ligand-free reaction:

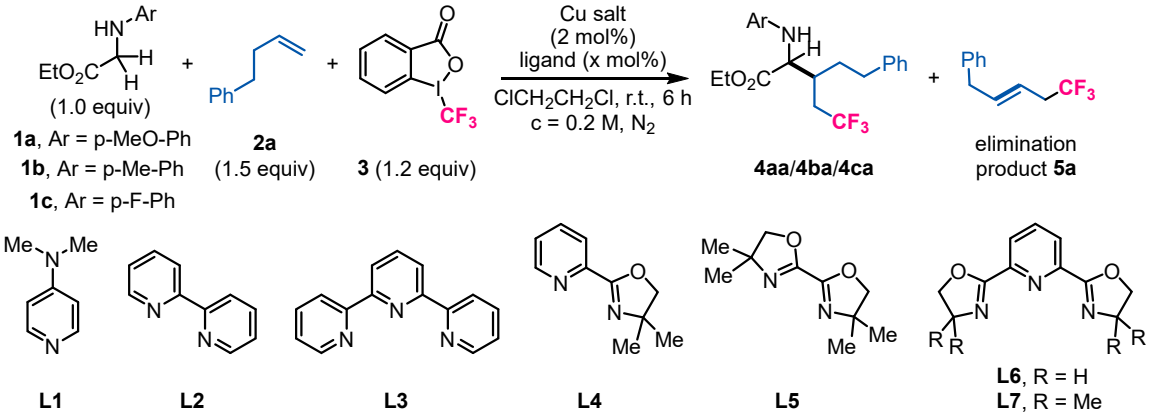
To a flame-dried reaction tube charged with a stir bar were added an ethyl glycinate **1** (0.2 mmol), Togni II reagent **3** (75.8 mg, 0.24 mmol), and a copper salt (0.004 mmol). The tube was sealed with a septum, evacuated, and backfilled with N_2 three times. Freshly distilled 1,2-dichloroethane (1.0 mL) and alkene **2a** (45 μL, 0.3 mmol) were then added, and the reaction was let stirred at room temperature (23 to 26 °C). After indicated time, the reaction was quenched with saturated $NaHCO_3$ aqueous solution (1 mL) and $Na_2S_2O_3$ aqueous solution (1 mL). The organic phase was separated and the aqueous one was extracted with CH_2Cl_2 (1 mL ×3). The combined organic layers were concentrated *in vacuo,* filtered through a short silica gel pad, and washed with PE/EtOAc (4:1, 15 mL). After the solvent was removed *in vacuo*, the residue was dissolved in $CDCl_3$ (with *α,α,α*-trifluorotoluene as an internal standard) and submitted for quantitative ^{19}F NMR analysis.

b) General procedure for a ligand-promoted reaction:

In a N_2 atmosphere glovebox, a copper salt (0.004 mmol), and a ligand (0.0048 mmol) were weighted into a 1-dram vial, which was then charged with a stir bar and sealed under N_2 with a septum. After the vial was taken out from the glovebox, freshly distilled 1,2-dichloroethane (1.0 mL) was added to afford a clear catalyst solution. To a flame-dried reaction tube charged with a stir bar were added an ethyl glycinate **1** (0.2 mmol) and Togni II reagent **3** (75.8 mg, 0.24 mmol). The tube was sealed with a septum, evacuated, and backfilled with N_2 three times. The above catalyst solution (1.0 mL) was transferred into the reaction tube together with alkene **2a** (45 μL, 0.3 mmol), and the reaction was kept stirring at room temperature (23 to 26 °C). After the indicated time, the reaction was quenched with saturated $NaHCO_3$ aqueous solution (1 mL) and $Na_2S_2O_3$ aqueous solution (1 mL). The organic phase was separated and the aqueous one was extracted with CH_2Cl_2 (1 mL ×3). The combined organic layers were concentrated *in vacuo,* filtered through a short silica gel pad, and washed with PE/EtOAc (4:1, 15 mL). After the solvent was removed *in vacuo*, the residue was dissolved in $CDCl_3$ (with *α,α,α*-trifluorotoluene as an internal standard) and submitted for quantitative ^{19}F NMR analysis.

Representative Cu salts and ligands were evaluated according to the above procedures and the obtained data are summarized in **Table S1**.

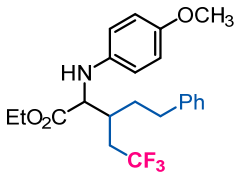
Table S1. Catalyst and ligand discovery[a]



entry	Cu salt (mol%)	**1**	ligand (mol%)	time (h)	**4aa/4ba/4ca** (%)[b]	**5** (%)[b]
1	none	**1a**	none	6	N.D.[c]	N.D.
2	$Cu(OTf)_2$ (2)	**1a**	none	12	30 (**4aa**)	36
3	$Cu(OTf)_2$ (2)	**1b**	none	12	11 (**4ba**)	60
4	$Cu(OTf)_2$ (2)	**1c**	none	12	8 (**4ca**)	47
5	$Cu(OTf)_2$ (2)	none	none	6	N.A.	N.D.
6	CuCl (2)	**1a**	none	6	49 (**4aa**)	39
7	$Cu(MeCN)_4PF_6$ (2)	**1a**	none	6	50 (**4aa**)	24
8	$Cu(MeCN)_4PF_6$ (2)	none	none	6	N.A.	6
9	$Cu(MeCN)_4PF_6$ (2)	**1a**	**L1** (4.8)	6	53 (**4aa**)	35
10	$Cu(MeCN)_4PF_6$ (2)	**1a**	**L2** (2.4)	12	7 (**4aa**)	N.D.
11	$Cu(MeCN)_4PF_6$ (2)	**1a**	**L3** (2.4)	12	<5 (**4aa**)	<5
12	$Cu(MeCN)_4PF_6$ (2)	**1a**	**L4** (2.4)	6	76 (**4aa**)	7
13	$Cu(MeCN)_4PF_6$ (2)	**1a**	**L5** (2.4)	6	74 (**4aa**)	7
14	$Cu(MeCN)_4PF_6$ (2)	**1a**	**L6** (2.4)	6	60 (**4aa**)	8
15	$Cu(MeCN)_4PF_6$ (2)	**1a**	**L7** (2.4)	6	92 (**4aa**)	N.D.
16	$Cu(MeCN)_4PF_6$ (1)	**1a**	**L7** (1.2)	12	88 (**4aa**)	N.D.
17[d]	$Cu(MeCN)_4PF_6$ (2)	**1a**	**L7** (2.4)	6	94[e] (**4aa**)	N.D.

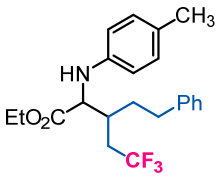
[a] unless otherwise stated, the reaction was carried out under N_2 with **1a** (0.2 mmol), **2a** (0.3 mmol), and **3** (0.24 mmol) in the presence of a copper catalyst (0.004 mol) and a ligand (0.0048 or 0.0096 mmol) in anhydrous $ClCH_2CH_2Cl$ (1 mL). [b] The yield of **4** and **5** were determined by quantitative ^{19}F NMR. [c] N.D. = Not detected on ^{19}F NMR. [d] 0.3 mmol of **3** was added. [e] isolated yield, *dr* = 1.2:1.

c) Characterization data of the related products:

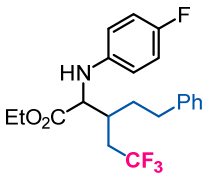


Ethyl 5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3-phenethylpentanoate (**4aa**): Compound **4aa** was isolated from the reaction described in ***entry 17*** through a silica gel flash column (PE: EtOAc = 50:1 to 30:1) as a colorless oil (76.9 mg, 94% yield, a mixture of two diastereomers, *dr* = 1.2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 – 7.15 (m, 2H), 7.15 – 7.04 (m, 3H), 6.74 – 6.63 (m, 2H), 6.59 – 6.50 (m, 2H), 4.18 – 3.91 (m, 3H), 3.89 – 3.68 (br, 1H), 3.65 (s, 3H, isomer 1), 3.64 (s, 3H, isomer 2), 2.76 – 2.37 (m, 3H), 2.29 – 1.97 (m, 2H), 1.95 – 1.82 (m, 1H, isomer 1), 1.73 – 1.52 (m, 1H + 1H, isomer 2), 1.15 (t, *J* = 7.2 Hz, 3H, isomer 1), 1.06 (t, *J* = 7.1 Hz, 3H, isomer 2); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.0 (isomer 1), 172.9 (isomer 2), 153.4 (isomer 2), 153.2 (isomer 1), 141.2 (isomer 1 + 2), 141.0 (isomer 2), 140.7 (isomer 1), 128.6 (isomer 2), 128.5 (isomer 1), 128.5 (isomer 2), 128.3 (isomer 1), 127.2 (q, *J* = 276.9, isomer 1 + 2), 126.2 (isomer 2), 126.1 (isomer 1), 116.2 (isomer 2), 115.8 (isomer 1), 115.0 (isomer 1), 114.9 (isomer 2), 61.5 (isomer 1), 61.4 (isomer 2), 60.6 (isomer 2), 60.3 (isomer 1), 55.7 (isomer 1), 55.7 (isomer 2), 35.8 (isomer 1), 34.9 (isomer 2), 34.3 (q, *J* = 27.7, isomer 2), 34.2 (q, *J* = 27.9, isomer 1), 33.0 (isomer 2), 32.9 (isomer 1), 32.7 (isomer 1), 31.6 (isomer 2), 14.2 (isomer 1), 14.2 (isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.6 (t, *J* = 11.3 Hz, 3F, isomer 1 + 2); IR ν_{max} (neat) cm^{-1}: 3371, 2938, 1725, 1510, 1453, 1389, 1245, 1134, 1030, 909, 821, 732, 696; HRMS (ESI, m/z): calcd for $C_{22}H_{27}F_3NO_3^+$ [M + H]$^+$ 410.1938, found 410.1940.

(E)-(5,5,5-trifluoropent-2-en-1-yl)benzene (**5a**): The elimination product **5a** is a known compound and the ^{1}H NMR & ^{19}F NMR data are in agreement with the literature.[15] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.34 (m, 2H), 7.33 – 7.22 (m, 3H), 5.94 (dt, *J* = 14.3, 6.9 Hz, 1H), 5.60 – 5.47 (m, 1H), 3.48 (d, *J* = 6.9 Hz, 2H), 2.88 (qd, *J* = 10.7, 7.1 Hz, 2H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -66.55 (t, *J* = 10.7 Hz, 3F).



Ethyl 5,5,5-trifluoro-3-phenethyl-2-(p-tolylamino)pentanoate (**4ba**): Compound **4ba** (11% yield based on ^{19}F NMR) was isolated from the reaction described in ***entry 3*** through a silica gel flash column (PE: EtOAc = 50:1 to 30:1) as colorless oil (6.3 mg, 8% isolated yield, a mixture of two diastereomers, *dr* = 1.3), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.24 (m, 2H), 7.24 – 7.10 (m, 3H), 7.06 – 6.93 (m, 2H), 6.63 – 6.52 (m, 2H), 4.29 – 3.90 (m, 4H), 2.87 – 2.46 (m, 3H), 2.39 – 2.08 (m, 5H), 2.05 – 1.91 (m, 1H, major), 1.83 – 1.62 (m, 1H, major + 2H, minor), 1.26 (t, *J* = 7.2 Hz, 3H, major), 1.18 (t, *J* = 7.1 Hz, 3H, minor); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.8 (isomer 1), 172.7 (isomer 2), 144.8 (isomer 1), 144.3 (isomer 2), 141.2 (isomer 1), 140.9 (isomer 2), 129.92 (isomer 1), 129.90 (isomer 2), 128.6 (isomer 2), 128.5 (isomer 1), 128.4 (isomer 2), 128.3 (isomer 1), 127.0 (q, *J* = 255.2 Hz, isomer 1+2), 126.2 (isomer 2), 126.1 (isomer 1), 114.5 (isomer 2), 114.2 (isomer 1), 61.5 (isomer 1), 61.4 (isomer 2), 59.5 (isomer 2), 59.3 (isomer 1), 35.7 (isomer 1), 34.9 (isomer 2), 34.3 (q, *J* = 27.7 Hz, isomer 2), 34.2 (d, *J* = 28.1 Hz, isomer 1), 33.0 (isomer 2), 32.9 (isomer 1), 32.7 (isomer 1), 31.7 (isomer 2), 20.4 (isomer 1+2), 14.22 (isomer 1), 14.2 (isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.70 (t, *J* = 11.7 Hz, isomer 1), -63.71 (t, *J* = 11.2 Hz, isomer 2); IR ν_{max} (neat) cm^{-1}: 3382, 2932, 1735, 1618, 1516, 1259, 1186, 1130, 1020, 809, 698; HRMS (ESI, m/z): calcd for $C_{22}H_{27}F_3NO_2^+$ [M + H]$^+$ 394.1988, found 394.1987.

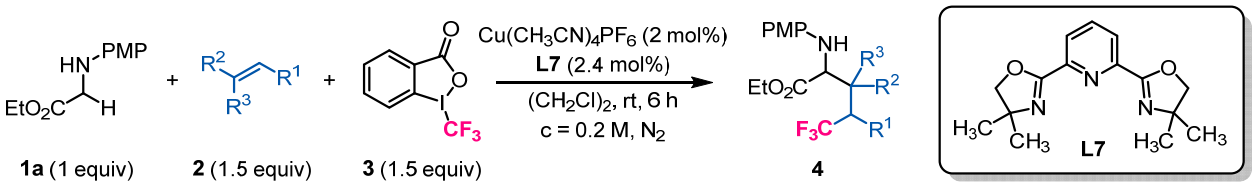


Ethyl 5,5,5-trifluoro-2-((4-fluorophenyl)amino)-3-phenethylpentanoate (**4ca**): Compound **4ca** (8% yield based on ^{19}F NMR) was isolated from the reaction described in ***entry 4*** through a silica gel flash column (PE: EtOAc = 50:1 to 30:1) as a colorless oil (4.7 mg, 6% isolated yield, a mixture of two diastereomers, *dr* = 1.5). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.27 (m, 2H), 7.23 – 7.11 (m, 3H), 6.94 – 6.82 (m, 2H), 6.64 – 6.51 (m, 2H), 4.28 – 4.03 (m, 3H), 2.84 – 2.46 (m, 3H), 2.39 – 2.08 (m, 2H), 1.81 – 1.56 (m, 2H), 1.25 (t, *J* = 6.8 Hz, 3H, isomer 1), 1.17 (t, *J* = 7.1 Hz, 2H, isomer 2); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.5, 158.0, 143.4, 140.8, 128.6, 128.5, 128.4, 128.3, 126.3, 126.2, 61.6, 61.5, 60.0, 59.8, 35.5, 34.7, 34.4, 34.1, 32.95, 32.86, 32.5, 31.6, 14.2, 14.1;

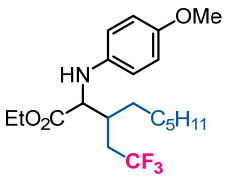
^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.70 (t, *J* = 11.6 Hz, isomer 1 + 2), -125.51 – -125.81 (m, isomer 1), -125.81 – -126.12 (m, isomer 2); IR ν_{max} (neat) cm^{-1}: 3376, 2926, 1733, 1514, 1457, 1389, 1249, 1138, 1022, 825, 702; HRMS (ESI, m/z): calcd for $C_{21}H_{24}F_4NO_2^+$ $[M + H]^+$ 398.1738, found 398.1736.

IV. Substrate Scope and Product Characterization

a) General procedure for the 3-component ligation with different alkenes

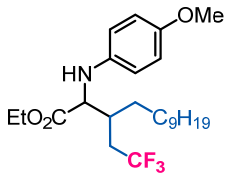


In a N_2 atmosphere glovebox, $Cu(CH_3CN)_4PF_6$ (1.5 mg, 0.004 mmol), and ligand **L7** (1.3 mg, 0.0048 mmol) were weighted into a 1-dram vial, which was then charged with a stir bar and sealed under N_2 with a septum. After the vial was taken out from the glovebox, freshly distilled 1,2-dichloroethane (1.0 mL) was added to afford a clear catalyst solution. To a flame-dried reaction tube charged with a stir bar were added *N*-PMP ethyl glycinate **1a** (41 mg, 0.2 mmol) and Togni II reagent **3** (94.8 mg, 0.3 mmol). The tube was sealed with a septum, evacuated, and backfilled with N_2 three times. The above catalyst solution (1.0 mL) was transferred into the reaction tube together with an alkene **2** (0.3 mmol, unless otherwise stated), and the reaction was kept stirring at room temperature (23 to 26 °C) for 6 h. After the reaction was quenched with saturated $NaHCO_3$ aqueous solution (1 mL) and $Na_2S_2O_3$ aqueous solution (1 mL), the organic phase was separated and the aqueous one was extracted with CH_2Cl_2 (1 mL × 3). The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo*, and then purified through a silica gel flash column.



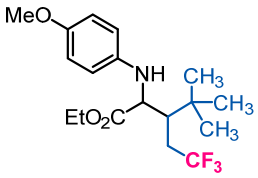
Ethyl 2-((4-methoxyphenyl)amino)-3-(2,2,2-trifluoroethyl)nonanoate (**4ab**): Following the general procedure A, compound **4ab** was prepared through a reaction between **1a**, 1-octene **2b** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 70:1 to 40:1) as a colorless oil (74.0 mg, 95% yield, a mixture of two diastereomers, *dr* = 1.2). ^{1}H NMR (400 MHz,

Chloroform-*d*) δ 6.84 – 6.71 (m, 2H), 6.70 – 6.57 (m, 2H), 4.27 – 4.10 (m, 2H + 1H, minor), 4.05 – 4.00 (m, 1H, major), 4.00 – 3.77 (br, 1H), 3.74 (s, 3H, major + 3H, minor), 2.61 – 2.40 (m, 1H), 2.33 – 1.96 (m, 2H), 1.46 – 1.17 (m, 13H), 0.95 – 0.75 (m, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 173.15 (major), 173.13 (minor), 153.3 (minor), 153.1 (major), 141.3 (minor), 140.8 (major), 127.2 (q, J = 276.4, major + minor), 116.1 (minor), 115.7 (major), 114.9 (major), 114.9 (minor), 61.33 (major), 61.27 (minor), 60.6 (minor), 60.2 (major), 55.69 (major), 55.66 (minor), 36.0 (major), 35.6 (minor), 34.2 (q, J = 27.6, minor), 34.1 (q, J = 28.2, major), 31.64 (major), 31.58 (minor), 30.7 (major), 29.6 (minor), 29.2 (major), 29.1 (minor), 26.8 (minor), 26.4 (major), 22.6 (major + minor), 14.24 (minor), 14.21 (major), 14.0 (major + minor); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.82 (t, J = 11.2 Hz, 3F, major), -63.89 (t, J = 11.5 Hz, 3F, minor); IR ν_{max} (neat) cm^{-1}: 3370, 2930, 1733, 1512, 1464, 1245, 1186, 1128, 1030, 821, 662; HRMS (ESI, m/z): calcd for $C_{20}H_{31}F_3NO_3^+$ $[M + H]^+$ 390.2251, found 390.2249.

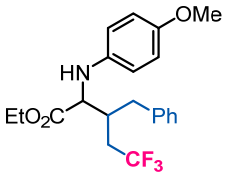


Ethyl 2-((4-methoxyphenyl)amino)-3-(2,2,2-trifluoroethyl)tridecanoate (**4ac**): Following the general procedure A, compound **4ac** was prepared through a reaction between **1a**, 1-dodecene **2c** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 70:1 to 40:1) as a colorless oil (85.5 mg, 96% yield, a mixture of two diastereomers, *dr* = 1.1). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.87 – 6.72 (m, 2H), 6.70 – 6.56 (m, 2H), 4.28 – 4.09 (m, 2H + 1H, isomer 1), 4.06 – 3.97 (m, 1H, isomer 2), 3.96 – 3.86 (m, 1H, isomer 1), 3.85 – 3.77 (m, 1H, isomer 2), 3.76 – 3.69 (m, 3H), 2.63 – 2.39 (m, 1H), 2.35 – 1.95 (m, 2H), 1.46 – 1.16 (m, 21H), 0.96 – 0.79 (m, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 173.2 (isomer 2), 173.1 (isomer 1), 153.3 (isomer 2), 153.1 (isomer 1), 141.3 (isomer 2), 140.8 (isomer 1), 127.2 (q, J = 278.0 Hz, isomer 1 + isomer 2), 116.1 (isomer 2), 115.7 (isomer 1), 114.9 (isomer 1), 114.9 (isomer 2), 61.3 (isomer 1), 61.2 (isomer 2), 60.6 (isomer 1), 60.2 (isomer 2), 55.7 (isomer 1), 55.6 (isomer 2), 36.0 (q, J = 2.2 Hz, isomer 1), 35.6 (q, J = 2.3 Hz, isomer 2), 34.2 (q, J = 27.6 Hz, isomer 1), 34.1 (q, J = 27.7 Hz, isomer 2), 31.9 (isomer 1 + isomer 2), 30.7 (isomer 1), 29.58, 29.56, 29.44, 29.43, 29.41, 29.32, 26.8 (isomer 1), 26.4 (isomer 2), 22.7 (isomer 1 + isomer 2), 14.2 (isomer 1), 14.2 (isomer 2), 14.1 (isomer 1 + isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.82 (t, J = 11.8 Hz, 3F, isomer 1), -63.90 (t, J = 11.4 Hz, 3F,

isomer 2); IR ν_{max} (neat) cm^{-1}: 3368, 2930, 2851, 1737, 1510, 1463, 1233, 1130, 1040, 817; HRMS (ESI, m/z): calcd for $C_{24}H_{39}F_3NO_3^+$ $[M + H]^+$ 446.2877, found 446.2875.

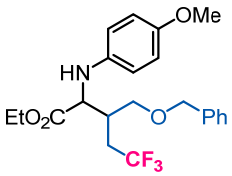


Ethyl 3-(tert-butyl)-5,5,5-trifluoro-2-((4-methoxyphenyl)amino)pentanoate (**4ad**): Following the general procedure A, compound **4ad** was prepared through a reaction between **1a**, 3,3-dimethyl-1-butene **2d** (3 equiv) and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 50 to 30:1) as a colorless oil (39.0 mg, 54% yield, a mixture of two diastereomers, *dr* = 2.0). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.85 – 6.72 (m, 2H), 6.70 – 6.59 (m, 2H), 4.29 – 4.20 (m, 1H), 4.20 – 4.05 (m, 2H), 3.90 - 3.60 (m, 4H), 2.80 – 2.60 (m, 1H, minor), 2.54 – 2.36 (m, 1H, major), 2.31 – 2.06 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H, minor), 1.23 (t, *J* = 7.2 Hz, 3H, major), 1.05 (s, 9H, major), 1.02 (s, 9H, minor); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.8 (major), 173.8 (minor), 153.1 (major + minor), 141.1 (minor), 140.9 (major), 127.6 (q, *J* = 276.5 Hz, minor), 127.3 (q, *J* = 276.3 Hz, major), 115.9 (major), 115.8 (minor), 114.9 (major), 114.8 (minor), 61.3 (major), 61.2 (minor), 59.5 (minor), 58.1 (major), 55.6 (minor + major), 44.8 (minor), 44.2 (major), 34.4 (major), 34.3 (minor), 31.4 (q, *J* = 27.9 Hz, minor), 30.0 (q, *J* = 28.6 Hz, major), 28.3 (minor), 28.1 (major), 14.0 (major + minor); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.82 (t, *J* = 11.7 Hz, 3F, minor), -64.18 (t, *J* = 11.6 Hz, 3F, major); IR ν_{max} (neat) cm^{-1}: 3390, 3950, 1721, 1524, 1244, 1080, 907, 815, 732, 688; HRMS (ESI, m/z): calcd for $C_{18}H_{27}F_3NO_3^+$ $[M + H]^+$ 362.1938, found 362.1937.



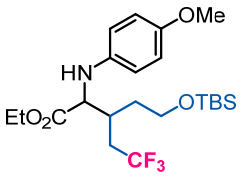
Ethyl 3-benzyl-5,5,5-trifluoro-2-((4-methoxyphenyl)amino)pentanoate (**4ae**): Following the general procedure A, compound **4ae** was prepared through a reaction between **1a**, allylbenzene **2e** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 50:1 to 30:1) as a colorless oil (73.5 mg, 93% yield, a mixture of two diastereomers, *dr* = 1.1). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.10 (m, 5H), 6.76 – 6.64 (m, 2H), 6.55 – 6.42 (m, 2H), 4.26 –

4.06 (m, 2H + 1H, isomer 1), 4.05 – 3.99 (m, 1H, isomer 2), 3.99 – 3.80 (br, 1H), 3.70 (s, 3H, isomer 1), 3.69 (s, 3H, isomer 2), 2.99 – 2.86 (m, 1H, isomer 1), 2.83 – 2.65 (m, 1H + 1H, isomer 2), 2.65 – 2.53 (m, 1H), 2.53 – 2.33 (m, 1H), 2.20 – 1.89 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H, isomer 1), 1.21 (t, J = 7.1 Hz, 3H, isomer 2); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 173.0 (isomer 1), 172.8 (isomer 2), 153.2 (isomer 2), 153.1 (isomer 1), 140.9 (isomer 1), 140.7 (isomer 2), 138.5 (isomer 2), 138.3 (isomer 1), 129.4 (isomer 2), 129.3 (isomer 1), 128.7 (isomer 1 + isomer 2), 127.1 (q, J = 276.9 Hz, isomer 1), 127.0 (q, J = 276.9 Hz, isomer 2), 126.9 (isomer 2), 126.7 (isomer 1), 115.9 (isomer 2), 115.8 (isomer 1), 114.9 (isomer 1 + isomer 2), 61.5 (isomer 2), 61.4 (isomer 1), 59.3 (isomer 2), 59.1 (isomer 1), 55.6 (isomer 1 + isomer 2), 37.8 (q, J = 2.3 Hz, isomer 1), 37.5 (q, J = 2.2 Hz, isomer 2), 37.1 (isomer 2), 35.9 (isomer 1), 33.7 (q, J = 28.3 Hz, isomer 1), 33.5 (q, J = 28.1 Hz, isomer 2), 14.3 (isomer 2), 14.2 (isomer 1); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.42 (t, J = 11.2 Hz, 3F), -63.53 (t, J = 11.2 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3366, 2938, 1735, 1512, 1247, 1128, 1078, 809, 734; HRMS (ESI, m/z): calcd for $C_{21}H_{25}F_3NO_3^+$ $[M + H]^+$ 396.1781, found 396.1780.



Ethyl 3-((benzyloxy)methyl)-5,5,5-trifluoro-2-((4-methoxyphenyl)amino)pentanoate (**4af**): Following the general procedure A, compound **4af** was prepared through a reaction between **1a**, allyl benzyl ether **2f** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 30:1 to 20:1) as a colorless oil (68.9 mg, 81% yield, a mixture of two diastereomers, *dr* = 1.6). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.28 (m, 5H), 6.82 – 6.68 (m, 2H + 2H, major), 6.65 – 6.56 (m, 2H, minor), 4.58 – 4.43 (m, 2H), 4.24 (d, J = 4.3 Hz, 1H, major), 4.19 (d, J = 4.5 Hz, 1H, minor), 4.16 – 4.06 (m, 2H), 3.75 (s, 3H, major), 3.74 (s, 3H, minor), 3.67 – 3.61 (m, 1H), 3.61 – 3.54 (m, 1H), 2.71 – 2.53 (m, 1H), 2.53 – 2.17 (m, 2H), 1.25 – 1.14 (m, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 172.6 (minor), 172.4 (major), 153.7 (major), 153.1 (minor), 140.9 (minor), 139.8 (major), 137.70 (major), 137.68 (minor), 128.48 (minor), 128.43 (major), 127.89 (major, 2C), 127.85 (minor), 127.78 (minor), 127.2 (q, J = 278.1 Hz, minor), 127.0 (q, J = 277.0 Hz, major), 116.5 (major), 115.7 (minor), 114.8 (major + minor), 73.5 (minor), 73.3 (major), 69.3 (minor), 68.9 (major), 61.6 (major), 61.3 (minor), 60.1 (minor), 59.4 (major), 55.7 (major + minor), 36.5 (major), 35.8 (minor), 32.7 (q, J = 28.5 Hz, minor), 31.8 (q, J = 28.7 Hz, major), 14.2 (minor), 14.1 (major); ^{19}F NMR (376

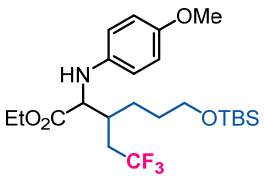
MHz, Chloroform-*d*) δ -64.06 (t, *J* = 11.3 Hz, 3F, minor), -64.16 (t, *J* = 11.4 Hz, 3F, major); IR ν_{max} (neat) cm^{-1}: 3374, 2934, 1729, 1512, 1239, 905, 823, 730, 694, 650; HRMS (ESI, m/z): calcd for $C_{22}H_{27}F_3NO_4^+$ $[M + H]^+$ 426.1887, found 426.1889.



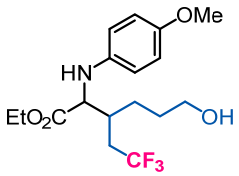
Ethyl 3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-5,5,5-trifluoro-2-((4-methoxyphenyl)amino) pentanoate (**4ag**): Following the general procedure A, compound **4ag** was prepared through a reaction between **1a**, alkene **2g** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 80:1 to 50:1).

Isomer 1 (less polar, colorless oil, 44.0 mg, 47% yield): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.86 – 6.71 (m, 2H), 6.67 – 6.59 (m, 2H), 4.27 – 4.12 (m, 3H), 4.10 – 3.84 (br, 1H), 3.79 – 3.65 (m, 5H), 2.54 – 2.35 (m, 2H), 2.33 – 2.14 (m, 1H), 1.96 – 1.80 (m, 1H), 1.65 – 1.54 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.89 (s, 9H), 0.063 (s, 3H), 0.059 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.1, 153.0, 140.9, 127.2 (q, *J* = 276.9 Hz), 115.6, 114.9, 61.3, 60.7, 60.1, 55.7, 34.4 (q, *J* = 27.9 Hz), 33.3, 33.2 (q, *J* = 2.5 Hz), 25.8, 18.2, 14.2, -5.50, -5.53; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.78 (t, *J* = 11.2 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3380, 2928, 1733, 1508, 1251, 831, 769, 728, 656; HRMS (ESI, m/z): calcd for $C_{22}H_{37}F_3NO_4Si^+$ $[M + H]^+$ 464.2438, found 464.2438.

Isomer 2 (more polar, colorless oil, 44.2 mg, 48%): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.76 – 6.66 (m, 2H), 6.63 – 6.54 (m, 2H), 4.20 – 4.01 (m, 3H), 3.93 – 3.79 (br, 1H), 3.73 – 3.56 (m, 2H), 3.67 (s, 3H), 2.60 – 2.35 (m, 2H), 2.20 – 1.98 (m, 1H), 1.76 – 1.55 (m, 1H), 1.55 – 1.40 (m, 1H), 1.18 (t, *J* = 7.1 Hz, 3H), 0.84 (s, 9H), 0.03 – -0.03 (m, 6H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.0, 153.2, 141.3, 127.2 (q, *J* = 277.1 Hz), 115.9, 114.9, 61.3, 60.4, 60.3, 55.7, 34.2 (q, *J* = 27.8 Hz), 32.6 (q, *J* = 2.4 Hz), 32.5, 25.8, 18.2, 14.2, -5.49, -5.52; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.6 (t, *J* = 10.9 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3354, 2950, 1737, 1662, 1520, 1226, 1110, 1014, 815; HRMS (ESI, m/z): calcd for $C_{22}H_{37}F_3NO_4Si^+$ $[M + H]^+$ 464.2438, found 464.2438.



Ethyl 6-((tert-butyldimethylsilyl)oxy)-2-((4-methoxyphenyl)amino)-3-(2,2,2-trifluoroethyl) hexanoate (**4ah**): Following the general procedure A, compound **4ah** was prepared through a reaction between **1a**, alkene **2h** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 80:1 to 60:1) as a colorless oil (92.7 mg, 97% yield, a mixture of two diastereomers, *dr* = 1.1). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.78 – 6.68 (m, 2H), 6.65 – 6.51 (m, 2H), 4.21 – 4.05 (m, 2H + 1H, minor), 3.97 (d, *J* = 4.8 Hz, 1H, major), 3.91 – 3.73 (br, 1H), 3.70 (s, 3H), 3.61 – 3.52 (m, 2H), 2.59 – 2.37 (m, 1H), 2.31 – 2.20 (m, 1H, minor), 2.20 – 1.95 (m, 1H + 1H, major), 1.70 – 1.44 (m, 3H), 1.44 – 1.32 (m, 1H), 1.21 (t, *J* = 7.2 Hz, 3H, major), 1.20 (t, *J* = 7.1 Hz, 3H, minor), 0.90 – 0.80 (m, 9H), 0.03 – -0.02 (m, 6H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.0 (major), 172.9 (minor), 153.3 (minor), 153.1 (major), 141.2 (minor), 140.8 (major), 127.2 (q, *J* = 276.7 Hz, major), 127.2 (q, *J* = 276.9 Hz, minor), 116.1 (minor), 115.7 (major), 114.9 (major), 114.8 (minor), 62.7 (major), 62.6 (minor), 61.4 (major), 61.3 (minor), 60.6 (minor), 60.3 (major), 55.7 (major), 55.6 (minor), 35.8 (q, *J* = 2.3 Hz, major), 35.6 (q, *J* = 2.4 Hz, minor), 34.3 (q, *J* = 27.7 Hz, minor), 34.1 (q, *J* = 28.0 Hz, major), 30.2 (minor), 29.7 (major), 27.1 (major), 26.2 (minor), 25.9 (major + minor), 18.3 (major + minor), 14.2 (minor), 14.1 (major), -5.4 (minor), -5.3 (major); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.80 (t, *J* = 11.3 Hz, 3F, major), -63.85 (t, *J* = 11.3 Hz, 3F, minor); IR ν_{max} (neat) cm^{-1}: 3370, 2936, 1733, 1516, 1249, 1098, 833, 775, 730, 658; HRMS (ESI, m/z): calcd for $C_{23}H_{39}F_3NO_4Si^+$ $[M + H]^+$ 478.2595, found 478.2592.

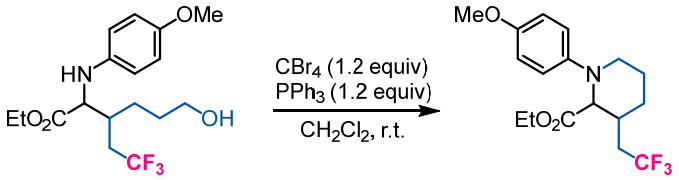


Ethyl 6-hydroxy-2-((4-methoxyphenyl)amino)-3-(2,2,2-trifluoroethyl)hexanoate (**4ai**): Following the general procedure A, compound **4ai** was prepared through a reaction between **1a**, pent-4-en-1-ol **2i** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 10:1 to 7:1).

Isomer 1 (less polar, brownish oil, 34.0 mg, 47% yield): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.85 – 6.71 (m, 2H), 6.68 – 6.56 (m, 2H), 4.27 – 4.10 (m, 2H), 4.02 (d, *J* = 5.0 Hz, 1H), 3.73 (s, 3H), 3.63 (t, *J* = 6.0 Hz, 2H), 2.51 (ddt, *J* = 18.8, 11.4, 5.5 Hz, 1H), 2.26 – 2.03 (m, 2H), 1.80 – 1.53 (m, 3H), 1.49 – 1.34 (m, 1H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.0, 153.2, 140.7, 127.1 (q, *J* = 276.8 Hz), 115.7, 114.9, 62.4, 61.5, 60.3, 55.7, 35.7 (q, *J* = 2.4 Hz), 34.2 (q, *J* =

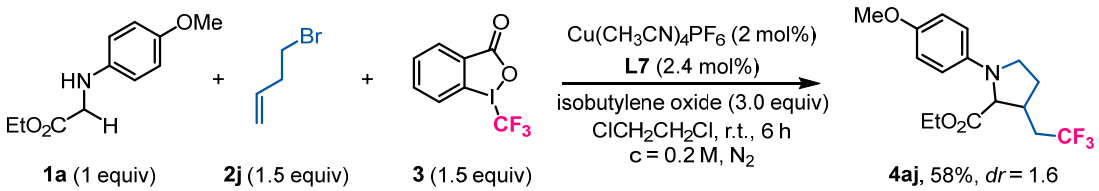
27.9 Hz), 29.5, 26.9, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.84 (t, *J* = 11.2 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3362, 2938, 1727, 1508, 1235, 1132, 1028, 823, 736; HRMS (ESI, m/z): calcd for $C_{17}H_{25}F_3NO_4^+$ $[M + H]^+$ 364.1730, found 364.1726.

Isomer 2 (more polar, brownish oil, 34.2 mg, 47% yield): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.83 – 6.72 (m, 2H), 6.69 – 6.59 (m, 2H), 4.26 – 4.05 (m, 3H), 3.74 (s, 3H), 3.69 – 3.57 (m, 2H), 2.64 – 2.44 (m, 1H), 2.36 – 2.25 (m, 1H), 2.16 – 1.97 (m, 1H), 1.75 – 1.38 (m, 4H), 1.24 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.1, 153.3, 141.1, 127.1 (q, *J* = 276.9 Hz), 116.1, 114.9, 62.3, 61.4, 60.6, 55.7, 35.5 (q, *J* = 2.6 Hz), 34.4 (q, *J* = 27.7 Hz), 29.8, 26.1, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.89 (t, *J* = 11.3 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3372, 2940, 1731, 1512, 1243, 1038, 819, 728; HRMS (ESI, m/z): calcd for $C_{17}H_{25}F_3NO_4^+$ $[M + H]^+$ 364.1730, found 364.1729.



4ai, isomer 1 **6**, 88%

Ethyl 1-(4-methoxyphenyl)-3-(2,2,2-trifluoroethyl)piperidine-2-carboxylate (**6**): To a solution of **4ai** (72.7 mg, 0.2 mmol, isomer 1) and PPh_3 (70.0 mg, 0.24 mmol) in CH_2Cl_2 (2 mL) was added CBr_4 (79.6 mg, 0.24 mmol) under N_2 atmosphere. The reaction was kept stirring for 2 h at room temperature before it was quenched with saturated aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2 (2 mL ×3). The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was then purified through a silica gel flash column (PE: EtOAc = 80:1 to 50:1) to give **6** as a colorless oil (60.7 mg, 88% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.95 – 6.86 (m, 2H), 6.85 – 6.77 (m, 2H), 4.34 (d, *J* = 4.6 Hz, 1H), 4.02 (qd, *J* = 7.1, 1.8 Hz, 2H), 3.76 (s, 3H), 3.39 (td, *J* = 11.5, 3.2 Hz, 1H), 3.20 (dt, *J* = 12.0, 3.2 Hz, 1H), 2.49 – 2.27 (m, 2H), 2.15 – 1.97 (m, 1H), 1.93 – 1.59 (m, 4H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 170.8, 153.8, 144.5, 126.9 (q, *J* = 277.0 Hz), 118.9, 114.3, 63.7, 60.2, 55.5, 44.7, 36.9 (q, *J* = 28.0 Hz), 33.1 (t, *J* = 2.6 Hz), 25.7, 24.9, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.80 (t, *J* = 11.1 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 2942, 1721, 1502, 1237, 1132, 1032, 815, 732; HRMS (ESI, m/z): calcd for $C_{17}H_{23}F_3NO_3^+$ $[M + H]^+$ 346.1625, found 346.1628.

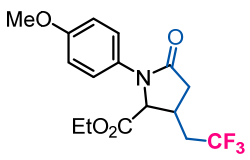


1a (1 equiv) **2j** (1.5 equiv) **3** (1.5 equiv) **4aj**, 58%, *dr* = 1.6

Ethyl 1-(4-methoxyphenyl)-3-(2,2,2-trifluoroethyl)pyrrolidine-2-carboxylate (**4aj**): Following the general procedure A, compound **4aj** was prepared through a reaction between **1a**, 4-bromobut-1-ene **2j**, Togni II reagent **3** and isobutylene oxide (3.0 equiv, as an acid absorbent), and it was isolated through a silica gel flash column (PE: EtOAc = 70:1 to 50:1).

Major isomer (less polar, yellow oil, 23.8 mg, 36% yield): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.91 – 6.77 (m, 2H), 6.55 – 6.44 (m, 2H), 4.25 (d, *J* = 8.0 Hz, 1H), 4.23 – 4.11 (m, 2H), 3.75 (s, 3H), 3.61 – 3.52 (m, 1H), 3.46 – 3.35 (m, 1H), 2.84 – 2.67 (m, 1H), 2.56 – 2.39 (m, 1H), 2.39 – 2.26 (m, 1H), 2.18 – 1.93 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.7, 151.6, 140.8, 126.5 (q, *J* = 277.0 Hz), 115.1, 112.5, 64.2, 61.0, 55.8, 47.8, 36.2 (q, *J* = 2.8 Hz), 34.5 (q, *J* = 29.0 Hz), 29.6, 14.3; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -64.69 (t, *J* = 10.8 Hz,3F); IR ν_{max} (neat)/cm^{-1}: 2938, 1737, 1518, 1365, 1245, 1040, 809, 779; HRMS (ESI, m/z): calcd for $C_{16}H_{21}F_3NO_3^+$ $[M + H]^+$ 332.1468, found 332.1469.

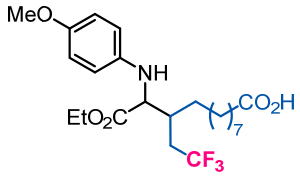
Minor isomer (more polar, yellow oil, 14.9 mg, 22% yield): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.86 – 6.78 (m, 2H), 6.53 – 6.44 (m, 2H), 4.18 (qd, *J* = 7.1, 1.2 Hz, 2H), 3.98 (d, *J* = 4.5 Hz, 1H), 3.75 (s, 3H), 3.62 – 3.53 (m, 1H), 3.50 - 3.43 (m, 1H), 2.75 – 2.64 (m, 1H), 2.56 – 2.33 (m, 2H), 2.31 – 2.11 (m, 1H), 1.80 - 1.92 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.3, 151.7, 140.9, 126.4 (d, *J* = 277.0 Hz), 112.9, 66.4, 61.2, 55.8, 47.7, 38.2 (q, *J* = 2.5 Hz), 37.7 (q, *J* = 28.2 Hz), 30.1, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -64.46 (t, *J* = 10.8 Hz); IR ν_{max} (neat)/cm^{-1}: 2988, 1729, 1518, 1369, 1237, 1152, 1132, 1032, 813; HRMS (ESI, m/z): calcd for $C_{16}H_{21}F_3NO_3^+$ $[M + H]^+$ 332.1468, found 332.1470.



Ethyl 1-(4-methoxyphenyl)-5-oxo-3-(2,2,2-trifluoroethyl)pyrrolidine-2-carboxylate (**4ak**): Following the general procedure A, compound **4ak** was prepared through a reaction between **1a**, but-3-enoic acid **2k** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 40:1 to 20:1).

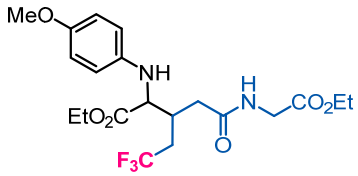
Minor isomer (less polar, white solid, 17.6 mg, 25% yield, m.p.: 78 – 81 °C): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.27 (m, 2H), 6.93 – 6.83 (m, 2H), 4.60 (d, *J* = 8.3 Hz, 1H), 4.31 – 4.12 (m, 2H), 3.79 (s, 3H), 3.13 – 2.95 (m, 1H), 2.75 (dd, *J* = 16.6, 8.3 Hz, 1H), 2.62 (dd, *J* = 16.6, 11.9 Hz, 1H), 2.47 (dqd, *J* = 14.7, 10.7, 4.4 Hz, 1H), 2.07 (dp, *J* = 14.7, 10.1 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.9, 170.0, 157.8, 130.5, 126.0 (q, *J* = 276.9 Hz), 124.3, 114.4, 65.8, 62.0, 55.5, 36.4, 34.7 (q, *J* = 29.4 Hz), 30.1 (q, *J* = 2.9 Hz), 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -64.82 (t, *J* = 10.4 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 2954, 1739, 1694, 1516, 1393, 1253, 1200, 1106, 1012, 843, 636; HRMS (ESI, m/z): calcd for $C_{16}H_{19}F_3NO_4^+$ $[M + H]^+$ 346.1261, found 346.1260.

Major isomer (more polar, white solid, 28.1 mg, 41% yield, m.p.: 85 – 88 °C): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.20 (m, 2H), 6.96 – 6.82 (m, 2H), 4.40 (d, *J* = 4.5 Hz, 1H), 4.26 – 4.07 (m, 2H), 3.78 (s, 3H), 2.96 (dd, *J* = 17.1, 8.8 Hz, 1H), 2.82 – 2.69 (m, 1H), 2.65 – 2.47 (m, 1H), 2.40 (dd, *J* = 17.1, 4.9 Hz, 1H), 2.40 – 2.26 (m, 1H), 1.17 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.2, 170.3, 157.9, 130.2, 125.9 (q, *J* = 277.1 Hz), 124.6, 114.4, 66.9, 62.0, 55.4, 38.1 (q, *J* = 28.3 Hz), 36.8, 31.0 (q, *J* = 2.8 Hz), 14.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -64.34 (t, *J* = 10.4 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 2960, 1747, 1690, 1518, 1395, 1239, 1186, 1108, 998, 825, 648; HRMS (ESI, m/z): calcd for $C_{16}H_{19}F_3NO_4^+$ $[M + H]^+$ 346.1261, found 346.1261.

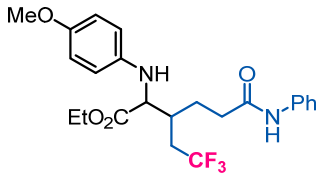


12-Ethoxy-11-((4-methoxyphenyl)amino)-12-oxo-10-(2,2,2-trifluoroethyl)dodecanoic acid (**4al**): Following the general procedure A, compound **4al** was prepared through a reaction between **1a**, undecenoic acid **2l** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 5:1 to 3:1) as a colorless oil (87.7 mg, 95% yield, a mixture of two diastereomers, *dr* = 1.1). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 – 7.35 (br, 1H), 6.91 – 6.73 (m, 2H), 6.69 – 6.58 (m, 2H), 4.28 – 4.09 (m, 2H + 1H, isomer 1), 4.02 (d, *J* = 4.9 Hz, 1H, isomer 2), 3.73 (s, 3H), 2.67 – 2.42 (m, 1H), 2.39 – 2.25 (m, 2H), 2.22 – 1.97 (m, 2H), 1.69 – 1.55 (m, 2H), 1.45 – 1.16 (m, 15H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 180.0 (isomer 1 + isomer 2), 173.3 (isomer 1), 173.2 (isomer 2), 153.3 (isomer 1), 153.1 (isomer 2), 141.3 (isomer 1), 140.8 (isomer 2), 127.3 (q, *J* = 276.8 Hz, isomer 1), 127.2 (q, *J* = 276.7 Hz, isomer 2), 116.1 (isomer 1), 115.7 (isomer 2), 114.9 (isomer 1),

114.8 (isomer 2), 61.4 (isomer 1), 61.3 (isomer 2), 60.5 (isomer 1), 60.2 (isomer 2), 55.6 (isomer 1), 55.5 (isomer 2), 35.9 (q, J = 2.2 Hz, isomer 1), 35.6 (q, J = 2.2 Hz, isomer 2), 34.2 (q, J = 27.9 Hz, isomer 1), 34.1 (q, J = 27.8 Hz, isomer 2), 34.0 (isomer 1 + isomer 2), 30.6 (isomer 1), 29.6 (isomer 2), 29.4 (isomer 1), 29.3 (isomer 2), 29.2 (isomer 1), 29.14 (isomer 2), 29.12 (isomer 1), 29.0 (isomer 2), 26.8 (isomer 1), 26.4 (isomer 2), 24.6 (isomer 1 + isomer 2), 14.2 (isomer 1), 14.1 (isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.80 (t, J = 11.4 Hz, 3F, isomer 1), -63.88 (t, J = 11.7 Hz, 3F, isomer 2); IR ν_{max} (neat) cm^{-1}: 3360, 2928, 2855, 1729, 1705, 1512, 1239, 1134, 1032, 825, 732; HRMS (ESI, m/z): calcd for $C_{23}H_{35}F_3NO_5^+$ $[M + H]^+$ 462.2462, found 462.2466.



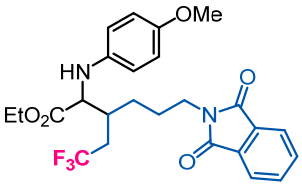
Ethyl 3-(2-((2-ethoxy-2-oxoethyl)amino)-2-oxoethyl)-5,5,5-trifluoro-2-((4-methoxyphenyl)amino) pentanoate (**4am**): Following the general procedure A, compound **4am** was prepared through a reaction between **1a**, ethyl but-3-enoyl glycinate **2m** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 10:1 to 5:1) as a yellow oil (62.5 mg, 64% yield, a mixture of two diastereomers, *dr* = 1.2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.84 – 6.55 (m, 4H), 6.37 – 6.10 (m, 1H), 4.44 – 3.86 (m, 8H), 3.77 – 3.66 (m, 3H), 2.92 – 2.69 (m, 1H), 2.69 – 2.12 (m, 4H), 1.34 – 1.16 (m, 6H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.1 (minor), 172.7 (major), 170.8 (major + minor), 169.8 (major), 169.7 (minor), 153.2 (minor), 153.1 (major), 140.9 (minor), 140.7 (major), 127.0 (q, J = 277.2 Hz, minor), 126.8 (q, J = 277.1 Hz, major), 115.9 (minor), 115.8 (major), 114.9 (major + minor), 61.7 (minor), 61.6 (2 major + 1 minor), 60.1 (major), 60.0 (minor), 55.7 (major + minor), 41.4 (major), 41.2 (minor), 36.3 (minor), 36.1 (major), 34.1 (q, J = 28.2 Hz, major), 33.6 (q, J = 28.2 Hz, minor), 33.2 (minor), 32.7 (major), 14.18 (major), 14.15 (minor), 14.10 (major + minor); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.46 (t, J = 11.1 Hz, 3F, major), -63.56 (t, J = 11.2 Hz, 3F, minor); IR ν_{max} (neat) cm^{-1}: 3340, 2986, 1731, 1660, 1512, 1373, 1231, 1196, 1132, 1018, 907, 819, 730; HRMS (ESI, m/z): calcd for $C_{20}H_{28}F_3N_2O_6^+$ $[M + H]^+$ 449.1894, found 449.1892.



Ethyl 2-((4-methoxyphenyl)amino)-6-oxo-6-(phenylamino)-3-(2,2,2-trifluoroethyl)hexanoate (**4an**): Following the general procedure A, compound **4an** was prepared through a reaction between **1a**, *N*-phenylpent-4-enamide **2n** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 15:1 to 7:1).

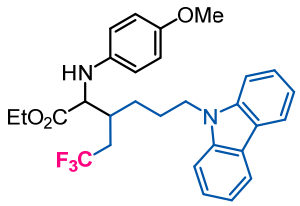
Minor isomer (less polar, white solid, 35.4 mg, 39% yield, m.p.: 77 – 79 °C): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (brs, 1H), 7.47 – 7.37 (m, 2H), 7.31 – 7.21 (m, 2H), 7.14 – 7.00 (m, 1H), 6.79 – 6.70 (m, 2H), 6.65 – 6.53 (m, 2H), 4.26 – 4.09 (m, 2H), 4.01 (d, *J* = 4.8 Hz, 1H), 3.71 (s, 3H), 2.63 – 2.30 (m, 3H), 2.30 – 2.19 (m, 1H), 2.19 – 1.96 (m, 2H), 1.83 – 1.67 (m, 1H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.7, 170.3, 153.2, 140.5, 137.8, 129.0, 127.0 (q, *J* = 276.7 Hz), 124.3, 120.0, 115.6, 115.0, 61.7, 60.6, 55.7, 35.4 (q, *J* = 2.3 Hz), 34.54, 34.49 (q, *J* = 28.1 Hz), 26.8, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.8 (t, *J* = 11.2 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3313, 2934, 1729, 1664, 1600, 1510, 1447, 1241, 1126, 1028, 907, 821, 728; HRMS (ESI, m/z): calcd for $C_{23}H_{28}F_3N_2O_4^+$ $[M + H]^+$ 453.1996, found 453.1997.

Major isomer (more polar, yellow solid, 42.4 mg, 47% yield, m.p.: 85 – 87 °C): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (brs, 1H), 7.52 – 7.43 (m, 2H), 7.37 – 7.27 (m, 2H), 7.16 – 7.04 (m, 1H), 6.83 – 6.70 (m, 2H), 6.69 – 6.58 (m, 2H), 4.23 – 4.13 (m, 2H), 4.11 (d, *J* = 4.3 Hz, 1H), 4.10 – 3.86 (br, 1H), 3.73 (s, 3H), 2.64 – 2.49 (m, 1H), 2.49 – 2.27 (m, 3H), 2.15 – 1.91 (m, 2H), 1.85 – 1.68 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.9, 170.1, 153.3, 141.0, 137.8, 129.0, 127.0 (q, *J* = 276.7 Hz), 124.4, 119.9, 116.0, 114.9, 61.6, 60.7, 55.7, 35.2 (q, *J* = 2.5 Hz), 34.6, 34.5 (q, *J* = 28.1 Hz), 25.8, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.75 (t, *J* = 11.3 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3315, 1942, 1731, 1666, 1512, 1437, 1237, 1132, 1030, 911, 823, 736; HRMS (ESI, m/z): calcd for $C_{23}H_{28}F_3N_2O_4^+$ $[M + H]^+$ 453.1996, found 453.1994.



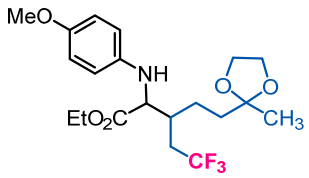
Ethyl 6-(1,3-dioxoisoindolin-2-yl)-2-((4-methoxyphenyl)amino)-3-(2,2,2-trifluoroethyl)hexanoate (**4ao**): Following the general procedure A, compound **4ao** was prepared through a reaction between

1a, alkene **2o** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 10:1 to 5:1) as brownish solid (90.6 mg, 92% yield, a mixture of two diastereomers, *dr* = 1.0). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 – 7.76 (m, 2H), 7.75 – 7.60 (m, 2H), 6.81 – 6.69 (m, 2H), 6.67 – 6.54 (m, 2H), 4.23 – 4.05 (m, 2H + 1H, isomer 1), 4.04 – 3.81 (m, 1H + 1H, isomer 2), 3.70 (s, 3H), 3.70 – 3.63 (m, 2H), 2.59 – 2.41 (m, 1H), 2.35 – 2.16 (m, 1H), 2.15 – 1.95 (m, 1H), 1.89 – 1.63 (m, 2H + 1H, isomer 1), 1.58 – 1.37 (m, 1H + 1H, isomer 2), 1.25 – 1.14 (m, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.9 (isomer 1), 172.8 (isomer 2), 168.3 (isomer 1 + isomer 2), 153.2 (isomer 1), 153.1 (isomer 2), 141.0 (isomer 1), 140.7 (isomer 2), 134.0 (isomer 1), 133.9 (isomer 2), 132.0 (isomer 1), 131.9 (isomer 2), 127.1 (q, *J* = 276.9 Hz, isomer 1), 127.0 (q, *J* = 277.0 Hz, isomer 2), 123.2 (isomer 1), 123.1 (isomer 2), 116.0 (isomer 1), 115.7 (isomer 2), 114.9 (isomer 1), 114.8 (isomer 2), 61.4 (isomer 1), 61.3 (isomer 2), 60.3 (isomer 1), 60.2 (isomer 2), 55.6 (isomer 1), 55.5 (isomer 2), 37.6 (isomer 1), 37.5 (isomer 2), 35.7 (isomer 1), 35.4 (isomer 2), 34.2 (q, *J* = 27.9 Hz, isomer 1), 34.0 (q, *J* = 27.7 Hz, isomer 2), 28.0 (isomer 1), 27.1 (isomer 2), 25.9 (isomer 1), 25.6 (isomer 2), 14.1 (isomer 1 + isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.83 (t, *J* = 11.3 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3332, 2916, 1779, 1701, 1514, 1235, 1158, 1108, 1028, 907, 821, 718; HRMS (ESI, m/z): calcd for $C_{25}H_{28}F_3N_2O_5^+$ $[M + H]^+$ 493.1945, found 493.1946.



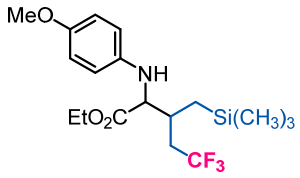
Ethyl 6-(9H-carbazol-9-yl)-2-((4-methoxyphenyl)amino)-3-(2,2,2-trifluoroethyl)hexanoate (**4ap**): Following the general procedure A, compound **4ap** was prepared through a reaction between **1a**, alkene **2p** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 20:1 to 15:1) as a colorless oil (58.4 mg, 57% yield, a mixture of two diastereomers, *dr* = 1.0). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 – 8.07 (m, 2H), 7.59 – 7.47 (m, 2H), 7.47 – 7.37 (m, 2H), 7.34 – 7.24 (m, 2H), 6.86 – 6.77 (m, 2H, isomer 1), 6.77 – 6.70 (m, 2H, isomer 2), 6.66 – 6.60 (m, 2H, isomer 1), 6.59 – 6.52 (m, 2H, isomer 2), 4.41 – 4.24 (m, 2H), 4.17 – 4.01 (m, 2H + 1H, isomer 1), 3.94 (d, *J* = 4.9 Hz, 1H, isomer 2), 3.94 – 3.77 (br, 1H), 3.77 (s, 3H), 2.66 – 2.41 (m, 1H), 2.40 – 2.29 (m, 1H, isomer 1), 2.29 – 2.19 (m, 1H, isomer 2), 2.16 – 1.92 (m, 3H), 1.85 – 1.71 (m, 1H, isomer 1), 1.64 – 1.46 (m, 1H + 1H, isomer 2), 1.17 (t, *J* = 7.2 Hz, 3H, isomer 1), 1.12 (t, *J* = 7.1 Hz, 3H, isomer 2); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.9 (isomer 1), 172.8 (isomer 2), 153.4 (isomer 1),

153.3 (isomer 2), 140.9 (isomer 1), 140.7 (isomer 2), 140.4 (isomer 1), 140.3 (isomer 2), 127.1 (q, J = 276.9 Hz, isomer 1), 127.0 (q, J = 277.0 Hz, isomer 2), 125.8 (isomer 1), 125.7 (isomer 2), 123.0 (isomer 1 + isomer 2), 120.5 (isomer 1),120.4 (isomer 2), 119.1 (isomer 1), 119.0 (isomer 2), 116.1 (isomer 1), 116.0 (isomer 2), 114.9 (isomer 1 + isomer 2), 108.6 (isomer 1), 108.5 (isomer 2), 61.5 (isomer 1), 61.4 (isomer 2), 60.6 (isomer 1), 60.3 (isomer 2), 55.7 (isomer 1), 55.7 (isomer 2), 42.8 (isomer 1), 42.8 (isomer 2), 36.0 (isomer 1), 35.7 (isomer 2), 34.3 (q, J = 28.0 Hz, isomer 1), 34.1 (q, J = 28.0 Hz, isomer 2), 28.6 (isomer 1), 27.6 (isomer 2), 26.2 (isomer 1), 26.0 (isomer 2), 14.12 (isomer 1), 14.11 (isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.65 (t, J = 11.3 Hz, 3F, isomer 1), -63.66 (t, J = 11.3 Hz, 3F, isomer 2); IR ν_{max} (neat) cm^{-1}: 2949, 1724, 1594, 1510, 1483, 1324, 1239, 1120, 1003, 834, 748, 721, 654; HRMS (ESI, m/z): calcd for $C_{29}H_{32}F_3N_2O_3^+$ $[M + H]^+$ 513.2360, found 513.2360.

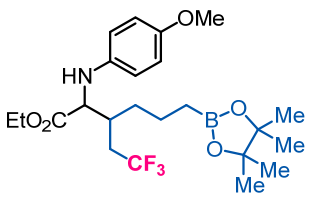


Ethyl 5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl) pentanoate (**4aq**): Following the general procedure A, compound **4aq** was prepared through a reaction between **1a**, alkene **2q** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 20:1 to 15:1) as a yellow oil (65.6 mg, 77% yield, a mixture of two diastereomers, *dr* = 1.0). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.85 – 6.72 (m, 2H), 6.68 – 6.57 (m, 2H), 4.30 – 4.08 (m, 2H + 1H, isomer 1), 4.03 – 3.83 (m, 5H + 1H, isomer 2), 3.73 (s, 3H), 2.64 – 2.39 (m, 1H), 2.35 – 2.25 (m, 1H, isomer 1), 2.25 – 2.16 (m, 1H, isomer 2), 2.16 – 1.95 (m, 1H), 1.80 – 1.65 (m, 2H + 1H, isomer 1), 1.60 – 1.39 (m, 1H + 1H, isomer 2), 1.31 (s, 3H), 1.25 (t, J = 7.1 Hz, 1H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.0 (isomer 1), 172.9 (isomer 2), 153.3 (isomer 1), 153.1 (isomer 2), 141.2 (isomer 1), 140.8 (isomer 2), 127.2 (q, J = 277.2 Hz, isomer 1), 127.1 (q, J = 277.1 Hz, isomer 2), 116.0 (isomer 1), 115.8 (isomer 2), 114.88 (isomer 1), 114.87 (isomer 2), 109.6 (isomer 1), 109.5 (isomer 2), 64.7 (isomer 1 + isomer 2), 61.4 (isomer 1), 61.3 (isomer 2), 60.5 (isomer 1), 60.4 (isomer 2), 55.7 (isomer 1), 55.6 (isomer 2), 36.3 (isomer 1), 35.9 (isomer 2), 35.8 (isomer 2), 35.7 (isomer 1), 34.3 (q, J = 27.9 Hz, isomer 1), 34.1 (q, J = 28.0 Hz, isomer 2), 25.1 (isomer 1), 24.1 (isomer 2), 23.9 (isomer 1), 23.8 (isomer 2), 14.2 (isomer 1), 14.1 (isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.84 (t, J = 11.3 Hz, 3F, isomer 1), -63.88 (t, J = 11.4 Hz, 3F,

isomer 2); IR ν_{max} (neat) cm^{-1}: 3364, 2982, 1729, 1514, 1379, 1235, 1120, 1032, 819, 732; HRMS (ESI, m/z): calcd for $C_{20}H_{29}F_3NO_5^+$ $[M + H]^+$ 420.1992, found 420.1994.

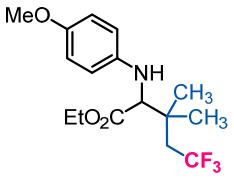


Ethyl 5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3-((trimethylsilyl)methyl)pentanoate (**4ar**): Following the general procedure A, compound **4ar** was prepared through a reaction between **1a**, allyl trimethyl silane **2r** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 70:1 to 50:1) as a yellow oil (74.4 mg, 95% yield, a mixture of two diastereomers, *dr* = 1.2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.85 – 6.71 (m, 2H), 6.78 – 6.66 (m, 1H, isomer 1), 6.63 – 6.55 (m, 1H, isomer 2), 4.30 – 4.10 (m, 2H + 1H, isomer 2), 4.10 – 4.04 (m, 1H, isomer 1), 4.04 – 3.95 (m, 1H, isomer 2), 3.88 – 3.78 (m, 1H, isomer 1), 3.74 (s, 3H), 2.74 – 2.45 (m, 1H + 1H, isomer 1), 2.44 – 2.33 (m, 1H, isomer 2), 2.19 – 2.04 (m, 1H, isomer 2), 2.04 – 1.85 (m, 1H, isomer 1), 1.28 (t, J = 7.2 Hz, 1H, isomer 2), 1.25 (t, J = 7.1 Hz, 1H, isomer 1), 0.93 (dd, J = 15.0, 5.2 Hz, 1H, isomer 1), 0.63 – 0.44 (m, 1H + 1H, isomer 2), 0.06 (s, 9H, isomer 1), 0.03 (s, 9H, isomer 2); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 174.6 (isomer 1), 173.8 (isomer 2), 154.6 (isomer 1), 154.2 (isomer 2), 142.7 (isomer 1), 141.8 (isomer 2), 128.4 (q, J = 277.2 Hz, isomer 1), 128.2 (q, J = 276.7 Hz, isomer 2), 117.6 (isomer 1), 116.6 (isomer 2), 116.2 (isomer 2), 116.1 (isomer 1), 62.7 (isomer 1), 62.63 (isomer 2), 62.60 (isomer 1), 62.5 (isomer 2), 56.95 (isomer 2), 56.92 (isomer 1), 37.8 (q, J = 33.7 Hz, isomer 1), 37.5 (q, J = 33.5 Hz, isomer 2), 33.2 (isomer 2), 33.0 (isomer 1), 19.5 (isomer 2), 18.0 (isomer 1), 15.5 (isomer 1 + 2), 0.2 (isomer 2), 0.0 (isomer 1); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.38 (t, J = 11.2 Hz, 3F, isomer 2), -63.83 (t, J = 11.2 Hz, 3F, isomer 1); IR ν_{max} (neat) cm^{-1}: 3370, 2954, 1735, 1516, 1249, 1126, 909, 837, 736, 648; HRMS (ESI, m/z): calcd for $C_{18}H_{29}F_3NO_3Si^+$ $[M + H]^+$ 392.1863, found 392.1863.

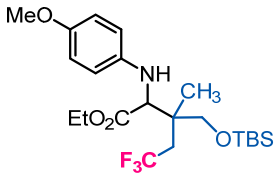


Ethyl 2-((4-methoxyphenyl)amino)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(2,2,2-trifluoroethyl)hexanoate (**4as**): Following the general procedure A, compound **4as** was

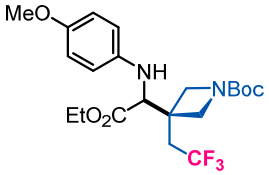
prepared through a reaction between **1a**, alkene **2s** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 20 to 15:1) as a yellow oil (74.8 mg, 79% yield, a mixture of two diastereomers, *dr* = 1.1). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.83 – 6.71 (m, 2H), 6.69 – 6.57 (m, 2H), 4.27 – 4.08 (m, 2H + 1H, isomer 1), 4.02 (d, *J* = 4.6 Hz, 1H, isomer 2), 3.73 (s, 3H), 2.61 – 2.35 (m, 1H), 2.35 – 2.23 (m, 1H, isomer 1), 2.23 – 1.99 (m, 1H + 1H, isomer 2), 1.71 – 1.58 (m, 1H, isomer 1), 1.58 – 1.31 (m, 3H + 1H, isomer 2), 1.29 – 1.16 (m, 15H), 0.85 - 0.69 (m, 2H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.1 (isomer 1 + isomer 2), 153.2 (isomer 1), 153.0 (isomer 2), 141.4 (isomer 1), 140.8 (isomer 2), 127.2 (q, *J* = 276.9 Hz, isomer 1), 127.1 (q, *J* = 276.9 Hz, isomer 2), 116.2 (isomer 1), 115.7 (isomer 2), 114.9 (isomer 1), 114.8 (isomer 2), 83.1 (isomer 1), 83.0 (isomer 2), 61.3 (isomer 1), 61.2 (isomer 2), 60.5 (isomer 1), 60.0 (isomer 2), 55.7 (isomer 1), 55.7 (isomer 2), 35.9 (q, *J* = 1.9 Hz, isomer 1), 35.5 (q, *J* = 2.1 Hz, isomer 2), 34.2 (q, *J* = 27.8 Hz, isomer 1), 34.1 (q, *J* = 27.5 Hz, isomer 2), 33.3 (isomer 1), 32.3 (isomer 2), 24.84 (isomer 1), 24.80 (isomer 1 + 2C, isomer 2), 21.4 (isomer 1), 21.0 (isomer 2), 14.2 (isomer 1), 14.2 (isomer 2), 11.1 (br, isomer 1 + isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.8 (t, *J* = 11.4 Hz, isomer 1), -63.8 (t, *J* = 11.3 Hz, isomer 2); IR ν_{max} (neat) cm^{-1}: 2978, 2935, 1732, 1151, 1370, 1318, 1236, 1161, 1034, 820, 753; HRMS (ESI, m/z): calcd for $C_{23}H_{36}BF_3NO_5^+$ $[M + H]^+$ 474.2633, found 474.2631.



Ethyl 5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3,3-dimethylpentanoate (**4at**): Following the general procedure A, compound **4at** was prepared through a reaction between **1a**, 2-methylpropene **2t** (3 equiv, 2 M solution in CH_2Cl_2) and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 50:1 to 30:1) as a yellowish oil (62.0 mg, 93% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.84 – 6.73 (m, 2H), 6.72 – 6.58 (m, 2H), 4.23 – 4.07 (m, 2H), 3.84 (s, 1H), 3.74 (s, 3H), 2.49 – 2.23 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.21 (s, 3H), 1.18 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.8, 153.4, 141.1, 127.1 (q, *J* = 278.4 Hz), 116.4, 114.8, 66.2, 61.0, 55.6, 41.3 (q, *J* = 26.5 Hz), 35.7, 24.3, 22.8, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.96 (t, *J* = 12.0 Hz; IR ν_{max} (neat) cm^{-1}: 3366, 2938, 1735, 1512, 1247, 1128, 1078, 809, 734; HRMS (ESI, m/z): calcd for $C_{16}H_{23}F_3NO_3^+$ $[M + H]^+$ 334.1625, found 334.1623.

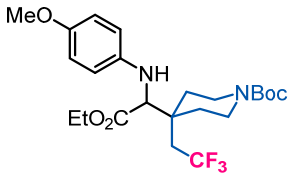


Ethyl 3-(((tert-butyldimethylsilyl)oxy)methyl)-5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3-methylpentanoate (**4au**): Following the general procedure A, compound **4au** was prepared through a reaction between **1a**, alkene **2u** and Togni II reagent, and it was isolated through a silica gel flash column (PE: EtOAc = 80:1 to 50:1) as a colorless oil (88.0 mg, 95% yield, a mixture of two diastereomers, *dr* = 2.0). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.75 – 6.62 (m, 2H), 6.61 – 6.54 (m, 2H, major), 6.53 – 6.46 (m, 2H, minor), 4.72 (brd, *J* = 11.0 Hz, 1H, minor), 4.06 (q, *J* = 7.0 Hz, 2H), 4.02 (s, 1H), 3.96 (brd, *J* = 10.1 Hz, 1H, major) 3.73 (d, *J* = 10.2 Hz, 1H, minor), 3.64 (s, 3H, major), 3.63 (s, 3H, minor), 3.58 (d, *J* = 10.1 Hz, 1H, major), 3.47 (d, *J* = 10.1 Hz, 1H, major), 3.37 (d, *J* = 10.2 Hz, 1H, minor), 2.60 – 2.19 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H, major), 1.11 (t, *J* = 7.1 Hz, 3H, minor), 1.03 (s, 3H, major), 0.99 (s, 3H, minor), 0.88 (s, 9H, minor), 0.86 (s, 9H, major), 0.04 – -0.04 (m, 6H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.9 (major), 172.8 (minor), 153.2 (major), 152.8 (minor), 141.5 (major), 141.4 (minor), 127.2 (d, *J* = 278.1 Hz, major), 127.2 (d, *J* = 278.1 Hz, minor), 116.1 (major), 115.3 (minor), 114.8 (minor), 114.7 (major), 67.2 (minor), 66.1 (major), 64.7 (minor), 62.9 (major), 61.0 (major), 60.9 (minor), 55.6 (major + minor), 40.9 (major), 39.2 (minor), 37.1 (q, *J* = 26.9 Hz, minor), 35.7 (q, *J* = 27.2 Hz, major), 25.8 (major + minor), 18.3 (major + minor), 18.2 (minor), 17.4 (major), 14.3 (minor), 14.2 (major), -5.7 (major + minor), -5.8 (major), -5.9 (minor); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.45 (t, *J* = 12.1 Hz, 3F, major), -58.82 (t, *J* = 12.0 Hz, 3F, minor); IR ν_{max} (neat) cm^{-1}: 3374, 2932, 1729, 1516, 1237, 1098, 835, 777, 672; HRMS (ESI, m/z): calcd for $C_{22}H_{37}F_3NO_4Si^+$ $[M + Na]^+$ 464.2438, found 464.2440.

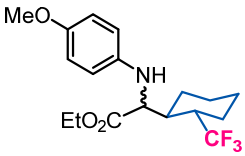


Tert-butyl 3-(2-ethoxy-1-((4-methoxyphenyl)amino)-2-oxoethyl)-3-(2,2,2-trifluoroethyl)azetidine-1-carboxylate (**4av**): Following the general procedure A, compound **4av** was prepared through a reaction between **1a**, alkene **2v** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 30:1 to 15:1) as a colorless oil (65.1 mg, 73% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.84 – 6.73 (m, 2H), 6.73 – 6.64 (m, 2H), 4.27 – 4.11 (m, 4H), 4.07 (d, *J* = 9.7 Hz,

1H), 4.00 – 3.90 (br, 1H), 3.87 (d, J = 9.7 Hz, 1H), 3.80 (d, J = 9.0 Hz, 1H), 3.74 (s, 3H), 2.79 (dq, J = 14.5, 11.0 Hz, 1H), 2.62 – 2.44 (m, 1H), 1.43 (s, 9H), 1.24 (t, J = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 171.6, 156.1, 153.7, 140.5, 126.2 (q, J = 278.6 Hz), 116.5, 114.9, 80.0, 61.8, 61.2, 55.6, 55.3 (br), 38.3 (q, J = 27.3 Hz), 37.1, 28.3, 14.1; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -60.41 (t, J = 11.0 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3251, 2948, 1648, 1554, 1508, 1359, 1263, 1233, 1108, 1062, 819, 694; HRMS (ESI, m/z): calcd for $C_{21}H_{30}F_3N_2O_5^+$ $[M + H]^+$ 447.2101, found 447.2104.



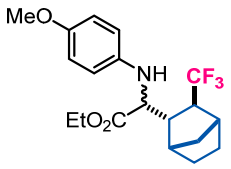
Tert-butyl 4-(2-ethoxy-1-((4-methoxyphenyl)amino)-2-oxoethyl)-4-(2,2,2-trifluoroethyl)piperidine -1-carboxylate (**4aw**): Following the general procedure A, compound **4aw** was prepared through a reaction between **1a**, alkene **2w** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 30:1 to 15:1) as a white solid (85.4 mg, 90% yield, m.p.: 72 – 75 °C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.81 – 6.72 (m, 2H), 6.70 – 6.61 (m, 2H), 4.24 (s, 1H), 4.21 – 4.06 (m, 2H), 3.96 – 3.64 (m, 3H), 3.73 (s, 3H), 3.28 – 3.01 (m, 2H), 2.66 (dq, J = 15.4, 11.9 Hz, 1H), 2.43 (dq, J = 15.4, 11.6 Hz, 1H), 1.84 (ddd, J = 14.5, 10.5, 4.3 Hz, 1H), 1.78 – 1.54 (m, 3H), 1.38 (s, 9H), 1.14 (t, J = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 172.6, 154.8, 153.6, 140.9, 127.0 (q, J = 278.8 Hz), 116.7, 114.8, 79.8, 62.9, 61.3, 55.6, 39.5 (br), 38.9 (br), 37.7, 34.6 (q, J = 26.5 Hz), 30.2, 29.8, 28.4, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.01 (t, J = 11.7 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3368, 2986, 1723, 1676, 1514, 1425, 1365, 1245, 1162, 1132, 1094, 811, 676; HRMS (ESI, m/z): calcd for $C_{23}H_{34}F_3N_2O_5^+$ $[M + H]^+$ 475.2414, found 475.2412.



Ethyl 2-((4-methoxyphenyl)amino)-2-(trifluoromethyl)cyclohexyl)acetate (**4ax**): Following the general procedure A, compound **4ax** was prepared through a reaction between **1a**, cyclohexene **2x** (3.0 equiv) and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 50:1 to 30:1).

Isomer 1 (less polar, colorless oil, 31.9 mg, 44% yield): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.88 – 6.71 (m, 2H), 6.67 – 6.53 (m, 2H), 4.34 (s, 1H), 4.31 – 4.10 (m, 3H), 3.74 (s, 3H), 2.54 (hd, *J* = 9.2, 4.0 Hz, 1H), 2.12 – 1.90 (m, 3H), 1.80 – 1.65 (m, 2H), 1.52 – 1.37 (m, 1H), 1.35 – 1.20 (m, 2H), 1.29 (t, *J* = 7.4 Hz, 3H) 1.10 – 0.90 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.4, 152.7, 140.8, 128.2 (q, *J* = 281.2 Hz), 115.1, 115.0, 61.3, 58.8, 55.7, 41.5 (q, *J* = 24.9 Hz), 39.2, 26.3, 24.7 (q, *J* = 3.4 Hz), 24.2, 24.1, 14.3; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -66.88 (d, *J* = 9.3 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3396, 2936, 1733, 1512, 1255, 1162, 1132, 1104, 1080, 1034, 813, 688; HRMS (ESI, m/z): calcd for $C_{18}H_{25}F_3NO_3^+$ $[M + H]^+$ 360.1781, found 360.1780.

Isomer 2 (more polar, white solid, 29.9 mg, 42% yield, m.p.: 69 – 73 °C): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.83 – 6.72 (m, 2H), 6.72 – 6.62 (m, 2H), 4.37 (s, 1H), 4.24 – 4.06 (m, 2H), 3.82 – 3.63 (m, 4H), 2.54 – 2.35 (m, 1H), 2.23 – 2.10 (m, 1H), 2.10 – 2.01 (m, 2H), 1.91 – 1.71 (m, 2H), 1.63 – 1.52 (m, 1H), 1.45 – 1.25 (m, 4H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.5, 153.3, 141.4, 127.8 (q, *J* = 281.2 Hz), 116.5, 114.7, 61.1, 59.4 (d, *J* = 2.3 Hz), 55.6, 41.8 (q, *J* = 24.6 Hz), 39.1, 25.7, 25.4 (q, *J* = 3.6 Hz), 25.1, 24.5, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -68.09 (d, *J* = 8.3 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3372, 2946, 1741, 1514, 1247, 1158, 1136, 1080, 1038, 815, 734; HRMS (ESI, m/z): calcd for $C_{18}H_{25}F_3NO_3^+$ $[M + H]^+$ 360.1781, found 360.1781.

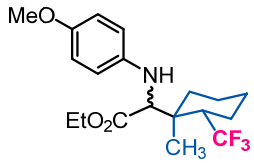


Ethyl 2-((4-methoxyphenyl)amino)-3-(trifluoromethyl)bicyclo[2.2.1]heptan-2-yl)acetate (**4ay**): Following the general procedure A, compound **4ay** was prepared through a reaction between **1a**, norbornene **2y** (3.0 equiv) and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 50:1 to 30:1).

Isomer 1 (less polar, colorless oil, 33.5 mg, 45%): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.87 – 6.68 (m, 2H), 6.65 – 6.51 (m, 2H), 4.24 – 4.10 (m, 2H), 4.05 – 3.87 (br, 1H), 3.80 (d, *J* = 10.8 Hz, 1H), 3.74 (s, 3H), 2.57 – 2.44 (m, 1H), 2.28 – 2.17 (m, 2H), 2.08 – 1.95 (m, 1H), 1.91 – 1.81 (m, 1H), 1.77 – 1.64 (m, 2H), 1.58 – 1.48 (m, 1H), 1.35 – 1.25 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.8, 152.8, 140.7, 127.4 (q, *J* = 278.3 Hz), 114.9, 114.8, 61.0, 59.7, 55.7, 50.4 (q, *J* = 26.2 Hz), 45.3, 38.9, 38.7 (q, *J* = 2.2 Hz), 37.7, 28.9, 23.2, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -67.96 (d, *J* = 9.7 Hz); IR ν_{max} (neat) cm^{-1}: 3370, 2964, 1731, 1514, 1237, 1140,

1106, 1028, 907, 819, 726; HRMS (ESI, m/z): calcd for $C_{19}H_{25}F_3NO_3^+$ $[M + H]^+$ 372.1781, found 372.1781.

Isomer 2 (more polar, colorless oil, 34.6 mg, 47% yield): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.86 – 6.69 (m, 2H), 6.67 – 6.47 (m, 2H), 4.20 – 3.99 (m, 2H), 3.80 – 3.68 (m, 2H), 3.73 (s, 3H), 2.64 – 2.55 (m, 1H), 2.51 (d, *J* = 4.5 Hz, 1H), 2.26 – 2.16 (m, 1H), 2.16 – 2.00 (m, 1H), 1.74 – 1.60 (m, 2H), 1.59 – 1.39 (m, 2H), 1.36 – 1.26 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.8, 153.1, 140.8, 127.3 (q, *J* = 278.7 Hz), 115.5, 114.9, 61.1, 60.0, 55.7, 49.0 (q, *J* = 26.6 Hz), 44.7, 38.8, 38.5 (q, *J* = 2.2 Hz), 36.9, 29.1, 22.3, 14.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -69.19 (d, *J* = 9.6 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3368, 2970, 1733, 1510, 1237, 1148, 1108, 1032, 907, 823, 724; HRMS (ESI, m/z): calcd for $C_{19}H_{25}F_3NO_3^+$ $[M + H]^+$ 372.1781, found 372.1783.

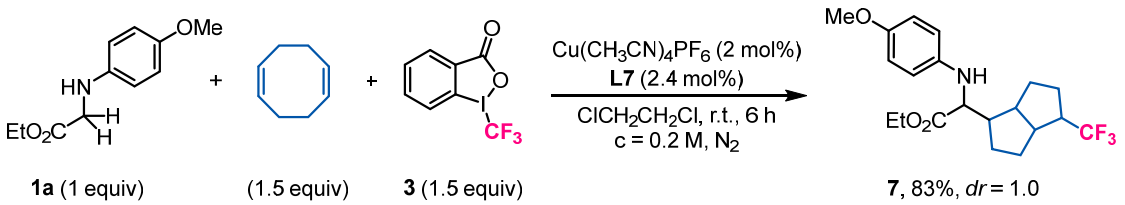


Ethyl 2-((4-methoxyphenyl)amino)-1-methyl-2-(trifluoromethyl)cyclohexyl)acetate (**4az**): Following the general procedure A, compound **4az** was prepared through a reaction between **1a**, 1-methylcyclohexene **2z** (3.0 equiv) and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 50:1 to 30:1).

Isomer 1 (less polar, colorless oil, 24.5 mg, 33% yield): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.84 – 6.72 (m, 2H), 6.72 – 6.59 (m, 2H), 4.36 (s, 1H), 4.28 – 4.17 (m, 1H), 4.17 – 4.05 (m, 1H), 4.04 – 3.82 (br, 1H), 3.74 (s, 3H), 2.70 – 2.40 (m, 1H), 1.92 – 1.56 (m, 5H), 1.52 – 1.33 (m, 3H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.21 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.8, 153.1, 141.8, 128.4 (q, *J* = 282.5 Hz), 116.2, 114.8, 64.5, 61.0, 55.7, 44.4 (q, *J* = 23.3 Hz), 39.2, 32.5, 23.8, 22.6 (q, *J* = 3.6 Hz), 21.0, 18.2, 14.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -61.49 (d, *J* = 9.3 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3382, 2934, 1721, 1516, 1230, 1156, 1076, 1034, 819, 738; HRMS (ESI, m/z): calcd for $C_{19}H_{27}F_3NO_3^+$ $[M + H]^+$ 374.1938, found 374.1936.

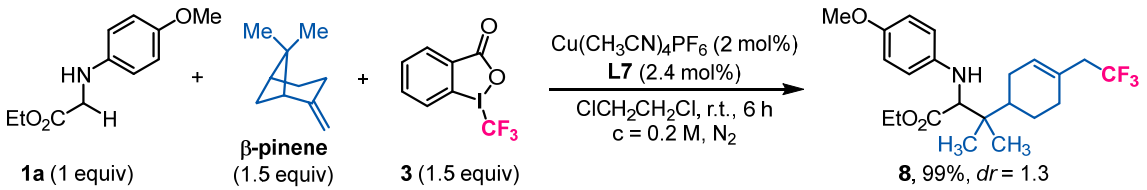
Isomer 2 (more polar, white solid, 27.0 mg, 36% yield, m.p.: 88 – 91 °C): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.82 – 6.73 (m, 2H), 6.73 – 6.62 (m, 2H), 4.31 (s, 1H), 4.21 – 4.00 (m, 2H), 3.99 – 3.78 (br, 1H), 3.74 (s, 3H), 2.97 – 2.77 (m, 1H), 1.96 – 1.85 (m, 1H), 1.85 – 1.74 (m, 1H), 1.69 – 1.55 (m, 2H), 1.53 – 1.35 (m, 3H), 1.31 – 1.24 (m, 1H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.18 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.1, 153.5, 141.0, 128.3 (q, *J* = 282.5 Hz), 117.0, 114.7, 64.9, 60.8,

55.6, 43.3 (q, J = 23.2 Hz), 38.2, 33.0, 24.7, 22.1 (q, J = 3.5 Hz), 21.0, 18.4, 14.3; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.91 (d, J = 9.5 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3358, 2928, 1719, 1508, 1231, 1202, 1160, 1130, 1074, 1034, 821, 748, 690; HRMS (ESI, m/z): calcd for $C_{19}H_{27}F_3NO_3^+$ [M + H]$^+$ 374.1938, found 374.1937.



1a (1 equiv) (1.5 equiv) **3** (1.5 equiv) **7**, 83%, *dr* = 1.0

Ethyl 2-((4-methoxyphenyl)amino)-2-(4-(trifluoromethyl)octahydropentalen-1-yl)acetate (**7**): Following the general procedure A, compound **7** was prepared through a reaction between **1a**, 1,5-cyclooctadiene and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 50:1 to 30:1) as a colorless oil (63.9 mg, 83% yield, a mixture of two diastereomers, *dr* = 1.0). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.85 – 6.68 (m, 2H), 6.68 – 6.52 (m, 2H), 4.23 – 4.05 (m, 2H), 3.93 – 3.76 (m, 2H), 3.73 (s, 3H), 2.73 – 2.41 (m, 2H), 2.35 – 2.16 (m, 1H), 2.12 – 1.71 (m, 6H), 1.66 – 1.52 (m, 1H), 1.44 – 1.30 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 174.2 (isomer 1), 174.1 (isomer 2), 152.8 (isomer 1 + isomer 2), 141.3 (isomer 1), 141.2 (isomer 2), 128.3 (q, J = 277.9 Hz, isomer 1), 128.2 (q, J = 277.6 Hz, isomer 2), 115.3 (isomer 1 + isomer 2), 114.9 (isomer 1 + isomer 2), 61.4 (isomer 1), 61.2 (isomer 2), 61.0 (isomer 1), 60.9 (isomer 2), 55.7 (isomer 1 + isomer 2), 50.6 (q, J = 26.3 Hz, isomer 1), 50.5 (isomer 1), 50.4 (q, J = 26.3 Hz, isomer 2), 50.3 (isomer 2), 47.4 (isomer 1), 46.4 (isomer 2), 44.7 (isomer 1), 44.5 (isomer 2), 33.1 (isomer 1), 32.5 (isomer 2), 32.3 (isomer 1), 31.8 (isomer 2), 31.4 (isomer 1), 31.3 (isomer 2), 28.5 (q, J = 2.5 Hz, isomer 1), 28.1 (q, J = 2.4 Hz, isomer 2), 14.3 (isomer 1 + isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -70.52 (m, 3F, isomer 1 + isomer 2); IR ν_{max} (neat) cm^{-1}: 3368, 2956, 1729, 1512, 1466, 1391, 1261, 1241, 1152, 1098, 899, 817, 728; HRMS (ESI, m/z): calcd for $C_{20}H_{27}F_3NO_3^+$ [M + H]$^+$ 386.1938, found 386.1936.

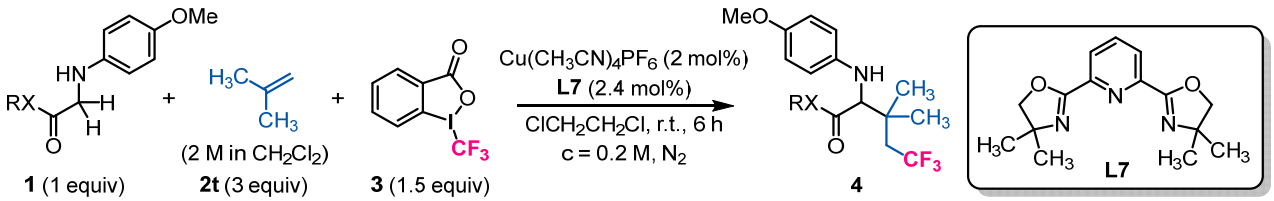


1a (1 equiv) β-pinene (1.5 equiv) **3** (1.5 equiv) **8**, 99%, *dr* = 1.3

Ethyl 2-((4-methoxyphenyl)amino)-3-methyl-3-(4-(2,2,2-trifluoroethyl)cyclohex-3-en-1-yl) butanoate (**8**): Following the general procedure A, compound **8** was prepared through a reaction

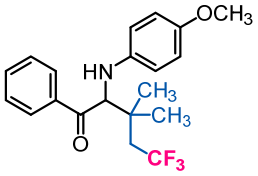
between **1a**, β-pinene and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 50:1 to 30:1) as a colorless oil (81.9 mg, 99% yield, a mixture of two diastereomers, *dr* = 1.3). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.84 – 6.70 (m, 2H), 6.68 – 6.53 (m, 2H), 5.69 (d, *J* = 6.6 Hz, 1H, isomer 2), 5.64 (d, *J* = 4.9 Hz, 1H, isomer 1), 4.21 – 4.05 (m, 2H), 4.02 – 3.94 (m, 1H), 3.92 – 3.79 (br, 1H), 3.73 (s, 3H), 2.70 (q, *J* = 11.2 Hz, 1H), 2.24 – 2.02 (m, 3H), 2.02 – 1.75 (m, 3H), 1.73 – 1.62 (m, 1H, isomer 2), 1.38 – 1.24 (m, 1H + 1H, isomer 1), 1.21 (t, *J* = 7.1 Hz, 1H), 1.06 (s, 3H, isomer 1), 1.01 (s, 3H, isomer 2), 0.93 (s, 3H, isomer 1), 0.92 (s, 3H, isomer 2); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 173.8 (isomer 2), 173.8 (isomer 1), 152.9 (isomer 1 + isomer 2), 141.7 (isomer 2), 141.5 (isomer 1), 129.0 (isomer 1 + isomer 2), 127.6 (d, *J* = 2.3 Hz, isomer 1 + isomer 2), 126.2 (q, *J* = 269.4 Hz, isomer 1), 126.1 (q, *J* = 270.0 Hz, isomer 2), 115.7 (isomer 2), 115.6 (isomer 1), 114.9 (isomer 1 + isomer 2), 63.7 (isomer 2), 63.6 (isomer 1), 60.6 (isomer 1 + isomer 2), 55.7 (isomer 1 + isomer 2), 41.60 (q, *J* = 28.7 Hz, isomer 1), 41.55 (q, *J* = 28.8 Hz, isomer 2), 39.8 (isomer 1), 39.1 (isomer 2), 38.9 (isomer 2), 38.8 (isomer 1), 30.1 (isomer 2), 30.0 (isomer 1), 26.7 (isomer 1), 26.5 (isomer 2), 24.1 (isomer 2), 23.8 (isomer 1), 20.3 (isomer 1), 20.2 (isomer 1 + isomer 2), 20.0 (isomer 2), 14.3 (isomer 1), 14.2 (isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -64.76 (t, *J* = 11.1 Hz, 3F, isomer 1), -64.81 (t, *J* = 11.2 Hz, 3F, isomer 2); IR ν_{max} (neat) cm^{-1}: 3378, 2938, 1725, 1516, 1235, 1122, 1030, 907, 821, 728, 638; HRMS (ESI, m/z): calcd for $C_{22}H_{31}F_3NO_3^+$ [M + H]$^+$ 414.2251, found 414.2252.

b) General procedure for the three-component ligation of different glycine derivatives

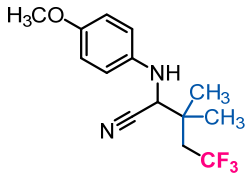


In a N_2 atmosphere glovebox, $Cu(CH_3CN)_4PF_6$ (1.5 mg, 0.004 mmol), and ligand **L7** (1.3 mg, 0.0048 mmol) were weighted into a 1-dram vial, which was then charged with a stir bar and sealed under N_2 with a septum. After the vial was taken out from the glovebox, freshly distilled 1,2-dichloroethane (1.0 mL) was added to afford a clear catalyst solution. To a flame-dried reaction tube charged with a stir bar were added an ethyl glycinate **1** (0.2 mmol) and Togni II reagent **3** (94.8 mg, 0.3 mmol). The tube was sealed with a septum, evacuated, and backfilled with N_2 three times. The above catalyst solution (1.0 mL) was transferred into the reaction tube together with alkene **2t**

(0.3 mL, 2.0 M solution in CH_2Cl_2, 0.6 mmol), and the reaction was kept stirring at room temperature (23 to 26 °C) for 6 h. After the reaction was quenched with saturated $NaHCO_3$ aqueous solution (1 mL) and $Na_2S_2O_3$ aqueous solution (1 mL), the organic phase was separated and the aqueous one was extracted with CH_2Cl_2 (1 mL × 3). The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo*, and then purified through a silica gel flash column.

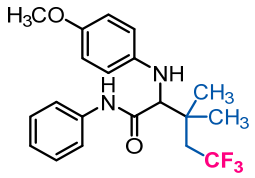


5,5,5-Trifluoro-2-((4-methoxyphenyl)amino)-3,3-dimethyl-1-phenylpentan-1-one (**4dt**): Following the general procedure B, compound **4dt** was prepared through a reaction between **1d**, 2-methylproene **2t** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 20:1 to 15:1) as a white solid (60.7 mg, 83% yield, m.p.: 61 – 64 °C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 – 7.73 (m, 2H), 7.57 – 7.44 (m, 1H), 7.42 – 7.33 (m, 2H), 6.72 – 6.56 (m, 4H), 4.86 (s, 1H), 4.52 – 3.95 (br, 1H), 3.63 (s, 3H), 2.61 (dq, J = 15.1, 12.0 Hz, 1H), 2.27 (dq, J = 15.1, 12.0 Hz, 1H), 1.10 (s, 3H), 1.08 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 203.1, 153.4, 141.5, 138.1, 133.6, 128.9, 128.2, 126.4 (q, J = 278.4 Hz), 116.9, 114.9, 64.8, 55.6, 41.2 (q, J = 26.1 Hz), 36.7, 25.4, 23.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.73 (t, J = 12.0 Hz); IR ν_{max} (neat) cm^{-1}: 3346, 2962, 1680, 1512, 1367, 1224, 1088, 819, 748, 690; HRMS (ESI, m/z): calcd for $C_{20}H_{23}F_3NO_2^+$ $[M + H]^+$ 366.1675, found 366.1677.

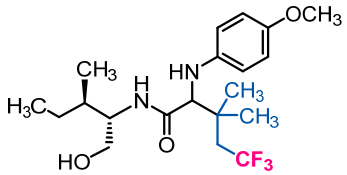


5,5,5-Trifluoro-2-((4-methoxyphenyl)amino)-3,3-dimethylpentanenitrile (**4et**): Following the general procedure B, compound **4et** was prepared through a reaction between **1e**, 2-methylpropene **2t** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 15:1 to 10:1) as a colorless oil (53.8 mg, 94% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.92 – 6.80 (m, 2H), 6.80 – 6.70 (m, 2H), 4.04 (s, 1H), 3.77 (s, 3H), 3.53 – 3.26 (brs, 1H), 2.55 – 2.24 (m, 2H), 1.35 (s, 3H), 1.29 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 154.8, 138.6, 126.5 (q, J = 278.4 Hz), 118.3, 117.7, 115.0, 57.8, 55.6, 40.7 (q, J = 27.3 Hz), 35.9, 24.2, 23.1; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -59.42 (t, J = 11.7 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3343, 2976, 2246, 1511, 1470, 1372,

1260, 1232, 1108, 819, 733, 691; HRMS (ESI, m/z): calcd for $C_{14}H_{18}F_3N_2O^+$ $[M + H]^+$ 287.1366, found 287.1366.

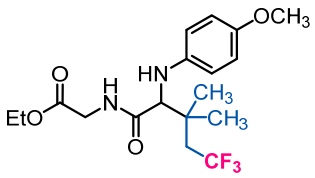


5,5,5-Trifluoro-2-((4-methoxyphenyl)amino)-3,3-dimethyl-N-phenylpentanamide (**4ft**): Following the general procedure B, compound **4ft** was prepared through a reaction between **1f**, 2-methylpropene **2t** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 20:1 to 15:1) as a white solid (71.5 mg, 94% yield, m.p.: 76 – 78 °C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.53 (s, 1H), 7.52 – 7.39 (m, 2H), 7.34 – 7.24 (m, 2H), 7.16 – 7.06 (m, 1H), 6.85 – 6.73 (m, 2H), 6.72 – 6.58 (m, 2H), 3.98 (d, *J* = 4.0 Hz, 1H), 3.73 (s, 3H), 3.60 (d, *J* = 4.0 Hz, 1H), 2.50 (q, *J* = 11.8 Hz, 2H), 1.31 (s, 3H), 1.28 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 170.0, 153.8, 140.7, 137.0, 129.0, 126.9 (q, *J* = 278.6 Hz), 124.8, 120.3, 116.0, 115.0, 68.9, 55.7, 41.7 (q, *J* = 26.6 Hz), 36.1, 24.4, 24.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.60 (t, *J* = 11.8 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3265, 2926, 1654, 1508, 1230, 1100, 1036, 809, 744, 690; HRMS (ESI, m/z): calcd for $C_{20}H_{24}F_3N_2O_2^+$ $[M + H]^+$ 381.1784, found 381.1784.

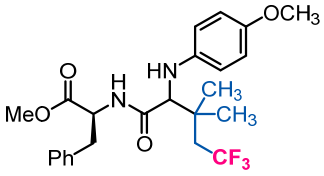


5,5,5-Trifluoro-N-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-2-((4-methoxyphenyl)amino)-3,3-dimethylpentanamide (**4gt**): Following the general procedure B, compound **4gt** was prepared through a reaction between **1g**, 2-methylpropene **2t** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 2:1 to 1:1) as a white solid (71.2 mg, 88% yield, mixture of two diastereomers, *dr* = 1.5). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.83 – 6.71 (m, 2H), 6.70 – 6.58 (m, 2H + 1H, minor), 6.57 – 6.48 (m, 1H, major), 3.79 - 3.68 (m, 4H), 3.64 – 3.52 (m, 2H), 3.49 (s, 1H), 2.75 – 2.20 (br, 1H), 2.43 (q, *J* = 11.9 Hz, 2H), 1.58 – 1.43 (m, 1H), 1.34 – 1.25 (m, 1H), 1.25 (s, 3H), 1.22 (s, 3H), 1.03 – 0.89 (m, 1H), 0.85 - 0.72 (m, 6H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.2 (minor), 172.0 (major), 153.7 (major), 153.6 (minor), 140.8 (major), 140.7 (minor), 127.0 (q, *J* = 279.2 Hz, major + minor), 116.3 (major), 116.0 (minor), 114.9 (major + minor), 68.7 (major),

68.4 (minor), 63.8 (minor), 63.4 (major), 55.9 (minor), 55.8 (major), 55.7 (minor), 55.6 (major), 41.6 (q, J = 26.4 Hz, major + minor), 35.4 (major + minor), 35.3 (minor), 35.2 (major), 25.4 (major), 25.3 (minor), 24.3 (2 major + minor), 24.1 (minor), 15.5 (minor), 15.4 (major), 11.0 (major + minor); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.63 – -58.78 (m, 3F, major + minor); IR ν_{max} (neat) cm^{-1}: 3275, 2968, 1640, 1508, 1367, 1263, 1235, 1106, 1060, 829, 676; HRMS (ESI, m/z): calcd for $C_{20}H_{32}F_3N_2O_3^+$ $[M + H]^+$ 405.2360, found 405.2357.



Ethyl (5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3,3-dimethylpentanoyl)glycinate (**4ht**): Following the general procedure B, compound **4ht** was prepared through a reaction between **1h**, 2-methylpropene **2t** and Togni II reagent, and it was isolated through a silica gel flash column (PE: EtOAc = 5:1 to 2:1) as a white solid (65.5 mg, 84% yield, m.p.: 72 – 74 °C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.87 (t, J = 5.6 Hz, 1H), 6.75 – 6.64 (m, 2H), 6.60 – 6.48 (m, 2H), 4.09 (q, J = 7.1 Hz, 2H), 3.95 (dd, J = 18.1, 5.7 Hz, 1H), 3.90 – 3.82 (br, 1H), 3.85 (dd, J = 18.1, 5.4 Hz, 1H), 3.66 (s, 3H), 3.47 (s, 1H), 2.47 – 2.26 (m, 2H), 1.23 – 1.06 (m, 9H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 171.8, 169.5, 153.4, 141.0, 127.0 (q, J = 278.6 Hz), 115.8, 114.9, 67.9, 61.5, 55.7, 41.3 (q, J = 26.6 Hz), 41.2, 35.8, 24.2, 24.1, 14.1; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.67 (t, J = 11.8 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3400, 3356, 2984, 1747, 1660, 1512, 1379, 1204, 1110, 1020, 817; HRMS (ESI, m/z): calcd for $C_{18}H_{26}F_3N_2O_4^+$ $[M + H]^+$ 391.1839, found 391.1837.

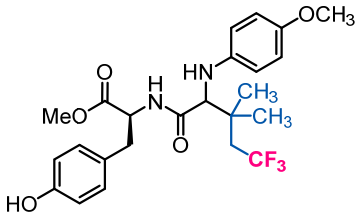


Methyl (5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3,3-dimethylpentanoyl)-L-phenylalaninate (**4it**): Following the general procedure B, compound **4it** was prepared through a reaction between **1i**, 2-methylpropene **2t** and Togni II reagent **3**, and it was isolated through a silica gel flash column (PE: EtOAc = 5:1 to 3:1).

Minor isomer (less polar, white soild, 28.9 mg, 31% yield, m.p.: 90 – 93 °C): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.07 (m, 3H), 6.92 – 6.82 (m, 2H), 6.82 – 6.75 (m, 2H), 6.69 – 6.60 (m, 2H),

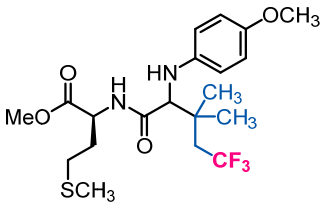
6.51 (d, J = 7.9 Hz, 1H), 4.99 – 4.80 (m, 1H), 3.91 – 3.79 (br, 1H), 3.76 (s, 3H), 3.68 (s, 3H), 3.40 (s, 1H), 3.10 (dd, J = 14.0, 5.3 Hz, 1H), 2.98 (dd, J = 14.0, 6.7 Hz, 1H), 2.30 (q, J = 11.9 Hz, 2H), 1.13 (s, 3H), 1.08 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 171.5, 171.3, 153.7, 141.2, 135.5, 129.1, 128.6, 127.1, 127.0 (q, J = 278.6 Hz), 116.9, 114.9, 68.9, 55.7, 53.0, 52.4, 41.1 (q, J = 26.6 Hz), 37.6, 35.7, 24.2, 23.8; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.68 (t, J = 11.9 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3378, 2956, 1733, 1652, 1510, 1104, 1036, 917, 811, 726, 698; HRMS (ESI, m/z): calcd for $C_{24}H_{30}F_3N_2O_4^+$ $[M + H]^+$ 467.2152, found 467.2150.

Major isomer (more polar, brownish soild, 43.8 mg, 47% yield, m.p.: 122 – 124 °C): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 – 7.05 (m, 3H), 6.97 (d, J = 8.5 Hz, 1H), 6.88 – 6.69 (m, 4H), 6.60 – 6.43 (m, 2H), 4.99 – 4.80 (m, 1H), 3.84 – 3.78 (br, 1H), 3.76 (s, 3H), 3.69 (s, 3H), 3.45 (s, 1H), 3.04 (dd, J = 13.9, 6.7 Hz, 1H), 2.97 (dd, J = 13.9, 5.4 Hz, 1H), 2.48 – 2.23 (m, 2H), 1.19 (s, 3H), 1.14 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 171.7, 171.0, 153.4, 140.6, 135.4, 129.0, 128.6, 127.0, 126.9 (q, J = 278.7 Hz), 115.3, 114.9, 67.8, 55.7, 52.5, 52.3, 41.4 (q, J = 26.4, 25.6 Hz), 37.8, 35.6, 24.4, 24.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.73 (t, J = 11.8 Hz); IR ν_{max} (neat) cm^{-1}: 3352, 2924, 1751, 1660, 1516, 1249, 1110, 1066, 809, 692; HRMS (ESI, m/z): calcd for $C_{24}H_{30}F_3N_2O_4^+$ $[M + H]^+$ 467.2152, found 467.2151.



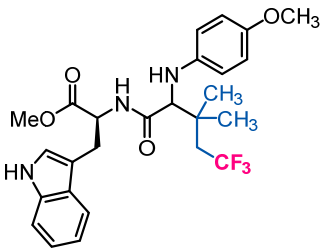
Methyl (5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3,3-dimethylpentanoyl)-L-tyrosinate (**4jt**): Following the general procedure B, compound **4jt** was prepared through a reaction between **1j**, 2-methylpropene **2t** and Togni II reagent **3**, and it was isolated through a silica gel flash column (CH_2Cl_2:MeOH = 50:1 to 30:1) as a white foam (84.9 mg, 88% yield, a mixture of two diastereomers, *dr* = 1.1). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.11 (d, J = 8.7 Hz, 1H, isomer 1), 6.84 – 6.73 (m, 2H), 6.73 – 6.45 (m, 7H + 1H, isomer 2), 4.95 – 4.78 (m, 1H), 3.95 – 3.80 (br, 1H), 3.80 – 3.76 (s, 3H), 3.70 (s, 3H, isomer 1), 3.68 (s, 3H, isomer 2), 3.48 (s, 1H, isomer 1), 3.44 (s, 1H, isomer 2), 3.11 – 2.82 (m, 2H), 2.45 – 2.24 (m, 2H), 1.20 (s, 3H, siomer 1), 1.17 (s, 3H, isomer 1), 1.15 (s, 3H, isomer 2), 1.11 (s, 3H, isomer 2); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 172.0 (isomer 2), 171.7 (isomer 1 + isomer 2), 171.5 (isomer 1), 155.3 (isomer 2), 155.2 (isomer 1), 153.6

(isomer 2), 153.3 (isomer 1), 141.2 (isomer 2), 140.6 (isomer 1), 130.2 (isomer 2), 130.1 (isomer 1), 127.0 (q, J = 278.7 Hz, isomer 2), 126.9 (q, J = 278.5 Hz, isomer 1), 126.8 (isomer 2), 126.7 (isomer 1), 116.9 (isomer 1), 115.7 (isomer 2), 115.6 (isomer 1), 115.2 (isomer 2), 115.1 (isomer 2), 115.0 (isomer 1), 68.7 (isomer 2), 67.7 (isomer 1), 55.8 (isomer 1), 55.7 (isomer 2), 53.3 (isomer 2), 52.8 (isomer 1), 52.4 (isomer 2), 52.3 (isomer 1), 41.4 (q, J = 26.4 Hz, isomer 1), 41.1 (q, J = 26.0 Hz, isomer 2), 36.9 (isomer 2), 36.8 (isomer 1), 35.7 (isomer 1), 35.6 (isomer 2), 24.3 (isomer 2), 24.2 (isomer 1), 24.1 (isomer 2), 23.7 (isomer 1); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.66 (t, J = 11.8 Hz, 3F, isomer 1), -58.71 (t, J = 11.2 Hz, 3F, isomer 2); IR ν_{max} (neat) cm^{-1}: 3350, 2978, 1731, 1686, 1512, 1393, 1235, 1016, 909, 819, 724; HRMS (ESI, m/z): calcd for $C_{24}H_{30}F_3N_2O_5^+$ $[M + H]^+$ 483.2101, found 483.2099.



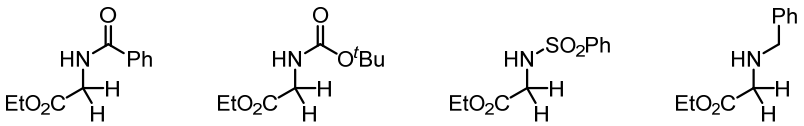
Methyl S-methyl-N-(5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3,3-dimethylpentanoyl)-L-cysteinate (**4kt**): Following the general procedure B, compound **4kt** was prepared through a reaction between **1k**, 2-methylpropene **2t** and Togni II reagent **3**, and it was isolated through a silica gel flash column (CH_2Cl_2:MeOH = 50:1 to 30:1) as a white foam (79.4 mg, 88% yield, a mixture of two diastereomers, *dr* = 1.5). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 (d, J = 8.3 Hz, 1H, major), 6.86 (d, J = 8.0 Hz, 1H, minor), 6.79 – 6.70 (m, 2H), 6.69 – 6.62 (m, 2H, minor), 6.61 – 6.51 (m, 2H, major), 4.75 – 4.58 (m, 1H), 3.96 – 3.81 (m, 1H), 3.71 (s, 3H), 3.69 (s, 3H, major), 3.67 (s, 3H, minor), 3.56 – 3.47 (m, 1H), 2.51 – 2.33 (m, 2H), 2.28 – 2.16 (m, 2H), 2.12 – 2.00 (m, 1H), 1.94 (s, 3H, minor), 1.90 (s, 3H, major), 1.90 – 1.78 (m, 1H), 1.28 – 1.17 (m, 6H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.0 (major), 171.9 (minor), 171.6 (minor), 171.2 (major), 153.7 (minor), 153.5 (major), 141.1 (minor), 140.5 (major), 127.1 (q, J = 278.8 Hz, minor), 126.9 (q, J = 278.6 Hz, major), 116.8 (minor), 115.4 (major), 114.9 (major), 114.8 (minor), 68.5 (minor), 67.8 (major), 55.7 (major), 55.6 (minor), 52.5 (major + minor), 51.5 (minor), 51.2 (major), 41.4 (q, J = 26.5 Hz, major), 41.3 (q, J = 26.4 Hz, minor), 35.7 (minor), 35.5 (major), 31.2 (minor), 30.9 (major), 29.8 (minor), 29.7 (major), 24.3 (major + minor), 24.2 (major), 23.8 (minor), 15.3 (minor), 15.2 (major); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.56 – -58.84 (m, 3F, major + minor); IR ν_{max} (neat) cm^{-1}: 3360, 2952, 1739,

1656, 1508, 1237, 1104, 907, 823, 730; HRMS (ESI, m/z): calcd for $C_{20}H_{30}F_3N_2O_4S^+$ $[M + H]^+$ 451.1873, found 451.1876.



Methyl (5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3,3-dimethylpentanoyl)-L-tryptophanate (**4lt**): Following the general procedure B, compound **4lt** was prepared through a reaction between **1l**, 2-methylpropene **2t** and Togni II reagent **3**, and it was isolated through a silica gel flash column (CH_2Cl_2:MeOH = 50:1 to 30:1) as a white powder (84.9 mg, 84% yield, a mixture of two diastereomers, *dr* = 1.4). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (s, 1H, minor), 7.96 (s, 1H, major), 7.45 – 7.36 (m, 1H), 7.34 – 7.24 (m, 1H + 1H, minor), 7.22 – 7.12 (m, 1H), 7.10 (d, *J* = 8.0 Hz, 1H, major), 7.07 – 6.99 (m, 1H), 6.83 – 6.69 (m, 2H), 6.67 – 6.59 (m, 2H, minor), 6.56 – 6.45 (m, 2H, major + 1H, minor), 6.41 (d, *J* = 2.5 Hz, 1H, major), 4.97 – 4.80 (m, 1H), 3.93 – 3.71 (m, 4H), 3.66 (s, 3H, minor), 3.65 (s, 3H, major), 3.49 – 3.37 (m, 1H), 3.33 – 3.20 (m, 1H + 1H minor), 3.14 (dd, *J* = 14.9, 5.1 Hz, 1H, major), 2.50 – 2.23 (m, 2H), 1.18 (s, 3H, major), 1.14 (s, 3H, major), 1.12 (s, 3H, minor), 1.08 (s, 3H, minor); ^{13}C{1H}NMR (100 MHz, Chloroform-*d*) δ 172.1 (major), 171.9 (minor), 171.4 (minor), 171.1 (major), 153.5 (minor), 153.3 (major), 141.5 (minor), 140.7 (major), 136.1 (major), 136.0 (minor), 127.3 (minor), 127.1 (major), 127.1 (q, *J* = 278.5 Hz, minor), 126.9 (q, *J* = 278.8 Hz, major), 123.0 (major), 122.9 (minor), 122.22 (minor), 122.18 (major), 119.67 (minor), 119.63 (major), 118.39 (major), 118.26 (minor), 117.0 (minor), 115.2 (major), 114.9 (major + minor), 111.3 (minor), 111.2 (major), 109.5 (minor), 109.4 (major), 68.6 (minor), 67.8 (major), 55.8 (minor), 55.7 (major), 52.8 (minor), 52.4 (minor), 52.3 (major), 52.2 (major), 41.4 (q, *J* = 26.5 Hz, major), 41.0 (q, *J* = 26.6 Hz, minor) 35.8 (minor), 35.5 (major), 27.4 (major), 27.3 (minor), 24.4 (major), 24.1 (minor), 24.0 (major), 23.7 (minor); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.65 (t, *J* = 12.4 Hz, 3F, minor), -58.69 (t, *J* = 12.0 Hz, 3F, major); IR ν_{max} (neat) cm^{-1}: 3404, 3366, 2955, 1739, 1647, 1514, 1502, 1441, 1263, 1244, 1202, 1181, 1101, 1076, 1037, 822, 743, 678, 586; HRMS (ESI, m/z): calcd for $C_{26}H_{31}F_3N_3O_4^+$ $[M + H]^+$ 506.2261, found 506.2260.

c) A few unsuccessful N-protected glycinates

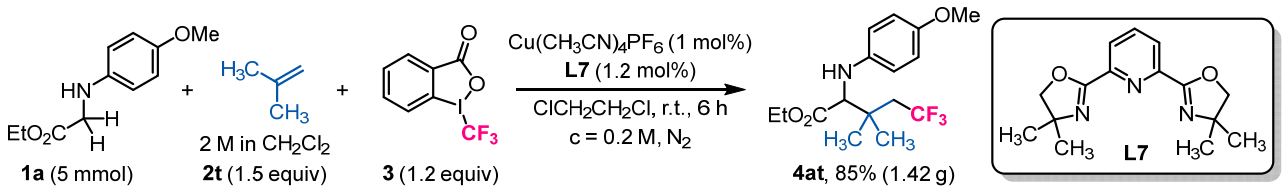


A few ethyl glycinates with other common protecting groups (**S8-S11**) were also evaluated under the optimized conditions, however, failed to give the desired trifluoromethyl alkylation products.

V. Studies on Synthetic Applications

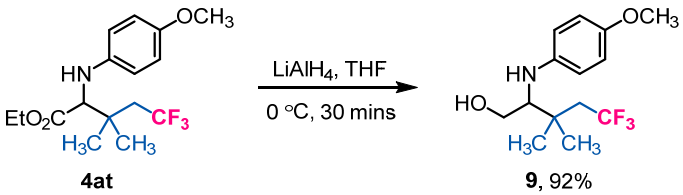
a) Product derivatizations

i) Gram-scale synthesis



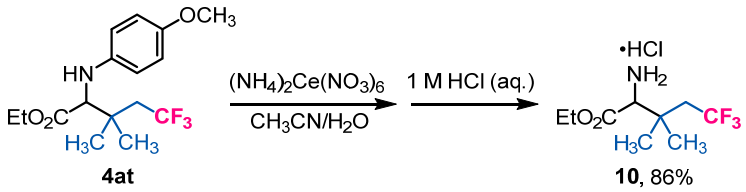
To a 50 mL round-bottomed flask charged with a stir bar were added **1a** (1.046 g, 5 mmol), **3** (1.90 g, 6 mmol), $Cu(CH_3CN)_4PF_6$ (18.6 mg, 0.05 mmol), and **L7** (16.3 mg, 0.06 mmol). After the flask was evacuated and refilled with N_2 three times, freshly distilled $ClCH_2CH_2Cl$ (21 mL) was added, followed by the addition of 2-methylpropene **2t** (3.75 mL, 7.5 mmol, 2 M in CH_2Cl_2) under N_2. The reaction mixture was let stirred at room temperature for 12 h and then quenched with saturated $NaHCO_3$ aqueous solution (10 mL) and $Na_2S_2O_3$ aqueous solution (10 mL). After the resulting mixture was extracted with CH_2Cl_2 (10 mL × 3), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*, the residue was purified through a silica gel flash column (PE: EtOAc from 50:1 to 30:1) to afford **4at** as a yellowish oil (1.42 g, 85%).

ii) $LiAlH_4$ reduction of the ester group



5,5,5-Trifluoro-2-((4-methoxyphenyl)amino)-3,3-dimethylpentan-1-ol (**9**): To a suspension of $LiAlH_4$ (7.6 mg, 0.2 mmol, in 1mL of anhydrous THF) cooled in an ice-bath was slowly added a solution of **4at** (66.7 mg, 0.2 mmol dissolved in 1 ml THF). The reaction was kept stirring for 30 min at the same temperature before it was quenched with saturated aqueous $NaHCO_3$ (2 mL). The mixture was extracted with CH_2Cl_2 (10 mL ×3) three times, washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Amino alcohol **9** was purified through a silica gel flash column (PE: EtOAc = 5:1 to 3:1) as a colorless oil (53.6 mg, 92% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.82 – 6.72 (m, 2H), 6.72 – 6.61 (m, 2H), 3.83 (d, *J* = 11.0 Hz, 1H), 3.75 (s, 3H), 3.58 (dd, *J* = 11.0, 6.6 Hz, 1H), 3.43 (s, 1H), 3.31 (dd, *J* = 6.9, 4.2 Hz, 1H), 2.21 (q, *J* = 12.0 Hz, 2H), 2.03 (brs, 1H), 1.14 (s, 3H), 1.11 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 152.6, 142.6, 127.1 (q, *J* = 278.7 Hz), 115.3, 115.1, 63.9, 61.5, 55.8, 41.9 (q, *J* = 26.0 Hz), 36.4, 24.4, 23.9; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.67 (t, *J* = 12.0 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3386, 2940, 1509, 1467, 1365, 1259, 1231, 1178, 1105, 1030, 817; HRMS (ESI, m/z): calcd for $C_{14}H_{21}F_3NO_2^+$ $[M + H]^+$ 292.1519, found 292.1518.

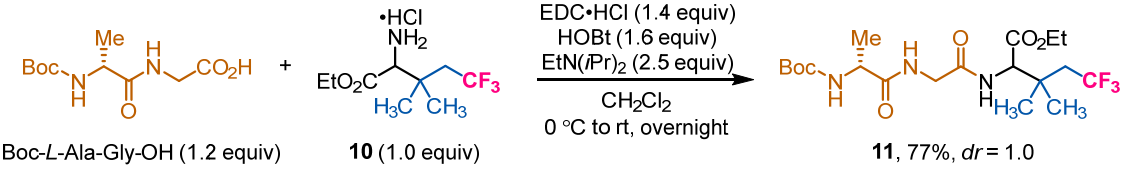
iii) Removal of PMP group



Ethyl 2-amino-5,5,5-trifluoro-3,3-dimethylpentanoate hydrochloride (**10**): To a solution of CAN (ceric ammonium nitrate, 6 mmol, dissolved in 10.5 mL of H_2O) cooled in an ice bath was slowly added a solution of **4at** (1.5 mmol dissolved in 4.5 mL CH_3CN) in 0.5 h. The reaction was kept stirring for 2 h at the same temperature before it was quenched with saturated aqueous Na_2CO_3. The mixture was extracted with CH_2Cl_2 (10 mL × 3), washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was dissolved in Et_2O (5 mL), and HCl (5 mL, 1 M aq.) was then slowly added into the above solution under vigorous stirring. After the organic phase was separated, the aqueous layer was washed with Et_2O (5 mL × 3). Lastly, water was removed *in vacuo* and the residue was further dried to afford the amino ester hydrochloride **10** as a beige powder (336 mg, 86% yield, m.p. = 71 – 74 °C). ^{1}H NMR (600 MHz, D_2O) δ 4.25 – 4.13 (m, 2H), 4.00 (s, 1H), 2.45 – 2.25 (m, 2H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.12 (s, 3H), 1.03 (s, 3H); ^{13}C{^{1}H}NMR (151 MHz,

D_2O) δ 168.4, 126.3 (q, J = 277.9 Hz), 63.8, 60.1, 40.4 (q, J = 27.0 Hz), 34.0, 23.2, 22.8, 13.2; ^{19}F NMR (565 MHz, D_2O) δ -59.22 (t, J = 11.6 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3400, 3356, 2934, 1723, 1518, 1235, 1072, 1024, 819, 690; HRMS (ESI, m/z): calcd for $C_9H_{17}F_3NO_2^+$ $[M + H]^+$ 228.1206, found 228.1208.

iv) Tripeptide synthesis

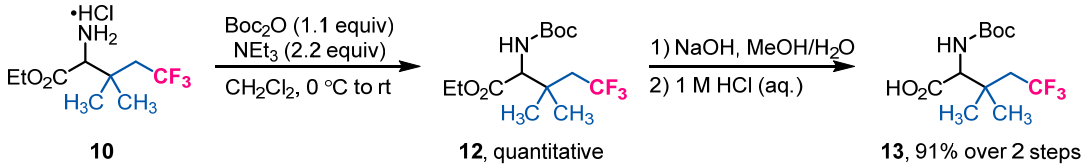


Boc-*L*-Ala-Gly-OH (1.2 equiv) **10** (1.0 equiv) **11**, 77%, *dr* = 1.0

Ethyl (6R)-2,2,6-trimethyl-4,7,10-trioxo-12-(4,4,4-trifluoro-2-methylbutan-2-yl)-3-oxa-5,8,11-triazatridecan-13-oate (**11**): In a 5 mL reaction tube, Boc-*L*-Ala-Gly-OH (59.1 mg, 0.24 mmol), EDC•HCl (43.5 mg, 0.28 mmol) and HOBt (43.2 mg, 0.32 mmol) were dissolved in dry CH_2Cl_2 (2 mL) under N_2. After the tube was cooled in an ice-water bath, EtN(*i*Pr)$_2$ (87 µL, 0.5 mmol) was slowly added in 5 minutes. The reaction mixture was allowed to stir for 30 minutes before **10** (52.7 mg, 0.2 mmol) was added. The reaction was warmed to room temperature and stirred for additional 16 hours. Then, the mixture was quenched with water (4 mL), and extracted with CH_2Cl_2 (2 mL × 3). The combined organic layers were washed with brine (2 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Tripeptide **11** was isolated through a silica gel flash column (PE: EtOAc = 5:1 to 3:1) as a white powder (70.1 mg, 77% yield, a mixture of two diastereomers, *dr* = 1.0). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.38 (d, J = 9.4 Hz, 1H, isomer 1), 7.34 (d, J = 9.3 Hz, 1H, isomer 2), 7.25 – 7.17 (br, 1H), 5.59 – 5.14 (br, 1H), 4.56 (d, J = 2.1 Hz, 1H, isomer 1), 4.55 (d, J = 2.1 Hz, 1H, isomer 2), 4.30 – 4.11 (m, 3H), 4.07 – 3.98 (m, 2H) 2.28 – 2.16 (m, 2H), 1.42 (s, 9H, isomer 1), 1.42 (s, 9H, isomer 2), 1.37 (s, 3H, isomer 1), 1.35 (s, 3H, isomer 2), 1.29 – 1.25 (m, 3H), 1.12 (s, 6H, isomer 1), 1.11 (s, 6H, isomer 2); $^{13}C\{^1H\}$NMR (151 MHz, Chloroform-*d*) δ 173.7 (isomer 1 + isomer 2), 170.4 (isomer 1), 170.3 (isomer 1), 169.0 (isomer 1 + isomer 2), 155.5 (isomer 1 + isomer 2), 126.8 (q, J = 279.1 Hz, isomer 1 + isomer 2), 80.2 (isomer 1 + isomer 2), 61.5 (isomer 1), 61.4 (isomer), 59.8 (isomer 1 + isomer 2), 50.2 (isomer 1 + isomer 2), 43.5 (isomer 1 + isomer 2), 40.8 (q, J = 27.1, 26.2 Hz, isomer 1 + isomer 2), 36.1 (isomer 1), 36.0 (isomer 2), 28.3(isomer 1 + isomer 2), 23.8 (isomer 1 + isomer 2), 23.3 (isomer 1), 23.2 (isomer 2), 18.5 (isomer 1 + isomer 2), 14.1 (isomer 1 + isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.93 (t, J = 11.8 Hz, 3F, isomer 1 + isomer 2);

IR ν_{max} (neat) cm^{-1}: 3380, 3313, 2982, 1713, 1634, 1367, 1337, 1269, 1212, 1166, 1110, 903, 726; HRMS (ESI, m/z): calcd for $C_{19}H_{33}F_3N_3O_6^+$ $[M + H]^+$ 456.2316, found 456.2313.

v) Preparation of N-Boc amino acid



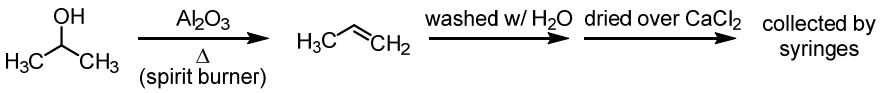
Ethyl 2-((tert-butoxycarbonyl)amino)-5,5,5-trifluoro-3,3-dimethylpentanoate (**12**): To a solution of **10** (52.7 mg, 0.2 mmol, dissolved in 2 mL CH_2Cl_2) cooled in an ice-water bath was slowly added NEt_3 (61 μL, 0.44 mmol) and Boc_2O (48 mg, 0.22 mmol). The reaction was kept stirring for 2 h at room temperature before it was quenched with saturated $NaHCO_3$ aqueous solution (2 mL) and 4-DMAP (2.4 mg, 0.02 mmol). The mixture was stirred for an additional 30 min at room temperature before it was extracted with CH_2Cl_2 (2 mL × 3), washed with brine (2 mL), dried over Na_2SO_4, and concentrated *in vacuo*. **12** was obtained in almost quantitative yield as a white solid (m.p.: 38 – 41 °C), which could be used for the next step without further purification. ^{1}H NMR (400 MHz, Chloroform-*d*) 5.16 (d, *J* = 9.8 Hz, 1H), 4.38 – 3.96 (m, 3H), 2.18 (q, *J* = 11.8 Hz, 2H), 1.42 (s, 9H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.08 (s, 6H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 171.0, 155.4, 126.8 (q, *J* = 278.4 Hz), 80.2, 61.4, 61.2, 40.9 (q, *J* = 26.9 Hz), 36.1, 28.2, 23.7, 22.9, 14.1; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.99 (t, *J* = 11.8 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3277, 2984, 1737, 1698, 1367, 1228, 1166, 1106, 869, 781, 600; HRMS (ESI, m/z): calcd for $C_{14}H_{24}F_3NNaO_4^+$ $[M + Na]^+$ 350.1550, found 350.1555.

2-((tert-Butoxycarbonyl)amino)-5,5,5-trifluoro-3,3-dimethylpentanoic acid (**13**): To a solution of compound **12** (dissolved in 1 mL MeOH) cooled in an ice-water bath was slowly added a solution of NaOH (1 mL, 50 wt% in water). The reaction was stirred for 2 h at room temperature before it was acidified with 1N HCl aqueous solution (to pH = 2). The mixture was extracted with EtOAc (2 mL × 3), washed with brine (2 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Compound **13** was obtained as a white solid (54.5 mg, 91% yield, m.p.: 107 – 110 °C) that is pure enough to be characterized. ^{1}H NMR (400 MHz, DMSO-d_6) δ 14.48 – 11.28 (br, 1H), 7.14 (d, *J* = 9.2 Hz, 1H), 3.97 (d, *J* = 9.2 Hz, 1H), 2.57 – 2.43 (m, 1H), 2.37 – 2.26 (m, 1H), 1.40 (s, 9H), 1.07 (s, 6H); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6) δ 172.7, 156.2, 127.8 (q, *J* = 278.7 Hz), 78.8, 61.8, 40.2 (overlapped with

DMSO residue peak), 34.8, 28.6, 24.5, 24.1; ^{19}F NMR (376 MHz, DMSO-d_6) δ -53.12 (t, J = 12.5 Hz, 3F); IR ν_{max} (neat) cm^{-1}: 3498, 3283, 1745, 1698, 1393, 1164, 1138, 1106, 939, 779; HRMS (ESI, m/z): calcd for $C_{12}H_{21}F_3NO_4^+$ $[M + H]^+$ 300.1417, found 300.1417.

b) Synthesis of (*rac*)-5,5,5-trifluoro-isoleucine

i) Small-scale preparation of propene gas



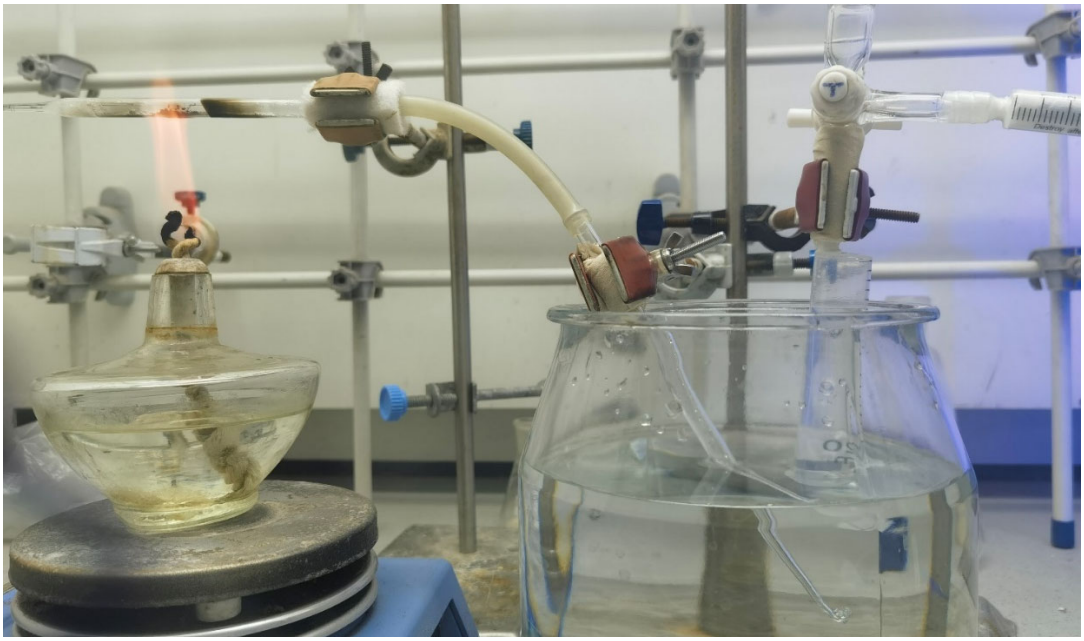


Figure S1. A small-scale preperation of propene gas

A glass Pasteur pipette was sealed at the thinner end using a blast burner. 0.5 mL of *i*-PrOH absorbed on mineral wool was added into the pipette, followed by the addition of Al_2O_3 (0.5 g) as the catalyst. The open end of the pipette was connected to a delivery tube. On the other side, a syringe and a dry tube were connected to a three-way, and the apparatus was fixed as shown in **Figure S1**. After the air was purged by a syringe from the drying tube and thoroughly exchanged with N_2, the glass pipette was heated by a spirit burner to generate propene gas. The gas collected in the inverted syringe was pulled into and stored in other syringes from the end of the drying tube. The collected propene was bubbled into $CDCl_3$ for ^{1}H NMR analysis, and it was pure enough to be used for the Cu-catalysed reaction (**Figure S2**).

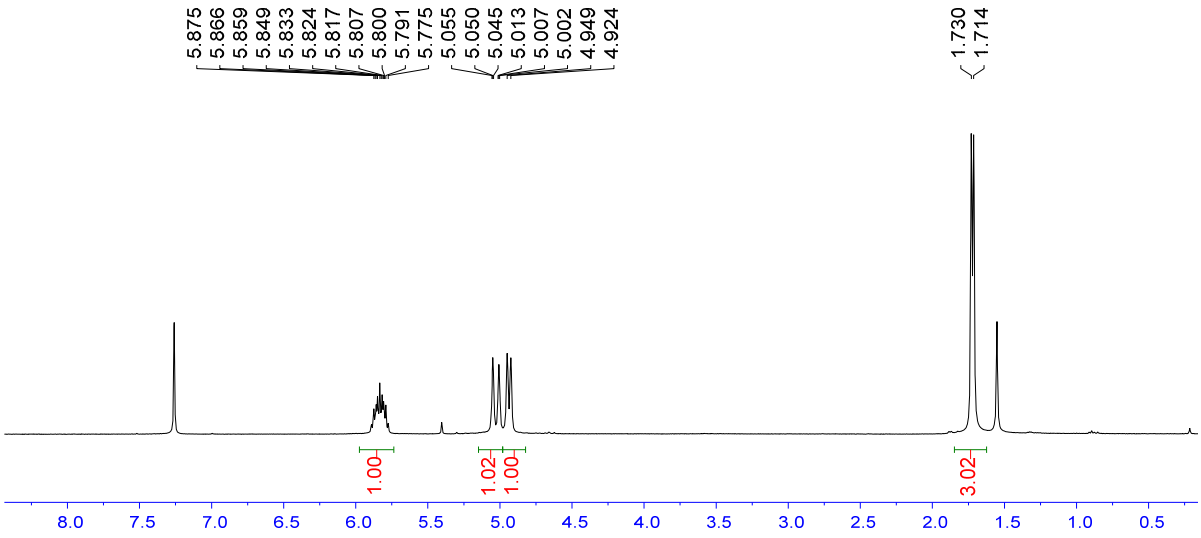
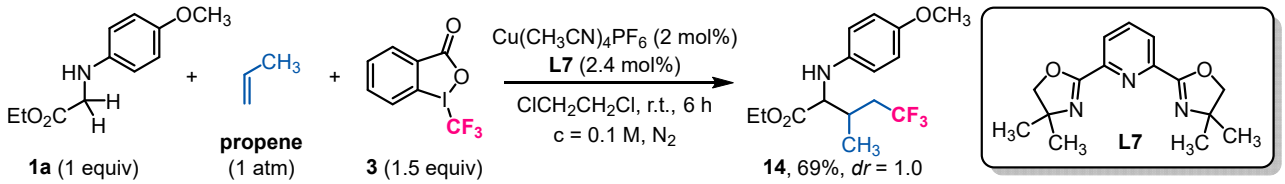


Figure S2. The ^{1}H NMR spectrum of propene

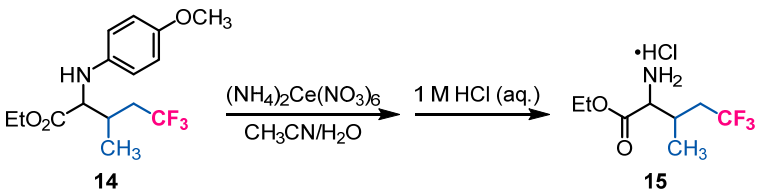
ii) The propene participated reaction



Ethyl 5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3-methylpentanoate (**14**): compound **14** was prepared according to the general procedure A, but under a propene atmosphere (injected by a syringe). After a silica gel flash column purification (PE: EtOAc = 5:1 to 3:1), **14** was isolated as a colorless oil (44.1 mg, 69% yield, a mixture of two diastereomers, *dr* = 1.0). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.87 – 6.71 (m, 2H), 6.71 – 6.55 (m, 2H), 4.32 – 4.09 (m, 2H), 4.04 – 3.84 (br, 1H), 4.00 (d, *J* = 3.5 Hz, 1H, isomer 1), 3.82 (d, *J* = 6.3 Hz, 1H, isomer 2), 3.74 (s, 3H), 2.68 – 2.53 (m, 1H, isomer 1), 2.53 – 2.39 (m, 1H), 2.35 – 2.22 (m, 1H, isomer 2), 2.17 – 1.95 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H, isomer 1), 1.08 (d, *J* = 6.7 Hz, 3H, isomer 2); ^{13}C{1H}NMR (100 MHz, Chloroform-*d*) δ 172.9 (isomer 1), 172.8 (isomer 2), 153.3 (isomer 1), 153.1 (isomer 2), 141.1 (isomer 1), 140.6 (isomer 2), 127.1 (q, *J* = 276.8 Hz, isomer 1), 127.0 (q, *J* = 277.1 Hz, isomer 2), 116.2 (isomer 1), 115.6 (isomer 2), 114.91 (isomer 1), 114.87 (isomer 2), 62.6 (isomer 1), 62.0 (isomer 2), 61.4 (isomer 1), 61.3 (isomer 2), 55.67 (isomer 1), 55.65 (isomer 2), 37.2 (q, *J* = 27.9 Hz, isomer 1), 36.9 (d, *J* = 27.8 Hz, isomer 2), 31.3 (q, *J* = 2.4 Hz, isomer 1), 30.7 (q, *J* = 2.4 Hz, isomer 2), 16.6 (isomer 1), 15.2 (isomer 2), 14.2 (isomer 1 + isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.58 (t, *J* = 10.3 Hz, 3F, isomer 1), -63.64 (t, *J* = 11.2 Hz, 3F, isomer 2); IR ν_{max} (neat) cm^{-1}: 3364,

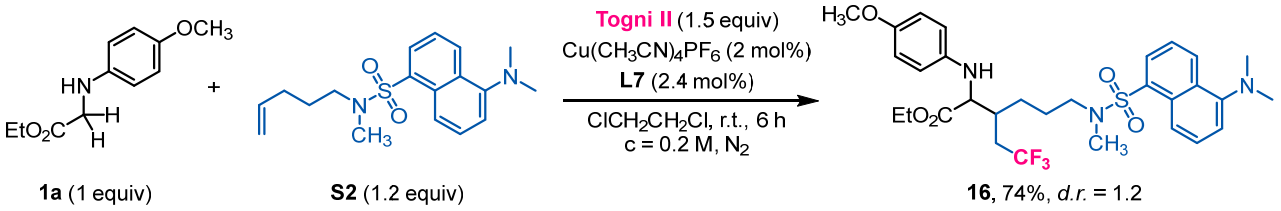
1741, 1514, 1180, 1110, 1089, 809, 734; HRMS (ESI, m/z): calcd for $C_{15}H_{21}F_3NO_3^+$ $[M + H]^+$ 320.1468, found 320.1467.

iii) Deprotection of the PMP group



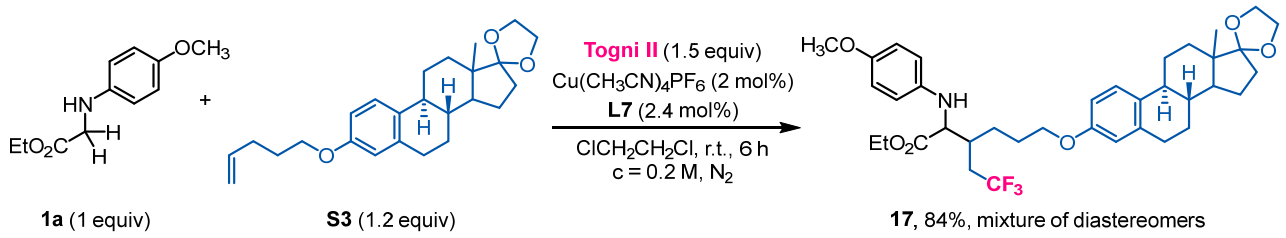
Ethyl 2-amino-5,5,5-trifluoro-3-methylpentanoate hydrochloride (**15**): Following the procedure described above (the preparation of **10**), the hydrochloride salt of amino ester (**15)** was obtained as a white foam (85% yield, *dr* = 1.3:1). ^{1}H NMR (400 MHz, D_2O) δ 4.17 – 4.08 (m, 2H), 4.05 (d, *J* = 2.8 Hz, 1H, isomer 1), 4.02 (d, *J* = 3.7 Hz, 1H, isomer 2), 2.60 – 2.21 (m, 2H), 2.21 – 1.98 (m, 1H), 1.10 (t, *J* = 7.2 Hz, 3H, isomer 1), 1.09 (t, *J* = 7.1 Hz, 3H, isomer 2), 0.91 (t, *J* = 6.4 Hz, 3H); ^{13}C{1H}NMR (100 MHz, D_2O) δ 168.9 (isomer 1), 168.5 (isomer 2), 126.6 (q, *J* = 276.5 Hz, isomer 1), 126.5 (q, *J* = 276.5 Hz, isomer 2), 56.8 (isomer 1), 56.5 (isomer 2), 36.2 (q, *J* = 28.1 Hz, isomer 1), 35.4 (q, *J* = 28.2 Hz, isomer 2), 29.0 (isomer 1), 28.7 (isomer 2), 14.5 (isomer 1), 14.0 (isomer 2), 13.3 (isomer 1), 13.2 (isomer 2); ^{19}F NMR (376 MHz, D_2O) δ -63.94 (t, *J* = 11.1 Hz, 3F, isomer 1), -64.13 (t, *J* = 11.0 Hz, 3F, isomer 2); IR ν_{max} (neat) cm^{-1}: 2976, 1741, 1504, 1428, 1386, 1243, 1135, 1050, 903, 854, 810; HRMS (ESI, m/z): calcd for $C_8H_{15}F_3NO_2^+$ $[M + H]^+$ 214.1049, found 214.1052.

c) The ligantion of complex functional molecules to glycinates



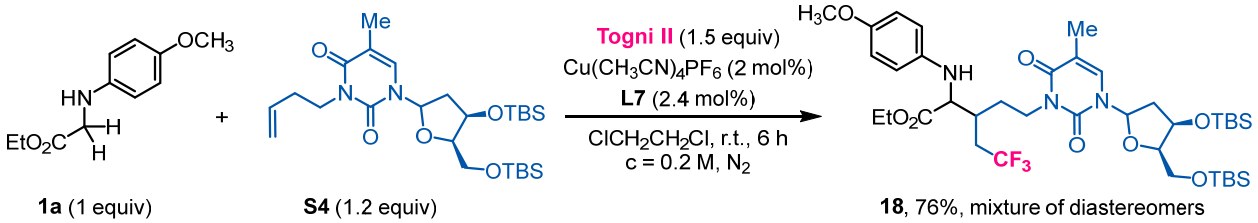
Ethyl 6-((5-(dimethylamino)-N-methylnaphthalene)-1-sulfonamido)-2-((4-methoxyphenyl)amino) -3-(2,2,2-trifluoroethyl)hexanoate (**16**): Following the general procedure A, compound **16** was prepared through a reaction between **1a**, an alkene-tagged dansyl amide **S2** and Togni II reagent **3**, **16** was purified through a silica gel flash column (PE: EtOAc = 10:1 to 5:1) as a brownish oil (90.1 mg, 74% yield, a mixture of two diastereomers, *dr* = 1.2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.65 – 8.45 (m, 1H), 8.42 – 8.29 (m, 1H), 8.22 – 8.10 (m, 1H), 7.63 – 7.46 (m, 2H), 7.23 – 7.10 (m, 1H),

6.85 – 6.71 (m, 2H), 6.69 – 6.51 (m, 2H), 4.25 – 4.10 (m, 2H), 4.07 (d, J = 4.2 Hz, 1H, isomer 1), 3.98 (d, J = 5.2 Hz, 1H, isomer 2), 3.76 – 3.66 (m, 3H), 3.28 – 3.10 (m, 2H), 2.92 - 2.84 (m, 6H), 2.82 (s, 3H, isomer 1), 2.81 (s, 3H, isomer 2), 2.58 – 2.38 (m, 1H), 2.30 – 2.12 (m, 1H), 2.09 – 1.87 (m, 1H), 1.73 – 1.51 (m, 2H + 1H, isomer 1), 1.45 – 1.17 (m, 5H + 1H, isomer 2); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 172.85 (isomer 1), 172.80 (isomer 2), 153.3 (isomer 1), 153.1 (isomer 2), 151.79 (isomer 1), 151.76 (isomer 2), 141.1 (isomer 1), 140.7 (isomer 2), 134.2 (isomer 1), 134.1 (isomer 2), 130.44 (isomer 2), 130.38 (isomer 1), 130.2 (isomer 1), 130.1 (isomer 2), 129.9 (isomer 1), 129.8 (isomer 2), 128.0 (isomer 2), 127.11 (q, J = 277.5 Hz, isomer 2), 127.06 (q, J = 276.9 Hz, isomer 1), 123.2 (isomer 1), 119.60 (isomer 2),119.59 (isomer 1), 116.1 (isomer 1), 115.6, 115.23 (isomer 1), 115.21 (isomer 2), 114.9 (isomer 1), 114.8 (isomer 2), 61.5 (isomer 2), 61.4 (isomer 1), 60.4 (isomer 1), 60.2 (isomer 2), 55.62 (isomer 2), 55.61 (isomer 1), 49.5 (isomer 1), 49.4 (isomer 2), 45.4 (2C, isomer 1 + isomer 2), 35.6 (isomer 1), 35.4 (isomer 2), 34.5 (isomer 1), 34.2 (isomer 2), 34.12 (isomer 2), 34.06 (isomer 1), 27.8 (isomer 2), 26.9 (isomer 1), 25.0 (isomer 1), 24.7 (isomer 2), 14.2 (2C, isomer 1 + isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.65 – -63.91 (m, 3F, isomer 1 + isomer 2); IR ν_{max} (neat) cm^{-1}: 3366, 2934, 1731, 1512, 1455, 1309, 1243, 1138, 907, 795, 724, 620, 564; HRMS (ESI, m/z): calcd for $C_{28}H_{41}F_3NO_9^+$ $[M + H]^+$ 610.2557, found 610.2557.



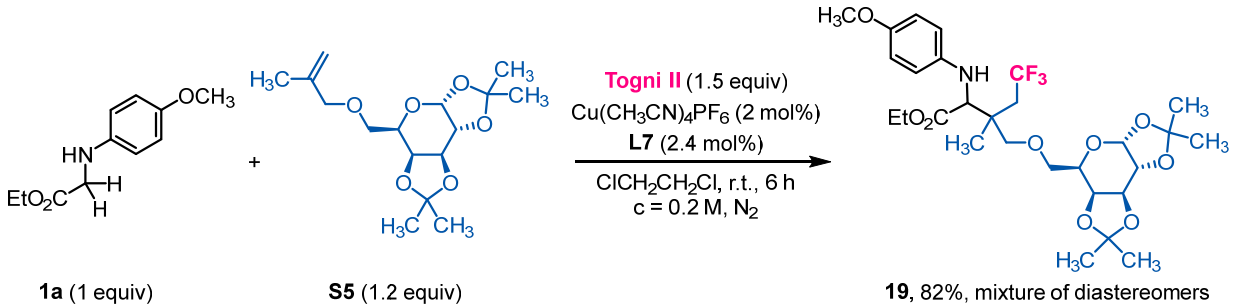
Ethyl 2-((4-methoxyphenyl)amino)-6-(((8R,9S,13S)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[a]phenanthrene-17,2'-[1,3]dioxolan]-3-yl)oxy)-3-(2,2,2-trifluoroethyl)hexanoate (**17**): Following the general procedure A, compound **17** was synthesized through a reaction between **1a**, an alkene-tagged estrone 17-ethylene ketal **S3** and Togni II reagent **3**. **17** was isolated through a silica gel flash column (PE: EtOAc = 15:1 to 10:1) as a white powder (110.8 mg, 84% yield, a mixture of diastereomers). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 – 7.16 (m, 1H), 6.84 – 6.74 (m, 2H), 6.73 – 6.58 (m, 4H), 4.29 – 4.03 (m, 3H), 4.02 – 3.81 (m, 7H), 3.75 (s, 3H), 2.98 – 2.73 (m, 2H), 2.69 – 2.45 (m, 1H), 2.44 – 2.09 (m, 4H), 2.09 – 1.99 (m, 1H), 1.97 – 1.74 (m, 6H), 1.71 – 1.32 (m, 8H), 1.28 (t, J = 6.9 Hz, 3H, isomer 1), 1.24 (t, J = 6.8 Hz, 3H, isomer 2), 0.91 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-*d*) δ 173.03, 172.97, 156.72 (isomer 1), 156.67 (isomer 2),

153.3 (isomer 1), 153.2 (isomer 2), 141.2 (isomer 1), 140.8 (isomer 2), 138.04 (isomer 1), 138.02 (isomer 2), 132.9 (isomer 1), 132.8 (isomer 2), 127.2 (q, J = 276.5 Hz), 126.37 (isomer 1), 126.35 (isomer 2), 119.4 (isomer 1 + isomer 2), 116.2 (isomer 1), 115.8 (isomer 2), 114.91 (isomer 1), 114.88 (isomer 2), 114.4 (isomer 1 + isomer 2), 111.99 (isomer 1), 111.97 (isomer 2), 67.3 (isomer 1), 67.2 (isomer 2), 65.3 (isomer 1 + isomer 2), 64.6 (isomer 1 + isomer 2), 61.5 (isomer 1), 61.4 (isomer 2), 60.6 (isomer 1), 60.3 (isomer 2), 55.66 (isomer 1), 55.64 (isomer 2), 49.4 (isomer 1 + isomer 2), 46.2 (isomer 1 + isomer 2), 43.7 (isomer 1 + isomer 2), 39.1 (isomer 1 + isomer 2), 35.8 (isomer 1), 35.5 (isomer 2), 34.31 (q, J = 27.8 Hz, isomer 1), 34.27 (isomer 1 + isomer 2), 34.19 (q, J = 27.4 Hz, isomer 2), 30.8 (isomer 1 + isomer 2), 29.8 (isomer 1 + isomer 2), 27.5 (isomer 1), 27.0 (isomer 1 + isomer 2), 26.8 (isomer 2), 26.5 (isomer 1 + isomer 2), 26.2 (isomer 1 + isomer 2), 22.4 (isomer 1 + isomer 2), 14.4 (isomer 1 + isomer 2), 14.2 (isomer 1 + isomer 2); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.7 – -63.8 (m, 3F, mixture of isomers); IR ν_{max} (neat) cm^{-1}: 2936, 1732, 1607, 1511, 1235, 1180, 1156, 1033, 907, 819, 728, 647; HRMS (ESI, m/z): calcd for $C_{37}H_{49}F_3NO_6^+$ [M + H]$^+$ 660.3506, found 660.3503.

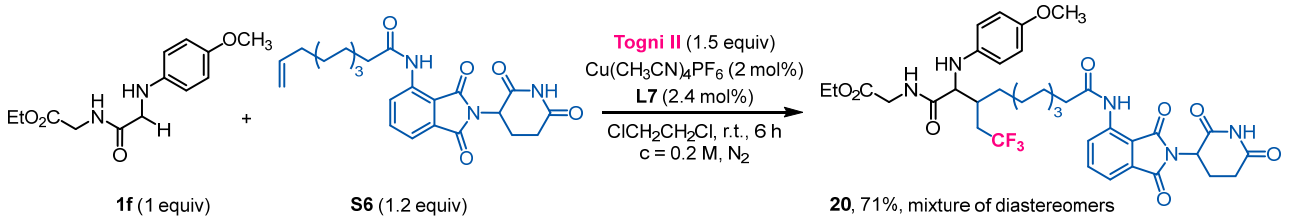


Ethyl 6-(3-((4R,5R)-4-((tert-butyldimethylsilyl)oxy)-5-(((tert-butyldimethylsilyl)oxy)methyl) tetrahydrofuran-2-yl)-5-methyl-2,6-dioxo-3,6-dihydropyrimidin-1(2H)-yl)-2-((4-methoxyphenyl)amino) -3-(2,2,2-trifluoroethyl)hexanoate (**18**): Following the general procedure A, compound **18** was prepared through a reaction between **1a**, an alkene-tagged thymidine **S4,** and Togni II reagent. **18** was isolated through a silica gel flash column (PE: EtOAc = 5:1 to 3:1) as a white powder (122.4 mg, 76% yield, a mixture of diastereomers). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 – 7.38 (m, 1H), 6.81 – 6.70 (m, 2H), 6.70 – 6.61 (m, 2H), 6.39 – 6.29 (m, 1H), 4.44 – 4.35 (m, 1H), 4.25 – 4.09 (m, 3H), 4.07 – 3.90 (m, 4H), 3.90 – 3.82 (m, 1H), 3.79 – 3.70 (m, 1H), 3.70 (s, 3H), 2.70 – 2.44 (m, 1H), 2.41 – 2.15 (m, 3H), 2.06 – 1.71 (m, 5H), 1.72 – 1.51 (m, 1H), 1.24 (t, J = 7.1 Hz, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.11 (s, 6H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.9, 172.6, 172.5, 163.3 – 163.2 (m), 153.2, 153.0, 150.8 – 150.6 (m), 141.3, 140.6, 140.5, 133.7 – 133.5 (m), 127.0 (q, J = 276.8 Hz), 116.2, 115.8, 114.9, 114.8, 110.0 – 109.7 (m), 87.8, 85.5, 72.2,

63.0, 61.5, 60.8, 60.3, 60.1, 55.6, 41.4, 39.3 – 38.3 (m), 35.1 – 33.3 (m), 28.9, 28.7, 28.1, 28.0, 25.9, 25.7, 18.4, 18.0, 14.2, 14.2, 13.2, -4.6, -4.8, -5.4, -5.5; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.78 – -64.02 (m, 3F); IR ν_{max} (neat) cm^{-1}: 3350, 2956, 1733, 1699, 1672, 1644, 1512, 1457, 1257, 1120, 1022, 905, 831, 734; HRMS (ESI, m/z): calcd for $C_{38}H_{63}F_3N_3O_8Si_2^+$ [M + H]$^+$ 802.4100, found 802.4113.



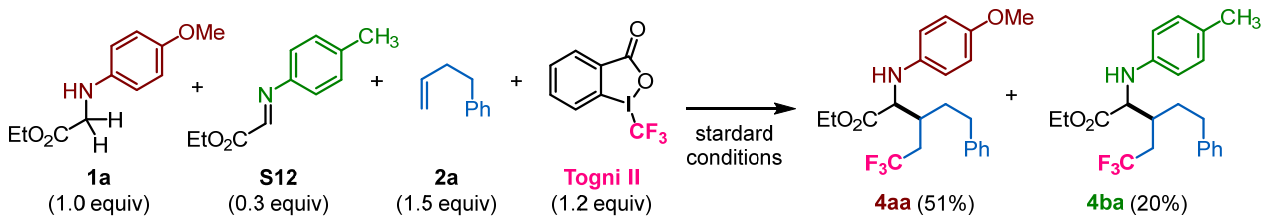
Ethyl 5,5,5-trifluoro-2-((4-methoxyphenyl)amino)-3-methyl-3-(((2,2,7,7-tetramethyltetrahydro-5H-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-5-yl)methoxy)methyl)pentanoate (**19**): Following the general procedure A, compound **19** was prepared through a reaction between **1a**, an alkene-tagged galactose **S5** and Togni II reagent **3**. Product **19** was isolated through a silica gel flash column (PE: EtOAc = 5:1 to 3:1) as a colorless oil (97.0 mg, 82% yield, a mixture of diastereomers). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.80 – 6.71 (m, 2H), 6.71 – 6.61 (m, 2H), 5.63 – 5.44 (m, 1H), 4.94 – 4.74 (br, 1H, 0.24H), 4.69 – 4.51 (m, 1H), 4.38 – 3.85 (m, 6.78H), 3.79 – 3.70 (m, 3H), 3.70 – 3.29 (m, 4H), 2.74 – 2.35 (m, 2H), 1.59 – 1.49 (m, 3H), 1.48 – 1.39 (m, 3H), 1.37 – 1.28 (m, 6H), 1.27 – 1.20 (m, 3H), 1.19 – 1.06 (m, 3H); ^{13}C{^{1}H}NMR (100 MHz, Chloroform-*d*) δ 172.9, 172.8, 172.7, 153.2, 153.1, 152.8, 152.7, 141.6 – 141.3 (m), 127.1 (q, *J* = 278.2 Hz), 116.2, 116.0, 115.7, 115.5, 114.9 – 114.6 (m), 109.4 – 109.1 (m), 108.7 – 108.5 (m), 96.4, 96.3, 75.4, 74.9, 74.4, 74.1, 71.5 – 70.9 (m), 70.8 – 70.4 (m), 70.1 – 69.8 (m), 66.9, 66.7, 66.5, 66.5, 64.8, 64.5, 63.3, 63.2, 61.1, 60.9, 55.9 – 55.2 (m), 40.2, 39.0, 38.8, 37.9 – 35.8 (m), 26.0, 26.0, 25.0, 25.0, 24.6, 24.4, 24.3, 18.7, 18.2, 18.1, 14.4 – 14.1 (m); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.53 (t, *J* = 12.0 Hz, 3F, isomer 1), -58.58 (t, *J* = 12.0 Hz, 3F, isomer 2), -58.94 (t, *J* = 12.1 Hz, isomer 3), -59.03 (t, *J* = 12.0 Hz, isomer 4); IR ν_{max} (neat) cm^{-1}: 3386, 2992, 1735, 1512, 1367, 1261, 1212, 1106, 1068, 993, 909, 728, 640; HRMS (ESI, m/z): calcd for $C_{28}H_{41}F_3NO_9^+$ [M + H]$^+$ 592.2728, found 592.2730.



Ethyl (12-((2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino)-2-((4-methoxyphenyl) amino)-12-oxo-3-(2,2,2-trifluoroethyl)dodecanoyl)glycinate (**20**): Following the general procedure A, compound **20** was prepared through a reaction between **1f**, an alkene-tagged pomalidomide **S6,** and Togni II reagent **3**. Product **20** was isolated through a silica gel flash column (PE: EtOAc = 5:1 to 3:1) as a beige powder (101.9 mg, 71% yield, a mixture of diastereomers). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.48 – 9.30 (m, 1H), 8.98 – 8.85 (m, 1H), 8.84 – 8.73 (m, 1H), 7.67 (t, *J* = 7.9 Hz, 1H), 7.51 (d, *J* = 7.3 Hz, 1H), 7.44 – 7.29 (m, 1H), 6.83 – 6.68 (m, 2H), 6.67 – 6.48 (m, 2H), 5.07 – 4.82 (m, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 4.12 – 3.76 (m, 4H), 3.70 (s, 3H), 2.92 – 2.49 (m, 4H), 2.49 – 2.04 (m, 6H), 1.77 – 1.63 (m, 2H), 1.55 – 1.43 (m, 1H), 1.36 – 1.17 (m, 13H); ^{13}C{1H}NMR (100 MHz, Chloroform-*d*) δ 172.5, 171.3, 169.7, 169.2, 168.3, 166.8, 153.3 (br), 140.6 (br), 137.8, 136.4, 131.1, 127.1 (q, 277.6 Hz), 125.3, 118.4, 115.3, 114.9 (br), 61.5, 61.5, 55.6, 49.3, 41.1, 41.1, 37.9, 36.3 – 35.7 (m, br), 34.9 – 33.7 (m, br), 31.3, 30.3, 30.0, 29.3, 29.2, 29.1, 27.0, 26.8, 25.2, 25.1, 22.6, 14.1; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.40 (t, *J* = 11.2 Hz, 3F, major), -63.76 (t, *J* = 11.0 Hz, 3F, minor); IR ν_{max} (neat) cm^{-1}: 3360, 2926, 1777, 1710, 1619, 1511, 1478, 1396, 1349, 1231, 1195, 1118, 1036, 912, 821, 740, 700, 605; HRMS (ESI, m/z): calcd for $C_{38}H_{47}F_3N_5O_9^+$ $[M+H]^+$ 774.3320, found 774.3321.

VI. Mechanistic studies

a) The participation of an exogenous glyoxo imine



The reaction between **1a** and **2a** was set up according to general procedure **A**, and a *p*-tolylimine ester **S12** (11.5 mg, 0.06 mmol) was added. The reaction was quenched with saturated $NaHCO_3$ aqueous solution and $Na_2S_2O_3$ aqueous solution after 6 h, worked-up following the general

procedure, and the crude product was submitted for ^{1}H NMR analysis. Besides the anticipated ligation product 4**aa** (51%), a cross-over coupling product **4ba** was also obtained in 20% yield (**Figure S3**).

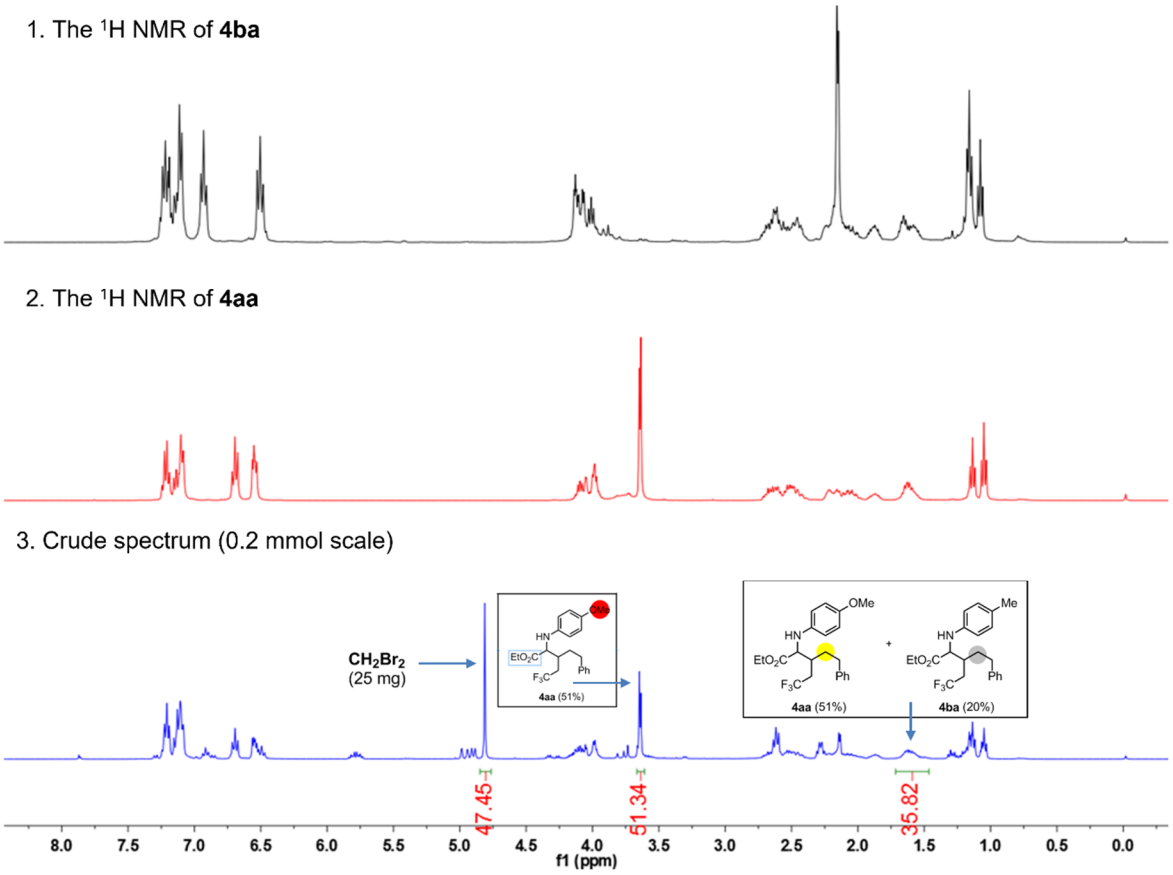
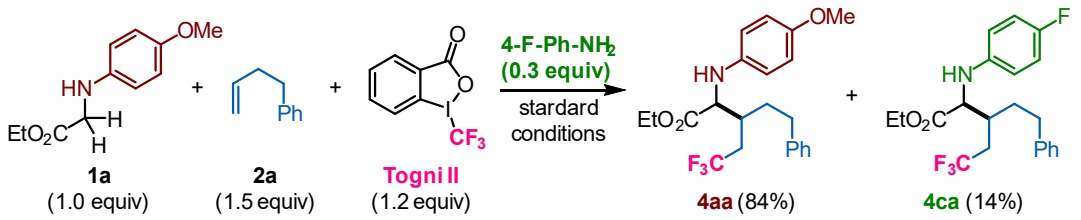


Figure S3. Stacked ^{1}H NMR to confirm the formation of 4ba

b) The participation of an exogenous aniline



The reaction between **1a** and **2a** was set up according to general procedure A, and a 4-fluoroaniline (5.7 μL, 0.06 mmol) was added. The reaction was quenched with saturated $NaHCO_3$ aqueous solution and $Na_2S_2O_3$ aqueous solution after 6 h, worked-up following the general procedure, and the crude product was submitted for ^{1}H and ^{19}F NMR analysis (**Figure S4** and **S5**). Besides the anticipated coupling product **4aa** (84%), fluorine-labelled product **4ca** was also obtained in 14% yield.

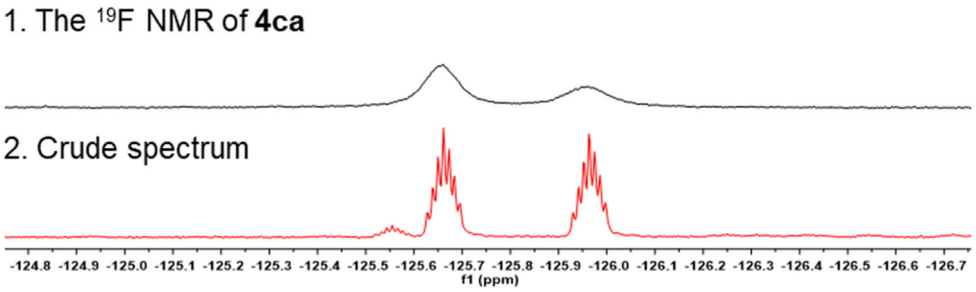


Figure S4. Stacked ^{19}F NMR to confirm the generation of 4ca

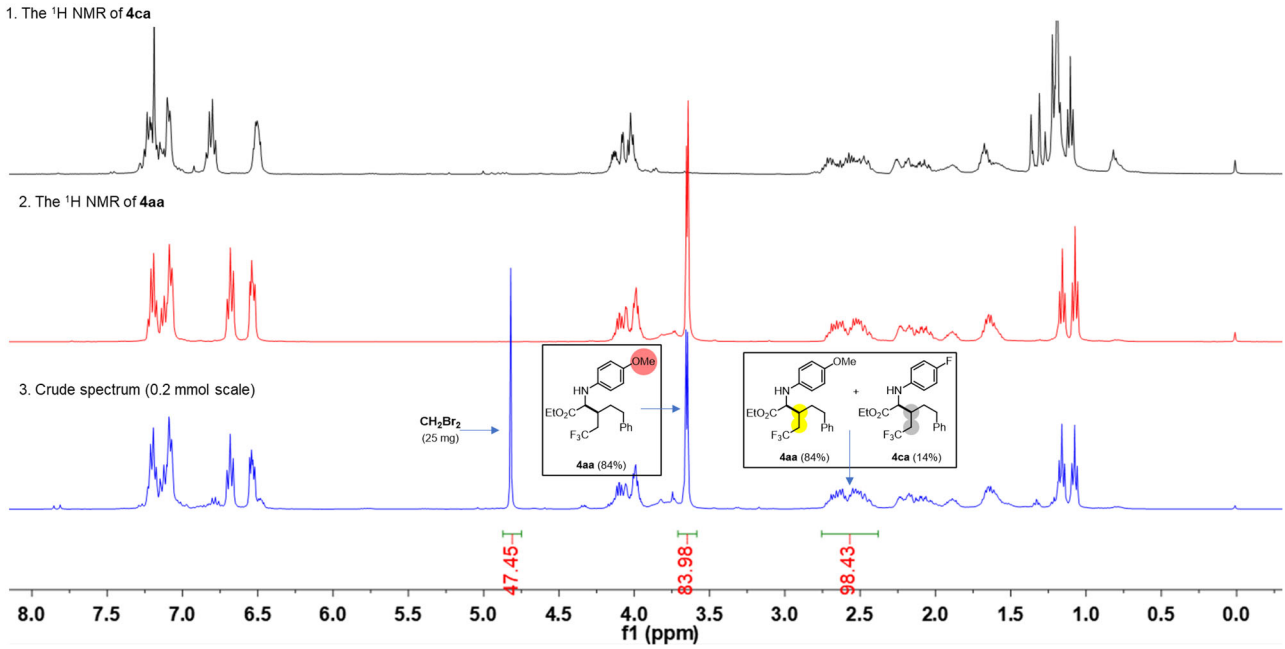
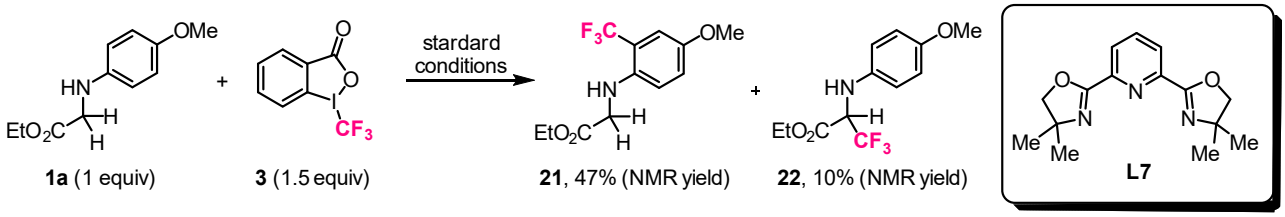


Figure S5. ^{1}H NMR analysis to determine the products distribution

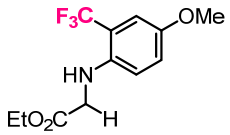
c) The trifluoromethylation of glycinate in the absence of an alkene



1a (1 equiv) **3** (1.5 equiv)

The control reaction in the absence of an alkene was set up according to general procedure A (0.2 mmol scale), but no alkene was added. The reaction was quenched with saturated $NaHCO_3$ aqueous solution and $Na_2S_2O_3$ aqueous solution after 6 h, worked-up following the general procedure, and the crude product was determined to be a mixture of **21** and **22** (47% for **21**, and 10% for **22** based

on ^{1}H NMR and ^{19}F NMR analysis). Compound **22** is known and its characterization data agree with the literature.[16]



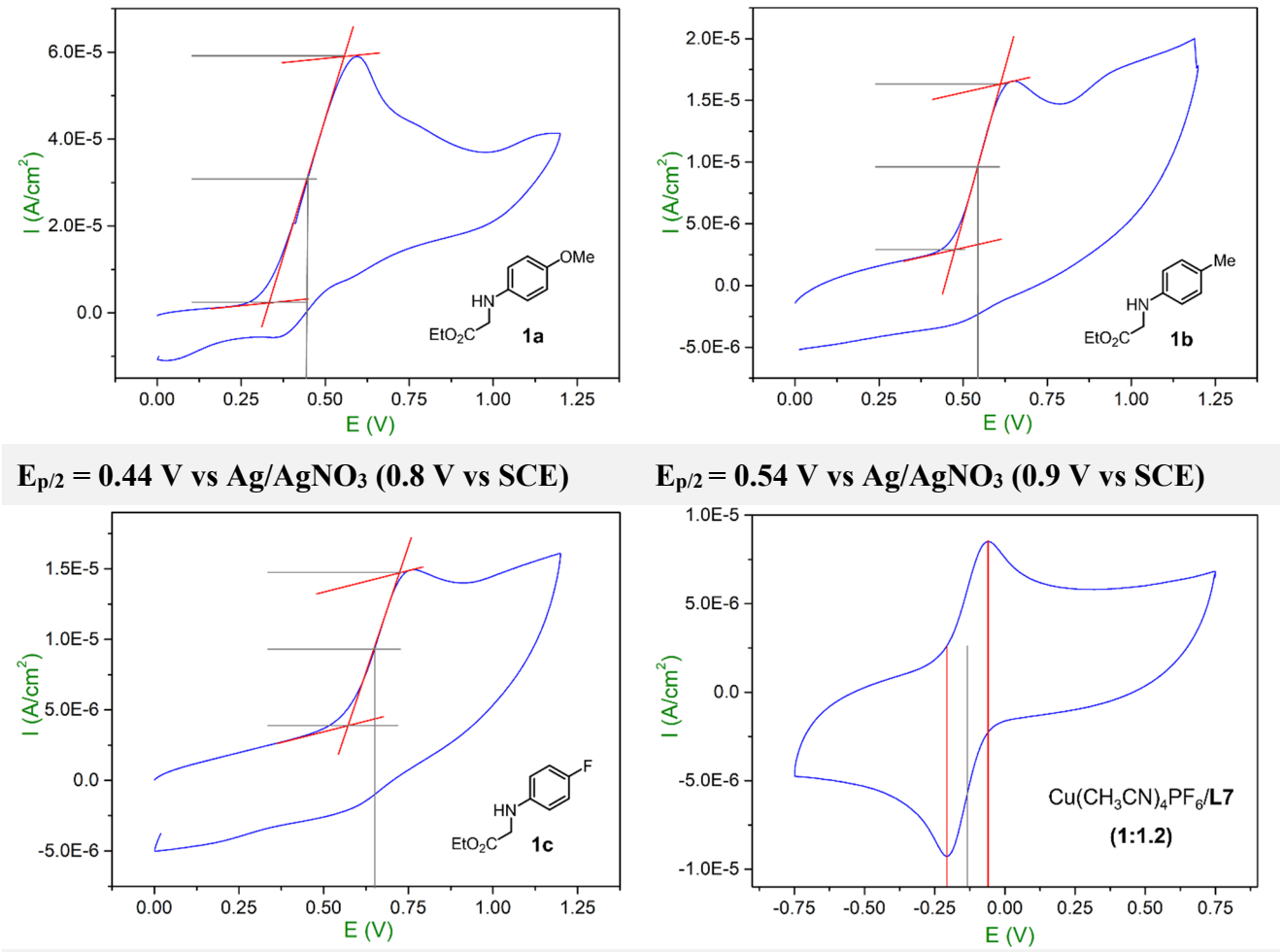
Ethyl (4-methoxy-2-(trifluoromethyl)phenyl)glycinate (**21**): The new compound **21** was further purified as a colorless solid. m.p. 42 – 45 °C. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.10 – 7.03 (m, 1H), 7.02 – 6.94 (m, 1H), 6.60 – 6.51 (m, 1H), 4.71 (brs, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.91 (s, 2H), 3.76 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, Chloroform-d) δ 170.5, 151.2, 138.7, 124.6 (q, J = 272.6 Hz), 119.1, 115.0 (q, J = 30.2 Hz), 113.5, 112.4 (q, J = 5.8 Hz), 61.5, 55.9, 46.0, 14.1; ^{19}F NMR (376 MHz, Chloroform-d) δ -62.38 (s, 3F); IR ν_{max} (neat) cm^{-1}: 3387, 1719, 1530, 1188, 1060, 875, 841, 726, 689; HRMS (ESI, m/z): calcd for $C_{12}H_{15}F_3NO_3^+$ $[M + H]^+$ 278.0999, found 278.0997.

d) The redox potential measurement of substrate and catalyst

The reduction/oxidation potentials of each compound were determined by cyclic voltammograms on a potentiostat. Conditions: glassy carbon as the working electrode, Pt plate as the counter electrode, $Ag/AgNO_3$ (0.1 M in MeCN) as the reference electrode, Bu_4NBF_4 in dichloroethane (0.1 M) was used as the supporting electrolyte, scan rate = 50 $mV{\cdot}s^{-1}$

First, the redox potentials of the substrates were measured in dichloroethane (0.025 M) with the supporting electrolyte. Irreversible oxidation of **1a**, **1b** and **1c** were recorded with half-wave potentials at 0.44 V, 0.54 V and 0.65V vs $Ag/AgNO_3$ (1.01 V vs SCE), respectively (**Figure S6**).

Next, representative $Cu(CH_3CN)_4PF_6$-**L7** complex was also evaluated with cyclic voltammetry. $Cu(CH_3CN)_4PF_6$ (1.5 mg, 0.02 mmol) and **L7** (1.3 mg, 0.024 mmol) were weighed into a 2-dram-vial and then dissolved by the electrolyte solution (4 mL). The clear solutions were then submitted for voltammograms scan. This complex undergoes a reversible oxidation and the half-wave potential was recoded at -0.13V vs $Ag/AgNO_3$ (0.23 V vs SCE) (see data in **Figure S6**).



$E_{p/2}$ = 0.44 V vs Ag/$AgNO_3$ (0.8 V vs SCE)

$E_{p/2}$ = 0.54 V vs Ag/$AgNO_3$ (0.9 V vs SCE)

$E_{p/2}$ = 0.65 V vs Ag/$AgNO_3$ (1.01 V vs SCE)

$E_{p/2}$ = -0.13 V vs Ag/$AgNO_3$ (0.23 V vs SCE)

Figure S6. The redox potentials of substrates and Cu catalyst

VII. References

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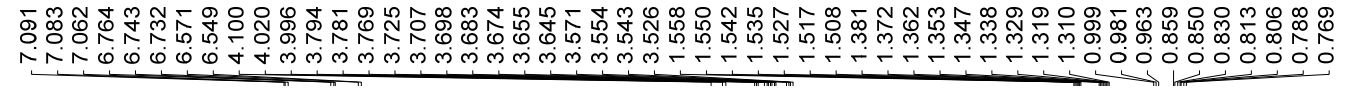
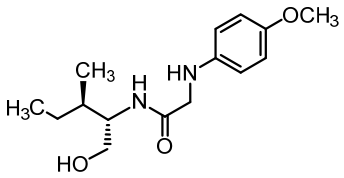
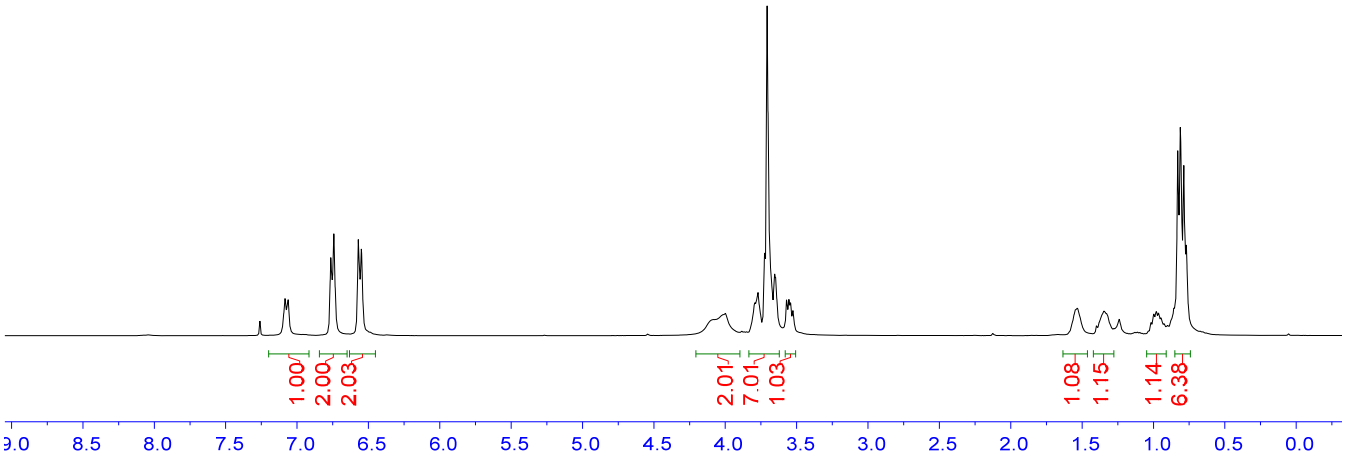
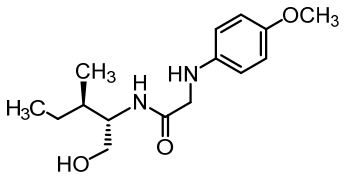
VIII. Copies of NMR spectra for New Compounds



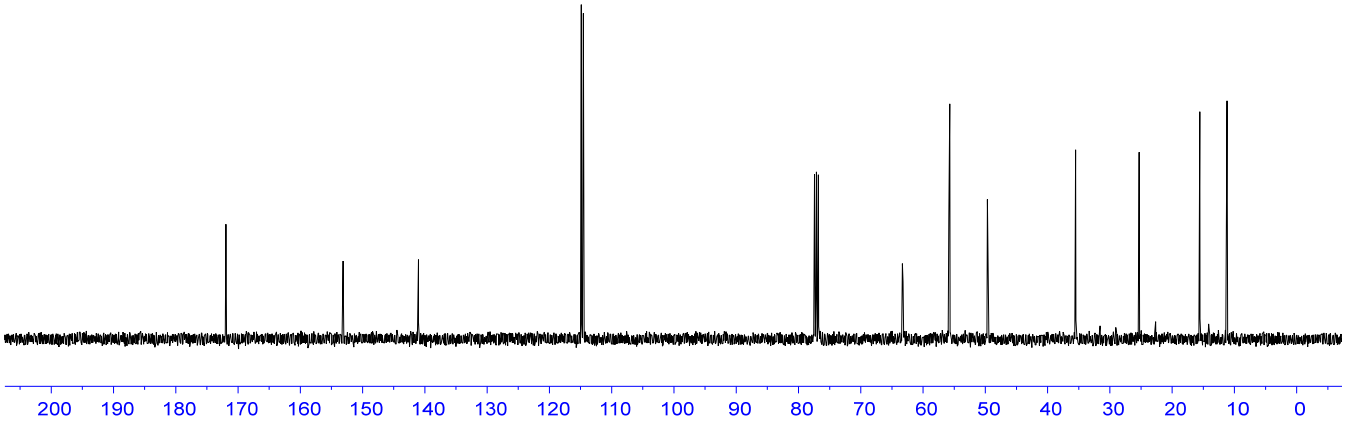


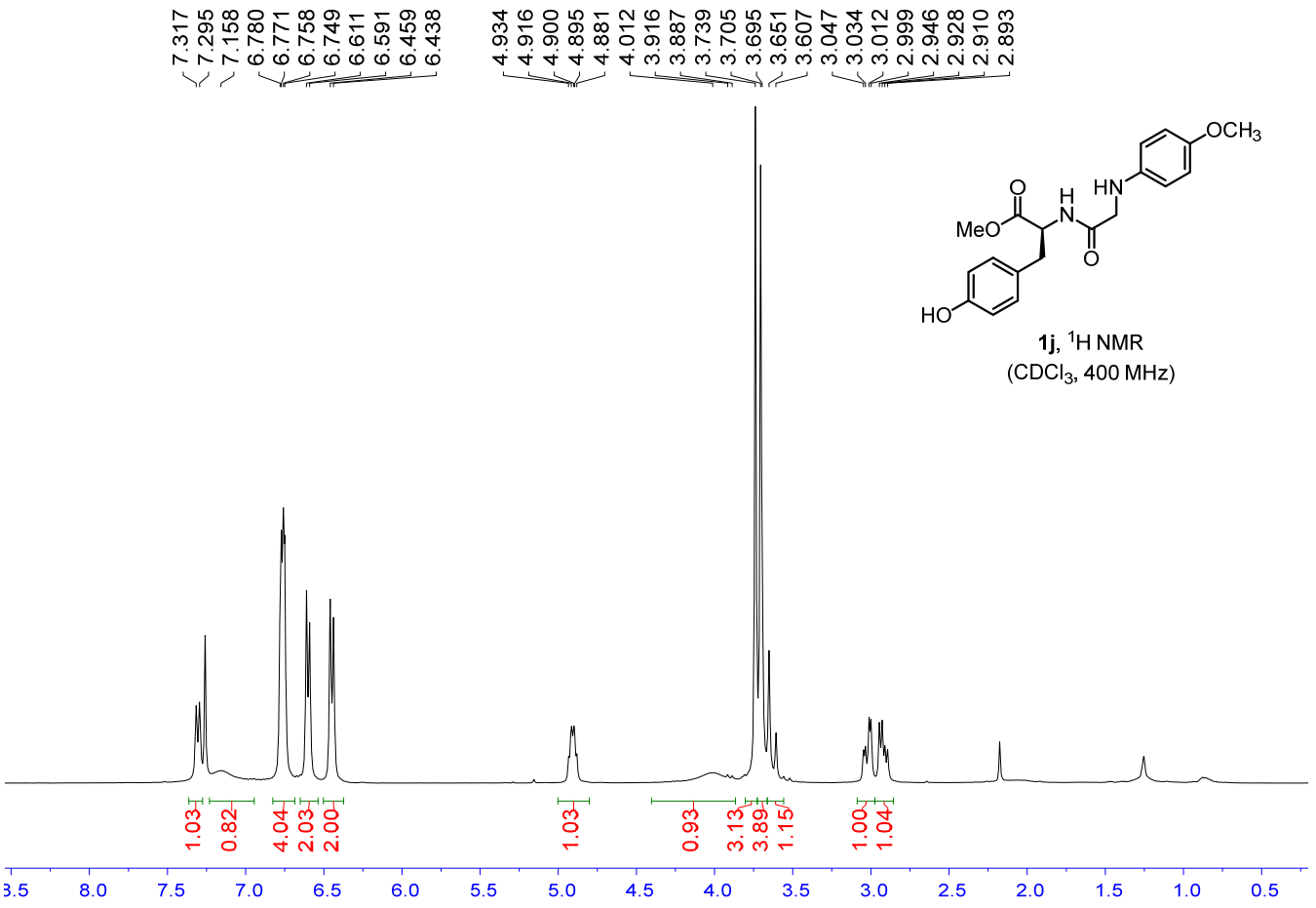
1g, ^{1}H NMR
($CDCl_3$, 400 MHz)





1g, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)




7.317
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4.900
4.895
4.881
4.012
3.916
3.887
3.739
3.705
3.695
3.651
3.607
3.047
3.034
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2.946
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2.910
2.893
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HN
H
N
MeO
O
O
HO
1j, 1H NMR
(CDCl3, 400 MHz)
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4.04
2.03
2.00
1.03
0.93
3.13
3.89
1.15
1.00
1.04
3.5
8.0
7.5
7.0
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5.0
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3.0
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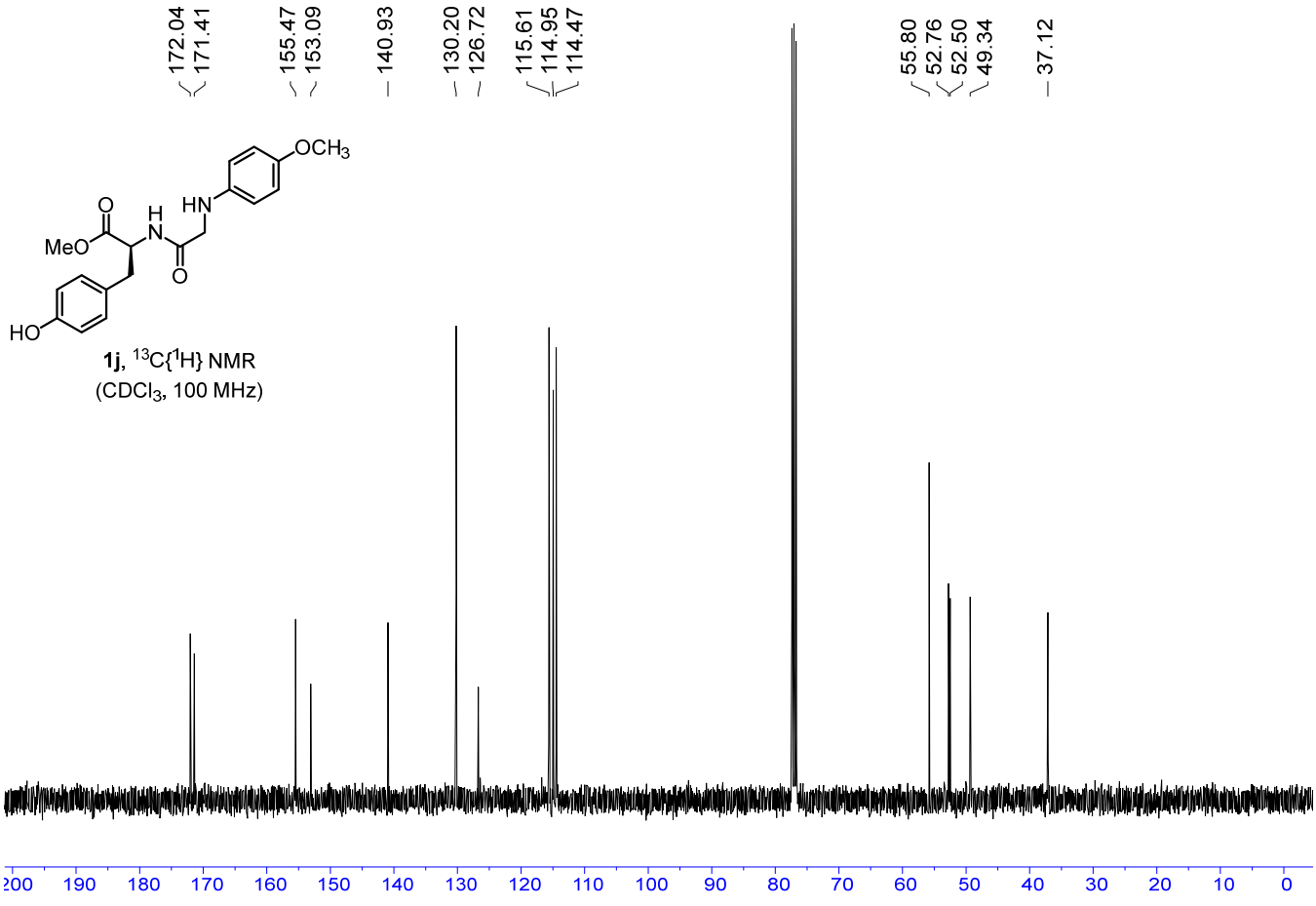
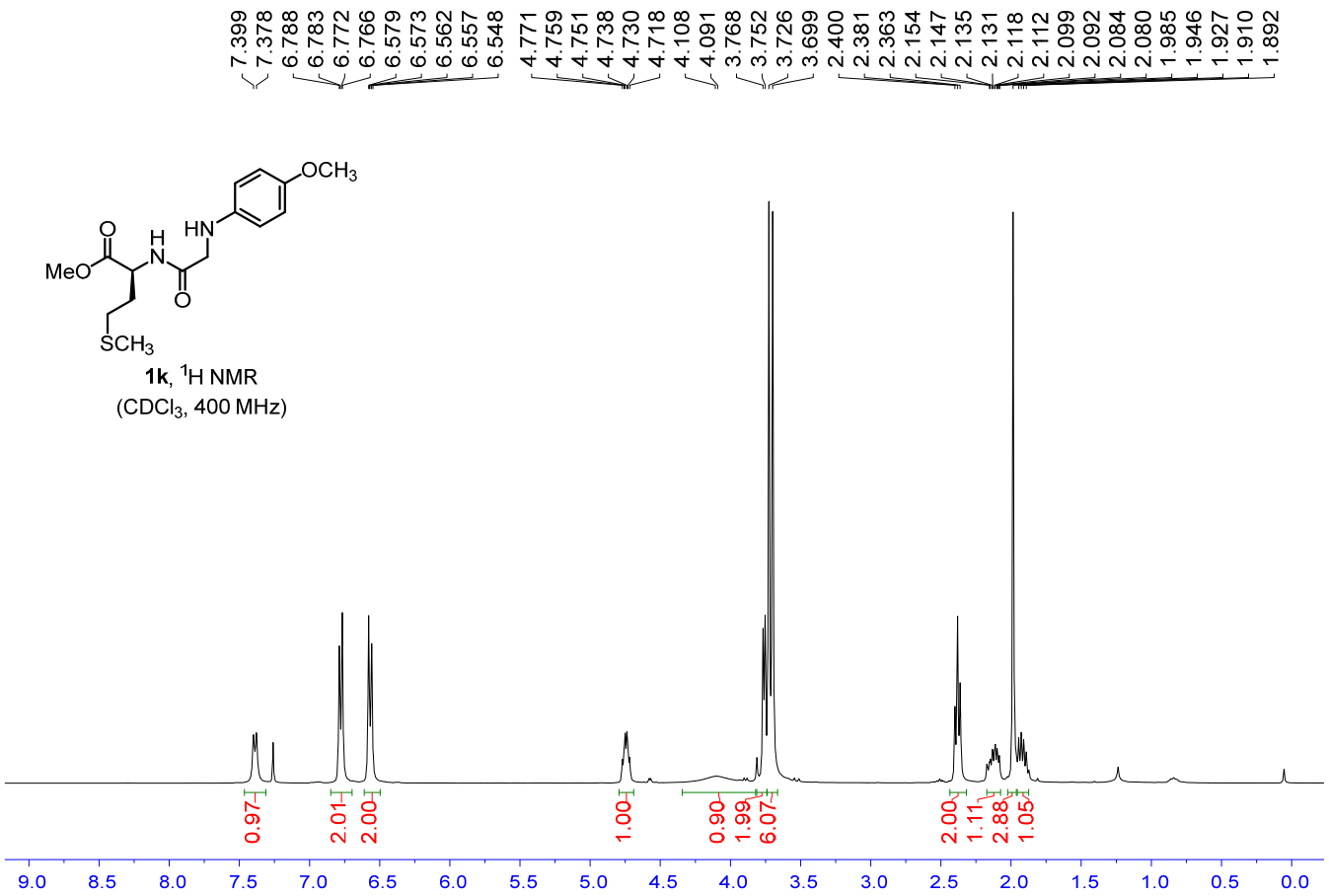
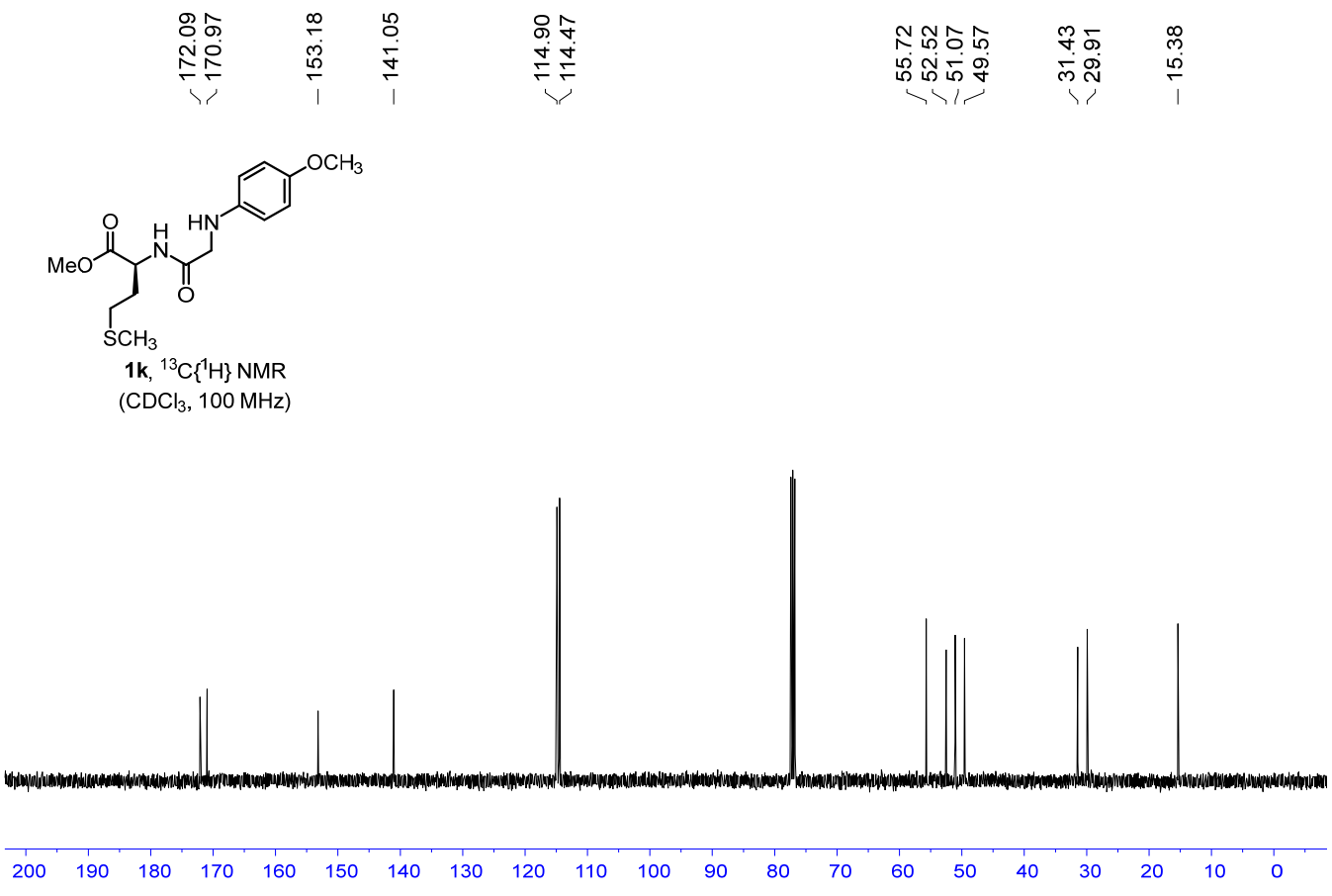
1.0
0.5

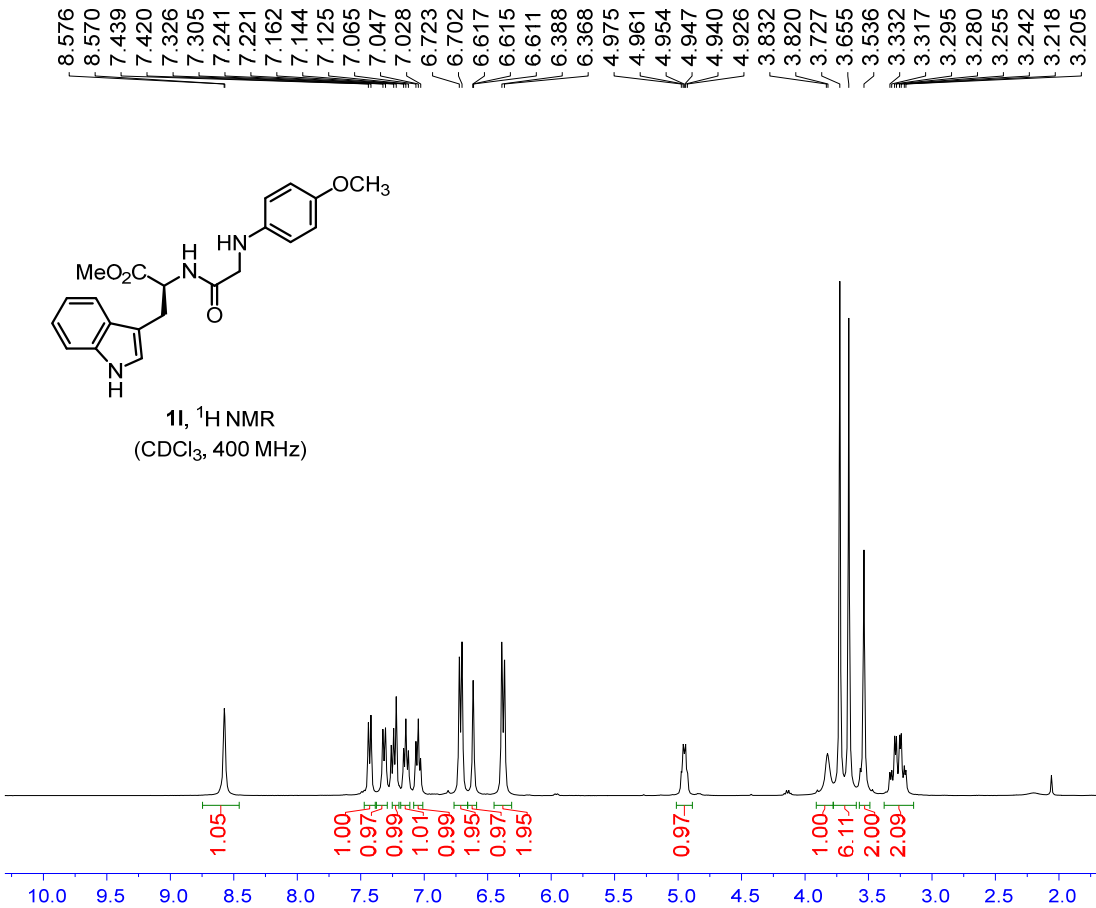

172.04
171.41
155.47
153.09
140.93
130.20
126.72
115.61
114.95
114.47
55.80
52.76
52.50
49.34
37.12
OCH3
HN
H
N
MeO
O
O
HO
1j, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



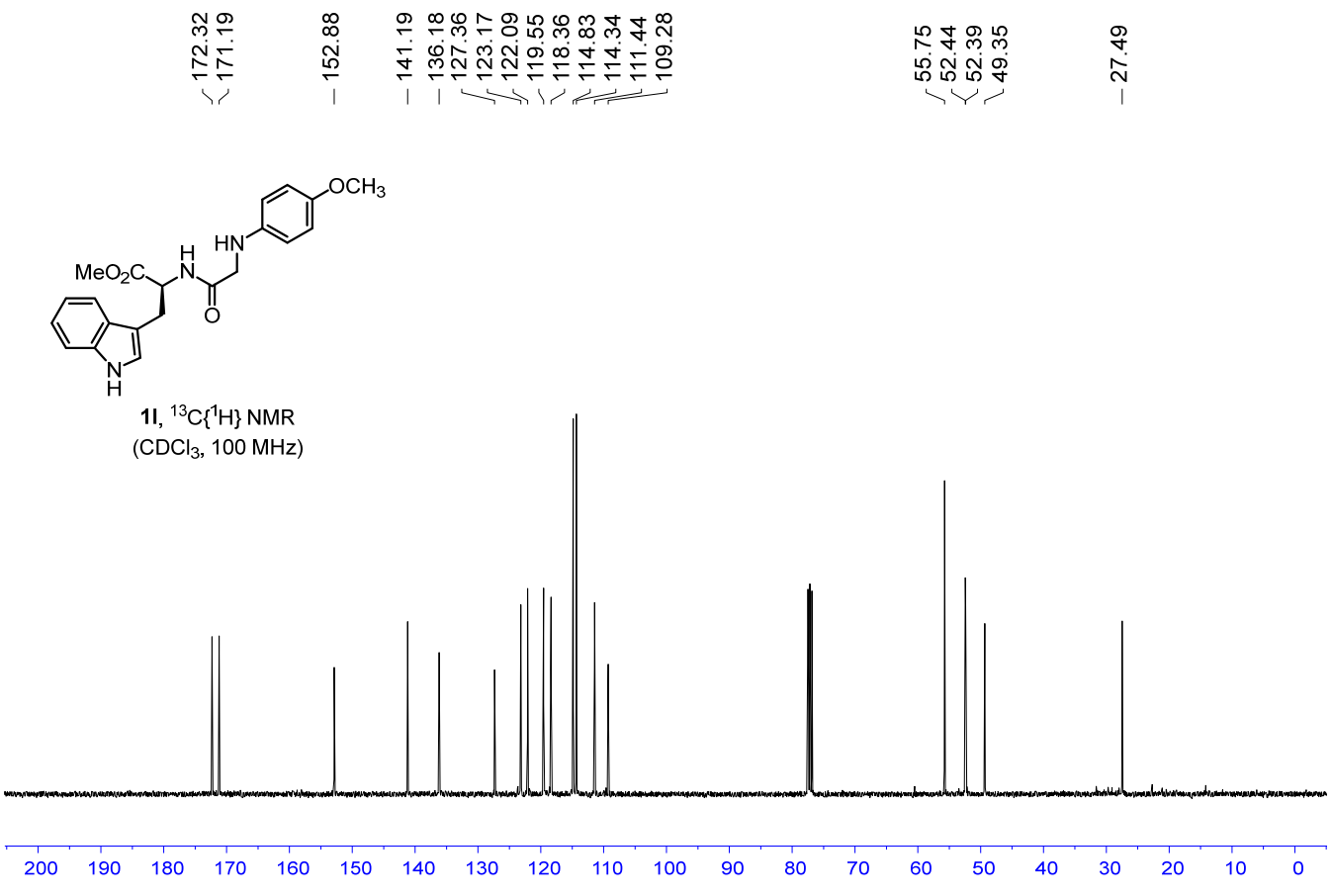
1k, ^{1}H NMR
($CDCl_3$, 400 MHz)



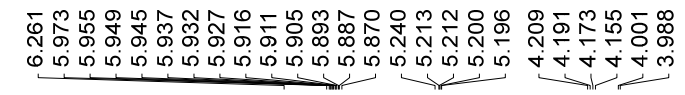
1k, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)

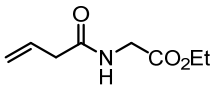


1l, ^{1}H NMR
($CDCl_3$, 400 MHz)

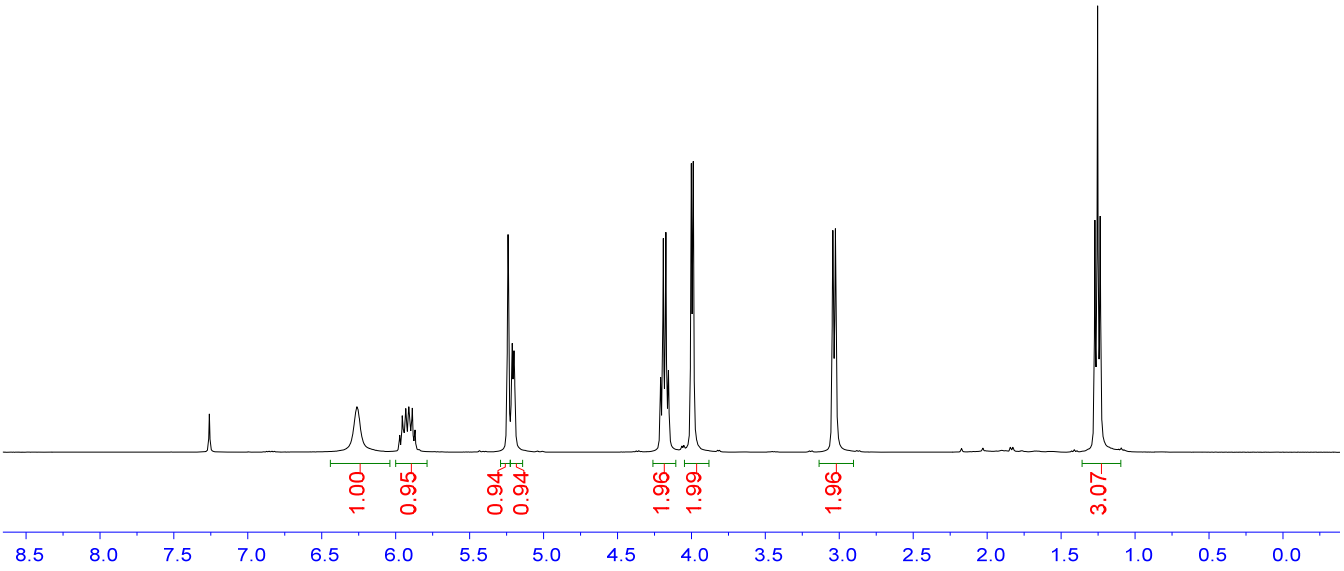


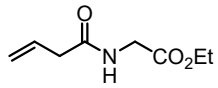
1l, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)



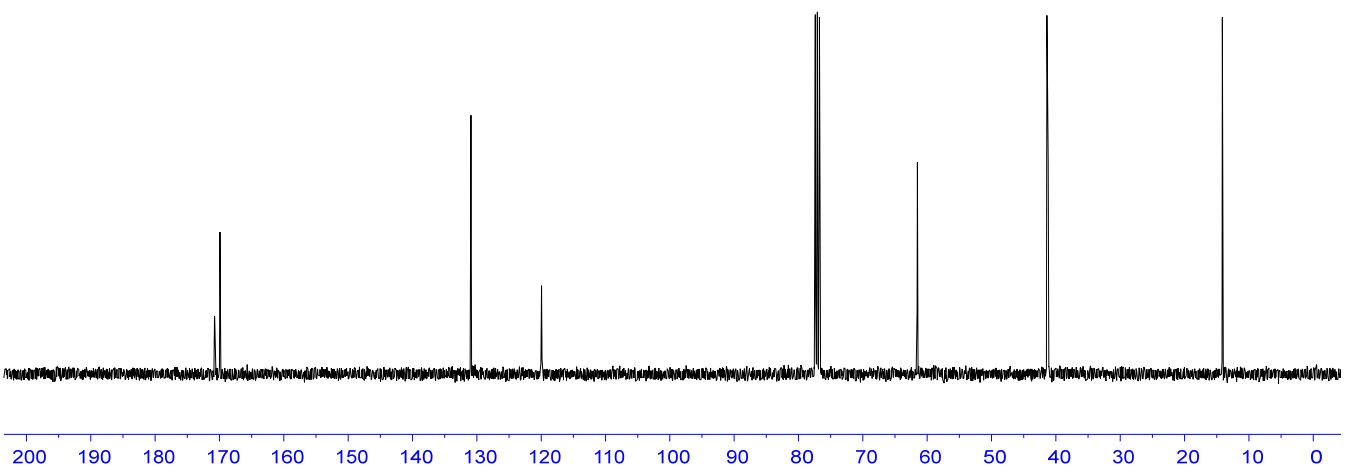


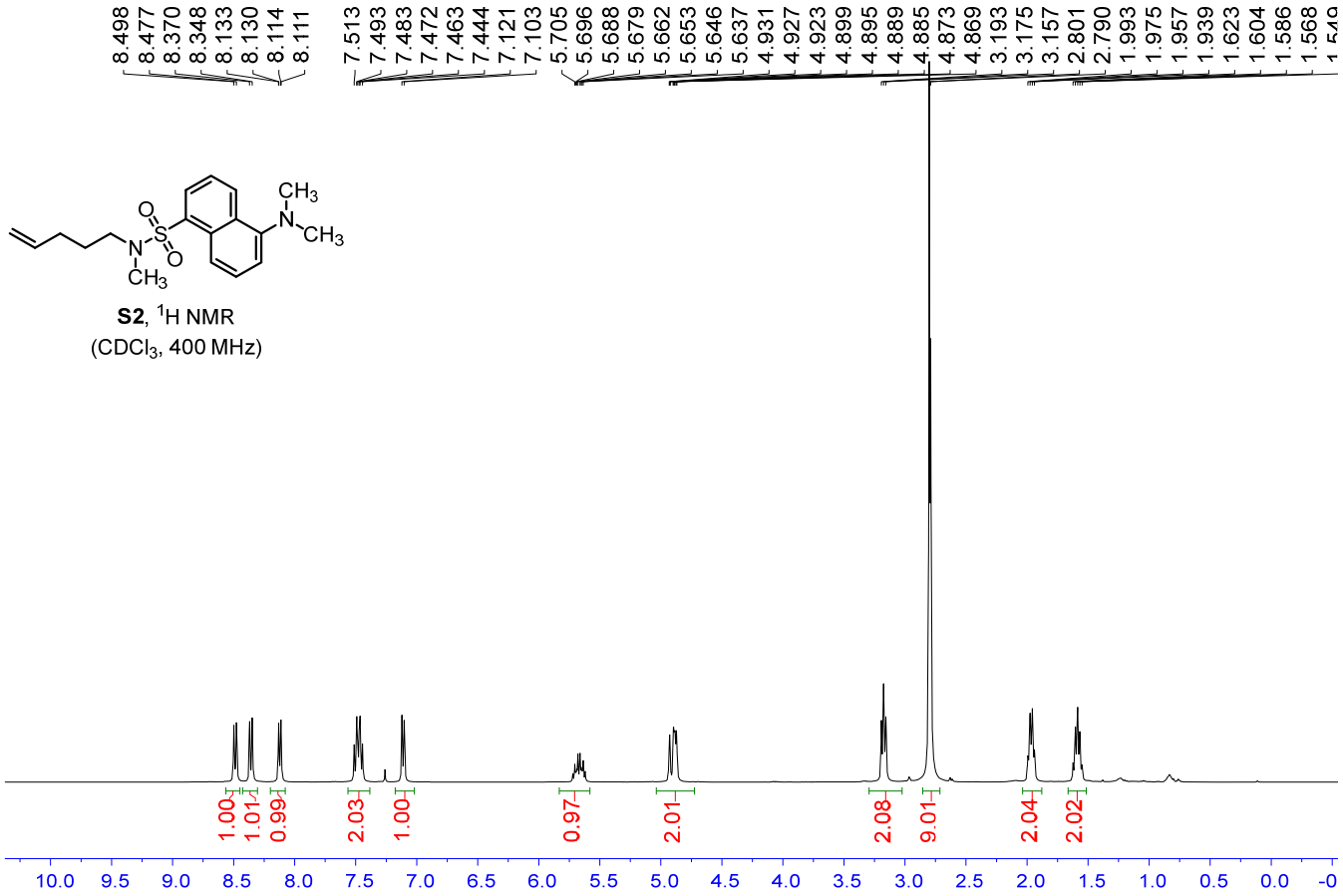
2m, ^{1}H NMR
($CDCl_3$, 400 MHz)



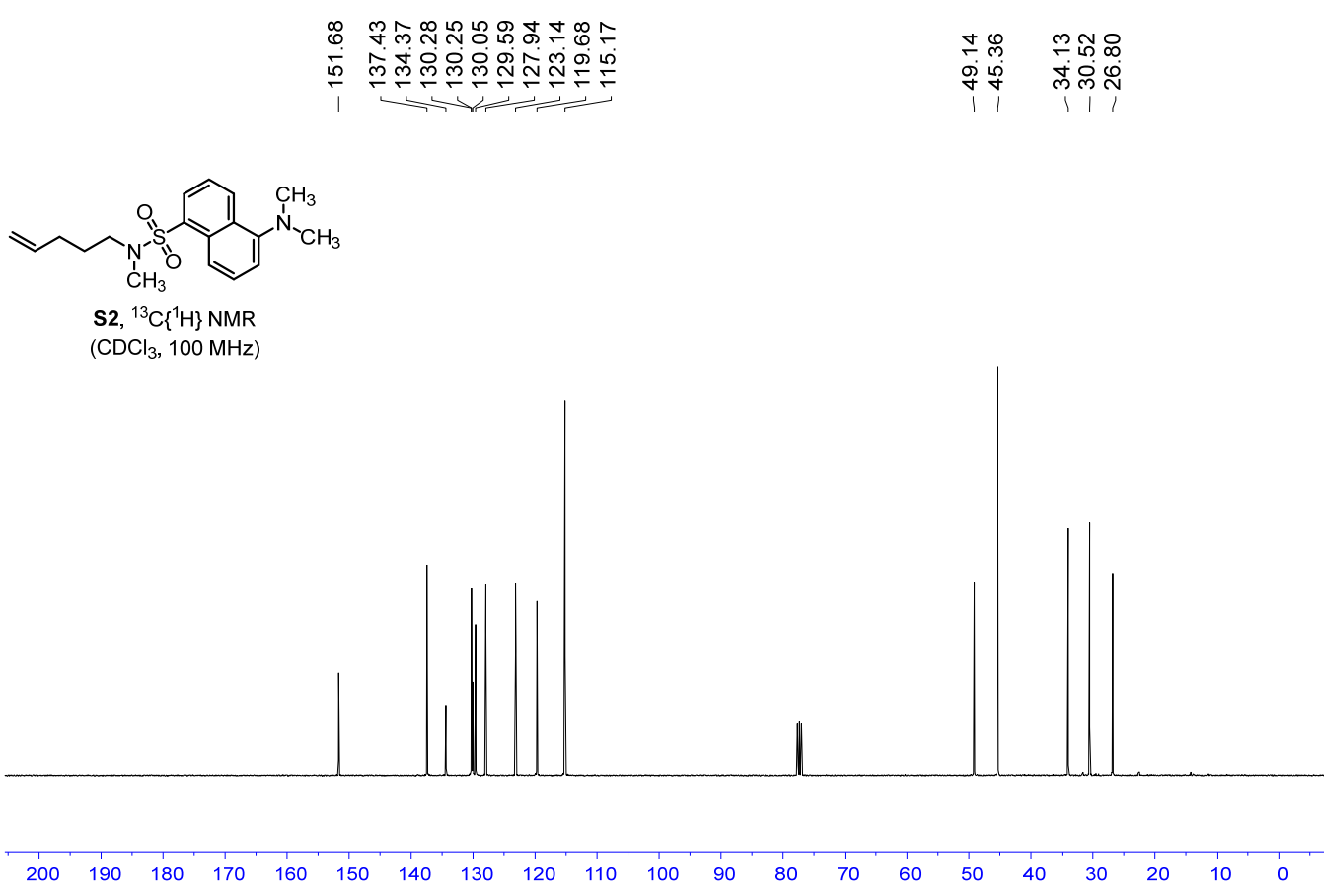


2m, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)

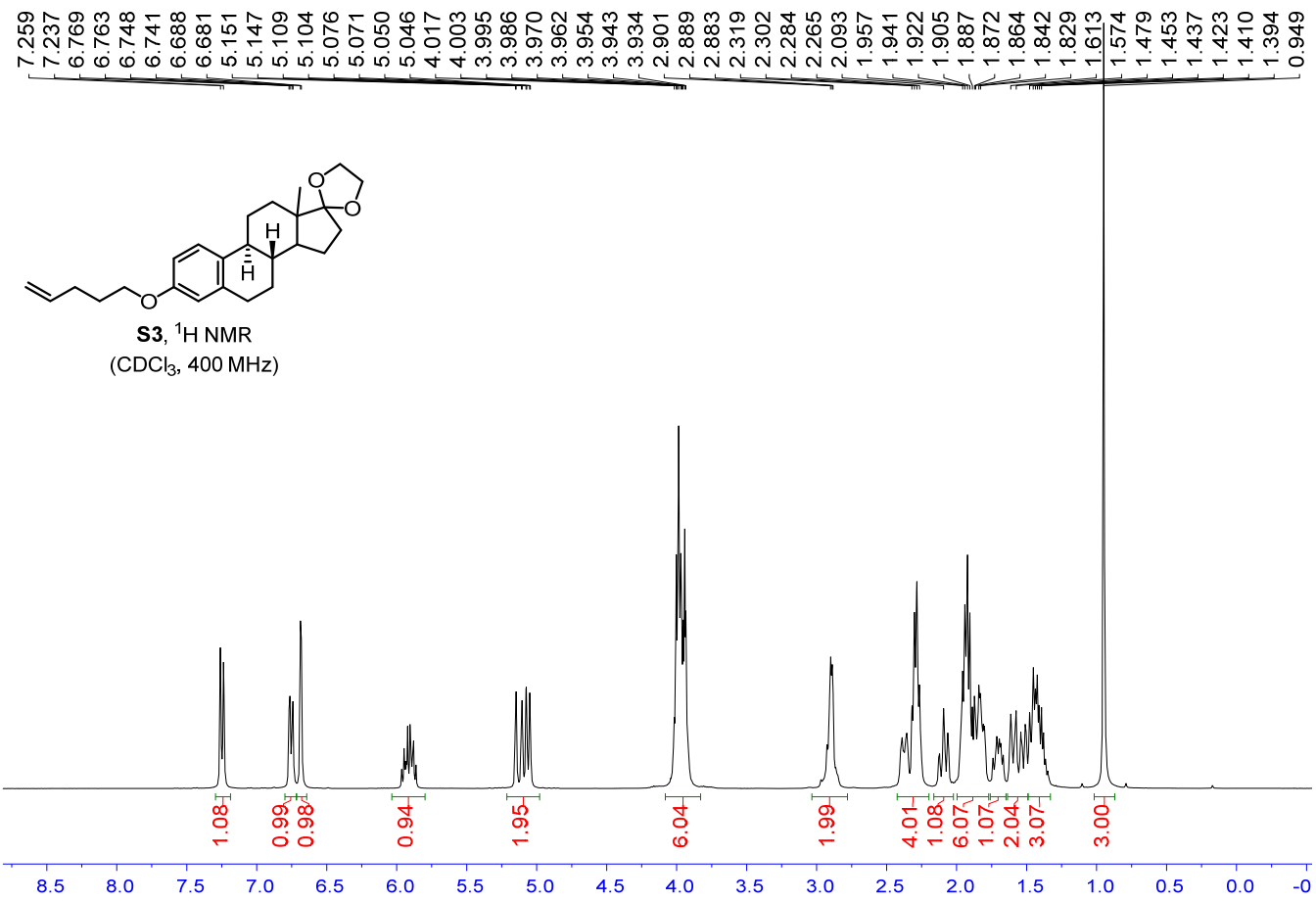




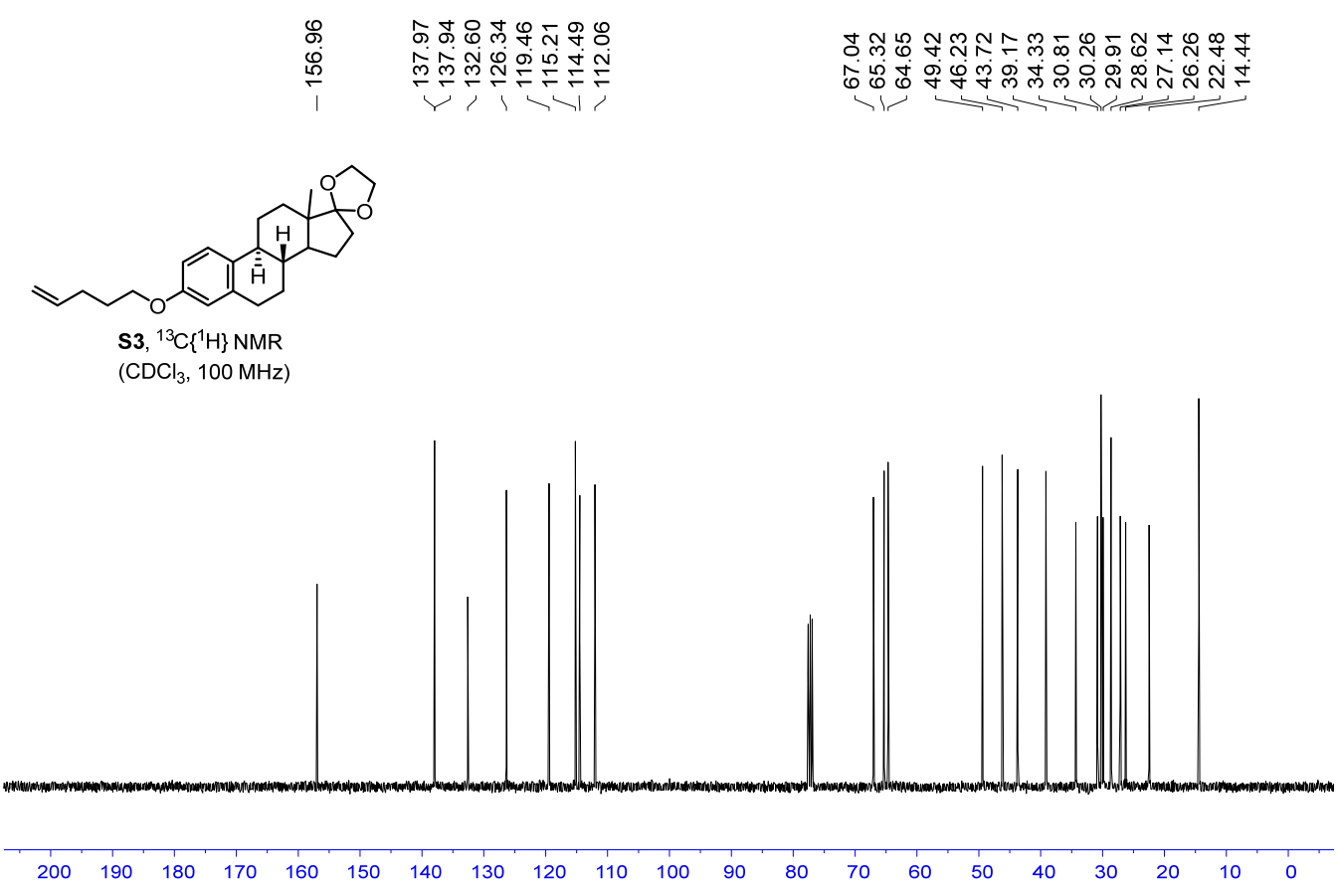
S2, ^{1}H NMR
($CDCl_3$, 400 MHz)



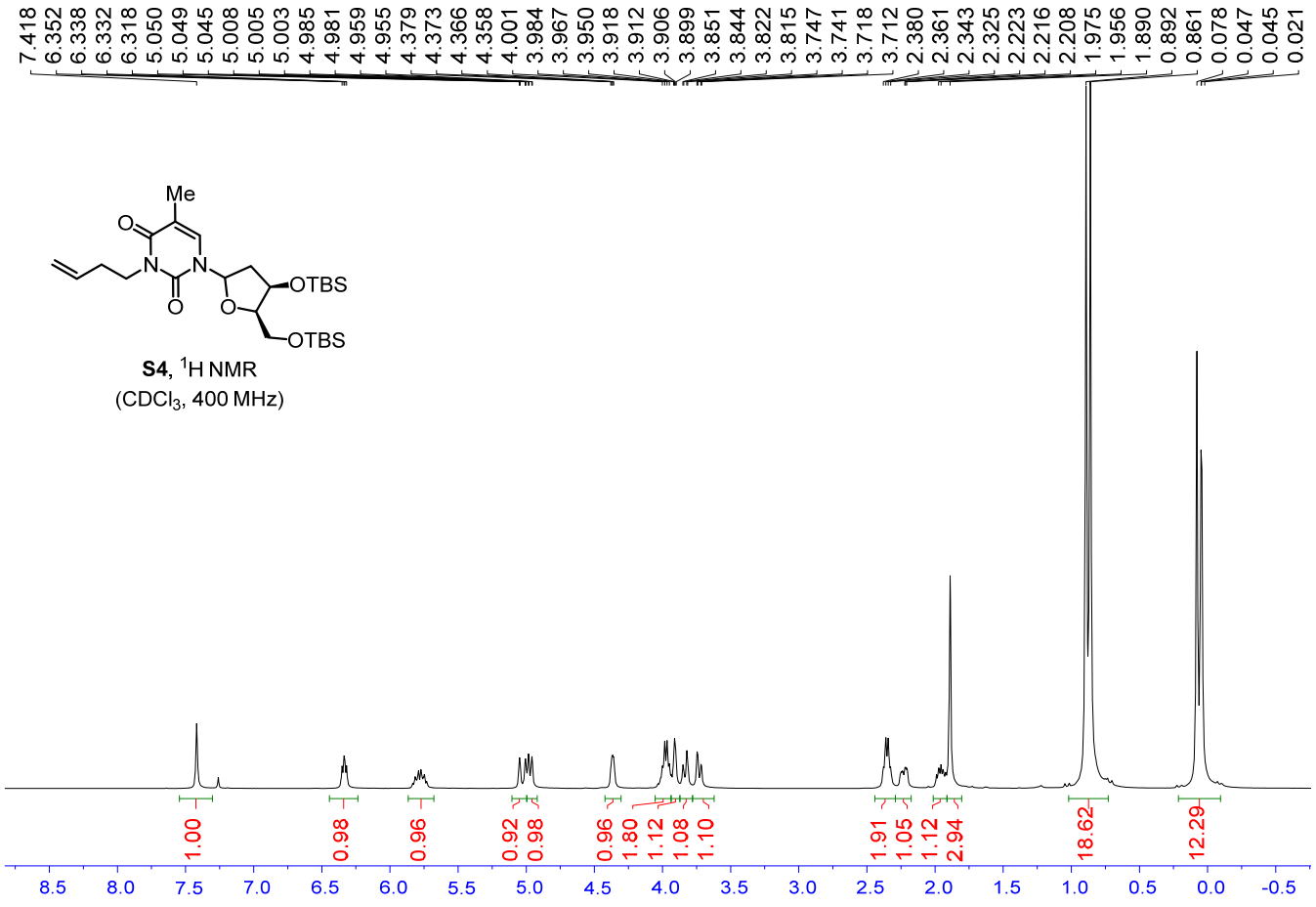
S2, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)



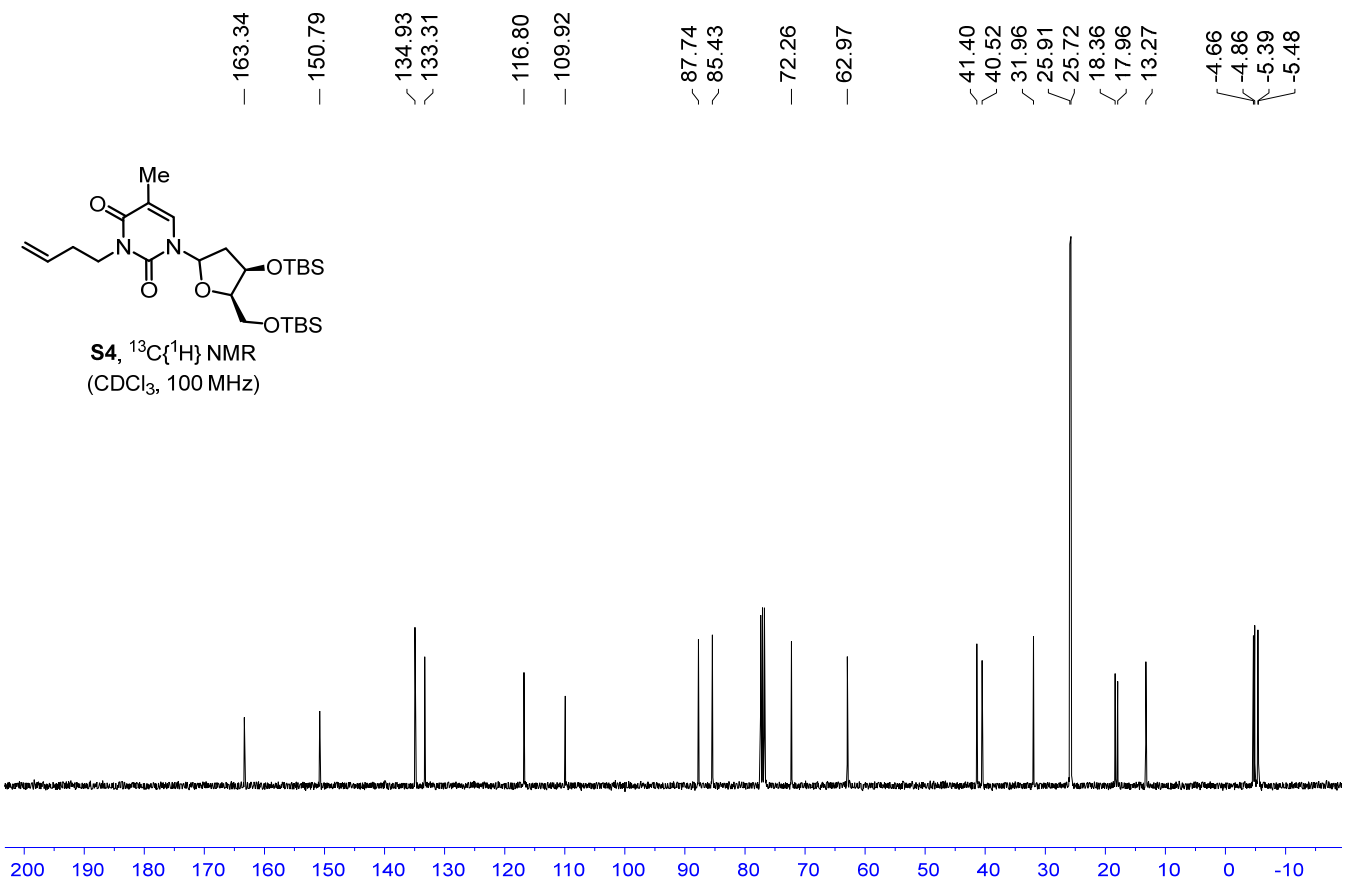
S3, ^{1}H NMR
($CDCl_3$, 400 MHz)



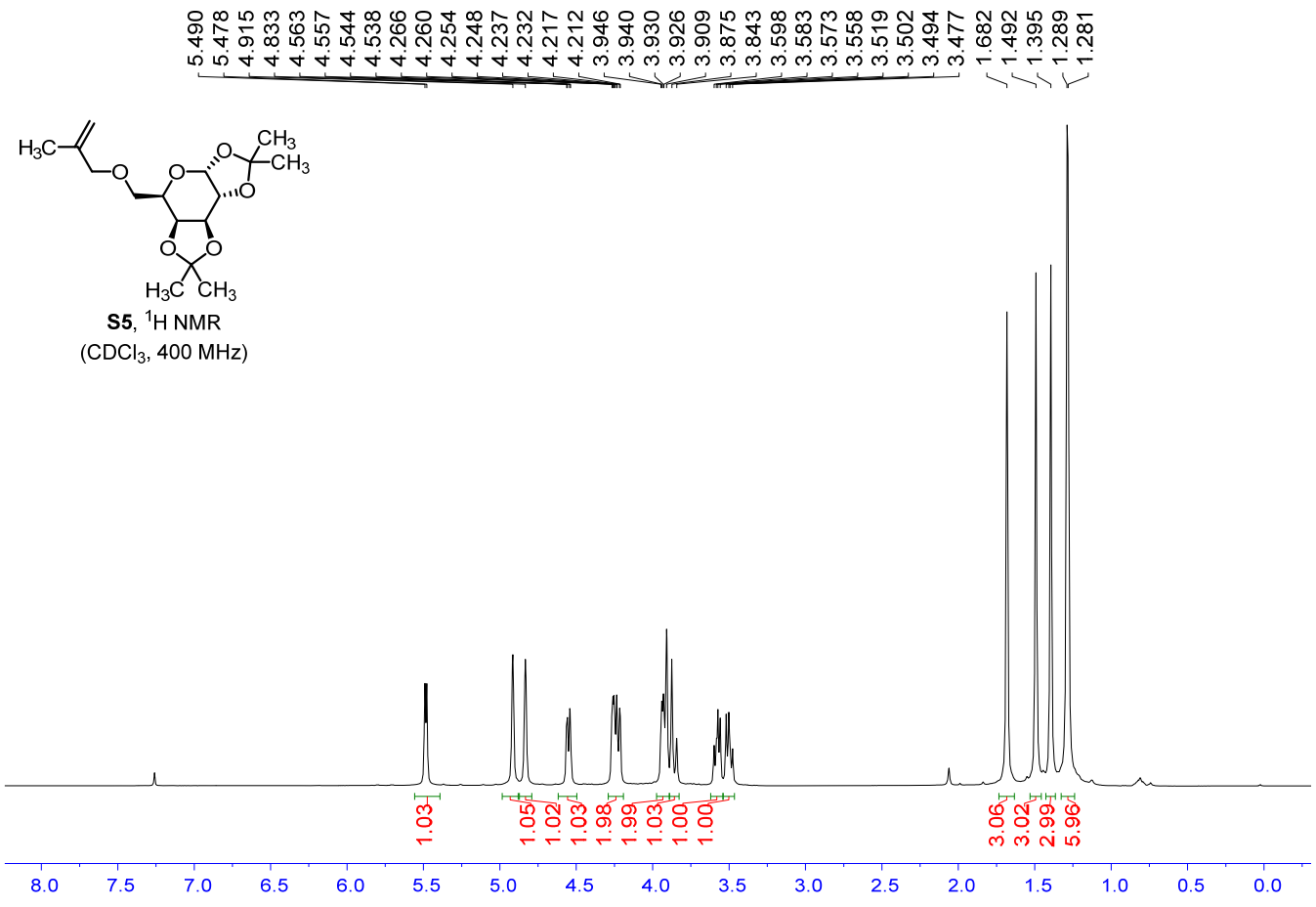
S3, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)



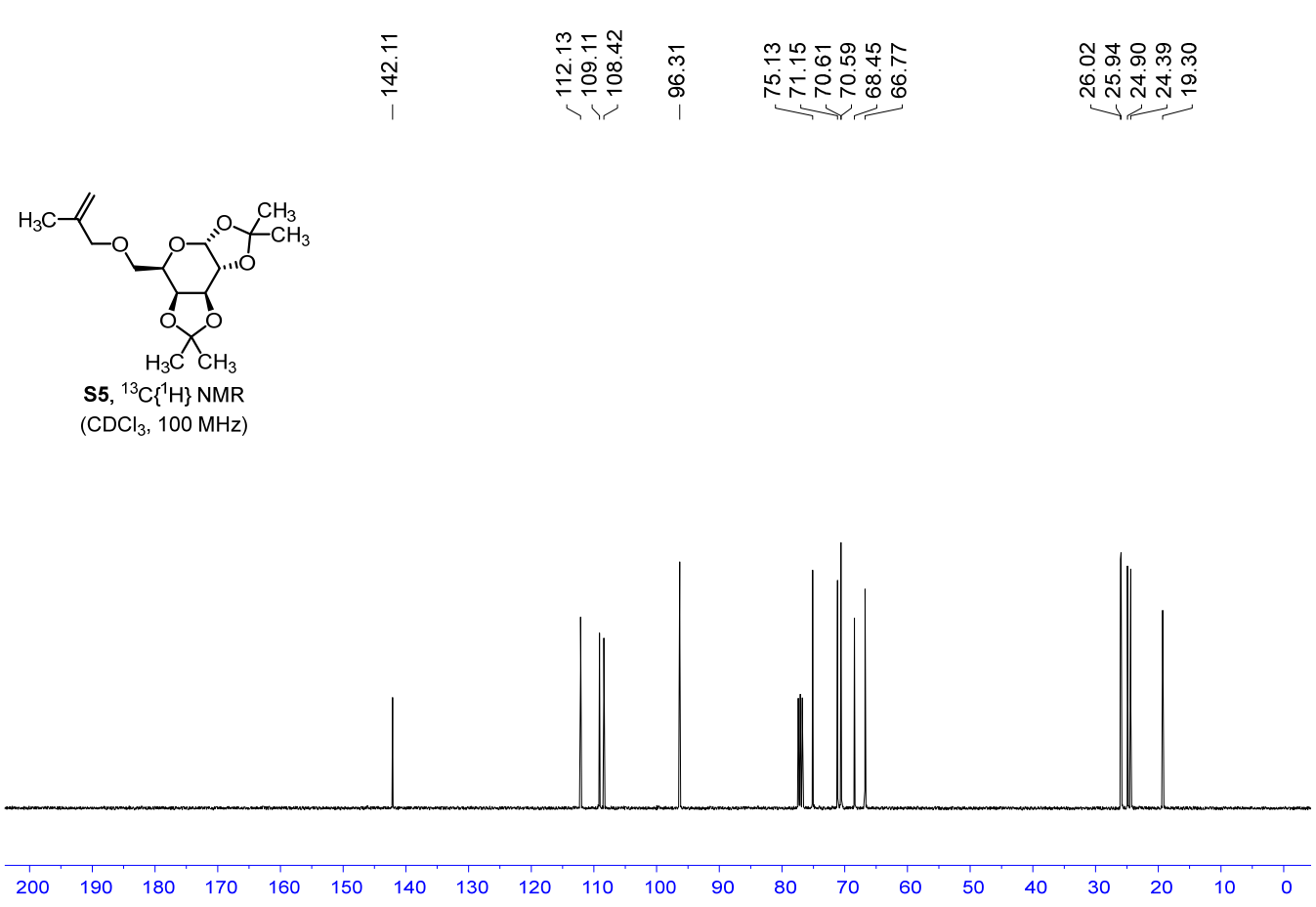
S4, ^{1}H NMR
($CDCl_3$, 400 MHz)



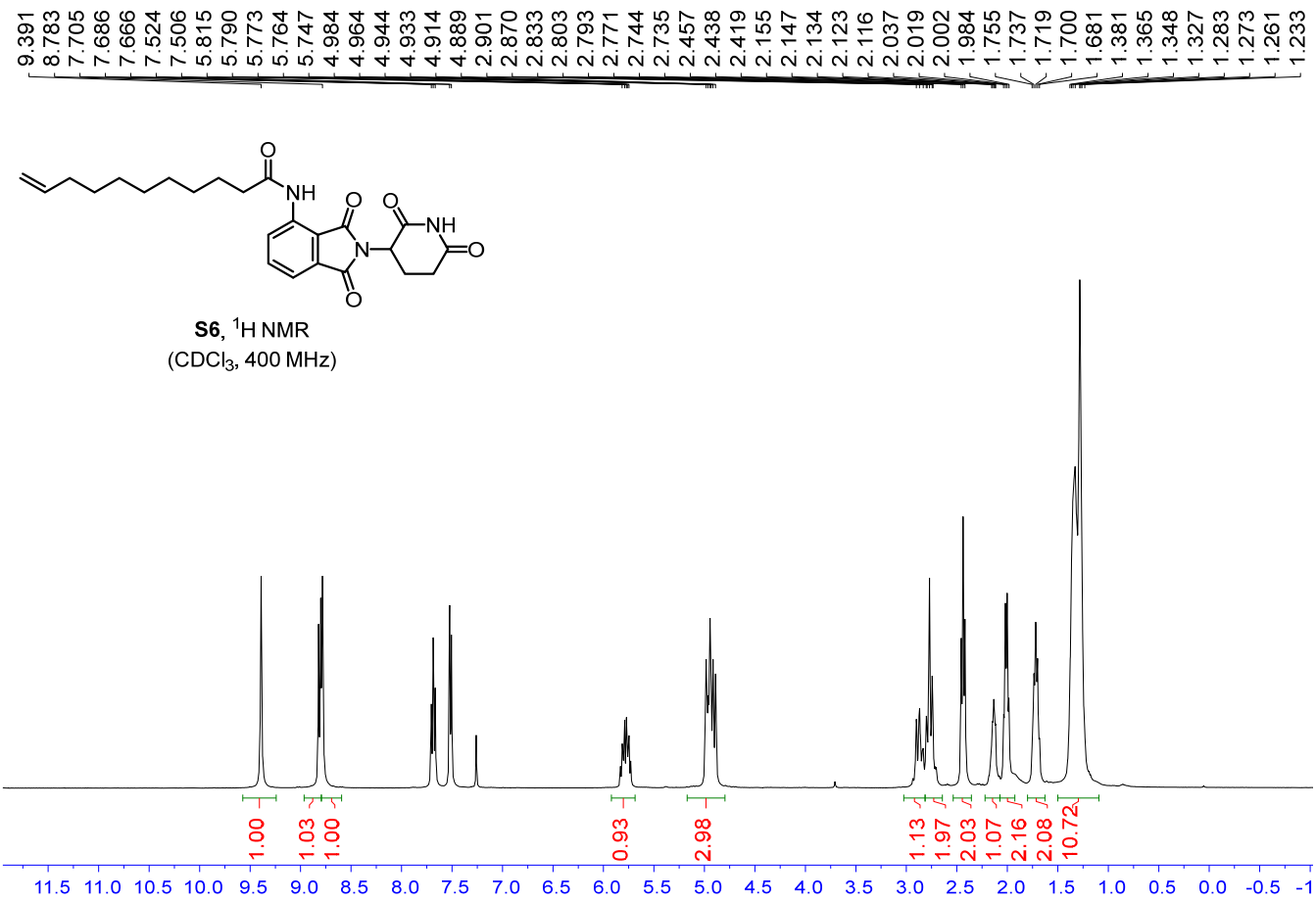
S4, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



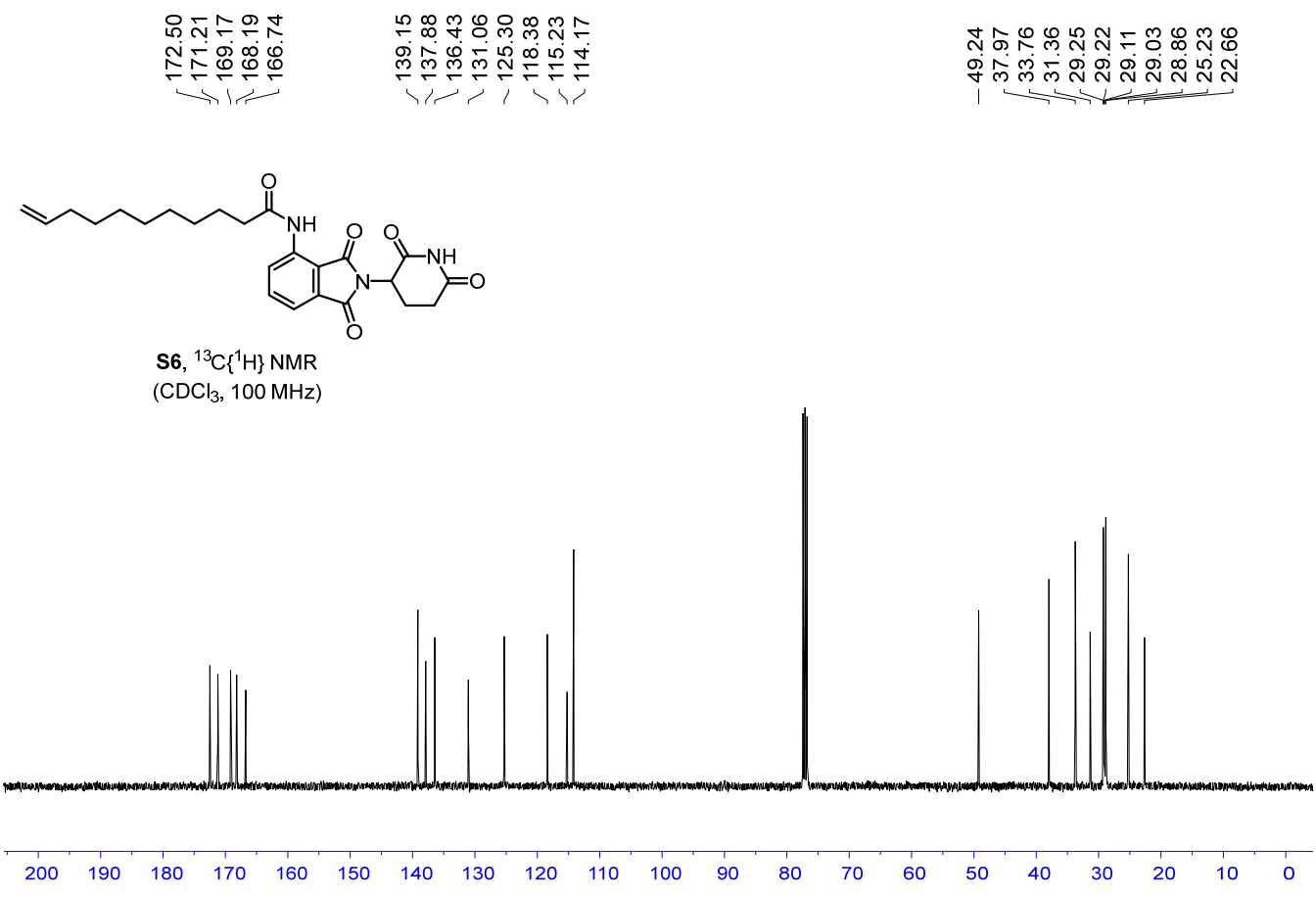
S5, ^{1}H NMR
($CDCl_3$, 400 MHz)



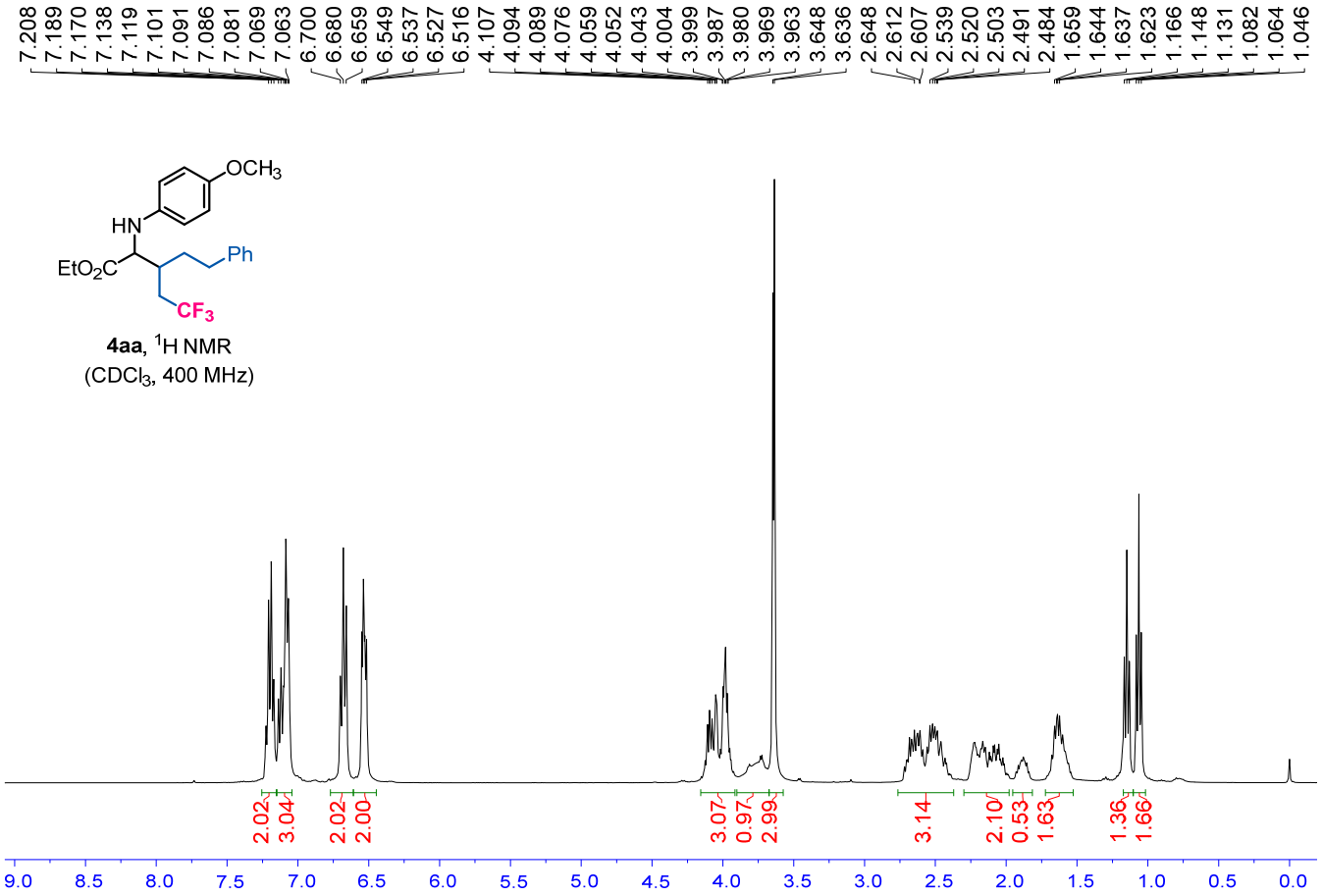
S5, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)

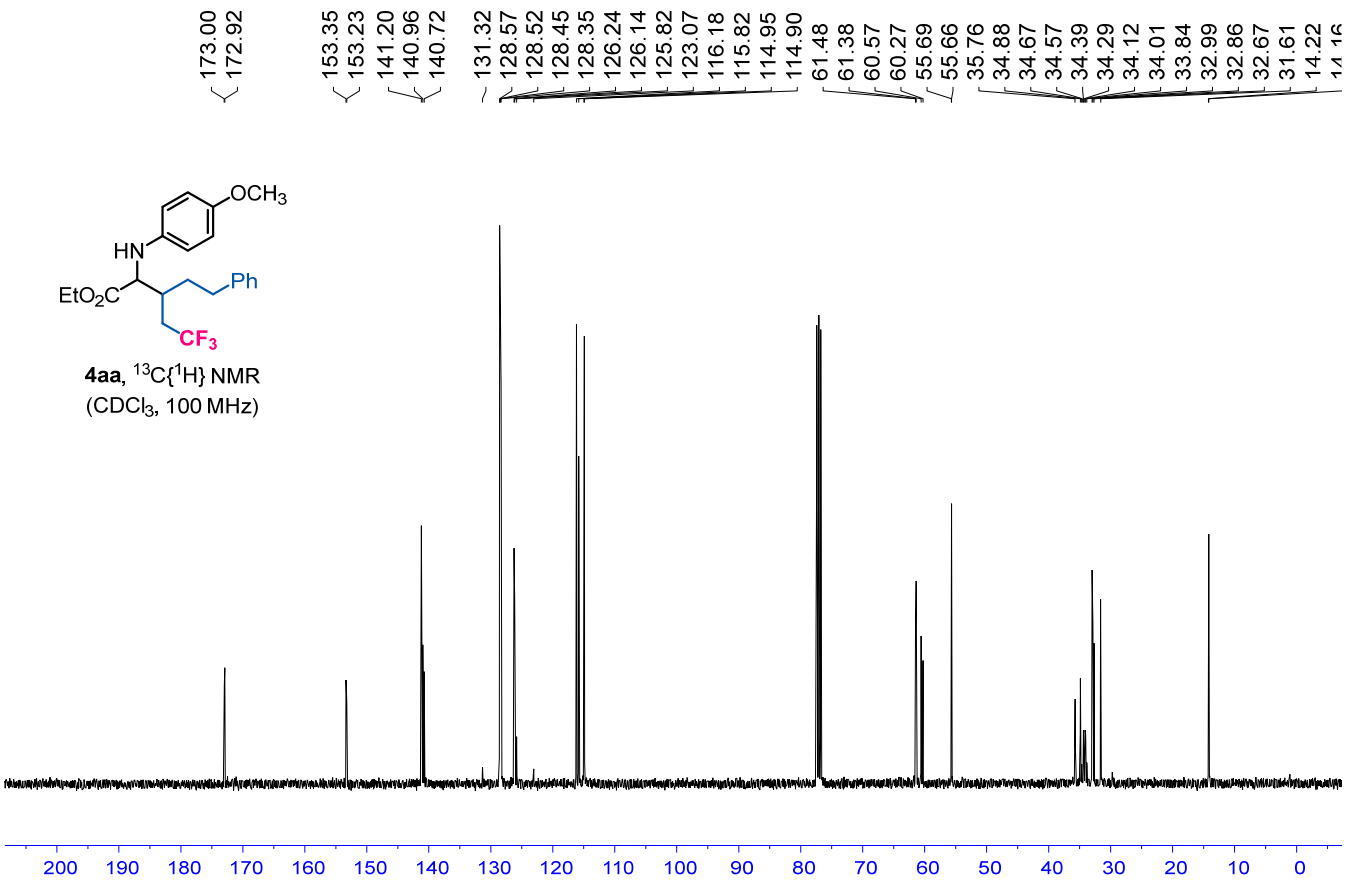


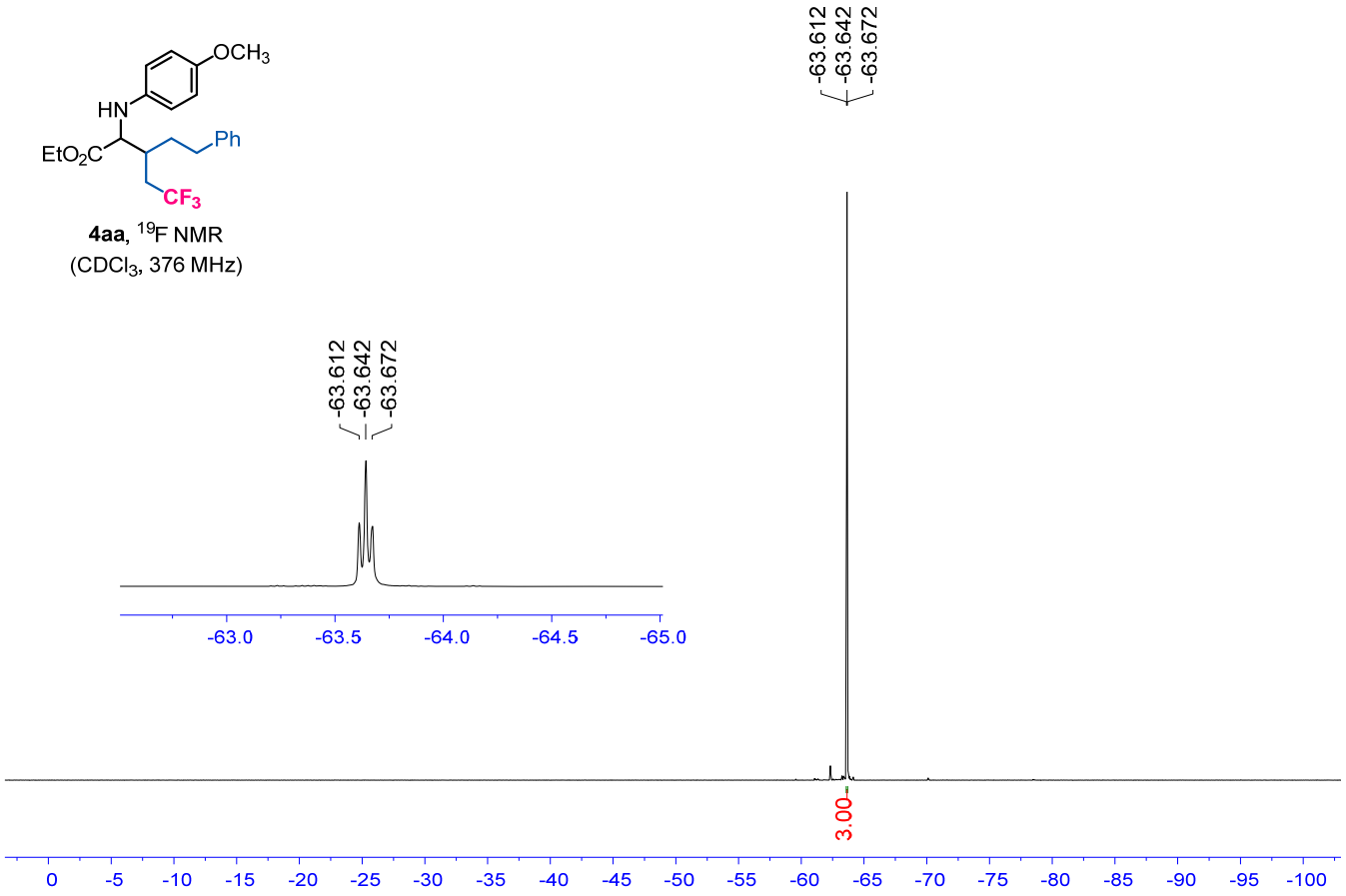
S6, ^{1}H NMR
($CDCl_3$, 400 MHz)



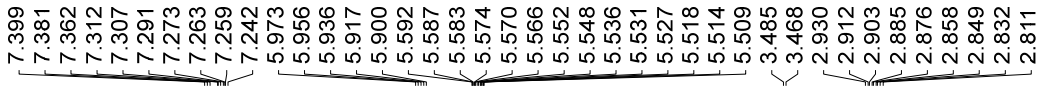
S6, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)


7.208
7.189
7.170
7.138
7.119
7.101
7.091
7.086
7.081
7.069
7.063
6.700
6.680
6.659
6.549
6.537
6.527
6.516
4.107
4.094
4.089
4.076
4.059
4.052
4.043
4.004
3.999
3.987
3.980
3.969
3.963
3.648
3.636
2.648
2.612
2.607
2.539
2.520
2.503
2.491
2.484
1.659
1.644
1.637
1.623
1.166
1.148
1.131
1.082
1.064
1.046
OCH3
HN
EtO2C
Ph
CF3
4aa, 1H NMR
(CDCl3, 400 MHz)
2.02
3.04
2.02
2.00
3.07
0.97
2.99
3.14
2.10
0.53
1.63
1.36
1.66
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

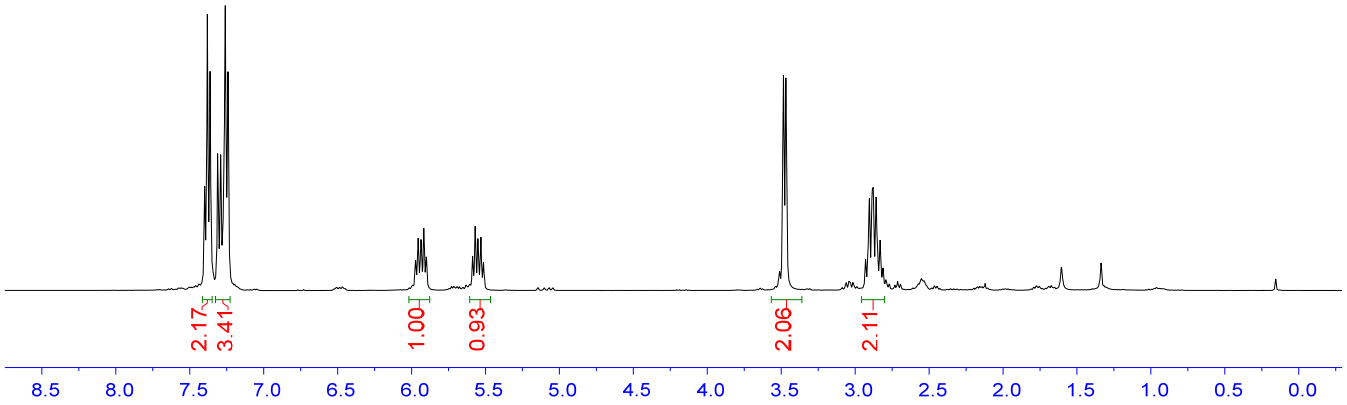

173.00
172.92
153.35
153.23
141.20
140.96
140.72
131.32
128.57
128.52
128.45
128.35
126.24
126.14
125.82
123.07
116.18
115.82
114.95
114.90
61.48
61.38
60.57
60.27
55.69
55.66
35.76
34.88
34.67
34.57
34.39
34.29
34.12
34.01
33.84
32.99
32.86
32.67
31.61
14.22
OCH3
HN
EtO2C
Ph
CF3
4aa, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



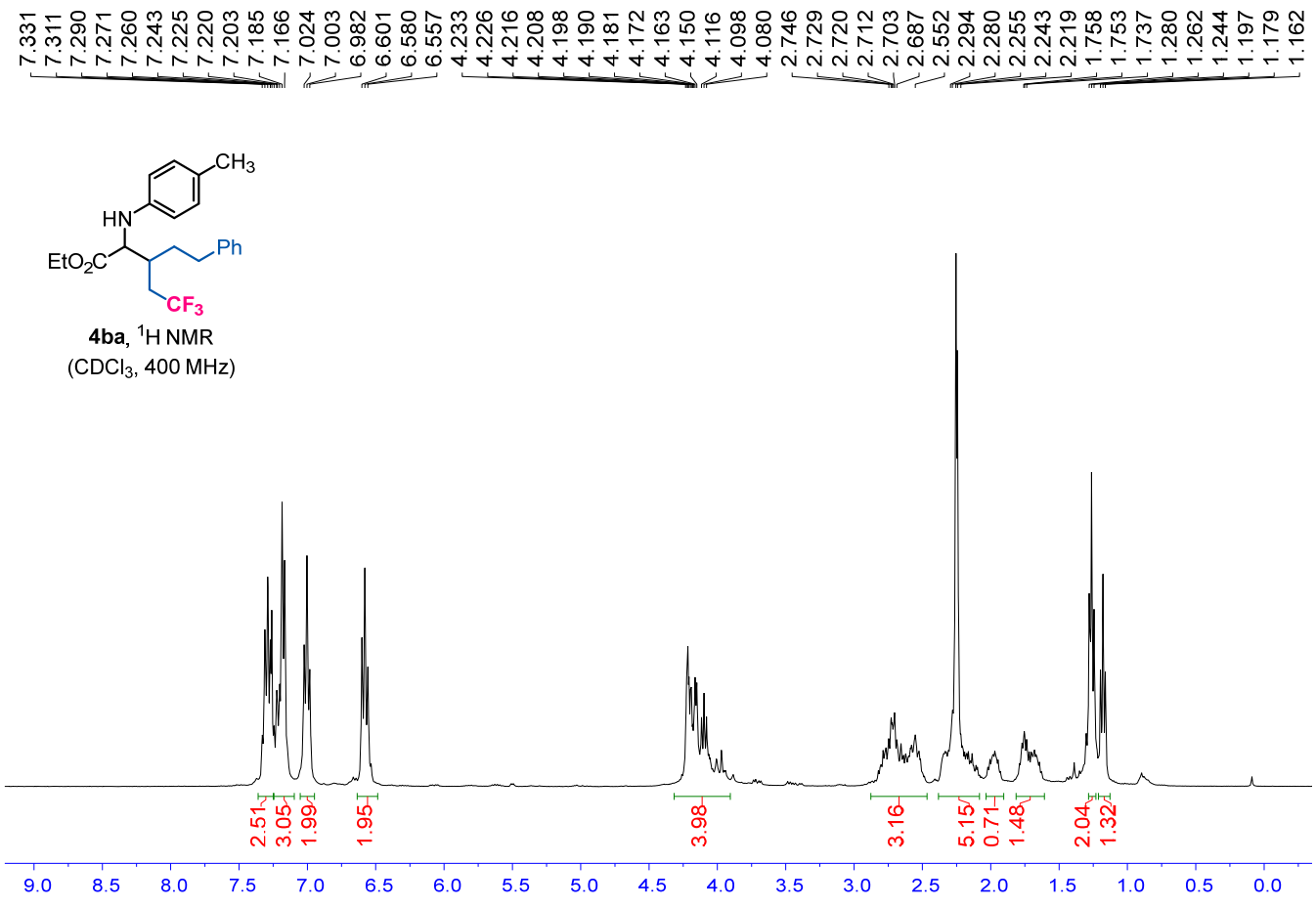
4aa, ^{19}F NMR
($CDCl_3$, 376 MHz)

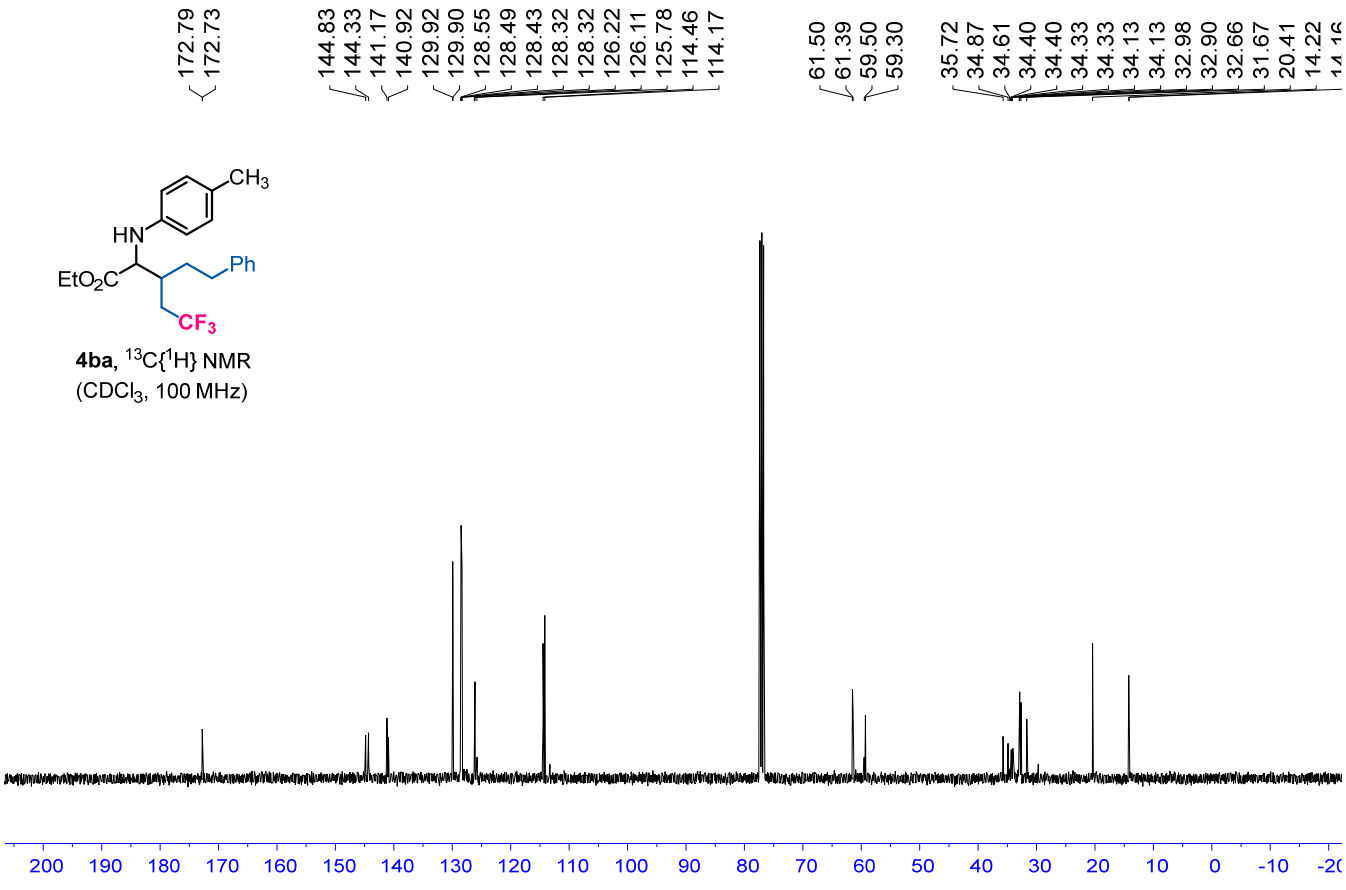


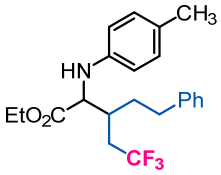
5a, ^{1}H NMR
($CDCl_3$, 400 MHz)



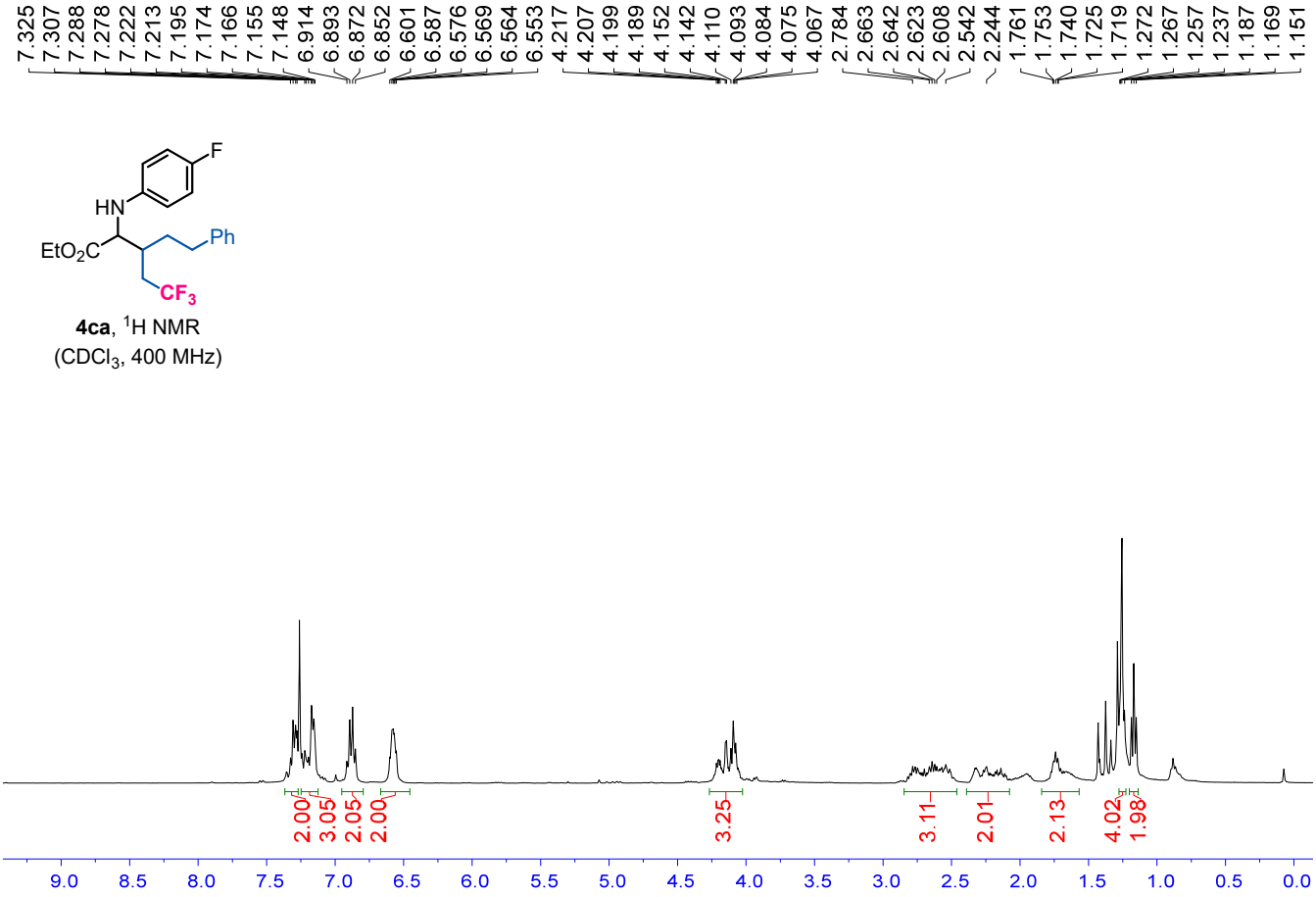
5a, ^{19}F NMR
($CDCl_3$, 376 MHz)


7.331
7.311
7.290
7.271
7.260
7.243
7.225
7.220
7.203
7.185
7.166
7.024
7.003
6.982
6.601
6.580
6.557
4.233
4.226
4.216
4.208
4.198
4.190
4.181
4.172
4.163
4.150
4.116
4.098
4.080
2.746
2.729
2.720
2.712
2.703
2.687
2.552
2.294
2.280
2.255
2.243
2.219
1.758
1.753
1.737
1.280
1.262
1.244
1.197
1.179
1.162
CH3
HN
EtO2C
Ph
CF3
4ba, 1H NMR
(CDCl3, 400 MHz)
2.51
3.05
1.99
1.95
3.98
3.16
5.15
0.71
1.48
2.04
1.32
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

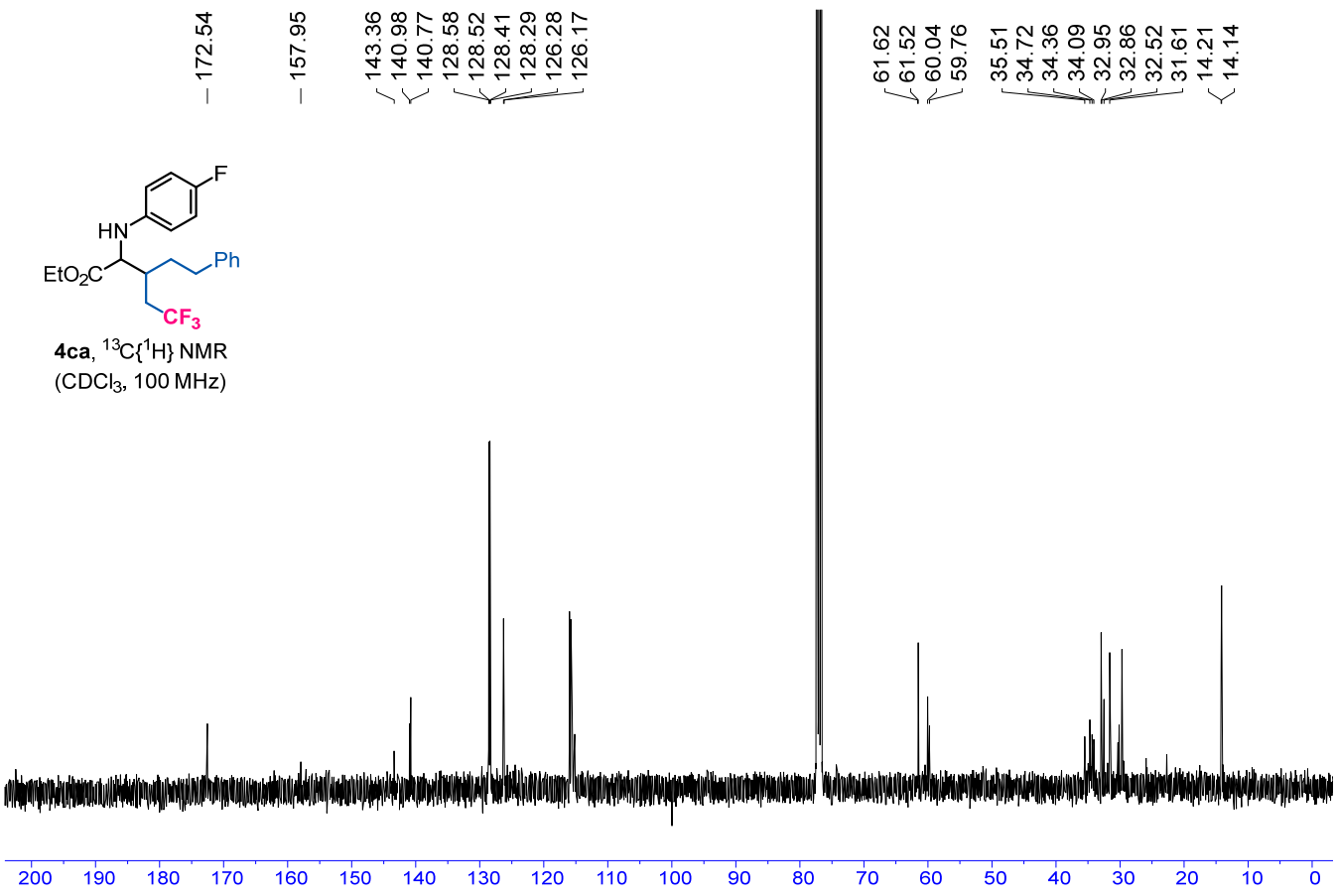

172.79
172.73
144.83
144.33
141.17
140.92
129.92
129.90
128.55
128.49
128.43
128.32
128.32
126.22
126.11
125.78
114.46
114.17
61.50
61.39
59.50
59.30
35.72
34.87
34.61
34.40
34.40
34.33
34.33
34.13
34.13
32.98
32.90
32.66
31.67
20.41
14.22
CH3
HN
EtO2C
Ph
CF3
4ba, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10



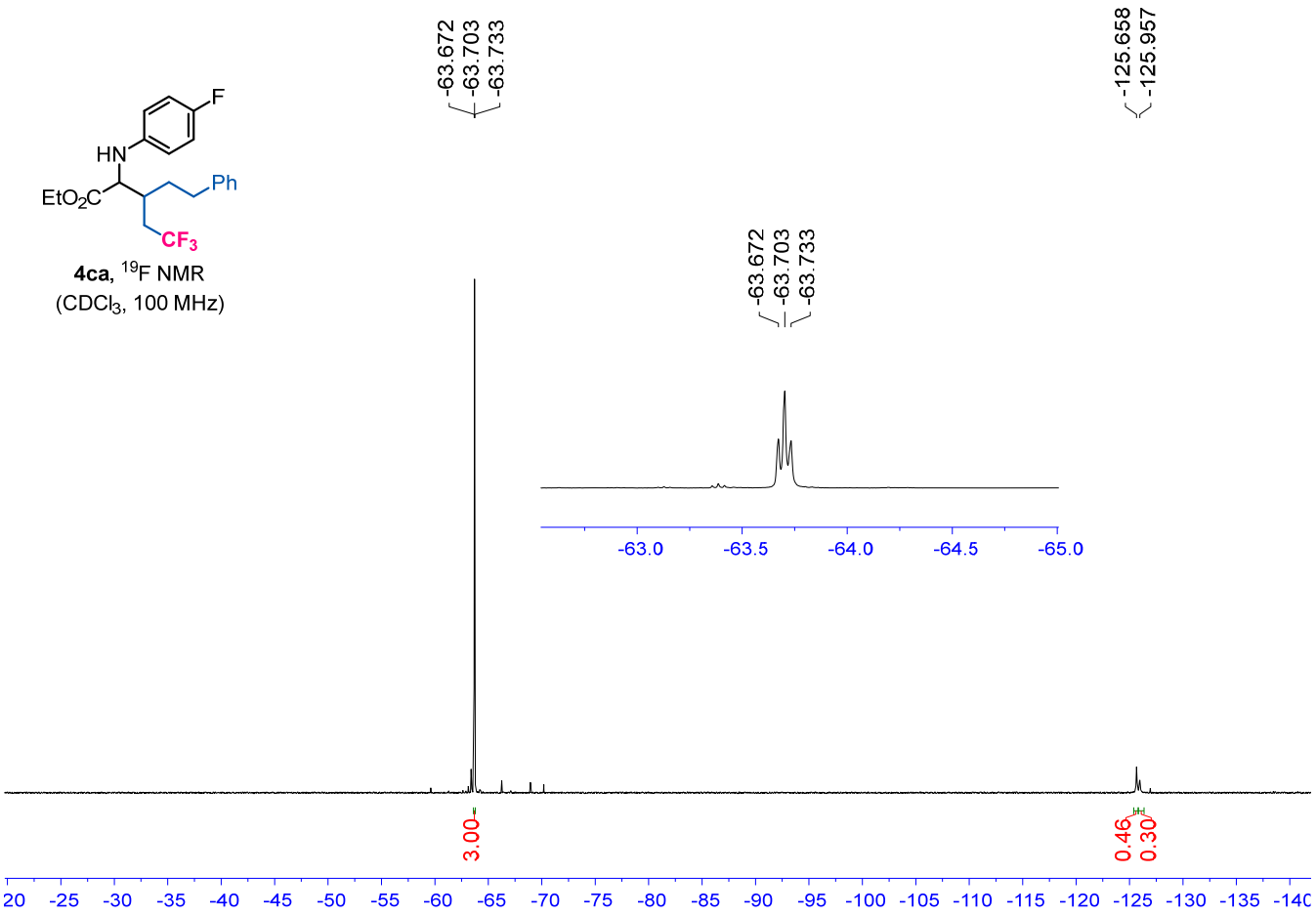
4ba, ^{19}F NMR
($CDCl_3$, 376 MHz)

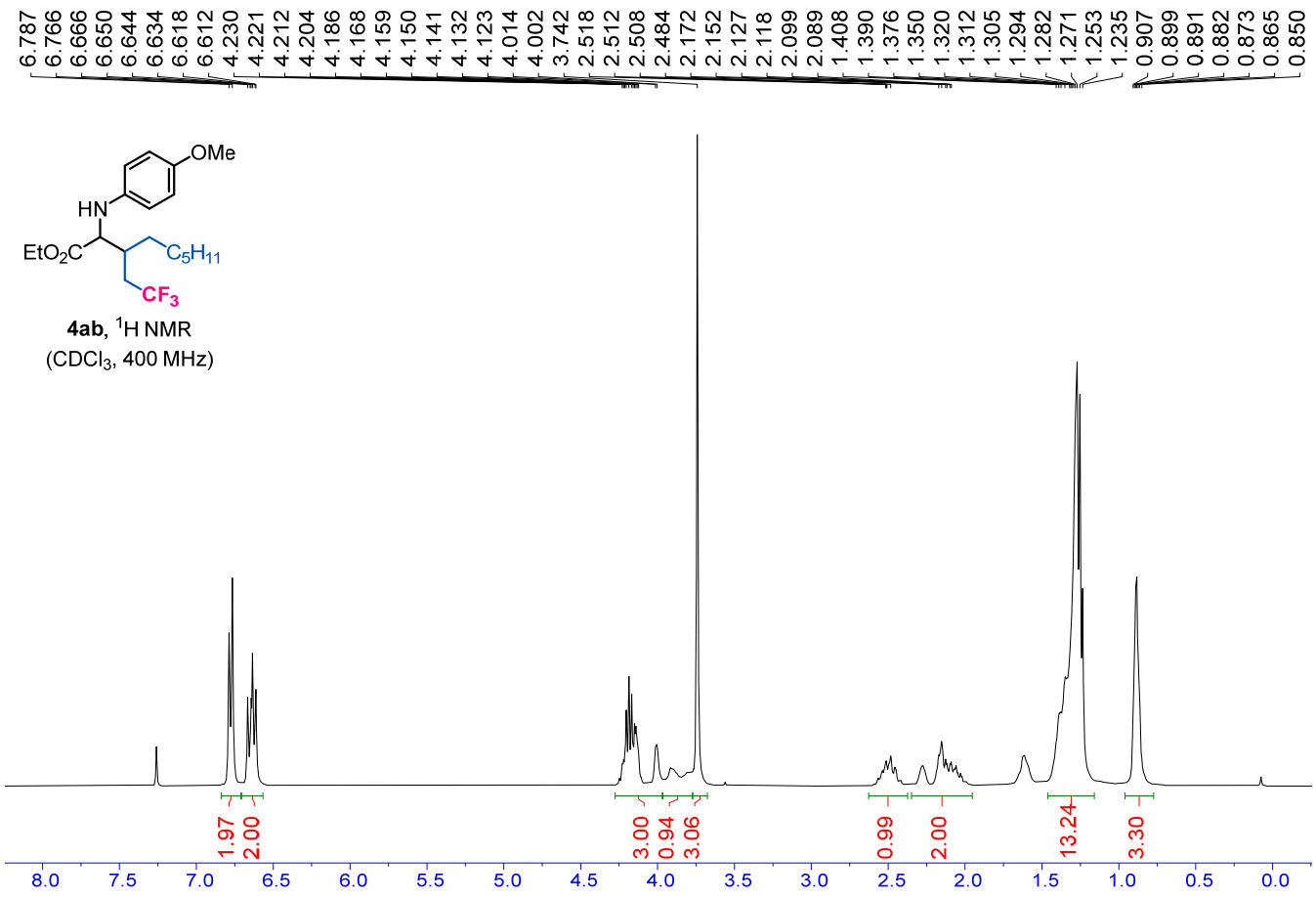


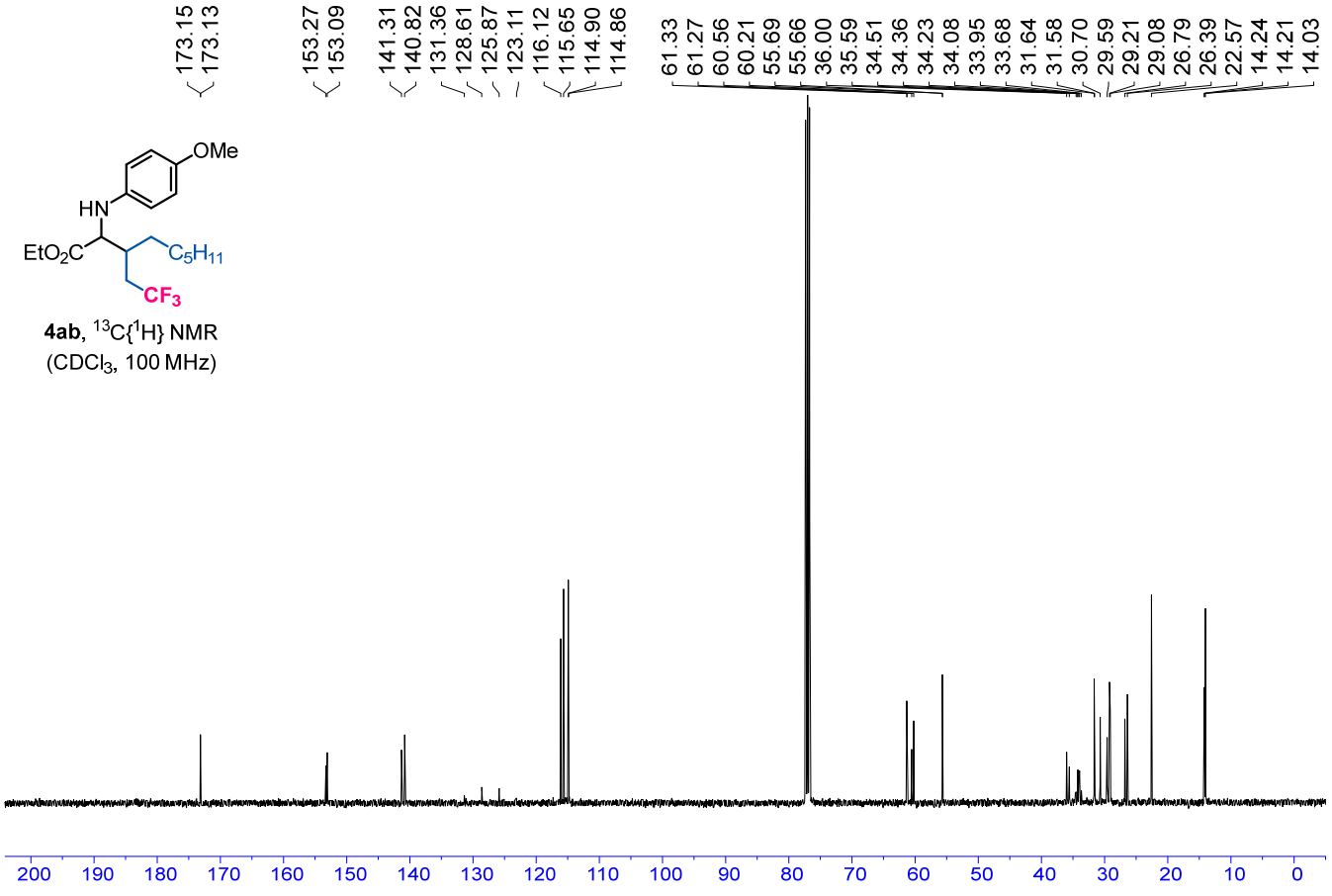
4ca, ^{1}H NMR
($CDCl_3$, 400 MHz)

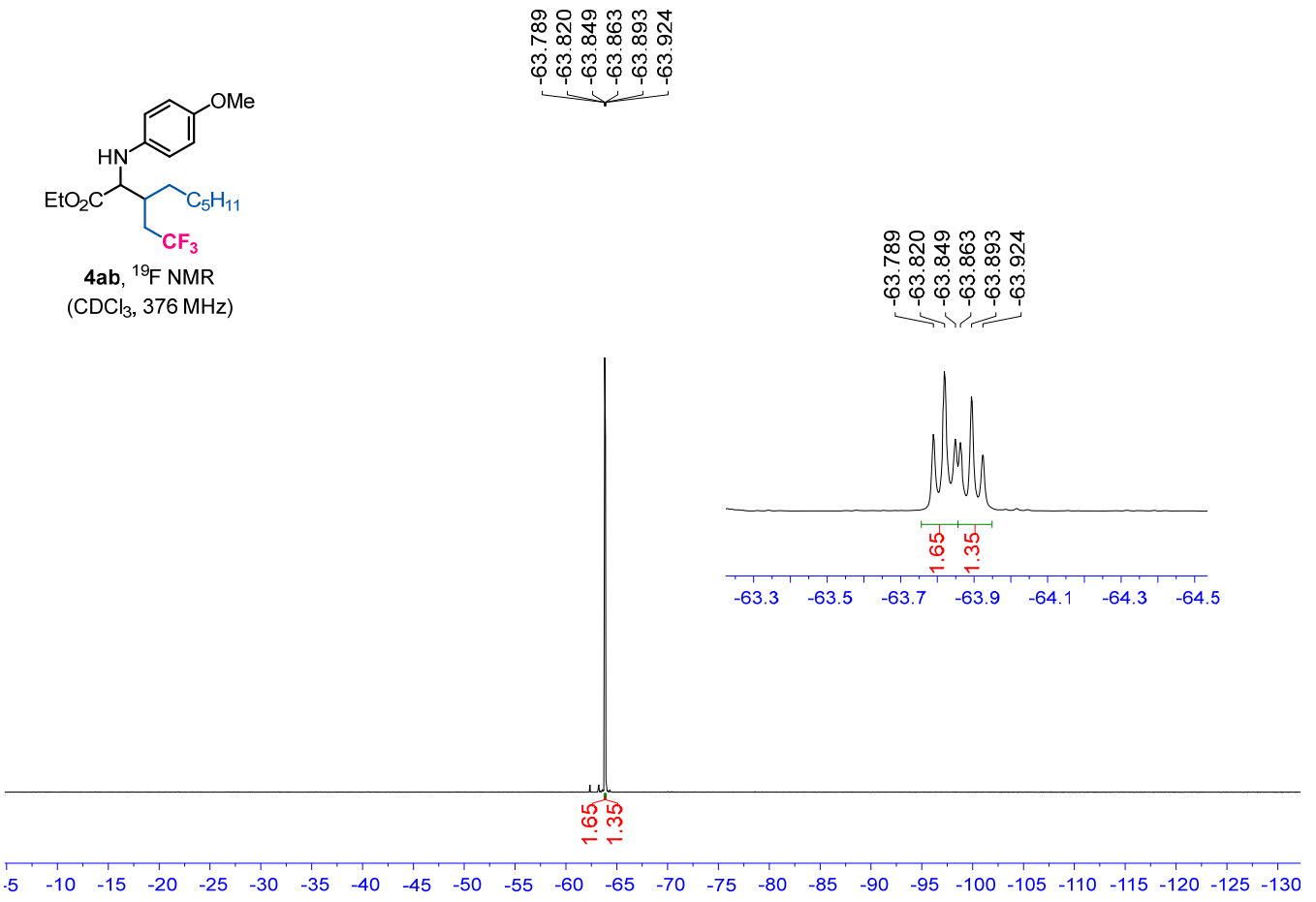


4ca, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)


F
HN
Ph
EtO2C
CF3
4ca, 19F NMR
(CDCl3, 100 MHz)
-63.672
-63.703
-63.733
-125.658
-125.957
-63.672
-63.703
-63.733
-63.0
-63.5
-64.0
-64.5
-65.0
3.00
0.46
0.30
20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140


6.787
6.766
6.666
6.650
6.644
6.634
6.618
6.612
4.230
4.221
4.212
4.204
4.186
4.168
4.159
4.150
4.141
4.132
4.123
4.014
4.002
3.742
2.518
2.512
2.508
2.484
2.172
2.152
2.127
2.118
2.099
2.089
1.408
1.390
1.376
1.350
1.320
1.312
1.305
1.294
1.282
1.271
1.253
1.235
0.907
0.899
0.891
0.882
0.873
0.865
0.850
OMe
HN
EtO2C
C5H11
CF3
4ab, 1H NMR
(CDCl3, 400 MHz)
1.97
2.00
3.00
0.94
3.06
0.99
2.00
13.24
3.30
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


173.15
173.13
153.27
153.09
141.31
140.82
131.36
128.61
125.87
123.11
116.12
115.65
114.90
114.86
61.33
61.27
60.56
60.21
55.69
55.66
36.00
35.59
34.51
34.36
34.23
34.08
33.95
33.68
31.64
31.58
30.70
29.59
29.21
29.08
26.79
26.39
22.57
14.24
14.21
14.03
OMe
HN
EtO2C
C5H11
CF3
4ab, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


-63.789
-63.820
-63.849
-63.863
-63.893
-63.924
OMe
HN
EtO2C
C5H11
CF3
4ab, 19F NMR
(CDCl3, 376 MHz)
1.65
1.35
-63.3
-63.5
-63.7
-63.9
-64.1
-64.3
-64.5
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
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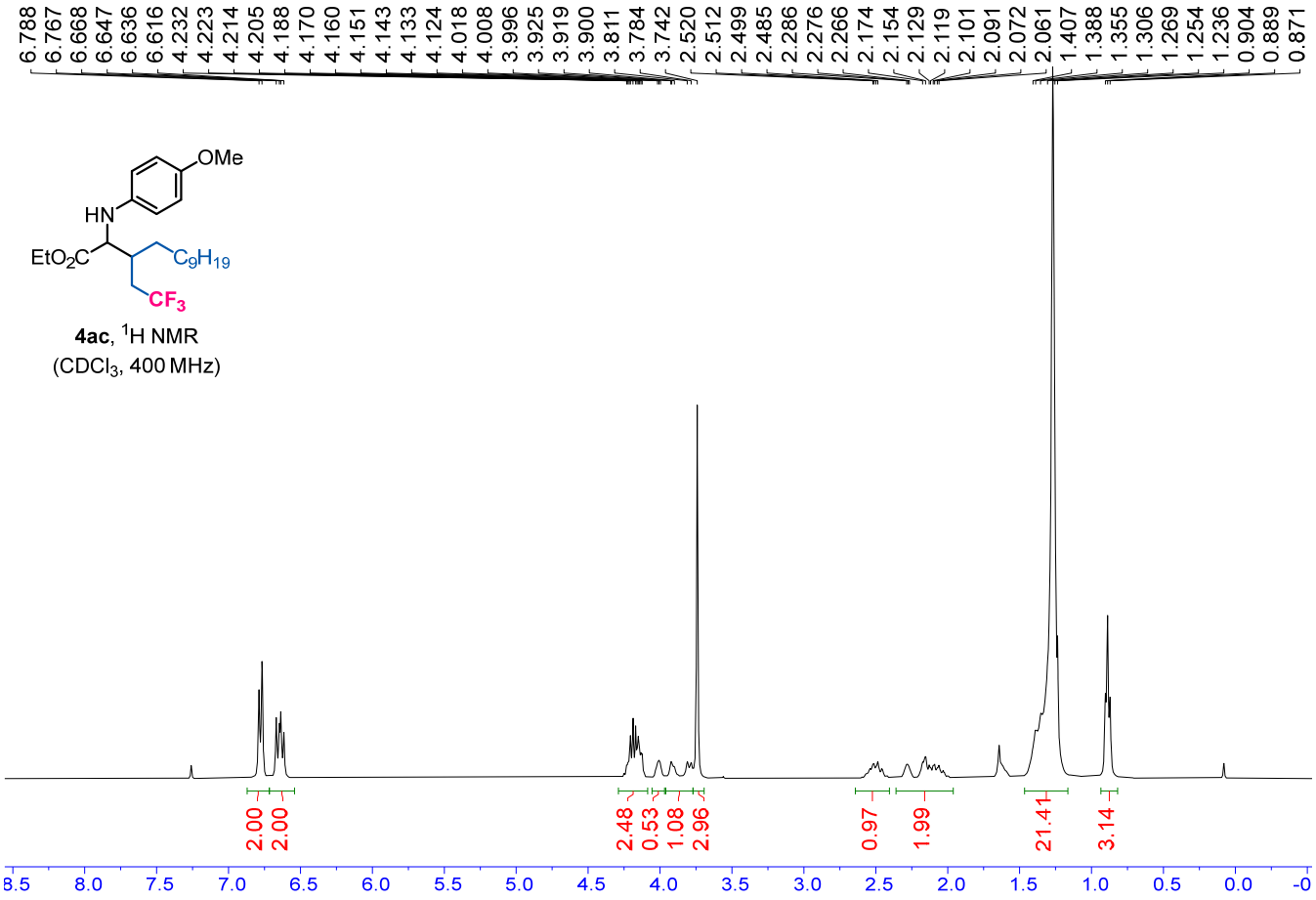
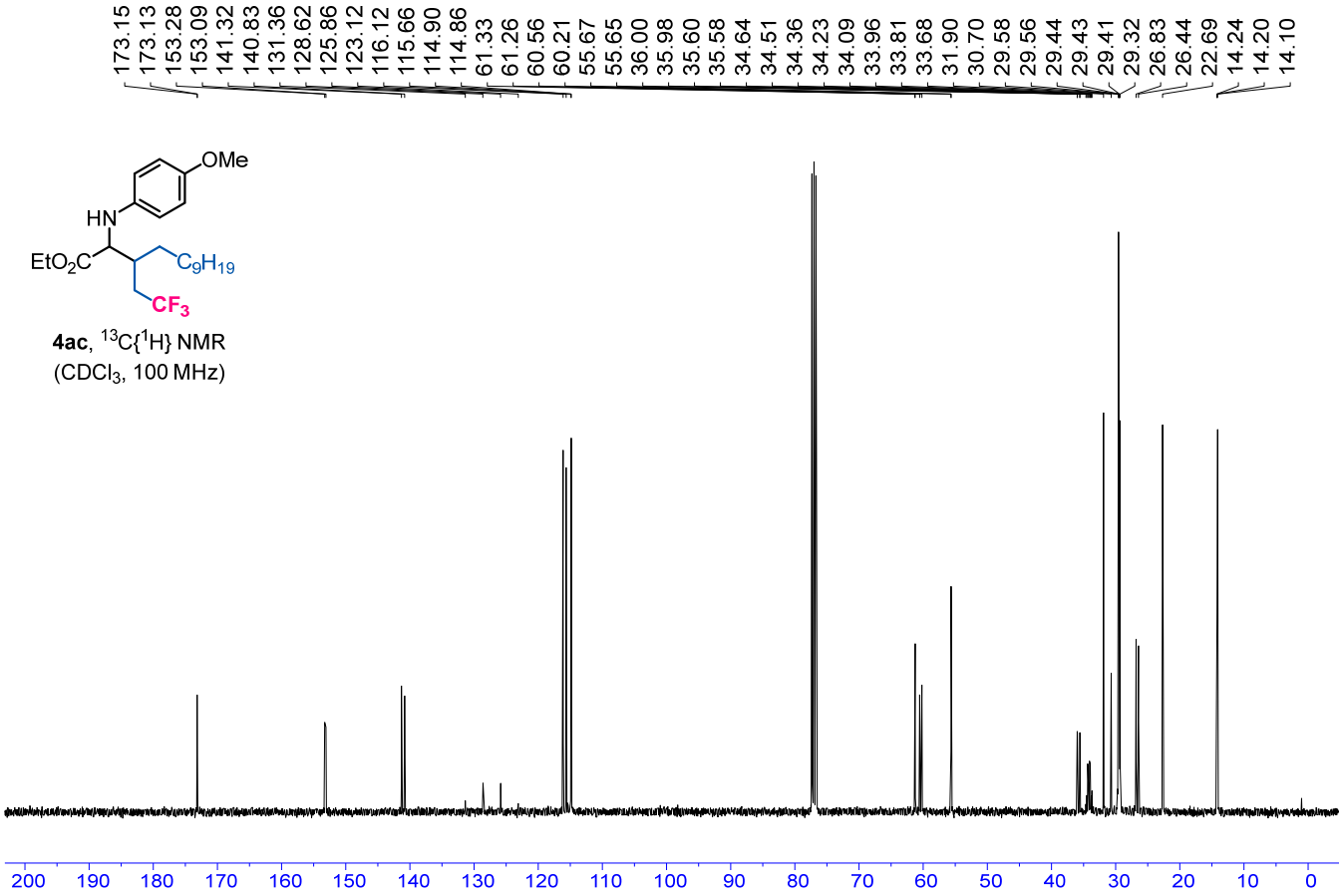
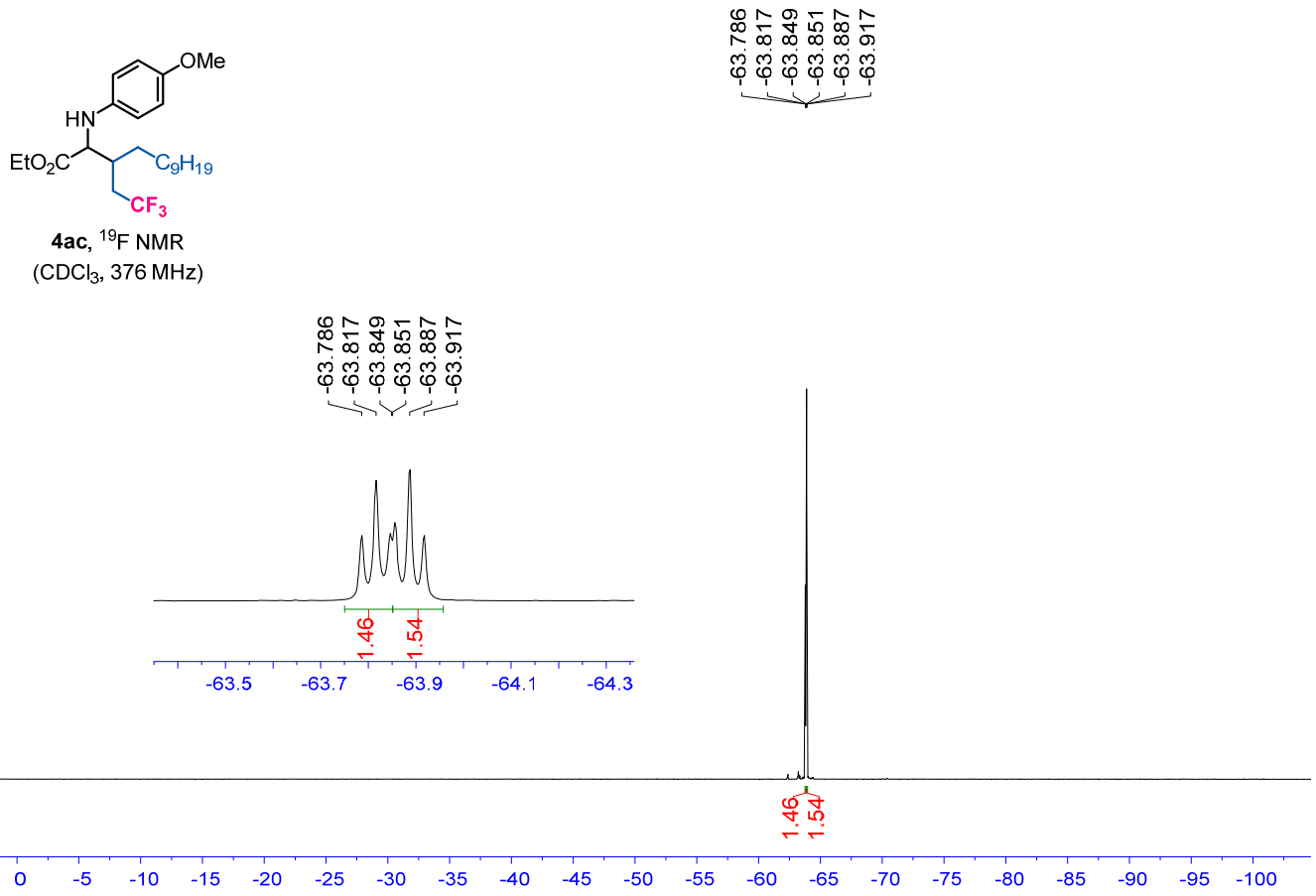
-100
-105
-110
-115
-120
-125
-130



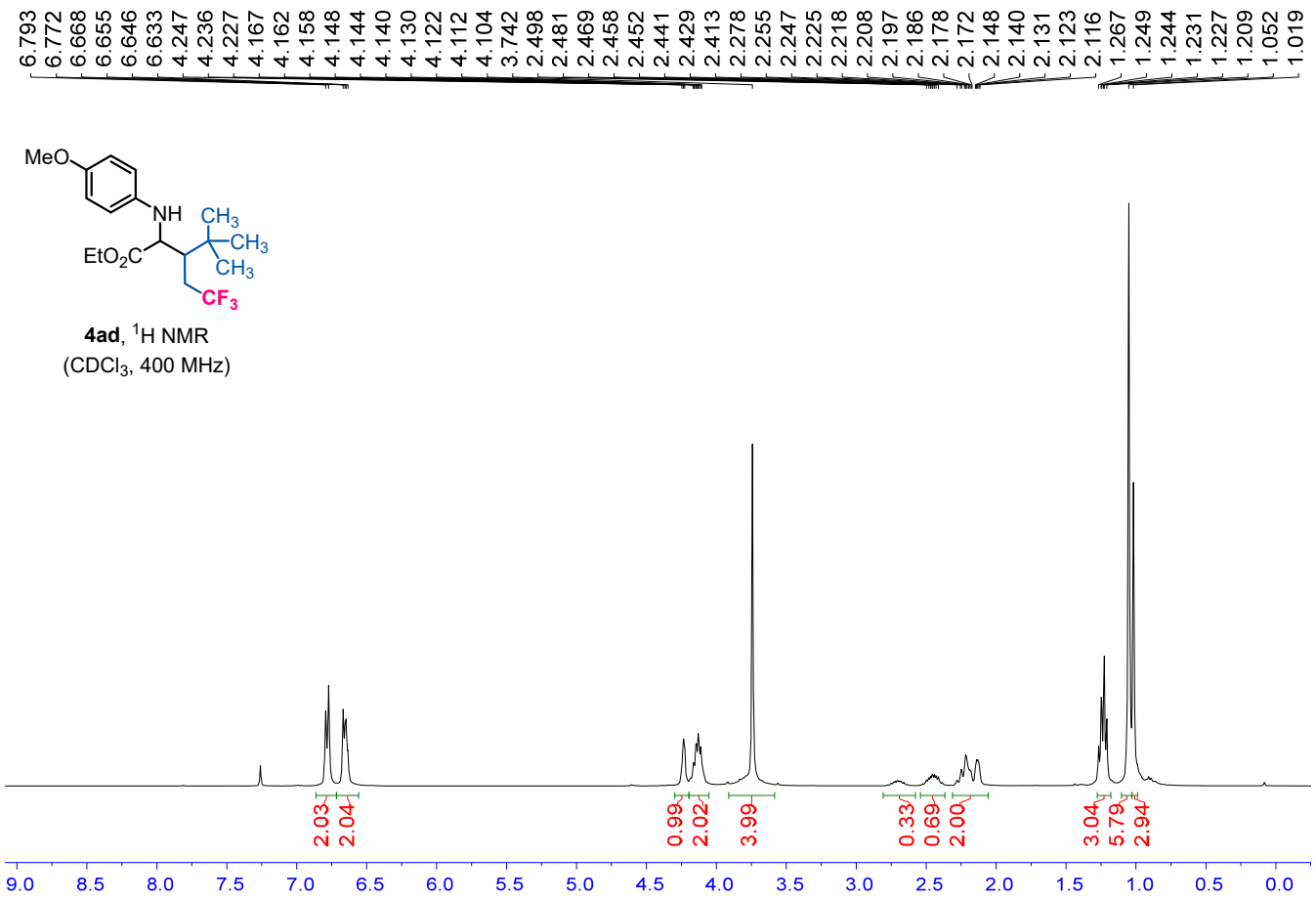
4ac, ^{1}H NMR
($CDCl_3$, 400 MHz)



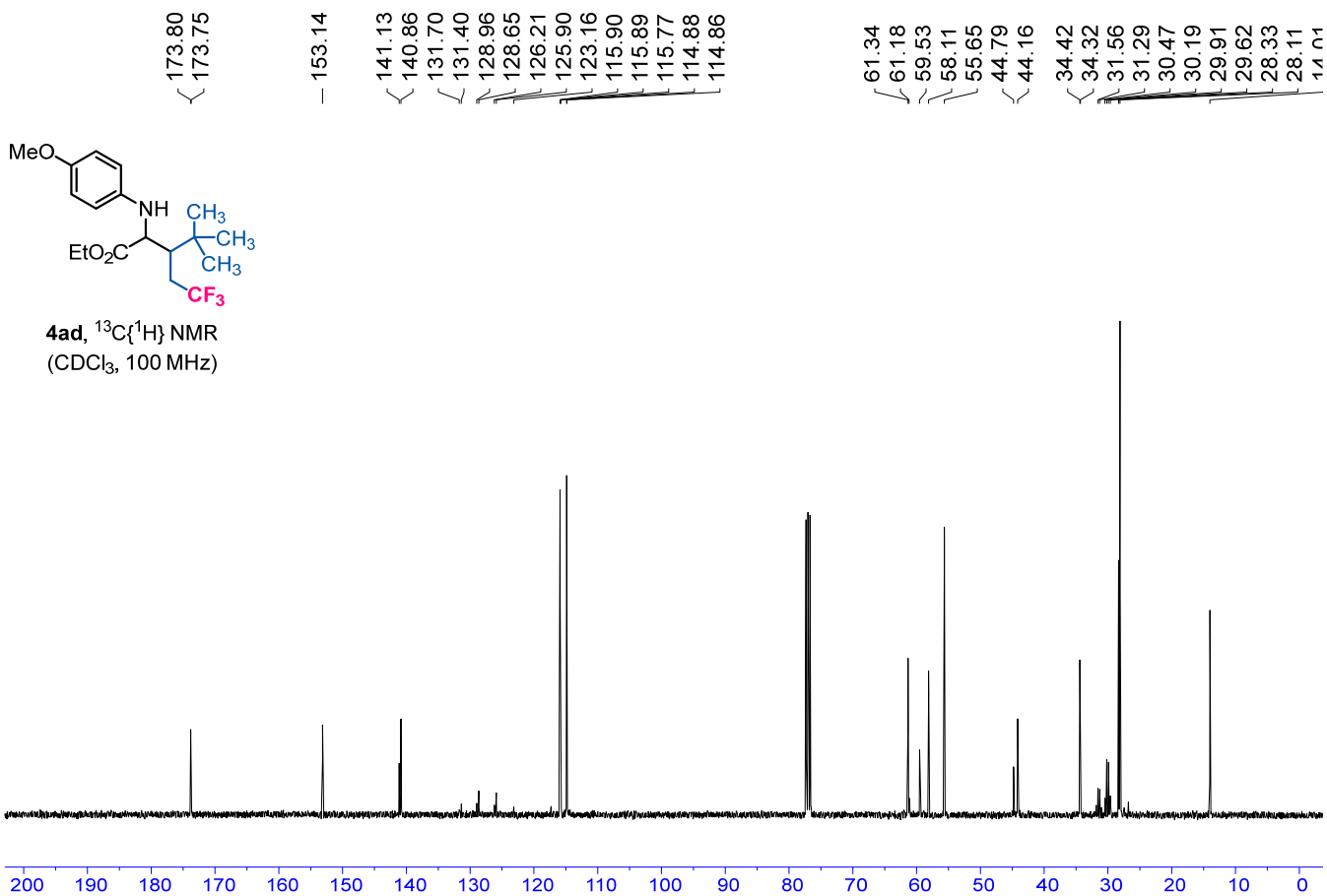
4ac, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



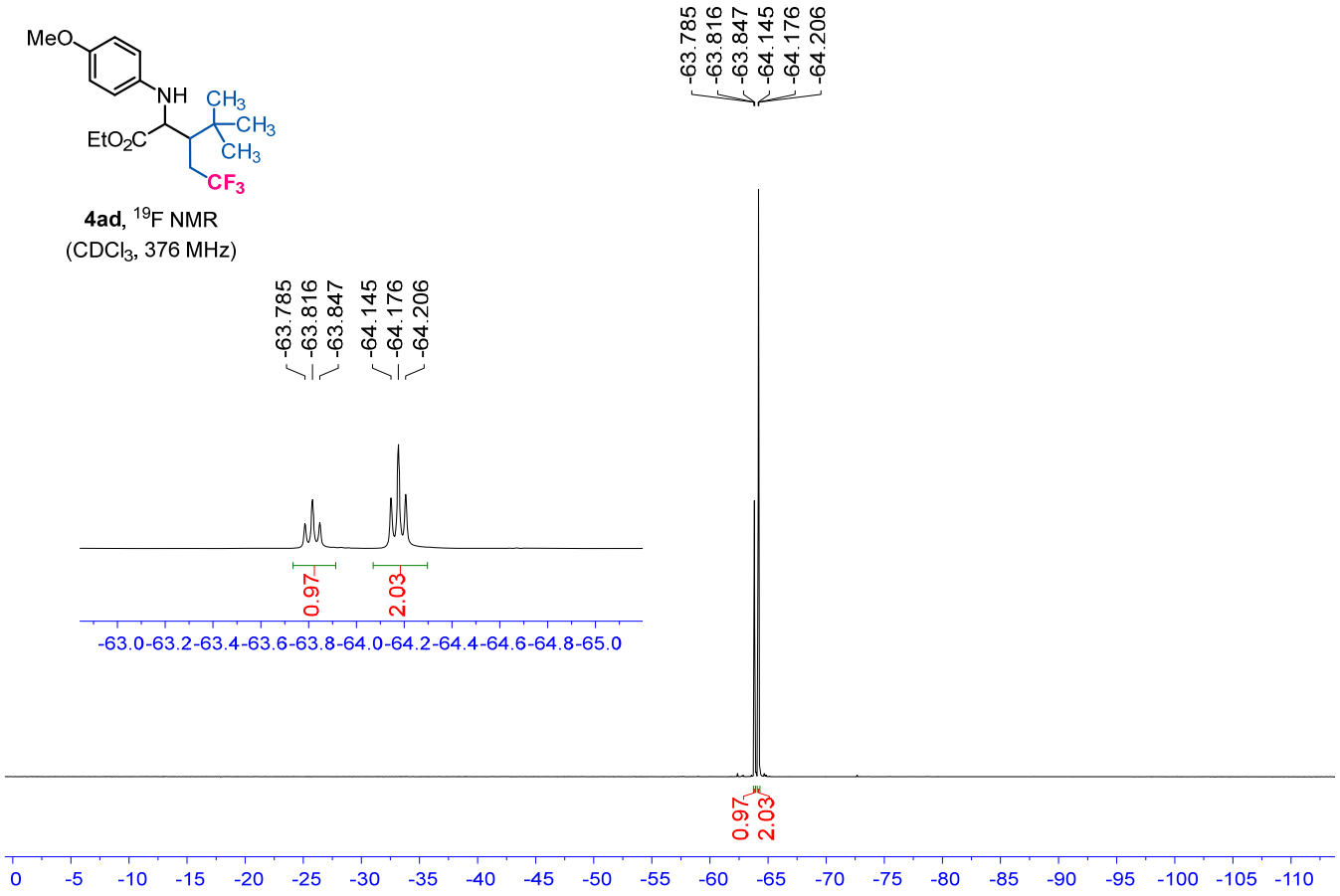
4ac, ^{19}F NMR
($CDCl_3$, 376 MHz)

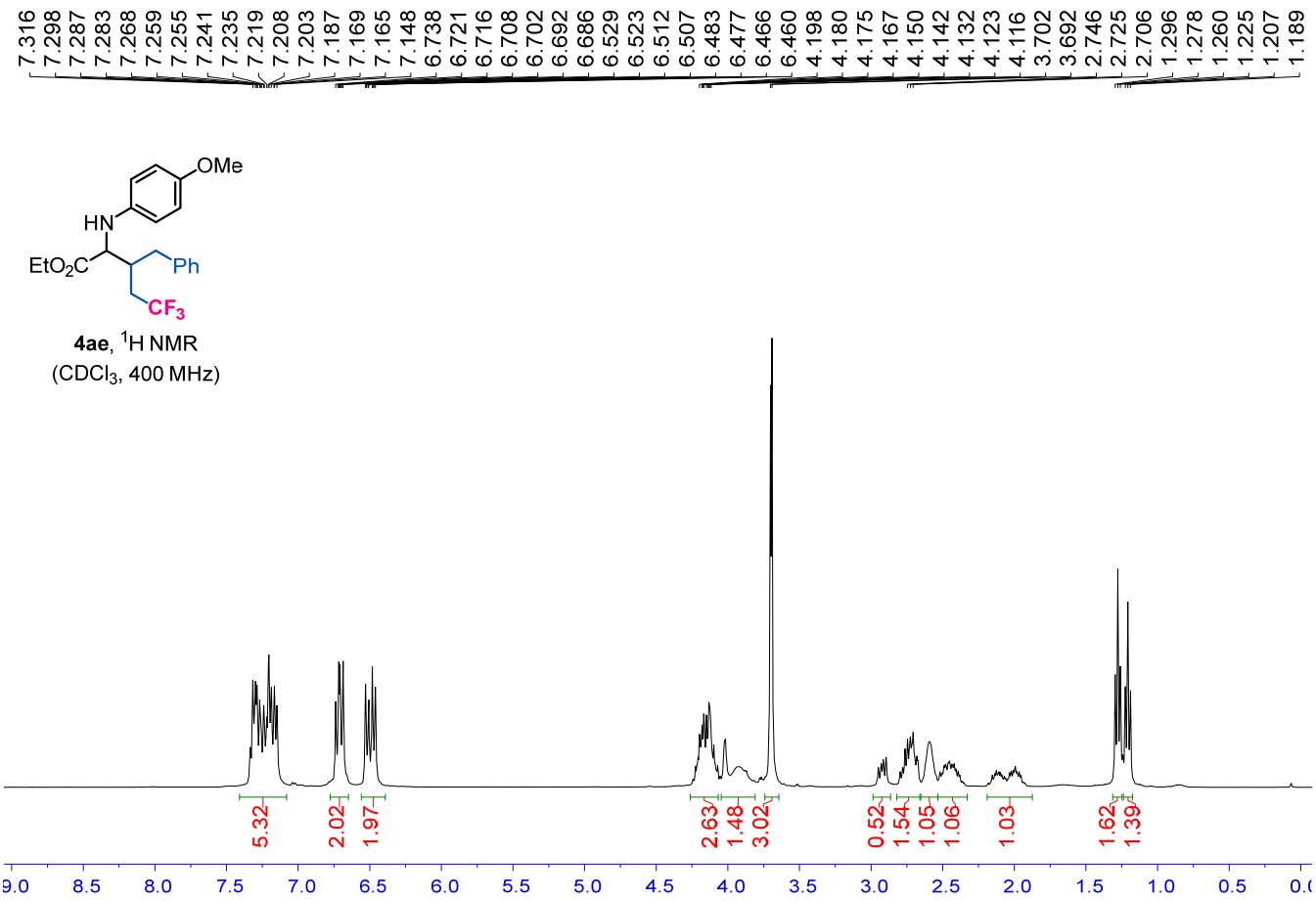


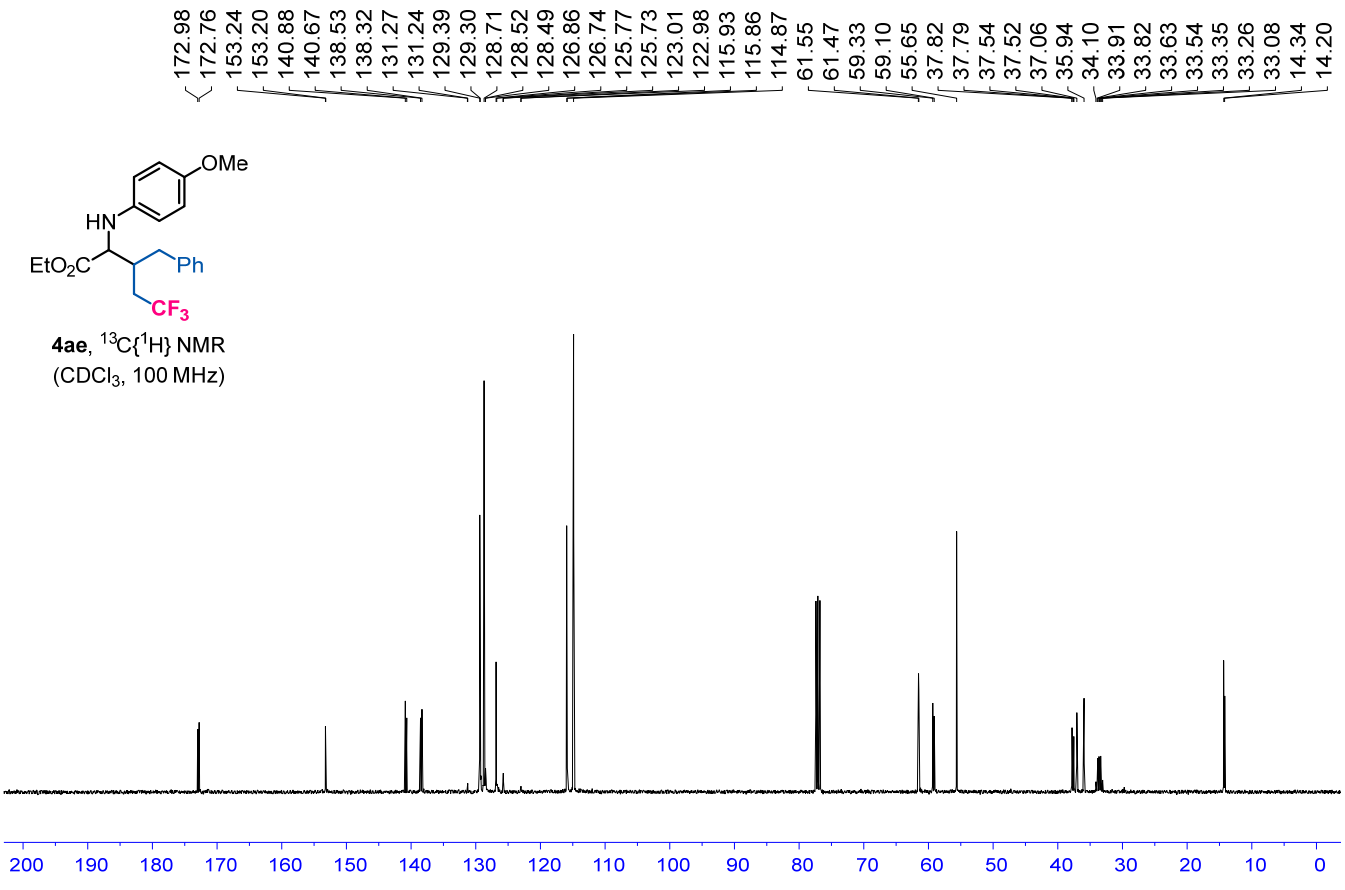
4ad, ^{1}H NMR
($CDCl_3$, 400 MHz)

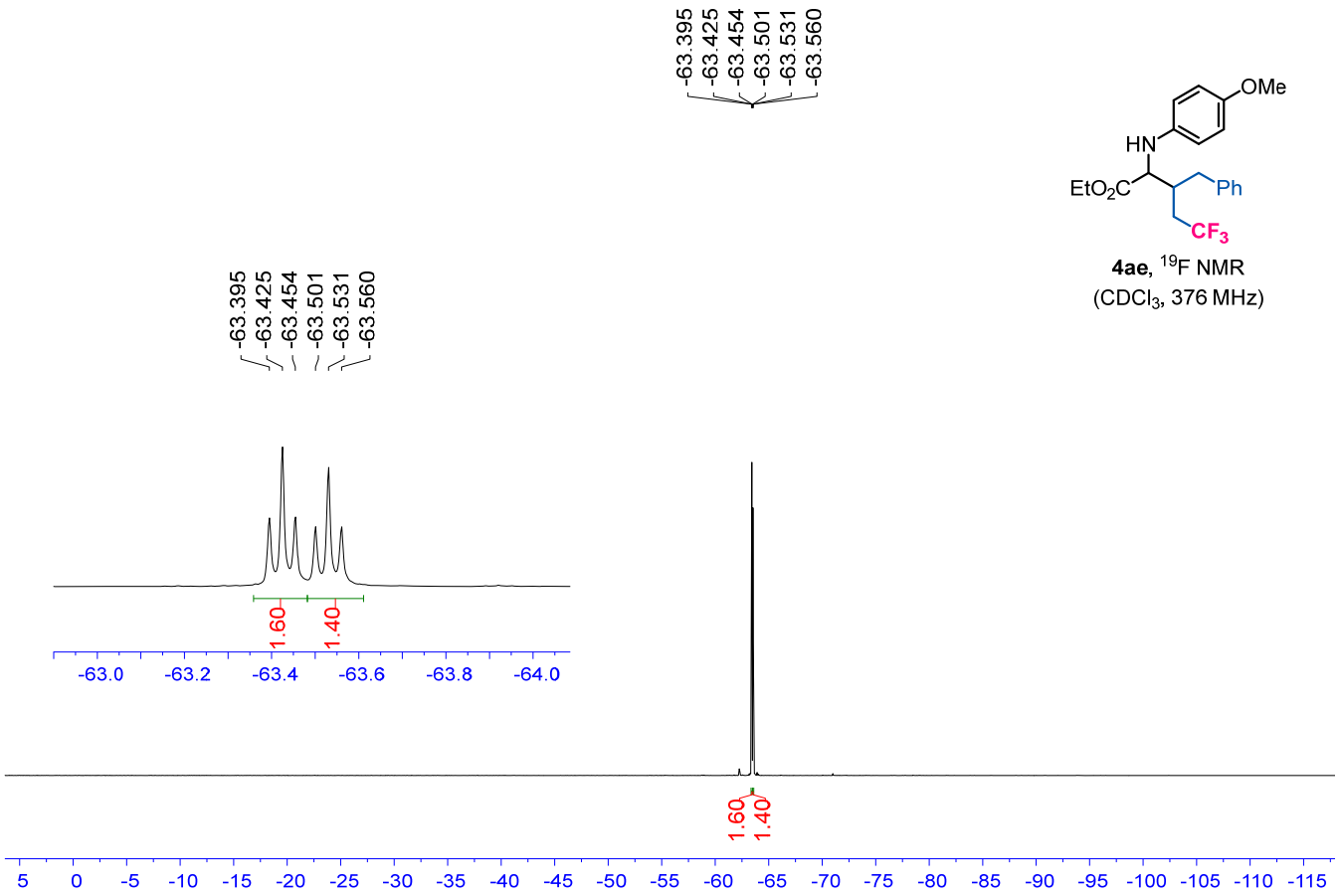


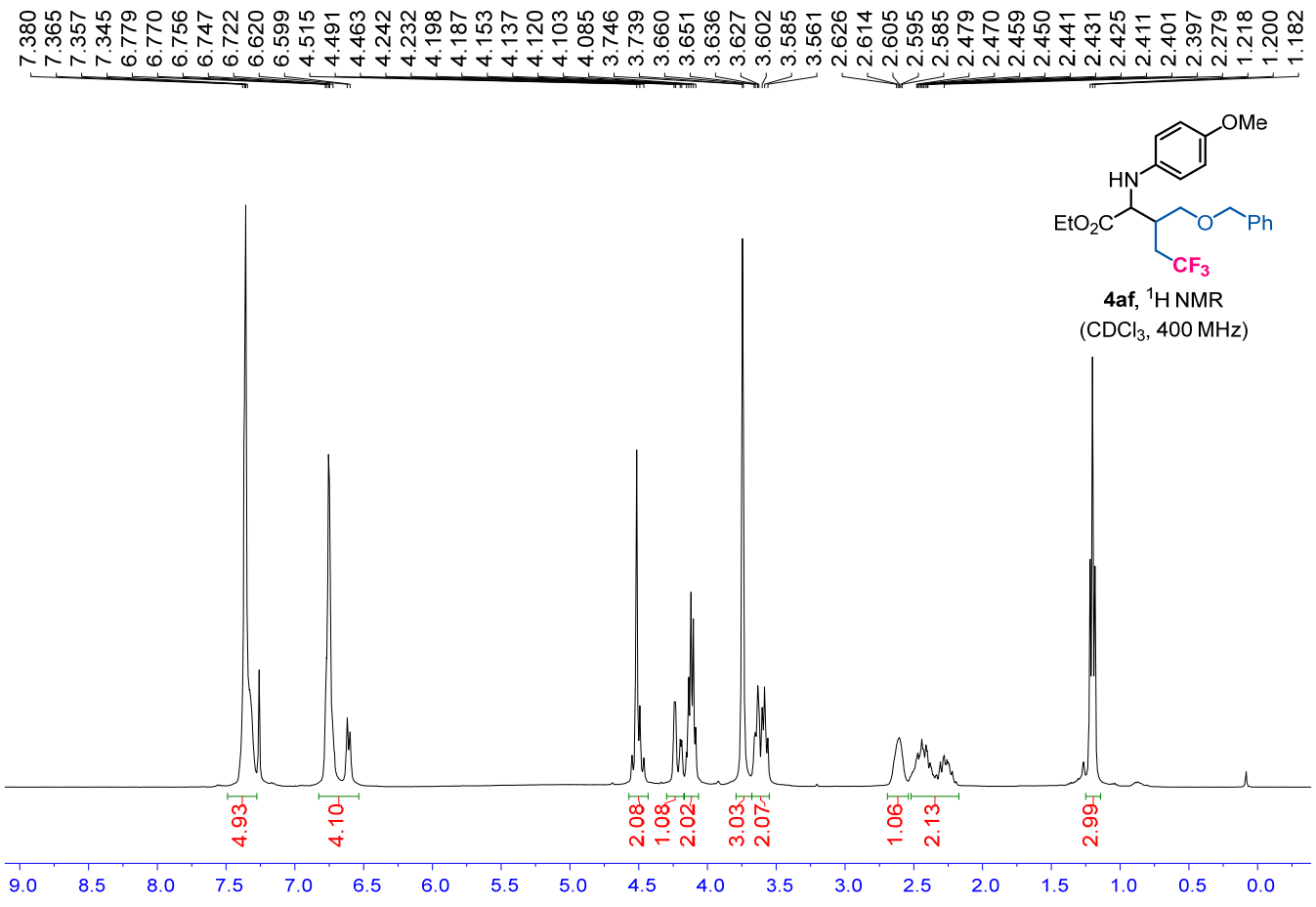
4ad, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)

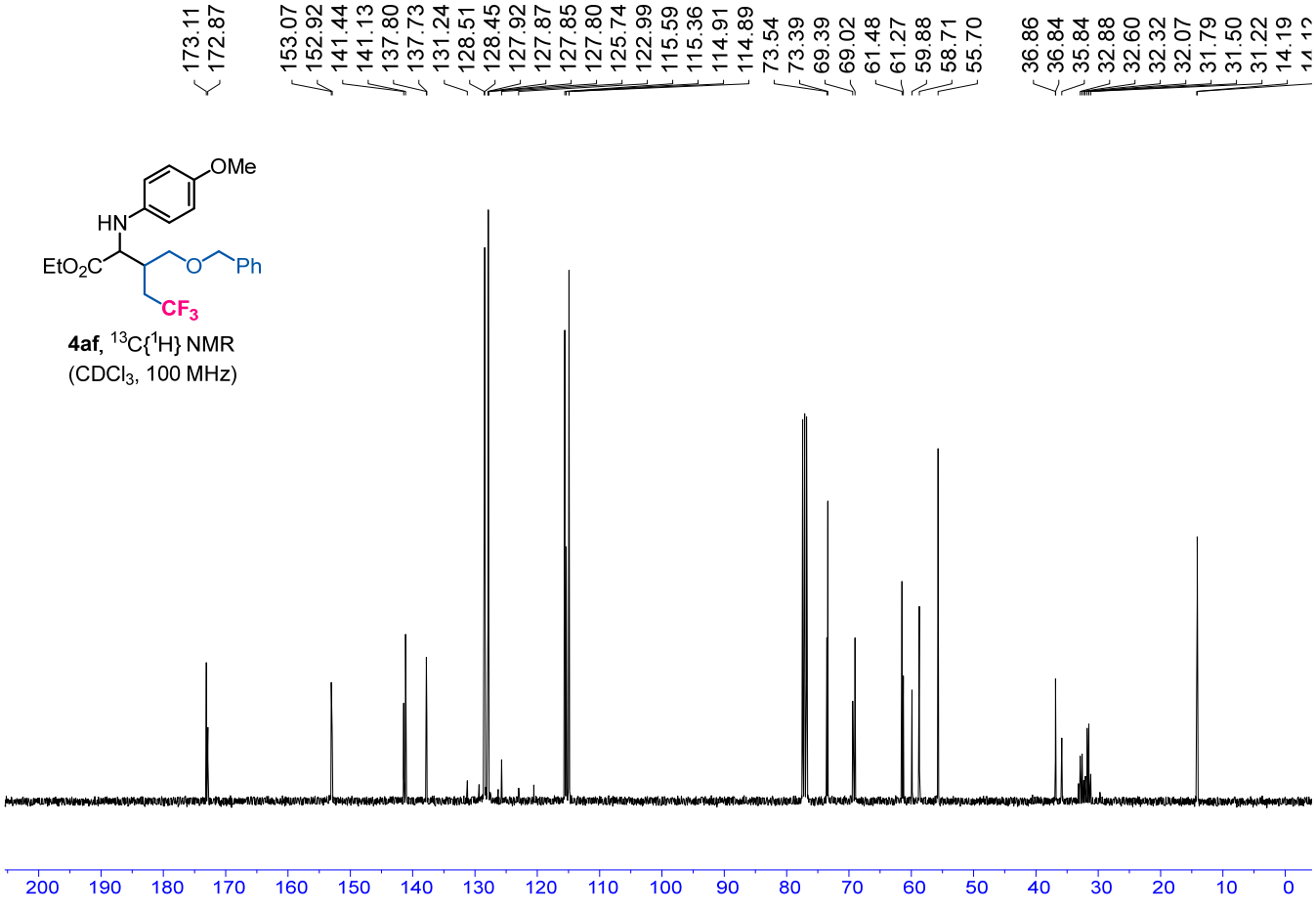

MeO
NH
CH3
CH3
CH3
EtO2C
CF3
4ad, 19F NMR
(CDCl3, 376 MHz)
-63.785
-63.816
-63.847
-64.145
-64.176
-64.206
0.97
2.03
-63.0 -63.2 -63.4 -63.6 -63.8 -64.0 -64.2 -64.4 -64.6 -64.8 -65.0
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110

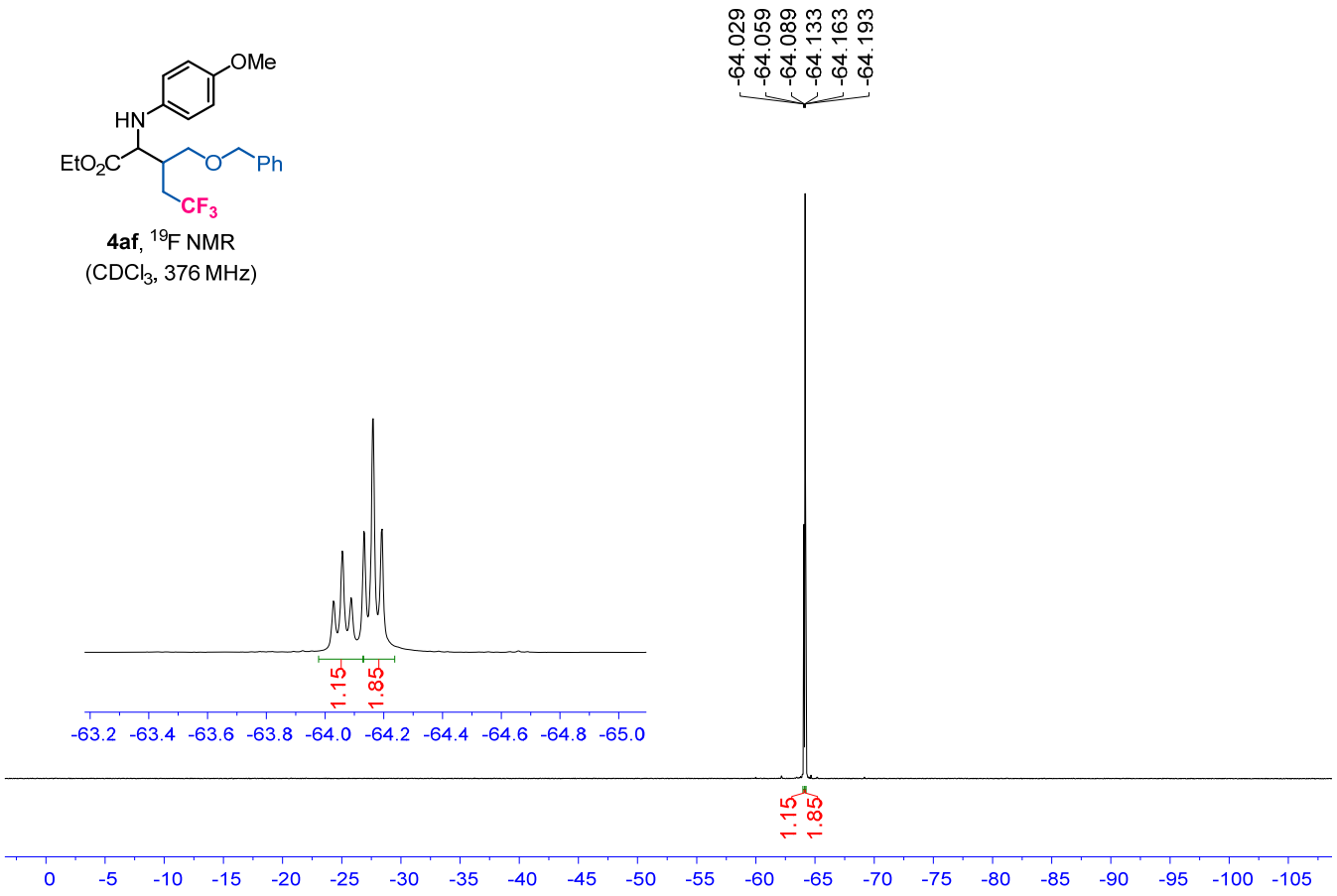

7.316
7.298
7.287
7.283
7.268
7.259
7.255
7.241
7.235
7.219
7.208
7.203
7.187
7.169
7.165
7.148
6.738
6.721
6.716
6.708
6.702
6.692
6.686
6.529
6.523
6.512
6.507
6.483
6.477
6.466
6.460
4.198
4.180
4.175
4.167
4.150
4.142
4.132
4.123
4.116
3.702
3.692
2.746
2.725
2.706
1.296
1.278
1.260
1.225
1.207
1.189
OMe
HN
EtO2C
Ph
CF3
4ae, 1H NMR
(CDCl3, 400 MHz)
5.32
2.02
1.97
2.63
1.48
3.02
0.52
1.54
1.05
1.06
1.03
1.62
1.39
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

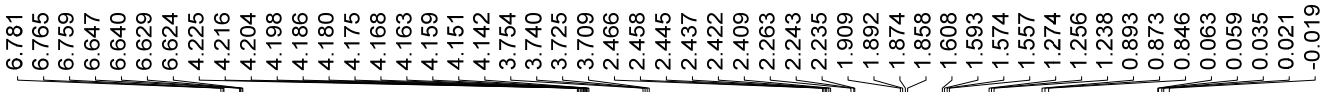

172.98
172.76
153.24
153.20
140.88
140.67
138.53
138.32
131.27
131.24
129.39
129.30
128.71
128.52
128.49
126.86
126.74
125.77
125.73
123.01
122.98
115.93
115.86
114.87
61.55
61.47
59.33
59.10
55.65
37.82
37.79
37.54
37.52
37.06
35.94
34.10
33.91
33.82
33.63
33.54
33.35
33.26
33.08
14.34
14.20
OMe
HN
EtO2C
Ph
CF3
4ae, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

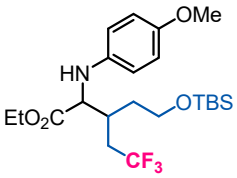

-63.395
-63.425
-63.454
-63.501
-63.531
-63.560
OMe
HN
EtO2C
Ph
CF3
4ae, 19F NMR
(CDCl3, 376 MHz)
1.60
1.40
-63.0
-63.2
-63.4
-63.6
-63.8
-64.0
5
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115


7.380
7.365
7.357
7.345
6.779
6.770
6.756
6.747
6.722
6.620
6.599
4.515
4.491
4.463
4.242
4.232
4.198
4.187
4.153
4.137
4.120
4.103
4.085
3.746
3.739
3.660
3.651
3.636
3.627
3.602
3.585
3.561
2.626
2.614
2.605
2.595
2.585
2.479
2.470
2.459
2.450
2.441
2.431
2.425
2.411
2.401
2.397
2.279
1.218
1.200
1.182
OMe
HN
EtO2C
O
Ph
CF3
4af, 1H NMR
(CDCl3, 400 MHz)
4.93
4.10
2.08
1.08
2.02
3.03
2.07
1.06
2.13
2.99
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

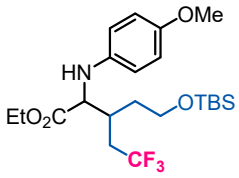

173.11
172.87
153.07
152.92
141.44
141.13
137.80
137.73
131.24
128.51
128.45
127.92
127.87
127.85
127.80
125.74
122.99
115.59
115.36
114.91
114.89
73.54
73.39
69.39
69.02
61.48
61.27
59.88
58.71
55.70
36.86
36.84
35.84
32.88
32.60
32.32
32.07
31.79
31.50
31.22
14.19
OMe
HN
EtO2C
O
Ph
CF3
4af, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


OMe
HN
EtO2C
O
Ph
CF3
4af, 19F NMR
(CDCl3, 376 MHz)
-64.029
-64.059
-64.089
-64.133
-64.163
-64.193
1.15
1.85
-63.2 -63.4 -63.6 -63.8 -64.0 -64.2 -64.4 -64.6 -64.8 -65.0
1.15
1.85
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105

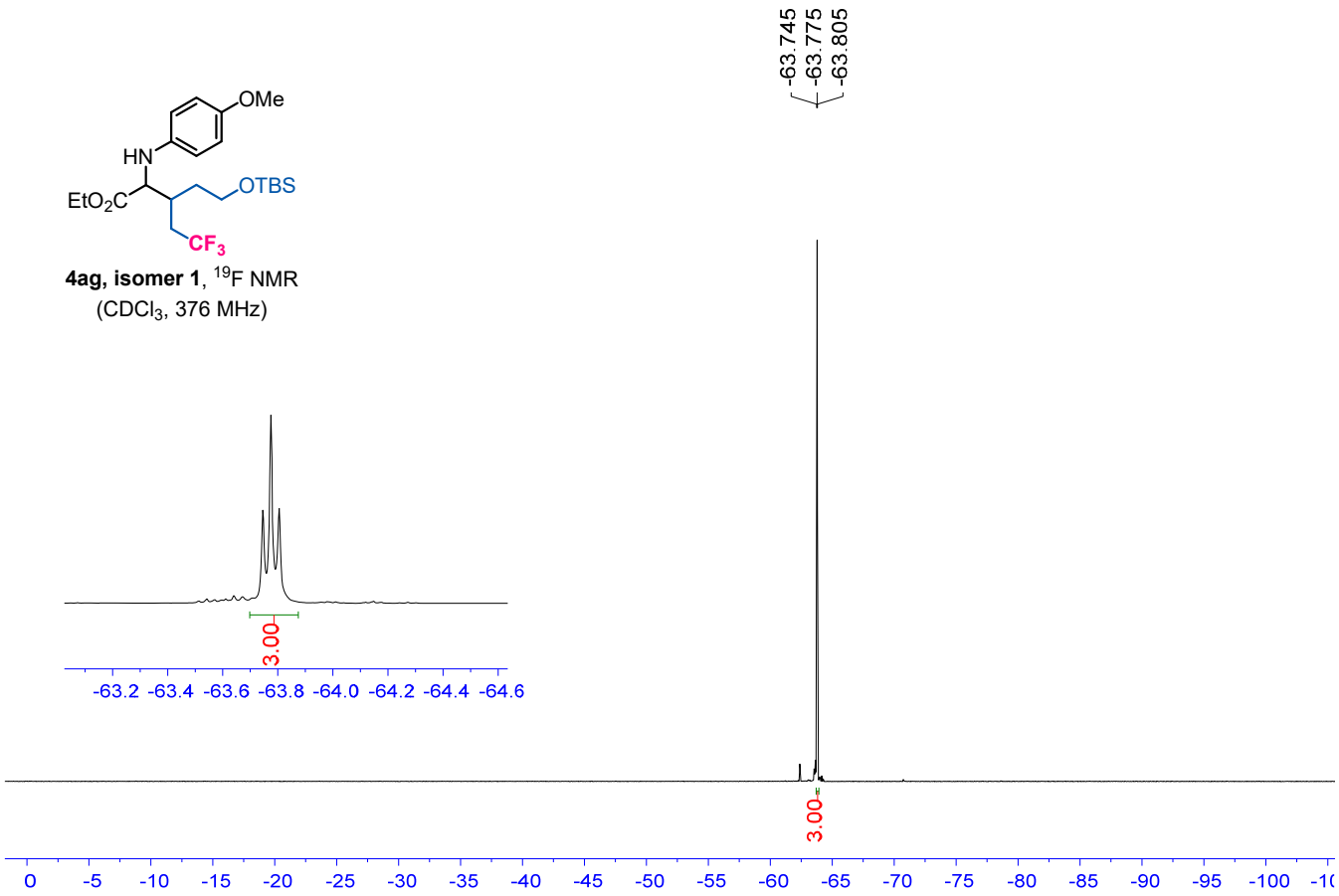




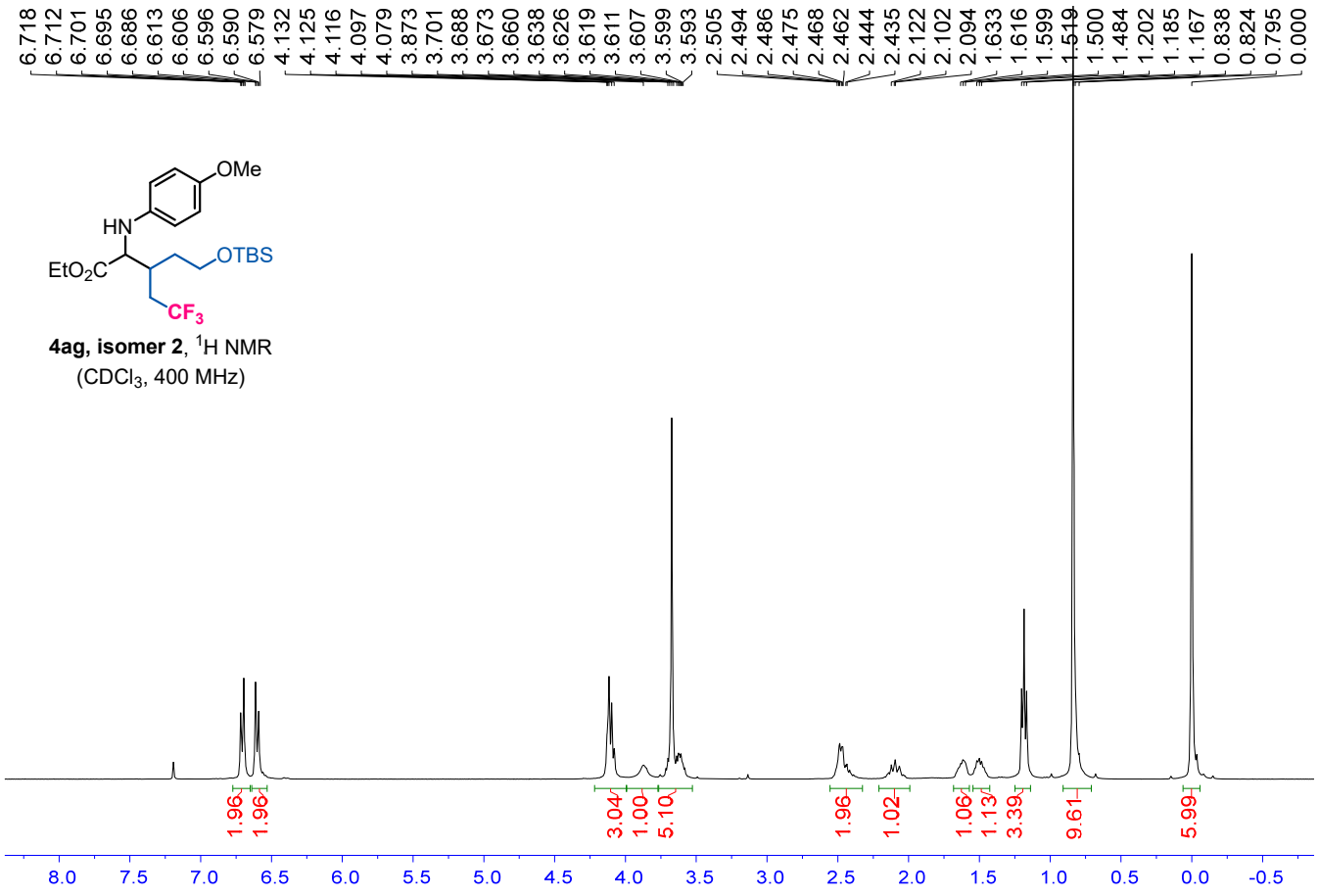
4ag, isomer 1, ^{1}H NMR
($CDCl_3$, 400 MHz)

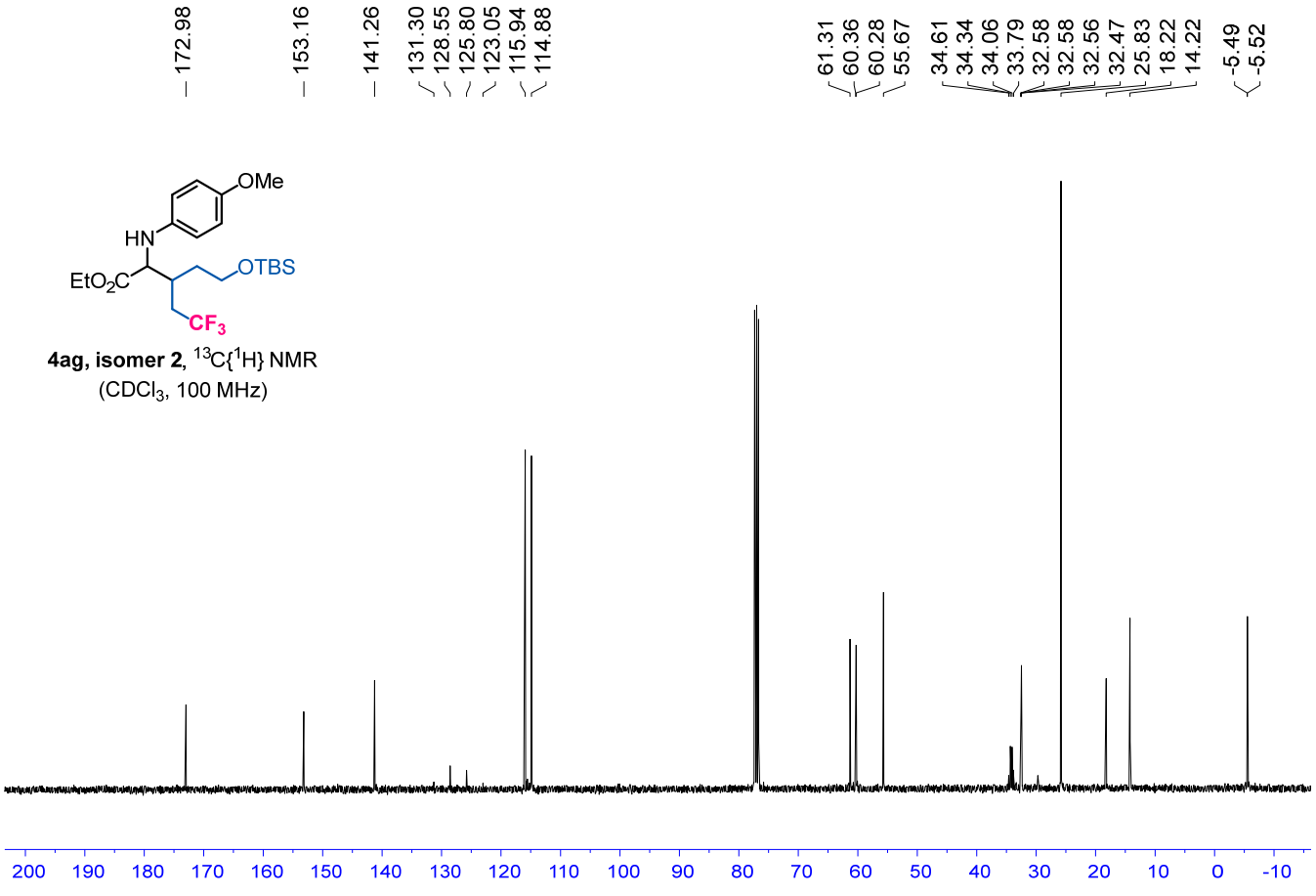


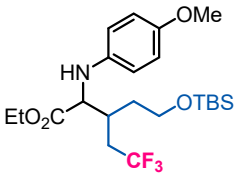
4ag, isomer 1, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



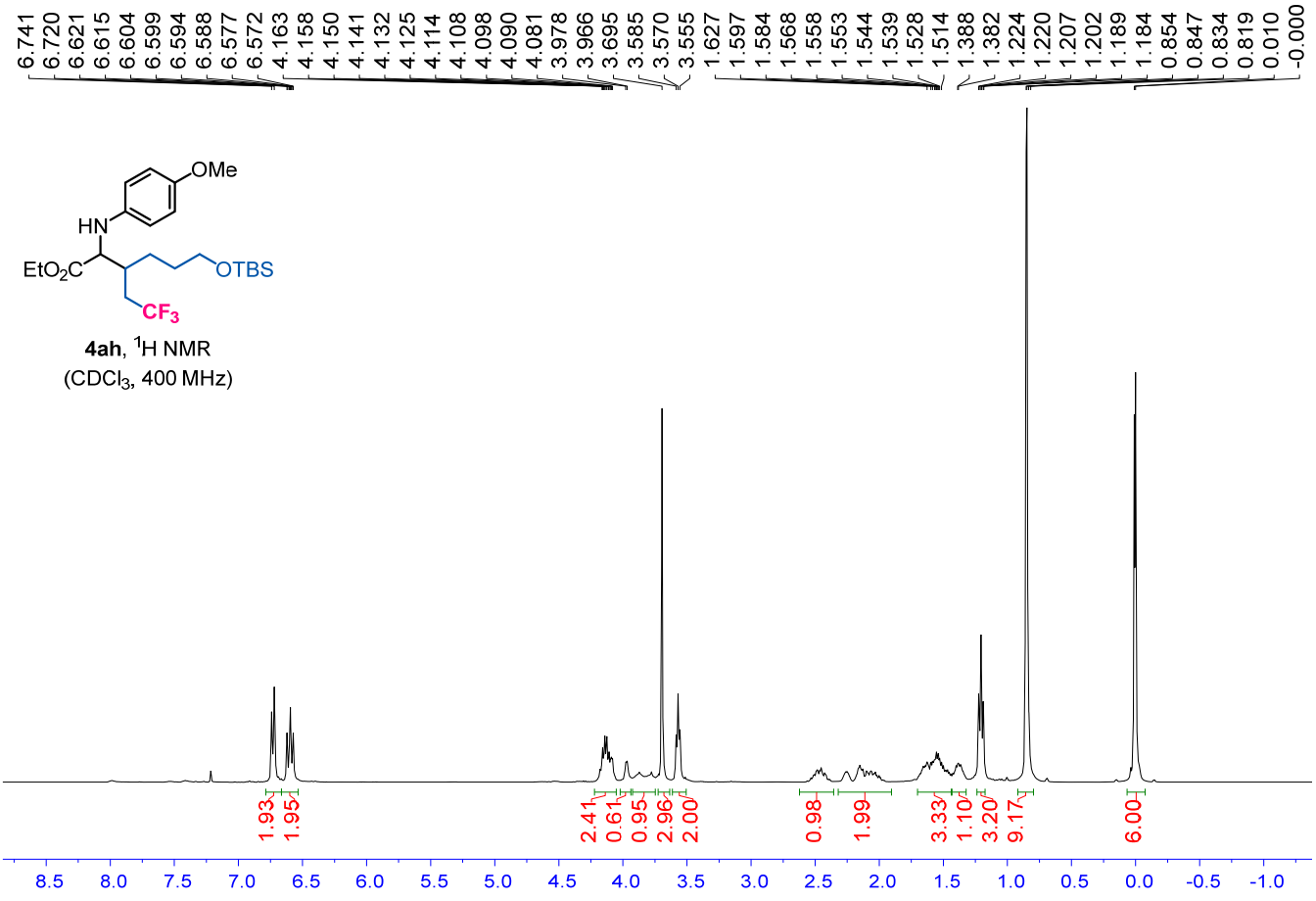
4ag, isomer 1, ^{19}F NMR
($CDCl_3$, 376 MHz)


6.718
6.712
6.701
6.695
6.686
6.613
6.606
6.596
6.590
6.579
4.132
4.125
4.116
4.097
4.079
3.873
3.701
3.688
3.673
3.660
3.638
3.626
3.619
3.611
3.607
3.599
3.593
2.505
2.494
2.486
2.475
2.468
2.462
2.444
2.435
2.122
2.102
2.094
1.633
1.616
1.599
1.519
1.500
1.484
1.202
1.185
1.167
0.838
0.824
0.795
0.000
OMe
HN
EtO2C
OTBS
CF3
4ag, isomer 2, 1H NMR
(CDCl3, 400 MHz)
1.96
1.96
3.04
1.00
5.10
1.96
1.02
1.06
1.13
3.39
9.61
5.99
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

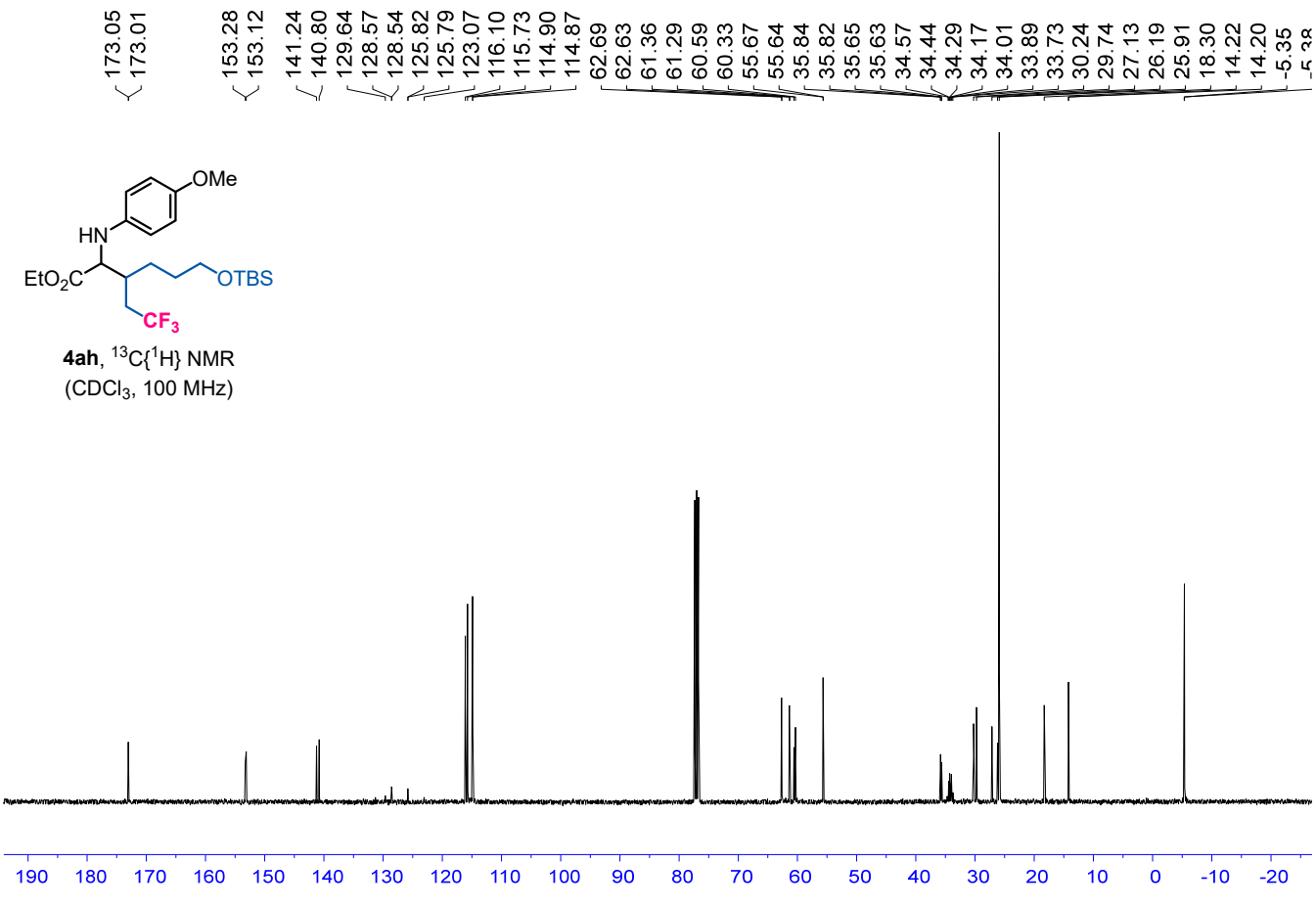

172.98
153.16
141.26
131.30
128.55
125.80
123.05
115.94
114.88
61.31
60.36
60.28
55.67
34.61
34.34
34.06
33.79
32.58
32.58
32.56
32.47
25.83
18.22
14.22
-5.49
-5.52
OMe
HN
EtO2C
OTBS
CF3
4ag, isomer 2, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10



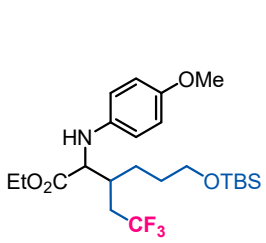
4ag, isomer 2, ^{1}H NMR
($CDCl_3$, 376 MHz)



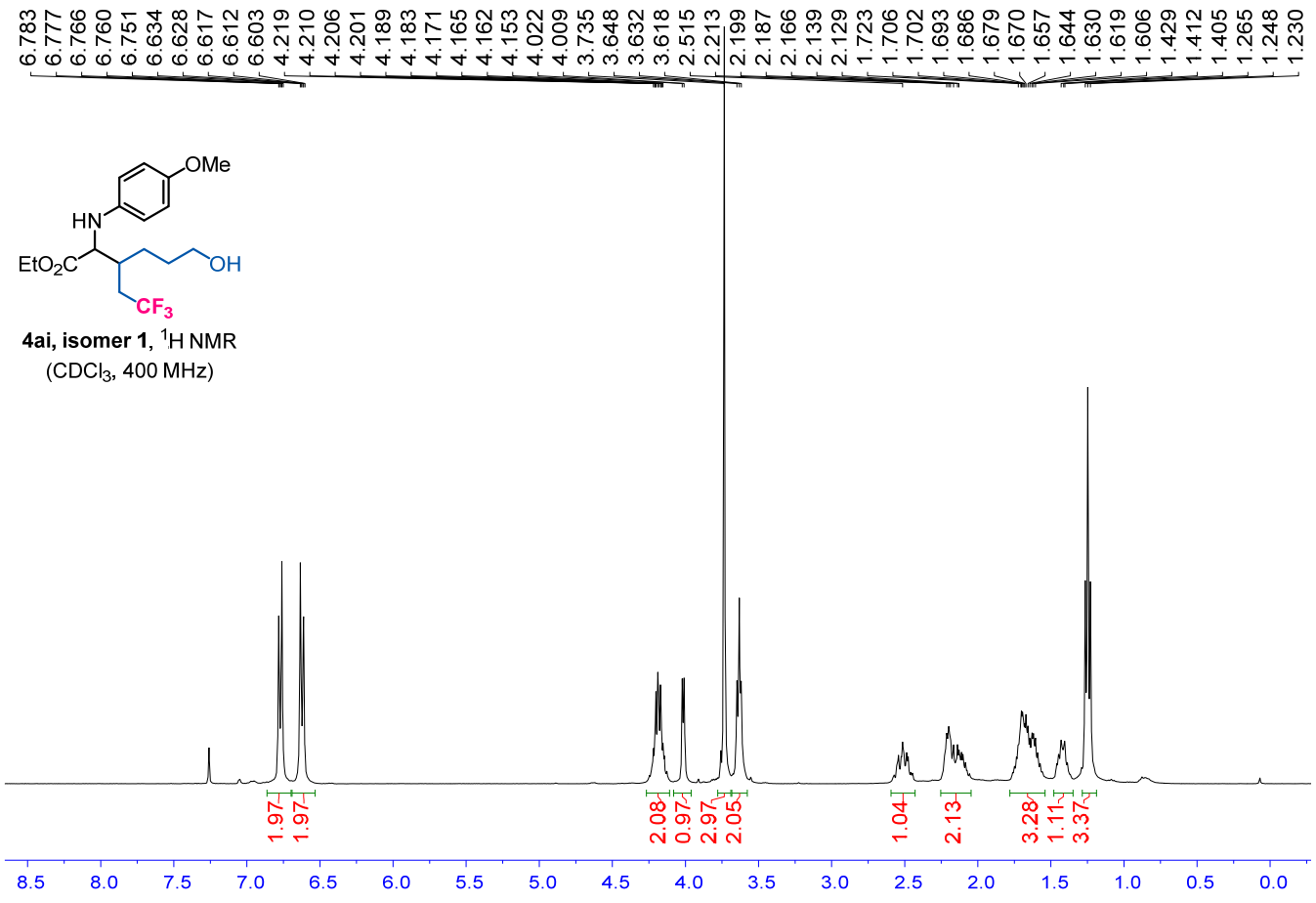
4ah, ^{1}H NMR
($CDCl_3$, 400 MHz)



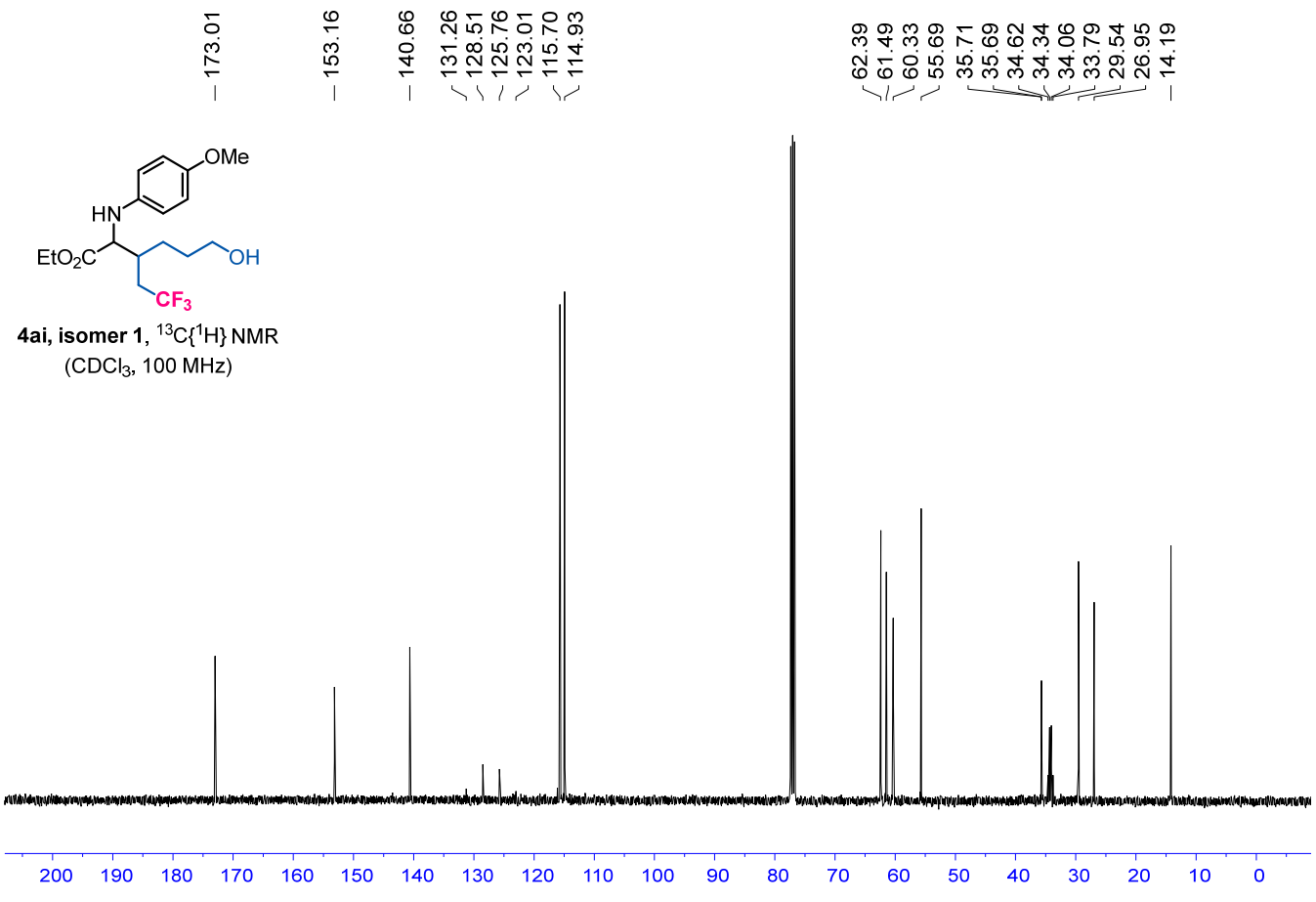
4ah, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



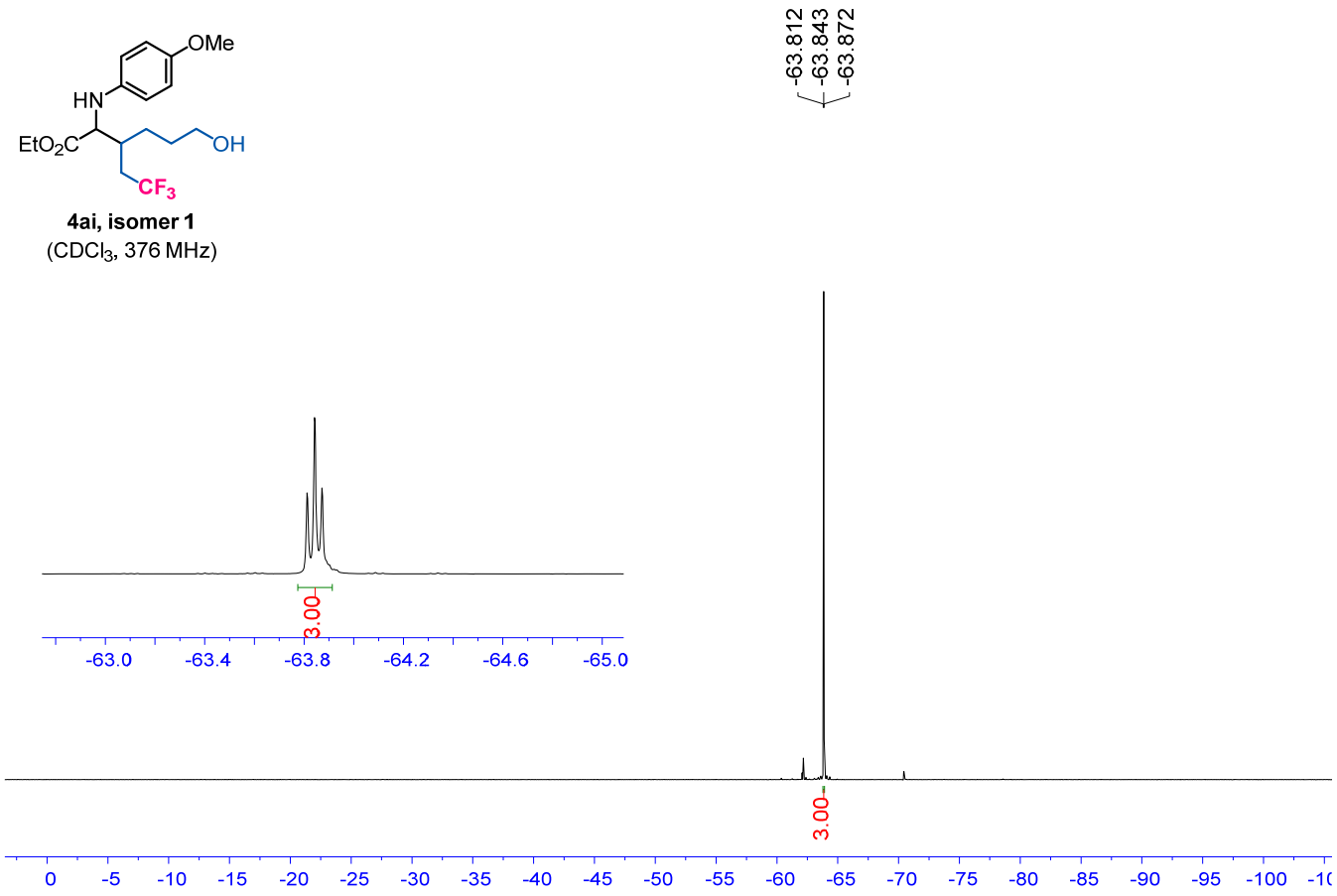
4ah, ^{19}F NMR
($CDCl_3$, 376 MHz)



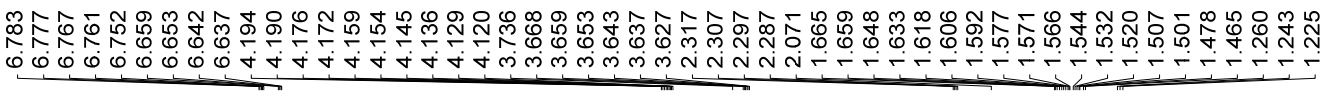
4ai, isomer 1, ^{1}H NMR
($CDCl_3$, 400 MHz)

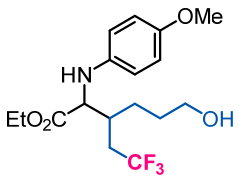


4ai, isomer 1, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)

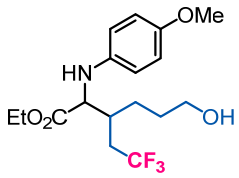


4ai, isomer 1
($CDCl_3$, 376 MHz)

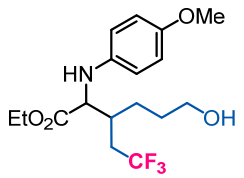




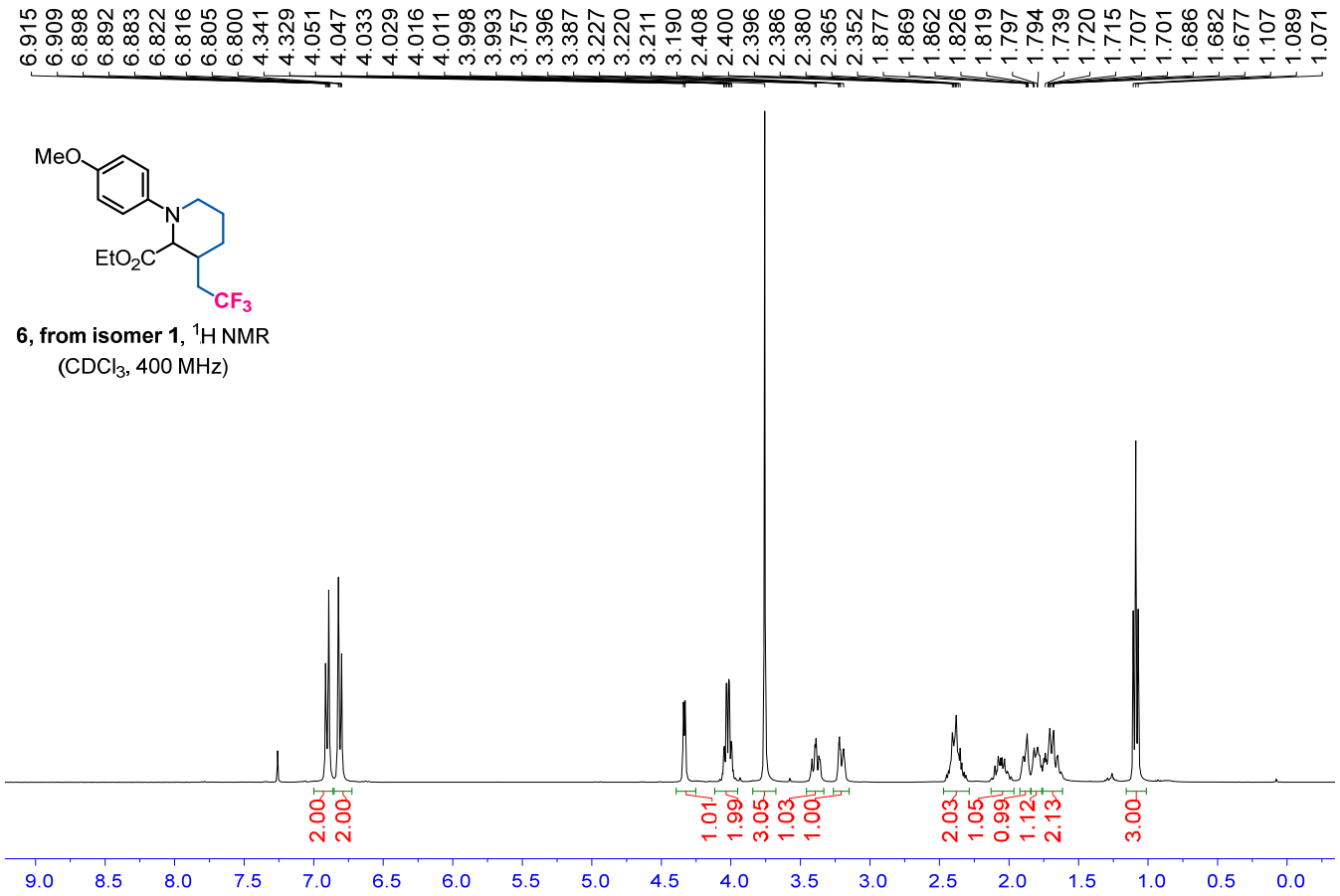
4ai, isomer 2, ^{1}H NMR
($CDCl_3$, 400 MHz)



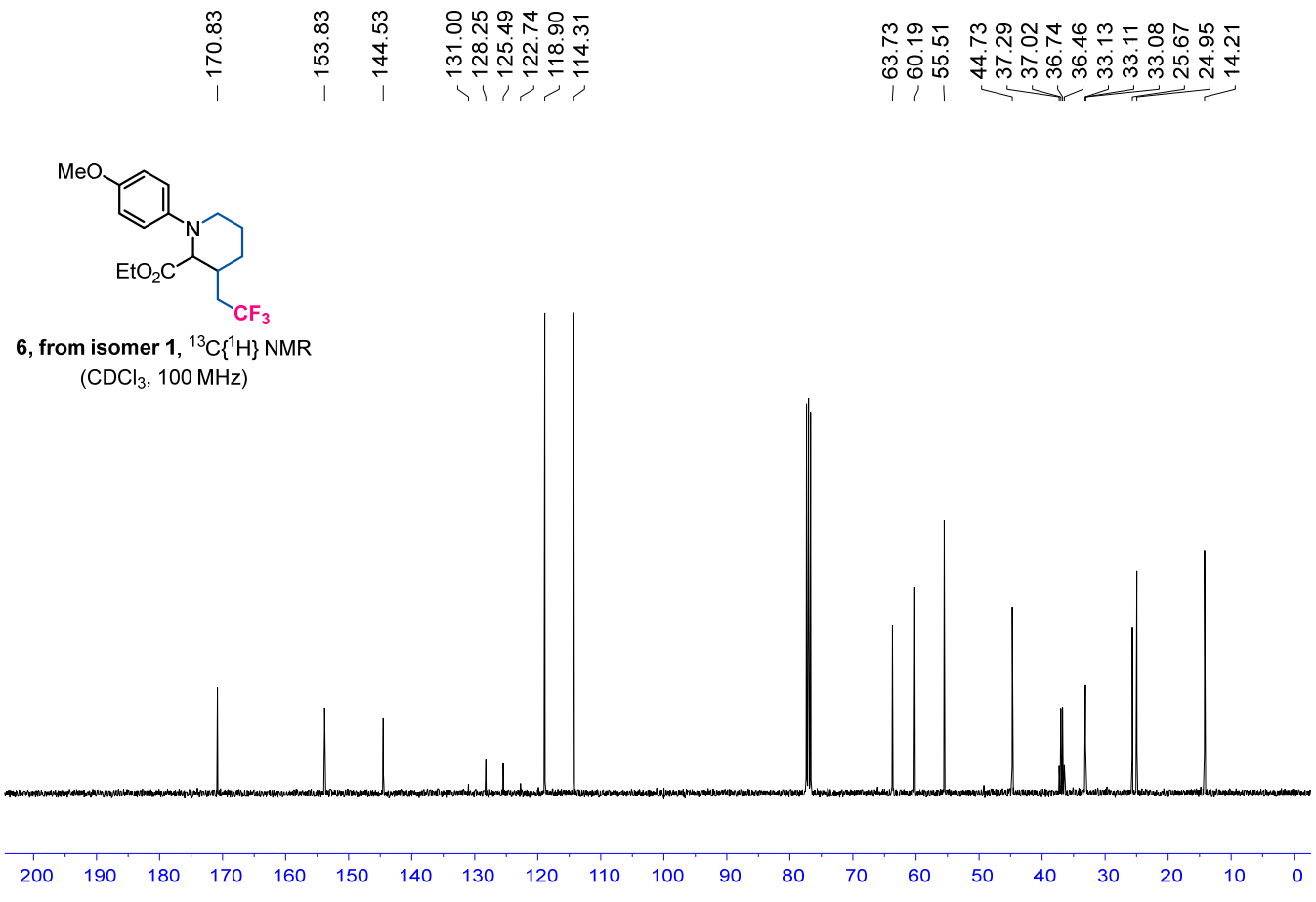
4ai, isomer 2, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



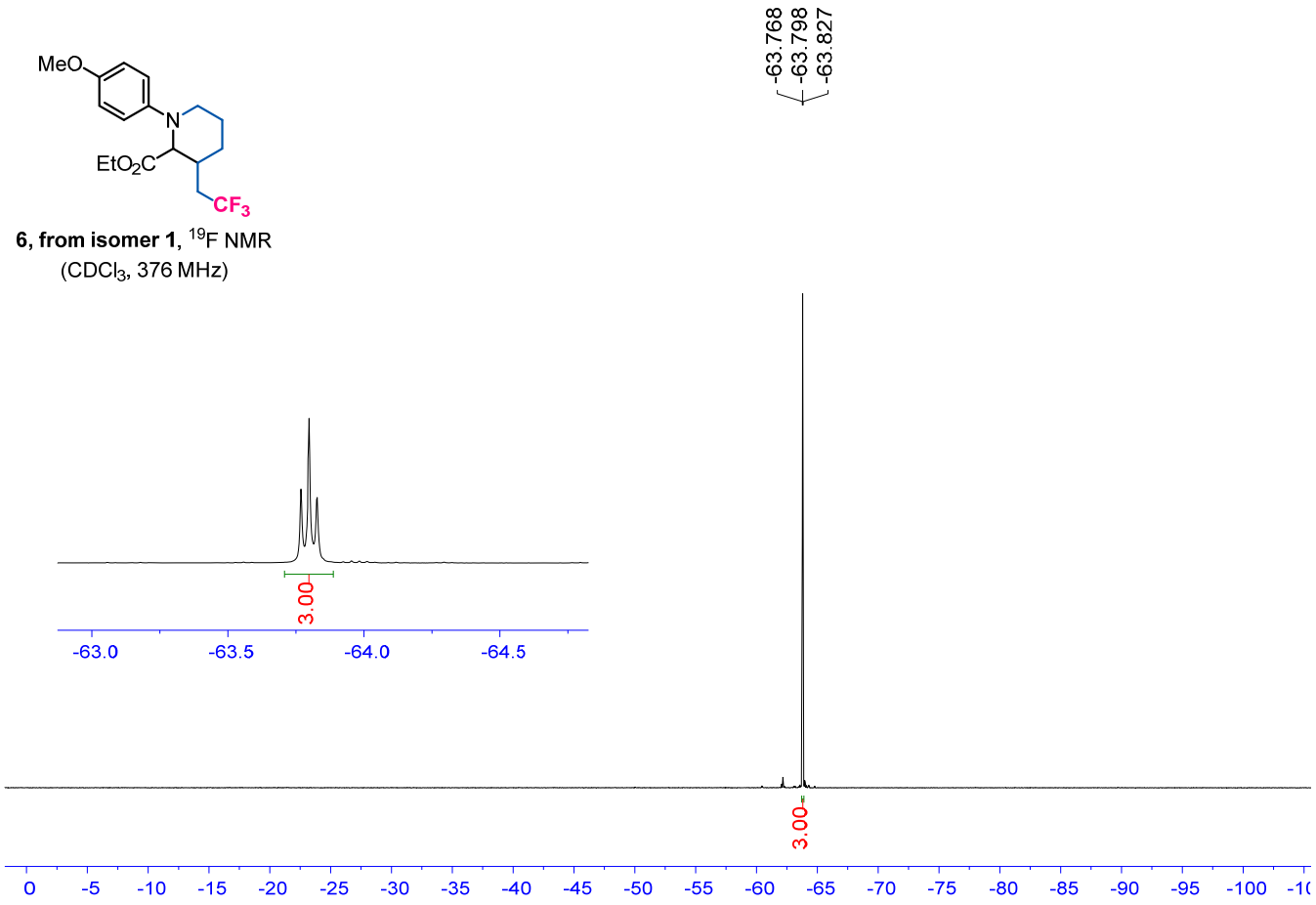
4ai, isomer 2, ^{1}1H NMR
($CDCl_3$, 376 MHz)



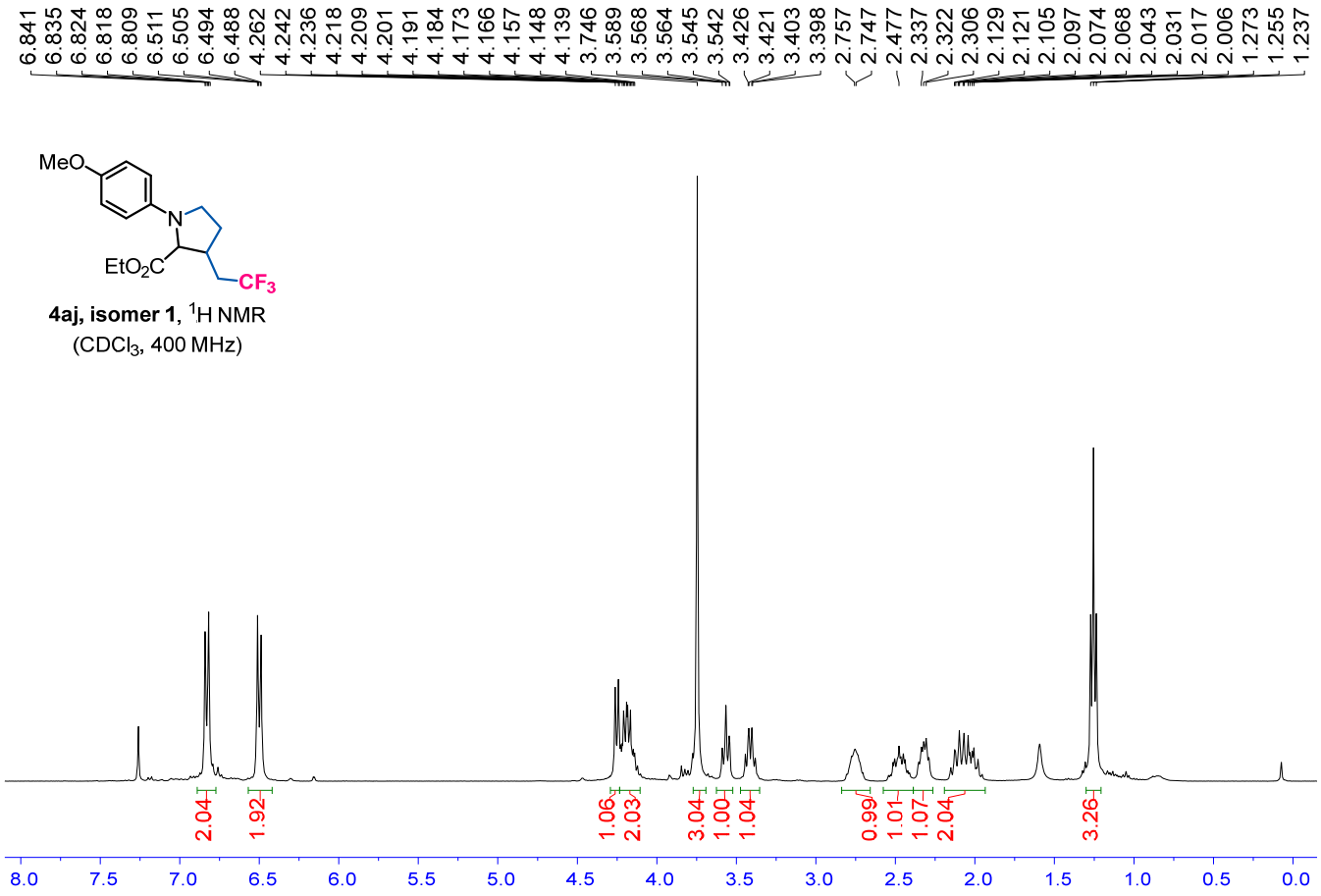
6, from isomer 1, ^{1}H NMR
($CDCl_3$, 400 MHz)

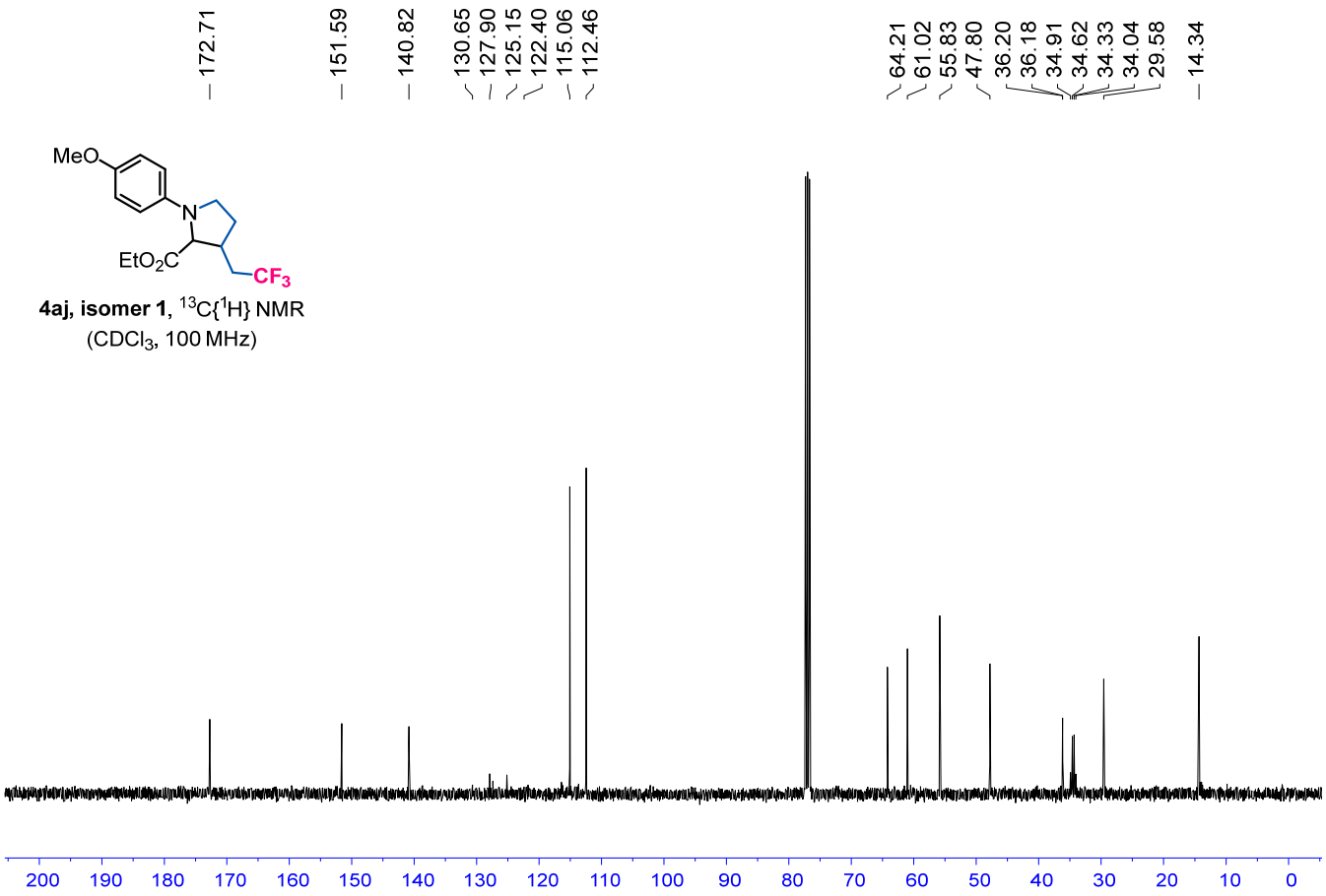


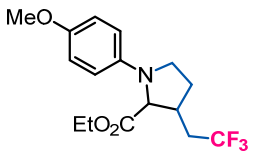
6, from isomer 1, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



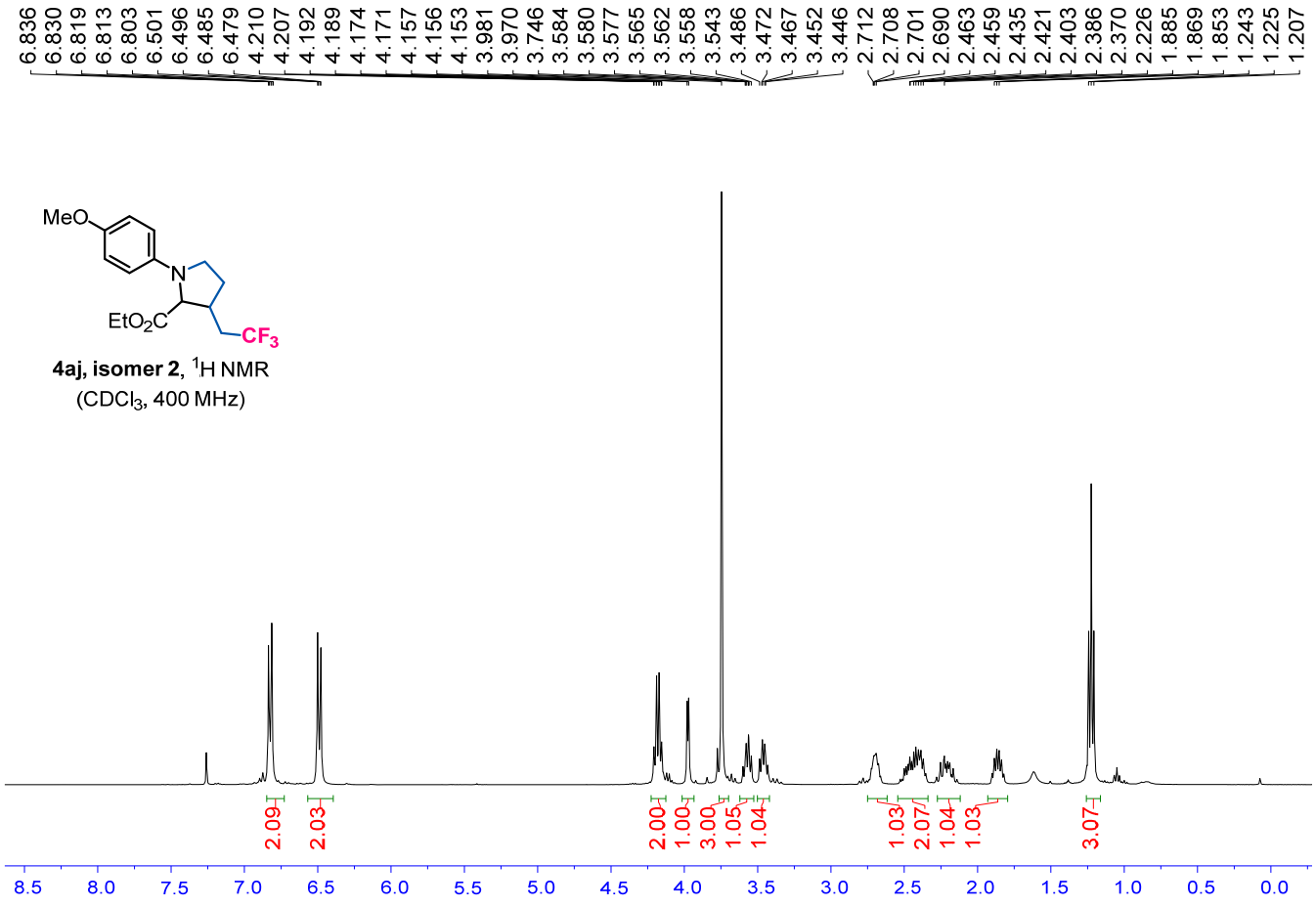
6, from isomer 1, ^{19}F NMR
($CDCl_3$, 376 MHz)

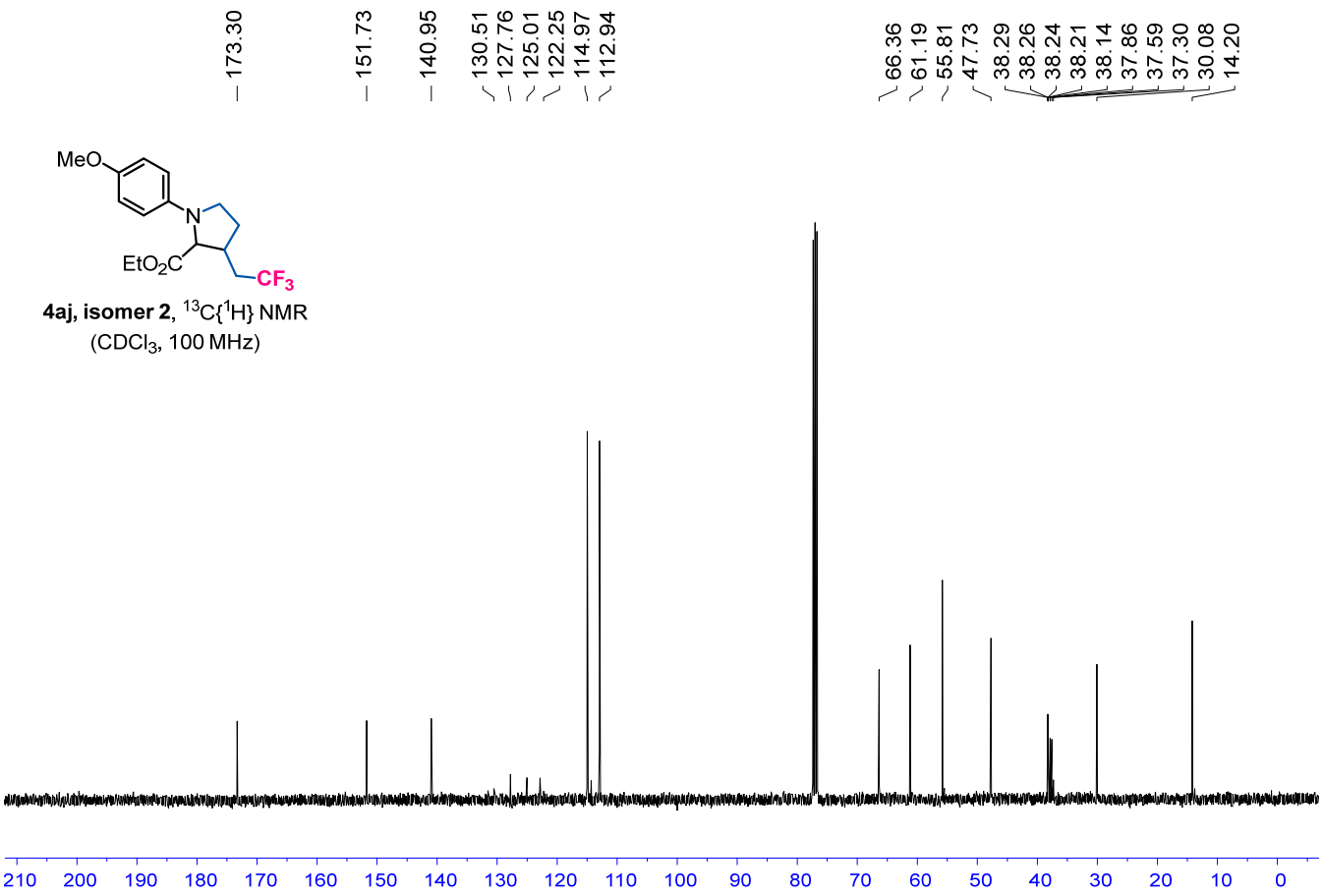

6.841
6.835
6.824
6.818
6.809
6.511
6.505
6.494
6.488
4.262
4.242
4.236
4.218
4.209
4.201
4.191
4.184
4.173
4.166
4.157
4.148
4.139
3.746
3.589
3.568
3.564
3.545
3.542
3.426
3.421
3.403
3.398
2.757
2.747
2.477
2.337
2.322
2.306
2.129
2.121
2.105
2.097
2.074
2.068
2.043
2.031
2.017
2.006
1.273
1.255
1.237
MeO
N
EtO2C
CF3
4aj, isomer 1, 1H NMR
(CDCl3, 400 MHz)
2.04
1.92
1.06
2.03
3.04
1.00
1.04
0.99
1.01
1.07
2.04
3.26
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

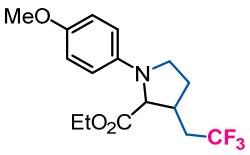

172.71
151.59
140.82
130.65
127.90
125.15
122.40
115.06
112.46
64.21
61.02
55.83
47.80
36.20
36.18
34.91
34.62
34.33
34.04
29.58
14.34
MeO
N
EtO2C
CF3
4aj, isomer 1, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



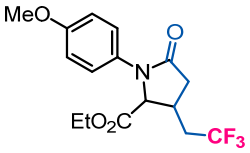
4aj, isomer 1, ^{19}F NMR
($CDCl_3$, 376 MHz)


6.836
6.830
6.819
6.813
6.803
6.501
6.496
6.485
6.479
4.210
4.207
4.192
4.189
4.174
4.171
4.157
4.156
4.153
3.981
3.970
3.746
3.584
3.580
3.577
3.565
3.562
3.558
3.543
3.486
3.472
3.467
3.452
3.446
2.712
2.708
2.701
2.690
2.463
2.459
2.435
2.421
2.403
2.386
2.370
2.226
1.885
1.869
1.853
1.243
1.225
1.207
MeO
N
EtO2C
CF3
4aj, isomer 2, 1H NMR
(CDCl3, 400 MHz)
2.09
2.03
2.00
1.00
3.00
1.05
1.04
1.03
2.07
1.04
1.03
3.07
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

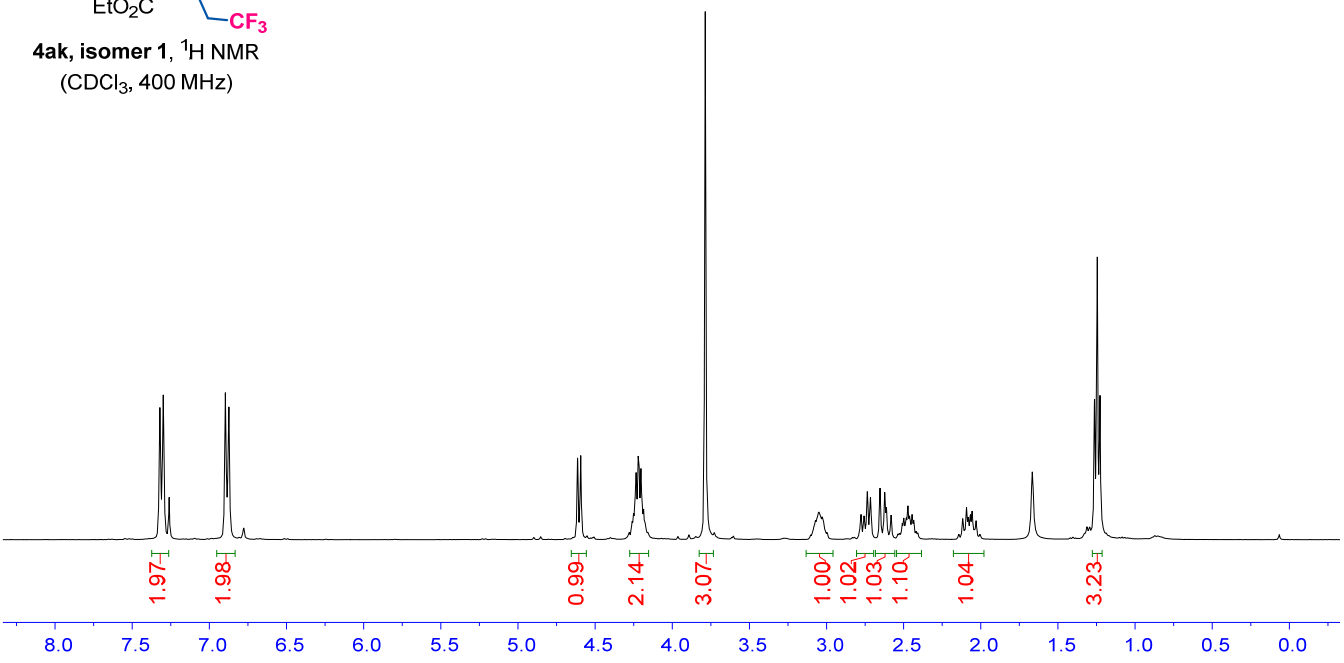

173.30
151.73
140.95
130.51
127.76
125.01
122.25
114.97
112.94
66.36
61.19
55.81
47.73
38.29
38.26
38.24
38.21
38.14
37.86
37.59
37.30
30.08
14.20
MeO
N
EtO2C
CF3
4aj, isomer 2, 13C{1H} NMR
(CDCl3, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

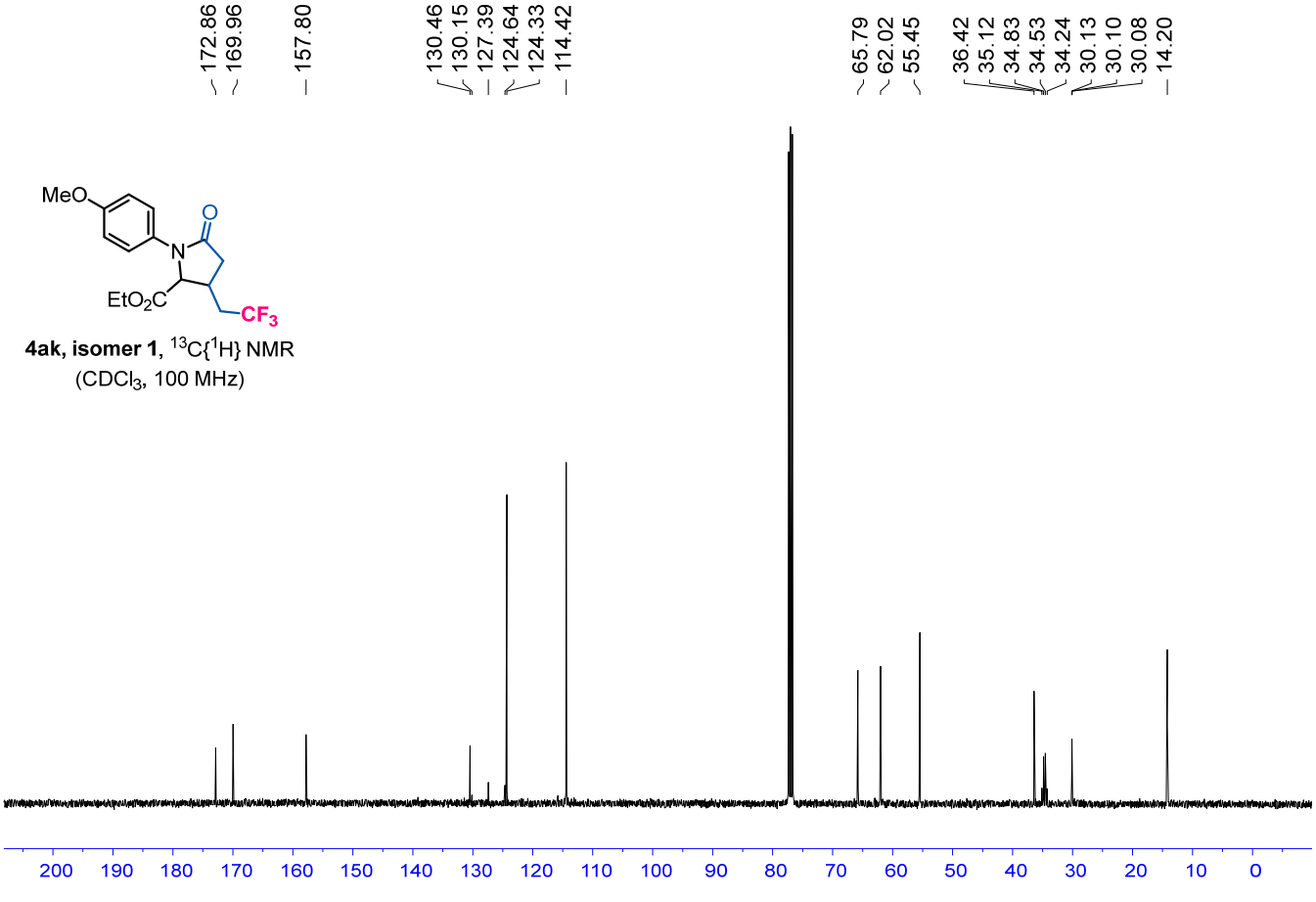


4aj, isomer 2, ^{19}F NMR
($CDCl_3$, 376 MHz)

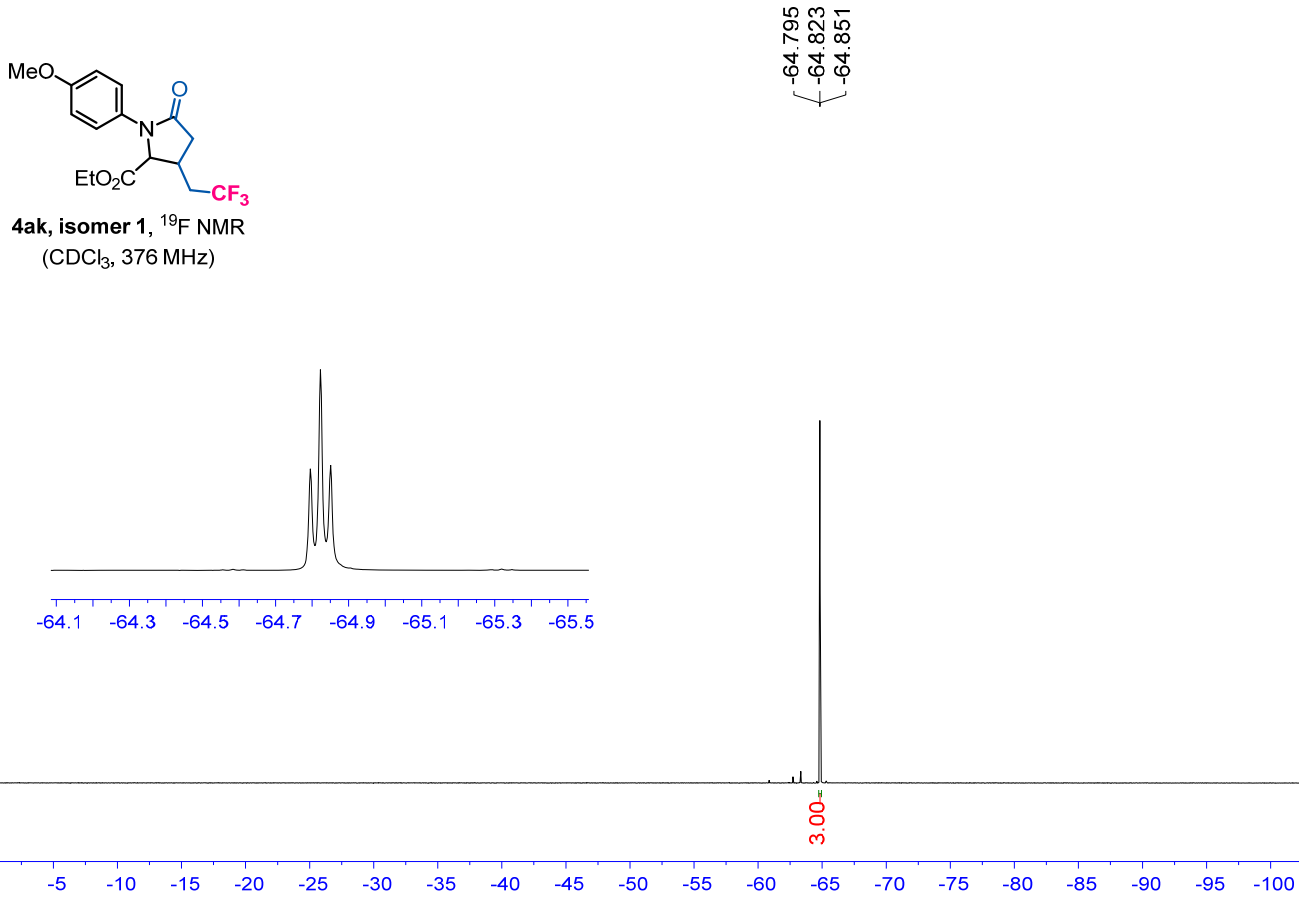


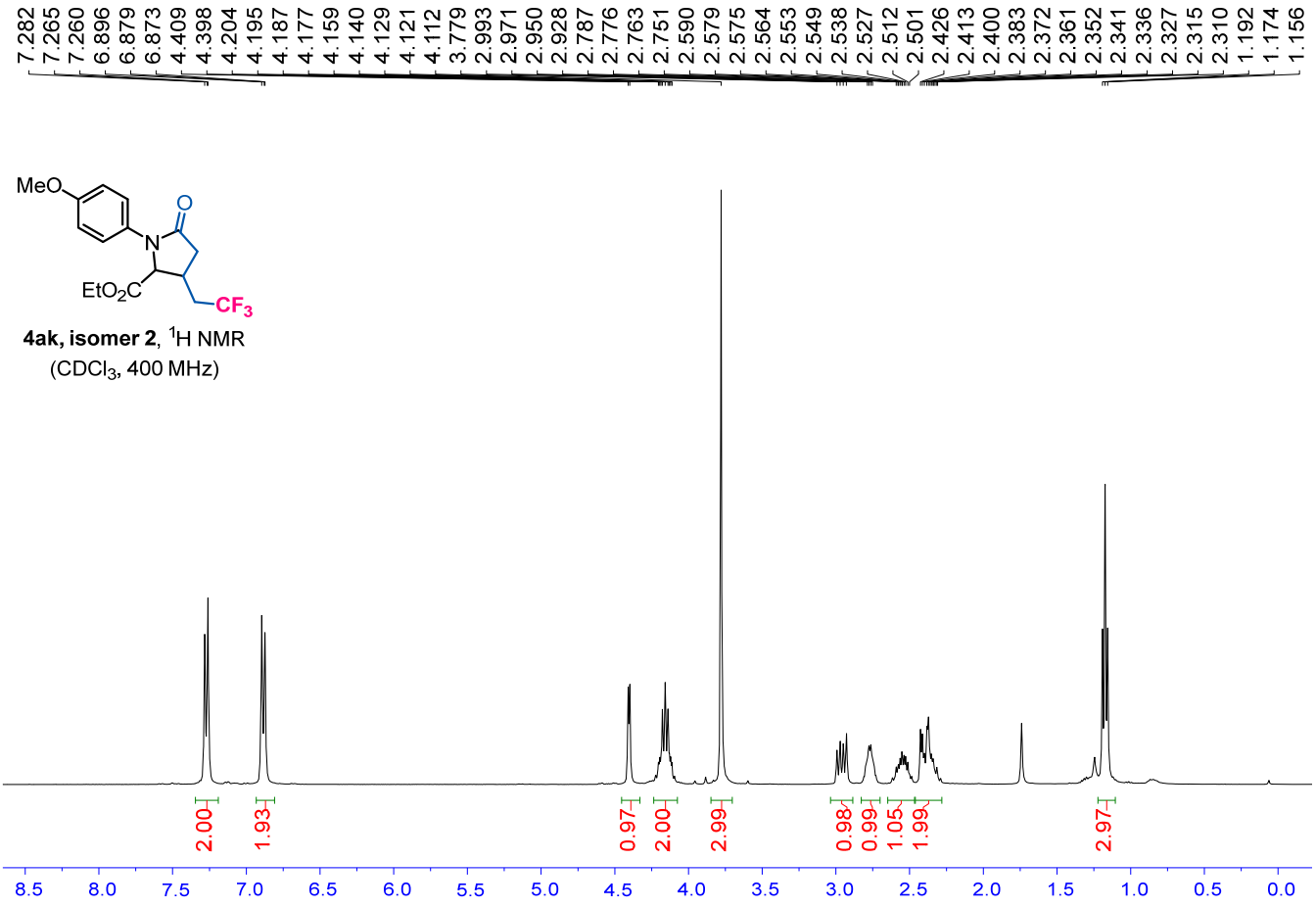
4ak, isomer 1, ^{1}H NMR
($CDCl_3$, 400 MHz)

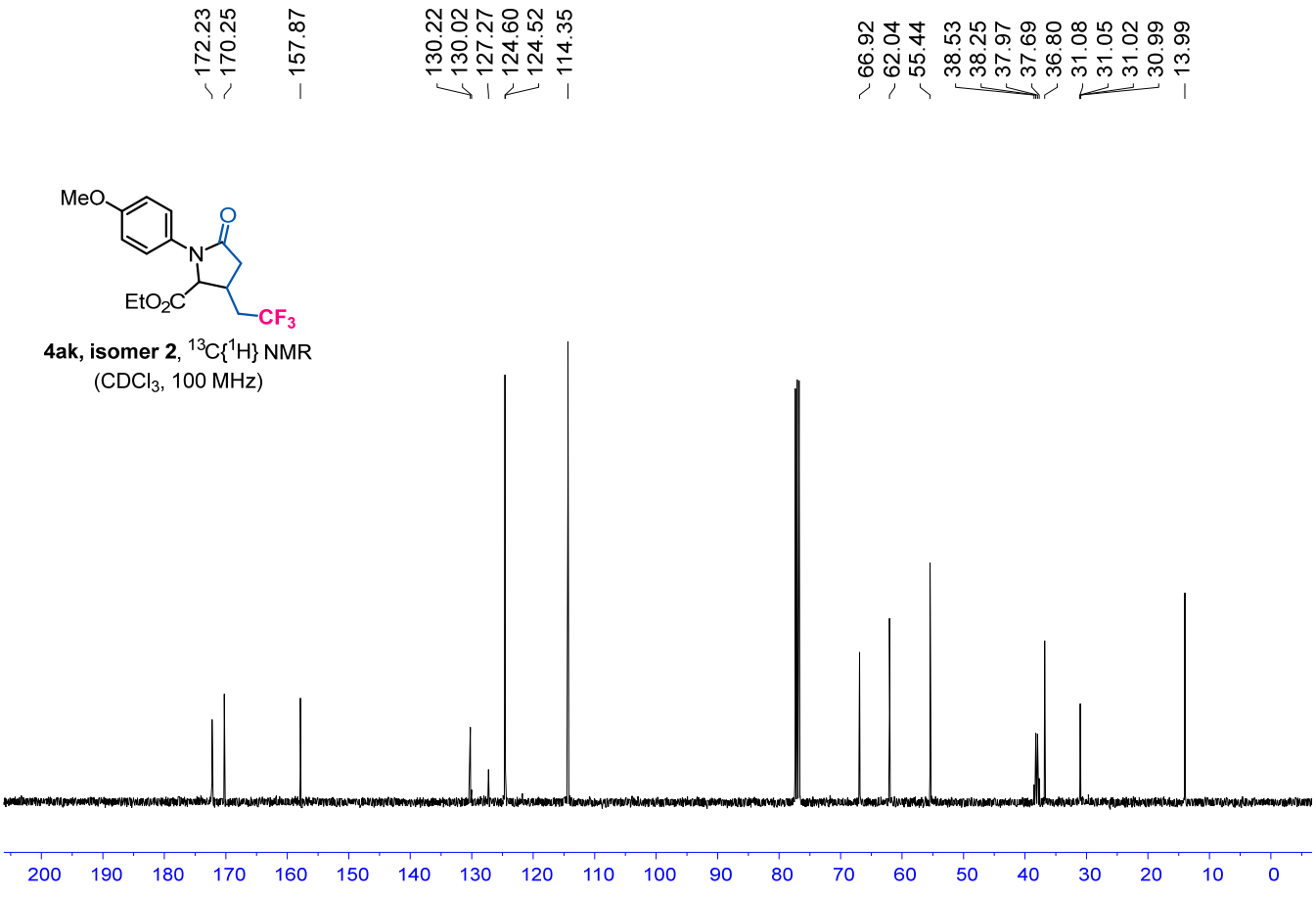


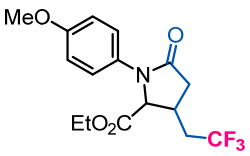


4ak, isomer 1, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)

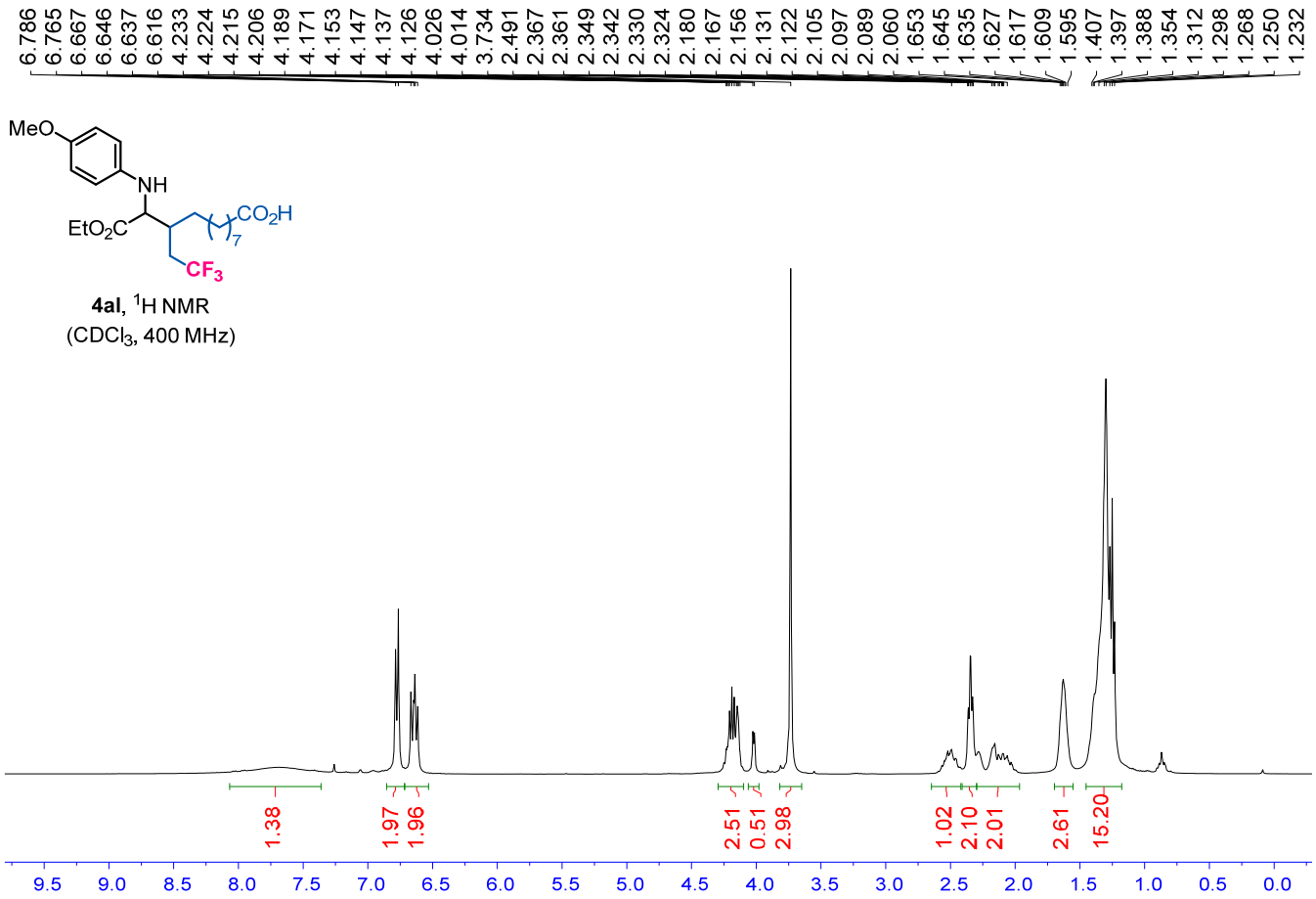

MeO
O
N
EtO2C
CF3
4ak, isomer 1, 19F NMR
(CDCl3, 376 MHz)
-64.795
-64.823
-64.851
-64.1
-64.3
-64.5
-64.7
-64.9
-65.1
-65.3
-65.5
3.00
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100

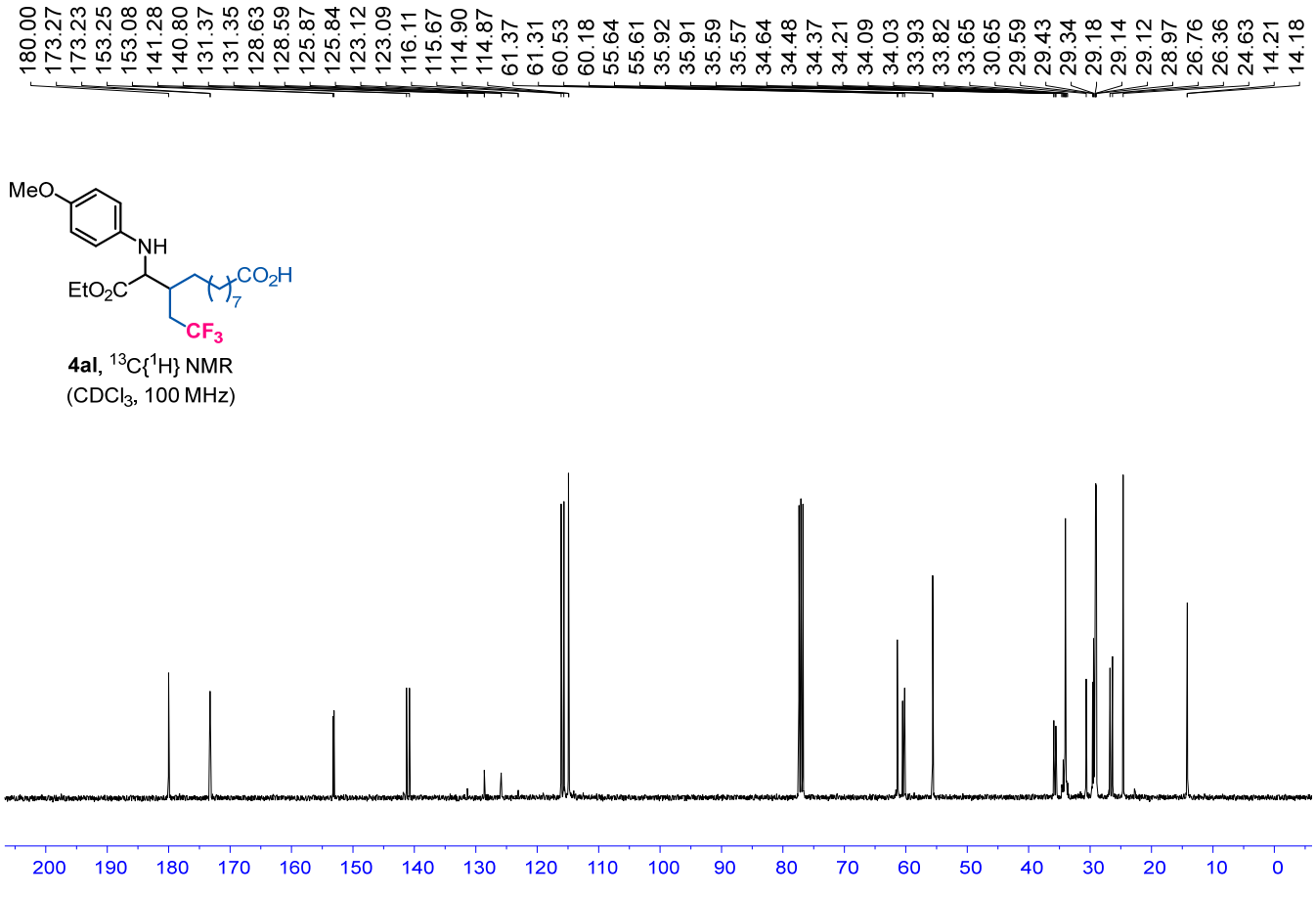

7.282
7.265
7.260
6.896
6.879
6.873
4.409
4.398
4.204
4.195
4.187
4.177
4.159
4.140
4.129
4.121
4.112
3.779
2.993
2.971
2.950
2.928
2.787
2.776
2.763
2.751
2.590
2.579
2.575
2.564
2.553
2.549
2.538
2.527
2.512
2.501
2.426
2.413
2.400
2.383
2.372
2.361
2.352
2.341
2.336
2.327
2.315
2.310
1.192
1.174
1.156
MeO
O
N
EtO2C
CF3
4ak, isomer 2, 1H NMR
(CDCl3, 400 MHz)
2.00
1.93
0.97
2.00
2.99
0.98
0.99
1.05
1.99
2.97
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

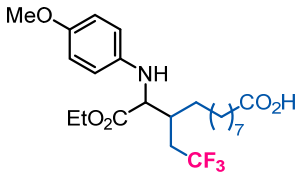

172.23
170.25
157.87
130.22
130.02
127.27
124.60
124.52
114.35
66.92
62.04
55.44
38.53
38.25
37.97
37.69
36.80
31.08
31.05
31.02
30.99
13.99
MeO
O
N
EtO2C
CF3
4ak, isomer 2, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



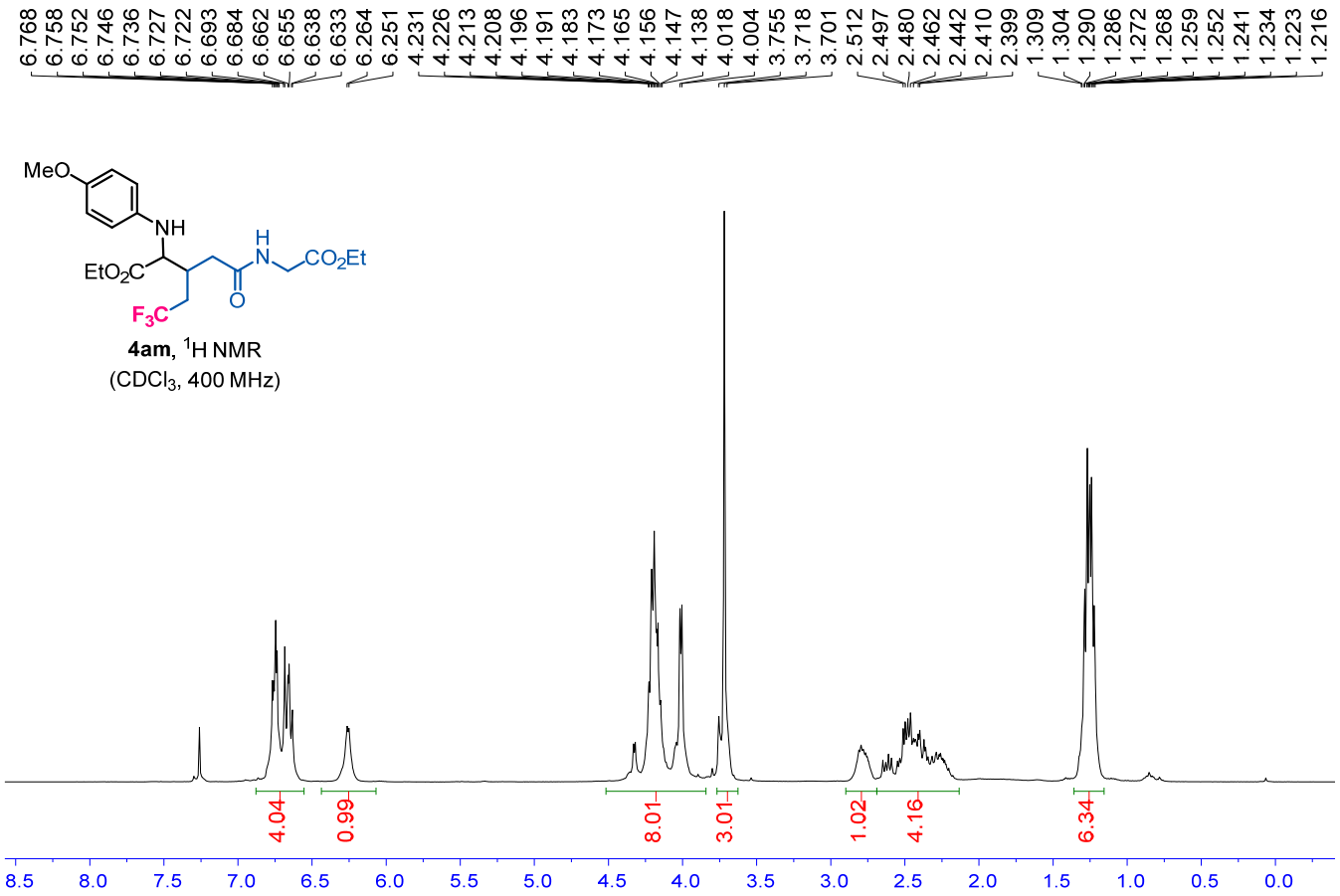
4ak, isomer 2, ^{19}F NMR
($CDCl_3$, 376 MHz)

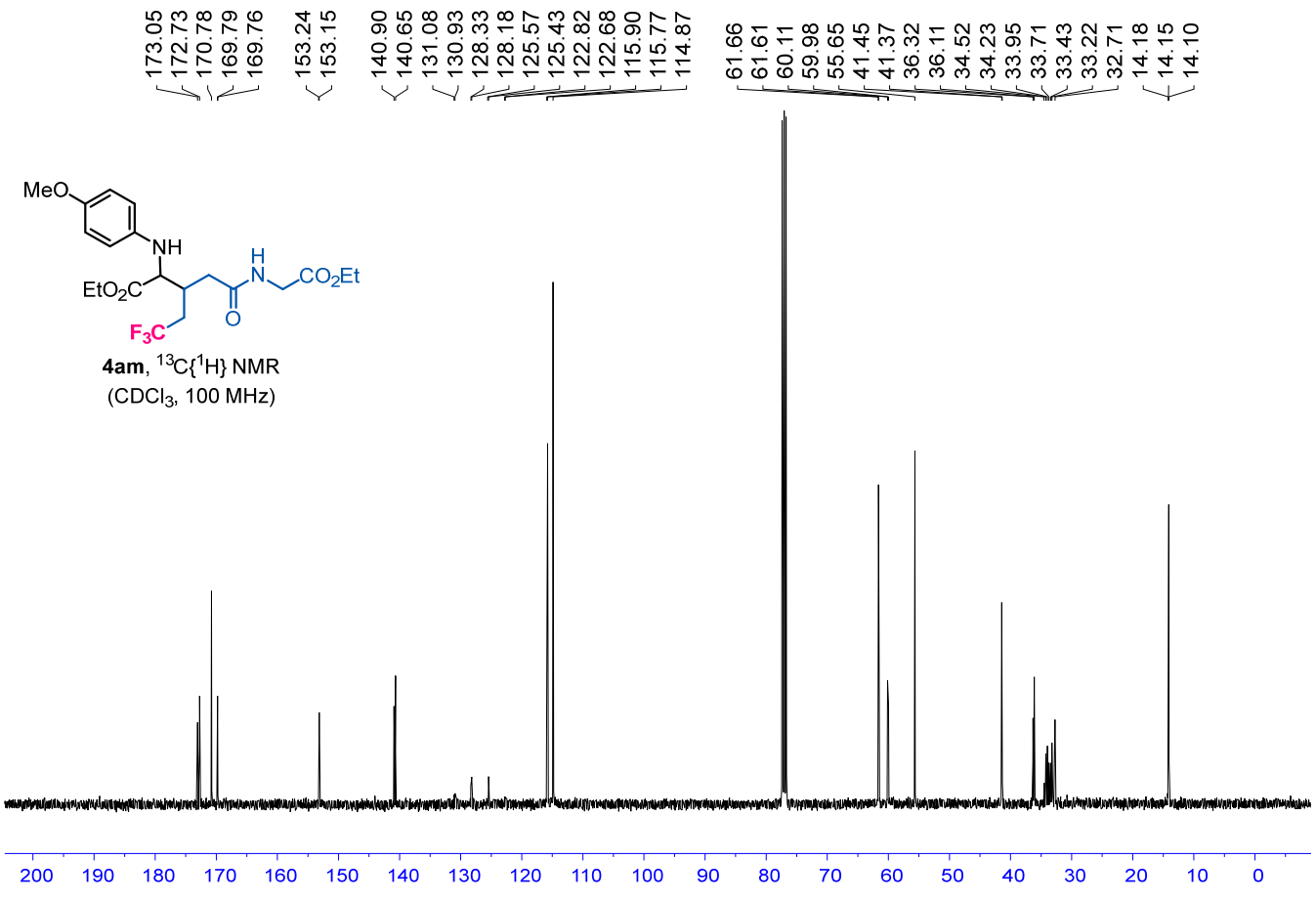

6.786
6.765
6.667
6.646
6.637
6.616
4.233
4.224
4.215
4.206
4.189
4.171
4.153
4.147
4.137
4.126
4.026
4.014
3.734
2.491
2.367
2.361
2.349
2.342
2.330
2.324
2.180
2.167
2.156
2.131
2.122
2.105
2.097
2.089
2.060
1.653
1.645
1.635
1.627
1.617
1.609
1.595
1.407
1.397
1.388
1.354
1.312
1.298
1.268
1.250
1.232
MeO
NH
EtO2C
CO2H
7
CF3
4al, 1H NMR
(CDCl3, 400 MHz)
1.38
1.97
1.96
2.51
0.51
2.98
1.02
2.10
2.01
2.61
15.20
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

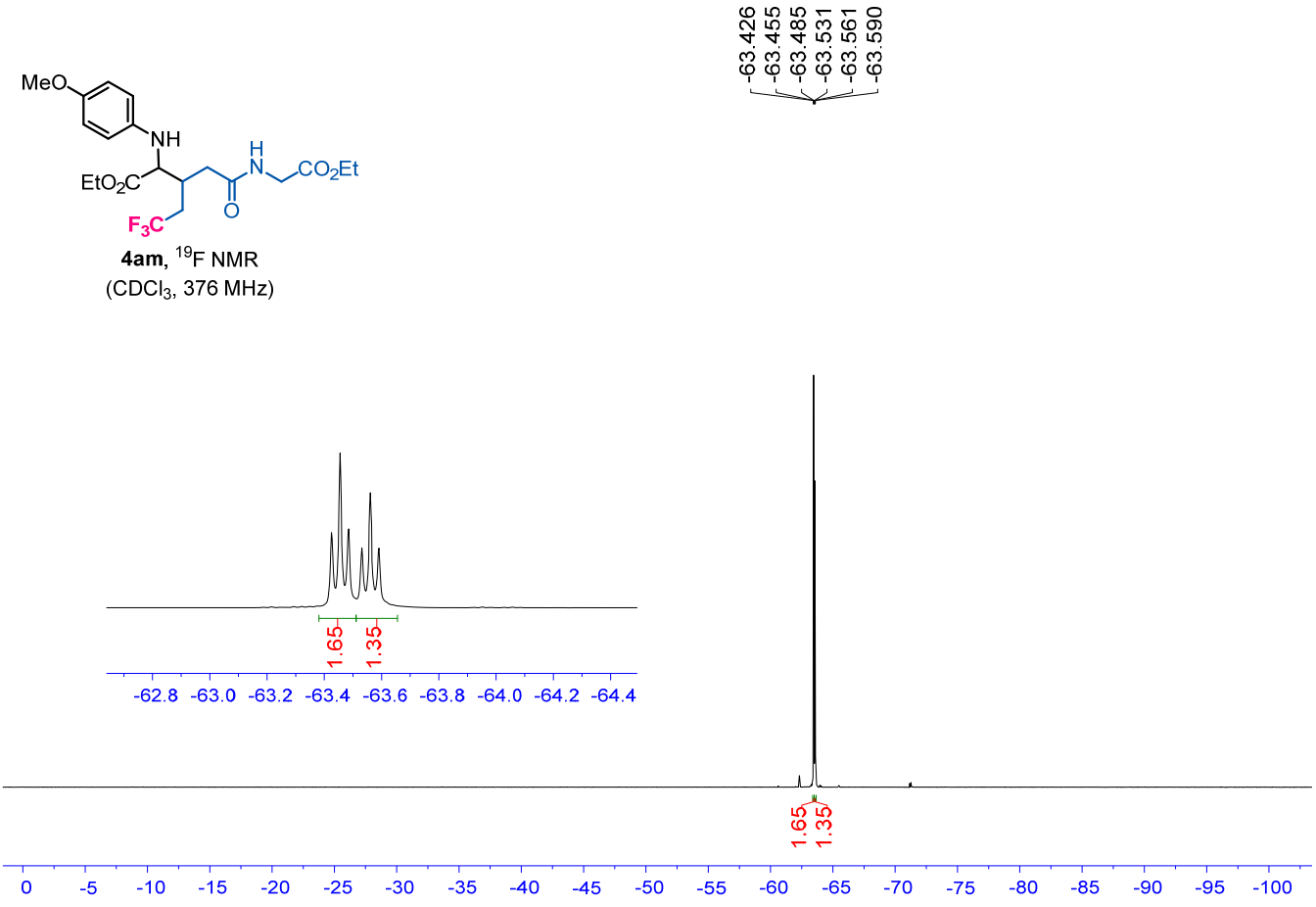

180.00
173.27
173.23
153.25
153.08
141.28
140.80
131.37
131.35
128.63
128.59
125.87
125.84
123.12
123.09
116.11
115.67
114.90
114.87
61.37
61.31
60.53
60.18
55.64
55.61
35.92
35.91
35.59
35.57
34.64
34.48
34.37
34.21
34.09
34.03
33.93
33.82
33.65
30.65
29.59
29.43
29.34
29.18
29.14
29.12
28.97
26.76
26.36
24.63
14.21
14.18
MeO
NH
EtO2C
CO2H
7
CF3
4al, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



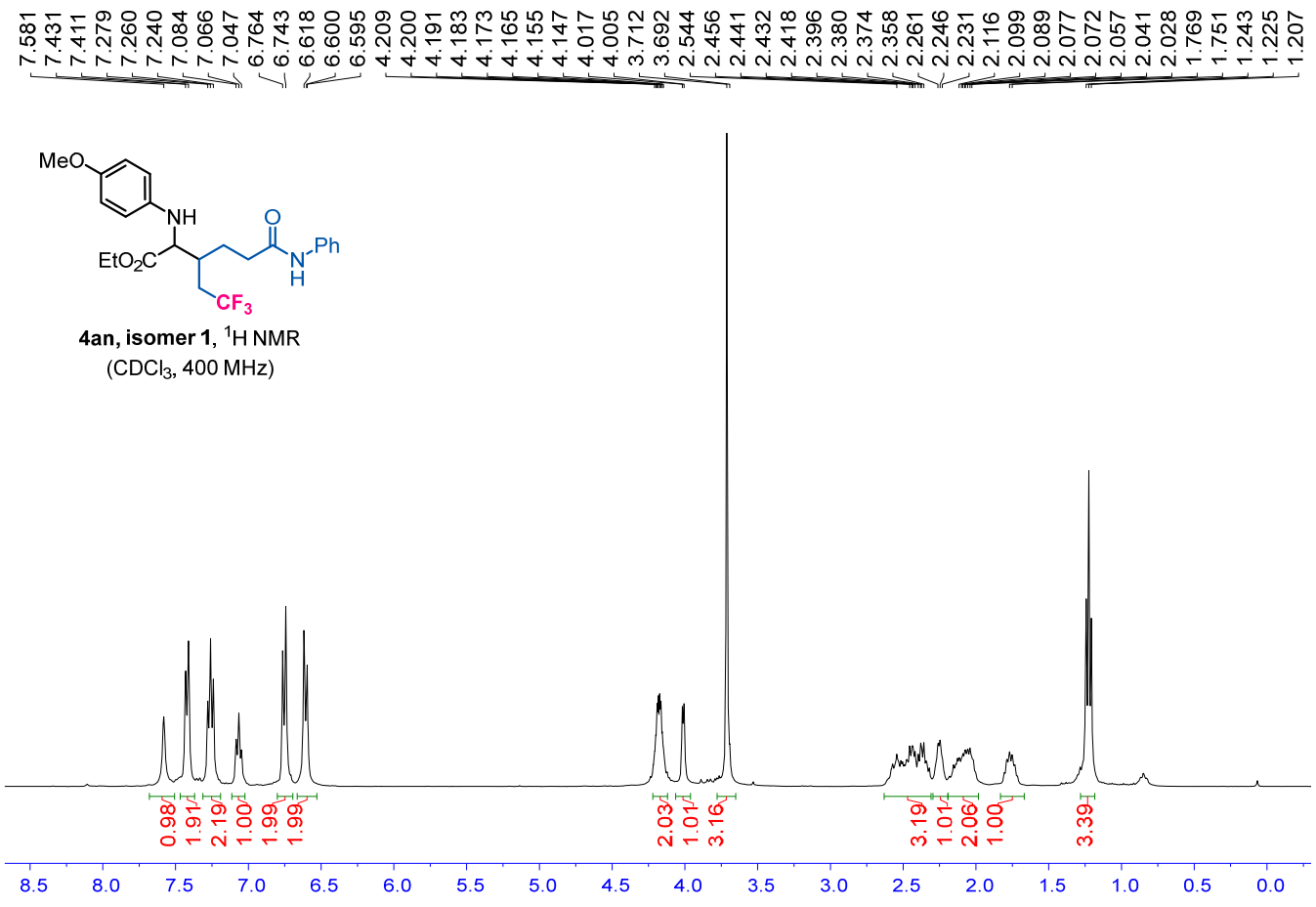
4al, ^{19}F NMR
($CDCl_3$, 376 MHz)


6.768
6.758
6.752
6.746
6.736
6.727
6.722
6.693
6.684
6.662
6.655
6.638
6.633
6.264
6.251
4.231
4.226
4.213
4.208
4.196
4.191
4.183
4.173
4.165
4.156
4.147
4.138
4.018
4.004
3.755
3.718
3.701
2.512
2.497
2.480
2.462
2.442
2.410
2.399
1.309
1.304
1.290
1.286
1.272
1.268
1.259
1.252
1.241
1.234
1.223
1.216
MeO
NH
EtO2C
H
N
CO2Et
O
F3C
4am, 1H NMR
(CDCl3, 400 MHz)
4.04
0.99
8.01
3.01
1.02
4.16
6.34
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

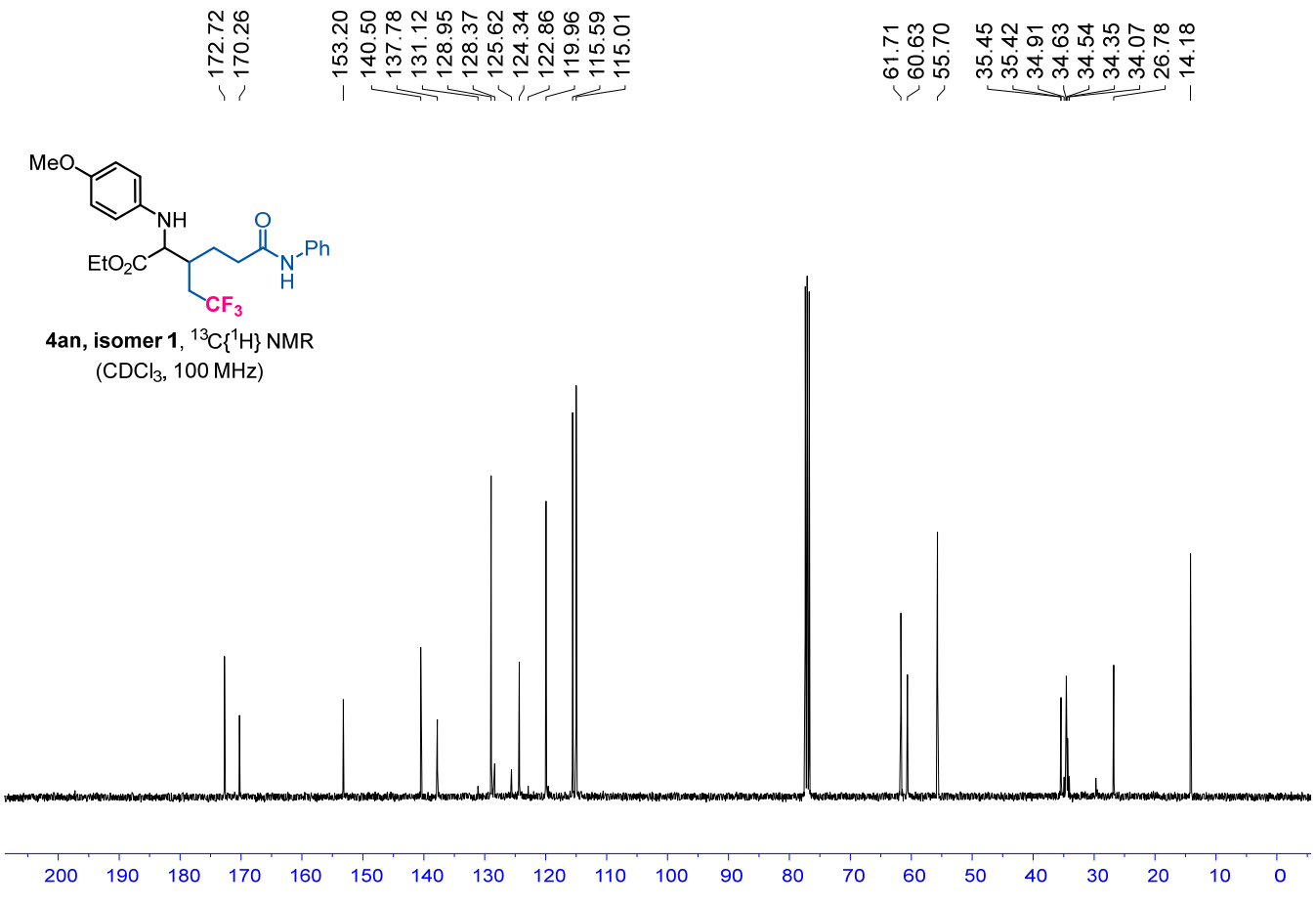

173.05
172.73
170.78
169.79
169.76
153.24
153.15
140.90
140.65
131.08
130.93
128.33
128.18
125.57
125.43
122.82
122.68
115.90
115.77
114.87
61.66
61.61
60.11
59.98
55.65
41.45
41.37
36.32
36.11
34.52
34.23
33.95
33.71
33.43
33.22
32.71
14.18
14.15
14.10
MeO
NH
EtO2C
H
N
CO2Et
O
F3C
4am, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



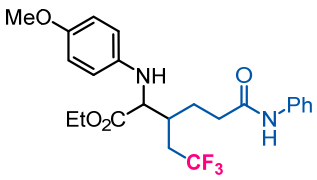
4am, ^{19}F NMR
($CDCl_3$, 376 MHz)



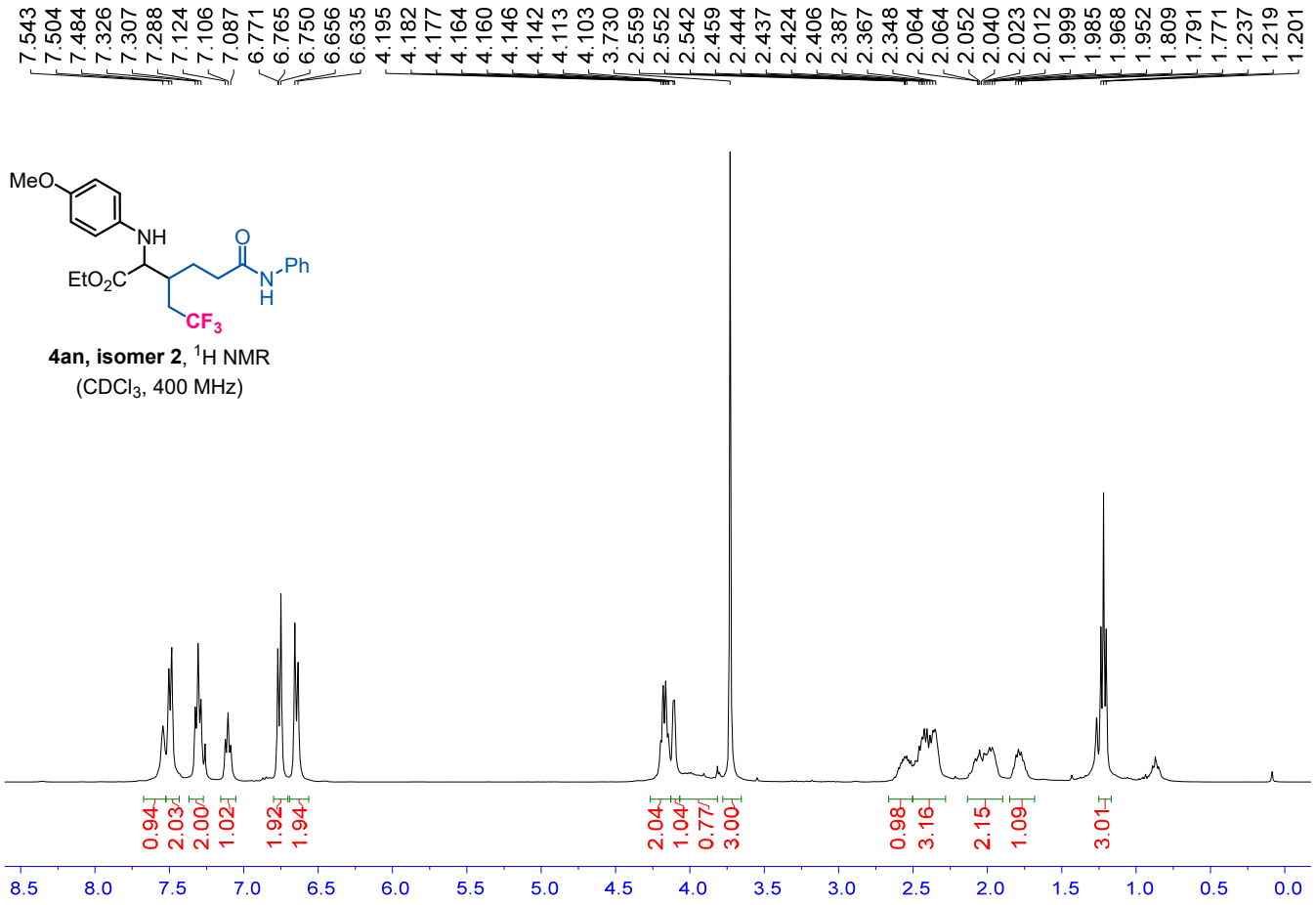
4an, isomer 1, ^{1}H NMR
($CDCl_3$, 400 MHz)



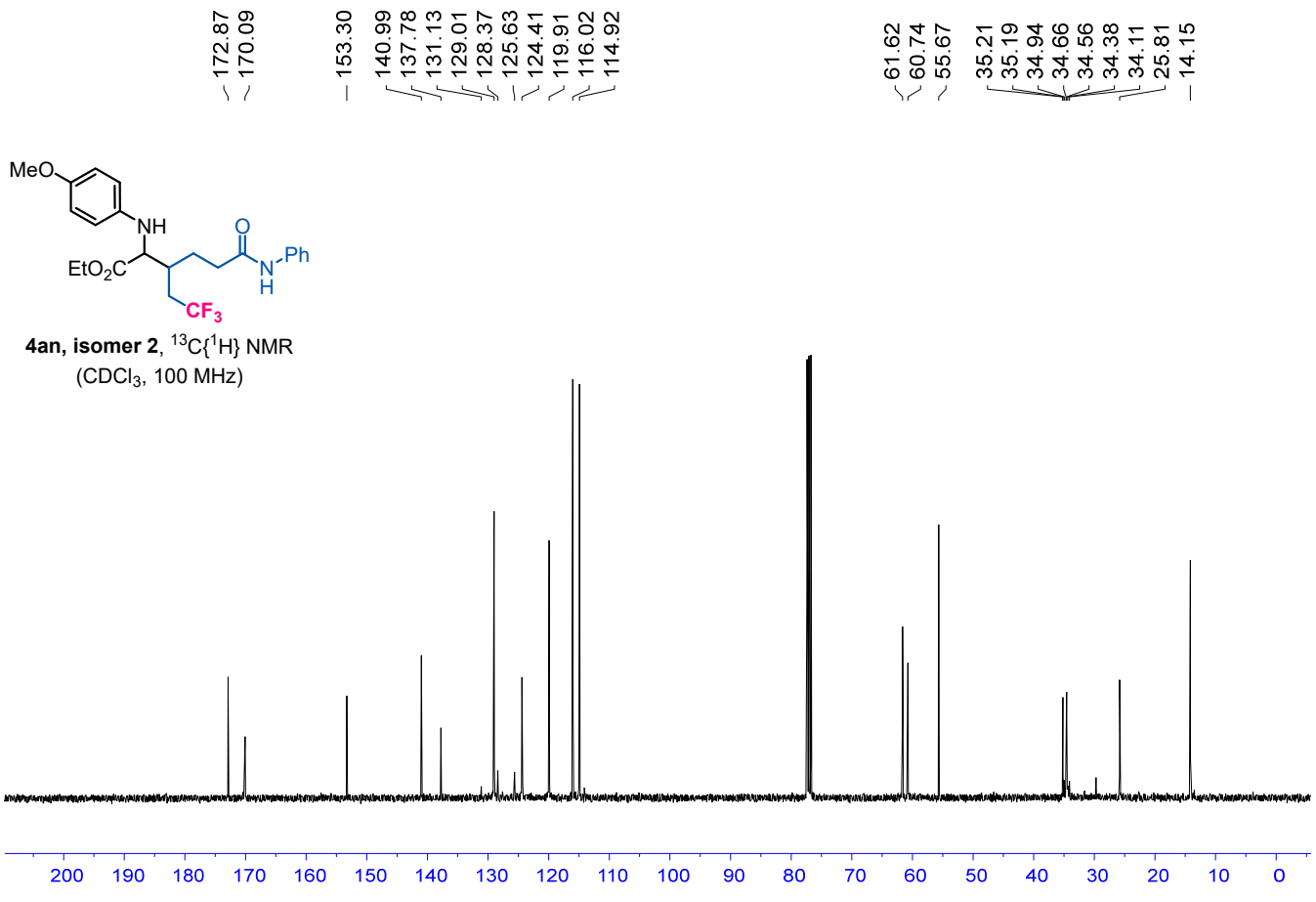
4an, isomer 1, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



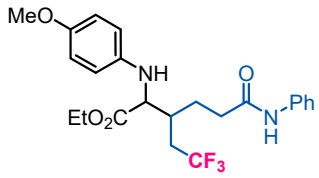
4an, isomer 1, ^{19}F NMR
($CDCl_3$, 376 MHz)



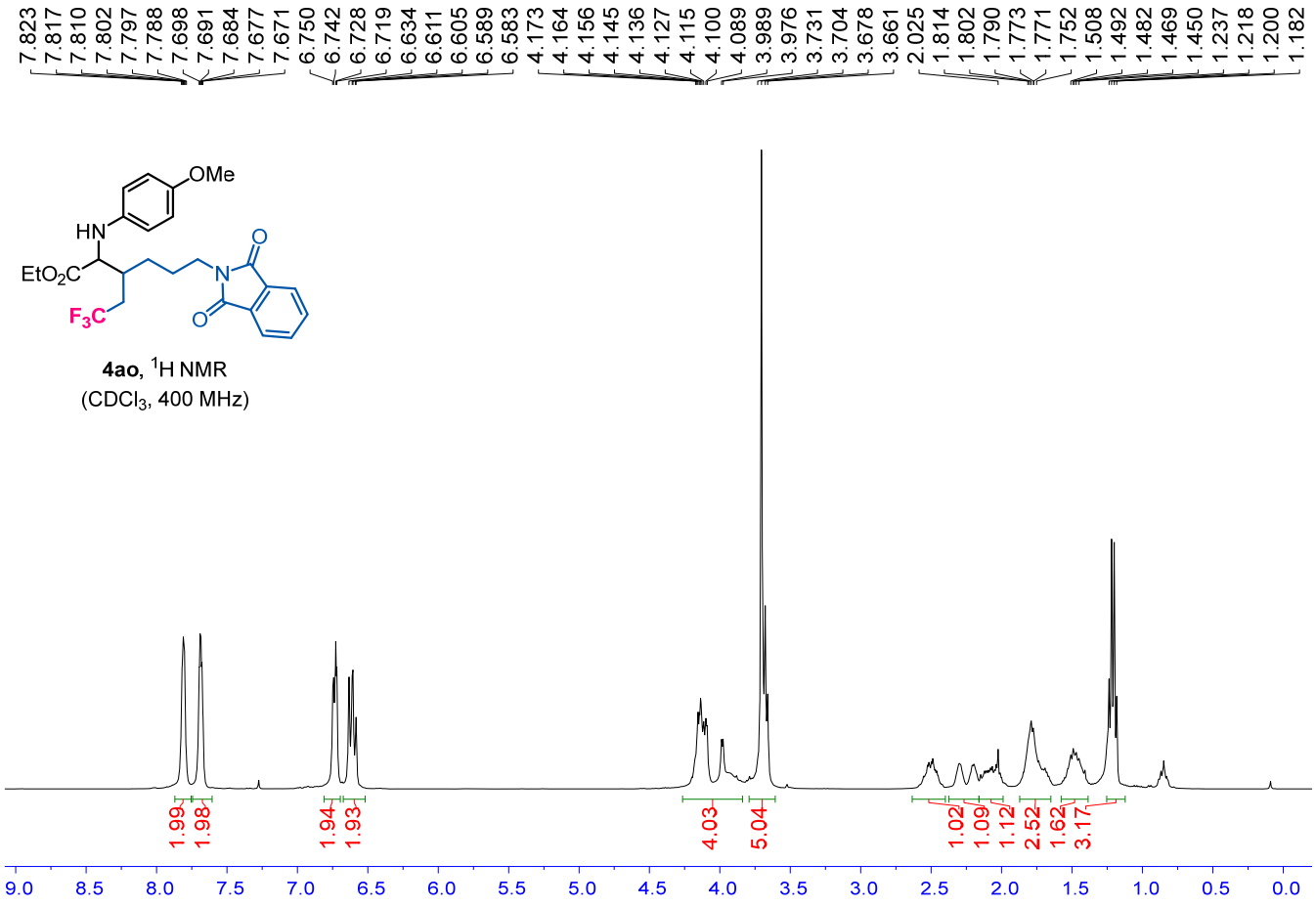
4an, isomer 2, ^{1}H NMR
($CDCl_3$, 400 MHz)

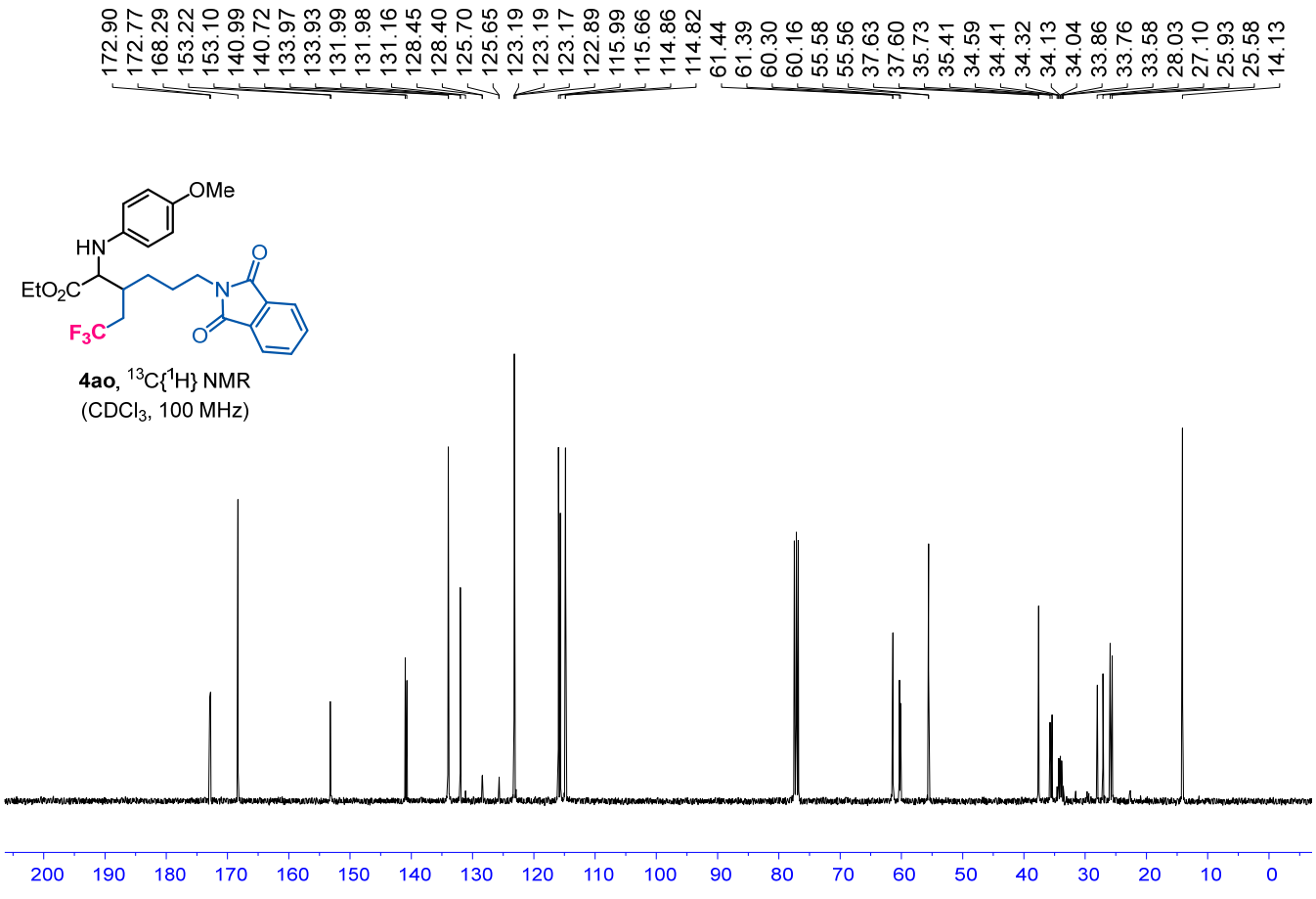


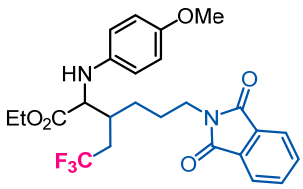
4an, isomer 2, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)



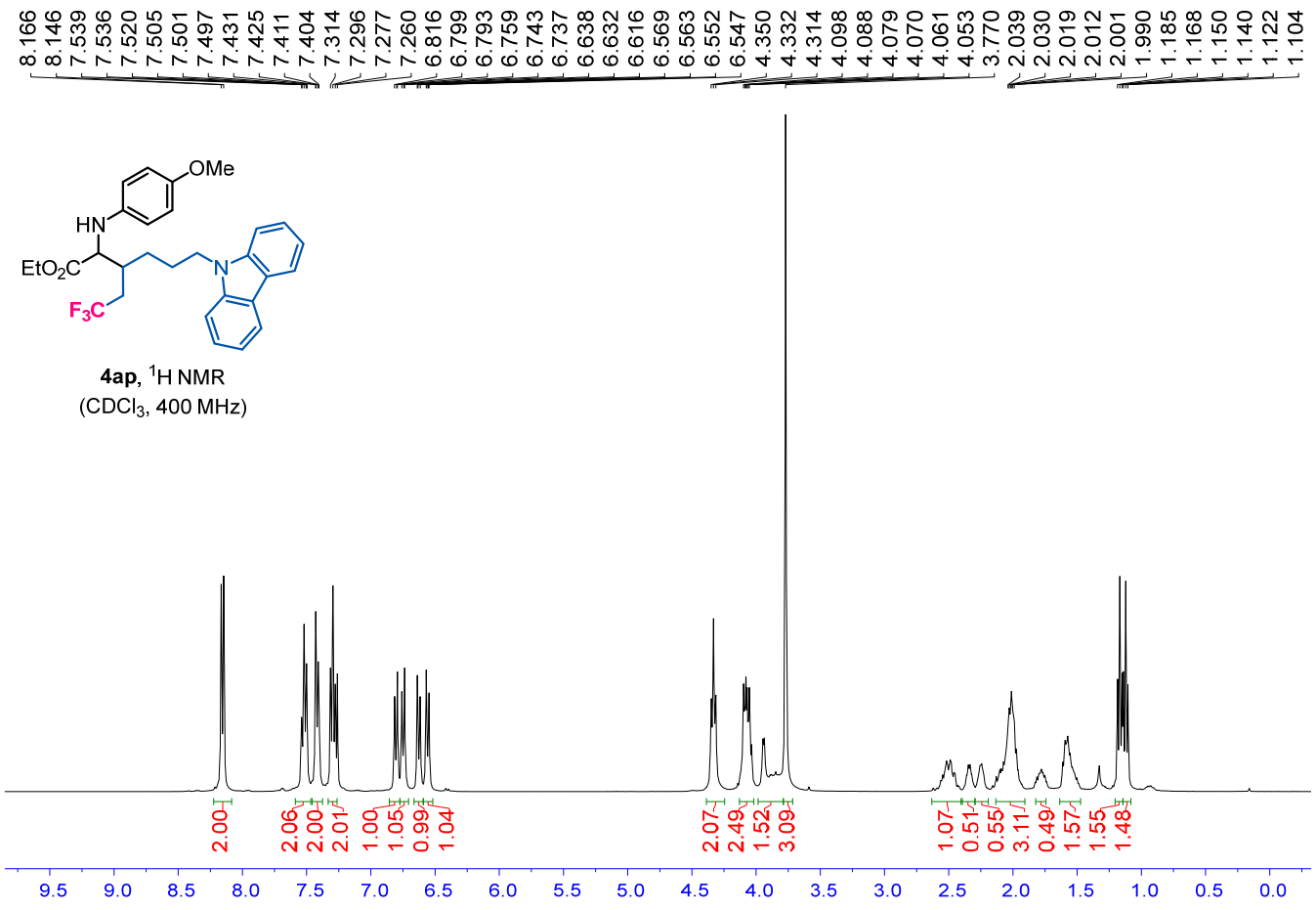
4an, isomer 2, ^{19}F NMR
($CDCl_3$, 376 MHz)


7.823
7.817
7.810
7.802
7.797
7.788
7.698
7.691
7.684
7.677
7.671
6.750
6.742
6.728
6.719
6.634
6.611
6.605
6.589
6.583
4.173
4.164
4.156
4.145
4.136
4.127
4.115
4.100
4.089
3.989
3.976
3.731
3.704
3.678
3.661
2.025
1.814
1.802
1.790
1.773
1.771
1.752
1.508
1.492
1.482
1.469
1.450
1.237
1.218
1.200
1.182
OMe
HN
EtO2C
F3C
O
N
O
4ao, 1H NMR
(CDCl3, 400 MHz)
1.99
1.98
1.94
1.93
4.03
5.04
1.02
1.09
1.12
2.52
1.62
3.17
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

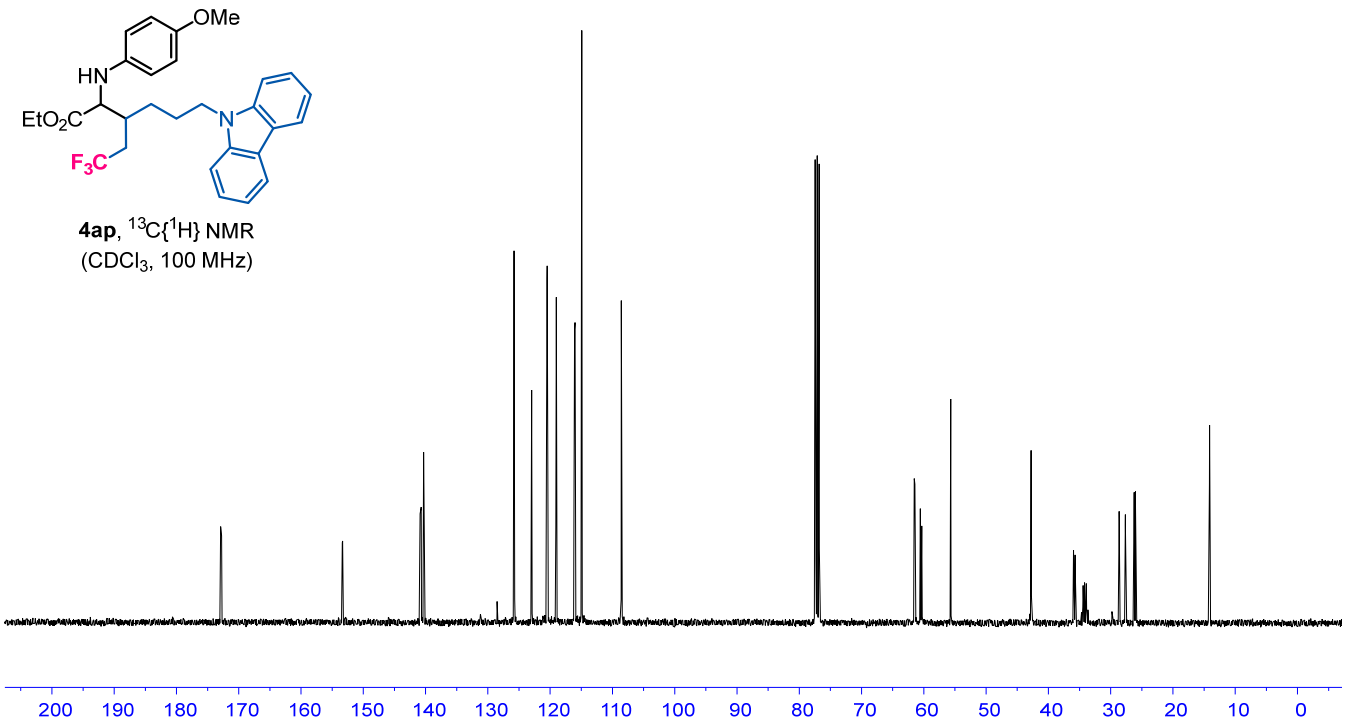

172.90
172.77
168.29
153.22
153.10
140.99
140.72
133.97
133.93
131.99
131.98
131.16
128.45
128.40
125.70
125.65
123.19
123.19
123.17
122.89
115.99
115.66
114.86
114.82
61.44
61.39
60.30
60.16
55.58
55.56
37.63
37.60
35.73
35.41
34.59
34.41
34.32
34.13
34.04
33.86
33.76
33.58
28.03
27.10
25.93
25.58
14.13
OMe
HN
EtO2C
F3C
O
N
O
4ao, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



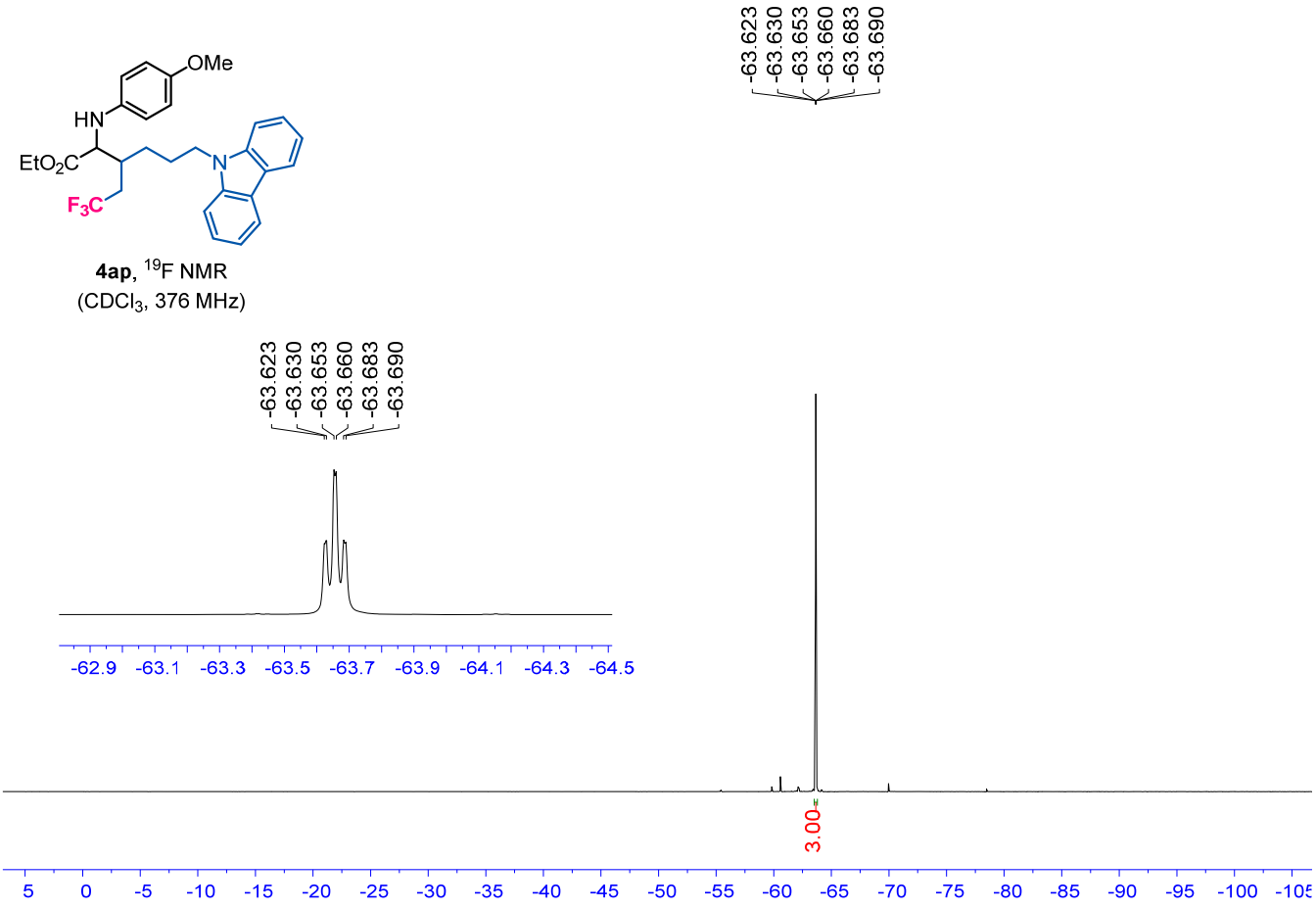
4ao, ^{19}F NMR
($CDCl_3$, 376 MHz)



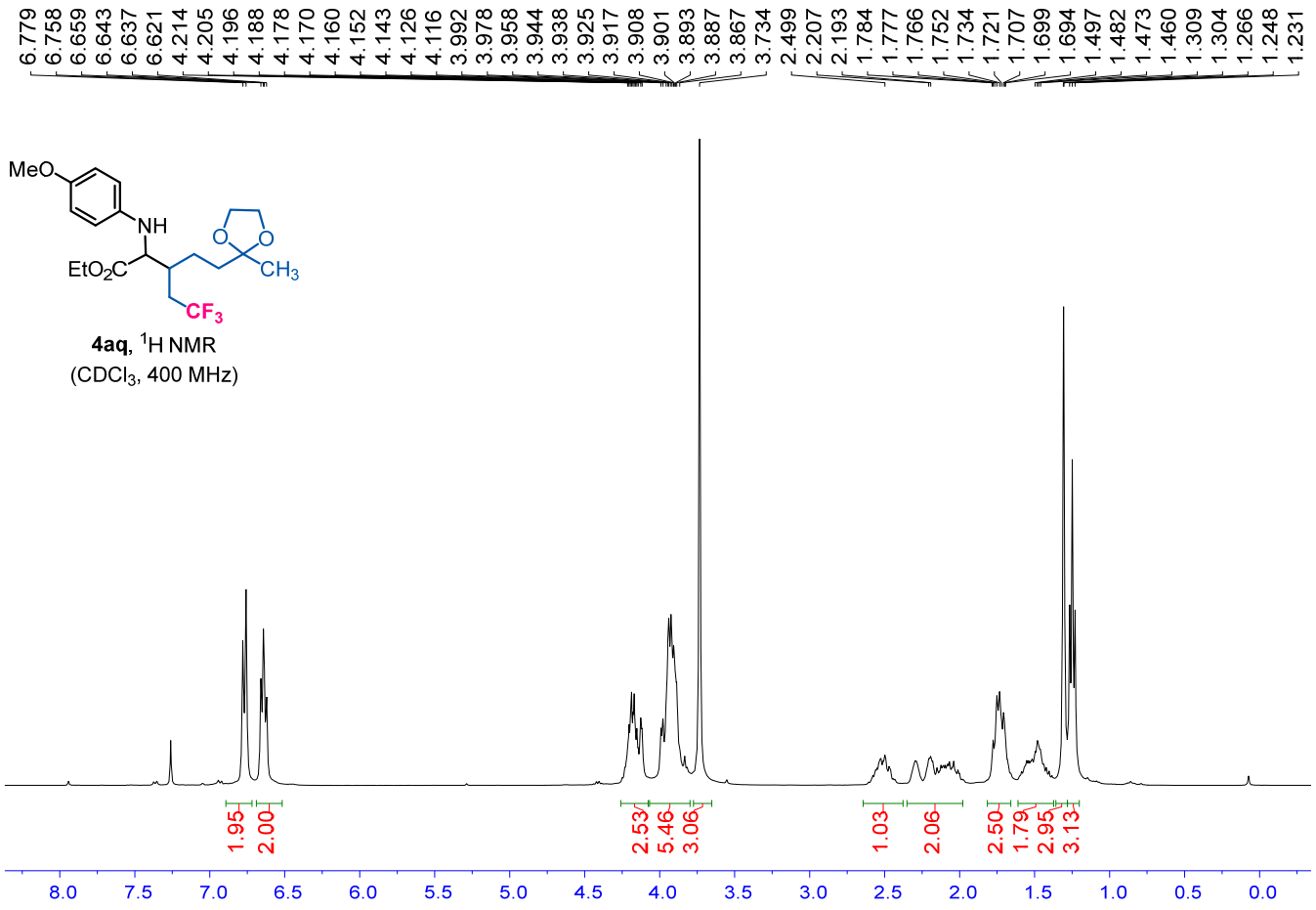
4ap, ^{1}H NMR
($CDCl_3$, 400 MHz)

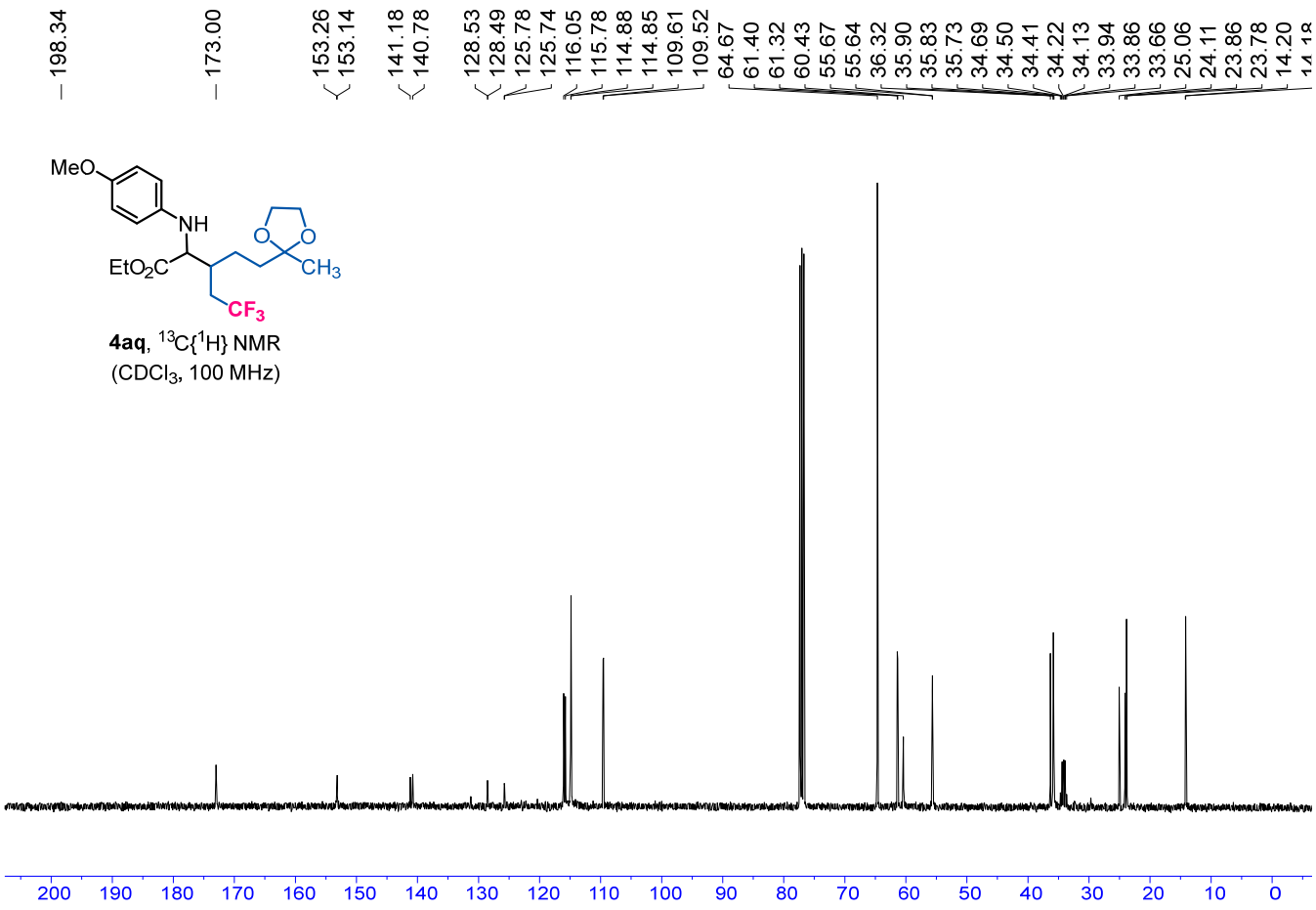


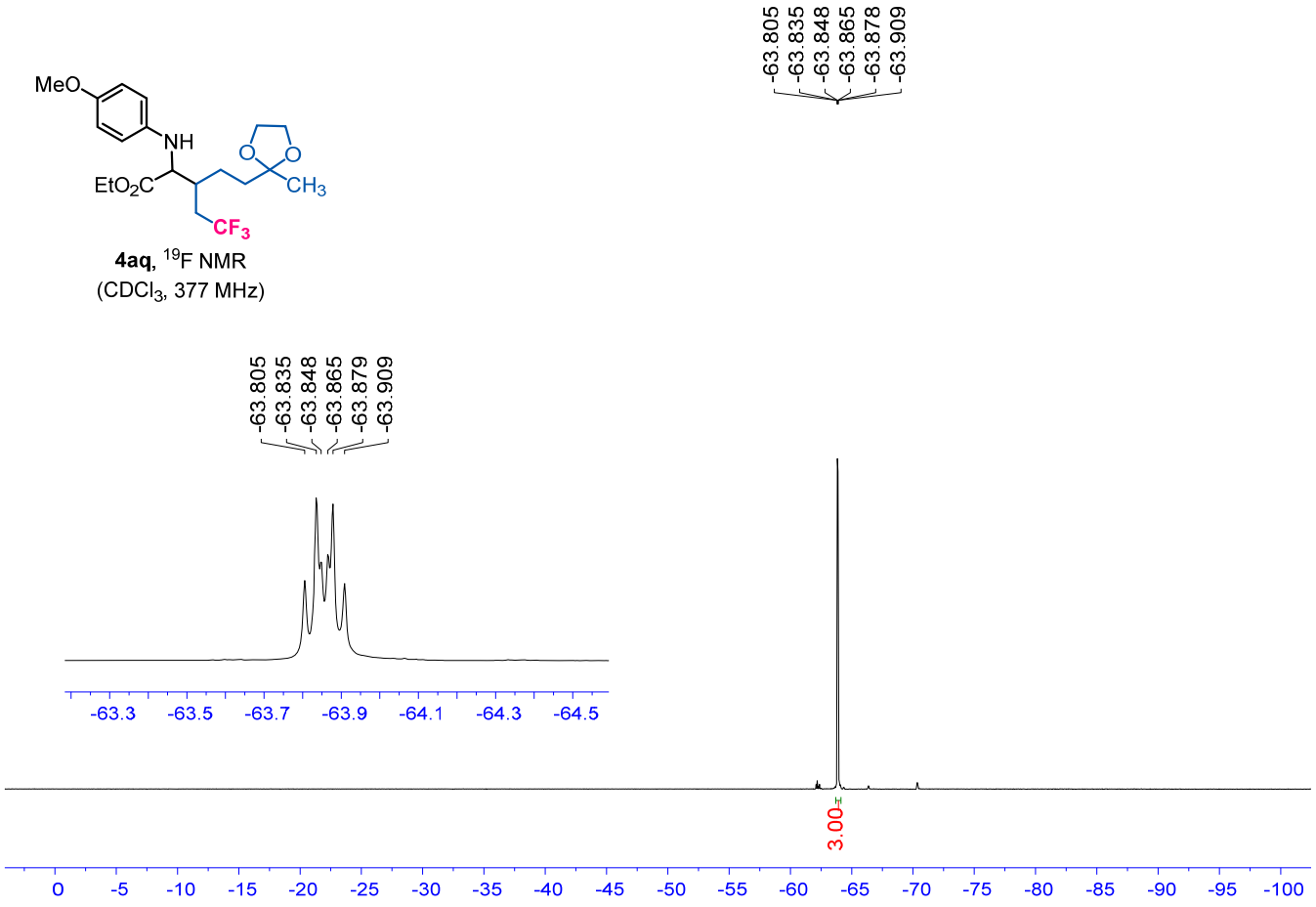
4ap, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



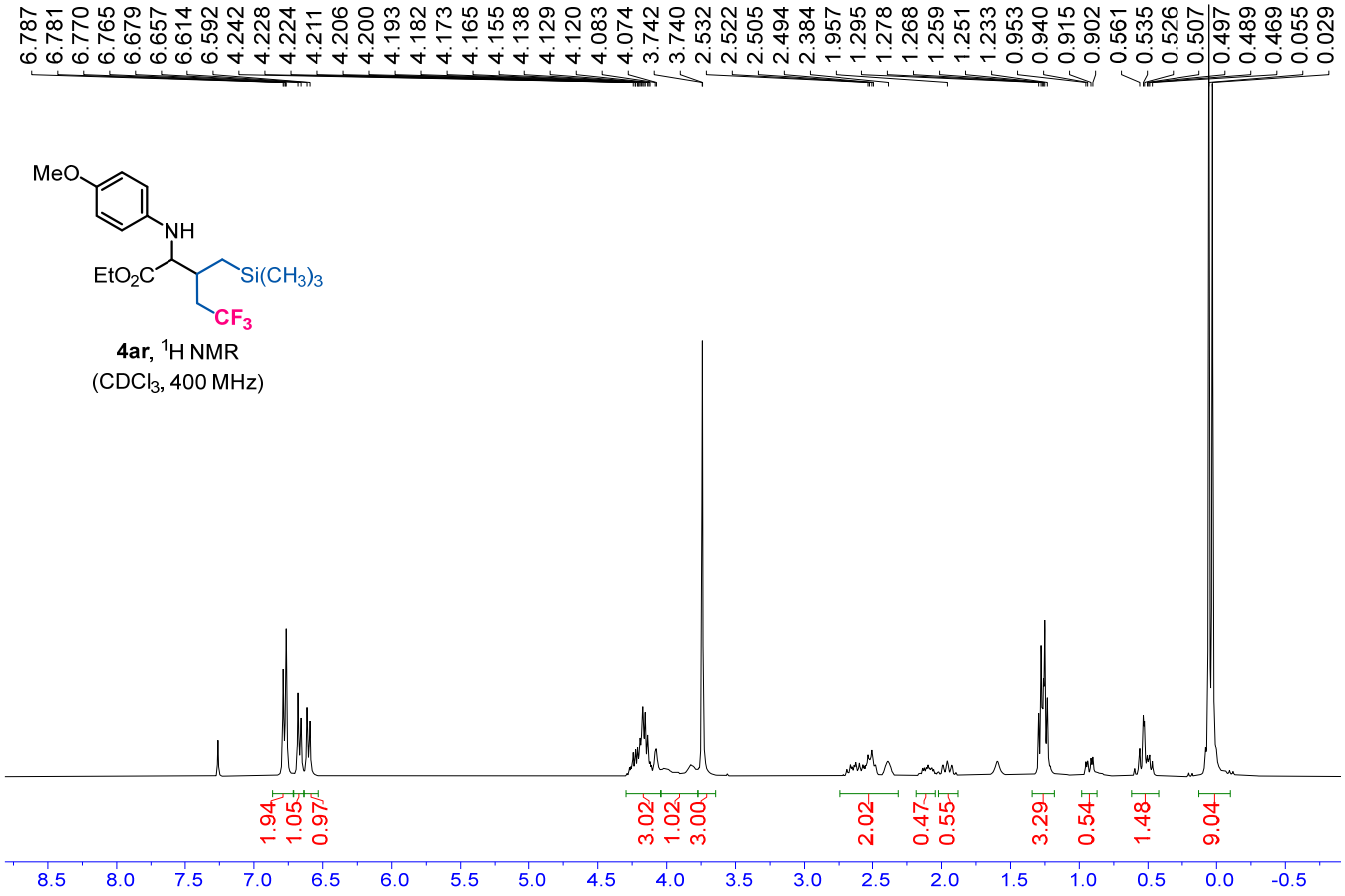
4ap, ^{19}F NMR
($CDCl_3$, 376 MHz)

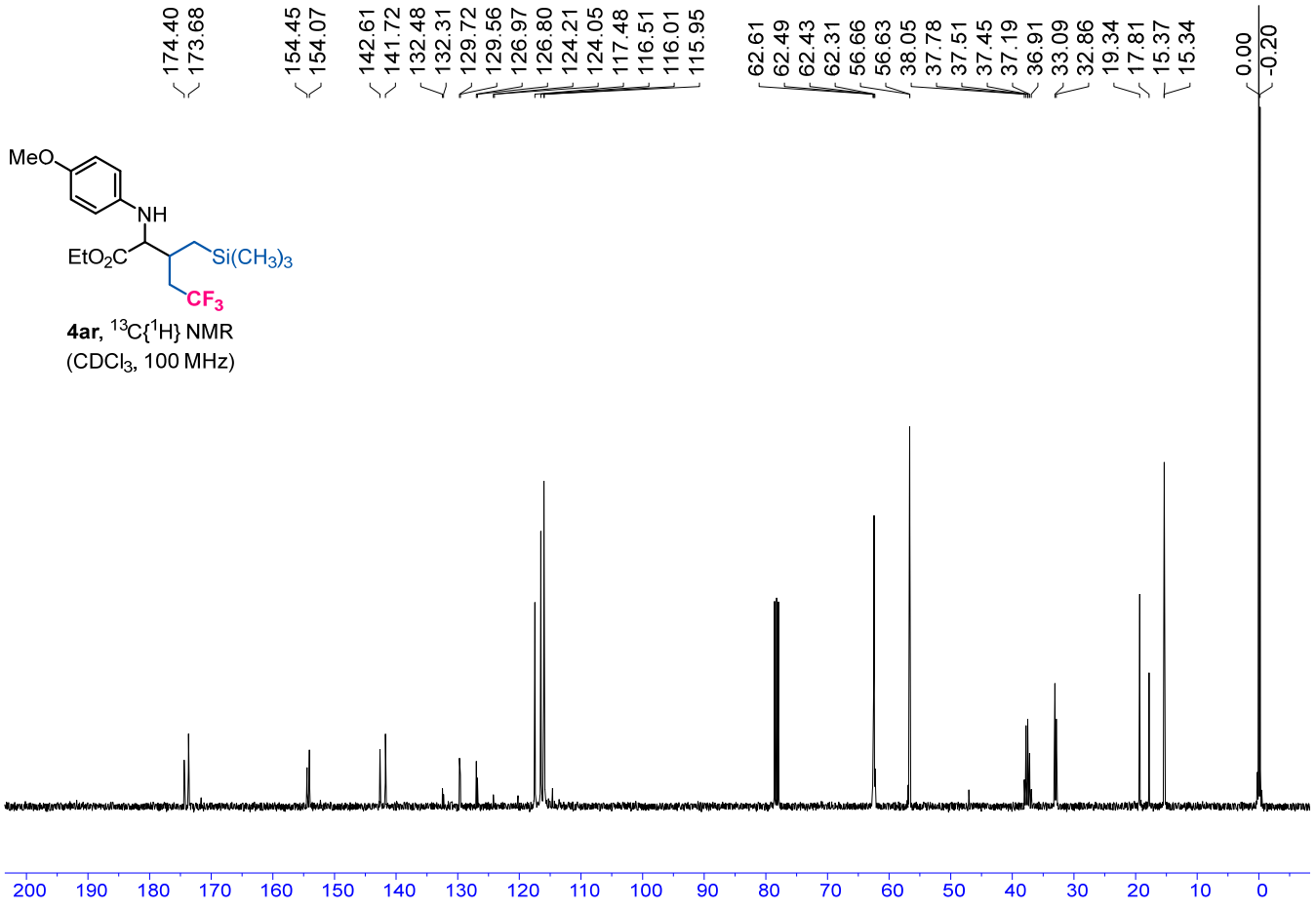

6.779
6.758
6.659
6.643
6.637
6.621
4.214
4.205
4.196
4.188
4.178
4.170
4.160
4.152
4.143
4.126
4.116
3.992
3.978
3.958
3.944
3.938
3.925
3.917
3.908
3.901
3.893
3.887
3.867
3.734
2.499
2.207
2.193
1.784
1.777
1.766
1.752
1.734
1.721
1.707
1.699
1.694
1.497
1.482
1.473
1.460
1.309
1.304
1.266
1.248
1.231
MeO
NH
EtO2C
O
O
CH3
CF3
4aq, 1H NMR
(CDCl3, 400 MHz)
1.95
2.00
2.53
5.46
3.06
1.03
2.06
2.50
1.79
2.95
3.13
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

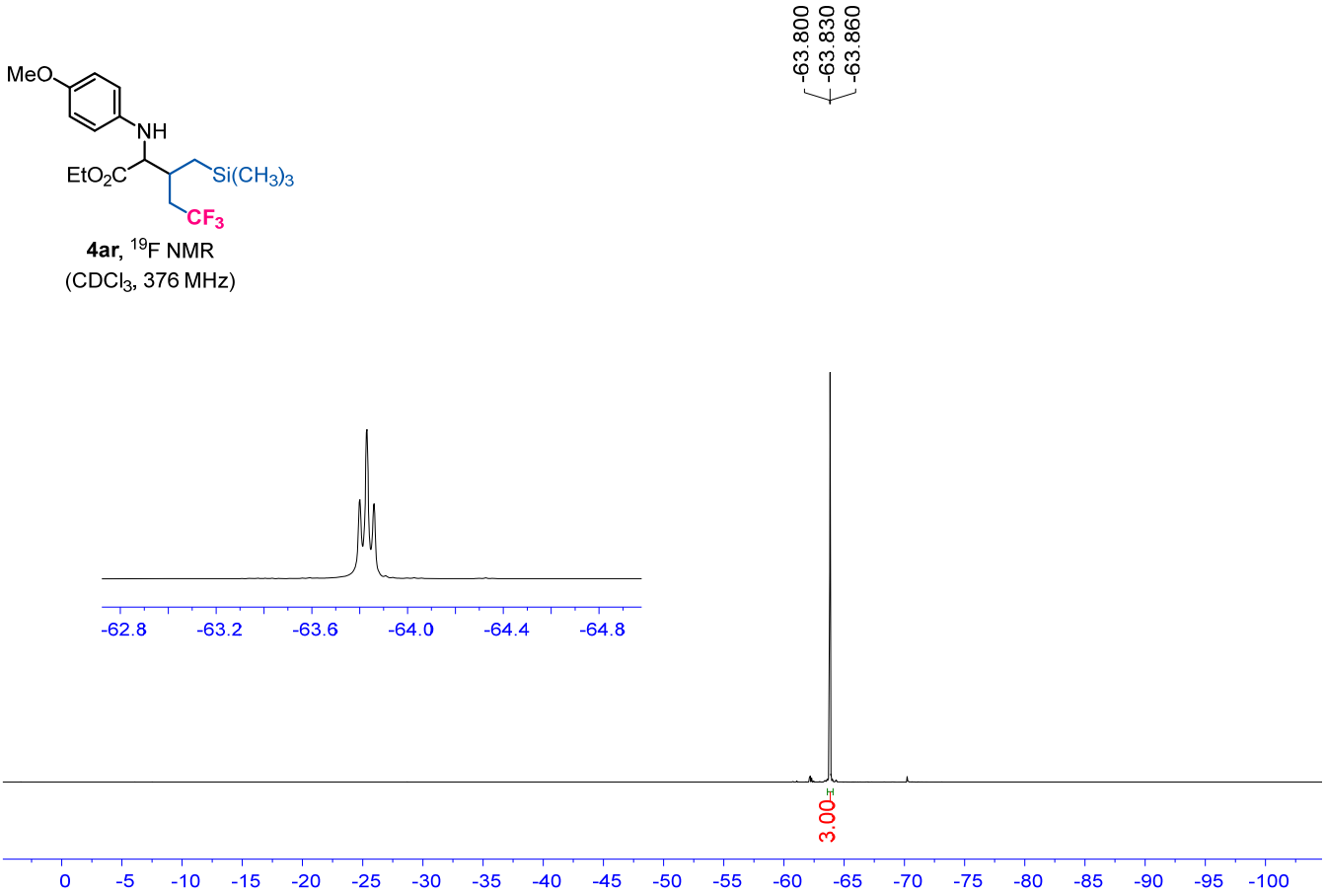

198.34
173.00
153.26
153.14
141.18
140.78
128.53
128.49
125.78
125.74
116.05
115.78
114.88
114.85
109.61
109.52
64.67
61.40
61.32
60.43
55.67
55.64
36.32
35.90
35.83
35.73
34.69
34.50
34.41
34.22
34.13
33.94
33.86
33.66
25.06
24.11
23.86
23.78
14.20
MeO
NH
EtO2C
O
O
CH3
CF3
4aq, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



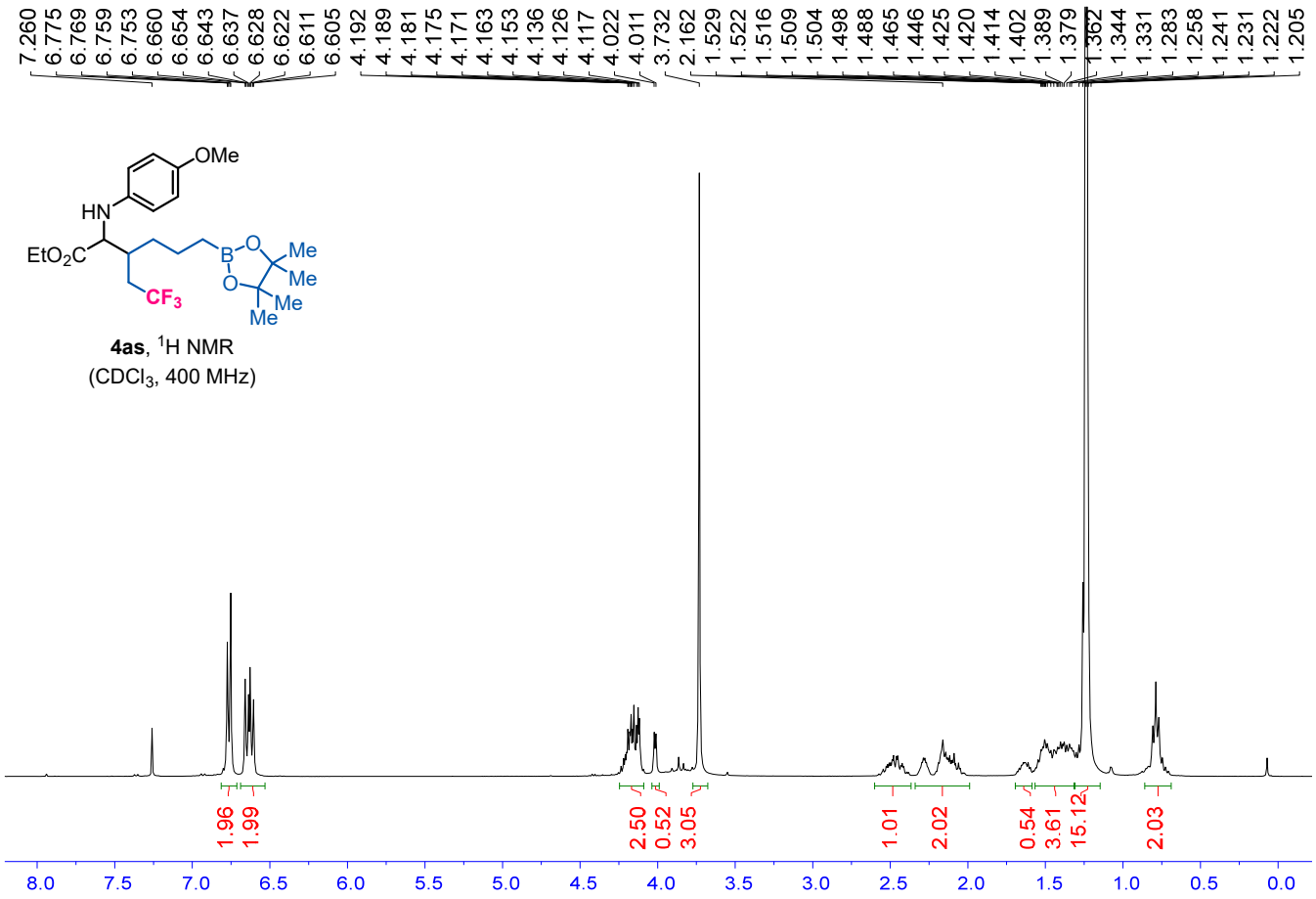
4aq, ^{19}F NMR
($CDCl_3$, 377 MHz)


6.787
6.781
6.770
6.765
6.679
6.657
6.614
6.592
4.242
4.228
4.224
4.211
4.206
4.200
4.193
4.182
4.173
4.165
4.155
4.138
4.129
4.120
4.083
4.074
3.742
3.740
2.532
2.522
2.505
2.494
2.384
1.957
1.295
1.278
1.268
1.259
1.251
1.233
0.953
0.940
0.915
0.902
0.561
0.535
0.526
0.507
0.497
0.489
0.469
0.055
0.029
MeO
NH
EtO2C
Si(CH3)3
CF3
4ar, 1H NMR
(CDCl3, 400 MHz)
1.94
1.05
0.97
3.02
1.02
3.00
2.02
0.47
0.55
3.29
0.54
1.48
9.04
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

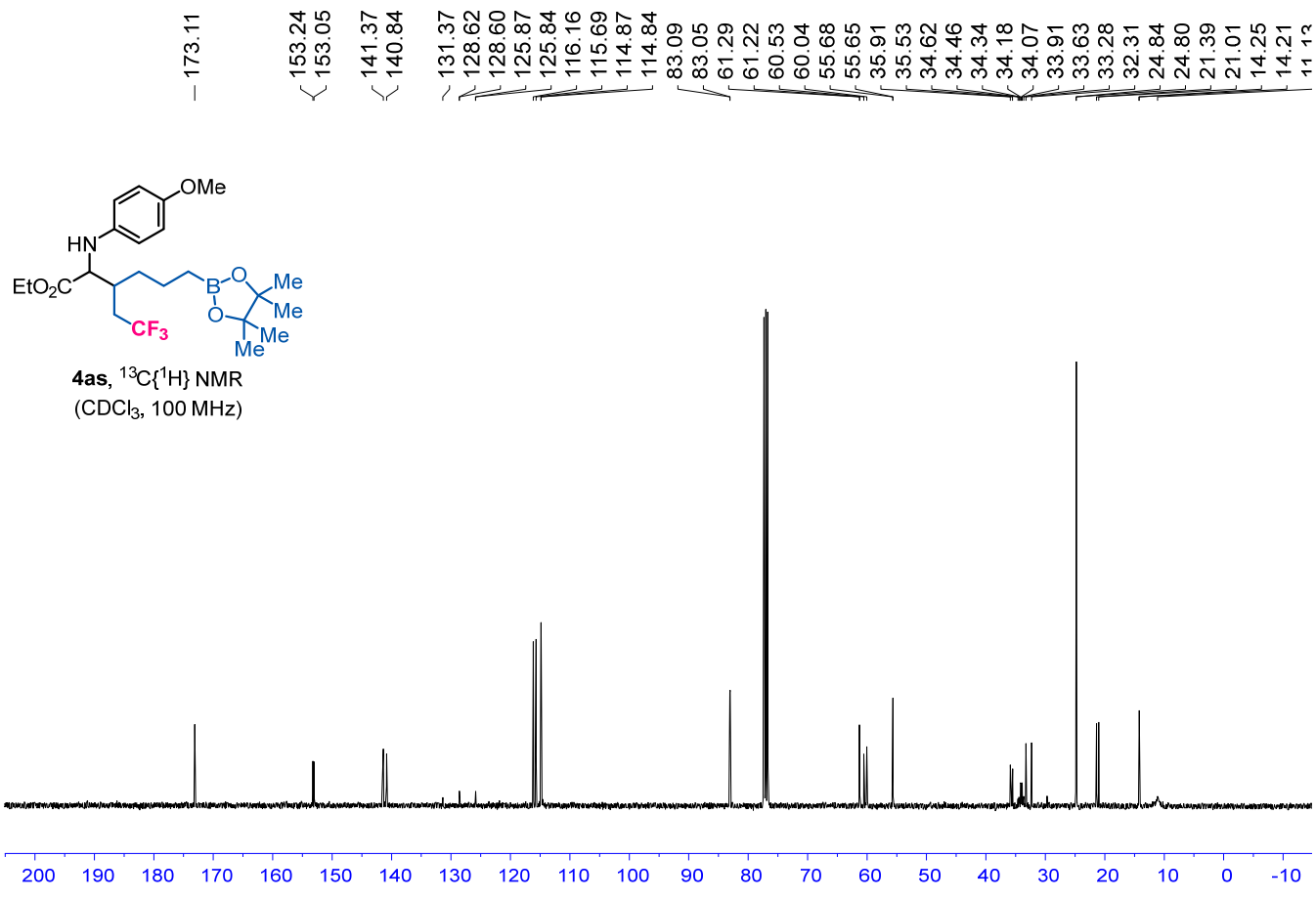

174.40
173.68
154.45
154.07
142.61
141.72
132.48
132.31
129.72
129.56
126.97
126.80
124.21
124.05
117.48
116.51
116.01
115.95
62.61
62.49
62.43
62.31
56.66
56.63
38.05
37.78
37.51
37.45
37.19
36.91
33.09
32.86
19.34
17.81
15.37
15.34
0.00
-0.20
MeO
NH
EtO2C
Si(CH3)3
CF3
4ar, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



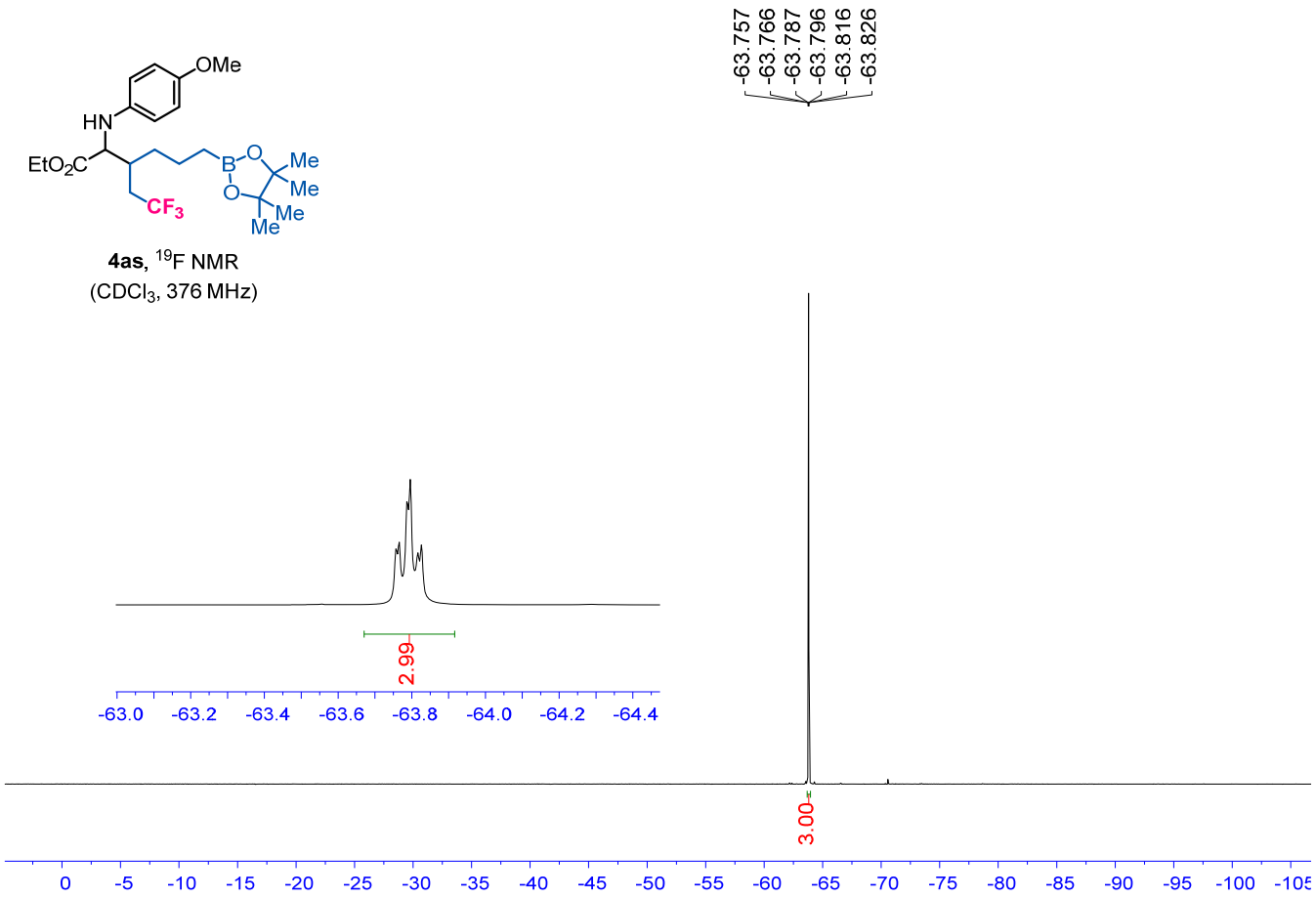
4ar, ^{19}F NMR
($CDCl_3$, 376 MHz)



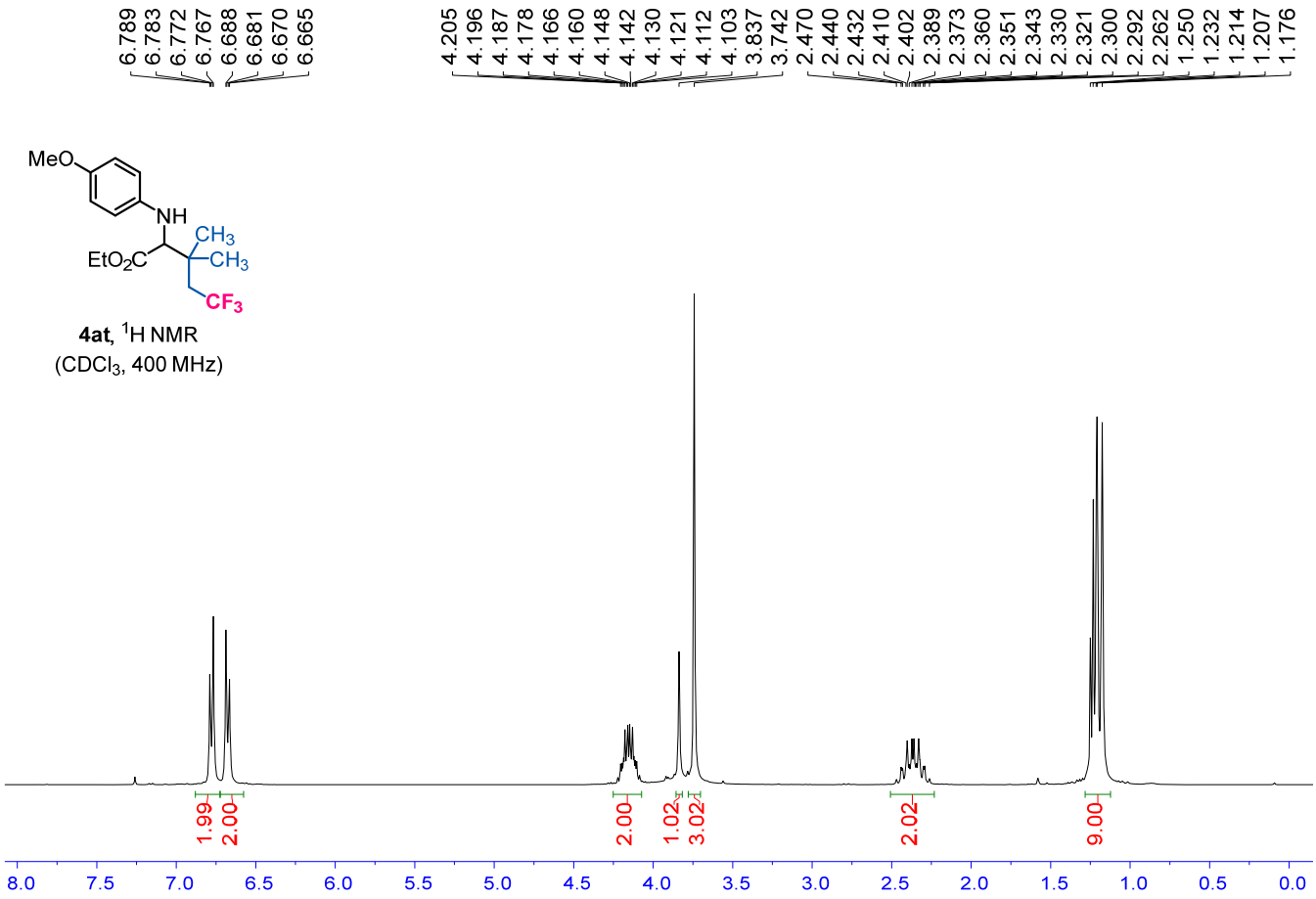
4as, ^{1}H NMR
($CDCl_3$, 400 MHz)

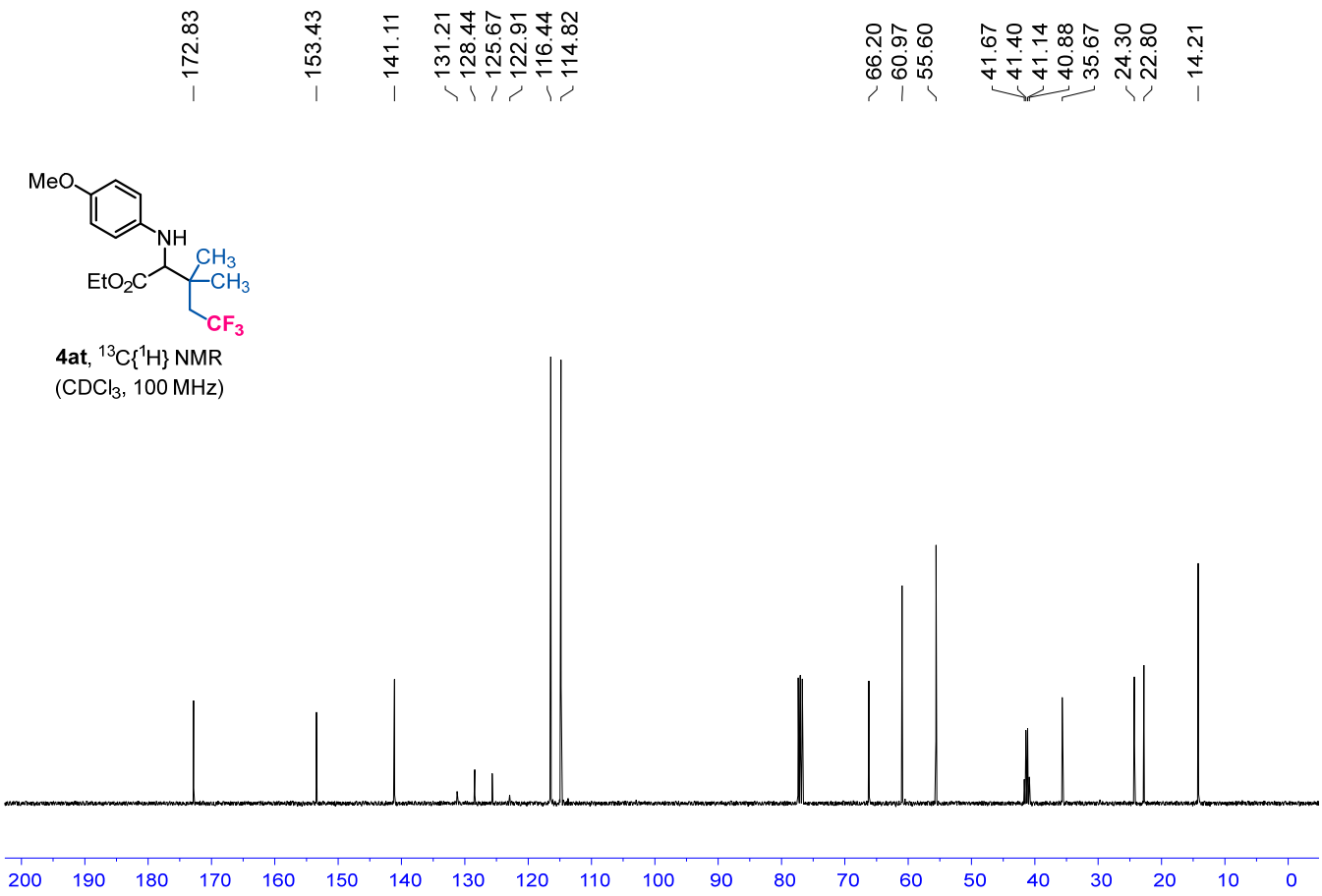


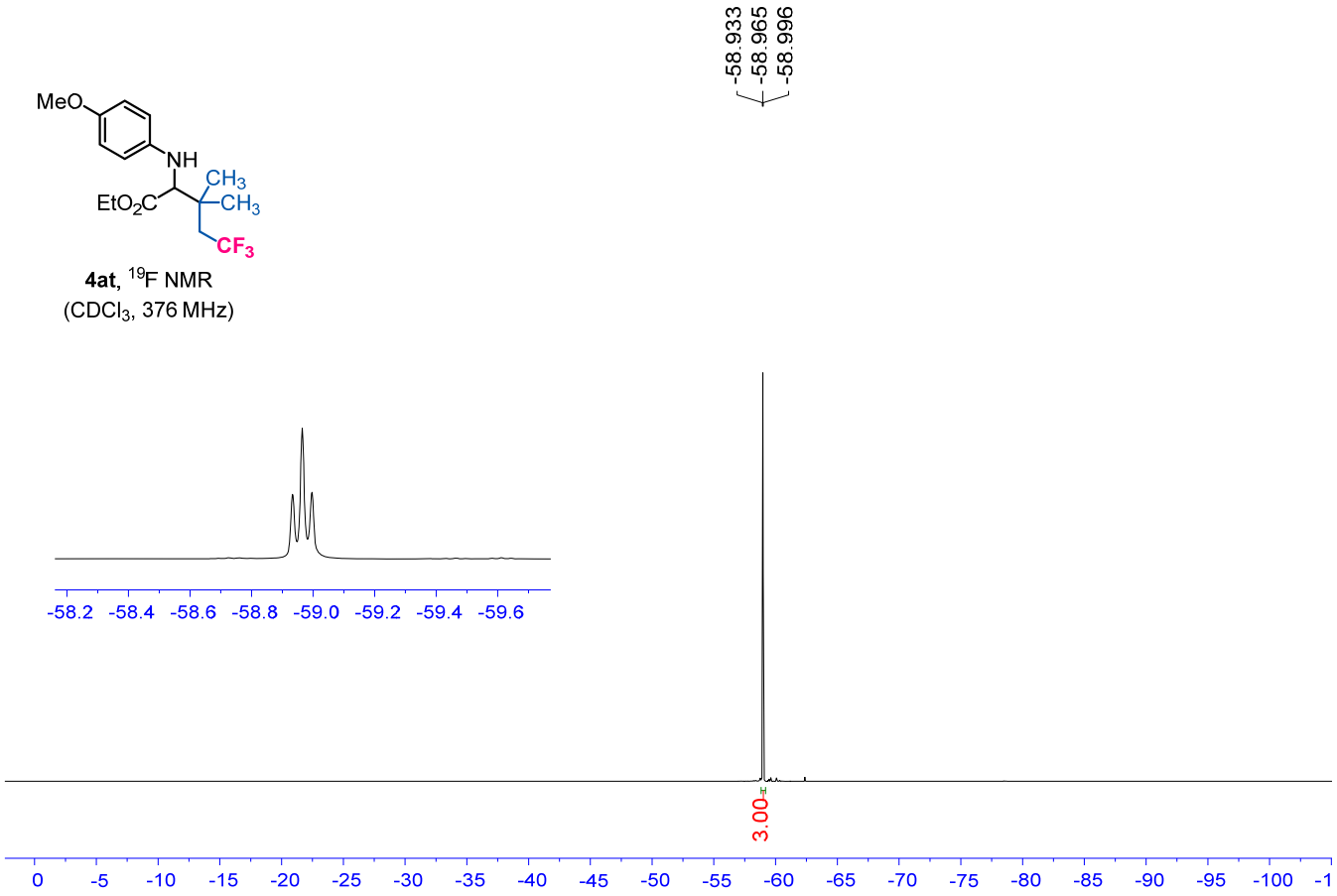
4as, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



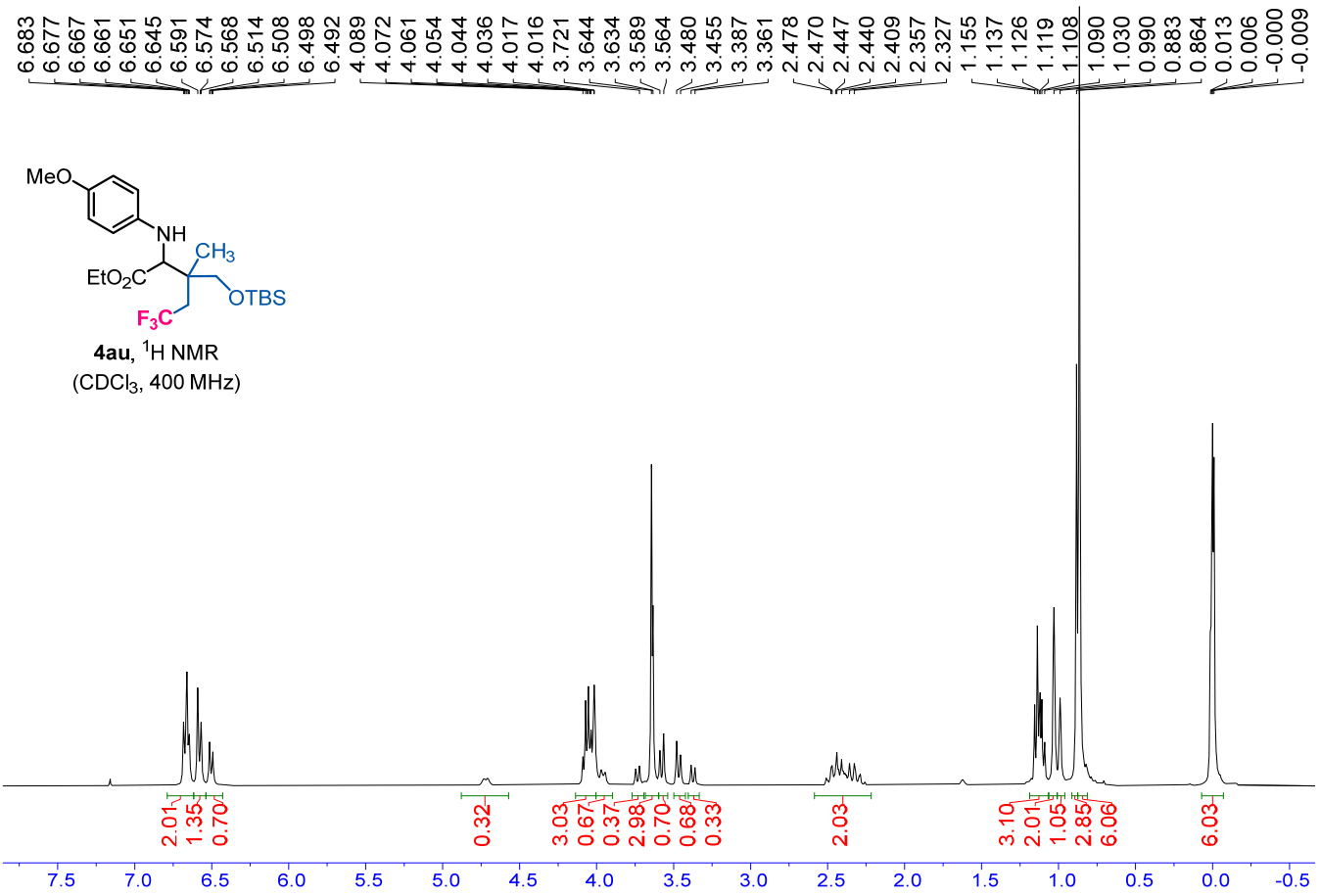
4as, ^{19}F NMR
($CDCl_3$, 376 MHz)


6.789
6.783
6.772
6.767
6.688
6.681
6.670
6.665
4.205
4.196
4.187
4.178
4.166
4.160
4.148
4.142
4.130
4.121
4.112
4.103
3.837
3.742
2.470
2.440
2.432
2.410
2.402
2.389
2.373
2.360
2.351
2.343
2.330
2.321
2.300
2.292
2.262
1.250
1.232
1.214
1.207
1.176
MeO
NH
CH3
EtO2C
CH3
CF3
4at, 1H NMR
(CDCl3, 400 MHz)
1.99
2.00
2.00
1.02
3.02
2.02
9.00
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

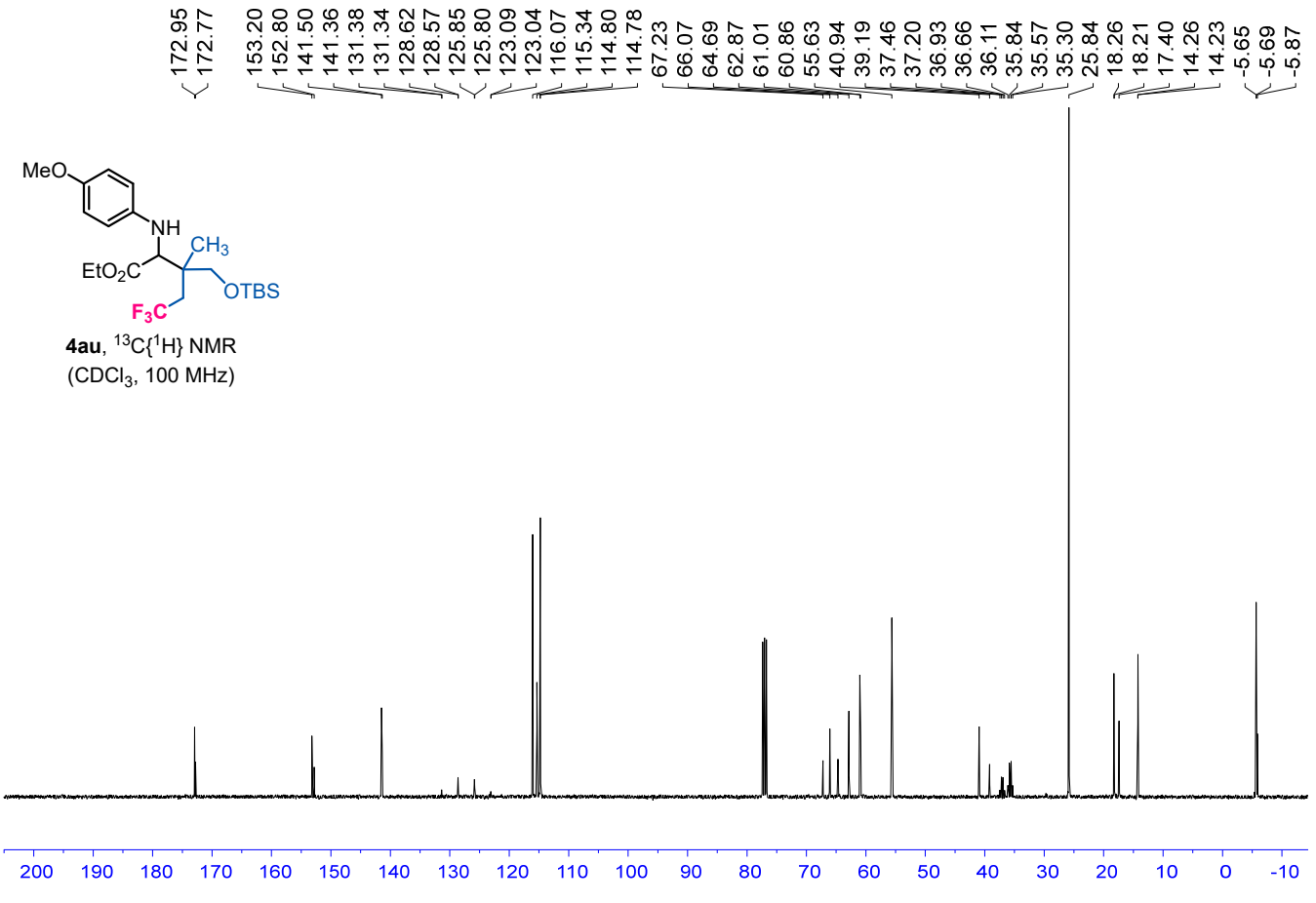

172.83
153.43
141.11
131.21
128.44
125.67
122.91
116.44
114.82
66.20
60.97
55.60
41.67
41.40
41.14
40.88
35.67
24.30
22.80
14.21
MeO
NH
CH3
EtO2C
CH3
CF3
4at, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



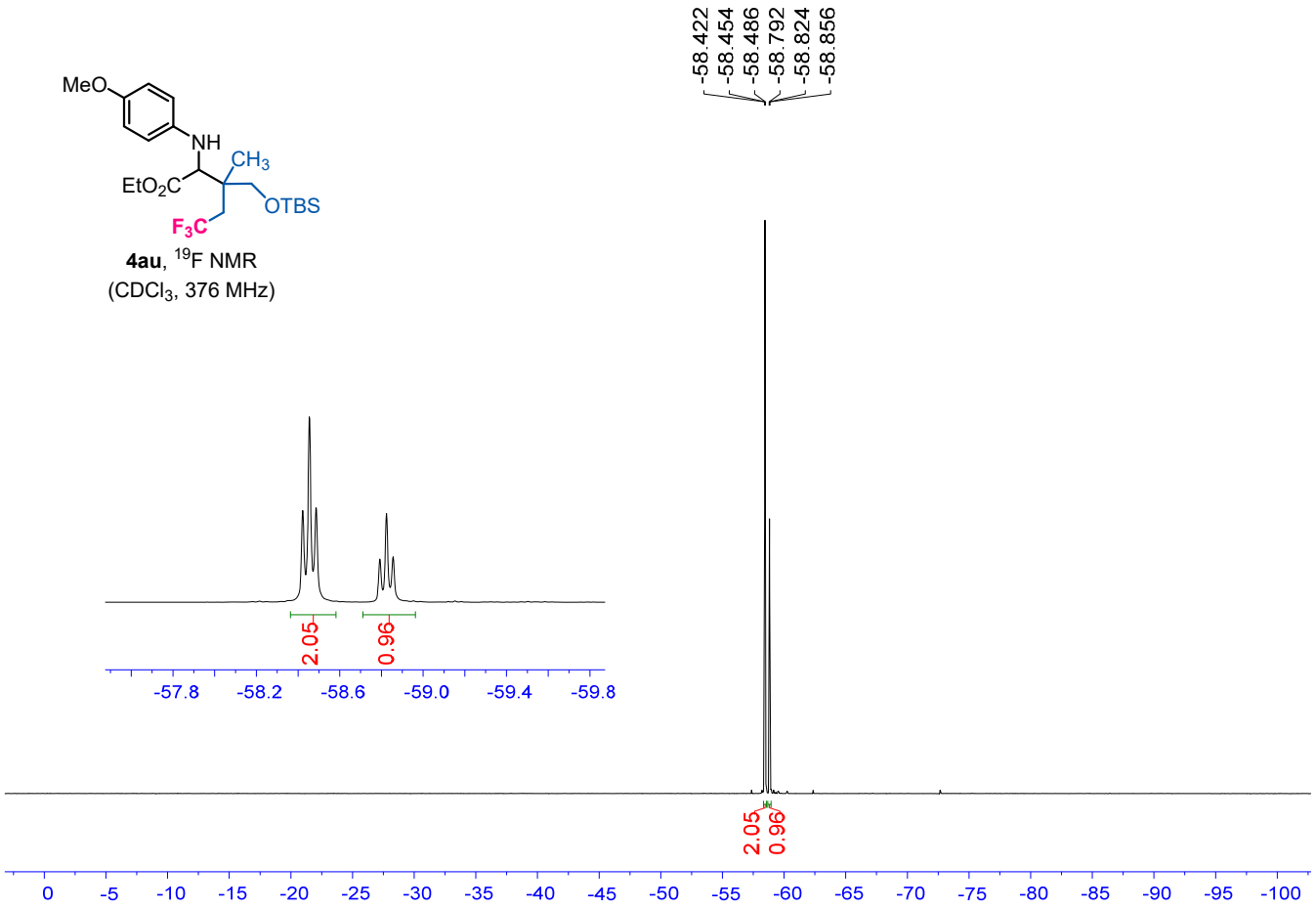
4at, ^{19}F NMR
($CDCl_3$, 376 MHz)



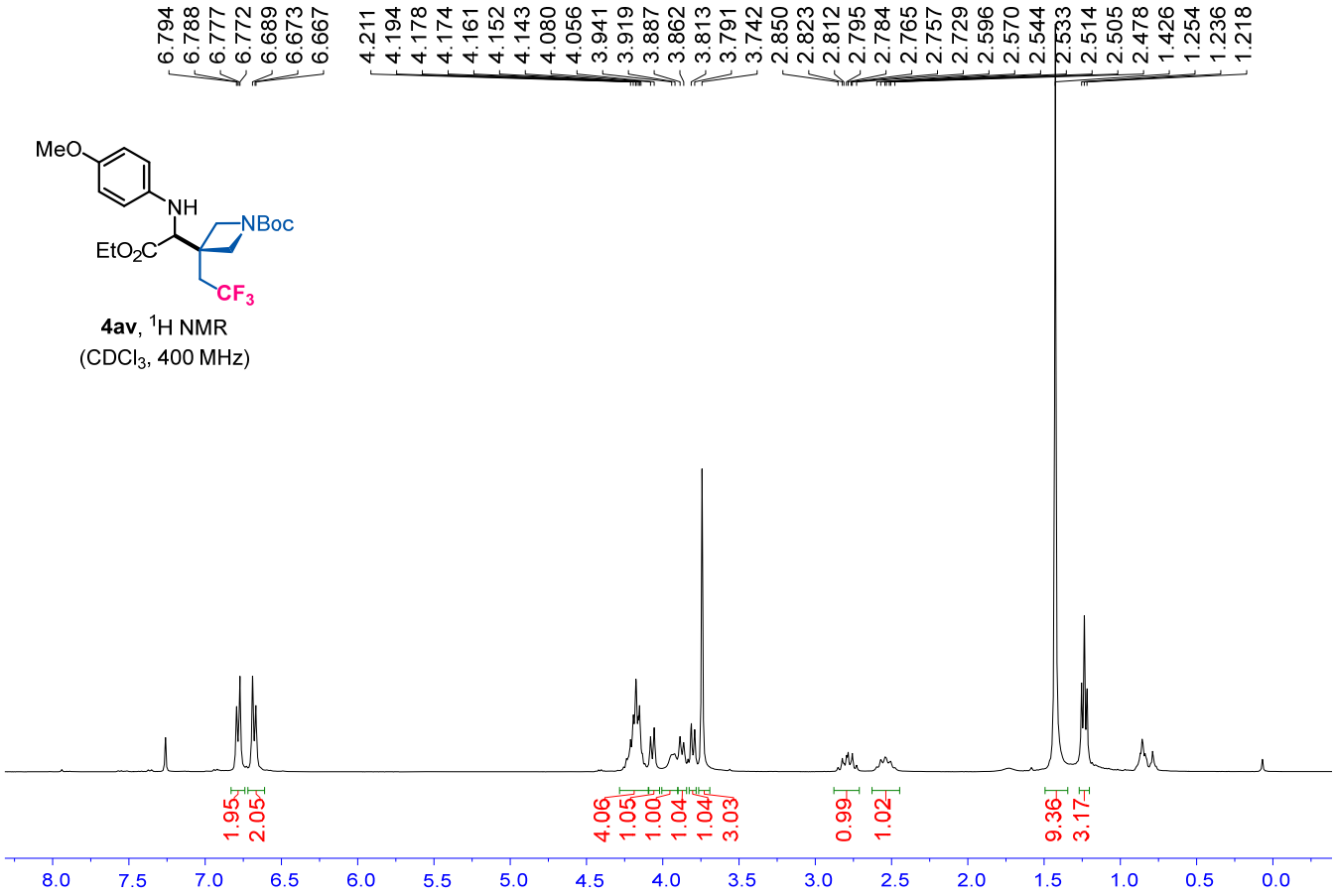
4au, ^{1}H NMR
($CDCl_3$, 400 MHz)

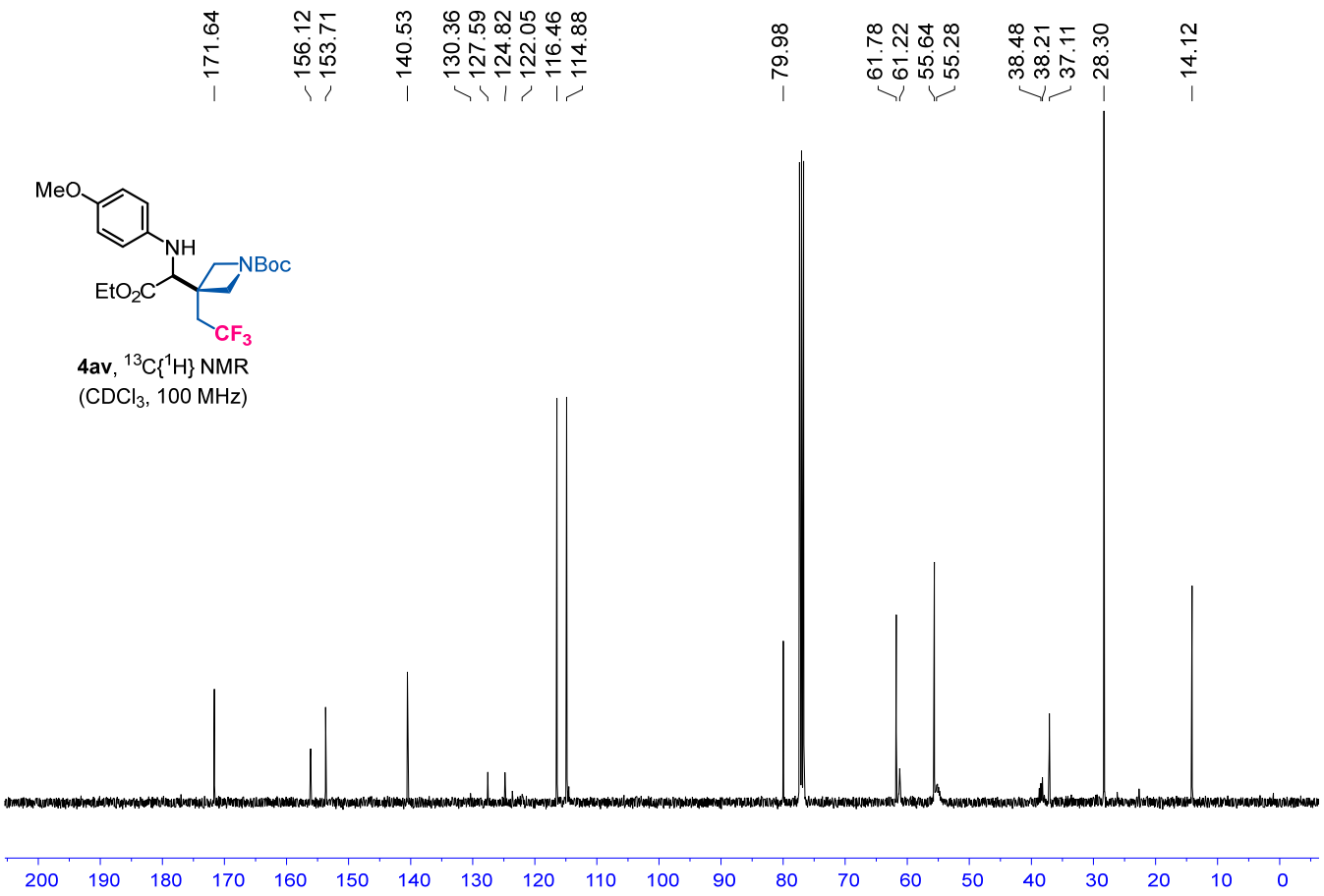


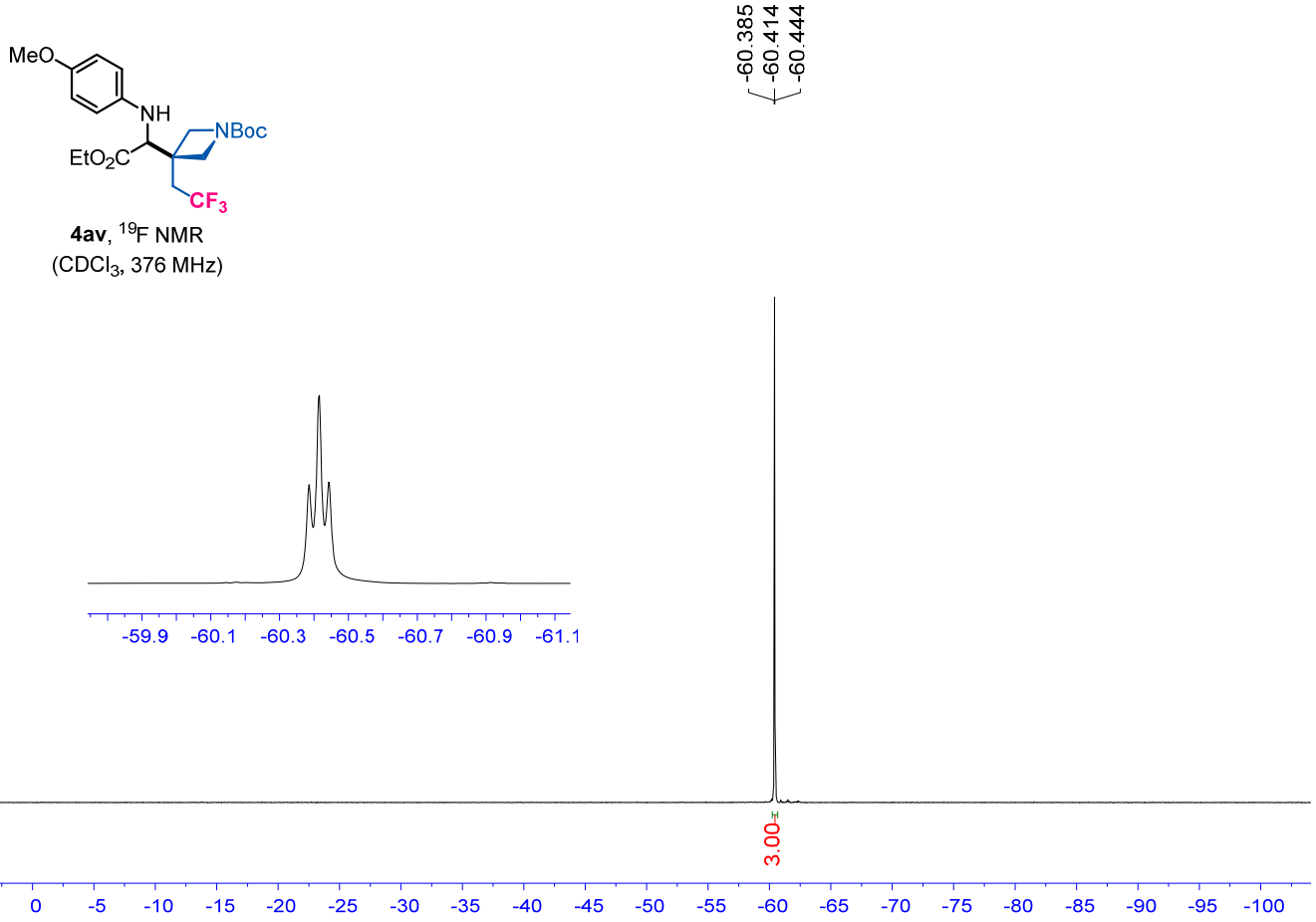
4au, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



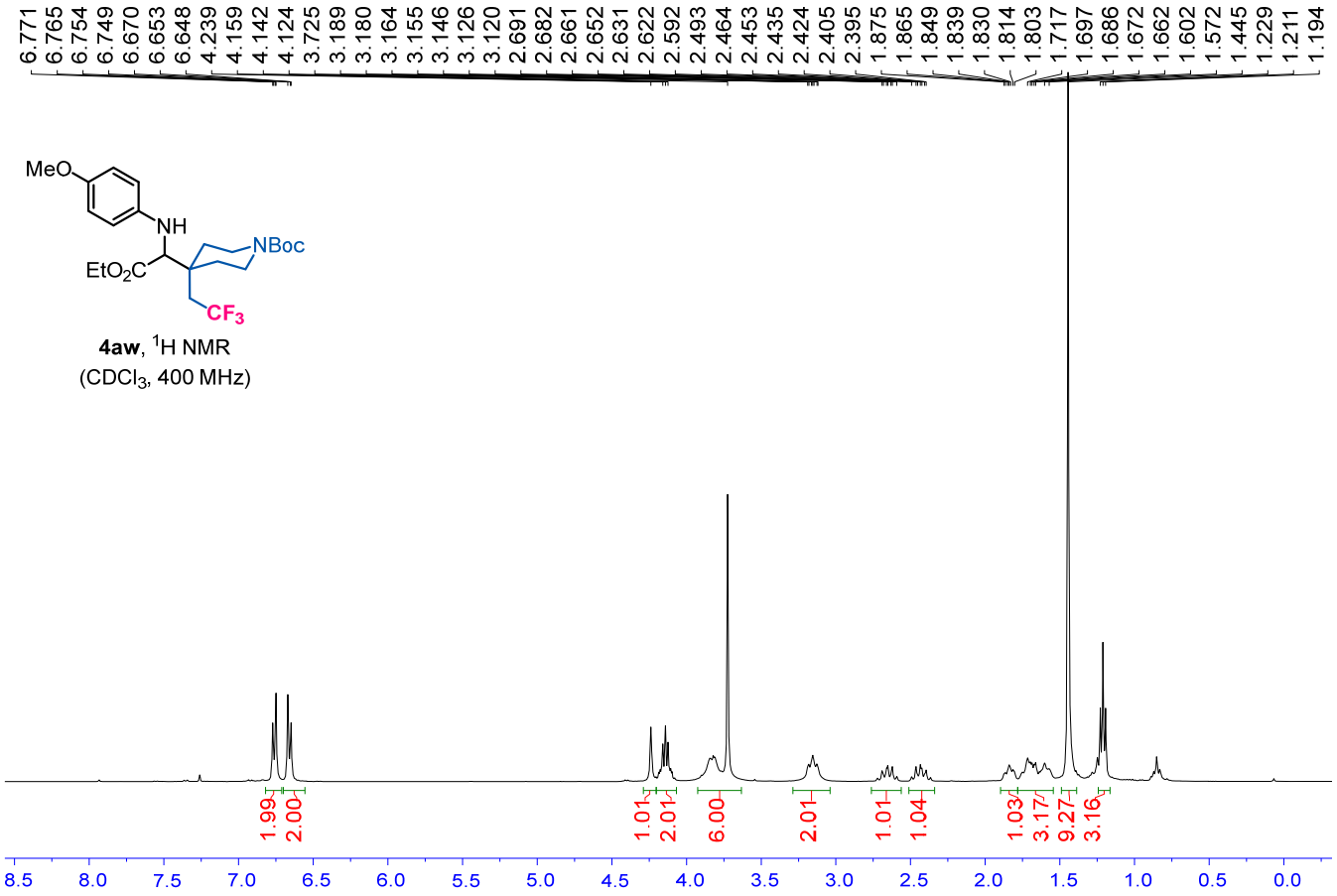
4au, ^{19}F NMR
($CDCl_3$, 376 MHz)


6.794
6.788
6.777
6.772
6.689
6.673
6.667
4.211
4.194
4.178
4.174
4.161
4.152
4.143
4.080
4.056
3.941
3.919
3.887
3.862
3.813
3.791
3.742
2.850
2.823
2.812
2.795
2.784
2.765
2.757
2.729
2.596
2.570
2.544
2.533
2.514
2.505
2.478
1.426
1.254
1.236
1.218
MeO
NH
NBoc
EtO2C
CF3
4av, 1H NMR
(CDCl3, 400 MHz)
1.95
2.05
4.06
1.05
1.00
1.04
1.04
3.03
0.99
1.02
9.36
3.17
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

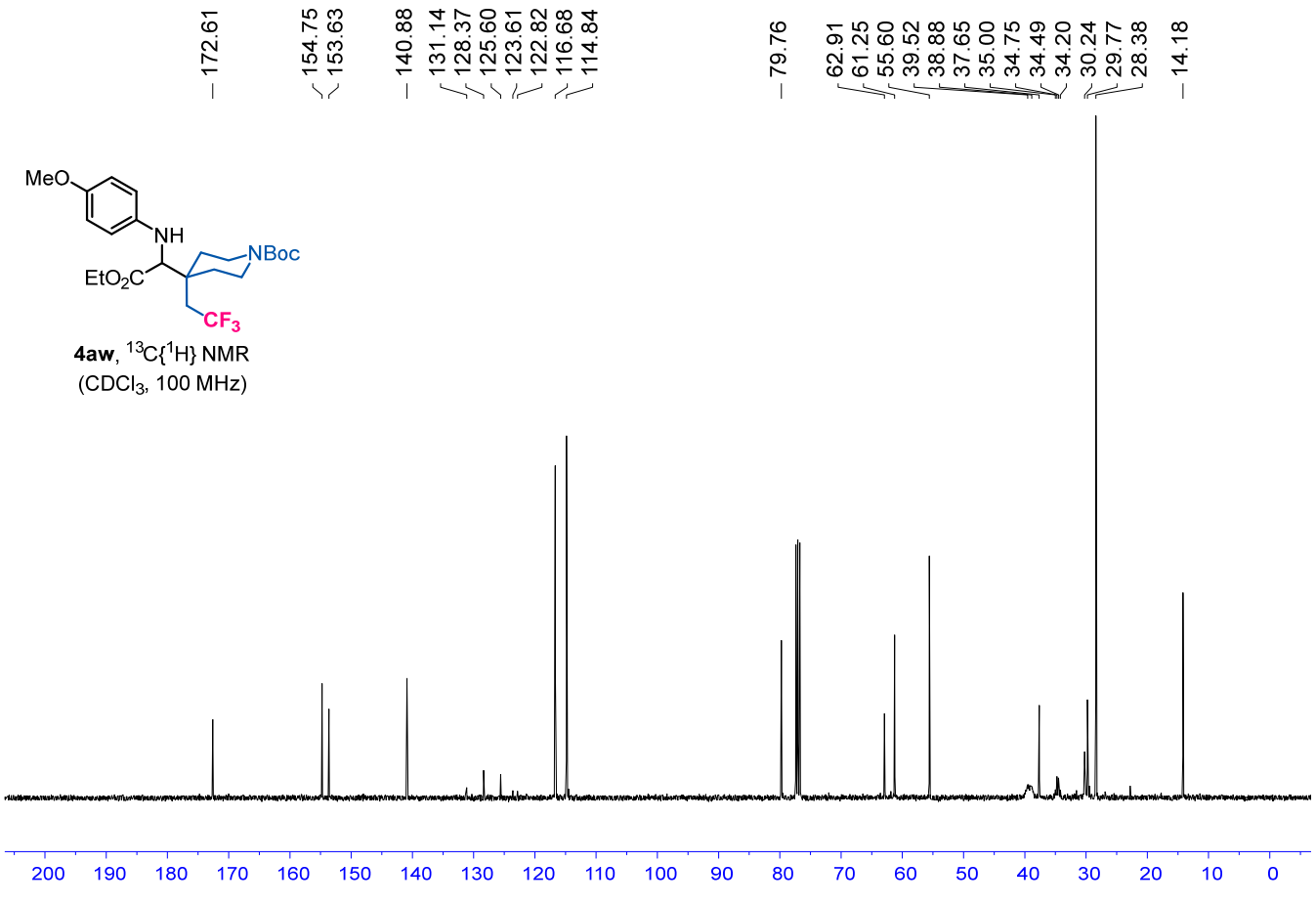

171.64
156.12
153.71
140.53
130.36
127.59
124.82
122.05
116.46
114.88
79.98
61.78
61.22
55.64
55.28
38.48
38.21
37.11
28.30
14.12
MeO
NH
NBoc
EtO2C
CF3
4av, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



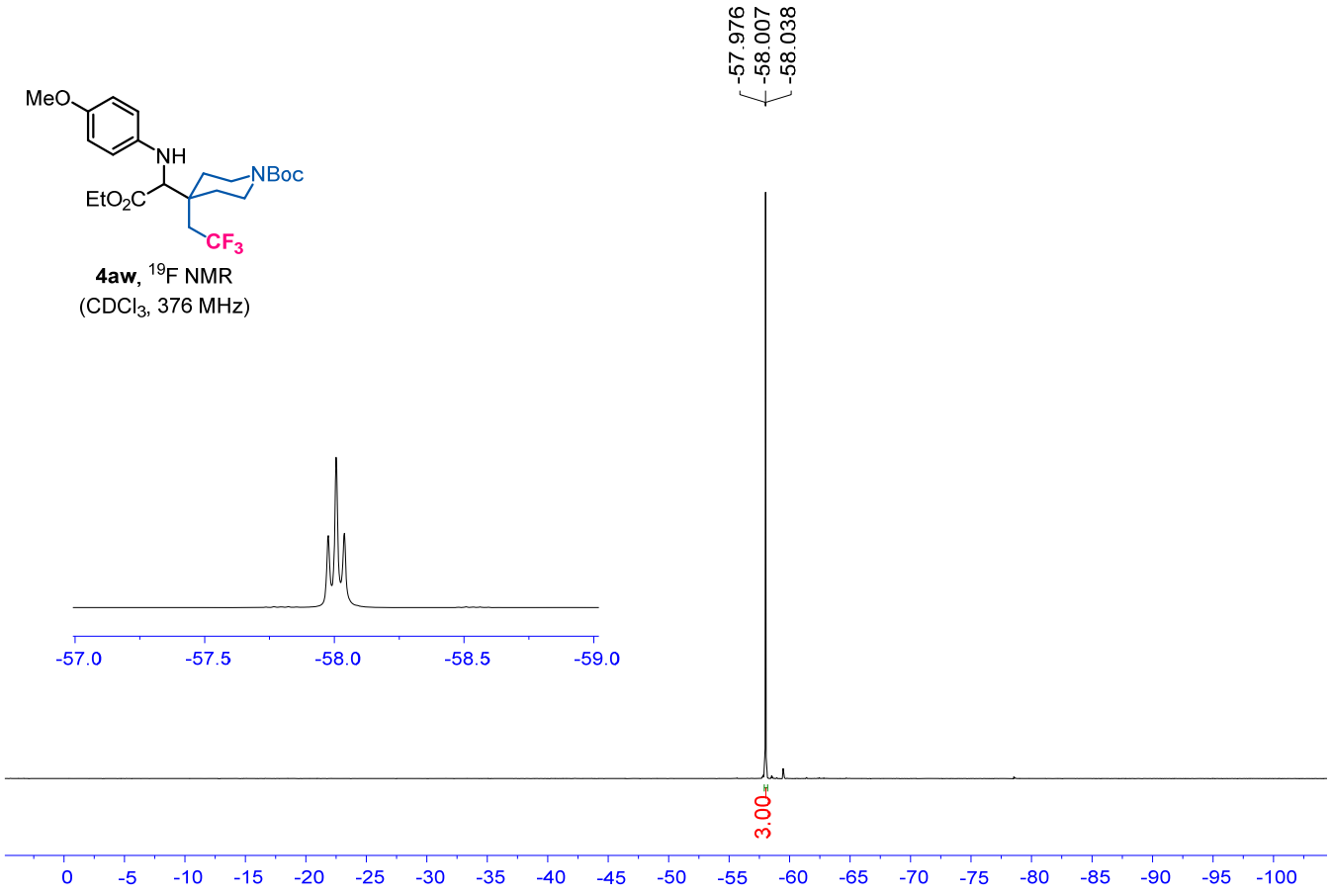
4av, ^{19}F NMR
($CDCl_3$, 376 MHz)

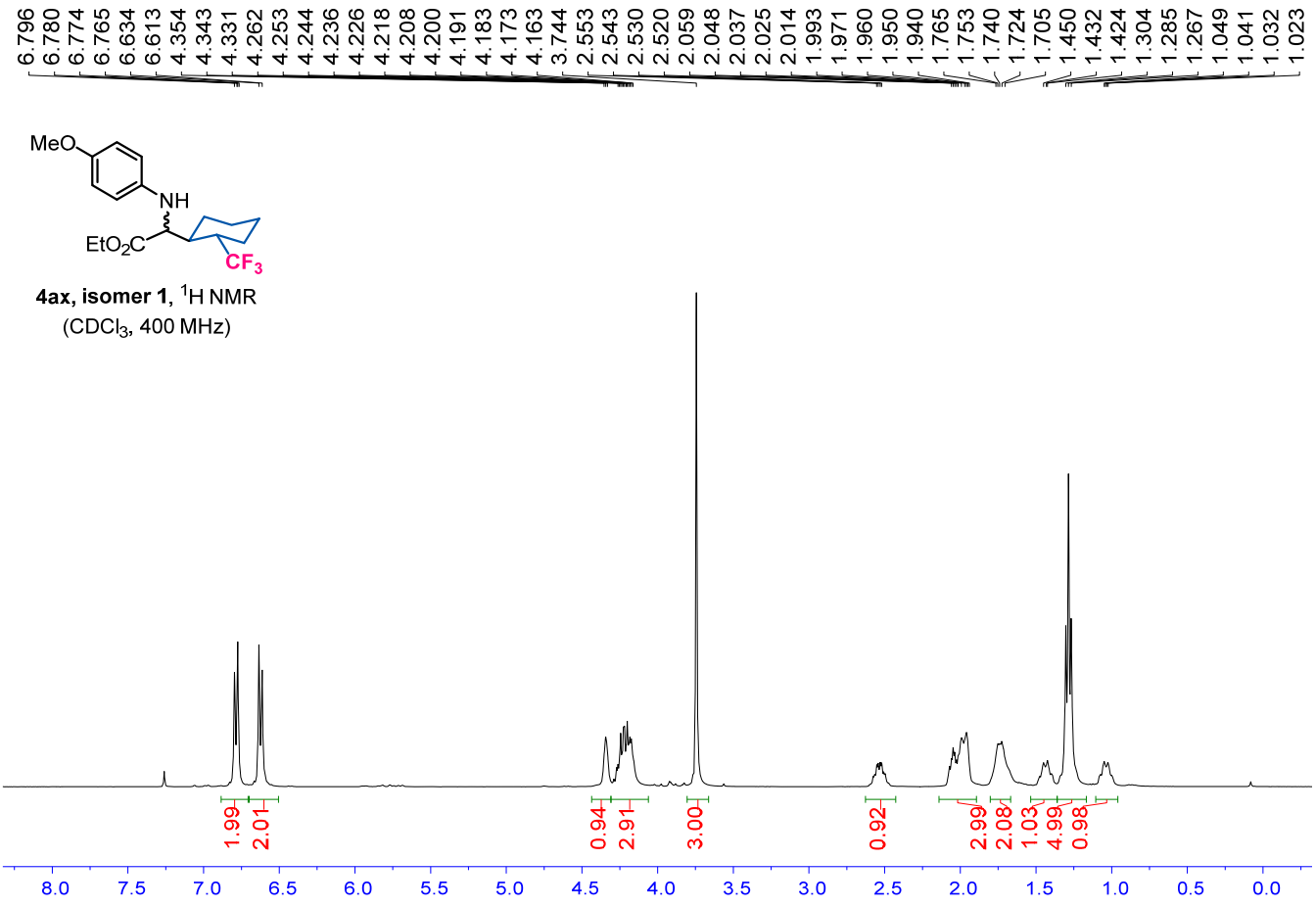


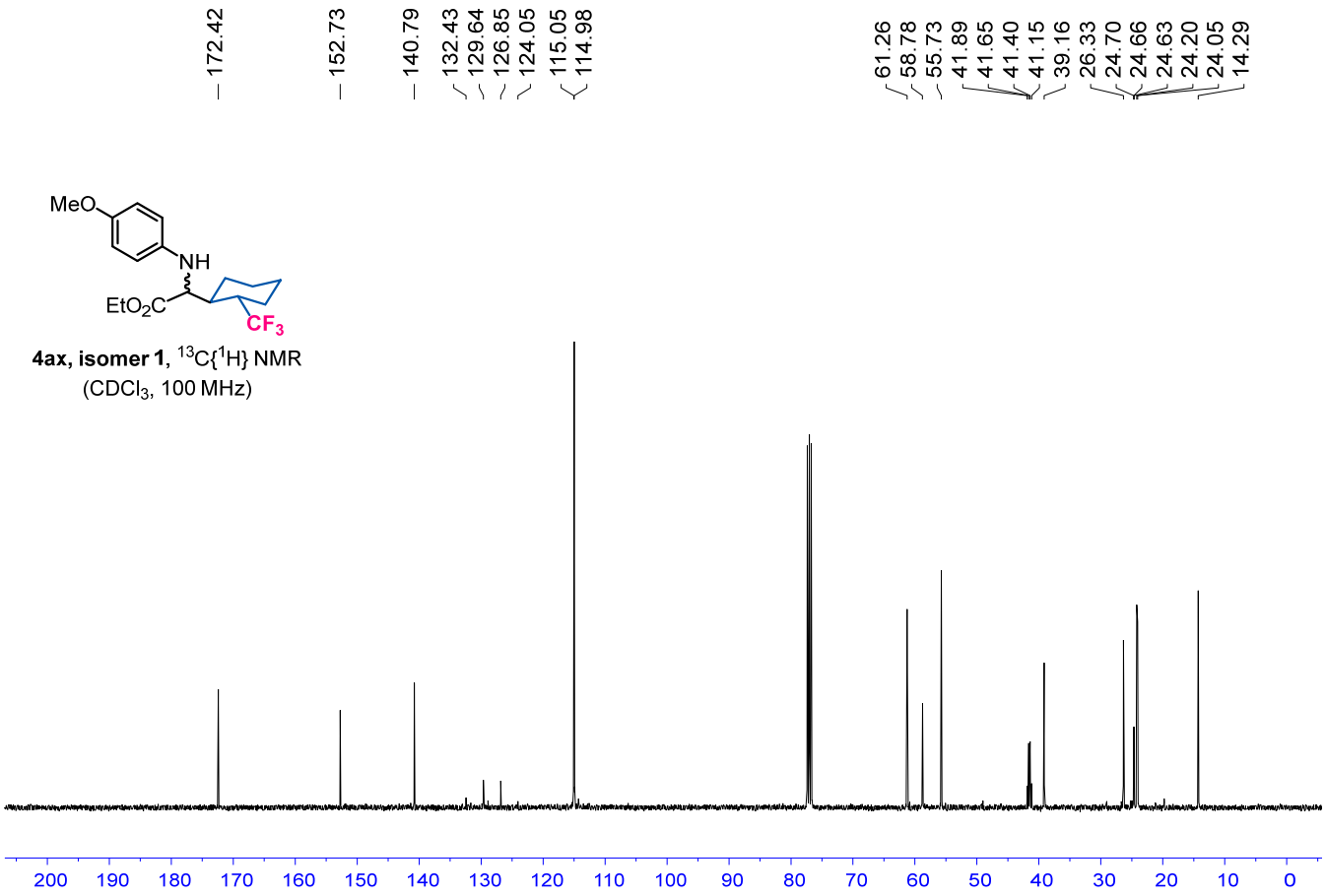
4aw, ^{1}H NMR
($CDCl_3$, 400 MHz)

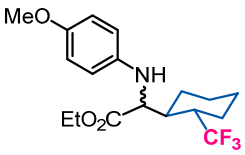


4aw, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)

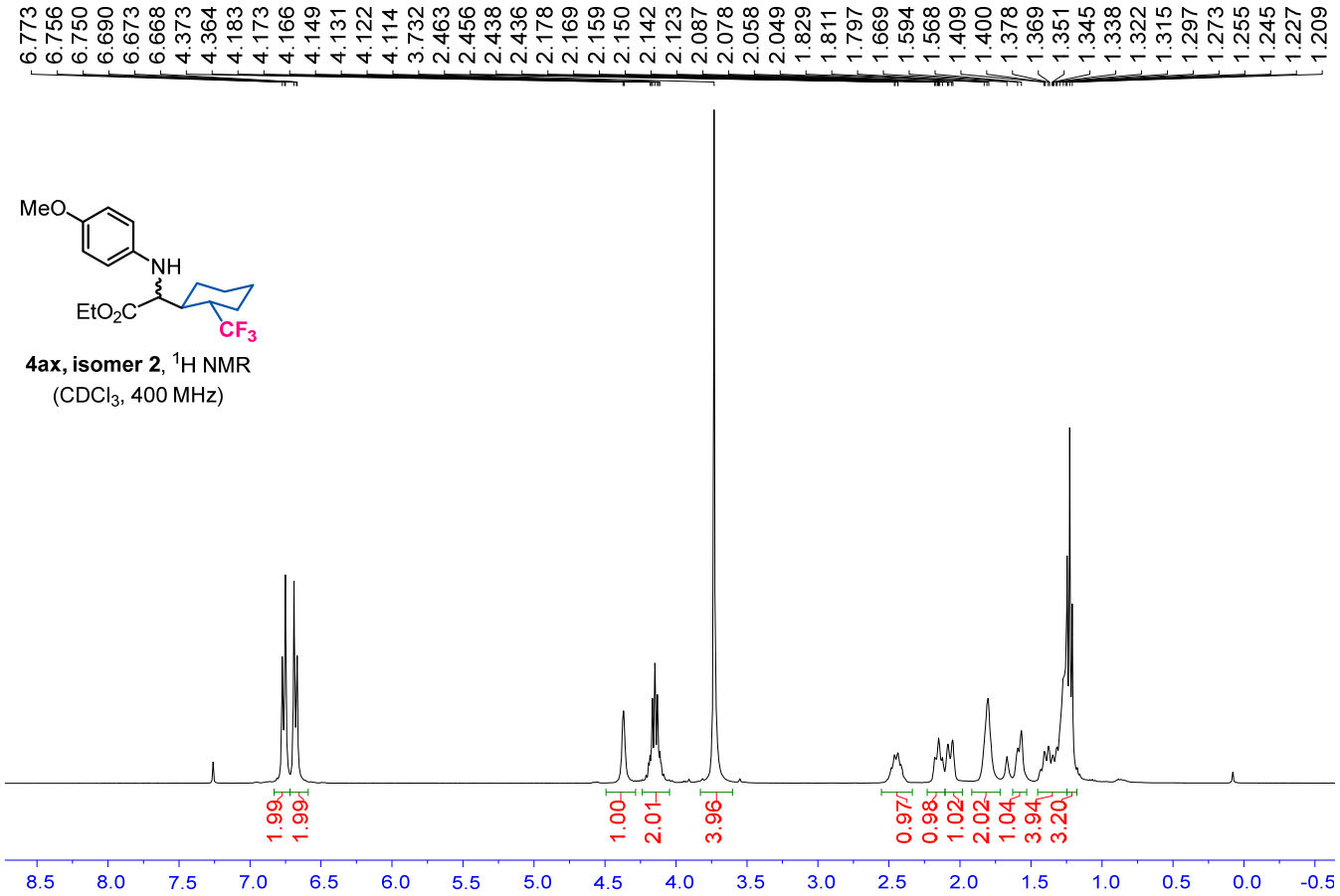

MeO
NH
NBoc
EtO2C
CF3
4aw, 19F NMR
(CDCl3, 376 MHz)
-57.976
-58.007
-58.038
3.00
-57.0
-57.5
-58.0
-58.5
-59.0
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100

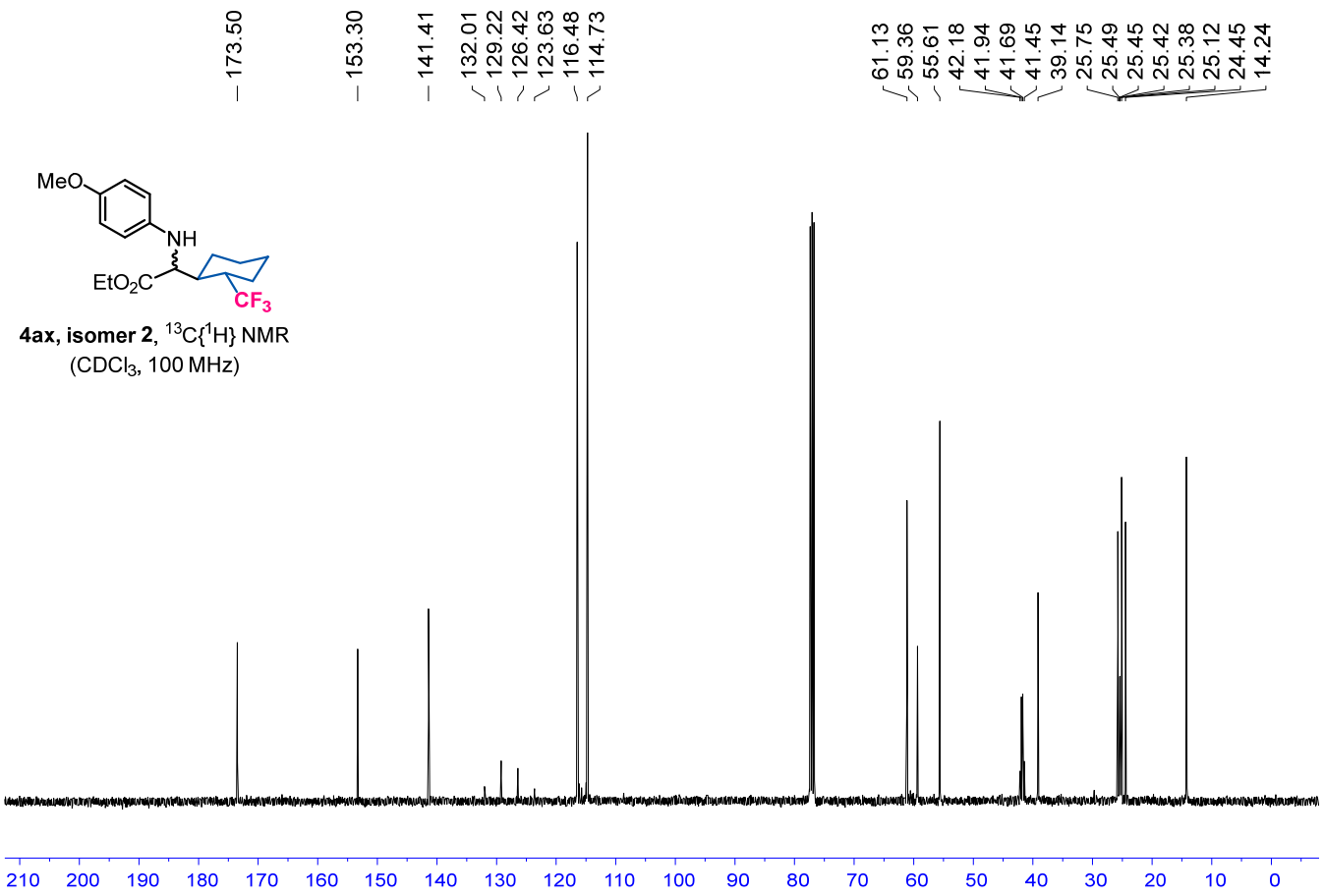

6.796
6.780
6.774
6.765
6.634
6.613
4.354
4.343
4.331
4.262
4.253
4.244
4.236
4.226
4.218
4.208
4.200
4.191
4.183
4.173
4.163
3.744
2.553
2.543
2.530
2.520
2.059
2.048
2.037
2.025
2.014
1.993
1.971
1.960
1.950
1.940
1.765
1.753
1.740
1.724
1.705
1.450
1.432
1.424
1.304
1.285
1.267
1.049
1.041
1.032
1.023
MeO
NH
EtO2C
CF3
4ax, isomer 1, 1H NMR
(CDCl3, 400 MHz)
1.99
2.01
0.94
2.91
3.00
0.92
2.99
2.08
1.03
4.99
0.98
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

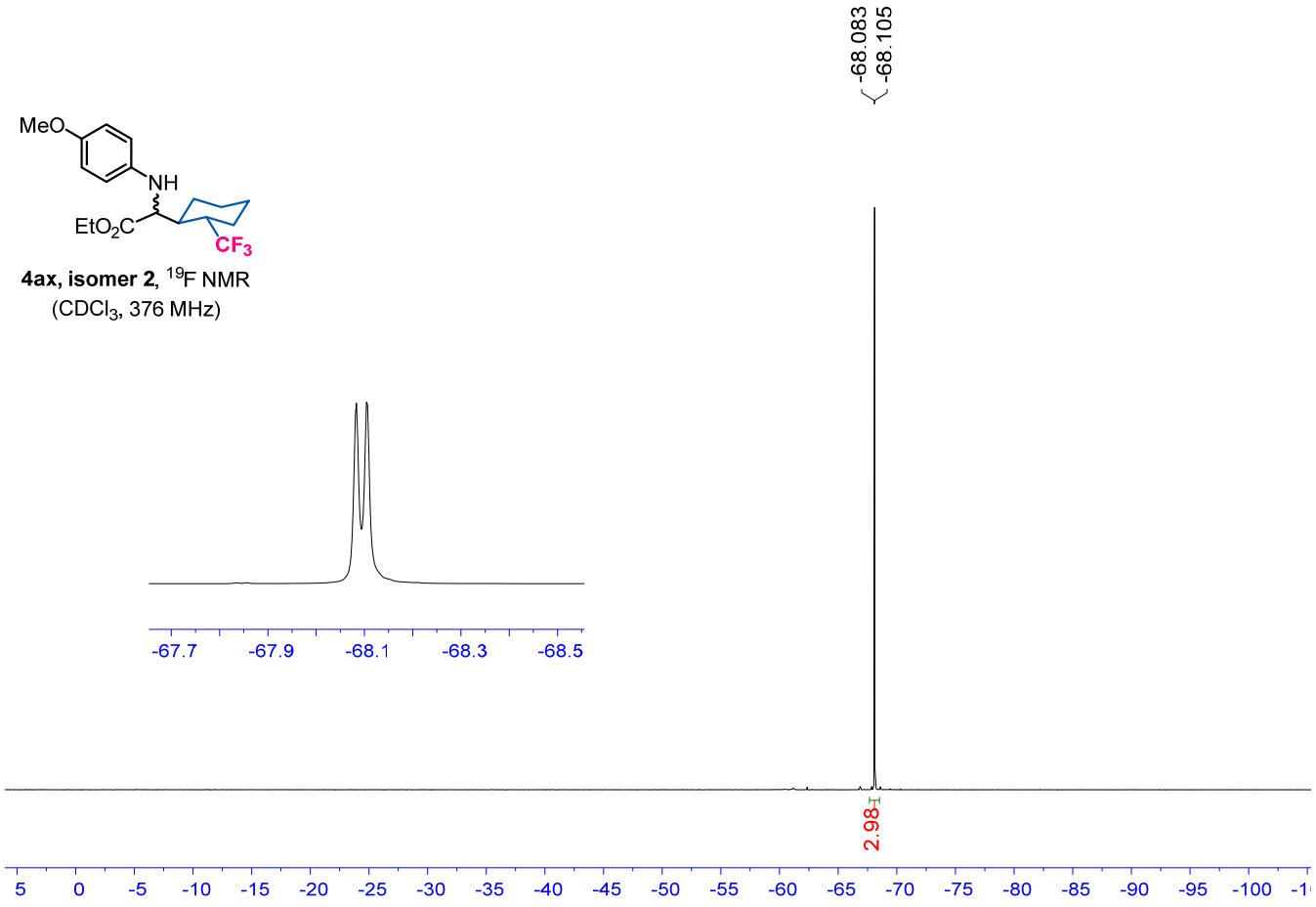

172.42
152.73
140.79
132.43
129.64
126.85
124.05
115.05
114.98
61.26
58.78
55.73
41.89
41.65
41.40
41.15
39.16
26.33
24.70
24.66
24.63
24.20
24.05
14.29
MeO
NH
EtO2C
CF3
4ax, isomer 1, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



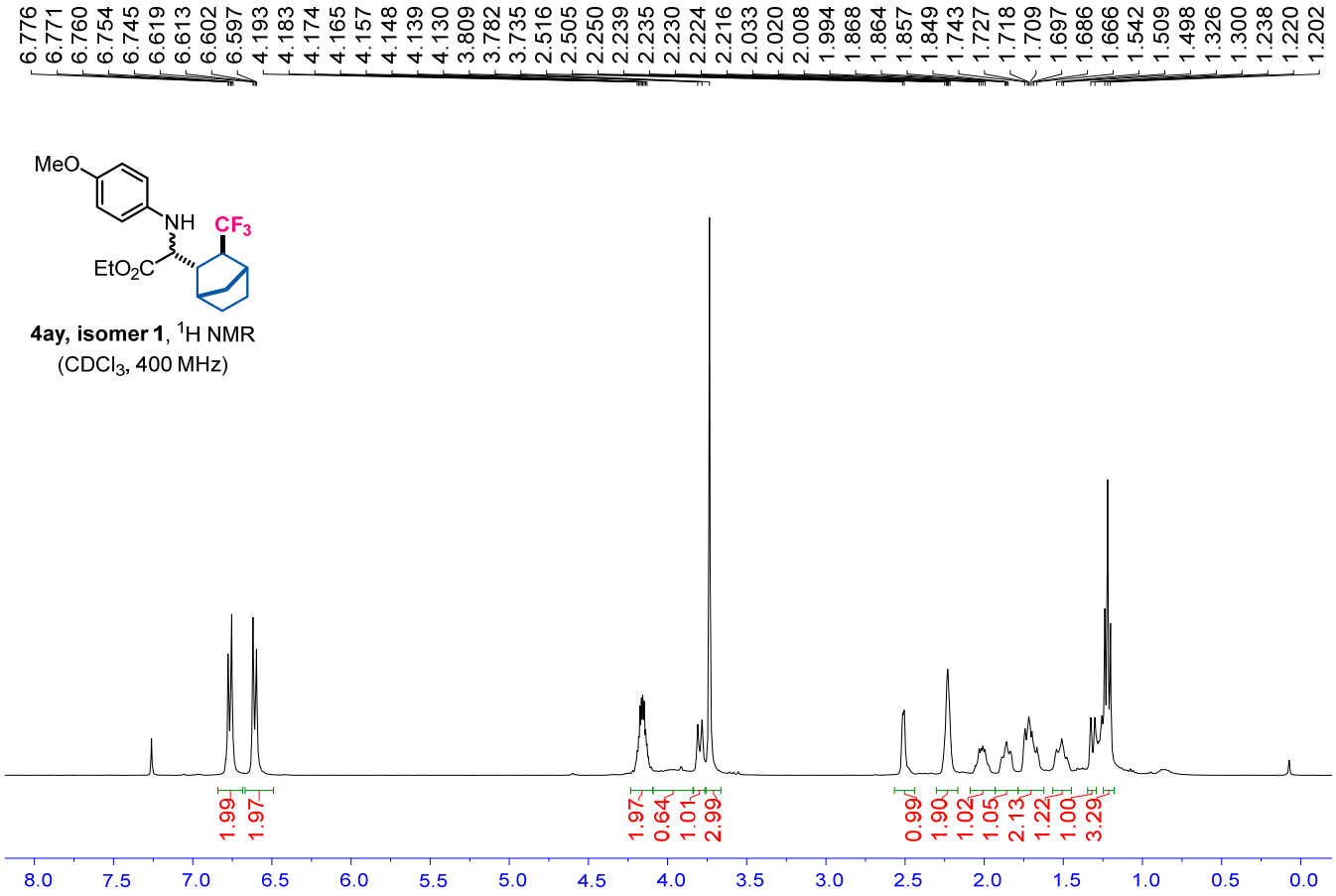
4ax, isomer 1, ^{19}F NMR
($CDCl_3$, 376 MHz)

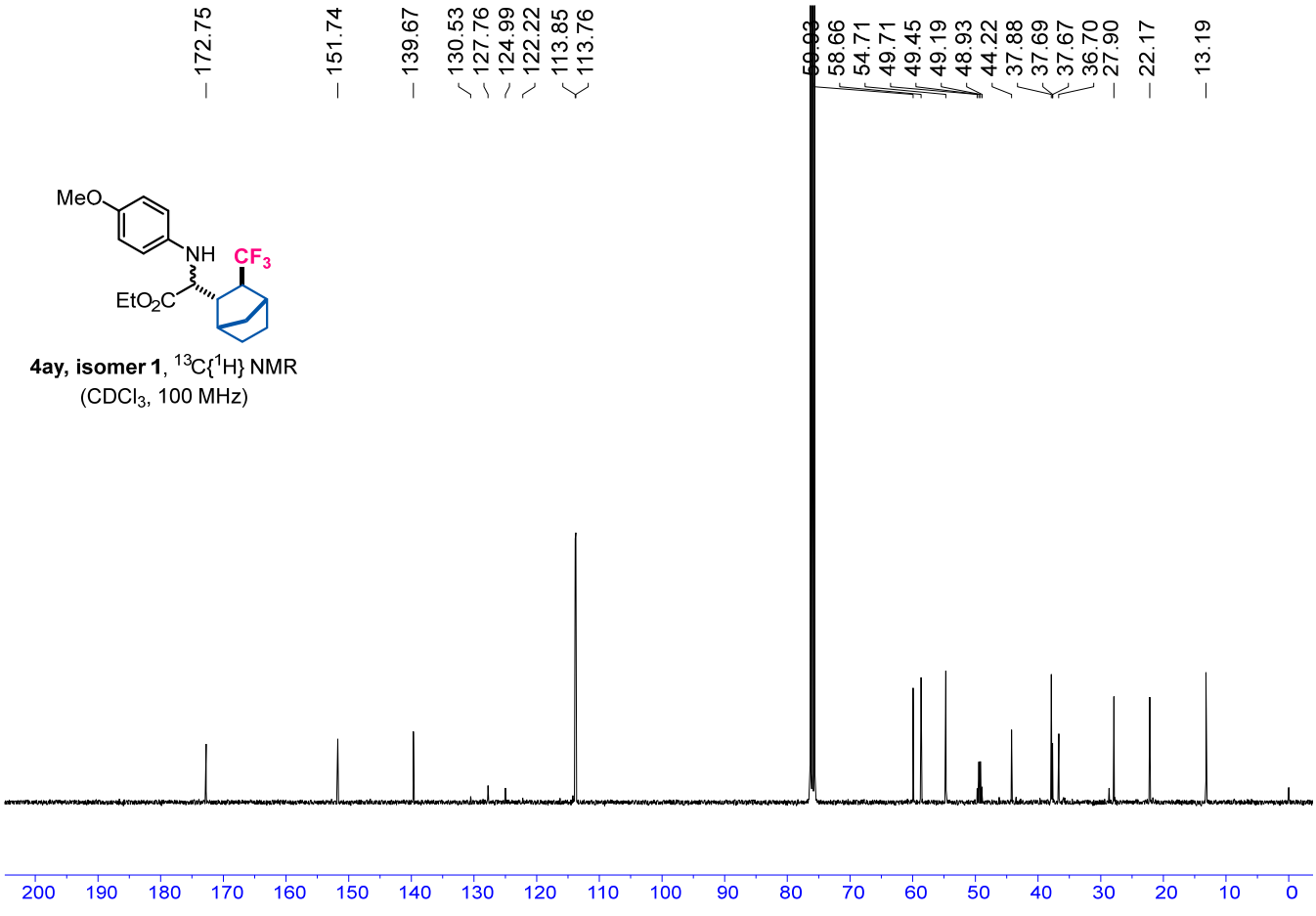

6.773
6.756
6.750
6.690
6.673
6.668
4.373
4.364
4.183
4.173
4.166
4.149
4.131
4.122
4.114
3.732
2.463
2.456
2.438
2.436
2.178
2.169
2.159
2.150
2.142
2.123
2.087
2.078
2.058
2.049
1.829
1.811
1.797
1.669
1.594
1.568
1.409
1.400
1.378
1.369
1.351
1.345
1.338
1.322
1.315
1.297
1.273
1.255
1.245
1.227
1.209
MeO
NH
EtO2C
CF3
4ax, isomer 2, 1H NMR
(CDCl3, 400 MHz)
1.99
1.99
1.00
2.01
3.96
0.97
0.98
1.02
2.02
1.04
3.94
3.20
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

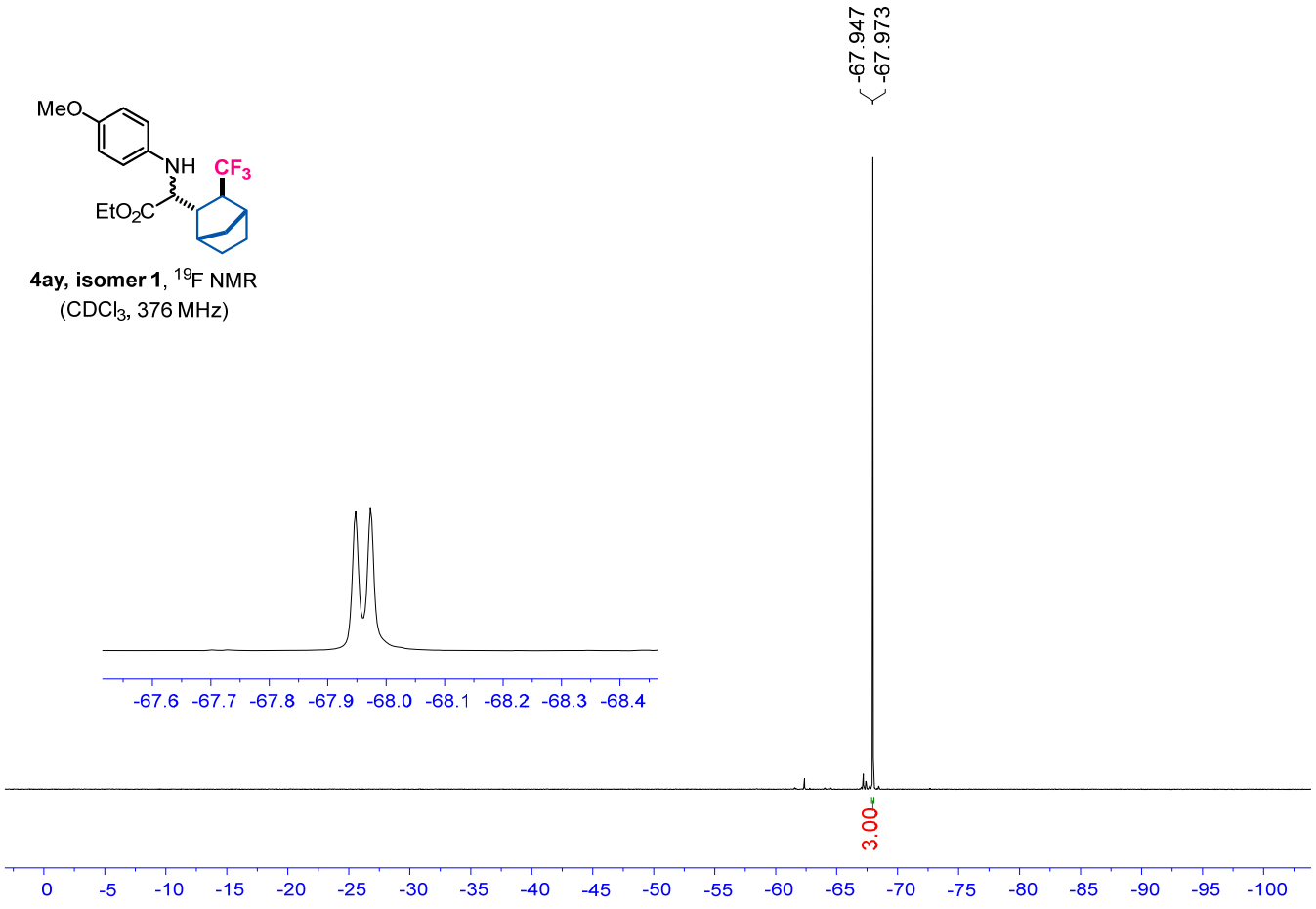

173.50
153.30
141.41
132.01
129.22
126.42
123.63
116.48
114.73
61.13
59.36
55.61
42.18
41.94
41.69
41.45
39.14
25.75
25.49
25.45
25.42
25.38
25.12
24.45
14.24
MeO
NH
EtO2C
CF3
4ax, isomer 2, 13C{1H} NMR
(CDCl3, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



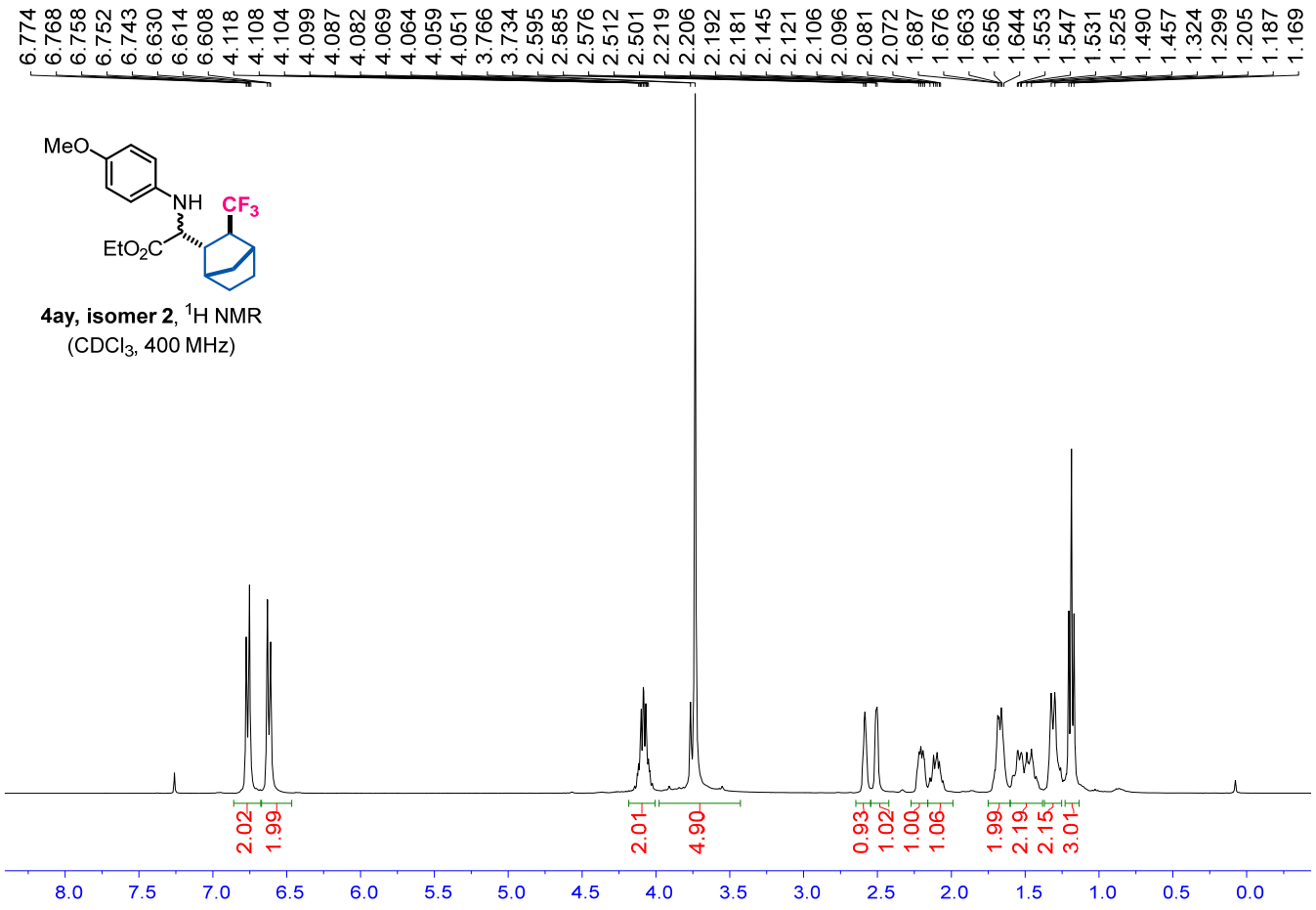
4ax, isomer 2, ^{19}F NMR
($CDCl_3$, 376 MHz)


6.776
6.771
6.760
6.754
6.745
6.619
6.613
6.602
6.597
4.193
4.183
4.174
4.165
4.157
4.148
4.139
4.130
3.809
3.782
3.735
2.516
2.505
2.250
2.239
2.235
2.230
2.224
2.216
2.033
2.020
2.008
1.994
1.868
1.864
1.857
1.849
1.743
1.727
1.718
1.709
1.697
1.686
1.666
1.542
1.509
1.498
1.326
1.300
1.238
1.220
1.202
MeO
NH
CF3
EtO2C
4ay, isomer 1, 1H NMR
(CDCl3, 400 MHz)
1.99
1.97
1.97
0.64
1.01
2.99
0.99
1.90
1.02
1.05
2.13
1.22
1.00
3.29
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

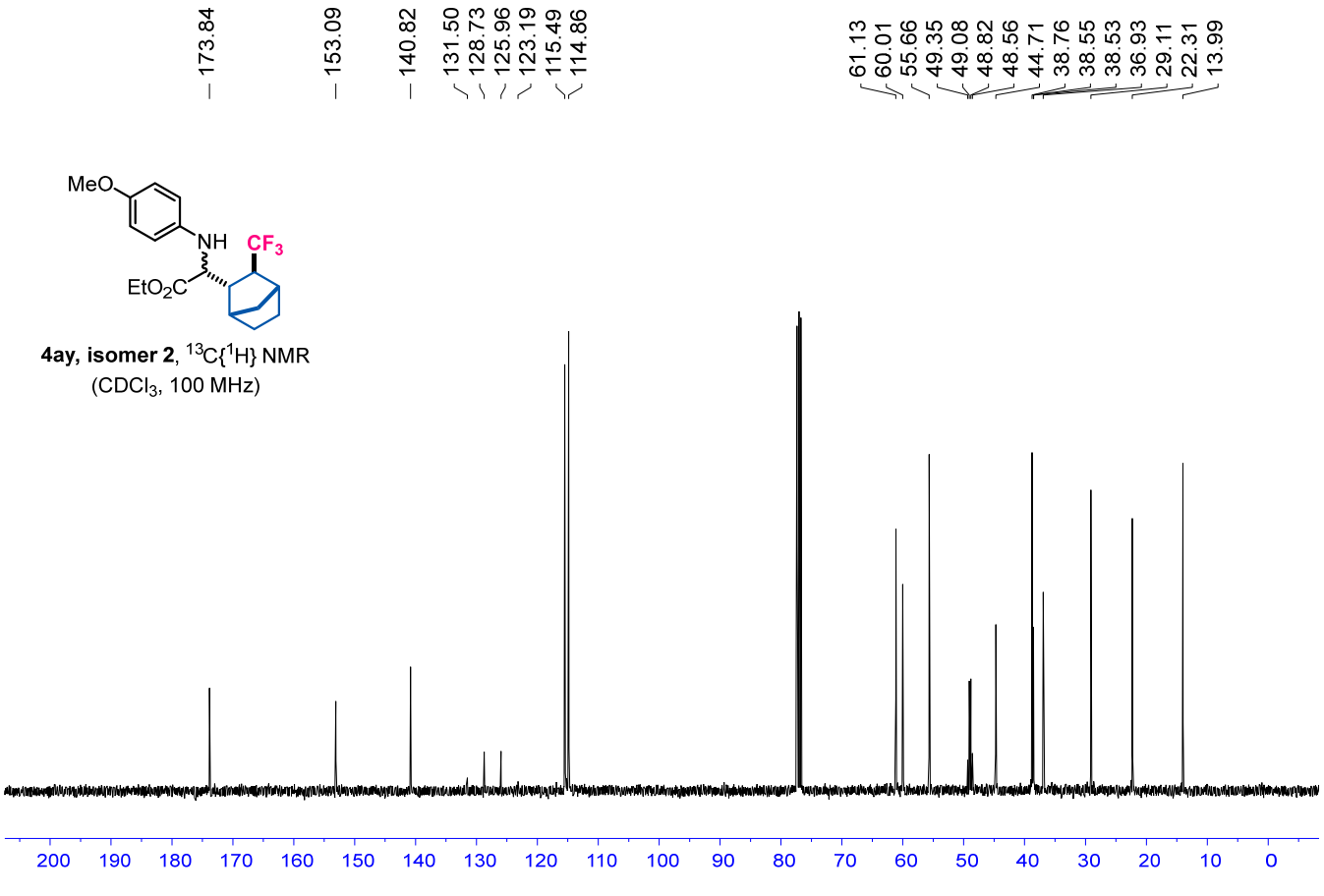

172.75
151.74
139.67
130.53
127.76
124.99
122.22
113.85
113.76
59.93
58.66
54.71
49.71
49.45
49.19
48.93
44.22
37.88
37.69
37.67
36.70
27.90
22.17
13.19
MeO
NH
CF3
EtO2C
4ay, isomer 1, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



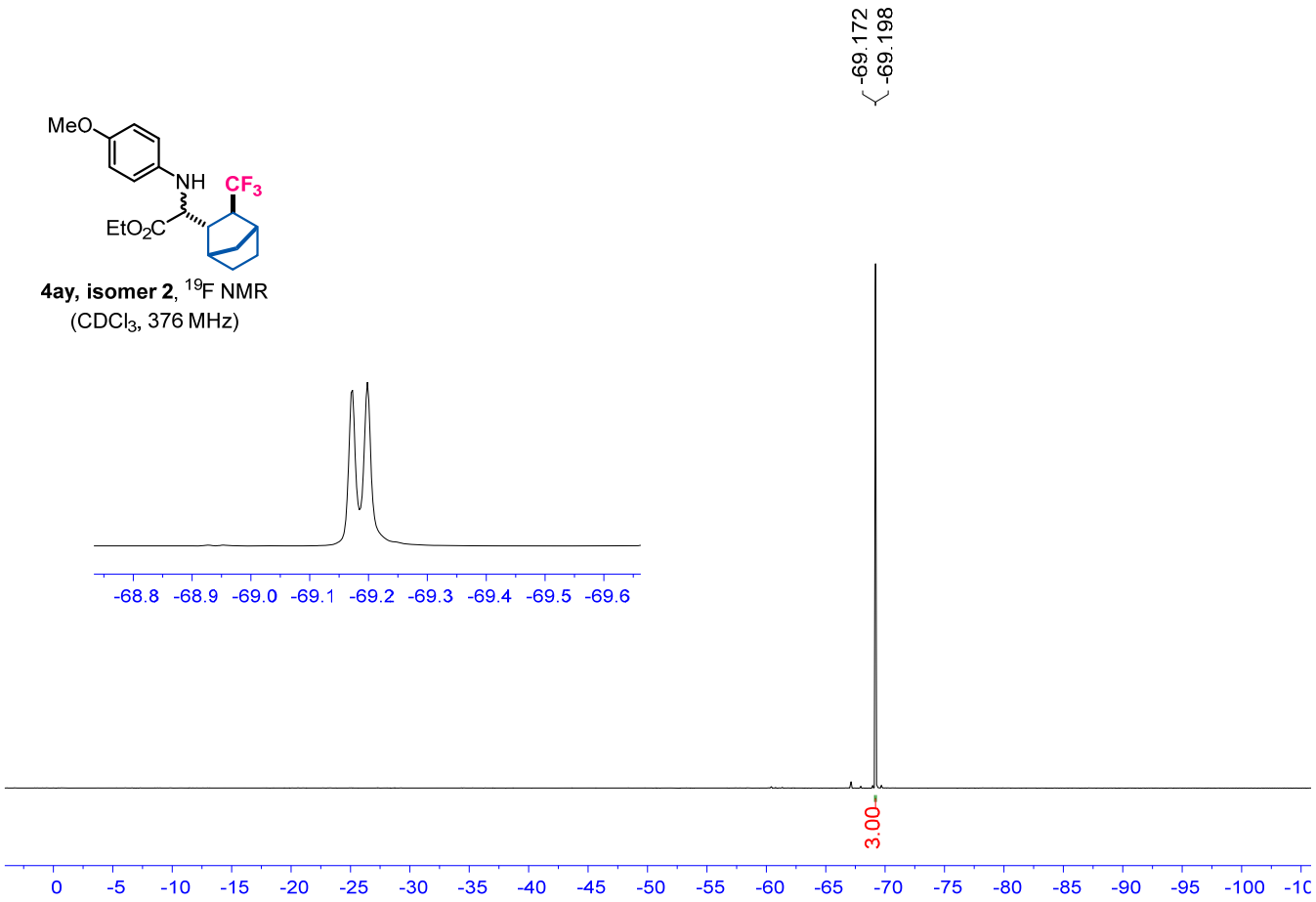
4ay, isomer 1, ^{19}F NMR
($CDCl_3$, 376 MHz)

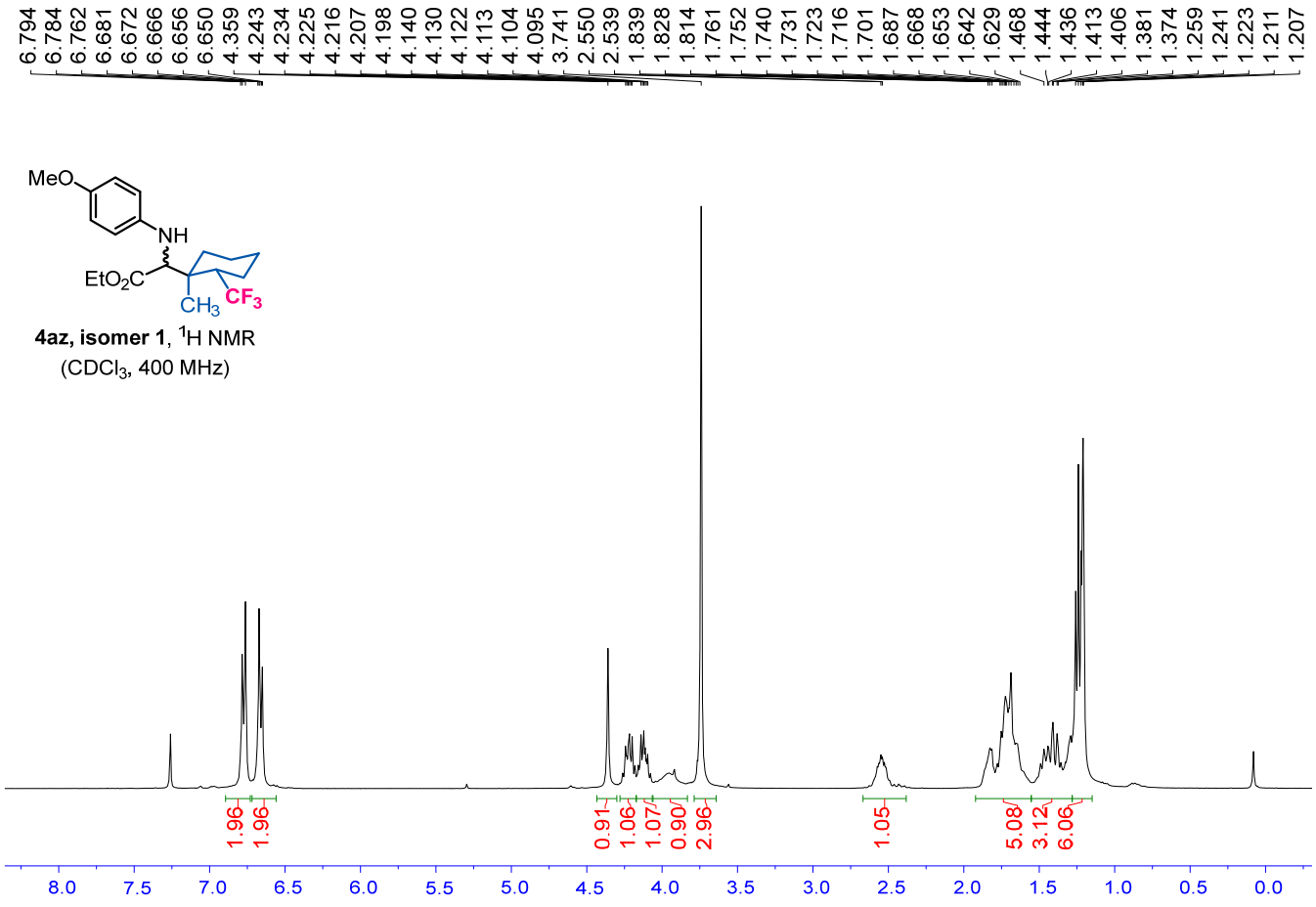


4ay, isomer 2, ^{1}H NMR
($CDCl_3$, 400 MHz)

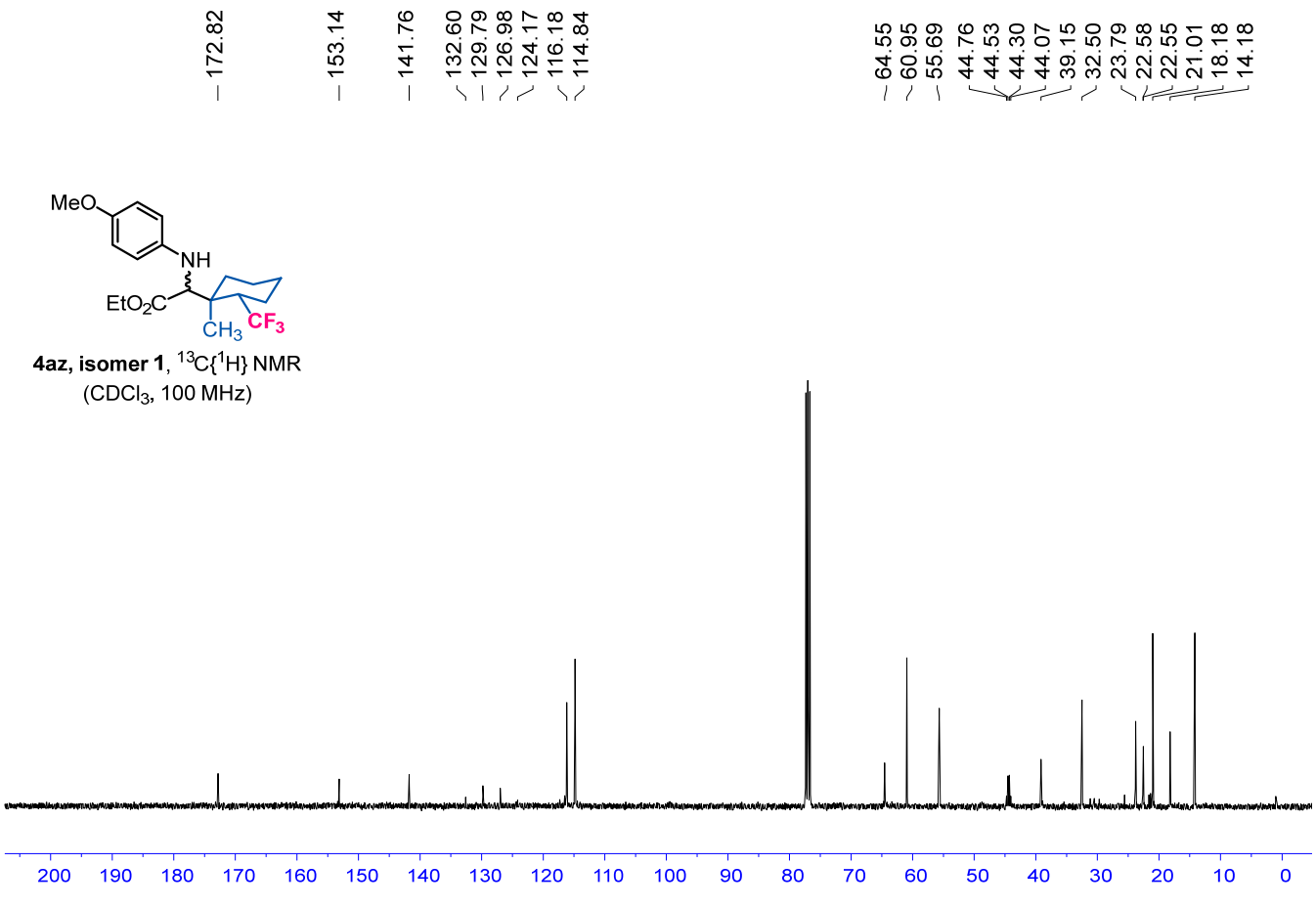


4ay, isomer 2, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)

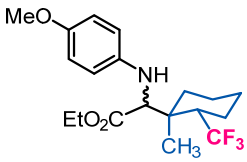

MeO
NH
CF3
EtO2C
4ay, isomer 2, 19F NMR
(CDCl3, 376 MHz)
-69.172
-69.198
-68.8 -68.9 -69.0 -69.1 -69.2 -69.3 -69.4 -69.5 -69.6
3.00
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100



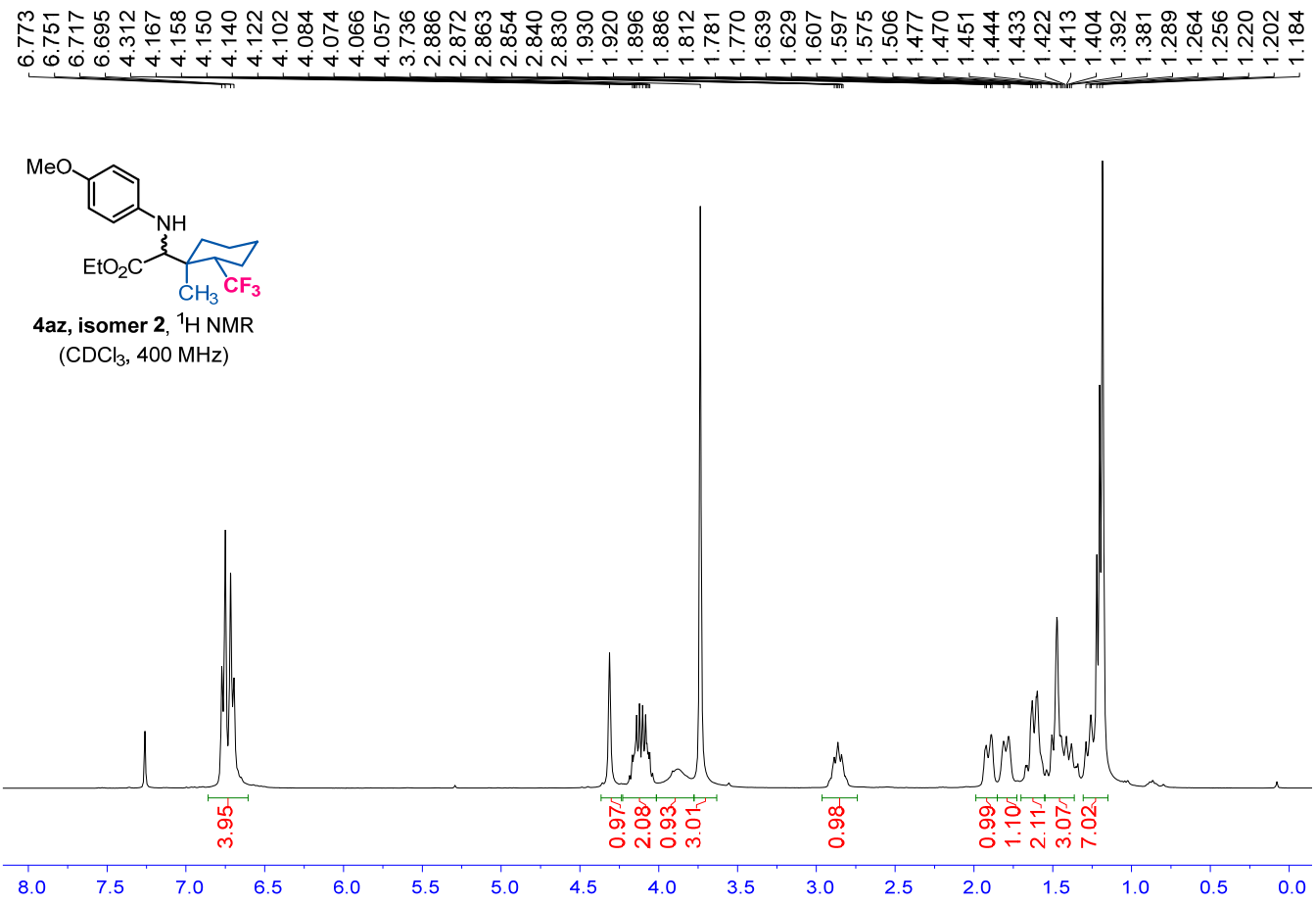
4az, isomer 1, ^{1}H NMR
($CDCl_3$, 400 MHz)



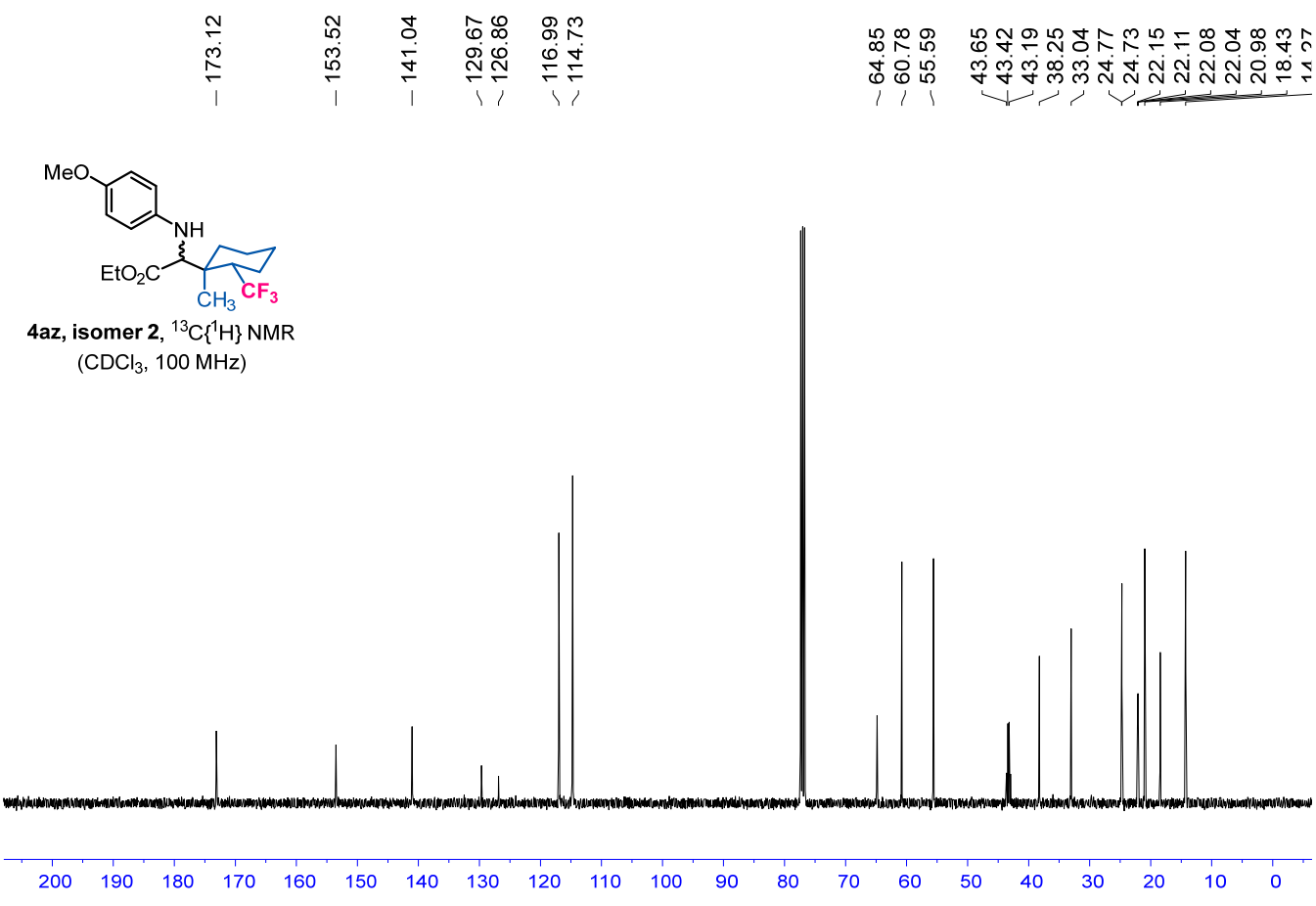
4az, isomer 1, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



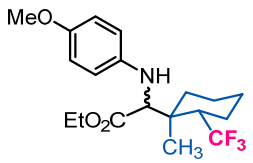
4az, isomer 1, ^{19}F NMR
($CDCl_3$, 367 MHz)



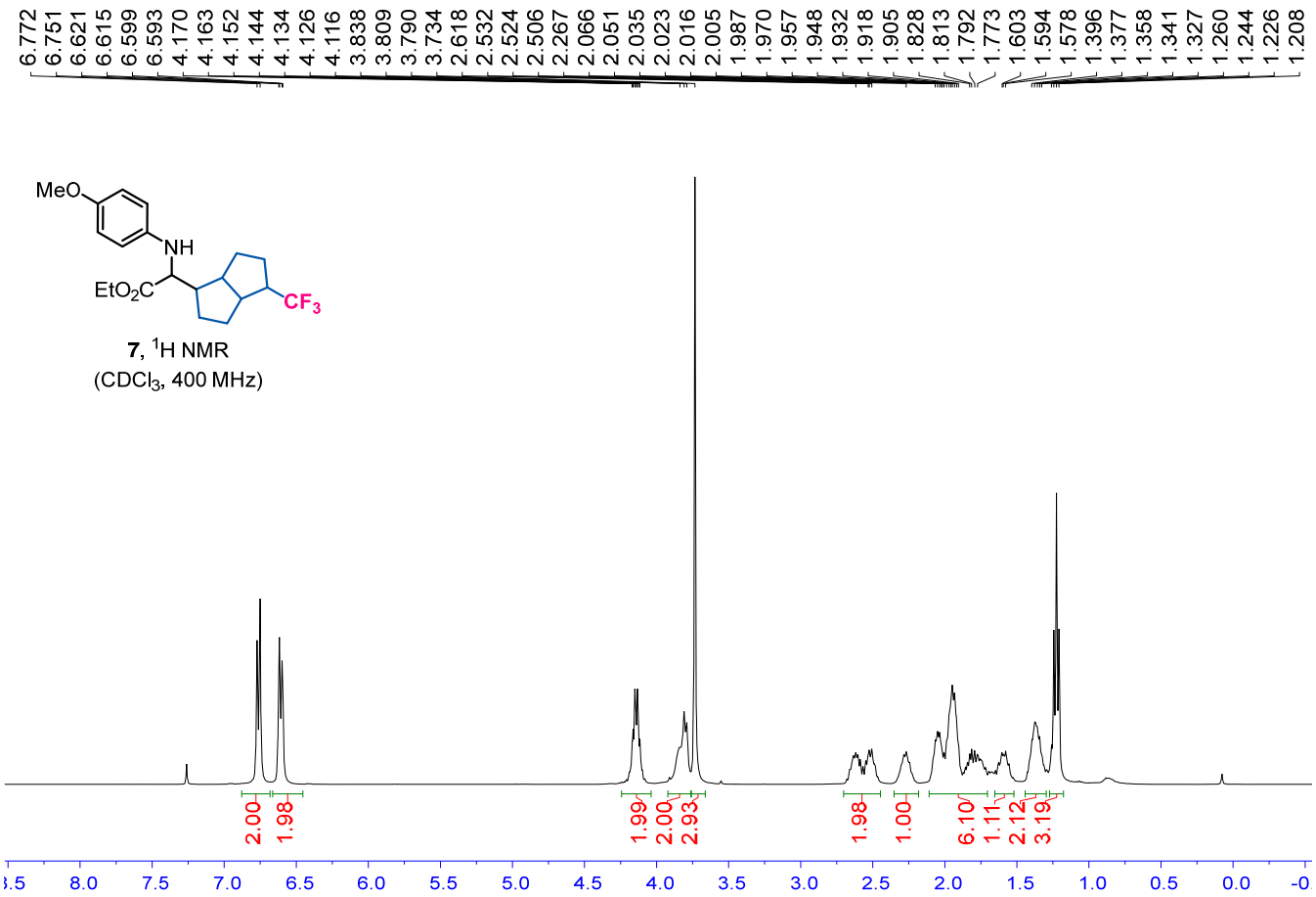
4az, isomer 2, ^{1}H NMR
($CDCl_3$, 400 MHz)

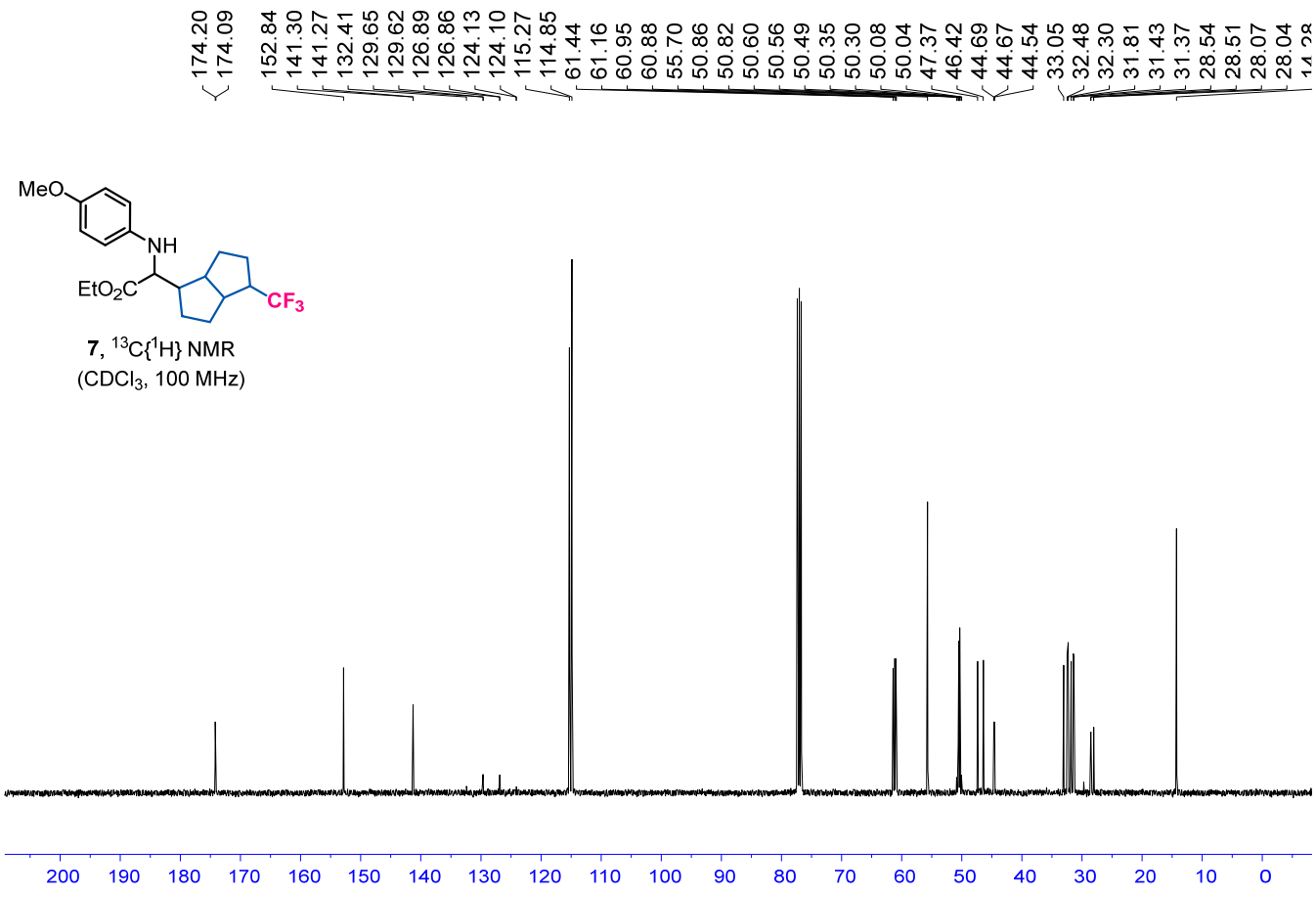


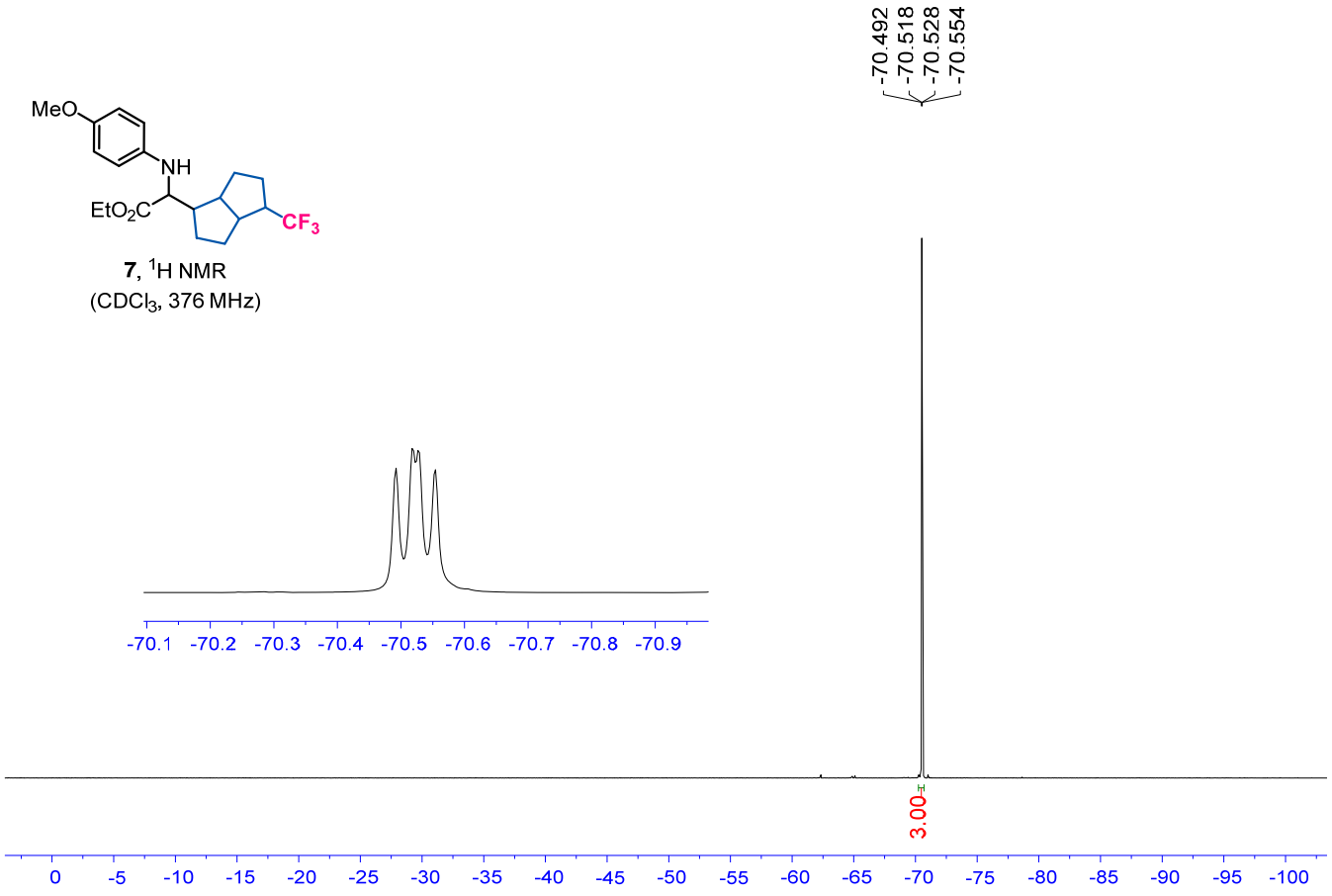
4az, isomer 2, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)

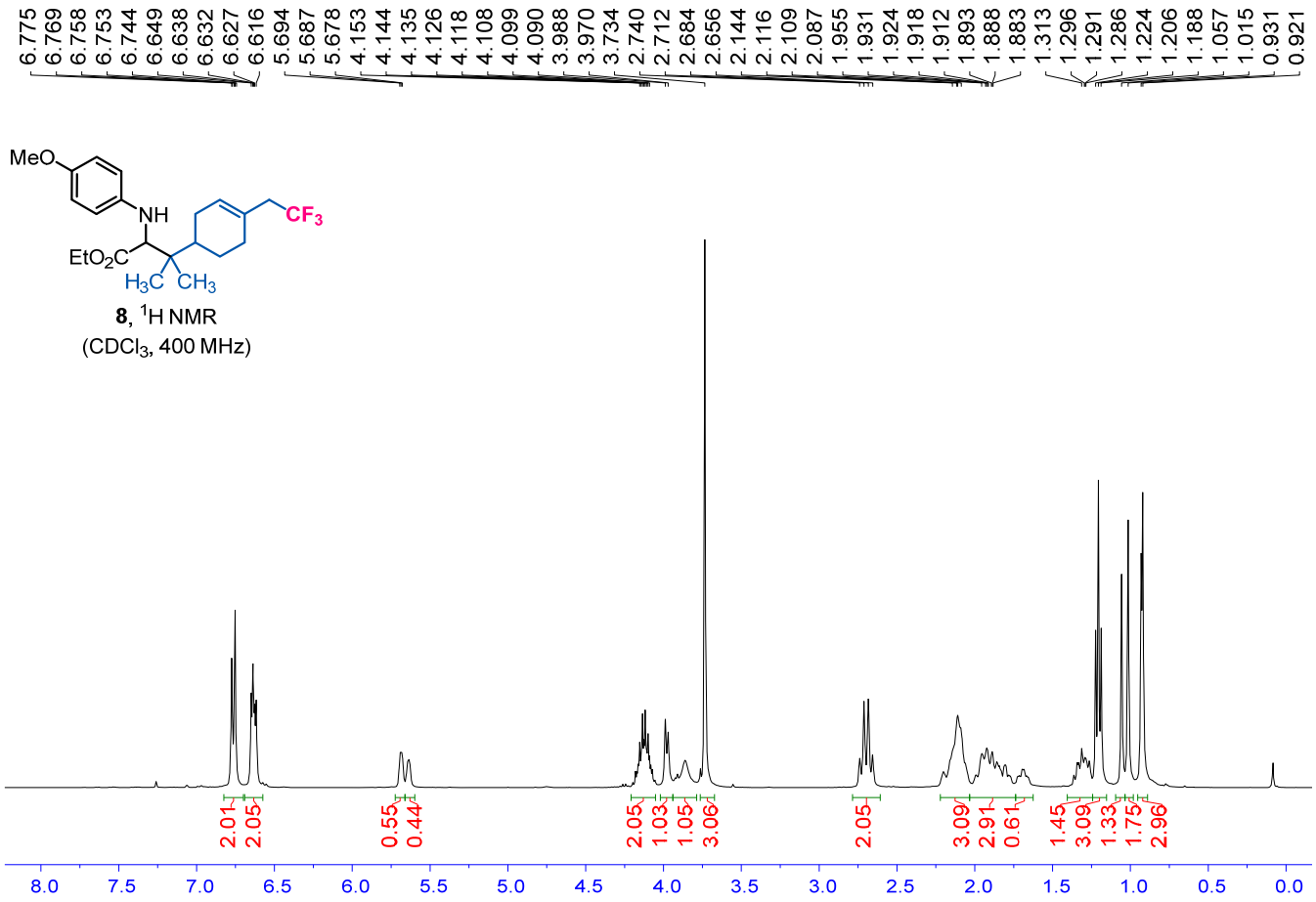


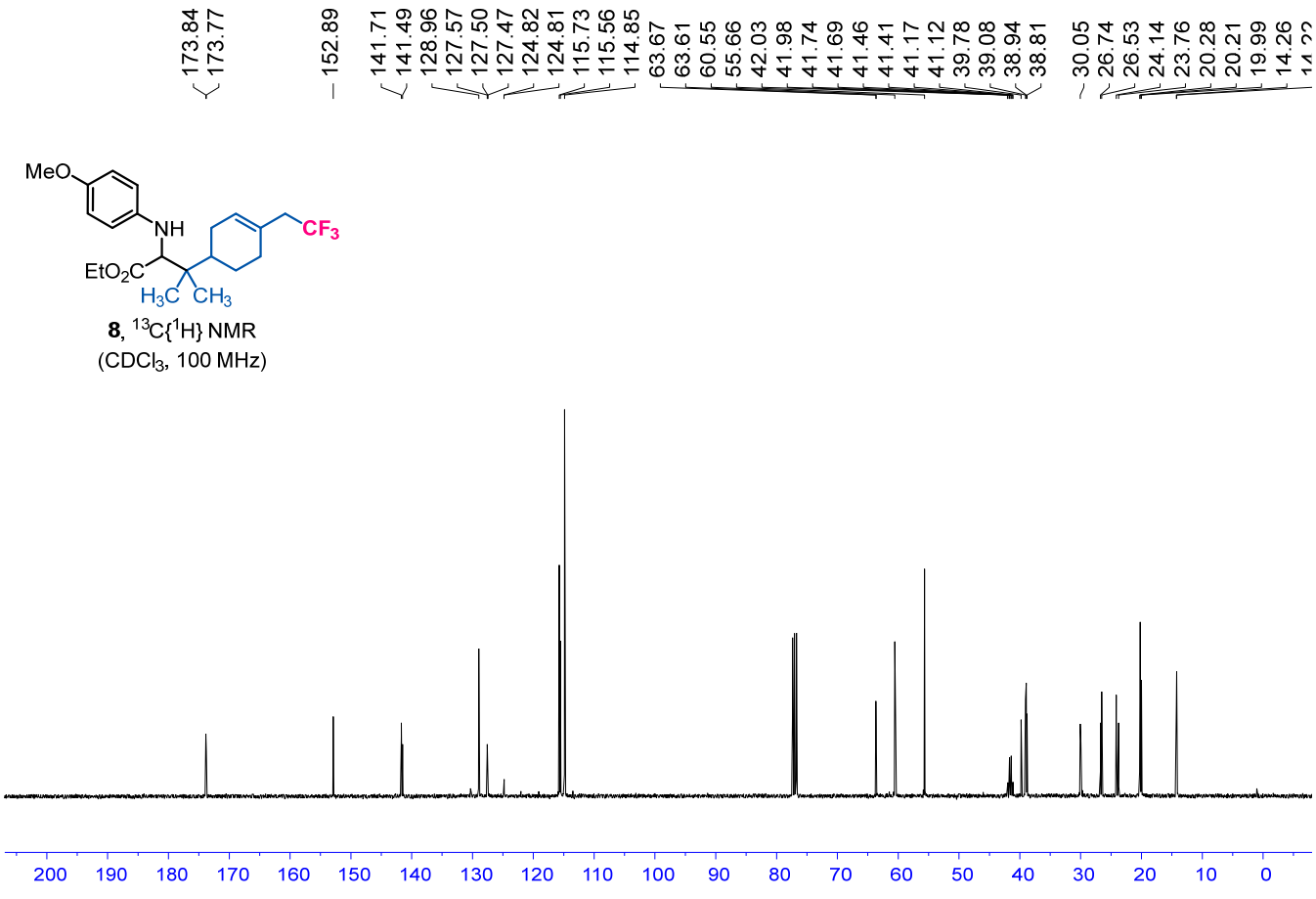
4az, isomer 2, ^{19}F NMR
($CDCl_3$, 376 MHz)

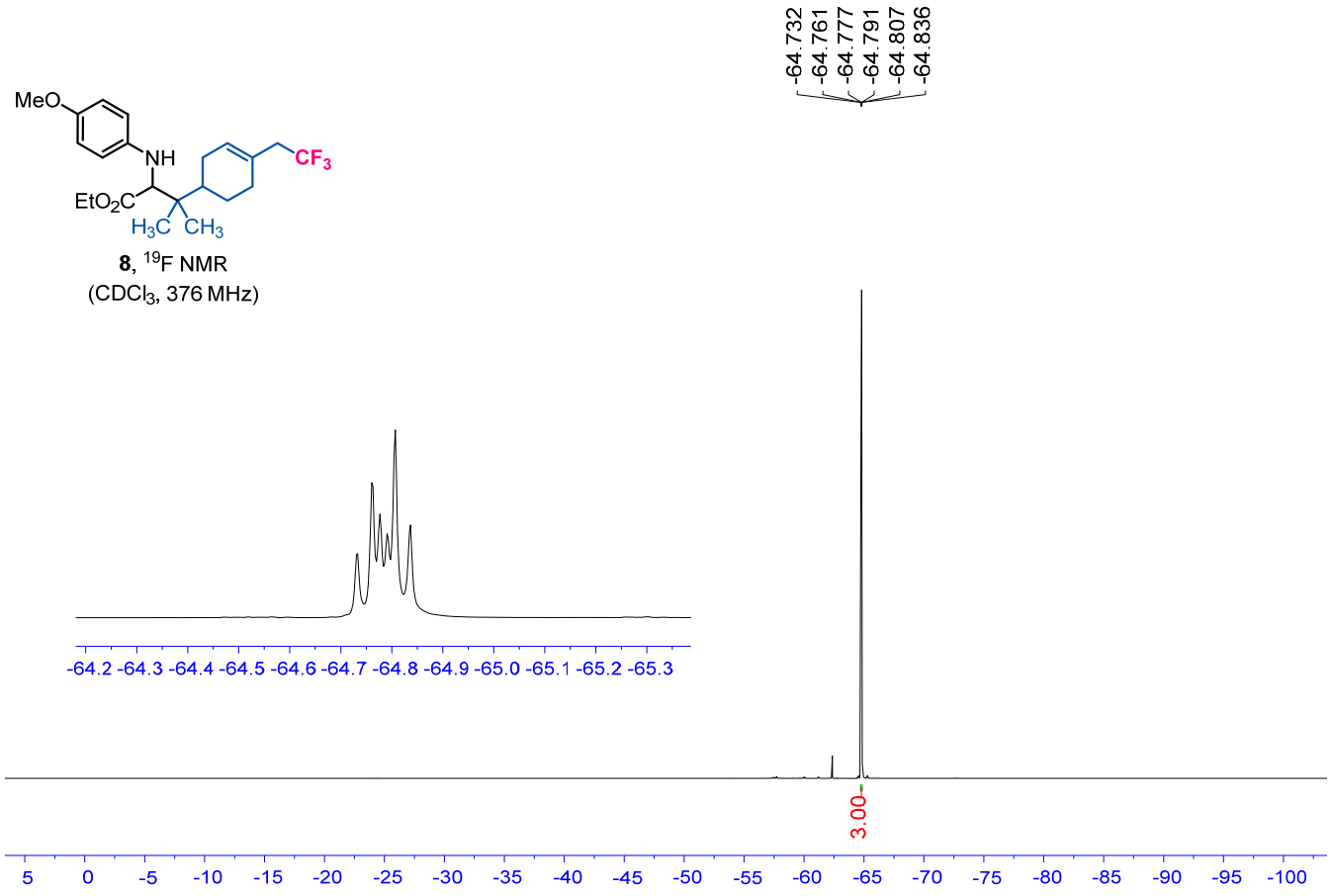

MeO
NH
EtO2C
CF3
7, 1H NMR
(CDCl3, 400 MHz)

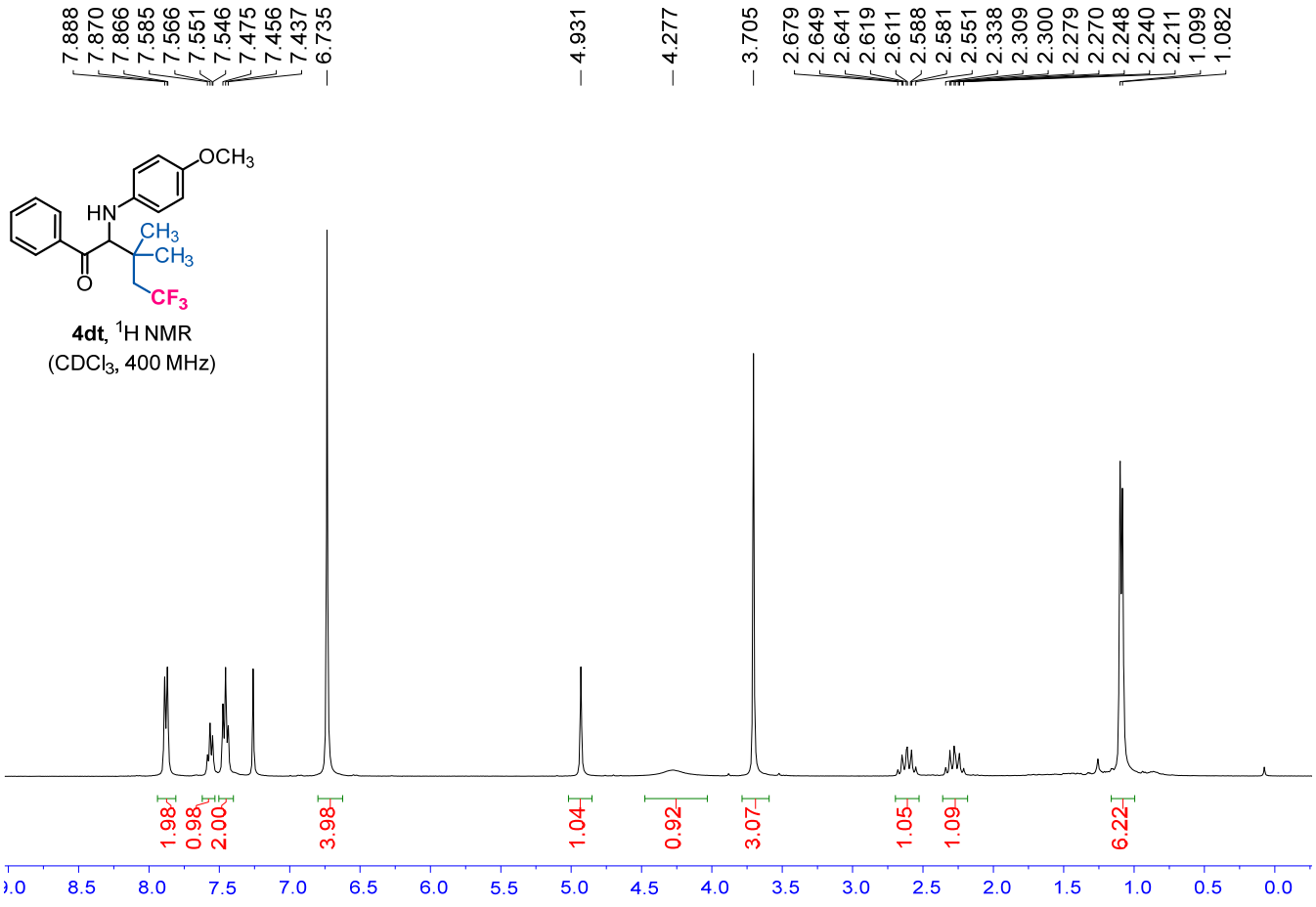

MeO
NH
EtO2C
CF3
7, 13C{1H} NMR
(CDCl3, 100 MHz)

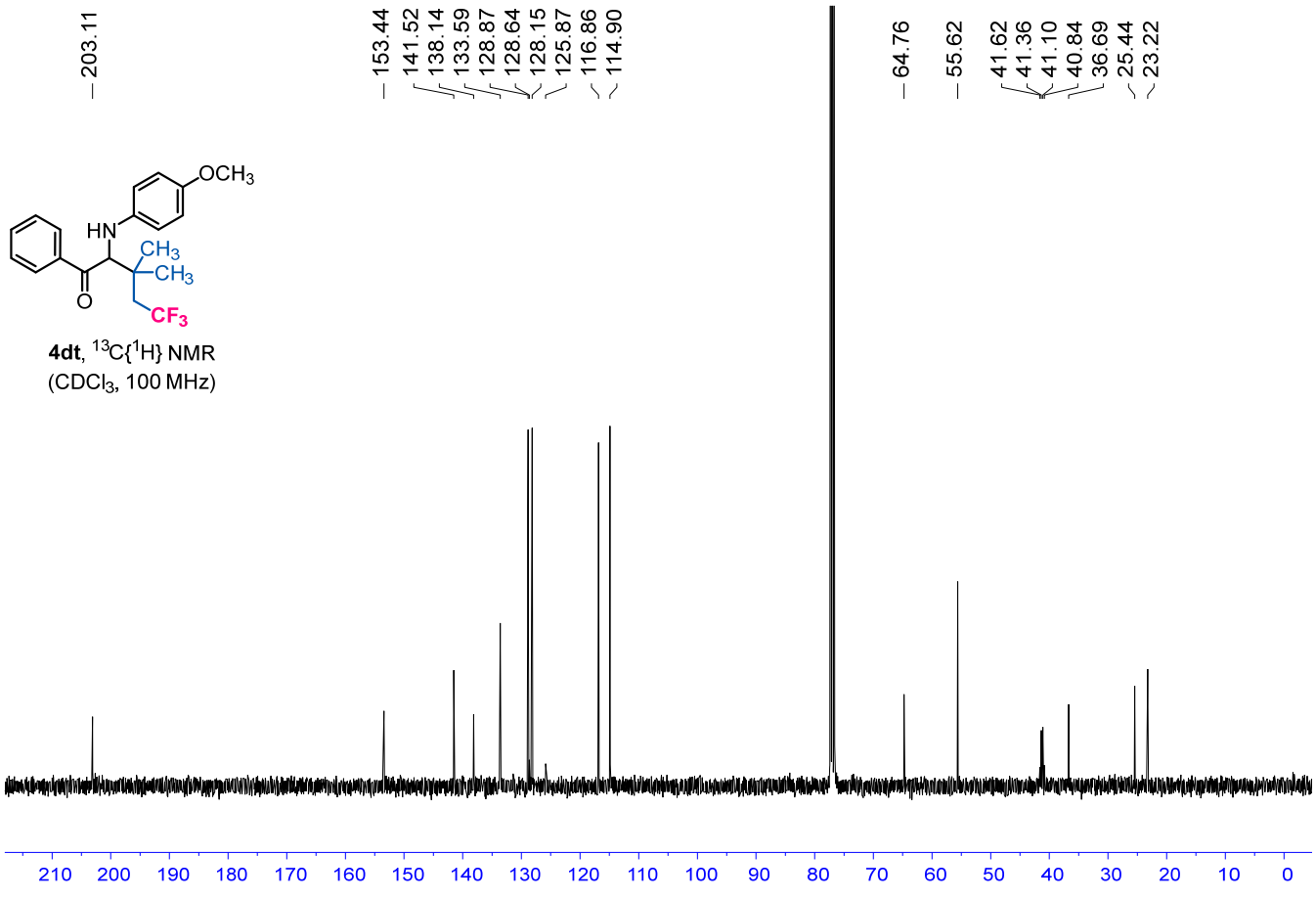

MeO
NH
EtO2C
CF3
7, 1H NMR
(CDCl3, 376 MHz)
-70.492
-70.518
-70.528
-70.554
-70.1 -70.2 -70.3 -70.4 -70.5 -70.6 -70.7 -70.8 -70.9
3.00
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100

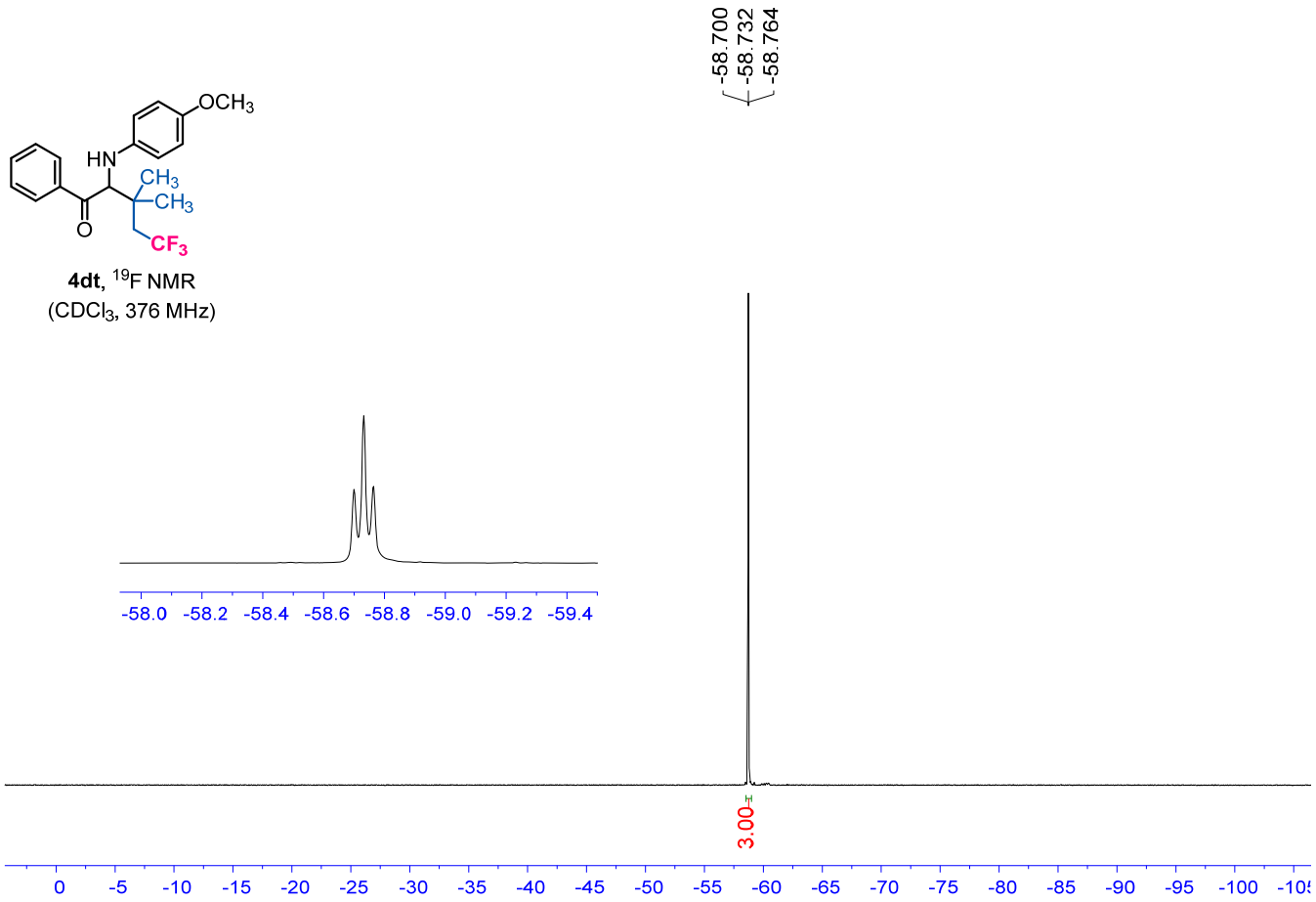

6.775
6.769
6.758
6.753
6.744
6.649
6.638
6.632
6.627
6.616
5.694
5.687
5.678
4.153
4.144
4.135
4.126
4.118
4.108
4.099
4.090
3.988
3.970
3.734
2.740
2.712
2.684
2.656
2.144
2.116
2.109
2.087
1.955
1.931
1.924
1.918
1.912
1.893
1.888
1.883
1.313
1.296
1.291
1.286
1.224
1.206
1.188
1.057
1.015
0.931
0.921
MeO
NH
CF3
EtO2C
H3C
CH3
8, 1H NMR
(CDCl3, 400 MHz)
2.01
2.05
0.55
0.44
2.05
1.03
1.05
3.06
2.05
3.09
2.91
0.61
1.45
3.09
1.33
1.75
2.96
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

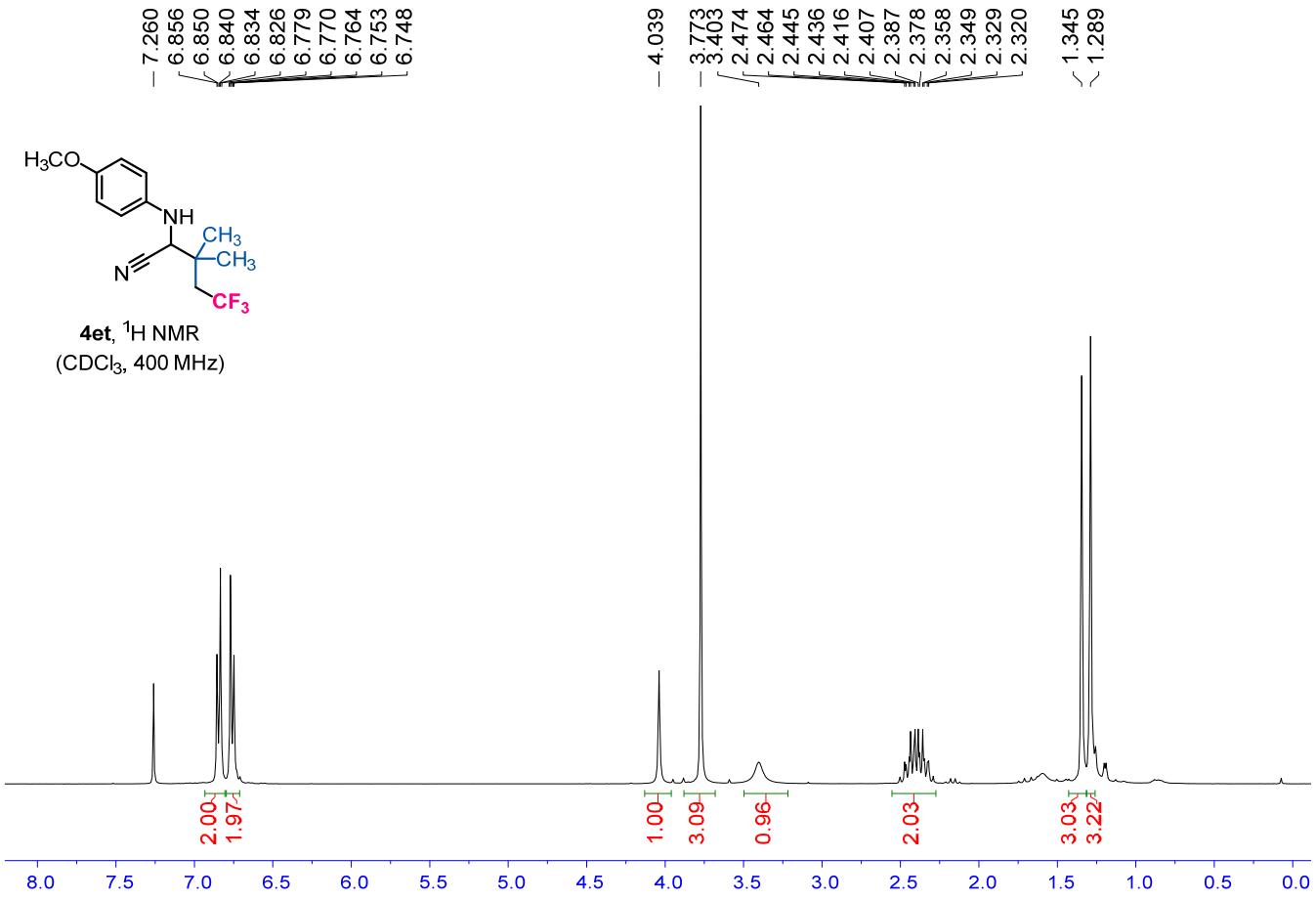

173.84
173.77
152.89
141.71
141.49
128.96
127.57
127.50
127.47
124.82
124.81
115.73
115.56
114.85
63.67
63.61
60.55
55.66
42.03
41.98
41.74
41.69
41.46
41.41
41.17
41.12
39.78
39.08
38.94
38.81
30.05
26.74
26.53
24.14
23.76
20.28
20.21
19.99
14.26
MeO
NH
CF3
EtO2C
H3C
CH3
8, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


-64.732
-64.761
-64.777
-64.791
-64.807
-64.836
MeO
NH
CF3
EtO2C
H3C CH3
8, 19F NMR
(CDCl3, 376 MHz)
-64.2 -64.3 -64.4 -64.5 -64.6 -64.7 -64.8 -64.9 -65.0 -65.1 -65.2 -65.3
3.00
5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100

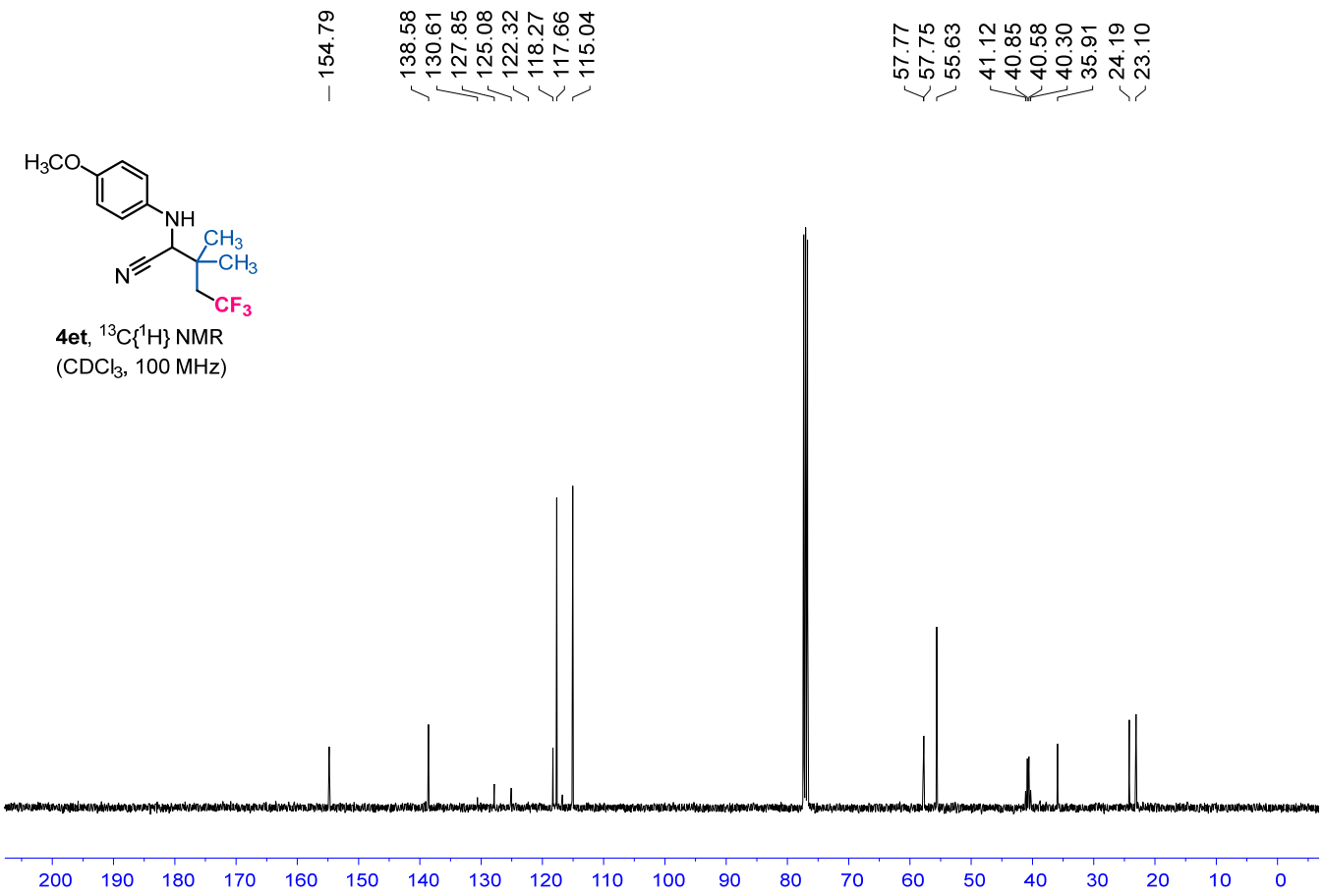

7.888
7.870
7.866
7.585
7.566
7.551
7.546
7.475
7.456
7.437
6.735
4.931
4.277
3.705
2.679
2.649
2.641
2.619
2.611
2.588
2.581
2.551
2.338
2.309
2.300
2.279
2.270
2.248
2.240
2.211
1.099
1.082
OCH3
HN
CH3
CH3
O
CF3
4dt, 1H NMR
(CDCl3, 400 MHz)
1.98
0.98
2.00
3.98
1.04
0.92
3.07
1.05
1.09
6.22
9.0
8.5
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


203.11
153.44
141.52
138.14
133.59
128.87
128.64
128.15
125.87
116.86
114.90
64.76
55.62
41.62
41.36
41.10
40.84
36.69
25.44
23.22
OCH3
HN
CH3
CH3
O
CF3
4dt, 13C{1H} NMR
(CDCl3, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

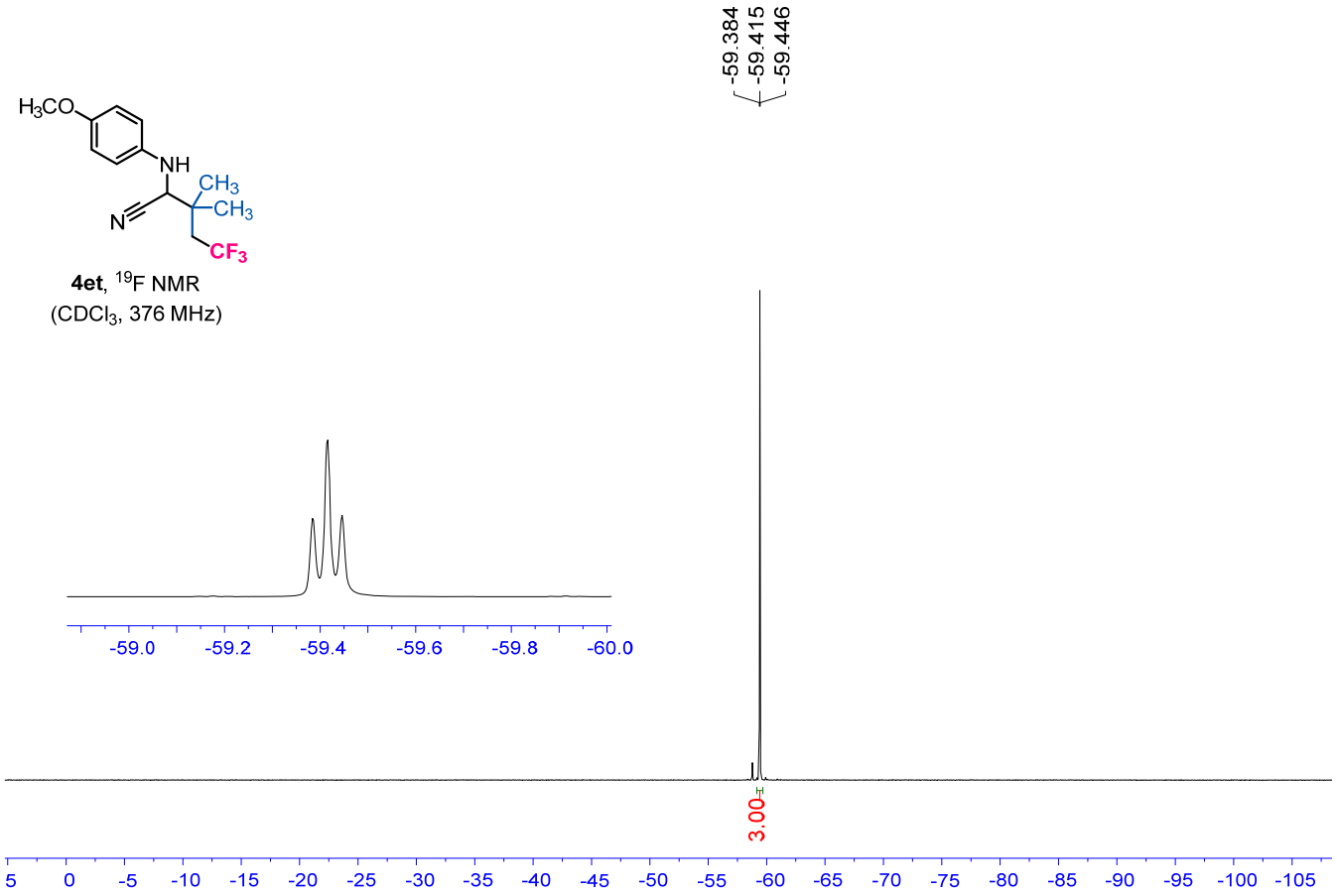

-58.700
-58.732
-58.764
OCH3
HN
CH3
CH3
O
CF3
4dt, 19F NMR
(CDCl3, 376 MHz)
-58.0 -58.2 -58.4 -58.6 -58.8 -59.0 -59.2 -59.4
3.00
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100



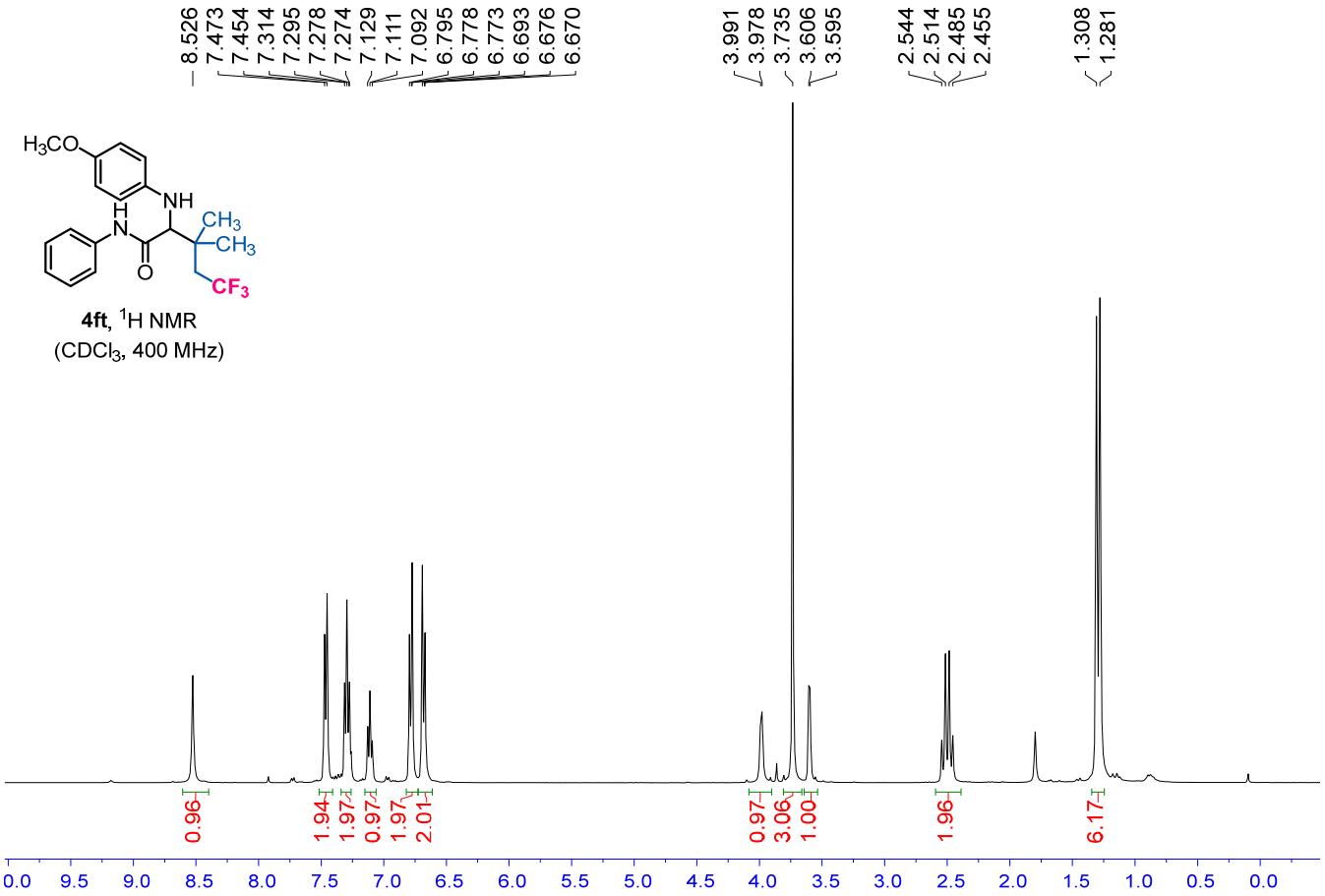
4et, ^{1}H NMR
($CDCl_3$, 400 MHz)



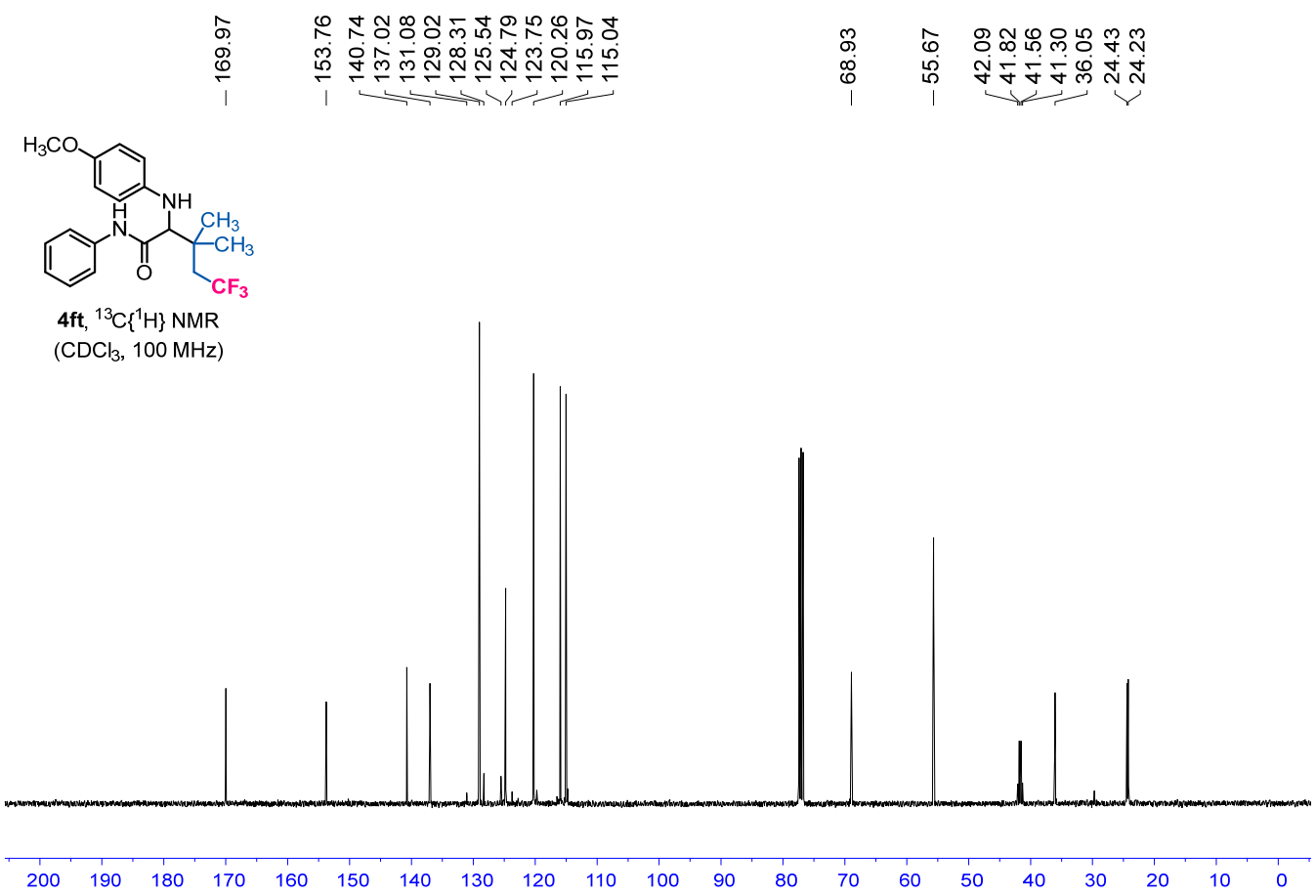
4et, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



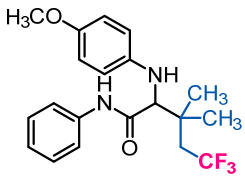
4et, ^{19}F NMR
($CDCl_3$, 376 MHz)



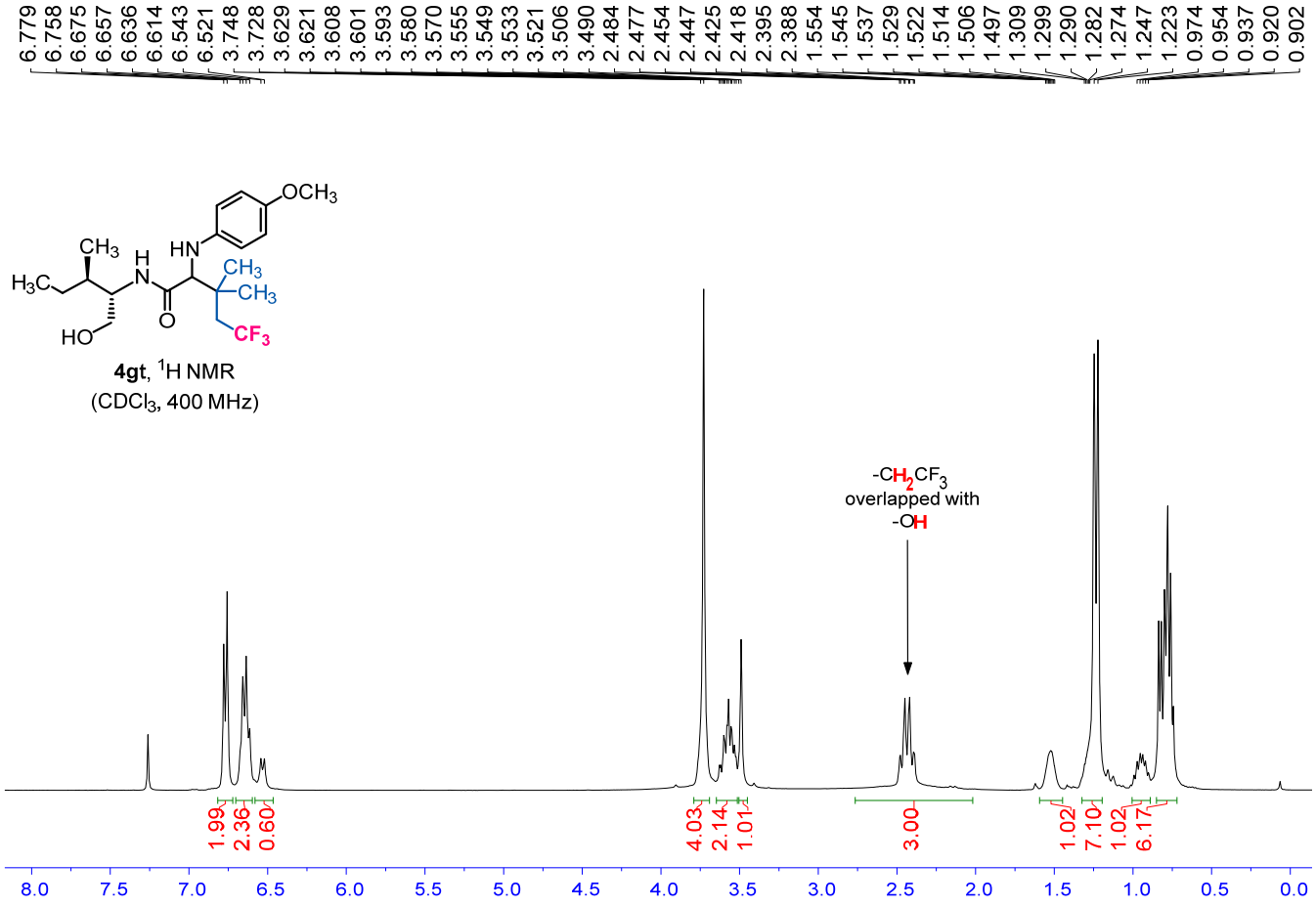
4ft, ^{1}H NMR
($CDCl_3$, 400 MHz)

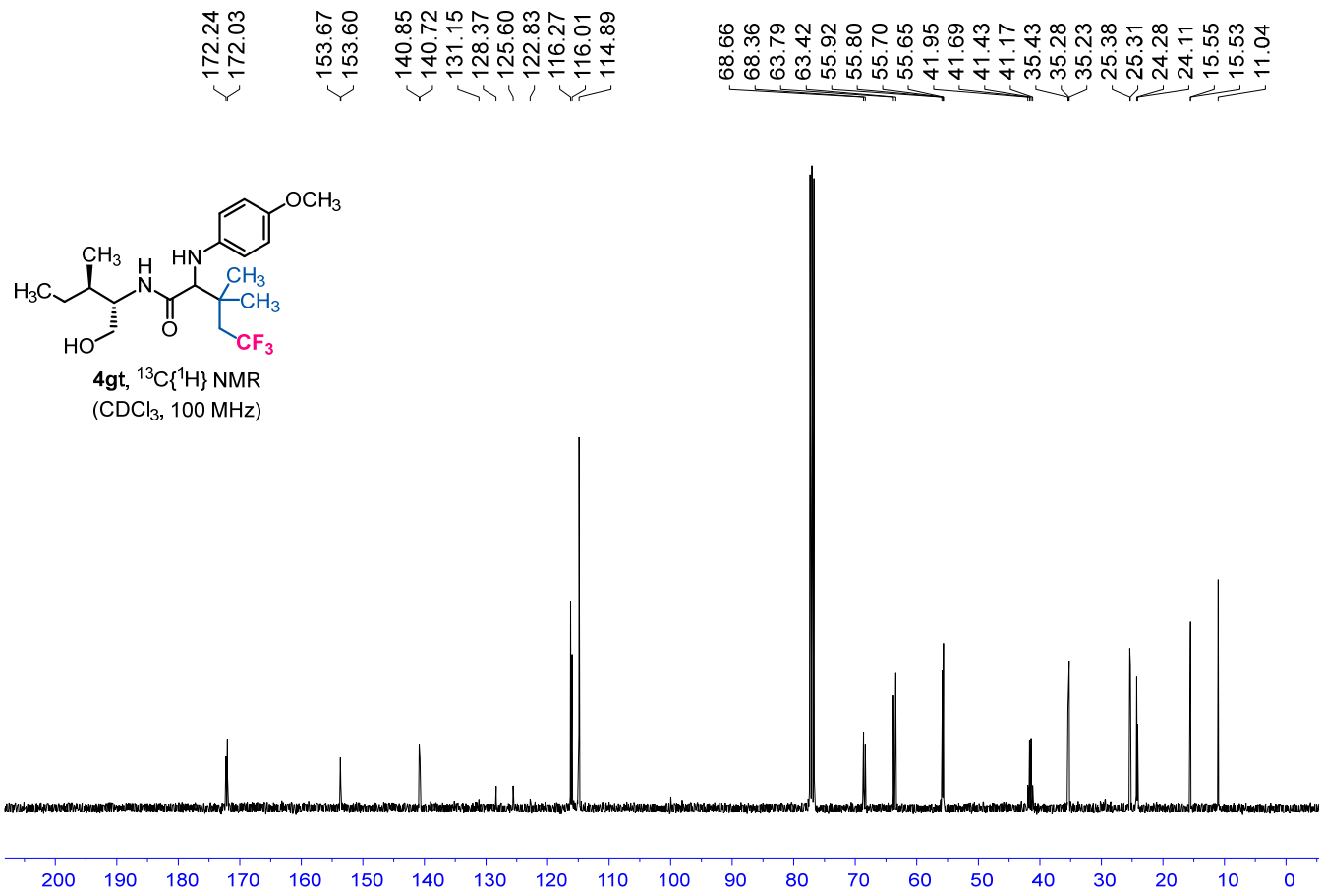


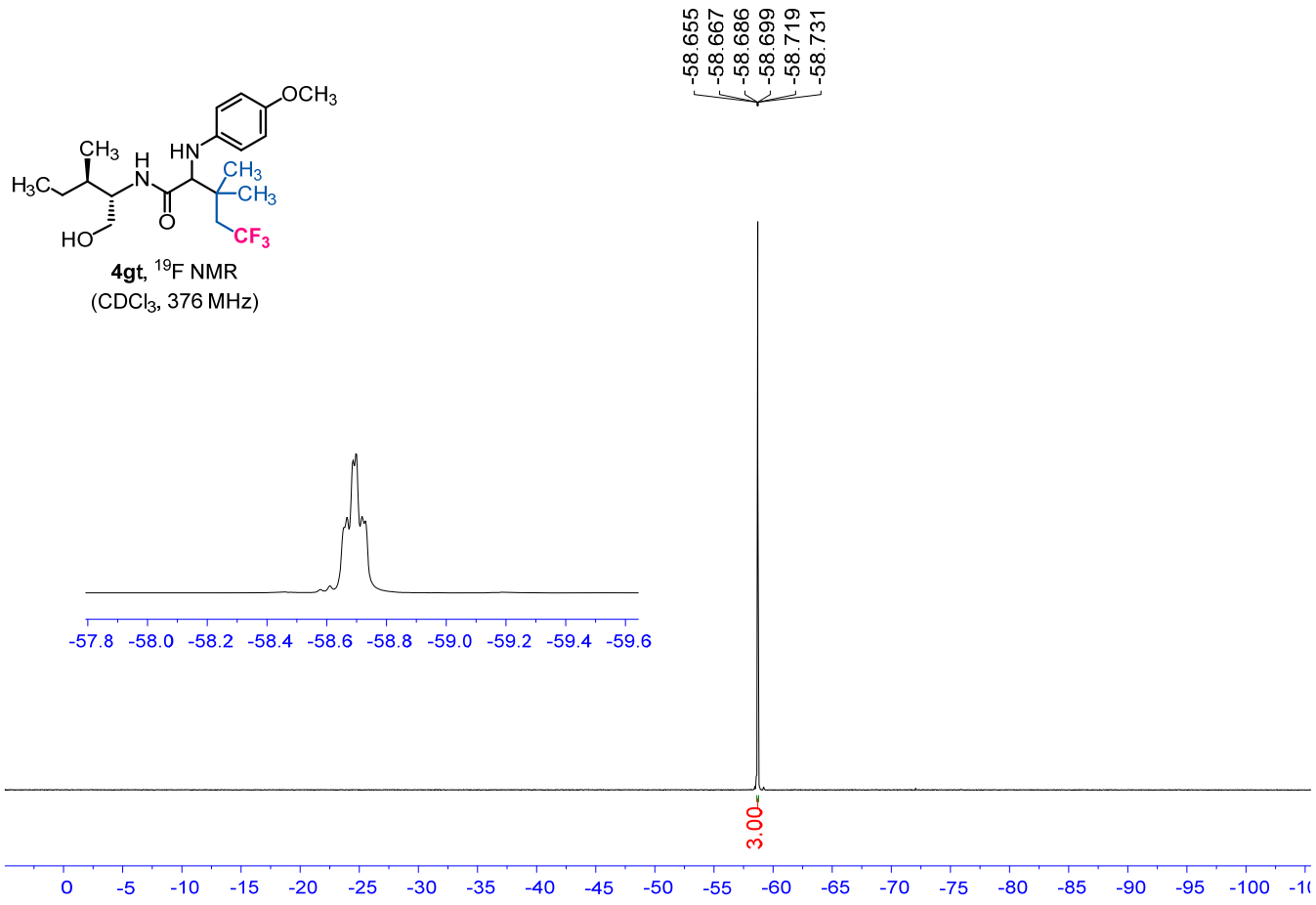
4ft, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)



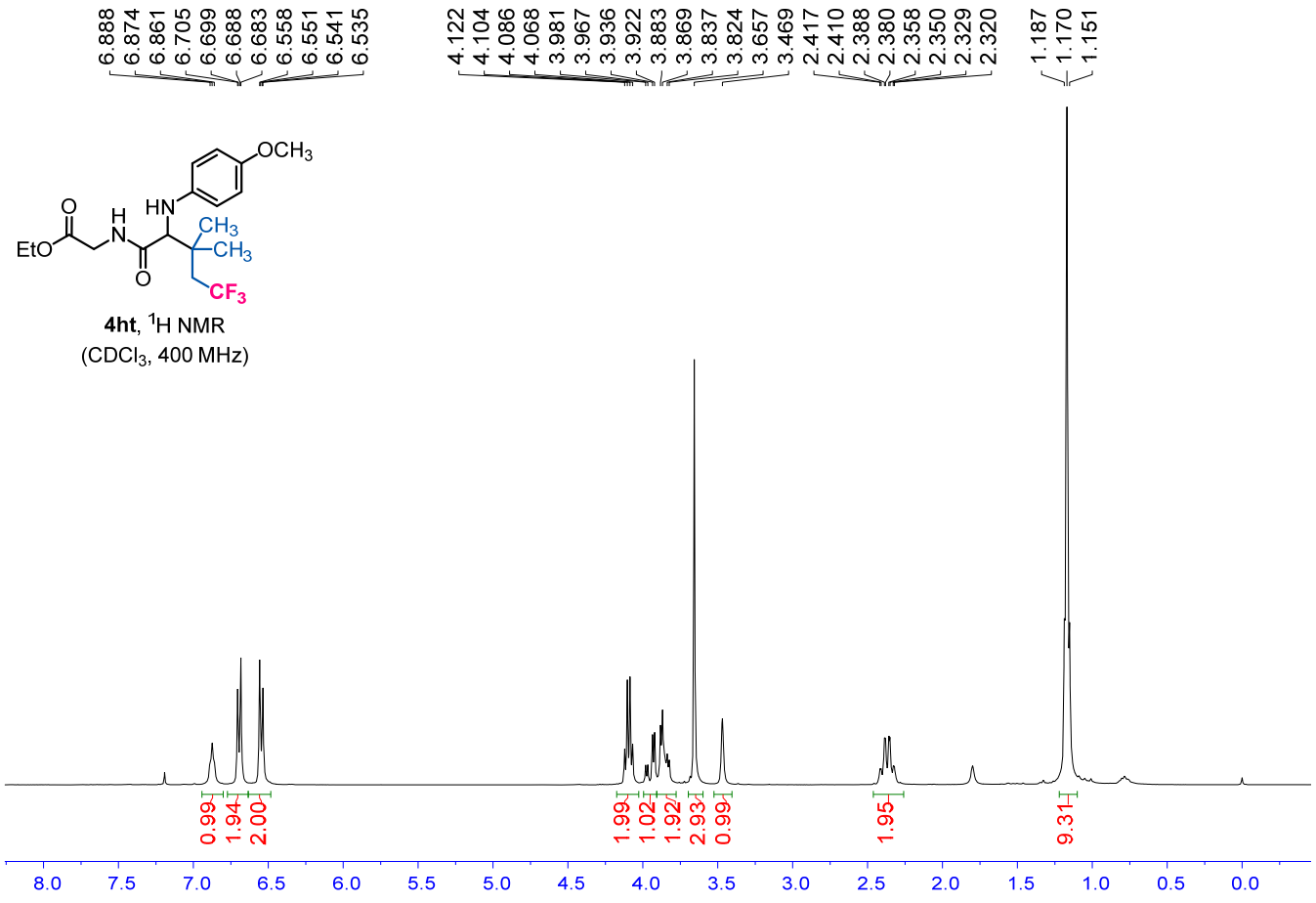
4ft, ^{19}F NMR
($CDCl_3$, 376 MHz)


6.779
6.758
6.675
6.657
6.636
6.614
6.543
6.521
3.748
3.728
3.629
3.621
3.608
3.601
3.593
3.580
3.570
3.555
3.549
3.533
3.521
3.506
3.490
2.484
2.477
2.454
2.447
2.425
2.418
2.395
2.388
1.554
1.545
1.537
1.529
1.522
1.514
1.506
1.497
1.309
1.299
1.290
1.282
1.274
1.247
1.223
0.974
0.954
0.937
0.920
0.902
OCH3
CH3
H
N
HN
H3C
CH3
CH3
HO
O
CF3
4gt, 1H NMR
(CDCl3, 400 MHz)
-CH2CF3
overlapped with
-OH
1.99
2.36
0.60
4.03
2.14
1.01
3.00
1.02
7.10
1.02
6.17
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

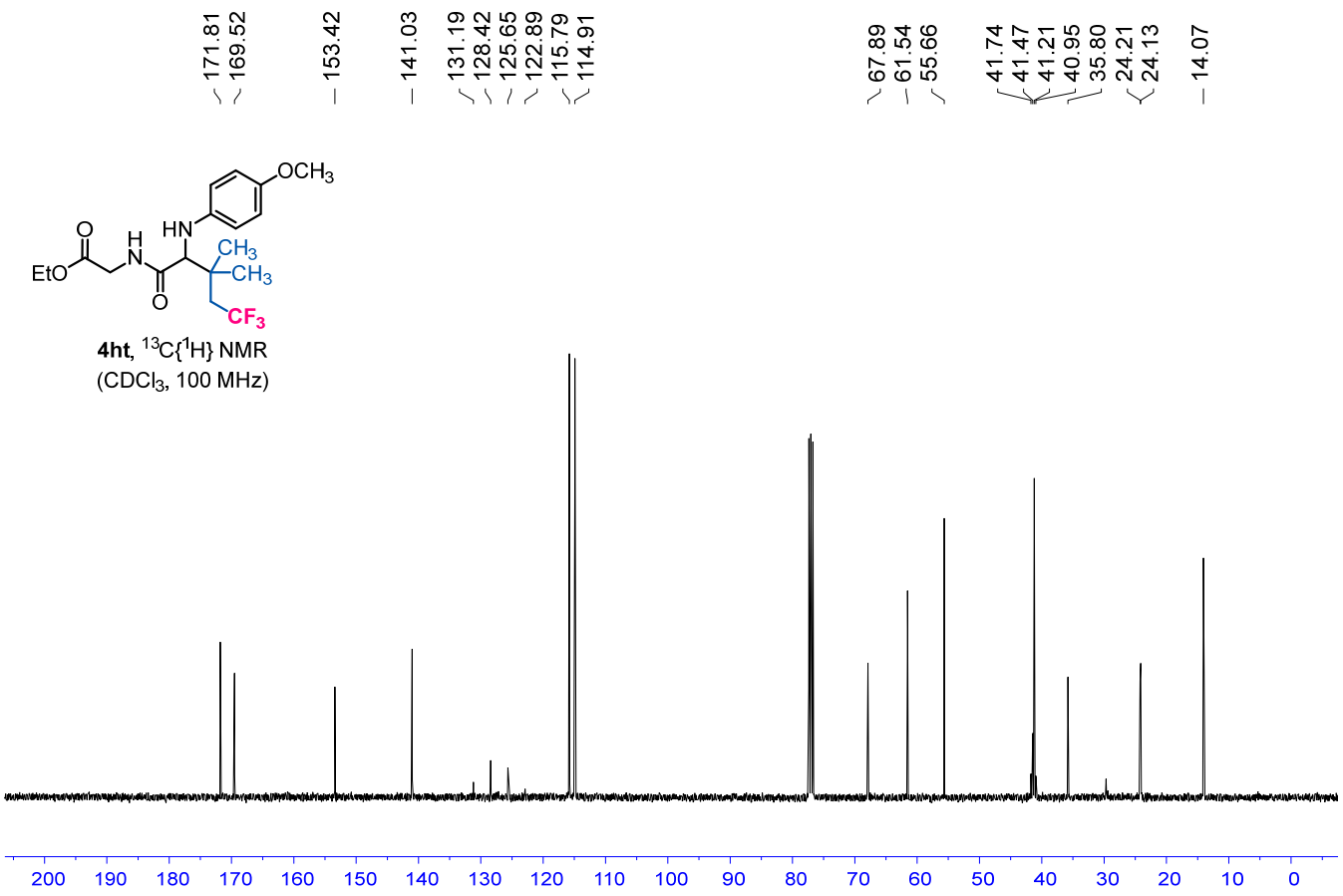

172.24
172.03
153.67
153.60
140.85
140.72
131.15
128.37
125.60
122.83
116.27
116.01
114.89
68.66
68.36
63.79
63.42
55.92
55.80
55.70
55.65
41.95
41.69
41.43
41.17
35.43
35.28
35.23
25.38
25.31
24.28
24.11
15.55
15.53
11.04
OCH3
CH3
H
N
HN
H3C
CH3
CH3
HO
O
CF3
4gt, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



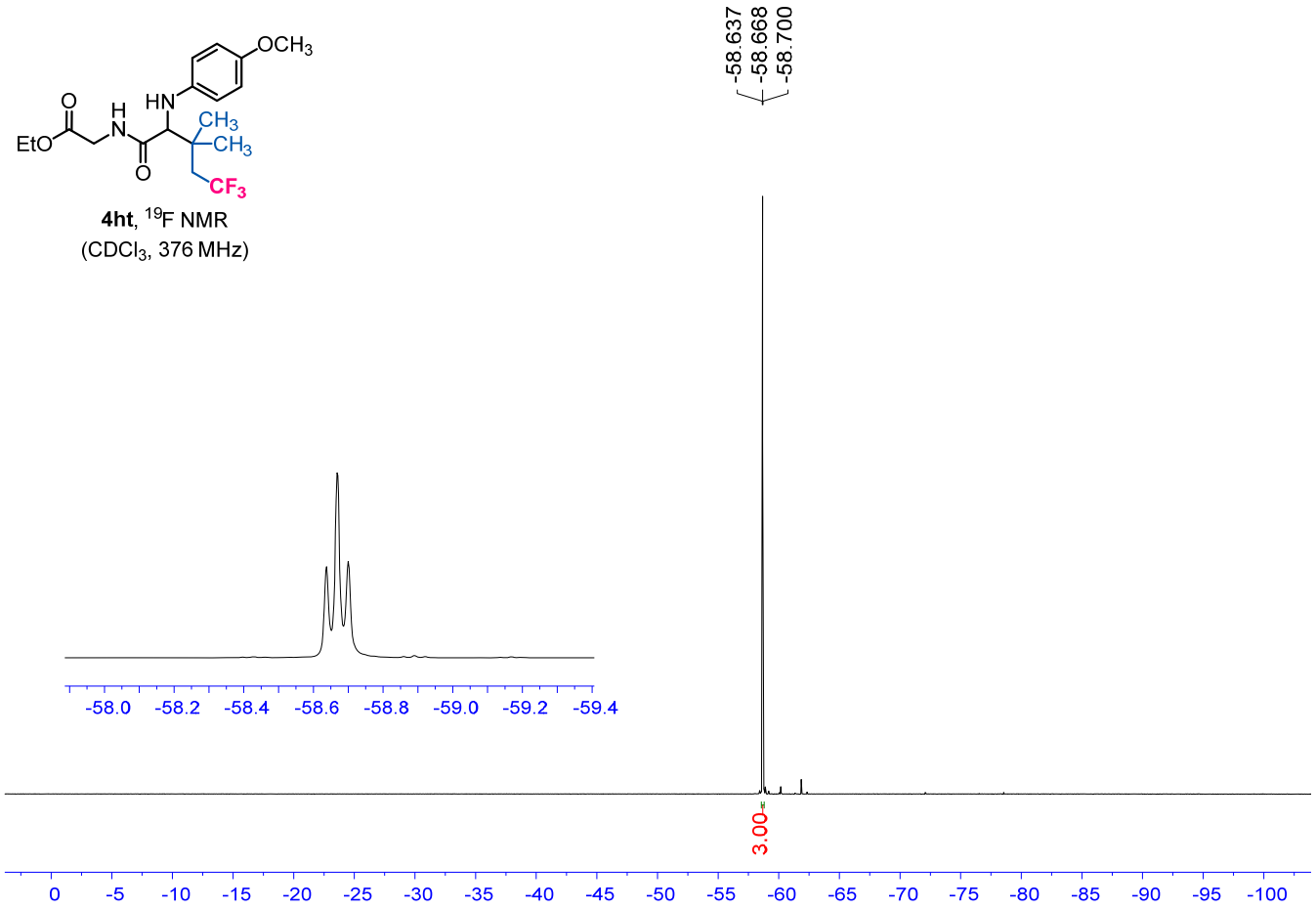
4gt, ^{19}F NMR
($CDCl_3$, 376 MHz)

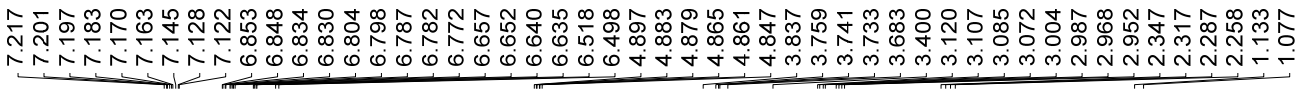


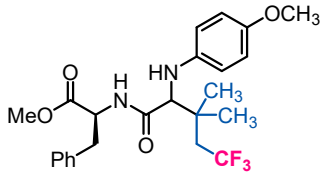
4ht, ^{1}H NMR
($CDCl_3$, 400 MHz)



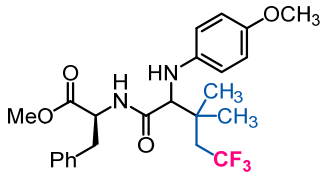
4ht, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)


OCH3
O
H
HN
EtO
N
CH3
CH3
O
CF3
4ht, 19F NMR
(CDCl3, 376 MHz)
-58.637
-58.668
-58.700
-58.0
-58.2
-58.4
-58.6
-58.8
-59.0
-59.2
-59.4
3.00
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100

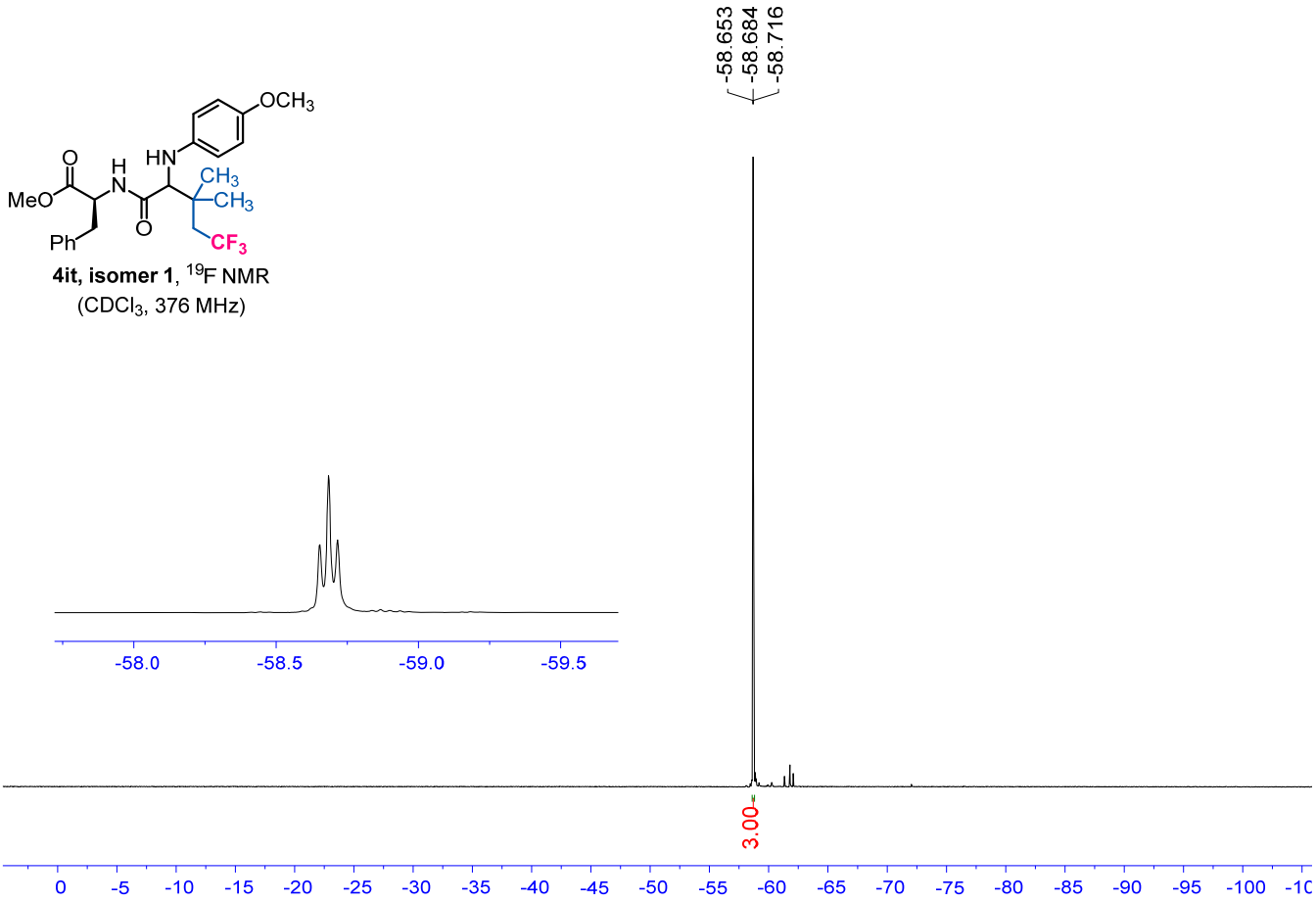




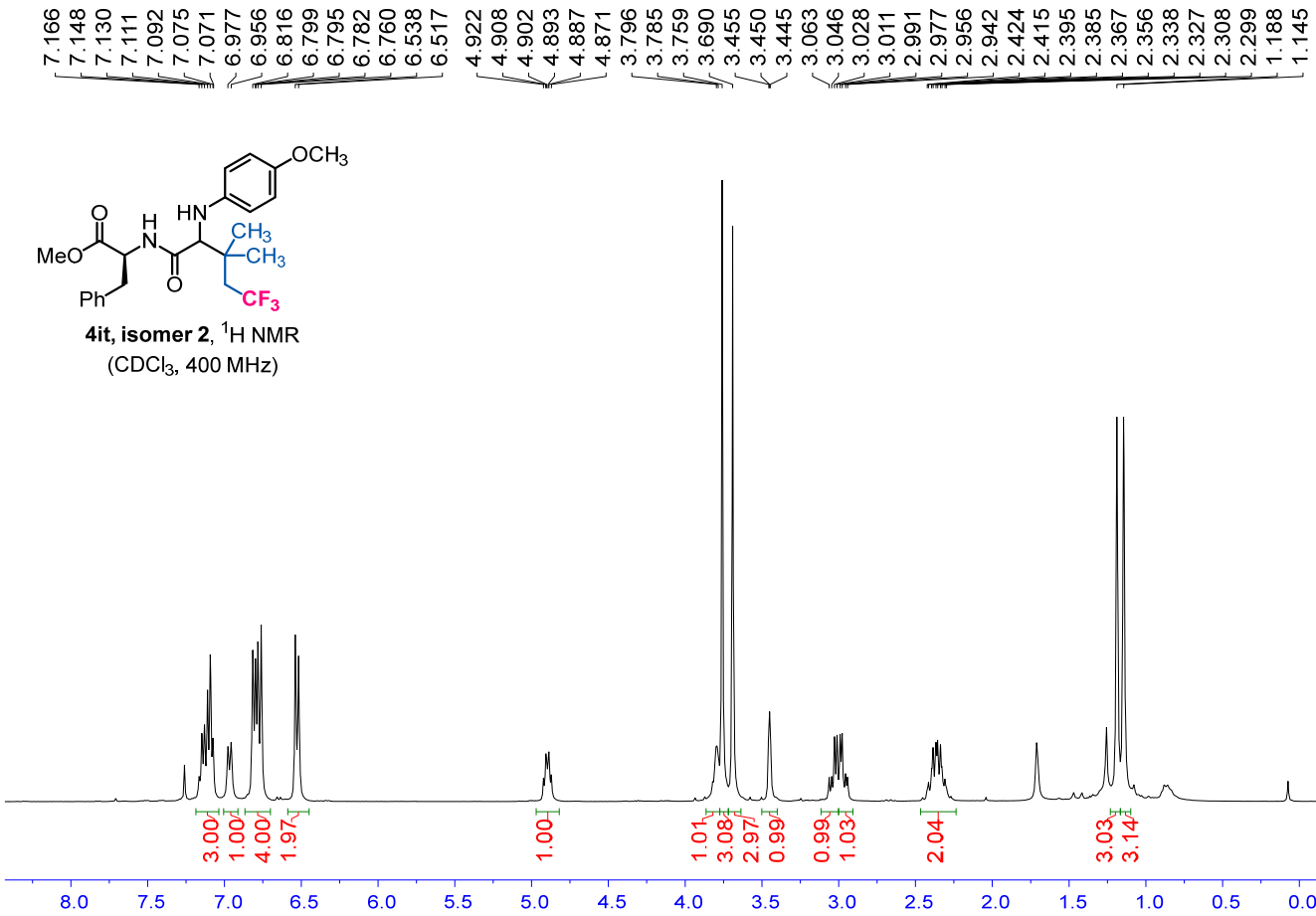
4it, isomer 1, ^{1}H NMR
($CDCl_3$, 400 MHz)



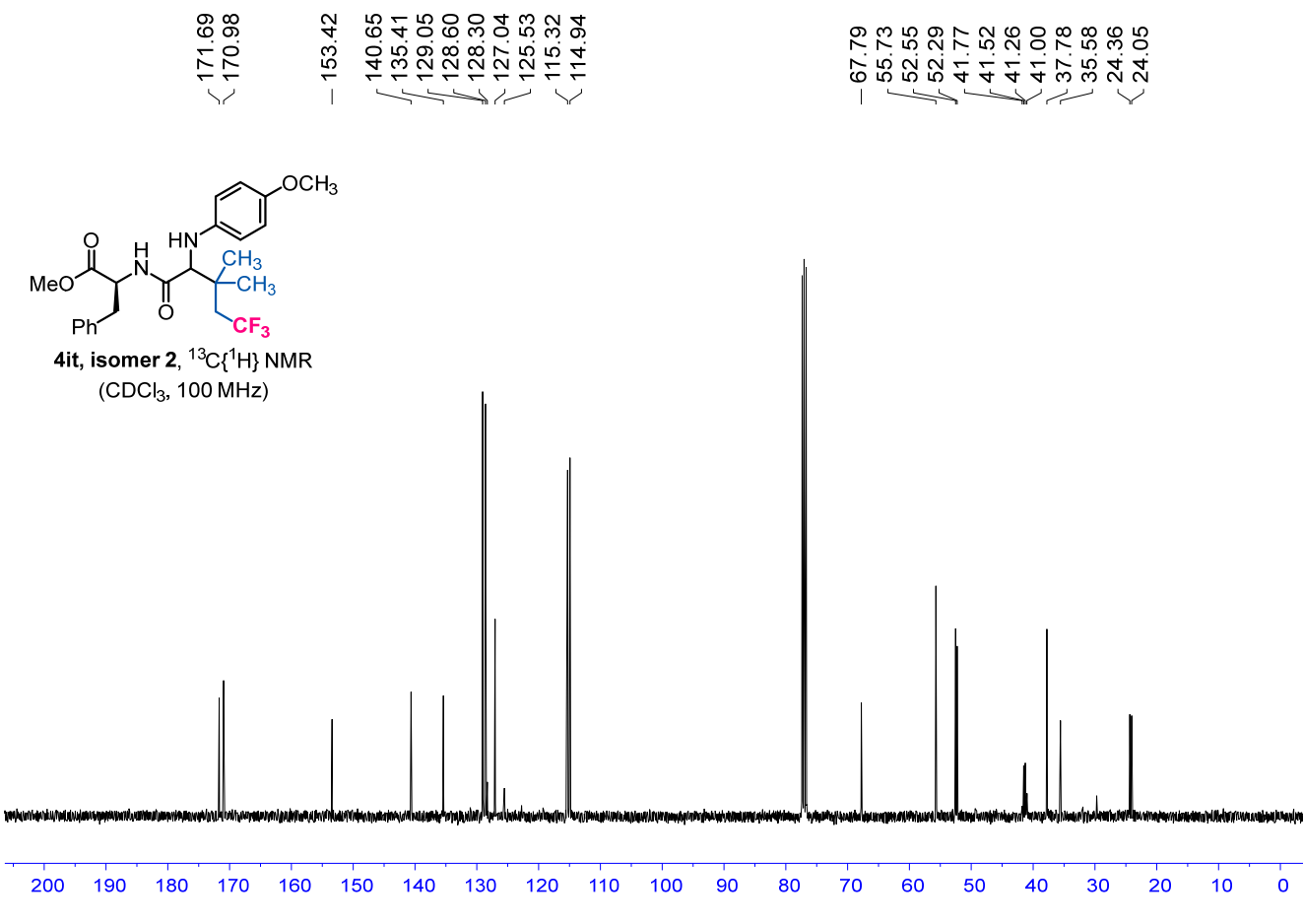
4it, isomer 1, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



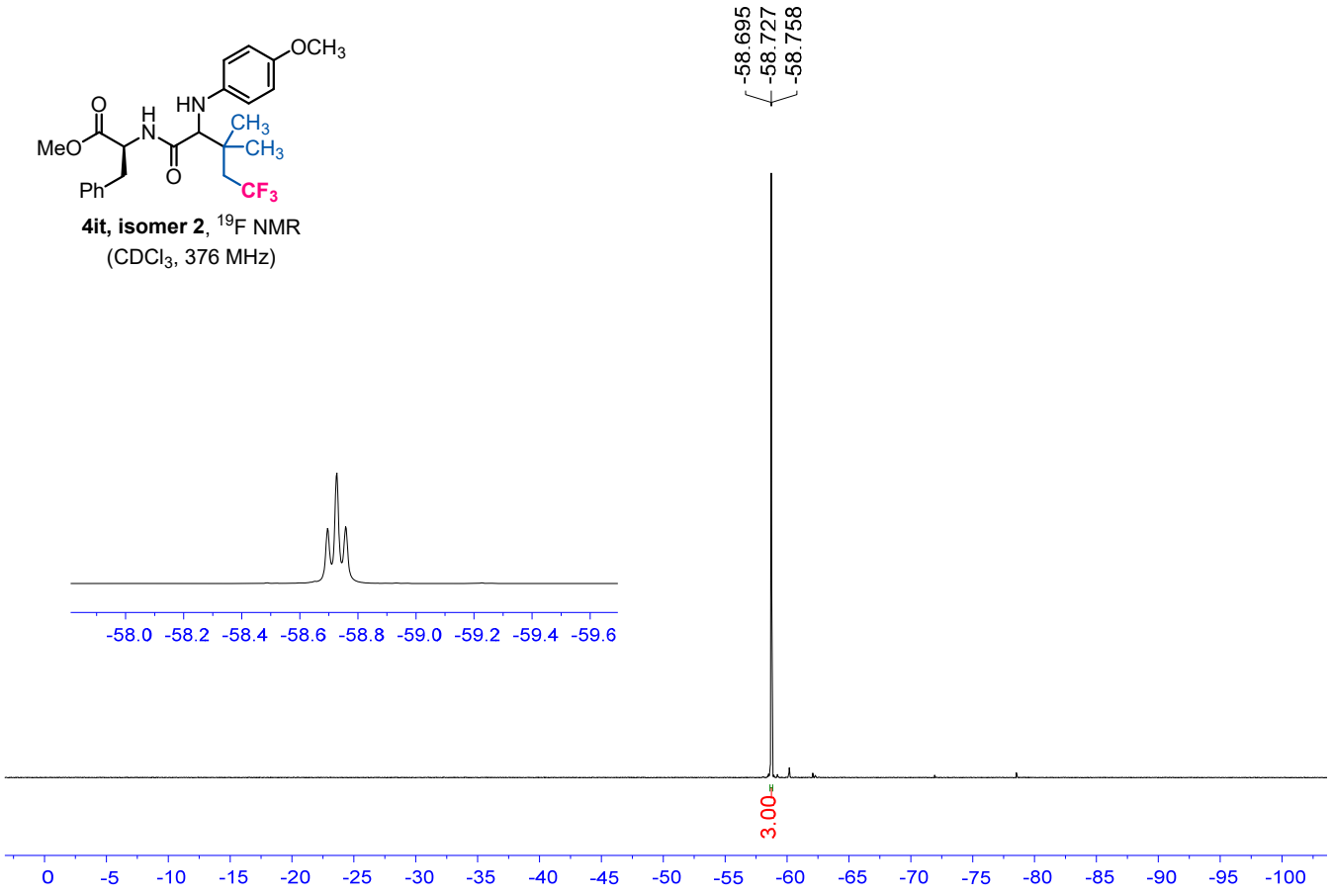
4it, isomer 1, ^{19}F NMR
($CDCl_3$, 376 MHz)



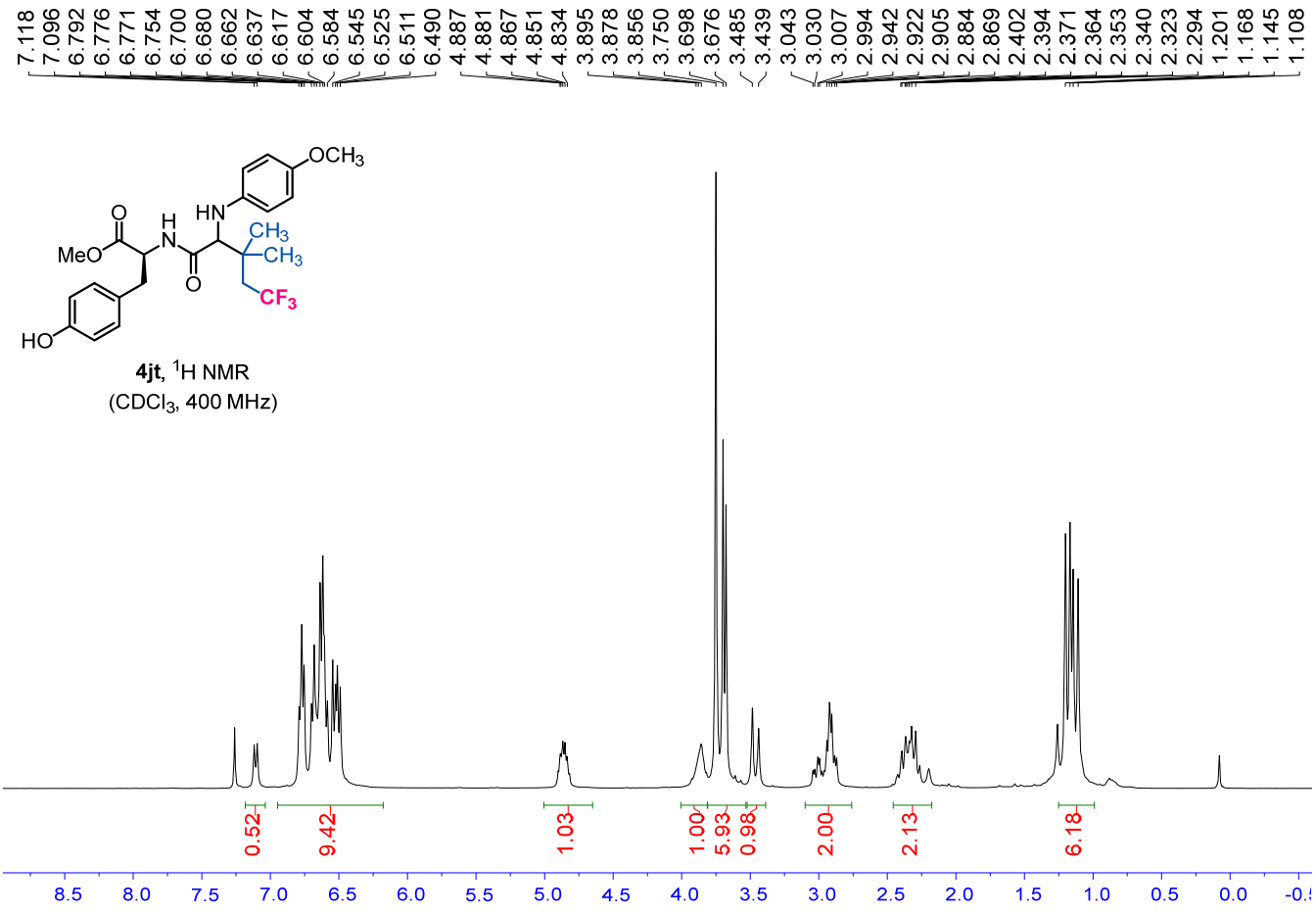
4it, isomer 2, ^{1}H NMR
($CDCl_3$, 400 MHz)

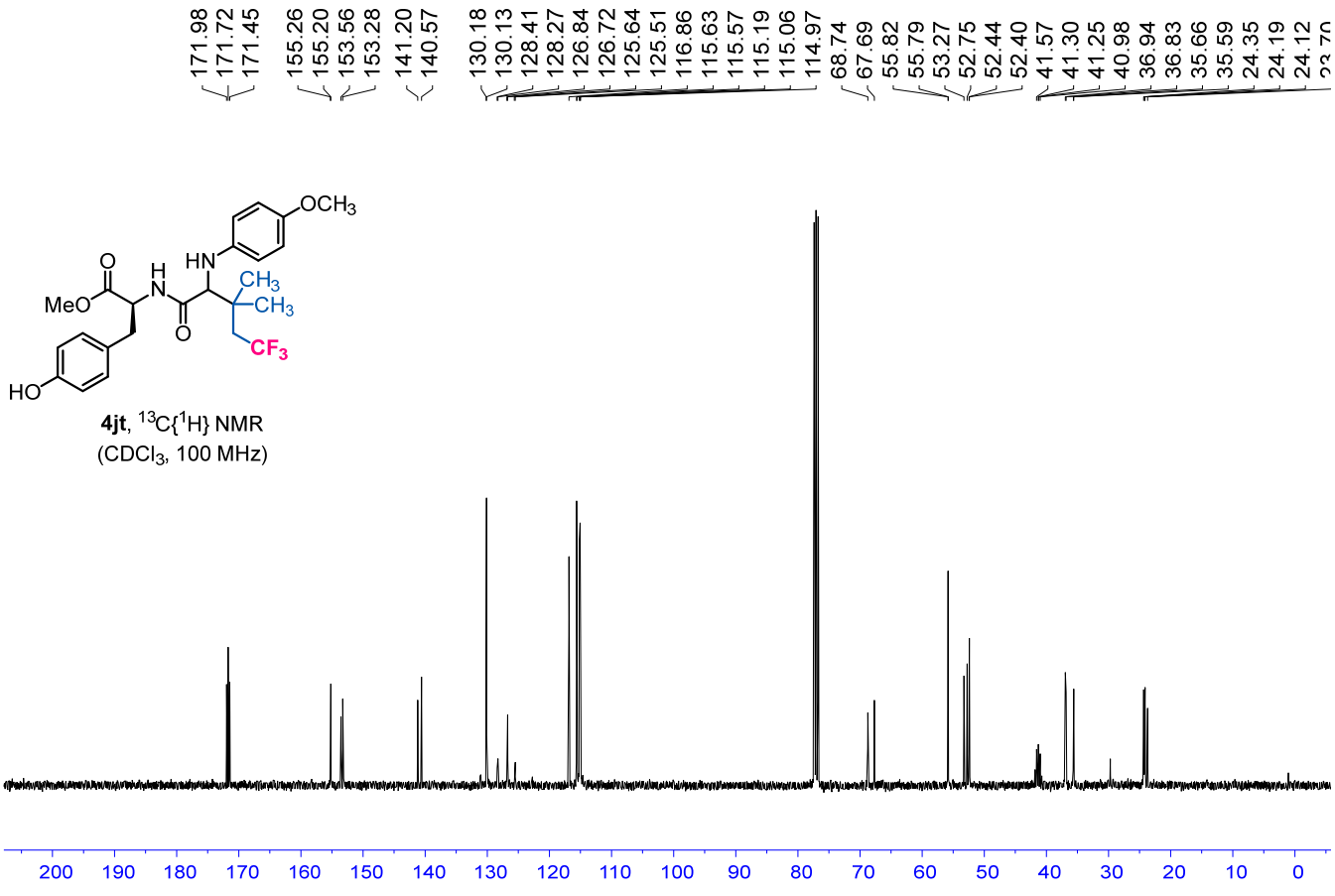


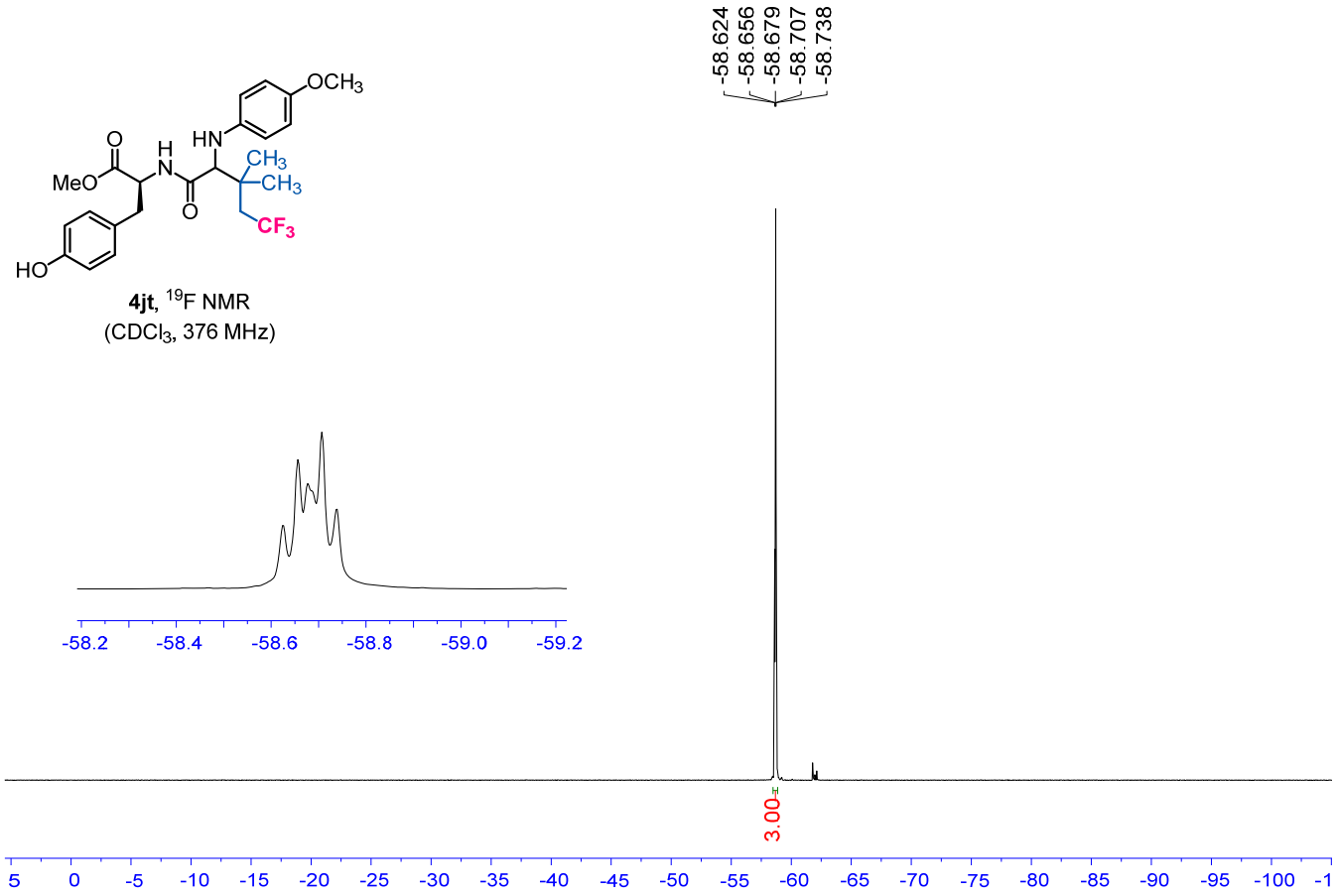
4it, isomer 2, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)

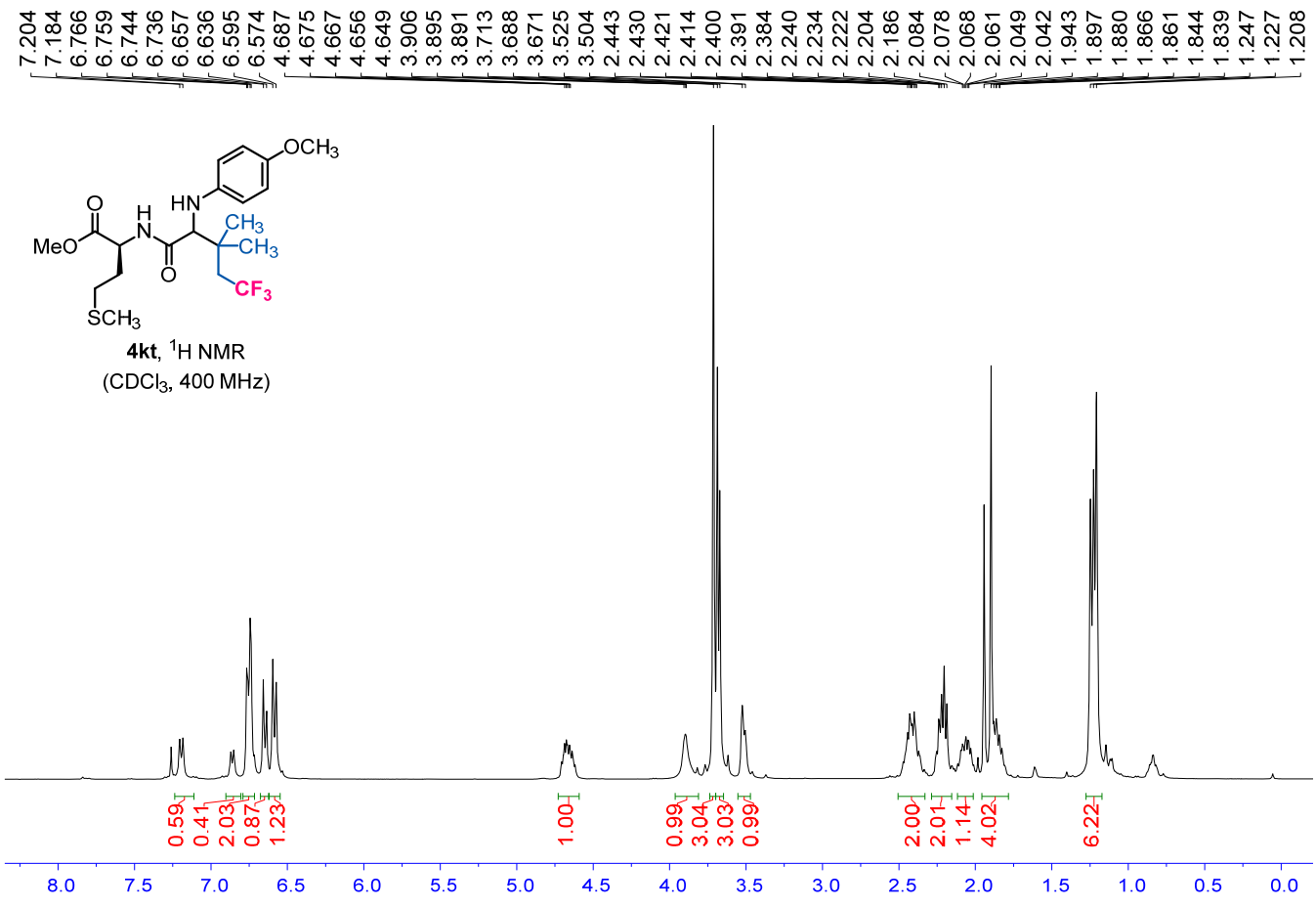


4it, isomer 2, ^{19}F NMR
($CDCl_3$, 376 MHz)

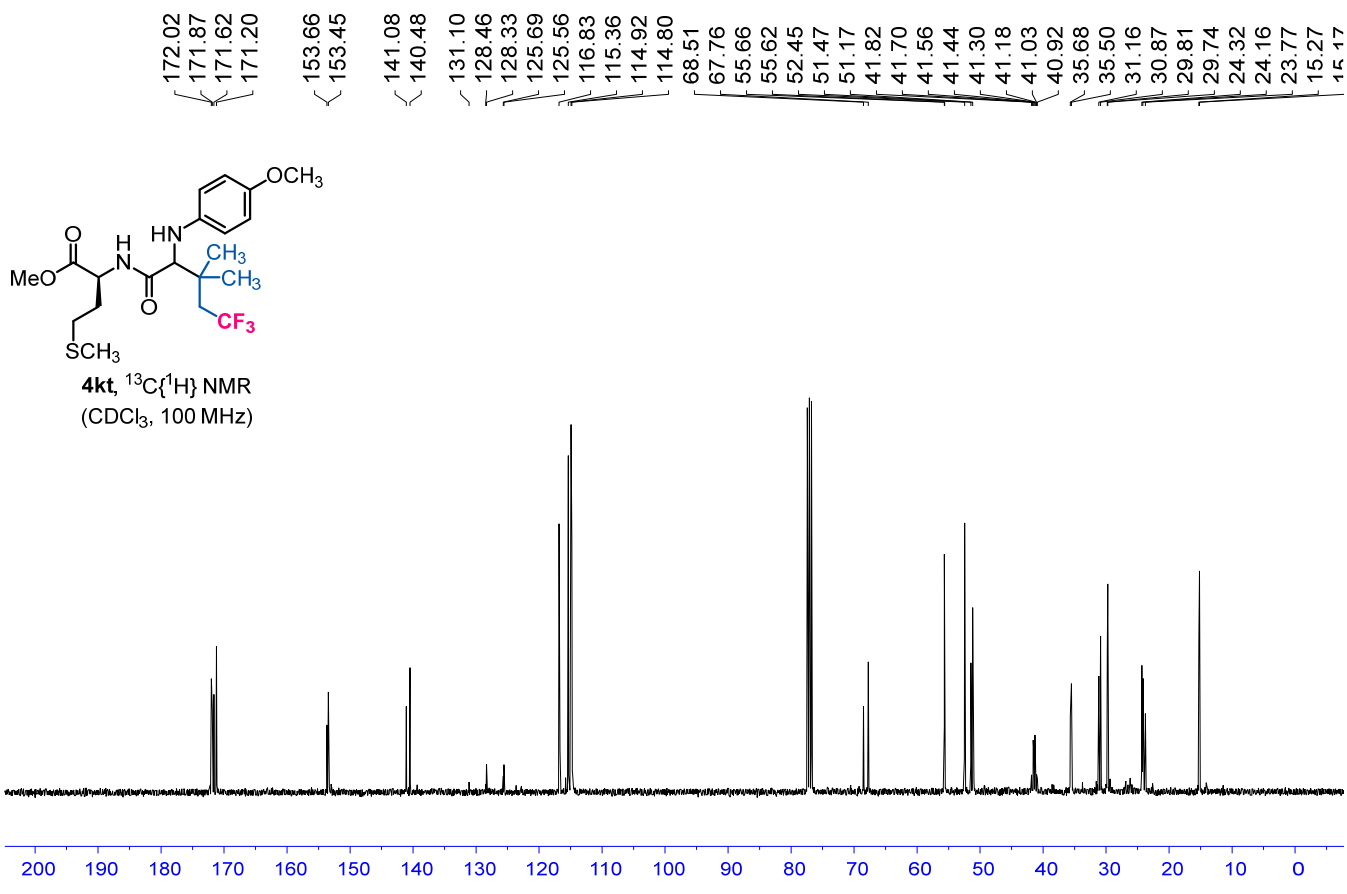

7.118
7.096
6.792
6.776
6.771
6.754
6.700
6.680
6.662
6.637
6.617
6.604
6.584
6.545
6.525
6.511
6.490
4.887
4.881
4.867
4.851
4.834
3.895
3.878
3.856
3.750
3.698
3.676
3.485
3.439
3.043
3.030
3.007
2.994
2.942
2.922
2.905
2.884
2.869
2.402
2.394
2.371
2.364
2.353
2.340
2.323
2.294
1.201
1.168
1.145
1.108
OCH3
HN
O
H
N
MeO
O
CH3
CH3
CF3
HO
4jt, 1H NMR
(CDCl3, 400 MHz)
0.52
9.42
1.03
1.00
5.93
0.98
2.00
2.13
6.18
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


171.98
171.72
171.45
155.26
155.20
153.56
153.28
141.20
140.57
130.18
130.13
128.41
128.27
126.84
126.72
125.64
125.51
116.86
115.63
115.57
115.19
115.06
114.97
68.74
67.69
55.82
55.79
53.27
52.75
52.44
52.40
41.57
41.30
41.25
40.98
36.94
36.83
35.66
35.59
24.35
24.19
24.12
OCH3
HN
O
H
N
MeO
O
CH3
CH3
CF3
HO
4jt, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

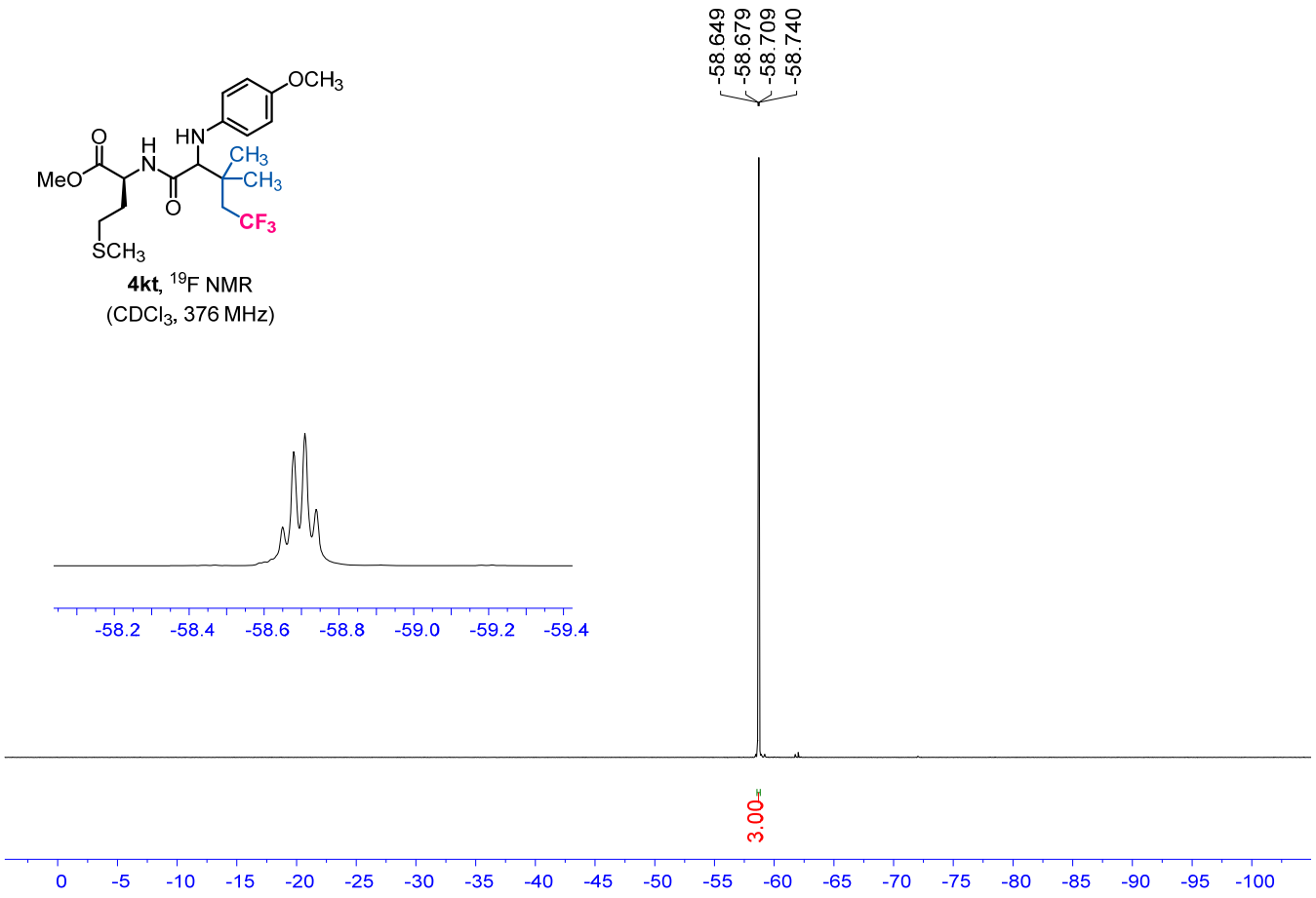

-58.624
-58.656
-58.679
-58.707
-58.738
OCH3
HN
H
N
O
MeO
O
CH3
CH3
CF3
HO
4jt, 19F NMR
(CDCl3, 376 MHz)
-58.2
-58.4
-58.6
-58.8
-59.0
-59.2
3.00
5
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-1

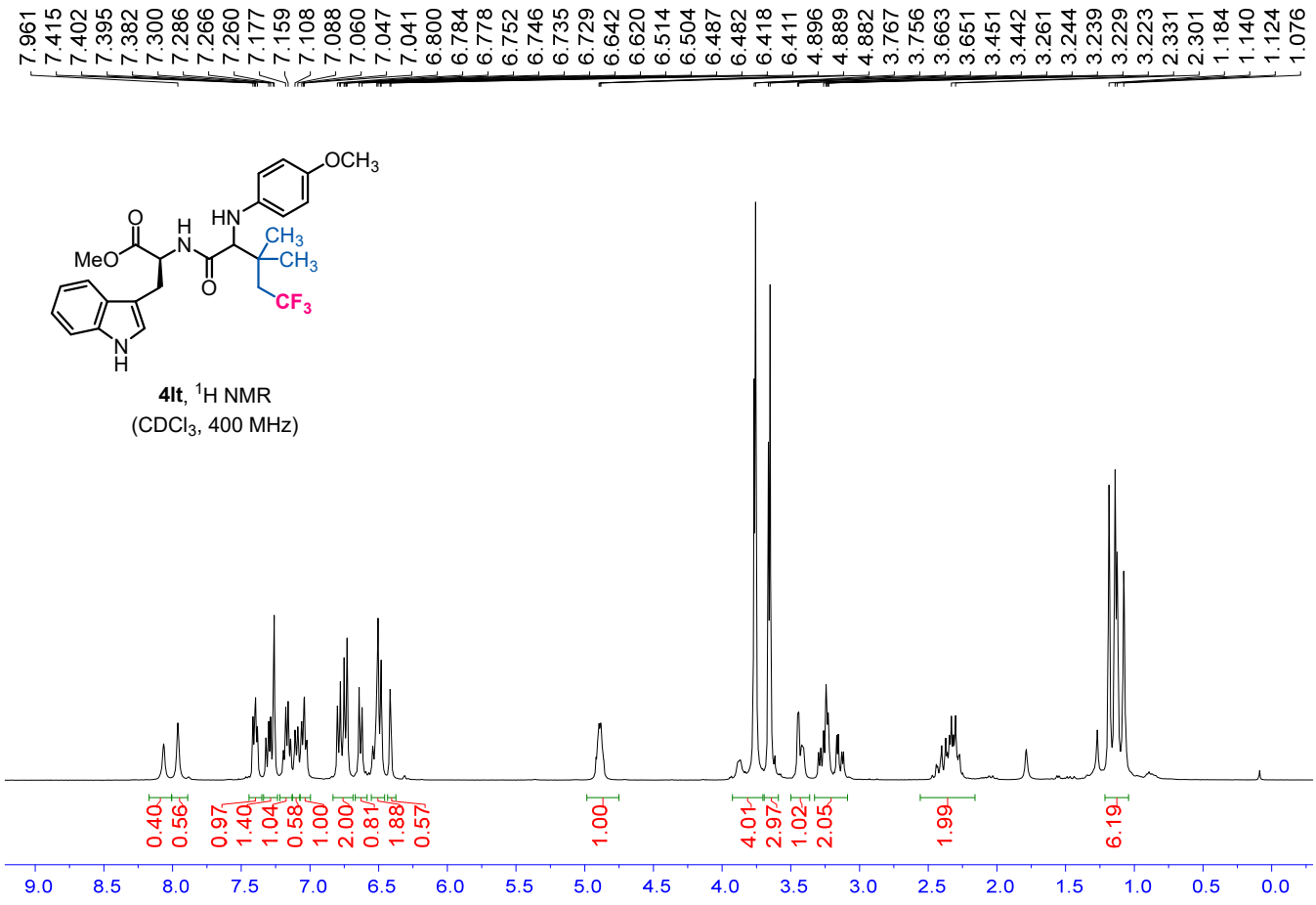


4kt, ^{1}H NMR
($CDCl_3$, 400 MHz)

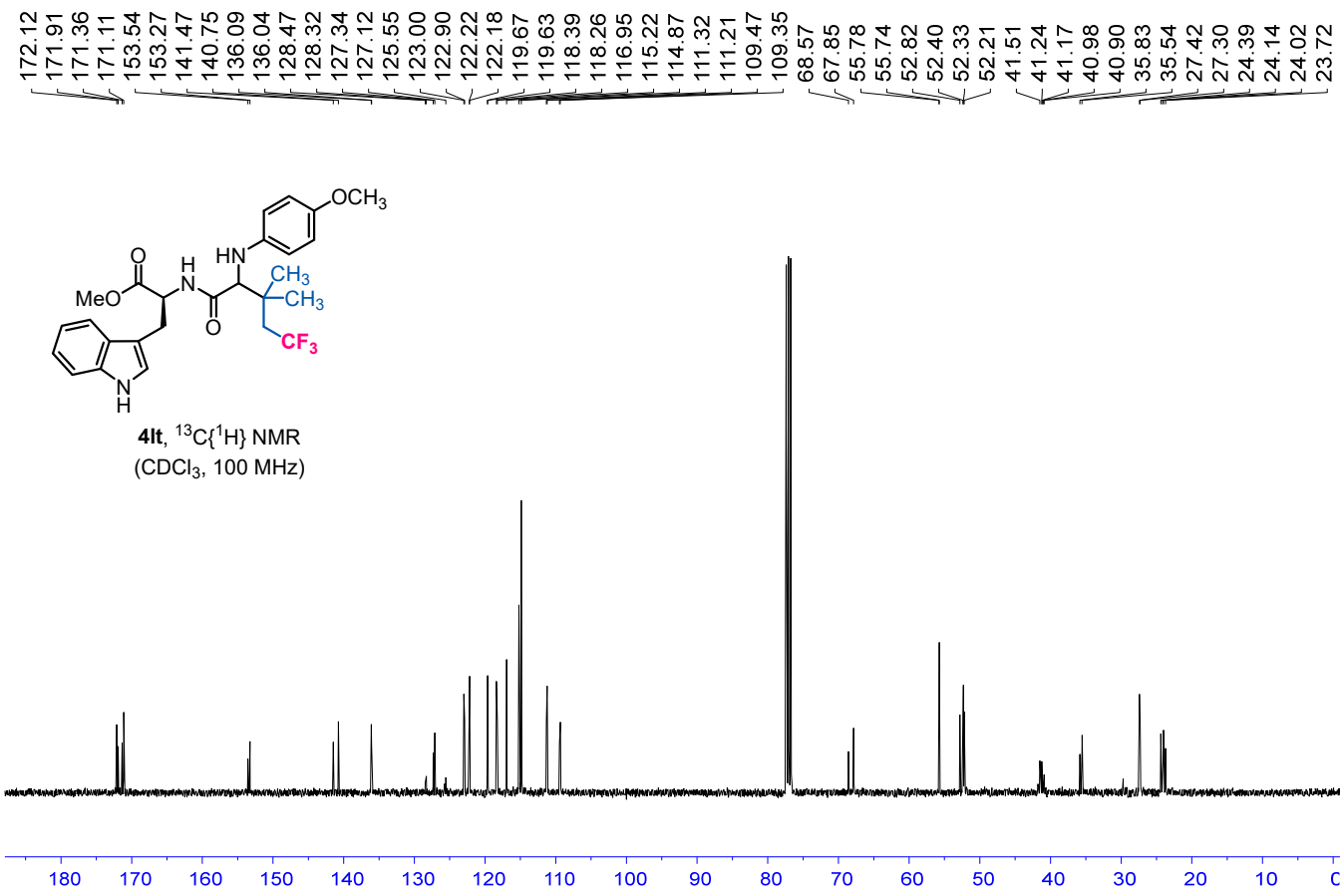


4kt, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)

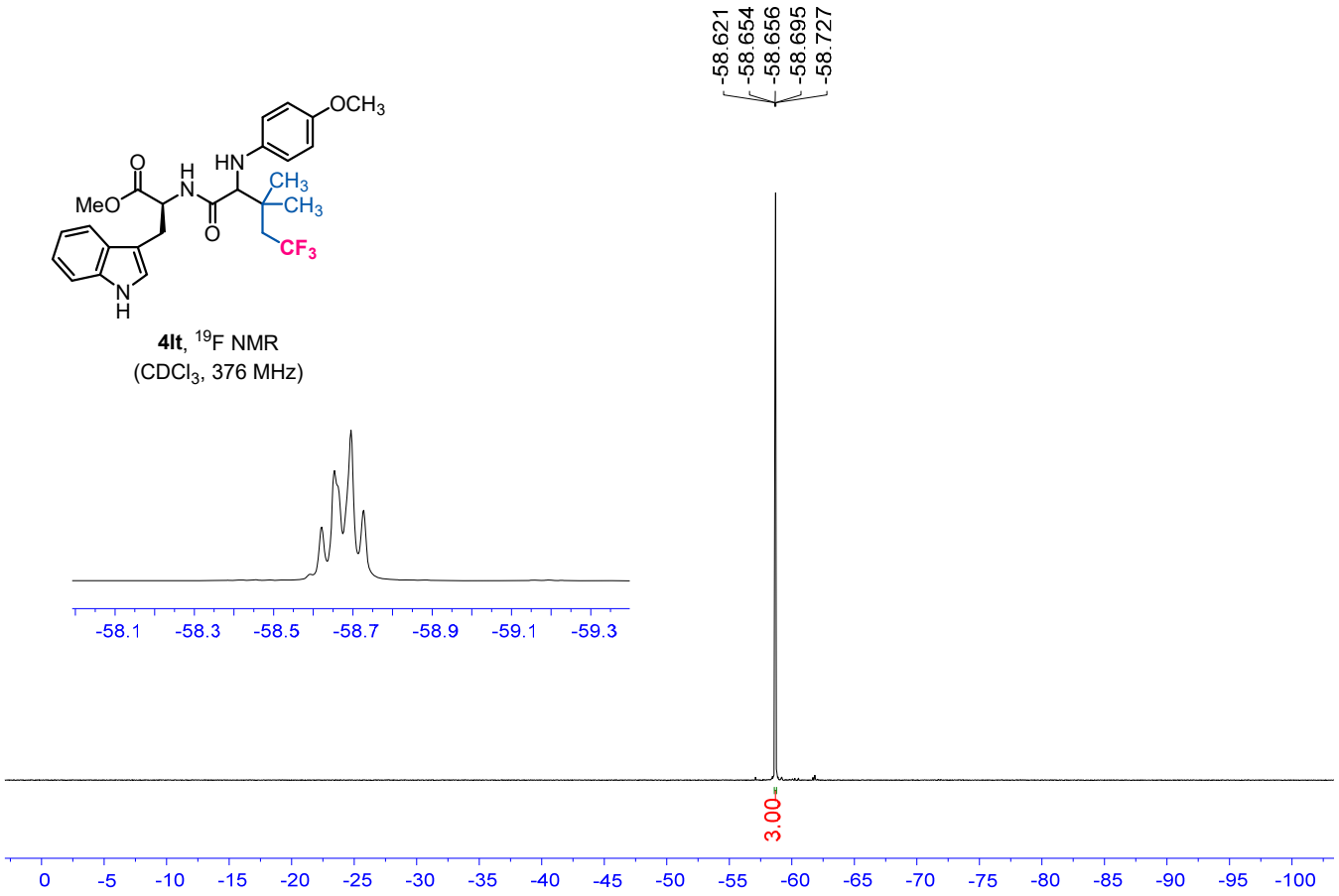

-58.649
-58.679
-58.709
-58.740
OCH3
HN
H
N
O
MeO
O
CH3
CH3
CF3
SCH3
4kt, 19F NMR
(CDCl3, 376 MHz)
-58.2
-58.4
-58.6
-58.8
-59.0
-59.2
-59.4
3.00
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100

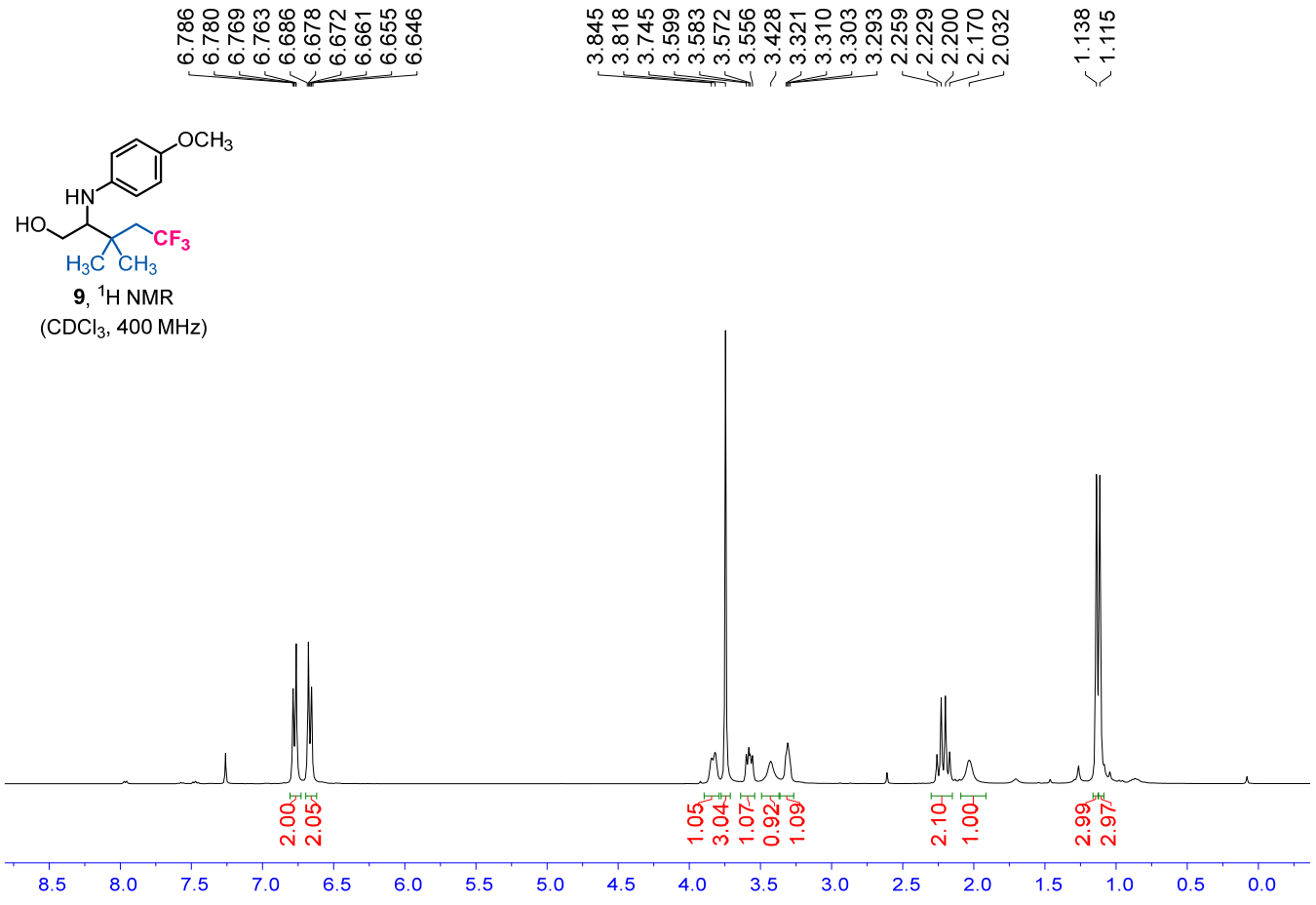


4lt, ^{1}H NMR
($CDCl_3$, 400 MHz)

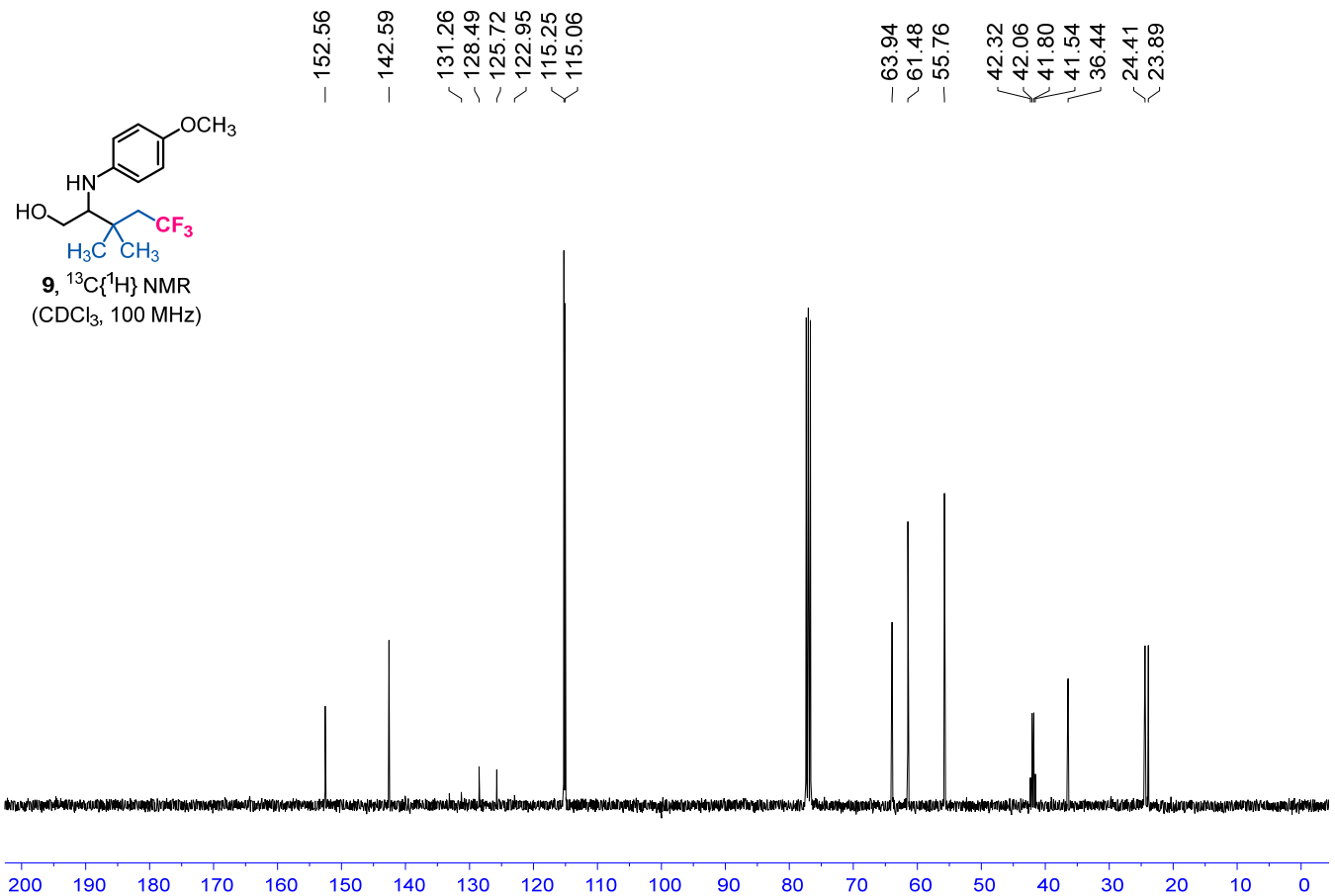


4lt, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)

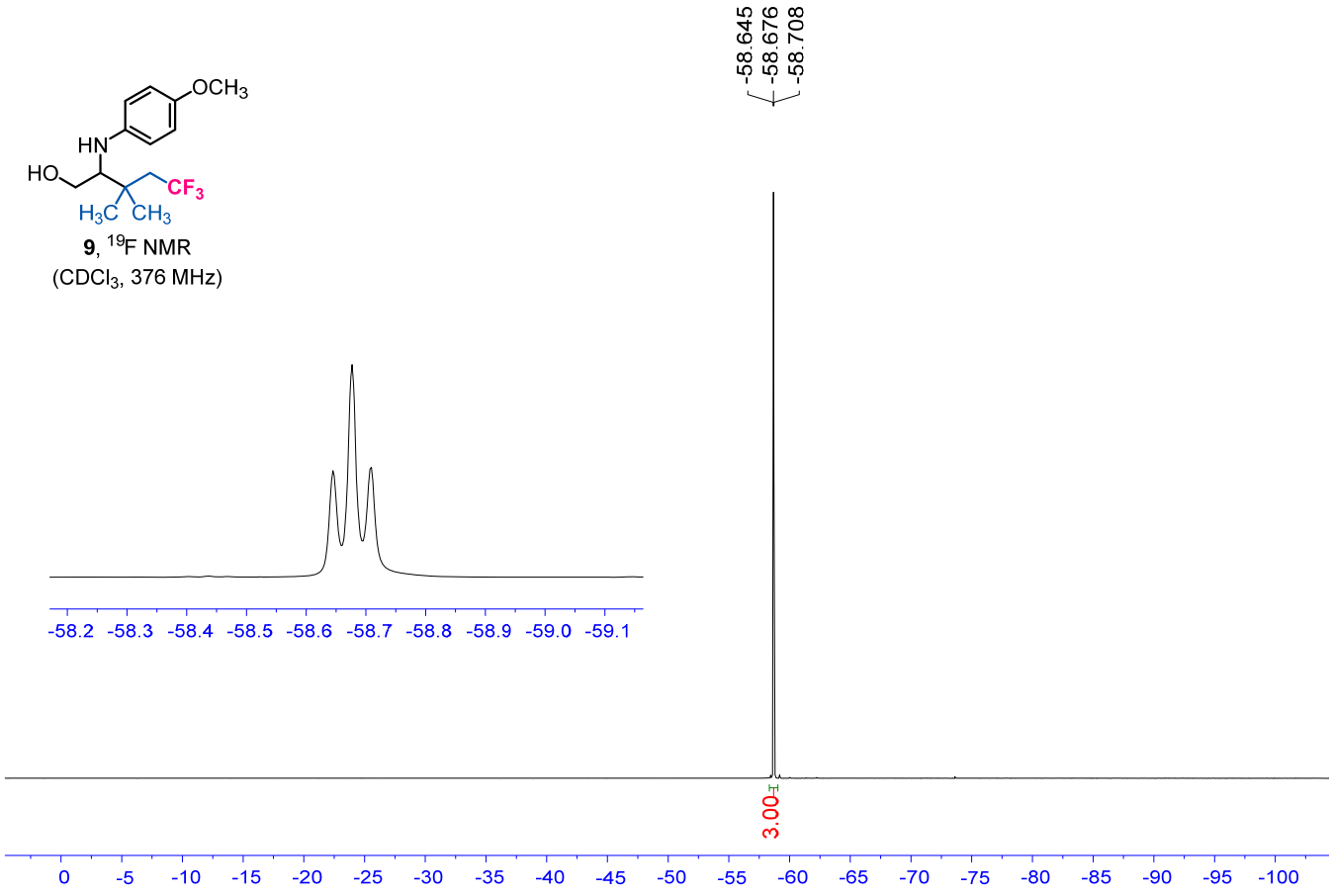

-58.621
-58.654
-58.656
-58.695
-58.727
OCH3
HN
H
N
MeO
O
O
CH3
CH3
CF3
N
H
4lt, 19F NMR
(CDCl3, 376 MHz)
-58.1
-58.3
-58.5
-58.7
-58.9
-59.1
-59.3
3.00
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100

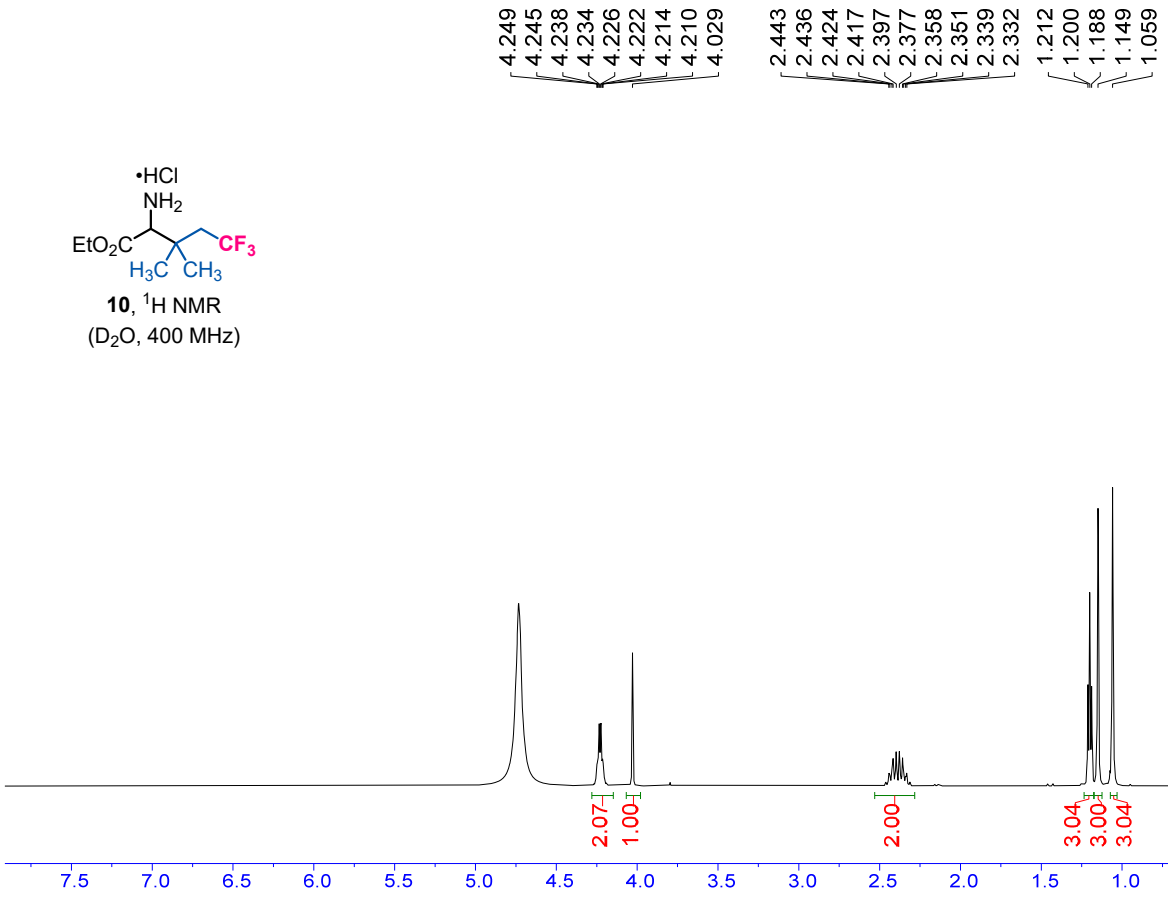


9, ^{1}H NMR
($CDCl_3$, 400 MHz)

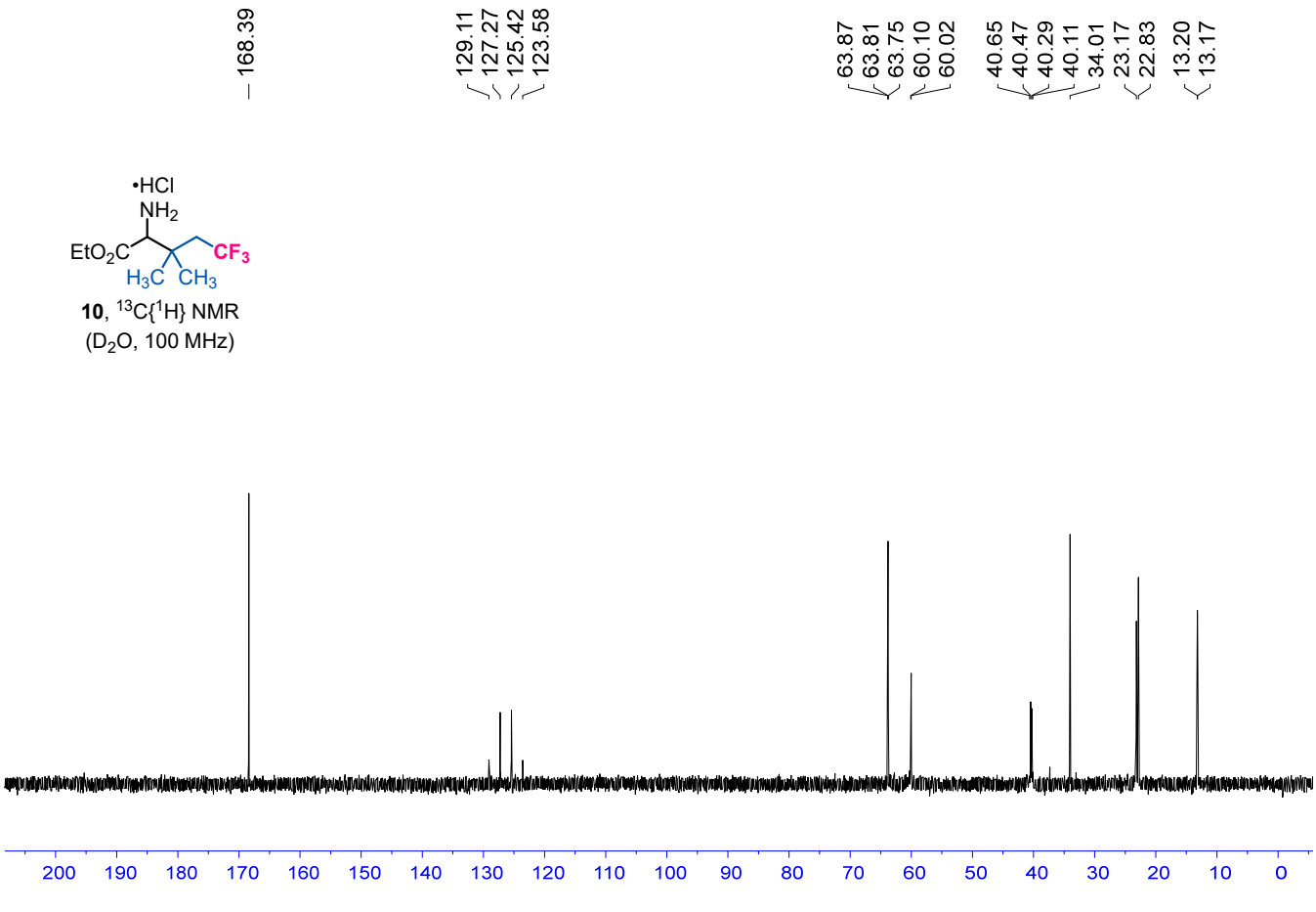


9, ^{13}C{^{1}H} NMR
($CDCl_3$, 100 MHz)

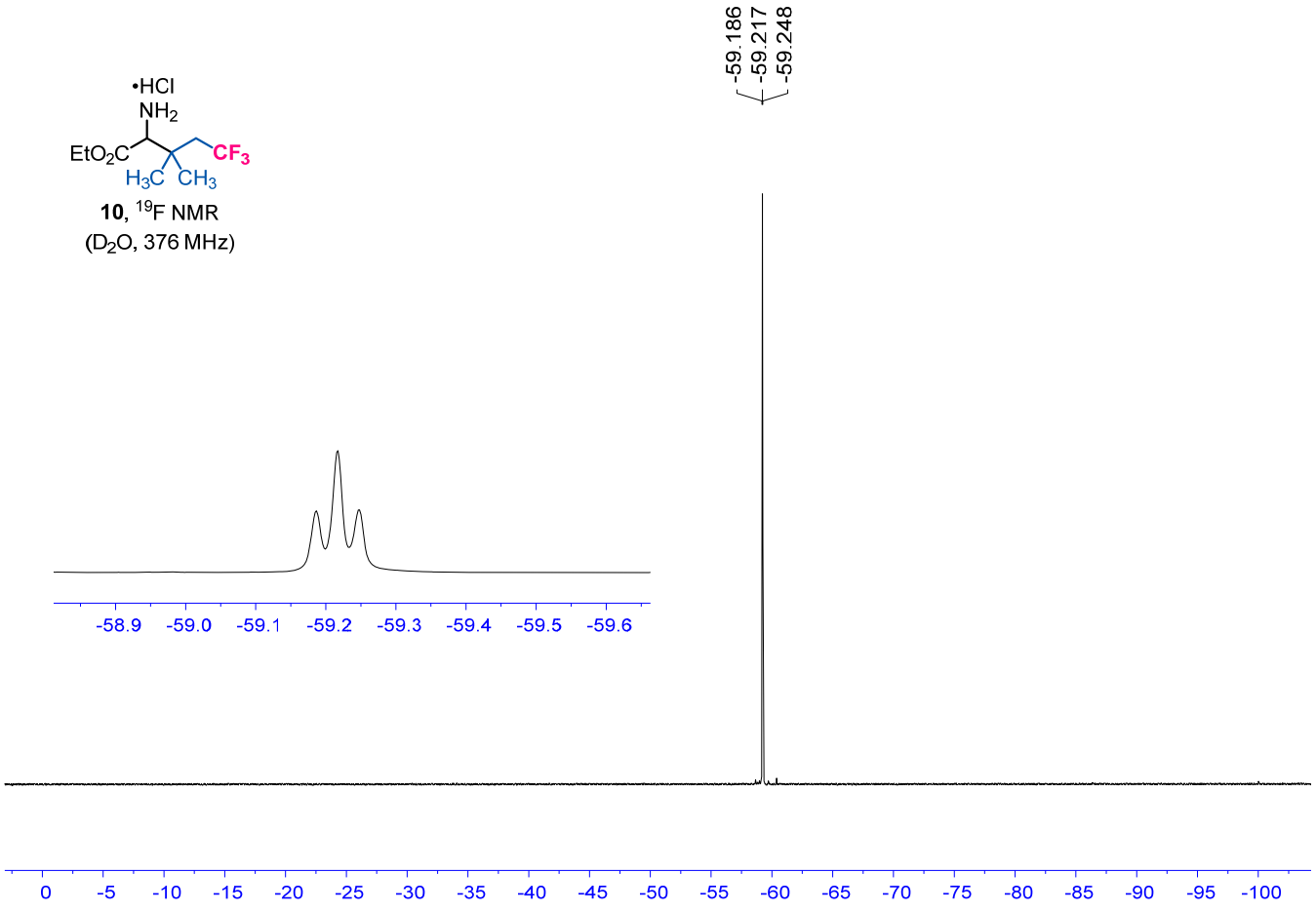

OCH3
HN
HO
CF3
H3C CH3
9, 19F NMR
(CDCl3, 376 MHz)
-58.645
-58.676
-58.708
3.00
-58.2 -58.3 -58.4 -58.5 -58.6 -58.7 -58.8 -58.9 -59.0 -59.1
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100

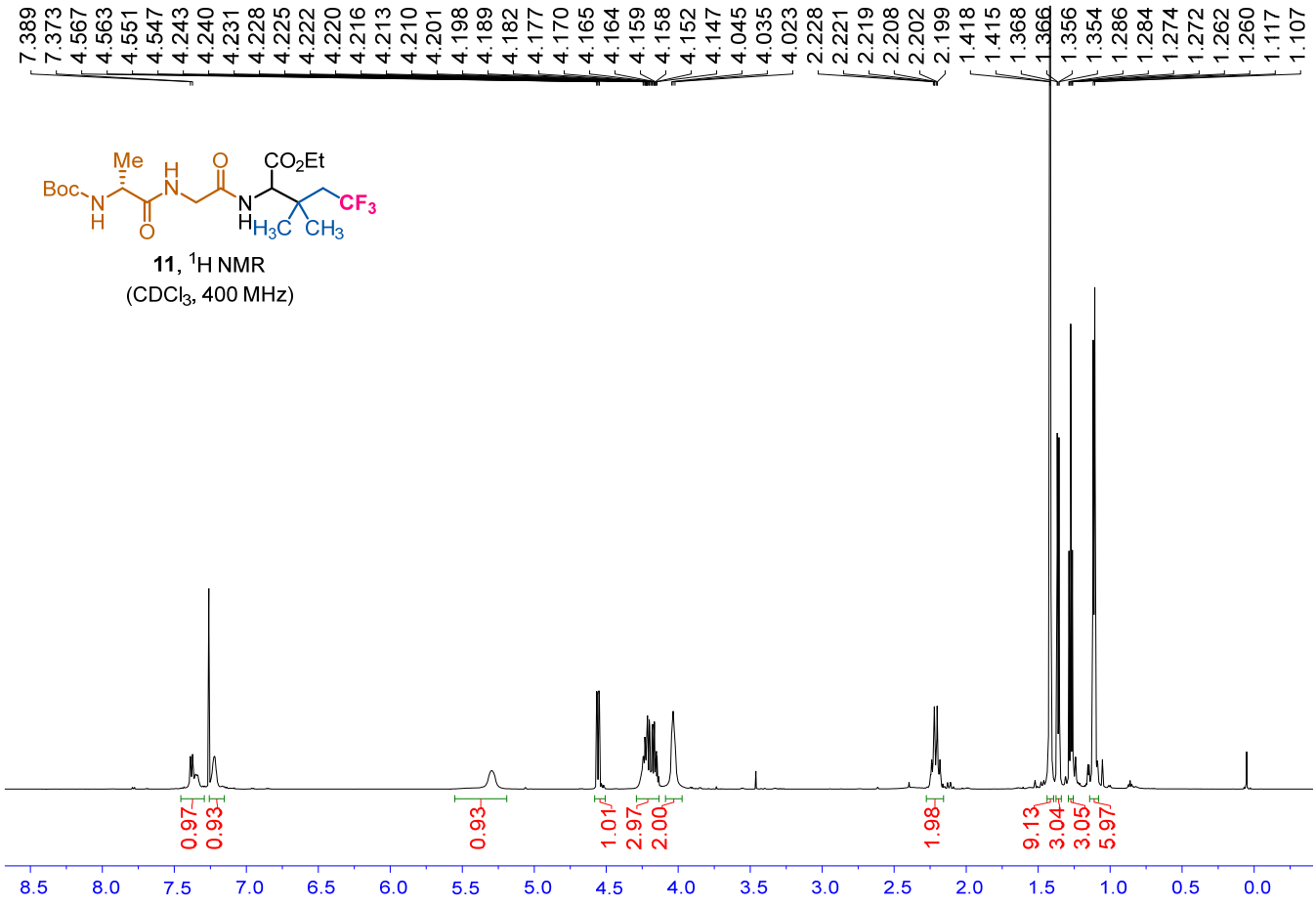


10, ^{1}H NMR
(D_2O, 400 MHz)

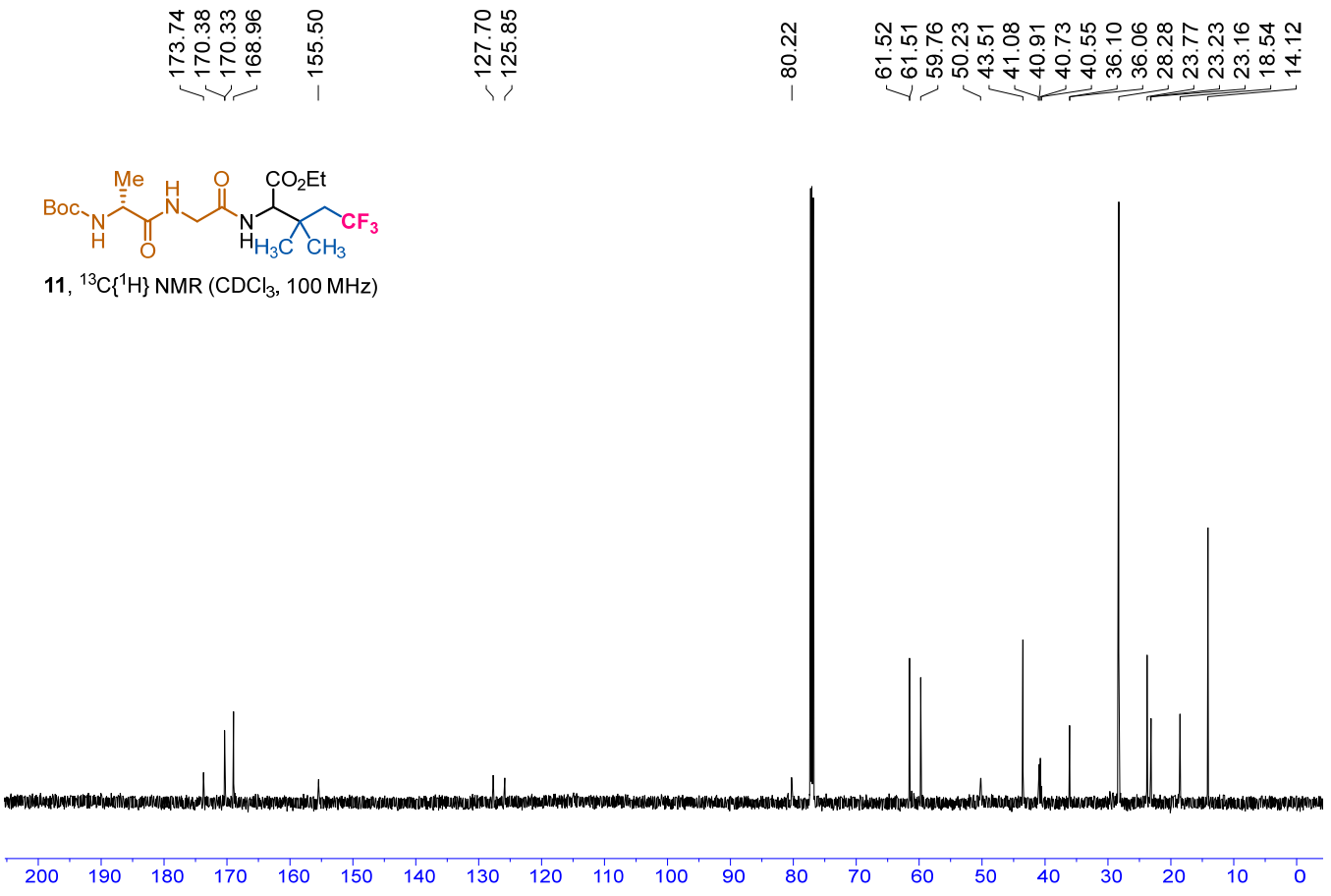


10, $^{13}C\{^{1}H\}$ NMR
(D_2O, 100 MHz)

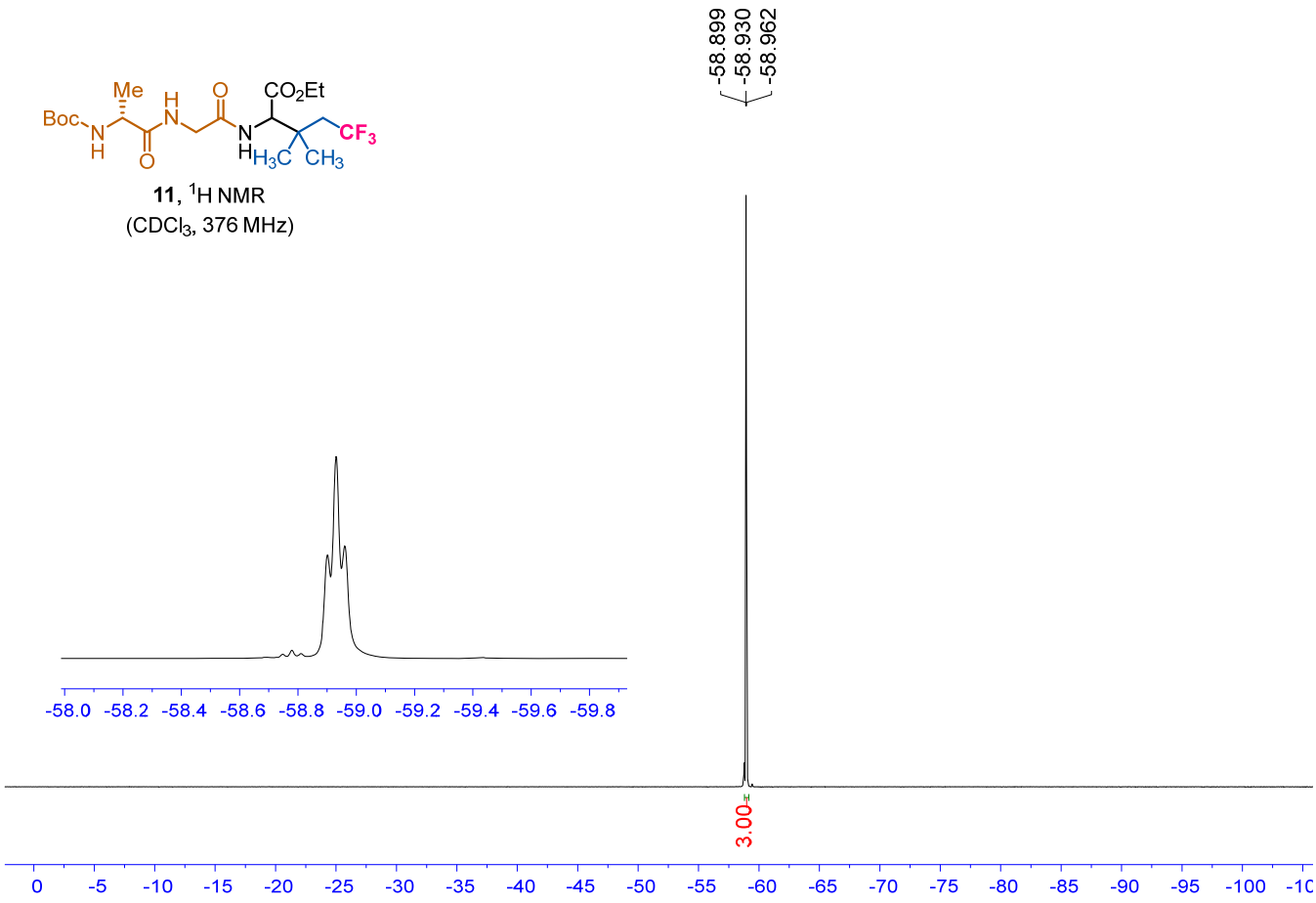

•HCl
NH2
EtO2C
CF3
H3C CH3
10, 19F NMR
(D2O, 376 MHz)
-59.186
-59.217
-59.248
-58.9 -59.0 -59.1 -59.2 -59.3 -59.4 -59.5 -59.6
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100

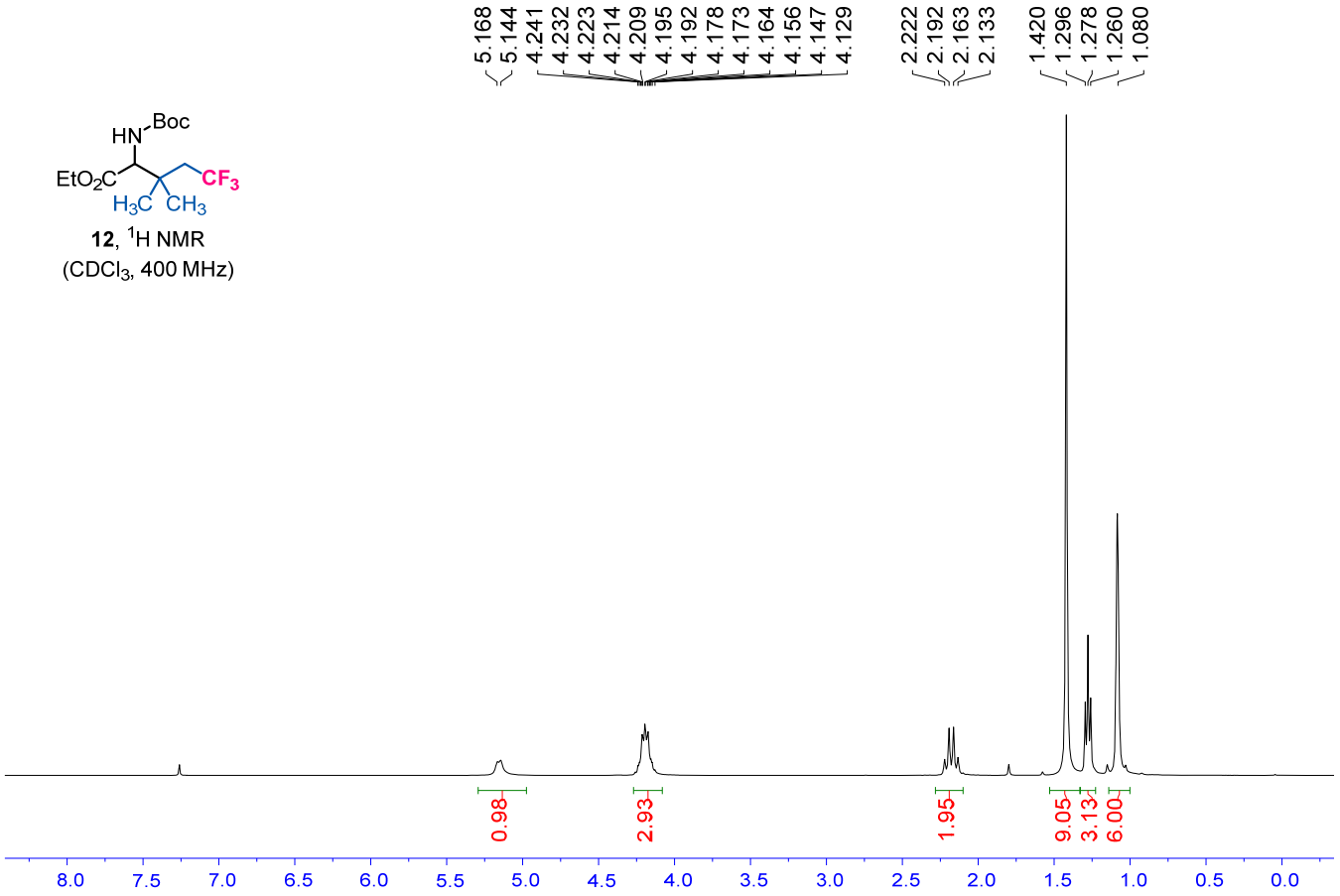


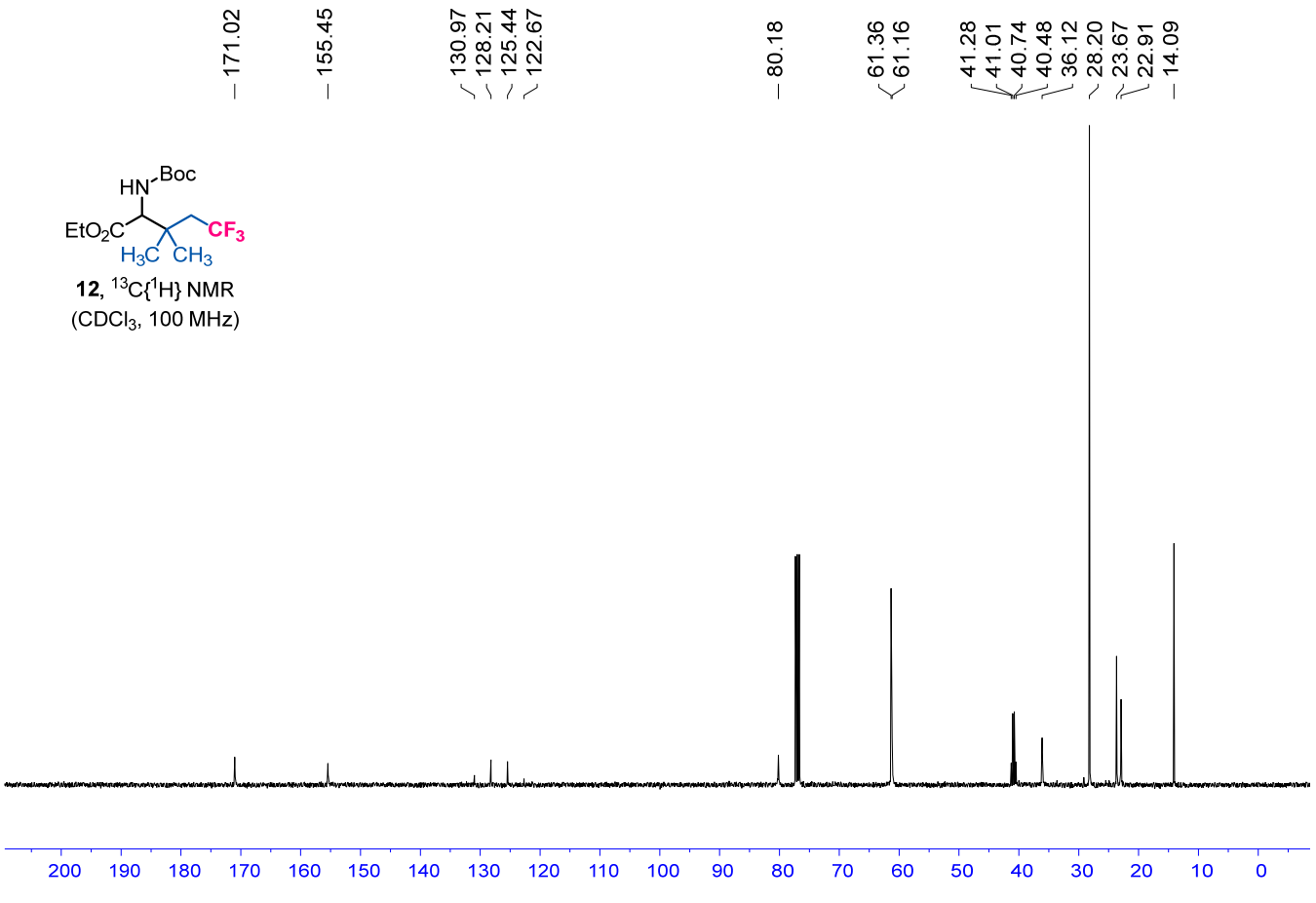
11, ^{1}H NMR
($CDCl_3$, 400 MHz)

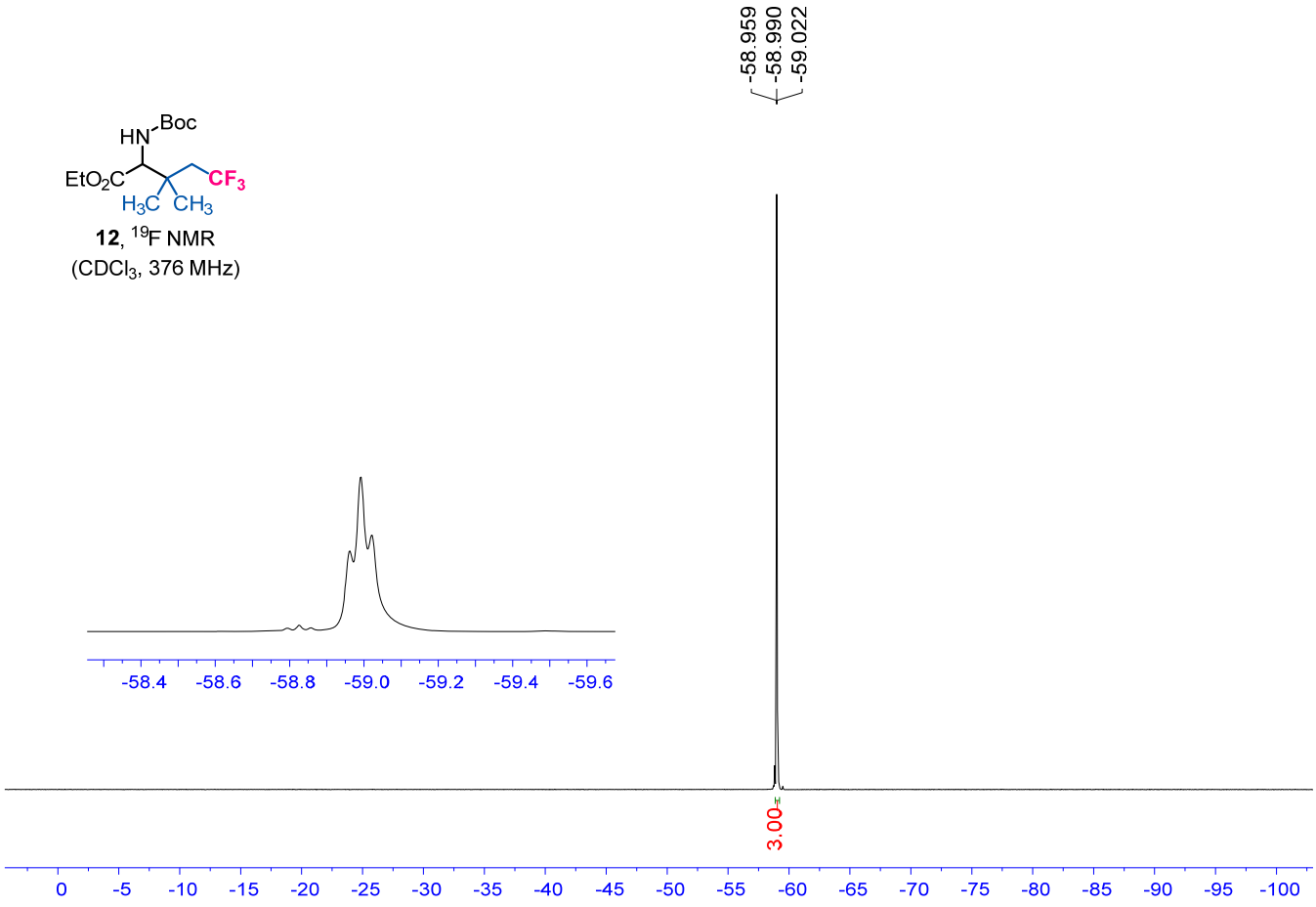


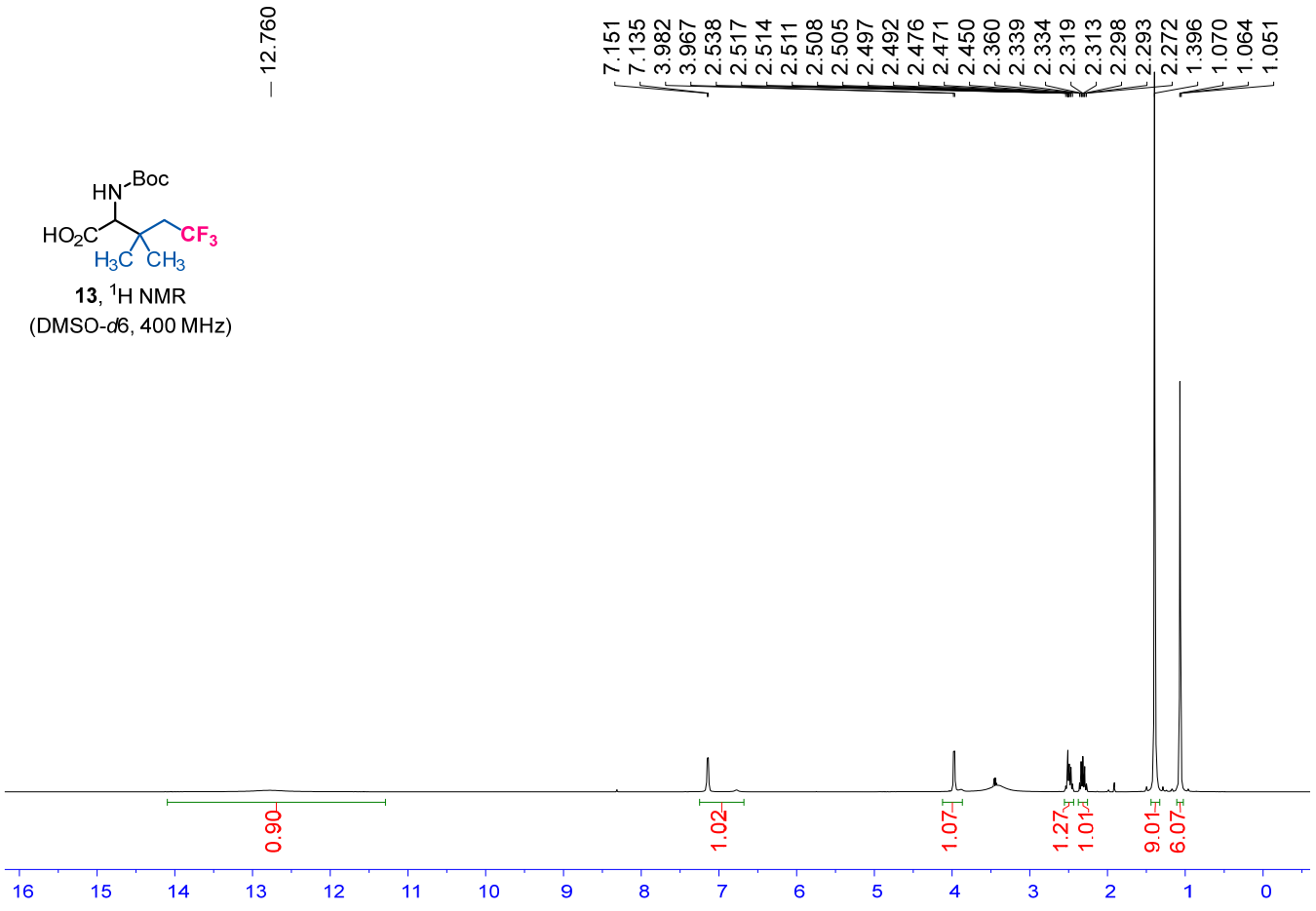
11, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz)


Me
H
O
CO2Et
Boc
N
H
N
O
N
H
CF3
H3C CH3
11, 1H NMR
(CDCl3, 376 MHz)
-58.899
-58.930
-58.962
-58.0 -58.2 -58.4 -58.6 -58.8 -59.0 -59.2 -59.4 -59.6 -59.8
3.00
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -10

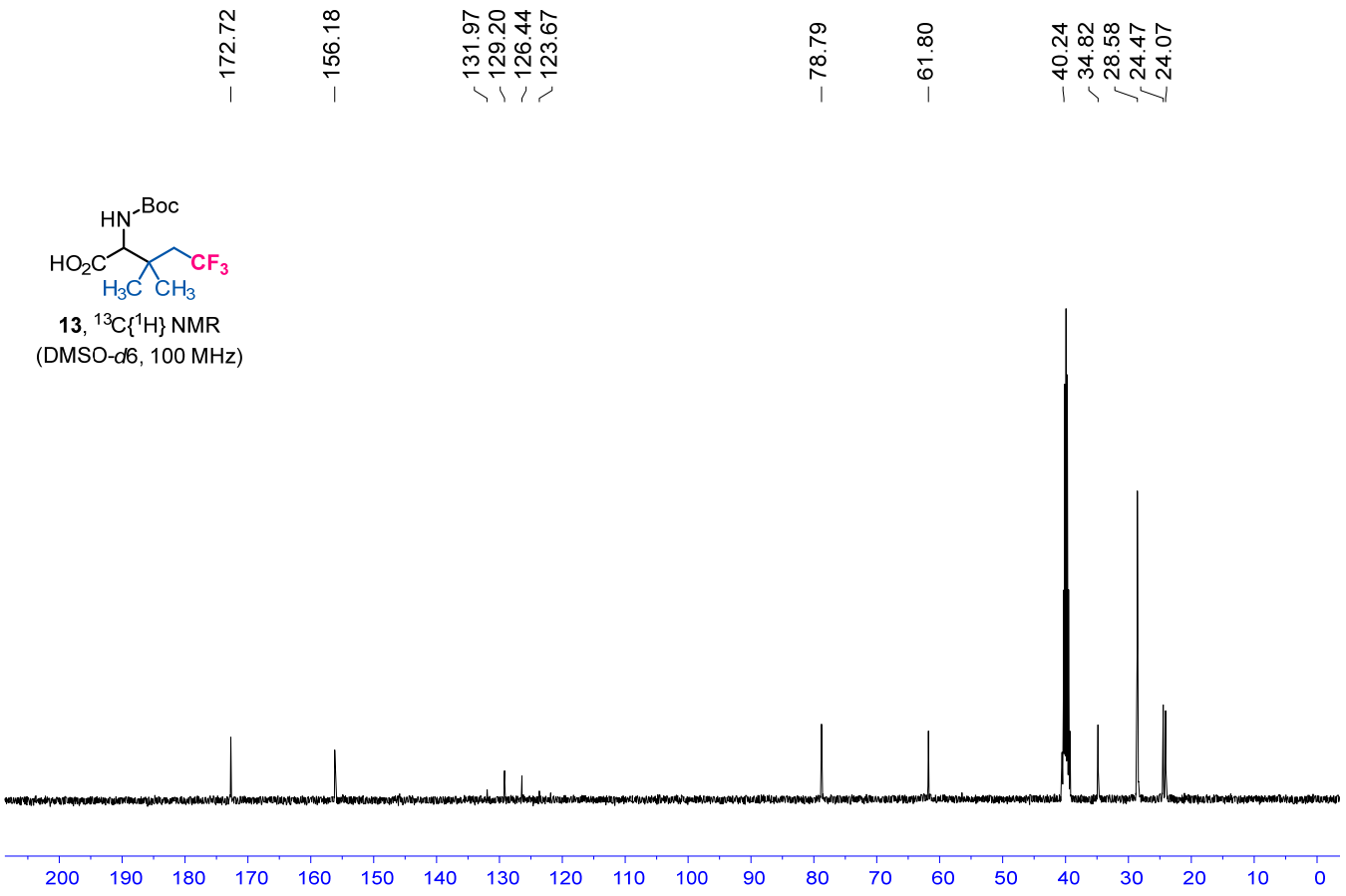

5.168
5.144
4.241
4.232
4.223
4.214
4.209
4.195
4.192
4.178
4.173
4.164
4.156
4.147
4.129
2.222
2.192
2.163
2.133
1.420
1.296
1.278
1.260
1.080
HN
Boc
EtO2C
CF3
H3C
CH3
12, 1H NMR
(CDCl3, 400 MHz)
0.98
2.93
1.95
9.05
3.13
6.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


171.02
155.45
130.97
128.21
125.44
122.67
80.18
61.36
61.16
41.28
41.01
40.74
40.48
36.12
28.20
23.67
22.91
14.09
HN
Boc
EtO2C
CF3
H3C
CH3
12, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

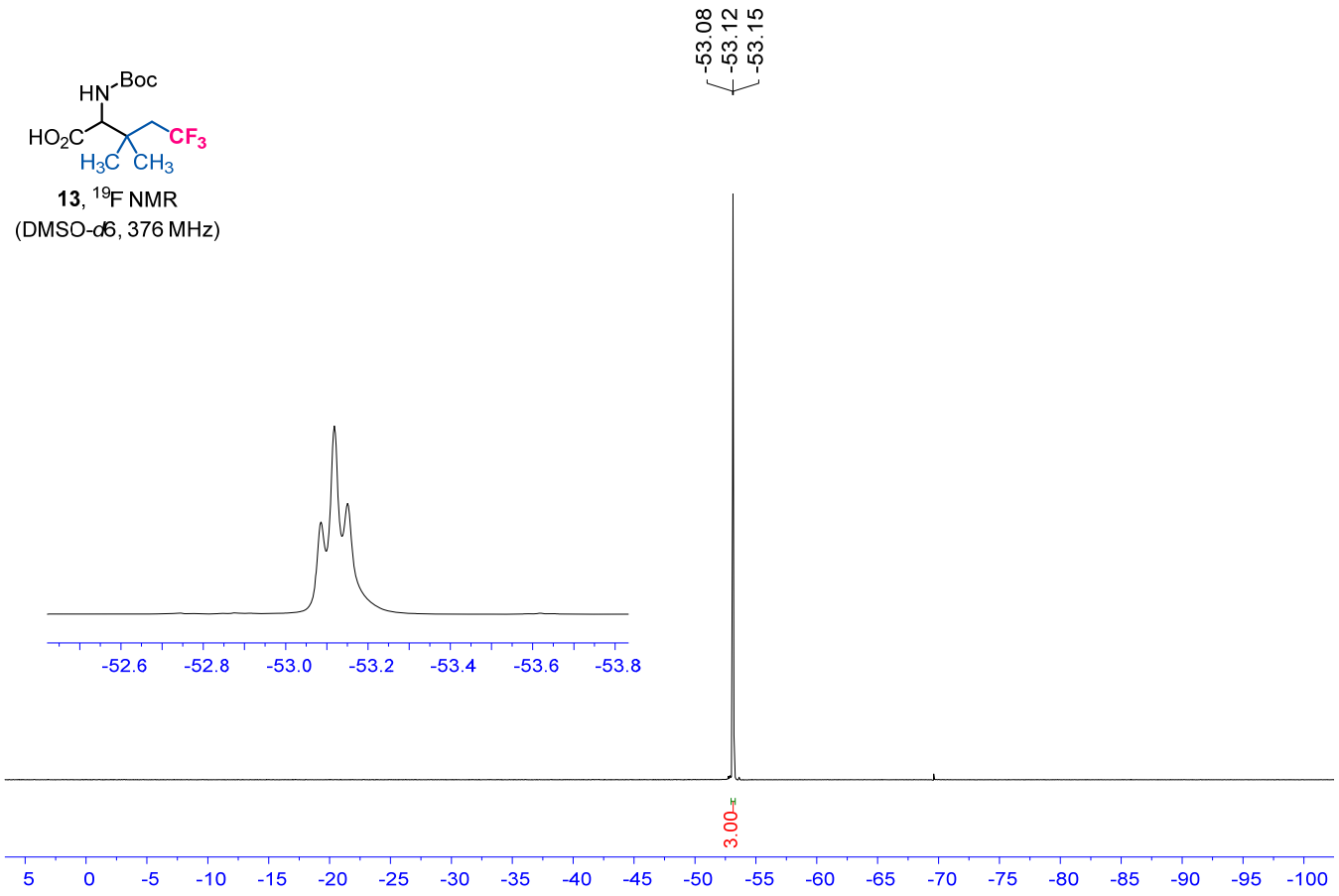

-58.959
-58.990
-59.022
HN
Boc
EtO2C
CF3
H3C
CH3
12, 19F NMR
(CDCl3, 376 MHz)
-58.4
-58.6
-58.8
-59.0
-59.2
-59.4
-59.6
3.00
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100

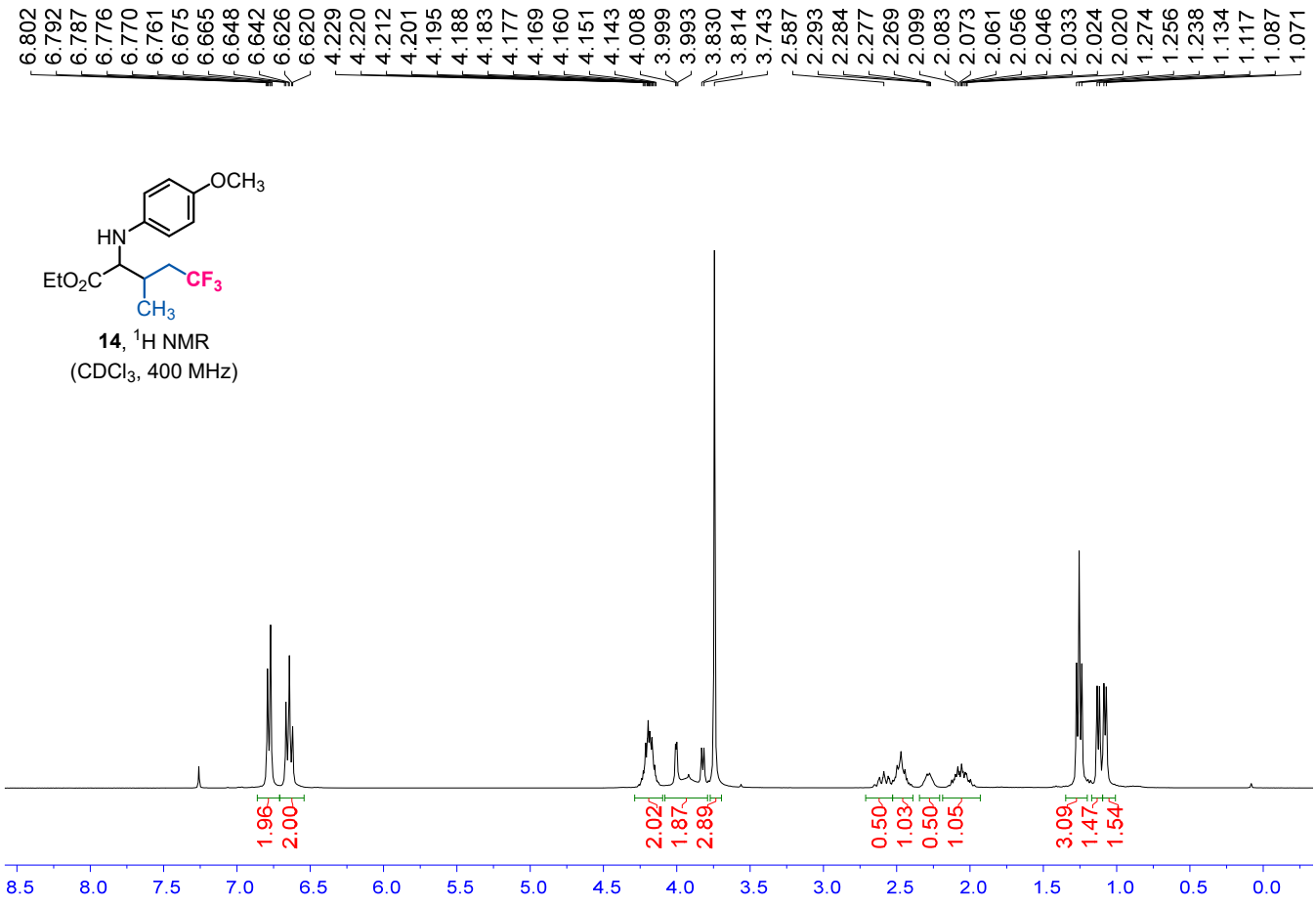


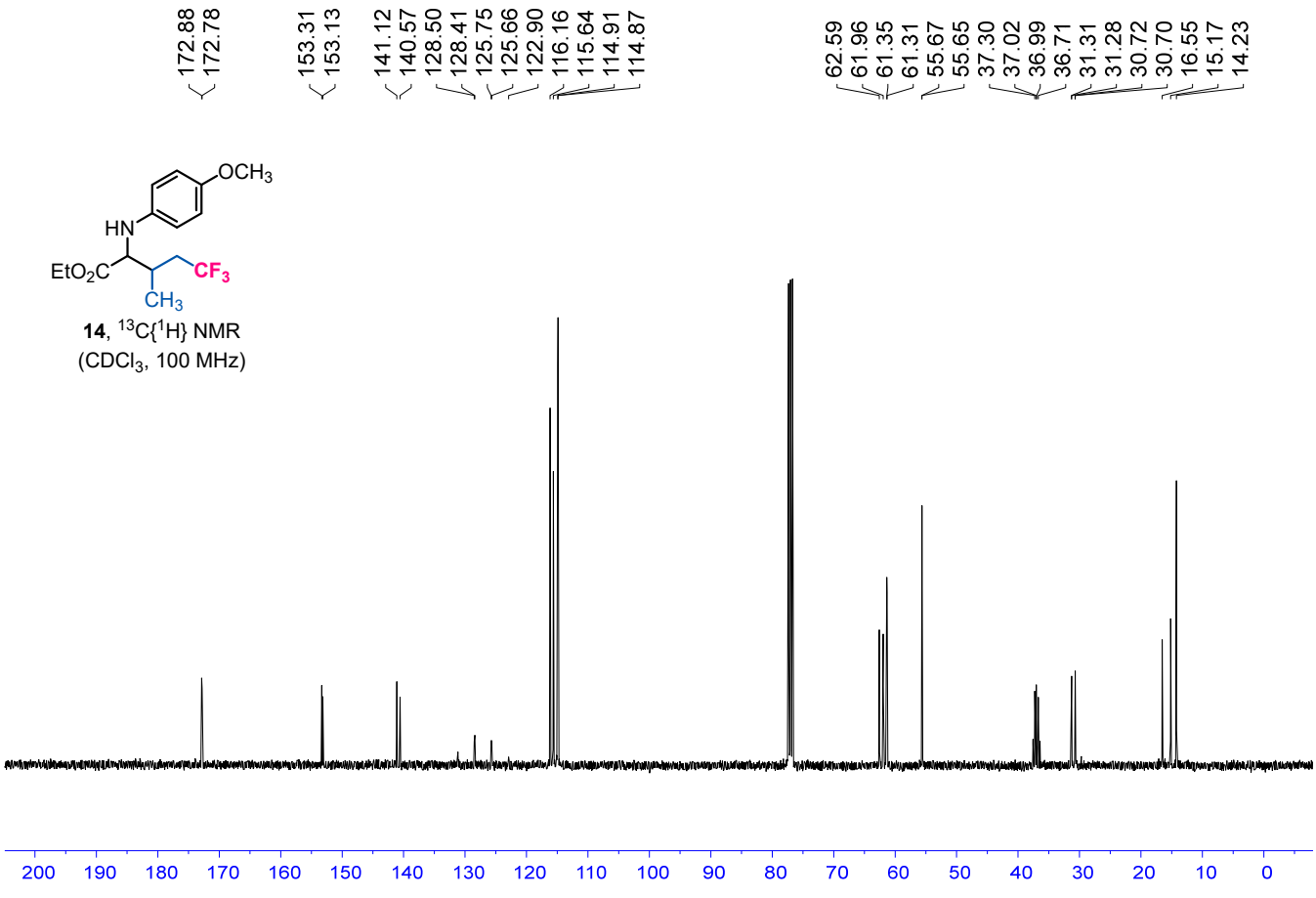
13, ^{1}H NMR
(DMSO-*d*6, 400 MHz)

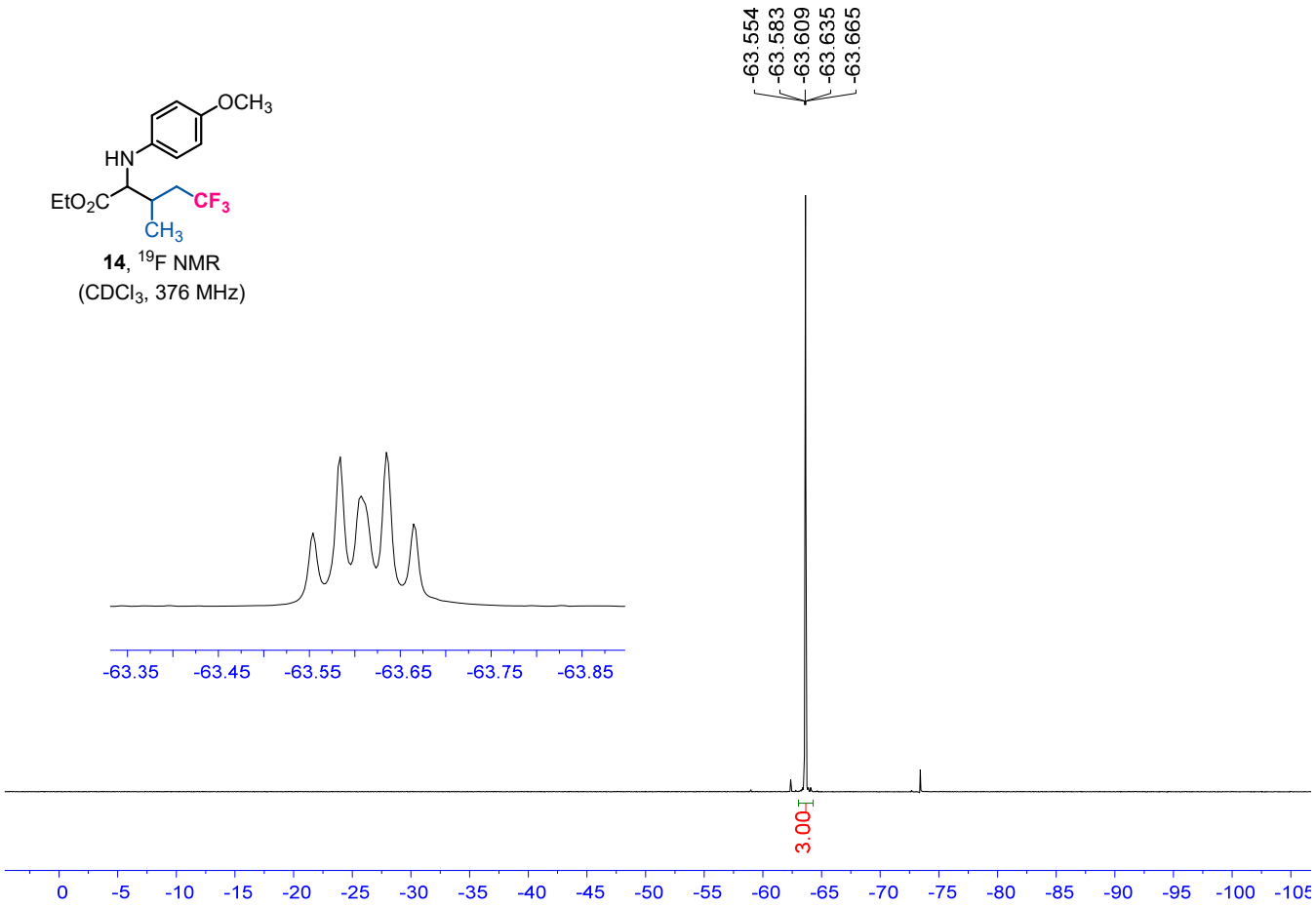


13, ^{13}C{^{1}H} NMR
(DMSO-*d*6, 100 MHz)

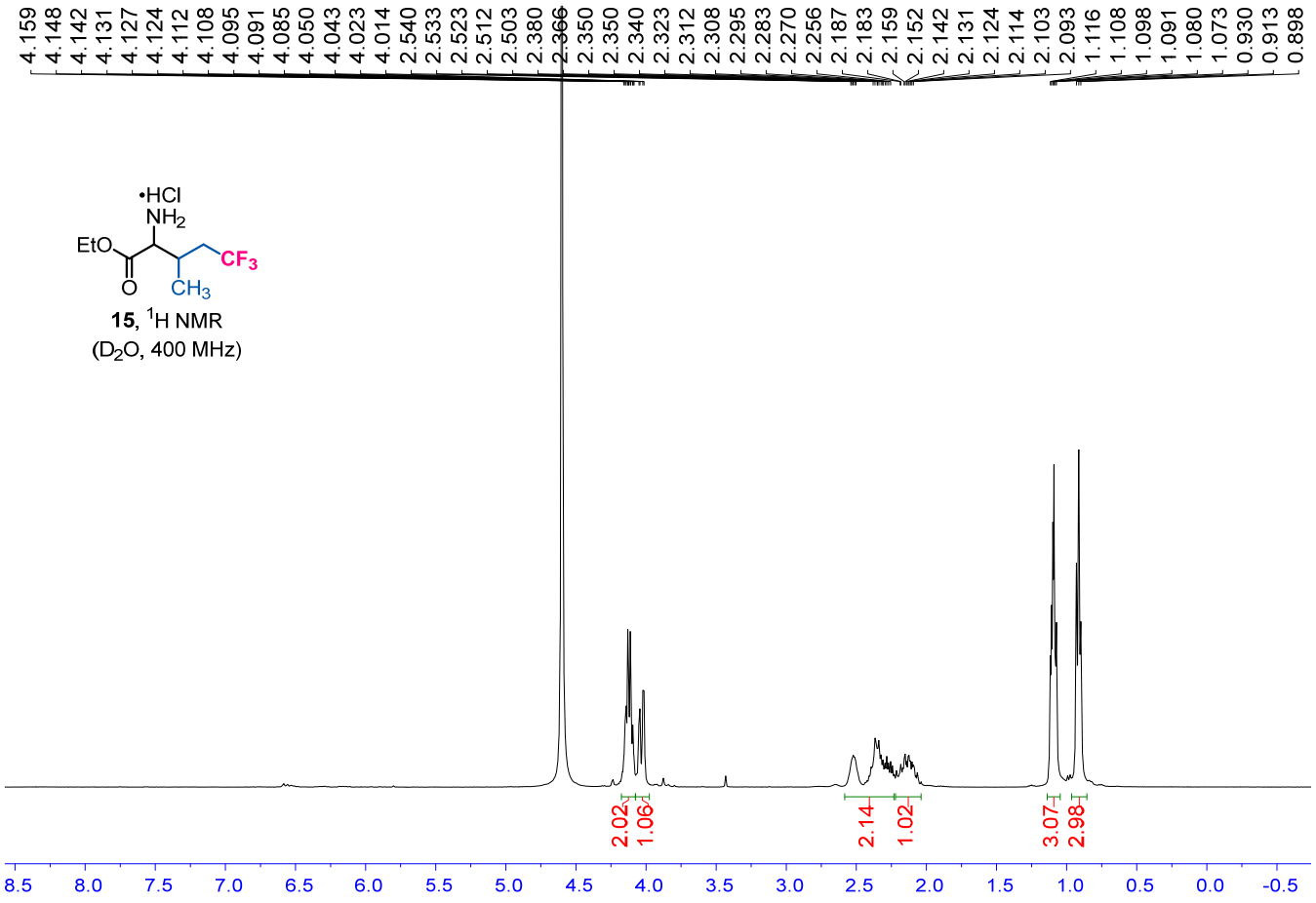

HN
Boc
HO2C
CF3
H3C
CH3
13, 19F NMR
(DMSO-d6, 376 MHz)
-53.08
-53.12
-53.15
-52.6
-52.8
-53.0
-53.2
-53.4
-53.6
-53.8
3.00
5
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100

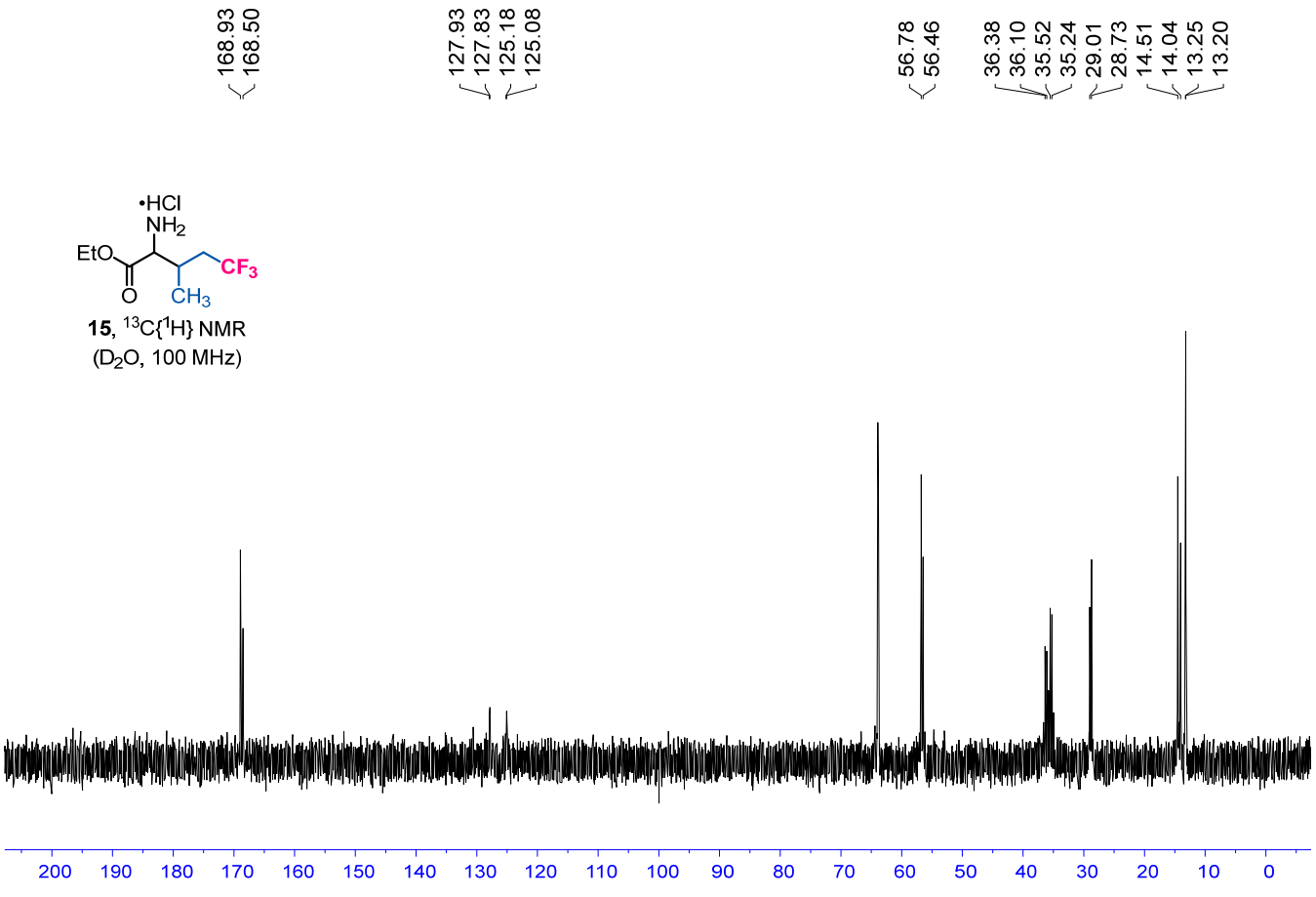

6.802
6.792
6.787
6.776
6.770
6.761
6.675
6.665
6.648
6.642
6.626
6.620
4.229
4.220
4.212
4.201
4.195
4.188
4.183
4.177
4.169
4.160
4.151
4.143
4.008
3.999
3.993
3.830
3.814
3.743
2.587
2.293
2.284
2.277
2.269
2.099
2.083
2.073
2.061
2.056
2.046
2.033
2.024
2.020
1.274
1.256
1.238
1.134
1.117
1.087
1.071
OCH3
HN
EtO2C
CF3
CH3
14, 1H NMR
(CDCl3, 400 MHz)
1.96
2.00
2.02
1.87
2.89
0.50
1.03
0.50
1.05
3.09
1.47
1.54
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

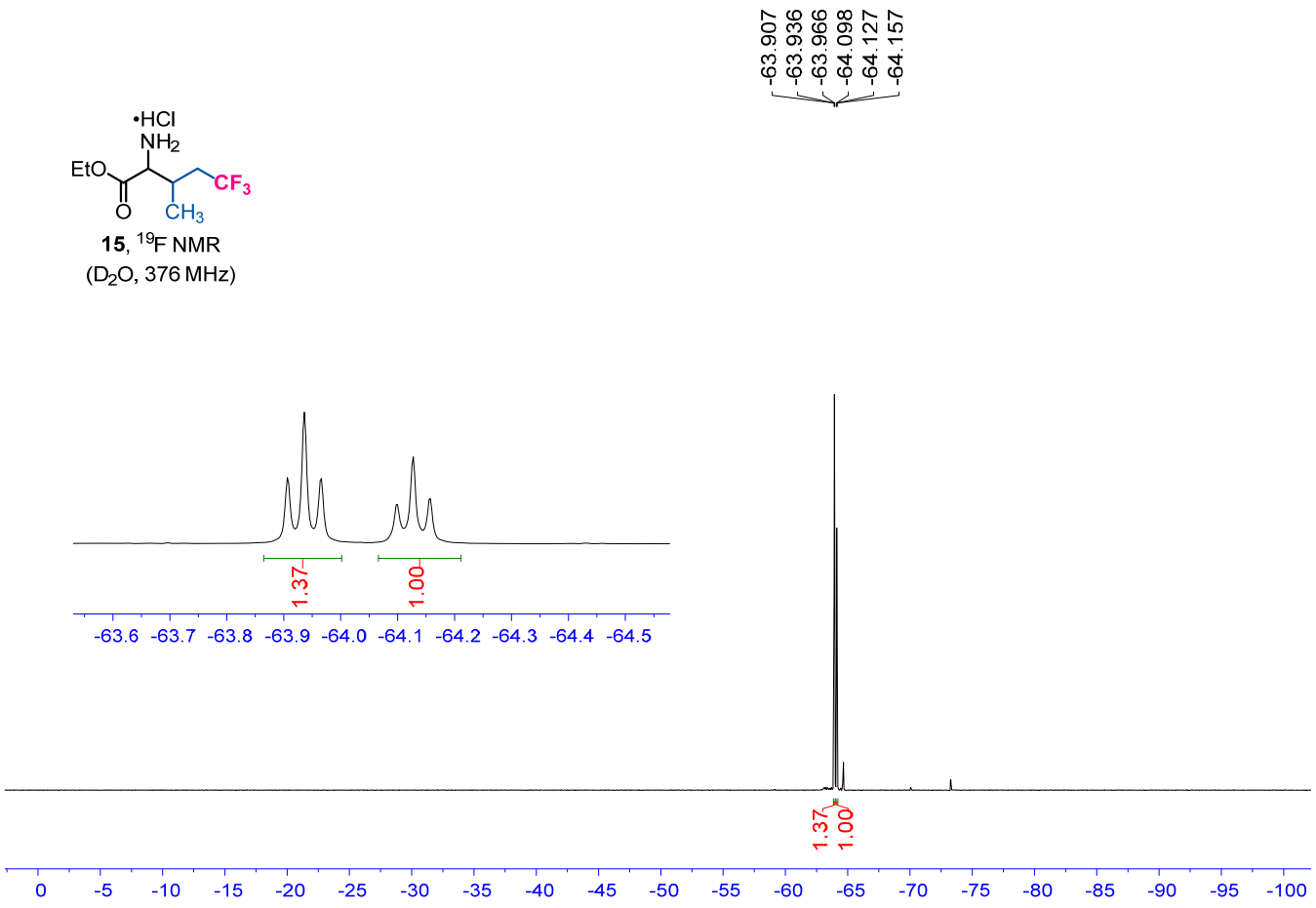

172.88
172.78
153.31
153.13
141.12
140.57
128.50
128.41
125.75
125.66
122.90
116.16
115.64
114.91
114.87
62.59
61.96
61.35
61.31
55.67
55.65
37.30
37.02
36.99
36.71
31.31
31.28
30.72
30.70
16.55
15.17
14.23
OCH3
HN
EtO2C
CF3
CH3
14, 13C{1H} NMR
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

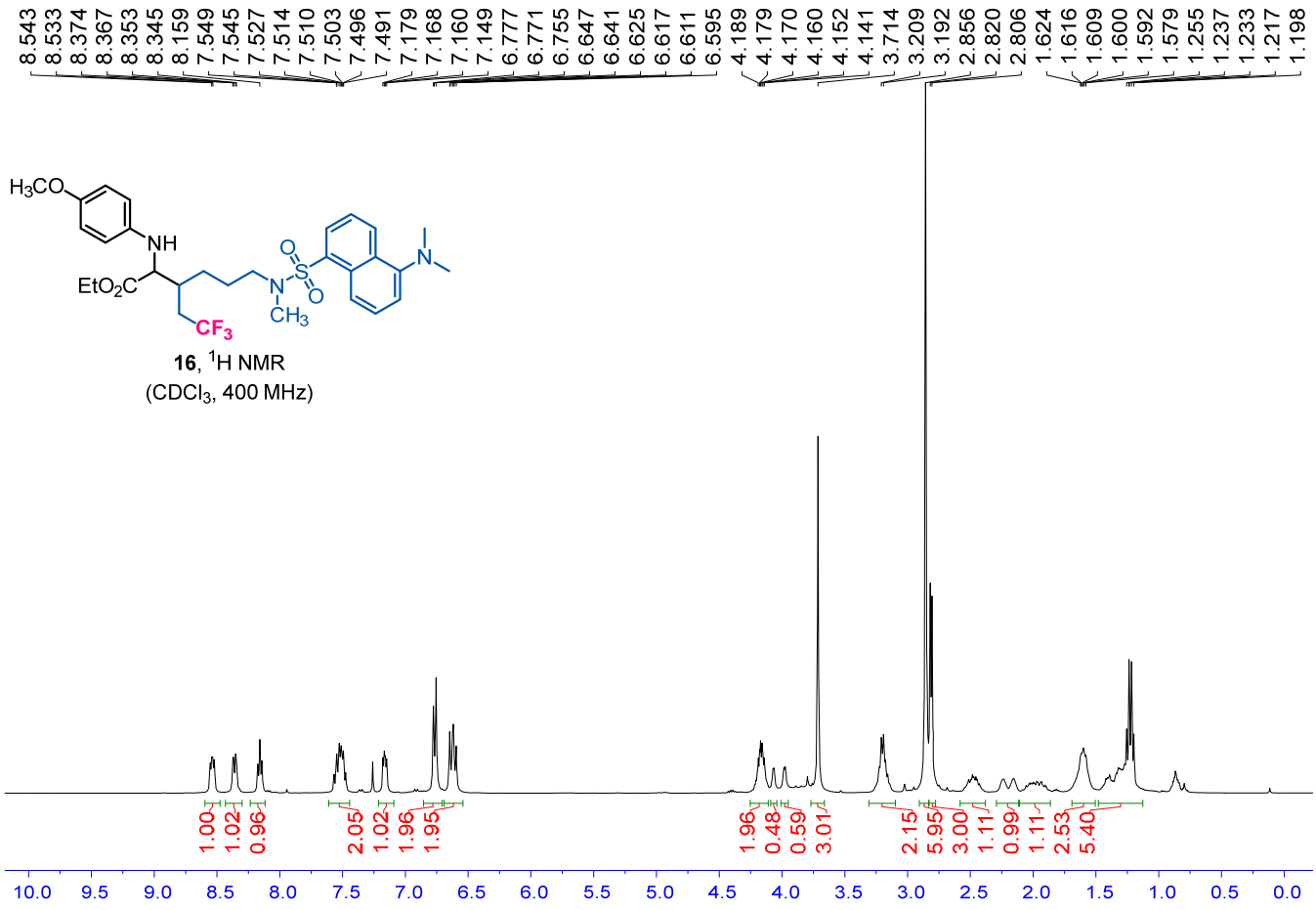


14, ^{19}F NMR
($CDCl_3$, 376 MHz)

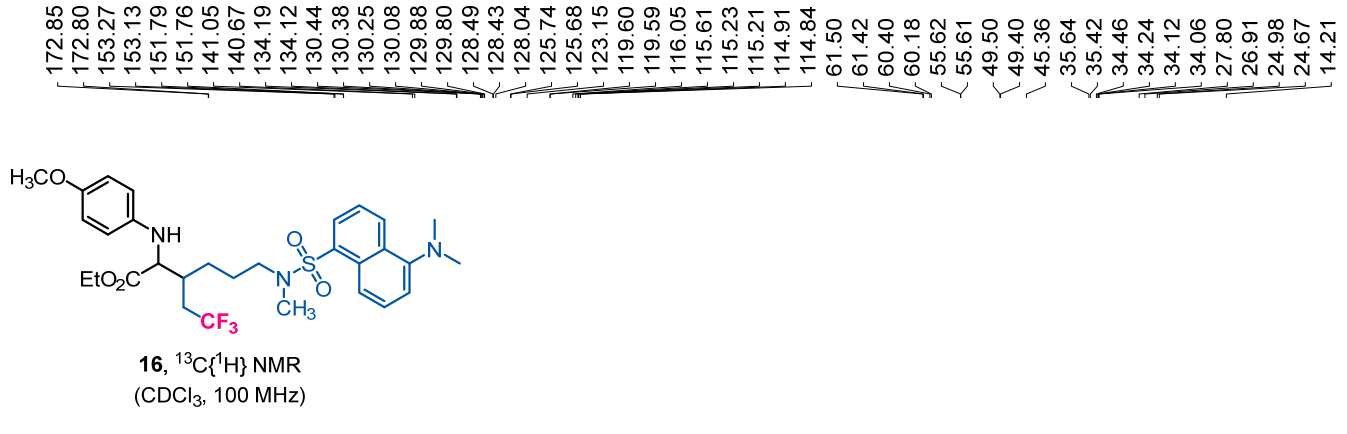

4.159
4.148
4.142
4.131
4.127
4.124
4.112
4.108
4.095
4.091
4.085
4.050
4.043
4.023
4.014
2.540
2.533
2.523
2.512
2.503
2.380
2.366
2.350
2.350
2.340
2.323
2.312
2.308
2.295
2.283
2.270
2.256
2.187
2.183
2.159
2.152
2.142
2.131
2.124
2.114
2.103
2.093
1.116
1.108
1.098
1.091
1.080
1.073
0.930
0.913
0.898
•HCl
NH2
EtO
CF3
O
CH3
15, 1H NMR
(D2O, 400 MHz)
2.02
1.06
2.14
1.02
3.07
2.98
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


168.93
168.50
127.93
127.83
125.18
125.08
56.78
56.46
36.38
36.10
35.52
35.24
29.01
28.73
14.51
14.04
13.25
13.20
•HCl
NH2
EtO
CF3
O
CH3
15, 13C{1H} NMR
(D2O, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

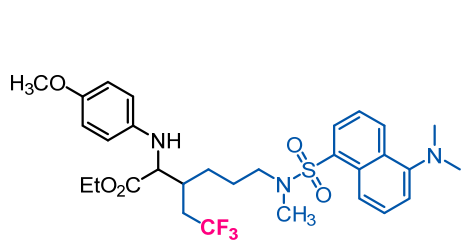

-63.907
-63.936
-63.966
-64.098
-64.127
-64.157
•HCl
NH2
EtO
CF3
O
CH3
15, 19F NMR
(D2O, 376 MHz)
1.37
1.00
-63.6 -63.7 -63.8 -63.9 -64.0 -64.1 -64.2 -64.3 -64.4 -64.5
1.37
1.00
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100



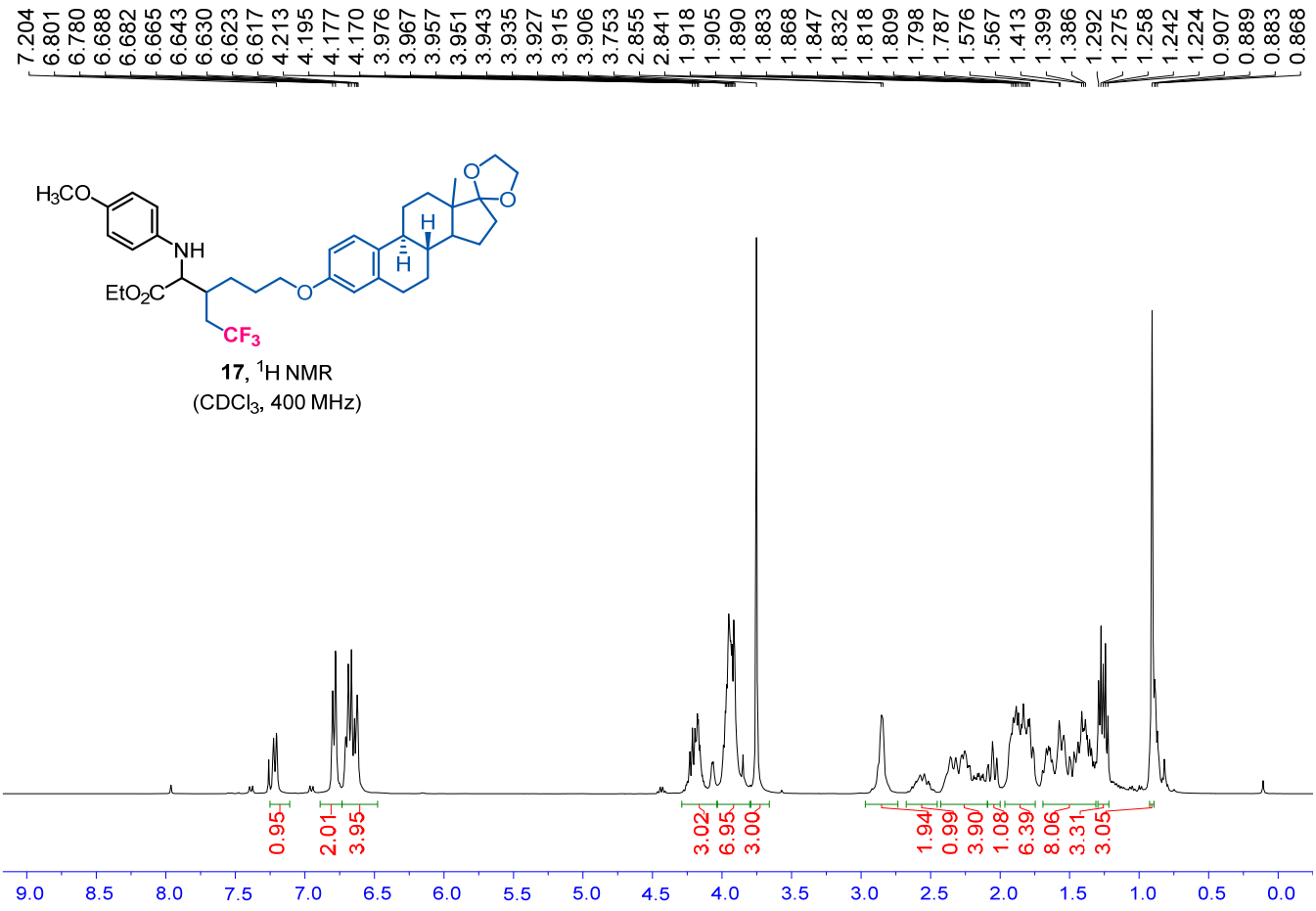
16, ^{1}H NMR
($CDCl_3$, 400 MHz)



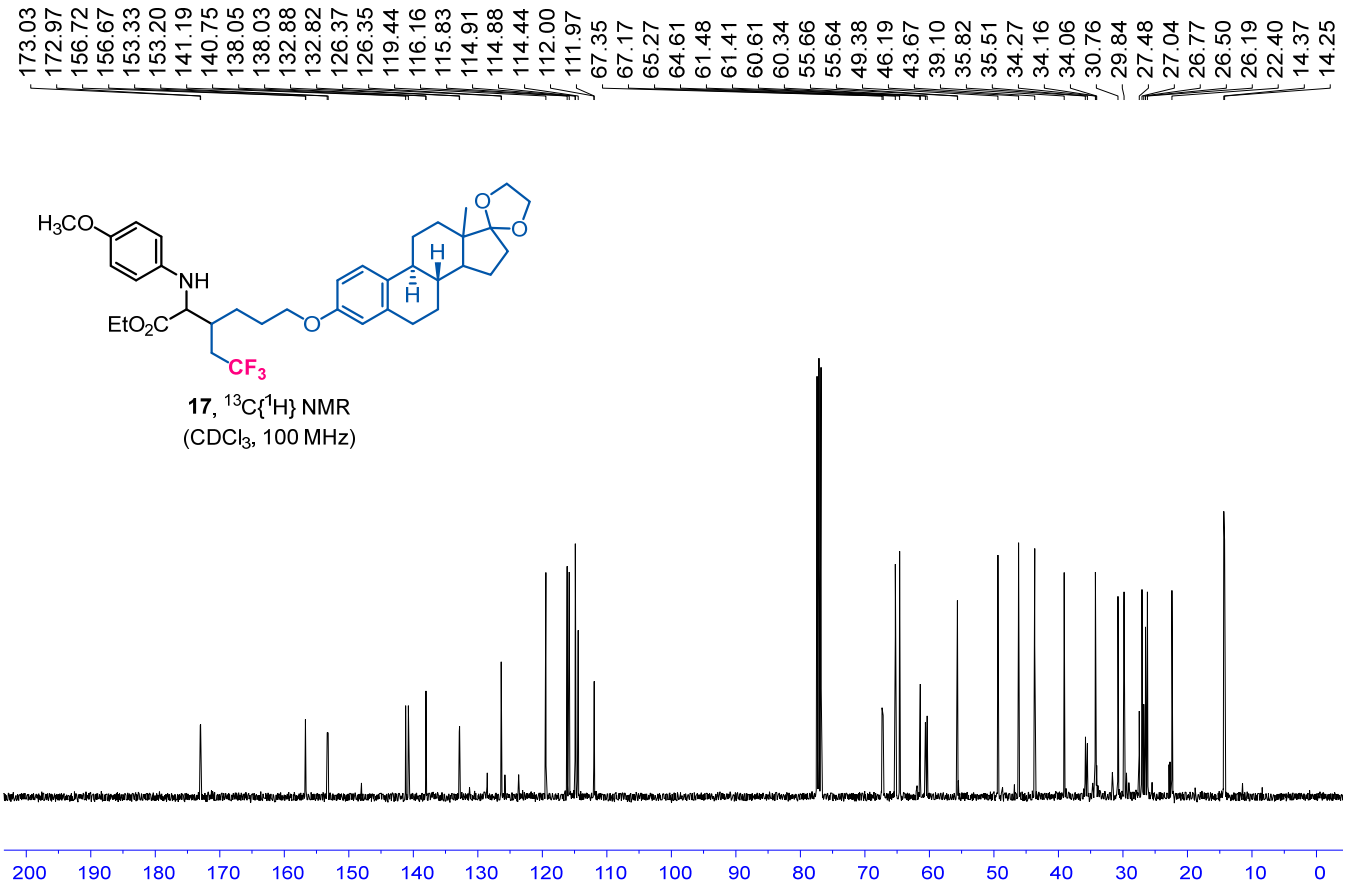
16, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



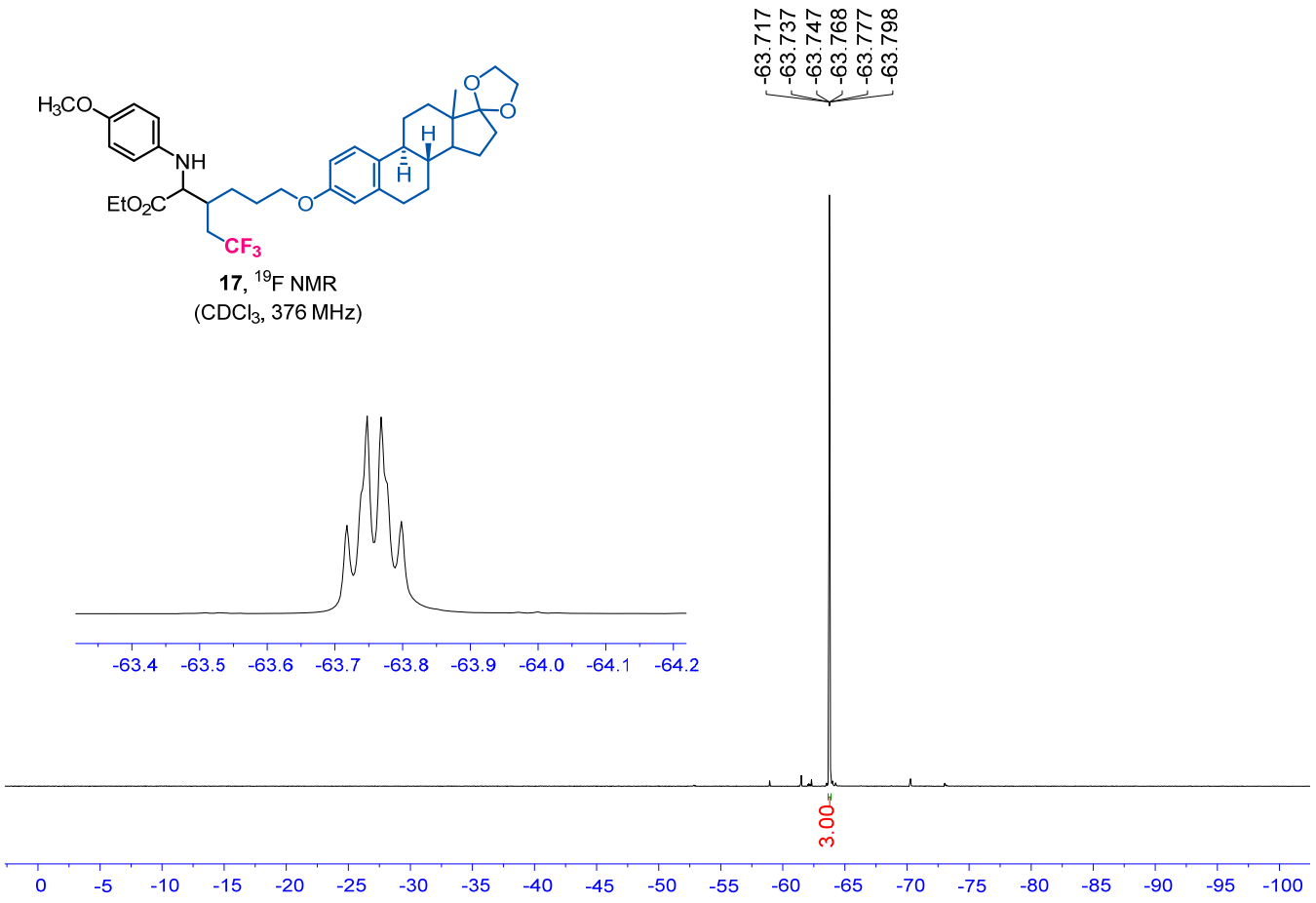
16, ^{19}F NMR
($CDCl_3$, 376 MHz)



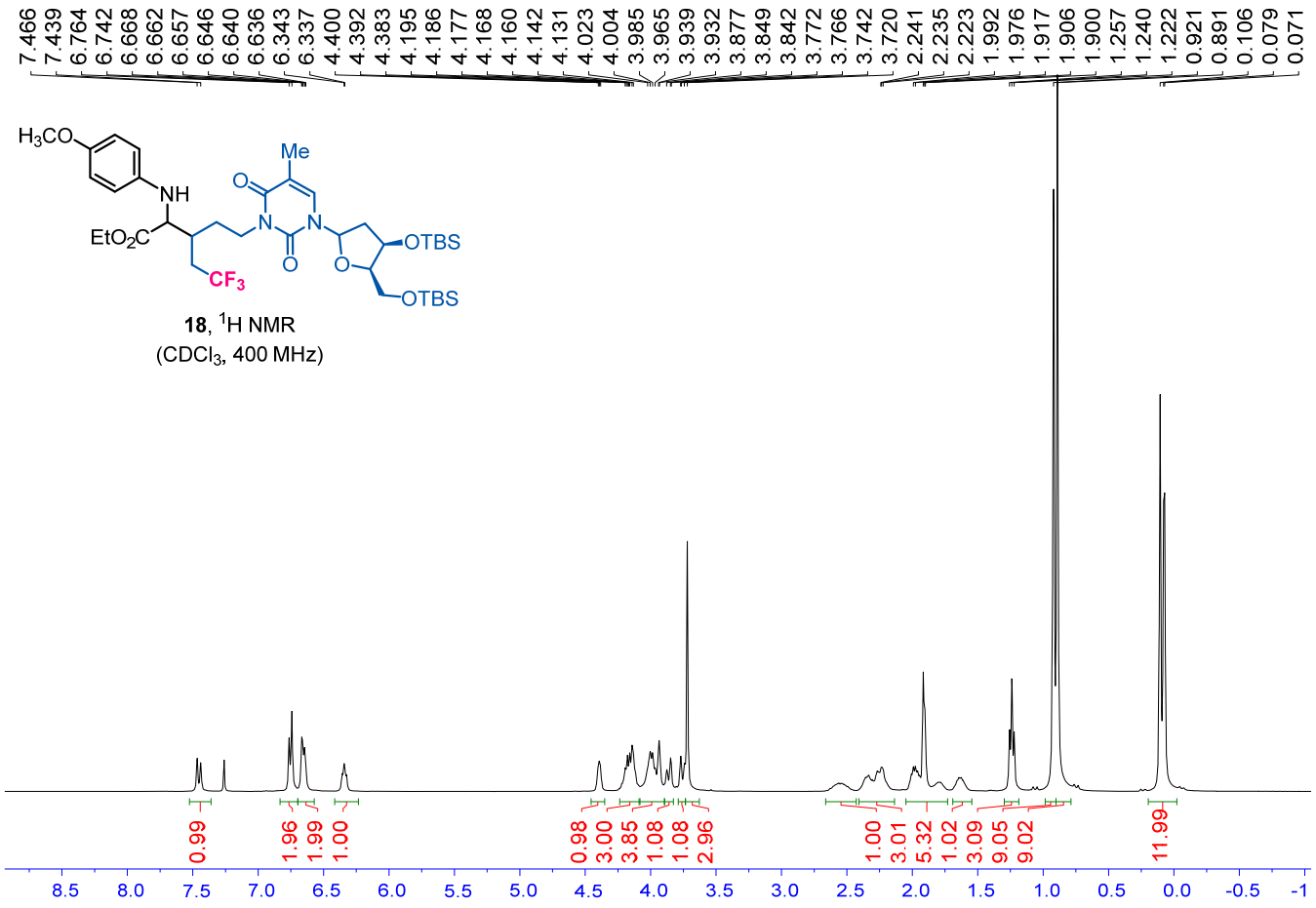
17, ^{1}H NMR
($CDCl_3$, 400 MHz)



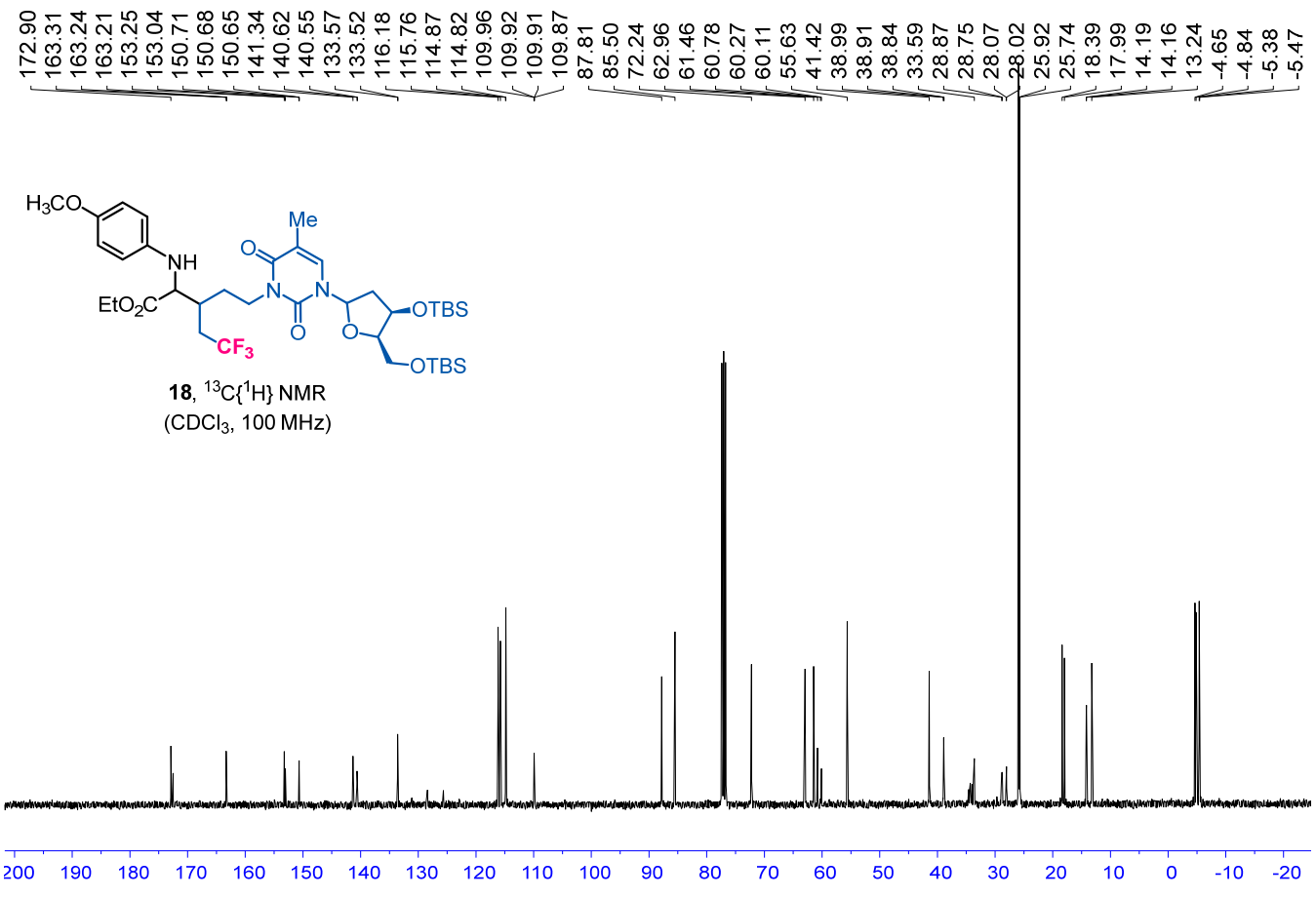
17, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)



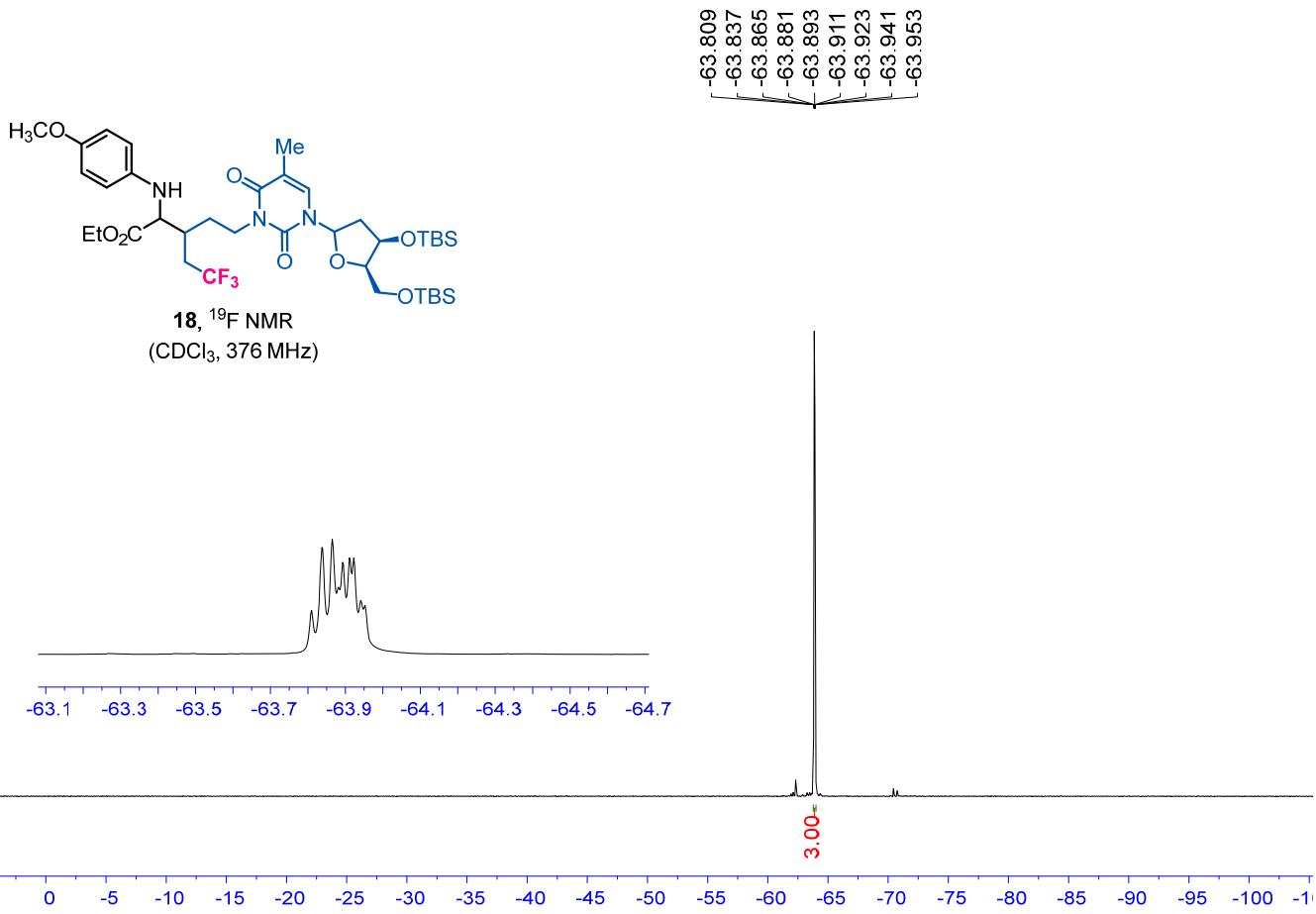
17, ^{19}F NMR
($CDCl_3$, 376 MHz)

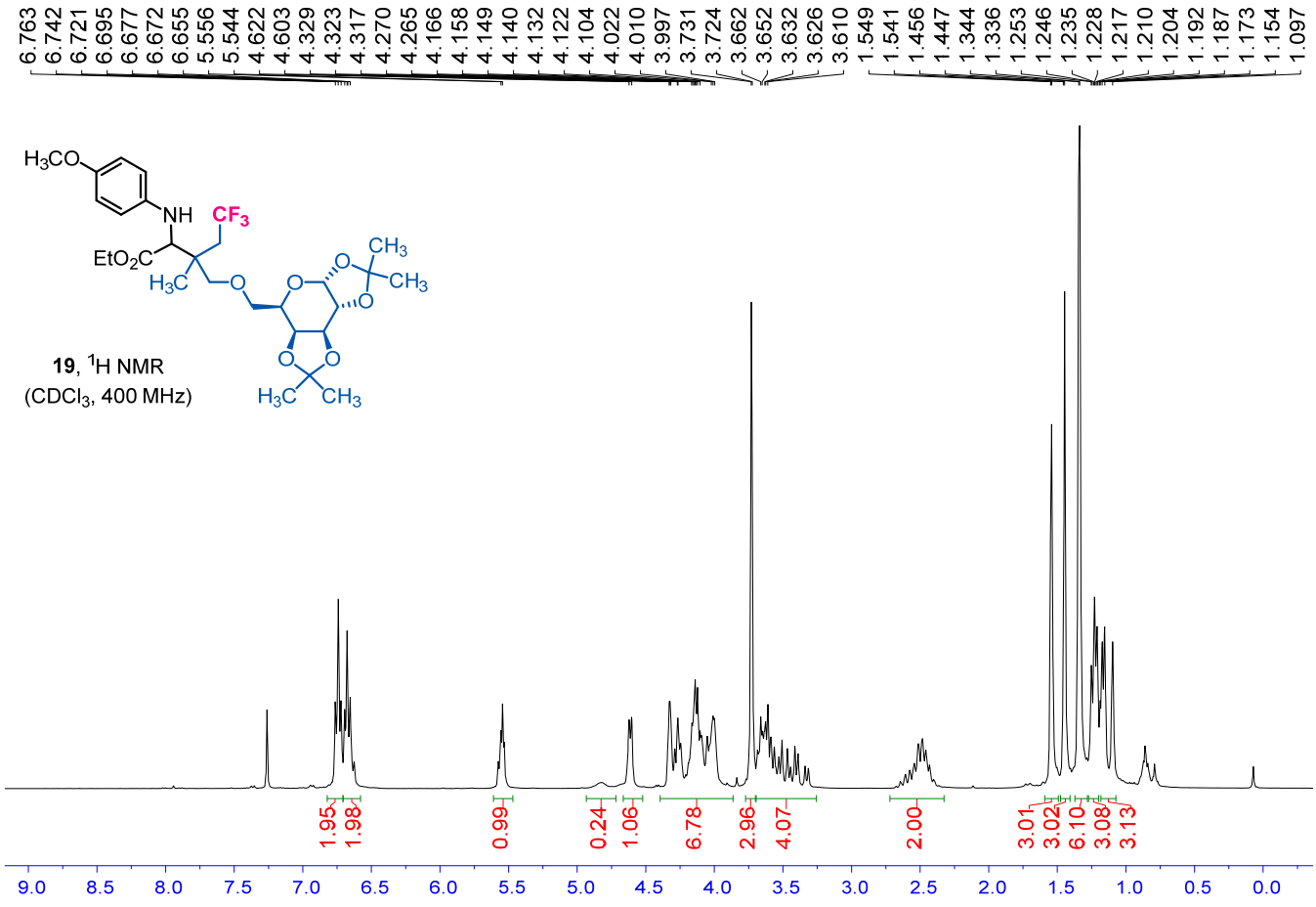


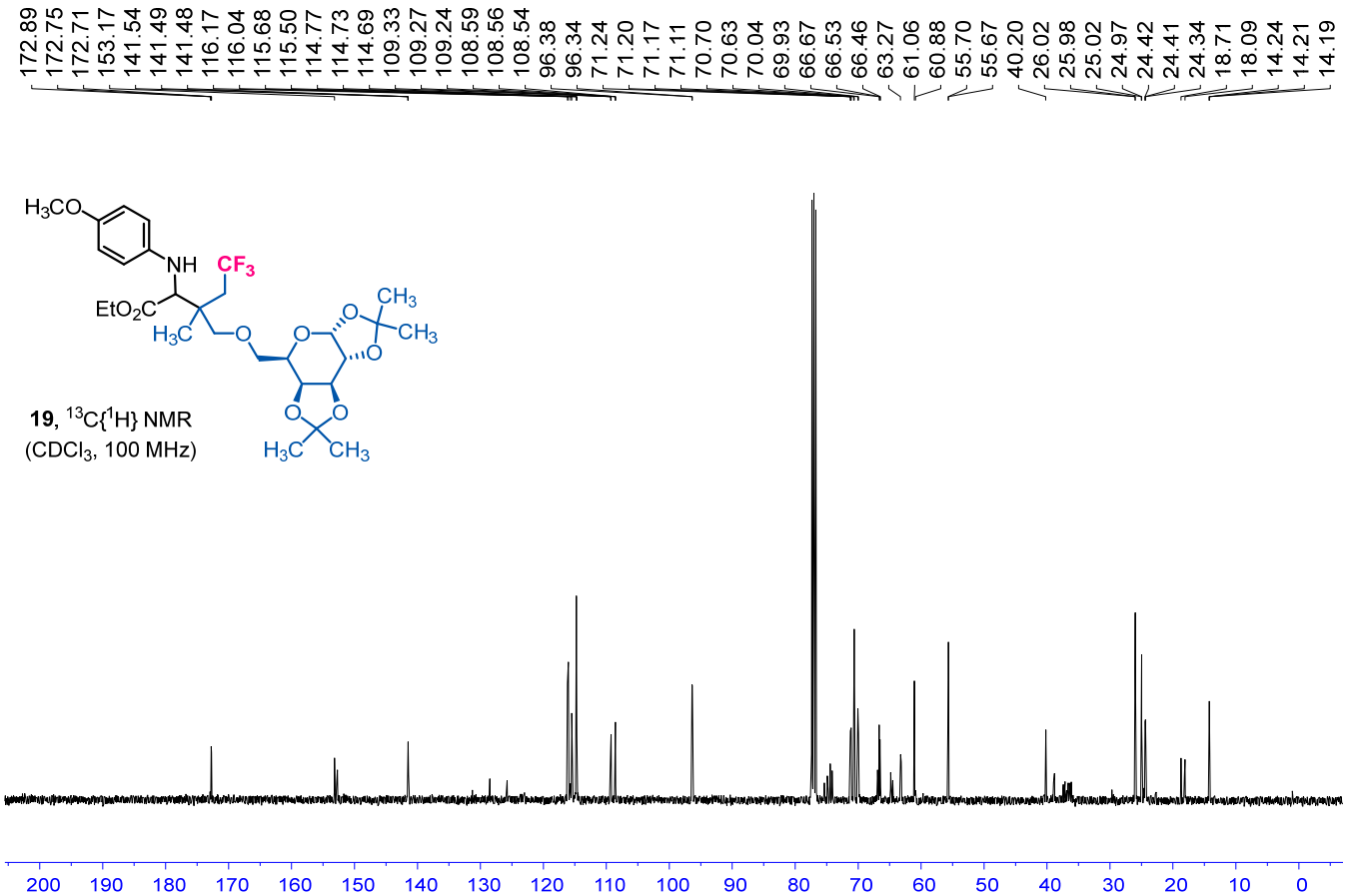
18, ^{1}H NMR
($CDCl_3$, 400 MHz)

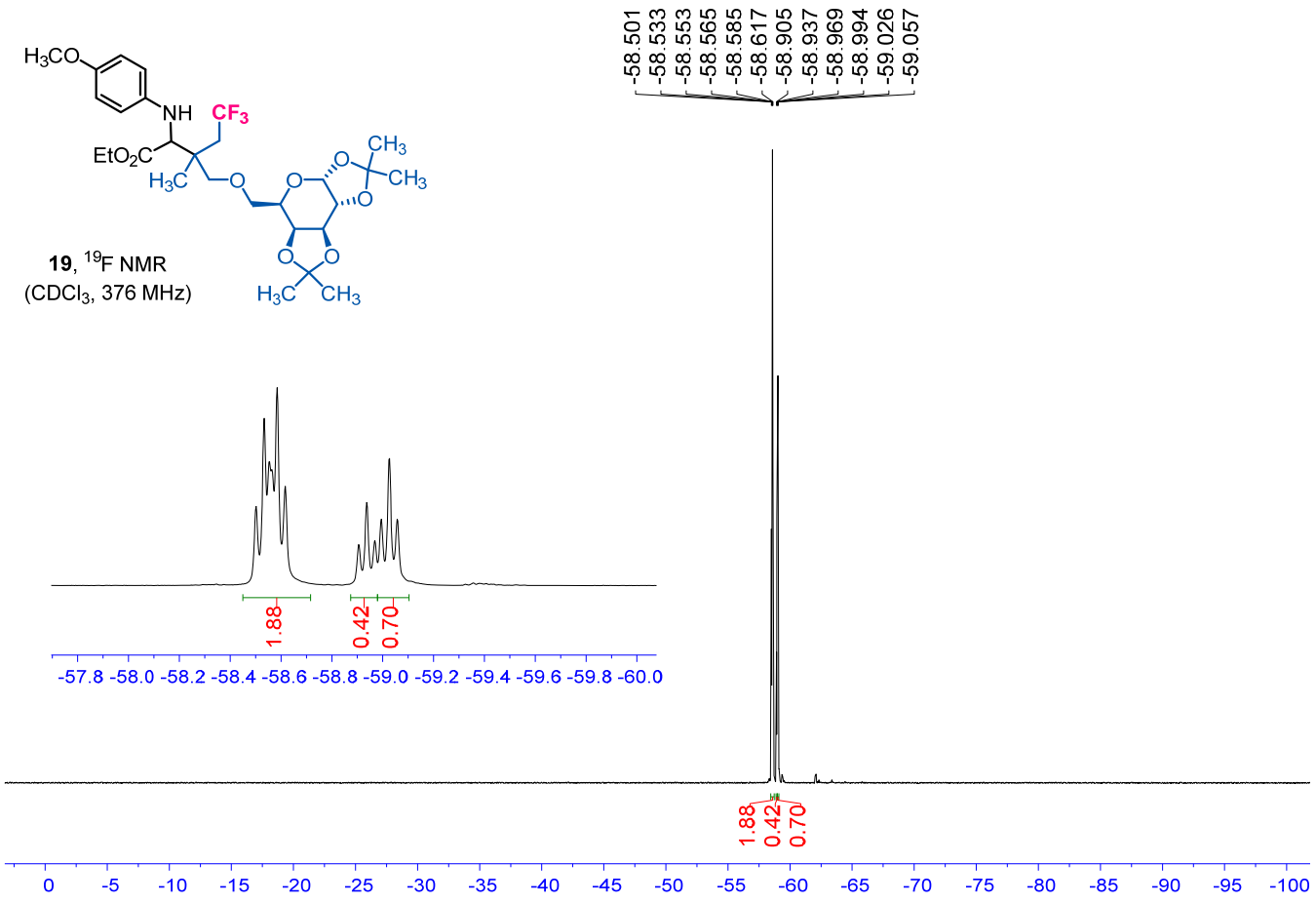


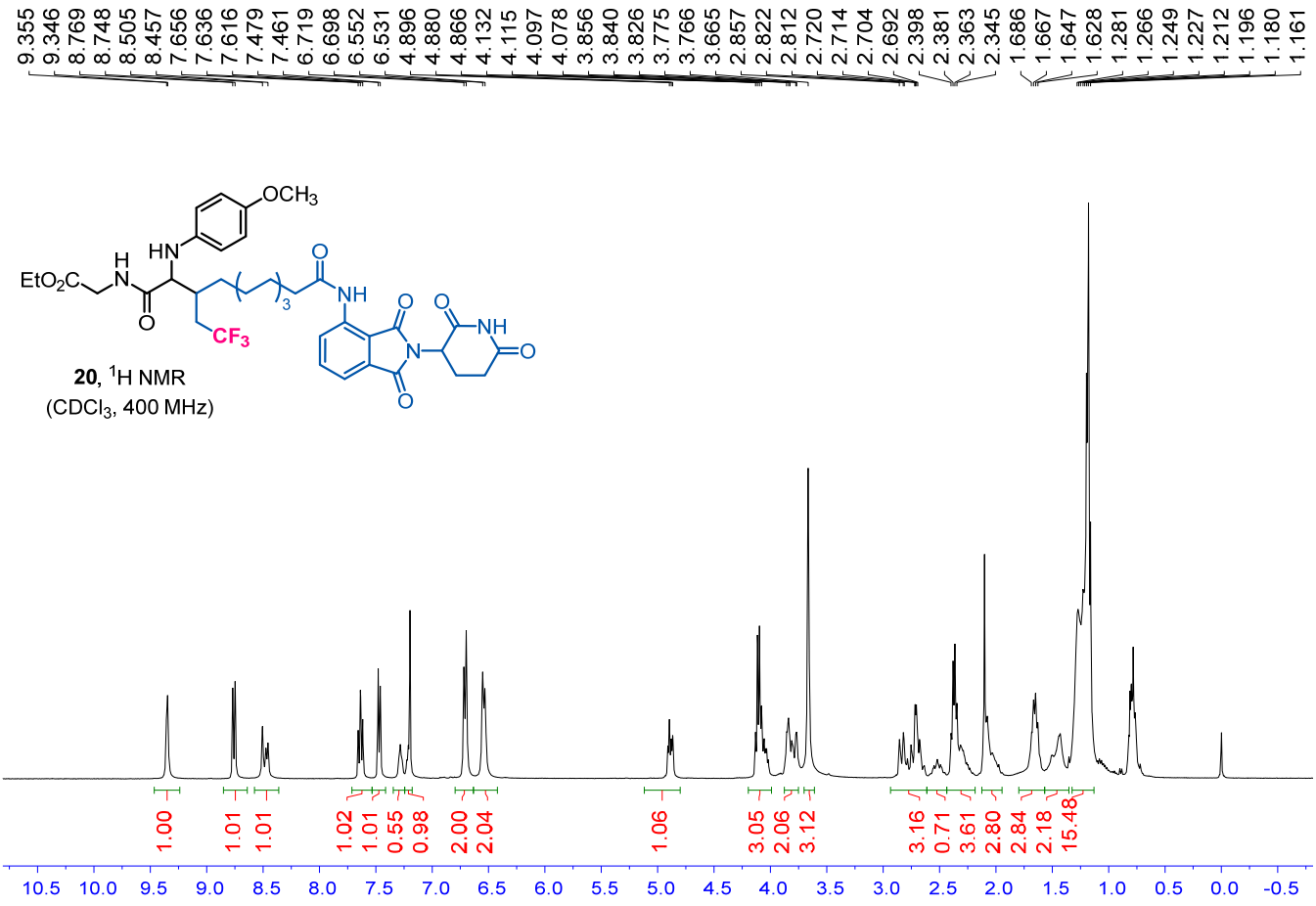
18, $^{13}C\{^{1}H\}$ NMR
($CDCl_3$, 100 MHz)

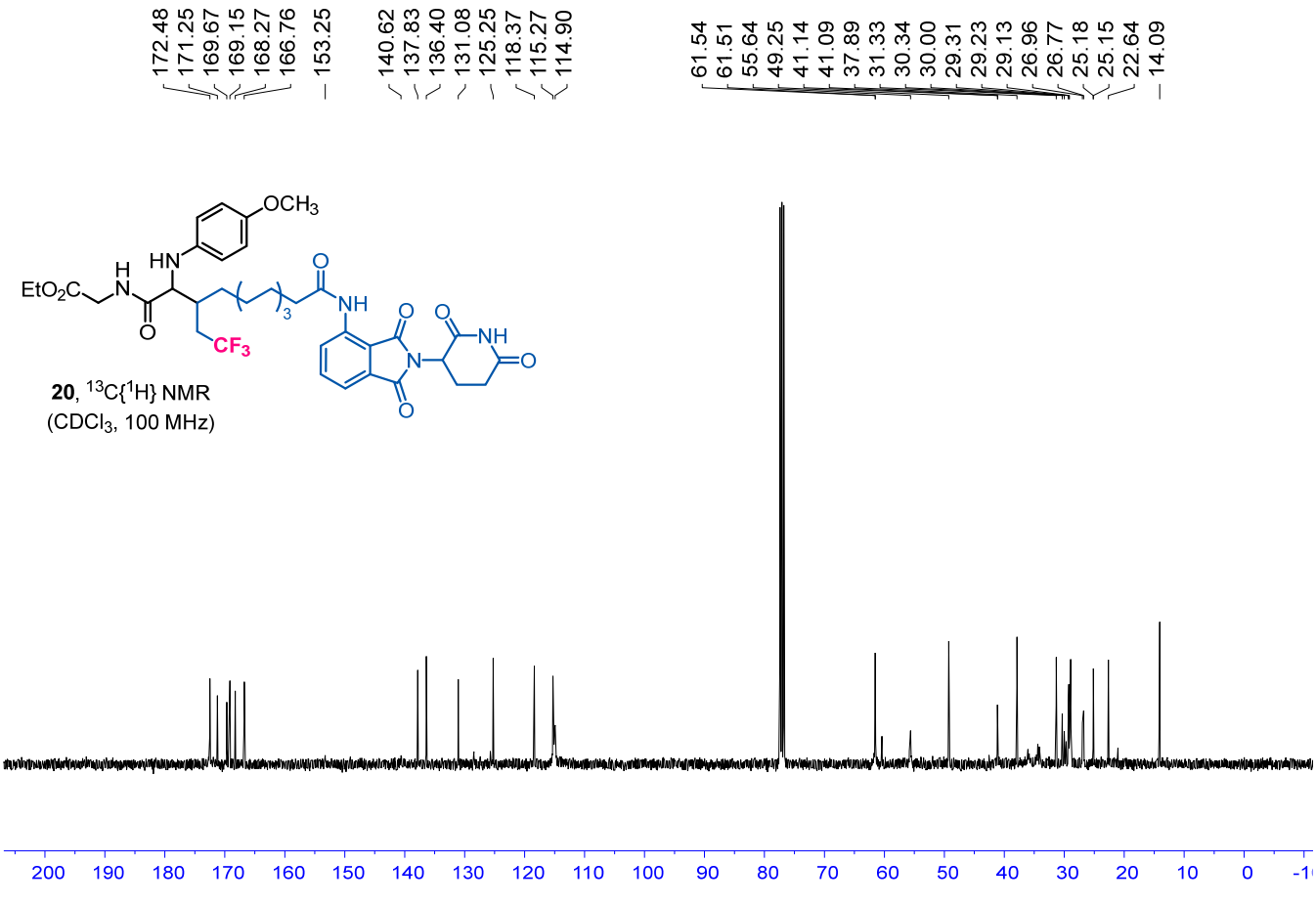

-63.809
-63.837
-63.865
-63.881
-63.893
-63.911
-63.923
-63.941
-63.953
H3CO
NH
EtO2C
Me
O
N
N
O
O
CF3
OTBS
OTBS
18, 19F NMR
(CDCl3, 376 MHz)
-63.1
-63.3
-63.5
-63.7
-63.9
-64.1
-64.3
-64.5
-64.7
3.00
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100

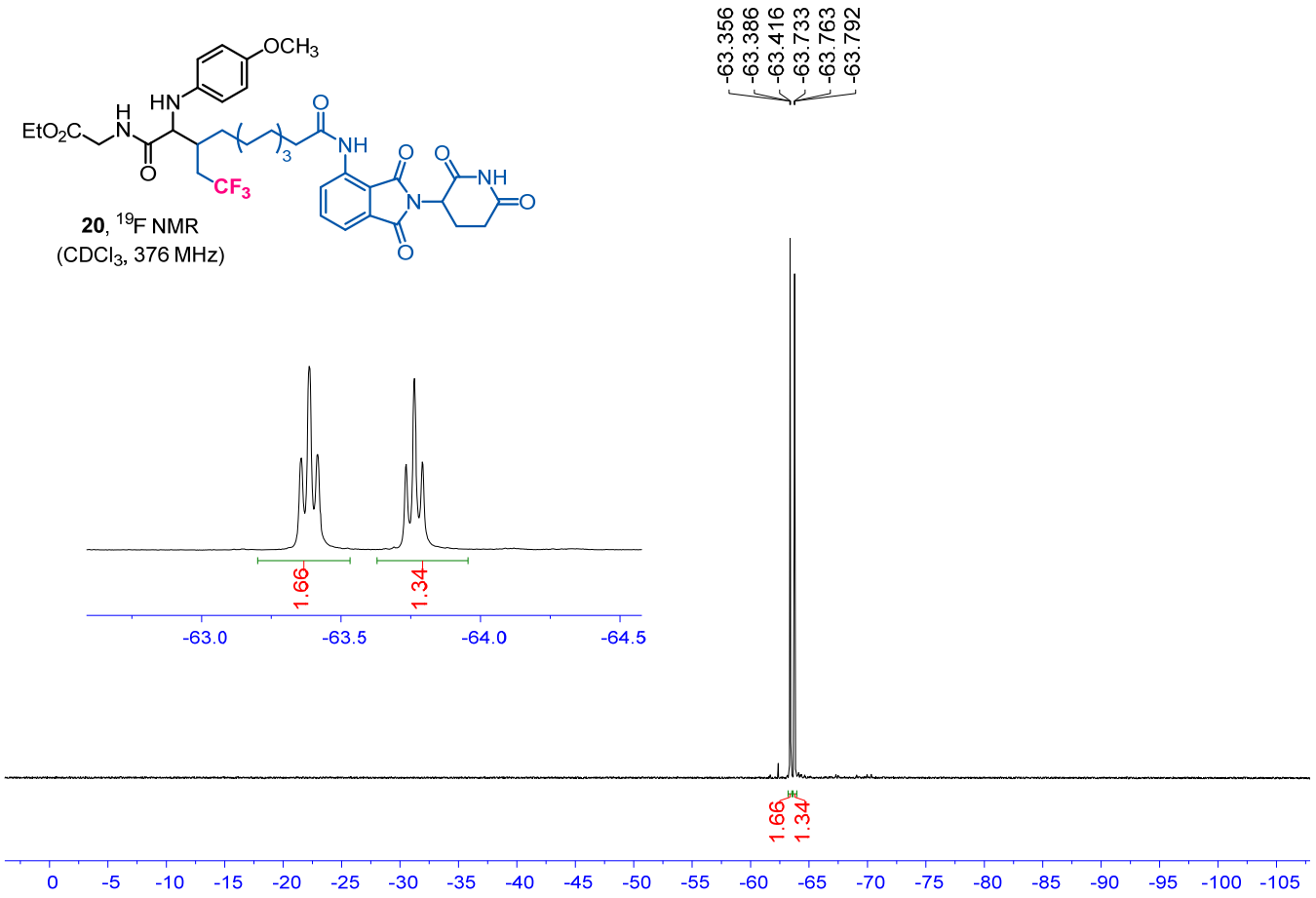

6.763 6.742 6.721 6.695 6.677 6.672 6.655 5.556 5.544 4.622 4.603 4.329 4.323 4.317 4.270 4.265 4.166 4.158 4.149 4.140 4.132 4.122 4.104 4.022 4.010 3.997 3.731 3.724 3.662 3.652 3.632 3.626 3.610 1.549 1.541 1.456 1.447 1.344 1.336 1.253 1.246 1.235 1.228 1.217 1.210 1.204 1.192 1.187 1.173 1.154 1.097
H3CO
NH
CF3
EtO2C
H3C
O
CH3
CH3
19, 1H NMR
(CDCl3, 400 MHz)
1.95 1.98 0.99 0.24 1.06 6.78 2.96 4.07 2.00 3.01 3.02 6.10 3.08 3.13
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

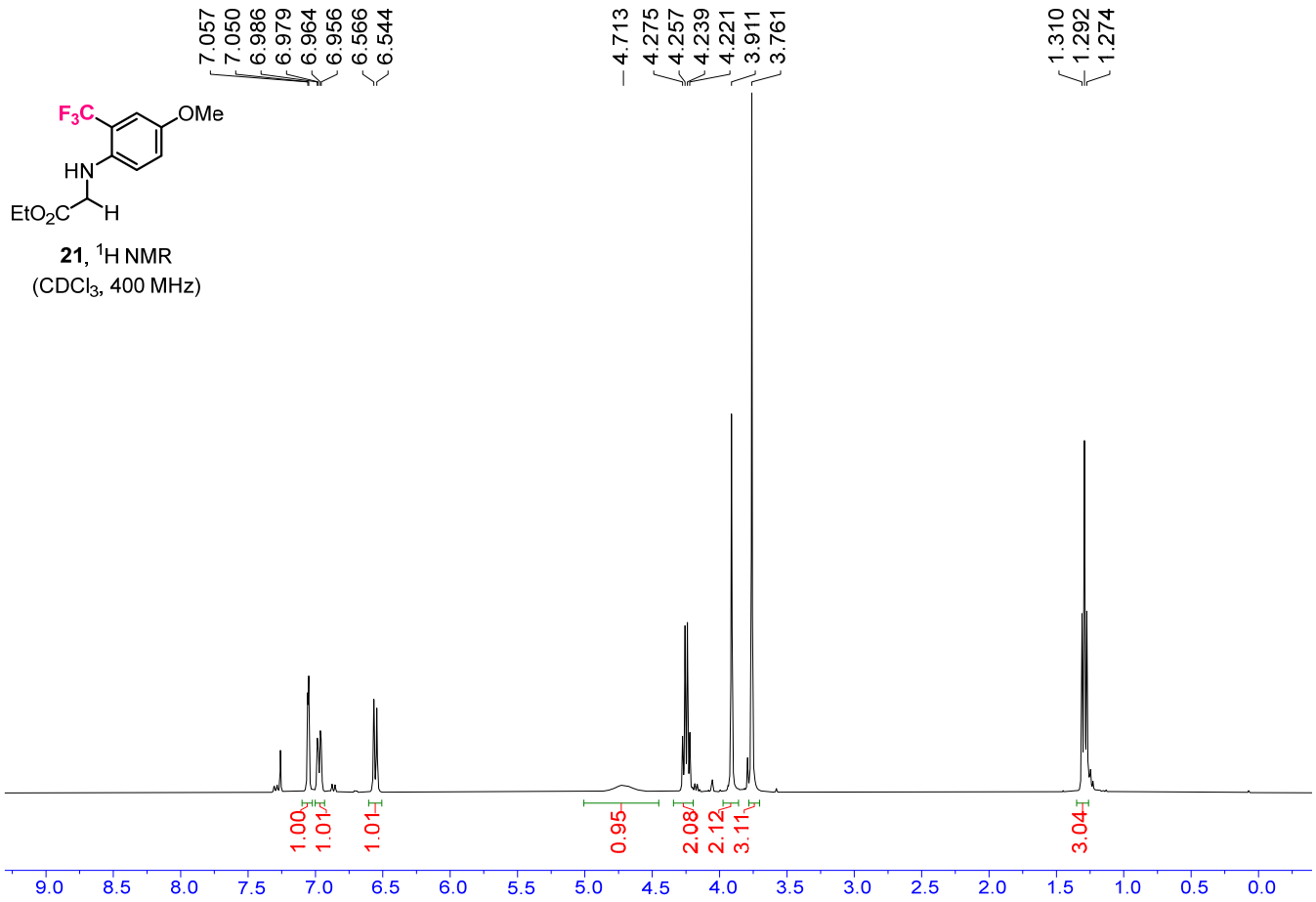

172.89 172.75 172.71 153.17 141.54 141.49 141.48 116.17 116.04 115.68 115.50 114.77 114.73 114.69 109.33 109.27 109.24 108.59 108.56 108.54 96.38 96.34 71.24 71.20 71.17 71.11 70.70 70.63 70.04 69.93 66.67 66.53 66.46 63.27 61.06 60.88 55.70 55.67 40.20 26.02 25.98 25.02 24.97 24.42 24.41 24.34 18.71 18.09 14.24 14.21 14.19
H3CO
NH
CF3
EtO2C
H3C
O
CH3
CH3
19, 13C{1H} NMR
(CDCl3, 100 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


-58.501
-58.533
-58.553
-58.565
-58.585
-58.617
-58.905
-58.937
-58.969
-58.994
-59.026
-59.057
H3CO
NH
CF3
EtO2C
H3C
O
O
O
O
O
CH3
CH3
O
O
H3C
CH3
19, 19F NMR
(CDCl3, 376 MHz)
1.88
0.42
0.70
-57.8 -58.0 -58.2 -58.4 -58.6 -58.8 -59.0 -59.2 -59.4 -59.6 -59.8 -60.0
1.88
0.42
0.70
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100

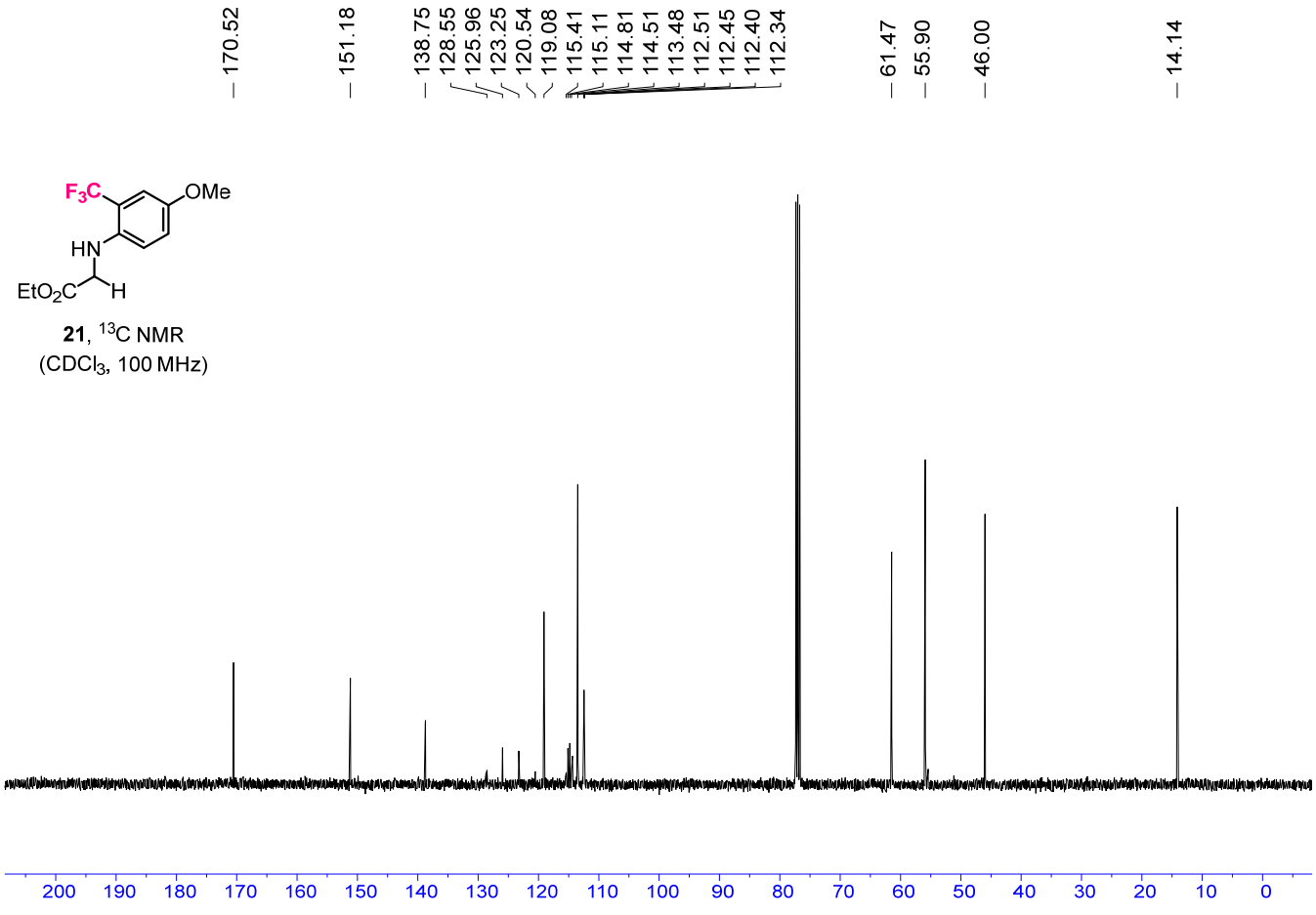

9.355
9.346
8.769
8.748
8.505
8.457
7.656
7.636
7.616
7.479
7.461
6.719
6.698
6.552
6.531
4.896
4.880
4.866
4.132
4.115
4.097
4.078
3.856
3.840
3.826
3.775
3.766
3.665
2.857
2.822
2.812
2.720
2.714
2.704
2.692
2.398
2.381
2.363
2.345
1.686
1.667
1.647
1.628
1.281
1.266
1.249
1.227
1.212
1.196
1.180
1.161
OCH3
HN
H
N
EtO2C
O
NH
CF3
20, 1H NMR
(CDCl3, 400 MHz)
1.00
1.01
1.01
1.02
1.01
0.55
0.98
2.00
2.04
1.06
3.05
2.06
3.12
3.16
0.71
3.61
2.80
2.84
2.18
15.48
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


172.48
171.25
169.67
169.15
168.27
166.76
153.25
140.62
137.83
136.40
131.08
125.25
118.37
115.27
114.90
61.54
61.51
55.64
49.25
41.14
41.09
37.89
31.33
30.34
30.00
29.31
29.23
29.13
26.96
26.77
25.18
25.15
22.64
14.09
OCH3
HN
H
N
EtO2C
O
NH
CF3
20, 13C{1H} NMR
(CDCl3, 100 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

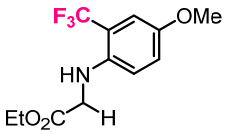

-63.356
-63.386
-63.416
-63.733
-63.763
-63.792
OCH3
HN
H
N
EtO2C
O
O
3
NH
O
O
N
NH
O
O
CF3
20, 19F NMR
(CDCl3, 376 MHz)
1.66
1.34
-63.0
-63.5
-64.0
-64.5
1.66
1.34
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105



21, ^{1}H NMR
($CDCl_3$, 400 MHz)



21, ^{13}C NMR
($CDCl_3$, 100 MHz)



21, ^{19}F NMR
($CDCl_3$, 376 MHz)