Electronic Supplementary Information

Iron-Catalysed Radical Cyclization/$C_{(sp3)}$–H Alkylation Cascade between γ,δ-Unsaturated Oxime Esters and Glycine Derivatives: Access to Pyrroline-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 and carbon nuclear magnetic resonance ($^{13}C\{^1H\}$ 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 (*Chloroform-d*: 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. IR spectra were recorded on a Bruker FT-IR spectrometer. HRMS was measured on a TOF-Q mass spectrometer equipped with an ESI source. Crystallographic data were collected on a Rigaku MM007 HF rotating anode. Electron paramagnetic resonance (EPR) signal was recorded on a Bruker EMXmicro-6/1/P/L spectrometer.

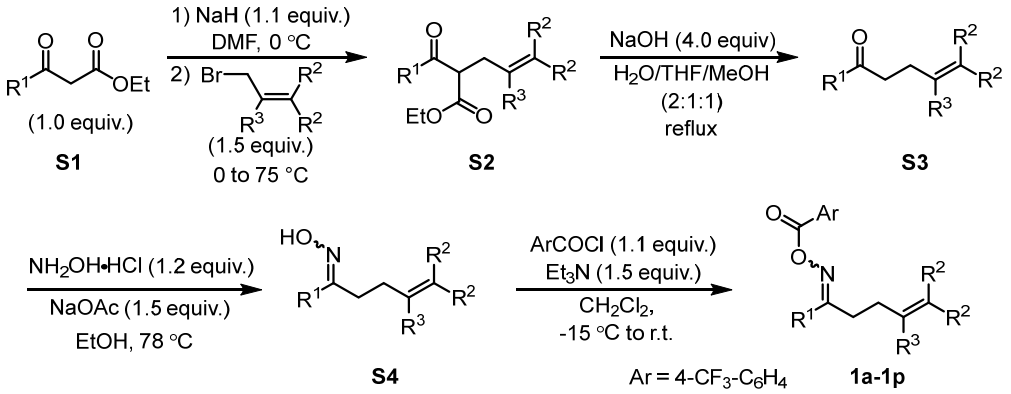
Abbreviations:

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; TEMPO–(2,2,6,6-tetramethylpiperidin-1-yl)oxyl; DMPO–5,5-Dimethyl-1-pyrroline N-oxide; CAN–ceric ammonium nitrate; LED–light-emitting diode

II. The Preparation of Substrates

a) General procedure for the synthesis of γ,δ-unsaturated oxime esters

γ,δ-Unsaturated oxime esters were prepared through a slightly modified 4-step procedure based on literature reports.[1-6]

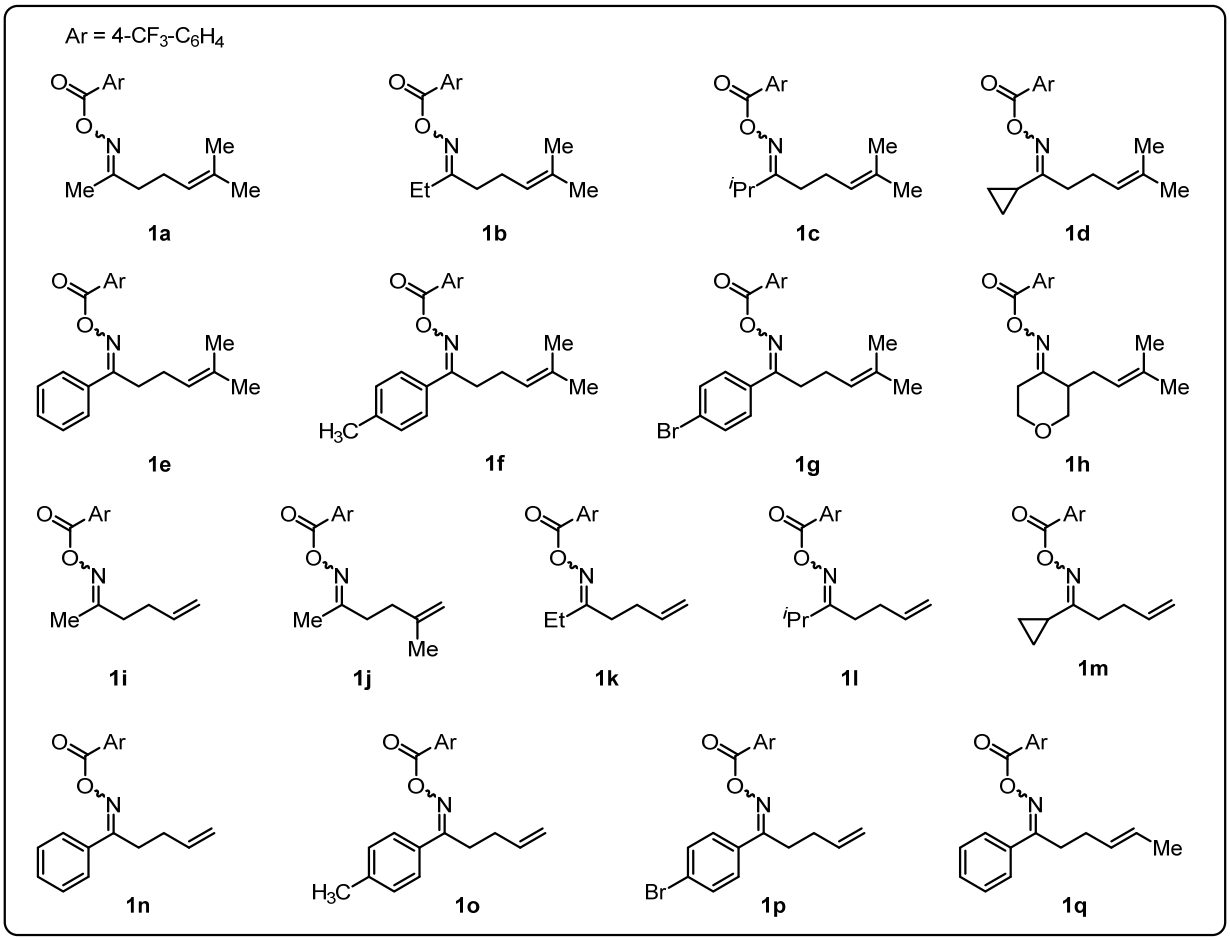


i) A solution of *β*-keto ester **S1** (20 mmol) in DMF (40 mL) was treated with NaH (22 mmol, 60 % in mineral oil) at 0 ˚C and stirred for 1 h, followed by the addtion of an allylic bromide (30 mmol). The resulted mixture was warmed up to 75 ºC and stirred for 6 h before it was cooled to room temperature and quenched with H_2O (100 mL). The aqueous phase was acidified with HCl (1 M, to pH = 3 to 4) and then extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with H_2O (2 × 25 mL), brine (2 × 25 mL), and then dried over anhydrous Na_2SO_4. After the removal of solvent, the residue was purified through a silica gel flash column with PE/ EtOAc (50:1) as the eluent to give compound **S2**.

ii) S2 (1.0 equiv) was dissoved in H_2O/THF/MeOH (40 mL, 2:1:1) with NaOH (4.0 equiv), and the mixture was heated under reflux for 2 to 4 h. Upon the consumption of **S2** (as indicated by TLC), the mixture was cooled down and the volatiles were removed *in vaco*. The aqueous layer was then extracted with EtOAc (3 × 20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. After the removal of solvent, the crude product was purified through a silica gel flash column with PE/EtOAc (100:1) as the eluent to give γ,δ-unsaturated ketone **S3.**

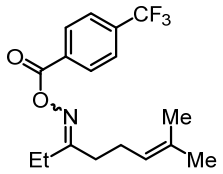
iii) To a stirred solution of unsaturated ketone **S3** (1.0 equiv) in EtOH (30 mL) were added NH_2OH•HCl (1.2 equiv) and NaOAc (1.5 equiv). The mixture was then heated under reflux and monitored with TLC. Upon consumption of **S3** (usually 4 h), the reaction was cooled down, quenched by $NaHCO_3$ (saturated aqueous solution, 80 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were then washed with H_2O (2 × 25 mL) and brine (25 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified through a silica gel flash column with PE/EtOAc (10:1 to 4:1) to afford a corresponding γ,δ-unsaturated oxime **S4**.

iv) Oxime **S4** (1.0 equiv) and a stir bar were placed in a flame-dried round bottom flask, which was then sealed under N_2 atmosphere, and cooled in an ice-salt bath. After dry CH_2Cl_2 (25 mL) and NEt_3 (1.5 equiv) were added, a solution of *p*-trifluoromethylbenzoyl chloride (1.1 equiv, dissolved in 10 to 15 mL CH_2Cl_2) was then added dropwise into the flask. The mixture was stirred at the same temperature for 10 min and then gradually warmed up to room temperature before it was quenched by $NaHCO_3$ (saturated aqueous solution). After the organic layer was separated, the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford crude product **1**, which was then purified through a silica gel flash column with PE/EtOAc (50:1 to 20:1).

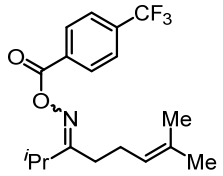


Compounds **1a**, **1d-1g**, **1n-1q** are known compounds and their characterization data are in agreement with the literatures. The rest of them are reported for the first time and fully characterized.

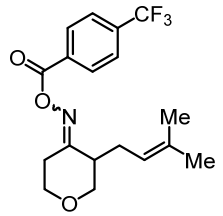
compound	**1a**, **1d**, **1o**	**1e**, **1f**, **1g**, **1n**, **1q**	**1p**
reference	[1]	[2]	[3]



7-Methyloct-6-en-3-one O-(4-(trifluoromethyl)benzoyl) oxime **(1b)**: According to the general procedure, compound **1b** was purified through a silica gel flash column (PE/EtOAc from 50:1 to 20:1) as colorless oil (2.0 g, 31% yield). ^{1}H NMR (400 MHz, *Chloroform-d*) δ 8.19 – 8.07 (m, 2H), 7.74 – 7.64 (m, 2H), 5.10 (t, *J* = 7.4 Hz, 1H), 2.57 – 2.37 (m, 4H), 2.32 – 2.18 (m, 2H), 1.63 (s, 3H), 1.56 (s, 3H), 1.19 (t, *J* = 7.5 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 171.9, 162.7, 134.5 (q, *J* = 32.7 Hz), 133.4, 132.6, 129.8, 125.4 (q, *J* = 3.8 Hz), 123.4 (q, *J* = 272.7 Hz), 122.1, 29.4, 27.8, 25.5, 24.6, 17.5, 10.7; ^{19}F NMR (376 MHz, *Chloroform-d*) δ -63.23 (s, 3F); IR ν_{max} (neat) cm^{-1}: 1746, 1635, 1410, 1322, 1255, 1166, 1127, 1073, 1015, 910, 859, 768, 698; MS (ESI, m/z): calcd for $C_{17}H_{20}F_3NO_2Na^+$ [M + Na]$^+$ 350.13, found 350.13.

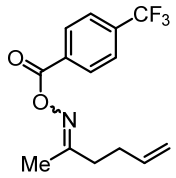


2,7-Dimethyloct-6-en-3-one O-(4-(trifluoromethyl)benzoyl) oxime **(1c)**: According to the general procedure, compound **1c** was purified through a silica gel flash column (PE/EtOAc from 50:1 to 20:1) as colorless oil (2.1 g, 31% yield). ^{1}H NMR (400 MHz, *Chloroform-d*) δ 8.18 – 8.05 (m, 2H), 7.73 – 7.60 (m, 2H), 5.10 (t, *J* = 7.3 Hz, 1H), 2.82 – 2.68 (m, 1H), 2.47 – 2.35 (m, 2H), 2.32 – 2.20 (m, 2H), 1.61 (s, 3H), 1.53 (s, 3H), 1.17 (d, *J* = 6.9 Hz, 6H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.5, 162.6, 134.4 (q, *J* = 32.8 Hz), 133.0, 132.7, 129.7, 125.3 (q, *J* = 3.8 Hz), 123.4 (q, *J* = 272.7 Hz), 122.4, 34.1, 28.1, 25.4, 25.2, 19.6, 17.4; ^{19}F NMR (376 MHz, *Chloroform-d*) δ -63.26 (s, 3F); IR ν_{max} (neat) cm^{-1}: 1746, 1630, 1410, 1322, 1255, 1166, 1128, 1065, 1015, 898, 859, 768, 698; MS (ESI, m/z): calcd for $C_{18}H_{22}F_3NO_2Na^+$ [M + Na]$^+$ 364.15, found 364.15.

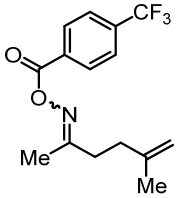


3-(3-Methylbut-2-en-1-yl)tetrahydro-4H-pyran-4-one O-(4-(trifluoromethyl)benzoyl) oxime **(1h)**: According to the general procedure, compound **1h** was purified through a silica gel flash column (PE/EtOAc from 50:1 to 20:1) as colorless oil (2.2 g, 31% yield). ^{1}H NMR (400 MHz, *Chloroform-d*) δ 8.22 – 8.11 (m, 2H), 7.78 – 7.68 (m, 2H), 5.14 (t, *J* = 7.3 Hz, 1H), 4.07 – 3.93 (m, 1H), 3.86 – 3.73 (m, 2H), 3.72 – 3.63 (m, 1H), 2.97 – 2.84 (m, 1H), 2.80 – 2.60 (m, 2H), 2.55 – 2.33 (m, 2H), 1.72 (s, 3H),

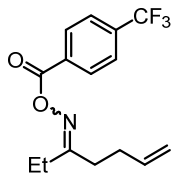
1.65 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 168.1, 162.8, 134.8 (q, *J* = 18.7 Hz), 134.7, 132.5, 130.0, 125.6 (q, *J* = 3.8 Hz), 123.5 (q, *J* = 272.7 Hz), 120.5, 71.1, 66.8, 42.4, 28.1, 26.4, 25.8, 17.9; ^{19}F NMR (376 MHz, *Chloroform-d*) δ -63.17 (s, 3F); IR ν_{max} (neat) cm^{-1}: 1741, 1637, 1412, 1328, 1262, 1240, 1125, 1077, 1014, 906, 866, 777, 698; MS (ESI, m/z): calcd for $C_{18}H_{20}F_3NO_3Na^+$ $[M + Na]^+$ 378.13, found 378.13



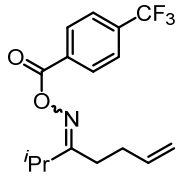
Hex-5-en-2-one O-(4-(trifluoromethyl)benzoyl) oxime **(1i)**: According to the general procedure, compound **1i** was purified through a silica gel flash column (PE/EtOAc from 50:1 to 20:1) as colorless oil (1.5 g, 27% yield). ^{1}H NMR (400 MHz, *Chloroform-d*) δ 8.17 – 8.03 (m, 2H), 7.70 – 7.58 (m, 2H), 5.77 (ddt, *J* = 16.8, 10.0, 6.5 Hz, 1H), 5.03 (d, *J* = 16.8 Hz, 1H), 4.96 (d, *J* = 10.0 Hz, 1H), 2.52 – 2.43 (m, 2H), 2.39 – 2.27 (m, 2H), 2.07 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 167.3, 162.4, 136.2, 134.3 (q, *J* = 32.8 Hz), 132.4, 129.7, 125.3 (q, *J* = 3.7 Hz), 123.3 (q, *J* = 272.7 Hz), 115.7, 34.9, 30.0, 15.4; ^{19}F NMR (376 MHz, *Chloroform-d*) δ -63.27 (s, 3F); IR ν_{max} (neat) cm^{-1}: 1745, 1641, 1410, 1320, 1253, 1241, 1179, 1122, 1079, 1014, 905, 862, 769, 698; MS (ESI, m/z): calcd for $C_{14}H_{14}F_3NO_2Na^+$ $[M + Na]^+$ 308.09, found 308.09.



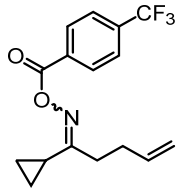
5-Methylhex-5-en-2-one O-(4-(trifluoromethyl)benzoyl) oxime **(1j)**: According to the general procedure, compound **1j** was purified through a silica gel flash column (PE/EtOAc from 50:1 to 20:1) as colorless oil (1.6 g, 27% yield).^{1}H NMR (400 MHz, *Chloroform-d*) δ 8.17 – 8.05 (m, 2H), 7.73 – 7.59 (m, 2H), 4.71 (s, 1H), 4.70 (s, 1H), 2.59 – 2.47 (m, 2H), 2.33 – 2.22 (m, 2H), 2.08 (s, 3H), 1.71 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 167.6, 162.5, 143.6, 134.4 (q, *J* = 32.6 Hz), 132.5, 129.7, 125.3 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 272.7 Hz), 110.9, 34.0, 33.9, 22.0, 15.3; ^{19}F NMR (376 MHz, *Chloroform-d*) δ -63.26 (s, 3F); IR ν_{max} (neat) cm^{-1}: 1745, 1641, 1410, 1320, 1253, 1179, 1122, 1078, 1014, 905, 862, 769, 698; MS (ESI, m/z): calcd for $C_{15}H_{16}F_3NO_2Na^+$ $[M + Na]^+$ 322.10, found 322.10.



Hept-6-en-3-one O-(4-(trifluoromethyl)benzoyl) oxime **(1k)**: According to the general procedure, compound **1k** was purified through a silica gel flash column (PE/EtOAc from 50:1 to 20:1) as colorless oil (1.7 g, 28% yield).^{1}H NMR (400 MHz, *Chloroform-d*) δ 8.21 – 8.11 (m, 2H), 7.78 – 7.69 (m, 2H), 5.86 (ddt, *J* = 16.7, 10.2, 6.5 Hz, 1H), 5.15 – 5.06 (m, 1H), 5.06 – 5.00 (m, 1H), 2.59 – 2.48 (m, 4H), 2.45 – 2.34 (m, 2H), 1.21 (t, *J* = 7.7 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 171.8, 162.8, 136.6, 134.6 (q, *J* = 32.9 Hz), 132.6, 129.9, 125.6 (q, *J* = 3.8 Hz), 123.5 (q, *J* = 272.9 Hz), 115.8, 33.3, 30.2, 23.1, 10.4; ^{19}F NMR (376 MHz, *Chloroform-d*) δ -63.18 (s, 3F); IR ν_{max} (neat) cm^{-1}: 1746, 1640, 1410, 1322, 1257, 1166, 1127, 1059, 1015, 904, 858, 768, 698; MS (ESI, m/z): calcd for $C_{15}H_{16}F_3NO_2Na^+$ [M + Na]$^+$ 322.10, found 322.10.



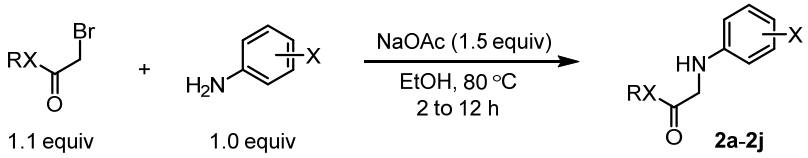
2-Methylhept-6-en-3-one O-(4-(trifluoromethyl)benzoyl) oxime **(1l)**: According to the general procedure, compound **1l** was purified through a silica gel flash column (PE/EtOAc from 50:1 to 20:1) as colorless oil (1.8 g, 29% yield, E/Z isomers, major:minor = 8:1). ^{1}H NMR (400 MHz, *Chloroform-d*) δ 8.13 – 7.02 (m, 2H), 7.67 – 7.57 (m, 2H), 5.77 (ddt, *J* = 17.0, 10.2, 6.5 Hz, 1H), 5.00 (d, *J* = 17.0 Hz, 1H), 4.94 (d, *J* = 10.2 Hz, 1H), 3.33 (hept, *J* = 7.1 Hz, 1H, minor), 2.71 (hept, *J* = 6.9 Hz, 1H, major), 2.51 – 2.42 (m, 2H, major), 2.41 – 2.34 (m, 4H, minor), 2.34 – 2.24 (m, 2H, major), 1.13 (d, *J* = 7.0 Hz, 6H, major), 1.11 (d, *J* = 7.0, 6H, minor); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.0 (major), 173.7 (minor), 162.34 (minor), 162.25 (major), 136.8 (minor), 136.4 (major), 134.2 (q, *J* = 32.7 Hz, major + minor), 132.5 (major + minor), 129.60 (minor), 129.55 (major), 125.3 (q, *J* = 3.7 Hz, major + minor), 123.3 (q, *J* = 272.7 Hz, major + minor), 115.4 (major), 115.1 (minor), 33.9 (major), 30.5 (major), 29.99 (minor), 29.96 (minor), 28.86 (minor), 27.2 (major), 19.4 (major), 18.7 (minor); ^{19}F NMR (376 MHz, *Chloroform-d*) δ -63.32 (s, 3F); IR ν_{max} (neat) cm^{-1}: 1746, 1641, 1410, 1322, 1254, 1166, 1127, 1055, 1015, 909, 859, 768, 698; MS (ESI, m/z): calcd for $C_{16}H_{18}F_3NO_2Na^+$ [M + Na]$^+$ 336.12, found 336.12.



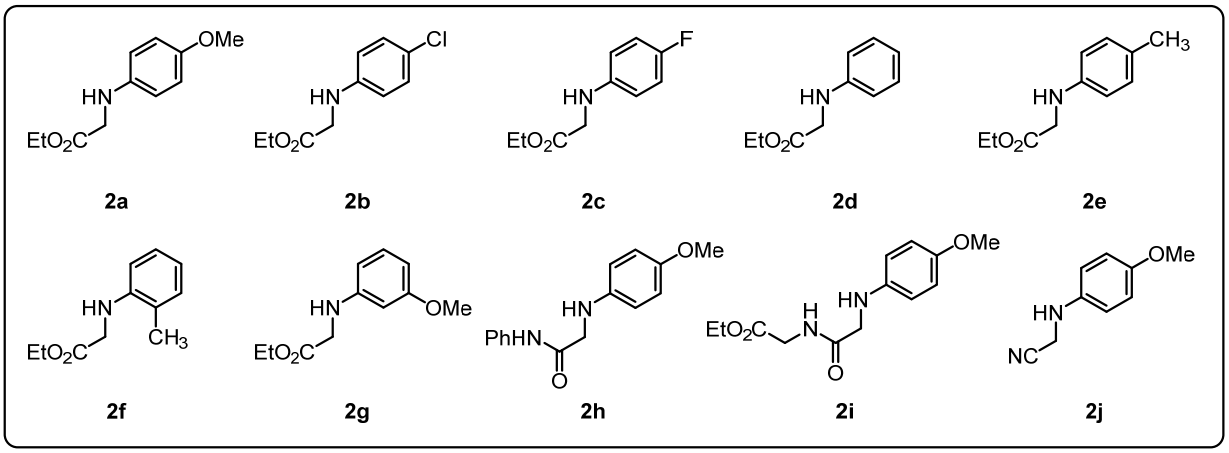
1-Cyclopropylpent-4-en-1-one O-(4-(trifluoromethyl)benzoyl) oxime **(1m)**: According to the general procedure, compound **1m** was purified through a silica gel flash column (PE/EtOAc from 50:1 to 20:1) as colorless oil (1.8 g, 29% yield).^{1}H NMR (400 MHz, *Chloroform-d*) δ 8.19 – 8.08 (m, 2H), 7.76 – 7.67 (m, 2H), 5.83 (ddt, *J* = 16.8, 10.2, 6.0 Hz, 1H), 5.09 (d, *J* = 16.8 Hz, 1H), 5.04 (d, *J* = 10.2 Hz, 1H), 2.48 – 2.30 (m, 4H), 1.83 – 1.69 (m, 1H), 0.98 – 0.86 (m, 4H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ

171.8, 162.5, 136.4, 134.5 (q, J = 32.7 Hz), 132.6, 129.8, 125.5 (q, J = 3.7 Hz), 123.5 (q, J = 272.9 Hz), 115.9, 30.6, 28.1, 14.4, 6.5; ^{19}F NMR (376 MHz, *Chloroform-d*) δ -63.16 (s, 3F); IR ν_{max} (neat) cm^{-1}: 1746, 1620, 1411, 1322, 1256, 1166, 1128, 1065, 1015, 903, 859, 768, 699; MS (ESI, m/z): calcd for $C_{16}H_{16}F_3NO_2Na^+$ $[M + Na]^+$ 334.10, found 334.10.

b) α-Amino carbonyl compounds



α-Amino carbonyl compounds **2** were prepared through nucleophilic substitution of corresponding anilines and α-bromo carbonyls according to literature procedures. All the compounds are known and their charachaterization data are in accordance with literatures.[7-12]



Compounds	**2a, 2b, 2c, 2d, 2e, 2f**	**2g**	**2h**	**2i**	**2j**
references	[7-8]	[9]	[10]	[11]	[12]

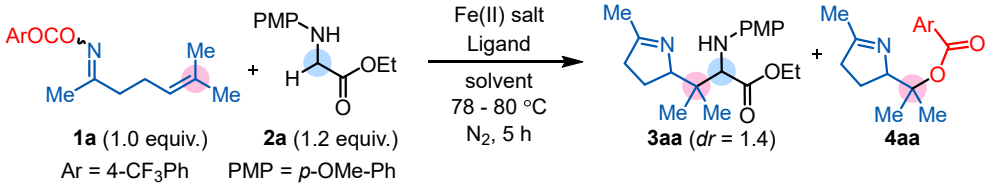
III. The Evaluation of Catalysts and Ligands

General procedures for iron salts screening: To a flame-dried reaction tube charged with a stir bar were added oxime ester **1a** (63 mg, 0.2 mmol), glycinate **2a** (51.6 mg, 0.24 mmol), and a corresponding Fe(II) salt (0.01 mmol). The tube was sealed with a septum, evacuated, and backfilled with N_2 three times. After anhydrous DCE (2 mL) was added, the reaction was stirred for 5 h in an 80 ˚C oil bath. The mixture was then quenched with $NaHCO_3$ (saturated aqueous solution, 2 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 1 mL) and the combined organic layers were dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was then filtered through a short silica gel pad, and washed with PE/EtOAc (1:1, 15 mL). After the volatiles were removed *in vacuo*, the crude product was dissolved in $CDCl_3$ with a specific amount of 1,3,5-trimethoxyl benzene and submitted for ^1H NMR analysis.

General procedures for ligands screening: In a N_2 atmosphere glove box, $Fe(NTf_2)_2$ (6.2 mg, 0.01 mmol) ***or*** $Fe(OAc)_2$ (1.7 mg, 0.01 mmol), and a ligand (0.02 mmol) were added into a 2-dram vial, which was then sealed with a septum. After the vial was then taken out of the glove box, freshly distilled DCE ***or*** EtOAc (0.7 mL) and dry DMA (0.3 mL) were added. The mixture was sonicated for 2 min to afford a clear **catalyst solution**. To a flame-dried reaction tube charged with a stir bar were added oxime ester **1a** (63 mg, 0.2 mmol) and glycinate **2a** (51.6 mg, 0.24 mmol). The tube was sealed with a septum, evacuated, and backfilled with N_2 three times. DCE or EtOAc (1 mL for 5 mol%, or 1.7 mL for 1.5 mol% catalyst loading) was then added through a syringe, followed by the addition of the above **catalyst solution** (1 mL for 5 mol%, or 0.3 mL for 1.5 mol% catalyst loading). The reaction mixture stirred for 5 h in an 80 ˚C oil bath before it was quenched with $NaHCO_3$ (saturated aqueous solution, 2 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 1 mL) and the combined organic layers were dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was then filtered through a short silica gel pad, and washed with PE/EtOAc (1:1, 15 mL). After the volatiles were removed *in vacuo*, the crude product was dissolved in $CDCl_3$ with a specific amount of 1,3,5-trimethoxyl benzene and submitted for ^1H NMR analysis.

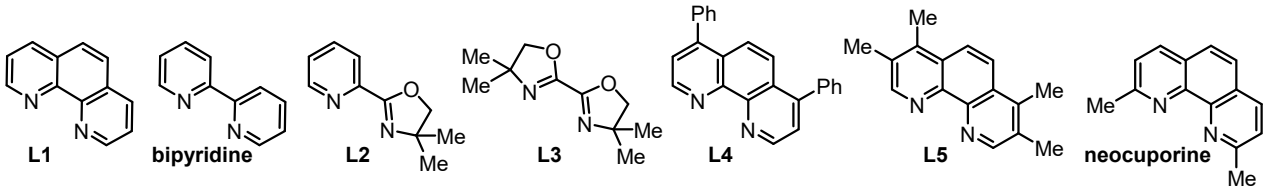
The results obtained with different Fe(II) salts, solvents and ligands are summarized in **Table S1**.

Table S1. The Discovery of Catalysts and Ligands[a]



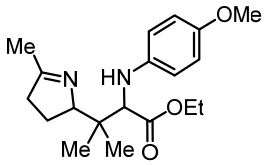
1a (1.0 equiv.) **2a** (1.2 equiv.) **3aa** (*dr* = 1.4) **4aa**

Ar = 4-CF_3Ph PMP = *p*-OMe-Ph



entry	metal salt (mol%)	ligand (mol%)	solvent (0.1 M)	yield (%)[b] **3aa** / **4aa**
1	none	none	DCE	n.d.[c] / n.d.
2	$FeCl_2$ (5)	none	DCE	5 / 63
3	CuCl (5)	none	DCE	<5 / <5[d]
4	$CoCl_2$ (5)	none	DCE	<5 / 34[e]
5	$Fe(OAc)_2$ (5)	none	DCE	10 / 67
6	$Fe(OTf)_2$ (5)	none	DCE	<5 / 68
7	$Fe(NTf_2)_2$ (5)	none	DCE	12 / 54
8	$Fe(NTf_2)_2$ (5)	**L1** (10)	DCE/DMA[f]	45 / 22
9	$Fe(OAc)_2$ (5)	**L1** (10)	DCE/DMA	58 / 11
10	$Fe(OAc)_2$ (5)	**L1** (10)	DMA	64 / 10
11	$Fe(OAc)_2$ (5)	**L1** (10)	EtOAc/DMA	73 / 8
12	$Fe(OAc)_2$ (1.5)	**L1** (3)	EtOAc/DMA	72 / 10
13	$Fe(OAc)_2$ (1.5)	**bipyridine** (3)	EtOAc/DMA	30 / 34
14	$Fe(OAc)_2$ (1.5)	**L2** (3)	EtOAc/DMA	49 / 28
15	$Fe(OAc)_2$ (1.5)	**L3** (3)	EtOAc/DMA	7 / 66
16	$Fe(OAc)_2$ (1.5)	**L4** (3)	EtOAc/DMA	84 / 8
17	$Fe(OAc)_2$ (1.5)	**L5** (3)	EtOAc/DMA	85 / <5
18	$Fe(OAc)_2$ (1.5)	**neocuporine** (3)	EtOAc/DMA	30 / 35
19[g]	$Fe(OAc)_2$ (1.5) **1a** (1.3 equiv), **2a** (1.0 equiv)	**L5** (3)	EtOAc/DMA	91 (88)[h]

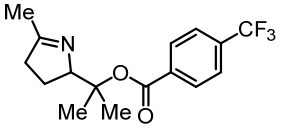
[a]Unless otherwise stated, the reaction was performed under N_2 with **1a** (0.20 mmol) and **2a** (0.24 mmol) in the presence of a corresponding catalyst in indicated solvent (2 mL) at 80°C for 5 h. DCE = 1,2-dichloroethane; DMA = N,N-dimethyl acetamide. [b]Yields were determined through ^{1}H NMR analysis with an internal standard; the *d.r.* of **3aa** was determined to be ~1.4:1. [c]Not Determined. [d]A cyclization-elimination product **S5** was detected. [e]45% of **1a** was recovered. [f]A small amount of DMA was added to dissolve the iron/ligand complex. [g]Reaction was performed on 0.4 mmol scale. [h]Isolated yield.



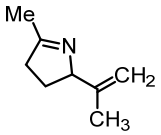
***Ethyl 2-((4-methoxyphenyl)amino)-3-methyl-3-(5-methyl-3,4-dihydro-2H-pyrrol-2-yl)butanoate* (3aa)**: Compound **3aa** was isolated from the 0.4 mmol scale reaction (entry 17) through a silica gel flash column (PE/EtOAc from 5:1 to 2:1) as a pair of diastereomers.

Isomer 1 (less polar, light yellow oil, 67.8 mg, 51%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.78 – 6.69 (m, 2H), 6.68 – 6.61 (m, 2H), 5.41 (brd, *J* = 6.2 Hz, 1H), 4.20 – 4.07 (m, 4H), 3.72 (s, 3H), 2.52 – 2.26 (m, 2H), 2.04 (d, *J* = 2.1 Hz, 3H), 1.89 (dddd, *J* = 12.9, 9.1, 7.7, 3.7 Hz, 1H), 1.59 (dq, *J* = 12.9, 9.2 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.00 (s, 3H), 0.89 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.0, 173.8, 152.1, 142.3, 114.8, 114.7, 77.1, 66.2, 60.3, 55.7, 39.7, 38.6, 24.5, 21.7, 19.9, 19.7, 14.3; IR ν_{max} (neat) cm^{-1}: 3291, 2965, 1723, 1652, 1510, 1234, 1034, 818; HRMS (ESI, m/z): calcd for $C_{19}H_{29}N_2O_3^+$ $[M + H]^+$ 333.2173, found 333.2154.

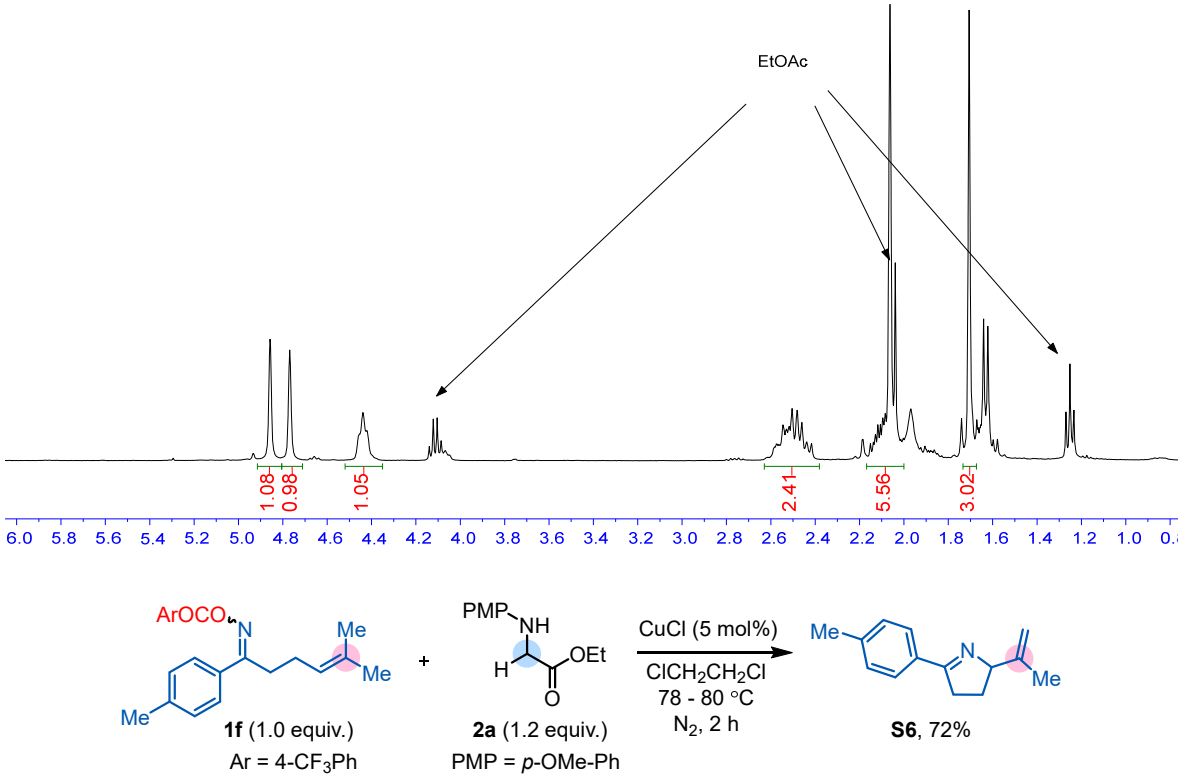
Isomer 2 (more polar, light yellow oil, 49.2 mg, 37%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.78 – 6.69 (m, 2H), 6.68 – 6.59 (m, 2H), 4.46 (brd, *J* = 7.8 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 4.08 – 4.01 (m, 1H), 3.91 (d, *J* = 7.0 Hz, 1H), 3.72 (s, 3H), 2.52 – 2.33 (m, 2H), 2.04 (s, 3H), 1.97 – 1.83 (m, 1H), 1.77 – 1.62 (m, 1H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.16 (s, 3H), 0.90 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.6, 173.4, 152.7, 141.7, 115.5, 114.7, 79.3, 65.0, 60.6, 55.7, 40.0, 39.0, 24.5, 20.7, 20.0, 19.8, 14.3; IR ν_{max} (neat) cm^{-1}: 3290, 2968, 1724, 1648, 1509, 1233, 1034, 820; HRMS (ESI, m/z): calcd for $C_{19}H_{29}N_2O_3^+$ $[M + H]^+$ 333.2173, found 333.2154.



***2-(5-Methyl-3,4-dihydro-2H-pyrrol-2-yl)propan-2-yl 4-(trifluoromethyl)benzoate* (4aa)**: Compound **4aa** was isolated from the $Fe(OTf)_2$ catalyzed reaction (entry 4) through a silica gel flash column (PE/EtOAc = 3:1) as a yellow oil (42.6 mg, 68%). ^{1}H NMR (400 MHz, *Chloroform-d*) δ 8.10 – 7.96 (m, 2H), 7.71 – 7.61 (m, 2H), 4.46 – 4.35 (m, 1H), 2.66 – 2.45 (m, 2H), 2.08 (s, 3H), 2.06 – 1.93 (m, 1H), 1.90 – 1.79 (m, 1H), 1.74 (s, 3H), 1.57 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 176.0, 164.4, 135.2, 134.0 (q, *J* = 32.5 Hz), 129.7, 125.2 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 272.6 Hz), 85.3, 80.4, 39.3, 24.0, 23.9, 22.1, 19.8; ^{19}F NMR (376 MHz, *Chloroform-d*) δ -63.07 (s, 3F); IR ν_{max} (neat) cm^{-1}: 2981, 1715, 1650, 1410, 1324, 1309, 1288, 1164, 1117, 1099, 1064, 1016, 862, 774, 703; HRMS (ESI, m/z): calcd for $C_{16}H_{19}F_3NO_2^+$ $[M + H]^+$ 314.1362, found 314.1333.

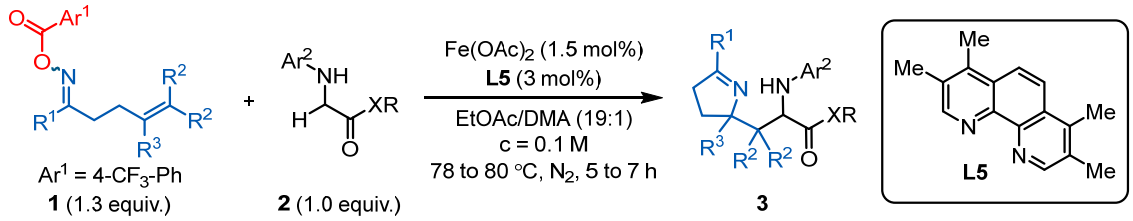


When CuCl was used as the catalyst, the oxime ester was quickly decomposed with the amino ester almost intact. A cyclization-eliminization product **S5** was detected on crude NMR, which is in accordance with Zaid's previous report.[13] However, this compound was volatile and difficult to purify.



In order to confirm the distinct selectivity exhibited by CuCl, a similar oxime exster with higher molecular weight (**1f**) was subjected into the same condition. A corresponding Hofmann elimination product **S6** was also isolated as the major product. **S6** is a known compound and its characterization data are in agreement with the literature.[4] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 4.94 (s, 1H), 4.82 (s, 1H), 4.71 (t, *J* = 7.6 Hz, 1H), 3.02 (dddd, *J* = 17.0, 9.9, 5.3, 2.1 Hz, 1H), 2.92 (dddd, *J* = 17.0, 9.3, 7.2, 1.8 Hz, 1H), 2.39 (s, 3H), 2.26 (dddd, *J* = 13.6, 9.9, 8.4, 5.4 Hz, 1H), 1.87 – 1.75 (m, 1H), 1.77 (s, 3H).

IV. Substrate Scope and Products Characterization

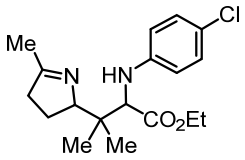


General procedure for synthesis of pyrroline-containing amino acids derivatives:

In a N_2 atmosphere glove box, $Fe(OAc)_2$ (8.7 mg, 0.05 mmol), and **L5** (23.6 mg, 0.10 mmol) were added into a 2-dram vial, which was then sealed with a septum. After the vial was then taken out of the glove box, freshly distilled EtOAc (3.5 mL) and dry DMA (1.5 mL) were added. The mixture was sonicated until fully dissolved to afford a **catalyst stock solution**.

To a flame-dried reaction tube charged with a stir bar were added an oxime ester **1** (0.26 mmol) and an glycinate **2** (0.20 mmol). The tube was sealed with a septum, evacuated, and backfilled with N_2 three times. EtOAc (1.7 mL) was then added through a syringe, followed by the addition of the **catalyst solution** (0.3 mL). The reaction mixture stirred for 5-7 h in an 80 ˚C oil bath before it was quenched with $NaHCO_3$ (saturated aqueous solution, 2 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 1 mL) and the combined organic layers were dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was then purified through a silica gel flash column with PE and EtOAc as eluent.

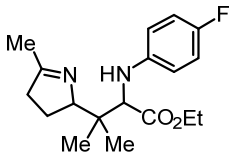
The substrate exploration was performed under optimized reaction conditions following the general procedure, and the obtained pyrroline-containing amino esters and peptides are fully characterized with ^1H, ^{13}C, ^{19}F NMR, FT-IR and HRMS.



***Ethyl 2-((4-chlorophenyl)amino)-3-methyl-3-(5-methyl-3,4-dihydro-2H-pyrrol-2-yl)butanoate* (3ab)**: Following the general procedure, compound **3ab** was prepared by reacting **1a** with **2b** and the product was isolated through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a pair of diastereomers:

Isomer 1 (less polar, yellow oil, 18.9 mg, 28%): ^1H NMR (400 MHz, *Chloroform-d*) δ 7.11 – 7.02 (m, 2H), 6.61 – 6.53 (m, 2H), 6.36 (brd, J = 9.3 Hz, 1H), 4.24 – 4.09 (m, 3H), 4.04 (d, J = 9.2 Hz, 1H), 2.52 – 2.28 (m, 2H), 2.05 (d, J = 2.1 Hz, 3H), 1.88 (dddd, J = 12.6, 9.1, 7.6, 3.5 Hz, 1H), 1.57 (dq, J = 12.6, 9.4 Hz, 1H), 1.23 (t, J = 7.2 Hz, 3H), 1.01 (s, 3H), 0.89 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, *Chloroform-d*) δ 174.1, 173.5, 146.8, 128.9, 121.6, 114.2, 76.8, 66.0, 60.6, 39.5, 38.3, 24.8, 22.6, 20.0, 19.7, 14.3; IR ν_{max} (neat) cm^{-1}: 3302, 2968, 1730, 1652, 1596, 1507, 1369, 1314, 1261, 1200, 1173, 1154, 1027; HRMS (ESI, m/z): calcd for $C_{18}H_{25}ClN_2O_2Na^+$ $[M + Na]^+$ 359.1497, found 359.1470.

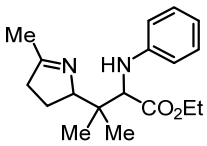
Isomer 2 (more polar, yellow oil, 18.2 mg, 27%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.13 – 7.05 (m, 2H), 6.60 – 6.53 (m, 2H), 5.07 (d, *J* = 8.9 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.03 – 3.91 (m, 2H), 2.54 – 2.31 (m, 2H), 2.04 (d, *J* = 2.0 Hz, 3H), 1.90 – 1.82 (m, 1H), 1.74 – 1.58 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.09 (s, 3H), 0.93 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.9, 172.9, 146.3, 129.0, 122.7, 114.8, 79.3, 64.4, 60.8, 40.0, 38.8, 24.6, 21.2, 19.8, 19.3, 14.3; IR ν_{max} (neat) cm^{-1}: 3377, 2972, 1717, 1647, 1599, 1521, 1490, 1367, 1248, 1192, 1139, 1092, 1015; HRMS (ESI, m/z): calcd for $C_{18}H_{25}ClN_2O_2Na^+$ $[M + Na]^+$ 359.1497, found 359.1470.



Ethyl 2-((4-fluorophenyl)amino)-3-methyl-3-(5-methyl-3,4-dihydro-2H-pyrrol-2-yl)butanoate **(3ac)**: Following the general procedure, compound **3ac** was prepared by reacting **1a** with **2c**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a pair of diastereomers:

Isomer 1 (less polar, yellow oil, 12.8 mg, 20%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.90 – 6.76 (m, 2H), 6.65 – 6.54 (m, 2H), 5.91 (brd, *J* = 9.5 Hz, 1H), 4.21 – 411 (m, 3H), 4.07 (d, *J* = 7.7 Hz, 1H), 2.51 – 2.28 (m, 2H), 2.05 (s, 3H), 1.94 – 1.83 (m, 1H), 1.65 – 1.51 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.01 (s, 3H), 0.89 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.0, 173.8, 155.8 (d, *J* = 234.5 Hz), 144.6 (d, *J* = 2.0 Hz), 115.5 (d, *J* = 22.2 Hz), 114.2 (d, *J* = 7.4 Hz), 77.0, 66.4, 60.5, 39.6, 38.5, 24.7, 22.3, 19.9, 19.7, 14.3; ^{19}F NMR (376 MHz, *Chloroform-d*) δ -128.26 – -128.36 (m, 1F); IR ν_{max} (neat) cm^{-1}: 3284, 2970, 1724, 1650, 1613, 1508, 1368, 1314, 1218, 1189, 1023; HRMS (ESI, m/z): calcd for $C_{18}H_{25}FN_2O_2Na^+$ $[M + Na]^+$ 343.1792, found 343.1764.

Isomer 2 (more polar, yellow oil, 12.2 mg, 19%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.90 – 6.80 (m, 2H), 6.64 – 6.53 (m, 2H), 4.83 (brd, *J* = 9.1 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.05 – 3.96 (m, 1H), 3.92 (d, *J* = 6.6 Hz, 1H), 2.54 – 2.32 (m, 2H), 2.03 (s, 3H), 1.89 (dtd, *J* = 12.5, 8.3, 3.8 Hz, 1H), 1.74 – 1.60 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.12 (s, 3H), 0.92 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 175.0, 173.2, 156.3 (d, *J* = 235.9 Hz), 144.0 (d, *J* = 1.8 Hz), 115.6 (d, *J* = 22.3 Hz), 114.9 (d, *J* = 7.5 Hz), 79.3, 65.0, 60.7, 40.0, 38.9, 24.6, 21.0, 19.8, 19.6, 14.3; ^{19}F NMR (376 MHz, *Chloroform-d*) δ -128.05 – -128.51 (m, 1F); IR ν_{max} (neat) cm^{-1}: 3284, 2970, 1724, 1650, 1613, 1508, 1368, 1314, 1218, 1189, 1023; HRMS (ESI, m/z): calcd for $C_{18}H_{25}FN_2O_2Na^+$ $[M + Na]^+$ 343.1792, found 343.1764.

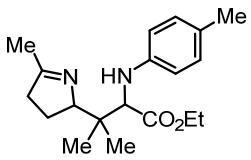


Ethyl 3-methyl-3-(5-methyl-3,4-dihydro-2H-pyrrol-2-yl)-2-(phenylamino)butanoate **(3ad)**: Following the general procedure, compound **3ad** was prepared by reacting **1a** with **2d**, and the product was isolated

through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 25.4 mg, 42%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.19 – 7.09 (m, 2H), 6.72 – 6.61 (m, 3H), 6.02 (d, *J* = 9.4 Hz, 1H), 4.21 – 4.10 (m, 4H), 2.52 – 2.29 (m, 2H), 2.05 (d, *J* = 2.0 Hz, 3H), 1.95 – 1.86 (m, 1H), 1.59 (dq, *J* = 12.7, 9.3 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.02 (s, 3H), 0.91 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.0, 173.8, 148.1, 129.1, 117.2, 113.2, 77.0, 65.4, 60.4, 39.6, 38.4, 24.7, 22.2, 19.9, 19.8, 14.3; IR ν_{max} (neat) cm^{-1}: 3281, 2968, 1729, 1654, 1601, 1520, 1326, 1290, 1200, 1154, 1012; HRMS (ESI, m/z): calcd for $C_{18}H_{26}N_2O_2Na^+$ $[M + Na]^+$ 325.1886, found 325.1878.

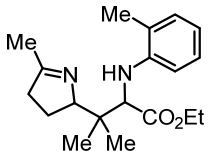
Isomer 2 (more polar, yellow oil, 15.7 mg, 26%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.20 – 7.10 (m, 2H), 6.77 – 6.68 (m, 1H), 6.68 – 6.59 (m, 2H), 4.81 (brd, *J* = 9.5 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.07 – 3.97 (m, 2H), 2.54 – 2.32 (m, 2H), 2.04 (d, *J* = 2.0 Hz, 3H), 1.94 – 1.82 (m, 1H), 1.77 – 1.62 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.15 (s, 3H), 0.92 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.7, 173.2, 147.6, 129.2, 118.2, 113.8, 79.2, 63.7, 60.6, 40.0, 38.9, 24.6, 20.8, 19.8, 14.3; IR ν_{max} (neat) cm^{-1}: 3284, 2967, 1728, 1652, 1601, 1498, 1314, 1251, 1181, 1152, 1026; HRMS (ESI, m/z): calcd for $C_{18}H_{26}N_2O_2Na^+$ $[M + Na]^+$ 325.1886, found 325.1878.



Ethyl 3-methyl-3-(5-methyl-3,4-dihydro-2H-pyrrol-2-yl)-2-(p-tolylamino)butanoate **(3ae)**: Following the general procedure, compound **3ae** was prepared by reacting **1a** with **2e**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 17.1 mg, 27%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.01 – 6.89 (m, 2H), 6.64 – 6.55 (m, 2H), 5.68 (brd, *J* = 8.7 Hz, 1H), 4.23 – 4.07 (m, 4H), 2.53 – 2.30 (m, 2H), 2.21 (s, 3H), 2.05 (d, *J* = 2.1 Hz, 3H), 1.95 – 1.82 (m, 1H), 1.59 (dq, *J* = 12.6, 9.3 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.01 (s, 3H), 0.91 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 173.9, 173.8, 145.8, 129.6, 126.4, 113.3, 77.1, 65.5, 60.4, 39.7, 38.5, 24.6, 21.9, 20.3, 19.9, 19.8, 14.3; IR ν_{max} (neat) cm^{-1}: 3291, 2967, 1724, 1652, 1616, 1520, 1367, 1302, 1196, 1147, 1024; HRMS (ESI, m/z): calcd for $C_{19}H_{28}N_2O_2Na^+$ $[M + Na]^+$ 339.2043, found 339.2040.

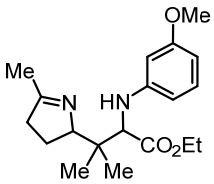
Isomer 2 (more polar, yellow oil, 15.8 mg, 25%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.01 – 6.91 (m, 2H), 6.62 – 6.53 (m, 2H), 4.56 (brs, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 4.08 – 4.00 (m, 1H), 3.98 (s, 1H), 2.52 – 2.31 (m, 2H), 2.22 (s, 3H), 2.04 (d, *J* = 2.0 Hz, 1H), 1.95 – 1.82 (m, 1H), 1.76 – 1.63 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.16 (s, 3H), 0.91 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.8, 173.3, 145.3, 129.7, 127.5, 114.0, 79.2, 64.0, 60.6, 40.0, 39.0, 24.5, 20.7, 20.4, 20.1, 19.8, 14.3; IR ν_{max} (neat) cm^{-1}: 3368, 2970, 1719, 1648, 1616, 1518, 1368, 1297, 1248, 1183, 1022; HRMS (ESI, m/z): calcd for $C_{19}H_{28}N_2O_2Na^+$ $[M + Na]^+$ 339.2043, found 339.2040.



Ethyl 3-methyl-3-(5-methyl-3,4-dihydro-2H-pyrrol-2-yl)-2-(o-tolylamino)butanoate **(3af)**: Following the general procedure, compound **3af** was prepared by reacting **1a** with **2f**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 13.3 mg, 21%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.09 – 6.99 (m, 2H), 6.74 (brs, 1H), 6.58 (t, *J* = 7.3 Hz, 1H), 6.54 (d, *J* = 8.0 Hz, 1H), 4.28 – 4.12 (m, 3H), 4.05 (d, *J* = 8.7 Hz, 1H), 2.52 – 2.31 (m, 2H), 2.23 (s, 3H), 2.05 (d, *J* = 2.2 Hz, 3H), 1.91 (dtd, *J* = 12.2, 8.3, 3.3 Hz, 1H), 1.69 – 1.53 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.05 (s, 3H), 0.94 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 173.9, 146.4, 130.0, 126.8, 122.7, 116.3, 109.0, 76.6, 66.4, 60.4, 39.4, 38.1, 25.0, 23.4, 19.9, 19.8, 18.1, 14.3; IR ν_{max} (neat) cm^{-1}: 3236, 2961, 1735, 1653, 1603, 1584, 1507, 1457, 1374, 1314, 1263, 1202, 1148, 1094, 1024; HRMS (ESI, m/z): calcd for $C_{19}H_{29}N_2O_2^+$ $[M + H]^+$ 317.2224, found. 317.2196.

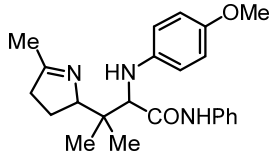
Isomer 2 (more polar, yellow oil, 12.0 mg, 19%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.10 – 7.00 (m, 2H), 6.65 (t, *J* = 7.3 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 4.91 (brd, *J* = 8.9 Hz, 1H), 4.23 – 4.09 (m, 2H), 4.09 – 3.99 (m, 2H), 2.56 – 2.30 (m, 2H), 2.23 (s, 3H), 2.05 (d, *J* = 2.1 Hz, 3H), 1.94 – 1.83 (m, 1H), 1.75 – 1.62 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.19 (s, 3H), 0.96 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 173.3, 145.7, 130.2, 127.0, 123.2, 117.5, 110.2, 79.3, 63.7, 60.6, 40.0, 38.9, 24.7, 21.2, 19.8, 19.7, 17.6, 14.3; IR ν_{max} (neat) cm^{-1}: 3291, 2970, 1725, 1651, 1605, 1587, 1512, 1446, 1368, 1314, 1189, 1144, 1095, 1024; HRMS (ESI, m/z): calcd for $C_{19}H_{29}N_2O_2^+$ $[M + H]^+$ 317. 2224, found 317.2196.



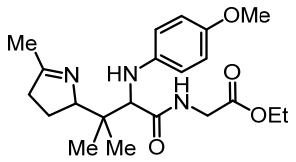
Ethyl 2-((3-methoxyphenyl)amino)-3-methyl-3-(5-methyl-3,4-dihydro-2H-pyrrol-2-yl)butanoate **(3ag)**: Following the general procedure, compound **3ag** was prepared by reacting **1a** with **2g**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 23.3 mg, 35%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.03 (t, *J* = 8.4 Hz, 1H), 6.31 – 6.19 (m, 3H), 6.13 (brd, *J* = 9.2 Hz, 1H), 4.24 – 4.08 (m, 4H), 3.75 (s, 3H), 2.52 – 2.28 (m, 2H), 2.05 (d, *J* = 2.1 Hz, 3H), 1.95 – 1.80 (m, 1H), 1.58 (dq, *J* = 12.9, 9.4 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.01 (s, 3H), 0.90 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 173.9, 173.7, 160.7, 149.5, 129.8, 106.2, 102.9, 98.7, 76.9, 65.4, 60.5, 55.0, 39.7, 38.4, 24.7, 22.2, 19.9, 19.8, 14.3; IR ν_{max} (neat) cm^{-1}: 3292, 2966, 1724, 1651, 1612, 1518, 1496, 1464, 1368, 1278, 1208, 1161, 1025; HRMS (ESI, m/z): calcd for $C_{19}H_{29}N_2O_3^+$ $[M + H]^+$ 333.2173, found 333.2160.

Isomer 2 (more polar, yellow oil, 16.0 mg, 24%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.05 (t, *J* = 8.1 Hz, 1H), 6.31 – 6.23 (m, 2H), 6.21 (t, *J* = 2.3 Hz, 1H), 4.89 (brd, *J* = 9.3 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.06 – 3.94 (m, 2H), 3.75 (s, 3H), 2.53 – 2.31 (m, 2H), 2.03 (d, *J* = 2.0 Hz, 3H), 1.95 – 1.82 (m, 1H), 1.74 – 1.61 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.14 (s, 3H), 0.92 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.7, 173.1, 160.7, 149.1, 129.9, 106.6, 103.5, 99.7, 79.2, 63.7, 60.7, 55.0, 40.0, 38.9, 24.6, 20.9, 19.8, 19.7, 14.3; IR ν_{max} (neat) cm^{-1}: 3280, 2968, 1725, 1650, 1597, 1513, 1495, 1464, 1368, 1258, 1207, 1160, 1037; HRMS (ESI, m/z): calcd for $C_{19}H_{29}N_2O_3^+$ [M + H]$^+$ 333.2173, found 333.2160.



2-((4-Methoxyphenyl)amino)-3-methyl-3-(5-methyl-3,4-dihydro-2H-pyrrol-2-yl)-N-phenylbutanamide **(3ah)**: Following the general procedure, compound **3ah** was prepared by reacting **1a** with **2h**, and the product was isolated through a silica gel flash column (PE: acetone, from 5:1 to 1:1) as a mixture of diastereomers (yellow oil, 66.8 mg, 88%, *dr* = 2.0). ^{1}H NMR (400 MHz, *Chloroform-d*) δ 9.50 (s, 1H, major), 9.04 (s, 1H, minor), 7.57 – 7.42 (m, 2H, major + minor), 7.31 – 7.19 (m, 2H, major + minor), 7.10 – 6.98 (m, 1H, major + minor), 6.80 – 6.71 (m, 2H, major + minor), 6.61 – 6.49 (m, 2H, major), 6.60 – 6.49 (m, 2H, minor), 6.22 (brs, 1H, major), 5.98 (brs, 1H, minor), 3.97 – 3.83 (m, 1H, major + minor), 3.79 (s, 1H, major), 3.70 (s, 3H, major + minor), 3.65 (d, *J* = 3.8 Hz, 1H, minor), 2.57 – 2.30 (m, 2H, major + minor), 2.11 (d, *J* = 1.9 Hz, 3H, major), 2.07 (d, *J* = 2.1 Hz, 3H, minor), 1.99 – 1.85 (m, 1H, major + minor), 1.75 – 1.52 (m, 1H, major + minor), 1.29 (s, 3H, minor), 1.08 (s, 3H, major), 0.99 (s, 3H, minor), 0.89 (s, 3H, major); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 175.8 (minor), 175.4 (major), 171.5 (minor), 171.3 (major), 152.7 (major), 152.4 (minor), 142.6 (major), 141.7 (minor), 137.9 (major), 137.7 (minor), 128.75 (major), 128.73 (minor), 123.9 (minor), 123.8 (major), 119.7 (minor), 119.5 (major), 115.6 (major), 114.8 (minor), 114.7 (major), 114.4 (minor), 79.8 (minor), 79.6 (major), 69.5 (major), 68.8 (minor), 55.60 (major), 55.58 (minor), 40.9 (major), 39.9 (minor), 38.5 (major), 38.4 (minor), 24.9 (minor), 24.8 (major), 23.9 (minor), 22.1 (minor), 22.0 (major), 20.0 (minor), 19.9 (major), 17.0 (major); IR ν_{max} (neat) cm^{-1}: 3314, 2966, 1681, 1652, 1598, 1506, 1465, 1438, 1378, 1266, 1223, 1177, 1115, 1035; HRMS (ESI, m/z): calcd for $C_{23}H_{30}N_3O_2^+$ [M + H]$^+$ 380.2333, found 380.2315.



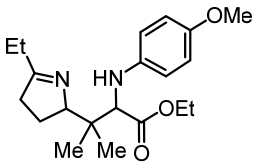
Ethyl (2-((4-methoxyphenyl)amino)-3-methyl-3-(5-methyl-3,4-dihydro-2H-pyrrol-2-yl)butanoyl)glycinate **(3ai)**: Following the general procedure, compound **3ai** was prepared by reacting **1a** with **2i**, and the product was isolated through a silica gel flash column (PE/EtOAc/Et_3N = 2 : 1 : 0.003)

as a mixture of diastereomers (foam, 69.2 mg, 89%, *dr* = 1.2). When using PE/acetone as the eluent, one diastereomer could be obtained in pure form, and the NMR data of each isomer was read by comparing the spectrum.

Isomer 1: ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.83 (t, *J* = 5.8 Hz, 1H), 6.83 – 6.72 (m, 2H), 6.65 – 6.55 (m, 2H), 6.32 (s, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.06 (dd, *J* = 18.0, 6.0 Hz, 1H), 3.93 (dd, *J* = 18.0, 5.6 Hz, 1H), 3.97 – 3.86 (m, 1H), 3.79 – 3.64 (m, 4H), 2.55 – 2.29 (m, 2H), 2.07 (s, 3H), 1.99 – 1.86 (m, 1H), 1.73 – 1.58 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.05 (s, 3H), 0.90 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.8, 173.2, 169.8, 152.6, 142.8, 115.4, 114.7, 79.8, 69.1, 61.1, 55.7, 41.2, 40.4, 38.4, 25.1, 22.3, 19.9, 16.7, 14.1;

Isomer 2: ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.46 (t, *J* = 5.9 Hz, 1H), 6.73 – 6.68 (m, 2H), 6.54 – 6.45 (m, 2H), 5.97 (brs, 1H), 4.20 – 4.08 (m, 3H), 3.99 – 3.94 (m, 1H), 3.81 (dd, *J* = 18.0, 5.2 Hz, 1H), 3.70 (s, 3H), 3.58 (d, *J* = 3.8 Hz, 1H), 2.42 – 2.29 (m, 2H), 2.03 (s, 3H), 1.98 – 1.85 (m, 1H), 1.62 – 1.49 (m, 1H), 1.25 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, *Chloroform-d*) δ 175.0, 173.5, 169.7, 152.1, 142.0, 114.8, 114.1, 79.8, 68.1, 61.1, 55.6, 41.2, 39.6, 38.4, 25.0, 23.8, 22.2, 20.1, 14.1.

The sample was characterized by IR and HRMS as a mixture of diastereomers: IR ν_{max} (neat) cm^{-1}: 3243, 2966, 1746, 1647, 1506, 1437, 1371, 1254, 1232, 1189, 1146, 1128, 1034; HRMS (ESI, m/z): calcd for $C_{21}H_{32}N_3O_4^+$ $[M + H]^+$ 390.2387, found 390.2379.

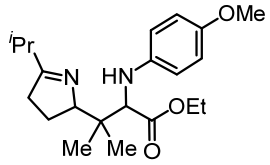


Ethyl 3-(5-ethyl-3,4-dihydro-2H-pyrrol-2-yl)-2-((4-methoxyphenyl)amino)-3-methylbutanoate **(3ba)**: Following the general procedure, compound **3ba** was prepared by reacting **1b** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 36.0 mg, 52%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.77 – 6.70 (m, 2H), 6.66 – 6.59 (m, 2H), 6.00 (brd, *J* = 9.4 Hz, 1H), 4.23 – 4.11 (m, 3H), 4.06 (d, *J* = 9.4 Hz, 1H), 3.72 (s, 3H), 2.52 – 2.27 (m, 4H), 1.88 (dddd, *J* = 12.8, 9.4, 7.7, 3.6 Hz, 1H), 1.57 (dq, *J* = 12.8, 9.2 Hz, 1H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.20 (t, *J* = 7.3 Hz, 3H), 1.01 (s, 3H), 0.89 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 177.8, 174.1, 151.8, 142.5, 114.8, 114.4, 76.5, 66.8, 60.3, 55.8, 39.6, 36.7, 26.9, 24.3, 22.5, 19.6, 14.3, 10.7; IR ν_{max} (neat) cm^{-1}: 3283, 2968, 1723, 1649, 1510, 1463, 1367, 1283, 1234, 1146, 1035; HRMS (ESI, m/z): calcd for $C_{20}H_{31}N_2O_3^+$ $[M + H]^+$ 347.2329, found 347.2328.

Isomer 2 (more polar, yellow oil, 25.6 mg, 37%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.79 – 6.70 (m, 2H), 6.66 – 6.56 (m, 2H), 5.06 (brs, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 4.02 (t, *J* = 8.0 Hz, 1H), 3.88 (s, 1H), 3.73 (s, 3H), 2.55 – 2.26 (m, 4H), 1.96 – 1.79 (m, 1H), 1.72 – 1.51 (m, 1H), 1.23 (t, *J* = 7.3 Hz, 3H), 1.16

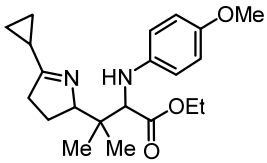
(t, J = 7.5 Hz, 3H), 1.12 (s, 3H), 0.91 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, *Chloroform-d*) δ 179.0, 173.5, 152.6, 142.0, 115.3, 114.8, 79.3, 66.0, 60.6, 55.7, 39.9, 36.8, 27.1, 24.4, 21.3, 19.1, 14.3, 10.9; IR ν_{max} (neat) cm^{-1}: 3279, 2969, 1724, 1646, 1510, 1463, 1367, 1234, 1182, 1140, 1034; HRMS (ESI, m/z): calcd for $C_{20}H_{31}N_2O_3^+$ $[M + H]^+$ 347.2329, found 347.2328.



***Ethyl 3-(5-isopropyl-3,4-dihydro-2H-pyrrol-2-yl)-2-((4-methoxyphenyl)amino)-3-methylbutanoate* (3ca)**: Following the general procedure, compound **3ca** was prepared by reacting **1c** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 32.4 mg, 45%): ^1H NMR (400 MHz, *Chloroform-d*) δ 6.78 – 6.70 (m, 2H), 6.66 – 6.57 (m, 2H), 6.14 (brs, 1H), 4.24 – 4.10 (m, 3H), 4.04 (s, 1H), 3.72 (s, 3H), 2.61 (hept, J = 6.9 Hz, 1H), 2.54 – 2.42 (m, 1H), 2.42 – 2.29 (m, 1H), 1.98 – 1.81 (m, 1H), 1.63 – 1.48 (m, 1H), 1.22 (t, J = 7.1 Hz, 3H), 1.18 (d, J = 6.9 Hz, 3H), 1.17 (d, J = 6.9 Hz, 3H), 1.01 (s, 3H), 0.88 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, *Chloroform-d*) δ 181.2, 174.1, 151.8, 142.6, 114.8, 114.3, 76.1, 67.0, 60.3, 55.8, 39.6, 34.4, 32.6, 24.3, 22.6, 20.2, 20.0, 19.6, 14.3; IR ν_{max} (neat) cm^{-1}: 3269, 2965, 1725, 1643, 1510, 1464, 1367, 1234, 1182, 1140, 1034, 819; HRMS (ESI, m/z): calcd for $C_{21}H_{33}N_2O_3^+$ $[M + H]^+$ 361.2486, found 2489.

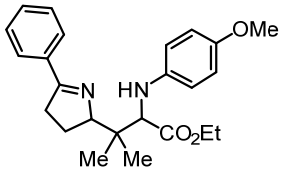
Isomer 2 (more polar, yellow oil, 31.7 mg, 44%): ^1H NMR (400 MHz, *Chloroform-d*) δ 6.80 – 6.71 (m, 2H), 6.65 – 6.57 (m, 2H), 5.36 (brs, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.99 (t, J = 7.5 Hz, 1H), 3.85 (s, 1H), 3.72 (s, 3H), 2.64 (hept, J = 6.9 Hz, 1H), 2.55 – 2.42 (m, 1H), 2.35 (dtd, J = 17.2, 9.2, 2.1 Hz, 1H), 1.96 – 1.84 (m, 1H), 1.70 – 1.57 (m, 1H), 1.24 (t, J = 7.0 Hz, 3H), 1.15 (d, J = 6.9 Hz, 3H), 1.14 (d, J = 6.9 Hz, 3H), 1.09 (s, 3H), 0.91 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, *Chloroform-d*) δ 182.4, 173.6, 152.5, 142.2, 115.1, 114.8, 79.1, 66.6, 60.6, 55.7, 39.9, 34.2, 32.7, 24.4, 21.6, 20.3, 20.0, 18.5, 14.3; IR ν_{max} (neat) cm^{-1}: 3269, 2965, 1725, 1643, 1510, 1464, 1367, 1234, 1182, 1140, 1034, 819; HRMS (ESI, m/z): calcd for $C_{21}H_{33}N_2O_3^+$ $[M + H]^+$ 361.2486, found 361.2489.



***Ethyl 3-(5-cyclopropyl-3,4-dihydro-2H-pyrrol-2-yl)-2-((4-methoxyphenyl)amino)-3-methylbutanoate* (3da)**: Following the general procedure, compound **3da** was prepared by reacting **1d** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 31.8 mg, 44%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.79 – 6.68 (m, 2H), 6.67 – 6.59 (m, 2H), 5.78 (brd, *J* = 8.1 Hz, 1H), 4.19 – 4.10 (m, 3H), 4.05 (d, *J* = 8.1 Hz, 1H), 3.72 (s, 3H), 2.42 – 2.16 (m, 2H), 1.86 (dddd, *J* = 12.8, 9.0, 7.6, 3.6 Hz, 1H), 1.79 – 1.70 (m, 1H), 1.54 (dq, *J* = 12.8, 9.3 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.99 (s, 3H), 0.94 – 0.79 (m, 4H), 0.87 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 178.1, 174.1, 151.9, 142.5, 114.8, 114.5, 76.3, 66.7, 60.3, 55.8, 39.7, 35.0, 24.1, 22.3, 19.7, 14.3, 13.9, 7.8, 7.6; IR ν_{max} (neat) cm^{-1}: 3289, 2965, 1722, 1639, 1510, 1464, 1367, 1283, 1234, 1195, 1146, 1096, 1023; HRMS (ESI, m/z): calcd for $C_{21}H_{30}N_2O_3Na^+$ $[M + Na]^+$ 381.2149, found 381.2128.

Isomer 2 (more polar, yellow oil, 31.5 mg, 44%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.80 – 6.69 (m, 2H), 6.65 – 6.56 (m, 2H), 5.00 (brs, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.01 – 3.92 (m, 1H), 3.85 (s, 1H), 3.72 (s, 3H), 2.38 – 2.15 (m, 2H), 1.87 (dddd, *J* = 12.7, 9.2, 7.5, 3.5 Hz, 1H), 1.63 (dq, *J* = 12.7, 9.2 Hz, 1H), 1.69 – 1.50 (m, 1H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.10 (s, 3H), 0.91 (s, 3H), 0.87 – 0.70 (m, 4H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 179.0, 173.5, 152.5, 142.0, 115.2, 114.7, 79.0, 65.9, 60.5, 55.7, 39.9, 34.6, 24.2, 21.4, 19.1, 14.3, 14.1, 7.4, 7.2; IR ν_{max} (neat) cm^{-1}: 3272, 2969, 1724, 1637, 1510, 1464, 1367, 1234, 1183, 1138, 1096, 1025; HRMS (ESI, m/z): calcd for $C_{21}H_{30}N_2O_3Na^+$ $[M + Na]^+$ 381.2149, found 381.2128.

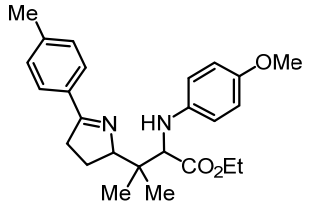


Ethyl 2-((4-methoxyphenyl)amino)-3-methyl-3-(5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)butanoate **(3ea)**: Following the general procedure, compound **3ea** was prepared by reacting **1e** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 10:1 to 5:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 33.1 mg, 42%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.96 – 7.86 (m, 2H), 7.49 – 7.40 (m, 3H), 6.81 – 6.74 (m, 2H), 6.74 – 6.68 (m, 2H), 5.69 (brs, 1H), 4.55 – 4.36 (m, 1H), 4.25 (s, 1H), 4.22 – 4.12 (m, 2H), 3.73 (s, 3H), 3.07 – 2.92 (m, 1H), 2.81 (dtd, *J* = 16.9, 9.4, 2.5 Hz, 1H), 2.12 – 2.00 (m, 1H), 1.75 (dq, *J* = 12.8, 9.3 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.08 (s, 3H), 0.94 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.1, 171.6, 152.1, 142.4, 134.6, 130.3, 128.4, 127.7, 114.8, 114.7, 77.1, 66.7, 60.4, 55.7, 40.3, 34.6, 24.2, 22.1, 19.7, 14.3; IR ν_{max} (neat) cm^{-1}: 3299, 2966, 1724, 1618, 1510, 1465, 1367, 1234, 1196, 1148, 1095, 1026; HRMS (ESI, m/z): calcd for $C_{24}H_{31}N_2O_3^+$ $[M + H]^+$ 395.2329, found 395.2300.

Isomer 2 (more polar, yellow oil, 30.7 mg, 39%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.94 – 7.82 (m, 2H), 7.53 – 7.36 (m, 3H), 6.86 – 6.72 (m, 2H), 6.71 – 6.59 (m, 2H), 4.99 (brs, 1H), 4.34 – 4.24 (m, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.98 (s, 1H), 3.74 (s, 3H), 2.99 (ddt, *J* = 15.8, 10.1, 2.8 Hz, 1H), 2.83 (dtd, *J* = 16.9, 9.3, 2.5 Hz, 1H), 2.15 – 2.03 (m, 1H), 1.84 (dq, *J* = 11.8, 9.2 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.22

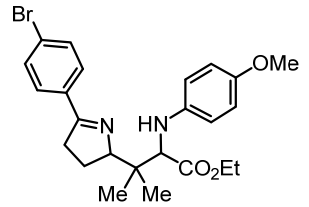
(s, 3H), 0.98 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 173.5, 172.4, 152.6, 141.9, 134.6, 130.3, 128.4, 127.6, 115.4, 114.8, 79.6, 65.8, 60.6, 55.7, 40.4, 34.9, 24.4, 21.4, 19.5, 14.3; IR ν_{max} (neat) cm^{-1}: 3287, 2969, 1724, 1617, 1509, 1464, 1367, 1233, 1180, 1151, 1095, 1026; HRMS (ESI, m/z): calcd for $C_{19}H_{29}N_2O_3^+$ $[M + H]^+$ 395.2329, found 395.2303.



***Ethyl 2-((4-methoxyphenyl)amino)-3-methyl-3-(5-(p-tolyl)-3,4-dihydro-2H-pyrrol-2-yl)butanoate* (3fa)**: Following the general procedure, compound **3fa** was prepared by reacting **1f** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 10:1 to 5:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 35.1 mg, 43%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.85 – 7.72 (m, 2H), 7.26 – 7.21 (m, 2H), 6.79 – 6.73 (m, 2H), 6.72 – 6.66 (m, 2H), 5.79 (brs, 1H), 4.49 – 4.39 (m, 1H), 4.21 (s, 1H), 4.20 – 4.13 (m, 2H), 3.73 (s, 3H), 2.97 (ddt, *J* = 16.8, 10.1, 2.6 Hz, 1H), 2.78 (dtd, *J* = 16.8, 9.4, 2.4 Hz, 1H), 2.41 (s, 3H), 2.11 – 1.97 (m, 1H), 1.73 (dq, *J* = 12.7, 9.3 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.07 (s, 3H), 0.93 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 174.1, 171.4, 152.0, 142.5, 140.5, 131.9, 129.1, 127.6, 114.8, 114.7, 77.2, 66.8, 60.4, 55.8, 40.3, 34.5, 24.3, 22.2, 21.4, 19.7, 14.3; IR ν_{max} (neat) cm^{-1}: 3307, 2933, 1729, 1614, 1510, 1447, 1337, 1235, 1180, 1154, 1034; HRMS (ESI, m/z): calcd for $C_{25}H_{33}N_2O_3^+$ $[M + H]^+$ 409.2486, found 409.2486.

Isomer 2 (more polar, yellow oil, 30.2 mg, 37%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.80 – 7.72 (m, 2H), 7.24 – 7.19 (m, 2H), 6.80 – 6.71 (m, 2H), 6.70 – 6.61 (m, 2H), 4.26 (t, *J* = 8.2 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 1H), 3.73 (s, 3H), 2.97 (ddt, *J* = 17.0, 9.9, 2.5 Hz, 1H), 2.81 (dtd, *J* = 17.0, 9.4, 2.4 Hz, 1H), 2.39 (s, 3H), 2.13 – 2.02 (m, 1H), 1.89 – 1.74 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 3H), 0.97 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 173.5, 172.2, 152.6, 142.0, 140.5, 131.9, 129.0, 127.6, 115.3, 114.8, 79.6, 66.0, 60.6, 55.7, 40.4, 34.8, 24.4, 21.5, 21.4, 19.3, 14.3; HRMS (ESI, m/z): calcd for $C_{25}H_{33}N_2O_3^+$ $[M + H]^+$ 409.2486, found 409.2486.

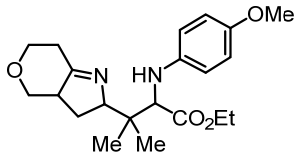


***Ethyl 3-(5-(4-bromophenyl)-3,4-dihydro-2H-pyrrol-2-yl)-2-((4-methoxyphenyl)amino)-3-methylbutanoate* (3ga)**: Following the general procedure, compound **3ga** was prepared by reacting **1g** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 10:1 to 5:1) as

a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 40.6 mg, 43%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.81 – 7.70 (m, 2H), 7.61 – 7.52 (m, 2H), 6.81 – 6.72 (m, 2H), 6.73 – 6.61 (m, 2H), 5.45 (brs, 1H), 4.44 (t, *J* = 8.4 Hz, 1H), 4.25 (d, *J* = 4.8, 1H), 4.21 – 4.11 (m, 2H), 3.73 (s, 3H), 3.03 – 2.87 (m, 1H), 2.83 – 2.70 (m, 1H), 2.13 – 1.96 (m, 1H), 1.82 – 1.69 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.06 (s, 3H), 0.91 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.1, 170.7, 152.2, 142.3, 133.5, 131.6, 129.2, 124.8, 115.0, 114.9, 77.2, 66.5, 60.5, 55.8, 40.3, 34.6, 24.3, 21.9, 19.6, 14.3; IR ν_{max} (neat) cm^{-1}: 3307, 2924, 1726, 1618, 1511, 1465, 1396, 1235, 1196, 1149, 1069, 1036, 1008; HRMS (ESI, m/z): calcd for $C_{24}H_{30}BrN_2O_3^+$ $[M + H]^+$ 473.1434, found 473.1449.

Isomer 2 (more polar, yellow oil, 39.6 mg, 42%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.80 – 7.63 (m, 2H), 7.60 – 7.48 (m, 2H), 6.80 – 6.70 (m, 2H), 6.68 – 6.59 (m, 2H), 4.75 (brd, *J* = 8.2 Hz, 1H), 4.27 (t, *J* = 8.0 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.97 (d, *J* = 8.2 Hz, 1H), 3.73 (s, 3H), 3.02 – 2.88 (m, 1H), 2.80 (dtd, *J* = 16.9, 9.3, 2.4 Hz, 1H), 2.16 – 2.03 (m, 1H), 1.85 (dq, *J* = 11.7, 9.2 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.21 (s, 3H), 0.97 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 173.4, 171.4, 152.7, 141.8, 133.5, 131.6, 129.1, 124.8, 115.4, 114.8, 79.7, 65.5, 60.6, 55.7, 40.5, 34.9, 24.5, 21.3, 19.7, 14.3; IR ν_{max} (neat) cm^{-1}: 3307, 2968, 1725, 1617, 1509, 1484, 1464, 1396, 1234, 1181, 1152, 1069, 1033, 1007; HRMS (ESI, m/z): calcd for $C_{24}H_{30}BrN_2O_3^+$ $[M + H]^+$ 473.1434, found 473.1449.

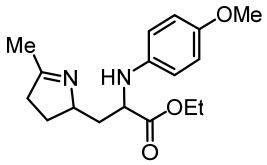


***Ethyl 3-(2,3,3a,4,6,7-hexahydropyrano[4,3-b]pyrrol-2-yl)-2-((4-methoxyphenyl)amino)-3-methylbutanoate* (3ha)**: Following the general procedure, compound **3ha** was prepared by reacting **1h** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a three diastereomers.

Isomer 1 (less polar, yellow oil, 26.9 mg, 36%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.78 – 6.70 (m, 2H), 6.69 – 6.61 (m, 2H), 5.29 (brs, 1H), 4.34 – 4.09 (m, 6H), 3.72 (s, 3H), 3.34 (td, *J* = 11.3, 4.0 Hz, 1H), 2.97 (t, *J* = 10.9 Hz, 1H), 2.87 – 2.74 (m, 1H), 2.67 – 2.49 (m, 2H), 1.94 (dt, *J* = 12.8, 8.3 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.11 (dt, *J* = 12.8, 9.4 Hz, 1H), 1.03 (s, 3H), 0.93 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 173.94, 173.90, 152.3, 142.1, 115.0, 114.8, 75.9, 74.0, 68.3, 66.0, 60.5, 55.7, 47.1, 39.4, 32.9, 26.6, 21.6, 20.0, 14.3; IR ν_{max} (neat) cm^{-1}: 3305, 2965, 1731, 1661, 1511, 1466, 1371, 1234, 1198, 1156, 1091, 1037; HRMS (ESI, m/z): calcd for $C_{21}H_{31}N_2O_4^+$ $[M + H]^+$ 375.2278, found. 375.2285

Isomers 2+3 (more polar, yellow oil, 25.4 mg, 34%, *dr* = 2.4:1):^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.79 – 6.70 (m, 2H), 6.68 – 6.58 (m, 2H), 4.38 – 4.09 (m, 5H), 4.08 – 4.00 (m, 1H), 3.94 (s, 1H, major), 3.92 (s, 1H, minor), 3.73 (s, 3H), 3.43 – 3.30 (m, 1H), 3.06 – 2.95 (m, 1H), 2.91 – 2.76 (m, 1H), 2.68 –

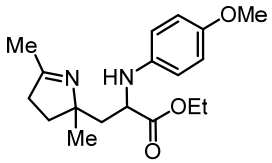
2.47 (m, 2H), 2.02 – 1.89 (m, 1H), 1.28 – 1.12 (m, 7H), 0.94 (s, 3H, major), 0.87 (s, 3H, minor); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 174.6 (major + minor), 173.3 (major + minor), 152.9 (minor), 152.8 (major), 141.49 (minor), 141.46 (major), 115.8 (minor), 115.6 (major), 114.8 (major + minor), 78.2 (minor), 77.9 (major), 74.4 (minor), 73.8 (major), 68.6 (minor), 68.2 (major), 64.7 (major), 64.3 (minor), 60.7 (minor), 60.6 (major), 55.7 (major +minor), 48.5 (minor), 47.5 (major), 40.9 (minor), 39.5 (major), 33.4 (minor), 32.9 (major), 26.8 (major), 25.8 (minor), 20.8 (major), 20.4 (minor), 20.2 (major), 20.3 (minor), 14.3 (major + minor); IR ν_{max} (neat) cm^{-1}: 3359, 2966, 1725, 1659, 1510, 1465, 1367, 1233, 1182, 1141, 1090, 1031; HRMS (ESI, m/z): calcd for $C_{21}H_{31}N_2O_4^+$ $[M + H]^+$ 375.2278, found. 375.2285



Ethyl 2-((4-methoxyphenyl)amino)-3-(5-methyl-3,4-dihydro-2H-pyrrol-2-yl)propanoate **(3ia)**: Following the general procedure, compound **3ia** was prepared by reacting **1i** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 2:1 to 1:1) as a pair of diastereomers.

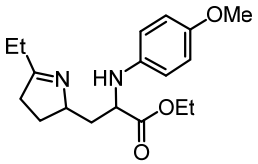
Isomer 1 (less polar, yellow oil, 15.8 mg, 26%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.82 – 6.71 (m, 2H), 6.66 – 6.56 (m, 2H), 4.57 (brs, 1H), 4.25 – 4.12 (m, 2H), 4.13 – 4.05 (m, 2H), 3.73 (s, 3H), 2.59 – 2.37 (m, 2H), 2.19 – 2.00 (m, 2H), 2.02 (s, 3H), 1.96 – 1.86 (m, 1H), 1.55 – 1.42 (m, 1H), 1.23 (t, J = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 174.6, 174.5, 152.5, 141.3, 115.0, 114.8, 70.1, 61.0, 57.0, 55.7, 39.7, 38.6, 29.5, 19.8, 14.2; IR ν_{max} (neat) cm^{-1}: 3225, 2938, 1741, 1646, 1534, 1508, 1456, 1443, 1313, 1260, 1239, 1179, 1147, 1030; HRMS (ESI, m/z): calcd for $C_{17}H_{25}N_2O_3^+$ $[M + H]^+$ 305.1860, found 305.1850.

Isomer 2 (more polar, yellow oil, 14.6 mg, 24%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.78 – 6.70 (m, 2H), 6.66 – 6.58 (m, 2H), 4.54 (brd, J = 6.1 Hz, 1H), 4.23 (q, J = 6.1 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 4.09 – 4.02 (m, 1H), 3.72 (s, 3H), 2.58 – 2.35 (m, 2H), 2.20 – 2.08 (m, 1H), 2.08 – 1.99 (m, 1H), 2.02 (s, 3H), 1.90 (ddd, J = 13.5, 7.3, 5.6 Hz, 1H), 1.51 – 1.39 (m, 1H), 1.21 (t, J = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 174.5, 174.4, 152.5, 141.4, 115.1, 114.7, 69.5, 60.9, 56.8, 55.7, 39.8, 38.8, 29.7, 19.8, 14.2; IR ν_{max} (neat) cm^{-1}: 3351, 2934, 1728, 1646, 1510, 1441, 1376, 1235, 1179, 1156, 1033; HRMS (ESI, m/z): calcd for $C_{17}H_{25}N_2O_3^+$ $[M + H]^+$ 305.1860, found 305.1850.

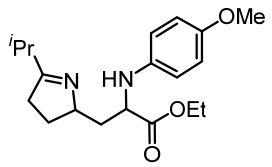


Ethyl 3-(2,5-dimethyl-3,4-dihydro-2H-pyrrol-2-yl)-2-((4-methoxyphenyl) amino) propanoate **(3ja)**: Following the general procedure, compound **3ja** was prepared by reacting **1j** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 2:1 to 1:1) as a mixture of diastereomers

(yellow oil, 28.6 mg, 45%, *dr* = 1:1). ^{1}H NMR (400 MHz, *Chloroform-d*) (mixture of 2 diastereomers) δ 6.81 – 6.69 (m, 2H, isomer 1 + isomer 2), 6.62 – 6.47 (m, 2H, isomer 1 + isomer 2), 5.37 (brs, 1H, isomer 1 + isomer 2), 4.26 – 4.08 (m, 2H, isomer 1 + isomer 2), 3.99 (dd, *J* = 9.7, 4.3 Hz, 1H, isomer 1), 3.91 (dd, *J* = 8.1, 4.6 Hz, 1H, isomer 2), 3.73 (s, 3H, isomer 1), 3.72 (s, 3H, isomer 2), 2.62 – 2.39 (m, 2H, isomer 1 + isomer 2), 2.11 – 1.88 (m, 2H, isomer 1 + isomer 2), 2.01 (s, 3H, isomer 1), 1.93 (s, 3H, isomer 2), 1.86 – 1.67 (m, 2H, isomer 1 + isomer 2), 1.25 (s, 3H, isomer 1), 1.24 (t, *J* = 7.1 Hz, 3H, isomer 1), 1.24 (t, *J* = 7.1 Hz, 3H, isomer 2), 1.18 (s, 3H, isomer 2); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 175.0 (isomer 1), 174.7 (isomer 2), 172.7 (isomer 1 + isomer 2), 152.4 (isomer 1 + isomer 2), 141.7 (isomer 1), 141.3 (isomer 2), 114.77 (isomer 1), 114.73 (isomer 2), 114.71 (isomer 1), 114.68 (isomer 2), 75.1 (isomer 2), 74.9 (isomer 1), 61.0 (isomer 1 + isomer 2), 56.6 (isomer 1), 56.2 (isomer 2), 55.7 (isomer 1 + isomer 2), 44.0 (isomer 1), 43.9 (isomer 2), 39.1 (isomer 2), 38.2 (isomer 1), 36.4 (isomer 1), 34.3 (isomer 2), 27.9 (isomer 2), 25.7 (isomer 1), 19.9 (isomer 1), 19.7 (isomer 2), 14.20 (isomer 1), 14.17 (isomer 2); IR ν_{max} (neat) cm^{-1}: 3303, 2932, 1727, 1649, 1510, 1442, 1372, 1234, 1180, 1152, 1033; HRMS (ESI, m/z): calcd for $C_{18}H_{27}N_2O_3^+$ [M + H]$^+$ 319.2016, found 319.1994.



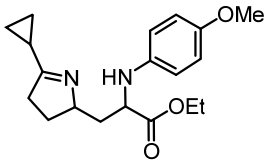
***Ethyl 3-(5-ethyl-3,4-dihydro-2H-pyrrol-2-yl)-2-((4-methoxyphenyl)amino)propanoate* (3ka)**: Following the general procedure, compound **3ka** was prepared by reacting **1k** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 2:1 to 1:1) as a mixture of diastereomers (yellow oil, 30.0 mg, 47%, *dr* = 1.1:1).^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.83 – 6.69 (m, 2H, isomer 1 + isomer 2), 6.69 – 6.54 (m, 2H, isomer 1 + isomer 2), 4.87 (br, 1H, isomer 1 + isomer 2), 4.31 – 4.01 (m, 4H, isomer 1 + isomer 2), 3.73 (s, 3H, isomer 1), 3.72 (s, 3H, isomer 2), 2.56 – 2.39 (m, 2H, isomer 1 + isomer 2), 2.38 – 2.27 (m, 2H, isomer 1 + isomer 2), 2.19 – 2.07 (m, 1H, isomer 1 + isomer 2), 2.08 – 1.89 (m, 2H, isomer 1 + isomer 2), 1.52 – 1.39 (m, 1H, isomer 1 + isomer 2), 1.24 – 1.20 (m, 3H, isomer 1 + isomer 2), 1.16 (t, *J* = 7.5 Hz, 3H, isomer 1 + isomer 2); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 178.7 (isomer 1 + isomer 2), 174.5 (isomer 1), 174.4 (isomer 2), 152.5 (isomer 1), 152.4 (isomer 2), 141.5 (isomer 1 + isomer 2), 114.9 (isomer 1 + isomer 2), 114.82 (isomer 1), 114.80 (isomer 2), 70.2 (isomer 1), 69.4 (isomer 2), 61.0 (isomer 1), 60.9 (isomer 2), 57.5 (isomer 1), 56.8 (isomer 2), 55.8 (isomer 1), 55.7 (isomer 2), 39.6 (isomer 1+ isomer 2), 36.9 (isomer 2), 36.8 (isomer 1), 29.4 (isomer 2), 29.3 (isomer 1), 26.97 (isomer 2), 26.95 (isomer 1), 14.3 (isomer 2), 14.2 (isomer 1), 10.7 (isomer 2), 10.6 (isomer 1); IR ν_{max} (neat) cm^{-1}: 3342, 2933, 1728, 1643, 1510, 1461, 1370, 1236, 1179, 1156, 1096, 1031; HRMS (ESI, m/z): calcd for $C_{18}H_{27}N_2O_3^+$ [M + H]$^+$ 319.2016, found. 319.2022



Ethyl 3-(5-isopropyl-3,4-dihydro-2H-pyrrol-2-yl)-2-((4-methoxyphenyl)amino)propanoate **(3la)**: Following the general procedure, compound **3la** was prepared by reacting **1l** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 5:1 to 2:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 20.0 mg, 30%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.79 – 6.69 (m, 2H), 6.65 – 6.54 (m, 2H), 4.97 (brs, 1H), 4.28 – 4.19 (m, 1H), 4.16 (q, *J* = 7.3 Hz, 2H), 4.09 – 3.97 (m, 1H), 3.73 (s, 3H), 2.73 – 2.48 (m, 2H), 2.41 (dtd, *J* = 17.2, 9.0, 1.8 Hz, 1H), 2.17 – 2.07 (m, 1H), 2.06 – 1.88 (m, 2H), 1.42 (dq, *J* = 12.3, 8.7 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 181.9, 174.4, 152.3, 141.5, 114.8 (2C), 69.1, 60.8, 56.8, 55.7, 39.4, 34.4, 32.6, 29.4, 20.1, 20.0, 14.2; IR ν_{max} (neat) cm^{-1}: 3311, 2963, 1730, 1637, 1510, 1464, 1367, 1236, 1178, 1155, 1035, 818; HRMS (ESI, m/z): calcd for $C_{19}H_{28}N_2O_3Na^+$ $[M + Na]^+$ 355.1992, found 355.2002.

Isomer 2 (more polar, yellow oil, 18.6 mg, 28%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.85 – 6.73 (m, 2H), 6.63 – 6.52 (m, 2H), 5.13 (brs, 1H), 4.26 – 4.14 (m, 2H), 4.12 – 4.00 (m, 2H), 3.73 (s, 3H), 2.66 – 2.47 (m, 2H), 2.41 (dt, *J* = 17.5, 9.4 Hz, 1H), 2.18 – 2.06 (m, 1H), 2.03 – 1.88 (m, 2H), 1.56 – 1.36 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 182.3, 174.5, 152.5, 141.6, 114.8, 114.7, 70.2, 61.0, 57.8, 55.7, 39.5, 34.4, 32.6, 29.3, 20.1, 20.0, 14.2; IR ν_{max} (neat) cm^{-1}: 3311, 2963, 1730, 1637, 1510, 1464, 1367, 1236, 1178, 1155, 1035, 818; HRMS (ESI, m/z): calcd for $C_{19}H_{28}N_2O_3Na^+$ $[M + Na]^+$ 355.1992, found 355.2002.

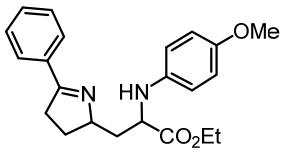


Ethyl 3-(5-cyclopropyl-3,4-dihydro-2H-pyrrol-2-yl)-2-((4-methoxyphenyl)amino)propanoate **(3ma)**: Following the general procedure, compound **3ma** was prepared by reacting **1m** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 2:1 to 1:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 20.5 mg, 31%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 6.80 – 6.70 (m, 2H), 6.66 – 6.57 (m, 2H), 4.68 (brs, 1H), 4.22 (dd, *J* = 6.9, 5.3 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.07 – 3.96 (m, 1H), 3.73 (s, 3H), 2.45 – 2.22 (m, 2H), 2.17 – 2.06 (m, 1H), 2.02 (ddd, *J* = 13.8, 8.5, 5.3 Hz, 1H), 1.92 (ddd, *J* = 13.8, 7.0, 5.5 Hz, 1H), 1.79 (ddd, *J* = 12.8, 7.9, 5.1 Hz, 1H), 1.41 (dq, *J* = 12.6, 8.6 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.89 – 0.69 (m, 4H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 179.0, 174.4, 152.4, 141.5, 115.0, 114.8, 69.0, 60.8, 56.8, 55.7, 39.6, 34.6, 29.2, 14.2, 14.1, 7.5, 7.4; IR ν_{max}

(neat) cm^{-1}: 3323, 2934, 1728, 1631, 1510, 1455, 1369, 1235, 1179, 1155, 1097, 1034; HRMS (ESI, m/z): calcd for $C_{19}H_{27}N_2O_3^+$ $[M + H]^+$ 331.2016, found 331.1999.

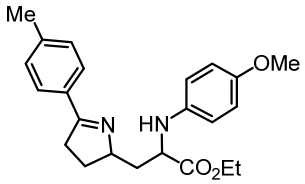
Isomer 2 (more polar, yellow oil, 19.8 mg, 30%): ^1H NMR (400 MHz, *Chloroform-d*) δ 6.80 – 6.72 (m, 2H), 6.62 – 6.55 (m, 2H), 4.84 (brs, 1H), 4.22 – 4.13 (m, 2H), 4.10 – 4.02 (m, 2H), 3.73 (s, 3H), 2.41 (dddd, *J* = 16.8, 9.9, 4.3, 1.9 Hz, 1H), 2.30 (dtd, *J* = 17.1, 8.9, 1.8 Hz, 1H), 2.15 – 2.05 (m, 1H), 2.02 – 1.88 (m, 2H), 1.76 (tt, *J* = 8.0, 5.3 Hz, 1H), 1.43 (ddt, *J* = 12.7, 9.8, 8.3 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.89 – 0.80 (m, 4H); $^{13}C\{^1H\}$NMR (100 MHz, *Chloroform-d*) δ 179.1, 174.5, 152.5, 141.5, 114.9, 114.8, 69.9, 61.0, 57.4, 55.7, 39.6, 34.6, 29.1, 14.2, 14.0, 7.5 (2C); IR ν_{max} (neat) cm^{-1}: 3304, 2935, 1727, 1631, 1510, 1463, 1369, 1235, 1180, 1154, 1096, 1030; HRMS (ESI, m/z): calcd for $C_{19}H_{27}N_2O_3^+$ $[M + H]^+$ 331.2016, found 331.1999.



Ethyl 2-((4-methoxyphenyl)amino)-3-(5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)propanoate **(3na)**: Following the general procedure, compound **3na** was prepared by reacting **1n** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 10:1 to 5:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 27.1 mg, 37%): ^1H NMR (400 MHz, *Chloroform-d*) δ 7.94 – 7.79 (m, 2H), 7.51 – 7.34 (m, 3H), 6.83 – 6.71 (m, 2H), 6.70 – 6.59 (m, 2H), 4.85 (brs, 1H), 4.43 – 4.27 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 3H), 3.12 – 2.95 (m, 1H), 2.94 – 2.75 (m, 1H), 2.37 – 2.25 (m, 1H), 2.18 – 2.01 (m, 2H), 1.69 – 1.52 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, *Chloroform-d*) δ 174.5, 172.2, 152.4, 141.5, 134.4, 130.4, 128.4, 127.7, 115.0, 114.8, 69.9, 60.9, 57.0, 55.7, 39.8, 34.8, 29.5, 14.2; IR ν_{max} (neat) cm^{-1}: 3350, 2931, 1728, 1614, 1510, 1447, 1323, 1236, 1178, 1155, 1034; HRMS (ESI, m/z): calcd for $C_{22}H_{27}N_2O_3^+$ $[M + H]^+$ 367.2016, found 367.2021.

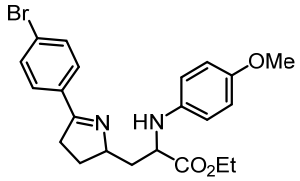
Isomer 2 (more polar, yellow oil, 24.2 mg, 33%): ^1H NMR (400 MHz, *Chloroform-d*) δ 7.91 – 7.80 (m, 2H), 7.49 – 7.36 (m, 3H), 6.83 – 6.71 (m, 2H), 6.70 – 6.57 (m, 2H), 4.97 (brs, 1H), 4.41 – 4.30 (m, 1H), 4.26 – 4.10 (m, 3H), 3.74 (s, 3H), 3.11 – 2.97 (m, 1H), 2.93 – 2.78 (m, 1H), 2.38 – 2.23 (m, 1H), 2.20 – 2.00 (m, 2H), 1.73 – 1.55 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, *Chloroform-d*) δ 174.4, 172.4, 152.5, 141.4, 134.3, 130.5, 128.4, 127.6, 114.9, 114.8, 70.8, 61.0, 57.4, 55.7, 39.5, 34.6, 29.3, 14.2; IR ν_{max} (neat) cm^{-1}: 3307, 2933, 1729, 1614, 1510, 1447, 1337, 1235, 1180, 1154, 1034; HRMS (ESI, m/z): calcd for $C_{19}H_{29}N_2O_3^+$ $[M + H]^+$ 367.2016, found 367.2021.



***Ethyl 2-((4-methoxyphenyl)amino)-3-(5-(p-tolyl)-3,4-dihydro-2H-pyrrol-2-yl)propanoate* (3oa)**: Following the general procedure, compound **3oa** was prepared by reacting **1o** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 10:1 to 5:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 29.7 mg, 39%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.81 – 7.72 (m, 2H), 7.25 – 7.19 (m, 2H), 6.80 – 6.72 (m, 2H), 6.70 – 6.62 (m, 2H), 4.88 (brs, 1H), 4.39 – 4.27 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 3H), 3.11 – 2.94 (m, 1H), 2.91 – 2.76 (m, 1H), 2.40 (s, 3H), 2.34 – 2.24 (m, 1H), 2.16 – 2.03 (m, 2H), 1.73 – 1.52 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (101 MHz, *Chloroform-d*) δ 174.5, 172.0, 152.4, 141.5, 140.6, 131.7, 129.0, 127.6, 115.0, 114.8, 69.8, 60.8, 56.9, 55.7, 39.8, 34.7, 29.4, 21.4, 14.2; IR ν_{max} (neat) cm^{-1}: 3336, 2933, 1731, 1610, 1510, 1456, 1333, 1236, 1179, 1155, 1109, 1036; HRMS (ESI, m/z): calcd for $C_{23}H_{29}N_2O_3^+$ $[M + H]^+$ 381.2173, found 381.2192.

Isomer 2 (more polar, yellow oil, 22.8 mg, 30%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.80 – 7.68 (m, 2H), 7.25 – 7.16 (m, 2H), 6.82 – 6.72 (m, 2H), 6.70 – 6.59 (m, 2H), 5.00 (brs, 1H), 4.45 – 4.30 (m, 1H), 4.25 – 4.09 (m, 3H), 3.74 (s, 3H), 3.02 (dddd, *J* = 16.5, 10.2, 4.3, 2.1 Hz, 1H), 2.84 (dt, *J* = 16.5, 8.9 Hz, 1H), 2.39 (s, 3H), 2.33 – 2.21 (m, 1H), 2.17 – 2.04 (m, 2H), 1.68 – 1.54 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (101 MHz, *Chloroform-d*) δ 174.4, 172.3, 152.5, 141.5, 140.7, 131.6, 129.1, 127.6, 114.9, 114.8, 70.7, 61.0, 57.5, 55.7, 39.6, 34.6, 29.3, 21.4, 14.2; IR ν_{max} (neat) cm^{-1}: 3306, 2932, 1730, 1611, 1510, 1456, 1333, 1235, 1179, 1153, 1109, 1034; HRMS (ESI, m/z): calcd for $C_{23}H_{29}N_2O_3^+$ $[M + H]^+$ 381.2173, found. 381.2192.

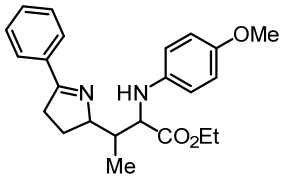


***Ethyl 3-(5-(4-bromophenyl)-3,4-dihydro-2H-pyrrol-2-yl)-2-((4-methoxyphenyl)amino)propanoate* (3pa)**: Following the general procedure, compound **3pa** was prepared by reacting **1p** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 10:1 to 5:1) as a pair of diastereomers.

Isomer 1 (less polar, yellow oil, 33.8 mg, 38%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.77 – 7.67 (m, 2H), 7.60 – 7.50 (m, 2H), 6.80 – 6.70 (m, 2H), 6.70 – 6.60 (m, 2H), 4.72 (brs, 1H), 4.38 – 4.28 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 3H), 3.06 – 2.92 (m, 1H), 2.89 – 2.76 (m, 1H), 2.38 – 2.24 (m, 1H), 2.15 – 2.01 (m, 2H), 1.70 – 1.53 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.4, 171.3, 152.5, 141.5, 133.3, 131.6, 129.3, 125.0, 115.1, 114.8, 70.1, 61.0, 56.9, 55.7, 39.8, 34.8, 29.5, 14.3; IR ν_{max} (neat) cm^{-1}: 3350, 2925, 1731, 1615, 1511, 1484, 1329, 1237, 1179, 1156, 1069, 1036, 1008; HRMS (ESI, m/z): calcd for $C_{22}H_{26}BrN_2O_3^+$ $[M + H]^+$ 445.1121, found 445.1101.

Isomer 2 (more polar, yellow oil, 30.2 mg, 34%): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.77 – 7.67 (m, 2H), 7.60 – 7.50 (m, 2H), 6.83 – 6.73 (m, 2H), 6.67 – 6.58 (m, 2H), 4.85 (brs, 1H), 4.46 – 4.28 (m, 1H),

4.26 – 4.07 (m, 3H), 3.74 (s, 3H), 3.01 (dddd, *J* = 17.0, 10.0, 4.1, 2.1 Hz, 1H), 2.84 (dddd, *J* = 17.0, 10.0, 8.3, 2.1 Hz, 1H), 2.42 – 2.21 (m, 1H), 2.18 – 2.05 (m, 2H), 1.70 – 1.58 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 174.3, 171.5, 152.6, 141.3, 133.2, 131.6, 129.2, 125.0, 114.9, 114.8, 70.8, 61.1, 57.3, 55.7, 39.5, 34.6, 29.3, 14.2; IR ν_{max} (neat) cm^{-1}: 3352, 2932, 1729, 1712, 1615, 1510, 1484, 1397, 1235, 1179, 1154, 1068, 1034, 1008; HRMS (ESI, m/z): calcd for $C_{22}H_{26}BrN_2O_3^+$ $[M + H]^+$ 445.1121, found 445.1101.



Ethyl 2-((4-methoxyphenyl)amino)-3-(5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)butanoate **(3qa)**: Following the general procedure, compound **3qa** was prepared by reacting **1q** with **2a**, and the product was isolated through a silica gel flash column (PE/EtOAc, from 15:1 to 10:1) as two sets of diastereomers.

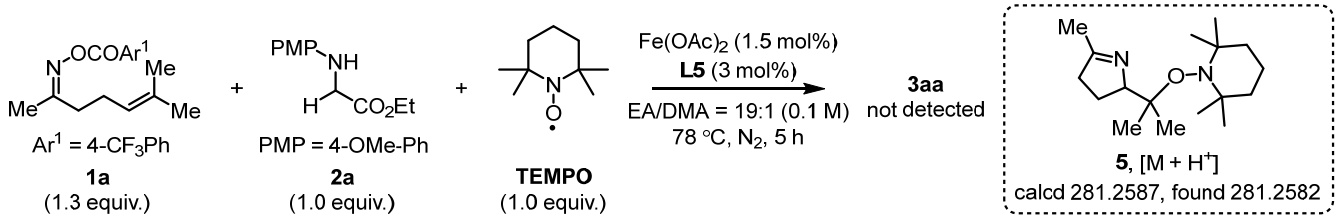
Isomer 1 + 2 (less polar, yellow oil, 27.5 mg, 36%, *dr* = 1.9): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 – 7.82 (m, 2H), 7.53 – 7.36 (m, 3H), 6.91 – 6.82 (m, 2H, major), 6.82 – 6.71 (m, 2H), 6.64 – 6.57 (m, 2H, minor), 5.45 (brs, 1H, minor), 4.79 – 4.56 (m, 2H, major), 4.56 – 4.45 (m, 1H, minor), 4.29 – 4.07 (m, 3H), 3.74 (s, 3H), 3.14 – 2.95 (m, 1H), 2.95 – 2.75 (m, 1H), 2.39 – 2.09 (m, 2H), 1.84 – 1.71 (m, 1H, minor), 1.64 (dq, *J* = 12.4, 9.7 Hz, 1H, major), 1.25 (t, *J* = 6.9 Hz, 3H, minor), 1.24 (t, *J* = 7.2 Hz, 3H, major), 1.02 (d, *J* = 7.0 Hz, 3H, major), 0.99 (d, *J* = 6.9 Hz, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5 (major), 174.4 (minor), 172.3 (minor), 171.8 (major), 152.6 (major), 152.0 (minor), 142.6 (major), 142.1 (minor), 134.7 (major), 134.4 (minor), 130.5 (minor), 130.4 (major), 128.43 (minor), 128.41 (major), 127.8 (major), 127.7 (minor), 115.9 (major), 114.9 (minor), 114.8 (major), 114.2 (minor), 74.8 (major), 73.5 (minor), 62.4 (minor), 61.8 (major), 60.9 (major), 60.8 (minor), 55.81 (minor), 55.75 (major), 42.7 (major), 40.7 (minor), 35.1 (major), 34.9 (minor), 27.7 (major), 26.9 (minor), 14.4 (minor), 14.3 (major), 12.5 (major), 12.0 (minor); IR ν_{max} (neat) cm^{-1}: 3384, 2966, 1727, 1616, 1511, 1447, 1338, 1236, 1152, 1023, 907, 820, 727, 692; HRMS (ESI, m/z): calcd for $C_{23}H_{29}N_2O_3^+$ $[M + H]^+$ 381.2173, found 381.2188.

Isomer 3 + 4 (less polar, yellow oil, 37.0 mg, 49%): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 – 7.80 (m, 2H), 7.51 – 7.33 (m, 3H), 6.84 – 6.69 (m, 3H), 6.67 – 6.59 (m, 1H), 4.98 (brd, *J* = 6.7 Hz, 1H, isomer 1), 4.71 (brs, 1H, isomer 2), 4.41 – 4.29 (m, 1H), 4.29 – 4.09 (m, 3H), 3.74 (s, 3H, isomer 1), 3.73 (s, 3H, isomer 2), 3.11 – 2.96 (m, 1H), 2.96 – 2.80 (m, 1H), 2.40 – 2.12 (m, 2H), 1.82 (ddt, *J* = 12.8, 10.2, 8.1 Hz, 1H, isomer 1), 1.68 (ddt, *J* = 12.8, 10.0, 8.2 Hz, 1H, isomer 2), 1.26 (t, *J* = 7.1 Hz, 3H, isomer 1), 1.22 (t, *J* = 7.1 Hz, 1H, isomer 2), 1.12 (d, *J* = 7.1 Hz, 3H, isomer 1), 1.00 (d, *J* = 6.9 Hz, 3H, isomer 2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 173.8, 172.8, 172.3, 152.6, 152.4, 142.0, 141.9, 134.5, 134.4, 130.5, 130.5, 128.4 (2C), 127.7, 127.7, 115.2 (2C), 114.9, 114.8, 75.9, 74.8, 61.9 (2C), 61.0, 60.9, 55.8, 55.7,

42.0, 41.2, 35.0, 34.9, 27.3, 26.6, 14.3 (2C), 13.4, 10.8; IR ν_{max} (neat) cm^{-1}: 3386, 2962, 1728, 1616, 1510, 1447, 1339, 1234, 1152, 1035, 907, 819, 726, 692; HRMS (ESI, m/z): calcd for $C_{23}H_{29}N_2O_3^+$ $[M + H]^+$ 381.2173, found 381.2188.

V. Mechanistic Studies

a) Radical trapping experiment with TEMPO as the reagent



The reaction between **1a** and **2a** was set up according to the general procedure, but in the presence of TEMPO (2,2,6,6-tetramethylpiperidin-1-yl)oxyl) (31.3 mg, 0.2 mmol). The reaction was quenched with $NaHCO_3$ (saturated aqueous solution) after 5 h and worked-up by following the general procedure. Starting materials **1a**, **2a** and TEMPO were mostly recovered and **3aa** was not detected by TLC by comparing with the authentic sample. The reaction mixture was then submitted for HRMS analysis, and a cyclized alkyl radical trapping product **5** was detected, which is a known compound.[14] HRMS (ESI, m/z): calcd for $C_{17}H_{33}N_2O^+$ $[M + H]^+$ 281.2587, found 281.2582 (**Figure S1**).

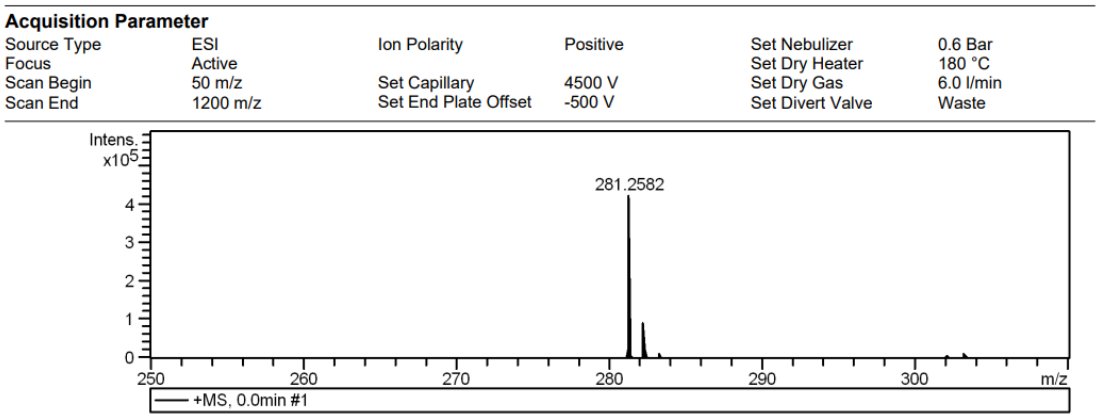
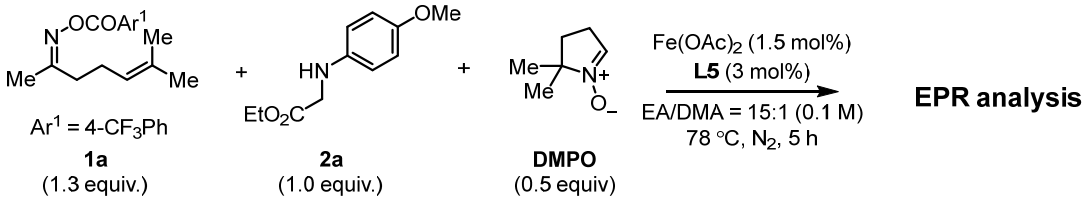


Figure S1. HRMS for radical trapping product

b) EPR study using DMPO as a trapping reagent



The reaction between **1a** and **2a** was set up according to the general procedure, and 5,5-dimethyl-1-pyrroline N-oxide (DMPO, 11.3 mg, 0.1 mmol, dissolved in 0.2 mL of EtOAc) was added after 1 h. The reaction was stirred for additional 10 min, cooled down to room temperature and submitted for ERP

analysis. The major radical species observed under standard conditions was identified as an adduct between a tertiary carbo radical and DMPO, which appears as a ***doublet of triplets***. The g factor was calculated to be 2.0066 by using the following equation [g = 71.4484υ(in GHz)/B (in mT)], and the hyperfine coupling constants are analyzed and presented in **Figure S2**.

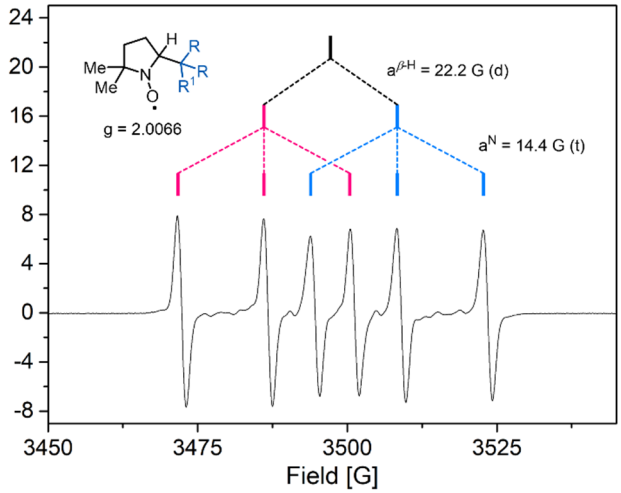
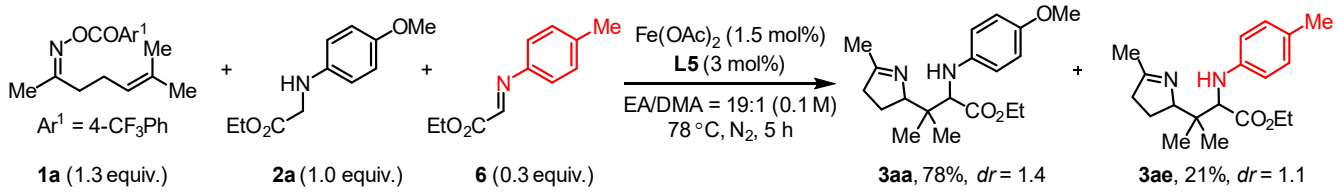


Figure S2. The hyperfine coupling analysis of the EPR signal

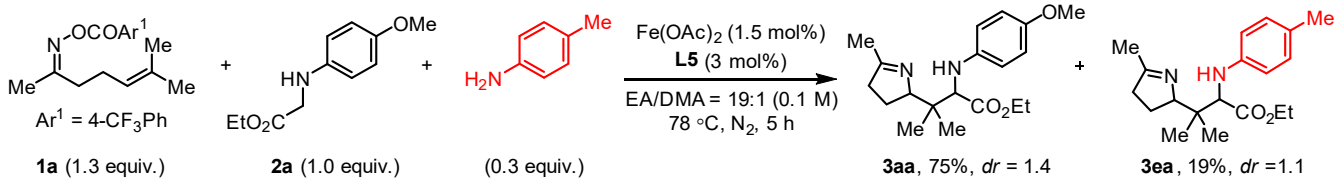
c) The participation of an exogenous imine in the coupling reaction



1a (1.3 equiv.) **2a** (1.0 equiv.) **6** (0.3 equiv.) **3aa**, 78%, *dr* = 1.4 **3ae**, 21%, *dr* = 1.1

The reaction was set up with **1a** and **2a** according to the general procedure, but in the presence of N-(4-methylphenyl) imine **6** (11.5 mg, 0.06 mmol). The reaction was quenched with $NaHCO_3$ (saturated aqueous solution) after 5 h and worked-up following the general procedure. The crude product was filtered through a short silica gel column to remove the less polar starting materials, and the more polar fractions were combined, concentrated and submitted for ^1H NMR analysis (with 1,3,5-trimethoxyl benzene as an internal standard). Beside the anticipated product **3aa** (78%), **3ea** was also formed in 21% yield.

d) Aniline exchange test



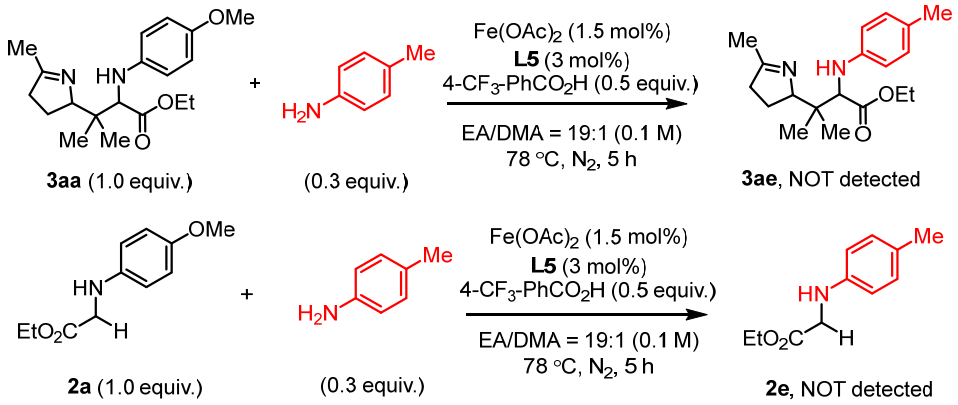
1a (1.3 equiv.) **2a** (1.0 equiv.) (0.3 equiv.) **3aa**, 75%, *dr* = 1.4 **3ea**, 19%, *dr* =1.1

The reaction was set up with **1a** and **2a** according to the general procedure, but in the presence of *p*-toluidine (6.4 mg, 0.06 mmol). The reaction was quenched with $NaHCO_3$ (saturated aqueous solution) after 5 h and worked-up following the general procedure. The crude product was filtered through a short

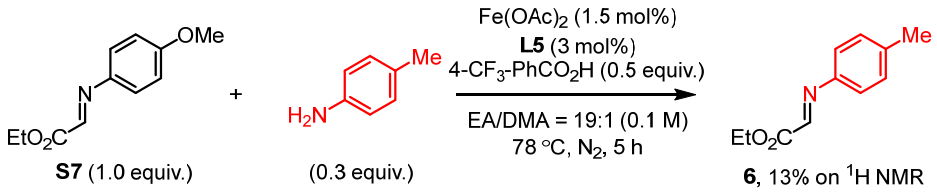
silica gel column to remove the less polar starting materials, and the more polar fractions were combined, concentrated and submitted for ^{1}H NMR analysis (with 1,3,5-trimethoxyl benzene as an internal standard). Beside the desired anticipated product **3aa** (75%), an aniline exchanged product **3ae** was also detected in 19% yield.

To defferentiate whether **3ae** was generated through nucleophilic substitution or imine addition, a few control experiments were performed.

On one hand, when **3aa** was treated with *p*-toluidine under the reaction conditions, **3ae** was *NOT* detected by either TLC or ^{1}H NMR. Treating glycinate **2a** with *p*-toluidine under the reaction conditions did *NOT* lead to any substitution product **2e** either.

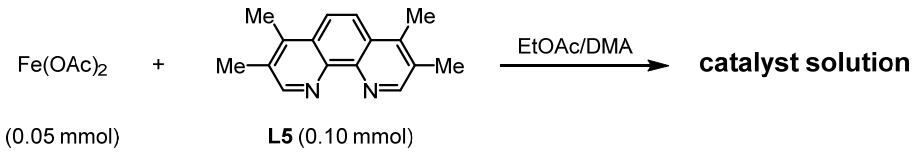


On the other hand, the *N*-(4-methoxylphenyl) imine **S7** underwent a rapid exchange with *p*-toluidine under the reaction conditions, affording an N-(4-methylphenyl) imine **6**, which is known to react with an alkyl radical to afford product **3ae**.



e) HRMS analysis of the catalyst solution

In a N_2 atmosphere glove box, $Fe(OAc)_2$ (8.7 mg, 0.05 mmol), and **L5** (23.6 mg, 0.10 mmol) were added into a 2-dram vial, which was then sealed with a septum. After the vial was then taken out of the glove box, freshly distilled EtOAc (3.5 mL) and dry DMA (1.5 mL) were added. The mixture was sonicated until fully dissolved to afford a **catalyst solution**. The catalyst solution was then submitted for HRMS analysis and the iron-containing species and their related intensity are listed in **Figure S3**.



	$[Fe(\mathbf{L5})_2]^{2+}$	$[Fe(\mathbf{L5})_3]^{2+}$	$[Fe(\mathbf{L5})OAc]^{+}$	$[Fe(\mathbf{L5})_2OAc]^{+}$
m/z, calcd	264.0983	382.1639	351.0790	587.2104
m/z, found	264.1009	382.1646	351.0797	587.2107
intensity	$3.7 * 10^6$	$3.2 * 10^5$	$1.3 * 10^5$	$1.7 * 10^5$

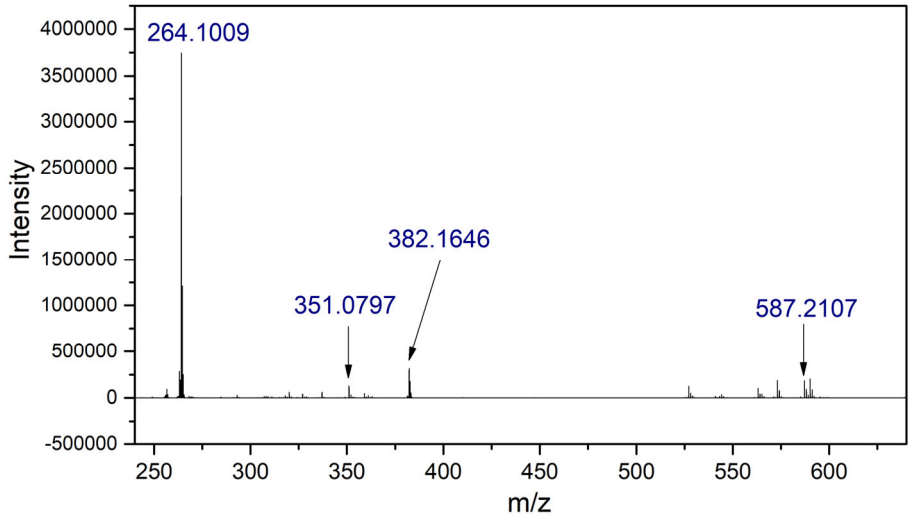
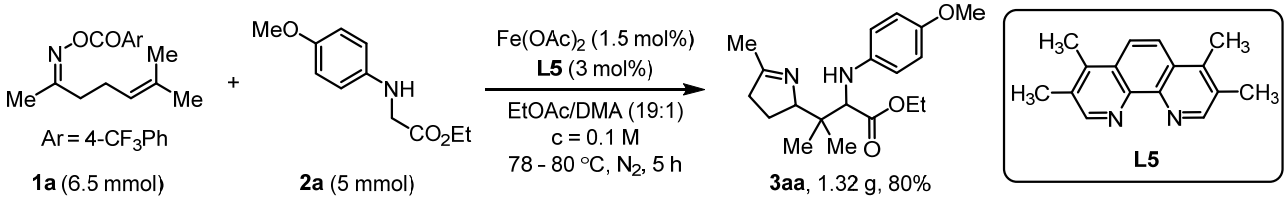


Figure S3. HRMS analysis of the catalyst solution

VI. Gram Scale Synthesis & Product Derivatizations

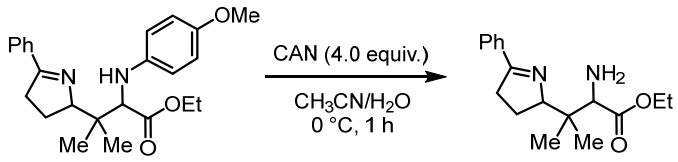
1) Gram Scale Synthesis



In a N_2 atmosphere glove box, $Fe(OAc)_2$ (13.1 mg, 0.075 mmol), and **L5** (35.4 mg, 0.15 mmol) were added into a 3-dram vial, which was then sealed with a septum. After the vial was then taken out of the glove box, freshly distilled EtOAc (5.5 mL) and dry DMA (2.5 mL) were added. The mixture was sonicated until fully dissolved to afford the **catalyst solution**. To a flame-dried round bottom flask charged with a stir bar were added oxime ester **1a** (1.87 g, 6.5 mmol) and glycinate **2a** (1.05 g, 5.0 mmol). The flask was sealed with a septum, evacuated, and backfilled with N_2 three times. EtOAc (42 mL) was then added through a syringe, followed by the addition of the **catalyst solution**. The reaction mixture was stirred in an 80 ˚C oil bath for 7 h before it was quenched with saturated $NaHCO_3$ (saturated aqueous solution, 40 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic

layers were dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was then purified through a silica gel flash column with PE and EtOAc (5:1 to 2:1) as eluent, affording compound **3aa** as a pair of diastereomers, isomer 1 (less polar, 78 mg, 47%), isomer 2 (more polar, 550 mg, 33%).

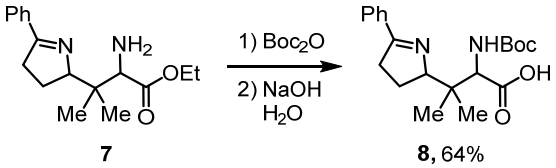
2) The Removal of the *N*-PMP group



3ea, isomer 1 **7**, 60%

Ethyl 2-amino-3-methyl-3-(5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)butanoate **(7)**:To a solution of CAN (ceric ammonium nitrate, 0.4 mmol, dissolved in 0.7 ml H_2O) stirred at 0 °C was added a solution of **3ea** (isomer 1, 0.1 mmol dissolved in 0.3 ml CH_3CN). The reaction was kept stirring for 1 h at the same temperature before it was modulated to alkalescence with saturated aqueous Na_2CO_3. Then the mixture was extracted with CH_2Cl_2 for three times, washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified through a silica gel flash column (PE/Acetone = 1:2) to give **7** as yellow oil (17 mg, 60%); ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.90 – 7.77 (m, 2H), 7.47 – 7.37 (m, 3H), 4.41 – 4.30 (m, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 1H), 3.04 – 2.80 (m, 2H), 2.14 – 1.99 (m, 1H), 1.83 (s, 2H), 1.79 – 1.70 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 0.98 (s, 3H), 0.86 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 175.3, 171.9, 134.7, 130.2, 128.3, 127.6, 77.9, 60.9, 60.3, 40.9, 35.2, 23.7, 19.9, 19.3, 14.3; IR ν_{max} (neat) cm^{-1}: 3386, 2966, 1723, 1617, 1575, 1495, 1466, 1447, 1385, 1339, 1205, 1155, 1095, 1025; HRMS (ESI, m/z): calcd for $C_{17}H_{25}N_2O_2^+$ $[M + H]^+$ 289.1911, found 289.1938.

3) Hydrolysis of the ester group

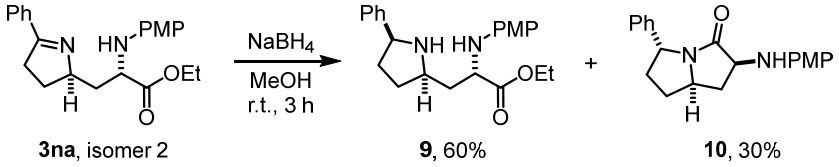


7 **8**, 64%

Product **7** was dissolved in CH_2Cl_2 (1 mL), and Boc_2O (33 mg, 0.15 mmol) was added. The reaction was stirred at room temperature for 2 h and concontrated *in vacuo*. The residue was dissolved in CH_3OH (0.8 mL), following by addition of NaOH (0.4 mL, 1 M aqueous solution). The mixture was then heated under reflux for 4 h until the ester was fully hydrolyzed. After it was cooled down and concentrated under reduced pressure to remove CH_3OH, the aqueous solution was acidified with HCl (2 M aqueous solution, to pH = 2). The acidic solution was then extracted with EtOAc (4 × 2 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residure was purified through a silica gen flash column (PE/acetone/AcOH = 3:1:0.02) to afford **8** (foam, 13.7 mg). ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.87 – 7.75 (m, 2H), 7.58 – 7.52 (m, 1H), 7.51 – 7.42 (m, 2H), 5.99 (brs, 1H), 4.58 (d, *J* = 7.5 Hz, 1H), 4.33 (t,

J = 8.5 Hz, 1H), 3.23 (dd, J = 17.7, 10.0 Hz, 1H), 3.10 – 2.93 (m, 1H), 2.36 – 2.18 (m, 1H), 1.83 (dq, J = 12.8, 10.2 Hz, 1H), 1.45 (s, 9H), 1.09 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, *Chloroform-d*) δ 176.3, 173.4, 156.5, 132.6, 131.1, 129.1, 128.5, 79.6, 79.5, 63.1, 40.9, 34.7, 28.3, 24.6, 23.2, 16.4; IR ν_{max} (neat) cm^{-1}: 3321, 2968, 2923, 2852, 1704, 1495, 1391, 1365, 1249, 1160, 1049, 1013, 917, 760, 730, 691; HRMS (ESI, m/z): calcd for $C_{20}H_{28}N_2O_4Na^+$ 383.1941, found 383.1920

4) The selective reduction of C=N bond



3na, isomer 2 **9**, 60% **10**, 30%

$NaBH_4$ (0.5 mmol) was added to the solution of **3na** (0.1 mmol) in MeOH (1 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 3 hours. After **3na** was consumed as indicated by TLC, the reaction was quenched with brine and extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified through a silica gel flash column (PE: Acetone, from 10:1 to 5:1) to give product **9** as yellow oil (22.1mg, 60%), and product **10** as yellow solid (9.6 mg, 30%).

Ethyl 2-((4-methoxyphenyl)amino)-3-(5-phenylpyrrolidin-2-yl)propanoate (9): ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.45 – 7.37 (m, 2H), 7.36 – 7.27 (m, 2H), 7.26 – 7.19 (m, 1H), 6.82 – 6.69 (m, 2H), 6.70 – 6.46 (m, 2H), 4.28 – 4.13 (m, 3H), 4.12 – 4.03 (m, 1H), 3.74 (s, 3H), 3.47 – 3.36 (m, 1H), 2.19 – 2.08 (m, 1H), 2.08 – 1.91 (m, 3H), 1.77 – 1.65 (m, 1H), 1.64 – 1.52 (m, 1H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 174.5, 152.7, 144.9, 141.0, 128.2, 126.8, 126.6, 115.1, 114.8, 62.6, 61.0, 57.4, 56.3, 55.7, 40.3, 33.7, 31.7, 14.2; IR ν_{max} (neat) cm^{-1}: 3361, 2932, 1728, 1510, 1463, 1235, 1179, 1028, 909, 819, 756, 730, 699; HRMS (ESI, m/z): calcd for $C_{22}H_{29}N_2O_3^+$ $[M + H]^+$ 369.2173, found 369.2172.

2-((4-methoxyphenyl)amino)-5-phenylhexahydro-3H-pyrrolizin-3-one (10): m.p. 135–138 °C; ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.38 – 7.28 (m, 2H), 7.28 – 7.21 (m, 3H), 6.88 – 6.70 (m, 2H), 6.72 – 6.59 (m, 2H), 5.02 (t, J = 7.8 Hz, 1H), 4.41 (brs, 1H), 4.30 (dd, J = 10.9, 7.4 Hz, 1H), 4.11 (td, J = 8.8, 4.5 Hz, 1H), 3.75 (s, 3H), 3.19 – 2.96 (m, 1H), 2.81 – 2.48 (m, 1H), 2.38 – 2.14 (m, 1H), 2.18 – 1.94 (m, 1H), 1.77 – 1.61 (m, 1H), 1.60 – 1.47 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 173.2, 152.6, 141.9, 141.6, 128.6, 127.1, 125.6, 114.9, 114.8, 59.3, 58.6, 57.7, 55.8, 40.0, 36.6, 33.1; IR ν_{max} (neat) cm^{-1}: 3359, 3334, 2927,1682, 1511, 1416, 1400, 1292, 1228, 1167, 1027, 827, 698; HRMS (ESI, m/z): calcd for $C_{20}H_{23}N_2O_2^+$ $[M + H]^+$ 323.1754, found 323.1729

The **relative configuration** of compound **10** was determined by single crystal X-ray diffraction (**Figure S4**), and the relative configuration of **9** was assigned to be opposite on the benzylic possition. It was hypothized that compound **9** doesn't undergo similar lactamization due to the steric hindrance (the phenyl

and N-PMP group would otherwise on the same side of the bicyclic ring).

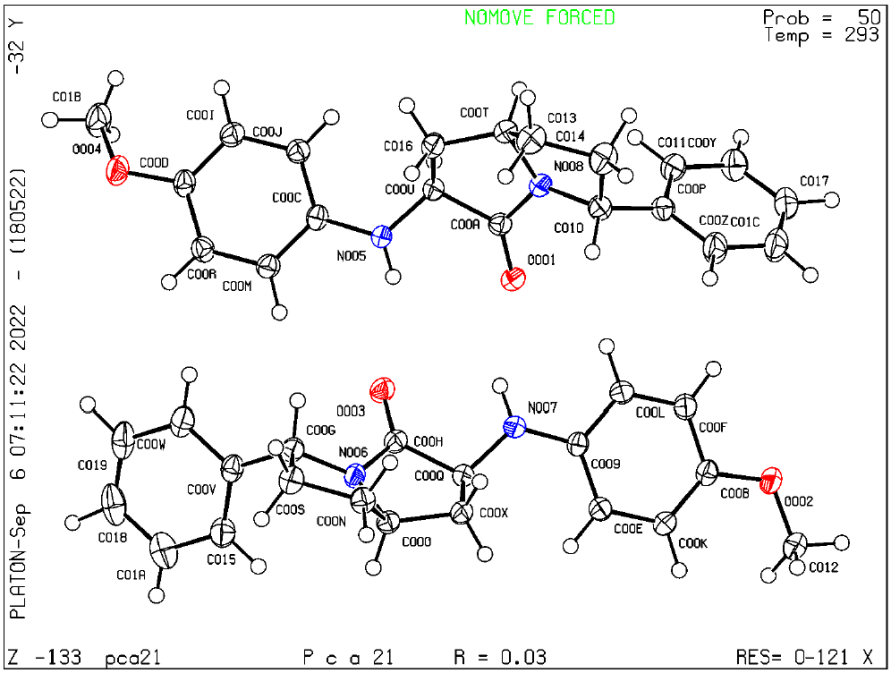
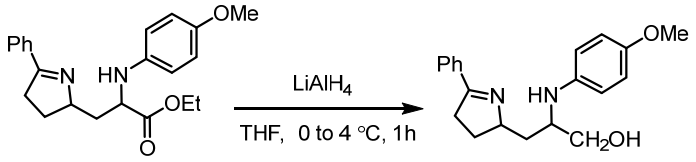


Figure S4 The crystal struction of compound 10

Bond precision:	C-C = 0.0031 A		Wavelength=1.54178
Cell:	a=13.7759(1)	b=9.0774(1)	c=26.8337(2)
	alpha=90	beta=90	gamma=90
Temperature:	293 K		
	Calculated		Reported
Volume	3355.54(5)		3355.54(5)
Space group	P c a 21		P c a 21
Hall group	P 2c -2ac		P 2c -2ac
Moiety formula	C20 H22 N2 O2		C20 H22 N2 O2
Sum formula	C20 H22 N2 O2		C20 H22 N2 O2
Mr	322.40		322.39
Dx,g cm-3	1.276		1.276
Z	8		8
Mu (mm-1)	0.660		0.660
F000	1376.0		1376.0
F000'	1379.95		
h,k,lmax	17,11,33		17,11,33
Nref	6850[3505]		6657
Tmin,Tmax			
Tmin'			
Correction method= Not given			
Data completeness= 1.90/0.97		Theta(max)= 74.183	
R(reflections)= 0.0304(6505)		wR2(reflections)=0.0936(6657)	
S = 0.850		Npar= 609	

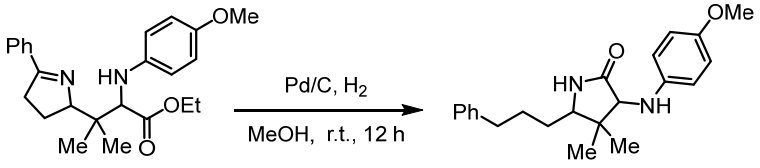
5) Reduction of the ester group



3na, isomer 2 **11**, 83%

2-((4-methoxyphenyl)amino)-3-(5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)propan-1-ol **(11)**: To a flame-dried reaction tube charged with a stir bar was added $LiAlH_4$ (0.6 mmol). After the tube was evacuated and backfilled with N_2 three times, freshly distilled THF (1 mL) was added through a syringe. Next, the tube was cooled and stirred in an ice-water bath, followed by the addition of **3na** (isomer 2, 0.1 mmol, dissolved in 1 mL THF). The mixture was kept at the same temperature and stirred for 1 hour. After **3na** was consumed as indicated by TLC, the reaction was quenched with brine and extracted with CH_2Cl_2 (2 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified through a silica gel flash column (PE/Acetone = 2:1) to give the product **11** as yellow oil (27.0 mg, 83%); ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.87 – 7.71 (m, 2H), 7.53 – 7.35 (m, 3H), 6.86 – 6.74 (m, 2H), 6.70 – 6.58 (m, 2H), 5.14 (br, 1H), 4.37 – 4.19 (m, 1H), 3.88 – 3.82 (m, 2H), 3.75 (s, 3H), 3.72 – 3.62 (m, 1H), 3.15 – 3.02 (m, 1H), 2.97 – 2.78 (m, 1H), 2.38 – 2.27 (m, 1H), 2.27 – 2.17 (m, 1H), 1.76 – 1.57 (m, 1H), 1.57 – 1.42 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, *Chloroform-d*) δ 172.9, 151.7, 141.5, 133.6, 130.9, 128.6, 127.8, 115.0, 114.6, 67.2, 65.0, 55.8, 53.2, 39.8, 35.0, 29.6; IR ν_{max} (neat) cm^{-1}: 3310, 2904, 1611, 1508, 1447, 1237, 1178, 1105, 1036, 814, 760, 733, 690; HRMS (ESI, m/z): calcd for $C_{20}H_{25}N_2O_2^+$ $[M + H]^+$ 325.1911, found 325.1884.

6) Pd-catalysed hydrogenation



3ea, isomer 1 **12**, 88%

3-((4-Methoxyphenyl)amino)-4,4-dimethyl-5-(3-phenylpropyl)pyrrolidin-2-one **(12)**: To a flame-dried reaction tube charged with a stir bar were added Pd/C (10%, 5.1 mg, 0.049 mmol). The tube was sealed with a septum, evacuated, and backfilled with N_2 three times. After **3ea** (isomer 1, 0.1 mmol, dissolved in 2 mL CH_3OH) was added, H_2 gas was bubbled through the reaction mixture for 10 seconds and the reaction was stirred vigorously under H_2 atmosphere (balloon) for 12 hours. Upon consumption of starting material (TLC) the reaction mixture was filtered through Celite and washed with CH_3OH. The filtrate was concentrated *in vacuo* and purified through a silica gel flash column (PE/Acetone = 1:1) to give product **12** as yellow oil (31.0 mg, 88%). ^{1}H NMR (400 MHz, *Chloroform-d*) δ 7.34 – 7.24 (m, 2H), 7.23 – 7.14 (m, 3H), 6.81 (s, 1H), 6.81 – 6.71 (m, 2H), 6.71 – 6.61 (m, 2H), 3.90 (br, 1H), 3.79 (s, 1H), 3.74

(s, 3H), 3.26 (dd, J = 9.9, 3.3 Hz, 1H), 2.73 – 2.52 (m, 2H), 1.87 – 1.74 (m, 1H), 1.74 – 1.61 (m, 1H), 1.62 – 1.49 (m, 1H), 1.46 – 1.25 (m, 1H), 1.22 (s, 3H), 0.81 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, *Chloroform-d*) δ 176.2, 152.4, 142.5, 141.5, 128.4, 128.3, 125.9, 114.8, 114.7, 66.6, 60.3, 55.7, 45.3, 35.7, 28.9, 28.6, 24.6, 15.3; IR ν_{max} (neat) cm^{-1}: 3192, 2981, 1727, 1694, 1641, 1495, 1367, 1321, 1225, 1192, 1037, 1008, 944, 737, 694; HRMS (ESI, m/z): calcd for $C_{22}H_{28}N_2O_2Na^+$ $[M + Na]^+$ 375.2043, found 375.2041.

VII. References

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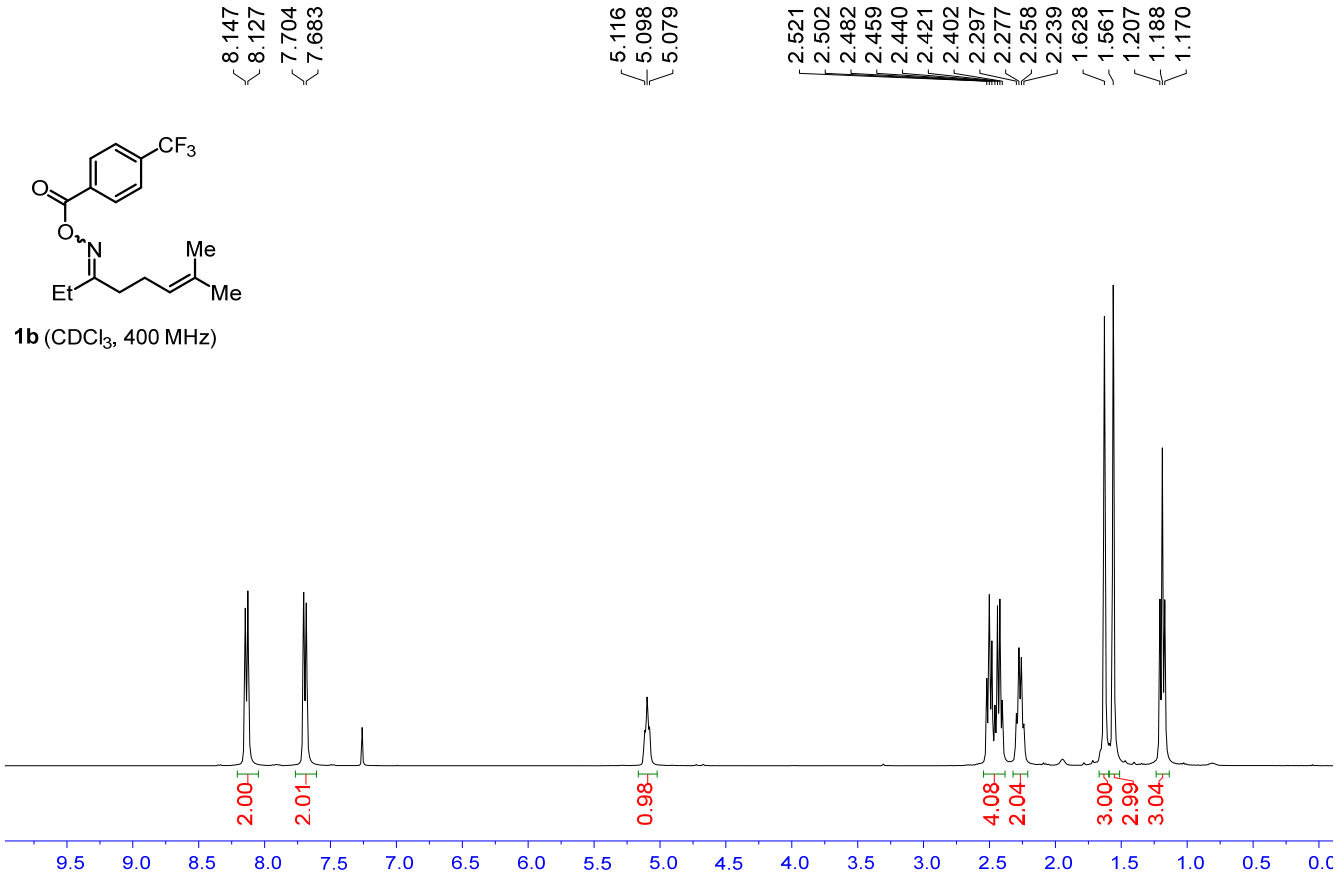
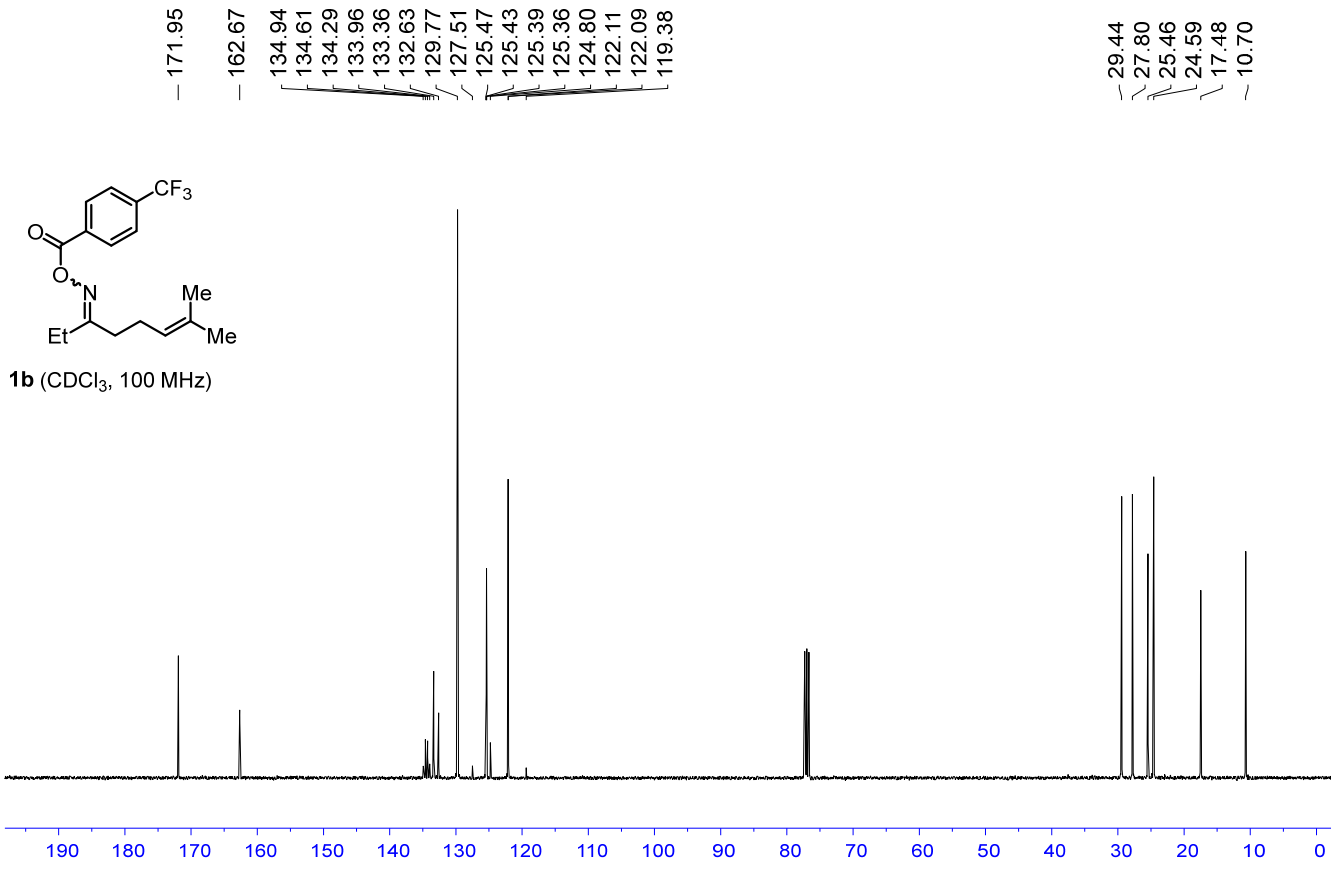
VIII. Copies of NMR spectra for New Compounds



1b ($CDCl_3$, 400 MHz)



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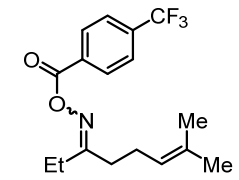
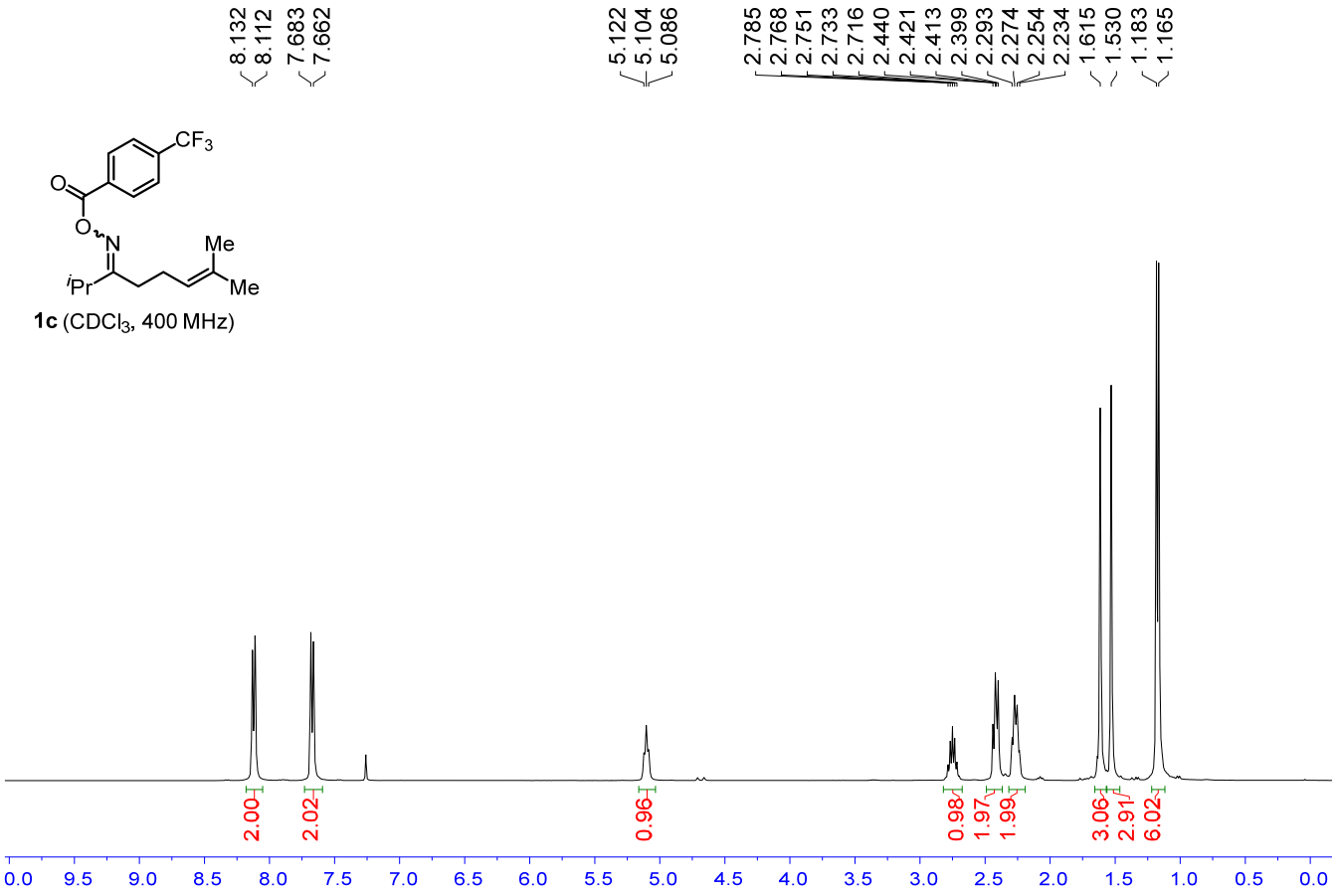


1b ($CDCl_3$, 376 MHz)



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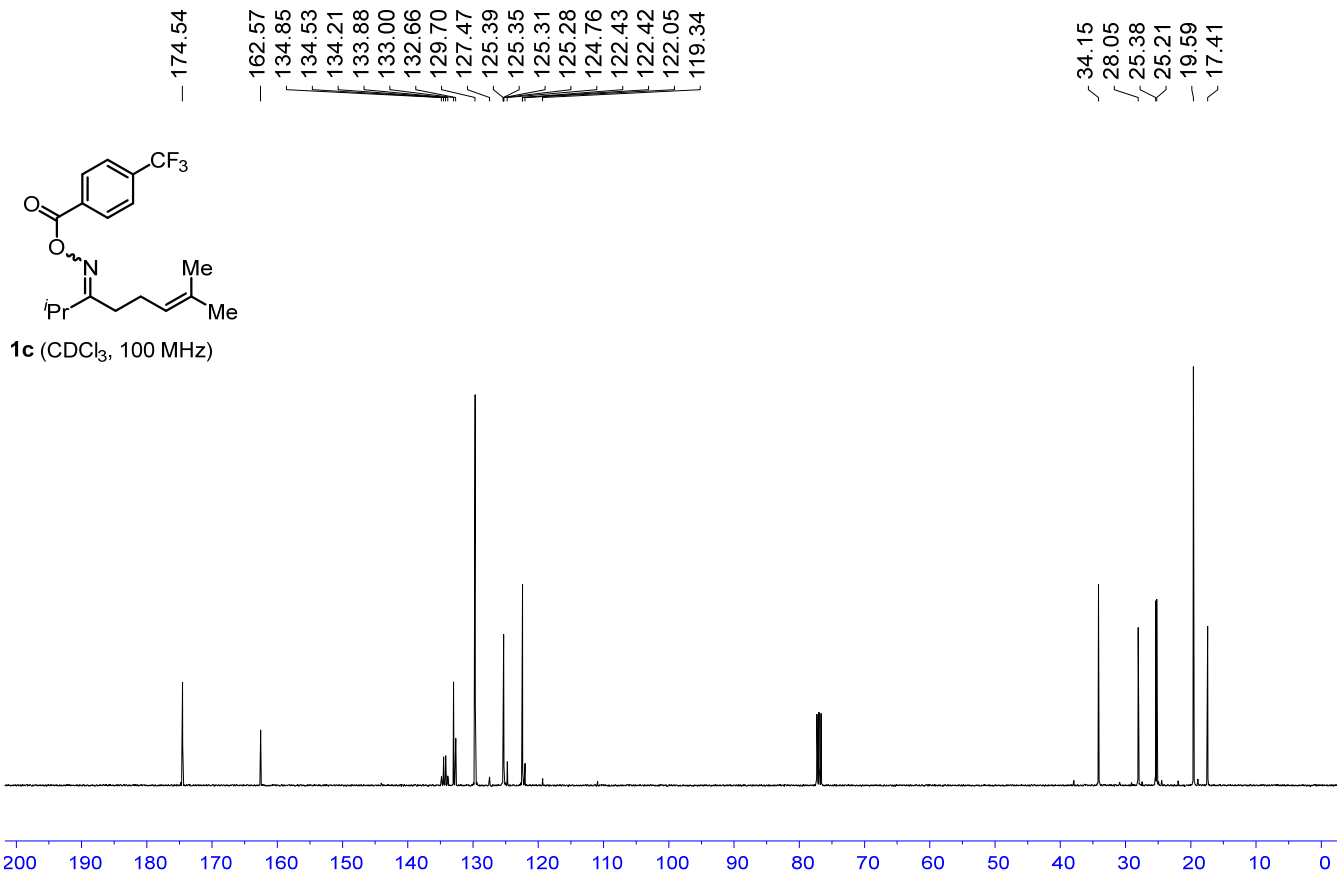

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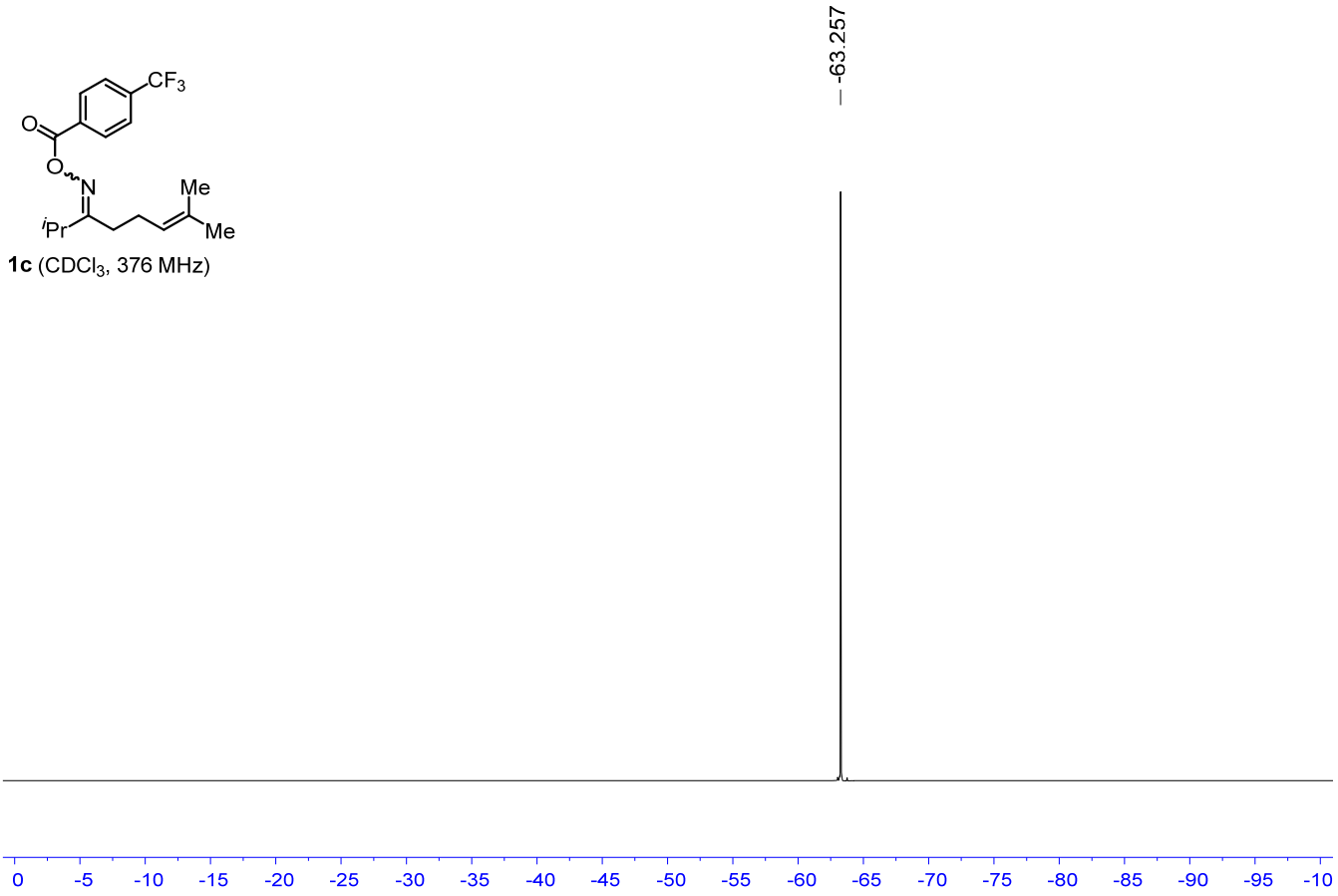

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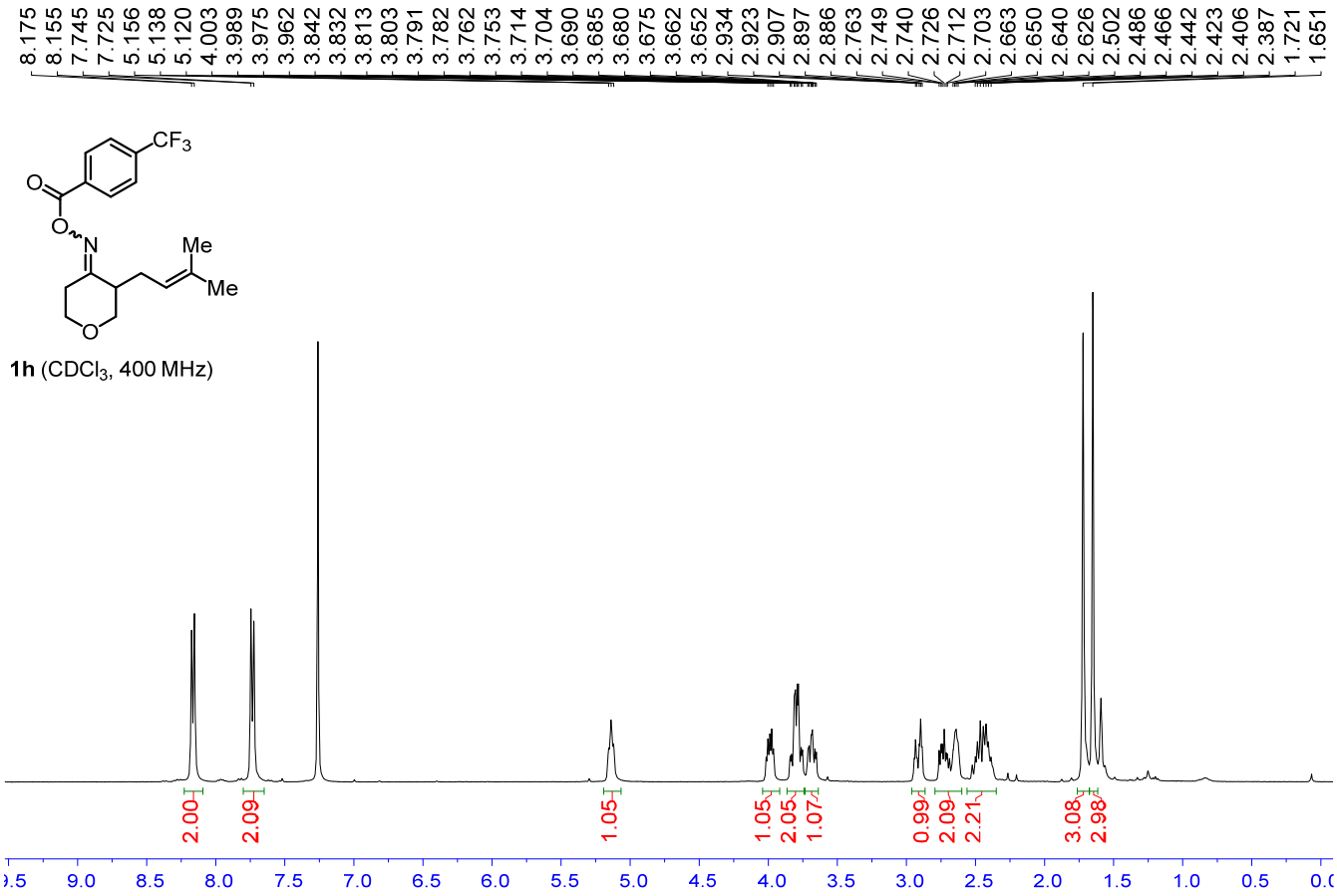
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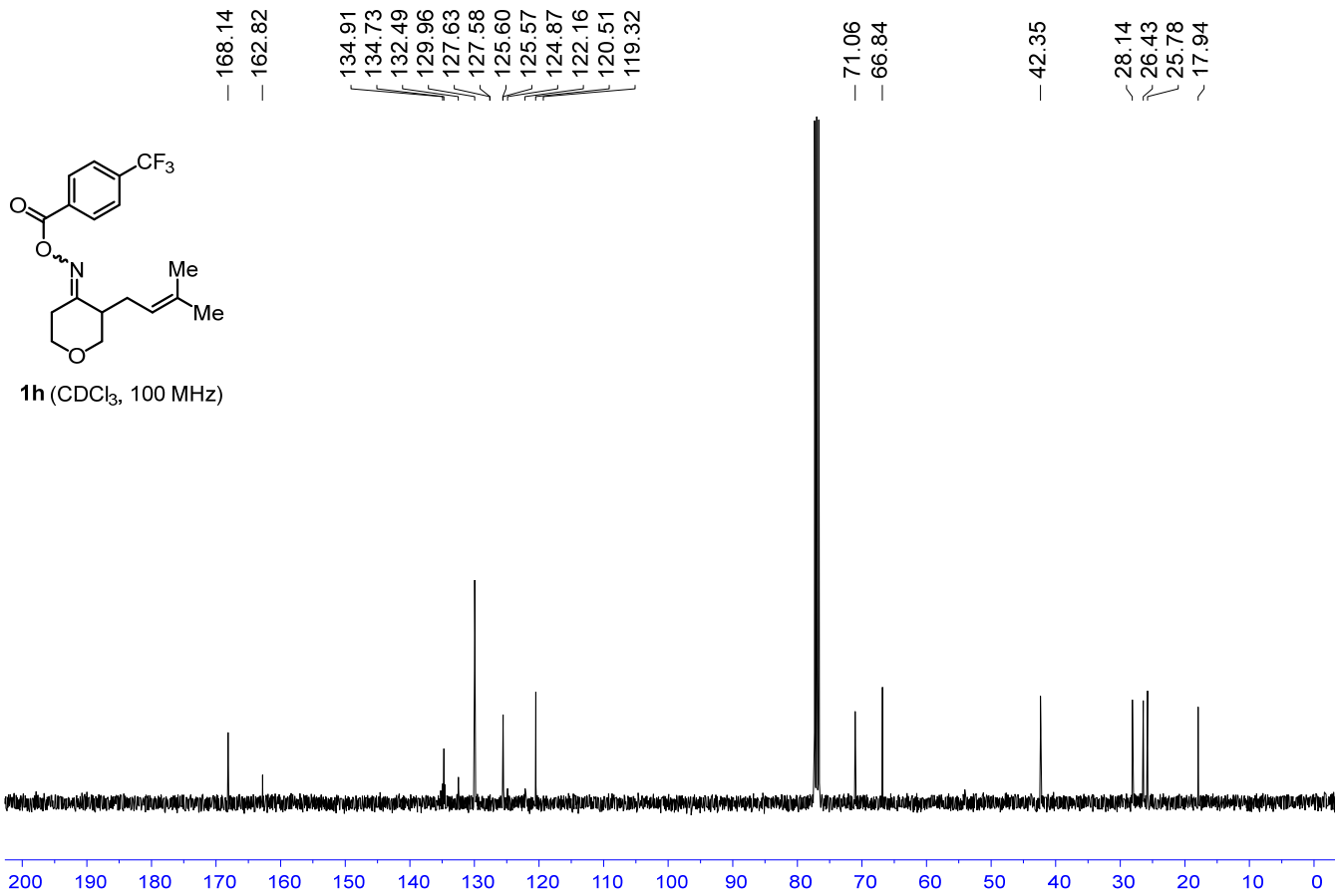
8.155
7.745
7.725
5.156
5.138
5.120
4.003
3.989
3.975
3.962
3.842
3.832
3.813
3.803
3.791
3.782
3.762
3.753
3.714
3.704
3.690
3.685
3.680
3.675
3.662
3.652
2.934
2.923
2.907
2.897
2.886
2.763
2.749
2.740
2.726
2.712
2.703
2.663
2.650
2.640
2.626
2.502
2.486
2.466
2.442
2.423
2.406
2.387
1.721
1.651
CF3
O
O
N
Me
Me
O
1h (CDCl3, 400 MHz)
2.00
2.09
1.05
1.05
2.05
1.07
0.99
2.09
2.21
3.08
2.98
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


168.14
162.82
134.91
134.73
132.49
129.96
127.63
127.58
125.60
125.57
124.87
122.16
120.51
119.32
71.06
66.84
42.35
28.14
26.43
25.78
17.94
CF3
O
O
N
Me
Me
O
1h (CDCl3, 100 MHz)
200
190
180
170
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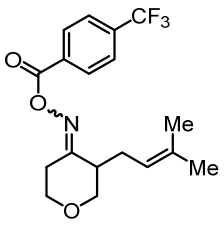
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



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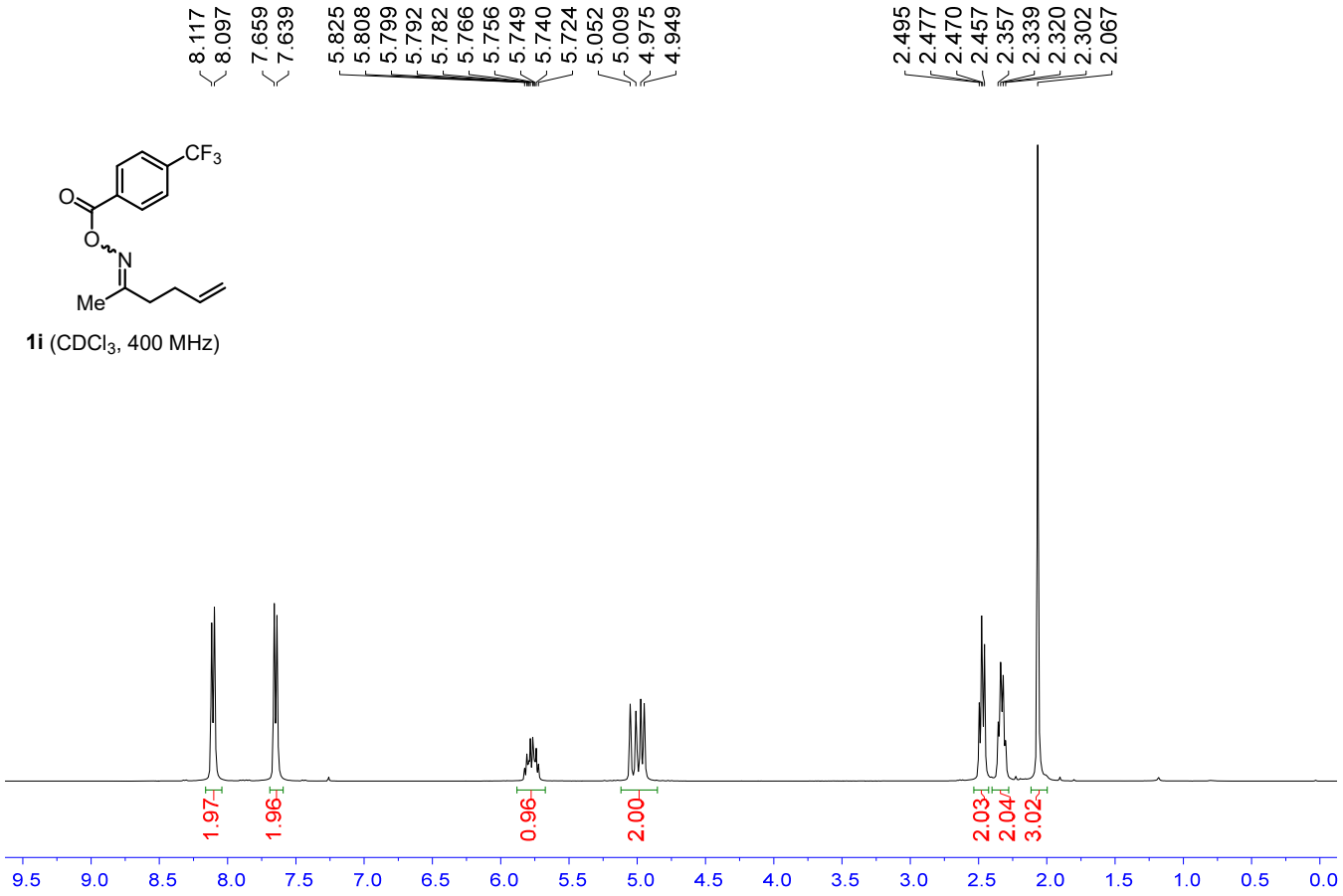

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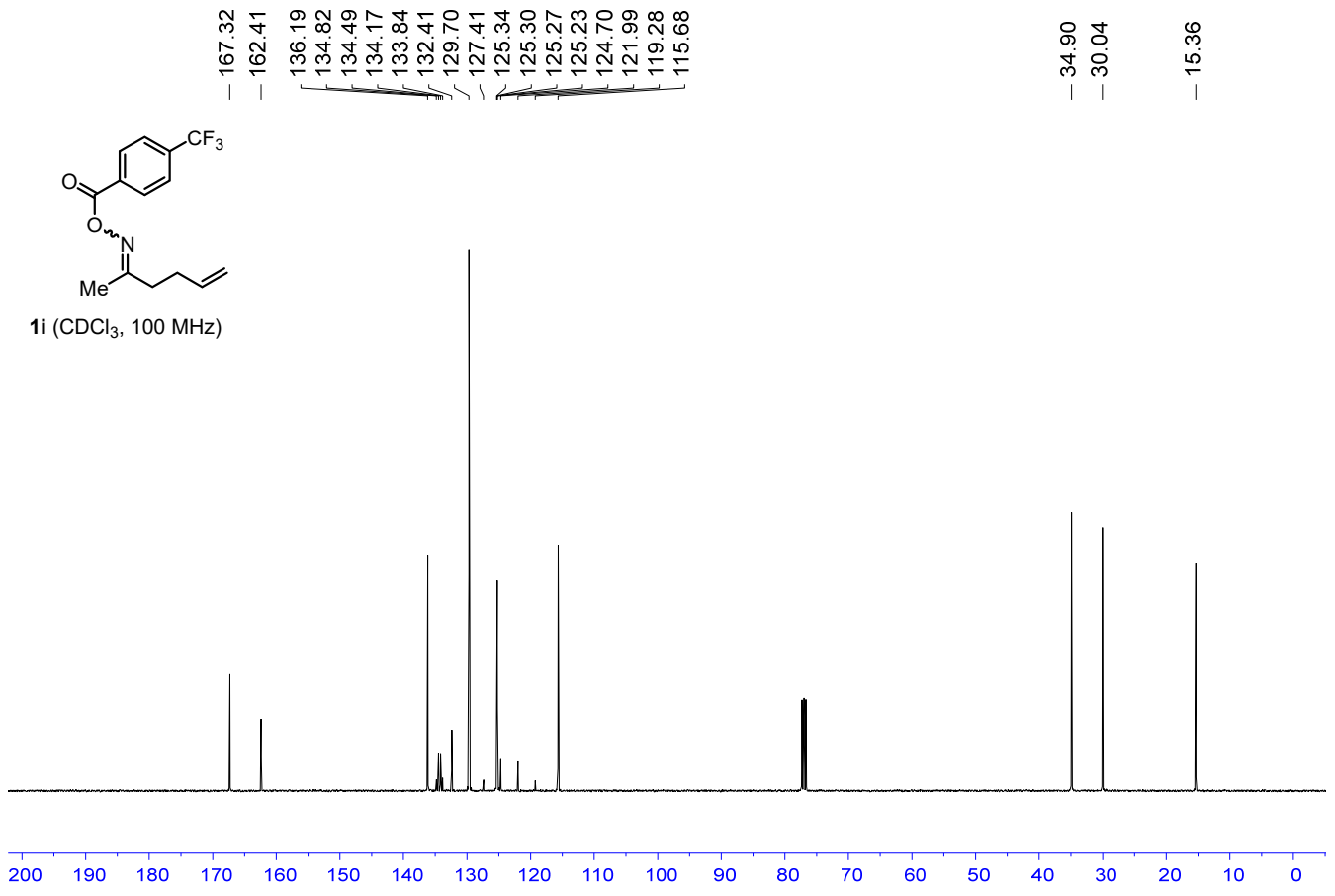
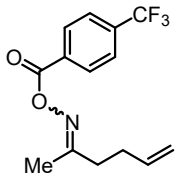
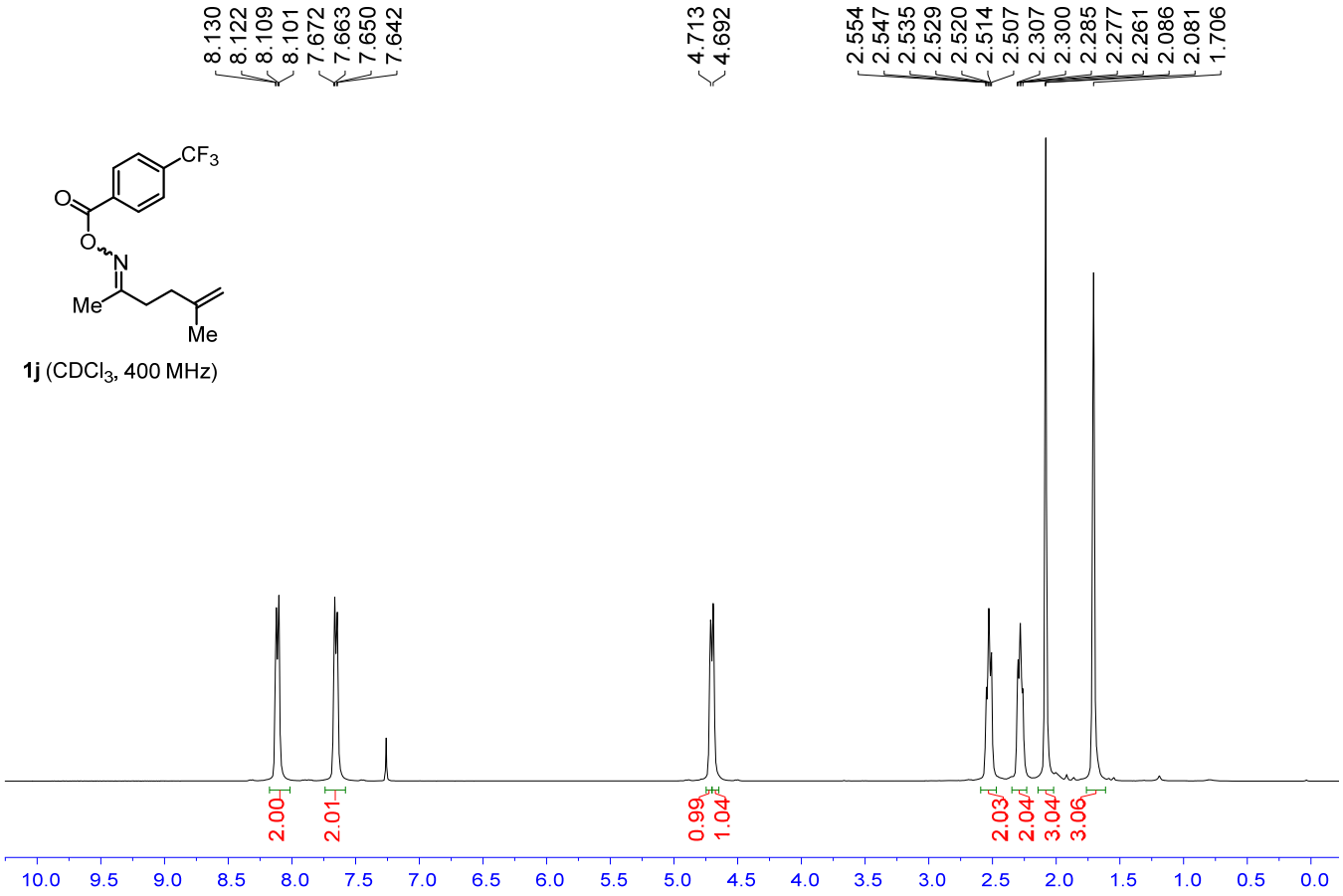


1i ($CDCl_3$, 100 MHz)



1i ($CDCl_3$, 376 MHz)



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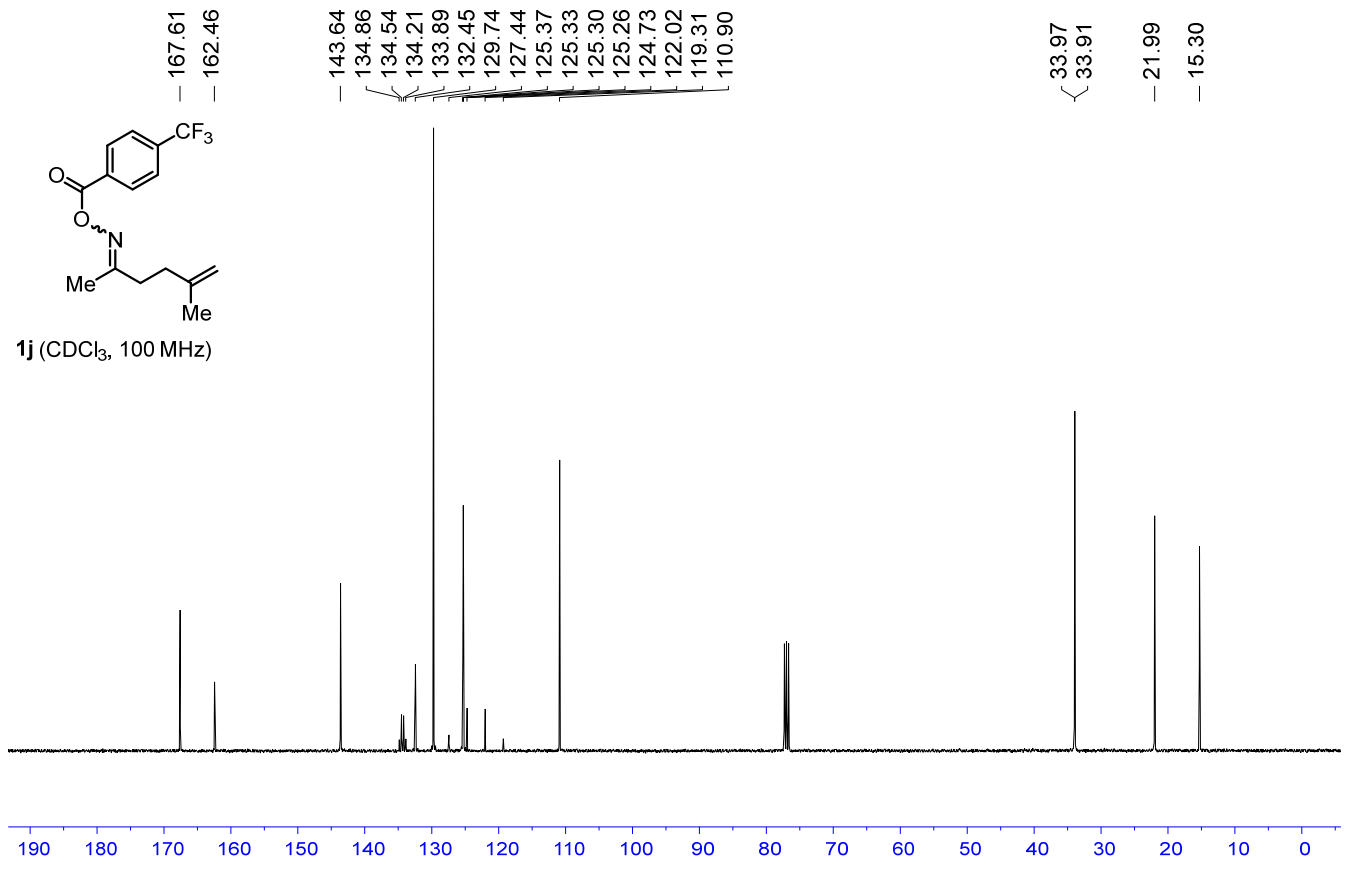
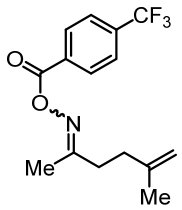


1j ($CDCl_3$, 100 MHz)



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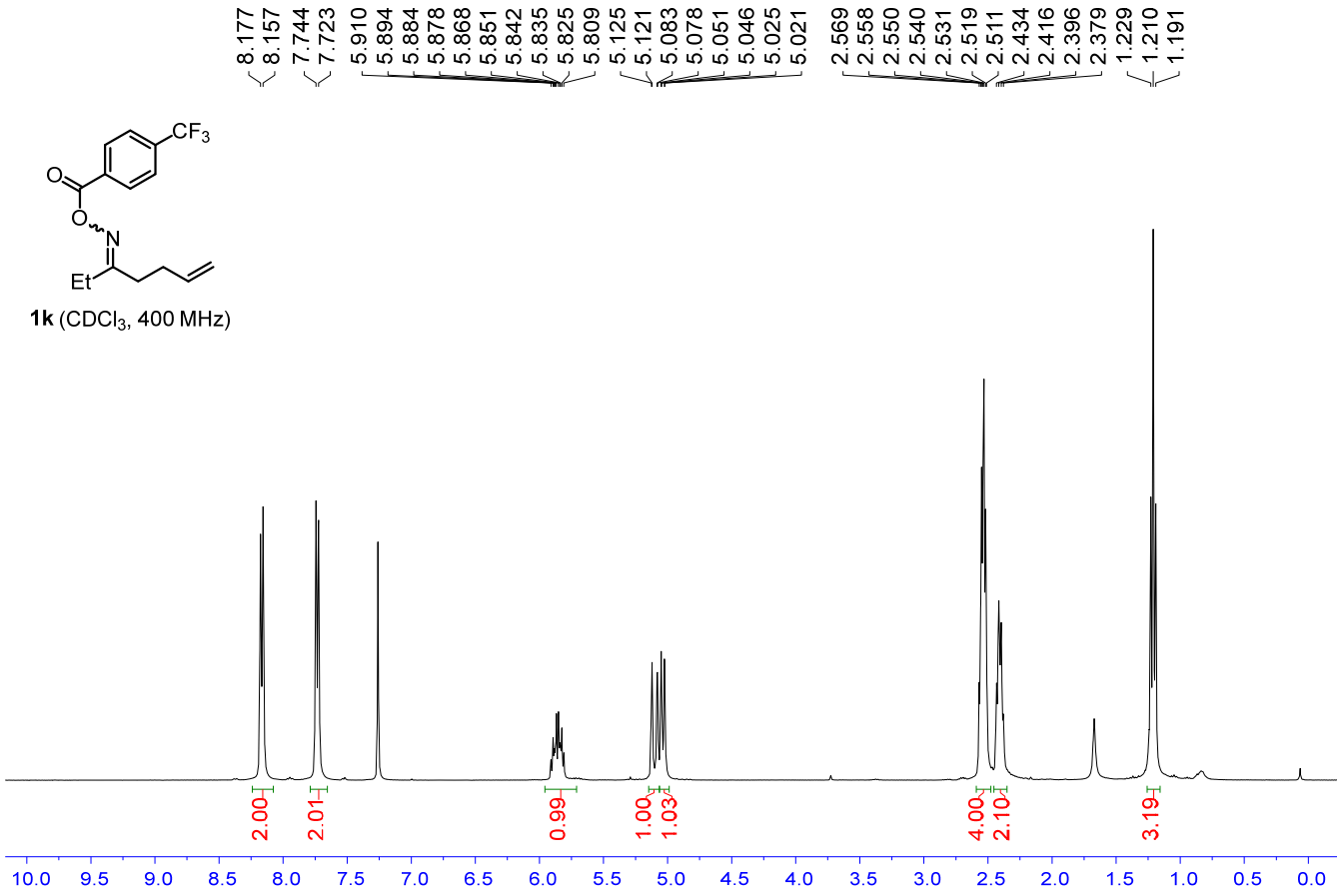

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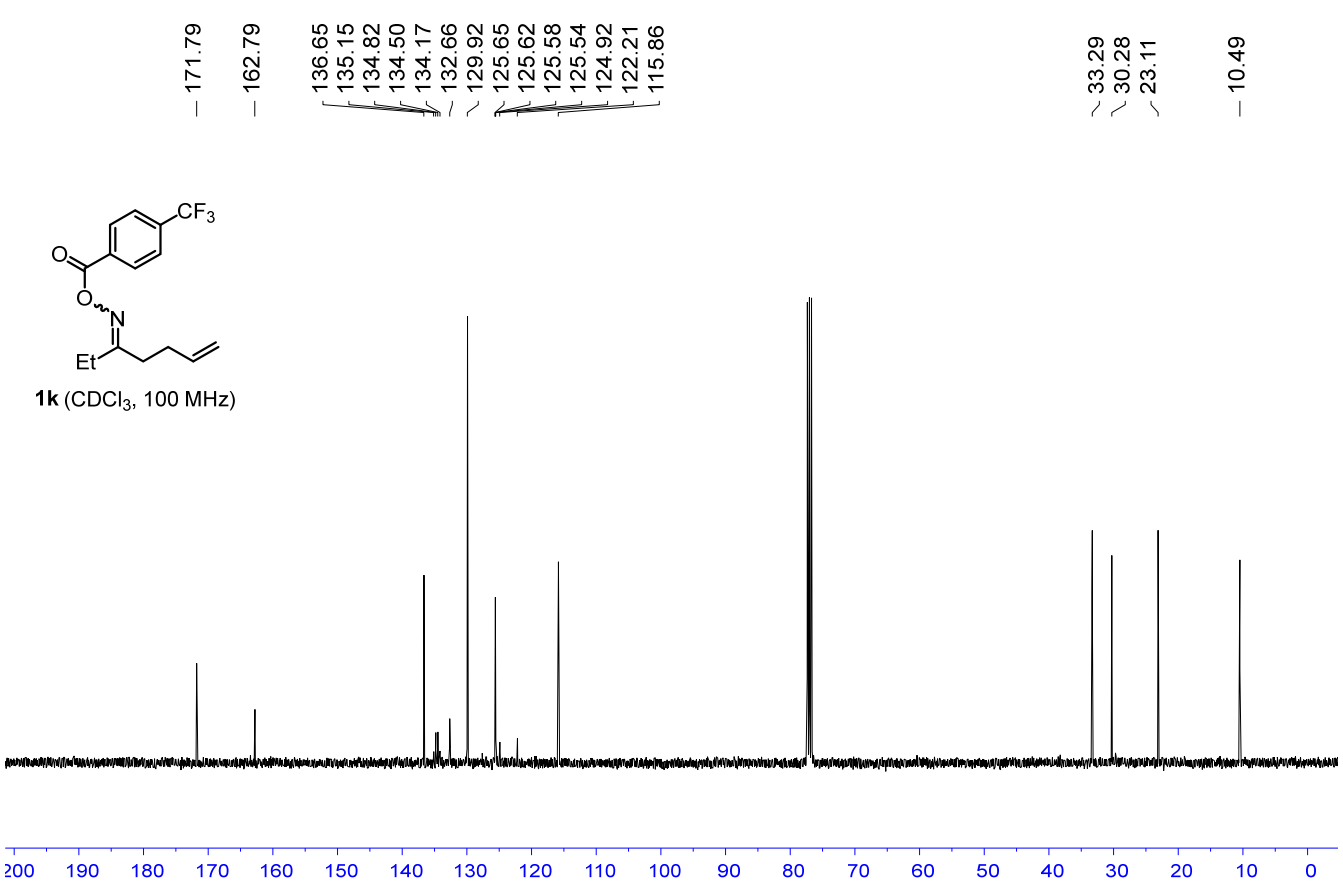

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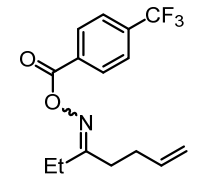

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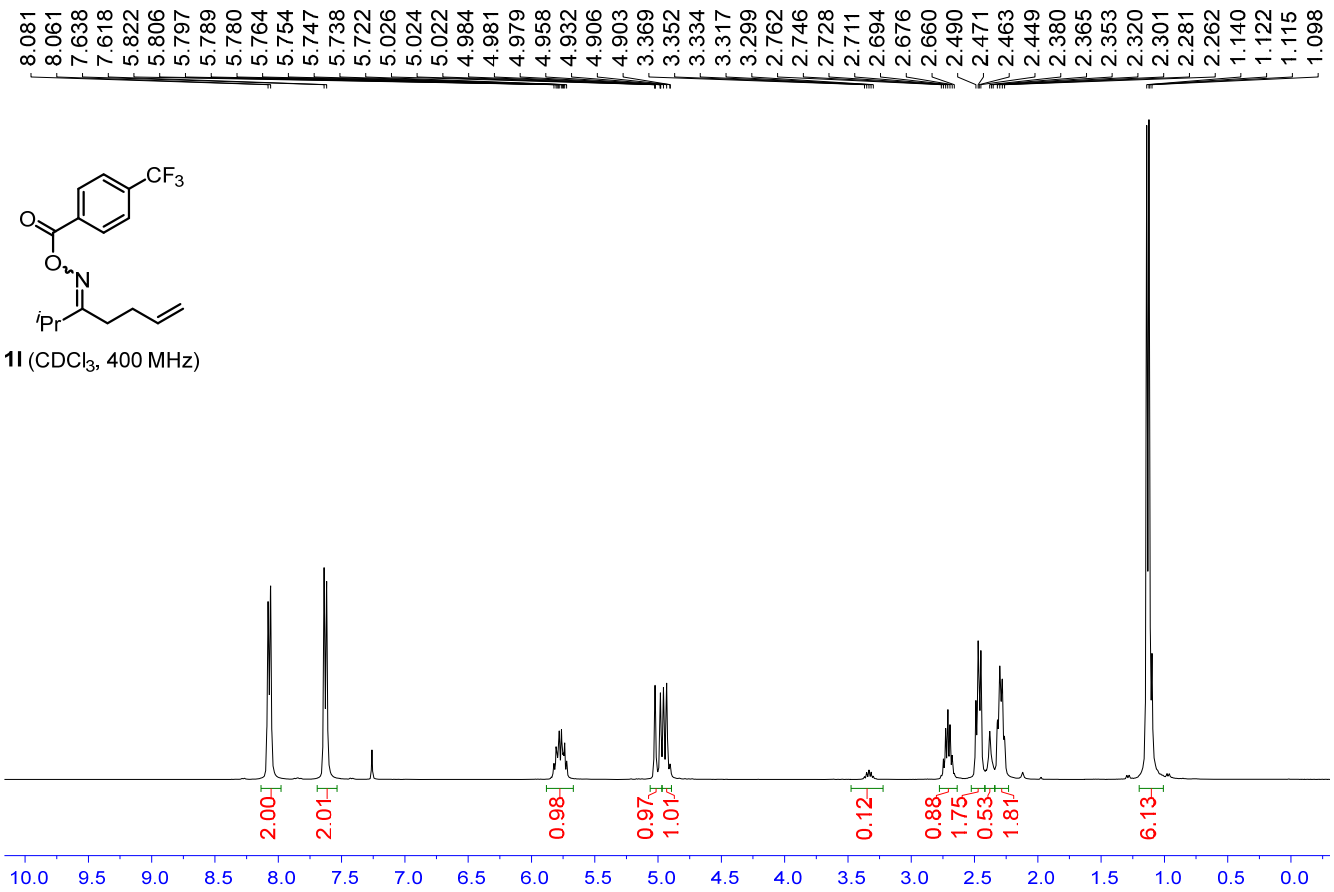

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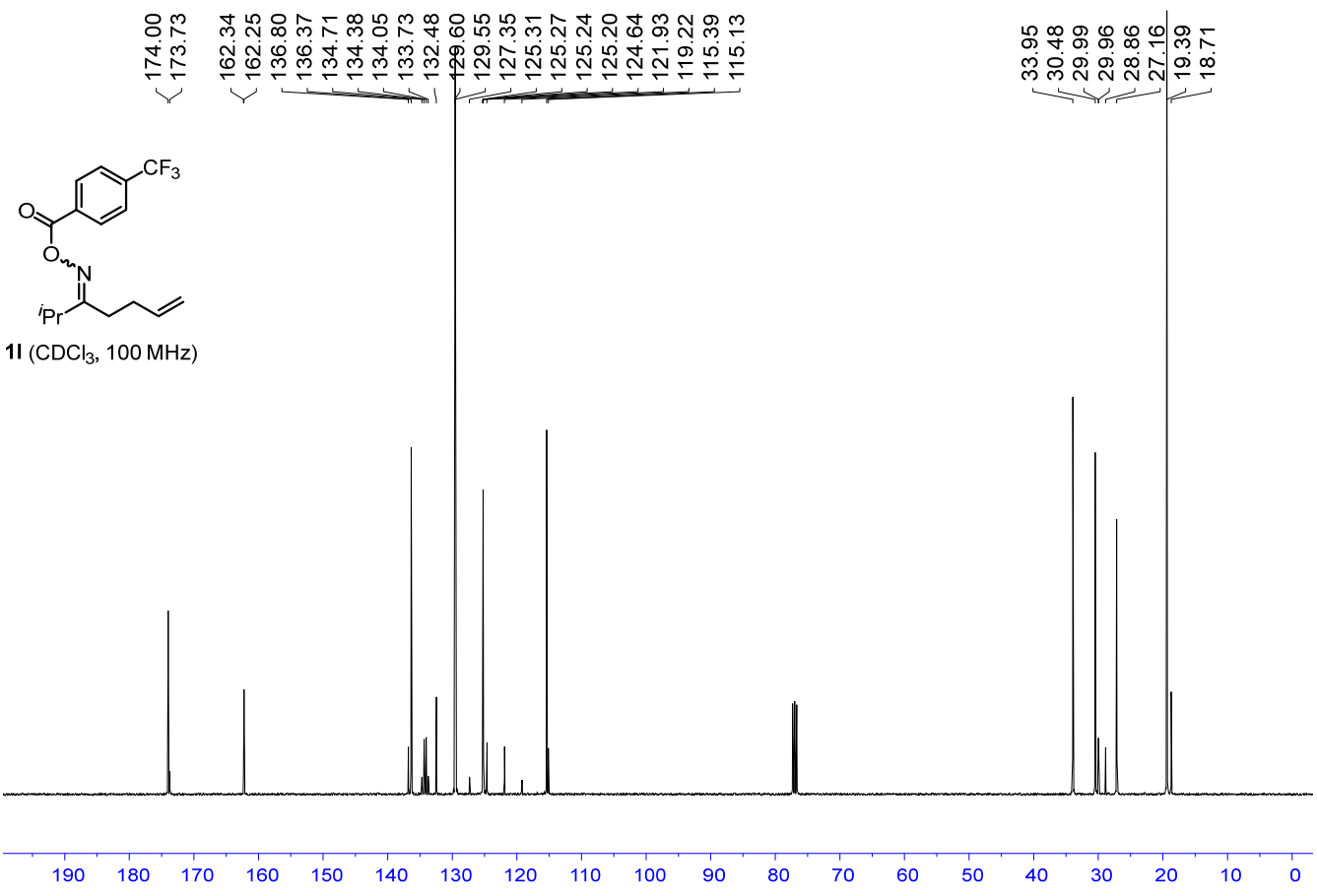

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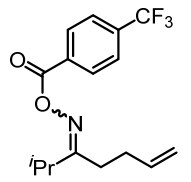

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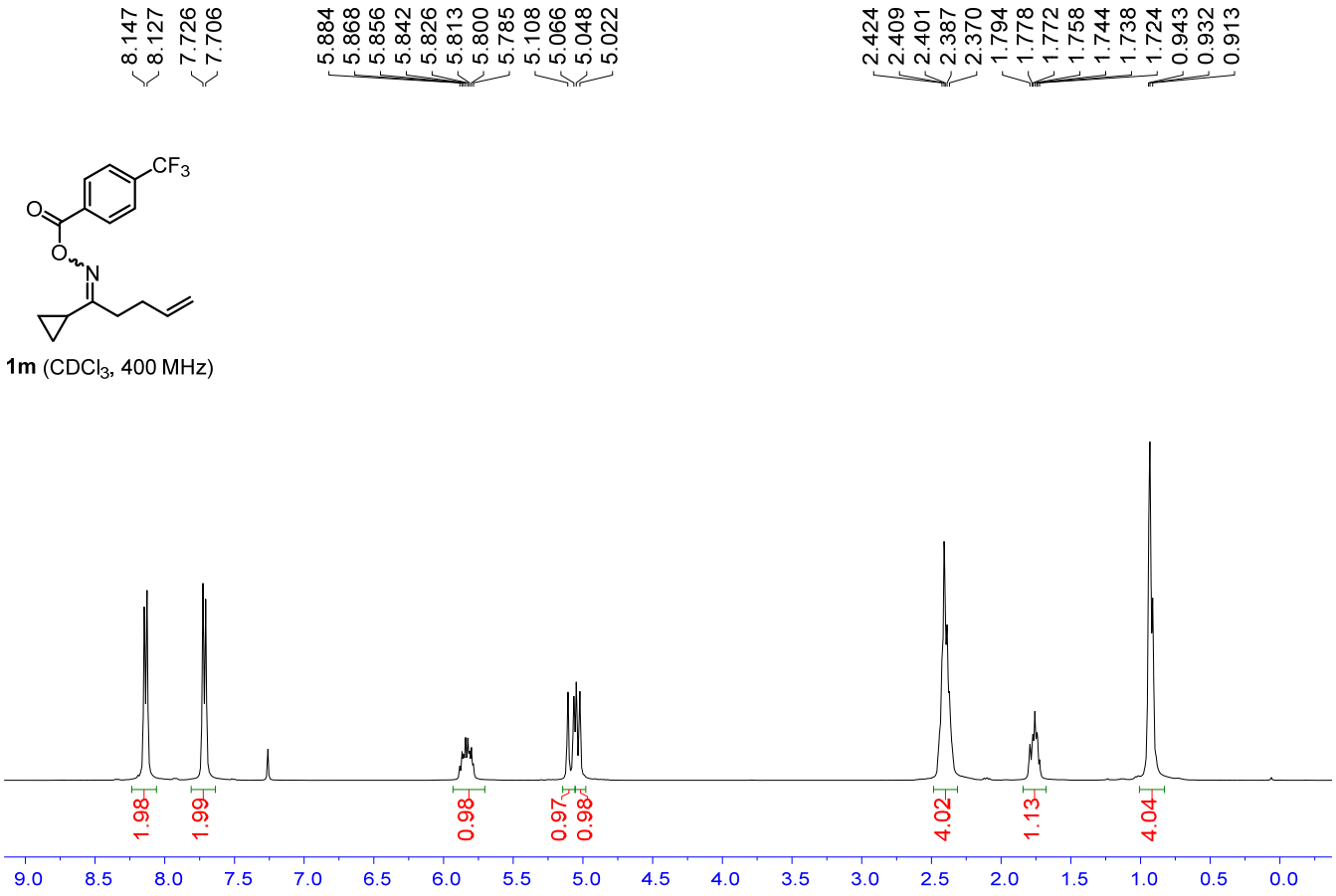
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5.868
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5.826
5.813
5.800
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5.066
5.048
5.022
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2.409
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2.387
2.370
1.794
1.778
1.772
1.758
1.744
1.738
1.724
0.943
0.932
0.913
CF3
O
O
N
1m (CDCl3, 400 MHz)
1.98
1.99
0.98
0.97
0.98
4.02
1.13
4.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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2.0
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1.0
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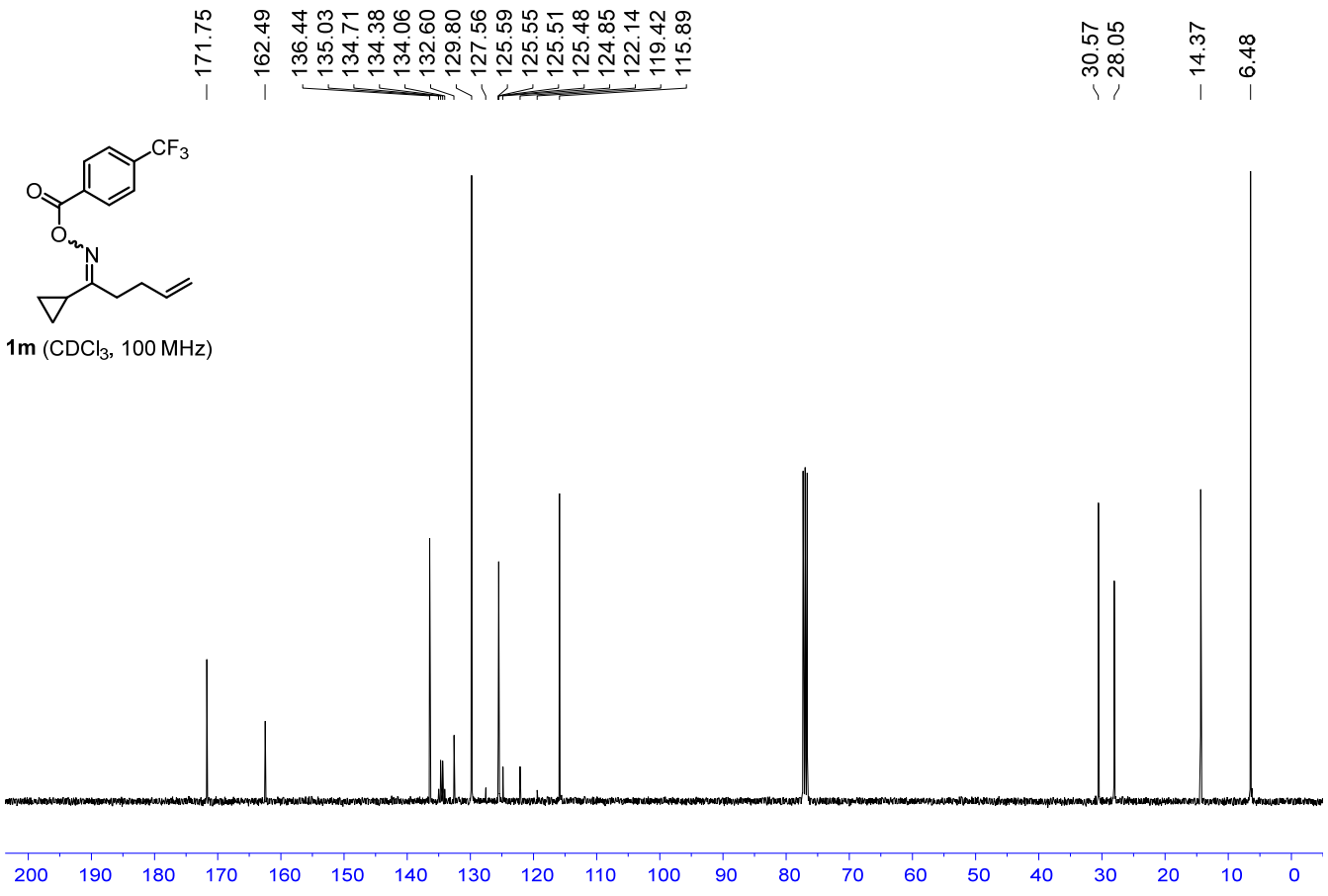
0.0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127.56
125.59
125.55
125.51
125.48
124.85
122.14
119.42
115.89
30.57
28.05
14.37
6.48
CF3
O
O
N
1m (CDCl3, 100 MHz)
200
190
180
170
160
150
140
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120
110
100
90
80
70
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50
40
30
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10
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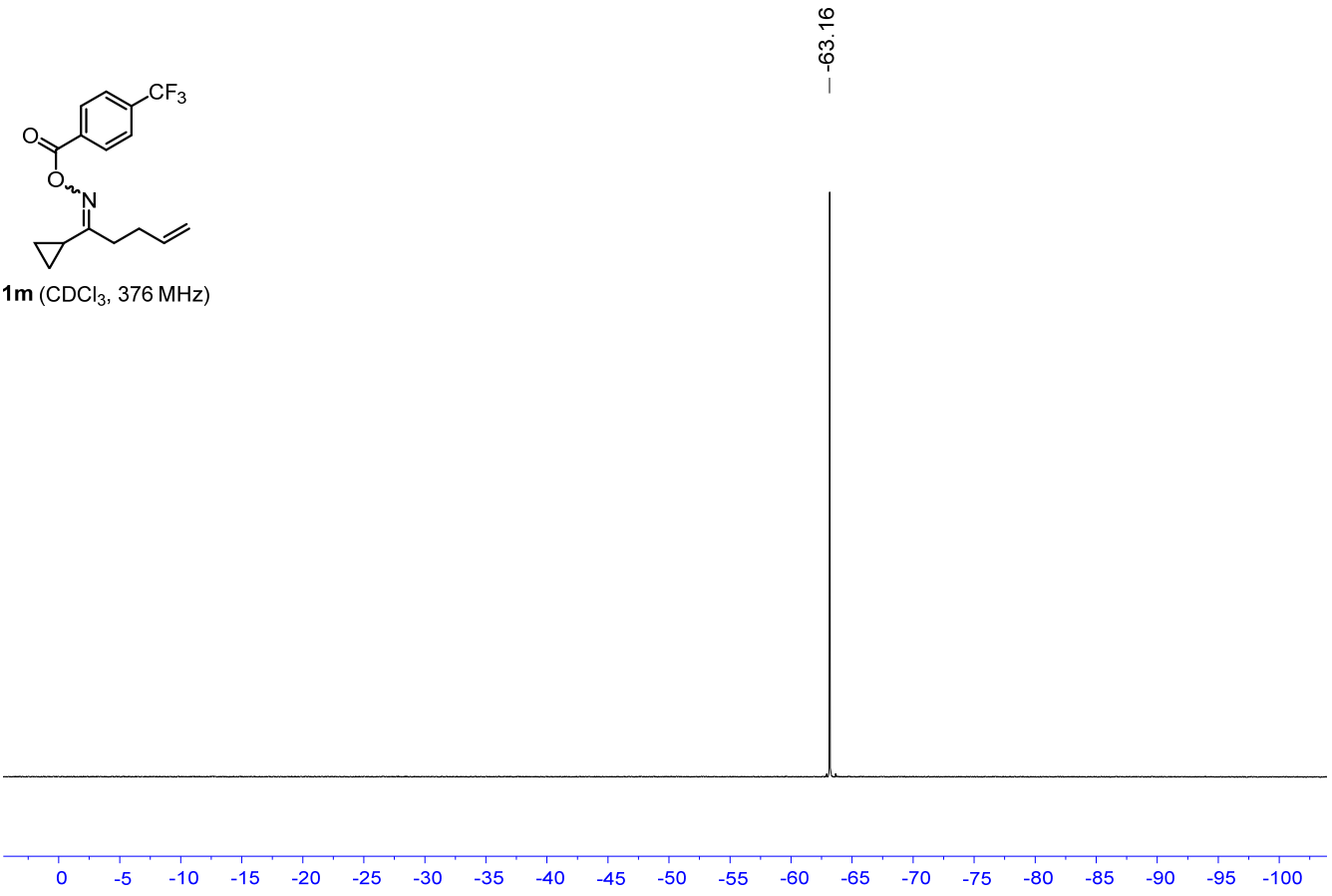

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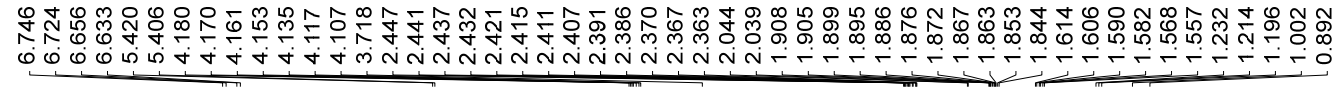
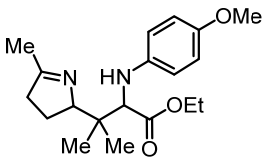
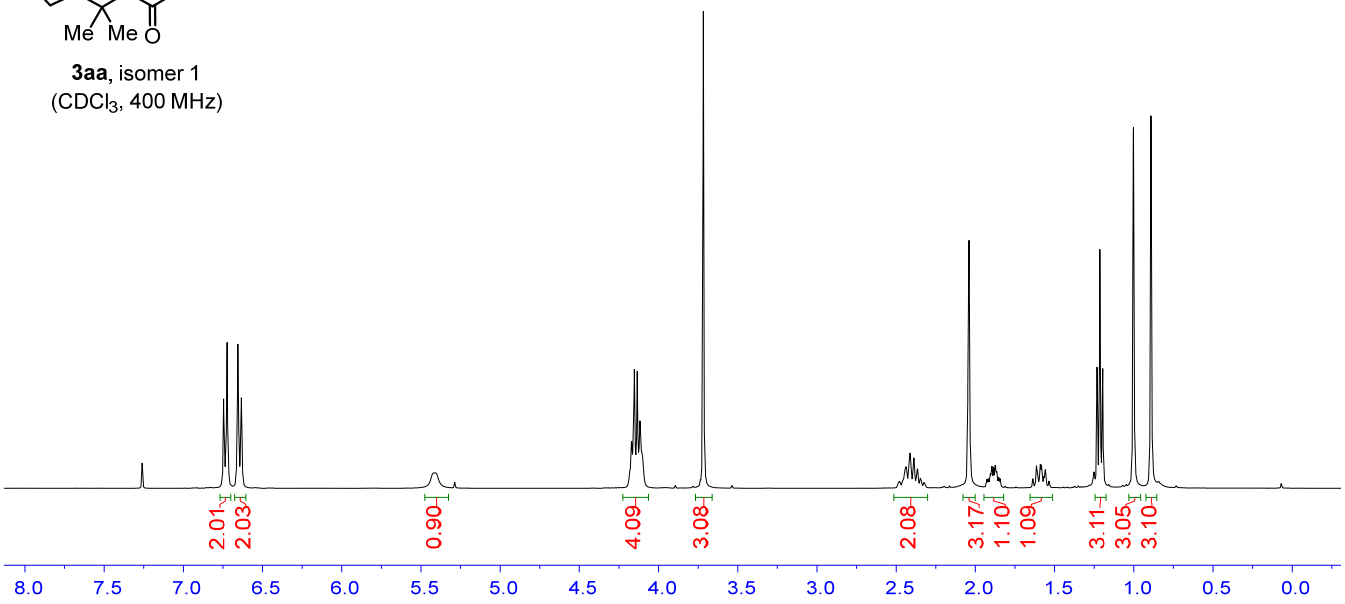
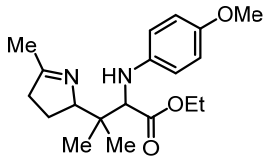


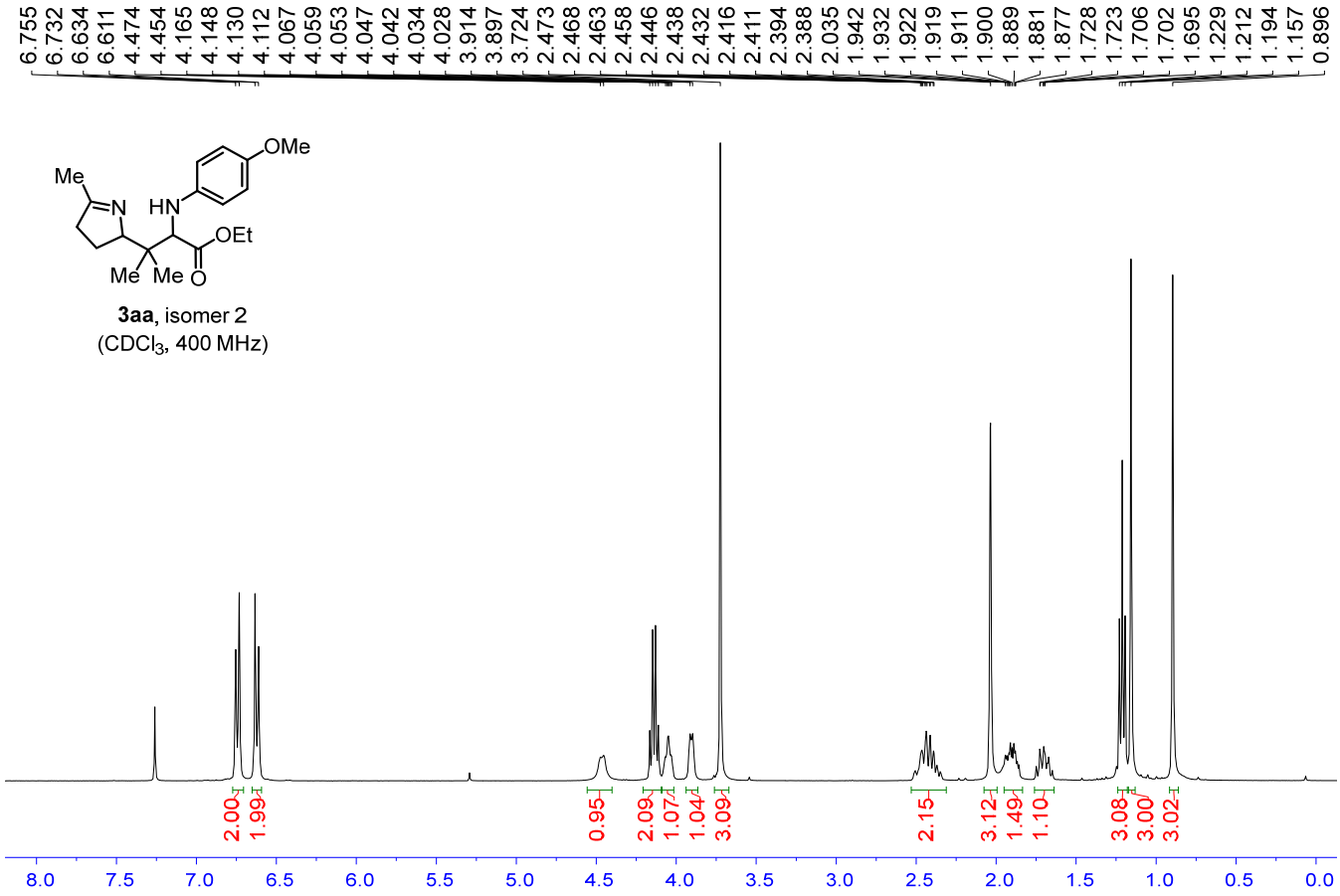


3aa, isomer 1
($CDCl_3$, 400 MHz)





3aa, isomer 1
($CDCl_3$, 100 MHz)



3aa, isomer 2
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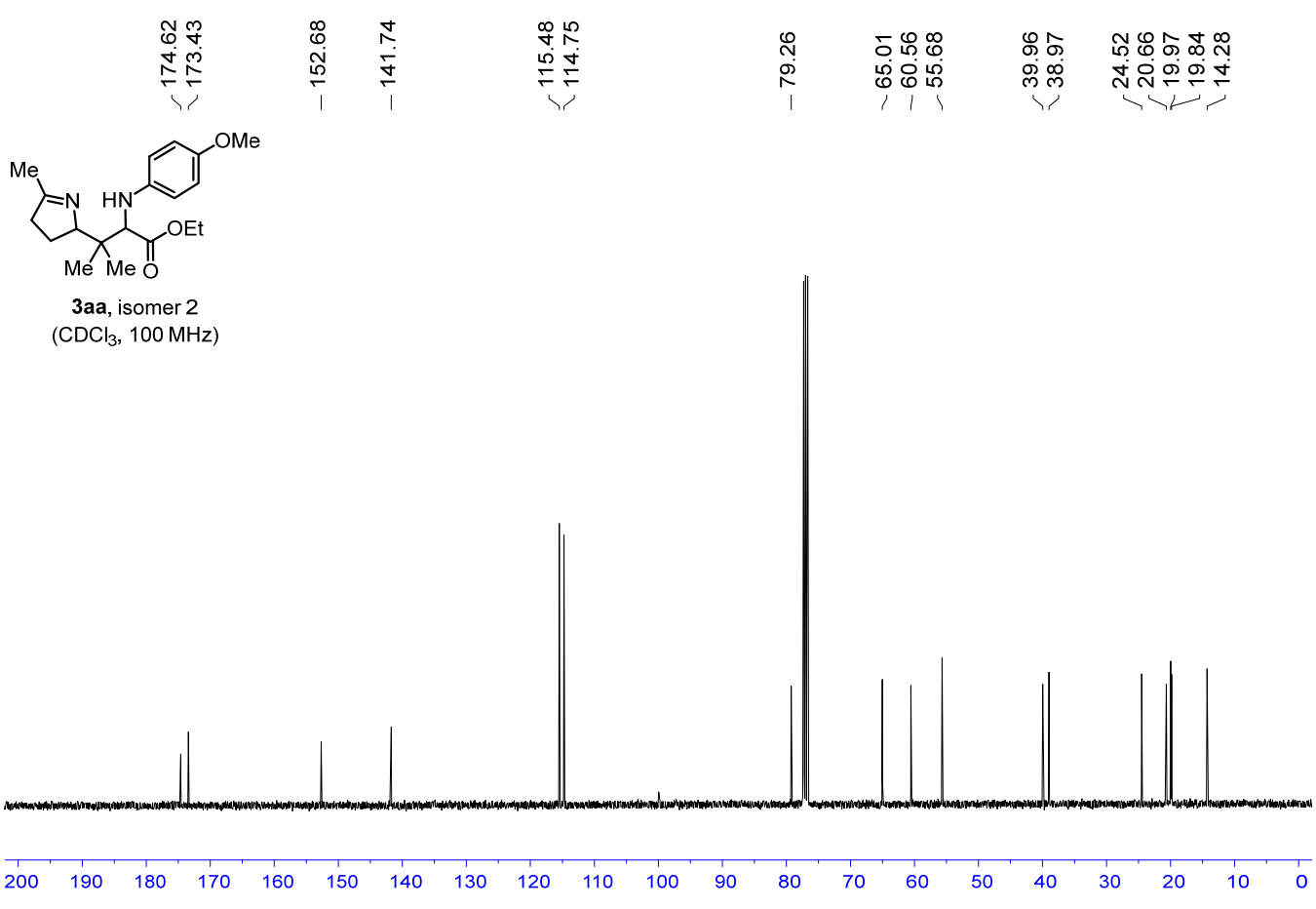
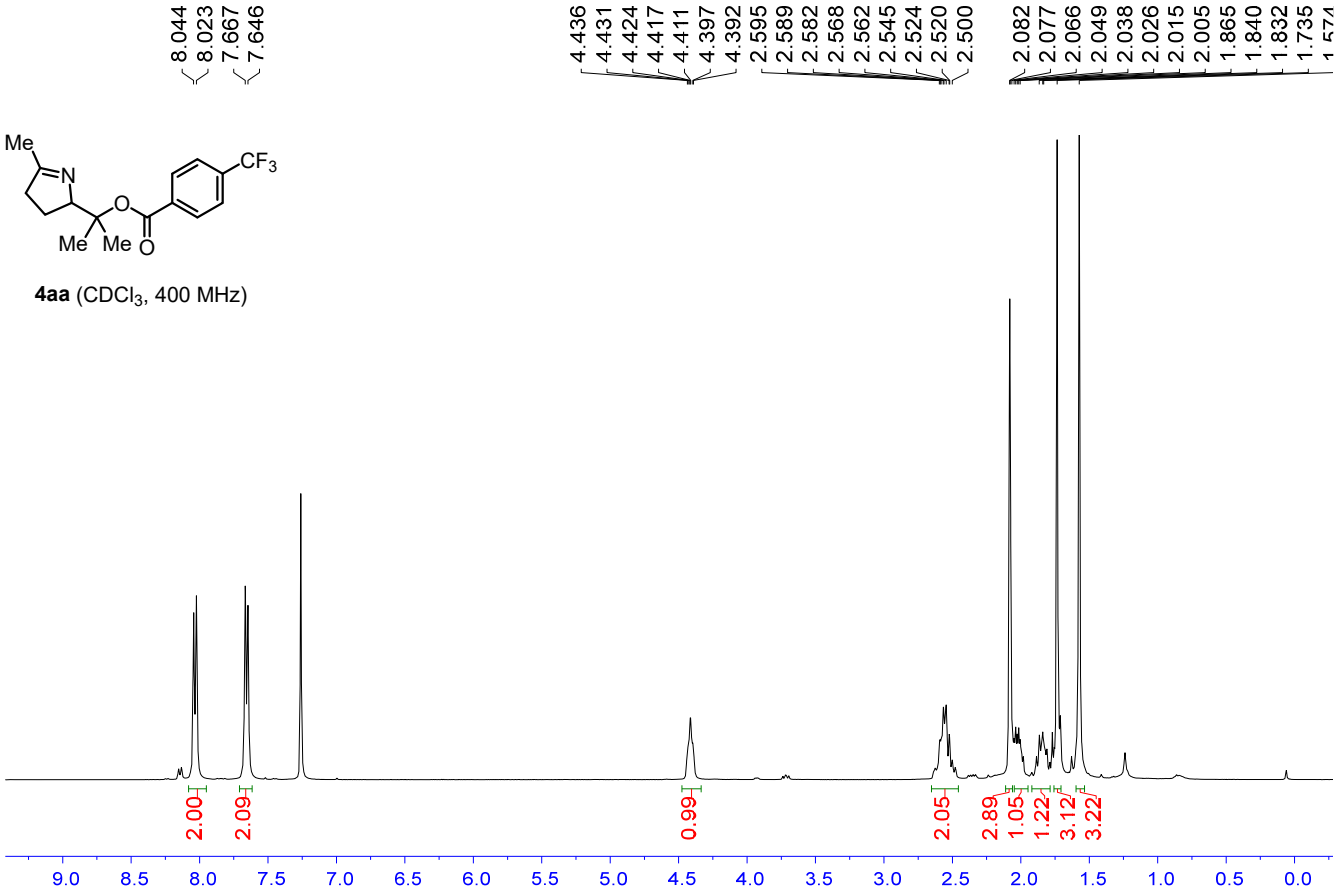
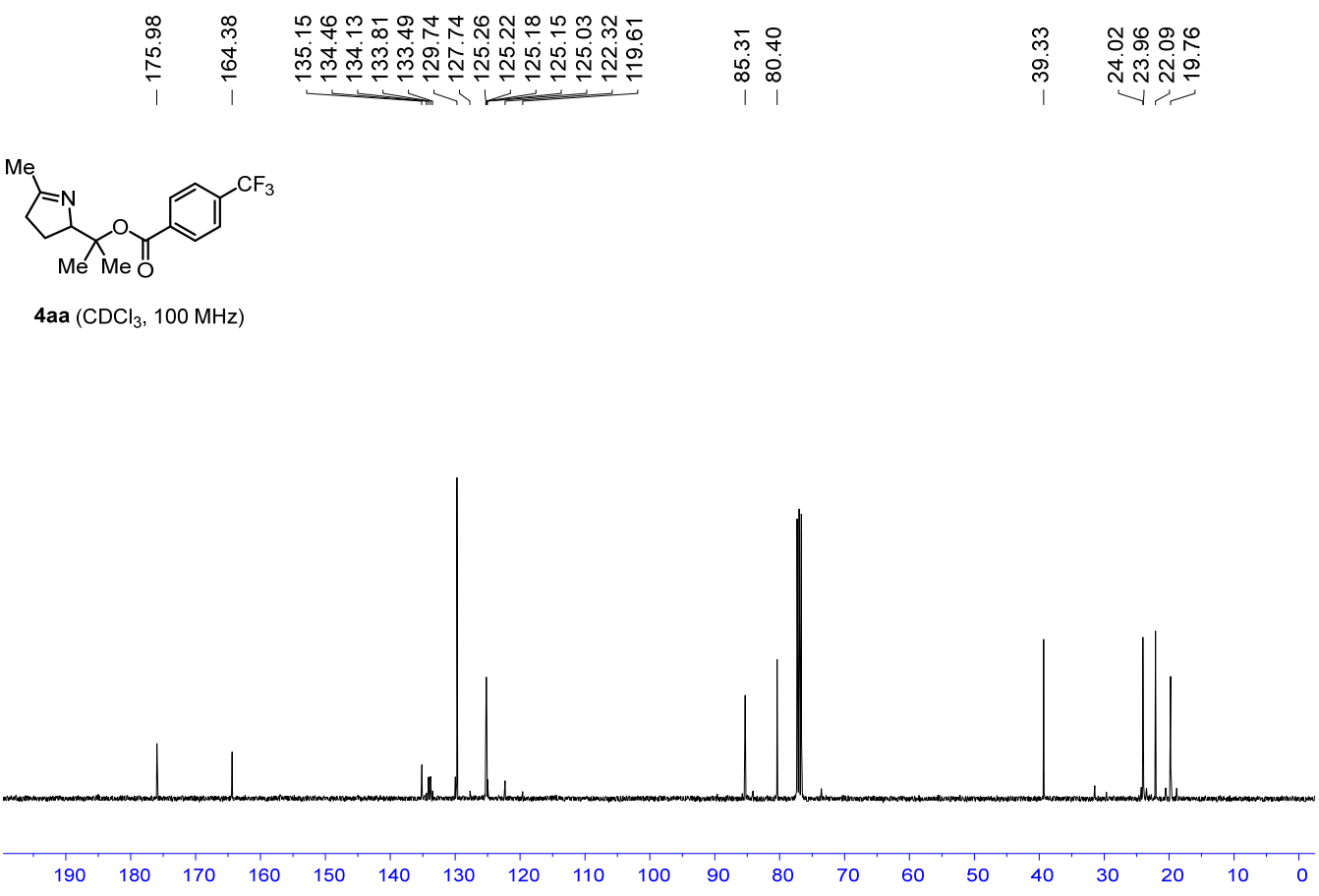


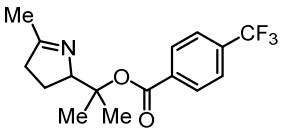
3aa, isomer 2
($CDCl_3$, 100 MHz)



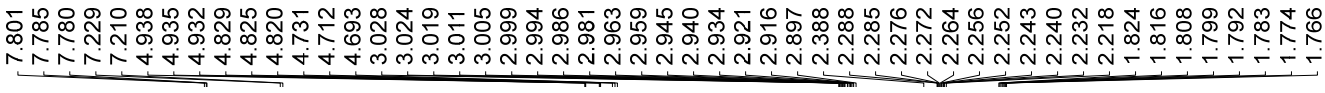
4aa ($CDCl_3$, 400 MHz)

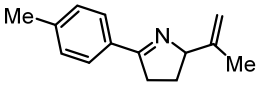


4aa ($CDCl_3$, 100 MHz)



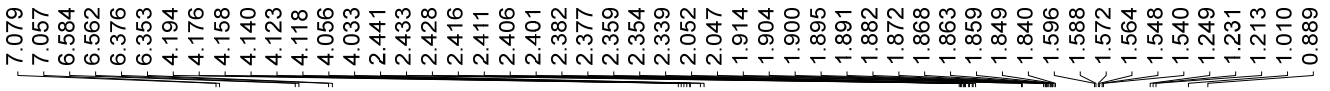
4aa ($CDCl_3$, 376 MHz)

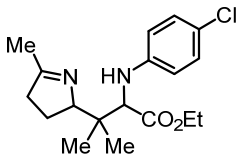




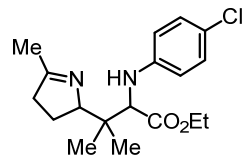
S6

($CDCl_3$, 400 MHz)

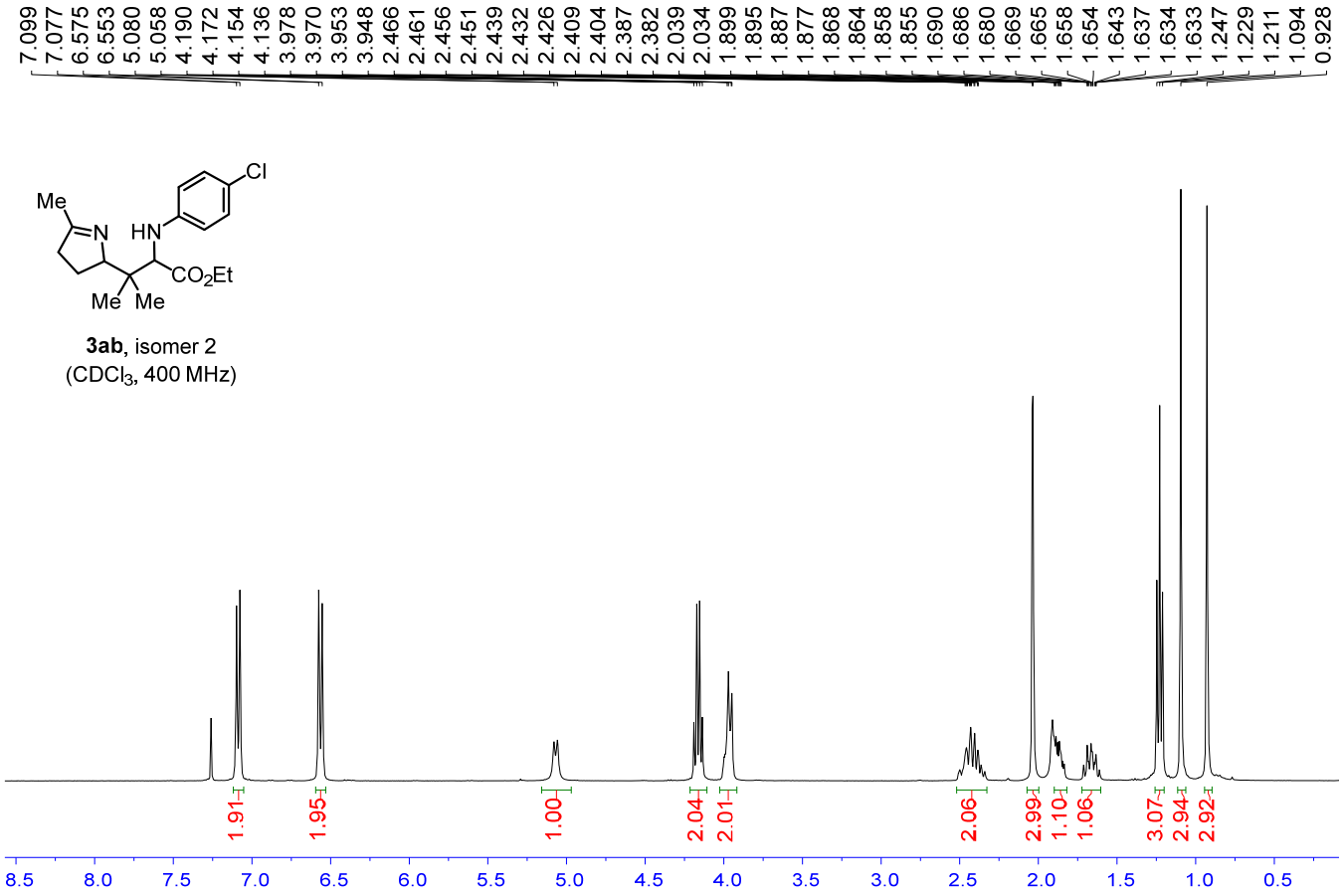


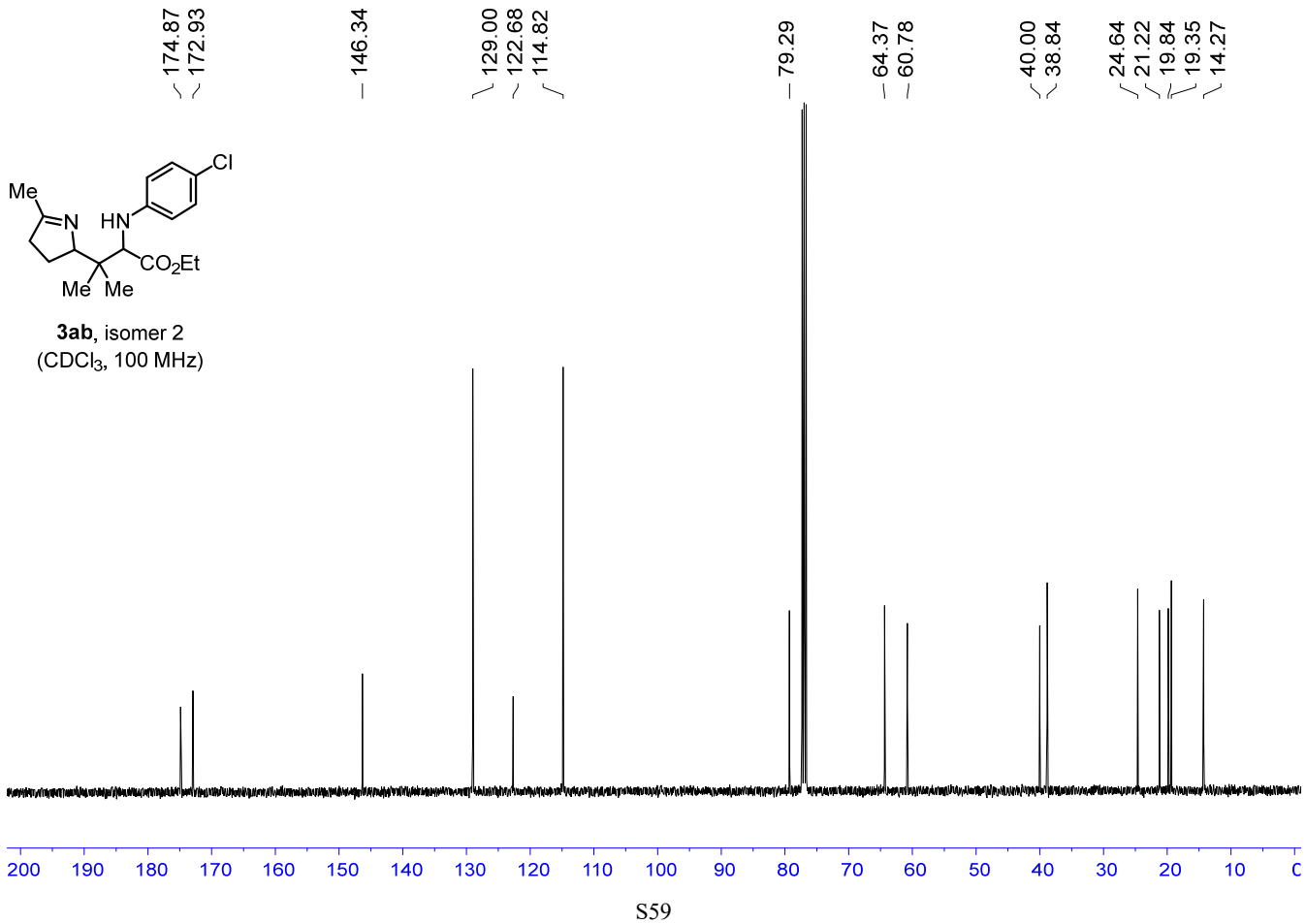


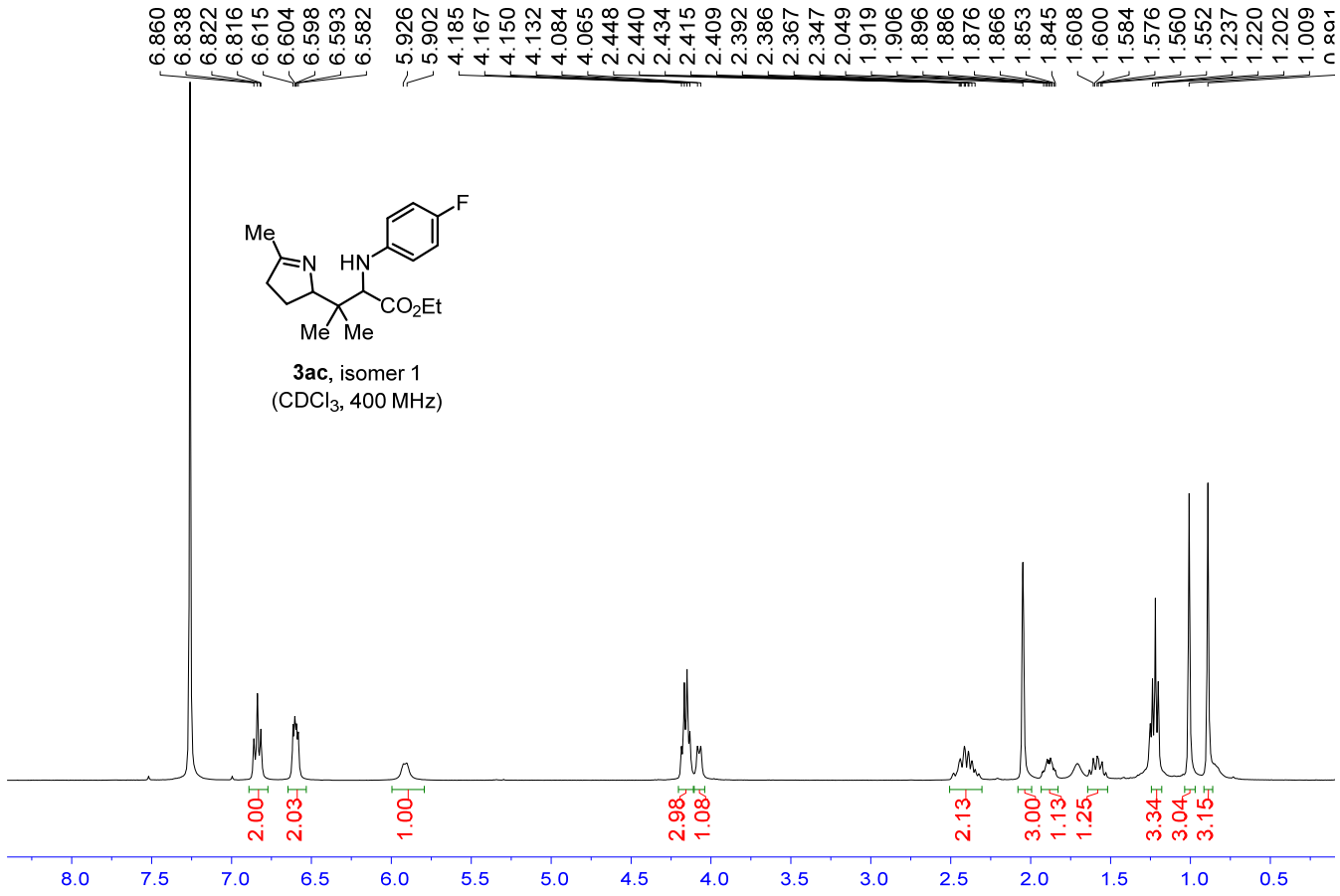
3ab, isomer 1
($CDCl_3$, 400 MHz)

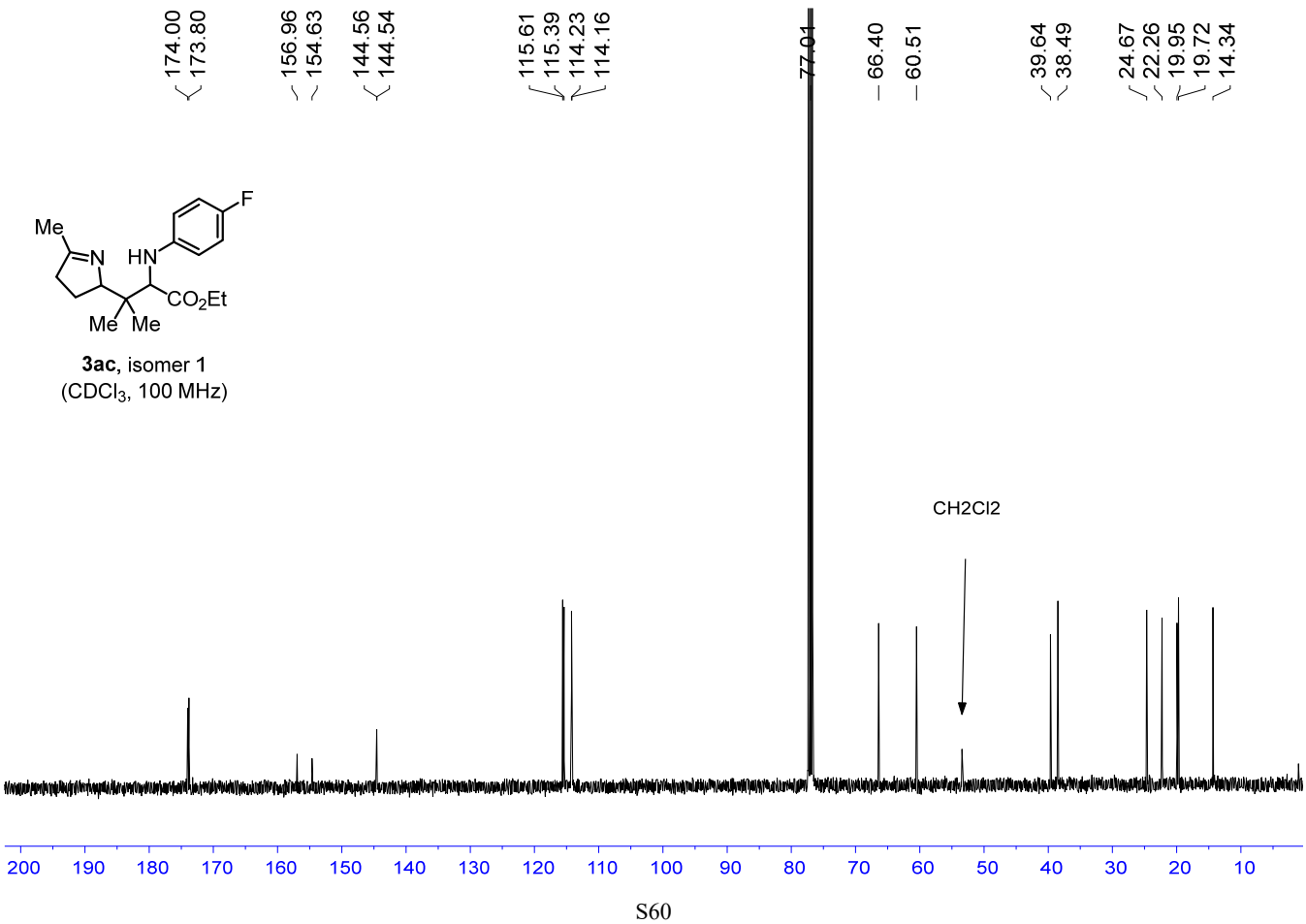


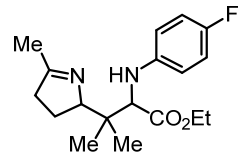
3ab, isomer 1
($CDCl_3$, 100 MHz)


7.099
7.077
6.575
6.553
5.080
5.058
4.190
4.172
4.154
4.136
3.978
3.970
3.953
3.948
2.466
2.461
2.456
2.451
2.439
2.432
2.426
2.409
2.404
2.387
2.382
2.039
2.034
1.899
1.895
1.887
1.877
1.868
1.864
1.858
1.855
1.690
1.686
1.680
1.669
1.665
1.658
1.654
1.643
1.637
1.634
1.633
1.247
1.229
1.211
1.094
0.928
Cl
Me
N
HN
CO2Et
Me Me
3ab, isomer 2
(CDCl3, 400 MHz)
1.91
1.95
1.00
2.04
2.01
2.06
2.99
1.10
1.06
3.07
2.94
2.92
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

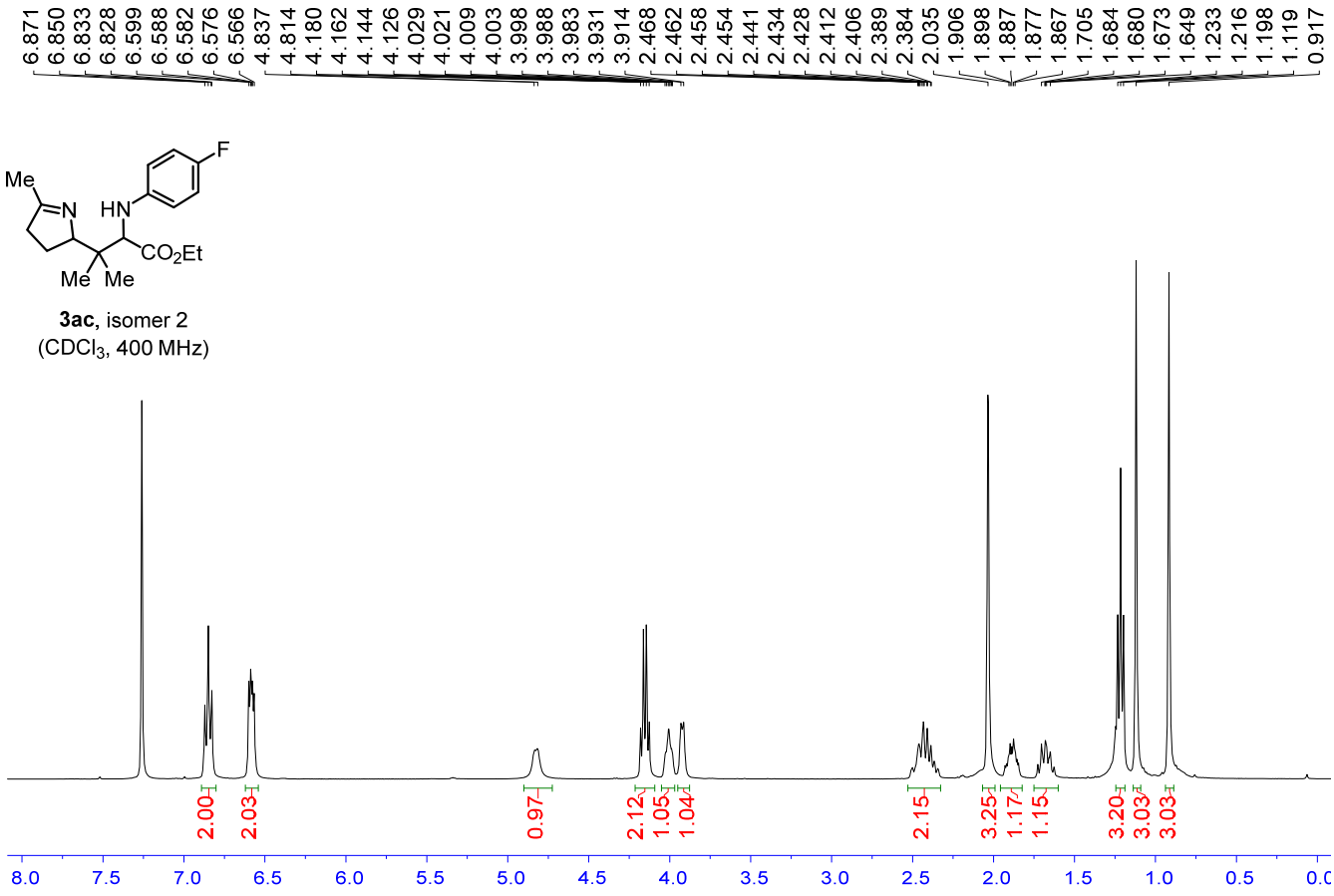

174.87
172.93
146.34
129.00
122.68
114.82
79.29
64.37
60.78
40.00
38.84
24.64
21.22
19.84
19.35
14.27
Cl
Me
N
HN
CO2Et
Me Me
3ab, isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

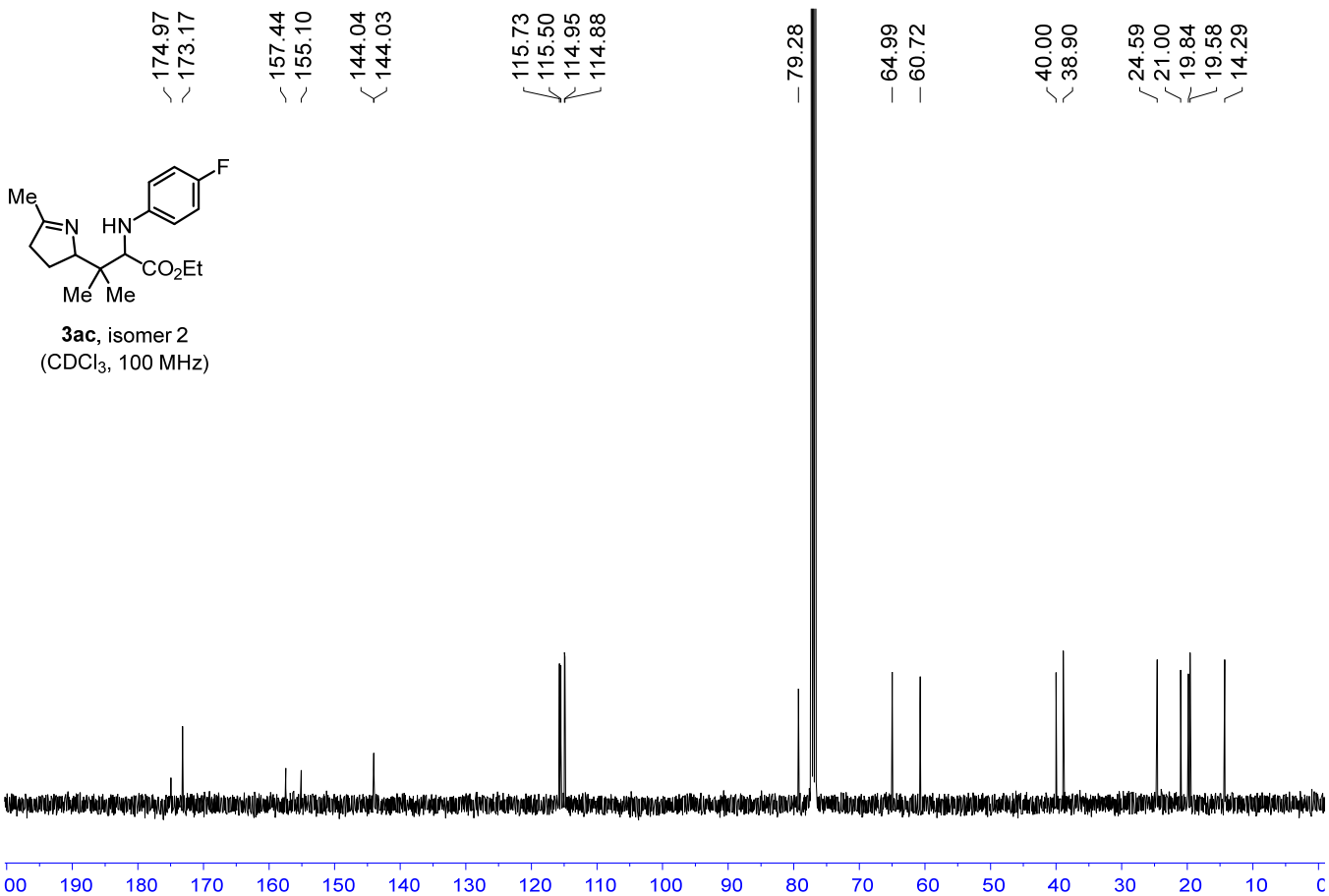

6.860
6.838
6.822
6.816
6.615
6.604
6.598
6.593
6.582
5.926
5.902
4.185
4.167
4.150
4.132
4.084
4.065
2.448
2.440
2.434
2.415
2.409
2.392
2.386
2.367
2.347
2.049
1.919
1.906
1.896
1.886
1.876
1.866
1.853
1.845
1.608
1.600
1.584
1.576
1.560
1.552
1.237
1.220
1.202
1.009
Me
N
HN
F
CO2Et
Me Me
3ac, isomer 1
(CDCl3, 400 MHz)
2.00
2.03
1.00
2.98
1.08
2.13
3.00
1.13
1.25
3.34
3.04
3.15
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

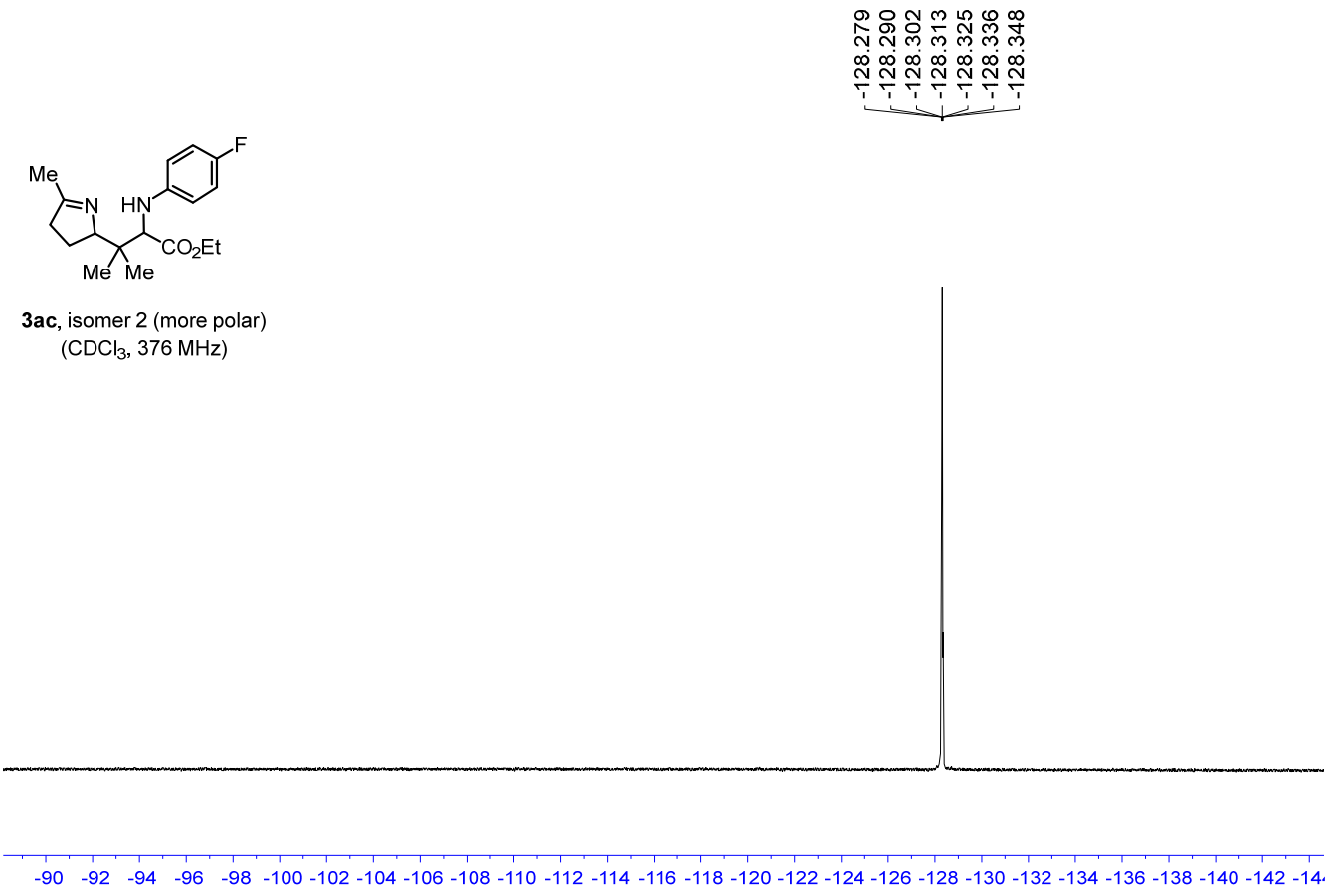

174.00
173.80
156.96
154.63
144.56
144.54
115.61
115.39
114.23
114.16
77.01
66.40
60.51
39.64
38.49
24.67
22.26
19.95
19.72
14.34
CH2Cl2
Me
N
HN
F
CO2Et
Me Me
3ac, isomer 1
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10



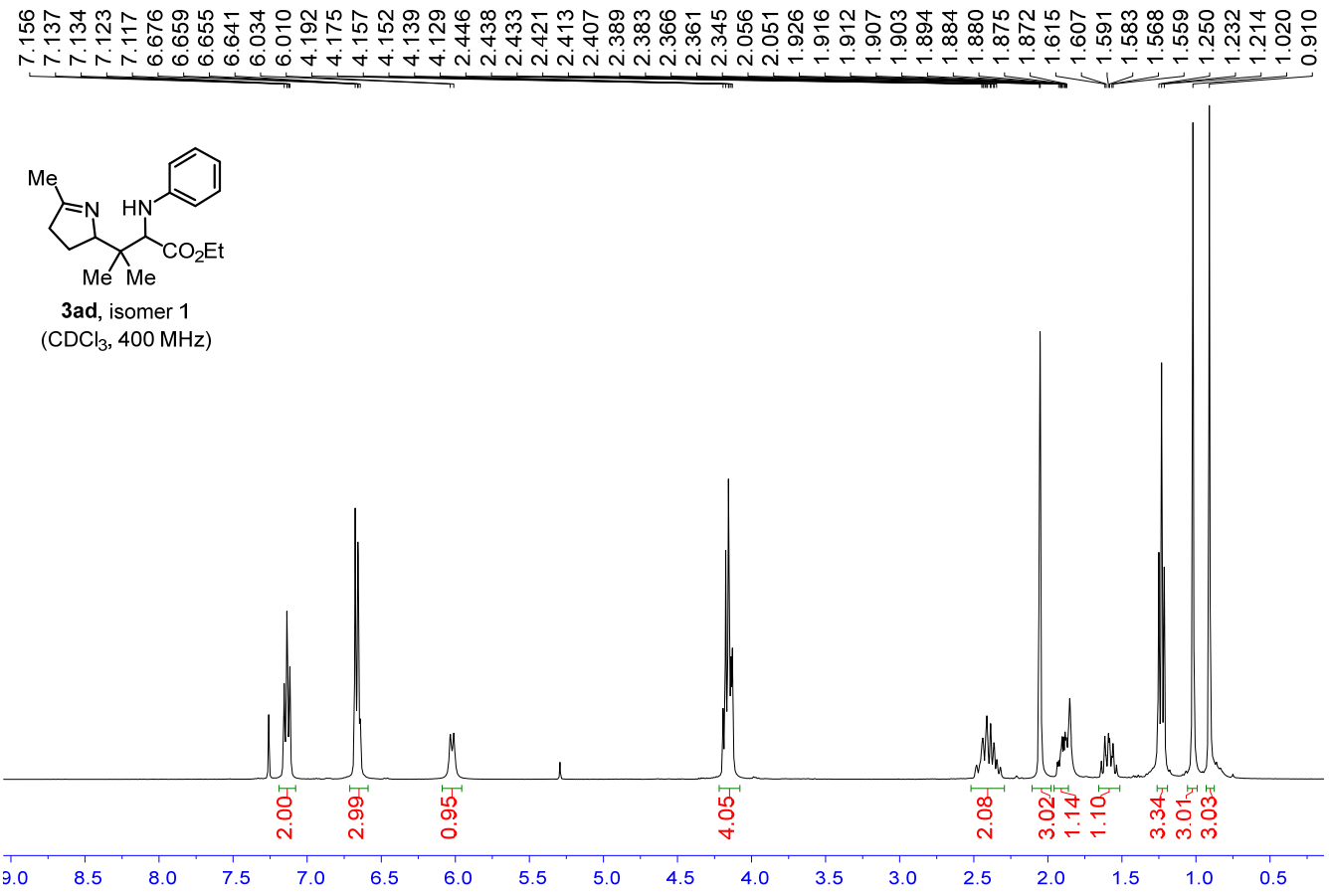
3ac, isomer **1**
($CDCl_3$, 376 MHz)

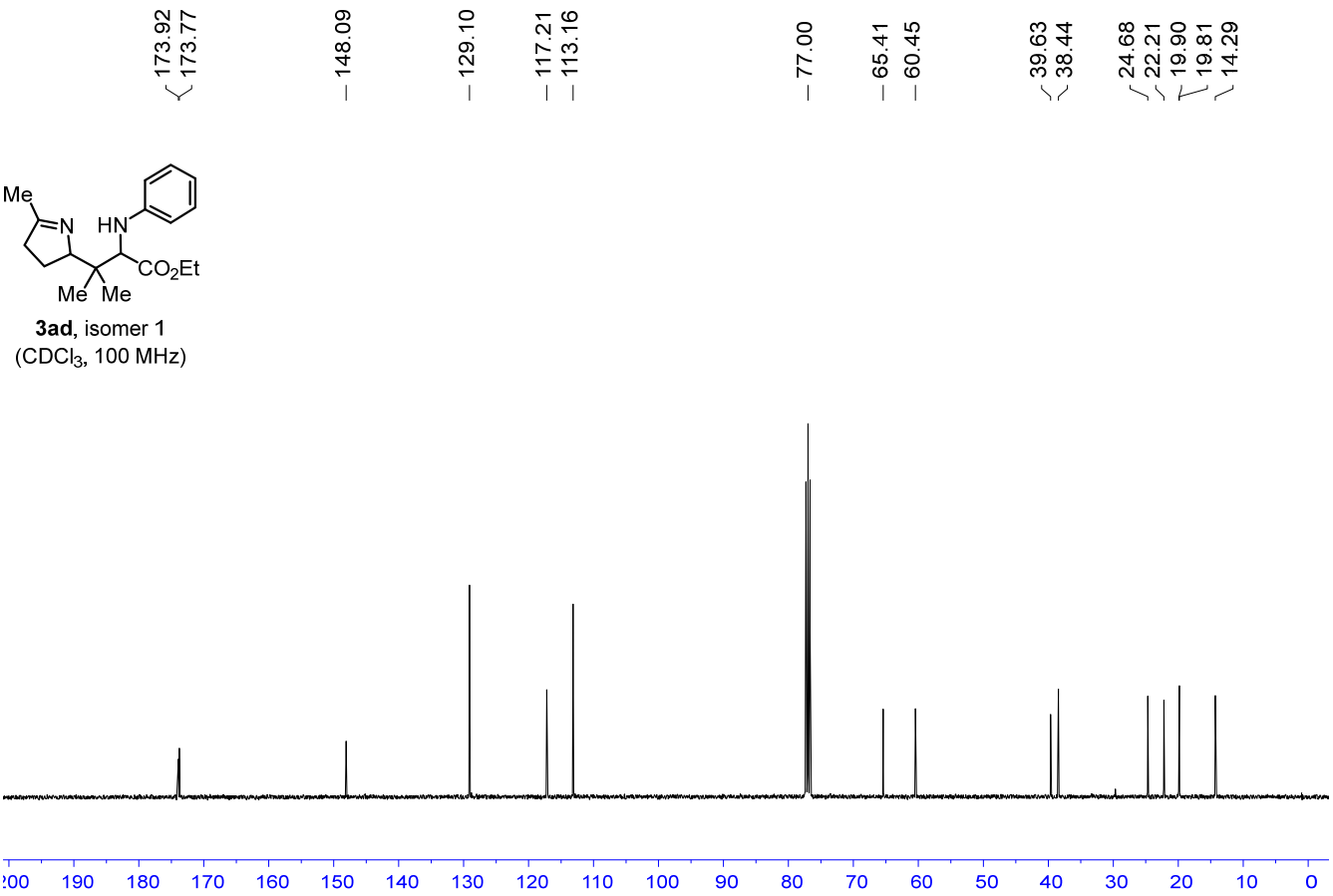

6.871
6.850
6.833
6.828
6.599
6.588
6.582
6.576
6.566
4.837
4.814
4.180
4.162
4.144
4.126
4.029
4.021
4.009
4.003
3.998
3.988
3.983
3.931
3.914
2.468
2.462
2.458
2.454
2.441
2.434
2.428
2.412
2.406
2.389
2.384
2.035
1.906
1.898
1.887
1.877
1.867
1.705
1.684
1.680
1.673
1.649
1.233
1.216
1.198
1.119
0.917
Me
N
HN
F
CO2Et
Me Me
3ac, isomer 2
(CDCl3, 400 MHz)
2.00
2.03
0.97
2.12
1.05
1.04
2.15
3.25
1.17
1.15
3.20
3.03
3.03
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

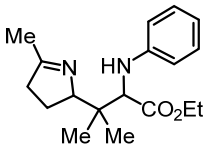

174.97
173.17
157.44
155.10
144.04
144.03
115.73
115.50
114.95
114.88
79.28
64.99
60.72
40.00
38.90
24.59
21.00
19.84
19.58
14.29
Me
N
HN
F
CO2Et
Me Me
3ac, isomer 2
(CDCl3, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10



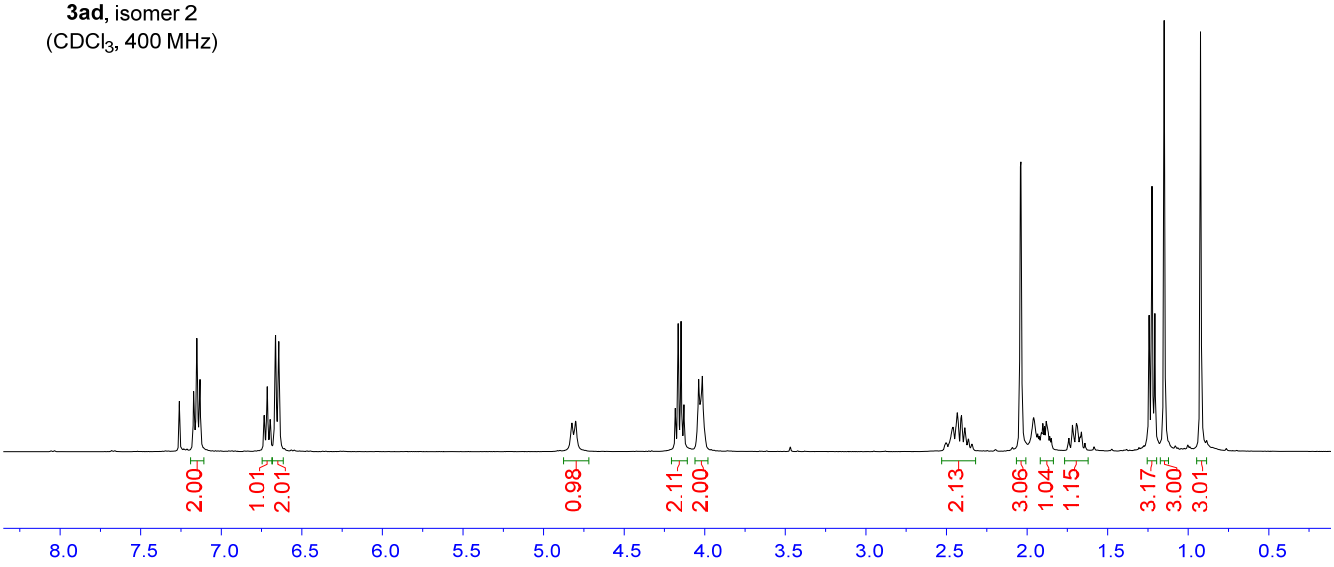
3ac, isomer 2 (more polar)
($CDCl_3$, 376 MHz)

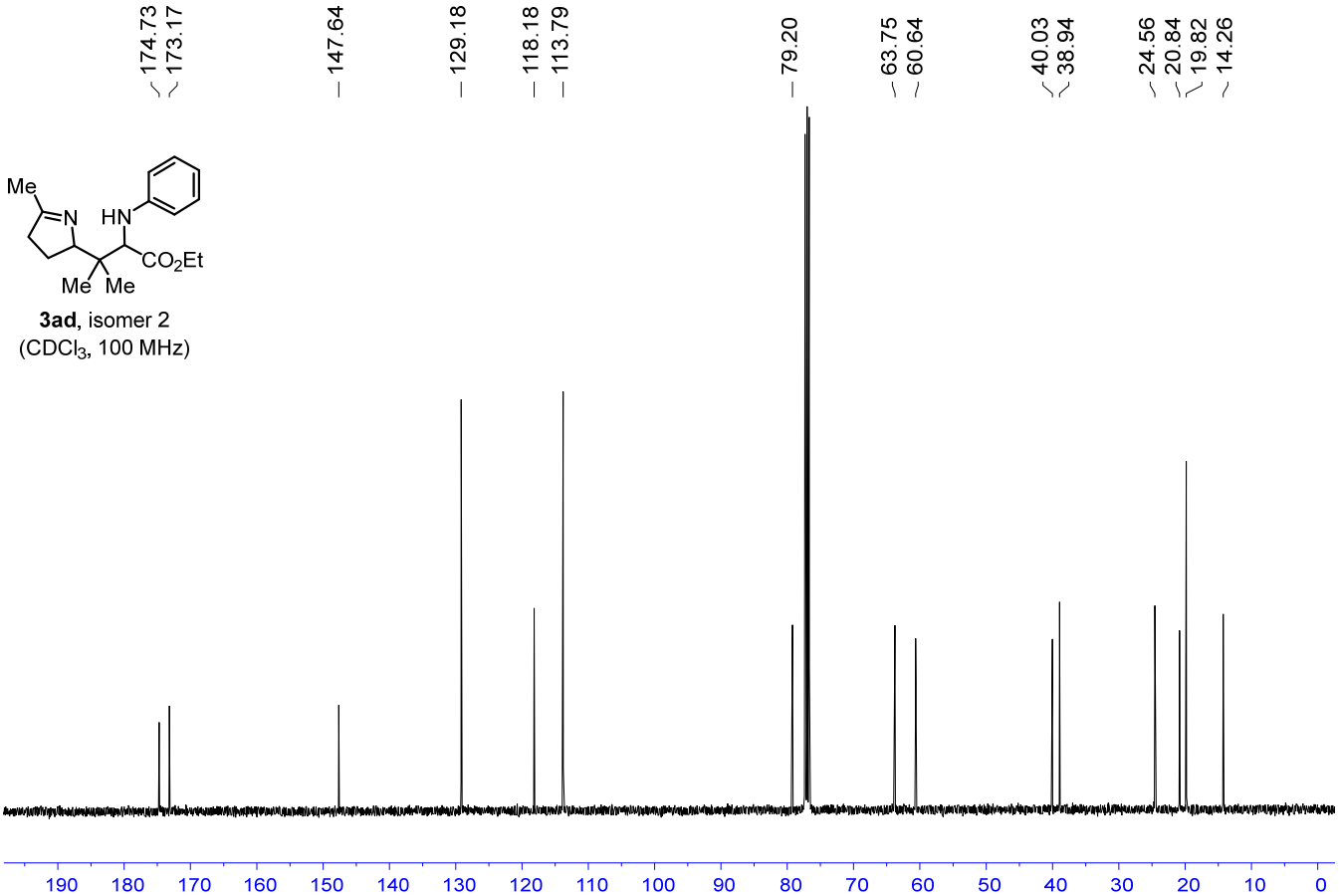

7.156
7.137
7.134
7.123
7.117
6.676
6.659
6.655
6.641
6.034
6.010
4.192
4.175
4.157
4.152
4.139
4.129
2.446
2.438
2.433
2.421
2.413
2.407
2.389
2.383
2.366
2.361
2.345
2.056
2.051
1.926
1.916
1.912
1.907
1.903
1.894
1.884
1.880
1.875
1.872
1.615
1.607
1.591
1.583
1.568
1.559
1.250
1.232
1.214
1.020
0.910
Me
N
HN
CO2Et
Me Me
3ad, isomer 1
(CDCl3, 400 MHz)
2.00
2.99
0.95
4.05
2.08
3.02
1.14
1.10
3.34
3.01
3.03
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


173.92
173.77
148.09
129.10
117.21
113.16
77.00
65.41
60.45
39.63
38.44
24.68
22.21
19.90
19.81
14.29
Me
N
HN
CO2Et
Me Me
3ad, isomer 1
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

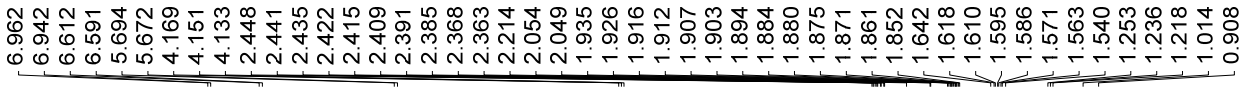


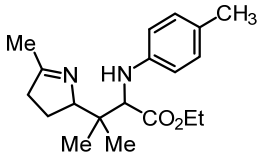
3ad, isomer 2
($CDCl_3$, 400 MHz)



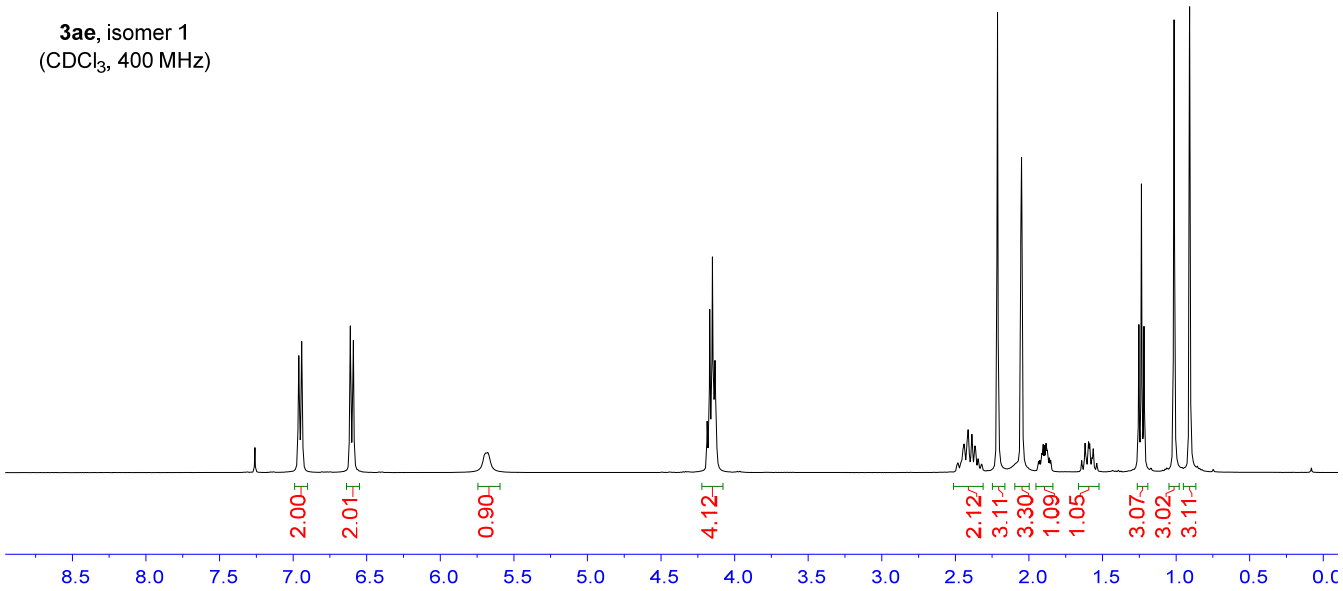


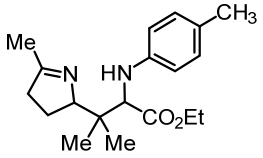
3ad, isomer 2
($CDCl_3$, 100 MHz)



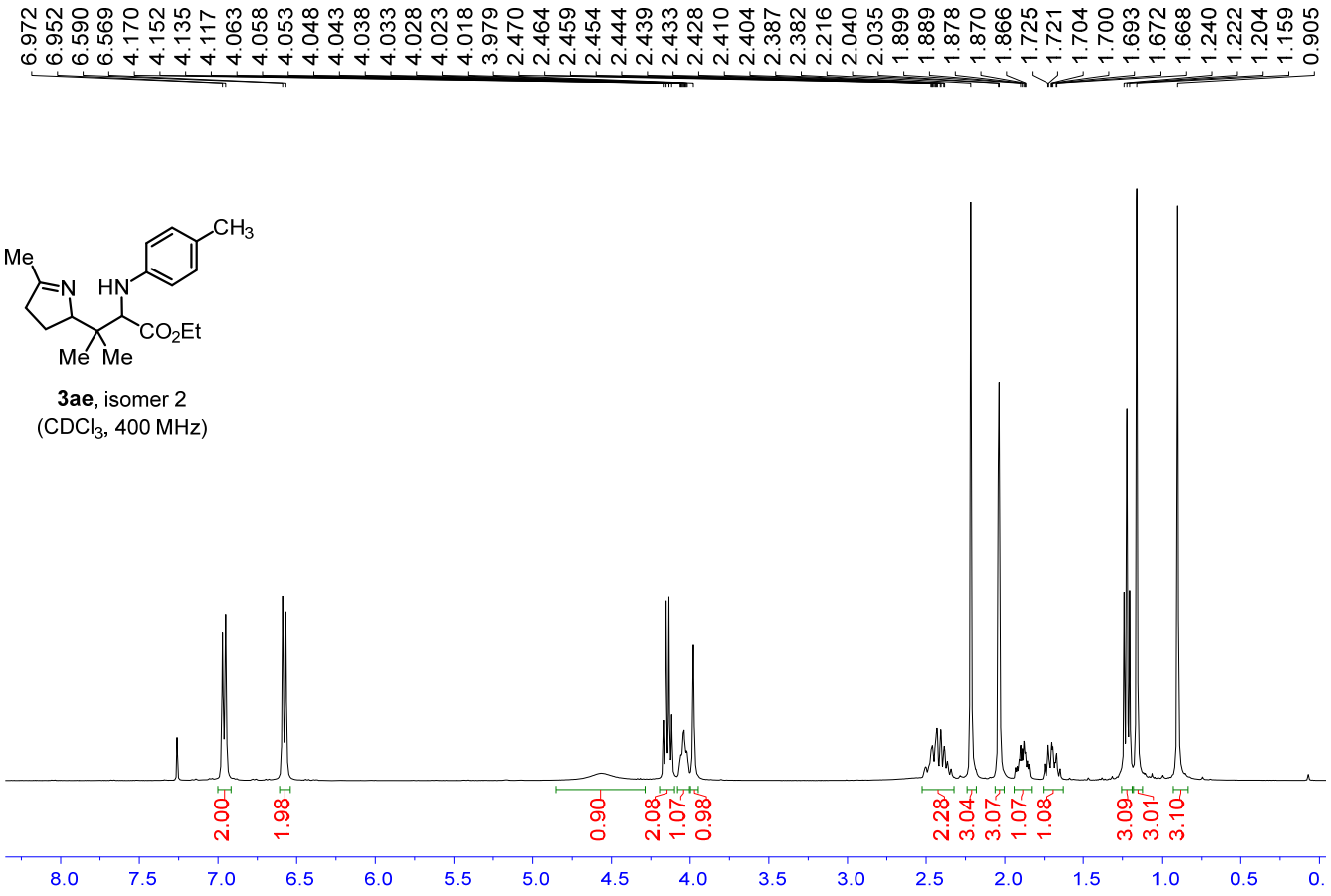


3ae, isomer 1
($CDCl_3$, 400 MHz)

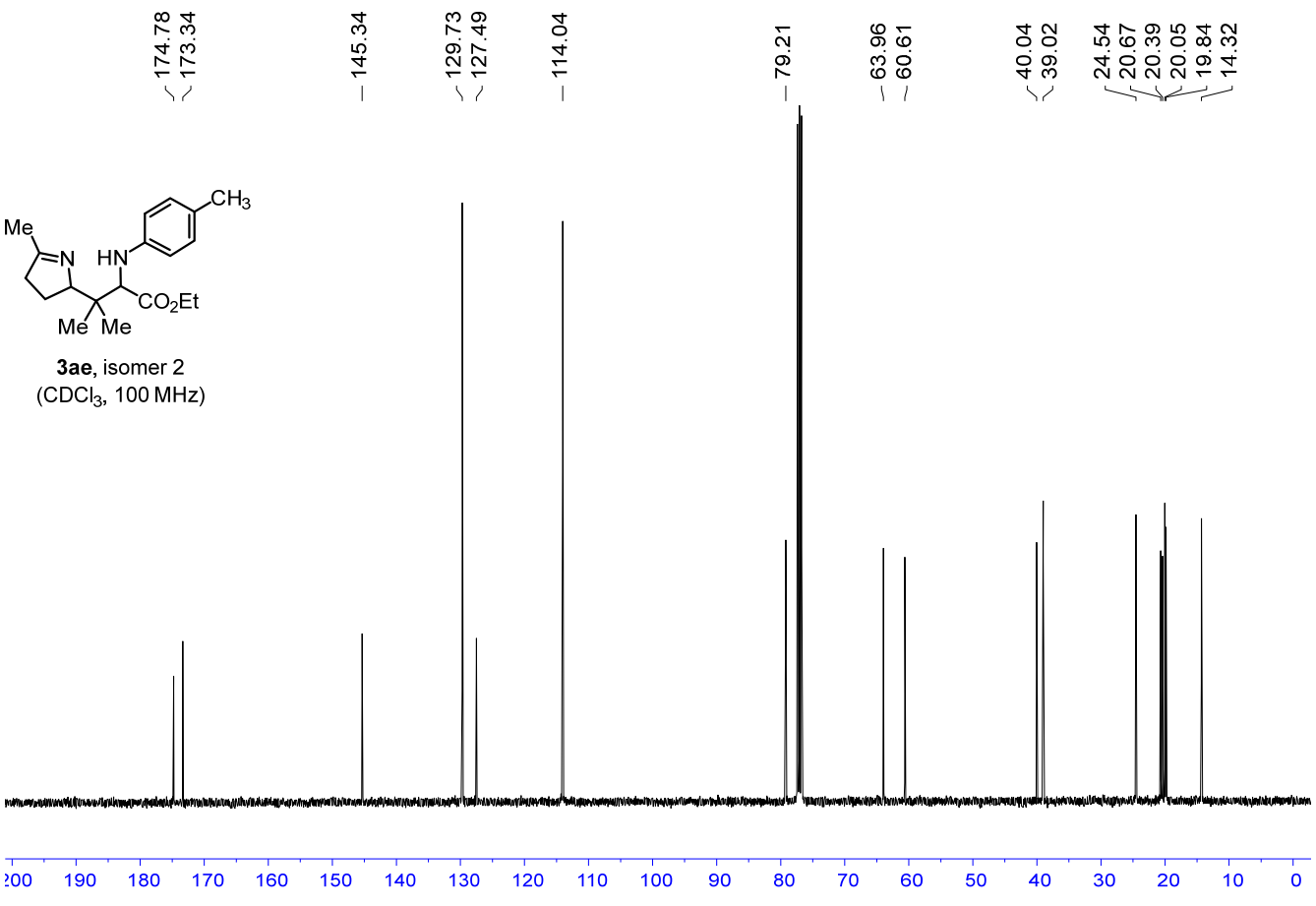




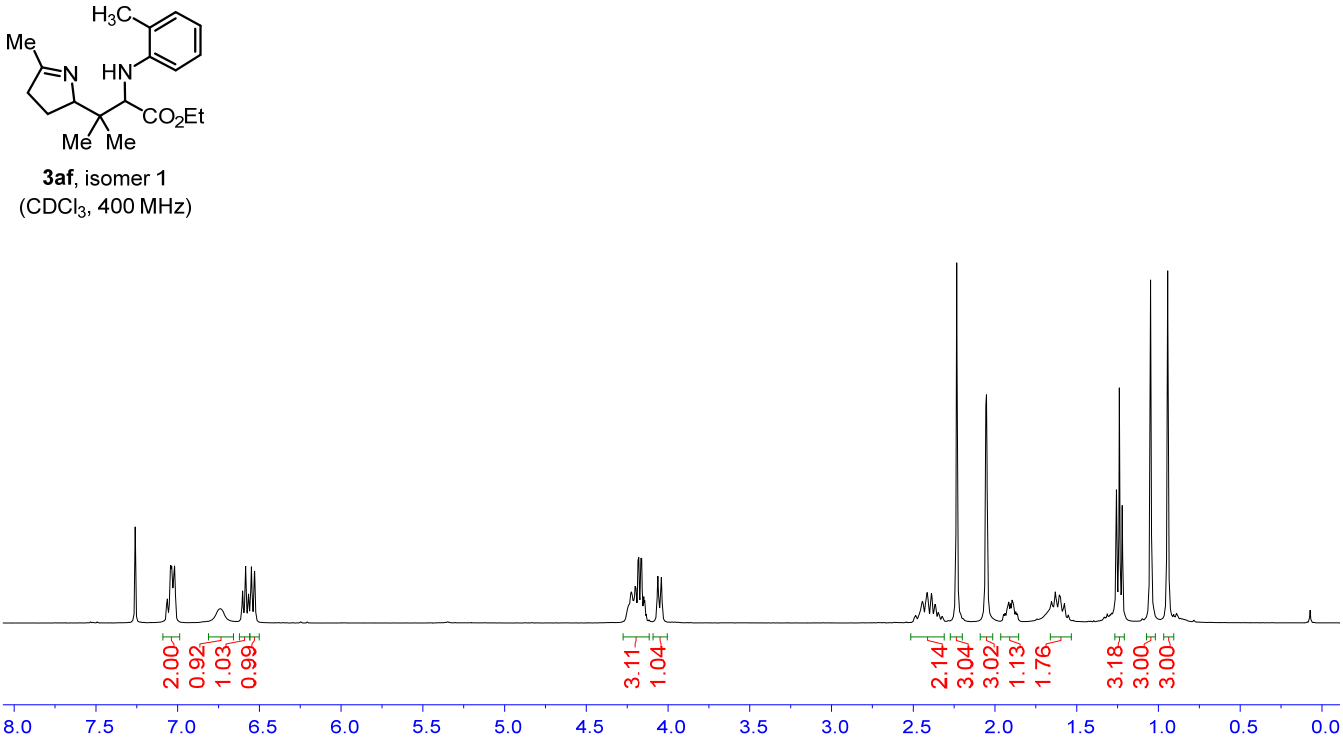
3ae, isomer 1
($CDCl_3$, 100 MHz)



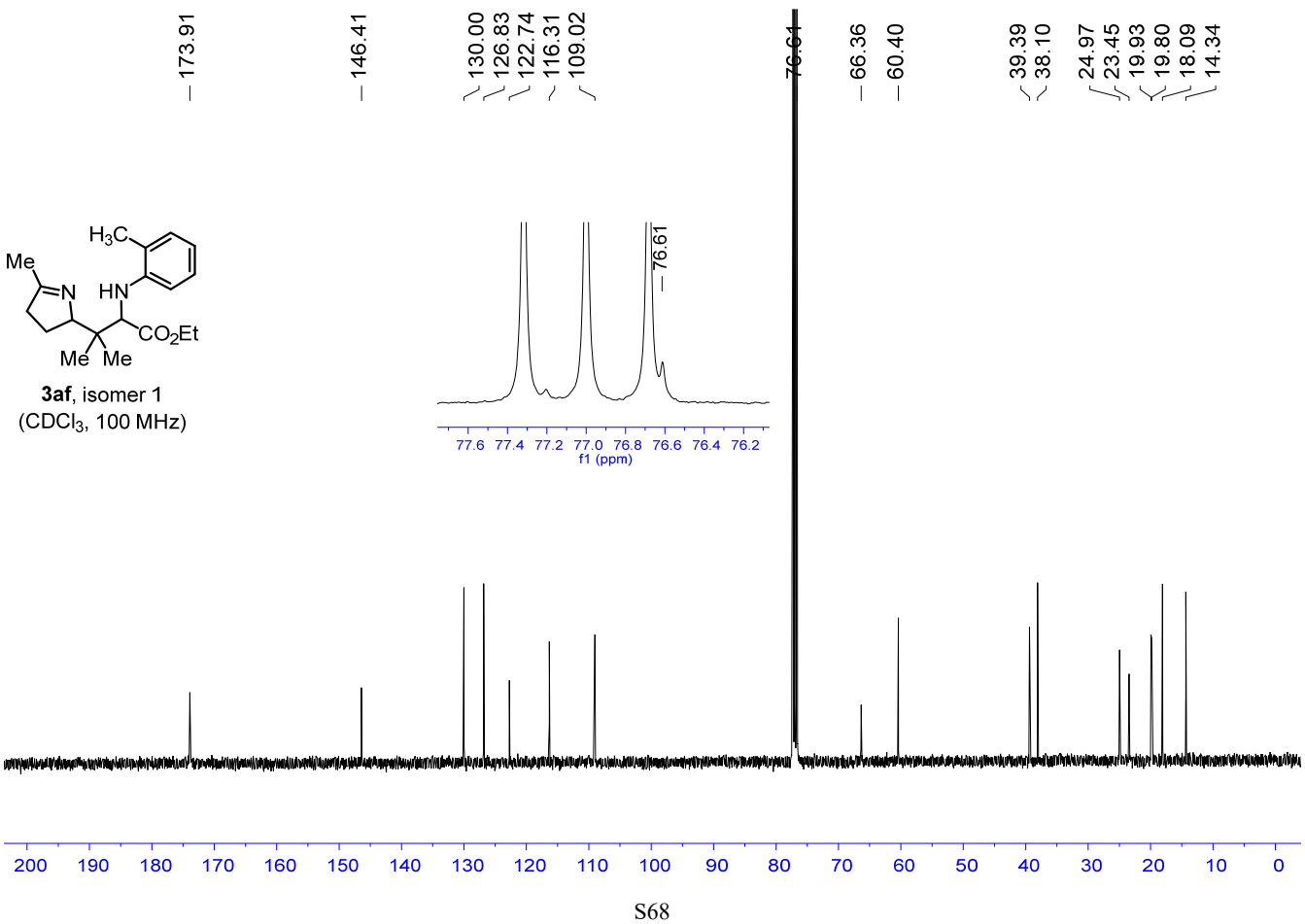
3ae, isomer 2
($CDCl_3$, 400 MHz)



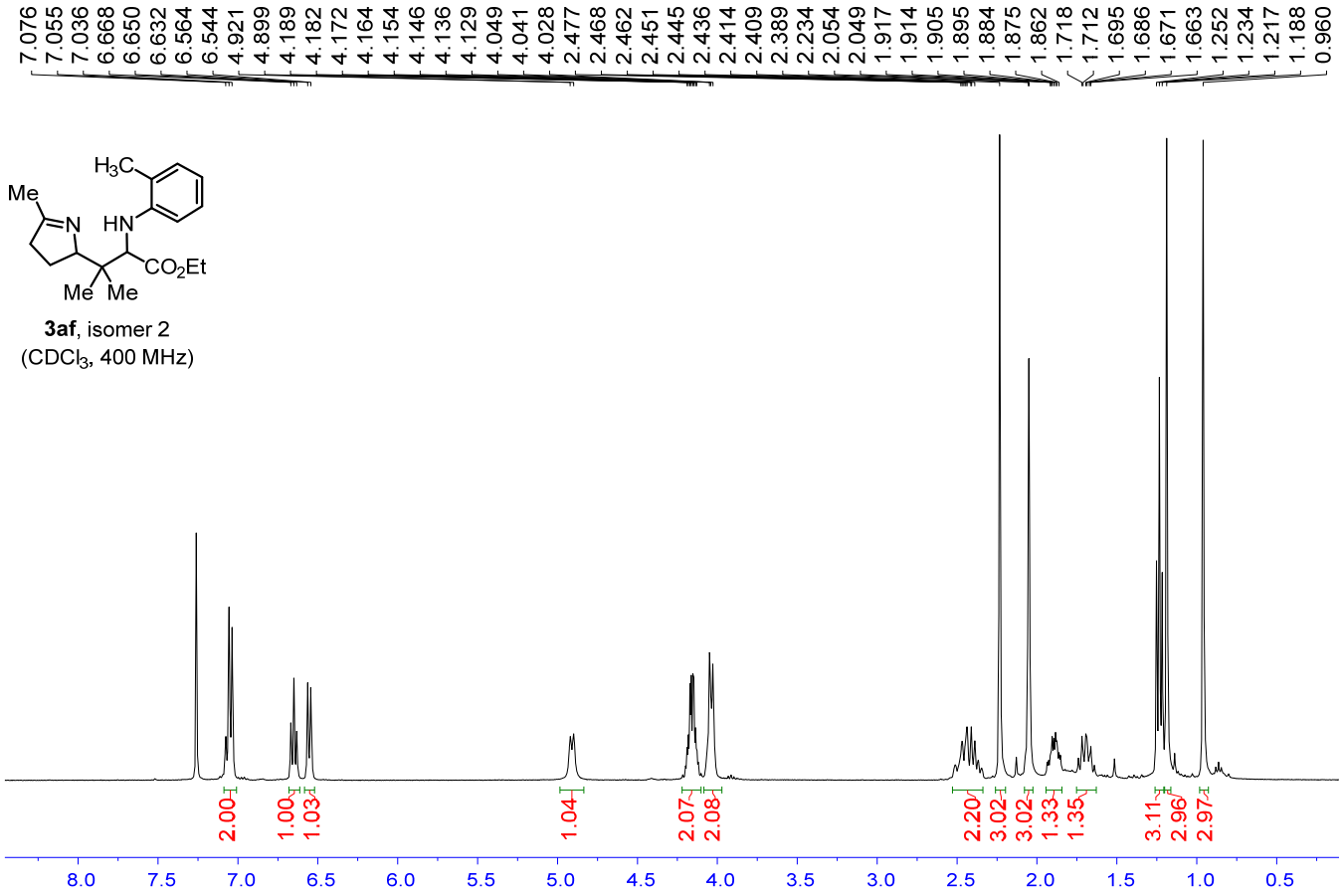
3ae, isomer 2
($CDCl_3$, 100 MHz)

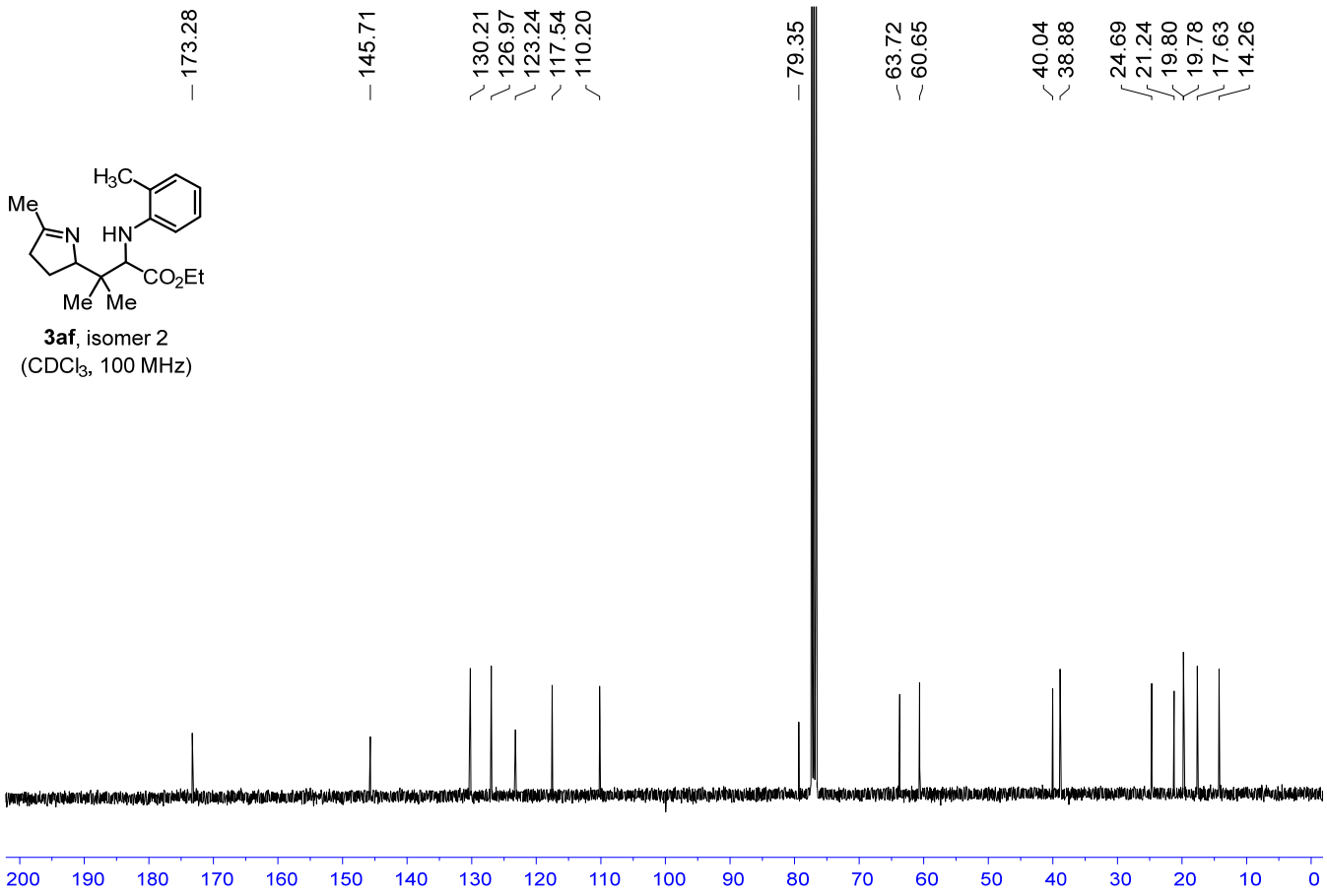


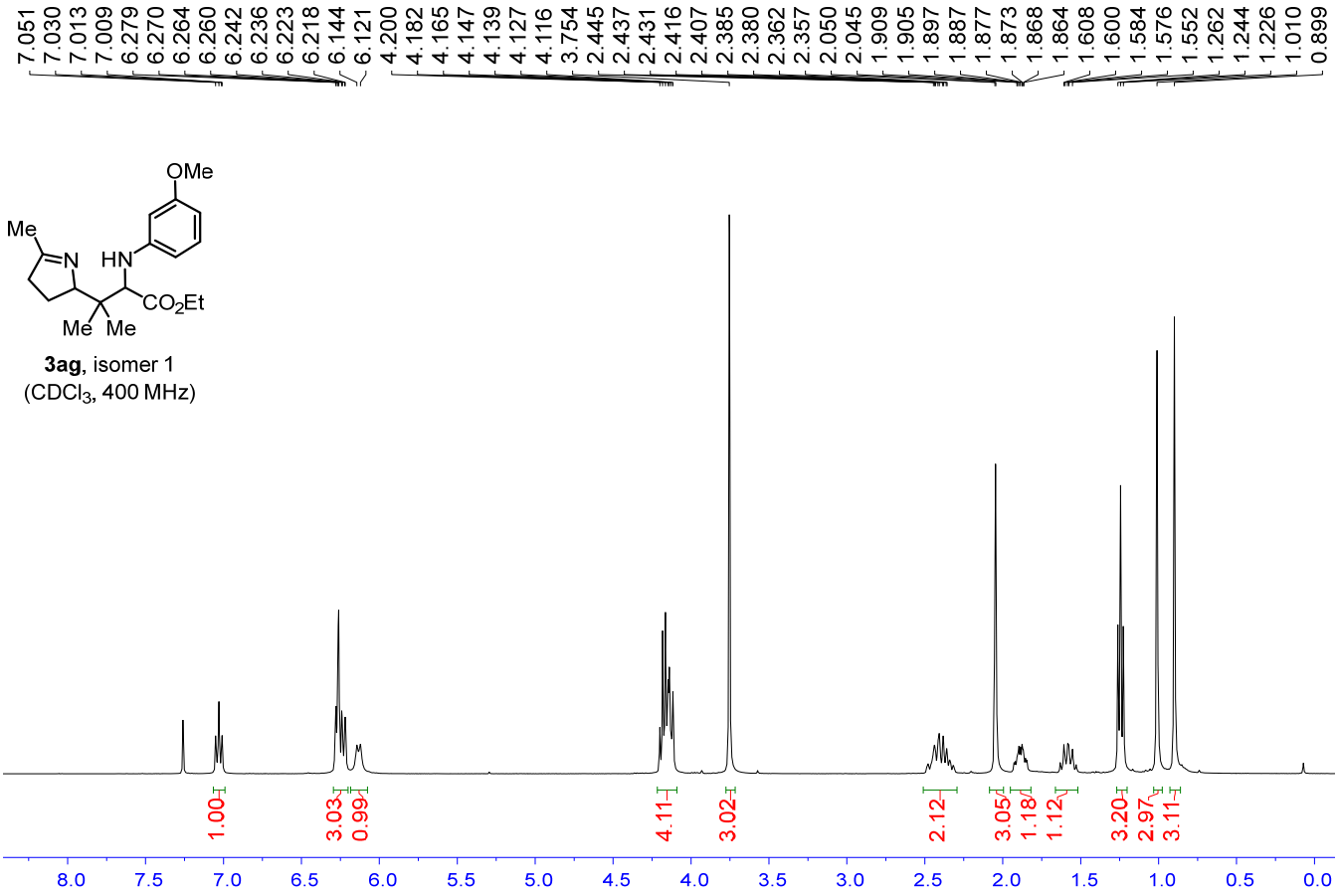
3af, isomer 1
($CDCl_3$, 400 MHz)

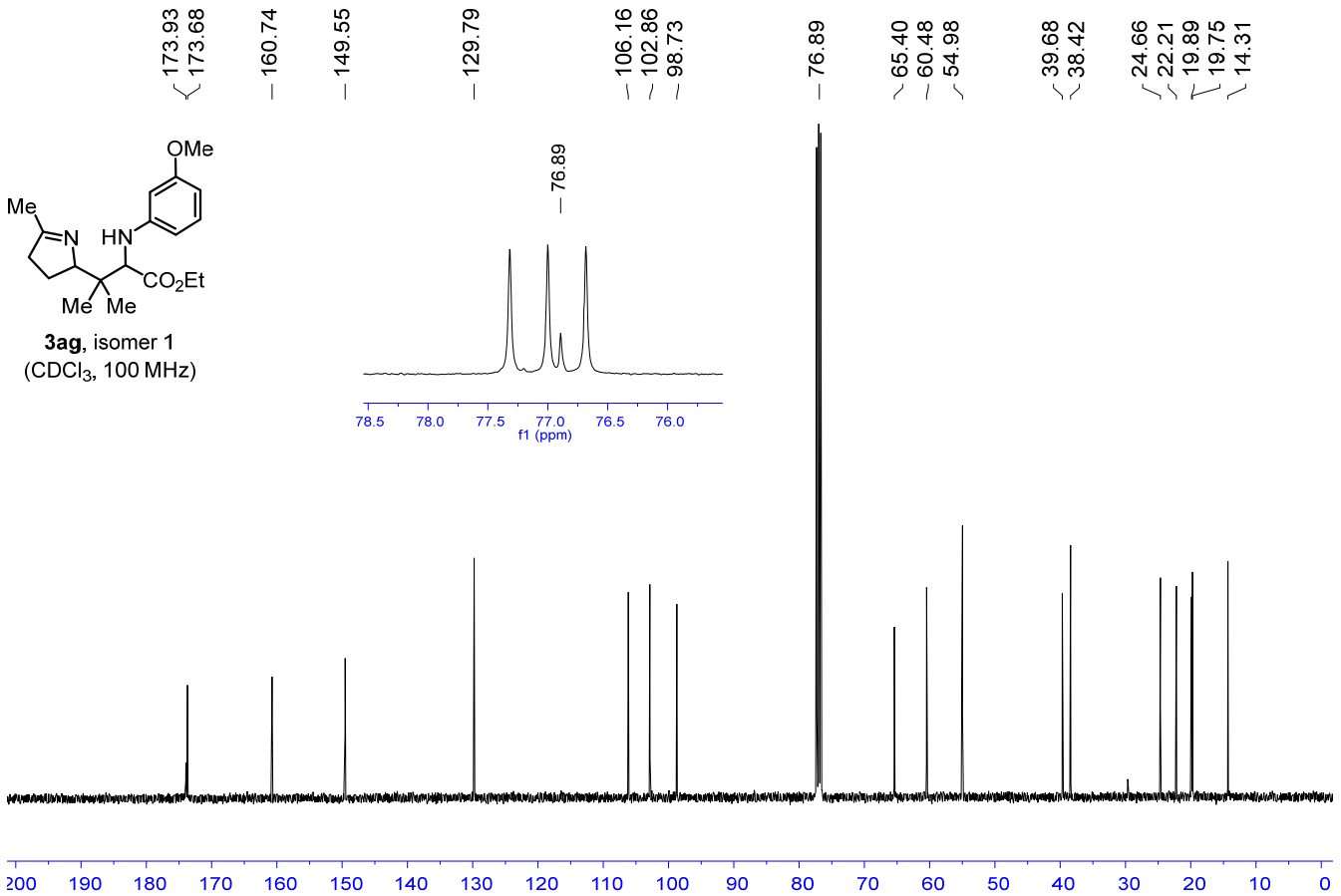


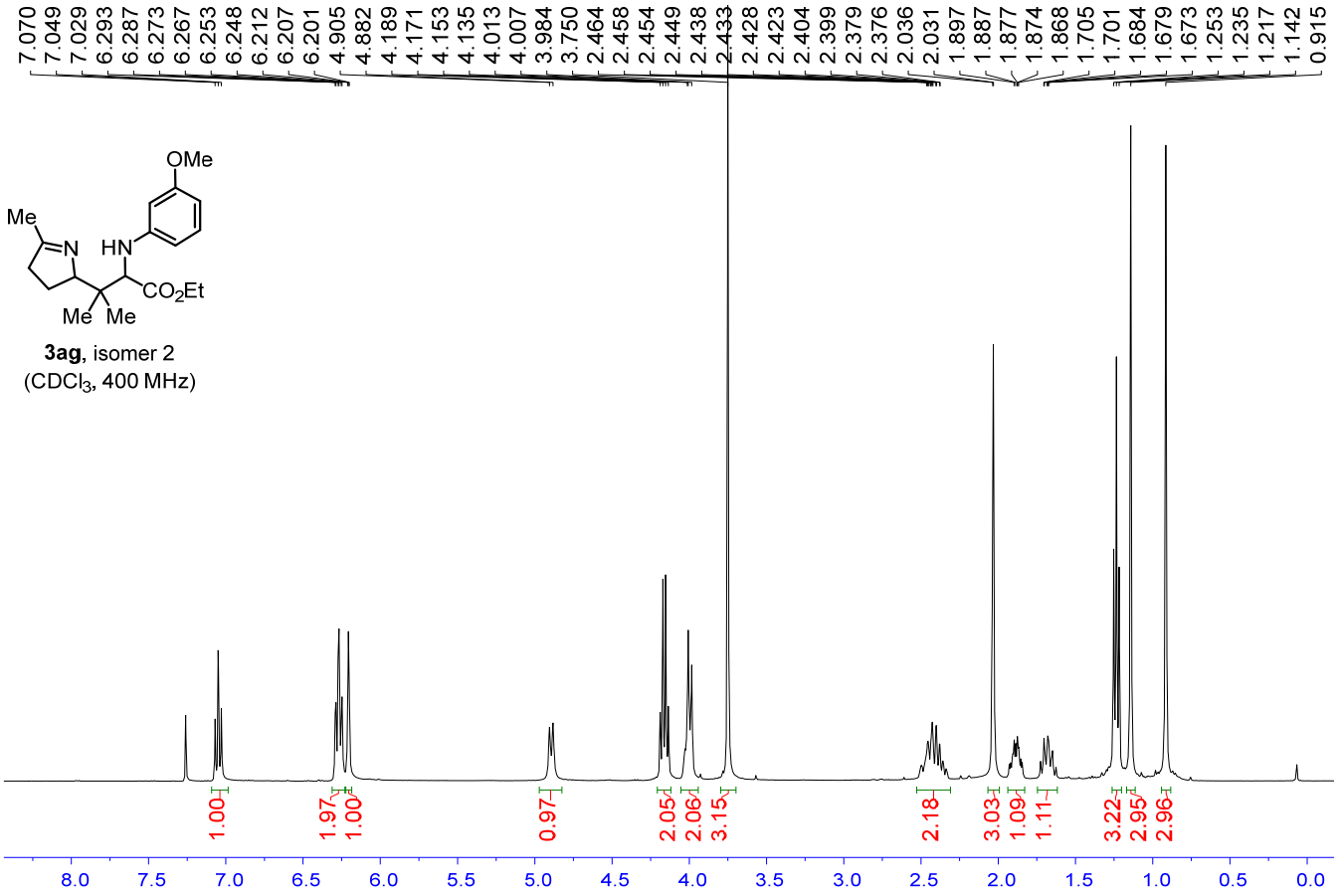
3af, isomer 1
($CDCl_3$, 100 MHz)

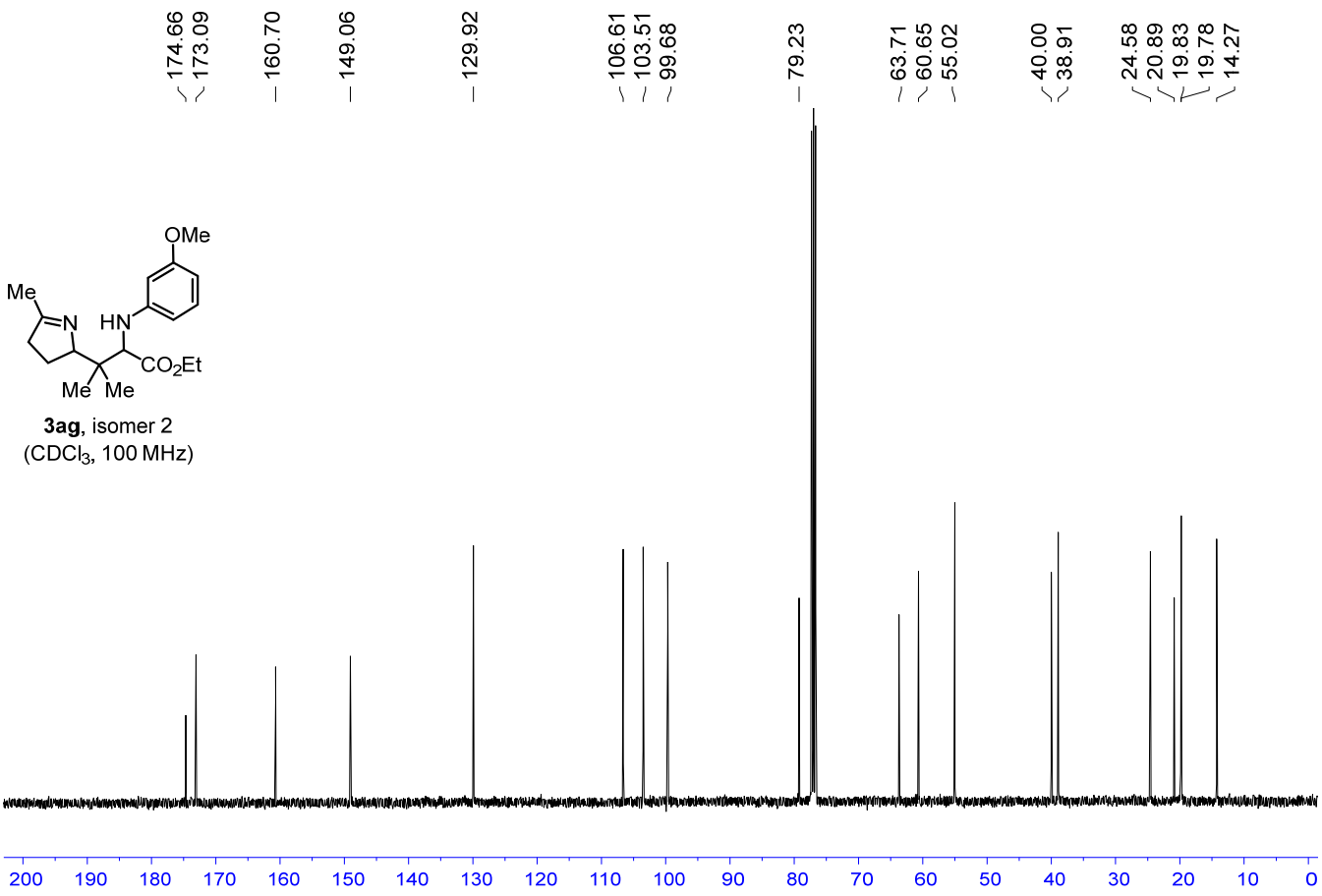

7.076
7.055
7.036
6.668
6.650
6.632
6.564
6.544
4.921
4.899
4.189
4.182
4.172
4.164
4.154
4.146
4.136
4.129
4.049
4.041
4.028
2.477
2.468
2.462
2.451
2.445
2.436
2.414
2.409
2.389
2.234
2.054
2.049
1.917
1.914
1.905
1.895
1.884
1.875
1.862
1.718
1.712
1.695
1.686
1.671
1.663
1.252
1.234
1.217
1.188
0.960
Me
H3C
N
HN
CO2Et
Me Me
3af, isomer 2
(CDCl3, 400 MHz)
2.00
1.00
1.03
1.04
2.07
2.08
2.20
3.02
3.02
1.33
1.35
3.11
2.96
2.97
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

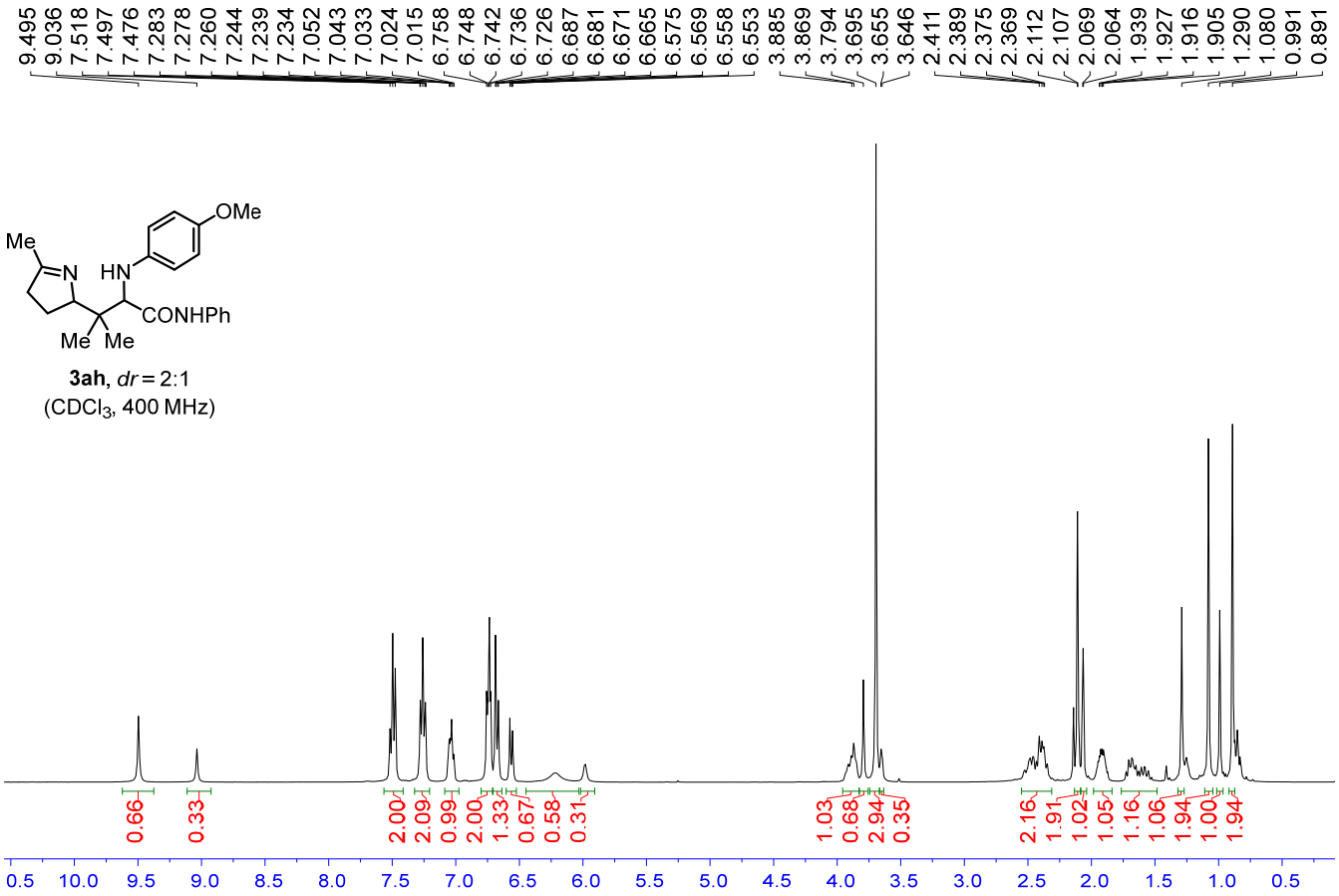

173.28
145.71
130.21
126.97
123.24
117.54
110.20
79.35
63.72
60.65
40.04
38.88
24.69
21.24
19.80
19.78
17.63
14.26
Me
H3C
N
HN
CO2Et
Me Me
3af, isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

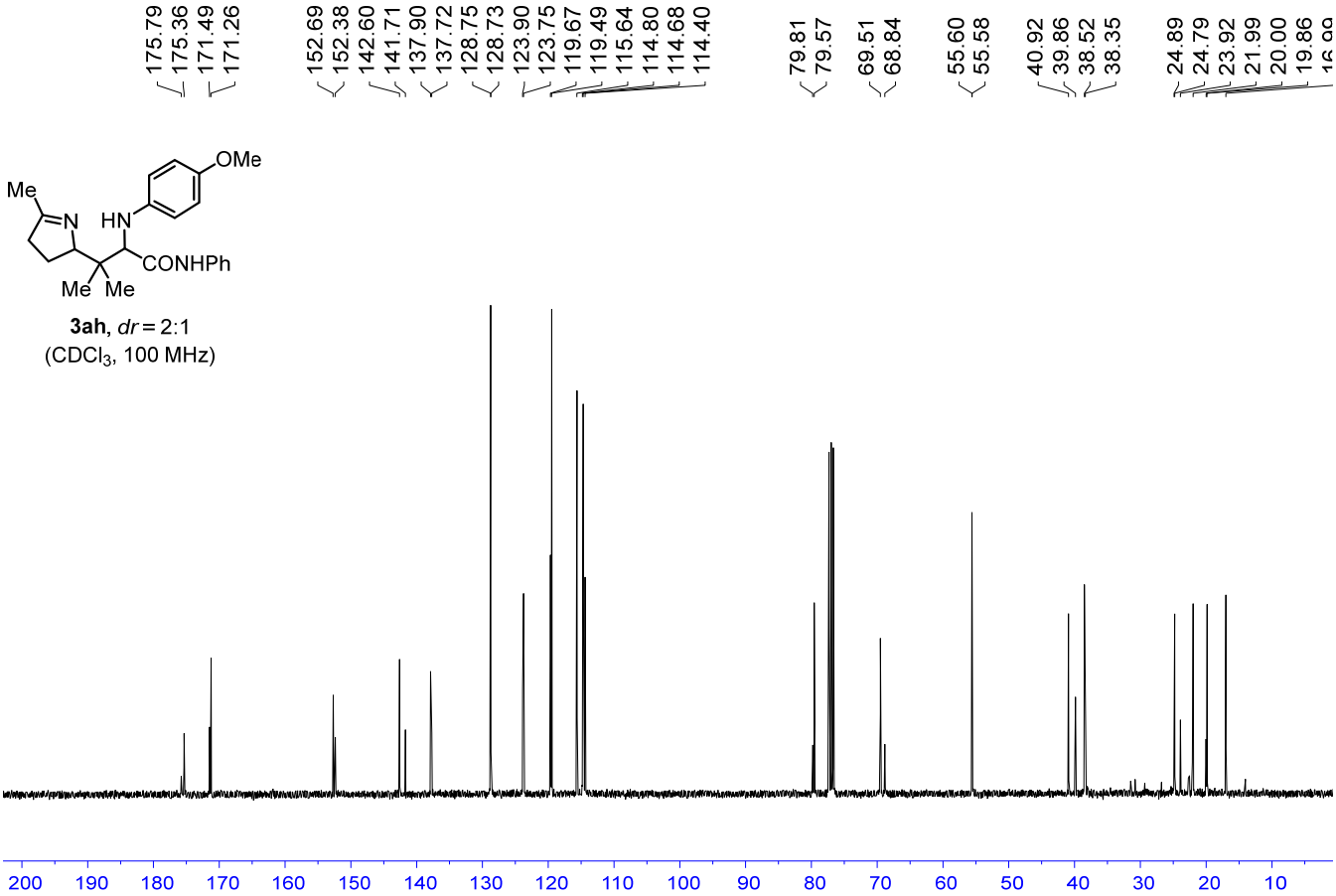

7.051
7.030
7.013
7.009
6.279
6.270
6.264
6.260
6.242
6.236
6.223
6.218
6.144
6.121
4.200
4.182
4.165
4.147
4.139
4.127
4.116
3.754
2.445
2.437
2.431
2.416
2.407
2.385
2.380
2.362
2.357
2.050
2.045
1.909
1.905
1.897
1.887
1.877
1.873
1.868
1.864
1.608
1.600
1.584
1.576
1.552
1.262
1.244
1.226
1.010
0.899
OMe
Me
N
HN
CO2Et
Me Me
3ag, isomer 1
(CDCl3, 400 MHz)
1.00
3.03
0.99
4.11
3.02
2.12
3.05
1.18
1.12
3.20
2.97
3.11
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

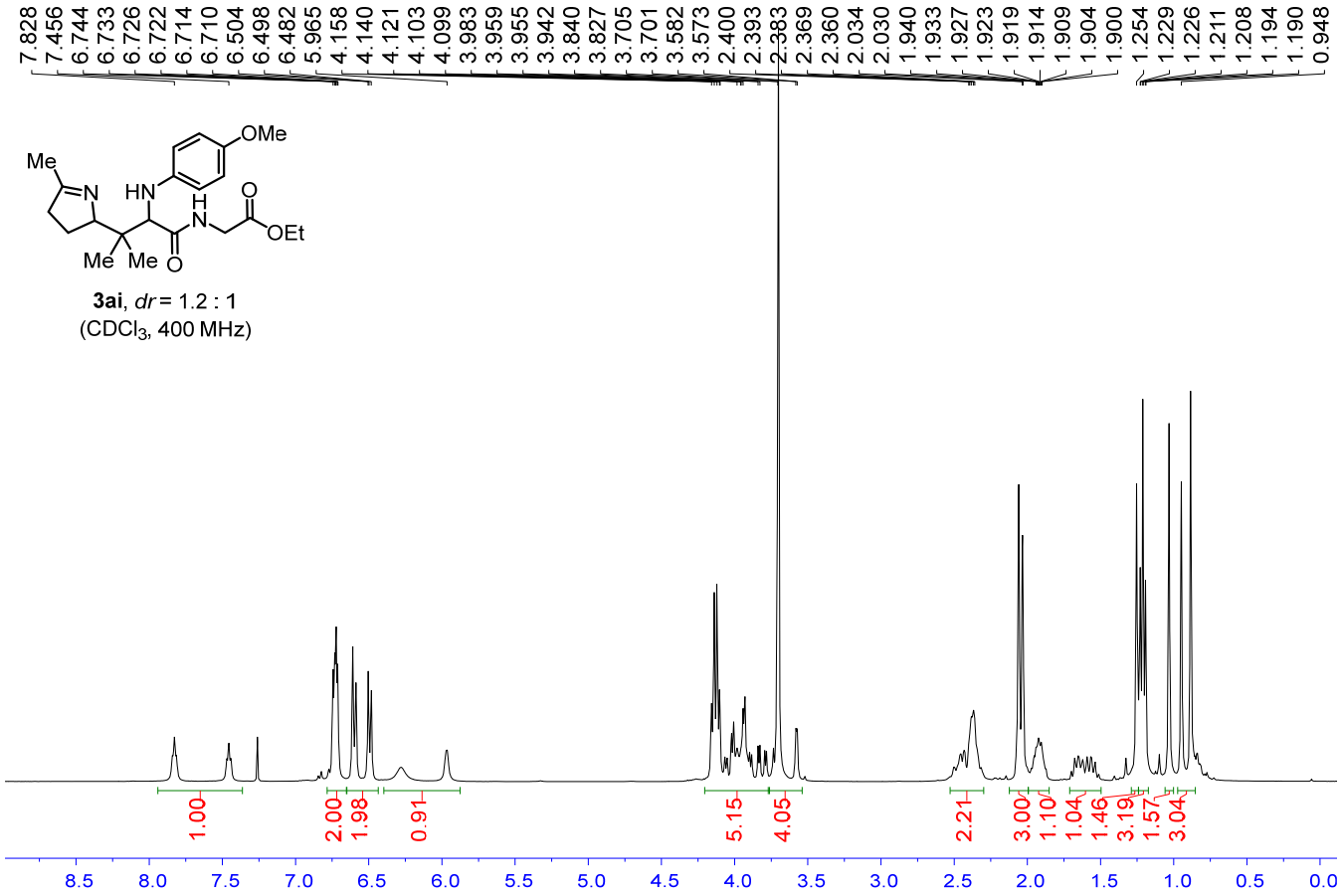

173.93
173.68
160.74
149.55
129.79
106.16
102.86
98.73
76.89
65.40
60.48
54.98
39.68
38.42
24.66
22.21
19.89
19.75
14.31
OMe
Me
N
HN
CO2Et
Me Me
3ag, isomer 1
(CDCl3, 100 MHz)
76.89
78.5
78.0
77.5
77.0
76.5
76.0
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.070
7.049
7.029
6.293
6.287
6.273
6.267
6.253
6.248
6.212
6.207
6.201
4.905
4.882
4.189
4.171
4.153
4.135
4.013
4.007
3.984
3.750
2.464
2.458
2.454
2.449
2.438
2.433
2.428
2.423
2.404
2.399
2.379
2.376
2.036
2.031
1.897
1.887
1.877
1.874
1.868
1.705
1.701
1.684
1.679
1.673
1.253
1.235
1.217
1.142
0.915
OMe
Me
N
HN
CO2Et
Me Me
3ag, isomer 2
(CDCl3, 400 MHz)
1.00
1.97
1.00
0.97
2.05
2.06
3.15
2.18
3.03
1.09
1.11
3.22
2.95
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

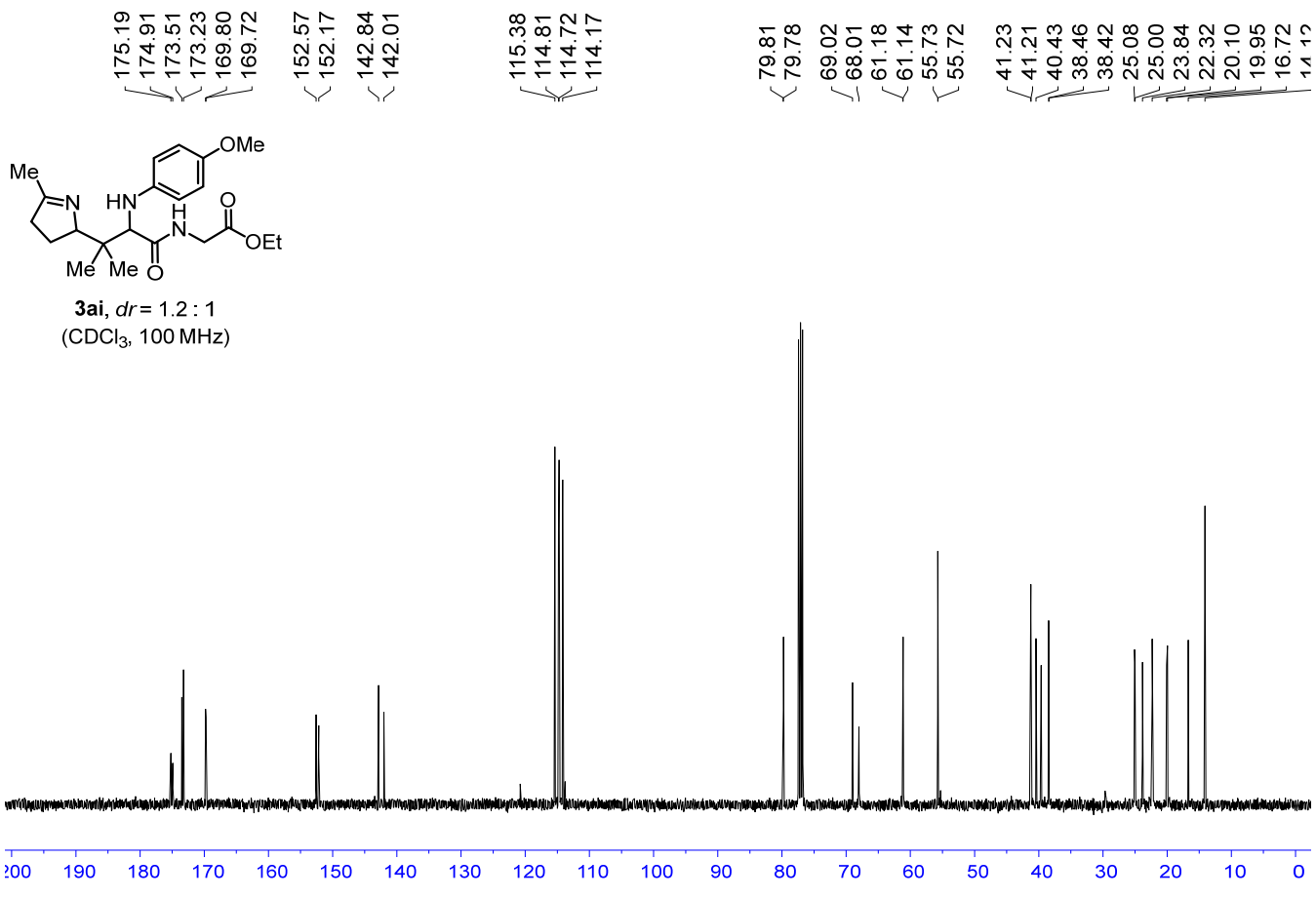

174.66
173.09
160.70
149.06
129.92
106.61
103.51
99.68
79.23
63.71
60.65
55.02
40.00
38.91
24.58
20.89
19.83
19.78
14.27
OMe
Me
N
HN
CO2Et
Me Me
3ag, isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


9.495
9.036
7.518
7.497
7.476
7.283
7.278
7.260
7.244
7.239
7.234
7.052
7.043
7.033
7.024
7.015
6.758
6.748
6.742
6.736
6.726
6.687
6.681
6.671
6.665
6.575
6.569
6.558
6.553
3.885
3.869
3.794
3.695
3.655
3.646
2.411
2.389
2.375
2.369
2.112
2.107
2.069
2.064
1.939
1.927
1.916
1.905
1.290
1.080
0.991
0.891
OMe
Me
N
HN
CONHPh
Me Me
3ah, dr = 2:1
(CDCl3, 400 MHz)
0.66
0.33
2.00
2.09
0.99
2.00
1.33
0.67
0.58
0.31
1.03
0.68
2.94
0.35
2.16
1.91
1.02
1.05
1.16
1.06
1.94
1.00
1.94
0.5
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

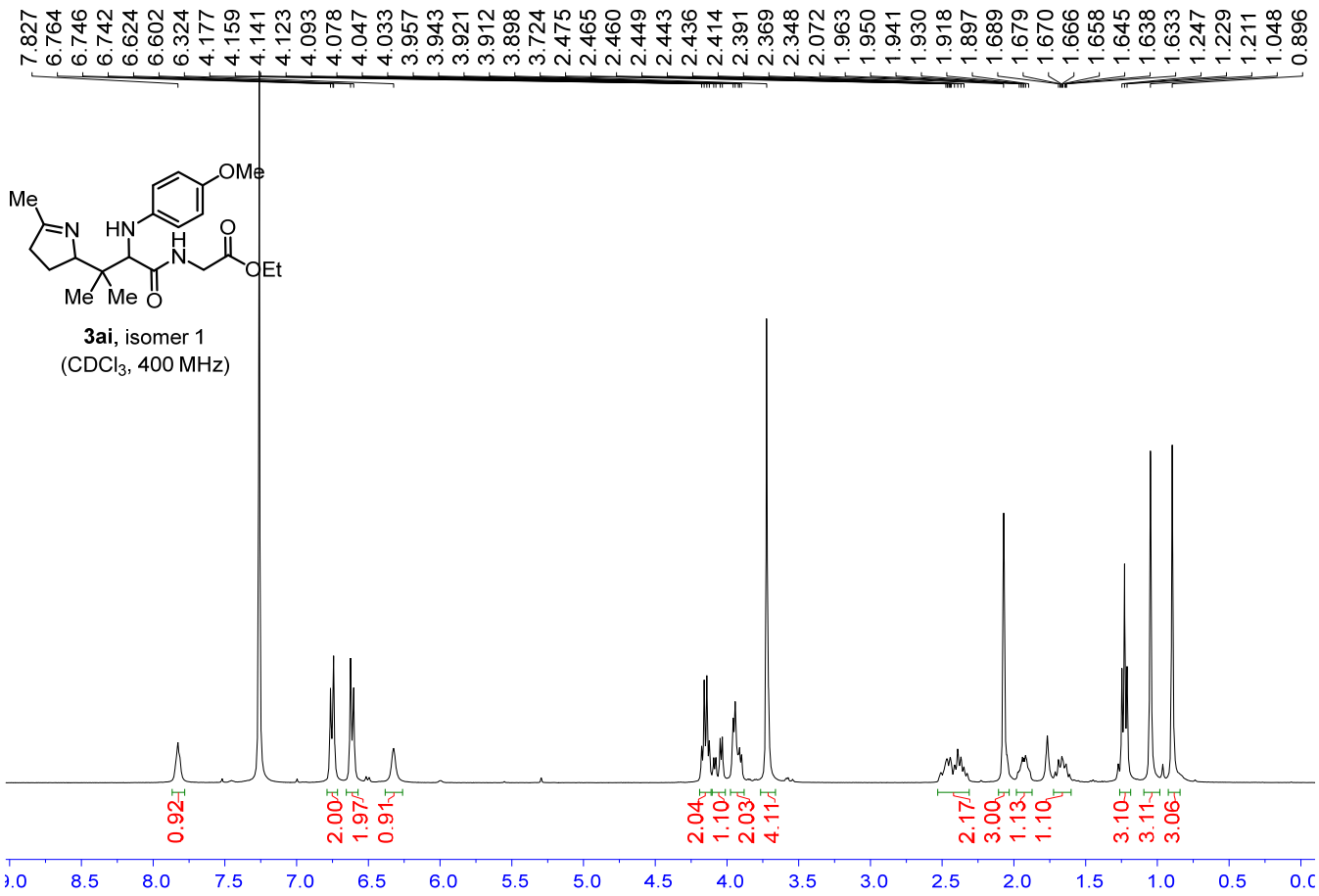

175.79
175.36
171.49
171.26
152.69
152.38
142.60
141.71
137.90
137.72
128.75
128.73
123.90
123.75
119.67
119.49
115.64
114.80
114.68
114.40
79.81
79.57
69.51
68.84
55.60
55.58
40.92
39.86
38.52
38.35
24.89
24.79
23.92
21.99
20.00
19.86
OMe
Me
N
HN
CONHPh
Me Me
3ah, dr = 2:1
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10



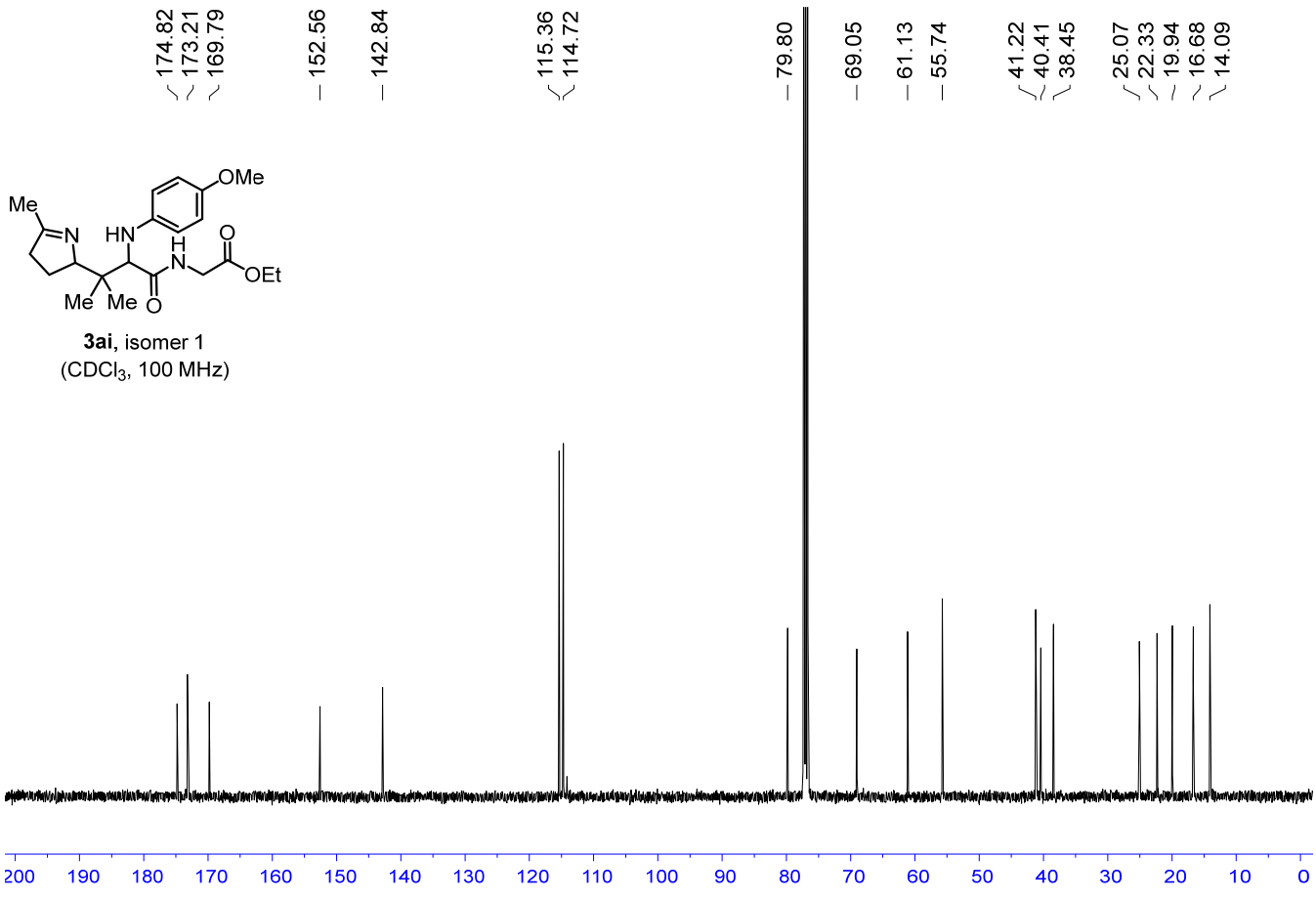
3ai, *dr* = 1.2 : 1
($CDCl_3$, 400 MHz)



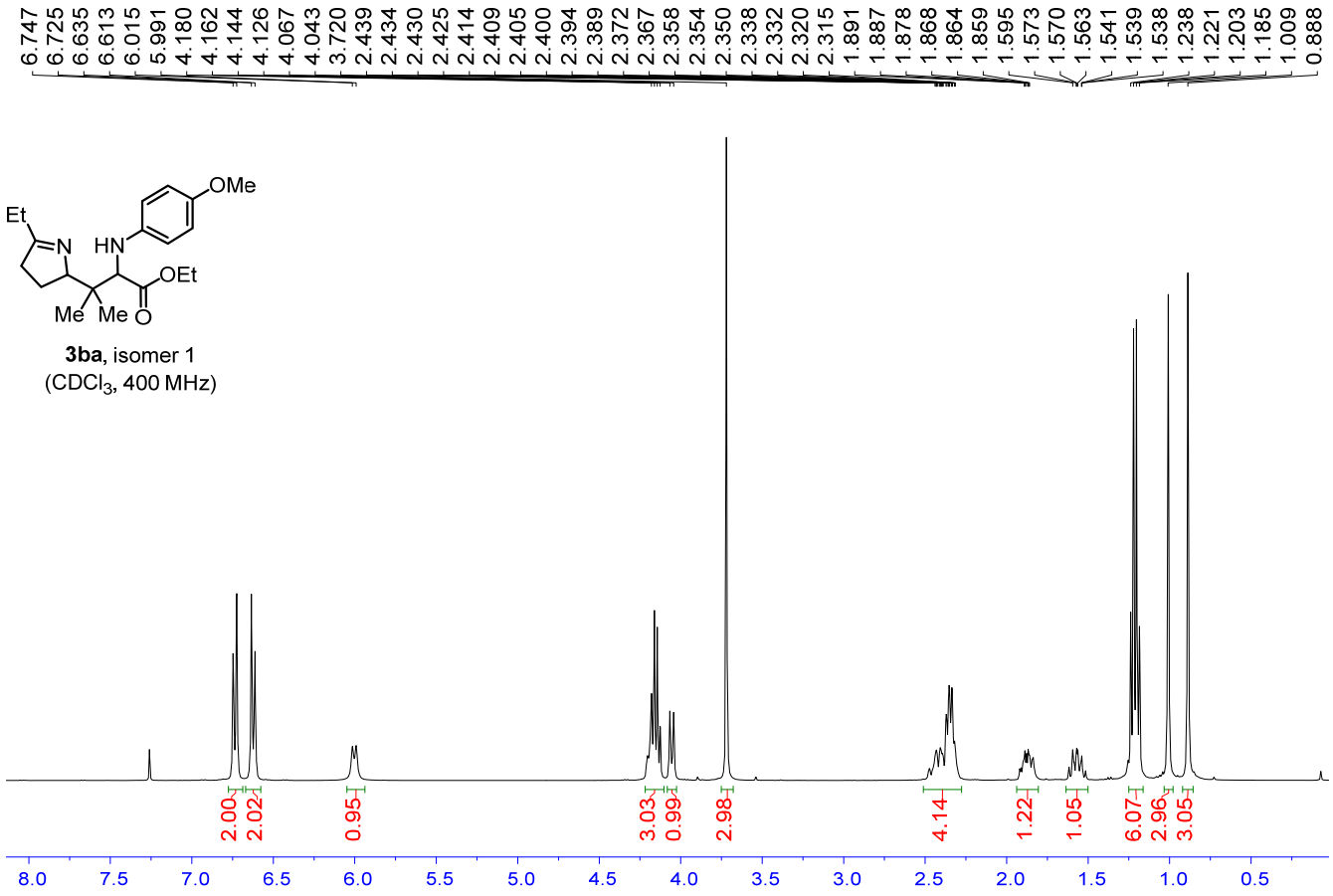
3ai, *dr* = 1.2 : 1
($CDCl_3$, 100 MHz)



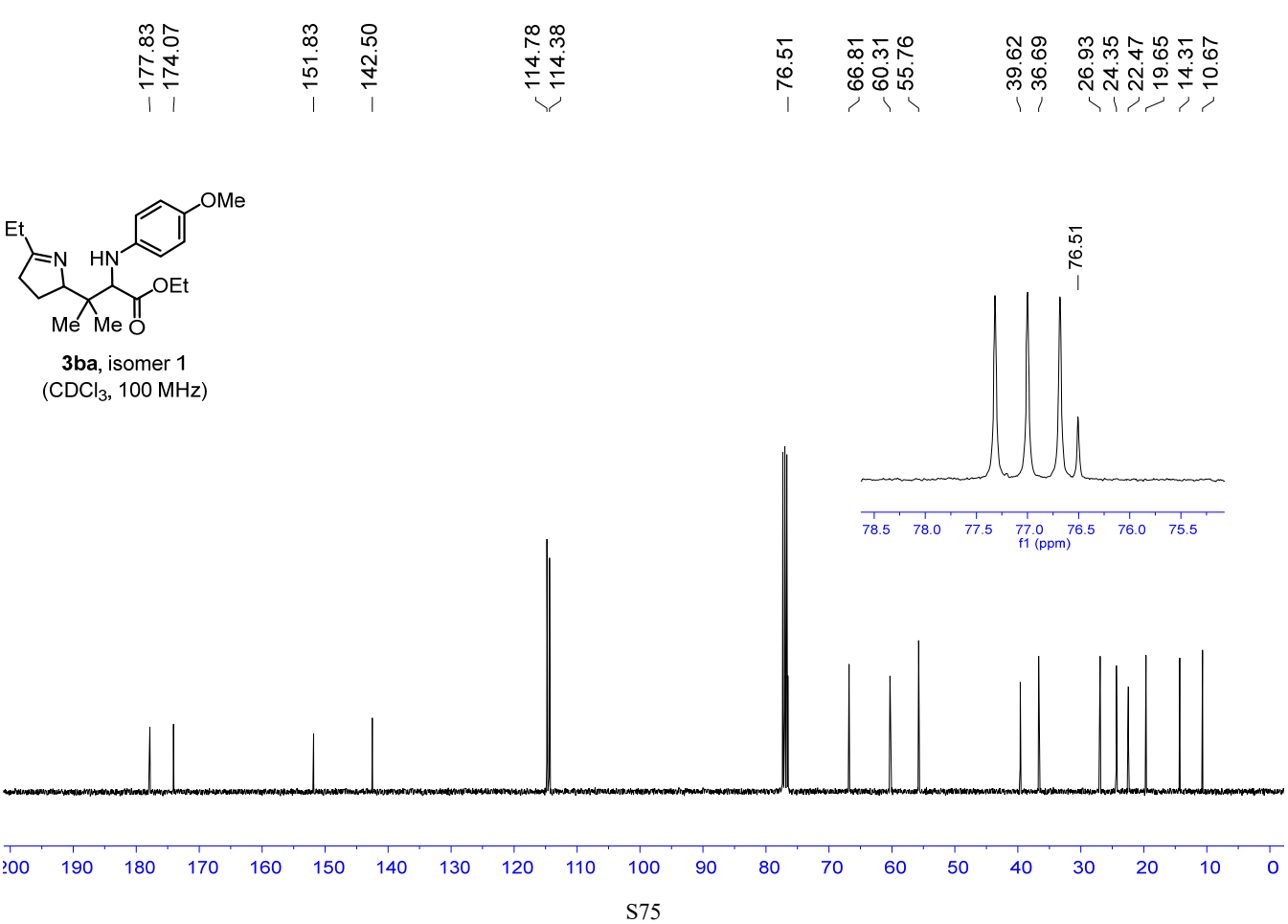
3ai, isomer 1
($CDCl_3$, 400 MHz)



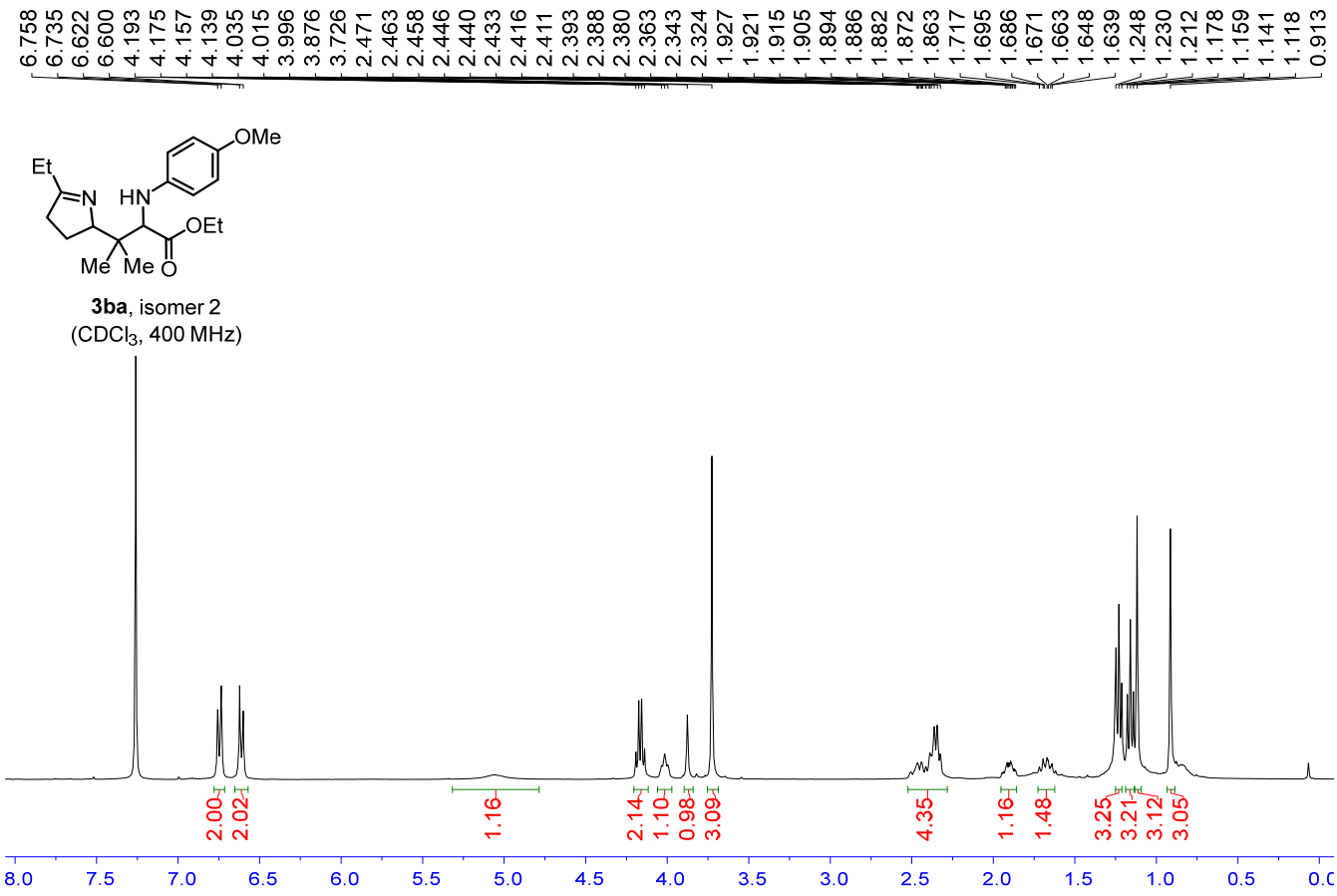
3ai, isomer 1
($CDCl_3$, 100 MHz)

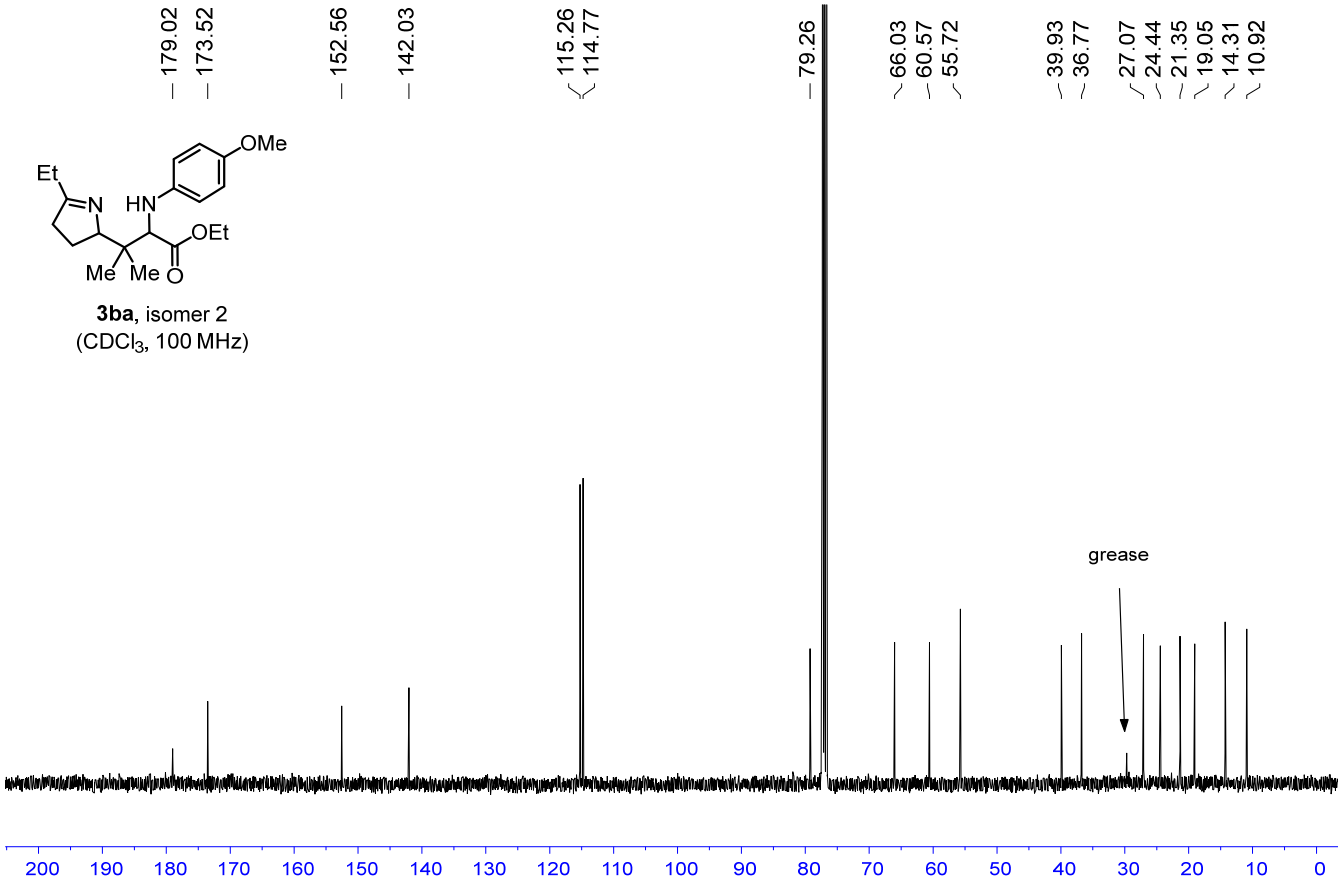


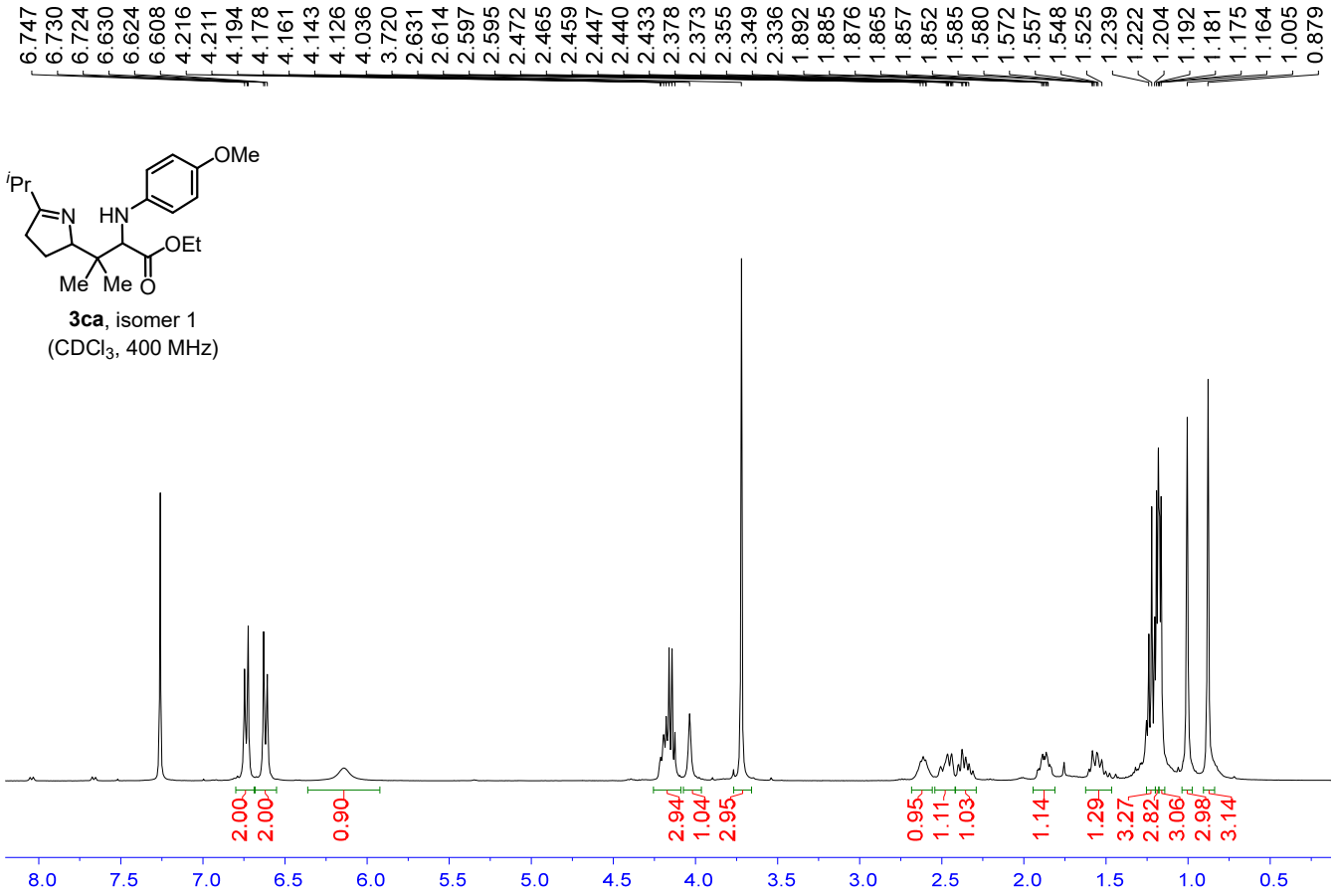
3ba, isomer 1
($CDCl_3$, 400 MHz)

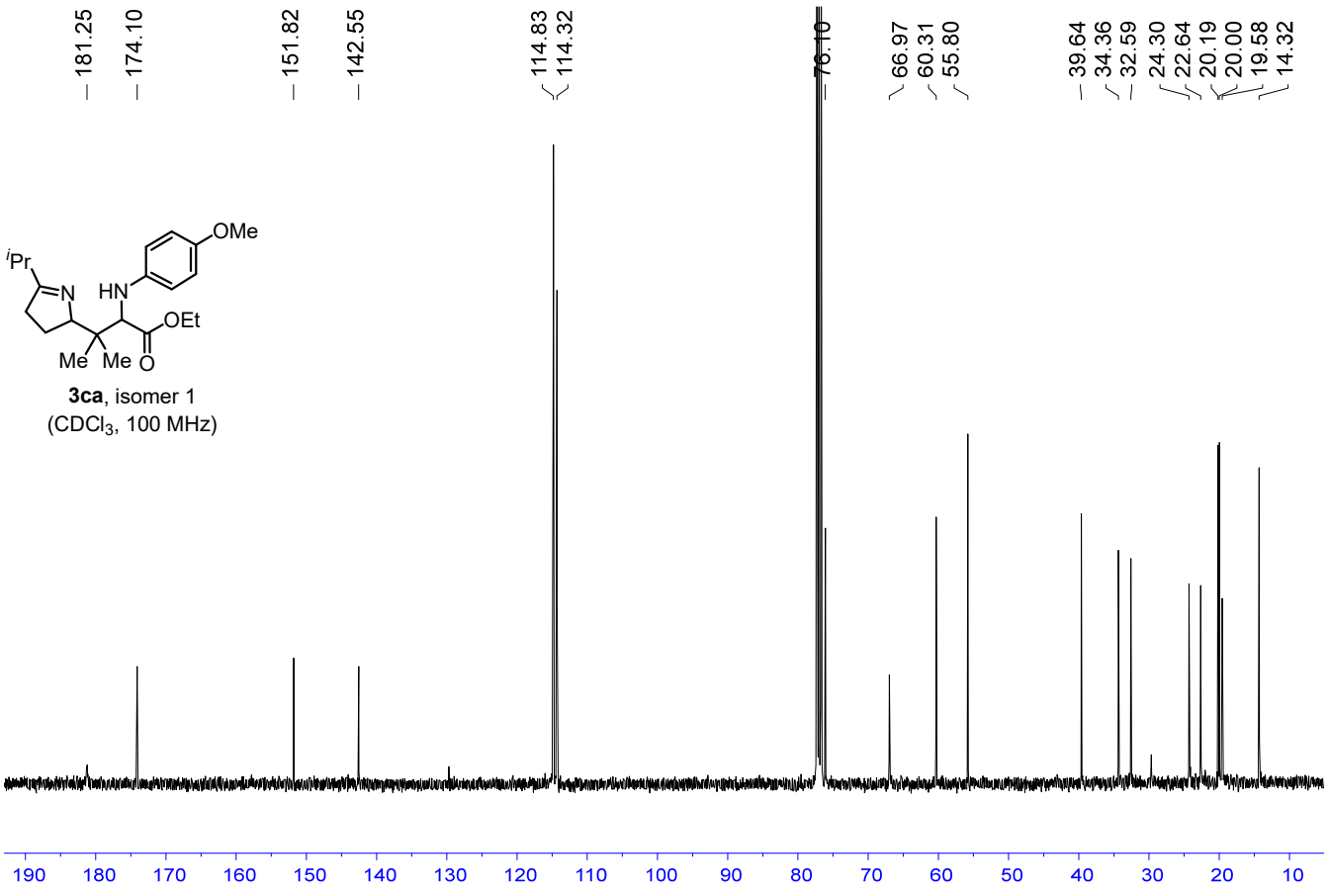


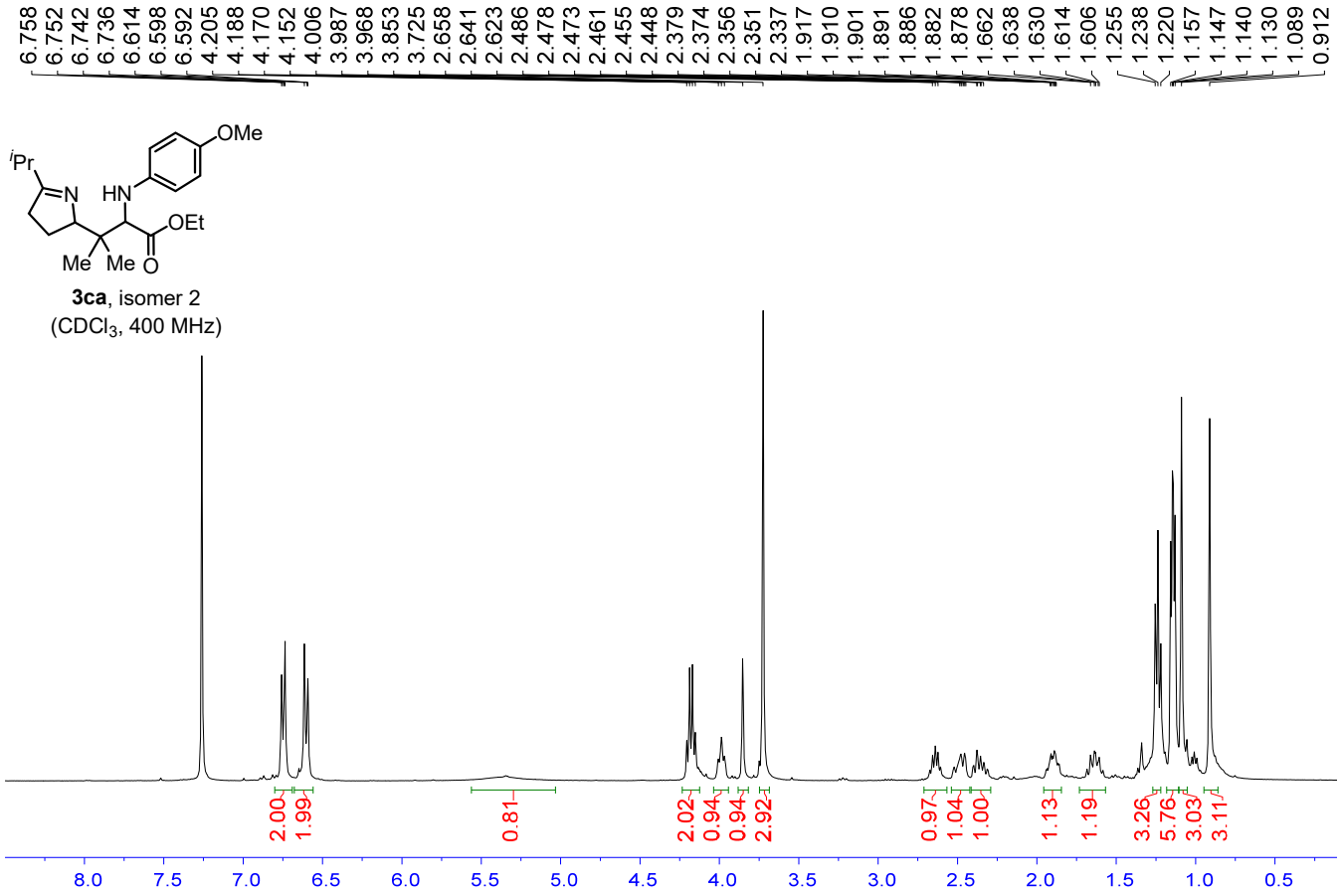
3ba, isomer 1
($CDCl_3$, 100 MHz)

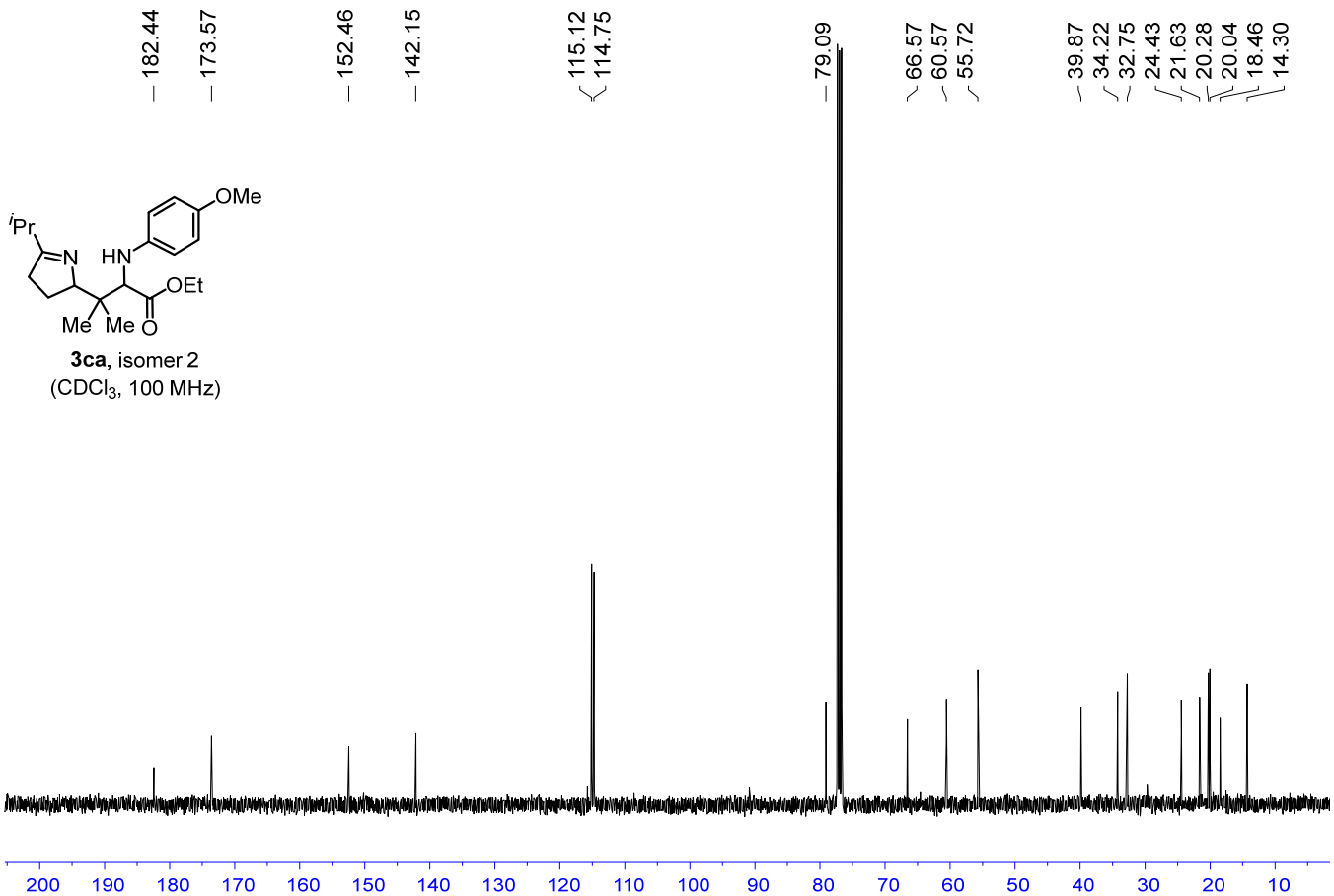

6.758
6.735
6.622
6.600
4.193
4.175
4.157
4.139
4.035
4.015
3.996
3.876
3.726
2.471
2.463
2.458
2.446
2.440
2.433
2.416
2.411
2.393
2.388
2.380
2.363
2.343
2.324
1.927
1.921
1.915
1.905
1.894
1.886
1.882
1.872
1.863
1.717
1.695
1.686
1.671
1.663
1.648
1.639
1.248
1.230
1.212
1.178
1.159
1.141
1.118
0.913
Et
N
HN
OMe
OEt
Me
Me
O
3ba, isomer 2
(CDCl3, 400 MHz)
2.00
2.02
1.16
2.14
1.10
0.98
3.09
4.35
1.16
1.48
3.25
3.21
3.12
3.05
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

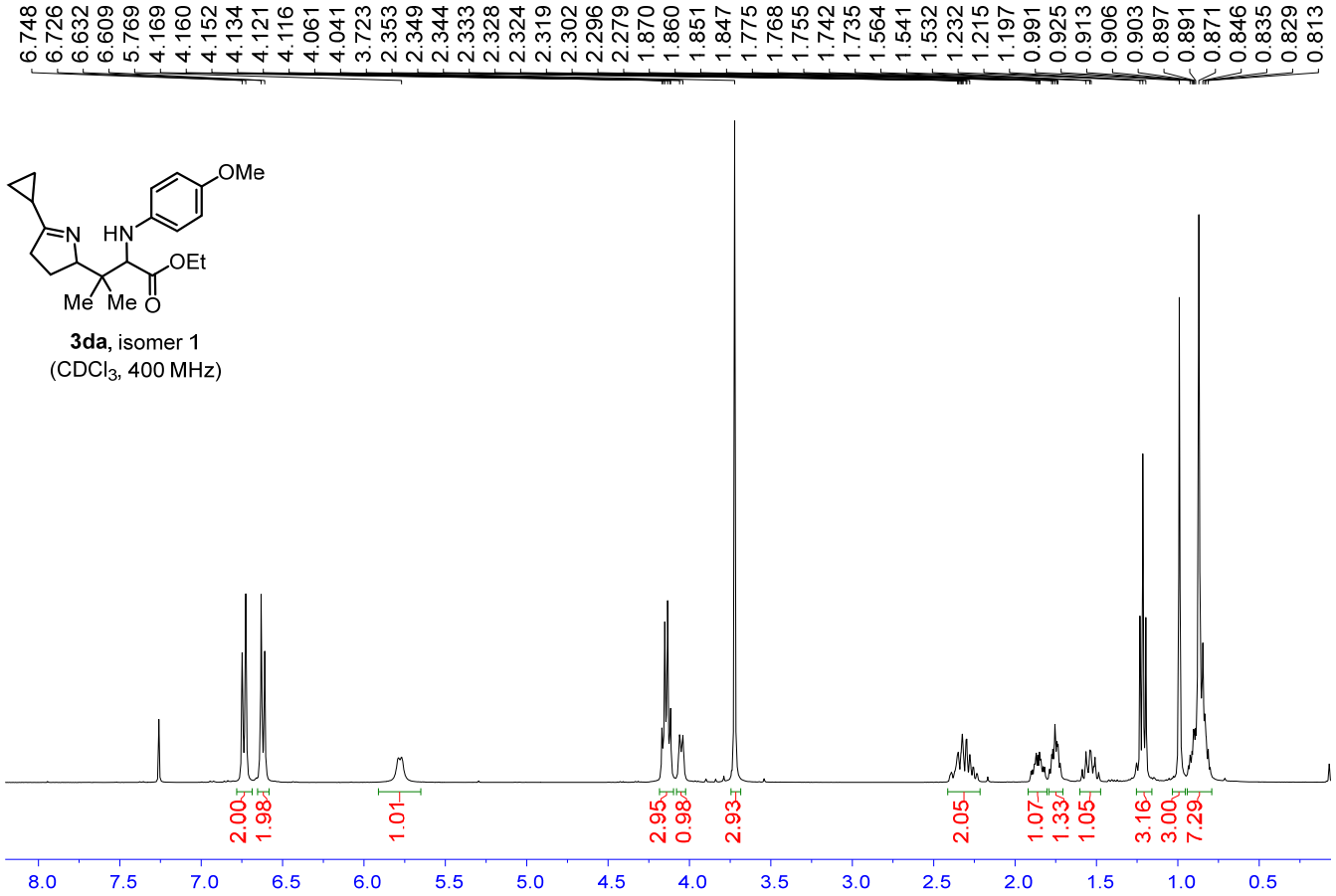

179.02
173.52
152.56
142.03
115.26
114.77
79.26
66.03
60.57
55.72
39.93
36.77
27.07
24.44
21.35
19.05
14.31
10.92
Et
N
HN
OMe
OEt
Me
Me
O
3ba, isomer 2
(CDCl3, 100 MHz)
grease
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

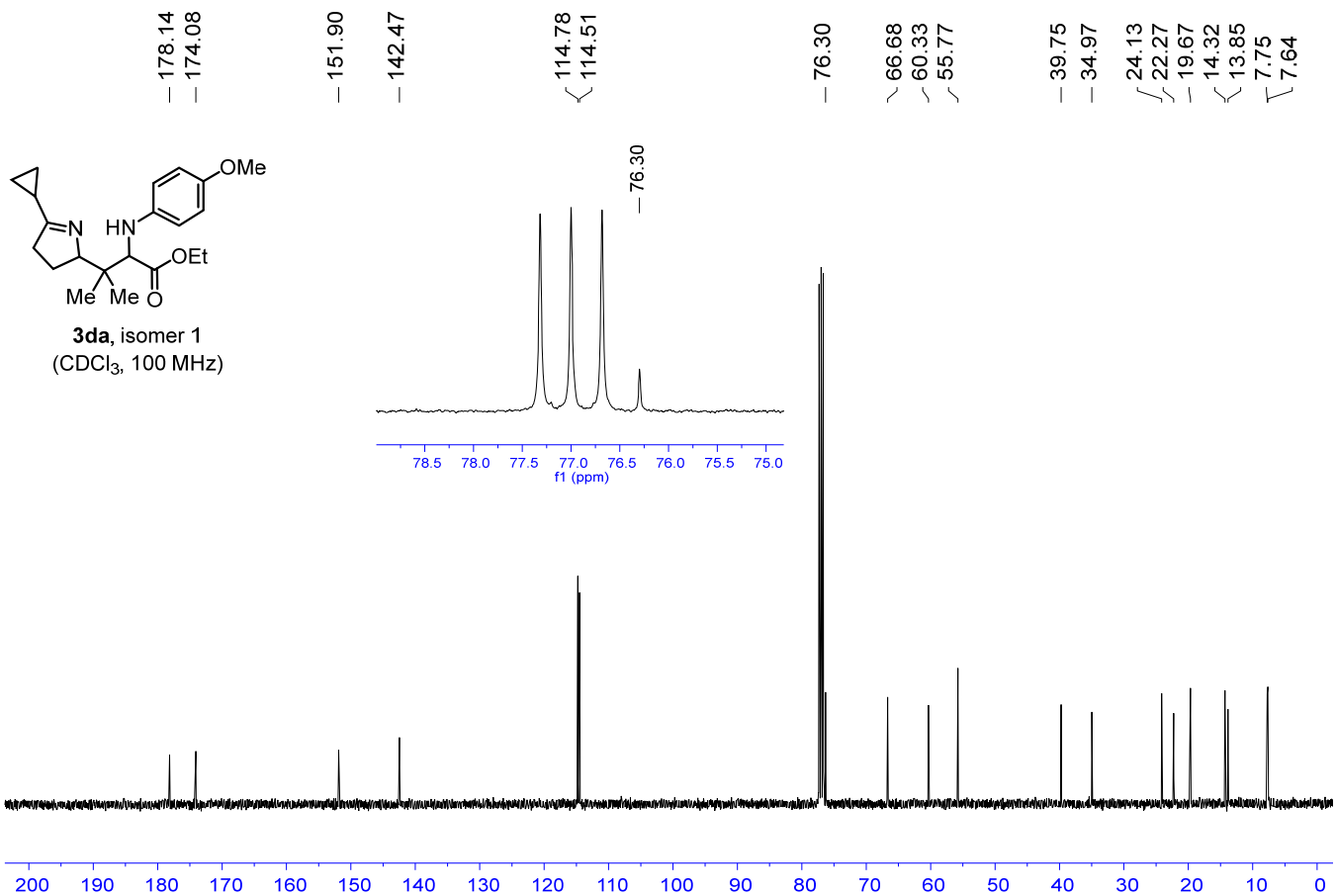

6.747
6.730
6.724
6.630
6.624
6.608
4.216
4.211
4.194
4.178
4.161
4.143
4.126
4.036
3.720
2.631
2.614
2.597
2.595
2.472
2.465
2.459
2.447
2.440
2.433
2.378
2.373
2.355
2.349
2.336
1.892
1.885
1.876
1.865
1.857
1.852
1.585
1.580
1.572
1.557
1.548
1.525
1.239
1.222
1.204
1.192
1.181
1.175
1.164
1.005
0.879
OMe
iPr
N
HN
OEt
Me Me O
3ca, isomer 1
(CDCl3, 400 MHz)
2.00
2.00
0.90
2.94
1.04
2.95
0.95
1.11
1.03
1.14
1.29
3.27
2.82
3.06
2.98
3.14
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

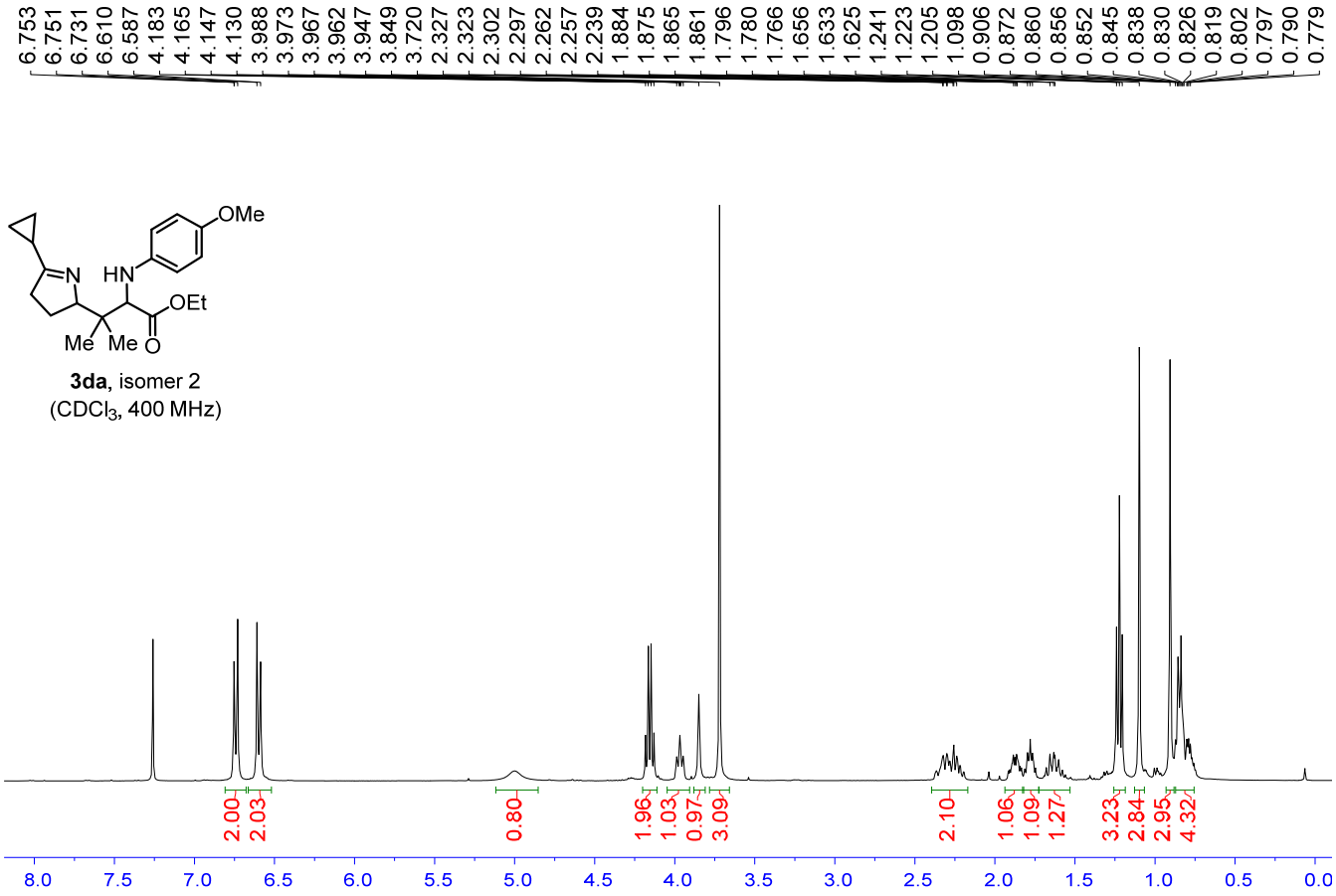

181.25
174.10
151.82
142.55
114.83
114.32
76.10
66.97
60.31
55.80
39.64
34.36
32.59
24.30
22.64
20.19
20.00
19.58
14.32
OMe
iPr
N
HN
OEt
Me Me O
3ca, isomer 1
(CDCl3, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

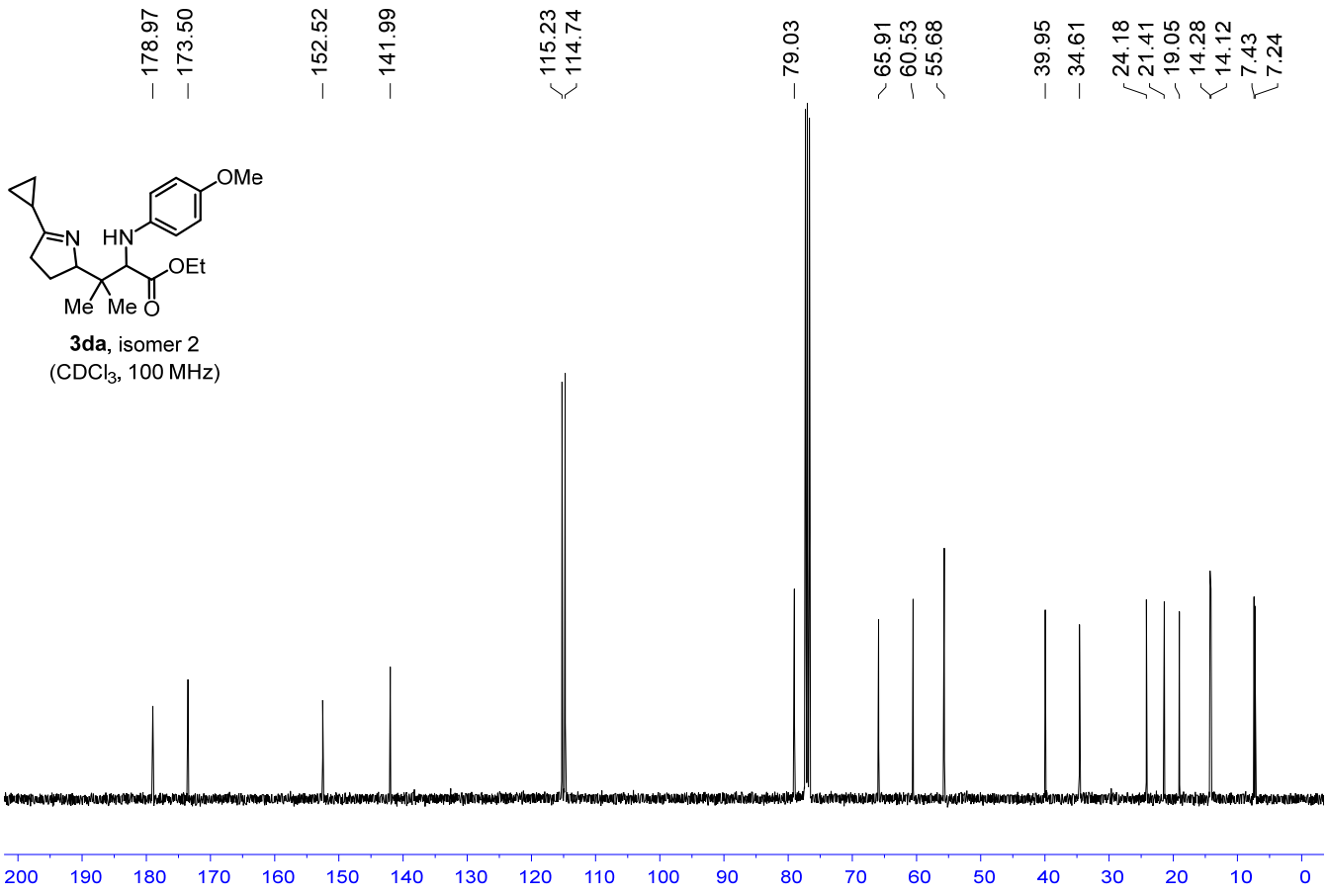

6.758
6.752
6.742
6.736
6.614
6.598
6.592
4.205
4.188
4.170
4.152
4.006
3.987
3.968
3.853
3.725
2.658
2.641
2.623
2.486
2.478
2.473
2.461
2.455
2.448
2.379
2.374
2.356
2.351
2.337
1.917
1.910
1.901
1.891
1.886
1.882
1.878
1.662
1.638
1.630
1.614
1.606
1.255
1.238
1.220
1.157
1.147
1.140
1.130
1.089
0.912
OMe
iPr
N
HN
OEt
Me
Me
O
3ca, isomer 2
(CDCl3, 400 MHz)
2.00
1.99
0.81
2.02
0.94
0.94
2.92
0.97
1.04
1.00
1.13
1.19
3.26
5.76
3.03
3.11
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

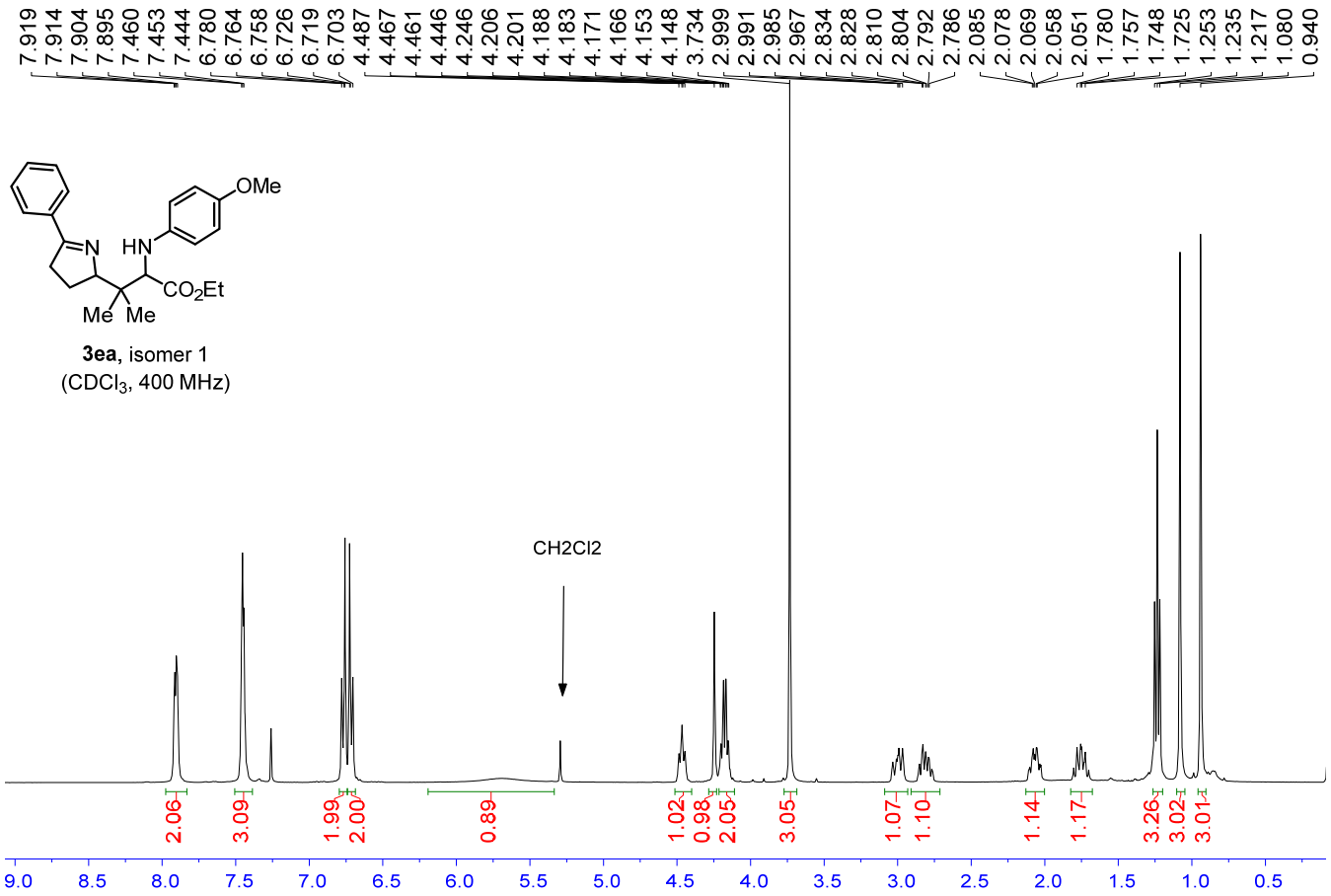

182.44
173.57
152.46
142.15
115.12
114.75
79.09
66.57
60.57
55.72
39.87
34.22
32.75
24.43
21.63
20.28
20.04
18.46
14.30
OMe
iPr
N
HN
OEt
Me
Me
O
3ca, isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

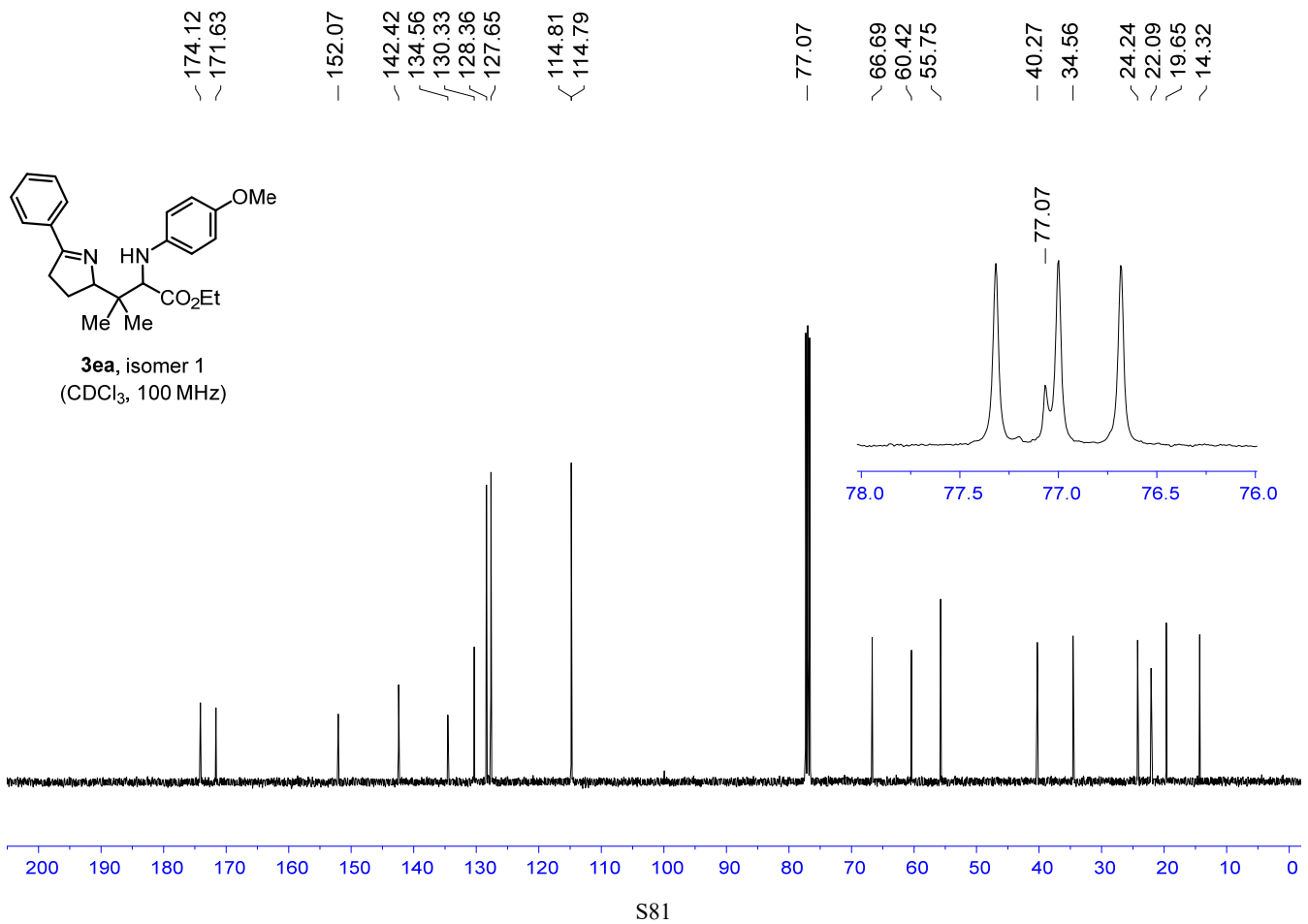

6.748
6.726
6.632
6.609
5.769
4.169
4.160
4.152
4.134
4.121
4.116
4.061
4.041
3.723
2.353
2.349
2.344
2.333
2.328
2.324
2.319
2.302
2.296
2.279
1.870
1.860
1.851
1.847
1.775
1.768
1.755
1.742
1.735
1.564
1.541
1.532
1.232
1.215
1.197
0.991
0.925
0.913
0.906
0.903
0.897
0.891
0.871
0.846
0.835
0.829
0.813
OMe
N
HN
OEt
Me
Me
O
3da, isomer 1
(CDCl3, 400 MHz)
2.00
1.98
1.01
2.95
0.98
2.93
2.05
1.07
1.33
1.05
3.16
3.00
7.29
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

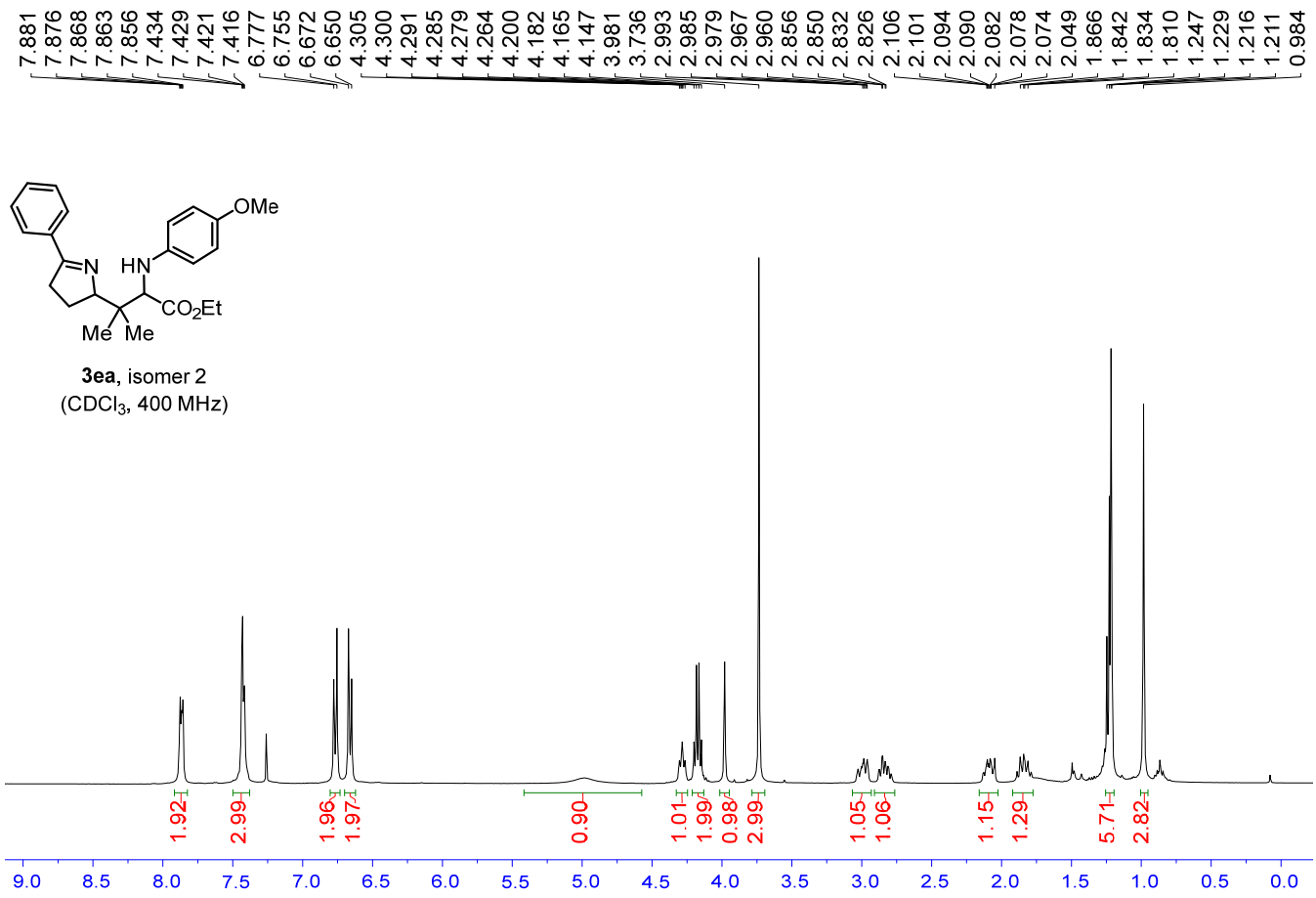

178.14
174.08
151.90
142.47
114.78
114.51
76.30
66.68
60.33
55.77
39.75
34.97
24.13
22.27
19.67
14.32
13.85
7.75
7.64
OMe
N
HN
OEt
Me
Me
O
3da, isomer 1
(CDCl3, 100 MHz)
76.30
78.5
78.0
77.5
77.0
76.5
76.0
75.5
75.0
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

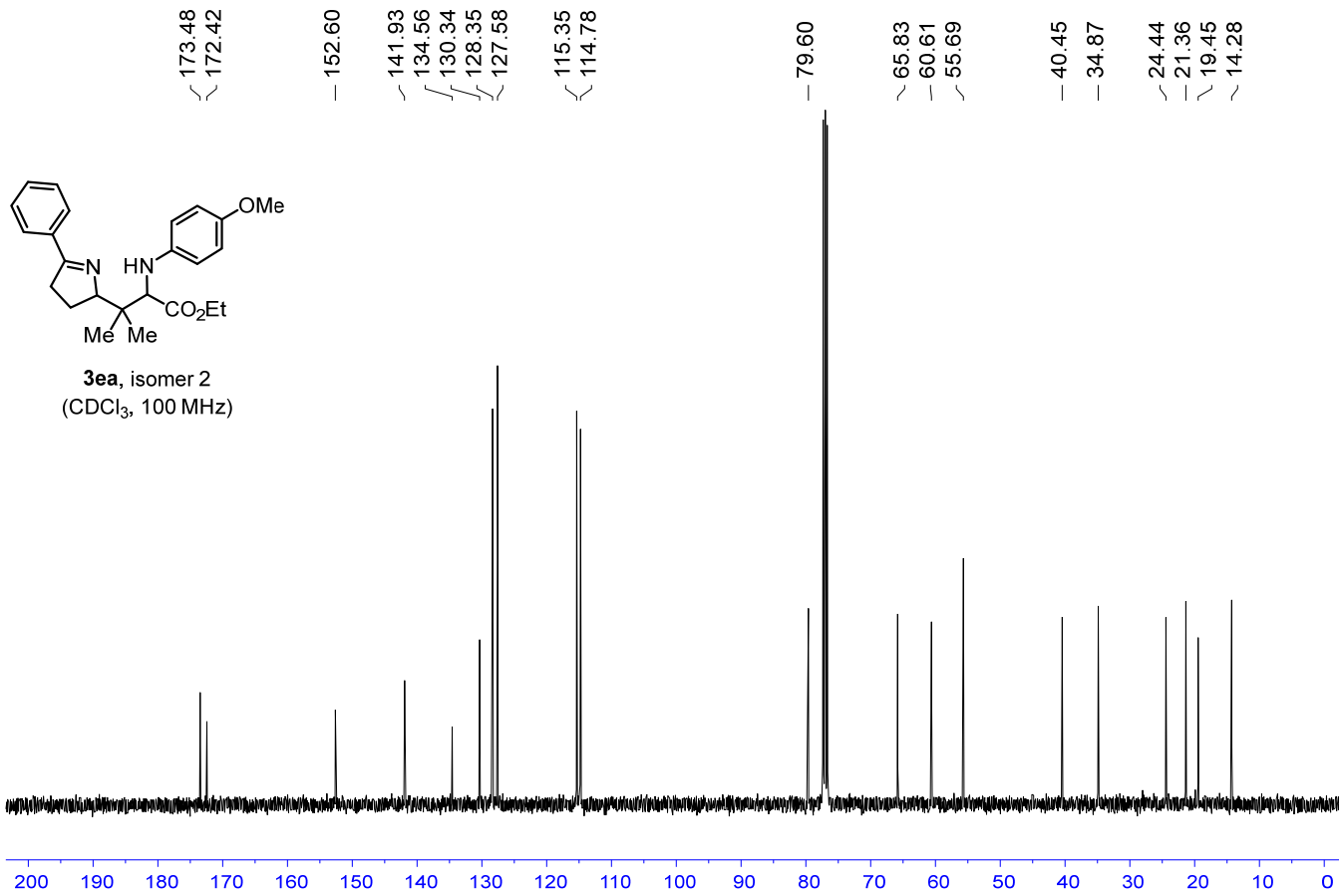

6.753
6.751
6.731
6.610
6.587
4.183
4.165
4.147
4.130
3.988
3.973
3.967
3.962
3.947
3.849
3.720
2.327
2.323
2.302
2.297
2.262
2.257
2.239
1.884
1.875
1.865
1.861
1.796
1.780
1.766
1.656
1.633
1.625
1.241
1.223
1.205
1.098
0.906
0.872
0.860
0.856
0.852
0.845
0.838
0.830
0.826
0.819
0.802
0.797
0.790
0.779
OMe
N
HN
OEt
Me Me O
3da, isomer 2
(CDCl3, 400 MHz)
2.00
2.03
0.80
1.96
1.03
0.97
3.09
2.10
1.06
1.09
1.27
3.23
2.84
2.95
4.32
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

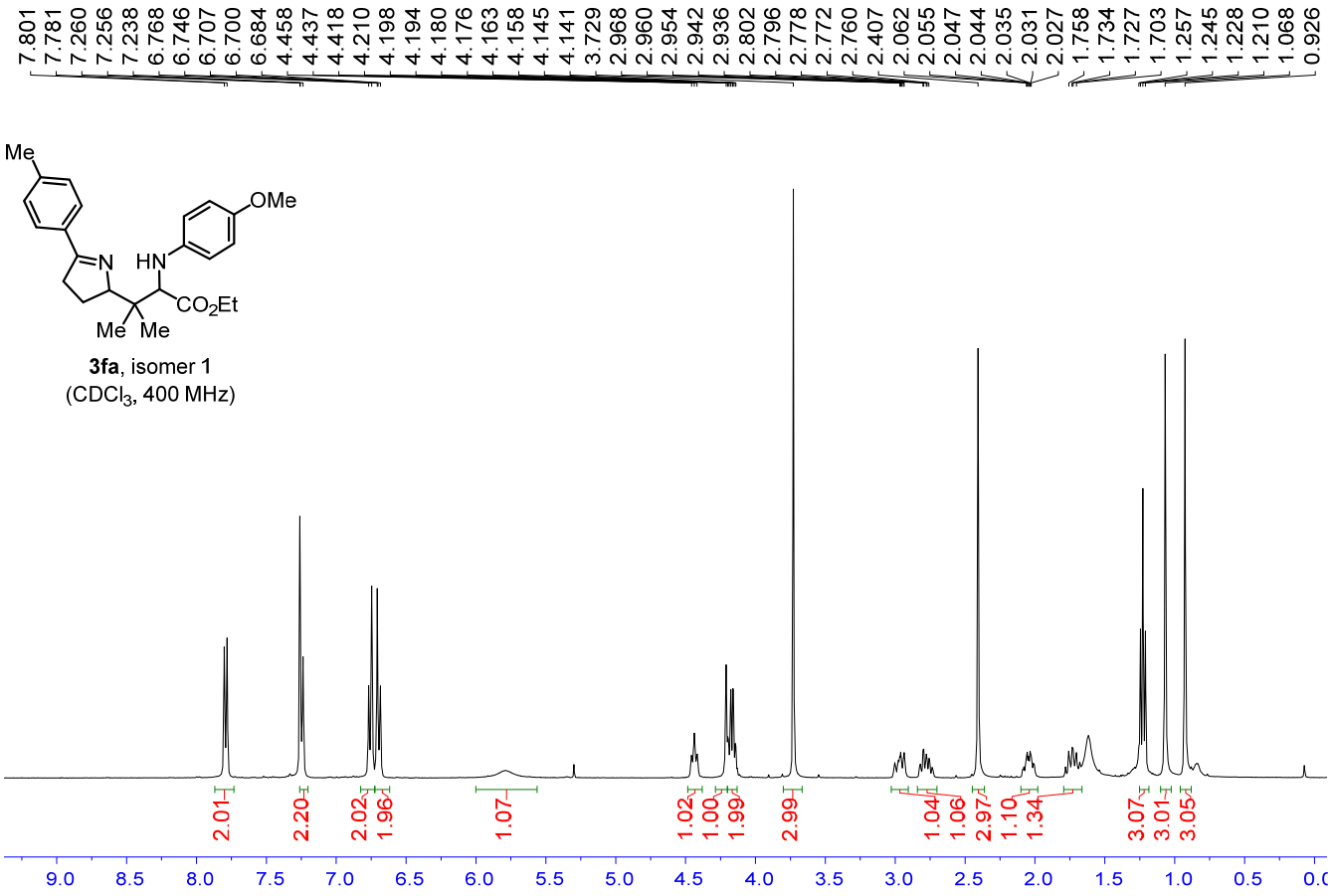

178.97
173.50
152.52
141.99
115.23
114.74
79.03
65.91
60.53
55.68
39.95
34.61
24.18
21.41
19.05
14.28
14.12
7.43
7.24
OMe
N
HN
OEt
Me Me O
3da, isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

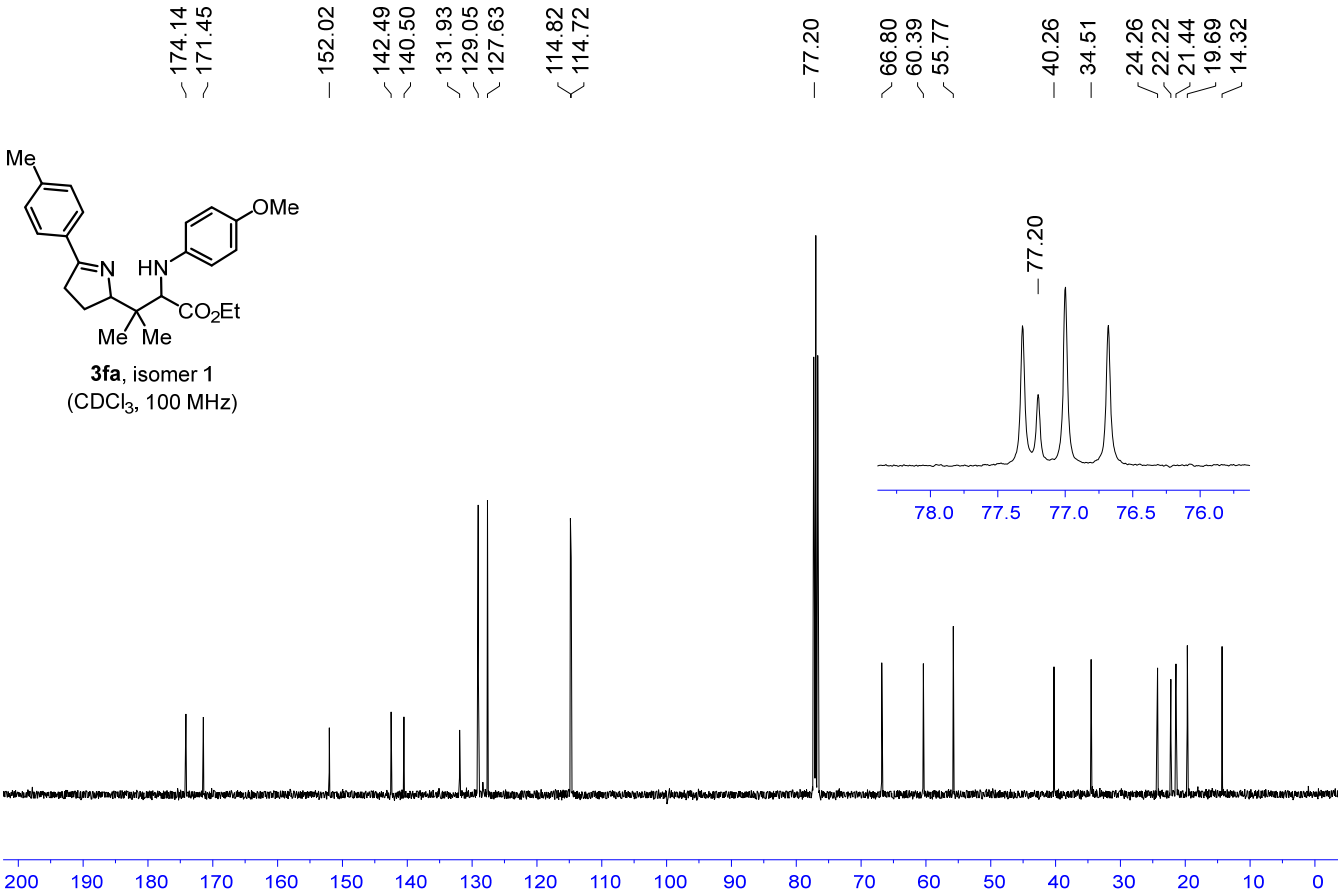

7.919
7.914
7.904
7.895
7.460
7.453
7.444
6.780
6.764
6.758
6.726
6.719
6.703
4.487
4.467
4.461
4.446
4.246
4.206
4.201
4.188
4.183
4.171
4.166
4.153
4.148
3.734
2.999
2.991
2.985
2.967
2.834
2.828
2.810
2.804
2.792
2.786
2.085
2.078
2.069
2.058
2.051
1.780
1.757
1.748
1.725
1.253
1.235
1.217
1.080
0.940
OMe
N
HN
CO2Et
Me Me
3ea, isomer 1
(CDCl3, 400 MHz)
CH2Cl2
2.06
3.09
1.99
2.00
0.89
1.02
0.98
2.05
3.05
1.07
1.10
1.14
1.17
3.26
3.02
3.01
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

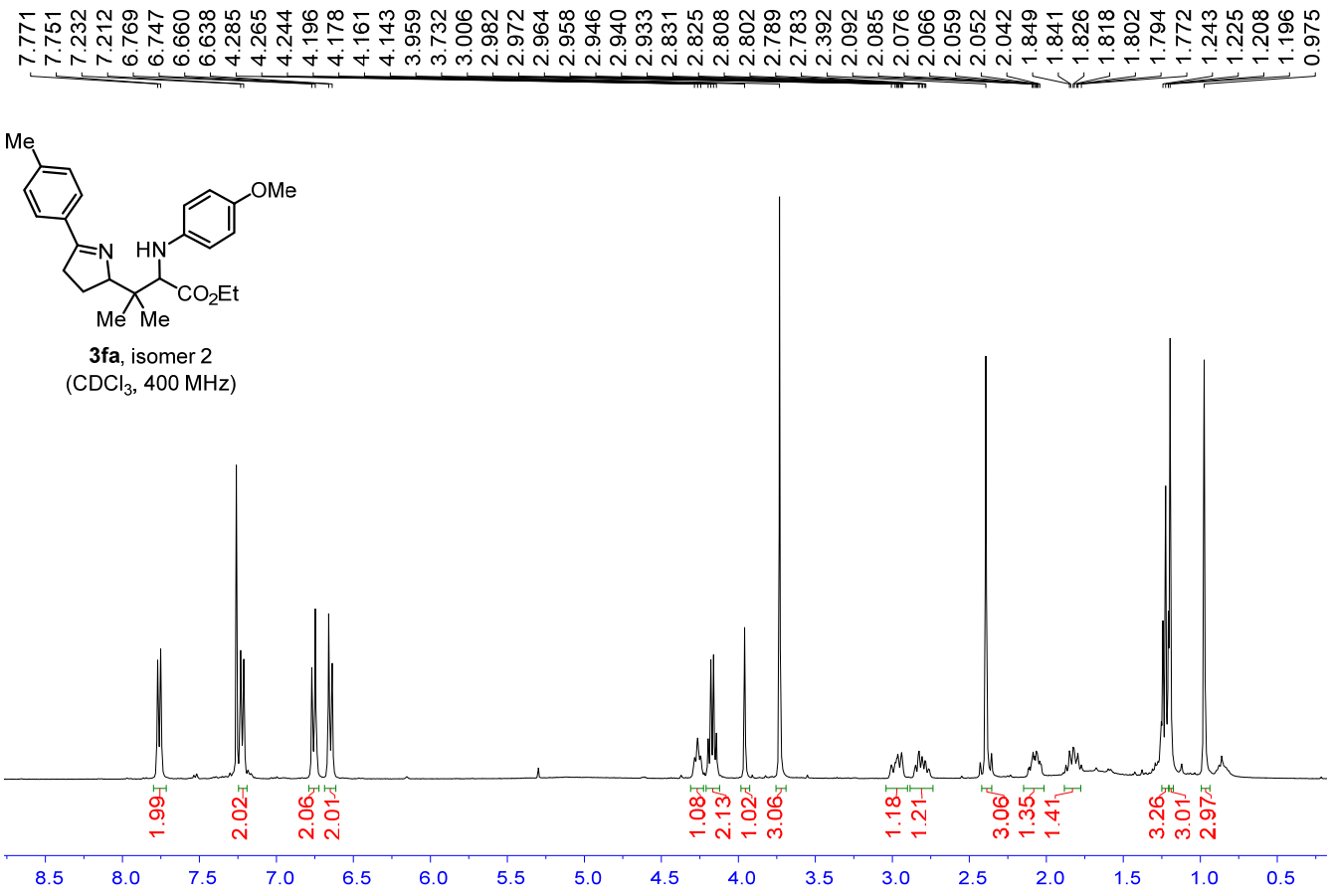

174.12
171.63
152.07
142.42
134.56
130.33
128.36
127.65
114.81
114.79
77.07
66.69
60.42
55.75
40.27
34.56
24.24
22.09
19.65
14.32
OMe
N
HN
CO2Et
Me Me
3ea, isomer 1
(CDCl3, 100 MHz)
77.07
78.0
77.5
77.0
76.5
76.0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

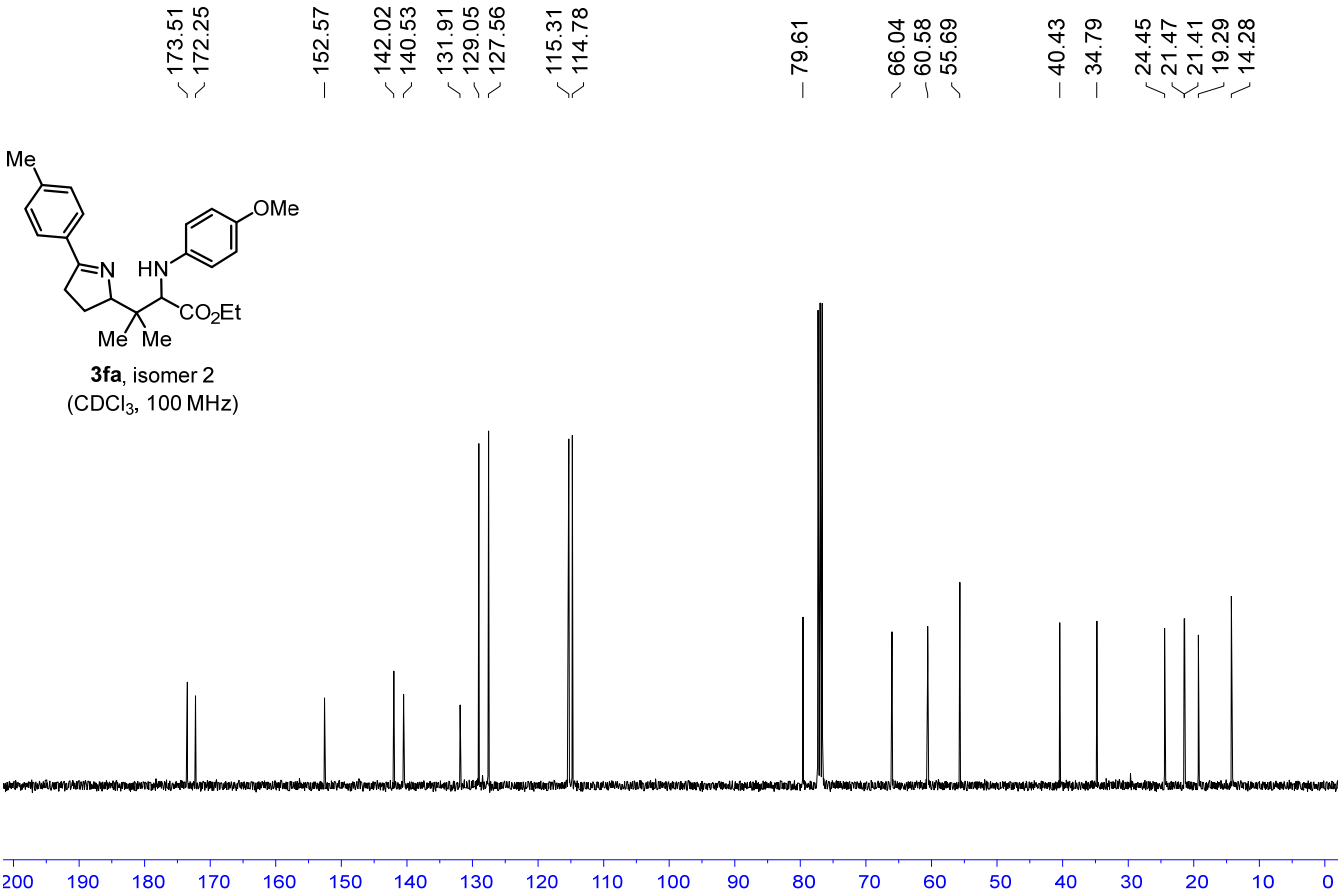

7.881
7.876
7.868
7.863
7.856
7.434
7.429
7.421
7.416
6.777
6.755
6.672
6.650
4.305
4.300
4.291
4.285
4.279
4.264
4.200
4.182
4.165
4.147
3.981
3.736
2.993
2.985
2.979
2.967
2.960
2.856
2.850
2.832
2.826
2.106
2.101
2.094
2.090
2.082
2.078
2.074
2.049
1.866
1.842
1.834
1.810
1.247
1.229
1.216
1.211
0.984
OMe
HN
N
CO2Et
Me Me
3ea, isomer 2
(CDCl3, 400 MHz)
1.92
2.99
1.96
1.97
0.90
1.01
1.99
0.98
2.99
1.05
1.06
1.15
1.29
5.71
2.82
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

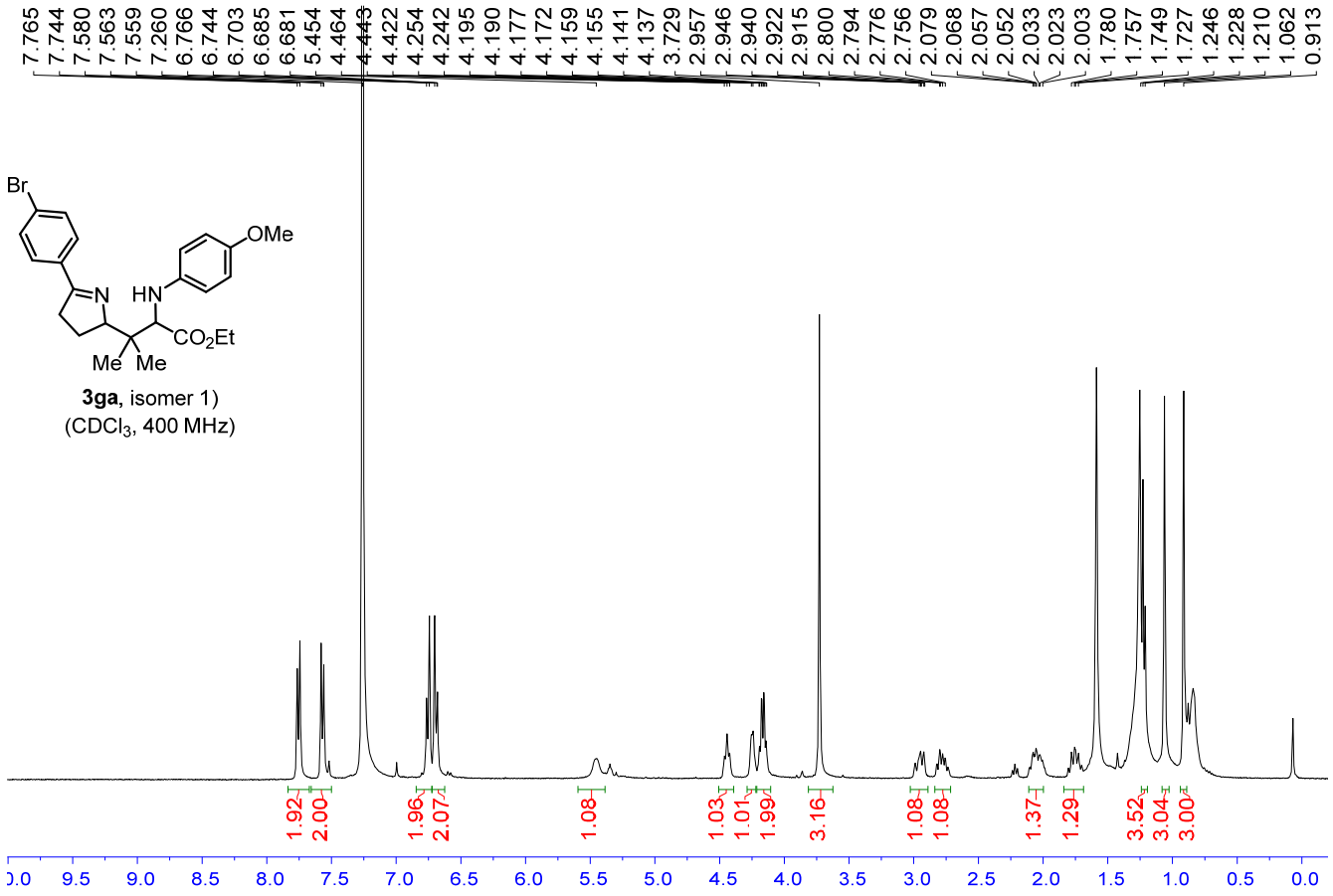

173.48
172.42
152.60
141.93
134.56
130.34
128.35
127.58
115.35
114.78
79.60
65.83
60.61
55.69
40.45
34.87
24.44
21.36
19.45
14.28
OMe
HN
N
CO2Et
Me Me
3ea, isomer 2
(CDCl3, 100 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

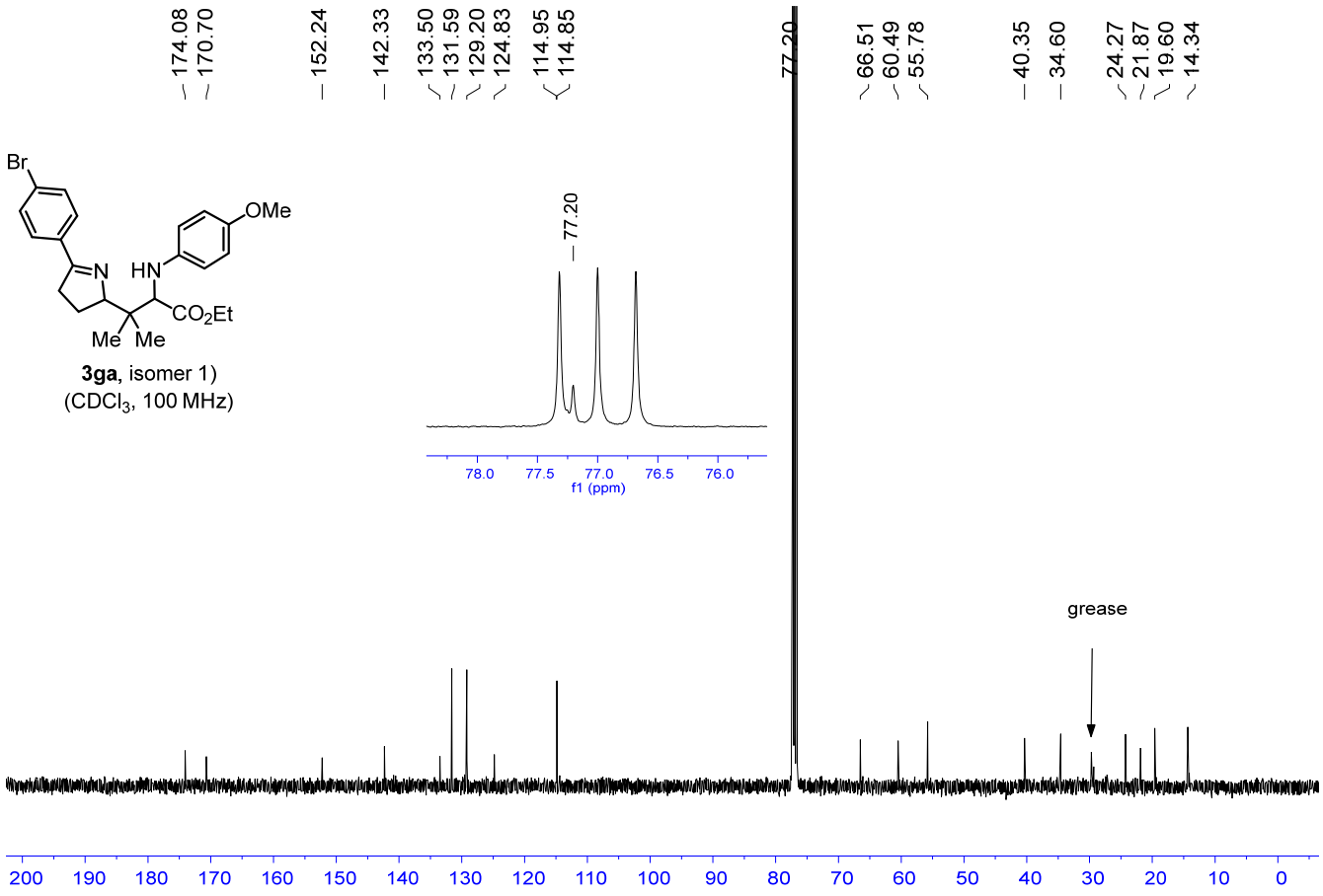

7.801
7.781
7.260
7.256
7.238
6.768
6.746
6.707
6.700
6.684
4.458
4.437
4.418
4.210
4.198
4.194
4.180
4.176
4.163
4.158
4.145
4.141
3.729
2.968
2.960
2.954
2.942
2.936
2.802
2.796
2.778
2.772
2.760
2.407
2.062
2.055
2.047
2.044
2.035
2.031
2.027
1.758
1.734
1.727
1.703
1.257
1.245
1.228
1.210
1.068
0.926
Me
OMe
N
HN
CO2Et
Me Me
3fa, isomer 1
(CDCl3, 400 MHz)
2.01
2.20
2.02
1.96
1.07
1.02
1.00
1.99
2.99
1.04
1.06
2.97
1.10
1.34
3.07
3.01
3.05
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

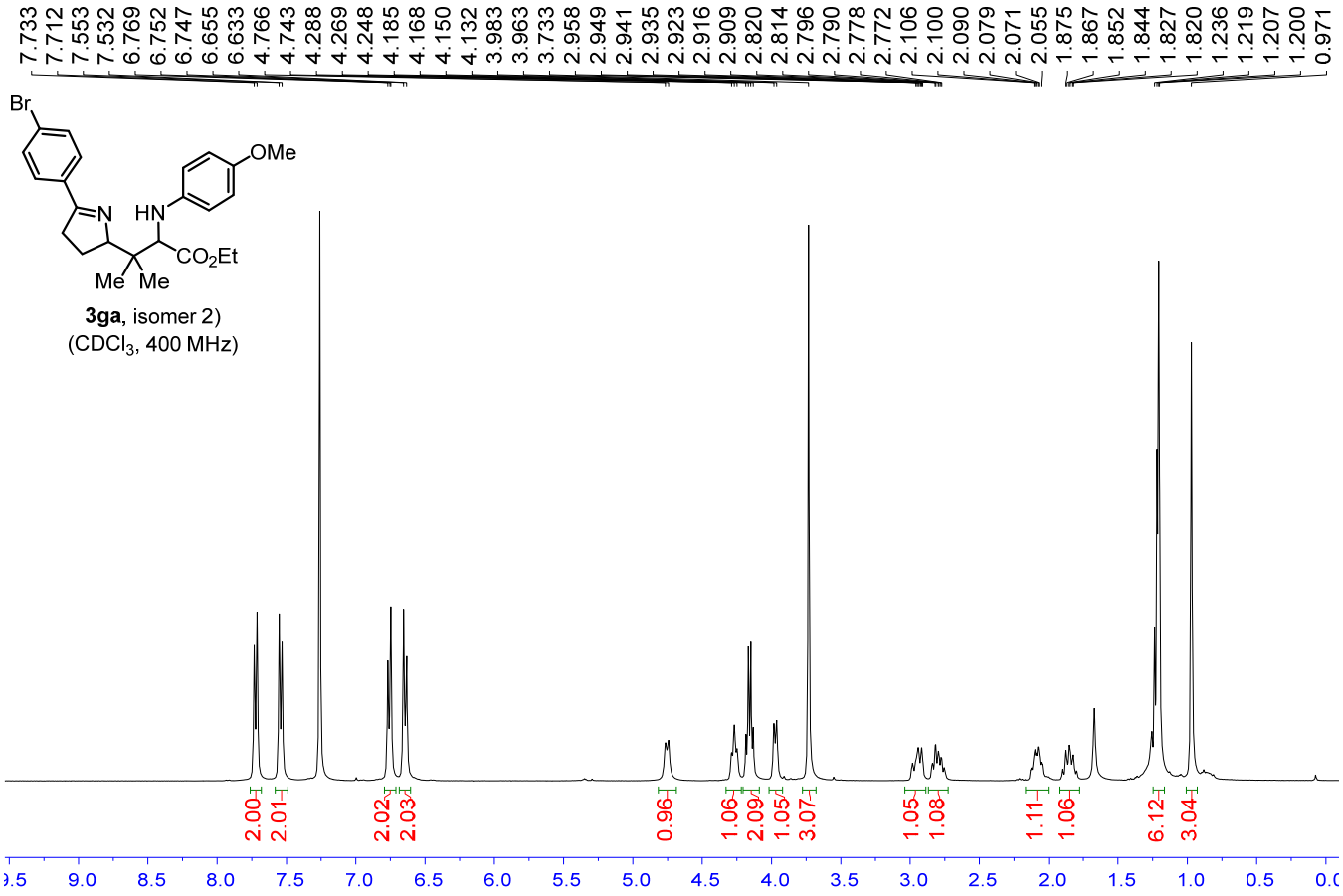

174.14
171.45
152.02
142.49
140.50
131.93
129.05
127.63
114.82
114.72
77.20
66.80
60.39
55.77
40.26
34.51
24.26
22.22
21.44
19.69
14.32
Me
OMe
N
HN
CO2Et
Me Me
3fa, isomer 1
(CDCl3, 100 MHz)
77.20
78.0
77.5
77.0
76.5
76.0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

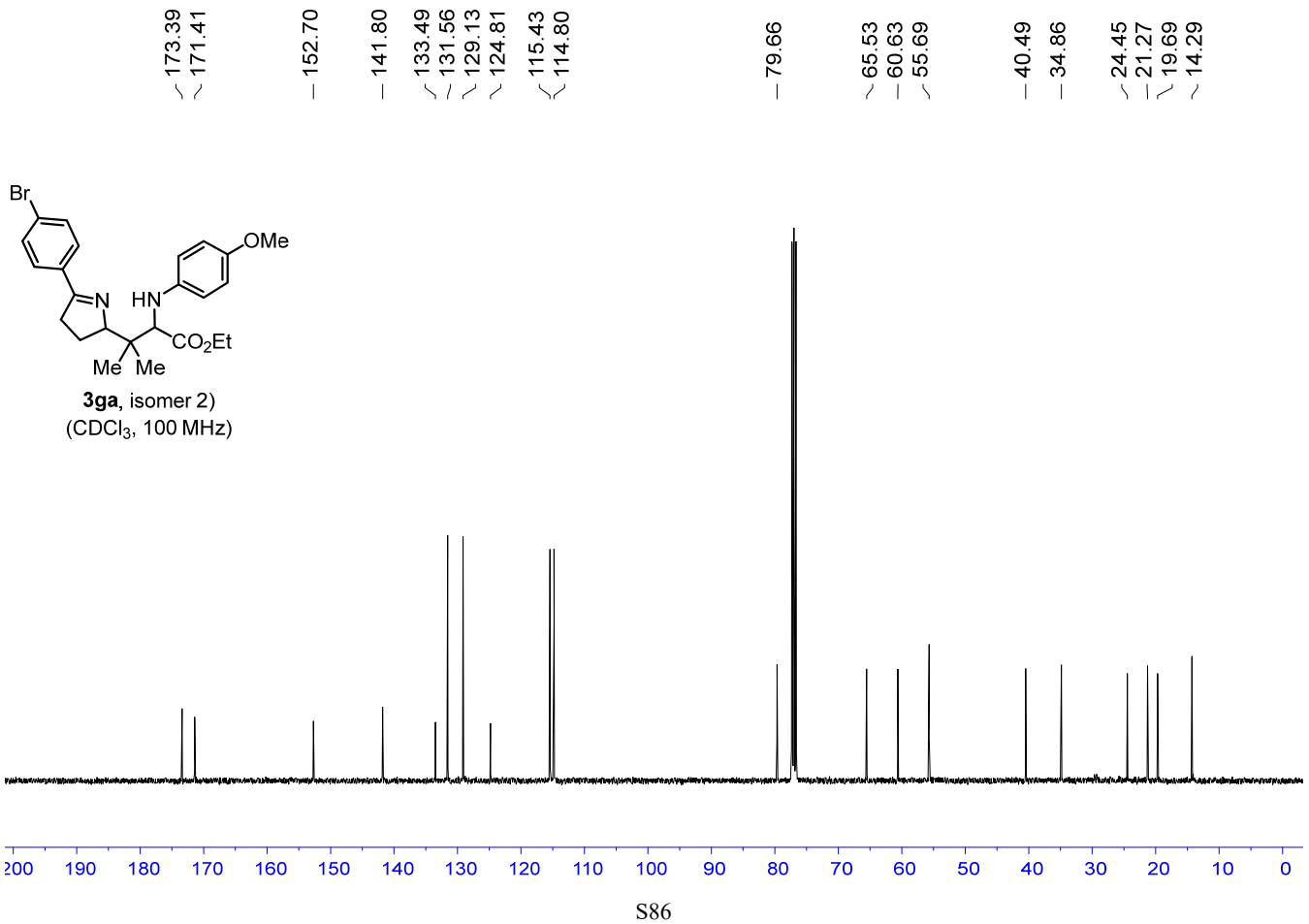

7.771
7.751
7.232
7.212
6.769
6.747
6.660
6.638
4.285
4.265
4.244
4.196
4.178
4.161
4.143
3.959
3.732
3.006
2.982
2.972
2.964
2.958
2.946
2.940
2.933
2.831
2.825
2.808
2.802
2.789
2.783
2.392
2.092
2.085
2.076
2.066
2.059
2.052
2.042
1.849
1.841
1.826
1.818
1.802
1.794
1.772
1.243
1.225
1.208
1.196
0.975
Me
OMe
N
HN
CO2Et
Me Me
3fa, isomer 2
(CDCl3, 400 MHz)
1.99
2.02
2.06
2.01
1.08
2.13
1.02
3.06
1.18
1.21
3.06
1.35
1.41
3.26
3.01
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

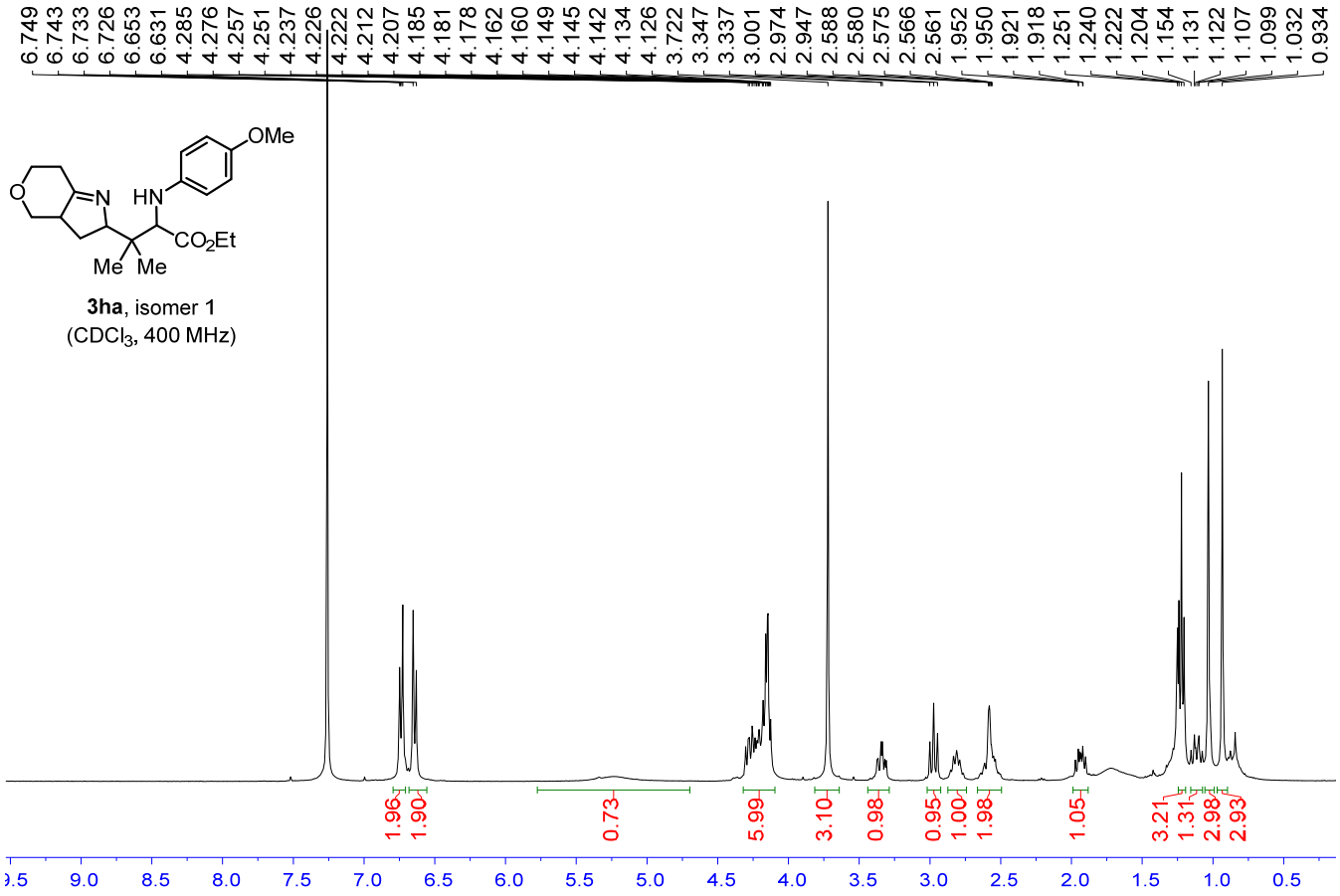

173.51
172.25
152.57
142.02
140.53
131.91
129.05
127.56
115.31
114.78
79.61
66.04
60.58
55.69
40.43
34.79
24.45
21.47
21.41
19.29
14.28
Me
OMe
N
HN
CO2Et
Me Me
3fa, isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.765 7.744 7.580 7.563 7.559 7.260 6.766 6.744 6.703 6.685 6.681 5.454 4.464 4.443 4.422 4.254 4.242 4.195 4.190 4.177 4.172 4.159 4.155 4.141 4.137 3.729 2.957 2.946 2.940 2.922 2.915 2.800 2.794 2.776 2.756 2.079 2.068 2.057 2.052 2.033 2.023 2.003 1.780 1.757 1.749 1.727 1.246 1.228 1.210 1.062 0.913
Br
OMe
N
HN
CO2Et
Me Me
3ga, isomer 1)
(CDCl3, 400 MHz)
1.92 2.00 1.96 2.07 1.08 1.03 1.01 1.99 3.16 1.08 1.08 1.37 1.29 3.52 3.04 3.00
0.0 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

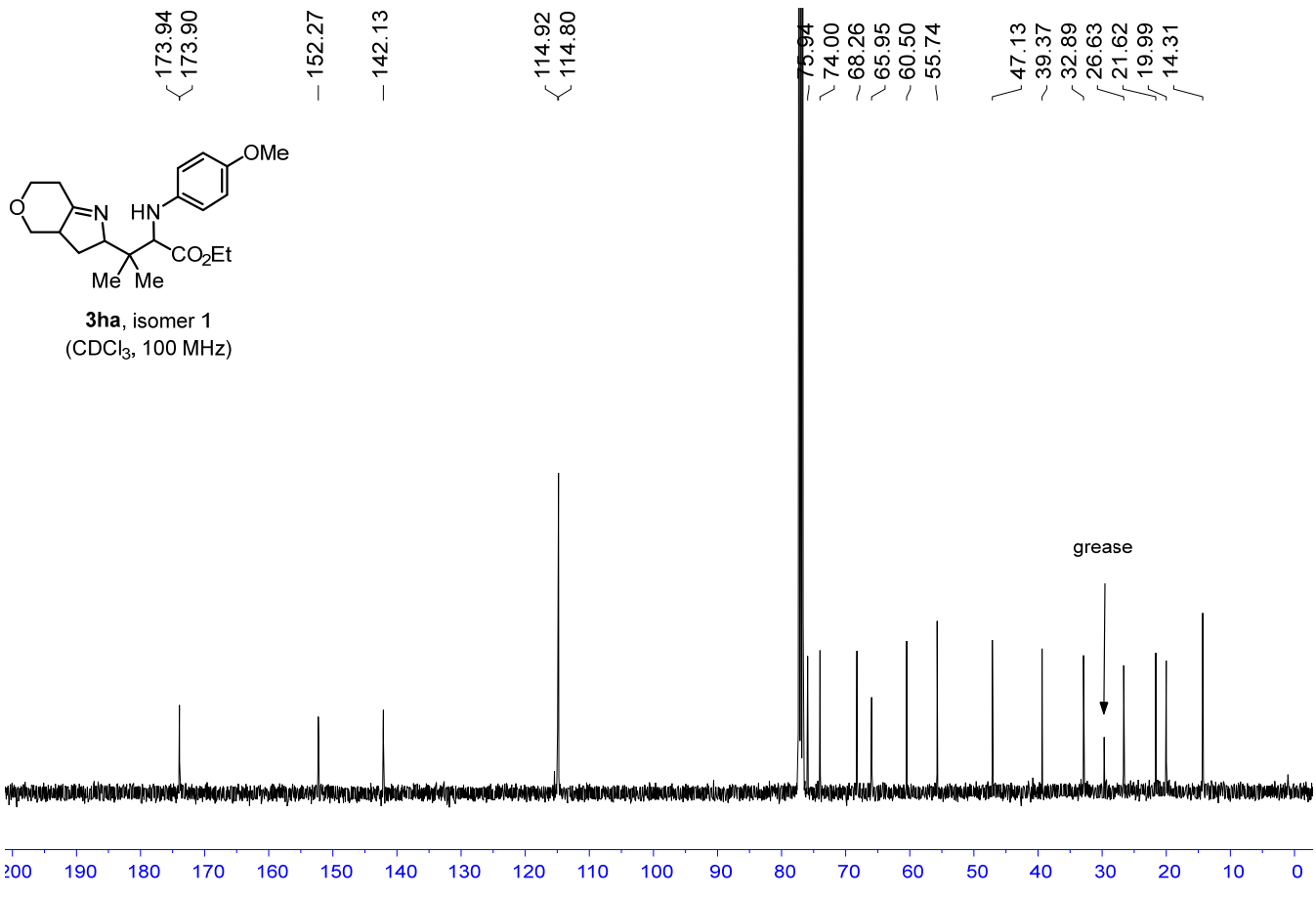

174.08 170.70 152.24 142.33 133.50 131.59 129.20 124.83 114.95 114.85 77.20 66.51 60.49 55.78 40.35 34.60 24.27 21.87 19.60 14.34
Br
OMe
N
HN
CO2Et
Me Me
3ga, isomer 1)
(CDCl3, 100 MHz)
77.20
78.0 77.5 77.0 76.5 76.0
f1 (ppm)
grease
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


7.733
7.712
7.553
7.532
6.769
6.752
6.747
6.655
6.633
4.766
4.743
4.288
4.269
4.248
4.185
4.168
4.150
4.132
3.983
3.963
3.733
2.958
2.949
2.941
2.935
2.923
2.916
2.909
2.820
2.814
2.796
2.790
2.778
2.772
2.106
2.100
2.090
2.079
2.071
2.055
1.875
1.867
1.852
1.844
1.827
1.820
1.236
1.219
1.207
1.200
0.971
Br
OMe
N
HN
CO2Et
Me Me
3ga, isomer 2)
(CDCl3, 400 MHz)
2.00
2.01
2.02
2.03
0.96
1.06
2.09
1.05
3.07
1.05
1.08
1.11
1.06
6.12
3.04

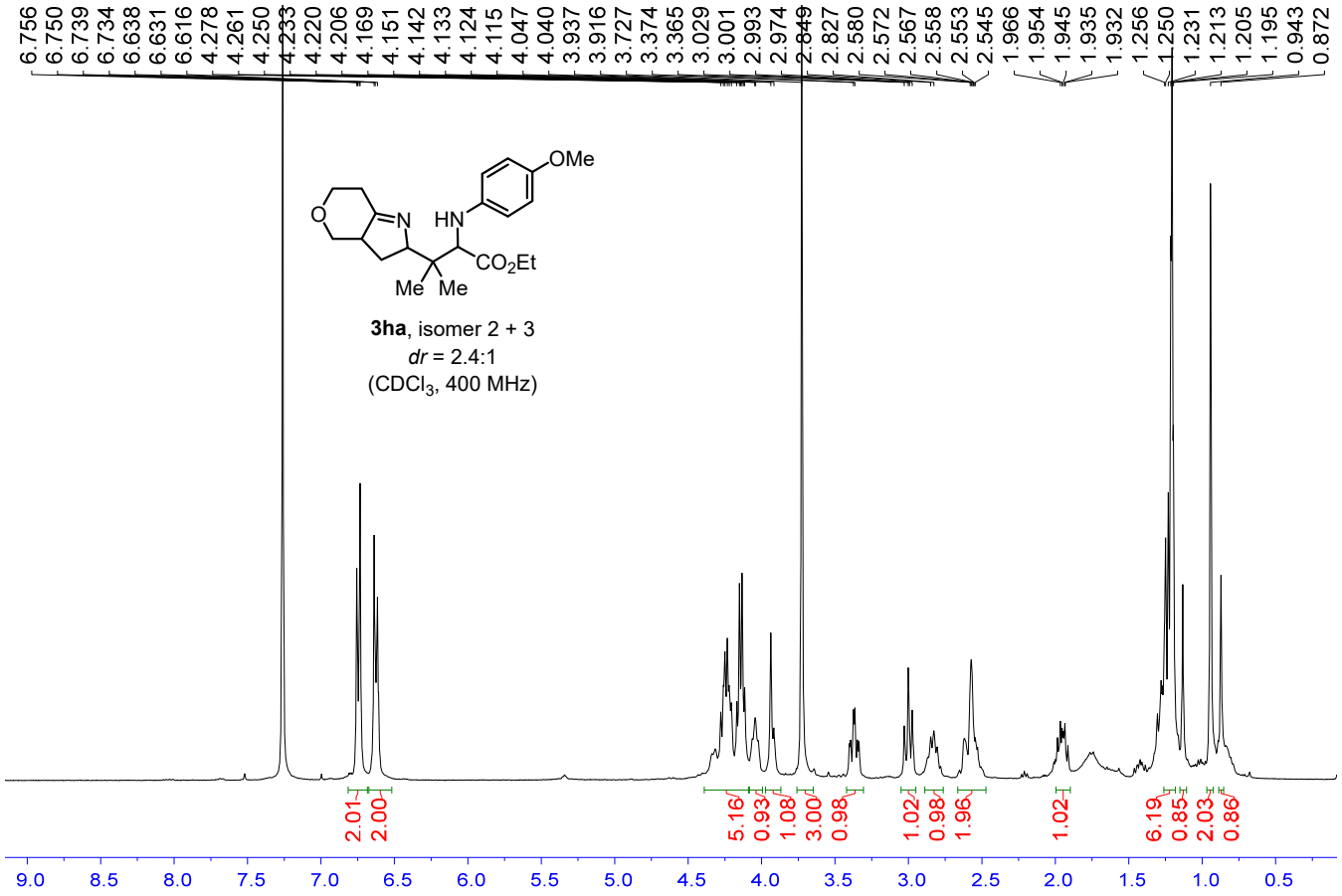

173.39
171.41
152.70
141.80
133.49
131.56
129.13
124.81
115.43
114.80
79.66
65.53
60.63
55.69
40.49
34.86
24.45
21.27
19.69
14.29
Br
OMe
N
HN
CO2Et
Me Me
3ga, isomer 2)
(CDCl3, 100 MHz)



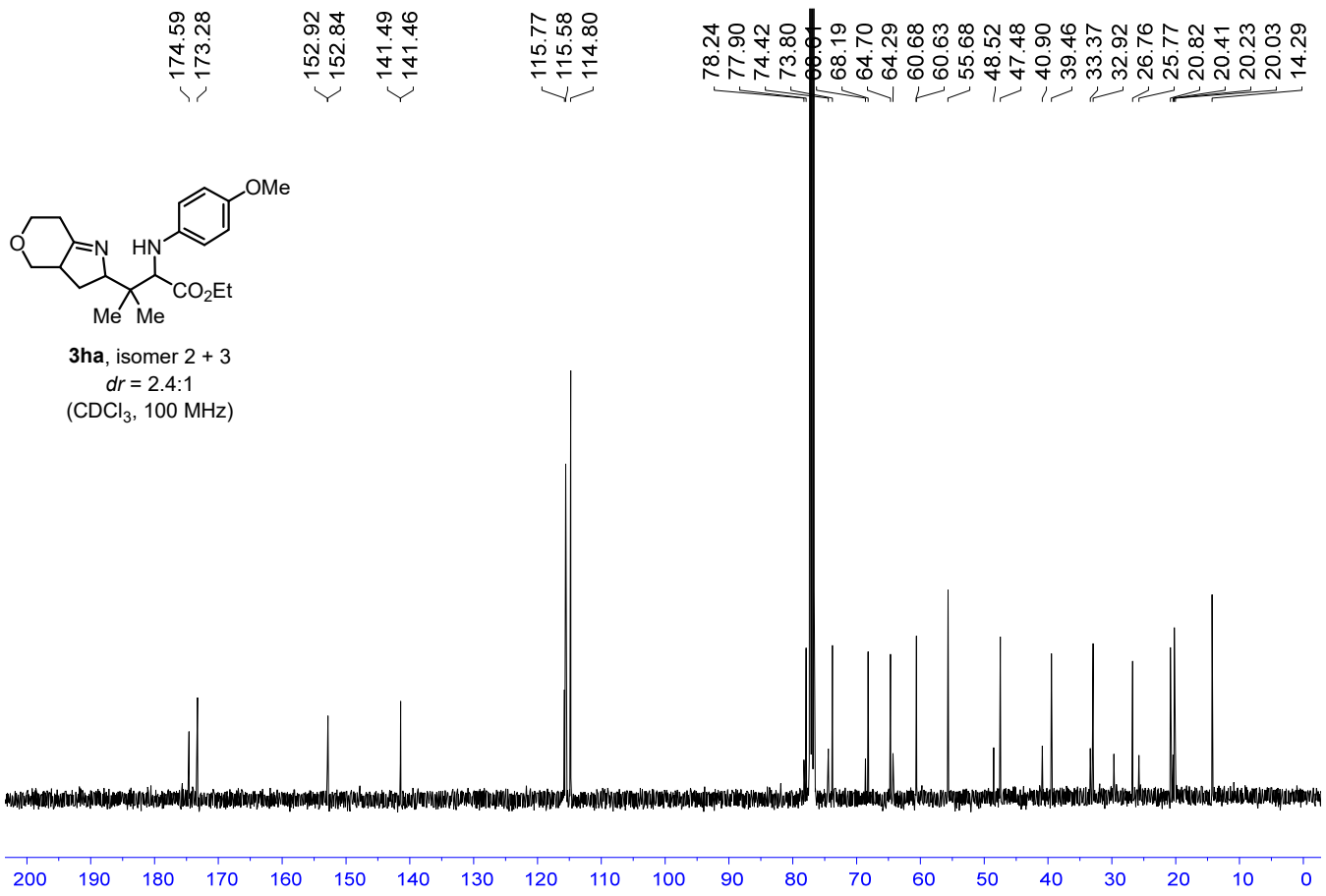
3ha, isomer 1
($CDCl_3$, 400 MHz)



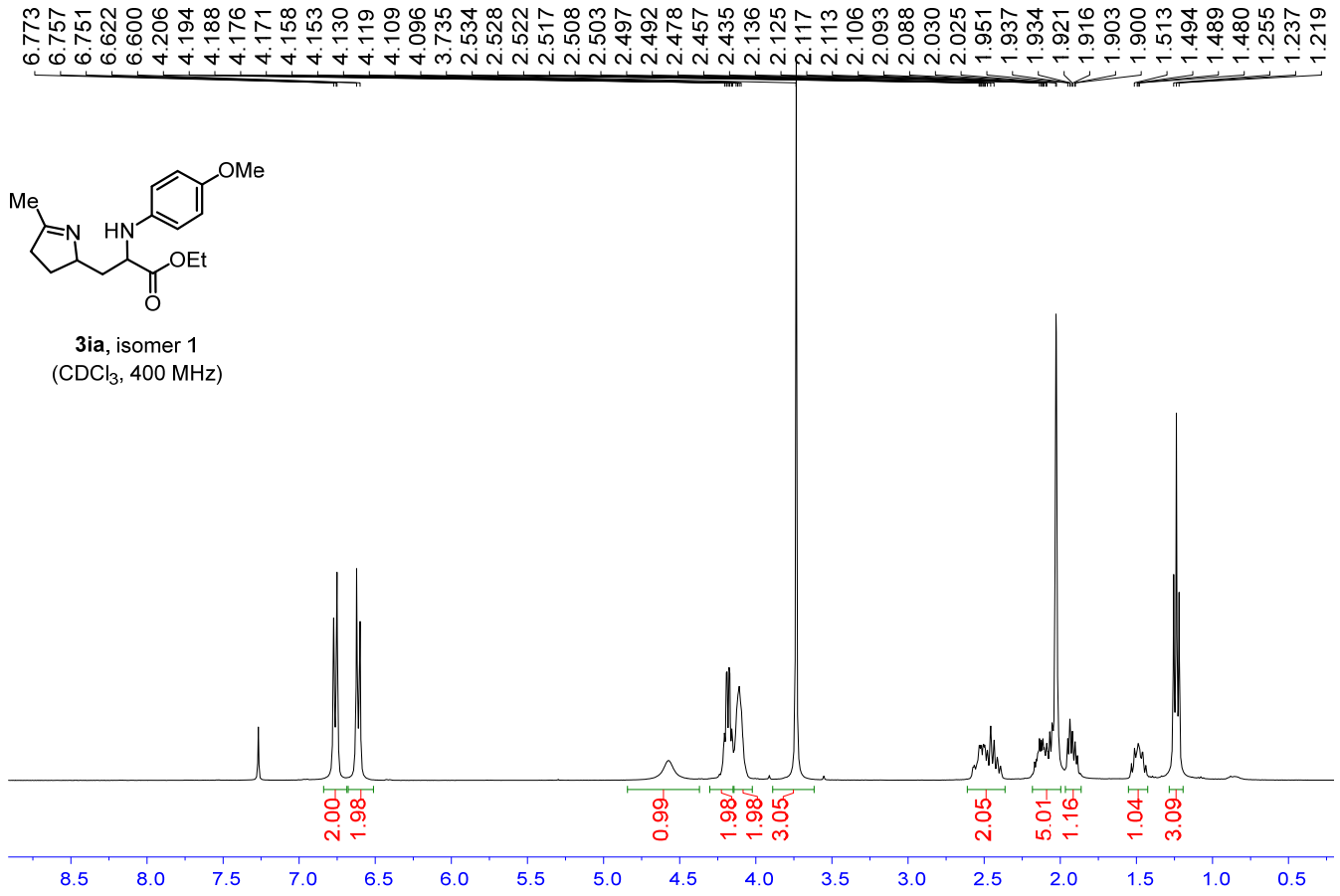
3ha, isomer 1
($CDCl_3$, 100 MHz)



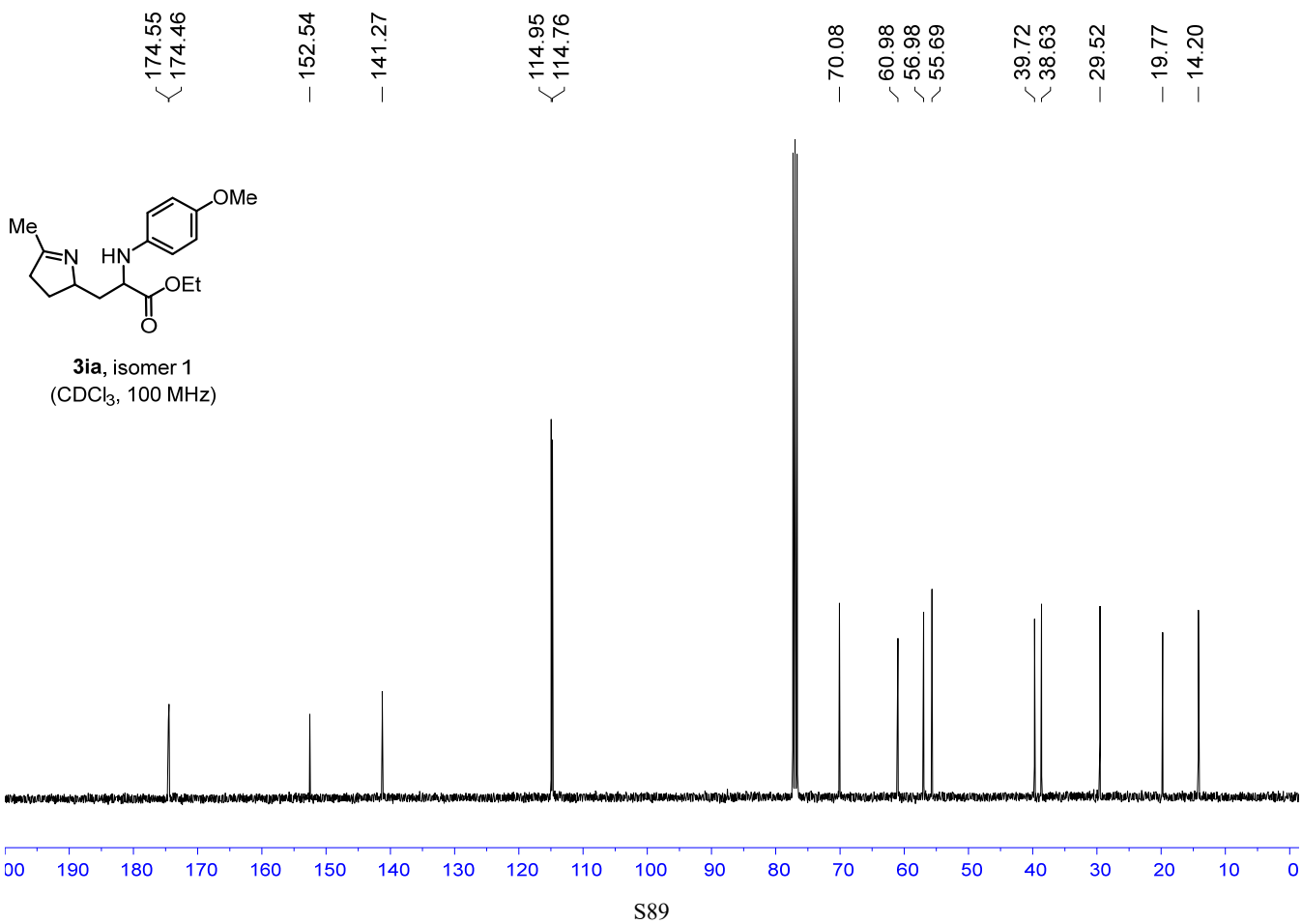
3ha, isomer 2 + 3
dr = 2.4:1
($CDCl_3$, 400 MHz)



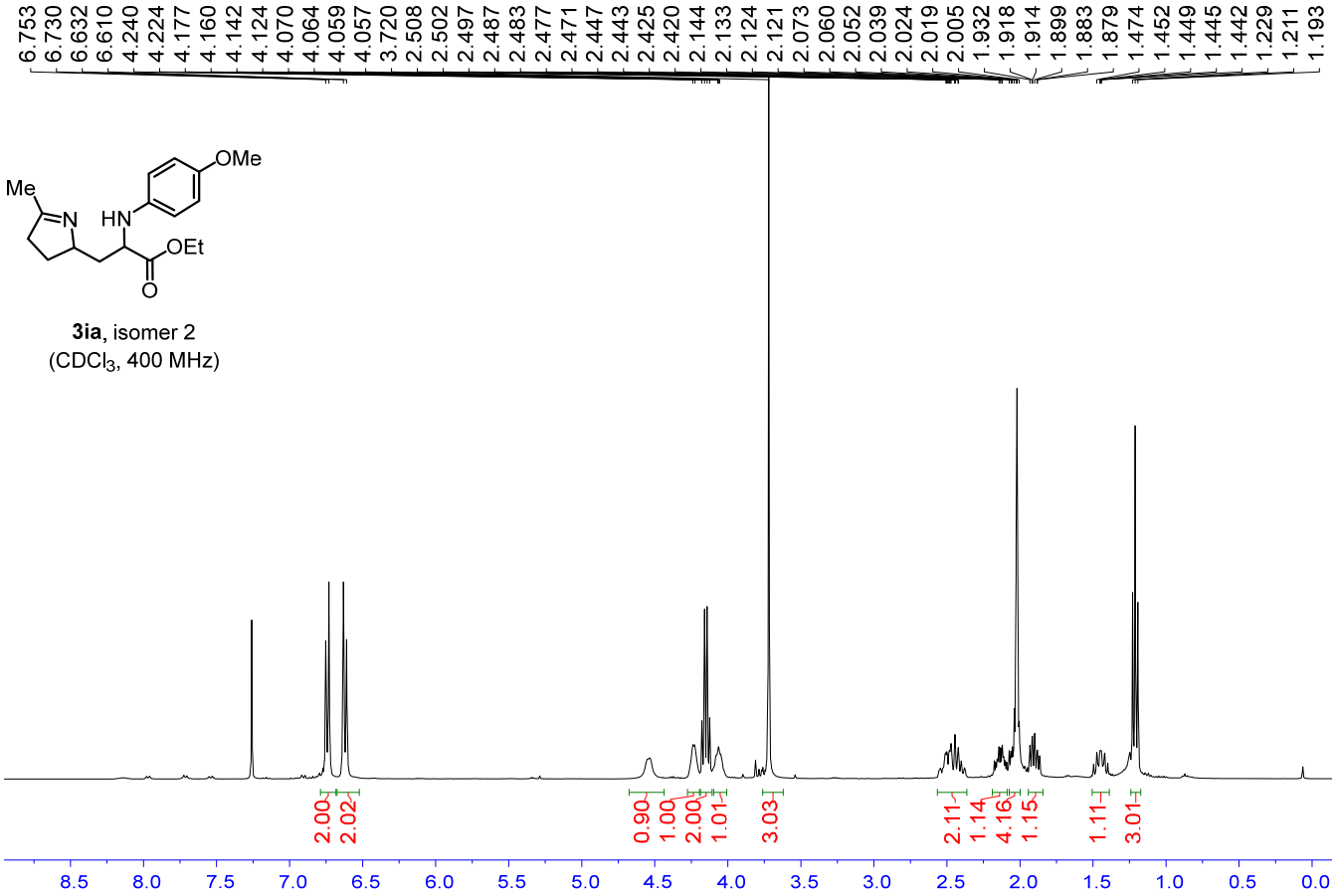
3ha, isomer 2 + 3
dr = 2.4:1
($CDCl_3$, 100 MHz)



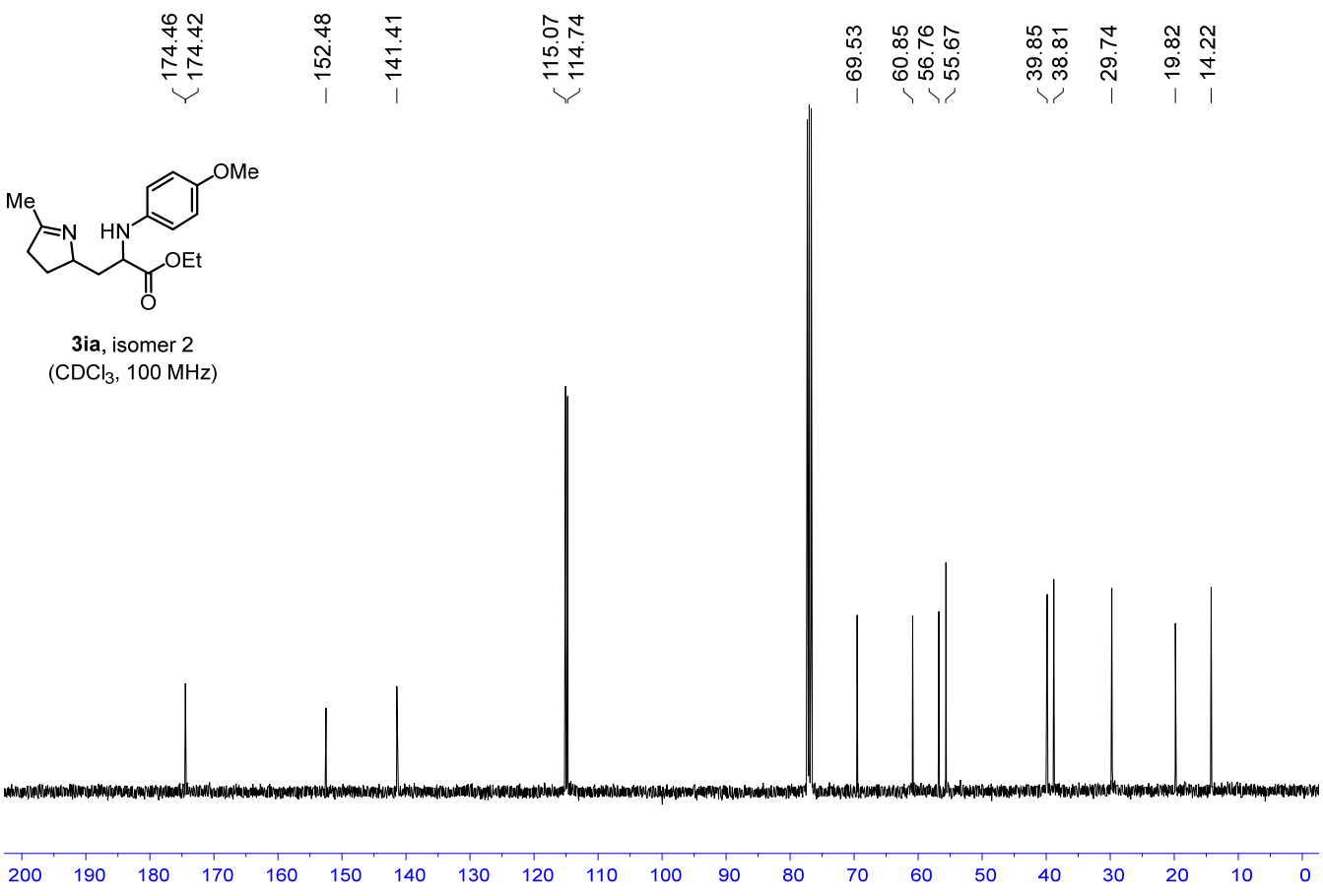
3ia, isomer 1
($CDCl_3$, 400 MHz)



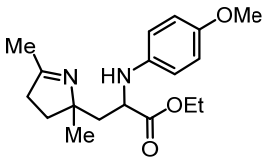
3ia, isomer 1
($CDCl_3$, 100 MHz)



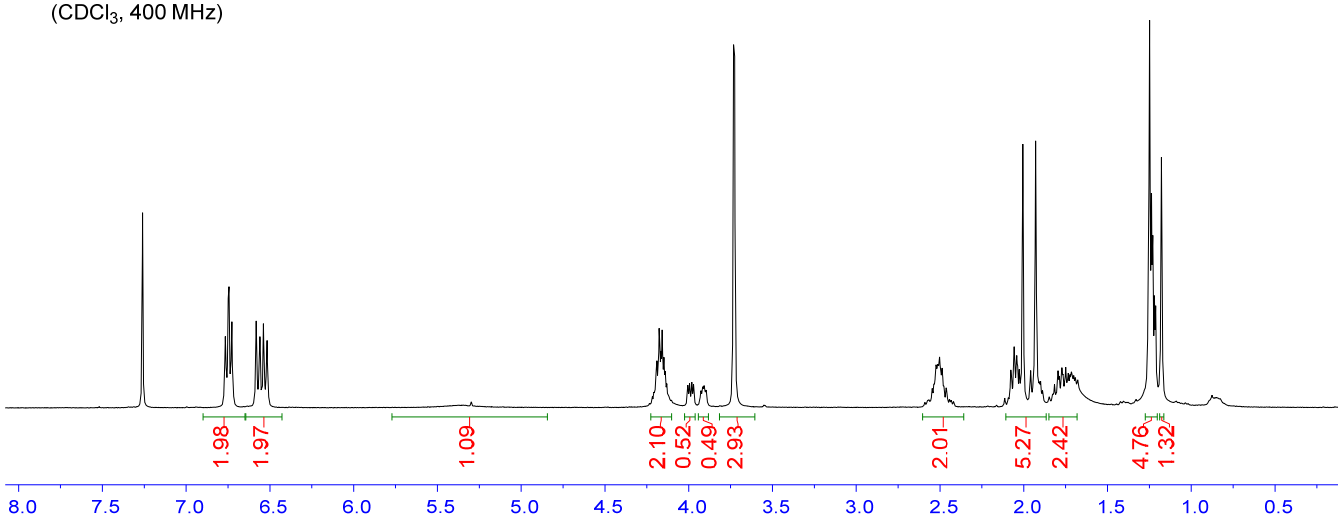
3ia, isomer 2
($CDCl_3$, 400 MHz)

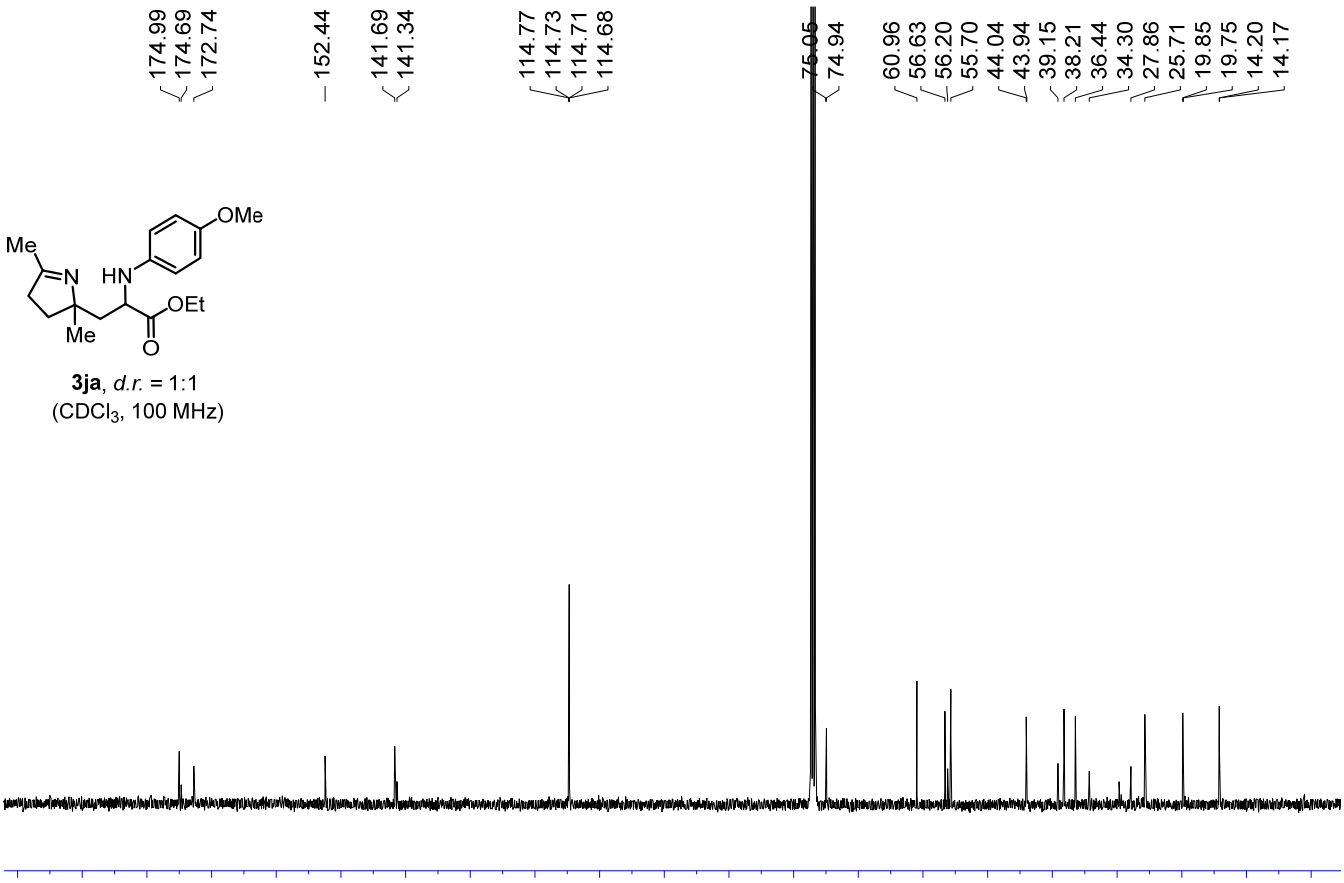


3ia, isomer 2
($CDCl_3$, 100 MHz)

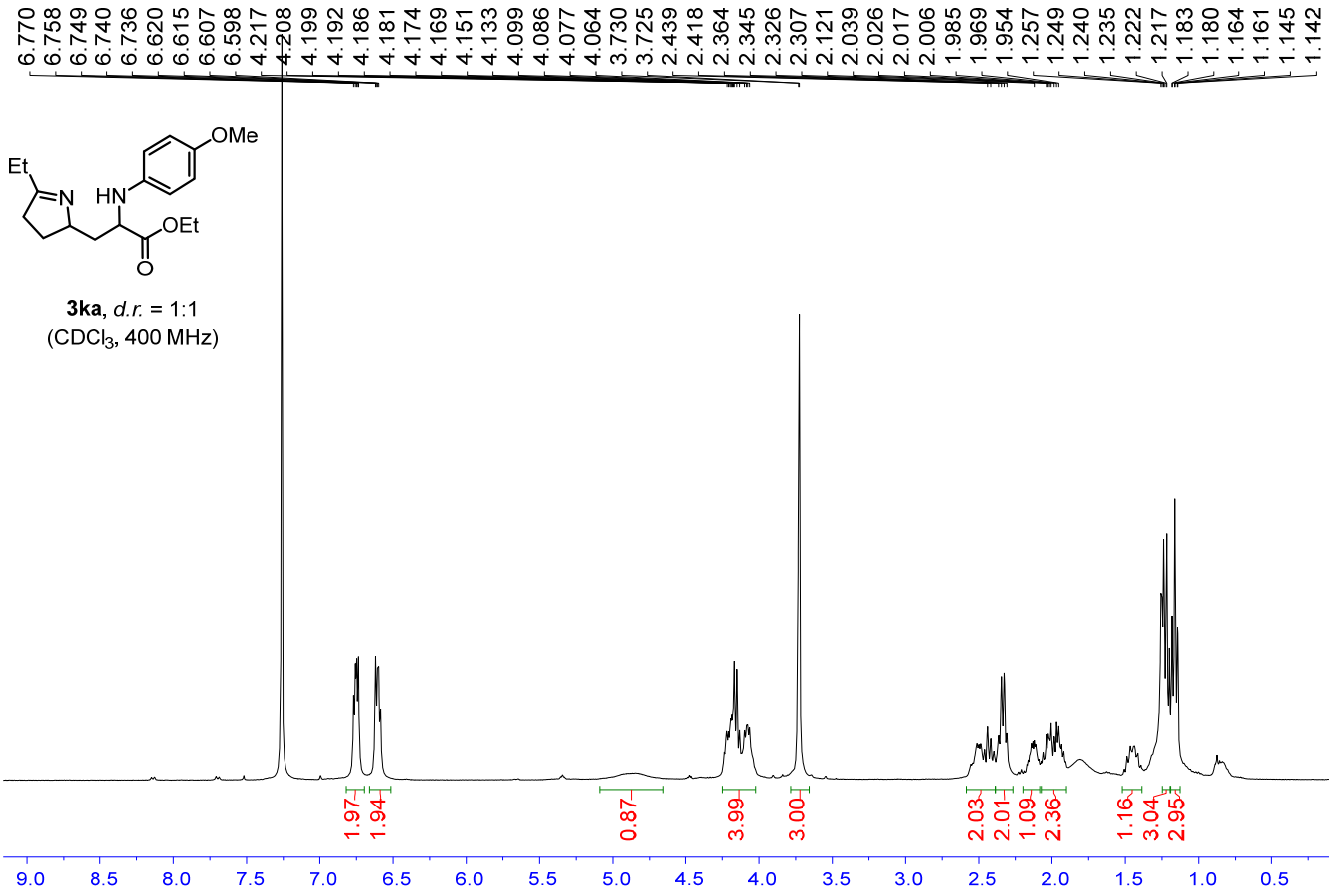


3ja, *d.r.* = 1:1
($CDCl_3$, 400 MHz)

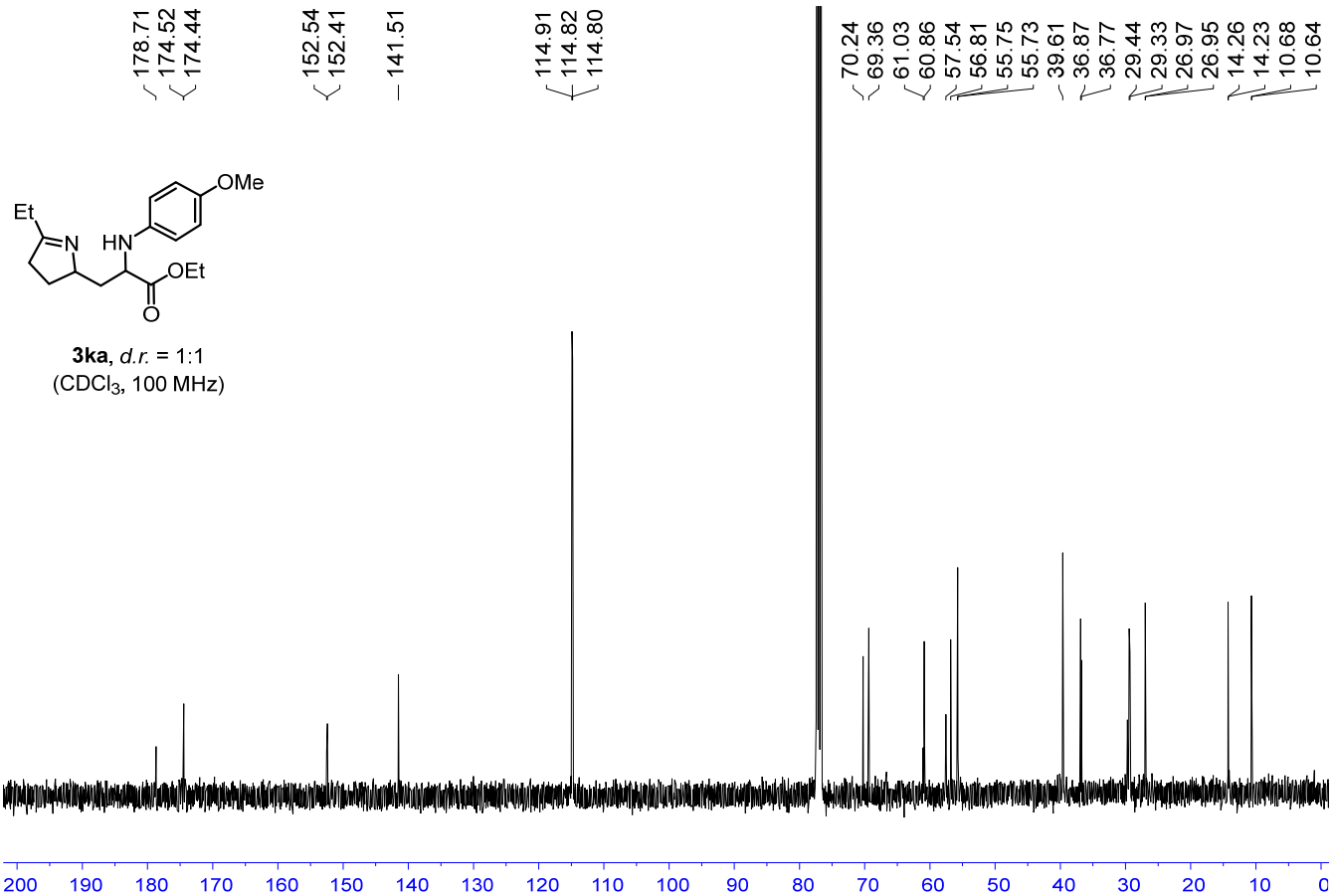




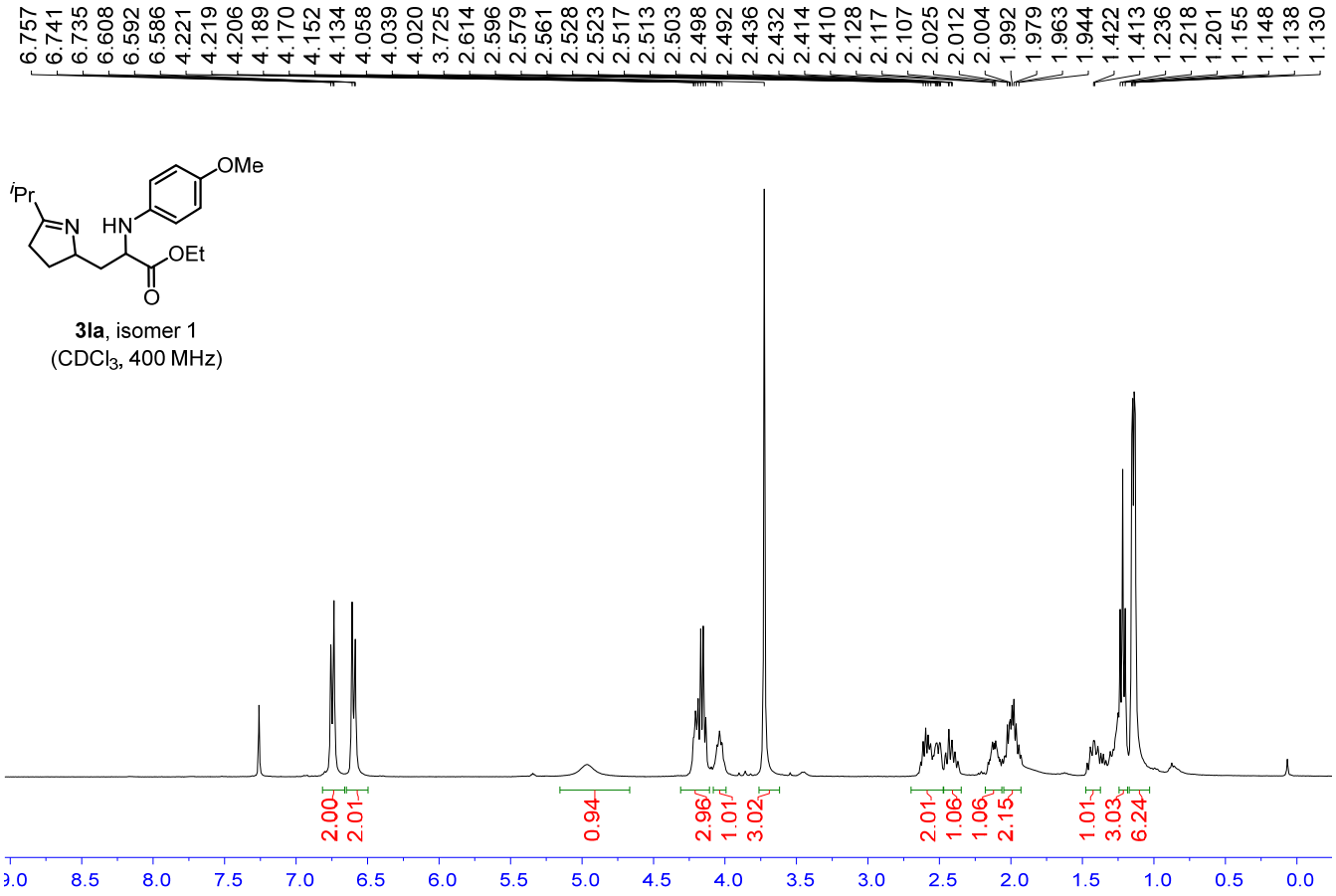
3ja, *d.r.* = 1:1
($CDCl_3$, 100 MHz)

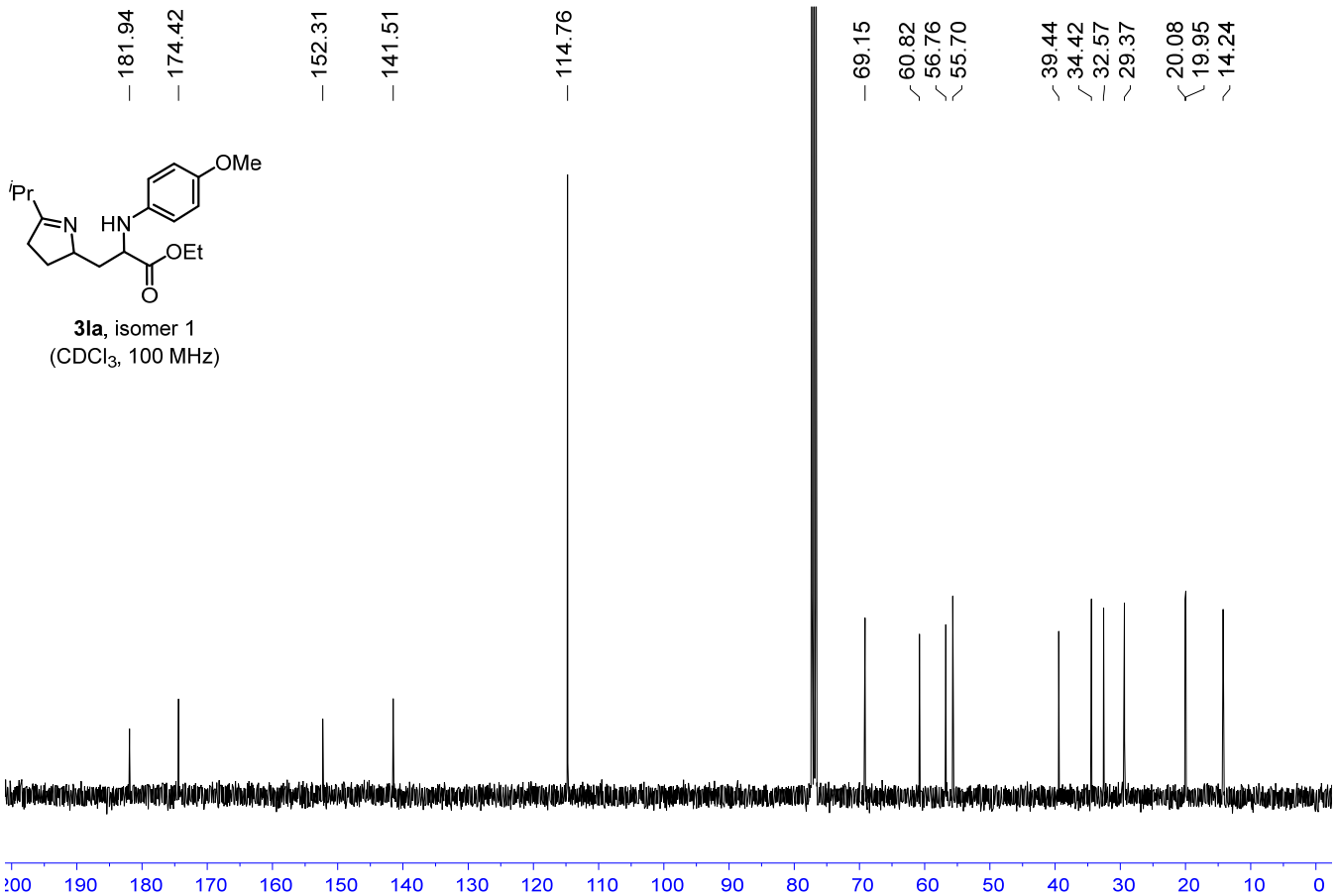


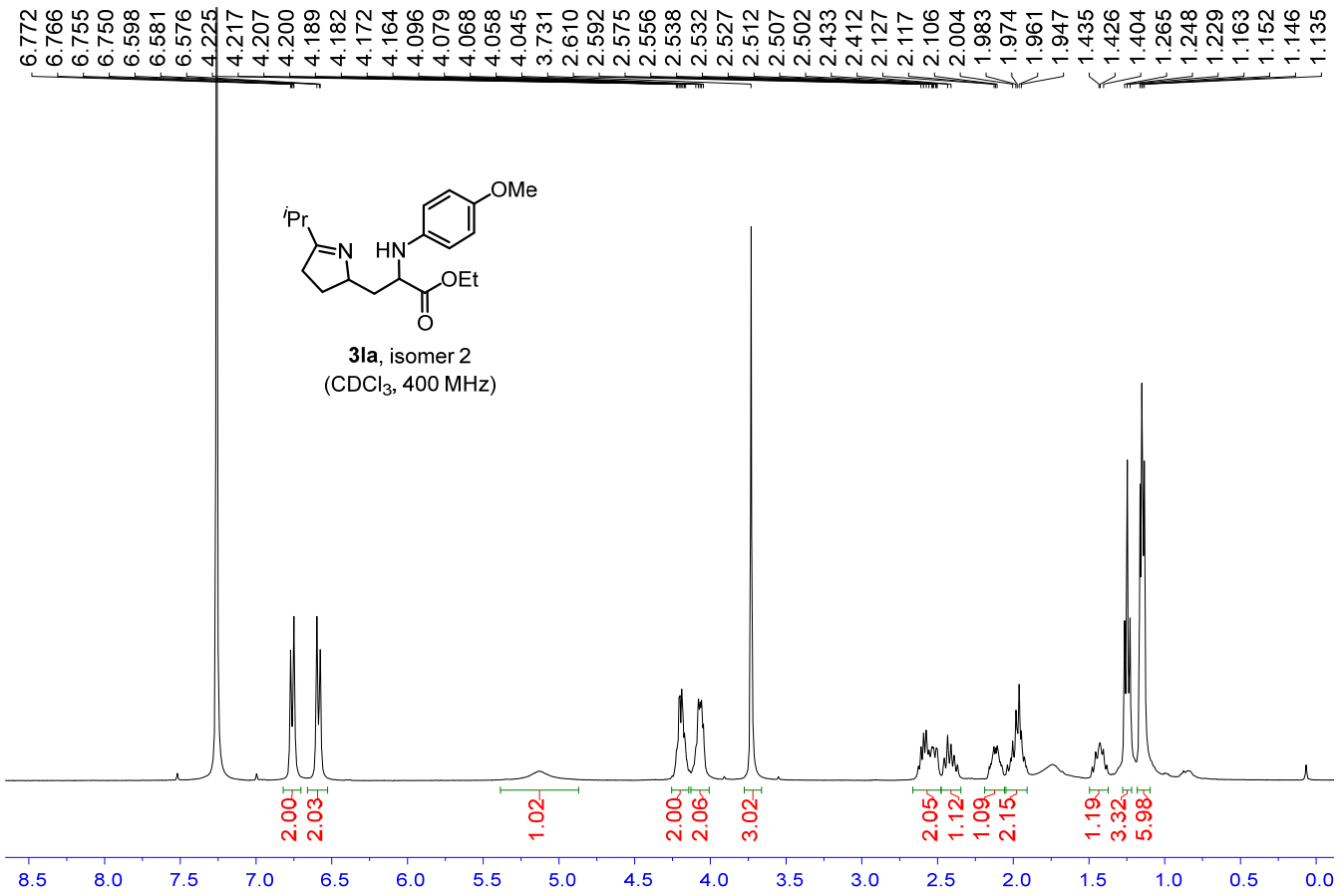
3ka, *d.r.* = 1:1
($CDCl_3$, 400 MHz)



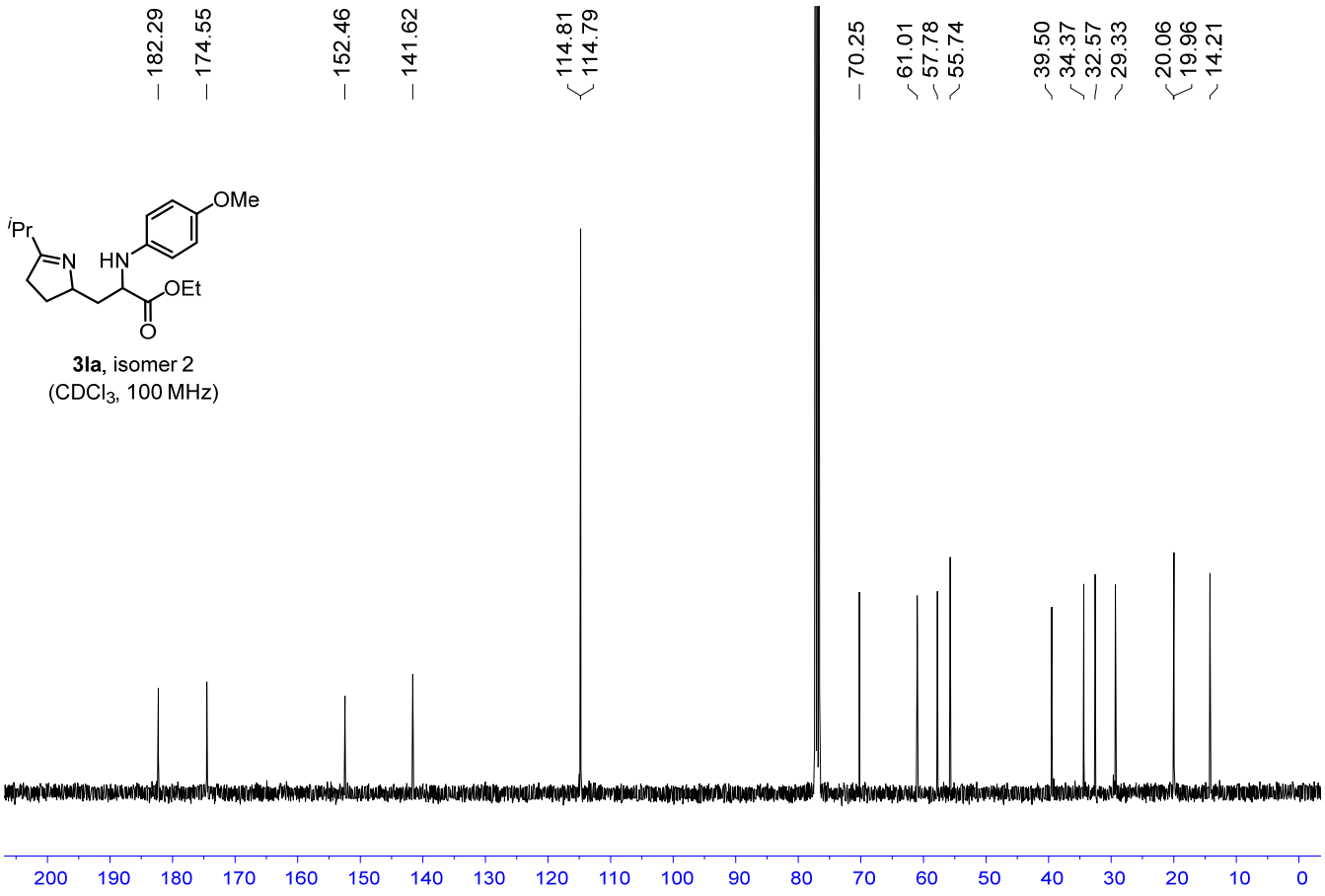
3ka, *d.r.* = 1:1
($CDCl_3$, 100 MHz)


6.757
6.741
6.735
6.608
6.592
6.586
4.221
4.219
4.206
4.189
4.170
4.152
4.134
4.058
4.039
4.020
3.725
2.614
2.596
2.579
2.561
2.528
2.523
2.517
2.513
2.503
2.498
2.492
2.436
2.432
2.414
2.410
2.128
2.117
2.107
2.025
2.012
2.004
1.992
1.979
1.963
1.944
1.422
1.413
1.236
1.218
1.201
1.155
1.148
1.138
1.130
OMe
iPr
N
HN
OEt
O
3la, isomer 1
(CDCl3, 400 MHz)
2.00
2.01
0.94
2.96
1.01
3.02
2.01
1.06
1.06
2.15
1.01
3.03
6.24
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

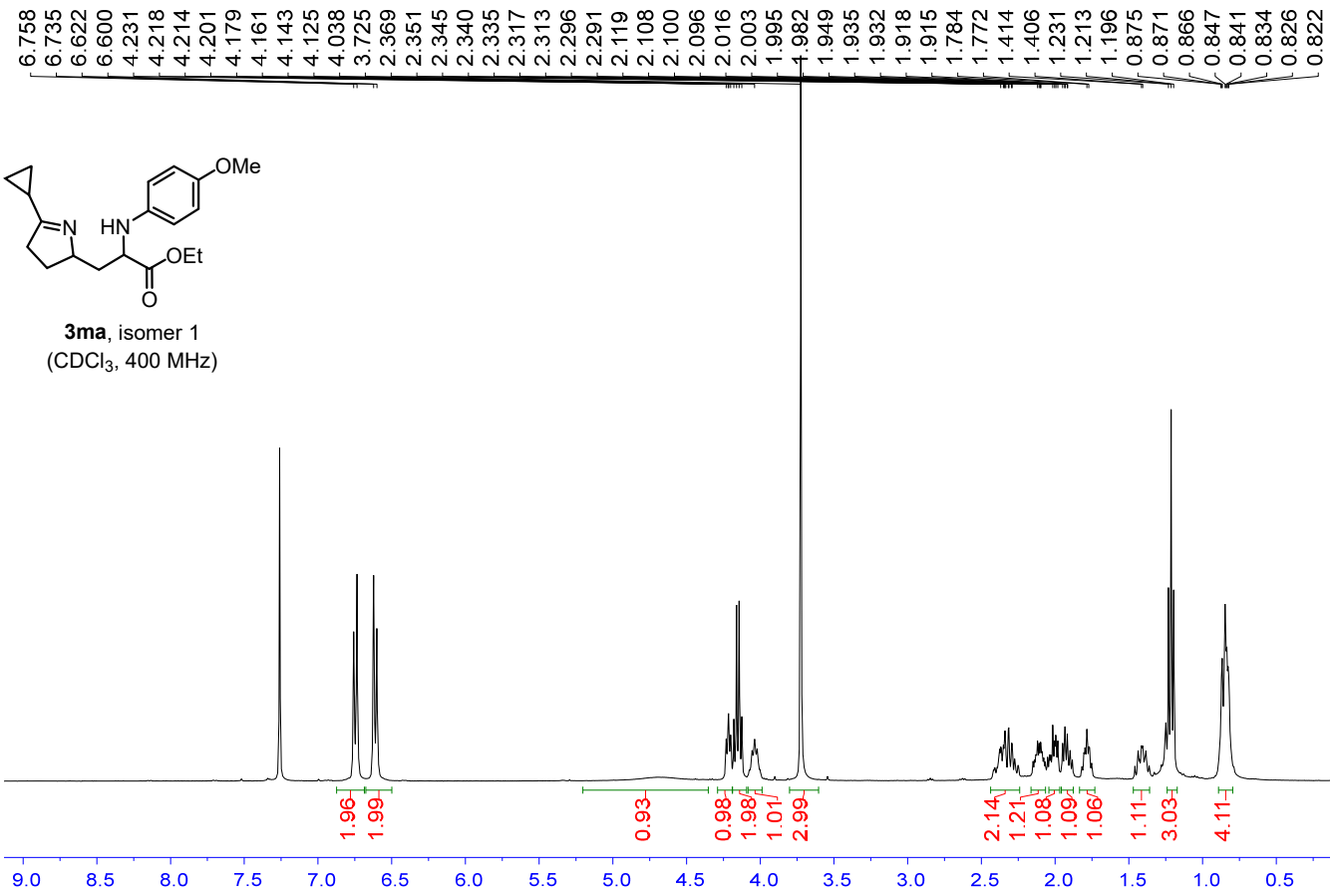

181.94
174.42
152.31
141.51
114.76
69.15
60.82
56.76
55.70
39.44
34.42
32.57
29.37
20.08
19.95
14.24
OMe
iPr
N
HN
OEt
O
3la, isomer 1
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



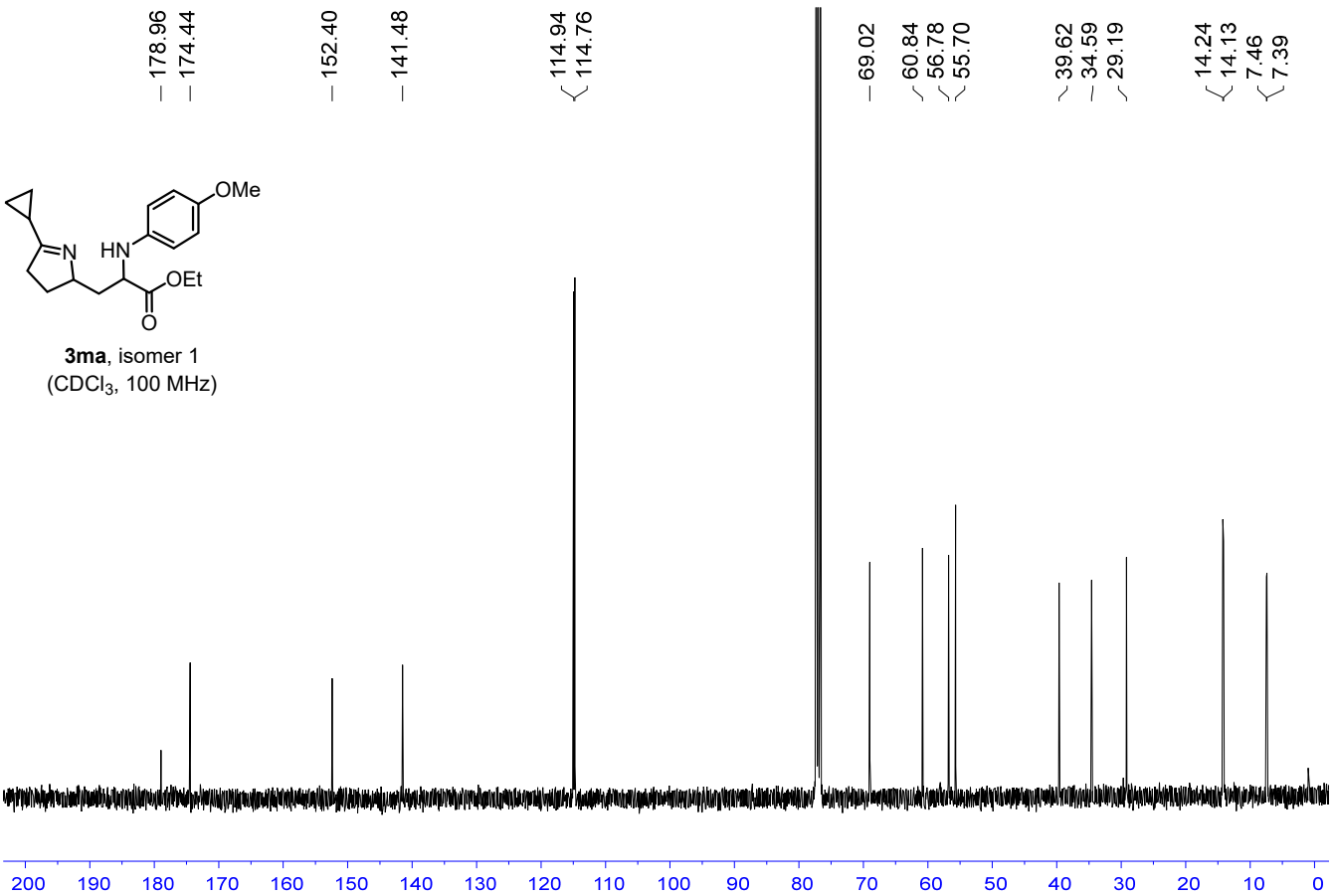
3la, isomer 2
($CDCl_3$, 400 MHz)



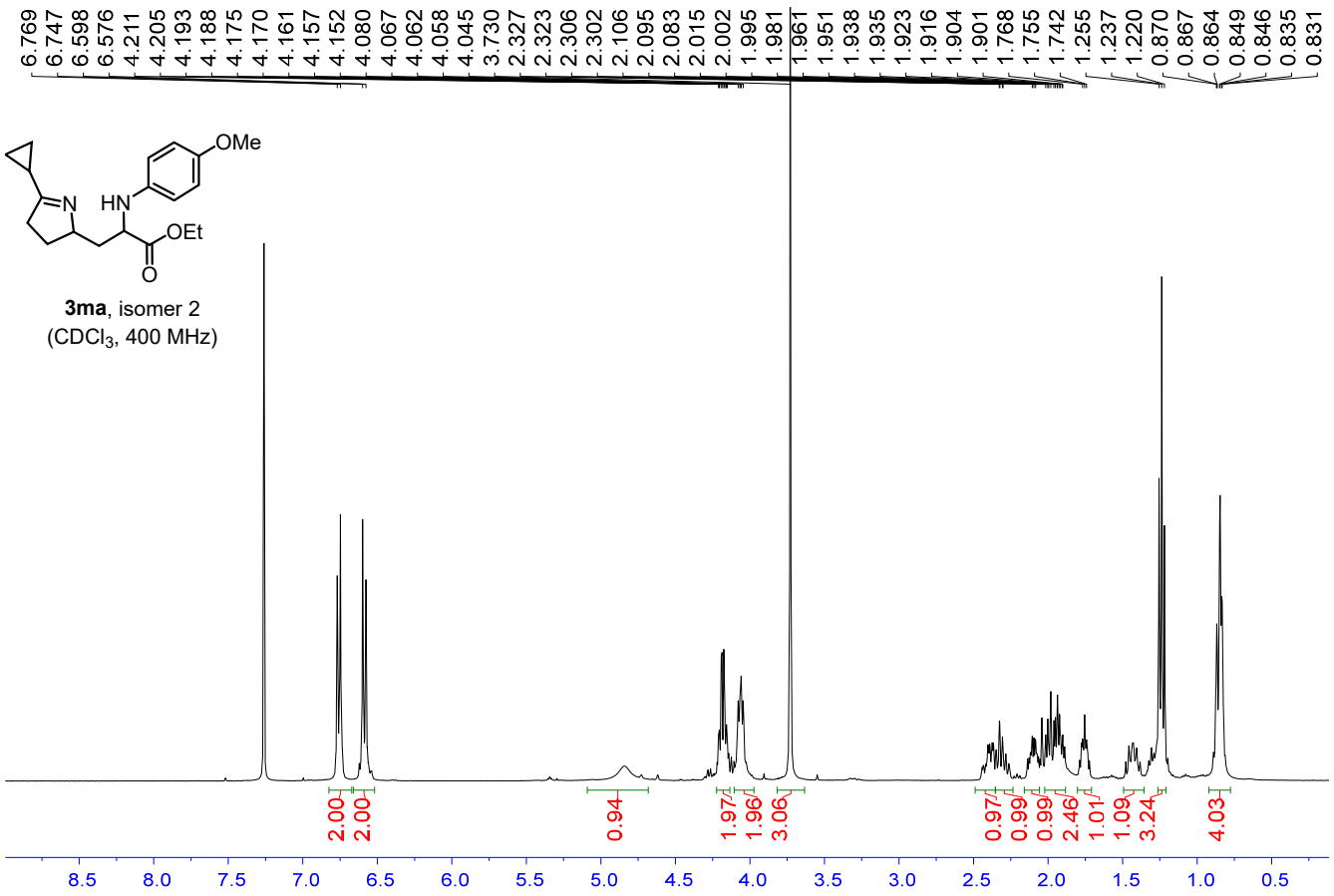
3la, isomer 2
($CDCl_3$, 100 MHz)



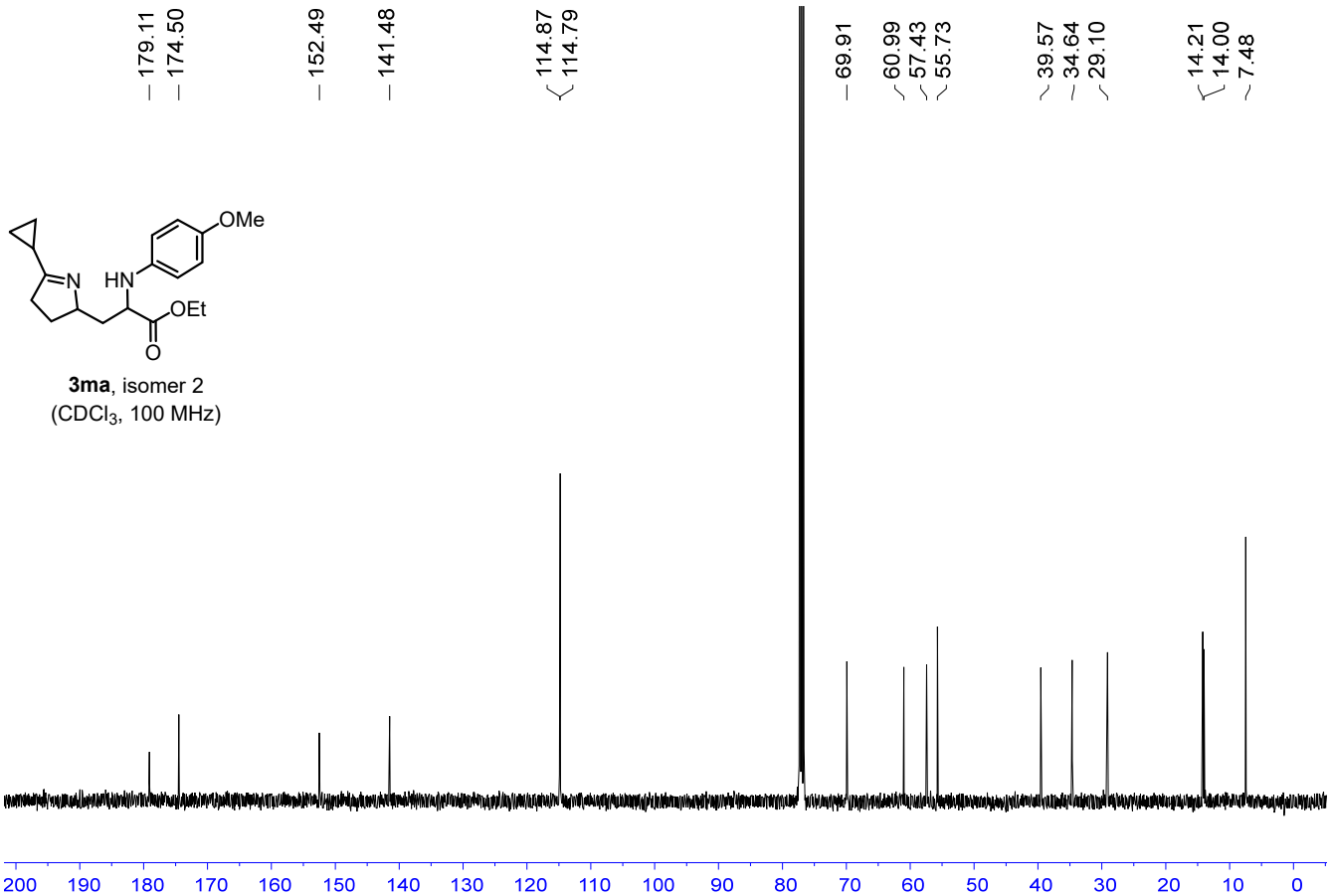
3ma, isomer 1
($CDCl_3$, 400 MHz)



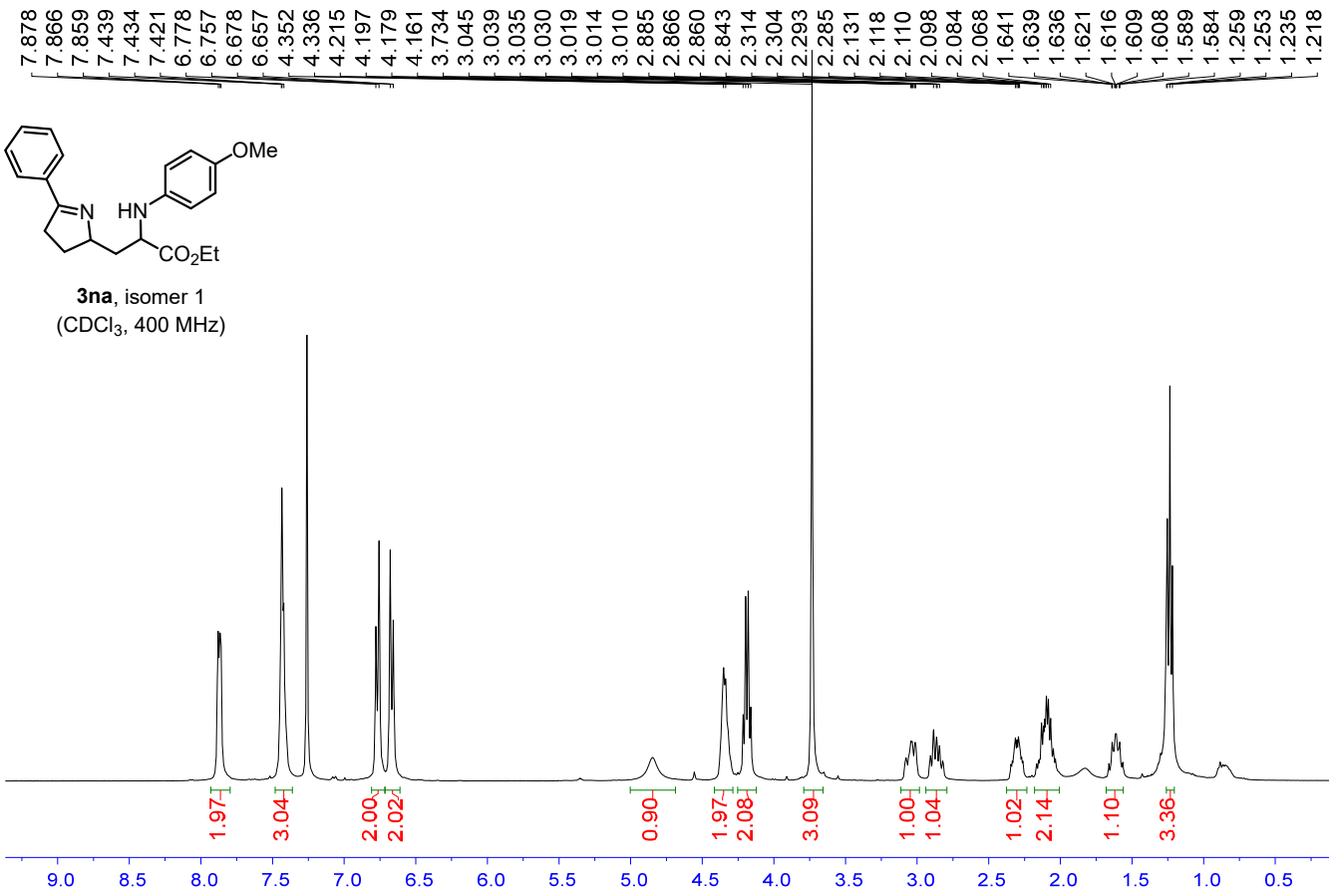
3ma, isomer 1
($CDCl_3$, 100 MHz)

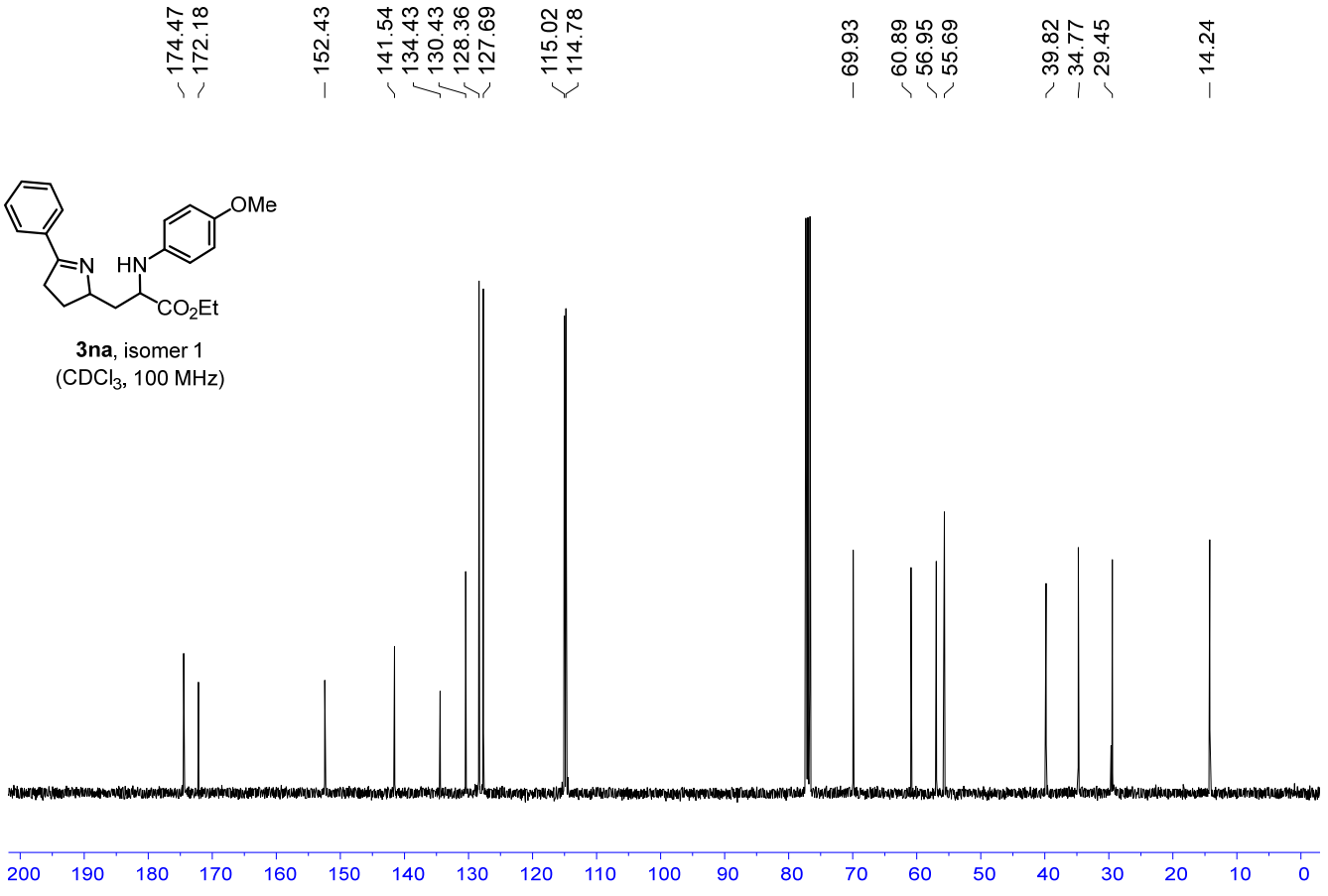


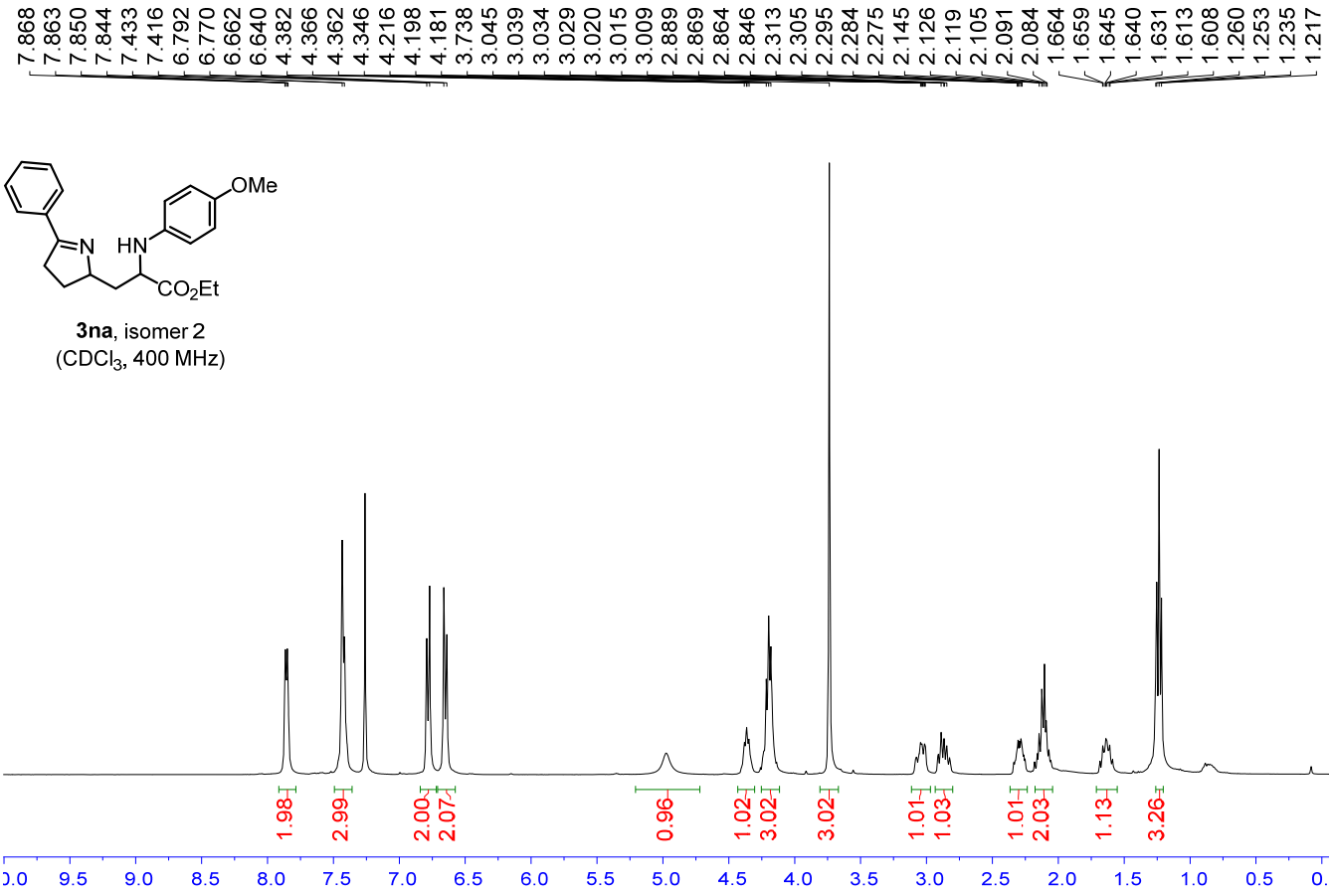
3ma, isomer 2
($CDCl_3$, 400 MHz)

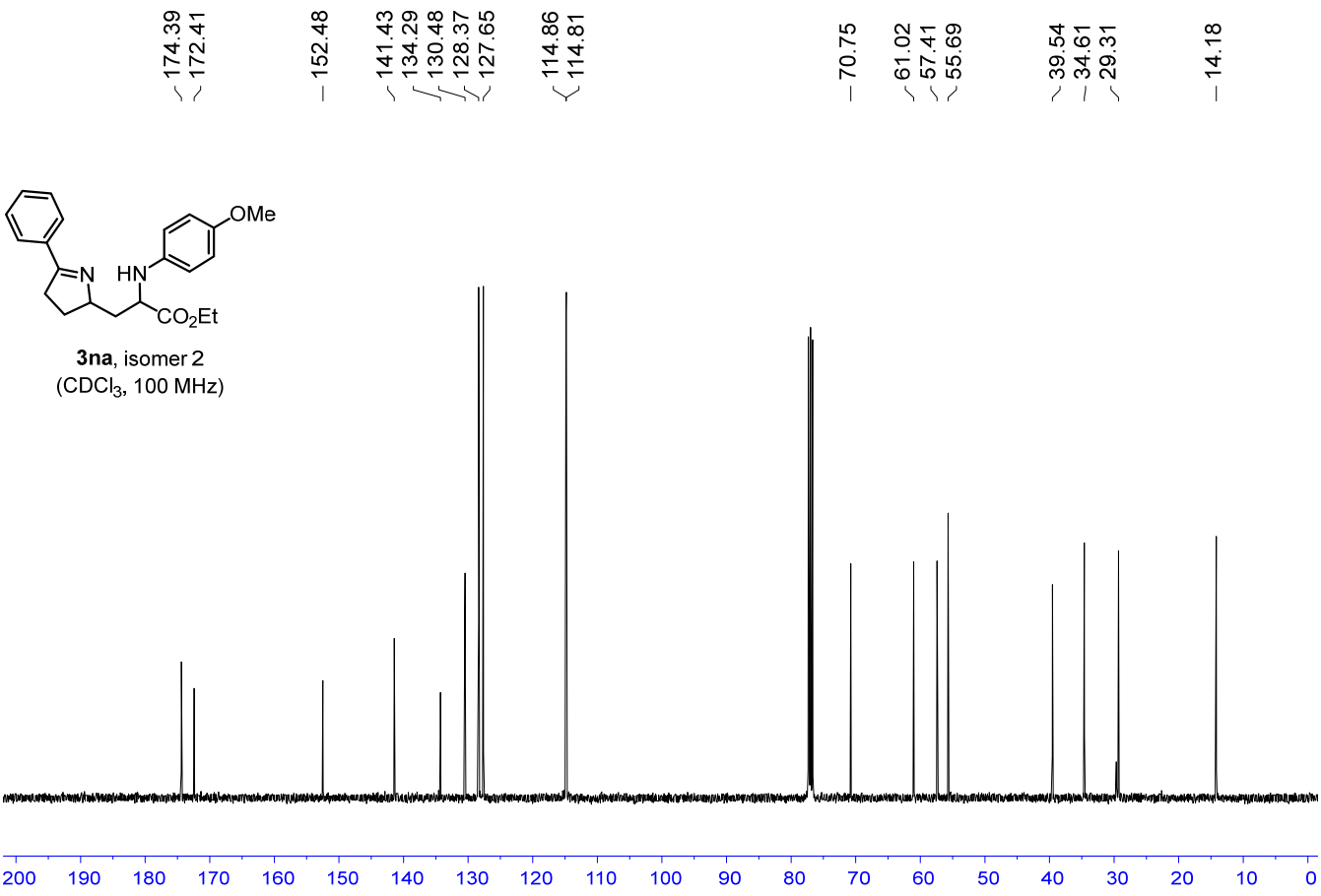


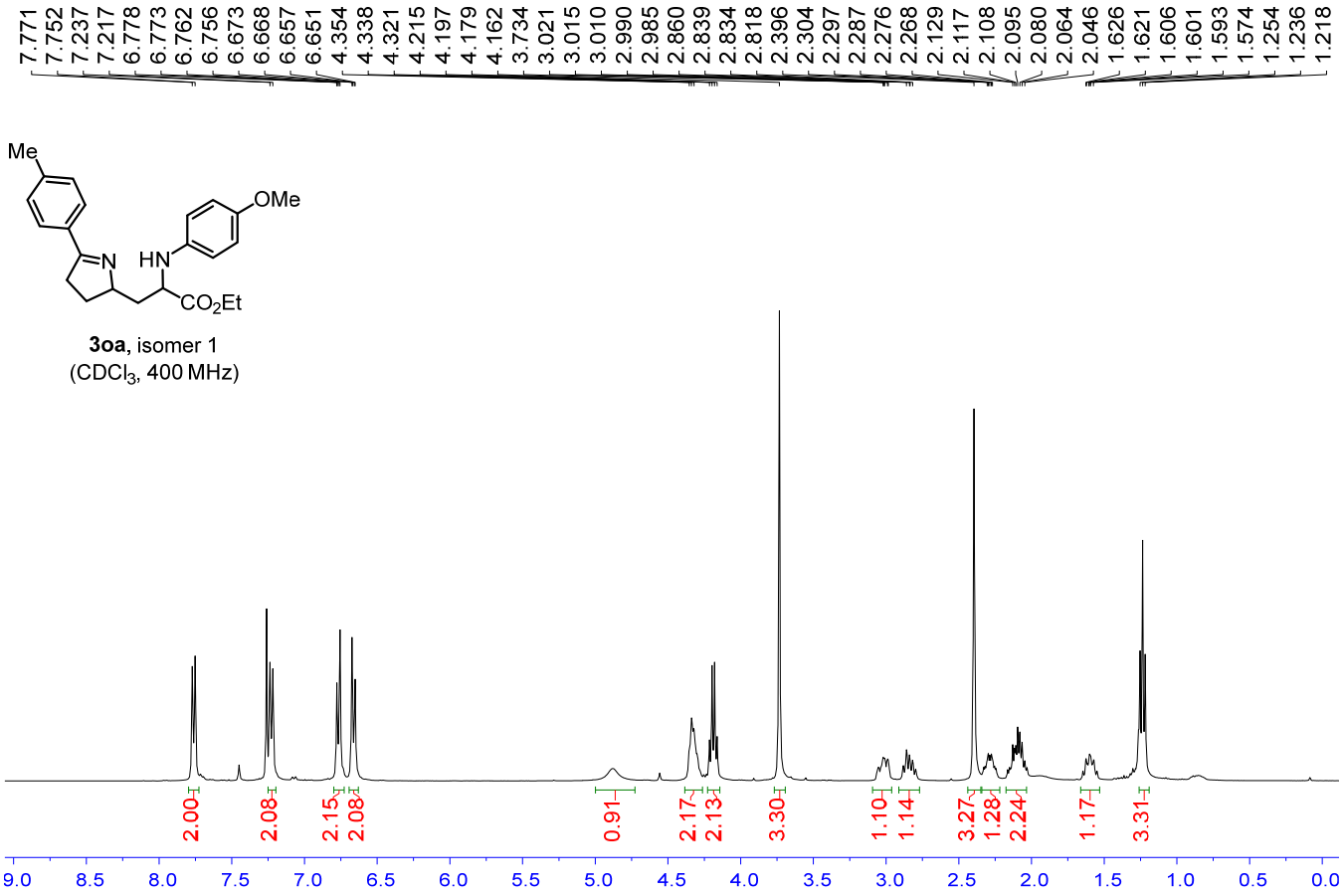
3ma, isomer 2
($CDCl_3$, 100 MHz)

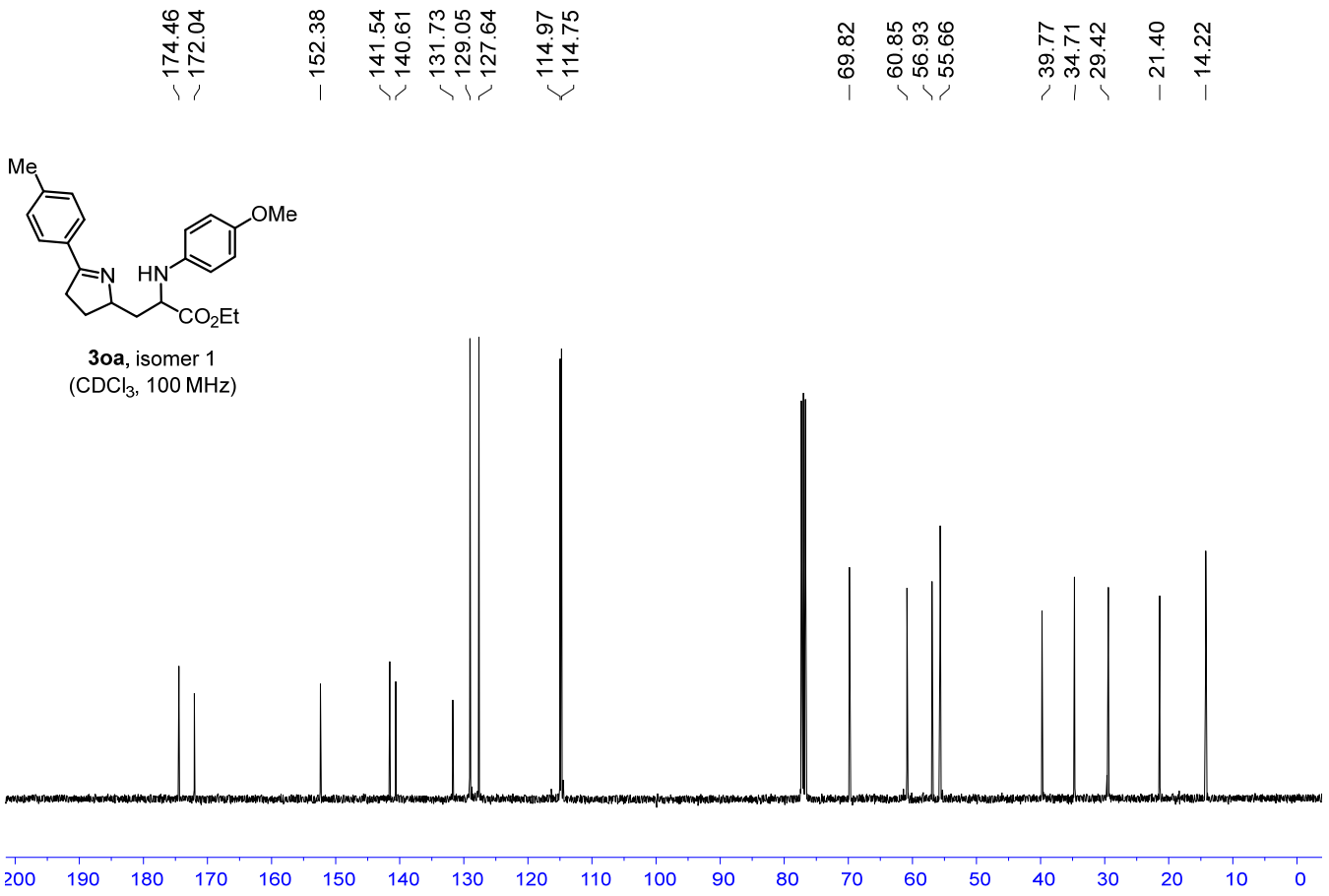

7.878
7.866
7.859
7.439
7.434
7.421
6.778
6.757
6.678
6.657
4.352
4.336
4.215
4.197
4.179
4.161
3.734
3.045
3.039
3.035
3.030
3.019
3.014
3.010
2.885
2.866
2.860
2.843
2.314
2.304
2.293
2.285
2.131
2.118
2.110
2.098
2.084
2.068
1.641
1.639
1.636
1.621
1.616
1.609
1.608
1.589
1.584
1.259
1.253
1.235
1.218
OMe
N
HN
CO2Et
3na, isomer 1
(CDCl3, 400 MHz)
1.97
3.04
2.00
2.02
0.90
1.97
2.08
3.09
1.00
1.04
1.02
2.14
1.10
3.36
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

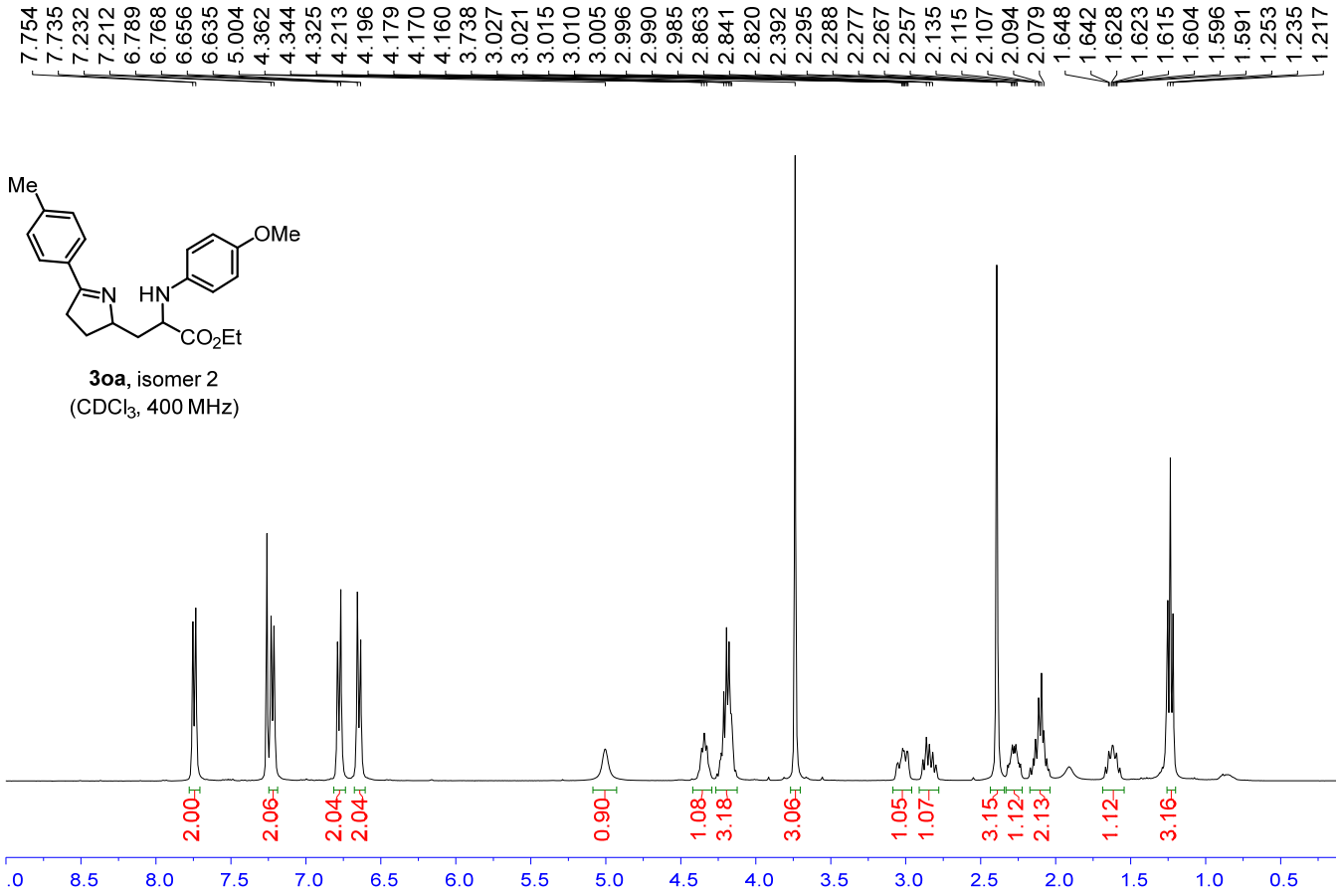

174.47
172.18
152.43
141.54
134.43
130.43
128.36
127.69
115.02
114.78
69.93
60.89
56.95
55.69
39.82
34.77
29.45
14.24
OMe
N
HN
CO2Et
3na, isomer 1
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

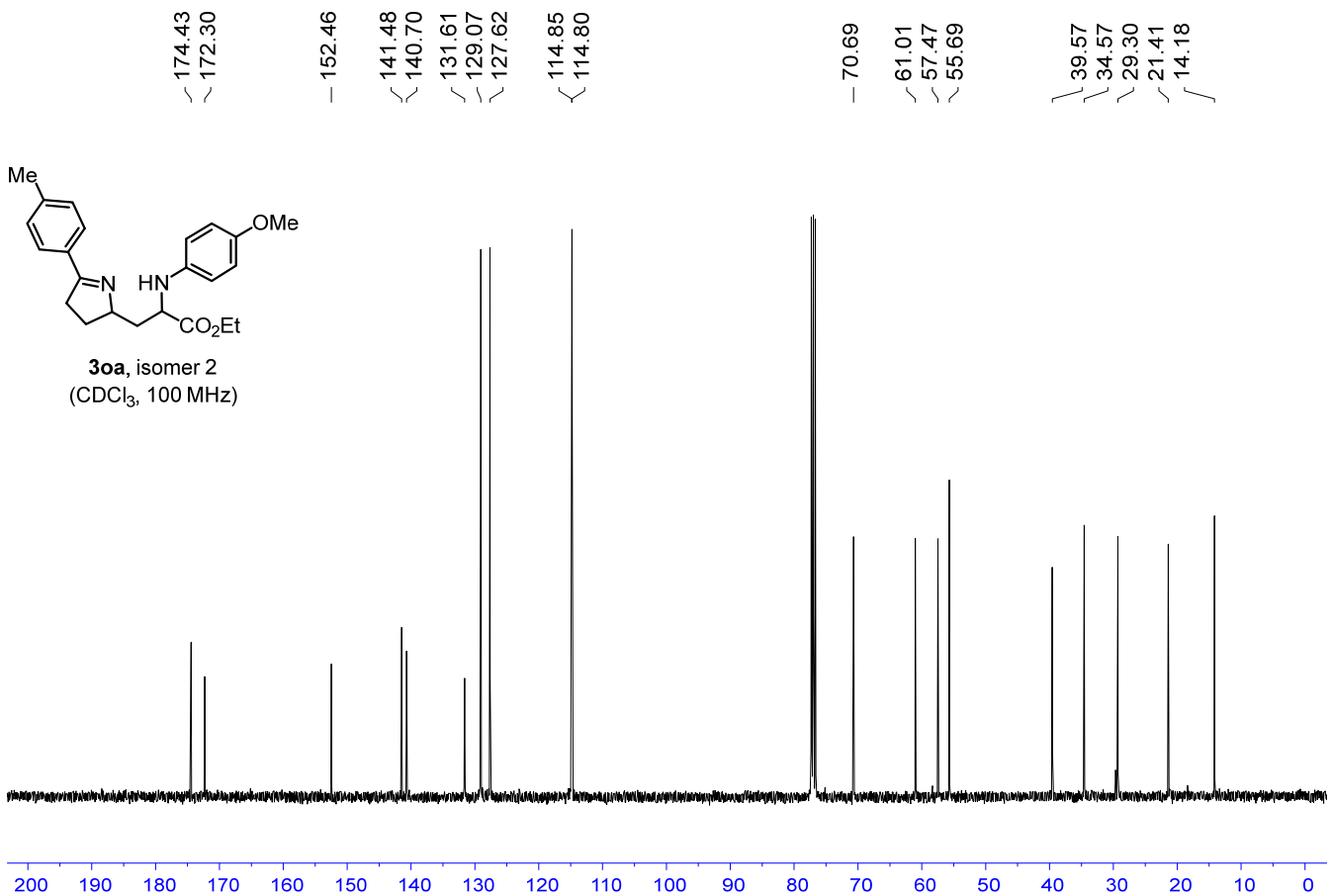

7.868
7.863
7.850
7.844
7.433
7.416
6.792
6.770
6.662
6.640
4.382
4.366
4.362
4.346
4.216
4.198
4.181
3.738
3.045
3.039
3.034
3.029
3.020
3.015
3.009
2.889
2.869
2.864
2.846
2.313
2.305
2.295
2.284
2.275
2.145
2.126
2.119
2.105
2.091
2.084
1.664
1.659
1.645
1.640
1.631
1.613
1.608
1.260
1.253
1.235
1.217
OMe
N
HN
CO2Et
3na, isomer 2
(CDCl3, 400 MHz)
1.98
2.99
2.00
2.07
0.96
1.02
3.02
3.02
1.01
1.03
1.01
2.03
1.13
3.26
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

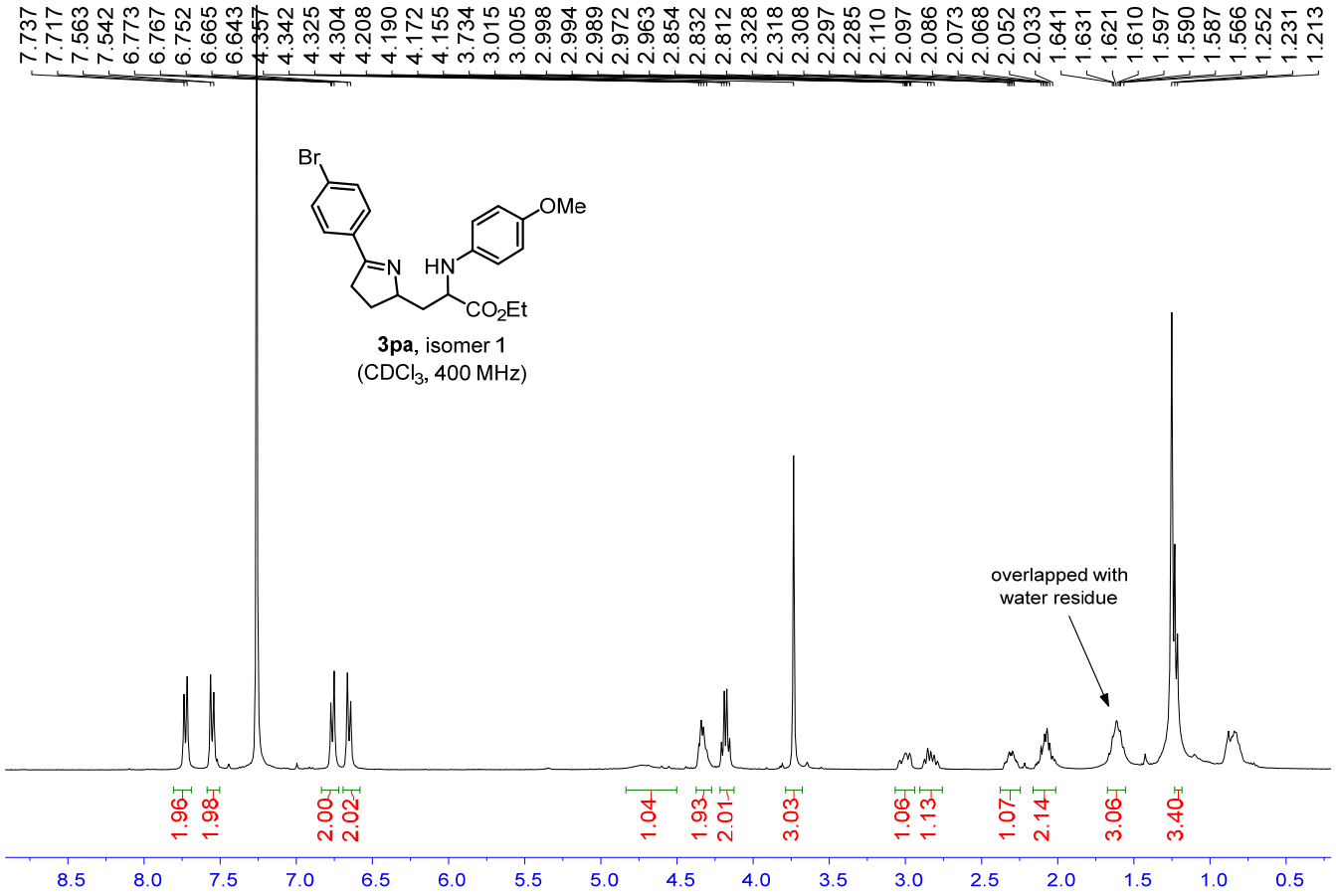

174.39
172.41
152.48
141.43
134.29
130.48
128.37
127.65
114.86
114.81
70.75
61.02
57.41
55.69
39.54
34.61
29.31
14.18
OMe
N
HN
CO2Et
3na, isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

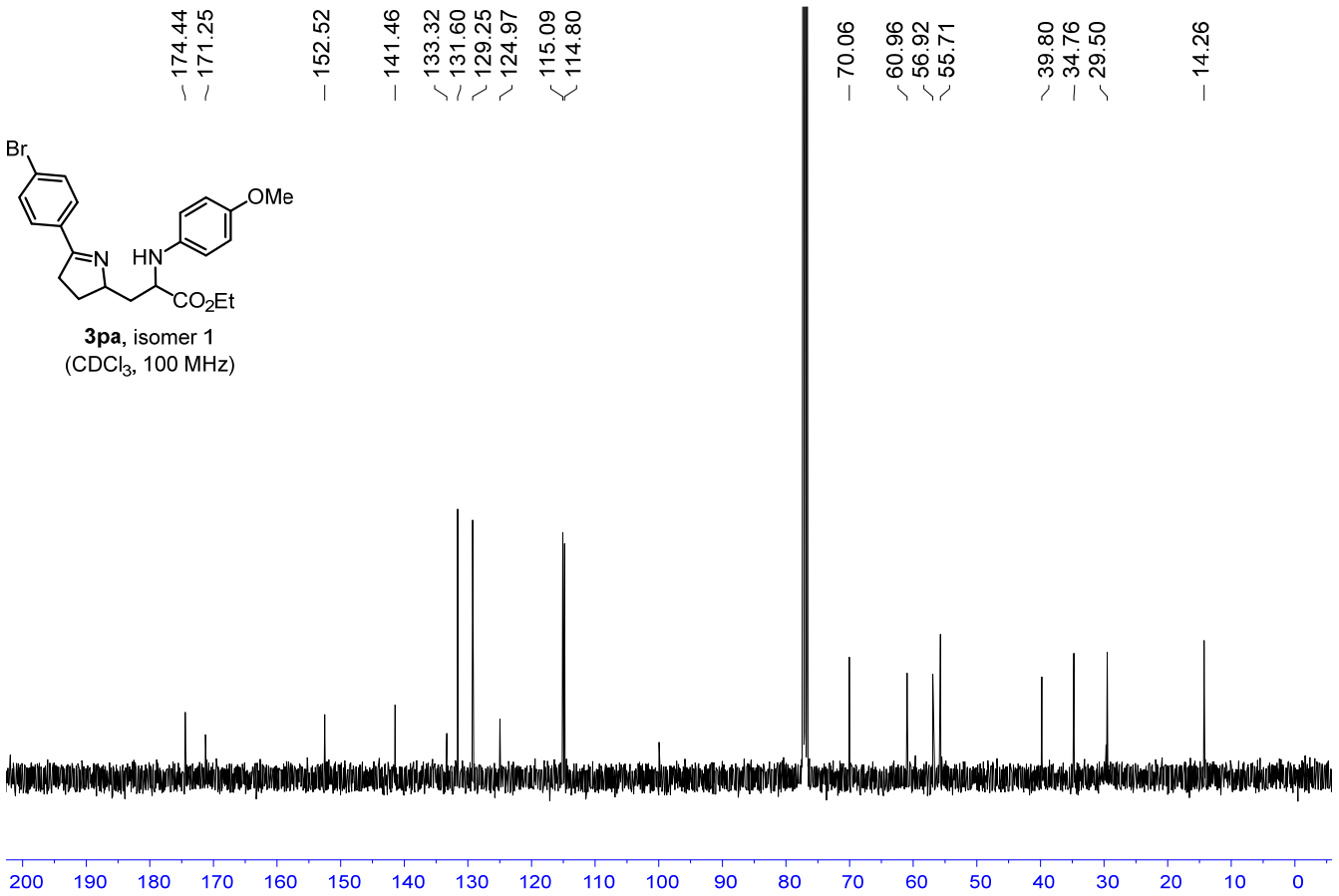

7.771
7.752
7.237
7.217
6.778
6.773
6.762
6.756
6.673
6.668
6.657
6.651
4.354
4.338
4.321
4.215
4.197
4.179
4.162
3.734
3.021
3.015
3.010
2.990
2.985
2.860
2.839
2.834
2.818
2.396
2.304
2.297
2.287
2.276
2.268
2.129
2.117
2.108
2.095
2.080
2.064
2.046
1.626
1.621
1.606
1.601
1.593
1.574
1.254
1.236
1.218
Me
OMe
N
HN
CO2Et
3oa, isomer 1
(CDCl3, 400 MHz)
2.00
2.08
2.15
2.08
0.91
2.17
2.13
3.30
1.10
1.14
3.27
1.28
2.24
1.17
3.31
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

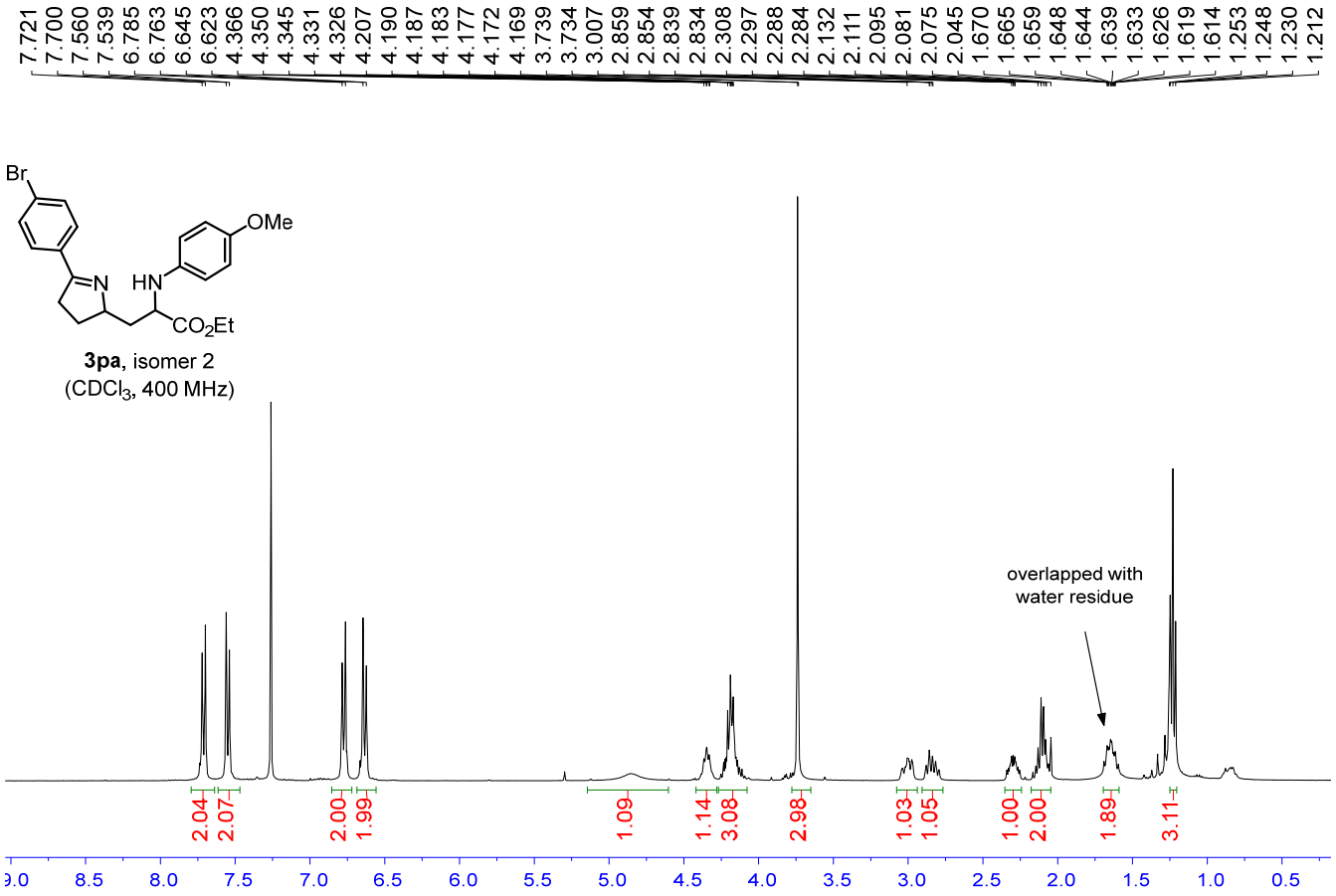

174.46
172.04
152.38
141.54
140.61
131.73
129.05
127.64
114.97
114.75
69.82
60.85
56.93
55.66
39.77
34.71
29.42
21.40
14.22
Me
OMe
N
HN
CO2Et
3oa, isomer 1
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

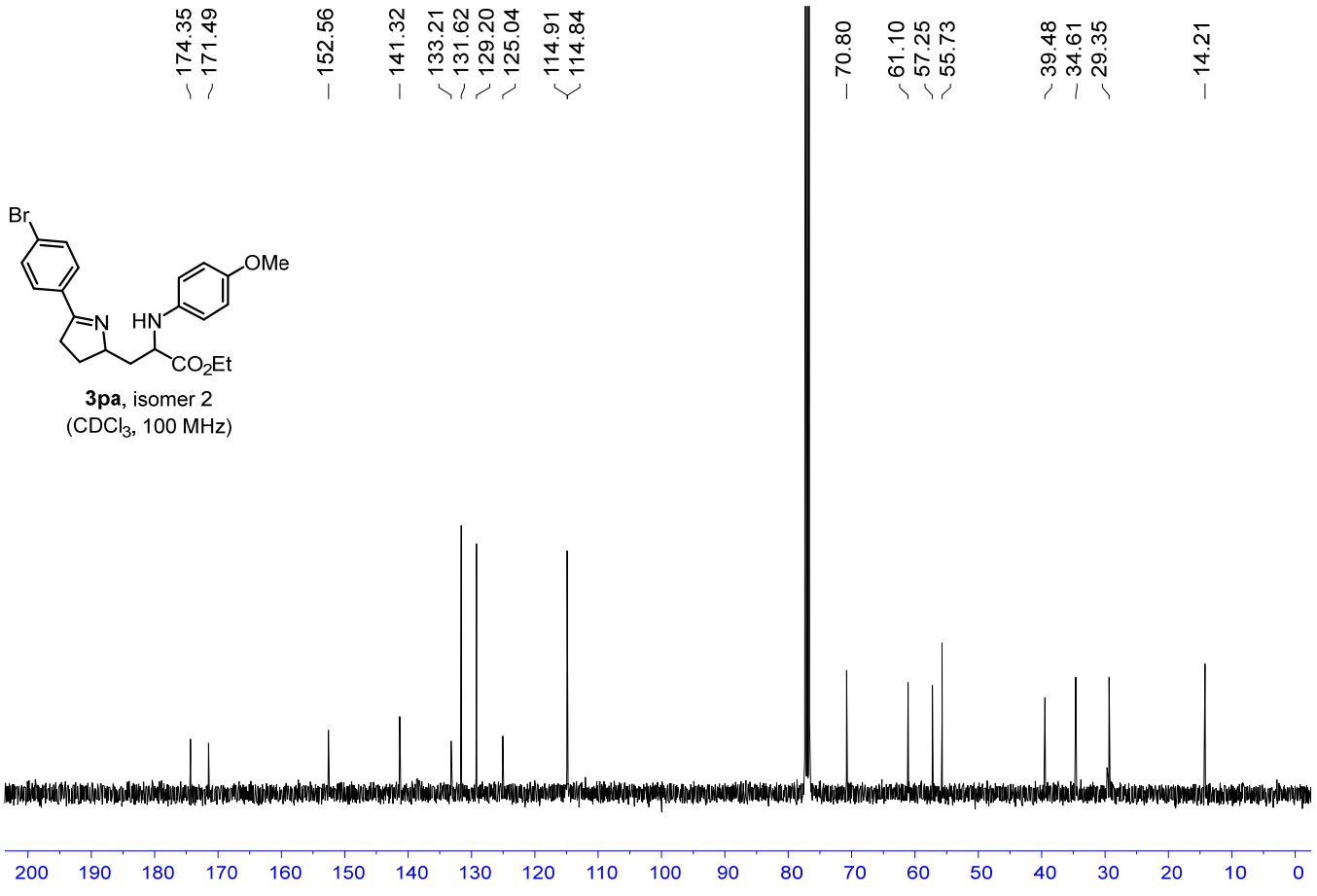

7.754
7.735
7.232
7.212
6.789
6.768
6.656
6.635
5.004
4.362
4.344
4.325
4.213
4.196
4.179
4.170
4.160
3.738
3.027
3.021
3.015
3.010
3.005
2.996
2.990
2.985
2.863
2.841
2.820
2.392
2.295
2.288
2.277
2.267
2.257
2.135
2.115
2.107
2.094
2.079
1.648
1.642
1.628
1.623
1.615
1.604
1.596
1.591
1.253
1.235
1.217
Me
OMe
N
HN
CO2Et
3oa, isomer 2
(CDCl3, 400 MHz)
2.00
2.06
2.04
2.04
0.90
1.08
3.18
3.06
1.05
1.07
3.15
1.12
2.13
1.12
3.16
.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

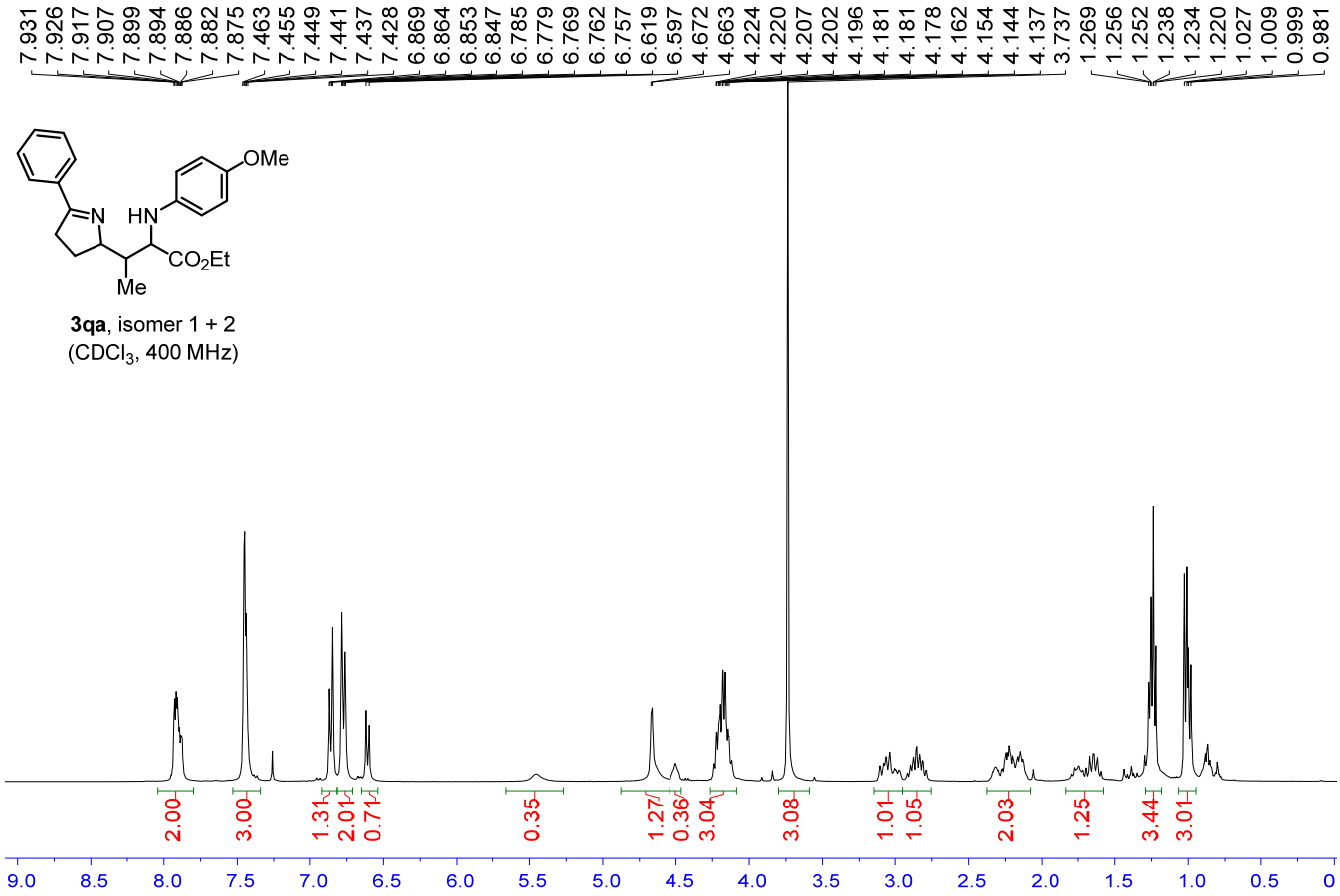

174.43
172.30
152.46
141.48
140.70
131.61
129.07
127.62
114.85
114.80
70.69
61.01
57.47
55.69
39.57
34.57
29.30
21.41
14.18
Me
OMe
N
HN
CO2Et
3oa, isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.737
7.717
7.563
7.542
6.773
6.767
6.752
6.665
6.643
4.357
4.342
4.325
4.304
4.208
4.190
4.172
4.155
3.734
3.015
3.005
2.998
2.994
2.989
2.972
2.963
2.854
2.832
2.812
2.328
2.318
2.308
2.297
2.285
2.110
2.097
2.086
2.073
2.068
2.052
2.033
1.641
1.631
1.621
1.610
1.597
1.590
1.587
1.566
1.252
1.231
1.213
Br
OMe
HN
N
CO2Et
3pa, isomer 1
(CDCl3, 400 MHz)
overlapped with
water residue
1.96
1.98
2.00
2.02
1.04
1.93
2.01
3.03
1.06
1.13
1.07
2.14
3.06
3.40
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

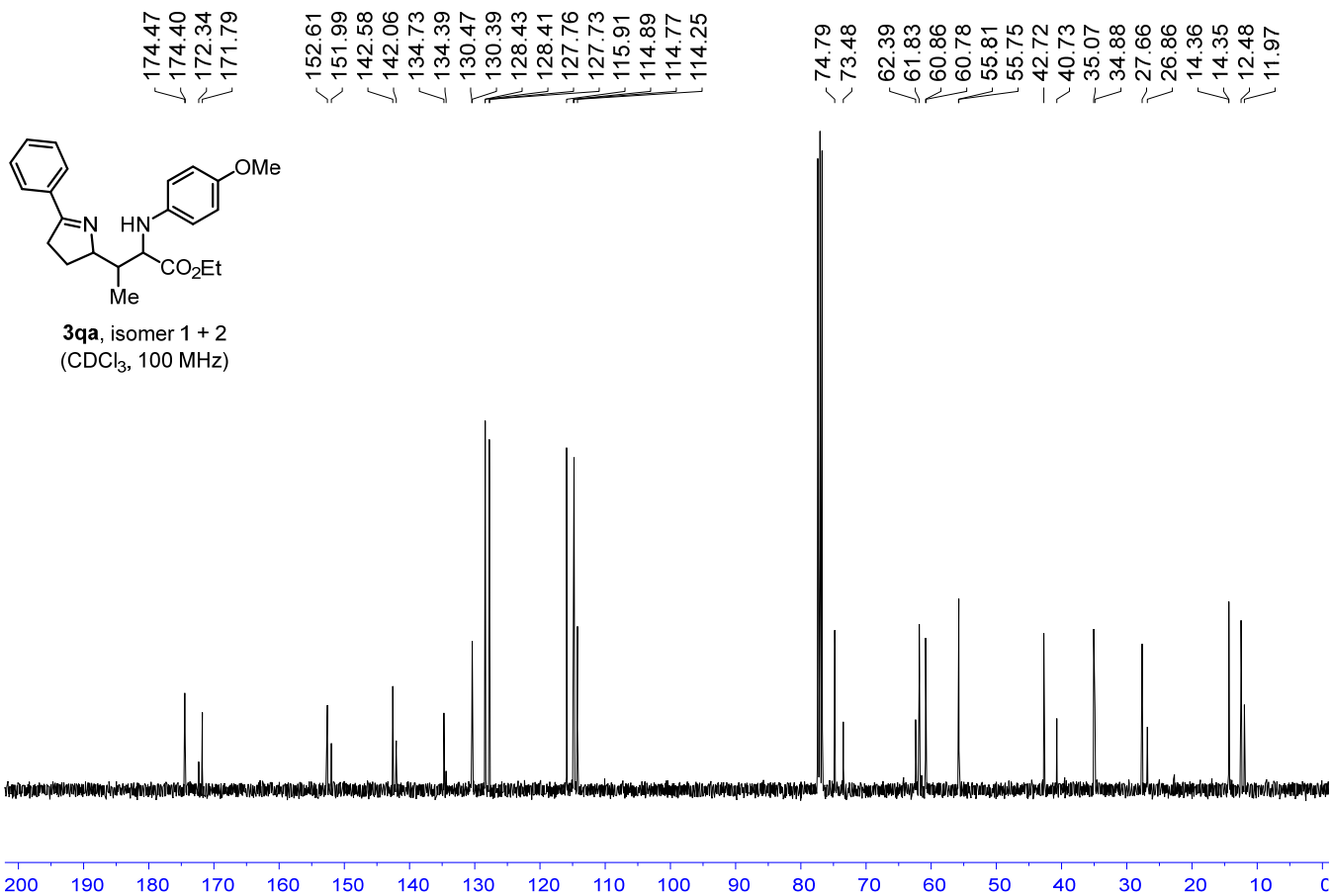

174.44
171.25
152.52
141.46
133.32
131.60
129.25
124.97
115.09
114.80
70.06
60.96
56.92
55.71
39.80
34.76
29.50
14.26
Br
OMe
HN
N
CO2Et
3pa, isomer 1
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.721
7.700
7.560
7.539
6.785
6.763
6.645
6.623
4.366
4.350
4.345
4.331
4.326
4.207
4.190
4.187
4.183
4.177
4.172
4.169
3.739
3.734
3.007
2.859
2.854
2.839
2.834
2.308
2.297
2.288
2.284
2.132
2.111
2.095
2.081
2.075
2.045
1.670
1.665
1.659
1.648
1.644
1.639
1.633
1.626
1.619
1.614
1.253
1.248
1.230
1.212
Br
OMe
N
HN
CO2Et
3pa, isomer 2
(CDCl3, 400 MHz)
overlapped with
water residue
2.04
2.07
2.00
1.99
1.09
1.14
3.08
2.98
1.03
1.05
1.00
2.00
1.89
3.11
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

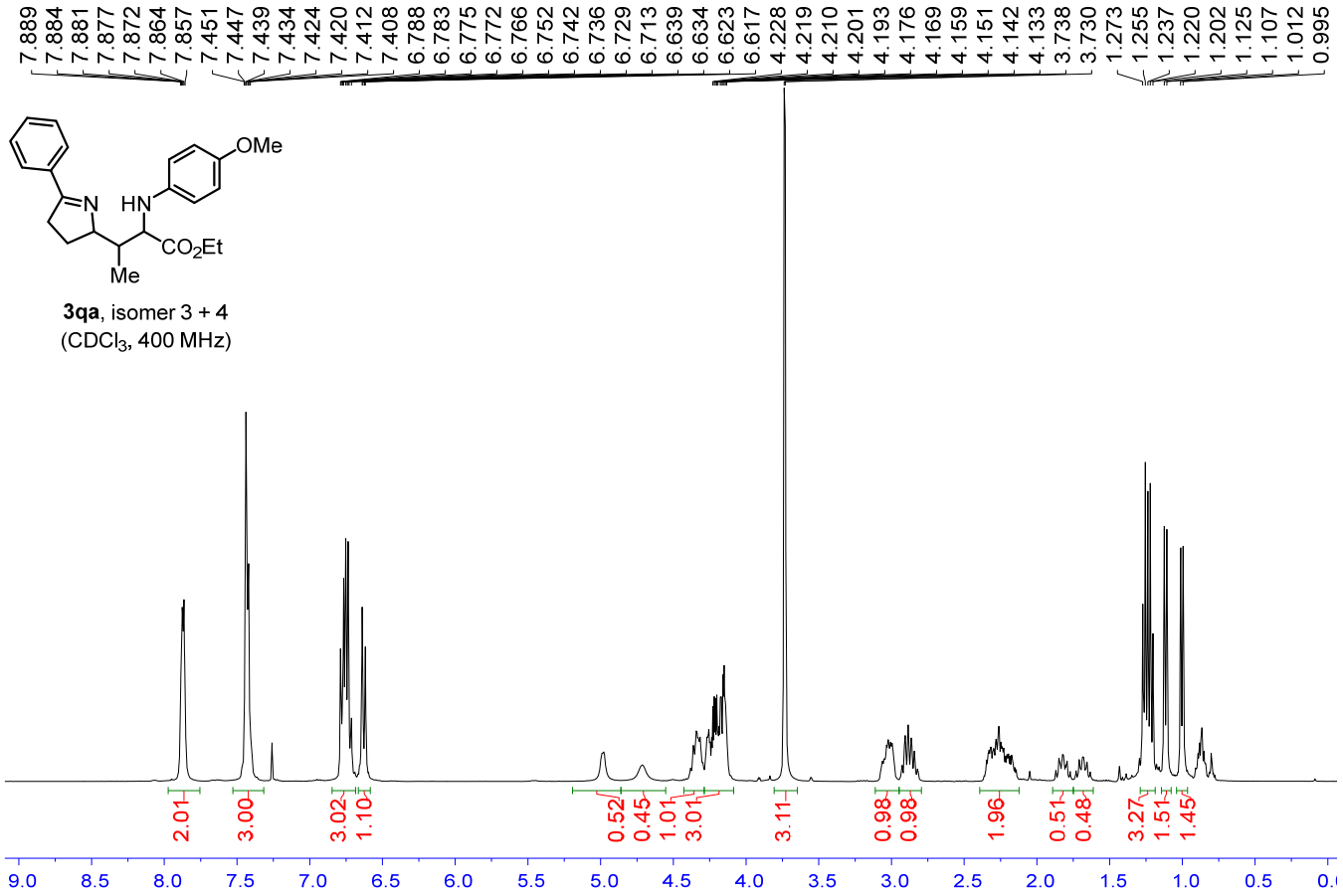

174.35
171.49
152.56
141.32
133.21
131.62
129.20
125.04
114.91
114.84
70.80
61.10
57.25
55.73
39.48
34.61
29.35
14.21
Br
OMe
N
HN
CO2Et
3pa, isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



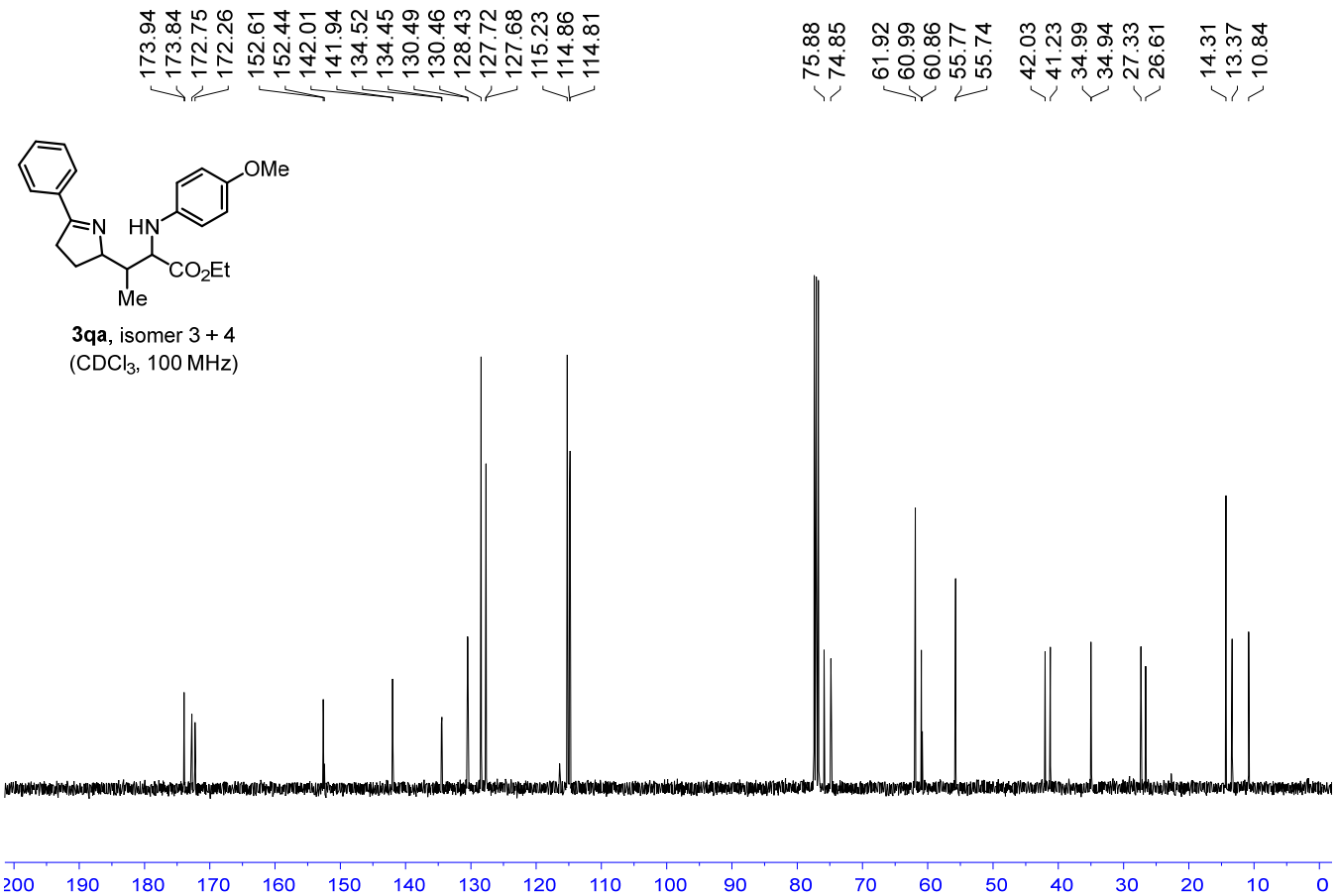
3qa, isomer 1 + 2
($CDCl_3$, 400 MHz)



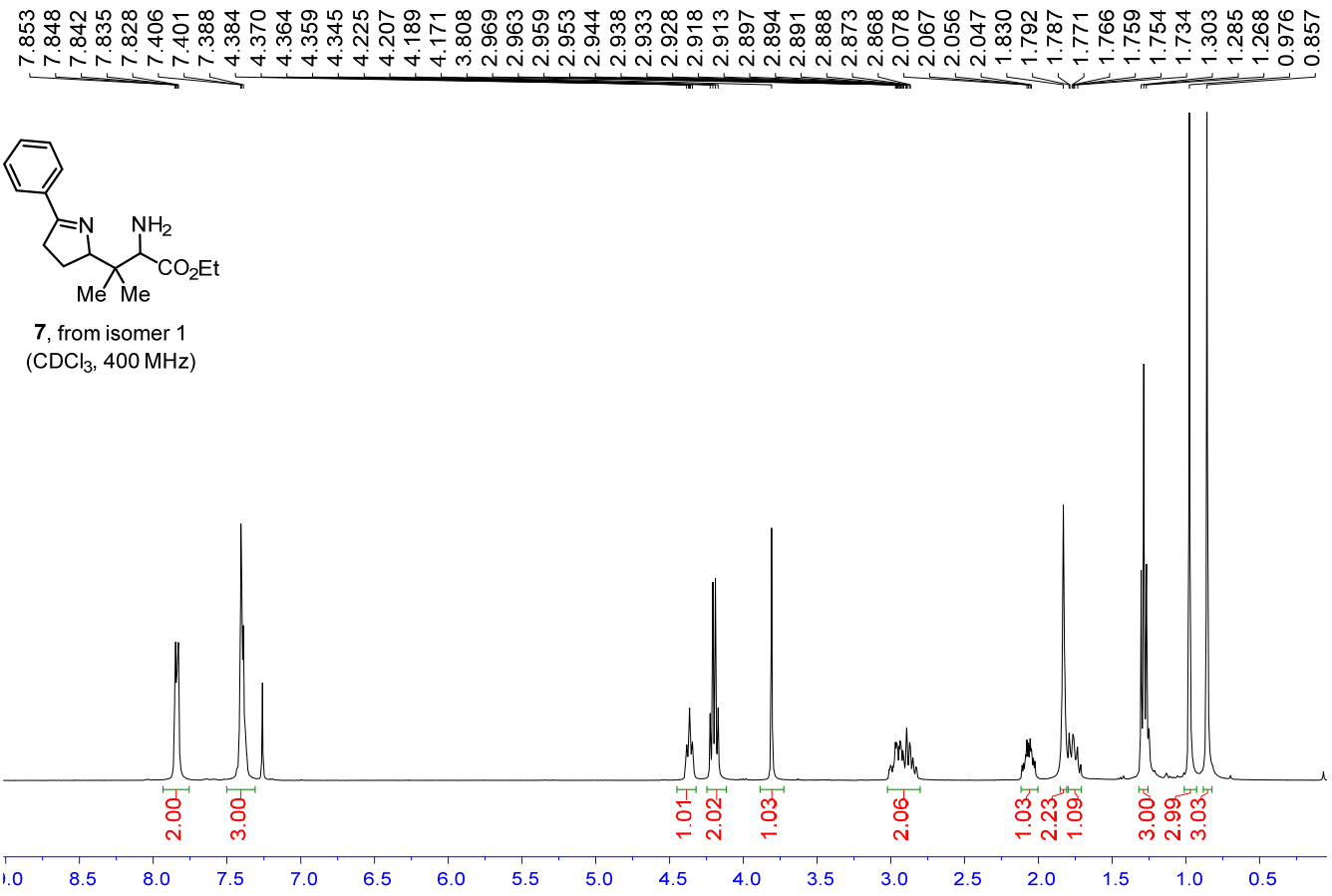
3qa, isomer 1 + 2
($CDCl_3$, 100 MHz)

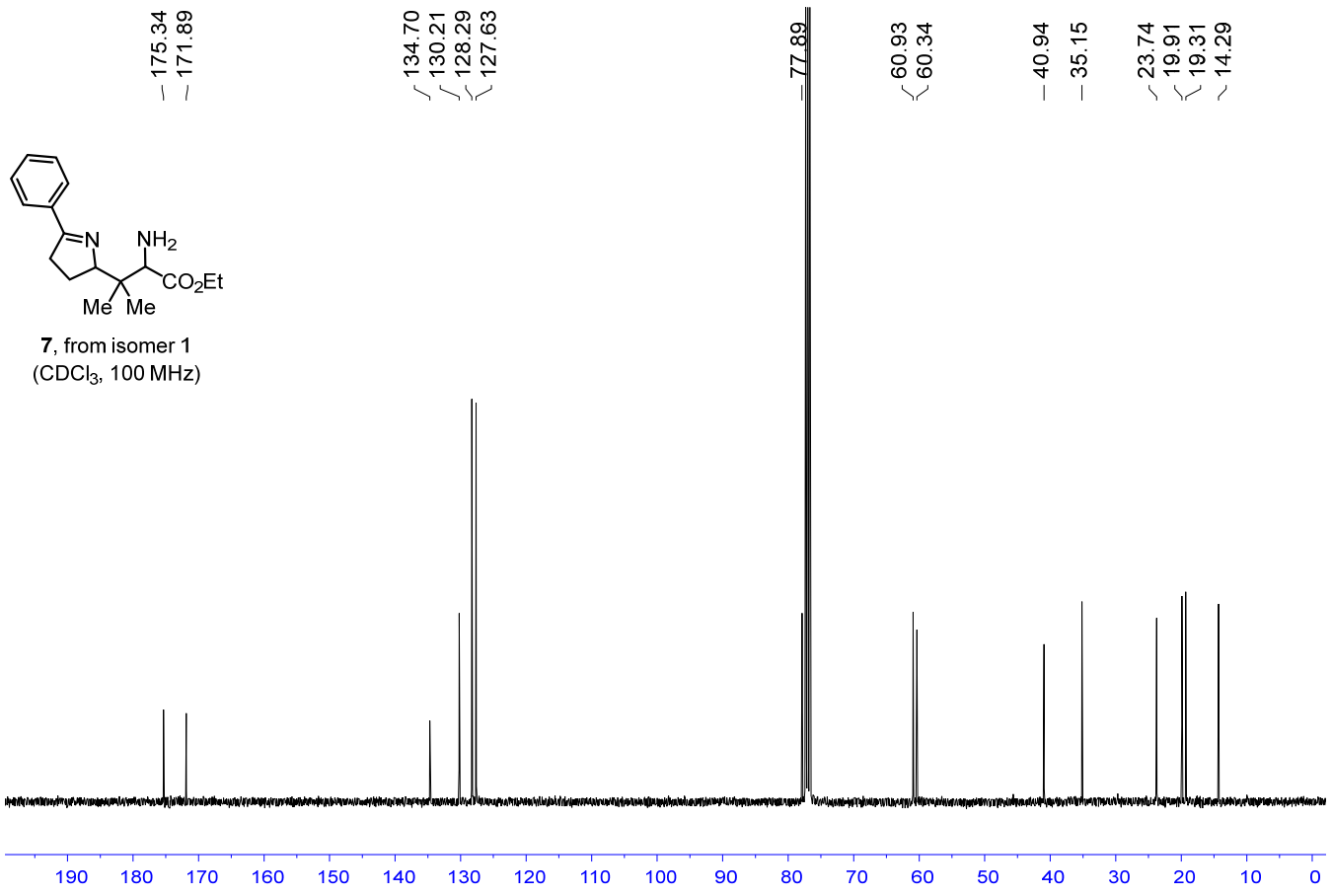


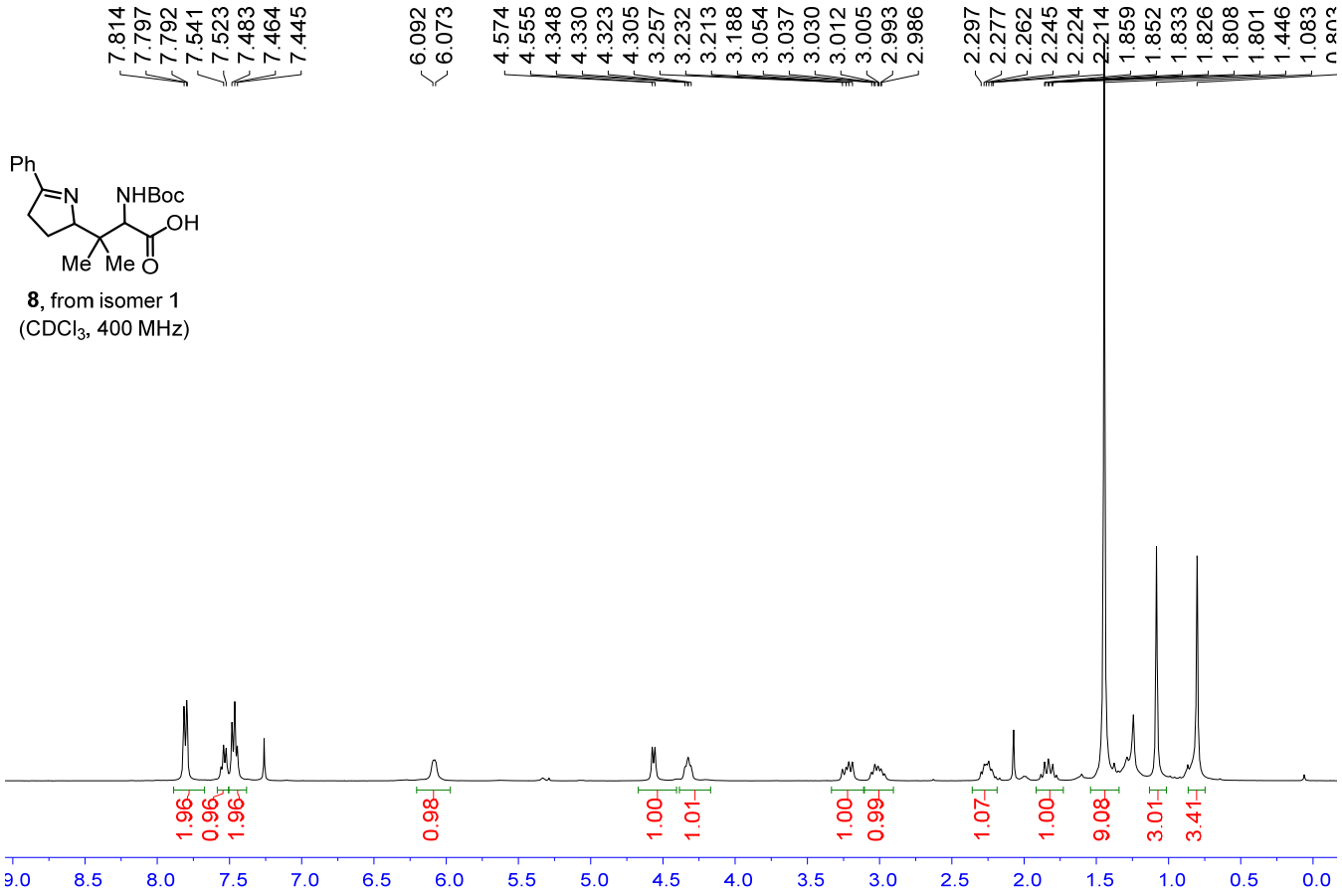
3qa, isomer 3 + 4
($CDCl_3$, 400 MHz)

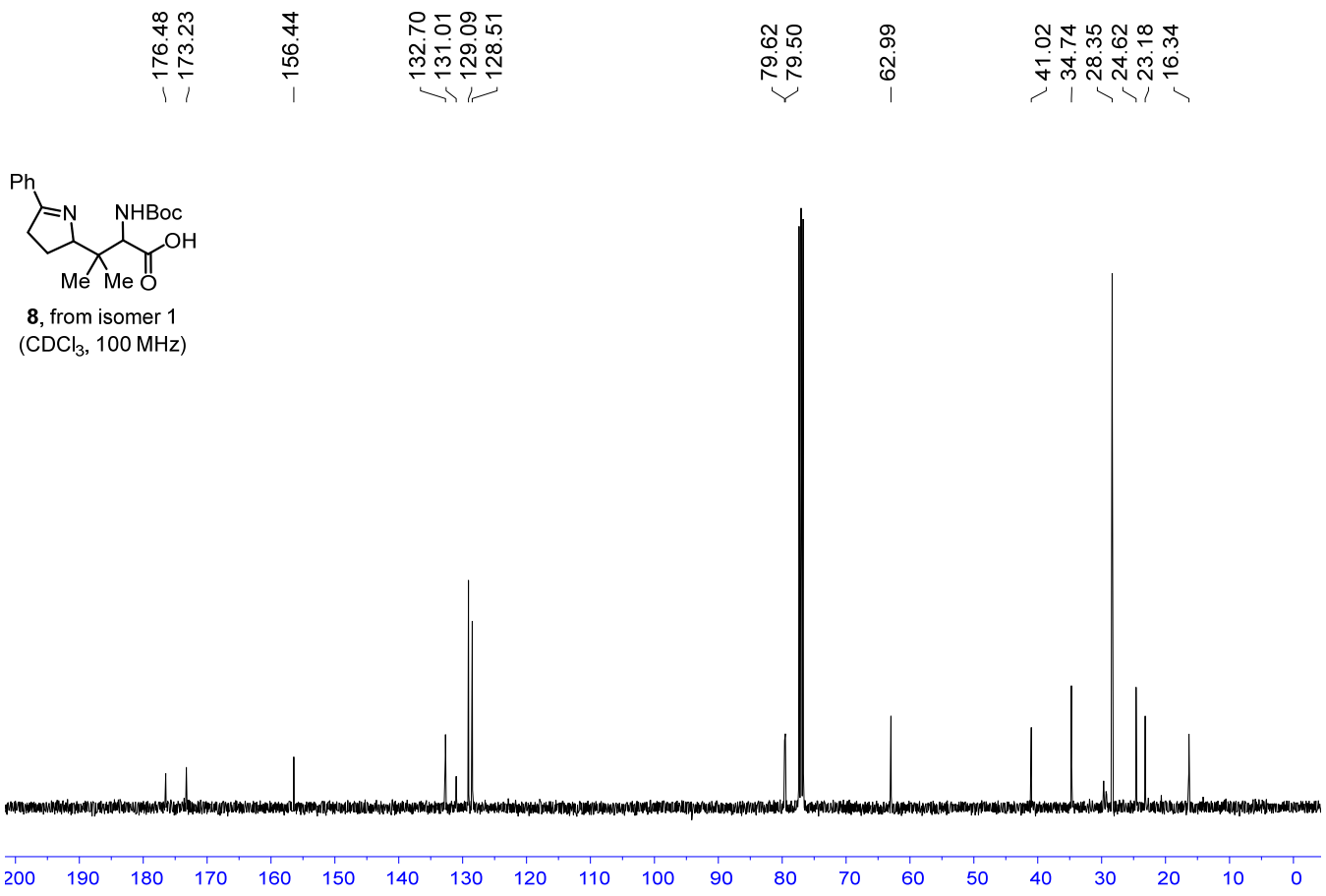


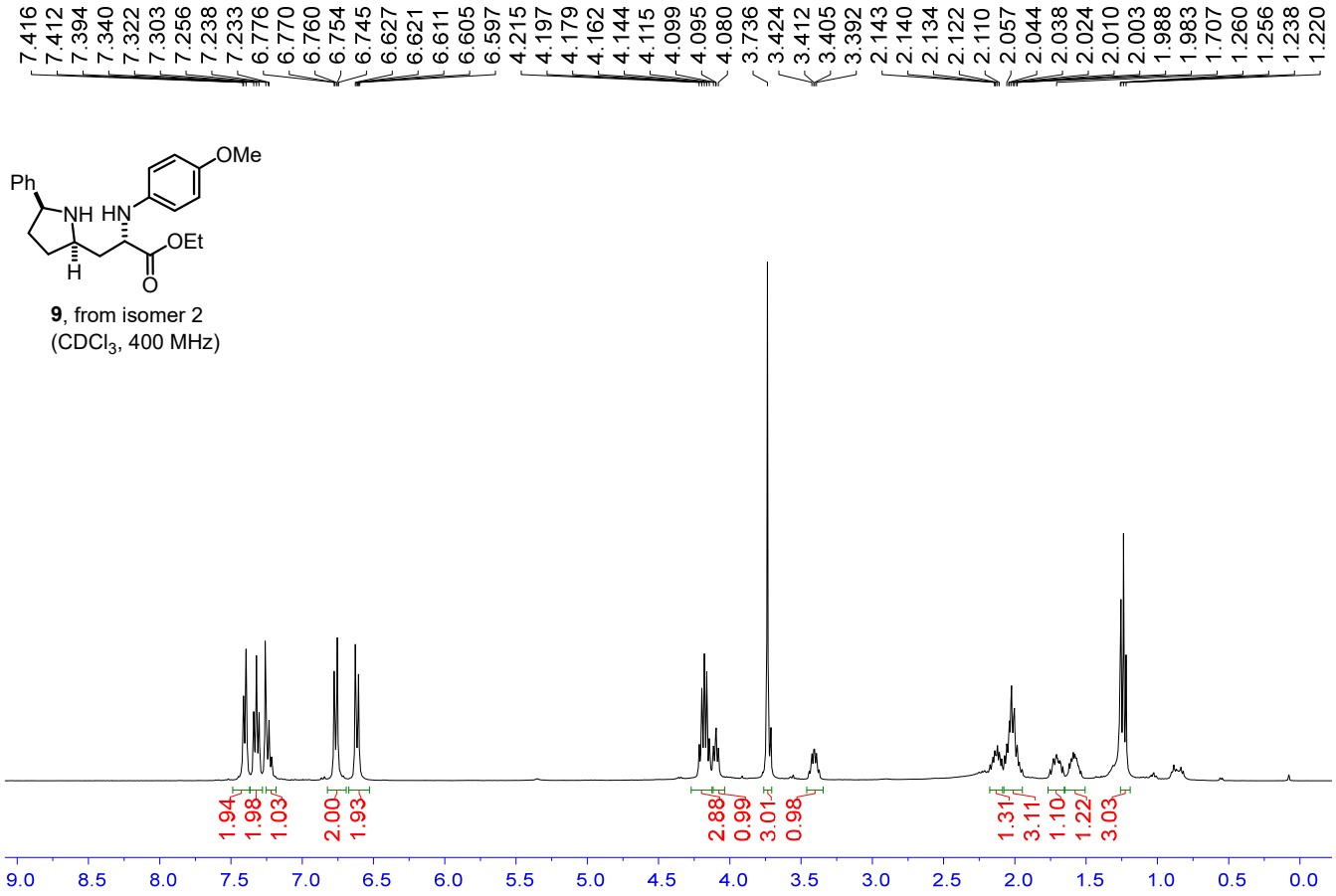
3qa, isomer 3 + 4
($CDCl_3$, 100 MHz)


7.853
7.848
7.842
7.835
7.828
7.406
7.401
7.388
4.384
4.370
4.364
4.359
4.345
4.225
4.207
4.189
4.171
3.808
2.969
2.963
2.959
2.953
2.944
2.938
2.933
2.928
2.918
2.913
2.897
2.894
2.891
2.888
2.873
2.868
2.078
2.067
2.056
2.047
1.830
1.792
1.787
1.771
1.766
1.759
1.754
1.734
1.303
1.285
1.268
0.976
0.857
N
NH2
CO2Et
Me Me
7, from isomer 1
(CDCl3, 400 MHz)
2.00
3.00
1.01
2.02
1.03
2.06
1.03
2.23
1.09
3.00
2.99
3.03
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

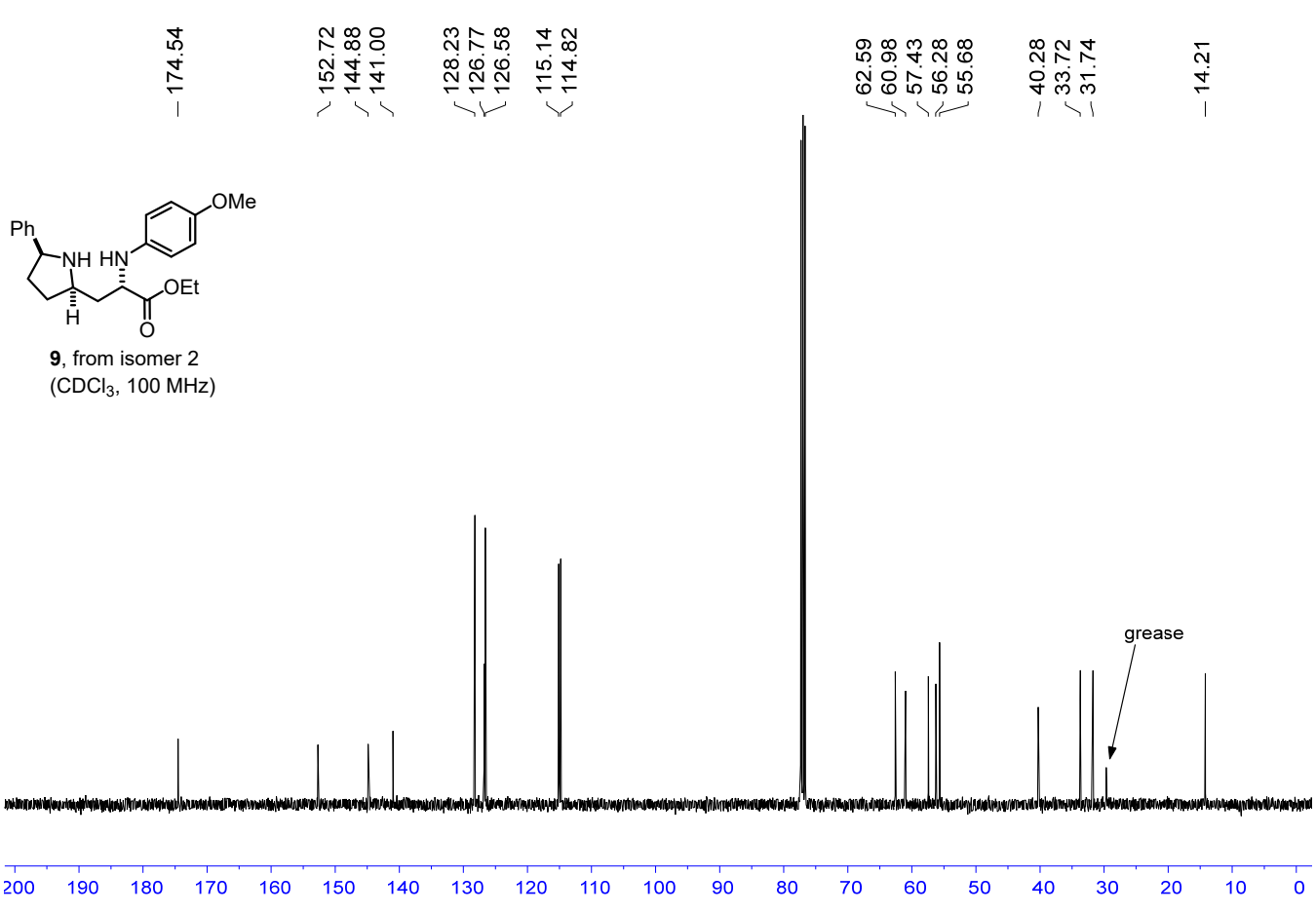

175.34
171.89
134.70
130.21
128.29
127.63
77.89
60.93
60.34
40.94
35.15
23.74
19.91
19.31
14.29
N
NH2
CO2Et
Me Me
7, from isomer 1
(CDCl3, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.814
7.797
7.792
7.541
7.523
7.483
7.464
7.445
6.092
6.073
4.574
4.555
4.348
4.330
4.323
4.305
3.257
3.232
3.213
3.188
3.054
3.037
3.030
3.012
3.005
2.993
2.986
2.297
2.277
2.262
2.245
2.224
2.214
1.859
1.852
1.833
1.826
1.808
1.801
1.446
1.083
Ph
N
NHBoc
OH
Me
Me
O
8, from isomer 1
(CDCl3, 400 MHz)
1.96
0.96
1.96
0.98
1.00
1.01
1.00
0.99
1.07
1.00
9.08
3.01
3.41
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

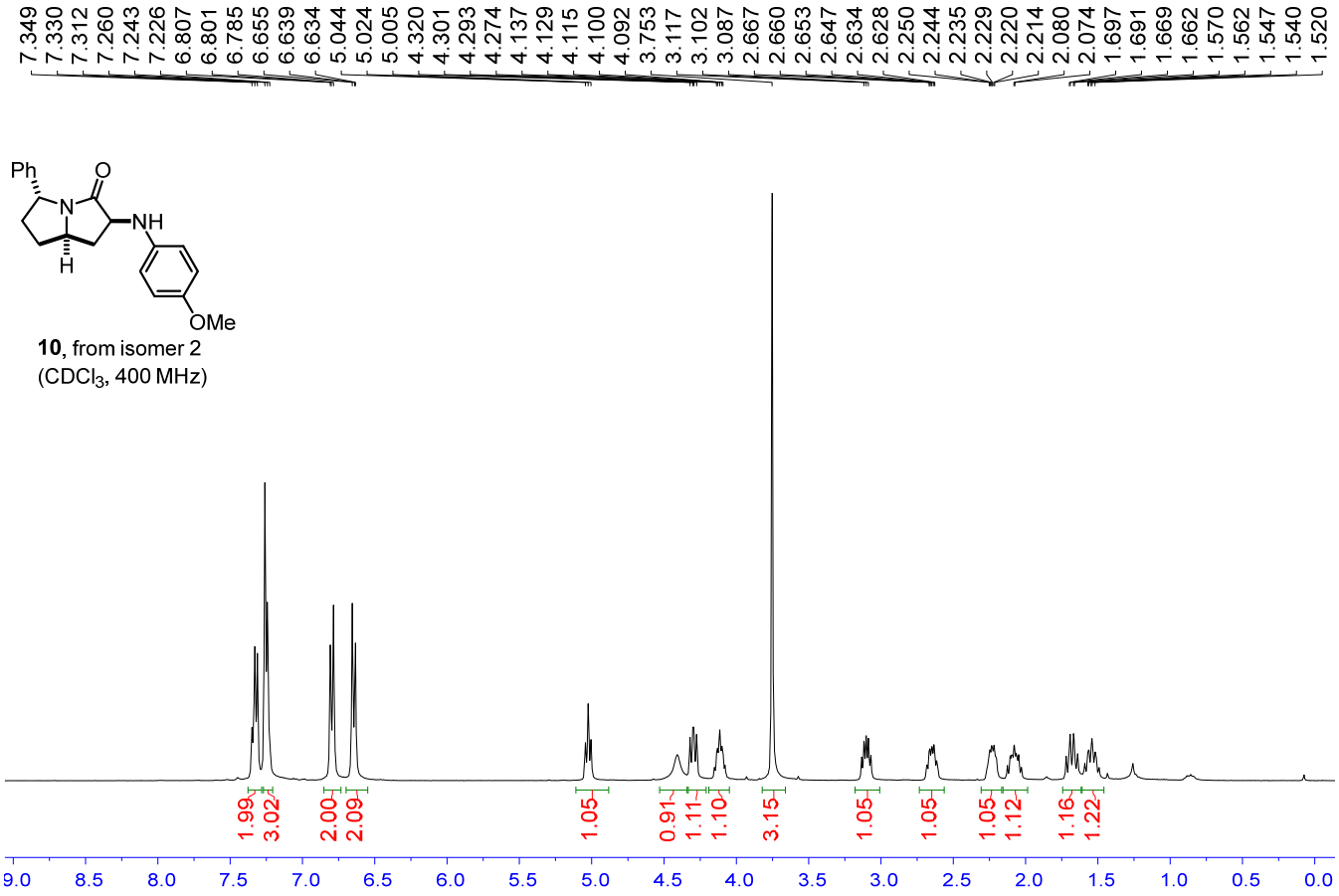

176.48
173.23
156.44
132.70
131.01
129.09
128.51
79.62
79.50
62.99
41.02
34.74
28.35
24.62
23.18
16.34
Ph
N
NHBoc
OH
Me
Me
O
8, from isomer 1
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

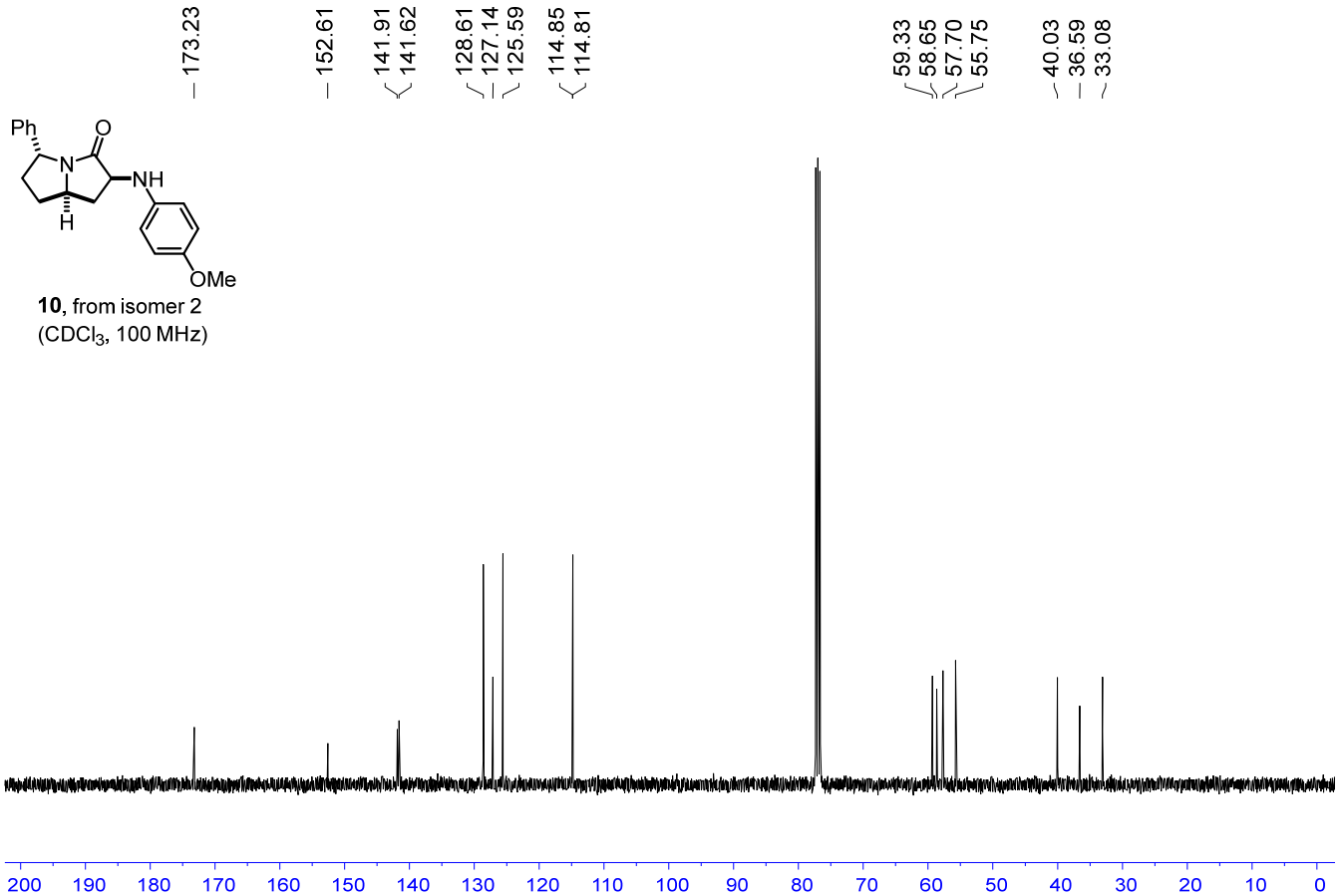


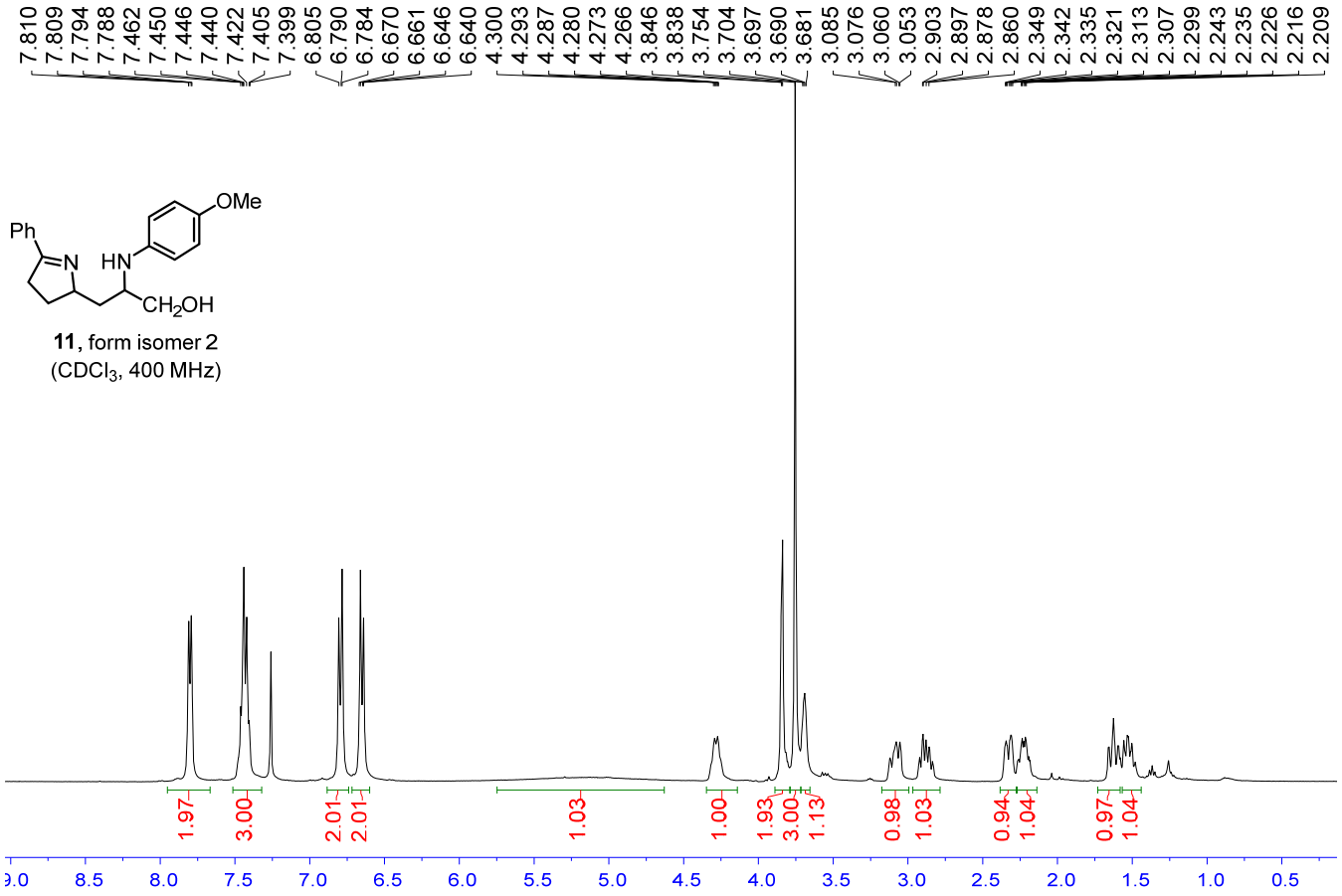
9, from isomer 2
($CDCl_3$, 400 MHz)

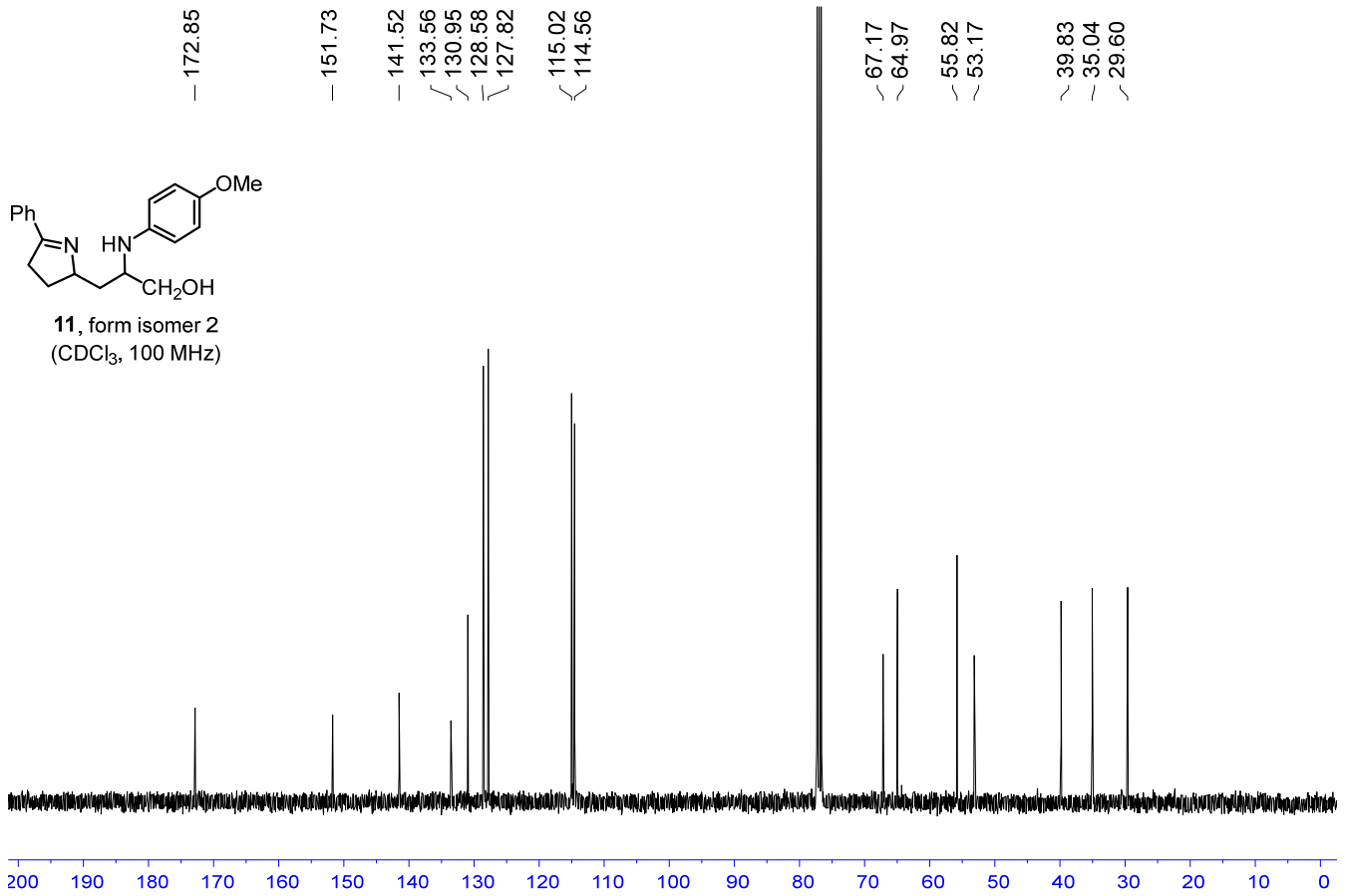


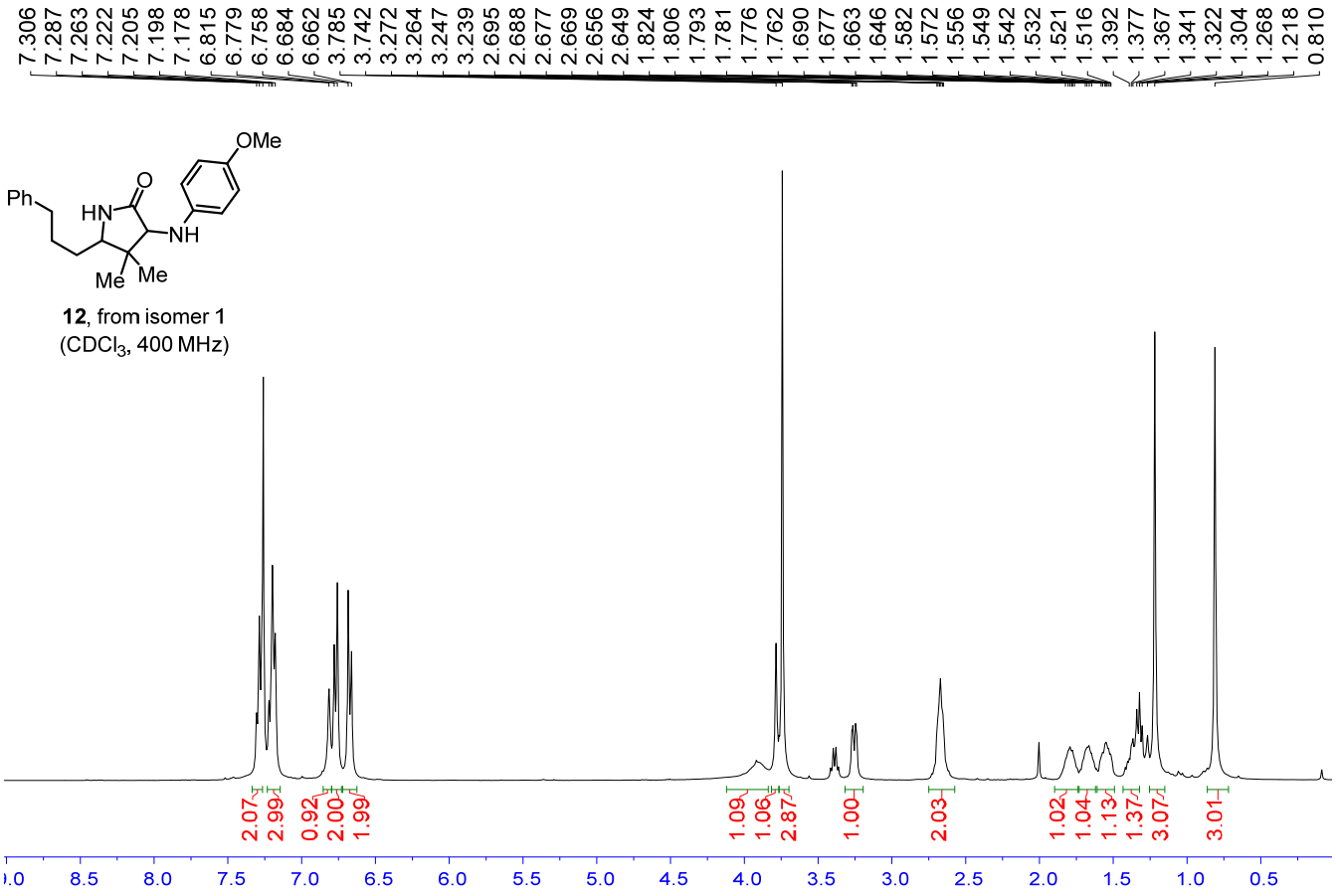
9, from isomer 2
($CDCl_3$, 100 MHz)

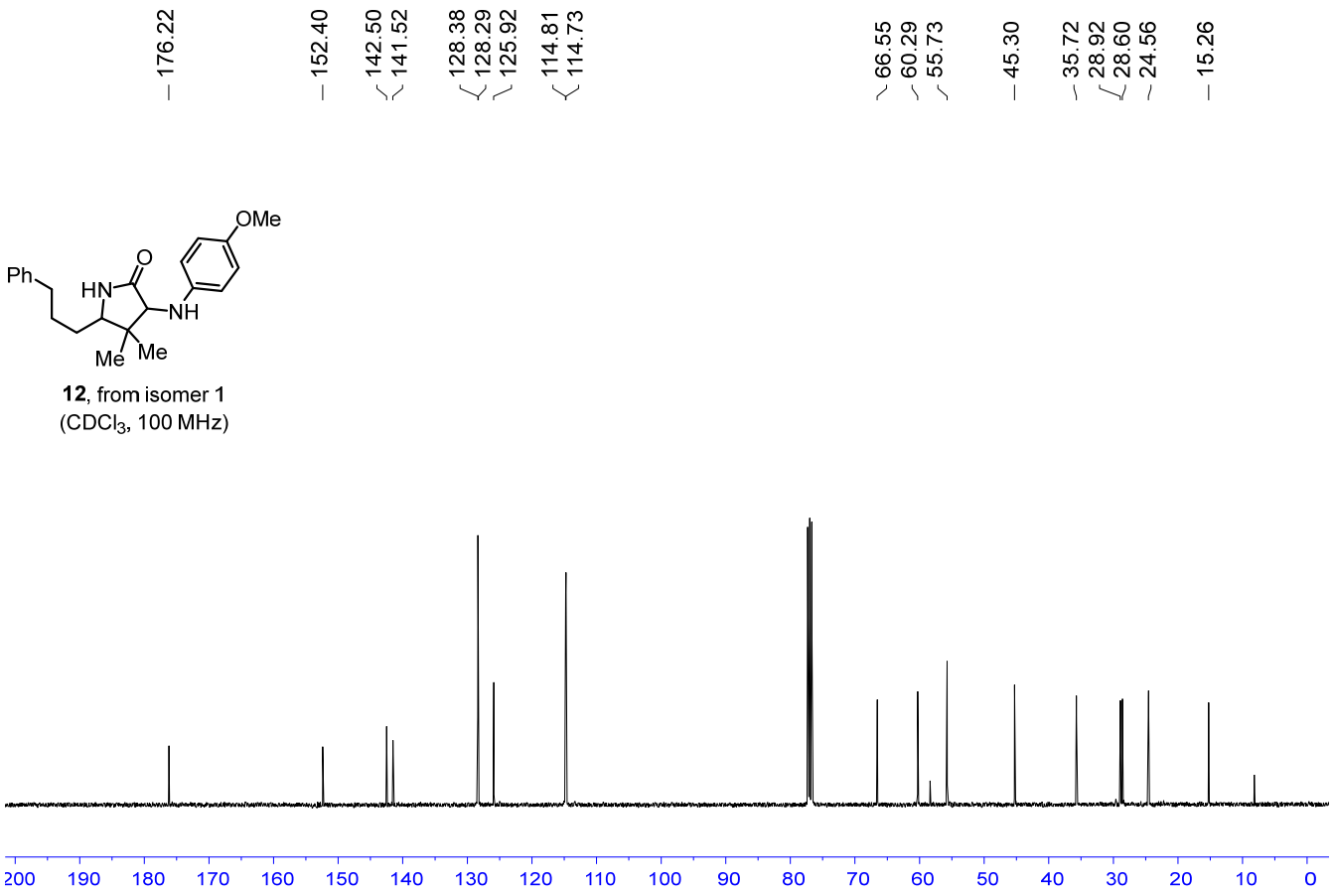

7.349
7.330
7.312
7.260
7.243
7.226
6.807
6.801
6.785
6.655
6.639
6.634
5.044
5.024
5.005
4.320
4.301
4.293
4.274
4.137
4.129
4.115
4.100
4.092
3.753
3.117
3.102
3.087
2.667
2.660
2.653
2.647
2.634
2.628
2.250
2.244
2.235
2.229
2.220
2.214
2.080
2.074
1.697
1.691
1.669
1.662
1.570
1.562
1.547
1.540
1.520
Ph
O
N
NH
H
OMe
10, from isomer 2
(CDCl3, 400 MHz)
1.99
3.02
2.00
2.09
1.05
0.91
1.11
1.10
3.15
1.05
1.05
1.05
1.12
1.16
1.22
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


173.23
152.61
141.91
141.62
128.61
127.14
125.59
114.85
114.81
59.33
58.65
57.70
55.75
40.03
36.59
33.08
Ph
O
N
NH
H
OMe
10, from isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.810
7.809
7.794
7.788
7.462
7.450
7.446
7.440
7.422
7.405
7.399
6.805
6.790
6.784
6.670
6.661
6.646
6.640
4.300
4.293
4.287
4.280
4.273
4.266
3.846
3.838
3.754
3.704
3.697
3.690
3.681
3.085
3.076
3.060
3.053
2.903
2.897
2.878
2.860
2.349
2.342
2.335
2.321
2.313
2.307
2.299
2.243
2.235
2.226
2.216
2.209
Ph
N
HN
OMe
CH2OH
11, form isomer 2
(CDCl3, 400 MHz)
1.97
3.00
2.01
2.01
1.03
1.00
1.93
3.00
1.13
0.98
1.03
0.94
1.04
0.97
1.04
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


172.85
151.73
141.52
133.56
130.95
128.58
127.82
115.02
114.56
67.17
64.97
55.82
53.17
39.83
35.04
29.60
Ph
N
HN
OMe
CH2OH
11, form isomer 2
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.306
7.287
7.263
7.222
7.205
7.198
7.178
6.815
6.779
6.758
6.684
6.662
3.785
3.742
3.272
3.264
3.247
3.239
2.695
2.688
2.677
2.669
2.656
2.649
1.824
1.806
1.793
1.781
1.776
1.762
1.690
1.677
1.663
1.646
1.582
1.572
1.556
1.549
1.542
1.532
1.521
1.516
1.392
1.377
1.367
1.341
1.322
1.304
1.268
1.218
0.810
OMe
Ph
HN
O
NH
Me
Me
12, from isomer 1
(CDCl3, 400 MHz)
2.07
2.99
0.92
2.00
1.99
1.09
1.06
2.87
1.00
2.03
1.02
1.04
1.13
1.37
3.07
3.01
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


176.22
152.40
142.50
141.52
128.38
128.29
125.92
114.81
114.73
66.55
60.29
55.73
45.30
35.72
28.92
28.60
24.56
15.26
OMe
Ph
HN
O
NH
Me
Me
12, from isomer 1
(CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0