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Supporting Information

for DOI: 10.1055/a-2230-4562

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

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Supporting Information for

Stereodivergent 1,5-Conjugate Addition with Iminoesters via Pd/Cu Dual Catalysis

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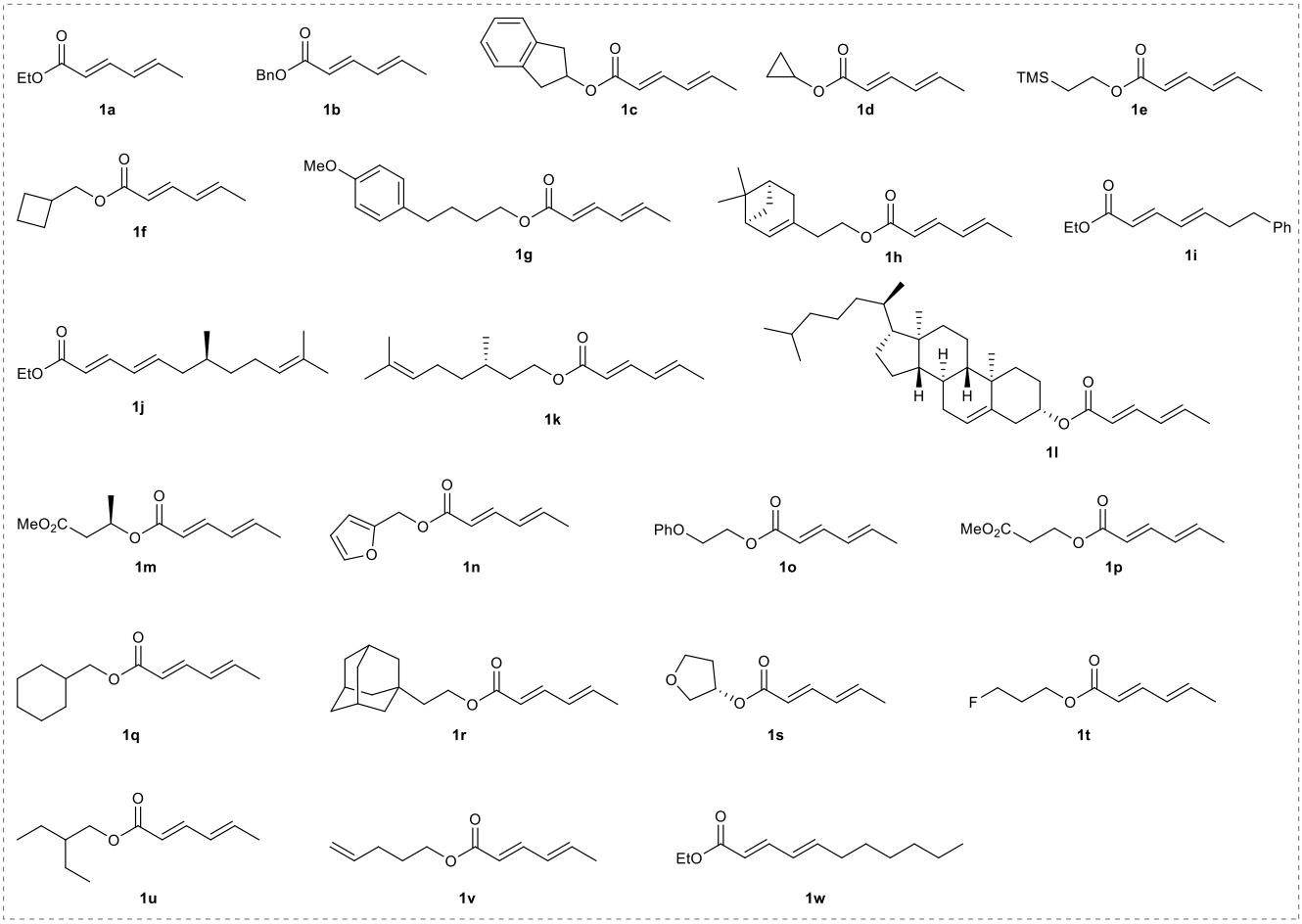
Table of Contents

1. General information

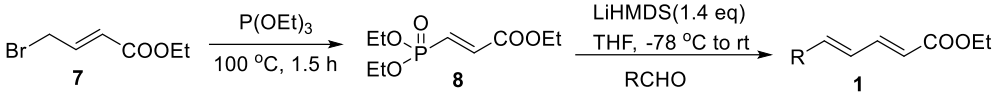
All air-sensitive procedures were conducted by Schlenk techniques under argon. Unless otherwise indicated, all commercially available starting materials and dry solvents were purchased and used directly without further purification. ^{1}H, ^{13}C and ^{19}F NMR spectra were acquired on 400 MHz Bruker or 500 MHz Agilent instruments at Shanghai Institute of Organic Chemistry. For High-resolution mass spectra: ESI mass spectra were recorded on Thermo Scientific Q Exactive HF Orbitrap-FTMS; MALDI was measured on Voyager-DE STR; EI mass spectra were recorded on Waters Premier GC-TOF MS; FI mass spectra were recorded on JEOL-AccuTOF-GCv4G-GCT MS. Optical rotation was measured using a 1 mL cell with 1.0 dm path length on a JASCO P-1030 polarimeter. HPLC analysis was conducted on a Shimadzu HPLC system equipped with Daicel or Chiralpak chiral-stationary-phase columns (ϕ 4.6 mm×250 mm). Chemical shifts are reported in δ (ppm) referenced to an internal TMS standard or $CHCl_3$ in $CDCl_3$ (7.26 ppm) for ^{1}H NMR, $CDCl_3$ (δ = 77.10 ppm) for ^{13}C NMR, and $CFCl_3$ (0 ppm) for ^{19}F NMR. Coupling constants (*J*) are reported in Hz. Multiplicities are reported using the following abbreviations: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Column chromatography was performed with 300-400 mesh silica gel using flash column chromatography technique. The X-ray crystal structure was measured on Bruker D8 VENTURE.

2. Synthesis of substrates

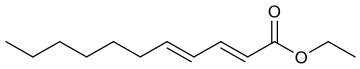


2.1 Synthesis of fluorinatedesters

Dienes **1a-1l** were known compounds.[1]

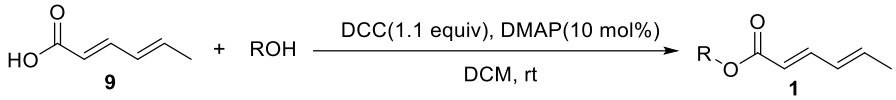


General procedure **A**: To a 25 mL flask with ethyl (*E*)-4-bromobut-2-enoate **7** (1.4 g, 7.0 mmol) was added triethyl phosphite (1.6 g, 9.8 mmol) under nitrogen. The reaction was stirred under refluxing for 1.5 h. After this time, the solution was directly condensed to provide the crude **8**. To another 100 mL Schlenk tube with **8** in dry THF (20 mL) was added LiHMDS (1 M in THF, 7.0 mL, 7.0 mmol) dropwise at -78 °C. The resulting mixture continued to stir at -78 °C for 30 min. Then aldehyde (5.0 mmol) in THF (15 mL) was added to the reaction and the resulting mixture was stirred at room temperature for 2 h. After this time, the reaction was quenched by 20% aqueous citric acid solution (30 mL), extracted with diethyl ether (3 ×20 mL), washed with saturated $NaHCO_3$ aqueous solution (20 mL), and dried over anhydrous magnesium sulfate, condensed and purified by flash column chromatography to provide pure **1**.

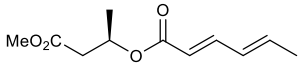


Ethyl (*2E,4E*)-undeca-2,4-dienoate (**1w**)

Colorless oil, 588 mg, 40% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.29 – 7.21 (q, *J* = 15.4 Hz, 1H), 6.19 – 6.08 (m, 2H), 5.77 (d, *J* = 15.4 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.15 (q, *J* = 6.9 Hz, 2H), 1.40 (q, *J* = 7.5 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 9H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 167.4, 145.2, 144.9, 128.4, 119.2, 60.2, 33.1, 31.7, 28.9, 28.7, 22.6, 14.4, 14.1. HRMS (FI): $[M]^{\oplus}$ calcd for $C_{13}H_{22}O_2^{\oplus}$ 210.1614, found 210.1608.

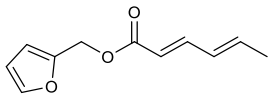


General procedure **B**: To a solution of sorbic acid **9** (4.4 mmol, 0.49 g, 1.1 eq), alcohol (4.0 mmol, 1.0 eq) and DMAP (0.40 mmol, 49 mg, 10 mol%) in CH_2Cl_2 (20 mL) at 0 °C was added DCC (4.4 mmol, 0.91 g, 1.1 eq) in five portions over 5 min. Then the reaction was stirred at room temperature for 12 h. After this time, the reaction was filtered through a pad of celite using CH_2Cl_2 as the eluent, concentrated, and purification by flash column chromatography to provide the pure **1**.



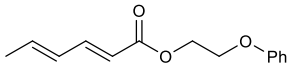
(*R*)-4-Methoxy-4-oxobutan-2-yl (2*E*,4*E*)-hexa-2,4-dienoate (**1m**)

Yellow oil, 297 mg, 35% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.19 (dd, *J* = 15.4, 9.8 Hz, 1H), 6.20 – 6.03 (m, 2H), 5.69 (d, *J* = 15.4 Hz, 1H), 5.38 – 5.20 (m, 1H), 3.63 (s, 3H), 2.65 (dd, *J* = 15.5, 6.3 Hz, 1H), 2.49 (dd, *J* = 15.5, 6.3 Hz, 1H), 1.81 (d, *J* = 5.6 Hz, 3H), 1.29 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 170.7, 166.4, 145.2, 139.5, 129.7, 118.9, 67.1, 51.7, 40.7, 20.0, 18.6. HRMS (EI): $[M]^{\oplus}$ calcd for $C_{11}H_{16}O_4^{\oplus}$ 212.1043, found 212.1048.



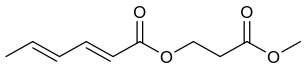
Furan-2-ylmethyl (2*E*,4*E*)-hexa-2,4-dienoate (**1n**)

Colorless oil, 599 mg, 78% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.41 (d, *J* = 1.8 Hz, 1H), 7.27 (dd, *J* = 15.4, 9.8 Hz, 1H), 6.40 (d, *J* = 3.2 Hz, 1H), 6.34 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.21 – 6.01 (m, 2H), 5.77 (d, *J* = 15.3 Hz, 1H), 5.11 (s, 2H), 1.83 (d, *J* = 5.6 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 166.9, 149.7, 145.8, 143.2, 139.9, 129.8, 118.3, 110.6, 57.9, 18.7 (one aromatic carbon signal was not observed). HRMS (EI): $[M]^{\oplus}$ calcd for $C_{11}H_{12}O_3^{\oplus}$ 192.0781, found 192.0779.



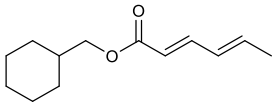
2-Phenoxyethyl (2*E*,4*E*)-hexa-2,4-dienoate (**1o**).

White solid, 622 mg, 67% yield. Mp = 57–59 ºC; ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.29 (t, *J* = 7.5 Hz, 1H), 6.97 (t, *J* = 7.3 Hz, 1H), 6.93 (d, *J* = 8.1 Hz, 2H), 6.25 – 6.05 (m, 2H), 5.82 (d, *J* = 15.4 Hz, 1H), 4.49 (t, *J* = 4.7 Hz, 2H), 4.20 (t, *J* = 4.7 Hz, 2H), 1.85 (d, *J* = 5.7 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 167.2, 158.6, 145.7, 139.9, 129.8, 129.5, 121.2, 118.4, 114.7, 66.0, 62.7, 18.7. HRMS (EI): $[M]^{\oplus}$ calcd for $C_{14}H_{16}O_3^{\oplus}$ 232.1094, found 232.1100.



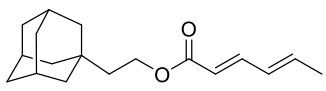
3-Methoxy-3-oxopropyl (2*E*,4*E*)-hexa-2,4-dienoate (**1p**).

Colorless oil, 444 mg, 56% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.27 – 7.20 (m, 1H), 6.23 – 6.06 (m, 2H), 5.75 (d, *J* = 15.4 Hz, 1H), 4.40 (t, *J* = 6.4 Hz, 2H), 3.70 (s, 3H), 2.68 (t, *J* = 6.4 Hz, 2H), 1.84 (d, *J* = 5.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 171.3, 167.1, 145.6, 139.9, 129.8, 118.5, 59.7, 52.0, 33.9, 18.8. HRMS (FI): $[M]^{\oplus}$ calcd for $C_{10}H_{14}O_4^{\oplus}$ 198.0887, found 198.0884.



Cyclohexylmethyl (2*E*,4*E*)-hexa-2,4-dienoate (**1q**).

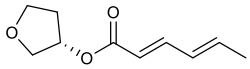
Colorless oil, 582 mg, 70% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.24 (dd, *J* = 15.4, 10.0 Hz, 1H), 6.23 – 6.09 (m, 2H), 5.77 (d, *J* = 15.4 Hz, 1H), 3.94 (d, *J* = 6.6 Hz, 2H), 1.85 (d, *J* = 5.9 Hz, 3H), 1.79 – 1.62 (m, 6H), 1.35 – 1.11 (m, 3H), 0.98 (qd, *J* = 13.3, 12.6, 3.8 Hz, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 167.6, 144.9, 139.3, 129.9, 119.2, 69.5, 37.3, 29.8, 26.5, 25.8, 18.7. HRMS (EI): $[M]^{\oplus}$ calcd for $C_{13}H_{20}O_2^{\oplus}$ 208.1458, found 208.1463.



2-((3*r*,5*r*,7*r*)-Adamantan-1-yl) ethyl (2*E*,4*E*)-hexa-2,4-dienoate (**1r**)

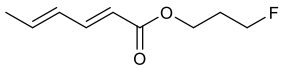
White solid, 690 mg, 63% yield. Mp = 59–60 ºC; ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.23 (dd, *J* = 15.4, 10.2 Hz, 1H), 6.25 – 6.04 (m, 2H), 5.76 (d, *J* = 15.4 Hz, 1H), 4.19 (t, *J* = 7.4 Hz, 2H), 1.97 – 1.92 (m, 3H), 1.85 (d, *J* = 6.0 Hz, 3H), 1.73 – 1.68 (m, 3H), 1.65 – 1.59 (m, 3H), 1.53 (d, *J* = 2.9 Hz, 6H), 1.45 (t, *J* = 7.4 Hz, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 167.6, 144.9, 139.3, 129.9, 119.2, 60.8,

42.6, 42.6, 37.4, 35.0, 31.9, 28.7, 25.5, 18.7. HRMS (EI): $[M]^{\oplus}$ calcd for $C_{18}H_{26}O_2^{\oplus}$ 274.1927, found 274.1929.



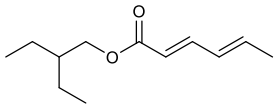
(*S*)-tetrahydrofuran-3-yl (2*E*,4*E*)-hexa-2,4-dienoate (**1s**)

Yellow oil, 255 mg, 35% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.24 (dd, *J* = 15.4, 9.9 Hz, 1H), 6.26 – 5.98 (m, 2H), 5.75 (d, *J* = 15.4 Hz, 1H), 5.35 (td, *J* = 4.6, 2.3 Hz, 1H), 3.95 – 3.89 (m, 2H), 3.87 – 3.81 (m, 2H), 2.18 (dtd, *J* = 14.7, 8.4, 6.3 Hz, 1H), 2.02 (dddd, *J* = 13.5, 6.6, 4.4, 1.7 Hz, 1H), 1.84 (d, *J* = 5.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 167.0, 145.6, 139.9, 129.7, 118.6, 74.6, 73.2, 67.1, 32.8, 18.7. HRMS (FI): $[M]^{\oplus}$ calcd for $C_{10}H_{14}O_3^{\oplus}$ 182.0937, found 182.0934.



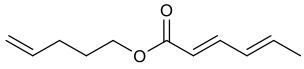
3-Fluoropropyl (2*E*,4*E*)-hexa-2,4-dienoate (**1t**)

Colorless oil, 440 mg, 64% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.24 (dd, *J* = 15.4, 9.8 Hz, 1H), 6.24 – 6.06 (m, 2H), 5.76 (d, *J* = 15.4 Hz, 1H), 4.58 (t, *J* = 5.8 Hz, 1H), 4.49 (t, *J* = 5.8 Hz, 1H), 4.26 (t, *J* = 6.3 Hz, 2H), 2.05 (dp, *J* = 24.8, 6.1 Hz, 1H), 1.84 (d, *J* = 5.7 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 167.2, 145.4, 139.8, 129.8, 118.6, 80.7 (d, *J* = 165.1 Hz), 60.2 (d, *J* = 5.5 Hz), 29.9 (d, *J* = 19.8 Hz), 18.7. ^{19}F NMR (376 MHz, chloroform-*d*) δ -222.2 (tt, *J* = 47.0, 25.6 Hz). HRMS (EI): $[M]^{\oplus}$ calcd for $C_9H_{13}O_2F^{\oplus}$ 172.0895, found 172.0894.



2-Ethylbutyl (2*E*,4*E*)-hexa-2,4-dienoate (**1u**)

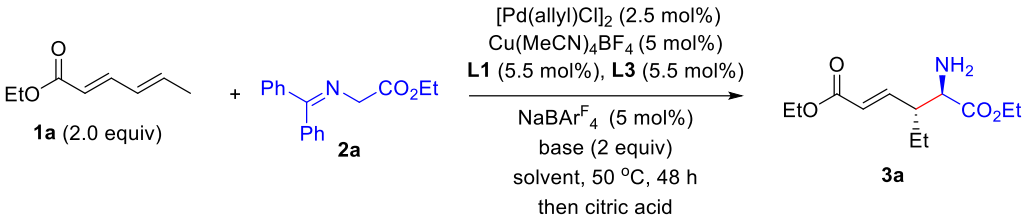
Colorless oil, 486 mg, 62% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.27 – 7.20 (q, *J* = 15.4, 10.0 Hz, 1H), 6.23 – 6.07 (m, 2H), 5.78 (d, *J* = 15.4 Hz, 1H), 4.06 (d, *J* = 5.9 Hz, 2H), 1.85 (d, *J* = 5.9 Hz, 2H), 1.59 (s, 1H), 1.54 (dq, *J* = 12.4, 6.3 Hz, 1H), 1.37 (p, *J* = 7.3 Hz, 4H), 0.90 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 167.6, 144.9, 139.3, 129.9, 119.2, 66.4, 40.5, 23.4, 18.7, 11.1. HRMS (EI): $[M]^{\oplus}$ calcd for $C_{12}H_{20}O_2^{\oplus}$ 196.1458, found 196.1461.

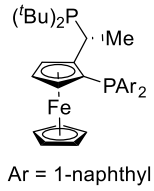


Pent-4-en-1-yl (2*E*,4*E*)-hexa-2,4-dienoate (**1v**)

Colorless oil, 454 mg, 63% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.32 – 7.13 (m, 1H), 6.31 – 6.04 (m, 2H), 5.96 – 5.65 (m, 2H), 5.23 – 4.92 (m, 2H), 4.15 (t, *J* = 6.6 Hz, 2H), 2.23 – 2.07 (m, 2H), 1.85 (d, *J* = 5.9 Hz, 3H), 1.80 – 1.73 (m, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 167.5, 145.1, 139.4, 137.7, 129.9, 119.0, 115.3, 63.6, 30.2, 28.0, 18.7. HRMS (FI): $[M]^{\oplus}$ calcd for $C_{11}H_{16}O_2^{\oplus}$ 180.1145, found 180.1143.

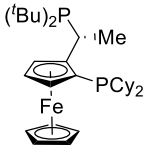
3. Development of reaction conditions



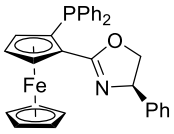


Ar = 1-naphthyl

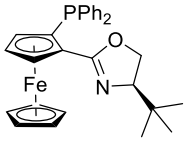
L1



L2



L3

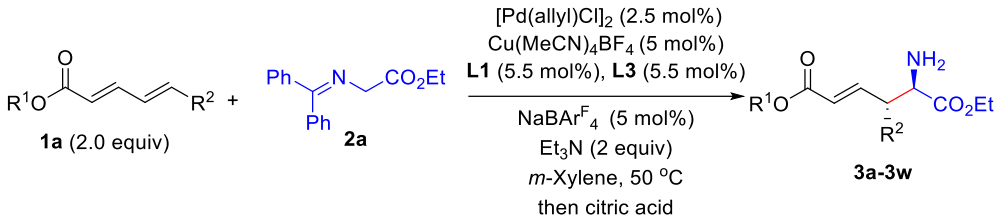


L4

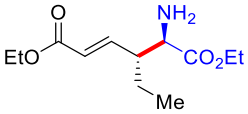
Entry[a]	Solvent	Base	Yield (%)[b]	dr	ee (%)[c]
1	$PhCF_3$	Et_3N	85	14:1	99
2[b]	$PhCF_3$	Et_3N	60	5:1	95
3[c]	$PhCF_3$	Et_3N	80	13:1	99
4	$PhCF_3$	$^{i}PrNEt_2$	36	7:1	99
5	$PhCF_3$	Cs_2CO_3	n.d.		
6	$PhCF_3$	DBU	n.d.		
7	$PhCF_3$	$^{t}BuOK$	n.d.		
8	hexane	Et_3N	trace		
9	THF	Et_3N	50	5:1	99
10	DMSO	Et_3N	n.d.		
11	CH_3CN	Et_3N	n.d.		
12	*m*-Xylene	Et_3N	90	>20:1	99

[a]Isolated yields. The yield and dr values were determined by ^{1}H NMR. The ee was determined by HPLC analysis. [b]**L2** was used instead of **L1**. [c]**L4** was used instead of **L3**. n.d., not detected.

4. General procedure for stereodivergent 1,5-conjugate addition

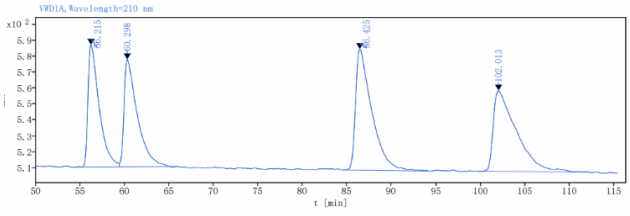


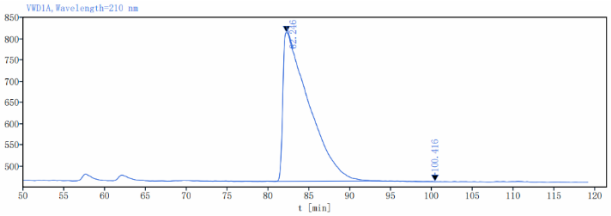
In a N_2-filled glovebox, to a 4 mL vial with $Cu(MeCN)_4BF_4$ (1.6 mg, 0.0050 mmol), **L3** (2.8 mg, 0.0055 mmol) and nucleophilic **2a** (0.10 mmol) was added dry *m*-Xylene (0.20 mL). The resulting mixture was stirred at room temperature for 0.5 h. To another 4 mL vial with $[Pd(\eta^3\text{-allyl})Cl]_2$ (0.9 mg, 0.0025 mmol), **L1** (3.5 mg, 0.0055 mmol) and sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ($NaBAr^F_4$, 4.4 mg, 0.0050 mmol) was added dry *m*-Xylene (0.20 mL), and the resulting mixture was stirred at room temperature for 0.5 h. Then to the vial with copper complex above were added Et_3N (28 μL, 0.20 mmol) and diene **1a** (0.20 mmol), and the resulting mixture continued to stir at room temperature for 5 min. After this time, the vial with palladium complex solution were transferred to the vial with copper solution aforementioned. The resulting mixture was stirred at 50 °C for 48 h. After this time, to the reaction was added citric acid solution (2 mL, 20 wt.%) and THF (1 mL). The mixture was stirred at room temperature for 3 h. Then the mixture was neutralized with solid K_2CO_3 and extracted with EtOAc (10 mL x 3). The combined organic extracts were dried over $MgSO_4$, concentrated, and purified by flash column chromatography to give the pure product **3a-3w**.



Diethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate ((*R*,*R*)-3a)

Pd/**L1** and Cu/**L3** were used. Yellow oil, 20 mg, 84% yield, >20:1 dr, $[\alpha]_D^{25}$ -2.59 (*c* 0.73, $CHCl_3$) for 99% ee; ^1H NMR (400 MHz, chloroform-*d*) δ 6.75 (dd, *J* = 15.7, 9.5 Hz, 1H), 5.84 (d, *J* = 15.7 Hz, 1H), 4.39 – 4.03 (m, 4H), 3.64 – 3.43 (m, 1H), 2.49 (dt, *J* = 9.5, 4.3 Hz, 1H), 1.67 – 1.41 (m, 4H), 1.28 (tt, *J* = 7.0, 1.4 Hz, 6H), 0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 166.1, 147.4, 124.1, 61.2, 60.5, 24.0, 14.4, 14.3, 11.9 (one carbonyl carbon and two alkyl carbon signals were not observed). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{12}H_{22}O_4N^{\oplus}$ 244.1543, found 244.1542. HPLC analysis: Chiracel IF-3 column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 56.2 min, 60.3 min, 86.4 min, 102.0 min. The ee value was determined based on peaks at 82.3 min (major) and 99.0 min (minor).



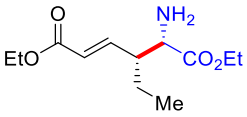


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	56.215	20.63
2	60.298	21.52
3	86.425	29.77
4	102.013	28.08

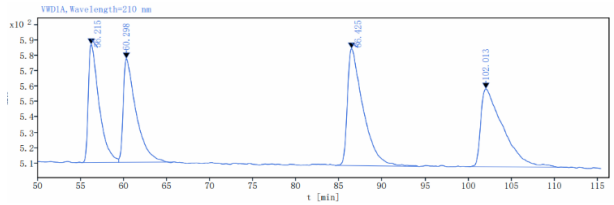
VWD1A, Wavelength=210 nm

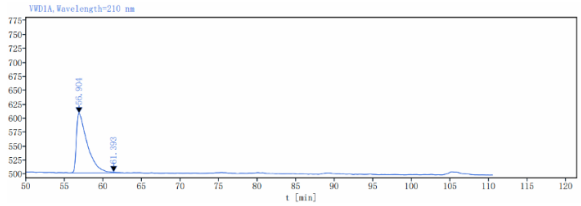
Number	Time	Area%
1	82.246	99.99
2	98.959	0.01



Diethyl (4*R*,5*S*,*E*)-5-amino-4-ethylhex-2-enedioate ((*R*,*S*)-3a)

Pd/**L1** and Cu/*ent*-**L3** were used. Yellow oil, 18 mg, 72% yield, 10:1 dr, $[\alpha]_D^{25}$ +22.09 (*c* 0.76, $CHCl_3$) for 99% ee; ^{1}H NMR (500 MHz, chloroform-*d*) δ 6.79 (dd, *J* = 15.6, 9.6 Hz, 1H), 5.86 (d, *J* = 15.6 Hz, 1H), 4.16 (dq, *J* = 12.0, 7.1 Hz, 4H), 3.47 (d, *J* = 5.5 Hz, 1H), 2.39 (tt, *J* = 9.6, 4.7 Hz, 1H), 1.78 (s, 2H), 1.67 – 1.37 (m, 2H), 1.26 (dt, *J* = 11.8, 7.1 Hz, 6H), 0.86 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.3, 166.1, 148.2, 123.7, 61.0, 60.4, 57.7, 48.9, 22.7, 14.30, 14.26, 11.9. HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{12}H_{22}O_4N^{\oplus}$ 244.1543, found 244.1545. HPLC analysis: Chiracel IF-3 column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; The ee value was determined based on peaks at 56.9 min (major) and 61.4 min (minor).



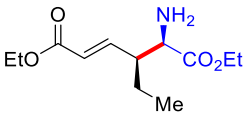


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	56.215	20.63
2	60.298	21.52
3	86.425	29.77
4	102.013	28.08

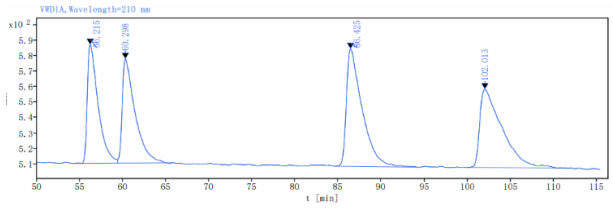
VWD1A, Wavelength=210 nm

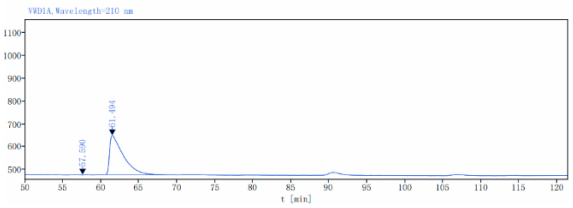
Number	Time	Area%
1	56.904	99.77
2	61.393	0.23



Diethyl (4*S*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate ((*S*,*R*)-3a)

Pd/*ent*-**L1** and Cu/**L3** were used. Yellow oil, 19 mg, 78% yield, 9:1 dr, $[\alpha]_D^{25}$ -23.16 (*c* 0.90, $CHCl_3$) for 99% ee; HPLC analysis: Chiracel IF-3 column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; The ee value was determined based on peaks at 57.6 min (minor) and 61.5 min (major).



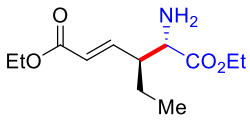


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	56.215	20.63
2	60.298	21.52
3	86.425	29.77
4	102.013	28.08

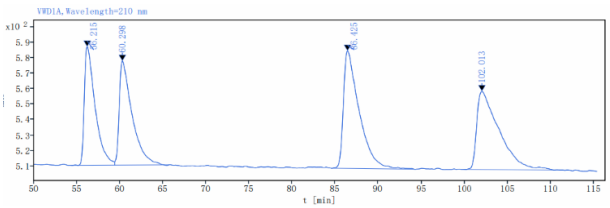
VWD1A, Wavelength=210 nm

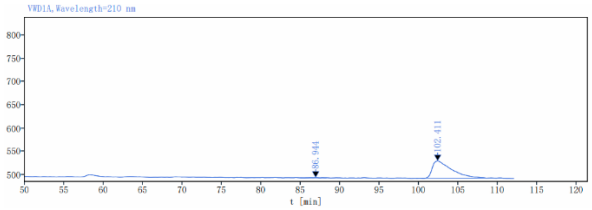
Number	Time	Area%
1	57.590	0.12
2	61.494	99.88



Diethyl (4*S*,5*S*,*E*)-5-amino-4-ethylhex-2-enedioate ((*S*,*S*)-3a)

Pd/*ent*-**L1** and Cu/*ent*-**L3** were used. Yellow oil, 21 mg, 87% yield, >20:1 dr, $[\alpha]_D^{25}$ +6.56 (*c* 0.72, $CHCl_3$) for 99% ee; HPLC analysis: Chiracel IF-3 column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; The ee value was determined based on peaks at 86.9 min (minor) and 102.4 min (major).



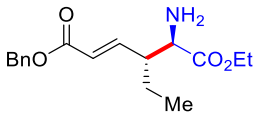


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	56.215	20.63
2	60.298	21.52
3	86.425	29.77
4	102.013	28.08

VWD1A, Wavelength=210 nm

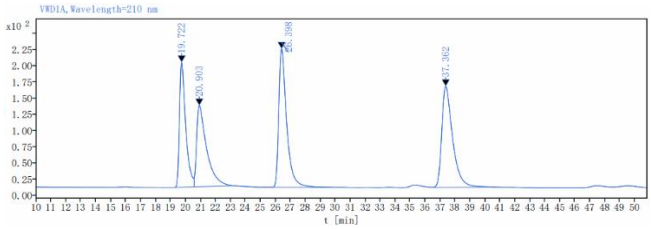
Number	Time	Area%
1	86.944	0.17
2	102.411	99.83

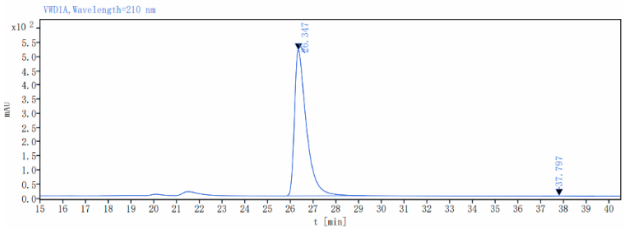


Denzyl 6-ethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3b)

Yellow oil, 19 mg, 63% yield, 15:1 dr, $[\alpha]_D^{25}$ -9.80 (*c* 0.72, $CHCl_3$) for 99% ee; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.43 – 7.29 (m, 5H), 6.82 (dd, *J* = 15.6, 9.2 Hz, 1H), 5.90 (d, *J* = 15.6 Hz, 1H), 5.17 (s, 2H), 4.19 (tq, *J* = 7.1, 3.3 Hz, 2H), 3.64 (s, 1H), 2.55 (s, 1H), 1.73 – 1.34 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 4H), 0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 165.9, 148.2, 136.0, 128.6, 128.3,

128.3, 123.7, 66.3, 61.2, 60.5, 23.9, 14.3, 11.9 (one carbonyl carbon and one alkyl carbon signals were not observed). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{17}H_{24}O_4N^{\oplus}$ 306.1700, found 306.1702. HPLC analysis: Chiracel IF-3 column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 19.7 min, 20.9 min, 36.4 min, 37.4 min. The ee value was determined based on peaks at 26.4 min (major) and 37.8 min (minor).



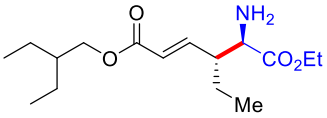


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	19.722	20.67
2	20.903	21.42
3	26.398	28.95
4	37.362	28.96

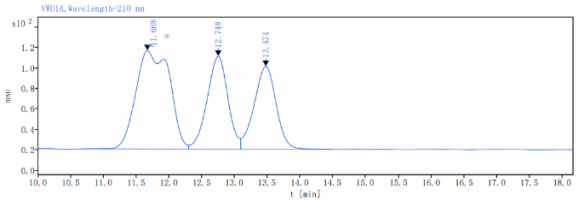
VWD1A, Wavelength=210 nm

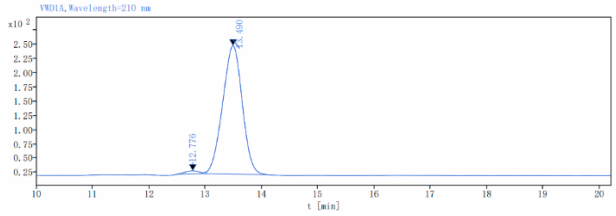
Number	Time	Area%
1	26.347	99.82
2	37.797	0.18



6-Ethyl 1-(2-ethylbutyl) (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (**3c**)

Yellow oil, 25 mg, 83% yield, >20:1 dr, $[\alpha]_D^{25}$ -3.10 (*c* 0.99, $CHCl_3$) for 95% ee; ^{1}H NMR (400 MHz, chloroform-*d*) δ 6.74 (dd, *J* = 15.6, 9.4 Hz, 1H), 5.84 (d, *J* = 15.6 Hz, 1H), 4.18 (p, *J* = 7.0 Hz, 2H), 4.07 – 3.99 (m, 2H), 3.69 – 3.38 (m, 1H), 2.50 (s, 1H), 1.63 – 1.43 (m, 3H), 1.35 (p, *J* = 7.1 Hz, 4H), 1.26 (t, *J* = 7.1 Hz, 4H), 0.89 (td, *J* = 7.5, 4.3 Hz, 10H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 166.3, 147.3, 124.1, 66.6, 61.1, 40.3, 23.9, 23.4, 23.4, 14.3, 14.2, 11.9, 11.1 (one carbonyl carbon signal was not observed). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{16}H_{30}O_4N^{\oplus}$ 300.2169, found 300.2168. HPLC analysis: Chiracel (OD-H) + (OD-H) column; detected at 210 nm, 20 °C; 5% ^{i}PrOH in *n*-hexane; flow = 1.3 mL/min; Retention time: 11.7 min, 12.8 min, 13.5 min. The ee value was determined based on peaks at 12.8 min (minor) and 13.5 min (major).



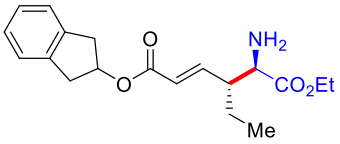


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	11.668	46.97
2	12.748	27.21
3	13.474	25.82

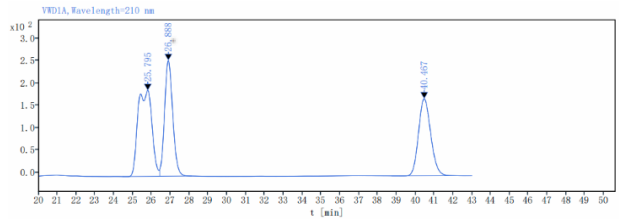
VWD1A, Wavelength=210 nm

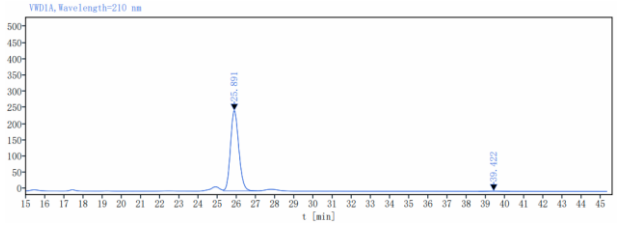
Number	Time	Area%
1	12.776	1.92
2	13.490	98.08



1-(2,3-Dihydro-1H-inden-2-yl) 6-ethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (**3d**)

Yellow oil, 30 mg, 90% yield, >20:1 dr, $[\alpha]_D^{25}$ -1.78 (*c* 0.56, $CHCl_3$) for 99% ee; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.30 – 7.06 (m, 4H), 6.75 (dd, *J* = 15.6, 9.3 Hz, 1H), 5.81 (d, *J* = 15.6 Hz, 1H), 5.58 (dt, *J* = 6.6, 3.3 Hz, 1H), 4.17 (qd, *J* = 7.1, 2.6 Hz, 2H), 3.54 (s, 1H), 3.34 (dd, *J* = 17.0, 6.6 Hz, 2H), 3.05 (dt, *J* = 17.0, 3.9 Hz, 2H), 2.48 (s, 1H), 1.70 – 1.43 (m, 3H), 1.25 (t, *J* = 7.1 Hz, 4H), 0.89 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.5, 166.0, 147.8, 140.5, 126.8, 124.7, 124.7, 75.4, 61.2, 57.4, 48.4, 39.7, 23.9, 14.3, 11.9. HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{19}H_{26}O_4N^{\oplus}$ 332.1856, found 332.1853. HPLC analysis: Chiracel (AD-H) + (AD-H) column; detected at 210 nm, 25 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 25.8 min, 26.9 min, 40.5 min. The ee value was determined based on peaks at 25.9 min (major) and 39.4 min (minor).



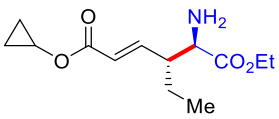


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	25.795	39.06
2	26.888	30.58
3	40.467	30.36

VWD1A, Wavelength=210 nm

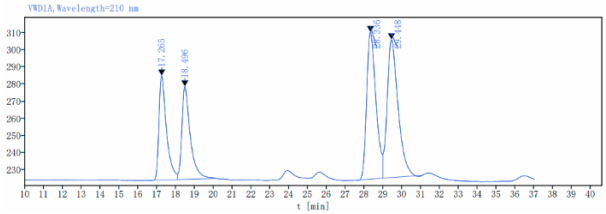
Number	Time	Area%
1	25.891	99.39
2	39.422	0.61



Cyclopropyl 6-ethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (**3e**)

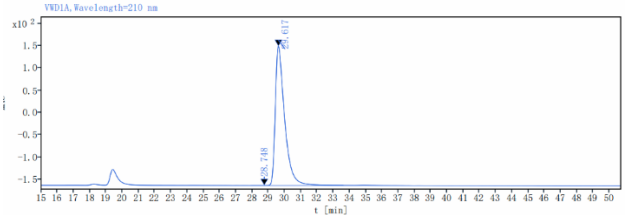
Yellow oil, 18 mg, 70% yield, 10:1 dr, $[\alpha]_D^{25}$ -4.76 (*c* 0.86, $CHCl_3$) for 99% ee; ^{1}H NMR (500 MHz, chloroform-*d*) δ 6.73 (dd, *J* = 15.7, 9 .5 Hz, 1H), 5.79 (d, *J* = 15.7 Hz, 1H), 4.17 (ttd, *J* = 13.6, 6.9, 3.8 Hz, 3H), 3.50 (d, *J* = 5.0 Hz, 1H), 2.47 (tt, *J* = 9.5, 5.2 Hz, 1H), 1.64 – 1.44 (m, 2H), 1.43 (s, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H), 0.79 – 0.66 (m, 4H). ^{13}C NMR (126 MHz, chloroform-*d*) δ

166.9, 147.9, 123.7, 61.2, 48.9, 23.9, 14.4, 11.9, 5.18, 5.16 (one carbonyl carbon and one alkyl carbon signals were not observed). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{13}H_{22}O_4N^{\oplus}$ 256.1543, found 256.1546. HPLC analysis: Chiracel IF-3 column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 17.3 min, 18.5 min, 28.3 min, 29.5 min. The ee value was determined based on peaks at 28.8 min (major) and 29.6 min (minor).



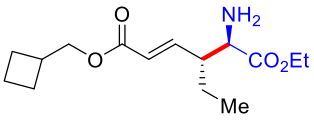
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	17.265	17.72
2	18.496	17.71
3	28.336	30.71
4	29.448	33.86



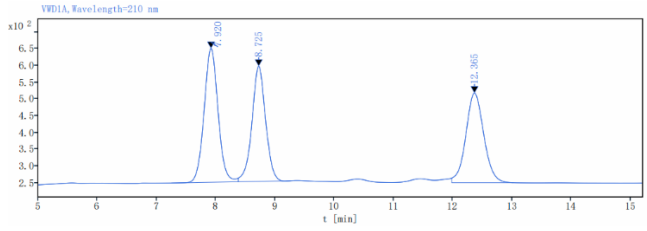
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	28.748	0.02
2	29.617	99.98



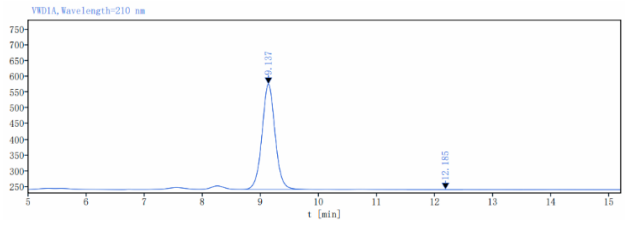
1-(Cyclobutylmethyl) 6-ethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3f)

Yellow oil, 25 mg, 86% yield, >20:1 dr, $[\alpha]_D^{25}$ -2.36 (*c* 0.70, $CHCl_3$) for 99% ee; ^{1}H NMR (400 MHz, chloroform-*d*) δ 6.74 (dd, *J* = 15.7, 9.4 Hz, 1H), 5.84 (d, *J* = 15.7 Hz, 1H), 4.18 (qd, *J* = 7.1, 5.0 Hz, 2H), 4.09 (d, *J* = 6.8 Hz, 2H), 3.52 (s, 1H), 2.62 (p, *J* = 7.4 Hz, 1H), 2.49 (dt, *J* = 9.3, 4.3 Hz, 1H), 2.05 (dtd, *J* = 12.6, 7.4, 6.9, 2.8 Hz, 2H), 1.95 – 1.71 (m, 4H), 1.66 – 1.42 (m, 3H), 1.27 (t, *J* = 7.2 Hz, 4H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.5, 166.3, 147.5, 124.1, 68.4, 61.2, 57.4, 48.3, 34.1, 24.9, 23.9, 18.5, 14.3, 11.9. HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{15}H_{26}O_4N^{\oplus}$ 284.1854, found 284.1857. HPLC analysis: Chiracel AD-H column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 7.9 min, 8.7 min, 12.3 min. The ee value was determined based on peaks at 9.1 min (major) and 12.2 min (minor).



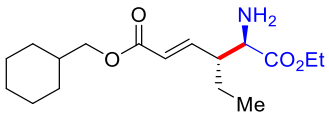
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	7.920	37.06
2	8.725	31.06
3	12.365	31.88



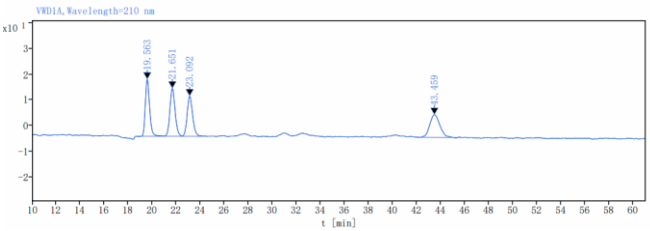
VWD1A, Wavelength=210 nm

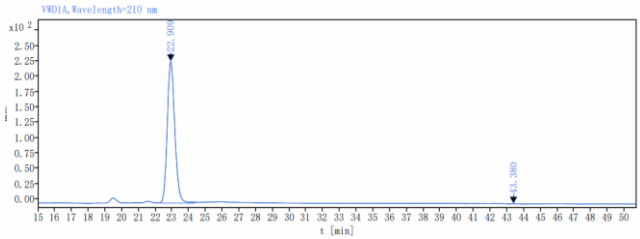
Number	Time	Area%
1	9.137	99.98
2	12.185	0.02



1-(Cyclohexylmethyl) 6-ethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3g)

Yellow oil, 23 mg, 73% yield, >20:1 dr, $[\alpha]_D^{25}$ -5.10 (*c* 0.86, $CHCl_3$) for 99% ee; ^{1}H NMR (500 MHz, chloroform-*d*) δ 6.75 (dd, *J* = 15.7, 9.4 Hz, 1H), 5.85 (d, *J* = 15.7 Hz, 1H), 4.24 – 4.14 (m, 2H), 3.93 (d, *J* = 6.6 Hz, 2H), 3.52 (d, *J* = 5.1 Hz, 1H), 2.50 (tt, *J* = 9.6, 5.2 Hz, 1H), 1.77 – 1.50 (m, 10H), 1.29 – 1.16 (m, 6H), 0.97 (qd, *J* = 10.7, 9.5, 5.0 Hz, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 166.2, 147.4, 124.1, 69.7, 61.2, 37.1, 29.7, 26.4, 25.7, 23.9, 14.3, 11.9. (one carbonyl carbon and two alkyl carbon signals were not observed because of overlapping). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{17}H_{30}O_4N^{\oplus}$ 312.2169, found 312.2170. HPLC analysis: Chiracel (AD-H) + (AD-H) column; detected at 210 nm, 20 °C; 5% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 19.6 min, 21.7 min, 23.1 min, 43.5 min. The ee value was determined based on peaks at 22.9 min (major) and 43.4 min (minor).



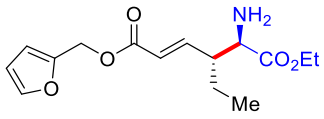


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	19.563	26.10
2	21.651	26.37
3	23.092	23.60
4	43.459	23.93

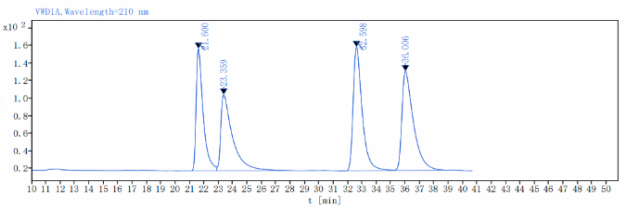
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	22.909	99.96
2	43.380	0.04



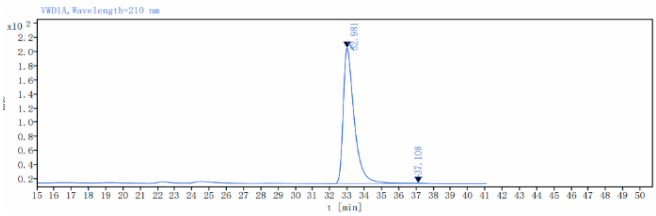
6-Ethyl 1-(furan-2-ylmethyl) (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3h)

Yellow oil, 19 mg, 65% yield, >20:1 dr, $[\alpha]_D^{25}$ -5.22 (*c* 0.94, $CHCl_3$) for 99% ee; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.42 (d, *J* = 1.8 Hz, 1H), 6.80 (dd, *J* = 15.6, 9.5 Hz, 1H), 6.41 (d, *J* = 3.3 Hz, 1H), 6.36 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.86 (d, *J* = 15.6 Hz, 1H), 5.11 (s, 2H), 4.17 (qd, *J* = 7.2, 2.2 Hz, 2H), 3.51 (s, 1H), 2.49 (tt, *J* = 9.6, 5.2 Hz, 1H), 1.66 – 1.39 (m, 4H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 165.6, 149.5, 148.5, 143.3, 123.4, 110.8, 110.6, 61.2, 58.1, 57.4, 48.4, 23.9, 14.3, 11.9 (one carbonyl carbon signal was not observed). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{15}H_{22}O_5N^{\oplus}$ 296.1493, found 296.1493. HPLC analysis: Chiracel IF-3 column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 21.6 min, 23.4 min, 32.6 min, 36.0 min. The ee value was determined based on peaks at 33.0 min (major) and 37.1 min (minor).



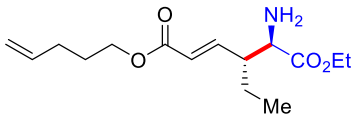
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	21.600	21.31
2	23.359	22.31
3	32.598	27.87
4	36.006	28.51



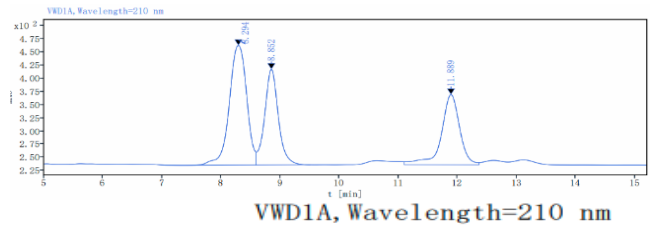
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	32.981	99.52
2	37.108	0.48



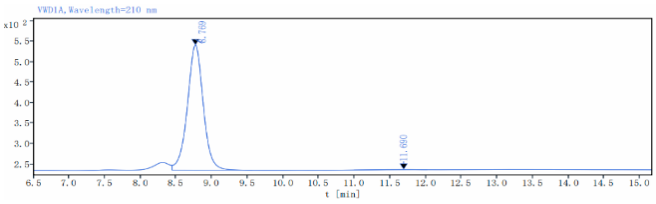
6-Ethyl 1-(pent-4-en-1-yl) (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3i)

Yellow oil, 23 mg, 80% yield, >20:1 dr, $[\alpha]_D^{25}$ -3.04 (*c* 0.67, $CHCl_3$) for 99% ee; ^1H NMR (400 MHz, chloroform-*d*) δ 6.75 (dd, *J* = 15.7, 9.5 Hz, 1H), 5.90 – 5.62 (m, 2H), 5.15 – 4.91 (m, 2H), 4.33 – 3.99 (m, 4H), 3.53 (s, 1H), 2.50 (tt, *J* = 9.5, 5.2 Hz, 1H), 2.28 – 2.03 (m, 2H), 1.83 – 1.69 (m, 2H), 1.66 – 1.47 (m, 4H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.5, 166.1, 147.6, 137.6, 124.0, 115.4, 63.9, 61.2, 57.4, 48.3, 30.1, 27.9, 23.9, 14.4, 11.9. HRMS (ESI): $[M+H]^+$ calcd for $C_{15}H_{26}O_4N^+$ 284.1856, found 284.1857. HPLC analysis: Chiracel AD-H column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 8.3 min, 8.9 min, 11.9 min. The ee value was determined based on peaks at 8.8 min (major) and 11.7 min (minor).



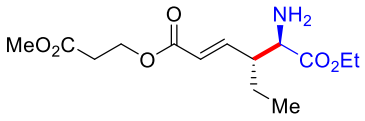
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	8.294	44.46
2	8.852	27.89
3	11.889	27.64



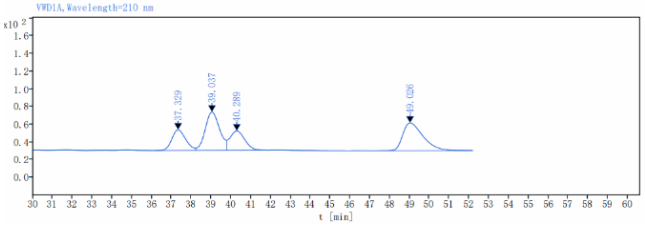
VWD1A, Wavelength=210 nm

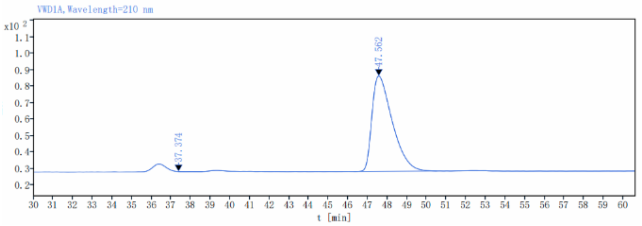
Number	Time	Area%
1	8.769	99.42
2	11.690	0.58



6-Ethyl 1-(3-methoxy-3-oxopropyl) (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3j)

Yellow oil, 20 mg, 65% yield, >20:1 dr, $[\alpha]_D^{25}$ -12.62 (*c* 1.04, $CHCl_3$) for 99% ee; ^1H NMR (400 MHz, chloroform-*d*) δ 6.76 (dd, *J* = 15.7, 9.5 Hz, 1H), 5.87 – 5.74 (d, *J* = 15.7 Hz, 1H), 4.39 (t, *J* = 6.4 Hz, 2H), 4.17 (qt, *J* = 7.3, 3.7 Hz, 2H), 3.70 (s, 3H), 3.51 (d, *J* = 5.1 Hz, 1H), 2.68 (t, *J* = 6.4 Hz, 2H), 2.48 (tt, *J* = 9.6, 5.1 Hz, 1H), 1.69 – 1.43 (m, 4H), 1.27 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 170.7, 165.1, 147.8, 123.9, 67.4, 61.2, 60.4, 51.8, 40.7, 23.8, 19.9, 14.3, 11.8 (one carbonyl carbon signal was not observed because of overlapping). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{14}H_{24}O_6N^{\oplus}$ 302.1598, found 302.1596. HPLC analysis: Chiracel (OD-H) + (OD-H) column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 37.3 min, 39.0 min, 40.3 min, 49.0 min. The ee value was determined based on peaks at 37.4 min (minor) and 47.6 min (major).



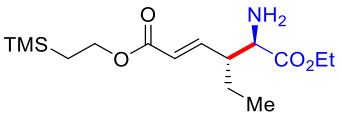


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	37.329	16.88
2	39.037	32.72
3	40.289	16.92
4	49.026	33.48

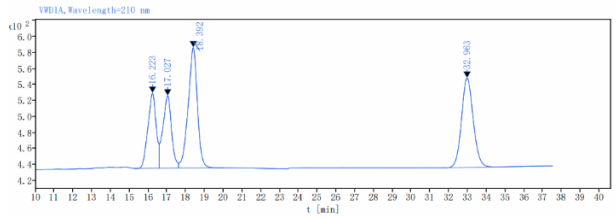
VWD1A, Wavelength=210 nm

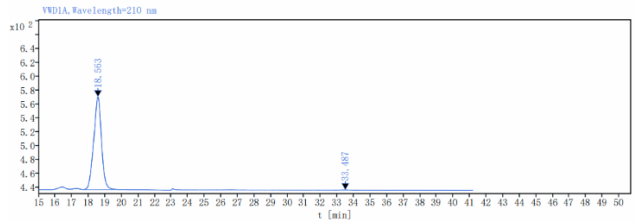
Number	Time	Area%
1	37.374	0.05
2	47.562	99.95



6-Ethyl 1-(2-(trimethylsilyl)ethyl) (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3k)

Yellow oil, 30 mg, 95% yield, >20:1 dr, $[\alpha]_D^{25}$ -3.64 (*c* 0.81, $CHCl_3$) for 99% ee; ^1H NMR (400 MHz, chloroform-*d*) δ 6.72 (dd, *J* = 15.6, 9.3 Hz, 1H), 5.81 (d, *J* = 15.6 Hz, 1H), 4.30 – 3.89 (m, 4H), 3.71 – 3.35 (m, 1H), 2.49 (s, 1H), 1.71 – 1.39 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 4H), 1.00 (dd, *J* = 9.2, 7.6 Hz, 2H), 0.89 (t, *J* = 7.4 Hz, 3H), 0.03 (s, 9H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.5, 166.2, 147.3, 124.3, 62.7, 61.2, 57.5, 48.3, 24.0, 17.4, 14.4, 11.9, -1.4. HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{15}H_{30}O_4NSi^{\oplus}$ 316.1939, found 316.1937. HPLC analysis: Chiracel (AD-H) + (AD-H) column; detected at 210 nm, 20 °C; 5% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 16.2 min, 17.0 min, 18.4 min, 33.0 min. The ee value was determined based on peaks at 18.6 min (major) and 33.5 min (minor).



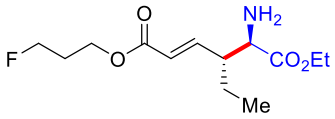


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	16.223	18.18
2	17.027	18.37
3	18.392	32.82
4	32.963	30.63

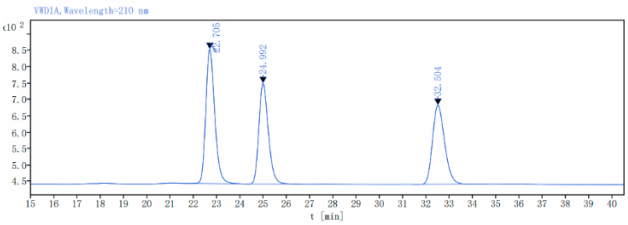
VWD1A, Wavelength=210 nm

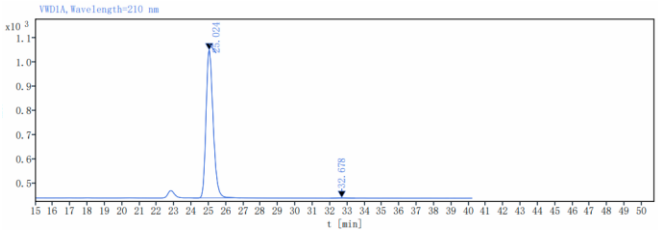
Number	Time	Area%
1	18.563	99.65
2	33.487	0.35



6-Ethyl 1-(3-fluoropropyl) (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3l)

Yellow oil, 22 mg, 80% yield, >20:1 dr, $[\alpha]_D^{25}$ -4.05 (*c* 1.04, $CHCl_3$) for 99% ee; ^1H NMR (400 MHz, chloroform-*d*) δ 6.77 (dd, *J* = 15.6, 9.5 Hz, 1H), 5.84 (d, *J* = 15.6 Hz, 1H), 4.59 (t, *J* = 5.8 Hz, 1H), 4.47 (t, *J* = 5.8 Hz, 1H), 4.25 (t, *J* = 6.3 Hz, 2H), 4.18 (tq, *J* = 7.2, 4.1 Hz, 2H), 3.52 (d, *J* = 5.0 Hz, 1H), 2.49 (tt, *J* = 9.6, 5.2 Hz, 1H), 2.04 (dp, *J* = 25.6, 6.1 Hz, 2H), 1.66 – 1.39 (m, 4H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.4, 165.9, 148.1, 123.6, 80.7 (d, *J* = 165.3 Hz), 61.2, 60.4 (d, *J* = 5.4 Hz), 57.4, 48.3, 29.8 (d, *J* = 20.1 Hz), 23.9, 14.3, 11.9. ^{19}F NMR (376 MHz, chloroform-*d*) δ -222.2 (tt, *J* = 49.1, 25.2 Hz). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{13}H_{23}O_4NF^{\oplus}$ 276.1606, found 276.1605. HPLC analysis: Chiracel (AD-H) + (AD-H) column; detected at 210 nm, 20 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 22.7 min, 25.0 min, 32.5 min. The ee value was determined based on peaks at 25.0 min (major) and 32.7 min (minor).



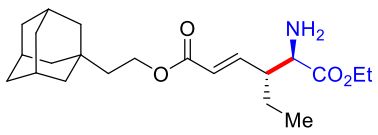


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	22.705	38.47
2	24.992	30.75
3	32.504	30.78

VWD1A, Wavelength=210 nm

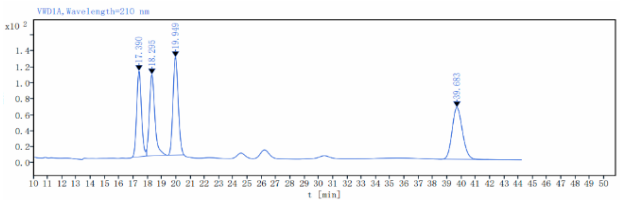
Number	Time	Area%
1	25.024	99.81
2	32.678	0.19



1-(2-((3*R*,5*R*,7*R*)-Adamantan-1-yl)ethyl) 6-ethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3m)

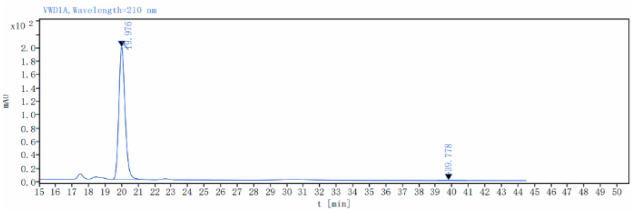
Yellow oil, 23 mg, 62% yield, >20:1 dr, $[\alpha]_D^{25}$ -5.20 (*c* 0.88, $CHCl_3$) for 99% ee; ^1H NMR (400 MHz, chloroform-*d*) δ 6.74 (dd, *J* = 15.6, 9.4 Hz, 1H), 5.83 (d, *J* = 15.6 Hz, 1H), 4.33 – 4.10 (m, 4H), 3.48 (dtt, *J* = 10.4, 7.1, 3.7 Hz, 1H), 2.51 (s, 1H), 2.04 – 1.87 (m, 4H), 1.78 – 1.57 (m, 8H), 1.53 (d, *J* = 2.9 Hz,

7H), 1.45 (t, *J* = 7.4 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 166.2, 147.3, 124.2, 61.2, 61.0, 42.6, 42.4, 37.1, 31.8, 28.6, 24.0, 14.4, 11.9 (one carbonyl carbon and two alkyl carbon signals were not observed because of overlapping). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{22}H_{36}O_4N^{\oplus}$ 378.2639, found 378.2635. HPLC analysis: Chiracel (AD-H) + (AD-H) column; detected at 210 nm, 20 °C; 10 % ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 17.4 min, 18.3 min, 20.0 min, 39.7 min. The ee value was determined based on peaks at 20.0 min (major) and 39.8 min (minor).



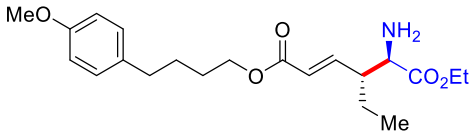
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	17.390	21.66
2	18.295	23.34
3	19.949	26.96
4	39.683	28.04



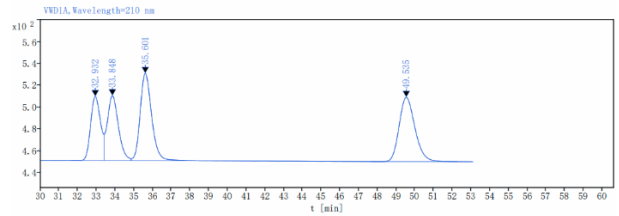
VWD1A, Wavelength=210 nm

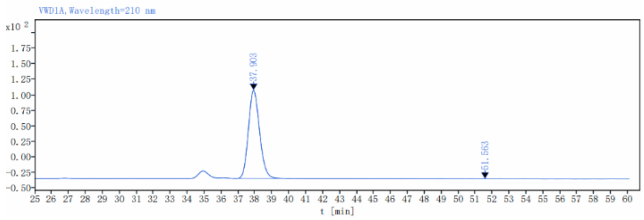
Number	Time	Area%
1	19.976	99.75
2	39.778	0.25



6-Ethyl 1-(4-(4-methoxyphenyl)butyl) (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (**3n**)

Yellow oil, 34 mg, 90% yield, >20:1 dr, $[\alpha]_D^{25}$ -1.80 (*c* 0.39, $CHCl_3$) for 99% ee; ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.09 (d, *J* = 8.1 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 6.75 (dd, *J* = 15.7, 9.5 Hz, 1H), 5.84 (d, *J* = 15.7 Hz, 1H), 4.22 – 4.12 (m, 4H), 3.79 (s, 3H), 3.53 (s, 1H), 2.59 (t, *J* = 6.9 Hz, 2H), 2.54 – 2.45 (m, 1H), 1.67 (dt, *J* = 8.0, 3.7 Hz, 4H), 1.62 – 1.52 (m, 4H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 166.2, 157.8, 147.5, 134.2, 129.4, 124.1, 113.8, 64.5, 61.2, 55.3, 34.6, 28.2, 28.0, 23.9, 14.4, 11.9 (one carbonyl carbon and two alkyl carbon signals were not observed). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{21}H_{32}O_5N^{\oplus}$ 378.2275, found 378.2273. HPLC analysis: Chiracel (AD-H) + (AD-H) column; detected at 210 nm, 20 °C; 10 % ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 32.9 min, 33.9 min, 35.6 min, 49.5 min. The ee value was determined based on peaks at 37.9 min (major) and 51.6 min (minor).



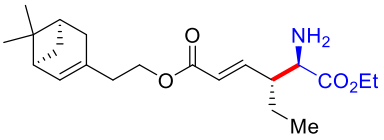


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	32.932	18.64
2	33.848	21.52
3	35.601	29.72
4	49.535	30.12

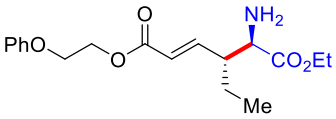
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	37.903	99.99
2	51.563	0.01



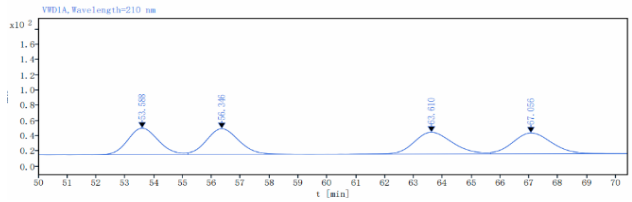
1-(2-((1*S*,5*R*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-3-yl)ethyl) 6-ethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3o)

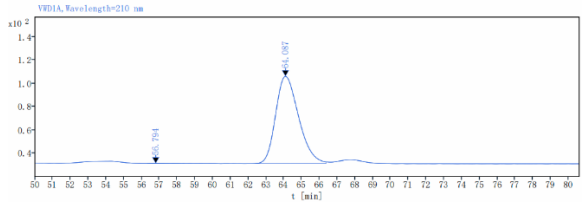
Yellow oil, 33 mg, 90% yield, >20:1 dr, $[\alpha]_D^{25}$ -22.30 (*c* 1.12, $CHCl_3$); ^1H NMR (500 MHz, chloroform-*d*) δ 6.73 (dd, *J* = 15.7, 9.5 Hz, 1H), 5.81 (d, *J* = 15.7 Hz, 1H), 5.28 (dd, *J* = 3.0, 1.5 Hz, 1H), 4.27 – 3.92 (m, 4H), 3.50 (d, *J* = 5.0 Hz, 1H), 2.48 (dt, *J* = 9.3, 4.4 Hz, 1H), 2.38 – 2.27 (m, 3H), 2.27 – 2.14 (m, 2H), 2.05 (dtd, *J* = 11.5, 5.7, 3.8 Hz, 2H), 1.64 – 1.42 (m, 4H), 1.31 – 1.23 (m, 6H), 1.13 (d, *J* = 8.6 Hz, 1H), 0.89 (t, *J* = 7.4 Hz, 3H), 0.80 (s, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 166.0, 147.4, 144.2, 124.1, 118.9, 62.8, 61.1, 57.4, 48.3, 45.7, 40.7, 38.0, 36.0, 31.7, 31.4, 26.3, 24.0, 21.2, 14.3, 11.8 (one carbonyl carbon signal was not observed). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{21}H_{34}O_4N^{\oplus}$ 364.2482, found 364.2477.



1-(2-(Benzyloxy)ethyl) 6-ethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3p)

Yellow oil, 27 mg, 81% yield, 16:1 dr, $[\alpha]_D^{25}$ -4.35 (*c* 1.22, $CHCl_3$); ^1H NMR (400 MHz, chloroform-*d*) δ 7.33 – 7.24 (m, 2H), 6.96 (t, *J* = 7.3 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 2H), 6.80 (dd, *J* = 15.7, 9.5 Hz, 1H), 5.88 (d, *J* = 15.7 Hz, 1H), 4.53 – 4.34 (m, 2H), 4.17 (dq, *J* = 14.2, 4.0, 3.1 Hz, 4H), 3.58 – 3.46 (m, 1H), 2.49 (tt, *J* = 9.5, 5.2 Hz, 1H), 1.64 – 1.41 (m, 4H), 1.25 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.4, 165.9, 158.6, 148.5, 129.6, 123.5, 121.2, 114.7, 65.9, 62.9, 61.2, 57.4, 48.4, 23.9, 14.4, 11.9. HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{18}H_{26}O_5N^{\oplus}$ 336.1806, found 336.1808. HPLC analysis: Chiracel (OD-H) + (OD-H) column; detected at 210 nm, 20 °C; 5% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 53.6 min, 56.3 min, 63.6 min, 67.1 min. The ee value was determined based on peaks at 56.8 min (minor) and 64.1 min (major).



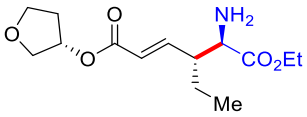


VWD1A, Wavelength=210 nm

Number	Time	Area%
1	53.588	24.68
2	56.346	25.34
3	63.610	25.37
4	67.056	24.61

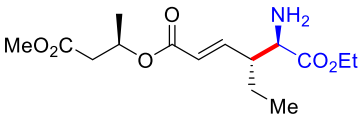
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	56.794	0.03
2	64.087	99.97



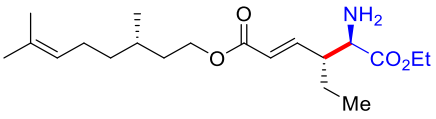
6-Ethyl 1-((*S*)-tetrahydrofuran-3-yl) (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (**3q**)

Yellow oil, 25 mg, 89% yield, >20:1 dr, $[\alpha]_D^{25}$ -12.6 (*c* 1.04, $CHCl_3$); ^1H NMR (400 MHz, chloroform-*d*) δ 6.77 (dd, *J* = 15.7, 9.5 Hz, 1H), 5.83 (d, *J* = 15.7 Hz, 1H), 5.33 (ddd, *J* = 6.6, 4.4, 2.2 Hz, 1H), 4.18 (dq, *J* = 7.0, 3.9 Hz, 2H), 4.02 – 3.73 (m, 4H), 3.51 (d, *J* = 5.1 Hz, 1H), 2.49 (dt, *J* = 9.3, 4.3 Hz, 1H), 2.34 – 2.11 (m, 1H), 2.09 – 1.93 (m, 1H), 1.82 – 1.43 (m, 4H), 1.27 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.4, 165.7, 148.3, 123.7, 74.9, 73.2, 67.1, 61.2, 57.3, 48.3, 32.8, 23.9, 14.3, 11.9. HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{14}H_{24}O_5N^{\oplus}$ 286.1649, found 286.1648.



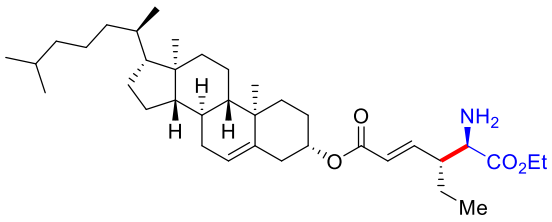
6-Ethyl 1-((*R*)-4-methoxy-4-oxobutan-2-yl) (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (**3r**)

Yellow oil, 19 mg, 61% yield, >20:1 dr, $[\alpha]_D^{25}$ -9.85 (*c* 0.83, $CHCl_3$); ^1H NMR (400 MHz, chloroform-*d*) δ 6.74 (dd, *J* = 15.7, 9.4 Hz, 1H), 5.80 (d, *J* = 15.6 Hz, 1H), 5.30 (h, *J* = 6.4 Hz, 1H), 4.17 (qt, *J* = 7.0, 3.6 Hz, 2H), 3.66 (s, 3H), 3.52 (d, *J* = 5.0 Hz, 1H), 2.68 (dd, *J* = 15.4, 7.1 Hz, 1H), 2.59 – 2.34 (m, 2H), 1.73 (s, 2H), 1.58 (dt, *J* = 13.7, 6.8 Hz, 1H), 1.48 (dt, *J* = 14.2, 7.6 Hz, 1H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 170.8, 165.2, 147.8, 124.0, 67.4, 61.2, 60.5, 51.8, 40.7, 23.9, 21.0, 20.0, 14.3, 11.9 (one carbonyl carbon signal was not observed because of overlapping). HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{15}H_{26}O_6N^{\oplus}$ 316.1755, found 316.1755.



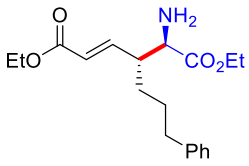
1-((*S*)-3,7-Dimethyloct-6-en-1-yl) 6-ethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (**3s**)

Yellow oil, 24 mg, 68% yield, >20:1 dr, $[\alpha]_D^{25}$ +11.6 (*c* 0.11, $CHCl_3$); ^1H NMR (400 MHz, chloroform-*d*) δ 6.74 (dd, *J* = 15.7, 9.3 Hz, 1H), 5.84 (d, *J* = 15.7 Hz, 1H), 5.14 – 4.90 (m, 1H), 4.33 – 3.94 (m, 4H), 3.77 – 3.35 (m, 1H), 2.51 (s, 1H), 1.98 (tq, *J* = 15.0, 7.5, 7.1 Hz, 2H), 1.67 (s, 4H), 1.60 (s, 3H), 1.57 – 1.32 (m, 7H), 1.30 – 1.13 (m, 5H), 0.95 – 0.86 (m, 5H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.4, 166.1, 147.4, 131.4, 124.6, 124.1, 63.1, 61.1, 57.4, 48.3, 37.0, 35.4, 29.6, 25.7 25.4, 23.9, 19.4, 17.7, 14.3, 11.8. HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{20}H_{36}O_4N^{\oplus}$ 354.2639, found 354.2642



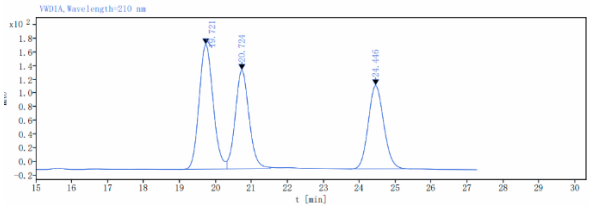
1-((3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl) 6-ethyl (4*R*,5*R*,*E*)-5-amino-4-ethylhex-2-enedioate (3t)

Yellow oil, 55 mg, 95% yield, >20:1 dr, $[\alpha]_D^{25}$ -14.8 (*c* 1.38, $CHCl_3$); ^1H NMR (500 MHz, chloroform-*d*) δ 6.73 (dd, *J* = 15.6, 9.4 Hz, 1H), 5.82 (d, *J* = 15.6 Hz, 1H), 5.37 (d, *J* = 5.0 Hz, 1H), 4.66 (td, *J* = 10.1, 9.2, 4.2 Hz, 1H), 4.19 (qd, *J* = 7.2, 4.2 Hz, 2H), 3.51 (d, *J* = 5.1 Hz, 1H), 2.63 – 2.41 (m, 1H), 2.34 (d, *J* = 7.0 Hz, 2H), 2.07 – 1.75 (m, 5H), 1.73 – 0.80 (m, 43H), 0.67 (s, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.4, 165.5, 147.2, 139.7, 124.6, 122.7, 74.1, 61.2, 57.4, 56.8, 56.2, 50.1, 48.3, 42.4, 39.8, 39.6, 38.2, 37.1, 36.7, 36.3, 35.9, 32.0, 31.9, 28.3, 28.1, 27.9, 24.4, 23.92, 23.89, 22.9, 22.6, 21.1, 19.4, 18.8, 14.4, 11.93, 11.91. HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{37}H_{62}O_4N^{\oplus}$ 584.4673, found 584.4672.



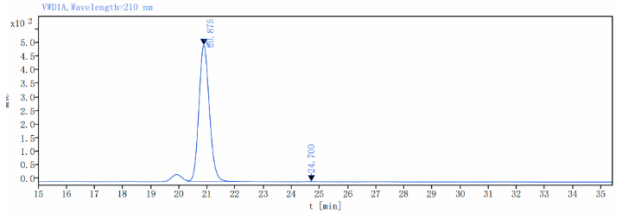
Diethyl (4*R*,5*R*,*E*)-5-amino-4-(3-phenylpropyl)hex-2-enedioate (3u)

Yellow oil, 27 mg, 80% yield, >20:1 dr, $[\alpha]_D^{25}$ -22.9 (*c* 1.34, $CHCl_3$); ^1H NMR (400 MHz, chloroform-*d*) δ 7.27 (t, *J* = 7.4 Hz, 2H), 7.20 – 7.12 (m, 3H), 6.75 (dd, *J* = 15.6, 9.6 Hz, 1H), 5.82 (d, *J* = 15.6 Hz, 1H), 4.17 (qdd, *J* = 8.1, 5.3, 2.9 Hz, 4H), 3.49 (s, 1H), 2.60 (d, *J* = 7.6 Hz, 3H), 1.71 – 1.46 (m, 6H), 1.27 (dt, *J* = 10.4, 7.1 Hz, 6H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.3, 166.0, 147.3, 142.0, 128.4, 128.4, 125.9, 124.1, 61.2, 60.5, 57.7, 46.6, 35.8, 30.5, 29.2, 14.3, 14.2. HRMS (ESI): $[M+H]^{\oplus}$ calcd for $C_{19}H_{28}O_4N^{\oplus}$ 334.2013, found 334.2010. HPLC analysis: Chiracel (AD-H) + (AD-H) column; detected at 210 nm, 25 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 19.7 min, 20.7 min, 24.5 min. The ee value was determined based on peaks at 20.9 min (major) and 24.7 min (minor).



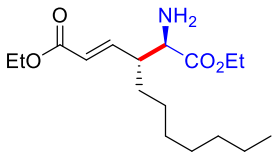
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	19.721	39.79
2	20.724	30.89
3	24.446	29.31



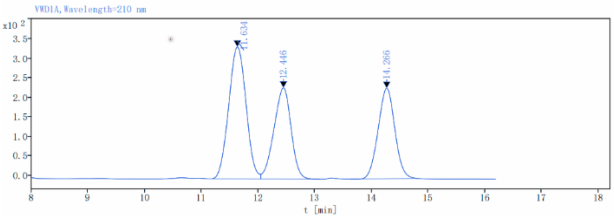
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	20.875	99.82
2	24.700	0.18



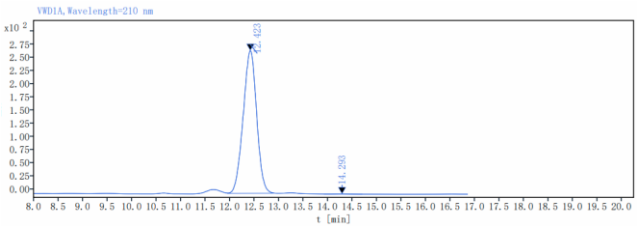
Diethyl (4*R*,5*R*,*E*)-5-amino-4-heptylhex-2-enedioate (3v)

Yellow oil, 20 mg, 65% yield, >20:1 dr, $[\alpha]_D^{25}$ -12.12 (*c* 0.84, $CHCl_3$); ^1H NMR (400 MHz, chloroform-*d*) δ 6.74 (dd, *J* = 15.6, 9.4 Hz, 1H), 5.82 (d, *J* = 15.6 Hz, 1H), 4.17 (q, *J* = 6.9 Hz, 4H), 3.51 (s, 1H), 2.57 (qd, *J* = 9.8, 6.5, 5.2 Hz, 1H), 1.68 – 1.35 (m, 4H), 1.27 (ddd, *J* = 9.9, 6.5, 3.1 Hz, 16H), 0.86 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 166.1, 147.7, 123.9, 61.1, 60.5, 57.7, 46.7, 31.8, 30.9, 29.5, 29.2, 27.3, 22.7, 14.32, 14.27, 14.1 (one carbonyl carbon signal was not observed). HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{32}O_4N^+$ 314.2326, found 314.2326. HPLC analysis: Chiracel (AD-H) + (AD-H) column; detected at 210 nm, 25 °C; 10% ^{i}PrOH in *n*-hexane; flow = 1.0 mL/min; Retention time: 11.6 min, 12.4 min, 14.3 min. The ee value was determined based on peaks at 12.4 min (major) and 14.3 min (minor).



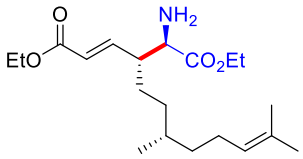
VWD1A, Wavelength=210 nm

Number	Time	Area%
1	11.634	42.68
2	12.446	29.15
3	14.266	28.18



VWD1A, Wavelength=210 nm

Number	Time	Area%
1	12.423	99.89
2	14.293	0.11

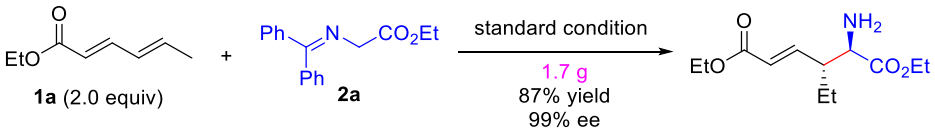


Diethyl (4*R*,5*R*,*E*)-5-amino-4-((*S*)-3,7-dimethyloct-6-en-1-yl)hex-2-enedioate (3w)

Yellow oil, 23 mg, 66% yield, >20:1 dr, $[\alpha]_D^{25}$ -4.74 (*c* 1.05, $CHCl_3$); ^1H NMR (400 MHz, chloroform-*d*) δ 6.75 (dd, *J* = 15.7, 9.5 Hz, 1H), 5.81 (d, *J* = 15.7 Hz, 1H), 5.07 (t, *J* = 7.2 Hz, 1H), 4.29 – 4.03 (m, 4H), 3.50 (d, *J* = 4.9 Hz, 1H), 2.54 (dt, *J* = 9.3, 4.4 Hz, 1H), 1.94 (qd, *J* = 14.9, 7.3 Hz, 2H), 1.67 (s, 3H), 1.58 (s, 5H), 1.48 –1.33 (m, 3H), 1.27 (td, *J* = 7.1, 2.9 Hz, 8H), 1.09 (tdd, *J* = 18.3, 8.0, 5.8 Hz, 2H), 0.86 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.4, 166.0, 147.6, 131.2, 124.8, 123.9, 61.1, 60.4, 57.6, 46.9, 36.8, 34.5, 32.4, 28.4, 25.7, 25.5, 19.5, 17.7, 14.3, 14.2. HRMS (ESI): $[M+H]^+$ calcd for $C_{20}H_{36}O_4N^+$ 354.2639, found 354.2635.

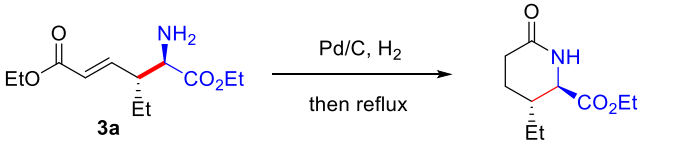
5. Gram-scale test and transformations

5.1 Gram-scale test



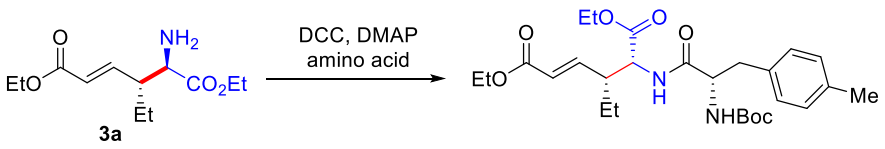
In a N_2-filled glovebox, to a 4 mL vial with $Cu(MeCN)_4BF_4$ (0.13 g, 0.40 mmol), **L3** (0.22 g, 0.44 mmol) and nucleophilic **2a** (8.0 mmol) was added dry *m*-Xylene (16 mL). The resulting mixture was stirred at room temperature for 0.5 h. To another 4 mL vial with $[Pd(\eta^3\text{-allyl})Cl]_2$ (72 mg, 0.20 mmol), **L1** (0.28 g, 0.44 mmol) and sodium $NaBAr^F_4$ (0.35 g, 0.40 mmol) was added dry *m*-Xylene (16 mL), and the resulting mixture was stirred at room temperature for 0.5 h. Then to the vial with copper complex above were added Et_3N (2.2 mL, 16 mmol) and diene **1a** (16 mmol), and the resulting mixture continued to stir at room temperature for 5 min. After this time, the vial with palladium complex solution were transferred to the vial with copper solution aforementioned. The reaction mixture was stirred at 50 °C for 48 h. To the reaction mixture was added citric acid solution (160 mL, 20 wt.%) and THF (80 mL) and the mixture was stirred for 6 h. The mixture was neutralized with solid K_2CO_3 and extracted with EtOAc (500 mL x 3). The combined extracts were dried over $MgSO_4$ and concentrated in vacuo to afford a residue. The residue was then purified by SiO_2 column chromatography (PE/EA = 1:1) to give the product **3a** (1.7 g) in 87% yield and >20:1 dr, 99% ee.

5.2 Transformations



4, 62% yield, >20:1 dr

Ethyl (2*R*,3*R*)-3-ethyl-6-oxopiperidine-2-carboxylate (**4**) A stirred solution of **3a** (0.20 mmol, 49 mg) in THF (2 mL) was added Pd/C (10 mg) under the atmosphere of H_2. The mixture was stirred at room temperature for 8 h, and then the mixture was refluxed directly at 70 °C for 12 h. After completion of the reaction indicated by TLC, the mixture to a silica gel chromatography column (silica gel, PE/EtOAc = 1/1) to afford the desired **4** (25 mg) in 62% yield as yellow oil. $[\alpha]_D^{25}$ -18.2 (*c* 1.01, $CHCl_3$), ^{1}H NMR (500 MHz, chloroform-*d*) δ 6.34 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.83 (dd, *J* = 5.4, 2.6 Hz, 1H), 2.48 – 2.24 (m, 2H), 2.03 – 1.83 (m, 2H), 1.62 (ddt, *J* = 15.0, 13.6, 6.4 Hz, 2H), 1.42 (ddd, *J* = 15.0, 13.3, 7.5 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 172.0, 171.8, 61.8, 59.3, 36.2, 28.8, 24.4, 22.9, 14.2, 11.4. HRMS (ESI): $[M+Na]^+$ calcd for $C_{10}H_{18}O_3N^+$ 200.1281, found 200.1275.



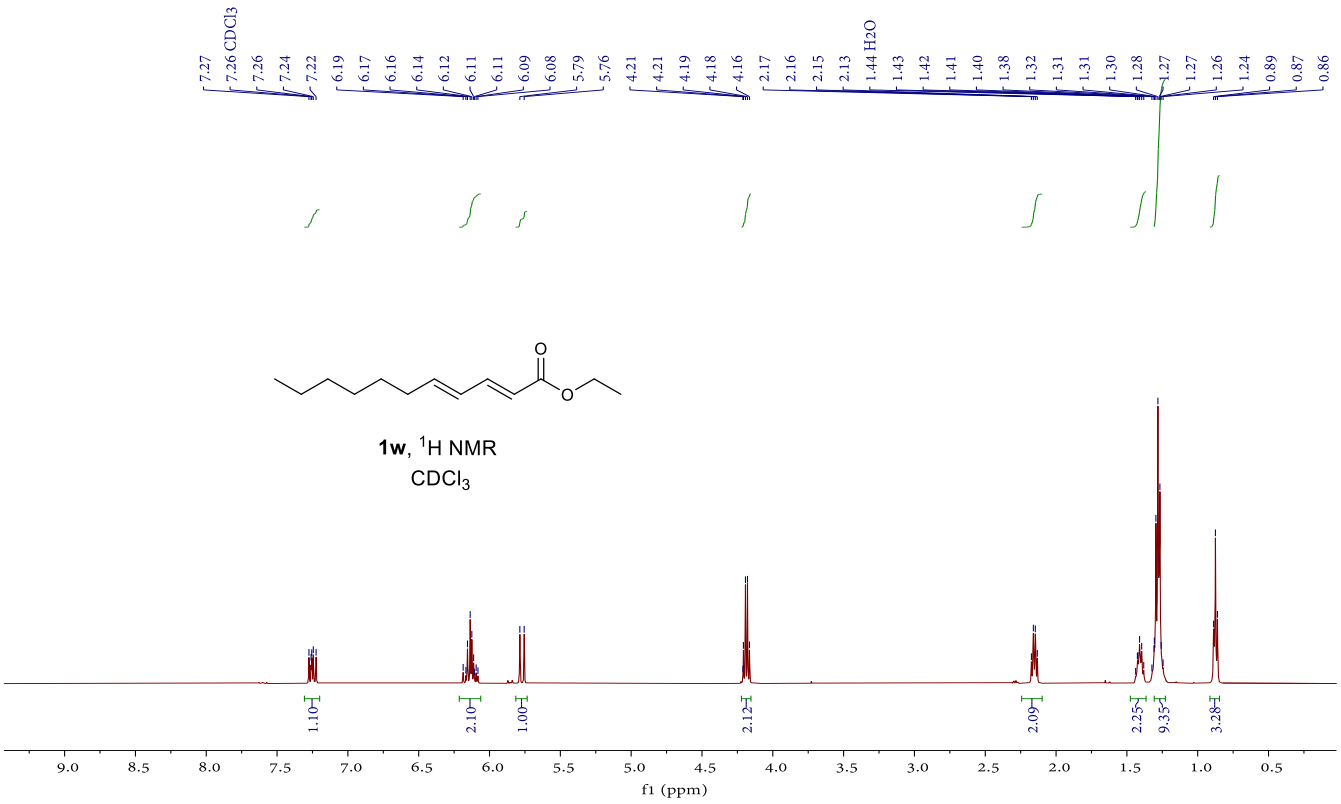
5, 82% yield, >20:1 dr

Diethyl (4*R*,5*R*,*E*)-5-((*S*)-2-((tert-butoxycarbonyl)amino)-3-(p-tolyl)propanamido)-4-ethylhex-2-enedioate (**5**) To a solution of sorbic acid amino acid (0.12 mmol, 33 mg, 1.1 eq), **3a** (0.10 mmol, 24 mg, 1.0 eq) and DMAP (1.2 mg, 10 mol%) in CH_2Cl_2 (2 mL) at 0 °C was added DCC (0.11 mmol, 23 mg, 1.1 eq) in five portions over 5 min. Then the reaction was stirred at room temperature for 12 h. After this time, the reaction was filtered through a pad of celite using CH_2Cl_2 as the eluent, concentrated, and purification by flash column chromatography to provide the pure **5** (41 mg) in 82% yield as a white solid. Mp = 112-114 ^oC; $[\alpha]_D^{25}$ -24.8 (*c* 0.28, $CHCl_3$); ^1H NMR (500 MHz, chloroform-*d*) δ 7.10 (d, *J* = 3.0 Hz, 4H), 6.49 (dd, *J* = 15.6, 9.3 Hz, 1H), 6.44 – 6.38 (m, 1H), 5.75 (d, *J* = 15.6 Hz, 1H), 4.99 (s, 1H), 4.73 (dd, *J* = 9.0, 3.9 Hz, 1H), 4.36 (s, 1H), 4.26 – 4.03 (m, 4H), 3.01 (d, *J* = 7.1 Hz, 2H), 2.58 (tt, *J* = 9.3, 4.7 Hz, 1H), 2.30 (s, 3H), 1.40 (s, 10H), 1.26 (dt, *J* = 14.2, 7.1 Hz, 6H), 1.16 (p, *J* = 7.5 Hz, 1H), 0.82 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 171.6, 170.5, 165.7, 145.8, 136.7, 133.3, 129.5, 129.1, 124.5, 80.3, 61.7, 60.5, 56.0, 54.6, 47.6, 46.6, 37.9, 28.3, 23.0, 21.1, 14.3, 14.2, 11.8; HRMS (ESI): $[M+Na]^{\oplus}$calcd for $C_{27}H_{41}O_7N_2^{\oplus}$ 505.2908, found 505.2909.

6. References

1. Wang, Y.-C.; Xiao, Z.-X.; Wang, M.; Yang, S.-Q.; Liu, J.-B.; He, Z.-T. *Angew. Chem. Int. Ed.* **2023**, *62*, e202215568

7. Copies of ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra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6.14
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6.11
6.11
6.09
6.08
5.79
5.76
4.21
4.21
4.19
4.18
4.16
2.17
2.16
2.15
2.13
1.44 H2O
1.43
1.42
1.41
1.40
1.38
1.32
1.31
1.31
1.30
1.28
1.27
1.27
1.26
1.24
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0.87
0.86
O
O
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1.10
2.10
1.00
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2.25
9.35
3.28
9.0
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8.0
7.5
7.0
6.5
6.0
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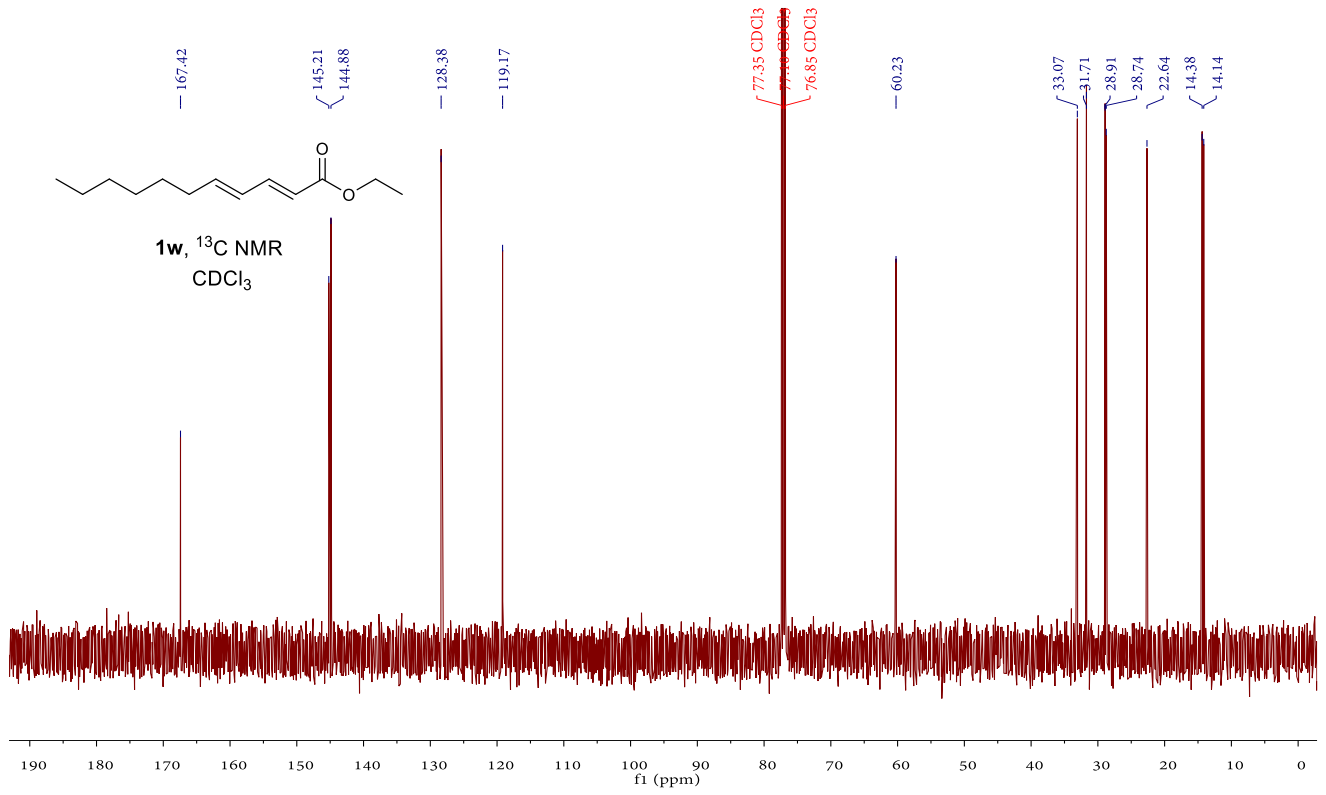
f1 (ppm)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128.38
119.17
77.35 CDCl3
76.85 CDCl3
60.23
33.07
31.71
28.91
28.74
22.64
14.38
14.14
O
O
1w, 13C NMR
CDCl3
190
180
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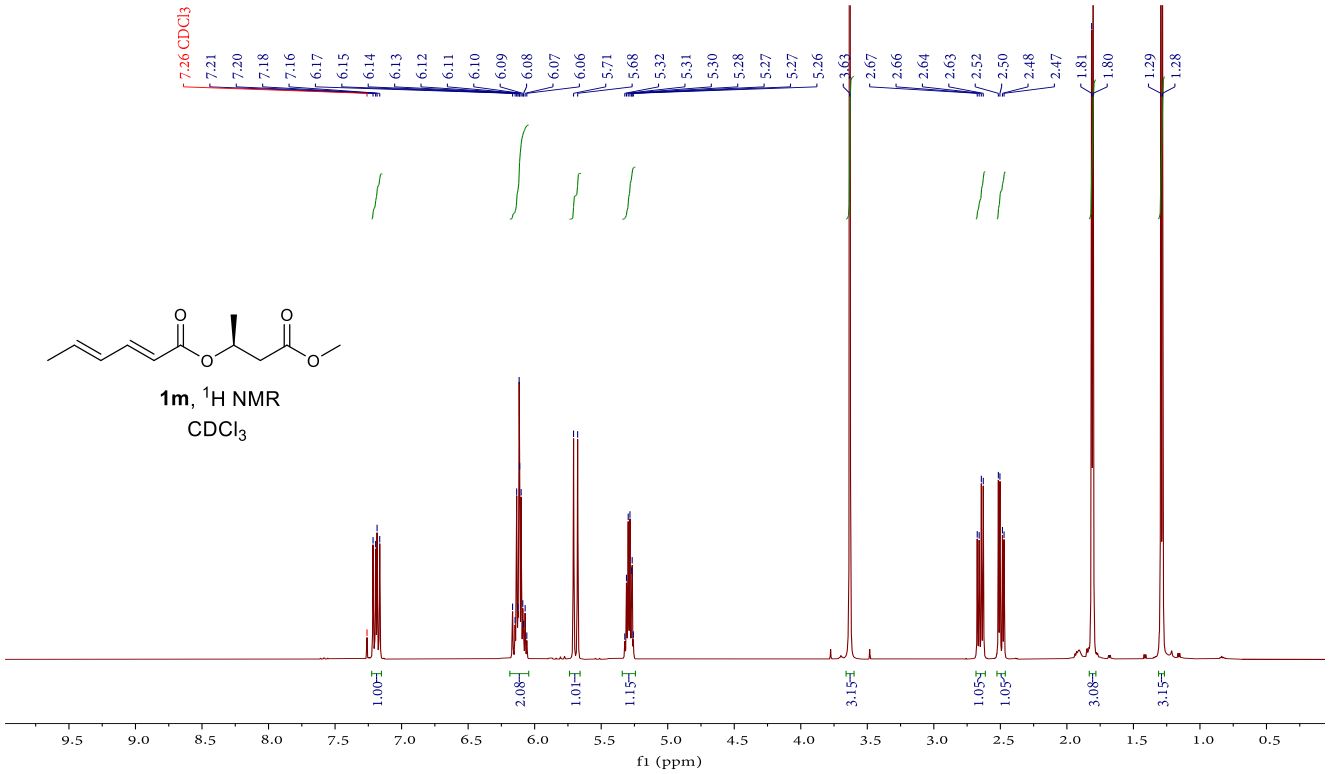
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.18
7.16
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6.14
6.13
6.12
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6.10
6.09
6.08
6.07
6.06
5.71
5.68
5.32
5.31
5.30
5.28
5.27
5.27
5.26
3.63
2.67
2.66
2.64
2.63
2.52
2.50
2.48
2.47
1.81
1.80
1.29
1.28
1m, 1H NMR
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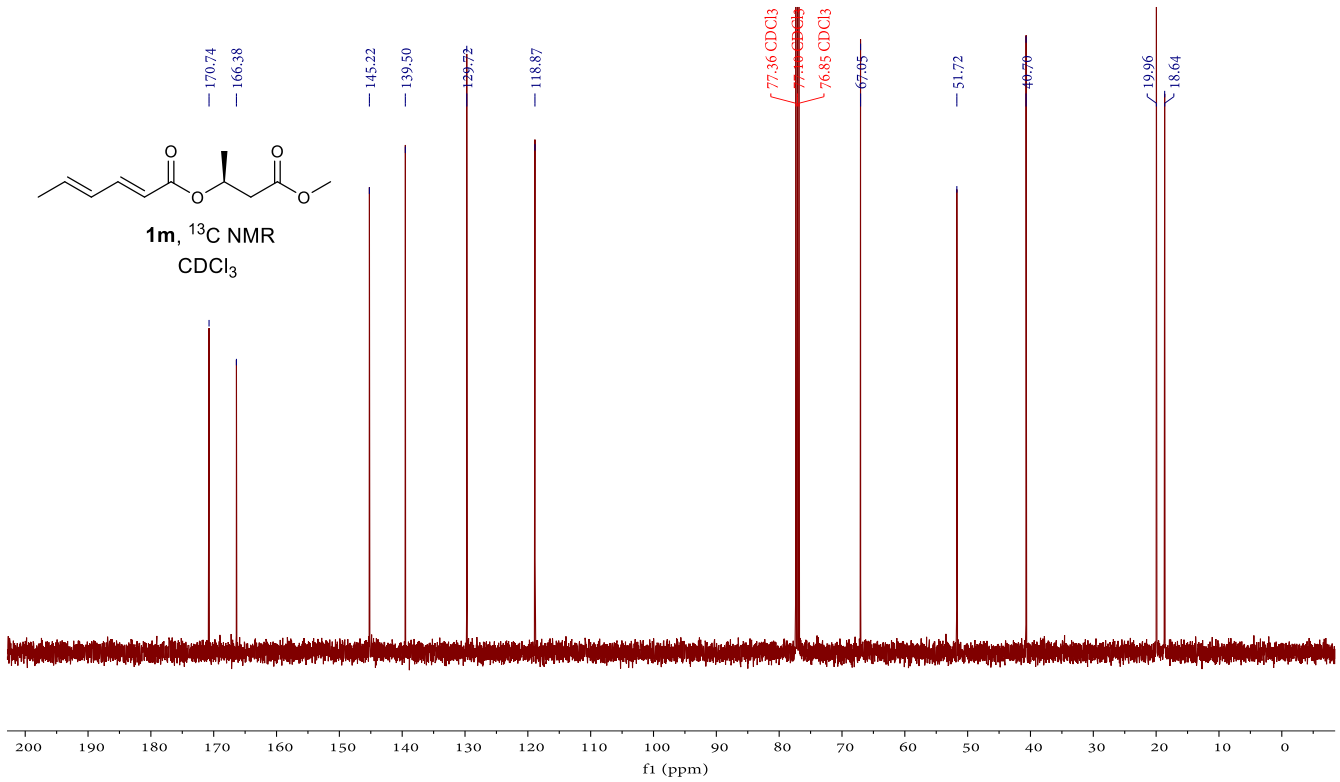
1.01
1.15
3.15
1.05
1.05
3.08
3.15
f1 (ppm)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139.50
129.72
118.87
77.36 CDCl3
76.85 CDCl3
67.05
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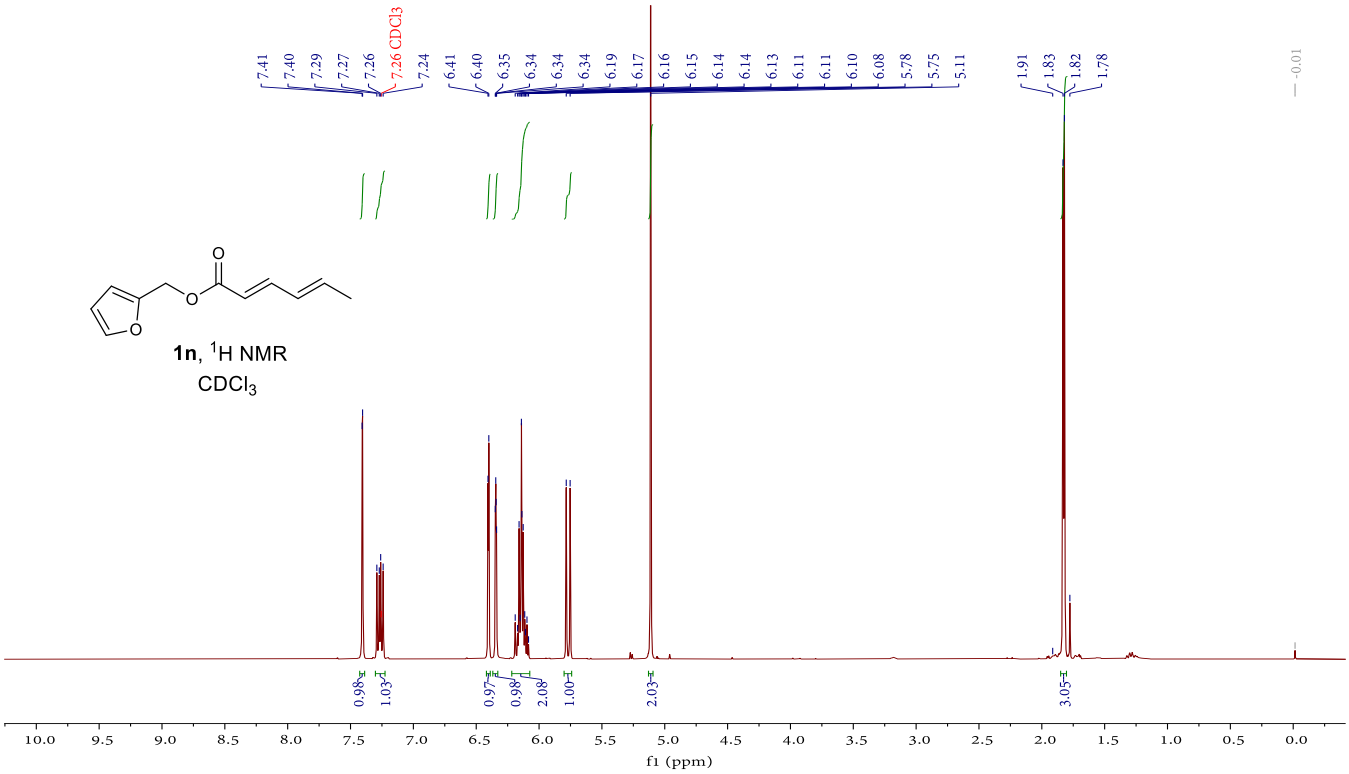
40.70
19.96
18.64
1m, 13C NMR
CDCl3
f1 (ppm)



1n, ^{1}H NMR
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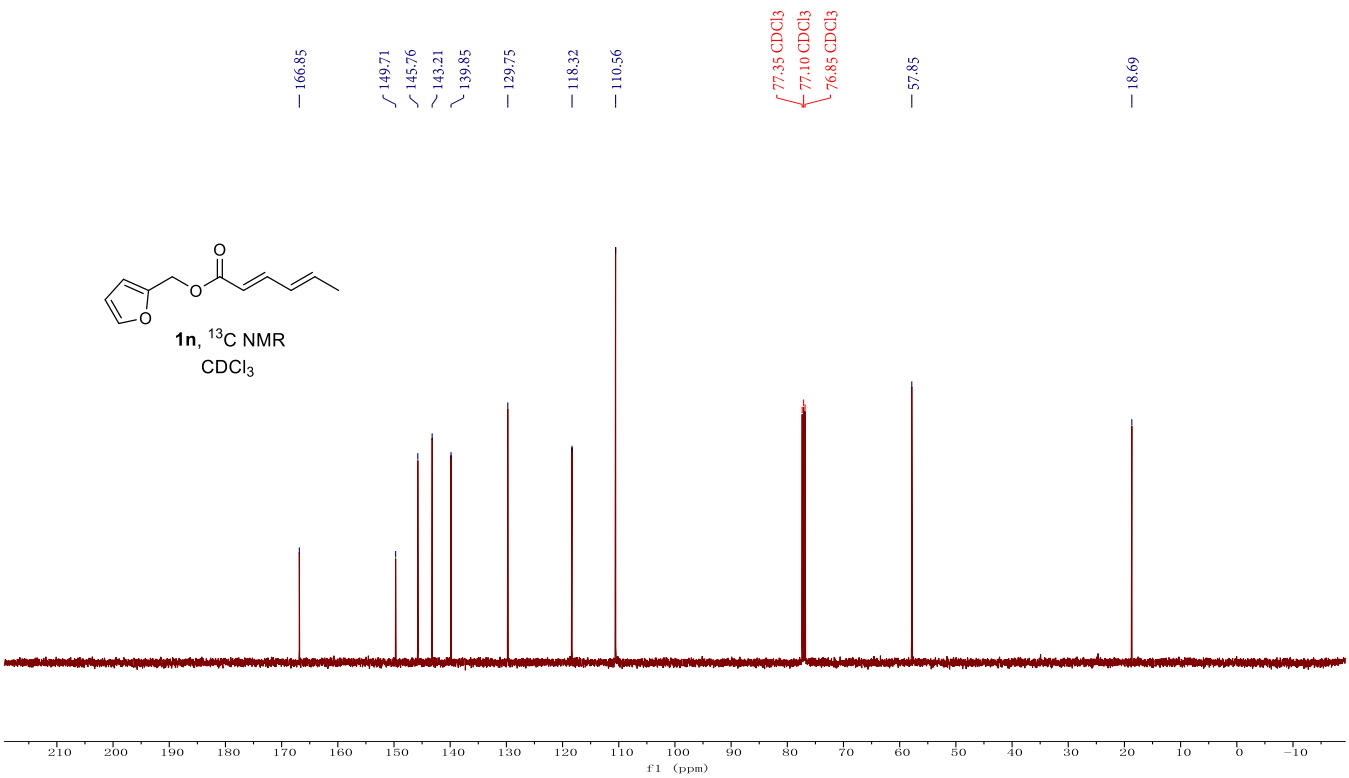

1n, ^{13}C NMR
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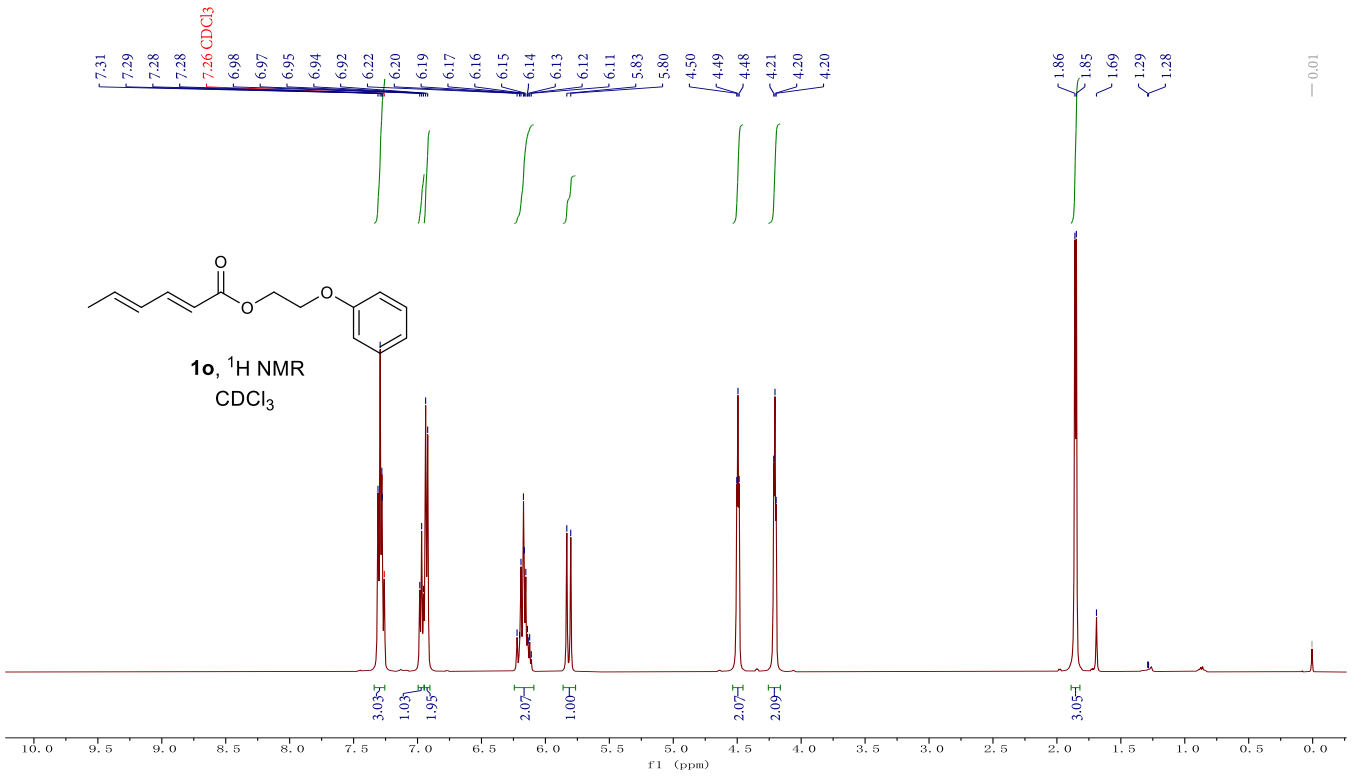
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6.19
6.17
6.16
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6.14
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4.21
4.20
4.20
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1.69
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1.28
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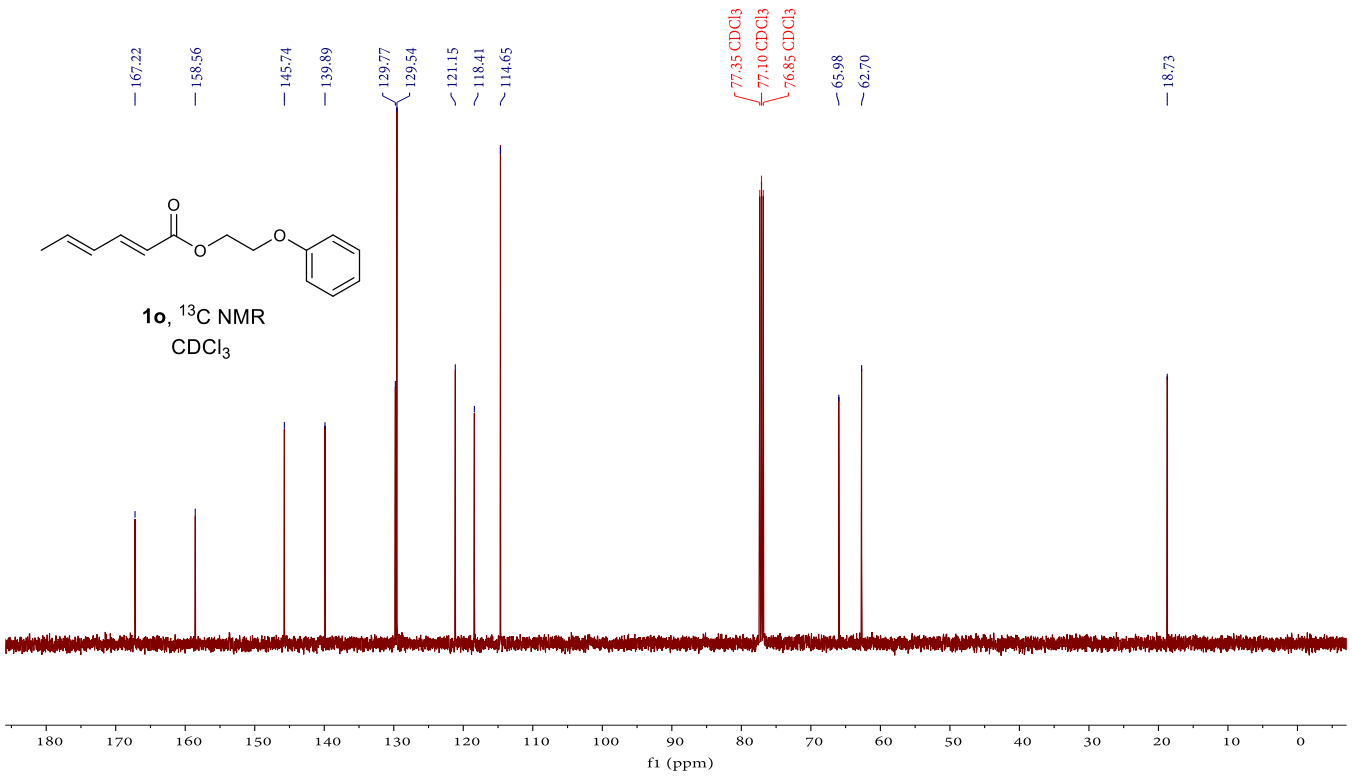
f1 (ppm)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65.98
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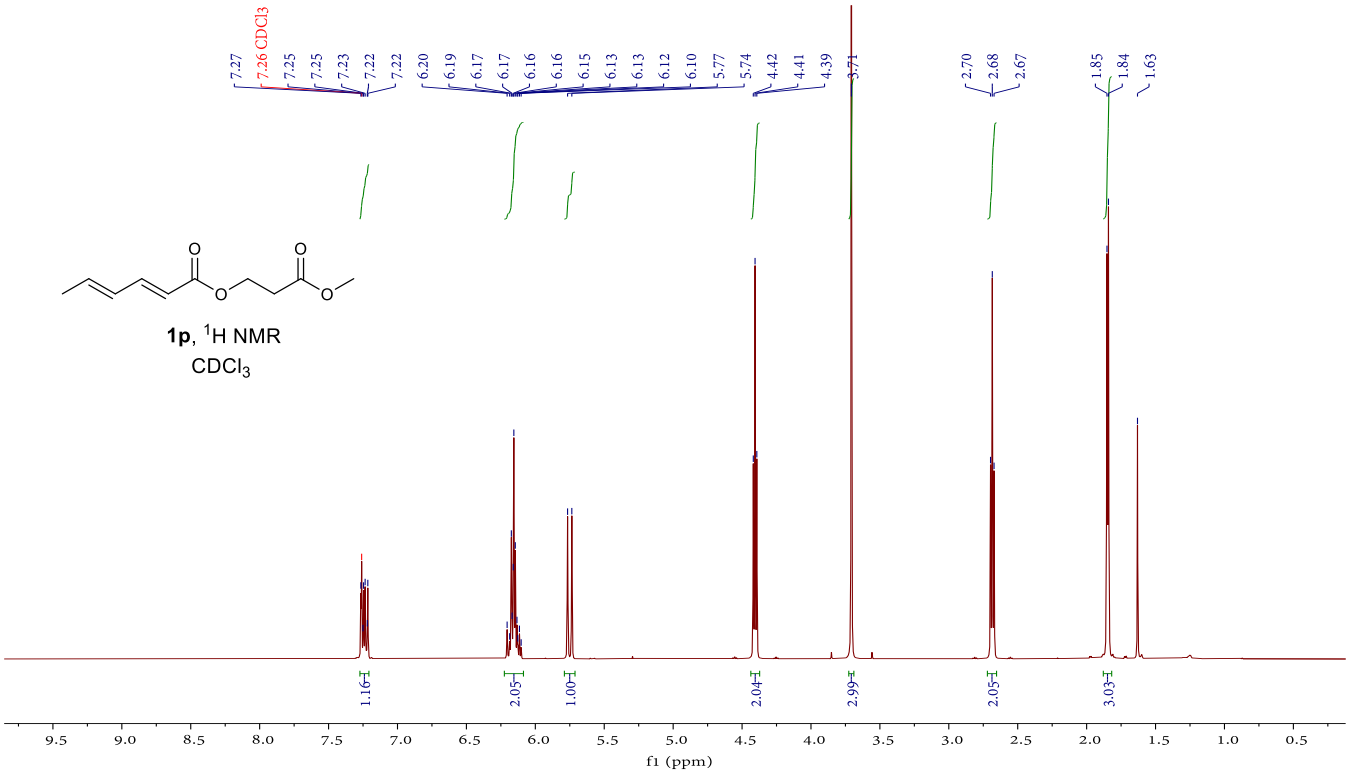
CDCl3
f1 (ppm)



1p, ^{1}H NMR
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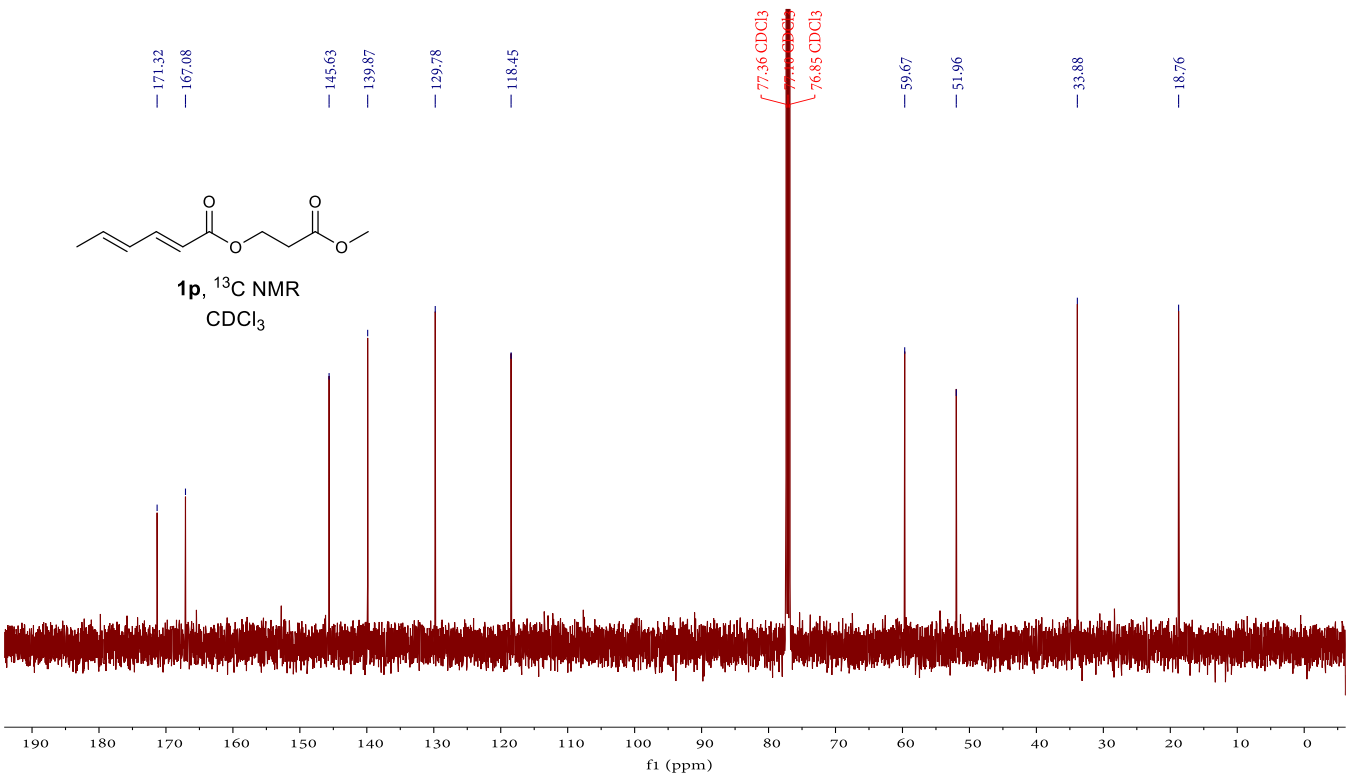

1p, ^{13}C NMR
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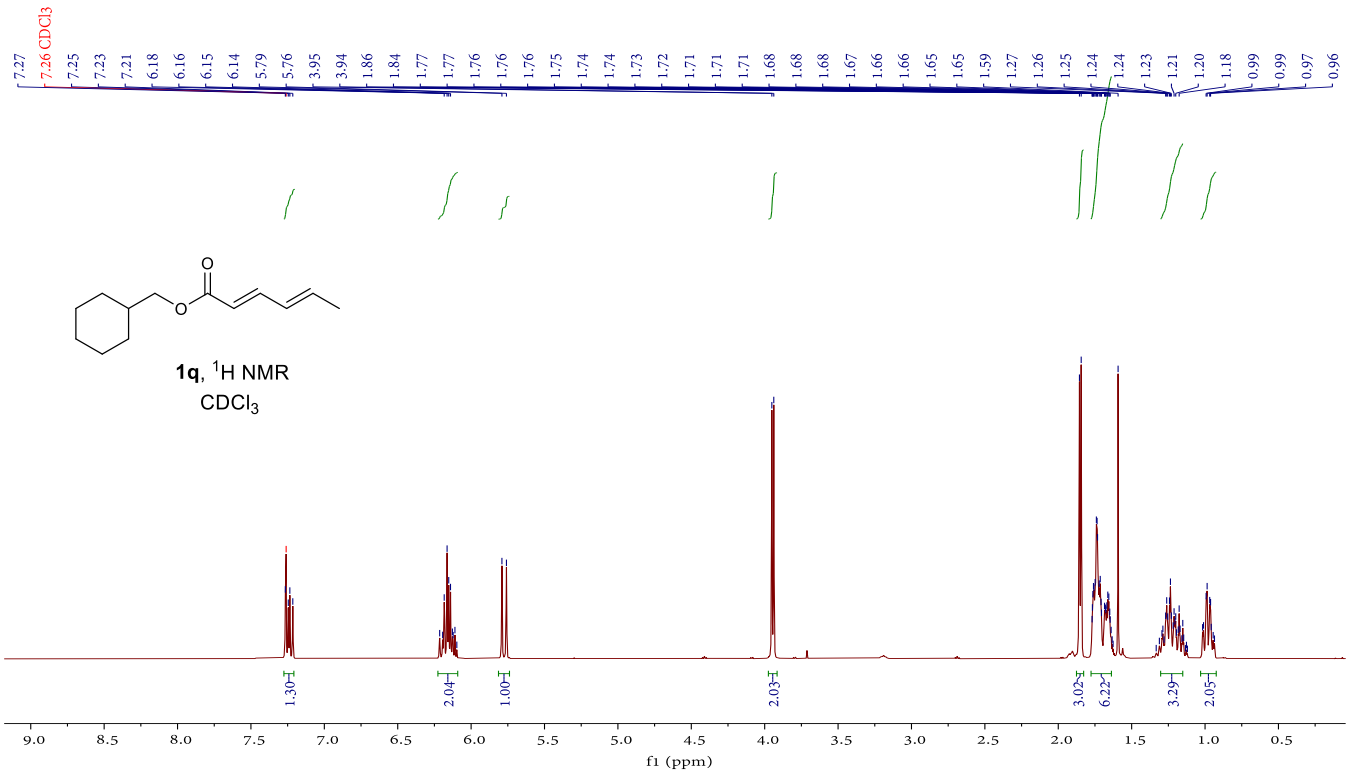
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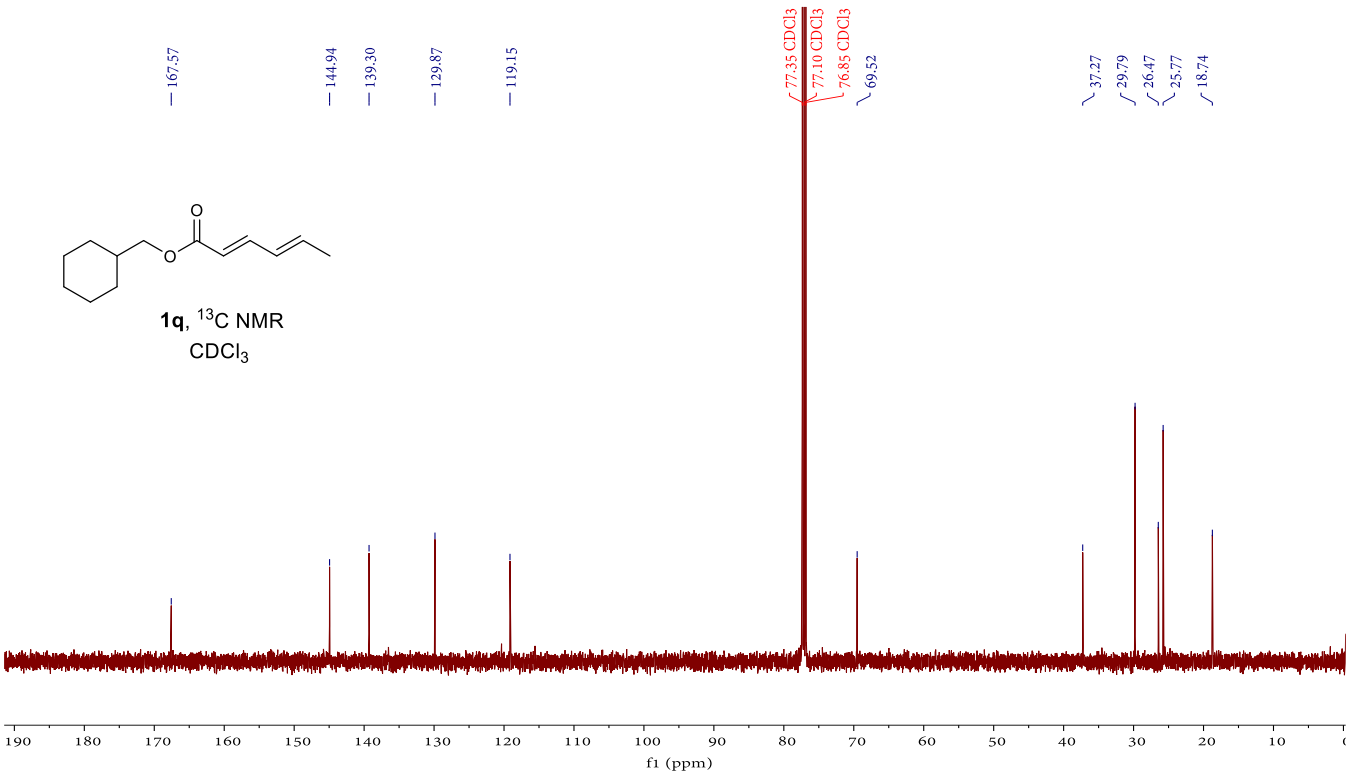
f1 (ppm)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37.27
29.79
26.47
25.77
18.74
O
O
1q, 13C NMR
CDCl3
190
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110
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90
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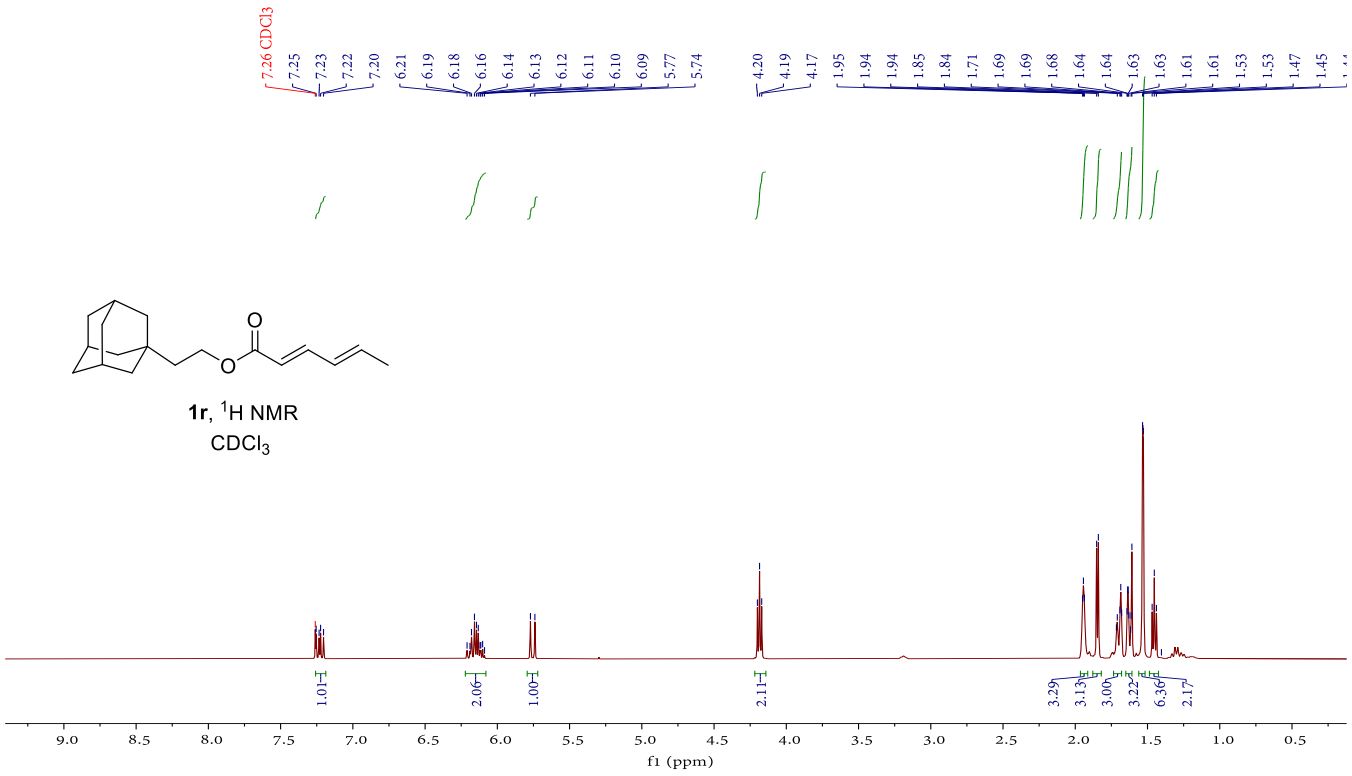
50
40
30
20
10
f1 (ppm)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6.11
6.10
6.09
5.77
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1.94
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1.63
1.63
1.61
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1.53
1.53
1.47
1.45
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O
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1.00
2.11
3.29
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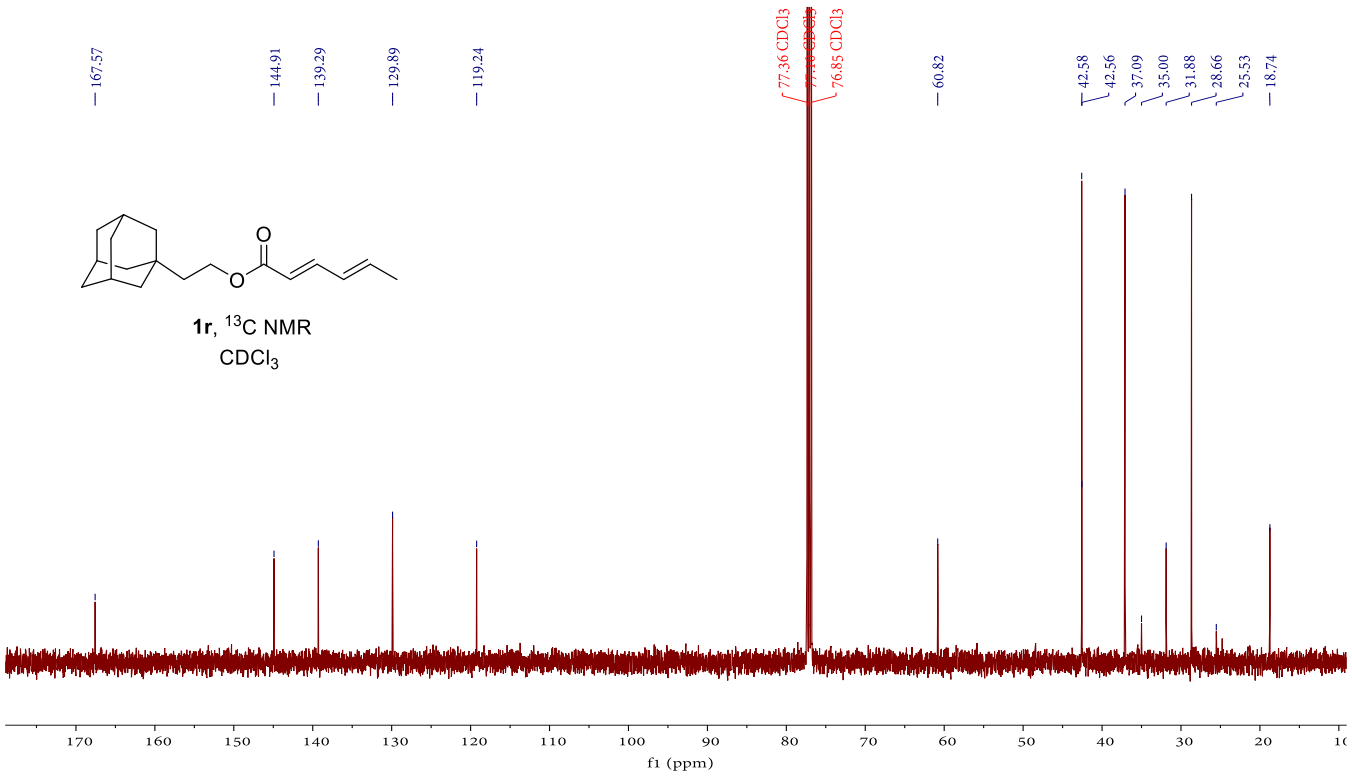
f1 (ppm)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28.66
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18.74
O
O
1r, 13C NMR
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50
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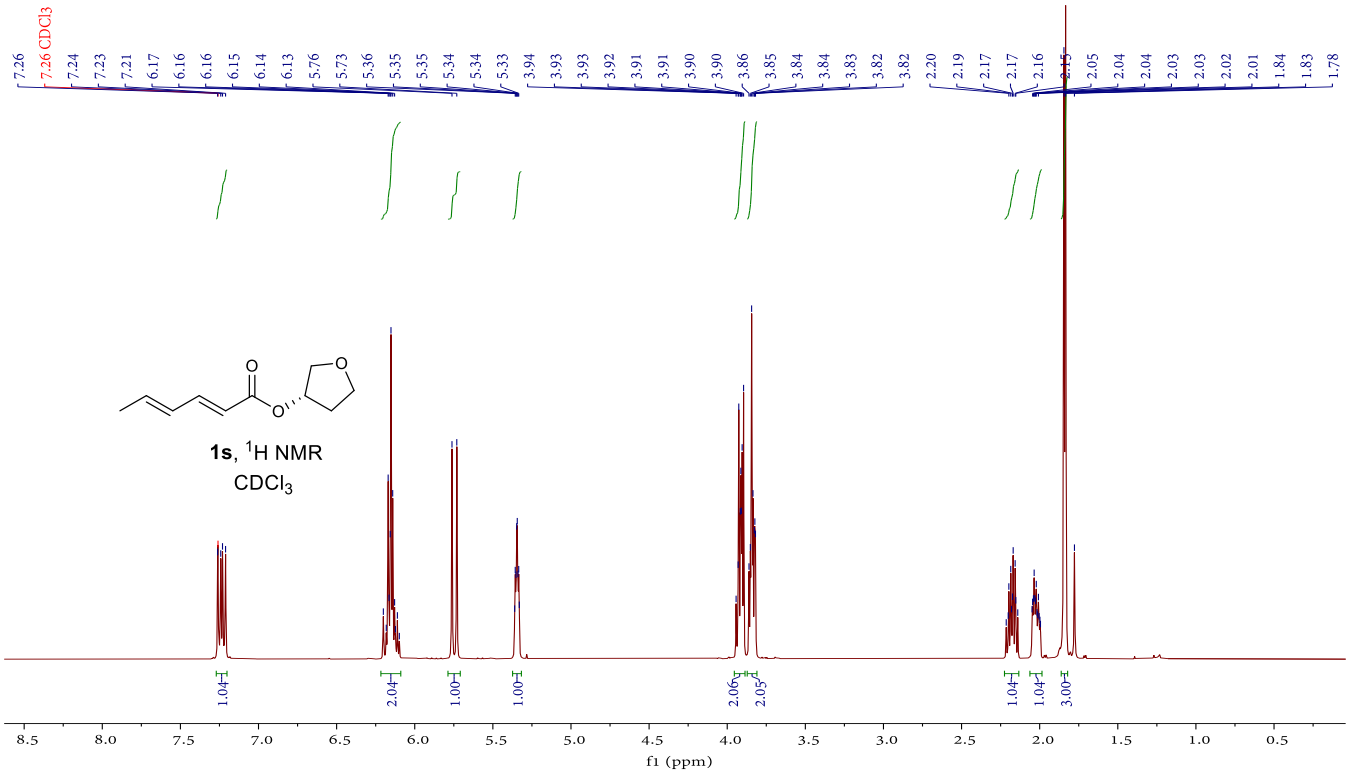
30
20
f1 (ppm)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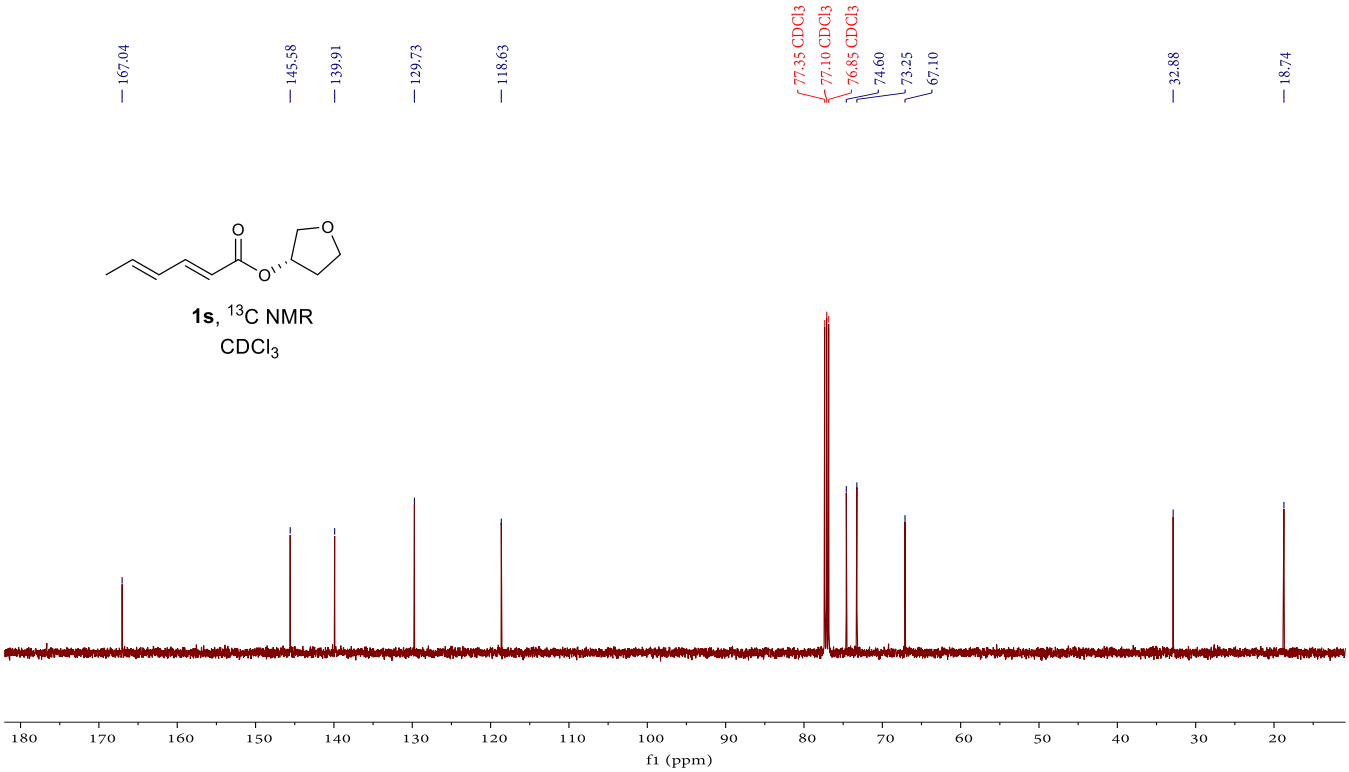
1s, 1H NMR
CDCl3
f1 (ppm)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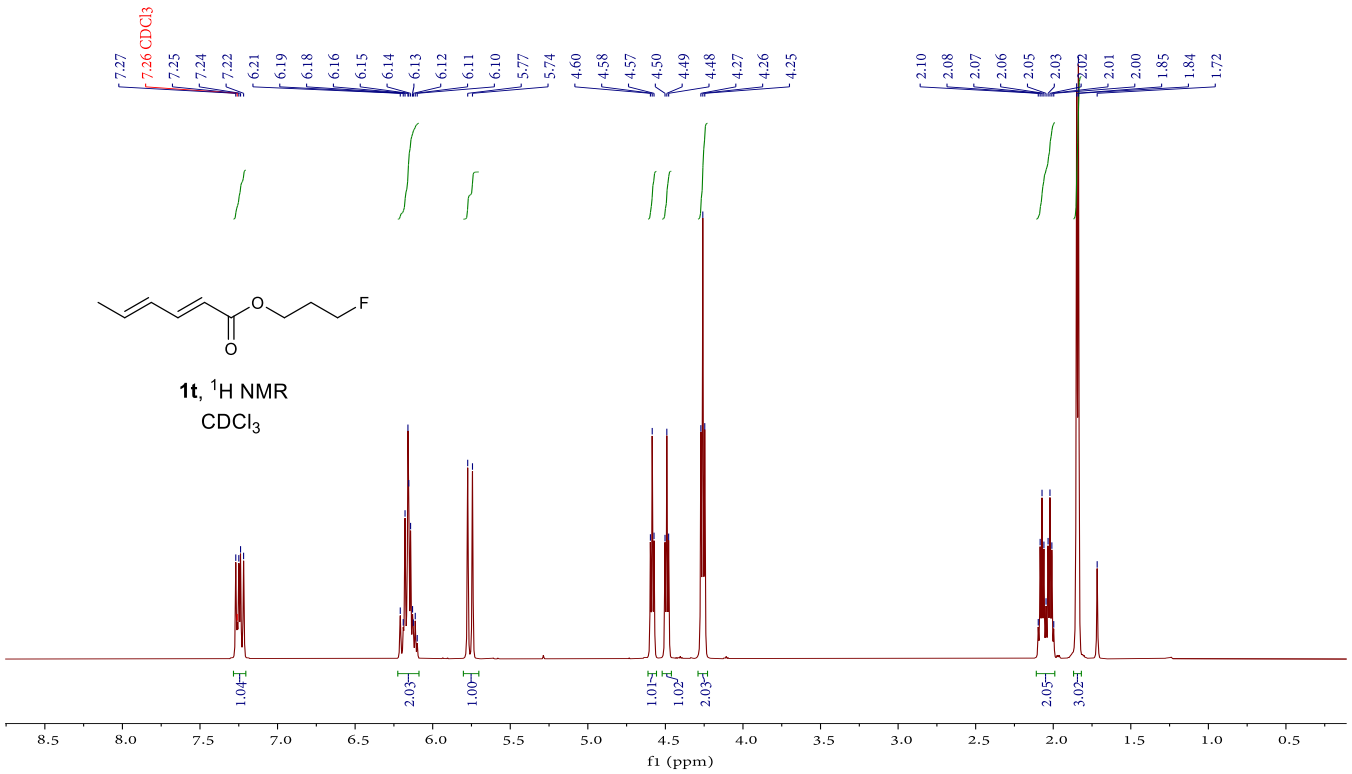
18.74
1s, 13C NMR
CDCl3
f1 (ppm)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2.06
2.05
2.03
2.02
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F
O
1t, 1H NMR
CDCl3
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1.01
1.02
2.03
2.05
3.02
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6.0
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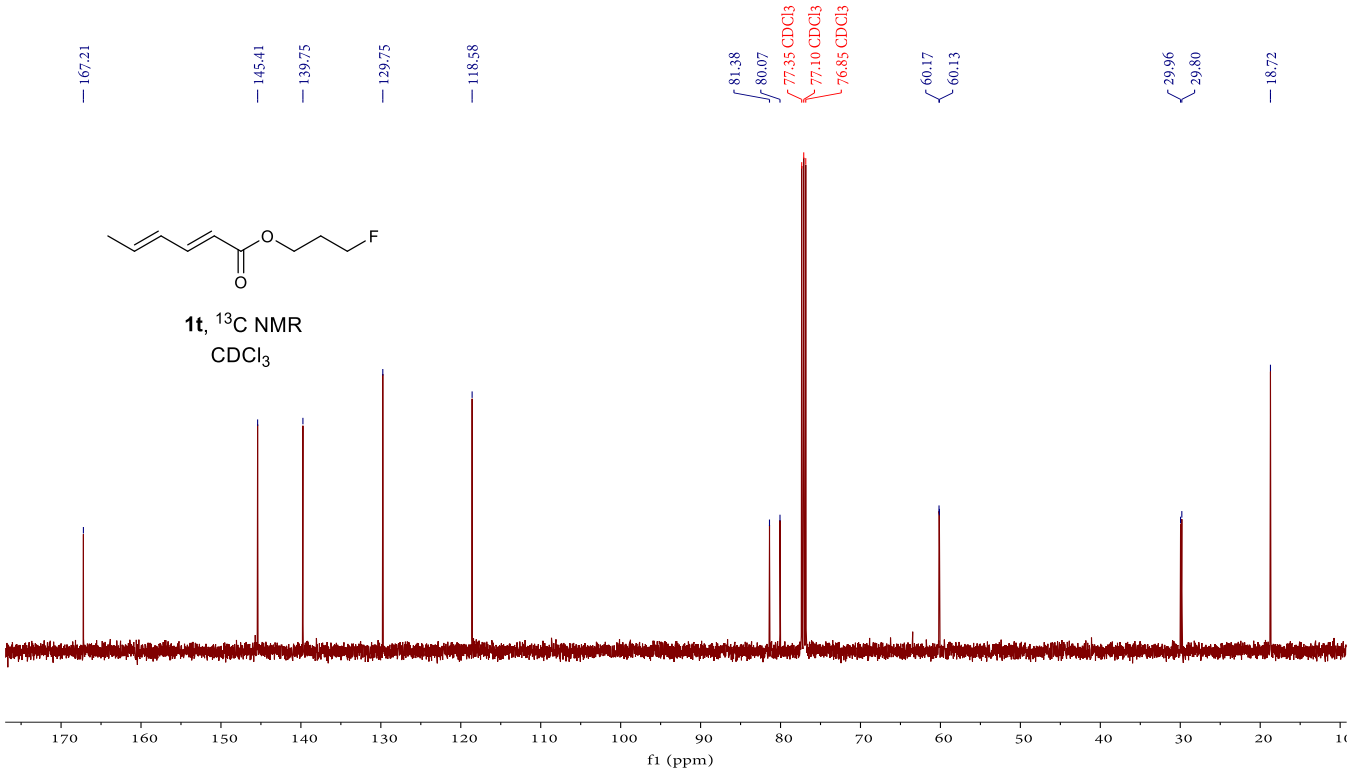
f1 (ppm)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29.96
29.80
18.72
O
F
O
1t, 13C NMR
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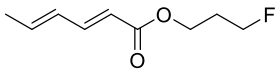
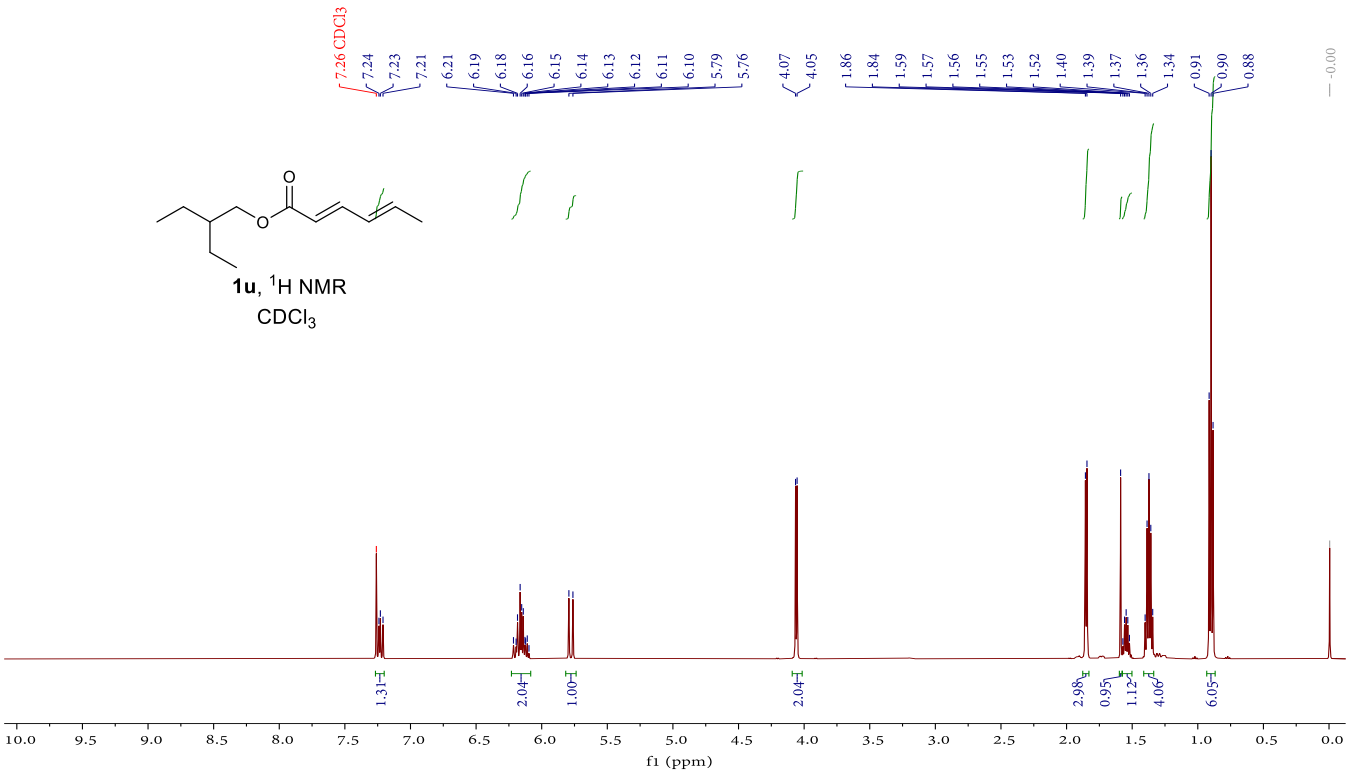
f1 (ppm)



1t, ^{19}F NMR

$CDCl_3$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1.00
2.04
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6.05
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3.0
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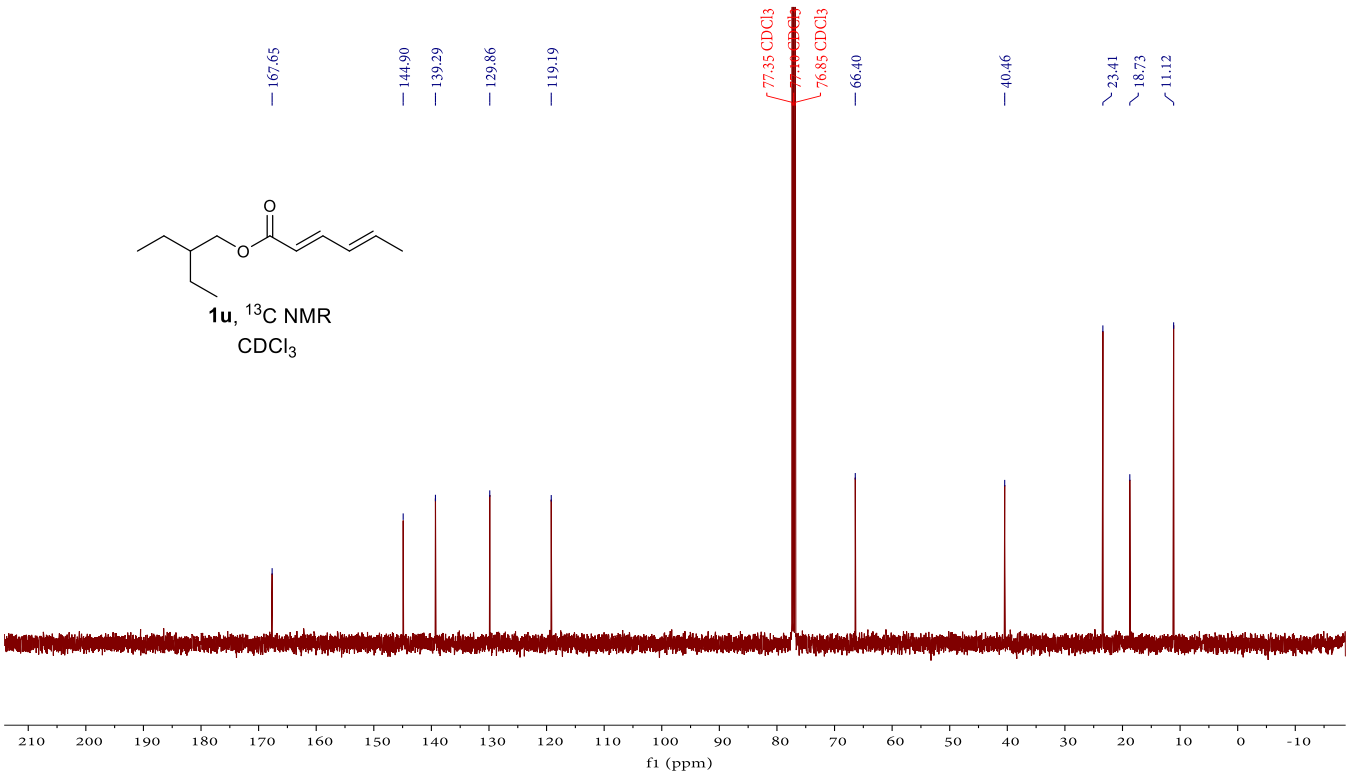
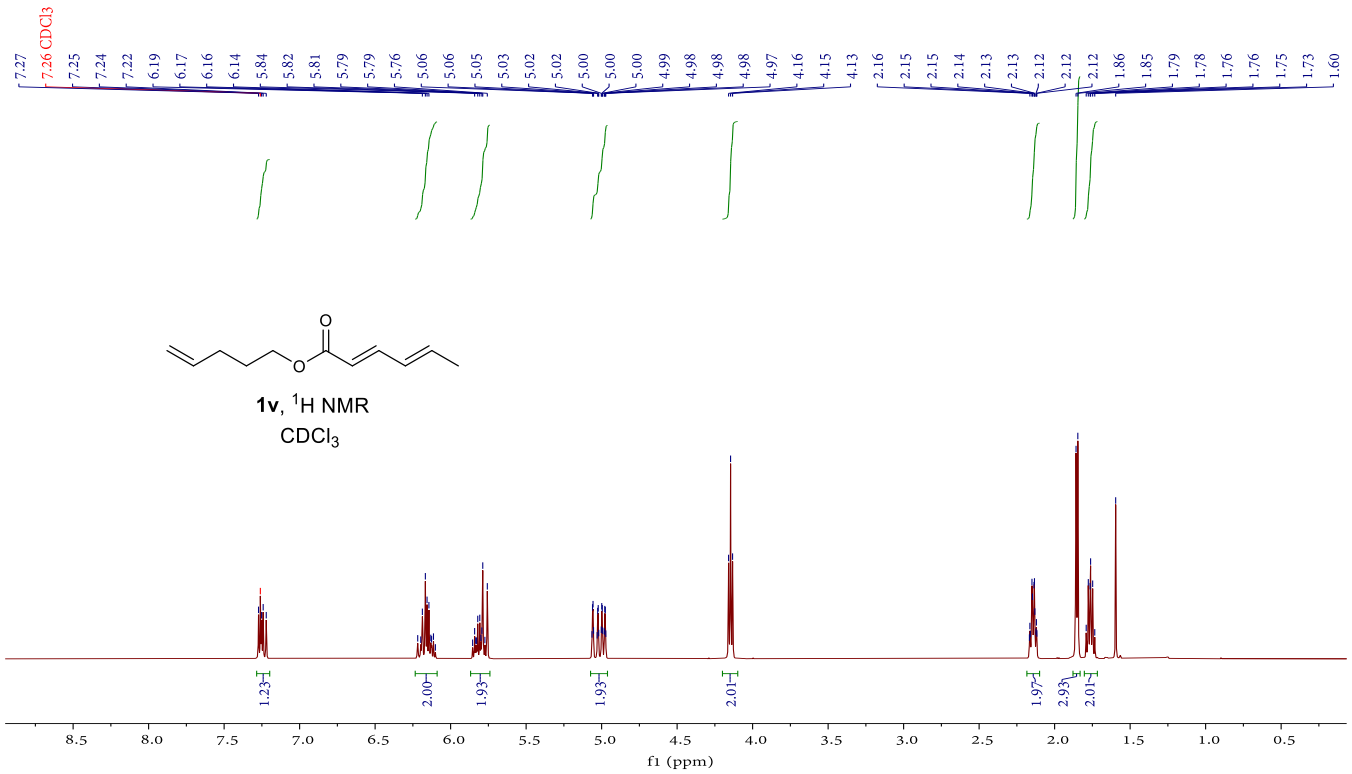
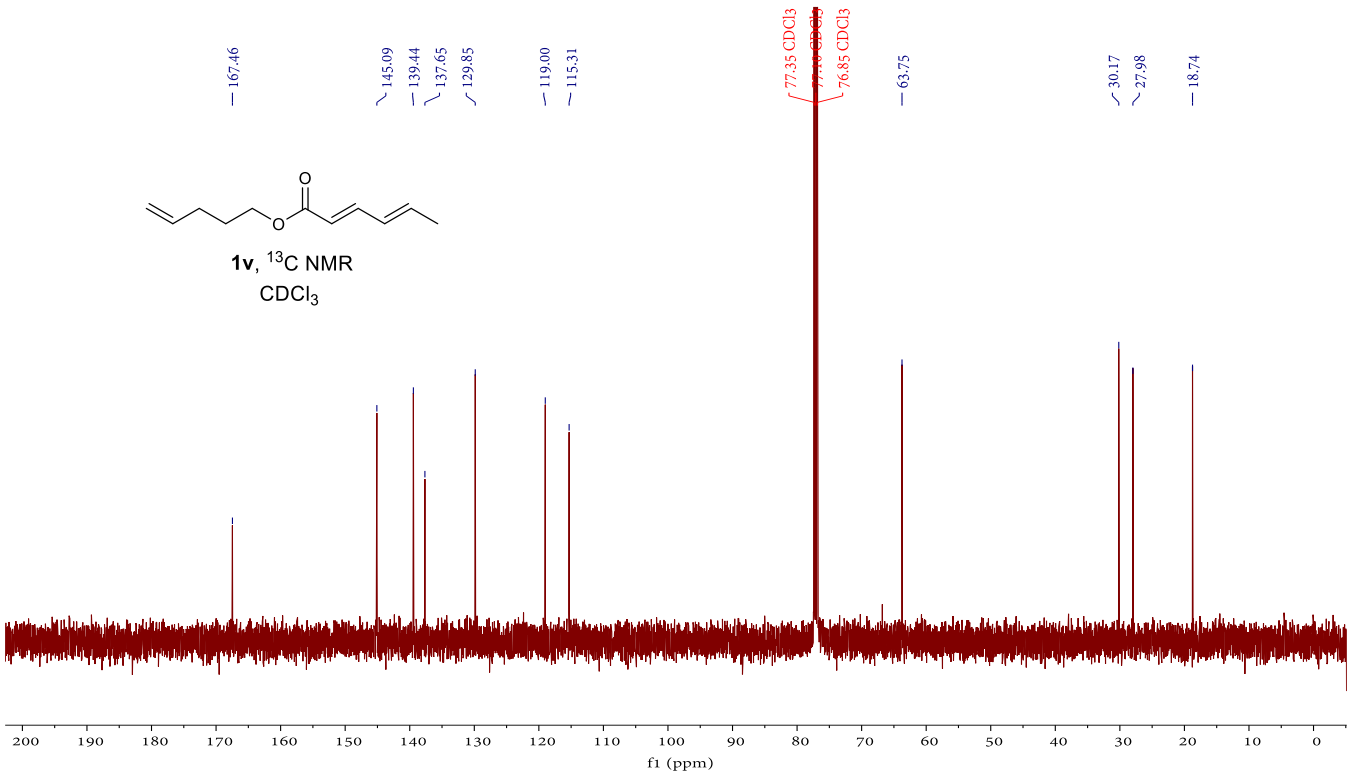
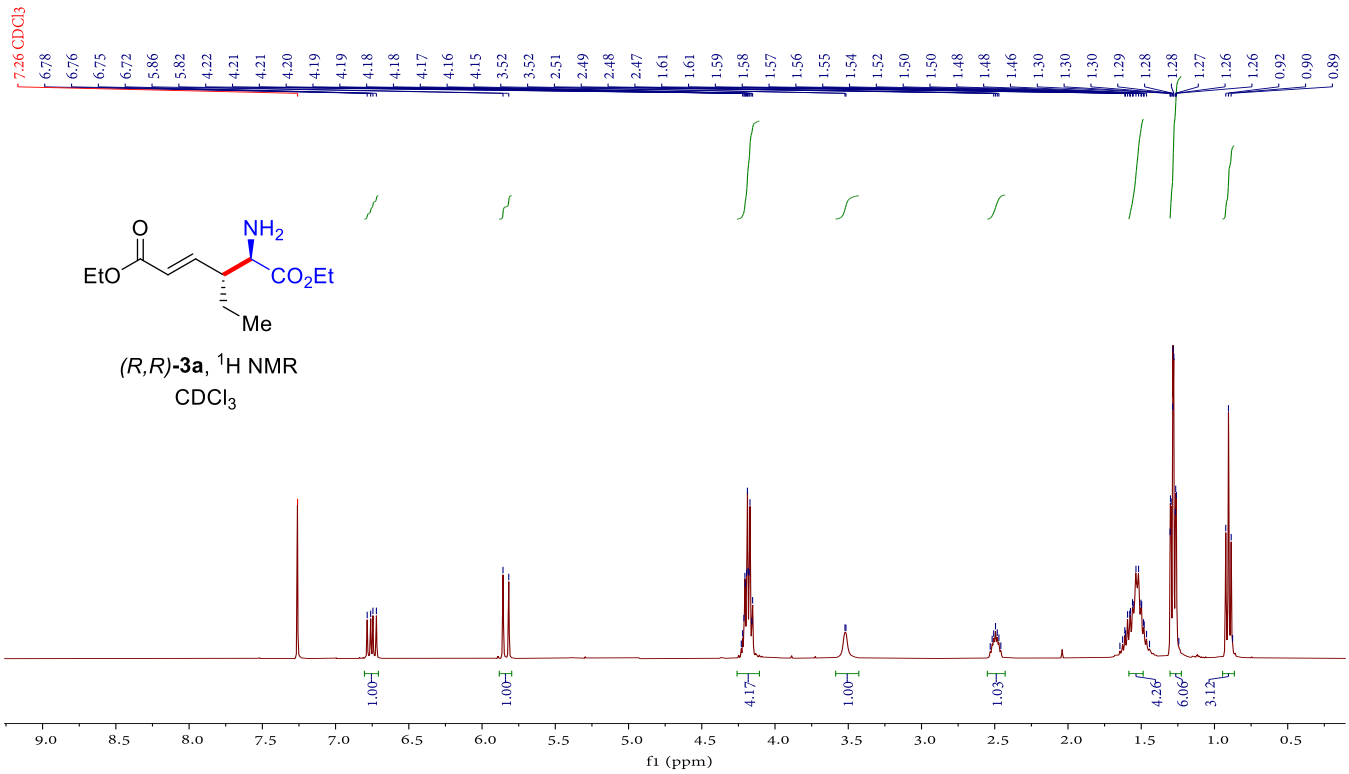
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
1u, 1H NMR
CDCl3

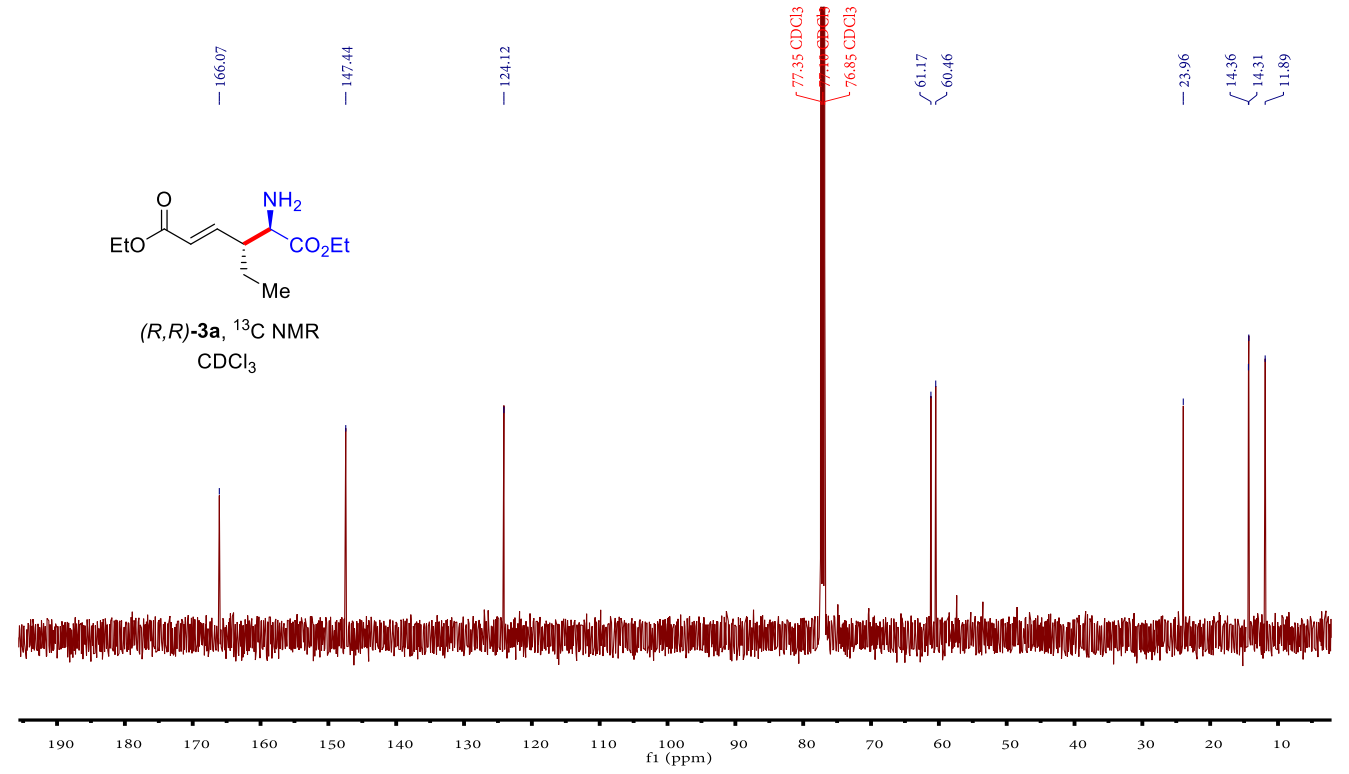

167.65
144.90
139.29
129.86
119.19
77.35 CDCl3
77.10 CDCl3
76.85 CDCl3
66.40
40.46
23.41
18.73
11.12
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
1u, 13C NMR
CDCl3


7.27
7.26 CDCl3
7.25
7.24
7.22
6.19
6.17
6.16
6.14
5.84
5.82
5.81
5.79
5.79
5.76
5.06
5.06
5.05
5.03
5.02
5.02
5.00
5.00
5.00
4.99
4.98
4.98
4.98
4.97
4.16
4.15
4.13
2.16
2.15
2.15
2.14
2.13
2.13
2.12
2.12
2.12
1.86
1.85
1.79
1.78
1.76
1.76
1.75
1.73
1.60
O
O
1v, 1H NMR
CDCl3
1.23
2.00
1.93
1.93
2.01
1.97
2.93
2.01
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
f1 (ppm)

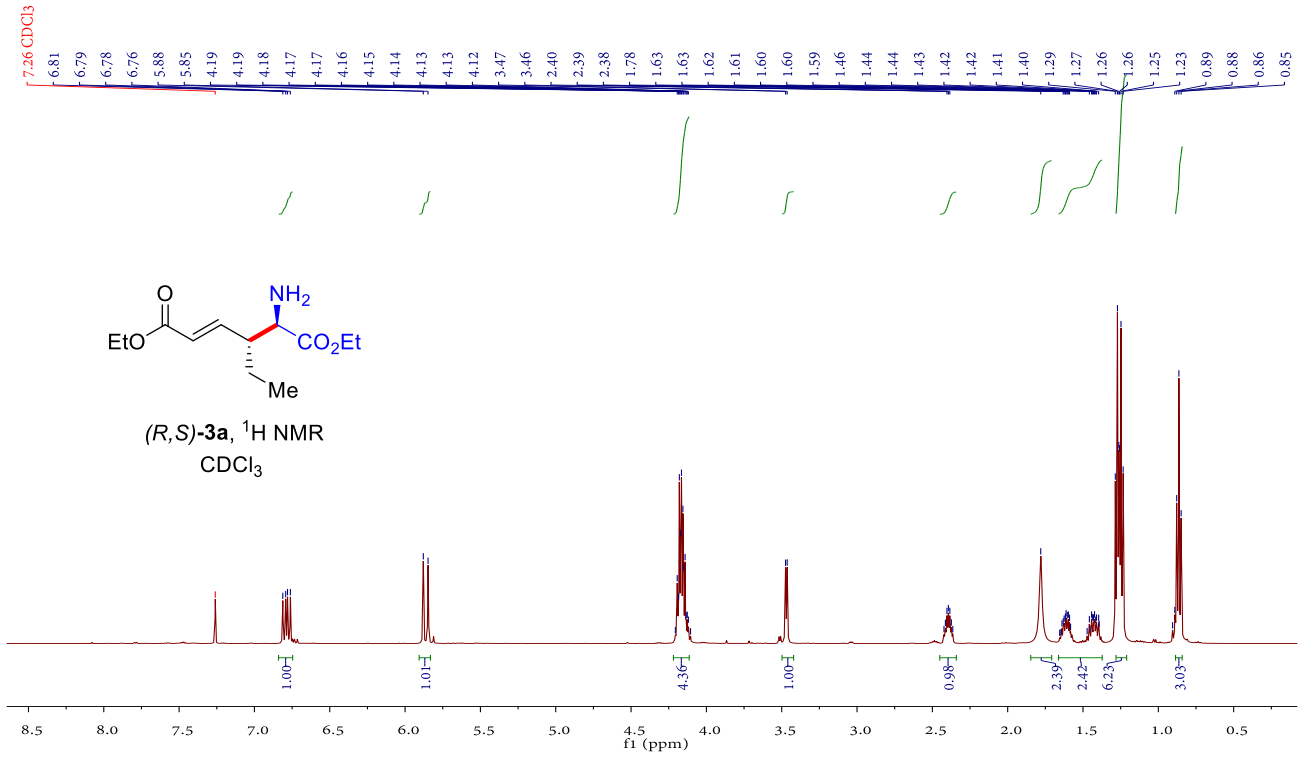

167.46
145.09
139.44
137.65
129.85
119.00
115.31
77.35 CDCl3
77.00 CDCl3
76.85 CDCl3
63.75
30.17
27.98
18.74
O
O
1v, 13C NMR
CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

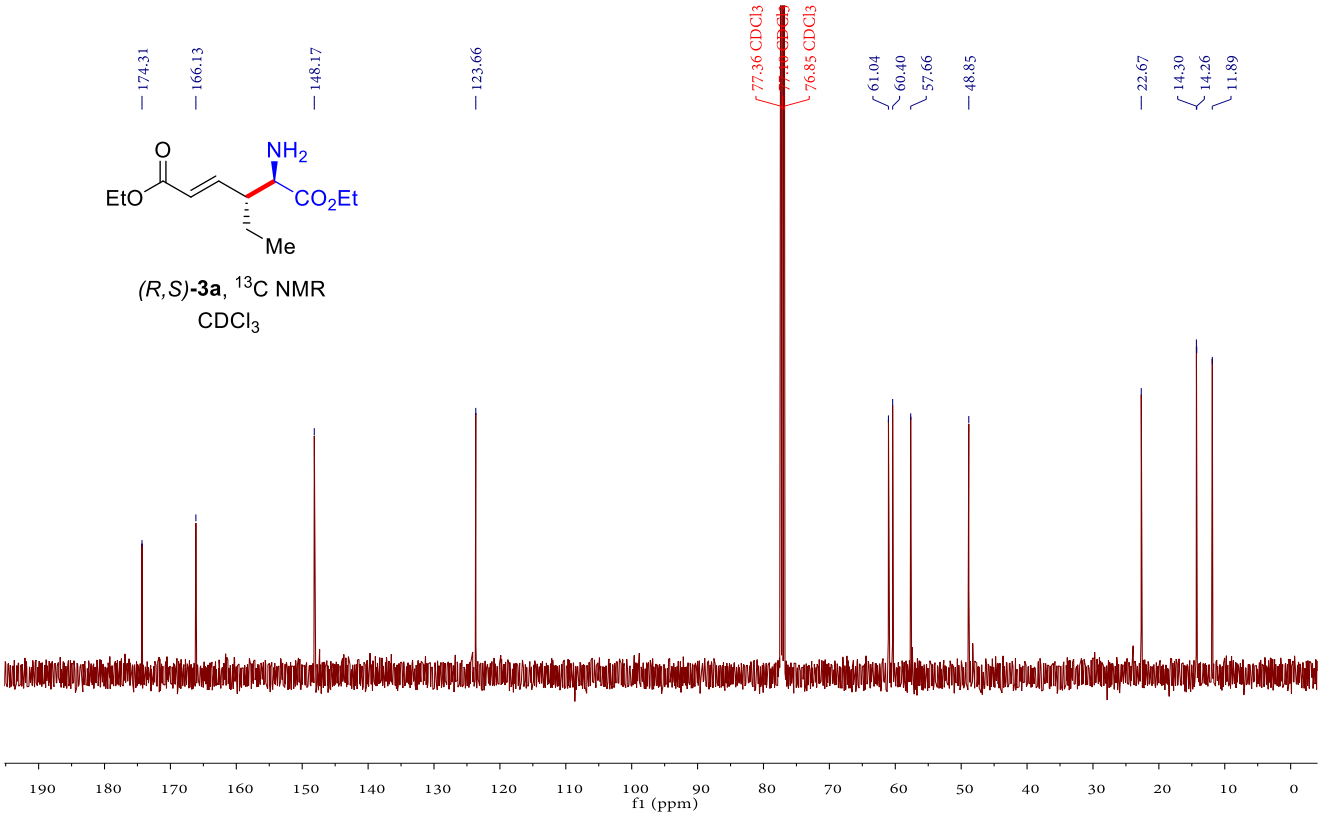


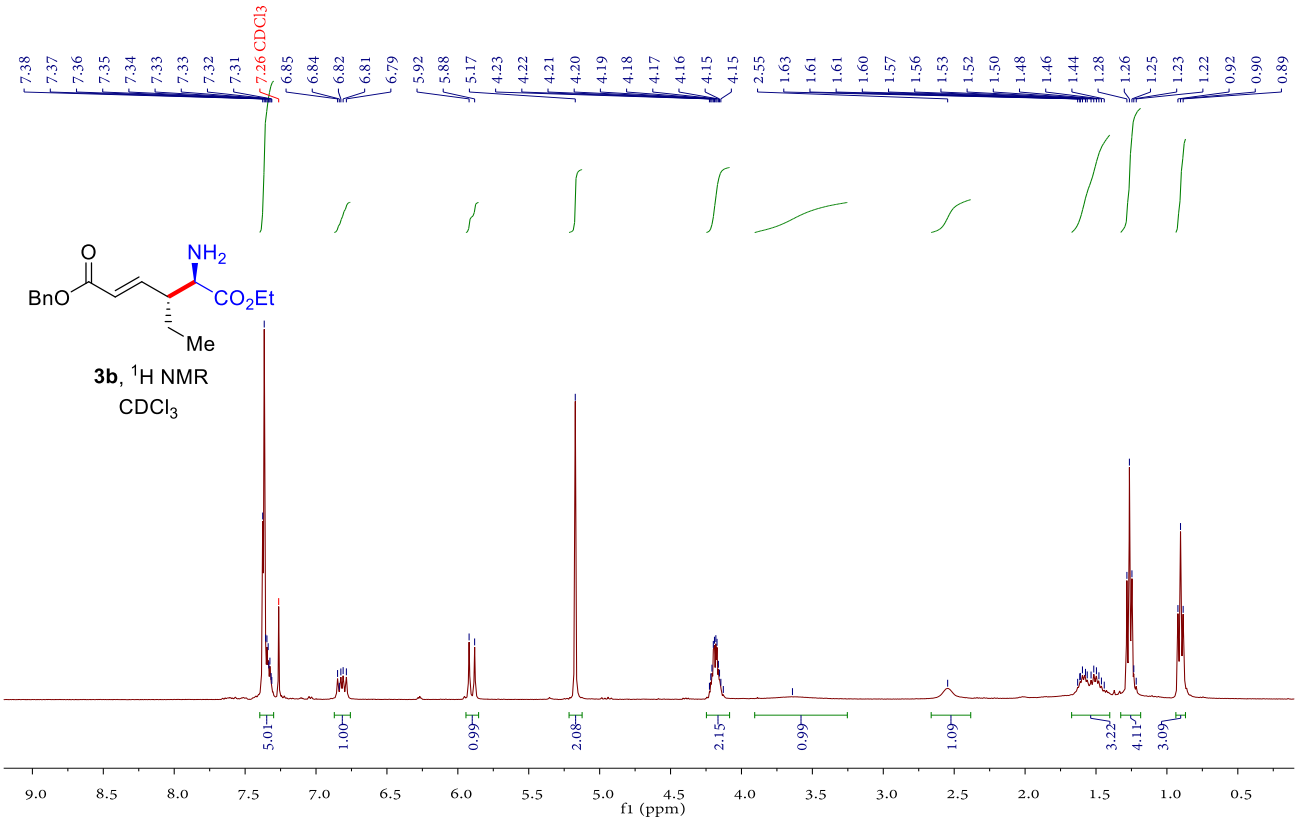
(R,R)-**3a**, ^{1}H NMR
$CDCl_3$

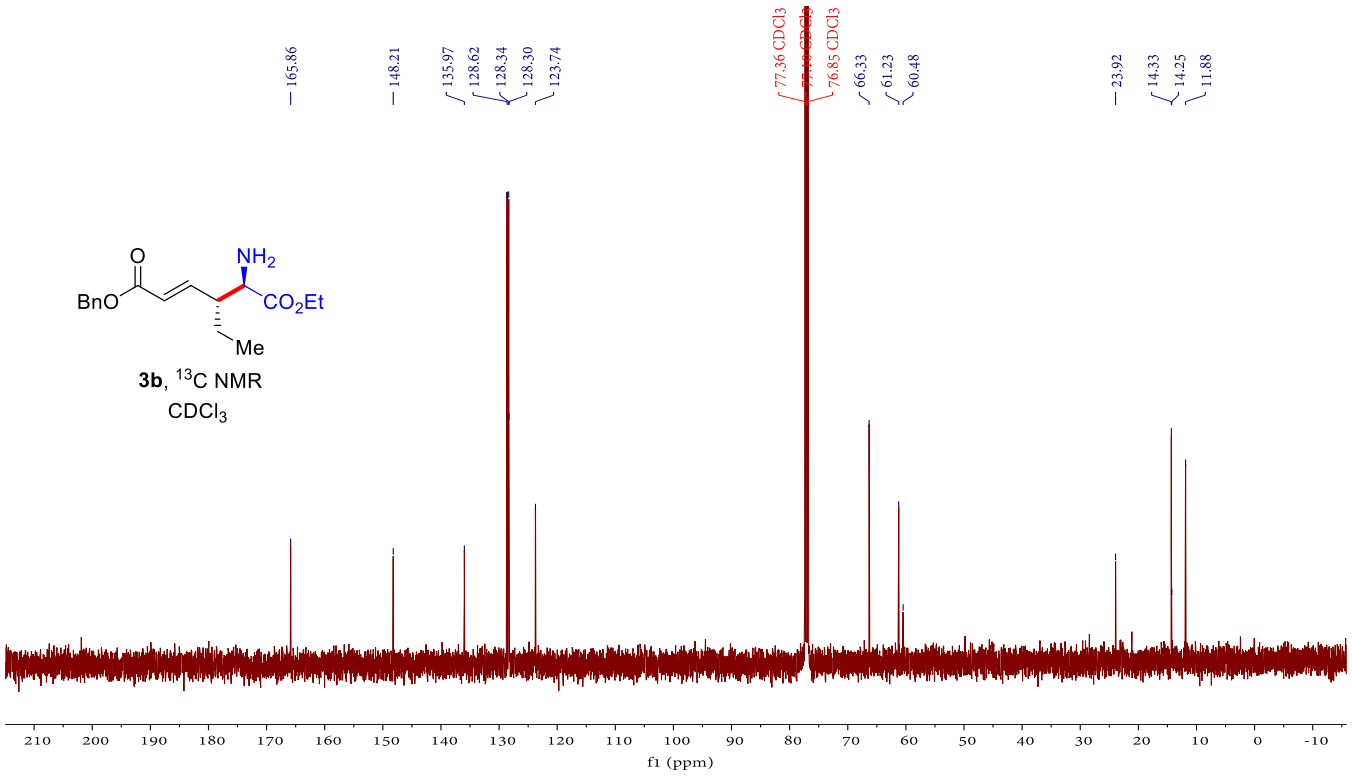


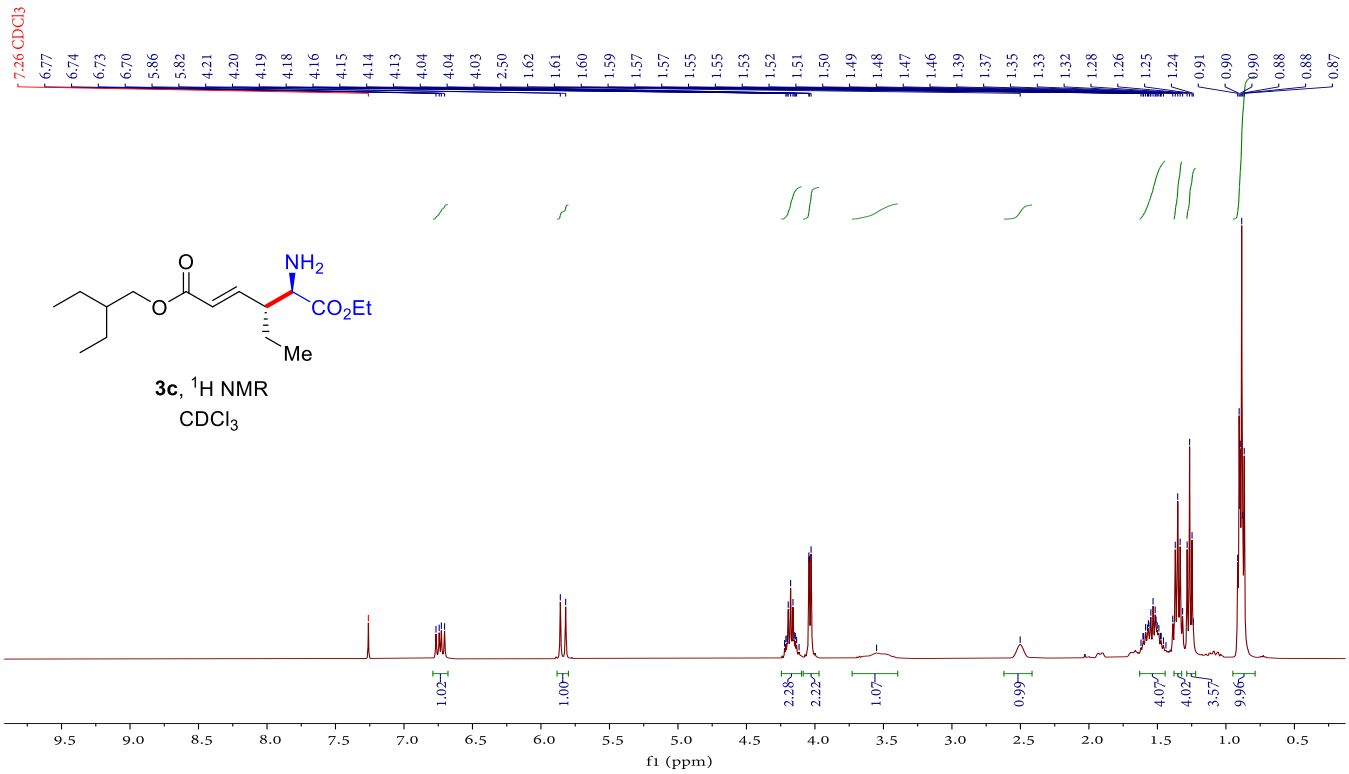
(R,R)-**3a**, ^{13}C NMR
$CDCl_3$


7.26 CDCl3
6.81 6.79 6.78 6.76 5.88 5.85 4.19 4.19 4.18 4.17 4.17 4.16 4.15 4.14 4.13 4.13 4.12 3.47 3.46 2.40 2.39 2.38 1.78 1.63 1.63 1.62 1.61 1.60 1.60 1.59 1.46 1.44 1.44 1.43 1.42 1.42 1.41 1.40 1.29 1.27 1.26 1.26 1.25 1.23 0.89 0.88 0.86 0.85
O
NH2
EtO
CO2Et
Me
(R,S)-3a, 1H NMR
CDCl3
1.00 1.01 4.36 1.00 0.98 2.39 2.42 6.23 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
f1 (ppm)

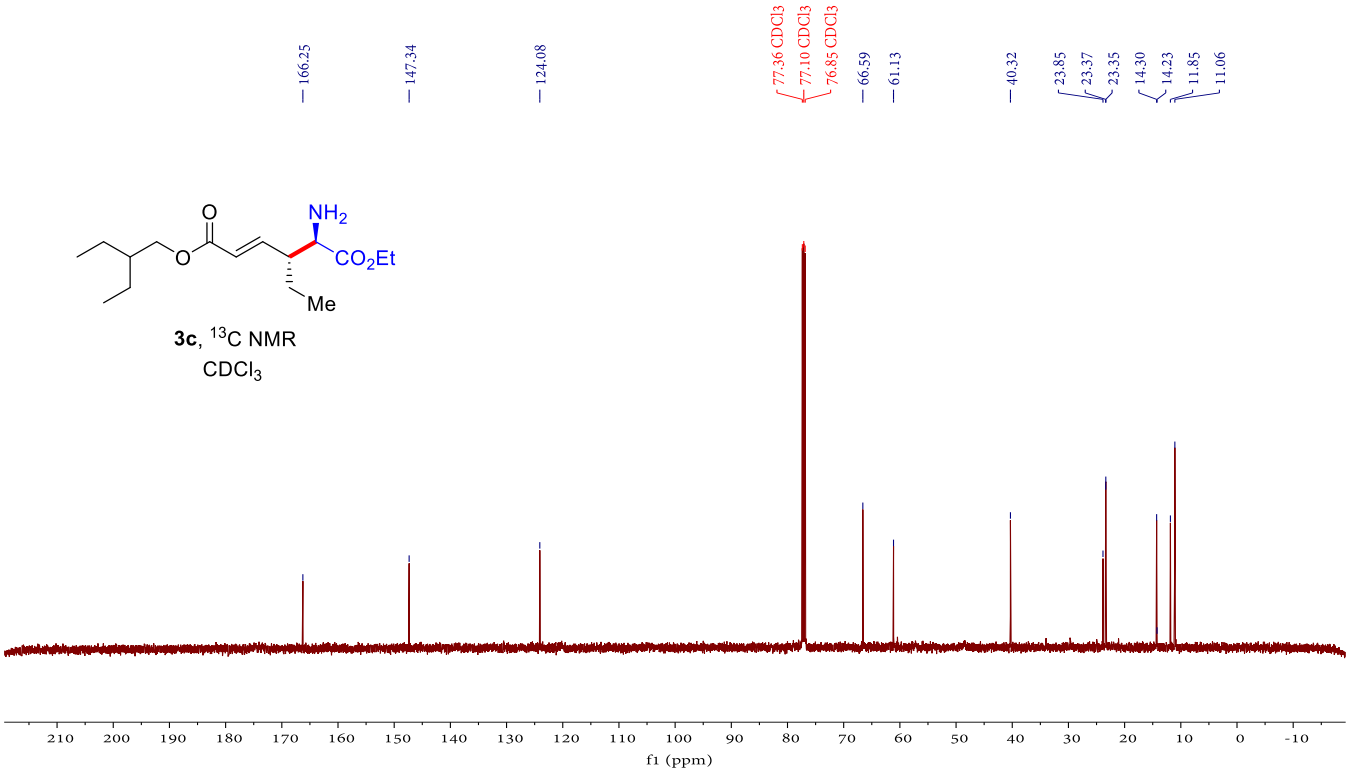

174.31 166.13 148.17 123.66
77.36 CDCl3
77.10 CDCl3
76.85 CDCl3
61.04 60.40 57.66 48.85 22.67 14.30 14.26 11.89
O
NH2
EtO
CO2Et
Me
(R,S)-3a, 13C NMR
CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.38 7.37 7.36 7.35 7.34 7.33 7.33 7.32 7.31 7.26 CDCl3 6.85 6.84 6.82 6.81 6.79 5.92 5.88 5.17 4.23 4.22 4.21 4.20 4.19 4.18 4.17 4.16 4.15 4.15 2.55 1.63 1.61 1.61 1.60 1.57 1.56 1.53 1.52 1.50 1.48 1.46 1.44 1.28 1.26 1.25 1.23 1.22 0.92 0.90 0.89
O
NH2
BnO
CO2Et
Me
3b, 1H NMR
CDCl3
5.01 1.00 0.99 2.08 2.15 0.99 1.09 3.22 4.11 3.09
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
f1 (ppm)

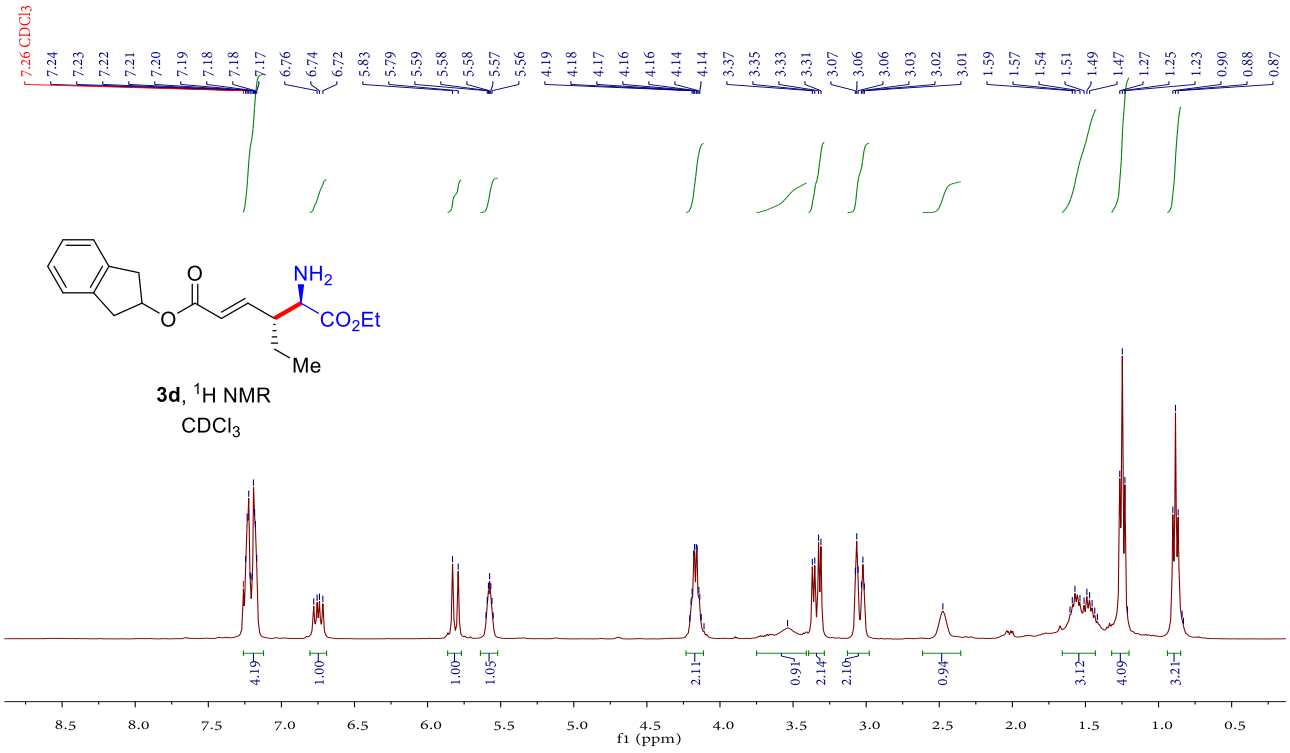

165.86 148.21 135.97 128.62 128.34 128.30 123.74 77.36 CDCl3 76.85 CDCl3 66.33 61.23 60.48 23.92 14.33 14.25 11.88
O
NH2
BnO
CO2Et
Me
3b, 13C NMR
CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

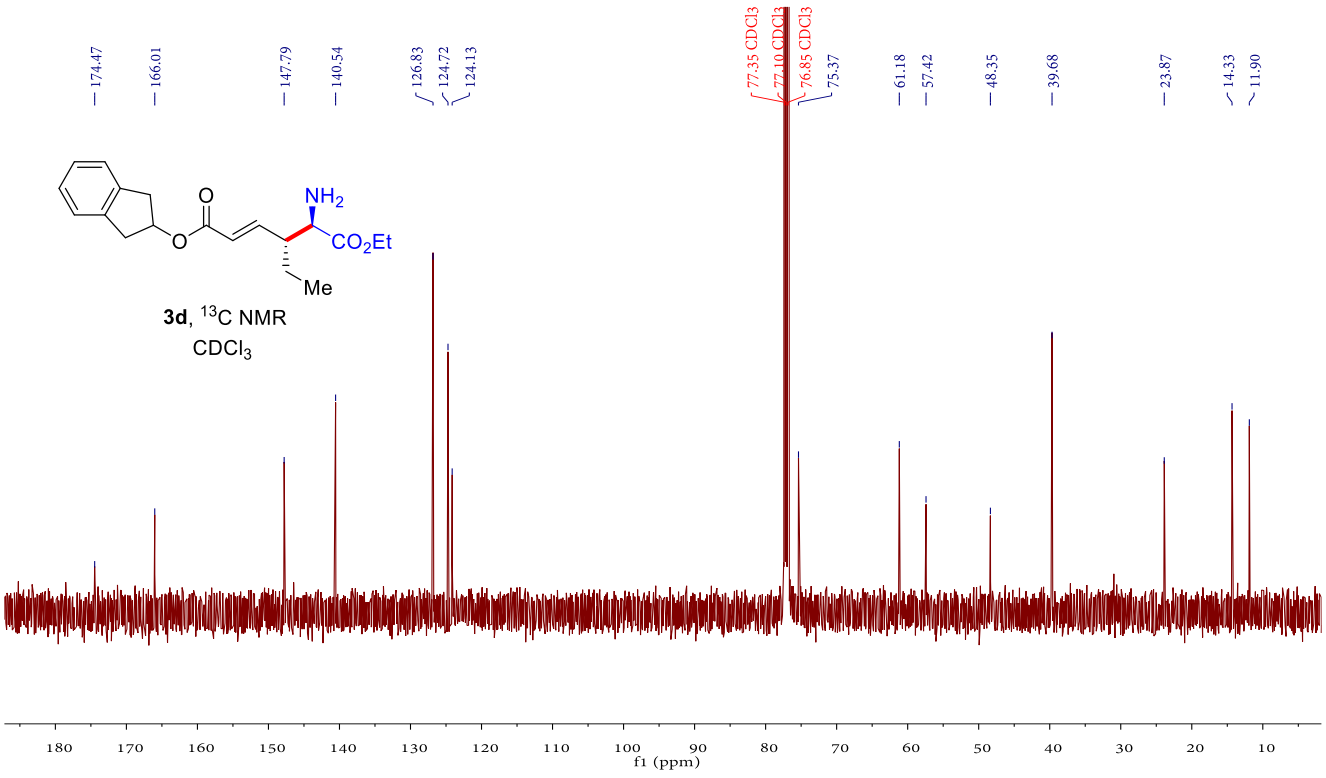


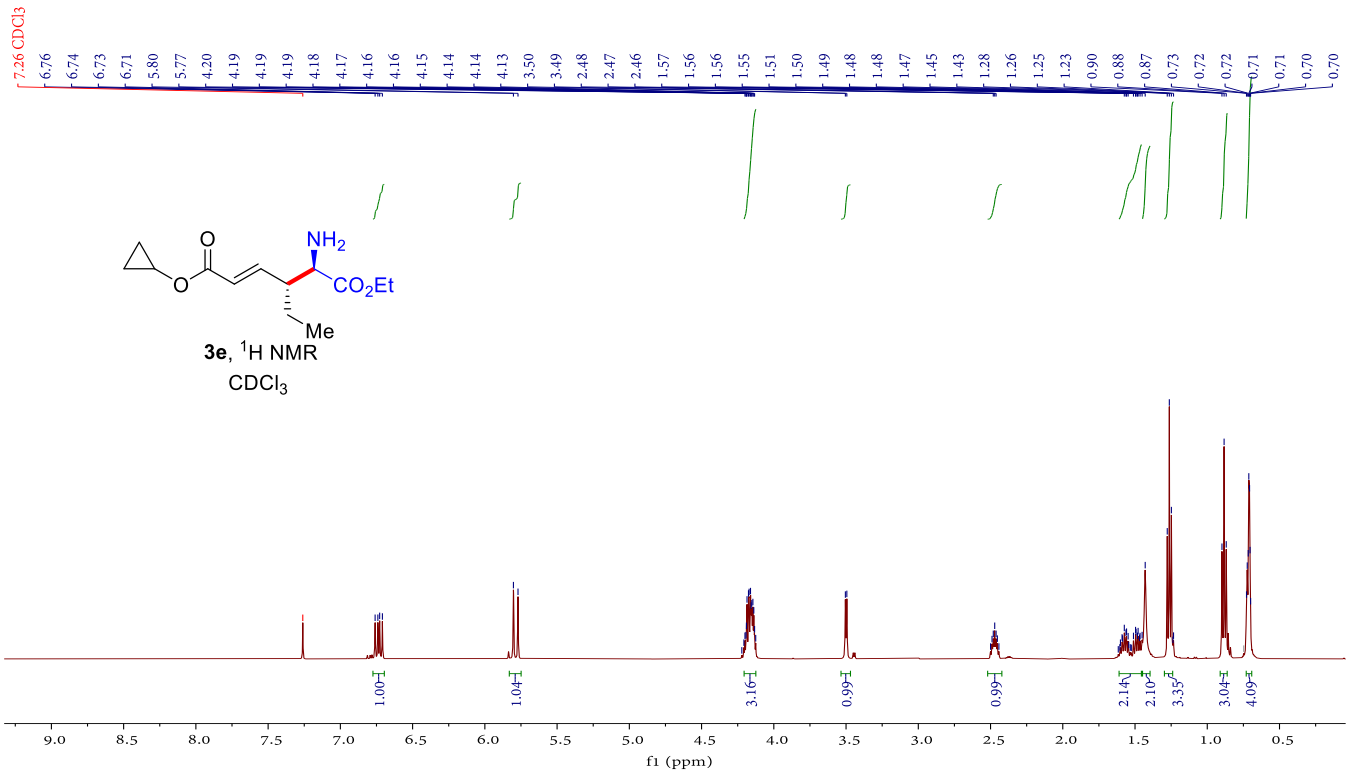
3c, ^{1}H NMR
$CDCl_3$

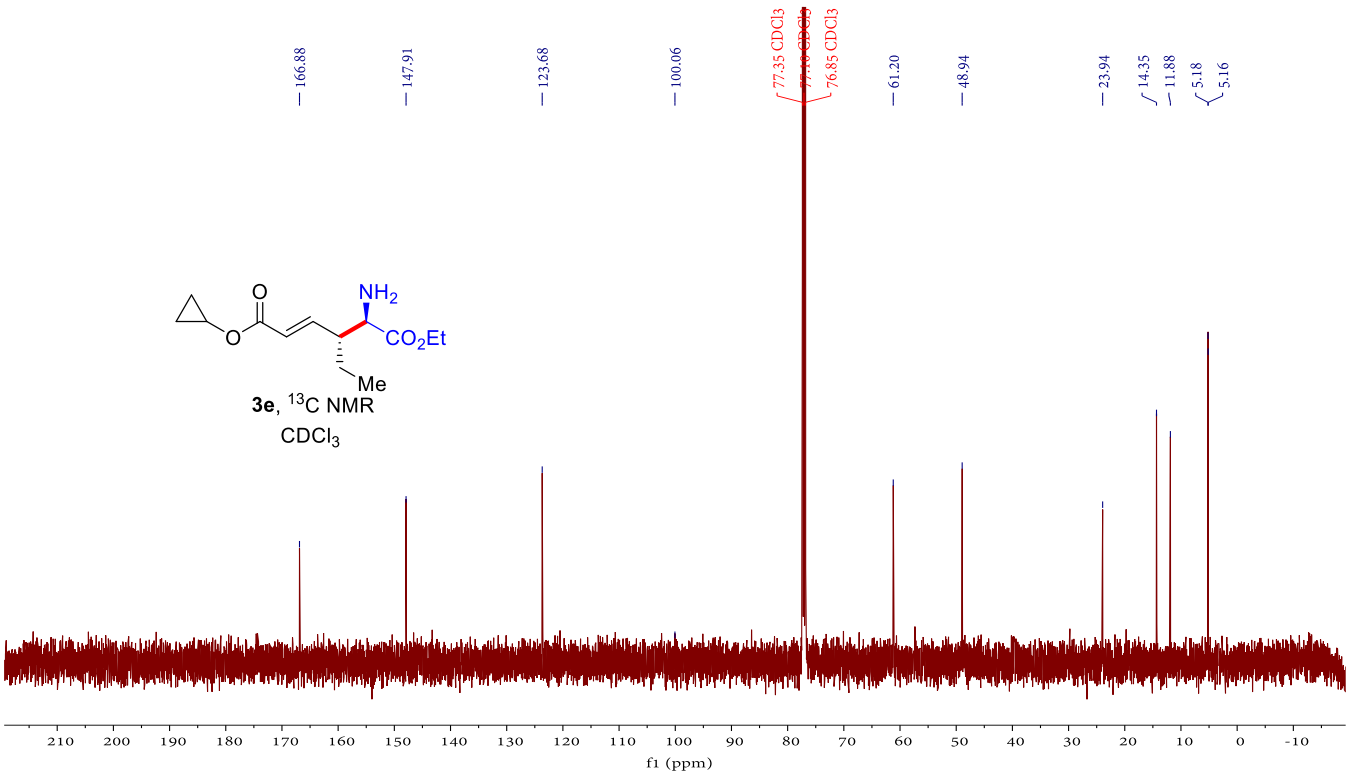


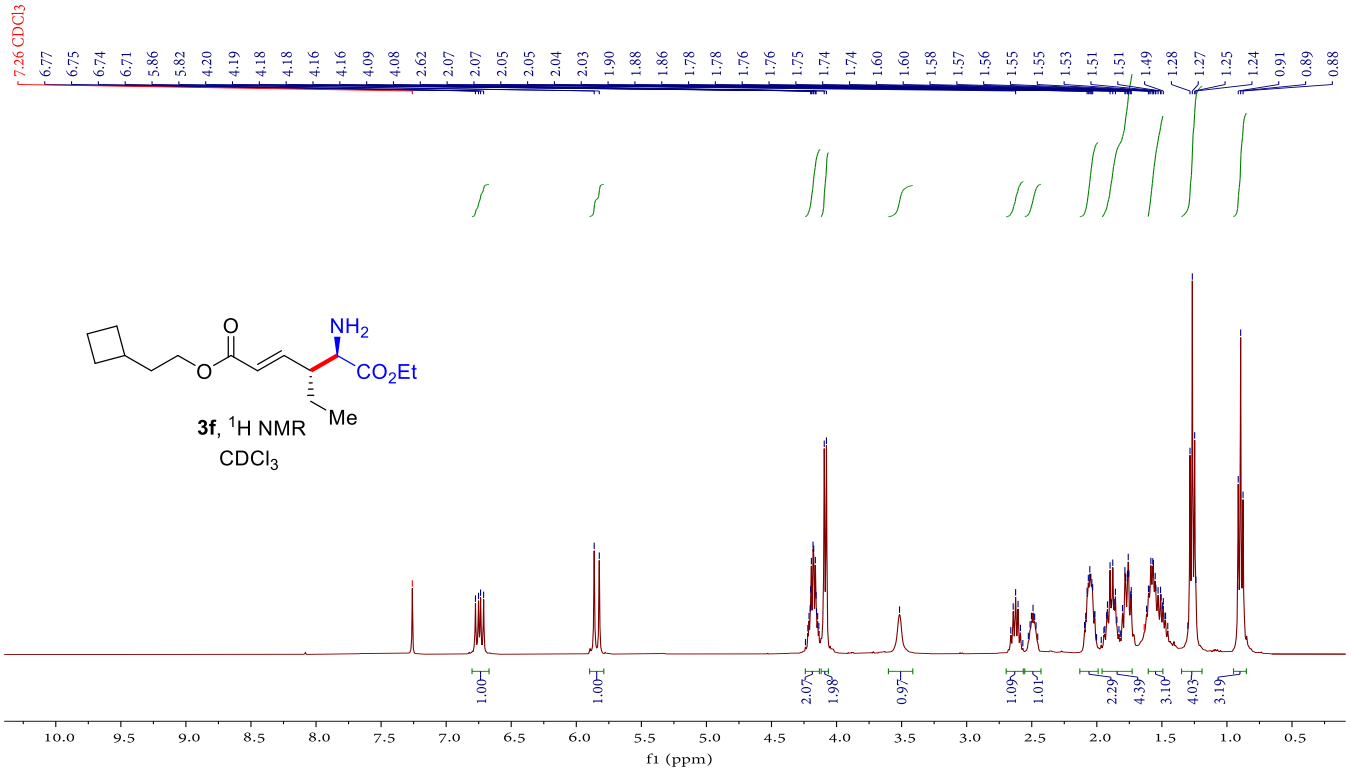
3c, ^{13}C NMR
$CDCl_3$

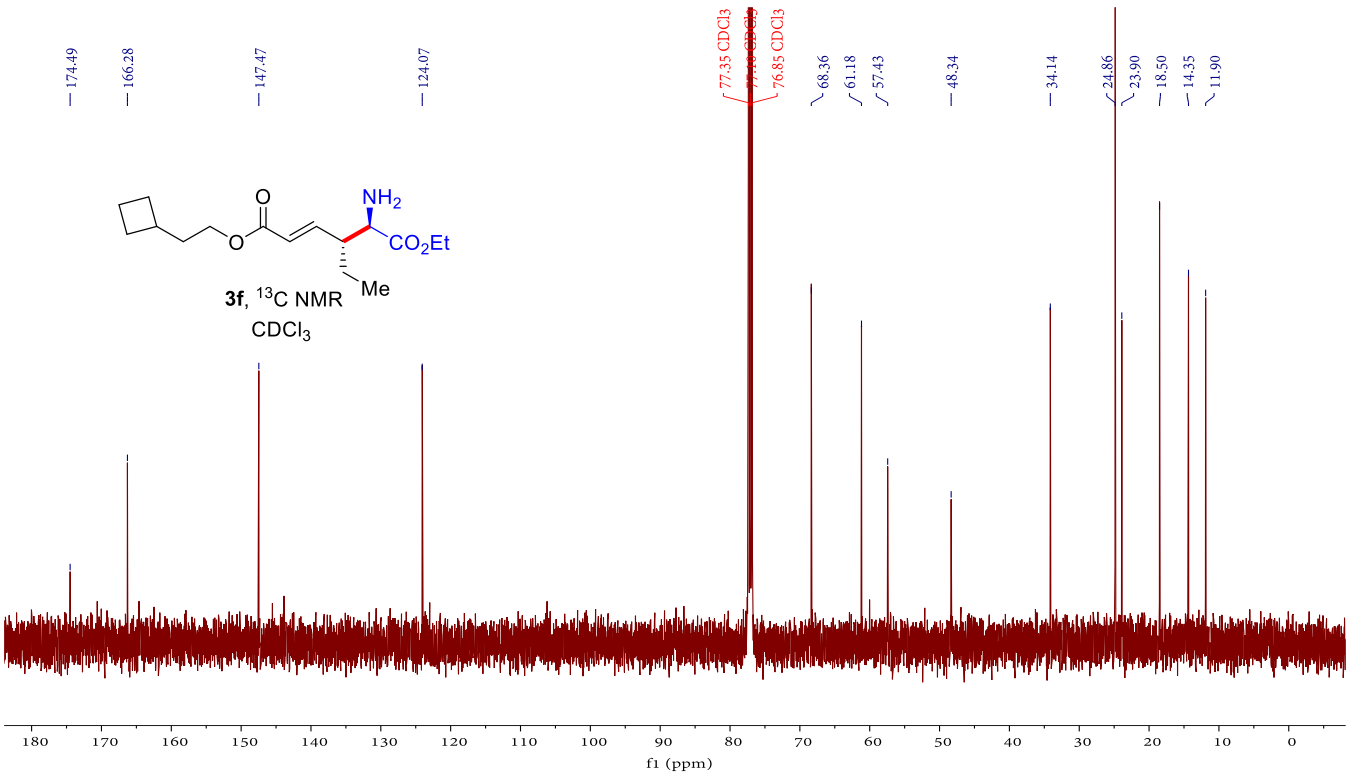

7.26 CDCl3
7.24
7.23
7.22
7.21
7.20
7.19
7.18
7.18
7.17
6.76
6.74
6.72
5.83
5.79
5.59
5.58
5.58
5.57
5.56
4.19
4.18
4.17
4.16
4.16
4.14
4.14
3.37
3.35
3.33
3.31
3.07
3.06
3.06
3.03
3.02
3.01
1.59
1.57
1.54
1.51
1.49
1.47
1.27
1.25
1.23
0.90
0.88
0.87
O
O
NH2
CO2Et
Me
3d, 1H NMR
CDCl3
4.19
1.00
1.00
1.05
2.11
0.91
2.14
2.10
0.94
3.12
4.09
3.21
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
f1 (ppm)

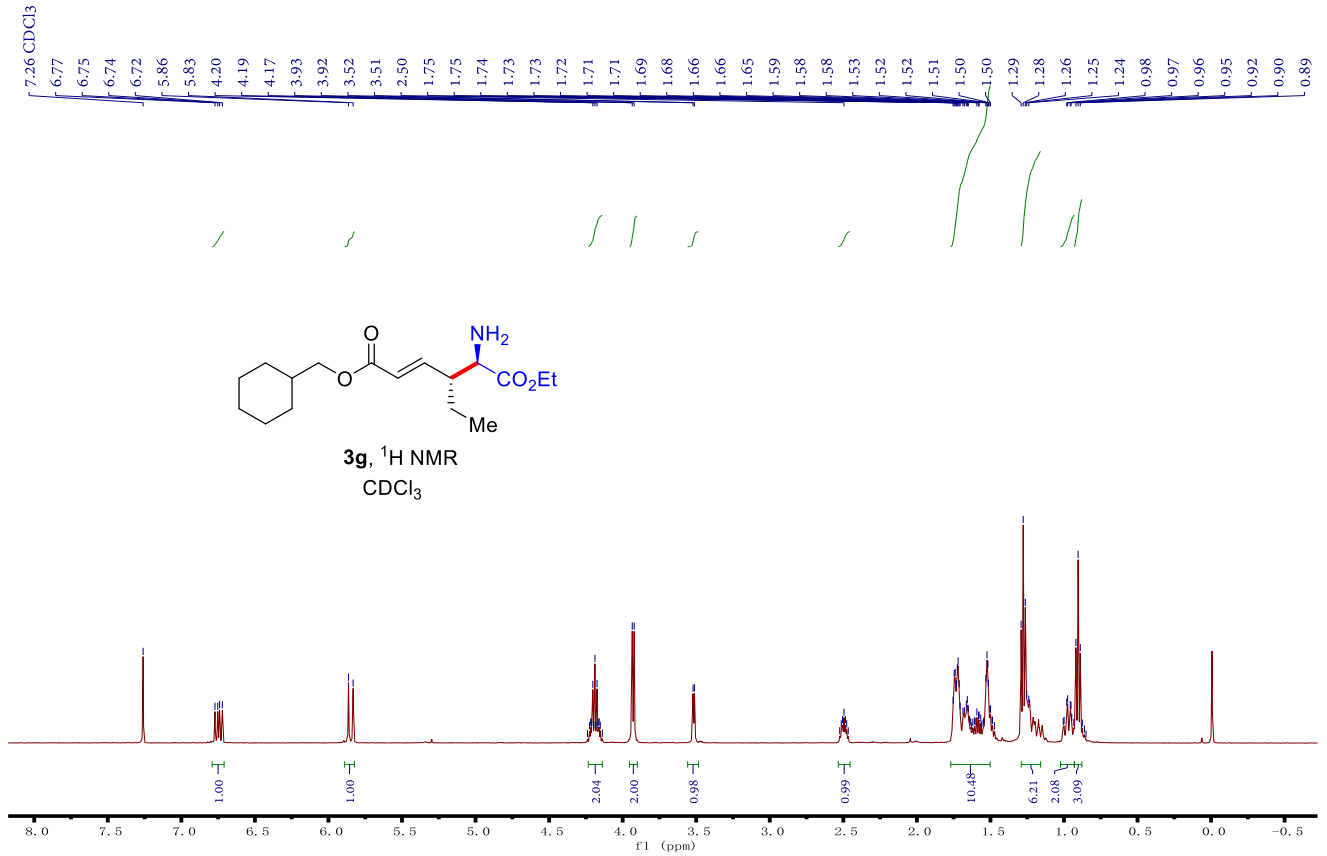

174.47
166.01
147.79
140.54
126.83
124.72
124.13
77.35 CDCl3
77.10 CDCl3
76.85 CDCl3
75.37
61.18
57.42
48.35
39.68
23.87
14.33
11.90
O
O
NH2
CO2Et
Me
3d, 13C NMR
CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.26 CDCl3
6.76 6.74 6.73 6.71 5.80 5.77 4.20 4.19 4.19 4.19 4.18 4.17 4.16 4.16 4.15 4.14 4.14 4.13 3.50 3.49 2.48 2.47 2.46 1.57 1.56 1.56 1.55 1.51 1.50 1.49 1.48 1.48 1.47 1.45 1.43 1.28 1.26 1.25 1.23 0.90 0.88 0.87 0.73 0.72 0.72 0.71 0.71 0.70 0.70
O
O
NH2
CO2Et
Me
3e, 1H NMR
CDCl3
1.00 1.04 3.16 0.99 0.99 2.14 2.10 3.35 3.04 4.09
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
f1 (ppm)

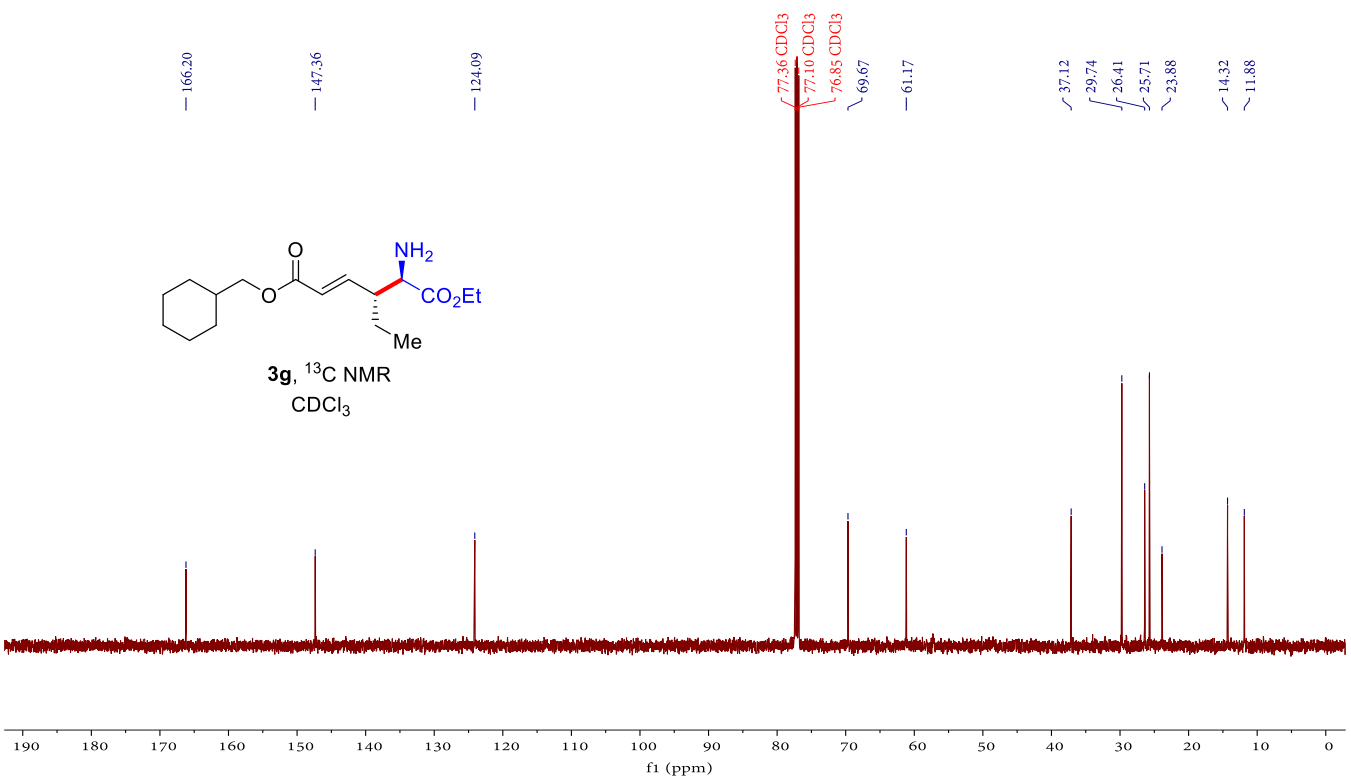

166.88 147.91 123.68 100.06 77.35 CDCl3 77.18 CDCl3 76.85 CDCl3 61.20 48.94 23.94 14.35 11.88 5.18 5.16
O
O
NH2
CO2Et
Me
3e, 13C NMR
CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.26 CDCl3
6.77
6.75
6.74
6.71
5.86
5.82
4.20
4.19
4.18
4.18
4.16
4.16
4.09
4.08
2.62
2.07
2.07
2.05
2.05
2.04
2.03
1.90
1.88
1.86
1.78
1.78
1.76
1.76
1.75
1.74
1.74
1.60
1.60
1.58
1.57
1.56
1.55
1.55
1.53
1.51
1.51
1.49
1.28
1.27
1.25
1.24
0.91
0.89
0.88
O
NH2
O
CO2Et
Me
3f, 1H NMR
CDCl3
1.00
1.00
2.07
1.98
0.97
1.09
1.01
2.29
4.39
3.10
4.03
3.19
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
f1 (ppm)

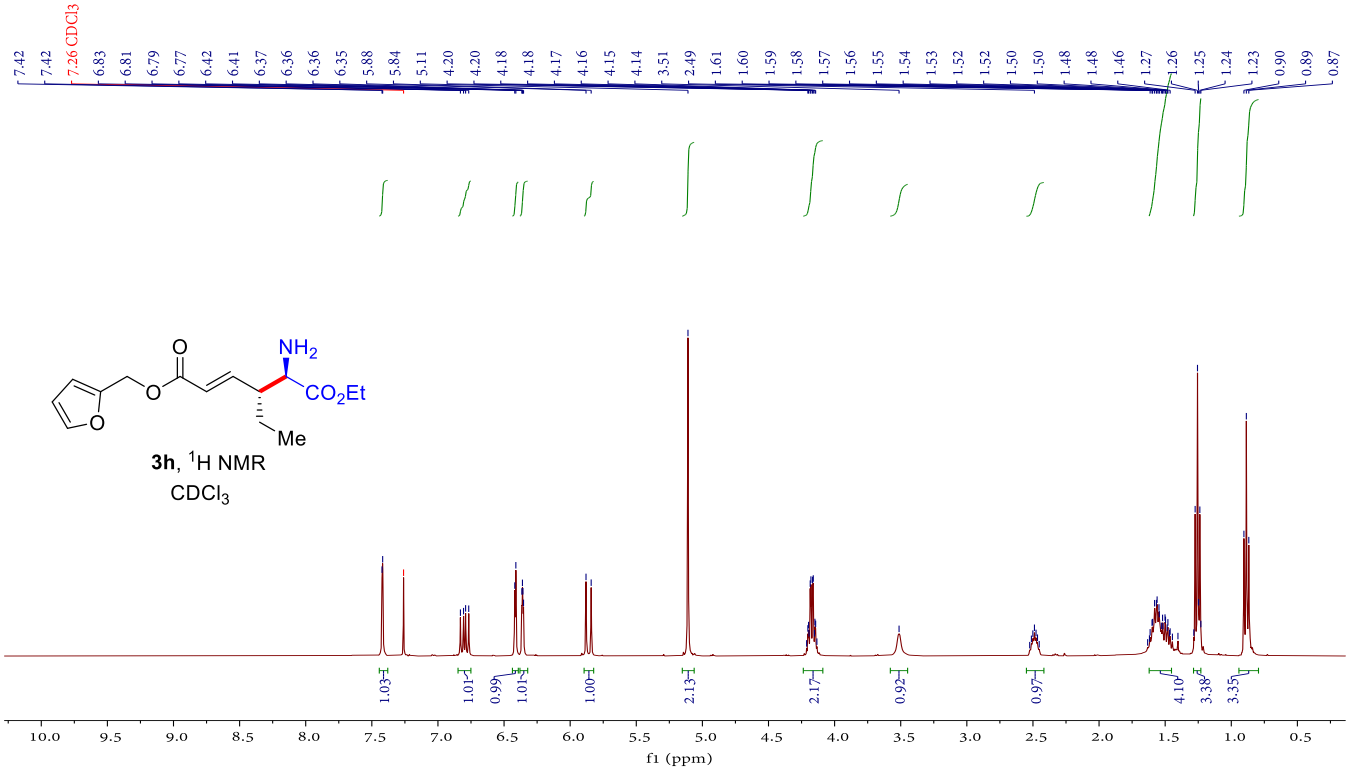

174.49
166.28
147.47
124.07
77.35 CDCl3
76.85 CDCl3
68.36
61.18
57.43
48.34
34.14
24.86
23.90
18.50
14.35
11.90
O
NH2
O
CO2Et
Me
3f, 13C NMR
CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

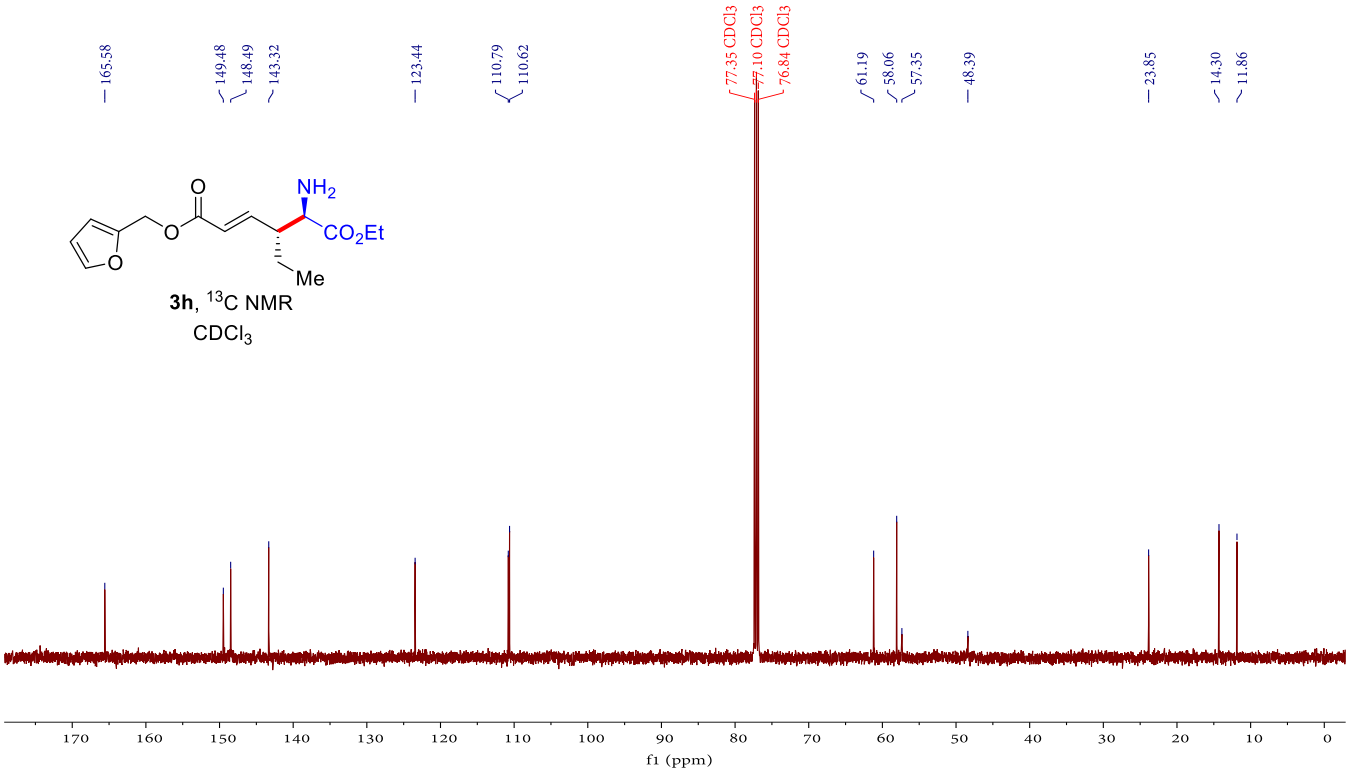


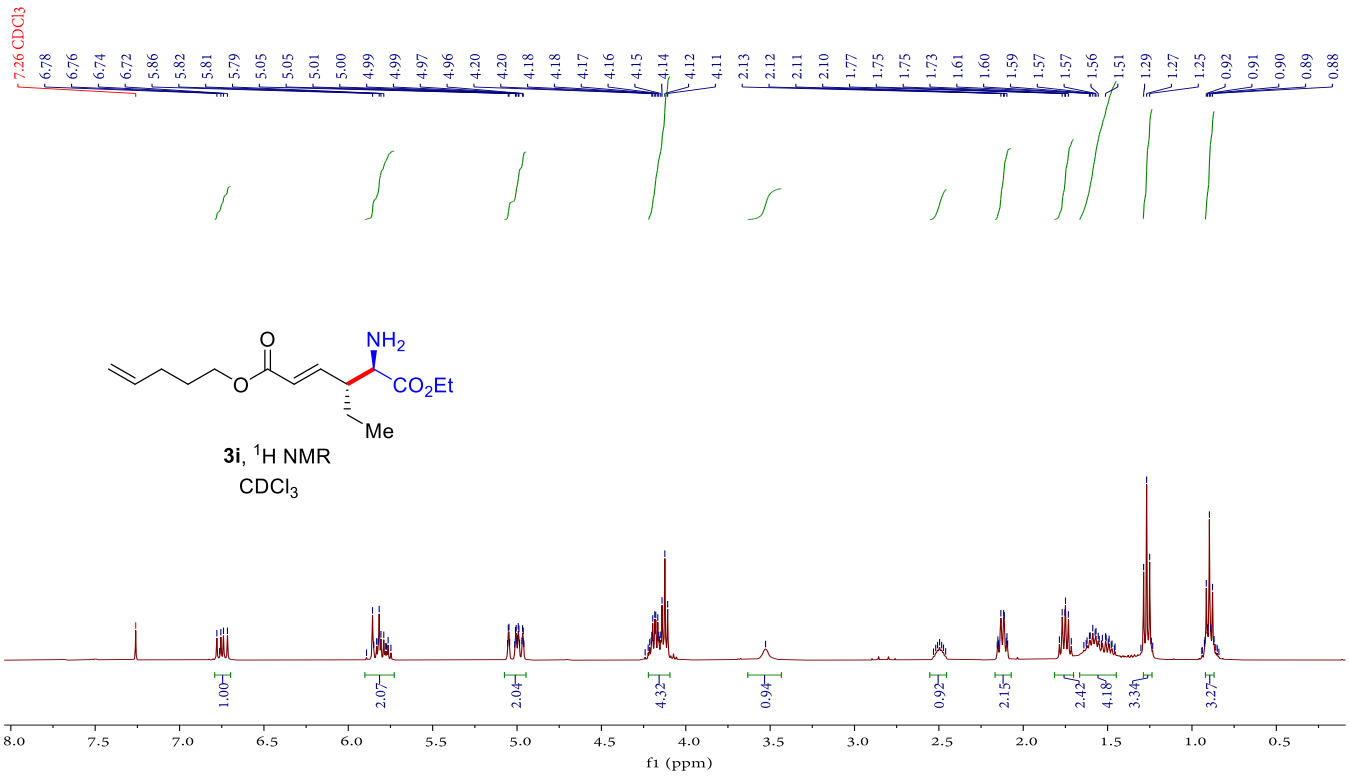
3g, ^{1}H NMR
$CDCl_3$

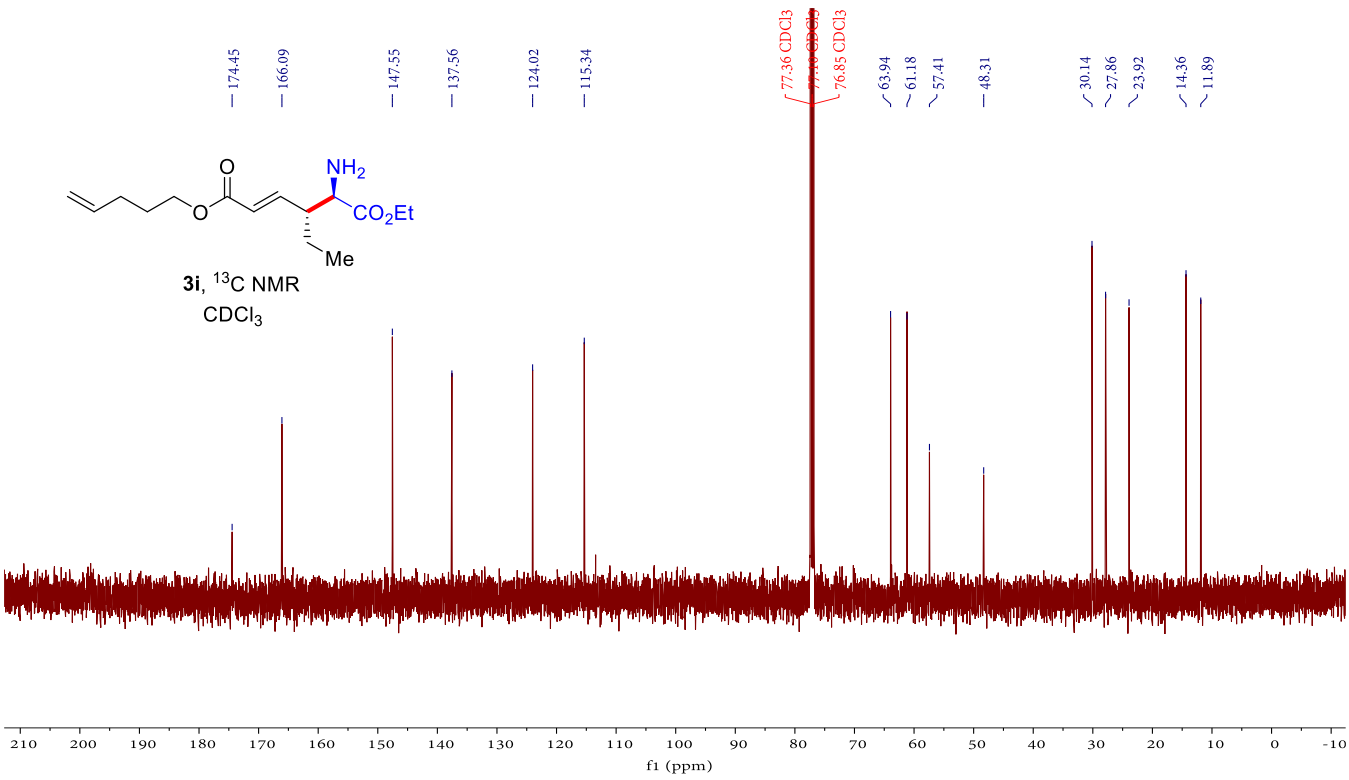


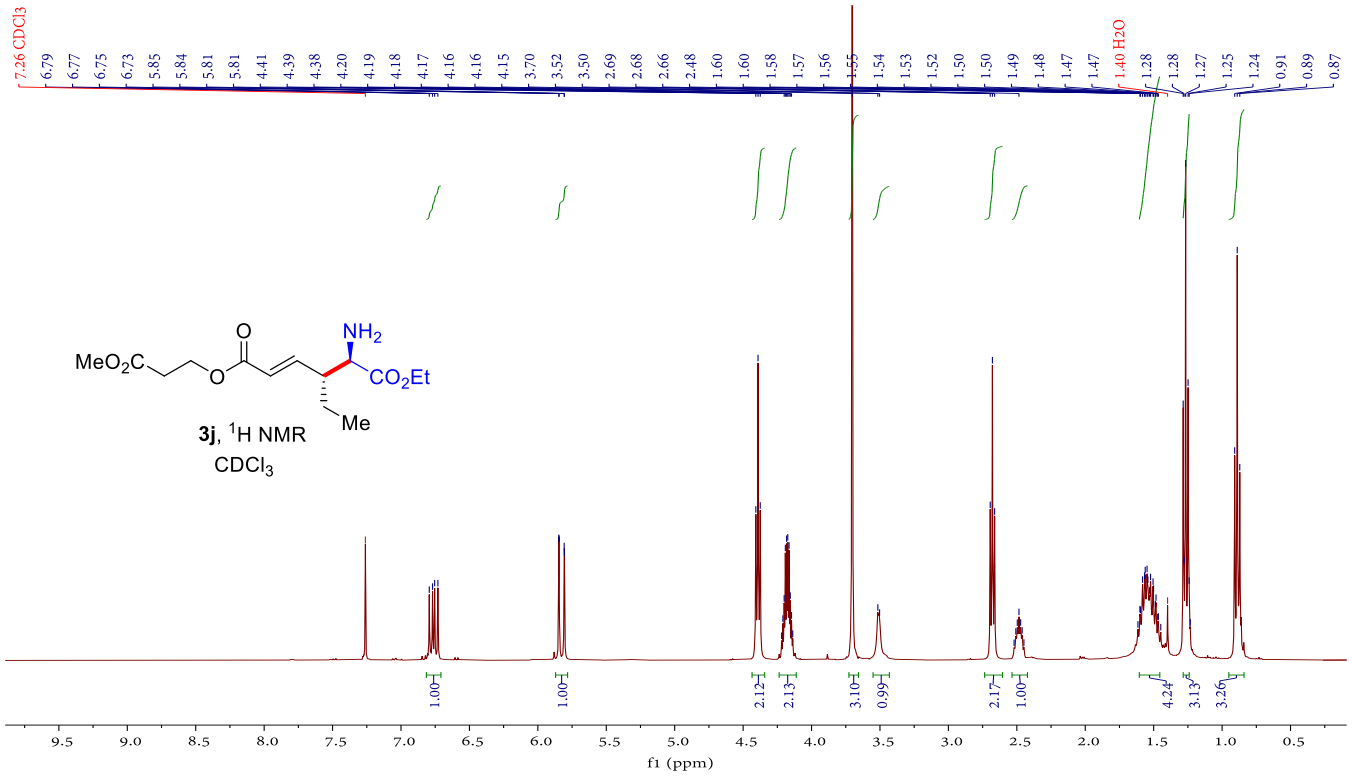
3g, ^{13}C NMR
$CDCl_3$

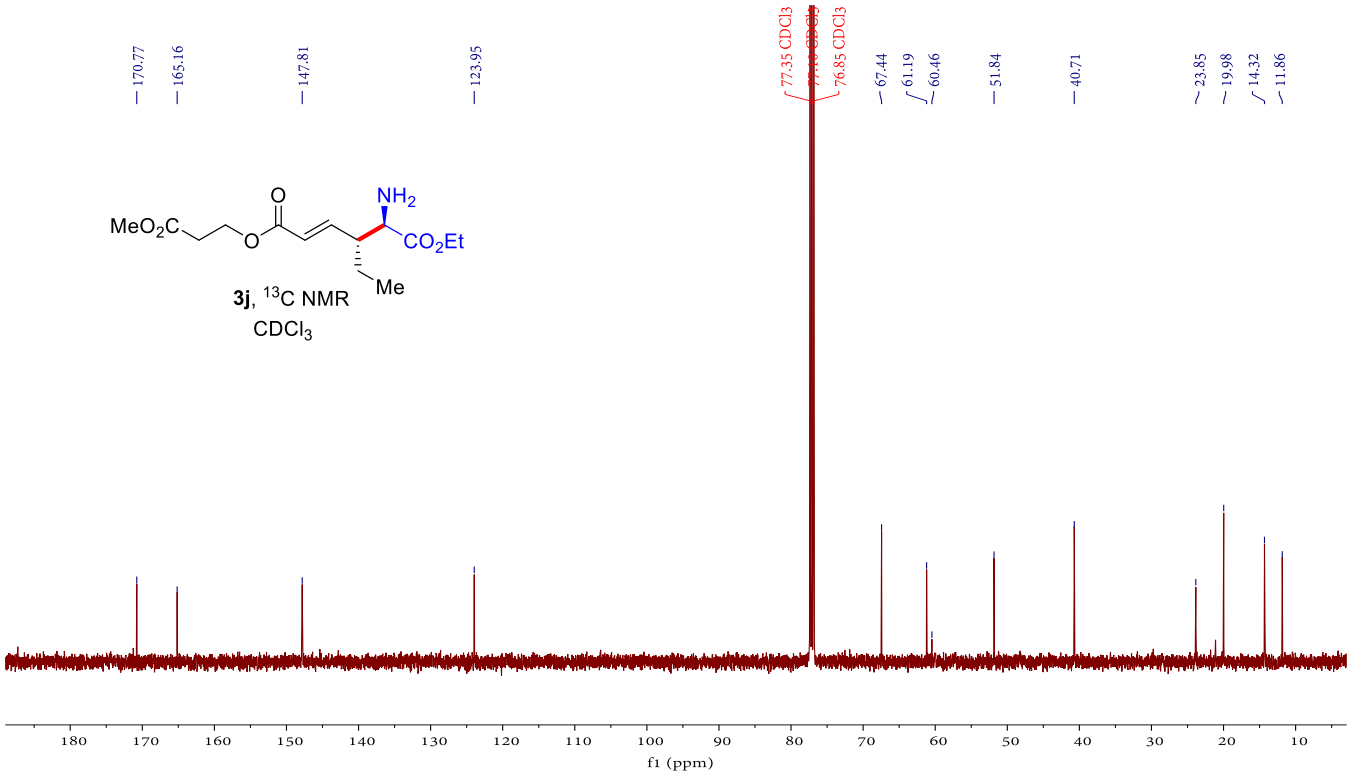

7.42 7.42 7.26 CDCl3 6.83 6.81 6.79 6.77 6.42 6.41 6.37 6.36 6.36 6.35 5.88 5.84 5.11 4.20 4.20 4.18 4.18 4.17 4.16 4.15 4.14 3.51 2.49 1.61 1.60 1.59 1.58 1.57 1.56 1.55 1.54 1.53 1.52 1.52 1.50 1.50 1.48 1.48 1.46 1.27 1.26 1.25 1.24 1.23 0.90 0.89 0.87
O
O
O
NH2
CO2Et
Me
3h, 1H NMR
CDCl3
1.03 1.01 0.99 1.01 1.00 2.13 2.17 0.92 0.97 4.10 3.38 3.35
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
f1 (ppm)

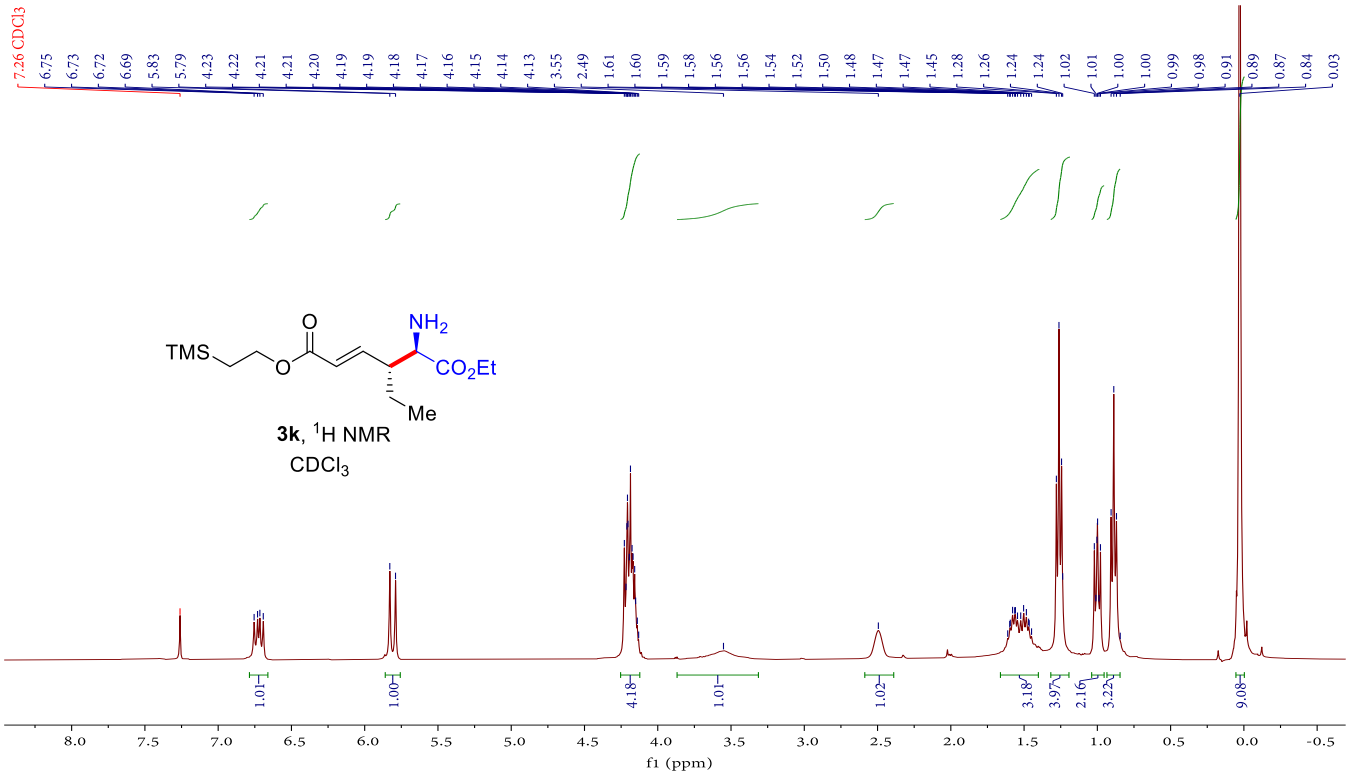

165.58 149.48 148.49 143.32 123.44 110.79 110.62 77.35 CDCl3 77.10 CDCl3 76.84 CDCl3 61.19 58.06 57.35 48.39 23.85 14.30 11.86
O
O
O
NH2
CO2Et
Me
3h, 13C NMR
CDCl3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

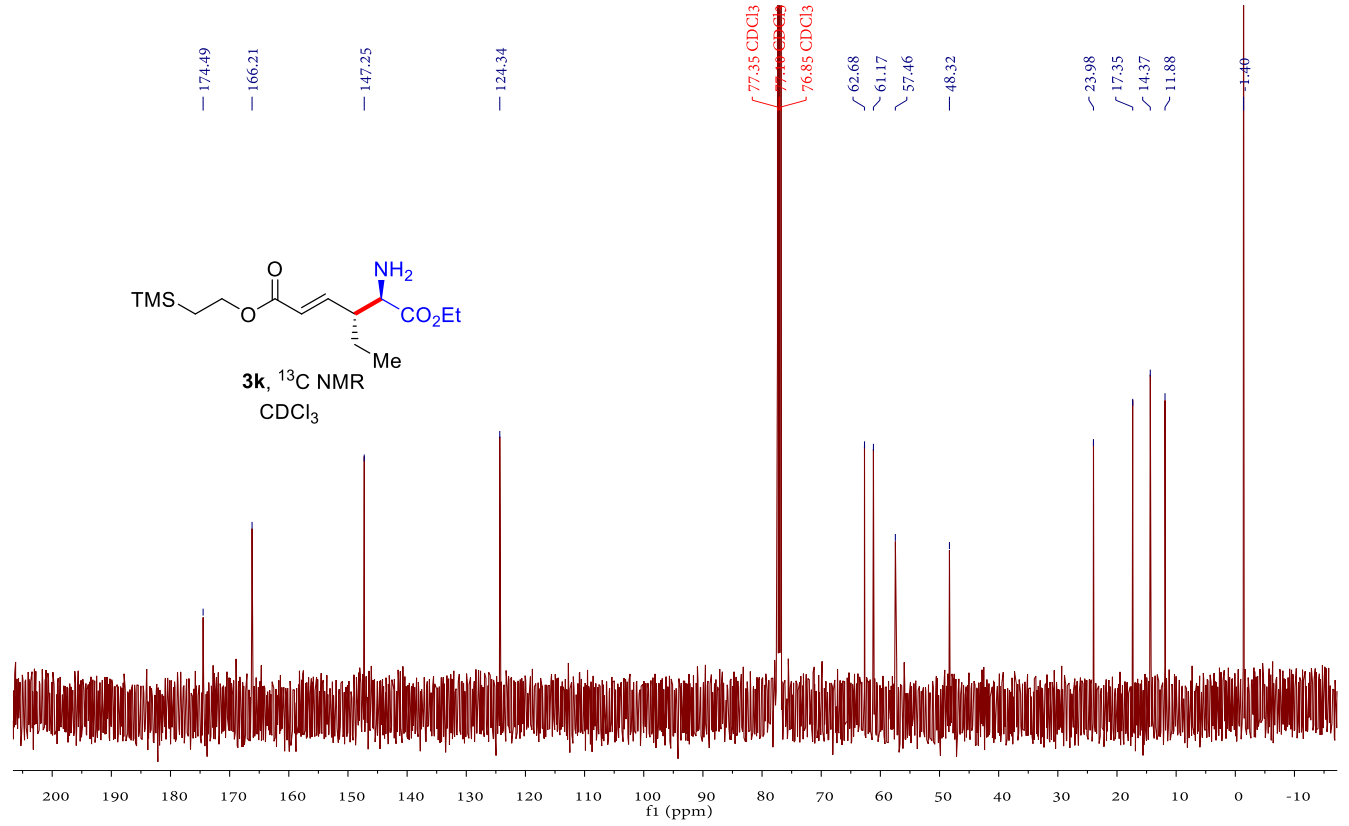

7.26 CDCl3
6.78 6.76 6.74 6.72 5.86 5.82 5.81 5.79 5.05 5.05 5.01 5.00 4.99 4.99 4.97 4.96 4.20 4.20 4.18 4.18 4.17 4.16 4.15 4.14 4.12 4.11
2.13 2.12 2.11 2.10 1.77 1.75 1.75 1.73 1.61 1.60 1.59 1.57 1.57 1.56 1.51 1.29 1.27 1.25 0.92 0.91 0.90 0.89 0.88
O
NH2
O
CO2Et
Me
3i, 1H NMR
CDCl3
1.00 2.07 2.04 4.32 0.94 0.92 2.15 2.42 4.18 3.34 3.27
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
f1 (ppm)

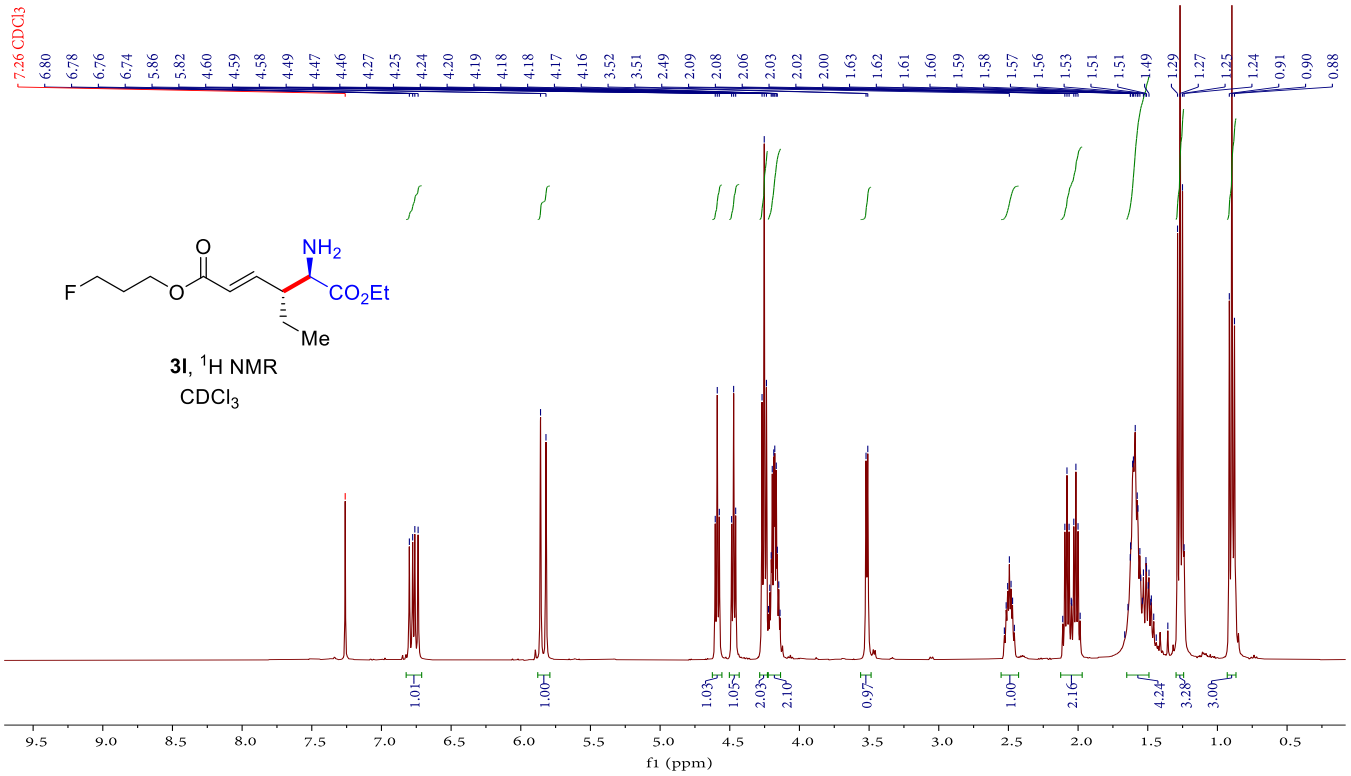

174.45 166.09 147.55 137.56 124.02 115.34
77.36 CDCl3 77.16 CDCl3 76.85 CDCl3
63.94 61.18 57.41 48.31 30.14 27.86 23.92 14.36 11.89
O
NH2
O
CO2Et
Me
3i, 13C NMR
CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

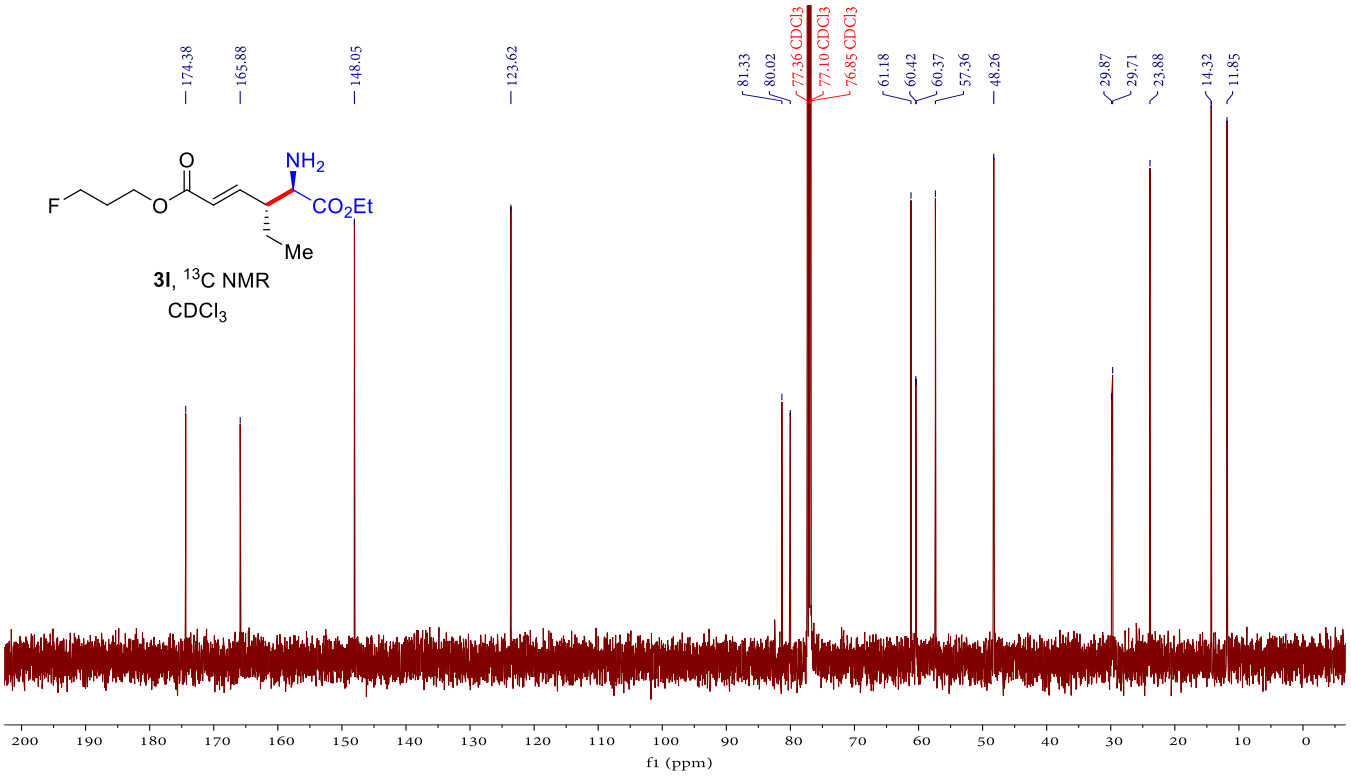

7.26 CDCl3
1.40 H2O
MeO2C
O
NH2
CO2Et
Me
3j, 1H NMR
CDCl3
1.00
1.00
2.12
2.13
3.10
0.99
2.17
1.00
4.24
3.13
3.26
f1 (ppm)


170.77
165.16
147.81
123.95
77.35 CDCl3
76.85 CDCl3
67.44
61.19
60.46
51.84
40.71
23.85
19.98
14.32
11.86
MeO2C
O
NH2
CO2Et
Me
3j, 13C NMR
CDCl3
f1 (ppm)


7.26 CDCl3
TMS
O
NH2
CO2Et
Me
3k, 1H NMR
CDCl3
f1 (ppm)


174.49
166.21
147.25
124.34
77.35 CDCl3
76.85 CDCl3
62.68
61.17
57.46
48.32
23.98
17.35
14.37
11.88
TMS
O
NH2
CO2Et
Me
3k, 13C NMR
CDCl3
f1 (ppm)


7.26 CDCl3
6.80 6.78 6.76 6.74 5.86 5.82 4.60 4.59 4.58 4.49 4.47 4.46 4.27 4.25 4.24 4.20 4.19 4.18 4.18 4.17 4.16 3.52 3.51 2.49 2.09 2.08 2.06 2.03 2.02 2.00 1.63 1.62 1.61 1.60 1.59 1.58 1.57 1.56 1.53 1.51 1.51 1.49 1.29 1.27 1.25 1.24 0.91 0.90 0.88
O
NH2
F
O
CO2Et
Me
3l, 1H NMR
CDCl3
1.01 1.00 1.03 1.05 2.03 2.10 0.97 1.00 2.16 4.24 3.28 3.00
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
f1 (ppm)


174.38 165.88 148.05 123.62 81.33 80.02 77.36 CDCl3 77.10 CDCl3 76.85 CDCl3 61.18 60.42 60.37 57.36 48.26 29.87 29.71 23.88 14.32 11.85
O
NH2
F
O
CO2Et
Me
3l, 13C NMR
CDCl3
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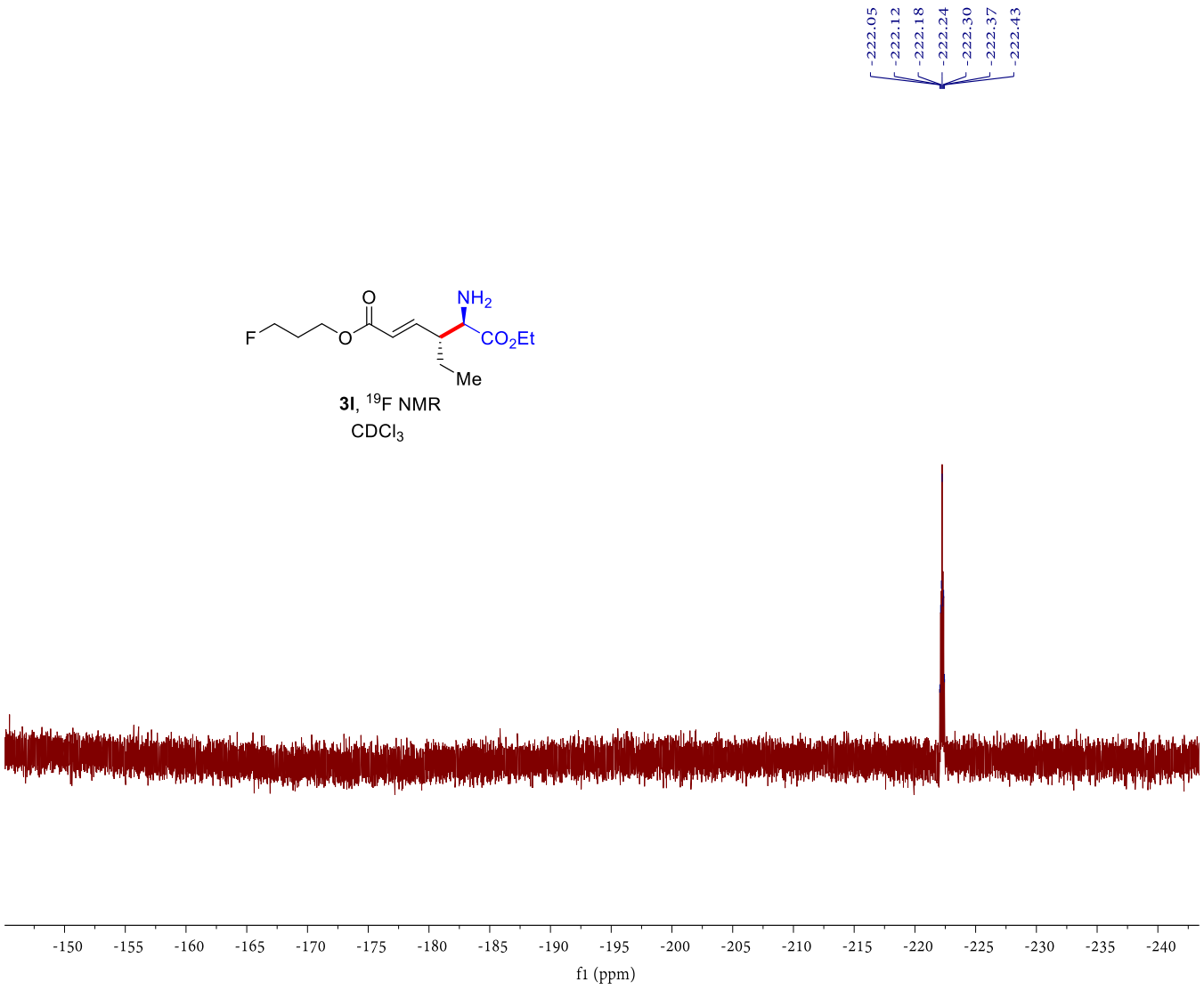
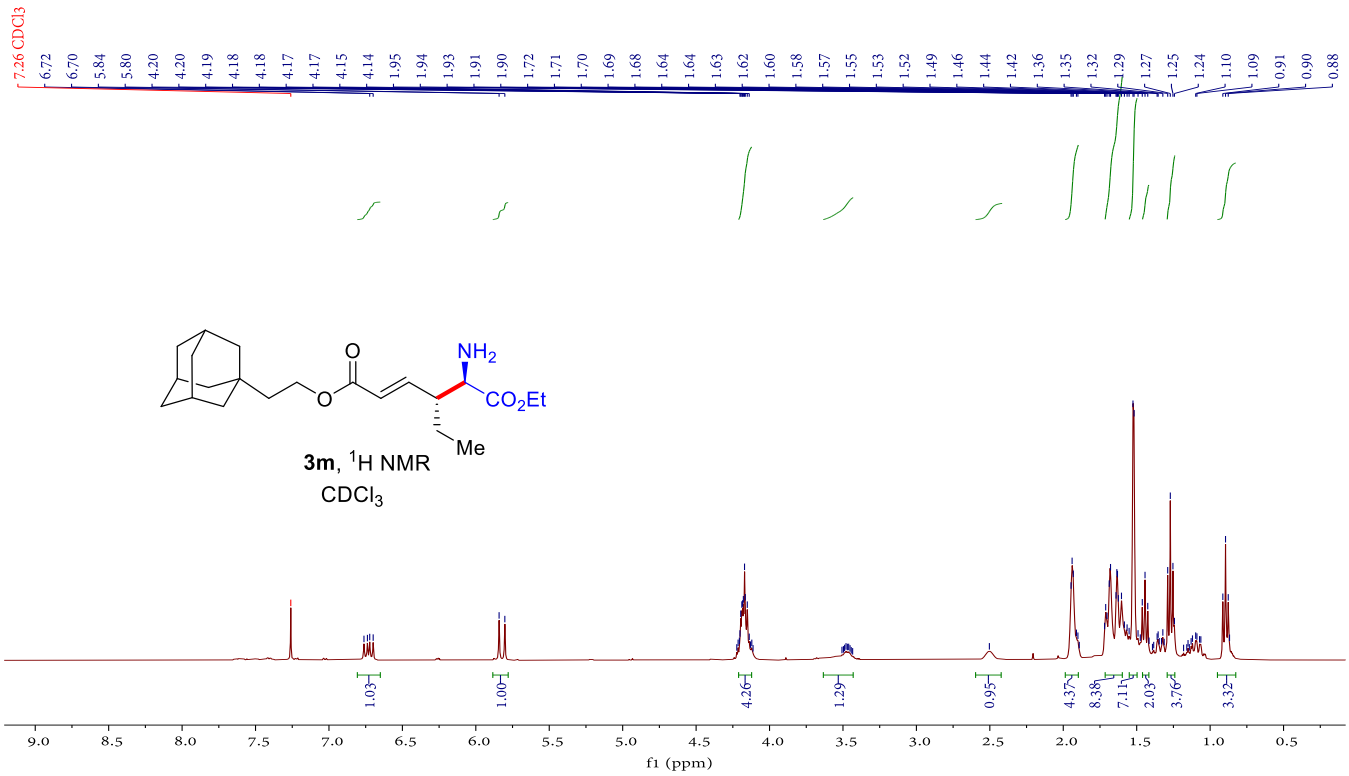
f1 (ppm)


-222.05
-222.12
-222.18
-222.24
-222.30
-222.37
-222.43
F
O
O
NH2
CO2Et
Me
3l, 19F NMR
CDCl3
-150
-155
-160
-165
-170
-175
-180
-185
-190
-195
-200
-205
-210
-215
-220
-225
-230
-235
-240
f1 (ppm)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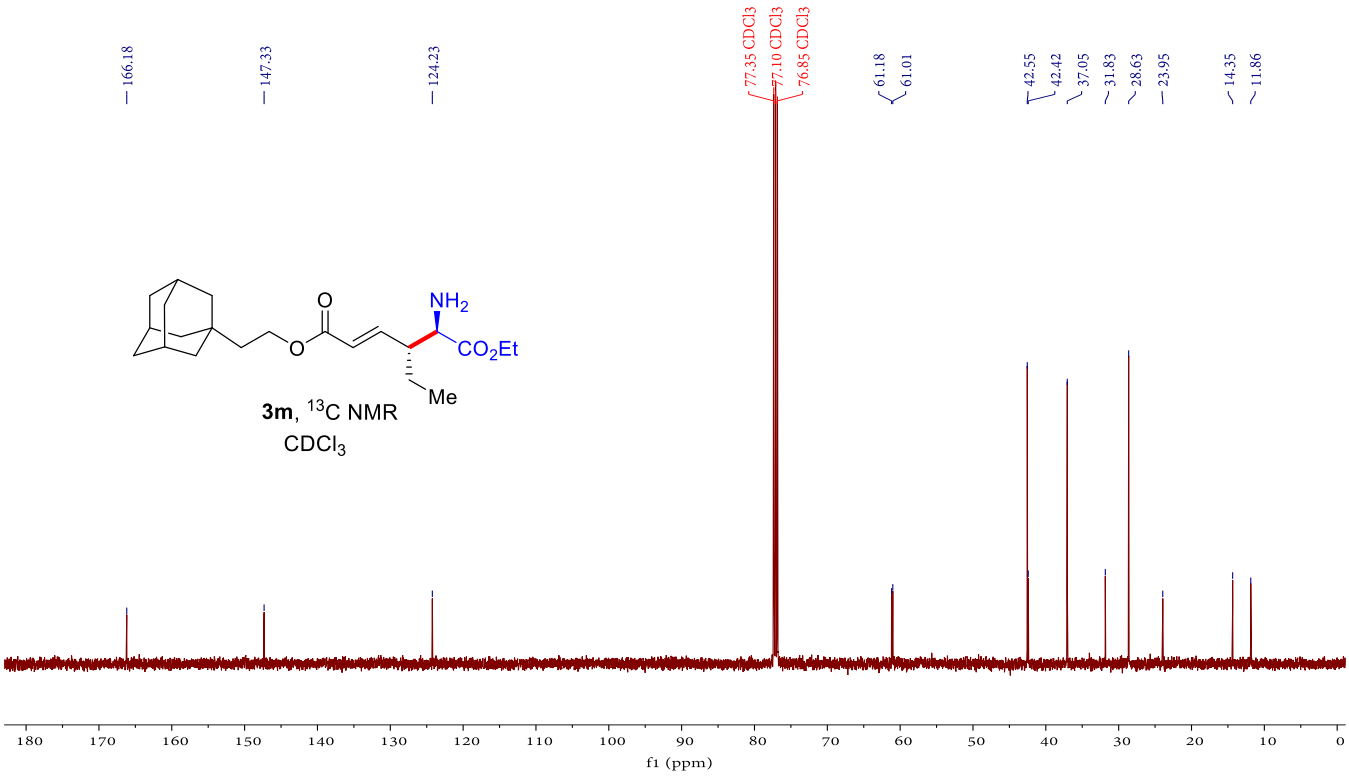
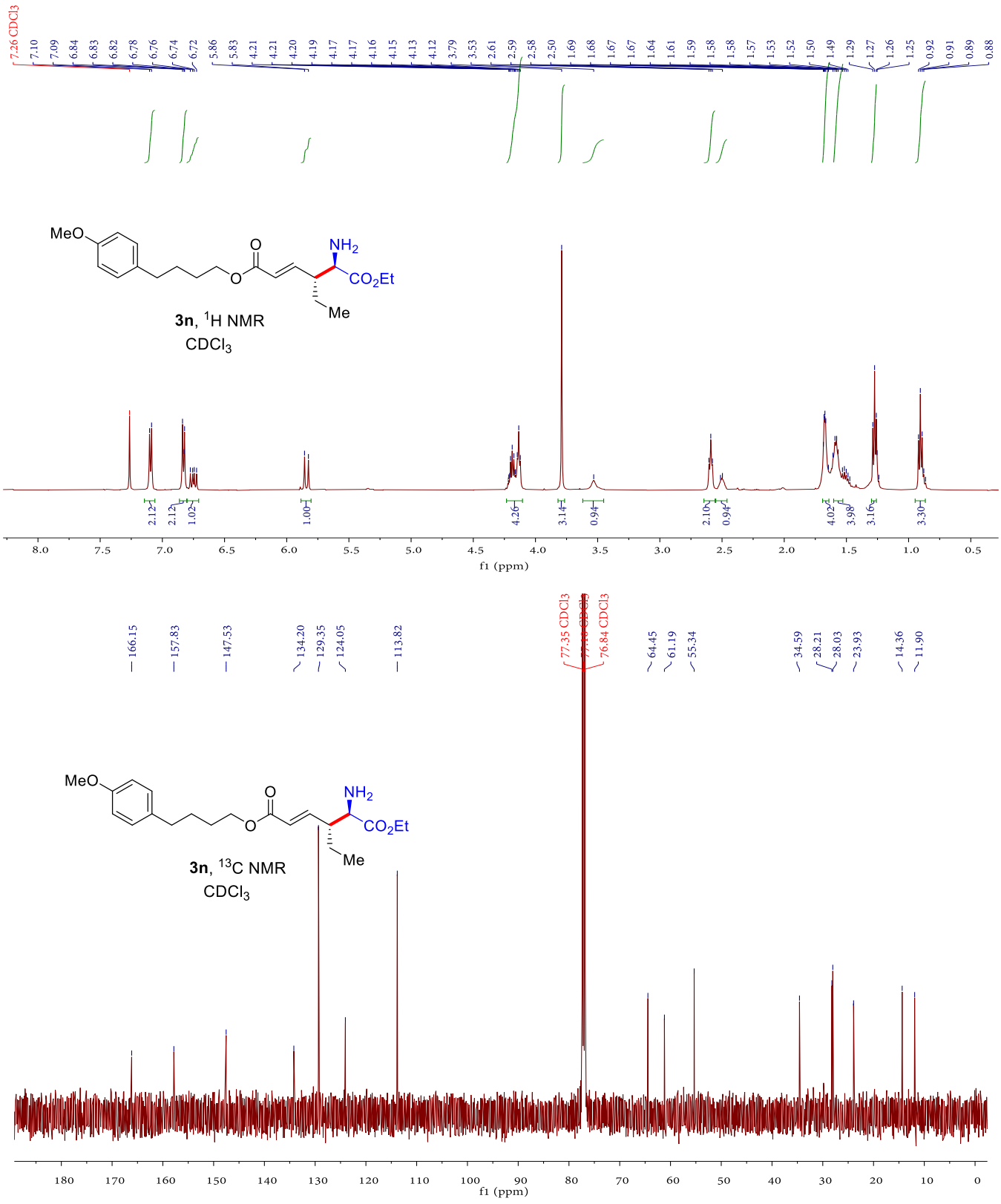
6.72 6.70 5.84 5.80 4.20 4.20 4.19 4.18 4.18 4.17 4.17 4.15 4.14 1.95 1.94 1.93 1.91 1.90 1.72 1.71 1.70 1.69 1.68 1.64 1.64 1.63 1.62 1.60 1.58 1.57 1.55 1.53 1.52 1.49 1.46 1.44 1.42 1.36 1.35 1.32 1.29 1.27 1.25 1.24 1.10 1.09 0.91 0.90 0.88
O
O
NH2
CO2Et
Me
3m, 1H NMR
CDCl3
1.03 1.00 4.26 1.29 0.95 4.37 8.38 7.11 2.03 3.76 3.32
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


166.18
147.33
124.23
77.35 CDCl3
77.10 CDCl3
76.85 CDCl3
61.18
61.01
42.55
42.42
37.05
31.83
28.63
23.95
14.35
11.86
O
O
NH2
CO2Et
Me
3m, 13C NMR
CDCl3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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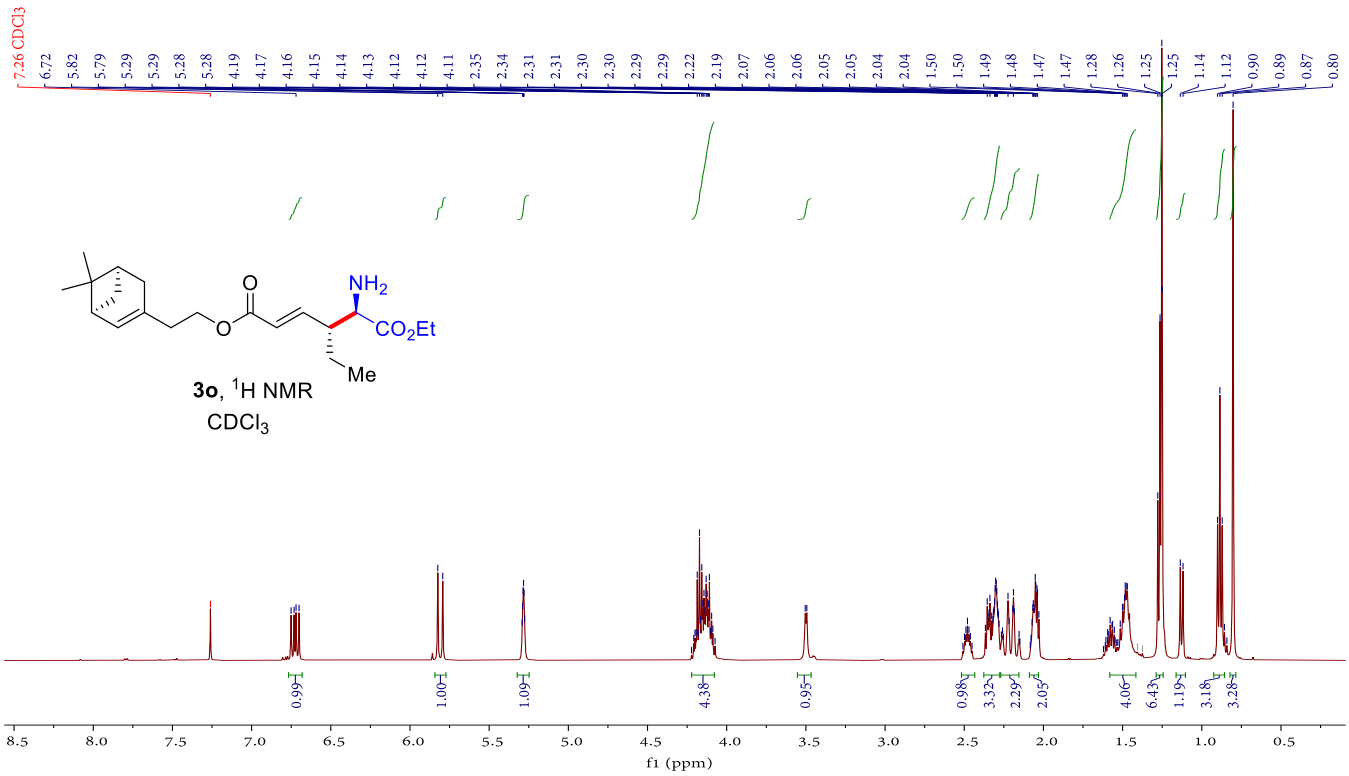
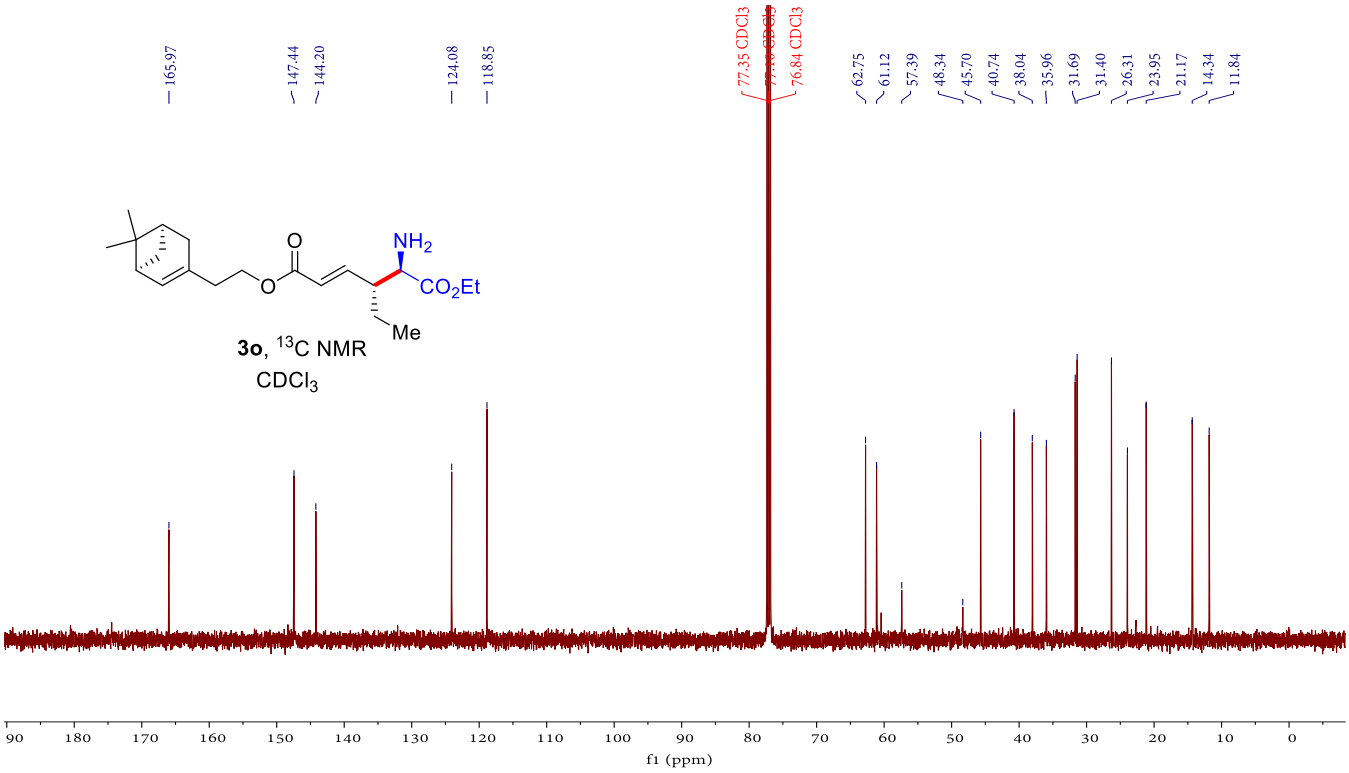
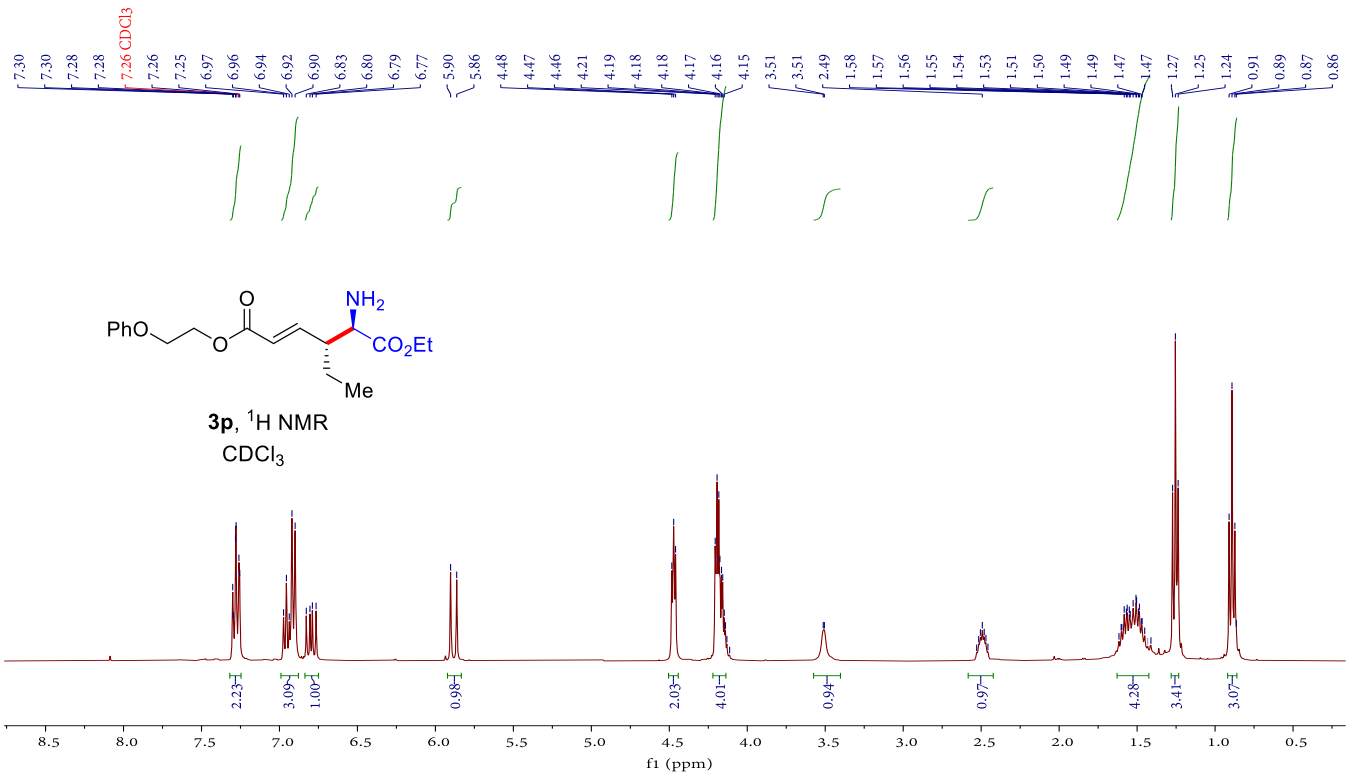
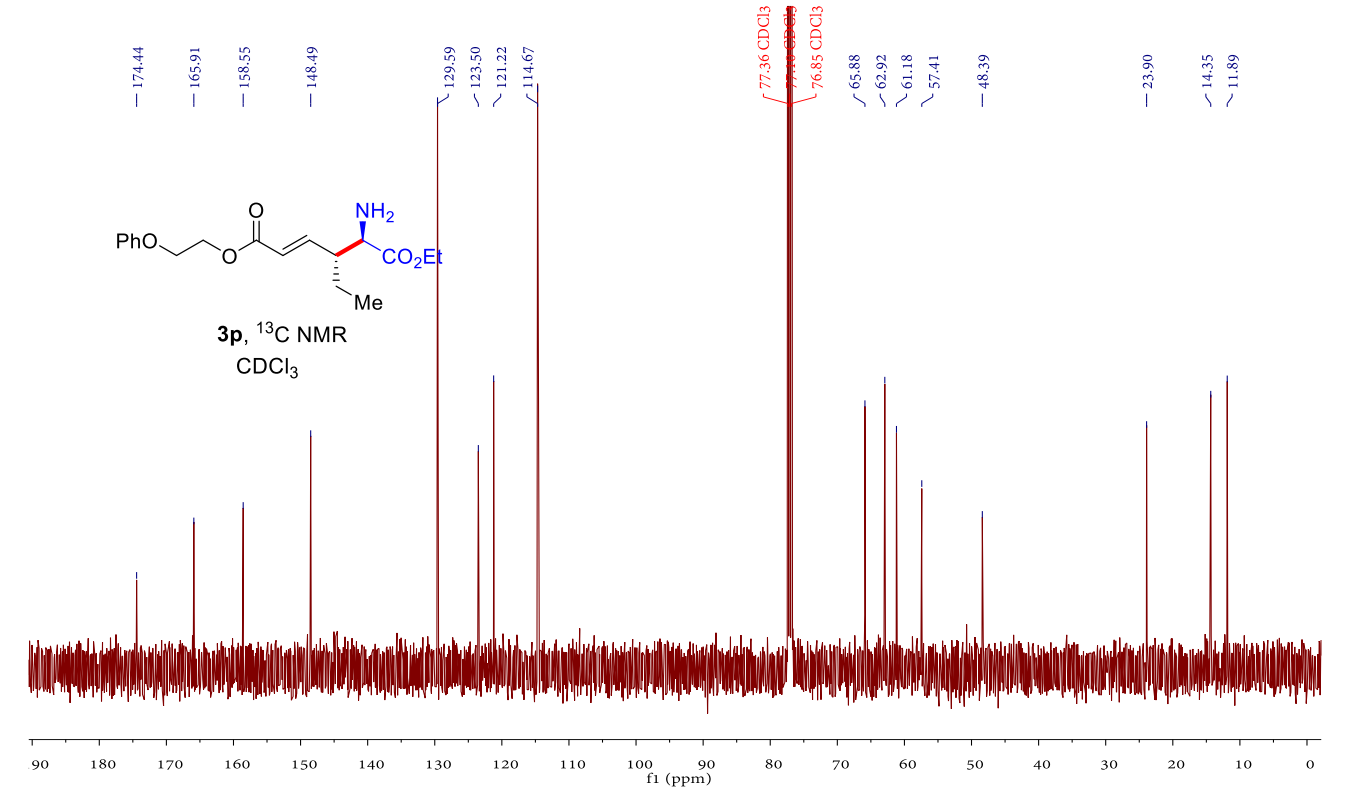
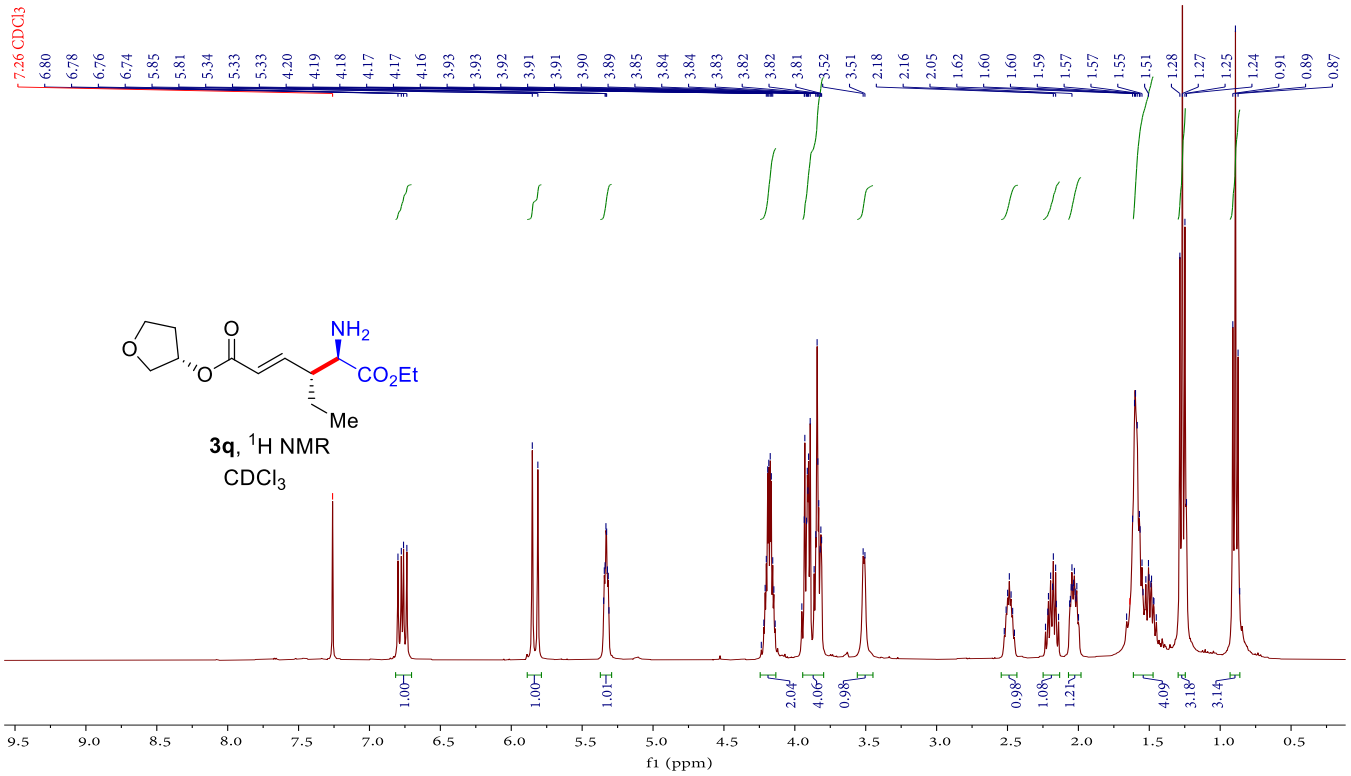
7.10
7.09
6.84
6.83
6.82
6.78
6.76
6.74
6.72
5.86
5.83
4.21
4.21
4.20
4.19
4.17
4.17
4.16
4.15
4.13
4.12
3.79
3.53
2.61
2.59
2.58
2.50
1.69
1.68
1.67
1.67
1.64
1.61
1.59
1.58
1.58
1.57
1.53
1.52
1.50
1.49
1.29
1.27
1.26
1.25
0.92
0.91
0.89
0.88
MeO
O
O
NH2
CO2Et
Me
3n, 1H NMR
CDCl3
2.12
2.12
1.02
1.00
4.26
3.14
0.94
2.10
0.94
4.02
3.98
3.16
3.30
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
166.15
157.83
147.53
134.20
129.35
124.05
113.82
77.35 CDCl3
76.84 CDCl3
64.45
61.19
55.34
34.59
28.21
28.03
23.93
14.36
11.90
MeO
O
O
NH2
CO2Et
Me
3n, 13C NMR
CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

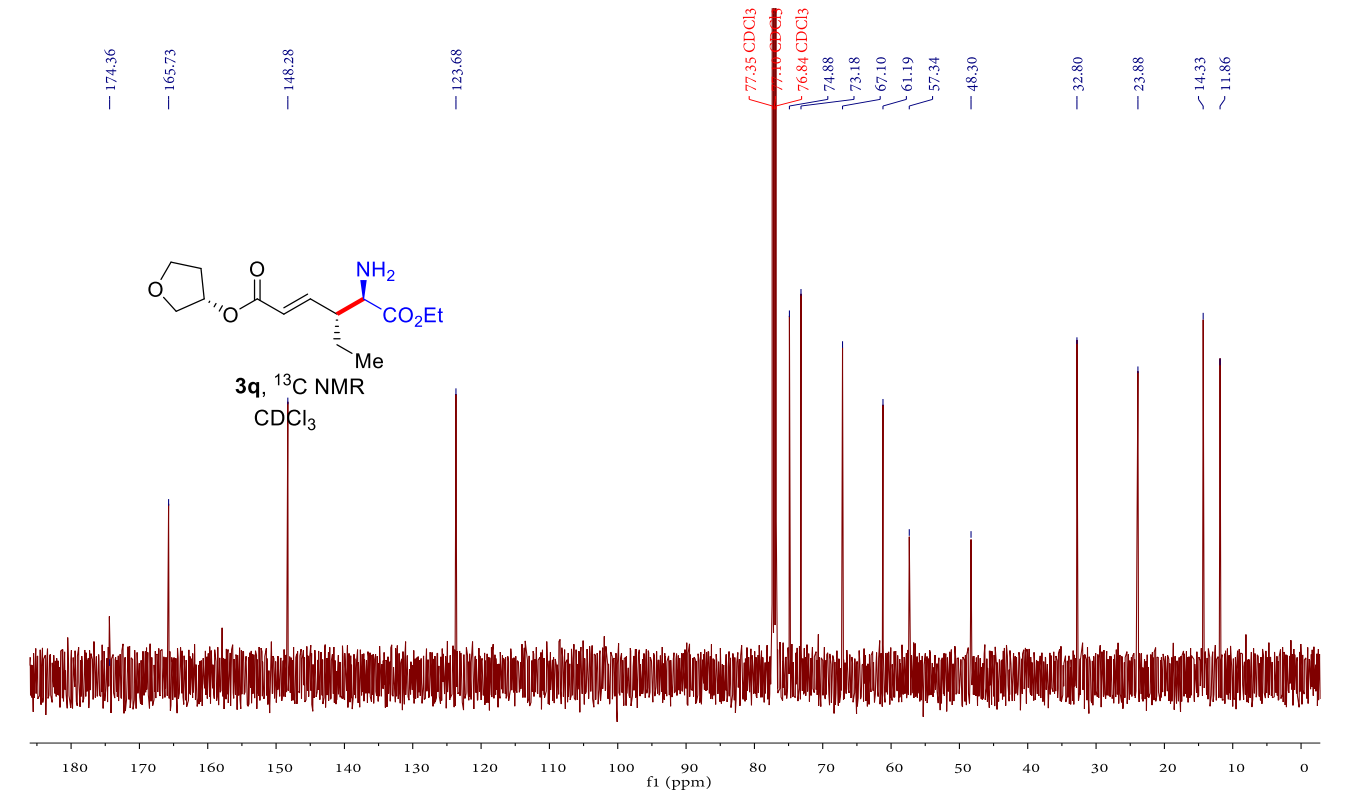

7.26 CDCl3
6.72
5.82
5.79
5.29
5.29
5.28
5.28
4.19
4.17
4.16
4.15
4.14
4.13
4.12
4.12
4.11
2.35
2.34
2.31
2.31
2.30
2.30
2.29
2.29
2.22
2.19
2.07
2.06
2.06
2.05
2.05
2.04
2.04
1.50
1.50
1.49
1.48
1.47
1.47
1.28
1.26
1.25
1.25
1.14
1.12
0.90
0.89
0.87
0.80
O
O
NH2
CO2Et
Me
3o, 1H NMR
CDCl3
0.99
1.00
1.09
4.38
0.95
0.98
3.32
2.29
2.05
4.06
6.43
1.19
3.18
3.28
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
f1 (ppm)

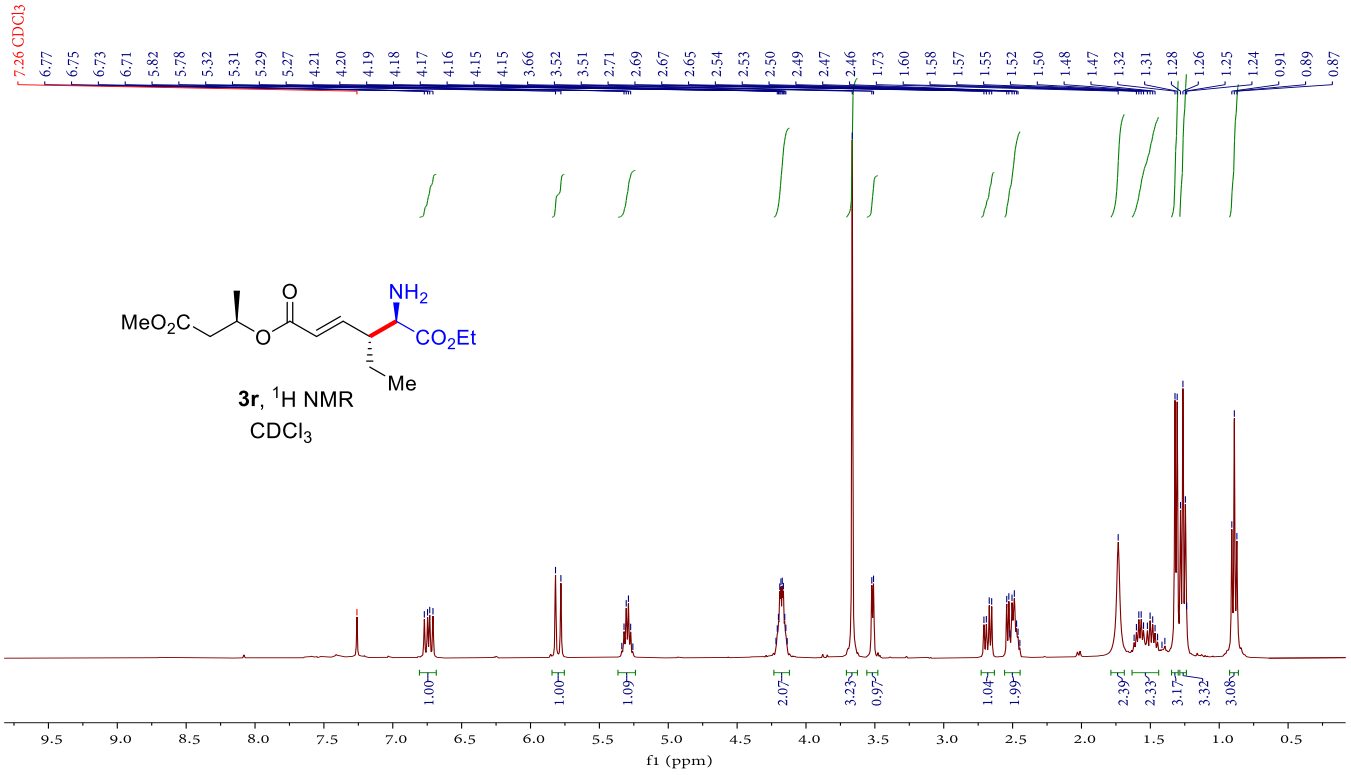

165.97
147.44
144.20
124.08
118.85
77.35 CDCl3
77.16 CDCl3
76.84 CDCl3
62.75
61.12
57.39
48.34
45.70
40.74
38.04
35.96
31.69
31.40
26.31
23.95
21.17
14.34
11.84
O
O
NH2
CO2Et
Me
3o, 13C NMR
CDCl3
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

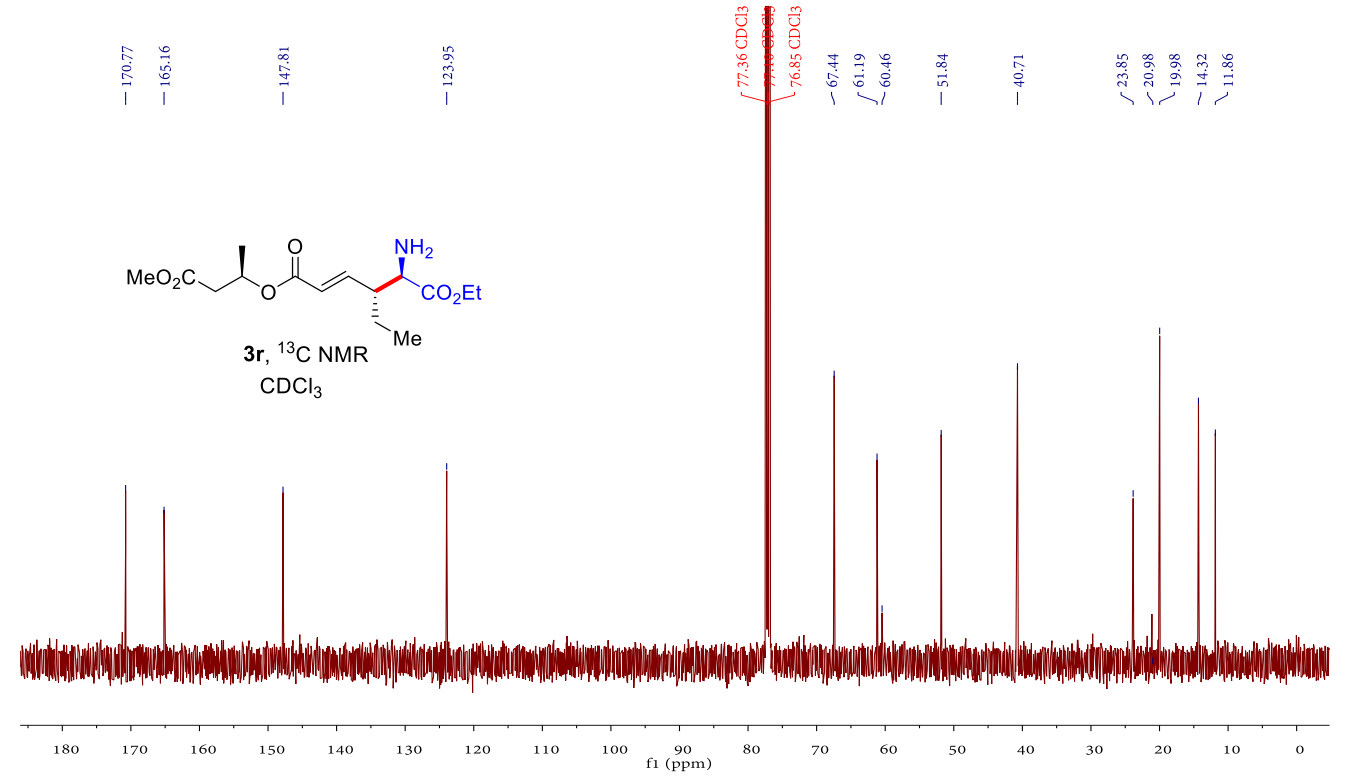

7.30 7.30 7.28 7.28 7.26 CDCl3 7.26 7.25 6.97 6.96 6.94 6.92 6.90 6.83 6.80 6.79 6.77 5.90 5.86 4.48 4.47 4.46 4.21 4.19 4.18 4.18 4.17 4.16 4.15 3.51 3.51 2.49 1.58 1.57 1.56 1.55 1.54 1.53 1.51 1.50 1.49 1.49 1.47 1.47 1.27 1.25 1.24 0.91 0.89 0.87 0.86
PhO
O
O
NH2
CO2Et
Me
3p, 1H NMR
CDCl3
2.23 3.09 1.00 0.98 2.03 4.01 0.94 0.97 4.28 3.41 3.07
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

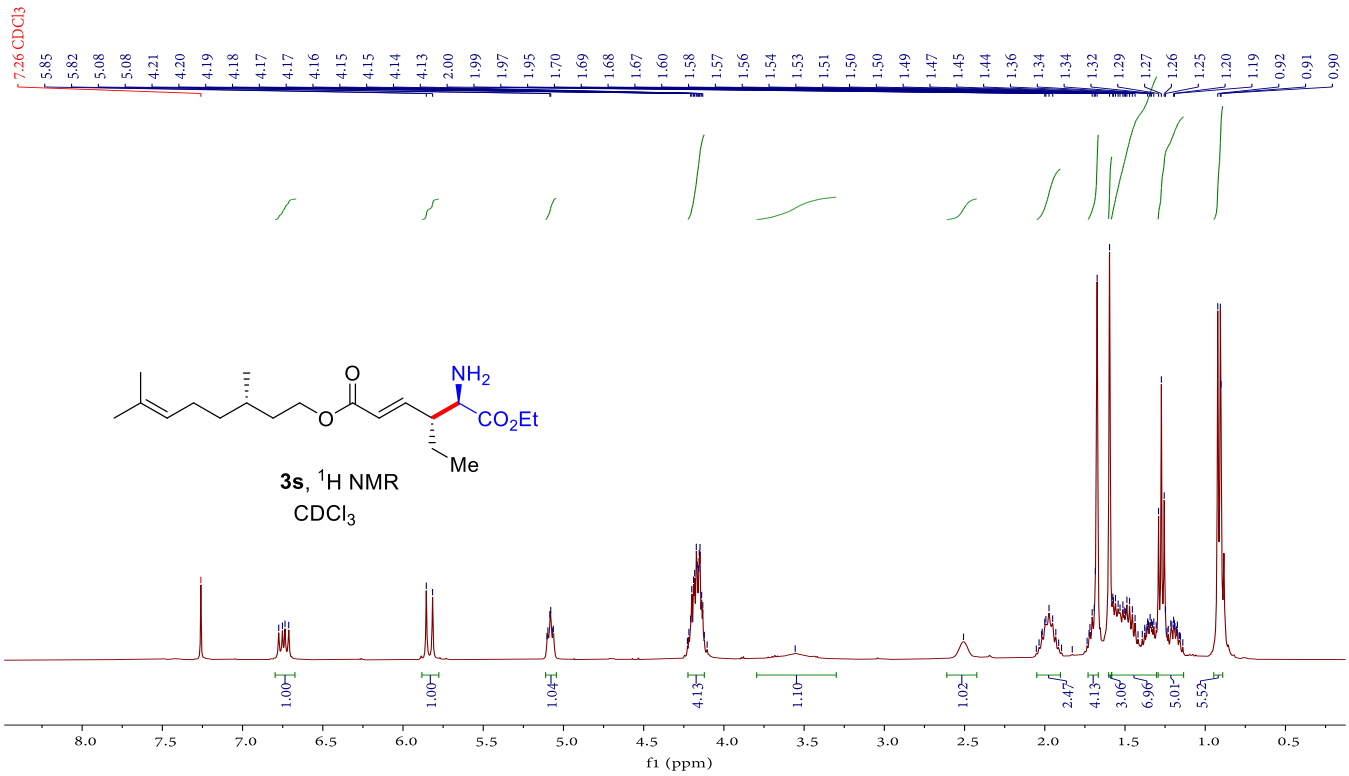

174.44 165.91 158.55 148.49 129.59 123.50 121.22 114.67 77.36 CDCl3 76.85 CDCl3 65.88 62.92 61.18 57.41 48.39 23.90 14.35 11.89
PhO
O
O
NH2
CO2Et
Me
3p, 13C NMR
CDCl3
90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

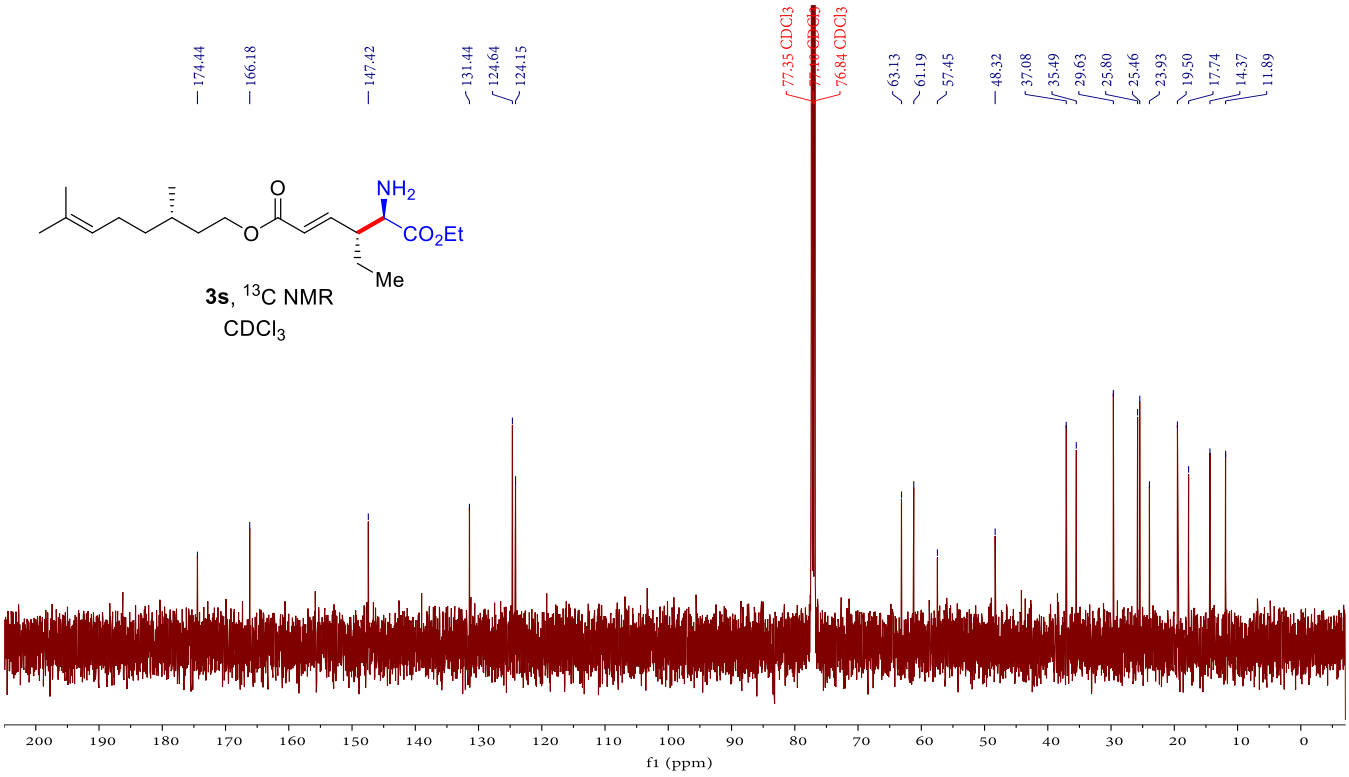

7.26 CDCl3
6.80 6.78 6.76 6.74 5.85 5.81 5.34 5.33 5.33 4.20 4.19 4.18 4.17 4.17 4.16 3.93 3.93 3.92 3.91 3.91 3.90 3.89 3.85 3.84 3.84 3.83 3.82 3.82 3.81 3.52 3.51 2.18 2.16 2.05 1.62 1.60 1.60 1.59 1.57 1.57 1.55 1.51 1.28 1.27 1.25 1.24 0.91 0.89 0.87
NH2
CO2Et
Me
3q, 1H NMR
CDCl3
1.00 1.00 1.01 2.04 4.06 0.98 0.98 1.08 1.21 4.09 3.18 3.14
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
f1 (ppm)

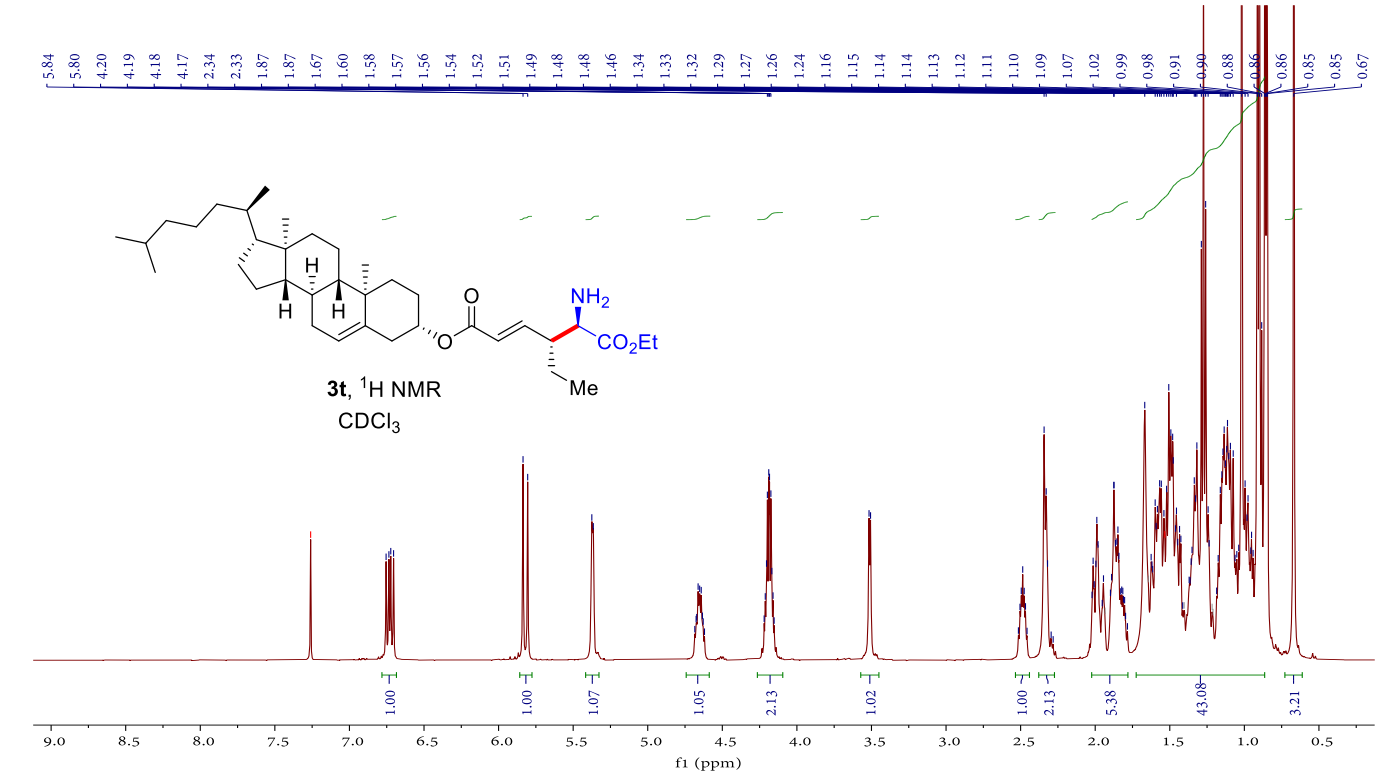

174.36
165.73
148.28
123.68
77.35 CDCl3
76.84 CDCl3
74.88
73.18
67.10
61.19
57.34
48.30
32.80
23.88
14.33
11.86
NH2
CO2Et
Me
3q, 13C NMR
CDCl3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

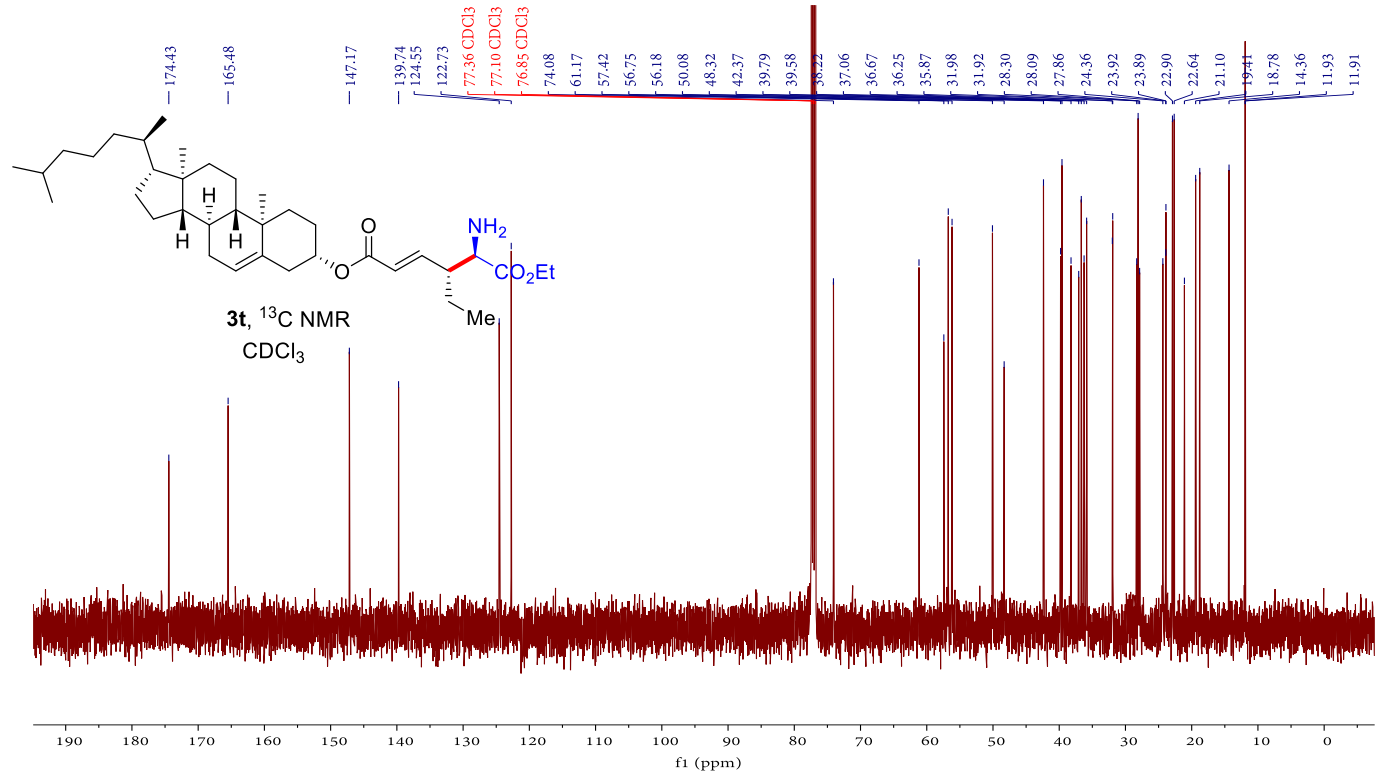

7.26 CDCl3
6.77
6.75
6.73
6.71
5.82
5.78
5.32
5.31
5.29
5.27
4.21
4.20
4.19
4.18
4.17
4.16
4.15
4.15
3.66
3.52
3.51
2.71
2.69
2.67
2.65
2.54
2.53
2.50
2.49
2.47
2.46
1.73
1.60
1.58
1.57
1.55
1.52
1.50
1.48
1.47
1.32
1.31
1.28
1.26
1.25
1.24
0.91
0.89
0.87
MeO2C
O
O
NH2
CO2Et
Me
3r, 1H NMR
CDCl3
1.00
1.00
1.09
2.07
3.23
0.97
1.04
1.99
2.39
2.33
3.17
3.32
3.08
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
f1 (ppm)

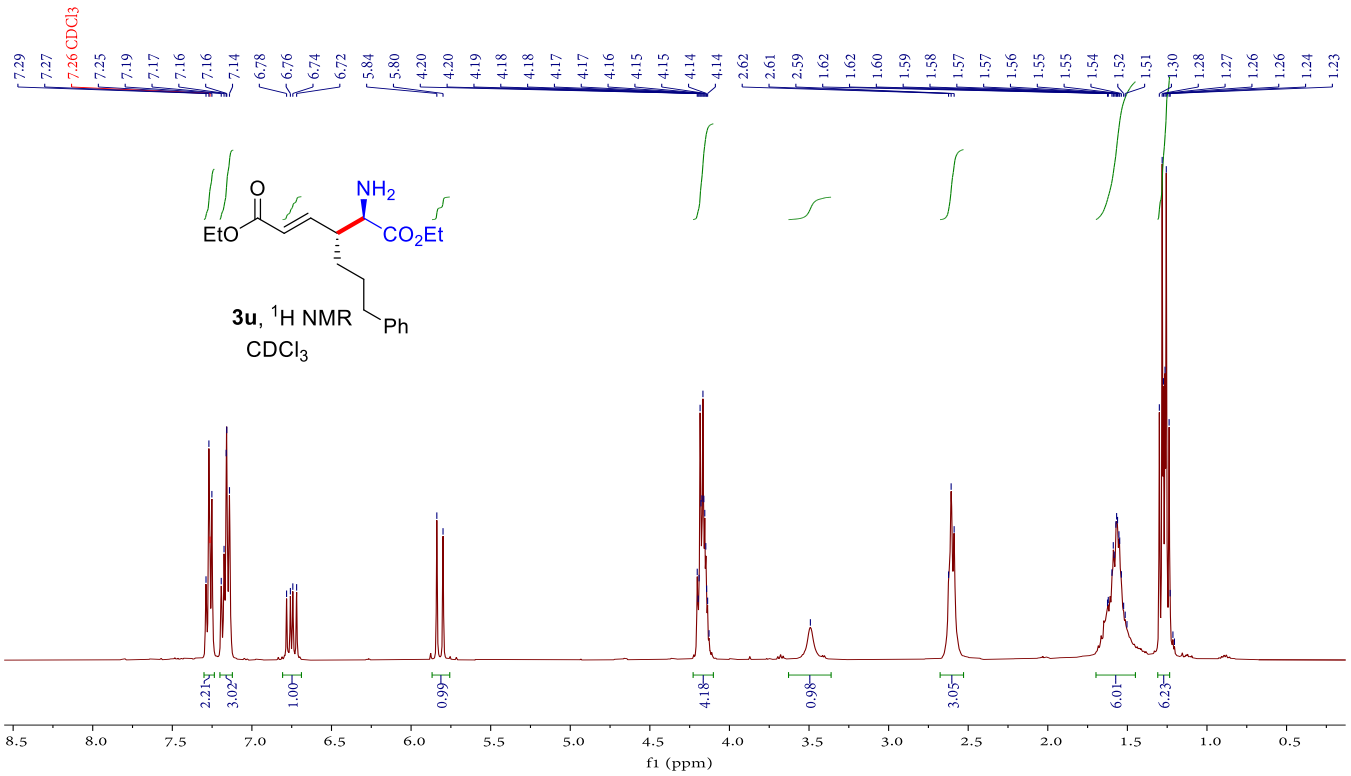

170.77
165.16
147.81
123.95
77.36 CDCl3
76.85 CDCl3
67.44
61.19
60.46
51.84
40.71
23.85
20.98
19.98
14.32
11.86
MeO2C
O
O
NH2
CO2Et
Me
3r, 13C NMR
CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

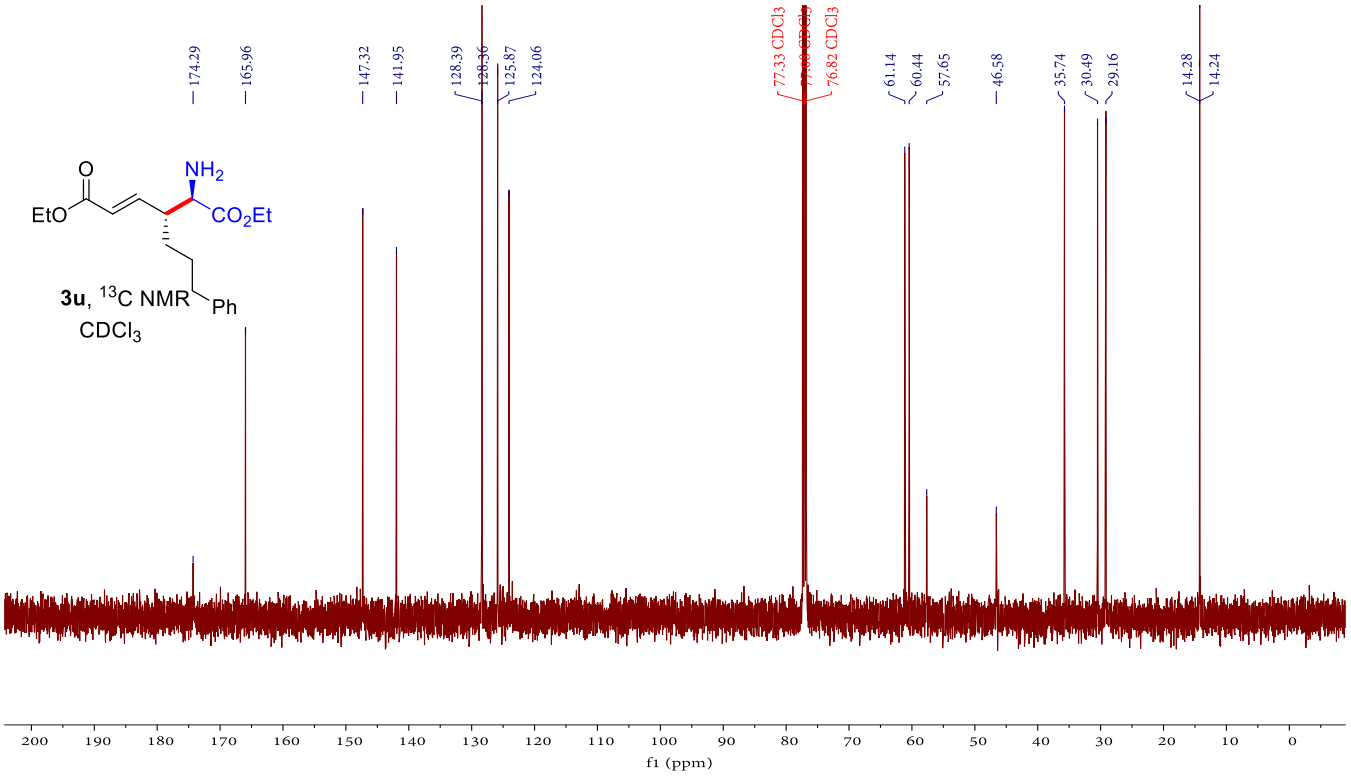

7.26 CDCl3
5.85 5.82 5.08 5.08 4.21 4.20 4.19 4.18 4.17 4.17 4.16 4.15 4.15 4.14 4.13 2.00 1.99 1.97 1.95 1.70 1.69 1.68 1.67 1.60 1.58 1.57 1.56 1.54 1.53 1.51 1.50 1.50 1.49 1.47 1.45 1.44 1.36 1.34 1.34 1.32 1.29 1.27 1.26 1.25 1.20 1.19 0.92 0.91 0.90
NH2
CO2Et
O
O
Me
3s, 1H NMR
CDCl3
1.00 1.00 1.04 4.13 1.10 1.02 2.47 4.13 3.06 6.96 5.01 5.52
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
f1 (ppm)

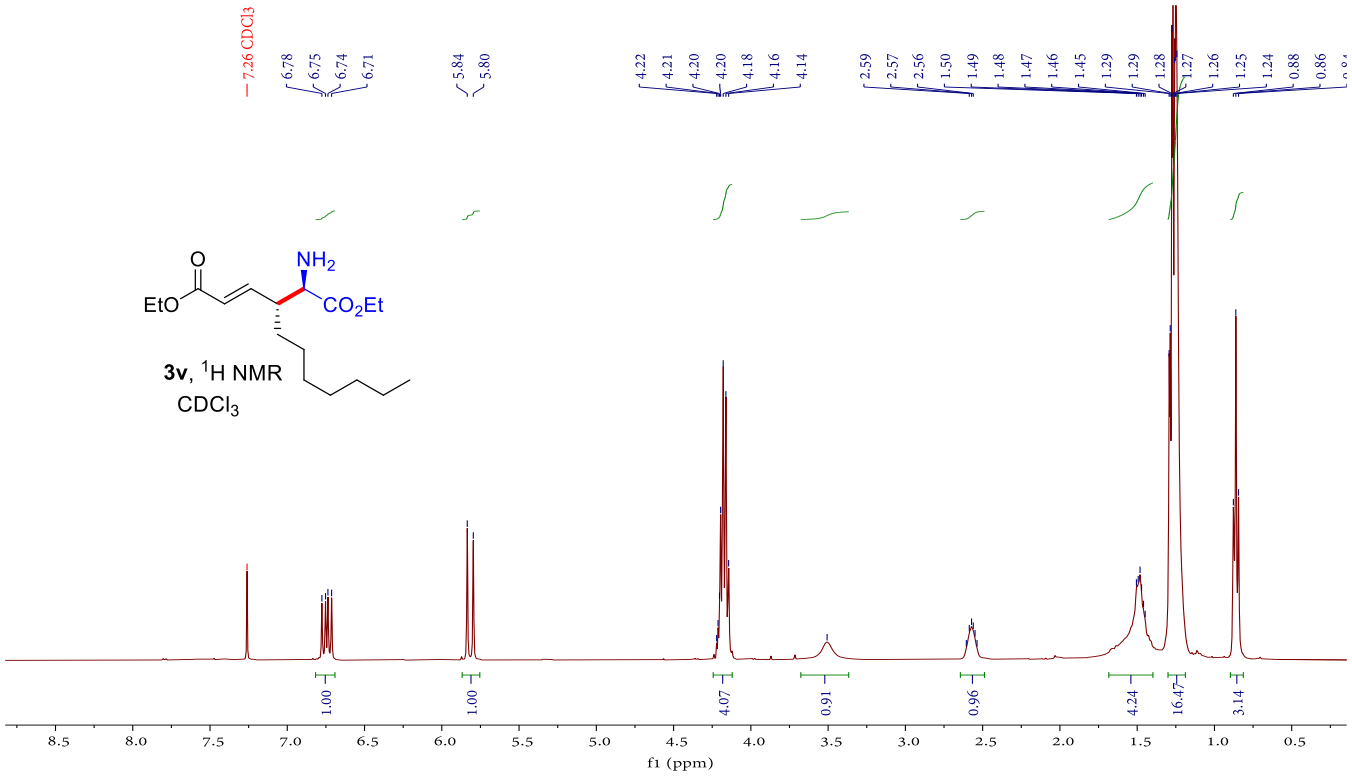

174.44 166.18 147.42 131.44 124.64 124.15
77.35 CDCl3
76.84 CDCl3
63.13 61.19 57.45 48.32 37.08 35.49 29.63 25.80 25.46 23.93 19.50 17.74 14.37 11.89
NH2
CO2Et
O
O
Me
3s, 13C NMR
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

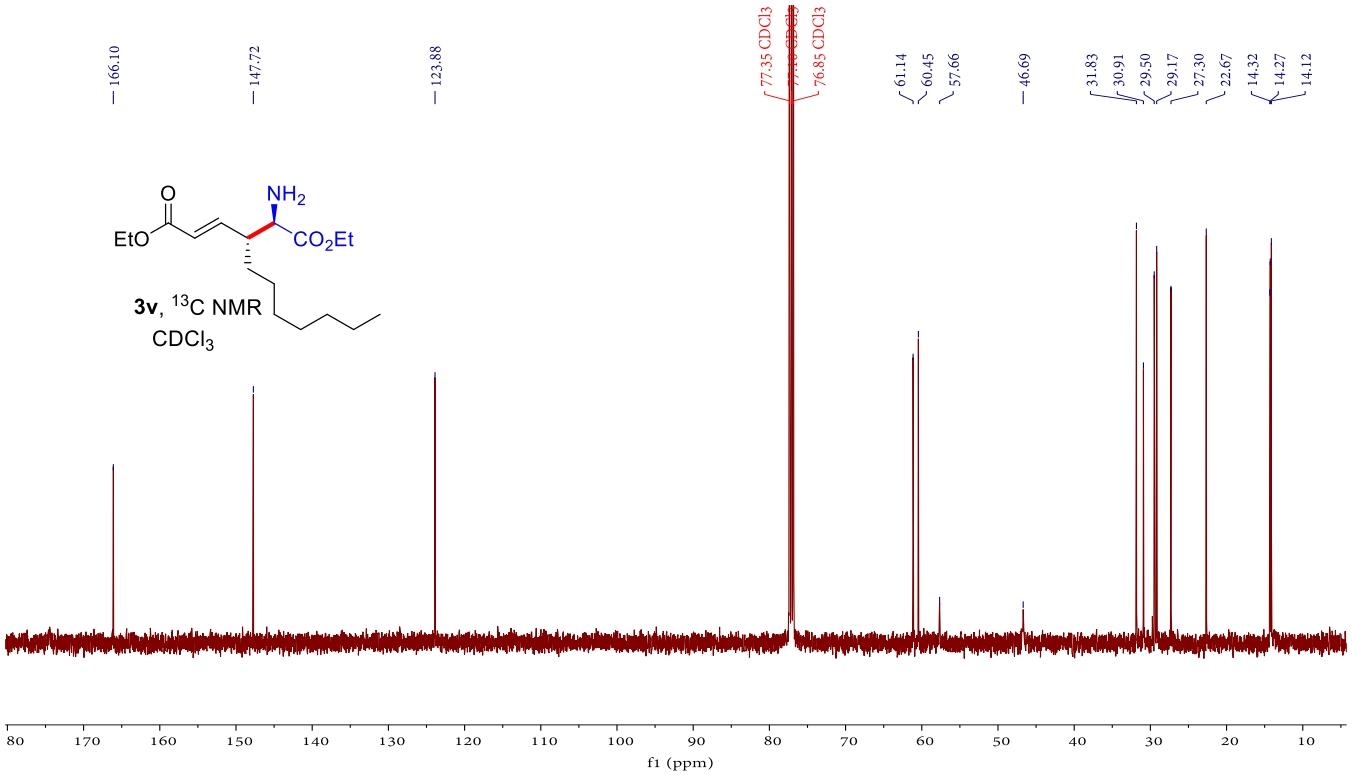

3t, 1H NMR
CDCl3
f1 (ppm)

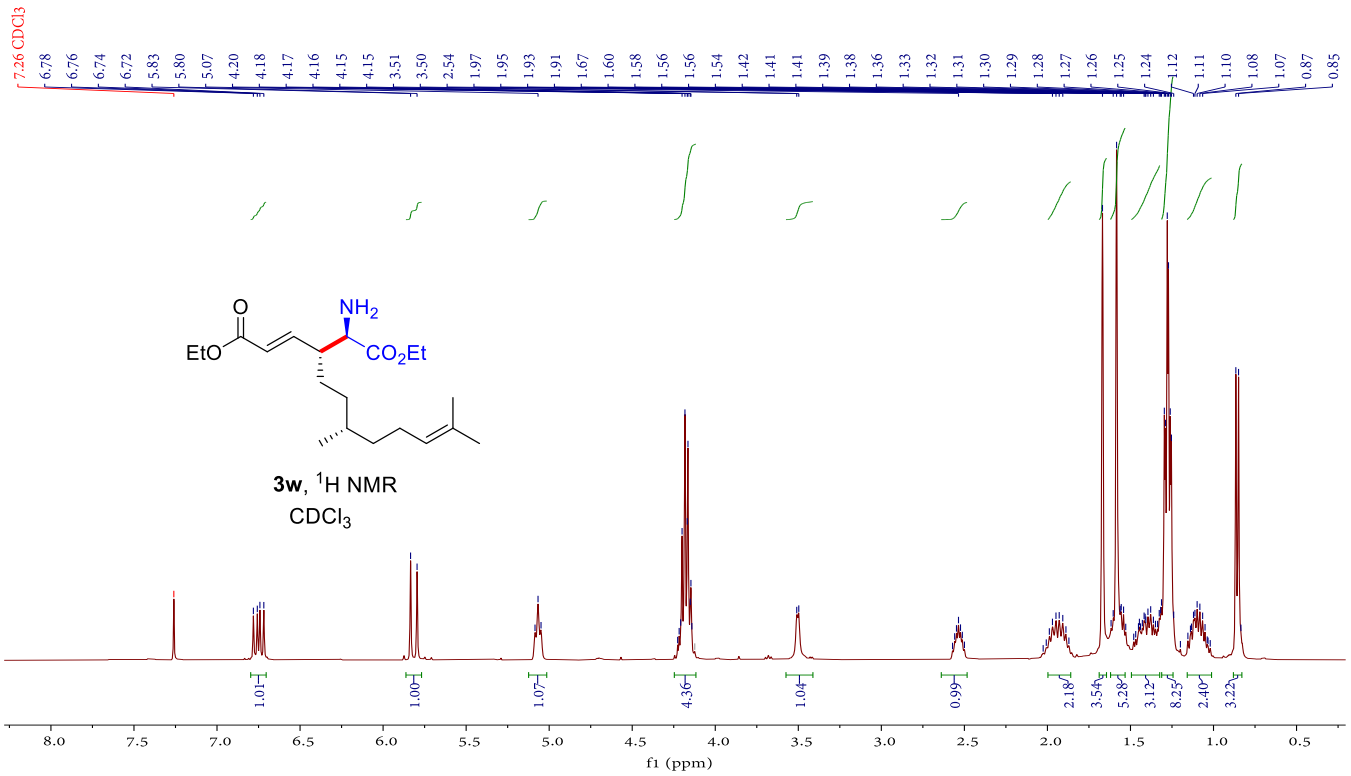

3t, 13C NMR
CDCl3
f1 (ppm)

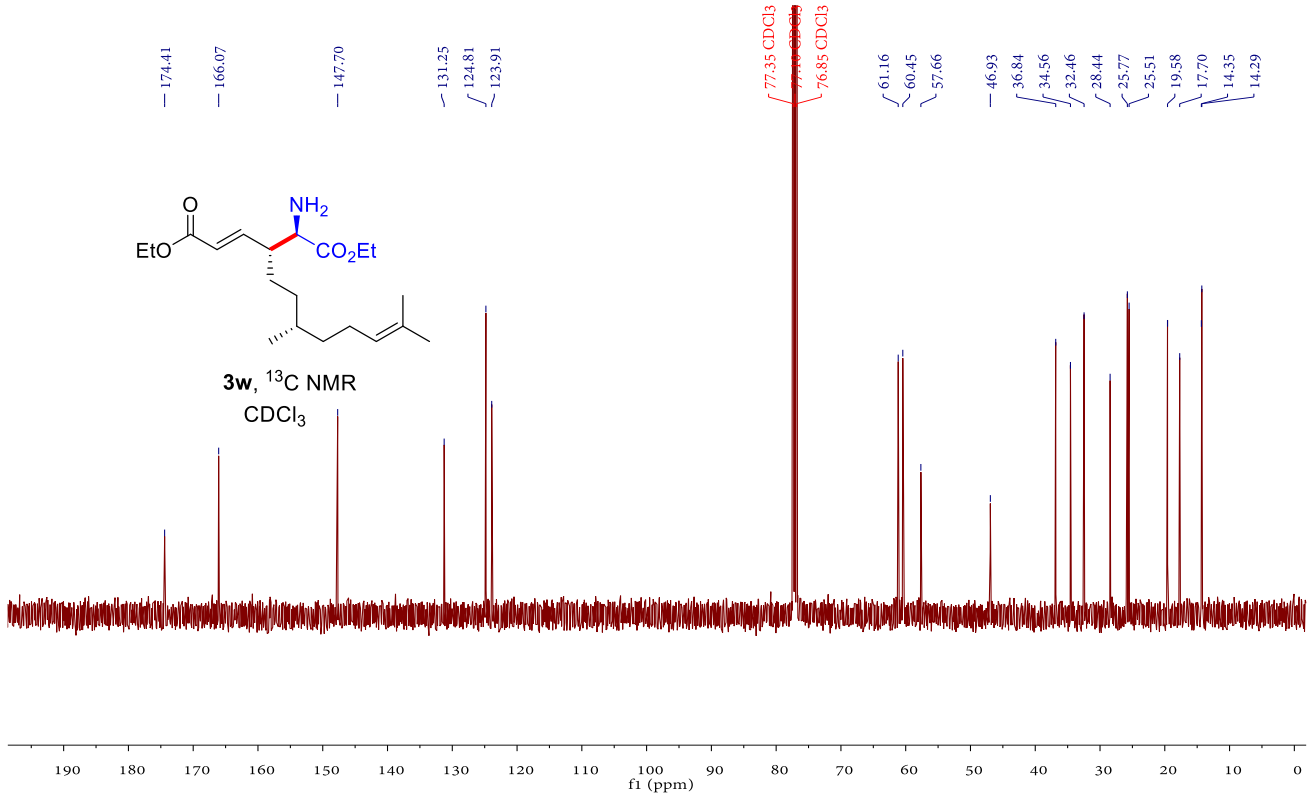

7.29 7.27 7.26 CDCl3 7.25 7.19 7.17 7.16 7.16 7.14 6.78 6.76 6.74 6.72 5.84 5.80 4.20 4.20 4.19 4.18 4.18 4.17 4.17 4.16 4.15 4.15 4.14 4.14 2.62 2.61 2.59 1.62 1.62 1.60 1.59 1.58 1.57 1.57 1.56 1.55 1.55 1.54 1.52 1.51 1.30 1.28 1.27 1.26 1.26 1.24 1.23
NH2
O
EtO
CO2Et
Ph
3u, 1H NMR
CDCl3
2.21 3.02 1.00 0.99 4.18 0.98 3.05 6.01 6.23
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
f1 (ppm)

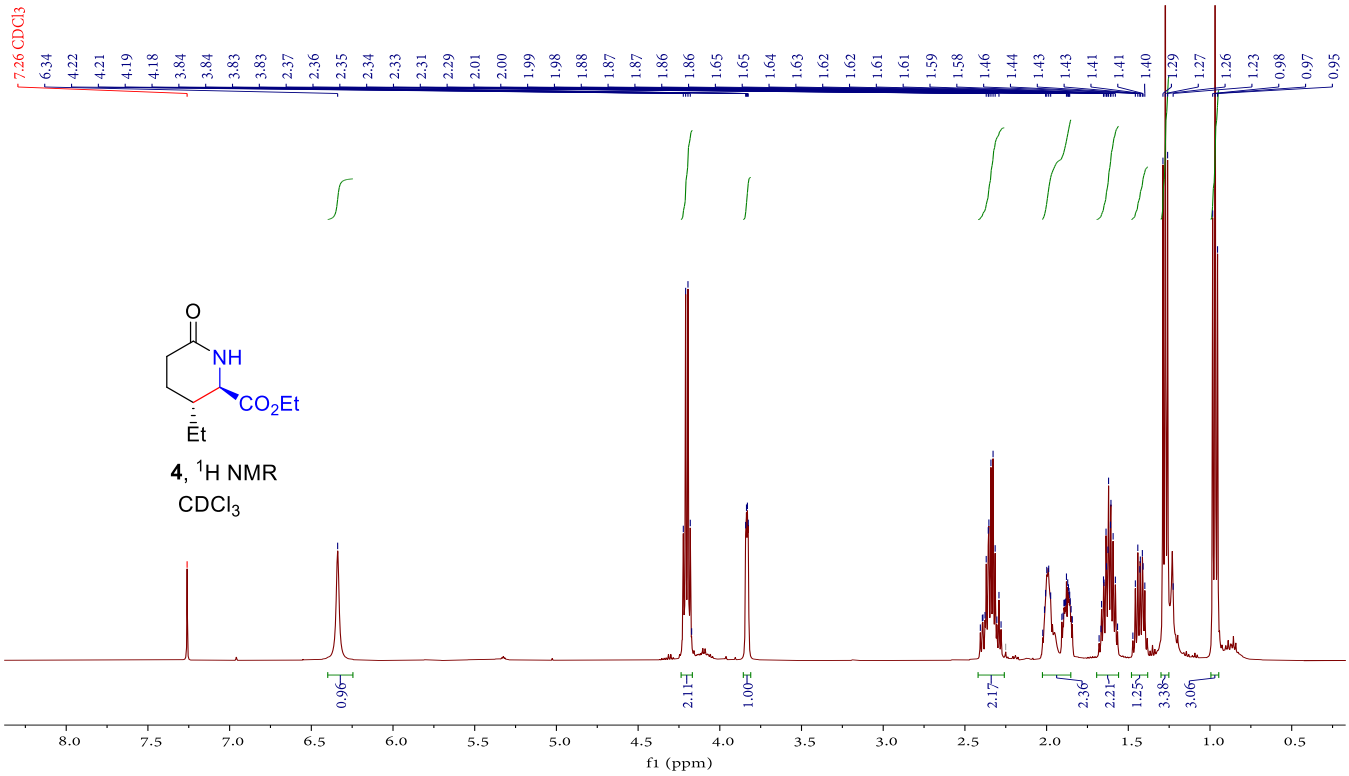

174.29 165.96 147.32 141.95 128.39 128.36 125.87 124.06 77.33 CDCl3 77.08 CDCl3 76.82 CDCl3 61.14 60.44 57.65 46.58 35.74 30.49 29.16 14.28 14.24
NH2
O
EtO
CO2Et
Ph
3u, 13C NMR
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

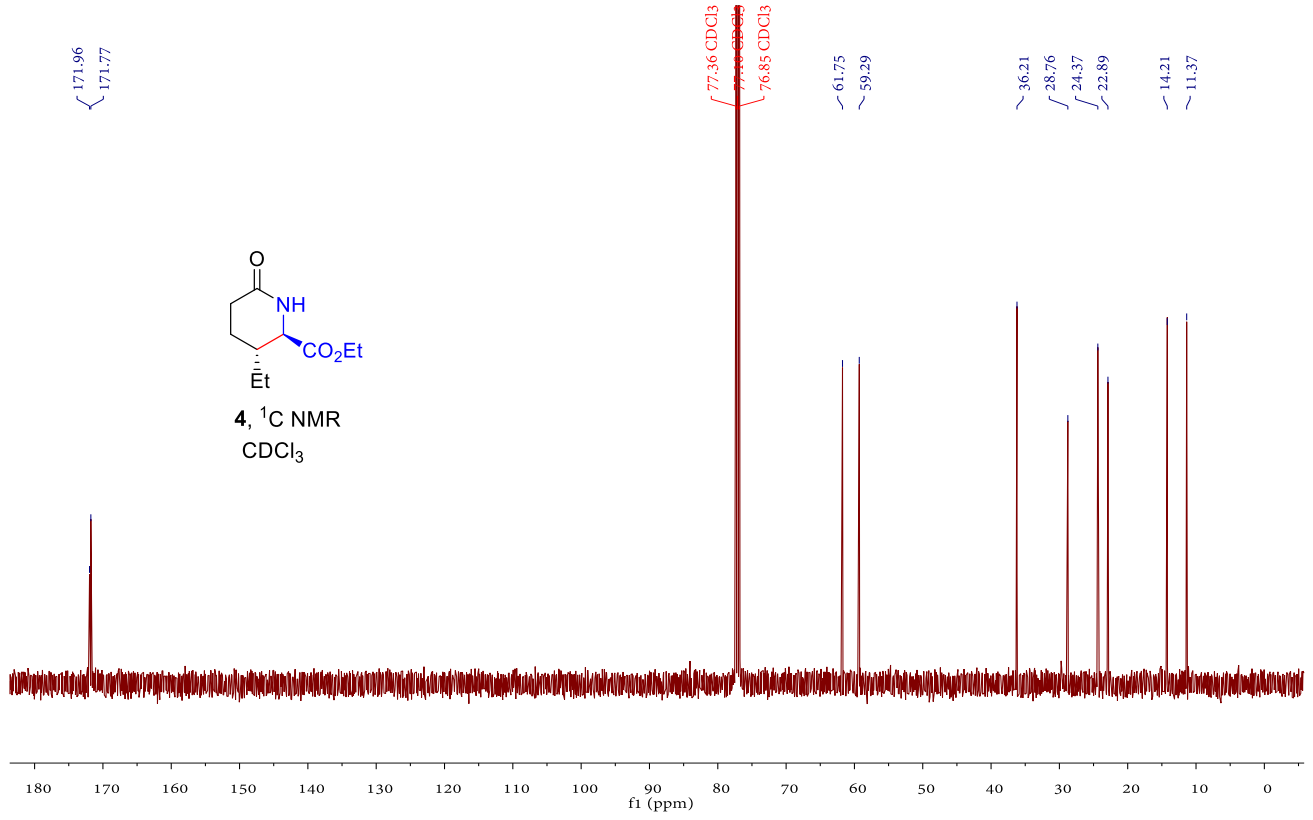

7.26 CDCl3
6.78
6.75
6.74
6.71
5.84
5.80
4.22
4.21
4.20
4.20
4.18
4.16
4.14
2.59
2.57
2.56
1.50
1.49
1.48
1.47
1.46
1.45
1.29
1.29
1.28
1.27
1.26
1.25
1.24
0.88
0.86
O
NH2
EtO
CO2Et
3v, 1H NMR
CDCl3
1.00
1.00
4.07
0.91
0.96
4.24
16.47
3.14
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

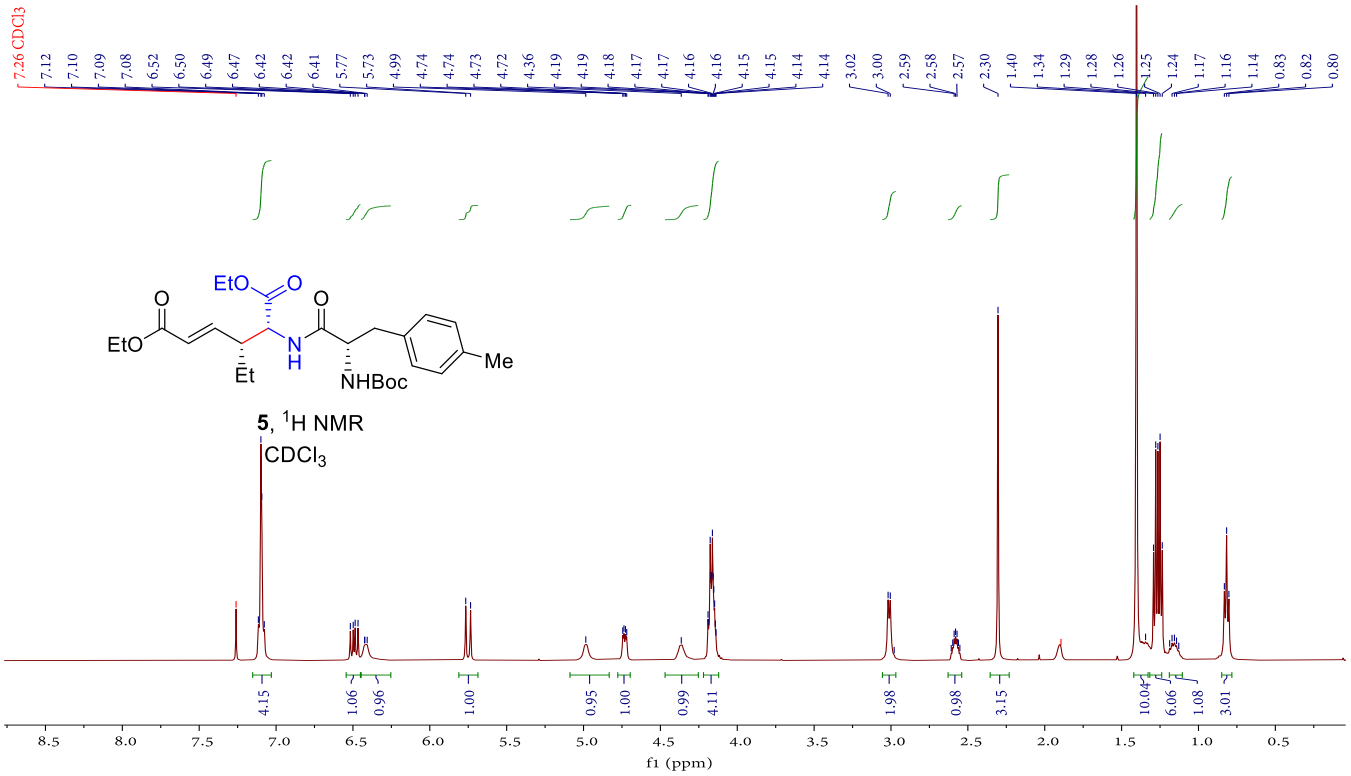

166.10
147.72
123.88
77.35 CDCl3
77.10 CDCl3
76.85 CDCl3
61.14
60.45
57.66
46.69
31.83
30.91
29.50
29.17
27.30
22.67
14.32
14.27
14.12
O
NH2
EtO
CO2Et
3v, 13C NMR
CDCl3
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

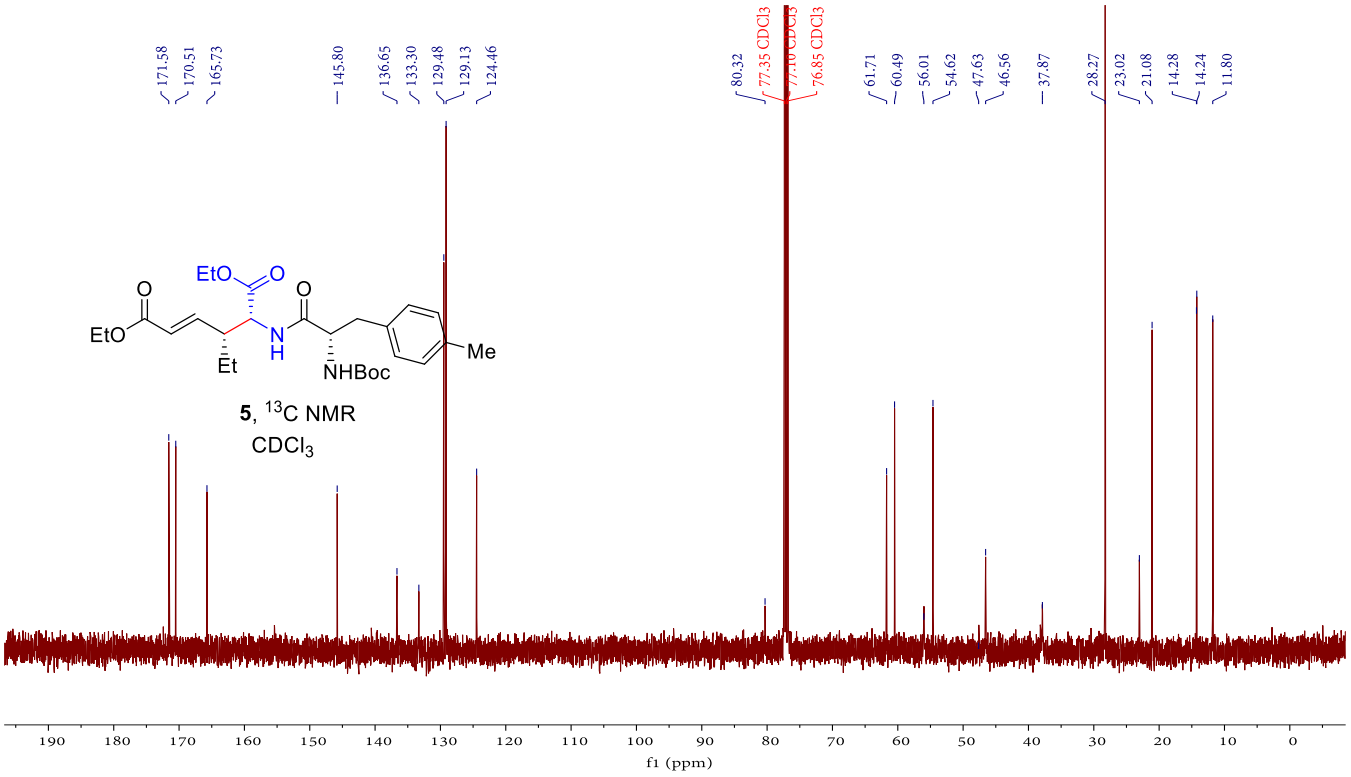

7.26 CDCl3
O
NH2
EtO
CO2Et
3w, 1H NMR
CDCl3
f1 (ppm)


174.41
166.07
147.70
131.25
124.81
123.91
77.35 CDCl3
76.85 CDCl3
61.16
60.45
57.66
46.93
36.84
34.56
32.46
28.44
25.77
25.51
19.58
17.70
14.35
14.29
O
NH2
EtO
CO2Et
3w, 13C NMR
CDCl3
f1 (ppm)


7.26 CDCl3
6.34
4.22
4.21
4.19
4.18
3.84
3.84
3.83
3.83
2.37
2.36
2.35
2.34
2.33
2.31
2.29
2.01
2.00
1.99
1.98
1.88
1.87
1.87
1.86
1.86
1.65
1.65
1.64
1.63
1.62
1.62
1.61
1.61
1.59
1.58
1.46
1.44
1.43
1.43
1.41
1.41
1.40
1.29
1.27
1.26
1.23
0.98
0.97
0.95
O
NH
CO2Et
Et
4, 1H NMR
CDCl3
0.96
2.11
1.00
2.17
2.36
2.21
1.25
3.38
3.06
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
f1 (ppm)


171.96
171.77
77.36 CDCl3
77.16 CDCl3
76.85 CDCl3
61.75
59.29
36.21
28.76
24.37
22.89
14.21
11.37
O
NH
CO2Et
Et
4, 1C NMR
CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.26 CDCl3
7.12 7.10 7.09 7.08 6.52 6.50 6.49 6.47 6.42 6.42 6.41 5.77 5.73 4.99 4.74 4.74 4.73 4.72 4.36 4.19 4.19 4.18 4.17 4.17 4.16 4.16 4.15 4.15 4.14 4.14 3.02 3.00 2.59 2.58 2.57 2.30 1.40 1.34 1.29 1.28 1.26 1.25 1.24 1.17 1.16 1.14 0.83 0.82 0.80
EtO
O
O
EtO
N
H
O
Et
NHBoc
Me
5, 1H NMR
CDCl3
4.15 1.06 0.96 1.00 0.95 1.00 0.99 4.11 1.98 0.98 3.15 10.04 6.06 1.08 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
f1 (ppm)


171.58 170.51 165.73 145.80 136.65 133.30 129.48 129.13 124.46
80.32 77.35 CDCl3 76.85 CDCl3 61.71 60.49 56.01 54.62 47.63 46.56 37.87 28.27 23.02 21.08 14.28 14.24 11.80
EtO
O
O
EtO
N
H
O
Et
NHBoc
Me
5, 13C NMR
CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)