Supporting Information

Cu(I)-catalyzed asymmetric *exo*-selective synthesis of substituted pyrrolidines *via* 1,3-dipolar cycloaddition reaction

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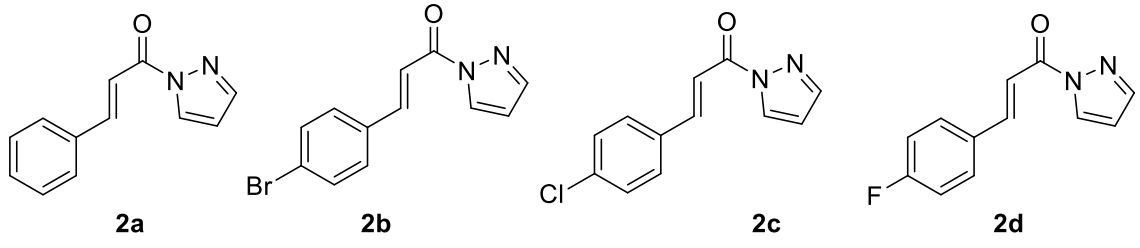
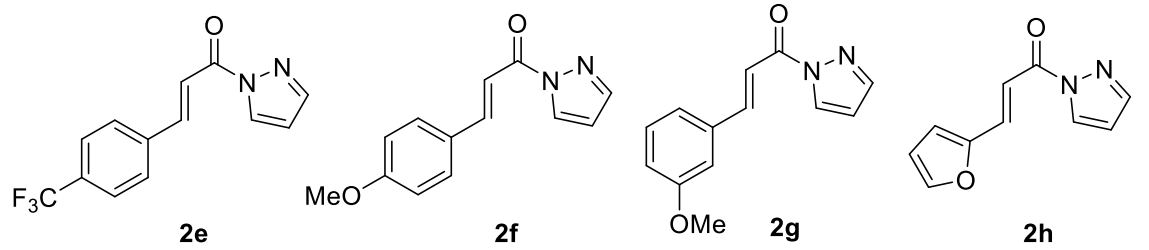
Materials andMethods:

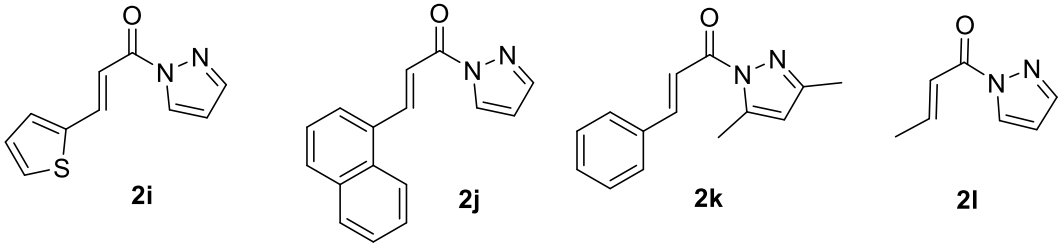
All reactions were carried out in oven dried glassware with magnetic stirring. All solventswere purified and dried according to standard methods prior to use. Starting materials α,β-unsaturated pyrazolamide **2a-l** and azomethine ylides **3b-m** were prepared by reported methods.[1,2] Catalysts **L1**-**L7** are commercially available. ^{1}H spectra were recorded on 400 MHz or 500 MHz in $CDCl_3$ and ^{13}C NMR spectra were recorded on 100 or 125 MHz in $CDCl_3$ using TMS or residual solvent signals as internal standard. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m =multiplet or unresolved, coupling constant (s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High resolution mass spectra (HRMS) were obtained by the ESI (Q-TOF) ionization sources. IR spectra were measured with PerkinElmer FT/IR Vector 22 spectrometer. Optical rotations were measured on a commercial automatic polarimeter and reported as follows: $[\alpha]_D^T$ (c = g/100 mL, solvent). Routine monitoring of reactions we reperformed using precoated silica gel TLC plates from E-Merck. All the chromatographic separations were carried out by using silica gel (Acme's, 100-200 mesh). Melting points were recorded by using a melting point apparatus and are uncorrected. The enantioselectivity was determined by chiral HPLC analysis using chiralpak AD-H. OD-H, IA, IC and ID column with a 200 UV-detector by using *iso*-propanol and *n*-hexane as eluents at 25 °C.

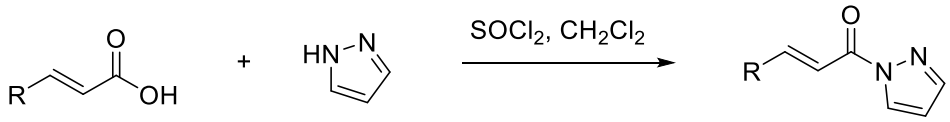
General procedure and characterization data of α,β-unsaturated pyrazolamide 2a-l:

α,β-unsaturated pyrazolamides **2a-l** were synthesiszed according to modified literature procedure.[1]

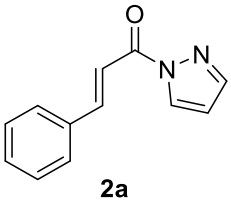






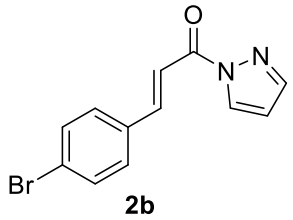


To a solution of pyrazole (5.0 g, 73.5 mmol) in CH_2Cl_2 (150 mL) was added $SOCl_2$ (8.0 mL, 110 mmol) at 0 °C, then the reaction mixture was brought to room temperature and stirred at room temperature for 1 h. *Trans*-Cinnamic acid (24.5 mmol) was added in one portion. The mixture was further stirred for additional 3 hours. The resulting solution was diluted with CH_2Cl_2 (150 mL), washed with aqueous NaOH solution (0.5 M, 3 x 100 mL), water (3 x 100 mL), then dried over Na_2SO_4. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel (*n*-hexane/CH_2Cl_2) to afford product **2a-l**.



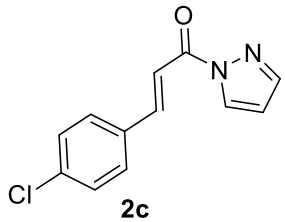
(*E*)-3-phenyl-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (2a): White solid, 6.01 g, 90% yield. **MP**: 42−45 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 2.9, 0.7 Hz, 1H), 8.06 (d, *J* = 16.0 Hz, 1H), 7.94

(d, *J* = 16.0 Hz, 1H), 7.81 (d, *J* = 1.4 Hz, 1H), 7.78 – 7.66 (m, 2H), 7.50 – 7.37 (m, 3H), 6.52 (dd, *J* = 2.8, 1.5 Hz, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 163.63, 147.88, 143.86, 134.44, 131.06, 128.98, 128.83, 128.74, 115.74, 109.86. **IR** (film) ν_{max} 3621, 3132, 1954, 1705, 1623, 1385, 1351, 935, 767 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{12}H_{10}N_2O$ [M+Na]$^+$: 221.0685. Found: 221.0700.



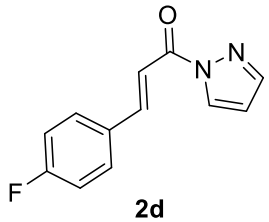
2b

(*E*)-3-(4-bromophenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (2b): White solid, 2.07 g, 75% yield. **MP**: 104-107 °C.**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 2.8 Hz, 1H), 8.01 – 7.78 (m, 2H), 7.75 (d,*J* = 1.5 Hz, 1H), 7.52 (s, 4H), 6.48 (dd, *J* = 2.8, 1.5 Hz, 1H).**^{13}C NMR** (100 MHz, Chloroform-*d*) δ 163.35, 146.28, 143.94, 133.32, 132.24, 130.11, 128.74, 125.44, 116.42, 110.00. **IR** (film) ν_{max} 3381, 2106, 1907, 1693, 1623, 1485, 1386, 1349, 819, 762 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{12}H_9BrN_2O$ [M+Na]$^+$: 298.9790. Found: 298.9795.



2c

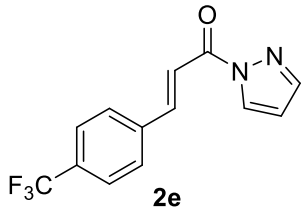
(*E*)-3-(4-chlorophenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (2c): White solid, 4.46 g, 96% yield. **MP**: 104-107 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 2.8 Hz, 1H), 8.01 – 7.80 (m, 2H), 7.76 (d, *J* = 1.4 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.43 – 7.33 (m, 2H), 6.48 (dd, *J* = 2.8, 1.5 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 163.36, 146.21, 143.93, 137.00, 132.91, 129.93, 129.27, 128.73, 116.31, 109.97, 99.99. **IR** (film) ν_{max}3138, 1695, 1623, 1386, 1349, 823, 763 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{12}H_9ClN_2O$ [M+Na]$^+$: 255.0296. Found: 255.0315.



2d

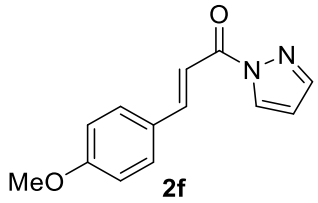
(*E*)-3-(4-fluorophenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (2d): White solid, 3.30 g, 85% yield. **MP**: 117-120 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 2.7 Hz, 1H), 7.99 (d, *J* = 16.0 Hz, 1H), 7.84 (d, *J* = 16.0 Hz, 1H), 7.79 (d, *J* = 1.5 Hz, 1H), 7.73 – 7.64 (m, 2H), 7.17 – 7.07 (m, 2H), 6.51

(dd, *J* = 2.9, 1.5 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 165.35, 163.45, 163.34, 146.40, 143.86, 130.81, 130.74, 116.25, 116.08, 115.49, 109.89. **^{19}F NMR** (470 MHz, Chloroform-*d*) δ -108.13. **IR** (film) ν_{max} 3428, 2361, 1699, 1626, 1387, 828, 745 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{12}H_9FN_2O$ [M+Na]$^+$: 239.0591. Found: 239.0583.



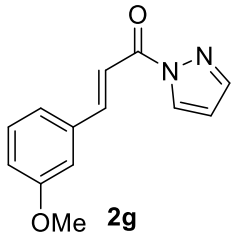
2e

(*E*)-1-(1*H*-pyrazol-1-yl)-3-(4-(trifluoromethyl)phenyl)prop-2-e*n*-1-one (2e): White solid, 0.36 g, 55% yield. **MP**: 90-93 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 2.7 Hz, 1H), 7.97 (d, *J* = 2.8 Hz, 2H), 7.75 (d, *J* = 8.9 Hz, 3H), 7.65 (d, *J* = 8.1 Hz, 2H), 6.52 – 6.43 (m, 1H).**^{13}C NMR** (125 MHz, Chloroform-*d*) δ 163.07, 145.57, 144.09, 137.69, 132.43, 132.17, 128.79, 125.90, 118.35, 110.16. **^{19}F NMR** (470 MHz, Chloroform-*d*) δ -62.92. **IR** (film) ν_{max} 3361, 2112, 1910, 1697, 1622, 1430, 1355, 801, 749 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{13}H_9F_3N_2O$ [M+Na]$^+$: 289.0559. Found: 289.0568.



2f

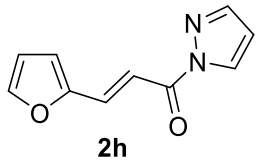
(*E*)-3-(4-methoxyphenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (2f): White solid, 5.76 g, 90% yield. **MP**: 79-82 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 2.8, 0.7 Hz, 1H), 8.02 (d, *J* = 15.9 Hz, 1H), 7.82 – 7.78 (m, 2H), 7.71 – 7.67 (m, 2H), 6.99 – 6.93 (m, 2H), 6.51 (dd, *J* = 2.8, 1.5 Hz, 1H), 3.89 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 163.88, 162.09, 147.74, 143.66, 130.71, 128.69, 127.30, 114.43, 113.02, 109.62, 55.45. **IR** (film) ν_{max} 3425, 2563, 1701, 1602, 1513, 1259, 826, 765 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{13}H_{12}N_2O_2$ [M+Na]$^+$: 251.0791. Found: 251.0810.



2g

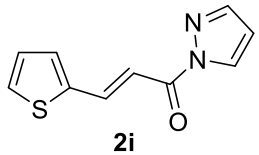
(*E*)-3-(3-methoxyphenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (2g): White solid, 4.7 g, 73% yield. **MP**: 62-65 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 2.8, 0.7 Hz, 1H), 8.03 (d, *J* = 16.0 Hz, 1H), 7.91 (d, *J* = 16.0 Hz, 1H), 7.84 – 7.76 (m, 1H), 7.37 (t, *J* = 7.9 Hz, 1H), 7.31 (dt, *J* = 7.6, 1.3

Hz, 1H), 7.23 (dd, *J* = 2.6, 1.7 Hz, 1H), 7.02 (ddd, *J* = 8.1, 2.6, 1.1 Hz, 1H), 6.53 (dd, *J* = 2.9, 1.5 Hz, 1H), 3.89 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 163.60, 159.97, 147.86, 143.87, 135.76, 129.96, 128.76, 121.66, 117.17, 115.95, 113.37, 109.88, 55.41. **IR** (film) ν_{max} 3424, 2085, 1705, 1622, 1384, 774 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{13}H_{12}N_2O_2$ [M+Na]$^+$: 251.0791. Found: 251.0787.



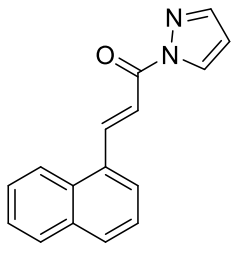
2h

(*E*)-3-(furan-2-yl)-1-(1*H*-pyrazol-1-yl)prop-2-en-1-one (2h): White solid, 1.63 g, 87% yield. **MP**: 67-70 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 2.8 Hz, 1H), 7.72 (d, *J* = 6.3 Hz, 3H), 7.50 (d, *J* = 1.7 Hz, 1H), 6.73 (d, *J* = 3.4 Hz, 1H), 6.45 (ddd, *J* = 11.9, 3.2, 1.7 Hz, 2H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 163.64, 151.38, 145.60, 143.78, 133.38, 128.56, 116.69, 113.33, 112.69, 109.75. **IR** (film) ν_{max}3418, 3174, 2095, 1761, 1622, 1348, 759, 593 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{10}H_8N_2O_2$ [M+Na]$^+$: 211.0478. Found: 211.0495.



2i

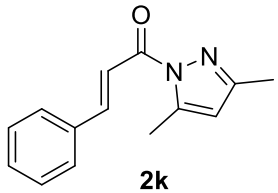
(*E*)-1-(1*H*-pyrazol-1-yl)-3-(thiophen-2-yl)prop-2-en-1-one(2i): White solid, 1.41 g, 69% yield. **MP**: 66-69 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.34 (d, *J* = 2.8 Hz, 1H), 8.10 (dd, *J* = 15.5, 3.1 Hz, 1H), 7.75 (d, *J* = 2.5 Hz, 1H), 7.65 (dd, *J* = 15.6, 2.6 Hz, 1H), 7.41 (dt, *J* = 22.7, 4.5 Hz, 2H), 7.13 – 7.02 (m, 1H), 6.52 – 6.40 (m, 1H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 163.50, 143.82, 140.04, 139.94, 132.50, 129.95, 128.67, 128.33, 114.28, 109.80. **IR** (film) ν_{max} 3428, 3148, 2117, 1699, 1609, 1385, 1201, 710 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{10}H_8N_2OS$ [M+Na]$^+$: 227.0250. Found: 227.0273.



2j

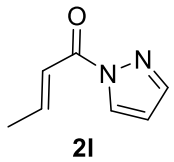
(*E*)-3-(naphthalen-1-yl)-1-(1*H*-pyrazol-1-yl)prop-2-en-1-one (2j): White solid, 1.8 g, 72% yield. **MP**: 71-74 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.93 (d, *J* = 15.7 Hz, 1H), 8.47 (dd, *J* = 2.9, 0.7 Hz, 1H), 8.34 (dd, *J* = 8.5, 1.1 Hz, 1H), 8.10 – 8.05 (m, 1H), 8.05 – 8.03 (m, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.95 – 7.91 (m, 1H), 7.83 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.65 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 7.61 –

7.53 (m, 2H), 6.55 (dd, *J* = 2.8, 1.5 Hz, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 163.54, 144.53, 143.94, 133.75, 131.69, 131.56, 131.40, 128.83, 128.80, 127.15, 126.33, 125.81, 125.47, 123.29, 118.04, 109.92. **IR** (film) ν_{max} 3404, 3055, 1704, 1616, 1416, 1385, 1352, 768 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{16}H_{12}N_2O$ $[M+Na]^+$: 271.0842. Found: 271.0863.



2k

(*E*)-1-(3,5-dimethyl-1*H*-pyrazol-1-yl)-3-phenylprop-2-en-1-one (2k) White solid, 3.8 g, 70% yield. **MP**: 53-56 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.05 – 7.86 (m, 2H), 7.77 – 7.61 (m, 2H), 7.44 (q, *J* = 3.2 Hz, 3H), 6.04 (s, 1H), 2.65 (s, 3H), 2.32 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 165.5, 151.9, 146.1, 144.4, 134.8, 130.6, 128.9, 128.7, 118.0, 111.4, 14.7, 13.9. **IR** (film) ν_{max} 3622, 3135, 1952, 1700, 1621, 1389, 1348, 932, 765 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{14}H_{14}N_2O$ $[M+Na]^+$: 249.0998. Found: 249.1026.

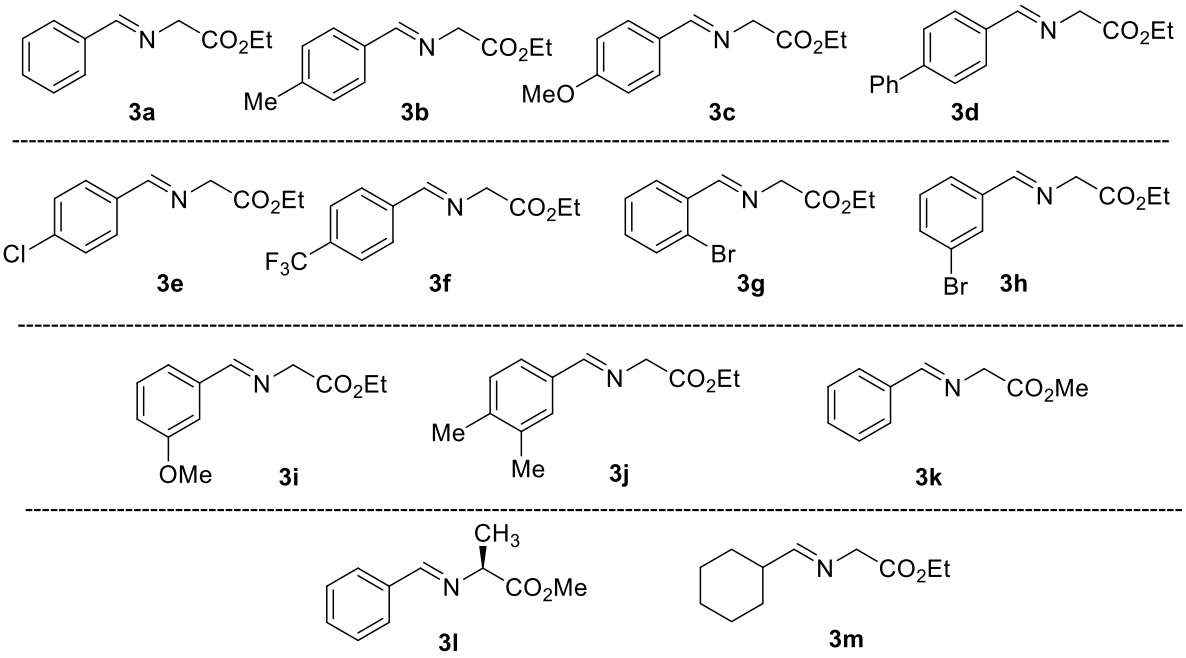


2l

(*E*)-1-(1*H*-pyrazol-1-yl)but-2-e*n*-1-one (3m): Yellowish oil, 2.68 g, 68% yield. R_f = 0.70 (10% EtOAc in hexanes). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.35 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.76 (d, *J* = 1.2 Hz, 1H), 7.38 (dq, *J* = 15.6, 6.3 Hz, 1H), 7.34 – 7.30 (m, 1H), 6.48 (dd, *J* = 2.8, 1.5 Hz, 1H), 2.07 (dd, *J* = 6.4, 1.2 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 163.2, 148.8, 143.7, 128.6, 120.8, 109.6, 18.7. **IR** (film) ν_{max} 3543, 3133, 2941, 1711, 1645, 1384, 910, 809, 772 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_7H_9N_2O$ 137.07096; Found 137.0696.

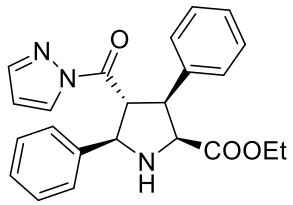
General procedure alkyl *N*-benzylideneglycinate 3a-m:

The following azomethine ylides (3a-m) were prepared according to literature procedure.[2]



General procedure for the synthesis of highly substituted pyrrolidine:

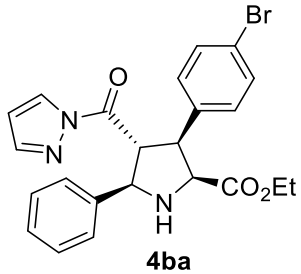
In a round bottomed flask, $Cu(CH_3CN)_4BF_4$ (6.28 mg, 0.02 mmol, 10 mol %) and (*R*)-DM-BINAP (L5) (11.37 mg, 0.024 mmol, 12 mol %) and 50 mg 4Å MS were taken and toluene (2.0 mL) was added to it. The mixture was stirred at room temperature (25 °C) for 1 hour under nitrogen atmosphere. Then azomethine ylide (57.3 mg, 0.3 mmol, 1.5 equiv.) was added slowly and stirred for 5 minutes followed by α,β-unsaturated pyrazolamides (40 mg, 0.2 mmol, 1.0 equiv) and DBU (3 µL, 0.02 mmol, 10 mol %) were added. The reaction mixture was allowed to stir for additional 24 hours at -20 °C. After completion of reaction, the residue was charged over a column packed with silica gel. The cycloaddition products **4aa-4gm** were isolated by flash column chromatography using ethyl acetate and hexane as eluents.



4aa

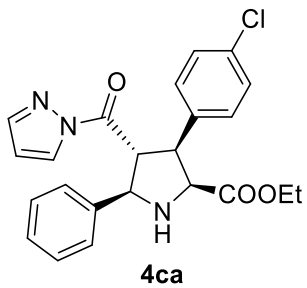
Ethyl (2*S*,3*S*,4*R*,5*R*)-3,5-diphenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4aa): White solid, 55 mg, 70% yield. **MP**: 157−160 °C. dr = 85:15 $[\alpha]_D^{25}$ = +42.54 ($CHCl_3$, c = 3.11 for 98%

ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 13.06 min (major), 23.33 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 38.8 Hz, 2H), 7.42 (d, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 3H), 7.29 – 7.25 (m, 1H), 7.23 – 7.10 (m, 5H), 6.24 (s, 1H), 5.17 (d, *J* = 9.4 Hz, 1H), 4.98 (t, *J* = 9.7 Hz, 1H), 4.25 (t, *J* = 8.6 Hz, 1H), 4.13 (dq, *J* = 20.8, 10.1, 8.2 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.8, 169.7, 143.7, 139.9, 139.0, 128.7, 128.6, 128.3, 128.3, 128.1, 128.1, 128.1, 127.8, 127.3, 127.1, 109.6, 67.6, 65.6, 61.2, 57.5, 51.8, 14.1. **IR** (film) ν_{max} 3433, 2119, 1721, 1645, 1207, 755 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{23}H_{23}N_3O_3$ $[M+H]^+$: 390.1812. Found: 390.1817



4ba

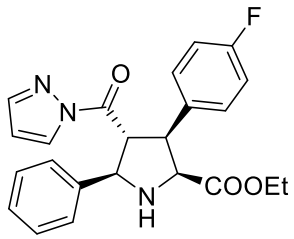
Ethyl (2*S*,3*S*,4*R*,5*R*)-3-(4-bromophenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ba): White solid, 66 mg, 70% yield. **MP**: 123−126 °C. dr = 85:15. $[\alpha]_D^{25}$ = +27.69 ($CHCl_3$, c = 0.82 for 98% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 11.03 min (major), 20.94 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 2.8 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.49 (d, *J* = 1.5 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.30 – 7.24 (m, 3H), 6.32 (dd, *J* = 2.9, 1.5 Hz, 1H), 4.96 (t, *J* = 9.8 Hz, 1H), 4.71 (d, *J* = 9.5 Hz, 1H), 4.40 (d, *J* = 9.3 Hz, 1H), 4.25 (t, *J* = 9.7 Hz, 1H), 3.93 – 3.82 (m, 1H), 3.78 – 3.64 (m, 1H), 0.88 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.42, 171.72, 144.08, 139.02, 136.71, 131.32, 130.11, 128.62, 128.59, 128.16, 128.07, 127.14, 121.33, 110.25, 68.16, 65.37, 61.04, 54.24, 53.88, 13.60. **IR** (film) ν_{max} 3429, 2095, 1725, 1643, 1490, 1389, 1202, 755 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{23}H_{22}BrN_3O_3$ $[M+H]^+$: 468.0917. Found: 468.0904.



4ca

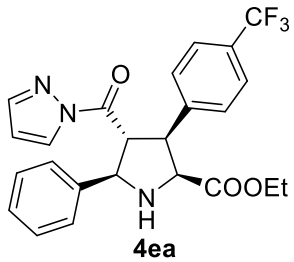
Ethyl (2*S*,3*S*,4*R*,5*R*)-3-(4-chlorophenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ca): White solid, 61 mg, 72% yield. **MP**: 135−138 °C. dr = 90:10 $[\alpha]_D^{25}$ = +51.66

($CHCl_3$, c = 0.48 for 98% ee); **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 10.42 min (major), 19.30 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 2.9 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.49 (d, *J* = 1.4 Hz, 1H), 7.32 (dd, *J* = 8.1, 6.3 Hz, 4H), 7.30 – 7.26 (m, 1H), 7.26 – 7.21 (m, 2H), 6.31 (dd, *J* = 2.8, 1.4 Hz, 1H), 4.96 (t, *J* = 9.7 Hz, 1H), 4.71 (d, *J* = 9.5 Hz, 1H), 4.46 – 4.35 (m, 1H), 4.26 (t, *J* = 9.5 Hz, 1H), 3.91 – 3.80 (m, 1H), 3.70 (dq, *J* = 10.7, 7.2 Hz, 1H), 2.83 (s, 1H), 0.88 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.5, 171.8, 144.1, 139.1, 136.2, 133.2, 129.8, 128.6, 128.4, 128.2, 128.1, 127.1, 110.2, 61.0, 13.6. **IR** (film) ν_{max} 3438, 2356, 2117, 1732, 1649, 1207, 751 cm^{-1};**HRMS** (ES+): Exact mass calcd for $C_{23}H_{22}ClN_3O_3$ $[M+H]^+$: 424.1422. Found: 424.1400.



4da

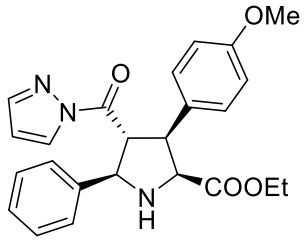
Ethyl (2*S*,3*S*,4*R*,5*R*)-3-(4-fluorophenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4da): White solid, 53 mg, 65% yield. **MP**: 88−91 °C. dr = 83:17 $[\alpha]_D^{25}$ = -70.10 ($CHCl_3$, c = 0.19 for 96% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 9.90 min (major), 17.78 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 2.8 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 2H), 7.49 (s, 1H), 7.37 – 7.30 (m, 4H), 7.27 (s, 1H), 6.95 (t, *J* = 8.5 Hz, 2H), 6.31 (d, *J* = 2.7 Hz, 1H), 4.99 (t, *J* = 9.9 Hz, 1H), 4.70 (d, *J* = 9.6 Hz, 1H), 4.40 (d, *J* = 9.4 Hz, 1H), 4.29 (t, *J* = 9.8 Hz, 1H), 3.86 (ddd, *J* = 14.6, 9.0, 5.5 Hz, 1H), 3.75 – 3.62 (m, 1H), 0.87 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.6, 171.8, 144.0, 139.1, 133.3, 130.0, 129.9, 128.6, 128.2, 128.1, 127.2, 115.2, 115.0, 110.2, 68.2, 65.4, 61.0, 54.1, 54.0, 29.7, 13.6. **IR** (film) ν_{max} 3429, 2114, 1645, 1514, 1267, 752 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{23}H_{22}FN_3O_3$ $[M+H]^+$: 408.1718. Found: 408.1743.



4ea

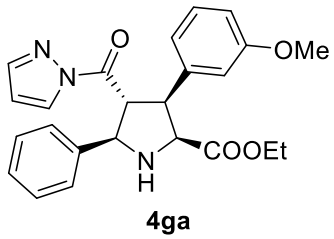
Ethyl (2*S*,3*S*,4*R*,5*R*)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)-3-(4-(trifluoromethyl)phenyl)pyrrolidine-2-carboxylate (4ea): White solid, 55 mg, 60% yield. **MP**: 85−88 °C. dr = 88:12 $[\alpha]_D^{25}$ = -835.13 ($CHCl_3$, c = 0.15 for 96% ee). **HPLC** (Chiralpak ID, *n*-hexane/

iso-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 7.49 min (major), 13.44 min (minor); **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 2.8 Hz, 1H), 7.61 – 7.56 (m, 2H), 7.53 (s, 4H), 7.49 (d, *J* = 1.3 Hz, 1H), 7.38 – 7.23 (m, 3H), 6.32 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.00 (t, *J* = 9.6 Hz, 1H), 4.74 (s, 1H), 4.45 (d, *J* = 9.4 Hz, 1H), 4.34 (t, *J* = 9.4 Hz, 1H), 3.82 (ddd, *J* = 14.1, 8.9, 5.4 Hz, 1H), 3.74 – 3.59 (m, 1H), 2.86 (s, 1H), 0.80 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.3, 171.6, 144.1, 142.0, 138.9, 128.8, 128.7, 128.2, 128.1, 127.1, 125.2, 125.1, 123.0, 110.3, 68.1, 65.4, 61.0, 54.3, 54.0, 13.4. **^{19}F NMR** (470 MHz, Chloroform-*d*) δ -62.58. **IR** (film) ν_{max} 3431, 2101, 1732, 1647, 1328, 753, cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{24}H_{22}F_3N_3O_3$ [M+Na]$^+$: 480.1505. Found: 480.1480



4fa

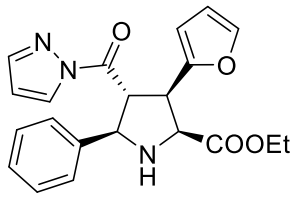
Ethyl (2*S*,3*S*,4*R*,5*R*)-3-(4-methoxyphenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4fa): White solid, 63 mg, 75% yield. **MP**: 130-133 °C. dr = 90:10 $[\alpha]_D^{25}$ = +79.8 ($CHCl_3$, c = 0.62 for 99% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 12.13 min (major), 24.63 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.08 (d, *J* = 2.9 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.49 (d, *J* = 1.4 Hz, 1H), 7.34 – 7.25 (m, 5H), 6.82 – 6.75 (m, 2H), 6.29 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.02 (t, *J* = 9.9 Hz, 1H), 4.69 (d, *J* = 9.9 Hz, 1H), 4.38 (d, *J* = 9.4 Hz, 1H), 4.29 (t, *J* = 9.7 Hz, 1H), 3.93 – 3.82 (m, 1H), 3.76 (s, 3H), 3.72 – 3.63 (m, 1H), 0.88 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.9, 172.0, 158.9, 143.9, 139.2, 129.4, 129.3, 128.6, 128.1, 128.0, 127.2, 113.6, 110.0, 60.9, 55.2, 54.4, 53.8, 13.7. **IR** (film) ν_{max} 3422, 2925, 2063, 1731, 1257, 753 cm^{-1};**HRMS** (ES+): Exact mass calcd for $C_{24}H_{25}N_3O_4$ [M+H]$^+$: 420.1918. Found: 420.1926.



4ga

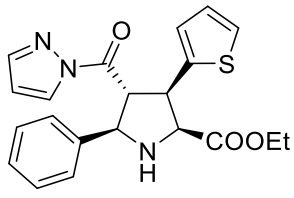
Ethyl (2*S*,3*S*,4*R*,5*R*)-3-(3-methoxyphenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ga): White solid, 43.70 mg, 52% yield. **MP**: 145−148 °C. dr = 75:25 $[\alpha]_D^{25}$ = +26.06 ($CHCl_3$, c = 1.42 for 98% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 12.81 min (major), 20.68 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 2.9 Hz, 1H), 7.61 – 7.52 (m, 2H), 7.47 (d, *J* = 1.5 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.24 (dd, *J* = 8.4, 6.2 Hz,

2H), 7.14 (t, *J* = 7.9 Hz, 1H), 6.97 – 6.87 (m, 2H), 6.73 (dd, *J* = 8.0, 2.6 Hz, 1H), 6.28 (dd, *J* = 2.8, 1.4 Hz, 1H), 5.05 (t, *J* = 10.0 Hz, 1H), 4.67 (d, *J* = 9.6 Hz, 1H), 4.38 (d, *J* = 9.5 Hz, 1H), 4.30 (t, *J* = 9.8 Hz, 1H), 3.83 (dd, *J* = 10.7, 7.2 Hz, 1H), 3.74 (s, 3H), 3.71 – 3.63 (m, 1H), 0.83 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.7, 169.7, 159.7, 143.7, 140.6, 139.9, 129.7, 128.1, 128.1, 127.7, 127.1, 120.2, 114.0, 112.6, 109.6, 67.5, 65.6, 61.2, 57.4, 55.2, 51.8, 14.1. **IR** (film) ν_{max} 3436, 3385, 2926, 1734, 1608, 1264, 747, 702 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{24}H_{25}N_3O_4$ $[M+H]^+$: 420.1918 Found: 420.1922.



4ha

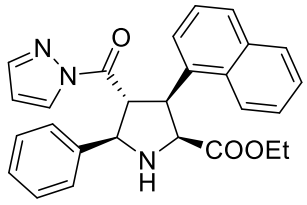
Ethyl (2*S*,3*R*,4*R*,5*R*)-3-(furan-2-yl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ha) : White solid, 34.11 mg, 45% yield. **MP**: 160−163 °C. dr = 64:36 $[\alpha]_D^{25}$ = +15.84 ($CHCl_3$, c = 0.40 for 40% ee). **HPLC** (Chiralcel OD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 8.07 min (minor), 12.31 min (major).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 2.8 Hz, 1H), 7.61 (d, *J* = 1.4 Hz, 1H), 7.35 (d, *J* = 1.8 Hz, 1H), 7.21 – 7.03 (m, 5H), 6.29 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.25 – 6.19 (m, 2H), 5.03 (dt, *J* = 17.5, 9.3 Hz, 2H), 4.30 (dd, *J* = 10.8, 7.2 Hz, 1H), 4.21 (dt, *J* = 10.6, 7.1 Hz, 3H), 2.94 (s, 1H), 1.25 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.4, 169.9, 152.2, 143.8, 142.1, 139.2, 128.1, 127.7, 127.0, 110.3, 109.7, 107.1, 65.4, 64.9, 61.4, 54.3, 45.4, 14.2. **IR** (film) ν_{max} 3432, 2085, 1645, 1028, 697, 598 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{21}H_{21}N_3O_4$ $[M+Na]^+$: 402.1424. Found: 402.1433.



4ia

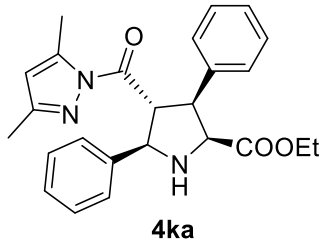
Ethyl (2*S*,3*R*,4*R*,5*R*)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)-3-(thiophen-2-yl)pyrrolidine-2-carboxylate (4ia): White solid, 32 mg, 40% yield. **MP**: 166−169 °C. dr = 50:50 $[\alpha]_D^{25}$ = +39.73 ($CHCl_3$, c = 0.60 for 52% ee). **HPLC** (Chiralpak AD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 13.8 min (major), 16.3 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 2.9 Hz, 1H), 7.65 (d, *J* = 1.4 Hz, 1H), 7.23 – 7.09 (m, 6H), 7.03 (dd, *J* = 3.5, 1.2 Hz, 1H), 6.94 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.24 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.11 (d, *J* = 9.4 Hz, 1H), 4.93 (t, *J* = 9.7 Hz, 1H), 4.43 (t, *J* = 9.9 Hz, 1H), 4.32 – 4.24 (m, 1H), 4.24 – 4.18 (m, 1H), 4.14 (d, *J* = 9.8 Hz, 1H), 2.58 (s, 1H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.3, 169.5, 143.9, 142.2, 139.6, 128.1, 128.1,

127.8, 127.0, 126.9, 125.4, 124.2, 109.7, 68.0, 65.2, 61.4, 58.2, 46.8, 14.2. **IR** (film) ν_{max} 3435, 2089, 1641, 1021, 695, 595 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{21}H_{21}N_3O_3S$ $[M+Na]^+$: 418.1196. Found: 418.1215.



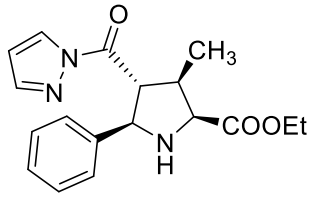
4ja

Ethyl (2*S*,3*S*,4*R*,5*R*)-3-(naphthalen-1-yl)-5-phenyl-4-(1H-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ja): White solid, 57 mg, 65% yield. **MP**: 146−149 °C. dr = 66:34 $[\alpha]_D^{27}$ = +7.20 ($CHCl_3$, c = 0.70 for 96% ee). **HPLC** (Chiralpak AD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 17.2 min (major), 33.4 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.25 (d, *J* = 8.6 Hz, 1H), 7.77 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 7.63 – 7.57 (m, 2H), 7.51 (d, *J* = 1.4 Hz, 1H), 7.50 – 7.45 (m, 1H), 7.41 (ddd, *J* = 10.0, 8.7, 6.6 Hz, 2H), 7.21 – 7.18 (m, 2H), 7.12 – 7.05 (m, 3H), 6.10 (dd, *J* = 2.9, 1.4 Hz, 1H), 5.18 (d, *J* = 9.4 Hz, 1H), 5.11 (t, *J* = 9.4 Hz, 1H), 4.96 (t, *J* = 9.5 Hz, 1H), 4.16 (d, *J* = 9.4 Hz, 1H), 3.89 (qd, *J* = 7.2, 1.2 Hz, 2H), 0.68 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 173.1, 170.2, 143.7, 139.6, 135.7, 133.9, 132.4, 128.8, 128.2, 128.1, 127.8, 127.8, 127.1, 126.3, 125.7, 125.4, 123.2, 109.6, 68.6, 66.0, 61.3, 57.7, 13.5, 1.0. **IR** (film) ν_{max} 3431, 2106, 1645, 610 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{27}H_{25}N_3O_3$ $[M+H]^+$: 440.1969. Found: 440.1952.



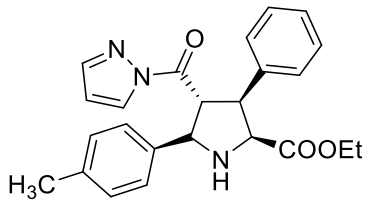
4ka

Ethyl (2*S*,3*S*,4*R*,5*R*)-4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-3,5-diphenylpyrrolidine-2-carboxylate (4ka): White solid, 30 mg, 36% yield. **MP**: 65−68 °C. dr = 67:33 $[\alpha]_D^{25}$ = +9.30 ($CHCl_3$, c = 1.54 for 6% ee). **HPLC** (Chiralcel OD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 5.30 min (minor), 6.12 min (major). **^{1}H NMR** (700 MHz, Chloroform-*d*) δ 7.41 (d, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.19 – 7.09 (m, 5H), 5.71 (s, 1H), 5.09 (s, 1H), 4.98 (t, *J* = 10.0 Hz, 1H), 4.21 (ddd, *J* = 14.2, 8.9, 5.4 Hz, 1H), 4.10 (dq, *J* = 10.7, 7.1 Hz, 2H), 4.01 (t, *J* = 10.4 Hz, 1H), 2.23 (s, 3H), 1.95 (s, 3H), 1.12 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (175 MHz, Chloroform-*d*) δ 170.9, 151.8, 143.9, 128.6, 128.2, 127.9, 127.7, 127.2, 127.1, 110.7, 61.1, 14.1, 13.8, 13.6. **IR** (film) ν_{max} 3435, 2120, 1723, 1642, 1208, 750 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{25}H_{27}N_3O_3$ $[M+H]^+$: 418.2125. Found: 418.2152



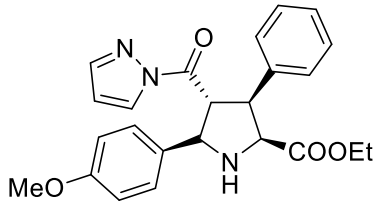
4la

Ethyl (2*S*,3*R*,4*R*,5*R*)-3-methyl-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4la) Viscous colourless oil, 45 mg, 68% yield. dr = 72:28 $[\alpha]_D^{25}$ = +1.52 ($CHCl_3$, c = 2.24 for 96% ee). **HPLC** (Chiralcel OD-H, *n*-hexane/ *iso*-propanol = 85/15, 1.0 mL/min, 254 nm): t_R = 7.65 min (major), 9.14 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 2.9 Hz, 1H), 7.68 (s, 1H), 7.45 – 7.32 (m, 1H), 7.13 – 7.06 (m, 4H), 6.28 (d, *J* = 3.0 Hz, 1H), 4.93 (d, *J* = 9.1 Hz, 1H), 4.40 – 4.23 (m, 3H), 3.63 (d, *J* = 9.6 Hz, 1H), 2.93 (td, *J* = 9.7, 6.6 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.28 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-d) δ 173.2, 170.3, 143.8, 140.2, 128.1, 127.6, 126.9, 109.6, 109.6, 67.0, 64.8, 61.3, 57.0, 40.9, 16.9, 14.3. **IR** (film) ν_{max} 3426, 2978, 1724, 1417, 1387, 1335, 1199, 1027, 760 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{18}H_{21}N_3O_3$ $[M+H]^+$: 328.1656. Found: 328.1673



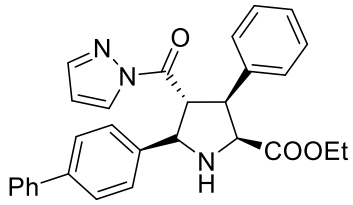
4ab

Ethyl (2*S*,3*S*,4*R*,5*S*)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)-5-(p-tolyl)pyrrolidine-2-carboxylate (4ab): White solid, 52 mg, 64% yield. **MP**: 159−162 °C. dr = 95:5 $[\alpha]_D^{25}$ = +11.76 ($CHCl_3$, c = 1.22 for 94% ee). **HPLC** (Chiralpak AD-H, *n*-hexane/ *iso*-propanol = 85/15, 1.0 mL/min, 254 nm): t_R = 17.02 min (major), 18.55 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 2.8 Hz, 1H), 7.42 – 7.36 (m, 3H), 7.26 (d, *J* = 7.2 Hz, 2H), 7.18 – 7.08 (m, 4H), 7.03 (d, *J* = 7.8 Hz, 2H), 6.20 (dd, *J* = 2.9, 1.5 Hz, 1H), 4.96 (t, *J* = 10.0 Hz, 1H), 4.57 (d, *J* = 9.7 Hz, 1H), 4.30 (d, *J* = 9.5 Hz, 1H), 4.23 (t, *J* = 9.9 Hz, 1H), 3.72 (dd, *J* = 10.7, 7.1 Hz, 1H), 3.51 (dd, *J* = 10.7, 7.2 Hz, 1H), 2.22 (s, 3H), 0.71 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 172.8, 172.1, 143.9, 137.8, 137.4, 135.9, 129.3, 128.3, 128.2, 128.0, 127.4, 127.2, 110.0, 68.4, 65.7, 60.9, 55.3, 53.5, 21.1, 13.5. **IR** (film) ν_{max} 3430, 1722, 1651, 1381, 1209, 757 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{24}H_{25}N_3O_3$ $[M+Na]^+$: 426.1788. Found: 426.1800.



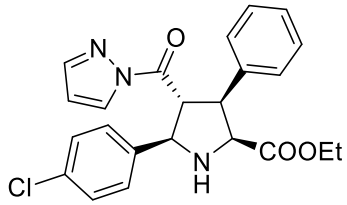
4ac

Ethyl (2*S*,3*S*,4*R*,5*S*)-5-(4-methoxyphenyl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ac): White solid, 50.4 mg, 60% yield. **MP**: 128−131 °C. dr = 87:13 $[\alpha]_D^{23}$ = +90.05 ($CHCl_3$, c = 0.50 for 99% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 12.11 min (major), 24.63 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.04 (d, *J* = 2.9 Hz, 1H), 7.55 – 7.46 (m, 3H), 7.38 – 7.29 (m, 2H), 7.23 (t, *J* = 7.3 Hz, 2H), 7.20 – 7.15 (m, 1H), 6.82 (d, *J* = 8.3 Hz, 2H), 6.27 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.03 (t, *J* = 9.9 Hz, 1H), 4.61 (s, 1H), 4.32 (q, *J* = 12.6, 9.4 Hz, 2H), 3.85 – 3.79 (m, 1H), 3.77 (s, 3H), 3.58 (dd, *J* = 10.6, 7.2 Hz, 1H), 0.78 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 172.8, 169.7, 159.0, 143.7, 139.0, 132.1, 128.6, 128.2, 128.1, 128.0, 127.3, 67.5, 65.0, 61.1, 57.6, 55.1, 51.8, 14.1. **IR** (film) ν_{max} 3421, 2929, 2306, 2121, 1730, 1642, 1515, 1261, 1027, 743 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{24}H_{25}N_3O_4$ $[M+H]^+$: 420.1918. Found: 420.1937.



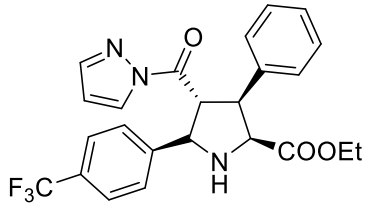
4ad

Ethyl (2*S*,3*S*,4*R*,5*S*)-5-([1,1'-biphenyl]-4-yl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ad): White solid, 45 mg, 48% yield. **MP**: 159−162 °C. dr = 70:30 $[\alpha]_D^{22}$ = +125.40 ($CHCl_3$, c = 0.70 for 94% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 9.95 min (major), 20.50 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 2.9 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.59 – 7.51 (m, 4H), 7.47 (d, *J* = 1.4 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.38 – 7.32 (m, 3H), 7.24 (t, *J* = 7.3 Hz, 2H), 7.21 – 7.16 (m, 1H), 6.27 (dd, *J* = 2.9, 1.4 Hz, 1H), 5.09 (t, *J* = 9.9 Hz, 1H), 4.73 (d, *J* = 9.7 Hz, 1H), 4.42 (d, *J* = 9.5 Hz, 1H), 4.34 (t, *J* = 9.8 Hz, 1H), 3.82 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.61 (dq, *J* = 10.7, 7.2 Hz, 1H), 2.35 (s, 1H), 0.80 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.8, 171.9, 144.0, 140.9, 140.7, 138.1, 137.3, 128.7, 128.3, 128.3, 128.1, 127.7, 127.4, 127.3, 127.0, 110.1, 68.2, 65.6, 60.9, 55.1, 53.6, 13.5. **IR** (film) ν_{max} 3412, 2119, 1725, 1641, 1387, 1209, 1027, 740 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{29}H_{27}N_3O_3$ $[M+H]^+$: 466.2125. Found: 466.2151.



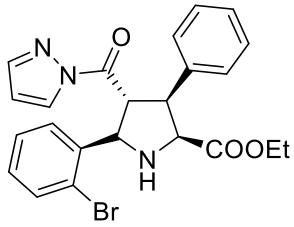
4ae

Ethyl (2*S*,3*S*,4*R*,5*R*)-5-(4-chlorophenyl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ae): White solid, 47.5 mg, 56% yield. **MP**: 118−121 °C. dr = 77:23 $[\alpha]_D^{25}$ = +105.23 ($CHCl_3$, c = 0.43 for 96% ee). **HPLC** (Chiralcel OD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 6.01 min (major), 7.44 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.08 (d, *J* = 2.9 Hz, 1H), 7.62 – 7.53 (m, 2H), 7.49 (d, *J* = 1.5 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.28 – 7.17 (m, 3H), 7.00 (t, *J* = 8.7 Hz, 2H), 6.30 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.05 (t, *J* = 10.0 Hz, 1H), 4.66 (d, *J* = 9.7 Hz, 1H), 4.37 (dt, *J* = 19.7, 9.6 Hz, 2H), 3.82 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.62 (dq, *J* = 10.7, 7.2 Hz, 1H), 2.59 (s, 1H), 0.80 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 172.7, 169.4, 143.9, 138.7, 138.7, 133.5, 128.7, 128.5, 128.3, 128.2, 128.0, 127.4, 109.8, 67.4, 64.6, 61.2, 57.2, 51.3, 14.1. **IR** (film) ν_{max} 3111, 2928, 1727, 1391, 1208, 758 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{23}H_{22}ClN_3O_3$ $[M+H]^+$: 424.1422. Found: 424.1439.



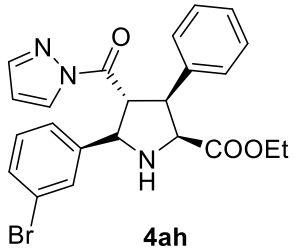
4af

Ethyl (2*S*,3*S*,4*R*,5*S*)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)-5-(4-(trifluoromethyl)phenyl)pyrrolidine-2-carboxylate (4af): White solid, 68.5 mg, 75% yield. **MP**: 118−121 °C. dr = 94:6 $[\alpha]_D^{23}$ = +25.21 ($CHCl_3$, c = 0.94 for 99% ee). **HPLC** (Chiralpak AD-H, *n*-hexane/ *iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 12.03 min (major), 14.23 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 2.8 Hz, 1H), 7.67 (s, 1H), 7.42 (dd, *J* = 8.0, 3.8 Hz, 4H), 7.38 – 7.32 (m, 4H), 7.28 (d, *J* = 7.0 Hz, 1H), 6.42 – 5.95 (m, 1H), 5.23 (d, *J* = 9.5 Hz, 1H), 5.00 (t, *J* = 9.8 Hz, 1H), 4.35 – 3.94 (m, 4H), 3.00 (s, 1H), 1.18 (t, *J* = 7.1 Hz, 3H).**^{13}C NMR** ^{13}C NMR (126 MHz, Chloroform-*d*) δ 172.7, 169.3, 144.0, 138.6, 128.8, 128.2, 128.1, 127.6, 127.5, 125.0, 109.9, 67.4, 64.7, 61.3, 57.1, 51.2. **IR** (film) ν_{max} 3427, 2924, 2306, 2128, 1739, 1643, 1510, 1265, 1022, 745 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{24}H_{22}F_3N_3O_3$ $[M+Na]^+$: 480.1505. Found: 480.1511.



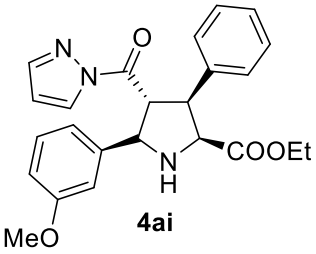
4ag

Ethyl (2*S*,3*S*,4*R*,5*S*)-5-(2-bromophenyl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ag): White solid, 47 mg, 50% yield. **MP**: 150−153 °C. dr = 77:23 $[\alpha]_D^{25}$ = +12.35 ($CHCl_3$, c = 0.16 for 98% ee). **HPLC** (Chiralpak AD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 10.93min (major), 12.43 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 2.9 Hz, 1H), 7.60 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.52 (d, *J* = 1.4 Hz, 1H), 7.44 (dt, *J* = 8.4, 1.9 Hz, 2H), 7.41 – 7.32 (m, 3H), 7.30 – 7.23 (m, 2H), 7.01 (td, *J* = 7.7, 1.7 Hz, 1H), 6.19 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.48 (d, *J* = 8.5 Hz, 1H), 5.17 (dd, *J* = 8.6, 6.6 Hz, 1H), 4.36 – 4.26 (m, 1H), 4.21 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.17 – 4.08 (m, 2H), 3.10 (s, 1H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.3, 170.7, 143.7, 140.1, 137.7, 132.4, 129.1, 128.8, 128.4, 127.8, 127.7, 127.3, 124.2, 109.8, 68.0, 64.8, 61.3, 54.8, 53.0, 14.2. **IR** (film) ν_{max} 3441, 2113, 1729, 1647, 1390, 1264, 1027, 740 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{23}H_{22}BrN_3O_3$ $[M+H]^+$: 468.0917. Found: 468.0926



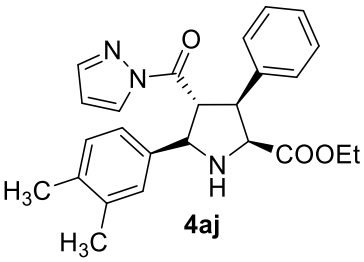
4ah

Ethyl (2*S*,3*S*,4*R*,5*S*)-5-(3-bromophenyl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ah): White solid, 72 mg, 77% yield. **MP**: 140−143 °C. dr = 77:23 $[\alpha]_D^{25}$ = +0.5 ($CHCl_3$, c = 1.1 for 92% ee). **HPLC** (Chiralpak AD-H, *n*-hexane/ *iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 15.73 min (major), 16.72 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 2.8 Hz, 1H), 7.72 – 7.62 (m, 1H), 7.39 (d, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.26 – 7.17 (m, 4H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.33 – 6.14 (m, 1H), 5.12 (s, 1H), 4.95 (s, 1H), 4.29 – 4.09 (m, 3H), 4.06 (s, 1H), 2.88 (s, 1H), 1.16 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 169.3, 144.0, 130.8, 130.5, 129.7, 128.7, 128.2, 128.1, 127.4, 125.6, 122.2, 109.9, 61.3, 14.1. **IR** (film) ν_{max} 3440, 2115, 1728, 1648, 1391, 1265, 1028, 740 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{23}H_{22}BrN_3O_3$ $[M+H]^+$: 468.0917. Found: 468.0924



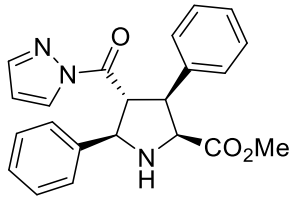
4ai

Ethyl (2*S*,3*S*,4*R*,5*S*)-5-(3-methoxyphenyl)-3-phenyl-4-(1H-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ai): White solid, 34 mg, 40% yield. **MP**: 119−122 °C. dr = 68:32 $[\alpha]_D^{25}$ = +105 ($CHCl_3$, c = 0.60 for 98% ee). **HPLC** (Chiralcel OD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 7.21 min (major), 15.55 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 2.8 Hz, 1H), 7.50 – 7.48 (m, 1H), 7.35 – 7.31 (m, 2H), 7.25 – 7.20 (m, 3H), 7.18 (d, *J* = 6.9 Hz, 1H), 7.16 – 7.11 (m, 2H), 6.78 (ddd, *J* = 8.1, 2.6, 1.1 Hz, 1H), 6.28 (dd, *J* = 2.8, 1.4 Hz, 1H), 5.04 (t, *J* = 9.8 Hz, 1H), 4.67 (s, 1H), 4.38 (s, 1H), 4.30 (t, *J* = 9.7 Hz, 1H), 3.83 – 3.78 (m, 1H), 3.77 (s, 3H), 3.61 – 3.55 (m, 1H), 0.78 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.0, 159.8, 144.0, 140.7, 137.3, 129.6, 128.3, 128.2, 128.1, 127.4, 119.5, 114.1, 112.4, 110.1, 68.5, 65.6, 60.9, 13.5. **IR** (film) ν_{max} 3429, 2926, 2307, 2132, 1728, 1654, 1511, 1265, 1022, 745 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{24}H_{25}N_3O_4$ $[M+H]^+$: 420.1918. Found: 420.1937.



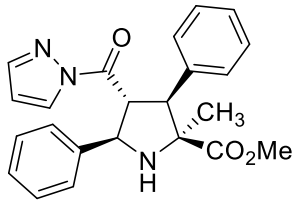
4aj

Ethyl (2*S*,3*S*,4*R*,5*S*)-5-(3,4-dimethylphenyl)-3-phenyl-4-(1H-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4aj): White solid, 33.5 mg, 40% yield. **MP**: 158−161 °C. dr = 66:34 $[\alpha]_D^{25}$ = +80 ($CHCl_3$, c = 1.08 for 95% ee). **HPLC** (Chiralpak AD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 10.50 min (minor), 11.40 min (major).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 2.8 Hz, 1H), 7.41 (s, 1H), 7.26 (d, *J* = 7.4 Hz, 2H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 2H), 7.10 (d, *J* = 7.1 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.19 (dd, *J* = 2.9, 1.4 Hz, 1H), 4.95 (t, *J* = 10.0 Hz, 1H), 4.55 (d, *J* = 9.7 Hz, 1H), 4.30 (d, *J* = 9.6 Hz, 1H), 4.21 (t, *J* = 9.9 Hz, 1H), 3.75 – 3.63 (m, 1H), 3.56 – 3.43 (m, 1H), 2.13 (s, 3H), 2.12 (s, 3H), 0.70 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.7, 172.2, 143.9, 137.4, 136.7, 136.4, 136.2, 129.8, 128.6, 128.4, 128.2, 128.1, 127.3, 124.5, 110.0, 68.4, 65.7, 60.9, 55.5, 53.4, 19.7, 19.4, 13.5. **IR** (film) ν_{max} 3429, 2924, 2309, 2125, 1731, 1647, 1515, 1266, 1021, 748 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{25}H_{27}N_3O_3$ $[M+H]^+$: 418.2125. Found: 418.2142.



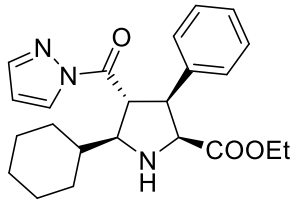
4ak

Methyl (2*S*,3*S*,4*R*,5*R*)-3,5-diphenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4ak): White solid, 65.2 mg, 87% yield. **MP**: 130−133 °C. dr = 90:10 $[\alpha]_D^{25}$ = +81.01 ($CHCl_3$, c = 0.65 for 93% ee). **HPLC** (Chiralpak AD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 11.17 min (major), 14.94 min (inor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 2.9 Hz, 1H), 7.60 – 7.45 (m, 2H), 7.36 (d, *J* = 1.5 Hz, 1H), 7.30 – 7.19 (m, 4H), 7.15 (dd, *J* = 8.1, 6.8 Hz, 3H), 7.13 – 7.07 (m, 1H), 6.16 (dd, *J* = 2.9, 1.5 Hz, 1H), 4.97 (t, *J* = 9.9 Hz, 1H), 4.61 (d, *J* = 9.6 Hz, 1H), 4.42 – 4.25 (m, 1H), 4.22 (d, *J* = 9.8 Hz, 1H), 3.14 (s, 3H), 2.72 (s, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 173.2, 171.9, 144.0, 139.2, 137.2, 128.6, 128.3, 128.2, 128.1, 128.0, 127.4, 127.2, 110.1, 68.6, 65.7, 55.1, 51.6. **IR** (film) ν_{max} 3428, 2926, 2855, 2114, 1737, 1651, 1390, 1208, 752 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{22}H_{21}N_3O_3$ $[M+Na]^+$: 398.1475. Found: 398.1488



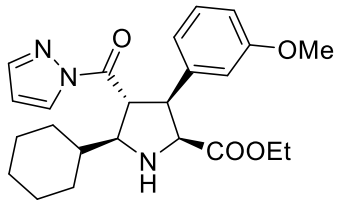
4al

Methyl (2*S*,3*S*,4*R*,5*R*)-2-methyl-3,5-diphenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4al): White solid, 40 mg, 51% yield. **MP**: 127−130 °C. dr = 80:20 $[\alpha]_D^{25}$ = +12.22 ($CHCl_3$, c = 3.20 for 4% ee). **HPLC** (Chiralpak AD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 7.28 min (major), 17.35 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.72 (s, 1H), 7.68 (d, *J* = 2.8 Hz, 1H), 7.33 (d, *J* = 6.5 Hz, 4H), 7.29 – 7.25 (m, 1H), 7.25 – 7.20 (m, 2H), 7.16 (d, *J* = 7.0 Hz, 3H), 6.24 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.33 (dd, *J* = 11.9, 9.8 Hz, 1H), 5.18 (s, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 3.84 (s, 3H), 3.15 (s, 1H), 1.36 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 175.4, 169.7, 143.8, 143.7, 140.1, 136.7, 128.7, 128.4, 128.2, 128.1, 127.7, 127.4, 127.3, 109.6, 109.5, 68.8, 52.5, 52.5. **IR** (film) ν_{max} 3365, 2928, 2342, 1737, 1410, 1390, 1259, 752 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{23}H_{23}N_3O_3$ $[M+H]^+$:390.1812. Found: 390.1838



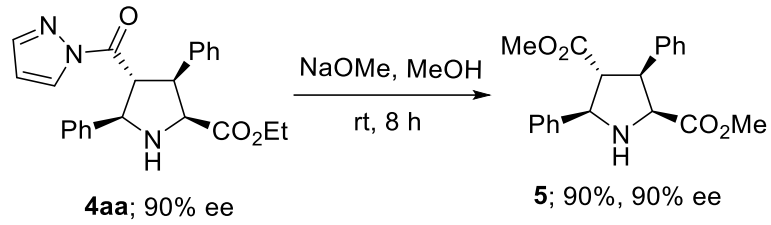
4am

Ethyl (2S,3S,4R,5S)-5-cyclohexyl-3-phenyl-4-(1H-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4am): Viscous yollowish oil, 42 mg, 53% yield. dr = 83:17 $[\alpha]_D^{25}$ = -50.00 ($CHCl_3$, c = 1.27 for 96% ee). **HPLC** (Chiralpak AD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 7.71 min (major), 8.65 min (minor).**^{1}H NMR** (700 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 2.9 Hz, 1H), 7.62 (d, *J* = 1.4 Hz, 1H), 7.25 – 7.18 (m, 4H), 7.18 – 7.13 (m, 1H), 6.38 (dd, *J* = 2.9, 1.5 Hz, 1H), 4.58 (t, *J* = 9.0 Hz, 1H), 4.26 (d, *J* = 9.2 Hz, 1H), 4.02 (t, *J* = 9.1 Hz, 1H), 3.75 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.60 – 3.45 (m, 2H), 2.63 (s, 1H), 2.12 – 2.02 (m, 1H), 1.78 – 1.73 (m, 1H), 1.61 (p, *J* = 4.2, 3.8 Hz, 1H), 1.58 – 1.52 (m, 1H), 1.27 – 1.05 (m, 7H), 0.77 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (175 MHz, Chloroform-*d*) δ 173.3, 172.1, 144.1, 138.3, 128.3, 128.1, 127.2, 110.2, 70.1, 65.8, 60.8, 55.8, 51.2, 41.6, 30.1, 29.8, 26.3, 26.2, 26.1, 13.5. **IR** (film) ν_{max} 3366, 2925, 2852, 1724, 1450, 1387, 1341, 1198, 1027, 769 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{23}H_{29}N_3O_3$ $[M+H]^+$: 396.2282. Found: 396.2298



4gm

Ethyl (2*S*,3*S*,4*R*,5*S*)-5-cyclohexyl-3-(3-methoxyphenyl)-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (4gm): Viscous yollowish oil, 50 mg, 59% yield. dr = 87:13 $[\alpha]_D^{25}$ = +47.09 ($CHCl_3$, c = 2.39 for 91% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 7.38 min (minor), 17.72 min (major). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.16 (s, 1H), 7.63 (s, 1H), 7.11 (t, *J* = 7.8 Hz, 1H), 6.86 – 6.75 (m, 2H), 6.69 (d, *J* = 8.2 Hz, 1H), 6.39 (s, 1H), 4.71 – 4.48 (m, 1H), 4.20 (d, *J* = 19.2 Hz, 1H), 4.02 (s, 1H), 3.77 (d, *J* = 7.9 Hz, 1H), 3.72 (s, 3H), 3.61 (t, *J* = 8.9 Hz, 2H), 2.50 (s, 1H), 2.07 (s, 1H), 1.74 (d, *J* = 13.1 Hz, 1H), 1.61 – 1.49 (m, 2H), 1.30 – 1.04 (m, 7H), 0.81 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 159.33, 144.05, 144.03, 129.06, 128.35, 120.79, 113.65, 113.14, 110.19, 60.76, 55.14, 41.64, 26.33, 26.22, 26.06, 13.58. **IR** (film) ν_{max} 3365, 2926, 2853, 1725, 1602, 1387, 1199, 1040, 774, 697 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{24}H_{31}N_3O_4$ $[M+H]^+$: 426.2387. Found: 426.2403.

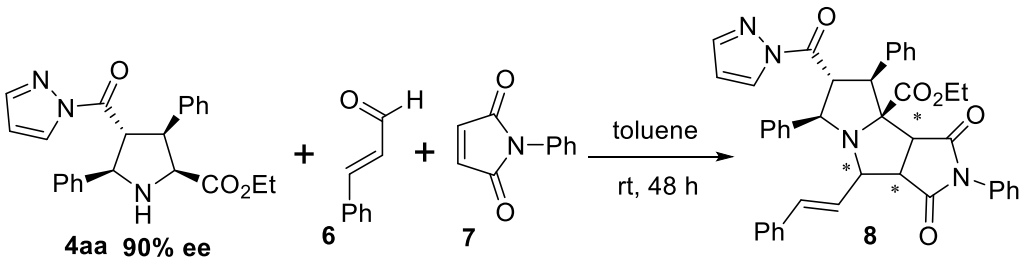


4aa; 90% ee

5; 90%, 90% ee

To a solution of **4aa** (77.9 mg, 0.2mol) in MeOH (2 mL) was added NaOMe (21.68 mg, 0.4 mol) at °C. After stirred for 8 hours at room temperature, the reaction was quenched with saturated aqueous NH_4Cl and extracted three times with EtOAc. Combined organic layers were washed with brine and dried over Na_2SO_4. After filtration and evaporation, the residue was purified through a small pad of silica gel by column chromatography (PE/EtOAc) to afford **5** as a colorless viscous gel (61.2 mg, 90%)

Dimethyl (2*S*,3*S*,4*R*,5*R*)-3,5-diphenylpyrrolidine-2,4-dicarboxylate (5) Viscous gel, 61.2 mg, 90% yield. $[\alpha]_D^{25}$ = +152.27 ($CHCl_3$, c = 0.63 for 90% ee). **HPLC** (Chiralcel OD-H , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 210 nm): t_R = 3.6 min (minor), 5.3 min (major). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.66 – 7.58 (m, 2H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.39 – 7.21 (m, 7H), 4.55 (d, *J* = 9.7 Hz, 1H), 4.36 (d, *J* = 9.5 Hz, 1H), 4.12 (t, *J* = 9.7 Hz, 1H), 3.55 (s, 3H), 3.41 (t, *J* = 9.8 Hz, 1H), 3.25 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 173.2, 173.1, 140.2, 138.0, 128.8, 128.4, 128.1, 128.0, 127.4, 127.1, 66.9, 65.3, 57.3, 53.6, 52.0, 51.5. **IR** (film) ν_{max} 3381, 3037, 3031, 2927, 2105, 1958, 1739, 1440, 1266, 1170, 752, 703 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{20}H_{21}NO_4$ $[M+H]^+$: 340.1543. Found: 340.1563.

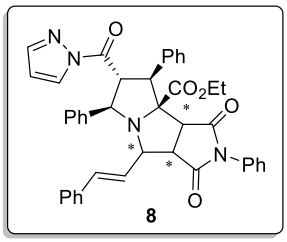


4aa 90% ee **6** **7** **8**

70%, 90:10 dr
90% ee

To a solution of **4aa** (77.9 mg, 0.2mol) in toluene (2 mL) were added *trans*-cinnamaldehyde (**6**) (21.68 mg, 0.4 mol) and *N*-phenylmaleimide (**7**) at room temperature. The reaction mixture was allowed to stir for 48 h at room temperature. After completion of the reaction, the residue was charged over a column packed with silica gel. The pyrrolizidine derivative **8** was isolated as white solid (70% yield by flash column chromatography using 25-30% EtOAc in hexanes as the eluent.

Ethyl (6*R*,7*R*,8*S*,8a*S*)-1,3-dioxo-2,6,8-triphenyl-7-(1*H*-pyrazole-1-carbonyl)-4-((*E*)-styryl)tetrahydro-1*H*,4*H*-3al3,4l3,8bl3-pyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (8): White solid, 95 mg, 70% yield. **MP**: 220-223 °C. dr = 90:10 $[\alpha]_D^{25}$ = +2.85 ($CHCl_3$, c = 1.11 for 90% ee). **HPLC** (Chiralpak AD-H , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 8.70 min (minor), 13.90 min (major).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 2.9 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.44 – 7.38 (m, 6H), 7.28 (t, *J* = 3.9 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 3H), 7.15 (dt, *J* = 4.3, 2.4 Hz, 4H), 6.81 (dd, *J* = 6.7, 2.9 Hz, 2H), 6.59 (d, *J* = 15.8 Hz, 1H), 6.35 (t, *J* = 2.1 Hz, 1H), 5.94 (dd, *J* = 15.8, 7.3 Hz, 1H), 5.13 (t, *J* = 9.2 Hz, 1H), 4.78 (d, *J* = 9.0 Hz, 1H), 4.61 (t, *J* = 7.5 Hz, 1H), 4.50 (d, *J* = 9.4 Hz, 1H), 4.32 (d, *J* = 10.2 Hz, 1H), 4.03 (dd, *J* = 10.2, 7.6 Hz, 1H), 3.87 – 3.73 (m, 2H), 0.82 (t, *J* = 7.2 Hz, 3H). **^{13}NMR** (125 MHz, Chloroform-*d*) δ 175.3, 171.6, 169.5, 144.3, 141.0, 138.4, 136.3, 132.2, 129.1, 128.6, 128.4, 128.3, 128.2, 128.0, 127.7, 127.6, 127.1, 126.7, 126.6, 126.5, 126.1, 84.8, 68.6, 66.1, 57.6, 57.2, 52.4, 13.4. **IR** (film) ν_{max} 3472, 3062, 2925, 2260, 1951, 1887, 1775, 1719, 1603, 1382, 1205, 747 cm^{-1}; **HRMS** (ES+): Exact mass calcd for $C_{42}H_{36}N_4O_5$ $[M+Na]^+$ 699.2578; Found 699.2564.

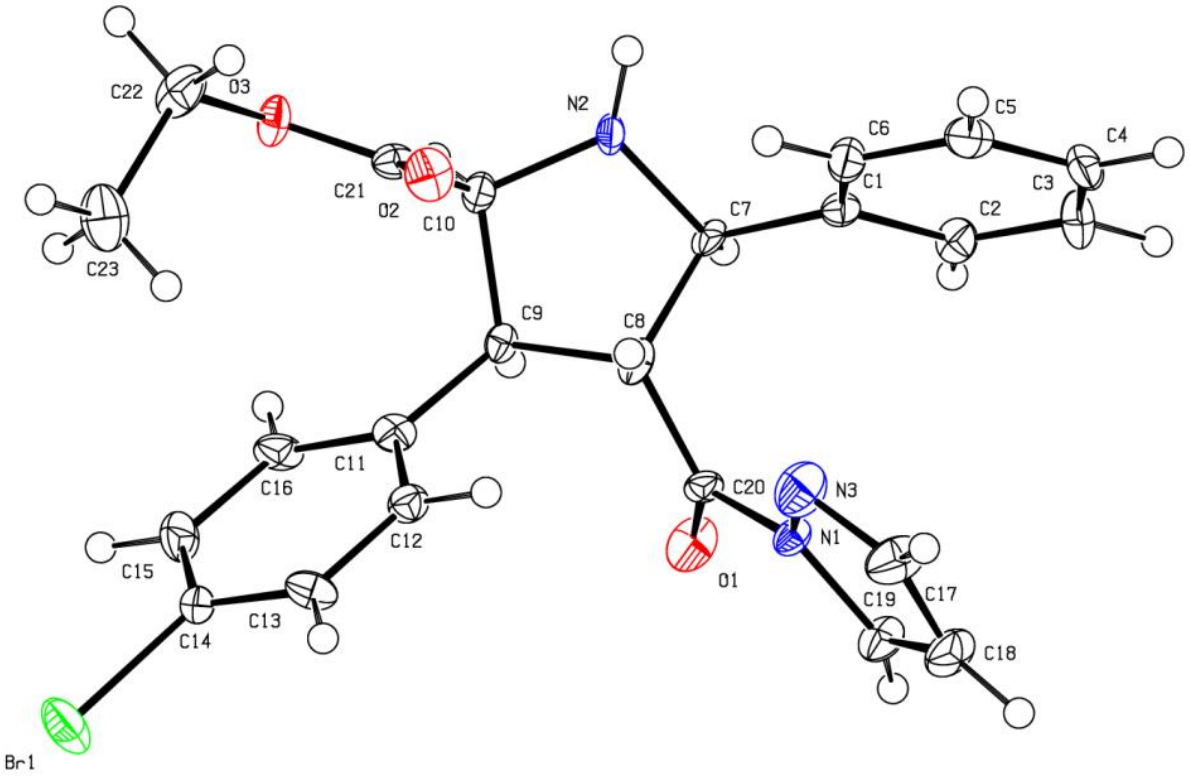


8

References:

[1] a) X. Ding, C. Tian, Y. Hu, L. Gong, E. Meggers, *Eur. J. Org. Chem.* **2016**, 887; b) Y. Zheng, Y. Yao, L. Ye, Z. Shi, X. Li, Z. Zhao, X. Li, *Tetrahedron* **2016**, *72*, 973.

[2] a) L. Dai, D. Xu, L. W. Tang, Z. M. Zhou, *Chem. Cat. Chem.* **2015**, *7*, 1078; (b) A. López-Pérez, J. Adrio, J. C. Carretero, *Angew. Chem. Int. Ed.* **2009**, *48*, 340; c) I. Oura, K. Shimizu, K. Ogata,S.-I. Fukuzawa, *Org. Lett.* **2010**, *12*, 175.

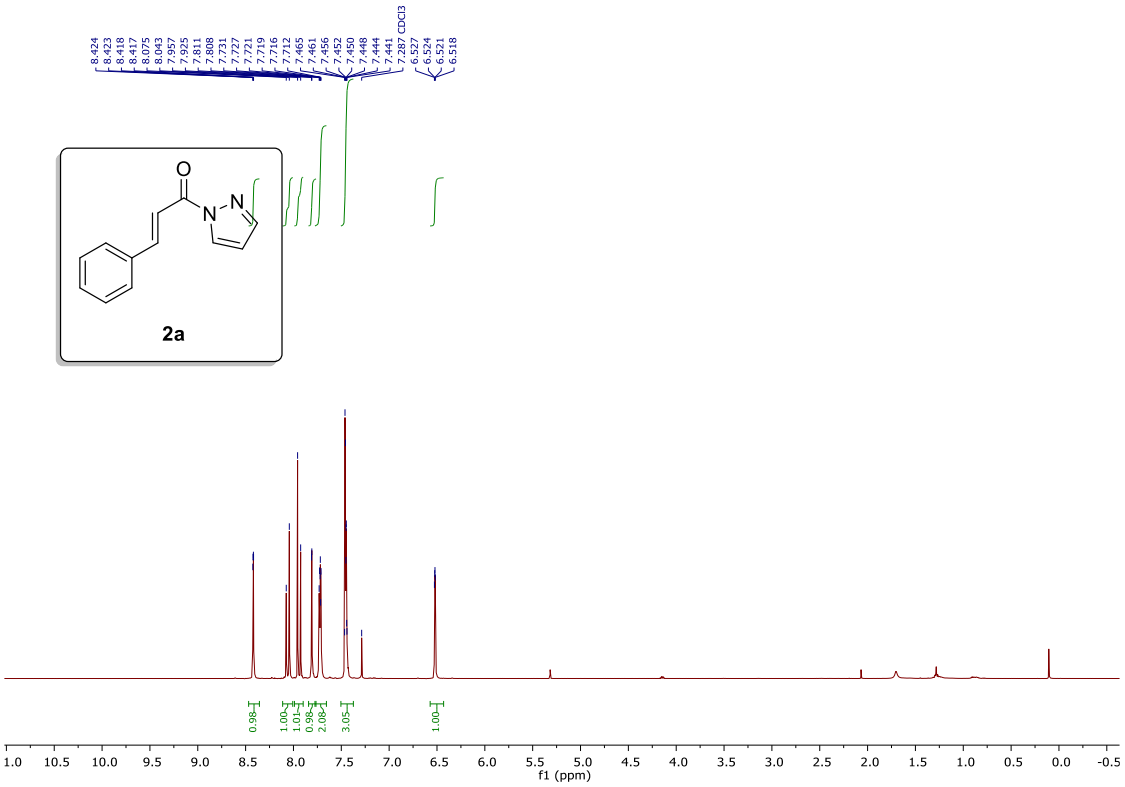


Crystal structure (with 50% ellipsoid probability) of **4ba(**CCDC No. **1578386)**

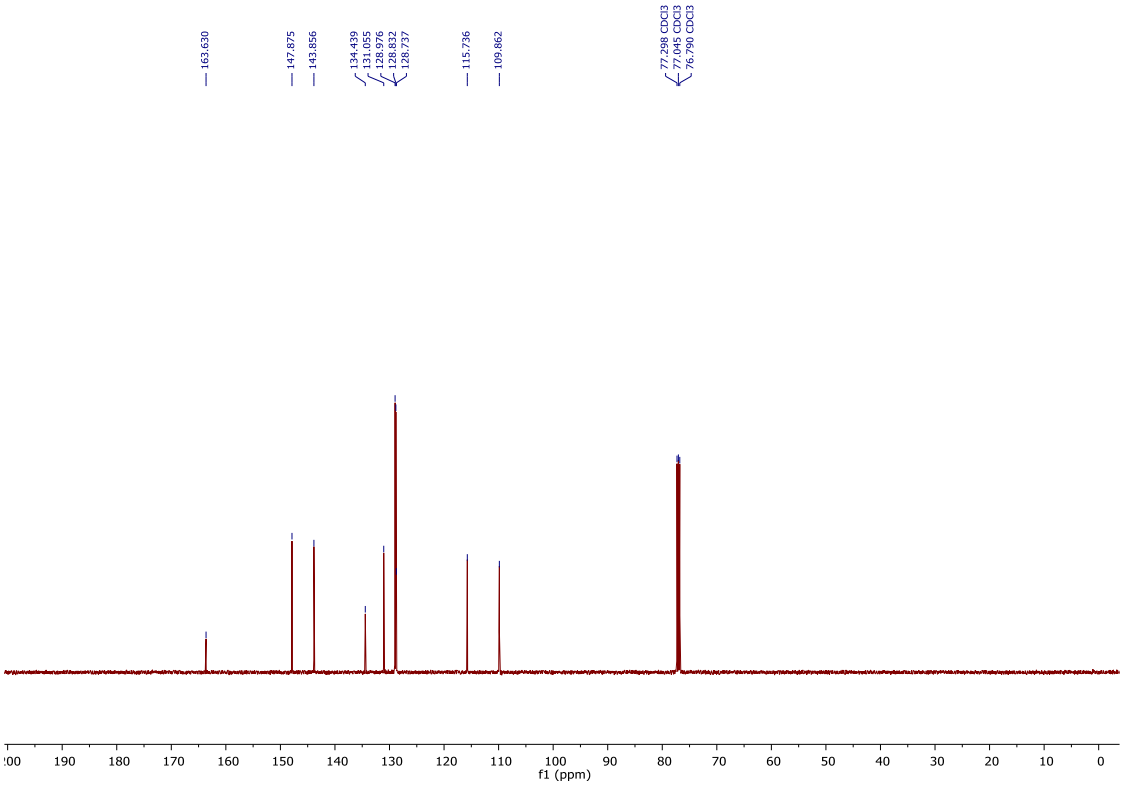
Table: Crystallographic data and structure refinement for **4ba** (CCDC No. **1578386**)

Empirical formula	$C_{23}H_{22}BrN_3O_3$
Formula weight	468.35
Temperature/K	140
Crystal system	triclinic
Space group	P_1
a/Å	5.6515(12)
b/Å	8.034(2)
c/Å	12.082(3)
α/°	81.886(8)
β/°	88.585(9)
γ/°	73.865(9)
Volume/Å^3	521.6(2)
Z	1
ρ_{calc}g/cm^3	1.491
μ/mm^{-1}	2.0
F(000)	240
Crystal size/mm^3	0.29 × 0.21 × 0.12
Radiation	MoKα (λ = 0.71073)
2 θ range for data collection/°	5.92 to 61.16
Index ranges	$-8 \leq h \leq 6$, $-10 \leq k \leq 10$, $-14 \leq l \leq 17$
Reflections collected	3016
Independent reflections	2978 [R_{int} = 0.0945, R_{sigma} = 0.1550]
Data/restraints/parameters	2978/3/271
Goodness-of-fit on F^2	0.926
Final R indexes [$I \geq 2\sigma$ (I)]	R_1 = 0.0615, wR_2 = 0.1341
Final R indexes [all data]	R_1 = 0.0922, wR_2 = 0.1497
Largest diff. peak/hole / e Å^{-3}	0.501/-0.585
Flack parameter	0.031(15)

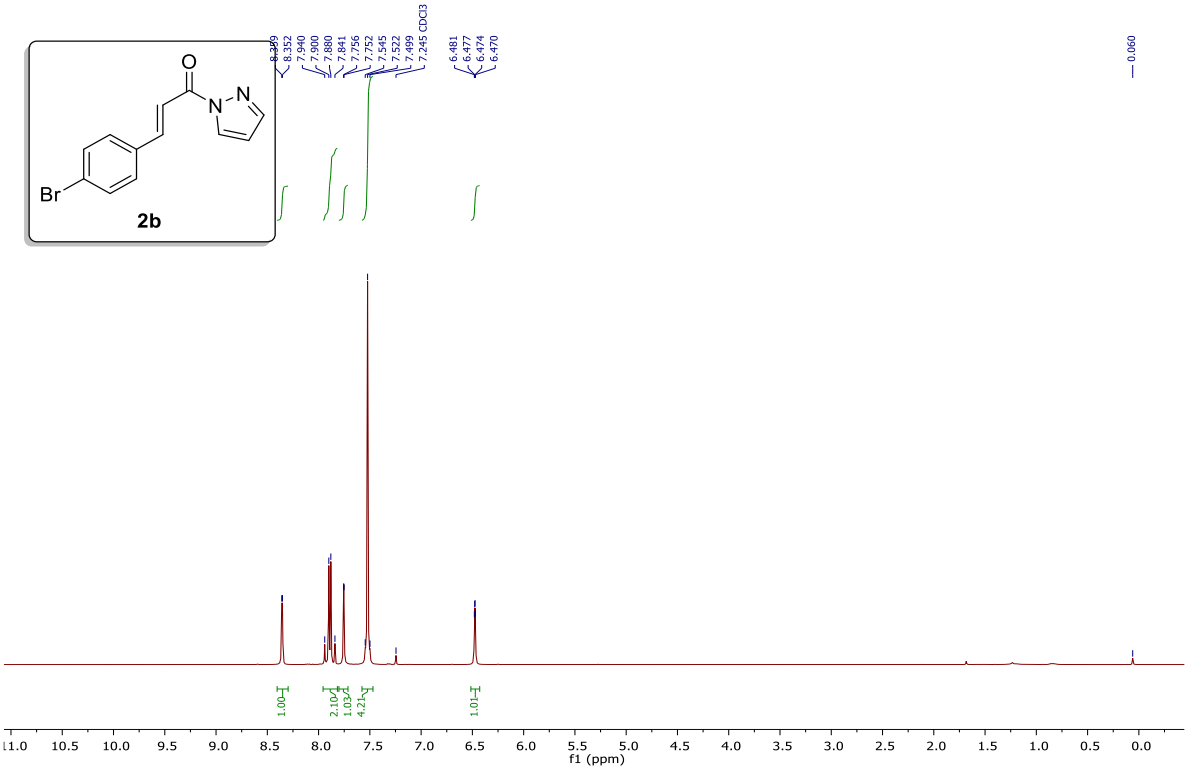
^{1}H NMR and ^{13}C NMR spectra of products:



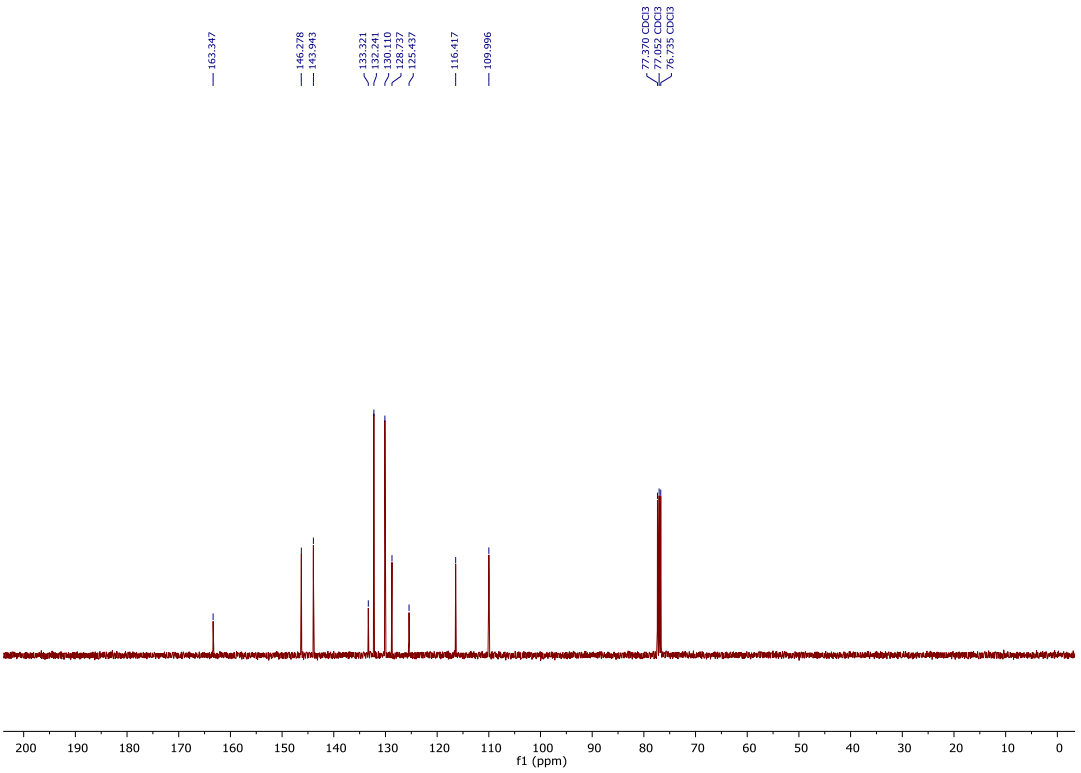
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2a**



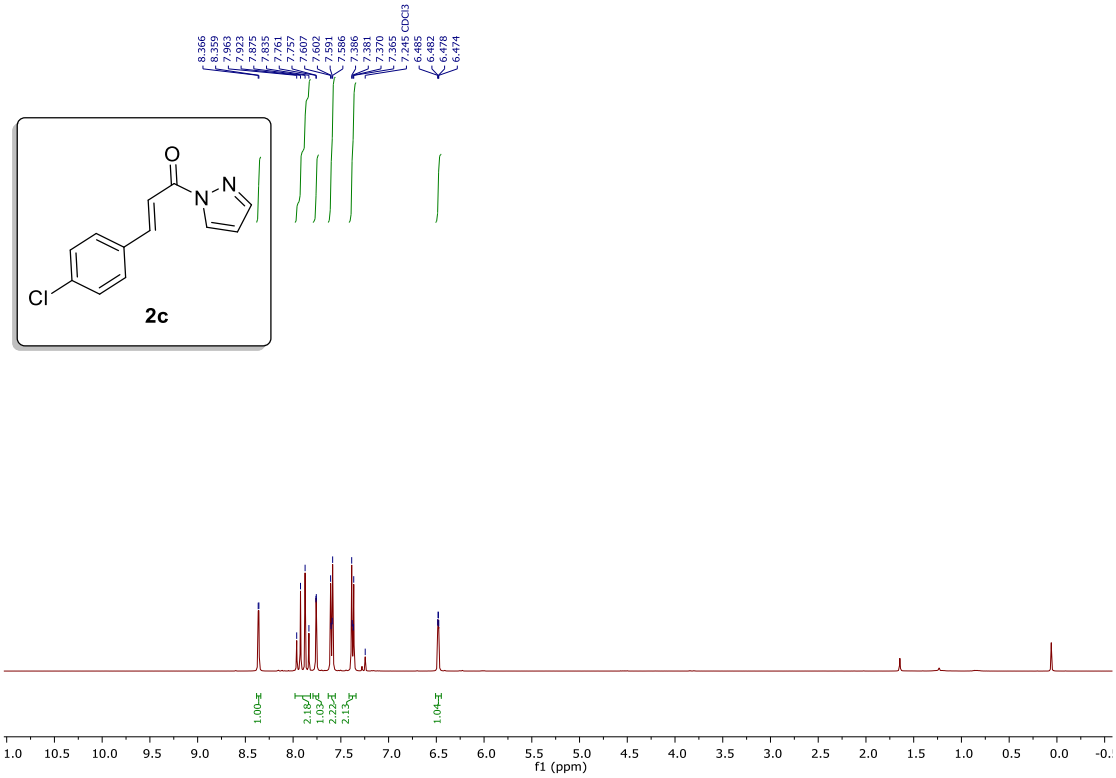
^{13}C NMR (125 MHz, CDCl3) of compound **2a**



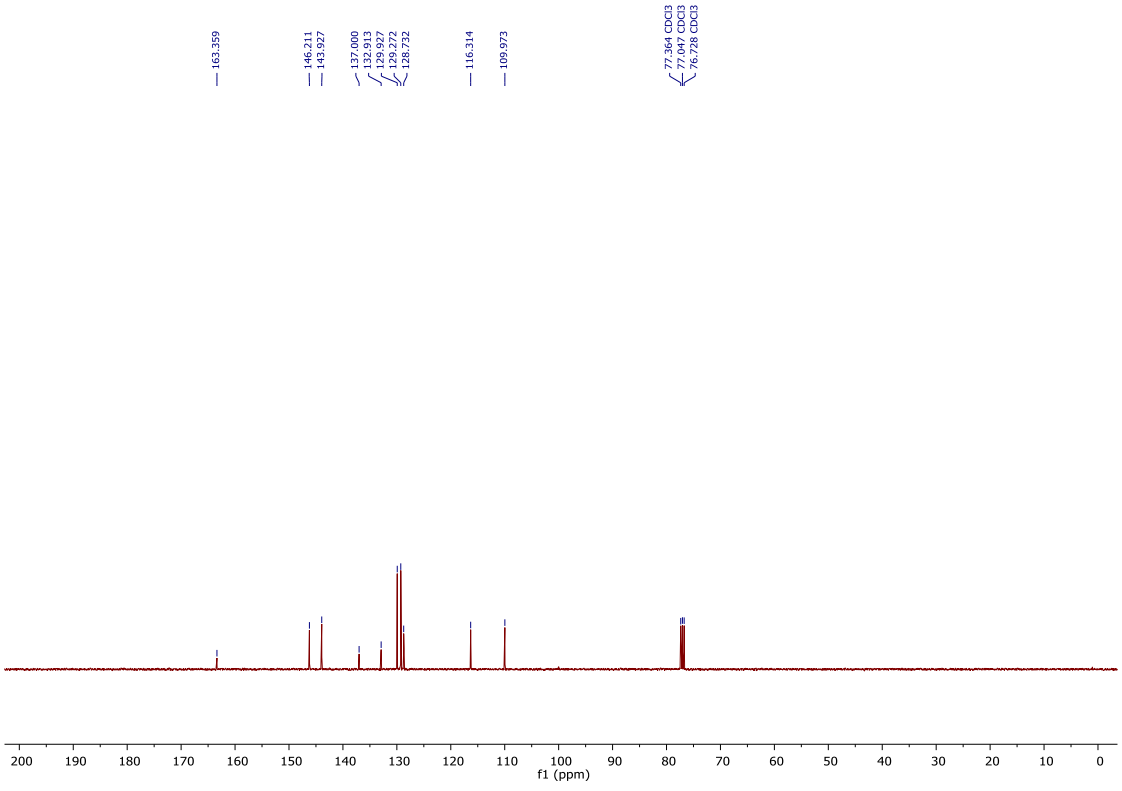
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2b**



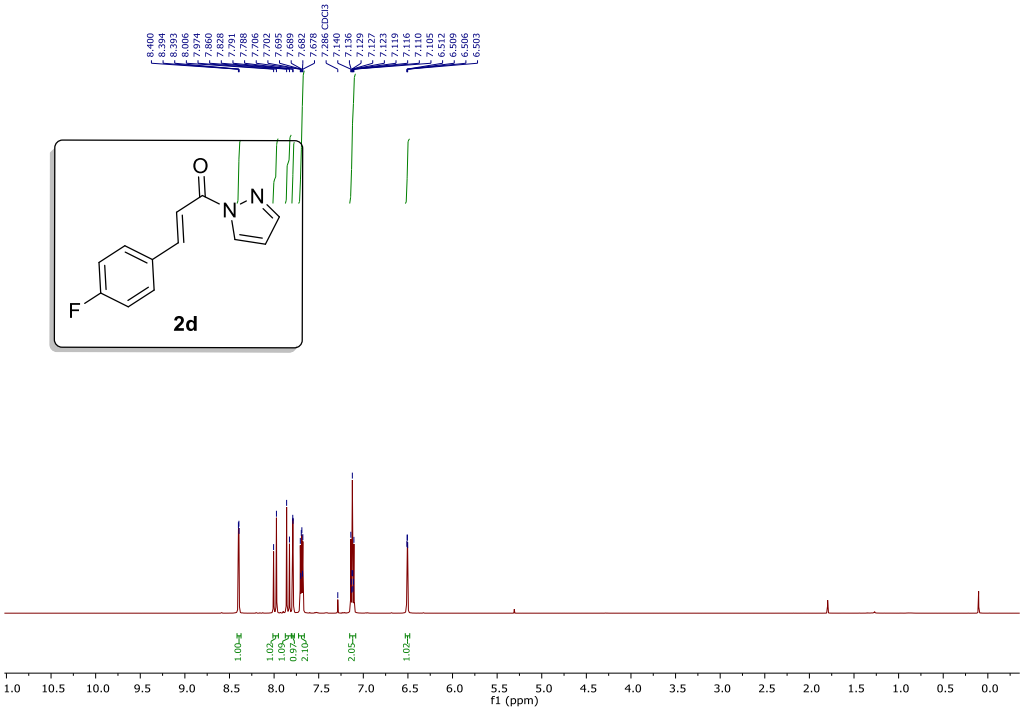
^{13}C NMR (100 MHz, $CDCl_3$) of compound **2b**



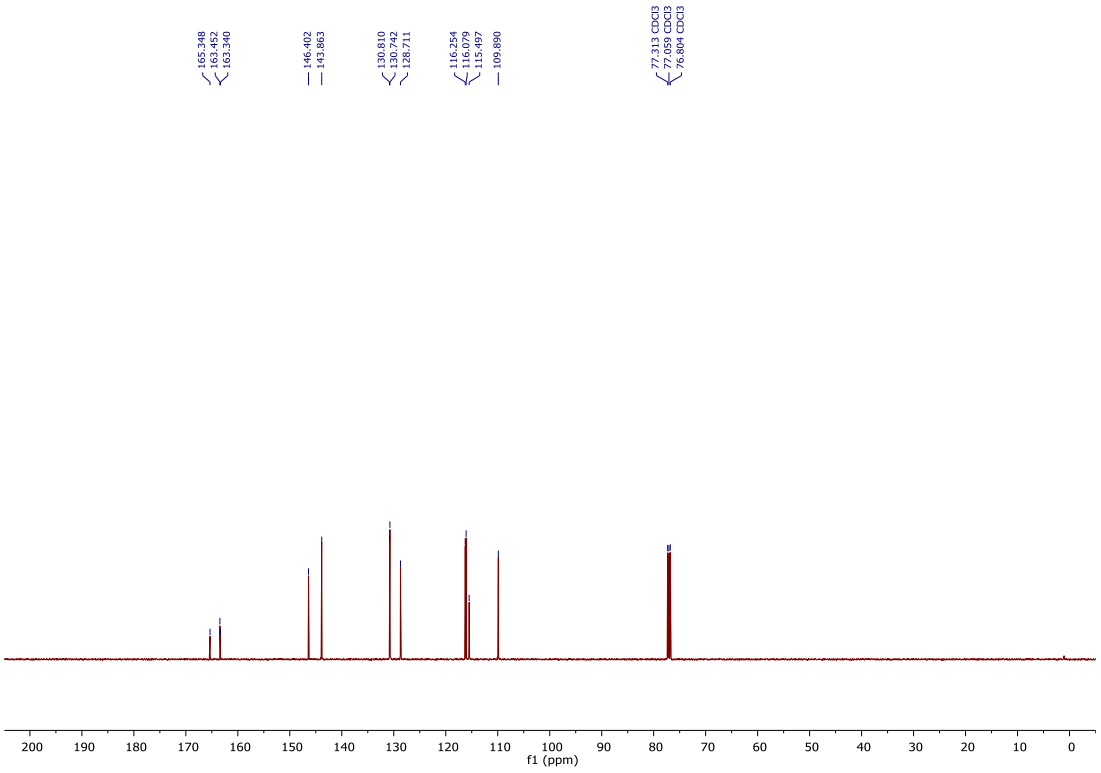
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2c**



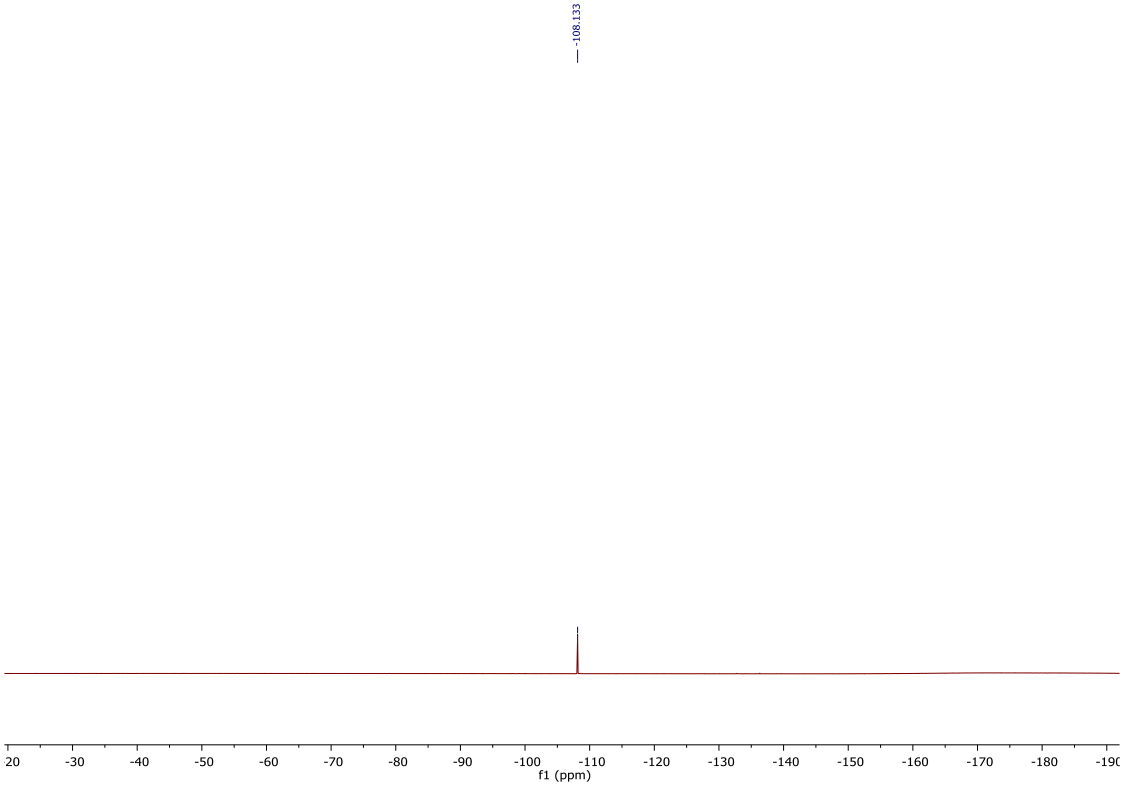
^{13}C NMR (100 MHz, $CDCl_3$) of compound **2c**



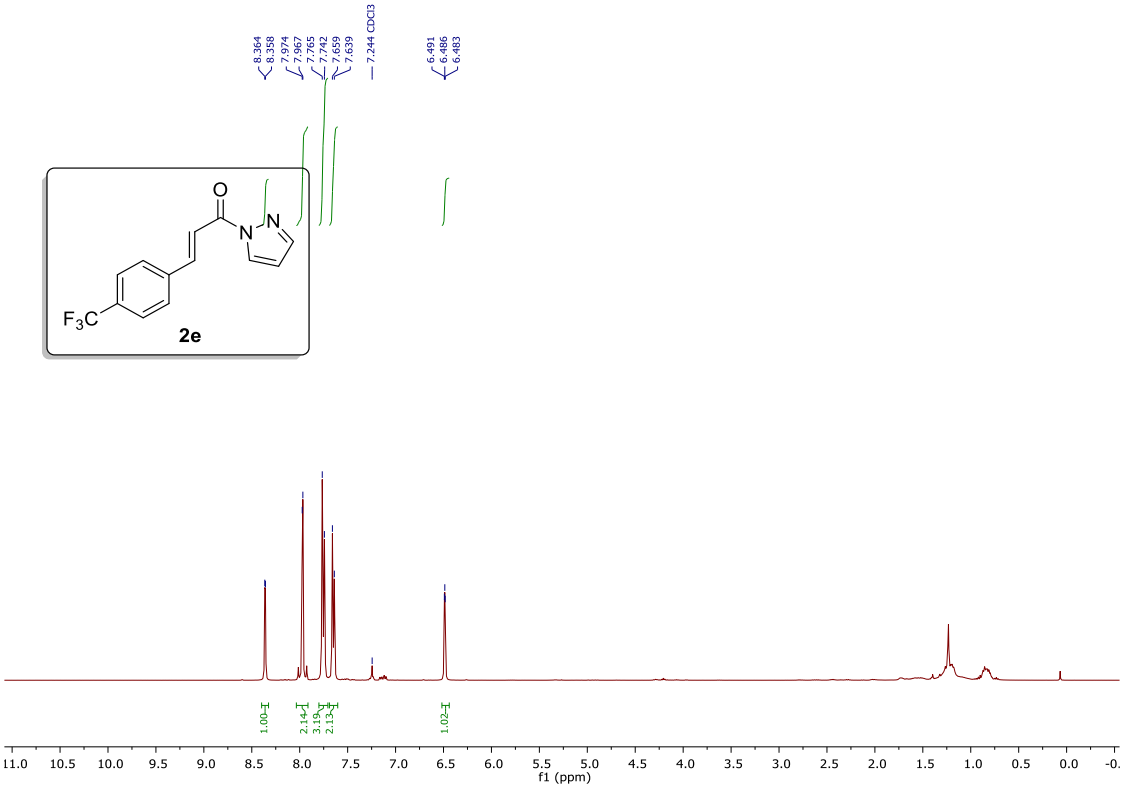
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2d**



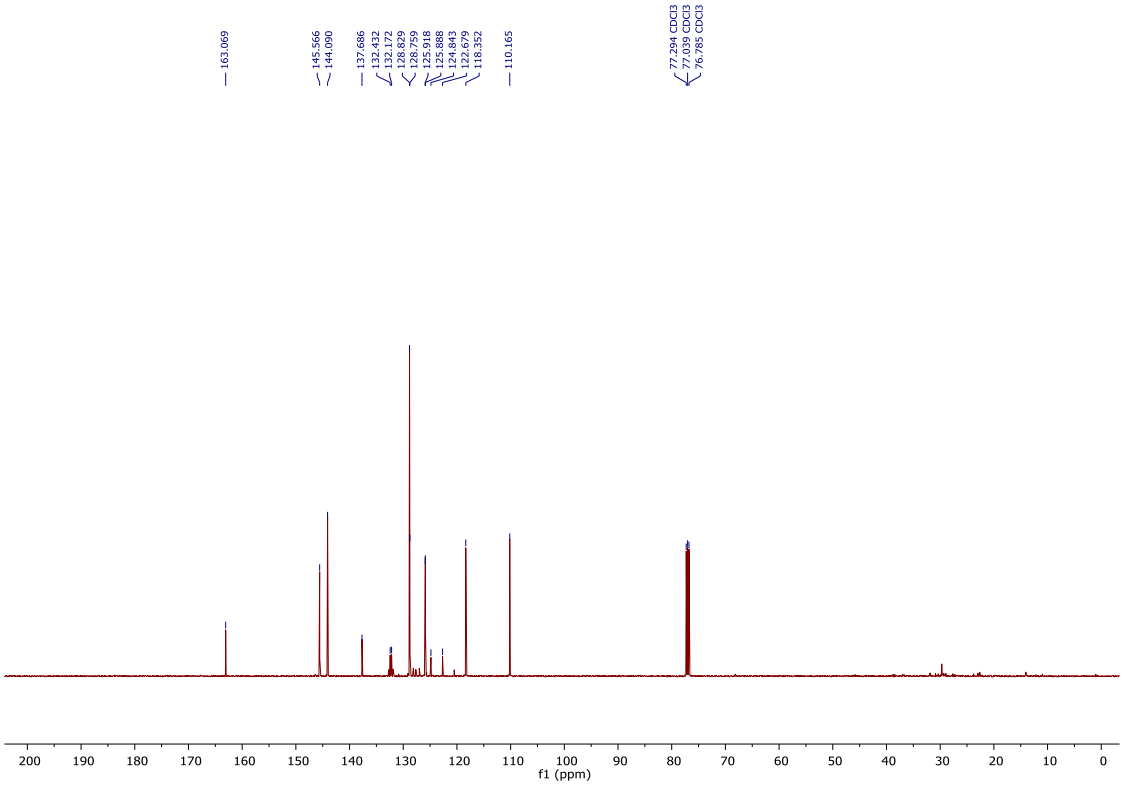
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2d**



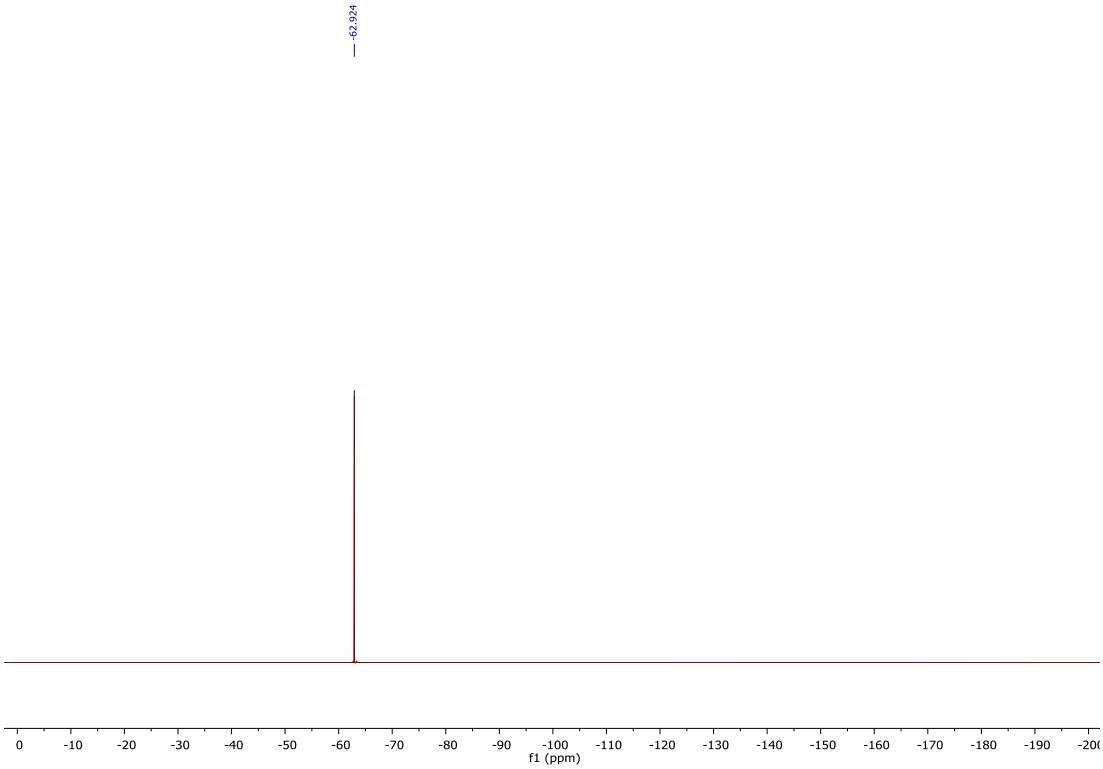
^{19}F NMR (470 MHz, $CDCl_3$) of compound **2d**



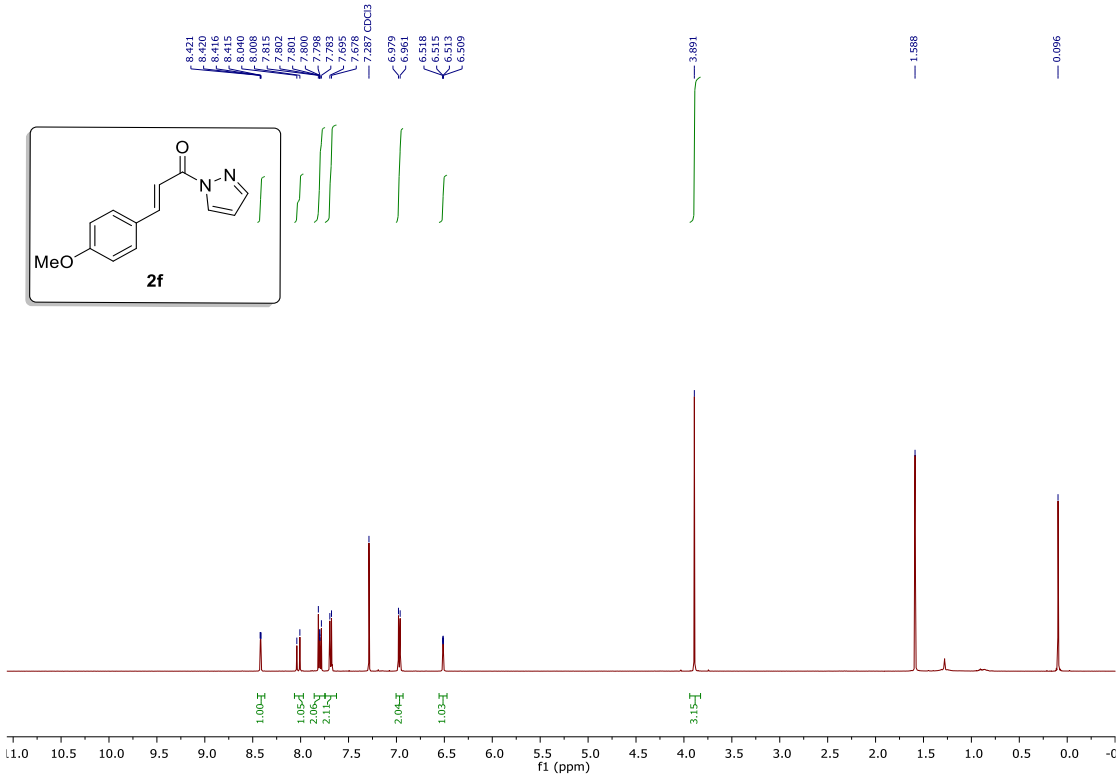
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2e**



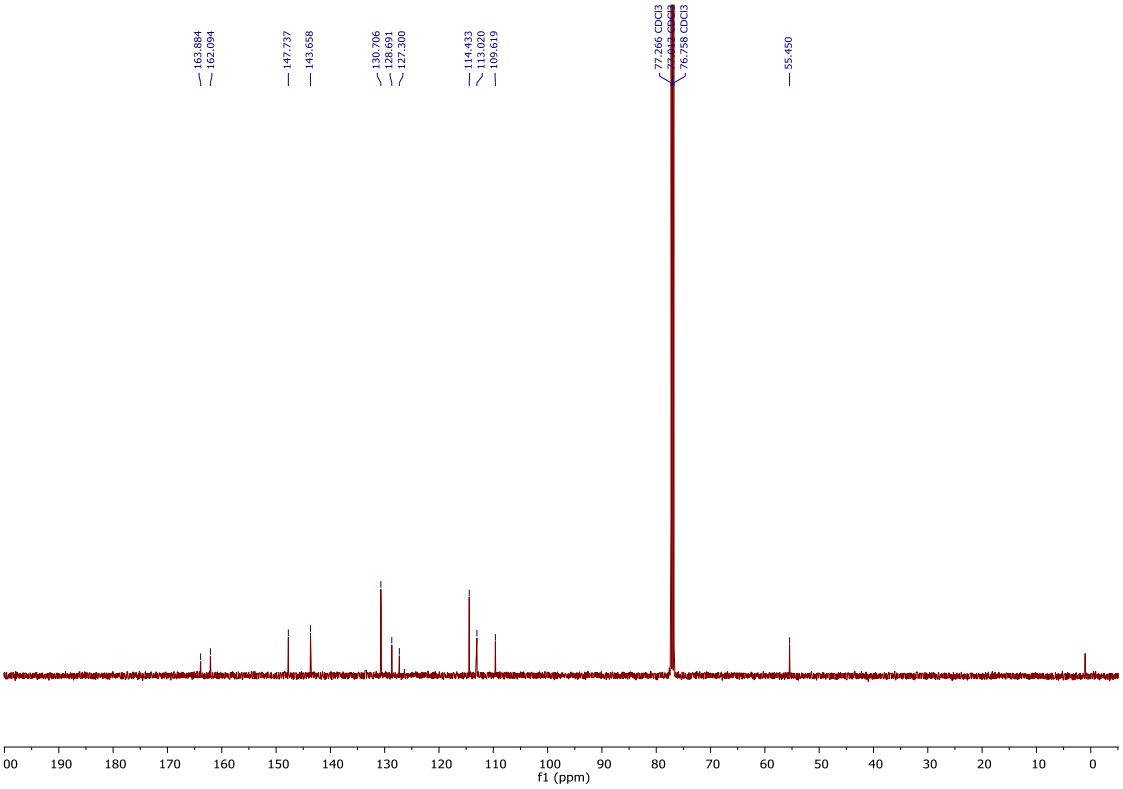
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2e**



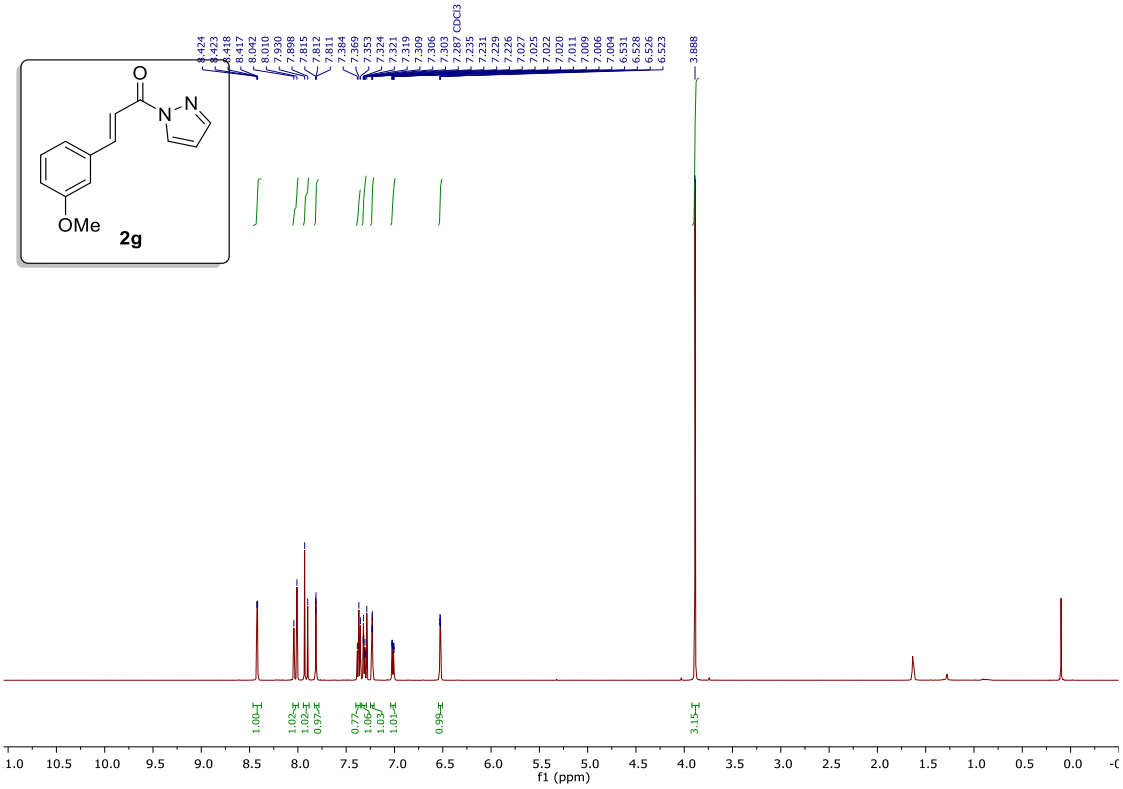
^{19}F NMR (470 MHz, $CDCl_3$) of compound **2e**



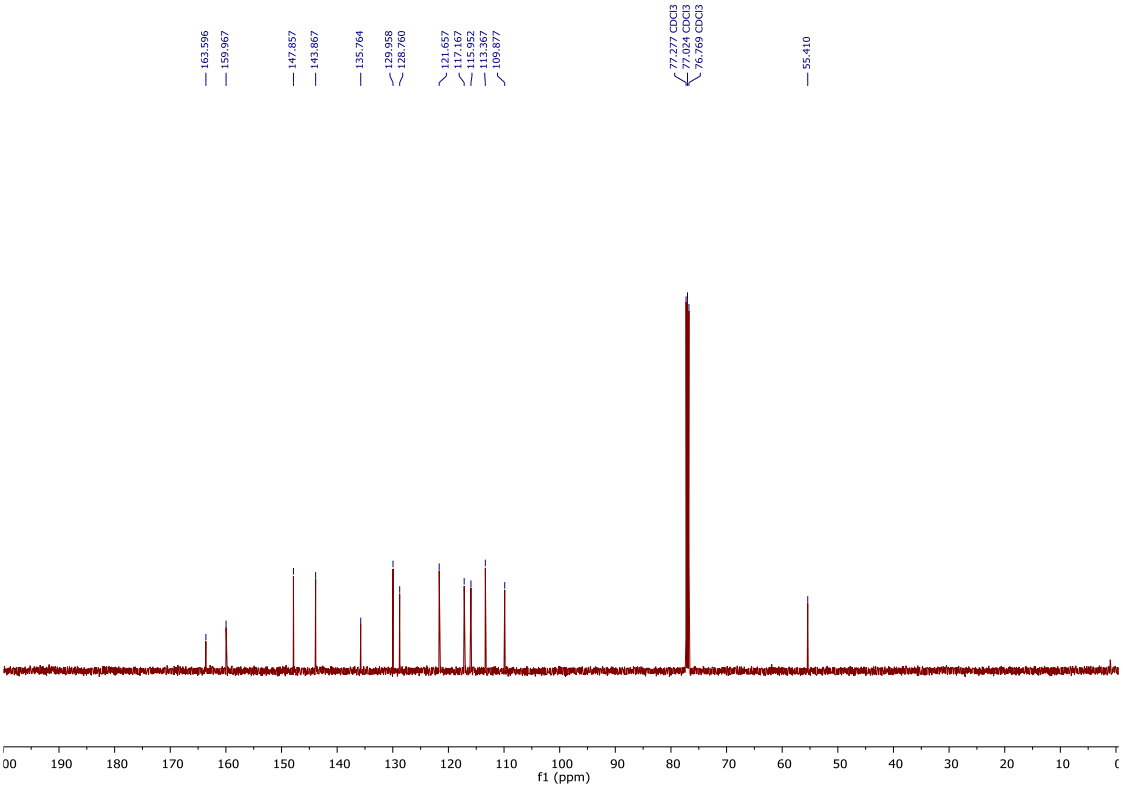
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2f**



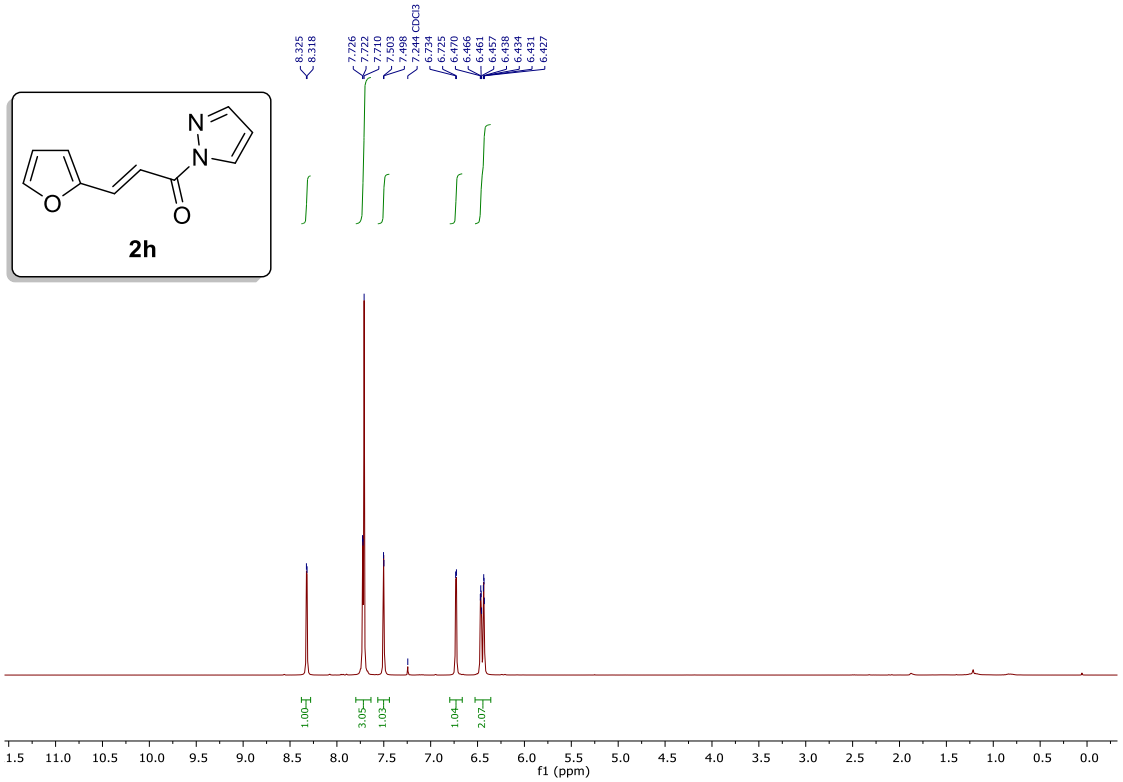
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2f**



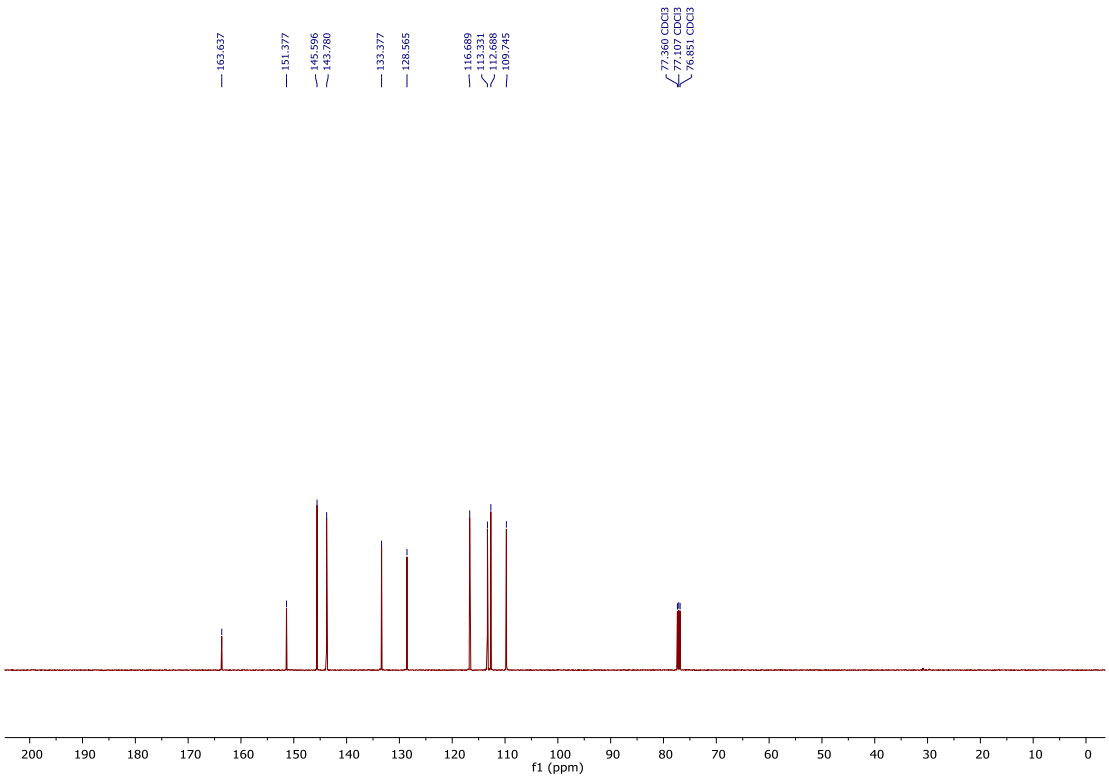
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2g**



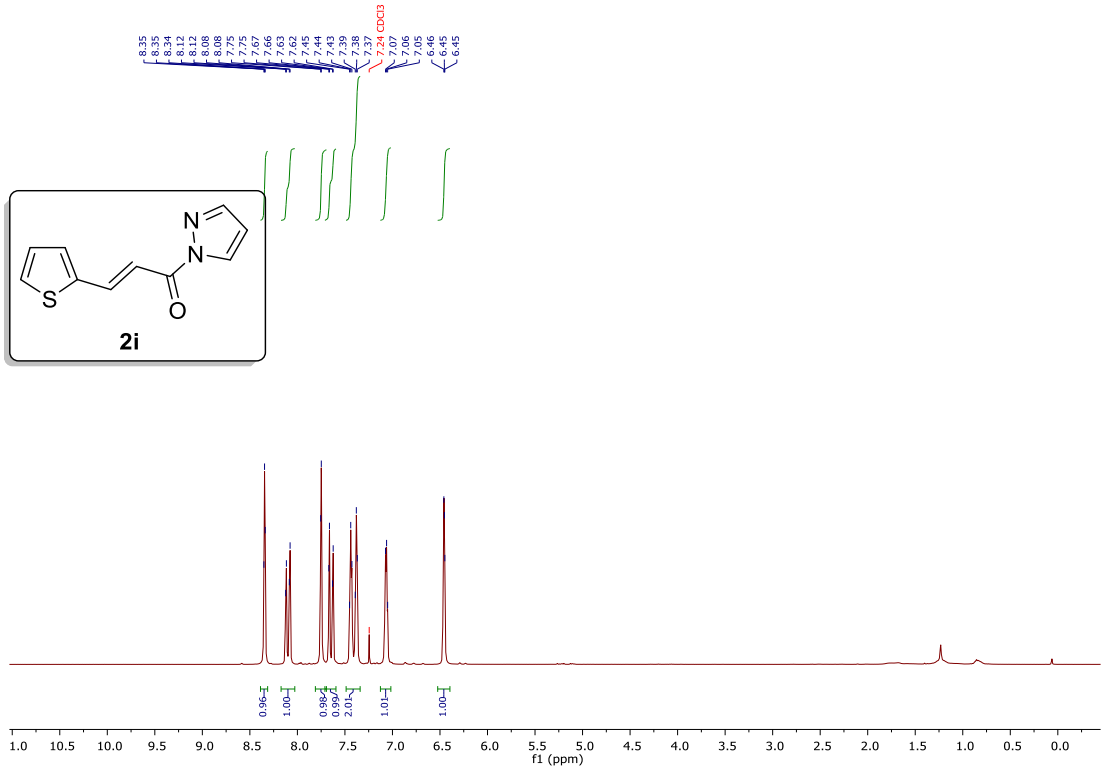
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2g**



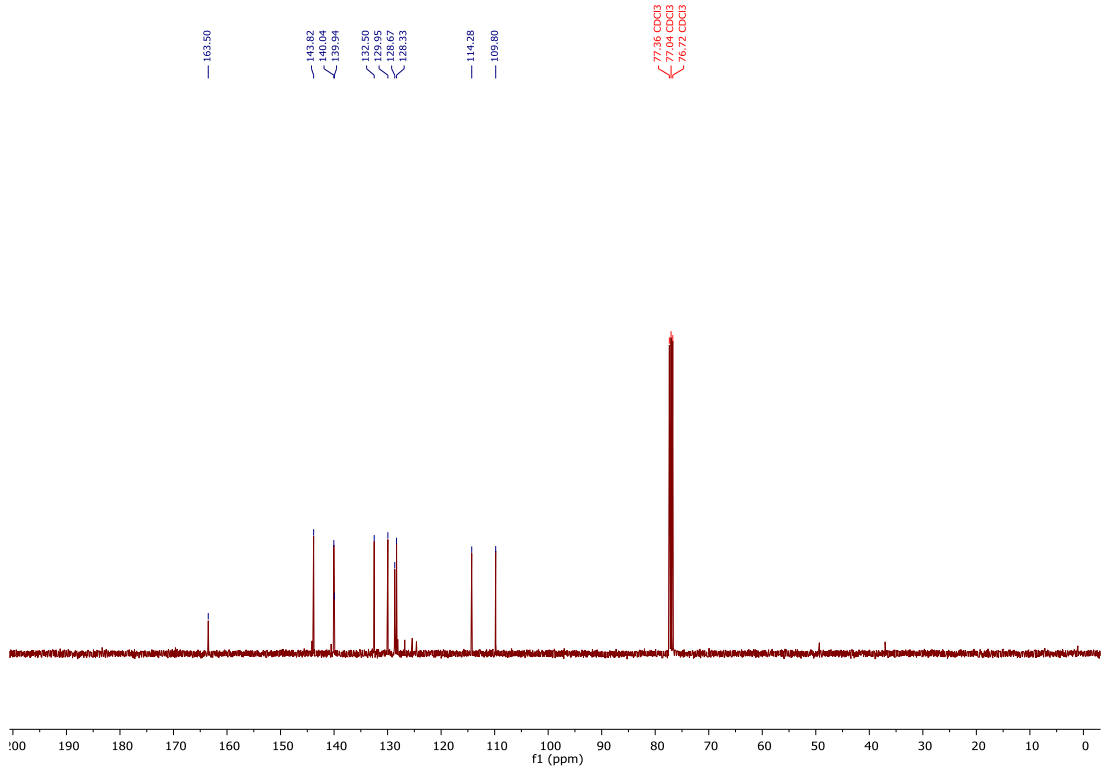
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2h**



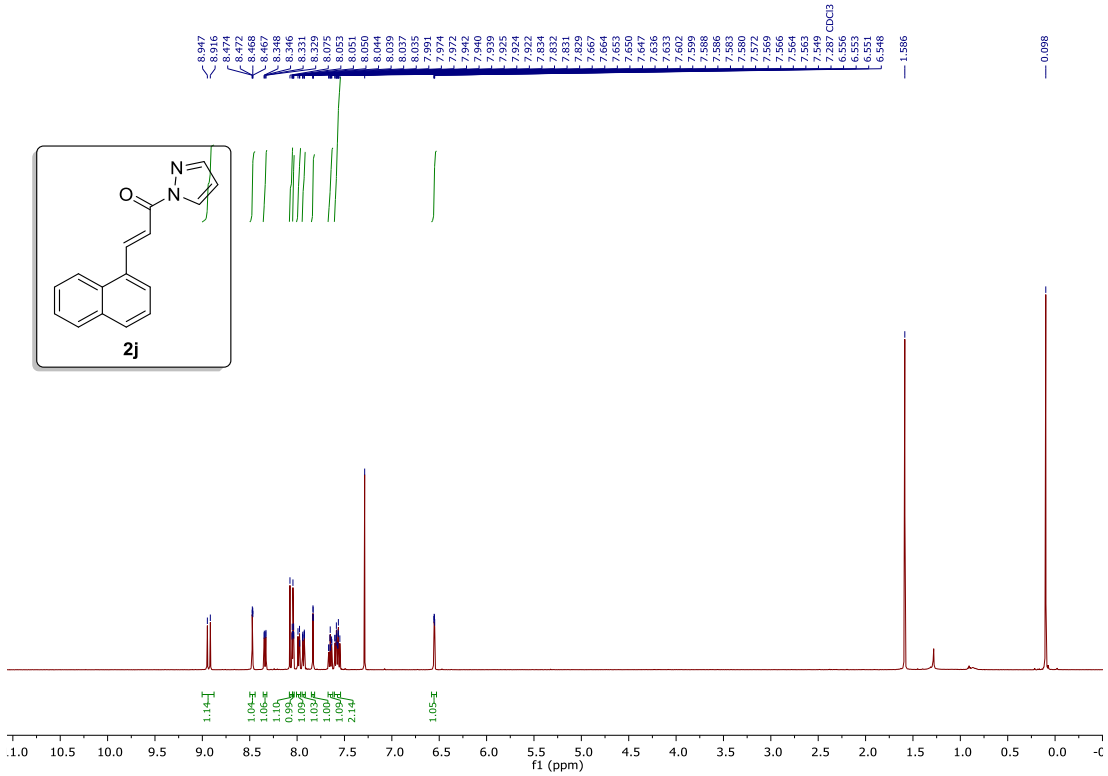
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2h**



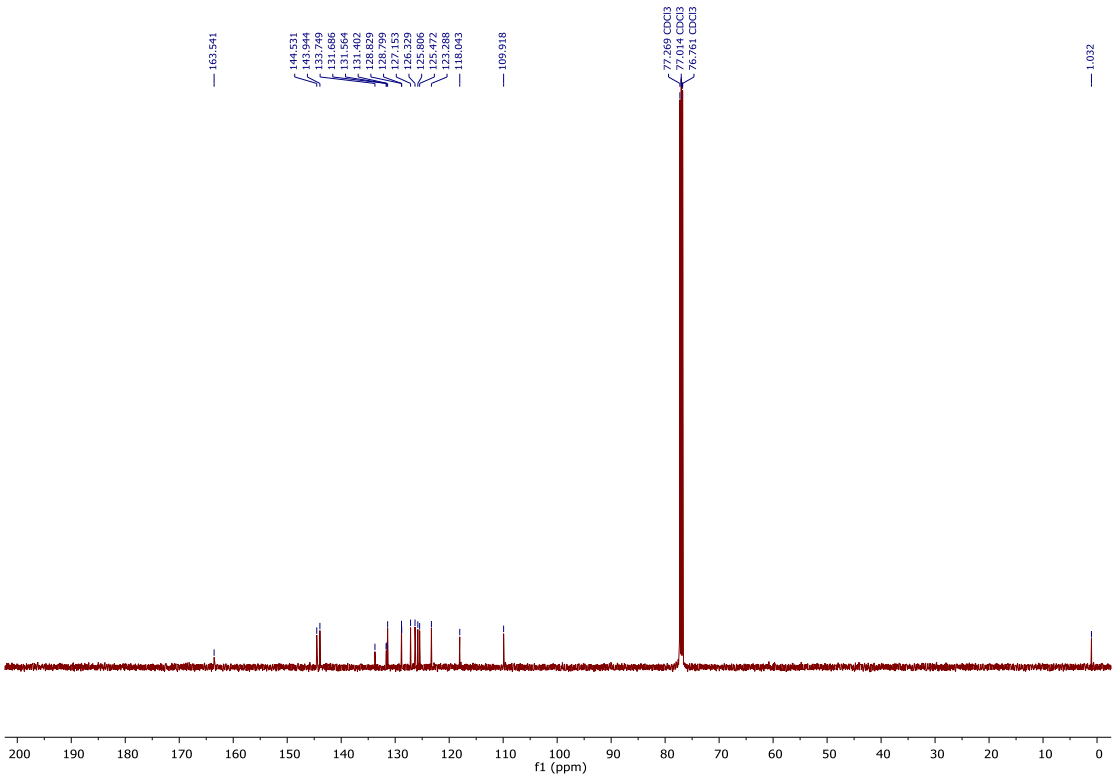
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2j**



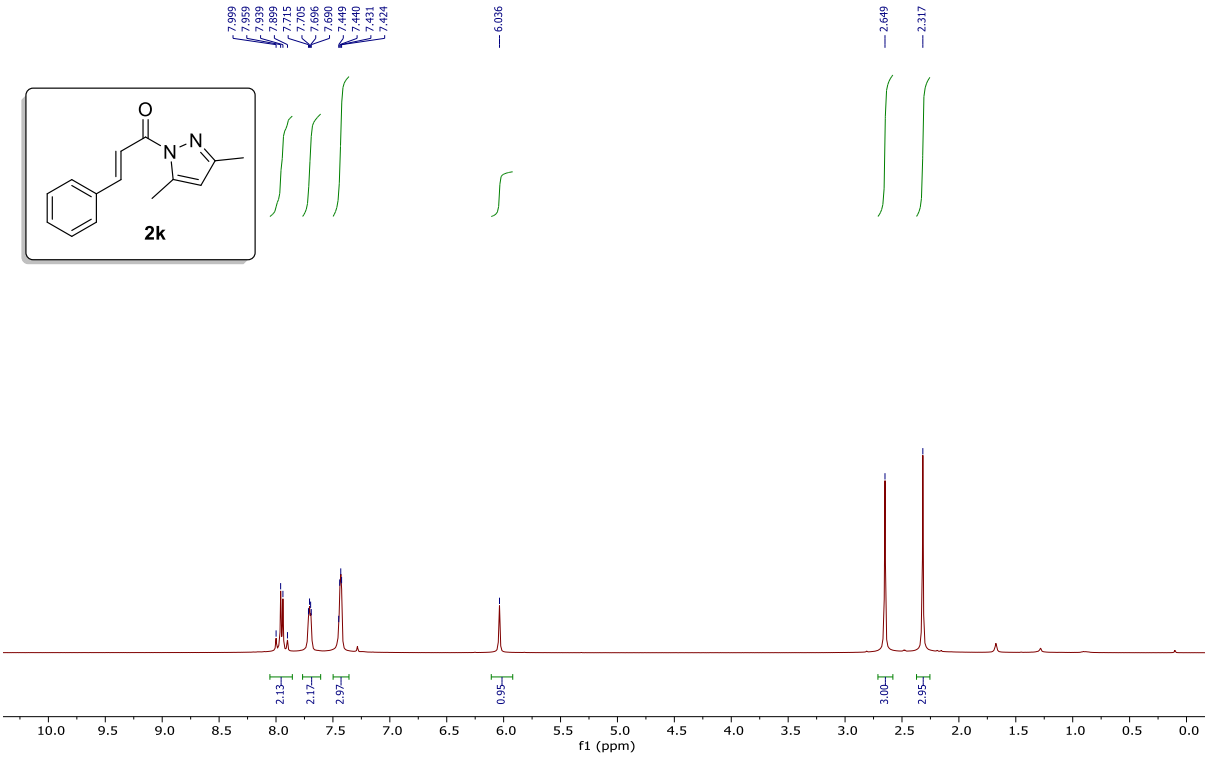
^{13}C NMR (100 MHz, $CDCl_3$) of compound **2j**



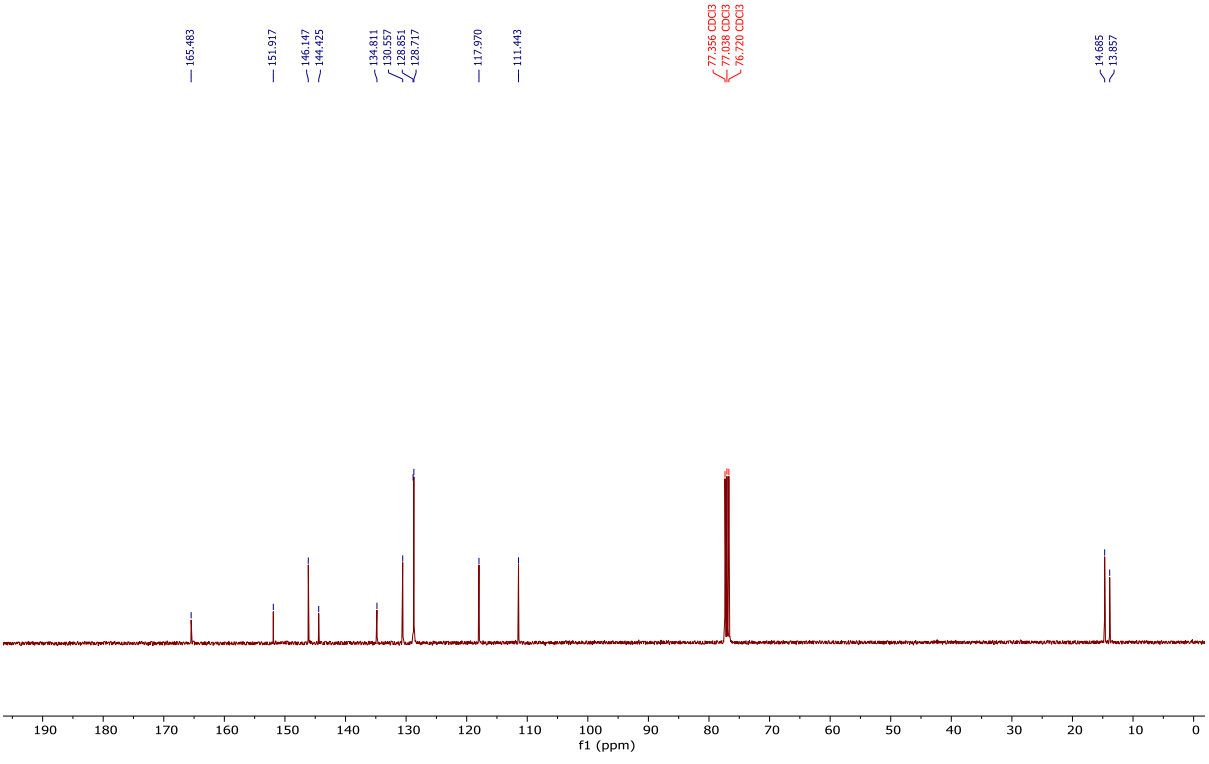
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2j**



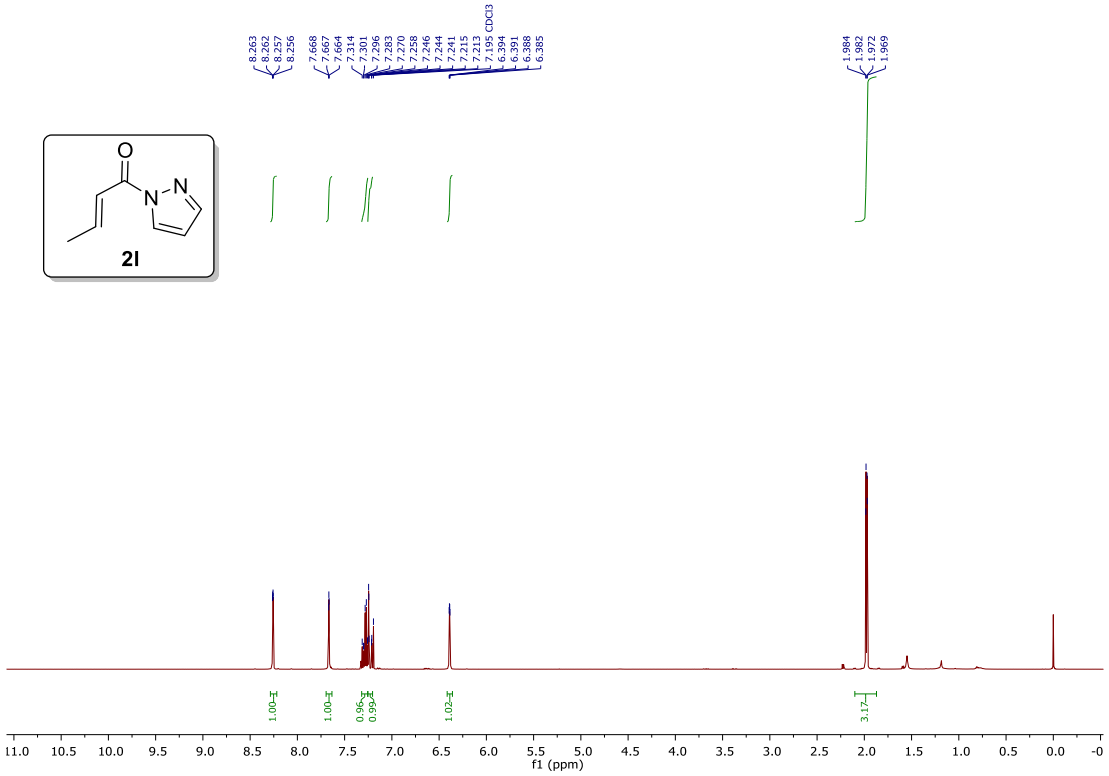
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2j**



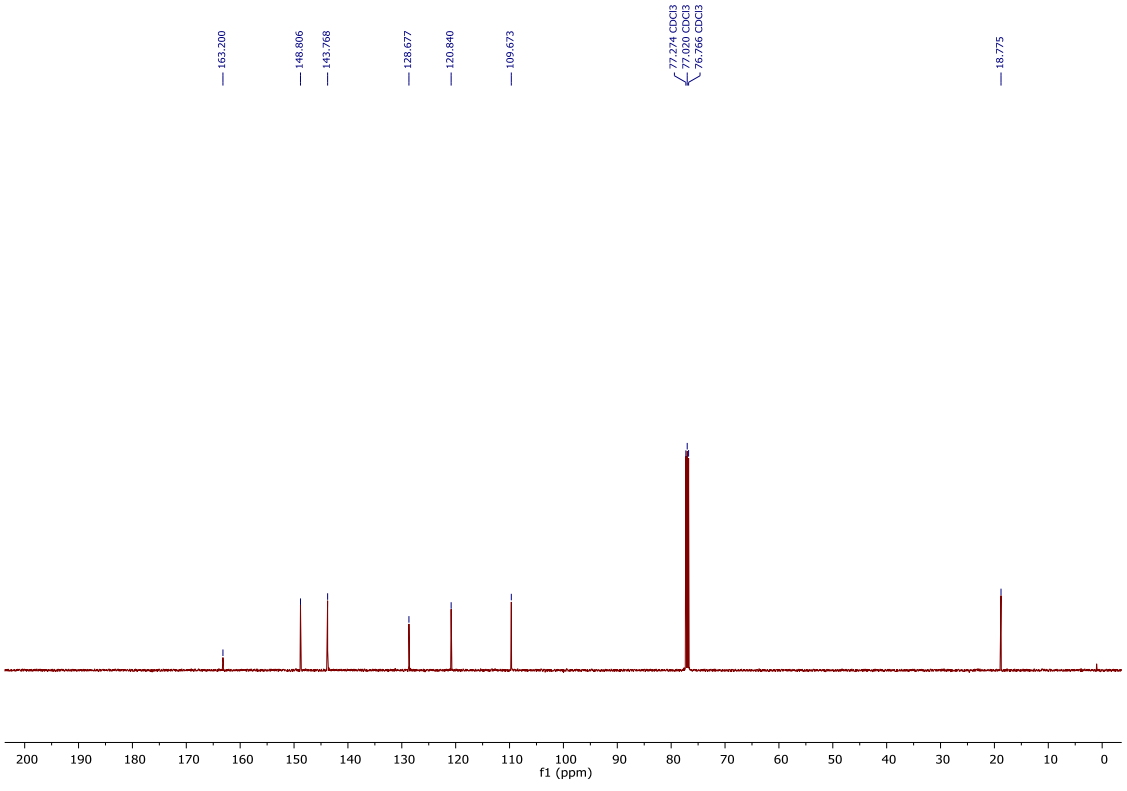
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2k**



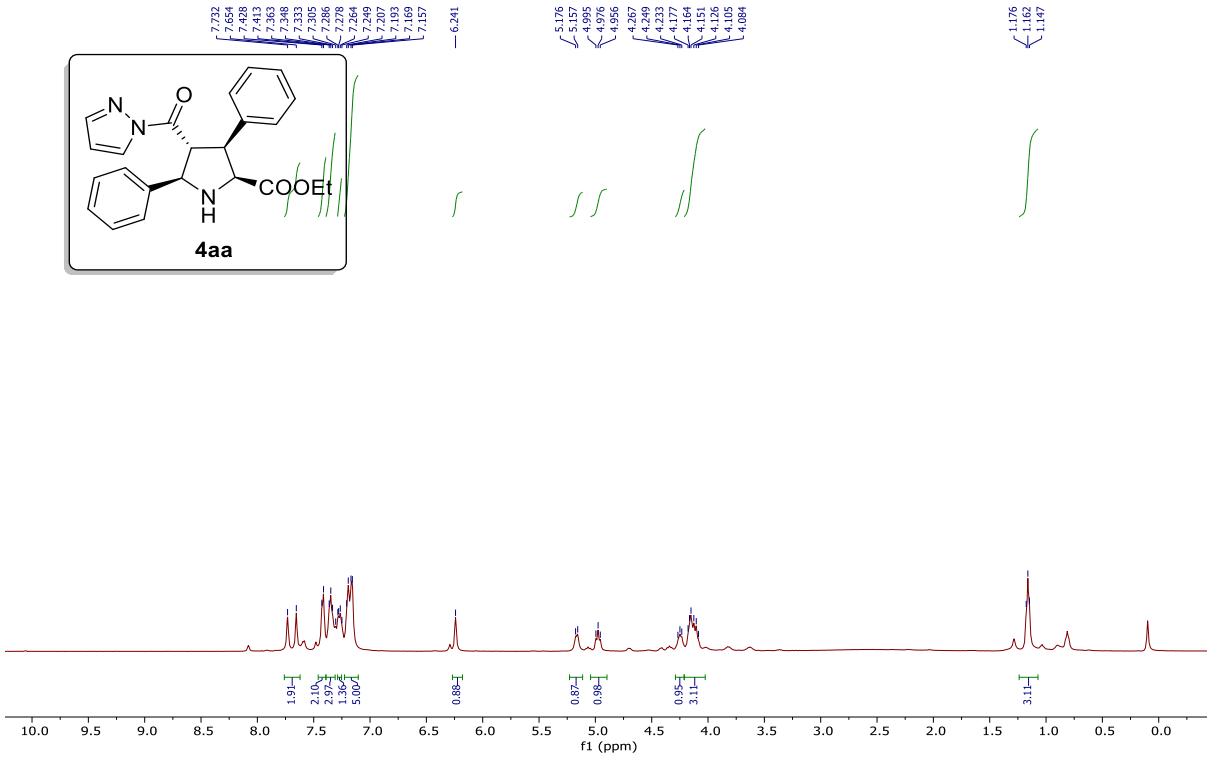
^{13}C NMR (100 MHz, $CDCl_3$) of compound **2k**



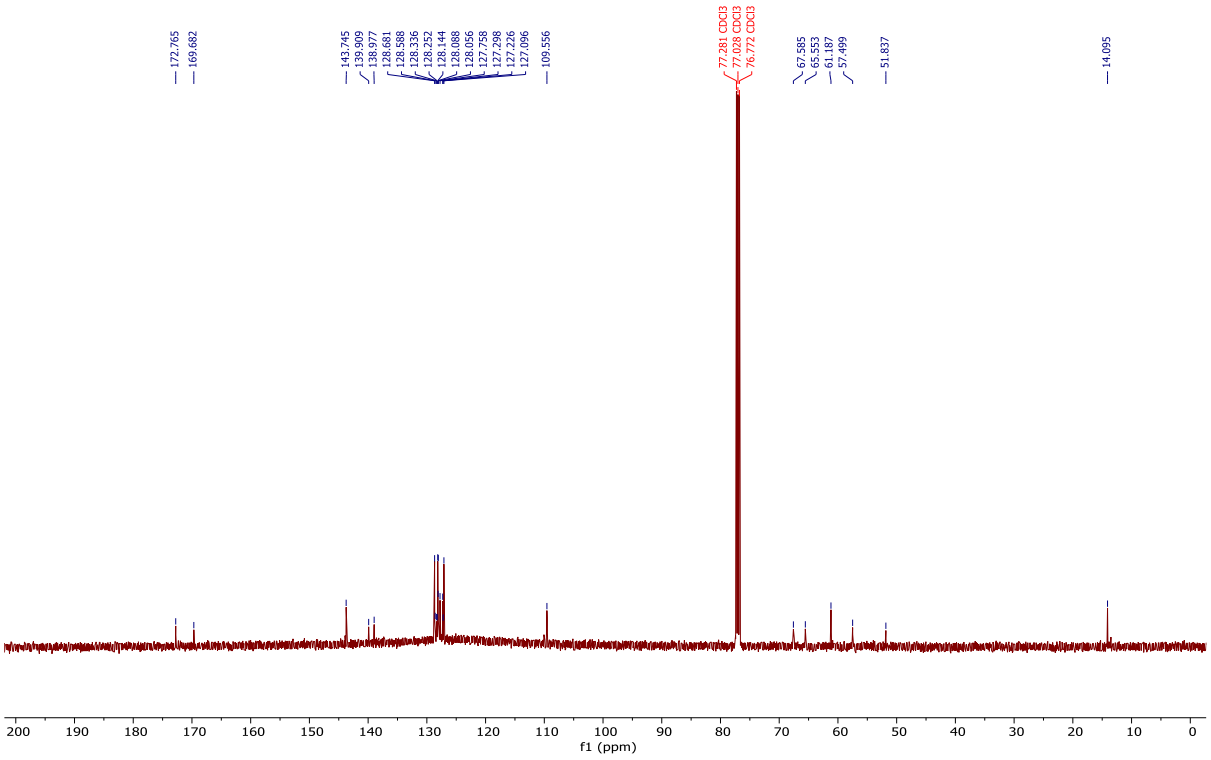
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2l**



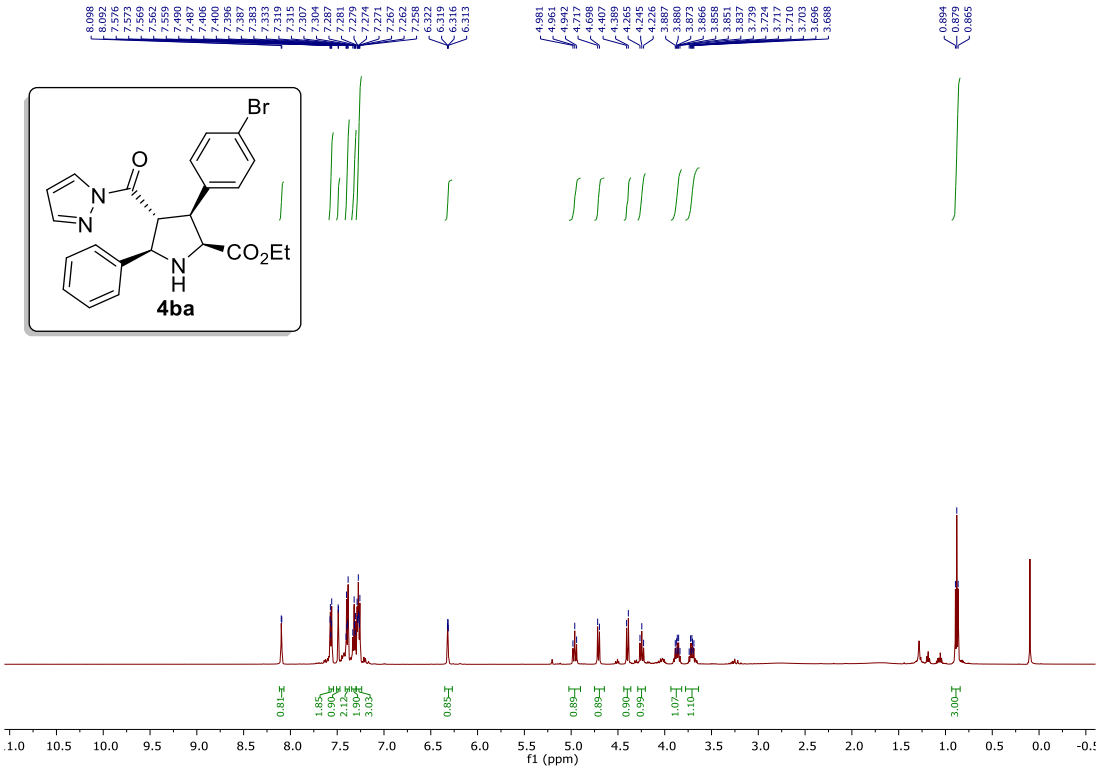
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2l**



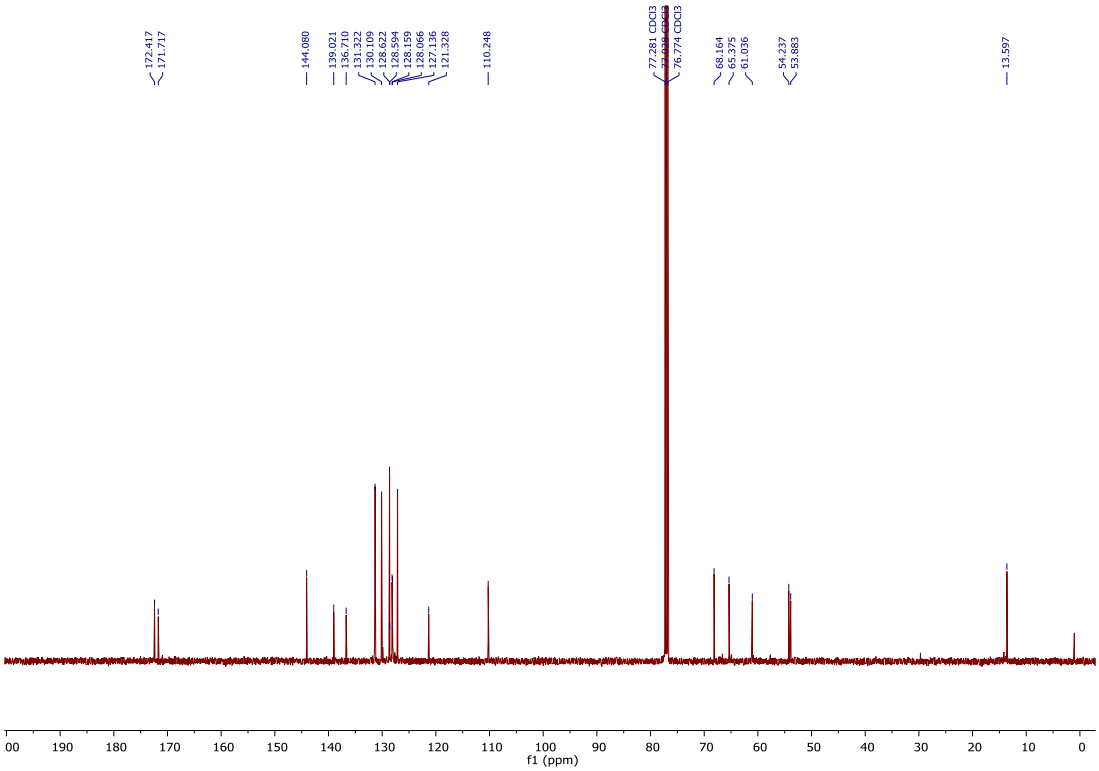
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4aa**



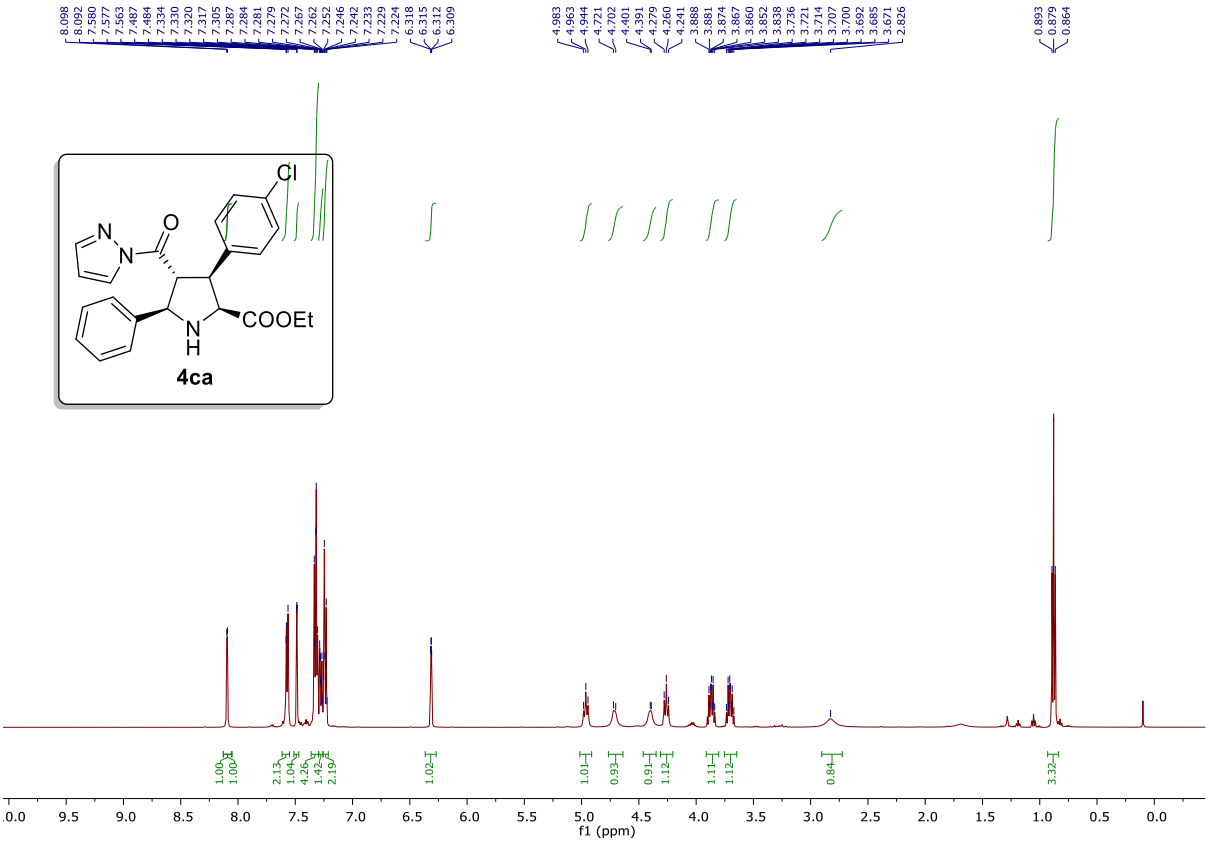
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4aa**



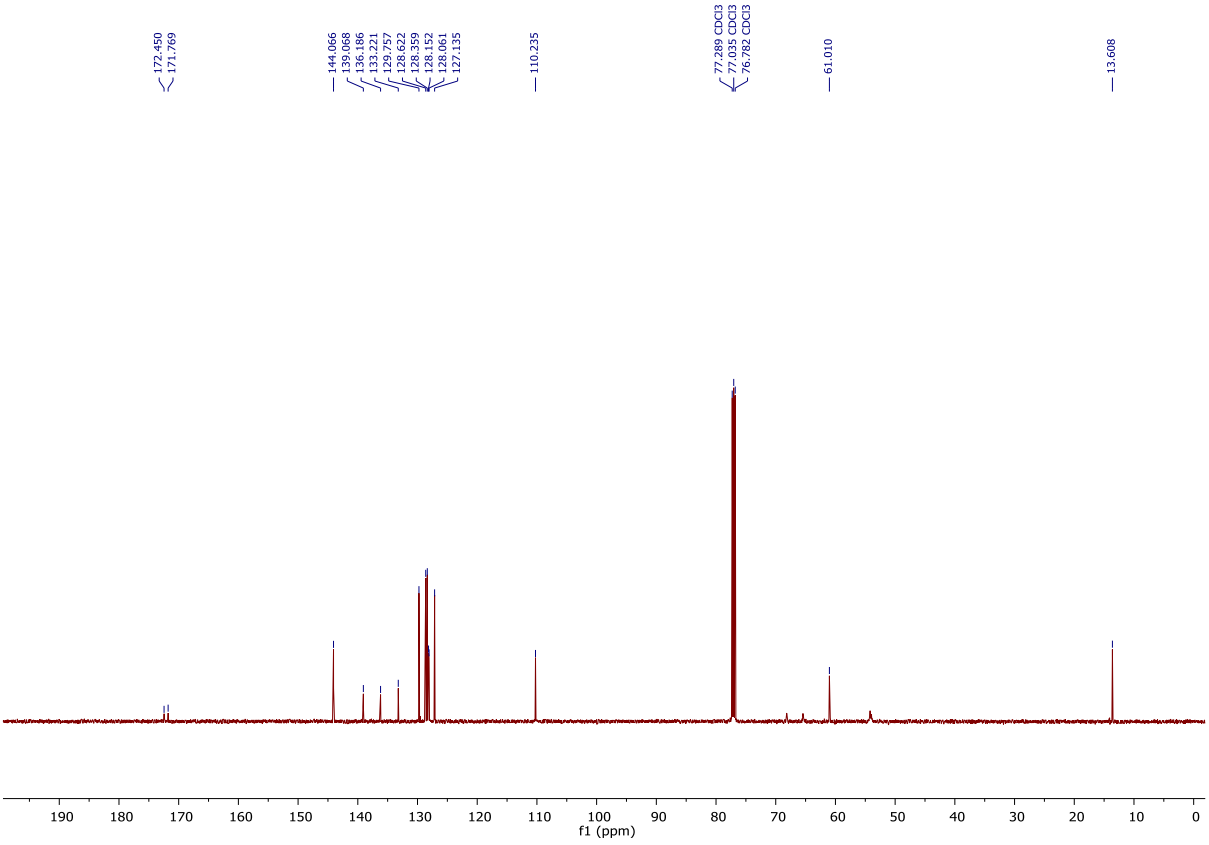
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ba**



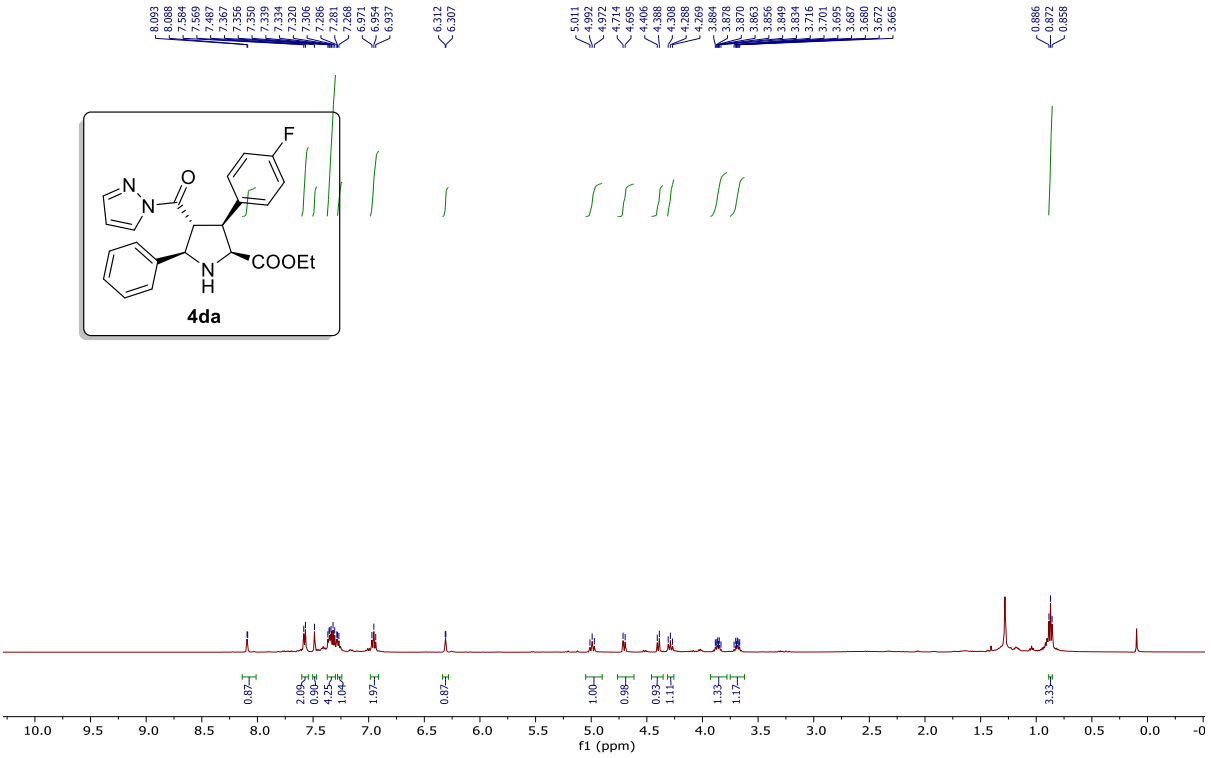
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ba**



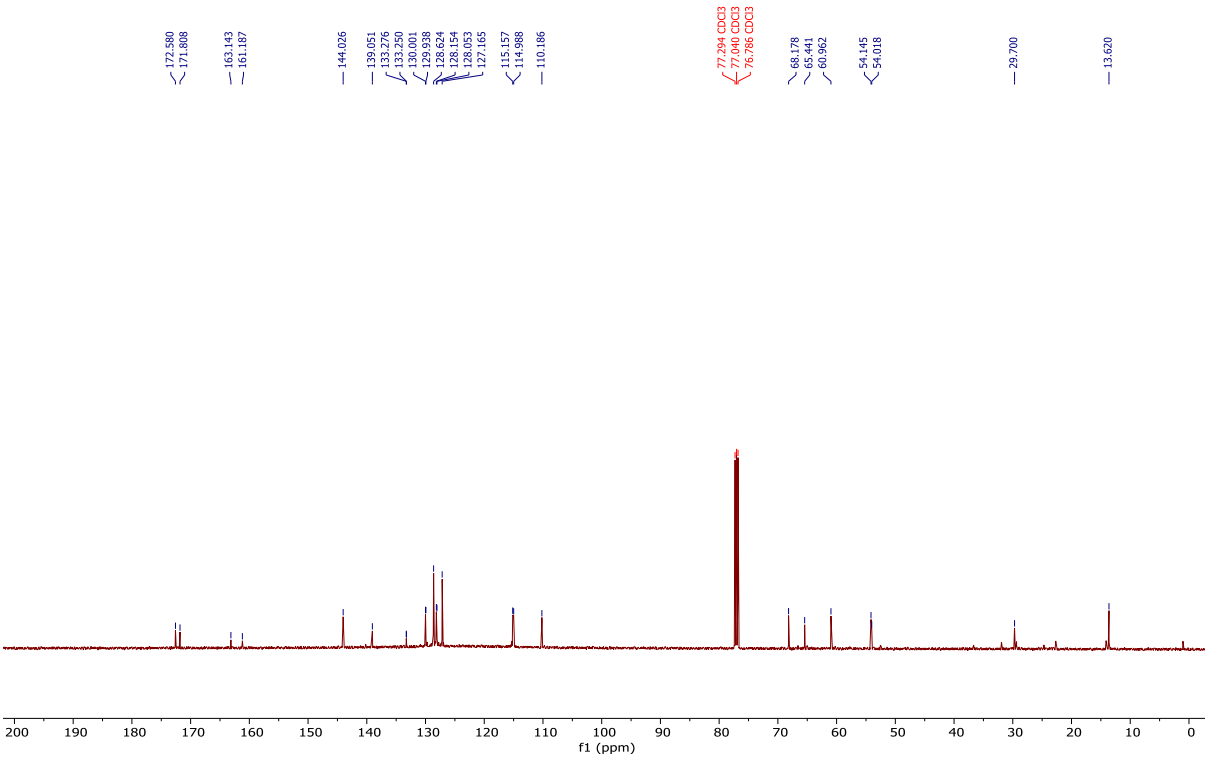
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ca**



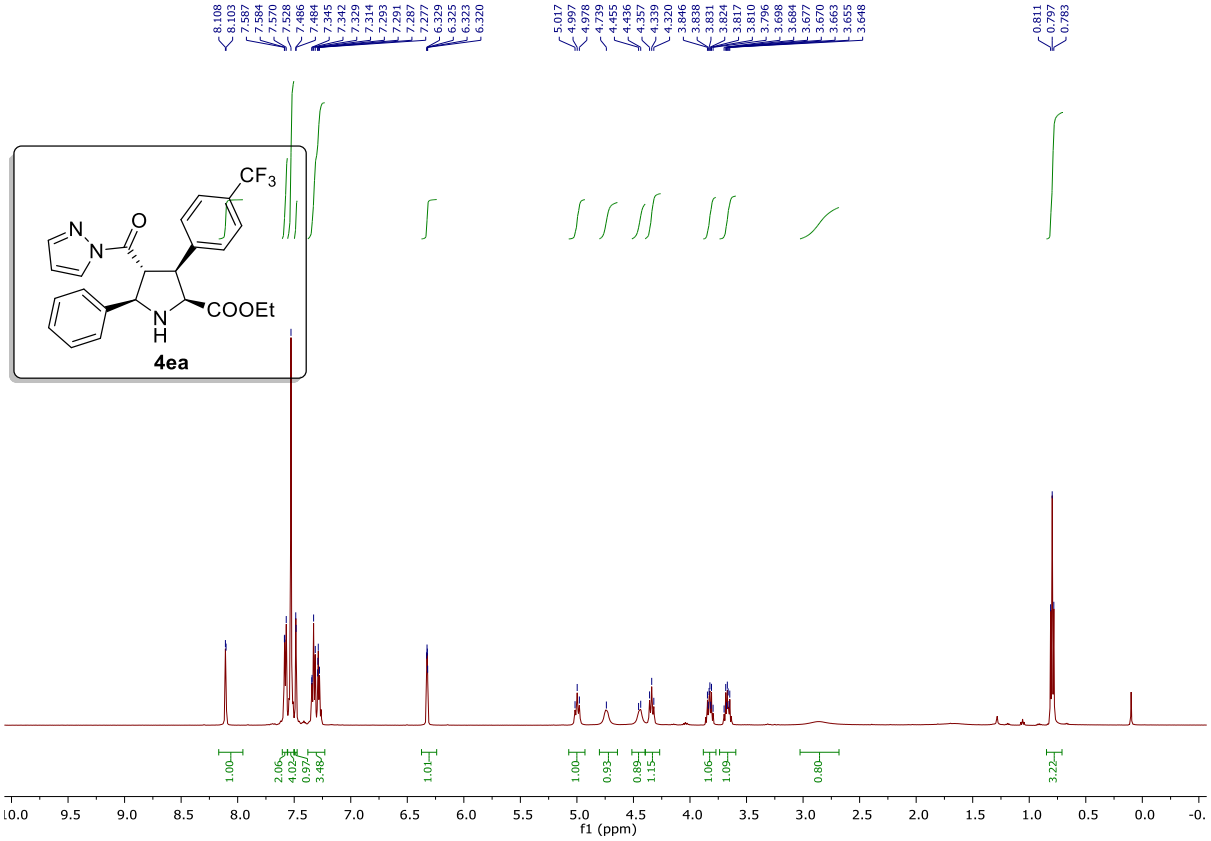
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ca**



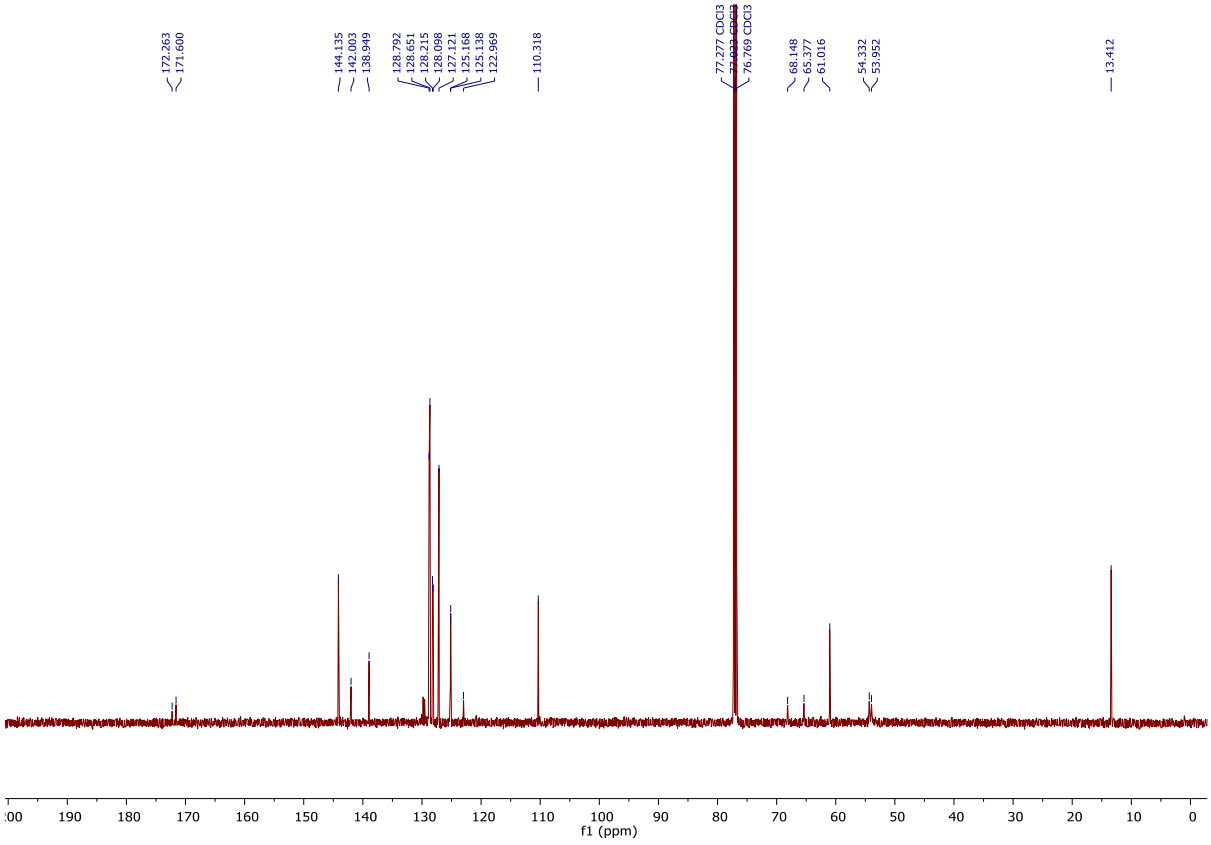
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4da**



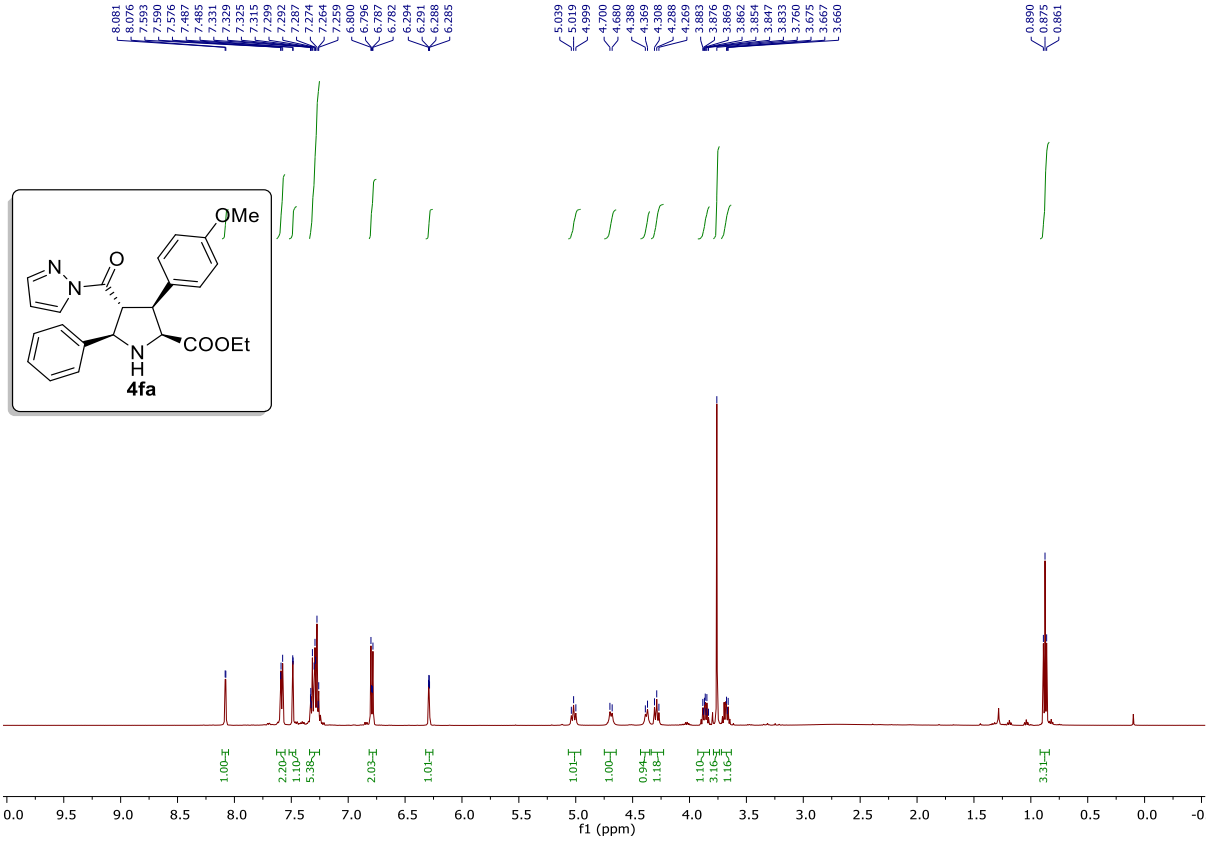
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4da**



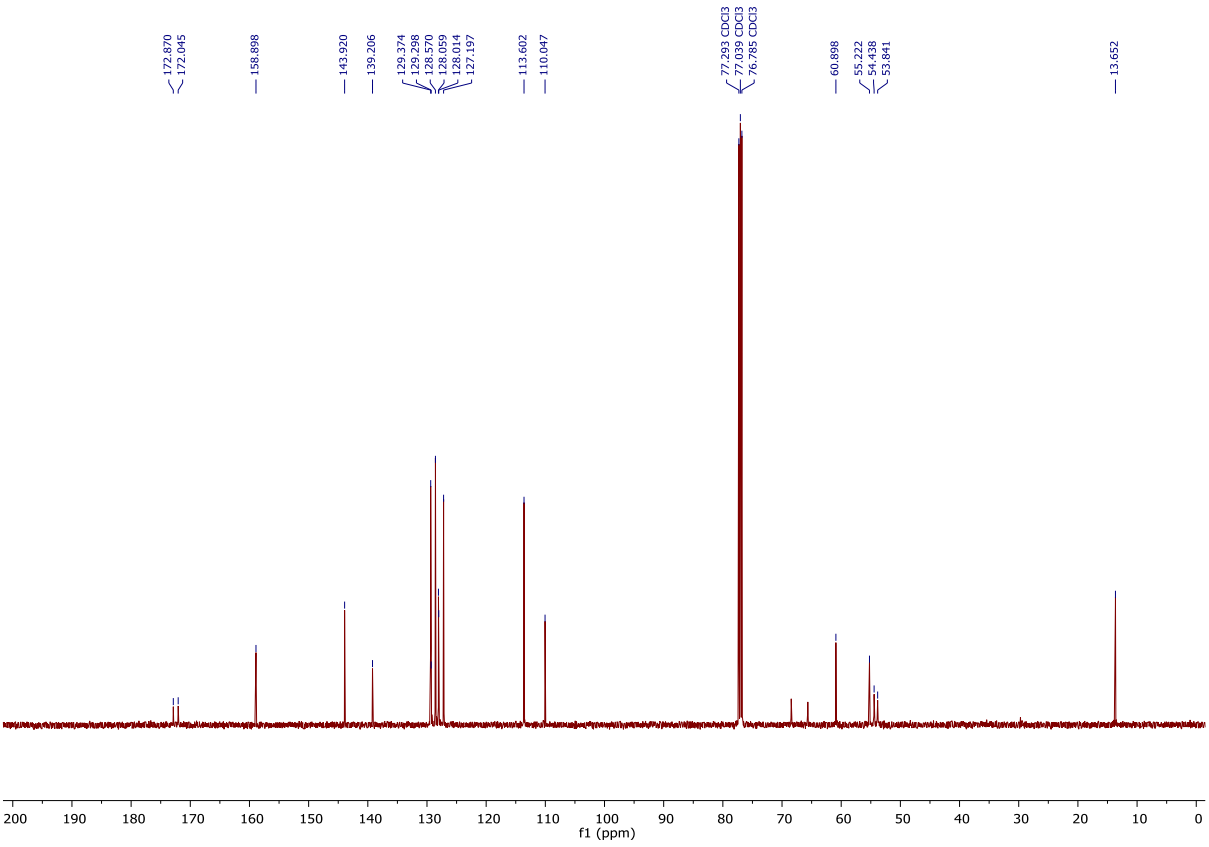
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ea**



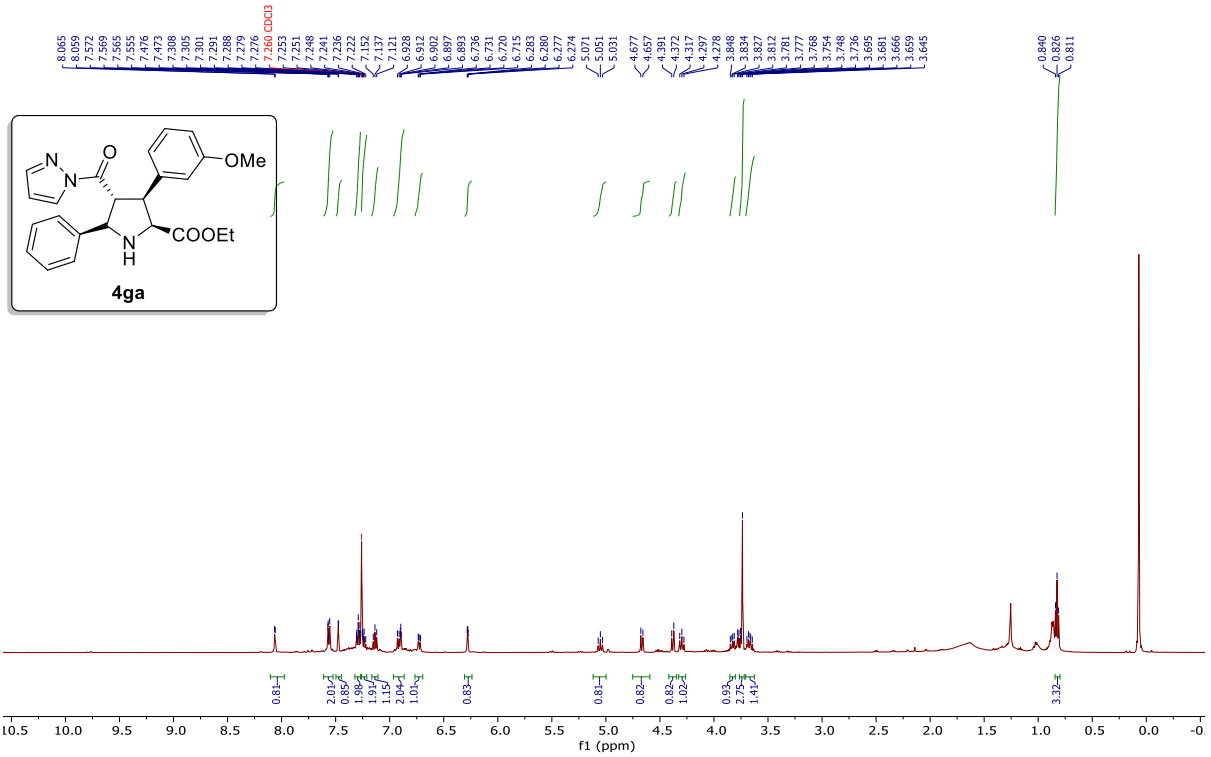
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ea**



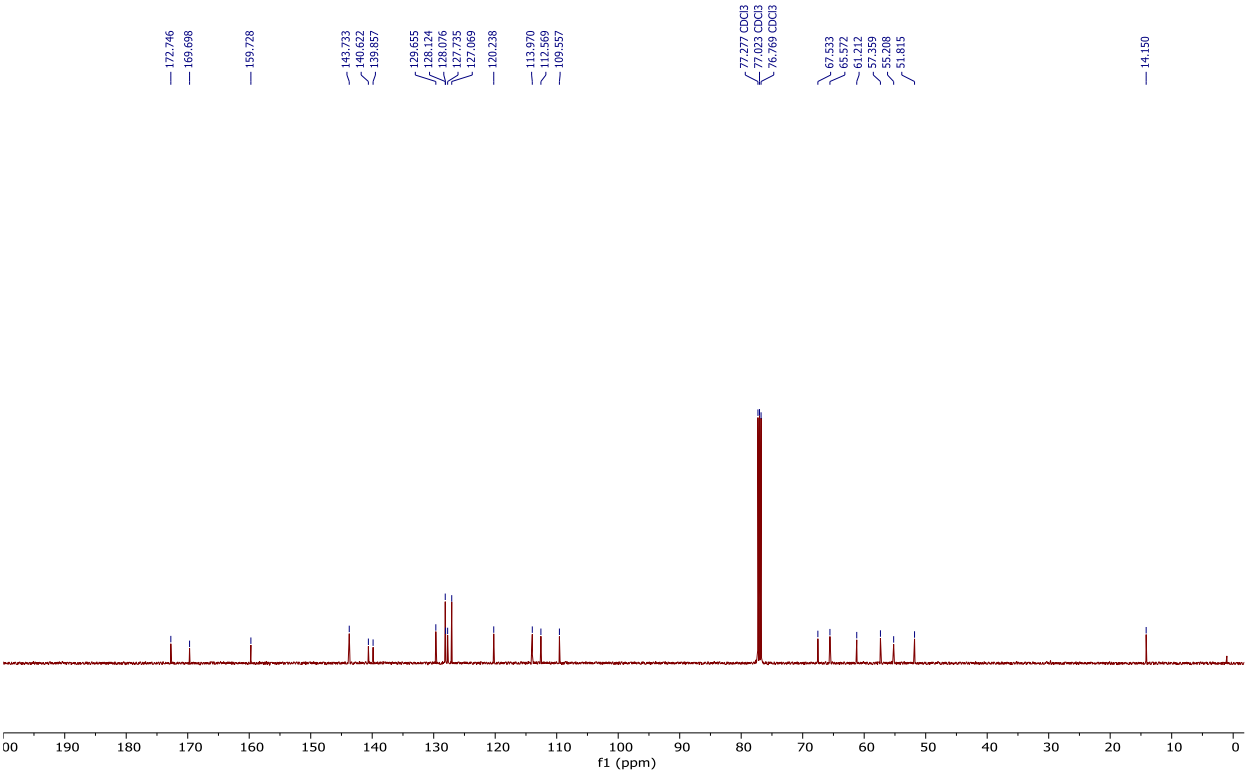
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4fa**



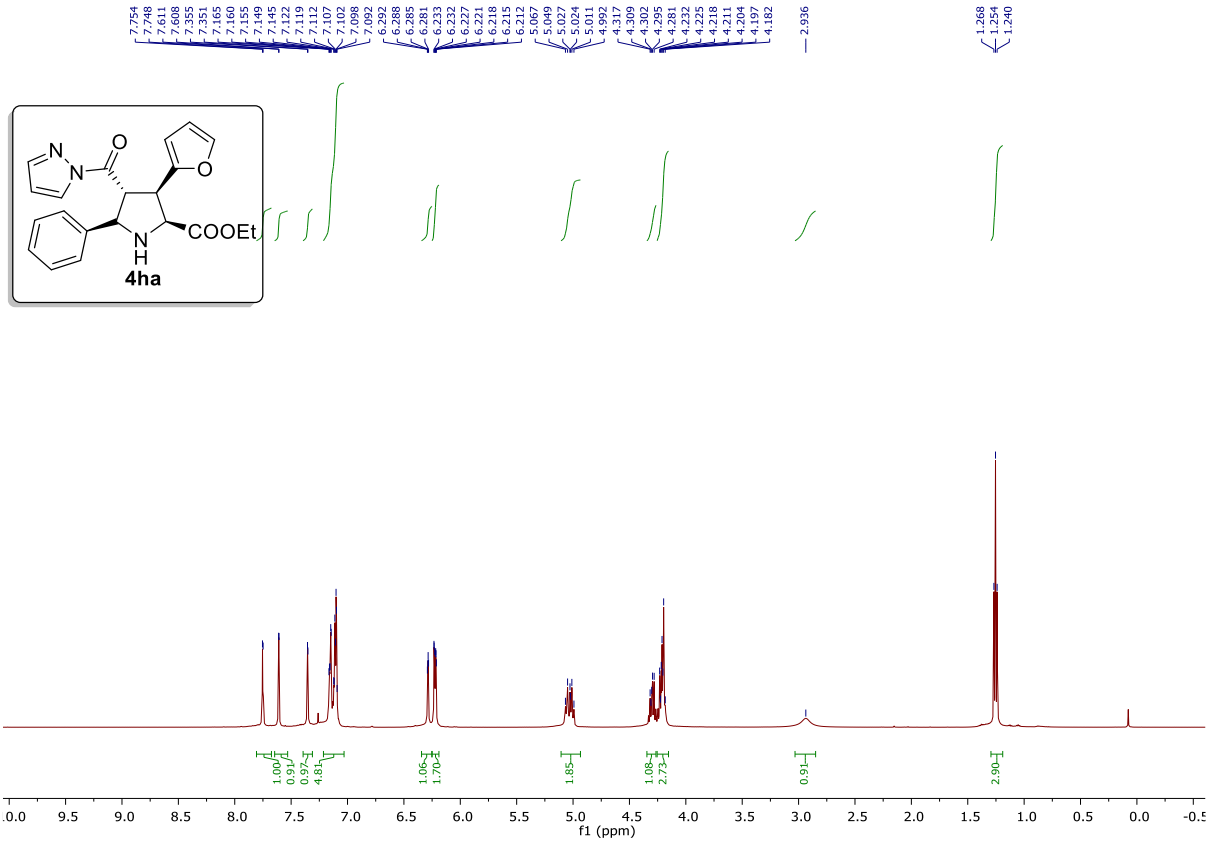
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4fa**



^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ga**

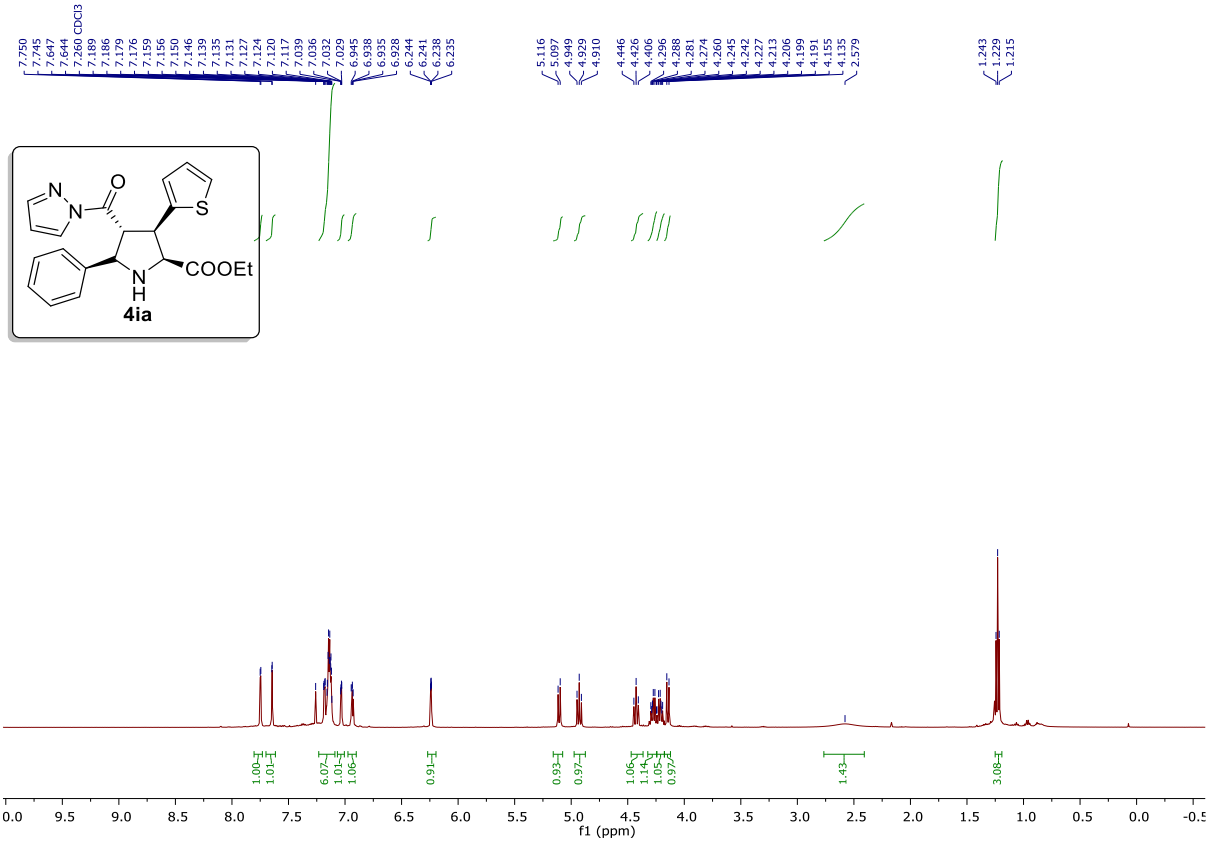


^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ga**

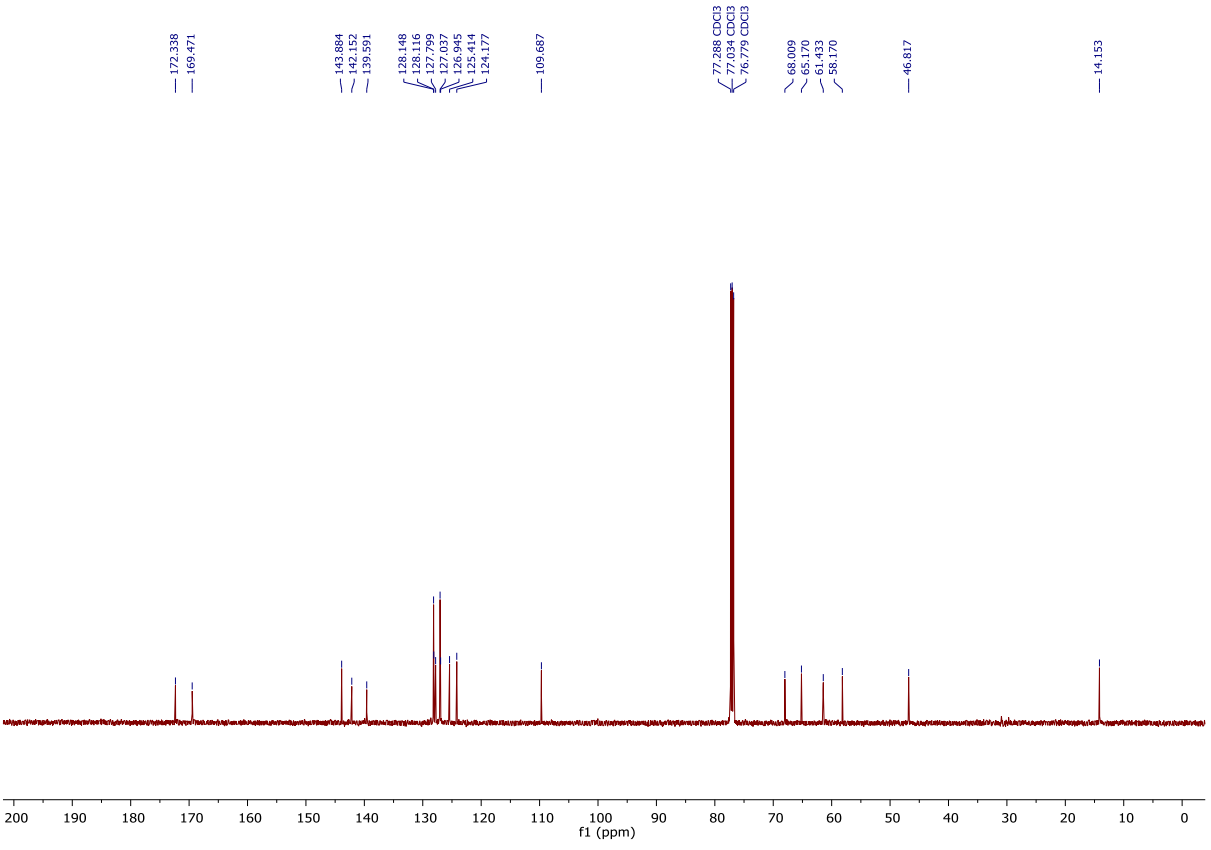


^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ha**

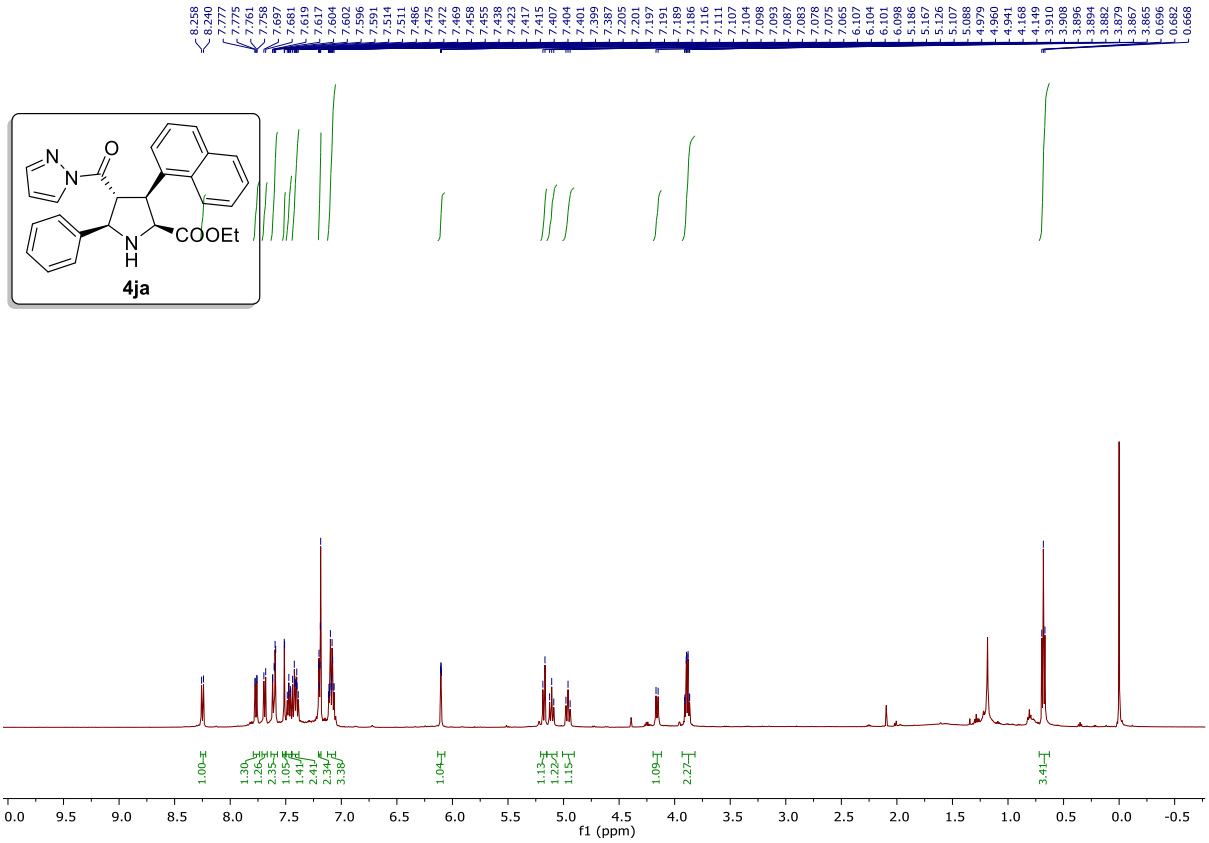
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ha**



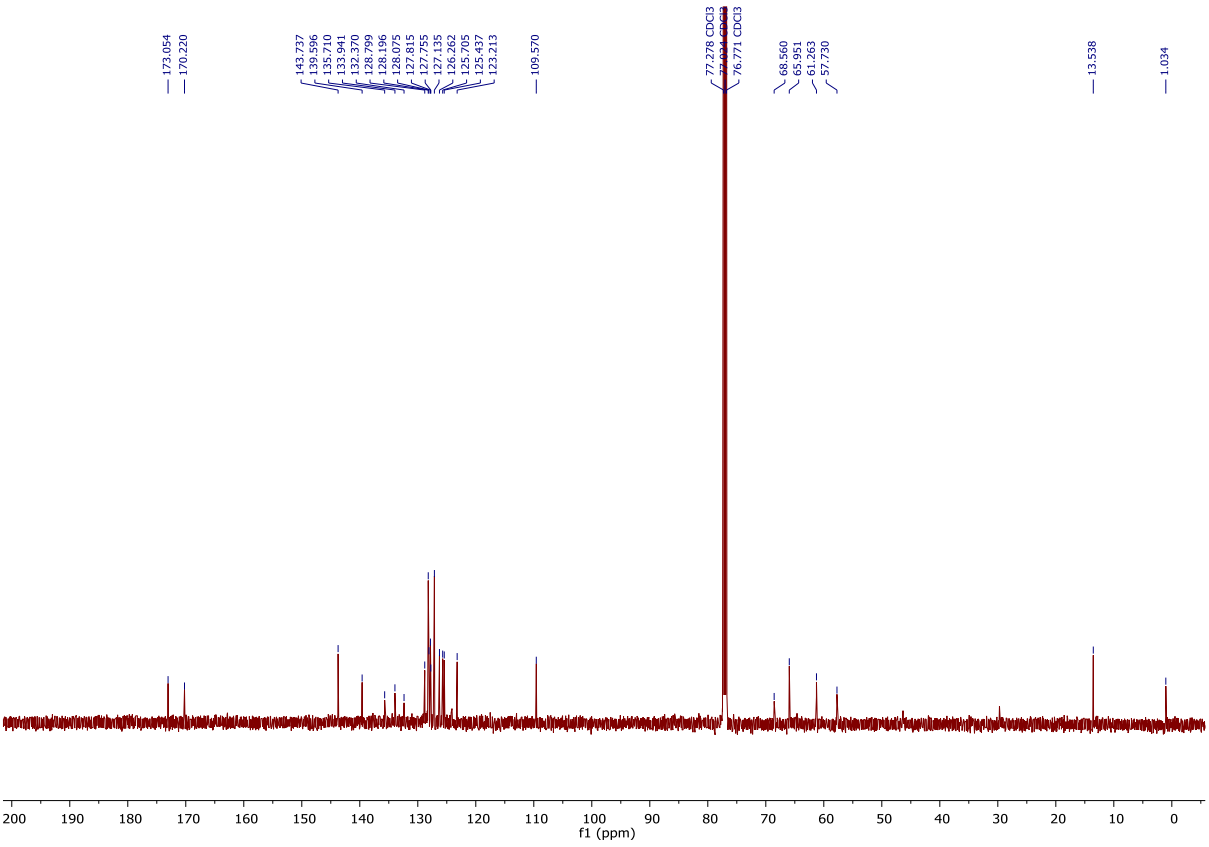
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ia**



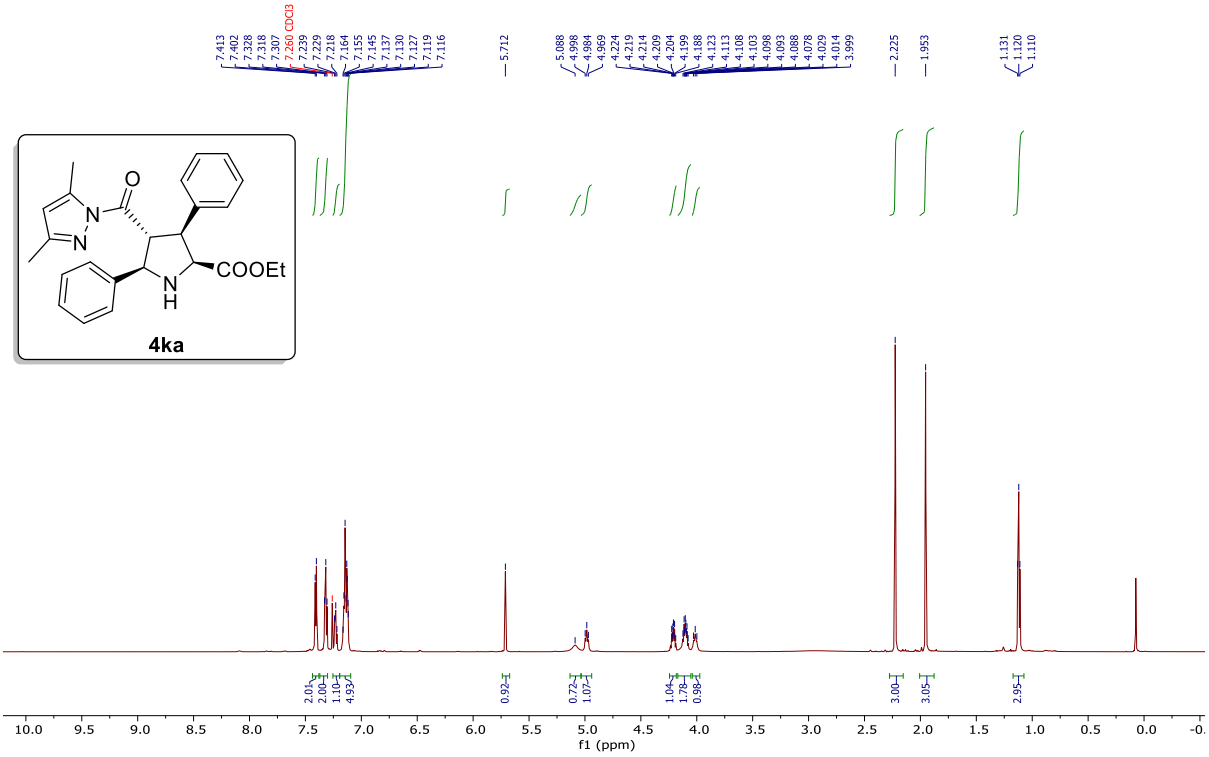
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ia**



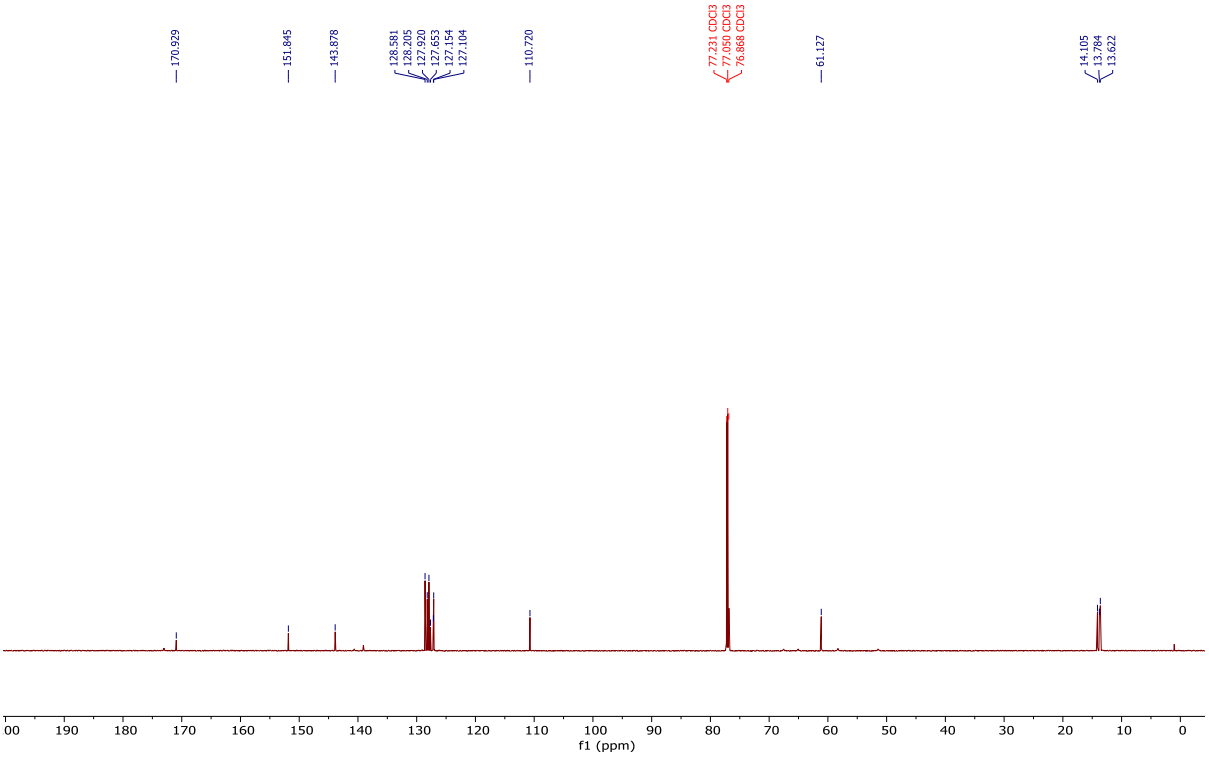
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ja**



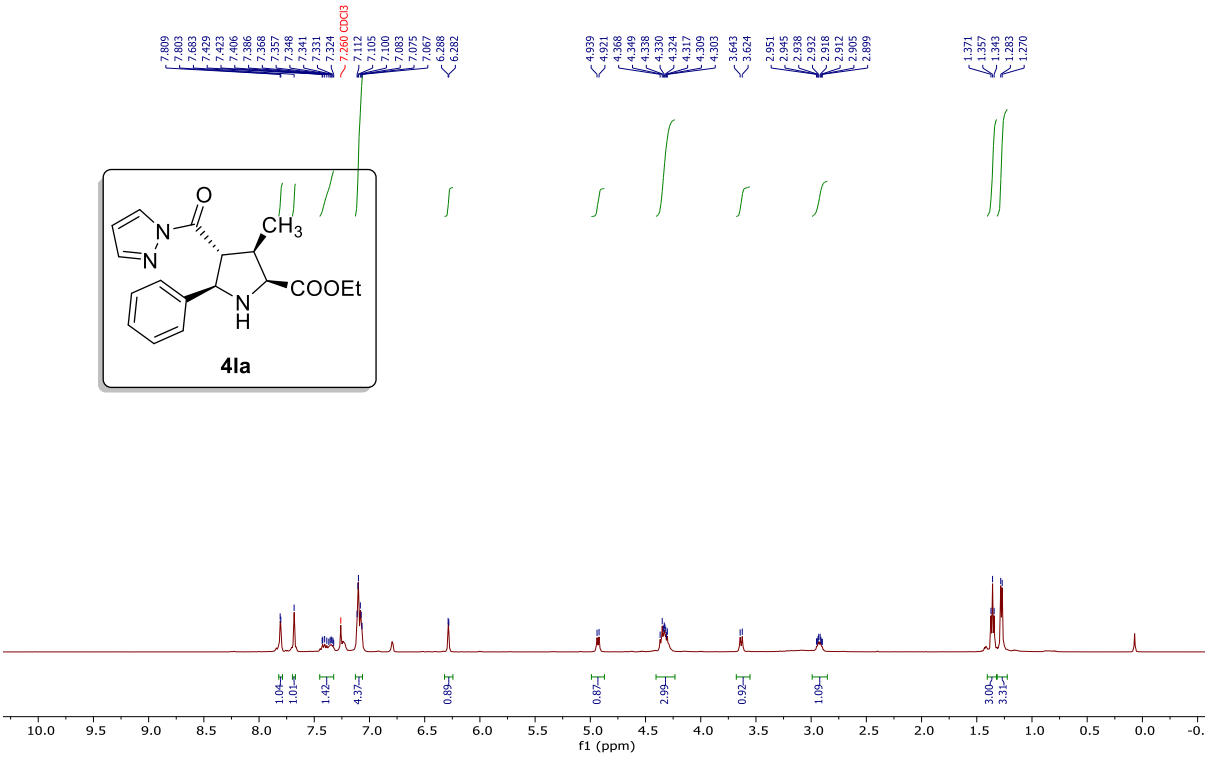
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ja**



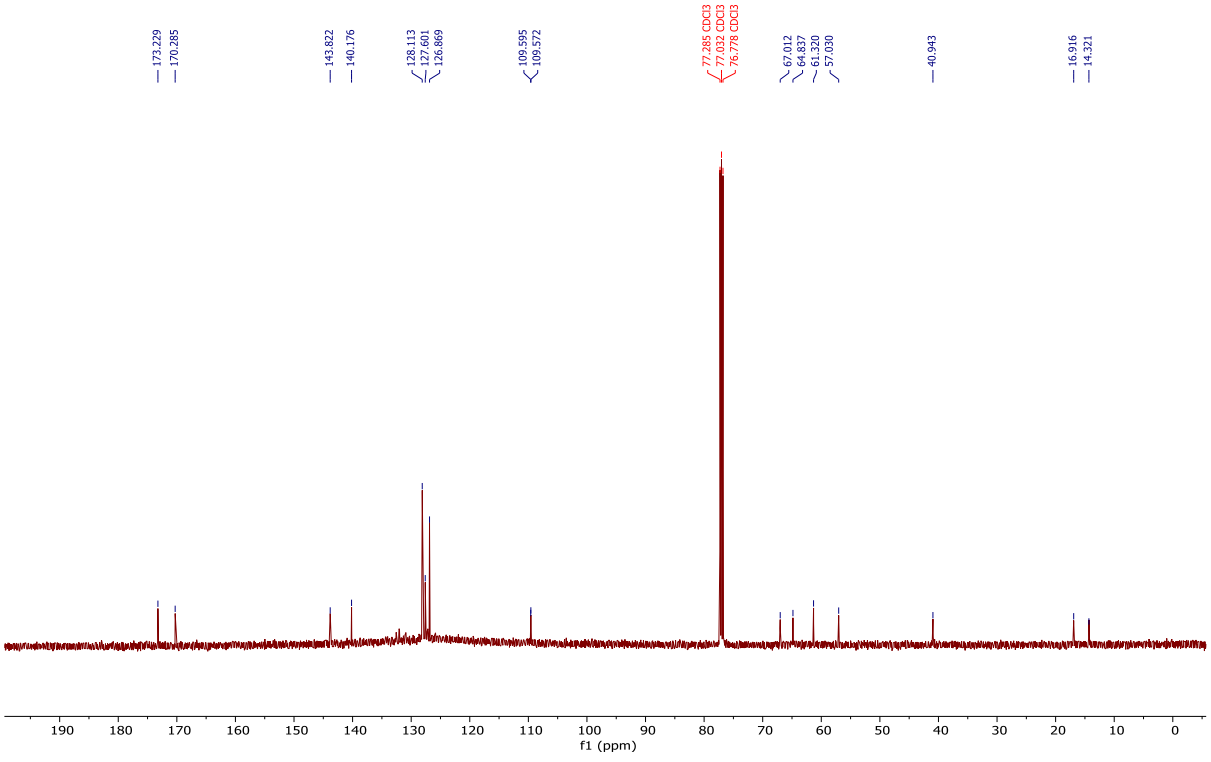
^{1}H NMR (700 MHz, $CDCl_3$) of compound **4ka**



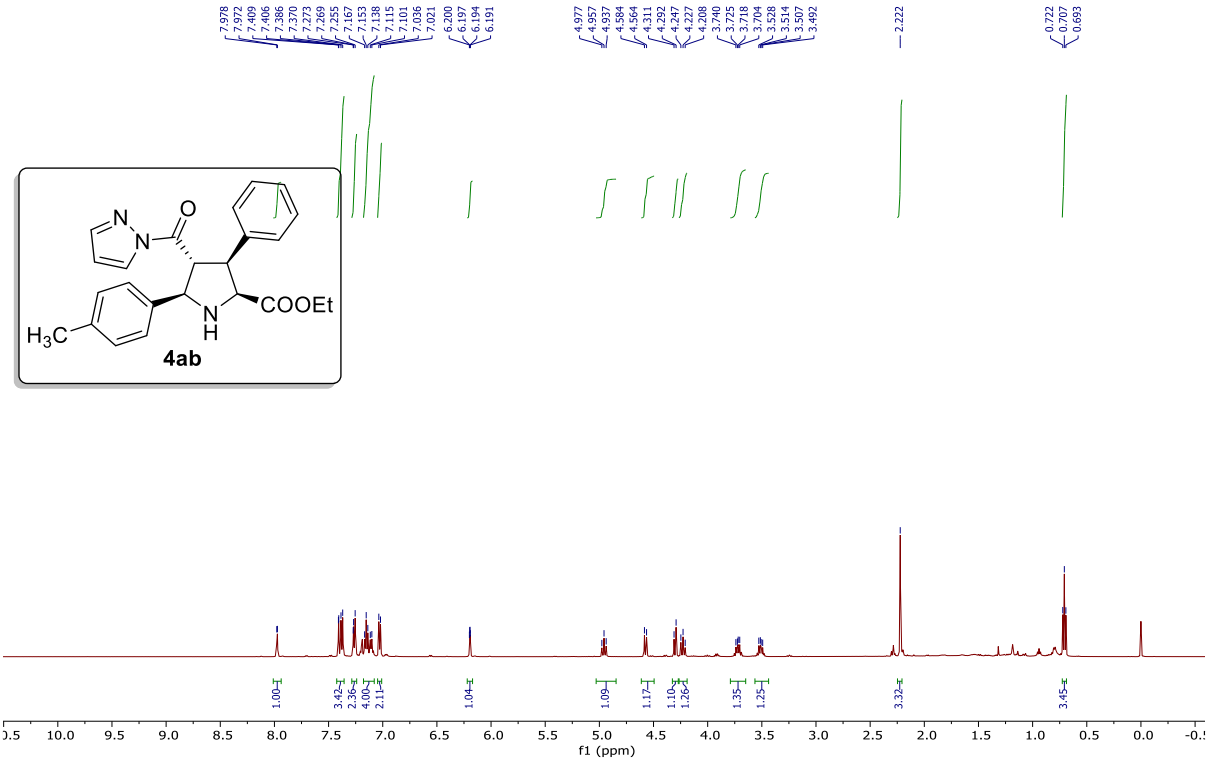
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4ka**



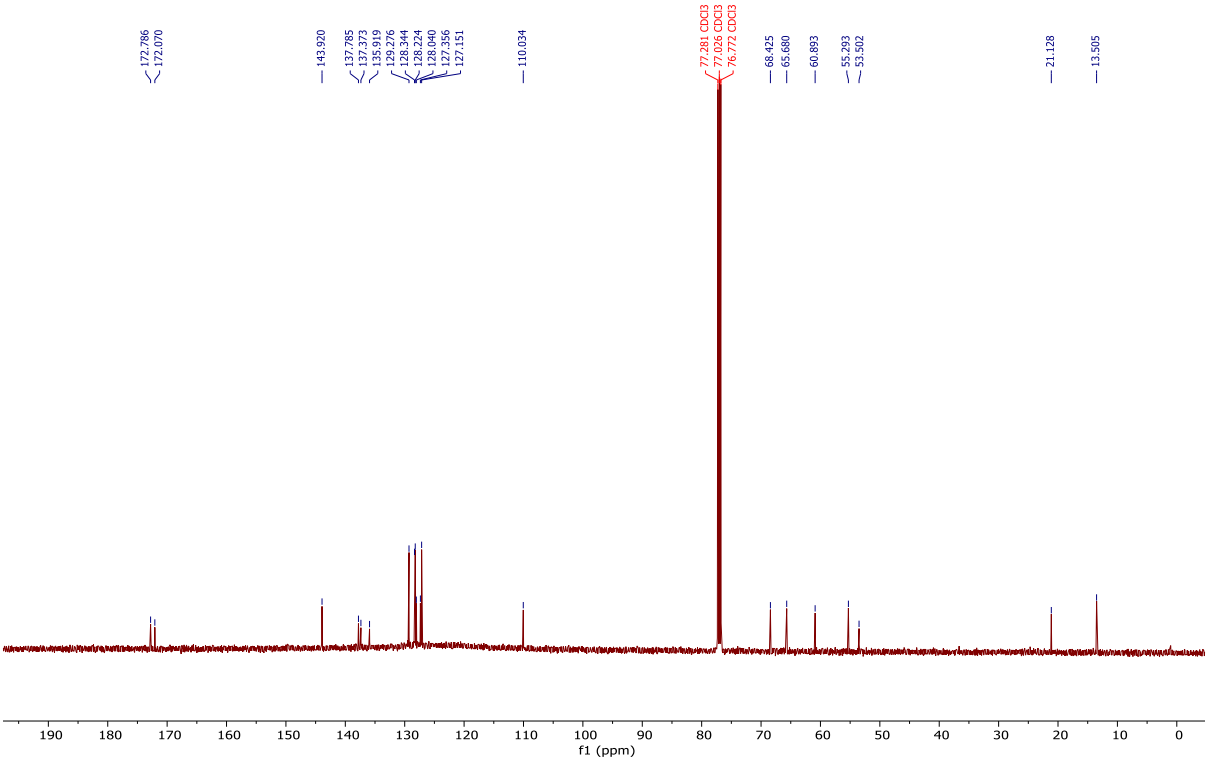
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4la**



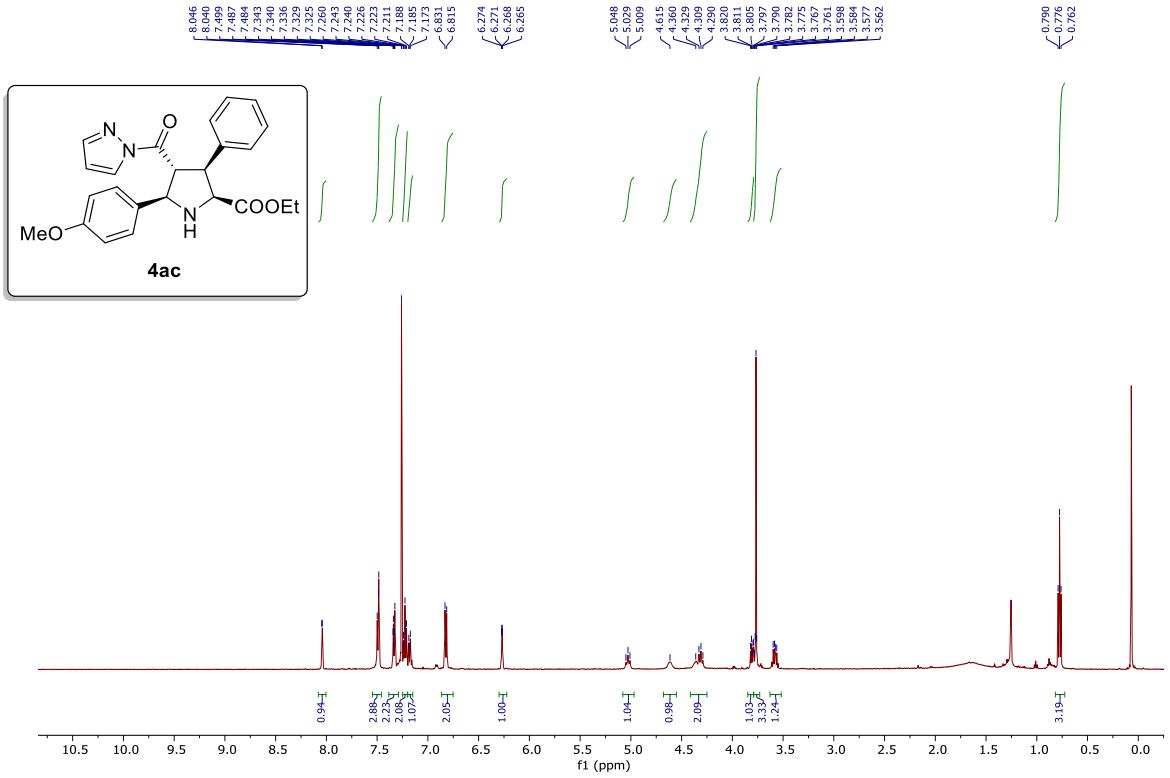
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4la**



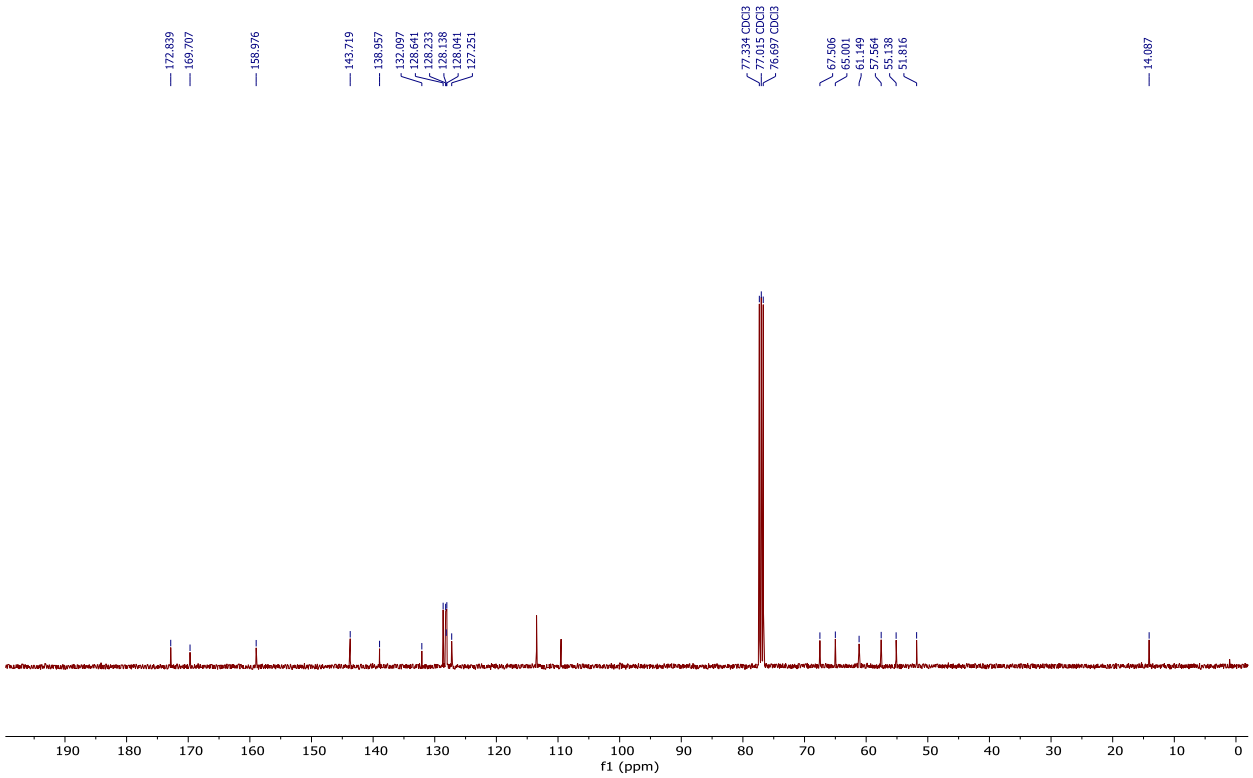
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ab**



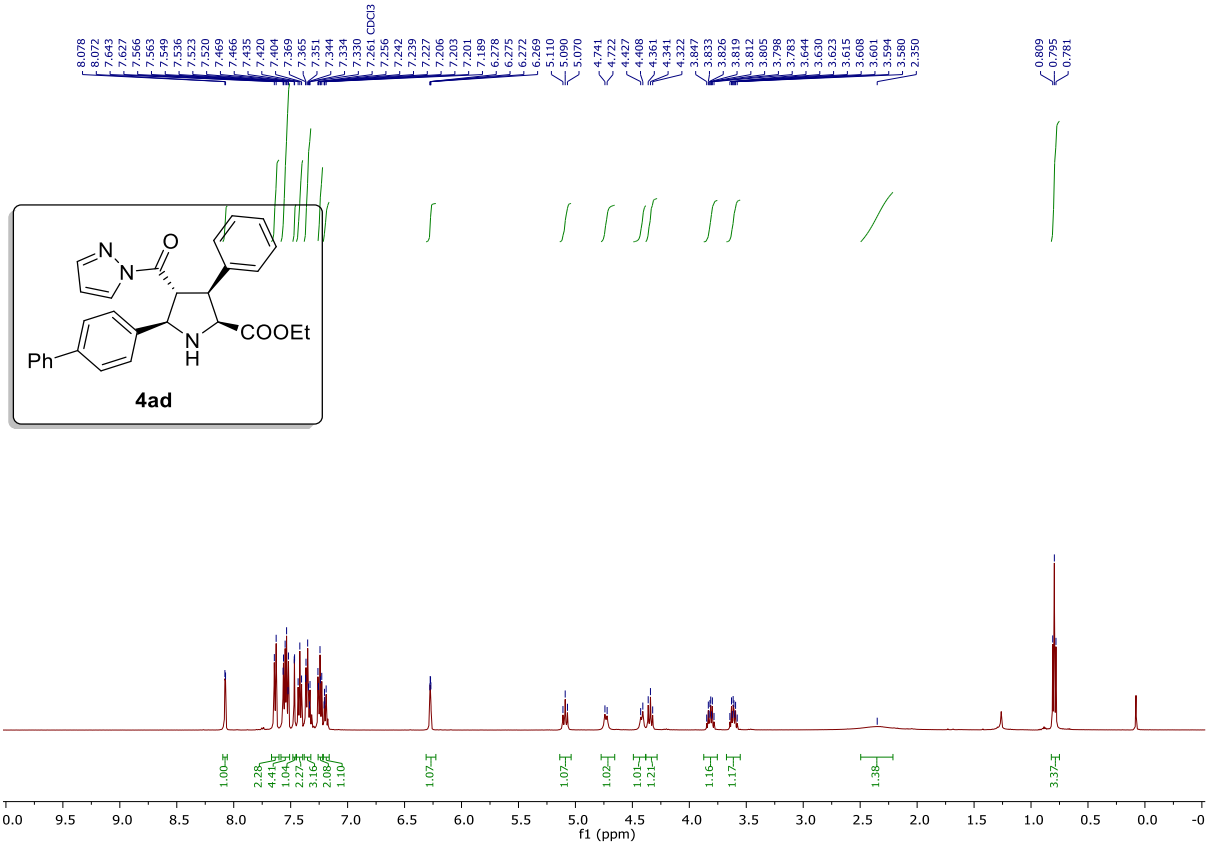
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ab**



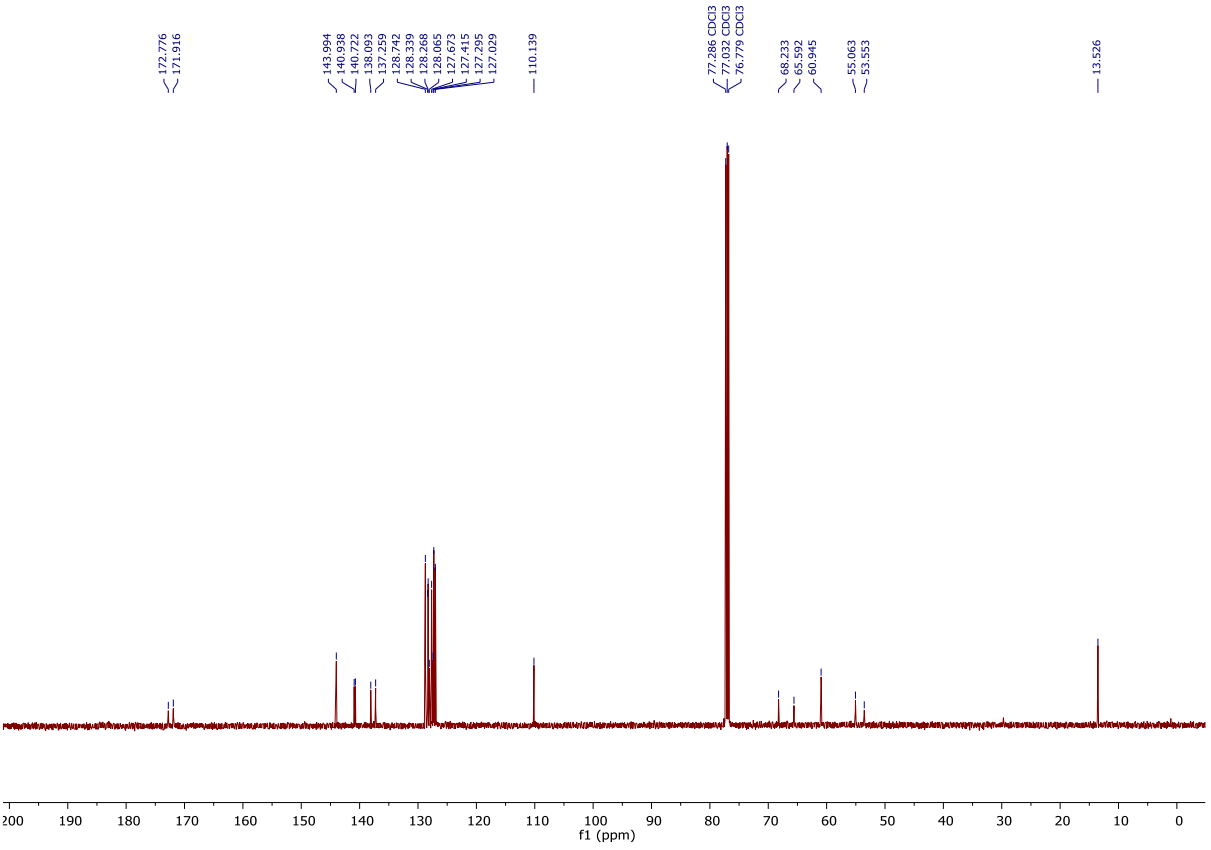
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4ac**



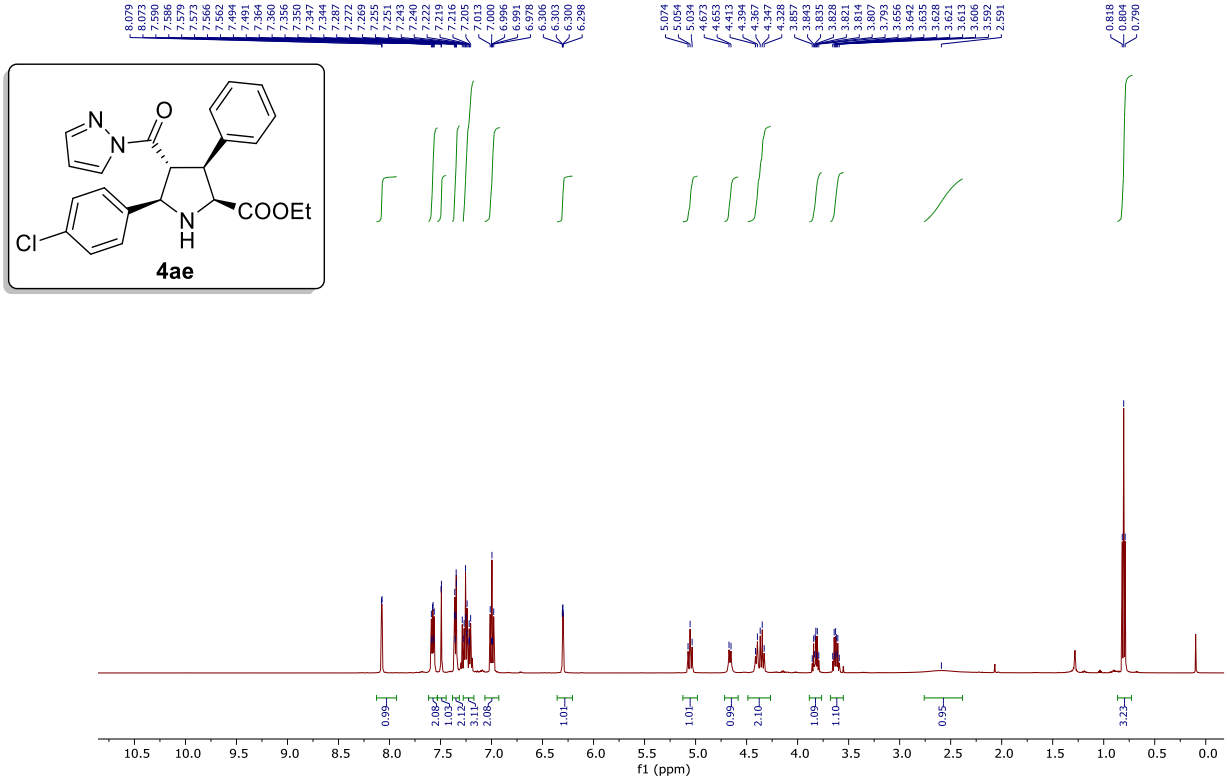
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4ac**



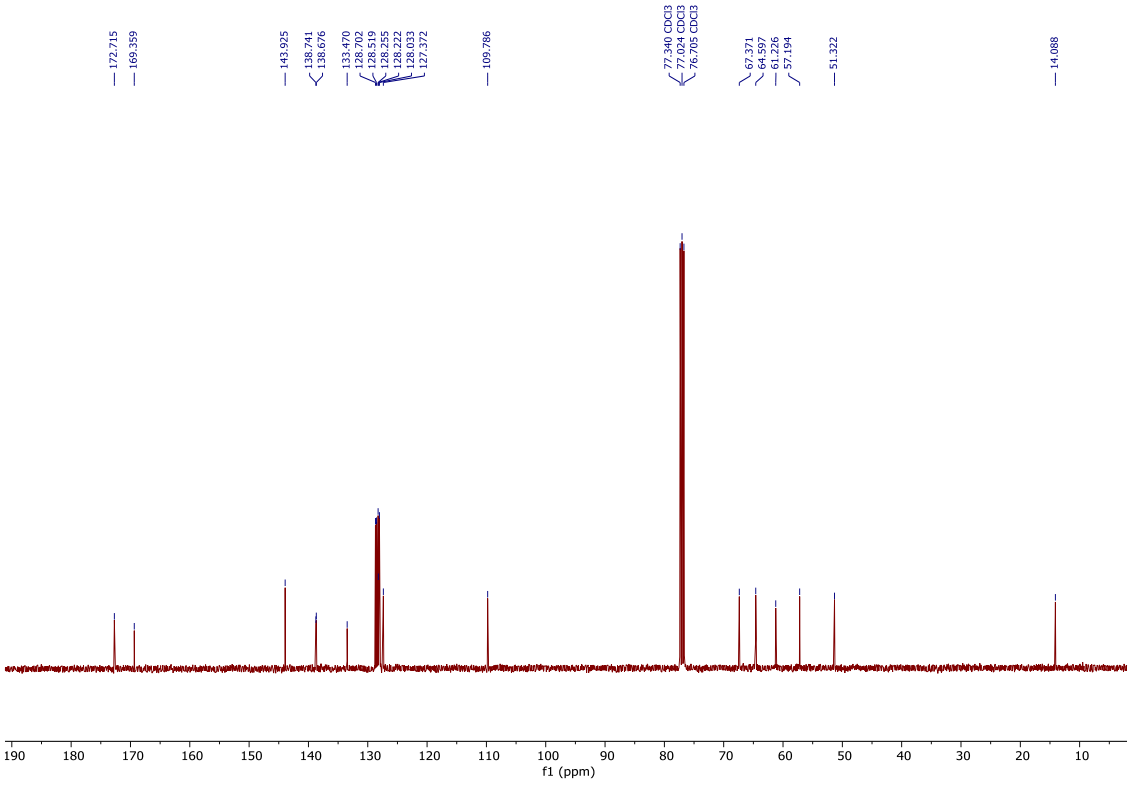
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ad**



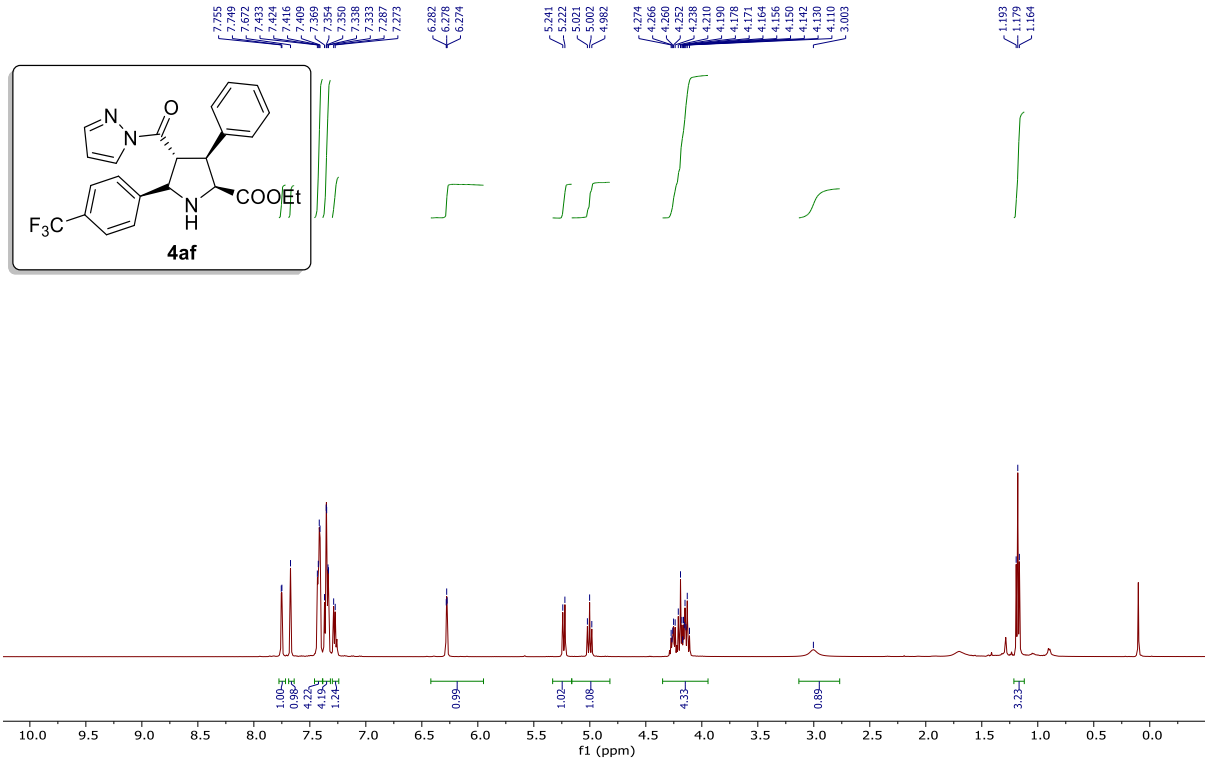
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ad**



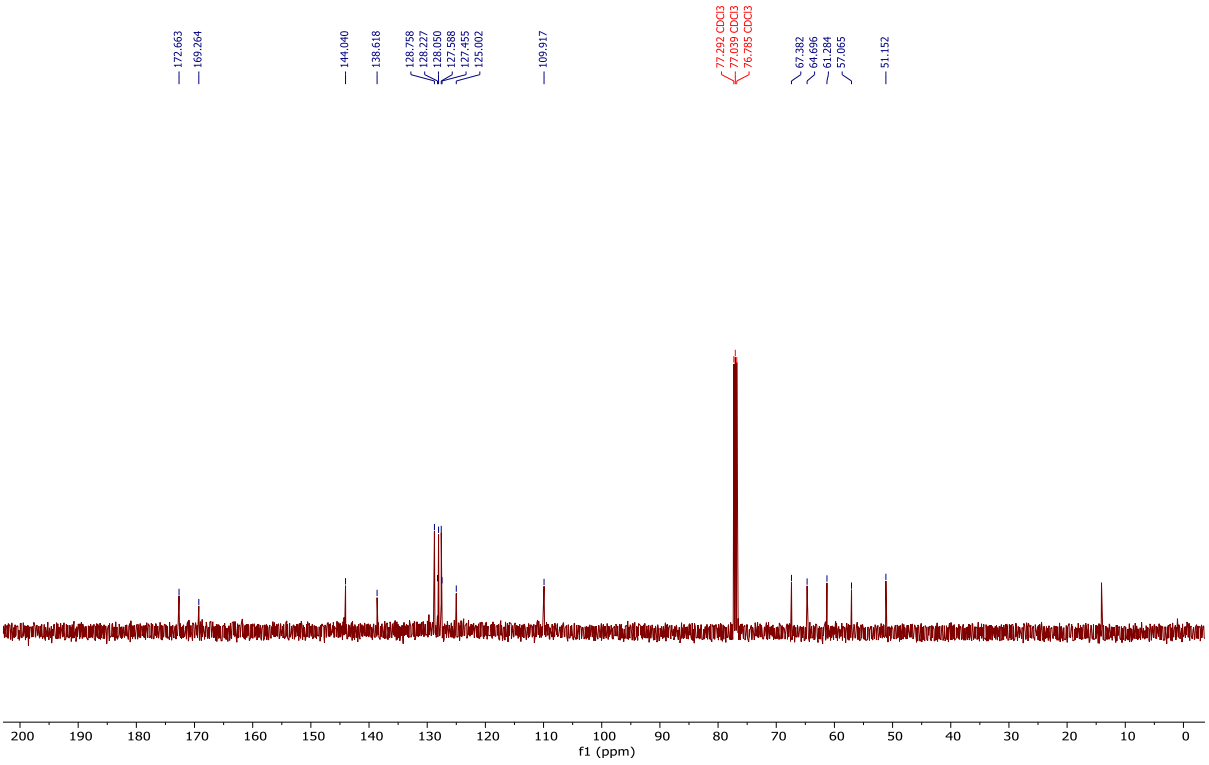
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ae**



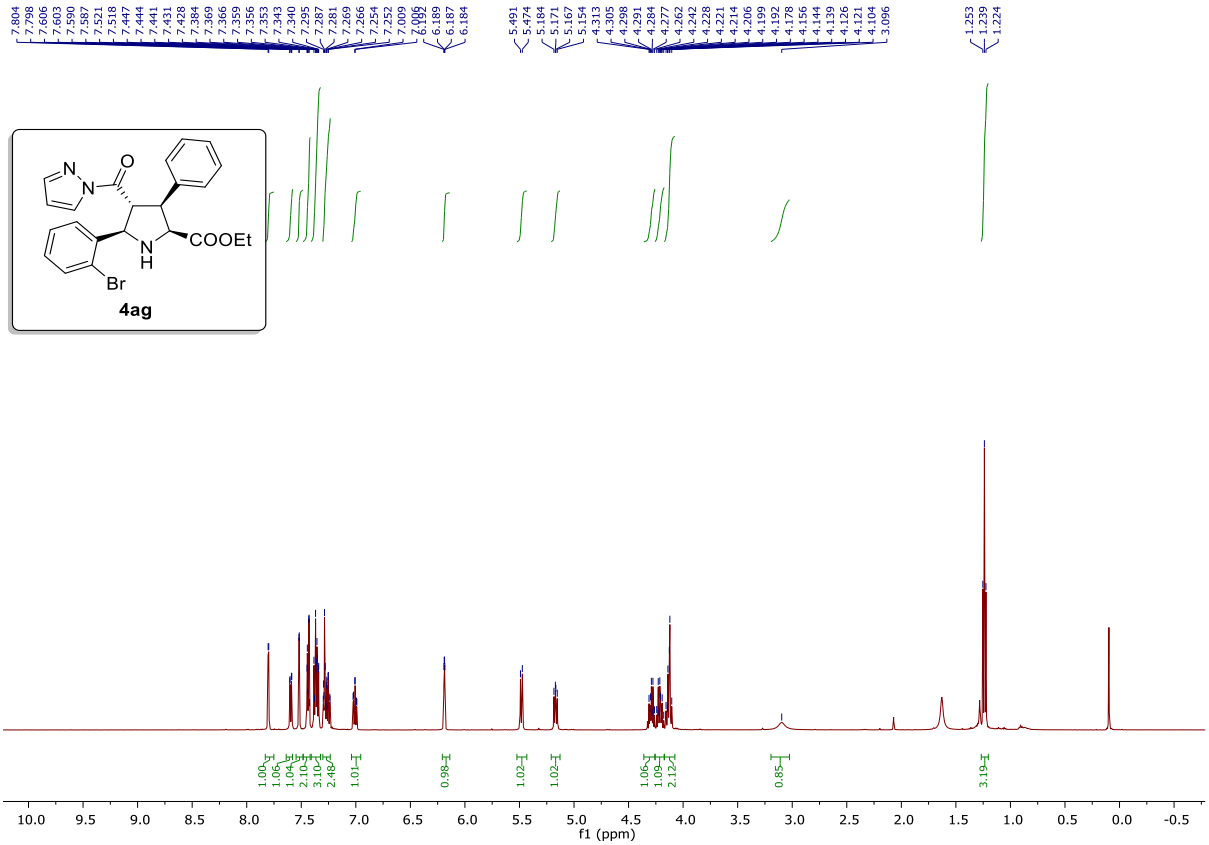
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4ae**



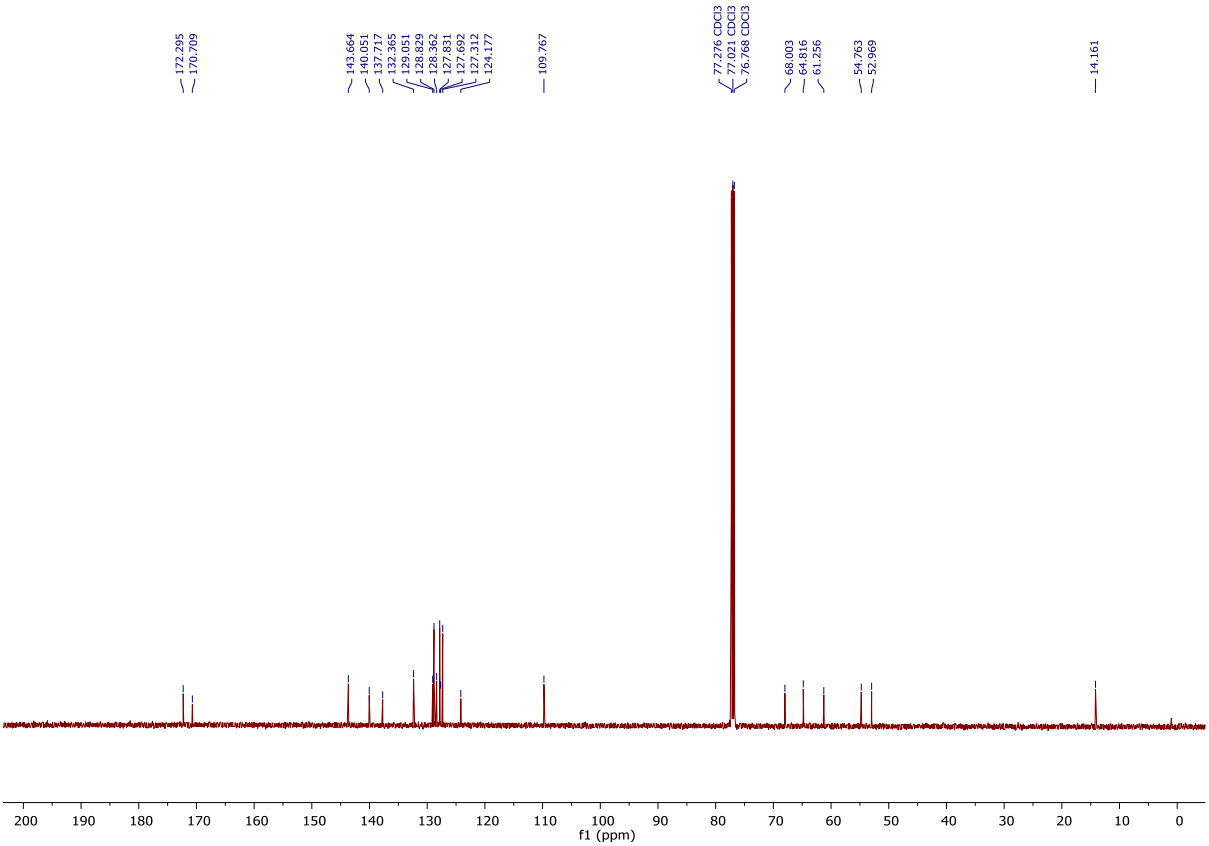
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4af**



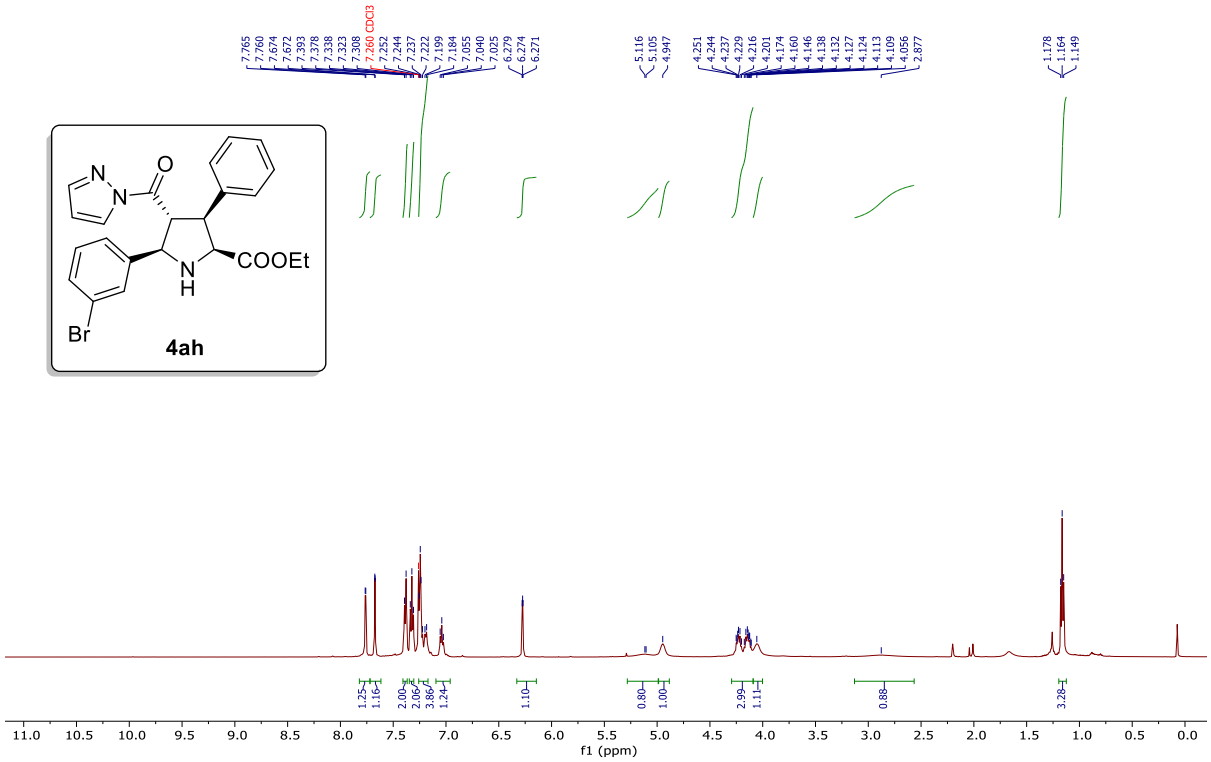
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4af**



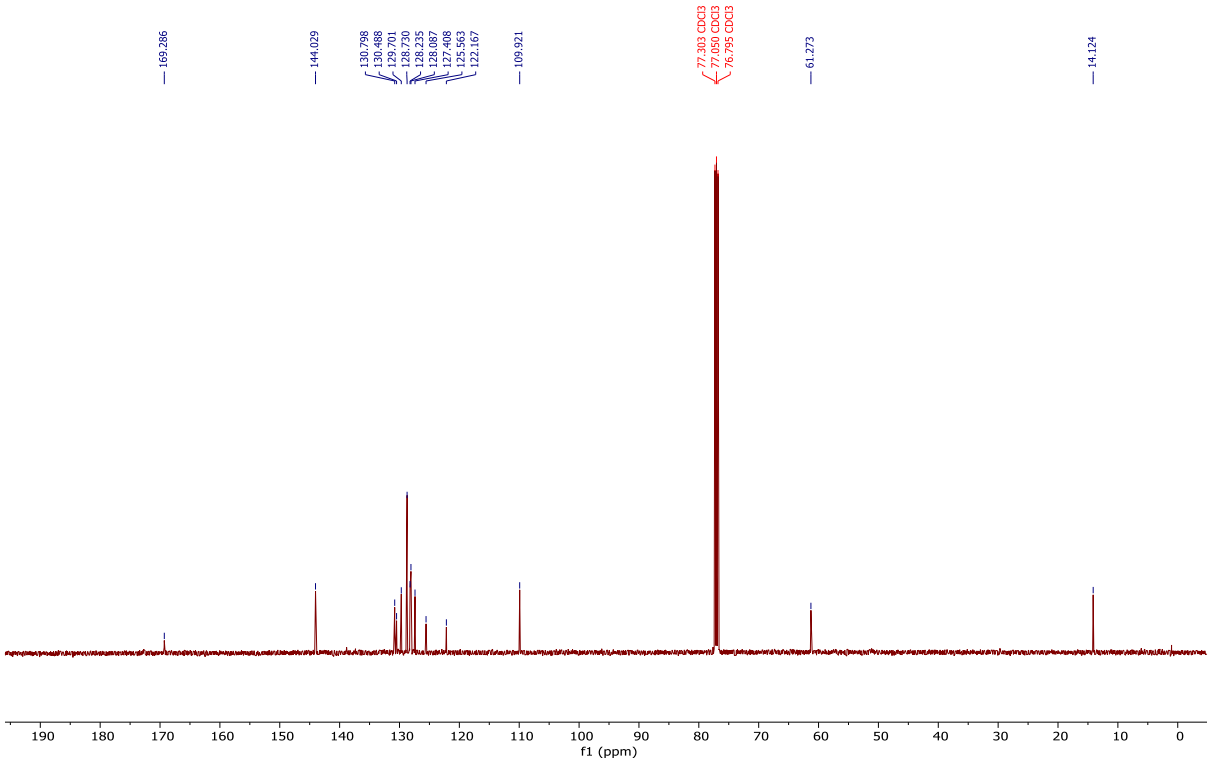
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ag**



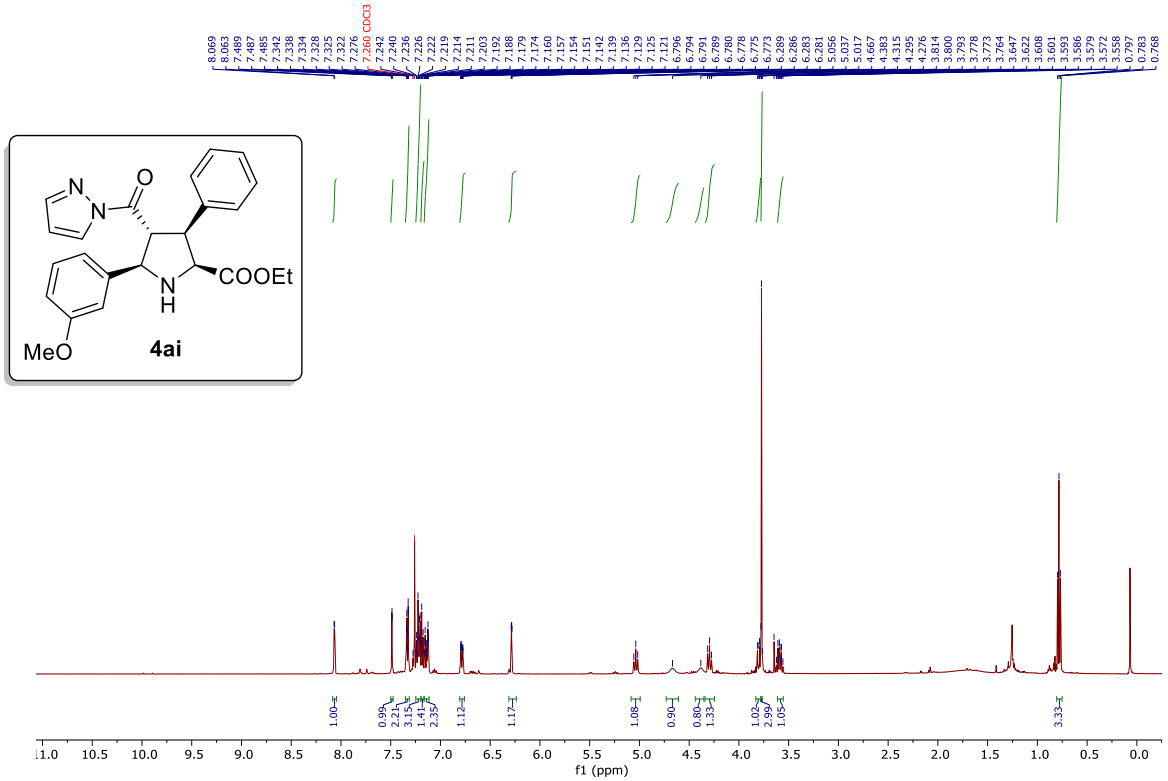
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ag**



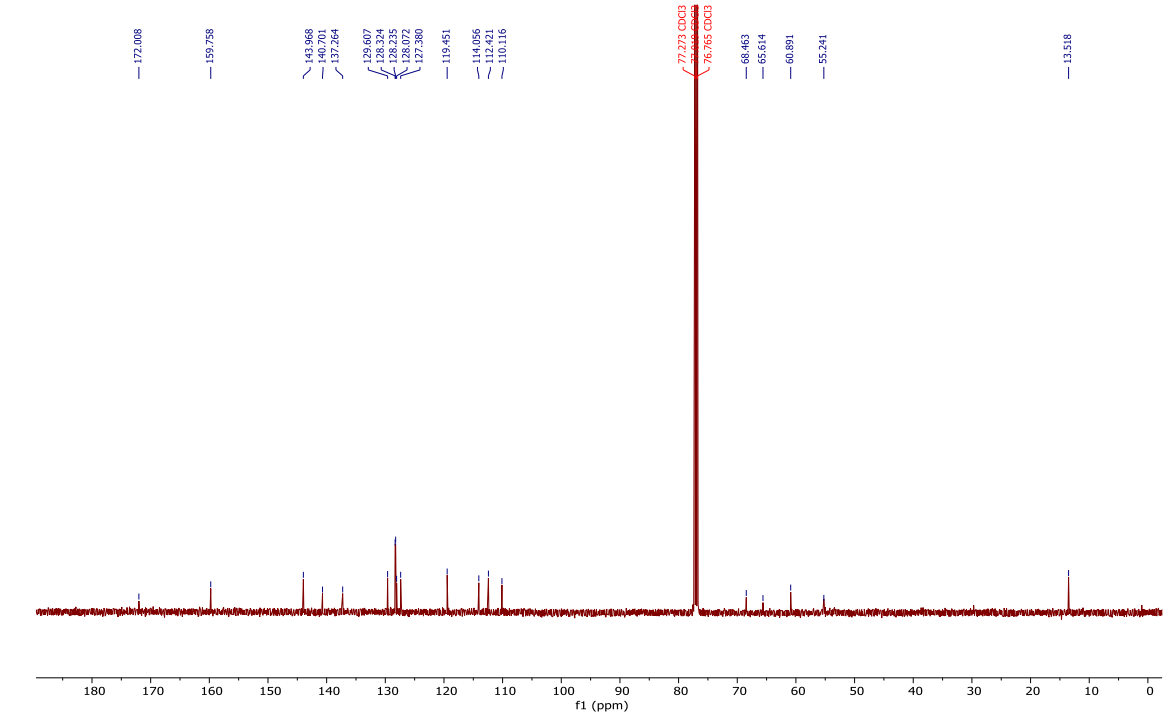
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ah**



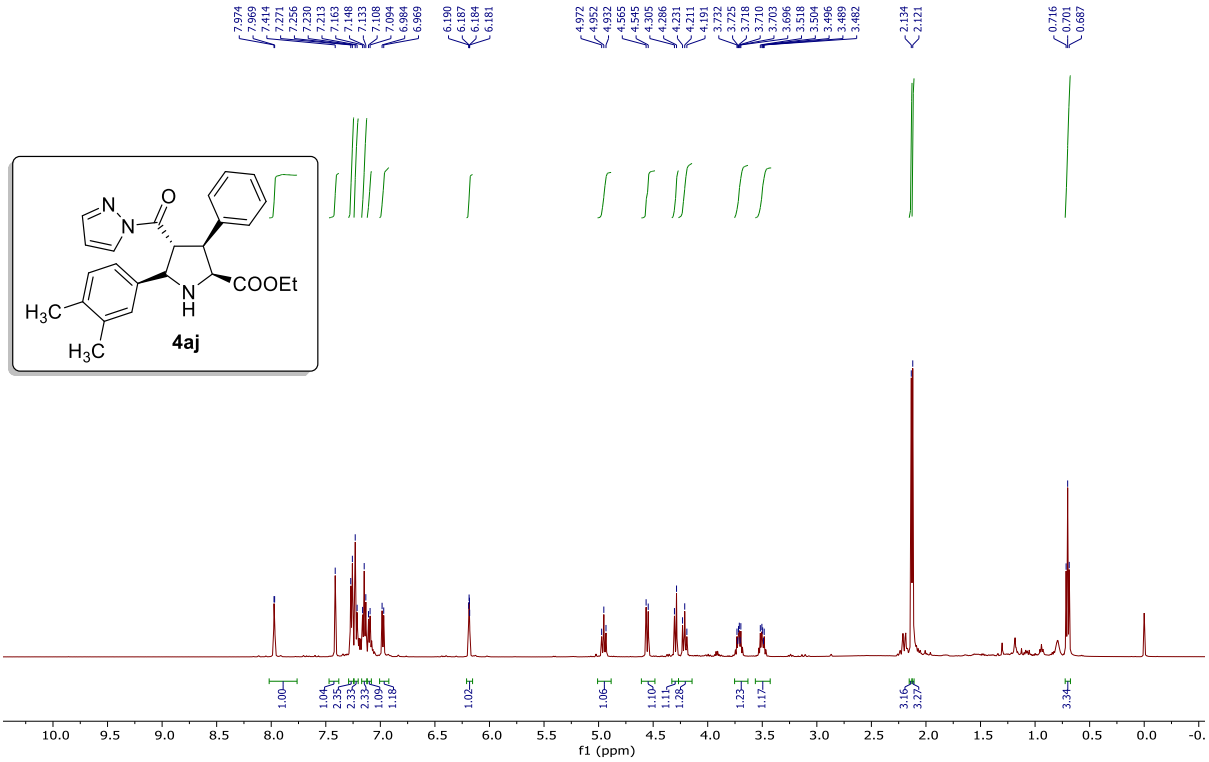
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ah**



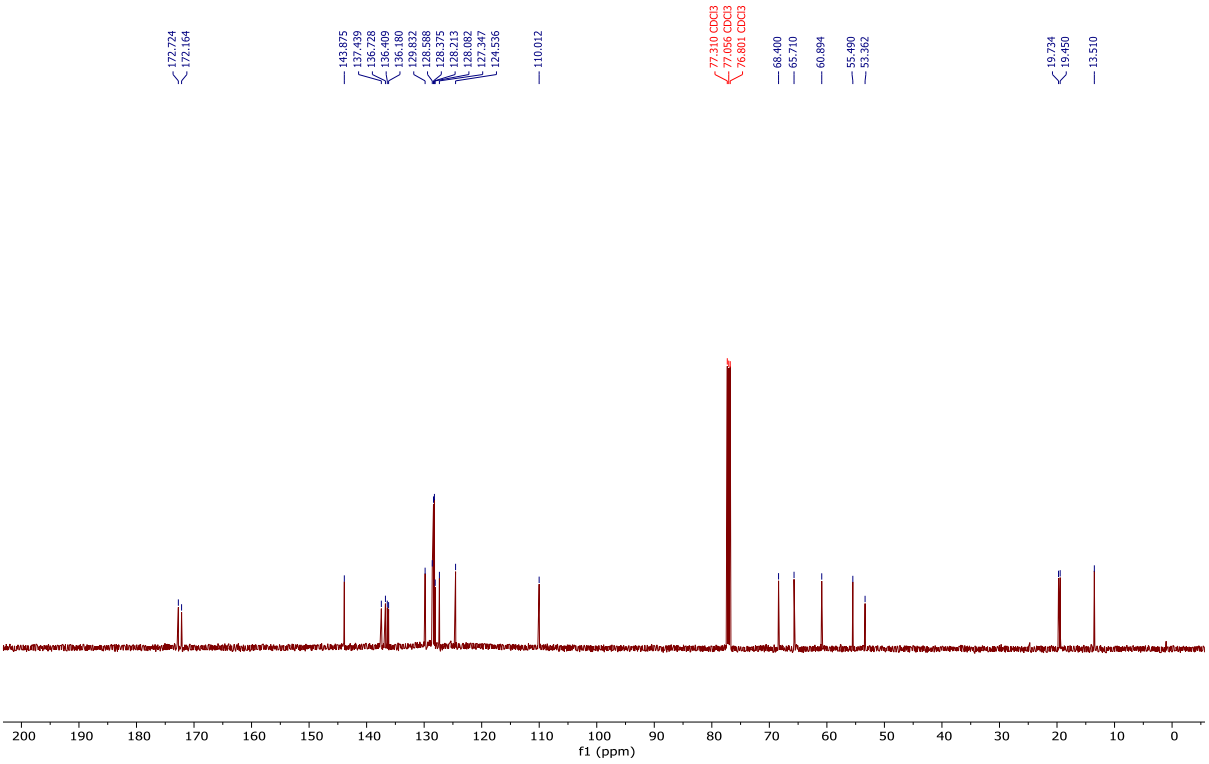
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ai**



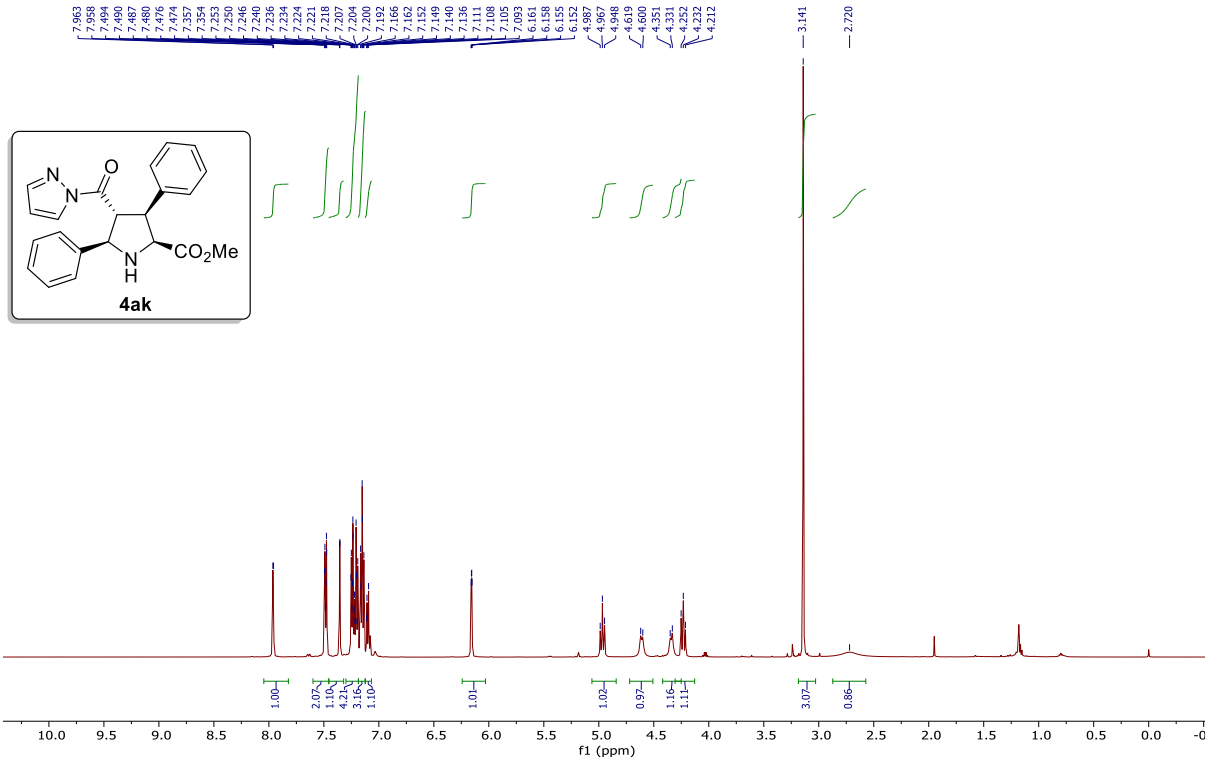
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4ai**



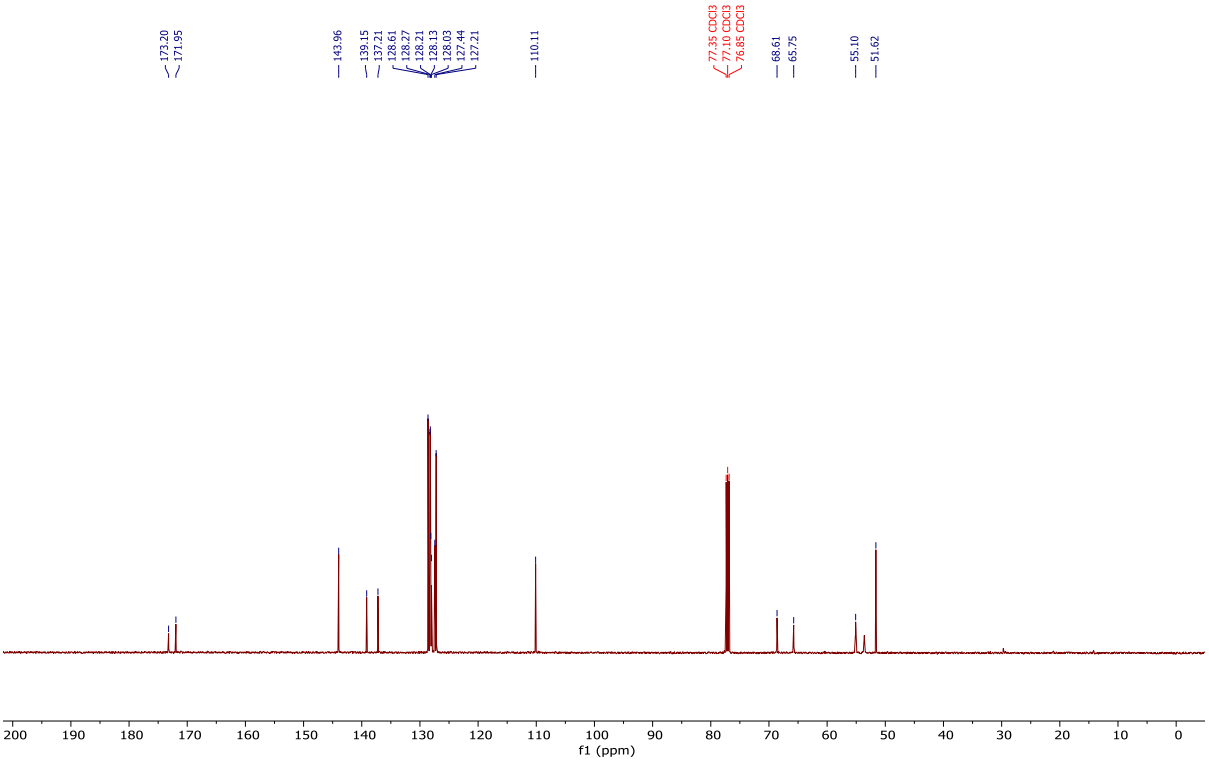
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4aj**



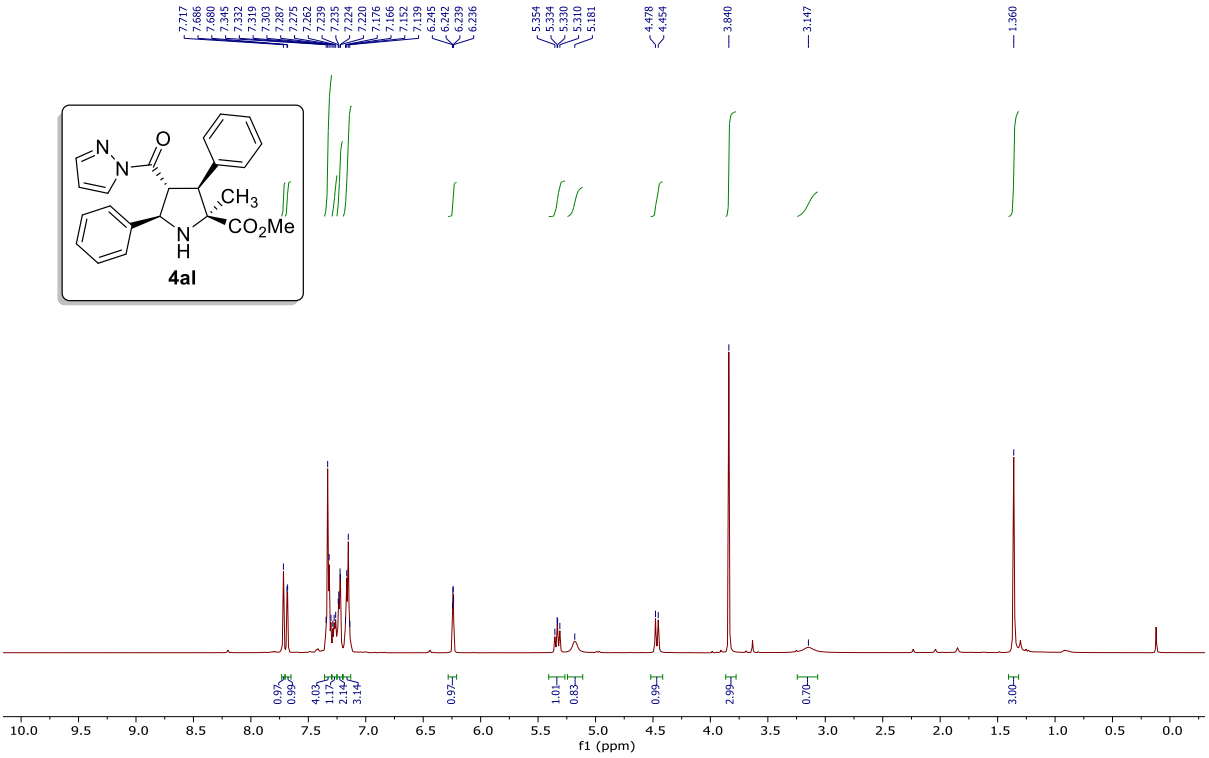
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4aj**



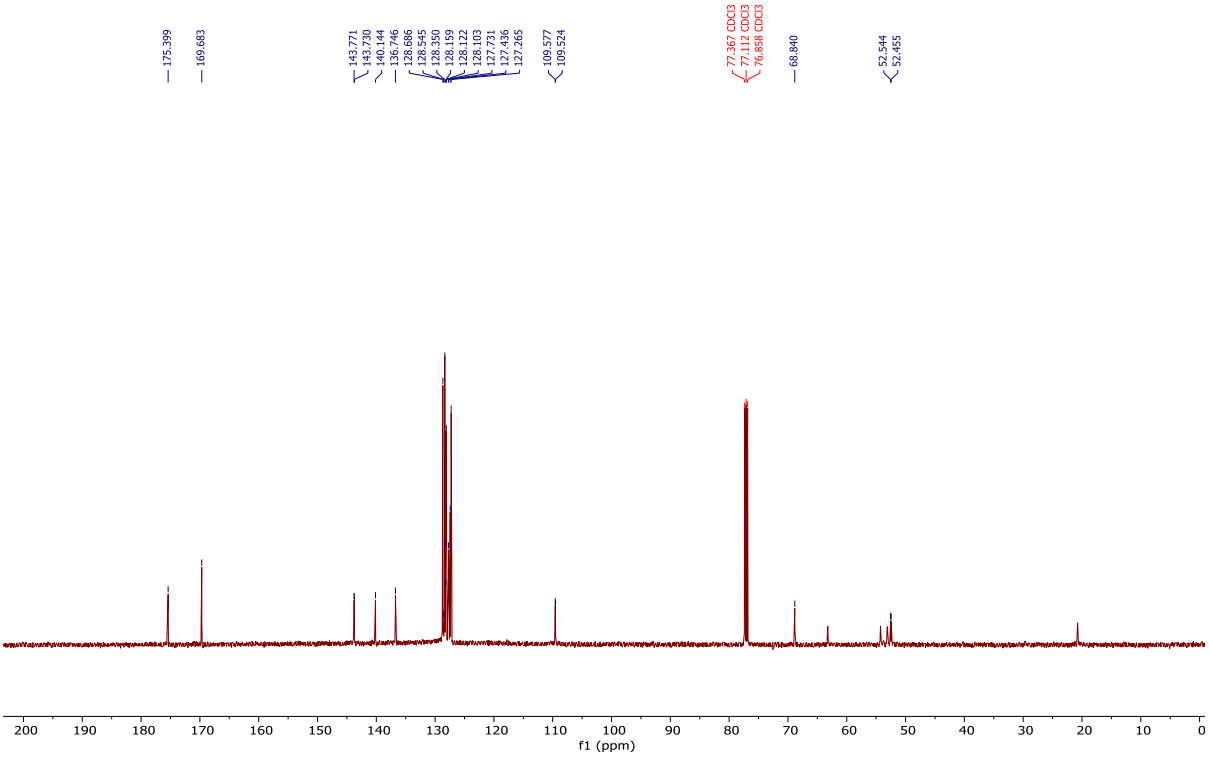
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4ak**



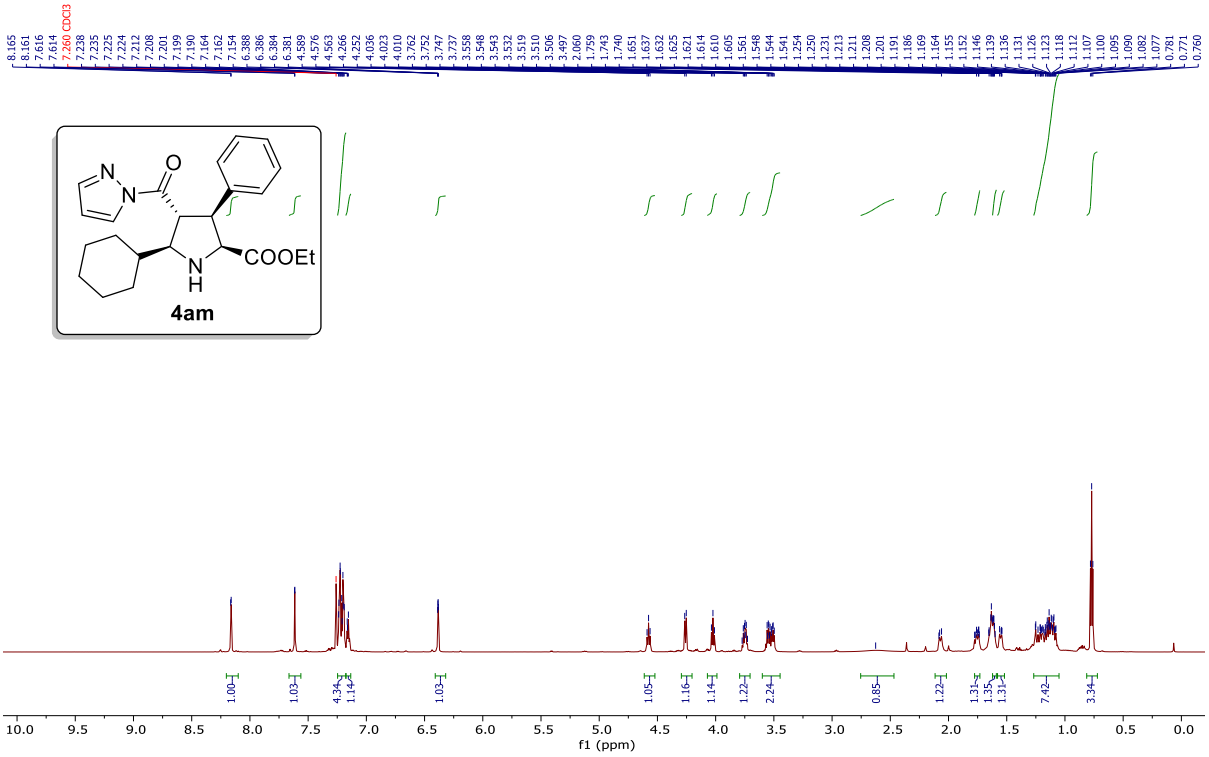
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4ak**



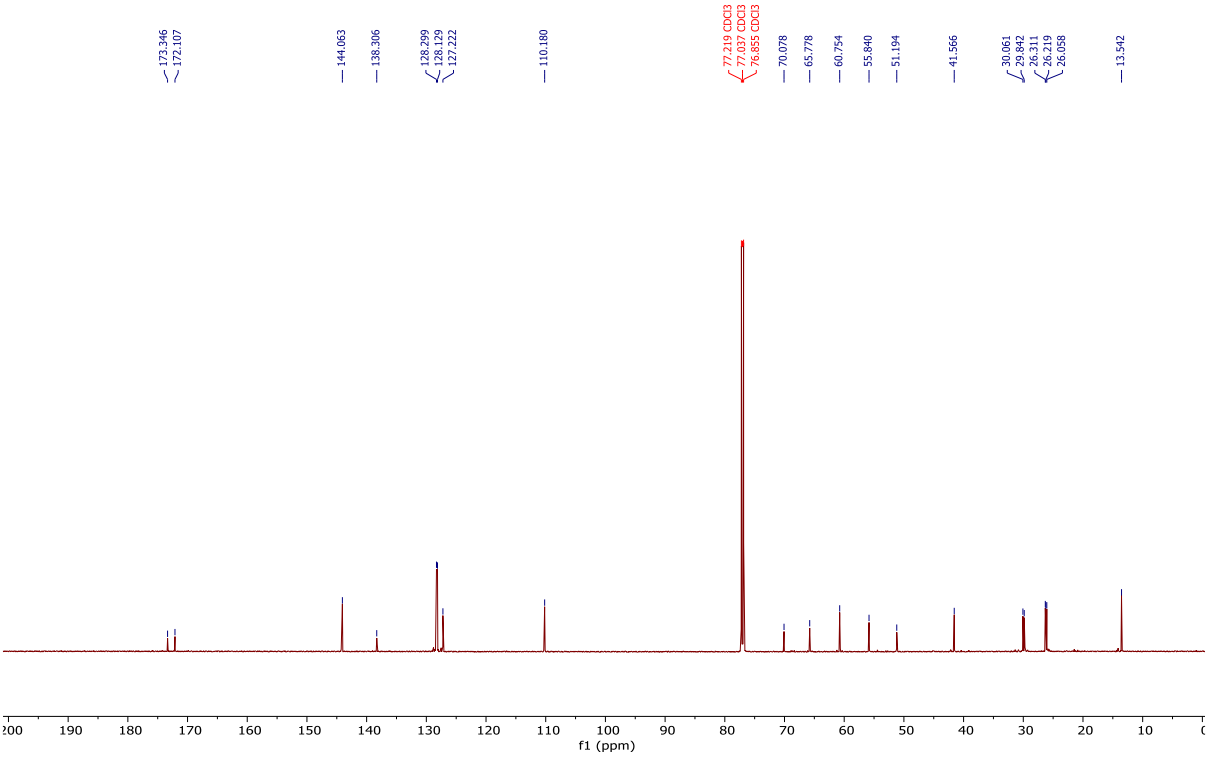
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4al**



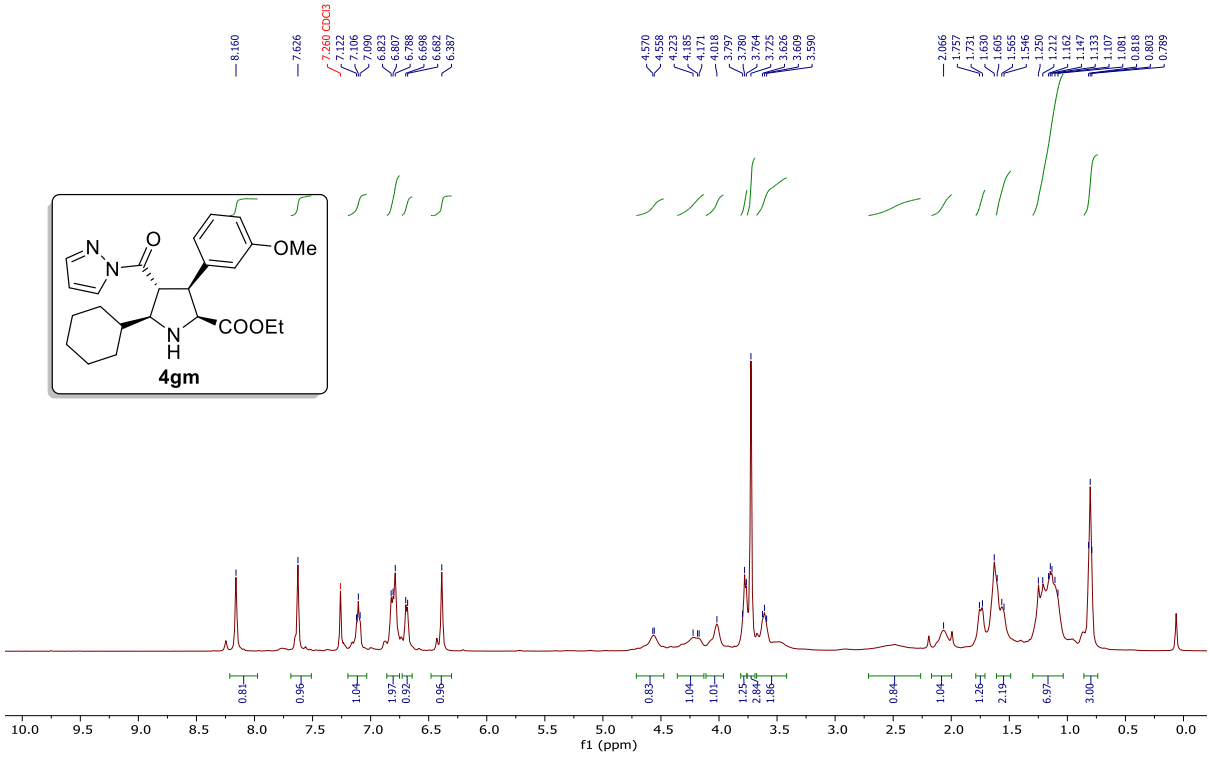
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4al**



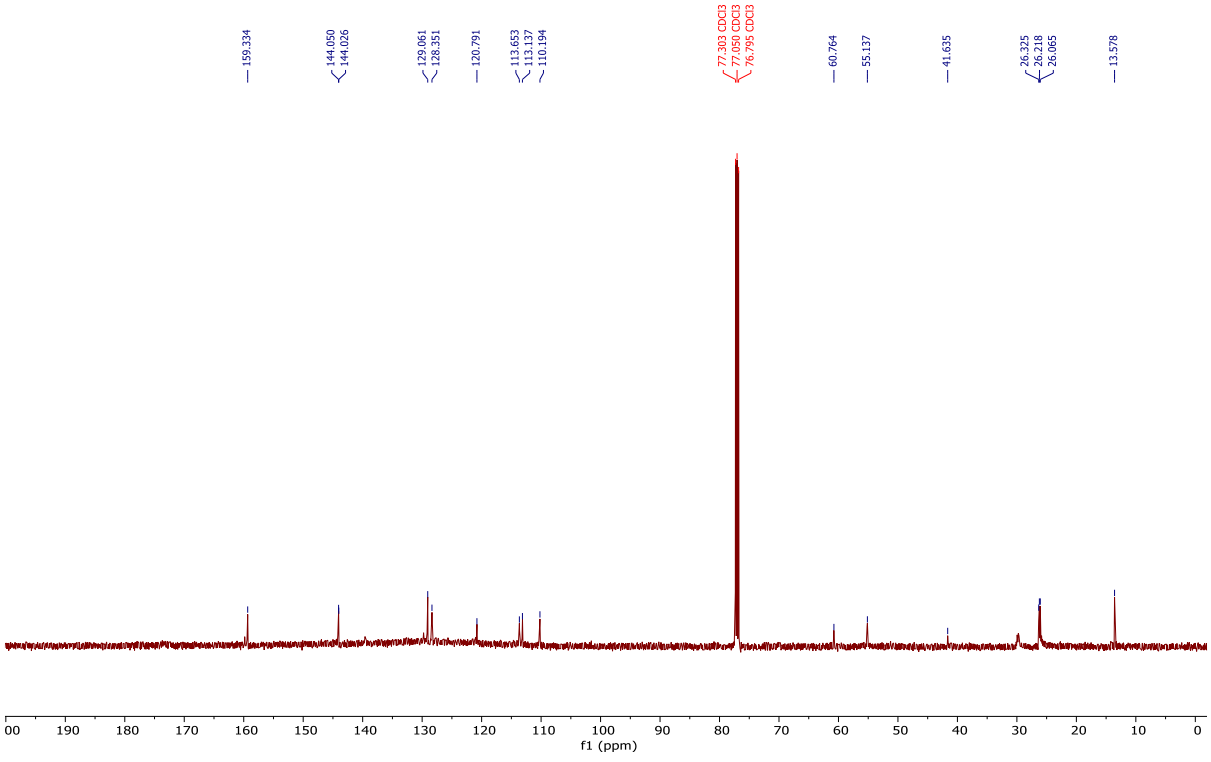
^{1}H NMR (700 MHz, $CDCl_3$) of compound **4am**



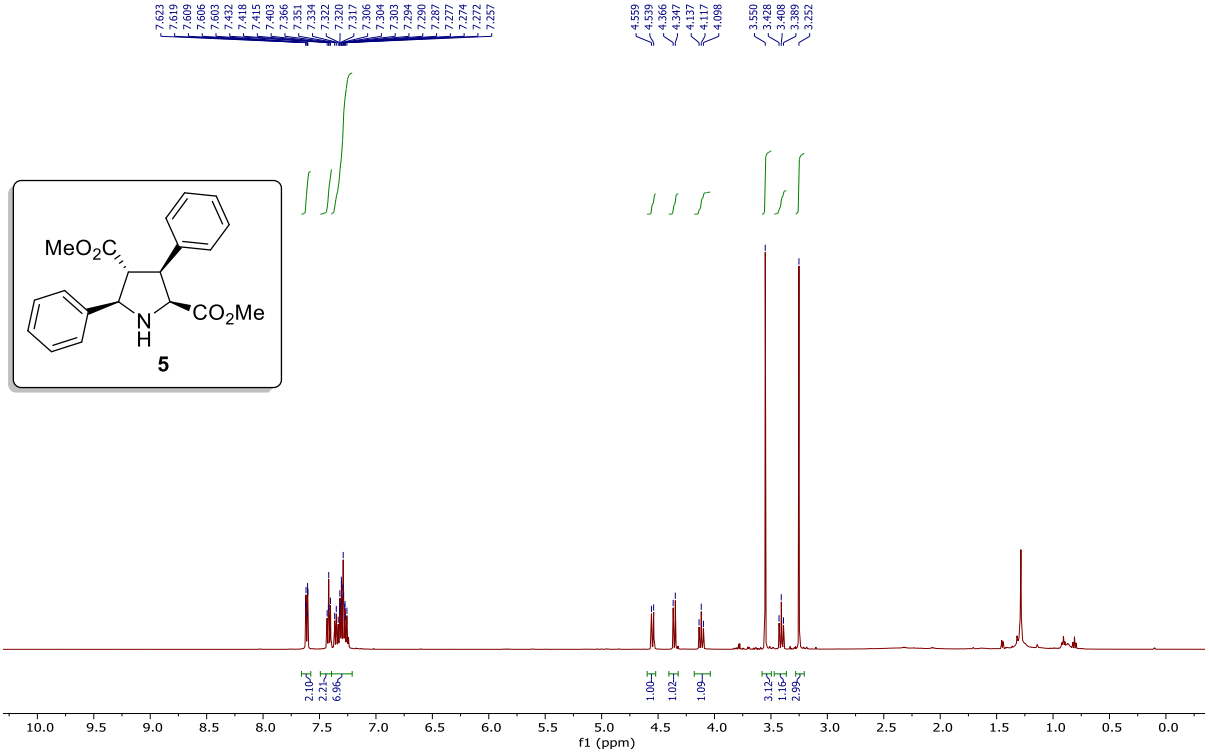
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4am**



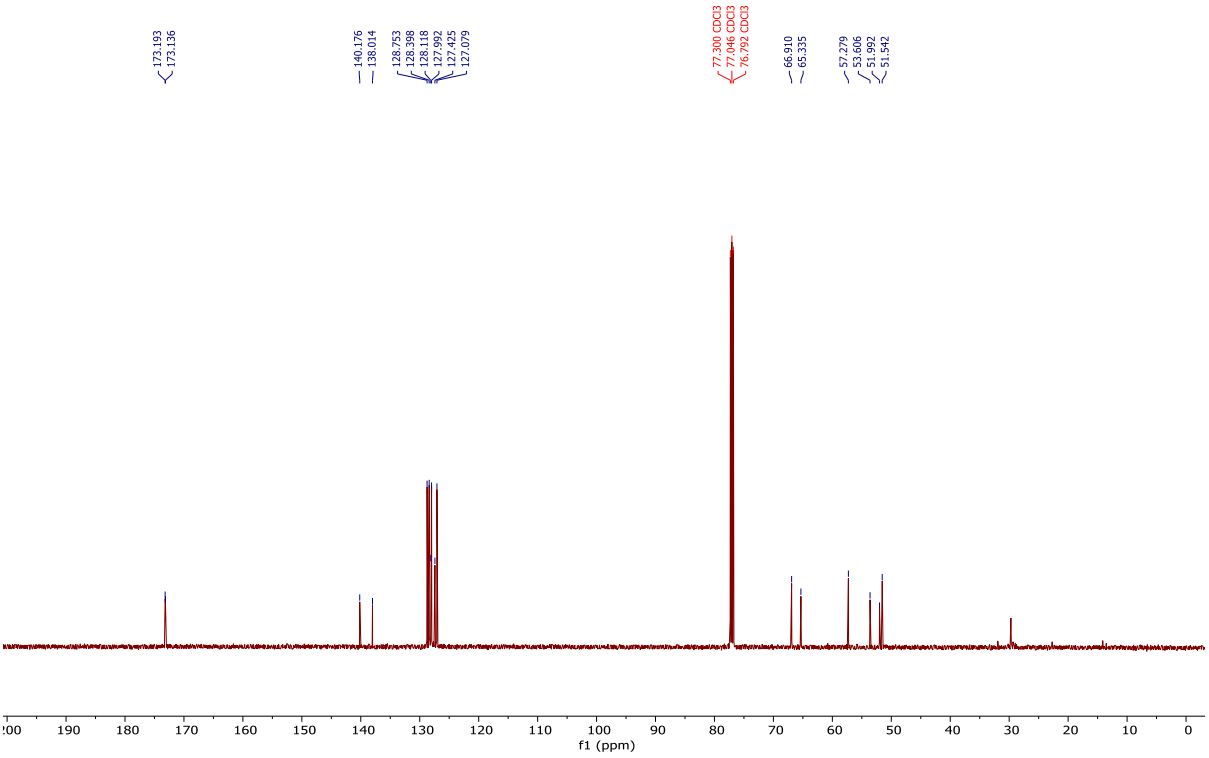
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4gm**



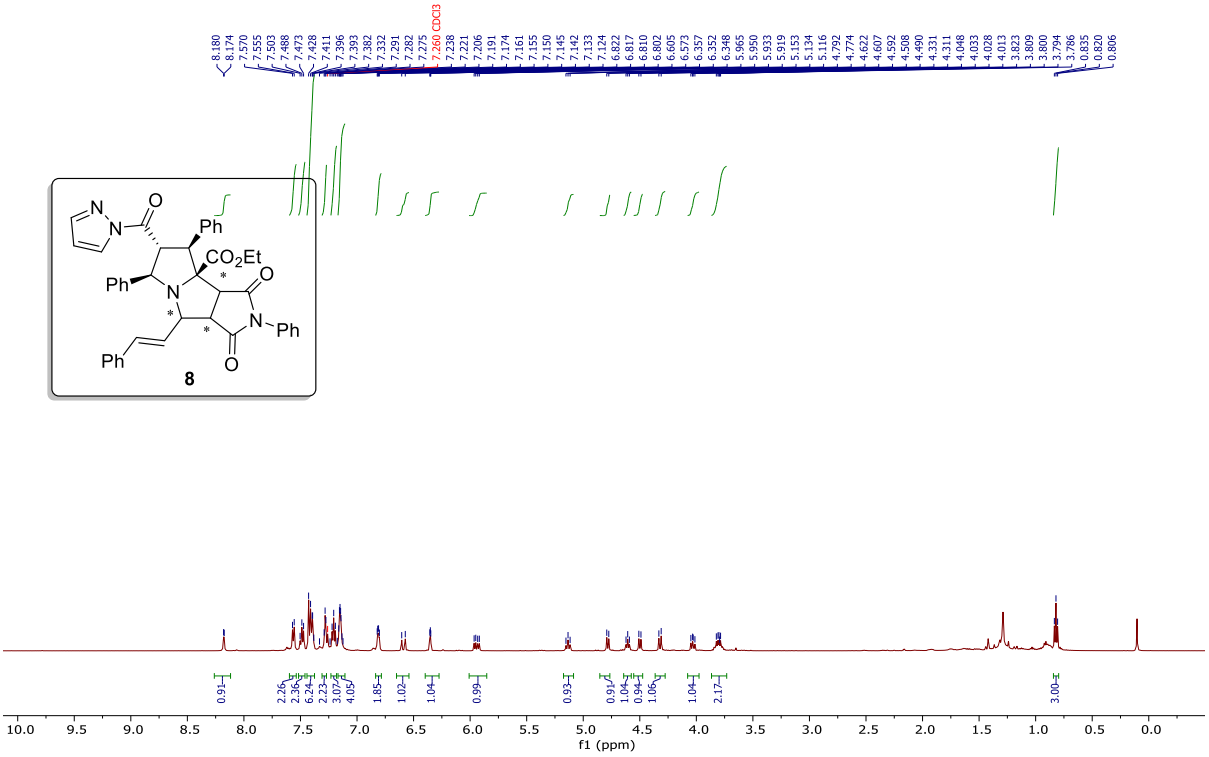
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4gm**



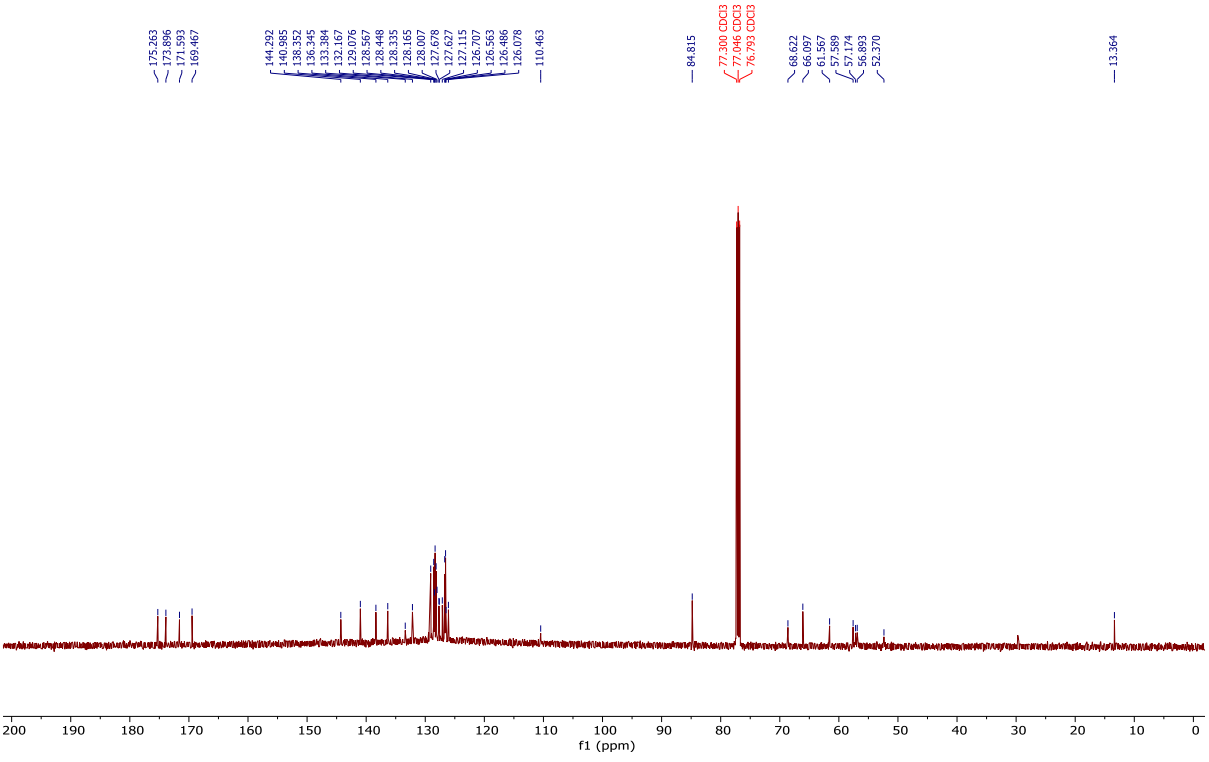
^{1}H NMR (500 MHz, $CDCl_3$) of compound **5**



^{13}C NMR (125 MHz, $CDCl_3$) of compound **5**

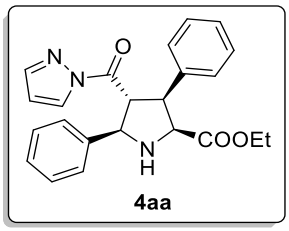


^{1}H NMR (500 MHz, $CDCl_3$) of compound **8**



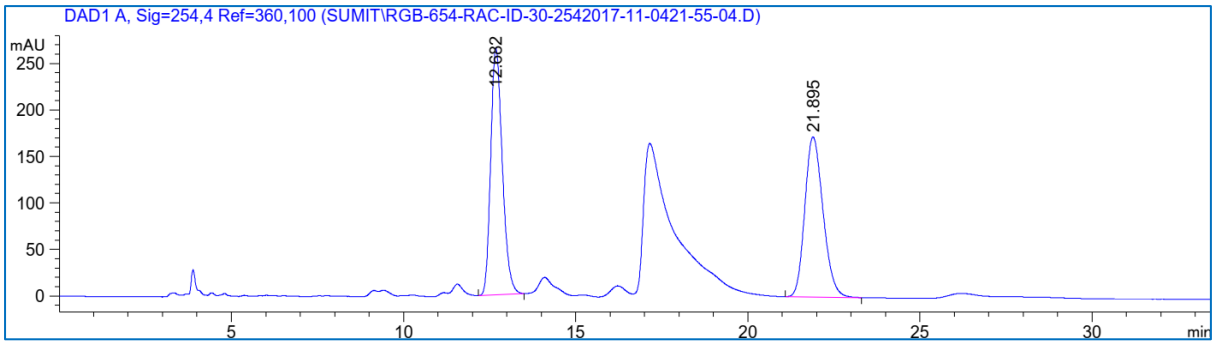
^{13}C NMR (125 MHz, $CDCl_3$) of compound **8**

HPLC Traces



4aa

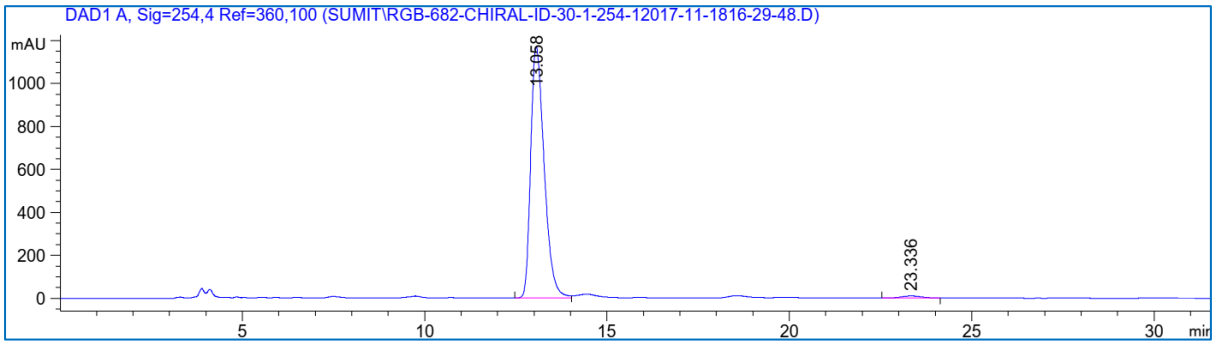
Sample Name: RGB-654-Rac-ID-30-254



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.682	BB	0.3613	6216.34717	265.38614	49.5260
2	21.895	BB	0.5713	6335.32617	172.18481	50.4740
Totals :				1.25517e4	437.57095	

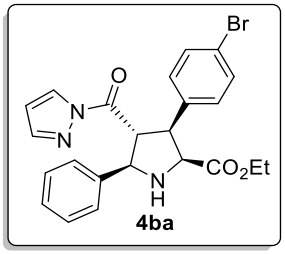
HPLC chromatogram of racemic **4aa**

Sample Name: RGB-682-Chiral-ID-30-1-254-1



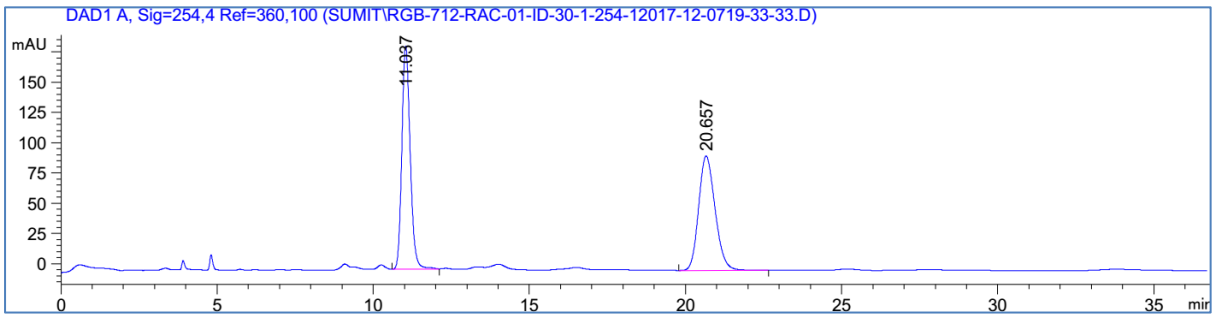
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.058	BV	0.3981	3.00512e4	1168.19214	98.7675
2	23.336	BB	0.5660	375.00452	9.80996	1.2325
Totals :				3.04262e4	1178.00209	

HPLC chromatogram of enantioenriched **4aa**



4ba

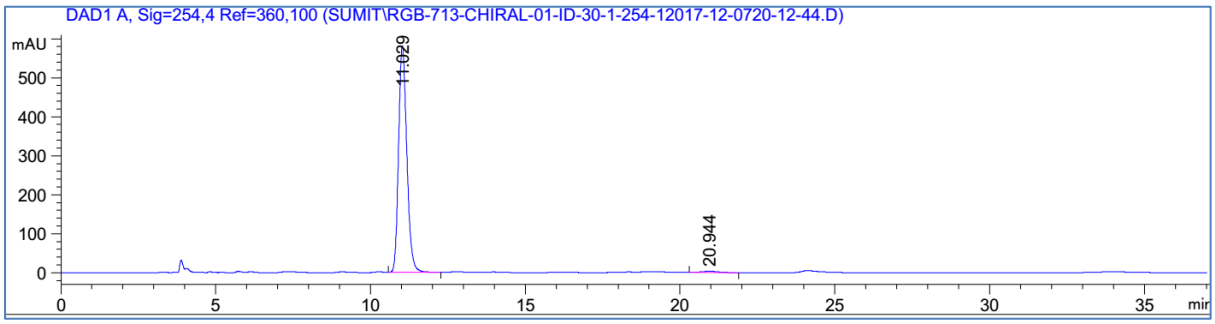
Sample Name: RGB-712-Rac-01-ID-30-1-254-1



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.037	BB	0.2867	3424.95728	184.37140	49.7447
2	20.657	BB	0.5672	3460.10669	94.50213	50.2553
Totals :				6885.06396	278.87353	

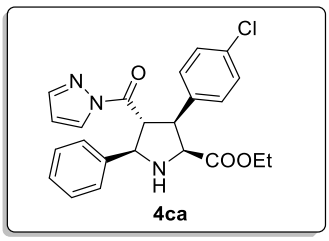
HPLC chromatogram of racemic **4ba**

Sample Name: RGB-713-Chiral-01-ID-30-1-254-1



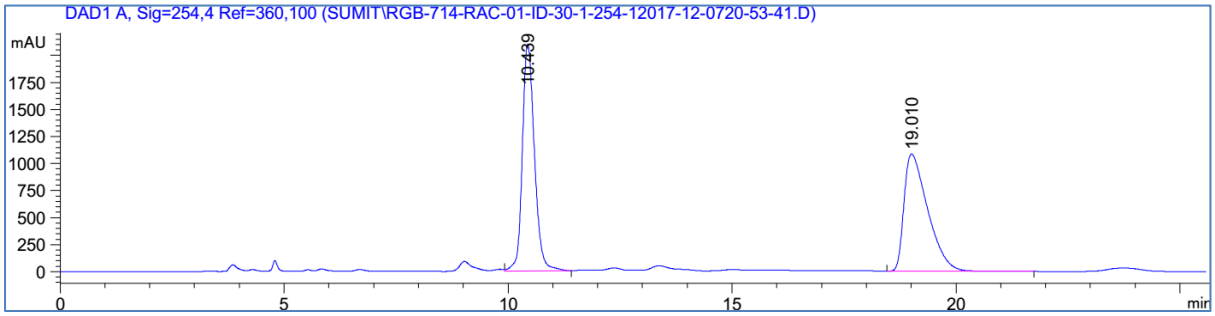
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.029	VB	0.2861	1.07659e4	581.19348	98.9331
2	20.944	BB	0.5448	116.10085	3.31311	1.0669
Totals :				1.08820e4	584.50659	

HPLC chromatogram of enantioenriched **4ba**



4ca

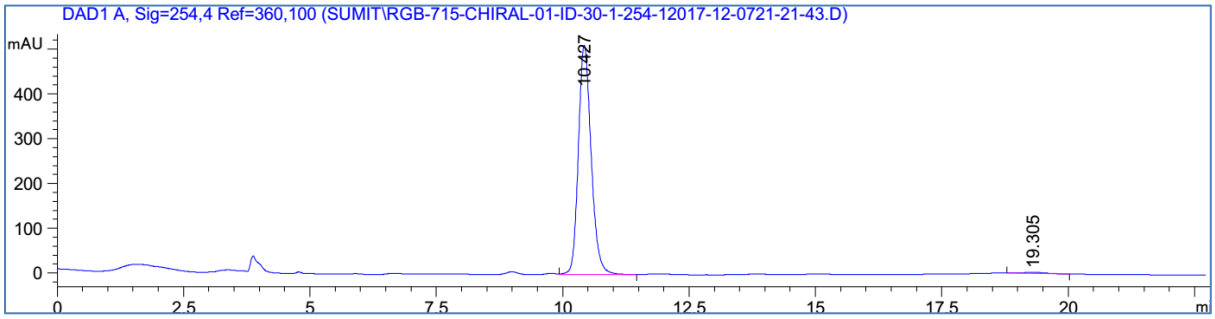
Sample Name: RGB-714-Rac-01-ID-30-1-254-1



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.439	VB	0.2889	3.93762e4	2098.60352	49.6437
2	19.010	BB	0.5571	3.99414e4	1086.06604	50.3563
Totals :				7.93176e4	3184.66956	

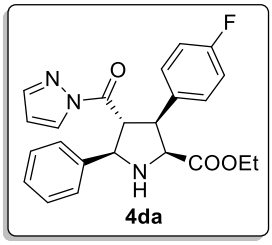
HPLC chromatogram of racemic **4ca**

Sample Name: RGB-715-Chiral-01-ID-30-1-254-1



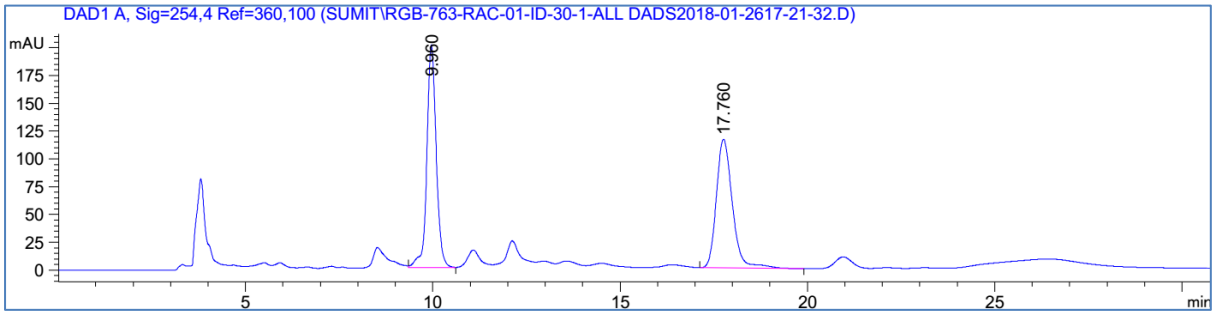
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.427	VB	0.2710	8994.06836	511.87506	99.1578
2	19.305	BBA	0.5000	76.39089	2.35785	0.8422
Totals :				9070.45925	514.23291	

HPLC chromatogram of enantioenriched **4ca**



4da

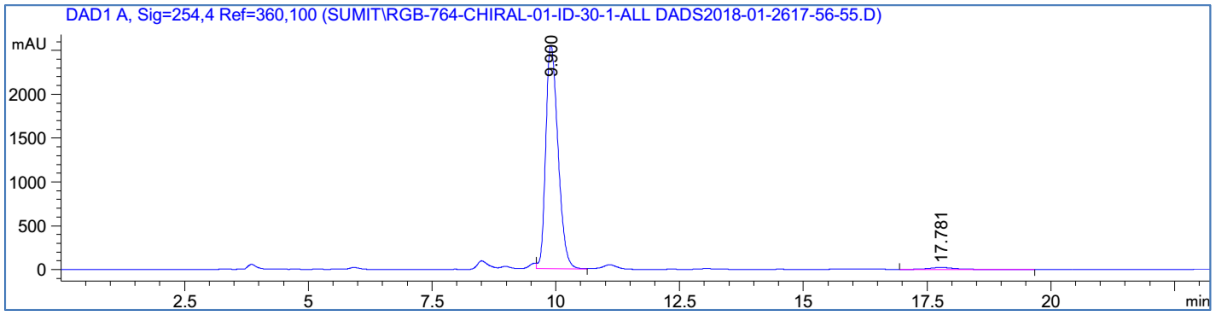
Sample Name: RGB-763-Rac-01-ID-30-1-All DADS



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.960	VB	0.2646	3476.53833	200.18739	50.2898
2	17.760	BB	0.4566	3436.47217	115.67691	49.7102
Totals :				6913.01050	315.86430	

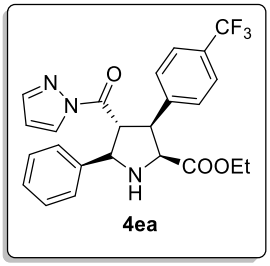
HPLC chromatogram of racemic **4da**

Sample Name: RGB-764-Chiral-01-ID-30-1-All DADS



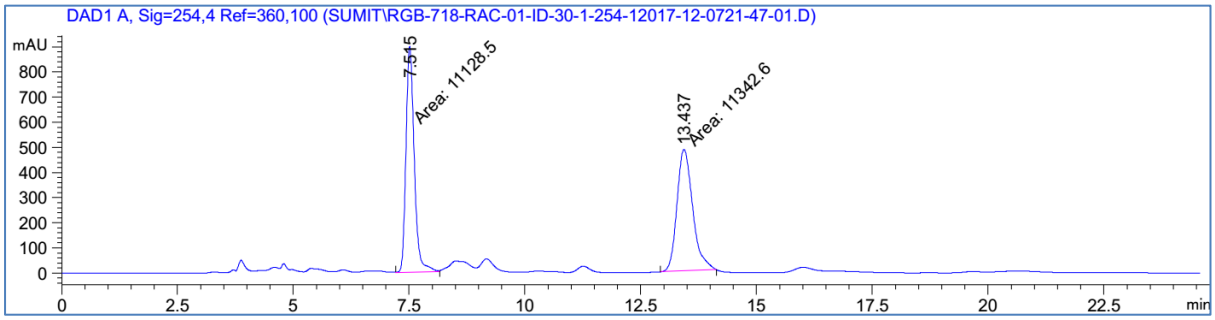
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.900	VV	0.2696	4.40283e4	2547.90869	97.9852
2	17.781	BB	0.5646	905.32892	23.54441	2.0148
Totals :				4.49336e4	2571.45311	

HPLC chromatogram of enantioenriched **4da**



4ea

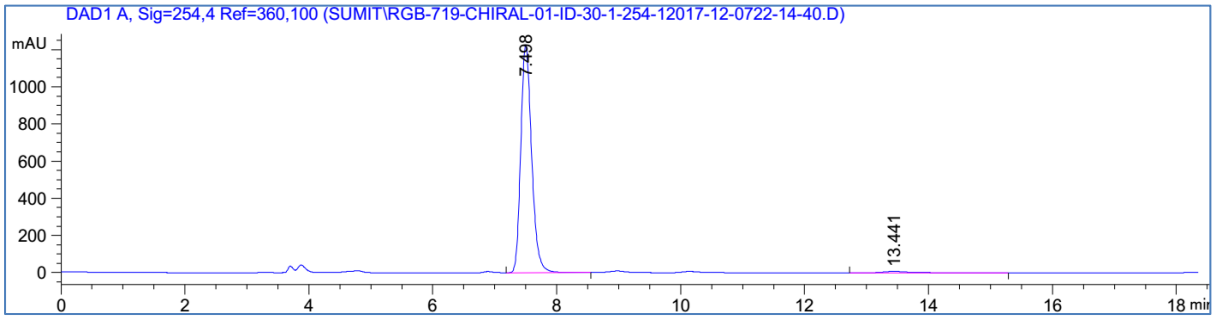
Sample Name: RGB-718-Rac-01-ID-30-1-254-1



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.515	MM	0.2066	1.11285e4	897.56287	49.5237
2	13.437	MM	0.3918	1.13426e4	482.55090	50.4763
Totals :				2.24711e4	1380.11377	

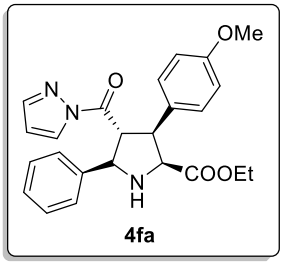
HPLC chromatogram of racemic **4ea**

Sample Name: RGB-719-Chiral-01-ID-30-1-254-1



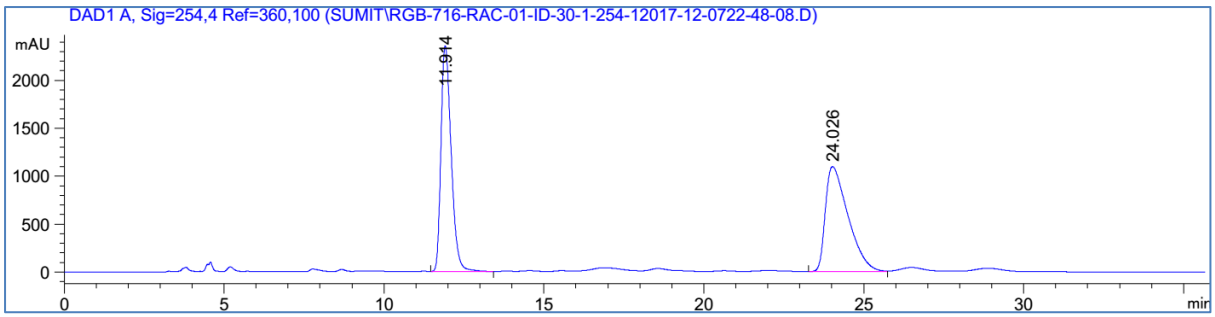
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.498	VB	0.1883	1.49448e4	1225.70117	98.4261
2	13.441	BB	0.4365	238.98112	7.95469	1.5739
Totals :				1.51838e4	1233.65586	

HPLC chromatogram of enantioenriched **4ea**



4fa

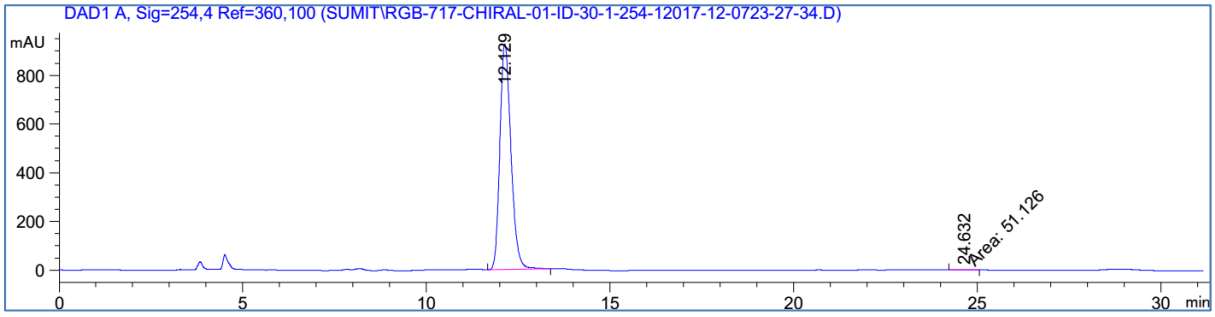
Sample Name: RGB-716-Rac-01-ID-30-1-254-1



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.914	VB	0.3452	5.23235e4	2354.89380	49.2638
2	24.026	BV	0.7442	5.38875e4	1094.90930	50.7362
Totals :				1.06211e5	3449.80310	

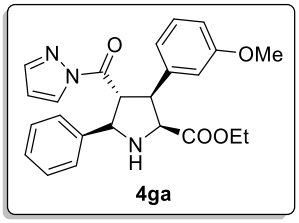
HPLC chromatogram of racemic **4fa**

Sample Name: RGB-717-Chiral-01-ID-30-1-254-1

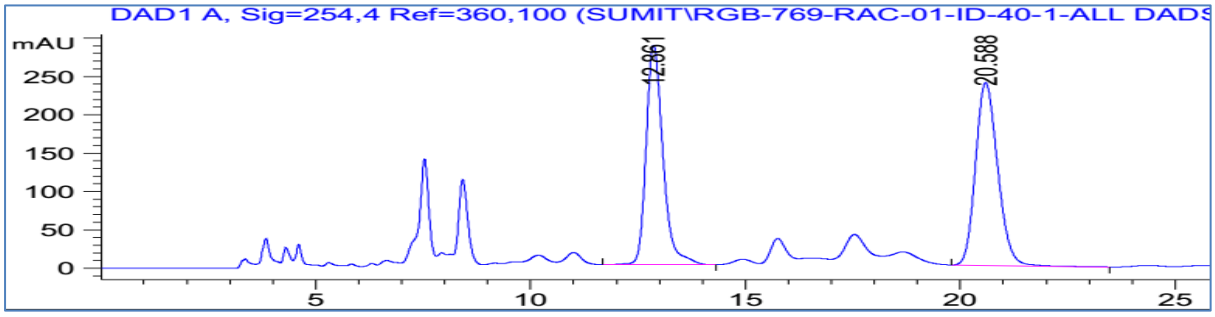


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.129	BB	0.3229	1.94481e4	926.48492	99.7378
2	24.632	MM	0.5613	51.12603	1.51806	0.2622
Totals :				1.94992e4	928.00299	

HPLC chromatogram of enantioenriched **4fa**



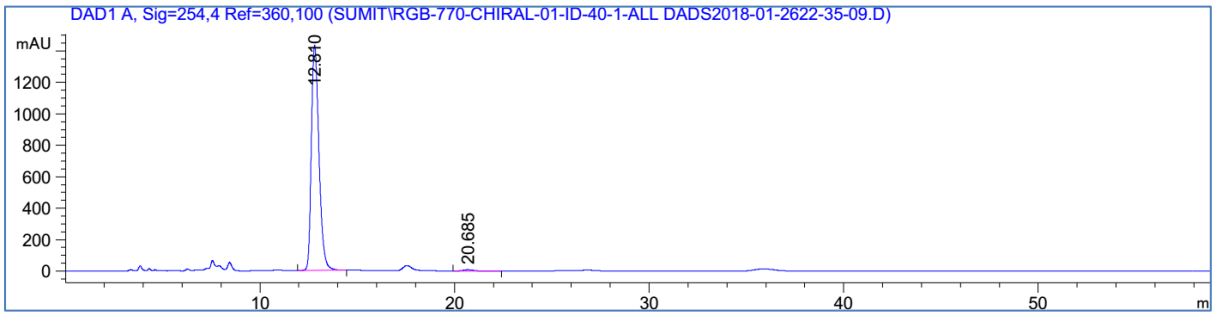
Sample Name: RGB-769-Rac-01-ID-40-1-All DADS



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.861	BB	0.4156	7782.02539	285.88452	47.6826
2	20.588	BB	0.5560	8538.43066	238.31888	52.3174
Totals :				1.63205e4	524.20340	

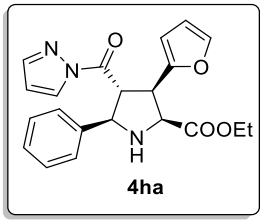
HPLC chromatogram of racemic **4ga**

Sample Name: RGB-770-Chiral-01-ID-40-1-All DADS



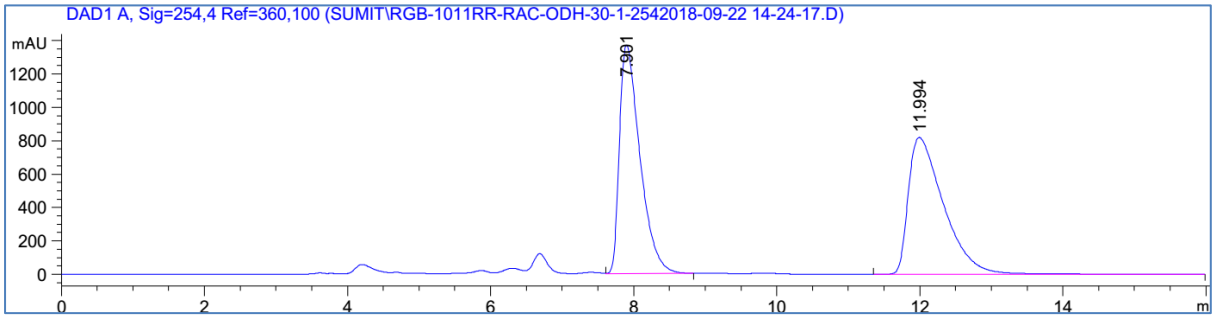
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.810	BB	0.4213	3.89910e4	1433.74976	99.1997
2	20.685	BB	0.5786	314.54861	8.29107	0.8003
Totals :				3.93055e4	1442.04083	

HPLC chromatogram of enantioenriched **4ga**



4ha

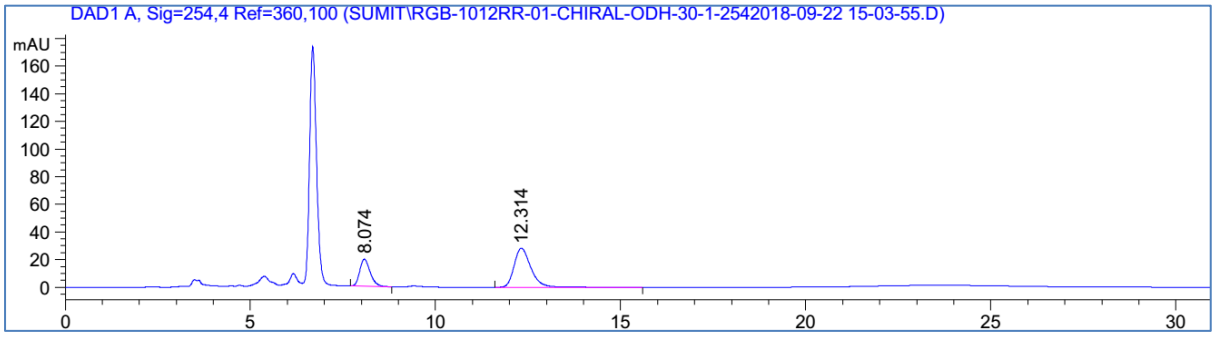
Sample Name: RGB-101011-RAC-ODH-30-1-254



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.901	VB	0.3020	2.71930e4	1367.61487	49.2628
2	11.994	BBA	0.5146	2.80069e4	819.67621	50.7372
Totals :				5.52000e4	2187.29108	

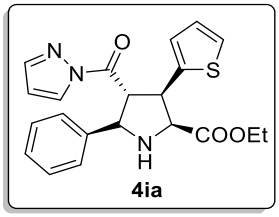
HPLC chromatogram of racemic **4ha**

Sample Name: RGB-1012RR-01-CHIRAL-ODH-30-1-254



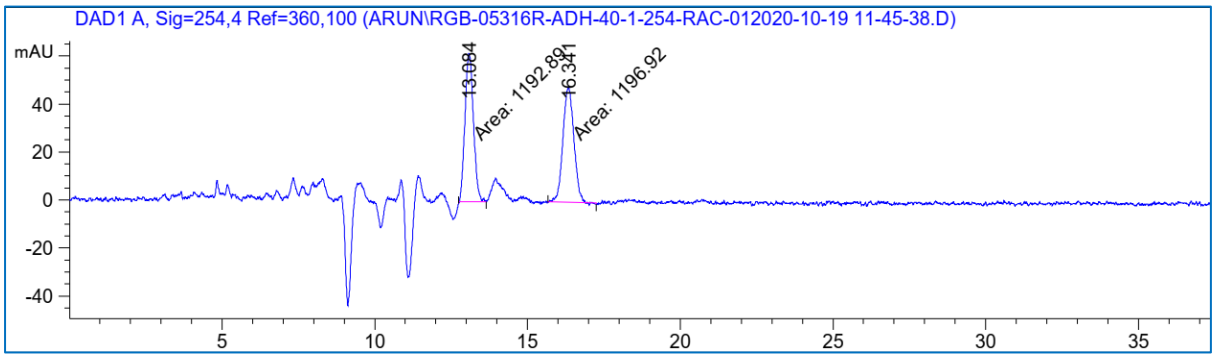
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.074	BB	0.2992	379.58481	19.49458	29.8797
2	12.314	BB	0.4810	890.79254	28.31792	70.1203
Totals :				1270.37735	47.81250	

HPLC chromatogram of enantioenriched **4ha**



4ia

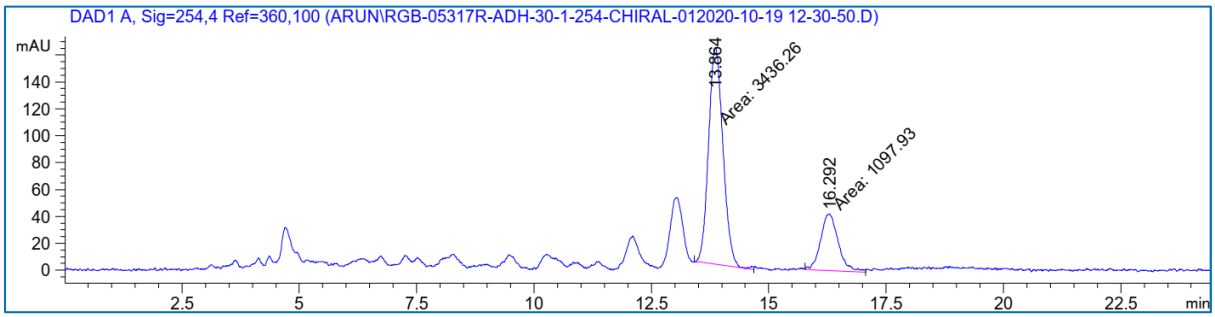
Sample Name: RGB-05316R-ADH-40-1-254-RAC-01



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.084	MM	0.3218	1192.88525	61.78625	49.9156
2	16.341	MM	0.4140	1196.92065	48.18714	50.0844
Totals :				2389.80591	109.97338	

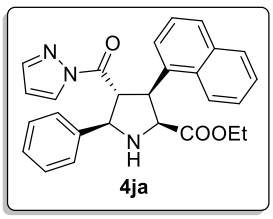
HPLC chromatogram of racemic **4ia**

Sample Name: RGB-05317R-ADH-30-1-254-CHIRAL-01



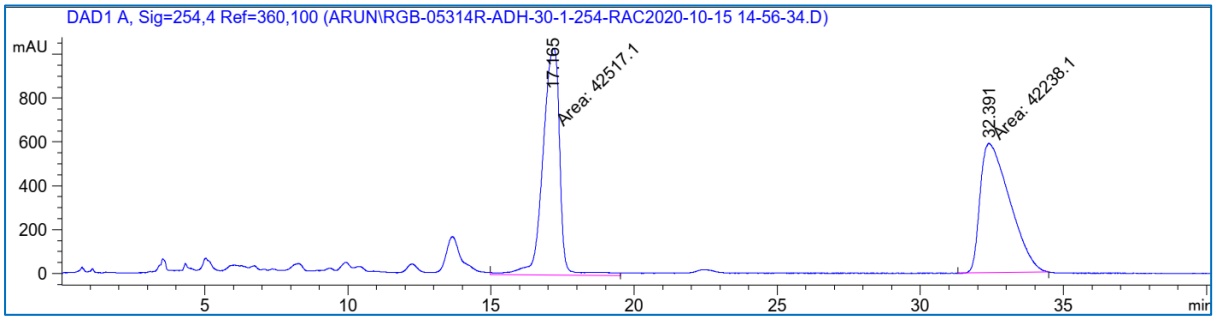
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.864	MM	0.3552	3436.26172	161.24118	75.7856
2	16.292	MM	0.4352	1097.92761	42.04232	24.2144
Totals :				4534.18933	203.28350	

HPLC chromatogram of enantioenriched **4ia**



4ja

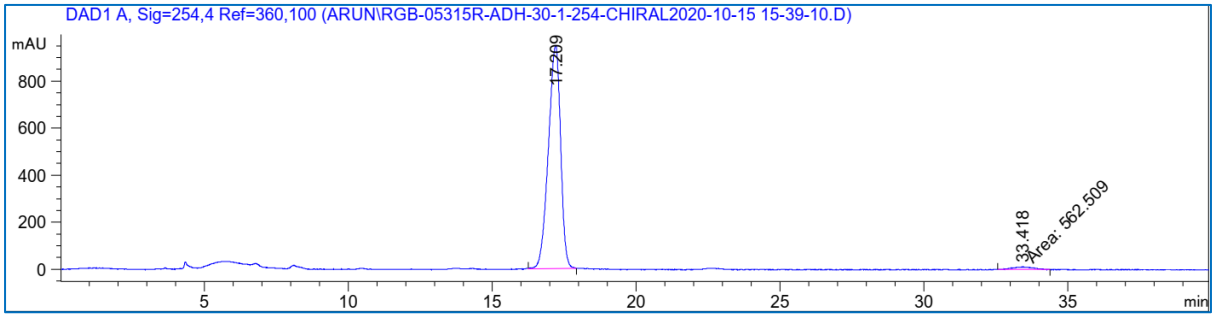
Sample Name: RGB-05314R-ADH-30-1-254-RAC



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.165	MM	0.6855	4.25171e4	1033.70703	50.1646
2	32.391	MM	1.1928	4.22381e4	590.15851	49.8354
Totals :				8.47552e4	1623.86554	

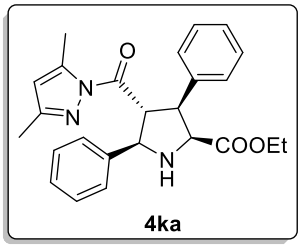
HPLC chromatogram of racemic **4ja**

Sample Name: RGB-05315R-ADH-30-1-254-CHIRAL



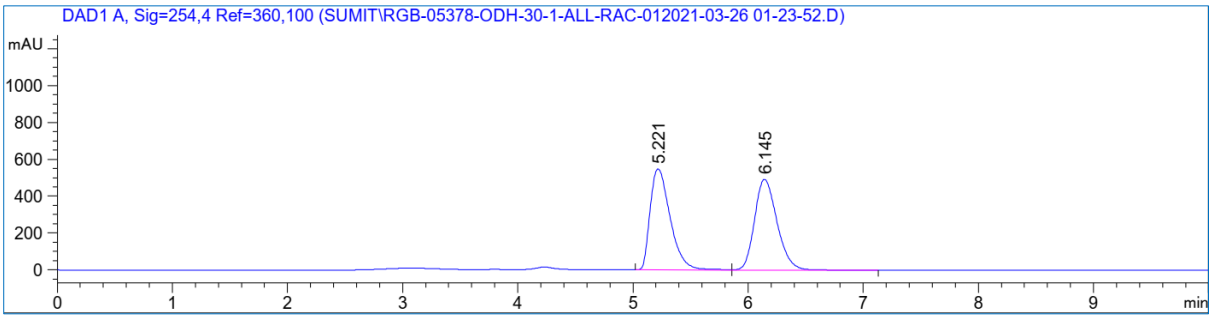
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.209	VV	0.3593	2.81136e4	949.91327	98.0384
2	33.418	MM	0.8267	562.50867	11.34066	1.9616
Totals :				2.86761e4	961.25393	

HPLC chromatogram of enantioenriched **4ja**



4ka

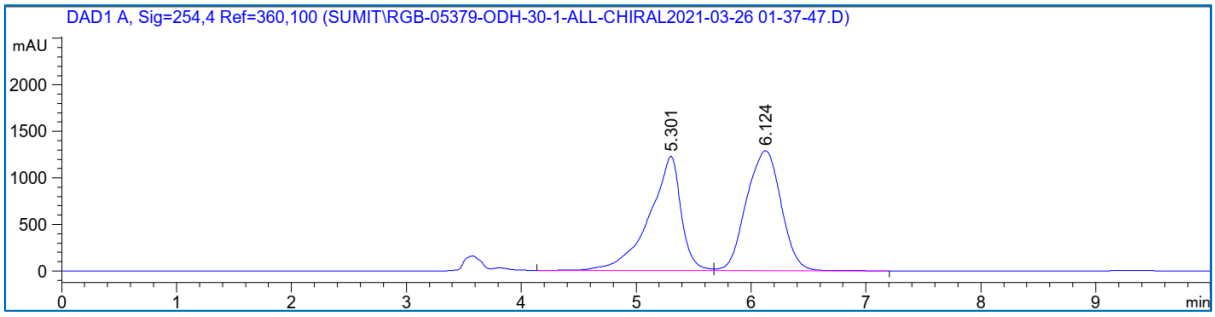
Sample Name: RGB-05378-ODH-30-1-ALL-RAC-01



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.221	BV	0.1895	6662.24170	549.38660	49.8950
2	6.145	VB	0.2103	6690.27539	493.15656	50.1050
Totals :				1.33525e4	1042.54315	

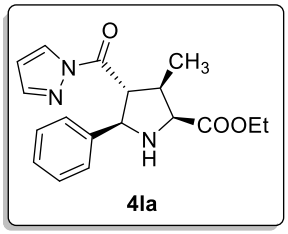
HPLC chromatogram of racemic **4ka**

Sample Name: RGB-05379-ODH-30-1-ALL-CHIRAL



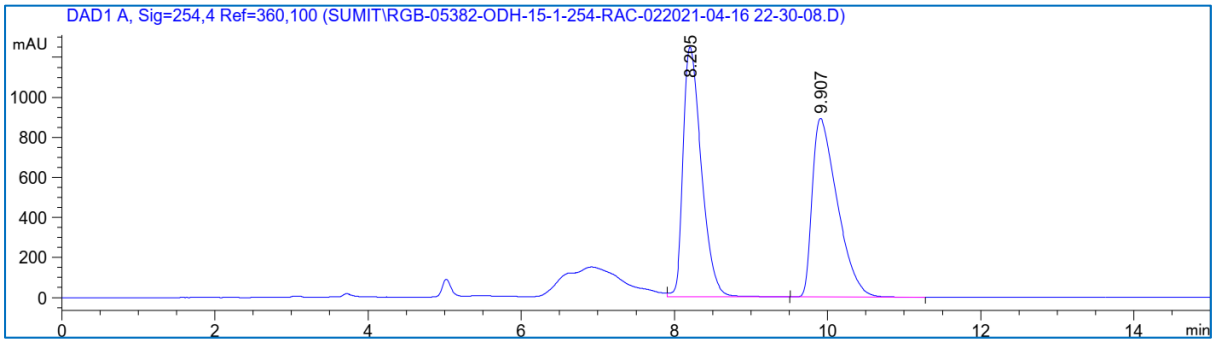
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.301	BV	0.2610	2.36801e4	1227.77466	46.7253
2	6.124	VB	0.3423	2.69993e4	1289.10754	53.2747
Totals :				5.06794e4	2516.88220	

HPLC chromatogram of enantioenriched **4ka**



4la

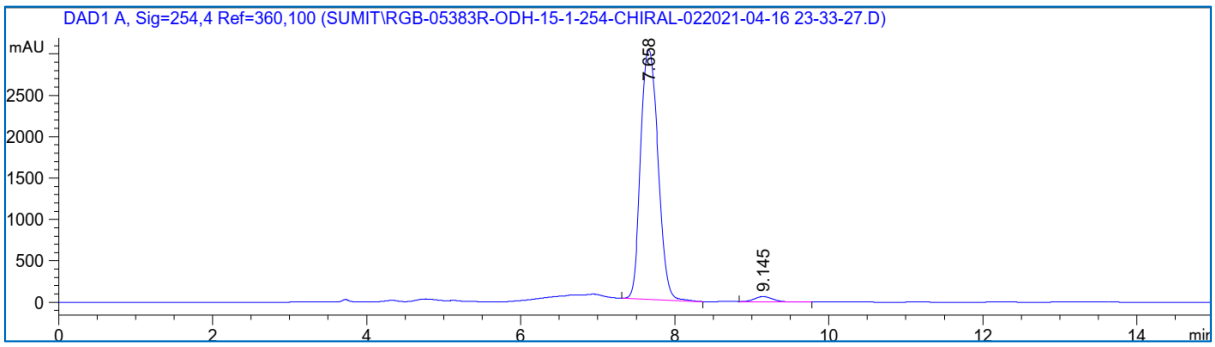
Sample Name: RGB-05382-ODH-15-1-254-RAC-02



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.205	VB	0.2551	2.06365e4	1247.11975	50.5214
2	9.907	BB	0.3444	2.02106e4	891.85541	49.4786
Totals :				4.08472e4	2138.97516	

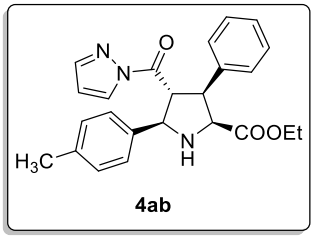
HPLC chromatogram of racemic **4la**

Sample Name: RGB-05383R-ODH-15-1-254-CHIRAL-02



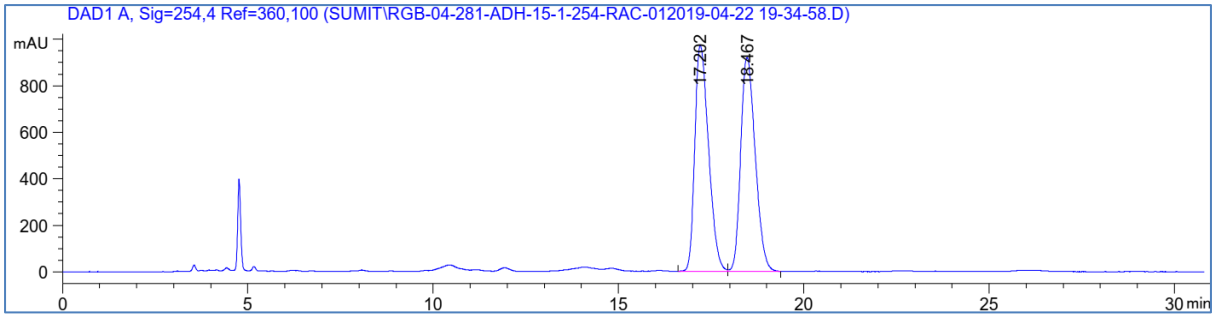
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.658	BB	0.2331	4.72384e4	3010.13818	97.7480
2	9.145	VB	0.2578	1088.33325	64.86351	2.2520
Totals :				4.83267e4	3075.00169	

HPLC chromatogram of enantioenriched **4la**



4ab

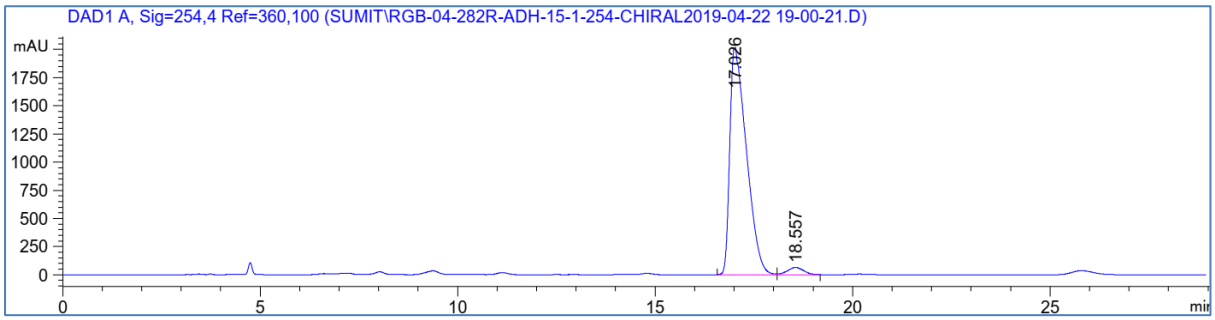
Sample Name: RGB-04-281-ADH-15-1-254-RAC-01



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.202	BV	0.3646	2.50872e4	973.68335	49.9541
2	18.467	VV	0.4231	2.51333e4	918.84070	50.0459
Totals :				5.02206e4	1892.52405	

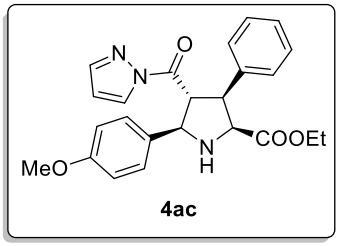
HPLC chromatogram of racemic **4ab**

Sample Name: RGB-04-282R-ADH-15-1-254-CHIRAL



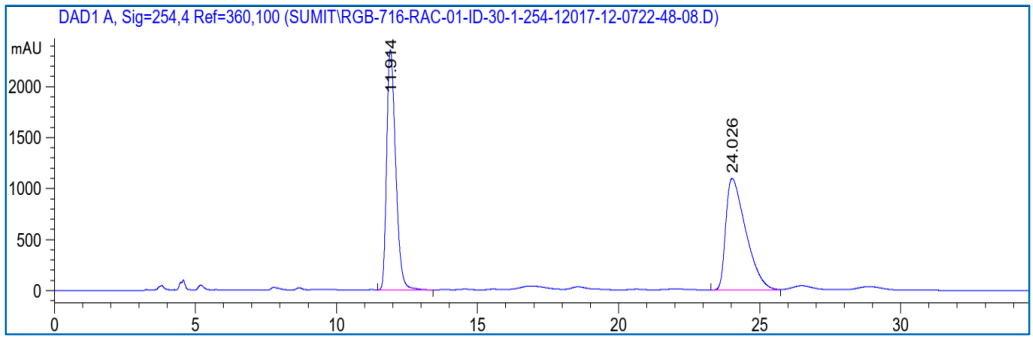
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.026	VV	0.3557	5.90412e4	2015.91211	96.9710
2	18.557	VV	0.4142	1844.20813	63.99843	3.0290
Totals :				6.08854e4	2079.91054	

HPLC chromatogram of enantioenriched **4ab**



4ac

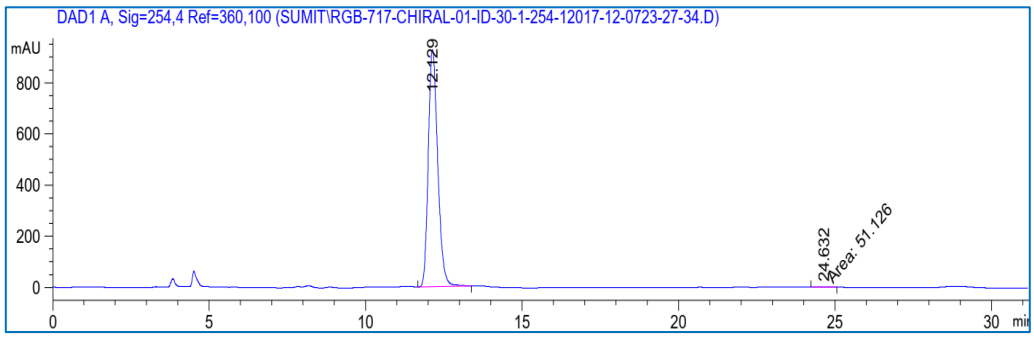
Sample Name: RGB-716-Rac-01-ID-30-1-254-1



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.914	VB	0.3452	5.23235e4	2354.89380	49.2638
2	24.026	BV	0.7442	5.38875e4	1094.90930	50.7362
Totals :				1.06211e5	3449.80310	

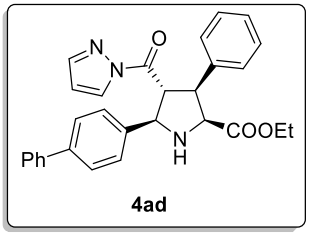
HPLC chromatogram of racemic **4ac**

Sample Name: RGB-717-Chiral-01-ID-30-1-254-1



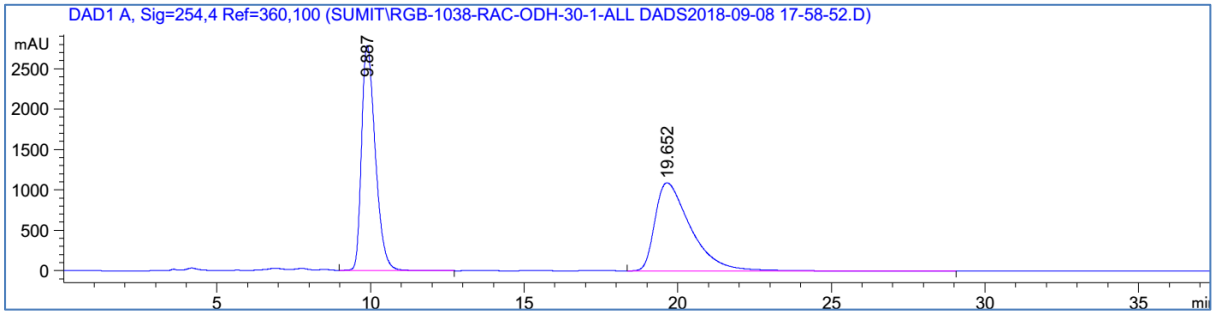
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.129	BB	0.3229	1.94481e4	926.48492	99.7378
2	24.632	MM	0.5613	51.12603	1.51806	0.2622
Totals :				1.94992e4	928.00299	

HPLC chromatogram of enantioenriched **4ac**



4ad

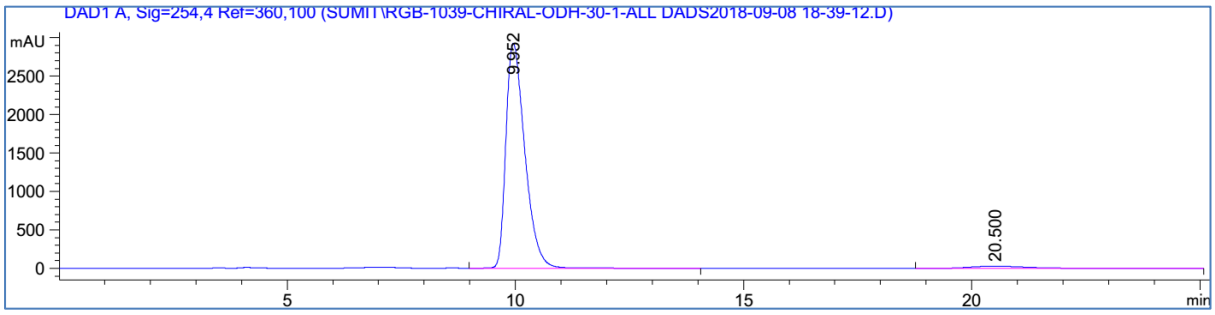
Sample Name: RGB-1038-RAC-ODH-30-1-ALL DADS



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.887	BB	0.4792	8.66547e4	2783.38159	49.6165
2	19.652	BB	1.2076	8.79942e4	1090.32007	50.3835
Totals :				1.74649e5	3873.70166	

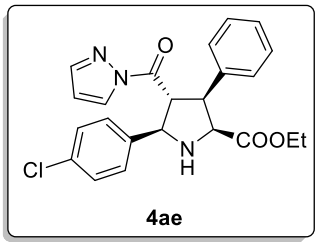
HPLC chromatogram of racemic **4ad**

Sample Name: RGB-1039-CHIRAL-ODH-30-1-ALL DADS



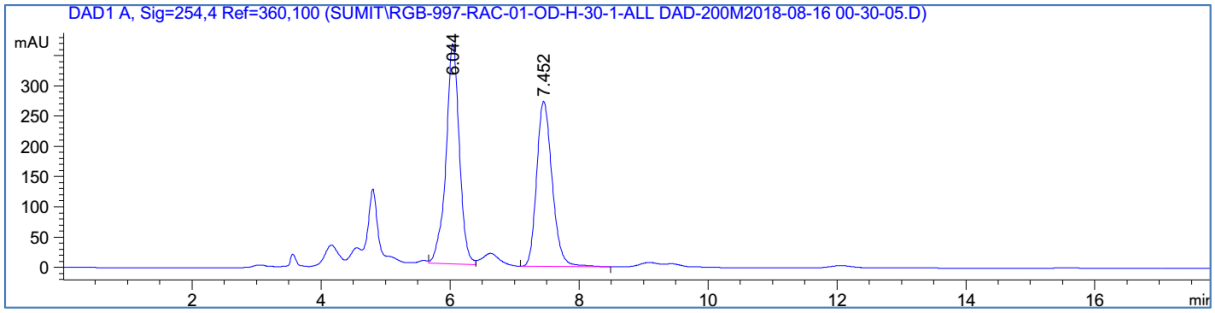
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.952	BB	0.4433	8.46024e4	2926.18433	96.9363
2	20.500	BBA	1.3583	2673.86499	29.70217	3.0637
Totals :				8.72762e4	2955.88649	

HPLC chromatogram of enantioenriched **4ad**



4ae

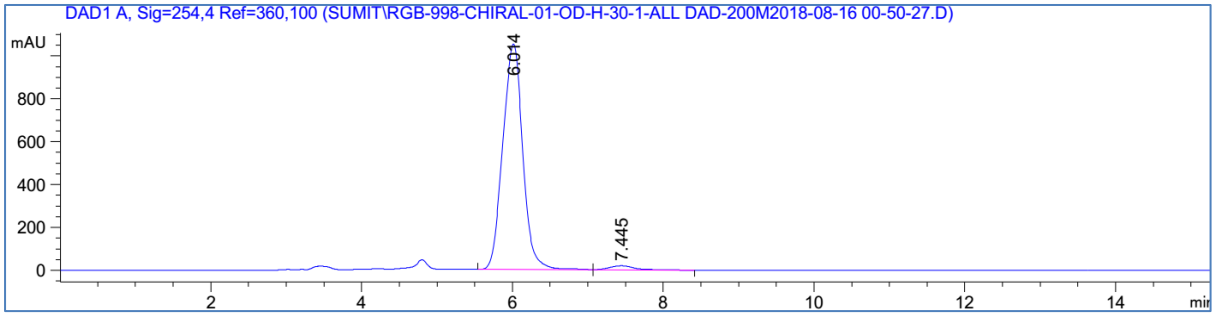
Sample Name: RGB-997-RAC-01-OD-H-30-1-ALL DAD-200M



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.044	VV	0.2161	5250.00342	364.30060	53.5258
2	7.452	BB	0.2569	4558.35010	272.85153	46.4742
Totals :				9808.35352	637.15213	

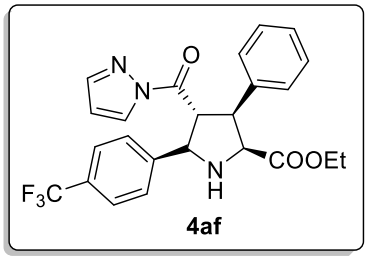
HPLC chromatogram of racemic **4ae**

Sample Name: RGB-998-CHIRAL-01-OD-H-30-1-ALL DAD-200M



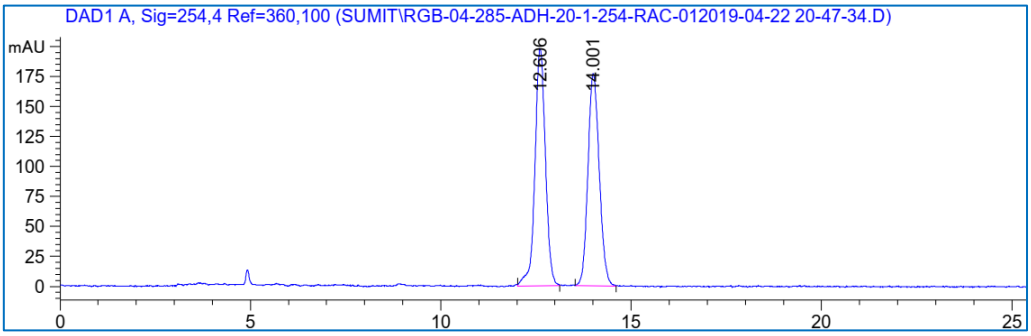
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.014	BV	0.2929	1.93831e4	1052.41187	97.6663
2	7.445	VB	0.3617	463.14618	19.45841	2.3337
Totals :				1.98463e4	1071.87028	

HPLC chromatogram of enantioenriched **4ae**



4af

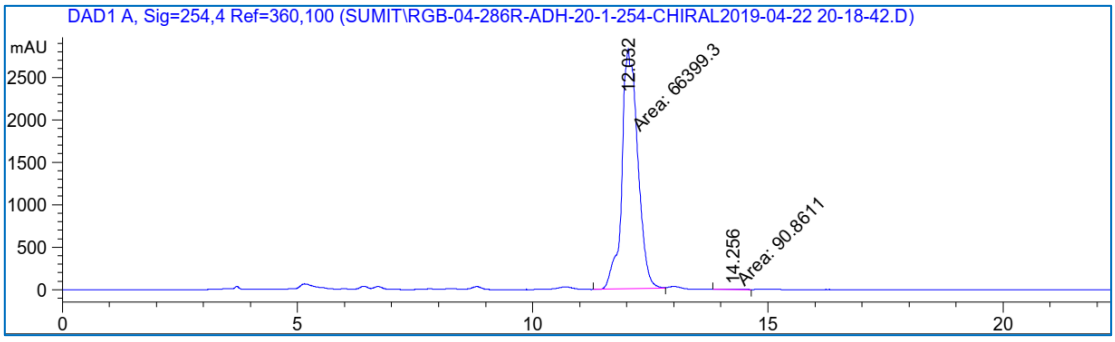
Sample Name: RGB-04-285-ADH-20-1-254-RAC-01



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.606	VV	0.2936	3788.91187	197.69821	50.7812
2	14.001	VV	0.3222	3672.34009	176.89294	49.2188
Totals :				7461.25195	374.59116	

HPLC chromatogram of racemic **4af**

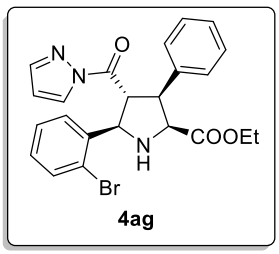
Sample Name: RGB-04-286R-ADH-20-1-254-CHIRAL



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

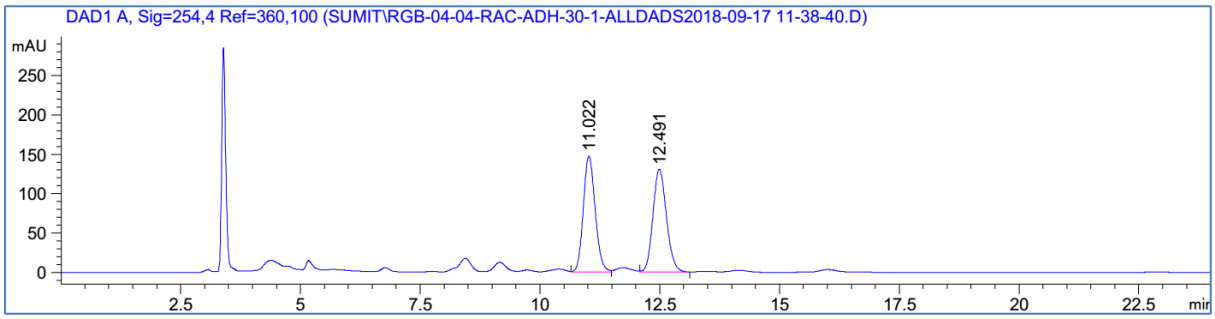
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.032	MM	0.3919	6.63993e4	2823.61865	99.8633
2	14.256	MM	0.3142	90.86106	4.81968	0.1367
Totals :				6.64901e4	2828.43833	

HPLC chromatogram of enantioenriched **4af**



4ag

Sample Name: RGB-04-04-RAC-ADH-30-1-ALLDADS

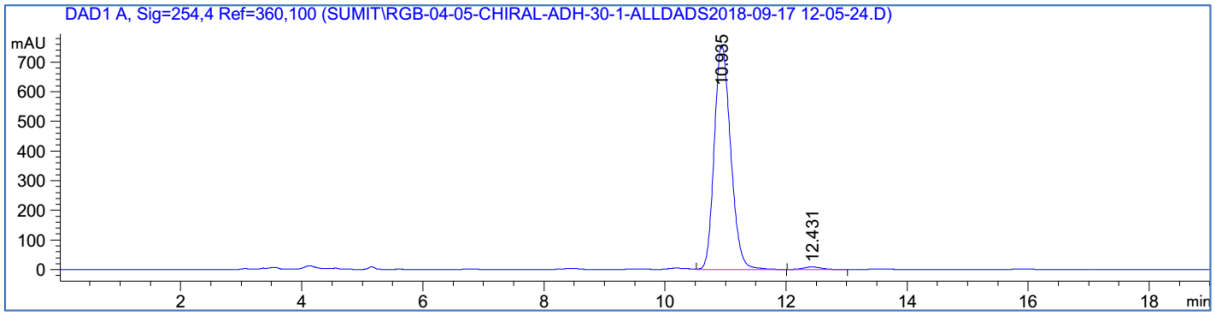


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.022	VV	0.2668	2524.68188	146.68004	49.7760
2	12.491	VB	0.3019	2547.40552	130.43153	50.2240
Totals :				5072.08740	277.11157	

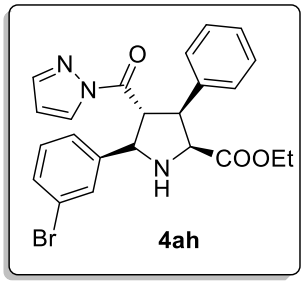
HPLC chromatogram of racemic **4ag**

Sample Name: RGB-04-05-CHIRAL-ADH-30-1-ALLDADS



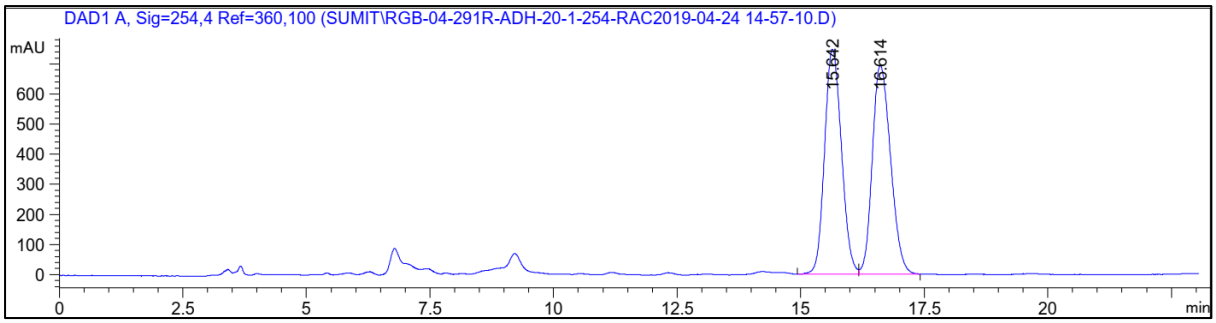
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.935	VB	0.2931	1.42278e4	757.59863	98.8045
2	12.431	BB	0.3161	172.15559	8.50736	1.1955
Totals :				1.44000e4	766.10599	

HPLC chromatogram of enantioenriched **4ag**



4ah

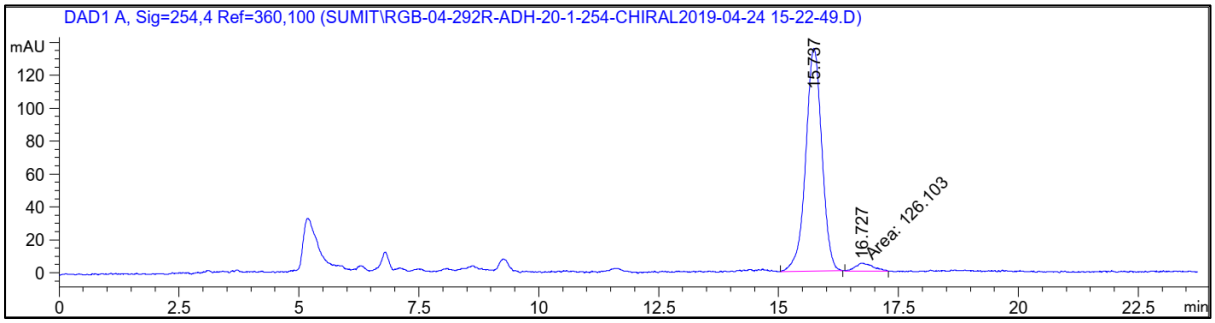
Sample Name: RGB-04-291R-ADH-20-1-254-RAC



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.642	BV	0.3738	1.78045e4	747.83887	49.8340
2	16.614	VV	0.4094	1.79232e4	693.82800	50.1660
Totals :				3.57277e4	1441.66687	

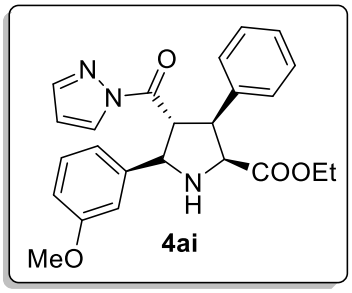
HPLC chromatogram of racemic **4ah**

Sample Name: RGB-04-292R-ADH-20-1-254-CHIRAL



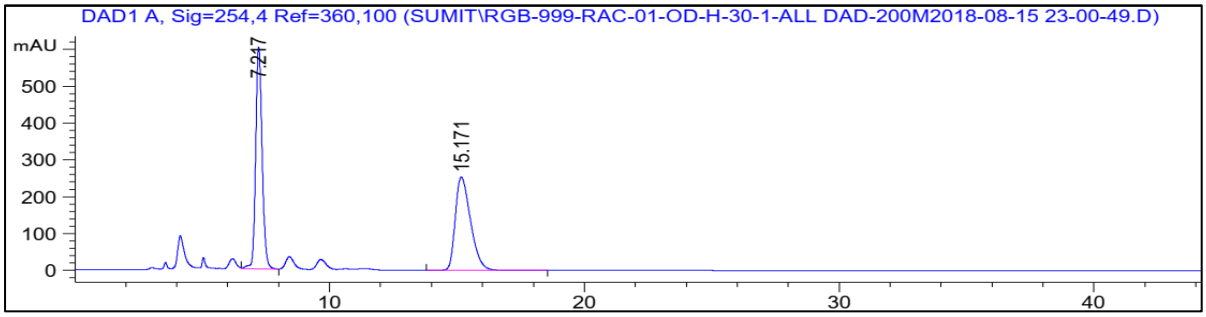
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.737	BB	0.3520	3182.90137	135.50673	96.1891
2	16.727	MM	0.4285	126.10264	4.90444	3.8109
Totals :				3309.00401	140.41117	

HPLC chromatogram of enantioenriched **4ah**



4ai

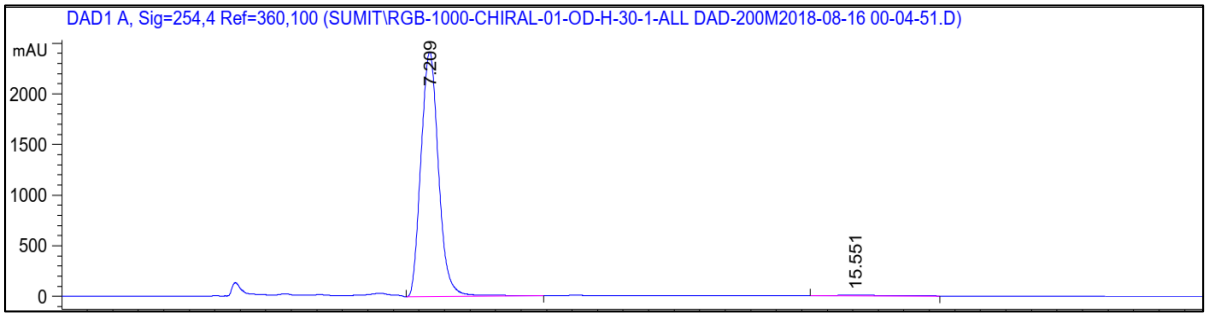
Sample Name: RGB-999-RAC-01-OD-H-30-1-ALL DAD-200M



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.217	VB	0.2714	1.06057e4	602.40930	50.2322
2	15.171	BB	0.6392	1.05076e4	253.70717	49.7678
Totals :				2.11133e4	856.11647	

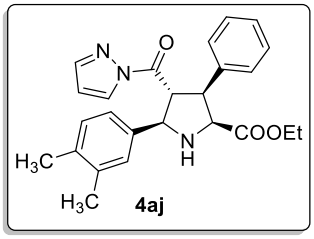
HPLC chromatogram of racemic **4ai**

Sample Name: RGB-1000-CHIRAL-01-OD-H-30-1-ALL DAD-200

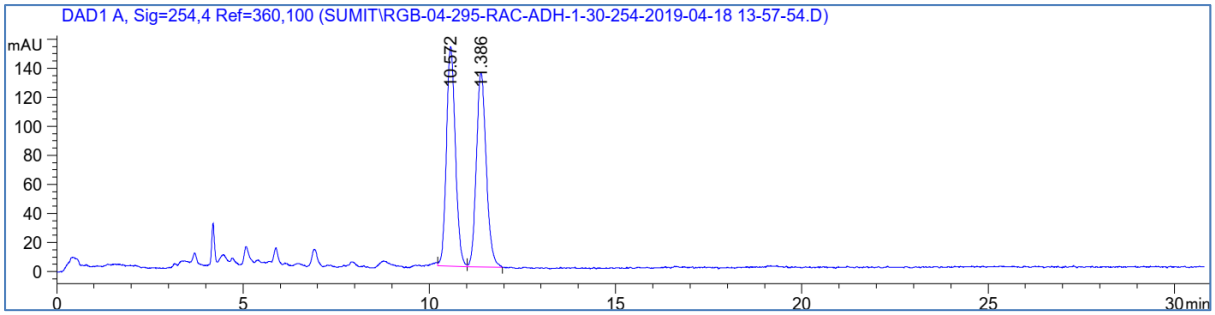


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.209	BB	0.3770	5.78007e4	2416.67603	99.2243
2	15.551	BBA	0.6927	451.86224	10.08587	0.7757
Totals :				5.82525e4	2426.76190	

HPLC chromatogram of enantioenriched **4ai**



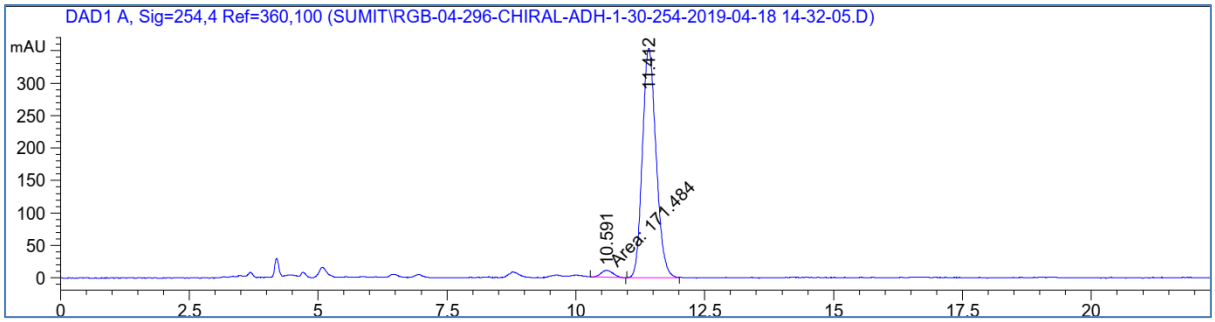
Sample Name: MMS-1090-ODH-05-1-254-RAC



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.572	VV	0.2519	2512.89160	151.18719	50.4549
2	11.386	VV	0.2815	2467.58252	133.58781	49.5451
Totals :				4980.47412	284.77501	

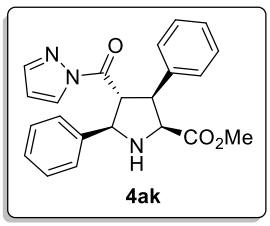
HPLC chromatogram of racemic **4aj**

Sample Name: RGB-04-296-CHIRAL-ADH-1-30-254



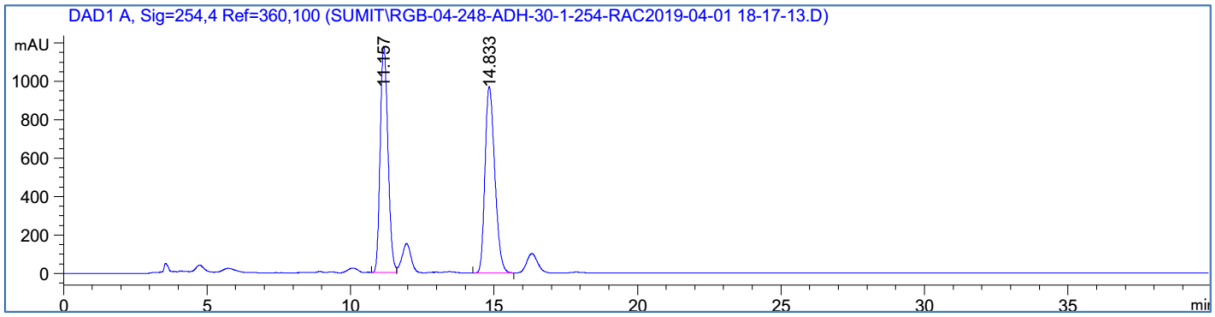
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.591	MM	0.2702	171.48396	10.57753	2.5551
2	11.412	VV	0.2878	6539.94678	353.51096	97.4449
Totals :				6711.43074	364.08848	

HPLC chromatogram of enantioenriched **4aj**



4ak

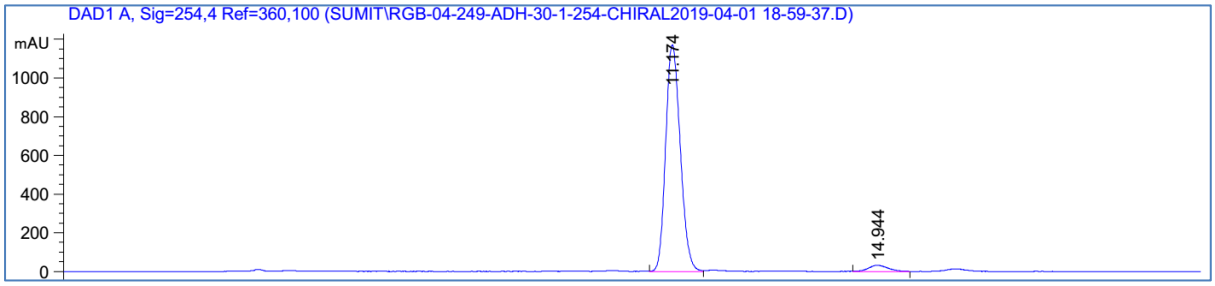
Sample Name: RGB-04-248-ADH-30-1-254-RAC



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.157	BV	0.2949	2.22693e4	1175.89355	49.0943
2	14.833	VV	0.3655	2.30909e4	970.69214	50.9057
Totals :				4.53602e4	2146.58569	

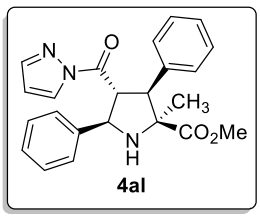
HPLC chromatogram of racemic **4ak**

Sample Name: RGB-04-249-ADH-30-1-254-CHIRAL



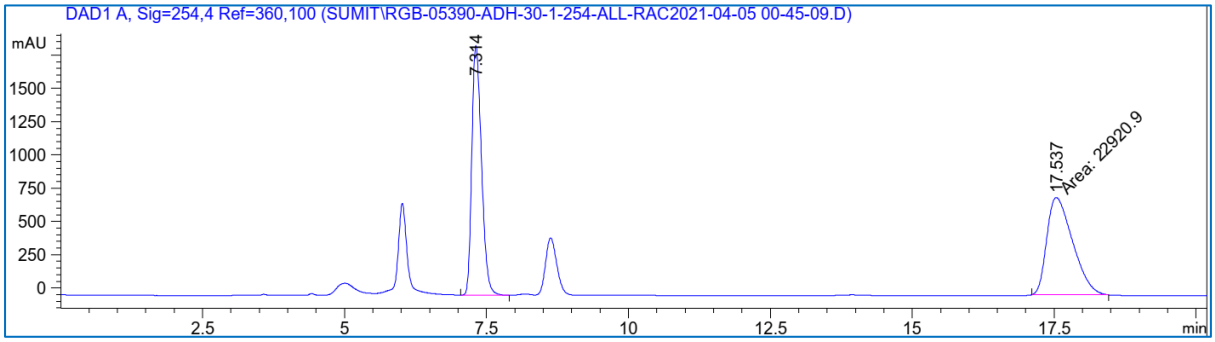
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.174	VV	0.2915	2.18301e4	1171.13110	96.4667
2	14.944	VV	0.3032	799.57819	32.25920	3.5333
Totals :				2.26297e4	1203.39031	

HPLC chromatogram of enantioenriched **4ak**



4al

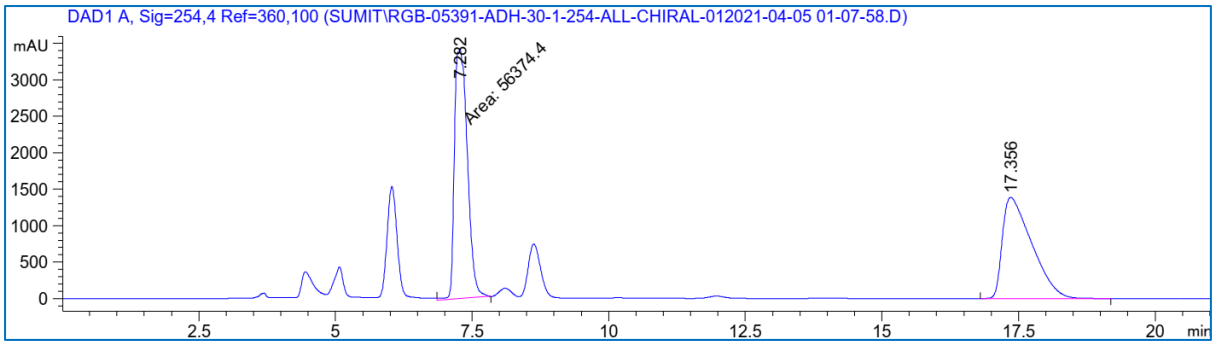
Sample Name: RGB-05390-ADH-30-1-254-ALL-RAC



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.314	BB	0.1864	2.22208e4	1873.29346	49.2245
2	17.537	MM	0.5241	2.29209e4	728.85791	50.7755
Totals :				4.51417e4	2602.15137	

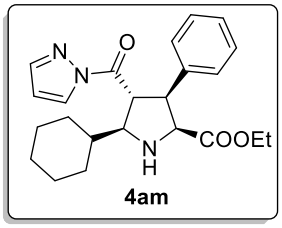
HPLC chromatogram of racemic **4al**

Sample Name: RGB-05391-ADH-30-1-254-ALL-CHIRAL-01



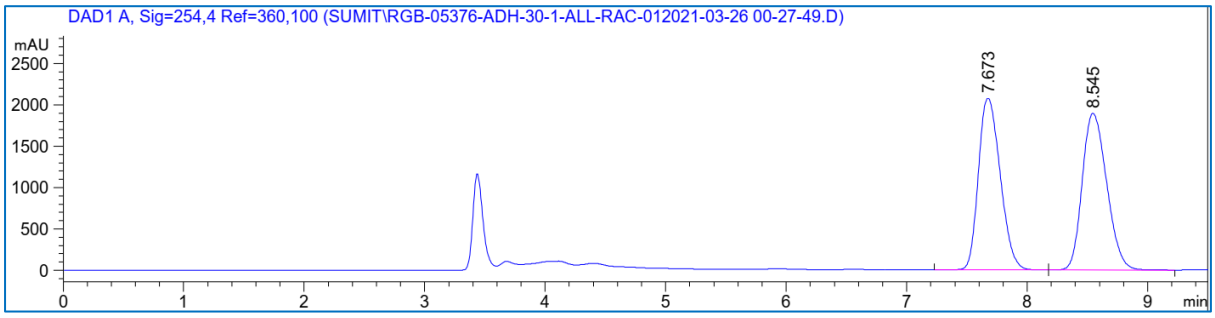
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.282	MM	0.2737	5.63744e4	3433.28027	52.1112
2	17.356	BB	0.5238	5.18065e4	1386.88477	47.8888
Totals :				1.08181e5	4820.16504	

HPLC chromatogram of enantioenriched **4al**



4am

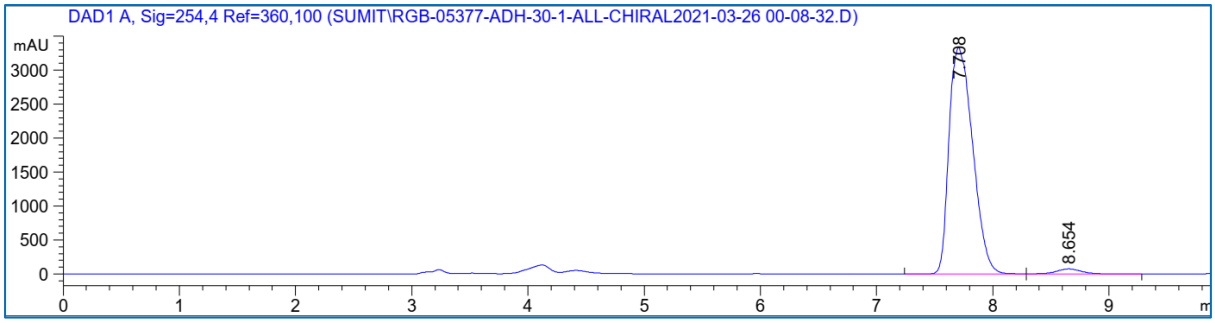
Sample Name: RGB-05376-ADH-30-1-ALL-RAC-01



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.673	VB	0.2008	2.61759e4	2079.66064	49.4174
2	8.545	BB	0.2228	2.67932e4	1896.49402	50.5826
Totals :				5.29691e4	3976.15466	

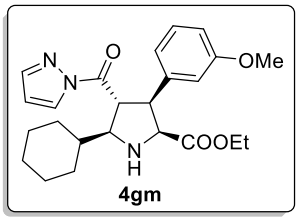
HPLC chromatogram of racemic **4am**

Sample Name: RGB-05377-ADH-30-1-ALL-CHIRAL

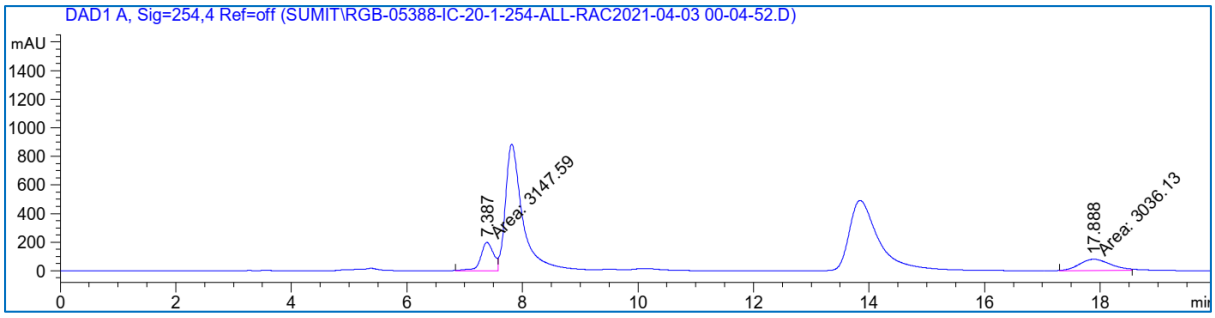


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.708	BV	0.1985	4.70510e4	3336.92432	97.6857
2	8.654	VB	0.2264	1114.68689	74.55148	2.3143
Totals :				4.81657e4	3411.47579	

HPLC chromatogram of enantioenriched **4am**



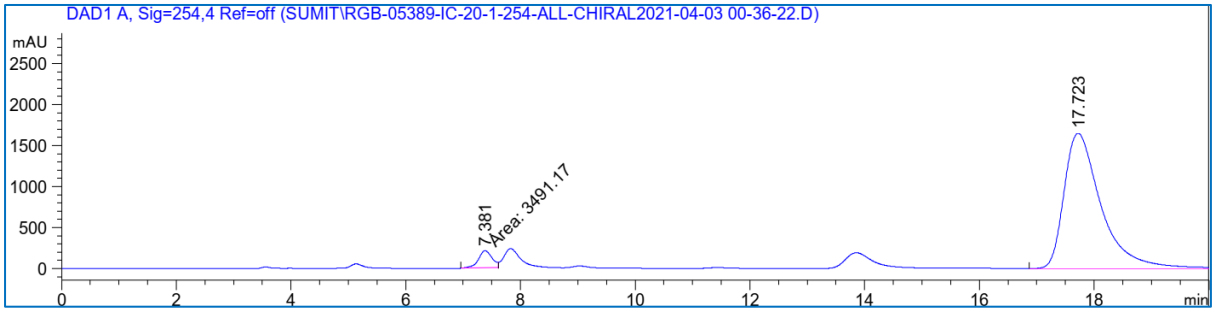
Sample Name: RGB-05388-IC-20-1-254-ALL-RAC



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.387	MF	0.2647	3147.59351	198.17479	50.9013
2	17.888	MM	0.6331	3036.12598	79.93145	49.0987
Totals :				6183.71948	278.10624	

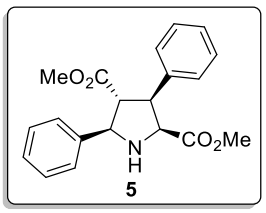
HPLC chromatogram of racemic **4gm**

Sample Name: RGB-05389-IC-20-1-254-ALL-CHIRAL



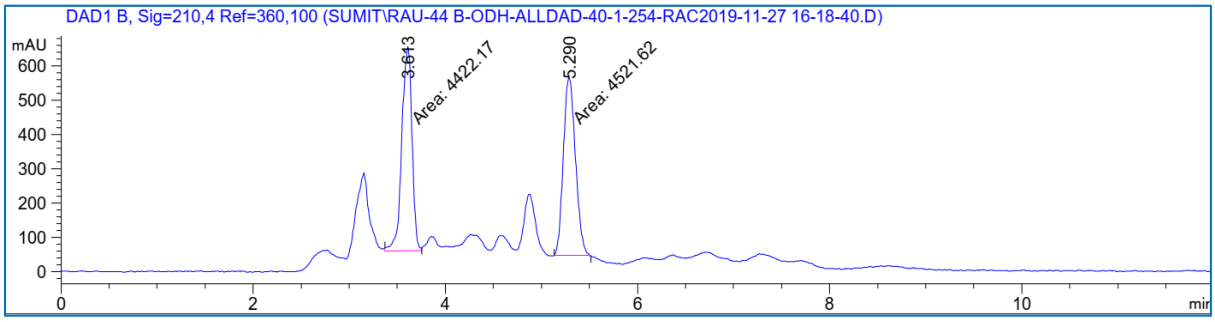
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.381	MF	0.2752	3491.16504	211.41292	4.4861
2	17.723	BB	0.6736	7.43306e4	1649.99048	95.5139
Totals :				7.78217e4	1861.40340	

HPLC chromatogram of enantioenriched **4gm**



5

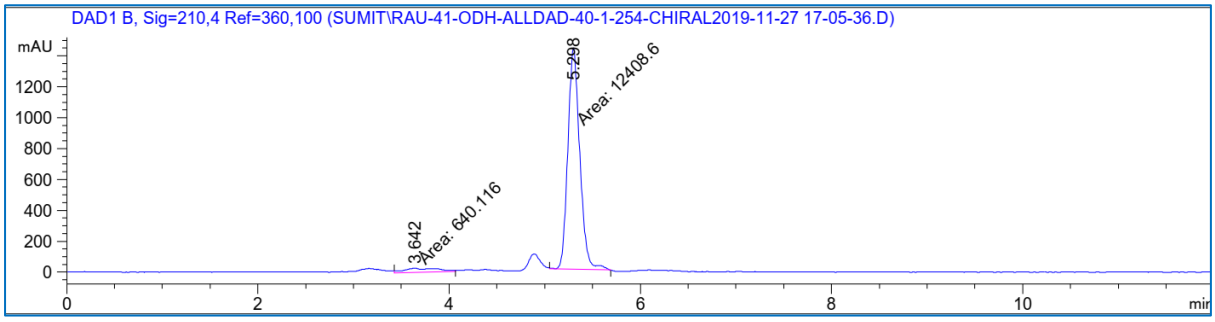
Sample Name: RAU-44 B-ODH-ALLDAD-40-1-254-RAC



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.613	MM	0.1235	4422.17480	596.82648	49.4440
2	5.290	MM	0.1456	4521.62451	517.67181	50.5560
Totals :				8943.79932	1114.49829	

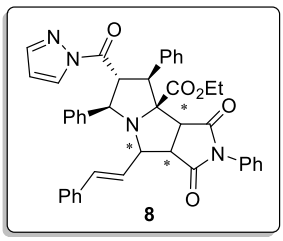
HPLC Chromatogram of racemic **5**

Sample Name: RAU-41-ODH-ALLDAD-40-1-254-CHIRAL

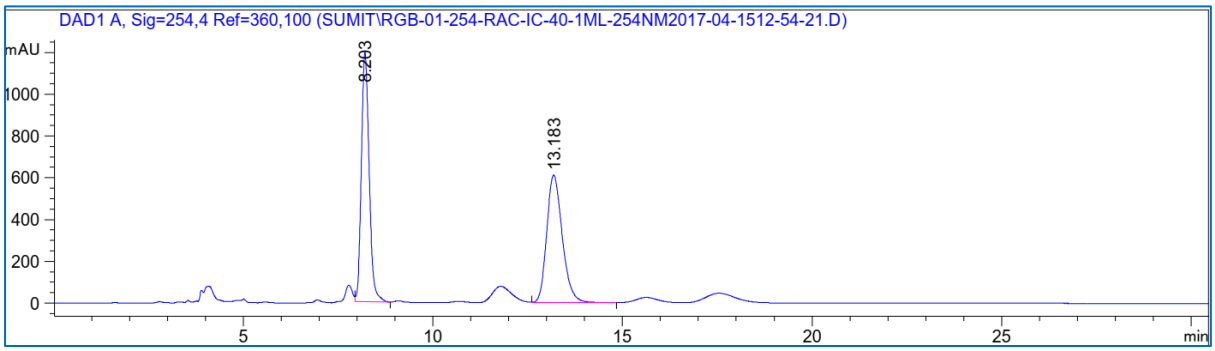


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.642	MM	0.4053	640.11560	26.32108	4.9056
2	5.298	MM	0.1446	1.24086e4	1430.54504	95.0944
Totals :				1.30487e4	1456.86612	

HPLC Chromatogram of enantioenriched **5**



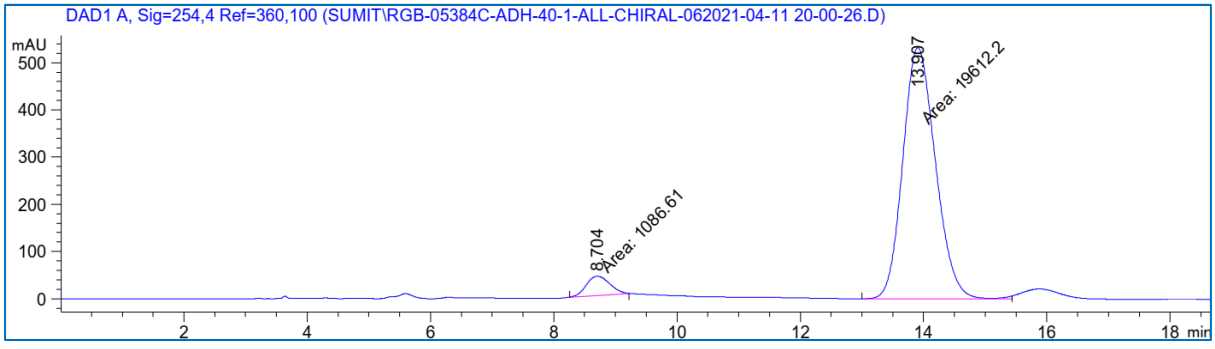
Sample Name: RGB-05384-ADH-40-1-254-RAC-1



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.203	VV	0.2210	1.70936e4	1194.22229	49.5228
2	13.183	VB	0.4389	1.74231e4	610.68768	50.4772
Totals :				3.45167e4	1804.90997	

HPLC Chromatogram of racemic **8**

Sample Name: RGB-05384C-ADH-40-1-ALL-CHIRAL-06



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.704	MM	0.4415	1086.61475	41.01876	5.2497
2	13.907	MM	0.6141	1.96122e4	532.25256	94.7503
Totals :				2.06988e4	573.27132	

HPLC Chromatogram of enantioenriched **8**