Asymmetric Construction of 3-Azabicyclo[3.1.0]hexane Skeleton with Five Contiguous Stereogenic Centers by Cu-Catalyzed 1,3-Dipolar Cycloaddition of Trisubstituted Cyclopropenes

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General information

^{1}H NMR spectrum were recorded on a Bruker AVANCE III 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6. Chemical shifts were reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The spectrums are interpreted as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, brs = broad singlet, coupling constant(s) *J* are reported in Hz and relative integrations are reported. ^{13}C NMR (100 MHz) spectrums were recorded on a Bruker AVANCE III 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6. Chemical shifts were reported in ppm with the internal chloroform signal at 77.16 ppm (DMSO signal at 39.52 ppm) as a standard. Optical rotations were measured on an AUTOPOL V. Diastereomeric ratios and enantiomeric excesses were determined from crude ^{1}H NMR spectroscopy interpretation or by analysis of HPLC traces, obtained by using chiralpak AS-H, AD-H, IA or chiralcel OD-H columns with *n*-hexane and *i*-propanol or ethanol as solvents. (Chiralpak AS-H, AD-H, IA and chiralcel OD-H columns were purchased from Daicel Chemical Industries, LTD.) Melting points were obtained in open capillary tubes using SGW X-4 micro melting point apparatus which were uncorrected. Mass spectrums were recorded on TOF mass Waters GCT Premier and Xevo G2 spectrometer. Solvents were dried and distilled following usual protocols. Commercially available materials purchased from Adamas-beta, TCI or Energy Chemical and were used as received.

Imino esters[1] and cyclopropenes: ethyl 2,3-diphenylcycloprop-2-ene-1-carboxylate (**2a**),[2] 2,3-diphenylcycloprop-2-ene-1-carbonitrile (**2d**) and *N*,*N*-dimethyl-2,3-diphenylcycloprop-2-ene-1-carboxamide (**2e**),[3] cycloprop-1-ene-1,2,3-triyltribenzene (**2f**),[4] ethyl 2,3-dimethylcycloprop-2-ene-1-carboxylate (**2i**),[5] were prepared according to the literature procedure.

Optimization of the reaction conditions

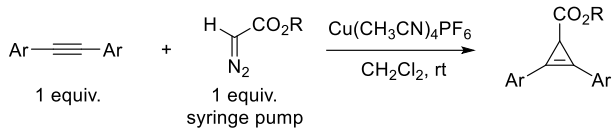
Table S1. Bases and solvents screening of the reaction conditions[a]

entry	base	solvent	yield[b] (%)	ee[c] (%)
1	Cs_2CO_3	CH_2Cl_2	95	97
2	Cs_2CO_3	CPME	93	97
3	Cs_2CO_3	MTBE	96	97
4	Cs_2CO_3	$ClCH_2CH_2Cl$	98	97
5	Cs_2CO_3	THF	98	98
6[d]	K_2CO_3	THF	98	98
7	DBU	THF	94	96
8[e]	*t*-BuOK	THF	99	89

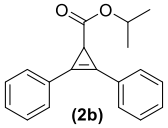
[a]All reactions were performed with **1a** (0.12 mmol), **2a** (0.10 mmol) in 1.0 mL of solvent, under an N_2 atmosphere at rt, $CuBF_4$ = $Cu(MeCN)_4BF_4$, CPME = cyclopentyl methyl ether, MTBE = methyl *tert*-butyl ether. [b]Isolated yield. [c]The ee was determined by chiral HPLC analysis. [d]2 equiv base was used. [e]10 mol % base was used.

The preparation of substrates

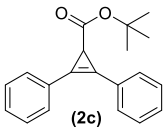
The preparation of cyclopropenes **2b**, **2c**, **2g**, **2h.**



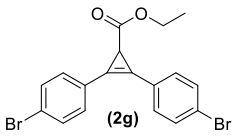
A 50 mL two-neck round bottom flask was charged with 1, 2-diarylacetylene[6] (16.85 mmol, 1.0 equiv), $Cu(CH_3CN)_4PF_6$ (63 mg, 0.169 mmol, 0.01 equiv) and dichloromethane (20 mL) under nitrogen atmosphere. A solution of diazoacetate[7] (84 mmol, 5 equiv) in dichloromethane (10 mL) was added *via* syringe pump over 10 h. The solvent was removed in vacuum and the residue was purified with flash column chromatography (50: 1 petroleum ether: ethyl acetate) to give white solid cyclopropene.



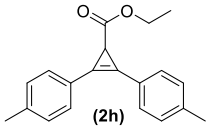
Isopropyl 2,3-diphenylcycloprop-2-ene-1-carboxylate White solid, yield: 288 mg, 52%; m.p.: 98-99 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 – 7.63 (m, 4H), 7.50 – 7.43 (m, 4H), 7.41 – 7.35 (m, 2H), 5.14 – 5.04 (m, 1H), 2.79 (s, 1H), 1.22 (d, *J* = 6.3 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.5, 130.0 (4C), 129.3 (2C), 129.0 (4C), 127.4 (2C), 107.9 (2C), 67.7, 22.1, 22.1 (2C); **HRMS** (EI-TOF, *m/z*) calcd for $C_{19}H_{18}O_2$ $[M]^+$: 278.1301, found: 278.1306.



***tert*-Butyl 2,3-diphenylcycloprop-2-ene-1-carboxylate** White solid, yield: 250 mg, 63%; m.p.: 78-80 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 – 7.64 (m, 4H), 7.51 – 7.43 (m, 4H), 7.42 – 7.33 (m, 2H), 2.73 (s, 1H), 1.46 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) 174.3, 130.0 (4C), 129.2 (2C), 129.0 (4C), 127.6 (2C), 108.2 (2C), 80.2, 28.3 (3C), 22.9; **HRMS** (EI-TOF, *m/z*) calcd for $C_{20}H_{20}O_2$ $[M]^+$: 292.1458, found: 292.1464.

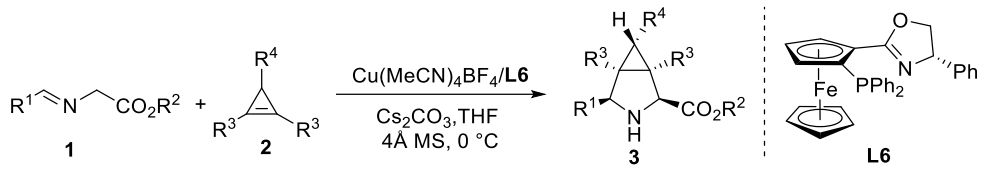


Ethyl 2,3-bis(4-bromophenyl)cycloprop-2-ene-1-carboxylate White solid, yield: 230 mg, 41%; m.p.: 148-150 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 – 7.57 (m, 4H), 7.55 – 7.46 (m, 4H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.79 (s, 1H), 1.24 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.3, 132.4 (4C), 131.4 (4C), 126.0 (2C), 124.0 (2C), 107.6 (2C), 60.8, 21.8, 14.5; **HRMS** (EI-TOF, *m/z*) calcd for $C_{18}H_{14}{}^{79}Br_2O_2$ $[M]^+$: 419.9355, found: 419.9364; for $C_{18}H_{14}{}^{79}Br^{81}BrO_2$ $[M]^+$: 421.9335, found: 421.9344; for $C_{18}H_{14}{}^{81}Br_2O_2$ $[M]^+$: 423.9314, found: 423.9330.

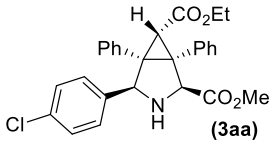


Ethyl 2,3-di-*p*-tolylcycloprop-2-ene-1-carboxylate White solid, yield: 300 mg, 47%; m.p.: 90-92 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 4H), 7.27 (d, *J* = 7.9 Hz, 4H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.76 (s, 1H), 2.40 (s, 6H), 1.22 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.3, 139.4 (2C), 129.9 (4C), 129.7 (4C), 124.7 (2C), 106.5 (2C), 60.4, 21.7, 21.7 (2C), 14.5; **HRMS** (EI-TOF, *m/z*) calcd for $C_{20}H_{20}O_2$ $[M]^+$: 292.1458, found: 292.1465.

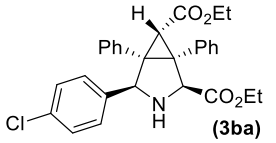
General procedure



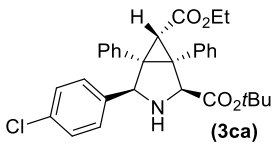
At a nitrogen atmosphere, $Cu(CH_3CN)_4BF_4$ (2.4 mg, 0.0075 mmol) and **L3** (4.3 mg, 0.00825mmol) were dissolved in 1.5 mL dry THF, subsequently add 4Å Ms (100 mg), and stirred at room temperature for about 1 h. Then, iminoester **1** (0.18 mmol) and Cs_2CO_3 (9.8 mg, 0.03 mmol) were added, the mixture was cooled to 0 ℃ and cyclopropene **2** (0.15 mmol) was added. Once starting material was consumed (monitored by TLC), the mixture was concentrated and the residue was purified by column chromatography (petroleum ether/ethyl acetate 15:1 to 6:1) on silica gel to afford the corresponding product **3**.



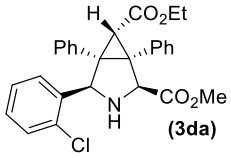
6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-chlorophenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 69.5 mg, 97%; m.p.: 157-159 °C; $[\alpha]_D^{25}$ = -72.6 (*c* 1.03, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.19 (m, 7H), 7.16 – 7.08 (m, 5H), 7.00 – 6.96 (m, 2H), 4.72 (s, 1H), 4.30 (s, 1H), 3.85 (q, *J* = 7.1 Hz, 2H), 3.66 (s, 3H), 2.97 (s, 1H), 2.58 (s, 1H), 0.87 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.6, 169.4, 136.2, 133.9, 133.8, 133.8, 131.0 (2C), 130.9 (2C), 128.9 (2C), 128.6 (2C), 127.9 (2C), 127.8 (2C), 127.4, 127.1, 71.7, 69.9, 60.4, 52.2, 51.5, 48.6, 25.2, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{28}H_{26}ClNO_4$ $[M]^+$: 475.1545, found: 475.1547; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 0.8 mL/min, 220 nm) t_R = 39.54 min, 42.38 min.



Diethyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-chlorophenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 72.8 mg, 99%; m.p.: 125-127 °C; $[\alpha]_D^{25}$ = -83.3 (*c* 0.97, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.18 (m, 7H), 7.17 – 7.08 (m, 5H), 7.02 – 6.94 (m, 2H), 4.71 (s, 1H), 4.27 (s, 1H), 4.24 – 4.04 (m, 2H), 3.91 – 3.81 (m, 2H), 2.95 (s, 1H), 2.59 (s, 1H), 1.12 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.2, 169.4, 136.2, 134.0, 133.9, 133.8, 131.2 (2C), 130.9 (2C), 128.9 (2C), 128.6 (2C), 127.8 (2C), 127.8 (2C), 127.4, 127.1, 71.8, 70.0, 61.4, 60.4, 51.6, 48.7, 25.1, 14.2, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{29}H_{28}ClNO_4$ $[M]^+$: 489.1701, found: 489.1709; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 80/20, 0.8 mL/min, 220 nm) t_R = 23.14 min, 25.41 min.

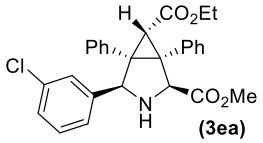


2-(*tert*-Butyl) 6-ethyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-chlorophenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 75.5 mg, 97%; m.p.: 68-70 °C; $[\alpha]_D^{25}$ = -68.2 (*c* 1.03, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.19 (m, 7H), 7.16 – 7.07 (m, 5H), 7.00 – 6.89 (m, 2H), 4.67 (s, 1H), 4.18 (s, 1H), 4.02 – 3.68 (m, 2H), 2.86 (s, 1H), 2.63 (s, 1H), 1.34 (s, 9H), 0.90 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.2, 169.4, 136.3, 134.0, 133.9, 133.9, 131.4 (2C), 130.8 (2C), 128.9 (2C), 128.7 (2C), 127.7 (2C), 127.7 (2C), 127.3, 127.0, 82.2, 72.0, 70.8, 60.4, 51.9, 49.0, 28.0 (3C), 24.9, 13.9; **HRMS** (EI-TOF, *m/z*) calcd for $C_{31}H_{32}ClNO_4$ $[M]^+$: 517.2014, found: 517.2027; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 0.8 mL/min, 220 nm) t_R = 15.31 min, 22.64 min.



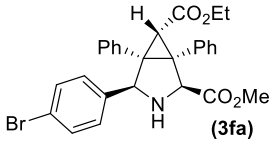
(3da)

6-Ethyl 2-methyl (1*S*,2*S*,4*R*,5*R*,6*S*)-4-(2-chlorophenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 67.8 mg, 95%; m.p.: 151-153 °C; $[\alpha]_D^{25}$ = +2.0 (*c* 0.94, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.36 – 7.18 (m, 8H), 7.11 – 7.06 (m, 3H), 7.06 – 7.01 (m, 2H), 5.30 (s, 1H), 4.30 (s, 1H), 3.94 – 3.85 (m, 2H), 3.63 (s, 3H), 3.16 (s, 1H), 2.52 (s, 1H), 0.89 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.5, 169.4, 135.5, 135.3, 133.7, 133.6, 131.3 (2C), 130.5 (2C), 129.9, 129.3, 128.2, 127.8 (2C), 127.7 (2C), 127.4, 127.3, 126.9, 70.1, 66.9, 60.5, 52.1, 49.9, 47.4, 25.9, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{28}H_{26}ClNO_4$ $[M]^+$: 475.1545, found: 475.1547; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 0.8 mL/min, 220 nm) t_R = 27.73 min, 39.92 min.



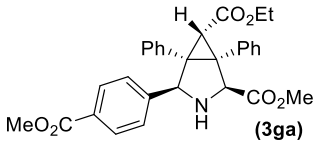
(3ea)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(3-chlorophenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 67.7 mg, 95%; m.p.: 59-61 °C; $[\alpha]_D^{25}$ = -74.9 (*c* 1.04, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.15 (m, 8H), 7.18 – 7.11 (m, 3H), 7.10 – 7.02 (m, 1H), 7.04 – 6.95 (m, 2H), 4.72 (s, 1H), 4.29 (s, 1H), 3.86 (q, *J* = 7.1 Hz, 2H), 3.66 (s, 3H), 2.99 (s, 1H), 2.53 (s, 1H), 0.89 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.5, 169.3, 139.8, 134.3, 133.7, 133.7, 131.1 (2C), 130.8 (2C), 129.7, 128.3, 127.9 (2C), 127.8, 127.8 (2C), 127.4, 127.2, 125.8, 71.5, 69.8, 60.5, 52.2, 50.9, 48.4, 25.3, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{28}H_{26}ClNO_4$ $[M]^+$: 475.1545, found: 475.1547; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 220 nm) t_R = 27.69 min, 40.19 min.



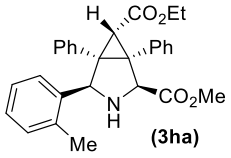
(3fa)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-bromophenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 77.2 mg, 99%; m.p.: 206-208 °C; $[\alpha]_D^{25}$ = -72.0 (*c* 0.94, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.36 (m, 2H), 7.31 – 7.18 (m, 5H), 7.18 – 7.09 (m, 3H), 7.05 (d, *J* = 8.2 Hz, 2H), 7.01 – 6.93 (m, 2H), 4.70 (d, *J* = 7.8 Hz, 1H), 4.30 (d, *J* = 7.4 Hz, 1H), 3.85 (q, *J* = 7.1 Hz, 2H), 3.66 (s, 3H), 2.97 (s, 1H), 2.55 (brs, 1H), 0.87 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.6, 169.4, 136.8, 133.8 (2C), 131.6 (2C), 131.1 (2C), 130.9 (2C), 129.3 (2C), 127.9 (2C), 127.8 (2C), 127.4, 127.2, 122.2, 71.8, 69.9, 60.4, 52.2, 51.4, 48.6, 25.2, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{28}H_{26}{}^{79}BrNO_4$ $[M]^+$: 519.1040, found: 519.1043, for $C_{28}H_{26}{}^{81}BrNO_4$ $[M]^+$: 521.1019, found: 521.1024; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 0.8 mL/min, 220 nm) t_R = 46.37 min, 50.47 min.



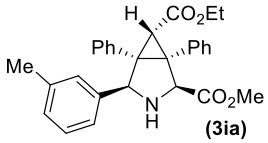
(3ga)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-(methoxycarbonyl)phenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 72.5 mg, 97%; m.p.: 152-153 °C; $[\alpha]_D^{25}$ = -106.8 (*c* 1.01, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 – 7.83 (m, 2H), 7.33 – 7.18 (m, 7H), 7.16 – 7.10 (m, 3H), 6.99 – 6.93 (m, 2H), 4.79 (s, 1H), 4.33 (s, 1H), 3.91 (s, 3H), 3.84 (q, *J* = 7.1 Hz, 2H), 3.67 (s, 3H), 3.01 (s, 1H), 2.72 (s, 1H), 0.87 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.6, 169.3, 167.0, 142.8, 133.7, 133.7, 131.0 (2C), 130.9 (2C), 130.0, 129.7 (2C), 127.9 (2C), 127.8 (2C), 127.6 (2C), 127.5, 127.2, 72.1, 69.9, 60.4, 52.3, 52.2, 51.6, 48.6, 25.2, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{30}H_{29}NO_6$ $[M]^+$: 499.1989, found: 499.1997; **HPLC** (Chiralpak AD-H, *n*-hexane/EtOH = 90/10, 1.0 mL/min, 220 nm) t_R = 40.55 min, 63.42 min.



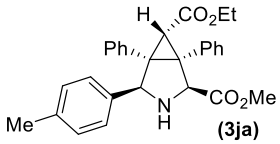
(3ha)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-1,5-diphenyl-4-(*o*-tolyl)-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 65.6 mg, 96%; m.p.: 97-99 °C; $[\alpha]_D^{25}$ = -23.1 (*c* 0.99, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.34 – 7.16 (m, 7H), 7.11 – 6.98 (m, 6H), 5.02 (s, 1H), 4.27 (s, 1H), 3.89 (q, *J* = 7.1 Hz, 2H), 3.64 (s, 3H), 3.05 (s, 1H), 2.74 (s, 1H), 1.95 (s, 3H), 0.90 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.7, 169.4, 138.0, 136.0, 134.3, 133.9, 131.2 (2C), 130.7, 130.5 (2C), 127.9, 127.8 (2C), 127.7 (2C), 127.3, 126.8, 126.3, 126.1, 70.5, 67.7, 60.4, 52.1, 51.0, 48.2, 25.9, 19.2, 13.9; **HRMS** (EI-TOF, *m/z*) calcd for $C_{29}H_{29}NO_4$ $[M]^+$: 455.2091, found: 455.2096; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 220 nm) t_R = 14.46 min, 16.69 min.



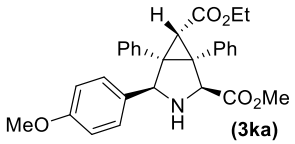
(3ia)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-1,5-diphenyl-4-(*m*-tolyl)-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 66.2 mg, 97%; m.p.: 63-65 °C; $[\alpha]_D^{25}$ = -53.9 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.19 (m, 5H), 7.20 – 7.14 (m, 1H), 7.14 – 7.07 (m, 4H), 7.05 – 6.96 (m, 4H), 4.73 (s, 1H), 4.28 (s, 1H), 3.85 (q, *J* = 7.1 Hz, 2H), 3.65 (s, 3H), 2.97 (s, 1H), 2.77 (s, 1H), 2.29 (s, 3H), 0.87 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.8, 169.5, 138.1, 137.4, 134.2, 134.0, 131.1 (2C), 130.9 (2C), 128.9, 128.4, 128.3, 127.8 (2C), 127.6 (2C), 127.3, 126.9, 124.6, 72.4, 70.2, 60.4, 52.1, 51.5, 48.8, 25.4, 21.6, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{29}H_{29}NO_4$ $[M]^+$: 455.2091, found: 455.2096; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 220 nm) t_R = 28.35 min, 44.11 min.



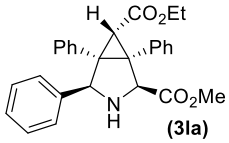
(3ja)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-1,5-diphenyl-4-(*p*-tolyl)-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 67.6 mg, 99%; m.p.: 143-145 °C; $[\alpha]_D^{25}$ = -42.0 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.18 (m, 6H), 7.17 – 7.05 (m, 6H), 7.04 – 6.97 (m, 2H), 4.72 (s, 1H), 4.28 (s, 1H), 3.84 (q, *J* = 7.1 Hz, 2H), 3.65 (s, 3H), 2.97 (s, 1H), 2.63 (s, 1H), 2.32 (s, 3H), 0.86 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.8, 169.5, 137.9, 134.5, 134.2, 134.0, 131.1 (2C), 130.9 (2C), 129.2 (2C), 127.8 (2C), 127.6 (2C), 127.5 (2C), 127.3, 126.9, 72.4, 70.2, 60.3, 52.1, 51.8, 48.8, 25.3, 21.3, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{29}H_{29}NO_4$ $[M]^+$: 455.2091, found: 455.2096; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 0.9 mL/min, 220 nm) t_R = 36.27 min, 45.84 min.



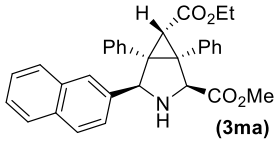
(3ka)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-methoxyphenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 67.8 mg, 96%; m.p.: 127-129 °C; $[\alpha]_D^{25}$ = -57.7 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.24 (m, 4H), 7.26 – 7.18 (m, 1H), 7.16 – 7.06 (m, 5H), 7.04 – 6.95 (m, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 4.70 (s, 1H), 4.28 (s, 1H), 3.85 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 3.65 (s, 3H), 2.97 (s, 1H), 2.64 (s, 1H), 0.86 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.8, 169.5, 159.5, 134.3, 134.0, 131.1 (2C), 130.8 (2C), 129.6, 128.7 (2C), 127.8 (2C), 127.6 (2C), 127.3, 126.9, 113.8 (2C), 72.0, 70.1, 60.4, 55.3, 52.1, 51.8, 48.7, 25.3, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{29}H_{29}NO_5$ $[M]^+$: 471.2040, found: 471.2041; **HPLC** (Chiralpak AS-H, *n*-hexane/*i*-propanol = 80/20, 1.0 mL/min, 220 nm) t_R = 7.70 min, 10.49 min.



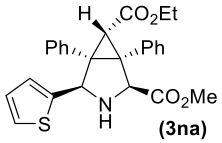
(3la)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-1,4,5-triphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 65.0 mg, 98%; m.p.: 65-67 °C; $[\alpha]_D^{25}$ = -50.8 (*c* 1.01, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.25 (m, 7H), 7.26 – 7.16 (m, 3H), 7.14 – 7.08 (m, 3H), 7.03 – 6.96 (m, 2H), 4.75 (s, 1H), 4.30 (s, 1H), 3.84 (q, *J* = 7.1 Hz, 2H), 3.65 (s, 3H), 3.00 (s, 1H), 2.63 (s, 1H), 0.85 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.7, 169.5, 137.5, 134.1, 133.9, 131.1 (2C), 130.9 (2C), 128.5 (2C), 128.2, 127.8 (2C), 127.6 (2C), 127.6 (2C), 127.4, 127.0, 72.5, 70.1, 60.4, 52.2, 51.7, 48.7, 25.3, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{28}H_{27}NO_4$ $[M]^+$: 441.1935, found: 441.1939; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 0.8 mL/min, 220 nm) t_R = 42.06 min, 46.45 min.



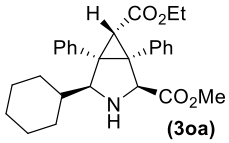
(3ma)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(naphthalen-2-yl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 73.0 mg, 99%; m.p.: 83-85 °C; $[\alpha]_D^{25}$ = -116.8 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 – 7.75 (m, 2H), 7.76 – 7.71 (m, 2H), 7.51 – 7.42 (m, 2H), 7.35 – 7.20 (m, 6H), 7.13 – 7.06 (m, 3H), 7.04 – 6.96 (m, 2H), 4.94 (s, 1H), 4.35 (s, 1H), 3.86 (q, *J* = 7.1 Hz, 2H), 3.68 (s, 3H), 3.10 (s, 1H), 2.87 (s, 1H), 0.88 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.8, 169.4, 135.1, 134.1, 133.9, 133.3, 133.3, 131.1 (2C), 130.9 (2C), 128.3, 128.0, 127.9 (2C), 127.7 (3C), 127.4, 127.0, 126.4, 126.2, 126.1, 125.9, 72.4, 70.1, 60.4, 52.2, 51.5, 48.7, 25.5, 13.9; **HRMS** (EI-TOF, *m/z*) calcd for $C_{32}H_{29}NO_4$ $[M]^+$: 491.2091, found: 491.2094; **HPLC** (Chiralpak AS-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 220 nm) t_R = 12.92 min, 28.58 min.



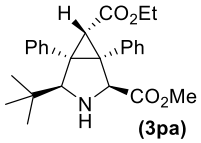
(3na)

6-Ethyl 2-methyl (1*S*,2*S*,4*R*,5*R*,6*R*)-1,5-diphenyl-4-(thiophen-2-yl)-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 65.7 mg, 98%; m.p.: 149-150 °C; $[\alpha]_D^{25}$ = -36.5 (*c* 1.01, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ7.30 – 7.19 (m, 6H), 7.19 – 7.10 (m, 3H), 7.12 – 7.05 (m, 2H), 6.91 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.81 (dd, *J* = 3.6, 1.0 Hz, 1H), 4.99 (s, 1H), 4.28 (s, 1H), 3.96 – 3.83 (m, 2H), 3.65 (s, 3H), 3.01 (s, 1H), 2.68 (s, 1H), 0.90 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.3, 169.3, 140.9, 133.8, 133.7, 131.0 (2C), 130.8 (2C), 127.9 (2C), 127.7 (2C), 127.4, 127.2, 126.7, 126.0, 125.1, 70.1, 68.9, 60.4, 52.2, 52.2, 49.5, 25.5, 13.9; **HRMS** (EI-TOF, *m/z*) calcd for $C_{26}H_{25}NO_4S$ $[M]^+$: 447.1499, found: 447.1507; **HPLC** (Chiralpak AD-H, *n*-hexane/EtOH = 90/10, 1.0 mL/min, 220 nm) t_R = 26.22 min, 39.10 min.



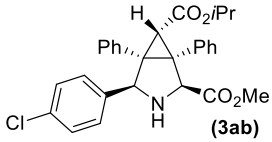
(3oa)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-cyclohexyl-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 66.4 mg, 99%; m.p.: 138-139 °C; $[\alpha]_D^{25}$ = +7.1 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.13 (m, 10H), 4.09 (s, 1H), 3.96 – 3.83 (m, 2H), 3.60 (s, 3H), 3.54 (d, *J* = 3.6 Hz, 1H), 2.62 (s, 1H), 2.29 (s, 1H), 2.07 – 1.94 (m, 1H), 1.89 – 1.71 (m, 1H), 1.70 – 1.59 (m, 2H), 1.53 – 1.44 (m, 2H), 1.32 – 1.05 (m, 5H), 0.89 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.9, 169.9, 135.1, 134.2, 130.8 (2C), 130.7 (2C), 128.0 (2C), 127.8 (2C), 127.1, 127.0, 74.3, 70.0, 60.3, 52.0, 50.2, 48.5, 38.1, 31.9, 27.2, 26.7, 26.4, 26.4, 25.0, 13.8; **HRMS** (EI-TOF, *m/z*) calcd for $C_{28}H_{33}NO_4$ $[M]^+$: 447.2404, found: 447.2412; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 20/1, 0.8 mL/min, 220 nm) t_R = 34.35 min, 37.07 min.



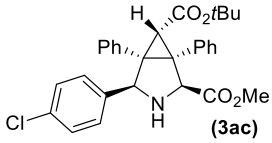
(3pa)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(*tert*-butyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 60.2 mg, 95%; m.p.: 168-170 °C; $[\alpha]_D^{25}$ = +67.3 (*c* 0.99, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.08 (m, 10H), 4.14 – 3.91 (m, 3H), 3.63 (s, 1H), 3.62 (s, 3H), 2.76 (s, 1H), 2.30 (s, 1H), 1.03 (t, *J* = 7.1 Hz, 3H), 0.85 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.1, 170.0, 135.4, 134.0, 131.6 (2C), 130.8 (2C), 127.7 (2C), 127.6 (2C), 127.1 (2C), 77.7, 69.1, 60.5, 52.0, 49.1, 48.6, 34.6, 28.0 (3C), 24.6, 14.0; **HRMS** (EI-TOF, *m/z*) calcd for $C_{26}H_{31}NO_4$ $[M]^+$: 421.2248, found: 421.2255; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 20/1, 0.8 mL/min, 220 nm) t_R = 20.97 min, 22.37 min.



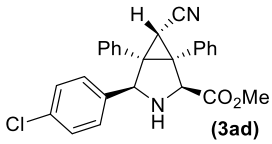
(3ab)

6-Isopropyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-chlorophenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 72.6 mg, 99%; m.p.: 158-160 °C; $[\alpha]_D^{25}$ = -69.6 (*c* 1.01, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.18 (m, 7H), 7.17 – 7.08 (m, 5H), 7.04 – 6.93 (m, 2H), 4.71 (s, 1H), 4.69 – 4.63 (m, 1H), 4.28 (s, 1H), 3.66 (s, 3H), 2.94 (s, 1H), 2.58 (s, 1H), 0.85 (dd, *J* = 8.6, 6.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.6, 168.9, 136.3, 134.0, 134.0, 134.0, 131.2 (2C), 130.9 (2C), 129.0 (2C), 128.6 (2C), 127.9 (2C), 127.8 (2C), 127.4, 127.1, 71.6, 70.0, 68.3, 52.2, 51.2, 48.4, 25.6, 21.4 (2C); **HRMS** (EI-TOF, *m/z*) calcd for $C_{29}H_{28}ClNO_4$ $[M]^+$: 489.1701, found: 489.1708; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 0.8 mL/min, 220 nm) t_R = 42.96 min, 75.35 min.



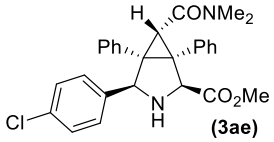
(3ac)

6-(*tert*-Butyl) 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-chlorophenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 72.0 mg, 95%; m.p.: 115-117 °C; $[\alpha]_D^{25}$ = -59.4 (*c* 0.99, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.22 (m, 7H), 7.16 – 7.09 (m, 5H), 7.04 – 6.96 (m, 2H), 4.68 (s, 1H), 4.26 (s, 1H), 3.66 (s, 3H), 2.86 (s, 1H), 2.43 (s, 1H), 1.00 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.6, 168.4, 136.3, 134.3, 134.2, 134.0, 131.3 (2C), 131.0 (2C), 129.1 (2C), 128.6 (2C), 127.8 (2C), 127.7 (2C), 127.3, 127.0, 81.0, 71.7, 70.0, 52.2, 51.2, 48.4, 27.5 (3C), 26.4; **HRMS** (EI-TOF, *m/z*) calcd for $C_{30}H_{30}ClNO_4$ $[M]^+$: 503.1858, found: 503.1862; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 80/20, 1.0 mL/min, 220 nm) t_R = 23.19 min, 25.53 min.



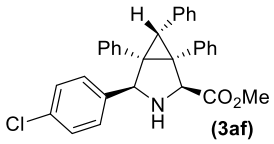
(3ad)

Methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-chlorophenyl)-6-cyano-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2-carboxylate White solid, yield: 63.6 mg, 99%; m.p.: 90-91 °C; $[\alpha]_D^{25}$ = -75.7 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.36 (m, 2H), 7.37 – 7.20 (m, 8H), 7.19 – 7.12 (m, 2H), 7.11 – 7.01 (m, 2H), 4.81 (d, *J* = 5.7 Hz, 1H), 4.42 (d, *J* = 5.7 Hz, 1H), 3.70 (s, 3H), 2.94 (s, 1H), 2.49 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.1, 135.5, 134.3, 132.0, 131.8, 130.6 (2C), 130.2 (2C), 128.8 (2C), 128.7 (2C), 128.6 (2C), 128.5 (2C), 128.3, 128.2, 118.1, 69.1, 67.3, 52.6, 49.1, 46.3, 11.3; **HRMS** (EI-TOF, *m/z*) calcd for $C_{26}H_{21}ClN_2O_2$ $[M]^+$: 428.1286, found: 428.1290; **HPLC** (Chiralpak AS-H, *n*-hexane/*i*-propanol = 90/10, 0.8 mL/min, 220 nm) t_R = 31.67 min, 43.36 min.



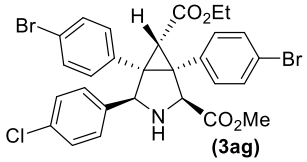
(3ae)

Methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-chlorophenyl)-6-(dimethylcarbamoyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2-carboxylate White solid, yield: 67.7 mg, 95%; m.p.: 79-80 °C; $[\alpha]_D^{25}$ = -59.7 (*c* 1.03, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27 – 7.22 (m, 2H), 7.20 – 7.09 (m, 10H), 7.05 – 7.00 (m, 2H), 4.60 (s, 1H), 4.55 (s, 1H), 3.71 (s, 3H), 3.14 (s, 1H), 2.97 (s, 3H), 2.81 (s, 3H), 2.57 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.8, 168.0, 136.8, 134.7, 133.8, 133.8, 132.1 (2C), 129.6 (2C), 128.8 (2C), 128.5 (2C), 127.7 (2C), 127.4 (2C), 126.9, 126.8, 71.8, 67.3, 52.3, 50.4, 46.3, 37.5, 36.0, 24.5; **HRMS** (EI-TOF, *m/z*) calcd for $C_{28}H_{27}ClN_2O_3$ $[M]^+$: 474.1705, found: 474.1707; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 220 nm) t_R = 20.30 min, 25.62 min.



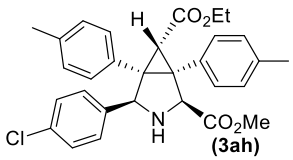
(3af)

Methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-chlorophenyl)-1,5,6-triphenyl-3-azabicyclo[3.1.0]hexane-2-carboxylate White solid, yield: 61.2 mg, 85%; m.p.: 83-85 °C; $[\alpha]_D^{25}$ = -63.9 (*c* 1.01, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.17 (m, 5H), 7.16 – 7.11 (m, 4H), 7.11 – 7.04 (m, 3H), 7.03 – 6.98 (m, 1H), 6.94 – 6.86 (m, 4H), 6.44 (d, *J* = 7.3 Hz, 2H), 4.79 (s, 1H), 4.41 (s, 1H), 3.58 (s, 3H), 3.21 (s, 1H), 2.84 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.3, 136.8, 135.9, 133.8, 133.7, 133.6, 132.7 (2C), 132.5 (2C), 131.5 (2C), 128.8 (2C), 128.5 (2C), 127.9 (2C), 127.8 (2C), 127.2, 127.0, 126.7 (2C), 125.6, 73.2, 70.7, 52.0, 51.0, 48.0, 27.2; **HRMS** (ESI-TOF, *m/z*) calcd for $C_{31}H_{26}ClNO_2$ $[M+H]^+$: 480.1725, found: 480.1729; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 0.8 mL/min, 220 nm) t_R = 13.32 min, 24.67 min.



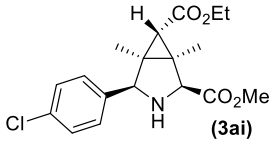
(3ag)

6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-1,5-bis(4-bromophenyl)-4-(4-chlorophenyl)-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 90.2 mg, 95%; m.p.: 205-206 °C; $[\alpha]_D^{25}$ = -79.8 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.38 (m, 2H), 7.30 – 7.25 (m, 4H), 7.16 – 7.08 (m, 4H), 6.83 – 6.77 (m, 2H), 4.66 (d, *J* = 6.1 Hz, 1H), 4.25 (d, *J* = 6.0 Hz, 1H), 3.96 – 3.85 (m, 2H), 3.68 (s, 3H), 2.99 (s, 1H), 2.54 (brs, 1H), 0.99 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.2, 169.0, 135.7, 134.3, 132.7 (2C), 132.6, 132.5, 132.4 (2C), 131.3 (2C), 131.2 (2C), 128.8 (4C), 121.9, 121.6, 71.2, 69.5, 60.9, 52.4, 50.8, 47.7, 25.2, 14.0; **HRMS** (EI-TOF, *m/z*) calcd for $C_{28}H_{24}{}^{79}Br_2ClNO_4$ $[M]^+$: 630.9755, found: 630.9709; for $C_{28}H_{24}{}^{79}Br^{81}BrClNO_4$ $[M]^+$: 632.9735, found: 632.9745; for $C_{28}H_{24}{}^{81}Br_2ClNO_4$ $[M]^+$: 634.9714, found: 634.9692. **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 0.8 mL/min, 220 nm) t_R = 32.37 min, 39.90 min.



(3ah)

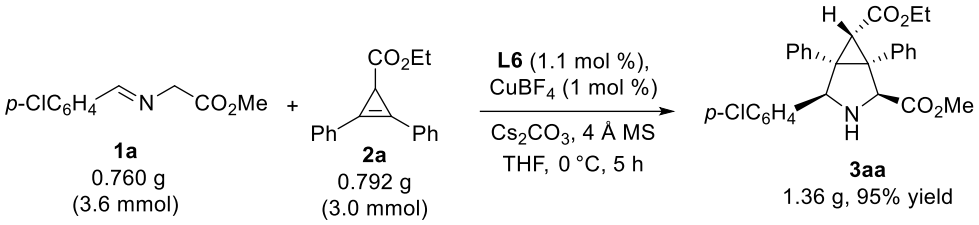
6-Ethyl 2-methyl (1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-chlorophenyl)-1,5-di-*p*-tolyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 74.0 mg, 98%; m.p.: 79-81°C; $[\alpha]_D^{25}$ = -61.7 (*c* 1.01, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 7.17 – 7.11 (m, 4H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.86 (d, *J* = 8.2 Hz, 2H), 4.70 (s, 1H), 4.26 (s, 1H), 3.90 (q, *J* = 7.1 Hz, 2H), 3.66 (s, 3H), 2.91 (s, 1H), 2.48 (s, 1H), 2.28 (s, 3H), 2.22 (s, 3H), 0.97 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.7, 169.3, 137.0, 136.7, 136.4, 133.9, 130.9 (2C), 130.7 (2C), 130.6 (2C), 129.0 (2C), 128.6 (2C), 128.6 (2C), 128.5 (2C), 71.6, 69.9, 60.5, 52.2, 51.1, 48.2, 25.1, 21.3, 21.2, 14.0; **HRMS** (EI-TOF, *m/z*) calcd for $C_{30}H_{30}ClNO_4$ $[M]^+$: 503.1858, found: 503.1859; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 220 nm) t_R = 18.15 min, 28.50 min.



(3ai)

6-Ethyl 2-methyl (1*R*,2*S*,4*S*,5*S*,6*S*)-4-(4-chlorophenyl)-1,5-dimethyl-3-azabicyclo[3.1.0]hexane-2,6-dicarboxylate White solid, yield: 42.1 mg, 80%; m.p.: 93-95 °C; $[\alpha]_D^{25}$ = -2.8 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.28 (m, 4H), 4.15 (s, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 3.77 (s, 1H), 2.20 (s, 1H), 1.99 (s, 1H), 1.46 (s, 3H), 1.28 – 1.18 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.3, 170.6, 137.2, 133.8, 128.9 (2C), 128.9 (2C), 68.4, 66.9, 60.4, 52.4, 39.6, 37.6, 23.6, 14.4, 10.1, 9.7; **HRMS** (EI-TOF, *m/z*) calcd for $C_{18}H_{22}ClNO_4$ $[M]^+$: 351.1232, found: 351.1227; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 40/1, 0.8 mL/min, 220 nm) t_R = 18.40 min, 25.60 min.

Gram scale procedure



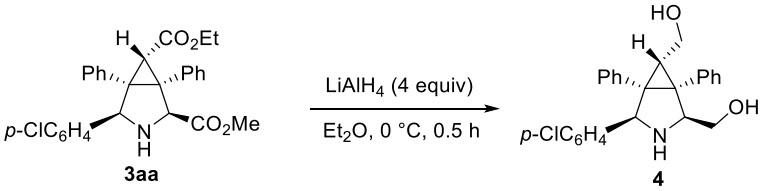
1a
0.760 g
(3.6 mmol)

2a
0.792 g
(3.0 mmol)

3aa
1.36 g, 95% yield

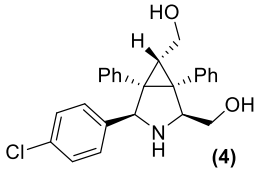
Under a nitrogen atmosphere, $Cu(CH_3CN)_4BF_4$ (9.4 mg, 0.03 mmol) and **L6** (17 mg, 0.033 mmol) were dissolved in dry THF (10 mL), subsequently add 4Å Ms (700 mg), and stirred at room temperature for about 1 h. Then, glycine imine **1a** (0.760 g, 3.6 mmol) dissolved in THF (30 mL) and Cs_2CO_3 (196 mg, 0.6 mmol) were added, the mixture was cooled to 0 ℃ and cyclopropene **2a** (0.792 g, 3.0 mmol) was added. Once starting material was consumed (monitored by TLC, about 5 h), the mixture was filtered through celite and the filtrate was concentrated, then the residue was purified by column chromatography (petroleum ether/ethyl acetate 6:1) on silica gel to afford the corresponding product **3aa** in 95% yield.

Synthetic transformations of the cycloadduct 3aa



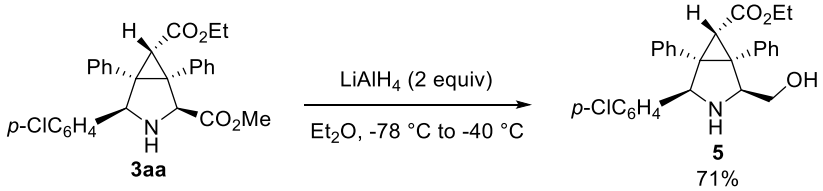
3aa **4**

To a solution of **3aa** (380.8 mg, 0.8 mmol) in dry Et_2O (10 mL) under nitrogen, $LiAlH_4$ (121.4 mg, 3.2 mmol) was added in small portions. The reaction mixture was stirred for 0.5 h at 0 ℃. Then water (0.5 mL) and 10% aqueous sodium hydroxide (0.7 mL) and more water (0.5 mL) was added carefully. The mixture was filtered over anhydrous Na_2SO_4, and the filtrate was concentrated. The residue was purified by column chromatography (petroleum ether/ethyl acetate 2:1 to 1:1) on silica gel to afford **4** in 90% yield.



(4)

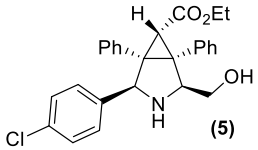
((1*S*,2*S*,4*S*,5*R*,6*S*)-4-(4-Chlorophenyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-2,6-diyl)dimethanol White solid, yield: 292 mg, 90%; m.p.: 176-177 °C; $[\alpha]_D^{25}$ = -79.7 (*c* 1.06, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 – 7.48 (m, 2H), 7.30 – 7.24 (m, 2H), 7.23 – 7.08 (m, 10H), 4.69 (s, 1H), 3.86 – 3.63 (m, 5H), 2.73 (brs, 3H), 2.34 (dd, *J* = 8.0, 6.3 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.9, 136.1, 135.8, 133.5, 131.2 (2C), 131.0 (2C), 129.0 (2C), 128.6 (2C), 128.5 (2C), 128.2 (2C), 127.2, 126.9, 69.6, 68.0, 62.2, 60.8, 44.7, 42.9, 24.3; **HRMS** (ESI-TOF, *m/z*) calcd for $C_{25}H_{24}ClNO_2$ $[M+H]^+$: 406.1568, found: 406.1573; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 220 nm) t_R = 23.03 min, 47.72 min.



3aa **5**
71%

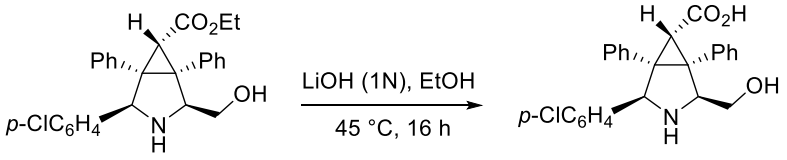
A solution of **3aa** (95.2 mg, 0.2 mmol) in dry Et_2O (3 mL) under nitrogen was cooled to -78 ℃, then $LiAlH_4$ (15.2 mg, 0.4 mmol) was added in small portions. The reaction mixture was stirred at -78 ℃ for

40 min and moved to -40 ℃ for another 10 min. Then water (0.5 mL) and 10% aqueous sodium hydroxide (0.7 mL) and more water (0.5 mL) was added carefully. The mixture was filtered over anhydrous Na_2SO_4, and the filtrate was concentrated. the residue was subjected to the preparative thin layer chromatography (petroleum ether/ethyl acetate 3:1) to afford **5** in 71% yield.



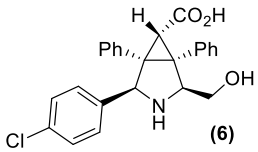
(5)

Ethyl (1*R*,2*S*,4*S*,5*S*,6*S*)-2-(4-chlorophenyl)-4-(hydroxymethyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-6-carboxylate White solid, yield: 63.6 mg, 71%; m.p.: 94-95 °C; $[\alpha]_D^{25}$ = -82.0 (*c* 0.98, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H), 7.30 – 7.24 (m, 2H), 7.23 – 7.10 (m, 6H), 7.03 – 6.95 (m, 4H), 4.64 (s, 1H), 3.84 – 3.61 (m, 5H), 3.02 (s, 1H), 1.97 (brs, 2H), 0.78 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.3, 137.2, 135.1, 134.3, 133.5, 131.3 (2C), 130.9 (2C), 129.0 (2C), 128.3 (2C), 128.1 (2C), 127.7 (2C), 127.2, 127.0, 70.2, 68.0, 62.7, 60.2, 50.7, 47.1, 24.6, 13.7; **HRMS** (ESI-TOF, *m/z*) calcd for $C_{27}H_{26}ClNO_3$ $[M+H]^+$: 448.1674, found: 448.1680; **HPLC** (Chiralcel OD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 220 nm) t_R = 13.54 min, 44.61 min.



5
> 99% ee
6
86% yield

To a solution of **5** (33.6 mg, 0.1 mmol) in EtOH (1.5 mL), LiOH (1N, 0.5 mL) was added. The reaction mixture was stirred at 45 ℃ for 16 h. the reaction mixture was subjected to the preparative thin layer chromatography (dichloromethane/methanol 10:1) to afford **6** in 86% yield.



(6)

(1*R*,2*S*,4*S*,5*S*,6*S*)-2-(4-Chlorophenyl)-4-(hydroxymethyl)-1,5-diphenyl-3-azabicyclo[3.1.0]hexane-6-carboxylic acid White solid, yield: 36.1 mg, 86%; m.p.: 278-280 ℃; $[\alpha]_D^{25}$ = -9.8 (*c* 1.00, DMSO); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.85 (brs, 1H), 7.49 – 7.32 (m, 8H), 7.29 – 7.20 (m, 2H), 7.21 – 7.12 (m, 3H), 7.11 – 6.98 (m, 1H), 5.60 (s, 1H), 5.23 (brs, 1H), 4.41 (dd, *J* = 10.1, 3.3 Hz, 1H), 3.82 – 3.73 (m, 1H), 3.49 – 3.36 (m, 1H), 2.87 (s, 1H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 172.5, 136.1, 135.7, 133.7, 133.0, 130.6 (2C), 129.5 (2C), 129.2 (2C), 128.4 (2C), 128.3 (2C), 128.2 (2C), 127.4, 127.1, 66.0, 64.1, 58.7, 45.3, 44.5, 35.0; **HRMS** (ESI-TOF, *m/z*) calcd for $C_{25}H_{22}ClNO_3$ $[M+H]^+$: 420.1361, found: 420.1367.

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The absolute configuration determination of (1*S*,2*S*,4*S*,5*R*,6*S*)-3fa

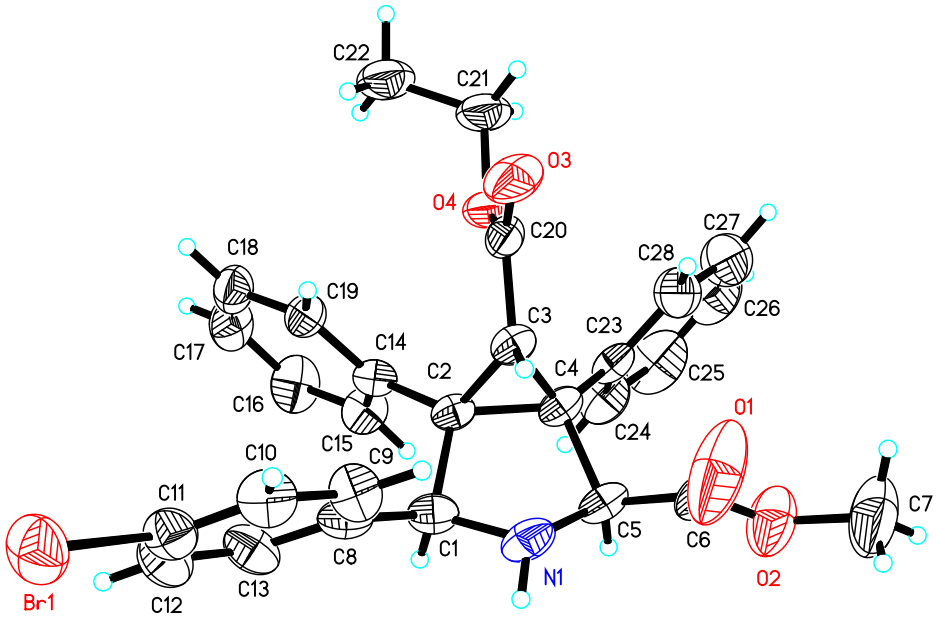


Fig S1. X-ray structure of (1*S*,2*S*,4*S*,5*R*,6*S*)-**3fa**
Ellipsoids are drawn at the 30% probability level.

Crystal data and structure refinement for CCDC 1844508

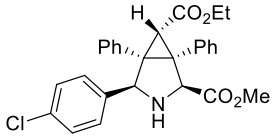
(CCDC 1844508 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.)

Table S2. Crystal data and structure refinement for (1*S*,2*S*,4*S*,5*R*,6*S*)-**3fa**.

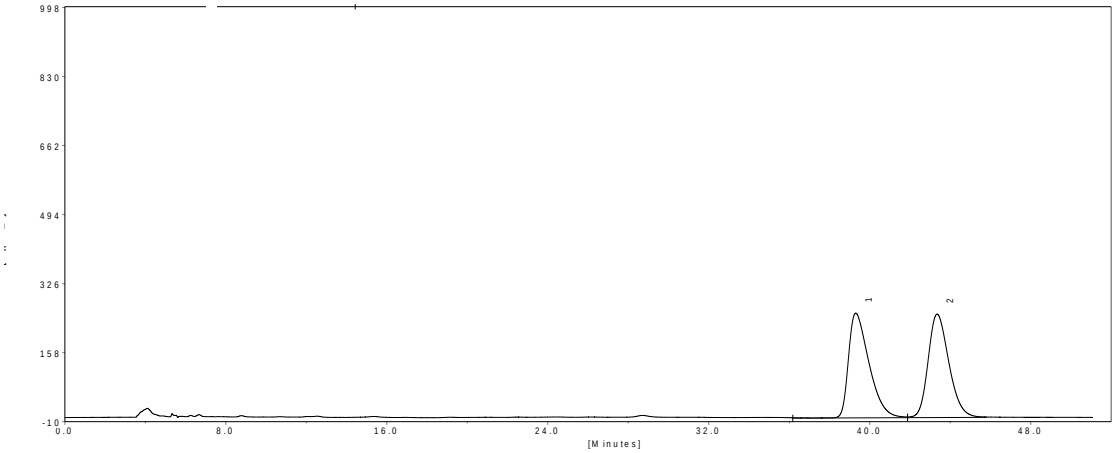
Identification code	(1*S*,2*S*,4*S*,5*R*,6*S*)-**3fa**	
Empirical formula	C28 H26 Br N O4	
Formula weight	520.41	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 9.0966(12) Å	α= 90 °.
	b = 14.1081(19) Å	β= 90 °.
	c = 20.070(3) Å	γ = 90 °.
Volume	2575.8(6) $Å^3$	
Z	4	
Density (calculated)	1.342 Mg/m^3	
Absorption coefficient	1.629 mm^{-1}	
F(000)	1072	
Crystal size	0.20 x 0.16 x 0.11 mm^3	
Theta range for data collection	1.764 to 25.497 °.	

Index ranges	-11<=h<=10, -17<=k<=17, -22<=l<=24
Reflections collected	18159
Independent reflections	4783 [R(int) = 0.0467]
Completeness to theta = 25.242 °	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6310
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4783 / 40 / 333
Goodness-of-fit on F^2	1.006
Final R indices [I>2sigma(I)]	R1 = 0.0436, wR2 = 0.0993
R indices (all data)	R1 = 0.0961, wR2 = 0.1209
Absolute structure parameter	0.009(6)
Extinction coefficient	0.0043(11)
Largest diff. peak and hole	0.423 and -0.218 e.$Å^{-3}$

Chiral HPLC Chromatograms



(3aa)



#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
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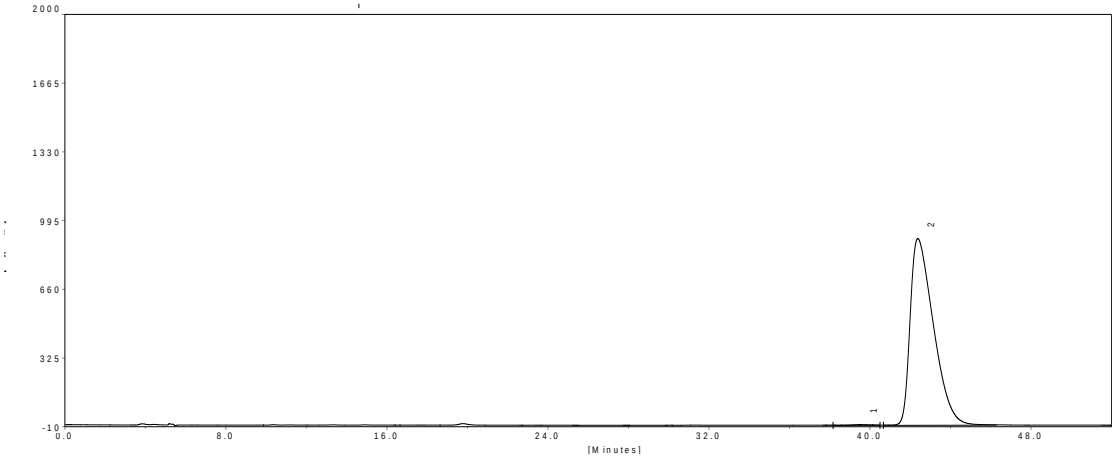
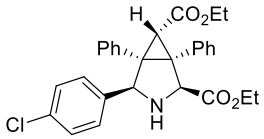
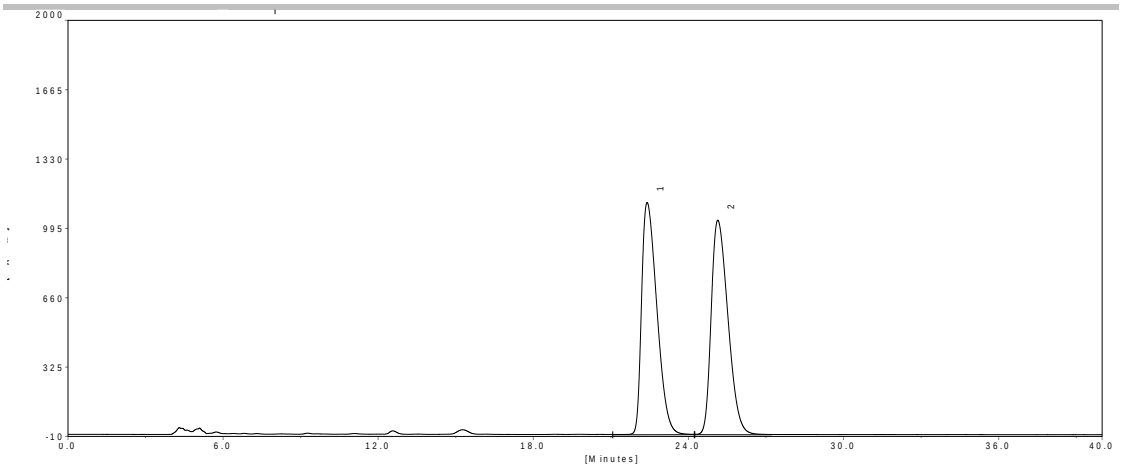
2	43.34583	251.18	17834.27	50.1092



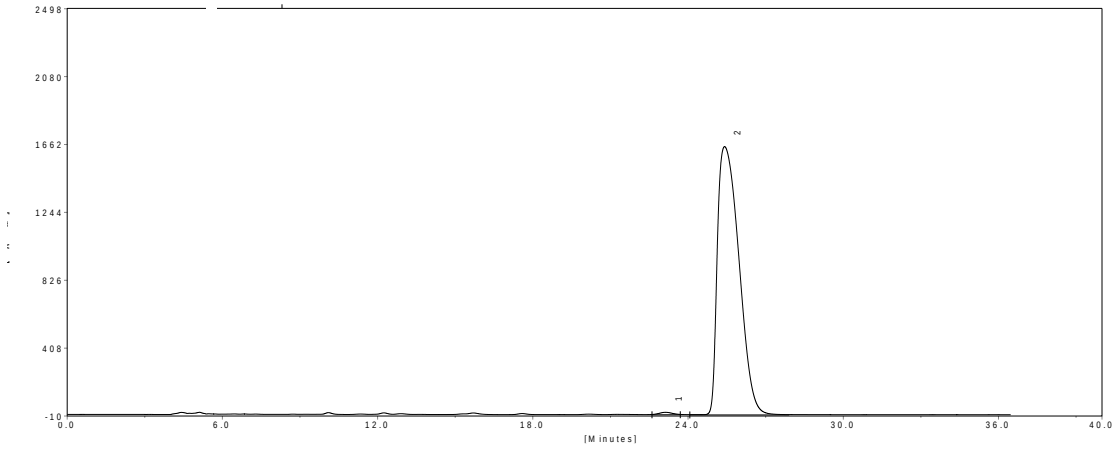
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	39.53750	2.20	127.06	0.1749
2	42.37583	909.04	72511.12	99.8251



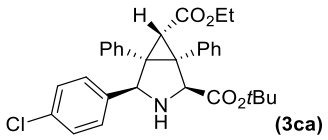
(3ba)



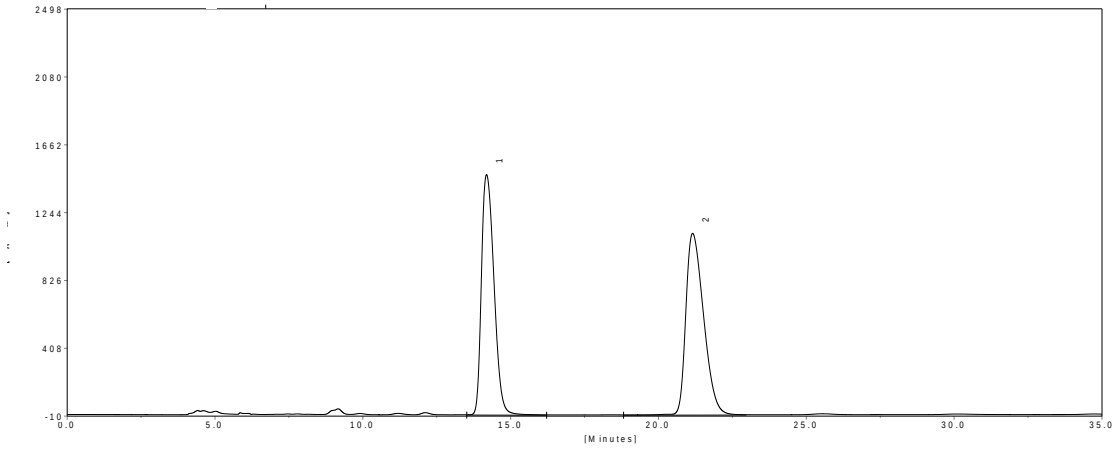
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	22.40167	1121.00	45950.96	49.7406
2	25.13667	1035.13	46430.29	50.2594



#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	23.13583	13.18	422.65	0.4425
2	25.41083	1650.41	95083.44	99.5575

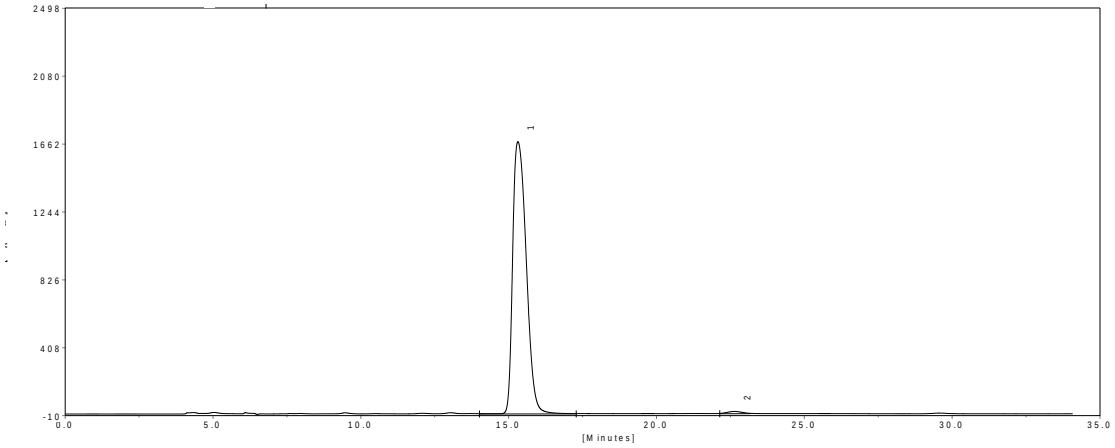


(3ca)

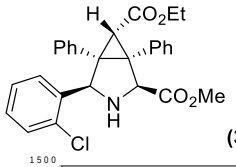


#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)

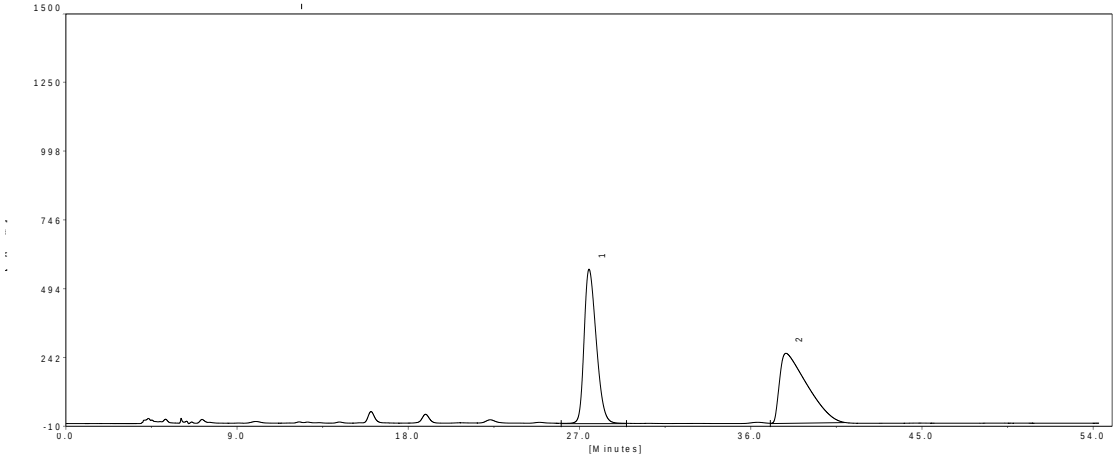
1	14.18583	1481.09	43551.62	49.4500
2	21.15583	1100.10	44520.39	50.5500



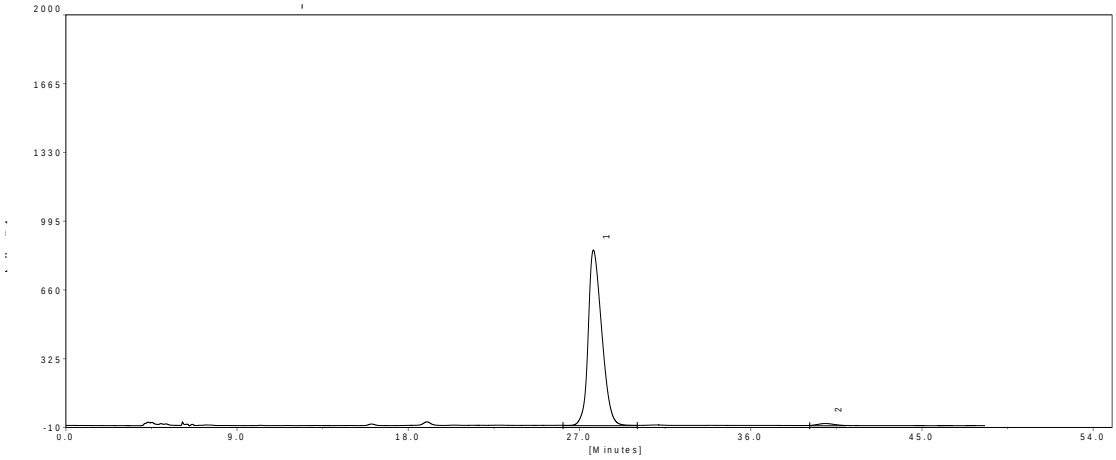
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	15.31417	1675.13	53187.85	99.3003
2	22.64250	11.77	374.80	0.6997



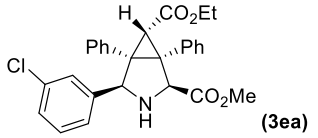
(3da)



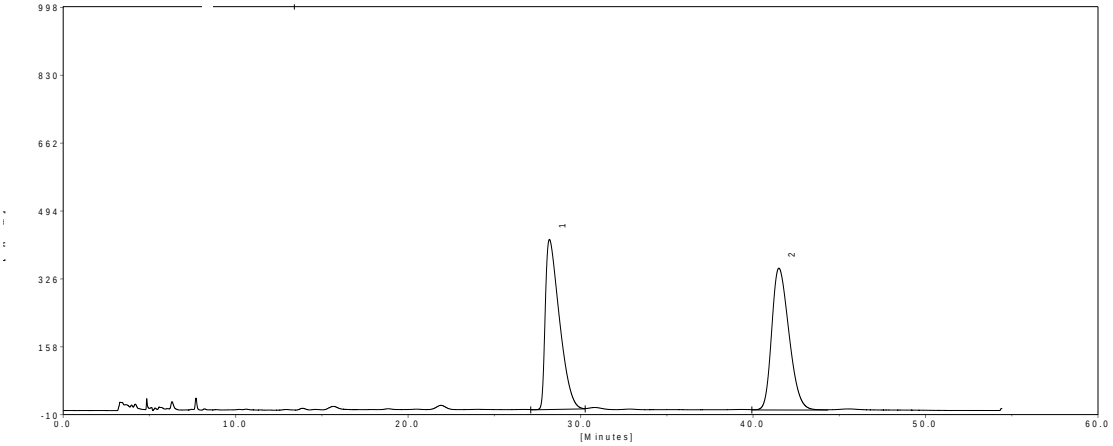
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	27.50083	564.52	24904.38	49.5216
2	37.85500	255.48	25385.52	50.4784



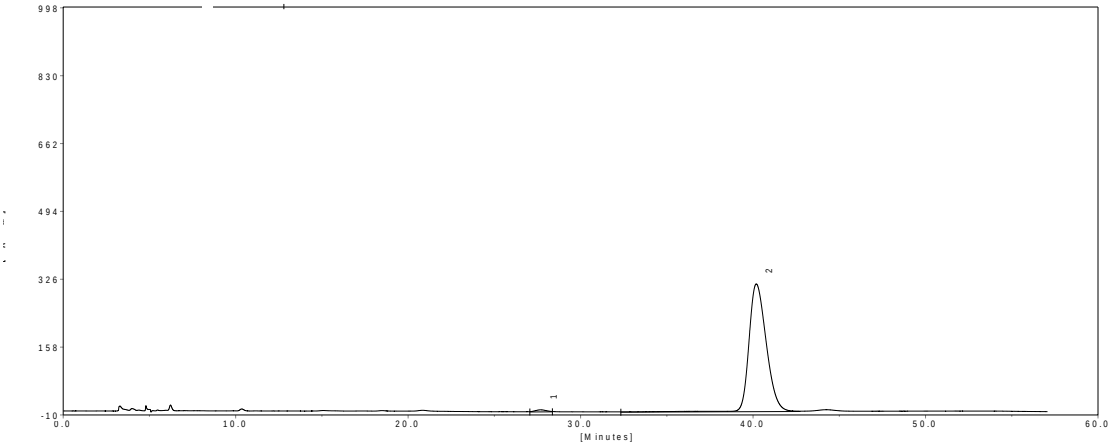
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	27.73000	854.19	41961.72	98.7959
2	39.92333	9.17	511.41	1.2041



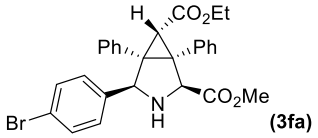
(3ea)



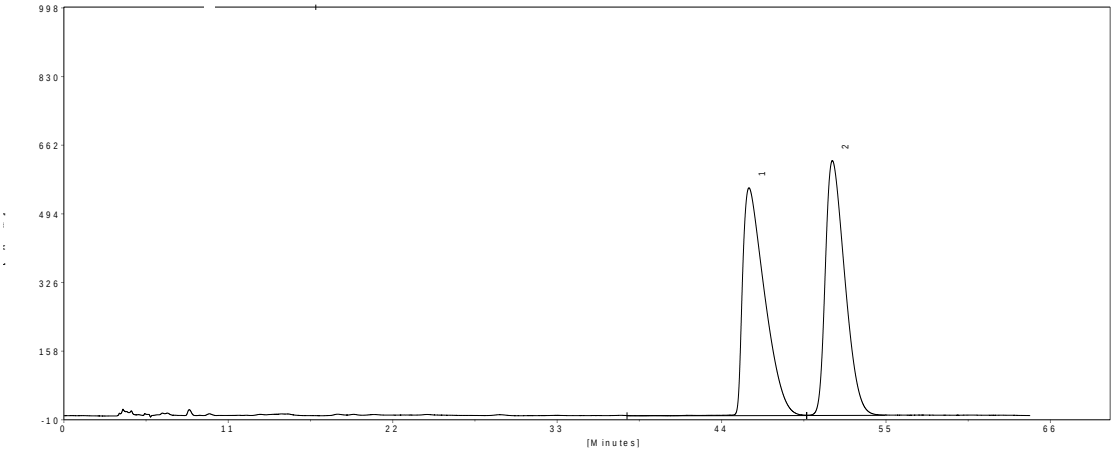
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	28.19583	420.49	23793.22	49.5978
2	41.49833	350.52	24179.12	50.4022



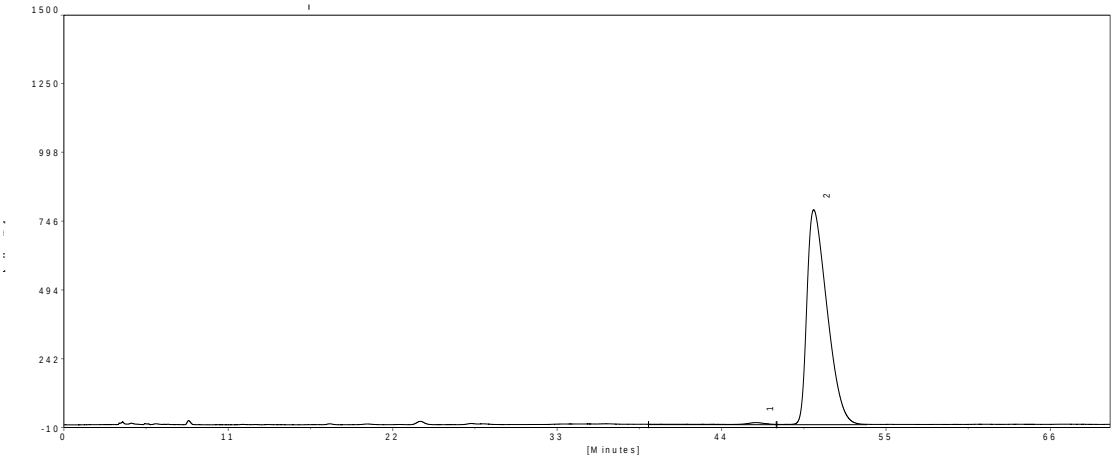
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	27.68833	4.02	146.79	0.6715
2	40.19083	315.55	21714.38	99.3285



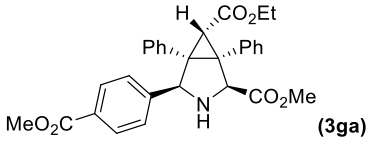
(3fa)



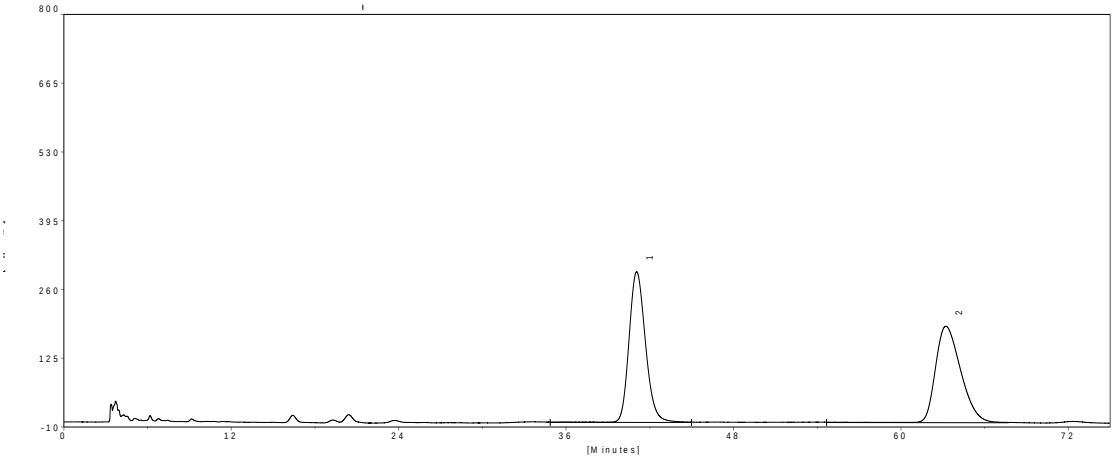
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	45.83333	556.77	56311.50	50.0691
2	51.11000	622.95	56155.98	49.9309



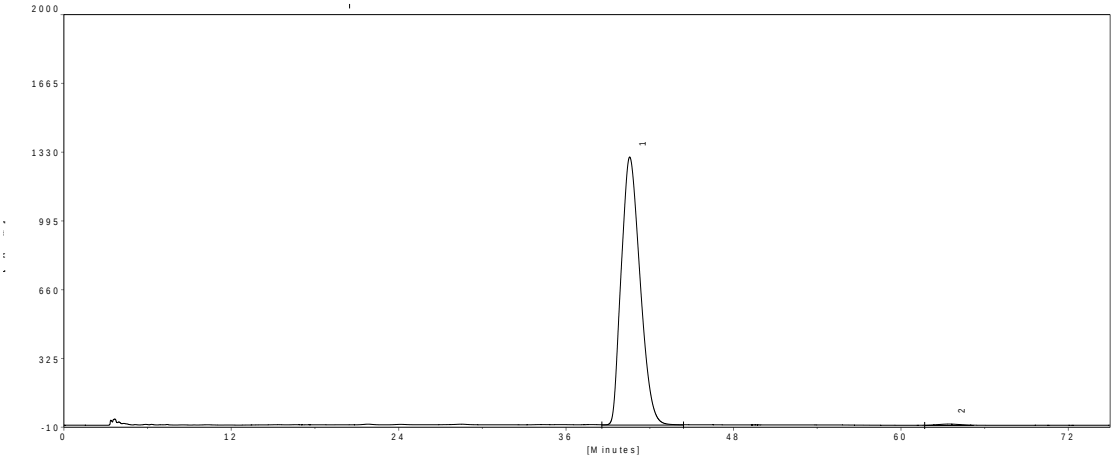
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	46.36833	6.34	441.58	0.6009
2	50.46583	786.01	73048.48	99.3991



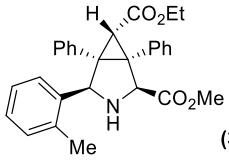
(3ga)



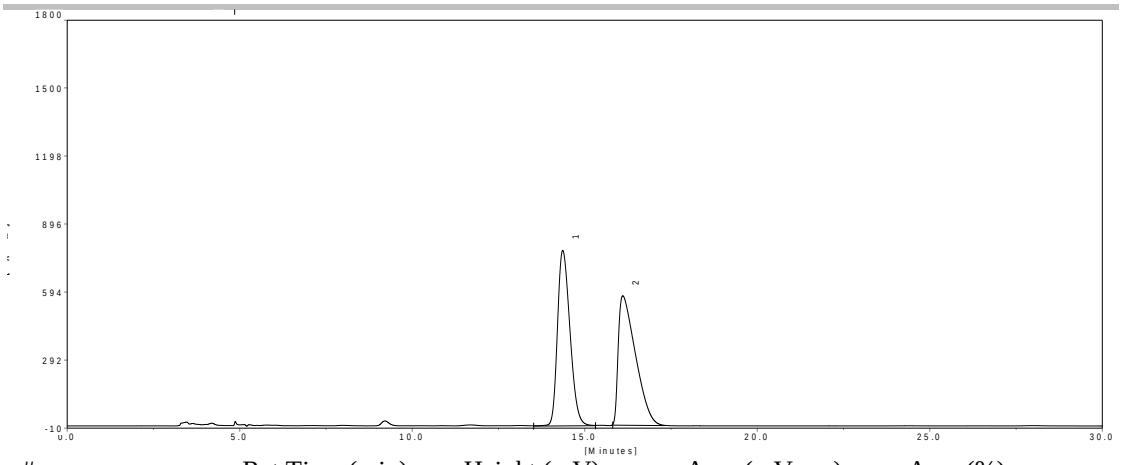
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	41.05333	295.38	23954.64	50.6360
2	63.22083	188.73	23352.88	49.3640



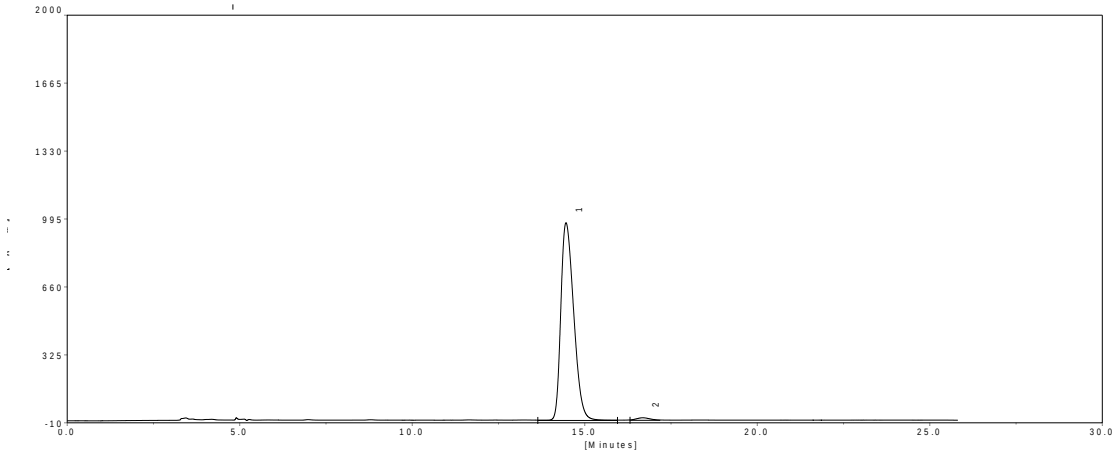
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	40.55833	1304.57	121758.46	99.5476
2	63.42417	5.37	553.29	0.4524



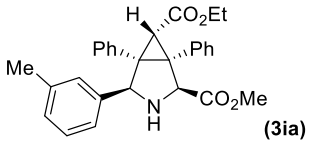
(3ha)



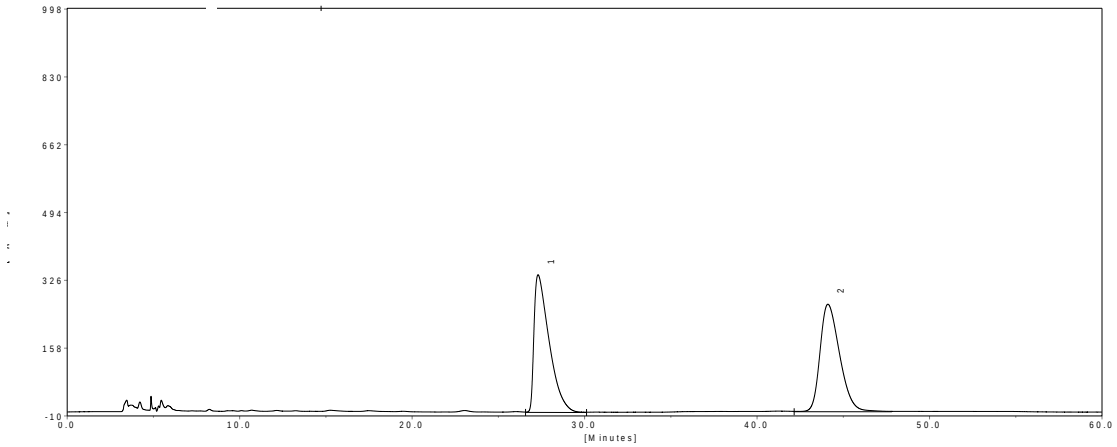
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	14.36250	777.95	19459.45	49.5412
2	16.10417	573.14	19819.88	50.4588



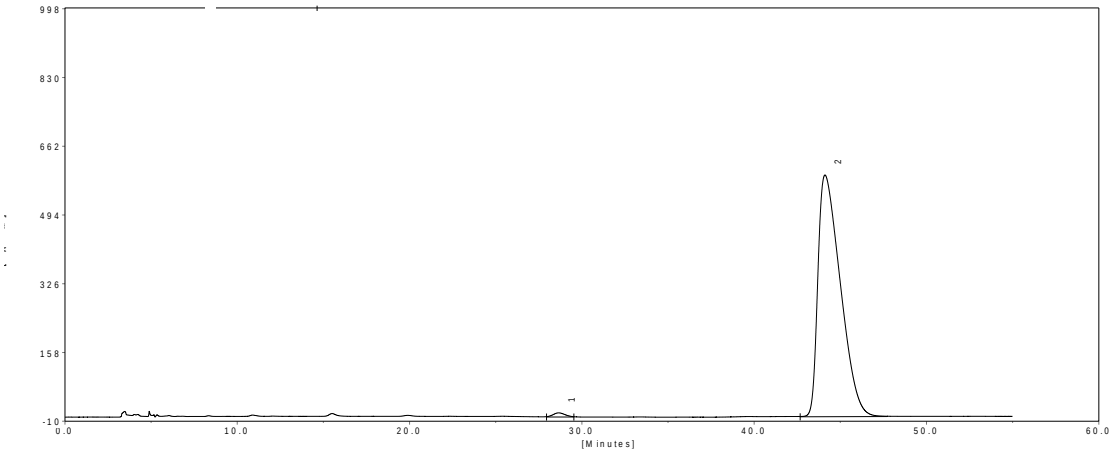
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	14.45750	973.48	25126.65	98.9401
2	16.68583	10.80	269.18	1.0599



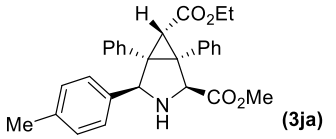
(3ia)



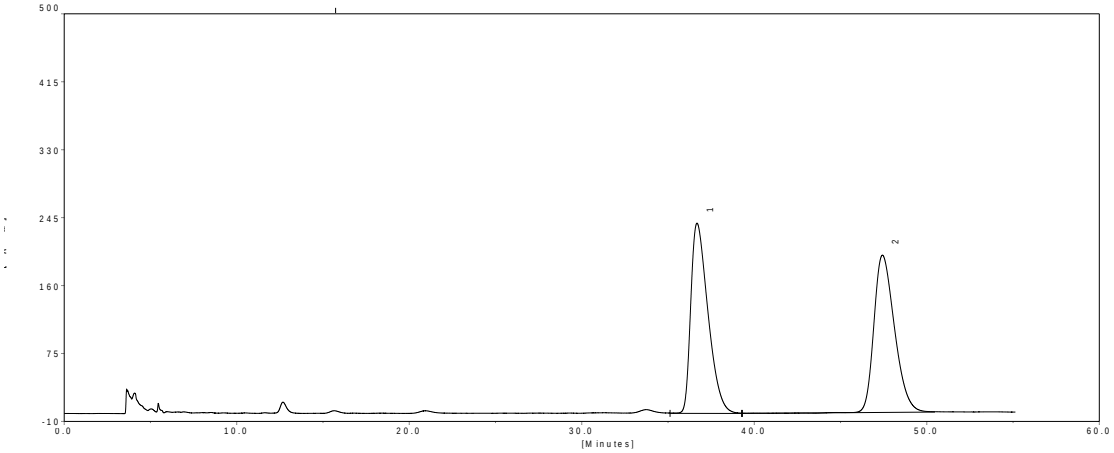
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	27.60500	340.35	20639.99	49.8362
2	44.10833	265.56	20775.63	50.1638



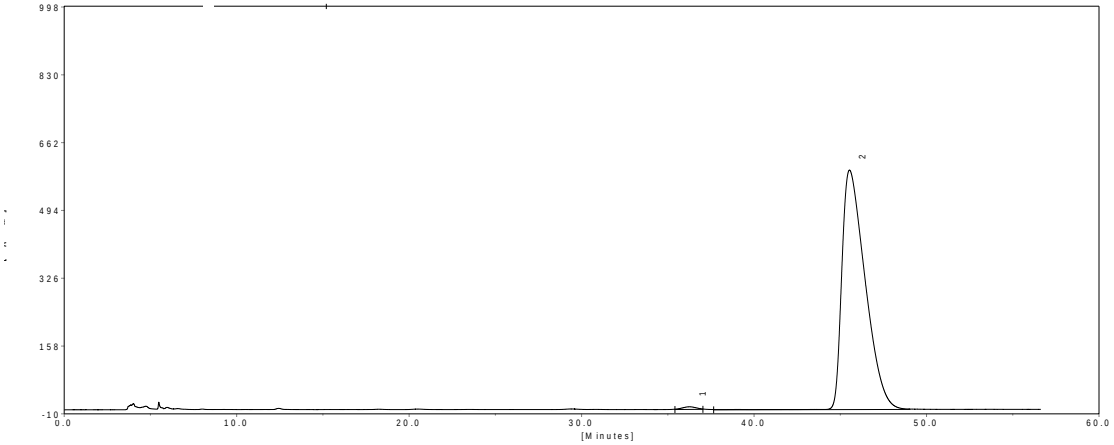
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	28.35167	8.50	351.02	0.6569
2	44.11000	589.91	53083.04	99.3431



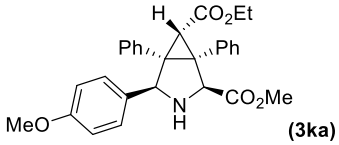
(3ja)



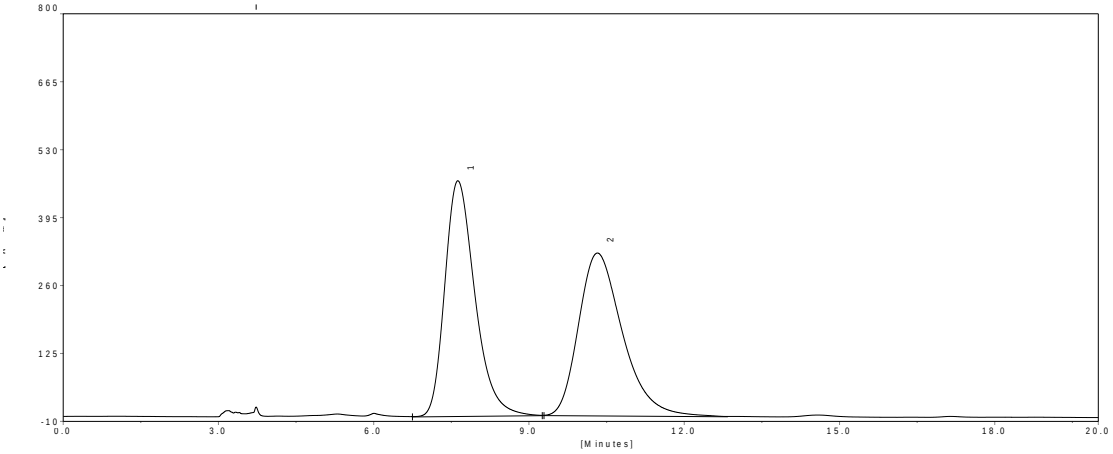
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	36.68583	237.66	16380.22	50.4914
2	46.93083	196.42	16061.40	49.5086



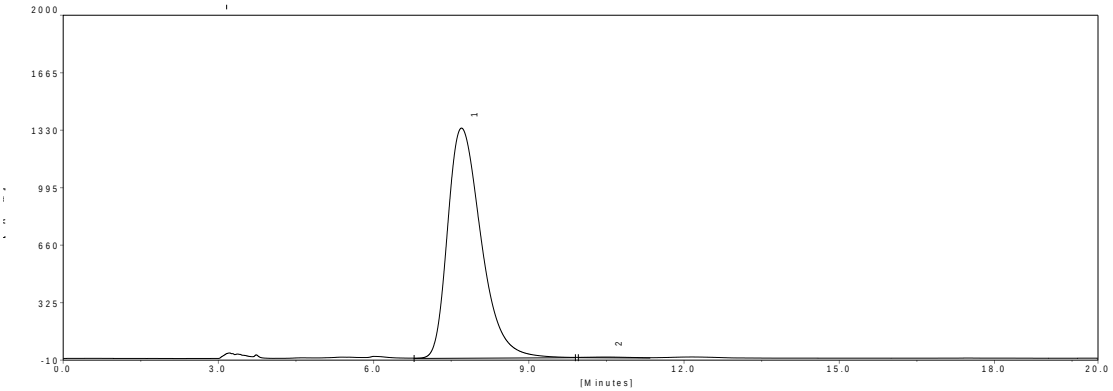
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	36.26750	5.70	289.59	0.5234
2	45.83583	592.56	55041.38	99.4766



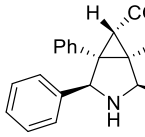
(3ka)



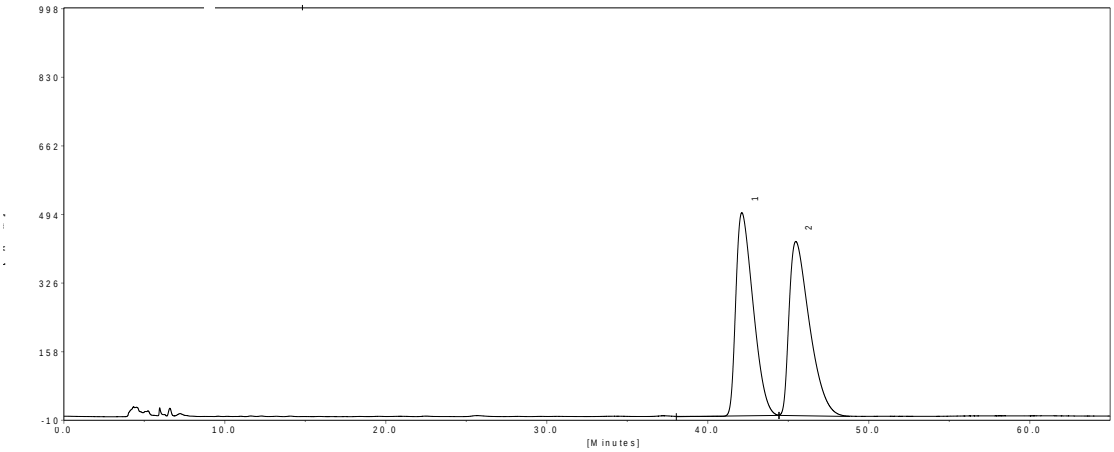
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	7.62583	467.79	18873.39	49.8548
2	10.32250	323.17	18983.32	50.1452



#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	7.69833	1339.53	60048.11	99.8090
2	10.48833	2.57	114.91	0.1910

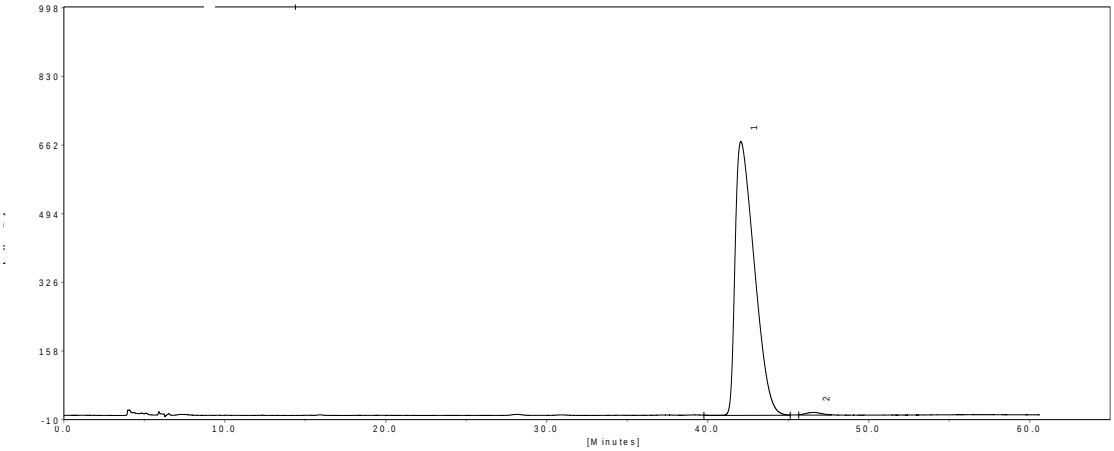


(3la)

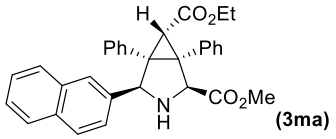


#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	42.11833	496.99	36728.96	49.5510

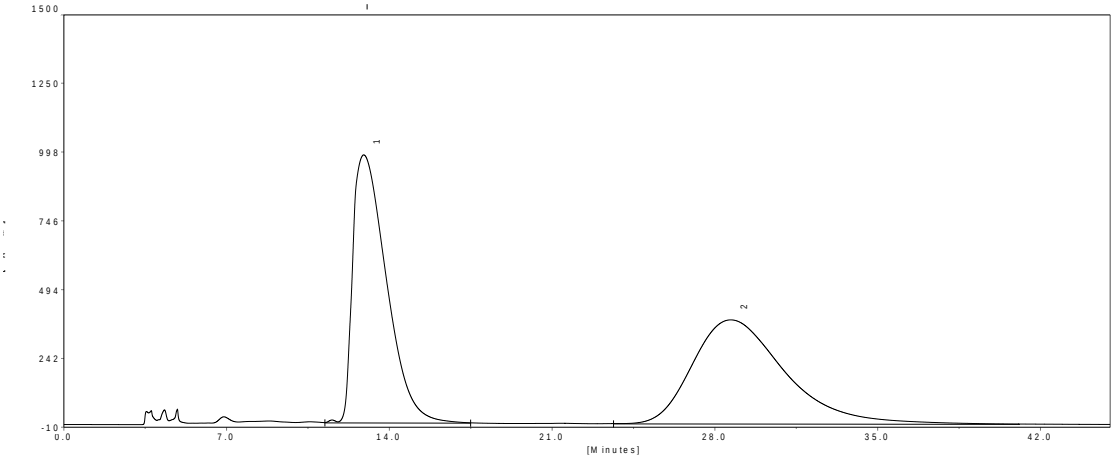
2	45.57000	425.90	37394.52	50.4490



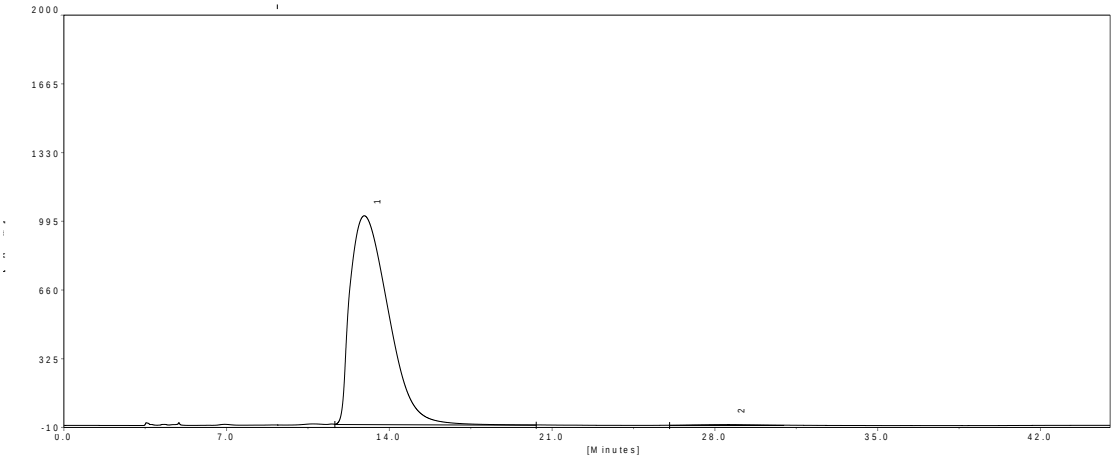
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	42.05500	669.52	55076.77	99.3518
2	46.45000	5.73	359.35	0.6482



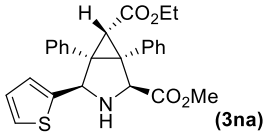
(3ma)



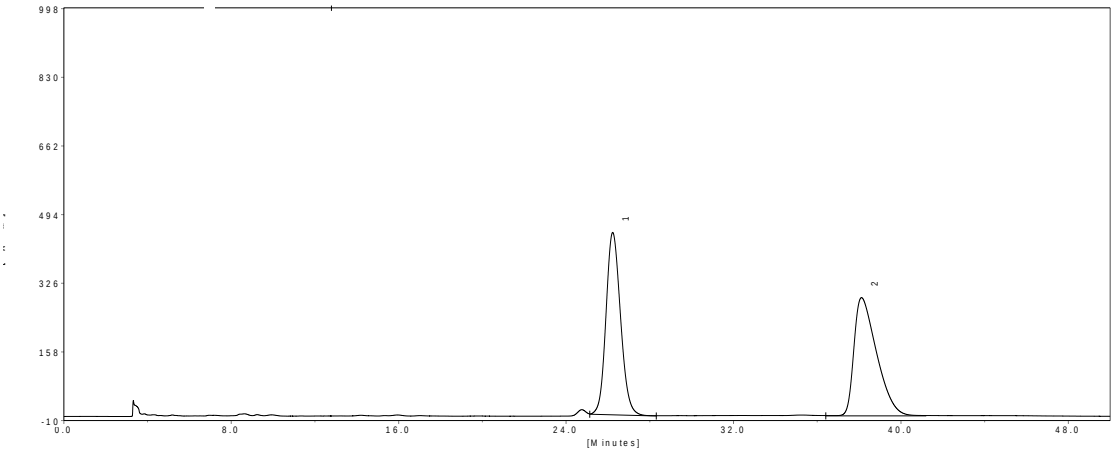
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.89583	980.60	98446.70	48.4951
2	28.68250	380.30	104556.82	51.5049



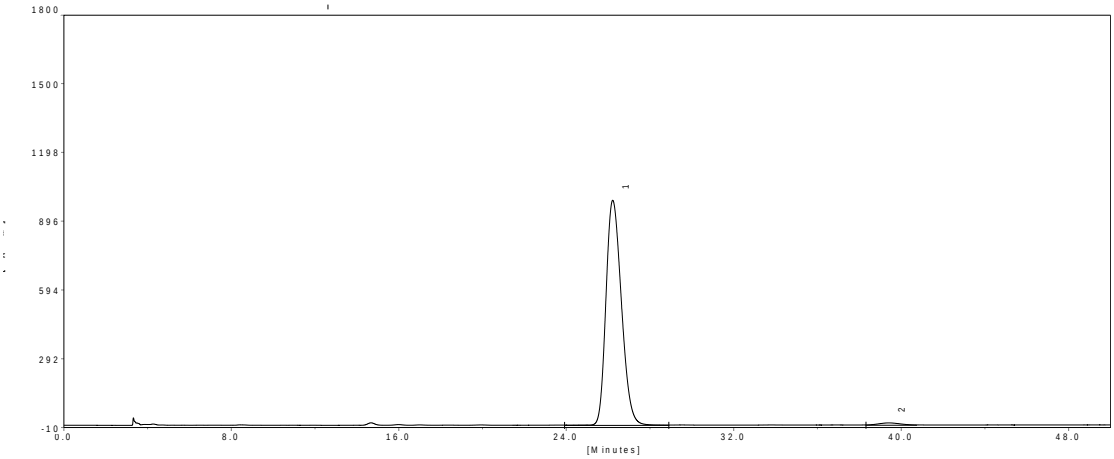
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.92417	1016.48	114941.80	99.5767
2	28.57500	3.05	488.57	0.4233



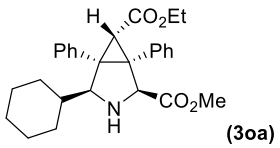
(3na)



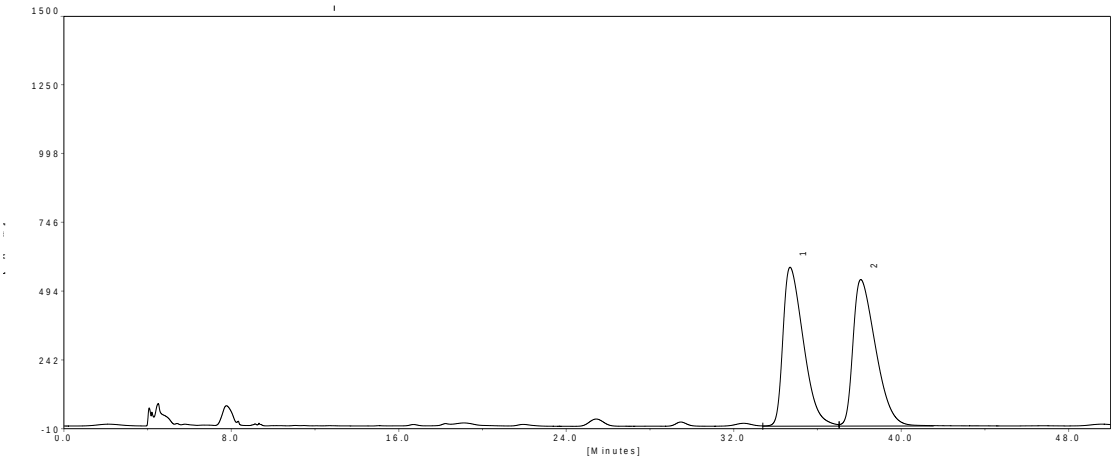
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	26.22583	445.67	21373.42	49.8524
2	38.41583	288.64	21500.01	50.1476



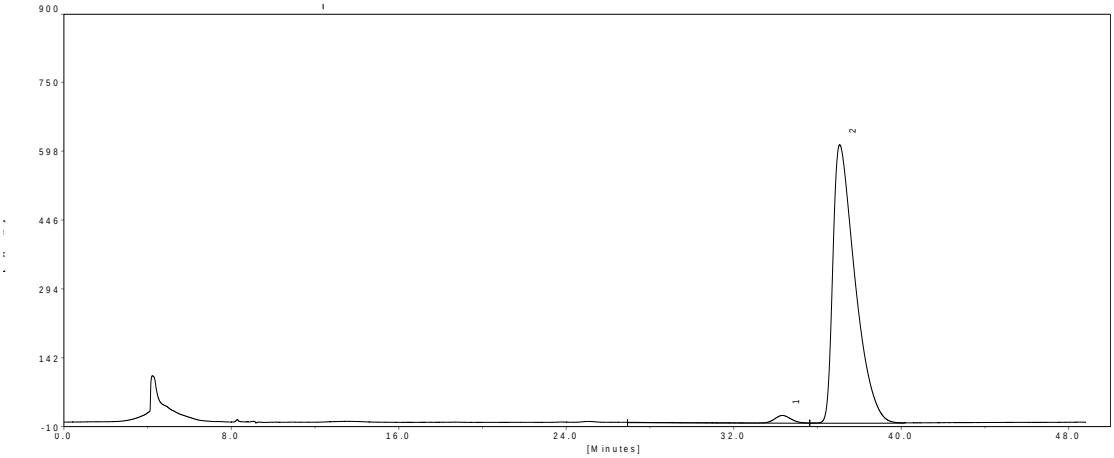
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	26.22000	986.96	50416.10	98.8443
2	39.10417	8.82	589.47	1.1557



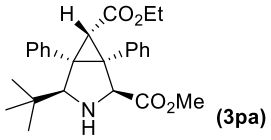
(3oa)



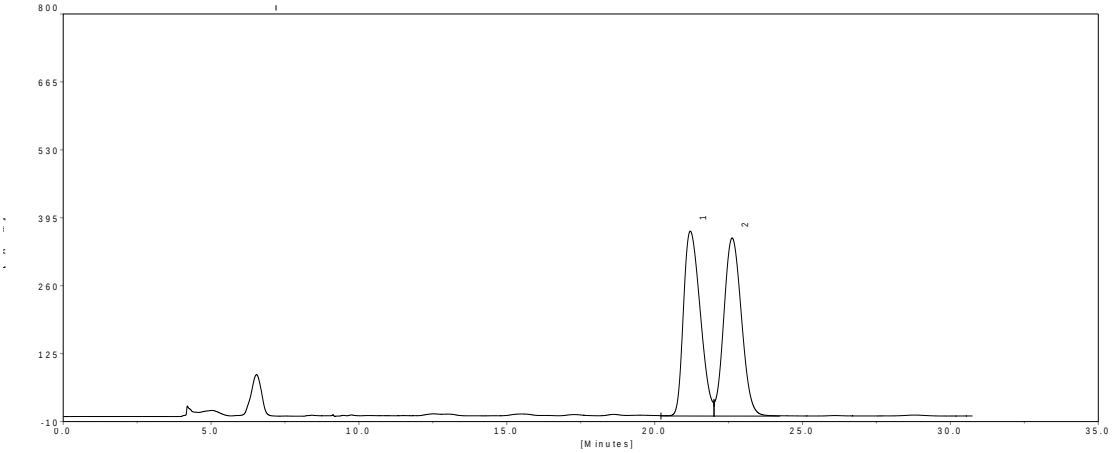
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	34.69000	581.08	39196.70	49.5582
2	38.07333	535.57	39895.50	50.4418



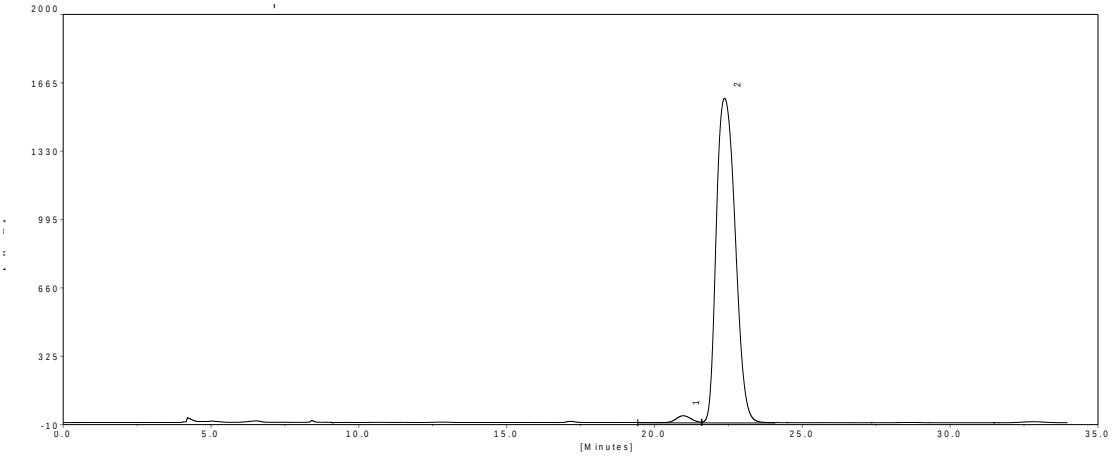
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	34.34833	16.27	687.42	1.5104
2	37.06500	614.09	44825.32	98.4896



(3pa)

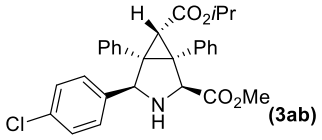


#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	21.20500	366.76	14383.76	49.6582
2	22.62000	353.32	14581.75	50.3418

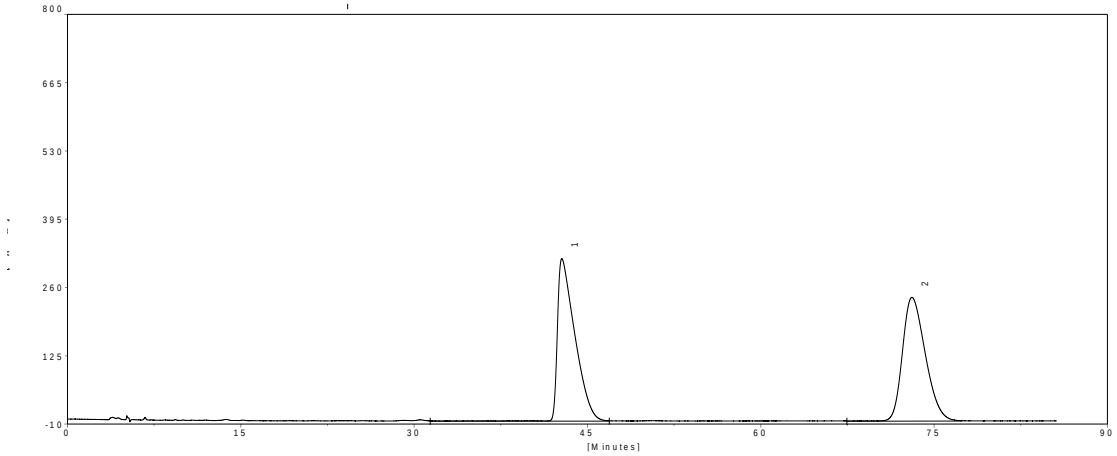


#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)

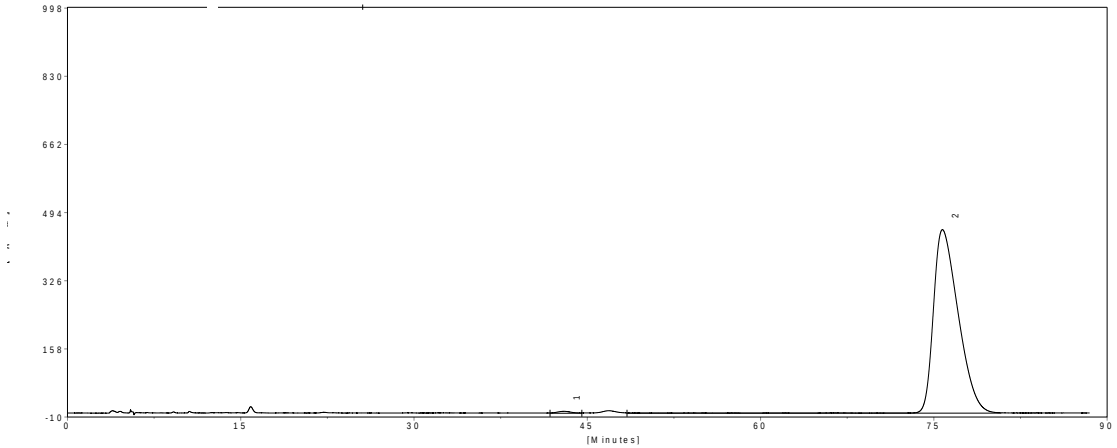
1	20.97083	33.33	1136.65	1.5862
2	22.37000	1589.48	70523.76	98.4138



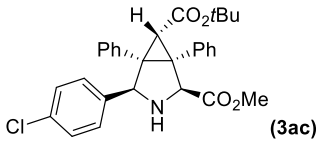
(3ab)



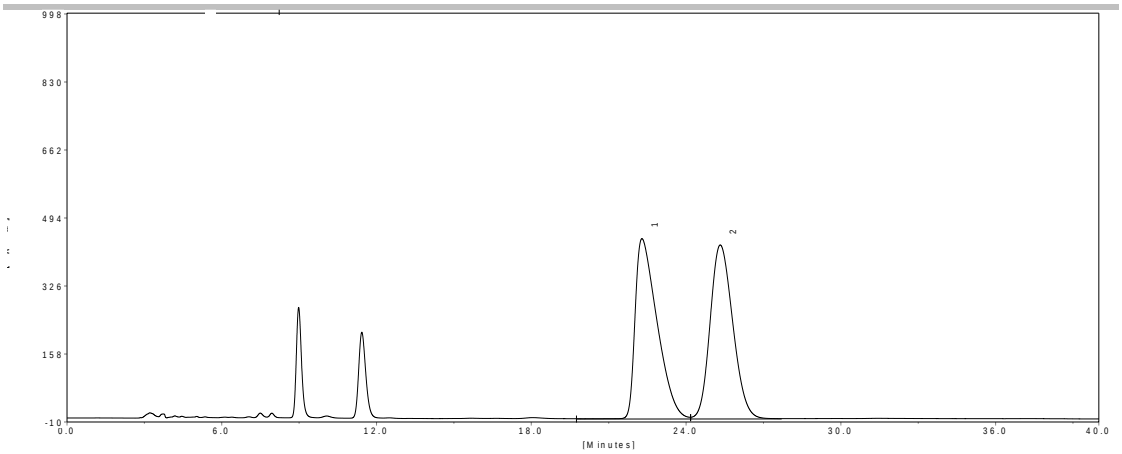
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	42.78500	320.70	33176.44	49.8957
2	73.58583	244.15	33315.20	50.1043



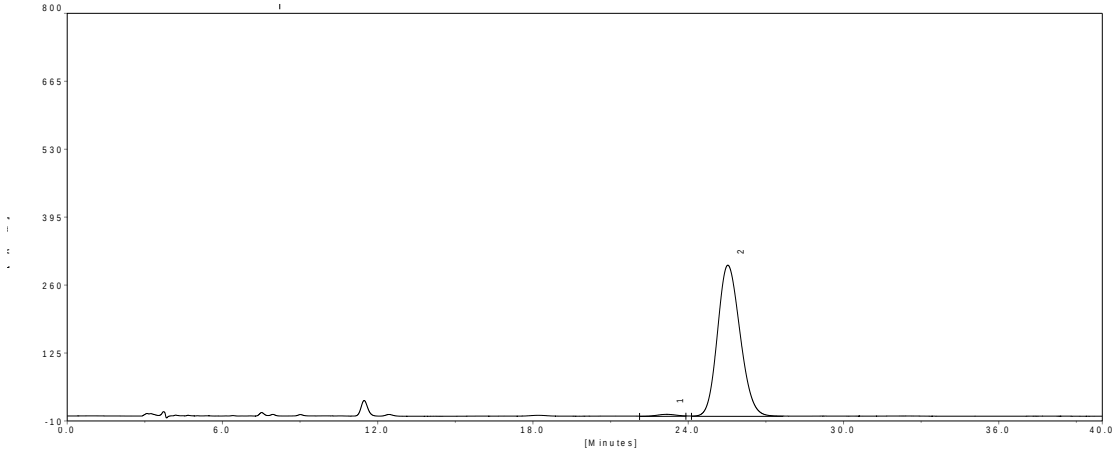
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	42.96000	4.03	289.18	0.4346
2	75.34750	451.67	66247.29	99.5654



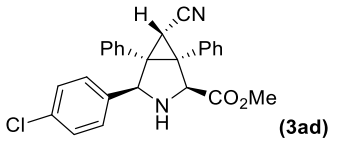
(3ac)



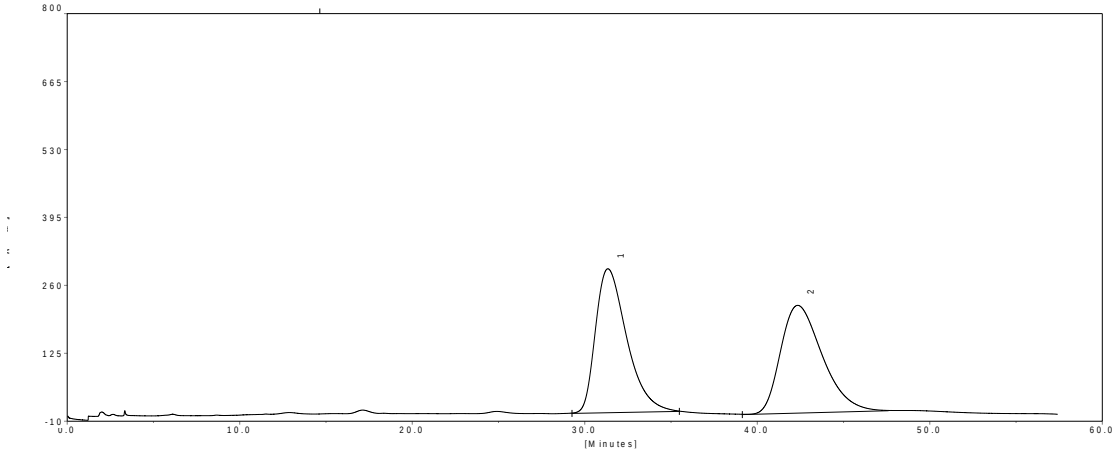
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	22.29000	444.95	26145.08	49.9802
2	25.32583	429.25	26165.84	50.0198



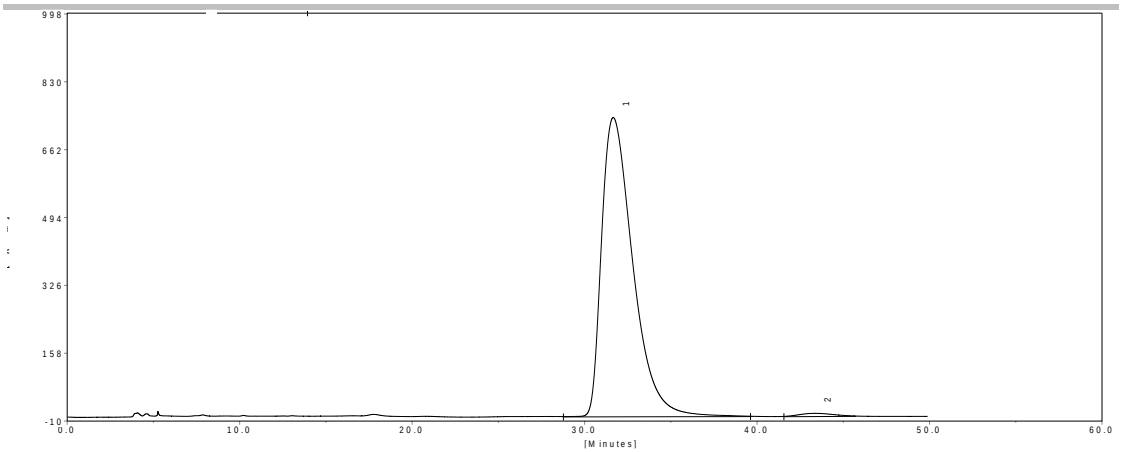
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	23.18583	3.32	152.51	0.8361
2	25.53167	299.85	18088.35	99.1639



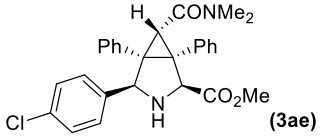
(3ad)



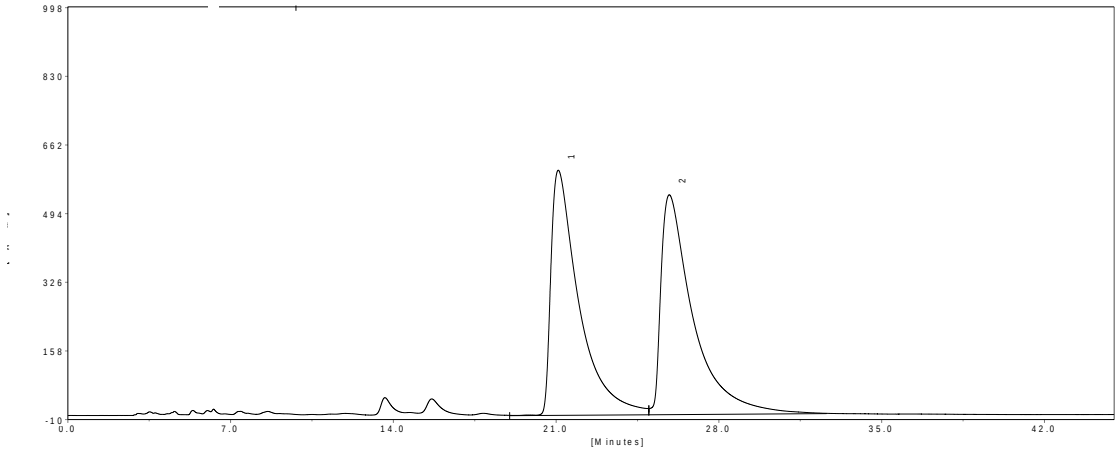
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	31.33917	285.50	35809.25	50.0980
2	42.35917	213.52	35669.22	49.9020



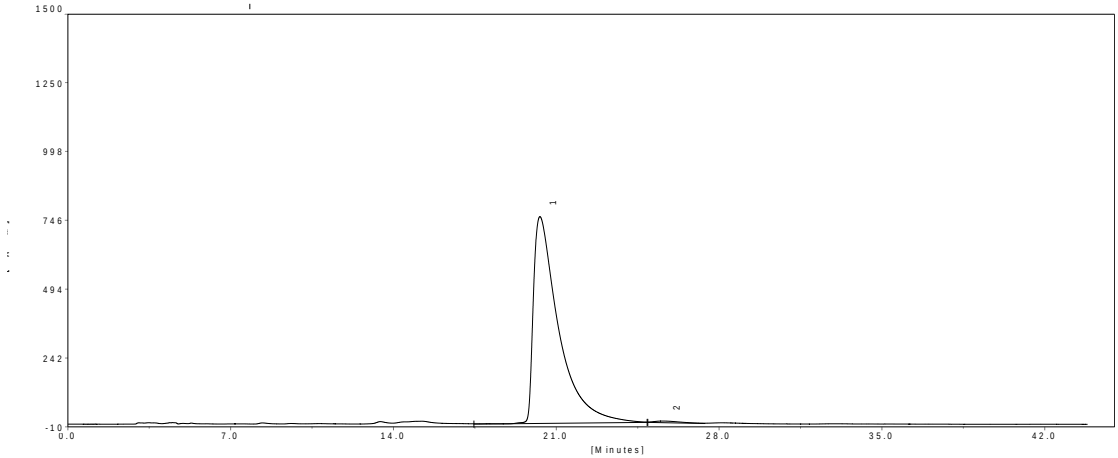
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	31.66500	740.24	93135.34	99.0011
2	43.35750	7.19	939.69	0.9989



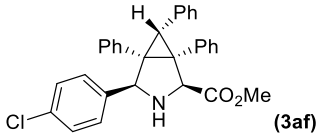
(3ae)



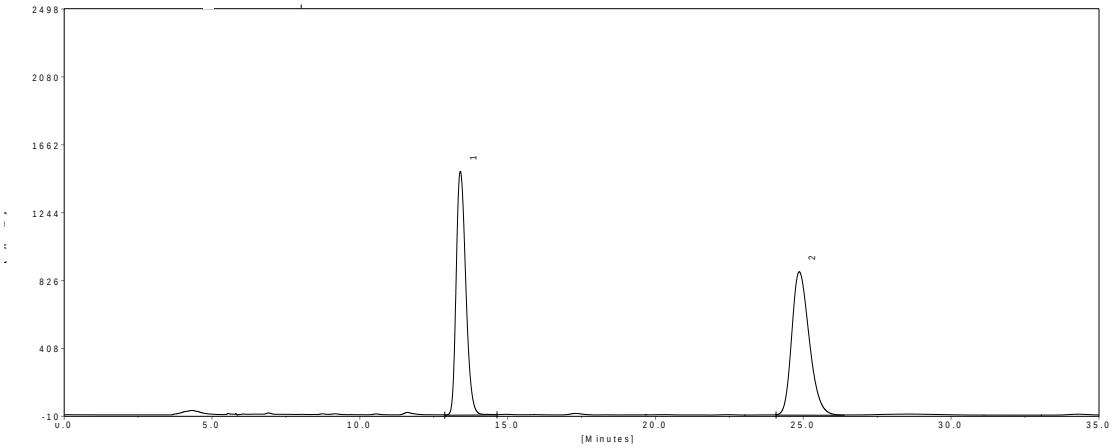
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	20.99083	599.19	50046.64	49.3264
2	25.86500	537.26	51413.44	50.6736



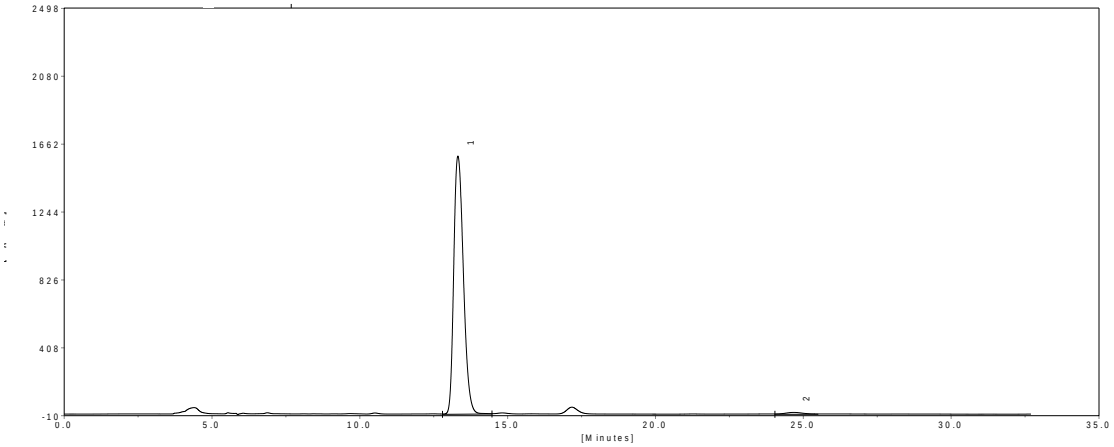
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	20.29667	755.91	56631.48	99.4359
2	25.62333	4.86	321.26	0.5641



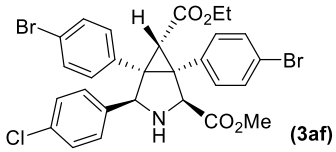
(3af)



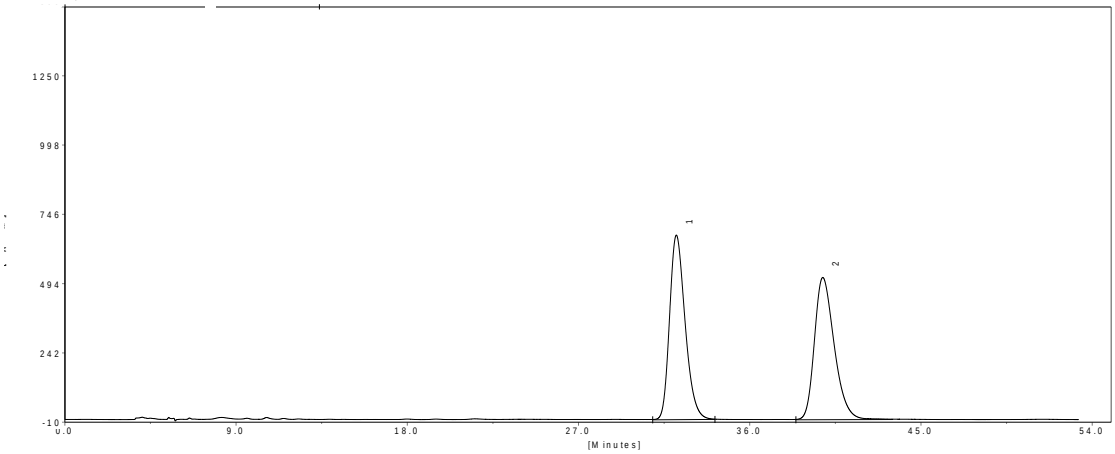
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	13.40000	1498.99	33700.98	48.3722
2	24.86333	881.45	35969.14	51.6278



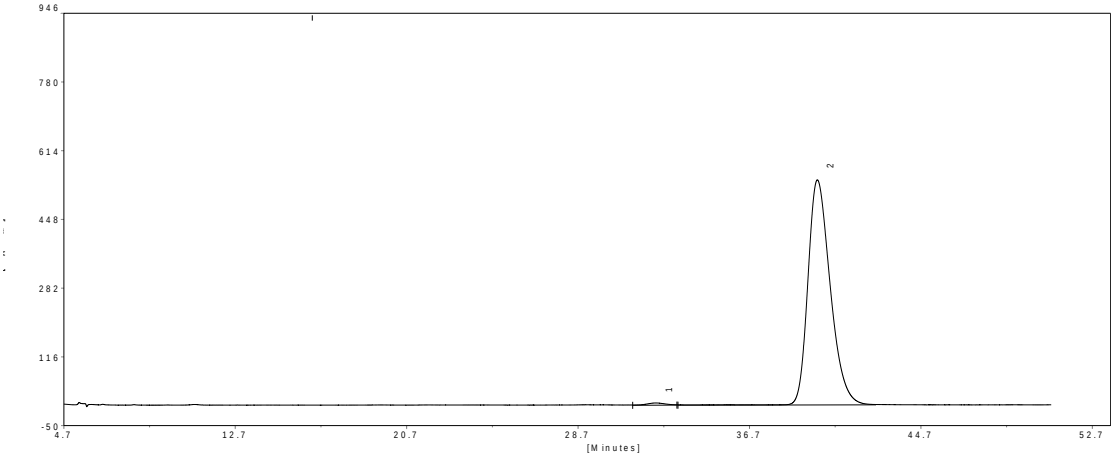
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	13.31833	1588.05	35931.64	99.0451
2	24.67083	9.50	346.40	0.9549



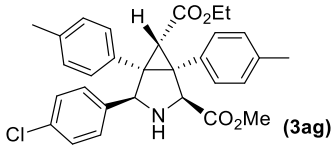
(3af)



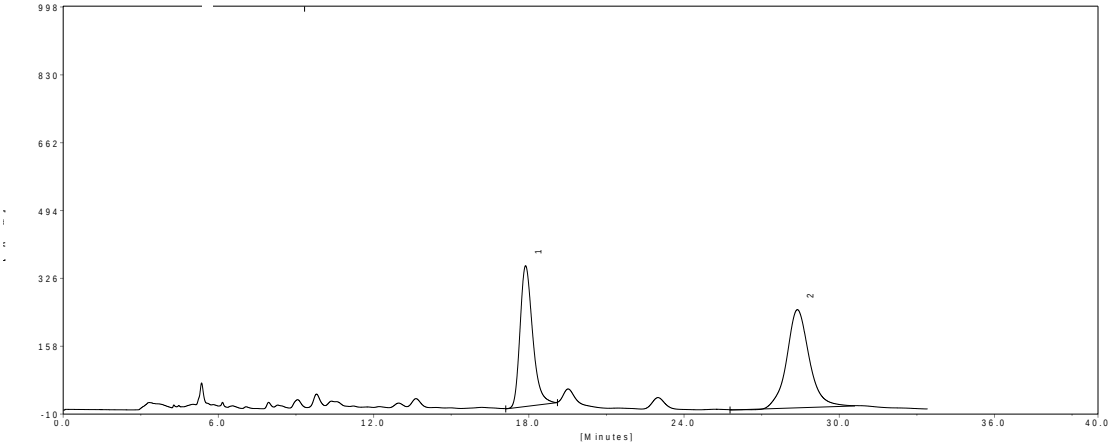
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	32.14083	670.11	37891.13	50.5765
2	39.84083	516.22	37027.25	49.4235



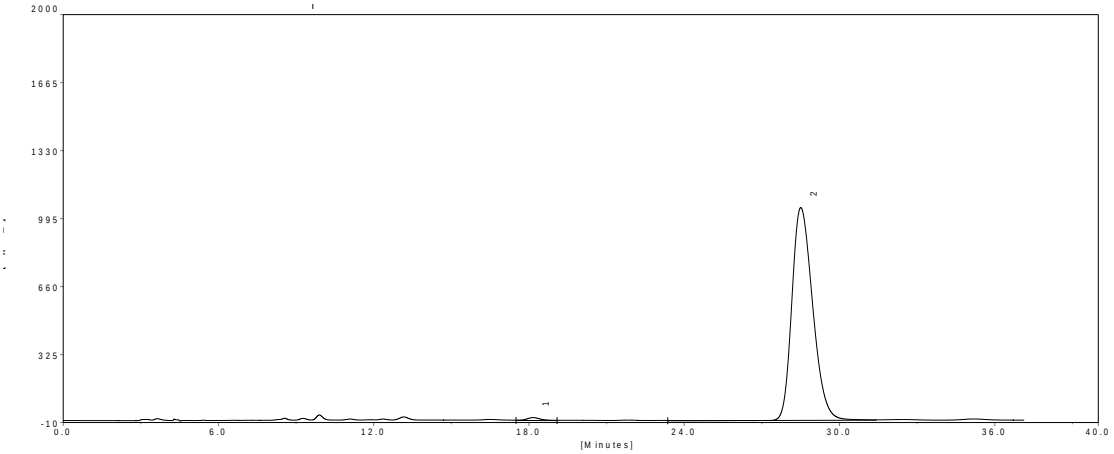
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	32.36917	4.64	239.02	0.6113
2	39.90250	542.85	38864.03	99.3887



(3ag)

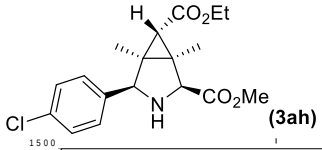


#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	17.87500	353.21	14437.09	50.0296
2	28.38250	242.33	14420.04	49.9704

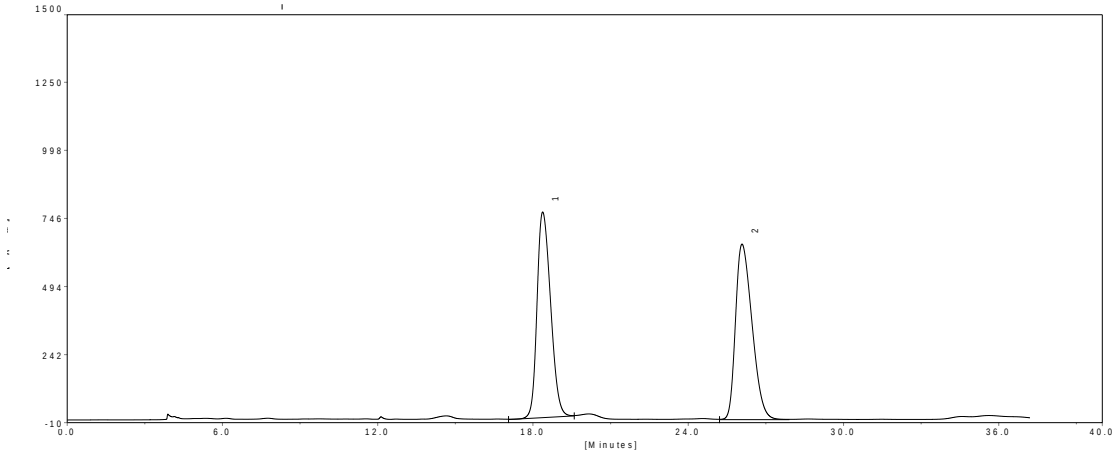


#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)

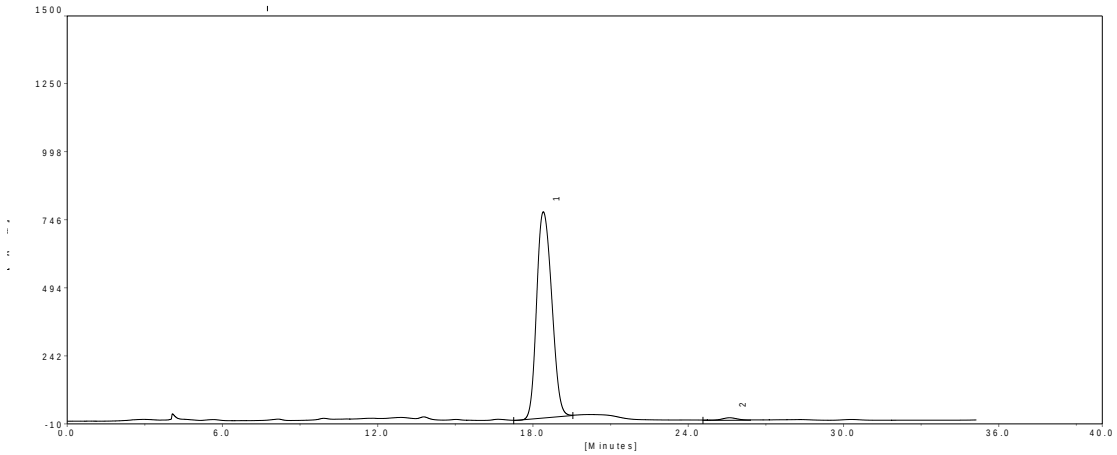
1	18.15167	12.78	409.41	0.7009
2	28.50333	1047.32	58000.12	99.2991



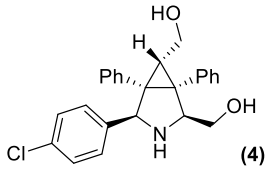
(3ah)



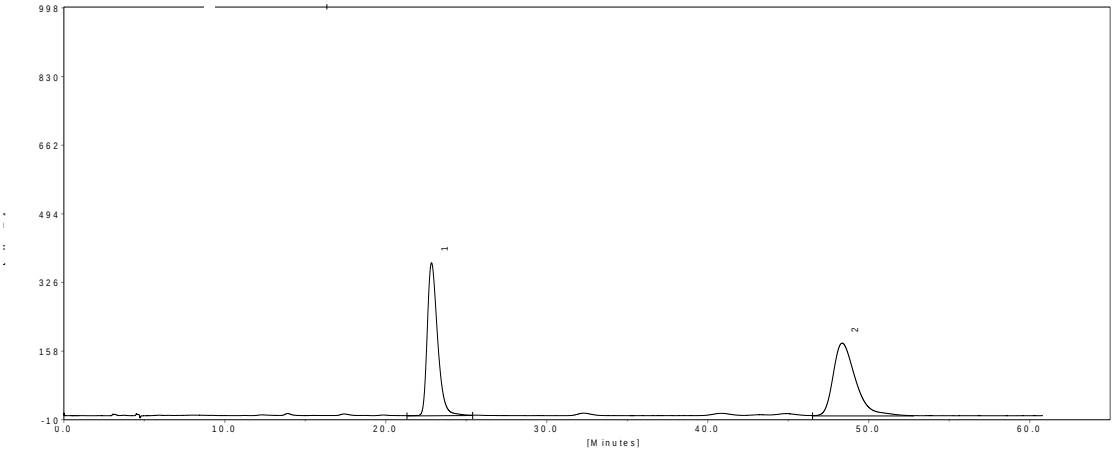
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	18.37500	765.81	29121.77	50.4353
2	26.07833	648.90	28619.08	49.5647



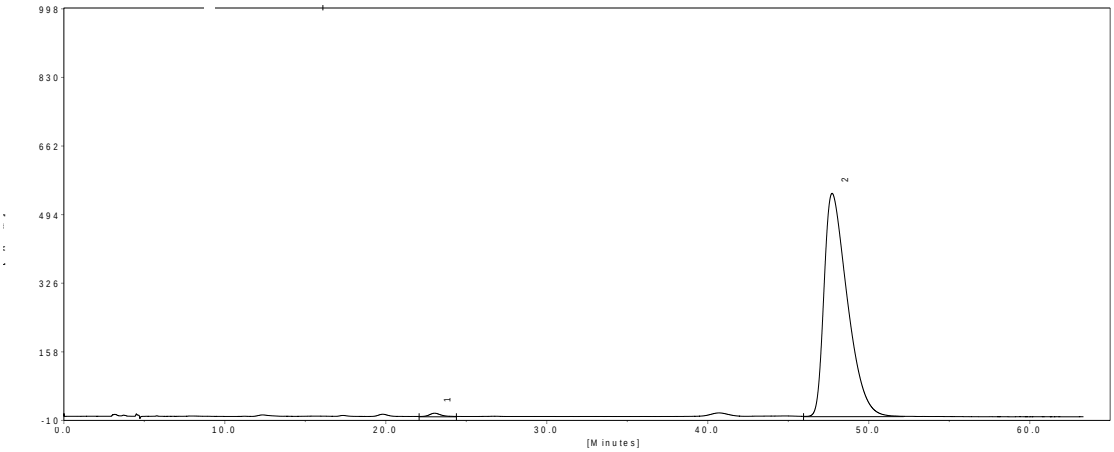
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	18.40083	762.35	30768.49	99.0649
2	25.60333	8.22	290.44	0.9351



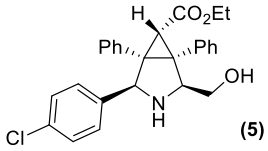
(4)



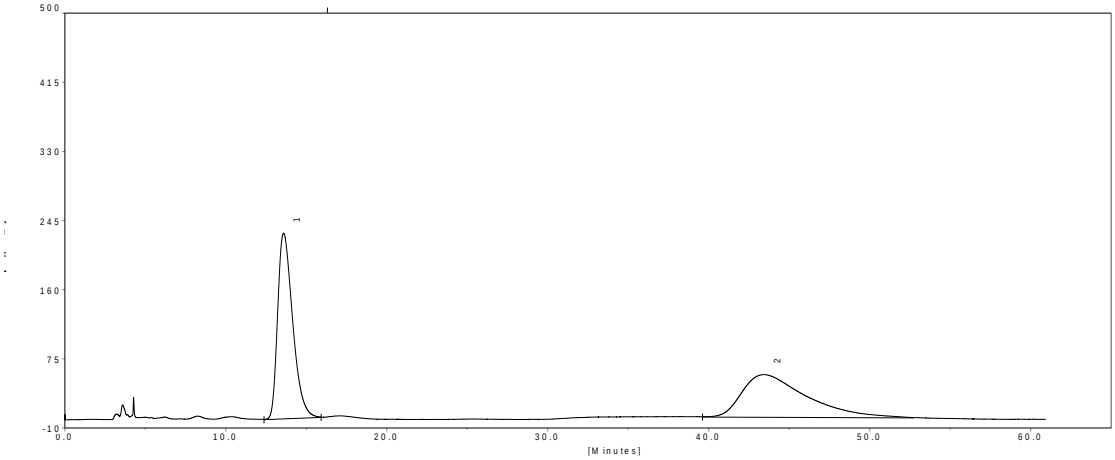
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	22.84000	373.79	16549.05	49.3101
2	48.34750	177.44	17012.13	50.6899



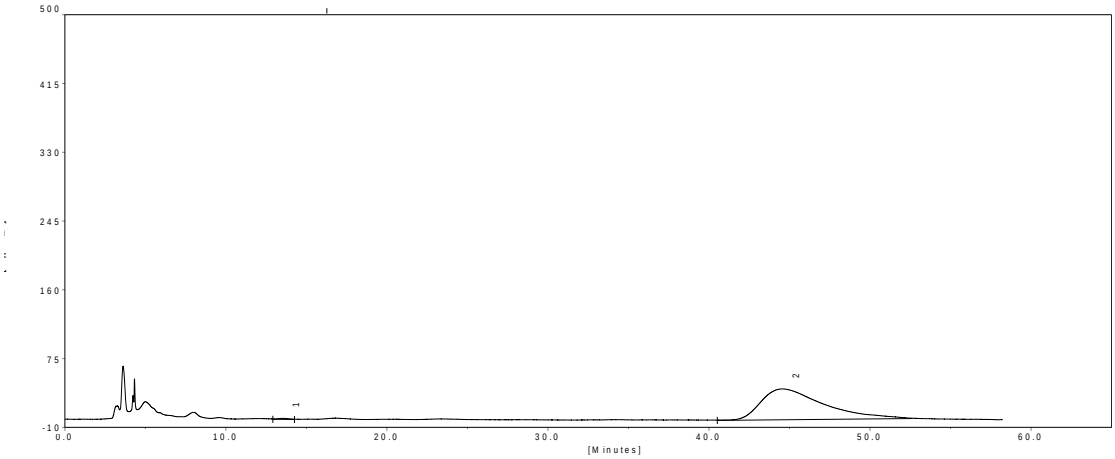
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	23.02667	7.96	366.66	0.6669
2	47.72333	546.22	54613.66	99.3331



(5)



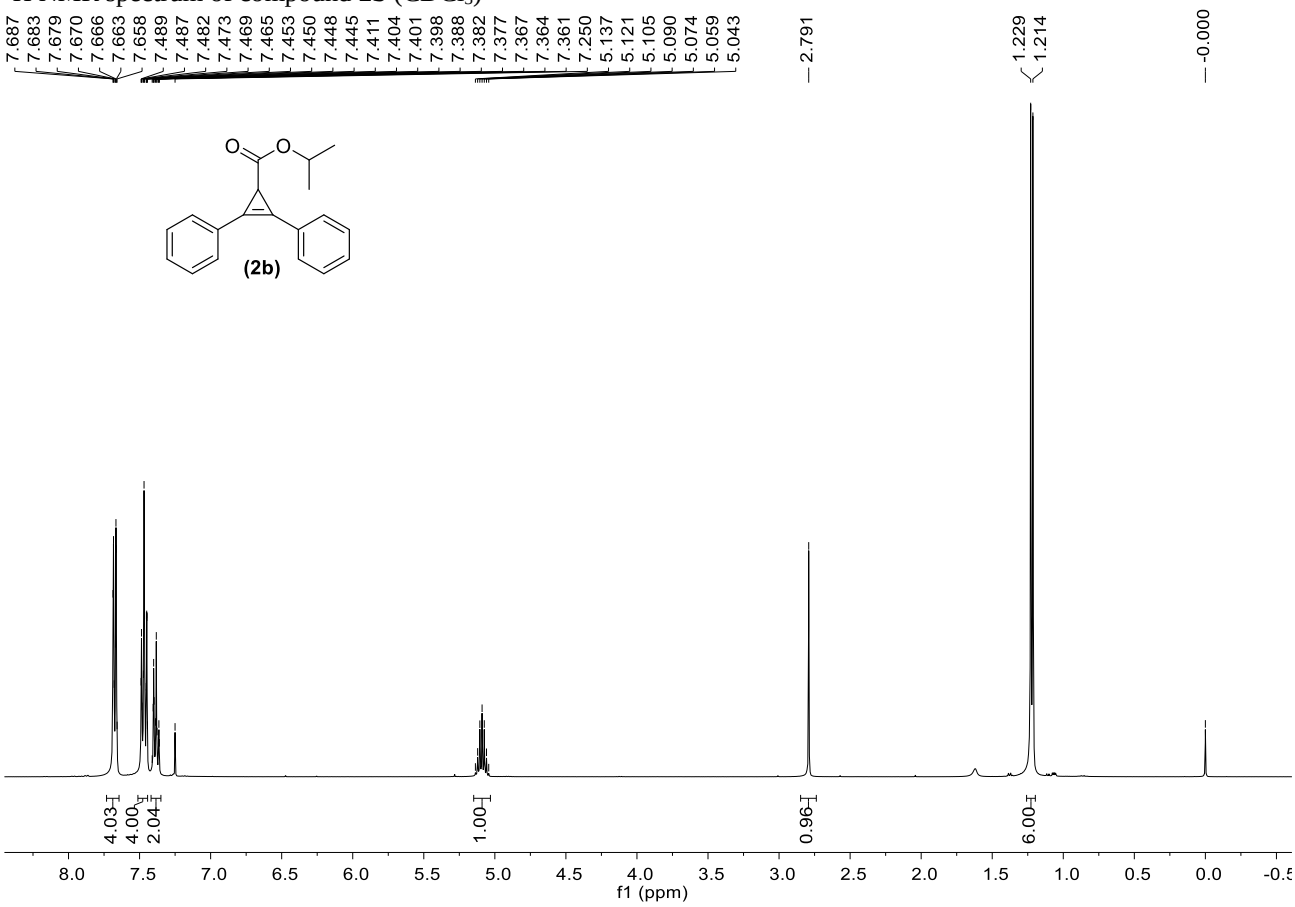
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	13.59250	227.94	14715.20	50.6912
2	43.44250	52.06	14313.90	49.3088



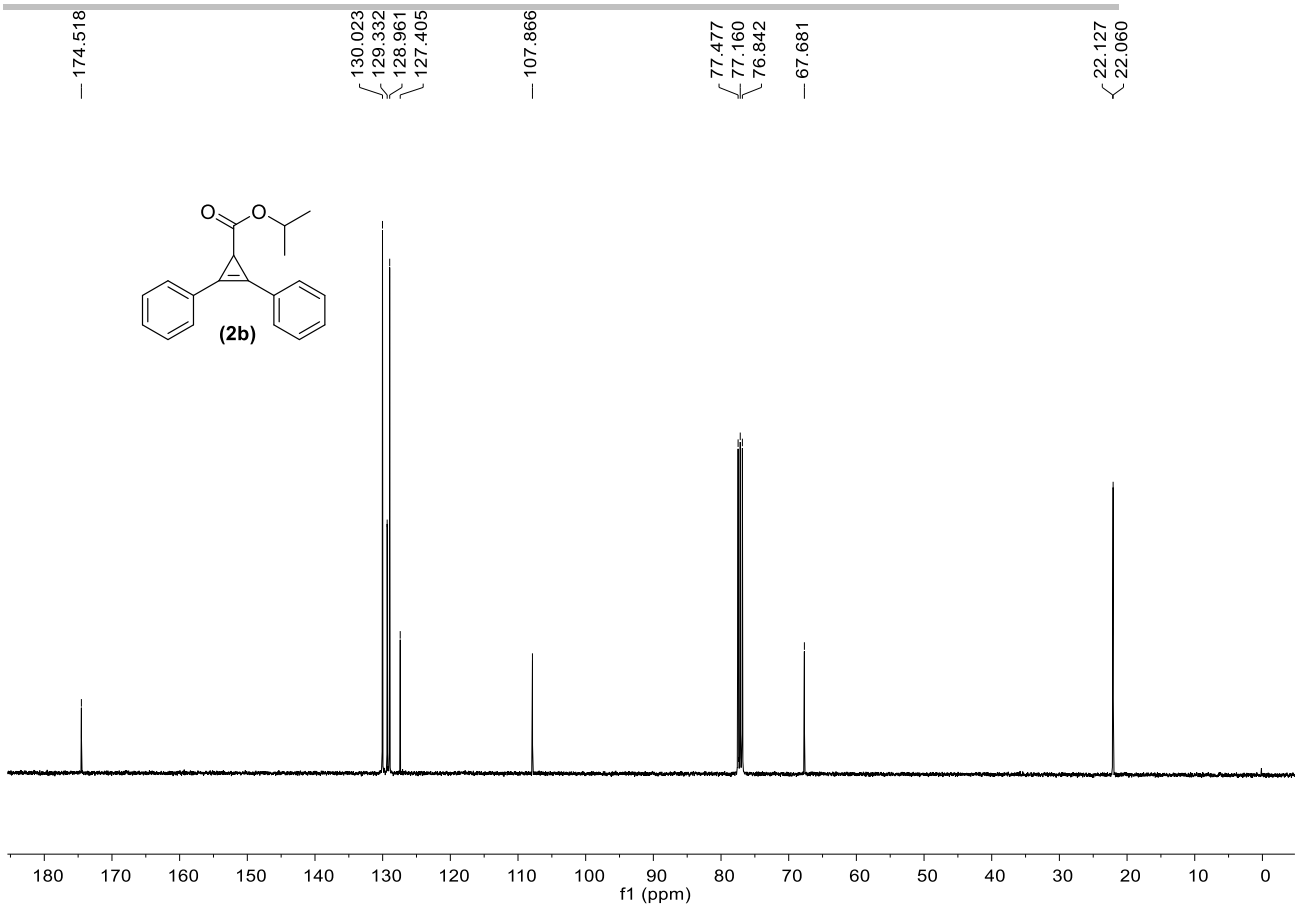
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	13.54250	0.88	34.91	0.3466
2	44.60500	37.76	10037.35	99.6534

^{1}H NMR and ^{13}C NMR spectra

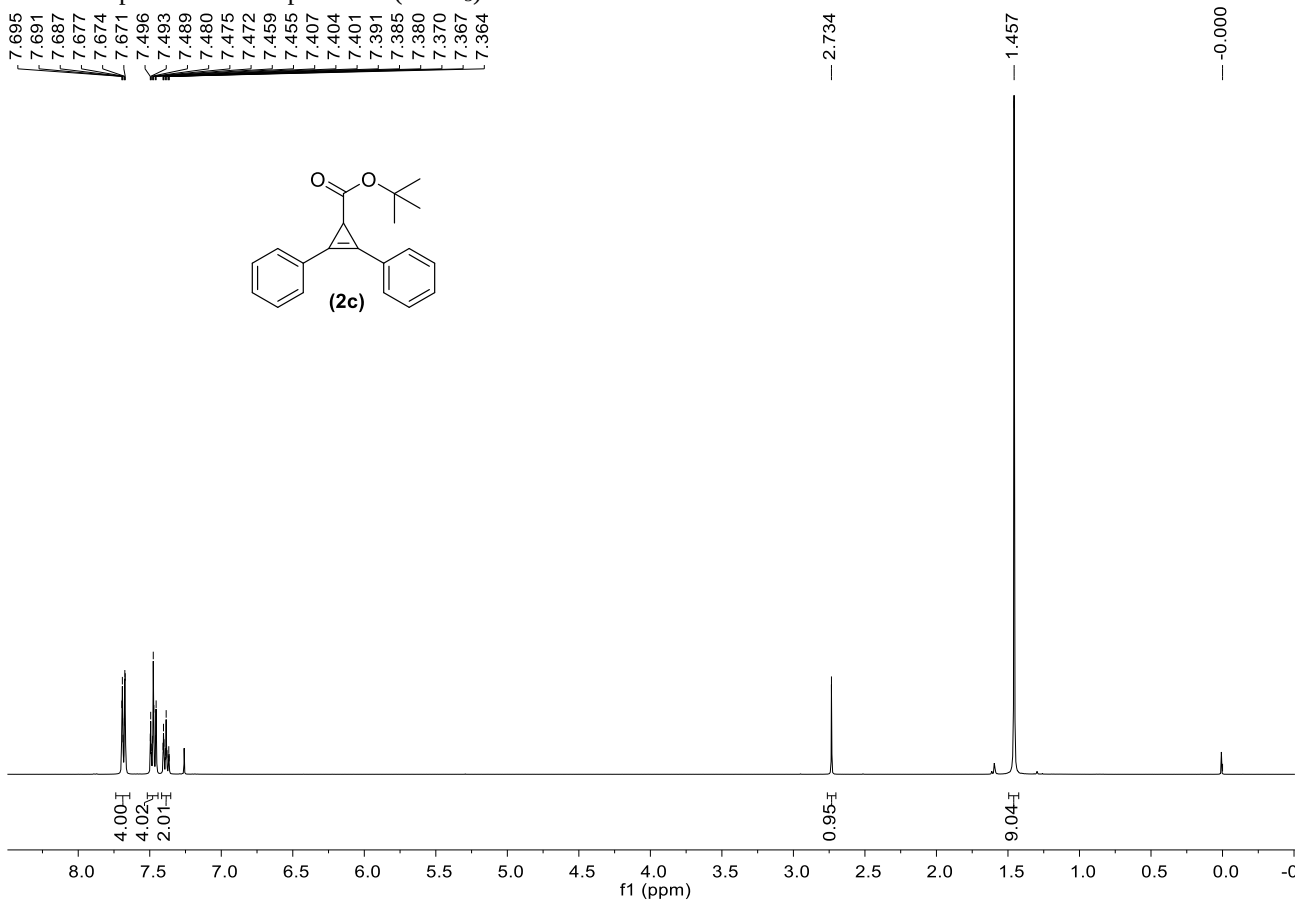
^{1}H NMR spectrum of compound **2b** ($CDCl_3$)



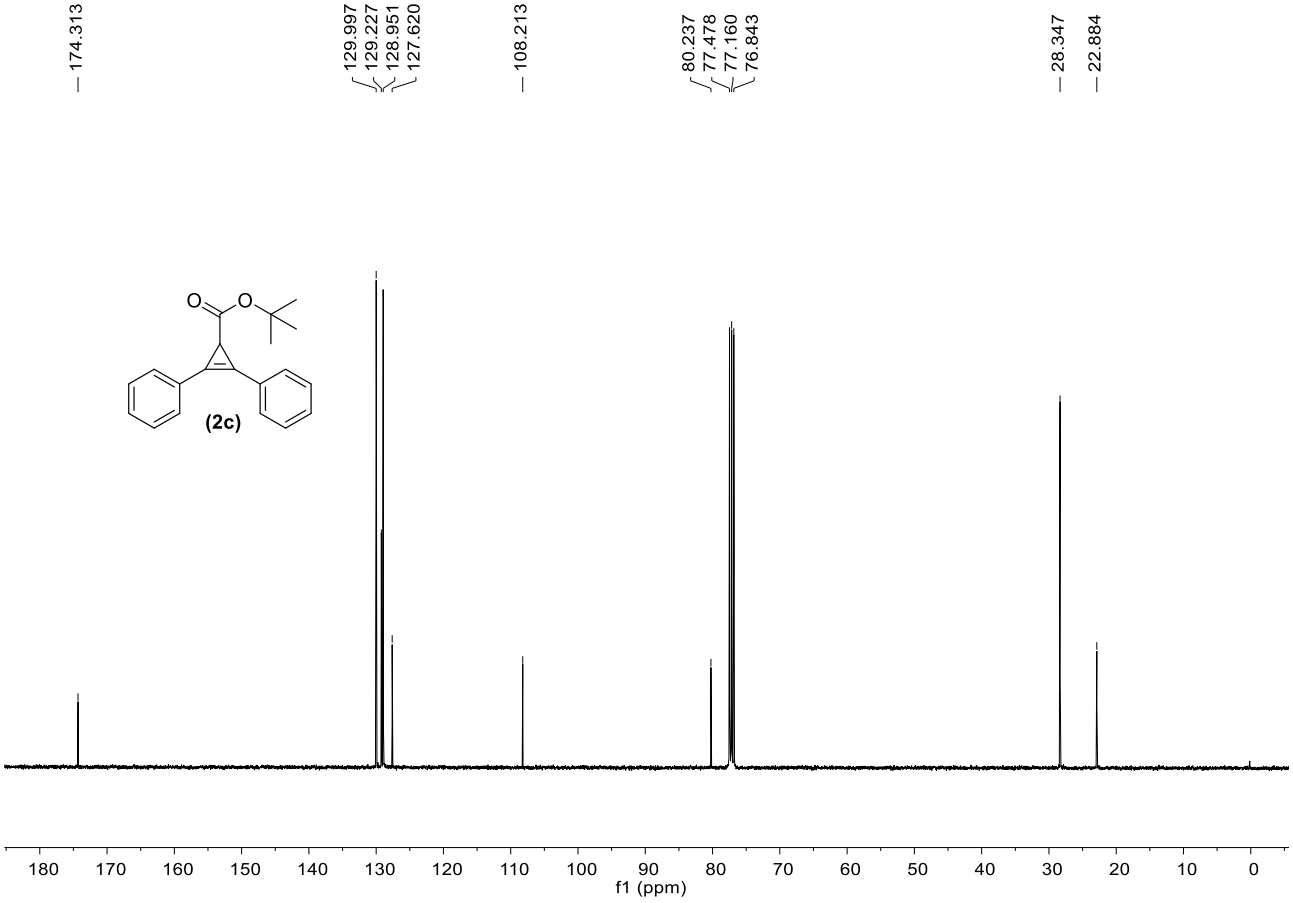
^{13}C NMR spectrum of compound **2b** ($CDCl_3$)



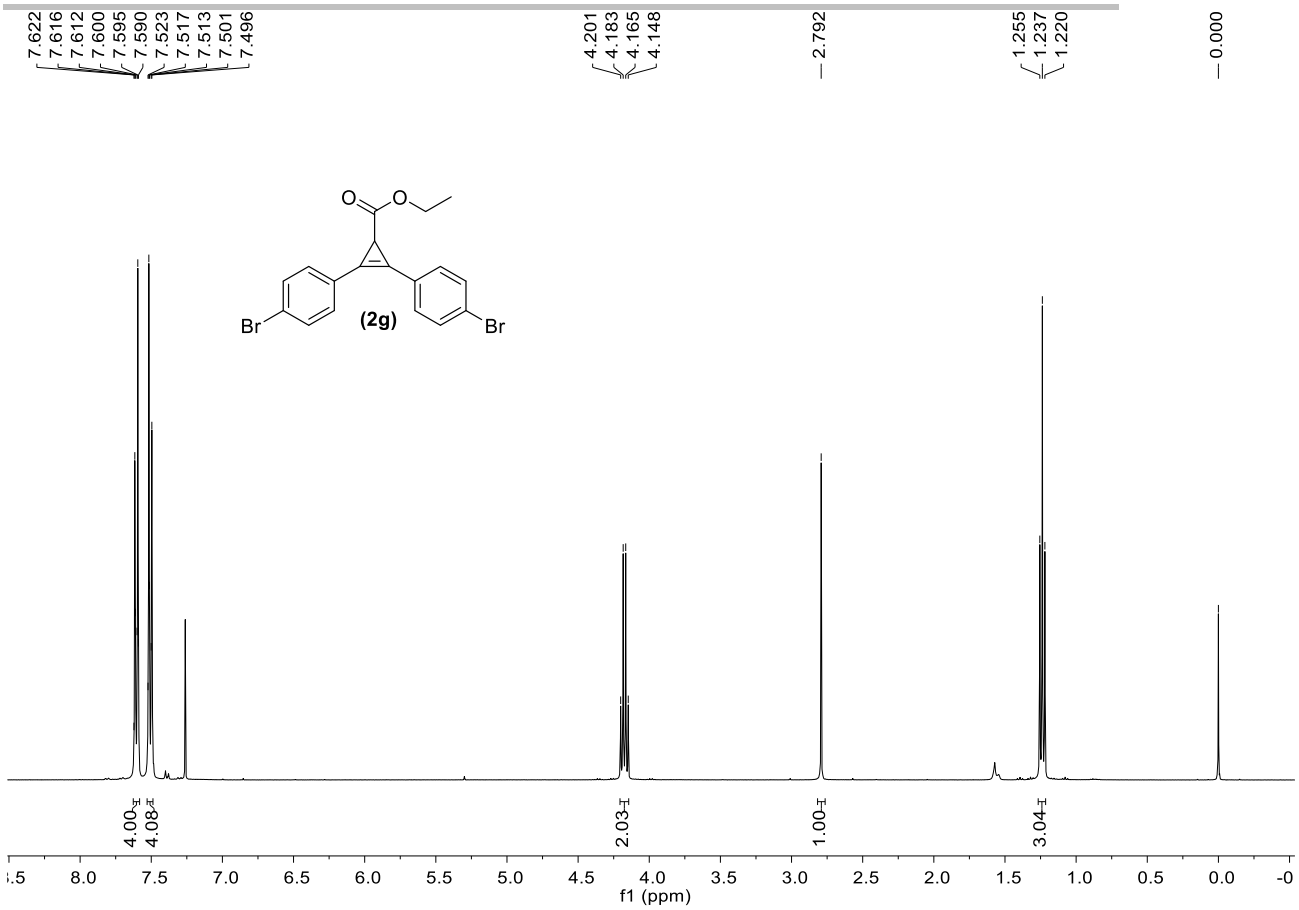
^{1}H NMR spectrum of compound **2c** ($CDCl_3$)



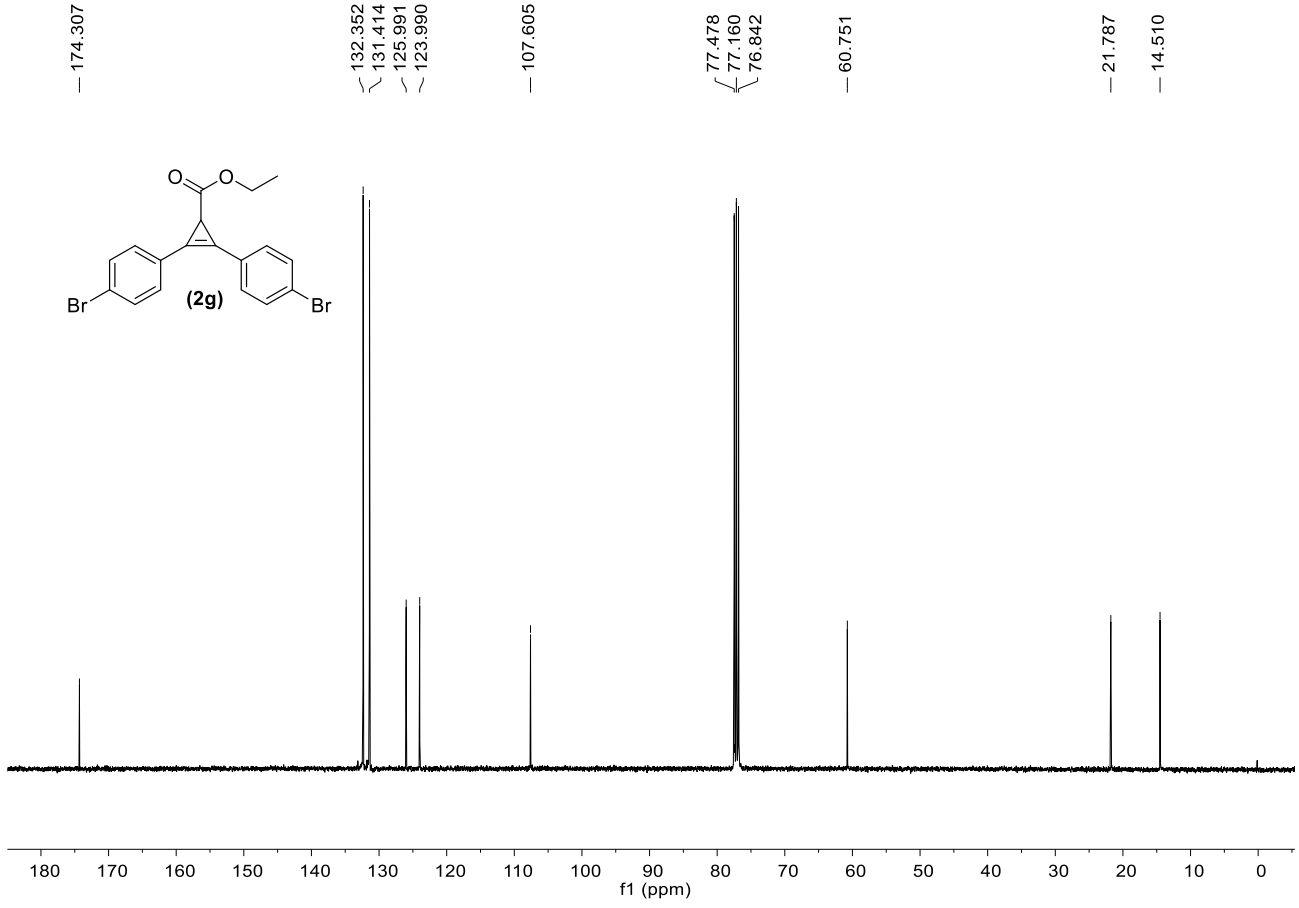
^{13}C NMR spectrum of compound **2c** ($CDCl_3$)



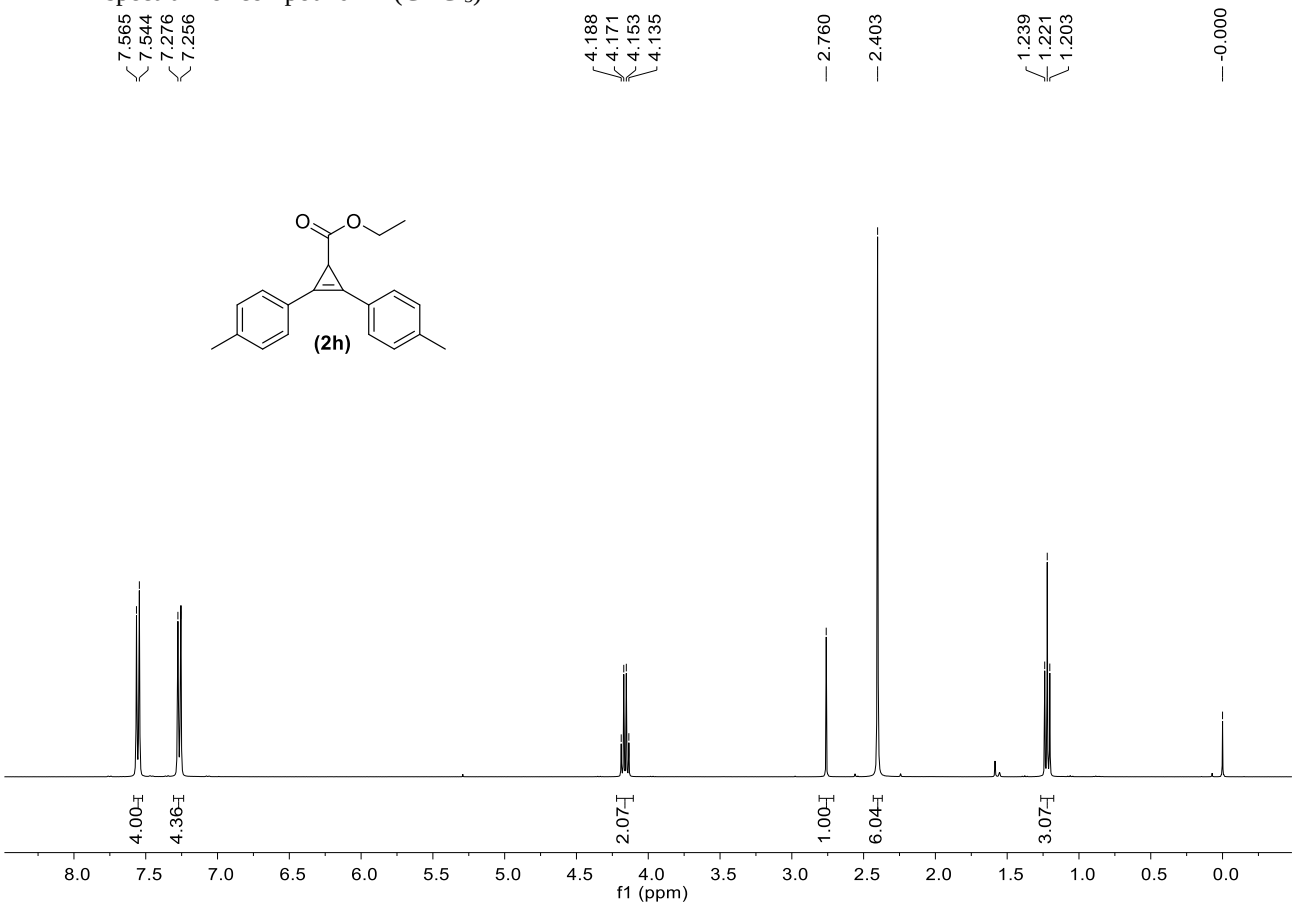
^{1}H NMR spectrum of compound **2g** ($CDCl_3$)



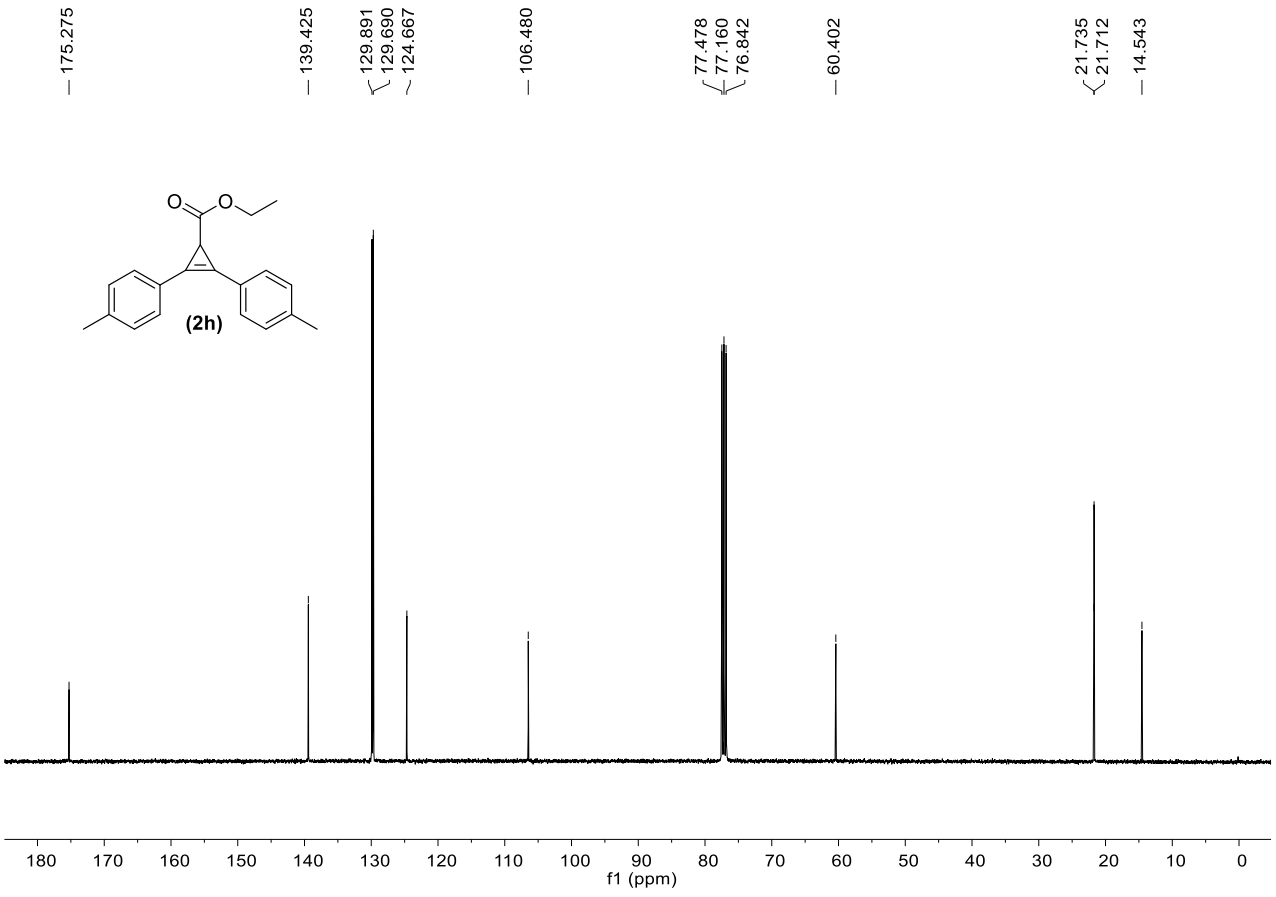
^{13}C NMR spectrum of compound **2g** ($CDCl_3$)



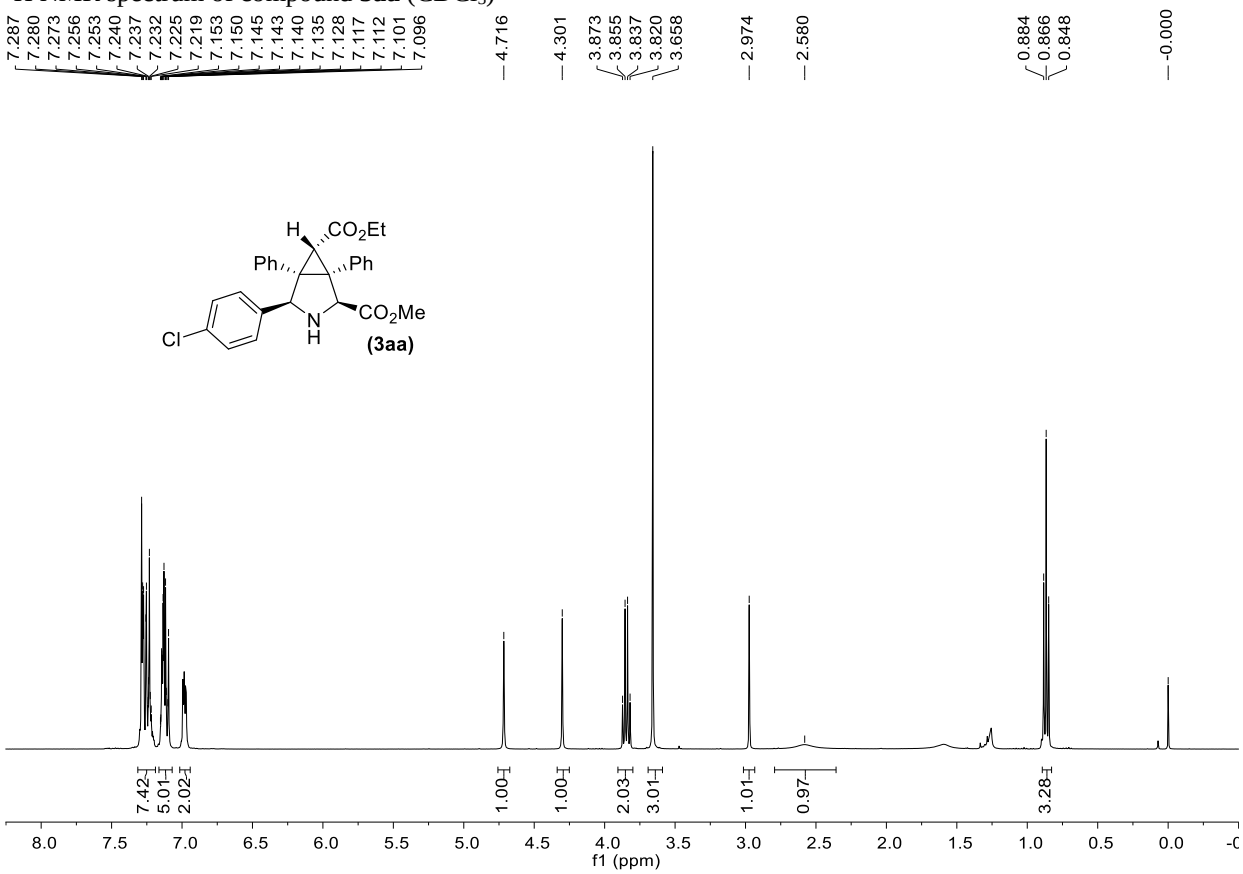
^{1}H NMR spectrum of compound **2h** ($CDCl_3$)



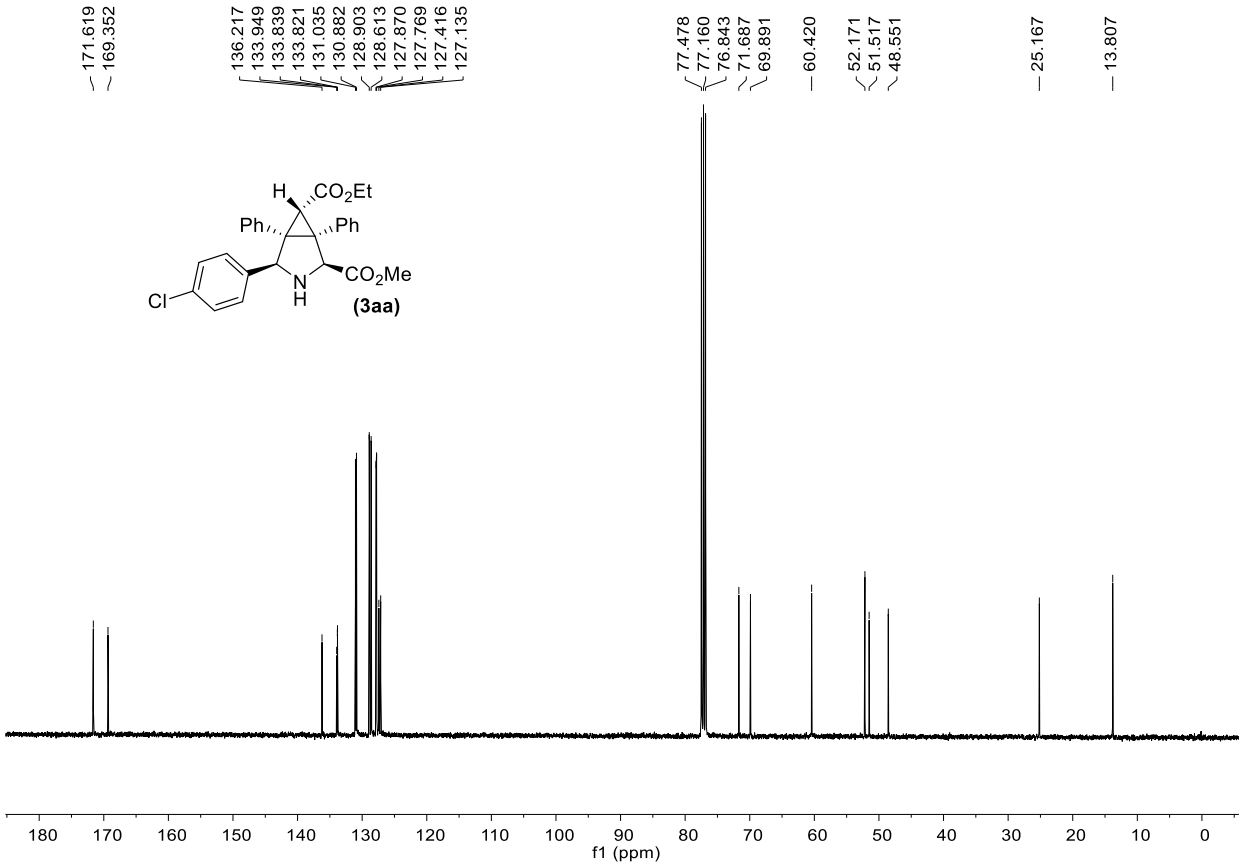
^{13}C NMR spectrum of compound **2h** ($CDCl_3$)



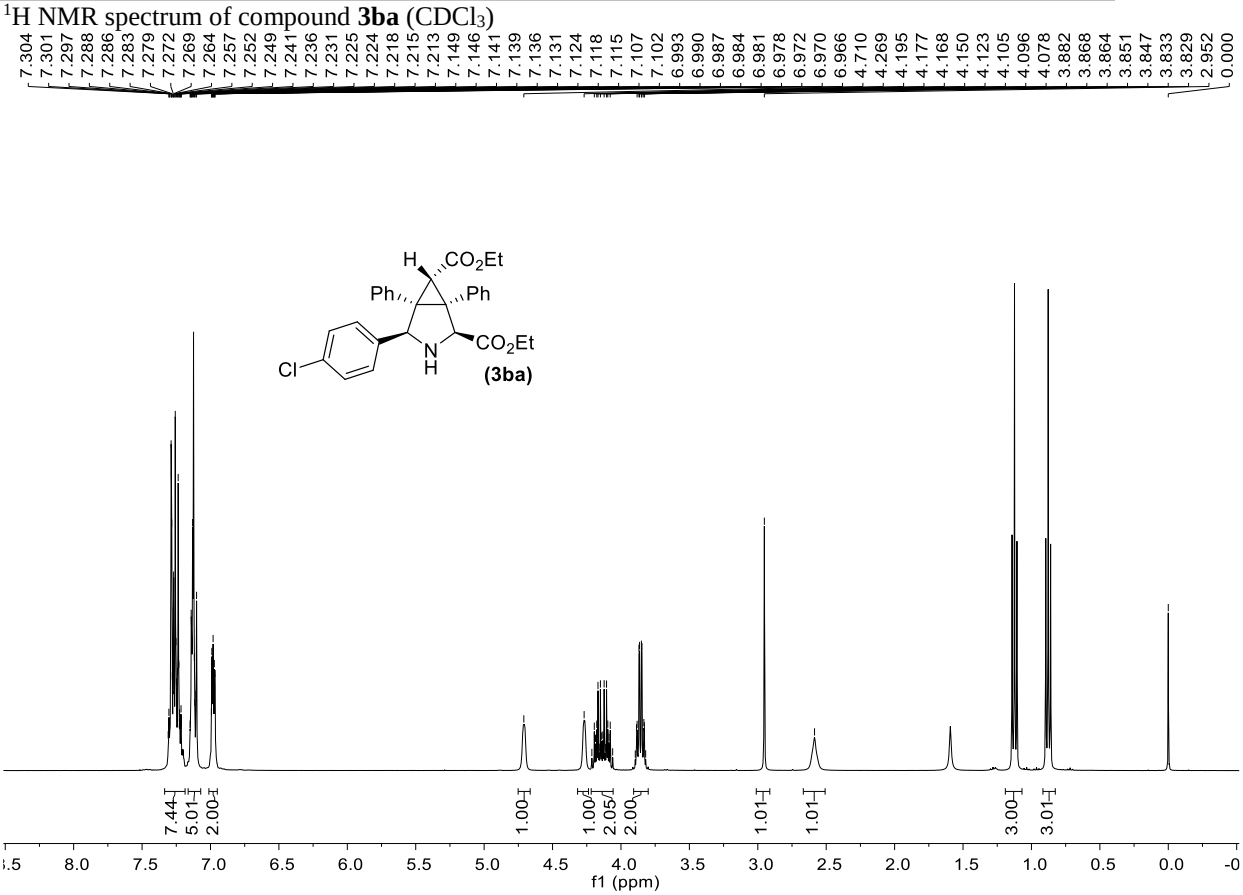
^{1}H NMR spectrum of compound **3aa** ($CDCl_3$)



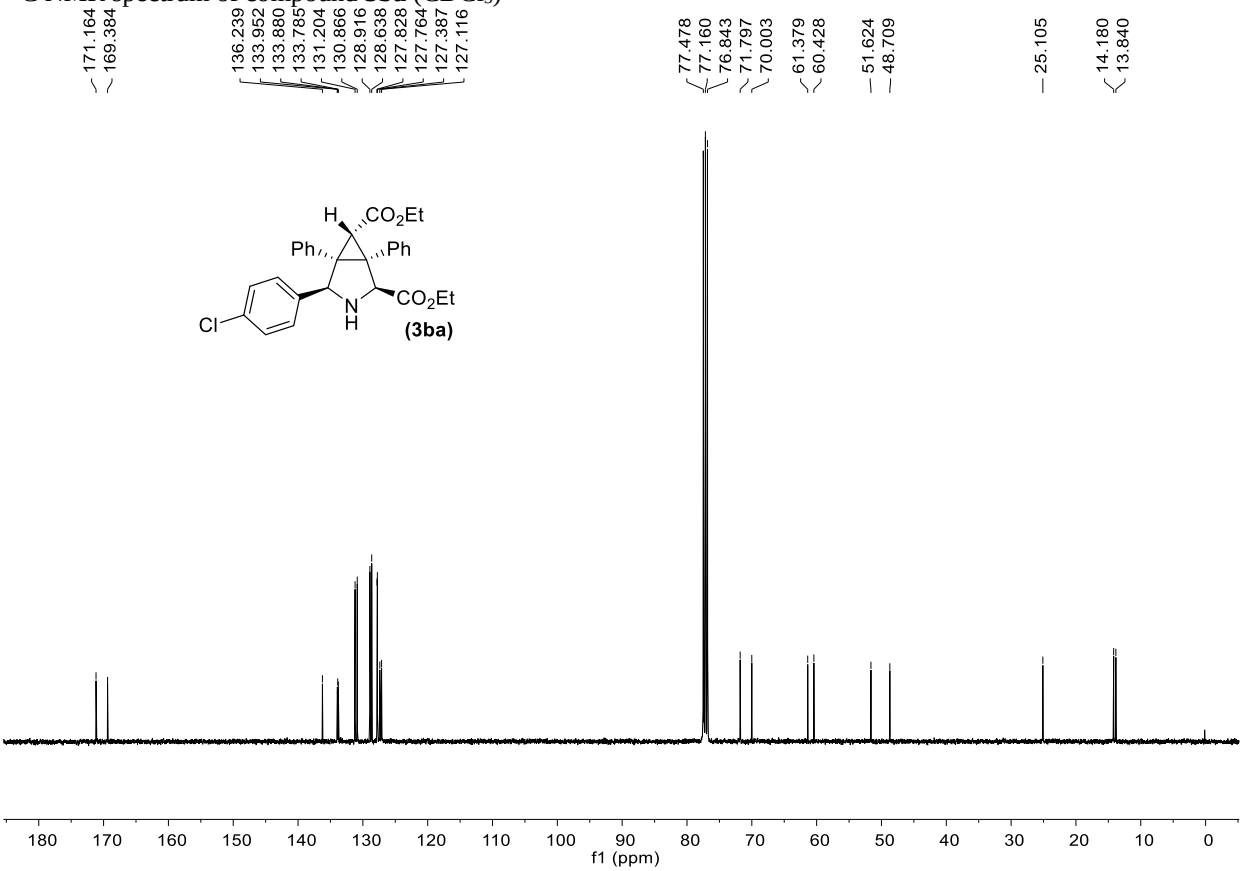
^{13}C NMR spectrum of compound **3aa** ($CDCl_3$)



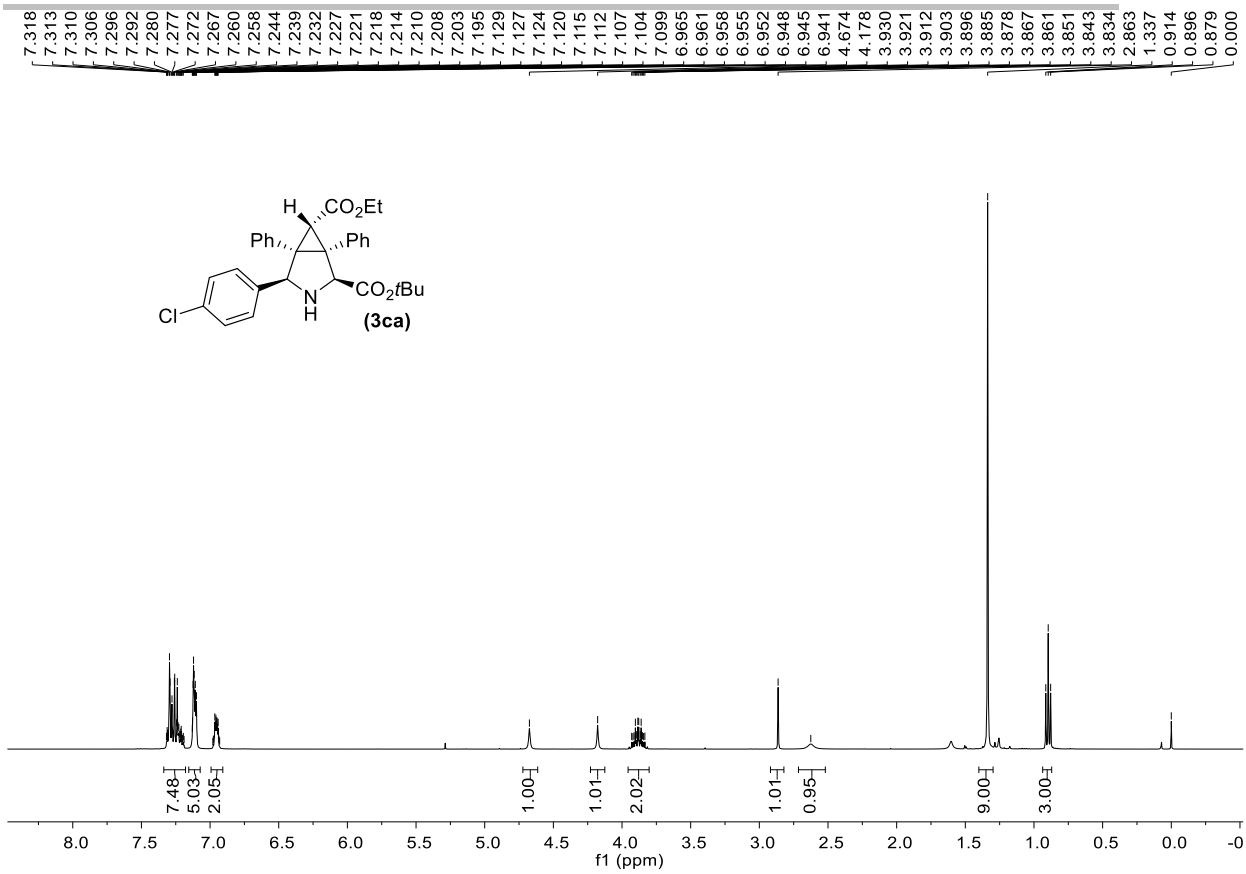
^{1}H NMR spectrum of compound **3ba** ($CDCl_3$)



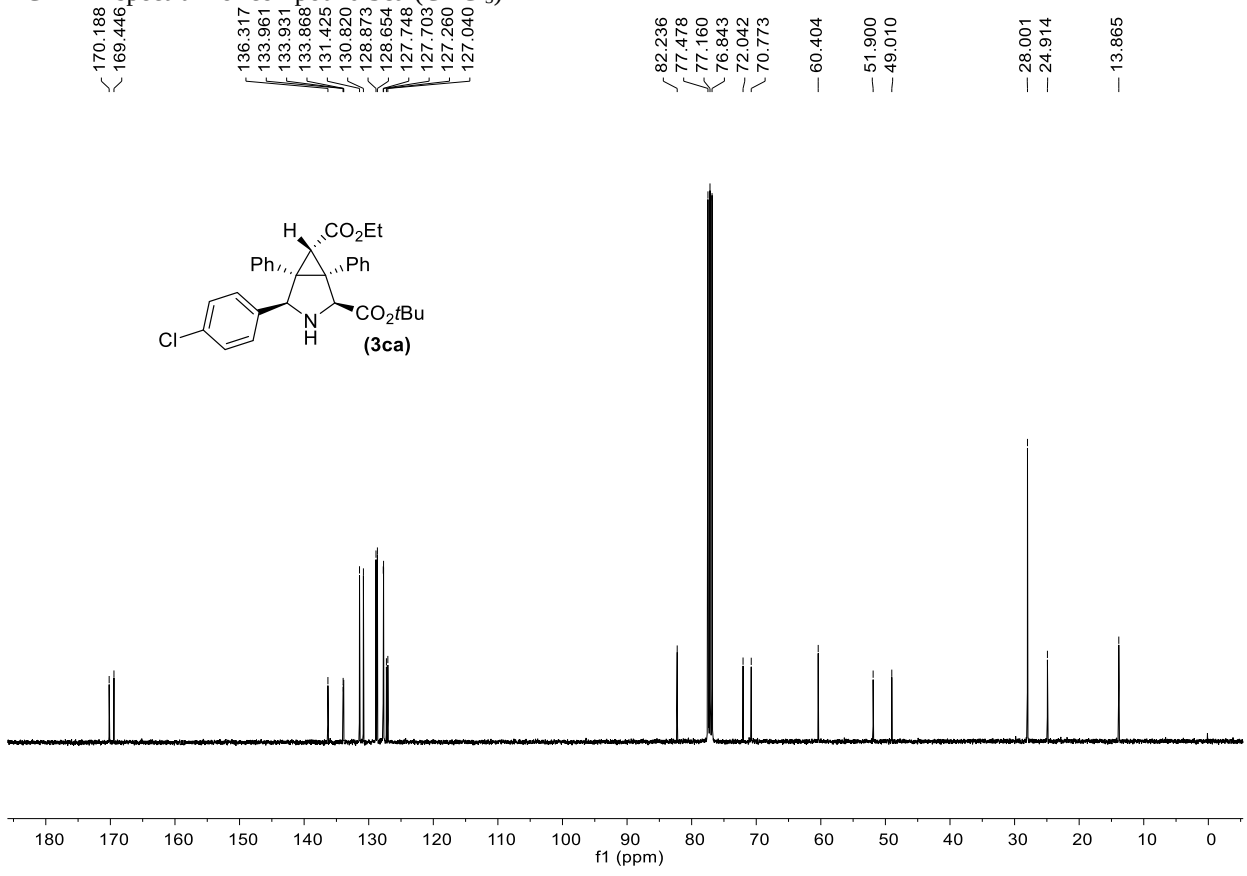
^{13}C NMR spectrum of compound **3ba** ($CDCl_3$)



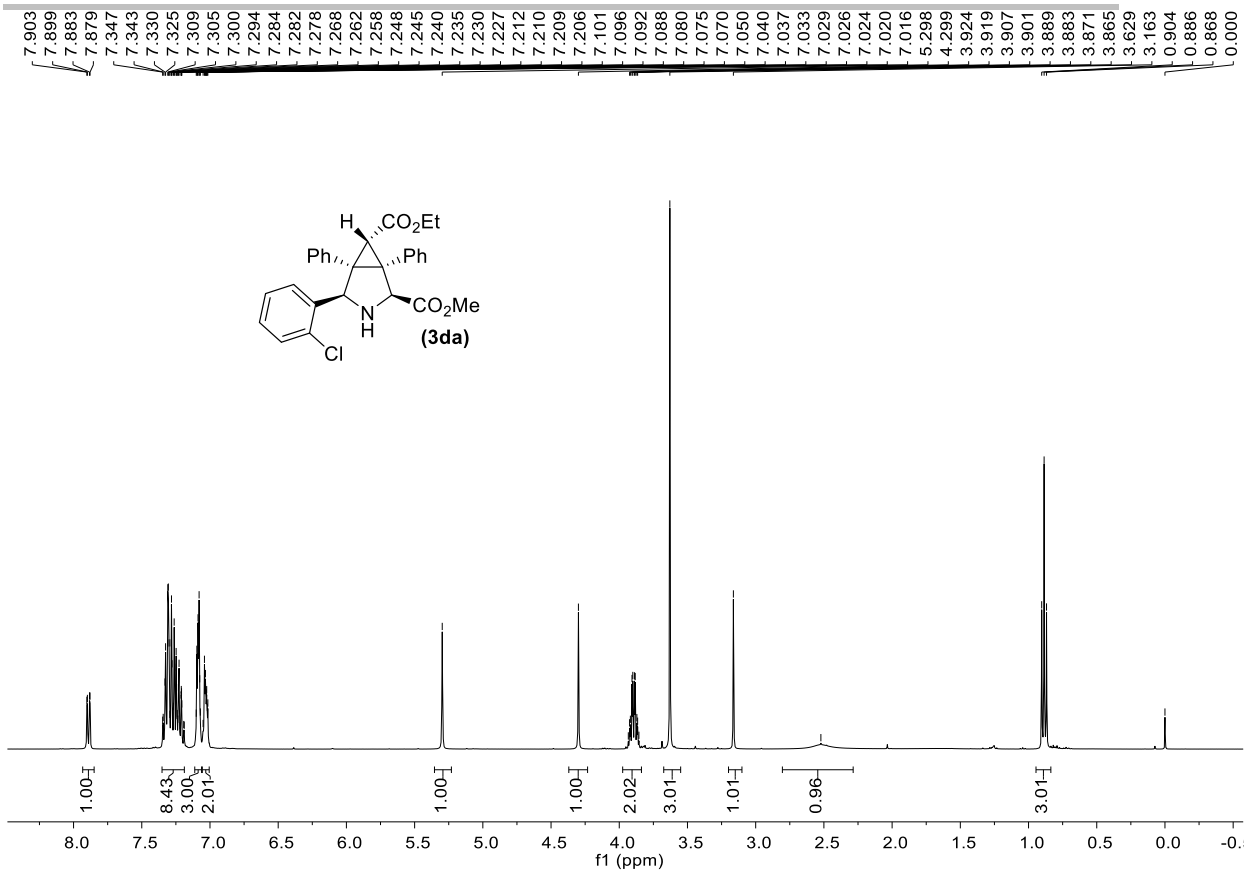
^{1}H NMR spectrum of compound **3ca** ($CDCl_3$)



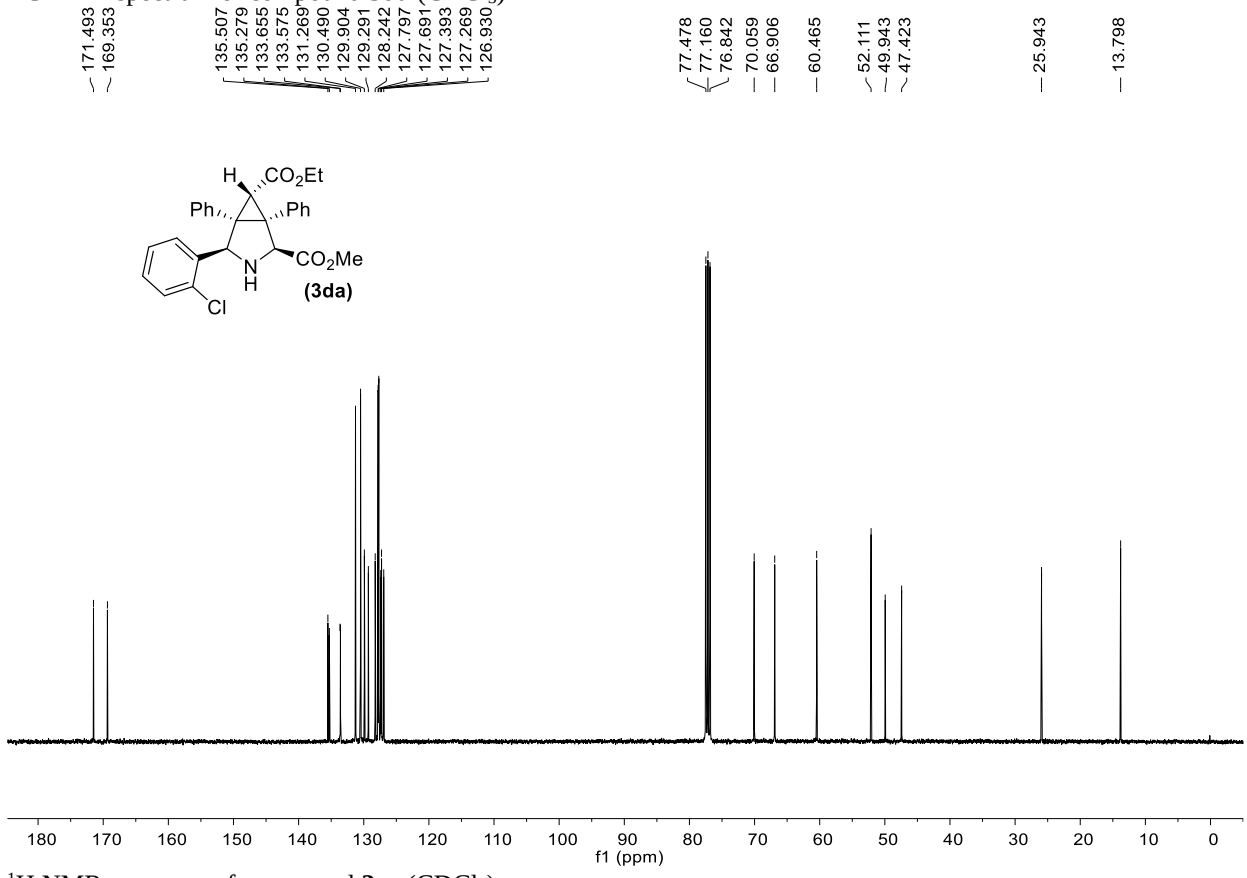
^{13}C NMR spectrum of compound **3ca** ($CDCl_3$)



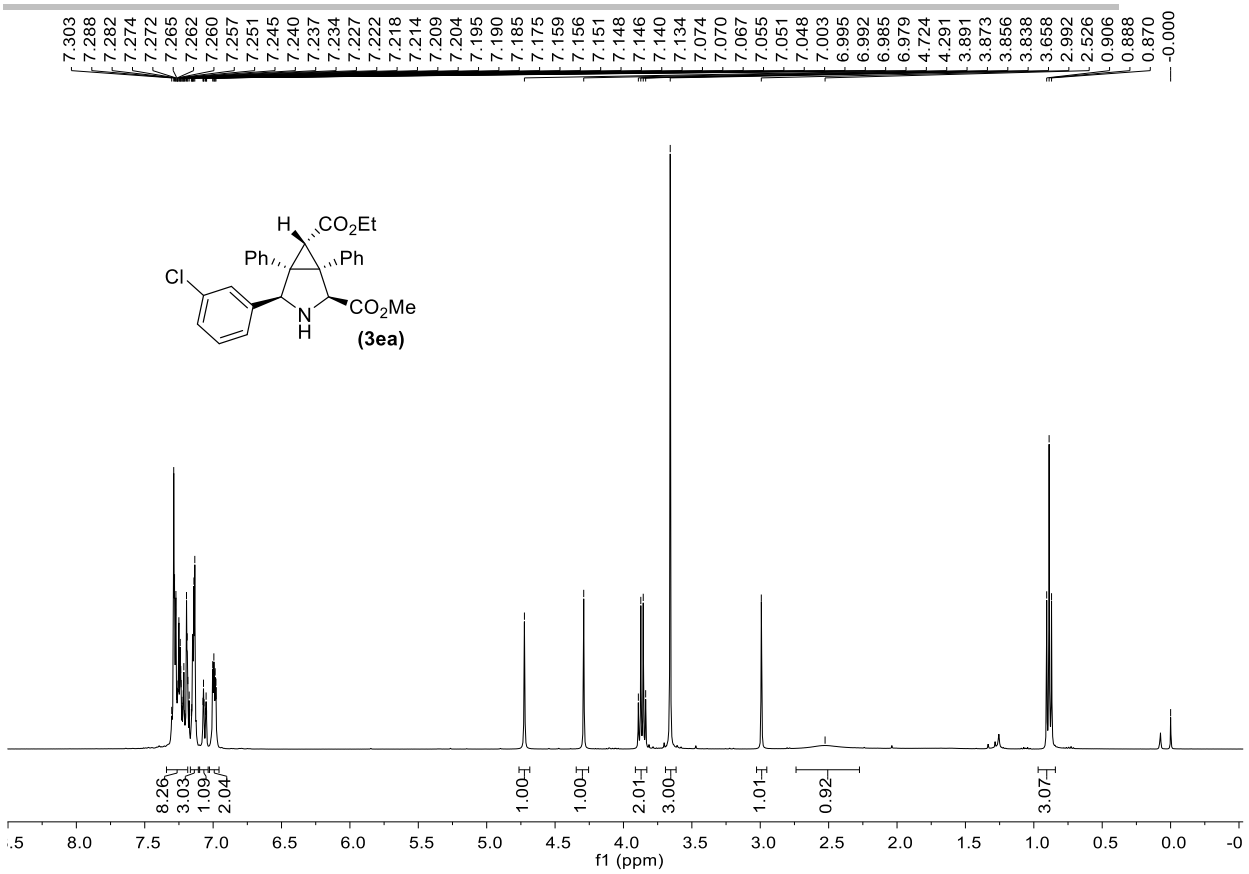
^{1}H NMR spectrum of compound **3da** ($CDCl_3$)



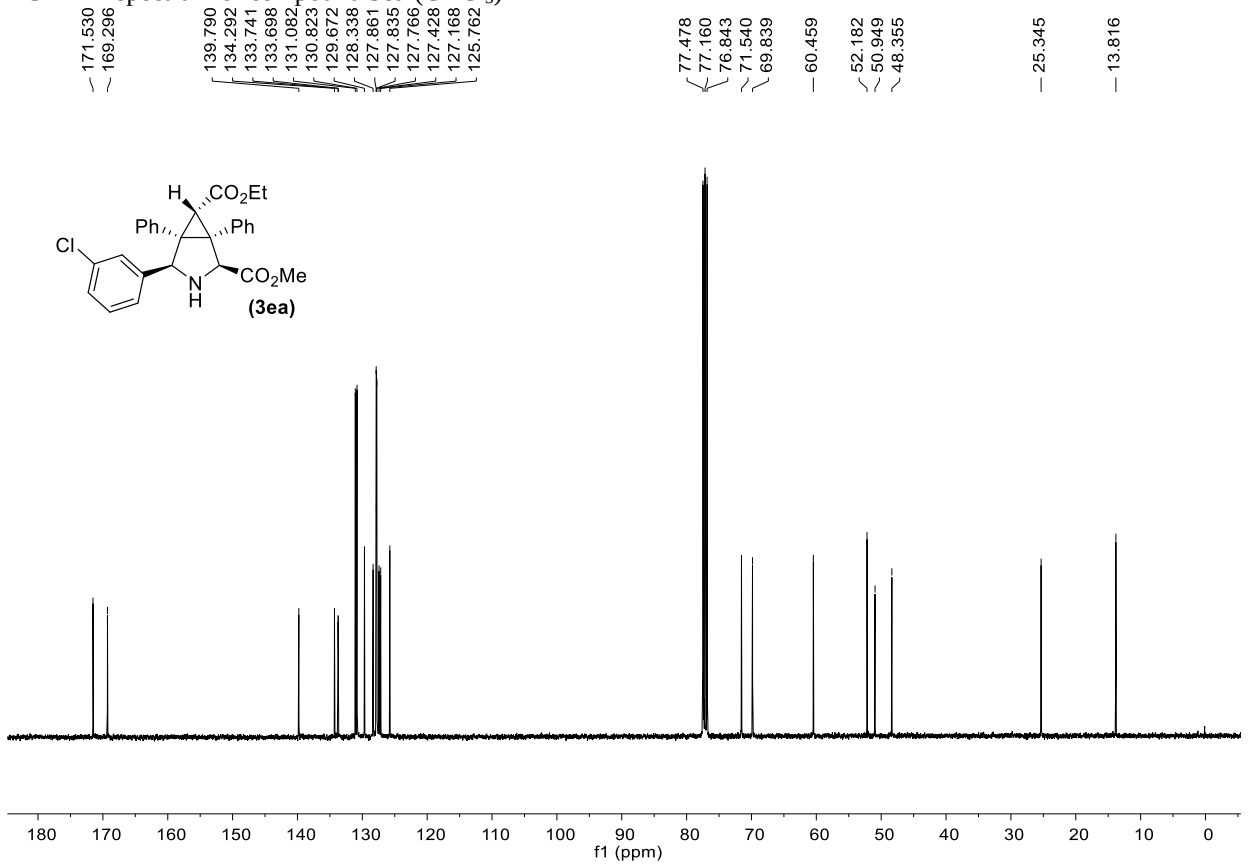
^{13}C NMR spectrum of compound **3da** ($CDCl_3$)



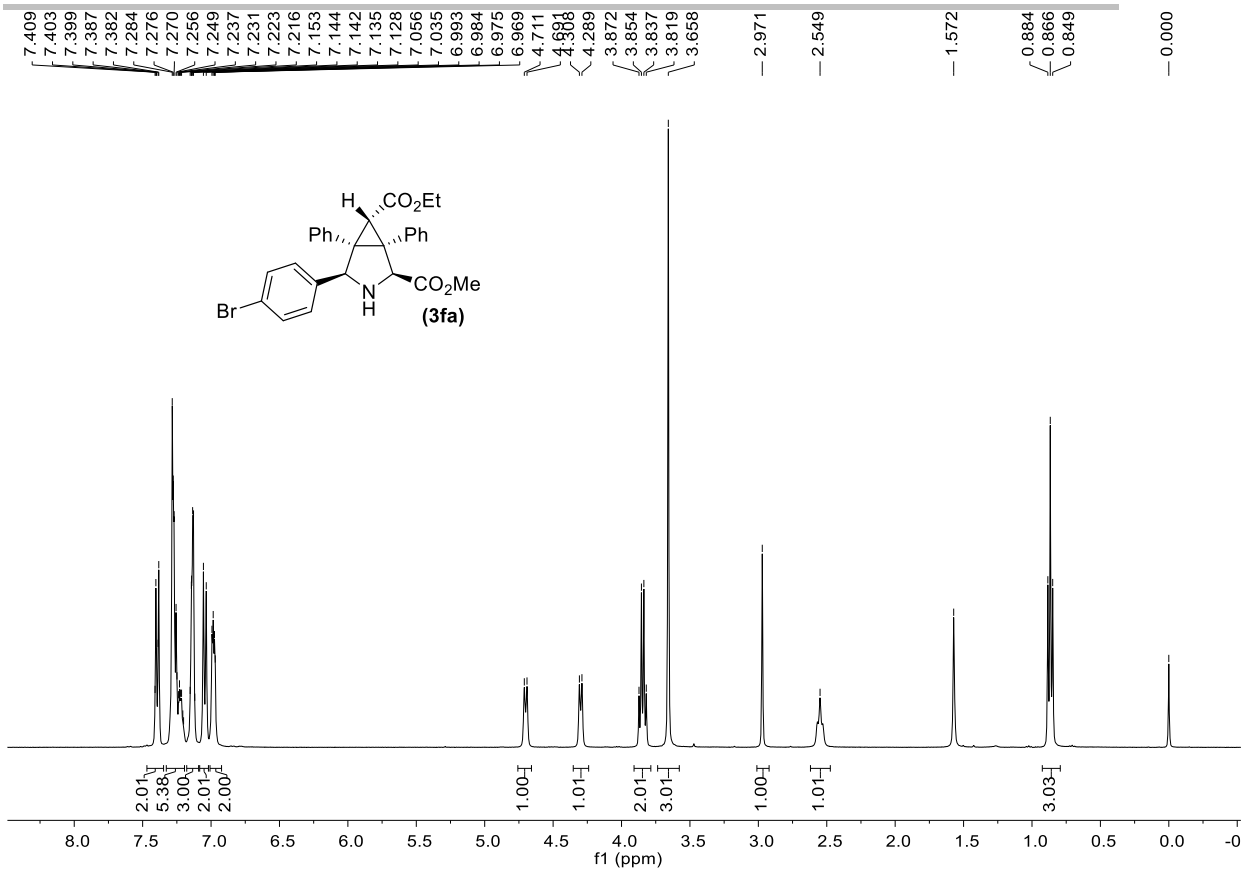
^{1}H NMR spectrum of compound **3ea** ($CDCl_3$)



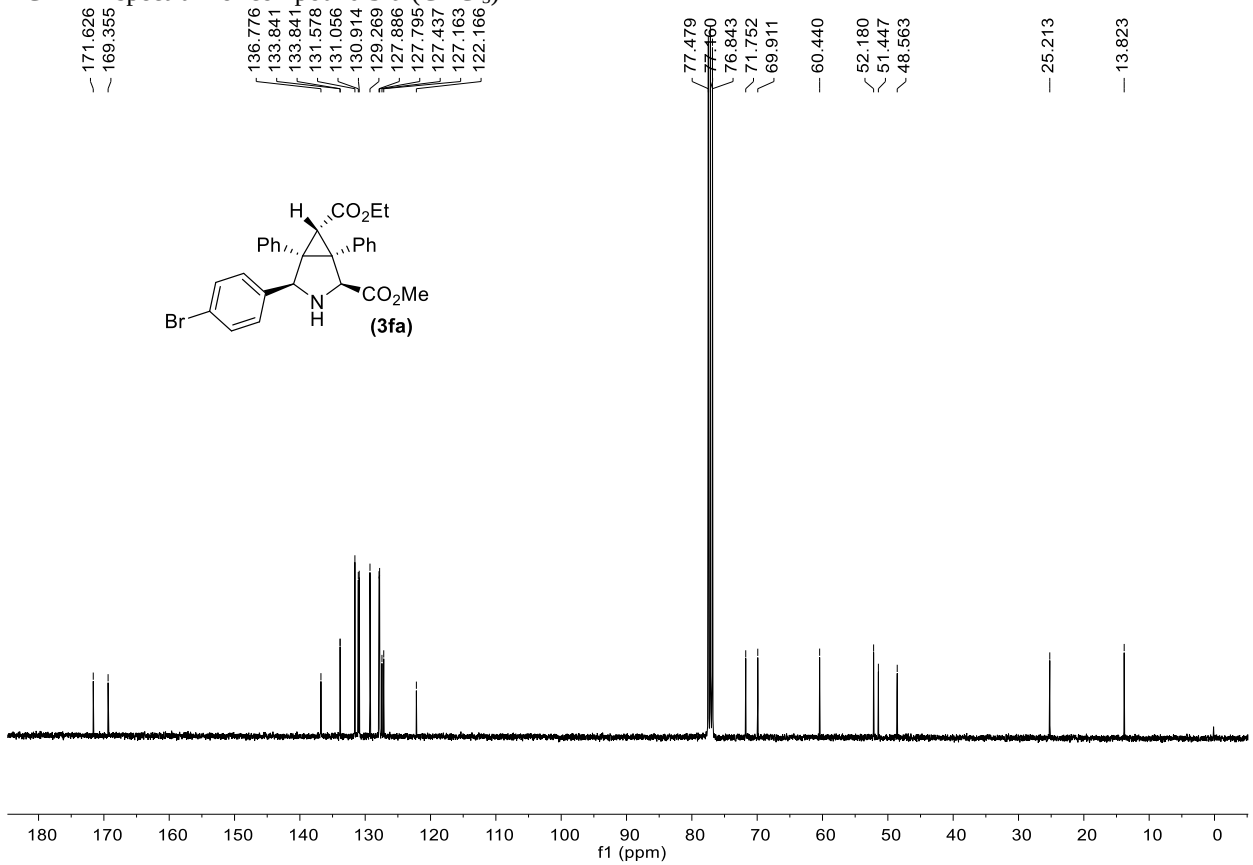
^{13}C NMR spectrum of compound **3ea** ($CDCl_3$)



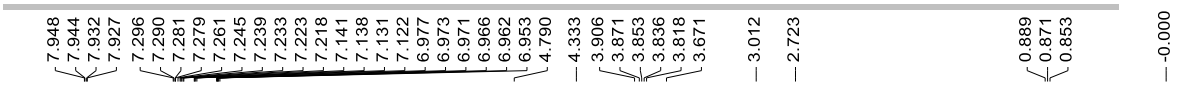
^{1}H NMR spectrum of compound **3fa** ($CDCl_3$)

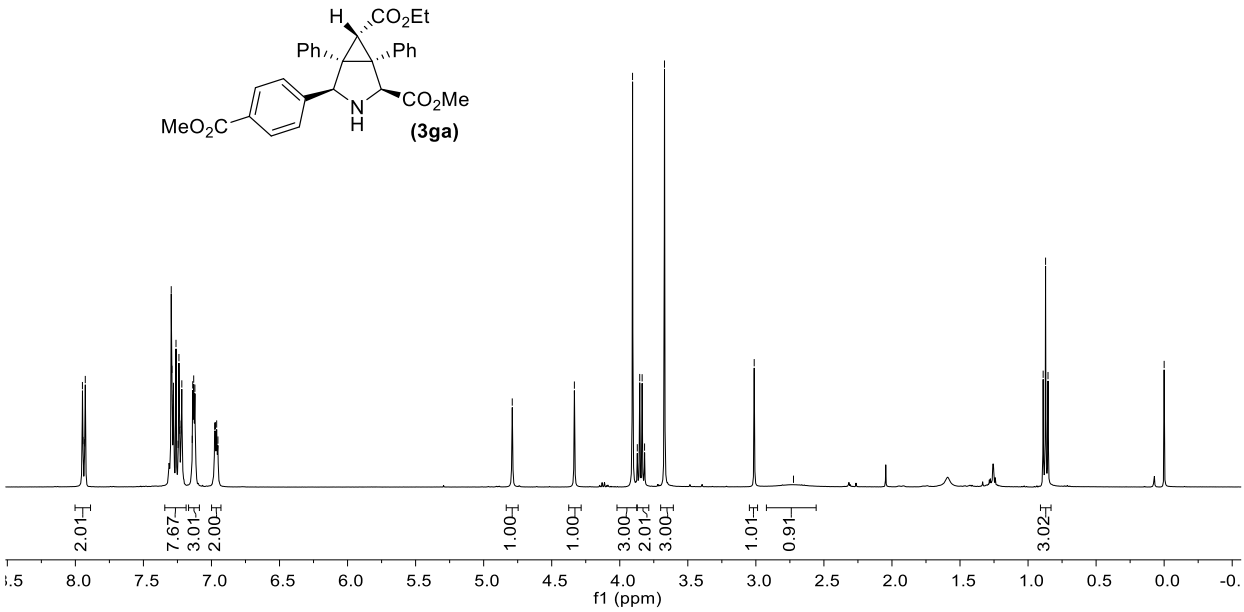


^{13}C NMR spectrum of compound **3fa** ($CDCl_3$)

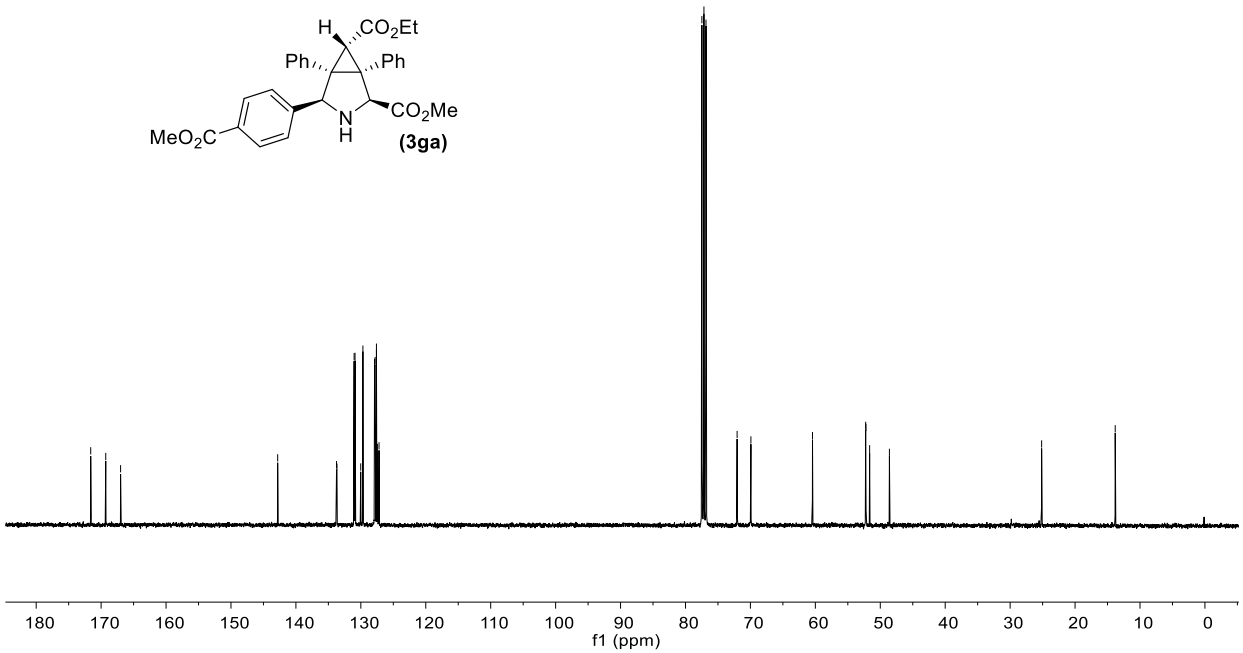


^{1}H NMR spectrum of compound **3ga** ($CDCl_3$)

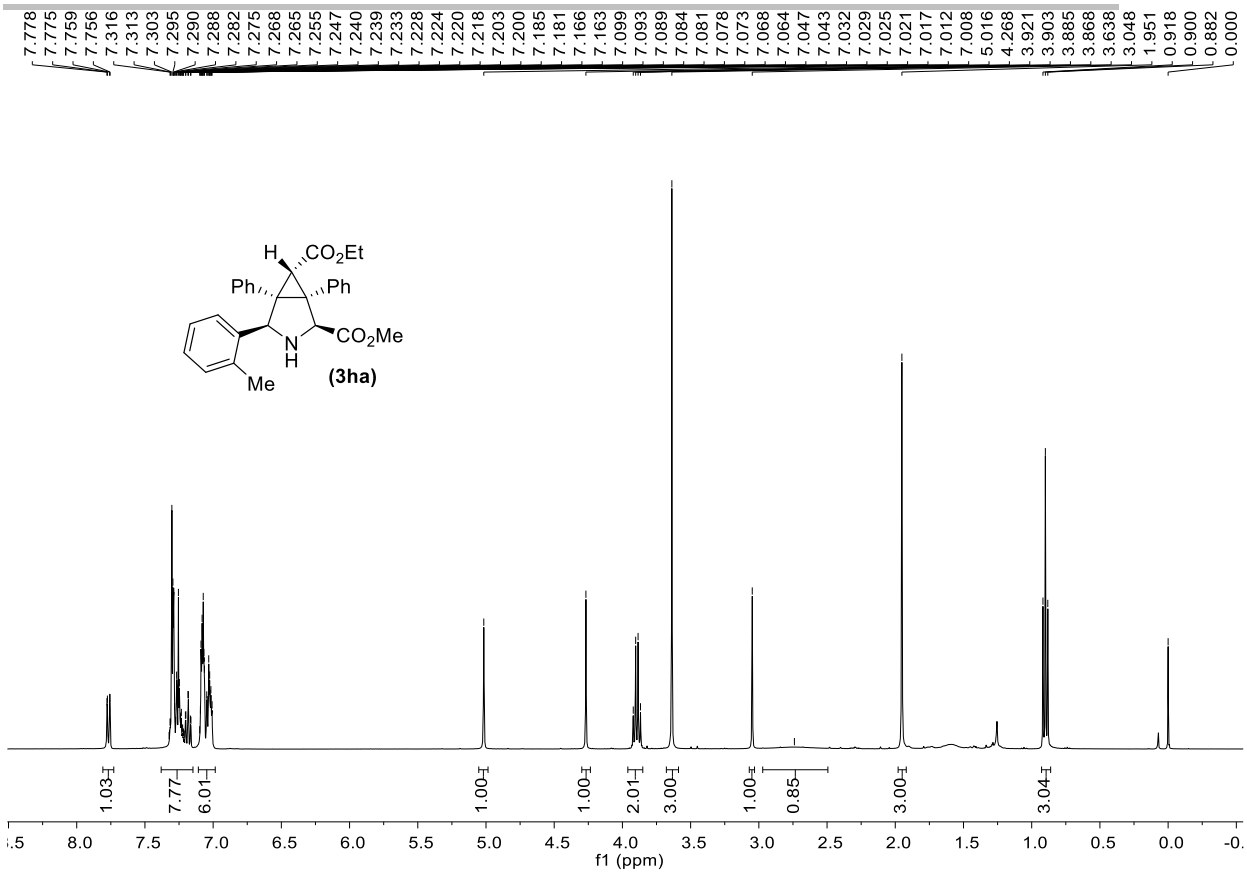




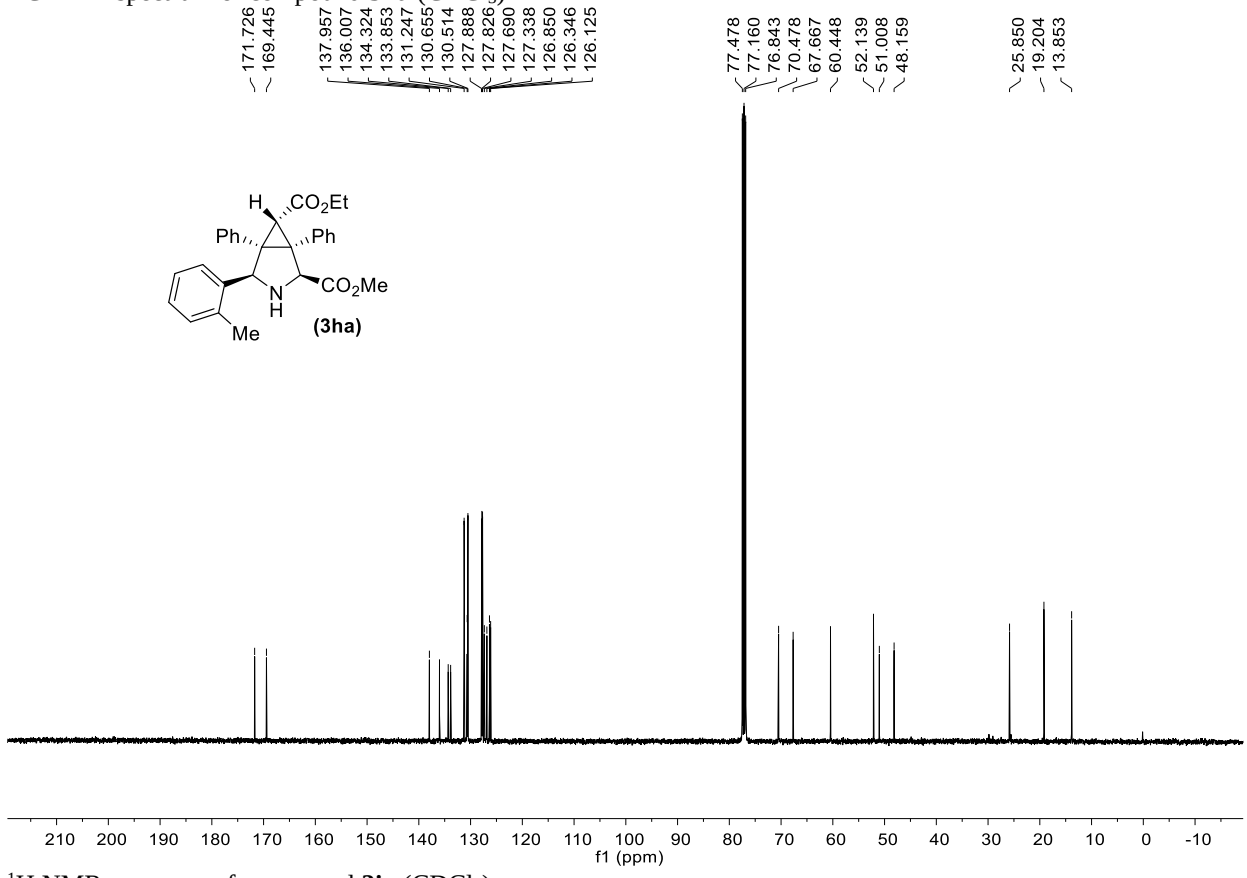
^{13}C NMR spectrum of compound **3ga** ($CDCl_3$)



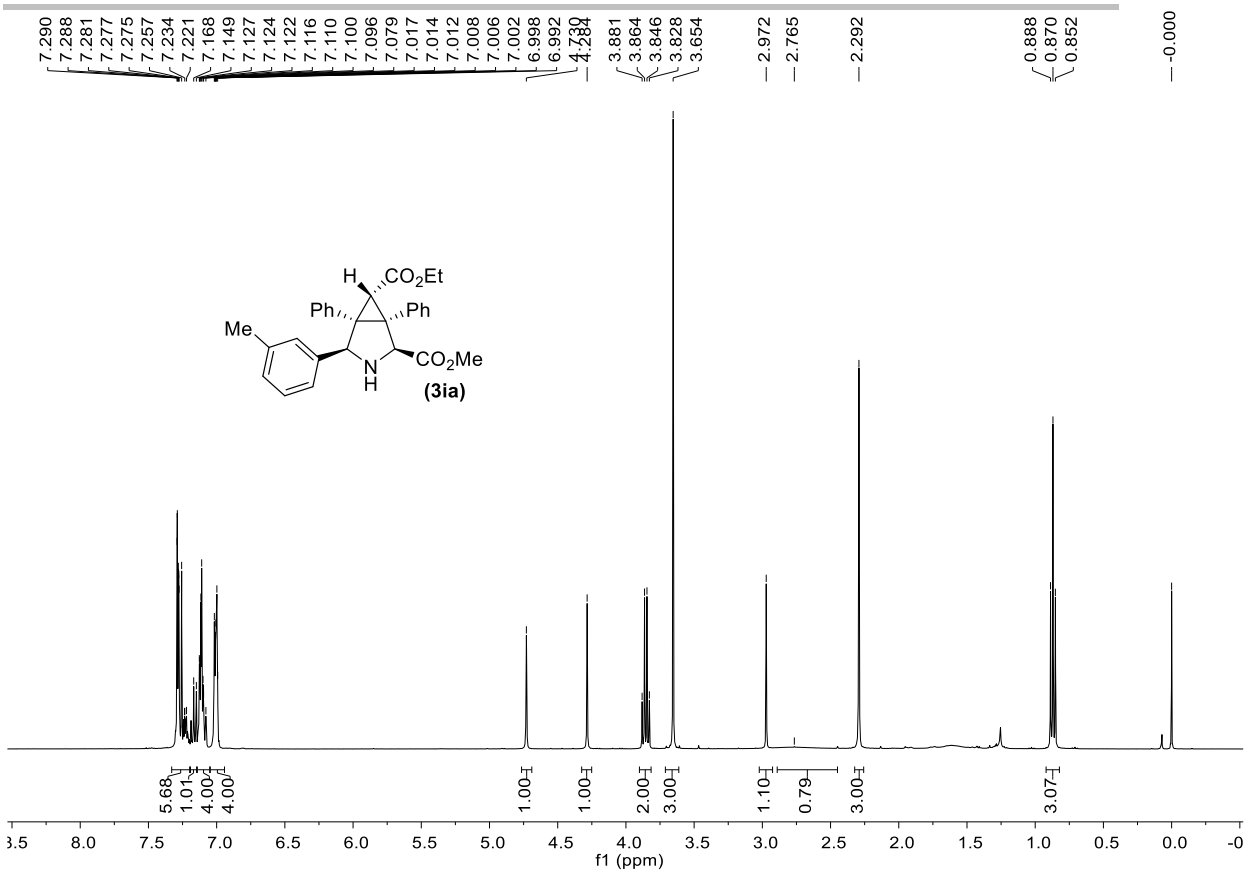
^{1}H NMR spectrum of compound **3ha** ($CDCl_3$)



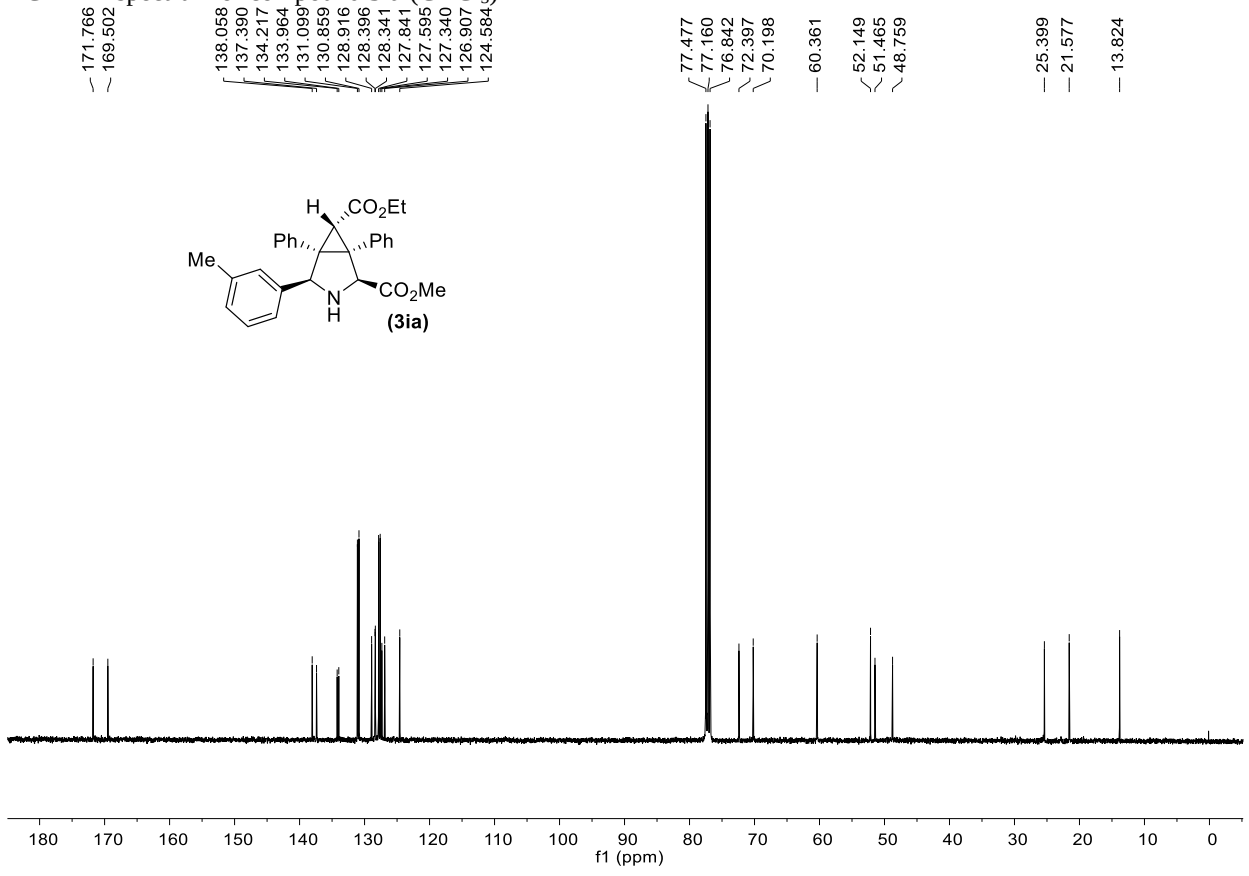
^{13}C NMR spectrum of compound **3ha** ($CDCl_3$)



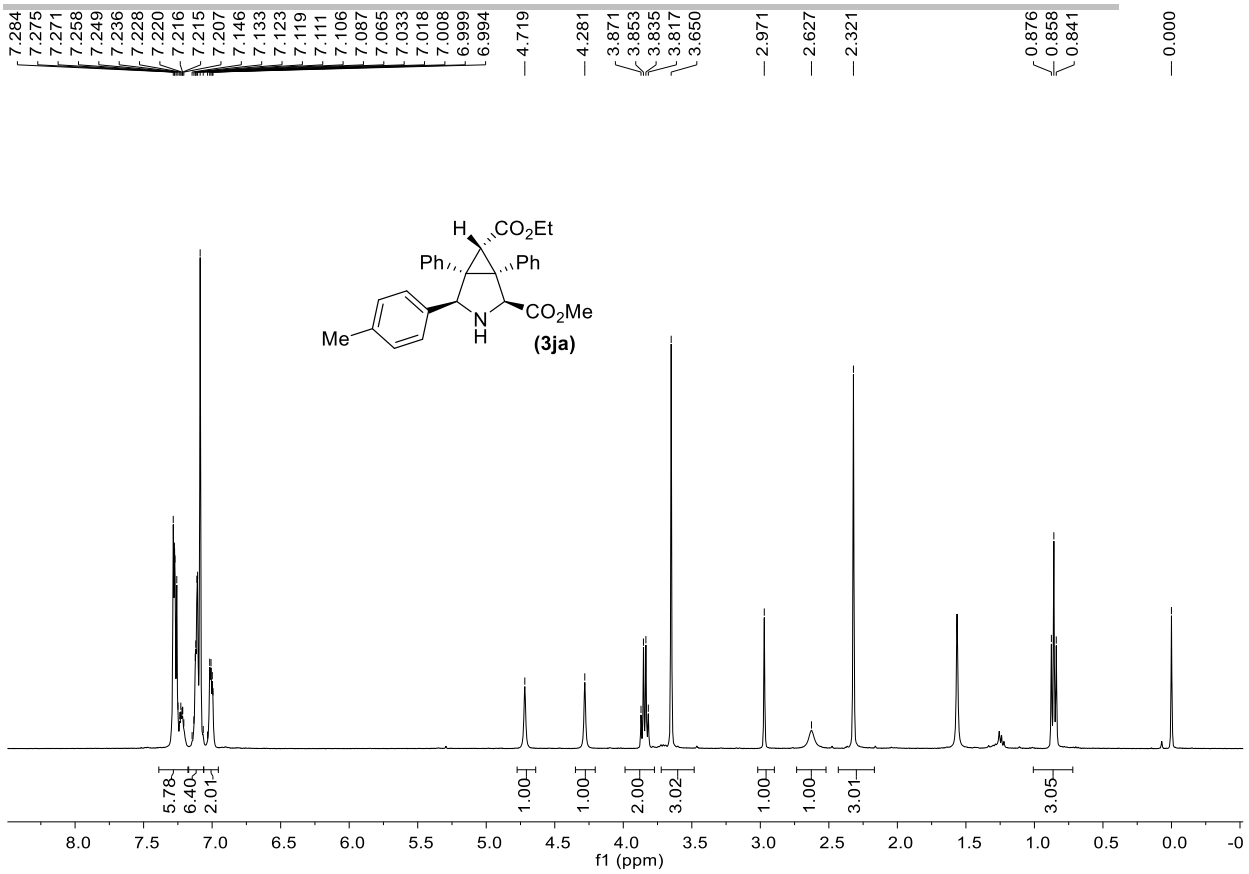
^{1}H NMR spectrum of compound **3ia** ($CDCl_3$)



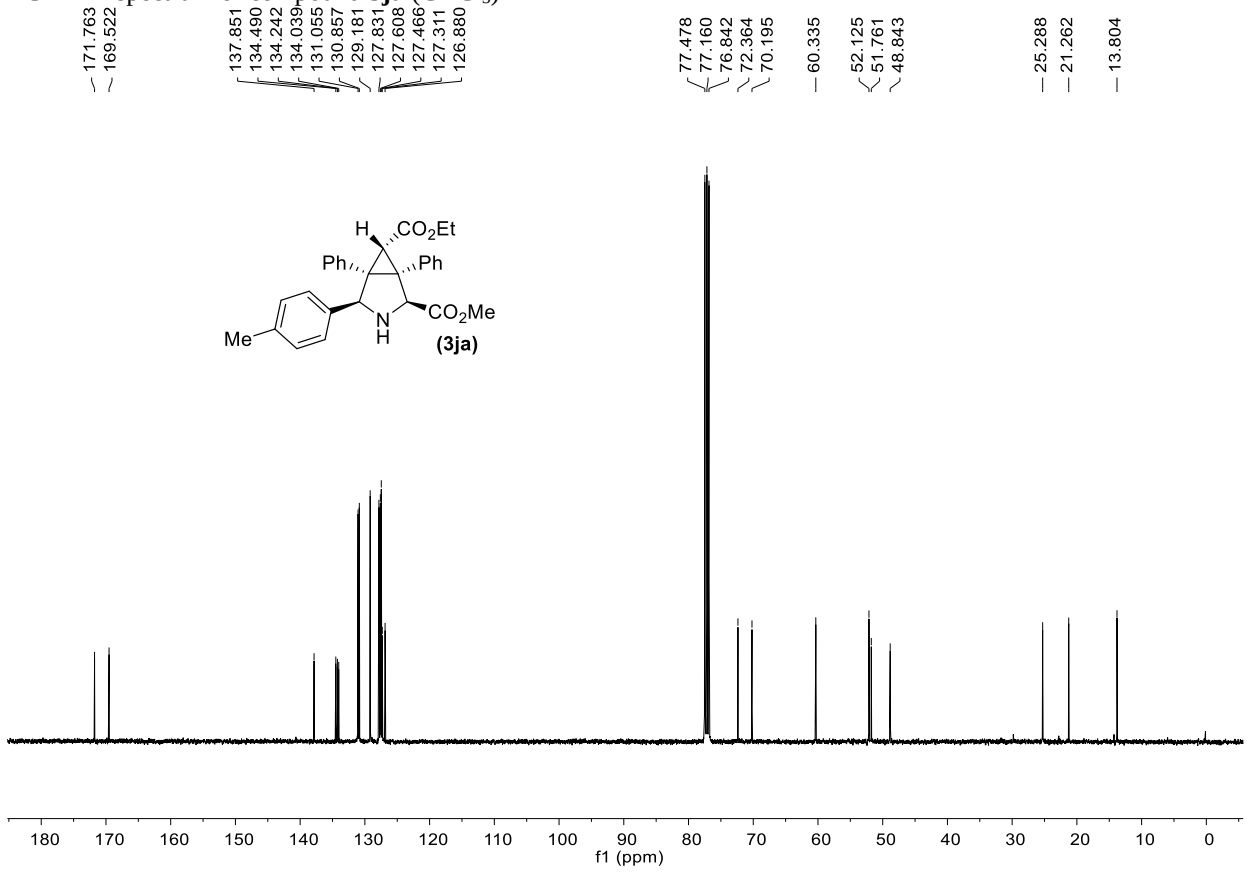
^{13}C NMR spectrum of compound **3ia** ($CDCl_3$)



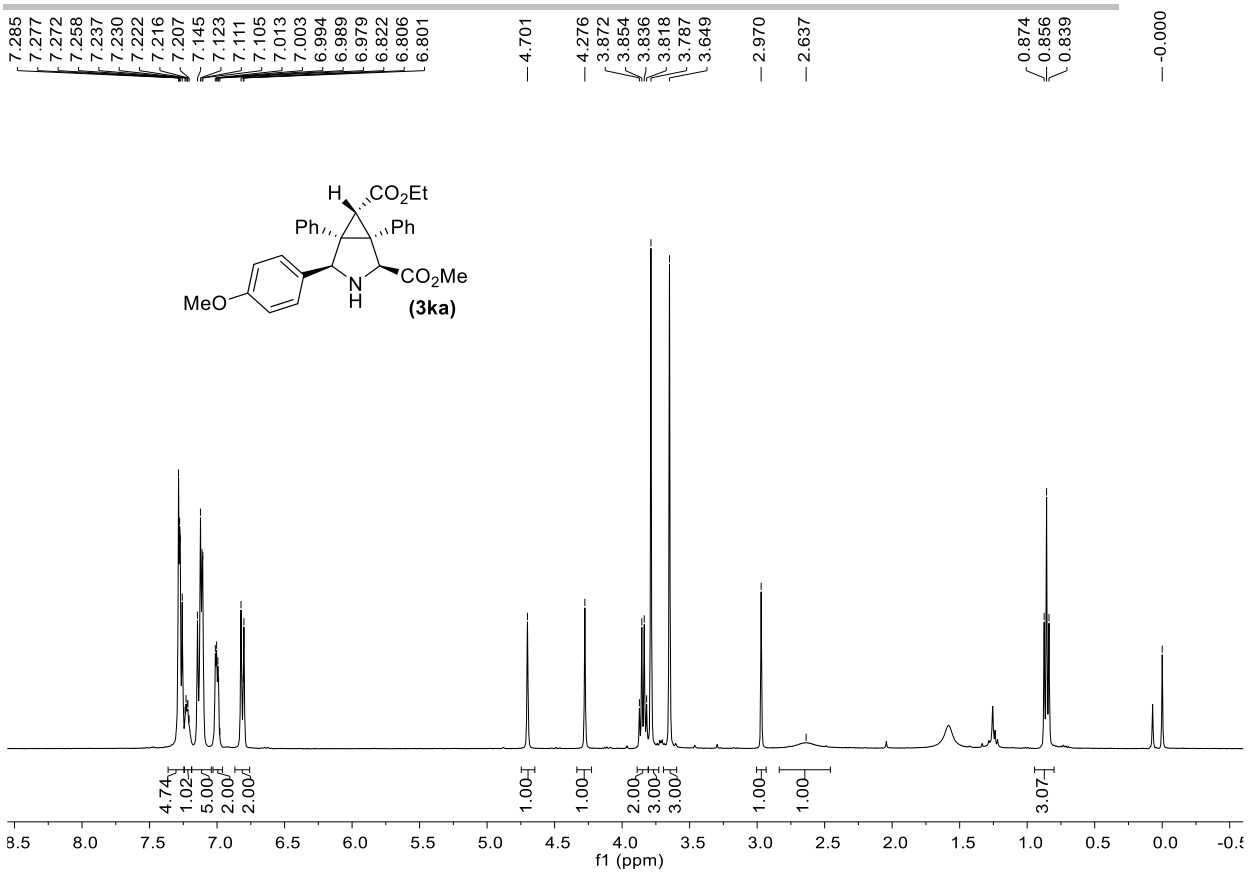
^{1}H NMR spectrum of compound **3ja** ($CDCl_3$)



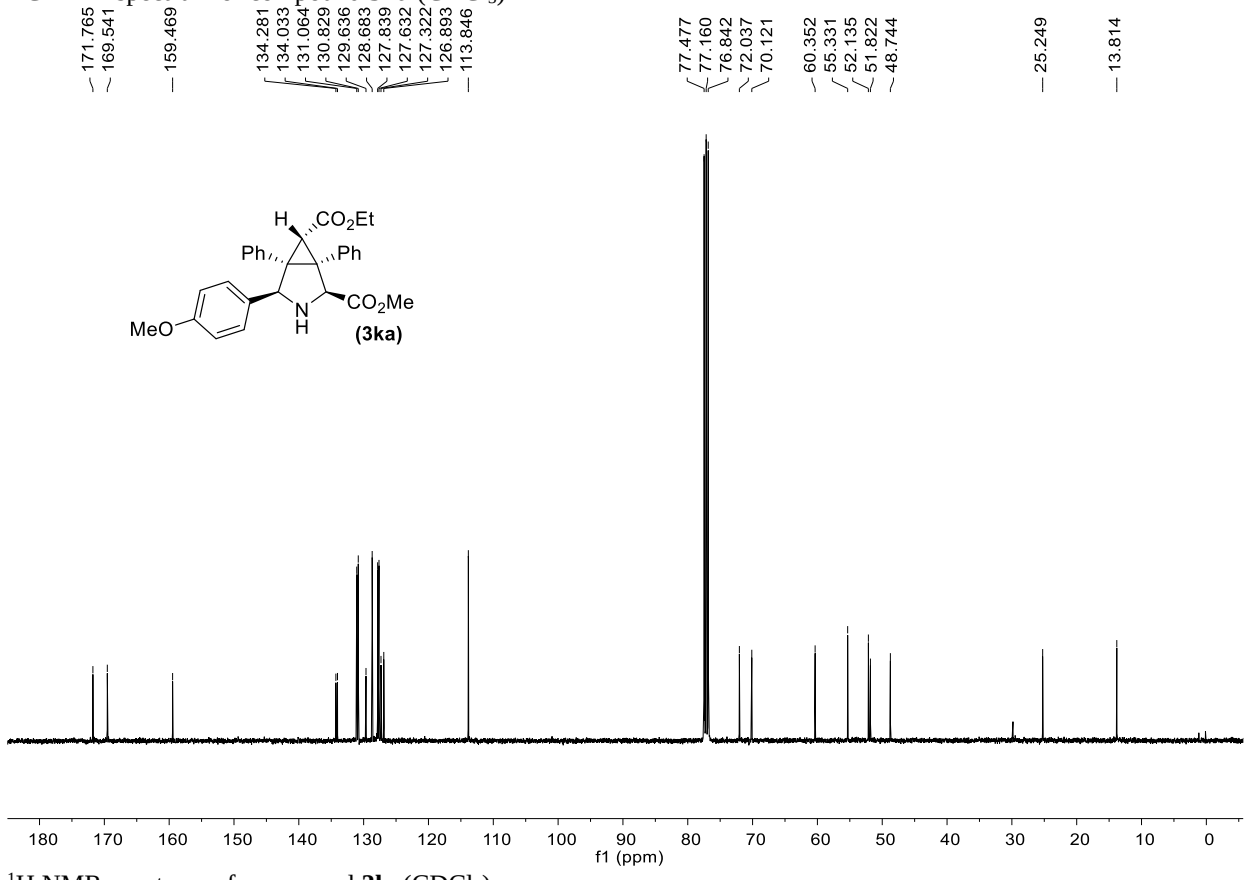
^{13}C NMR spectrum of compound **3ja** ($CDCl_3$)



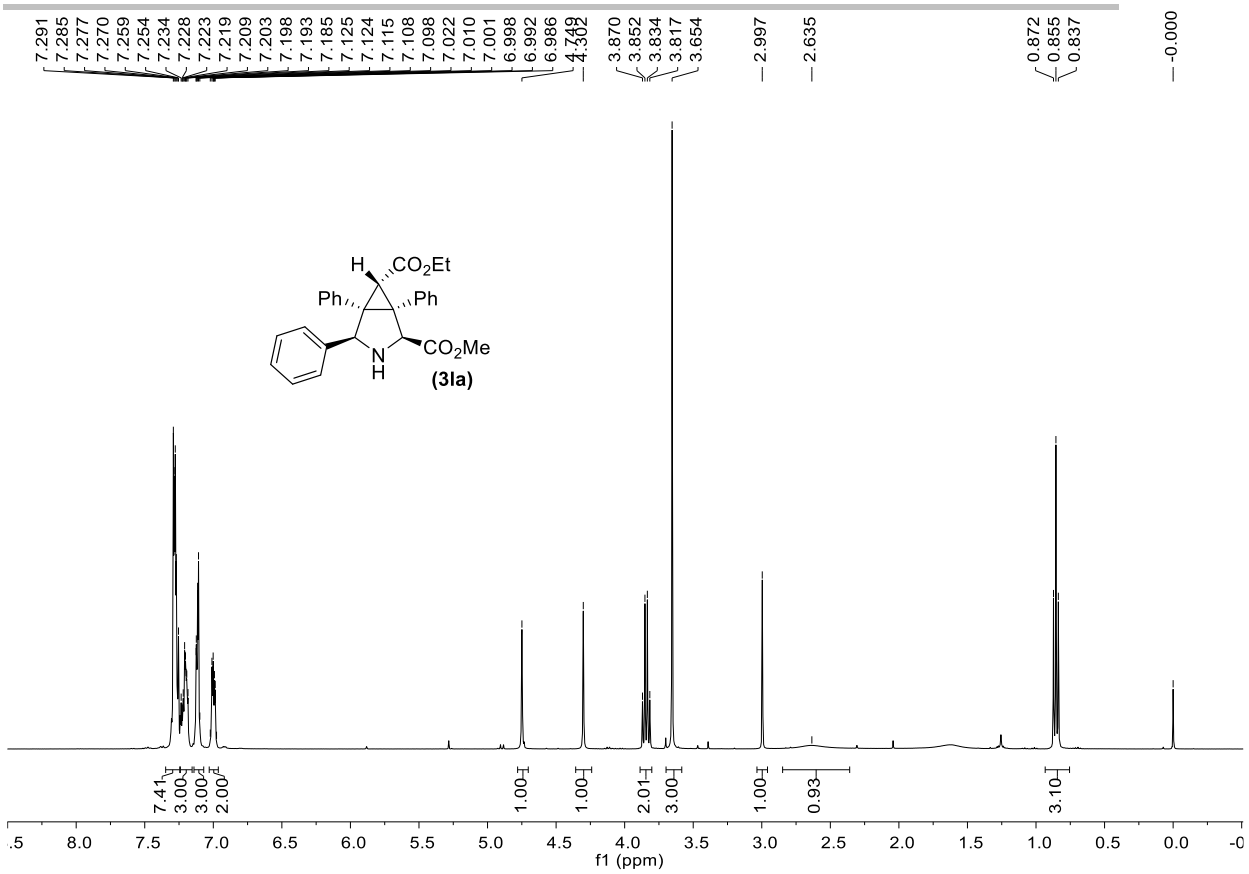
^{1}H NMR spectrum of compound **3ka** ($CDCl_3$)



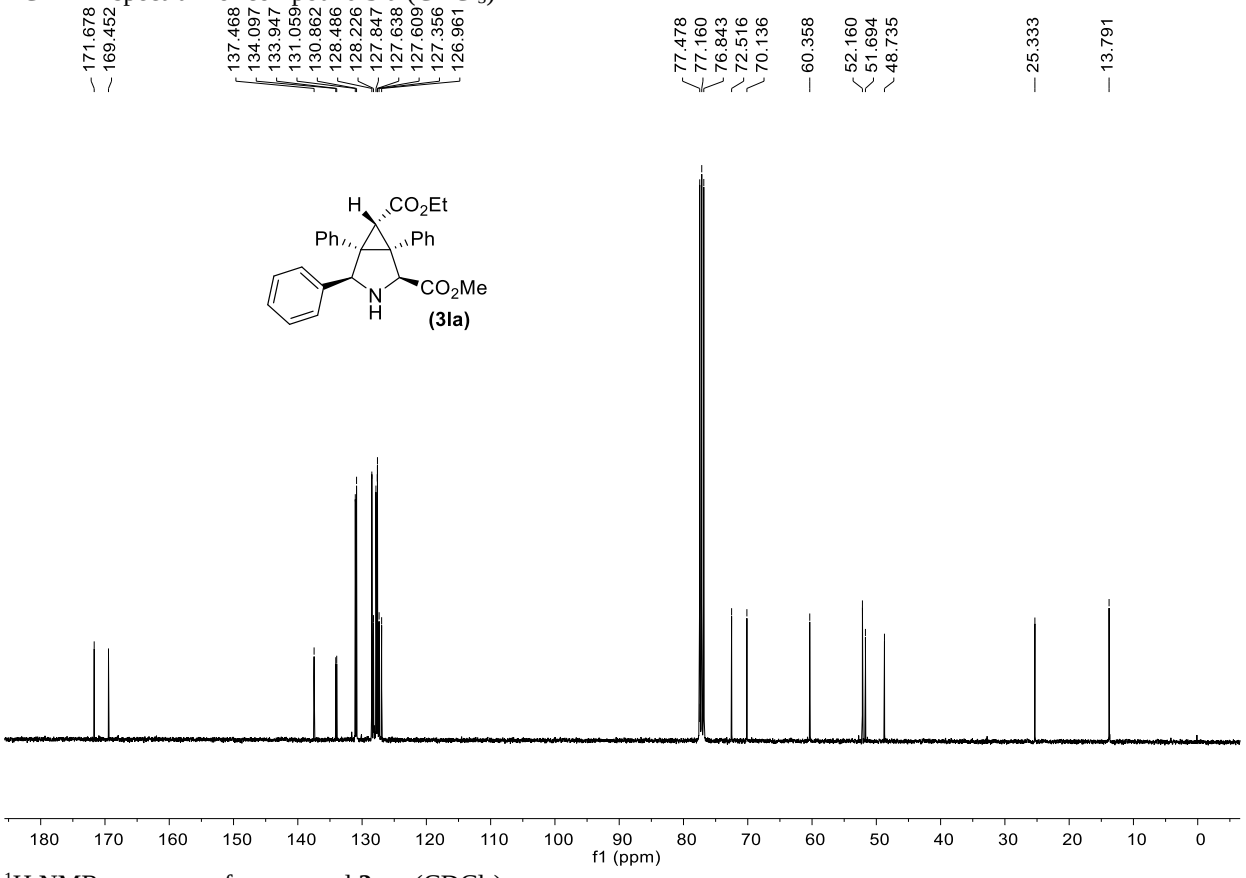
^{13}C NMR spectrum of compound **3ka** ($CDCl_3$)



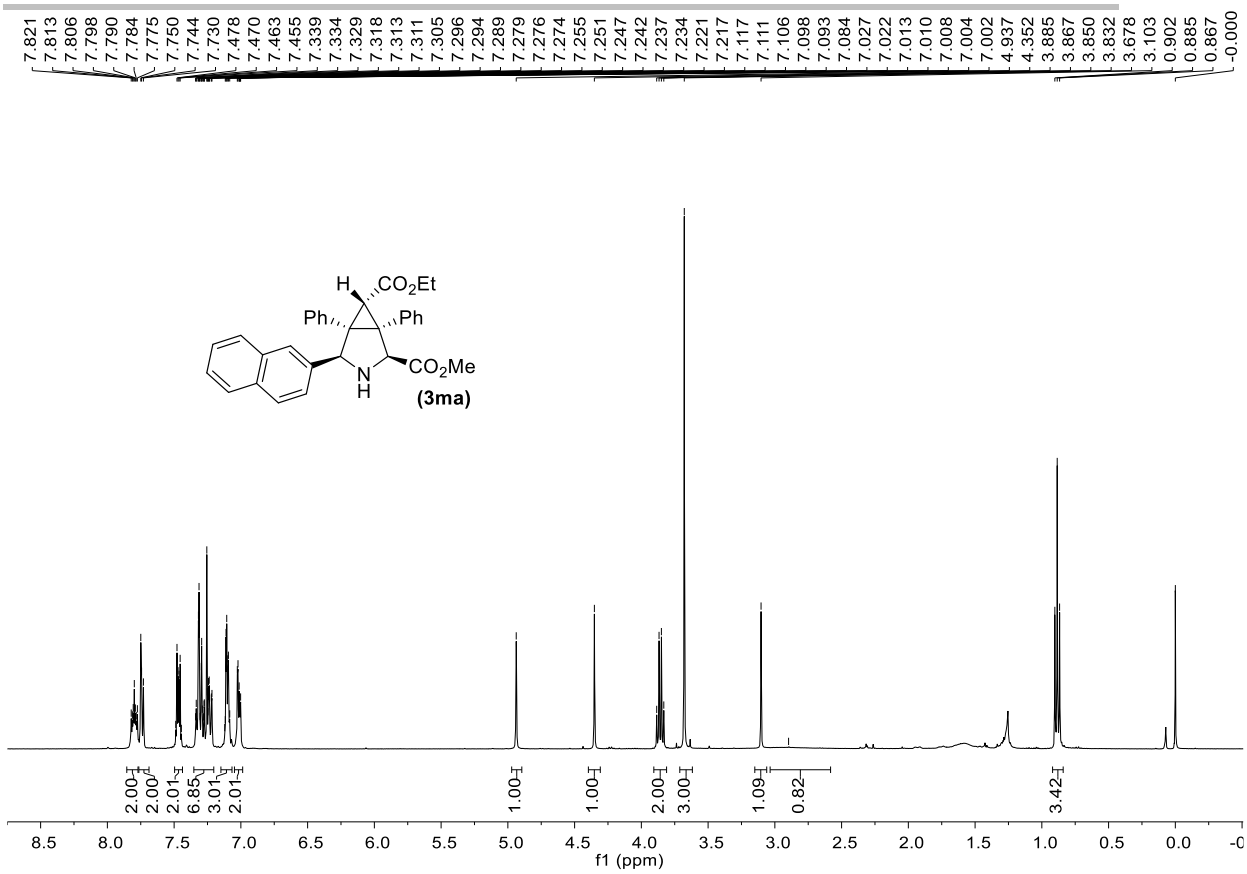
^{1}H NMR spectrum of compound **3la** ($CDCl_3$)



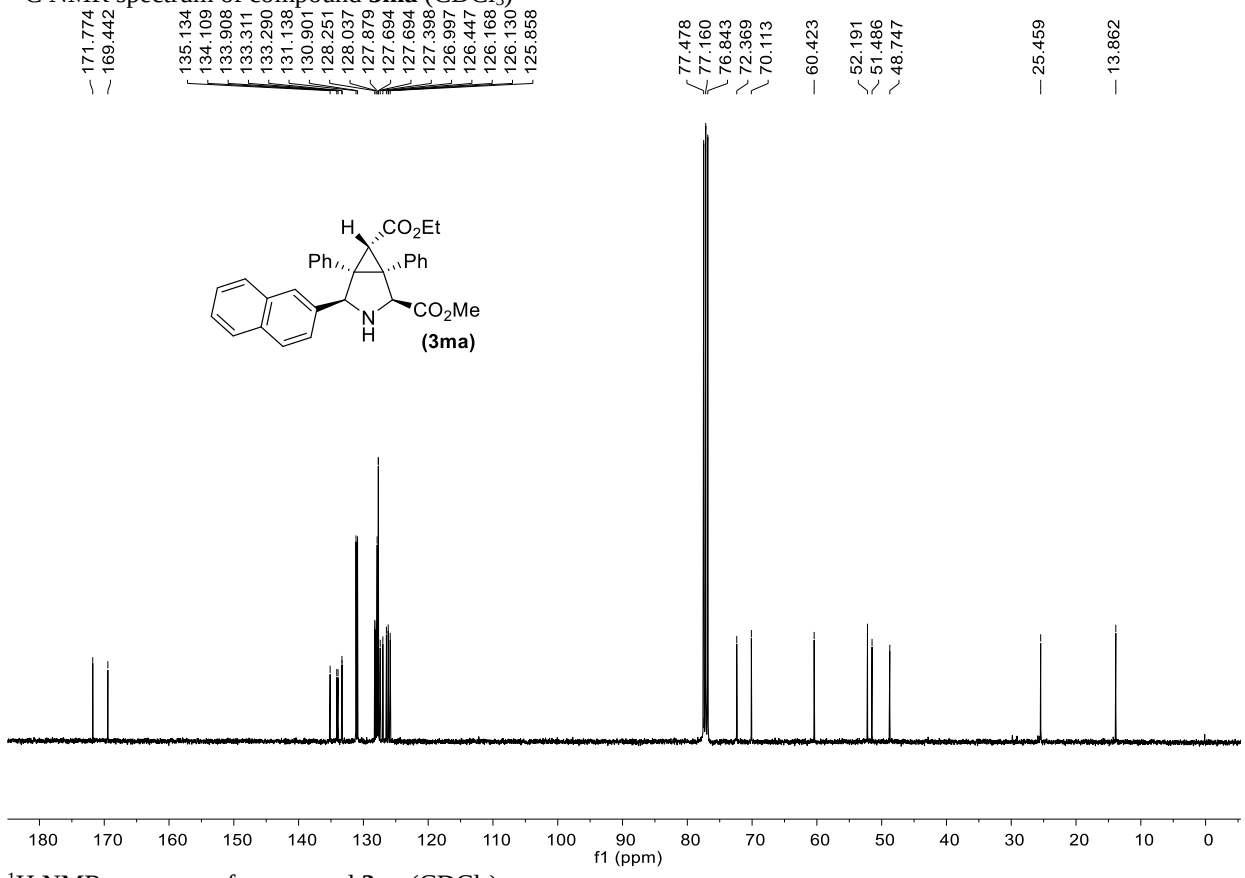
^{13}C NMR spectrum of compound **3la** ($CDCl_3$)



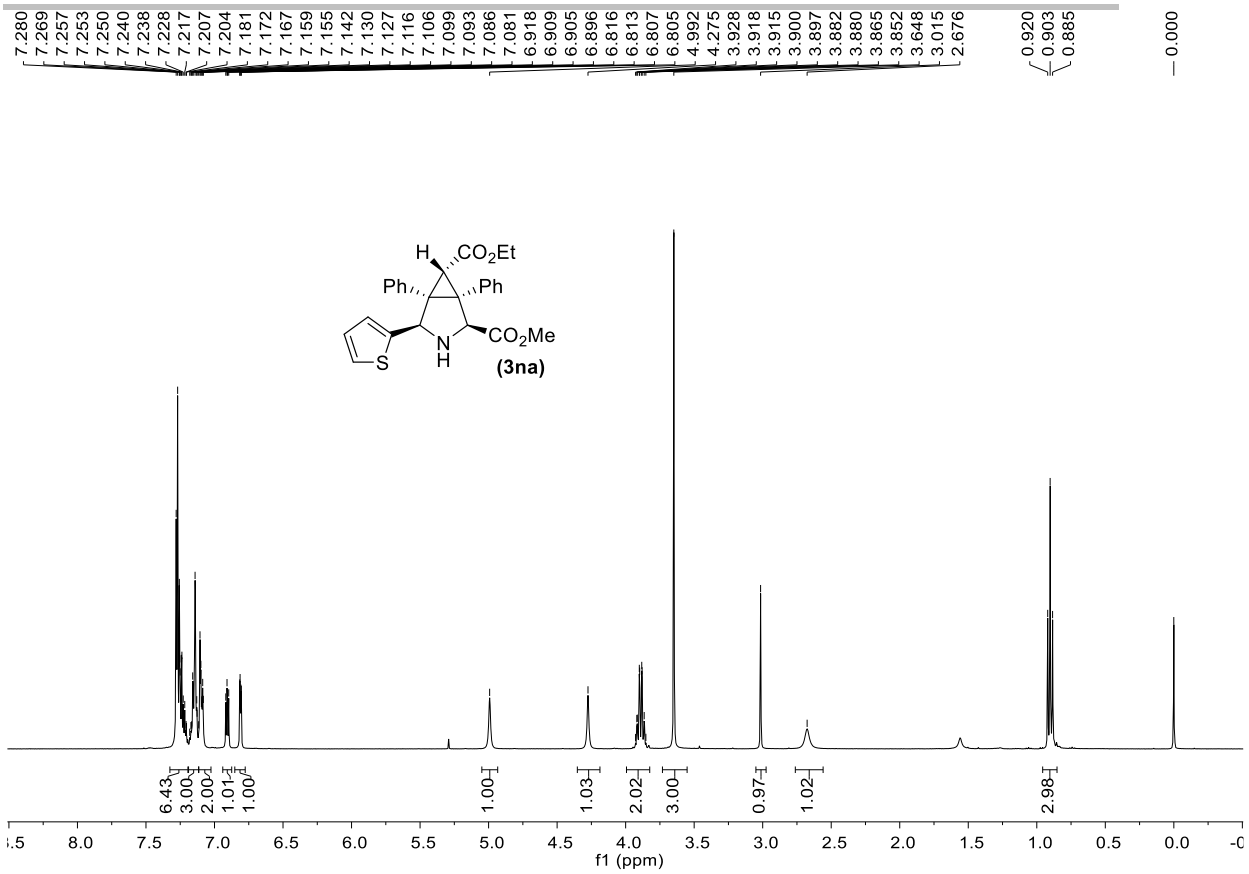
^{1}H NMR spectrum of compound **3ma** ($CDCl_3$)



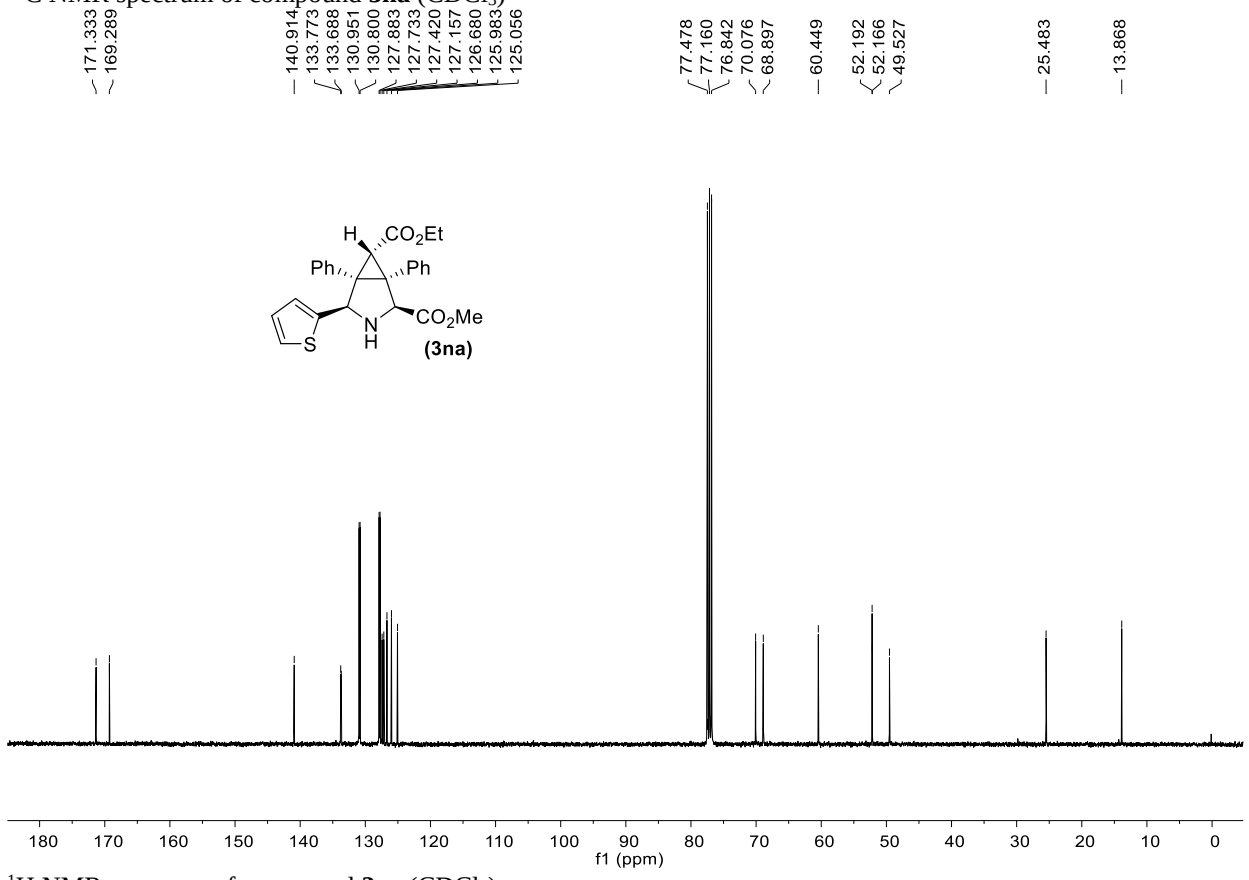
^{13}C NMR spectrum of compound **3ma** ($CDCl_3$)



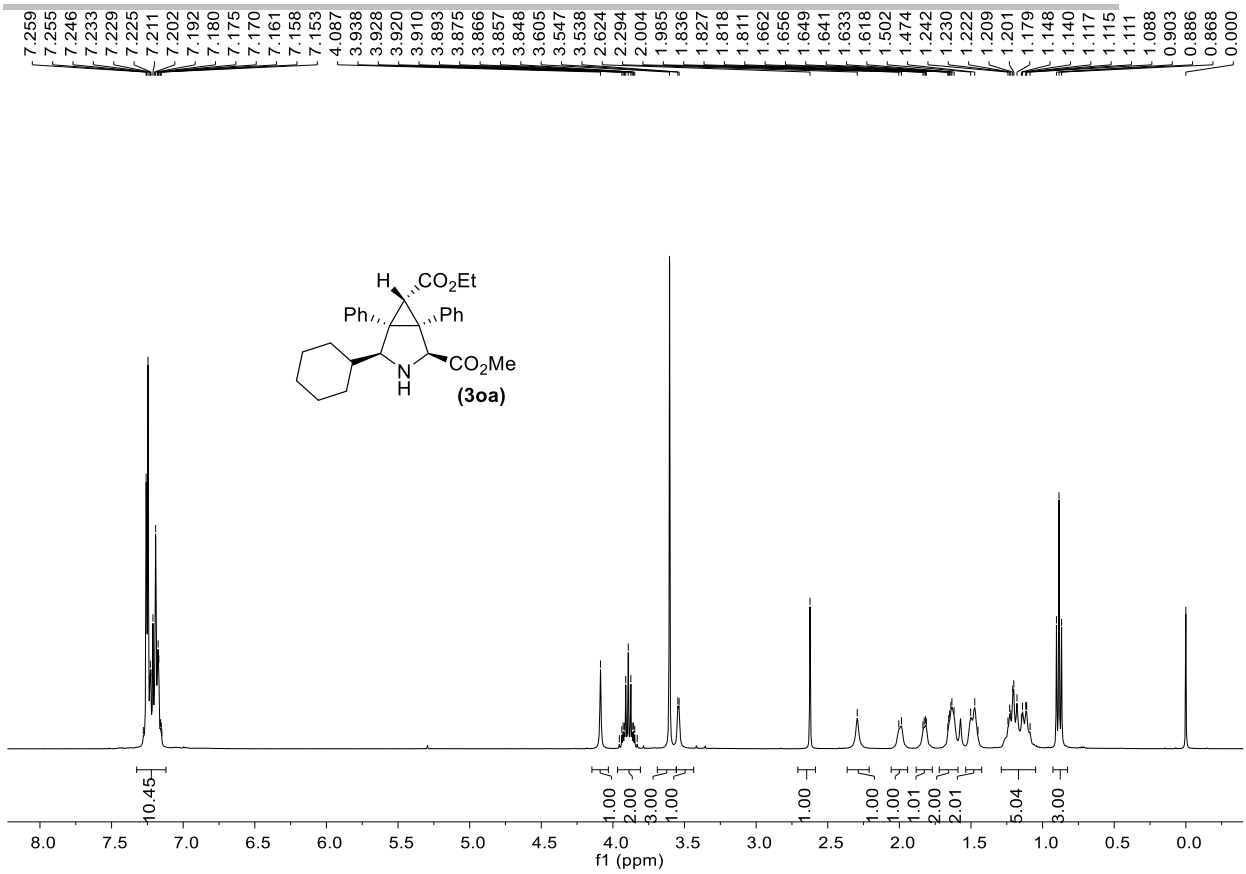
^{1}H NMR spectrum of compound **3na** ($CDCl_3$)



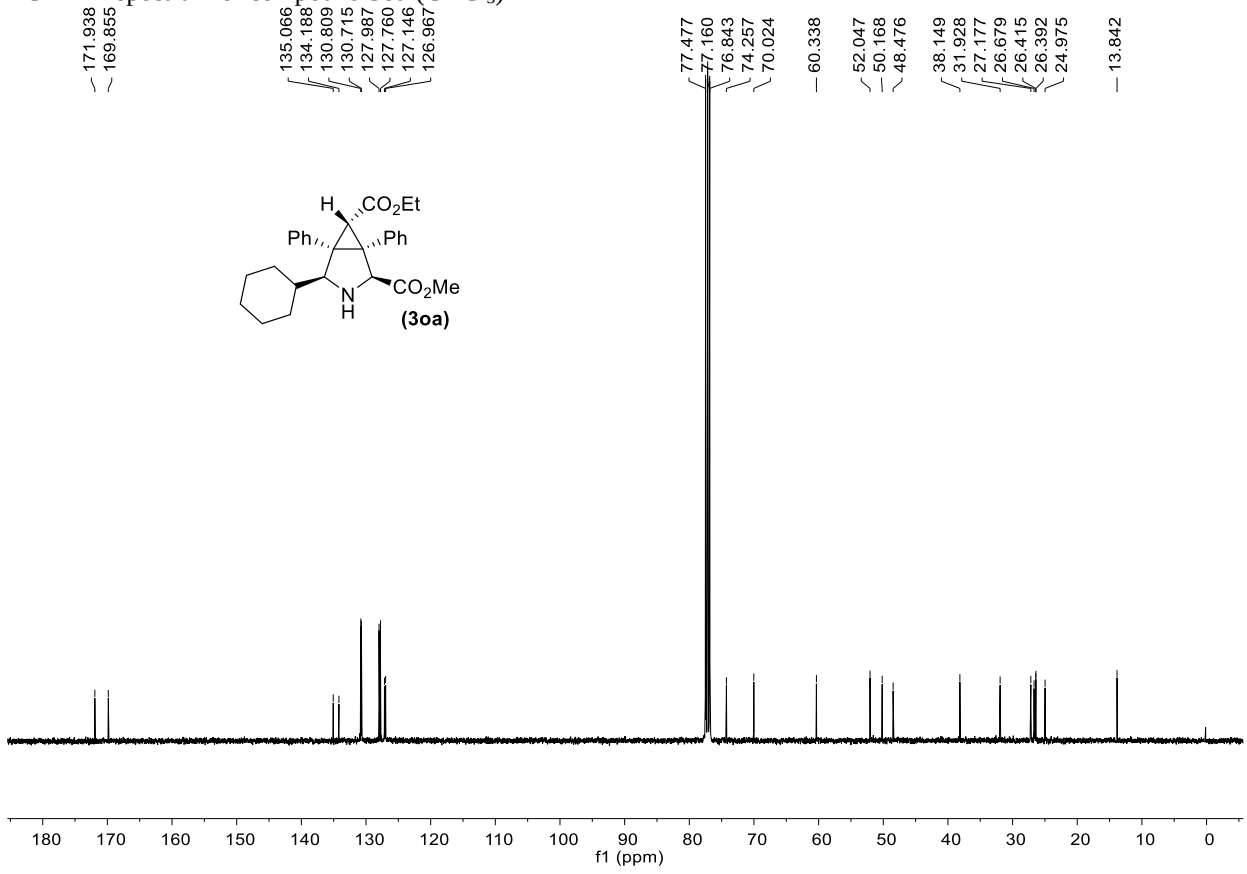
^{13}C NMR spectrum of compound **3na** ($CDCl_3$)



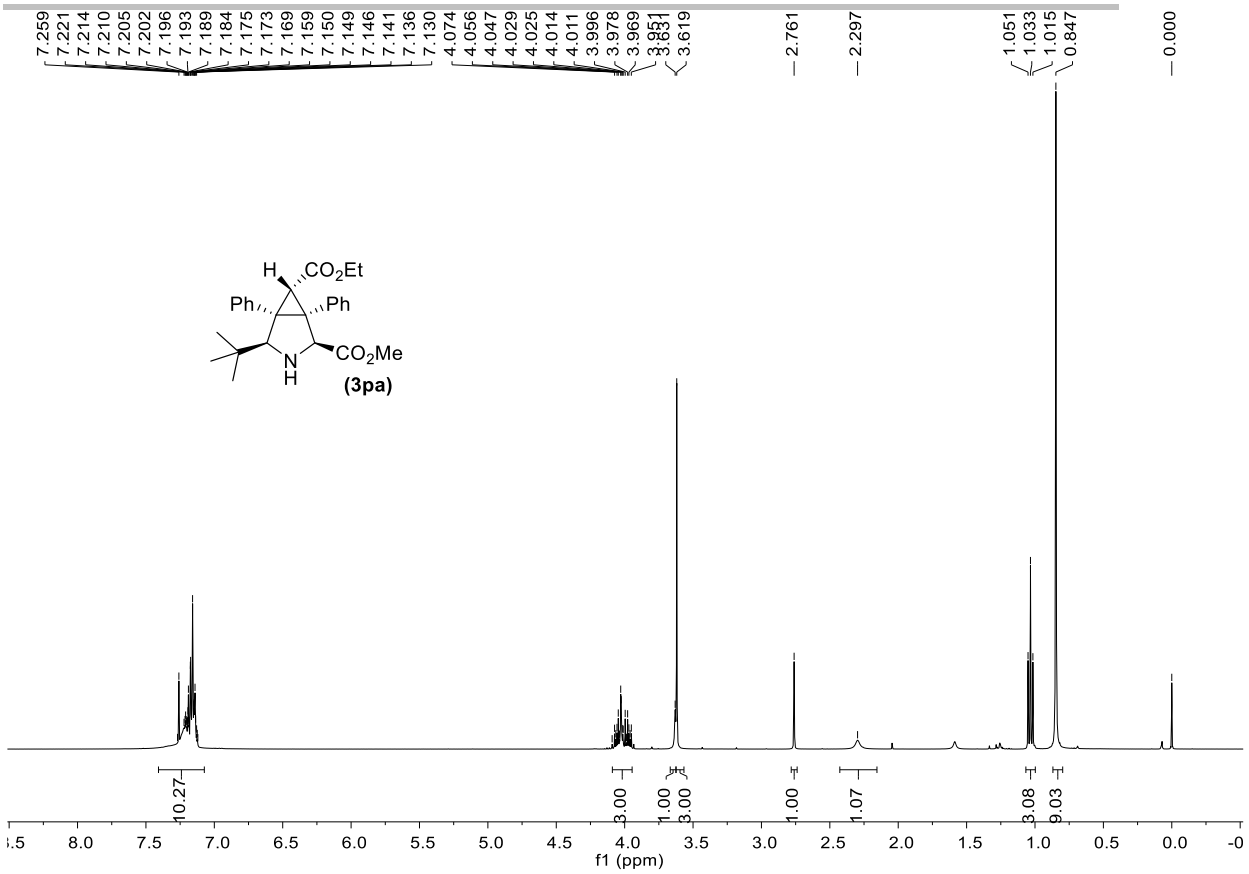
^{1}H NMR spectrum of compound **3oa** ($CDCl_3$)



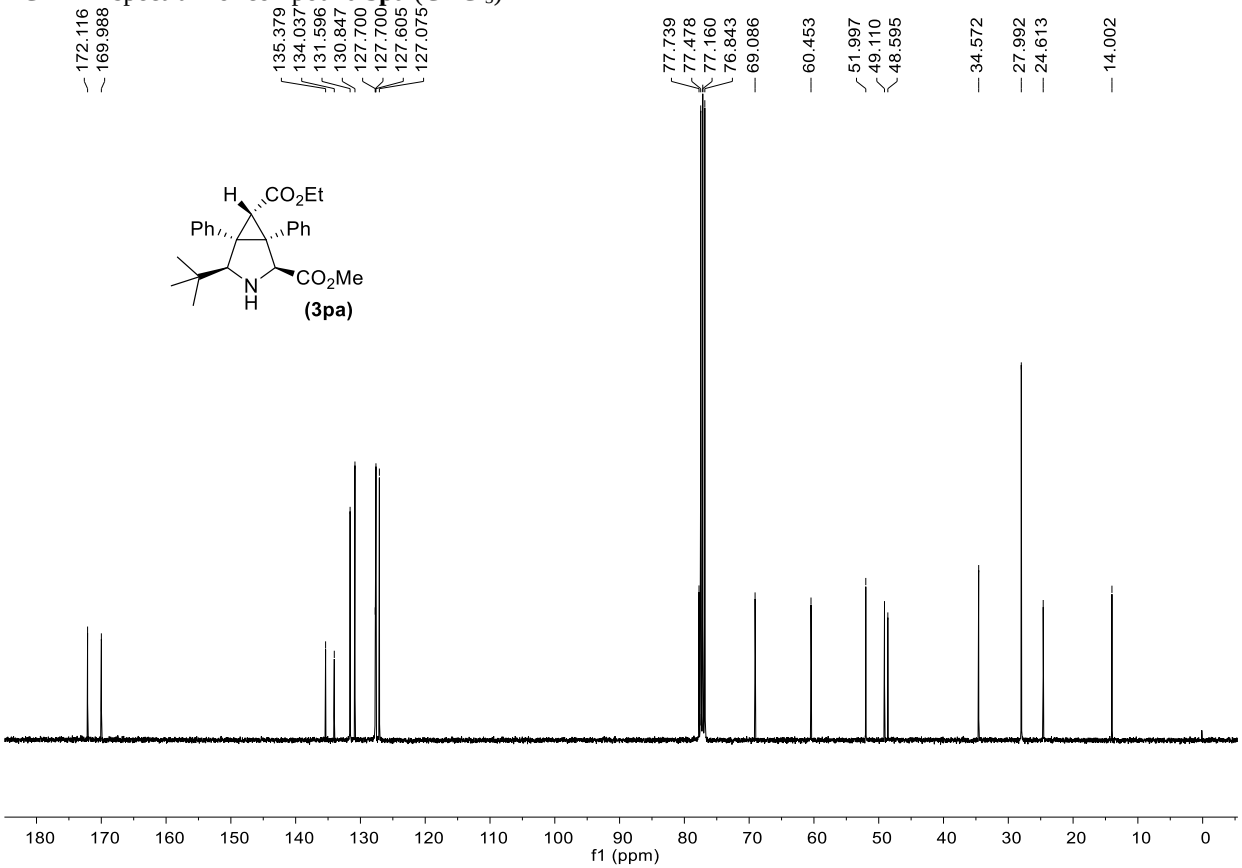
^{13}C NMR spectrum of compound **3oa** ($CDCl_3$)



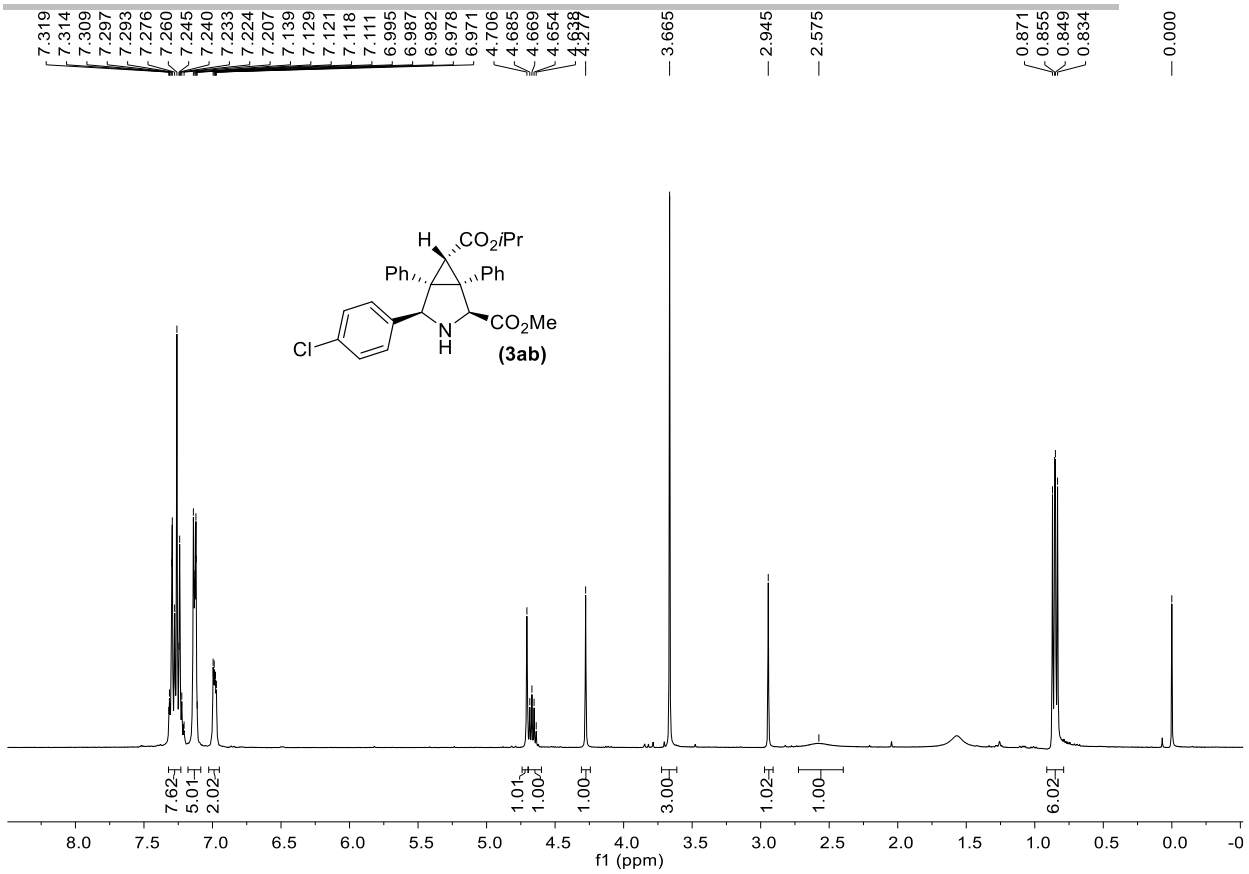
^{1}H NMR spectrum of compound **3pa** ($CDCl_3$)



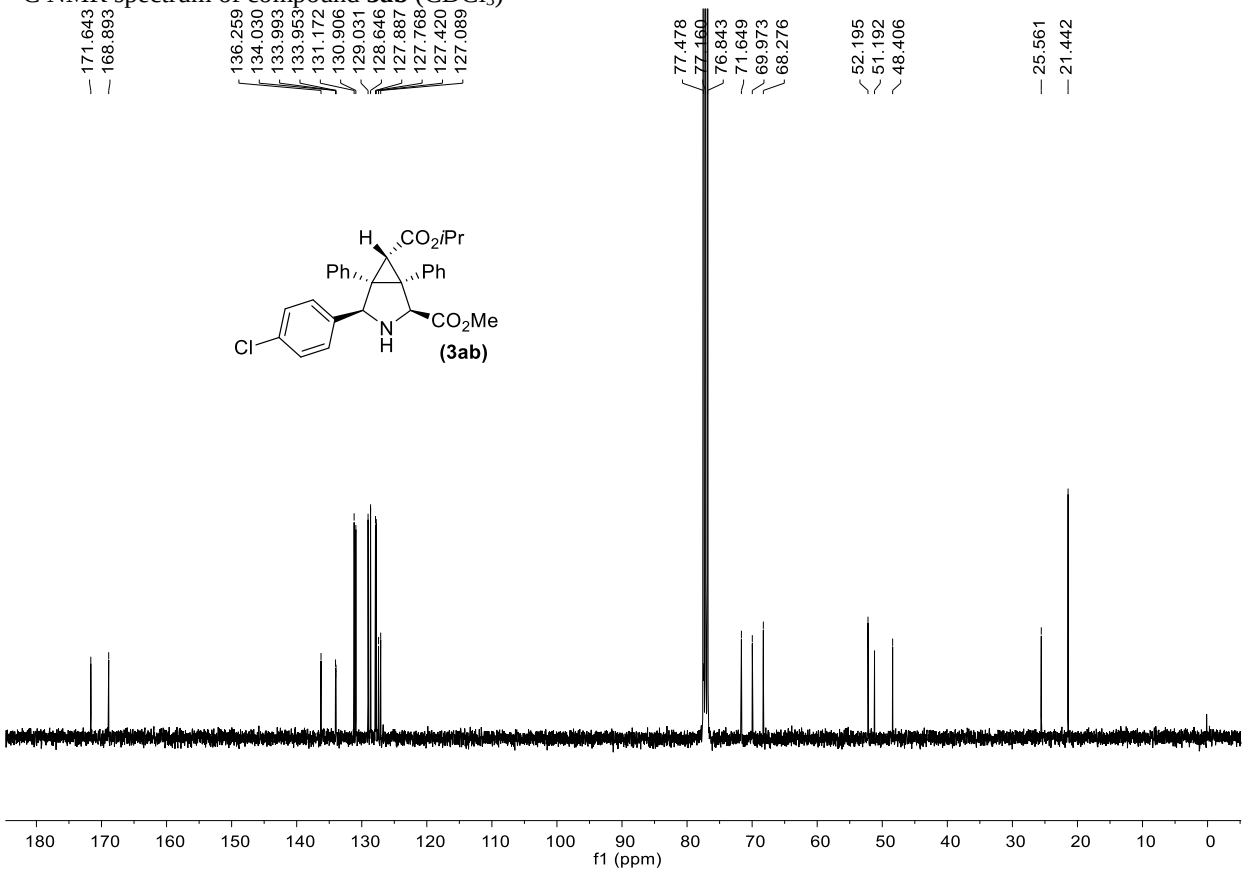
^{13}C NMR spectrum of compound **3pa** ($CDCl_3$)



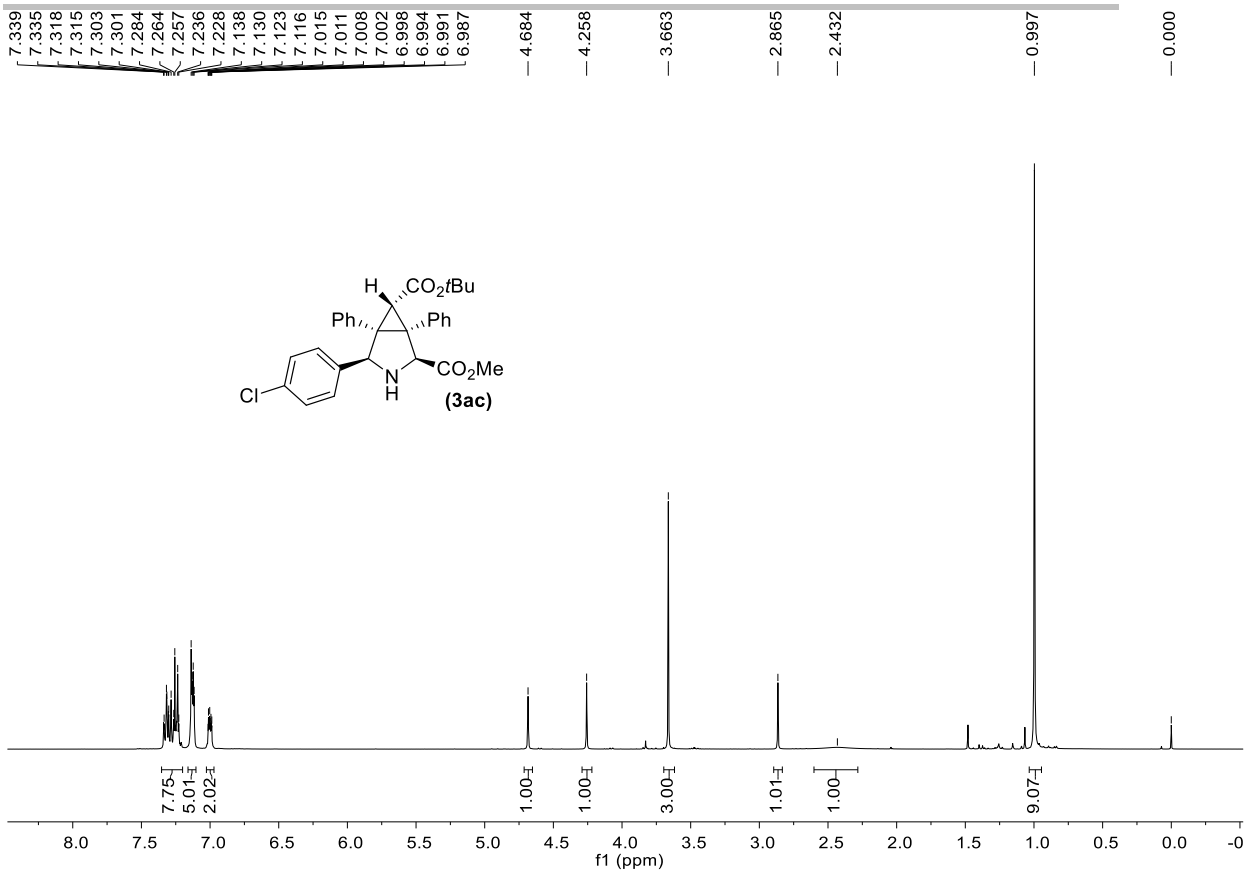
^{1}H NMR spectrum of compound **3ab** ($CDCl_3$)



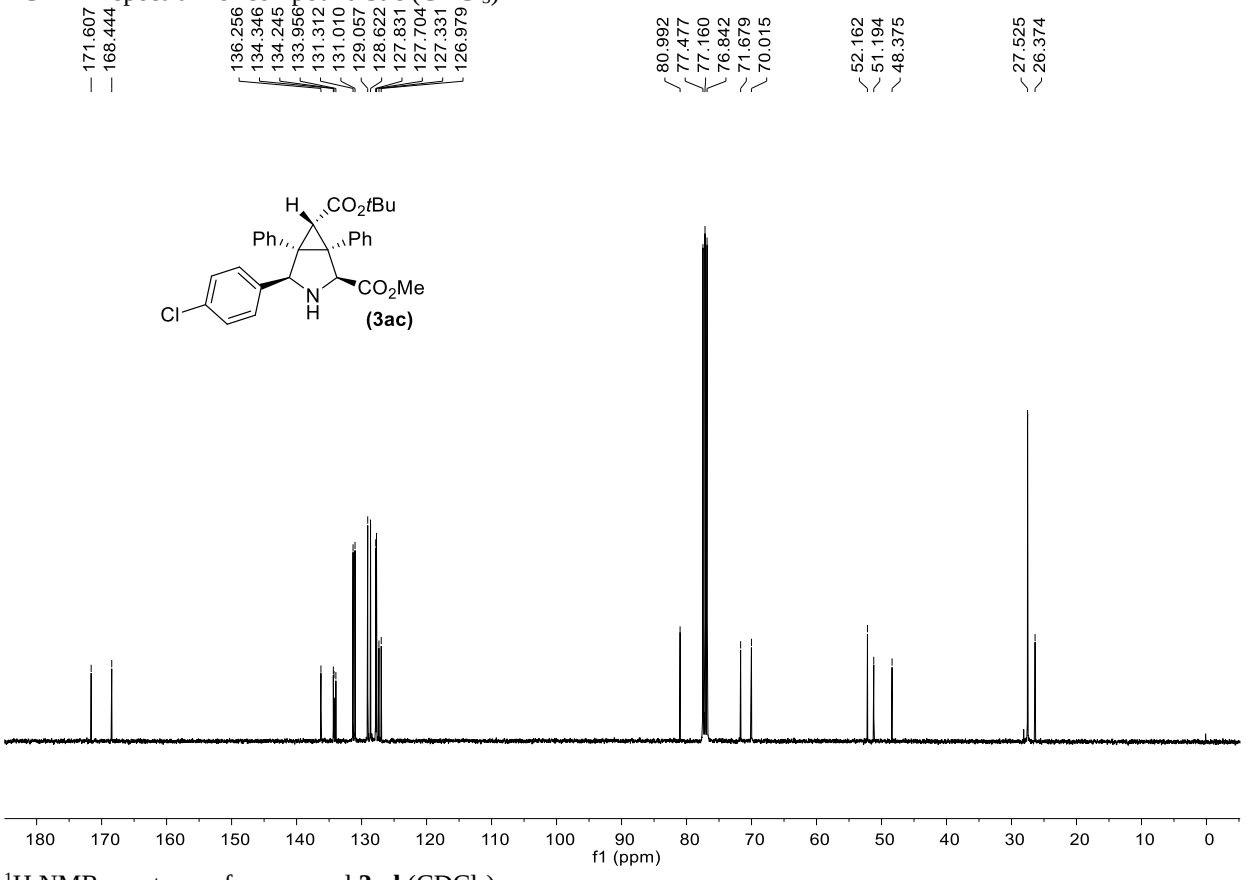
^{13}C NMR spectrum of compound **3ab** ($CDCl_3$)



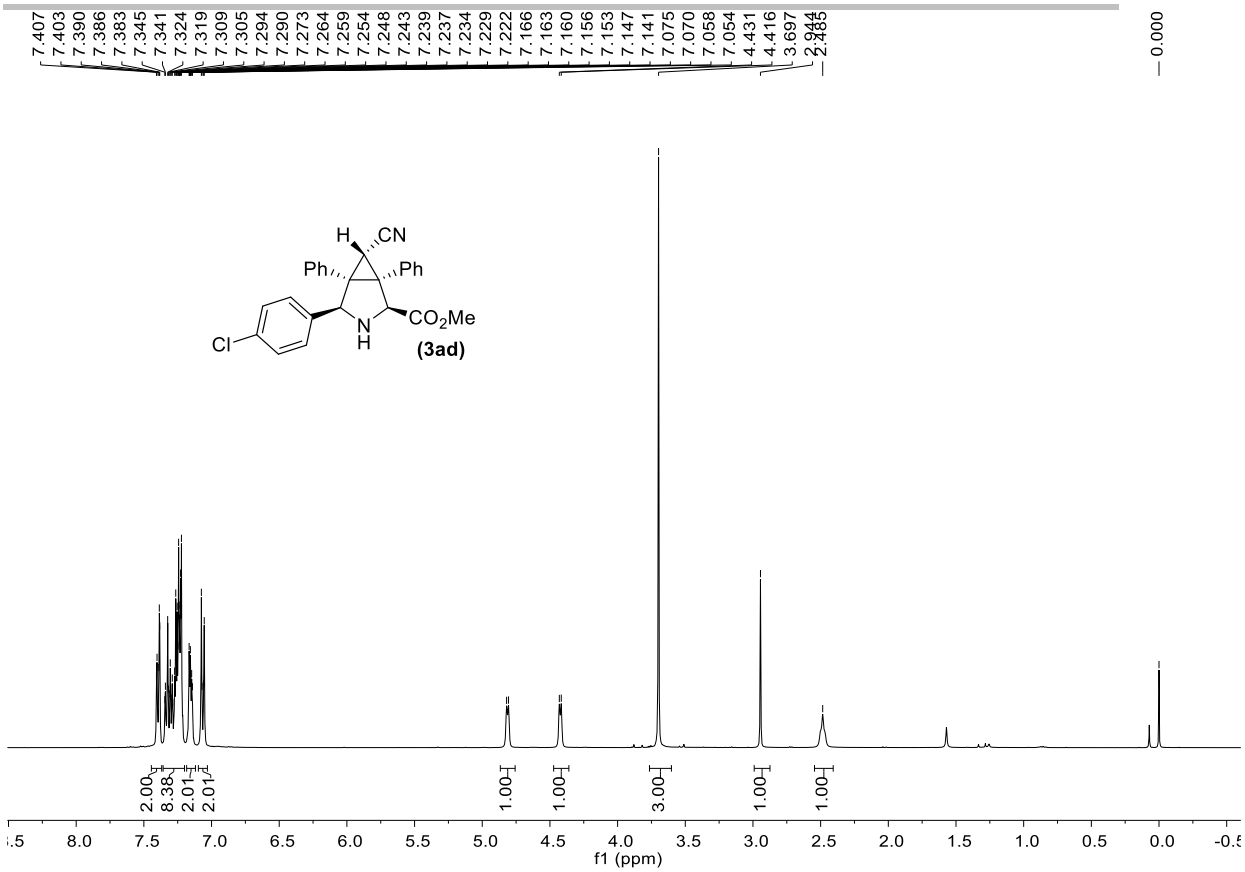
^{1}H NMR spectrum of compound **3ac** ($CDCl_3$)



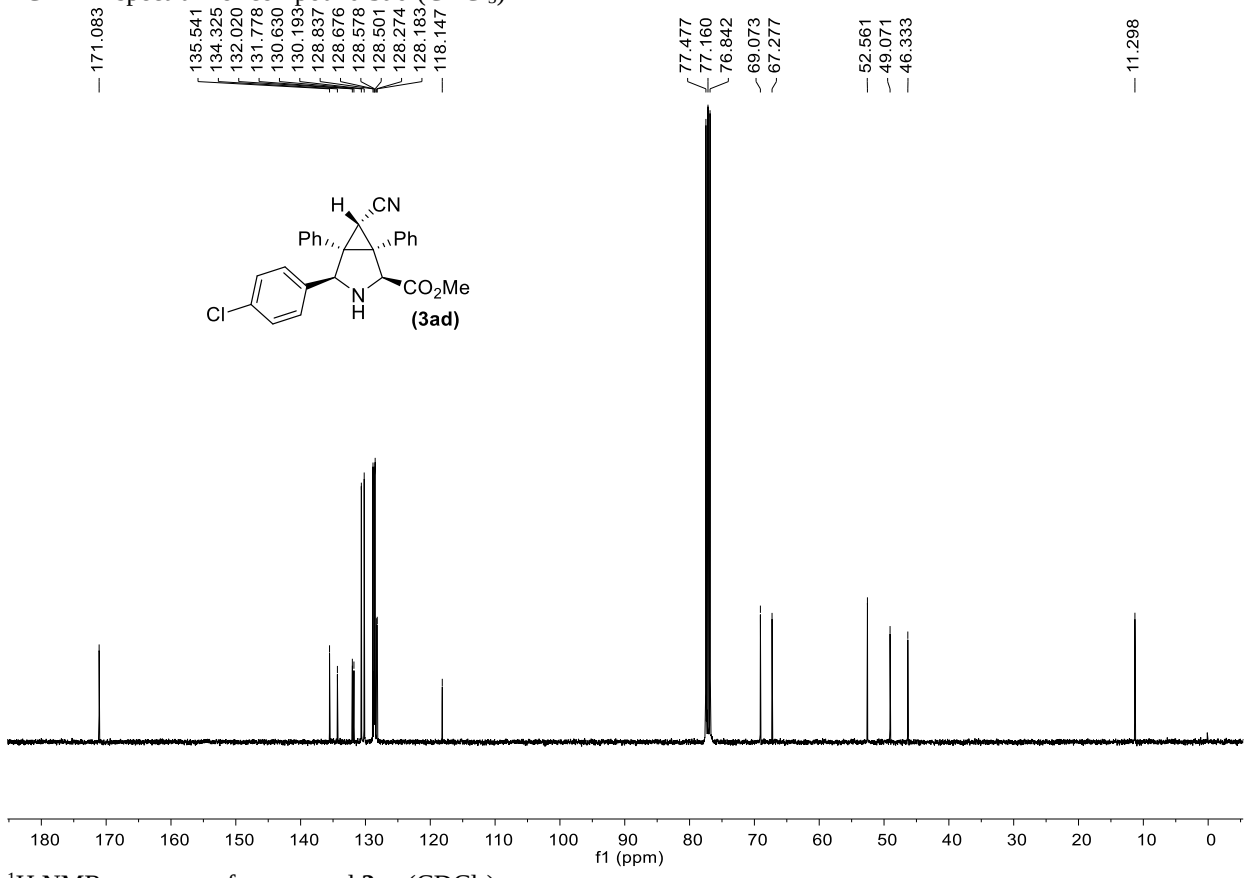
^{13}C NMR spectrum of compound **3ac** ($CDCl_3$)



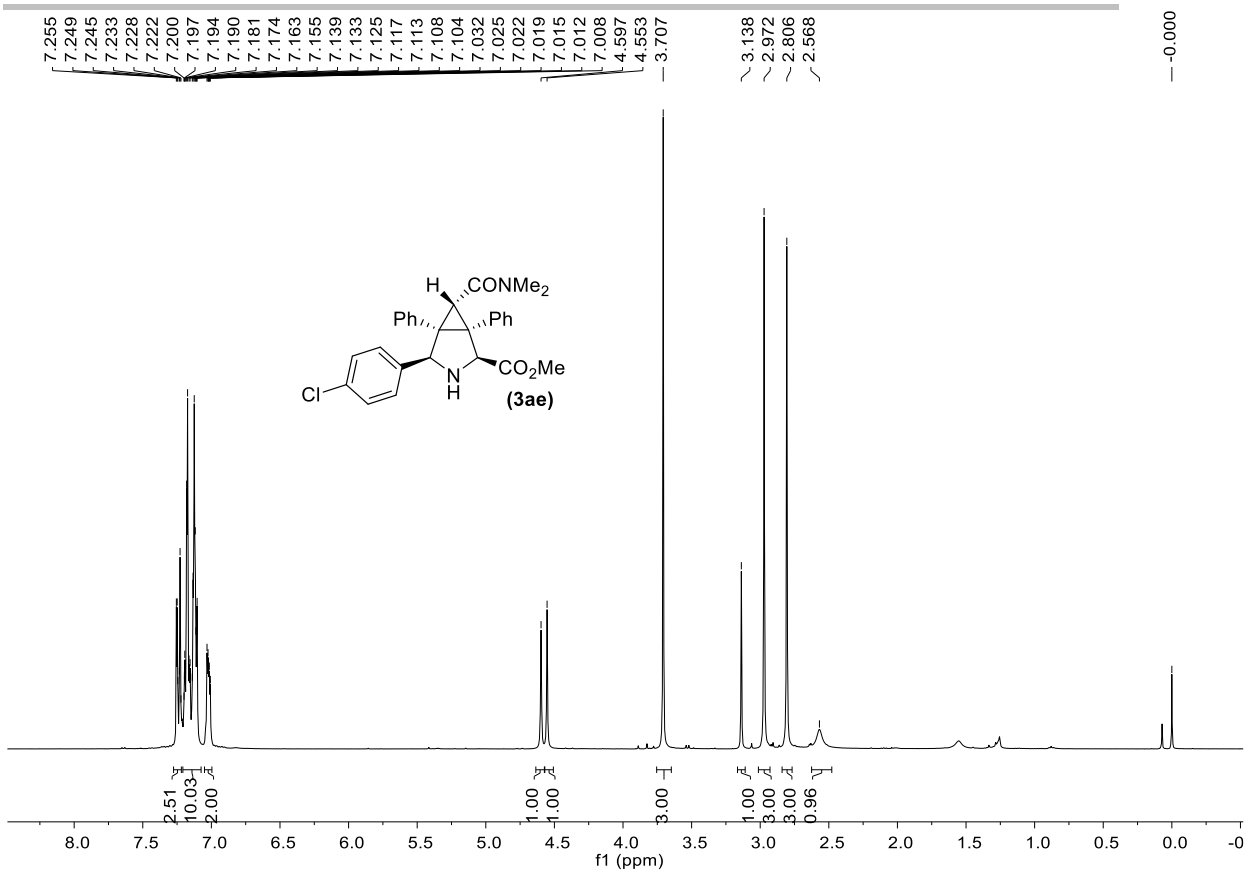
^{1}H NMR spectrum of compound **3ad** ($CDCl_3$)



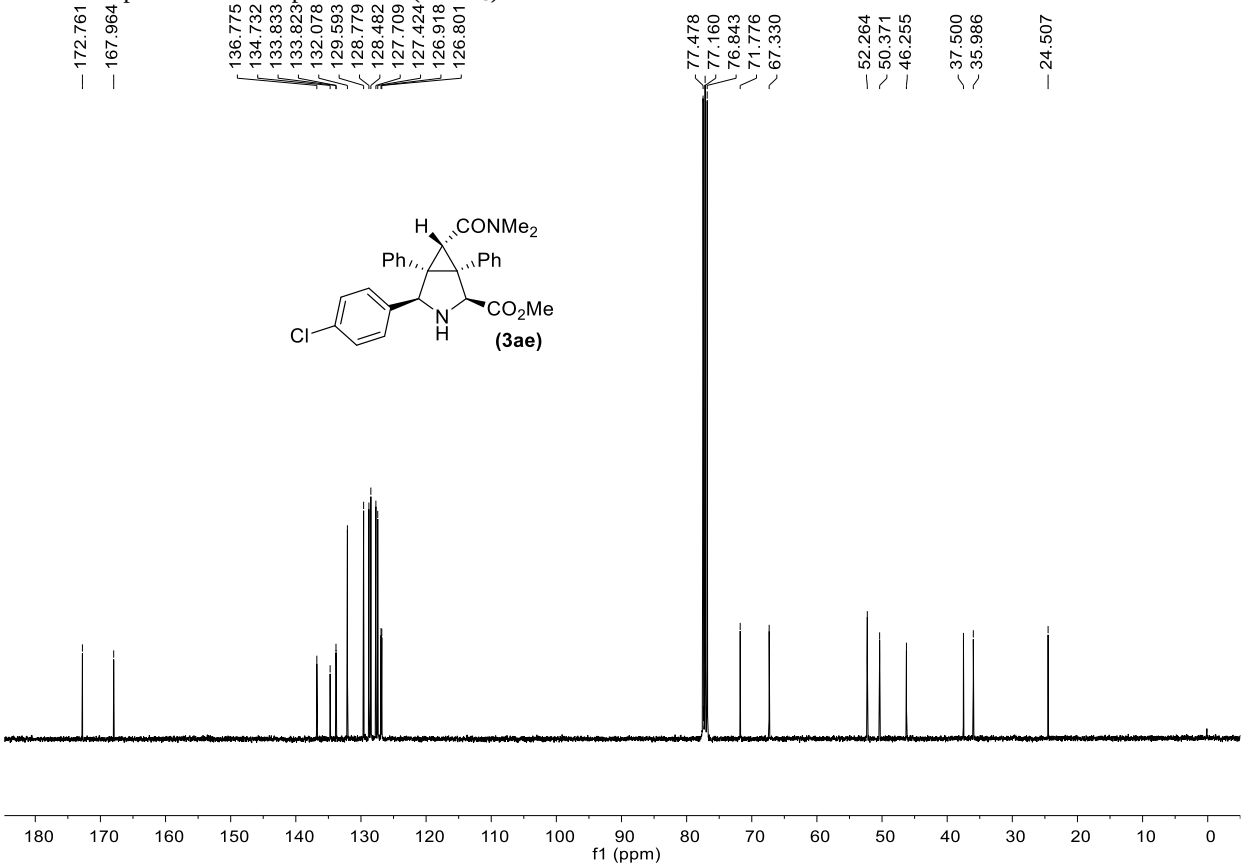
^{13}C NMR spectrum of compound **3ad** ($CDCl_3$)



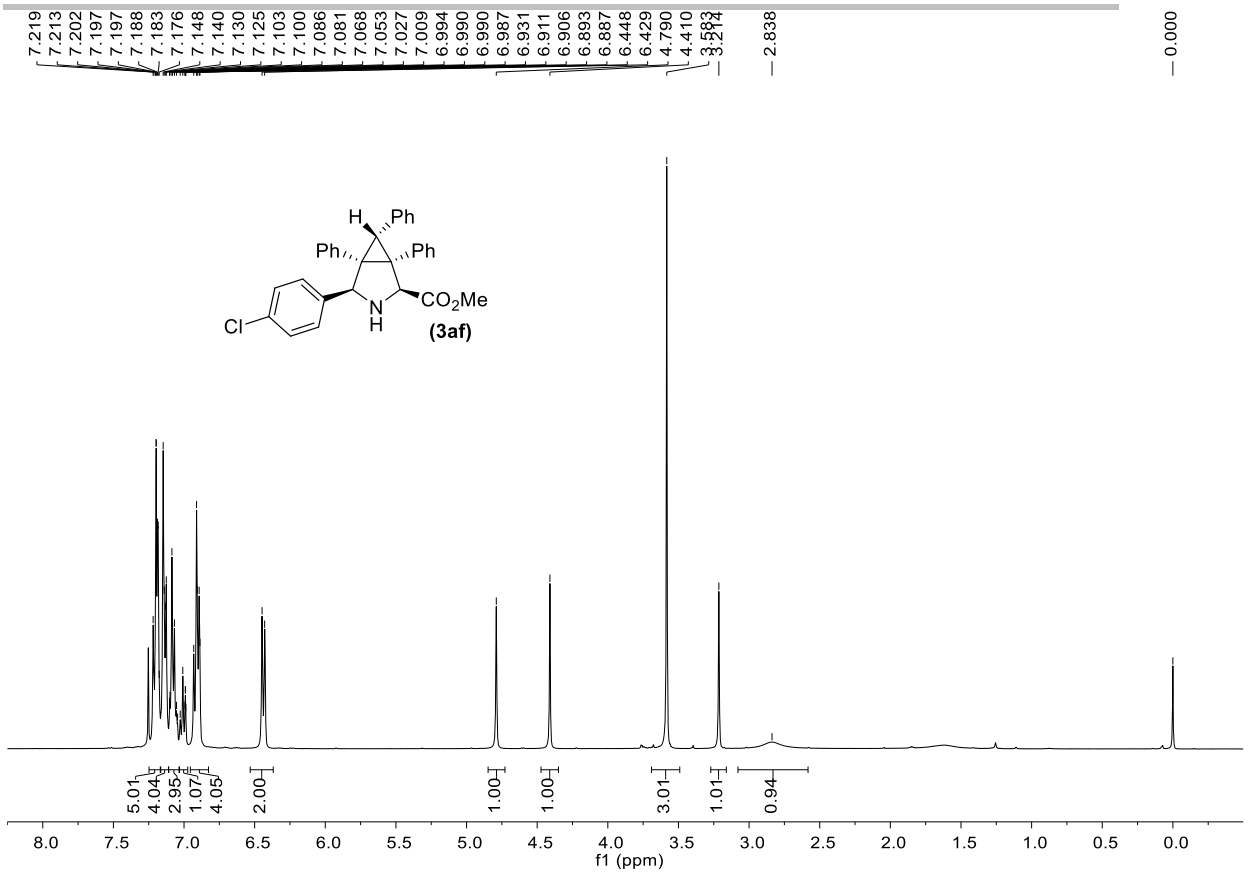
^{1}H NMR spectrum of compound **3ae** ($CDCl_3$)



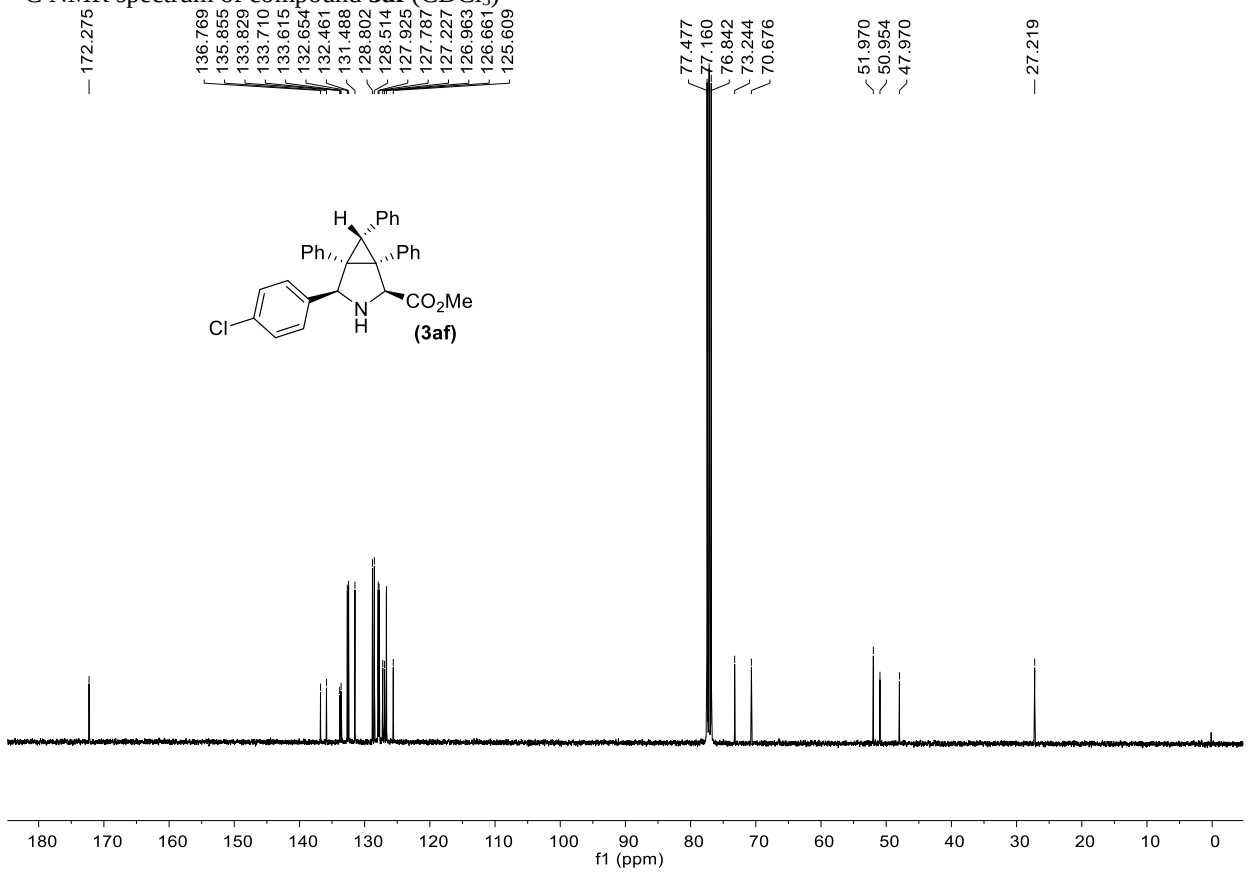
^{13}C NMR spectrum of compound **3ae** ($CDCl_3$)



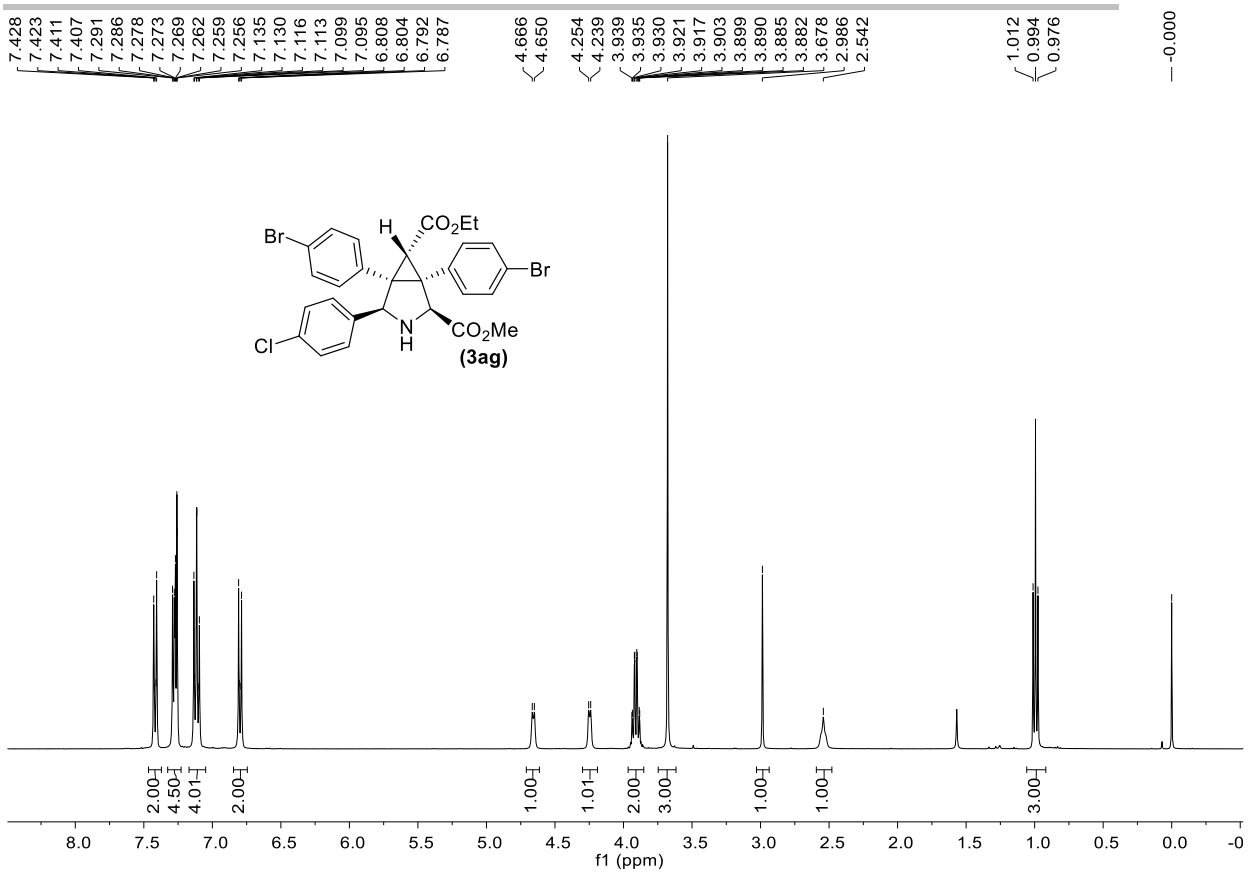
^{1}H NMR spectrum of compound **3af** ($CDCl_3$)



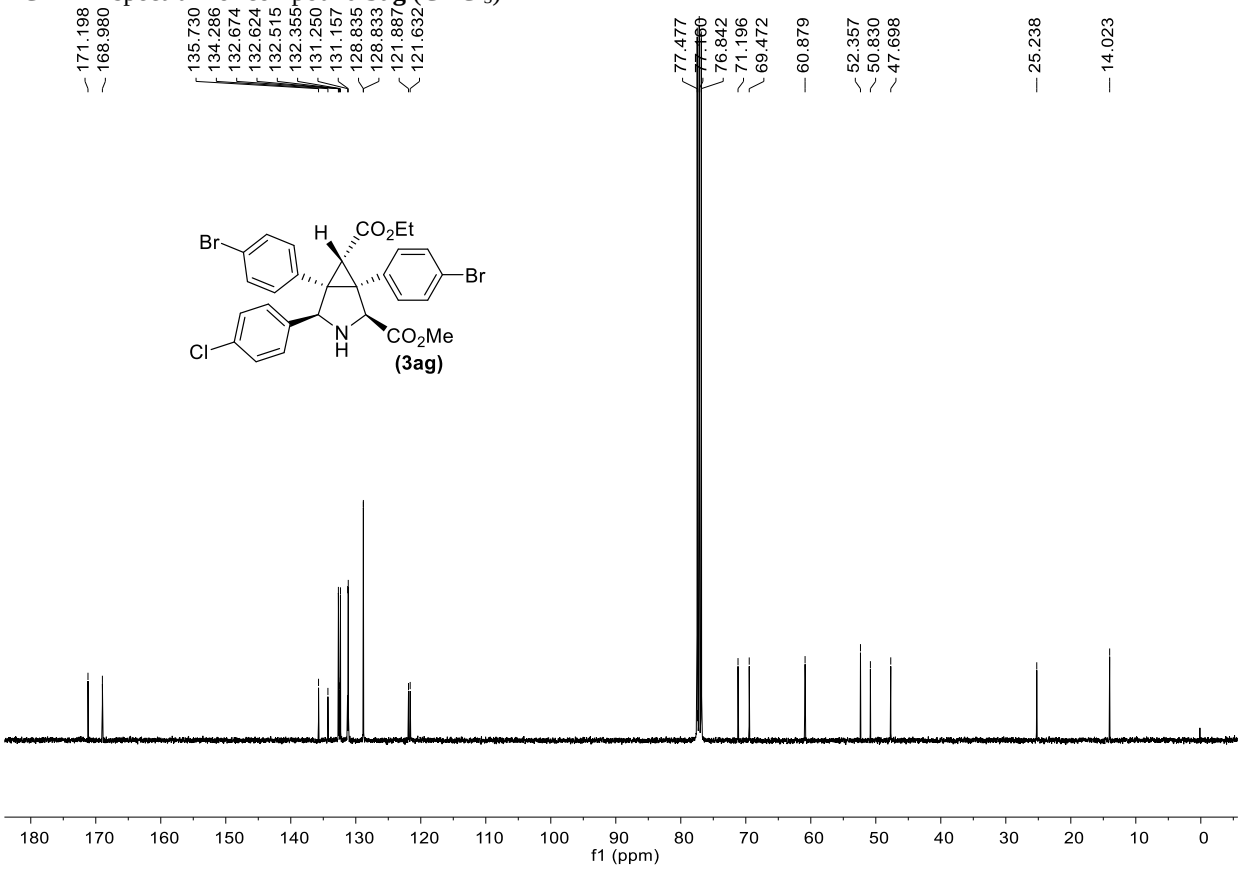
^{13}C NMR spectrum of compound **3af** ($CDCl_3$)



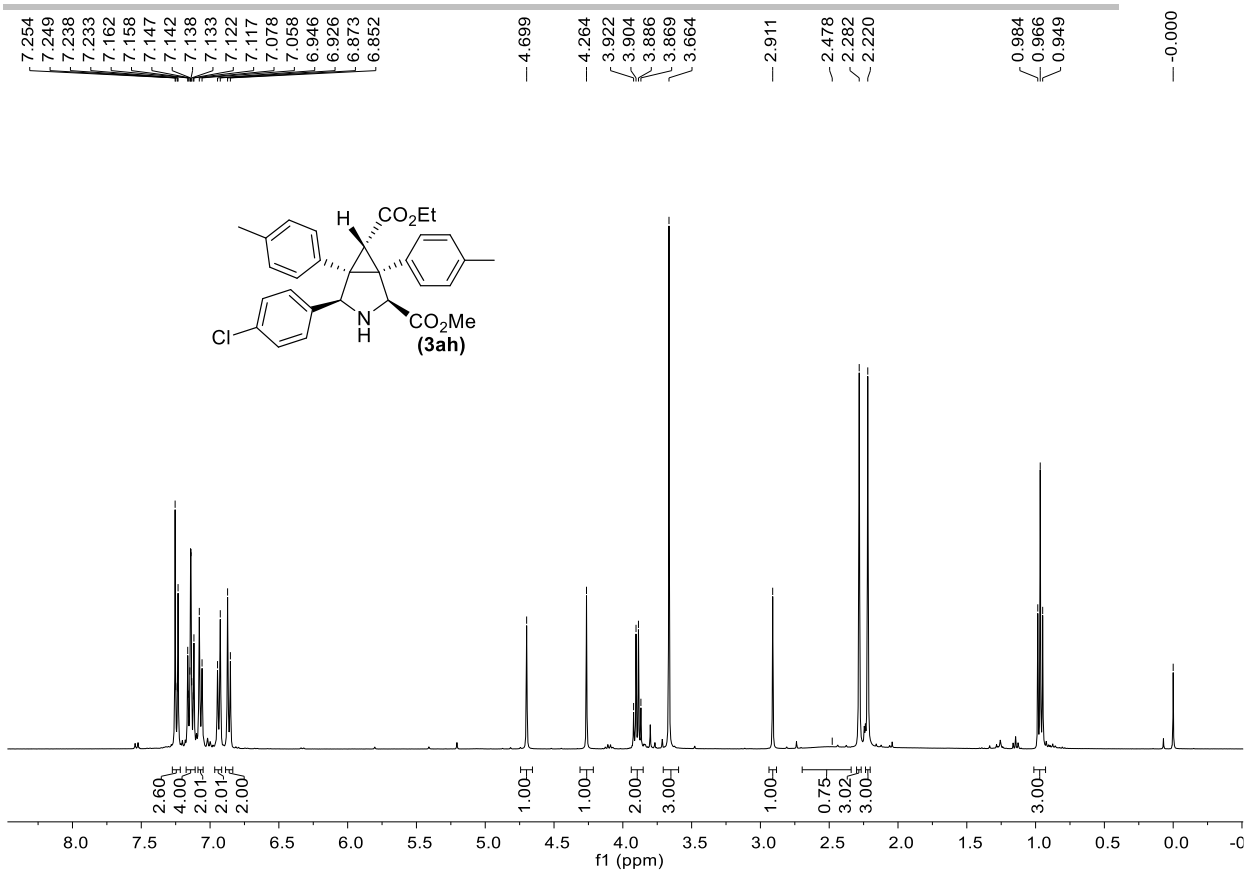
^{1}H NMR spectrum of compound **3ag** ($CDCl_3$)



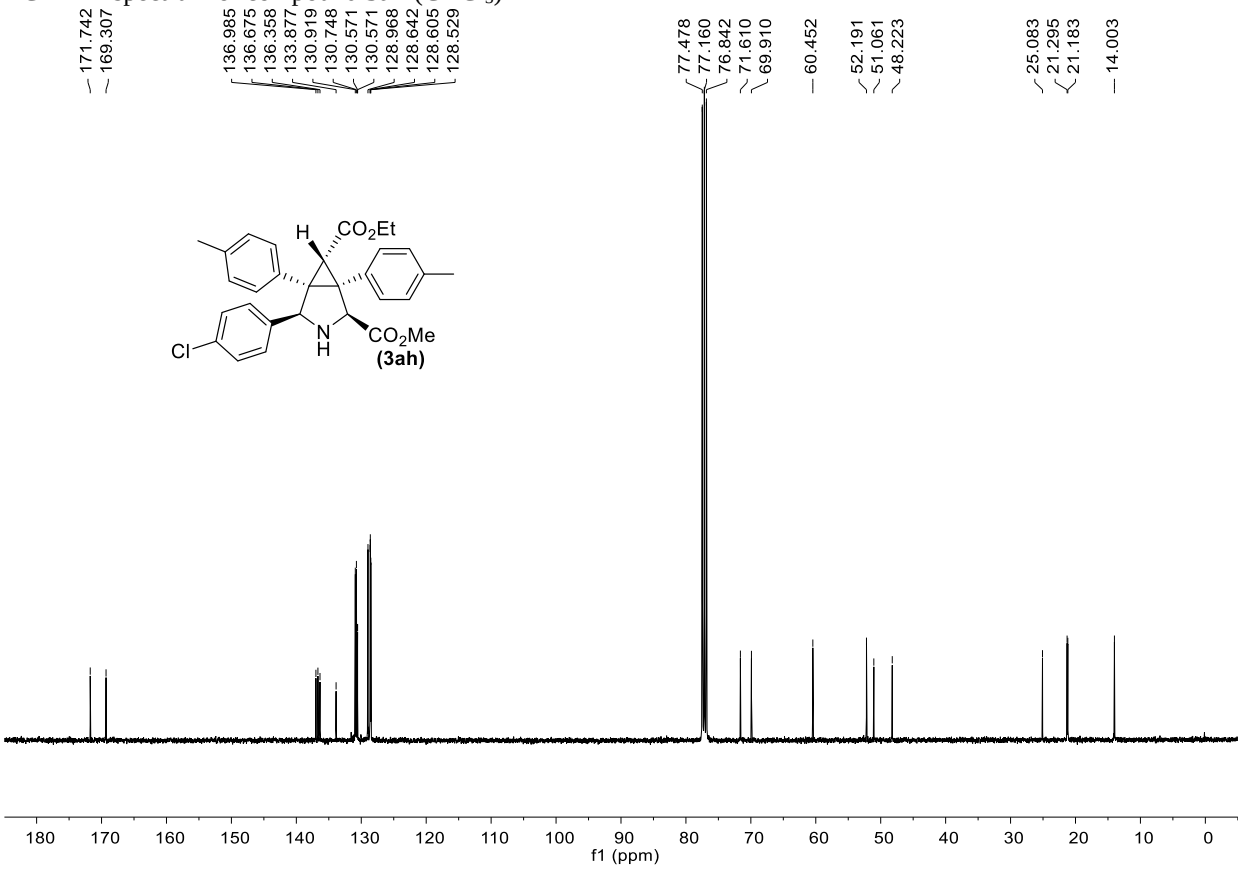
^{13}C NMR spectrum of compound **3ag** ($CDCl_3$)



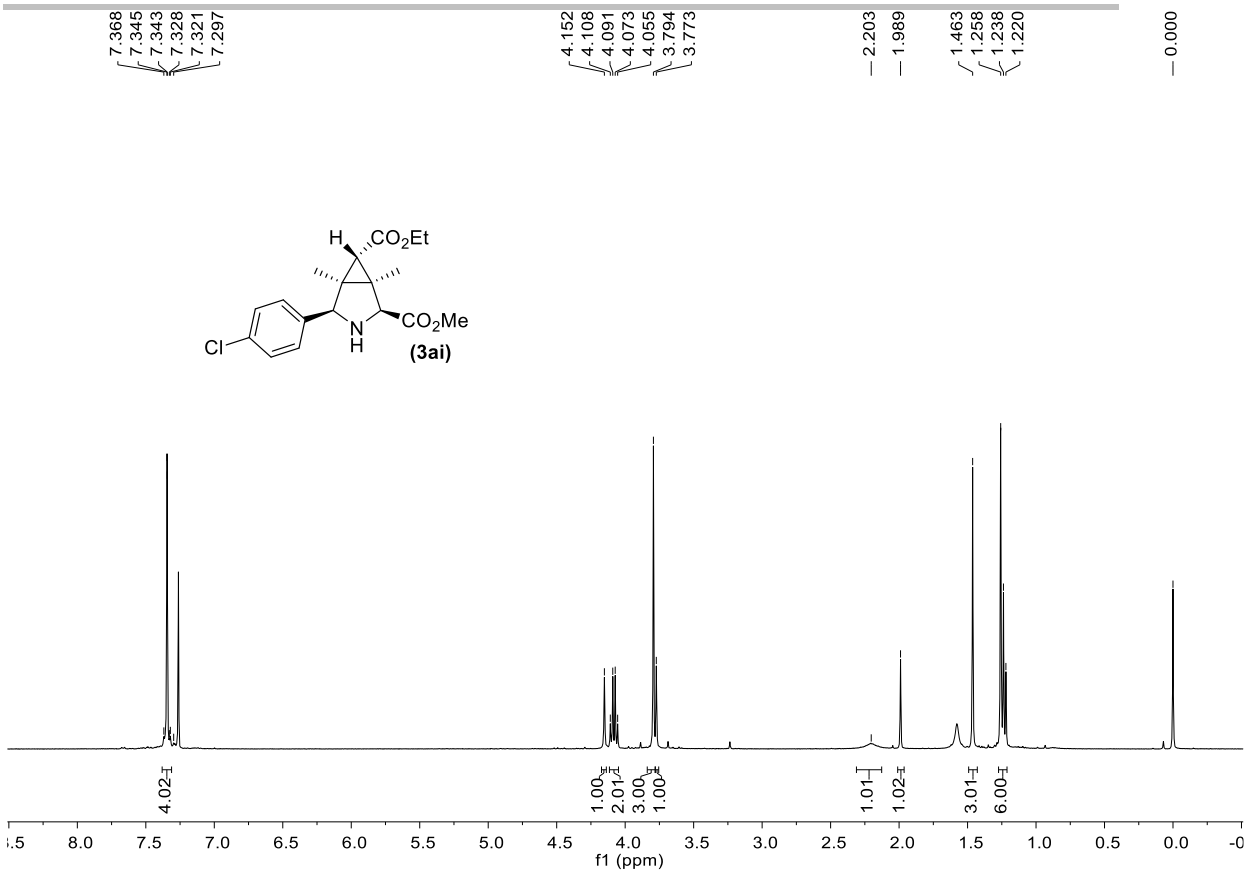
^{1}H NMR spectrum of compound **3ah** ($CDCl_3$)



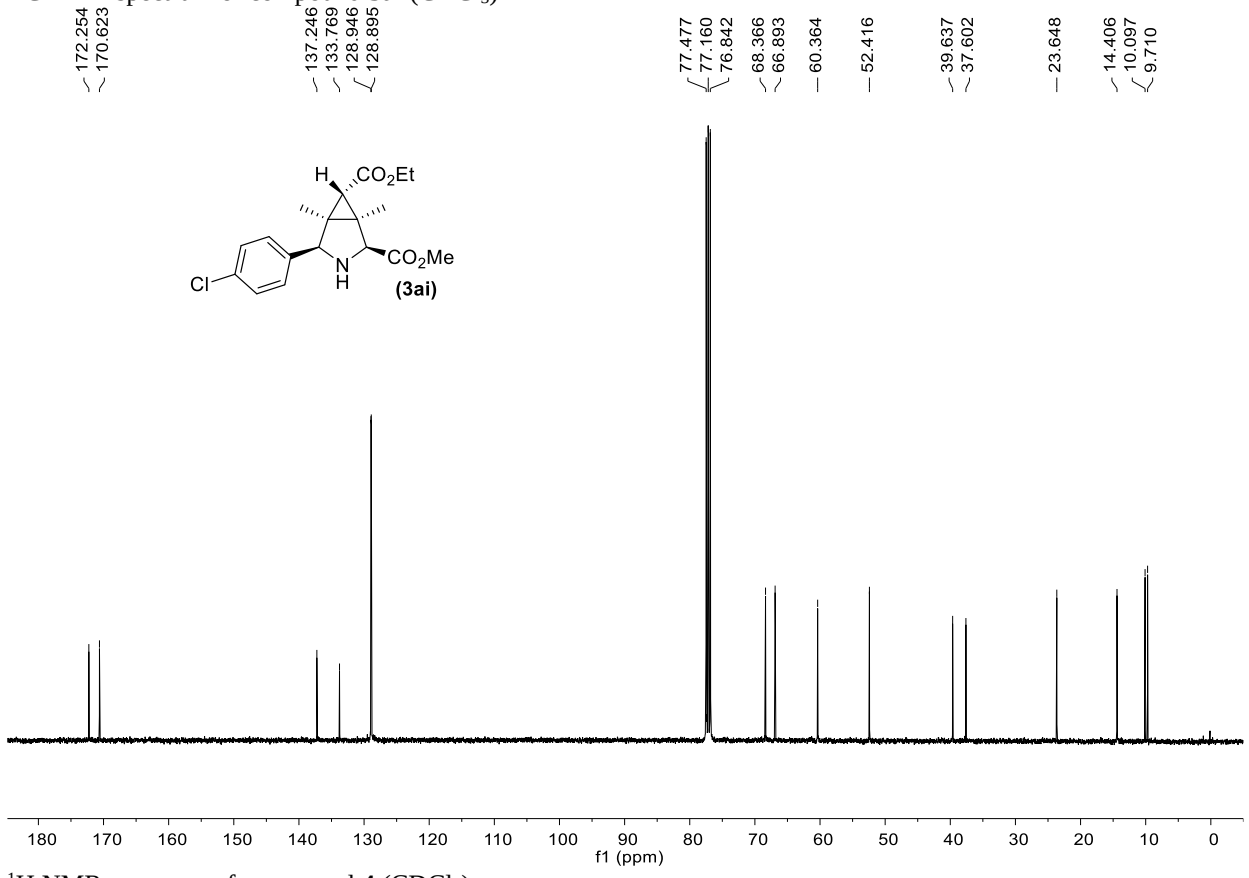
^{13}C NMR spectrum of compound **3ah** ($CDCl_3$)



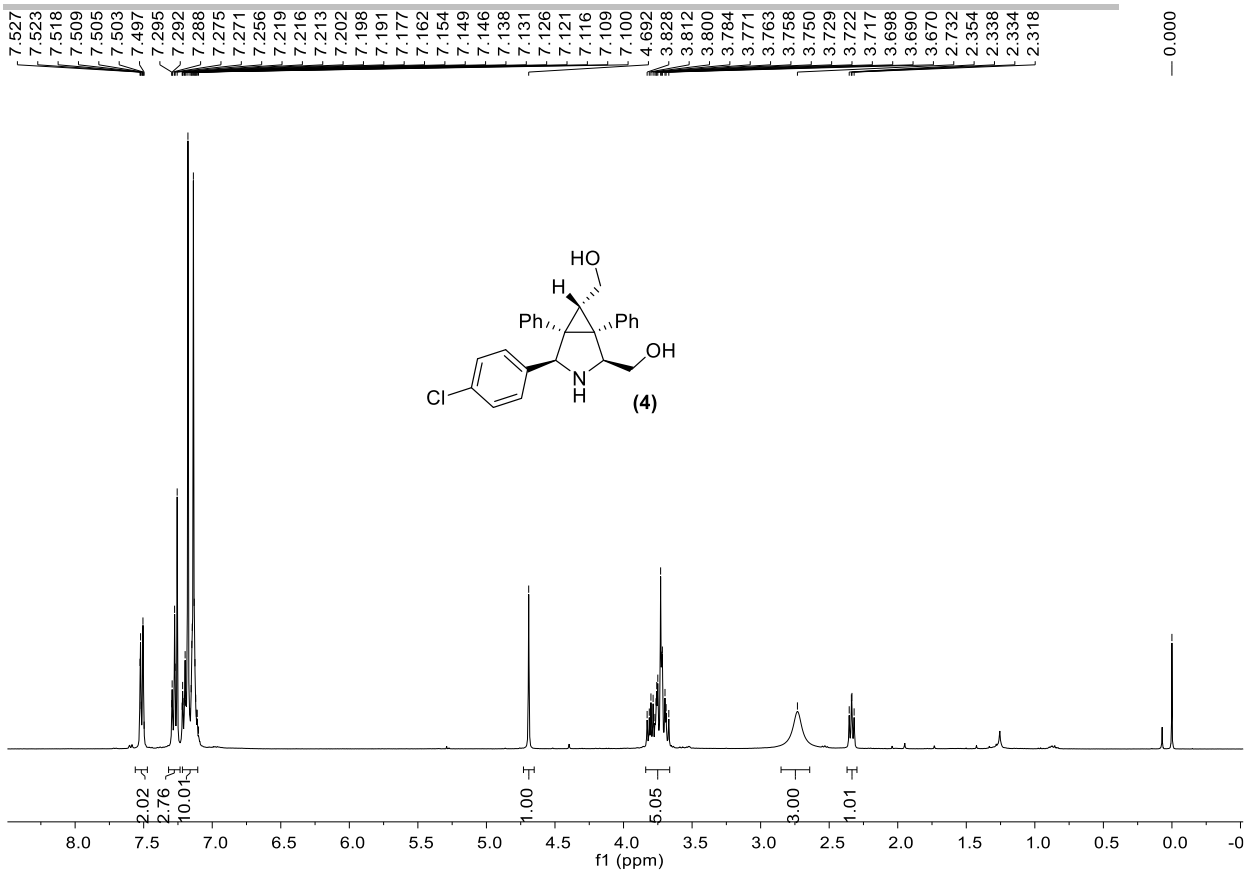
^{1}H NMR spectrum of compound **3ai** ($CDCl_3$)



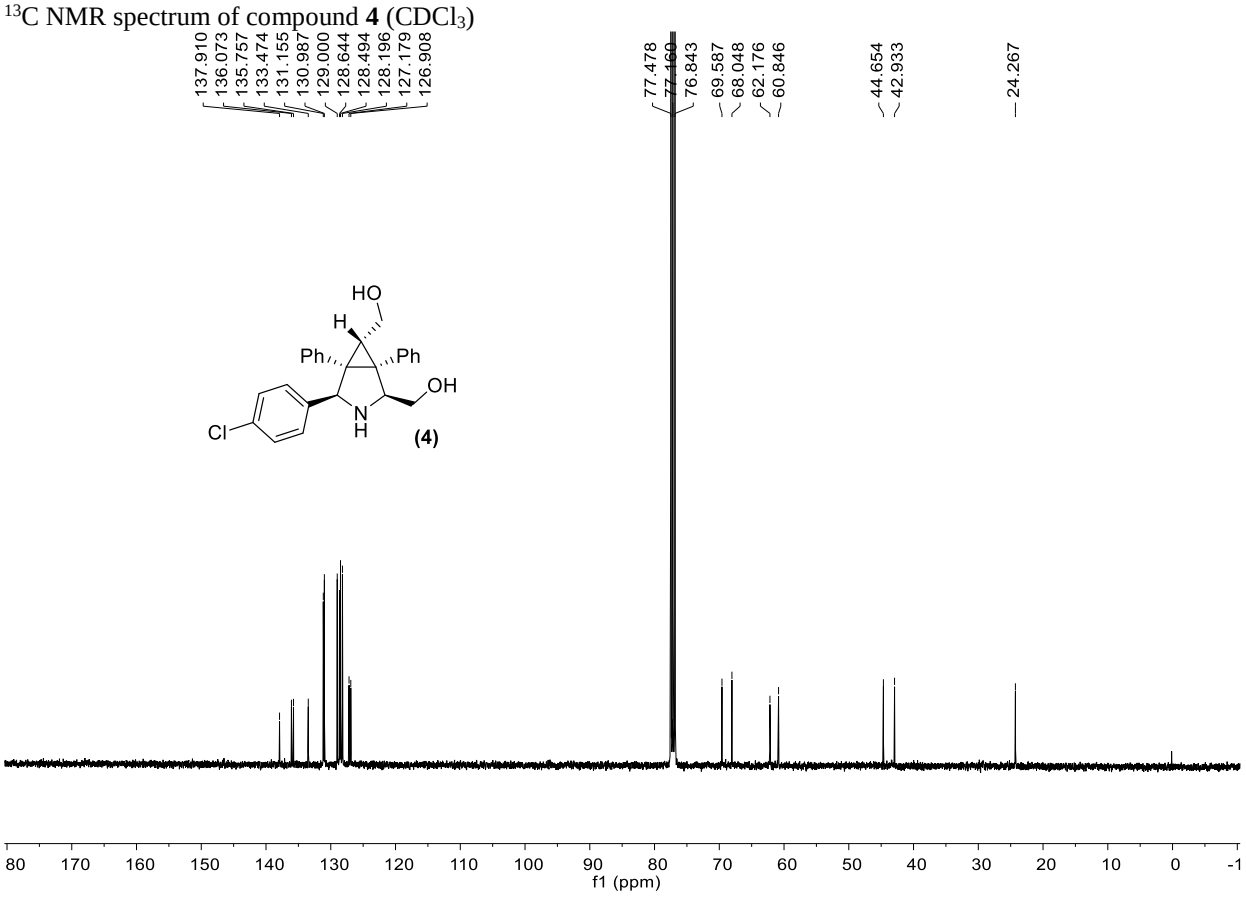
^{13}C NMR spectrum of compound **3ai** ($CDCl_3$)



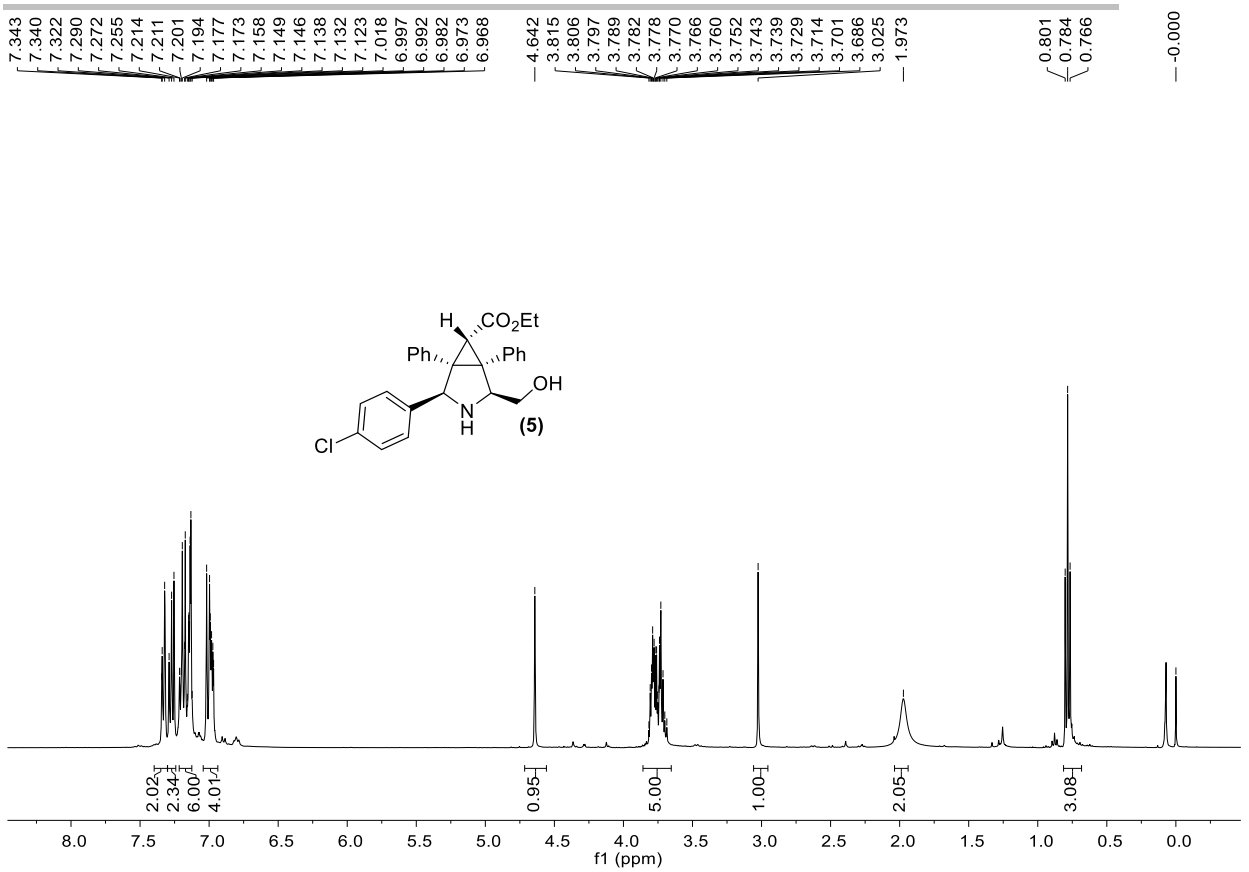
^{1}H NMR spectrum of compound **4** ($CDCl_3$)



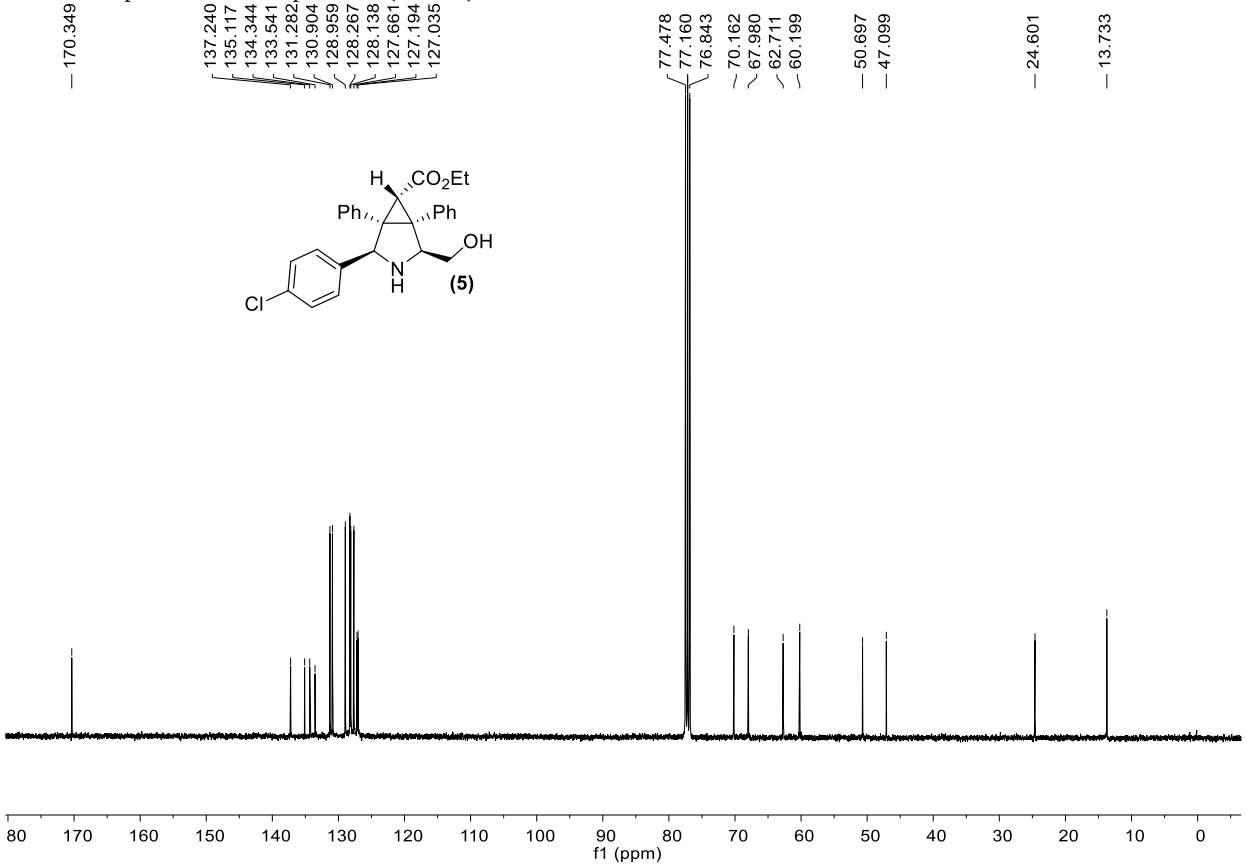
^{13}C NMR spectrum of compound **4** ($CDCl_3$)



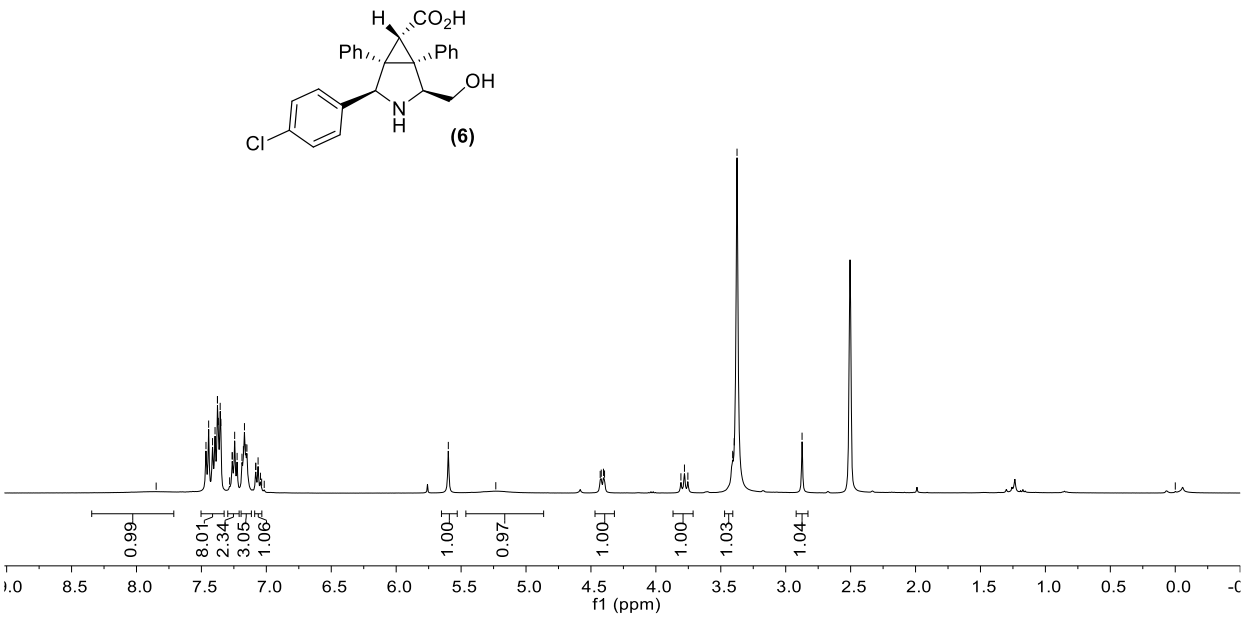
^{1}H NMR spectrum of compound **5** ($CDCl_3$)



^{13}C NMR spectrum of compound **5** ($CDCl_3$)



^{1}H NMR spectrum of compound **6** (DMSO-d_6)



^{13}C NMR spectrum of compound **6** (DMSO-d_6)