Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

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1. General information

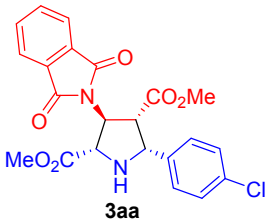
^{1}H NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ or D_2O. Chemical shifts were reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The spectrums are interpreted as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet. ^{13}C NMR (100 MHz) spectra were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ or D_2O. Chemical shifts are reported in ppm with the internal chloroform signal at 77.16 ppm as a standard. Optical rotations were measured on an AUTOPOL V. Diastereomeric ratios were determined from crude ^{1}H NMR spectroscopy interpretation. Enantiomer ratios were determined by analysis of HPLC traces, obtained by using chiralpak AD-H, IA or IF columns with *n*-hexane and *i*-propanol as solvents. (Chiralpak AD-H, IA and IF 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 are uncorrected. Mass spectrometry was performed on a TOF mass spectrometer.

Commercially available materials purchased from Adamas-beta, TCI or Energy Chemical and were used as received. The *β*-phthaliminoacrylate esters **2** were synthesised according to reported literature methods.[1]

2. General procedure for the asymmetric 1,3-dipolar addition of azomethine ylides 1 with *β*-phthaliminoacrylate esters 2

Under a nitrogen atmosphere, $Cu(CH_3CN)_4BF_4$ (3.1 mg, 0.01 mmol) and **L5** (5.7 mg, 0.011 mmol) were dissolved in 2 mL THF, and stirred at room temperature for about 1 h. Then, imino ester **1** (0.3 mmol) and K_2CO_3 (0.4 mmol) were added, the mixture was cooled to 0 °C and *β*-phthaliminoacrylate ester **2** (0.2 mmol) was added. Once starting material was consumed (monitored by TLC), the mixture was filtered through celite and the filtrate was concentrated to dryness. The crude product was analysed by ^{1}H NMR spectroscopy to determine the diastereomeric ratio, then the residue was purified by column chromatography (petroleum ether/ethyl acetate 6:1 to 2:1) on silica gel to give the corresponding product **3**, which was then directly analysed by chiral HPLC to determine the enantiomeric excess.

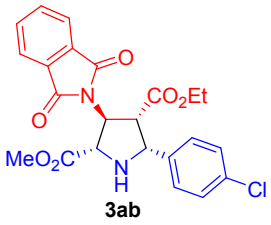
Dimethyl (2*S*,3*S*,4*R*,5*R*)-5-(4-chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl)pyrrolidine-2,4-dicarboxylate (3aa): 84.1 mg, 95% yield, >99% ee, white solid, m.p.: 70-72 °C; $[\alpha]_D^{27}$ = -83.4 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.32 (s, 4H), 5.24 (dd, *J* = 8.5, 6.1 Hz, 1H), 5.13 (t, *J* = 8.6 Hz, 1H), 4.34 (t, *J* = 8.6 Hz, 1H), 3.90 (dd, *J* = 8.3, 6.3 Hz, 1H), 3.74 (s, 3H), 3.24 (s, 3H), 2.90 (t, *J* = 8.7 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.8, 171.5, 167.7, 136.9, 134.5, 133.7, 131.7, 128.5, 128.5, 123.7, 63.7, 62.0, 55.4, 53.3, 52.7, 51.9; **HRMS** (EI,



3aa

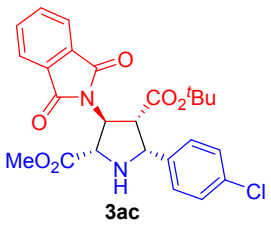
m/z): Calcd for $C_{22}H_{19}ClN_2O_6$ $[M]^+$: 442.0932, found: 442.0931; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 17.55 min, 30.27 min.

4-Ethyl 2-methyl (2*S*,3*S*,4*R*,5*R*)-5-(4-chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl)pyrrolidine-2,4-dicarboxylate (3ab): 83.0 mg, 91% yield, 99% ee, white solid, m.p.: 56-58 °C; $[\alpha]_D^{27}$ = -67.5 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.77 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.36 – 7.29 (m, 4H), 5.24 (dd, *J* = 8.4, 6.1 Hz, 1H), 5.14 (d, *J* = 8.5 Hz, 1H), 4.34 (d, *J* = 8.6 Hz, 1H), 3.87 (dd, *J* = 8.2, 6.2 Hz, 1H), 3.74 (s, 3H), 3.73 – 3.60 (m, 2H), 2.96 (brs, 1H), 0.83 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.5, 171.4, 167.7, 136.9, 134.5, 133.7, 131.7, 128.6, 128.5, 123.7, 63.7, 62.0, 61.1, 55.5, 53.3, 52.7, 13.7; **HRMS** (ESI, m/z): Calcd for $C_{23}H_{21}ClN_2O_6Na$ $[M+Na]^+$: 479.0986, found: 479.0981; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 17.18 min, 28.18 min.



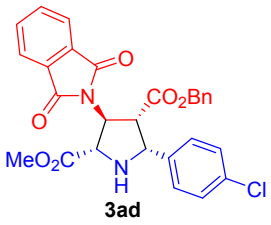
3ab

4-(*tert*-Butyl) 2-methyl (2*S*,3*S*,4*R*,5*R*)-5-(4-chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl) pyrrolidine-2,4-dicarboxylate (3ac): 91.0 mg, 94% yield, >99% ee, white soild, m.p.: 68-70 °C; $[\alpha]_D^{27}$ = -53.0 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.77 (dd, *J* = 5.2, 3.1 Hz, 2H), 7.38 – 7.31 (m, 4H), 5.15 (dd, *J* = 8.5, 5.9 Hz, 1H), 5.12 (d, *J* = 8.4 Hz, 1H), 4.30 (d, *J* = 8.5 Hz, 1H), 3.77 (dd, *J* = 8.3, 5.8 Hz, 1H), 3.74 (s, 3H), 1.04 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.6, 170.5, 167.7, 137.1, 134.5, 133.4, 131.7, 128.8, 128.4, 123.7, 81.9, 63.7, 62.2, 56.2, 53.9, 52.7, 27.5; **HRMS** (ESI, m/z): Calcd for $C_{25}H_{26}ClN_2O_6$ $[M+H]^+$: 485.1479, found: 485.1477; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 12.17 min, 14.38 min.



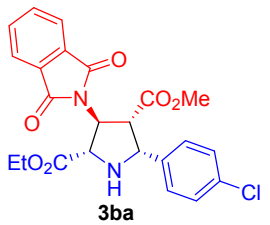
3ac

4-Benzyl 2-methyl (2*S*,3*S*,4*R*,5*R*)-5-(4-chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl) pyrrolidine-2,4-dicarboxylate (3ad): 99.4 mg, 96% yield, >99% ee, white soild, m.p.: 57-59 °C; $[\alpha]_D^{27}$ = -77.3 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 5.1, 3.2 Hz, 2H), 7.76 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.30 – 7.23 (m, 5H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 6.7 Hz, 2H), 5.28 (dd, *J* = 8.4, 5.9 Hz, 1H), 5.12 (d, *J* = 8.4 Hz, 1H), 4.72 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.33 (d, *J* = 8.5 Hz, 1H), 3.90 (dd, *J* = 8.3, 5.9 Hz, 1H), 3.74 (s, 3H), 2.95 (brs, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.4, 171.4, 167.7, 136.6, 134.7, 134.5, 133.7, 131.7, 128.7, 128.5, 128.5, 128.5, 128.4, 123.7, 67.1, 63.8, 62.1, 55.6, 53.3, 52.7; **HRMS** (EI, m/z): Calcd for $C_{28}H_{23}ClN_2O_6$ $[M]^+$: 518.1245, found: 518.1248; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 21.43 min, 31.43 min.



3ad

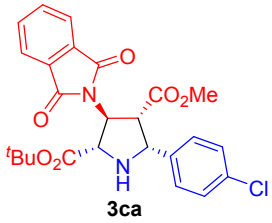
2-Ethyl 4-methyl (2*S*,3*S*,4*R*,5*R*)-5-(4-chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl)pyrrolidine-2,4-dicarboxylate (3ba): 83.0 mg, 91% yield, 96% ee, white soild, m.p.: 58-60 °C; $[\alpha]_D^{27}$ = -75.8 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.1, 3.2 Hz, 2H), 7.77 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.32 (s, 4H), 5.23 (dd, *J* = 8.5, 6.5 Hz, 1H), 5.12 (d, *J* = 8.6 Hz, 1H), 4.32 (d, *J* = 8.7 Hz, 1H), 4.29 – 4.10 (m, 2H), 3.93 (dd, *J* = 8.2, 6.6 Hz, 1H), 3.24 (s, 3H), 2.95 (brs, 1H), 1.16 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.8, 171.0, 167.7, 137.0, 134.5, 133.7, 131.7, 128.5, 128.5, 123.7, 63.6, 62.0, 61.7, 55.4, 53.2, 51.9, 14.0; **HRMS** (EI, m/z): Calcd for $C_{23}H_{21}ClN_2O_6$ $[M]^+$: 456.1088, found: 456.1089; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R =



3ba

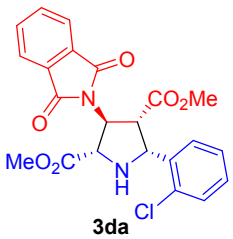
20.01 min, 32.80 min.

2-(*tert*-Butyl) 4-methyl (2*S*,3*S*,4*R*,5*R*)-5-(4-chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl) pyrrolidine-2,4-dicarboxylate (3ca): 89.1 mg, 92% yield, 92% ee, white soild, m.p.: 142-144 °C; $[\alpha]_D^{27}$ = -83.0 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.32 (s, 4H), 5.16 (dd, *J* = 8.7, 6.5 Hz, 1H), 5.10 (d, *J* = 8.6 Hz, 1H), 4.22 (d, *J* = 8.8 Hz, 1H), 3.94 (dd, *J* = 8.4, 6.6 Hz, 1H), 3.24 (s, 3H), 1.37 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.9, 170.1, 167.7, 137.1, 134.5, 133.6, 131.7, 128.5, 128.4, 123.6, 82.6, 63.5, 62.4, 55.5, 53.3, 51.8, 27.8; **HRMS** (EI, m/z): Calcd for $C_{25}H_{25}ClN_2O_6$ $[M]^+$: 484.1401, found: 484.1405; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 14.02 min, 29.80 min.



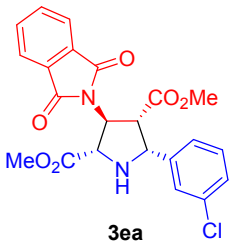
3ca

Dimethyl (2*S*,3*S*,4*R*,5*R*)-5-(2-chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl)pyrrolidine-2,4-dicarboxylate (3da): 85.0 mg, 96% yield, >99% ee, white soild, m.p.: 71-72 °C; $[\alpha]_D^{27}$ = -70.8 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 5.2, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.2, 3.1 Hz, 2H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.24 (t, *J* = 7.8 Hz, 1H), 5.52 (d, *J* = 8.0 Hz, 1H), 5.30 (dd, *J* = 8.2, 4.5 Hz, 1H), 4.35 (d, *J* = 8.2 Hz, 1H), 3.97 (dd, *J* = 8.0, 4.5 Hz, 1H), 3.76 (s, 3H), 3.14 (s, 3H), 3.00 (brs, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.2, 171.3, 167.7, 135.4, 134.5, 133.8, 131.8, 129.3, 129.0, 127.2, 126.8, 123.7, 62.3, 61.7, 55.5, 52.7, 52.0, 51.8; **HRMS** (EI, m/z): Calcd for $C_{22}H_{19}ClN_2O_6$ $[M]^+$: 442.0932, found: 442.0930; **HPLC** (Chiralpak IF, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 220 nm) t_R = 51.53 min, 59.16 min.



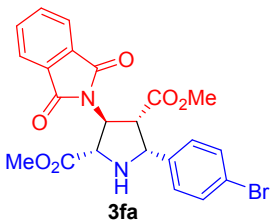
3da

Dimethyl (2*S*,3*S*,4*R*,5*R*)-5-(3-chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl)pyrrolidine-2,4-dicarboxylate (3ea): 81.4 mg, 92% yield, 95% ee, white soild, m.p.: 126-129 °C; $[\alpha]_D^{27}$ = -61.7 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.77 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.39 (s, 1H), 7.27 (d, *J* = 5.6 Hz, 3H), 5.25 (dd, *J* = 8.5, 6.0 Hz, 1H), 5.13 (d, *J* = 8.5 Hz, 1H), 4.34 (d, *J* = 8.6 Hz, 1H), 3.89 (dd, *J* = 8.3, 6.0 Hz, 1H), 3.75 (s, 3H), 3.26 (s, 3H), 2.96 (brs, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.7, 171.4, 167.7, 140.4, 134.5, 134.3, 131.7, 129.7, 128.1, 127.3, 125.2, 123.7, 63.8, 62.0, 55.3, 53.3, 52.7, 51.9; **HRMS** (EI, m/z): Calcd for $C_{22}H_{19}ClN_2O_6$ $[M]^+$: 442.0932, found: 442.0929; **HPLC** (Chiralpak IF, *n*-hexane/*i*-propanol = 80/20, 1.0 mL/min, 220 nm) t_R = 27.83 min, 42.50 min.



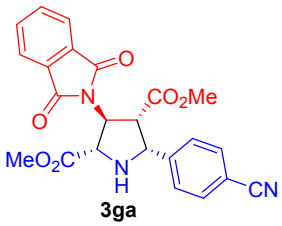
3ea

Dimethyl (2S,3S,4R,5R)-5-(4-bromophenyl)-3-(1,3-dioxoisoindolin-2-yl)pyrrolidine-2,4-dicarboxylate (3fa): 95.3 mg, 98% yield, 99% ee, white soild, m.p.: 69-70 °C; $[\alpha]_D^{27}$ = -67.3 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.0, 3.2 Hz, 2H), 7.77 (dd, *J* = 5.1, 3.1 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 3H), 5.24 (dd, *J* = 8.4, 6.1 Hz, 1H), 5.11 (d, *J* = 8.5 Hz, 1H), 4.34 (d, *J* = 8.6 Hz, 1H), 3.90 (dd, *J* = 8.2, 6.3 Hz, 1H), 3.74 (s, 3H), 3.25 (s, 3H), 2.96 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.8, 171.5, 167.7, 137.4, 134.5, 131.7, 131.5, 128.8, 123.7, 121.9, 63.7, 62.0, 55.4, 53.2, 52.7, 51.9; **HRMS** (EI, m/z): Calcd for $C_{22}H_{19}BrN_2O_6$ $[M]^+$: 486.0426, found: 486.0430; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 19.91 min, 33.08 min.



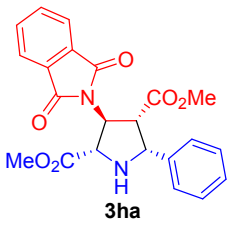
3fa

Dimethyl (2*S*,3*S*,4*R*,5*R*)-5-(4-cyanophenyl)-3-(1,3-dioxoisoindolin-2-yl)pyrrolidine-2,4-dicarboxylate (3ga): 84.2 mg, 97% yield, >99% ee, white soild, m.p.: 82-85 °C; $[\alpha]_D^{27}$ = -80.3 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.0, 2.9 Hz, 2H), 7.78 (dd, *J* = 4.9, 2.9 Hz, 2H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 5.26 (dd, *J* = 8.2, 6.2 Hz, 1H), 5.20 (d, *J* = 7.5 Hz, 1H), 4.37 (d, *J* = 7.7 Hz, 1H), 3.94 (dd, *J* = 8.1, 6.2 Hz, 1H), 3.75 (s, 3H), 3.22 (s, 3H), 2.93 (brs, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.4, 171.3, 167.7, 144.0, 134.6, 132.2, 131.7, 128.0, 123.8, 118.7, 111.8, 63.7, 61.9, 55.1, 53.1, 52.8, 52.0; **HRMS** (ESI, m/z): Calcd for $C_{23}H_{20}N_3O_6$ $[M+H]^+$: 434.1352, found: 434.1350; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 36.90 min, 77.02 min.



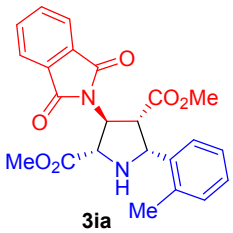
3ga

Dimethyl (2*S*,3*S*,4*R*,5*R*)-3-(1,3-dioxoisoindolin-2-yl)-5-phenylpyrrolidine-2,4-dicarboxylate (3ha): 78.1 mg, 96% yield, >99% ee, white soild, m.p.: 58-61 °C; $[\alpha]_D^{27}$ = -67.0 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.77 (dd, *J* = 5.2, 3.1 Hz, 2H), 7.40 – 7.27 (m, 5H), 5.25 (dd, *J* = 8.5, 6.2 Hz, 1H), 5.16 (d, *J* = 8.5 Hz, 1H), 4.35 (d, *J* = 8.7 Hz, 1H), 3.93 (dd, *J* = 8.3, 6.3 Hz, 1H), 3.74 (s, 3H), 3.18 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.0, 171.6, 167.7, 138.1, 134.5, 131.8, 128.4, 128.0, 127.0, 123.7, 64.5, 62.2, 55.6, 53.6, 52.7, 51.8; **HRMS** (ESI, m/z): Calcd for $C_{22}H_{21}N_2O_6$ $[M+H]^+$: 409.1400, found: 409.1401; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 13.25 min, 22.63 min.



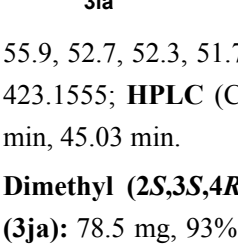
3ha

Dimethyl (2*S*,3*S*,4*R*,5*R*)-3-(1,3-dioxoisoindolin-2-yl)-5-(*o*-tolyl)pyrrolidine-2,4-dicarboxylate (3ia): 80.1 mg, 95% yield, >99% ee, white soild, m.p.: 164-167 °C; $[\alpha]_D^{27}$ = -81.6 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.38 – 7.31 (m, 1H), 7.23 – 7.14 (m, 3H), 5.34 (d, *J* = 7.9 Hz, 1H), 5.28 (dd, *J* = 8.3, 4.6 Hz, 1H), 4.28 (d, *J* = 8.2 Hz, 1H), 3.82 (dd, *J* = 8.0, 4.6 Hz, 1H), 3.76 (s, 3H), 3.11 (s, 3H), 3.06 (brs, 1H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.3, 171.4, 167.8, 136.2, 135.5, 134.5, 131.8, 130.1, 127.7, 126.0, 125.0, 123.7, 62.7, 61.9, 55.9, 52.7, 52.3, 51.7, 19.6; **HRMS** (ESI, m/z): Calcd for $C_{23}H_{23}N_2O_6$ $[M+H]^+$: 423.1556, found: 423.1555; **HPLC** (Chiralpak IF, *n*-hexane/*i*-propanol = 80/20, 0.8 mL/min, 220 nm) t_R = 41.13 min, 45.03 min.



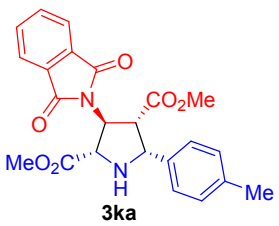
3ia

Dimethyl (2*S*,3*S*,4*R*,5*R*)-3-(1,3-dioxoisoindolin-2-yl)-5-(*m*-tolyl)pyrrolidine-2,4-dicarboxylate (3ja): 78.5 mg, 93% yield, 94% ee, white soild, m.p.: 51-54 °C; $[\alpha]_D^{27}$ = -71.9 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.17 (s, 1H), 7.15 (d, *J* = 7.7 Hz, 1H), 7.09 (d, *J* = 7.4 Hz, 1H), 5.24 (dd, *J* = 8.6, 5.9 Hz, 1H), 5.14 (d, *J* = 8.4 Hz, 1H), 4.34 (d, *J* = 8.6 Hz, 1H), 3.90 (dd, *J* = 8.4, 5.9 Hz, 1H), 3.75 (s, 3H), 3.21 (s, 3H), 2.36 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.1, 171.5, 167.7, 138.0, 137.8, 134.5, 131.8, 128.7, 128.3, 127.6, 124.0, 123.7, 64.6, 62.2, 55.7, 53.62, 52.7, 51.8, 21.5; **HRMS** (ESI, m/z): Calcd for $C_{23}H_{23}N_2O_6$ $[M+H]^+$: 423.1556, found: 423.1557; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 15.05 min, 18.04 min.



3ja

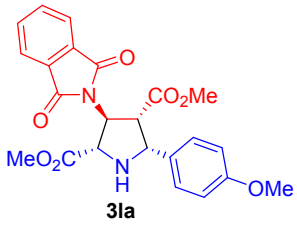
Dimethyl (2*S*,3*S*,4*R*,5*R*)-3-(1,3-dioxoisoindolin-2-yl)-5-(*p*-



3ka

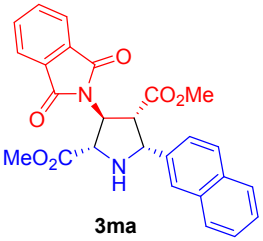
tolyl)pyrrolidine-2,4-dicarboxylate (3ka): 80.3 mg, 95% yield, 99% ee, white soild, m.p.: 64-66 °C; $[\alpha]_D^{27}$ = -66.7 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 5.24 (dd, *J* = 8.6, 6.2 Hz, 1H), 5.12 (d, *J* = 8.5 Hz, 1H), 4.34 (d, *J* = 8.7 Hz, 1H), 3.92 (dd, *J* = 8.4, 6.2 Hz, 1H), 3.74 (s, 3H), 3.22 (s, 3H), 2.33 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.1, 171.6, 167.7, 137.6, 135.0, 134.5, 131.8, 129.1, 126.9, 123.7, 64.3, 62.1, 55.6, 53.5, 52.7, 51.8, 21.2; **HRMS** (ESI, m/z): Calcd for $C_{23}H_{23}N_2O_6$ $[M+H]^+$: 423.1556, found: 423.1555; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 18.13 min, 30.73 min.

Dimethyl (2*S*,3*S*,4*R*,5*R*)-3-(1,3-dioxoisoindolin-2-yl)-5-(4-methoxyphenyl)pyrrolidine-2,4-dicarboxylate (3la): 85.0 mg, 97% yield, >99% ee, white soild, m.p.: 160-162 °C; $[\alpha]_D^{27}$ = -66.2 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.29 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.25 (dd, *J* = 8.7, 6.4 Hz, 1H), 5.10 (d, *J* = 8.6 Hz, 1H), 4.34 (d, *J* = 8.8 Hz, 1H), 3.92 (dd, *J* = 8.5, 6.4 Hz, 1H), 3.80 (s, 3H), 3.74 (s, 3H), 3.23 (s, 3H), 2.89 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.1, 171.6, 167.7, 159.2, 134.5, 131.8, 130.3, 128.2, 123.7, 113.7, 63.9, 62.0, 55.5, 55.4, 53.4, 52.7, 51.9; **HRMS** (ESI, m/z): Calcd for $C_{23}H_{23}N_2O_7$ $[M+H]^+$: 439.1505, found: 439.1507; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 24.28 min, 47.93 min.



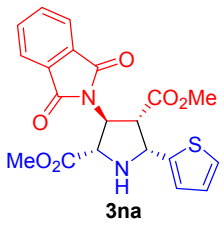
3la

Dimethyl (2*S*,3*S*,4*R*,5*R*)-3-(1,3-dioxoisoindolin-2-yl)-5-(naphthalen-2-yl)pyrrolidine-2,4-dicarboxylate (3ma): 86.0 mg, 94% yield, 98% ee, white soild, m.p.: 88-90 °C; $[\alpha]_D^{27}$ = -94.9 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.85 (d, *J* = 5.7 Hz, 2H), 7.82 (d, *J* = 8.6 Hz, 2H), 7.77 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.51 – 7.43 (m, 3H), 5.37 – 5.29 (m, 2H), 4.41 (d, *J* = 8.6 Hz, 1H), 3.99 (dd, *J* = 8.4, 5.8 Hz, 1H), 3.77 (s, 3H), 3.09 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.1, 171.6, 167.8, 135.6, 134.5, 133.3, 133.0, 131.8, 128.2, 128.0, 127.7, 126.3, 126.2, 125.7, 125.2, 123.7, 64.7, 62.4, 55.8, 53.7, 52.7, 51.8; **HRMS** (ESI, m/z): Calcd for $C_{26}H_{23}N_2O_6$ $[M+H]^+$: 459.1556, found: 459.1559; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 31.09 min, 40.44 min.



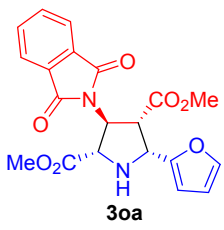
3ma

Dimethyl (2*S*,3*S*,4*R*,5*R*)-3-(1,3-dioxoisoindolin-2-yl)-5-(thiophen-2-yl)pyrrolidine-2,4-dicarboxylate (3na): 81.4 mg, 93% yield, >99% ee, yellow soild, m.p.: 60-62 °C; $[\alpha]_D^{27}$ = -62.7 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.24 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.05 (d, *J* = 3.5 Hz, 1H), 6.98 (dd, *J* = 5.0, 3.6 Hz, 1H), 5.33 (d, *J* = 8.2 Hz, 1H), 5.28 (dd, *J* = 8.7, 6.9 Hz, 1H), 4.33 (d, *J* = 8.7 Hz, 1H), 4.01 (dd, *J* = 8.2, 6.9 Hz, 1H), 3.73 (s, 3H), 3.40 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.5, 171.4, 167.7, 141.9, 134.5, 131.8, 127.0, 125.2, 125.0, 123.7, 61.6, 60.1, 55.0, 53.2, 52.8, 52.1; **HRMS** (ESI, m/z): Calcd for $C_{20}H_{18}N_2O_6SNa$ $[M+Na]^+$: 437.0783, found: 437.0783; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 18.99 min, 23.31 min.



3na

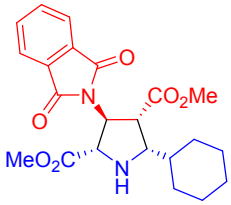
Dimethyl (2*S*,3*S*,4*R*,5*R*)-3-(1,3-dioxoisoindolin-2-yl)-5-(furan-2-yl)pyrrolidine-2,4-dicarboxylate (3oa): 64.5 mg, 81% yield, 98% ee, yellow soild, m.p.: 59-62 °C; $[\alpha]_D^{27}$ = -20.5 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 5.5, 3.0 Hz, 2H),



3oa

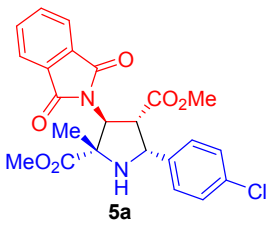
7.76 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.38 (dd, *J* = 1.7, 0.8 Hz, 1H), 6.35 (d, *J* = 3.1 Hz, 1H), 6.33 (dd, *J* = 3.2, 1.8 Hz, 1H), 5.34 (dd, *J* = 8.4, 7.6 Hz, 1H), 5.08 (d, *J* = 8.2 Hz, 1H), 4.27 (d, *J* = 8.6 Hz, 1H), 4.07 – 3.99 (m, 1H), 3.72 (s, 3H), 3.46 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.8, 171.2, 167.7, 152.0, 142.5, 134.4, 131.8, 123.7, 110.5, 107.9, 61.6, 58.3, 54.9, 52.8, 52.3, 51.6; **HRMS** (ESI, m/z): Calcd for $C_{20}H_{19}N_2O_7$ $[M+H]^+$: 399.1192, found: 399.1194; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 14.64 min, 18.65 min.

Dimethyl (2*S*,3*S*,4*R*,5*S*)-5-cyclohexyl-3-(1,3-dioxoisoindolin-2-yl)pyrrolidine-2,4-dicarboxylate (3pa): 72.0 mg, 87% yield, 98% ee, white soild, m.p.: 65-67 °C; $[\alpha]_D^{27}$ = -79.6 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.4, 3.0 Hz, 2H), 4.96 (dd, *J* = 7.7, 3.3 Hz, 1H), 4.07 (d, *J* = 7.7 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.33 (dd, *J* = 6.7, 3.3 Hz, 1H), 2.60 (s, 1H), 2.06 (d, *J* = 10.9 Hz, 1H), 1.88 – 1.57 (m, 5H), 1.35 – 1.19 (m, 4H), 1.18 – 1.02 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.2, 171.5, 167.6, 134.5, 131.8, 123.7, 68.7, 63.7, 57.7, 52.6, 52.2, 52.1, 39.5, 31.1, 31.1, 26.4, 26.0, 25.9; **HRMS** (ESI, m/z): Calcd for $C_{22}H_{27}N_2O_6$ $[M+H]^+$: 415.1869, found: 415.1868; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 7.27 min, 12.99 min.



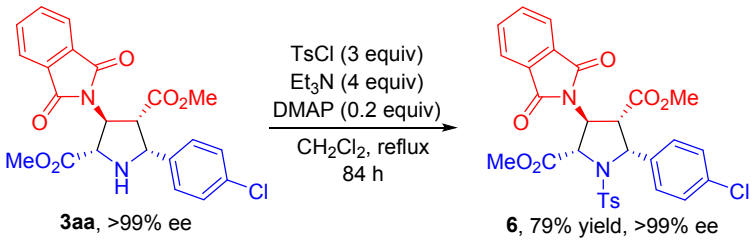
3pa

Dimethyl (2*S*,3*S*,4*R*,5*R*)-5-(4-chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl)-2-methylpyrrolidine-2,4-dicarboxylate (5a): 75.5 mg, 83% yield, >99% ee, white soild, m.p.: 167-169 °C; $[\alpha]_D^{27}$ = -44.1 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.39 – 7.30 (m, 4H), 5.28 (d, *J* = 8.9 Hz, 1H), 5.04 (d, *J* = 9.3 Hz, 1H), 4.74 (t, *J* = 9.1 Hz, 1H), 3.81 (s, 3H), 3.20 (s, 3H), 3.17 (brs, 1H), 1.47 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.4, 171.5, 168.3, 138.0, 134.5, 133.9, 131.6, 128.8, 128.6, 123.7, 68.1, 61.4, 59.0, 53.2, 51.8, 49.8, 20.8; **HRMS** (ESI, m/z): Calcd for $C_{23}H_{22}ClN_2O_6$ $[M+H]^+$: 457.1166, found: 457.1167; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 220 nm) t_R = 11.56 min, 15.14 min.



5a

3. Tosylation of cycloadduct 3aa for X-ray Determination



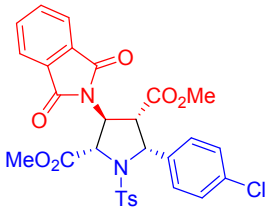
3aa, >99% ee

6, 79% yield, >99% ee

To a solution of compound **3aa** (177 mg, 0.4 mmol) in 3 mL CH_2Cl_2 was added TsCl (229 mg, 1.2 mmol), Et_3N (223 μL, 1.6 mmol), DMAP (10 mg, 0.08 mmol) sequentially, the mixture was

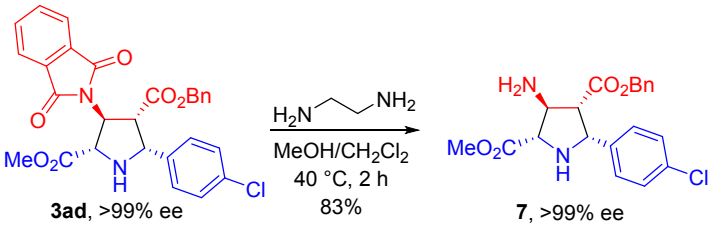
refluxed for 84 h. Then, the solvent was evaporated and the residue was purified by column chromatography (petroleum ether/ethyl acetate 6:1 to 2:1) to give the corresponding tosylated product **6** in 79% yield (189 mg). Recrystallisation in a mixture of Et_2O and *n*-hexane afforded crystal suitable for X-ray analysis.

Dimethyl (2*S*,3*S*,4*S*,5*R*)-5-(4-chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl)-1-tosylpyrrolidine-2,4-dicarboxylate (6): 189 mg, 79% yield, white soild, m.p.: 154-156 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.21 (t, *J* = 8.6 Hz, 4H), 5.33 (dd, *J* = 11.9, 10.1 Hz, 1H), 5.27 (d, *J* = 9.6 Hz, 1H), 4.86 (d, *J* = 10.0 Hz, 1H), 4.49 (dd, *J* = 11.9, 9.7 Hz, 1H), 3.77 (s, 3H), 3.29 (s, 3H), 2.42 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.6, 167.5, 167.3, 144.6, 135.7, 134.7, 134.4, 134.3, 131.4, 129.7, 129.2, 128.6, 128.2, 123.9, 62.0, 60.8, 53.3, 52.3, 52.2, 49.2, 21.7; **HRMS** (ESI, m/z): Calcd for $C_{29}H_{26}ClN_2O_8S$ $[M+H]^+$: 597.1093, found: 597.1092 ; **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 220 nm) t_R = 54.13 min, 64.00 min.



6

4. Transformation of cycloadduct 3ad

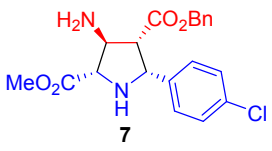


3ad, >99% ee

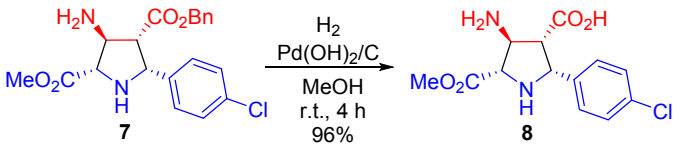
7, >99% ee

To a solution of compound **3ad** (207.6 mg, 0.4 mmol) in in a 1:1 mixture of CH_2Cl_2/MeOH (3 mL total) was added ethylenediamine (133 µL, 2.0 mmol). The reaction mixture was heated to 40 °C for 2 h. and then cooled to room temperature. After removing the solvent *in vacuo*, the residue was purified by column chromatography (CH_2Cl_2/MeOH = 60:1 to 20:1) to give the corresponding product **7** as a white solid in 83% yield (128.6 mg).

4-Benzyl 2-methyl (2*S*,3*S*,4*S*,5*R*)-3-amino-5-(4-chlorophenyl)pyrrolidine-2,4-dicarboxylate (7): 128.6 mg, 83% yield, white soild, m.p.: 104-106 °C; $[\alpha]_D^{27}$ = -36.9 (*c* 1.00, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 3H), 7.21 – 7.15 (m, 4H), 7.03 (dt, *J* = 4.5, 2.9 Hz, 2H), 4.77 (d, *J* = 12.0 Hz, 1H), 4.67 (t, *J* = 9.8 Hz, 2H), 3.97 (t, *J* = 7.6 Hz, 1H), 3.84 (s, 3H), 3.64 (d, *J* = 7.9 Hz, 1H), 3.17 (dd, *J* = 8.7, 7.3 Hz, 1H), 1.91 (brs, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.0, 171.1, 138.5, 135.1, 133.6, 128.8, 128.7, 128.6, 128.6, 128.5, 67.9, 66.8, 62.6, 59.0, 58.2, 52.7; **HRMS** (ESI, m/z): Calcd for $C_{20}H_{22}ClN_2O_4$ $[M+H]^+$: 389.1268, found: 389.1269; **HPLC** (Chiralpak AD-H, *n*-hexane/*i*-propanol = 80/20, 1.0 mL/min, 220 nm) t_R = 16.08 min, 22.49 min.

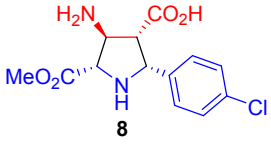


7



A Schlenk tube was charged with $Pd(OH)_2/C$ (7.0 mg, 20 wt%, 10 mol%) under vacuum and then refilled with hydrogen. Compound **7** (38.8 mg, 0.1 mmol) in MeOH was added, followed by vigorous stirring for 4 h at room temperature. The reaction mixture was pushed through a celite pad to remove $Pd(OH)_2/C$ and the filtrate was concentrated under reduced pressure to afford pyrrolidine *β*-amino acid **8** as a white solid in 96% yield (28.8 mg).

(2*R*,3*S*,4*S*,5*S*)-4-amino-2-(4-chlorophenyl)-5-(methoxycarbonyl)pyrrolidine-3-carboxylic



acid (8): 28.8 mg, 96% yield, white soild, m.p.: 180-182 °C; $[\alpha]_D^{27}$ = +16.9 (*c* 1.00, H_2O); **^{1}H NMR** (400 MHz, D_2O) δ 7.36 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.3 Hz, 2H), 4.70 (d, *J* = 8.2 Hz, 1H), 4.26 (t, *J* = 6.9 Hz, 1H), 4.10 (d, *J* = 7.5 Hz, 1H), 3.84 (s, 3H), 3.34 – 3.25 (m, 1H); **^{13}C NMR** (100 MHz, D_2O) δ 175.4, 171.9, 136.8, 133.0, 128.4, 128.3, 62.7, 62.0, 56.6, 55.9, 53.2; **HRMS** (ESI, m/z): Calcd for $C_{13}H_{16}ClN_2O_4$ $[M+H]^+$: 299.0799, found: 299.0798.

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

(CCDC 1495843 (**6**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.)

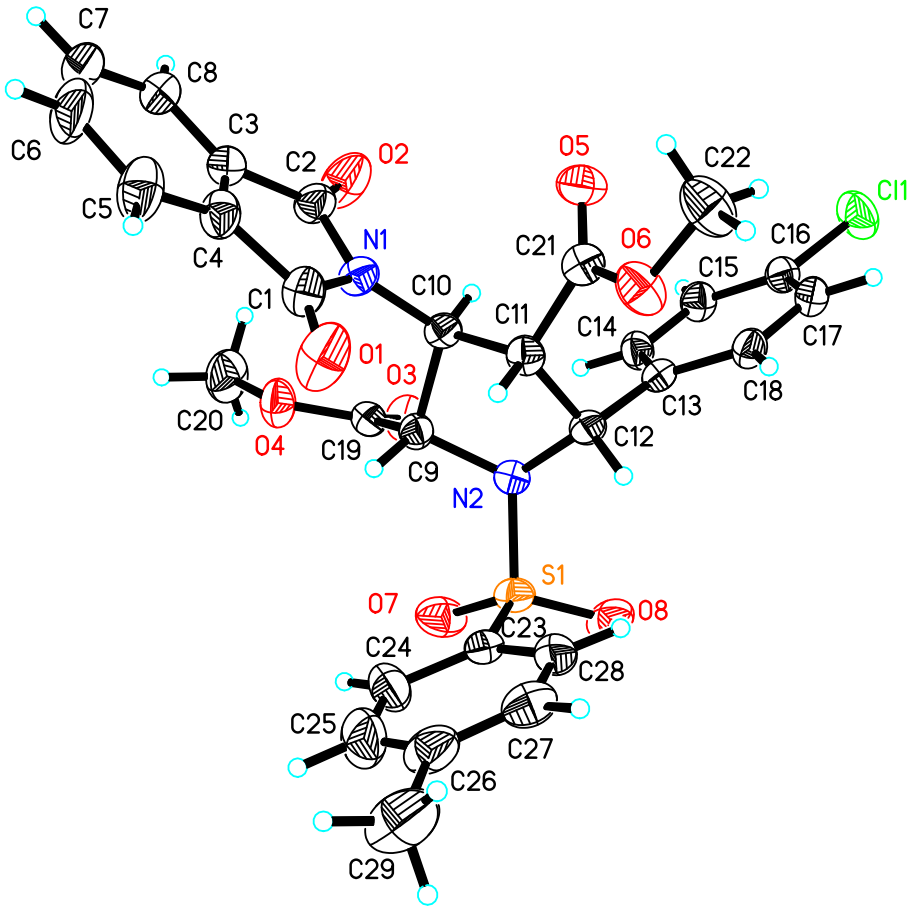


Figure S1. X-Ray crystal structure of (2*S*,3*S*,4*S*,5*R*)-**6** drawn at 30% probability for thermal ellipsoids.

Table S1. Crystal data and structure refinement for (2*S*,3*S*,4*S*,5*R*)-**6**.

Identification code	cd16374	
Empirical formula	C29 H25 Cl N2 O8 S	
Formula weight	597.02	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 11.4186(19) Å	a= 90°.
	b = 9.7011(17) Å	b= 92.473(4)°.
	c = 13.152(2) Å	g = 90°.
Volume	1455.6(4) Å^3	
Z	2	

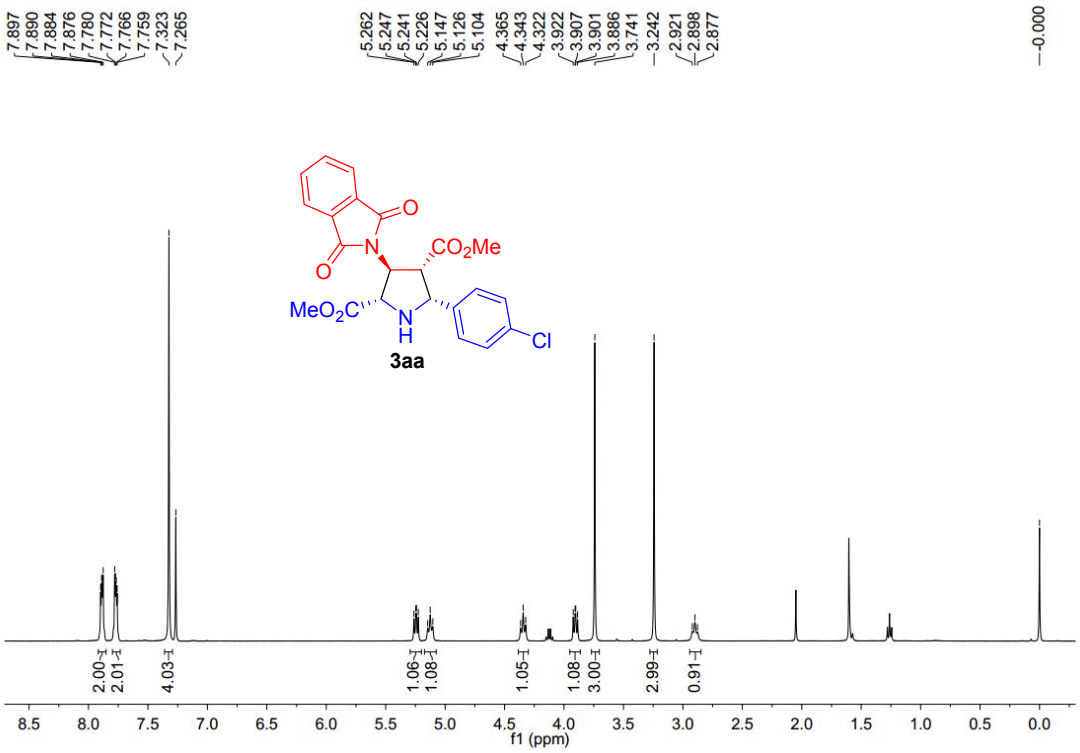
Density (calculated)	1.362 Mg/m^3
Absorption coefficient	0.255 mm^{-1}
F(000)	620
Crystal size	0.220 x 0.150 x 0.100 mm^3
Theta range for data collection	1.785 to 25.494°.
Index ranges	-13<=h<=10, -11<=k<=11, -15<=l<=15
Reflections collected	8415
Independent reflections	5122 [R(int) = 0.0294]
Completeness to theta = 25.242°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6221
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5122 / 1 / 373
Goodness-of-fit on F^2	1.000
Final R indices [I>2sigma(I)]	R1 = 0.0461, wR2 = 0.1112
R indices (all data)	R1 = 0.0552, wR2 = 0.1179
Absolute structure parameter	0.00(5)
Extinction coefficient	n/a
Largest diff. peak and hole	0.208 and -0.145 $e.Å^{-3}$

6. Reference

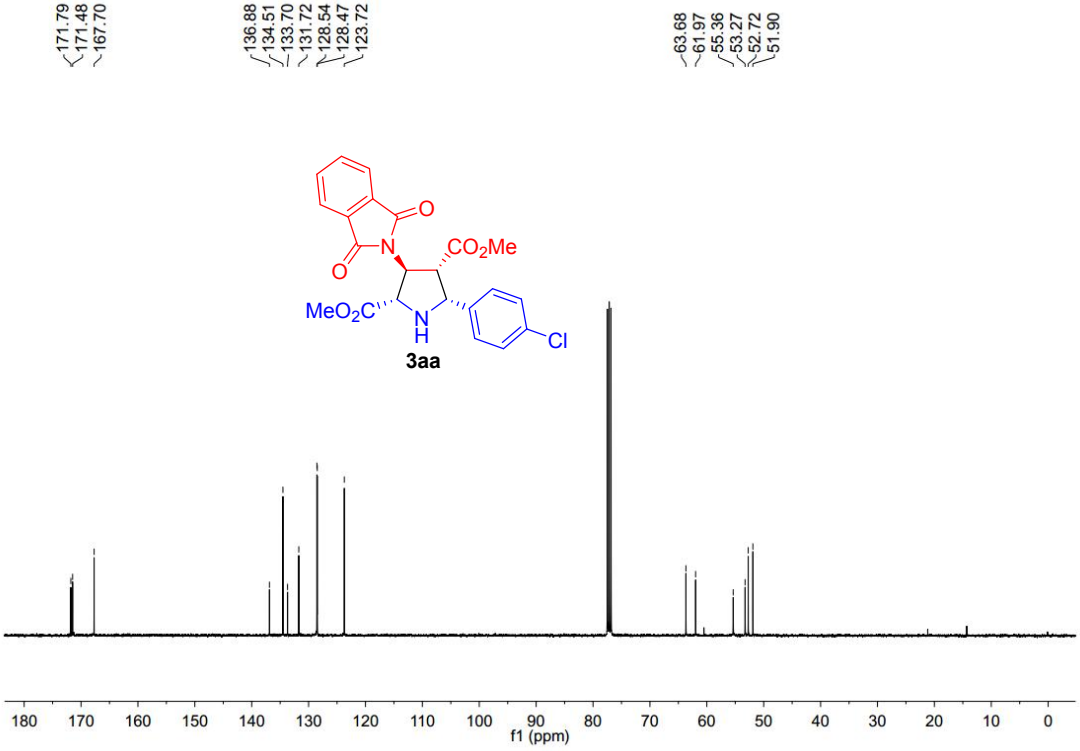
1. (a) M.-J. Fan, G.-Q. Li and Y.-M. Liang, *Tetrahedron* 2006, **62**, 6782; (b) T. Nishimura, J. Wang, M. Nagaosa, K. Okamoto, R. Shintani, F. Kwong, W. Yu, A. S. C. Chan and T. Hayashi, *J. Am. Chem. Soc.* 2010, **132**, 464; (c) L. Mola, J. Font, L. Bosch, J. Caner, A. M. Costa, G. Etxebarría-Jardí, O. Pineda, D. Vicente and J. Vilarrasa, *J. Org. Chem.* 2013, **78**, 5832.

7. ^{1}H NMR and ^{13}C NMR spectra

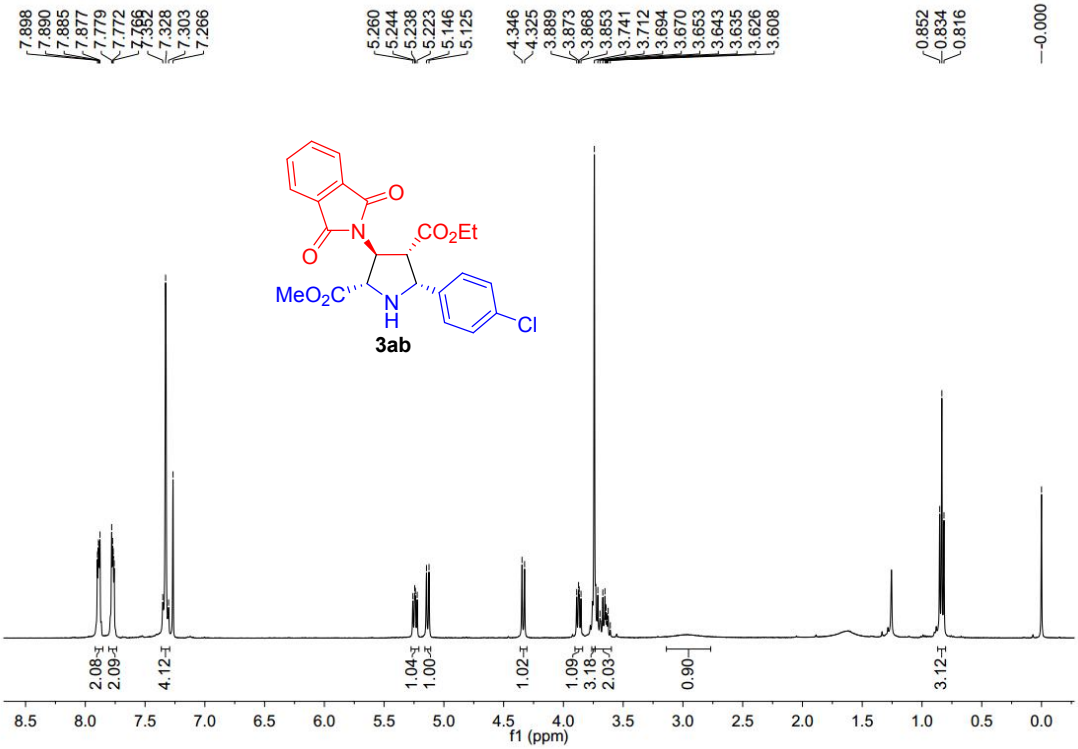
^{1}H NMR spectrum of compound **3aa**



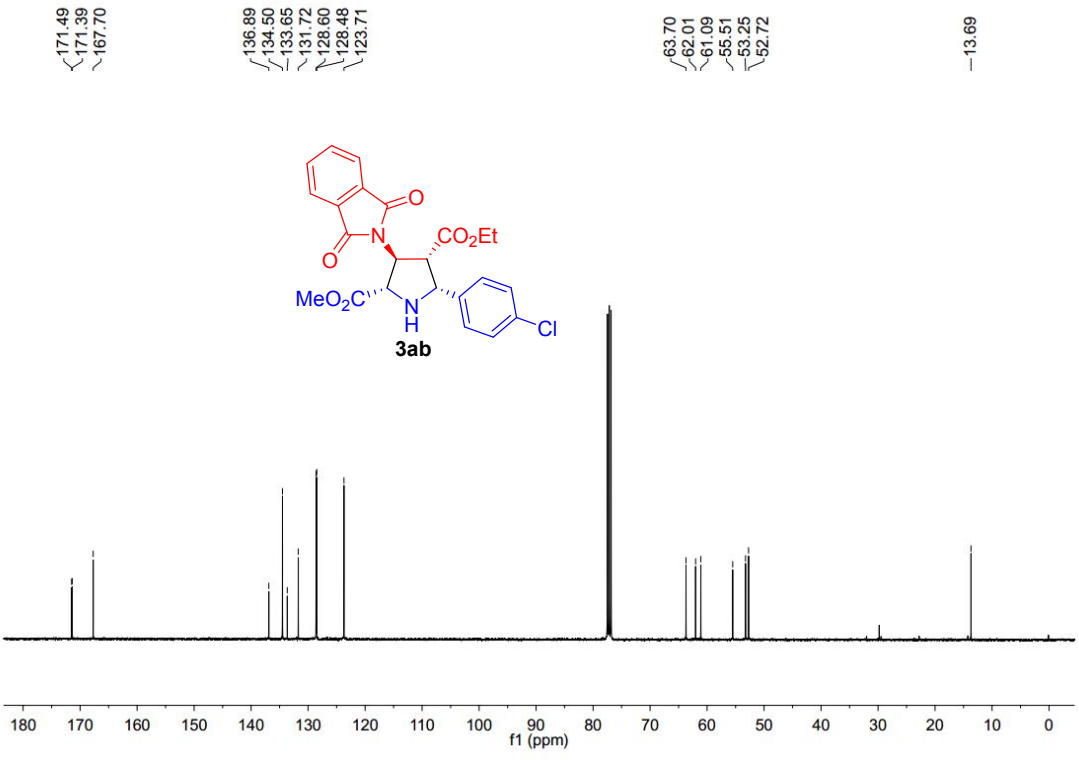
^{13}C NMR spectrum of compound **3aa**



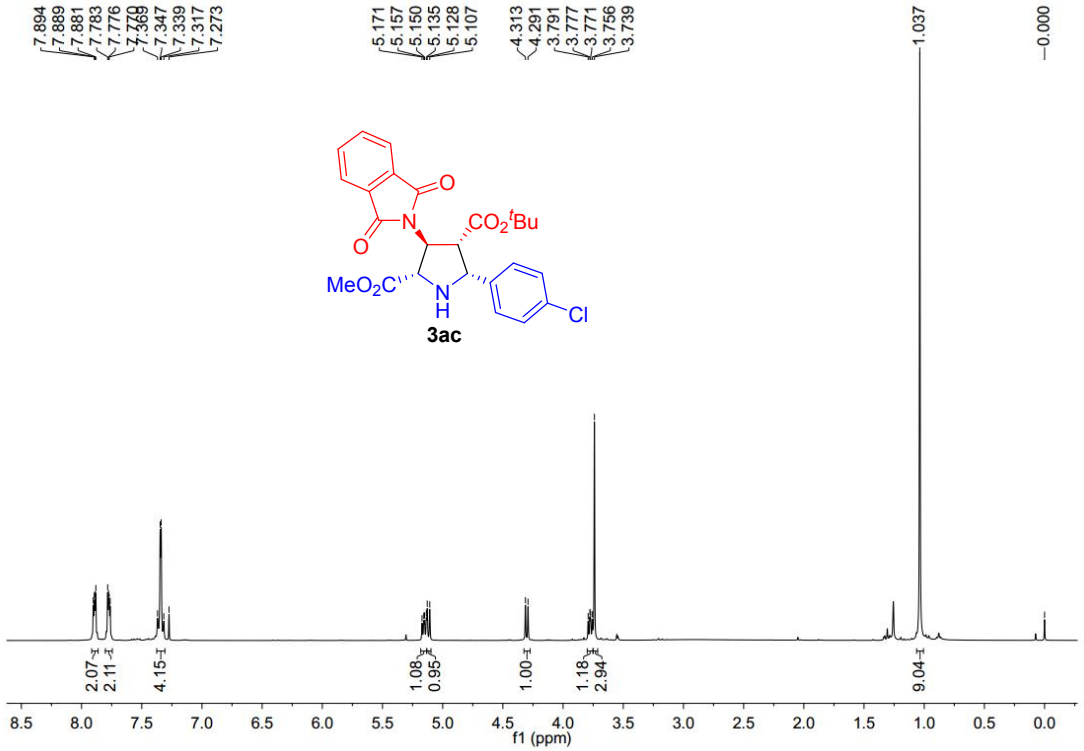
^{1}H NMR spectrum of compound **3ab**



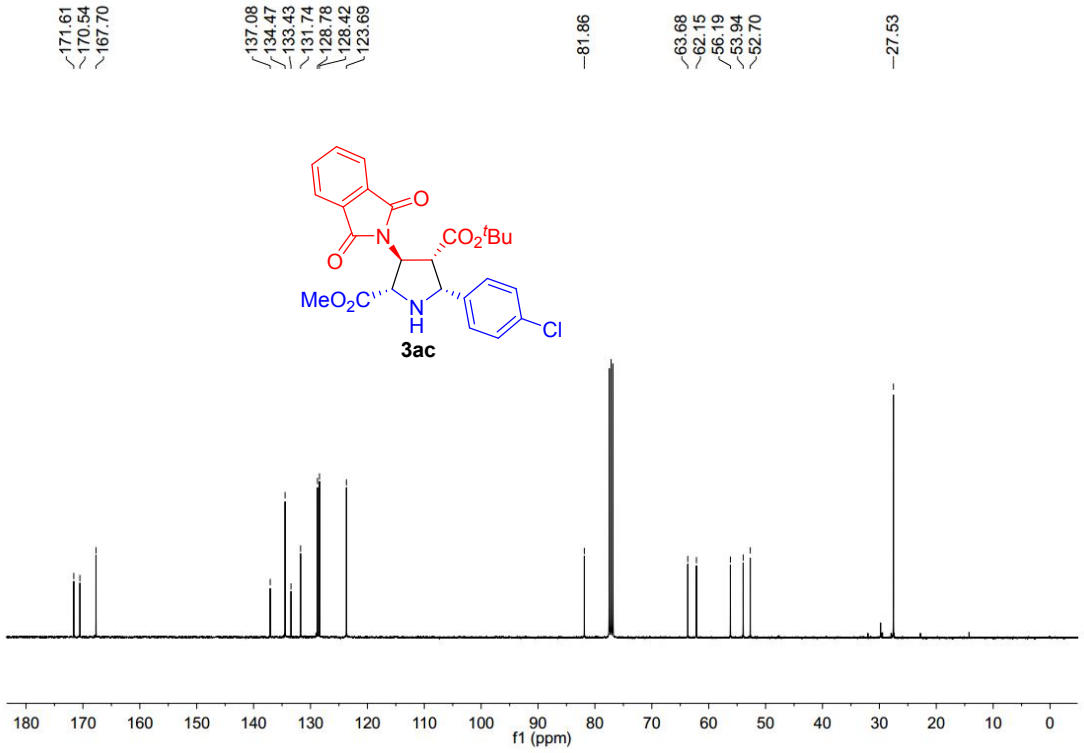
^{13}C NMR spectrum of compound **3ab**



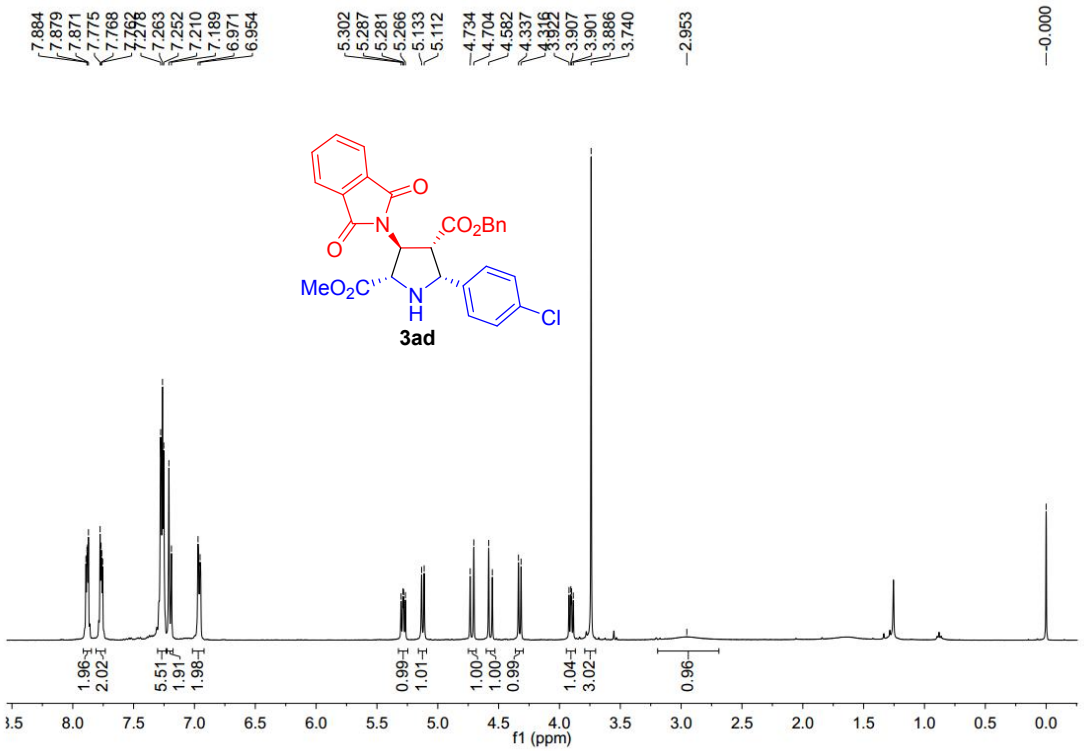
^{1}H NMR spectrum of compound **3ac**



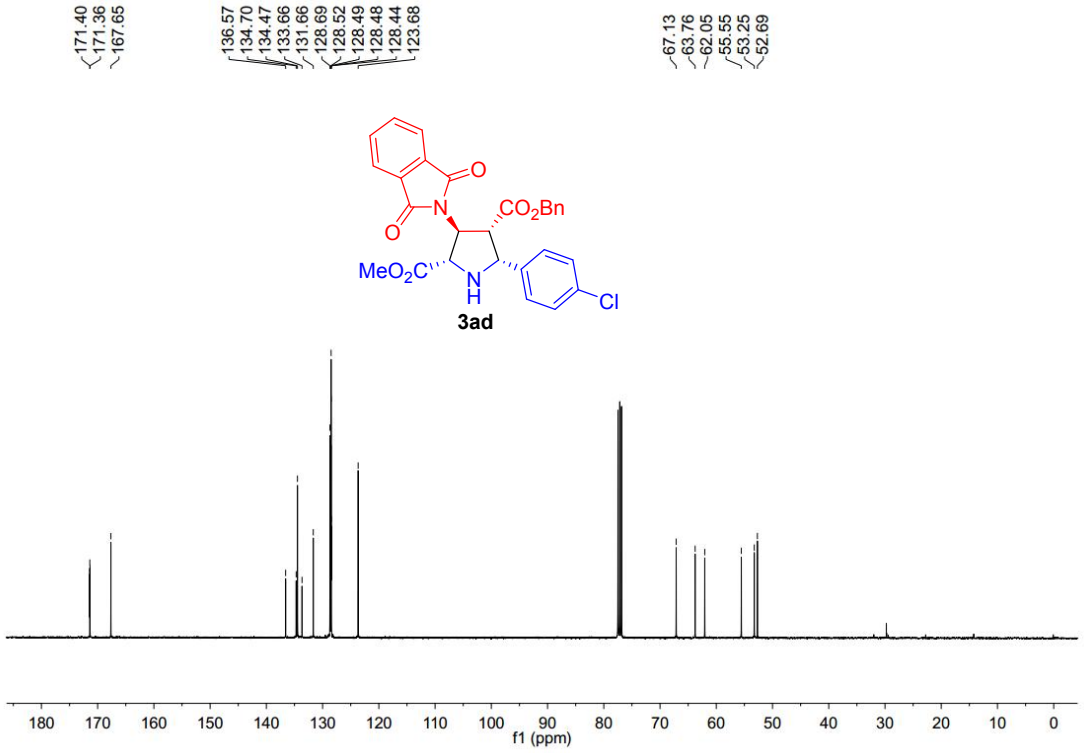
^{13}C NMR spectrum of compound **3ac**



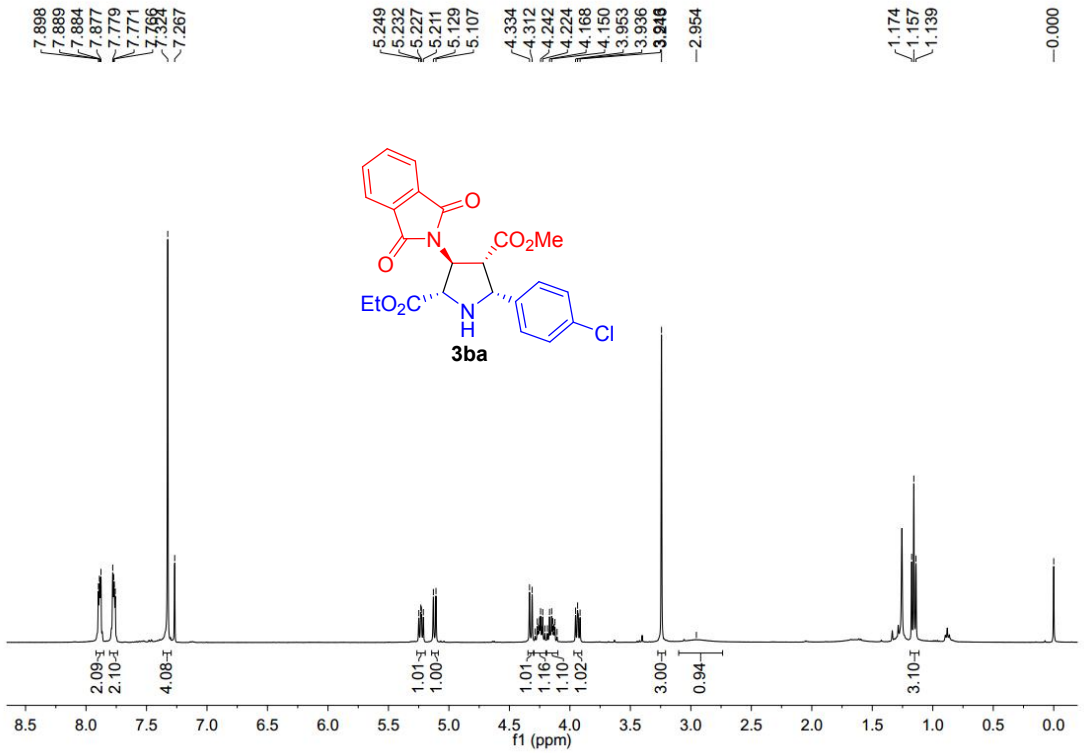
^{1}H NMR spectrum of compound **3ad**



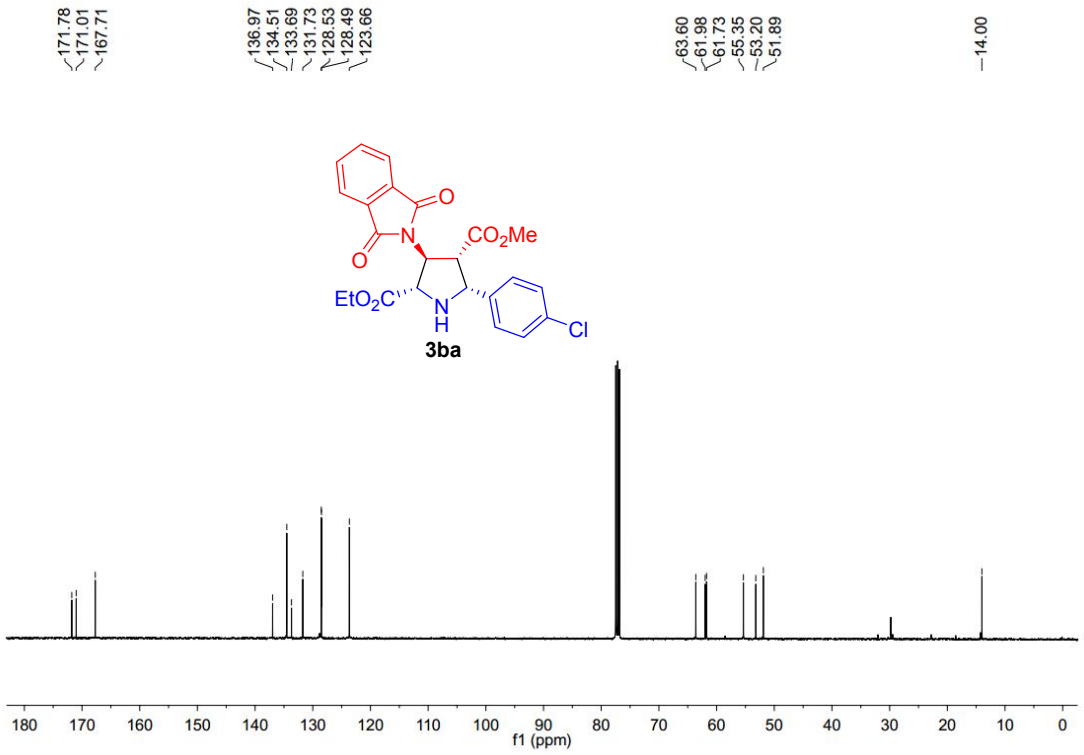
^{13}C NMR spectrum of compound **3ad**



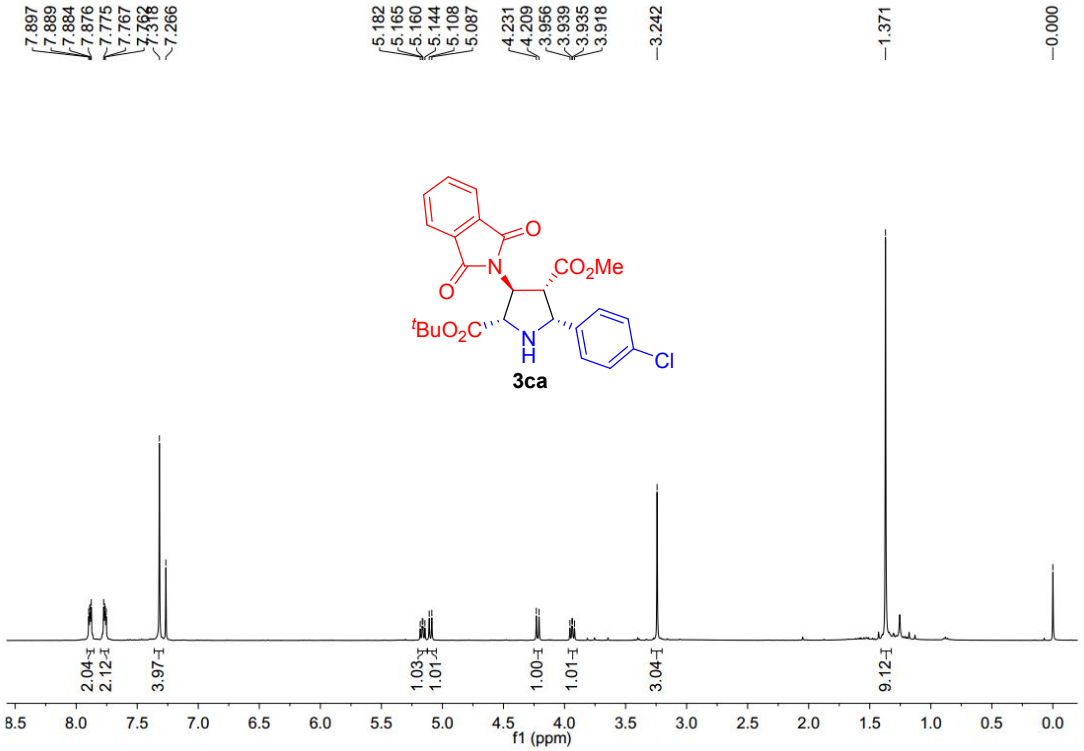
^{1}H NMR spectrum of compound **3ba**



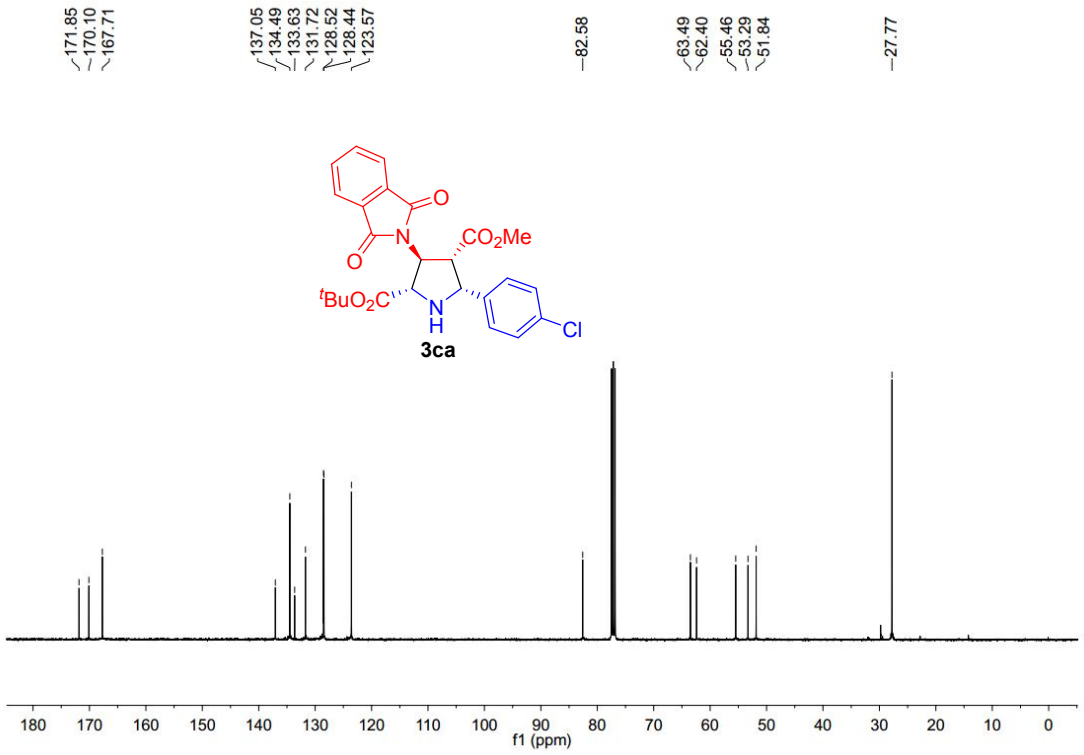
^{13}C NMR spectrum of compound **3ba**



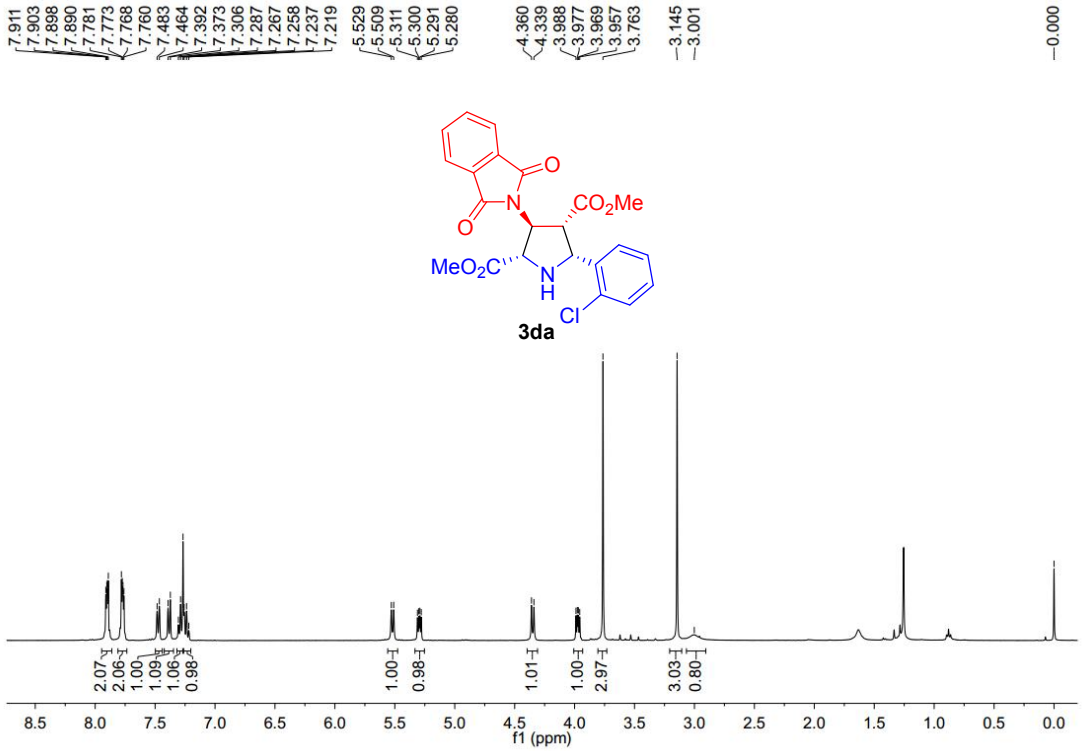
^{1}H NMR spectrum of compound **3ca**



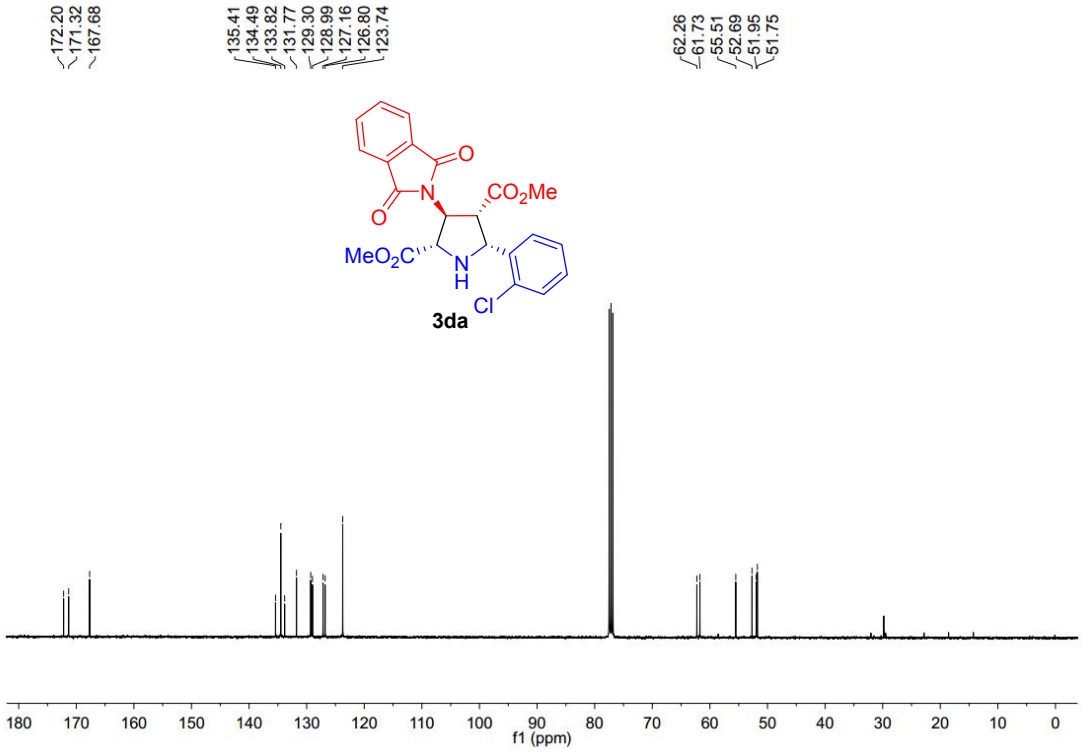
^{13}C NMR spectrum of compound **3ca**



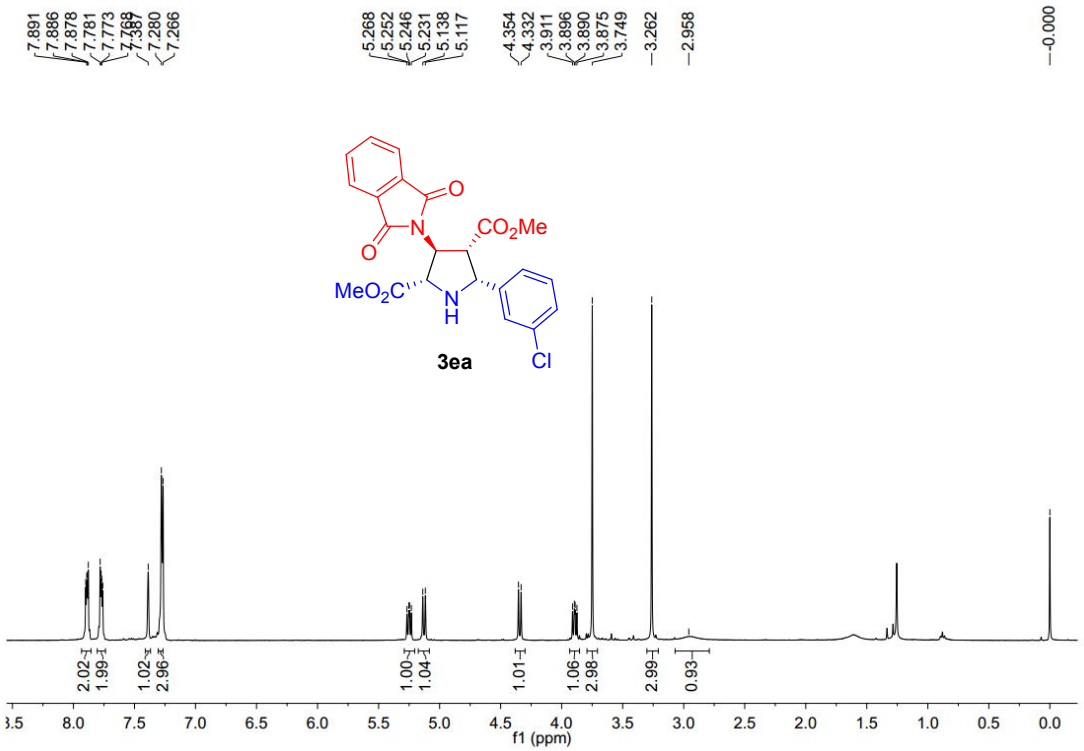
^{1}H NMR spectrum of compound **3da**



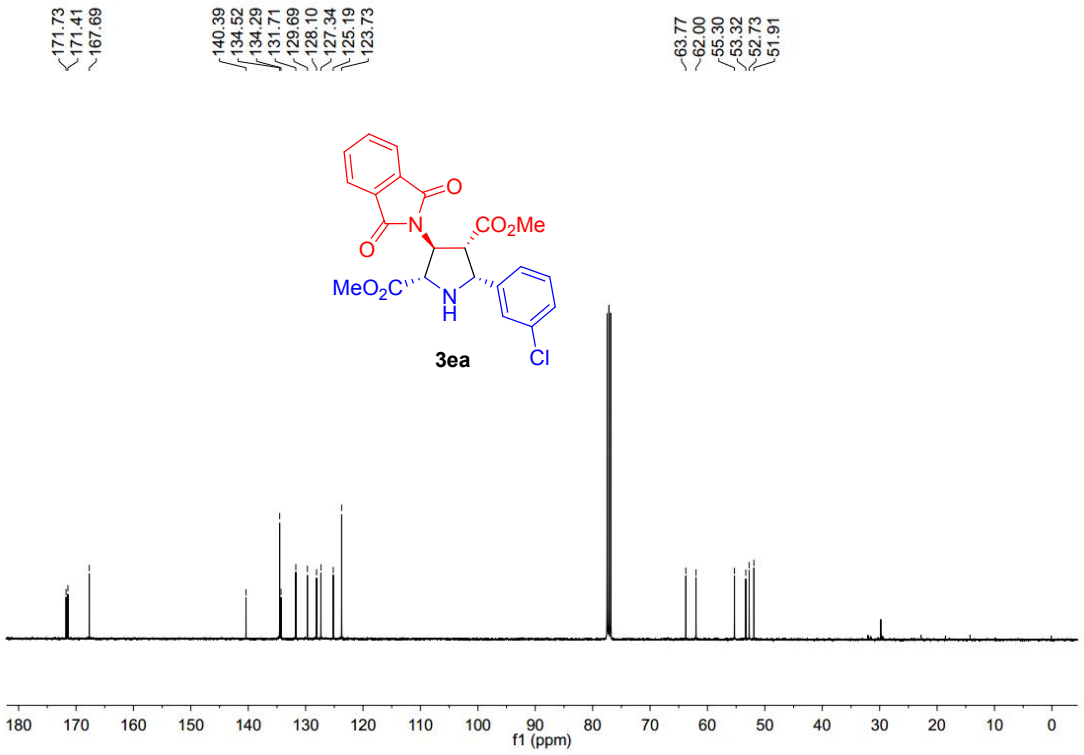
^{13}C NMR spectrum of compound **3da**



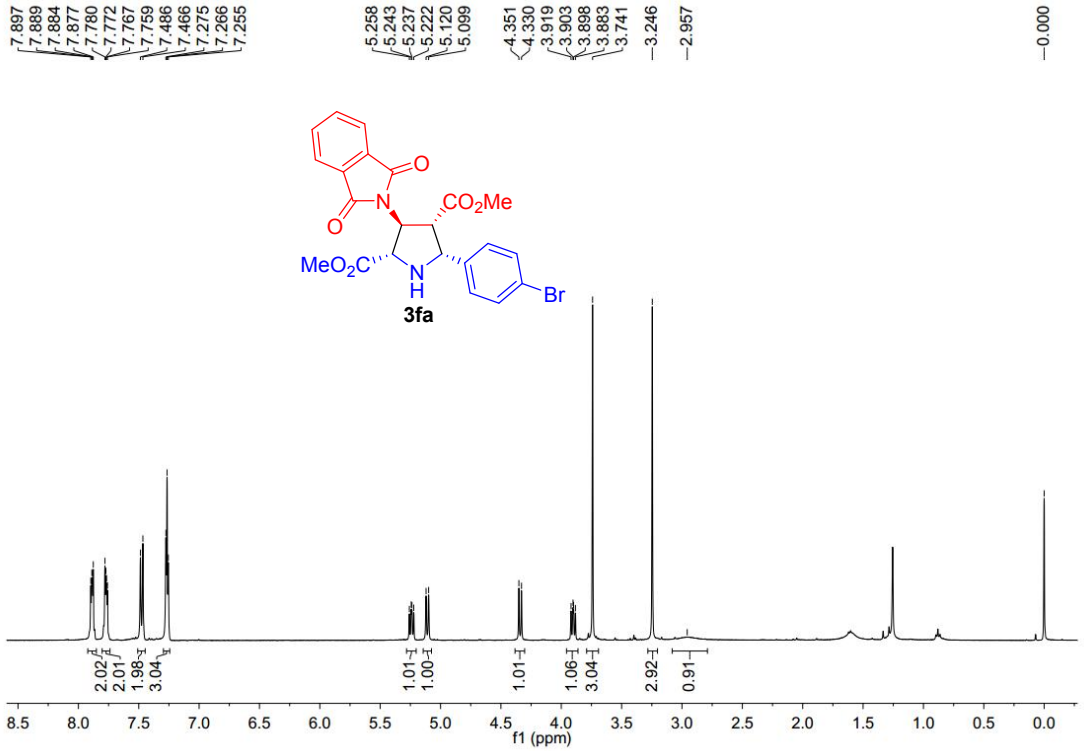
^{1}H NMR spectrum of compound **3ea**



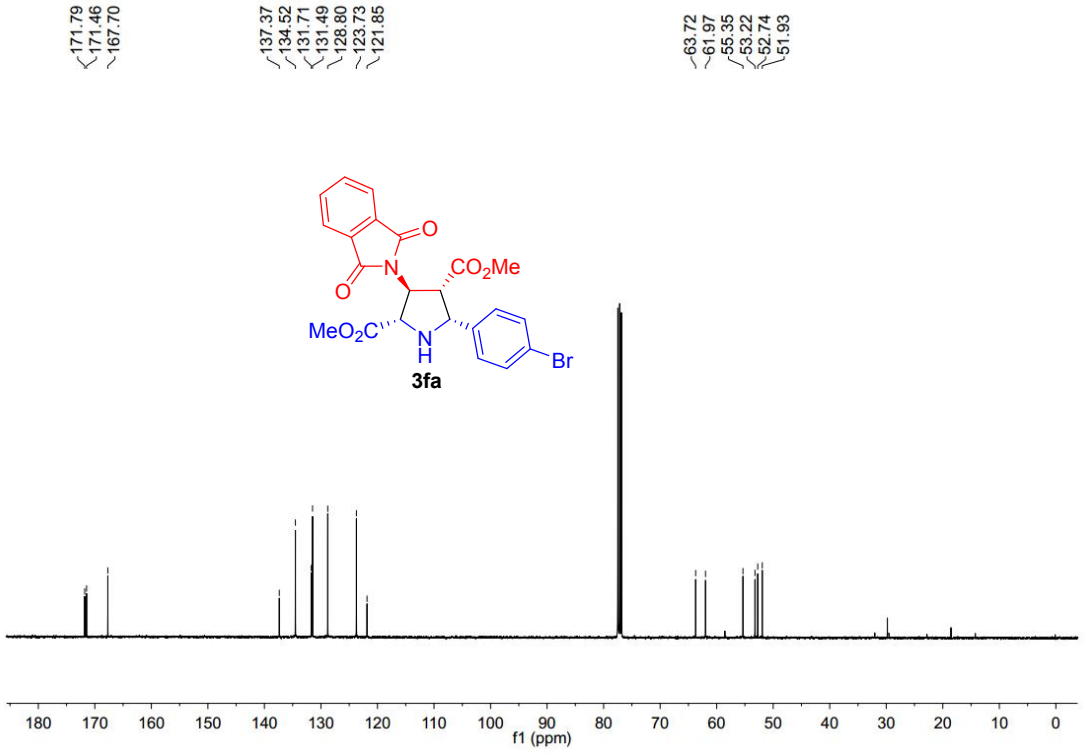
^{13}C NMR spectrum of compound **3ea**



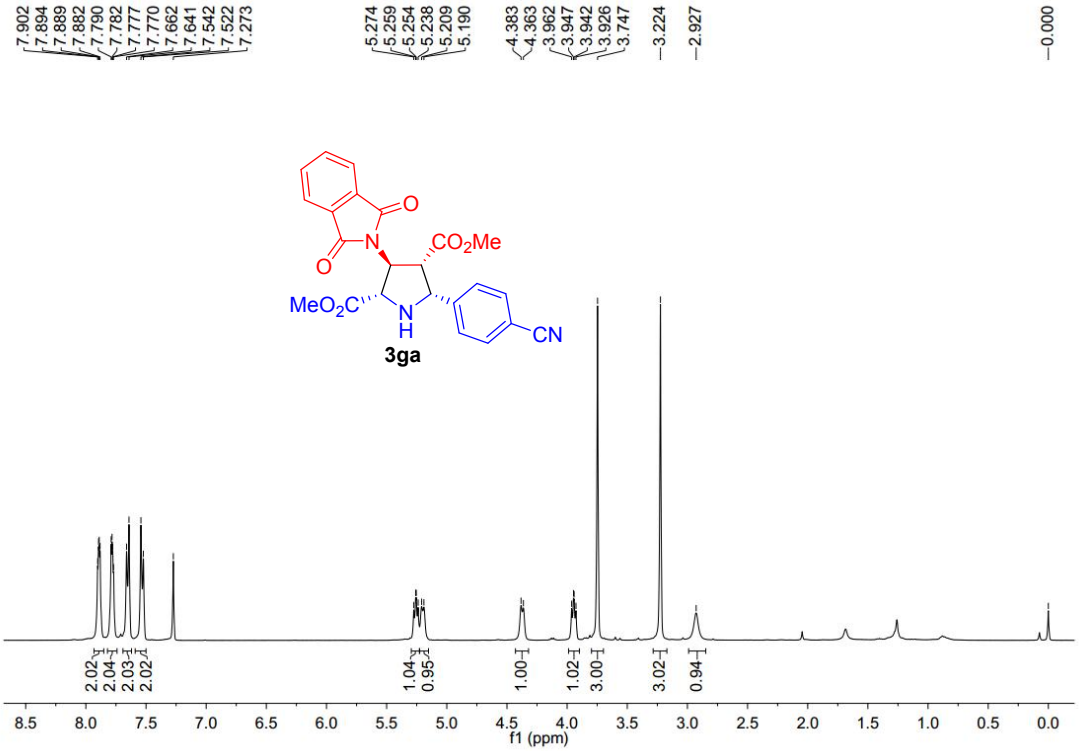
^{1}H NMR spectrum of compound **3fa**



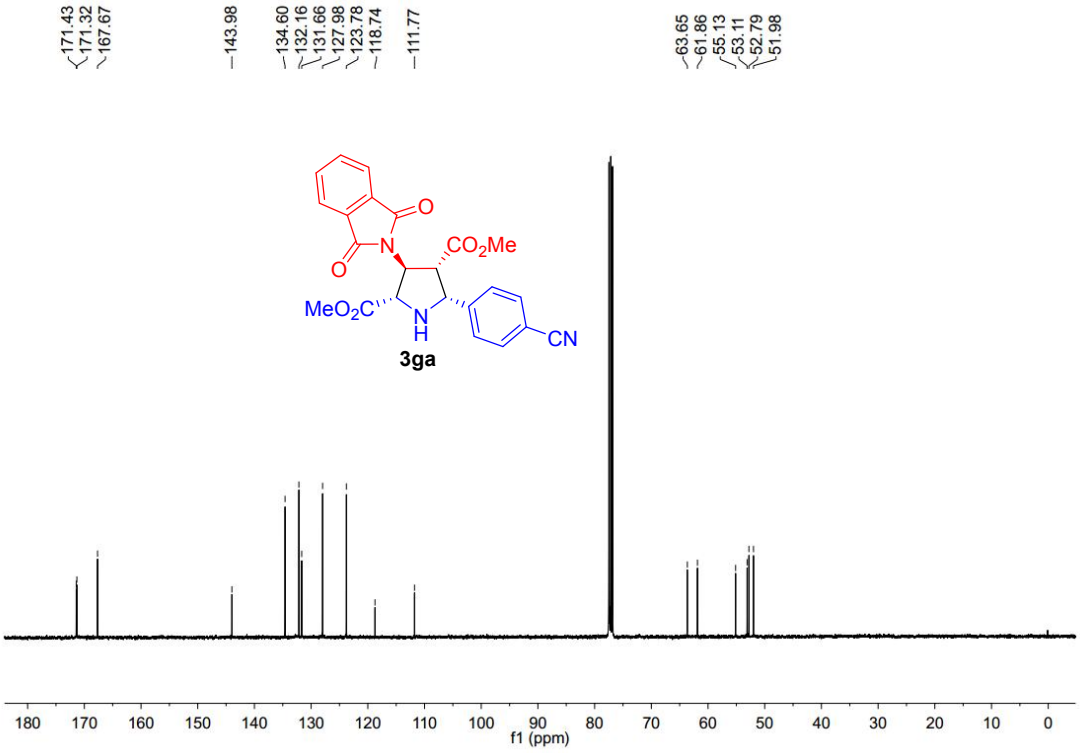
^{13}C NMR spectrum of compound **3fa**



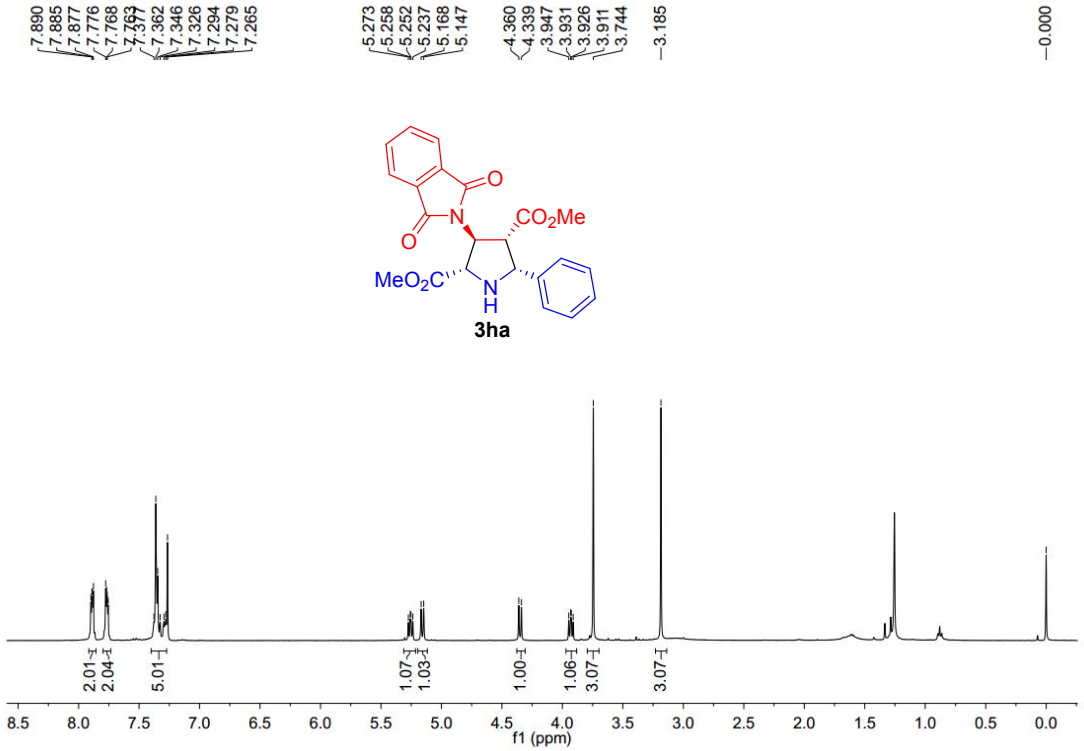
^{1}H NMR spectrum of compound **3ga**



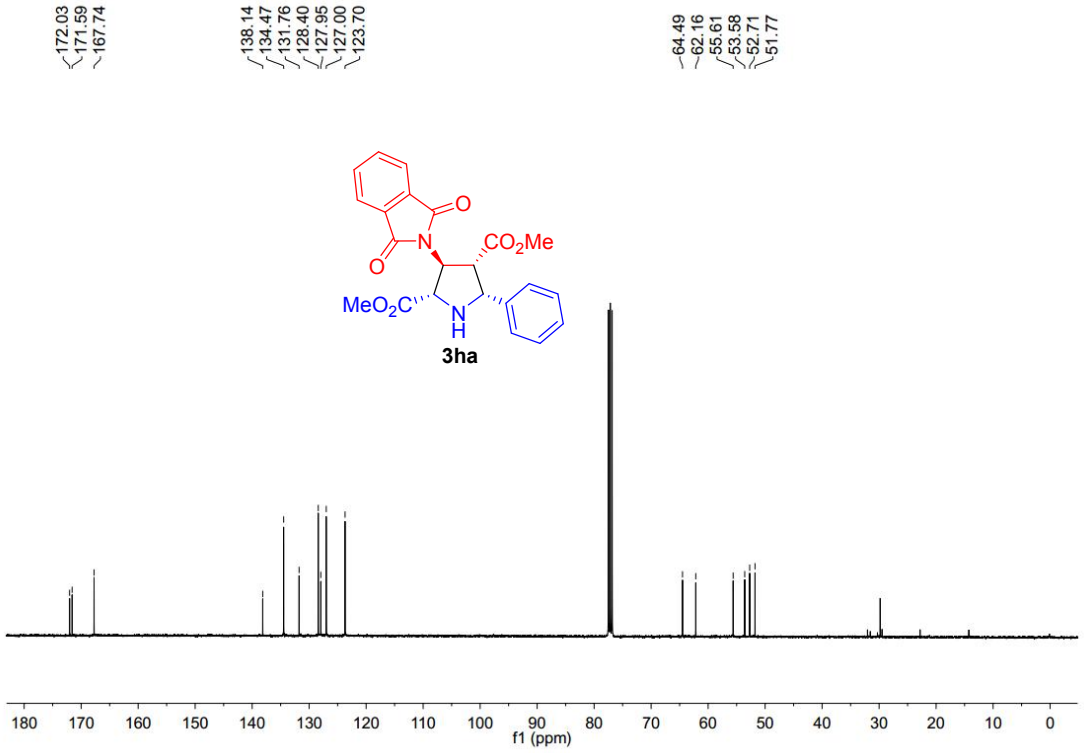
^{13}C NMR spectrum of compound **3ga**



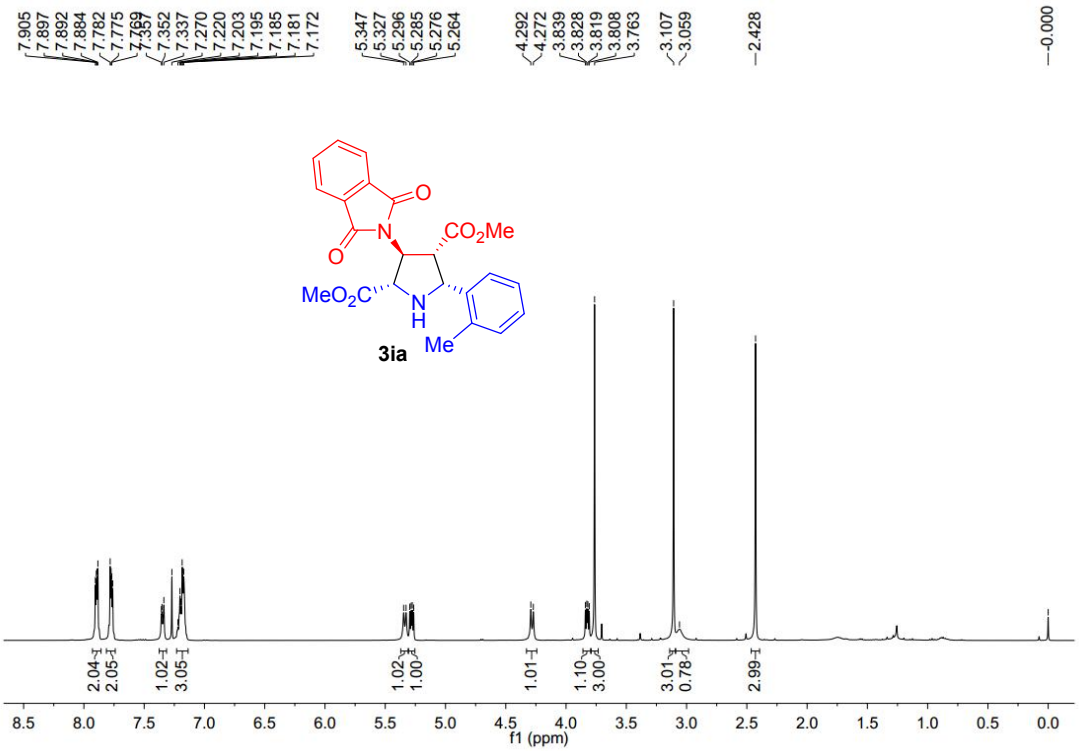
^{1}H NMR spectrum of compound **3ha**



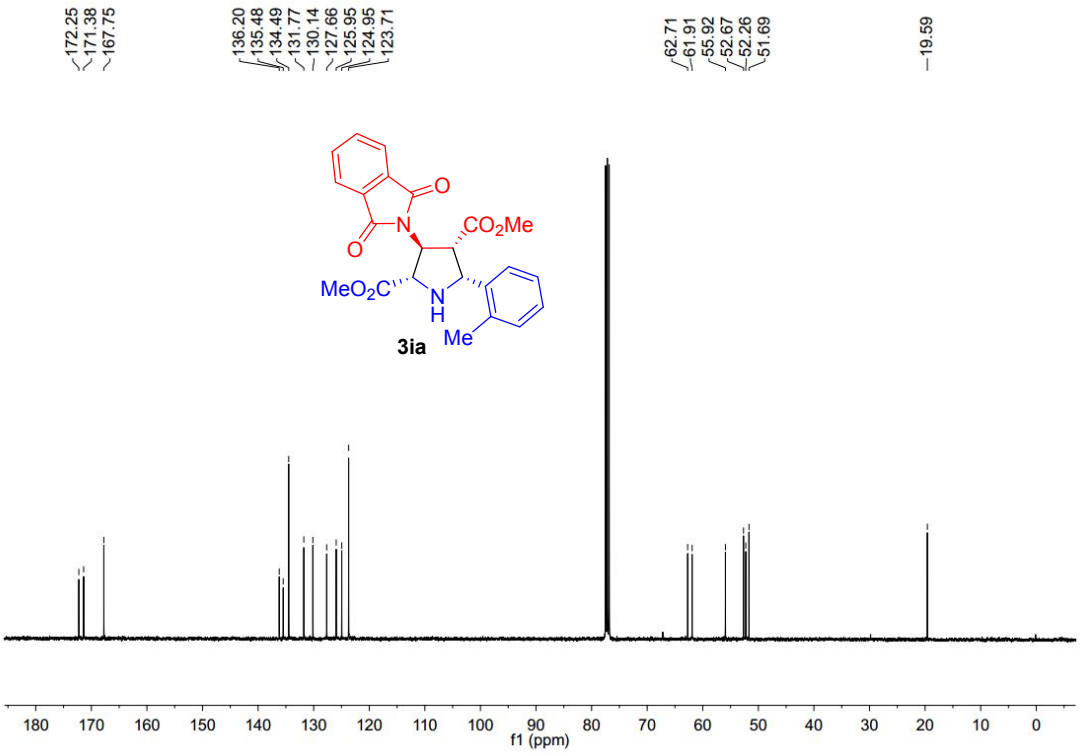
^{13}C NMR spectrum of compound **3ha**



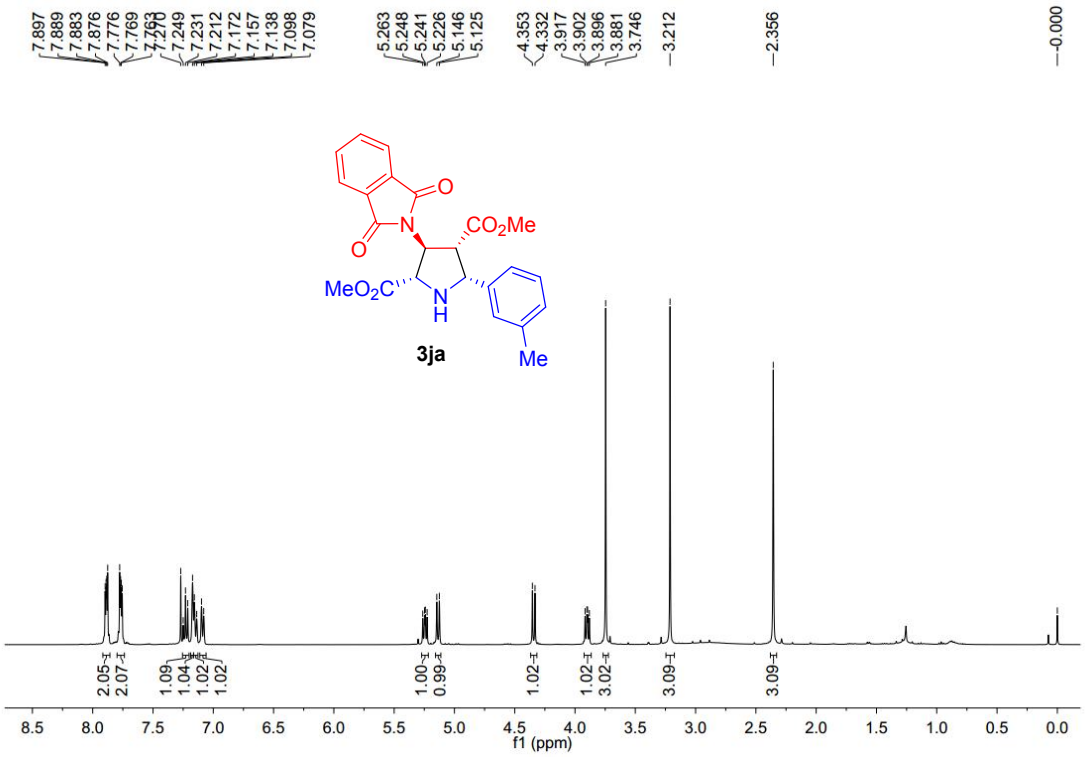
^{1}H NMR spectrum of compound **3ia**



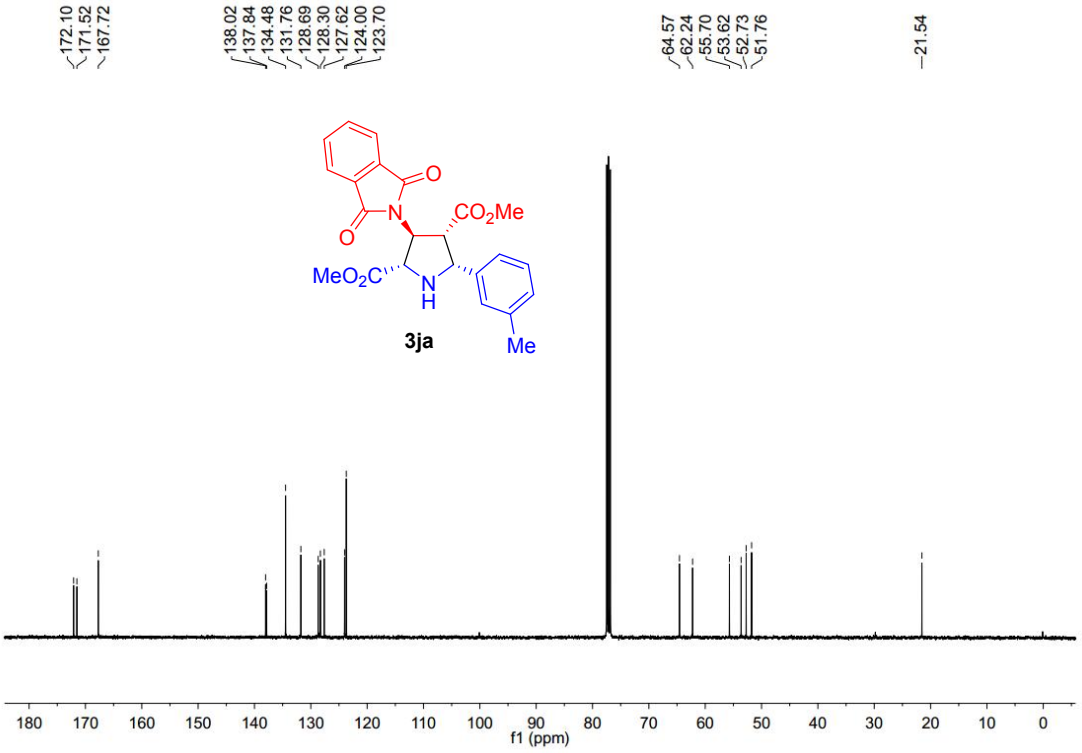
^{13}C NMR spectrum of compound **3ia**



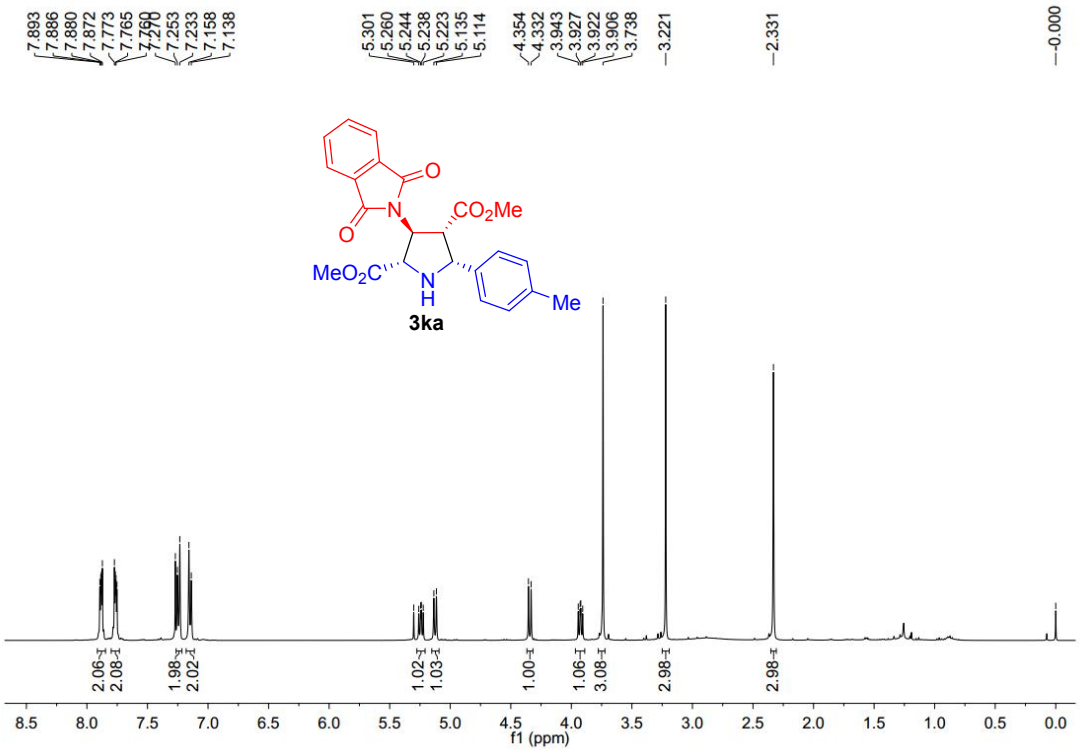
^{1}H NMR spectrum of compound **3ja**



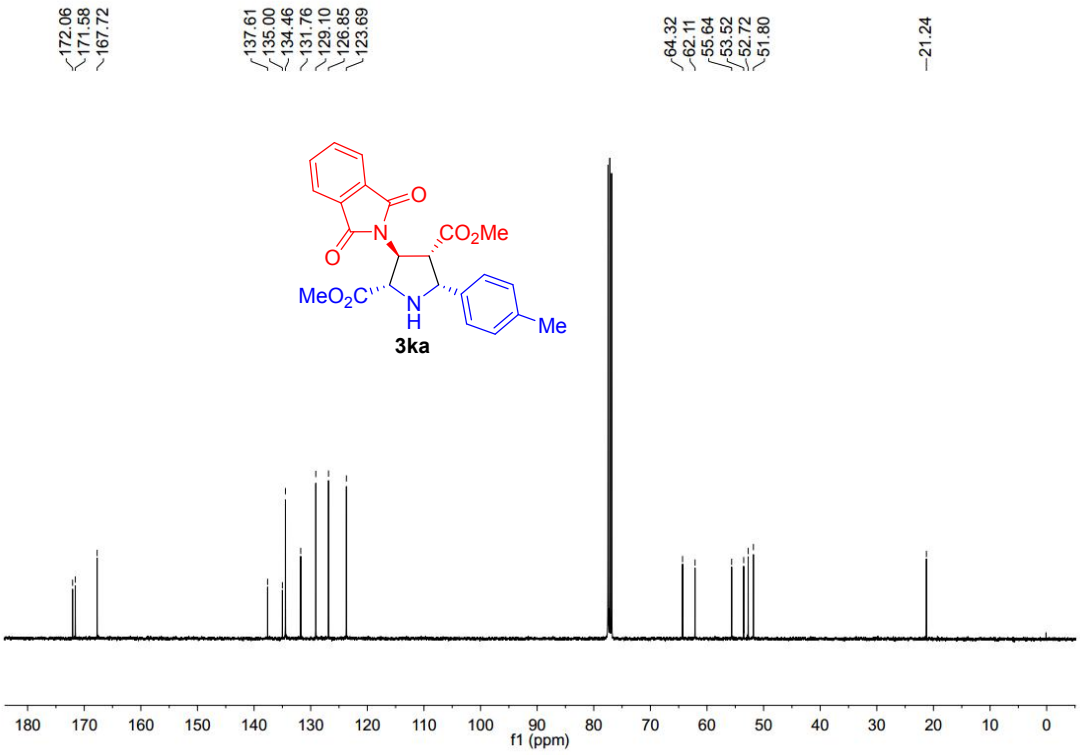
^{13}C NMR spectrum of compound **3ja**



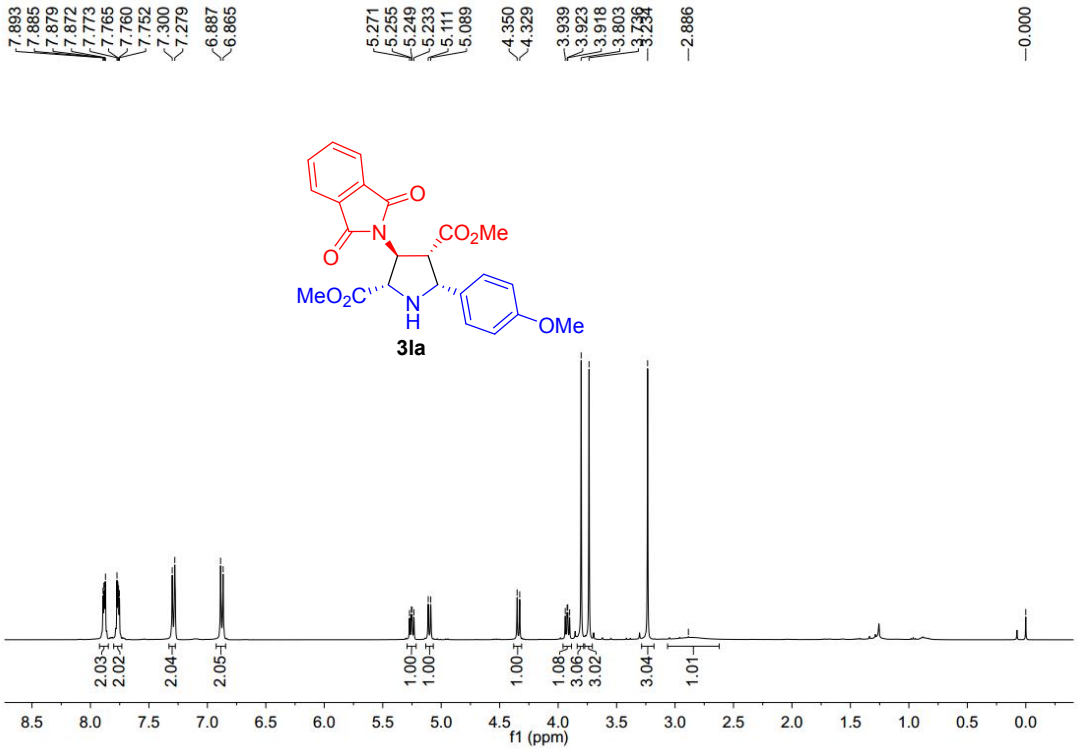
^{1}H NMR spectrum of compound **3ka**



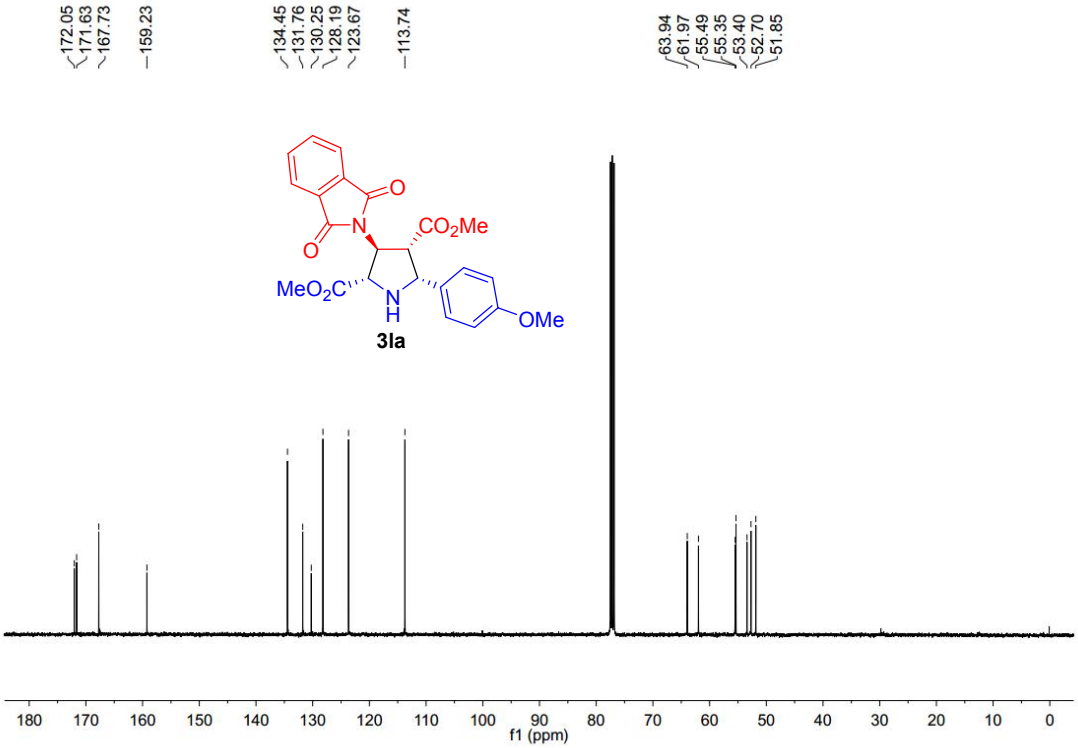
^{13}C NMR spectrum of compound **3ka**



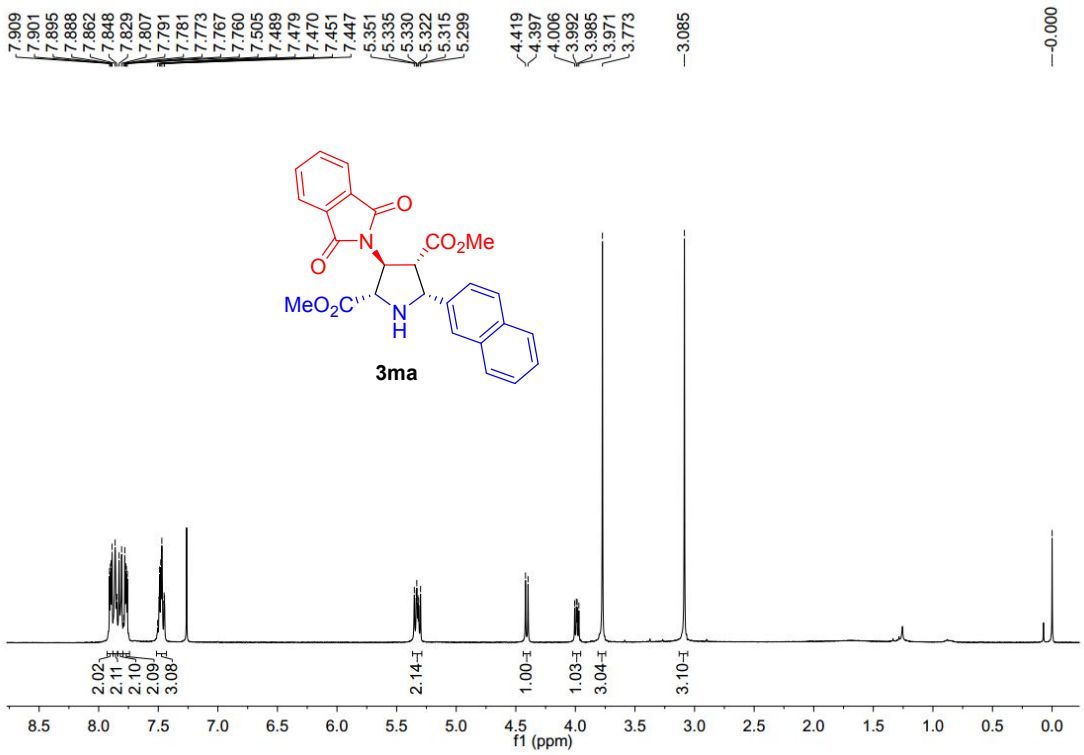
^{1}H NMR spectrum of compound **3la**



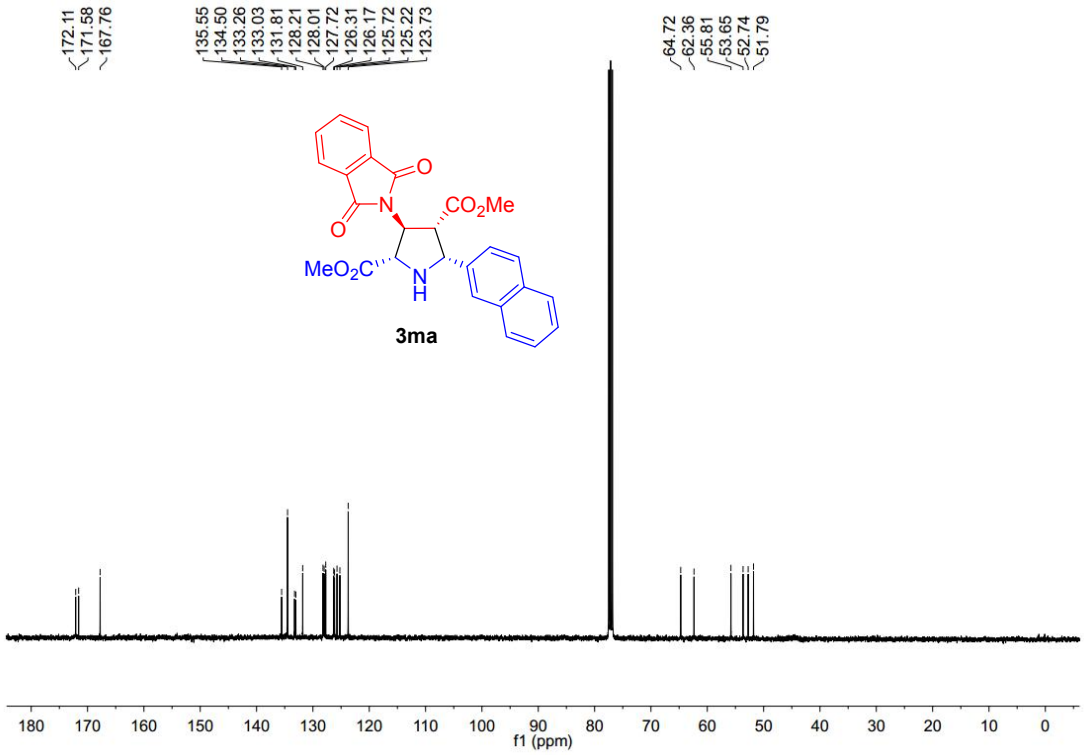
^{13}C NMR spectrum of compound **3la**



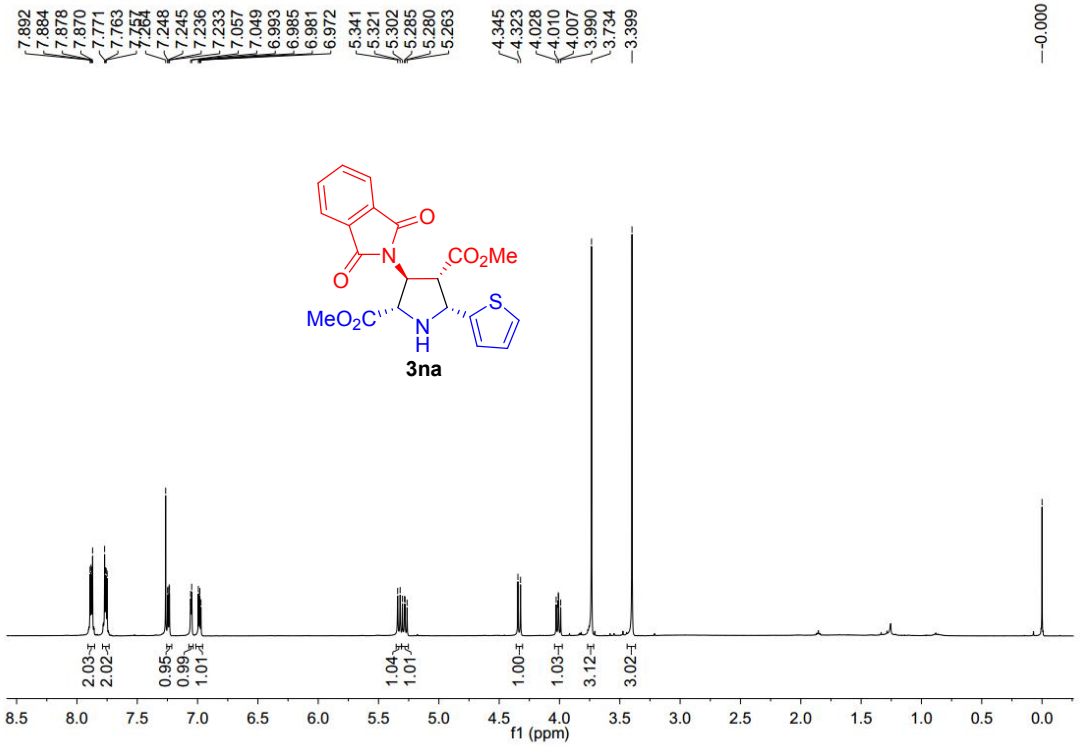
^{1}H NMR spectrum of compound **3ma**



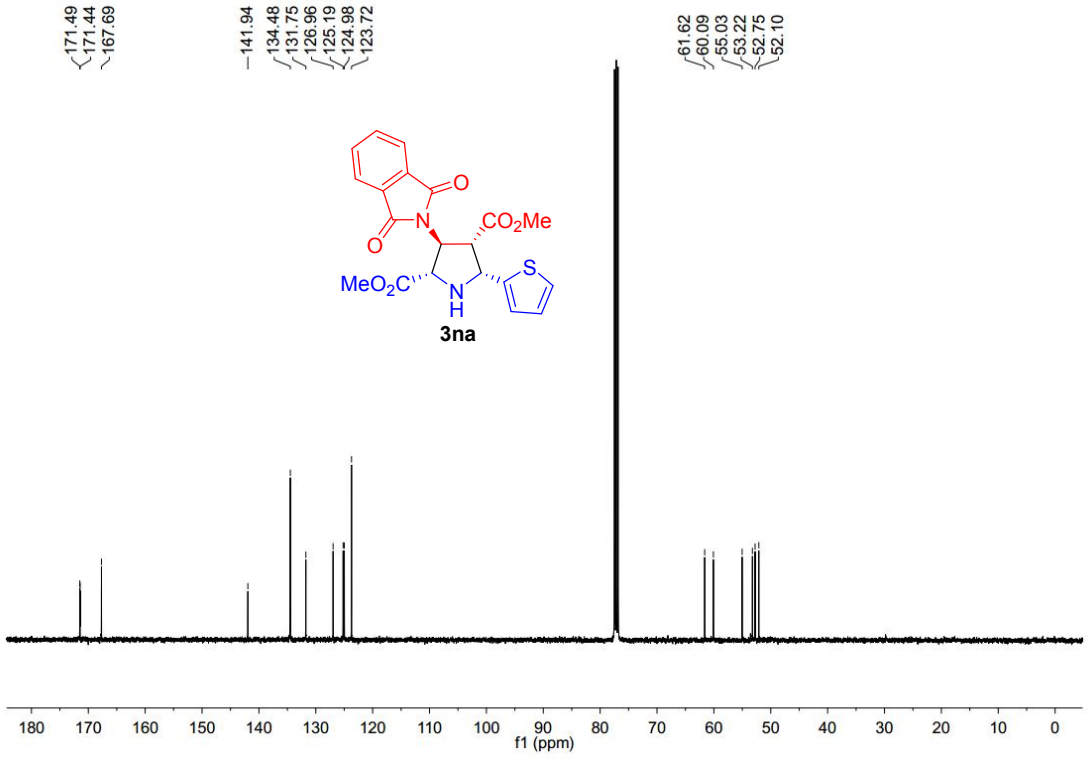
^{13}C NMR spectrum of compound **3ma**



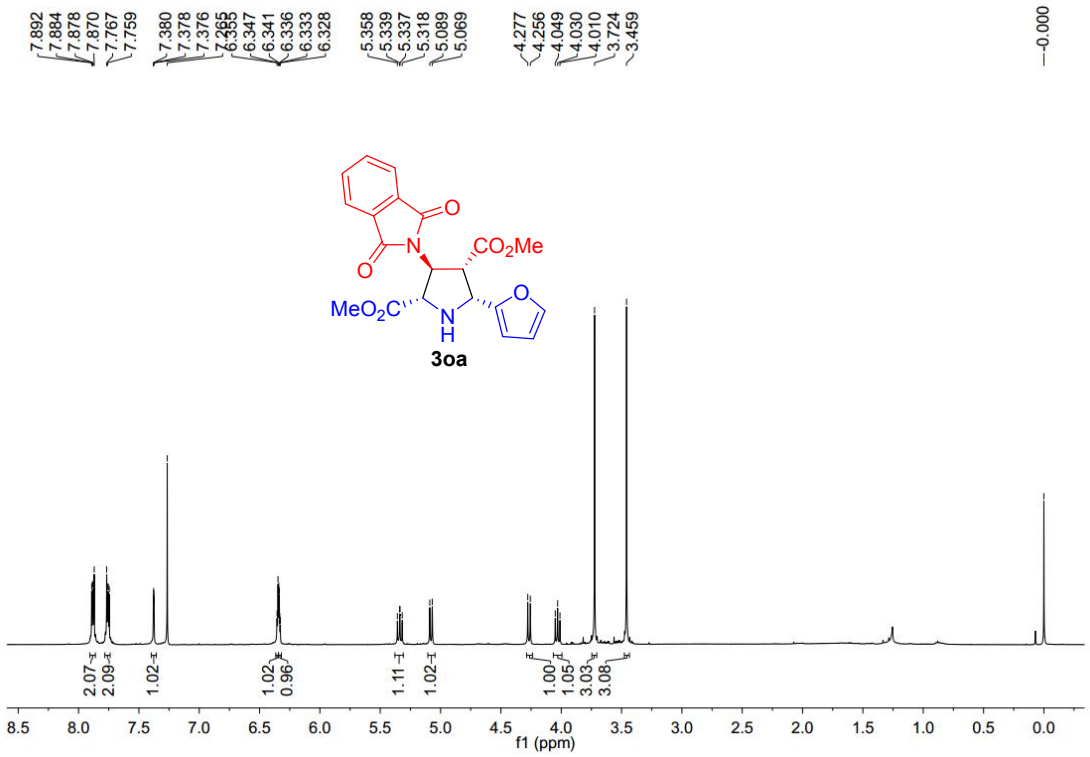
^{1}H NMR spectrum of compound **3na**



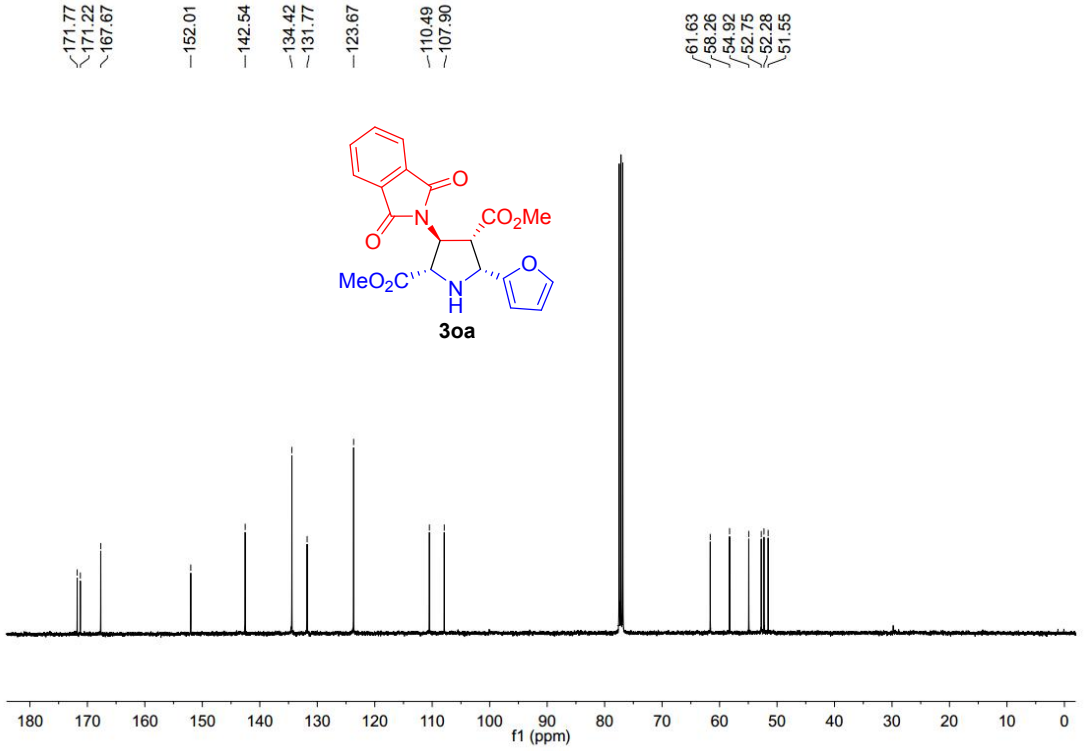
^{13}C NMR spectrum of compound **3na**



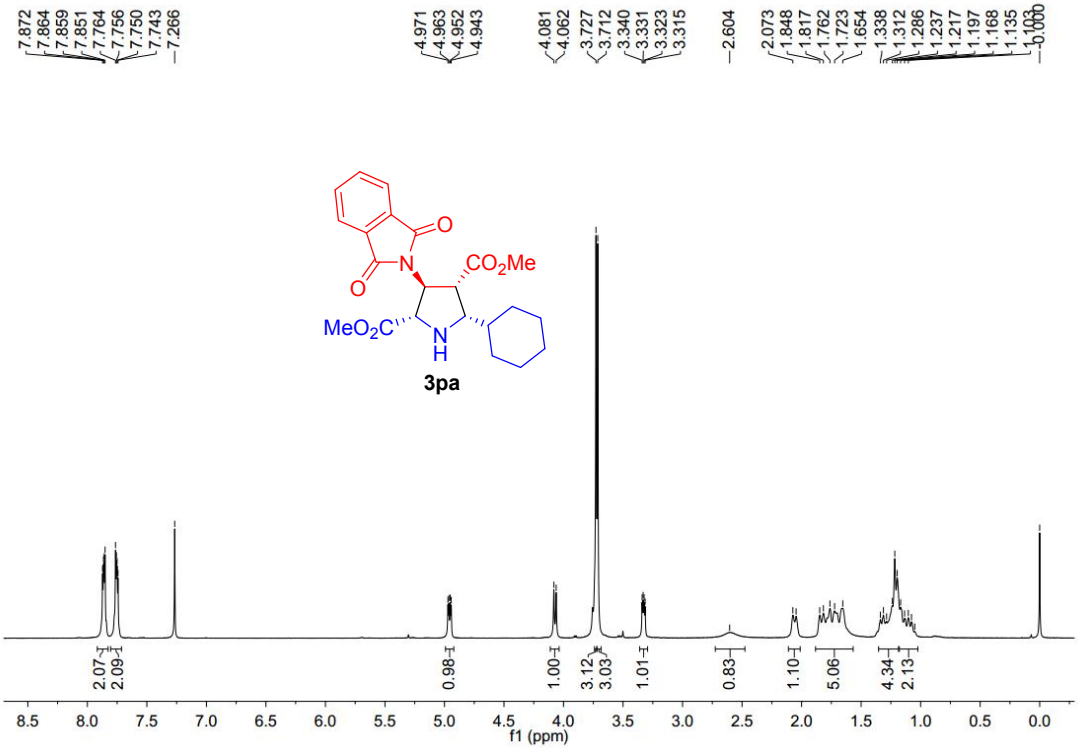
^{1}H NMR spectrum of compound **3oa**



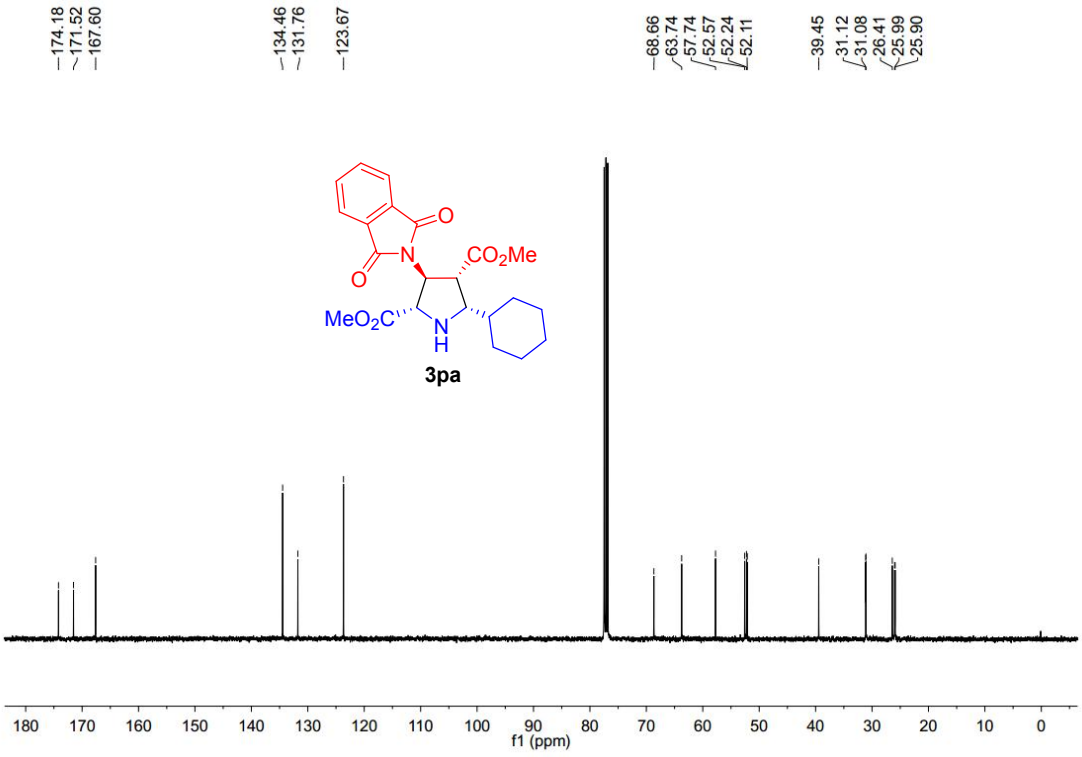
^{13}C NMR spectrum of compound **3oa**



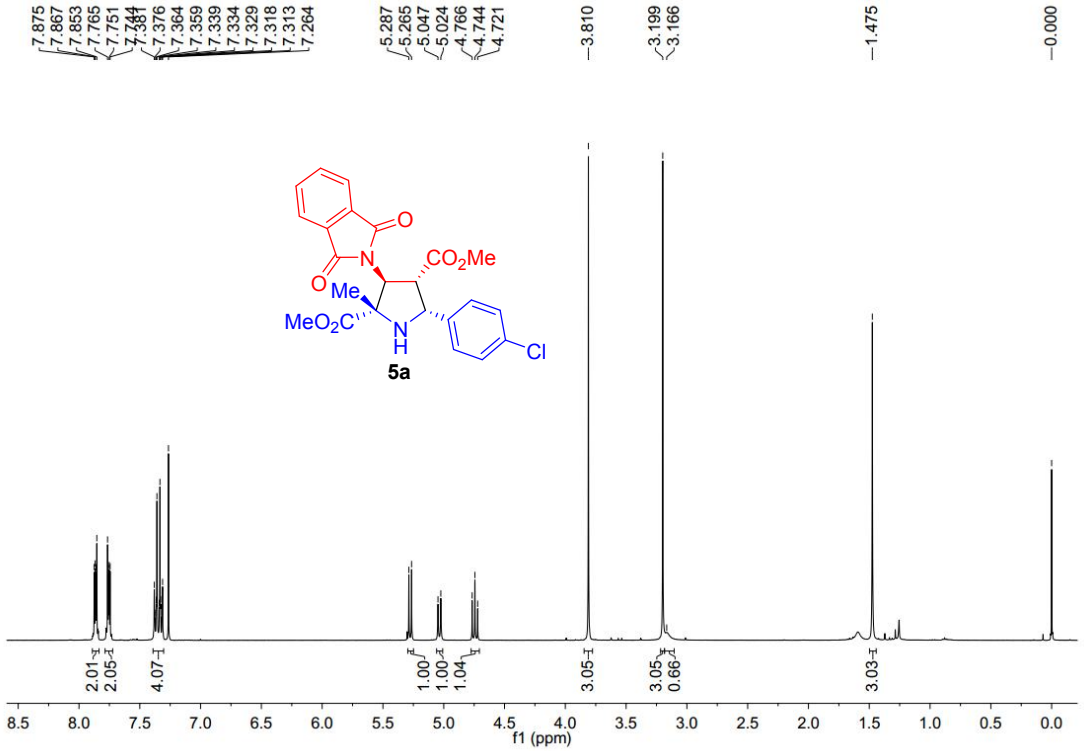
^{1}H NMR spectrum of compound **3pa**



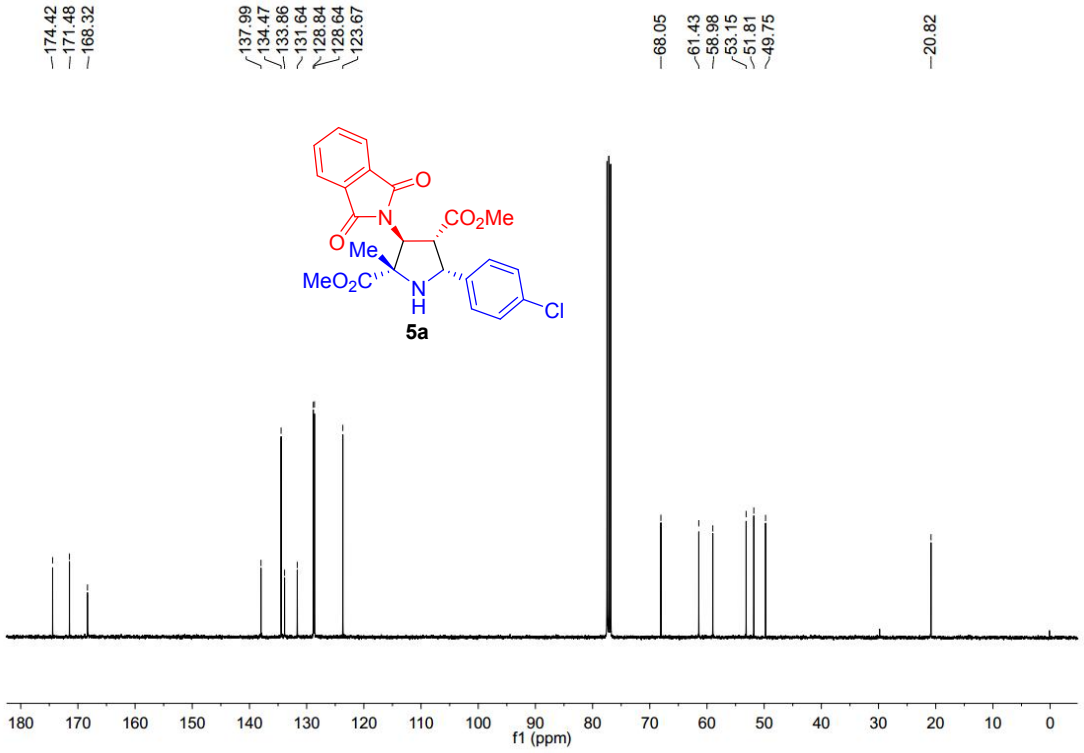
^{13}C NMR spectrum of compound **3pa**



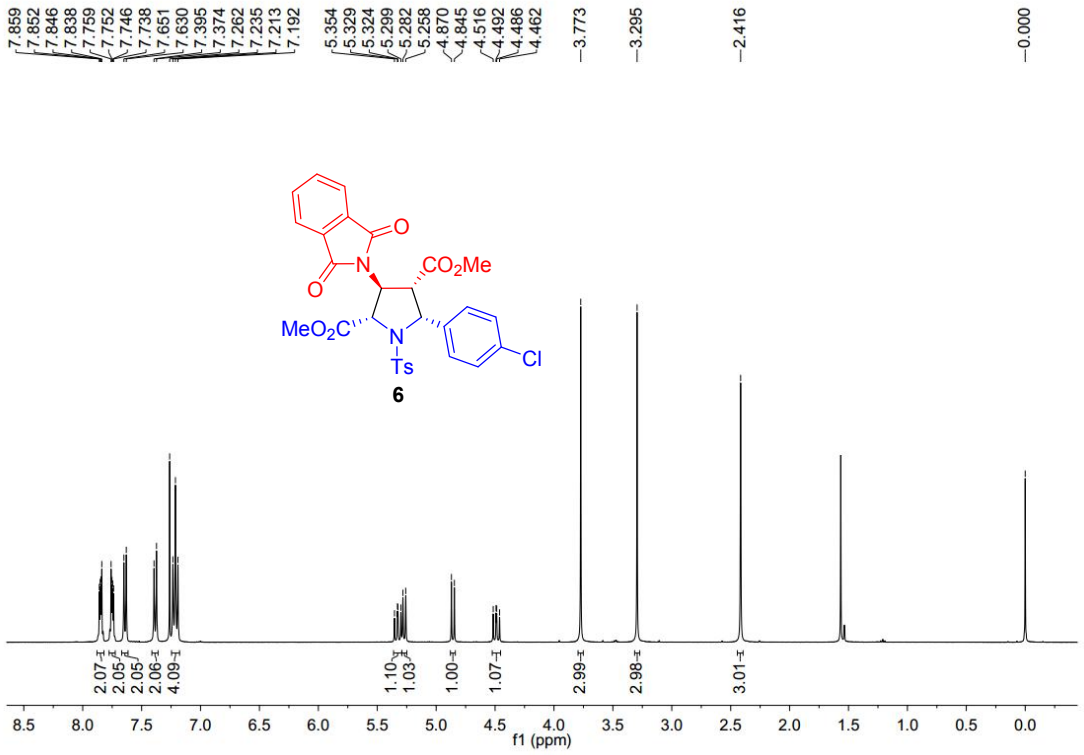
^{1}H NMR spectrum of compound **5a**



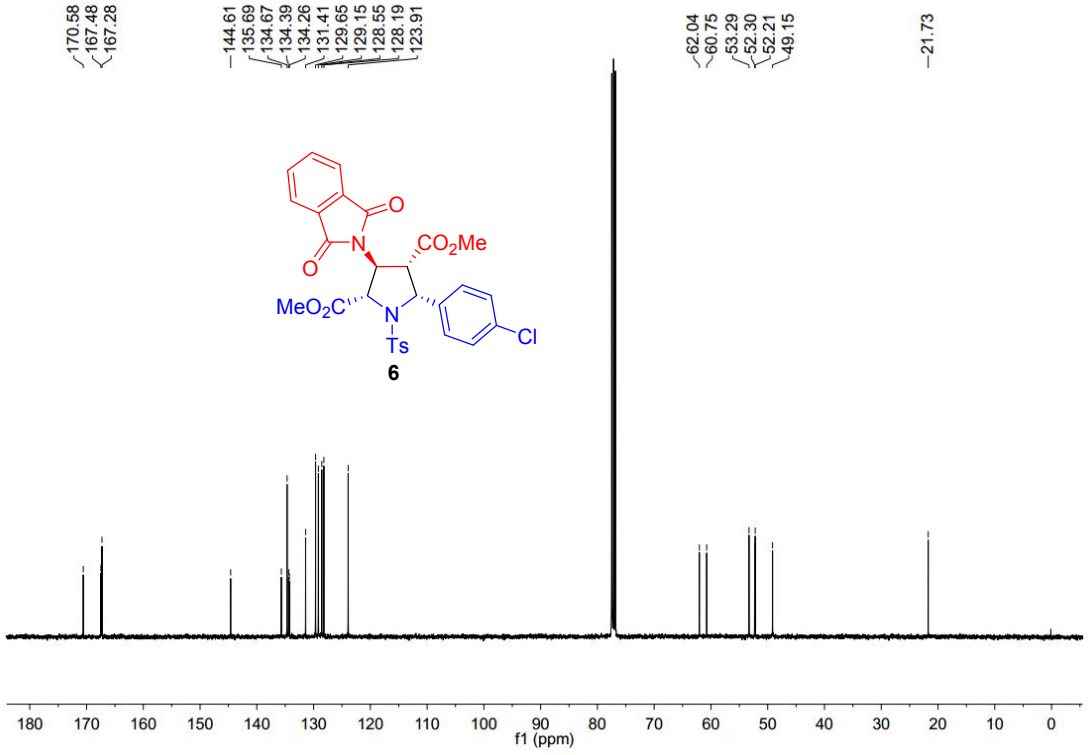
^{13}C NMR spectrum of compound **5a**



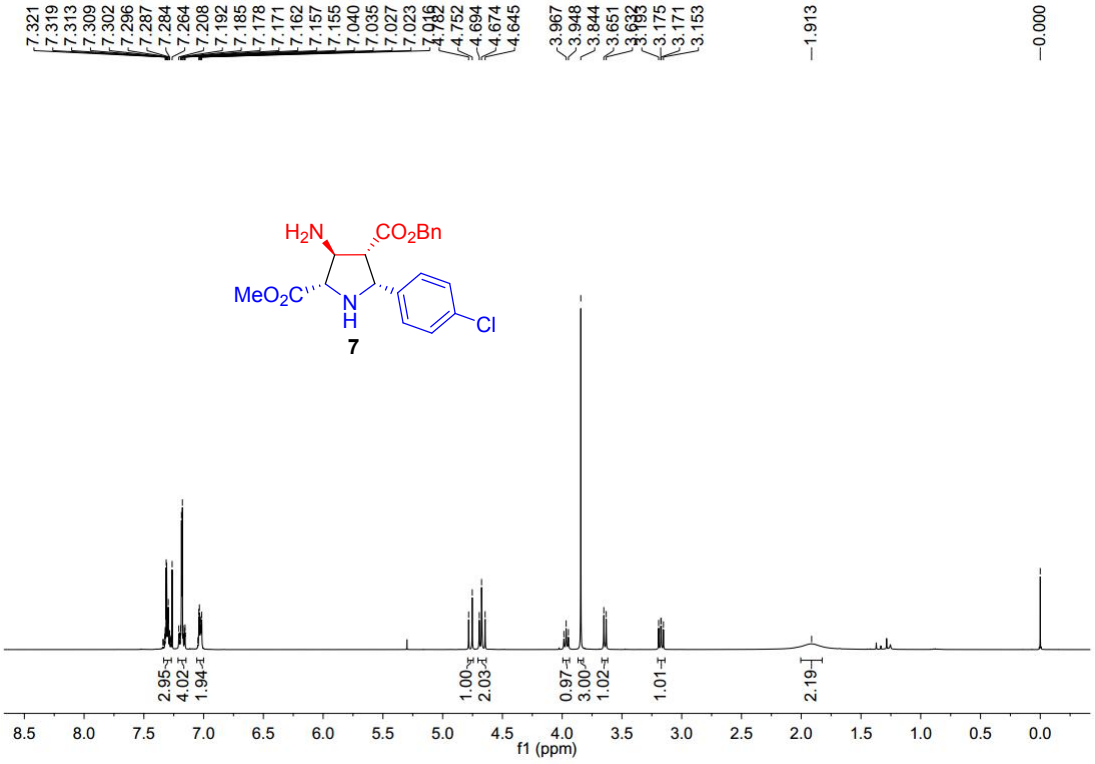
^{1}H NMR spectrum of compound **6**



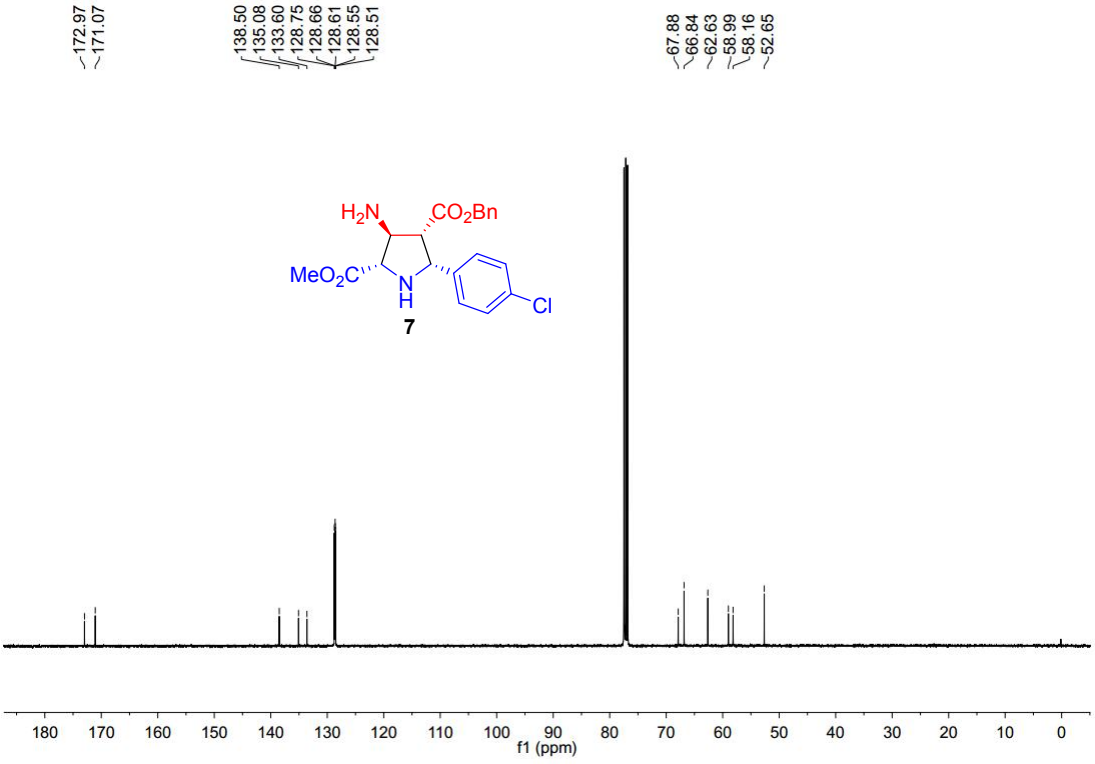
^{13}C NMR spectrum of compound **6**



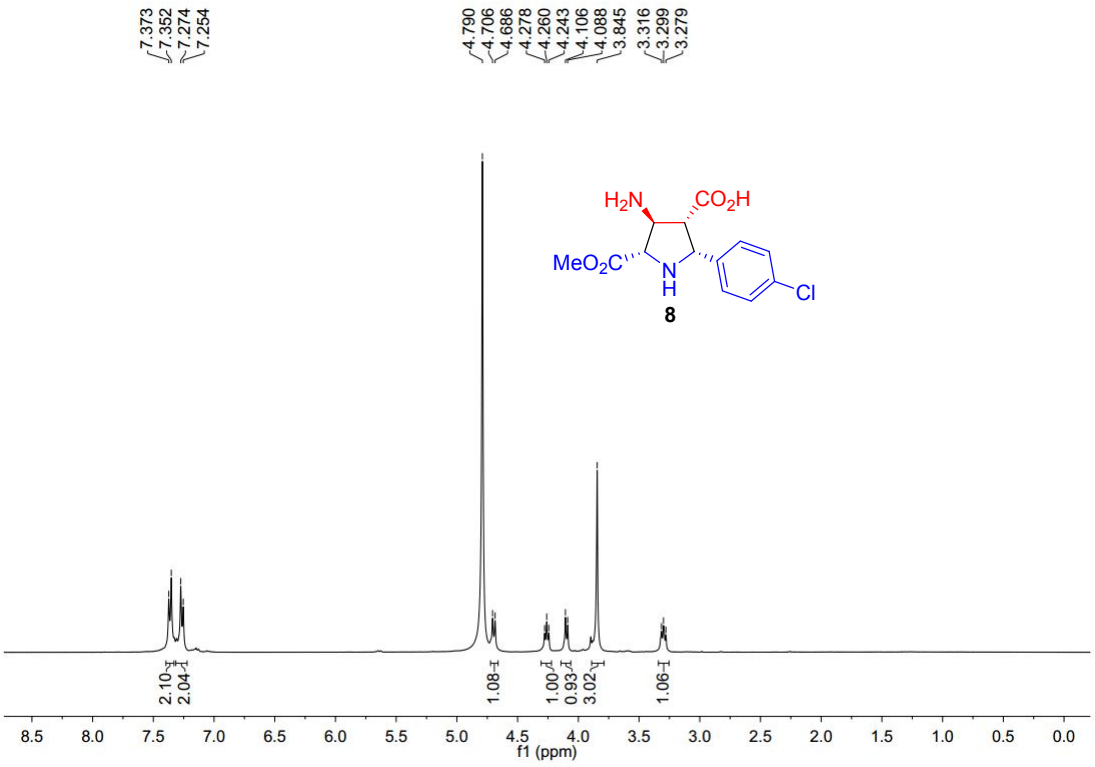
^{1}H NMR spectrum of compound **7**



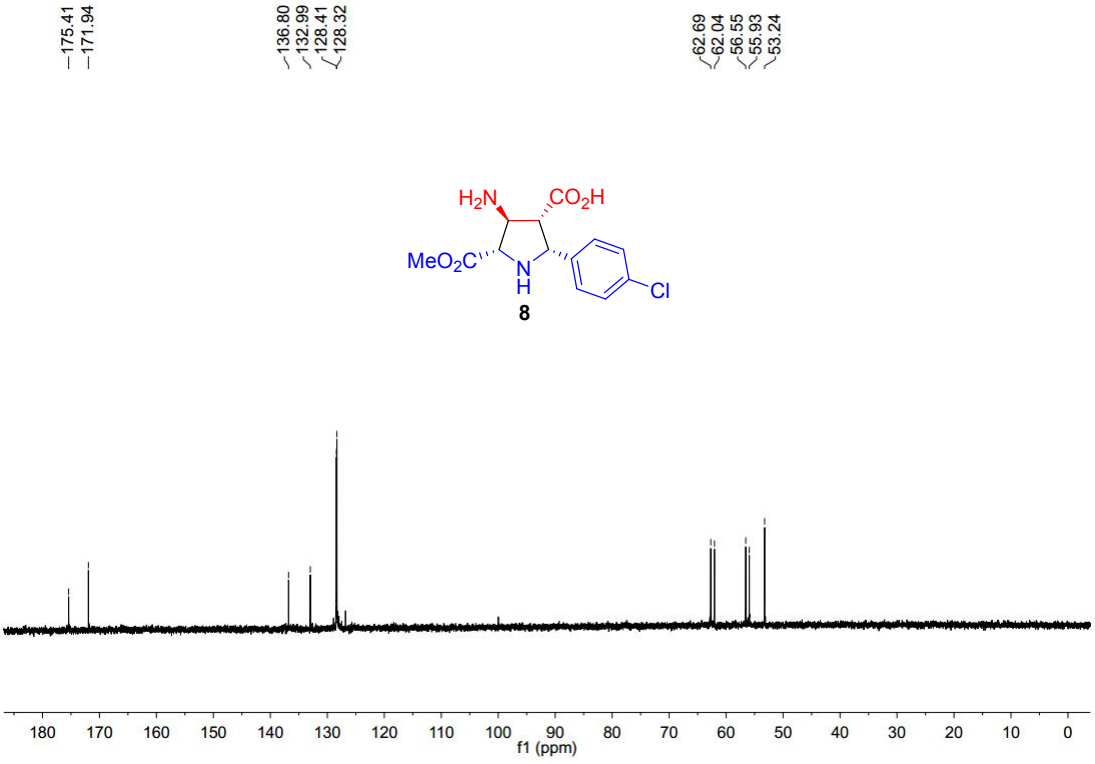
^{13}C NMR spectrum of compound **7**



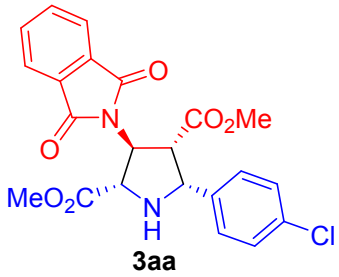
^{1}H NMR spectrum of compound **8**



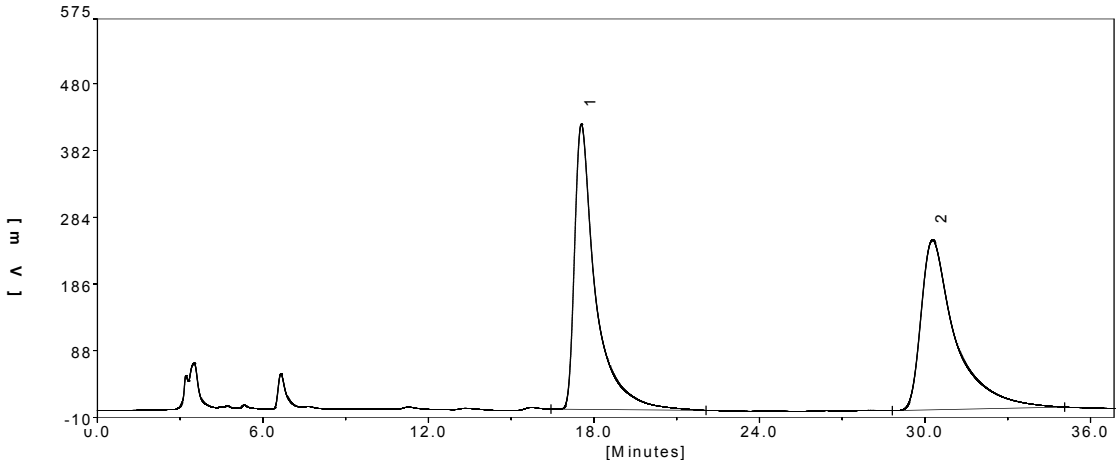
^{13}C NMR spectrum of compound **8**



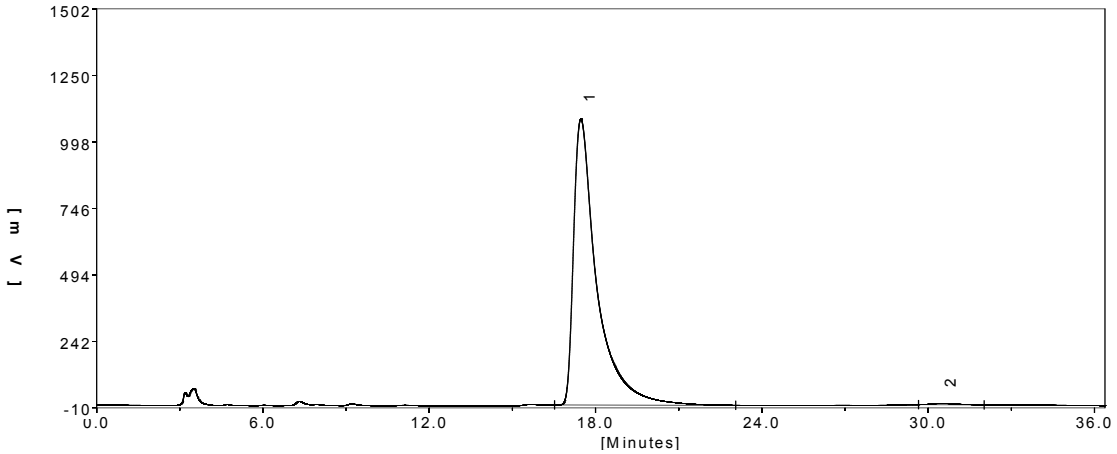
8. Chiral HPLC Chromatograms



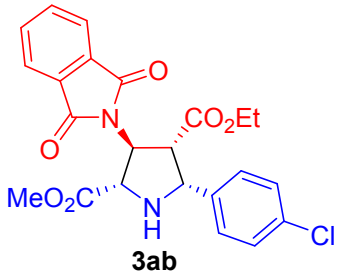
3aa



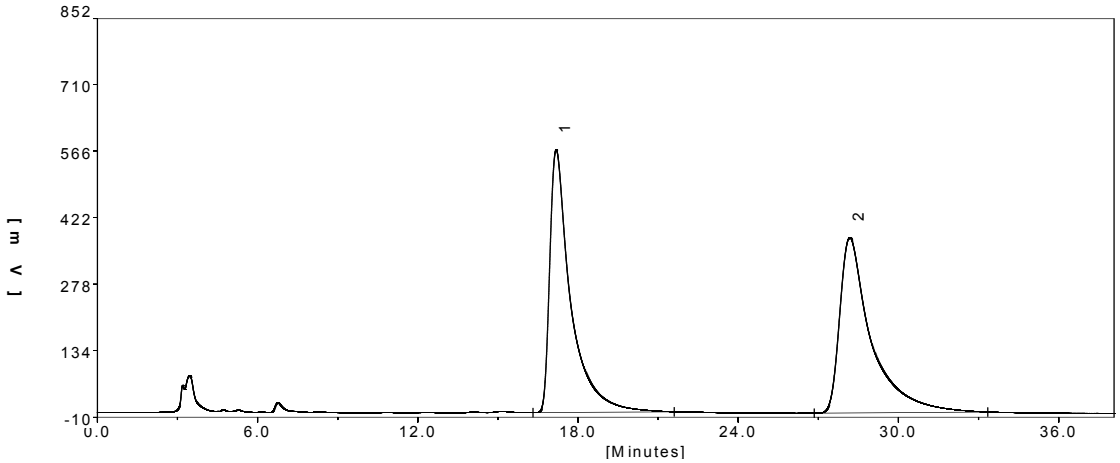
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	17.54667	418.92	22041.32	50.6864
2	30.27167	249.55	21444.34	49.3136



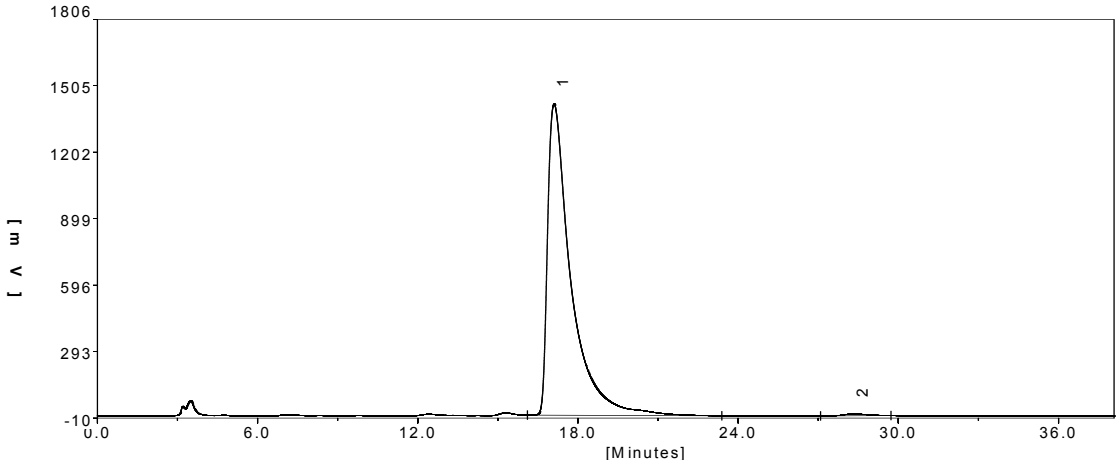
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	17.47167	1084.25	62918.97	99.5164
2	30.48917	4.82	305.74	0.4836



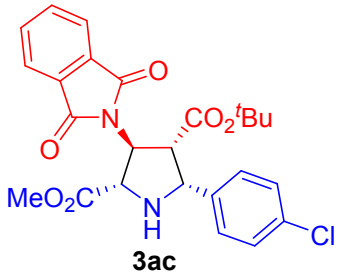
3ab



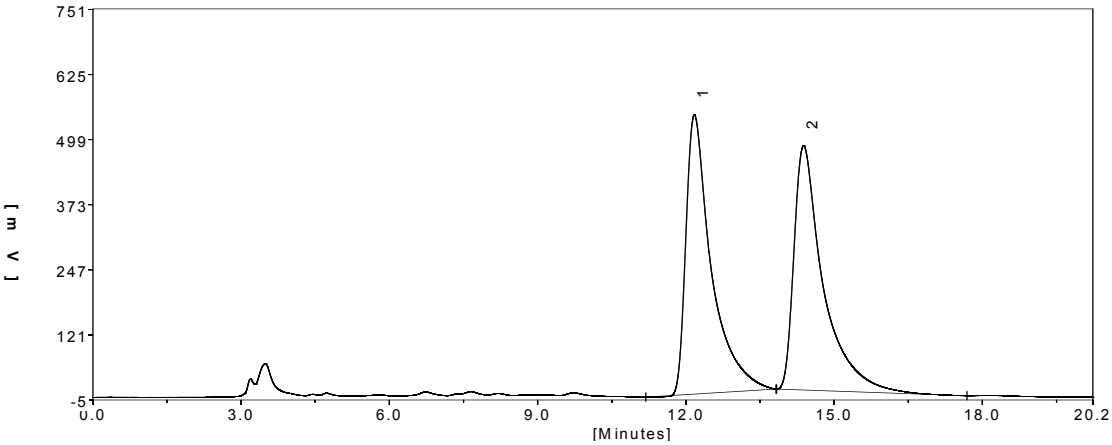
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	17.18333	568.68	30850.04	49.9791
2	28.17750	379.45	30875.89	50.0209



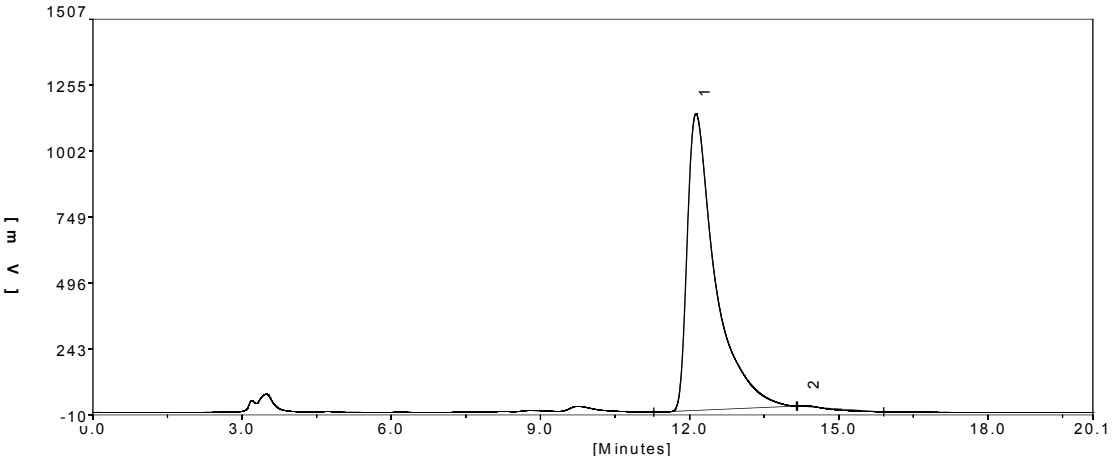
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	17.10833	1418.28	85991.13	99.4094
2	28.32833	8.68	510.84	0.5906



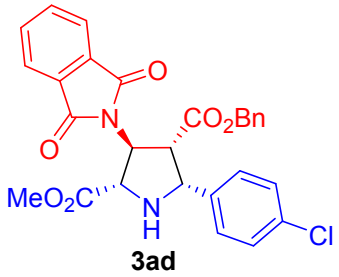
3ac



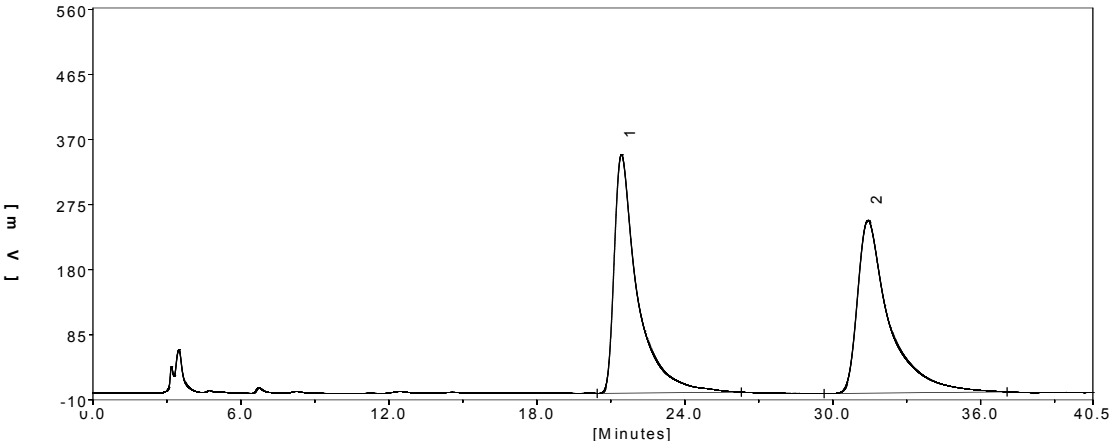
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	12.17167	540.98	19295.28	49.8655
2	14.38167	473.36	19399.35	50.1345



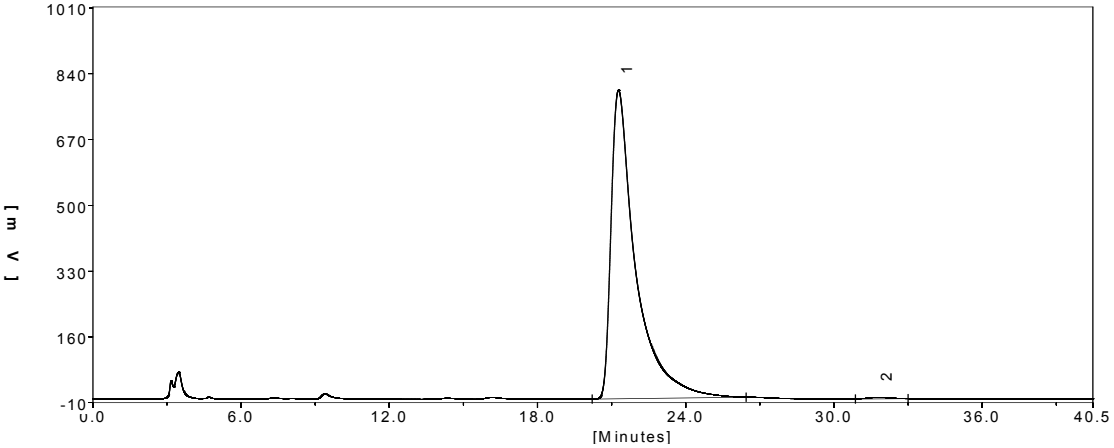
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	12.13000	1138.18	44535.93	99.5516
2	14.31917	2.80	200.61	0.4484



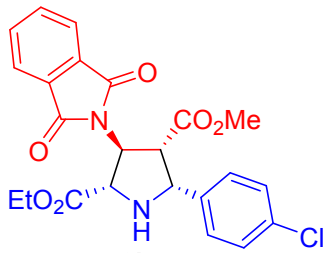
3ad



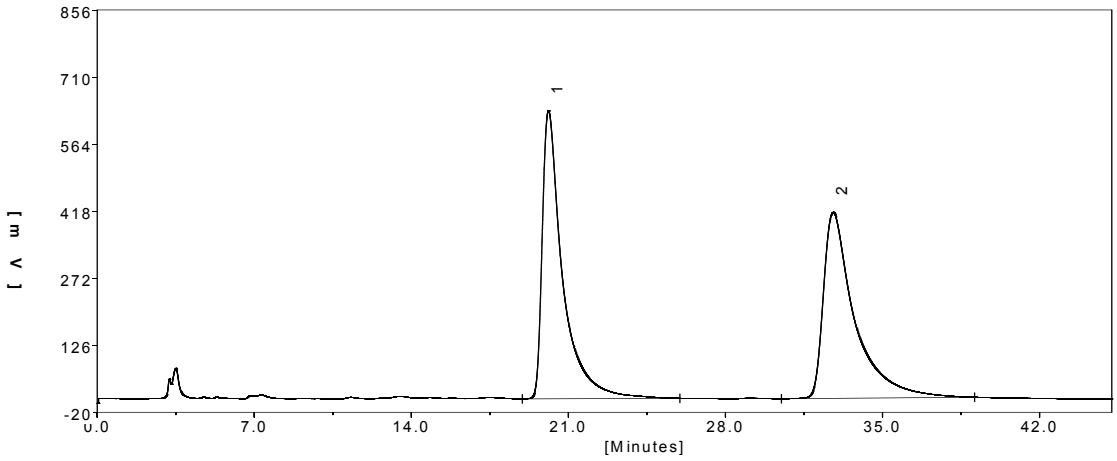
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	21.43333	348.42	22780.88	50.4512
2	31.43000	252.48	22373.39	49.5488



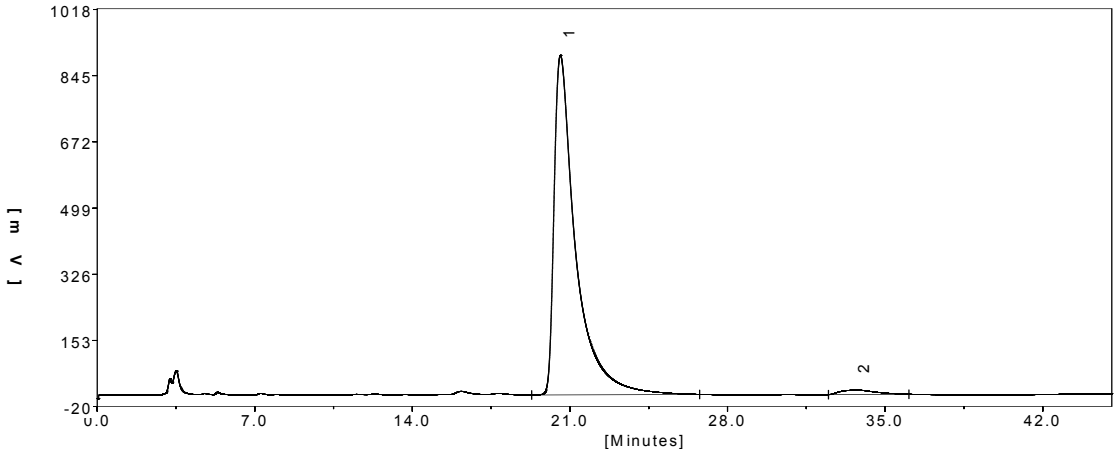
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	21.27750	797.87	55083.17	99.5624
2	31.78250	3.75	242.12	0.4376



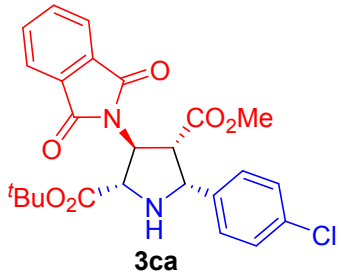
3ba



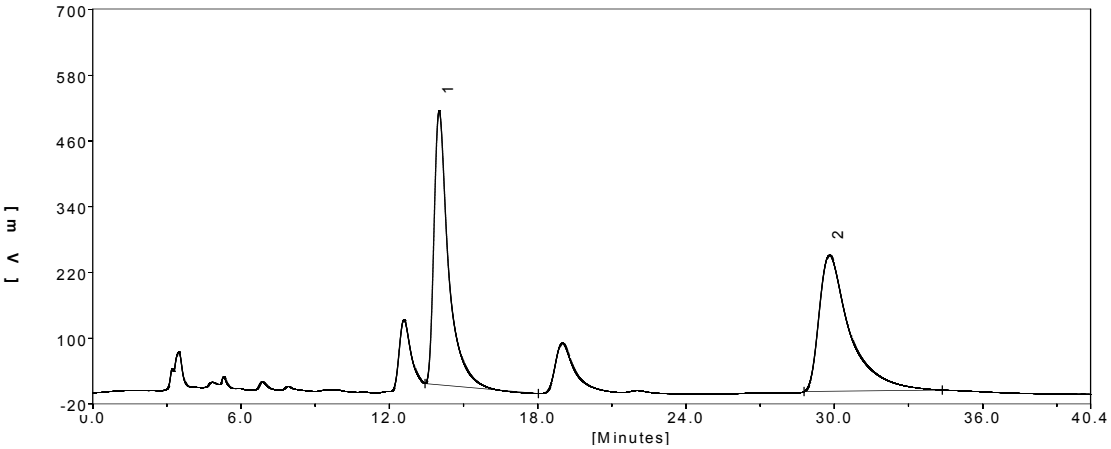
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	20.11333	628.40	39567.54	50.4039
2	32.80250	405.64	38933.46	49.5961



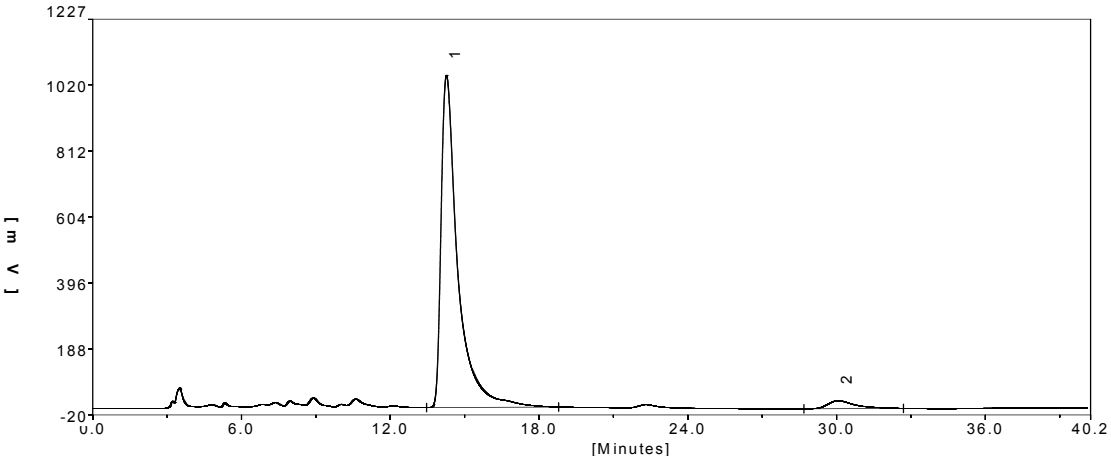
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	20.58000	888.96	59128.24	97.9145
2	33.66750	11.87	1259.36	2.0855



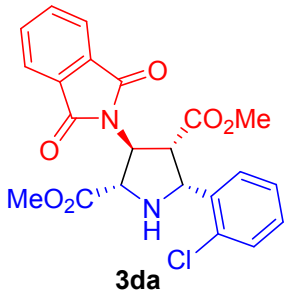
3ca



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	14.01583	500.45	20169.89	48.6057
2	29.80333	248.57	21327.08	51.3943



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	14.26833	1046.85	48961.71	96.2251
2	30.05833	25.18	1920.79	3.7749



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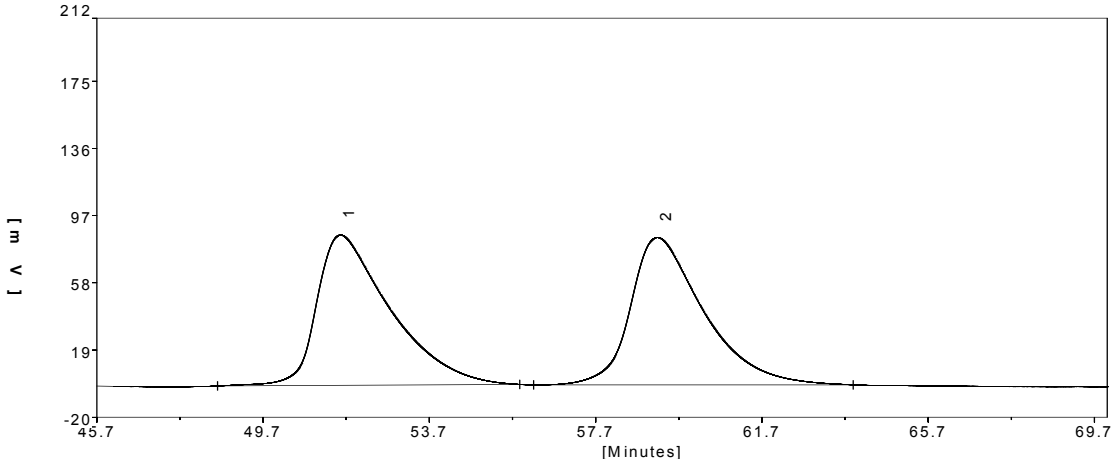
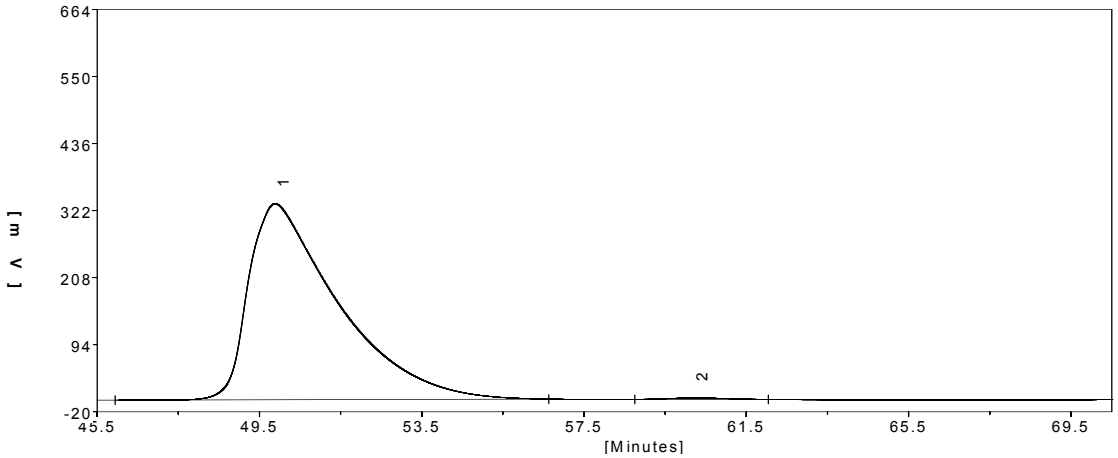
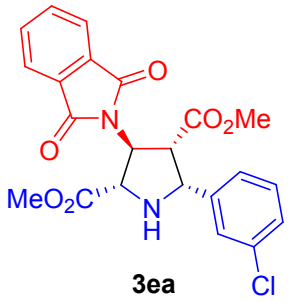


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	51.53083	87.23	10671.65	50.4737
2	59.15917	85.51	10471.33	49.5263



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	49.92333	333.50	50912.32	99.5206
2	60.24917	2.56	245.23	0.4794



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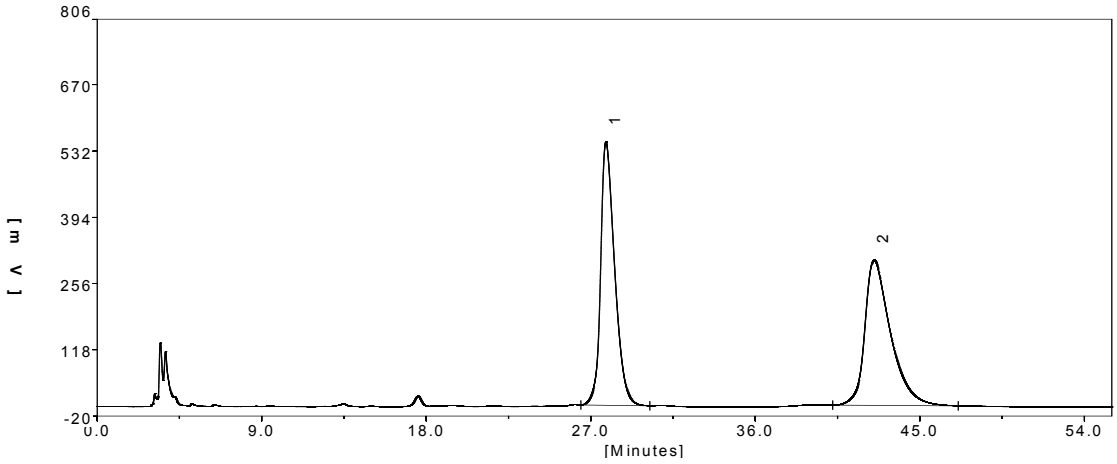
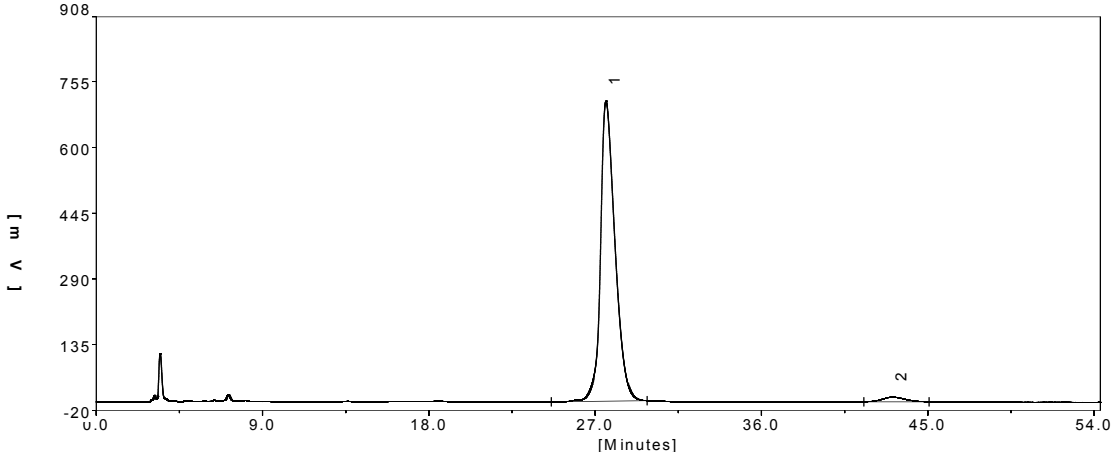
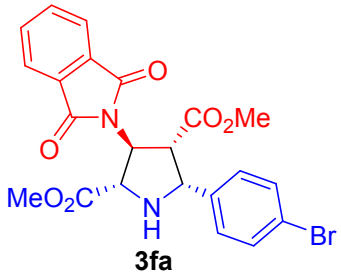


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	27.83083	548.59	29292.69	49.7473
2	42.49667	302.65	29590.28	50.2527



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	27.58750	707.50	38698.33	97.5696
2	43.09833	11.22	963.94	2.4304



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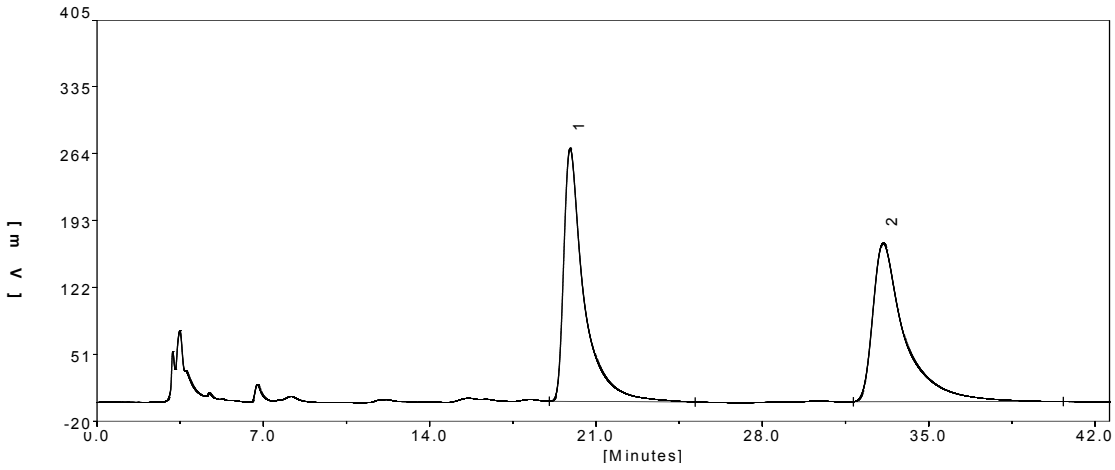
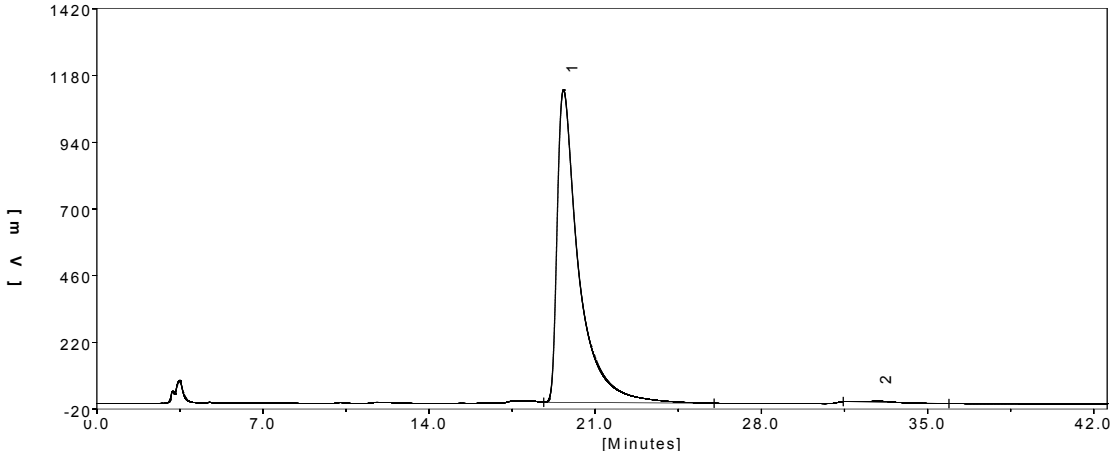
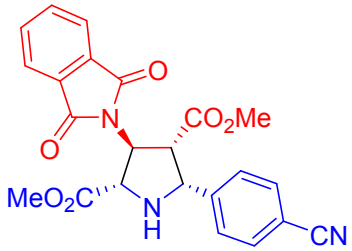


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	19.91167	268.33	15816.11	50.3791
2	33.08250	168.15	15578.06	49.6209



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	19.66500	1124.83	70810.17	99.7058
2	32.87583	3.83	208.95	0.2942



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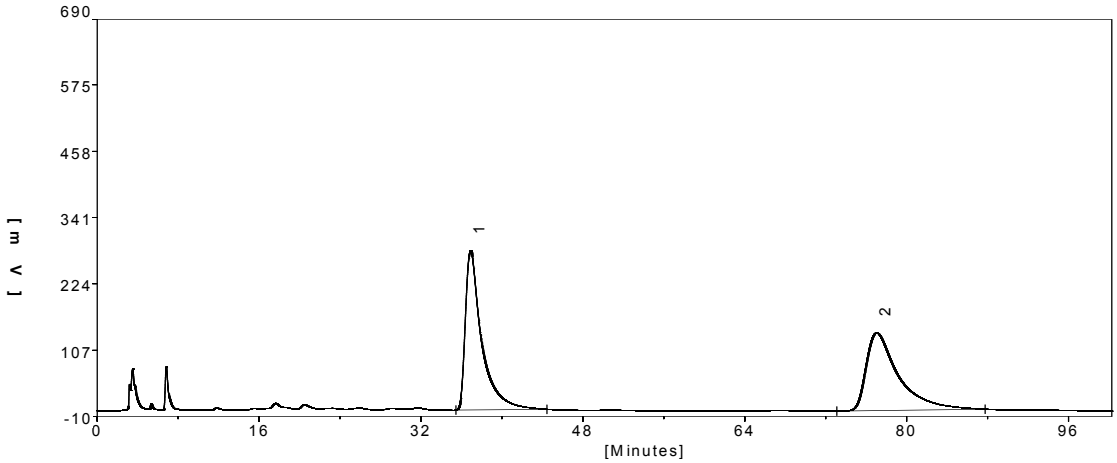
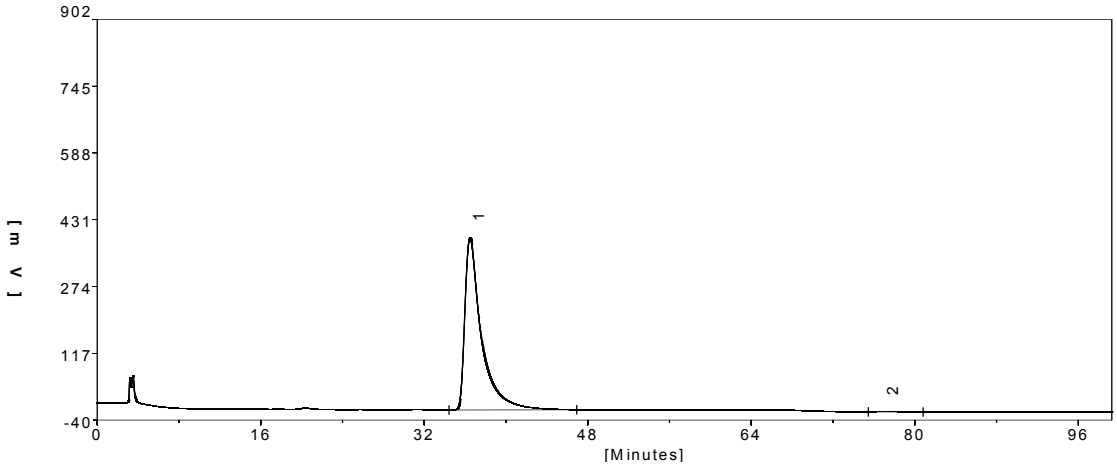
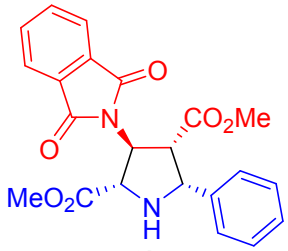


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	36.90083	281.18	31340.05	50.8597
2	77.02083	137.19	30280.58	49.1403



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	36.48333	404.75	45603.45	99.6316
2	77.00917	1.18	168.64	0.3684



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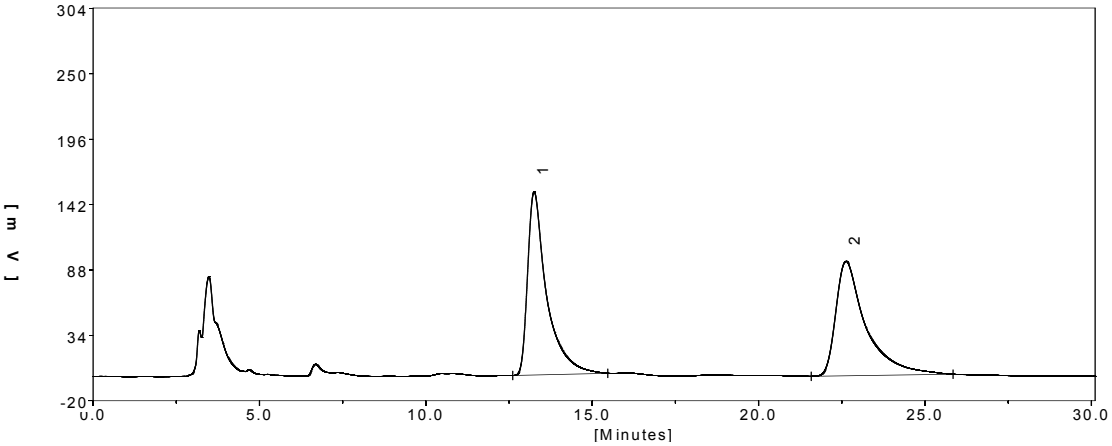
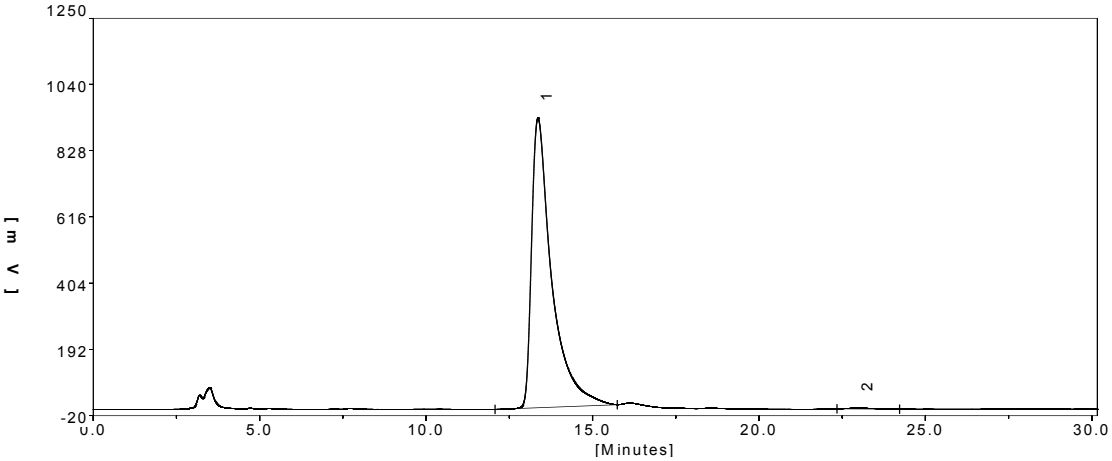
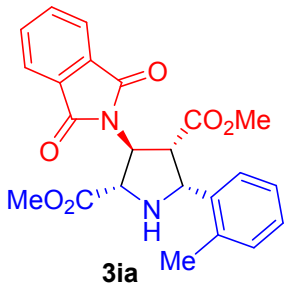


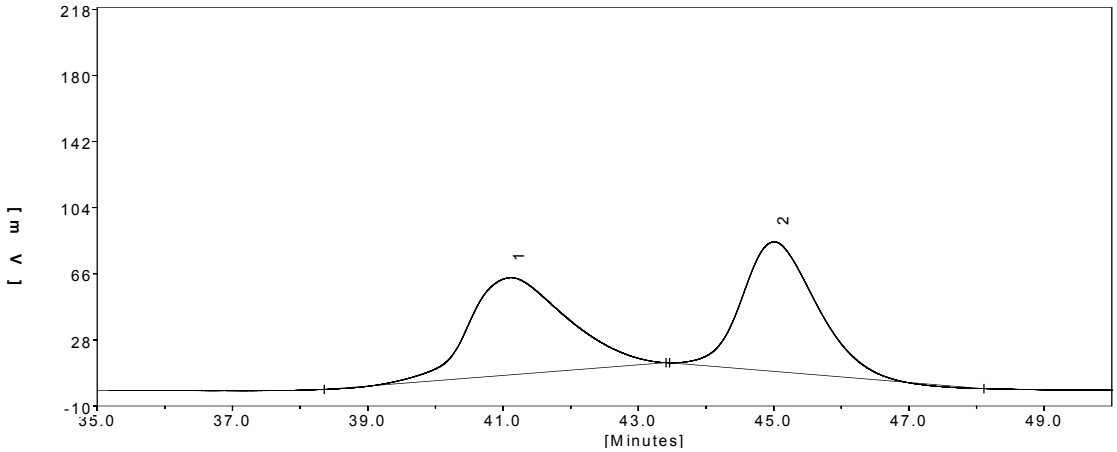
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	13.25417	151.34	6016.90	50.3360
2	22.62750	94.60	5936.57	49.6640



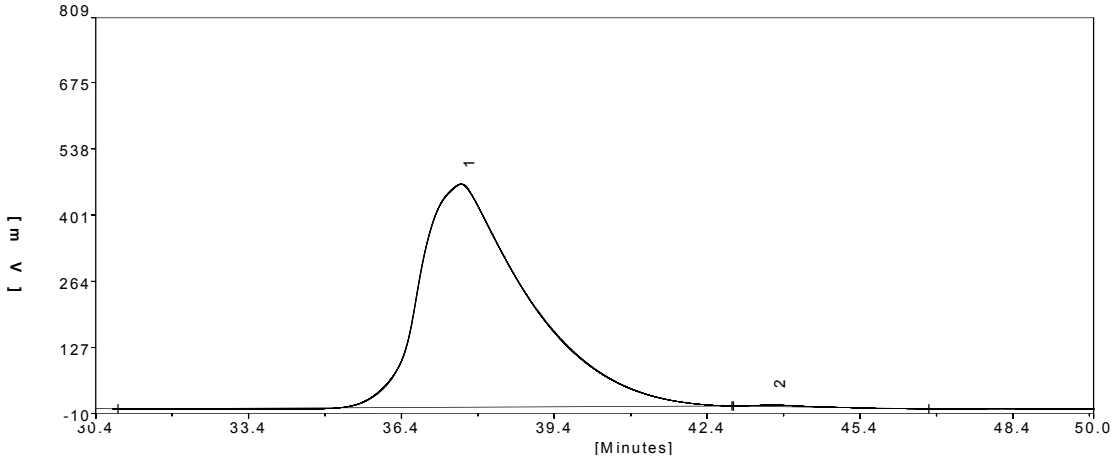
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	13.36250	926.29	38860.91	99.6319
2	22.98750	3.02	143.56	0.3681



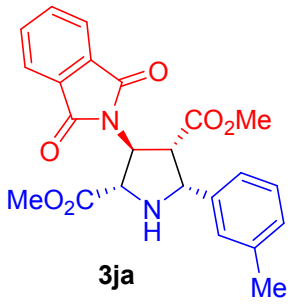
3ia



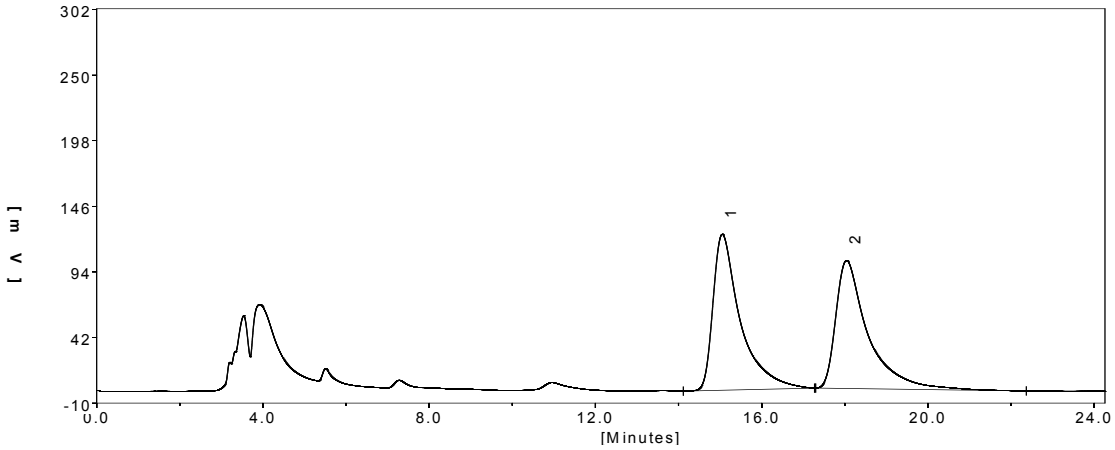
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	41.13083	55.89	5608.03	49.6370
2	45.03333	74.50	5690.05	50.3630



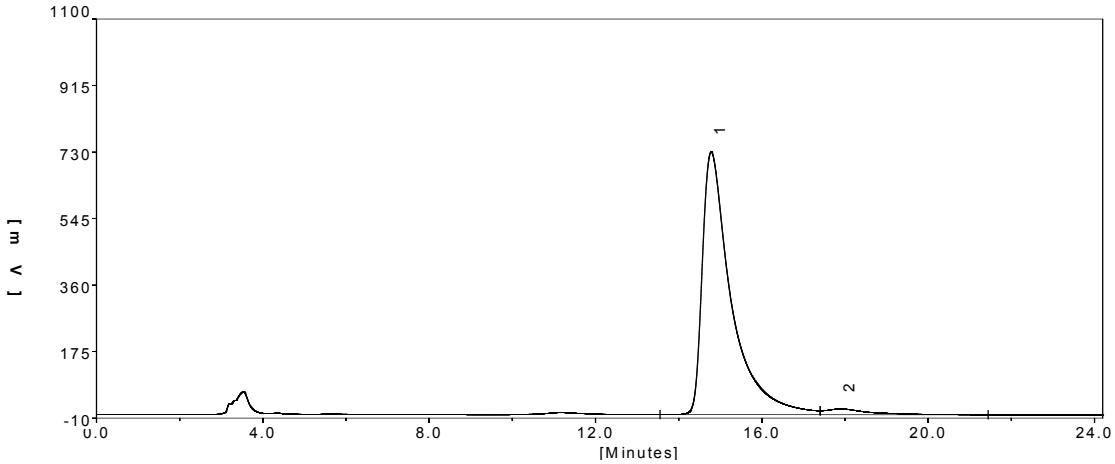
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	37.55583	461.92	67424.51	99.7638
2	43.64917	3.09	159.67	0.2362



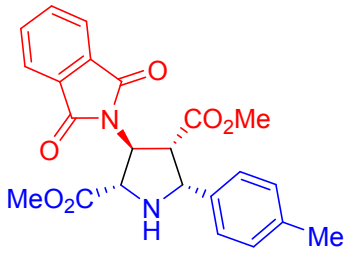
3ja



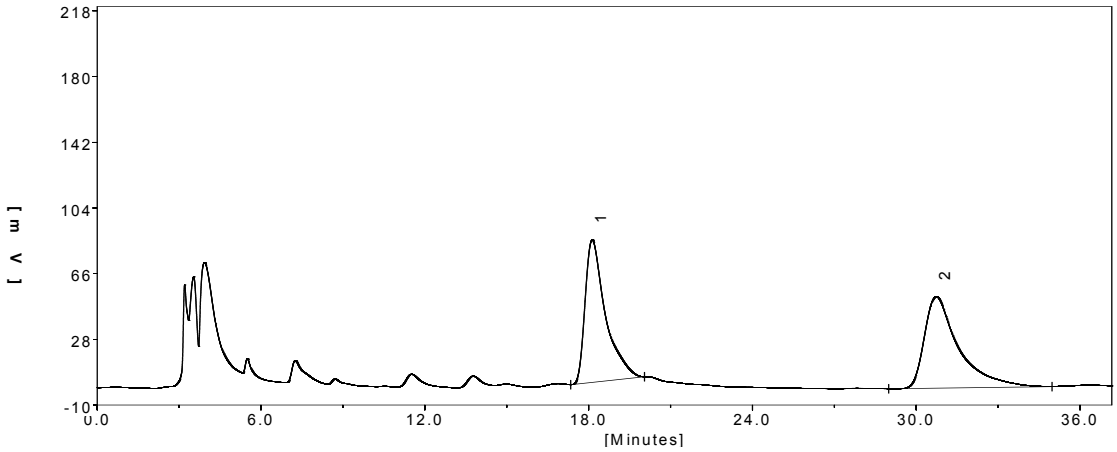
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	15.05417	123.68	5640.57	50.8405
2	18.04250	101.51	5454.08	49.1595



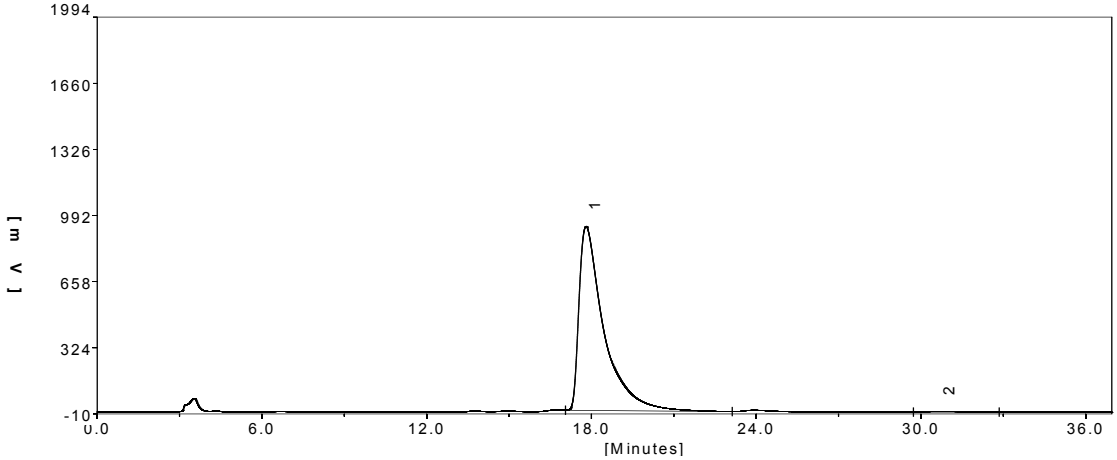
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	14.78417	730.75	35367.84	96.7911
2	17.89500	16.17	1172.55	3.2089



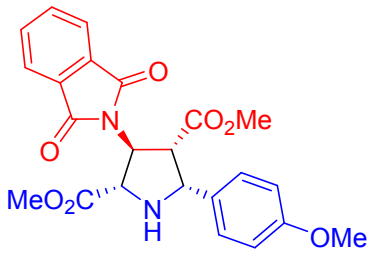
3ka



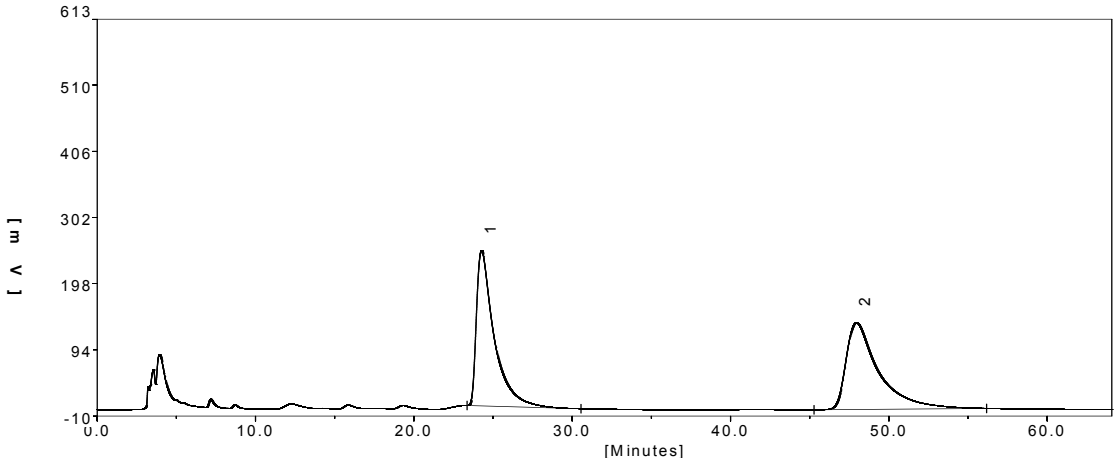
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	18.13417	82.48	4263.74	48.1811
2	30.73167	52.96	4585.66	51.8189



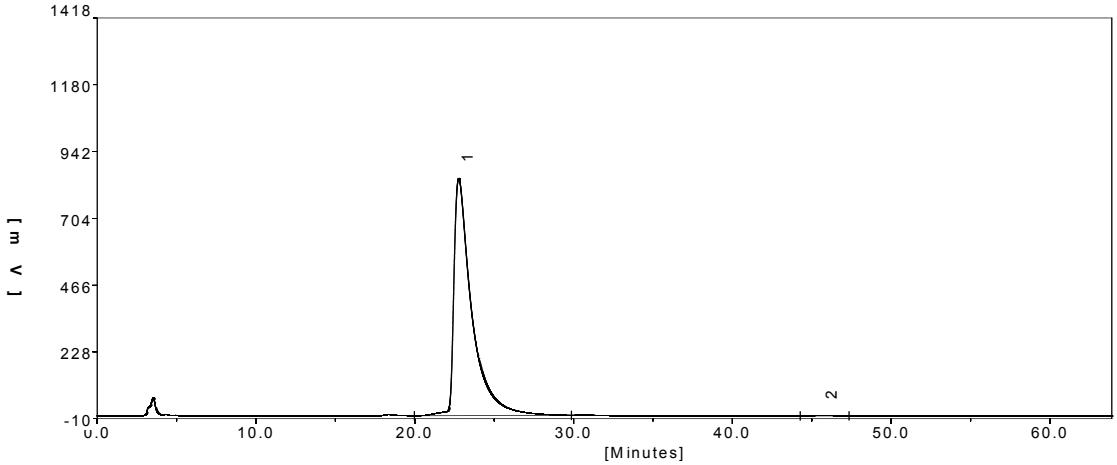
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	17.80417	929.78	58207.44	99.4914
2	30.70417	3.93	297.57	0.5086



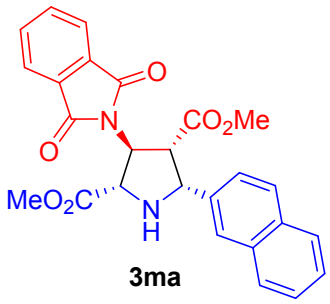
3la



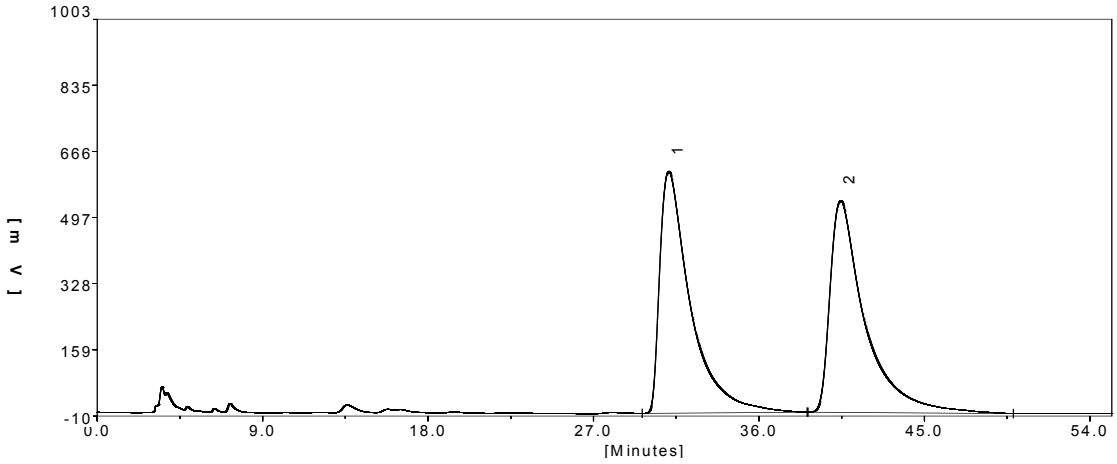
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	24.27583	244.22	18860.63	49.4325
2	47.93333	136.31	19293.66	50.5675



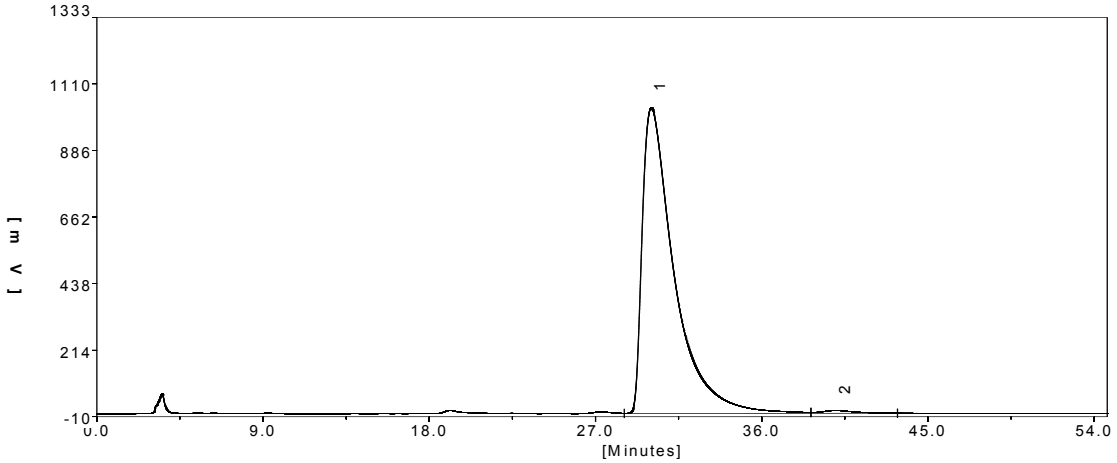
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	22.76917	845.75	66088.70	99.8076
2	45.68417	1.42	127.41	0.1924



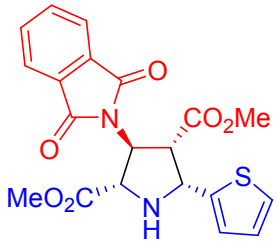
3ma



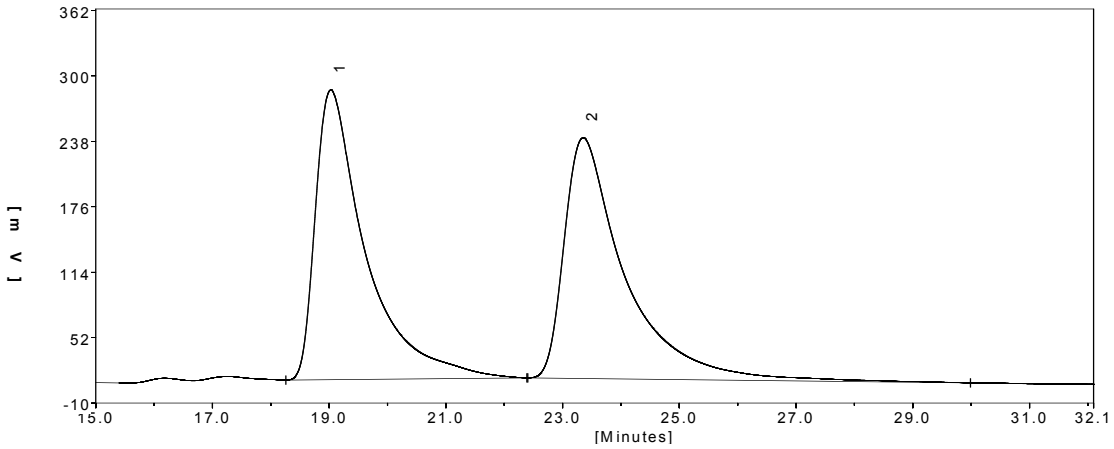
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	31.08917	617.72	71174.78	50.1400
2	40.44000	541.03	70777.21	49.8600



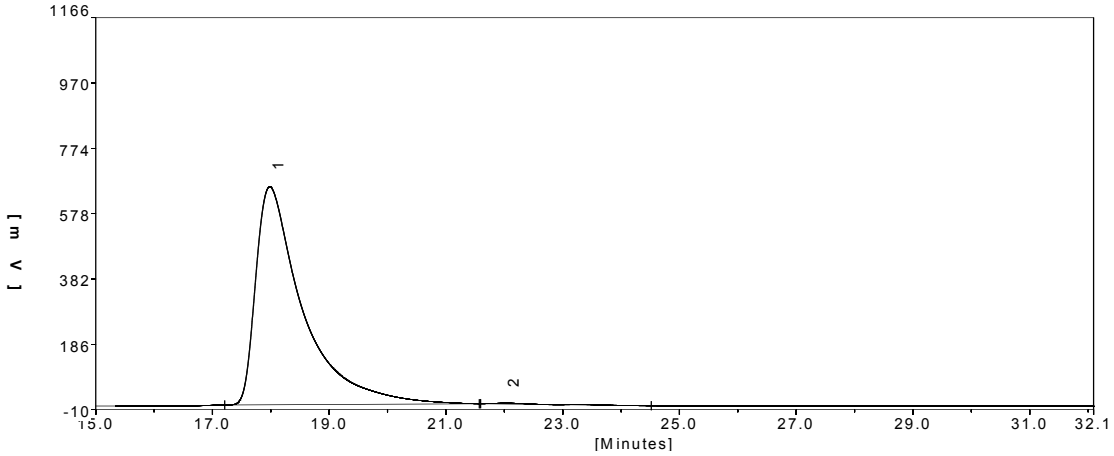
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	30.02333	1028.55	123123.69	99.0763
2	40.03167	9.59	1147.87	0.9237



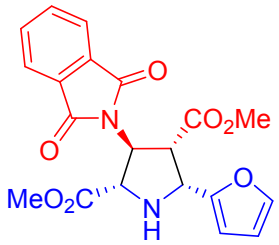
3na



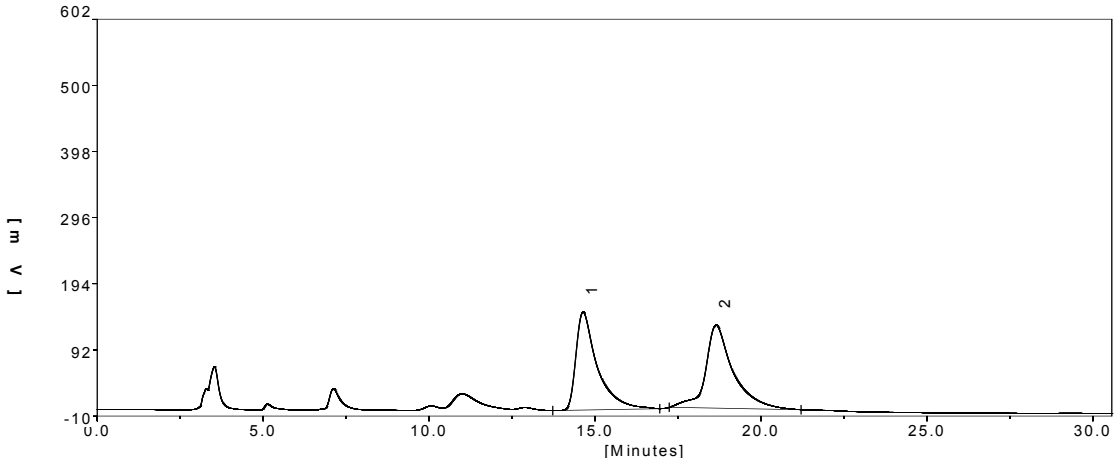
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	18.98833	274.54	16394.00	49.8470
2	23.31083	228.13	16494.66	50.1530



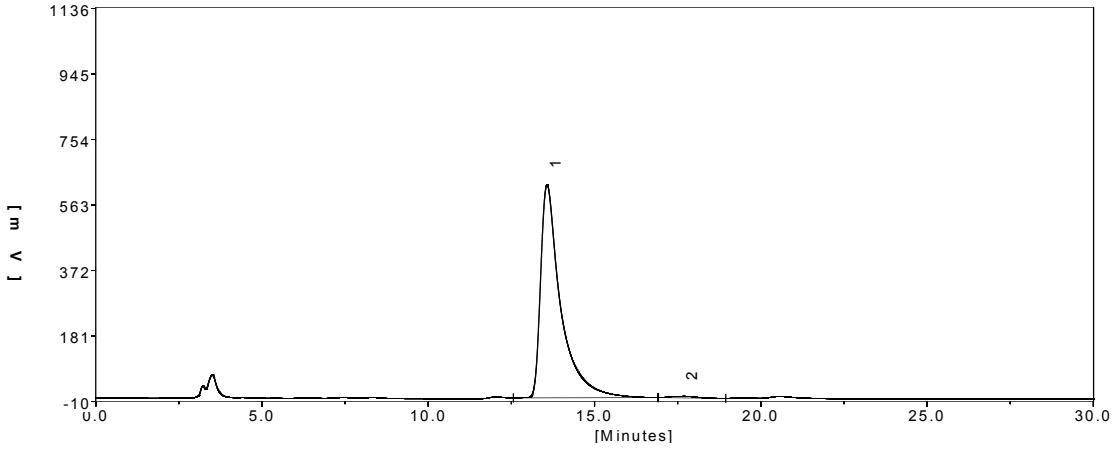
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	18.00083	654.27	36500.02	99.6825
2	22.03083	2.63	116.27	0.3175



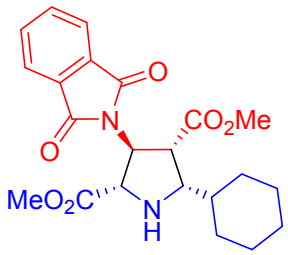
3oa



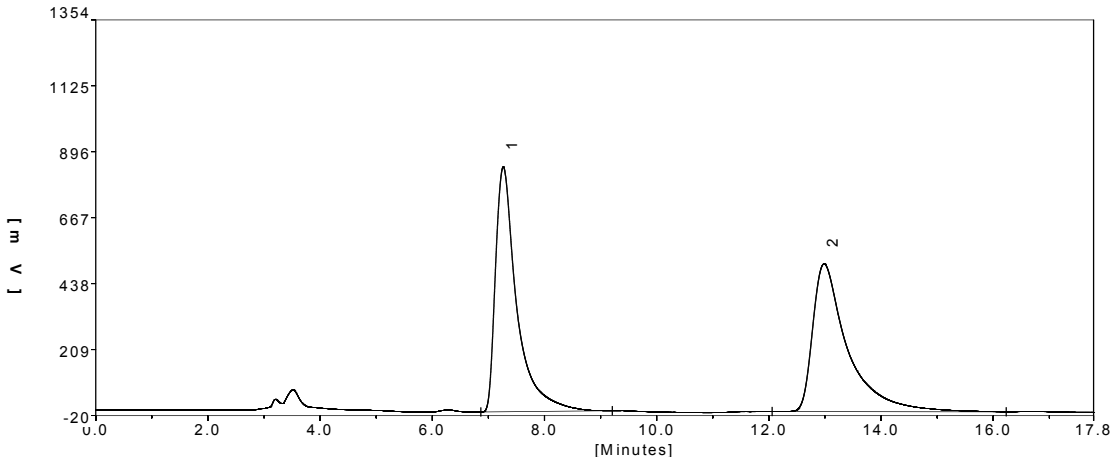
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	14.64083	151.15	6726.10	47.7546
2	18.64750	128.06	7358.61	52.2454



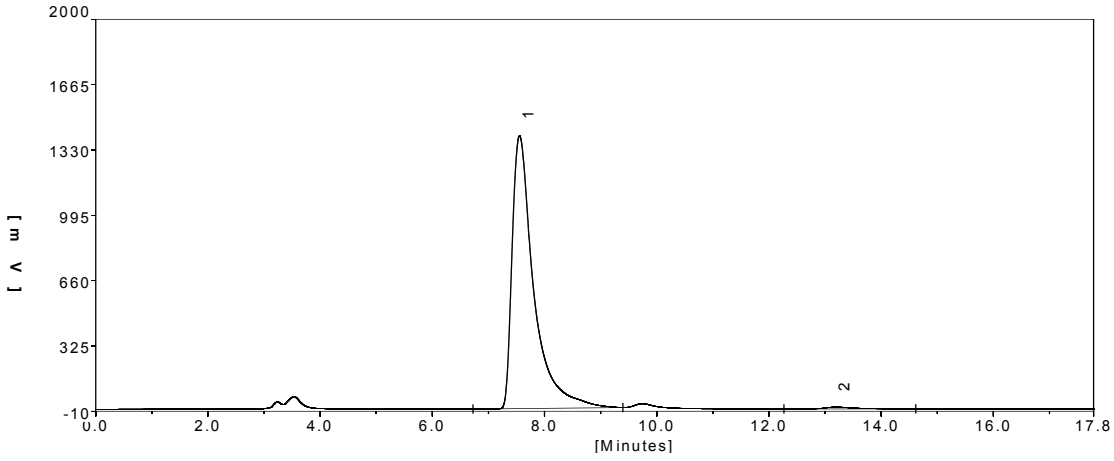
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	13.57333	622.01	26055.56	99.1111
2	17.66750	4.66	233.69	0.8889



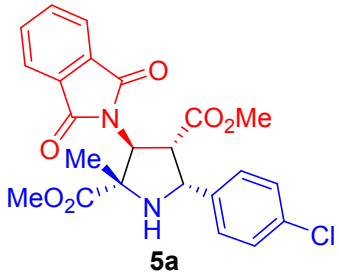
3pa



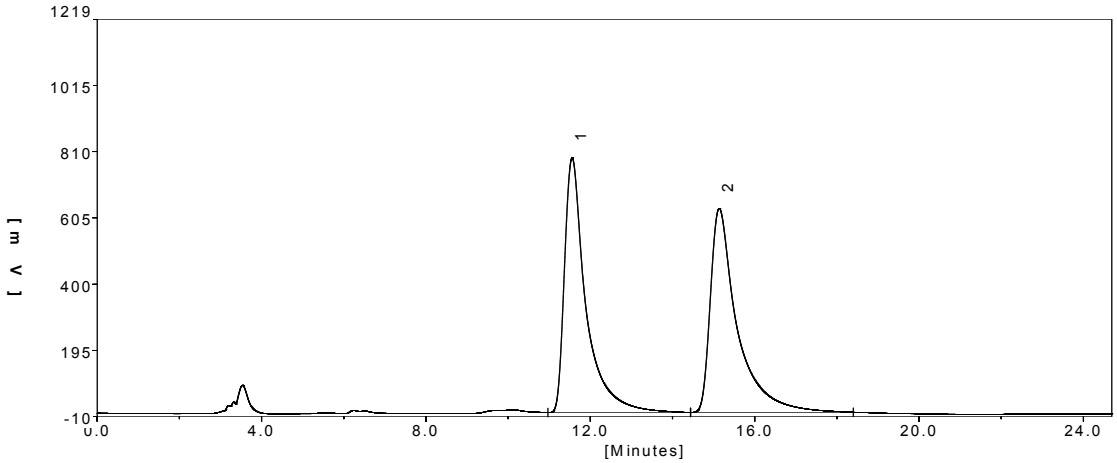
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	7.26500	850.14	22425.82	50.3112
2	12.98500	513.16	22148.38	49.6888



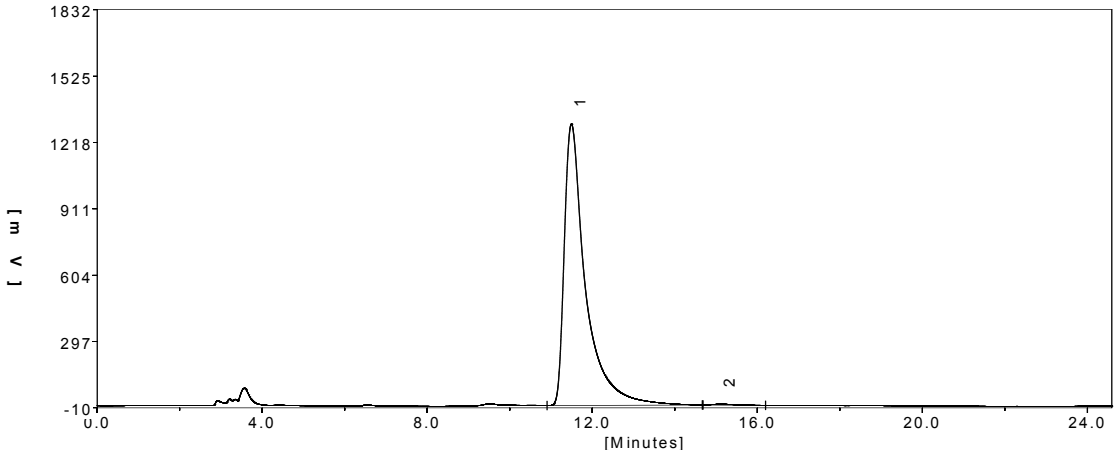
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	7.55417	1398.79	37434.94	99.0824
2	13.19000	9.48	346.68	0.9176



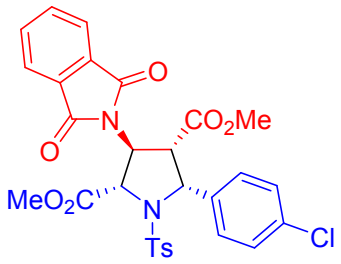
5a



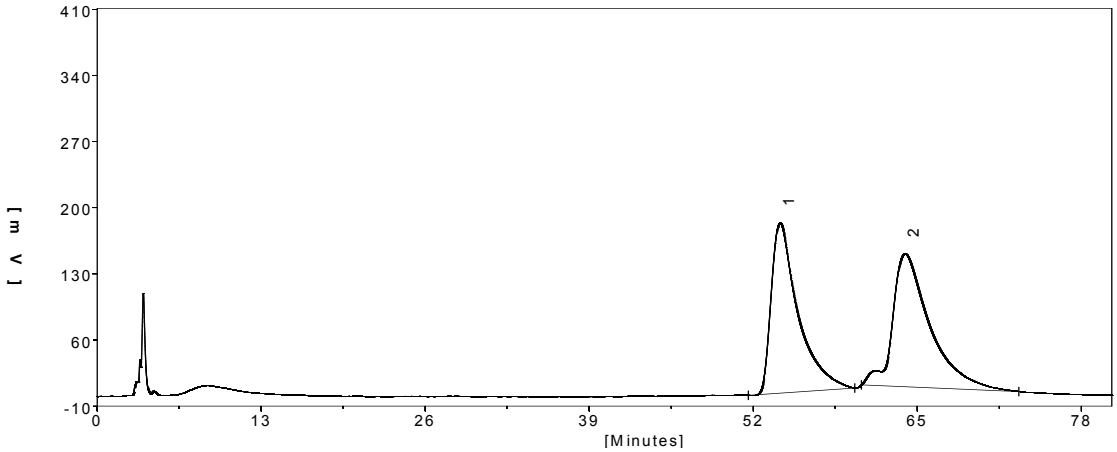
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	11.55750	789.25	28522.35	49.9864
2	15.13667	631.99	28537.87	50.0136



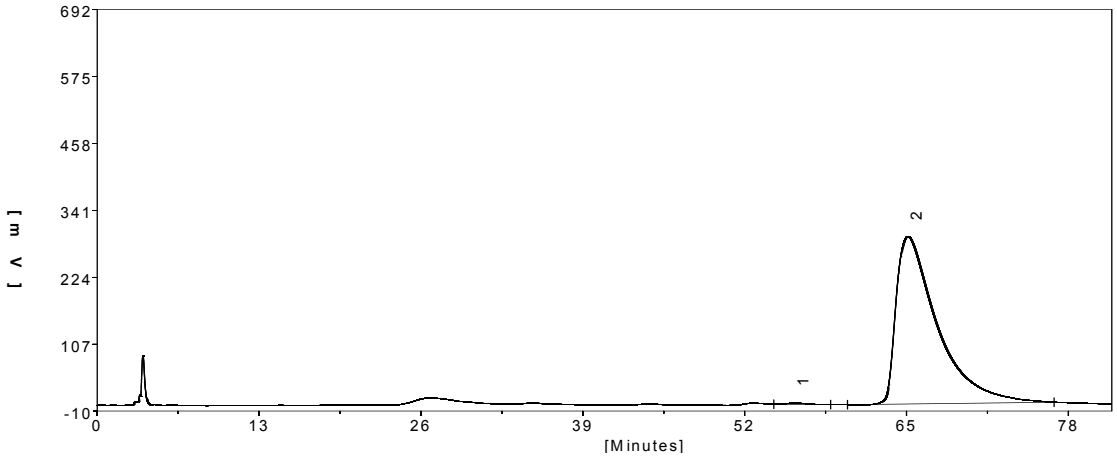
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	11.49417	1302.58	46514.35	99.6785
2	15.11417	4.59	150.01	0.3215



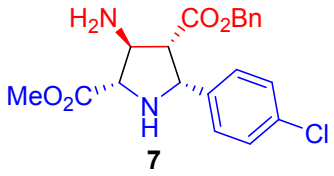
6



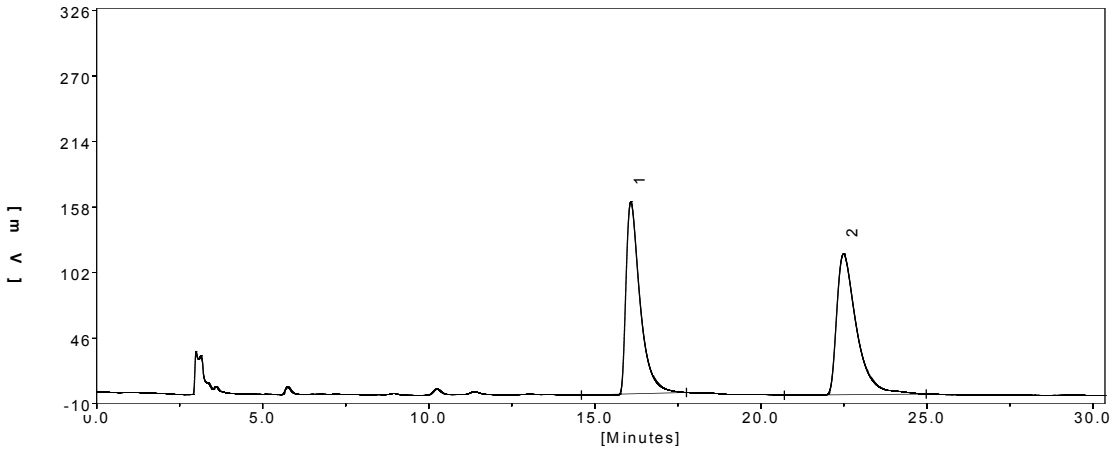
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	54.12625	180.11	26482.78	47.9194
2	63.99750	140.70	28782.50	52.0806



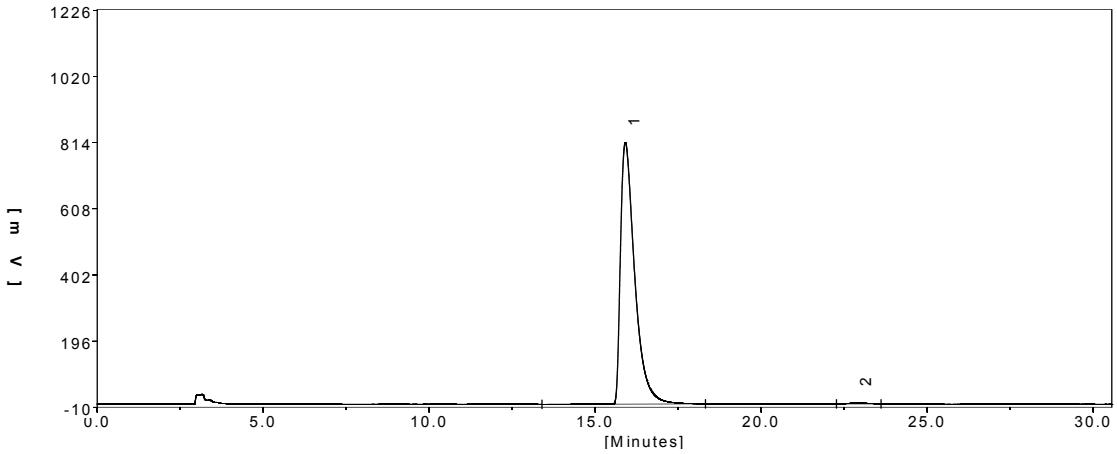
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	55.98417	2.50	239.29	0.3569
2	65.09583	292.99	66815.65	99.6431



7



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	16.08417	164.12	4781.39	49.0436
2	22.49000	120.38	4967.88	50.9564



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	15.90833	814.77	24232.67	99.5162
2	22.88583	3.15	117.81	0.4838