Copper-catalyzed asymmetric construction of dispiropyrrolidine skeleton *via* 1,3-dipolar cycloaddition of azomethine ylides with α-alkylidene succinimides

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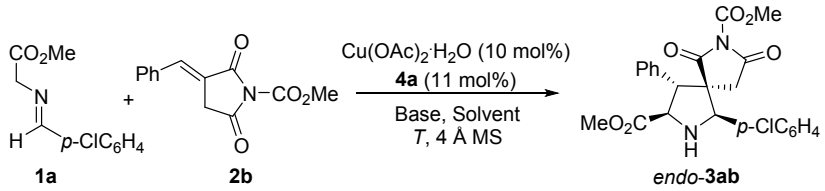
General information

^{1}H NMR spectrum were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ or $(CD_3)_2SO$. Chemical shifts were reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The spectrum are interpreted as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet, coupling constant(s) *J* are reported in Hz and relative integrations are reported. ^{13}C NMR (100 MHz) spectrum were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ or $(CD_3)_2SO$. Chemical shifts were reported in ppm with the internal chloroform signal at 77.16 ppm or DMSO signal at 39.52 ppm as a standard. Optical rotations were measured on an AUTOPOL V. Diastereomeric ratios were determined from crude ^{1}H NMR spectroscopy interpretation. Enantiomeric excess were determined by analysis of HPLC traces, obtained by using chiralcel AD-H, AS-H, or IF columns with *n*-hexane and *i*-propanol or EtOAc as solvents. (Chiralcel AD-H, AS-H, 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 were uncorrected. Mass spectrum were recorded on TOF mass spectrometer. All reagents and starting materials were obtained commercially and used as received unless otherwise stated. Toluene, THF, CPME, 1,4-dioxane and MeTHF were distilled over sodium/benzophenone. CH_3CN, CH_2Cl_2 and EtOAc were distilled over calcium hydride.

Table S1. Optimization of the asymmetric 1,3-dipolar cycloaddition of azomethine ylide 1a to α-alkylidene succinimide 2b

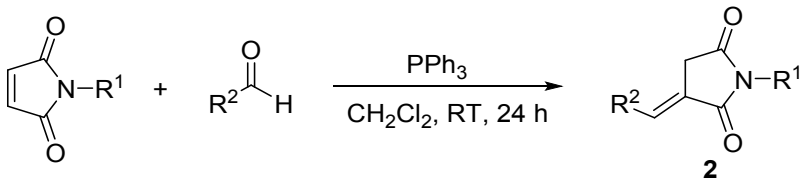


Entry[a]	Base (mol%)	Solvent	*T* (°C)	Yield (%)[b]	ee (%)[c]
1	K_2CO_3 (2 equiv.)	THF	RT	85	93
2	Et_3N (20)	THF	RT	50	93
3	KO^{t}Bu (10)	THF	RT	78	93
4	Cs_2CO_3 (20)	THF	RT	80	93
5	NaHMDS (10)	THF	RT	82	93
6	K_2CO_3 (2 equiv.)	CH_2Cl_2	RT	trace	-
7	K_2CO_3 (2 equiv.)	EtOAc	RT	32	91
8	K_2CO_3 (2 equiv.)	toluene	RT	68	95
9	K_2CO_3 (2 equiv.)	1,4-dioxane	RT	trace	-
10	K_2CO_3 (2 equiv.)	CH_3CN	RT	63	81

11	K_2CO_3 (2 equiv.)	MeTHF	RT	85	95
12[d]	K_2CO_3 (2 equiv.)	MeTHF	RT	85	95

[a] All reactions were carried out with 0.2 mmol of **1a** and 0.1 mmol of **2a** in 1 mL of solvent. MeTHF = 2-Methyltetrahydrofuran. [b] Isolated yield. [c] Determined by chiral HPLC analysis, and >20:1 dr was determined by ^{1}H NMR of crude product. [d] 5 mol% catalyst was used

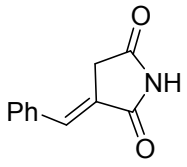
Procedure for the synthesis of α-alkylidene succinimides[1-3]



2

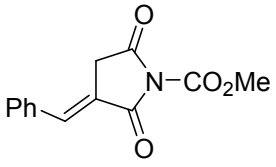
A maleimide derivative (10 mmol, 1.0 equiv.), corresponding aldehyde (10 mmol, 1.0 equiv.) and triphenylphosphine (10 mmol, 1.0 equiv.), were dissolved in anhydrous CH_2Cl_2 (30 mL) and stirred at room temperature for 24 h. The solvent was removed *in vacuo* and purification of the crude product by flash column chromatography yielded the α-alkylidene succinimides **2**.

(*E*)-3-Benzylidenepyrrolidine-2,5-dione (2a). White solid, yield (75%), m.p: > 200 °C; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 11.44 (s, 1H,), 7.66-7.56 (m, 2H), 7.53-7.35 (m, 4H), 3.65 (d, *J* = 2.4, 2H). ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 176.2, 172.4, 134.6, 132.0, 130.6, 130.1, 129.4, 127.5, 121.6, 35.3. The NMR data are in agreement with the literature report.[3]



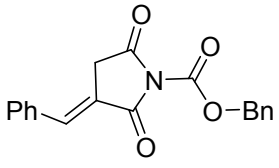
2a

Methyl (*E*)-3-benzylidene-2,5-dioxopyrrolidine-1-carboxylate (2b). White solid, yield (72%), m.p: 149-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.74 (m, 1H), 7.53-7.45 (m, 5H), 4.03 (s, 3H), 3.70 (d, *J* = 2.4, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 166.5, 149.0, 137.4, 133.6, 130.8, 130.5, 129.3, 121.6, 55.0, 34.4; HRMS (EI, m/z): Calcd for $C_{13}H_{11}NO_4$ $[M]^+$: 245.0683, found: 245.0687.



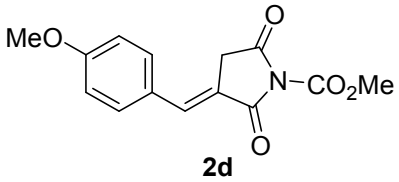
2b

Benzyl (*E*)-3-benzylidene-2,5-dioxopyrrolidine-1-carboxylate (2c). White solid, yield (80%), m.p: 157-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (t, *J* = 2.4, 1H), 7.49-7.46 (m, 7H), 7.44-7.32 (m, 3H), 5.43 (s, 2H), 3.67 (d, *J* = 2.4, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 166.5, 148.4, 137.4, 134.1, 133.6, 130.8, 130.5, 129.3, 128.8, 128.7, 128.4, 121.6, 69.9, 34.4; HRMS (EI, m/z): Calcd for $C_{19}H_{15}NO_4$ $[M]^+$: 321.0996, found: 321.0997.



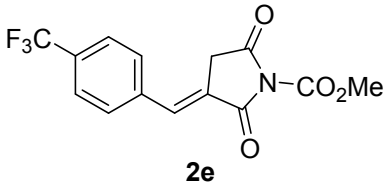
2c

Methyl (*E*)-3-(4-methoxybenzylidene)-2,5-dioxopyrrolidine-1-carboxylate (2d). White solid, yield (67%), m.p: 155-157 °C;[1]H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 1.9, 1H), 7.51-7.40 (m, 2H), 7.06-6.92 (m, 2H), 4.03 (d, *J* = 2.0, 3H), 3.87 (d, *J* = 1.9, 3H), 3.65 (s, 2H);[13]C NMR (100 MHz, $CDCl_3$) δ 170.0, 166.8, 161.7, 149.1, 137.1, 132.5, 126.4, 118.5, 114.8, 55.5, 54.9, 34.5; HRMS (EI, m/z): Calcd for $C_{14}H_{13}NO_5$ $[M]^+$: 275.0789, found: 275.0789.



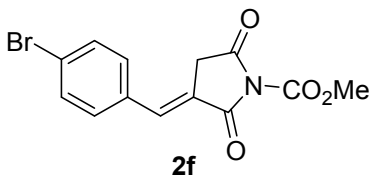
2d

Methyl (*E*)-2,5-dioxo-3-(4-(trifluoromethyl)benzylidene)pyrrolidine-1-carboxylate (2e).White solid, yield (70%), m.p: 200-202 °C; [1]H NMR (400 MHz, $CDCl_3$) δ 7.76-7.78 (m, 2H), 7.73 (s, 1H), 7.62 (d, *J* = 8.2, 2H), 4.04 (s, 3H), 3.73 (d, *J* = 2.4, 2H); [13]C NMR (100 MHz, $CDCl_3$) δ 169.1, 166.1, 148.8, 136.8, 135.4, 132.1 (q, $J_{C\text{-}F}$ = 32.9), 130.5, 126.2 (q, $J_{C\text{-}F}$ = 3.7), 124.2, 123.6 (q, $J_{C\text{-}F}$ = 272.4), 55.1, 34.3; HRMS (EI, m/z): Calcd for $C_{14}H_{10}F_3NO_4$ $[M]^+$: 313.0557, found: 313.0560.



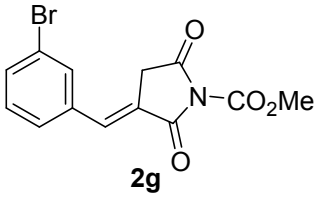
2e

Methyl (*E*)-3-(4-bromobenzylidene)-2,5-dioxopyrrolidine-1-carboxylate (2f). White solid, yield (63%), m.p: 193-195 °C; [1]H NMR (400 MHz, $CDCl_3$) δ 7.71-7.68 (m, 1H), 7.64 (d, *J* = 8.4, 2H), 7.38 (d, *J* = 8.4, 2H), 4.05 (s, 3H), 3.68 (d, *J* = 2.3, 2H); [13]C NMR (100 MHz, $CDCl_3$) δ 169.3, 166.3, 148.9, 136.0, 132.6, 132.4, 131.7, 125.5, 122.2, 55.1, 34.3; HRMS (EI, m/z): Calcd for $C_{13}H_{10}BrNO_4$ $[M]^+$: 322.9788, found: 322.9794.



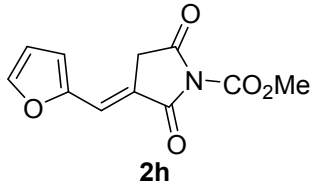
2f

Methyl (*E*)-3-(3-bromobenzylidene)-2,5-dioxopyrrolidine-1-carboxylate (2g). White solid, yield (65%), m.p: 160-162 °C; [1]H NMR (400 MHz, $CDCl_3$) δ 7.66-7.67 (m, 1H), 7.62 (s, 1H), 7.59 (d, *J* = 7.9, 1H), 7.43 (d, *J* = 7.8, 1H), 7.36 (t, *J* = 7.8, 1H), 4.03 (s, 3H), 3.70 (d, *J* = 2.4, 2H); [13]C NMR (100 MHz, $CDCl_3$) δ 169.3, 166.2, 148.9, 135.6, 135.5, 133.7, 133.0, 130.7, 128.9, 123.3, 123.1, 55.1, 34.3; HRMS (EI, m/z): Calcd for $C_{13}H_{10}BrNO_4$ $[M]^+$: 322.9788, found: 322.9792.



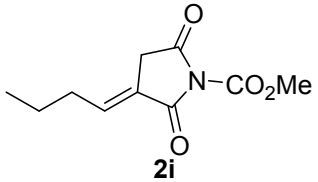
2g

Methyl (*E*)-3-(furan-2-ylmethylene)-2,5-dioxopyrrolidine-1-carboxylate (2h). Yellow solid, yield (75%), m.p: 141-143 °C;[1]H NMR(400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 1.4, 1H), 7.48 (t, *J* = 2.4, 1H), 6.81 (d, *J* = 3.5, 1H), 6.58 (dd, *J* = 3.5, 1.8, 1H), 4.02 (s, 3H), 3.75 (d, *J* = 2.4, 2H); [13]C NMR (100 MHz, $CDCl_3$) δ 170.2, 166.3, 150.6, 149.1, 146.6, 123.0, 118.7, 118.4, 113.0, 54.9, 34.5; HRMS (EI, m/z): Calcd for $C_{11}H_9NO_5$ $[M]^+$: 235.0476, found: 235.0480.



2h

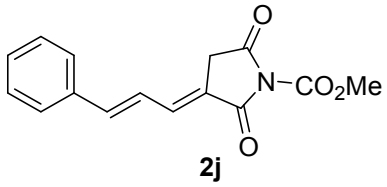
Methyl (*E*)-3-butylidene-2,5-dioxopyrrolidine-1-carboxylate (2i).



2i

Colorless oil, yield (68%), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02-6.92 (m, 1H), 4.00 (s, 3H), 3.34 (dt, *J* = 2.6, 1.4, 2H), 2.20 (q, *J* = 7.4, 2H), 1.65-1.49 (m, 2H), 0.97 (t, *J* = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 165.3, 149.0, 142.6, 124.2, 54.9, 32.3, 32.1, 21.3, 13.8; HRMS (EI, m/z): Calcd for $C_{10}H_{13}NO_4$ $[M]^+$: 211.0840, found: 211.0843.

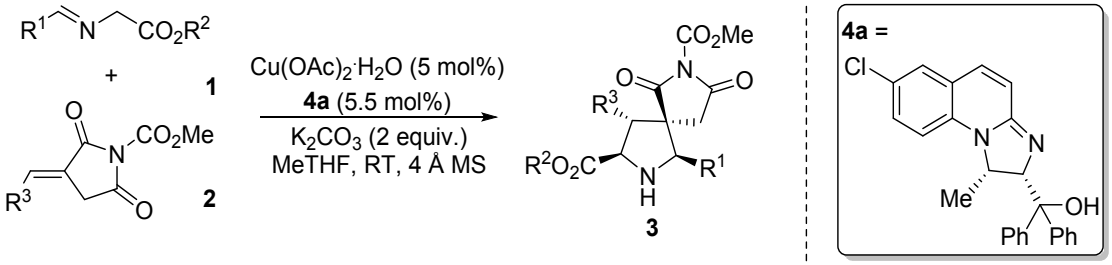
Methyl (*E*)-2,5-dioxo-3-((*E*)-3-phenylallylidene)pyrrolidine-1-carboxylate(2j). Yellow solid,



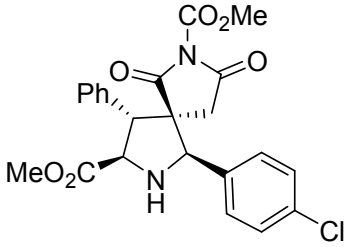
2j

yield (70%), m.p: 196-198 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (m, 3H), 7.43-7.34 (m, 3H), 7.08 (d, *J* = 15.4, 1H), 6.78 (dd, *J* = 15.4, 11.7, 1H), 4.02 (s, 3H), 3.53 (d, *J* = 2.2, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 165.8, 149.1, 144.3, 137.0, 135.4, 130.1, 129.0, 127.7, 122.5, 121.9, 54.9, 32.8; HRMS (EI, m/z): Calcd for $C_{15}H_{13}NO_4$ $[M]^+$: 271.0840, found: 271.0847.

Procedure for the asymmetric 1,3-dipolar cycloaddition of azomethine ylides to α-alkylidene succinimides



Under a nitrogen atmosphere, $Cu(OAc)_2 \cdot H_2O$ (2.0 mg, 0.01 mmol), ligand **4a** (4.4 mg, 0.011 mmol), K_2CO_3 (55.3 mg, 0.4 mmol) and 4 Å MS were dissolved in MeTHF (2 mL), and stirred at room temperature for approximately 1 h. Then, iminoester **1** (0.4 mmol) and α-alkylidene succinimides **2** (0.2 mmol) were added sequentially. Once starting material was consumed (monitored by TLC), the mixture was concentrated and purified by column chromatography to give the corresponding cycloaddition product.

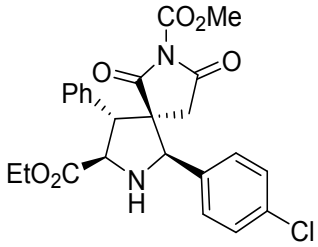


(3ab)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(4-chlorophenyl)-1,3-dioxo-9-phenyl-2,7-diazaspiro[4.4]nonane-

2,8-dicarboxylate

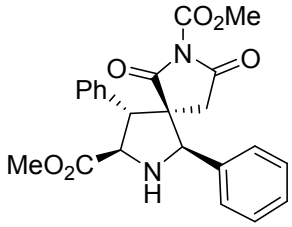
Yield (88%); White solid, m.p: 82-84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.40 (m, 2H), 7.37-7.32 (m, 3H), 7.29-7.24 (m, 4H), 4.45 (s, 1H), 4.28 (d, *J* = 5.7, 1H), 4.08 (d, *J* = 5.7, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 2.47 (d, *J* = 18.7, 1H), 2.30 (d, *J* = 18.7, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 172.3, 169.6, 147.6, 139.0, 135.2, 133.1, 129.5, 129.3, 128.6, 128.3, 128.0, 73.7, 67.1, 60.2, 54.9, 54.7, 52.7, 37.3; HRMS (EI, m/z): Calcd for $C_{23}H_{21}ClN_2O_6$ $[M]^+$: 456.1083, found: 456.1091; $[\alpha]_D^{25}$ = +52.9 (*c* 1.58, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 21.23 min, 34.28 min.



(3bb)

8-Ethyl 2-methyl (5*R*,6*R*,8*R*,9*R*)-6-(4-chlorophenyl)-1,3-dioxo-9-phenyl-2,7-diazaspiro[4.4] nonane-2,8-dicarboxylate

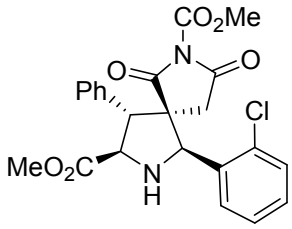
Yield (72%); White solid, m.p: 36-38 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.40 (m, 2H), 7.37-7.32 (m, 3H), 7.29-7.24 (m, 4H), 4.45 (s, 1H), 4.36-4.19 (m, 3H), 4.06 (d, *J* = 5.9, 1H), 3.77 (s, 3H), 2.49 (d, *J* = 18.6, 1H), 2.32 (d, *J* = 18.7, 1H), 1.26 (t, *J* = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 171.8, 169.7, 147.6, 139.0, 135.2, 133.1, 129.5, 129.3, 128.6, 128.2, 128.0, 73.9, 67.3, 61.7, 60.2, 55.2, 54.8, 37.4, 14.2; HRMS (EI, m/z): Calcd for $C_{24}H_{23}ClN_2O_6$ $[M]^+$: 470.1240, found: 470.1252; $[\alpha]_D^{25}$ = +58.7 (*c* 1.13, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 18.57 min, 38.30 min.



(3cb)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-1,3-dioxo-6,9-diphenyl-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

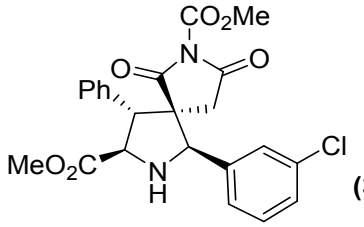
Yield (83%); White solid, m.p: 60-62 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.40 (m, 2H), 7.37-7.31 (m, 6H), 7.27-7.25 (m, 2H), 4.46 (s, 1H), 4.29 (d, *J* = 5.6, 1H), 4.07 (d, *J* = 5.7, 1H), 3.82 (s, 3H), 3.73 (s, 3H), 2.46 (d, *J* = 18.6, 1H), 2.33 (d, *J* = 18.7, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 172.4, 169.8, 147.7, 139.3, 134.1, 129.5, 129.3, 129.2, 128.6, 128.2, 126.5, 74.5, 67.5, 60.2, 55.3, 54.5, 52.7, 37.3; HRMS (EI, m/z): Calcd for $C_{23}H_{22}N_2O_6$ $[M]^+$: 422.1473, found: 422.1476; $[\alpha]_D^{25}$ = +56.2 (*c* 1.22, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 19.09 min, 29.40 min.



(3db)

Dimethyl (5*R*,6*S*,8*R*,9*R*)-6-(2-chlorophenyl)-1,3-dioxo-9-phenyl-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

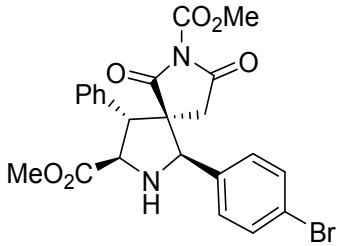
Yield (81%); White solid, m.p: 60-62 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.43-7.30 (m, 5H), 7.29-7.22 (m, 3H), 5.20 (s, 1H), 4.35 (d, *J* = 7.8, 1H), 4.15 (d, *J* = 7.8, 1H), 3.78 (s, 6H), 2.84 (d, *J* = 18.5, 1H), 2.53 (d, *J* = 18.5, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 172.3, 169.8, 147.9, 137.1, 134.0, 133.3, 129.9, 129.8, 129.4, 128.7, 128.6, 128.3, 127.5, 68.2, 65.3, 60.7, 54.7, 54.6, 52.6, 37.56; HRMS (EI, m/z): Calcd for $C_{23}H_{21}ClN_2O_6$ $[M]^+$: 456.1083, found: 456.1088; $[\alpha]_D^{25}$ = +32.3 (*c* 1.22, CH_2Cl_2); HPLC (Chiralcel AD-H, hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 17.16 min, 22.63 min.



(3eb)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(3-chlorophenyl)-1,3-dioxo-9-phenyl-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

Yield (80%); White solid, m.p: 124-126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.40 (m, 2H), 7.37-7.29 (m, 3H), 7.27-7.24 (m, 3H), 7.22-7.19 (m, *J* = 7.5 Hz, 1H), 4.43 (s, 1H), 4.29 (d, *J* = 5.7 Hz, 1H), 4.08 (d, *J* = 5.7 Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 2.48 (d, *J* = 18.6 Hz, 1H), 2.30 (d, *J* = 18.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 172.2, 169.5, 147.7, 139.0, 136.6, 135.3, 130.4, 129.5, 129.5, 128.6, 128.3, 126.8, 125.1, 73.7, 67.1, 60.1, 54.8, 54.7, 52.7, 37.2; HRMS (EI, m/z): Calcd for $C_{23}H_{21}ClN_2O_6$ $[M]^+$: 456.1083, found: 456.1083; $[\alpha]_D^{25}$ = +64.3 (*c* 0.94, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 16.58 min, 35.59 min.

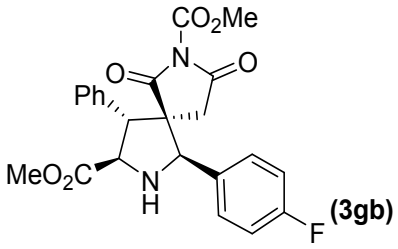


(3fb)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(4-bromophenyl)-1,3-dioxo-9-phenyl-2,7-diazaspiro[4.4]nonane-

2,8-dicarboxylate

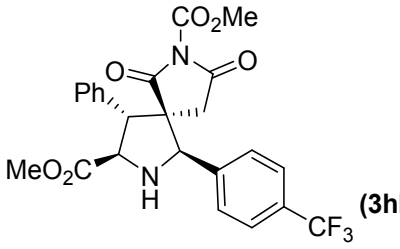
Yield (77%); White solid, m.p: 58-60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.47 (m, 2H), 7.43-7.40 (m, 2H), 7.37-7.33 (m, 1H), 7.26-7.21 (m, 4H), 4.43 (s, 1H), 4.28 (d, *J* = 5.7, 1H), 4.08 (d, *J* = 5.8, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 2.47 (d, *J* = 18.6, 1H), 2.30 (d, *J* = 18.7, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 172.3, 169.6, 147.6, 139.0, 133.6, 132.3, 129.5, 128.6, 128.3, 128.3, 123.3, 73.8, 67.1, 60.1, 54.9, 54.8, 52.7, 37.3; HRMS (EI, m/z): Calcd for $C_{23}H_{21}BrN_2O_6$ $[M]^+$: 500.0578, found: 500.0584; $[\alpha]_D^{25}$ = +51.1 (*c* 1.12, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 25.10 min, 42.67 min.



(3gb)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(4-fluorophenyl)-1,3-dioxo-9-phenyl-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

Yield (72%); White solid, m.p: 53-55 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.42 (m, 2H), 7.37-7.31 (m, 3H), 7.27-7.25 (m, 2H), 7.06-7.02 (m, 2H), 4.45 (s, 1H), 4.28 (d, *J* = 5.7, 1H), 4.08 (d, *J* = 5.7, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 2.47 (d, *J* = 18.6, 1H), 2.30 (d, *J* = 18.6, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 172.3, 169.7, 163.2 (d, $J_{C\text{-}F}$ = 248.5), 147.6, 139.1, 130.2 (d, $J_{C\text{-}F}$ = 3.3), 129.5, 128.6, 128.4 (d, $J_{C\text{-}F}$ = 8.3), 128.2, 116.1 (d, $J_{C\text{-}F}$ = 21.6), 73.8, 67.2, 60.1, 55.0, 54.7, 52.7, 37.3; HRMS (EI, m/z): Calcd for $C_{23}H_{21}FN_2O_6$ $[M]^+$: 440.1379, found: 440.1385; $[\alpha]_D^{25}$ = +49.8 (*c* 1.35, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 19.78 min, 35.70 min.

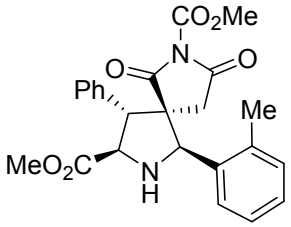


(3hb)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-1,3-dioxo-9-phenyl-6-(4-(trifluoromethyl)phenyl)-2,7-diazaspiro[4.4] nonane-2,8-dicarboxylate:

Yield (82%); White solid, m.p: 54-56 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1, 2H), 7.49 (d, *J* = 8.1, 2H), 7.43 (t, *J* = 7.4, 2H), 7.36 (t, *J* = 7.2, 1H), 7.26 (d, *J* = 6.4, 2H), 4.55 (s, 1H), 4.31 (d, *J* = 5.8, 1H), 4.11 (d, *J* = 5.8, 1H), 3.82 (s, 3H), 3.70 (s, 3H), 2.50 (d, *J* = 18.7, 1H), 2.36 (d, *J* = 18.7, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 172.3, 169.5, 147.5, 138.9, 138.8, 131.4

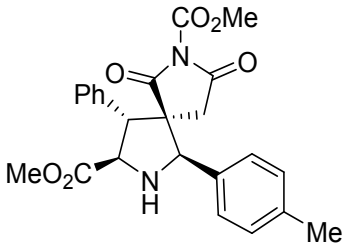
(q, $J_{C\text{-}F}$ = 32.7), 129.6, 128.6, 128.3, 127.1, 126.1 (q, $J_{C\text{-}F}$ = 3.6), 123.8 (q, $J_{C\text{-}F}$ = 272.1), 73.8, 67.1, 60.4, 54.7, 54.7, 52.8, 37.5; HRMS (EI, m/z): Calcd for $C_{24}H_{21}F_3N_2O_6$ $[M]^+$: 490.1347, found: 490.1354; $[\alpha]_D^{25}$ = +50.9 (*c* 1.70, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 15.47 min, 29.13 min.



(3ib)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-1,3-dioxo-9-phenyl-6-(o-tolyl)-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

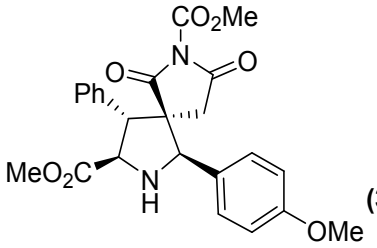
Yield (71%); White solid, m.p: 45-47 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.48 (m, 1H), 7.43-7.40 (m, 2H), 7.37-7.33 (m, 1H), 7.28 (d, *J* = 8.5, 2H), 7.24-7.14 (m, 3H), 4.89 (s, 1H), 4.31 (d, *J* = 6.3, 1H), 4.14 (d, *J* = 6.3, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 2.45 (d, *J* = 18.4, 1H), 2.37 (s, 3H), 2.34 (d, *J* = 18.4, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 172.4, 169.7, 147.7, 138.7, 135.7, 133.0, 131.4, 129.4, 128.6, 128.6, 128.2, 126.8, 126.3, 69.0, 66.7, 61.2, 55.2, 54.5, 52.7, 37.6, 20.1; HRMS (EI, m/z): Calcd for $C_{24}H_{24}N_2O_6$ $[M]^+$: 436.1629, found: 436.1638; $[\alpha]_D^{25}$ = +19.3 (*c* 1.17, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 80/20, 1.0 mL/min, 254 nm) t_R= 15.64 min, 27.51 min.



(3jb)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-1,3-dioxo-9-phenyl-6-(p-tolyl)-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

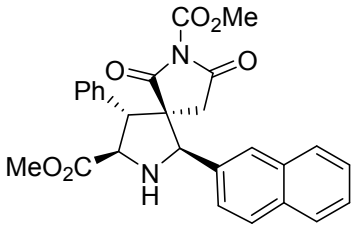
Yield (77%); White solid, m.p: 53-55 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.40 (m, 2H), 7.37-7.33 (m, 1H), 7.26 (d, *J* = 7.1, 2H), 7.19 (d, *J* = 8.1, 2H), 7.14 (d, *J* = 8.1, 2H), 4.41 (s, 1H), 4.28 (d, *J* = 5.5, 1H), 4.04 (d, *J* = 5.6, 1H), 3.82 (s, 3H), 3.75 (s, 3H), 2.43 (d, *J* = 18.7, 1H), 2.32 (s, 3H), 2.30 (d, *J* = 18.6, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 172.4, 169.9, 147.7, 139.4, 139.2, 130.9, 129.8, 129.4, 128.6, 128.1, 126.4, 74.4, 67.5, 60.2, 55.4, 54.5, 52.7, 37.2, 21.2; HRMS (EI, m/z): Calcd for $C_{24}H_{24}N_2O_6$ $[M]^+$: 436.1629, found: 436.1633; $[\alpha]_D^{25}$ = +56.2 (*c* 1.28, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 17.08 min, 29.70 min.



(3kb)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(4-methoxyphenyl)-1,3-dioxo-9-phenyl-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

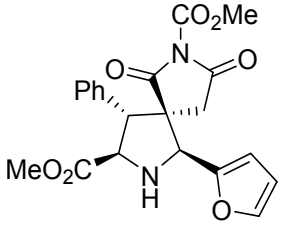
Yield (74%); White solid, m.p: 92-94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, *J* = 7.3, 2H), 7.37-7.33 (m, 1H), 7.27-7.23 (m, 4H), 6.86 (d, *J* = 8.7, 2H), 4.40 (s, 1H), 4.28 (d, *J* = 5.5, 1H), 4.05 (d, *J* = 5.6, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 3.76 (s, 3H), 2.44 (d, *J* = 18.6, 1H), 2.28 (d, *J* = 18.7, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 172.4, 169.9, 160.3, 147.7, 139.4, 129.4, 128.6, 128.1, 127.8, 125.9, 114.5, 74.2, 67.4, 60.1, 55.3, 55.3, 54.6, 52.7, 37.2; HRMS (EI, m/z): Calcd for $C_{24}H_{24}N_2O_7$ $[M]^+$: 452.1579, found: 436.1581; $[\alpha]_D^{25}$ = +53.3 (*c* 1.06, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 23.00 min, 48.21 min.



(3lb)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(naphthalen-2-yl)-1,3-dioxo-9-phenyl-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

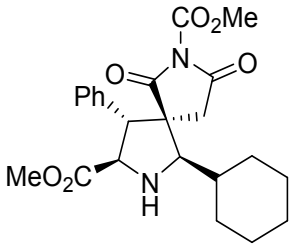
Yield (74%); White solid, m.p: 51-53 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 4H), 7.49-7.36 (m, 6H), 7.30-7.26 (m, 2H), 4.63 (d, *J* = 6.9, 1H), 4.35 (s, 1H), 4.12 (d, *J* = 4.5, 1H), 3.85 (s, 3H), 3.52 (brs, 1H), 3.42 (s, 3H), 2.48 (d, *J* = 18.5, 1H), 2.41 (d, *J* = 18.6, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 172.4, 169.7, 147.5, 139.3, 133.7, 133.3, 131.6, 129.5, 129.1, 128.6, 128.2, 128.2, 127.7, 126.6, 126.6, 126.1, 123.9, 74.7, 67.5, 60.5, 55.1, 54.3, 52.7, 37.4; HRMS (EI, m/z): Calcd for $C_{27}H_{24}N_2O_6$ $[M]^+$: 472.1629, found: 472.1635; $[\alpha]_D^{25}$ = +51.8 (*c* 1.12, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 27.41 min, 53.78 min.



(3mb)

Dimethyl (5*R*,6*S*,8*R*,9*R*)-6-(furan-2-yl)-1,3-dioxo-9-phenyl-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

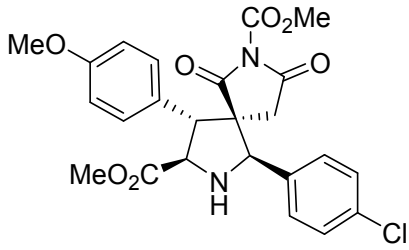
Yield (90%); White solid, m.p: 43-45 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.31 (m, 4H), 7.21 (d, *J* = 7.3, 2H), 6.41 (s, 1H), 6.34 (s, 1H), 4.54 (s, 1H), 4.29 (d, *J* = 5.8, 1H), 4.00 (d, *J* = 5.7, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 2.46 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 171.8, 170.1, 148.4, 148.0, 143.2, 138.9, 129.5, 128.6, 128.2, 110.7, 108.5, 68.0, 67.7, 59.3, 55.7, 54.8, 52.7, 36.9; HRMS (EI, m/z): Calcd for $C_{21}H_{20}N_2O_7$ $[M]^+$: 412.1266, found: 412.1273; $[\alpha]_D^{25}$ = +63.4 (*c* 1.56, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 16.72 min, 27.47 min.



(3nb)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-cyclohexyl-1,3-dioxo-9-phenyl-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

Yield (40%); White solid, m.p: 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (t, *J* = 7.3, 2H), 7.31 (t, *J* = 7.3, 1H), 7.13 (d, *J* = 7.3, 2H), 4.06 (d, *J* = 7.6, 1H), 3.99 (s, 3H), 3.81 (d, *J* = 7.8, 1H), 3.70 (s, 3H), 3.07 (d, *J* = 7.7, 1H), 2.76 (brs, 1H), 2.48 (d, *J* = 19.2, 1H), 2.32 (d, *J* = 19.2, 1H), 2.09 (d, *J* = 12.6, 1H), 1.81-1.60 (m, 4H), 1.34-1.06 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 171.9, 170.9, 148.3, 137.9, 129.4, 128.7, 128.3, 76.0, 66.3, 59.8, 57.9, 55.2, 52.5, 39.1, 38.3, 31.8, 31.0, 26.0, 25.9, 25.8; HRMS (EI, m/z): Calcd for $C_{23}H_{28}N_2O_6$ $[M]^+$: 428.1942, found: 428.1950; $[\alpha]_D^{25}$ = +27.6 (*c* 0.50, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 80/20, 1.0 mL/min, 254 nm) t_R= 15.71 min, 34.47 min.

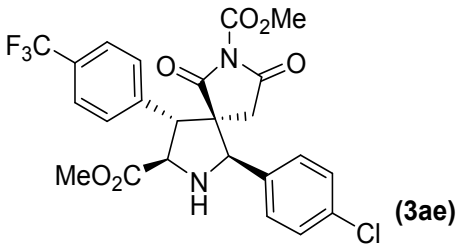


(3ad)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(4-chlorophenyl)-9-(4-methoxyphenyl)-1,3-dioxo-2,7-diazaspiro [4.4]nonane-2,8-dicarboxylate

Yield (77%); White solid, m.p: 75-77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.6, 2H), 7.27 (d, *J* = 8.6, 2H), 7.16 (d, *J* = 8.7, 2H), 6.93 (d, *J* = 8.7, 2H), 4.41 (s, 1H), 4.23 (d, *J* = 5.7, 1H), 4.03 (d, *J* = 5.9, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.77 (s, 3H), 2.50 (d, *J* = 18.6, 1H), 2.31 (d, *J* = 18.7, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 172.3, 169.7, 159.3, 147.6, 135.1, 133.2, 130.8, 129.7, 129.3, 128.0, 114.8, 73.6, 67.2, 60.3, 55.4, 54.7, 54.3, 52.7, 37.3; HRMS (EI, m/z): Calcd

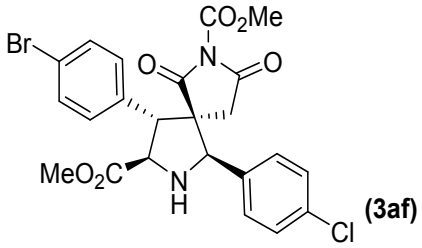
for $C_{24}H_{23}ClN_2O_7$ $[M]^+$: 486.1189, found: 486.1190; $[\alpha]_D^{25}$ = +36.6 (*c* 1.05, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 23.39 min, 42.67 min.



(3ae)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(4-chlorophenyl)-1,3-dioxo-9-(4-(trifluoromethyl)phenyl)-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

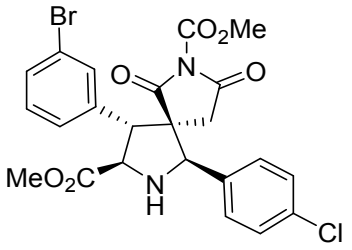
Yield (68%); White solid, m.p: 87-89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.1, 2H), 7.41 (d, *J* = 8.1, 2H), 7.34 (d, *J* = 8.6, 2H), 7.28 (d, *J* = 8.5, 2H), 4.46 (s, 1H), 4.26 (d, *J* = 5.7, 1H), 4.17 (d, *J* = 5.7, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 2.43 (d, *J* = 18.5, 1H), 2.34 (d, *J* = 18.5, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 171.9, 169.1, 147.5, 143.0, 135.4, 132.8, 130.5 (q, $J_{C\text{-}F}$ = 32.8), 129.4, 129.1, 127.9, 126.44 (q, $J_{C\text{-}F}$ = 3.6), 123.8 (q, $J_{C\text{-}F}$ = 272.7), 73.9, 67.0, 59.9, 54.8, 54.2, 52.8, 37.3; HRMS (EI, m/z): Calcd for $C_{24}H_{20}ClF_3N_2O_6$ $[M]^+$: 524.0957, found: 524.0966; $[\alpha]_D^{25}$ = +42.6 (*c* 1.12, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 14.19 min, 35.96 min.



(3af)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-9-(4-bromophenyl)-6-(4-chlorophenyl)-1,3-dioxo-2,7-diazaspiro[4.4] nonane-2,8-dicarboxylate

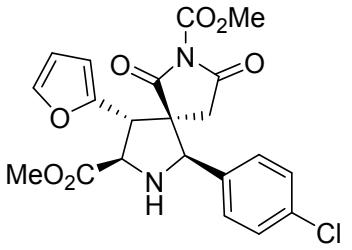
Yield (88%); White solid, m.p: 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2, 2H), 7.33 (d, *J* = 8.4, 2H), 7.27 (d, *J* = 8.5, 2H), 7.14 (d, *J* = 8.3, 2H), 4.41 (d, *J* = 10.0, 1H), 4.23-4.18 (m, 1H), 4.05 (d, *J* = 5.8, 1H), 3.82 (s, 3H), 3.77 (s, 3H), 3.30-3.21 (m, 1H), 2.46 (d, *J* = 18.5, 1H), 2.33 (d, *J* = 18.5, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 172.0, 169.3, 147.5, 137.9, 135.3, 132.9, 132.6, 130.3, 129.4, 128.0, 122.3, 73.8, 67.1, 59.9, 54.8, 54.1, 52.8, 37.3; HRMS (EI, m/z): Calcd for $C_{23}H_{20}BrClN_2O_6$ $[M]^+$: 534.0188, found: 534.0181; $[\alpha]_D^{25}$ = +78.9 (*c* 1.18, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 23.87 min, 43.44 min.



(3ag)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-9-(3-bromophenyl)-6-(4-chlorophenyl)-1,3-dioxo-2,7-diazaspiro[4.4] nonane-2,8-dicarboxylate

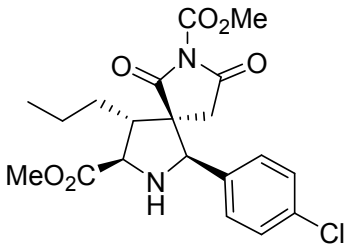
Yield (85%); White solid, m.p: 80-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0, 1H), 7.42 (s, 1H), 7.35-7.25 (m, 5H), 7.20 (d, *J* = 7.7, 1H), 4.43 (d, *J* = 9.7, 1H), 4.22 (t, *J* = 6.2, 1H), 4.05 (d, *J* = 5.7, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 3.33-3.20 (m, 1H), 2.48 (d, *J* = 18.5, 1H), 2.35 (d, *J* = 18.5, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 172.0, 169.3, 147.5, 141.4, 135.3, 132.9, 131.6, 131.4, 131.0, 129.4, 128.0, 127.3, 123.5, 73.8, 67.1, 60.0, 54.8, 54.2, 52.8, 37.3; HRMS (EI, m/z): Calcd for $C_{23}H_{20}BrClN_2O_6$ $[M]^+$: 534.0188, found: 534.0196; $[\alpha]_D^{25}$ = +60.6 (*c* 1.32, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 80/20, 1.0 mL/min, 254 nm) t_R= 54.26 min, 59.42 min.



(3ah)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(4-chlorophenyl)-9-(furan-2-yl)-1,3-dioxo-2,7-diazaspiro[4.4] nonane-2,8- dicarboxylate

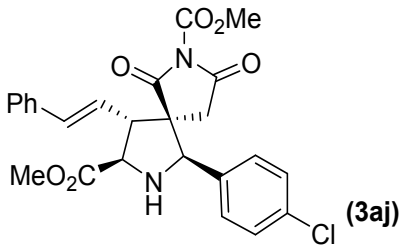
Yield (60%); Yellow solid, m.p: 56-58 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.33 (d, *J* = 8.5, 2H), 7.27 (d, *J* = 8.4, 2H), 6.39-6.38 (m, 1H), 6.31-6.30 (m, 1H), 4.47 (s, 1H), 4.30 (d, *J* = 6.0, 1H), 4.14 (d, *J* = 6.0, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 2.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 171.6, 169.7, 151.9, 147.6, 143.3, 135.3, 132.6, 129.3, 128.0, 110.7, 109.6, 72.8, 64.4, 59.5, 54.8, 52.8, 48.5, 36.4; HRMS (EI, m/z): Calcd for $C_{21}H_{19}ClN_2O_7$ $[M]^+$: 446.0876, found: 446.0877; $[\alpha]_D^{25}$ = +35.7 (*c* 1.00, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 16.67 min, 34.82 min.



(3ai)

Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(4-chlorophenyl)-1,3-dioxo-9-propyl-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

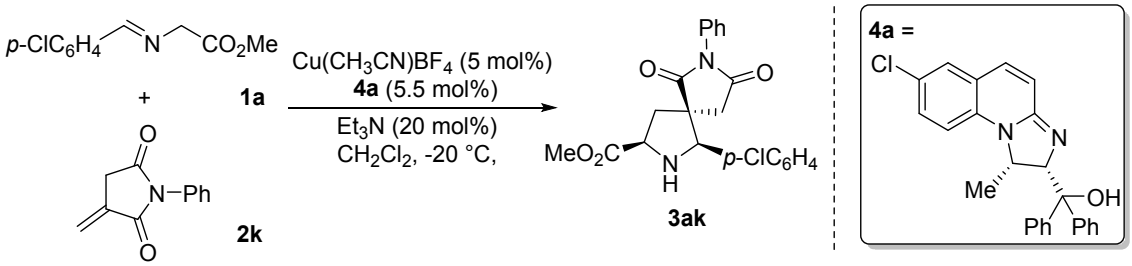
Yield (50%); White solid, m.p: 47-49 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.4, 2H), 7.25 (d, *J* = 7.4, 2H), 4.18 (s, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 3.77 (s, 1H), 3.00 (d, *J* = 18.2, 1H), 2.90-2.82 (m, 1H), 2.60 (d, *J* = 18.2, 1H), 1.61-1.30 (m, 4H), 1.09-0.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 172.9, 169.9, 147.7, 135.1, 133.3, 129.2, 128.0, 72.6, 65.1, 58.8, 54.8, 52.7, 47.4, 36.0, 33.4, 20.5, 14.0; HRMS (EI, m/z): Calcd for $C_{20}H_{23}ClN_2O_6$ $[M]^+$: 422.1240, found: 422.1246; $[\alpha]_D^{25}$ = +51.7 (*c* 1.52, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 80/20, 1.0 mL/min, 254 nm) t_R= 16.77 min, 35.28 min.



(3aj)

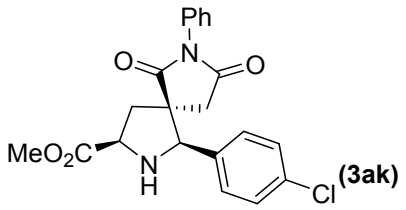
Dimethyl (5*R*,6*R*,8*R*,9*R*)-6-(4-chlorophenyl)-1,3-dioxo-9-((E)-styryl)-2,7-diazaspiro[4.4]nonane-2,8-dicarboxylate

Yield (30%); Yellow solid, m.p: 74-76 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.23 (m, 9H), 6.59 (d, *J* = 15.6 Hz, 1H), 6.10 (dd, *J* = 14.6, 11.0 Hz, 1H), 4.30 (s, 1H), 3.94 (d, *J* = 3.5 Hz, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.76 (s, 1H), 3.70-3.68 (m, 1H), 3.05 (d, *J* = 18.4 Hz, 1H), 2.61 (d, *J* = 18.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 172.0, 169.7, 147.7, 135.7, 135.6, 135.2, 132.9, 129.3, 128.8, 128.5, 128.0, 126.6, 125.8, 72.8, 65.9, 59.2, 54.8, 53.2, 52.8, 36.4; HRMS (EI, m/z): Calcd for $C_{25}H_{23}ClN_2O_6$ $[M]^+$: 482.1240, found: 482.1239; $[\alpha]_D^{25}$ = +17.9 (*c* 0.62, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 18.78 min, 36.62 min.



Under a nitrogen atmosphere, $Cu(CH_3CN)_4BF_4$ (3.1 mg, 0.01 mmol), ligand **4a** (4.4 mg, 0.011 mmol), and Et_3N (5.6 μL, 0.04 mmol) were dissolved in CH_2Cl_2 (2 mL), and stirred at room temperature for approximately 1 h. Then, iminoester **1a** (84.7 mg, 0.4 mmol) was added, the mixture was cooled to -20 °C and α-alkylidene succinimide **2k** (37.4 mg, 0.2 mmol) was then

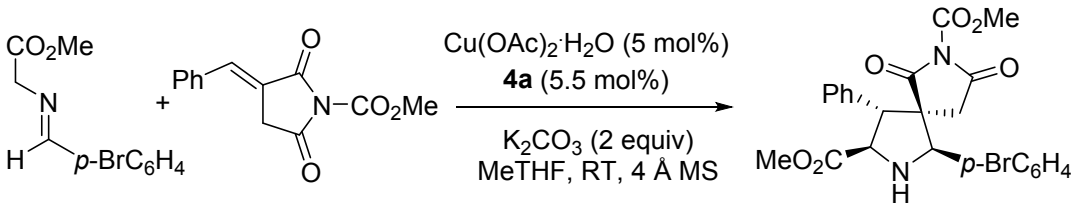
added. Once starting material was consumed (monitored by TLC), the mixture was concentrated and purified by column chromatography to give the corresponding cycloaddition product.



Methyl (1*R*,3*R*,5*S*)-1-(4-chlorophenyl)-6,8-dioxo-7-phenyl-2,7-diazaspiro[4.4]nonane-3-carboxylate

Yield (90%); White solid, m.p: 74-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 7H), 6.62-6.56 (m, 2H), 4.28 (s, 1H), 4.15 (dd, *J* = 9.9, 5.1, 1H), 3.83 (s, 3H), 2.99 (dd, *J* = 38.5, 17.1, 2H), 2.91 (dd, *J* = 12.3, 6.4, 1H), 2.47 (dd, *J* = 13.7, 9.9, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 172.5, 171.8, 133.9, 132.8, 130.1, 128.1, 128.0, 127.7, 127.0, 125.2, 72.1, 57.8, 53.2, 51.56, 38.2, 38.0; HRMS (EI, m/z): Calcd for $C_{21}H_{19}ClN_2O_4$ $[M]^+$: 398.1028, found: 398.1032; $[\alpha]_D^{25}$ = -21.8 (*c* 1.25, CH_2Cl_2); HPLC (Chiralcel IF, *n*-hexane/EtOAc = 50/50, 0.8 mL/min, 254 nm) t_R= 9.63 min, 10.55 min.

Scheme S1. Scaled up asymmetric 1,3-dipolar cycloaddition of azomethine ylide 1f to α-alkylidene succinimide 2b



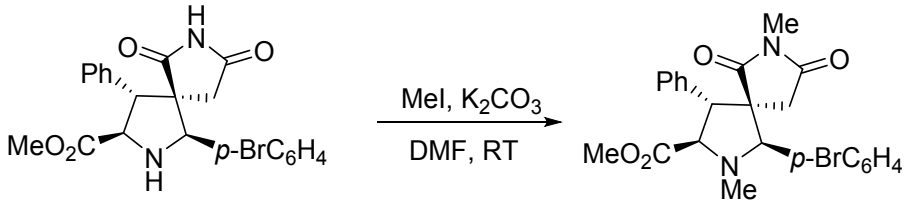
1f	**2b**	*endo*-**3fb**
10 mmol	5 mmol	81% yield, 2.03 g
2.56 g	1.23 g	95% ee

Synthetic transformations of the cycloadduct

3fa, 95% ee **6**, 85% yield, 95% ee

Compound **3fa** (100.3 mg, 0.2 mmol), CH_2Cl_2 (5 mL), triethylamine (27.9 μL, 0.2 mmol) and benzylamine (24.1 μL, 0.22 mmol) were placed in a 10 mL round-bottom flask with magnetic stir bar at room temperature. The resulting mixture was allowed to stir for 24 h. Then, the solvent was removed *in vacuo* and the residue was purified by column chromatography to give **6**.

Methyl (1*R*,3*R*,4*R*,5*R*)-1-(4-bromophenyl)-6,8-dioxo-4-phenyl-2,7-diazaspiro[4.4]nonane-3-carboxylate (6): Yield (85%); White solid, m.p: 95-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (brs, 1H), 7.48-7.38 (m, 4H), 7.38-7.32 (m, 1H), 7.26-7.19 (m, 4H), 4.38 (s, 1H), 4.23 (d, *J* = 6.2, 1H), 4.02 (d, *J* = 6.2, 1H), 3.79 (s, 3H), 3.29 (brs, 1H), 2.43 (d, *J* = 18.7, 1H), 2.27 (d, *J* = 18.7, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 173.3, 171.3, 138.0, 133.3, 131.1, 128.4, 127.6, 127.4, 127.1, 122.0, 71.9, 65.9, 59.9, 54.2, 51.6, 36.8; HRMS (EI, m/z): Calcd for $C_{21}H_{19}BrN_2O_4$ $[M]^+$: 442.0523, found: 442.0526; $[\alpha]_D^{25}$ = +64.7 (*c* 1.33, CH_2Cl_2); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 70/30, 1.0 mL/min, 254 nm) t_R= 14.43 min, 15.09 min.

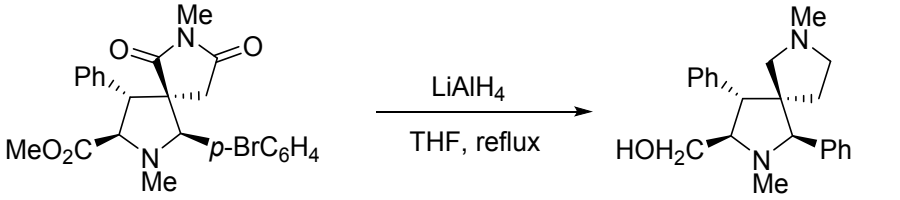


6 **7**, 92% yield

To a solution of **6** (88.7 mg, 0.2 mmol) and K_2CO_3 (165.9 mg, 1.2mmol) in DMF (2 mL) MeI (37.5 μL, 0.6 mmol) was added at room temperature. The mixture was stirred for 4 h and was then quenched with water, the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by column chromatography to afford **7**.

Methyl (1*R*,3*R*,4*R*,5*R*)-1-(4-bromophenyl)-2,7-dimethyl-6,8-dioxo-4-phenyl-2,7-diazaspiro [4.4]nonane-3-carboxylate (7): Yield (92%); White solid, m.p: 131-133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.5, 2H), 7.41-7.34 (m, 2H), 7.34-7.28 (m, 3H), 7.17-7.15 (m, 2H), 4.27 (d, *J* = 7.9, 1H), 3.76 (s, 1H), 3.73 (s, 1H), 3.65 (d, *J* = 7.9, 1H), 2.45 (s, 3H), 2.36 (s, 3H), 2.33 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 173.2, 170.8, 137.2, 134.2, 130.8, 128.3, 128.2, 127.9, 127.0, 121.8, 79.8, 72.5, 58.1, 51.3, 50.7, 38.3, 37.4, 23.3. HRMS (EI, m/z): Calcd for

$C_{23}H_{23}BrN_2O_4$ $[M]^+$: 470.0836, found: 470.0849; $[\alpha]_D^{25}$ = +43.0 (*c* 1.50, CH_2Cl_2).



7 **8**, 65% yield, 95% ee

Compound **7** (94.2 mg, 0.2 mmol) was dissolved in dry THF (4 mL) at 0 °C under a nitrogen atmosphere. Lithium aluminium hydride (60.7 mg, 1.6 mmol) was added in portions. Cooling was removed and the mixture was heated at reflux for 48 h protected from air. The mixture was cooled to 0 °C and the following were slowly added dropwise: water (0.1 mL), 15% NaOH aq (0.1 mL) and water (0.3 mL). The resulting slurry was filtered, the solids were washed with THF (10 mL) and the combined filtrates were concentrated *in vacuo* and the residue was purified by column chromatography to afford **8**.

((1*R*,3*R*,4*R*,5*S*)-2,7-dimethyl-1,4-diphenyl-2,7-diazaspiro[4.4]nonan-3-yl)methanol (8): Yield (65%), Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.17 (m, 10H), 3.80 (dd, *J* = 11.1, 3.6, 1H), 3.67 (s, 1H), 3.52 (dd, *J* = 11.1, 1.5, 1H), 3.41 (d, *J* = 7.7, 1H), 2.93 (ddd, *J* = 7.6, 3.5, 1.5, 1H), 2.86 (brs, 1H), 2.61 (d, *J* = 9.3, 1H), 2.27 (s, 3H), 2.17-2.08 (m, 2H), 2.04 (s, 3H), 1.86 (td, *J* = 8.7, 5.8, 1H), 1.57-1.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 138.2, 129.0, 127.9, 127.2, 127.1, 126.4, 125.5, 78.8, 71.7, 64.1, 59.1, 56.2, 54.9, 53.0, 41.3, 38.3, 31.1. HRMS (EI, m/z): Calcd for $C_{22}H_{28}N_2O$ $[M]^+$: 336.2197, found: 336.2206; $[\alpha]_D^{25}$ = -35.2 (*c* 1.20, CH_2Cl_2); HPLC (Chiralcel AS-H, *n*-hexane/*i*-propanol = 90/10, 0.8 mL/min, 254 nm) t_R= 5.24 min, 12.39 min.

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

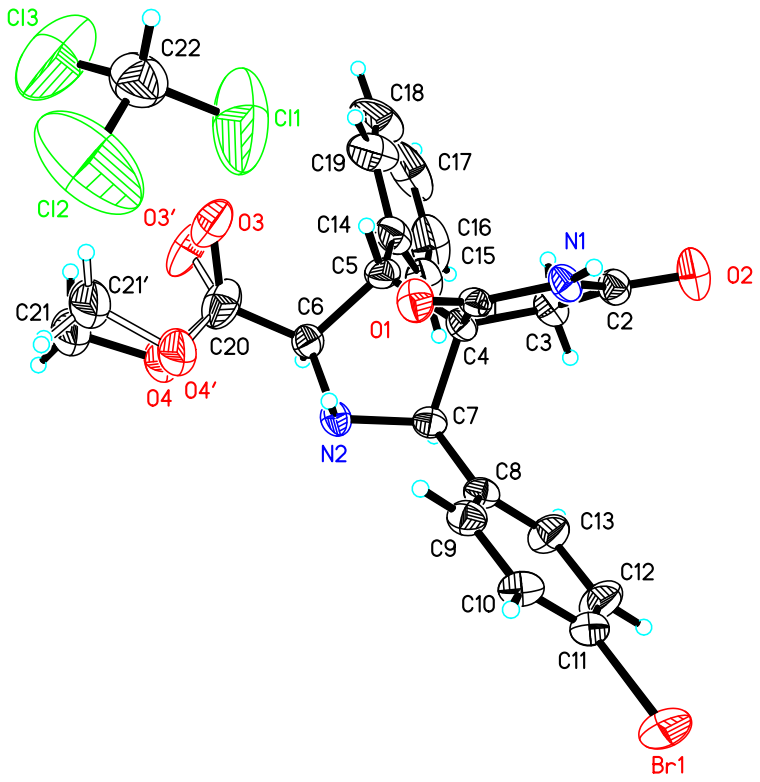


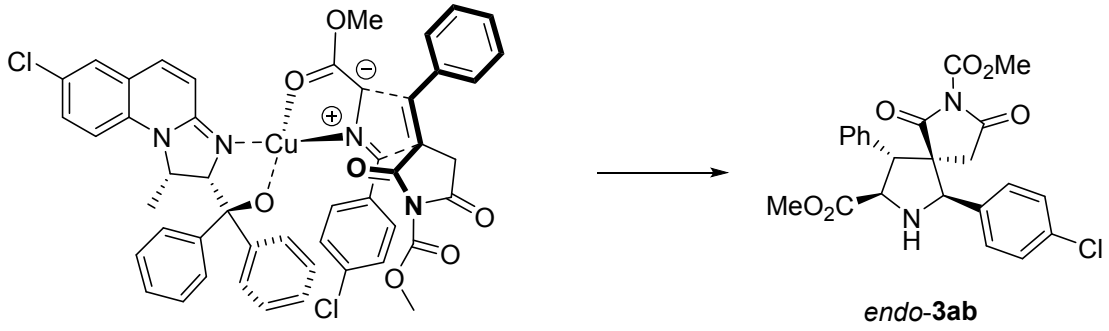
Fig S1. X-ray structure of (1*R*,3*R*,4*R*,5*R*)-**6**

Crystal data and structure refinement for cd21432

(CCDC 1019642 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.)

Empirical formula	$C_{22}H_{19}BrCl_3N_2O_4$
Formula weight	561.65
Temperature	293(2) K
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 10.2175(12) Å; b = 12.1386(14) Å; c = 19.641(2) Å
Volume	2436.0(5) Å^3
Z, Calculated density	4, 1.531 Mg/m^3
Reflections collected / unique	14495 / 3494 [R (int) = 0.0401]
Refinement method	Full-matrix least-squares on F^2
Final R indices [I>2 sigma(I)]	R1 = 0.0638, wR2 = 0.1817
R indices (all data)	R1 = 0.0877, wR2 = 0.1980

Scheme S2. Proposed transition state leading to the major product *endo*-3ab

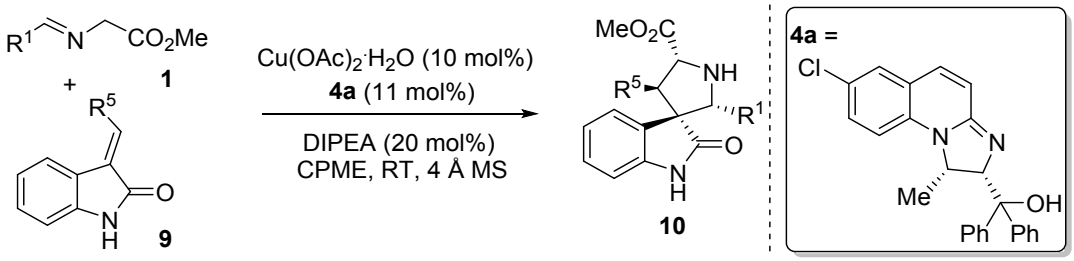


N,O-ligand 4a **1a** + **2b**

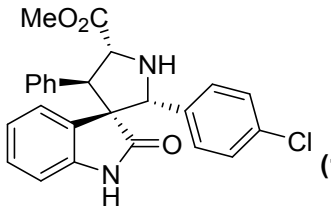
transition state **I**

The excellent diastereoselectivities and enantioselectivities observed in this 1,3-dipolar cycloaddition can be rationalised by considering the proposed transition state **I** shown in Scheme S2. According to a previous report,[4] the 1,3-dipolar cycloaddition is proposed to favor an *endo* cycloaddition mode, and two phenyl groups adjacent to the oxygen in the ligand might block the dipolarophile's approach from the "bottom" face (as drawn) and form *endo*-(5*R*,6*R*,8*R*,9*R*)-**3ab** through approach from the "top" face.

Procedure for the asymmetric 1,3-dipolar cycloaddition of azomethine ylides to 2-oxoindolin-3-ylidenes



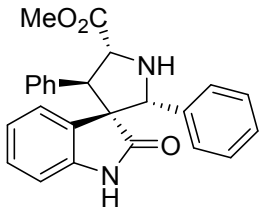
Under a nitrogen atmosphere, $Cu(OAc)_2 \cdot H_2O$ (2.0 mg, 0.01 mmol), ligand **4a** (4.4 mg, 0.011 mmol), DIPEA (3.3 μL, 0.02 mmol) and 4 Å MS were dissolved in CPME (1 mL), and stirred at room temperature for approximately 1 h. Next, iminoester **1** (0.2 mmol) and 2-oxoindolin-3-ylidene **9** (0.1 mmol) were added sequentially. Once starting material was consumed (monitored by TLC), the mixture was concentrated and purified by column chromatography to give the corresponding cycloaddition product **10**.



(10aa)

Methyl (2'*R*,3*S*,4'*R*,5'*R*)-2'-(4-chlorophenyl)-2-oxo-4'-phenylspiro[indoline-3,3'-pyrrolidine]-5'-carboxylate

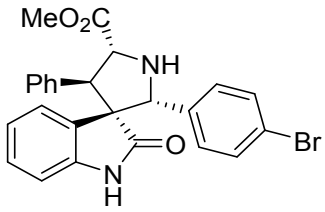
Yield (95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 3H), 7.23-7.20 (m, 2H), 7.11-7.07 (m, 2H), 7.03 (td, *J* = 7.7, 1.1, 1H), 6.97 (s, 1H), 6.90 (d, *J* = 8.5, 2H), 6.68 (td, *J* = 7.7, 0.9, 1H), 6.57 (d, *J* = 7.7, 1H), 6.04 (d, *J* = 7.6, 1H), 4.69 (s, 1H), 4.58 (d, *J* = 4.8, 1H), 4.18 (d, *J* = 5.0, 1H), 3.84 (s, 3H); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 80/20, 1.0 mL/min, 254 nm) t_R = 13.42 min, 17.84 min. $[\alpha]_D^{25}$ = +132.6 (*c* 1.00, $CHCl_3$). The absolute stereochemistry was determined by comparing optical rotations with literature report ($[\alpha]_D^{25}$ = +153.3 (*c* 1.00, $CHCl_3$), 91% ee).[5,6]



(10ca)

Methyl (2'*R*,3*S*,4'*R*,5'*R*)-2-oxo-2',4'-diphenylspiro[indoline-3,3'-pyrrolidine]-5'-carboxylate

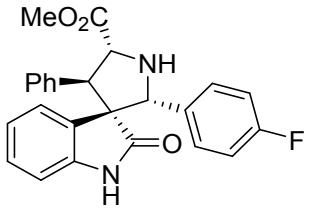
Yield (95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 4H), 7.25-7.20 (m, 2H), 7.17-7.06 (m, 3H), 7.02 (t, *J* = 7.7, 1H), 6.95 (d, *J* = 7.4, 2H), 6.68 (t, *J* = 7.6, 1H), 6.55 (d, *J* = 7.7, 1H), 6.06 (d, *J* = 7.6, 1H), 4.72 (s, 1H), 4.59 (d, *J* = 4.1, 1H), 4.18 (d, *J* = 5.0, 1H), 3.84 (s, 3H), 3.74 (brs, 1H); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 254 nm) t_R = 23.51 min, 27.16 min.



(10fa)

Methyl (2'*R*,3*S*,4'*R*,5'*R*)-2'-(4-bromophenyl)-2-oxo-4'-phenylspiro[indoline-3,3'-pyrrolidine]-5'-carboxylate

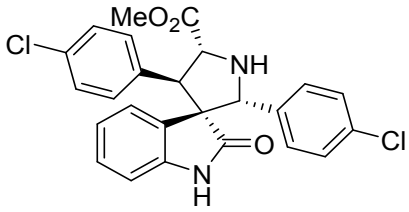
Yield (93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 3H), 7.25-7.15 (m, 4H), 7.04 (t, *J* = 7.6, 1H), 6.84 (d, *J* = 8.4, 2H), 6.68 (t, *J* = 7.6, 1H), 6.58 (d, *J* = 7.8 Hz, 1H), 6.08-6.00 (m, 1H), 4.67 (s, 1H), 4.58 (d, *J* = 4.8, 1H), 4.17 (d, *J* = 4.9, 1H), 3.84 (s, 3H), 3.65 (brs, 1H). HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 254 nm) t_R = 28.96 min, 40.40 min.



(10ga)

Methyl (2'*R*,3*S*,4'*R*,5'*R*)-2'-(4-fluorophenyl)-2-oxo-4'-phenylspiro[indoline-3,3'-pyrrolidine]-5'-carboxylate

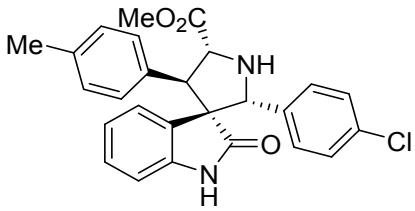
Yield (99%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 3H), 7.24-7.20 (m, 2H), 7.13 (s, 1H), 7.03 (td, *J* = 7.7, 0.9, 1H), 6.98-6.90 (m, 2H), 6.80 (t, *J* = 8.7, 2H), 6.68 (td, *J* = 7.6, 0.7, 1H), 6.57 (d, *J* = 7.7, 1H), 6.03 (d, *J* = 7.6, 1H), 4.70 (s, 1H), 4.58 (d, *J* = 4.6, 1H), 4.18 (d, *J* = 4.8, 1H), 3.84 (s, 3H), 3.66 (brs, 1H); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 254 nm) t_R = 23.33 min, 28.32 min.



(10ab)

Methyl (2'*R*,3*S*,4'*R*,5'*R*)-2',4'-bis(4-chlorophenyl)-2-oxospiro[indoline-3,3'-pyrrolidine]- 5'-carboxylate

Yield (95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.27 (d, *J* = 5.9, 2H), 7.16-7.05 (m, 5H), 6.90 (d, *J* = 8.2, 2H), 6.78 (t, *J* = 7.6, 1H), 6.60 (d, *J* = 7.8, 1H), 6.23 (d, *J* = 7.5, 1H), 4.65 (s, 1H), 4.52 (d, *J* = 4.7, 1H), 4.13 (d, *J* = 5.5, 1H), 3.83 (s, 3H), 3.58 (brs, 1H); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 254 nm) t_R = 26.06 min, 32.18 min.



(10ac)

Methyl (2'*R*,3*S*,4'*R*,5'*R*)-2'-(4-chlorophenyl)-2-oxo-4'-(*p*-tolyl)spiro[indoline-3,3'-pyrrolidine]-5'-carboxylate

Yield (88%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (s, 1H), 7.13-7.02 (m, 7H), 6.89 (d, *J* = 8.4, 2H), 6.71 (t, *J* = 7.6, 1H), 6.57 (d, *J* = 7.7, 1H), 6.12 (d, *J* = 7.6, 1H), 4.68 (d, *J* = 8.0, 1H), 4.55 (s, 1H), 4.13 (d, *J* = 5.0, 1H), 3.83 (s, 3H), 2.34 (s, 3H), 3.64 (brs, 1H); HPLC (Chiralcel AD-H, *n*-hexane/*i*-propanol = 90/10, 1.0 mL/min, 254 nm)t_R= 19.48 min, 31.16 min.

References

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2. Y. Liu, W. Zhang, *Angew. Chem., Int. Ed.,* 2013, **52,** 2203.

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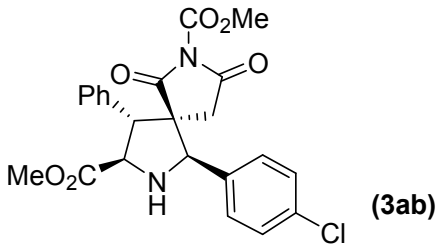
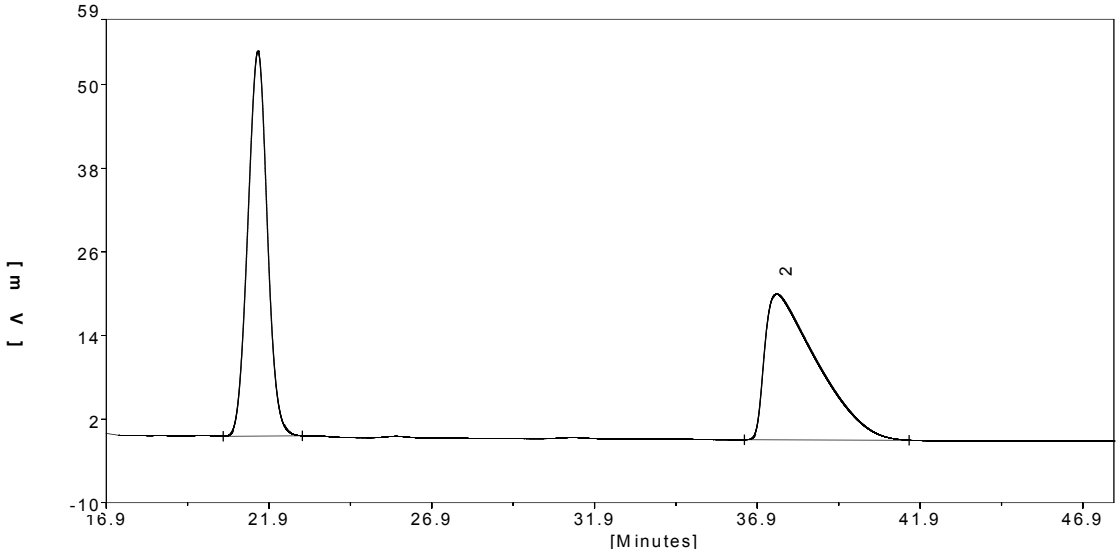
6. T.-L. Liu, Z.-Y. Xue, H.-Y. Tao and C.-J. Wang, *Org. Biomol. Chem.,* 2011, **9**, 1980.

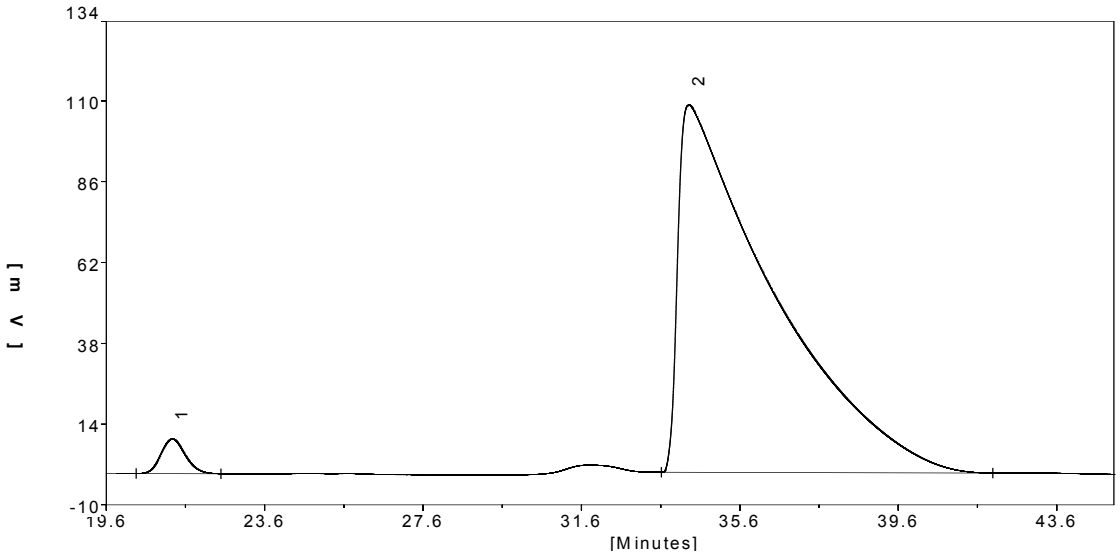
Chiral HPLC Chromatograms



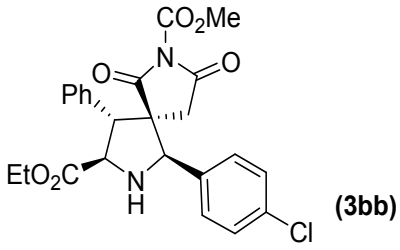
(3ab)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	21.55833	55.24	2297.06	49.7748
2	37.48583	20.93	2317.85	50.2252



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	21.23333	10.31	438.03	2.3783
2	34.28000	109.13	17980.00	97.6217



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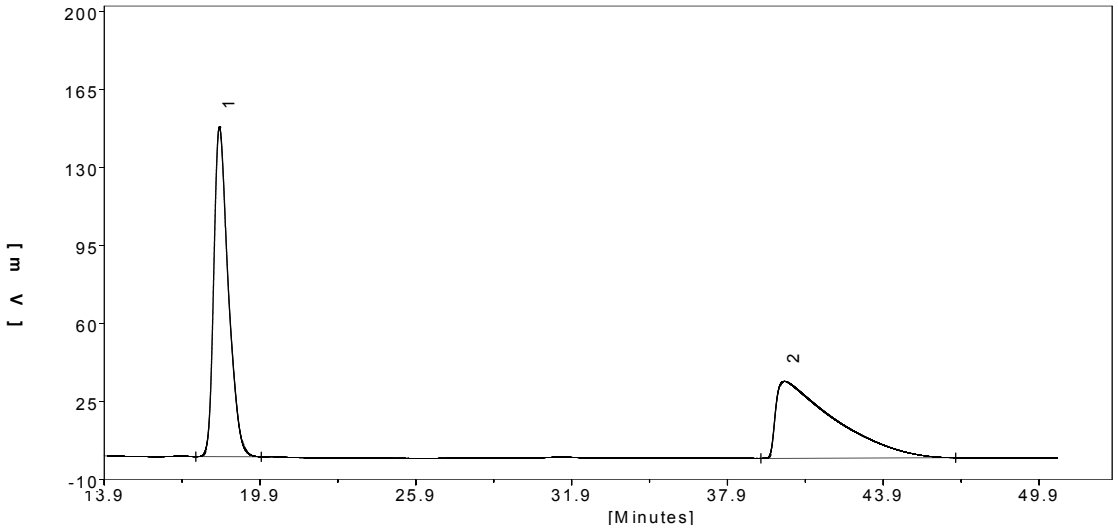

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1	18.37500	148.01	5730.43	51.8077
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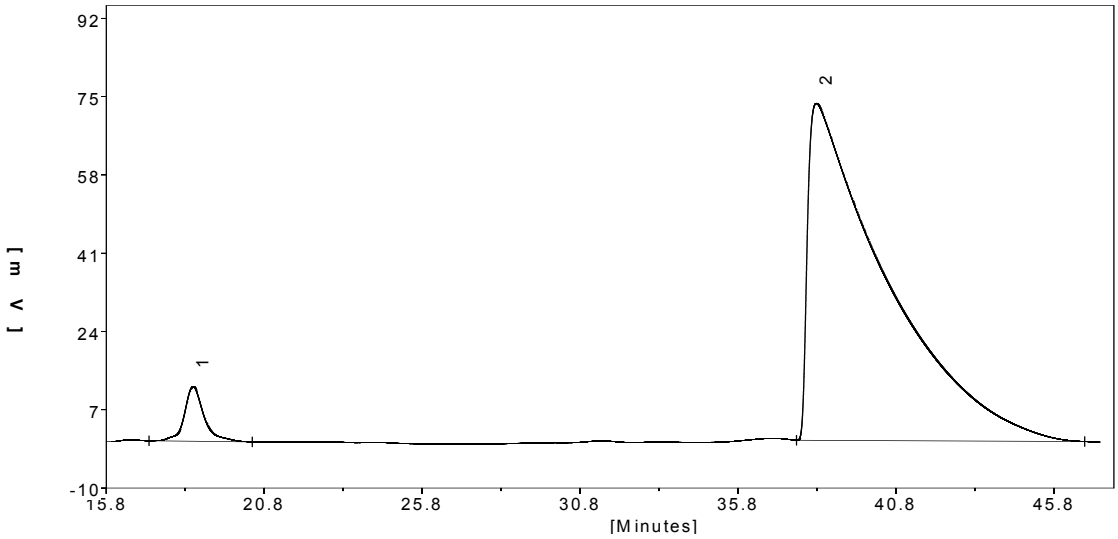

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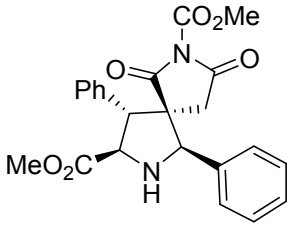
1	18.57000	11.89	509.97	3.9301
2	38.30167	73.18	12466.00	96.0699



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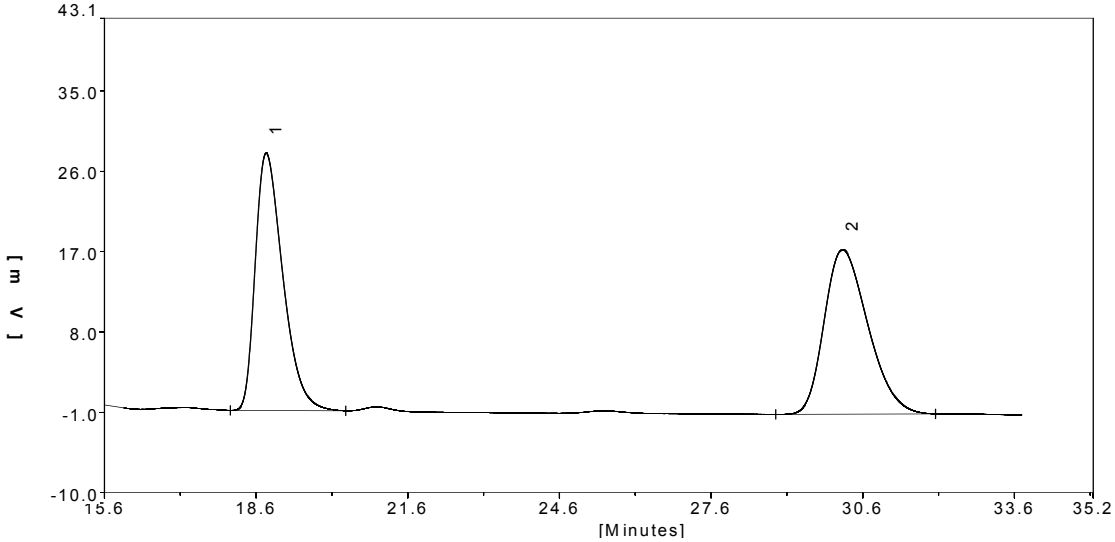
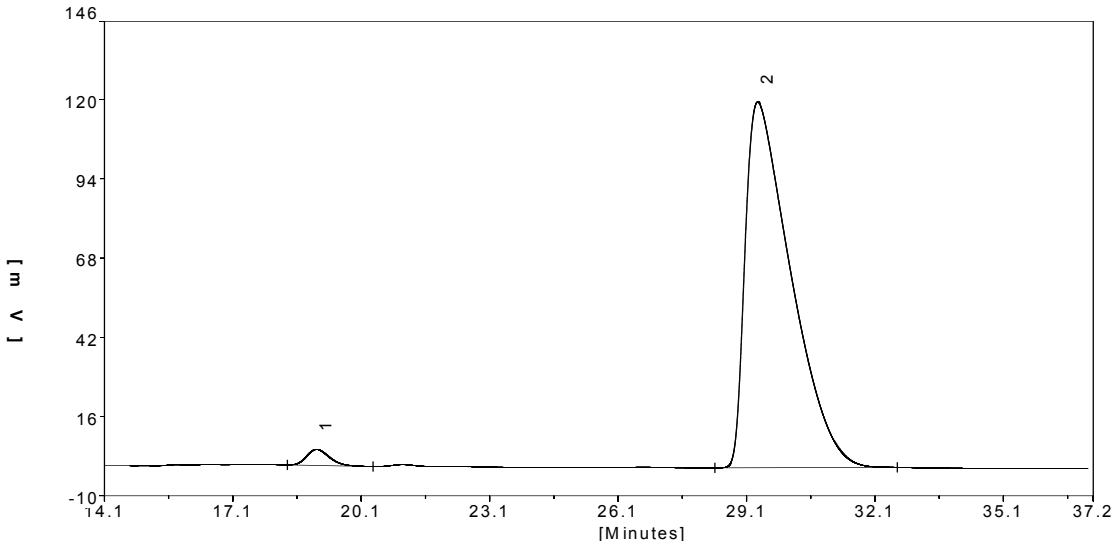
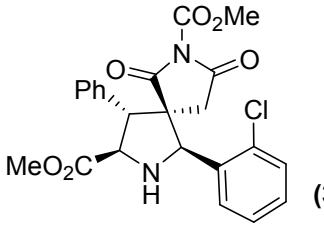


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	18.81167	28.85	1093.41	49.7038
2	30.21333	18.44	1106.45	50.2962



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	19.08500	5.25	193.09	2.1298
2	29.39750	120.02	8873.17	97.8702



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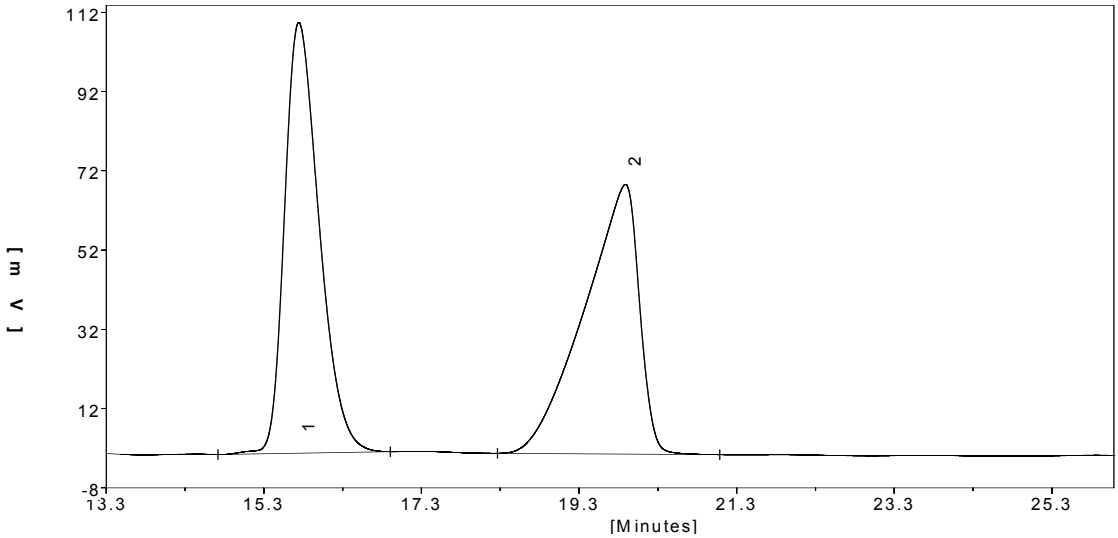

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1	15.70167	108.68	3318.56	50.1620
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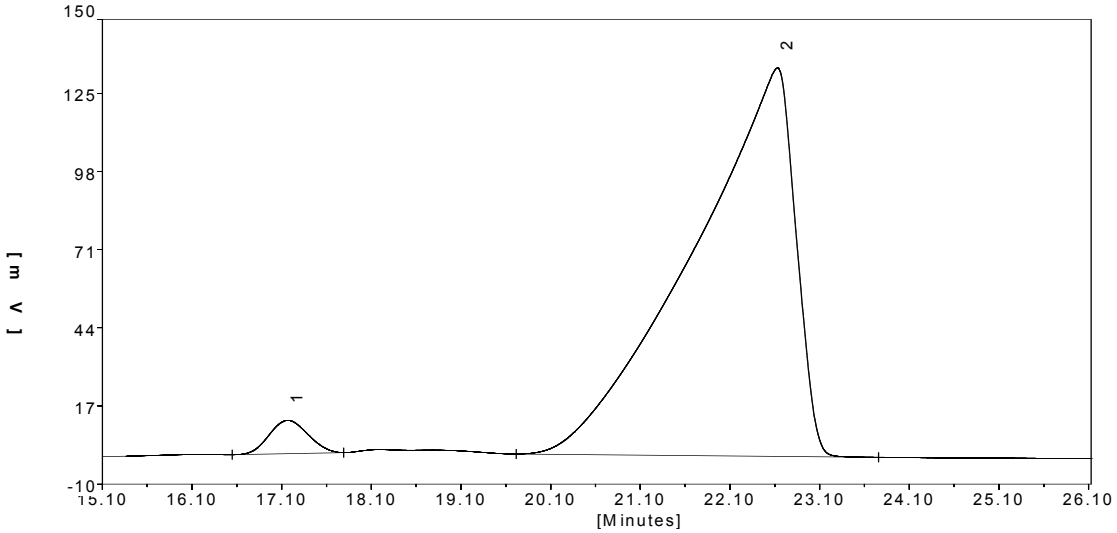
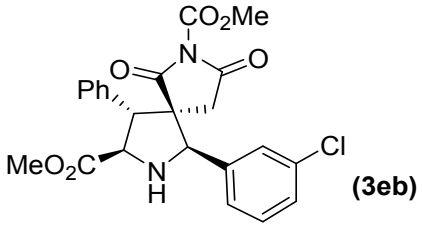


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	17.16250	11.51	345.16	3.1303
2	22.62583	134.16	10681.18	96.8697



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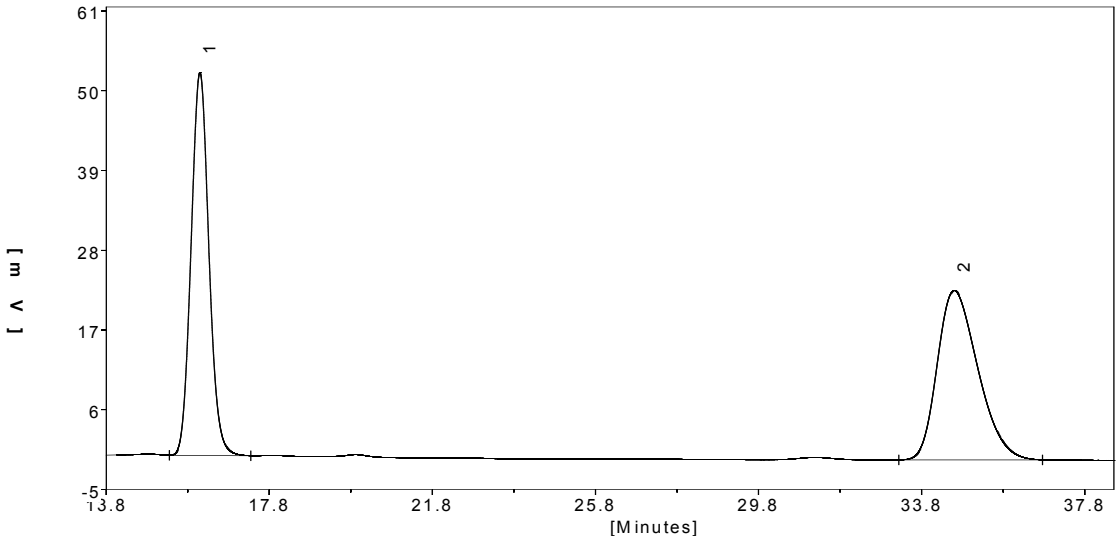
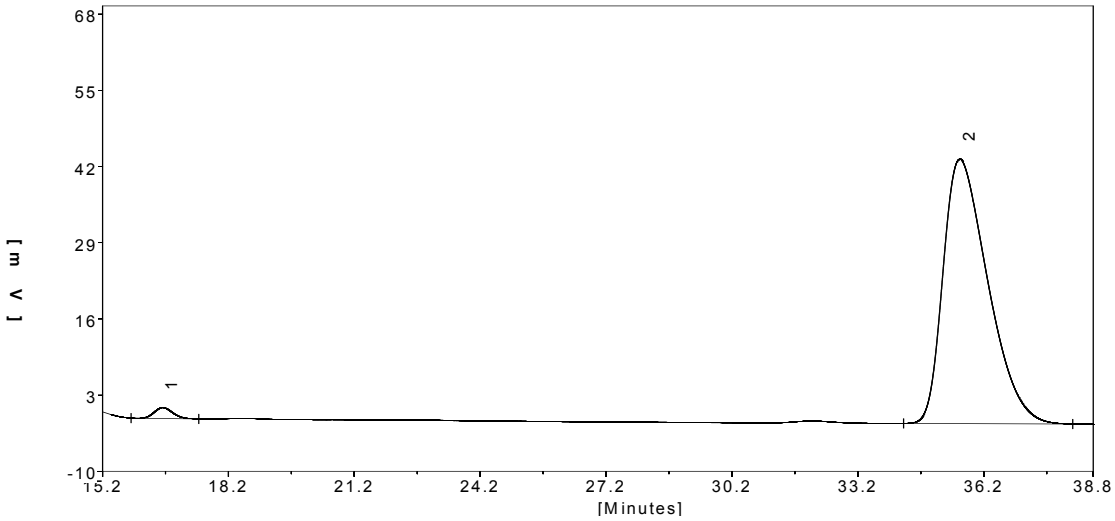
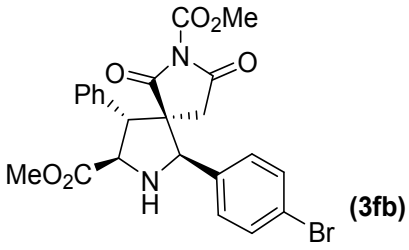


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	16.12083	52.84	1602.91	49.8293
2	34.62333	23.37	1613.89	50.1707



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	16.57833	1.85	56.31	1.6587
2	35.58583	45.14	3338.77	98.3413



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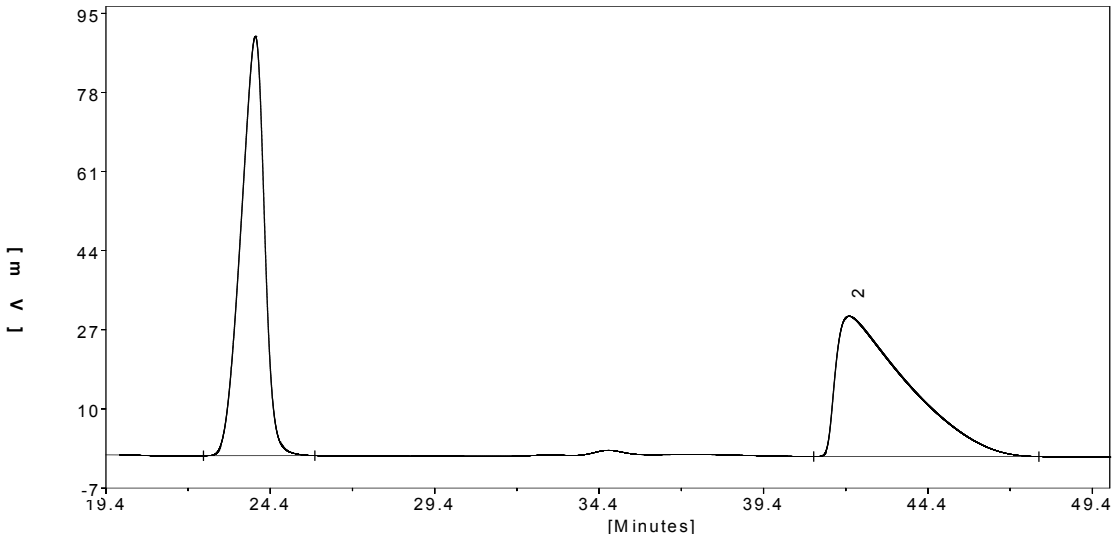
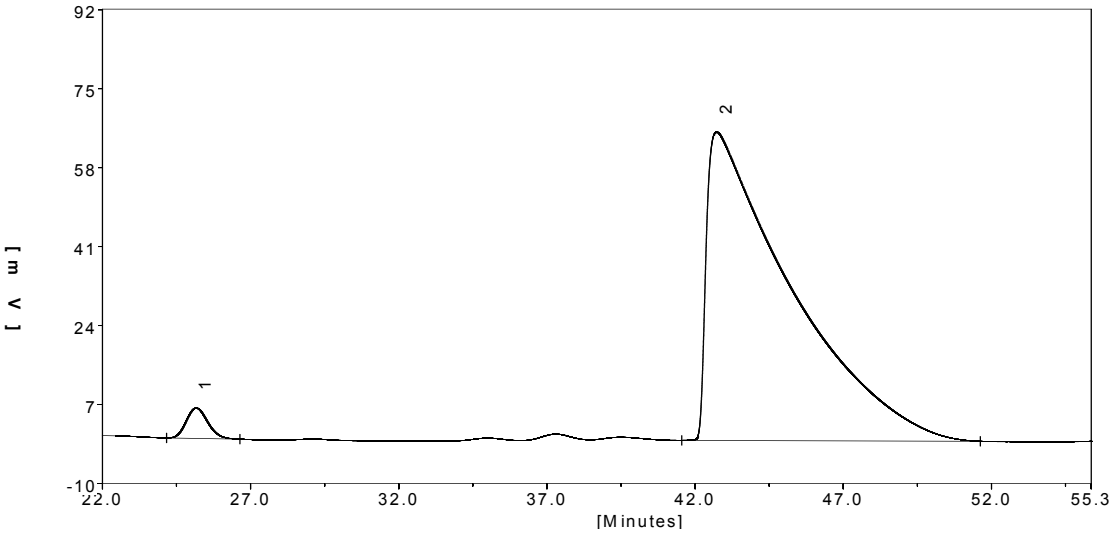


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	23.96083	90.09	4491.62	49.9751
2	42.00667	30.15	4496.09	50.0249



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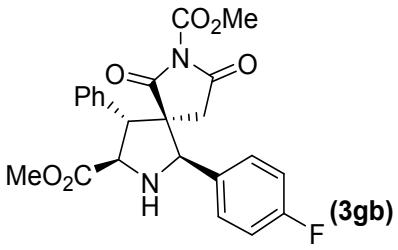
1	25.10458	6.55	328.95	2.4632
2	42.67417	66.42	13025.50	97.5368



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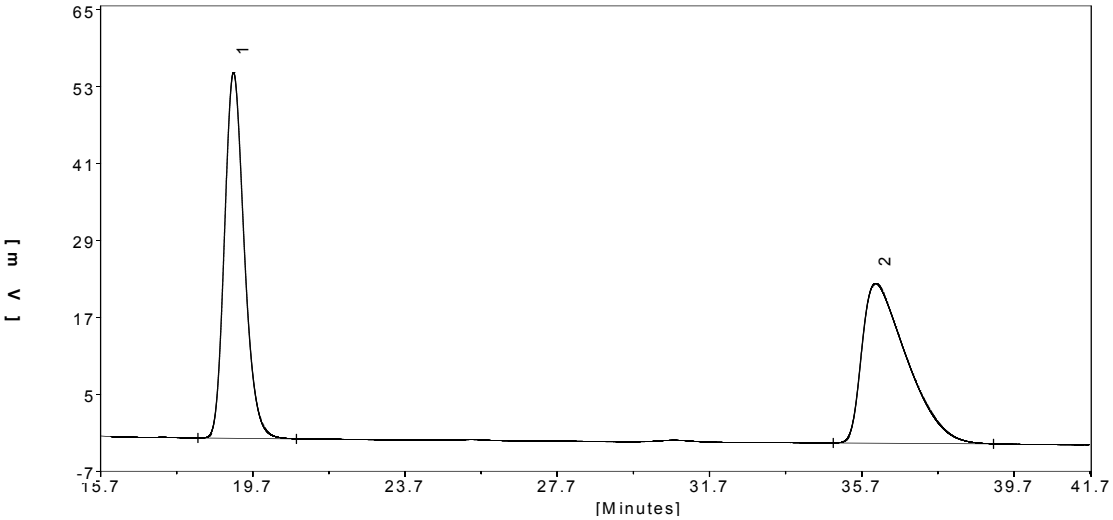

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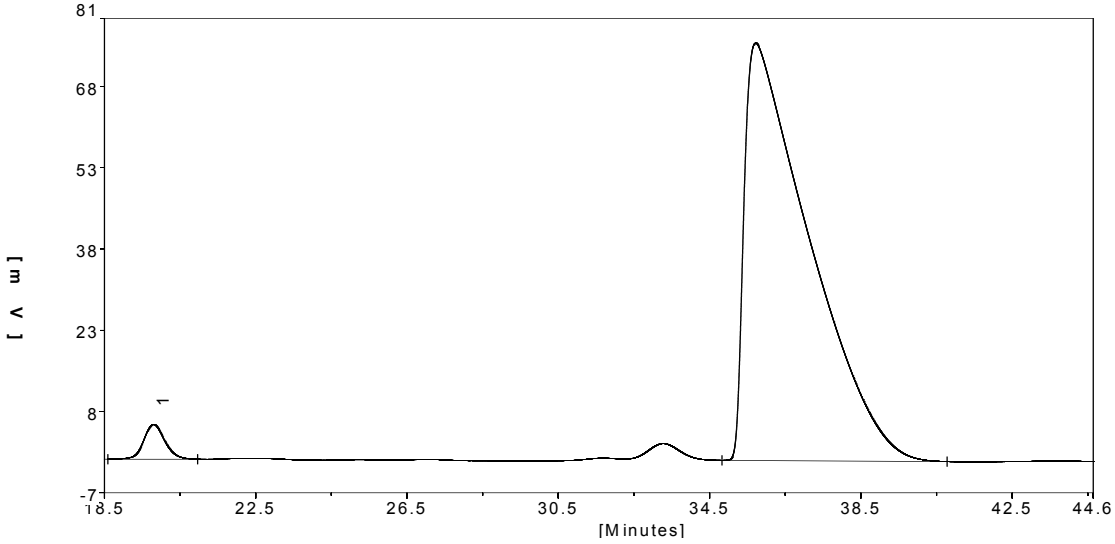
1	19.21500	57.04	2055.64	50.2915
2	36.08417	24.91	2031.81	49.7085



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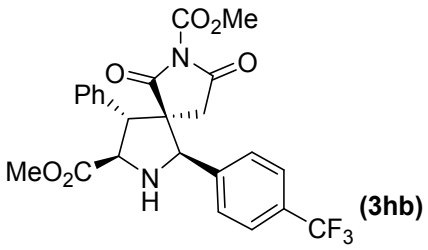
1	19.77583	6.41	248.78	2.6336
2	35.69750	77.05	9197.55	97.3664



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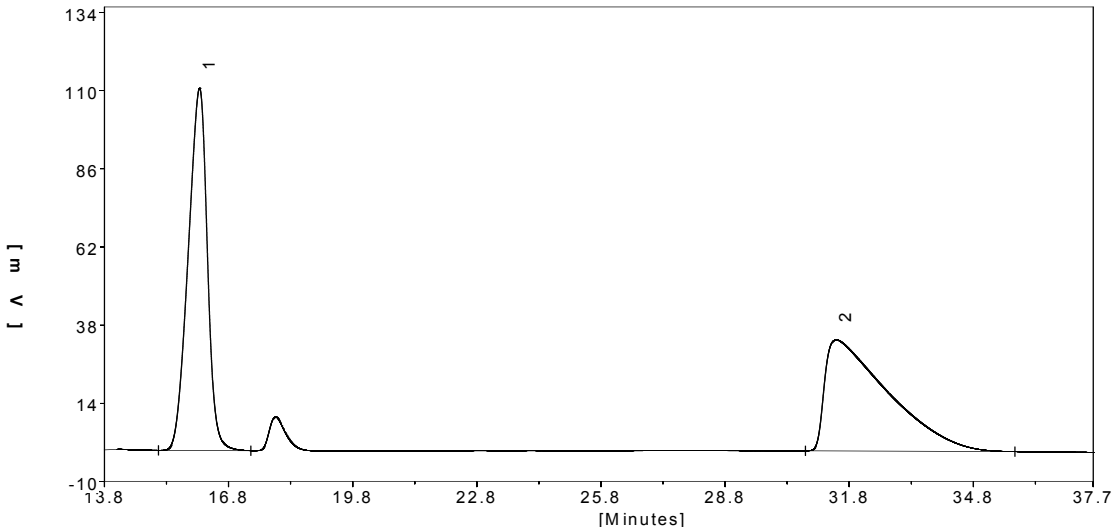

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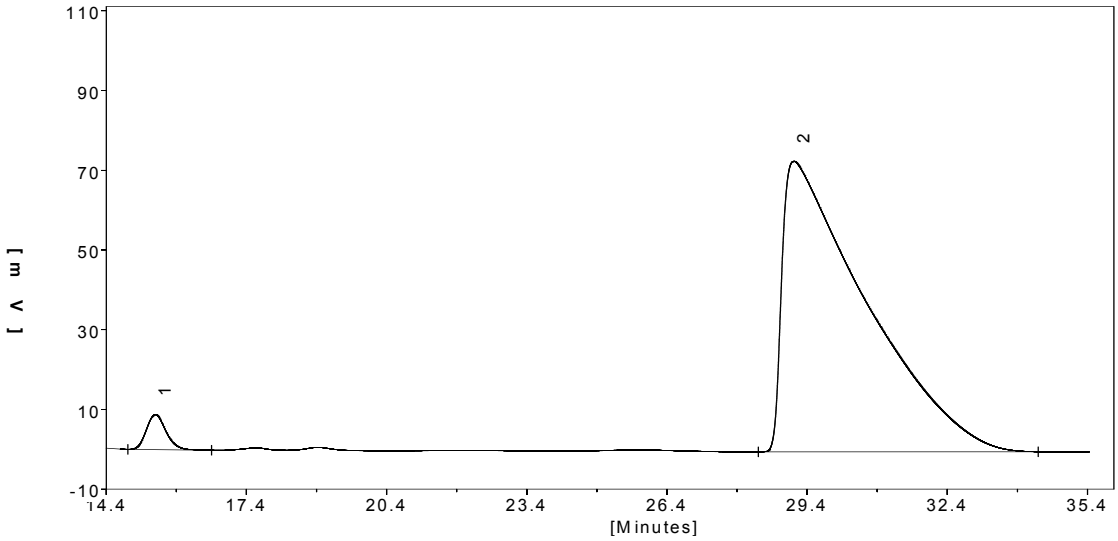
1	16.07250	111.32	3574.25	49.8421
2	31.45083	34.14	3596.90	50.1579



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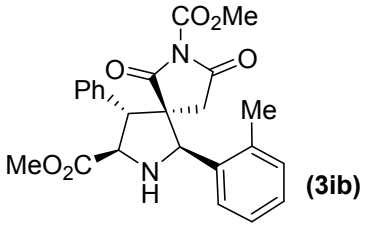

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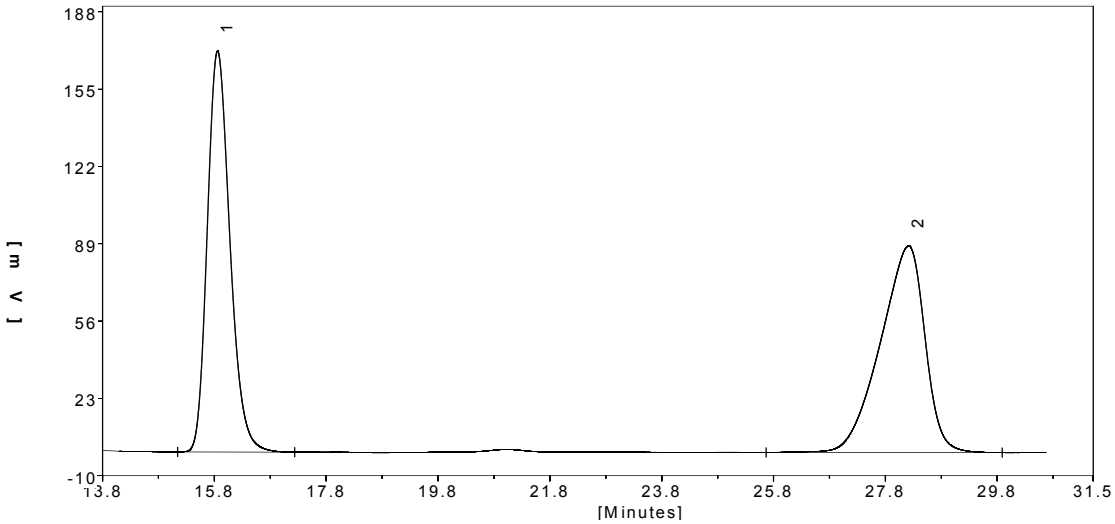

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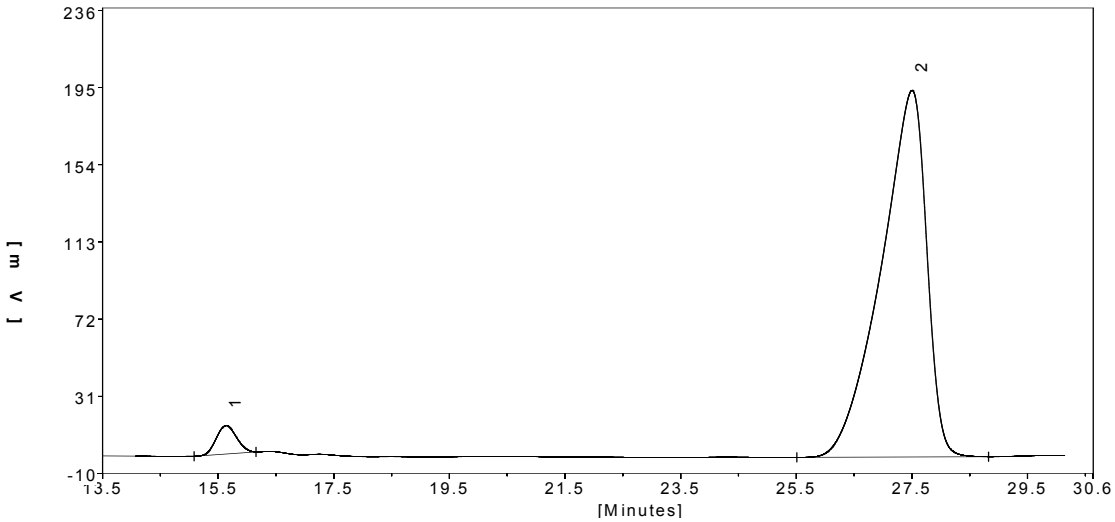
1	15.83667	171.16	4812.12	49.5879
2	28.19333	88.23	4892.10	50.4121



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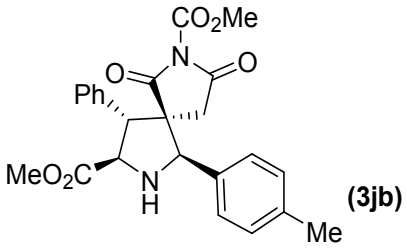

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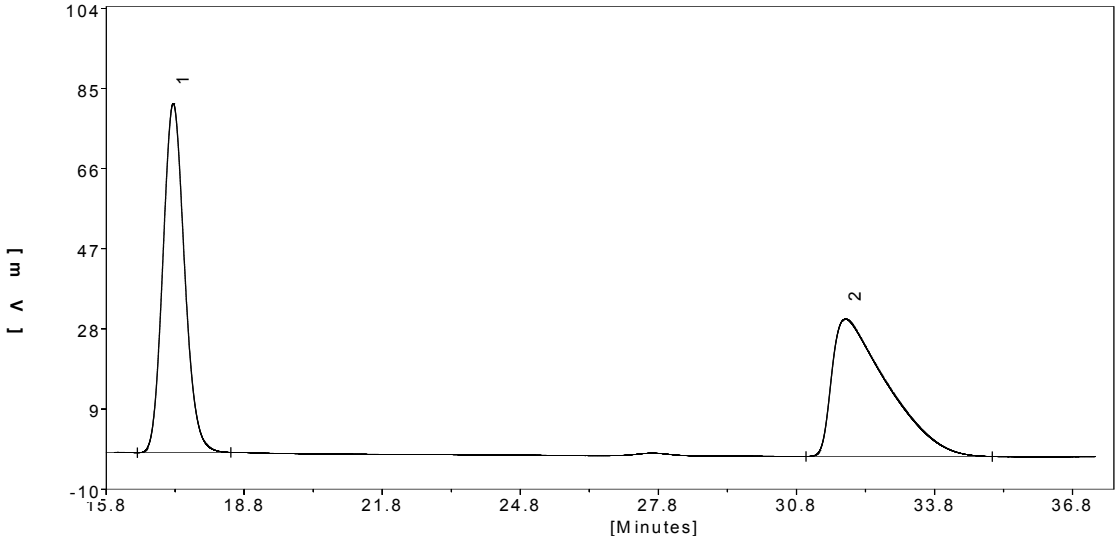
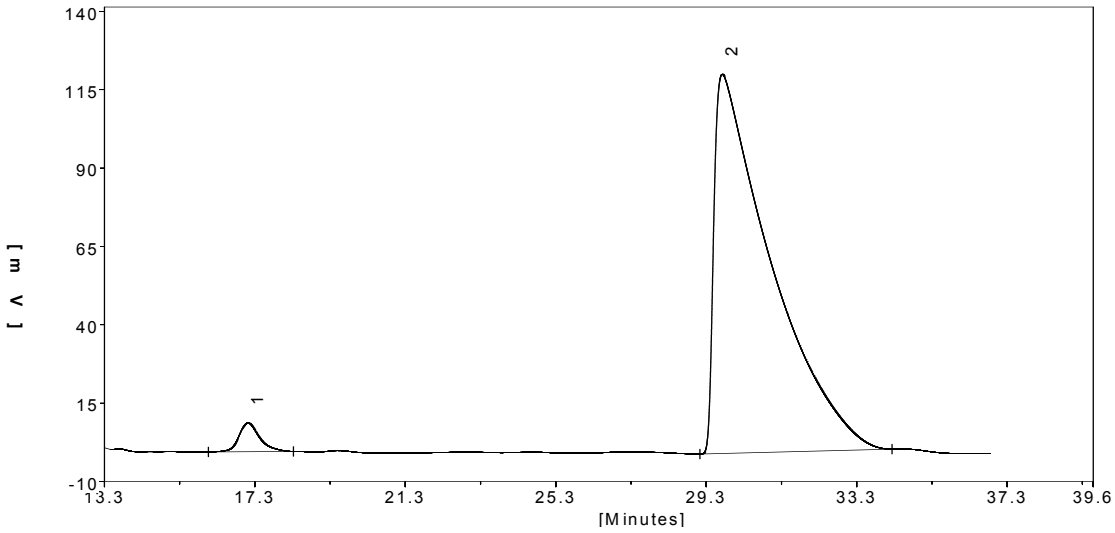


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	17.27833	82.82	2699.23	49.8694
2	31.88333	32.60	2713.37	50.1306



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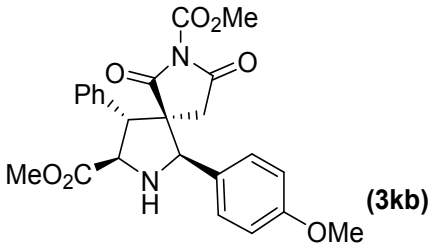
1	17.08333	9.19	349.93	2.6901
2	29.69667	121.02	12658.20	97.3099



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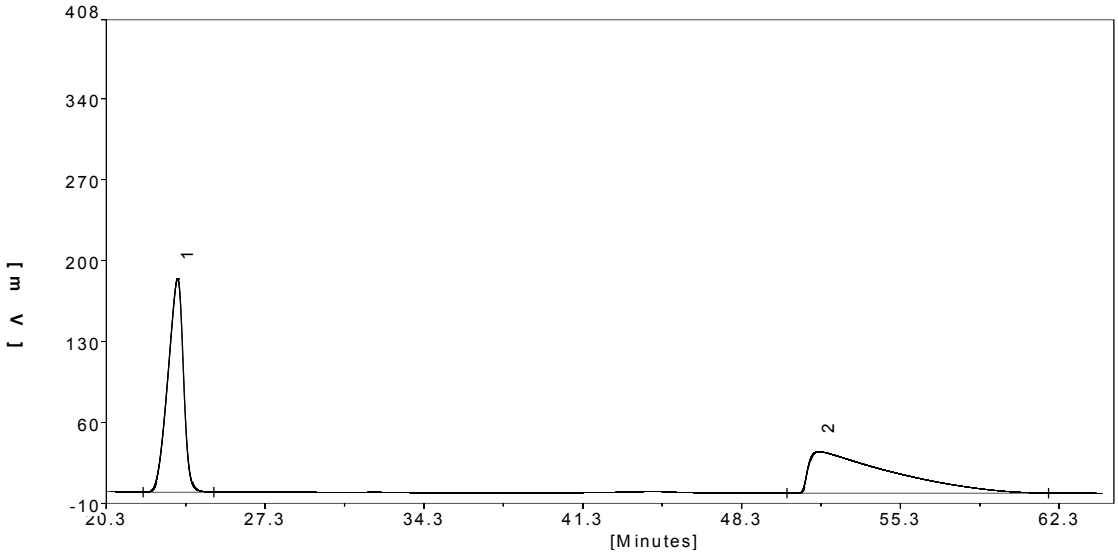

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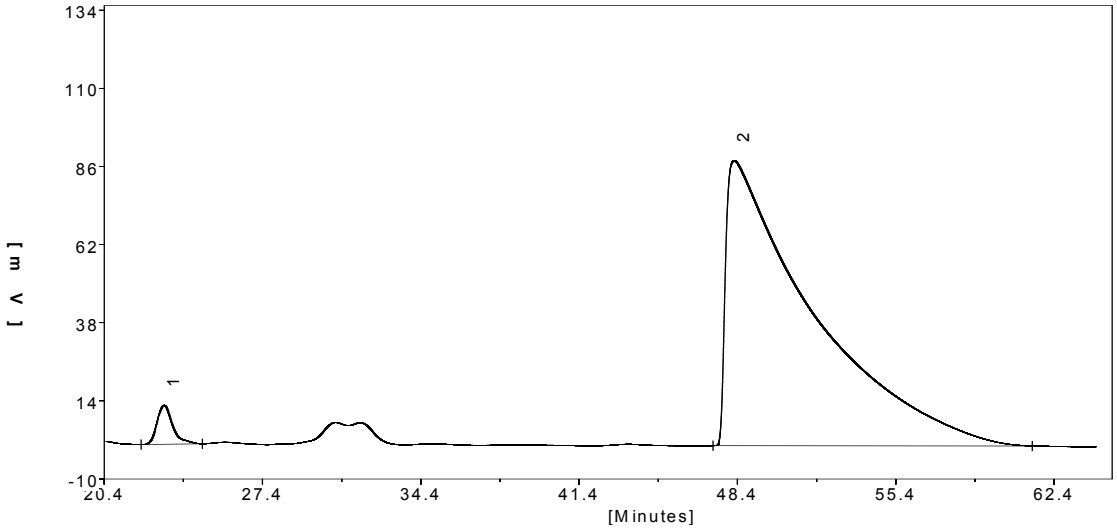
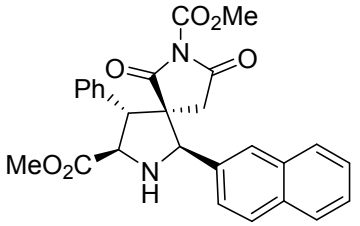
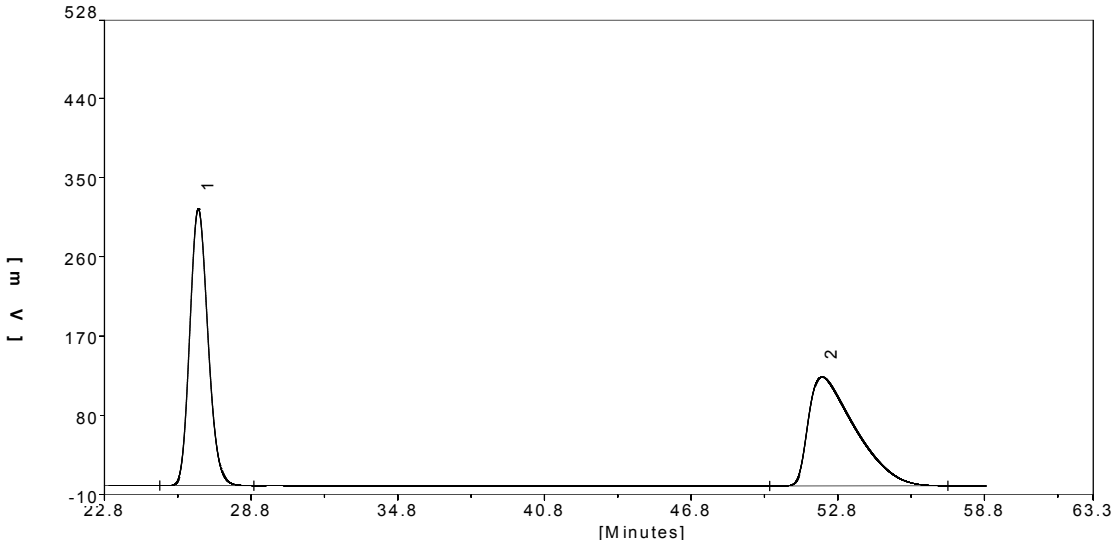
2	51.67667	35.86	8956.67	50.5132



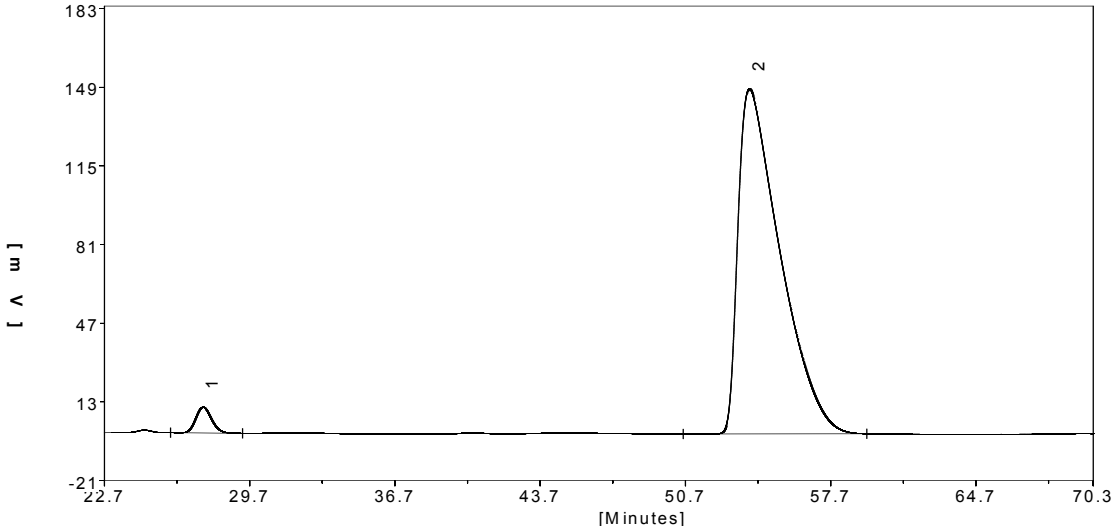
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	22.99917	11.99	569.50	2.4110
2	48.20583	87.62	23051.68	97.5890



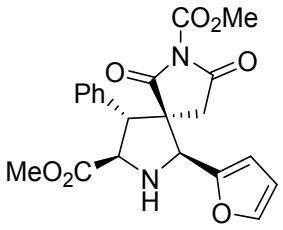
(3lb)



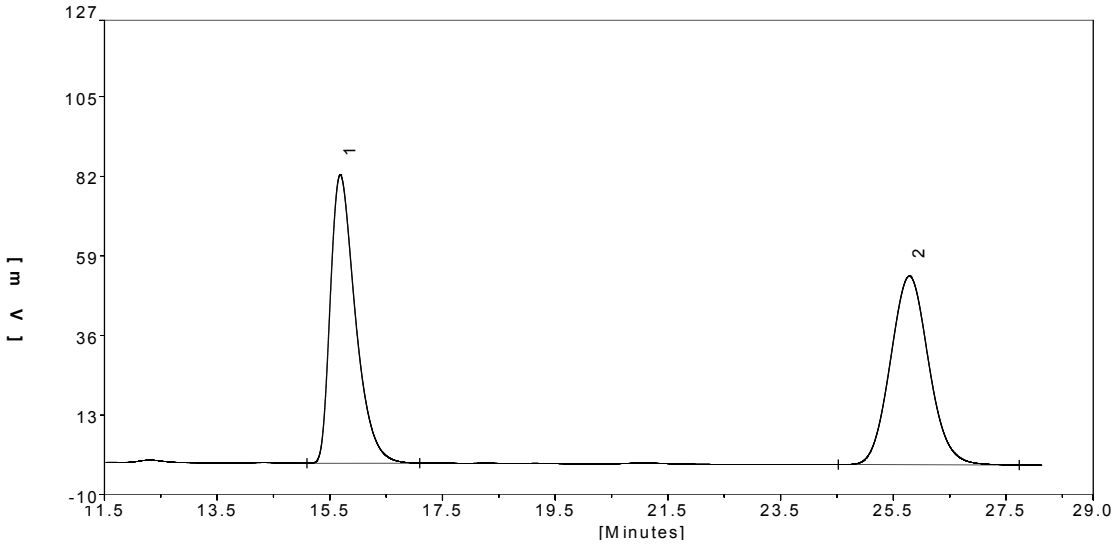
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	26.68083	314.30	16221.89	49.9088
2	52.18083	123.76	16281.16	50.0912



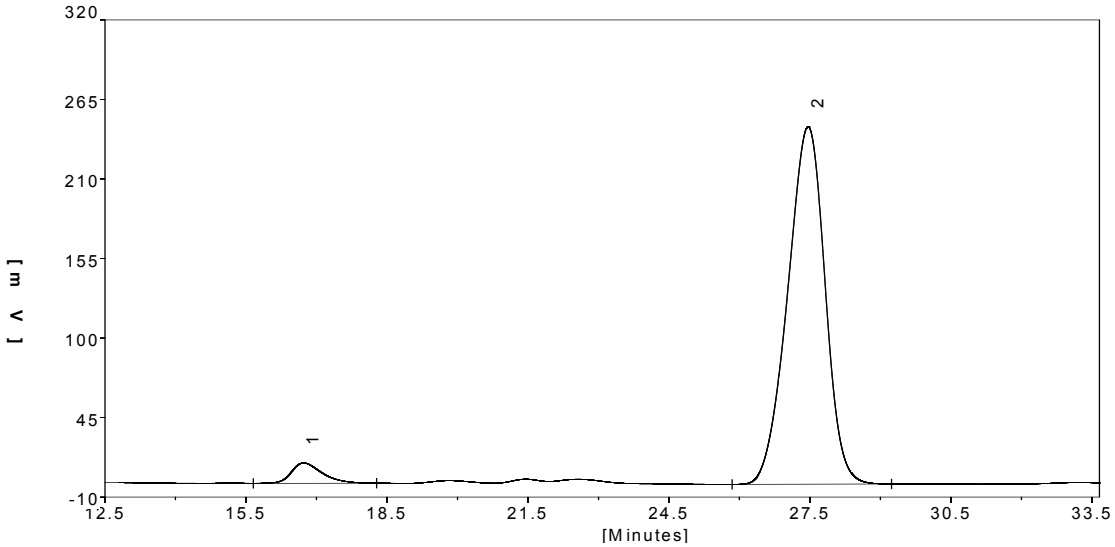
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	27.41417	11.17	585.62	2.7222
2	53.75750	149.12	20926.84	97.2778



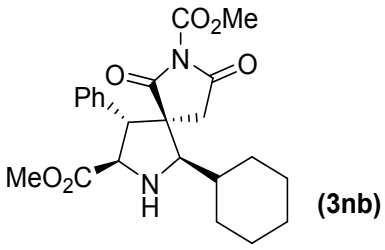
(3mb)



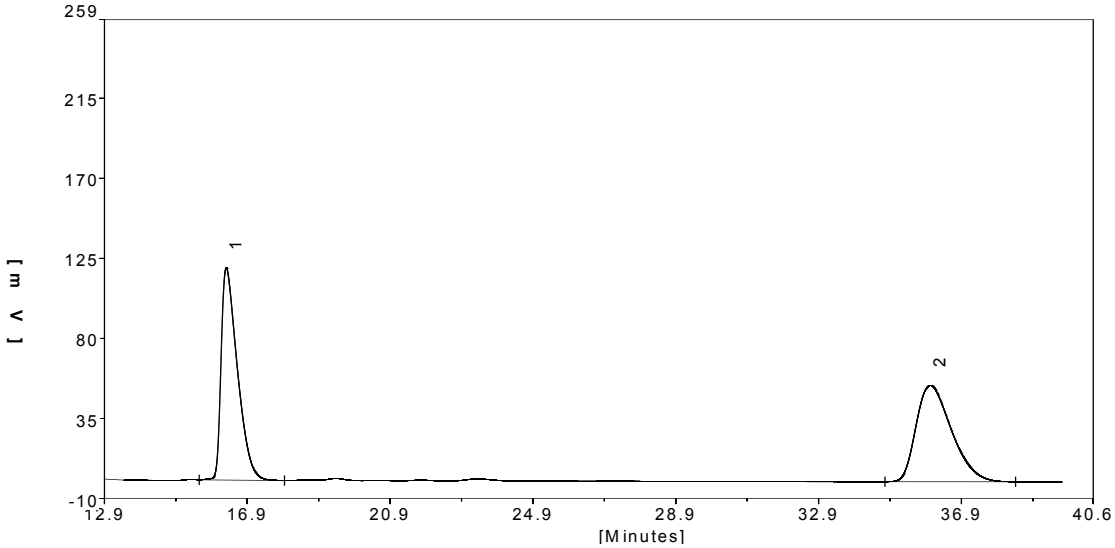
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	15.66917	83.38	2562.53	49.8880
2	25.76917	54.54	2574.03	50.1120



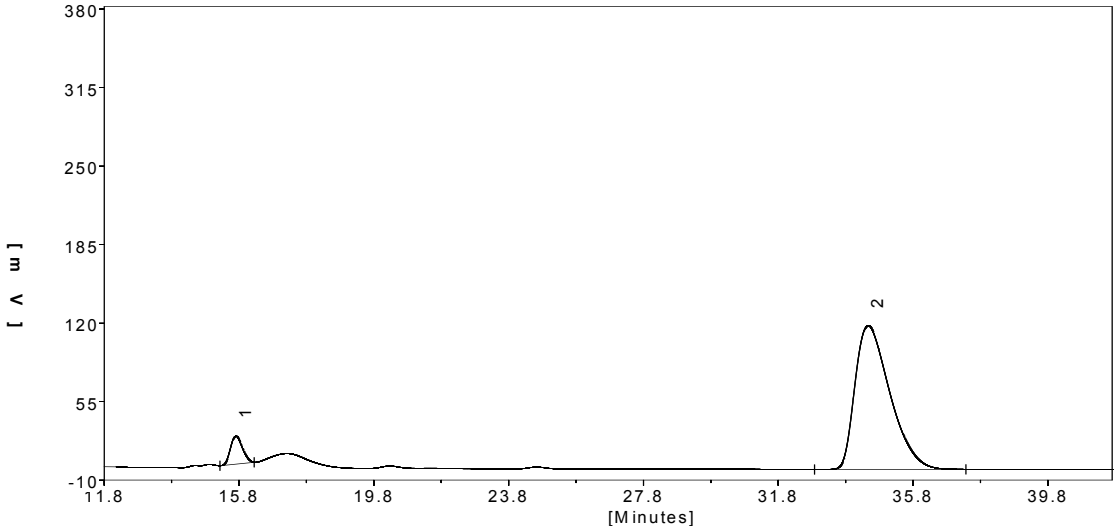
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	16.72333	14.08	637.49	4.4627
2	27.46500	247.32	13647.17	95.5373



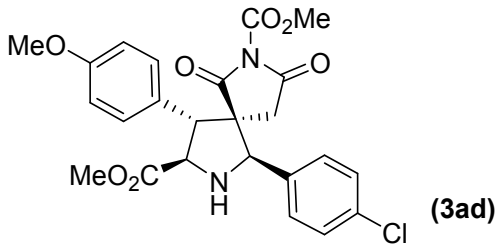
(3nb)



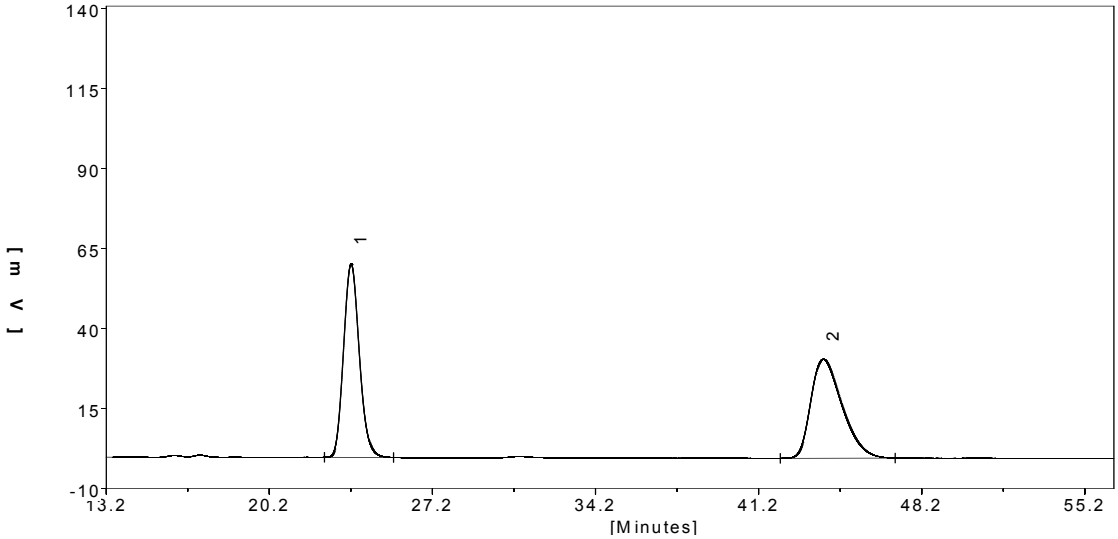
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	16.30083	119.24	3771.08	50.3421
2	36.01000	54.19	3719.83	49.6579



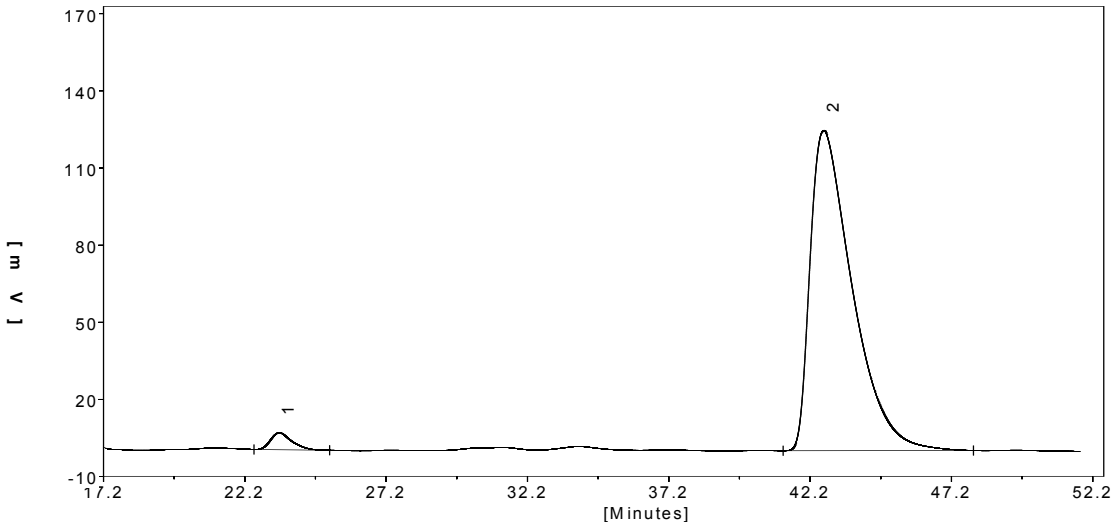
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	15.70583	23.18	570.92	6.2601
2	34.46500	119.03	8549.00	93.7399



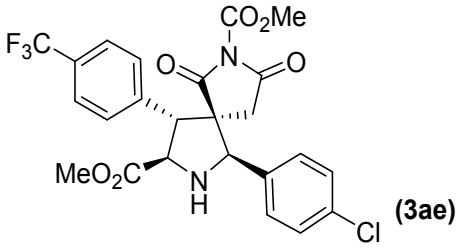
(3ad)



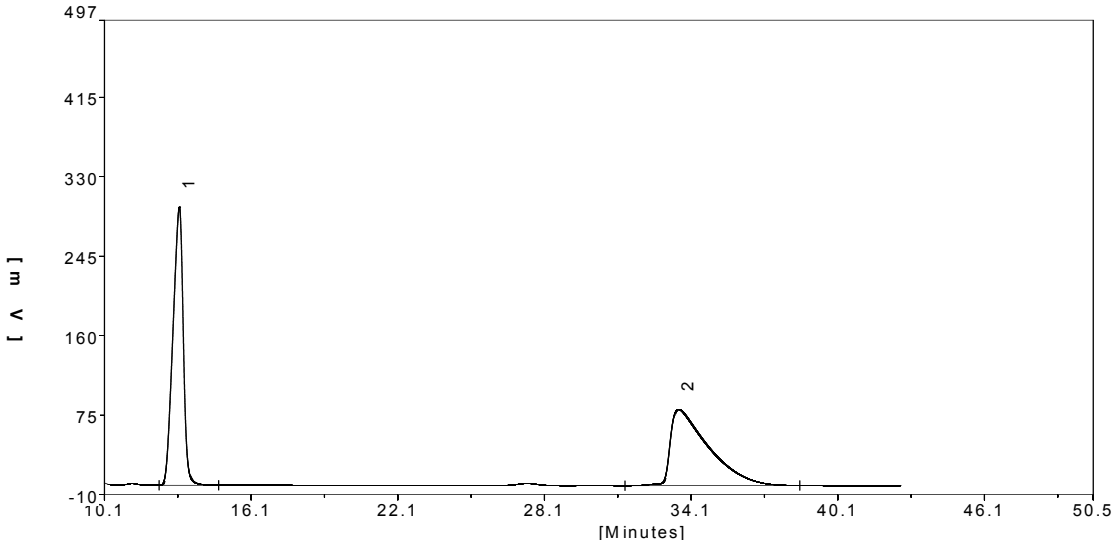
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	23.66250	60.46	2844.88	49.8462
2	43.91917	30.94	2862.44	50.1538



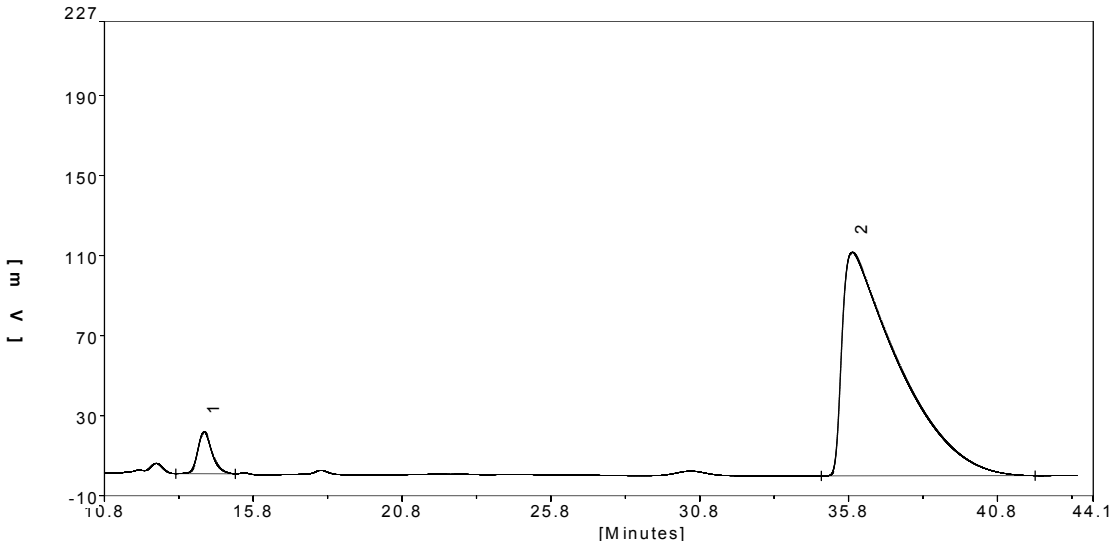
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	23.39167	6.60	343.82	2.5985
2	42.66583	124.67	12887.57	97.4015



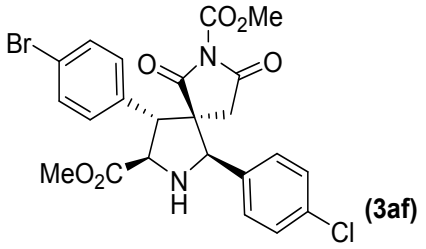
(3ae)



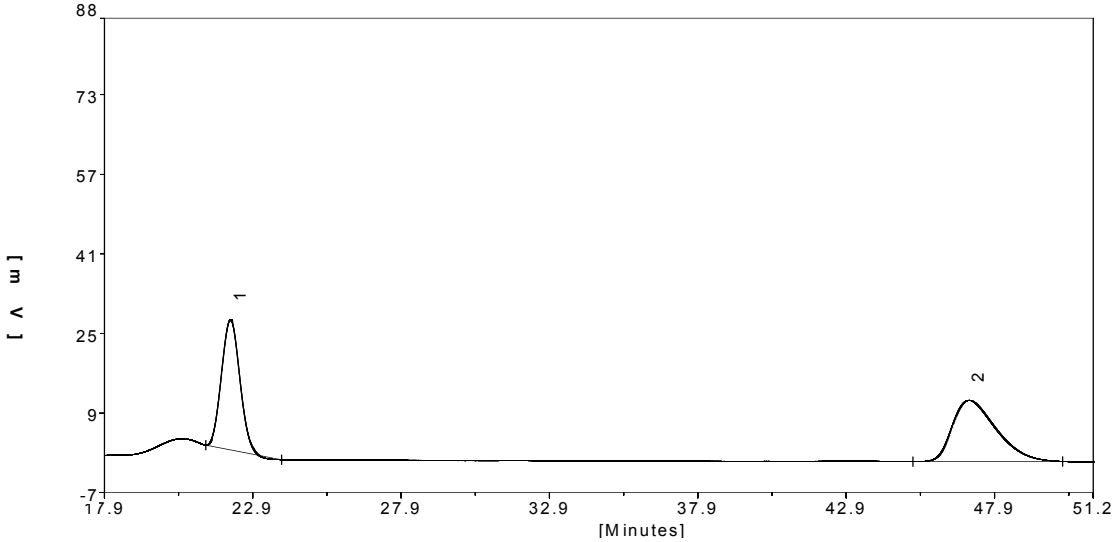
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	13.14583	297.45	8701.88	49.8960
2	33.55917	81.54	8738.16	50.1040



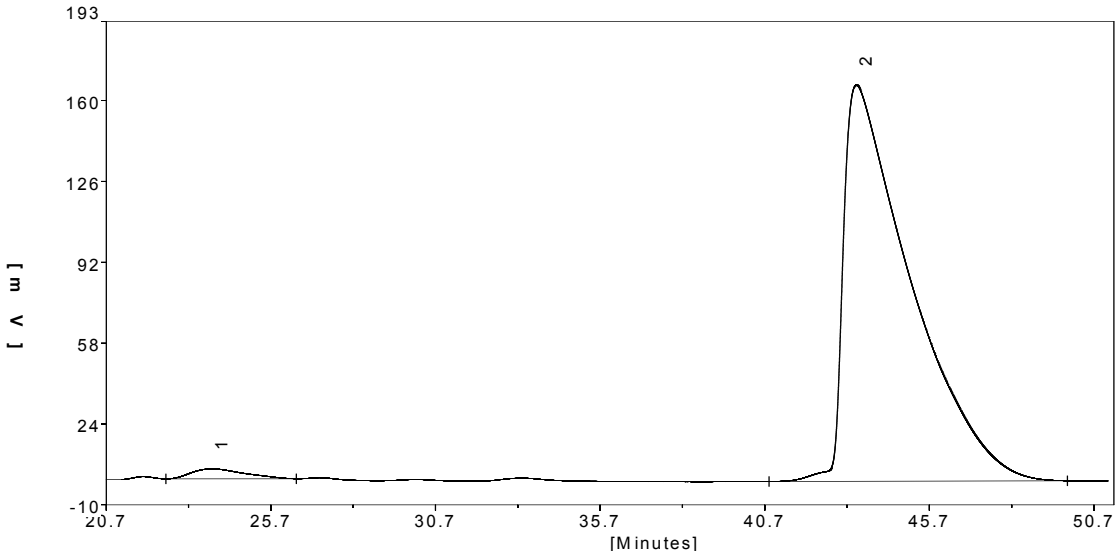
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	14.19417	20.96	696.78	4.5654
2	35.96250	111.77	14565.41	95.4346



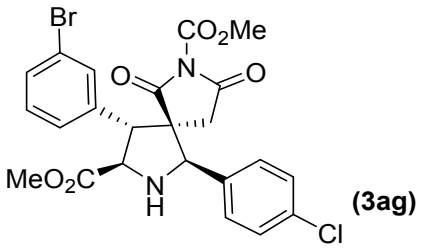
(3af)



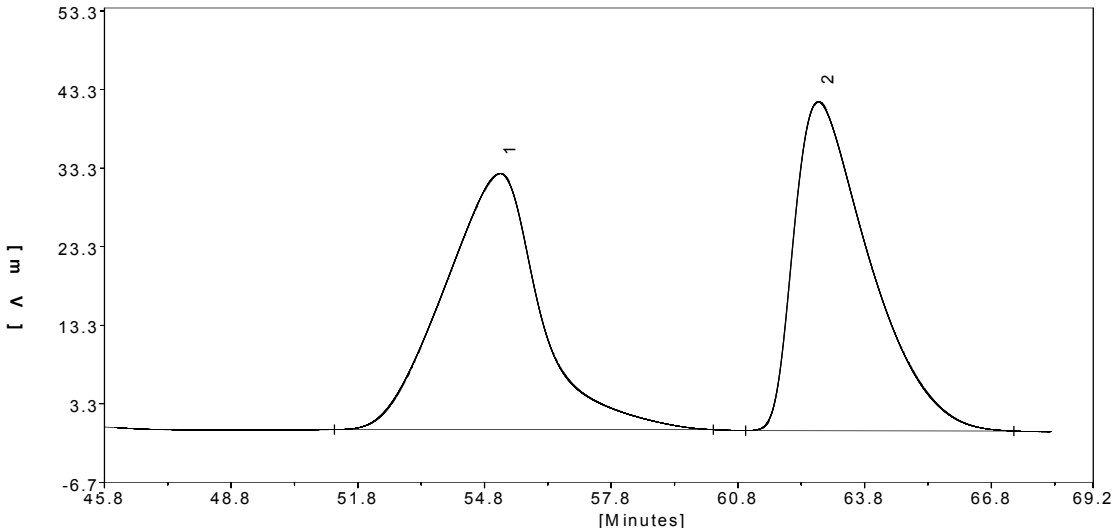
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	22.11333	26.18	1119.86	47.1218
2	46.99083	12.32	1256.66	52.8782



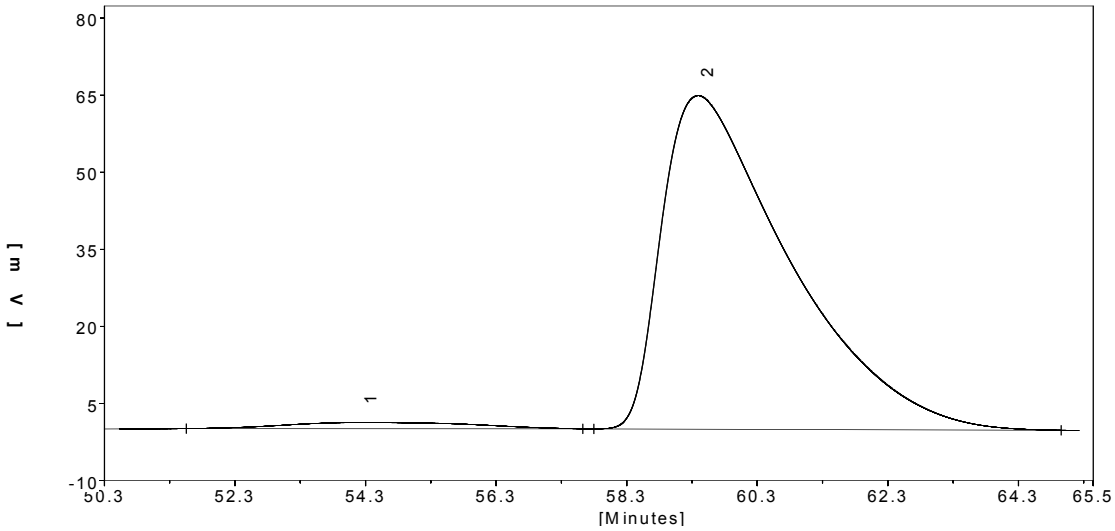
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	23.86583	4.21	469.48	1.9539
2	43.44083	166.56	23558.04	98.0461



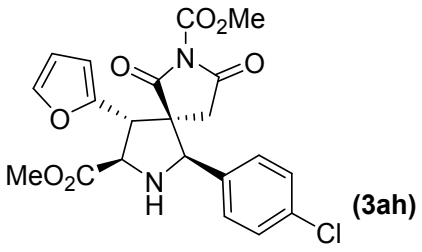
(3ag)



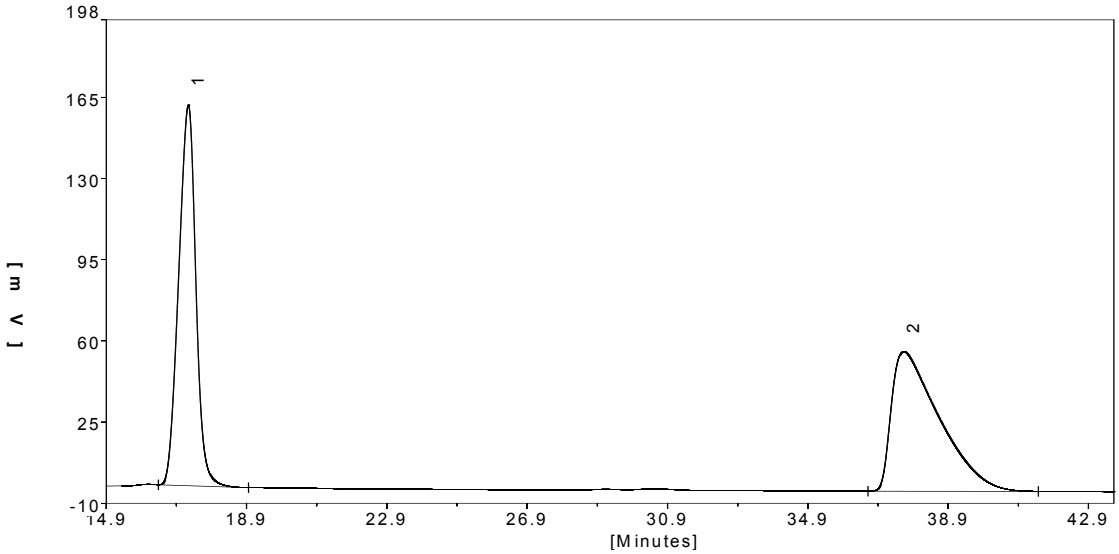
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	55.19833	32.59	5177.42	49.8907
2	62.73250	41.86	5200.10	50.1093



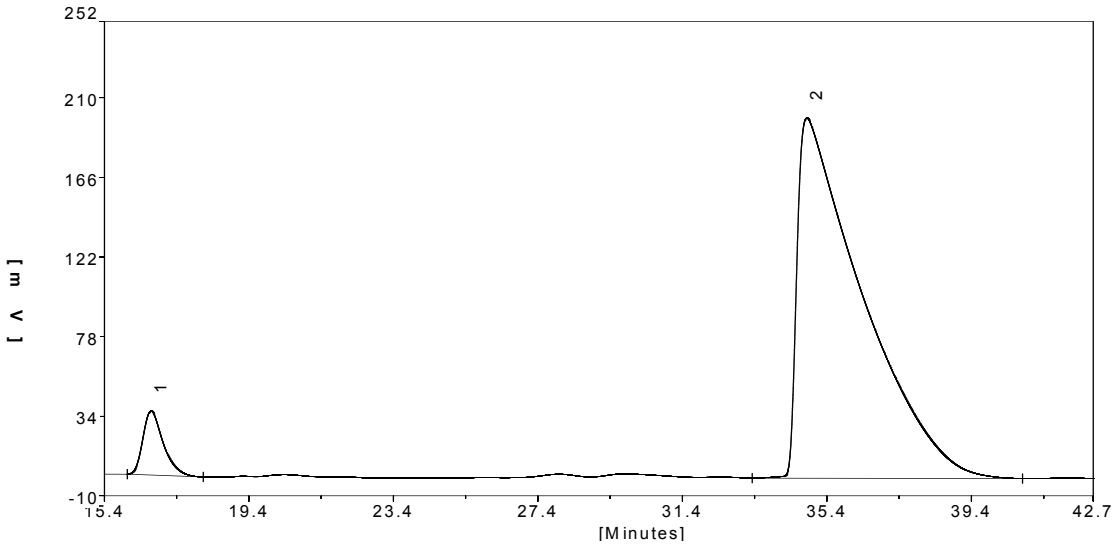
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	54.26000	1.22	242.69	2.6843
2	59.42250	64.94	8798.38	97.3157



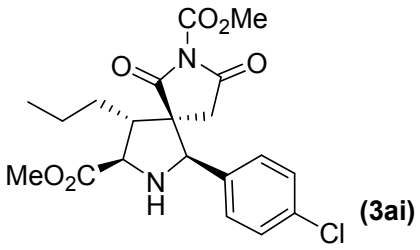
(3ah)



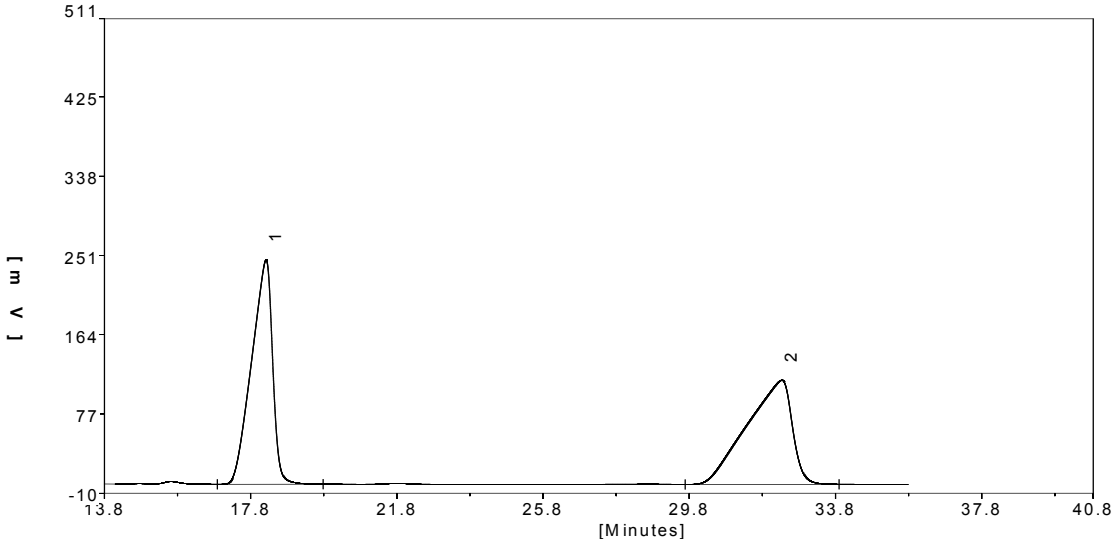
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	17.25500	164.07	5580.35	49.6205
2	37.64250	60.18	5665.71	50.3795



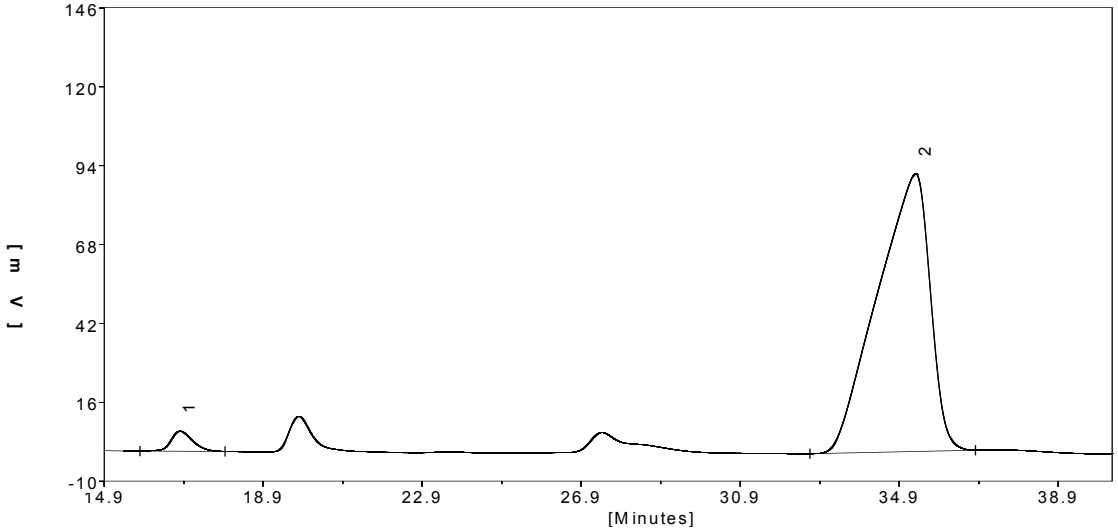
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	16.66583	35.44	1381.90	5.2712
2	34.81750	199.08	24833.99	94.7288



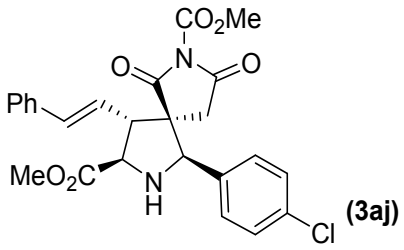
(3ai)



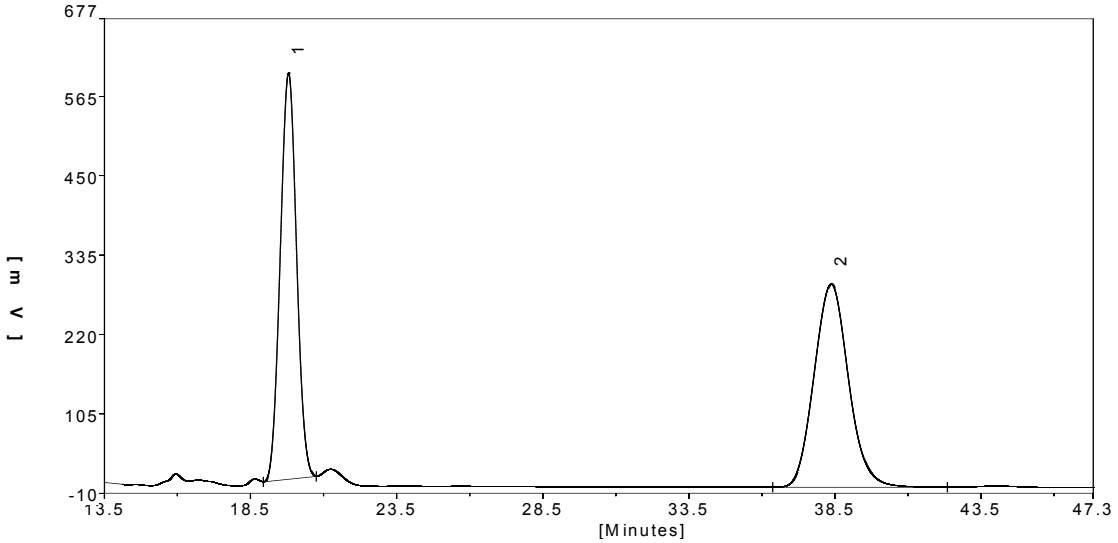
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	18.20333	246.30	9821.95	49.8643
2	32.30750	114.37	9875.40	50.1357



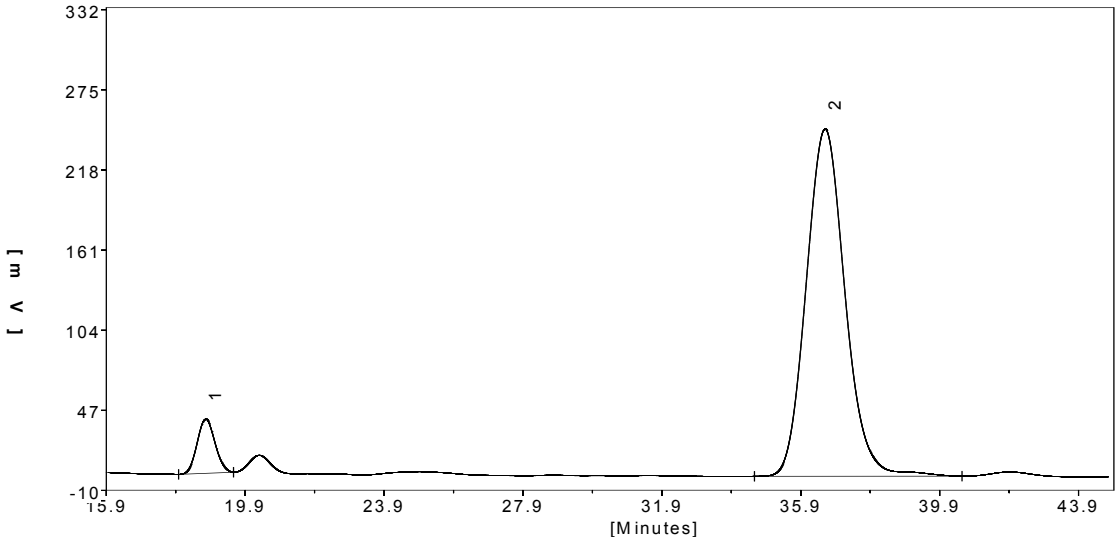
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	16.76750	6.61	248.32	2.8667
2	35.27750	91.61	8413.68	97.1333



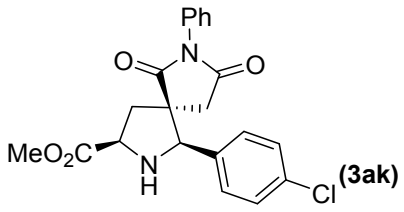
(3aj)



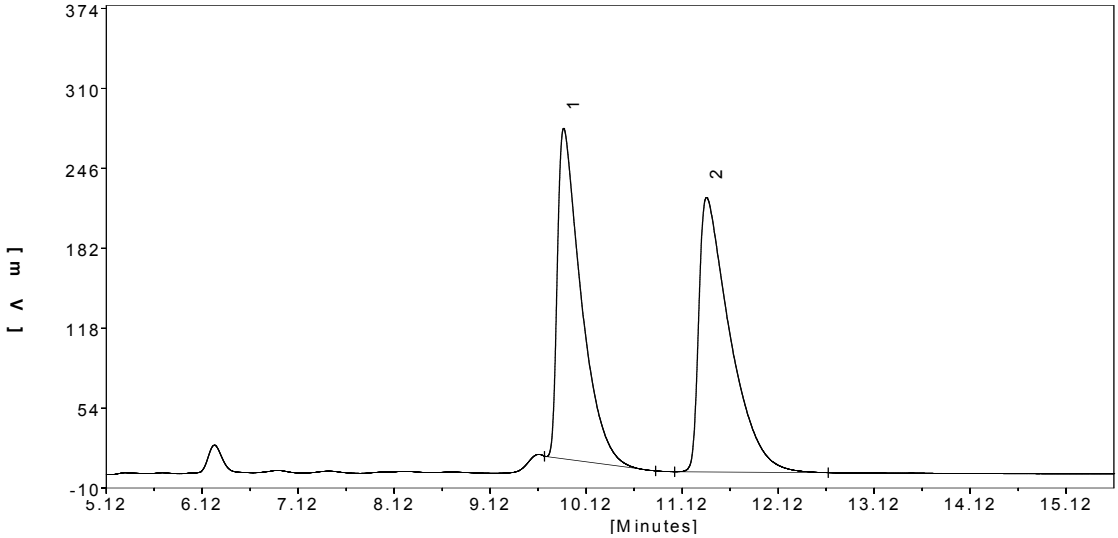
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	19.76583	588.45	22823.82	48.6902
2	38.33583	294.42	24051.73	51.3098



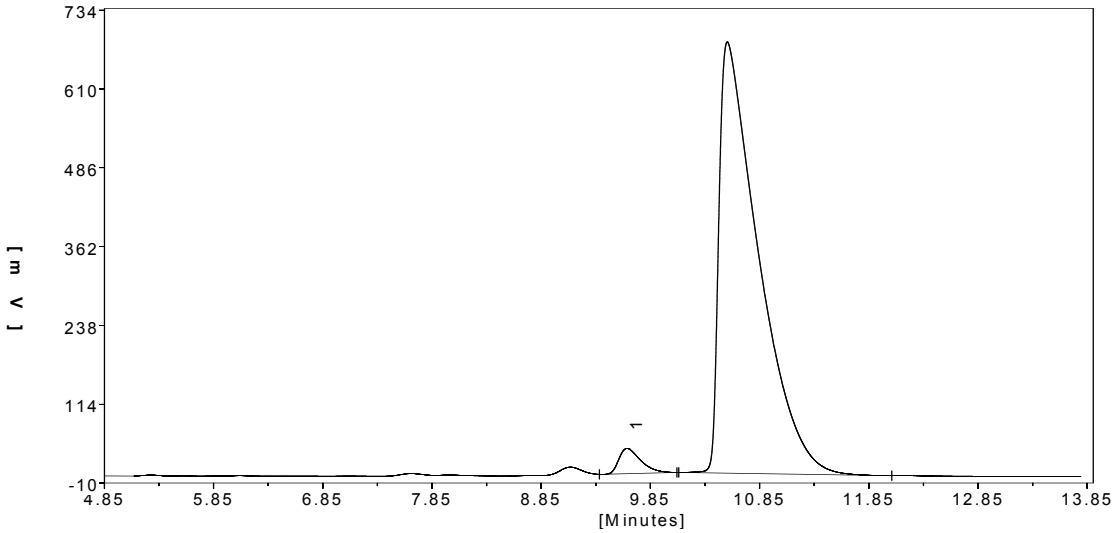
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	18.78167	38.66	1381.95	6.7092
2	36.62000	247.30	19215.96	93.2908



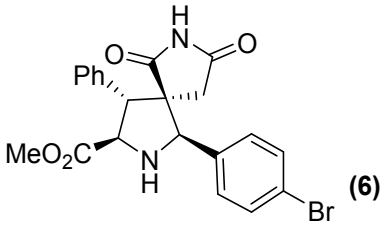
(3ak)



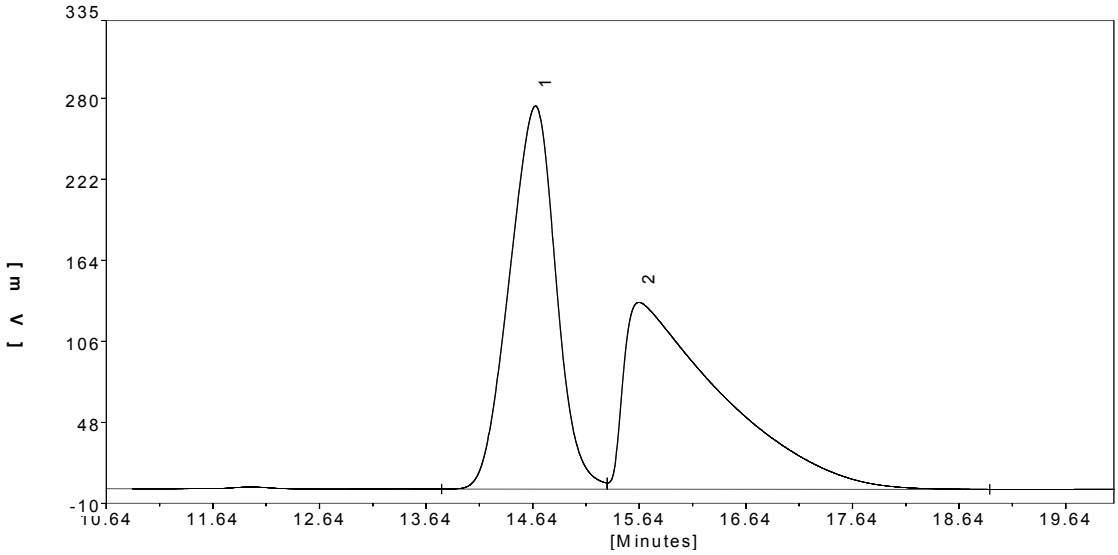
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	9.88250	264.58	4521.86	47.7510
2	11.37167	219.78	4947.80	52.2490



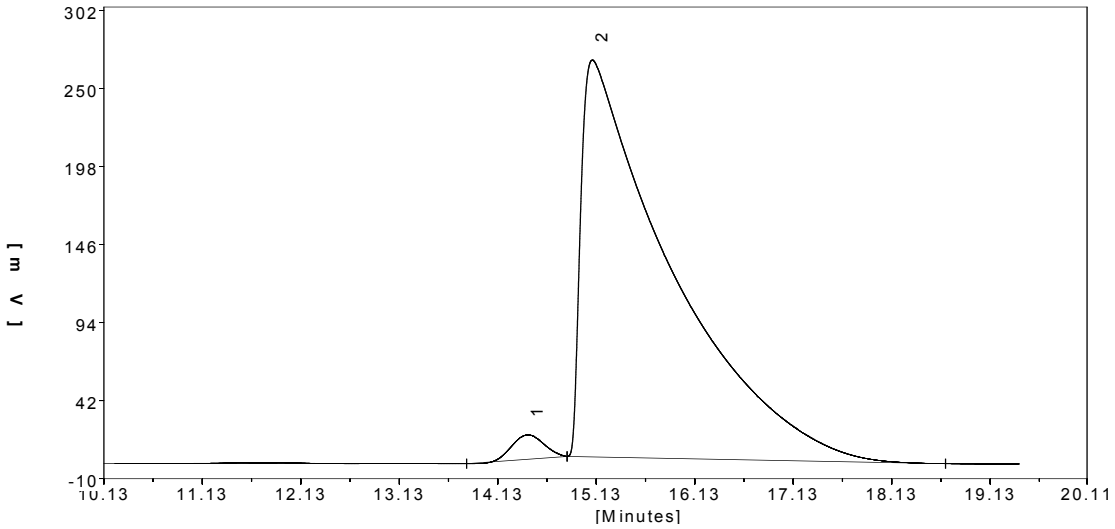
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	9.63417	39.70	548.85	3.1291
2	10.55333	678.44	16991.22	96.8709



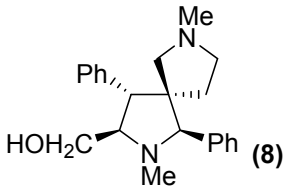
(6)



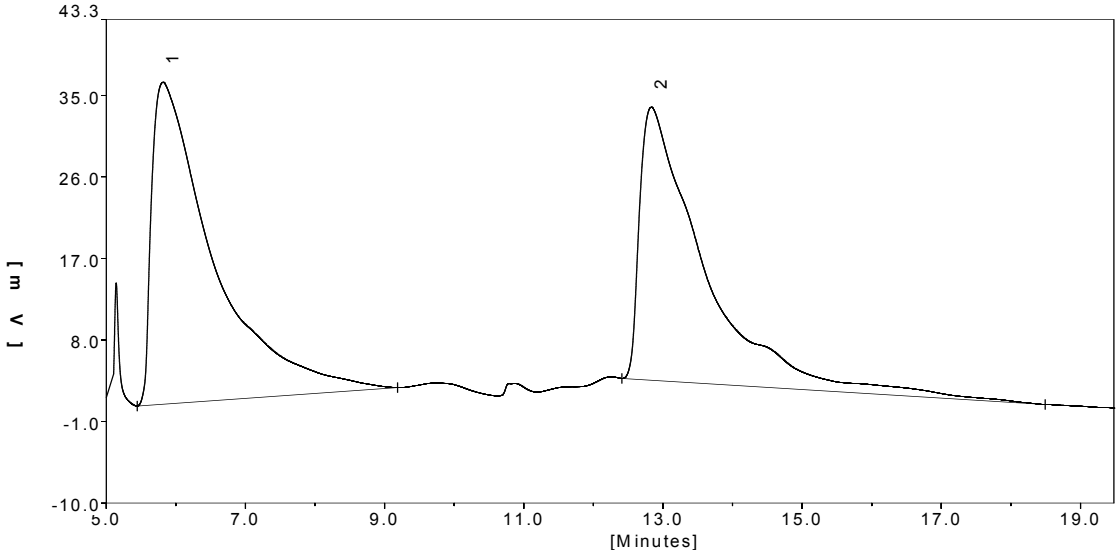
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	14.66167	274.22	8332.12	49.4531
2	15.63250	133.65	8516.42	50.5469



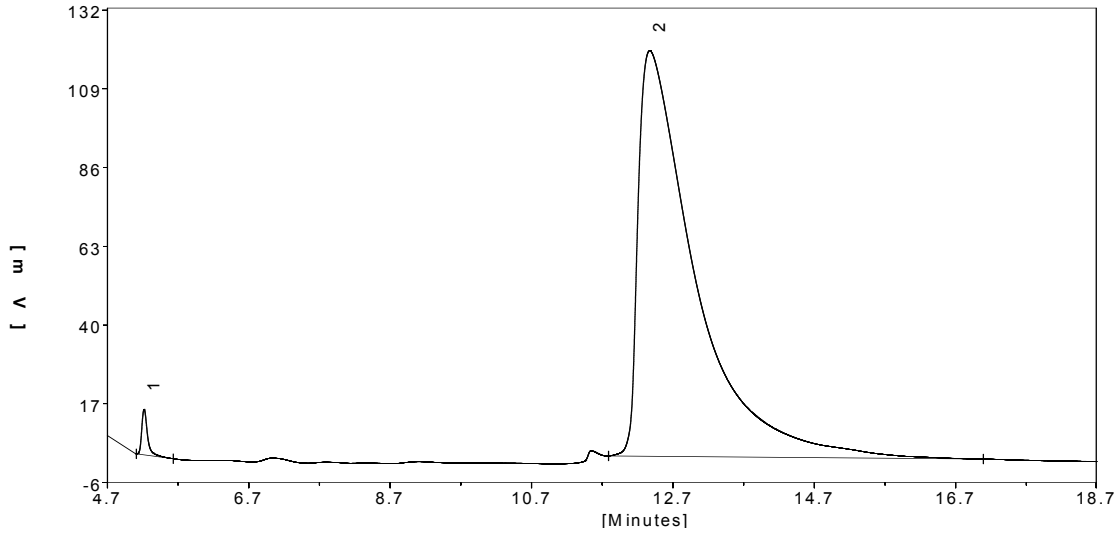
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	14.43083	16.27	362.42	2.1247
2	15.08667	264.47	16695.14	97.8753



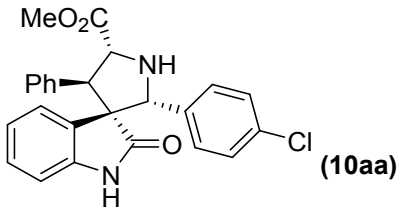
(8)



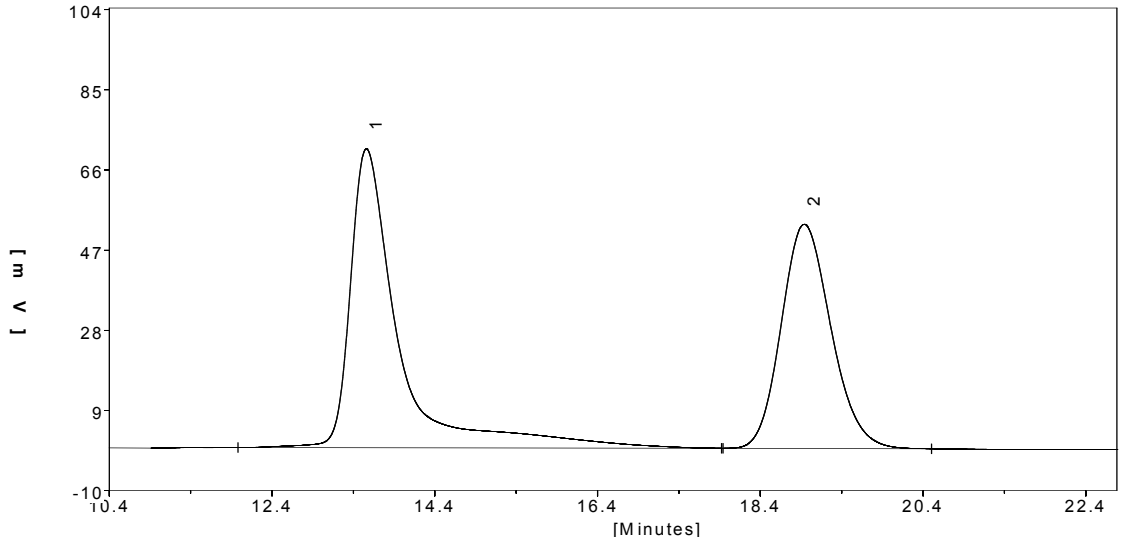
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	5.82917	35.53	2188.69	52.9741
2	12.84750	30.14	1942.93	47.0259



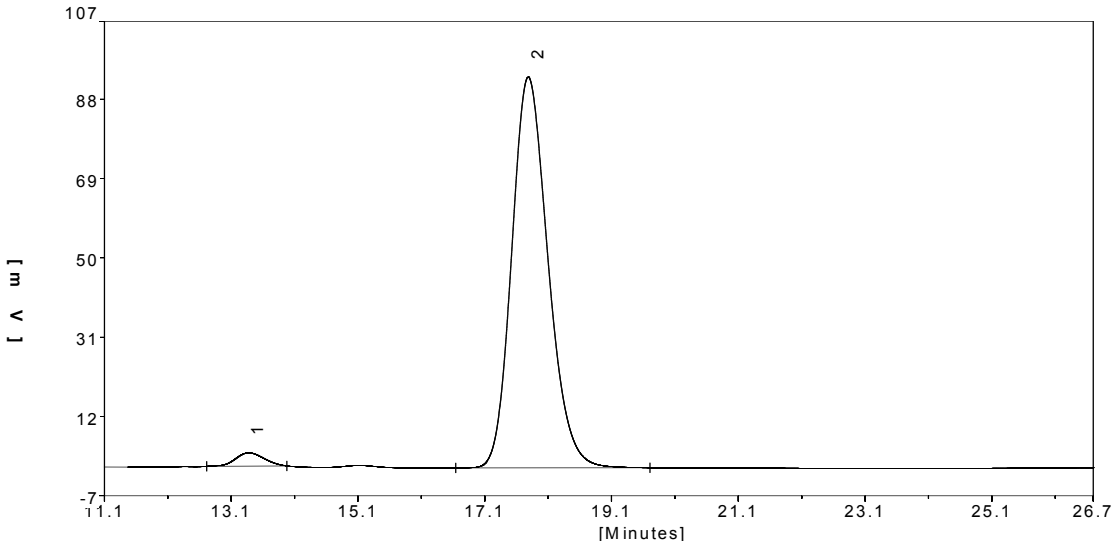
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	5.23917	13.33	150.50	2.2228
2	12.39167	118.51	6620.40	97.7772



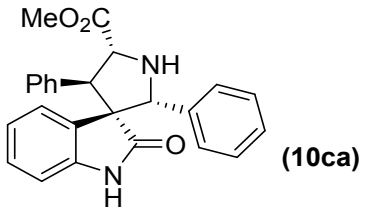
(10aa)



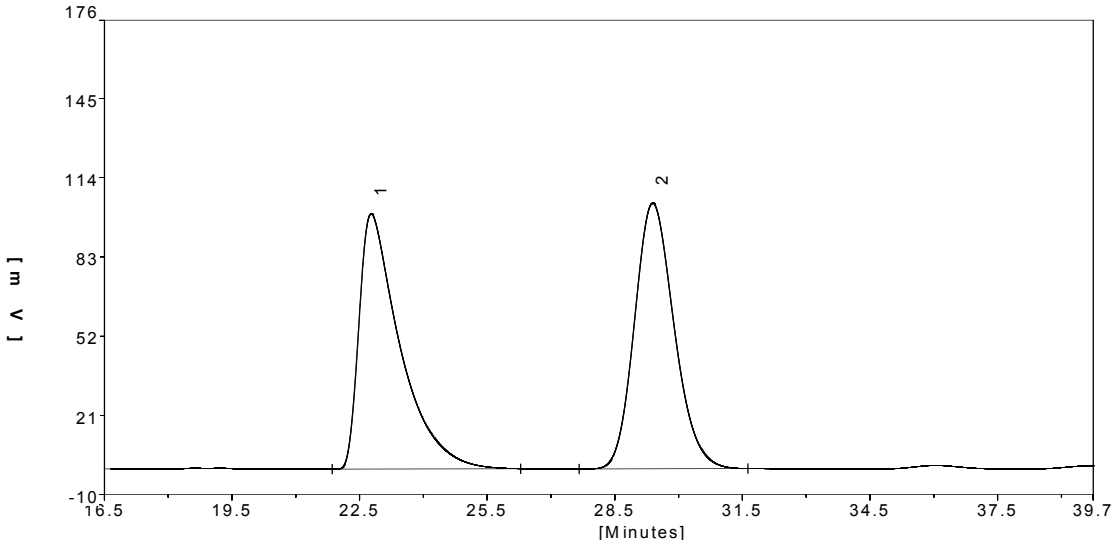
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	13.52500	70.87	2925.63	56.4685
2	18.90583	53.15	2255.37	43.5315



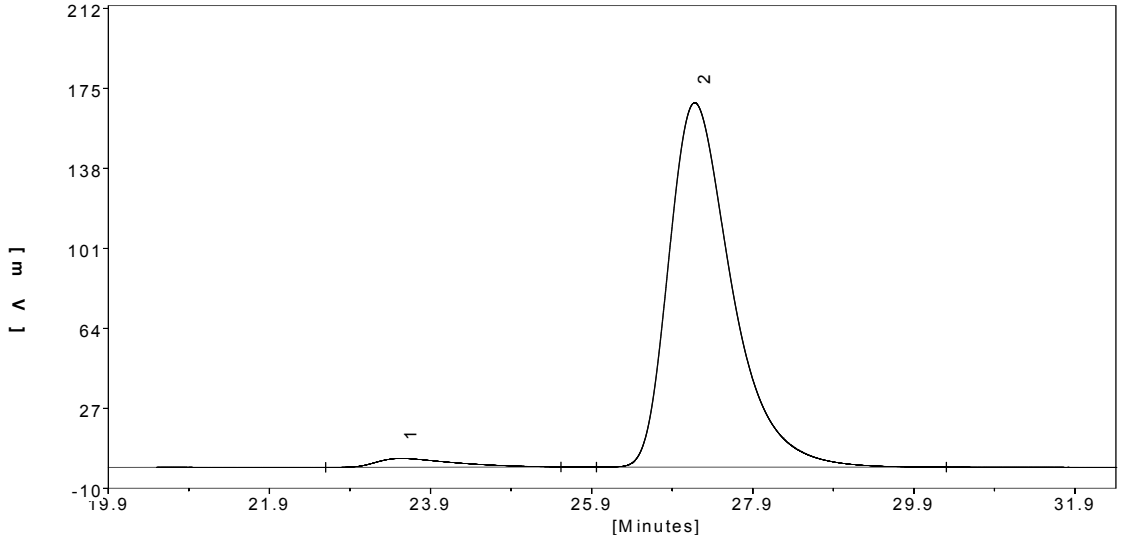
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	13.41500	3.19	99.75	2.6109
2	17.83583	93.61	3720.79	97.3891



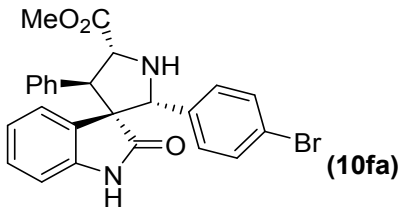
(10ca)



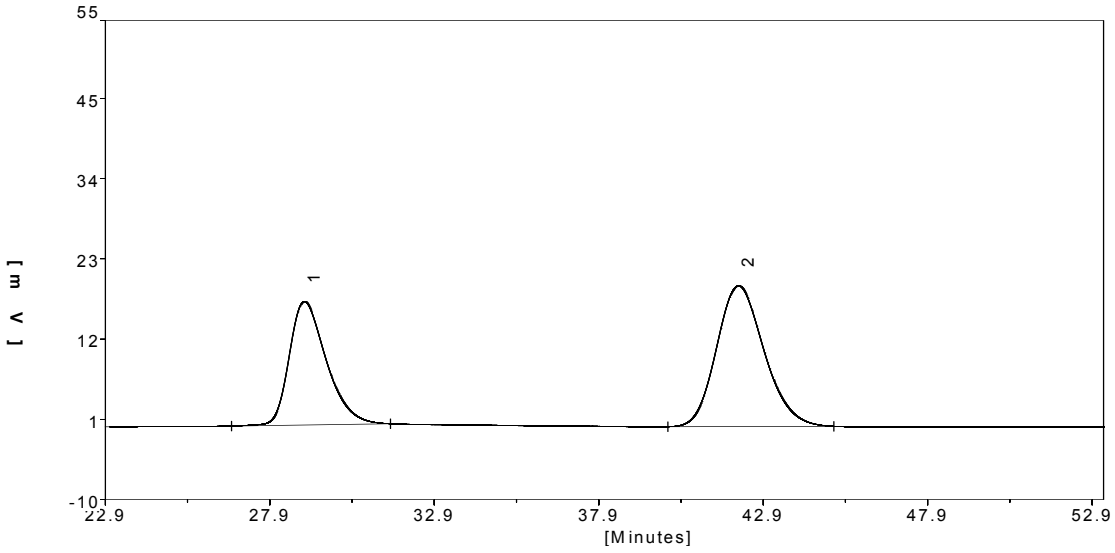
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	22.76167	99.88	6659.68	49.7605
2	29.38083	103.99	6723.78	50.2395



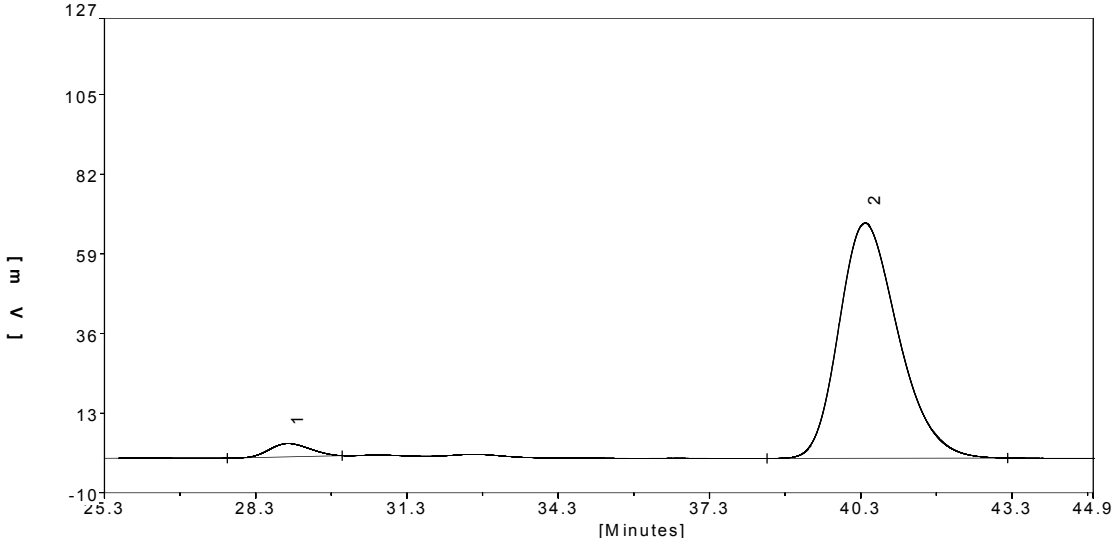
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	23.51250	4.05	267.26	2.8357
2	27.16000	168.50	9157.49	97.1643



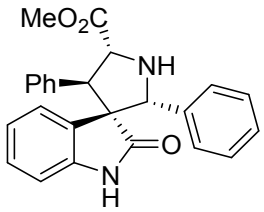
(10fa)



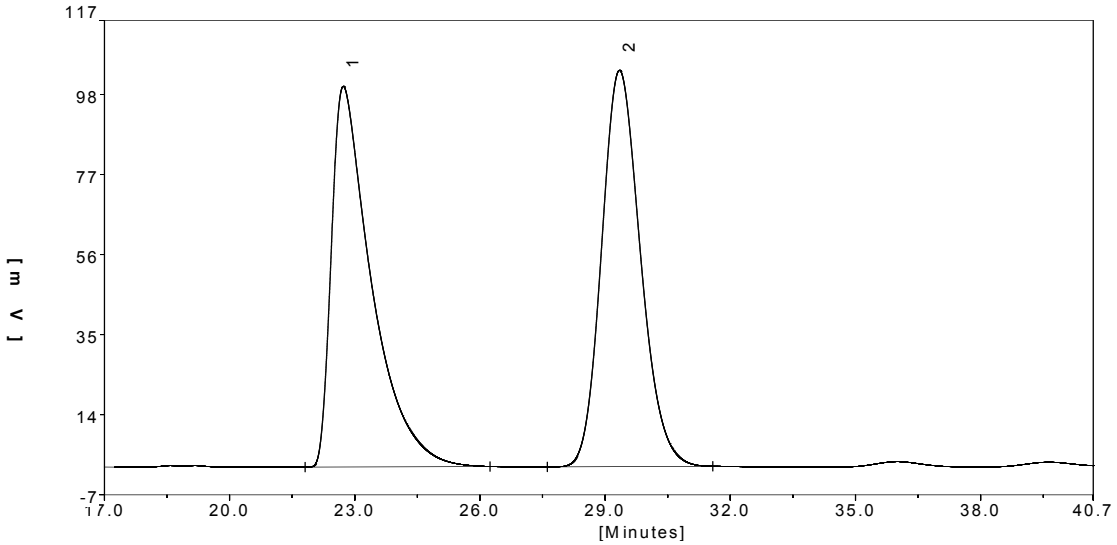
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	28.96167	16.93	1323.22	40.5555
2	42.15333	19.30	1939.52	59.4445



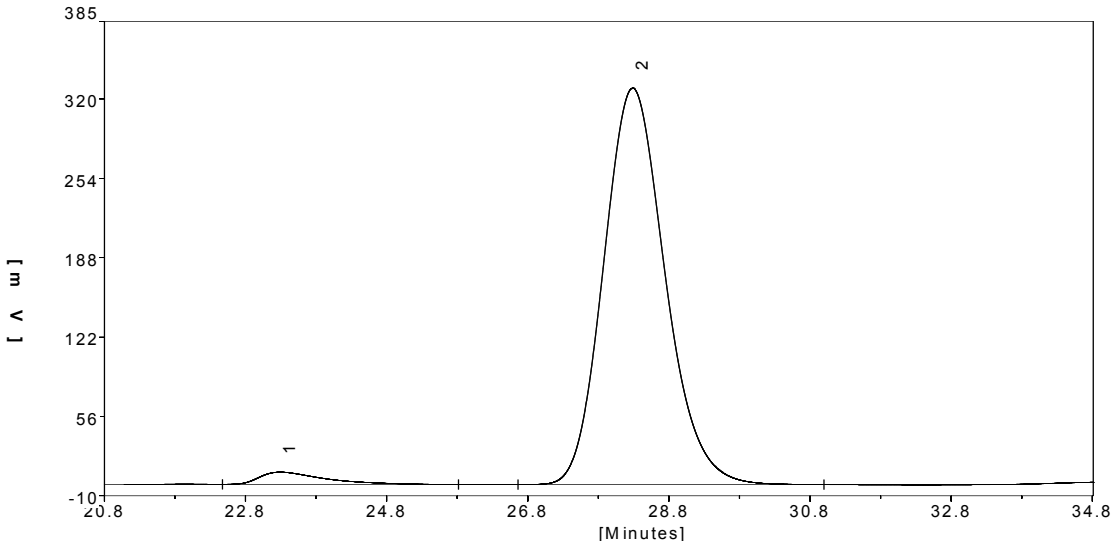
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	28.95833	3.85	213.82	3.7183
2	40.40417	67.92	5536.69	96.2817



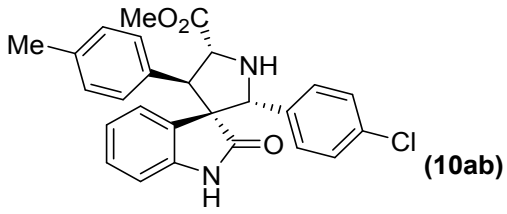
(10ga)



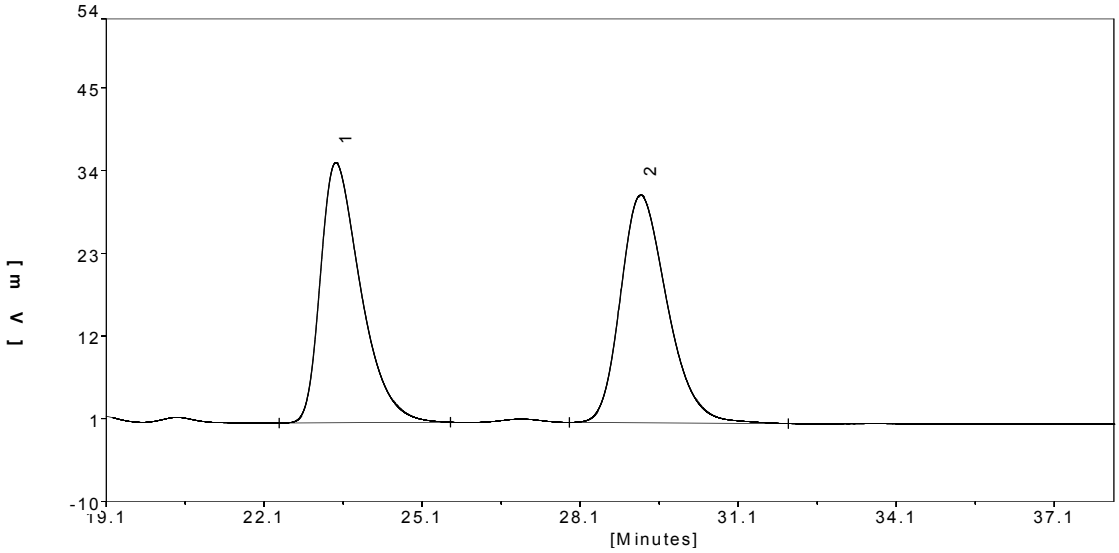
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	22.76167	99.88	6659.68	49.7605
2	29.38083	103.99	6723.78	50.2395



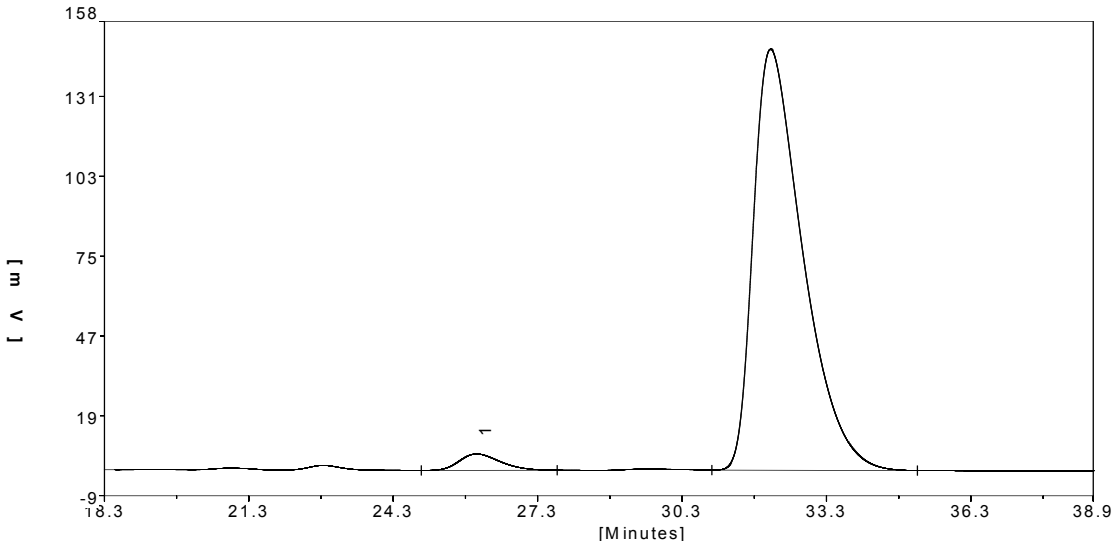
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	23.32750	10.22	647.03	3.1471
2	28.32417	329.72	19912.41	96.8529



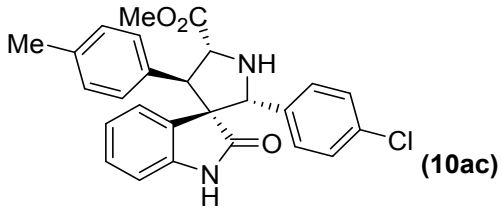
(10ab)



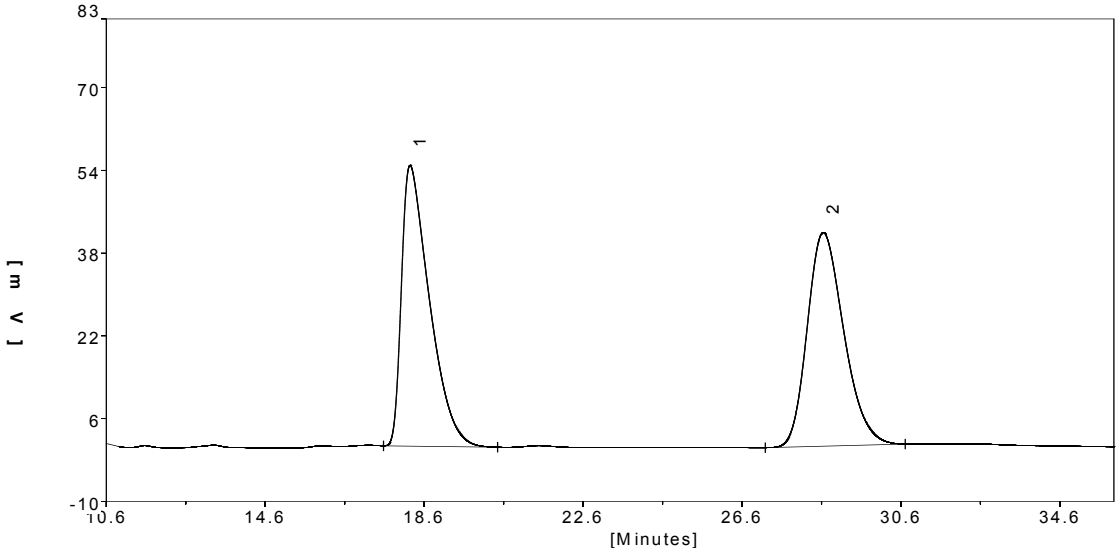
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	23.43500	34.59	1834.84	49.5794
2	29.22417	30.28	1865.97	50.4206



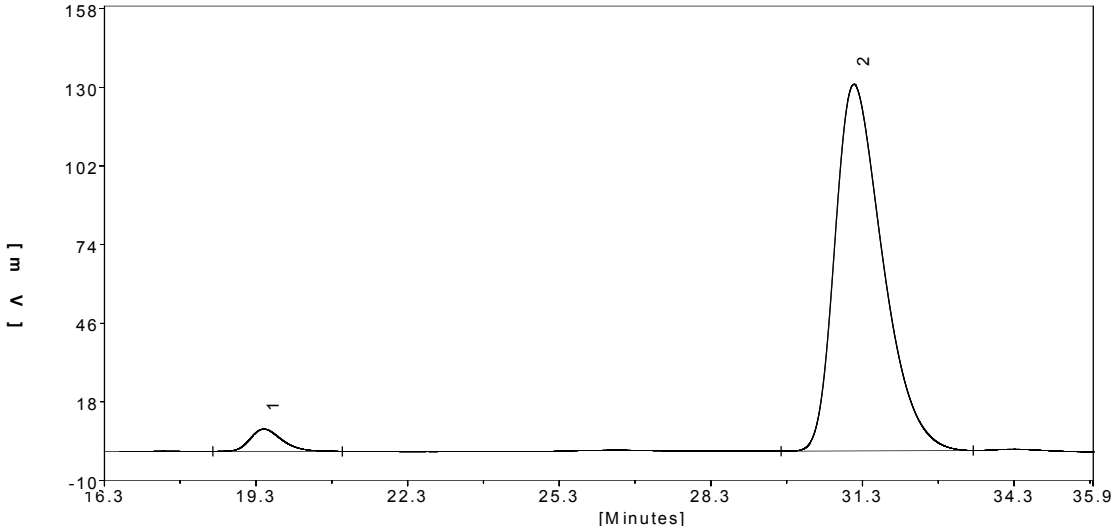
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	26.05750	5.75	338.63	3.1159
2	32.18000	147.56	10529.25	96.8841



(10ac)



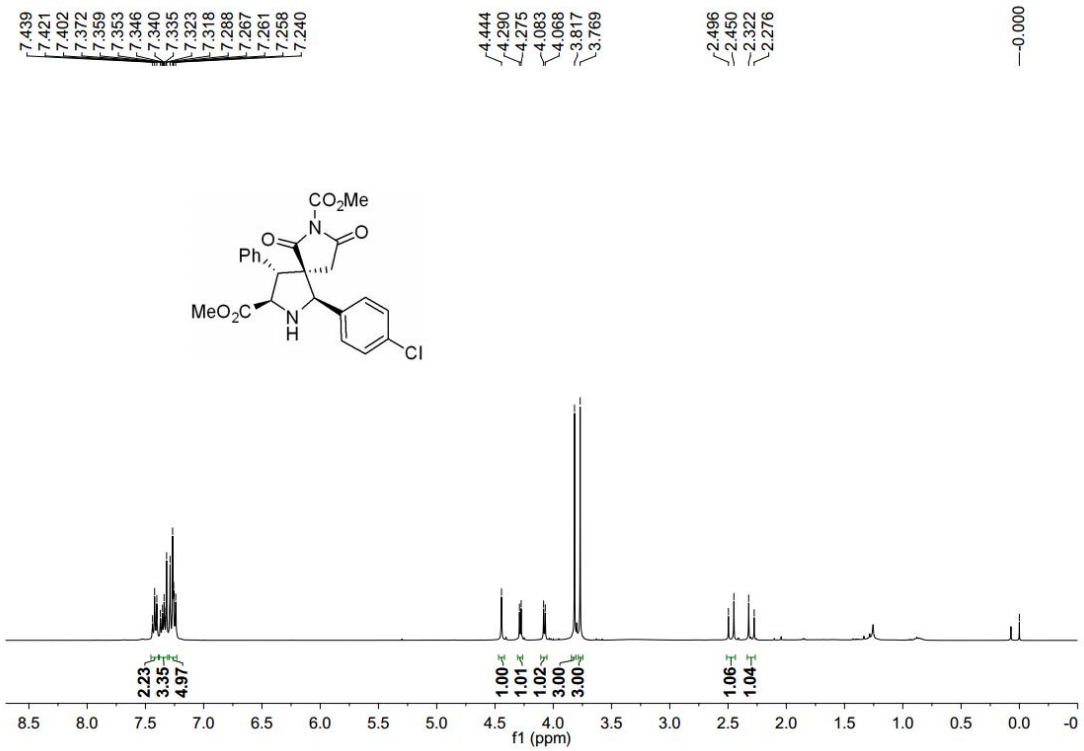
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	18.22000	54.29	2648.11	50.0990
2	28.61917	41.30	2637.65	49.9010



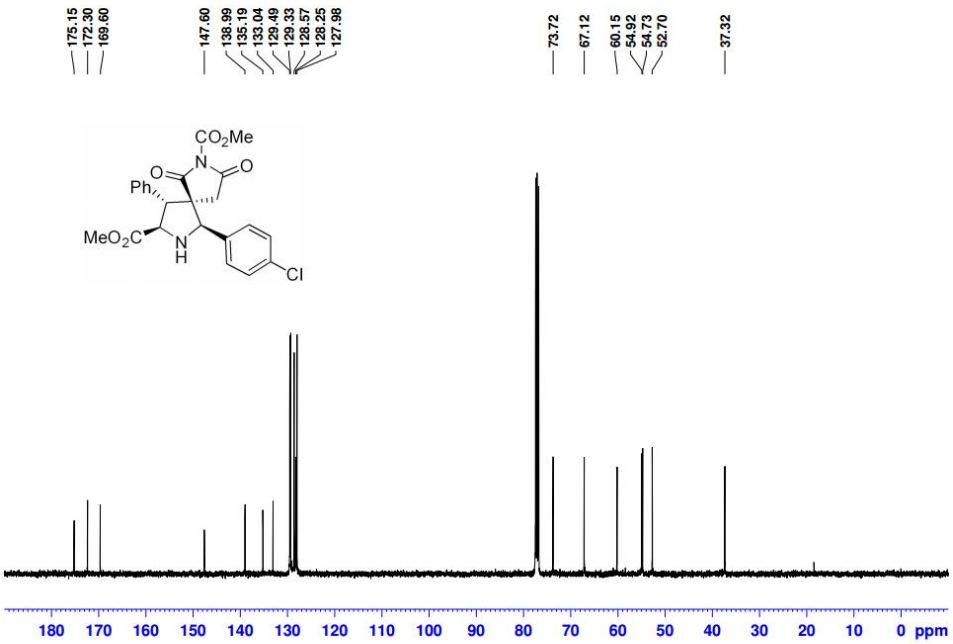
#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area (%)
1	19.48000	7.94	347.62	3.9018
2	31.16250	130.59	8561.53	96.0982

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

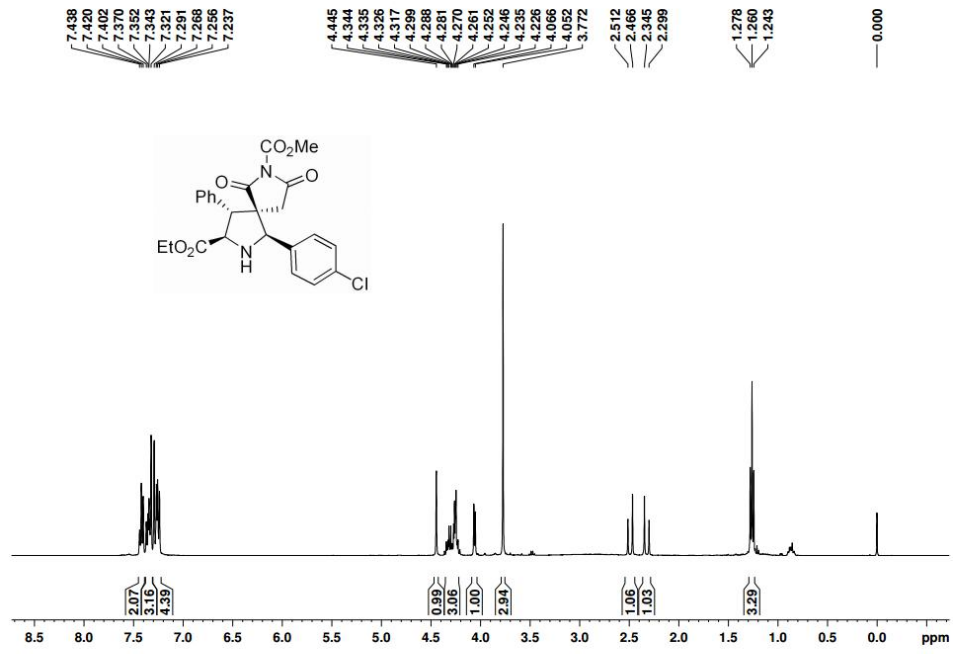
^{1}H NMR spectrum of compound **3ab** ($CDCl_3$)



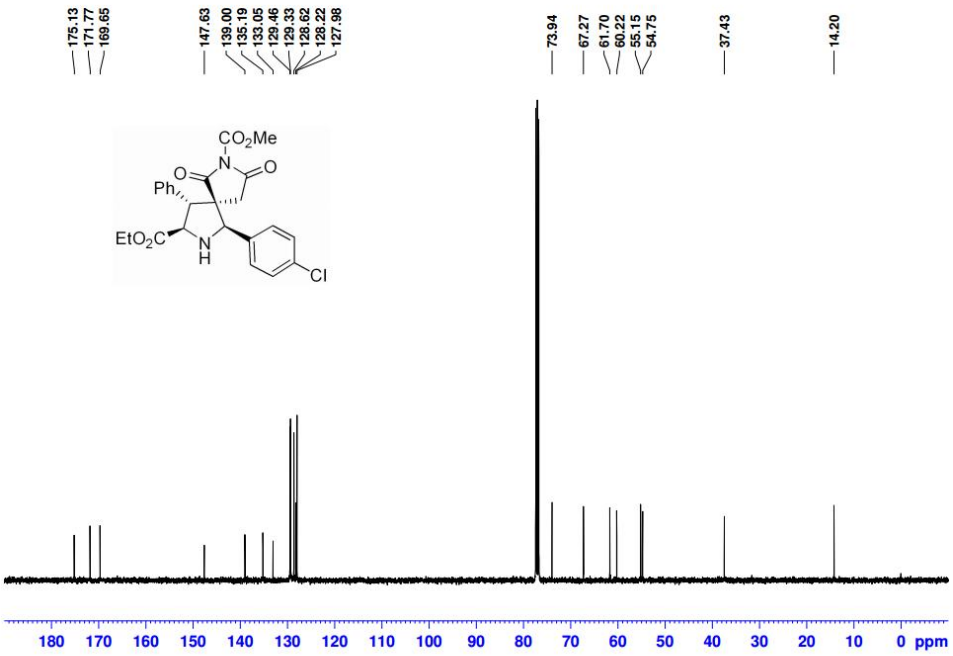
^{13}C NMR spectrum of compound **3ab** ($CDCl_3$)



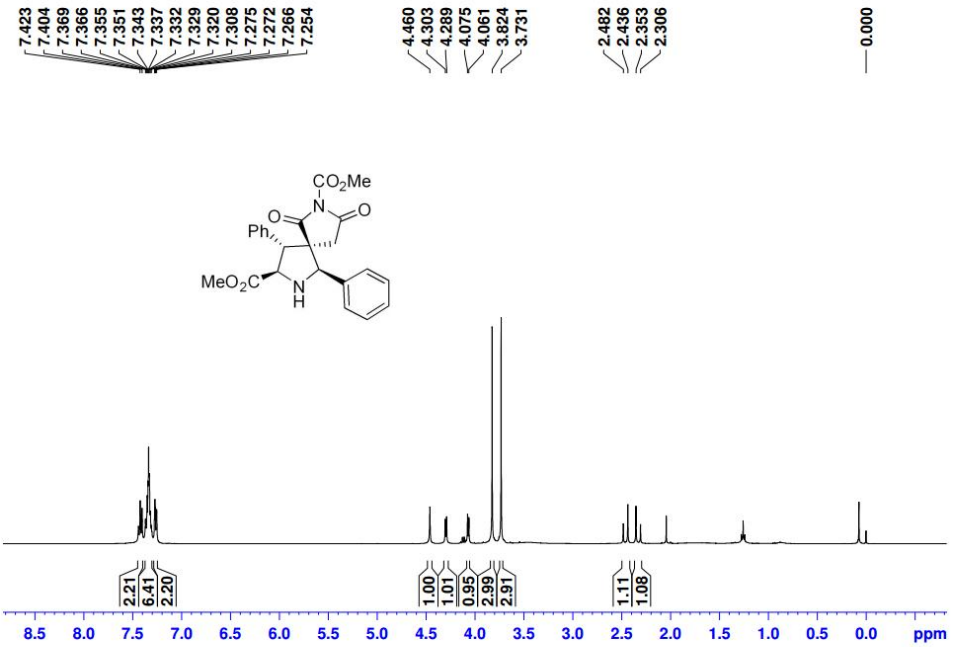
^{1}H NMR spectrum of compound **3bb** ($CDCl_3$)



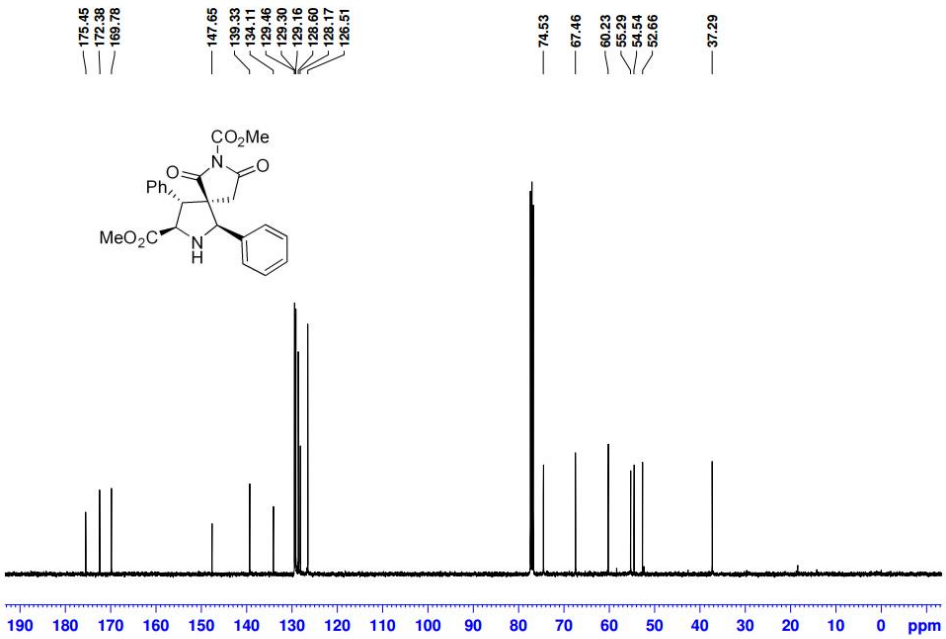
^{13}C NMR spectrum of compound **3bb** ($CDCl_3$)



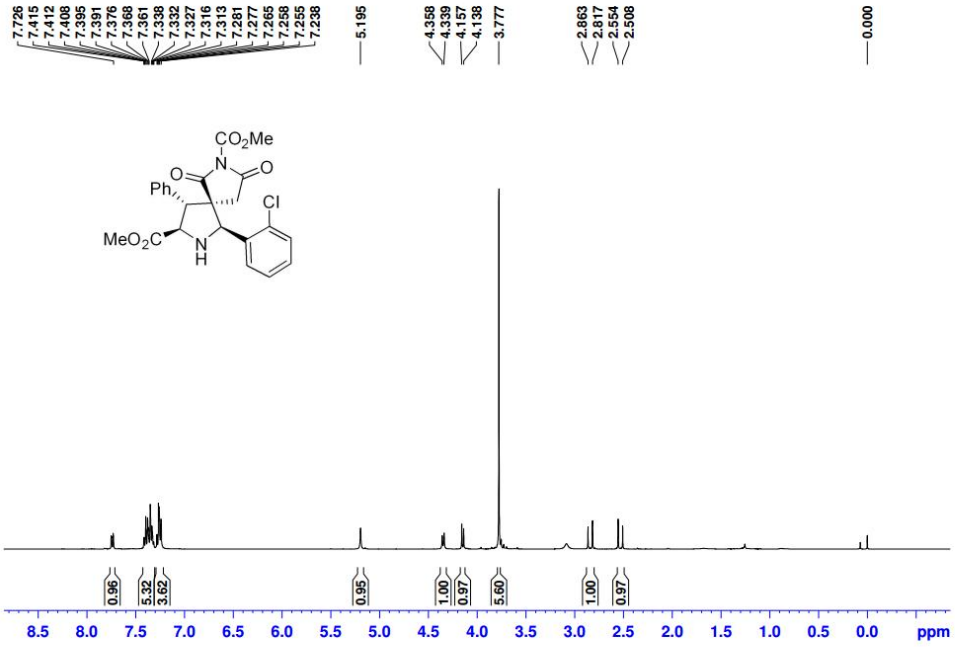
^{1}H NMR spectrum of compound **3cb** ($CDCl_3$)



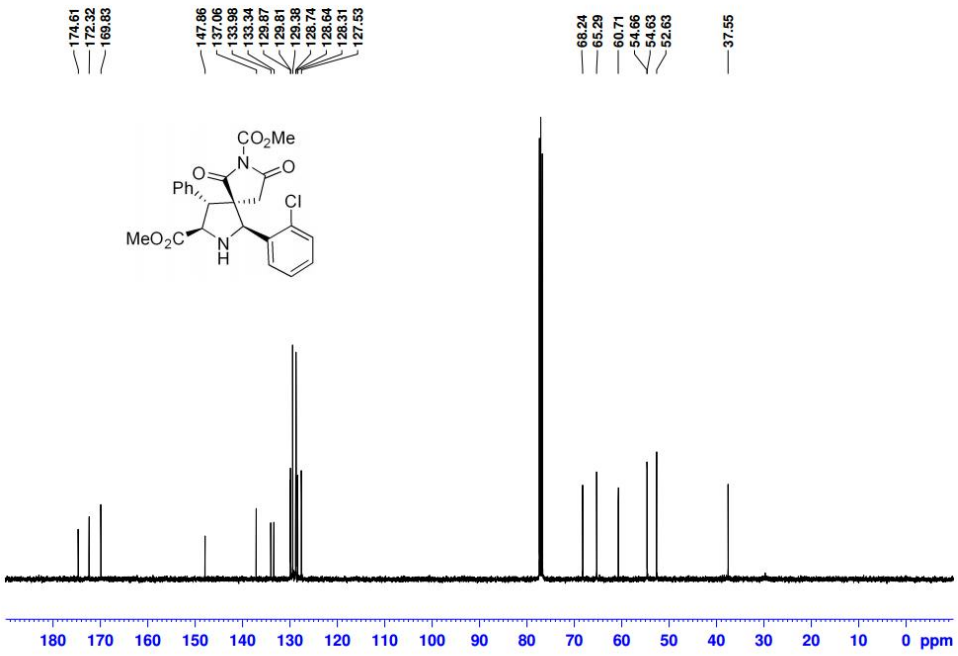
^{13}C NMR spectrum of compound **3cb** ($CDCl_3$)



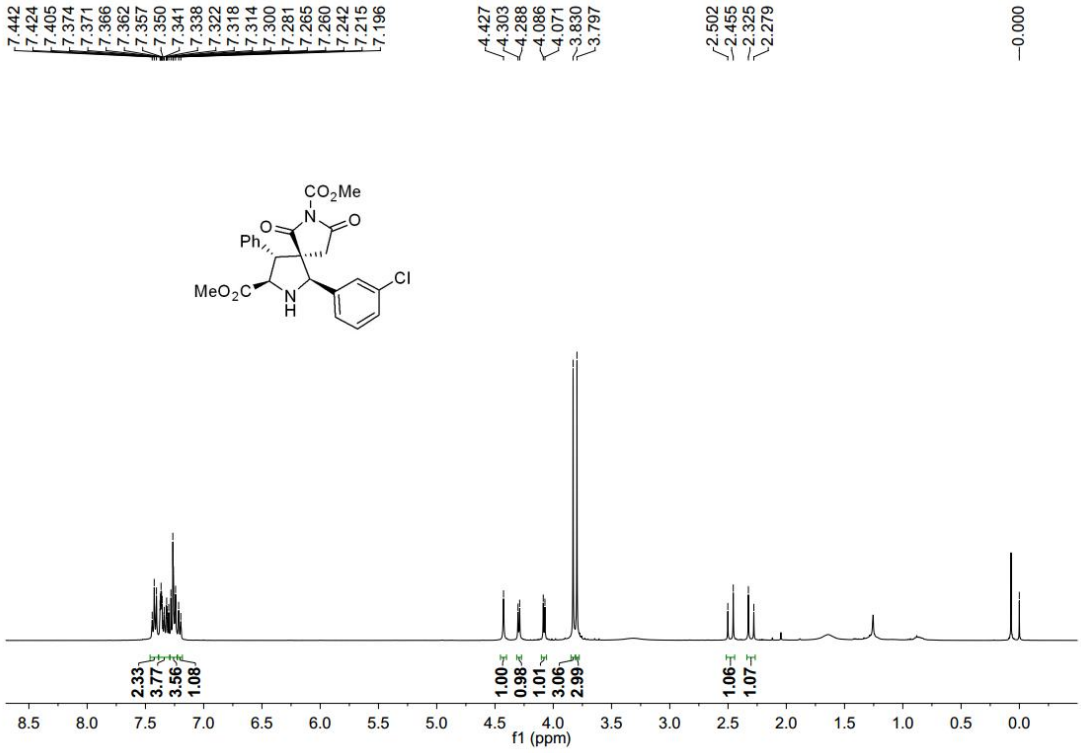
^{1}H NMR spectrum of compound **3db** ($CDCl_3$)



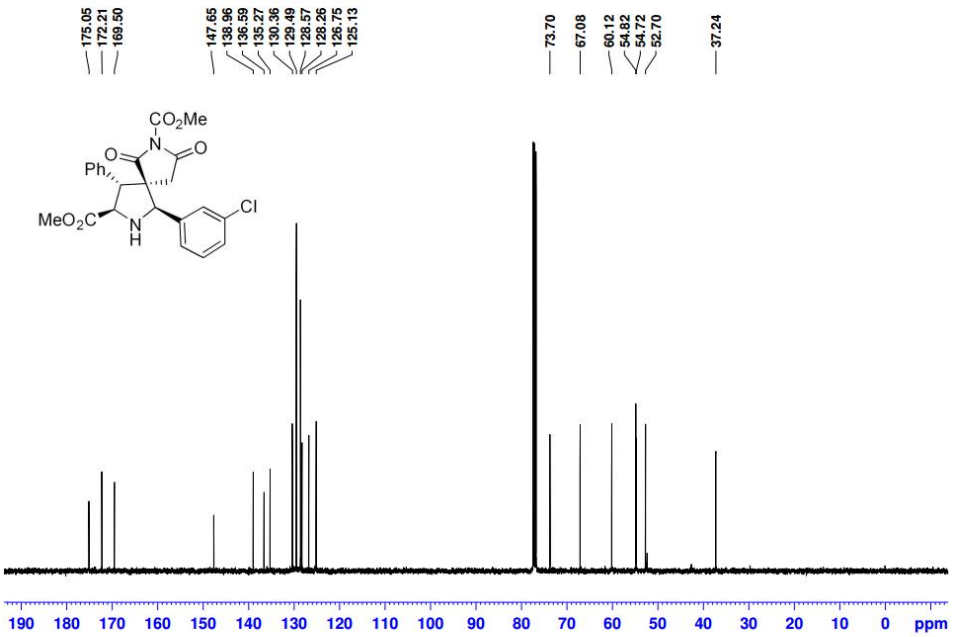
^{13}C NMR spectrum of compound **3db** ($CDCl_3$)



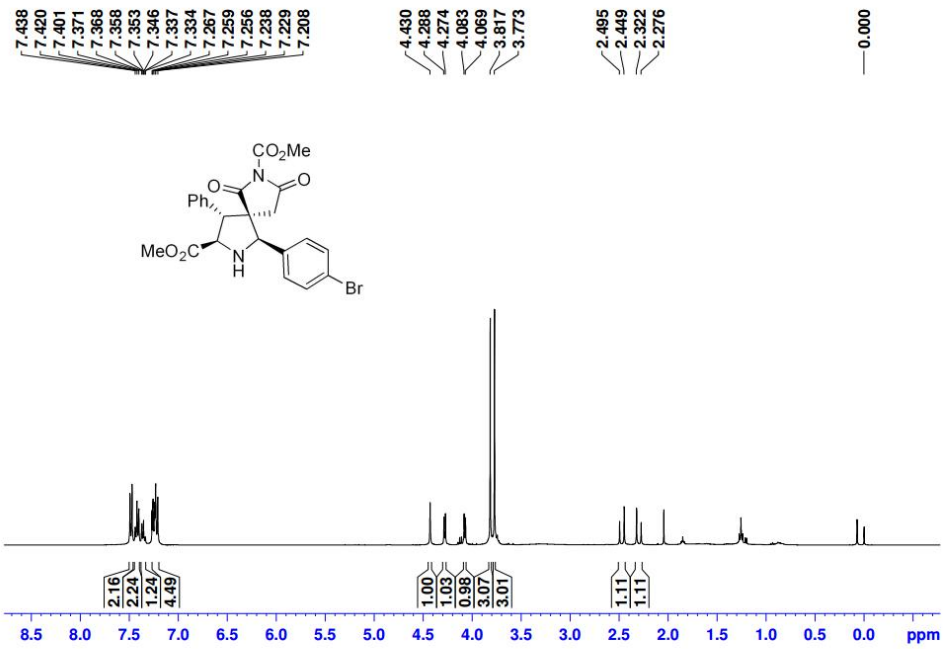
^{1}H NMR spectrum of compound **3eb** ($CDCl_3$)



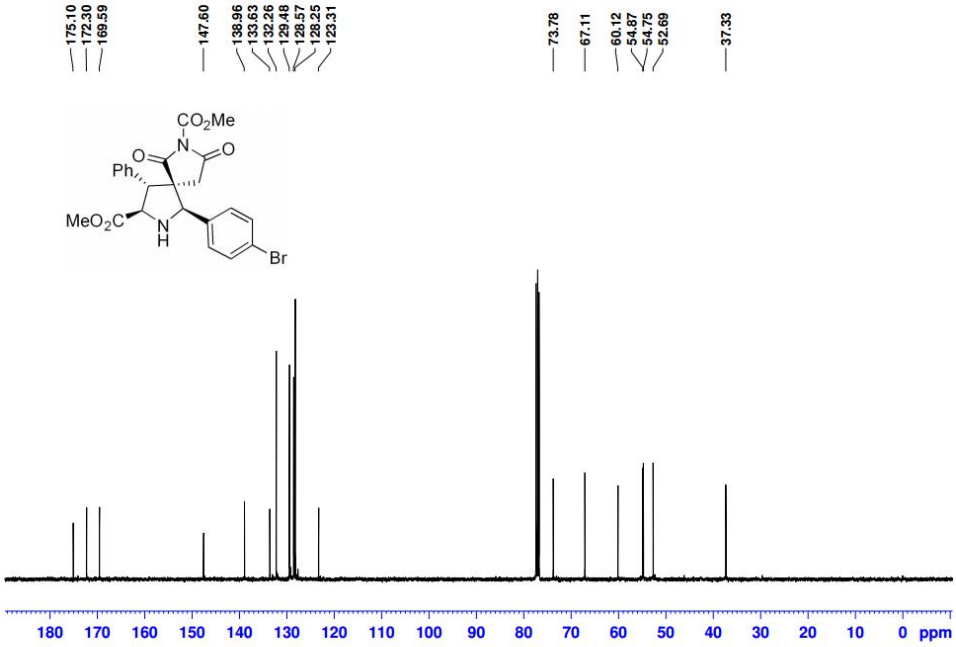
^{13}C NMR spectrum of compound **3eb** ($CDCl_3$)



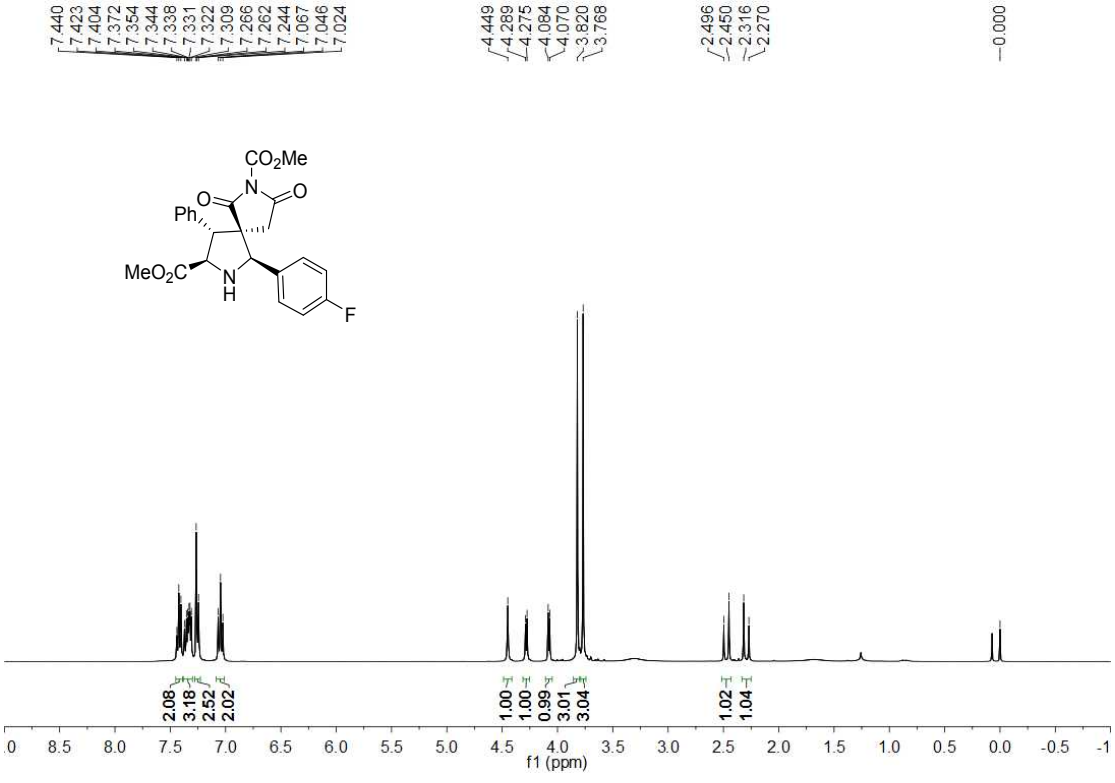
^{1}H NMR spectrum of compound **3fb** ($CDCl_3$)



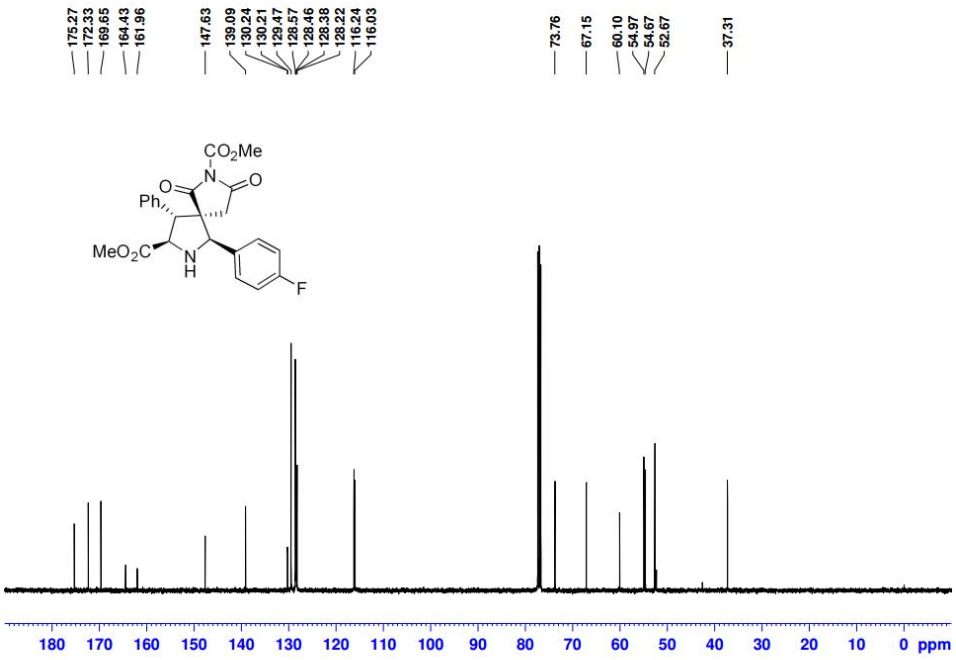
^{13}C NMR spectrum of compound **3fb** ($CDCl_3$)



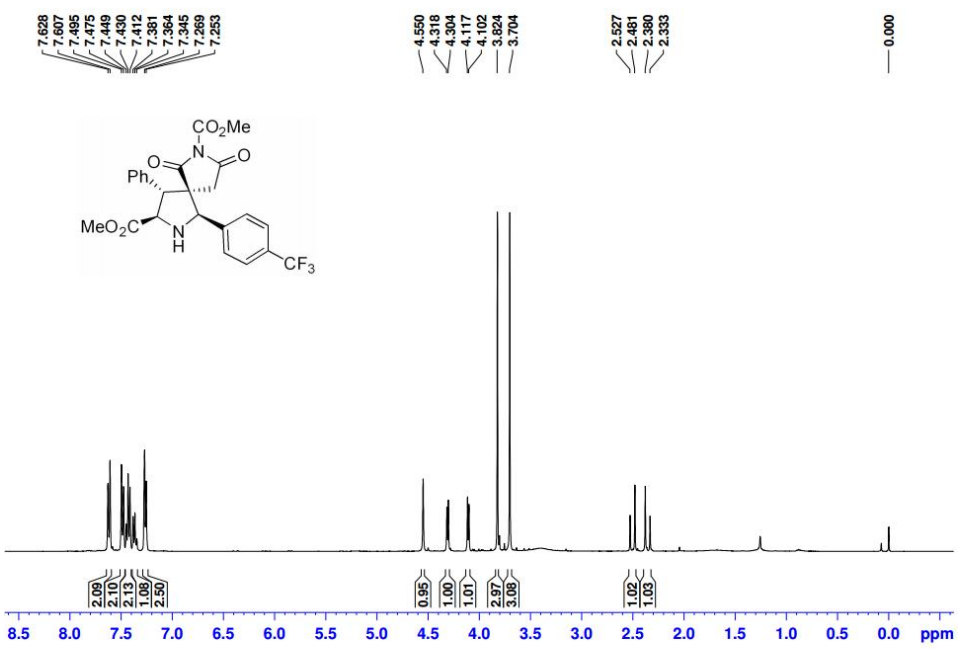
^{1}H NMR spectrum of compound **3gb** ($CDCl_3$)



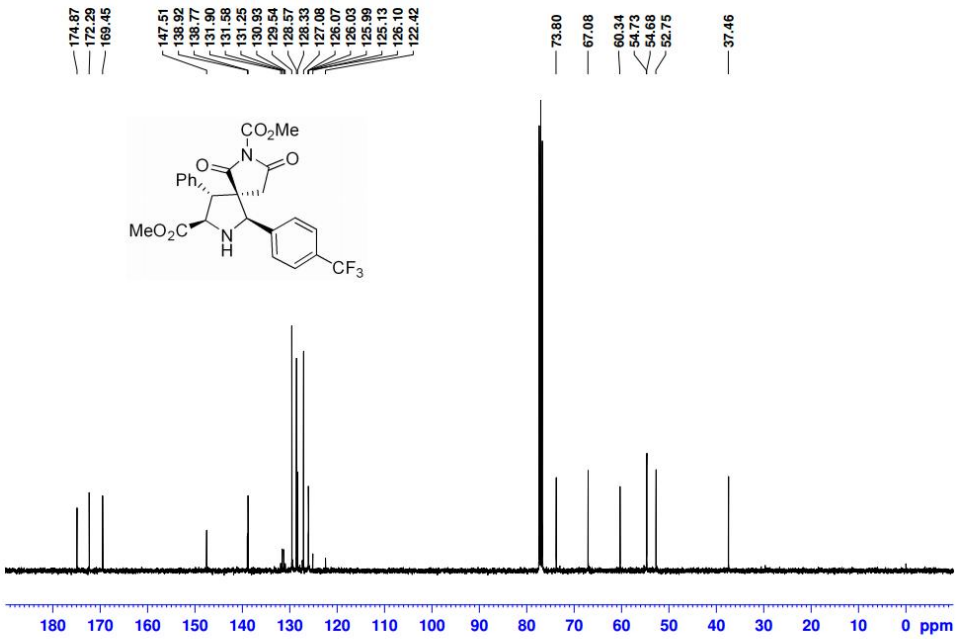
^{13}C NMR spectrum of compound **3gb** ($CDCl_3$)



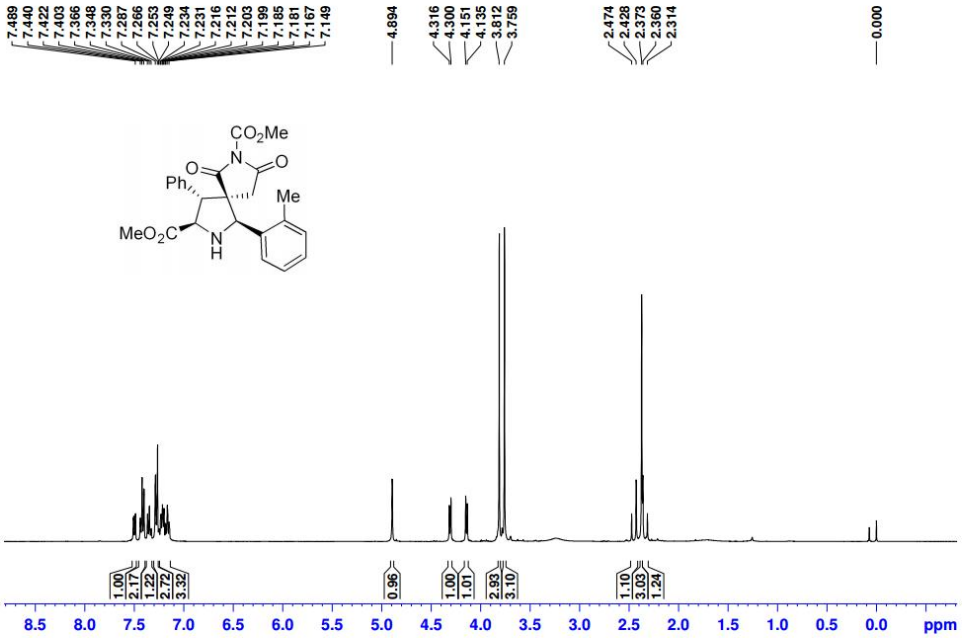
^{1}H NMR spectrum of compound **3hb** ($CDCl_3$)



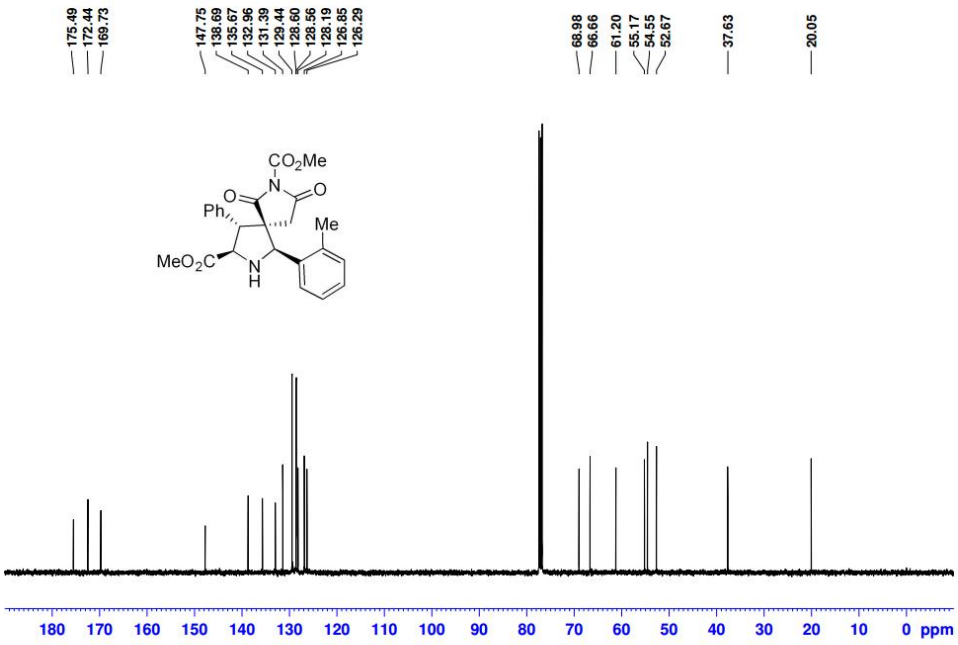
^{13}C NMR spectrum of compound **3hb** ($CDCl_3$)



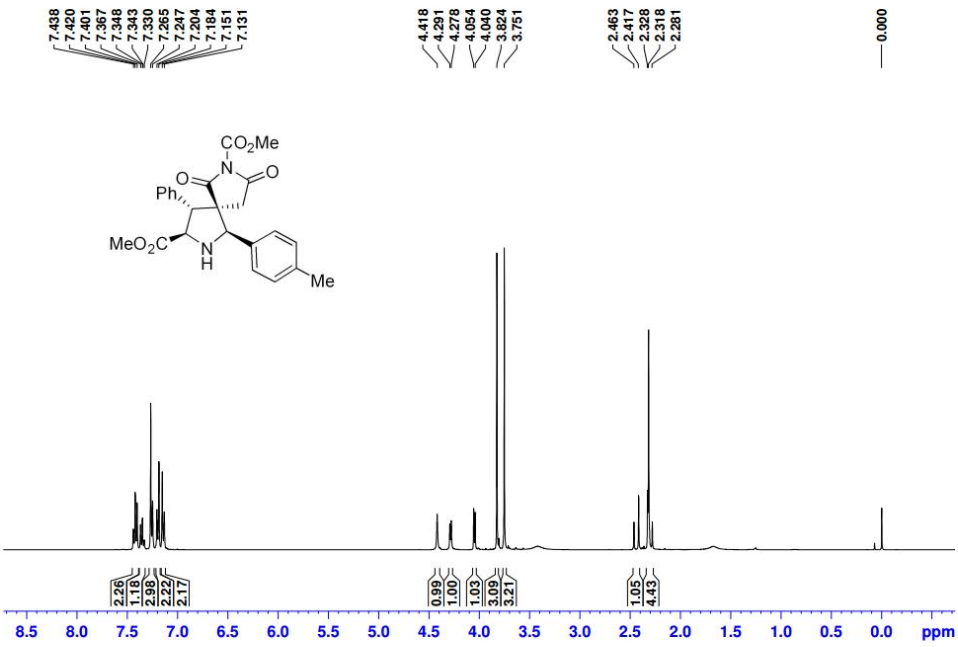
^{1}H NMR spectrum of compound **3ib** ($CDCl_3$)



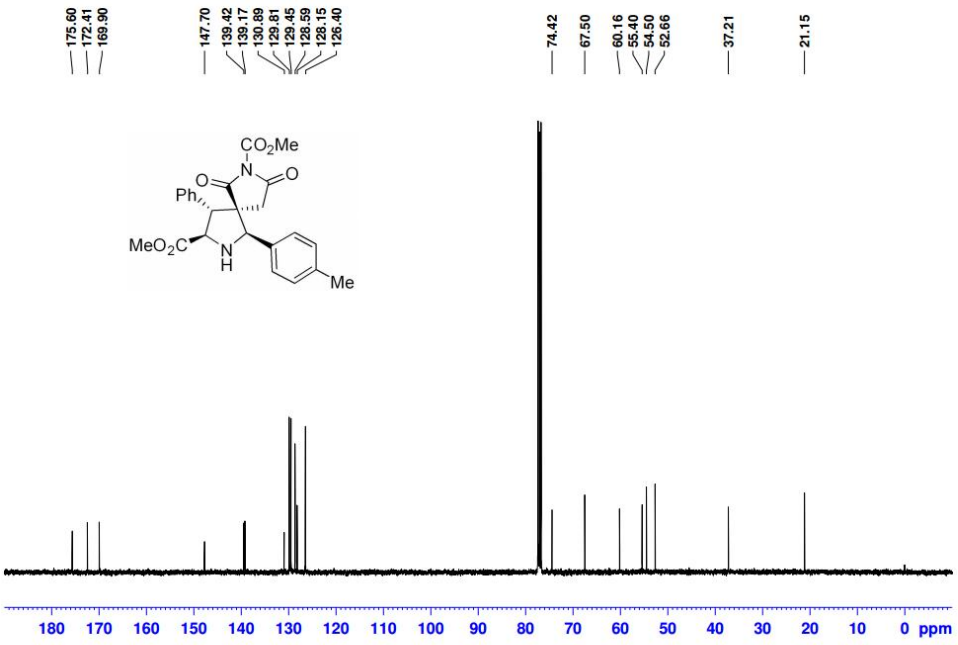
^{13}C NMR spectrum of compound **3ib** ($CDCl_3$)



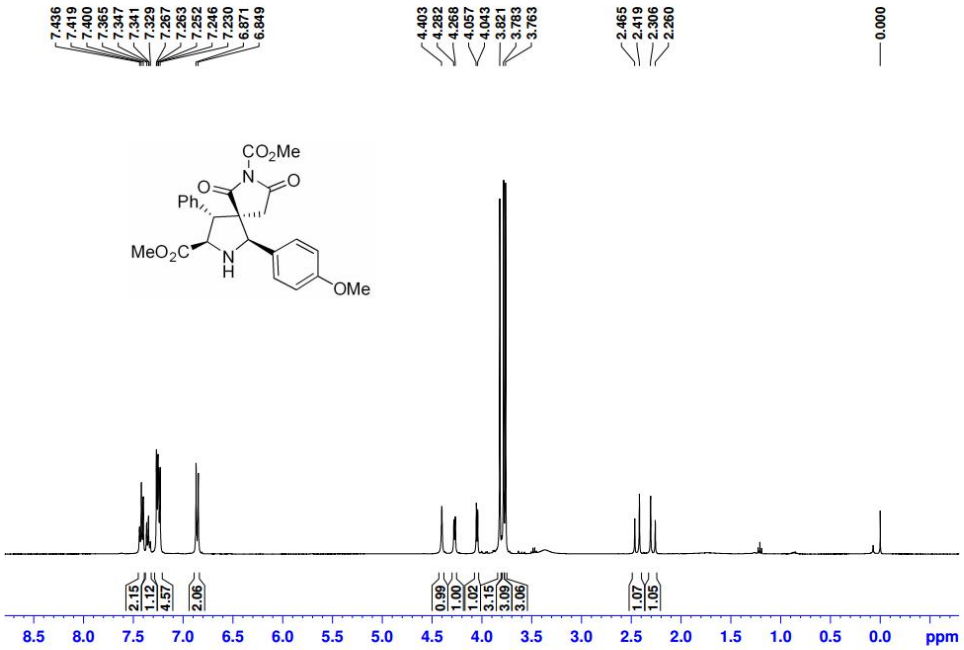
^{1}H NMR spectrum of compound **3jb** ($CDCl_3$)



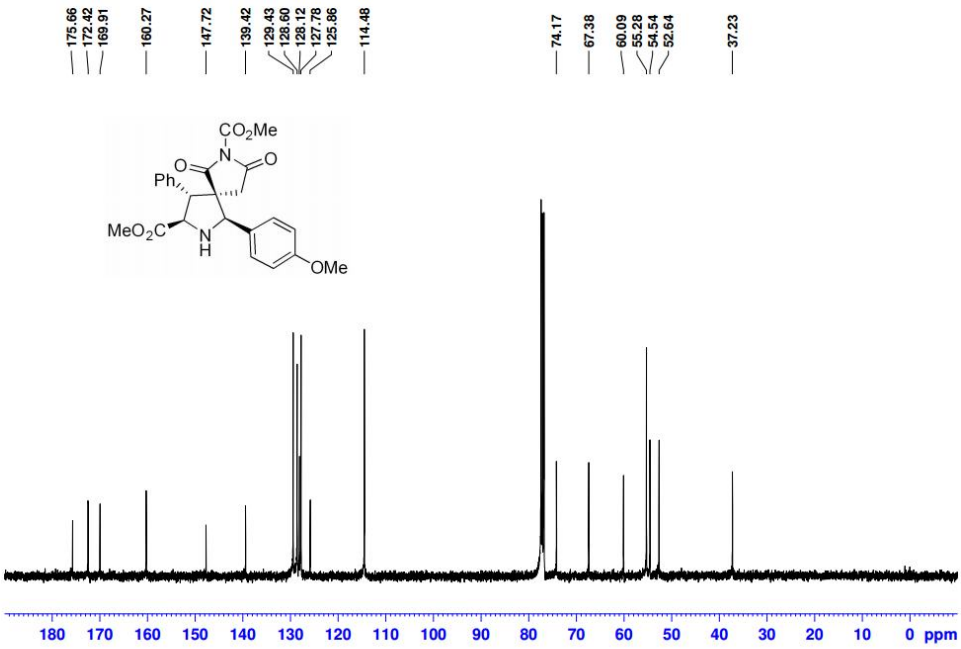
^{13}C NMR spectrum of compound **3jb** ($CDCl_3$)



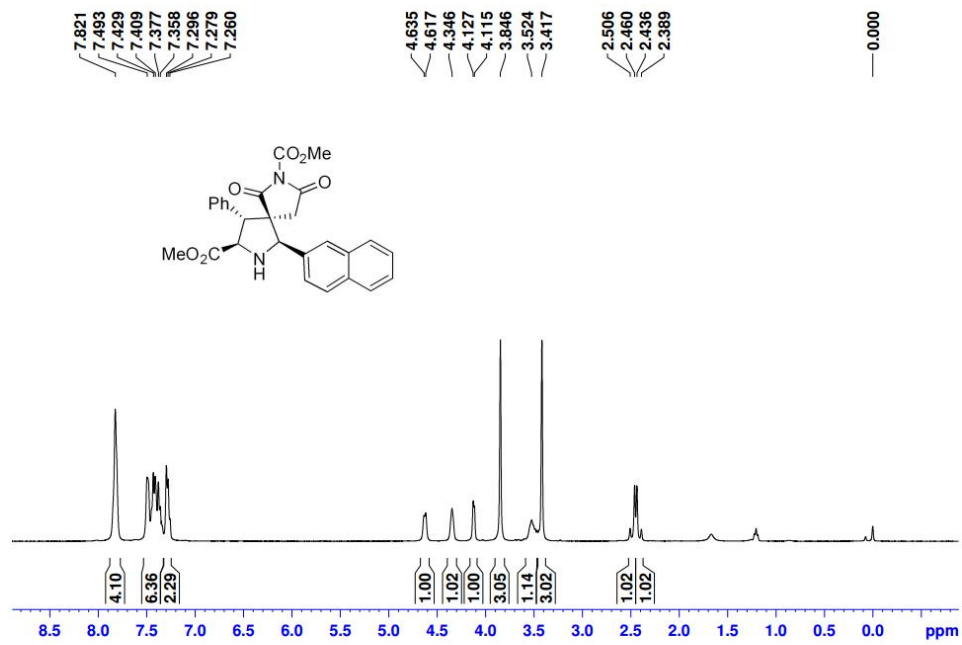
^{1}H NMR spectrum of compound **3kb** ($CDCl_3$)



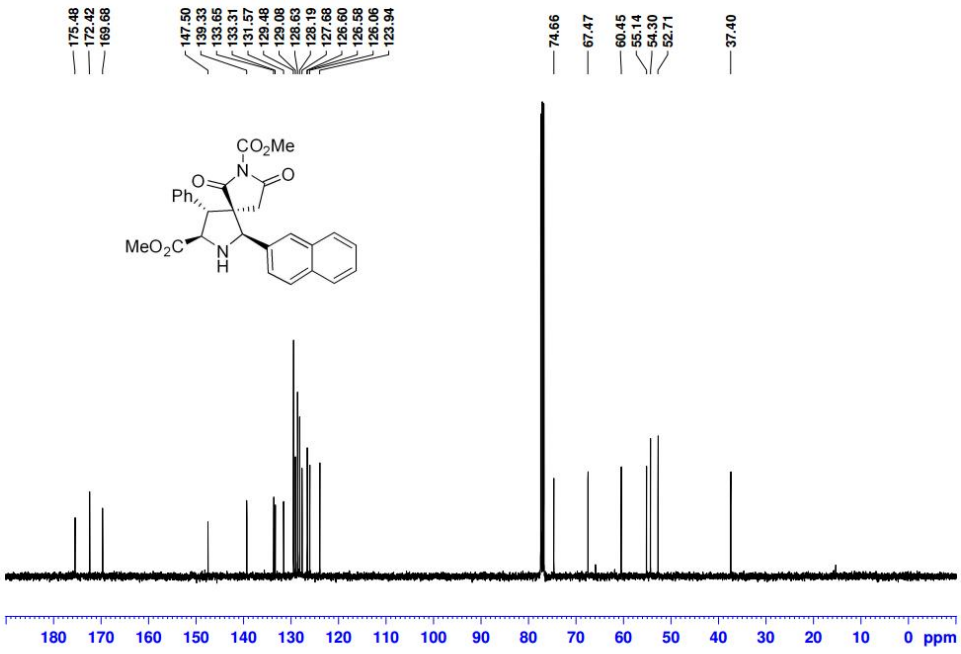
^{13}C NMR spectrum of compound **3kb** ($CDCl_3$)



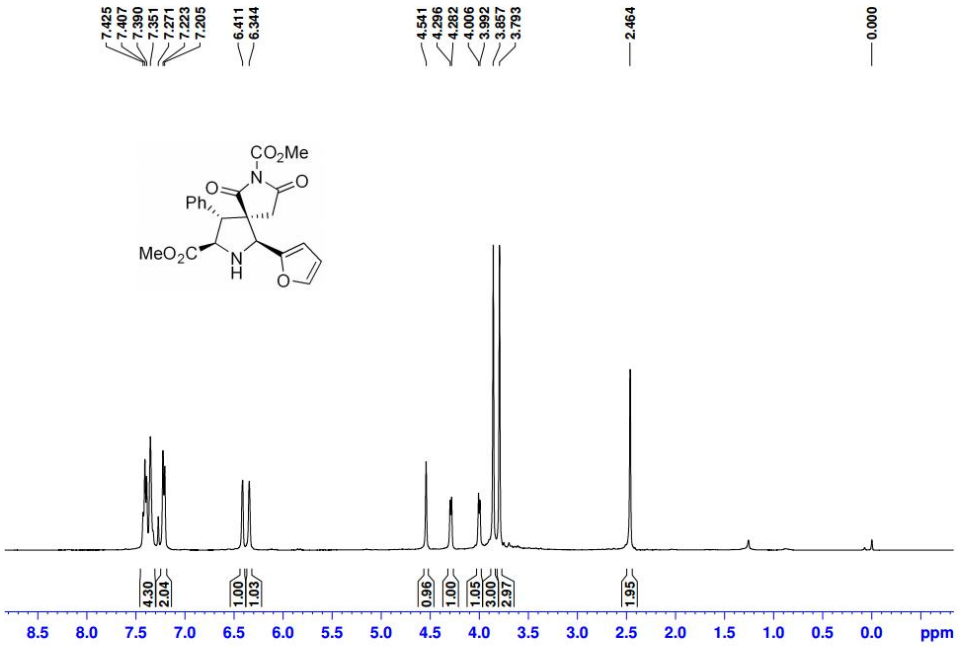
^{1}H NMR spectrum of compound **3lb** ($CDCl_3$)



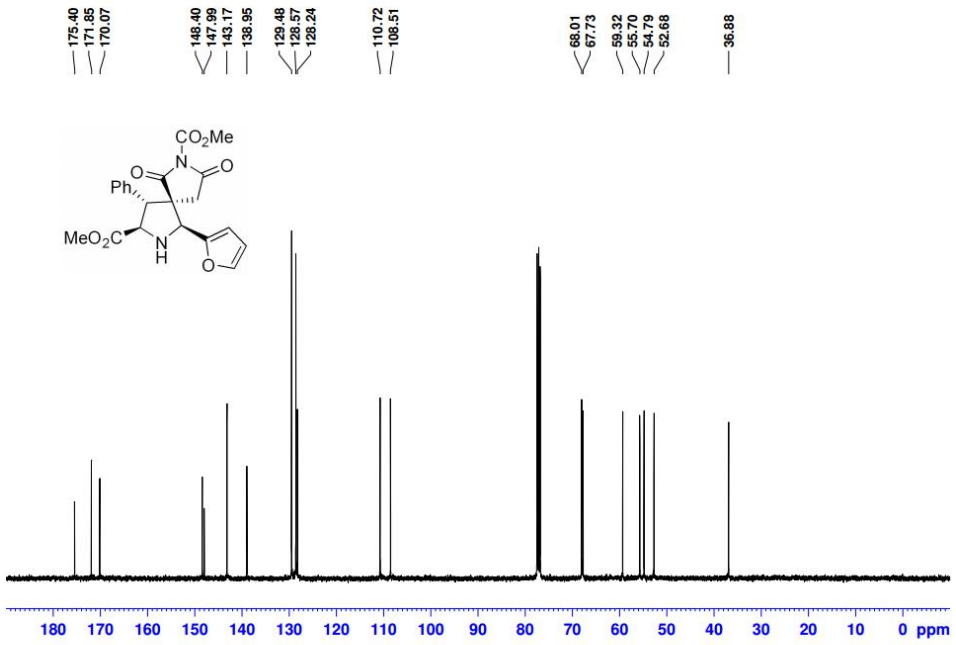
^{13}C NMR spectrum of compound **3lb** ($CDCl_3$)



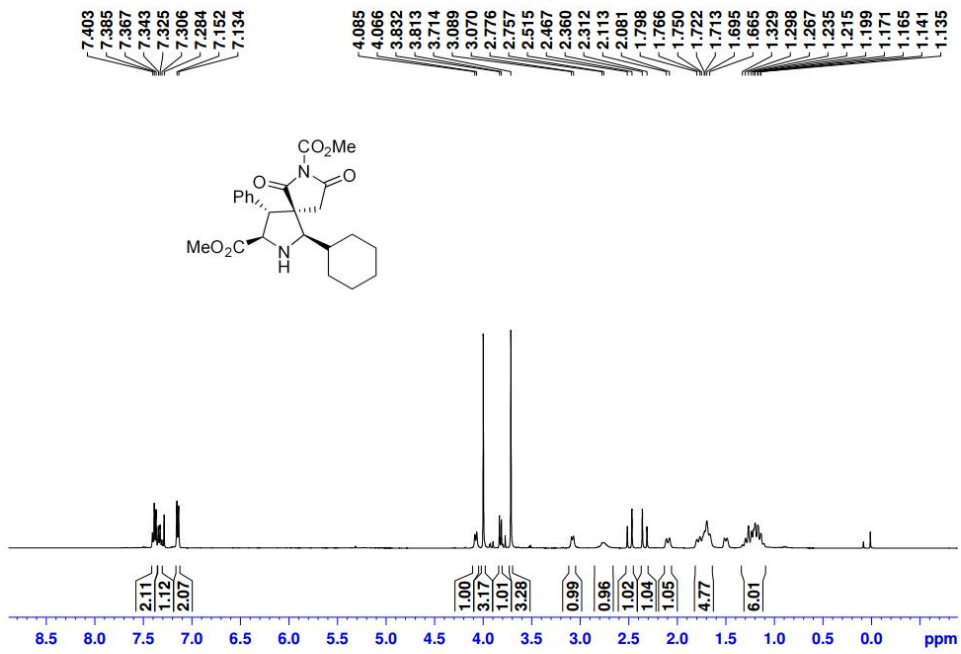
^{1}H NMR spectrum of compound **3mb** ($CDCl_3$)



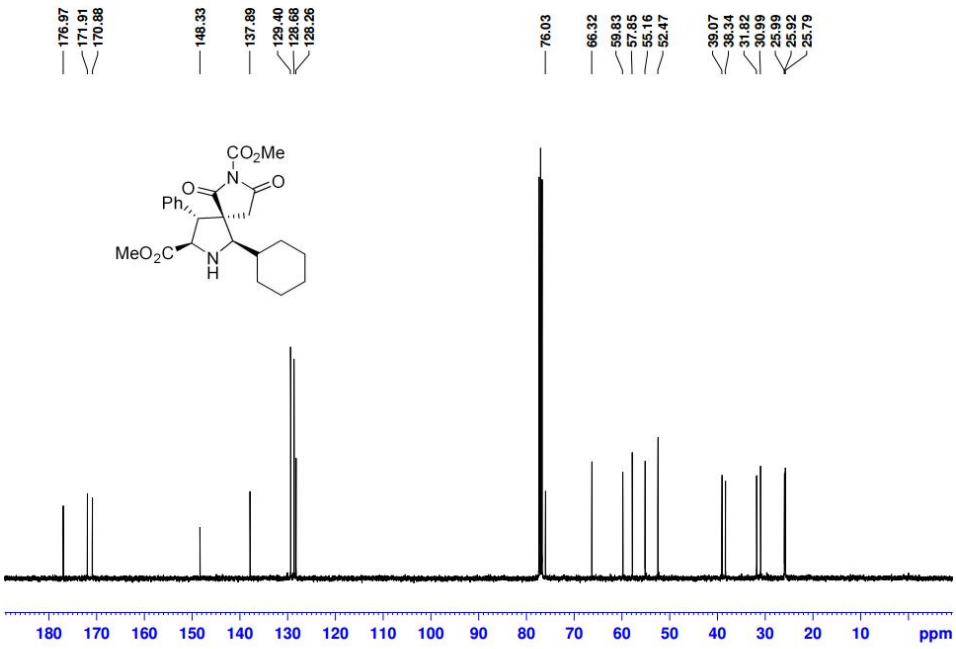
^{13}C NMR spectrum of compound **3mb** ($CDCl_3$)



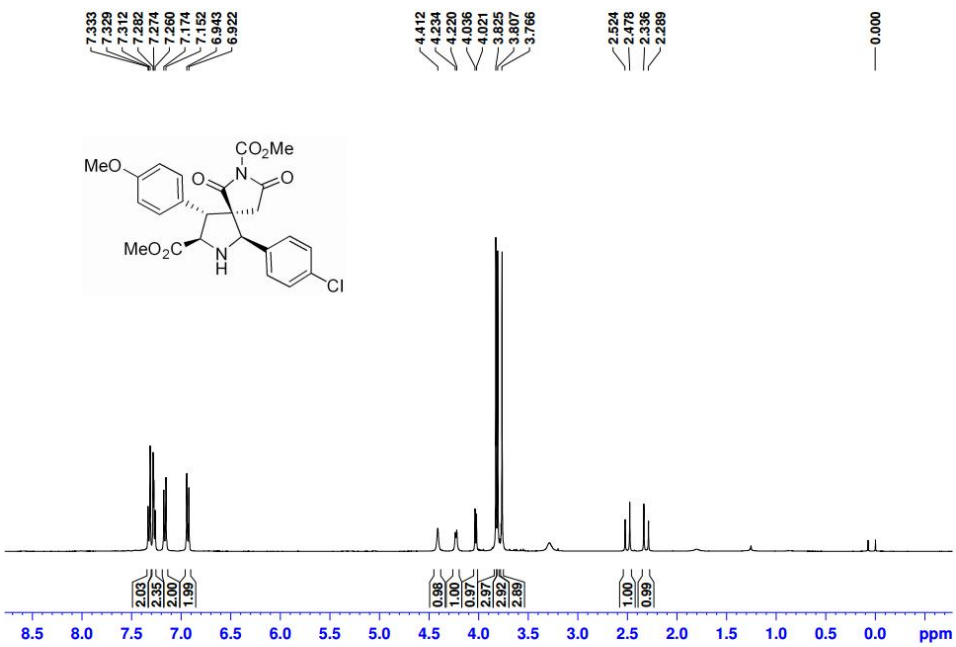
^{1}H NMR spectrum of compound **3nb** ($CDCl_3$)



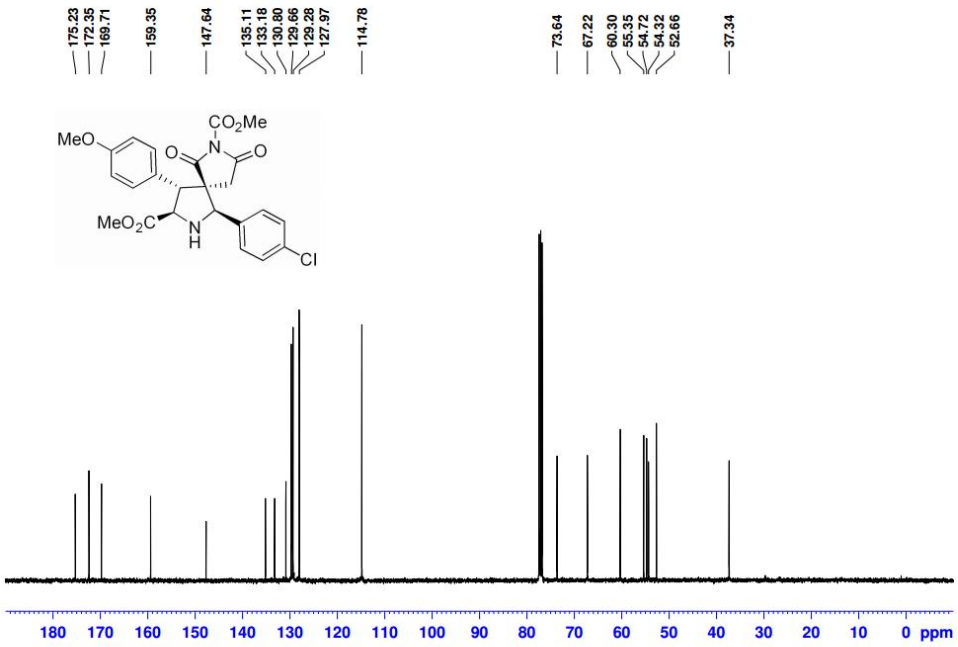
^{13}C NMR spectrum of compound **3nb** ($CDCl_3$)



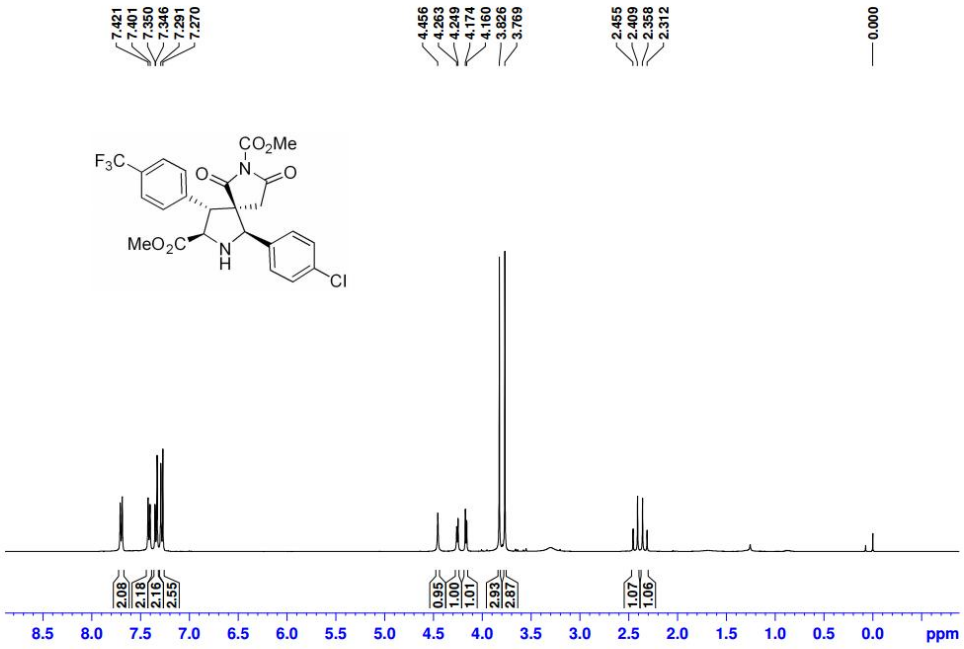
^{1}H NMR spectrum of compound **3ad** ($CDCl_3$)



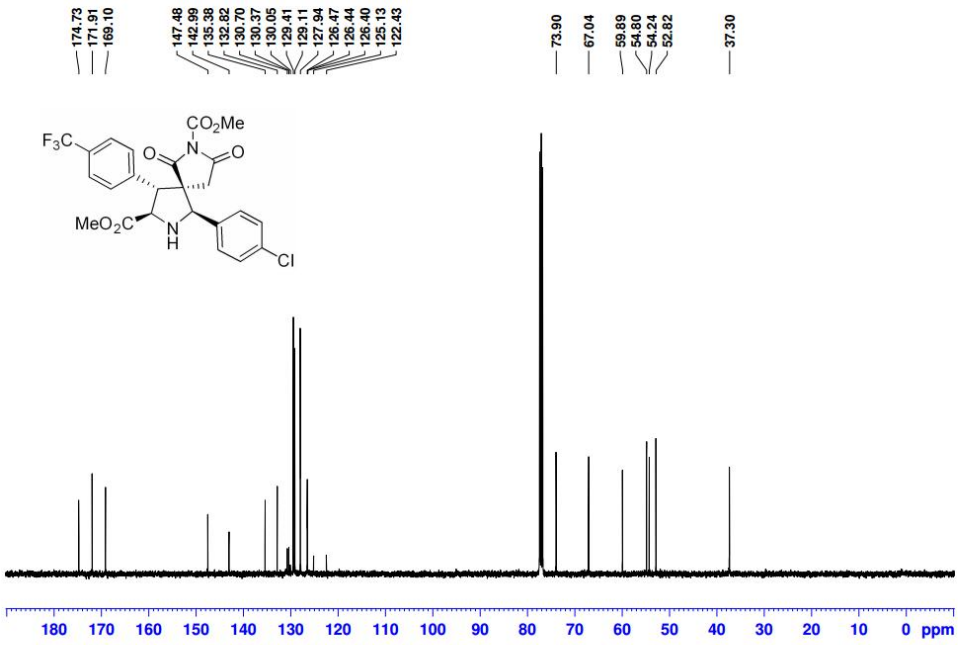
^{13}C NMR spectrum of compound **3ad** ($CDCl_3$)



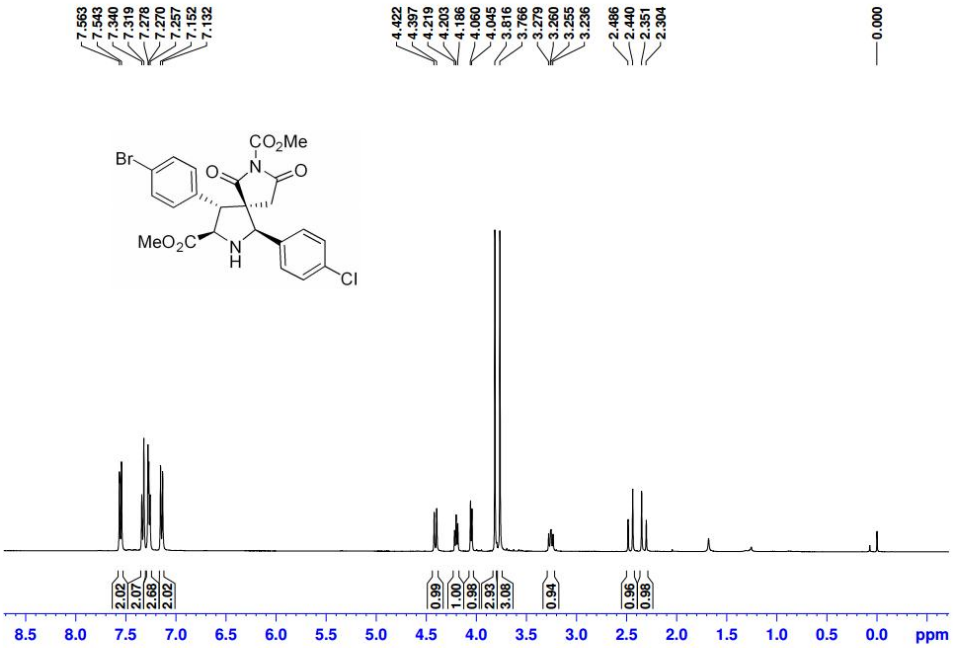
^{1}H NMR spectrum of compound **3ae** ($CDCl_3$)



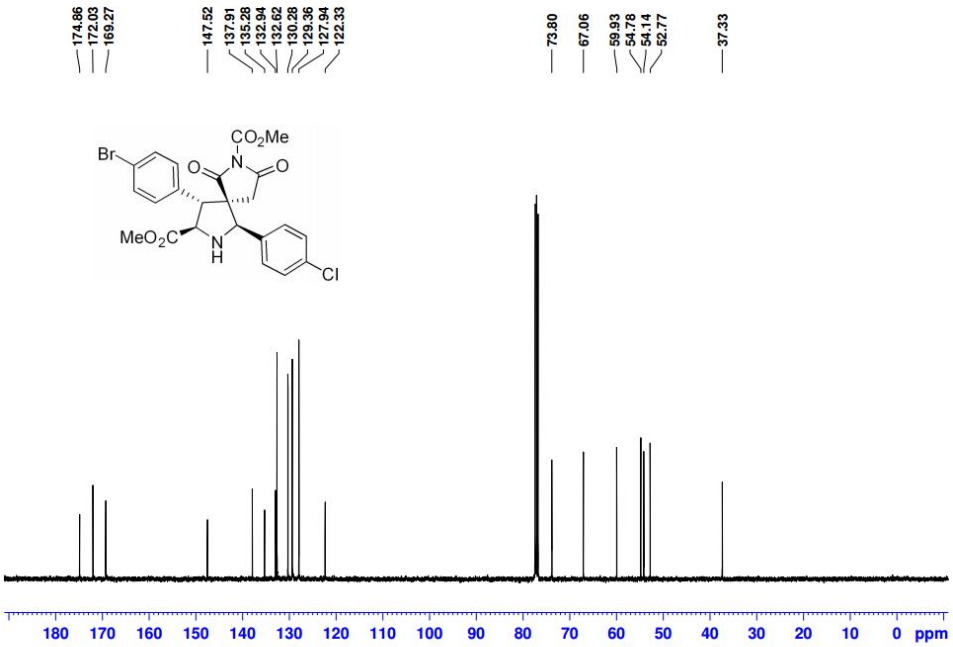
^{13}C NMR spectrum of compound **3ae** ($CDCl_3$)



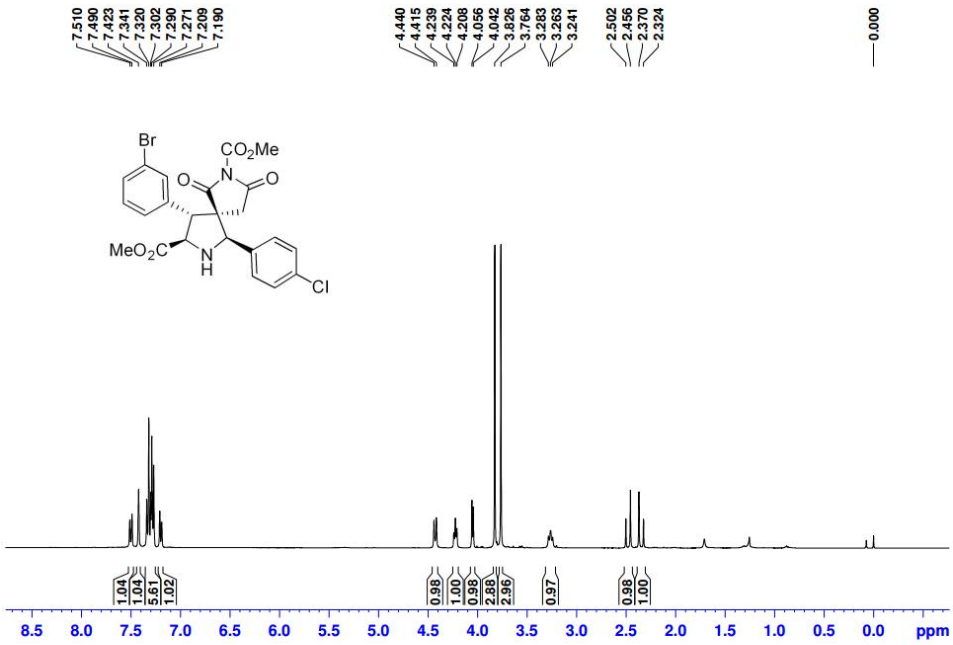
^{1}H NMR spectrum of compound **3af** ($CDCl_3$)



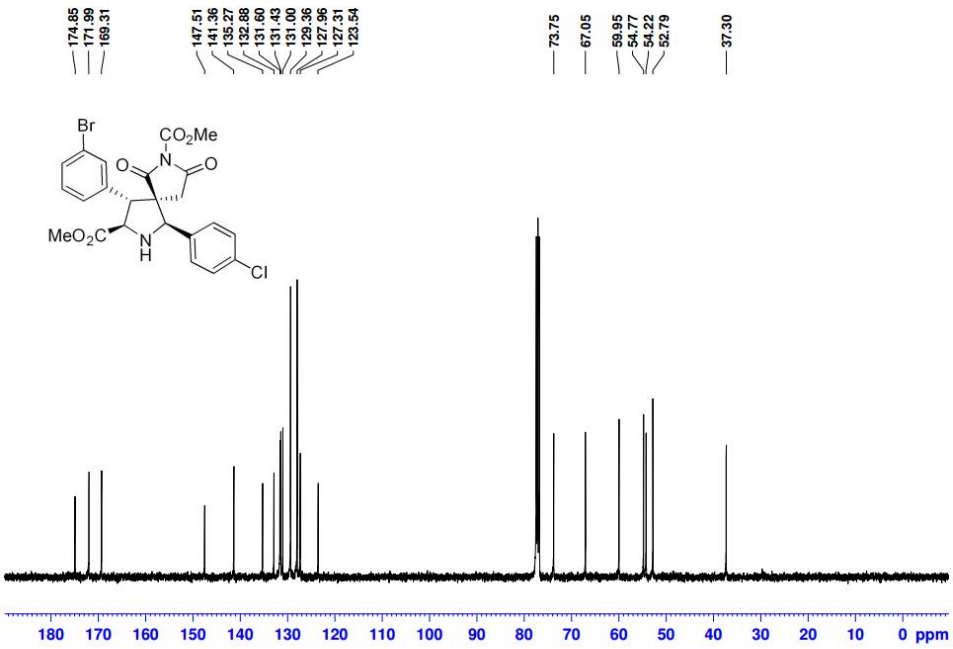
^{13}C NMR spectrum of compound **3af** ($CDCl_3$)



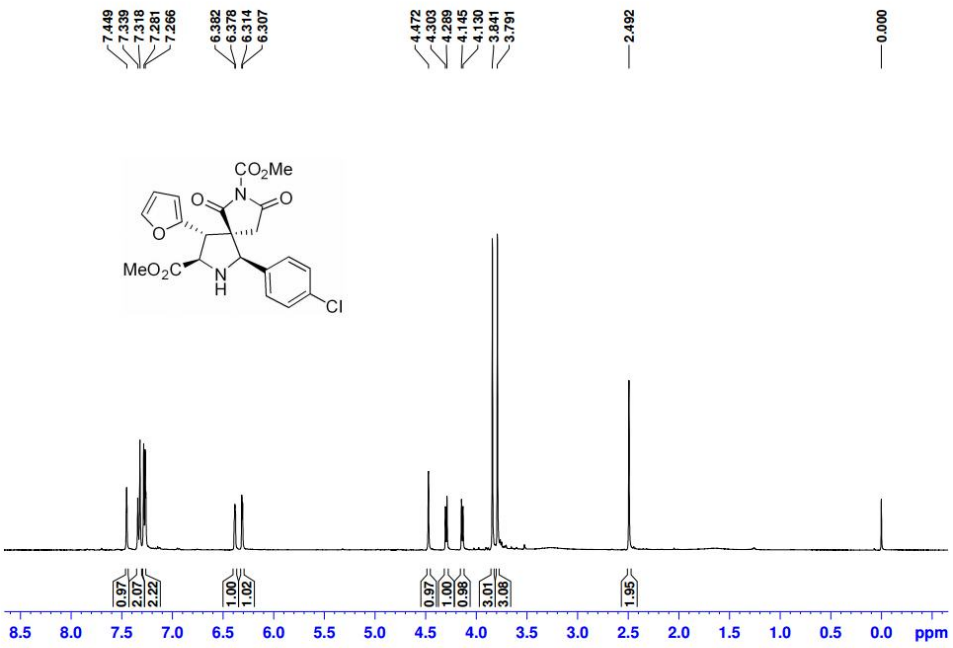
^{1}H NMR spectrum of compound **3ag** ($CDCl_3$)



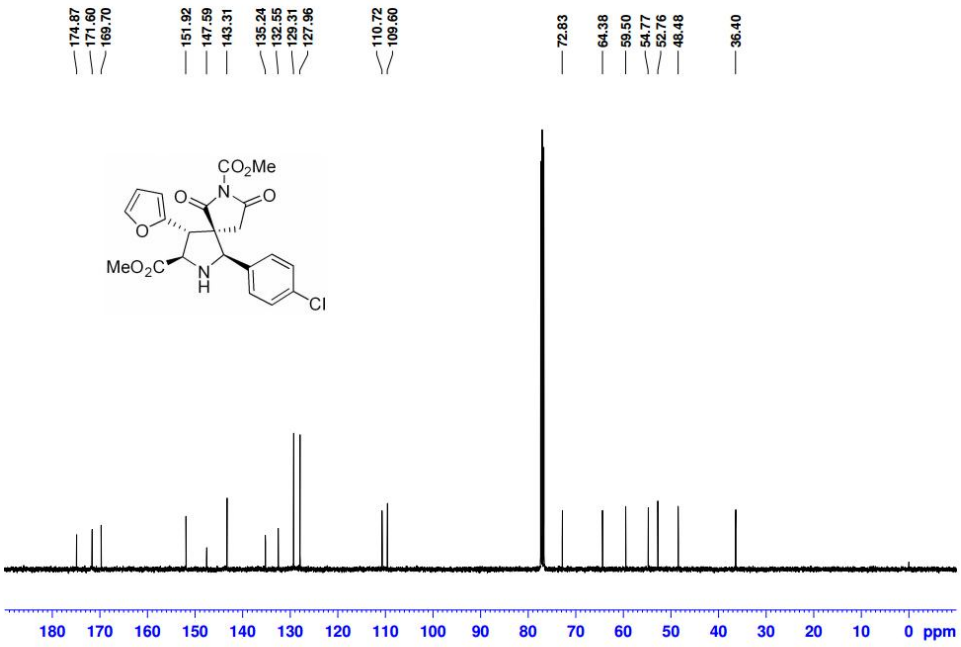
^{13}C NMR spectrum of compound **3ag** ($CDCl_3$)



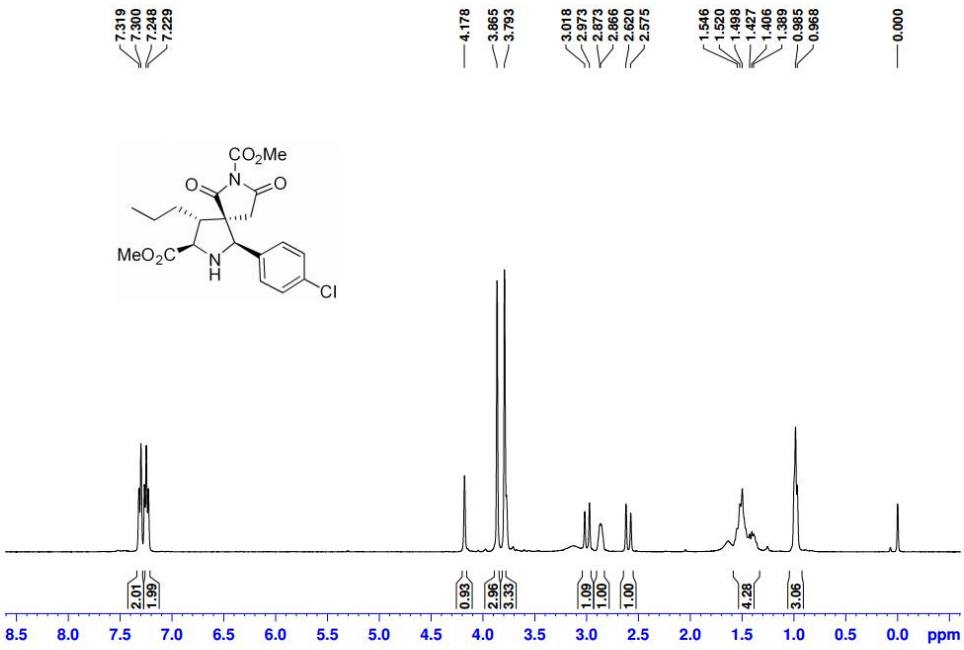
^{1}H NMR spectrum of compound **3ah** ($CDCl_3$)



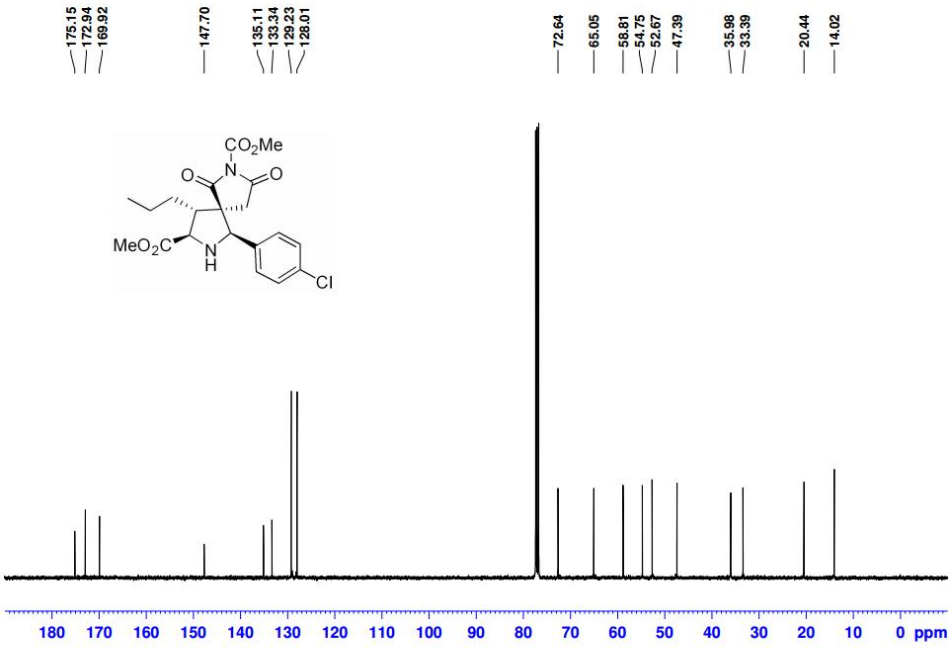
^{13}C NMR spectrum of compound **3ah** ($CDCl_3$)



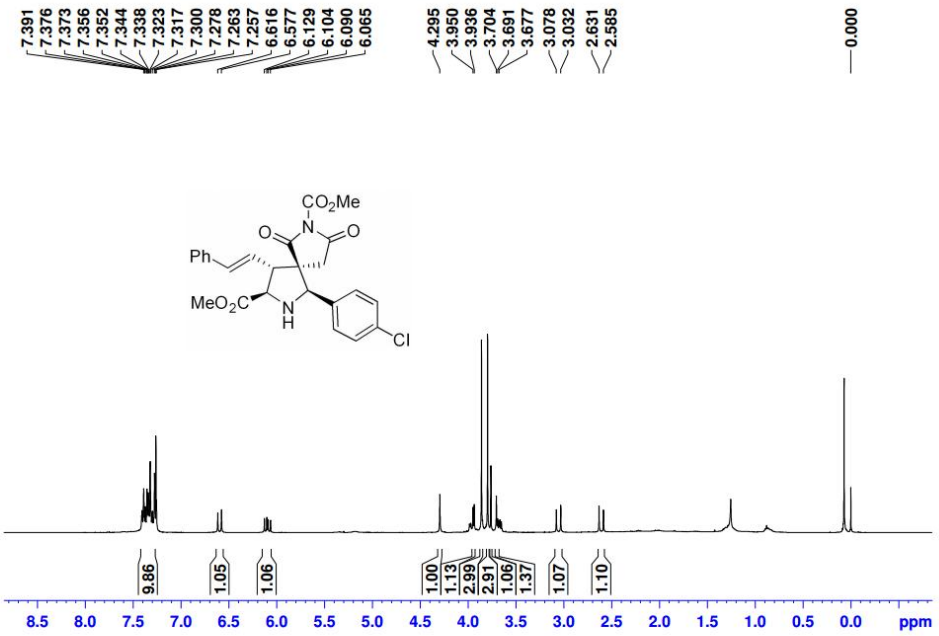
^{1}H NMR spectrum of compound **3ai** ($CDCl_3$)



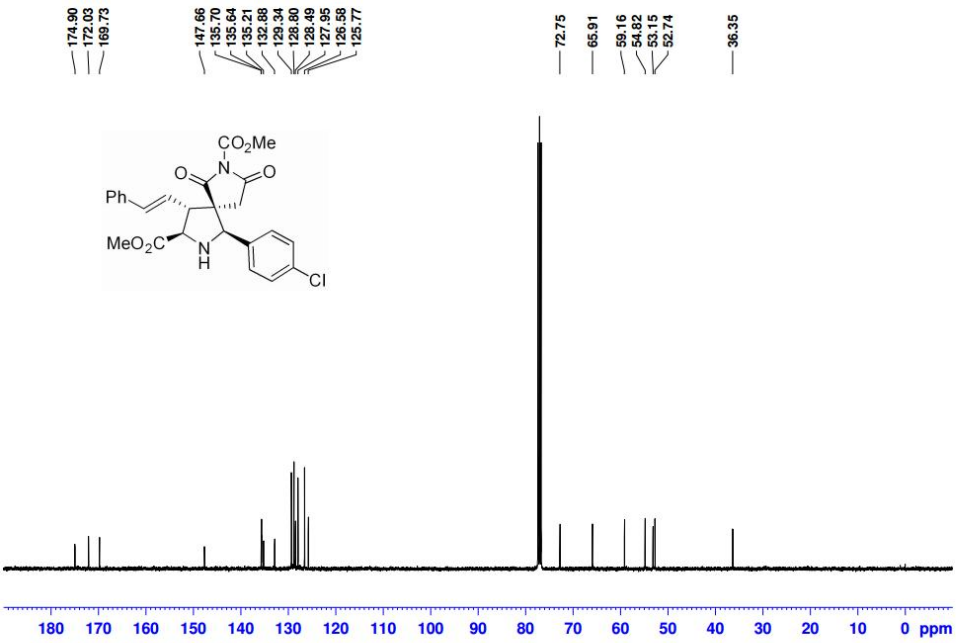
^{13}C NMR spectrum of compound **3ai** ($CDCl_3$)



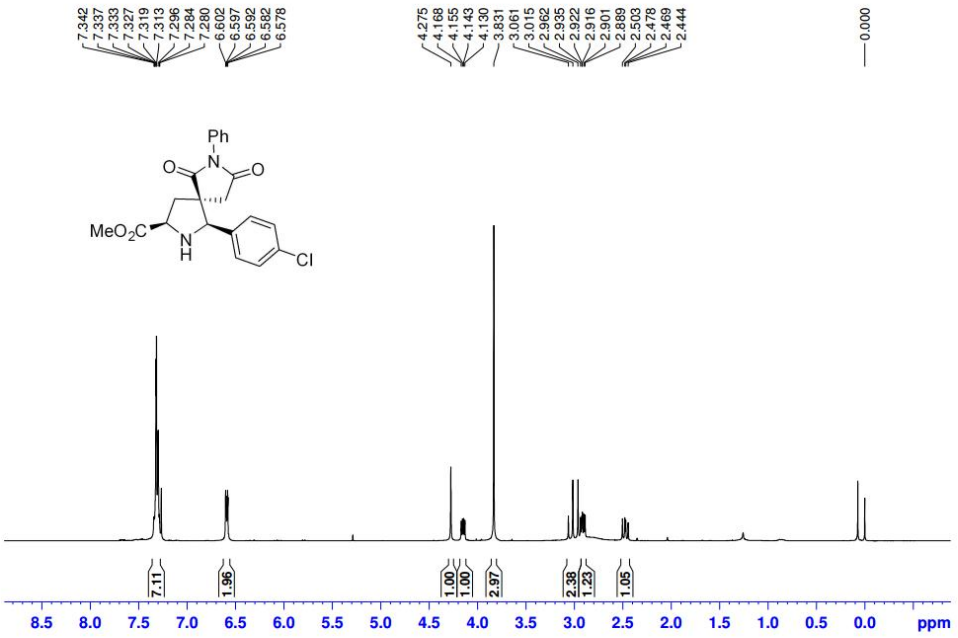
^{1}H NMR spectrum of compound **3aj** ($CDCl_3$)



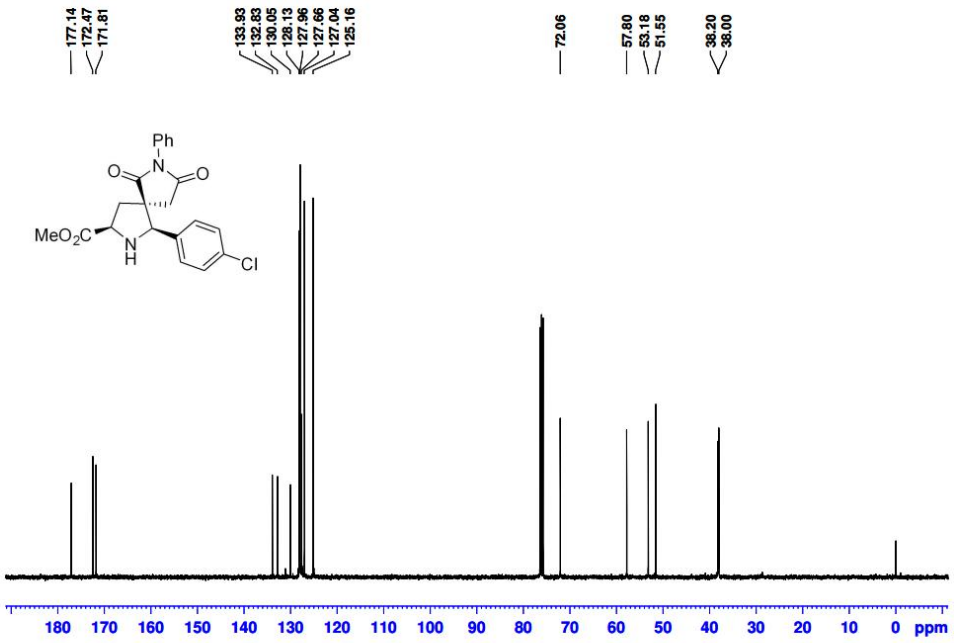
^{13}C NMR spectrum of compound **3aj** ($CDCl_3$)



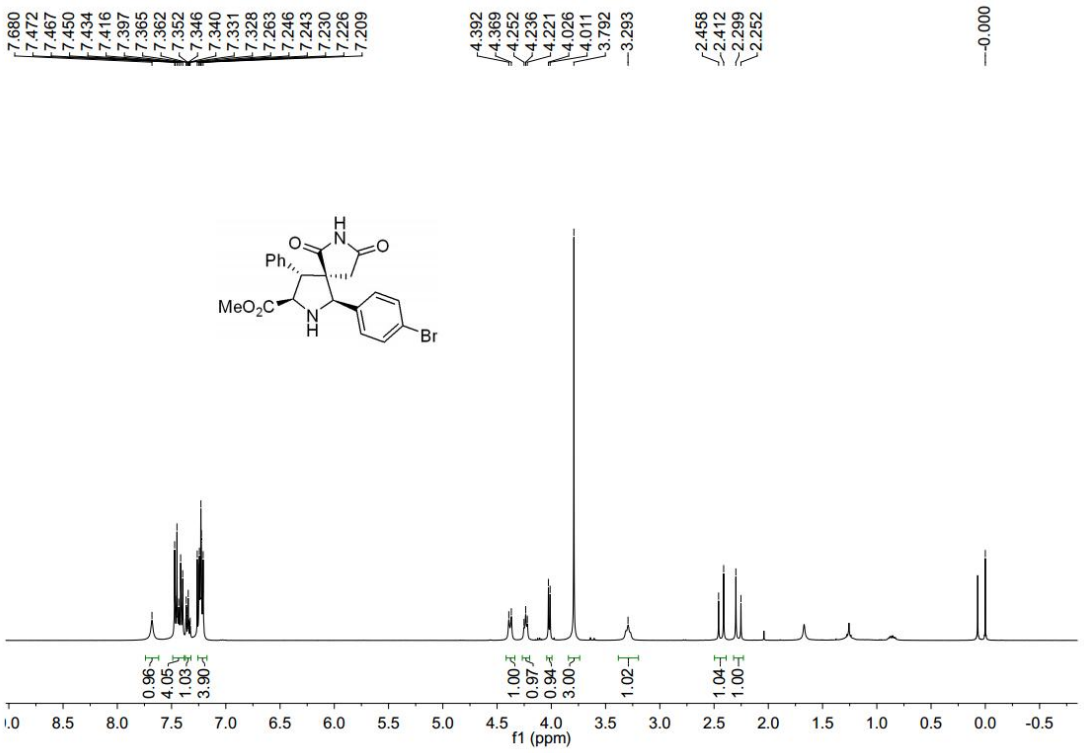
^{1}H NMR spectrum of compound **3ak** ($CDCl_3$)



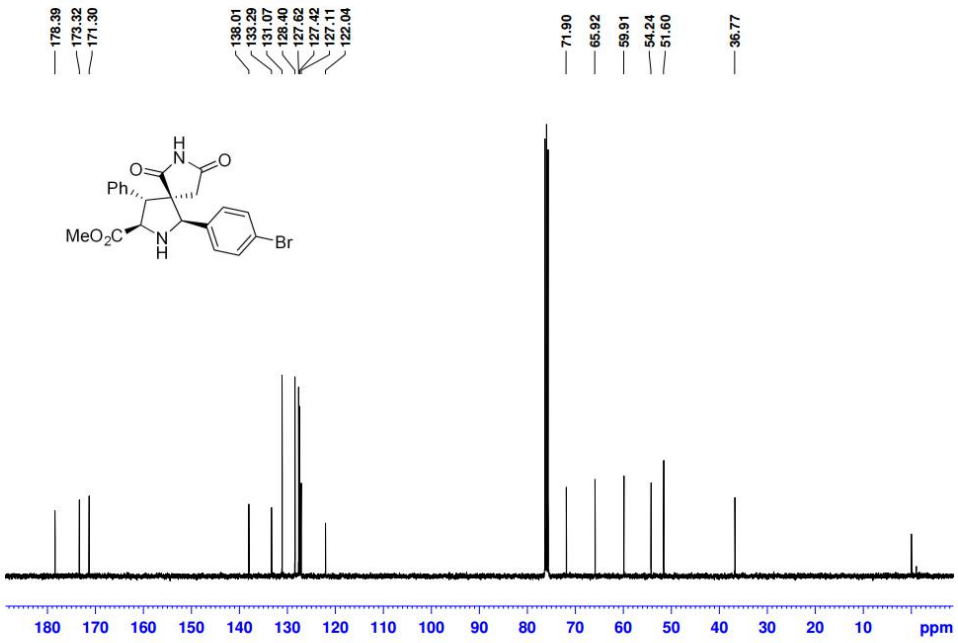
^{13}C NMR spectrum of compound **3ak** ($CDCl_3$)



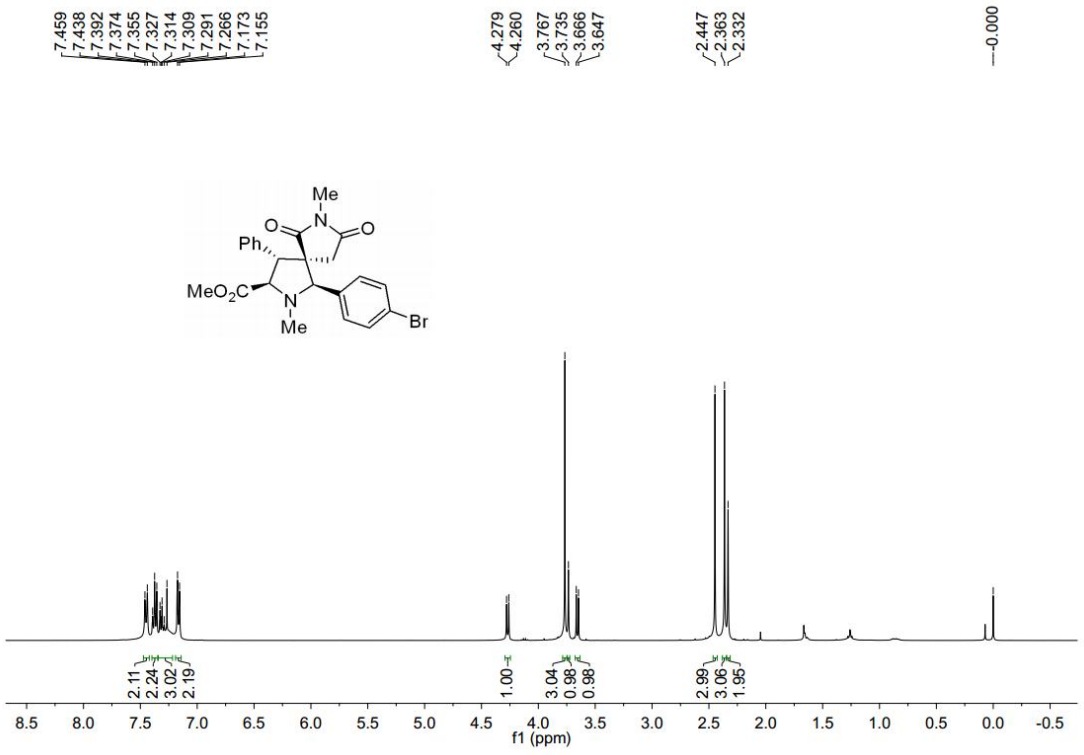
^{1}H NMR spectrum of compound **6** ($CDCl_3$)



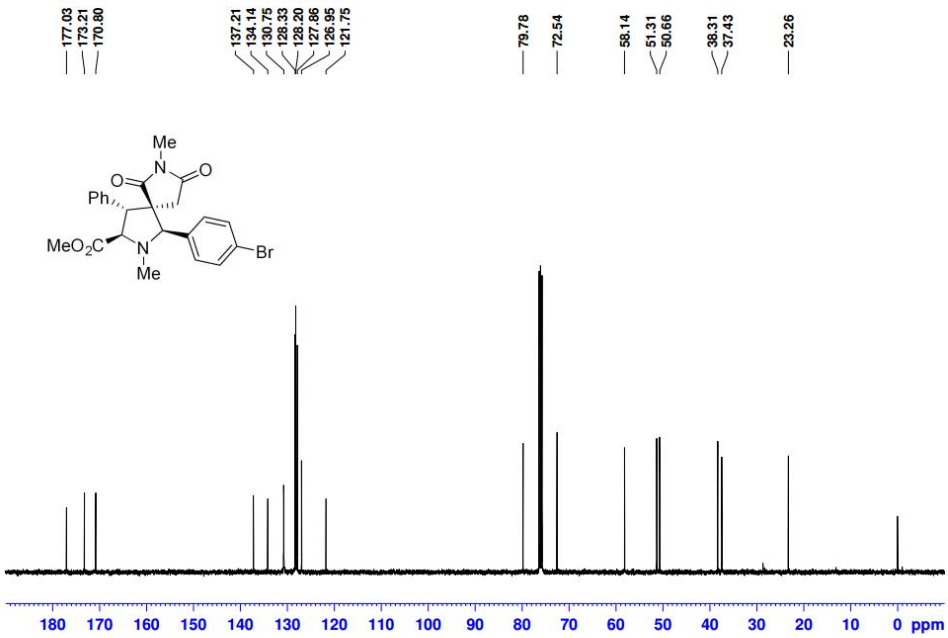
^{13}C NMR spectrum of compound **6** ($CDCl_3$)



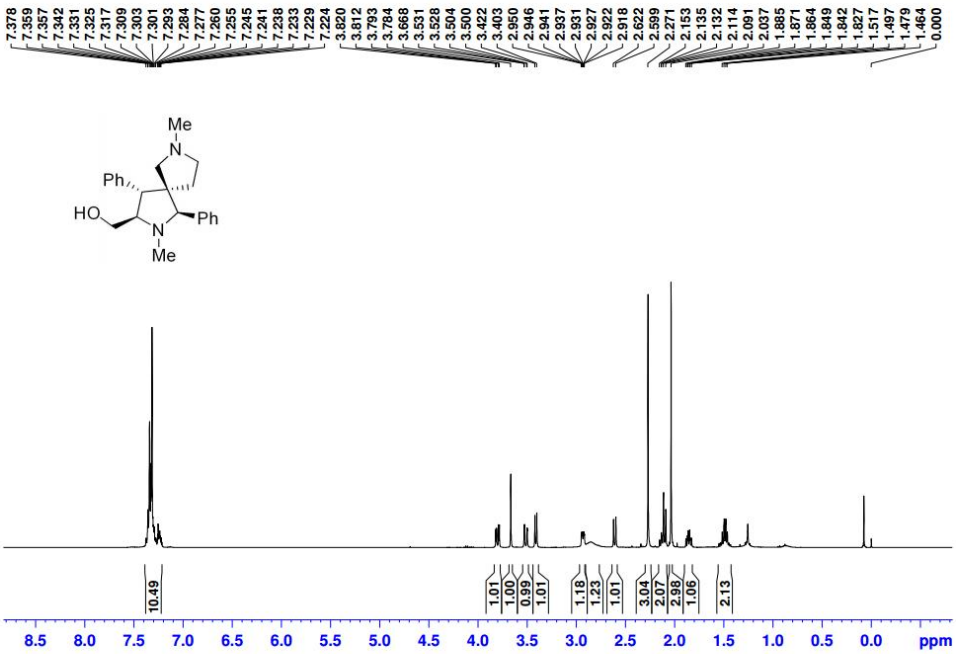
^{1}H NMR spectrum of compound **7** ($CDCl_3$)



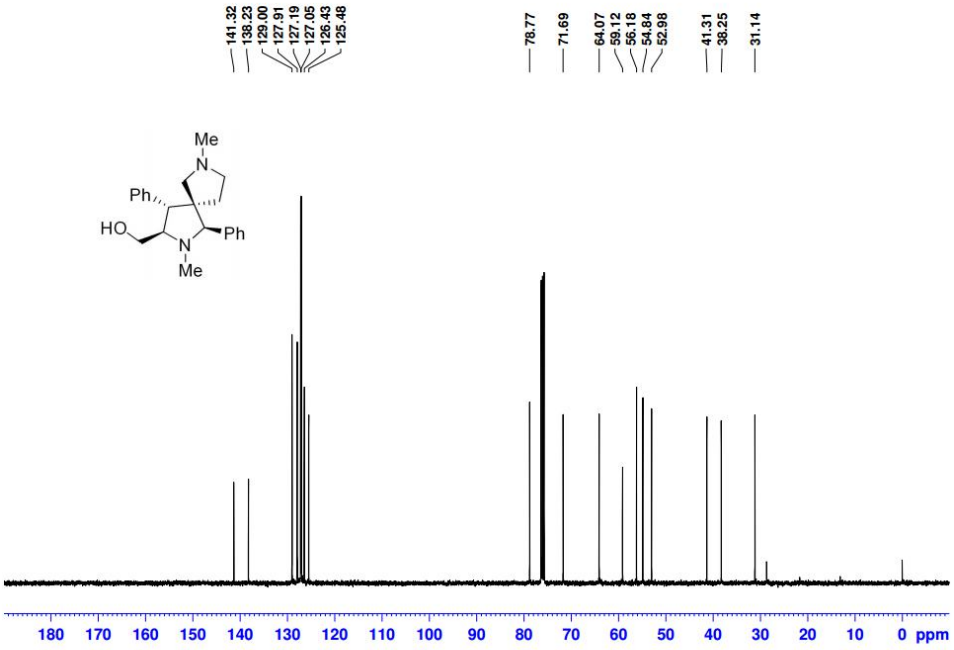
^{13}C NMR spectrum of compound **7** ($CDCl_3$)



^{1}H NMR spectrum of compound **8** ($CDCl_3$)



^{13}C NMR spectrum of compound **8** ($CDCl_3$)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129.00
127.91
127.19
127.05
126.43
125.48
78.77
71.69
64.07
59.12
56.18
54.84
52.98
41.31
38.25
31.14
Me
N
Ph
HO
Ph
N
Me
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm