Supporting Information

Organocatalyzed Asymmetric Formal [3+2] Cycloaddition of Isocyanoacetates with *N*-Itaconimides: A Facile Access to Optically Active Spiropyrroline Succinimide Derivatives

Mei-Xin Zhao,*,† Qiang Liu,† Kun-Ming Yu,† Xiao-Li Zhao,‡ and Min Shi†,§

† Key Laboratory for Advanced Materials and Institute of Fine Chemicals, School of Chemistry & Molecular Engineering, East China University of Science and Technology, 130 Mei Long Road, Shanghai, 200237, P. R. China
E-mail: mxzhao@ecust.edu.cn

‡ Department of Chemistry, East China Normal University, 3663 N. Zhongshan Road, Shanghai, 200062, P. R. China

§ State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, P. R. China

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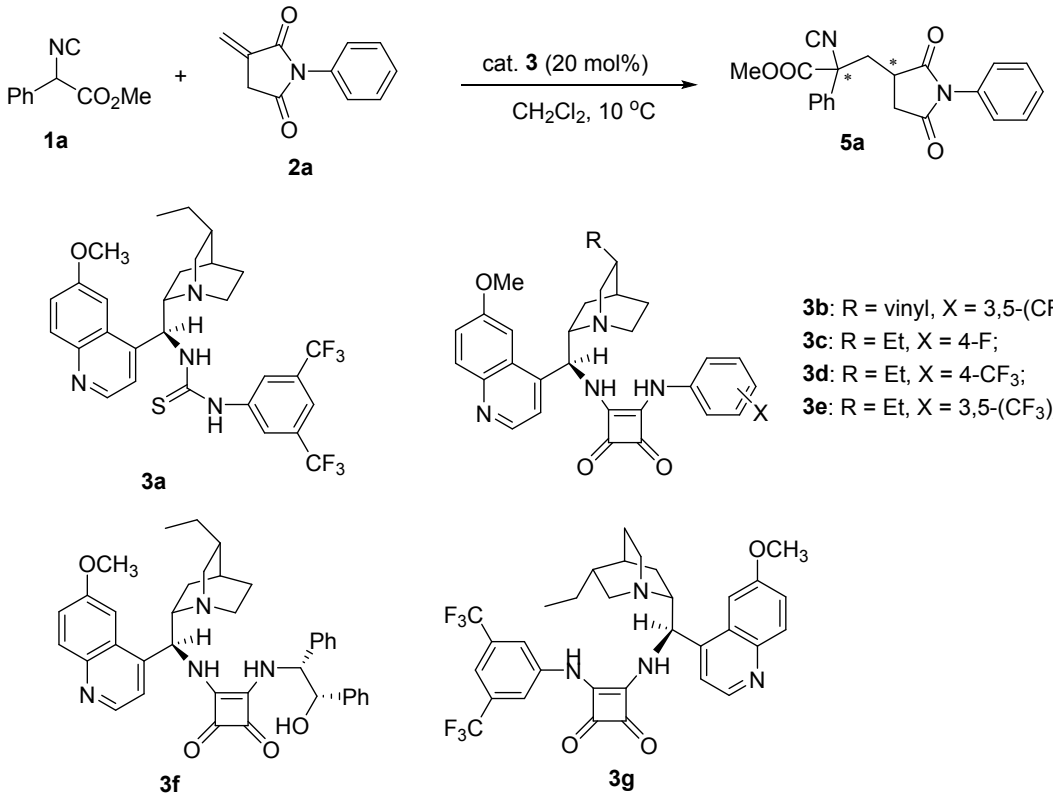
1. Optimization Reaction Conditions of Michael Addition of α-Phenyl Isocyanoacetate 1a to *N*-Phenyl Itaconimide 2a

Table S1. Catalysts screening[a]



Entry	Cat.	*t* (h)	Yield (%)[b]	*dr* [c]	*ee* (%) [d]
1	**3a**	96	62	4.8:1	91
2	**3b**	96	59	2:1	53
3	**3c**	94	52	9:1	97
4	**3d**	90	61	10:1	97
5	**3e**	90	63	10:1	99
6	**3f**	120	45	6.1:1	95
7	**3g**	90	58	6.5:1	-97

[a] All reactions were carried out with *N*-phenyl itaconimide **2a** (0.10 mmol), isocyanoacetate **1a** (0.20 mmol) and cat. **3** (20 mol%) in CH_2Cl_2 (1.0 mL) at 10 °C. [b] Isolated yields. [c] Determined by ^{1}H NMR analysis of purified product. [d] Determined by chiral HPLC analysis.

Table S2. Optimization of Reaction Conditions[a]

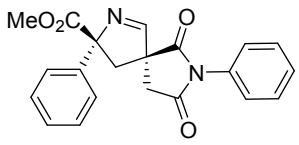
Entry	solvent	*T* (ºC)	*t* (h)	Yield (%)	*dr* (%)[b]	*ee* (%)[c]
1	$CHCl_3$	10	90	60	9:1	99
2	DCE	10	90	54	9:1	99
3	TCE	10	90	57	3.3:1	99
4	THF	10	99	51	5:1	85
5	toluene	10	120	41	9:1	97
6	MeCN	10	96	66	1.7:1	31
7	CH_2Cl_2	r.t.	90	62	6:1	99
8	CH_2Cl_2	0	97	54	11:1	99
9[d]	CH_2Cl_2	10	90	59	10:1	99
10[e]	CH_2Cl_2	10	90	61	10:1	99
11[f]	CH_2Cl_2	10	94	58	10:1	99
12[g]	CH_2Cl_2	10	94	62	10:1	99
13[h]	CH_2Cl_2	10	86	55	9:1	99
14[i]	CH_2Cl_2	10	90	60	9.8:1	99
15[j]	CH_2Cl_2	10	98	45	11.5:1	99

[a] Unless otherwise stated, all reactions were carried out with itaconimide **2a** (0.10 mmol), isocyanoacetate **1a** (0.20 mmol) and cat. **3e** (20 mol%) in CH_2Cl_2 (1.0 mL) at 10 °C. [b] Determined by ^1H NMR analysis of purified product. [c] Determined by chiral HPLC analysis. [d] 0.5 ml of CH_2Cl_2 was used. [e] 2.0 ml of CH_2Cl_2 was used. [f] 30 mg of 3Å molecular sieves was added. [g] 30 mg of 4Å molecular sieves was added. [h] **2a**: **1a** = 1:3. [i] **2a**: **1a** = 1:1.2. [j] 10 mol% of catalyst.

2. General Procedure for the Asymmetric Formal [3+2] Cycloaddition Reaction of Isocyanoacetates 1 with *N*-Itaconimides 2 Catalyzed by 3e.

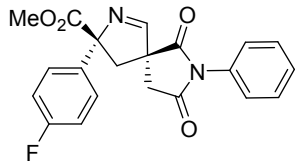
To a solution of isocyanoacetates **1** (0.20 mmol), *N*-itaconimides **2** (0.40 mmol) in 2.0 mL of $CHCl_3$ was added catalyst **3e** (20 mol%). The resulting mixture was stirred at 50 ºC for 5-8 days until the reaction completed (monitored by TLC). After concentration, the residue was directly subjected to flash column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1~3:1 as eluent) to furnish the corresponding products **4**.

*(2R,4R)-Methyl 6,8-dioxo-3,7-diphenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4a**)*.



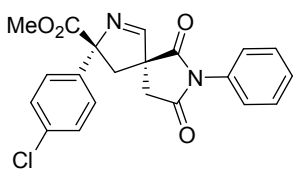
White solid; yield: 58.2 mg (80%); mp 217.3-218.5 ºC; $[\alpha]_D^{20}$ -55.8 (*c* 1.00, CH_2Cl_2) (99% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 42.30 min; t_{minor} = 54.86 min); 9:1 *dr*; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.70 (s, 1H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.43-7.37 (m, 3H), 7.35-7.29 (m, 3H), 3.76 (s, 3H), 3.70 (d, *J* = 13.6 Hz, 1H), 2.98 (d, *J* = 18.8 Hz, 1H), 2.64 (d, *J* = 18.4 Hz, 1H), 2.41 (d, *J* = 13.6 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 176.3, 174.5, 172.4, 166.4, 142.2, 132.5, 128.9, 128.63, 128.59, 127.8, 127.3, 125.8, 86.2, 60.9, 52.6, 45.2, 38.0; IR (Film) ν 1714, 1499, 1448, 1387, 1265, 1191, 1127 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{19}N_2O_4$ 363.1339; Found 363.1340.

*(2R,4R)-Methyl 3-(4-fluorophenyl)-6,8-dioxo-7-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4b**)*.



White solid; yield 59.3 mg (78%); mp 219.5-220.6 ºC; $[\alpha]_D^{20}$ -46.6 (*c* 1.00, CH_2Cl_2) (97% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 36.34 min; t_{minor} = 48.02 min); 7:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz) *δ* 7.92 (s, 1H), 7.54-7.48 (m, 4H), 7.45-7.43 (m, 1H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 8.8 Hz, 2H), 3.60 (s, 3H), 3.44 (d, *J* = 13.6 Hz, 1H), 3.10 (d, *J* = 18.4 Hz, 1H), 2.79 (d, *J* = 18.4 Hz, 1H), 2.42 (d, *J* = 14.0 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 176.3, 174.7, 172.5, 166.8, 161.8 (d, *J* = 243.0 Hz), 138.5 (d, *J* = 3.1 Hz), 132.6, 129.1, 128.8, 128.2 (d, *J* = 8.2 Hz), 127.4, 115.5 (d, *J* = 21.1 Hz), 85.7, 61.1, 52.8, 45.3, 38.1; ^{19}F NMR (d_6-DMSO, 376 MHz) *δ* -113.7; IR (Film) ν 1736, 1708, 1507, 1398, 1260, 1198, 1144, 1074, 1014 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{18}FN_2O_4$ 381.1245; Found 381.1245.

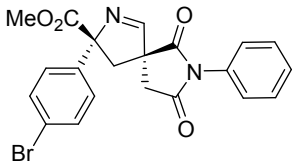
*(2R,4R)-Methyl 3-(4-chlorophenyl)-6,8-dioxo-7-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4c**)*.



White solid; yield 60.2 mg (76%); mp 234.0-234.8 ºC; $[\alpha]_D^{20}$ -51.4 (*c* 1.00, CH_2Cl_2)

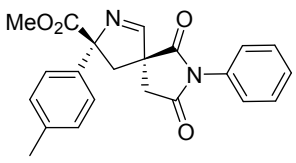
(98% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 43.24 min; t_{minor} = 77.35 min); 10:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz) δ 7.93 (s, 1H), 7.53-7.42 (m, 7H), 7.33 (d, J = 7.2 Hz, 2H), 3.60 (s, 3H), 3.44 (d, J = 14.0 Hz, 1H), 3.09 (d, J = 18.0 Hz, 1H), 2.79 (d, J = 18.4 Hz, 1H), 2.41 (d, J = 14.0 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) δ 176.3, 174.6, 172.3, 167.0, 141.2, 132.8, 132.6, 129.1, 128.7, 128.0, 127.4, 85.8, 61.1, 52.8, 45.1, 38.0; IR (Film) ν 1738, 1709, 1498, 1399, 1258, 1199, 1144, 1093, 1015 cm^{-1}; HRMS (ESI-TOF) m/z: $[M-H]^-$ calcd for $C_{21}H_{16}ClN_2O_4$ 395.0804; Found 395.0801.

*(2R,4R)-Methyl 3-(4-bromophenyl)-6,8-dioxo-7-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4d**)*.



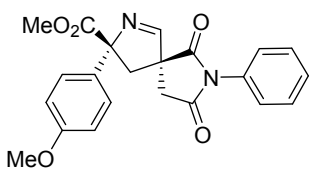
White solid; yield 72.3 mg (82%); mp 222.6-223.4 ºC; $[\alpha]_D^{20}$ -49.0 (*c* 1.00, CH_2Cl_2) (98% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (80/20 hexane/*i*-PrOH; 1.0 mL/min; λ = 230 nm; t_{major} = 50.30 min; t_{minor} = 106.90 min); 15:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz) δ 7.92 (s, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.51 (t, J = 7.6 Hz, 2H), 7.45-7.42 (m, 3H), 7.33 (d, J = 7.2 Hz, 2H), 3.60 (s, 3H), 3.43 (d, J = 14.0 Hz, 1H), 3.09 (d, J = 18.4 Hz, 1H), 2.78 (d, J = 18.4 Hz, 1H), 2.40 (d, J = 14.0 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) δ 176.1, 174.5, 172.0, 166.9, 141.5, 132.5, 131.5, 128.9, 128.6, 128.2, 127.2, 121.2, 85.7, 61.0, 52.7, 44.9, 38.0; IR (Film) ν 1735, 1713, 1499, 1384, 1257, 1190, 1068, 1014 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{18}BrN_2O_4$ 441.0444; Found 441.0442.

*(2R,4R)-Methyl 6,8-dioxo-7-phenyl-3-(p-tolyl)-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4e**)*.



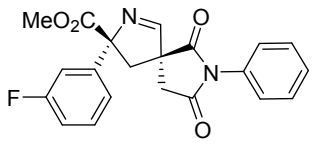
White solid; yield 50.4 mg (67%); mp 208.0-210.2 ºC; $[\alpha]_D^{20}$ -50.2 (*c* 1.00, CH_2Cl_2) (97% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (5/1 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 70.58 min; t_{minor} = 113.23 min); 10:1 *dr*; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68 (s, 1H), 7.46 (d, J = 7.6 Hz, 2H), 7.42-7.39 (m, 3H), 7.29 (d, J = 7.6 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 3.74 (s, 3H), 3.64 (d, J = 13.6 Hz, 1H), 2.94 (d, J = 18.4 Hz, 1H), 2.61 (d, J = 18.8 Hz, 1H), 2.39 (d, J = 13.6 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (d_6-DMSO, 100 MHz) δ 176.3, 174.4, 172.5, 166.1, 139.3, 137.0, 132.5, 129.1, 128.9, 128.5, 127.2, 125.7, 86.0, 60.8, 52.4, 45.1, 38.1, 20.7; IR (Film) ν 1740, 1710, 1499, 1456, 1399, 1301, 1257, 1197, 1143, 1078, 1022 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}N_2O_4$ 377.1496; Found 377.1495.

*(2R,4R)-Methyl 3-(4-methoxyphenyl)-6,8-dioxo-7-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4f**)*.



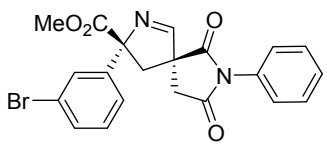
White solid; yield 43.1 mg (55%); mp 191.6-193.4 ºC; $[\alpha]_D^{20}$ -84.6 (*c* 1.00, CH_2Cl_2) (99% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (80/20 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 70.94 min; t_{minor} = 116.18 min); 5:1 *dr*; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.69 (s, 1H), 7.48-7.37 (m, 5H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H), 3.75 (s, 3H), 3.63 (d, *J* = 13.6 Hz, 1H), 2.96 (d, *J* = 19.2 Hz, 1H), 2.64 (d, *J* = 18.8 Hz, 1H), 2.40 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 175.4, 173.3, 172.5, 164.0, 159.5, 133.4, 131.5, 129.3, 129.0, 126.9, 126.3, 114.2, 86.2, 60.5, 55.4, 53.3, 46.4, 38.5; IR (Film) ν 1738, 1710, 1511, 1500, 1398, 1300, 1255, 1185, 1143, 1034 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}N_2O_5$ 393.1445; Found 393.1442.

*(2R,4R)-Methyl 3-(3-fluorophenyl)-6,8-dioxo-7-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4g**)*.



White solid; yield 54.7 mg (72%); mp 222.4-223.8 ºC; $[\alpha]_D^{20}$ -52.8 (*c* 1.00, CH_2Cl_2) (98% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 41.63 min; t_{minor} = 54.91 min); 6:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz) *δ* 7.93 (s, 1H), 7.50 (d, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.32 (s, 1H), 7.27-7.25 (m, 1H), 7.18 (td, *J* = 8.8, 2.0 Hz, 1H), 3.61 (s, 3H), 3.45 (d, *J* = 13.6 Hz, 1H), 3.11 (d, *J* = 18.4 Hz, 1H), 2.80 (d, *J* = 18.0 Hz, 1H), 2.43 (d, *J* = 13.6 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 176.1, 174.5, 172.0, 167.1, 162.1 (d, *J* = 234.5 Hz), 144.8 (d, *J* = 7.2 Hz), 132.5, 130.7 (d, *J* = 8.3 Hz), 128.9, 128.6, 127.2, 122.0 (d, *J* = 2.6 Hz), 114.7 (d, *J* = 20.7 Hz), 112.9 (d, *J* = 22.9 Hz), 85.7, 61.0, 52.7, 45.0, 37.9; ^{19}F NMR (d_6-DMSO, 376 MHz) *δ* -111.5; IR (Film) ν 1736, 1709, 1501, 1398, 1260, 1199, 1144, 1074, 1014 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{18}FN_2O_4$ 381.1245; Found 381.1245.

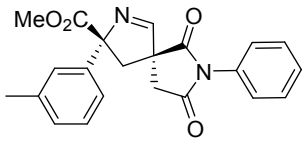
*(2R,4R)-Methyl 3-(3-bromophenyl)-6,8-dioxo-7-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4h**)*.



White solid; yield 71.4 mg (81%); mp 218.7-219.5 ºC; $[\alpha]_D^{20}$ -42.6 (*c* 1.00, CH_2Cl_2) (97% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 47.55 min; t_{minor} = 61.12 min); 5:1 *dr*; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.73 (t, *J* = 2.0 Hz, 1H), 7.70 (s, 1H), 7.51-7.45 (m, 4H), 7.44-7.42 (m, 1H), 7.32-7.28 (m, 3H), 3.77 (s, 3H), 3.72 (d, *J* = 13.2 Hz, 1H), 3.05 (d, *J* = 18.8 Hz, 1H), 2.69 (d, *J* = 18.4 Hz, 1H), 2.34 (d, *J* = 13.6 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 176.0, 174.5, 172.0, 167.2, 144.7,

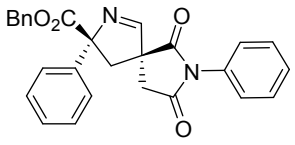
132.5, 130.9, 130.8, 128.9, 128.62, 128.57, 127.2, 125.1, 121.9, 85.6, 61.0, 52.8, 44.9, 37.9; IR (Film) ν 1738, 1713, 1490, 1447, 1384, 1257, 1189, 1069, 1014 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{18}BrN_2O_4$ 441.0444; Found 441.0455.

*(2R,4R)-Methyl 6,8-dioxo-7-phenyl-3-(m-tolyl)-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4i**)*.



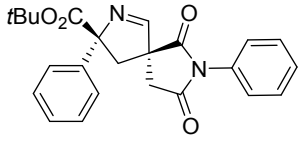
White solid; yield 51.1 mg (68%); mp 215.2-216.6 ºC; $[\alpha]_D^{20}$ -55.4 (*c* 1.00, CH_2Cl_2) (95% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 37.53 min; t_{minor} = 45.49 min); 6:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz) *δ* 7.89 (s, 1H), 7.53-7.49 (m, 2H), 7.45-7.43 (m, 1H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.29-7.26 (m, 3H), 7.14-7.13 (m, 1H), 3.59 (s, 3H), 3.43 (d, *J* = 14.0 Hz, 1H), 3.09 (d, *J* = 18.4 Hz, 1H), 2.78 (d, *J* = 18.4 Hz, 1H), 2.41 (d, *J* = 14.0 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 176.3, 174.5, 172.5, 166.2, 142.2, 137.8, 132.5, 128.9, 128.6, 128.5, 128.4, 127.2, 126.3, 122.9, 86.1, 60.9, 52.5, 45.1, 38.0, 21.3; IR (Film) ν 1739, 1710, 1499, 1455, 1399, 1257, 1197, 1143, 1105, 1022 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}N_2O_4$ 377.1496; Found 377.1492.

*(2R,4R)-Benzyl 6,8-dioxo-3,7-diphenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4k**)*.



White solid; yield 48.2 mg (55%); mp 204.8-205.5 ºC; $[\alpha]_D^{20}$ -53.6 (*c* 1.00, CH_2Cl_2) (99% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 97.45 min; t_{minor} = 82.61 min); 20:1 *dr*; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.71 (s, 1H), 7.51-7.47 (m, 4H), 7.43-7.40 (m, 1H), 7.38-7.30 (m, 6H), 7.26-7.24 (m, 2H), 7.19-7.16 (m, 2H), 5.24 (d, *J* = 12.4 Hz, 1H), 5.14 (d, *J* = 12.4 Hz, 1H), 3.69 (d, *J* = 13.2 Hz, 1H), 2.97 (d, *J* = 18.8 Hz, 1H), 2.63 (d, *J* = 18.4 Hz, 1H), 2.44 (d, *J* = 13.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ* 175.2, 173.1, 171.2, 164.0, 141.1, 135.4, 131.4, 129.2, 128.9, 128.7, 128.4, 128.2, 128.0, 127.8, 126.2, 125.7, 86.7, 67.5, 60.4, 46.0, 38.4; IR (Film) ν 1728, 1705, 1621, 1500, 1454, 1446, 1397, 1252, 1212, 1189, 1144, 1024 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{27}H_{23}N_2O_4$ 439.1652; Found 439.1650.

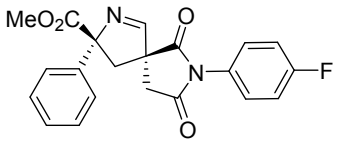
*(2R,4R)-tert-Butyl 6,8-dioxo-3,7-diphenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4l**)*.



White solid; yield 53.3 mg (33%); mp 193.9-194.6 ºC; $[\alpha]_D^{20}$ -60.6 (*c* 1.00, CH_2Cl_2) (96% *ee*); the *ee* was determined by HPLC analysis with a Chiralcel OD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 35.54 min; t_{minor} = 32.51

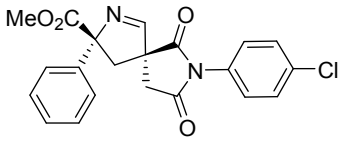
min); 17:1 *dr*; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68 (s, 1H), 7.50-7.46 (m, 4H), 7.43-7.41 (m, 1H), 7.39-7.35 (m, 2H), 7.32-7.30 (m, 3H), 3.62 (d, J = 13.2 Hz, 1H), 2.92 (d, J = 19.2 Hz, 1H), 2.59 (d, J = 18.8 Hz, 1H), 2.39 (d, J = 13.6 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.3, 173.2, 170.2, 163.4, 141.8, 131.4, 129.1, 128.8, 128.5, 127.8, 126.2, 125.5, 87.2, 82.4, 60.2, 45.8, 38.5, 27.7; IR (Film) ν 1711, 1500, 1447, 1395, 1298, 1261, 1202, 1189, 1165, 1142, 1058, 1031 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{24}H_{25}N_2O_4$ 405.1809; Found 405.1806.

*(2R,4R)-Methyl 7-(4-fluorophenyl)-6,8-dioxo-3-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4n**)*.



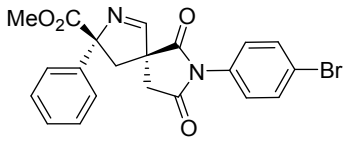
White solid; yield 50.2 mg (66%); mp 216.1-217.2 ºC; $[\alpha]_D^{20}$ -43.6 (*c* 1.00, CH_2Cl_2) (99% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (85/15 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 103.10 min; t_{minor} = 124.80 min); 10:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz) δ 7.89 (s, 1H), 7.47 (d, J = 7.6 Hz, 2H), 7.41-7.30 (m, 7H), 3.59 (s, 3H), 3.45 (d, J = 13.6 Hz, 1H), 3.08 (d, J = 18.4 Hz, 1H), 2.77 (d, J = 18.0 Hz, 1H), 2.41 (d, J = 13.6 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) δ 176.1, 174.4, 172.3, 166.2, 161.5 (d, J = 243.9 Hz), 142.1, 129.3 (d, J = 8.9 Hz), 128.6 (d, J = 2.9 Hz), 128.5, 127.7, 125.7, 115.8 (d, J = 22.7 Hz), 86.1, 60.7, 52.4, 45.1, 37.9; ^{19}F NMR (d_6-DMSO, 376 MHz) δ -113.0; IR (Film) ν 1736, 1709, 1505, 1398, 1260, 1199, 1158, 1144, 1074, 1014 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{18}FN_2O_4$ 381.1245; Found 381.1243.

*(2R,4R)-Methyl 7-(4-chlorophenyl)-6,8-dioxo-3-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4o**)*.



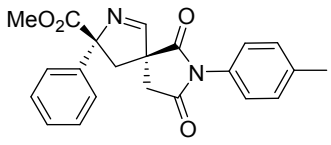
White solid; yield 60.3 mg (76%); mp 235.2-236.6 ºC; $[\alpha]_D^{20}$ -35.2 (*c* 1.00, CH_2Cl_2) (99% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (85/15 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 103.76 min; t_{minor} = 128.10 min); 9:1 *dr*; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68 (s, 1H), 7.53-7.51 (m, 2H), 7.45 (d, J = 8.8 Hz, 2H), 7.40-7.32 (m, 3H), 7.28 (d, J = 8.8 Hz, 2H), 3.76 (s, 3H), 3.69 (d, J = 13.6 Hz, 1H), 2.99 (d, J = 18.8 Hz, 1H), 2.64 (d, J = 18.8 Hz, 1H), 2.40 (d, J = 13.6 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) δ 176.1, 174.3, 172.4, 166.3, 142.2, 133.1, 131.3, 129.0, 128.6, 127.8, 126.1, 125.8, 86.2, 60.9, 52.6, 45.2, 38.1; IR (Film) ν 1738, 1710, 1490, 1399, 1258, 1199, 1144, 1093, 1075, 1015 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{18}ClN_2O_4$ 397.0950; Found 397.0949.

*(2R,4R)-Methyl 7-(4-bromophenyl)-6,8-dioxo-3-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4p**)*.



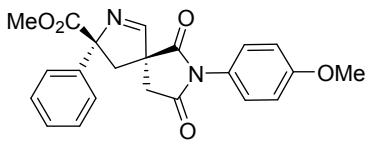
White solid; yield 64.4 mg (73%); mp 219.5-220.2 ºC; $[\alpha]_D^{20}$ -27.2 (*c* 1.00, CH_2Cl_2) (>99% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 75.02 min); 10:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz) *δ* 7.89 (s, 1H), 7.73 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.34-7.32 (m, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 3.59 (s, 3H), 3.45 (d, *J* = 13.6 Hz, 1H), 3.08 (d, *J* = 18.4 Hz, 1H), 2.76 (d, *J* = 18.4 Hz, 1H), 2.40 (d, *J* = 14.0 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 176.0, 174.3, 172.4, 166.3, 142.2, 132.0, 131.8, 129.3, 128.6, 127.8, 125.8, 121.5, 86.1, 60.9, 52.6, 45.2, 38.1; IR (Film) ν 1738, 1712, 1490, 1446, 1384, 1257, 1191, 1142, 1068, 1013 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{18}BrN_2O_4$ 441.0444; Found 441.0442.

*(2R,4R)-Methyl 6,8-dioxo-3-phenyl-7-(p-tolyl)-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4q**)*.



White solid; yield 54.1 mg (72%); mp 210.3-211.5 ºC; $[\alpha]_D^{20}$ -54.6 (*c* 1.00, CH_2Cl_2) (94% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 47.56 min; t_{minor} = 41.90 min); 5:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz) *δ* 7.90 (s, 1H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.34-7.27 (m, 3H), 7.20 (d, *J* = 8.4 Hz, 2H), 3.60 (s, 3H), 3.43 (d, *J* = 13.6 Hz, 1H), 3.06 (d, *J* = 18.0 Hz, 1H), 2.76 (d, *J* = 18.0 Hz, 1H), 2.42 (d, *J* = 13.6 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 176.3, 174.5, 172.4, 166.4, 142.2, 138.1, 129.9, 129.4, 128.6, 127.8, 127.0, 125.8, 86.1, 60.8, 52.5, 45.1, 38.0, 20.8; IR (Film) ν 1736, 1710, 1499, 1399, 1257, 1185, 1142, 1105, 1077, 1022 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}N_2O_4$ 377.1496; Found 377.1493.

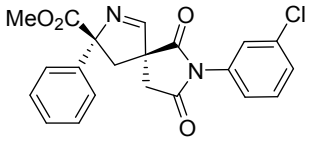
*(2R,4R)-Methyl 7-(4-methoxyphenyl)-6,8-dioxo-3-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4r**)*.



White solid; yield 55.8 mg (71%); mp 193.4-194.8 ºC; $[\alpha]_D^{20}$ -79.2 (*c* 1.00, CH_2Cl_2) (96% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 67.41 min; t_{minor} = 98.88 min); 5:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz) *δ* 7.89 (s, 1H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.33 (d, *J* = 7.2 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 3.60 (s, 3H), 3.43 (d, *J* = 14.0 Hz, 1H), 3.06 (d, *J* = 18.4 Hz, 1H), 2.75 (d, *J* = 18.0 Hz, 1H), 2.41 (d, *J* = 13.6 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 176.4, 174.7, 172.4, 166.4, 159.1, 142.2, 128.6, 128.4, 127.8, 125.8, 125.0, 114.2, 86.1, 60.8, 55.5, 52.5, 45.1, 37.9; IR (Film) ν 1739, 1710, 1511, 1500, 1455, 1398, 1300, 1254, 1185, 1143, 1077,

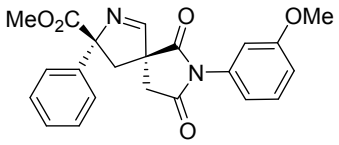
1034 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}N_2O_5$ 393.1445; Found 393.1443.

*(2R,4R)-Methyl 7-(3-chlorophenyl)-6,8-dioxo-3-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4s**)*.



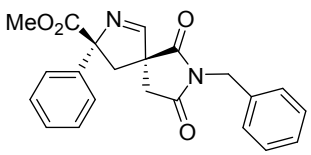
White solid; yield 47.6 mg (60%); mp 192.2-193.0 ºC; $[\alpha]_D^{20}$ -37.6 (*c* 1.00, CH_2Cl_2) (90% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 34.33 min; t_{minor} = 41.99 min); 3:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz, major isomer) *δ* 7.88 (s, 1H), 7.55 (d, *J* = 7.6 Hz, 2H), 7.48 (s, 1H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.35-7.33 (m, 2H), 3.60 (s, 3H), 3.47 (d, *J* = 13.6 Hz, 1H), 3.10 (d, *J* = 18.4 Hz, 1H), 2.78 (d, *J* = 18.4 Hz, 1H), 2.40 (d, *J* = 14.0 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 176.0, 174.3, 172.4, 166.2, 142.2, 133.8, 133.0, 130.6, 128.6, 128.5, 127.8, 127.2, 126.1, 125.8, 86.2, 60.9, 52.6, 45.2, 38.1; IR (Film) ν 1738, 1710, 1399, 1257, 1199, 1143, 1093, 1075, 1015 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{18}ClN_2O_4$ 397.0950; Found 397.0947.

*(2R,4R)-Methyl 7-(3-methoxyphenyl)-6,8-dioxo-3-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4t**)*.



White solid; yield 55.0 mg (70%); mp 190.6-191.2 ºC; $[\alpha]_D^{20}$ -76.2 (*c* 1.00, CH_2Cl_2) (> 99% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 64.39 min); 4:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz, major isomer) *δ* 7.90 (s, 1H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.40-7.38 (m, 1H), 7.33 (d, *J* = 7.2 Hz, 1H), 7.02 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.92 (s, 1H), 6.91 (d, *J* = 6.8 Hz, 1H), 3.78 (s, 3H), 3.60 (s, 3H), 3.44 (d, *J* = 13.6 Hz, 1H), 3.08 (d, *J* = 18.0 Hz, 1H), 2.77 (d, *J* = 18.4 Hz, 1H), 2.41 (d, *J* = 14.0 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 176.2, 174.4, 172.5, 166.4, 159.6, 142.2, 133.6, 129.8, 128.6, 127.8, 125.8, 119.5, 114.2, 113.2, 86.2, 60.9, 55.5, 52.6, 45.2, 38.1; IR (Film) ν 1738, 1711, 1603, 1588, 1492, 1454, 1391, 1284, 1257, 1196, 1132, 1042 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}N_2O_5$ 393.1445; Found 393.1442.

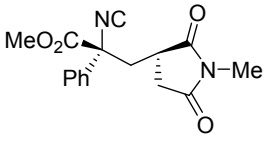
*(2R,4R)-Methyl 7-benzyl-6,8-dioxo-3-phenyl-2,7-diazaspiro[4.4]non-1-ene-3-carboxylate (**4u**)*.



White solid; yield 45.7 mg (60%); mp 226.5-227.8 ºC; $[\alpha]_D^{20}$ -69.6 (*c* 1.00, CH_2Cl_2) (98% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak AD-H column (75/25 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 28.64 min; t_{minor} = 36.35 min); >20:1 *dr*; ^{1}H NMR (d_6-DMSO, 400 MHz, major isomer) *δ* 7.78 (s, 1H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.39-7.36

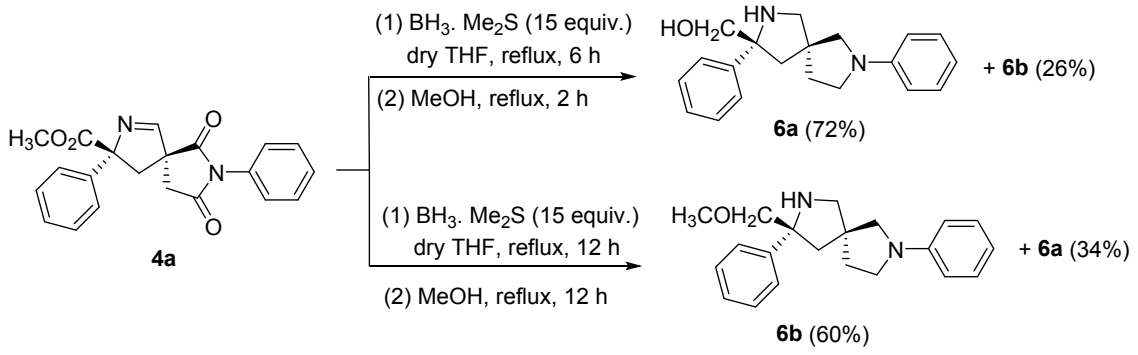
(m, 3H), 7.34 (d, J = 7.6 Hz, 2H), 7.31-7.28 (m, 1H), 7.27 (d, J = 8.0 Hz, 2H), 4.59 (s, 2H), 3.61 (s, 3H), 3.29 (d, J = 14.0 Hz, 1H), 3.03 (d, J = 18.4 Hz, 1H), 2.72 (d, J = 18.4 Hz, 1H), 2.40 (d, J = 14.0 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) δ 176.9, 175.2, 172.4, 166.1, 142.1, 135.9, 128.62, 128.57, 127.8, 127.6, 127.5, 125.8, 86.2, 60.8, 52.6, 44.7, 42.1, 37.7; IR (Film) ν 1762, 1740, 1702, 1494, 1432, 1396, 1345, 1261, 1171 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}N_2O_4$ 377.1496; Found 377.1493.

*Methyl (R)-2-isocyano-3-((R)-1-methyl-2,5-dioxopyrrolidin-3-yl)-2-phenylpropanoate (**5b**):*



Light yellow oil; yield 40.8 mg (68%); $[\alpha]_D^{20}$ -62.0 (c 1.00, CH_2Cl_2) (96% *ee*); the *ee* was determined by HPLC analysis with a Chiralpak IC-H column (85/15 hexane/*i*-PrOH; 0.8 mL/min; λ = 230 nm; t_{major} = 50.05 min; t_{minor} = 58.43 min); 6:1 *dr*; ^{1}H NMR ($CDCl_3$, 400 MHz, major isomer) δ 7.59-7.53 (m, 2H), 7.47-7.43 (m, 3H), 3.82 (s, 3H), 3.20 (dd, J = 14.4, 3.2 Hz, 1H), 3.03-2.93 (m, 1H), 2.96 (s, 3H), 2.47 (dd, J = 18.4, 9.2 Hz, 1H), 2.34 (dd, J = 18.8, 10.4 Hz, 1H), 2.00 (dd, J = 18.4, 5.6 Hz, 1H); ^{13}C NMR (d_6-DMSO, 100 MHz) δ 178.8, 176.4, 167.3, 162.0, 134.7, 129.4, 129.3, 124.9, 79.2, 69.8, 54.2, 36.6, 34.8, 24.5; IR (Film) ν 2135, 1745, 1696, 1561, 1437, 1279, 1256, 1117 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{16}H_{16}N_2NaO_4$ 323.1002; Found 323.1005.

3. Synthetic Transformation of Product 4a



To the solution of **4a** (0.2 mmol, 72.4 mg) in dry THF (5 mL) was added $BH_3{\cdot}Me_2S$ (15 equiv.) dropwise at 0°C under argon. The resulting slurry was stirred at 65 °C for 6 h and then the solution was allowed to cool to room temperature and quenched with dilute HCl. After neutralized by sat. Na_2CO_3, the resulting mixture was extracted with CH_2Cl_2 for three times (3 × 15 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was dissolved in MeOH and refluxed for 2 h, concentrated, and then purified by column chromatography (PE:EA = 2:1) to obtain compound **6a** as major product.

*((3R,5S)-3,7-Diphenyl-2,7-diazaspiro[4.4]nonan-3-yl)methanol (**6a**)*. Light yellow oil; yield 44.3 mg (72%); $[\alpha]_D^{20}$ -20.6 (*c* 1.00, CH_2Cl_2) (99% *ee*); the *ee* was determined by HPLC analysis with a Chiralcel OD-H column (70/30 hexane/*i*-PrOH; 0.8 mL/min; λ = 254 nm; t_{major} = 10.94 min; t_{minor} = 15.72 min); >20:1 *dr*; ^{1}H NMR ($CDCl_3$, 400 MHz, major isomer) δ 7.43-7.36 (m, 4H), 7.30-7.28 (m, 1H), 7.23 (dd, *J* = 8.4, 7.6 Hz, 2H), 6.67 (t, *J* = 7.6 Hz, 1H), 6.54 (d, *J* = 7.6 Hz, 2H), 3.64 (d, *J* = 10.8 Hz, 1H), 3.51 (d, *J* = 10.4 Hz, 1H), 3.36 (d, *J* = 9.2 Hz, 1H), 3.32-3.26 (m, 3H), 3.07 (d, *J* = 10.4 Hz, 1H), 2.98 (d, *J* = 10.4 Hz, 1H), 2.32 (d, *J* = 13.2 Hz, 1H), 2.23-2.18 (m, 3H), 1.80 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.8, 145.4, 129.3, 128.6, 127.0, 125.8, 115.7, 111.5, 69.4, 68.9, 58.8, 56.7, 50.2, 47.2, 46.2, 37.4; IR (Film) ν 3342, 1667, 1598, 1506, 1483, 1369, 1261, 1186, 1032 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{25}N_2O$ 309.1967; Found 309.1990.

To the solution of **4a** (0.2 mmol, 72.4 mg) in dry THF (5 mL) was added $BH_3{\cdot}Me_2S$ (15 equiv.) dropwise at 0°C under argon. The resulting slurry was stirred at 65 °C for 12 h and then the solution was allowed to cool to room temperature and quenched with dilute HCl. After neutralized by sat. Na_2CO_3, the resulting mixture was extracted with CH_2Cl_2 for three times (3 × 15 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was dissolved in MeOH and refluxed for 12 h, concentrated, and then purified by column chromatography (PE:EA = 5:1) to obtain compound **6b** as major product.

*(5S,8R)-8-(Methoxymethyl)-2,8-diphenyl-2,7-diazaspiro[4.4]nonane (**6b**)*. Light yellow oil; yield 38.6 mg (60%); $[\alpha]_D^{20}$ -26.0 (*c* 1.00, CH_2Cl_2) (98% *ee*); the *ee* was determined by HPLC analysis with a Chiralcel OD-H column (95/5 hexane/*i*-PrOH; 0.8 mL/min; λ = 254 nm; t_{major} = 13.35 min; t_{minor} = 21.62 min); >20:1 *dr*; ^{1}H NMR ($CDCl_3$, 400 MHz, major isomer) δ 7.51 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.2 Hz, 2H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.42 (d, *J* = 7.6 Hz, 2H), 3.49 (d, *J* = 9.6 Hz, 1H), 3.37 (d, *J* = 9.2 Hz, 1H), 3.34 (s, 3H), 3.33-3.31 (m, 2H), 3.03 (d, *J* = 11.2 Hz, 1H), 3.00 (d, *J* = 2.0 Hz, 1H), 2.89 (d, *J* = 11.2 Hz, 1H), 2.28-2.20 (m, 4H), 2.04 (td, *J* = 7.2, 2.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.9, 145.9, 129.2, 128.2, 126.7, 126.3, 115.5, 111.4, 79.2, 68.9, 59.3, 59.0, 57.3, 51.1, 47.3, 46.7, 37.1; IR (Film) ν 3326, 1597, 1507, 1483, 1448, 1369, 1192, 1101 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{27}N_2O$ 323.2123; Found 323.2159.

4. X-Ray Crystal Data of Compound 4d

Table 1. Crystal data and structure refinement for **4d** (CCDC 1909456).

Empirical formula	$C_{21}H_{17}BrN_2O_4$, $CHCl_3$	
Formula weight	560.64	
Temperature	293(2)	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 13.3229(3) Å	α = 90°.
	b = 6.20240(10) Å	β = 115.145(3)°.
	c = 15.4655(4) Å	γ = 90°.
Volume	1156.87(5) $Å^3$	
Z	2	
Density (calculated)	1.609 Mg/m^3	
Absorption coefficient	5.890 mm^{-1}	
F(000)	564	
Crystal size	0.36 x 0.06 x 0.04 mm^3	
Theta range for data collection	5.7210 to 74.2650°	
Index ranges	-16<=h<=16, -7<=k<=7, -19<=l<=19	
Reflections collected	23138	
Independent reflections	4644 [R(int) = 0.0832]	
Data / restraints / parameters	4644 / 1 / 290	
Goodness-of-fit on F^2	1.093	
Final R indices [I>2sigma(I)]	R1 = 0.0424, wR2 = 0.1112	
R indices (all data)	R1 = 0.0443, wR2 = 0.1096	
Largest diff. peak and hole	1.232 and -0.737 $e.Å^{-3}$	

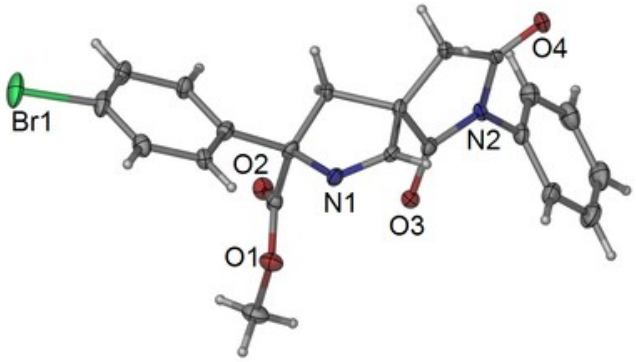
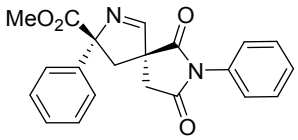


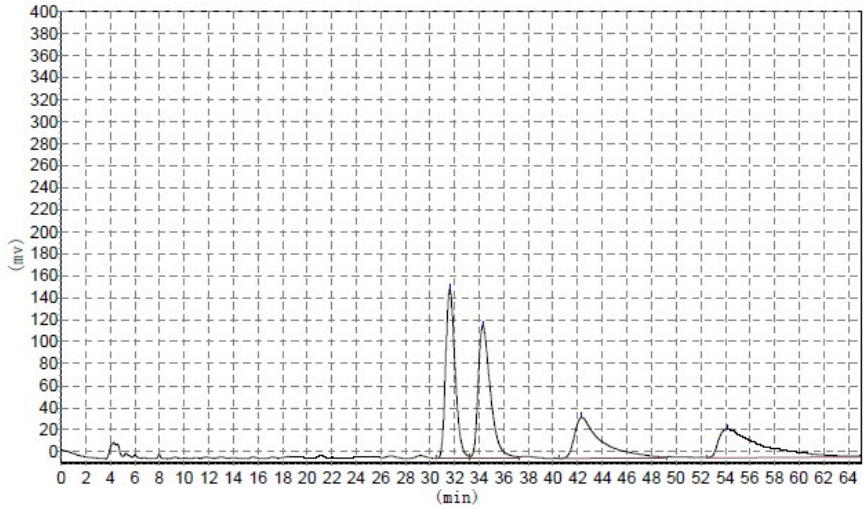
Figure S1. ORTEP plot of the X-ray crystal structure of **4d**. Displacement ellipsoids are drawn at the 50% probability level.

5. Copies of HPLC Analysis Spectra of Compounds 4 and 6

4a (Table 3, entry 1)

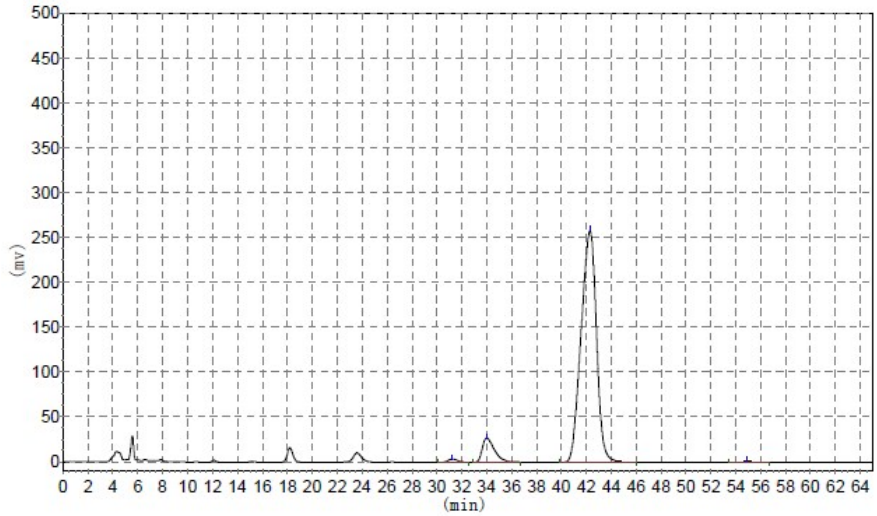


Racemic



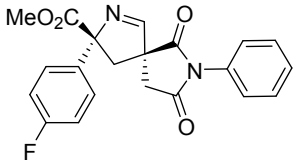
	Retention time	Height	Area	Area %
1	31.598	153434.578	8262419.000	29.3848
2	34.332	121067.500	8463428.000	30.0997
3	42.332	37194.117	5707667.500	20.2990
4	54.198	26189.795	5684487.000	20.2165
Total		337885.990	28118001.500	100.0000

Chiral



	Retention time	Height	Area	Area %
1	31.255	3636.297	190868.156	0.7884
2	34.008	26934.342	1812933.750	7.4884
3	42.297	257961.625	22114764.000	91.3461
4	54.855	974.679	91303.203	0.3771
Total		289506.942	24209869.109	100.0000

4b (Table 3, entry 2)



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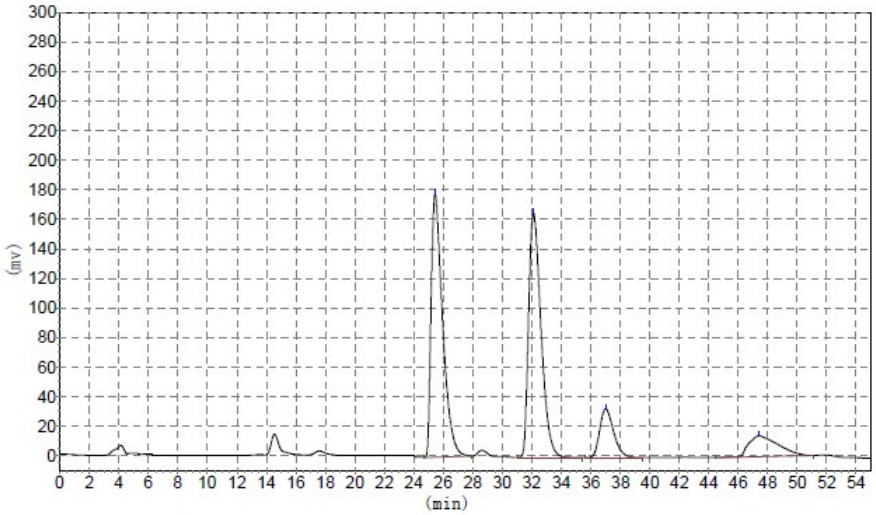
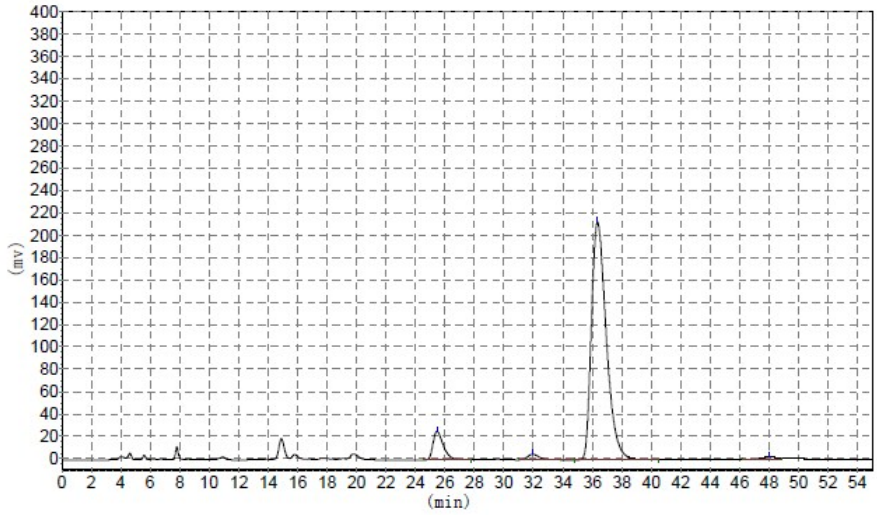


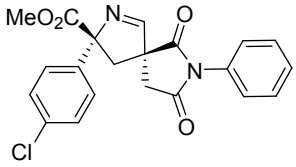
	Retention time	Height	Area	Area %
1	25.440	177896.422	9653028.000	40.6111
2	32.115	165650.234	9690515.000	40.7688
3	37.007	33106.090	2186340.500	9.1981
4	47.382	14818.422	2239566.000	9.4220
Total		391471.168	23769449.500	100.0000

Chiral



	Retention time	Height	Area	Area %
1	25.450	25559.480	1265328.875	7.5667
2	31.948	5050.777	288406.844	1.7247
3	36.343	212903.250	14953531.000	89.4229
4	48.020	2813.919	214988.141	1.2856
Total		246327.427	16722254.859	100.0000

4c (Table 3, entry 3)



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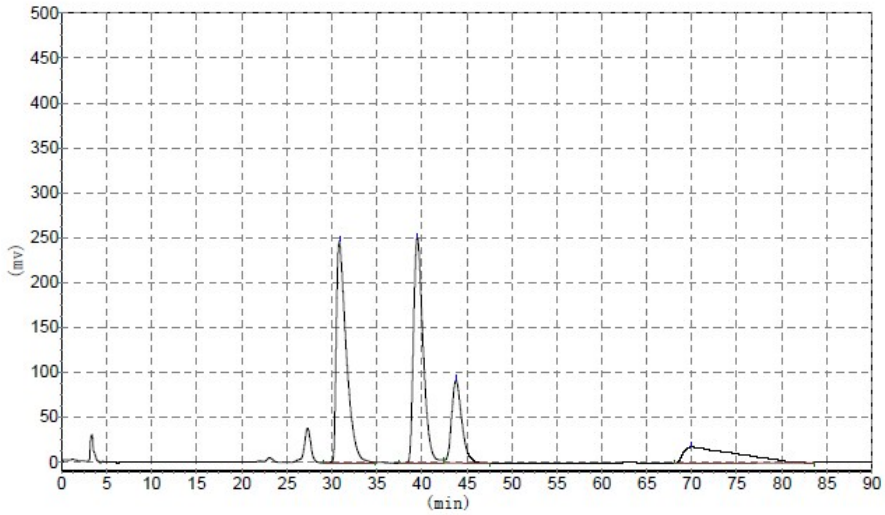
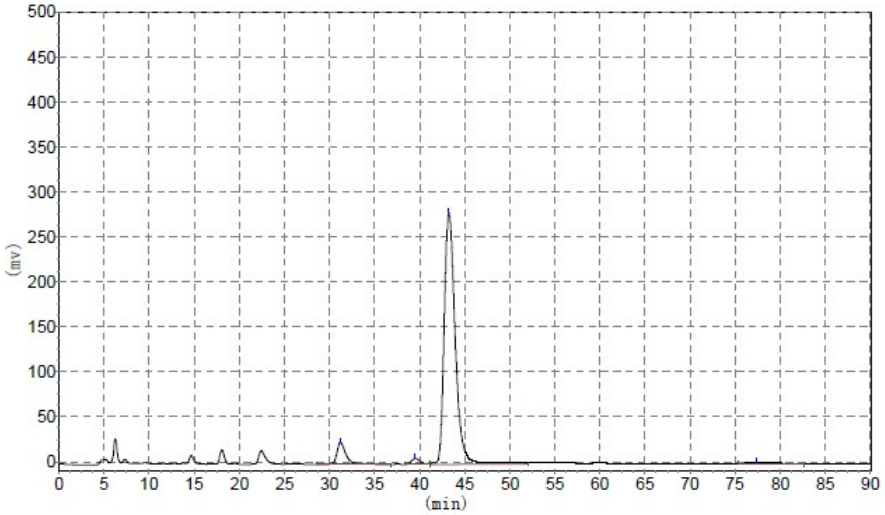


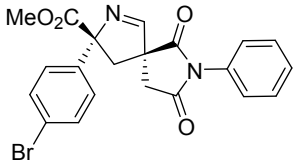
	Retention time	Height	Area	Area %
1	30.810	247155.516	19122664.000	34.8787
2	39.478	251239.828	18701630.000	34.1108
3	43.777	92378.750	7314045.500	13.3404
4	69.937	18377.641	7701996.000	14.0480
Total		647722.551	54826131.000	100.0000

Chiral



	Retention time	Height	Area	Area %
1	31.202	24440.611	1747105.875	6.6678
2	39.513	6618.770	431284.969	1.6460
3	43.237	279583.094	23813354.000	90.8838
4	77.350	1332.742	210229.016	0.8023
Total		311975.218	26201973.859	100.0000

4c (Table 3, entry 4)



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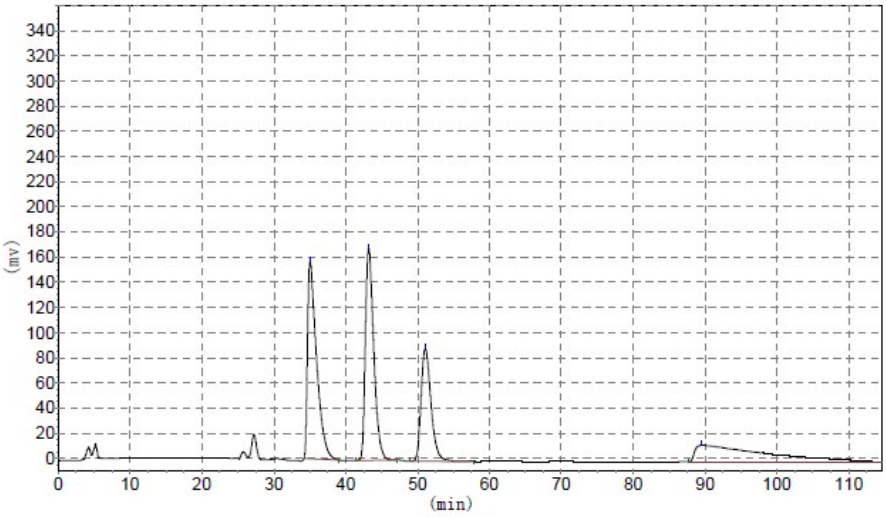
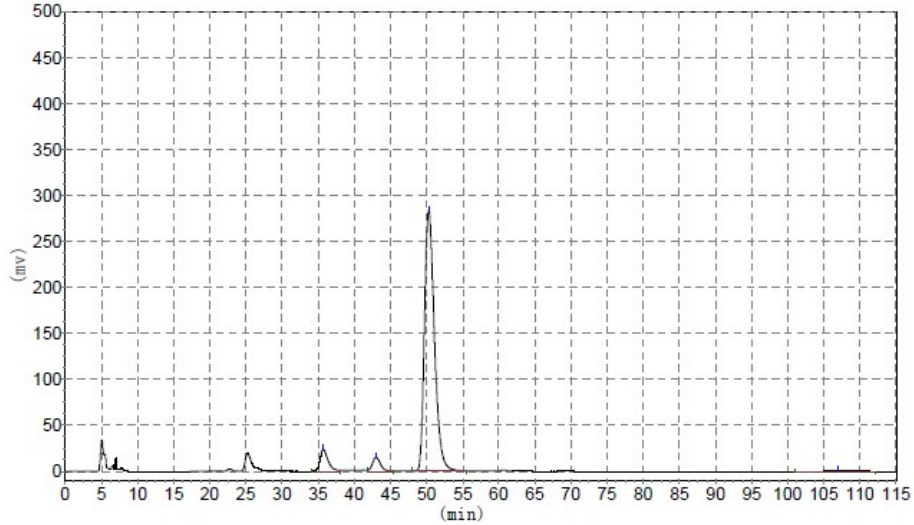


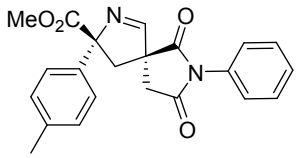
	Retention time	Height	Area	Area %
1	35.027	156756.016	13789073.000	30.5757
2	43.190	168318.750	13697918.000	30.3736
3	51.062	89401.883	8579670.000	19.0245
4	89.545	12950.749	8738575.000	19.3768
Total		427564.707	45098122.438	100.0000

Chiral



	Retention time	Height	Area	Area %
1	35.687	23501.455	1825004.375	6.0330
2	43.017	15146.762	1162499.125	3.8430
3	50.300	283475.531	27007384.000	89.2802
4	106.903	1116.855	255248.797	0.8438
Total		323240.603	30250136.297	100.0000

4e (Table 3, entry 5)



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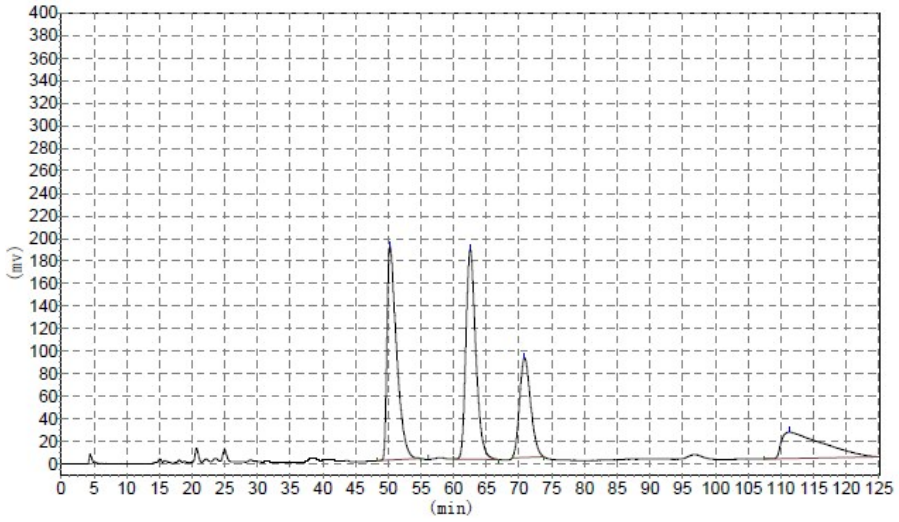
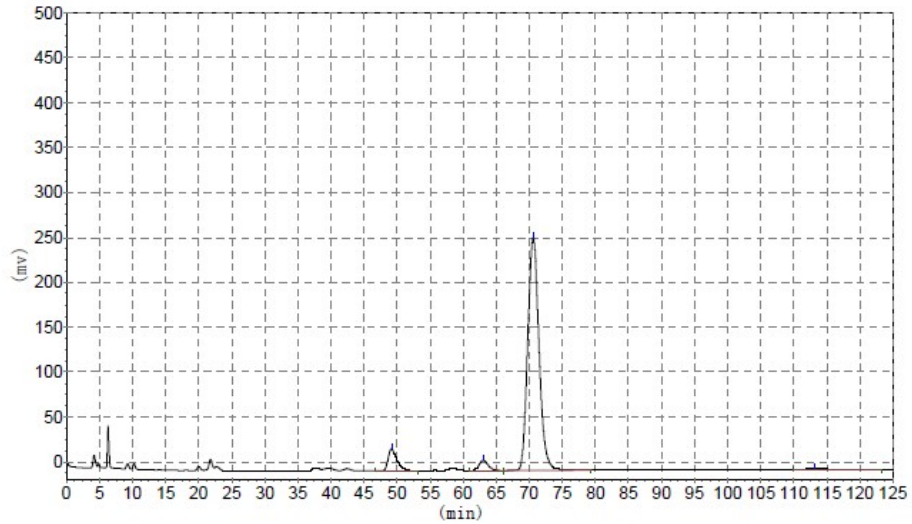


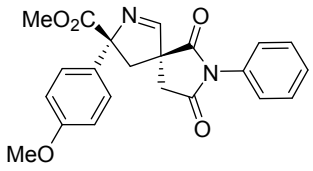
	Retention time	Height	Area	Area %
1	50.262	189695.609	19280042.000	32.3725
2	62.510	186330.734	19583622.000	32.8822
3	70.805	88646.305	10465072.000	17.5716
4	111.233	23263.613	10228135.000	17.1737
Total		487936.262	59556871.000	100.0000

Chiral



	Retention time	Height	Area	Area %
1	49.135	24113.643	2201348.250	6.3997
2	63.015	11307.252	1100530.125	3.1994
3	70.580	259269.172	30690948.000	89.2241
4	113.232	1514.536	404787.875	1.1768
Total		296204.603	34397614.250	100.0000

4f (Table 3, entry 6)



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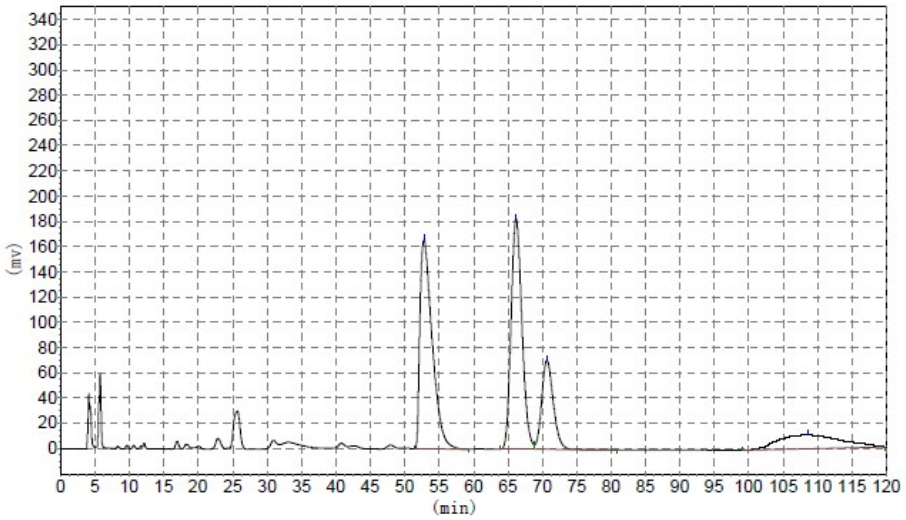
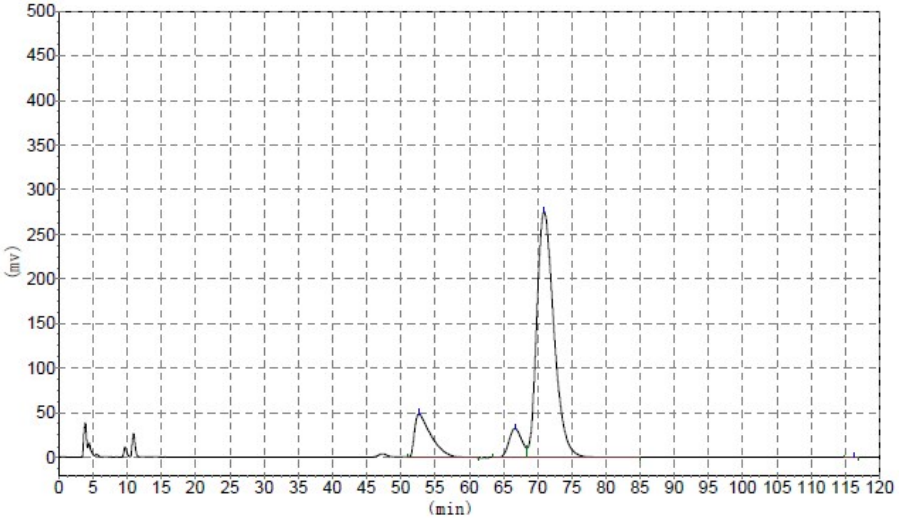


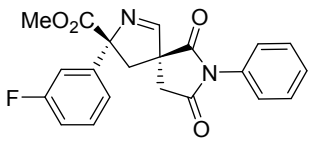
	Retention time	Height	Area	Area %
1	52.810	165522.234	20433144.000	36.6597
2	66.193	182782.125	20122846.000	36.1030
3	70.670	70889.852	8331564.500	14.9479
4	108.688	10906.421	6849729.500	12.2893
Total		430100.632	55737284.000	100.0000

Chiral



	Retention time	Height	Area	Area %
1	52.652	48658.523	8214130.500	13.5516
2	66.690	32638.502	4281476.000	7.0635
3	70.943	275856.750	48094824.000	79.3463
4	116.178	172.236	13981.157	0.0231
Total		357845.659	60613805.531	100.0000

4g (Table 3, entry 7)



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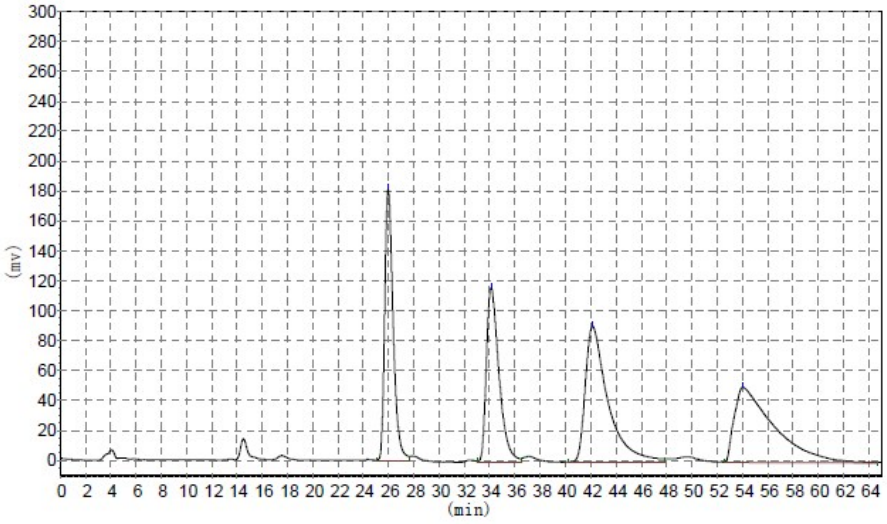
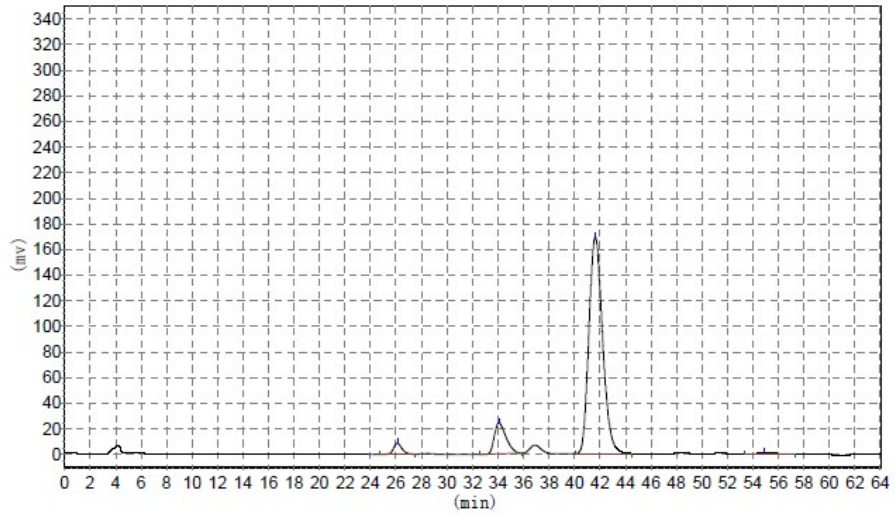


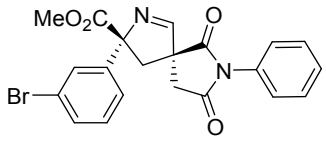
	Retention time	Height	Area	Area %
1	25.960	181085.391	8325117.500	22.6988
2	34.107	116784.234	8124444.000	22.1517
3	42.137	90897.500	11402499.000	31.0894
4	54.023	50346.156	10954324.000	29.8674
Total		557079.847	36676470.500	100.0000

Chiral

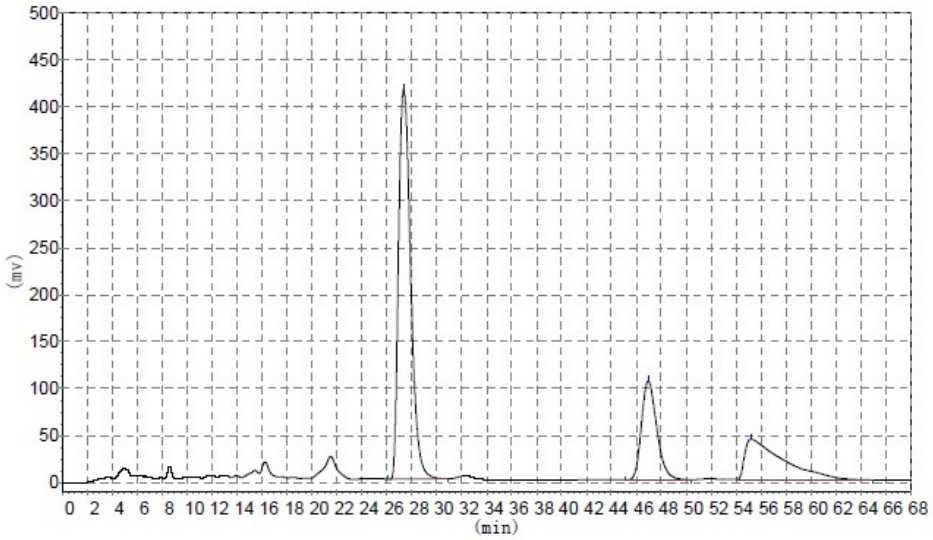


	Retention time	Height	Area	Area %
1	26.093	8630.867	382440.656	2.6099
2	34.075	24123.441	1545509.375	10.5472
3	41.628	169620.938	12609702.000	86.0540
4	54.912	1170.117	115586.492	0.7888
Total		203545.363	14653238.523	100.0000

4h (Table 3, entry 8)

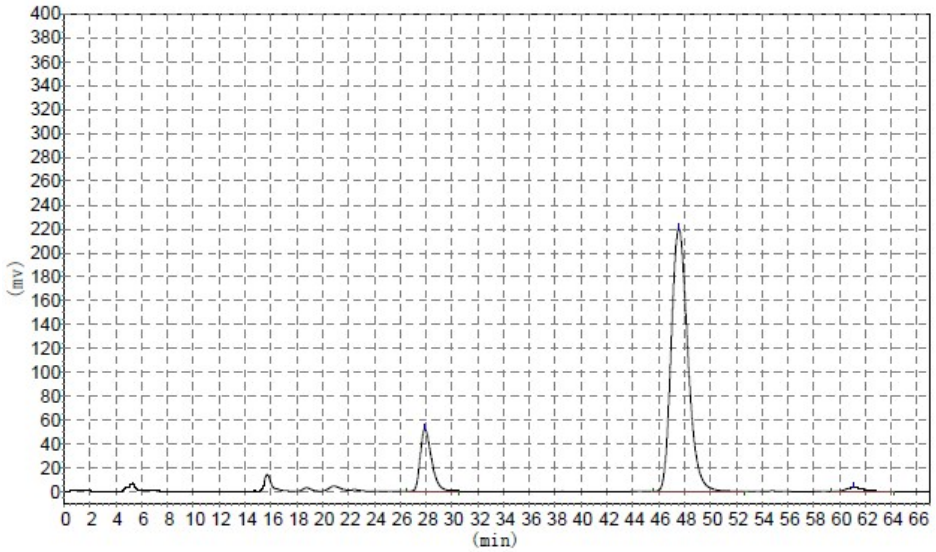


Racemic



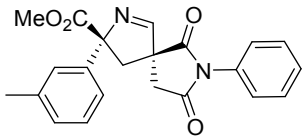
	Retention time	Height	Area	Area %
1	27.358	414828.125	27863978.000	60.6602
2	46.950	105195.281	8939775.000	19.4620
3	55.215	42863.590	9130742.000	19.8777
Total		562886.996	45934495.000	100.0000

Chiral



	Retention time	Height	Area	Area %
1	27.905	51925.957	3149579.000	13.6200
2	47.552	220292.719	19629770.000	84.8866
3	61.117	3168.851	345352.156	1.4934
Total		275387.526	23124701.156	100.0000

4i (Table 3, entry 9)



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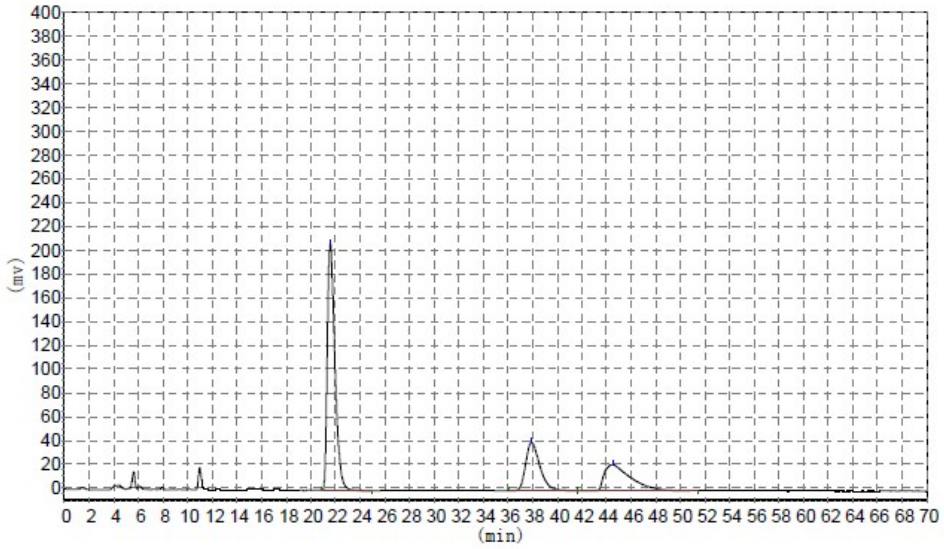
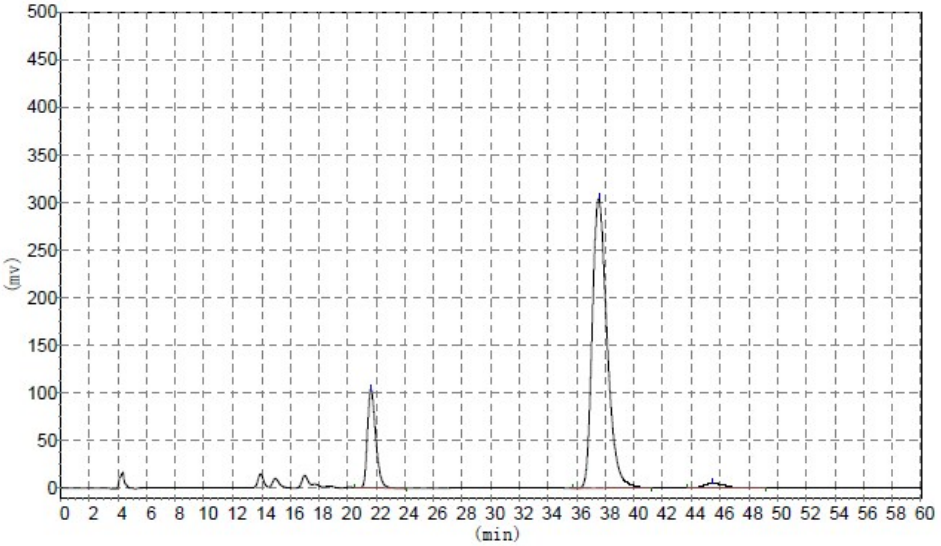


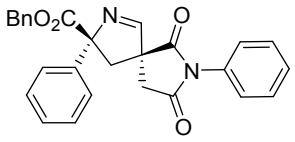
	Retention time	Height	Area	Area %
1	21.598	207805.156	8916301.000	57.5236
2	37.932	40555.484	3268461.000	21.0865
3	44.532	22156.643	3315491.000	21.3899
Total		270517.283	15500253.000	100.0000

Chiral

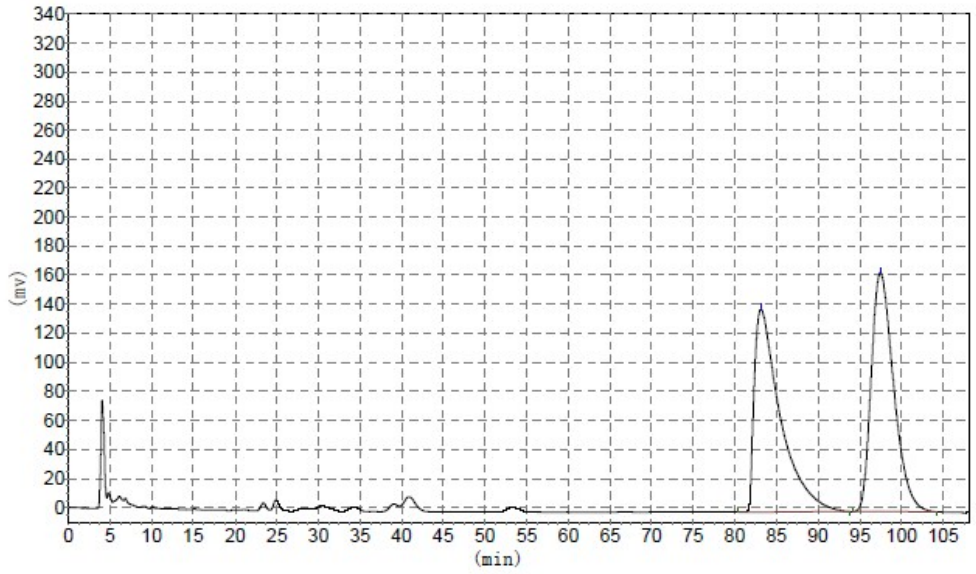


	Retention time	Height	Area	Area %
1	21.637	103207.781	4119187.250	15.5897
2	37.525	304082.438	21755050.000	82.3354
3	45.493	5264.083	548232.625	2.0749
Total		412554.302	26422469.875	100.0000

4k (Table 3, entry 11)

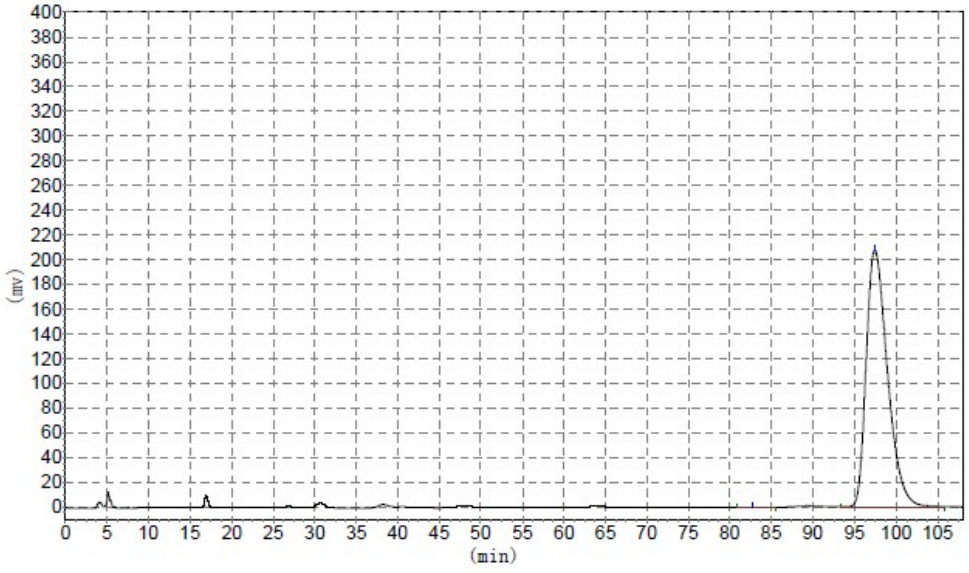


Racemic



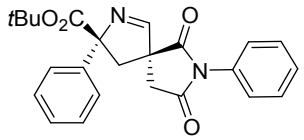
	Retention time	Height	Area	Area %
1	83.113	139814.469	30365838.000	49.6962
2	97.458	164624.047	30737100.000	50.3038
Total		304438.516	61102938.000	100.0000

Chiral

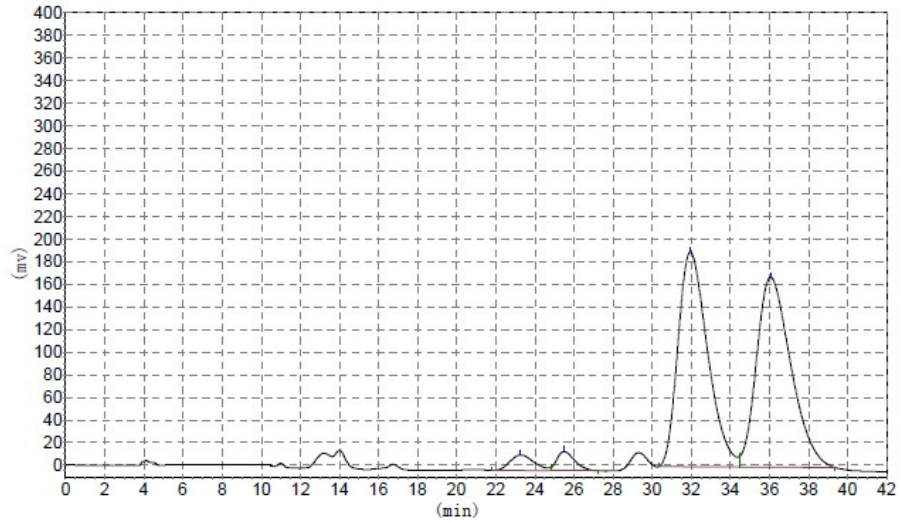


	Retention time	Height	Area	Area %
1	82.613	118.151	8593.600	0.0233
2	97.452	207636.234	36854520.000	99.9767
Total		207754.386	36863113.600	100.0000

4l (Table 3, entry 12)

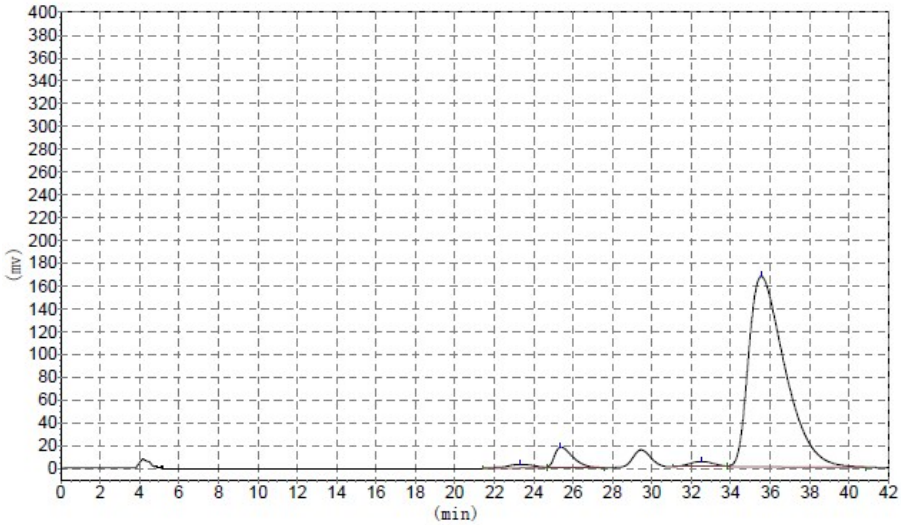


Racemic



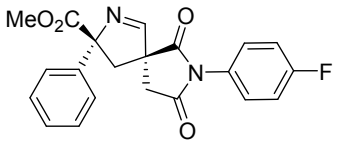
	Retention time	Height	Area	Area %
1	23.265	13504.556	1145165.625	2.6879
2	25.487	16894.695	1064512.750	2.4986
3	31.953	189812.828	20011708.000	46.9701
4	36.065	167891.719	20383798.000	47.8435
Total		388103.798	42605184.375	100.0000

Chiral

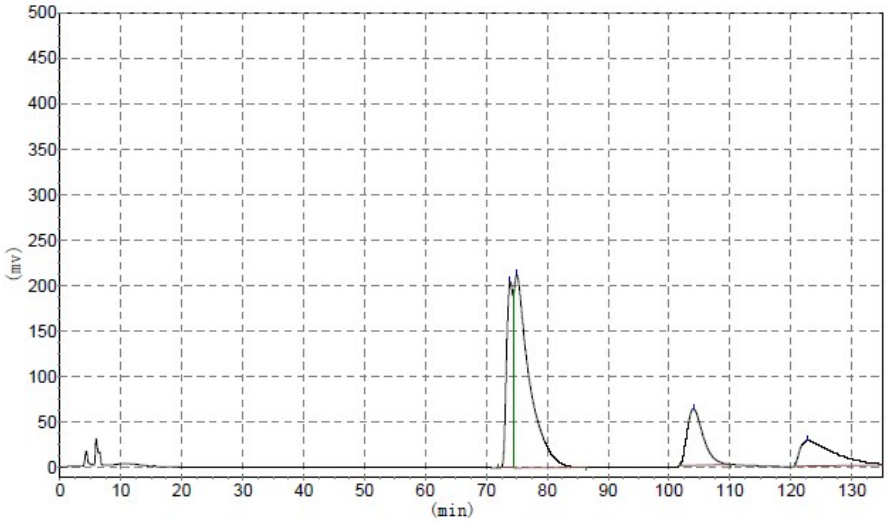


	Retention time	Height	Area	Area %
1	23.317	3262.273	321912.531	1.3830
2	25.375	18360.941	1183227.625	5.0832
3	32.513	4601.725	414376.313	1.7802
4	35.543	167227.594	21357498.000	91.7536
Total		193452.533	23277014.469	100.0000

4n (Table 4, entry 1)

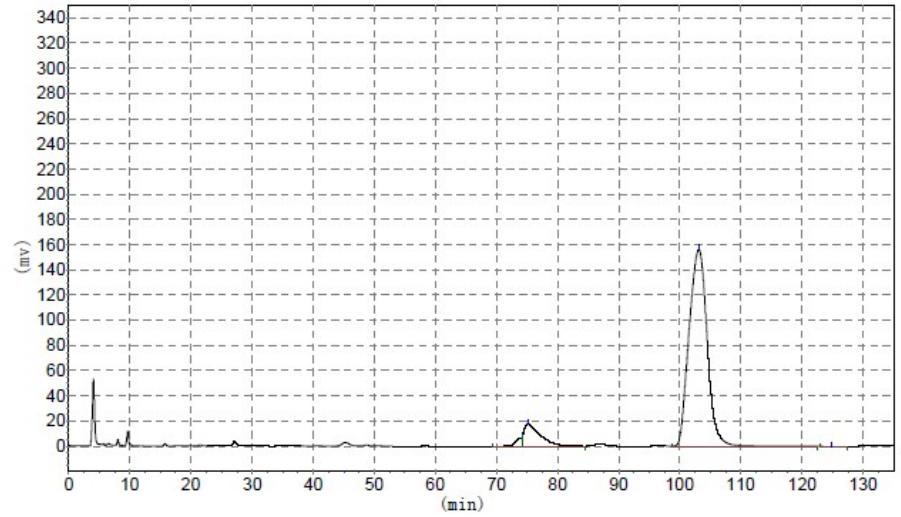


Racemic



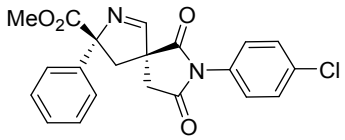
	Retention time	Height	Area	Area %
1	73.915	204185.047	15590406.000	21.1023
2	74.968	211920.750	36052064.000	48.7980
3	103.997	61874.652	11317497.000	15.3187
4	122.828	28230.711	10920220.000	14.7810
Total		506211.160	73880187.000	100.0000

Chiral

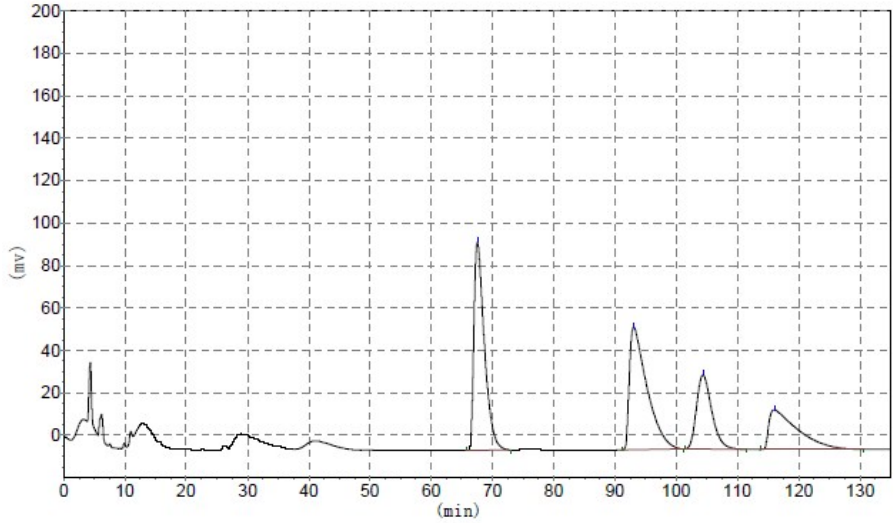


	Retention time	Height	Area	Area %
1	74.123	6637.056	422591.031	1.1706
2	75.127	17807.660	3295160.750	9.1281
3	103.095	156189.688	32121360.000	88.9814
4	124.795	31.638	4916.900	0.0136
Total		192337.880	36098978.259	100.0000

4o (Table 4, entry 2)

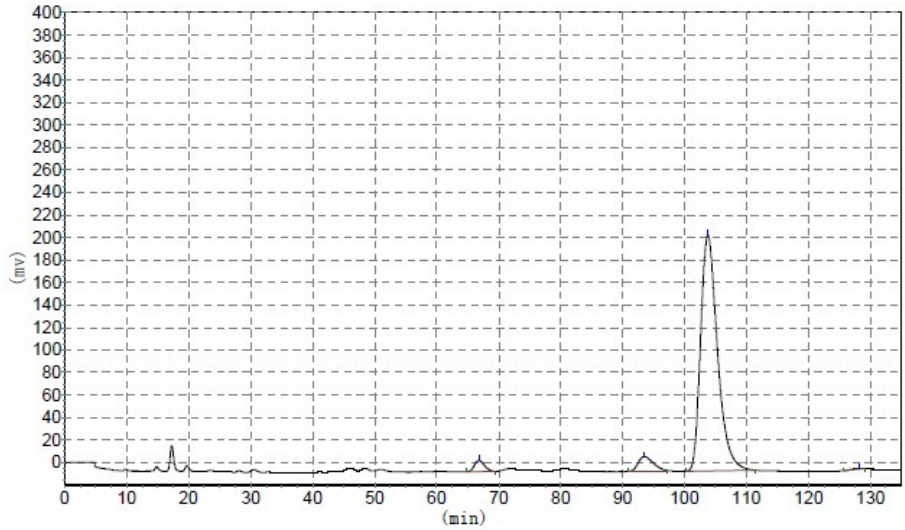


Racemic



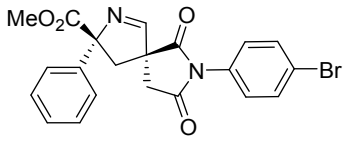
	Retention time	Height	Area	Area %
1	67.520	97756.664	11581517.000	32.7976
2	93.042	57789.734	11560930.000	32.7393
3	104.372	34957.930	6059267.000	17.1592
4	116.002	18725.674	6110374.000	17.3039
Total		209230.002	35312088.000	100.0000

Chiral

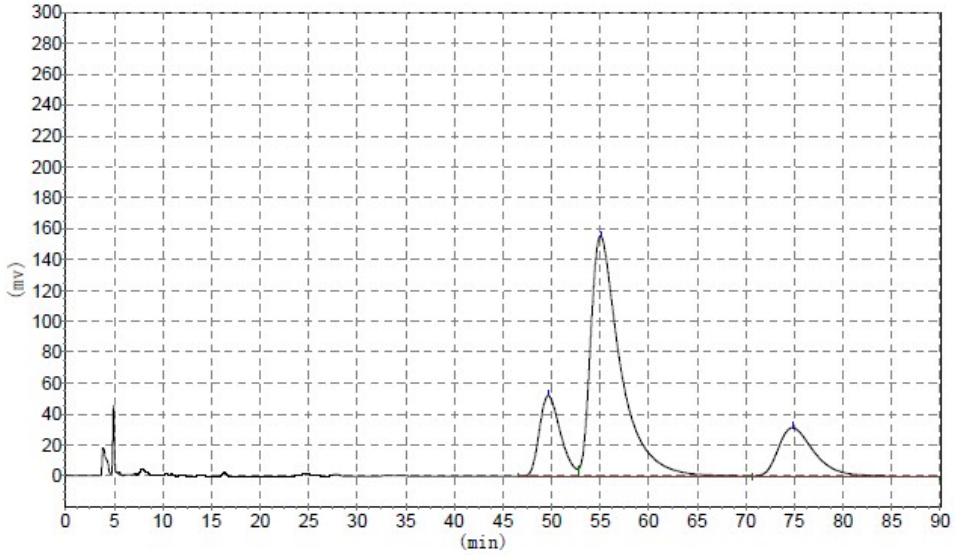


	Retention time	Height	Area	Area %
1	66.788	9747.520	1074881.250	2.5089
2	93.548	13049.151	2236789.000	5.2209
3	103.758	209587.656	39418560.000	92.0063
4	128.100	848.945	113070.180	0.2639
Total		233233.272	42843300.430	100.0000

4p (Table 4, entry 3)

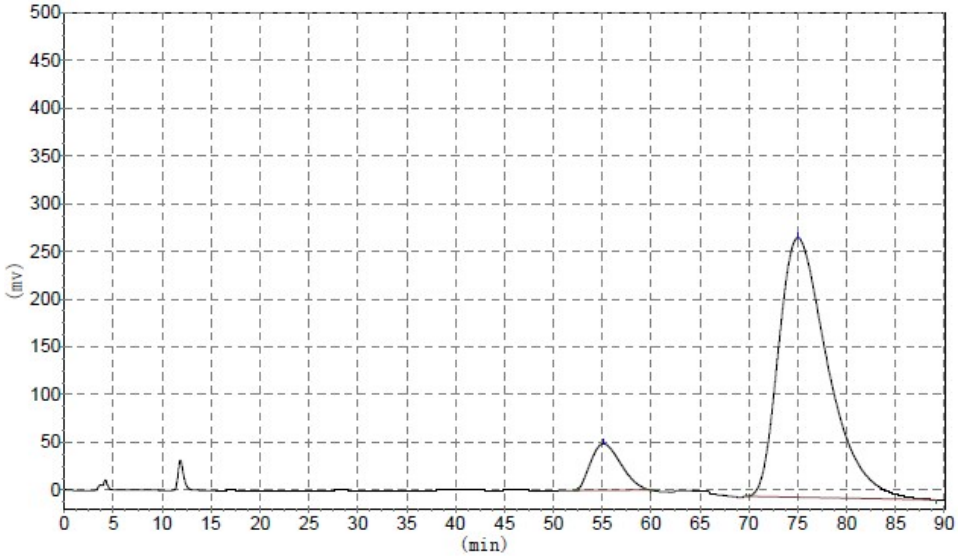


Racemic



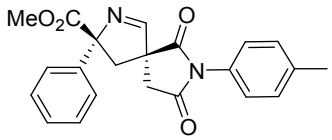
	Retention time	Height	Area	Area %
1	49.723	52189.402	7892572.500	16.0607
2	55.057	155581.625	33174672.000	67.5077
3	74.790	31435.391	8074849.500	16.4316
Total		239206.418	49142094.000	100.0000

Chiral

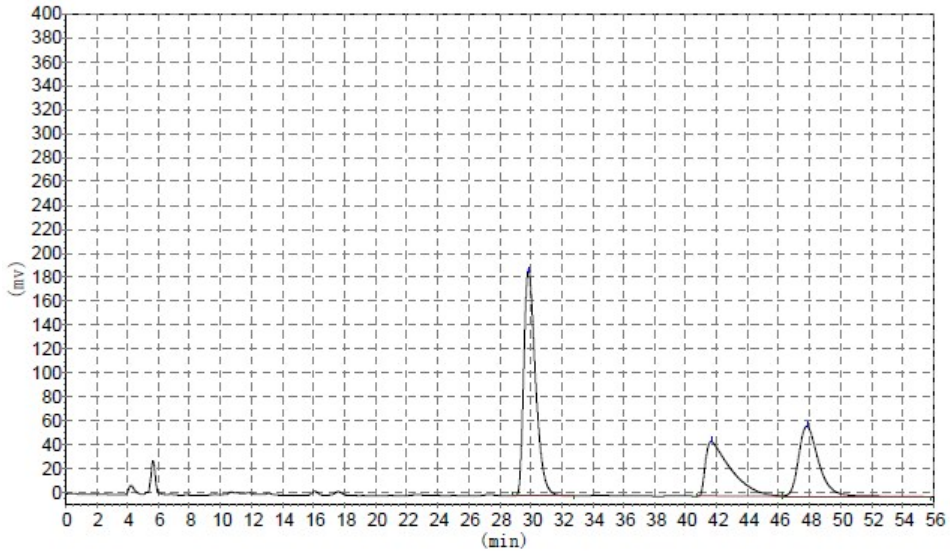


	Retention time	Height	Area	Area %
1	55.120	48886.105	10505936.000	9.9936
2	75.017	271732.125	94620376.000	90.0064
Total		320618.230	105126312.000	100.0000

4q (Table 4, entry 4)

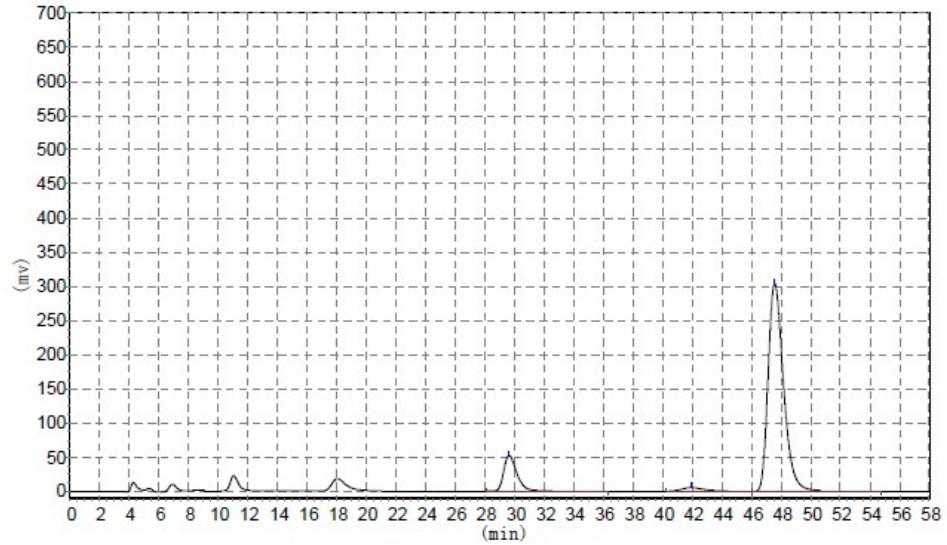


Racemic



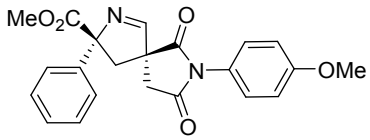
	Retention time	Height	Area	Area %
1	29.915	188730.719	9963227.000	48.9508
2	41.648	45588.941	5162542.500	25.3643
3	47.848	58550.133	5227768.000	25.6848
Total		292869.793	20353537.500	100.0000

Chiral

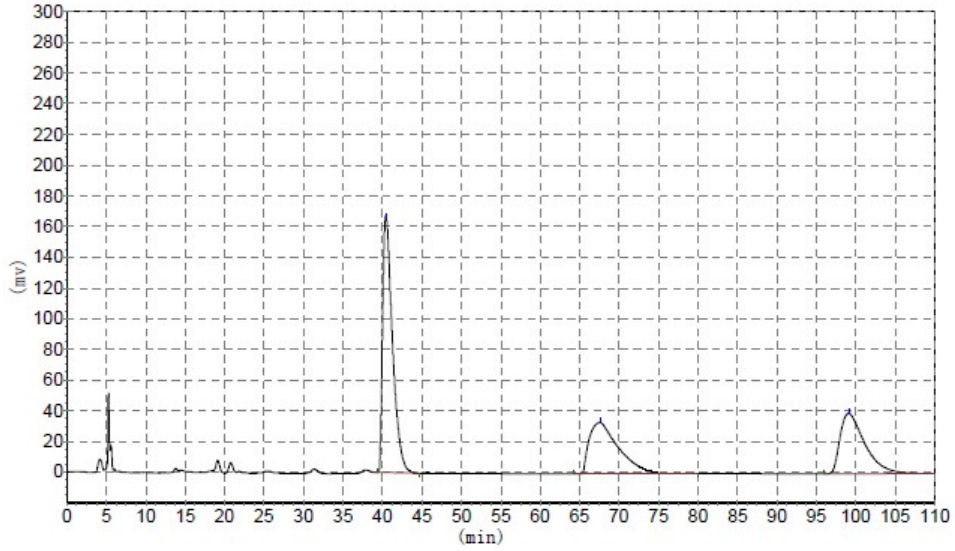


	Retention time	Height	Area	Area %
1	29.633	52466.211	3314411.250	12.8569
2	41.903	5492.313	624854.125	2.4239
3	47.563	304296.969	21839954.000	84.7192
Total		362255.493	25779219.375	100.0000

4r (Table 4, entry 5)

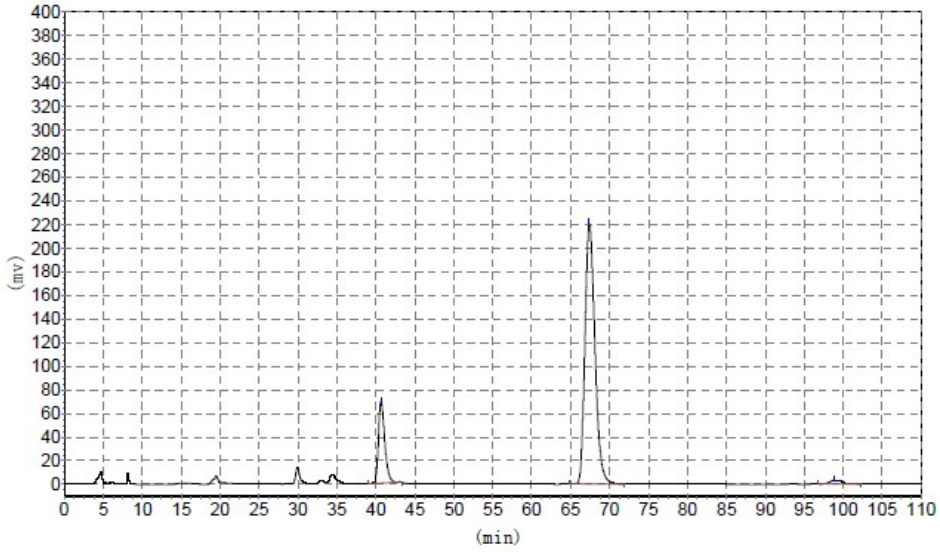


Racemic



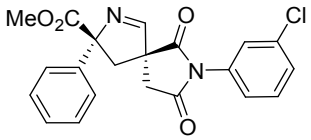
	Retention time	Height	Area	Area %
1	40.515	167938.953	14734355.000	45.8127
2	67.582	33420.172	8751329.000	27.2100
3	99.182	39464.215	8676457.000	26.9772
Total		240823.340	32162141.000	100.0000

Chiral

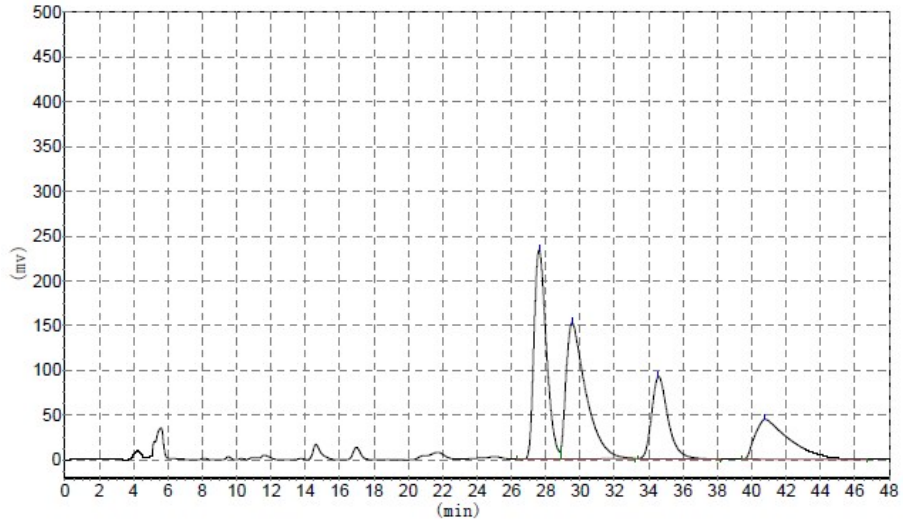


	Retention time	Height	Area	Area %
1	40.652	68961.180	3889175.500	16.2886
2	67.410	220405.609	19640948.000	82.2600
3	98.880	3163.151	346551.813	1.4514
Total		292529.940	23876675.313	100.0000

4s (Table 4, entry 6)

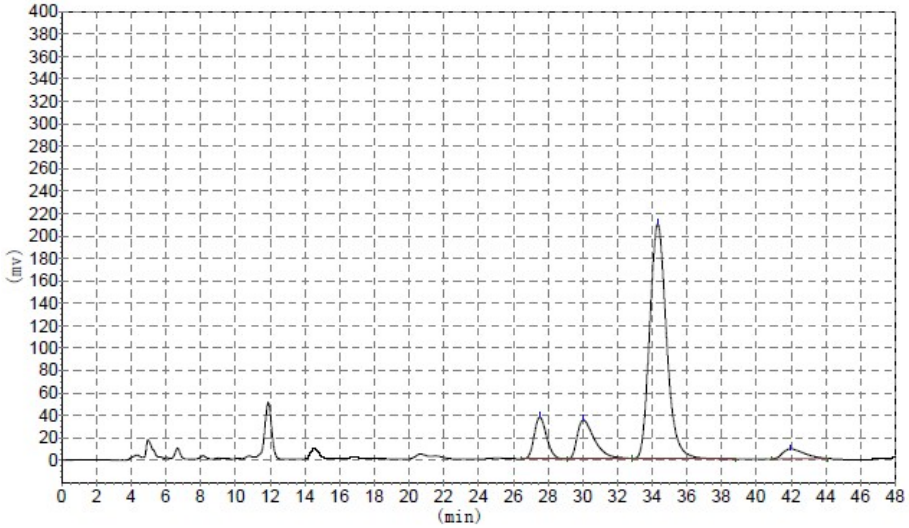


Racemic



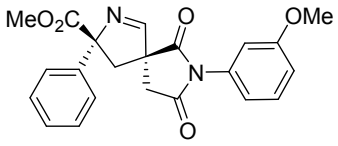
	Retention time	Height	Area	Area %
1	27.613	233280.328	11706223.000	32.5198
2	29.535	151850.906	12061943.000	33.5080
3	34.572	92106.453	6116046.500	16.9903
4	40.768	44477.320	6112985.000	16.9818
Total		521715.008	35997197.500	100.0000

Chiral

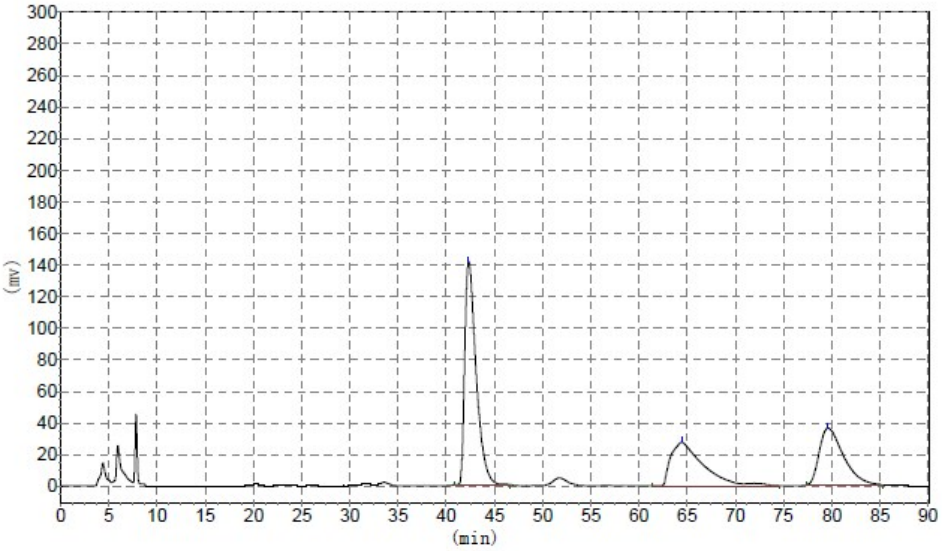


	Retention time	Height	Area	Area %
1	27.535	37305.121	1863199.000	9.6929
2	30.043	34817.625	2464022.750	12.8186
3	34.333	209592.219	14134456.000	73.5317
4	41.987	8816.754	760581.563	3.9568
Total		290531.719	19222259.313	100.0000

4t (Table 4, entry 7)

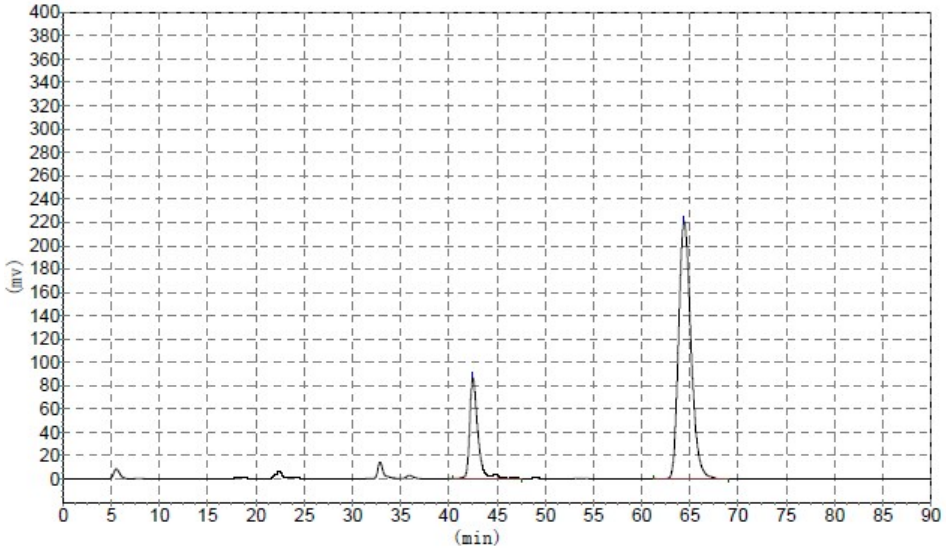


Racemic



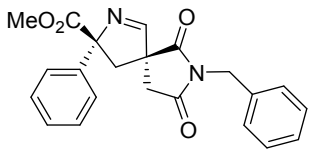
	Retention time	Height	Area	Area %
1	42.315	141201.531	11552185.000	43.4299
2	64.397	27483.164	6359936.000	23.9099
3	79.613	35896.031	6210495.000	23.3481
Total		293310.210	26599604.813	100.0000

Chiral

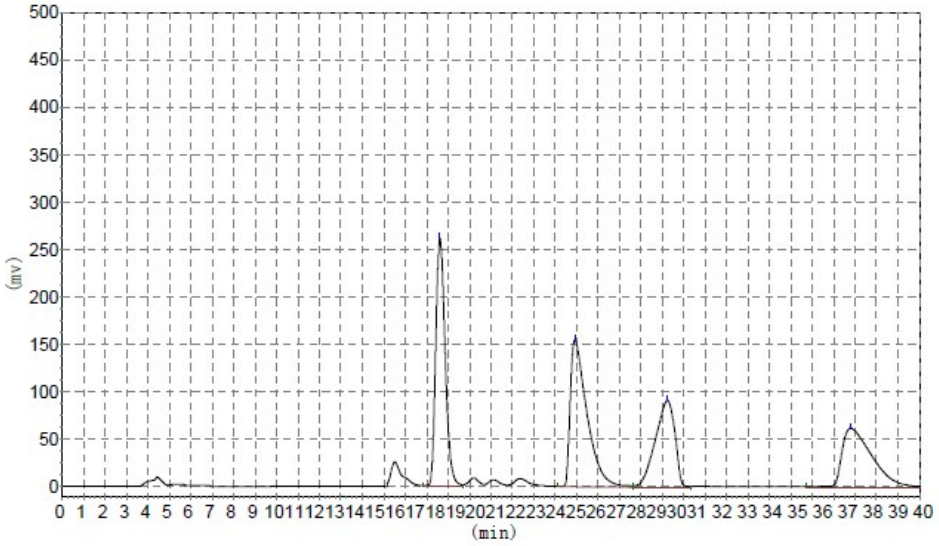


	Retention time	Height	Area	Area %
1	42.482	86216.125	5063314.500	20.4915
2	64.393	220421.656	19646074.000	79.5085
Total		306637.781	24709388.500	100.0000

4u (Table 4, entry 8)

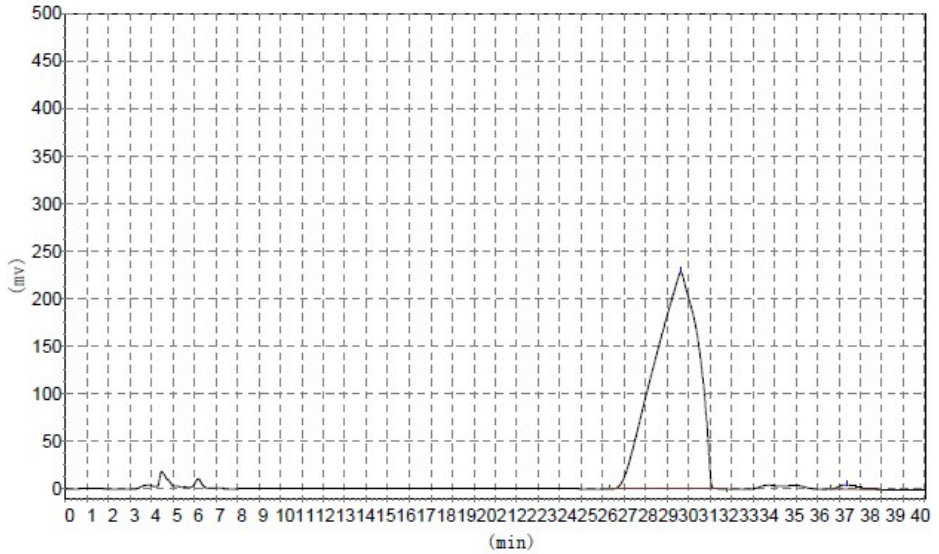


Racemic



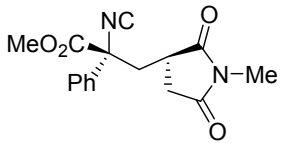
	Retention time	Height	Area	Area %
1	17.618	261673.750	8106926.500	28.7187
2	23.918	154887.219	8412767.000	29.8021
3	28.228	91267.852	5744226.000	20.3488
4	36.795	61795.234	5964846.500	21.1304
Total		569624.055	28228766.000	100.0000

Chiral

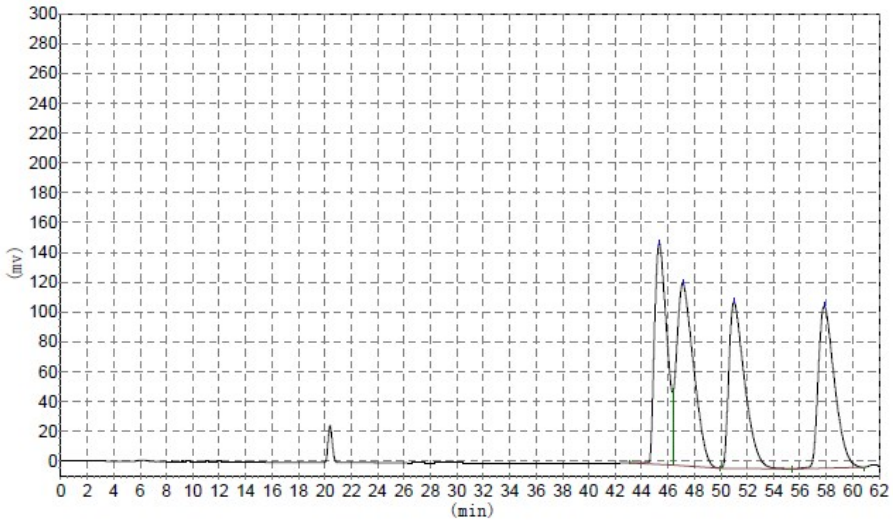


	Retention time	Height	Area	Area %
1	28.640	227896.297	32380596.000	99.1301
2	36.345	4632.177	284135.688	0.8699
Total		232528.474	32664731.688	100.0000

5b (Table 4, entry 9)

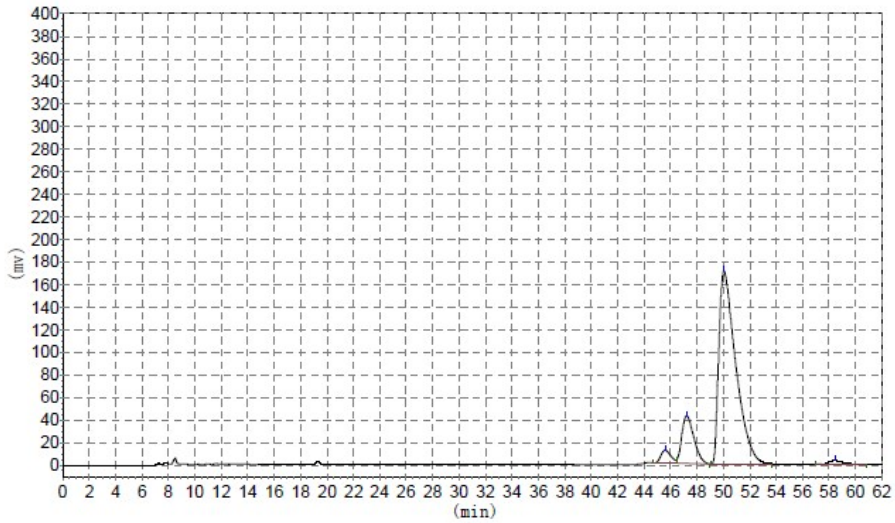


Racemic



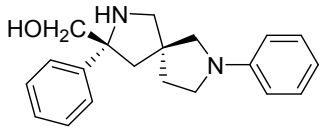
	Retention time	Height	Area	Area %
1	45.365	148486.156	9716581.000	24.6941
2	47.165	122505.313	11058268.000	28.1039
3	51.032	111422.242	9272898.000	23.5665
4	57.898	108511.359	9300110.000	23.6356
Total		490925.070	39347857.000	100.0000

Chiral

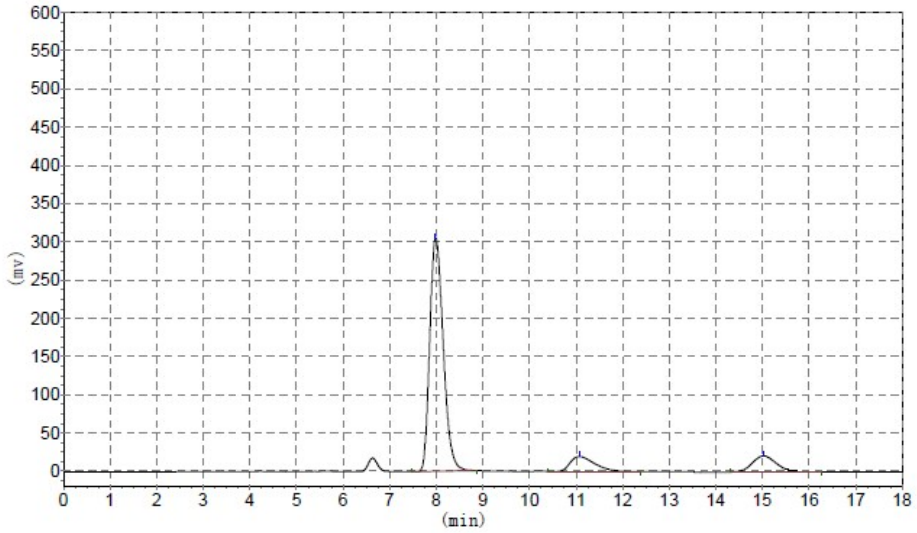


	Retention time	Height	Area	Area %
1	45.595	11344.293	596353.125	3.1865
2	47.222	42212.438	2691395.250	14.3809
3	50.053	170978.391	15157123.000	80.9887
4	58.427	3677.818	270242.313	1.4440
Total		228212.939	18715113.688	100.0000

6a (Scheme 3)

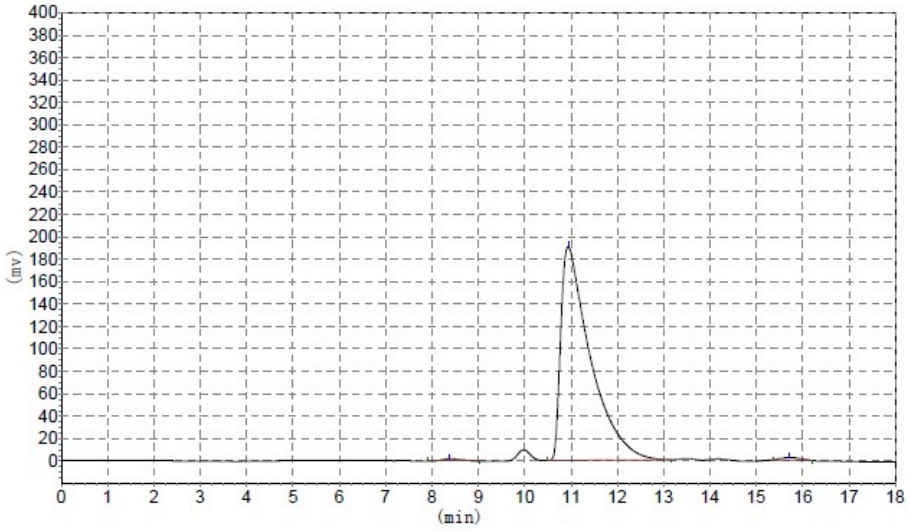


Racemic



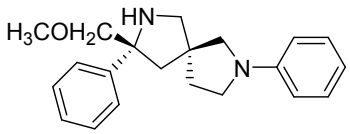
	Retention time	Height	Area	Area %
1	7.988	305286.750	6135550.500	80.4896
2	11.070	19773.064	729692.500	9.5725
3	15.025	21030.848	757538.750	9.9378
Total		346090.662	7622781.750	100.0000

Chiral

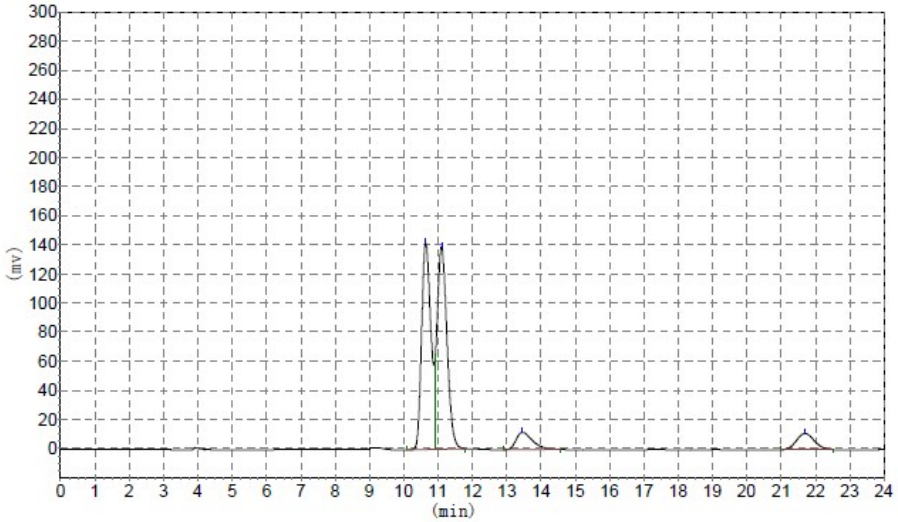


	Retention time	Height	Area	Area %
1	8.385	2149.348	58969.551	0.6883
2	10.938	190845.734	8447273.000	98.6023
3	15.720	2144.435	60775.102	0.7094
Total		195139.517	8567017.652	100.0000

6b (Scheme 3)

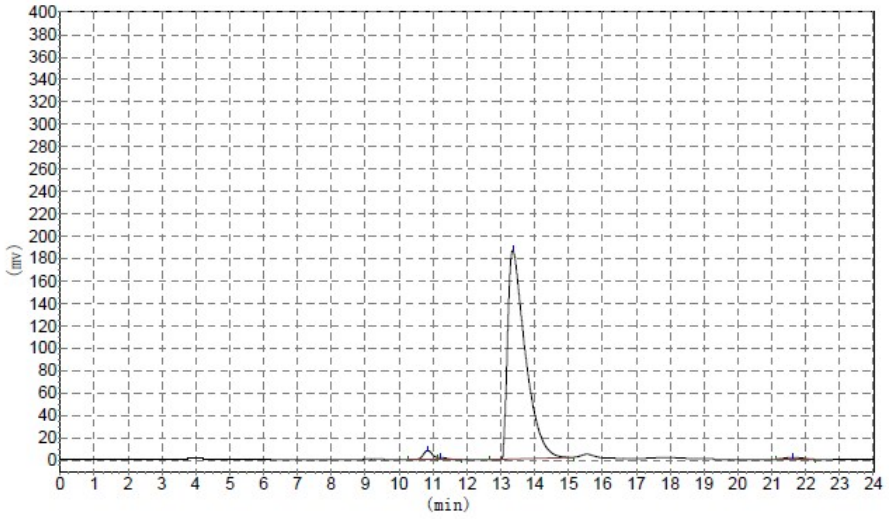


Racemic



	Retention time	Height	Area	Area %
1	10.643	141654.391	2728025.750	43.4988
2	11.103	139056.234	2737021.250	43.6422
3	13.463	11935.667	396898.750	6.3286
4	21.695	11209.421	409554.500	6.5304
Total		303855.713	6271500.250	100.0000

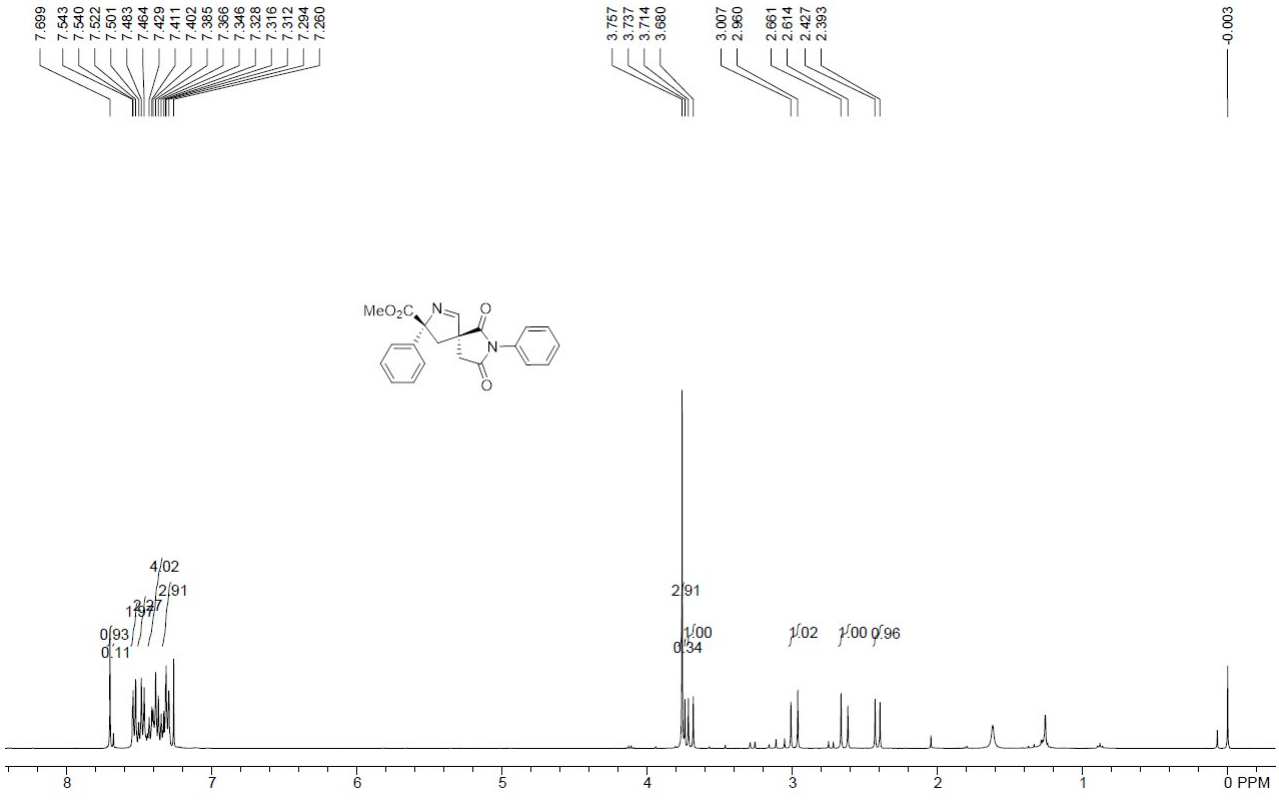
Chiral



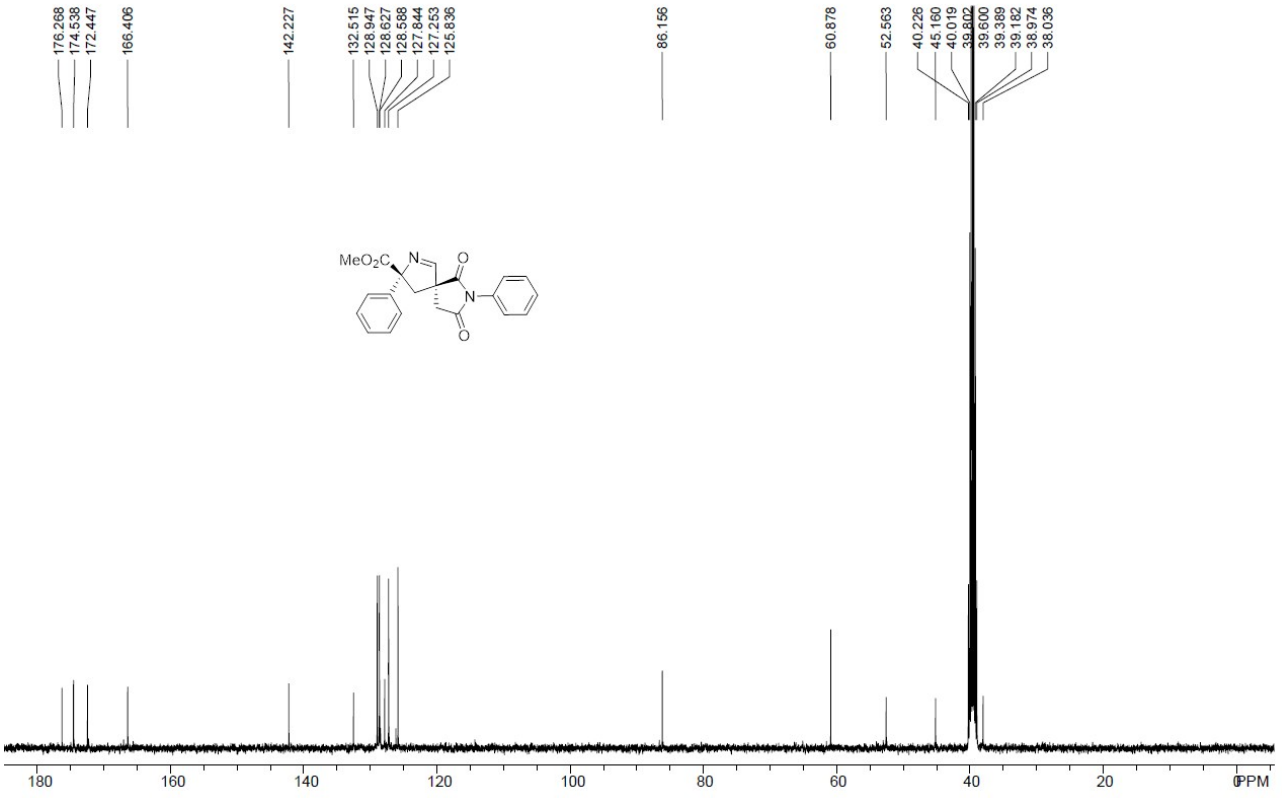
	Retention time	Height	Area	Area %
1	10.840	8111.668	156334.438	2.2302
2	11.230	1891.657	34500.027	0.4922
3	13.352	186452.313	6753637.000	96.3466
4	21.617	1682.312	65257.305	0.9310
Total		198137.949	7009728.770	100.0000

6. Copies of NMR Spectra for the Compounds 4 and 6

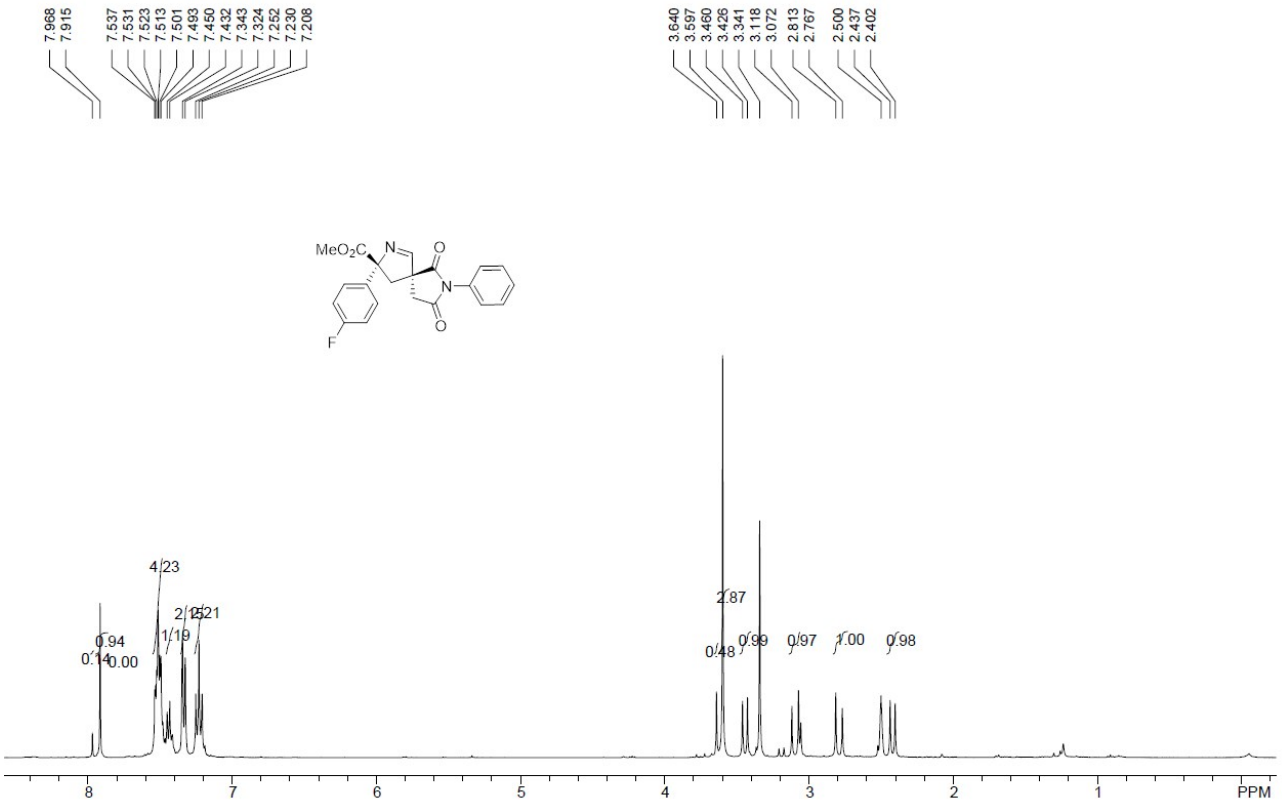
^{1}H NMR of **4a**



^{13}C NMR of **4a**



^{1}H NMR of **4b**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7.513
7.501
7.493
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7.343
7.324
7.252
7.230
7.208
3.640
3.597
3.460
3.426
3.341
3.118
3.072
2.813
2.767
2.500
2.437
2.402
MeO2C
N
O
O
N
O
F
4.23
2.87
0.94
0.14
0.00
1.19
0.48
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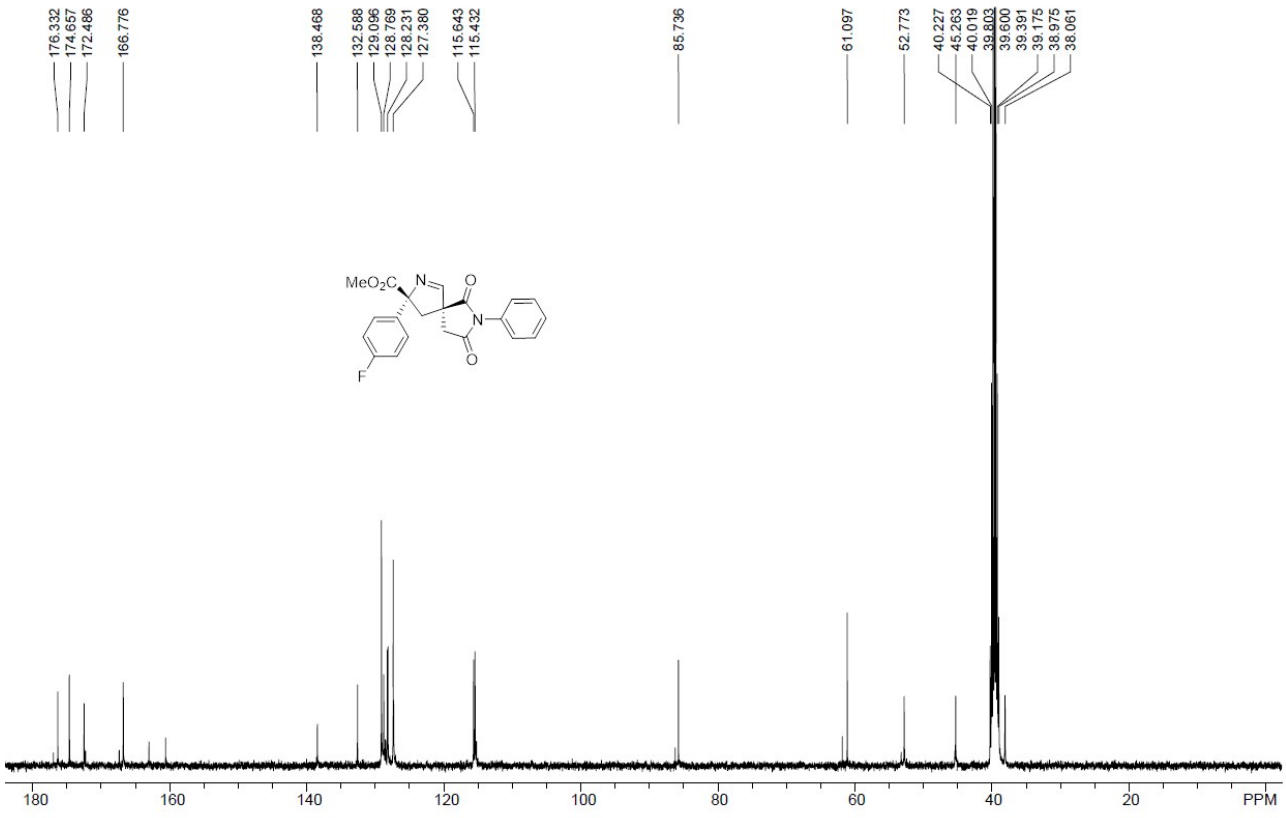
0.97
1.00
0.98
8
7
6
5
4
3
2
1
PPM

^{13}C NMR of **4b**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174.657
172.486
166.776
138.468
132.588
129.096
128.769
128.231
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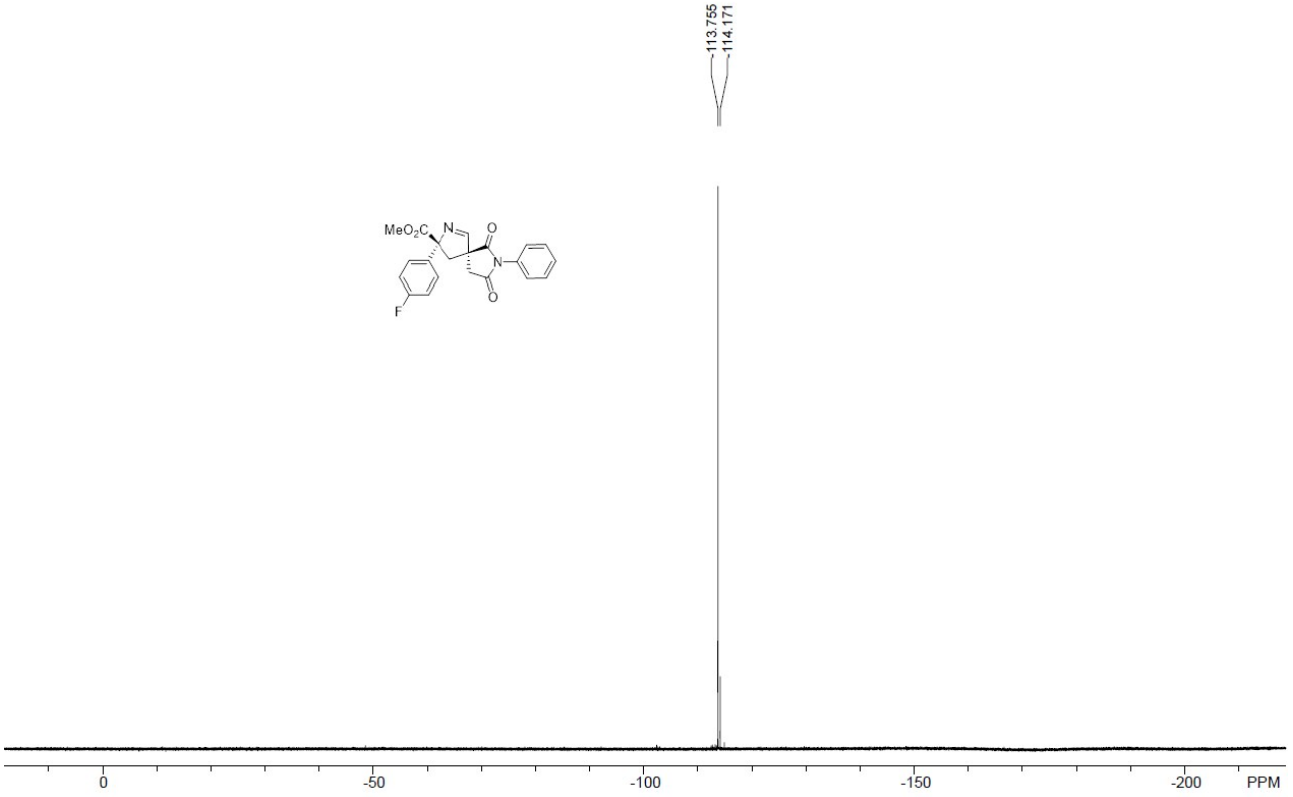
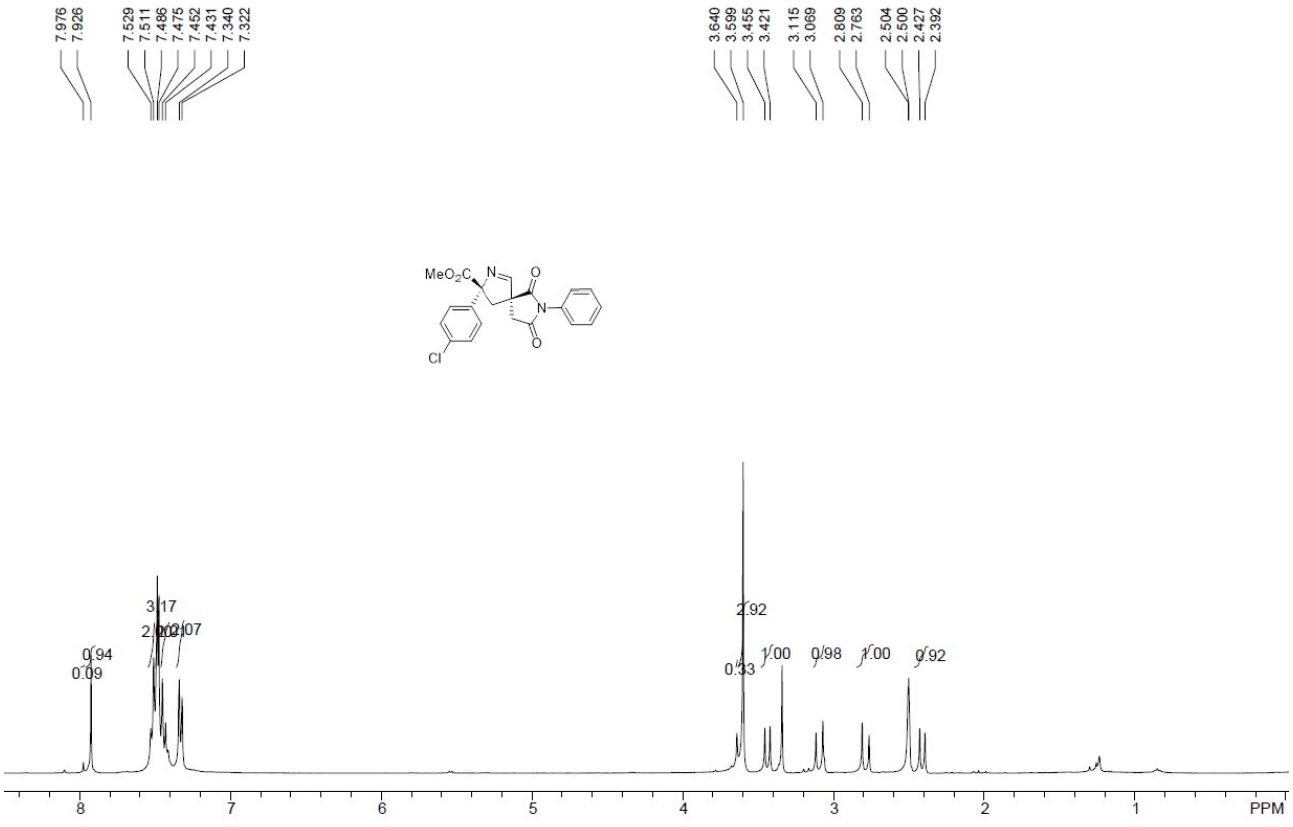
115.643
115.432
85.736
61.097
52.773
40.227
45.263
40.019
39.803
39.600
39.391
39.175
38.975
38.061
MeO2C
N
O
O
N
O
F
180
160
140
120
100
80
60
40
20
PPM

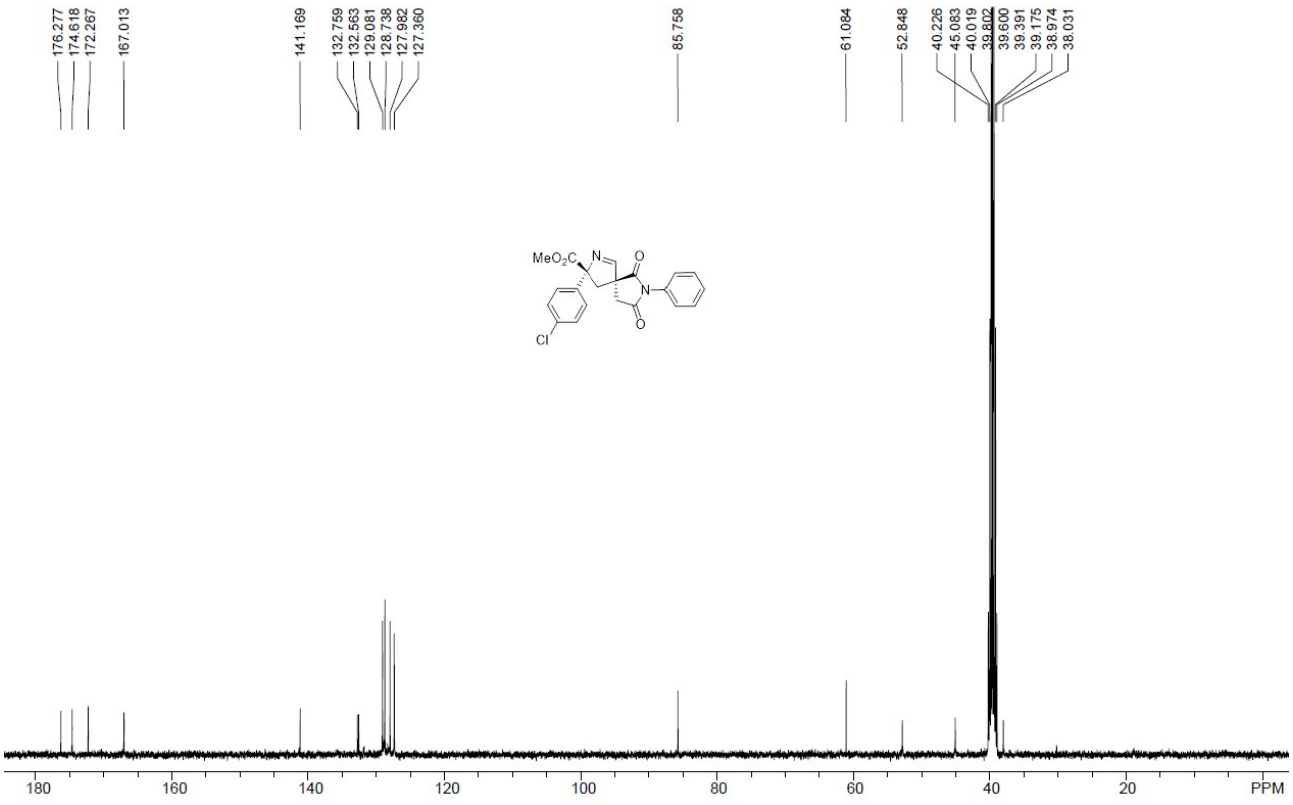
^{19}F NMR of **4b**



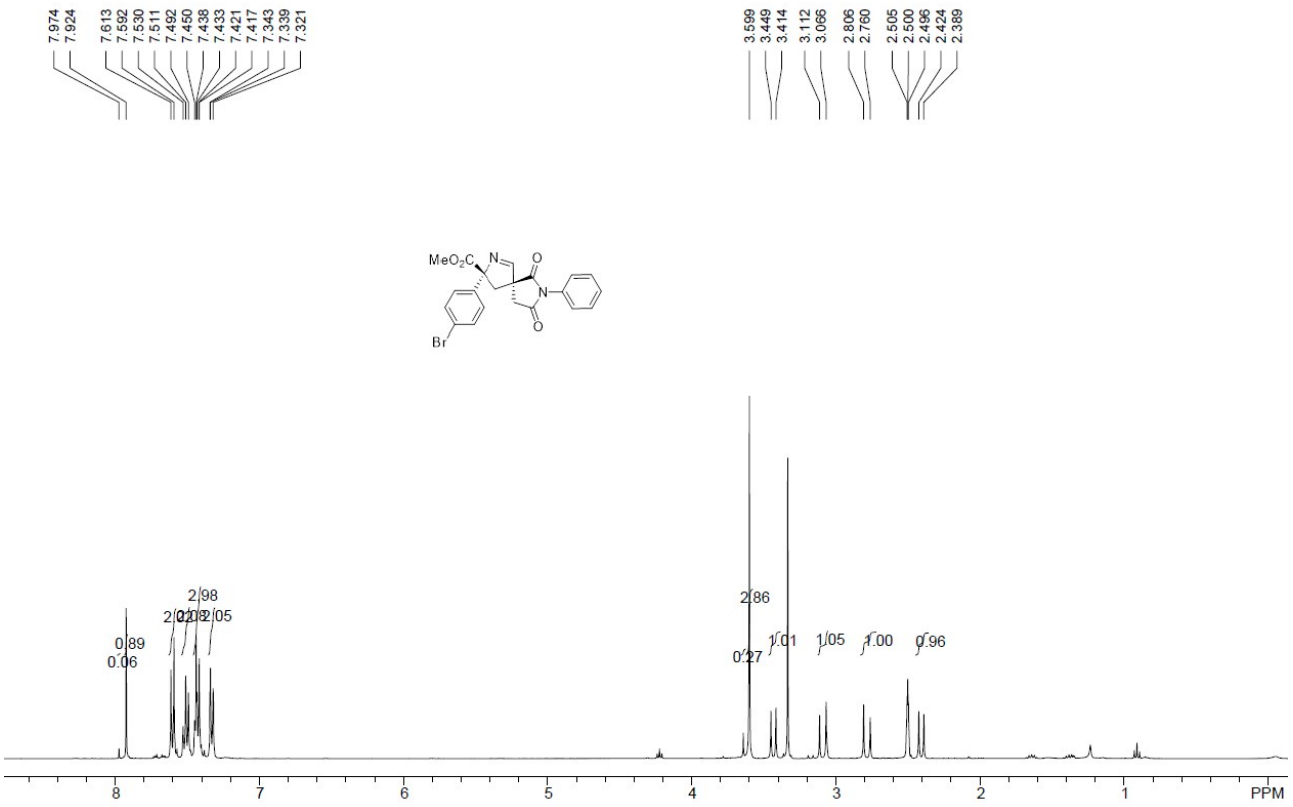
^{1}H NMR of **4c**



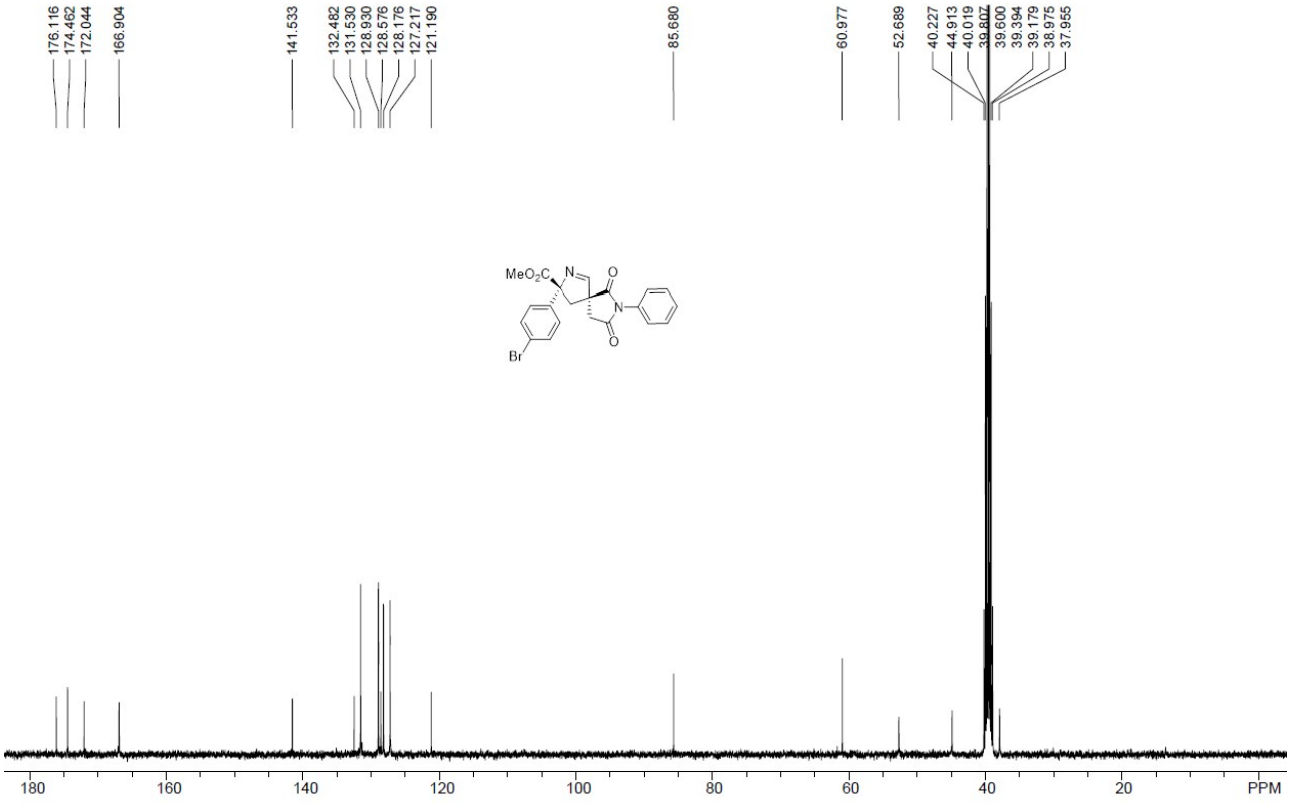
^{13}C NMR of **4c**



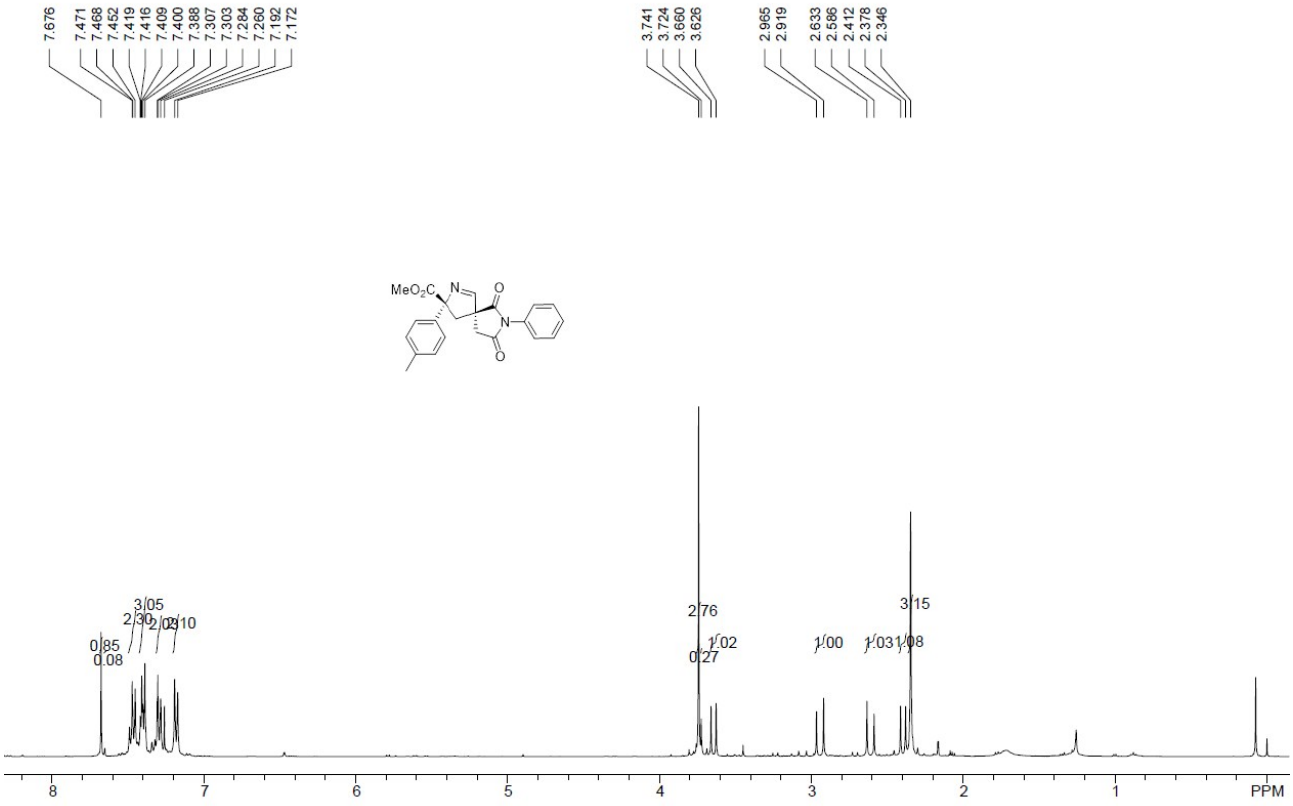
^{1}H NMR of **4d**



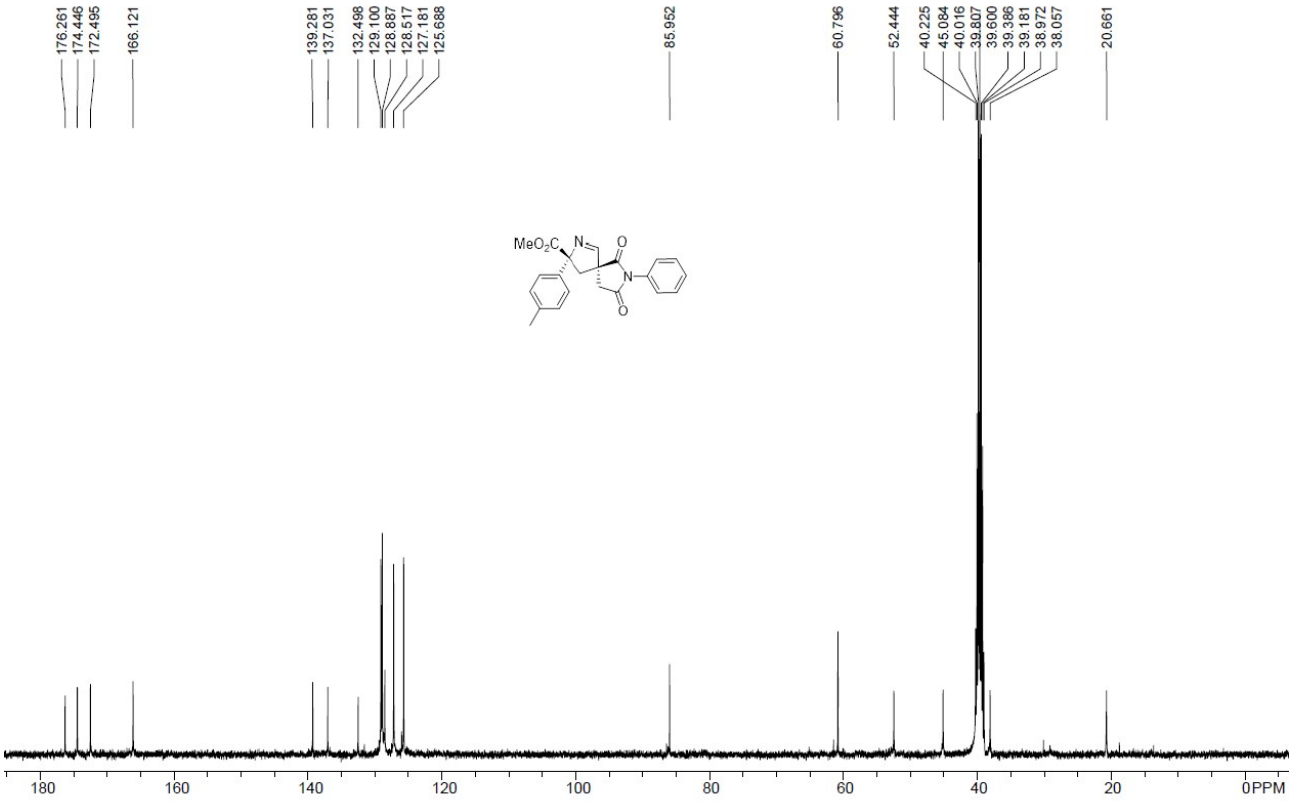
^{13}C NMR of **4d**



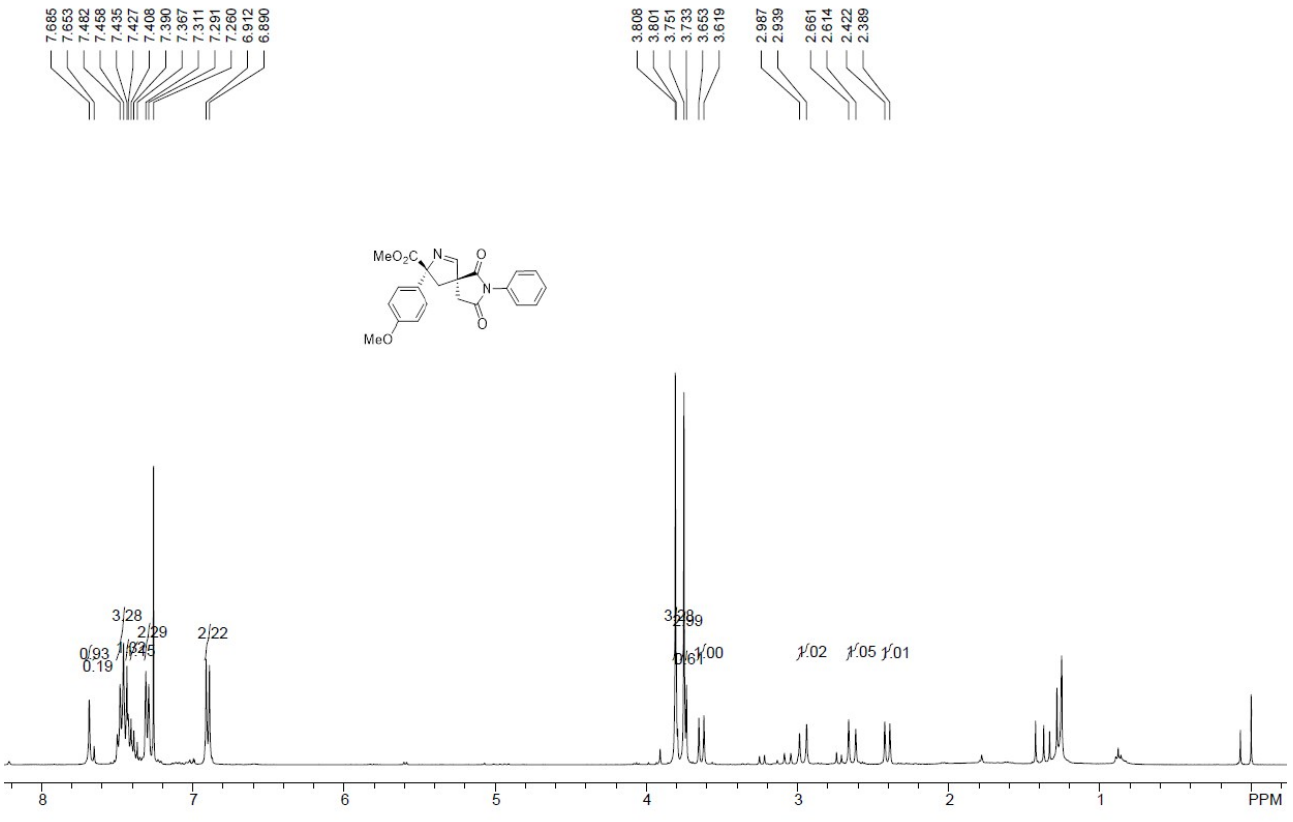
^{1}H NMR of **4e**



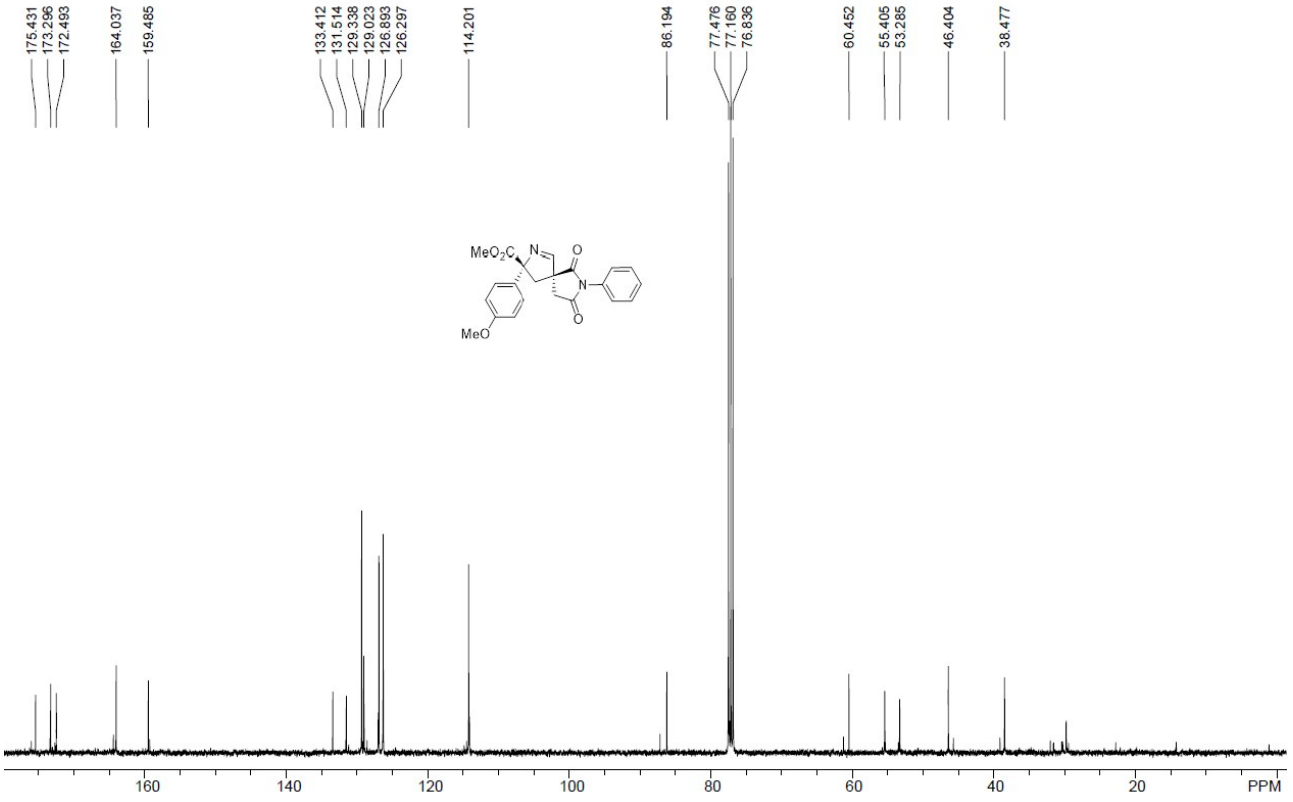
^{13}C NMR of **4e**



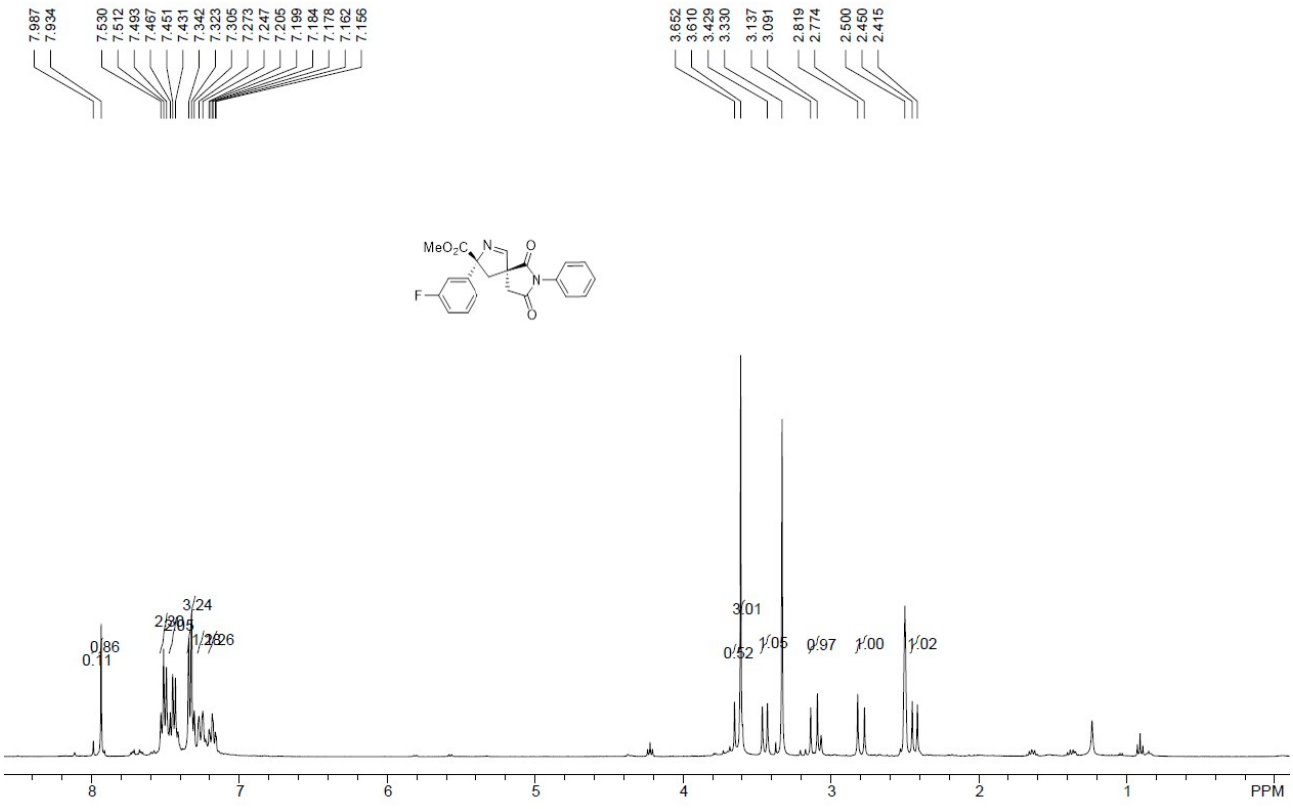
^{1}H NMR of **4f**



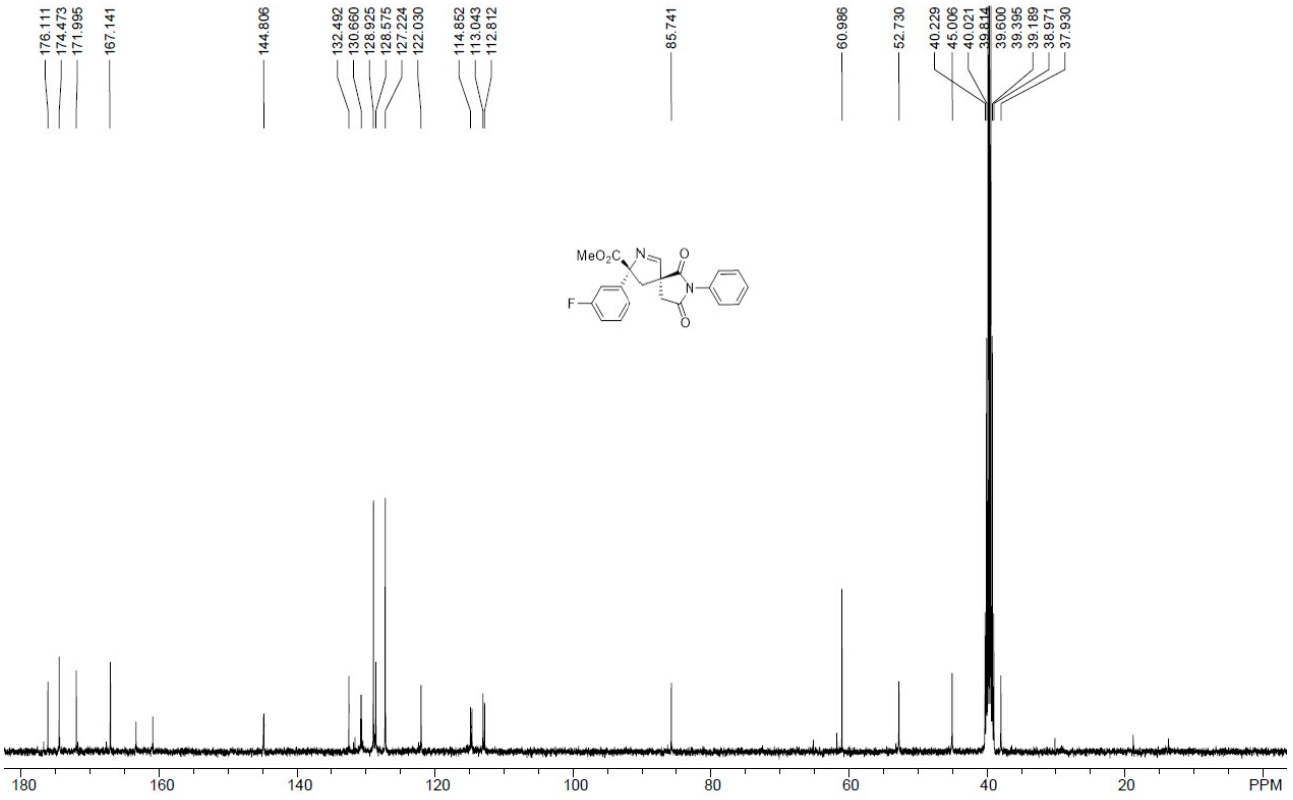
^{13}C NMR of **4f**



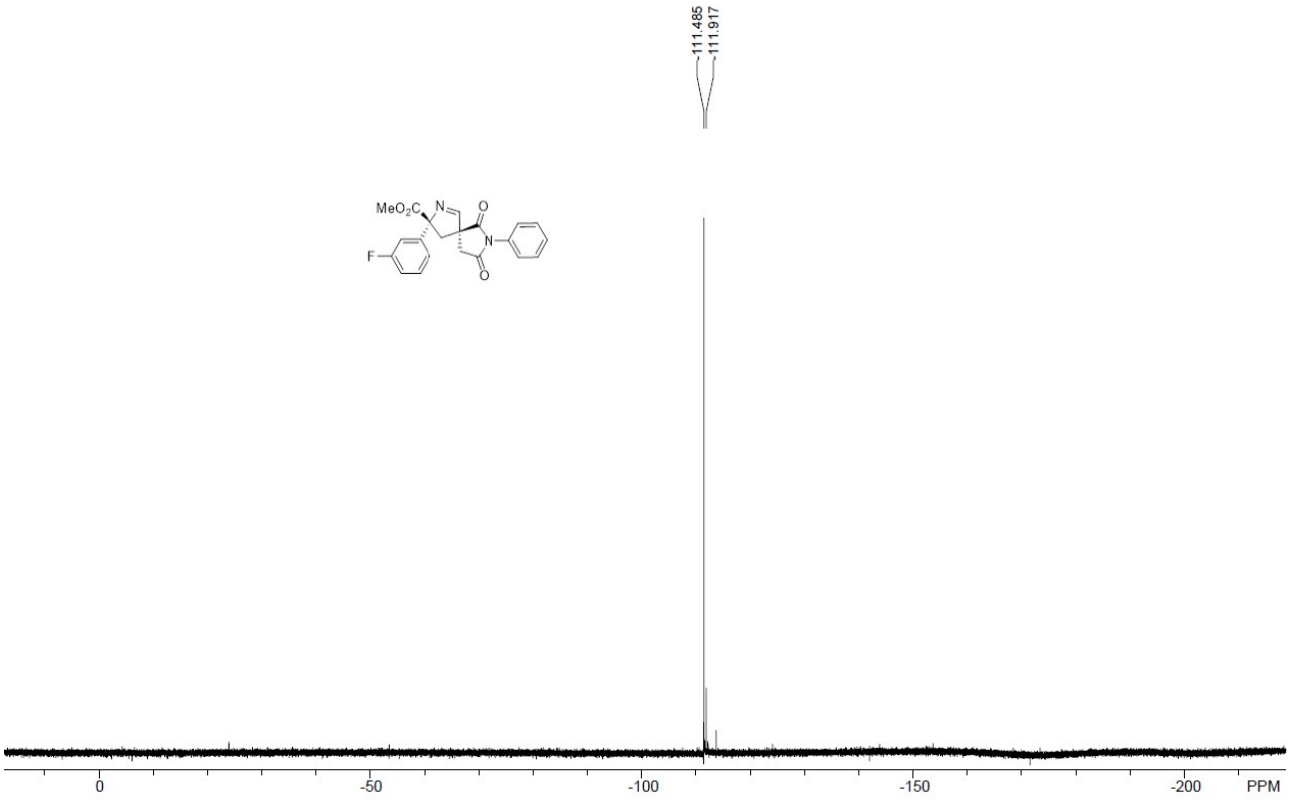
^{1}H NMR of **4g**



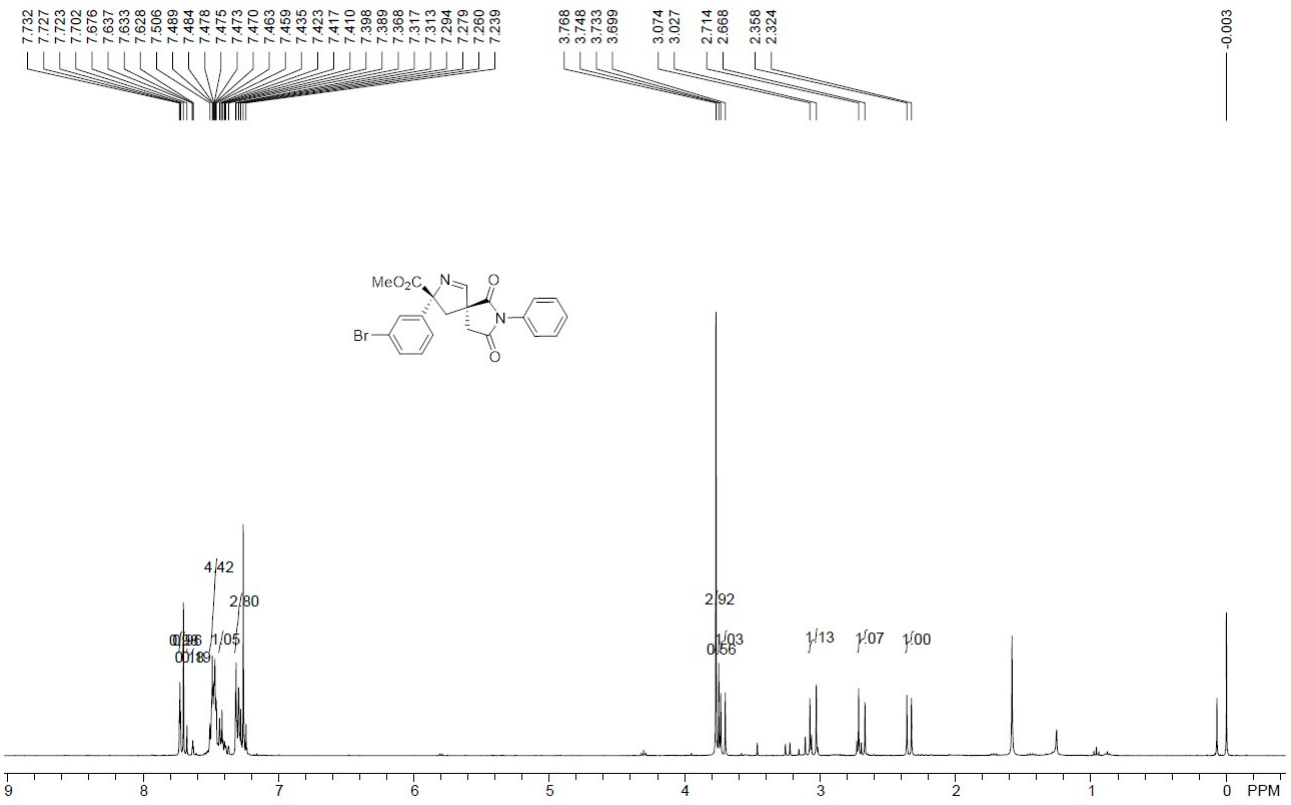
^{13}C NMR of **4g**



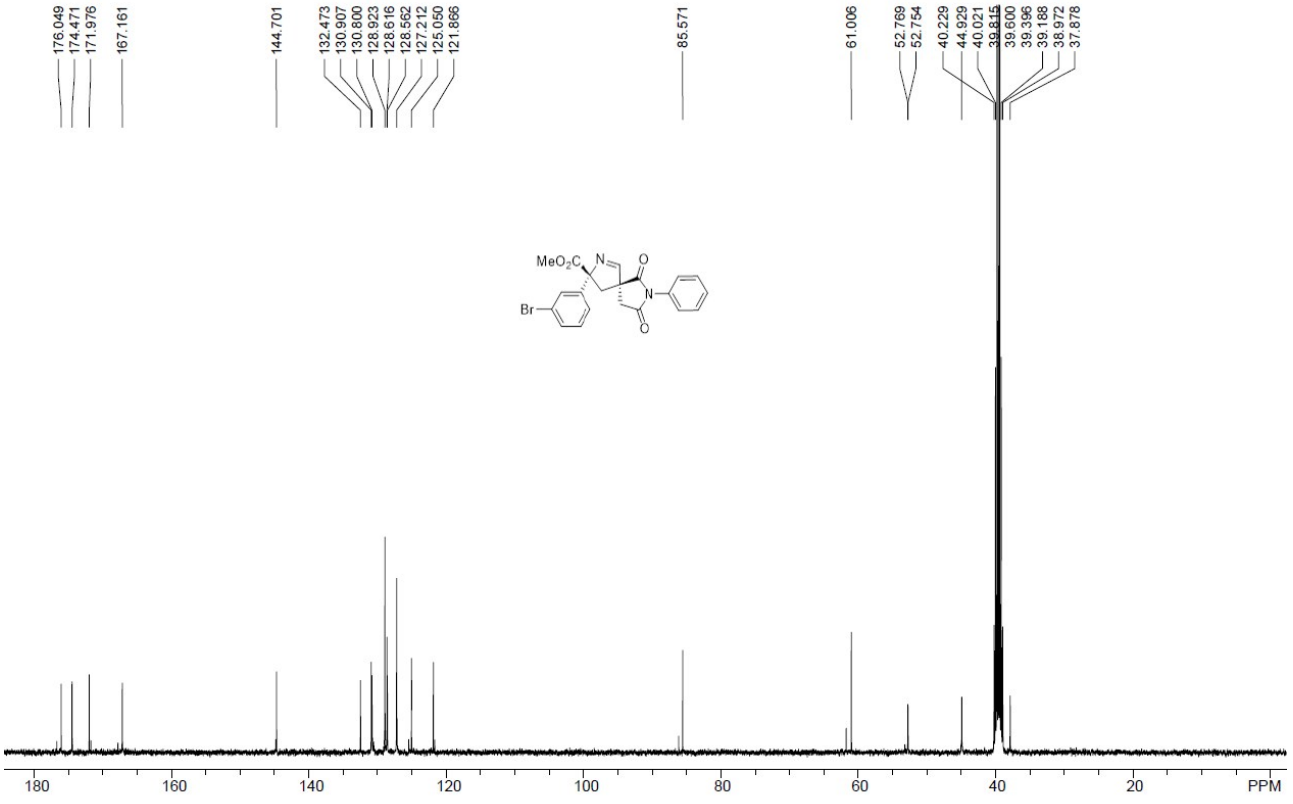
^{19}F NMR of **4g**



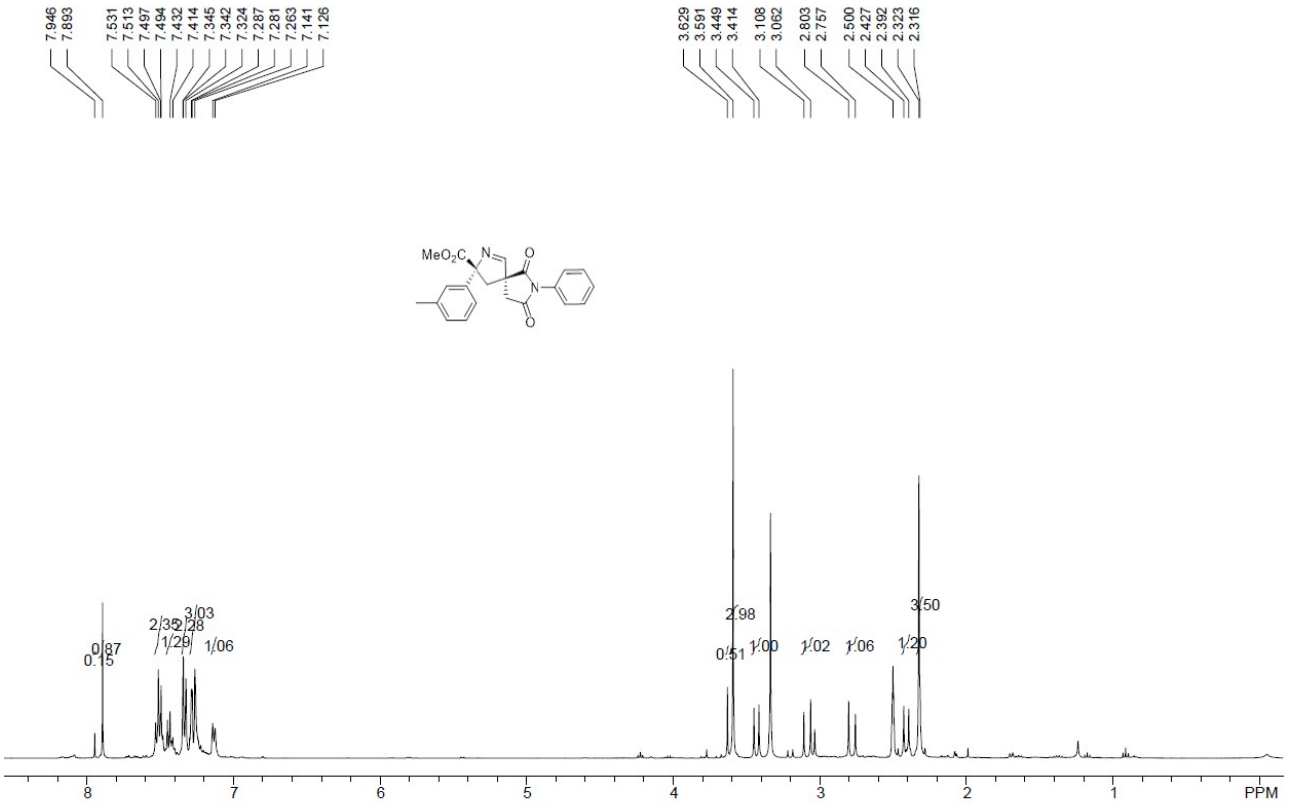
^{1}H NMR of **4h**



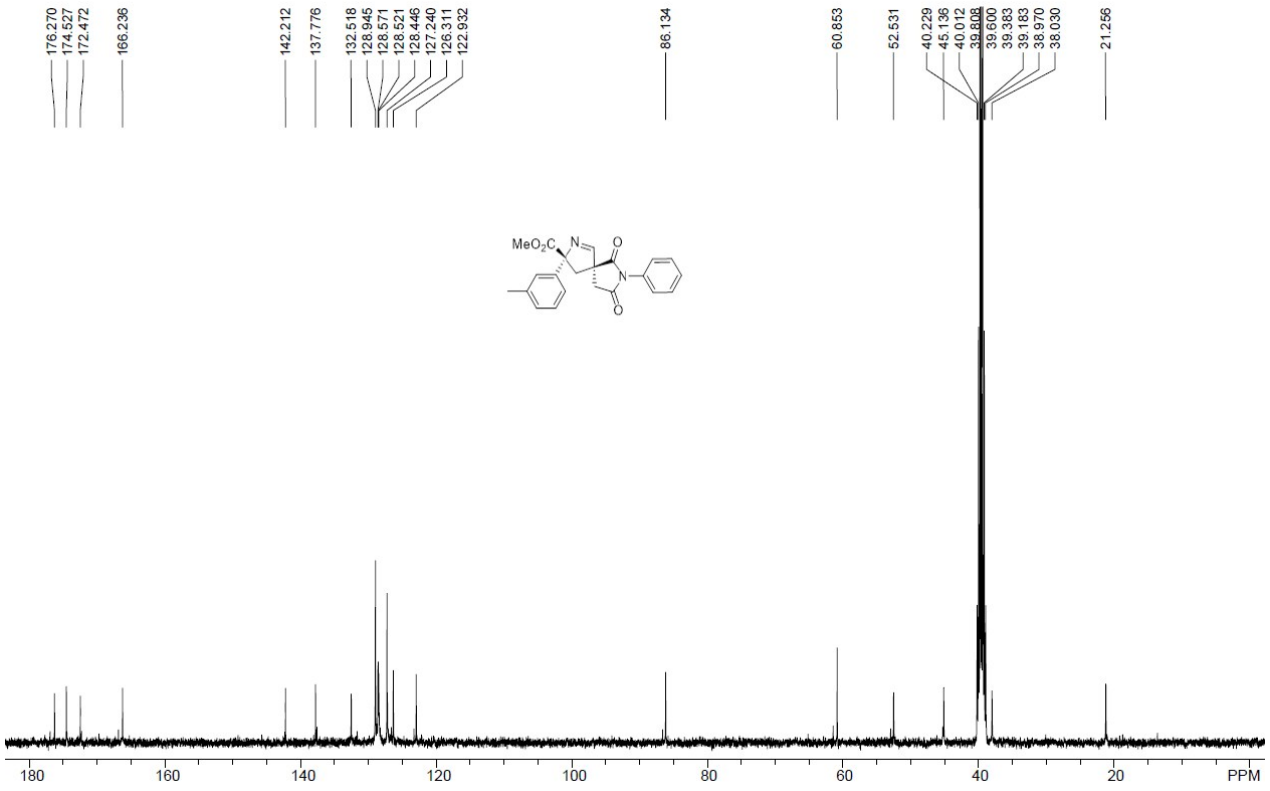
^{13}C NMR of **4h**



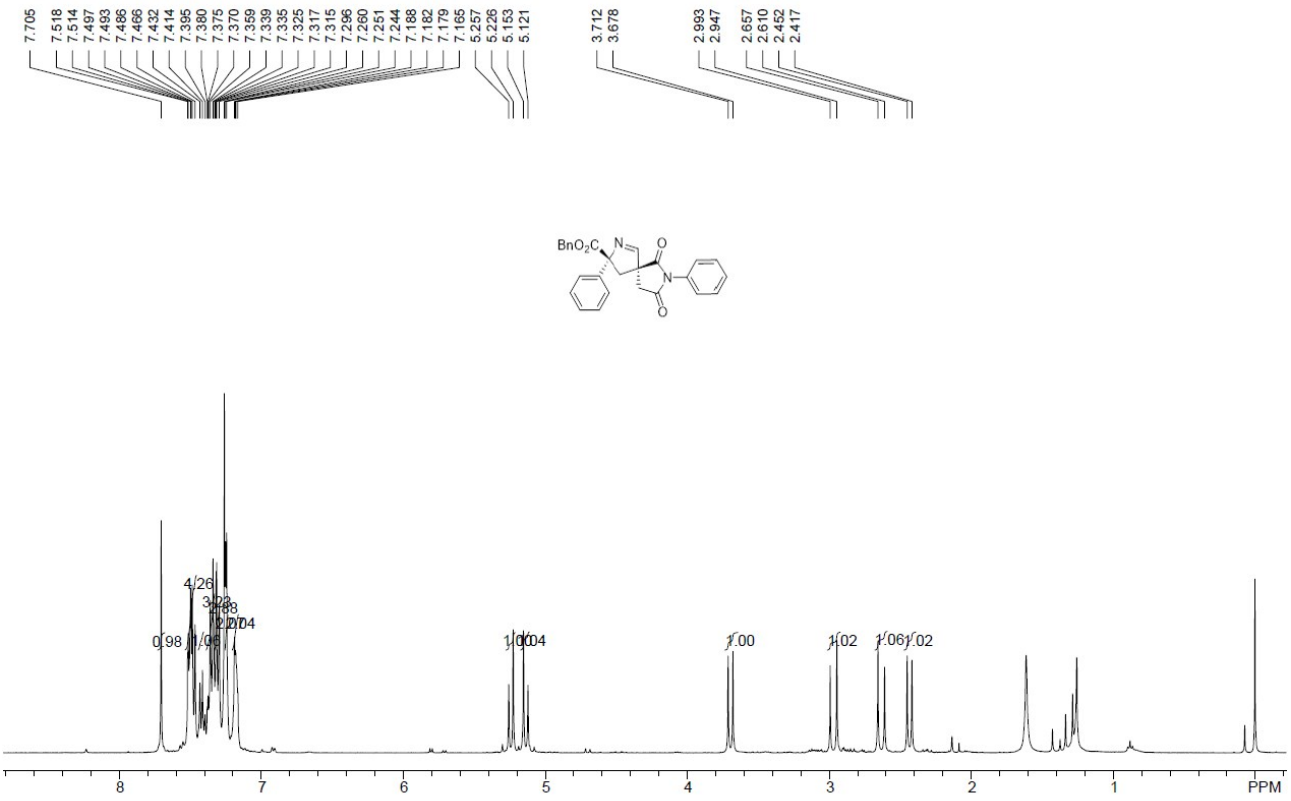
^{1}H NMR of **4i**



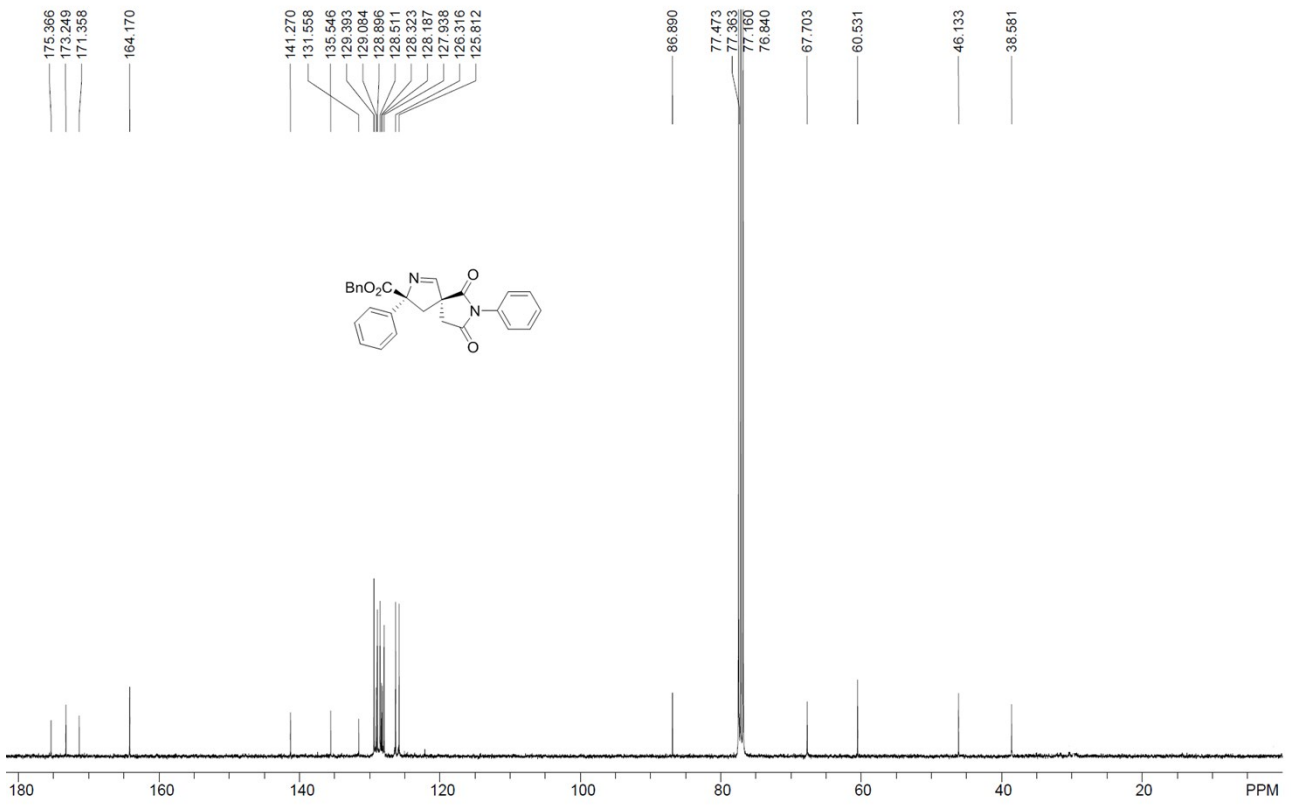
^{13}C NMR of **4i**



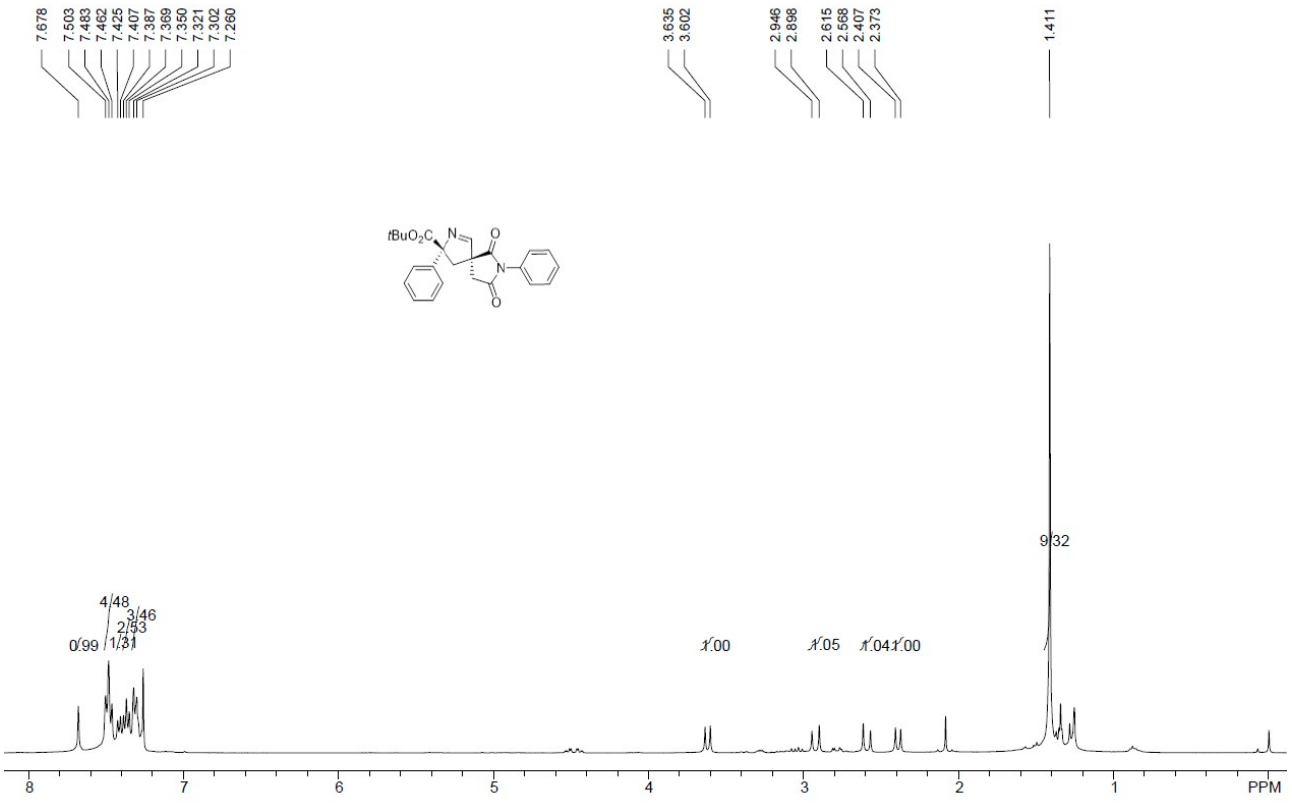
^{1}H NMR of **4k**



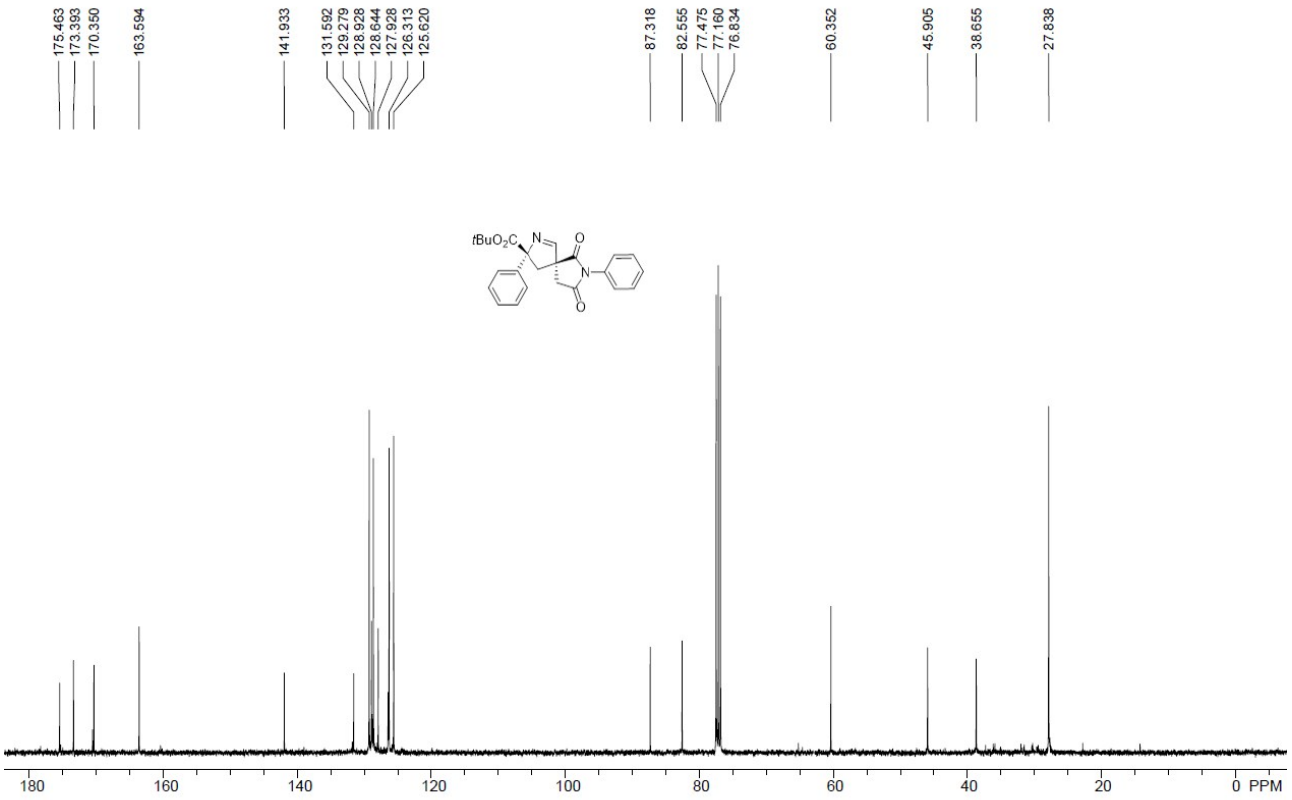
^{13}C NMR of **4k**



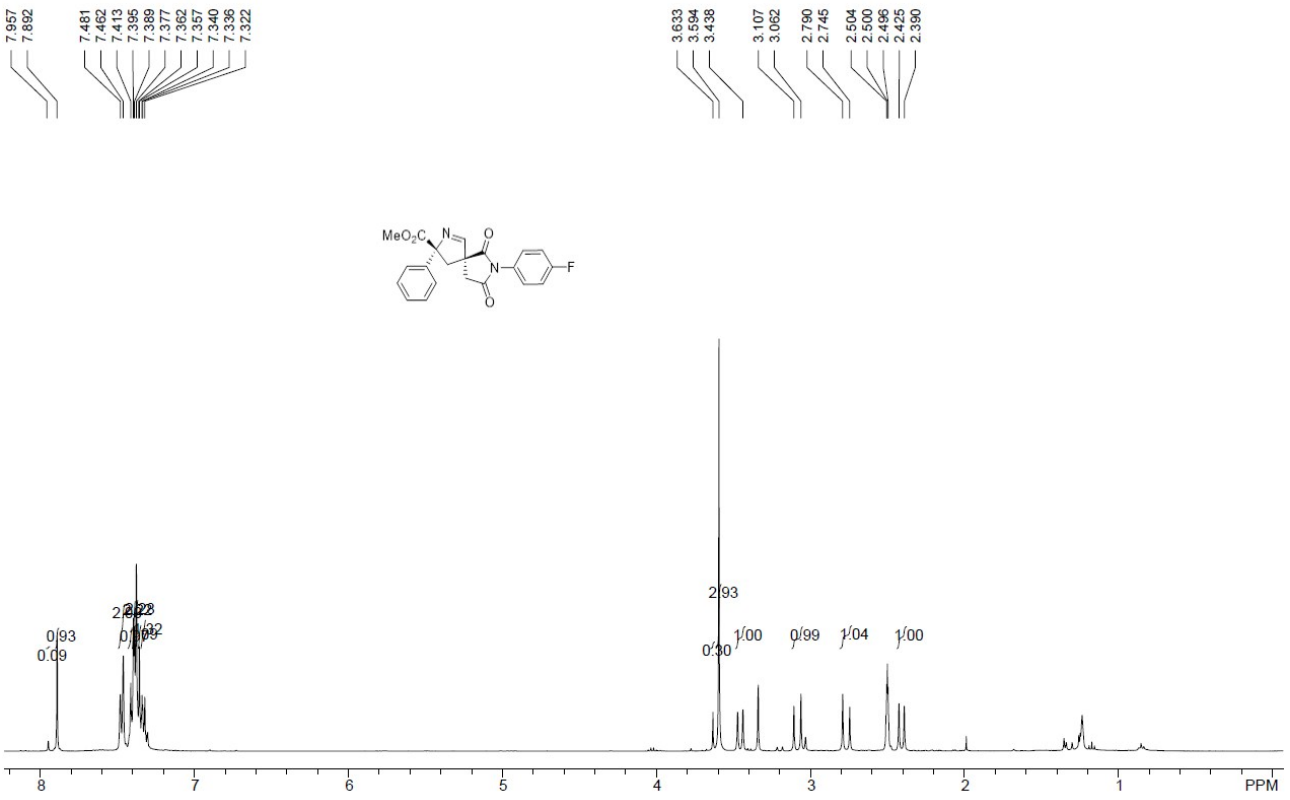
^{1}H NMR of **4l**



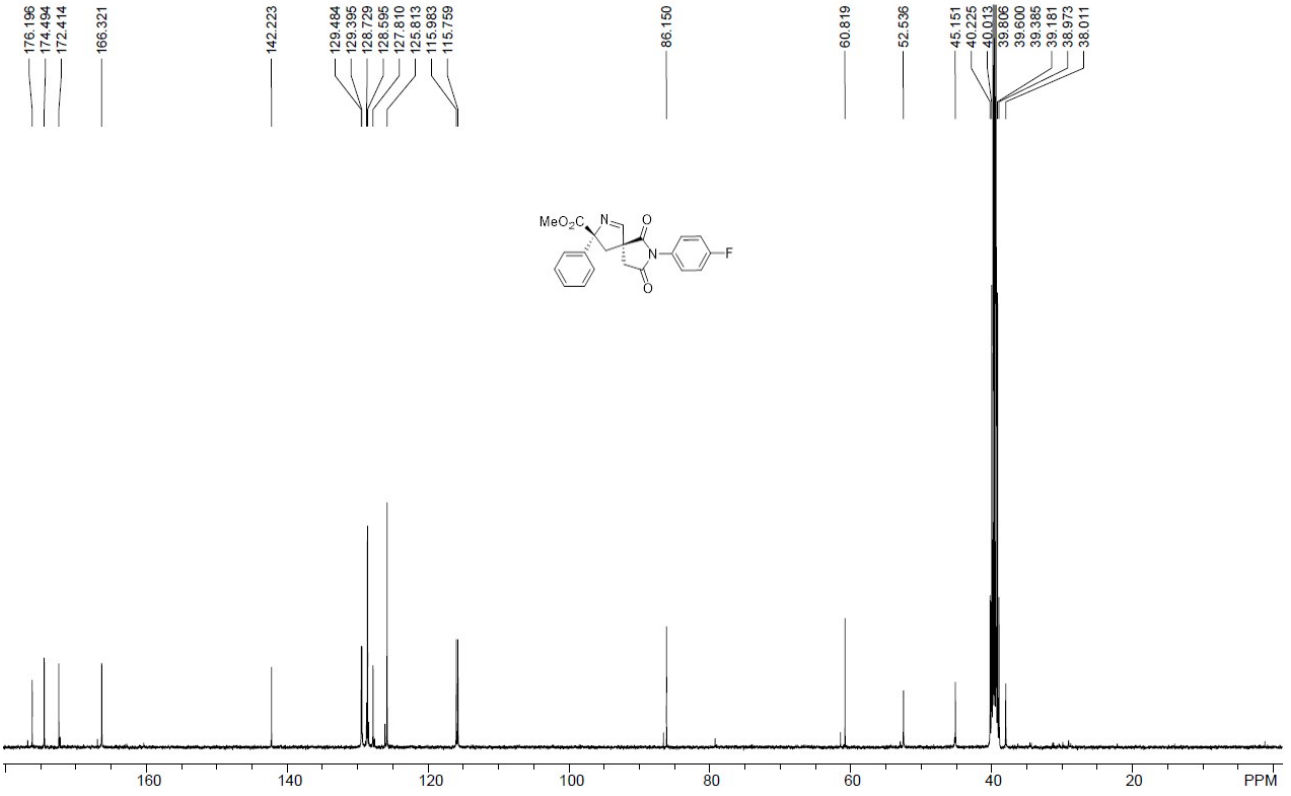
^{13}C NMR of **4l**



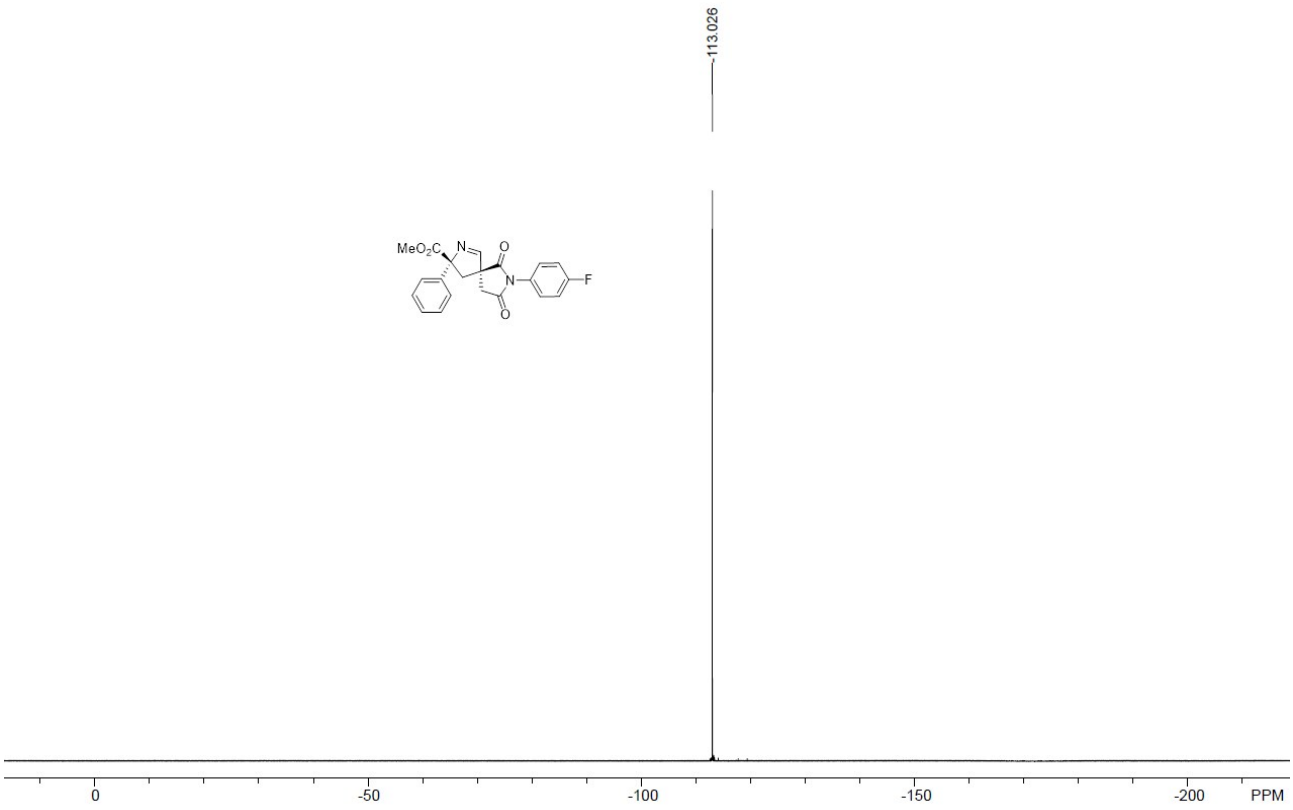
^{1}H NMR of **4n**



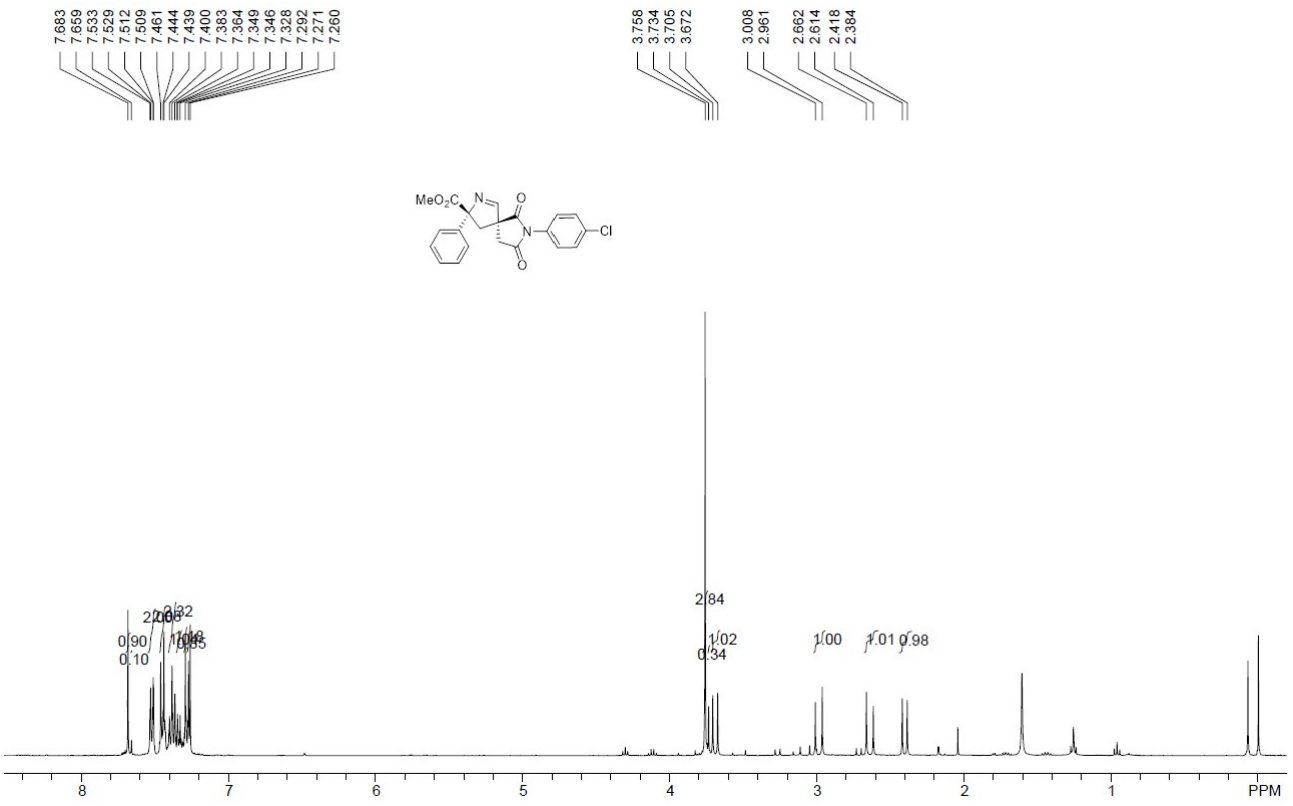
^{13}C NMR of **4n**



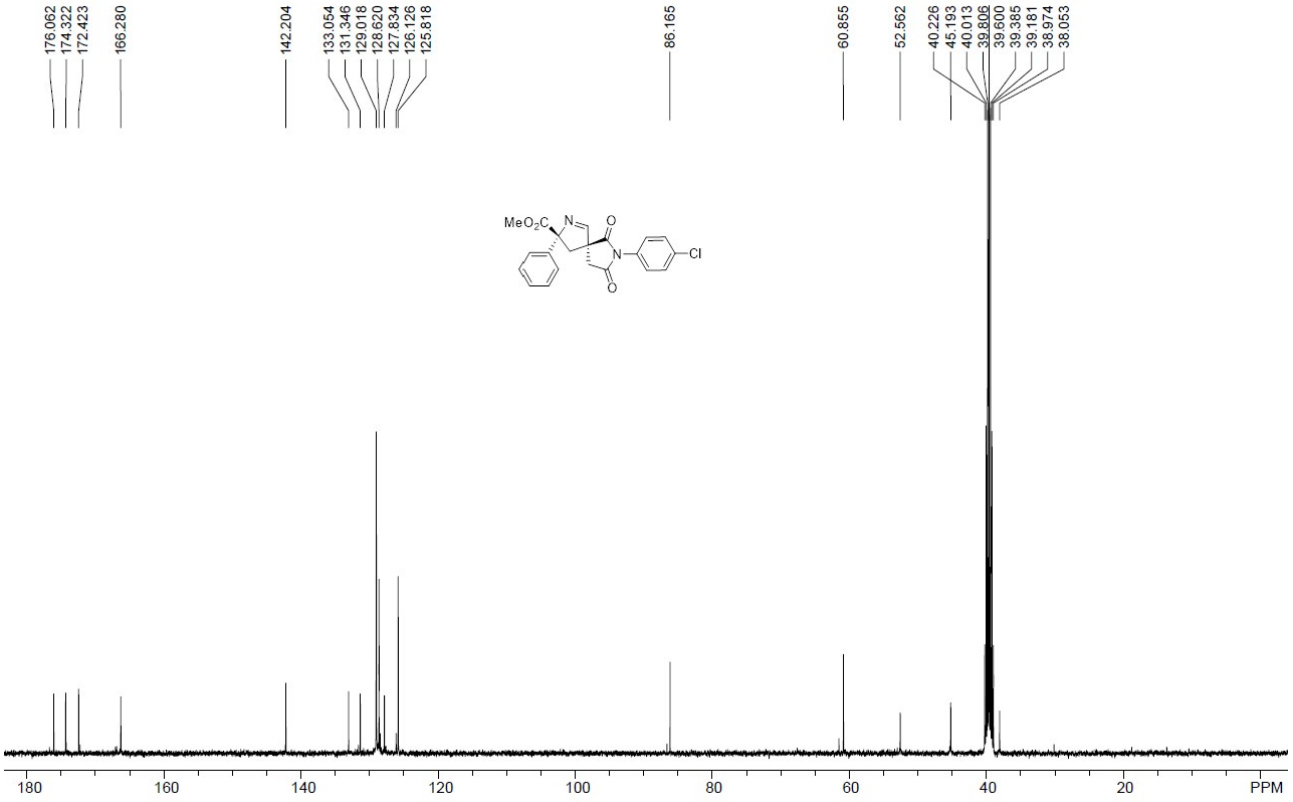
^{19}F NMR of **4n**



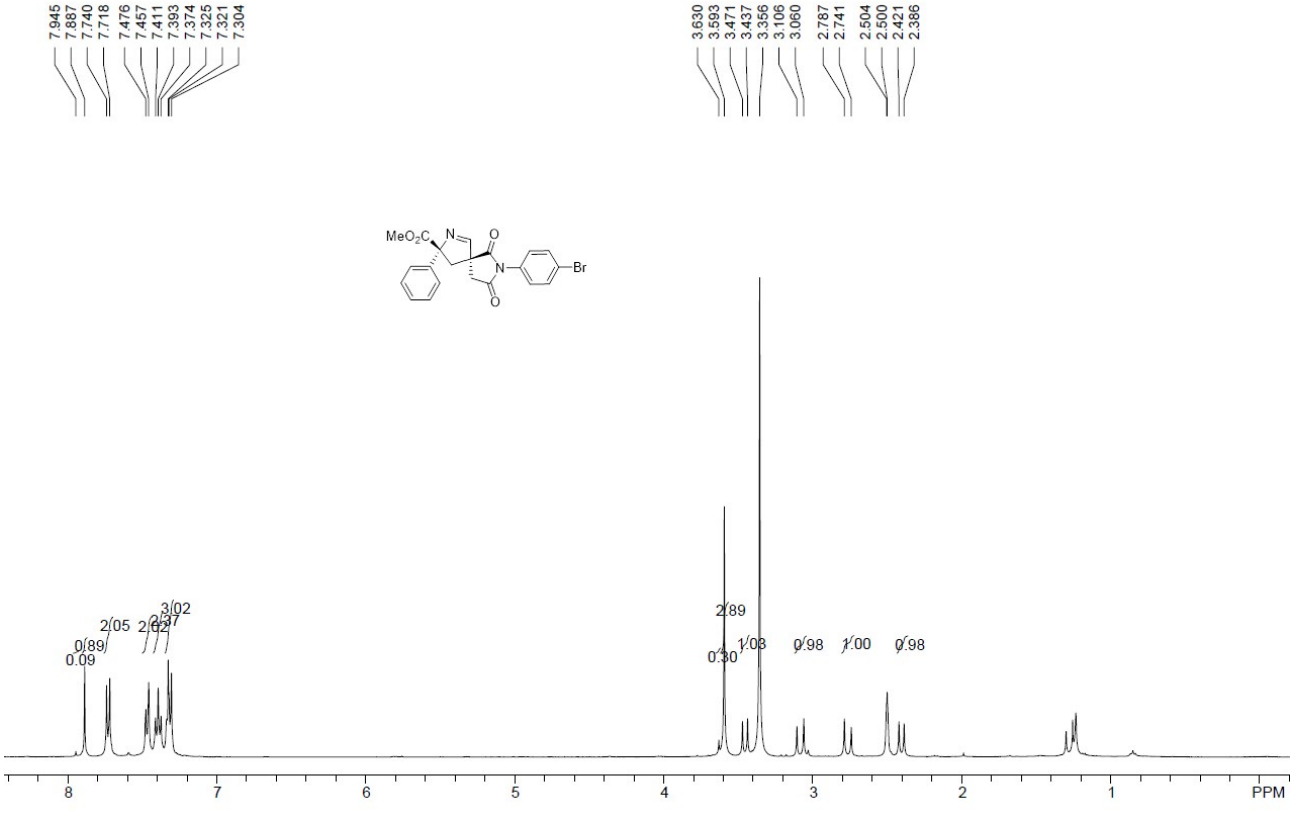
^{1}H NMR of **4o**



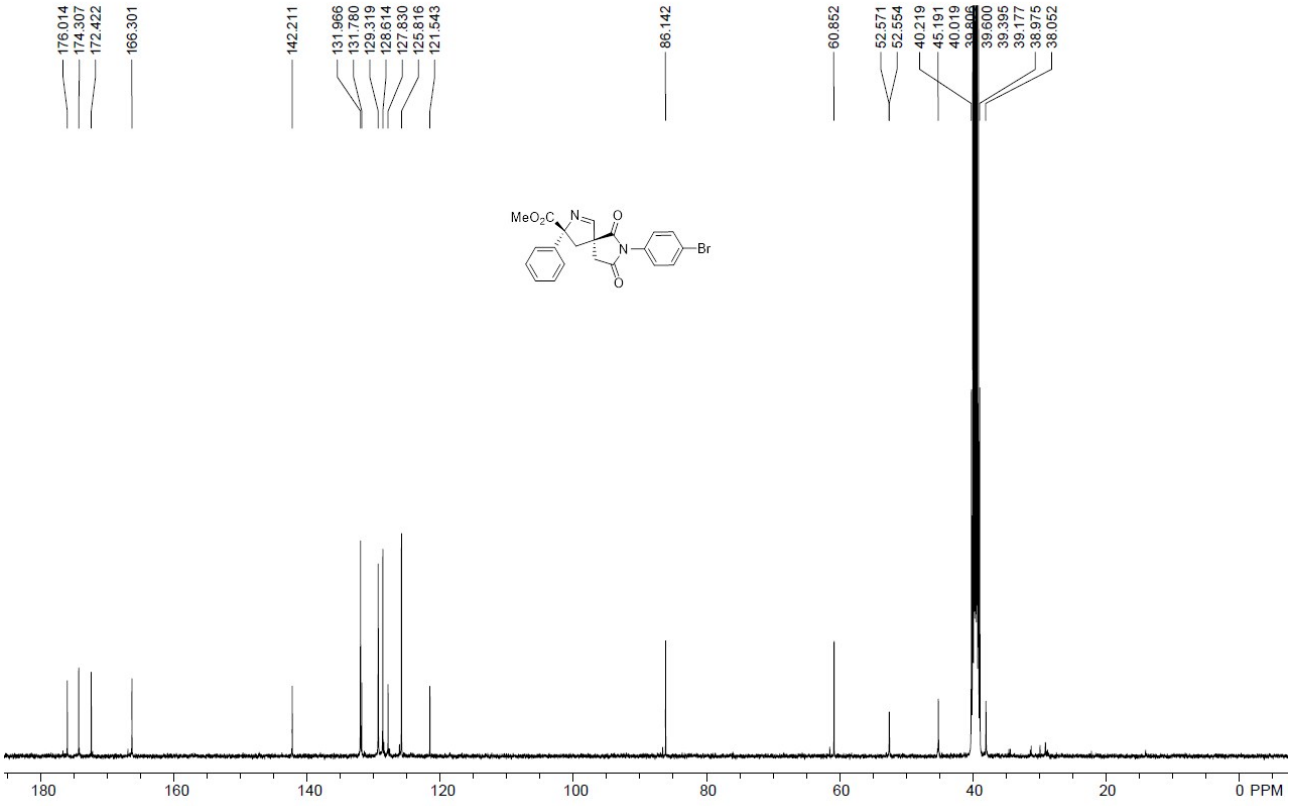
^{13}C NMR of **4o**



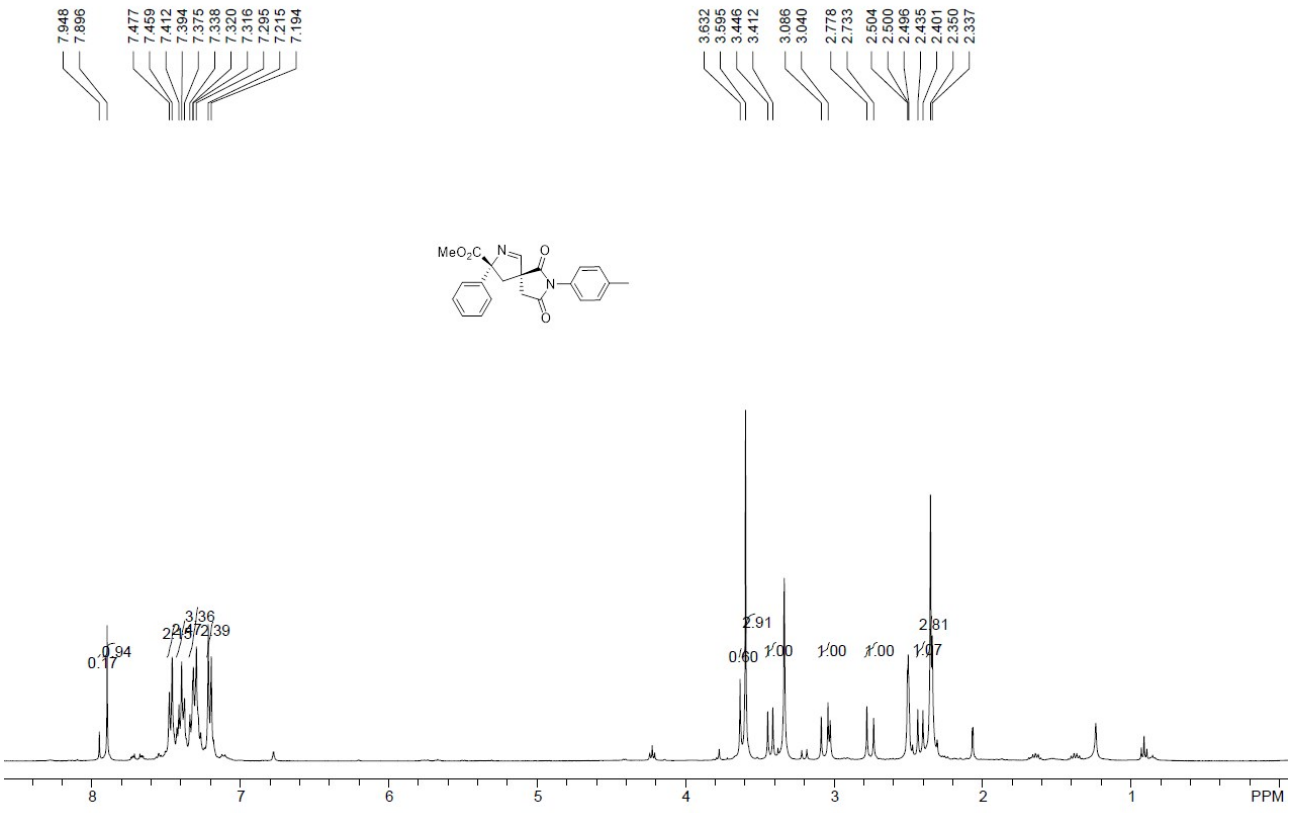
^{1}H NMR of **4p**



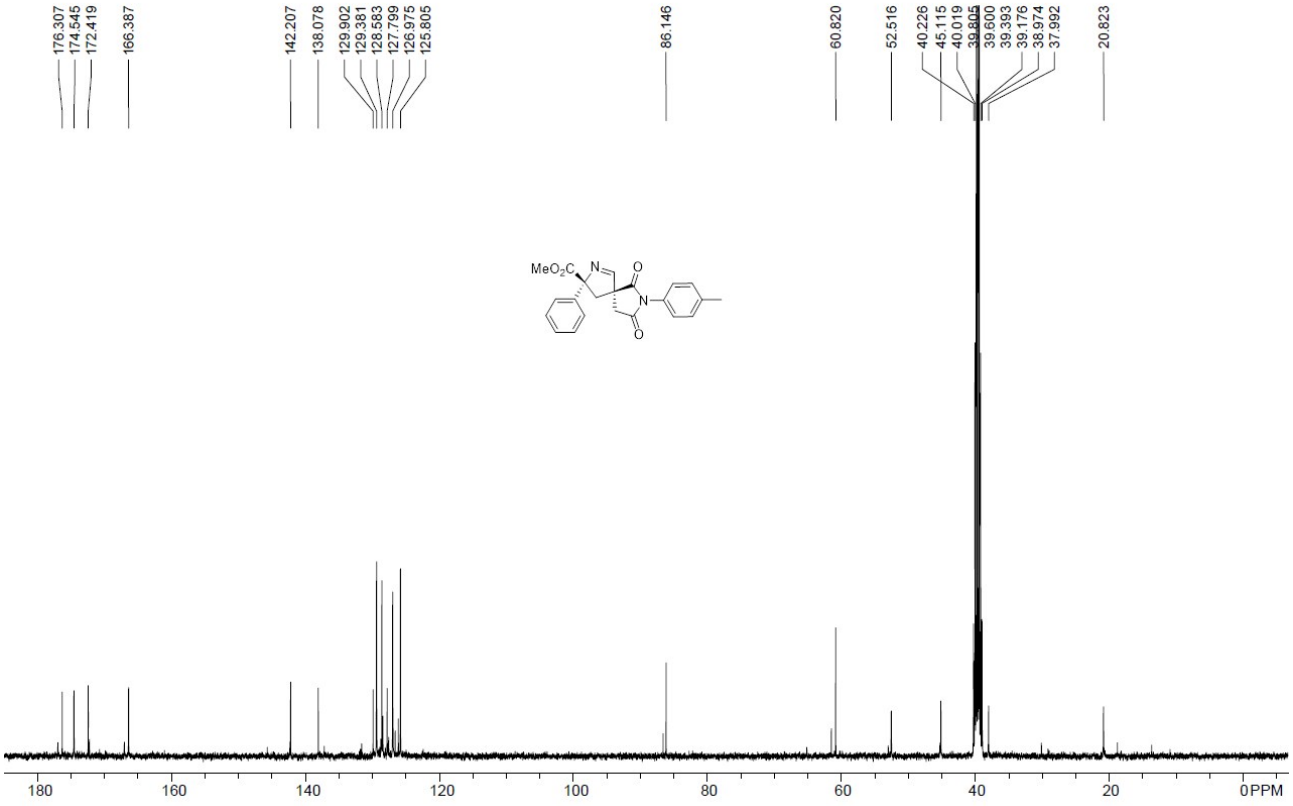
^{13}C NMR of **4p**



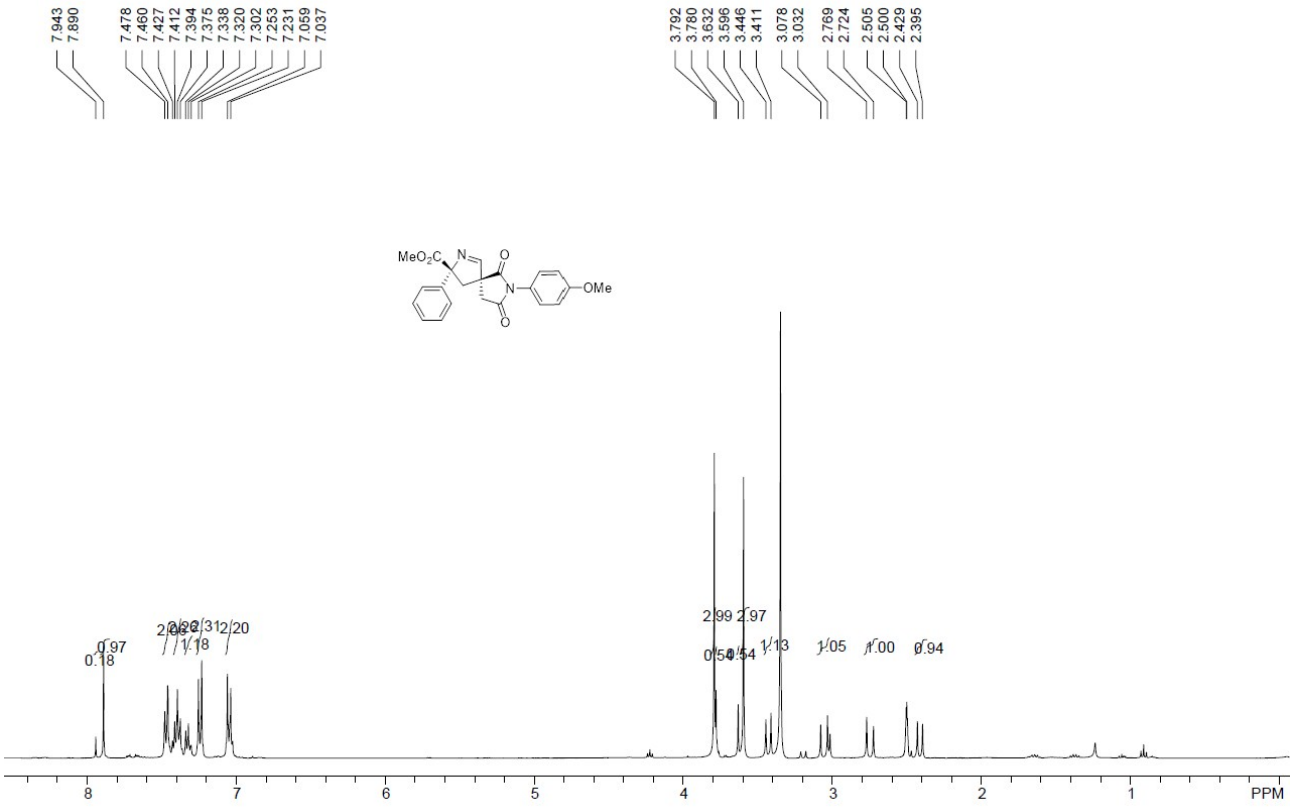
^{1}H NMR of **4q**



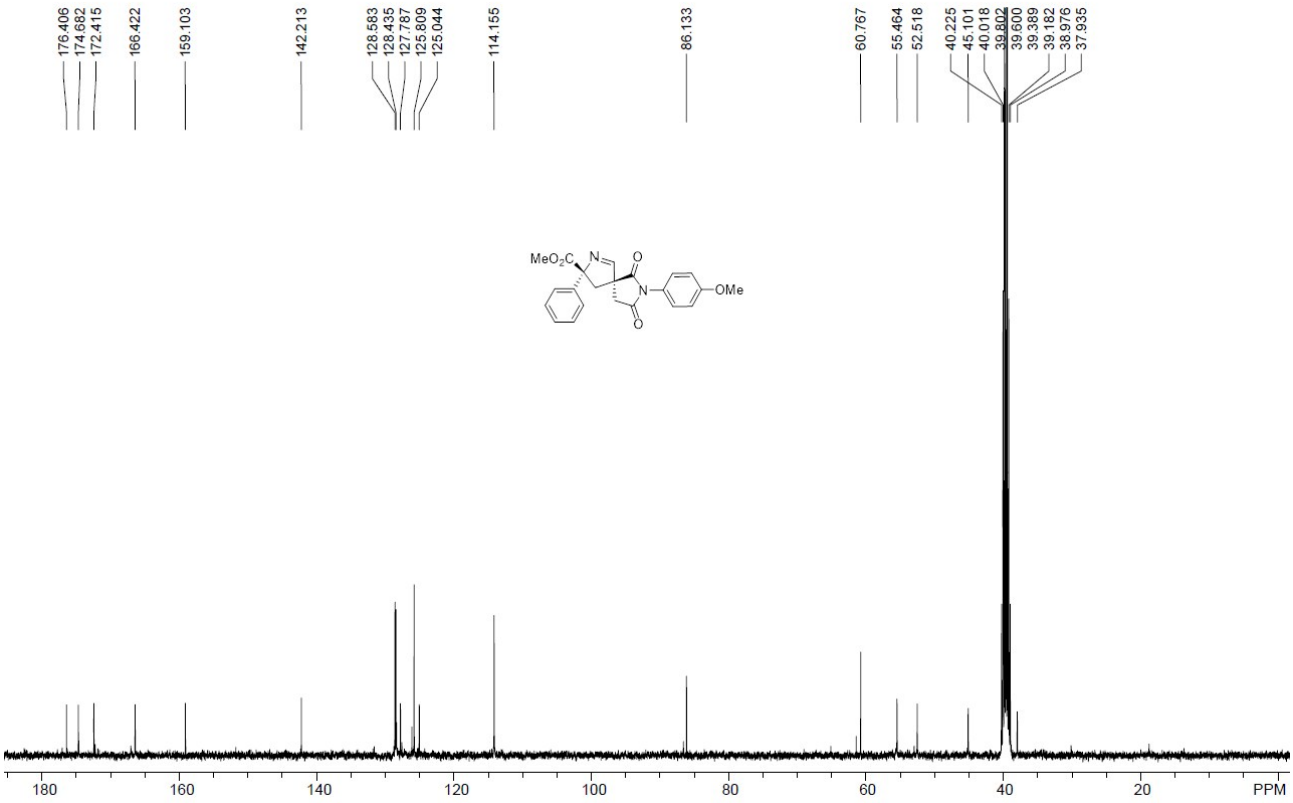
^{13}C NMR of **4q**



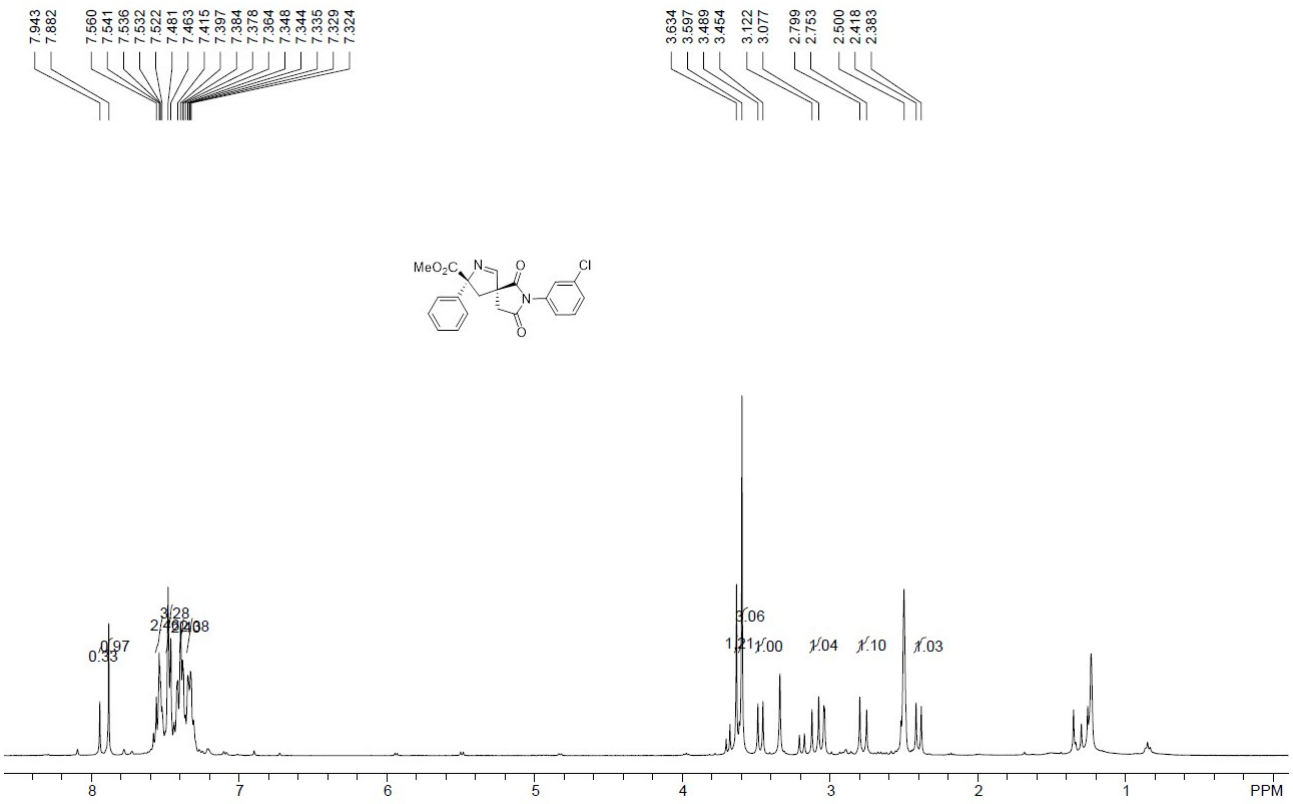
^{1}H NMR of **4r**



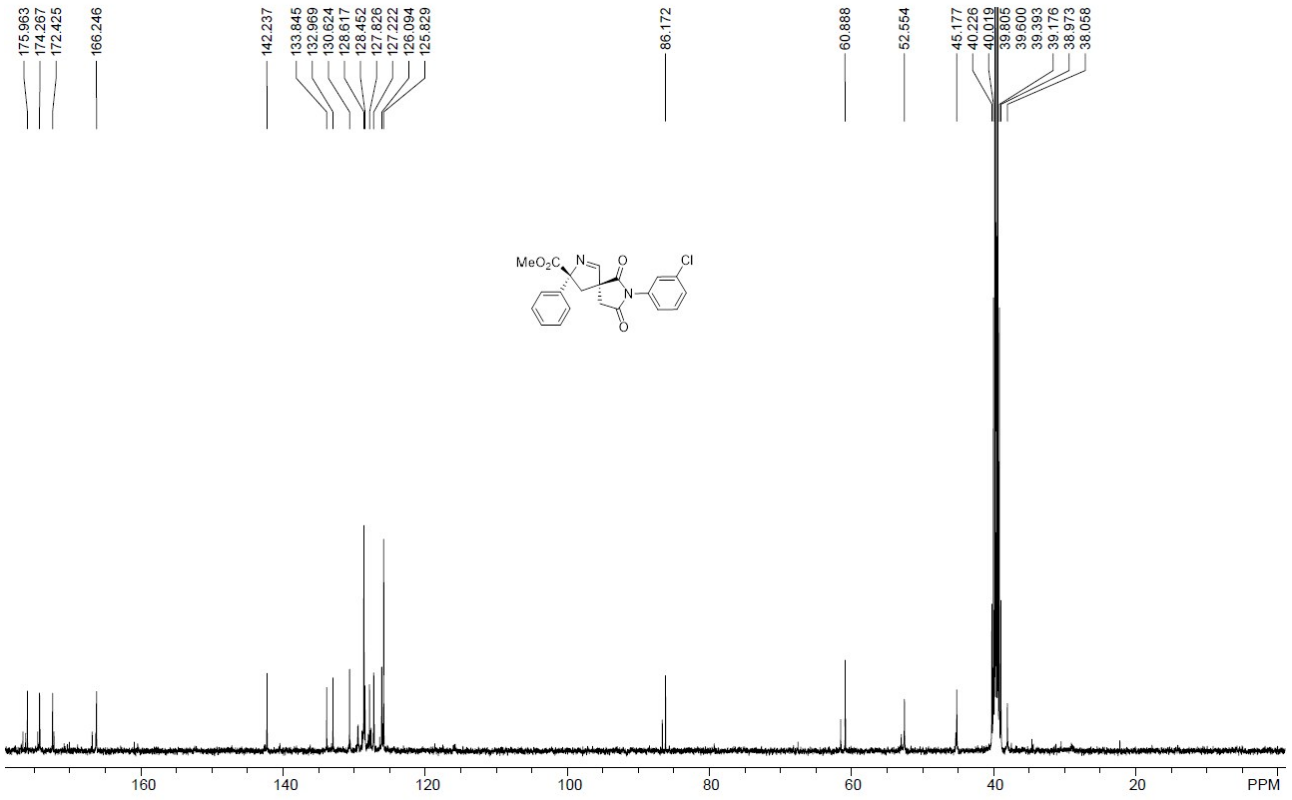
^{13}C NMR of **4r**



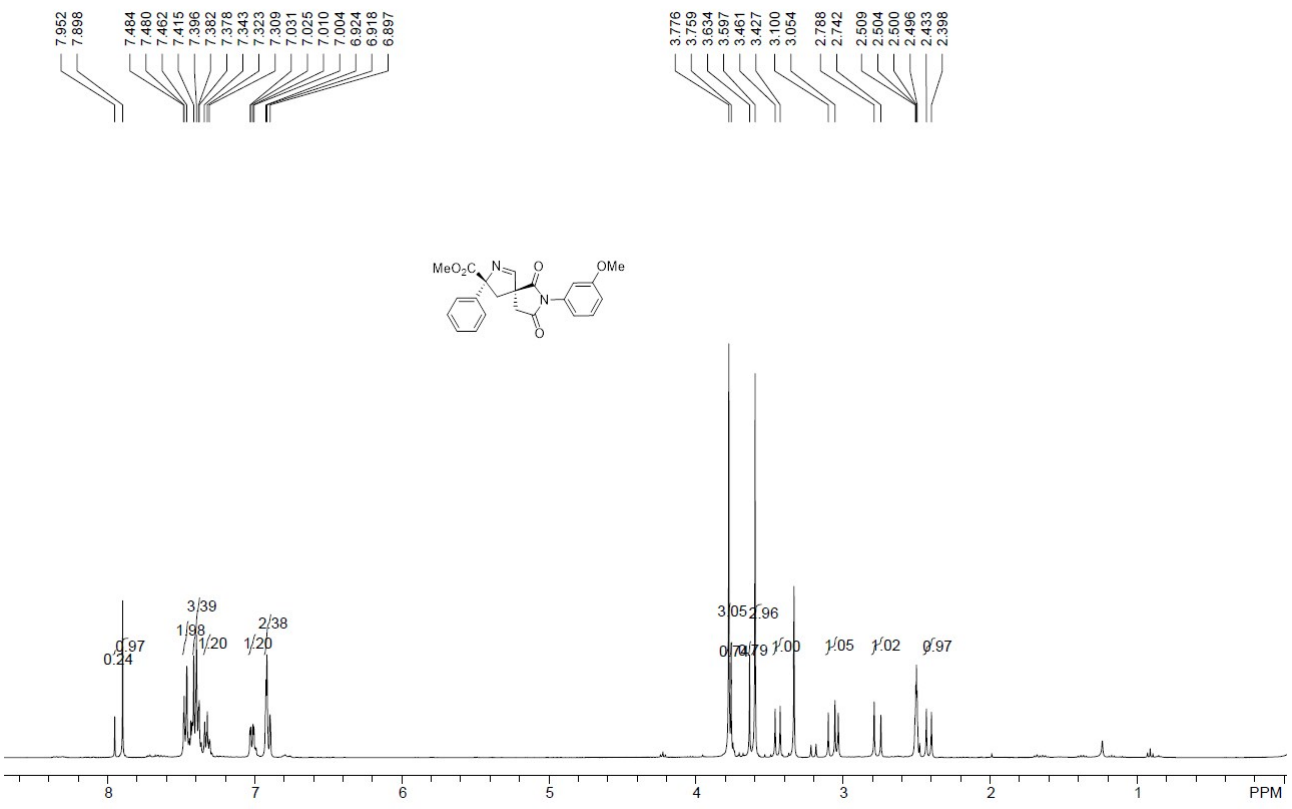
^{1}H NMR of **4s**



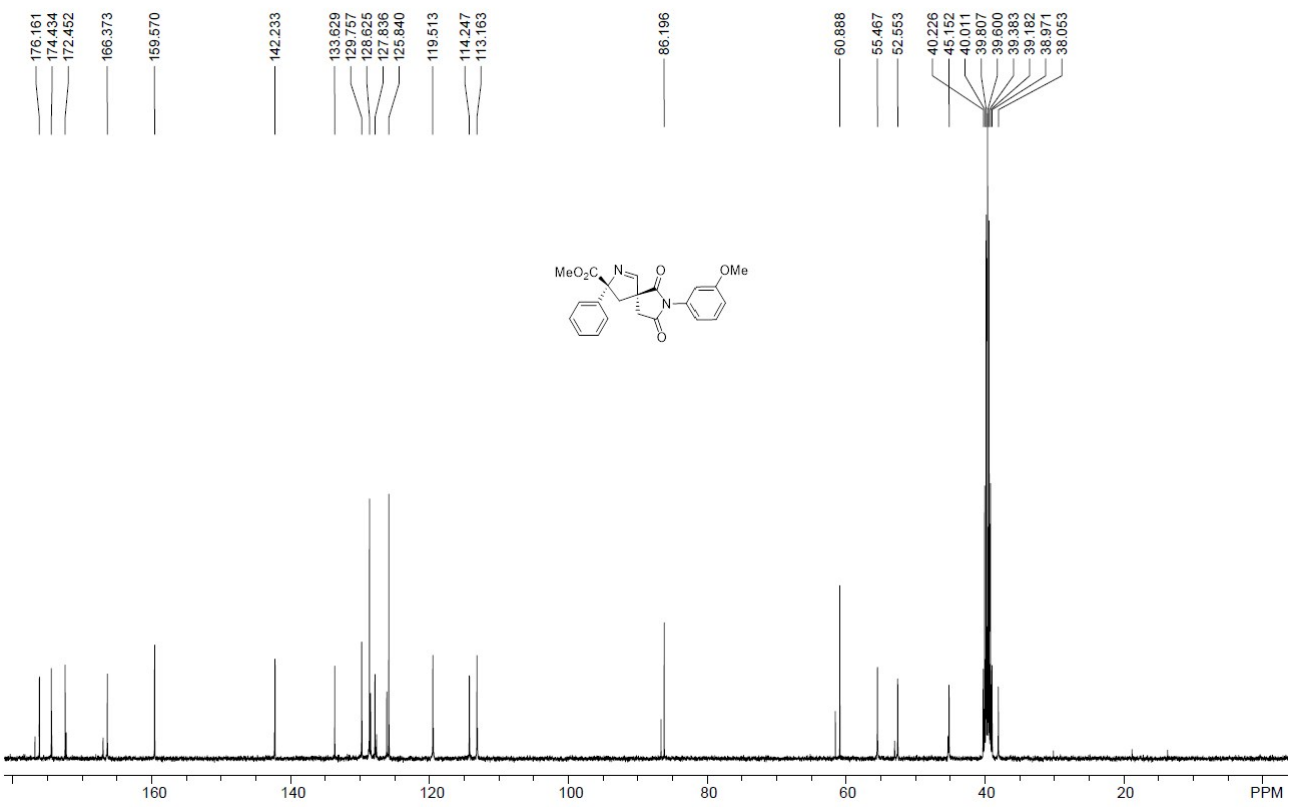
^{13}C NMR of **4s**



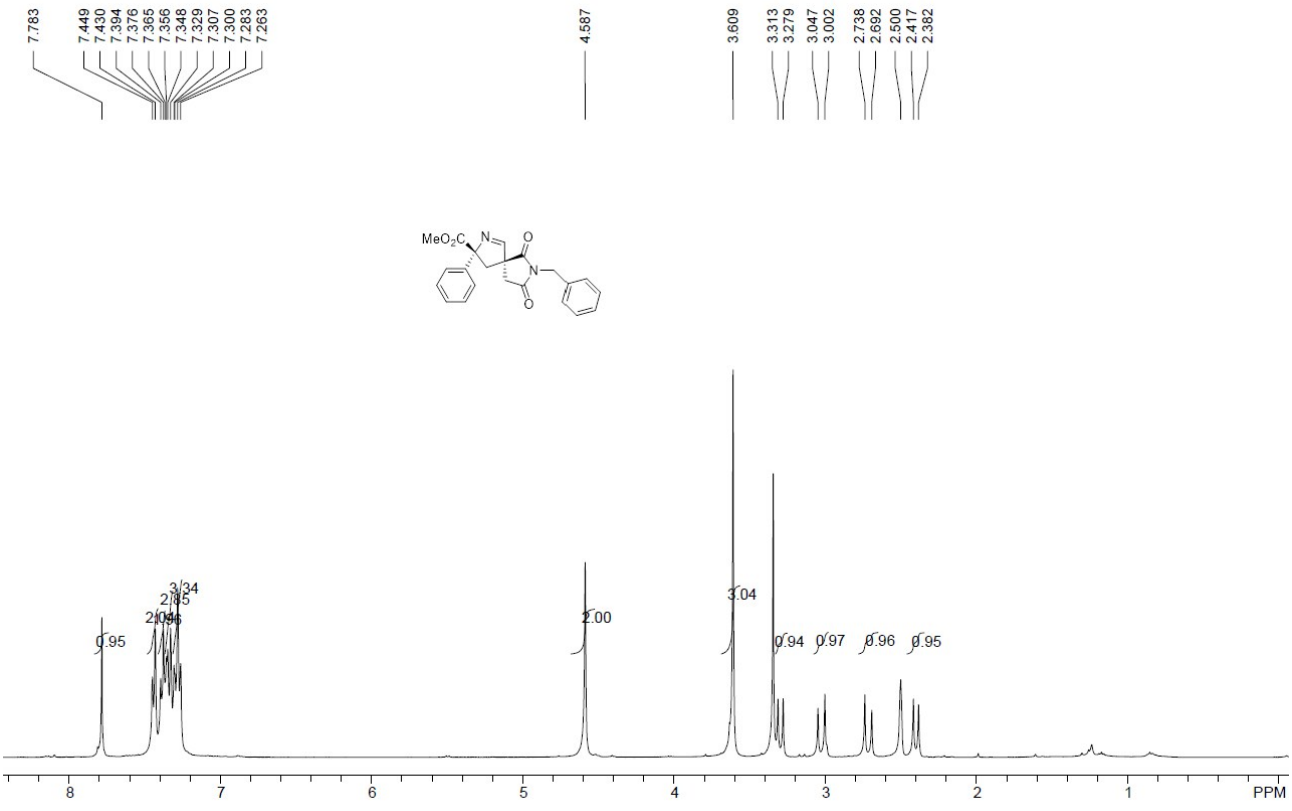
^{1}H NMR of **4t**



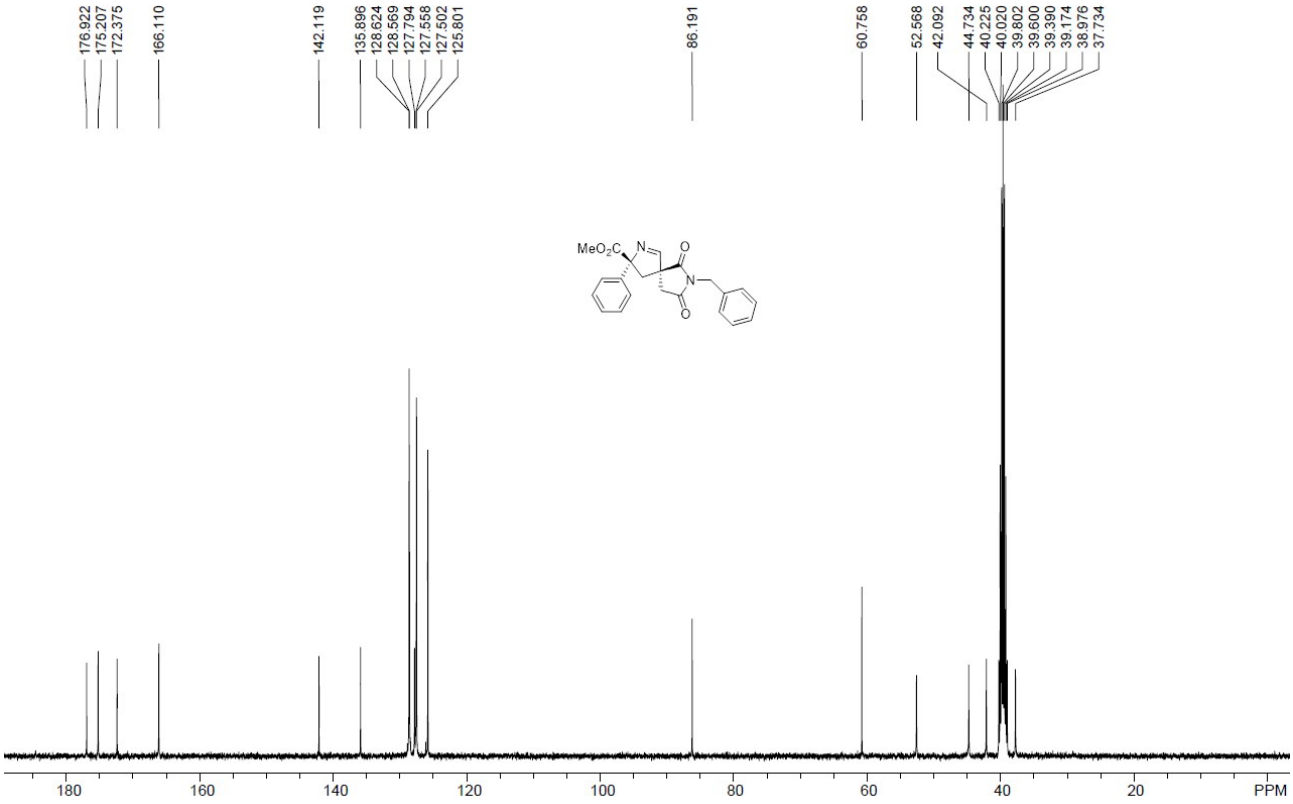
^{13}C NMR of **4t**



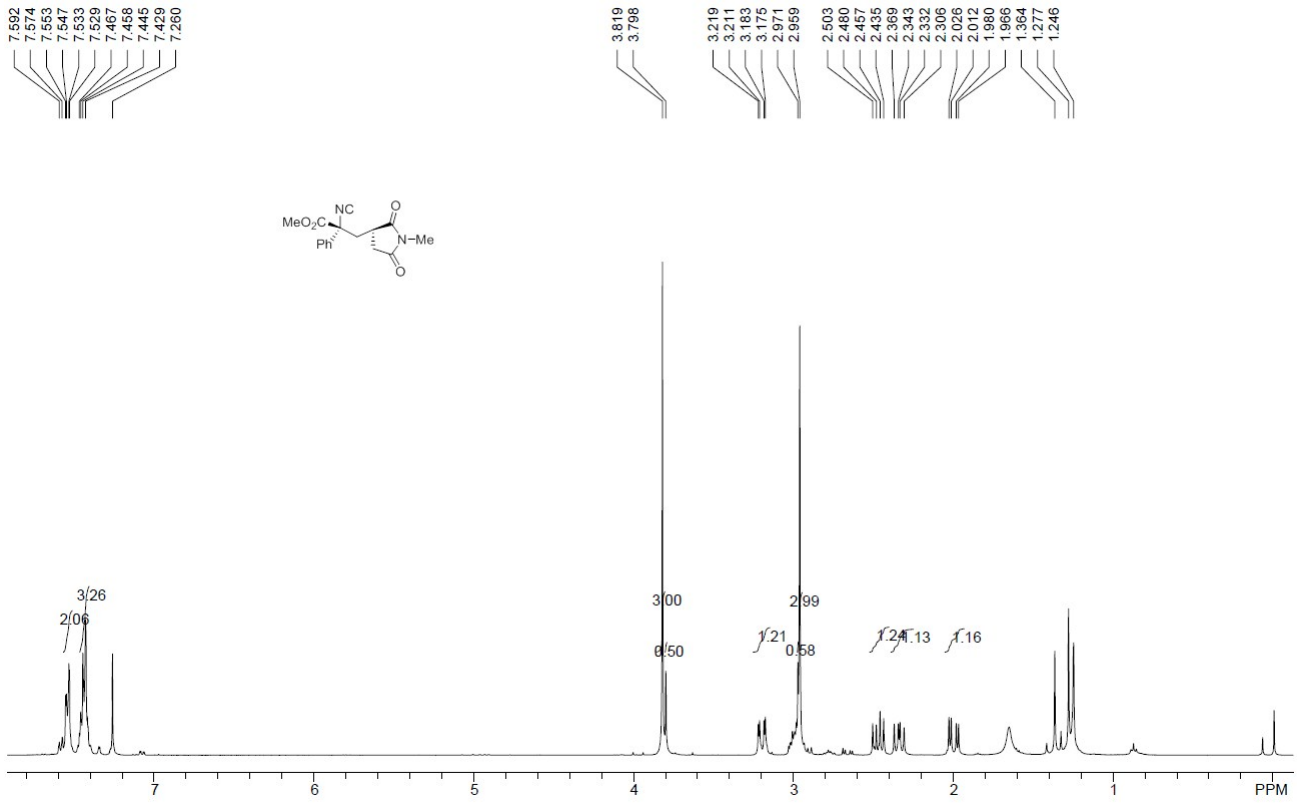
^{1}H NMR of **4u**



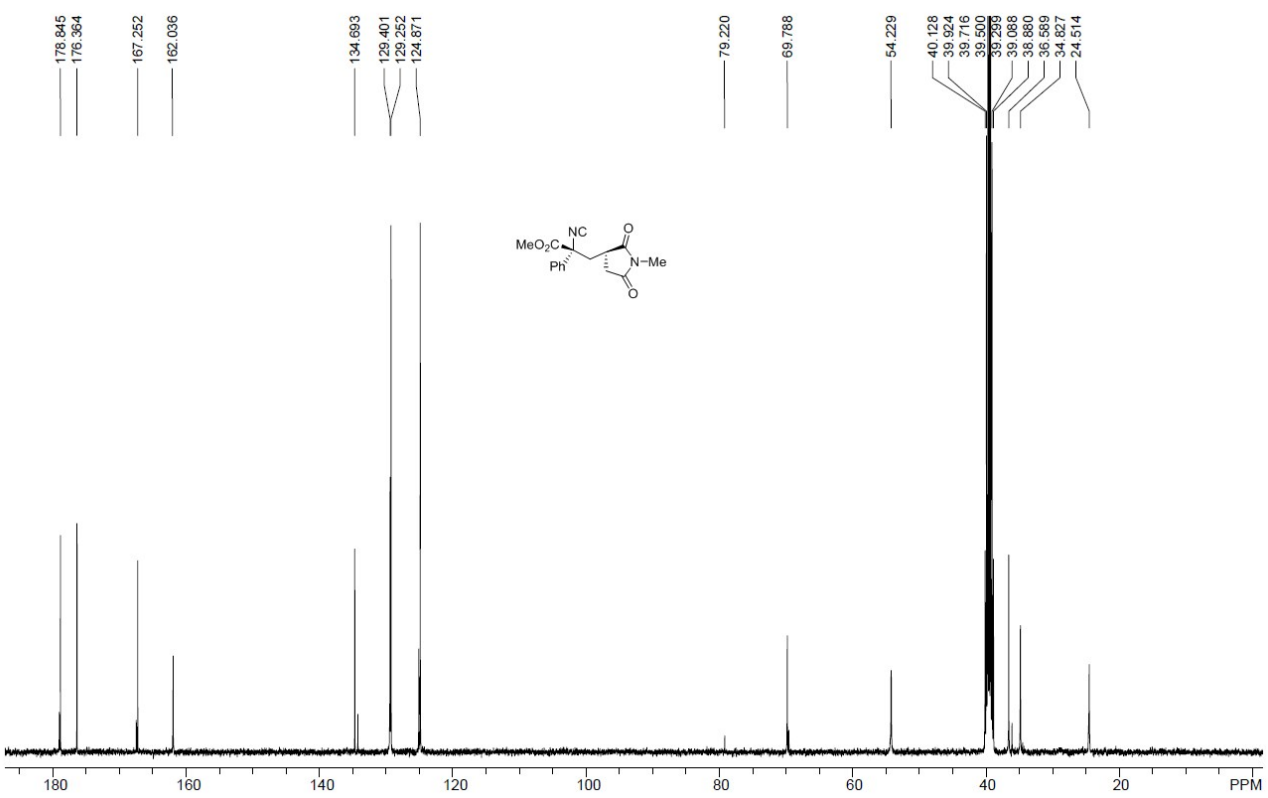
^{13}C NMR of **4u**



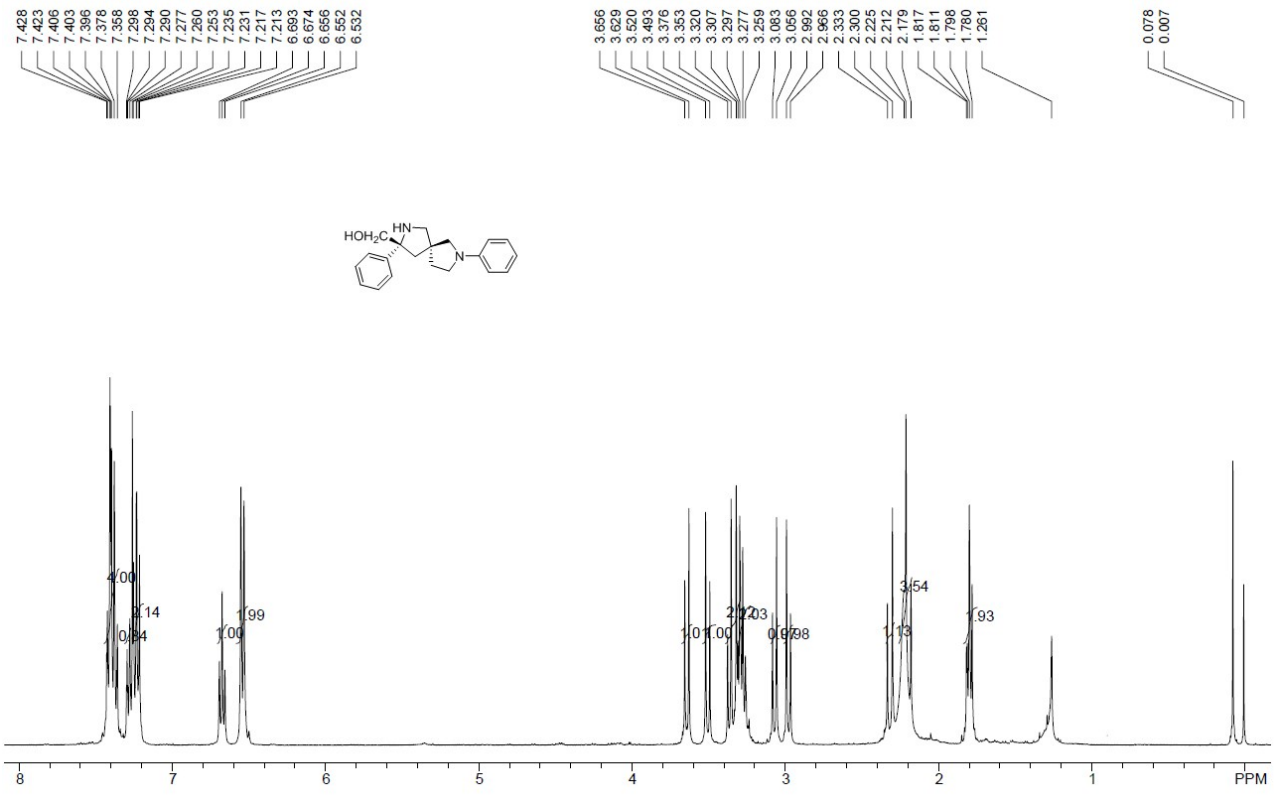
^{1}H NMR of **5b**



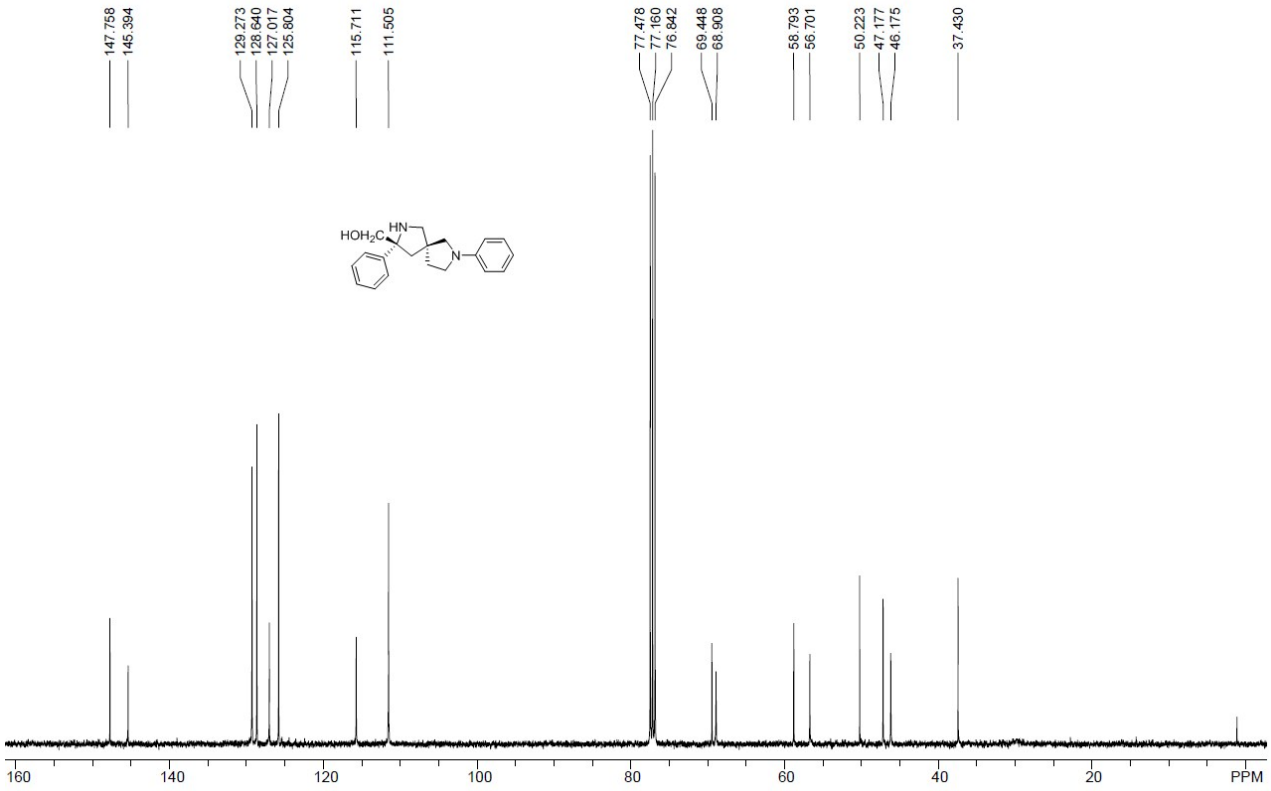
^{13}C NMR of **5b**



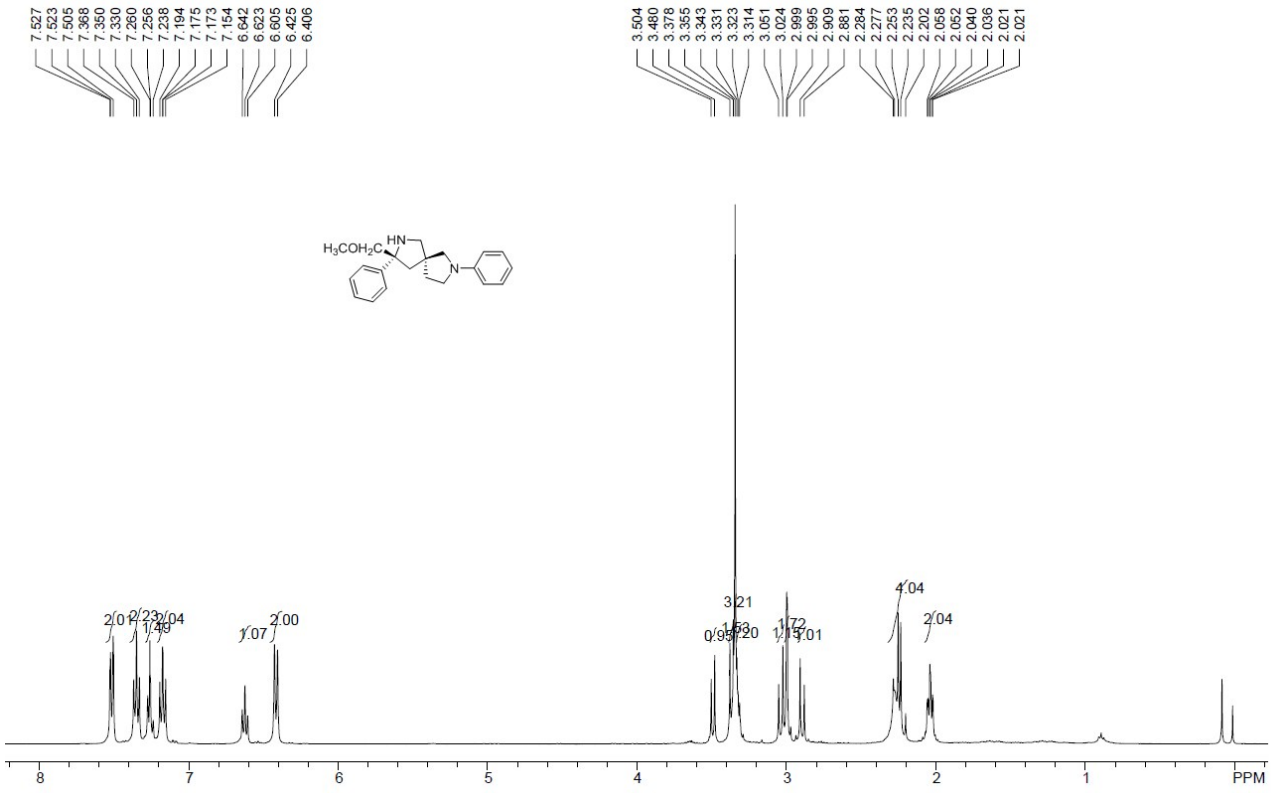
^{1}H NMR of **6a**



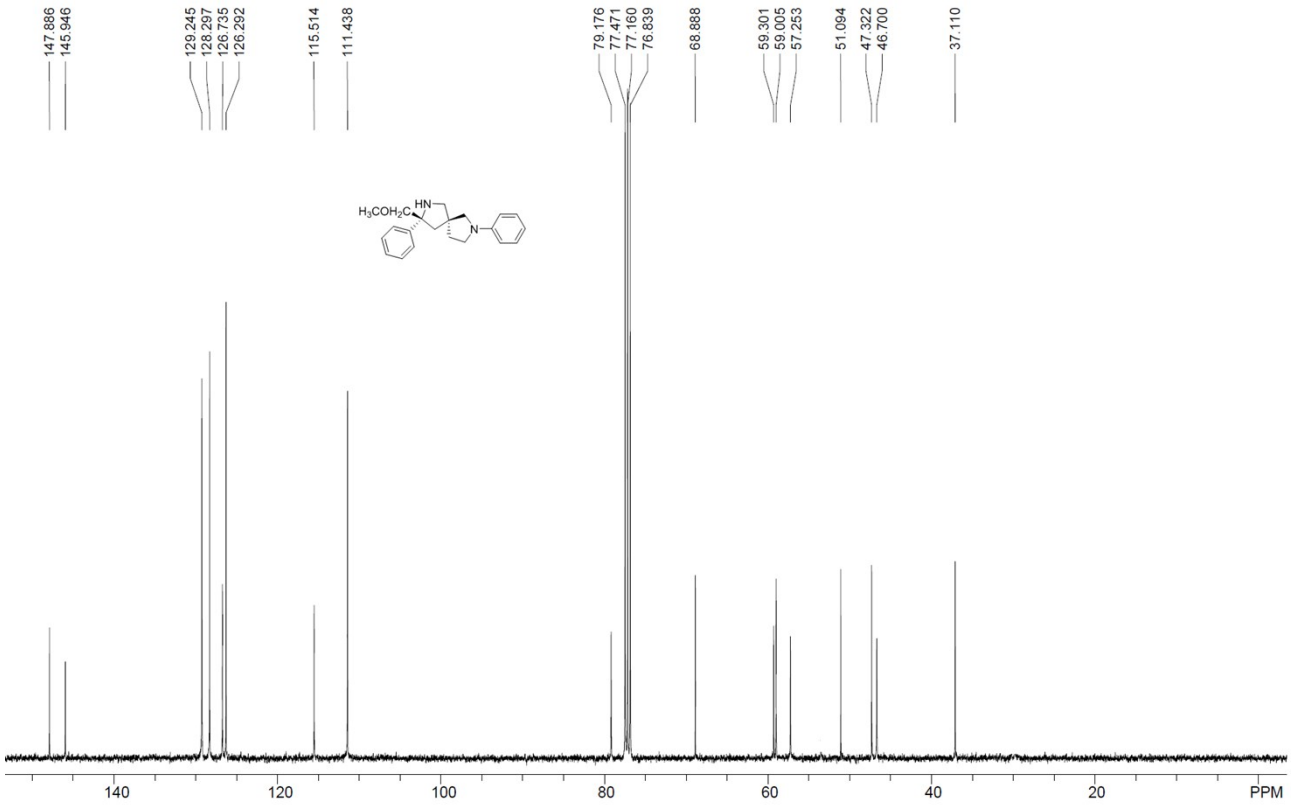
^{13}C NMR of **6a**



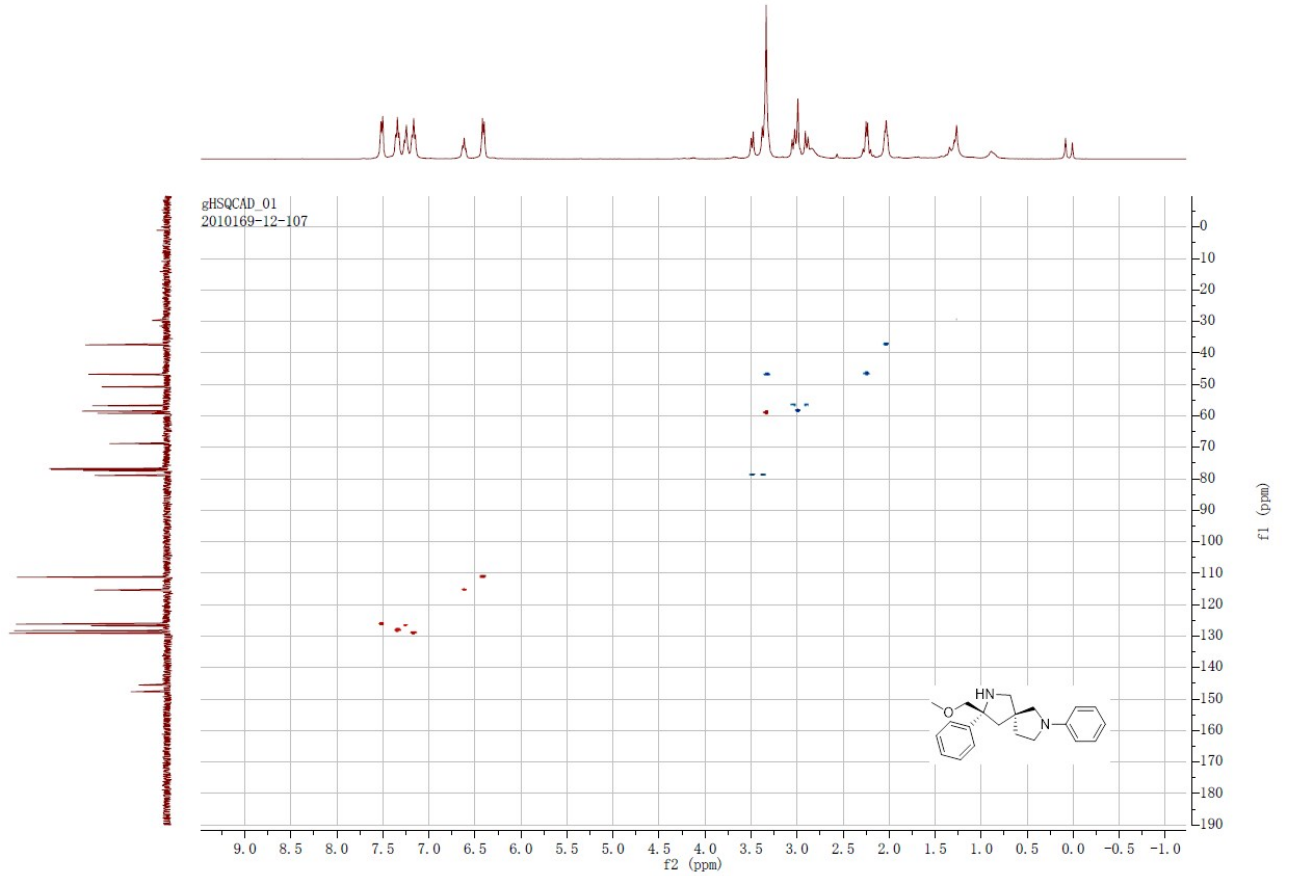
^{1}H NMR of **6b**



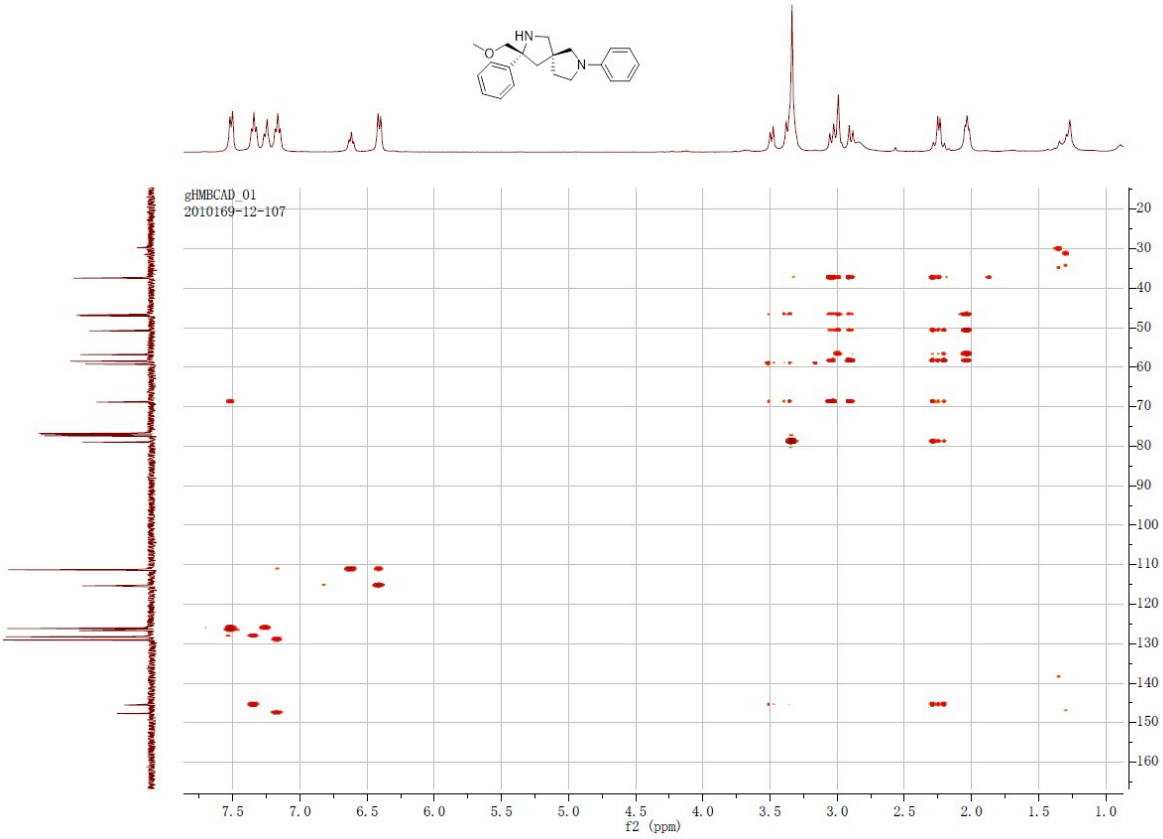
^{13}C NMR of **6b**



HSQC of **6b**



HMBC of **6b**



Extension HMBC of **6b**