Electronic Supplementary Information

Asymmetric Synthesis of Tetrasubstituted Cyclic Amines via Aza-Henry Reaction using Cinchona Alkaloid Sulfonamide/Zinc(II) Catalysts

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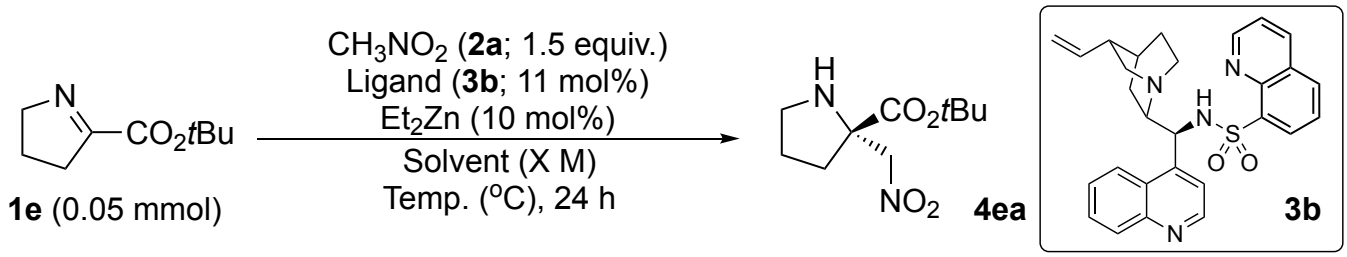
1. Experimental Section

General Information: All reactions were performed in oven-dried glassware under a positive pressure of argon or nitrogen. All chemicals, anhydrous solvents were purchased from commercial sources and used without further purification. Solvents were transferred via syringe and were introduced into the reaction vessels through a rubber septum. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica-gel (60-F254). The TLC plates were visualized with UV light and phosphomolybdic acid in ethanol, ninhydrin in acetic acid and butanol, or potassium permanganate in basic aqueous solution/heat. Column chromatography was carried out on a column packed with silica-gel 60N spherical neutral size 63-210 μm. The ^{1}H NMR (300 or 500 MHz) spectra for solution in $CDCl_3$ (chloroform-d_1), C_6D_6 (benzene-d_6) were recorded on Varian Mercury 300 or Bruker Avance 500 at room temperature or the ^{13}C NMR (125 MHz) spectra for solution in $CDCl_3$, C_6D_6, DMSO-d_6 (dimethyl solfoxide-d_6) were recorded on Bruker Avance 500 at room temperature. Chemical shifts (δ) are expressed in ppm downfield from internal TMS. HPLC analyses were performed on a SHIMADZU LC-2010A HT using 4.6 x 250 mm CHIRALPAK® AD-H, IF, IF-3, IG, and IH-3 column. ESI Mass spectra were recorded on a Waters SYNAPT G2 HDMS. Optical rotations were measured on a JASCO P-2200. Infrared spectra were recorded on a JASCO FT/IR-4600 spectrometer with ZnSe ATR unit. Iminoester (**1j**) derived from isatin was prepared by published procedures.[1)] Nitromethane (**2a**), nitroethane (**2b**), and 1-nitropropane (**2c**) are commercially available and other nitroalkanes (**2d, 2e**, and **2g**) were prepared by published procedures.[2)] Catalyst (**3a**) was prepared by published procedures.[3)] Catalysts (**3b**–**3f**) were also prepared by our previous methods.[4)]

2. Optimization

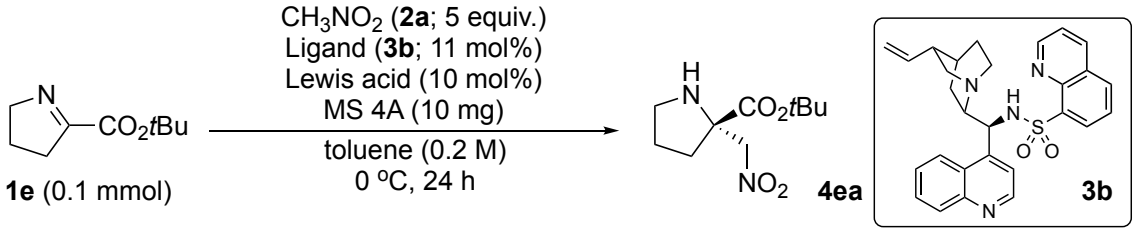
2-1. Optimization of solvent, concentration and reaction temperature



Entry	Solvent	X (M)	Temp. (°C)	Yield (%)[a]		Ee (%)[b]
				1e	**4ea**	
1	THF	0.025	r.t.	75	21	78
2	Et_2O	0.025	r.t.	87	11	73
3	CH_2Cl_2	0.025	r.t.	92	7	77
4	benzene	0.025	r.t.	73	25	78
5	toluene	0.025	r.t.	58	37	80
6	*o*-xylene	0.025	r.t.	61	30	68
7	*m*-xylene	0.025	r.t.	69	26	81
8	*p*-xylene	0.025	r.t.	50	13	n.a.
9	cyclohexane	0.025	r.t.	62	30	54
10	toluene	0.05	r.t.	39	60	88
11	toluene	0.1	r.t.	25	72	86
12	toluene	0.2	r.t.	18	76	88
13	toluene	0.4	r.t.	<1	90	84
14	toluene	0.2	10	23	74	88
15	toluene	0.2	0	31	67	94
16	toluene	0.2	–20	>99	<1	n.a.
17[c]	toluene	0.2	0	56	42	93
18[d]	toluene	0.2	0	13	81	92
19[e]	toluene	0.2	0	<1	92	90
20[e,f]	toluene	0.2	0	<1	91	94

[a] Yield was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [b] Enantiomeric excess (Ee) was determined by HPLC analysis using a chiral column. [c] 2.0 equiv. of **2a** were used. [d] 3.0 equiv. of **2a** were used. [e] 5.0 equiv. of **2a** were used. [f] 5 mg of MS 4A were added.

2-2. Screening of Lewis acids

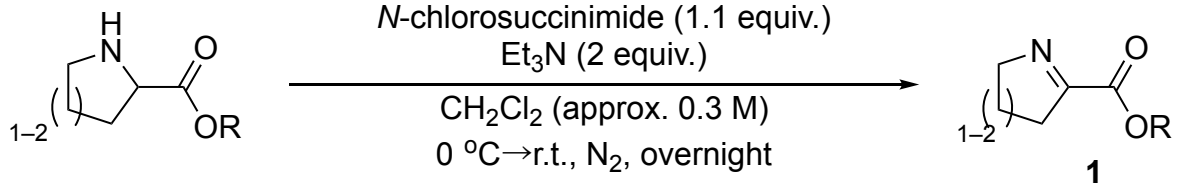


Entry	Lewis acid	Yield (%)[a]		Ee (%)[b]
		1e	**4ea**	
1	Et_2Zn	<1	91	94
2	$Zn(OTf)_2$	98	<1	n.a.
3	$Zn(OAc)_2$	99	<1	n.a.
4	ZnF_2	>99	<1	n.a.
5	Et_3Al	81	13	0
6	MeMgBr	98	<1	n.a.
7	*n*BuLi	>99	<1	n.a.
8	Et_3B	95	<1	n.a.

[a] Yield was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard. [b] Enantiomeric excess (Ee) was determined by HPLC analysis using a chiral column.

3. Preparation of Substrates

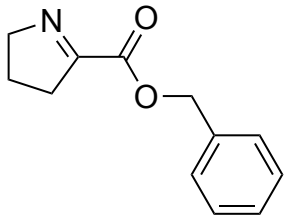
3-1. Synthesis of cyclic iminoester (1)[5)]



1

To a solution of cyclic α-amino acid ester (1.0 equiv.) in CH_2Cl_2 (approx. 0.3 M) were added triethylamine (2.0 equiv.) and *N*-chlorosuccinimide (1.1 equiv.) at 0 °C. After stirred under nitrogen at room temperature for overnight, the reaction mixture was concentrated under reduced pressure. Sat. NH_4Cl aq. was added to the residue, and the mixture was extracted with Et_2O. The combined organic layers were washed by sat. $NaHCO_3$ aq. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to give the corresponding cyclic iminoester (**1**).

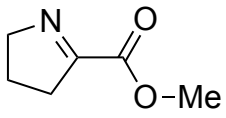
Benzyl 1-pyrroline 2-carboxylate (1a):



To a solution of *L*-proline benzyl ester hydrochloride (1.69 g, 7.0 mmol) in CH_2Cl_2 (21 mL) were added triethylamine (1.95 mL, 14.0 mmol) and *N*-chlorosuccinimide (1.03 g, 7.7 mmol) at 0 °C. After stirred under nitrogen at room temperature for overnight, the reaction mixture was concentrated under reduced pressure. Sat. NH_4Cl aq. (20 mL) was added to the residue, and the reaction mixture was extracted with Et_2O (20 mL × 3). The combined organic layers were washed by sat. $NaHCO_3$ aq. (30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (4/1 to 2/1) as a mixed eluent to give **1a** (0.79 g, 3.89 mmol) in 56% yield.

Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44–7.32 (m, 5H), 5.31 (s, 2H), 4.14–4.08 (s, 2H), 2.87–2.80 (m, 2H), 2.05–1.92 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 162.6, 135.1, 128.6, 128.6, 128.5, 67.3, 62.6, 35.4, 22.1; HRMS (ESI) m/z for $C_{12}H_{14}NO_2$ $[M+H]^+$: calcd. 204.1025, found 204.1022; IR (ATR) 3064, 3033, 2956, 2860, 1742, 1718, 1455, 1257, 1212, 1096 cm^{-1}.

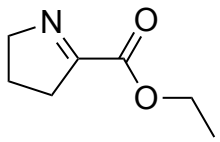
Methyl 1-pyrroline 2-carboxylate (1b):



To a solution of *L*-proline methyl ester hydrochloride (0.41 g, 2.5 mmol) in CH_2Cl_2 (7.5 mL) were added triethylamine (0.70 mL, 5.0 mmol) and *N*-chlorosuccinimide (0.37 g, 2.75 mmol) at 0 °C. After stirred at under nitrogen room temperature for 12 h, the reaction mixture was concentrated under reduced pressure. Sat. NH_4Cl aq. (10 mL) was added to the residue, and the reaction mixture was extracted with Et_2O (10 mL × 3). The combined organic layers were washed by sat. $NaHCO_3$ aq. (10 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (4/1 to 2/1) as a mixed eluent to give **1b** (0.14 g, 1.10 mmol) in 44% yield.

Brown oil; ^{1}H NMR (300 MHz, C_6D_6) δ 3.75–3.68 (m, 2H), 3.39 (s, 3H), 2.41–2.34 (m, 2H), 1.29–1.18 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6) δ 167.6, 163.8, 62.7, 51.7, 35.7, 22.1. Spectroscopic data of ^{1}H and ^{13}C NMR were identical to that reported in reference 5.

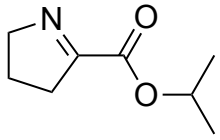
Ethyl 1-pyrroline 2-carboxylate (1c):



To a solution of *L*-proline ethyl ester (0.36 g, 2.5 mmol) in CH_2Cl_2 (7.5 mL) were added triethylamine (0.70 mL, 5.0 mmol) and *N*-chlorosuccinimide (0.37 g, 2.75 mmol) at 0 °C. After stirred under nitrogen at room temperature for 13 h, the reaction mixture was concentrated under reduced pressure. Sat. NH_4Cl aq. (10 mL) was added to the residue, and the reaction mixture was extracted with Et_2O (10 mL × 3). The combined organic layers were washed by sat. $NaHCO_3$ aq. (10 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 2/1) as a mixed eluent to give **1c** (0.26 g, 1.84 mmol) in 74% yield.

Yellow oil; ^{1}H NMR (300 MHz, C_6D_6) δ 4.03 (q, J = 7.2 Hz, 2H), 3.76–3.70 (m, 2H), 2.45–2.38 (m, 2H), 1.31–1.20 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 167.9, 163.5, 62.7, 61.1, 35.7, 22.1, 14.1; HRMS (ESI) m/z for $C_7H_{11}NO_2Na$ $[M+Na]^+$: calcd. 164.0687, found 164.0686; IR (ATR) 2980, 2864, 1744, 1719, 1631, 1374, 1341, 1258, 1102, 1022 cm^{-1}.

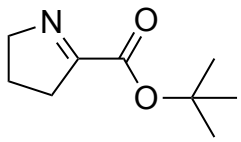
***iso*-Propyl pyrroline 2-carboxylate (1d):**



To a solution of *L*-proline *iso*-propyl ester (0.63 g, 4.0 mmol) in CH_2Cl_2 (12 mL) were added triethylamine (1.11 mL, 8.0 mmol) and *N*-chlorosuccinimide (0.59 g, 4.4 mmol) at 0 °C. After stirred under nitrogen at room temperature for 15 h, the reaction mixture was concentrated under reduced pressure. Sat. NH_4Cl aq. (20 mL) was added to the residue, and the reaction mixture was extracted with Et_2O (20 mL × 3). The combined organic layers were washed by sat. $NaHCO_3$ aq. (30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 2/1) as a mixed eluent to give **1d** (0.39 g, 2.52 mmol) in 63% yield.

Yellow oil; ^{1}H NMR (300 MHz, C_6D_6) δ 5.10 (sep., J = 6.3 Hz, 1H), 3.77–3.70 (m, 2H), 2.47–2.30 (m, 2H), 1.31–1.20 (m, 2H), 1.08 (d, J = 6.3 Hz, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 168.1, 163.2, 68.8, 62.7, 35.7, 22.1, 21.7; HRMS (ESI) m/z for $C_8H_{13}NO_2Na$ $[M+Na]^+$: calcd. 178.0844, found 178.0837; IR (ATR) 2980, 2938, 2871, 1740, 1713, 1629, 1374, 1319, 1259, 1097 cm^{-1}.

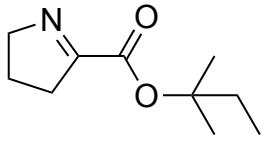
***tert*-Butyl pyrroline 2-carboxylate (1e):**



To a solution of *L*-proline *tert*-butyl ester (1.66 g, 9.7 mmol) in CH_2Cl_2 (30 mL) were added triethylamine (2.70 mL, 19.4 mmol) and *N*-chlorosuccinimide (1.43 g, 10.7 mmol) at 0 °C. After stirred under nitrogen at room temperature for 17 h, the reaction mixture was concentrated under reduced pressure. Sat. NH_4Cl aq. (20 mL) was added to the residue, and the reaction mixture was extracted with Et_2O (20 mL × 3). The combined organic layers were washed by sat. $NaHCO_3$ aq. (30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 4/1) as a mixed eluent to give **1e** (0.89 g, 5.24 mmol) in 54% yield.

Yellow oil; ^{1}H NMR (300 MHz, C_6D_6) δ 3.77–3.70 (m, 2H), 2.46–2.39 (m, 2H), 1.42 (s, 9H), 1.31–1.21 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6) δ 167.9, 163.1, 81.4, 62.6, 35.6, 28.0, 22.2; HRMS (ESI) m/z for $C_9H_{15}NO_2Na$ $[M+Na]^+$: calcd. 192.1000, found 192.0992; IR (ATR) 2978, 2933, 1738, 1712, 1631, 1478, 1367, 1254, 1165, 1105 cm^{-1}.

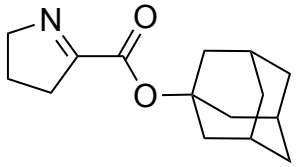
***tert*-Pentyl pyrroline 2-carboxylate (1f):**



To a solution of *L*-proline *tert*-pentyl ester (0.41 g, 2.0 mmol) in CH_2Cl_2 (6 mL) were added triethylamine (0.55 mL, 4.0 mmol) and *N*-chlorosuccinimide (0.29 g, 2.2 mmol) at 0 °C. After stirred under nitrogen at room temperature for 14 h, the reaction mixture was concentrated under reduced pressure. Sat. NH_4Cl aq. (10 mL) was added to the residue, and the reaction mixture was extracted with Et_2O (10 mL × 3). The combined organic layers were washed by sat. $NaHCO_3$ aq. (10 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (5/1 to 2/1) as a mixed eluent to give **1f** (0.22 g, 1.21 mmol) in 61 % yield.

Colorless oil; ^{1}H NMR (300 MHz, C_6D_6) δ 3.76–3.69 (m, 2H), 2.46–2.39 (m, 2H), 1.75 (q, J = 7.5 Hz, 2H), 1.43 (s, 6H), 1.31–1.20 (m, 2H), 0.85 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 168.9, 162.9, 83.9, 62.5, 35.6, 33.8, 25.5, 22.1, 8.4; HRMS (ESI) m/z for $C_{10}H_{17}NO_2Na$ $[M+Na]^+$: calcd. 206.1157, found 206.1153; IR (ATR) 2972, 2926, 2856, 1719, 1461, 1368, 1260, 1150, 1128, 832 cm^{-1}.

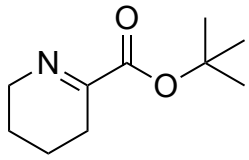
Adamanta-1-yl pyrroline 2-carboxylate (1g):



To a solution of *L*-proline adamanta-1-yl ester (0.50 g, 2.0 mmol) in CH_2Cl_2 (6 mL) were added triethylamine (0.56 mL, 4.0 mmol) and *N*-chlorosuccinimide (0.29 g, 2.2 mmol) at 0 °C. After stirred under nitrogen at room temperature for 10 h, the reaction mixture was concentrated under reduced pressure. Sat. NH_4Cl aq. (10 mL) was added to the residue, and the reaction mixture was extracted with Et_2O (10 mL × 3). The combined organic layers were washed by sat. $NaHCO_3$ aq. (10 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 4/1) as a mixed eluent to give **1g** (0.29 g, 1.16 mmol) in 58% yield.

Brown solid; M.p. 36.5–37.5 °C; ^{1}H NMR (300 MHz, C_6D_6) δ 3.78–3.71 (m, 2H), 2.48–2.41 (m, 2H), 2.37–2.30 (m, 6H), 1.93–1.91 (m, 3H), 1.51–1.36 (m, 6H), 1.32–1.21 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6) δ 169.0, 162.7, 81.6, 62.5, 41.5, 36.3, 35.7, 31.2, 22.2; HRMS (ESI) m/z for $C_{15}H_{21}NO_2Na$ $[M+Na]^+$: calcd. 270.1470, found 270.1471; IR (ATR) 2909, 2849, 1729, 1704, 1455, 1353, 1278, 1099, 1056, 794 cm^{-1}.

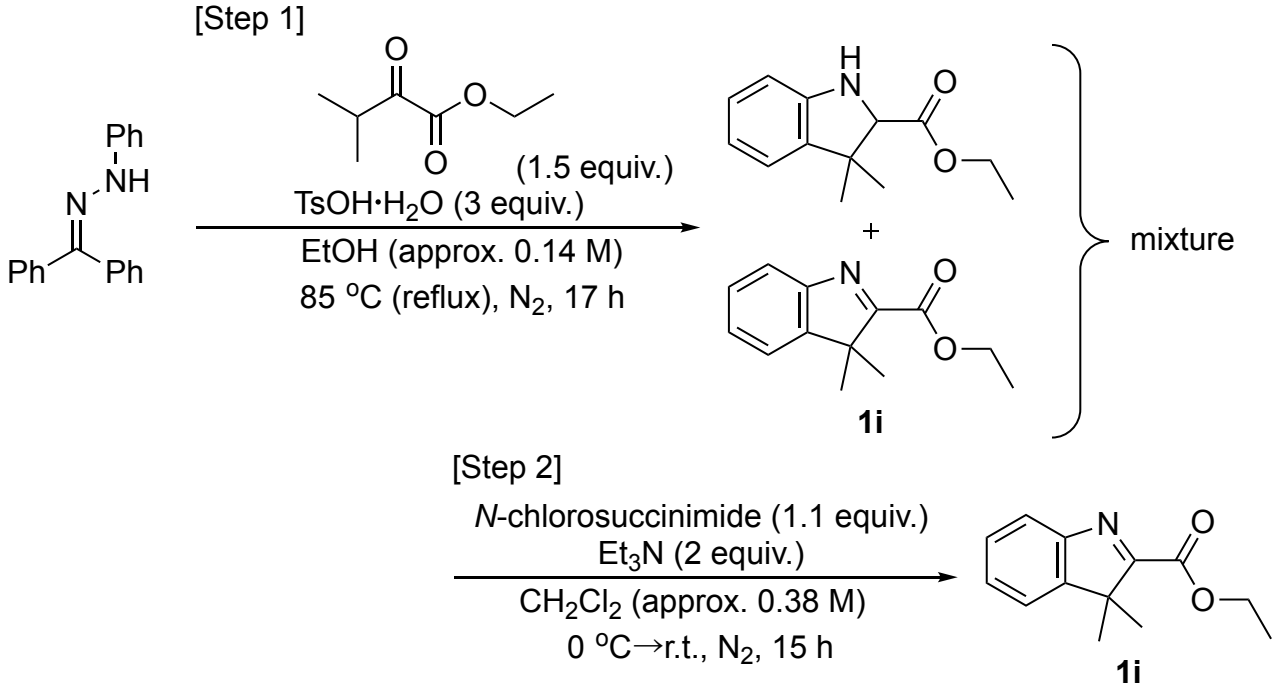
***tert*-Butyl 3,4,5,6-tetrahydropyridine 2-carboxylate (1h):**



To a solution of pipecoline *tert*-butyl ester (0.28 g, 1.5 mmol) in CH_2Cl_2 (4.5 mL) were added triethylamine (0.42 mL, 3.0 mmol) and *N*-chlorosuccinimide (0.22 g, 1.65 mmol) at 0 °C. After stirred under nitrogen at room temperature for 20 h, the reaction mixture was concentrated under reduced pressure. Sat. NH_4Cl aq. (10 mL) was added to the residue, and the reaction mixture was extracted with Et_2O (10 mL × 3). The combined organic layers were washed by sat. $NaHCO_3$ aq. (10 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (19/1 to 9/1) as a mixed eluent to give **1h** (0.081 g, 0.44 mmol) in 29% yield, which is contaminated with 70% of enamine form.

Orange solid; ^{1}H NMR (300 MHz, $CDCl_3$) of ketimine (**1h**) δ 3.85–3.78 (m, 0.6H), 2.46–2.40 (m, 0.6H), 1.75–1.67 (m, 0.6H), 1.54 (s, 2.7H); ^{1}H NMR (300 MHz, $CDCl_3$) of enamine δ 5.59 (t, J = 4.5 Hz, 0.7H), 3.18–3.14 (m, 1.4H), 2.20–2.15 (m, 1.4H), 1.83–1.77 (m, 1.4H), 1.65–1.57 (m, 0.7H), 1.49 (s, 6.3H); ^{13}C NMR (125 MHz, $CDCl_3$) of ketimine (**1h**) δ 163.0,163.0, 82.1, 27.9, 26.3, 21.3, 18.8; ^{13}C NMR (125 MHz, $CDCl_3$) of enamine δ 163.9, 135.3, 106.4, 80.9, 41.4, 28.0, 22.2, 21.7; HRMS (ESI) m/z for $C_{10}H_{17}NO_2Na$ $[M+Na]^+$: calcd. 206.1154, found 206.1157; IR (ATR) 3407, 2971, 2949, 2925, 2835, 1688, 1637, 1491, 1362, 1329, 1283, 1254, 1158, 1143, 1085, 848, 730 cm^{-1}.

3-2. Synthesis of ethyl 3,3-dimethyl-3*H*-indole-2-carboxylate (1i)[6)]



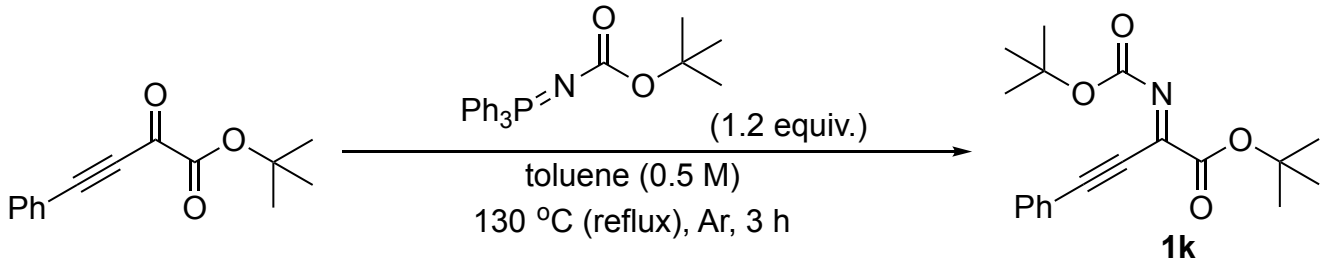
[Step 1] To a solution of benzophenone *N*-phenylhydrazone (0.82 g, 3.0 mmol), ethyl pyruvate (0.65 g, 4.5 mmol) in ethanol (21 mL) was added *p*-toluenesulfonic acid monohydrate (1.71 g, 9.0 mmol) at room temperature. After stirred and refluxed at 85 °C under nitrogen for 17 h, the reaction mixture was cooled down to room temperature and neutralized with sat. $NaHCO_3$ aq. (20 mL). The reaction mixture was extracted AcOEt (20 mL × 2), and the combined organic layers were washed with brine (20 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (15/1 to 9/1) as a mixed eluent and recrystallization to give ethyl 3,3-dimethylindoline-2-carboxylate (39.5 mg, 0.18 mmol) and **1i** (60.8 mg, 0.28 mmol) as an unseparated mixed product.

[Step 2] To a solution of the above-mentioned mixture (total 0.10 g, 0.46 mmol) in CH_2Cl_2 (1.2 mL) were added triethylamine (0.13 mL, 0.92 mmol) and *N*-chlorosuccinimide (0.07 g, 0.51 mmol) at 0 °C. After stirred under nitrogen at room temperature for 15 h, the reaction mixture was concentrated under reduced pressure. Sat. NH_4Cl aq. (10 mL) was added to the residue, and the reaction mixture was extracted with Et_2O (10 mL × 3). The combined organic layers were washed by sat. $NaHCO_3$ aq. (10 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (15/1 to 9/1) as a mixed eluent to give **1i** (65.3 mg, 0.30 mmol) in 10 % total yield (2 steps).

Yellow solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84–7.80 (m, 1H), 7.41–7.33 (m, 3H), 4.45 (q, J = 7.2 Hz,

2H), 1.51 (s, 6H), 1.45 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6, 161.6, 151.9, 147.6, 128.4, 128.0, 123.5, 121.3, 61.8, 54.2, 22.6, 14.3. Spectroscopic data of ^{1}H NMR was identical to that reported in reference 7.

3-3. Synthesis of *tert*-butyl 2-[(*tert*-butoxycarbonyl)imino]-4-phenylbut-3-ynoate (1k)[8)]

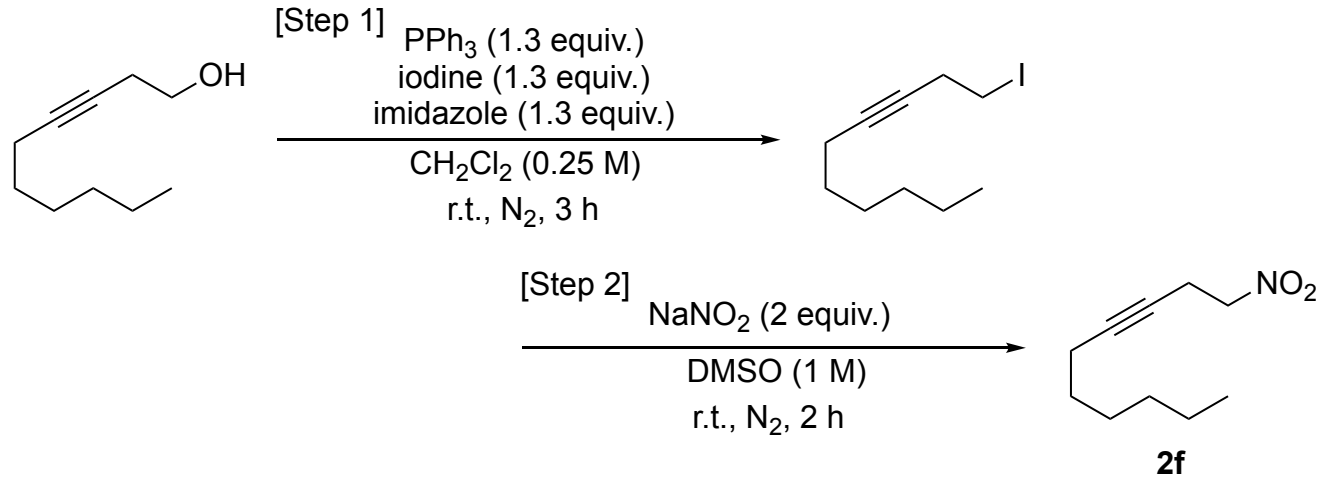


1k

To a solution of 3-phenylpropionic acid *tert*-butyl ester (0.35 g, 1.5 mmol) in toluene (3 mL) was added triphenyl(*tert*-butoxycarbonylimino)phosphorane (0.68 g, 1.8 mmol) at room temperature. After stirred and refluxed at 130 °C under argon for 3 h, the reaction mixture was cooled down to room temperature and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (19/1 to 9/1) as a mixed eluent to give **1k** (0.17 g, 0.516 mmol) in 34% yield.

Yellow solid; M.p. 92.0–93.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55–7.35 (m, 5H), 1.59 (s, 9H), 1.58 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 160.0, 132.7, 130.8, 128.6, 120.2, 100.6, 84.4, 83.9, 81.3, 28.1, 27.8; HRMS (ESI) m/z for $C_{19}H_{23}NO_4Na$ $[M+Na]^+$: calcd. 352.1525, found 352.1521; IR (ATR) 2980, 2935, 2203, 1721, 1609, 1591, 1488, 1370, 1252, 1146 cm^{-1}.

3-4. Synthesis of 1-nitrodec-3-yne (2f)[2b)]



2f

[Step 1] To a solution of triphenylphosphine (3.41 g, 13.0 mmol), iodine (3.30 g, 13.0 mmol), and

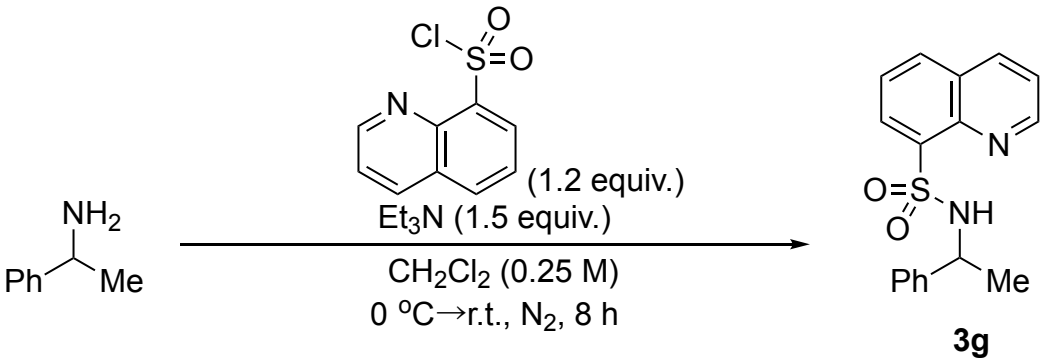
imidazole (0.89 g, 13.0 mmol) in CH_2Cl_2 (40 mL) was added 3-decyn-1-ol (1.77 mL, 10.0 mmol) at room temperature. After stirred under nitrogen at room temperature for 3 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane as an only eluent to give 1-iododec-3-yne (1.09 g, 5.6 mmol) in 56% yield.

Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.21 (t, J = 7.5 Hz, 2H), 2.74 (tt, J = 2.1, 7.5 Hz, 2H), 2.13 (t, J = 2.1, 7.5 Hz, 2H), 1.53–1.24 (m, 8H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 82.6, 78.7, 31.3, 28.7, 28.5, 24.1, 22.6, 18.7, 14.1, 2.8. Spectroscopic data of ^{1}H NMR was identical to that reported in reference 9.

[Step 2] To a solution of 1-iododec-3-yne (1.09 g, 5.6 mmol) in dimethylsulfoxide (5.6 mL) was added sodium nitrite (0.77 g, 11.2 mmol) at room temperature. After stirred under nitrogen at room temperature for 2 h, to the residue was added cooled water (10 mL) and the reaction mixture was extracted with Et_2O (10 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/Et_2O (19/1 to 14/1) as a mixed eluent to give **2f** (0.26 g, 2.3 mmol) in 41% yield.

Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.46 (t, J = 7.2 Hz, 2H), 2.87 (tt, J = 2.4, 7.2 Hz, 2H), 2.12 (t, J = 2.4, 7.2 Hz, 2H), 1.50–1.41 (m, 2H), 1.39–1.23 (m, 6H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 84.0, 73.9, 73.2, 31.3, 28.6, 28.4, 22.5, 18.6, 17.9, 14.0; HRMS (ESI) m/z for $C_{10}H_{17}NO_2Na$ $[M+Na]^+$: calcd. 206.1157, found 206.1154; IR (ATR) 2930, 2859, 1556, 1431, 1377, 1336, 1199, 861 cm^{-1}.

3-5. Synthesis of *N*-(1-phenylethyl)quinoline-8-sulfonamide (3g)



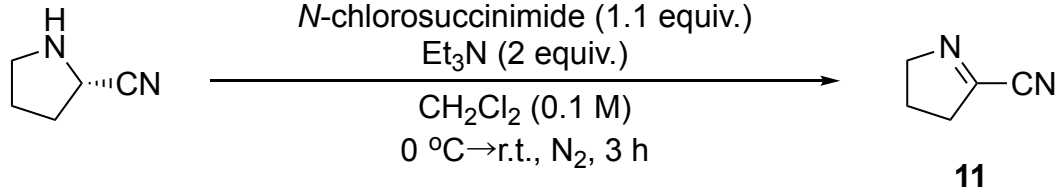
3g

To a solution of DL-1-phenylethylamine (0.30 g mL 2.5 mmol) in CH_2Cl_2 (10 mL) were added triethylamine (0.52 mL, 3.75 mmol) and 8-quinolinesulfornyl chloride (0.68 g, 3.0 mmol) at 0 °C. After stirred under nitrogen at room temperature for 8 h, to the reaction mixture was added sat. $NaHCO_3$ aq. (10

mL), and the reaction mixture was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (4/1 to 2/1) as a mixed eluent to give **3g** (0.71 g, 2.3 mmol) in 91% yield.

White solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.91 (dd, *J* = 1.8, 4.2 Hz, 1H), 8.26 (dd, *J* = 1.5, 7.5 Hz, 1H), 8.15 (dd, *J* = 1.8, 8.1 Hz, 1H), 7.90 (dd, *J* = 1.5, 8.1 Hz, 1H), 7.54–7.45 (m, 2H), 6.89–6.81 (m, 5H), 6.58 (d, *J* = 7.8 Hz, 1H), 4.47 (dq, *J* = 6.9, 7.8 Hz, 1H), 1.42 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.7, 142.9, 141.2, 136.7, 132.8, 130.6, 128.5, 127.6, 127.1, 125.9, 125.5, 121.9, 54.6, 23.1. Spectroscopic data of ^{1}H and ^{13}C NMR were identical to that reported in reference 10.

3-6. Synthesis of 2-cyano-1-pyrroline (11)[5)]

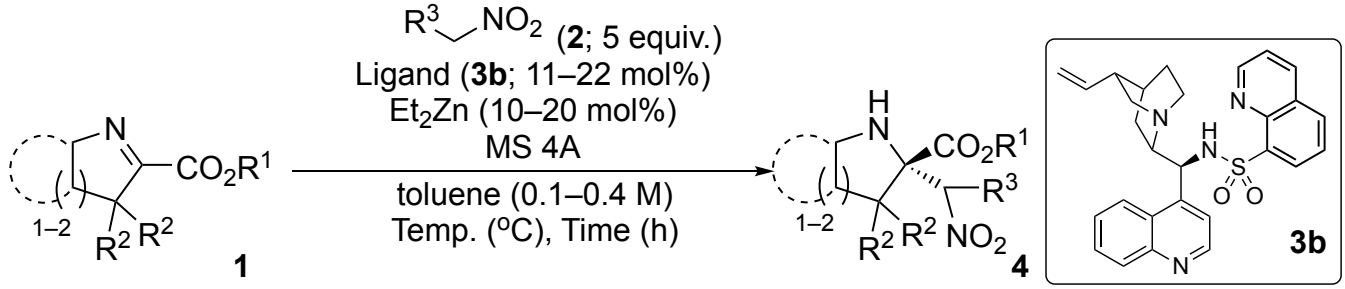


11

To a solution of (*S*)-pyrrolidine-2-carbonitrile (49.9 mg, 0.52 mmol) in CH_2Cl_2 (5.2 mL) were added triethylamine (0.15 mL, 1.08 mmol) and *N*-chlorosuccinimide (76.4 g, 0.572 mmol) at 0 °C. After stirred under nitrogen at room temperature for 3 h, the reaction mixture was concentrated under reduced pressure. To the residue was added sat. NH_4Cl aq. (10 mL) and the reaction mixture was extracted with Et_2O (20 mL × 2). The combined organic layers were washed by sat. $NaHCO_3$ aq. (10 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 2/1) as a mixed eluent to give **11** (9.8 mg, 0.10 mmol) in 20% yield.

Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.15–4.08 (m, 2H), 2.85–2.78 (m, 2H), 2.08–1.98 (m, 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.2, 114.2, 63.0, 38.9, 21.6. Spectroscopic data of ^{1}H and ^{13}C NMR were identical to that reported in reference 11.

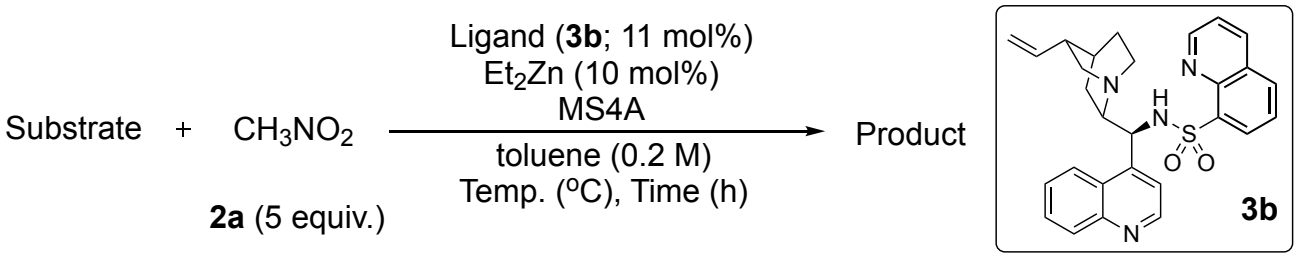
4. General Procedures for the Enantioselective Aza-Henry Reaction:

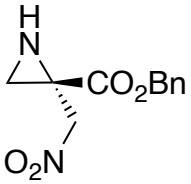
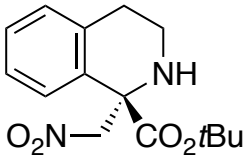
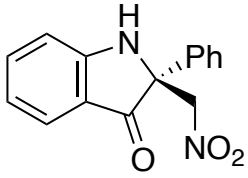
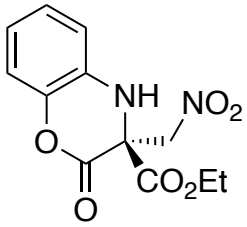


To a suspension of **3b** (11–22 mol%) and MS 4A in toluene (0.1–0.4 M) were added 1.0 M toluene solution of Et_2Zn (10–20 mol%) and the reaction mixture was stirred under argon at room temperature for 1 h. Ketimines (**1**; 1.0 equiv.) and nitroalkanes (**2**; 5.0 equiv.) were added at an adequate reaction temperature. After stirred for an adequate reaction time (in the case of $R^3 \neq H$; the reaction mixture was passed through a celite pad. The obtained filtrate was concentrated under reduced pressure to give the crude product and the diastereomer ratio was determined by ^1H NMR analysis.) the reaction mixture was purified by silica-gel column chromatography to give the corresponding chiral cyclic amines (**4**)

5. Limitation of Substrates:

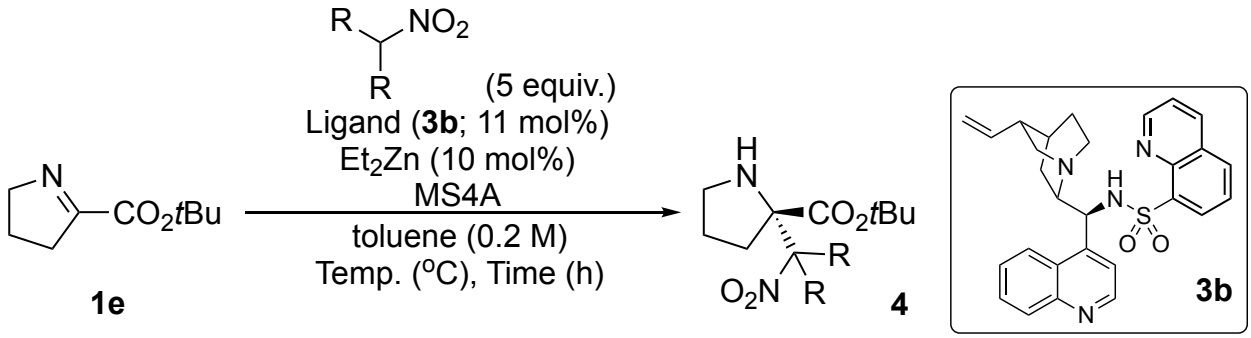
5-1. Scope of iminoesters as an electrophile

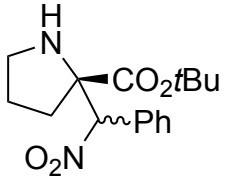
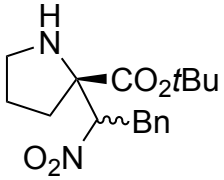
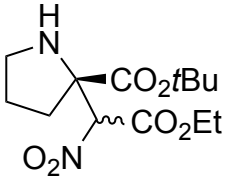
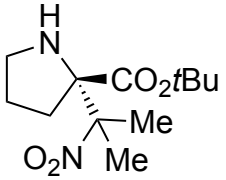


			
not obtained (–78 °C, 24 h)	24% yield 29% ee (r.t. to 50 °C, 48 h)	90% yield 25% ee (r.t., 120 h)	not obtained [a] (0 °C to 50 °C, 2 days)

[a] Ligand **3b**/Et_2Zn (22/20 mol%) were used.

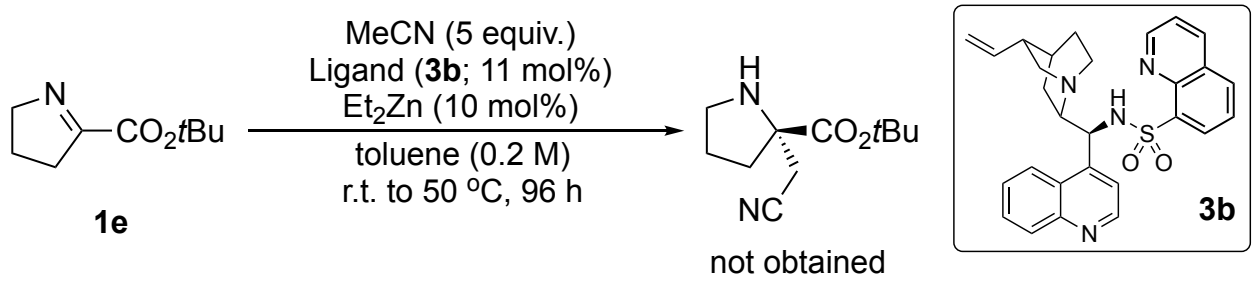
5-2. Scope of nitroalkanes as a nucleophile



			
not obtained (r.t., 96 h)	71% yield 64:36 dr 30/68% ee [a,b] (15 °C, 144 h)	not obtained (r.t., 120 h)	not obtained (r.t., 120 h)

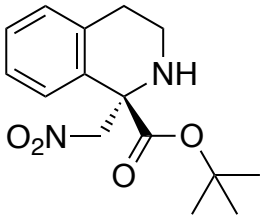
[a] Ligand **3b**/Et_2Zn (22/20 mol%) were used. [b] 0.1 M in toluene.

5-3. Reaction of 1e with acetonitrile



5-4. Characterization Data of the Synthesized Products in Tables 5-1 and 5-2:

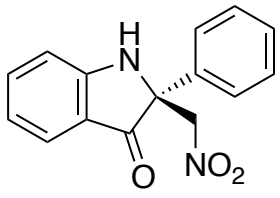
***tert*-Butyl (*S*)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline 1-carboxylate:**



To a suspension of **3b** (2.7 mg, 0.0055 mmol) and MS 4A (5.0 mg) in toluene (0.25 mL) were added 1.0 M toluene solution of Et_2Zn (5.0 μL, 0.005 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. *tert*-Butyl 1,2,3,4-tetrahydroisoquinoline 1-carboxylate (11.6 mg, 0.05 mmol) and nitromethane (**2a**; 13.4 μL, 0.25 mmol) were added at room temperature. After stirred at room temperature for 4 h, the reaction mixture was heated to 50 °C. After further stirred at 50 °C for 44 h (total 48 h), the reaction mixture was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 4/1) as a mixed eluent to give *tert*-butyl (*S*)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline 1-carboxylate (3.5 mg, 0.012 mmol) in 24% yield with 29% ee.

Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (dd, J = 1.8, 7.2 Hz, 1H), 7.26–7.14 (m, 3H), 5.23 (d, J = 13.8 Hz, 1H), 4.54 (d, J = 13.8 Hz, 1H), 3.43–3.35 (m, 1H), 3.07–2.99 (m, 1H), 2.92–2.71 (m, 3H), 1.49 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 137.1, 130.5, 130.2, 128.0, 126.5, 126.2, 83.4, 82.4, 62.7, 39.5, 29.9, 27.7; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 90:10, 1 mL/min, 40 °C, 235 nm), tR = 5.6 min (major), 7.0 min (minor).

(*S*)-2-(Nitromethyl)-2-phenylindolin-3-one:

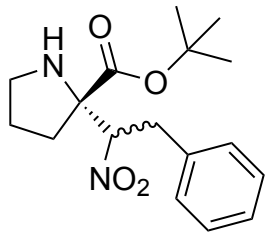


To a suspension of **3b** (2.7 mg, 0.0055 mmol) and MS 4A (5.0 mg) in toluene (0.25 mL) were added 1.0 M toluene solution of Et_2Zn (5.0 μL, 0.005 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. 2-Phenyl-3*H*-indol-3-one (10.4 mg, 0.05 mmol) and nitromethane (**2a**; 13.4 μL, 0.25 mmol) were added at room temperature. After stirred at room temperature for 120 h, the reaction mixture was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 4/1) as a mixed eluent to give *tert*-butyl (*S*)-2-(nitromethyl)- 2-phenylindolin-3-one (12.1 mg, 0.045 mmol) in 90% yield with 25% ee.

Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.52 (m, 4H), 7.40 (m, 3H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 5.94 (br, 1H), 5.24 (d, *J* = 13.8 Hz, 1H), 4.80 (d, *J* = 13.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.2, 160.1, 138.3, 134.4, 129.2, 128.8, 125.8, 125.1, 120.1, 118.3, 112.2, 80.3, 69.2; HPLC (DAICEL CHIRALPAK IC-3®, hexane:*i*-PrOH = 90:10, 1 mL/min, 40 °C, 240 nm), tR = 27.7 min (minor), 29.3 min (major).

Spectroscopic data of ^{1}H and ^{13}C NMR were identical to that reported in reference 12.

***tert*-Butyl (*S*)-2-(1-nitro-2-phenylethyl)pyrrolidine 2-carboxylate:**

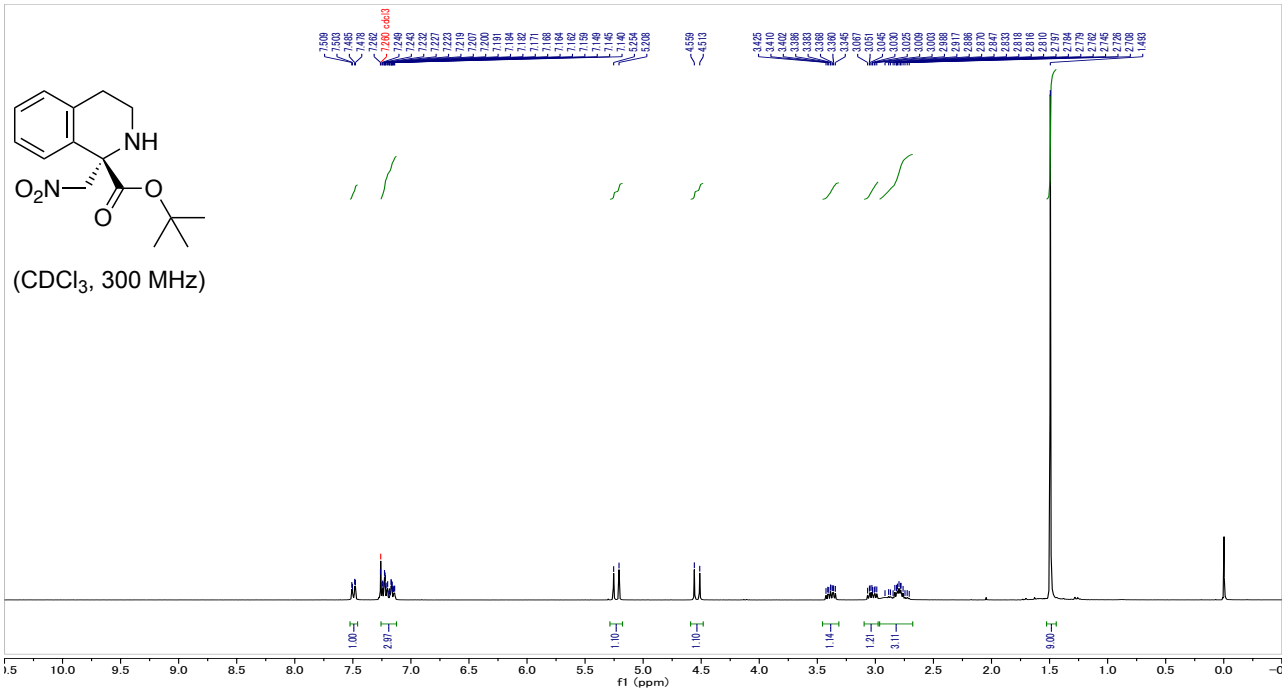


To a suspension of **3b** (5.3 mg, 0.011 mmol) and MS 4A (10.0 mg) in toluene (0.5 mL) were added 1.0 M toluene solution of Et_2Zn (10.0 μL, 0.01 mmol. **1e** (16.9 mg, 0.1 mmol) and 2-phenylnitroethane (75.6 mg, 0.5 mmol) were added at 15 °C. After stirred at 15 °C for 144 h, the reaction mixture was passed through a celite pad. The obtained filtrate was concentrated under reduced pressure to give the crude product and the diastereomer ratio was determined by ^{1}H NMR analysis. The crude product was purified by silica-gel column chromatography using hexane/AcOEt (9/1 to 4/1) as a mixed eluent to give *tert*-butyl (*S*)-2-(1-nitro-2-phenylethyl)pyrrolidine 2-carboxylate (22.7 mg, 0.071 mmol) in 71% yield with 64:36 dr, 30/68% ee.

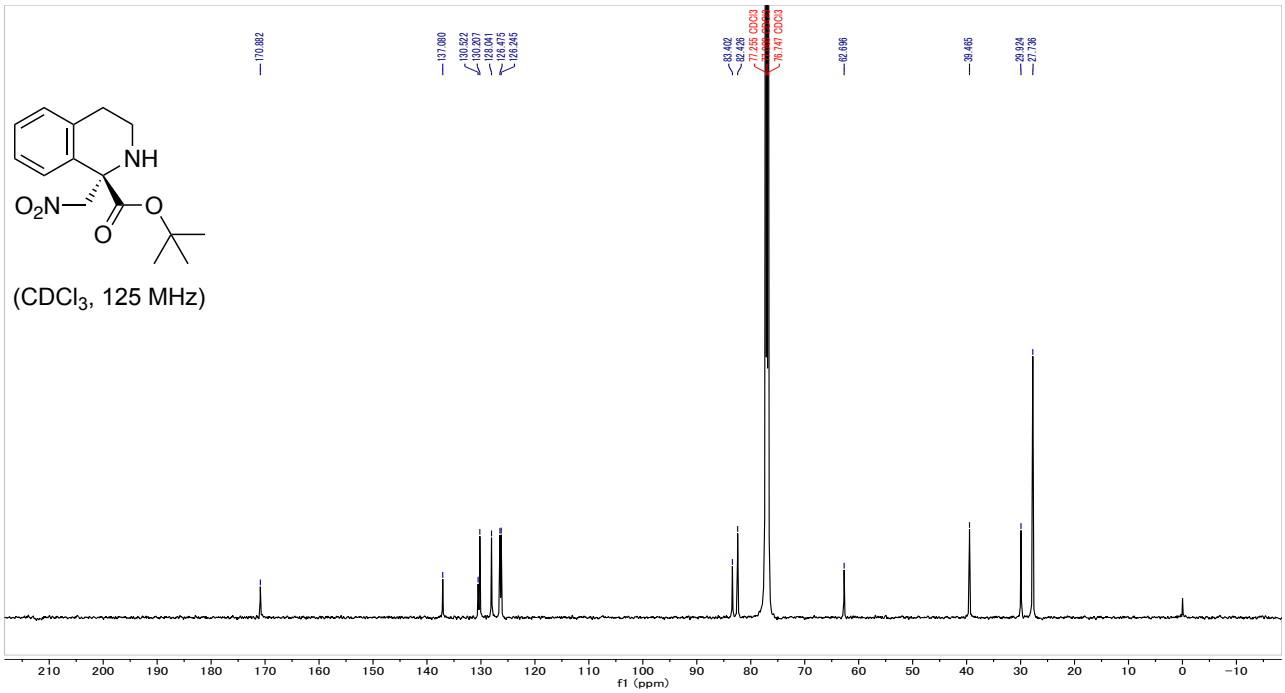
Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24–7.20 (m, 3H), 7.16–7.10 (m, 2H), 4.98–4.89 (m, 1H), 3.45–3.26 (m, 1H), 3.11–2.90 (m, 3H), 2.64 (br, 1H), 2.14–2.02 (m, 2H), 1.79–1.65 (m, 2H), 1.51 (s, 5.4H), 1.43 (s, 3.6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 172.5, 136.4, 136.1, 128.8, 128.8, 128.7, 128.7, 127.3, 127.2, 95.2, 94.3, 83.2, 82.9, 71.5, 71.0, 47.1, 35.9, 35.2, 34.0, 33.2, 27.9, 27.7, 25.3, 24.6; HPLC (DAICEL CHIRALPAK IA-3®, hexane:*i*-PrOH = 99.5:0.5, 0.7 mL/min, 230 nm), minor diastereomer: tR = 30.5 min (major), 35.3 min (miner), major diastereomer: tR = 36.5 min (major), 51.4 min (minor).

5-5. ^{1}H, ^{13}C NMR Spectra of the Synthesized Products in Tables 5-1 and 5-2:

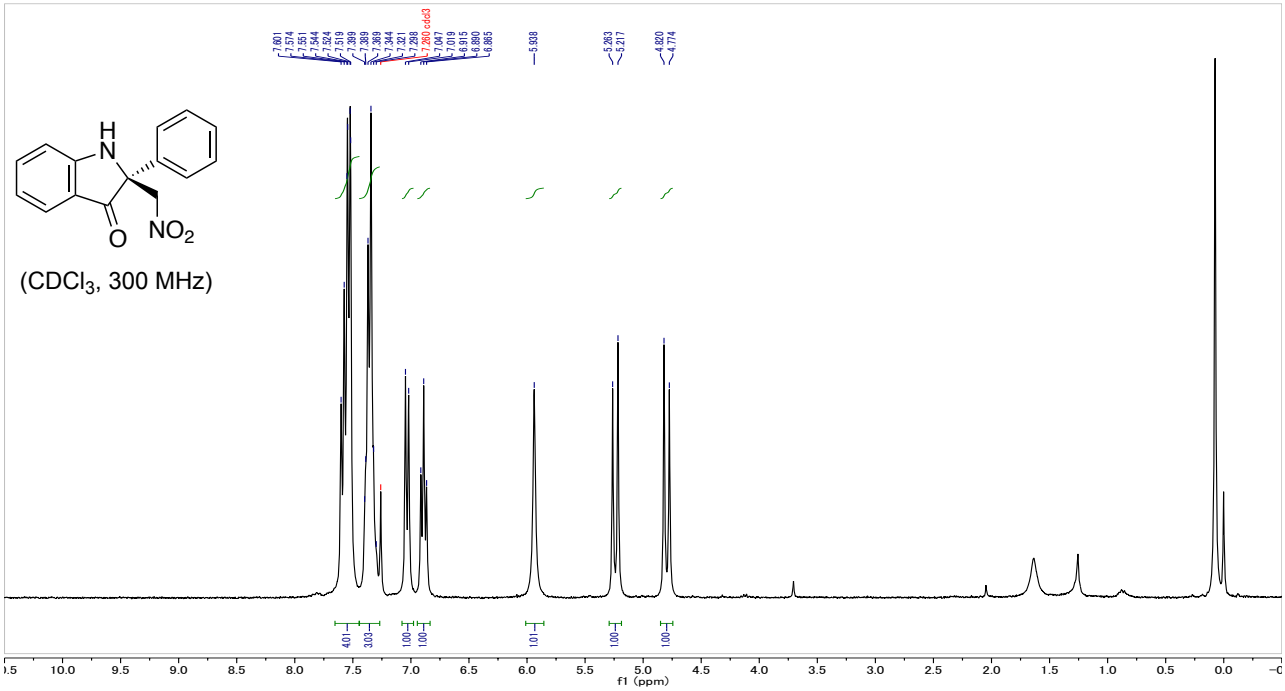
^{1}H NMR of *tert*-butyl (*S*)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline 1-carboxylate



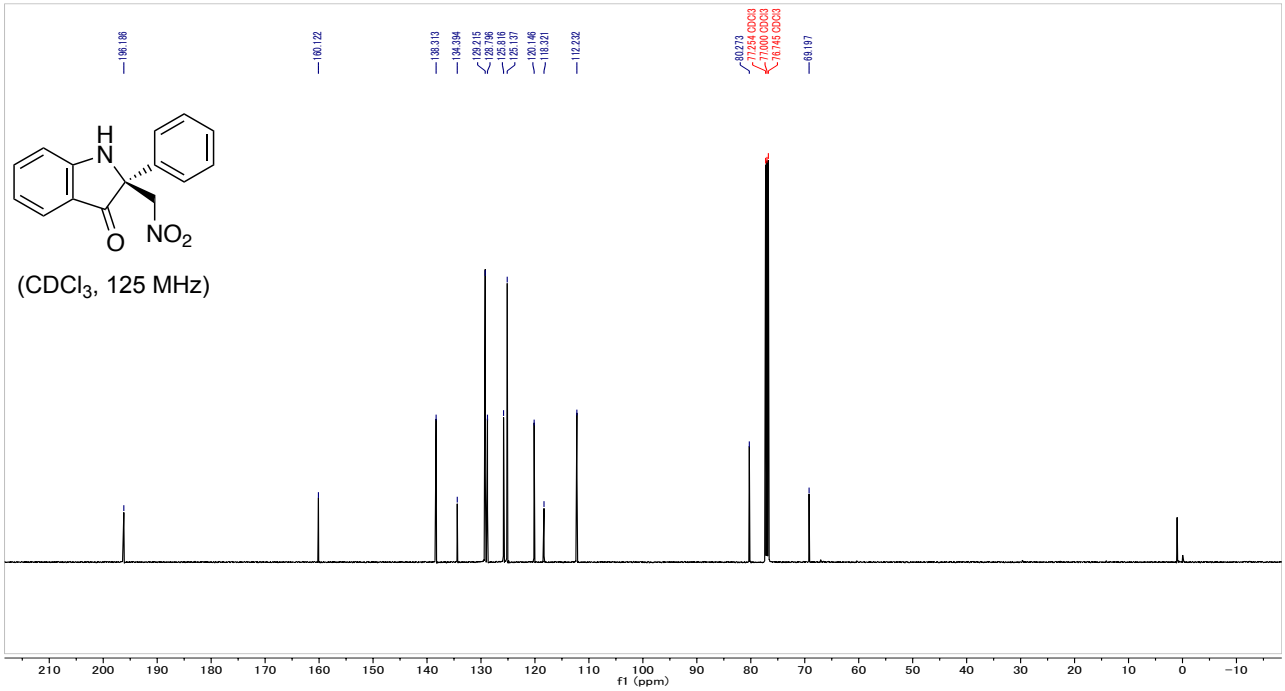
^{13}C NMR of *tert*-butyl (*S*)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline 1-carboxylate



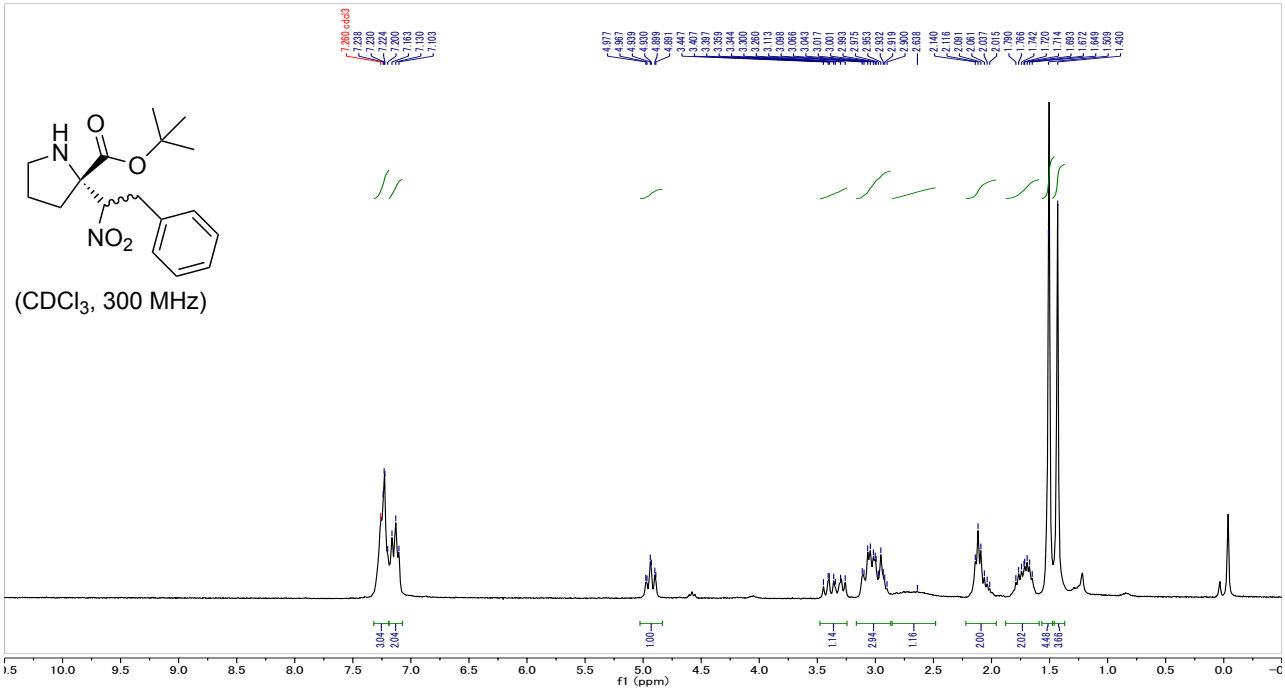
^{1}H NMR of (*S*)-2-(nitromethyl)-2-phenylindolin-3-one



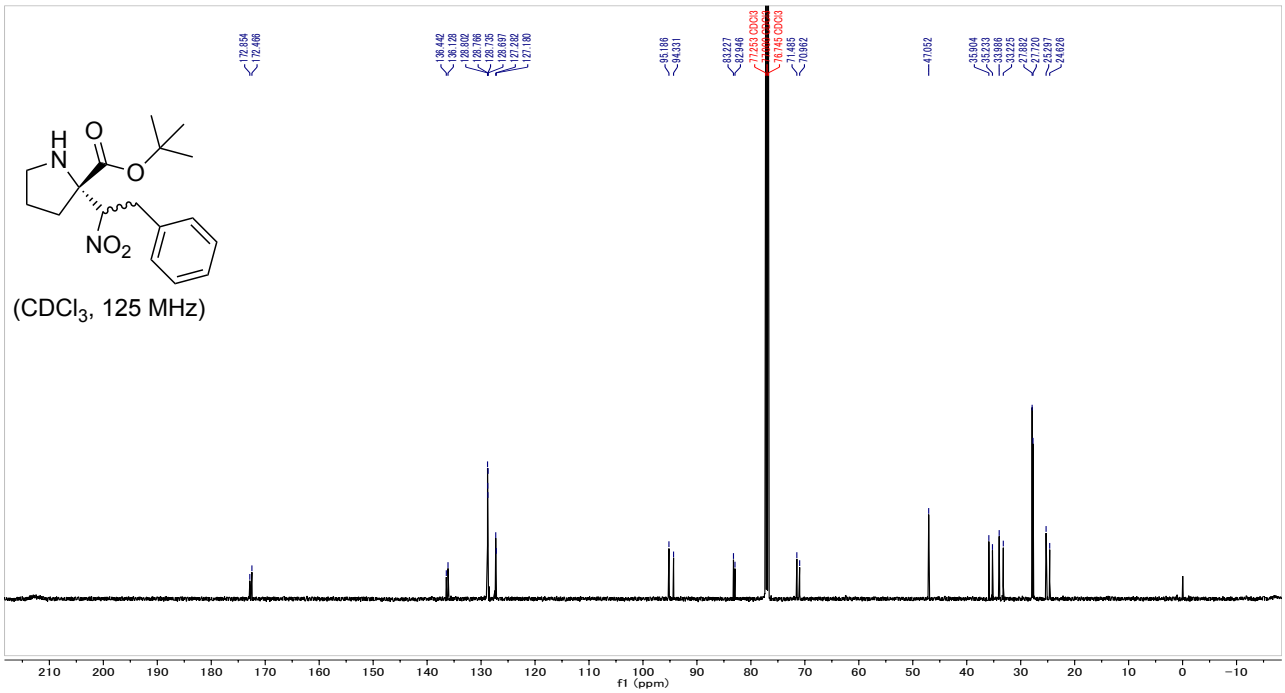
^{13}C NMR of (*S*)-2-(nitromethyl)-2-phenylindolin-3-one



^{1}H NMR of *tert*-butyl (*S*)-2-(1-nitro-2-phenylethyl)pyrrolidine 2-carboxylate

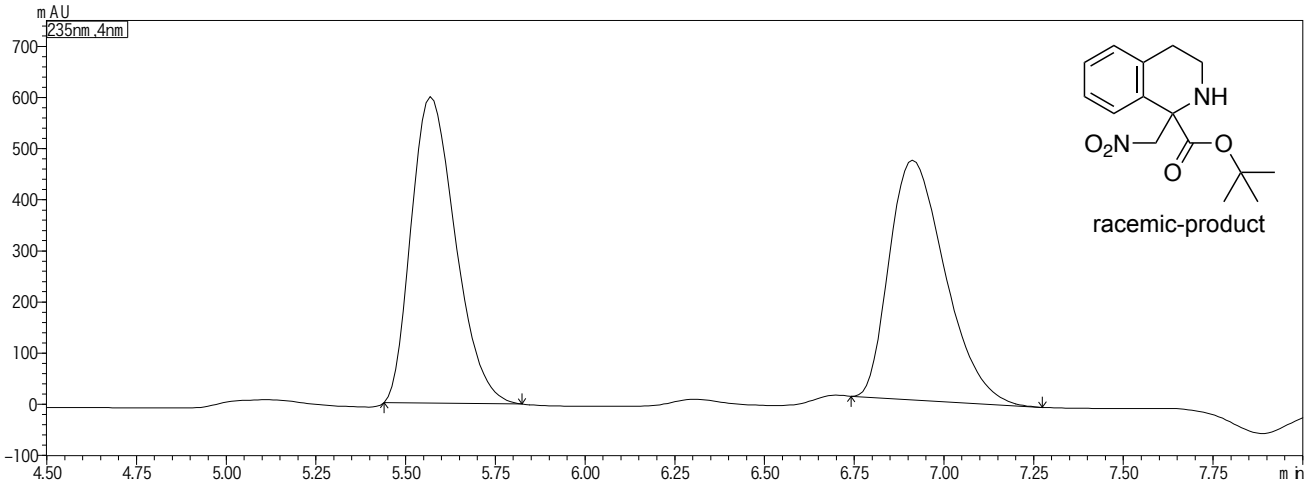


^{13}C NMR of *tert*-butyl (*S*)-2-(1-nitro-2-phenylethyl)pyrrolidine 2-carboxylate

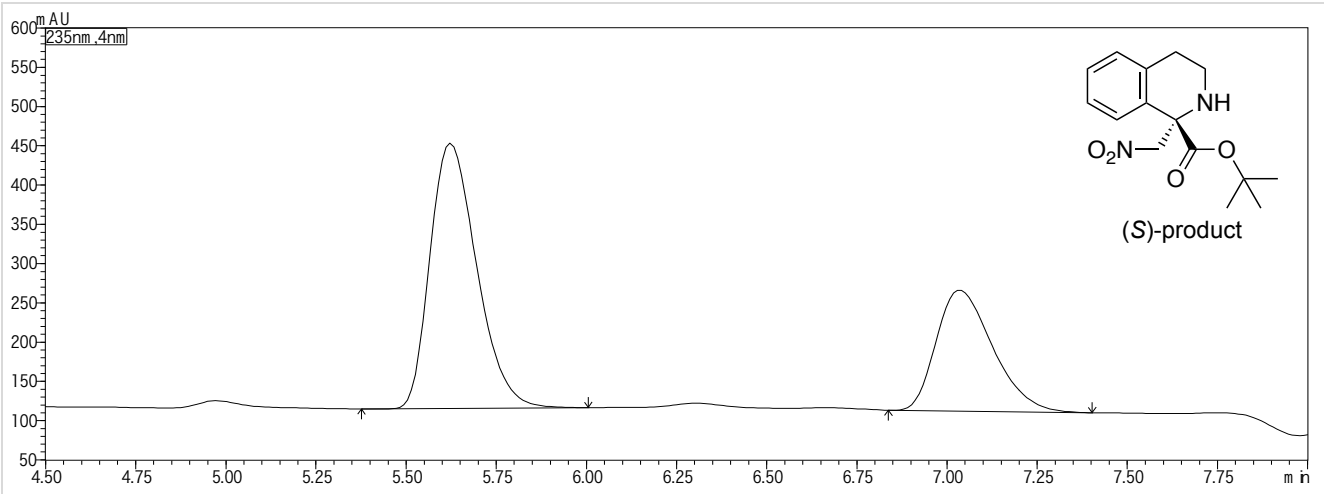


5-6. HPLC Charts of the Synthesized Products of Tables 5-1 and 5-2:

HPLC of *tert*-butyl 1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline 1-carboxylate



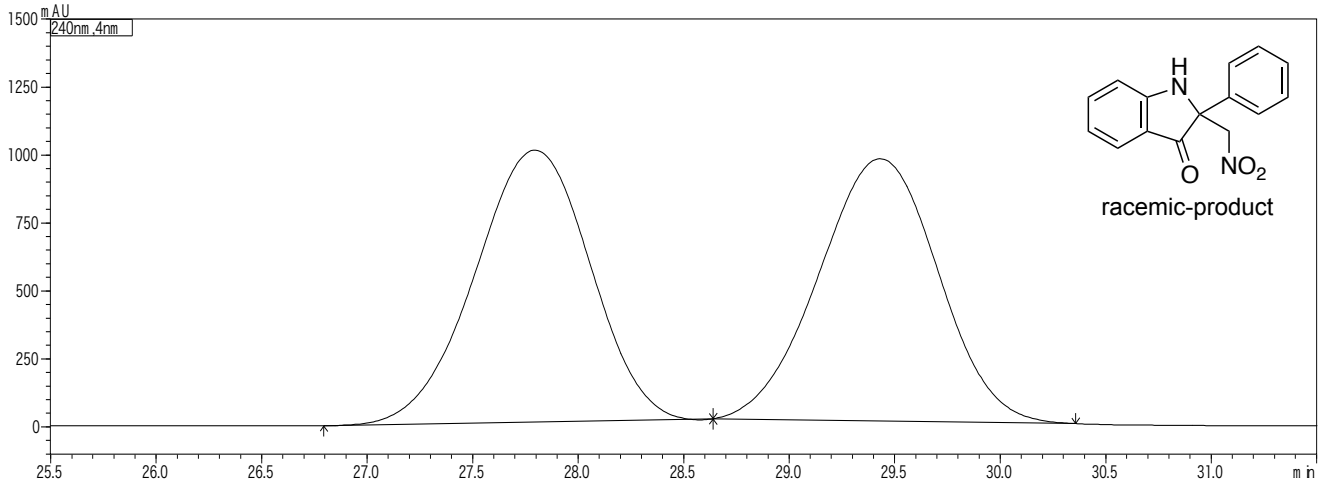
HPLC of *tert*-butyl (*S*)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline 1-carboxylate



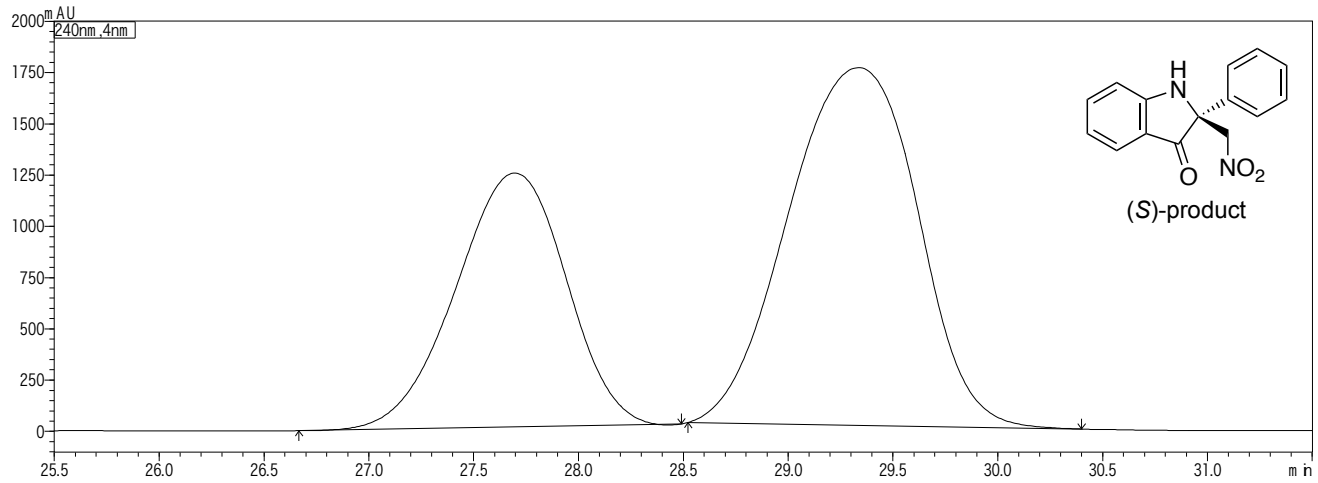
racemic-product		
Peak	tR (min)	Area (%)
1	5.6	50.2
2	6.9	49.8

(*S*)-product		
Peak	tR (min)	Area (%)
1	5.6	64.4
2	7.0	35.6

HPLC of 2-(nitromethyl)-2-phenylindolin-3-one



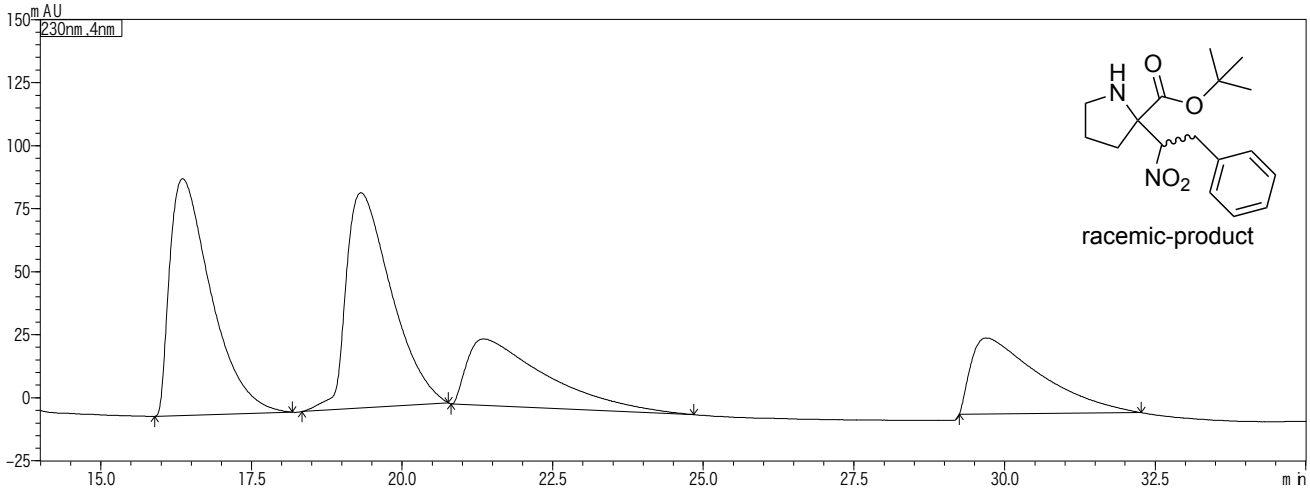
HPLC of ethyl (*S*)-2-(nitromethyl)-2-phenylindolin-3-one



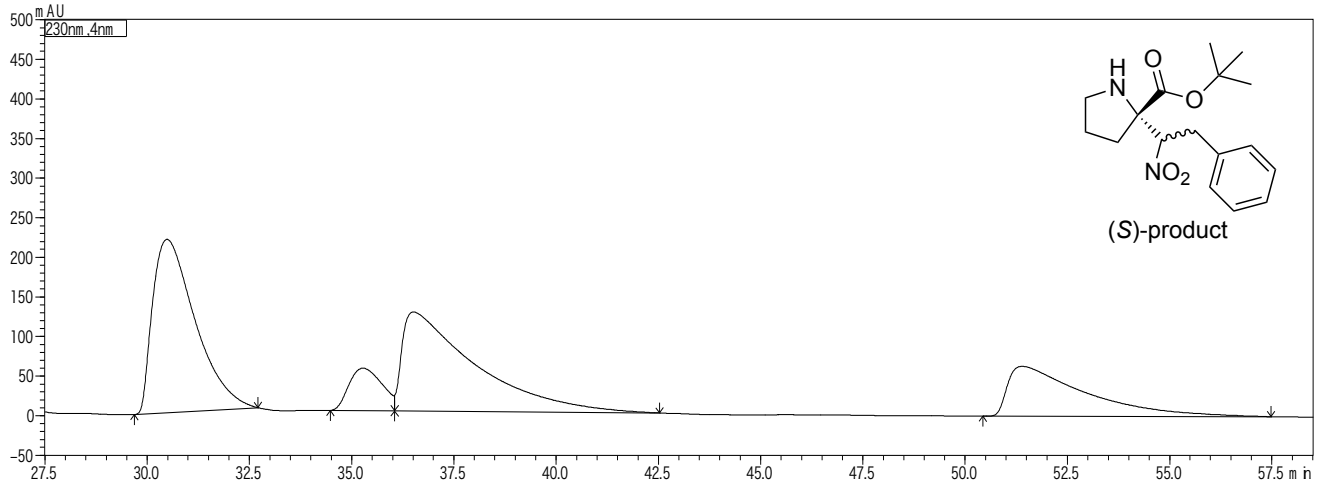
racemic-product		
Peak	tR (min)	Area (%)
1	27.8	50.0
2	29.4	50.0

(*S*)-product		
Peak	tR (min)	Area (%)
1	27.7	37.7
2	29.3	62.3

HPLC of *tert*-butyl 2-(1-nitro-2-phenylethyl)pyrrolidine 2-carboxylate[a]



HPLC of *tert*-butyl (*S*)-2-(1-nitro-2-phenylethyl)pyrrolidine 2-carboxylate[b]



racemic-product[a]		
Peak	tR (min)	Area (%)
1	16.4	32.6
2	19.3	32.6
3	21.3	17.4
4	29.7	17.4

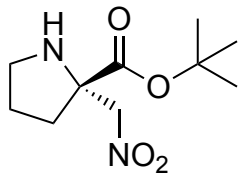
[a] Rate of racemic-sample = 1 mL/min.

(*S*)-product[b]		
Peak	tR (min)	Area (%)
1	30.5	37.2
2	35.3	7.1
3	36.5	36.3
4	51.4	19.4

[b] Rate of (*S*)-sample = 0.7 mL

6. Characterization Data of the Synthesized Products:

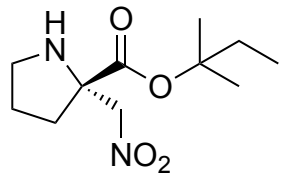
***tert*-Butyl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate (4ea):**



To a suspension of **3b** (5.3 mg, 0.011 mmol) and MS 4A (10.0 mg) in toluene (0.5 mL) were added 1.0 M toluene solution of Et_2Zn (10.0 μL, 0.01 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1e** (16.9 mg, 0.1 mmol) and nitromethane (**2a**; 26.8 μL, 0.5 mmol) were added at 0 °C. After stirred at 0 °C for 24 h, the reaction mixture was purified by silica-gel column chromatography using hexane/AcOEt (4/1 to 2/1) as a mixed eluent to give (*S*)-**4ea** (21.0 mg, 0.094 mmol) in 91% yield with 94% ee.

Colorless oil; $[\alpha]_D^{25}$ –80.3 (c 0.15, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.91 (d, *J* = 13.5 Hz, 1H), 4.34 (d, *J* = 13.5 Hz, 1H), 3.22–3.15 (m, 1H), 3.04–2.97 (m, 1H), 2.57 (br, 1H), 2.05–1.93 (m, 1H), 1.86–1.75 (m, 3H), 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1, 82.5, 82.1, 67.2, 47.4, 34.8, 27.8, 25.0; HRMS (ESI) m/z for $C_{10}H_{18}N_2O_4Na$ $[M+Na]^+$ calcd. 253.1164, found: 253.1168; IR (ATR) 3357, 2976, 2874, 1729, 1555, 1369, 1288, 1229, 1155, 1118 cm^{-1}; HPLC (DAICEL CHIRALPAK IH-3®, hexane:*i*-PrOH = 99:1, 0.7 mL/min, 40 °C, 210 nm), tR = 23.1 min (major), 27.9 min (minor).

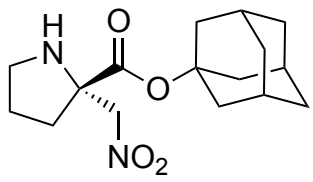
***tert*- Pentyl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate (4fa):**



To a suspension of **3b** (2.7 mg, 0.0055 mmol) and MS 4A (5.0 mg) in toluene (0.25 mL) were added 1.0 M toluene solution of Et_2Zn (5.0 μL, 0.005 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1f** (9.2 mg, 0.05 mmol) and nitromethane (**2a**; 13.4 μL, 0.25 mmol) were added at 0 °C. After stirred at 0 °C for 48 h, the reaction mixture was purified by silica-gel column chromatography using hexane/AcOEt (4/1 to 2/1) as a mixed eluent to give (*S*)-**4fa** (10.2 mg, 0.042 mmol) in 84% yield with 88% ee.

Colorless oil; $[\alpha]_D^{25}$ + 31.9 (c 0.85, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.89 (d, *J* = 13.8 Hz, 1H), 4.32 (d, *J* = 13.8 Hz, 1H), 3.21–3.13 (m, 1H), 3.02–2.95 (m, 1H), 2.54 (br, 1H), 2.05–1.92 (m, 1H), 1.88–1.67 (m, 5H), 1.45 (s, 3H), 1.43 (s, 3H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 85.1, 82.1, 67.3, 47.4, 34.9, 33.6, 25.1, 25.0, 8.2; HRMS (ESI) m/z for $C_{11}H_{20}N_2O_4Na$ $[M+Na]^+$ calcd. 267.1321, found: 267.1321; IR (ATR) 3365, 2975, 2943, 2881, 1729, 1556, 1378, 1223, 1152, 835 cm^{-1}; HPLC (DAICEL CHIRALPAK IH-3®, hexane:*i*-PrOH = 99:1, 0.5 mL/min, 210 nm), tR = 17.5 min (major), 23.0 min (minor).

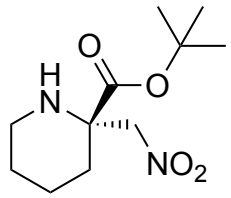
Adamanta-1-yl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate (4ga):



To a suspension of **3b** (2.7 mg, 0.0055 mmol) and MS 4A (5.0 mg) in toluene (0.25 mL) were added 1.0 M toluene solution of Et_2Zn (5.0 μL, 0.005 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1g** (12.4 mg, 0.05 mmol) and nitromethane (**2a**; 13.4 μL, 0.25 mmol) were added at 0 °C. After stirred at 0 °C for 48 h, the reaction mixture was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 4/1) as a mixed eluent to give (*S*)-**4ga** (13.2 mg, 0.043 mmol) in 86% yield with 88% ee.

White solid; M.p. 82.0–83.0 °C; $[\alpha]_D^{25}$ –21.8 (c 0.18, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.89 (d, *J* = 13.8 Hz, 1H), 4.32 (d, *J* = 13.8 Hz, 1H), 3.20–3.13 (m, 1H), 3.02–2.95 (m, 1H), 2.56 (br, 1H), 2.19–2.16 (m, 3H), 2.11–2.10 (m, 6H), 2.01–1.93 (m, 1H), 1.84–1.75 (m, 3H), 1.66–1.58 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 82.6, 82.1, 67.2, 47.4, 41.0, 36.0, 34.9, 30.8, 25.0; HRMS (ESI) m/z for $C_{16}H_{24}N_2O_4Na$ $[M+Na]^+$ calcd. 331.1634, found: 331.1630; IR (ATR) 3381, 3330, 2914, 2854, 1722, 1378, 1280, 1218, 1115, 1045, 878 cm^{-1}; HPLC (DAICEL CHIRALPAK IG®, hexane:*i*-PrOH = 90:10, 1 mL/min, 40 °C, 215 nm), tR = 14.8 min (major), 18.7 min (minor).

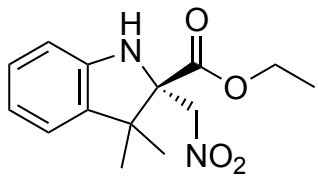
***tert*-Butyl (*S*)-2-(nitromethyl)piperidine 2-carboxylate (4ha):**



To a suspension of **3b** (5.3 mg, 0.011 mmol) and MS 4A (10.0 mg) in toluene (0.5 mL) were added 1.0 M toluene solution of Et_2Zn (10.0 μL, 0.01 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1h** (70% enamine form; 61.1 mg, 0.1 mmol) and nitromethane (**2a**; 26.8 μL, 0.5 mmol) were added at 0 °C. After stirred at 0 °C for 48 h, the reaction mixture was purified by silica-gel column chromatography using hexane/AcOEt (4/1 to 2/1) as a mixed eluent to give (*S*)-**4ha** (13.7 mg, 0.056 mmol) in 56% yield with 92% ee.

Colorless oil; $[\alpha]_D^{25}$ –100.5 (c 0.11, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.64 (d, *J* = 12.6 Hz, 1H), 4.49 (d, *J* = 12.6 Hz, 1H), 3.04–2.96 (m, 1H), 2.89–2.82 (m, 1H), 2.40 (br, 1H), 1.98–1.92 (m, 1H), 1.69–1.51 (m, 3H), 1.47 (s, 9H), 1.44–1.40 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 82.6, 82.4, 61.1, 42.2, 31.4, 27.8, 24.9, 20.9; HRMS (ESI) m/z for $C_{11}H_{20}N_2O_4Na$ $[M+Na]^+$ calcd. 267.1321, found: 267.1321; IR (ATR) 3353, 2977, 2935, 2863, 1731, 1553, 1368, 1231, 1147, 1130 cm^{-1}; HPLC (DAICEL CHIRALPAK IH-3®, hexane:*i*-PrOH = 99:1, 1 mL/min, 40 °C, 210 nm), tR = 10.6 min (major), 13.1 min (minor).

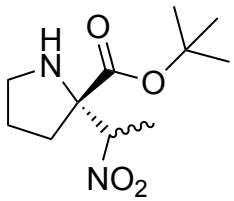
Ethyl (*S*)-3,3-dimethyl-2-(nitromethyl)indoline-2-carboxylate (4ia):



To a suspension of **3b** (2.7 mg, 0.0055 mmol) and MS 4A (2.5 mg) in toluene (62.5 μL) were added 1.0 M toluene solution of Et_2Zn (5.0 μL, 0.005 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1i** (6.1 mg, 0.025 mmol) and nitromethane (**2a**; 6.7 μL, 0.125 mmol) were added at 50 °C. After stirred at 50 °C for 168 h, the reaction mixture was purified by silica-gel column chromatography using hexane/AcOEt (9/1 to 4/1) as a mixed eluent to give (*S*)-**4ia** (3.3 mg, 0.011 mmol) in 42% yield with 83% ee.

Colorless oil; $[\alpha]_D^{25}$ + 68.2 (c 0.11, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.98 (d, *J* = 7.2 Hz, 1H), 6.83 (dd, *J* = 7.2, 7.5 Hz, 1H), 6.73 (d, *J* = 7.5 Hz, 1H), 5.07 (d, *J* = 14.1 Hz, 1H), 4.85 (br, 1H), 4.59 (d, *J* = 14.1 Hz, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 1.36 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 146.5, 135.3, 128.5, 121.8, 120.4, 111.0, 78.7, 74.2, 62.1, 48.8, 25.9, 22.0, 14.1; HRMS (ESI) m/z for $C_{14}H_{18}N_2O_4Na$ $[M+Na]^+$ calcd. 301.1164, found: 301.1155; IR (ATR) 3398, 2970, 2928, 1741, 1556, 1374, 1219, 1095, 1084, 750 cm^{-1}; HPLC (DAICEL CHIRALPAK IG®, hexane:*i*-PrOH = 97:3, 1 mL/min, 40 °C, 210 nm), tR = 18.8 min (minor), 23.5 min (major).

***tert*-Butyl (*S*)-2-(nitroethyl)pyrrolidine 2-carboxylate (4eb):**

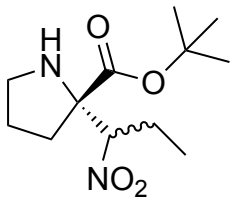


To a suspension of **3b** (10.7 mg, 0.022 mmol) and MS 4A (10.0 mg) in toluene (0.5 mL) were added 1.0 M toluene solution of Et_2Zn (20.0 μL, 0.02 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1e** (16.9 mg, 0.1 mmol) and nitroethane (**2b**; 35.7 μL, 0.5 mmol) were added at 10 °C. After stirred at 10 °C for 96 h, the reaction mixture was passed through a celite pad. The obtained filtrate was concentrated under reduced pressure to give the crude product and the diastereomer ratio was determined by ^{1}H NMR analysis. The crude product was purified by silica-gel column chromatography using hexane/AcOEt (9/1 to 4/1) as a mixed eluent to give (*S*)-**4eb** (19.0 mg, 0.078 mmol) in 78% yield with 60:40 dr, 92/85% ee.

Colorless oil; $[\alpha]_D^{25}$ +78.4 (c 0.16, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.95 (dd, *J* = 6.9, 13.8 Hz, 0.6H), 4.76 (dd, *J* = 6.9, 13.8 Hz, 0.4H), 3.18–2.90 (m, 2H), 2.41 (br, 1H), 2.18–1.85 (m, 2H), 1.79–1.70 (m, 2H), 1.64–1.54 (m, 3H), 1.49 (s, 3.6 H), 1.45 (s, 5.4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 172.4, 88.7, 87.4, 82.8, 82.4, 71.2, 70.3, 47.6, 46.8, 34.3, 33.6, 27.8, 27.7, 25.1, 24.9, 15.6, 13.9; HRMS (ESI) m/z for $C_{11}H_{21}N_2O_4$ $[M+H]^+$ calcd. 245.1501, found: 245.1482; IR (ATR) 3356, 2978, 2874, 1727, 1549,

1459, 1369, 1256, 1151, 846 cm^{-1}; HPLC (DAICEL CHIRALPAK IG®, hexane:*i*-PrOH = 97:3, 1 mL/min, 225 nm), major diastereomer: tR = 16.2 min (major), 17.0 min (miner), minor diastereomer: tR = 18.7 min (major), 28.8 min (minor).

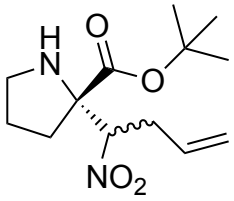
***tert*-Butyl (*S*)-2-(1-nitropropyl)pyrrolidine 2-carboxylate (4ec):**



To a suspension of **3b** (10.7 mg, 0.022 mmol) and MS 4A (10.0 mg) in toluene (0.5 mL) were added 1.0 M toluene solution of Et_2Zn (20.0 μL, 0.02 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1e** (16.9 mg, 0.1 mmol) and 1-nitropropane (**2c**; 44.5 μL, 0.5 mmol) were added at 10 °C. After stirred at 10 °C for 96 h, the reaction mixture was passed through a celite pad. The obtained filtrate was concentrated under reduced pressure to give the crude product and the diastereomer ratio was determined by ^{1}H NMR analysis. The crude product was purified by silica-gel column chromatography using hexane/AcOEt (9/1 to 4/1) as a mixed eluent to give (*S*)-**4ec** (15.7 mg, 0.061 mmol) in 61% yield with 60:40 dr, 62/76% ee.

Colorless oil; $[\alpha]_D^{25}$ +55.6 (c 0.13, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.64 (dd, *J* = 2.7, 11.1 Hz, 0.5H), 4.53 (dd, *J* = 2.4, 11.7 Hz, 0.5H), 3.11–2.89 (m, 2H), 2.29 (br, 1H), 2.27–1.91 (m, 3H), 1.85–1.61 (m, 3H), 1.49 (s, 4.5H), 1.45 (s, 4.5H), 1.03–0.95 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1, 172.4, 96.4, 94.7, 82.8, 82.7, 71.2, 70.9, 47.0, 46.8, 34.0, 33.3, 27.8, 27.7, 25.3, 24.6, 23.4, 22.3, 11.3, 11.2; HRMS (ESI) m/z for $C_{12}H_{23}N_2O_4$ $[M+H]^+$ calcd. 259.1658, found: 259.1661; IR (ATR) 3360, 2978, 2880, 1726, 1550, 1460, 1369, 1258, 1151, 737 cm^{-1}; HPLC (DAICEL CHIRALPAK IF-3®) hexane:^{i}PrOH =99:1, 1.0 mL/min, 220 nm, major diastereomer: tR = 16.4 min (major), 17.9 min (miner), minor diastereomer: tR = 20.6 min (major), 33.6 min (minor).

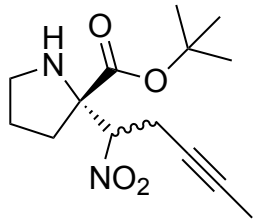
***tert*-Butyl (*S*)-2-(1-nitrobut-3-en-1-yl)pyrrolidine 2-carboxylate (4ed):**



To a suspension of **3b** (10.7 mg, 0.022 mmol) and MS 4A (10.0 mg) in toluene (1 mL) were added 1.0 M toluene solution of Et_2Zn (20.0 μL, 0.02 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1e** (16.9 mg, 0.1 mmol) and 4-nitrobut-1-ene (**2d**; 50.6 mg, 0.5 mmol) were added at –10 °C. After stirred at –10 °C for 120 h, the reaction mixture was passed through a celite pad. The obtained filtrate was concentrated under reduced pressure to give the crude product and the diastereomer ratio was determined by ^{1}H NMR analysis. The crude product was purified by silica-gel column chromatography using hexane/AcOEt (9/1 to 4/1) as a mixed eluent to give (*S*)-**4ed** (16.5 mg, 0.061 mmol) in 61% yield with 61:39 dr, 83/90% ee.

Colorless oil; $[\alpha]_D^{25}$ –69.4 (c 0.08, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.85–5.64 (m, 1H), 5.17–5.10 (m, 2H), 4.79 (dd, *J* = 3.0, 10.5 Hz, 0.6H), 4.67 (dd, *J* = 2.7, 11.4 Hz, 0.4H), 3.13–2.77 (m, 3H), 2.54–2.49 (m, 2H), 2.13–1.97 (m, 2H), 1.80–1.66 (m, 2H), 1.50 (s, 3.6 H), 1.44 (s, 5.4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 172.3, 132.6, 132.2, 119.1, 118.9, 93.7, 92.3, 83.0, 82.8, 71.1, 70.6, 47.1, 46.9, 34.2, 33.8, 33.5, 33.3, 27.8, 27.7, 25.3, 24.5; HRMS (ESI) m/z for $C_{13}H_{23}N_2O_4$ $[M+H]^+$ calcd. 271.1658, found: 271.1657; IR (ATR) 3360, 3083, 2979, 2873, 1726, 1552, 1369, 1151, 924, 845 cm^{-1}; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 98:2, 0.5 mL/min, 215 nm), minor diastereomer: tR = 44.3 min (minor), 47.0 min (major), major diastereomer: tR = 52.3 min (major), 91.2 min (minor).

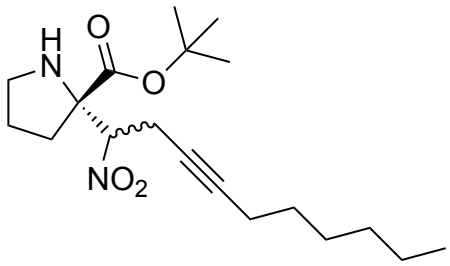
***tert*-Butyl (*S*)-2-(1-nitropent-3-yn-1-yl)pyrrolidine 2-carboxylate (4ee):**



To a suspension of **3b** (10.7 mg, 0.022 mmol) and MS 4A (10.0 mg) in toluene (0.5 mL) were added 1.0 M toluene solution of Et_2Zn (20.0 μL, 0.02 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1e** (16.9 mg, 0.1 mmol) and 5-nitropent-2-yne (**2e**; 56.6 mg, 0.5 mmol) were added at –10 °C. After stirred at –10 °C for 168 h, the reaction mixture was passed through a celite pad. The obtained filtrate was concentrated under reduced pressure to give the crude product and the diastereomer ratio was determined by ^1H NMR analysis. The crude product was purified by silica-gel column chromatography using hexane/AcOEt (14/1 to 7/1) as a mixed eluent to give (*S*)-**4ee** (16.6 mg, 0.059 mmol) in 59% yield with 52:48 dr, 82/92% ee.

Colorless oil; $[\alpha]_D^{25}$ +9.5 (c 0.20, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.88 (dd, *J* = 4.2, 9.6 Hz, 0.4H), 4.75 (dd, *J* = 3.3, 11.1 Hz, 0.6H), 3.12–2.89 (m, 3H), 2.72–2.56 (m, 1H), 2.09–2.03 (m, 2H), 1.79–1.65 (m, 7H), 1.49 (s, 5.4H), 1.45 (s, 3.6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 172.0, 93.0, 91.7, 83.3, 82.9, 79.1, 78.9, 73.6, 73.0, 70.8, 70.4, 47.2, 46.8, 33.9, 33.8, 27.8, 27.7, 25.3, 24.6, 20.7, 19.7, 3.5, 3.5; HRMS (ESI) m/z for $C_{14}H_{23}N_2O_4$ $[M+H]^+$ calcd. 283.1658, found: 283.1653; IR (ATR) 3360, 2978, 2874, 1729, 1553, 1368, 1251, 1151, 845 cm^{-1}; HPLC (DAICEL CHIRALPAK IF-3®–IF®, hexane:*i*-PrOH = 99:1, 0.7 mL/min, 210 nm), minor diastereomer: tR = 41.1 min (minor), 42.7 min (major), major diastereomer: tR = 61.9 min (major), 76.8 min (minor).

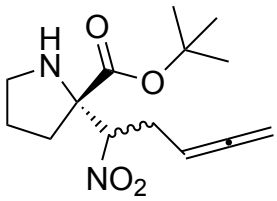
***tert*-Butyl (*S*)-2-(1-nitrodec-3-yn-1-yl)pyrrolidine 2-carboxylate (4ef):**



To a suspension of **3b** (10.7 mg, 0.022 mmol) and MS 4A (10.0 mg) in toluene (0.5 mL) were added 1.0 M toluene solution of Et_2Zn (20.0 μL, 0.02 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1e** (16.9 mg, 0.1 mmol) and 1-nitrodec-3-yne (**2f**; 91.6 mg, 0.5 mmol) were added at 0 °C. After stirred at 0 °C for 168 h, the reaction mixture was passed through a celite pad. The obtained filtrate was concentrated under reduced pressure to give the crude product and the diastereomer ratio was determined by ^{1}H NMR analysis. The crude product was purified by silica-gel column chromatography using hexane/AcOEt (14/1 to 7/1) as a mixed eluent to give (*S*)-**4ef** (18.3 mg, 0.052 mmol) in 52% yield with 60:40 dr, 70/86% ee.

Colorless oil; $[\alpha]_D^{25}$ +33.2 (c 0.13, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.89 (dd, *J* = 4.5, 9.3 Hz, 0.5H), 4.79 (dd, *J* = 3.6, 10.8 Hz, 0.5H), 3.15–2.85 (m, 3H), 2.75–2.62 (m, 1H), 2.16–1.99 (m, 4H), 1.80–1.62 (m, 3H), 1.50 (s, 4.5H), 1.45 (s, 4.5H), 1.38–1.22 (m, 8H), 0.92–0.86 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 171.8, 93.1, 91.7, 83.9, 83.7, 83.4, 83.0, 74.4, 73.8, 70.9, 70.4, 47.2, 46.8, 33.9, 33.7, 31.3, 28.6, 28.4, 28.3, 27.8, 27.7, 25.2, 24.6, 22.5, 20.9, 19.7, 18.6, 14.0; HRMS (ESI) m/z for $C_{19}H_{33}N_2O_4$ $[M+H]^+$ calcd. 353.2440, found: 353.2440; IR (ATR) 3357, 2931, 2859, 1729, 1556, 1369, 1251, 1152, 911, 733 cm^{-1}; HPLC (DAICEL CHIRALPAK IG®–IG®, hexane:*i*-PrOH = 99:5, 0.5 mL/min, 215 nm), major diastereomer: tR = 70.2 min (minor), 73.9 min (major), minor diastereomer: tR = 83.1 min (major), 119.8 min (minor).

***tert*-Butyl (*S*)-2-(1-nitropenta-3,4-dien-1-yl)pyrrolidine 2-carboxylate (4eg):**

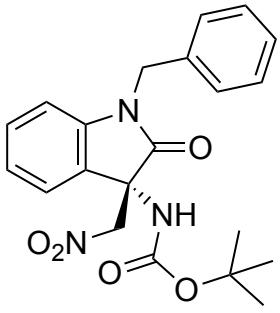


To a suspension of **3b** (10.7 mg, 0.022 mmol) and MS 4A (10.0 mg) in toluene (0.5 mL) were added 1.0 M toluene solution of Et_2Zn (20.0 μL, 0.02 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1e** (16.9 mg, 0.1 mmol) and 5-nitropenta-1,2-diene (**2g**; 56.6 mg, 0.5 mmol) were added at –10 °C. After stirred at –10 °C for 168 h, the reaction mixture was passed through a celite pad. The obtained filtrate was concentrated under reduced pressure to give the crude product and the diastereomer ratio was determined by ^{1}H NMR analysis. The crude product was purified by silica-gel column chromatography using hexane/AcOEt (14/1 to 7/1) as a mixed eluent to give (*S*)-**4eg** (16.0 mg, 0.057 mmol) in 57% yield with 60:40 dr, 76/91% ee.

Colorless oil; $[\alpha]_D^{25}$ –41.3 (c 0.28, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.18–5.02 (m, 1H), 4.84–4.72 (m, 3H), 3.12–2.91 (m, 2H), 2.86–2.38 (m, 3H), 2.13–1.96 (m, 2H), 1.84–1.62 (m, 2H), 1.49 (s, 3.6H),

1.45 (s, 5.4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.0, 209.0, 172.9, 172.2, 93.2, 92.1, 85.6, 85.2, 83.2, 82.9, 76.6, 76.5, 71.2, 70.7, 47.9, 46.9, 33.8, 33.6, 28.8, 27.9, 27.8, 27.7, 25.2, 24.7; HRMS (ESI) m/z for $C_{14}H_{23}N_2O_4$ $[M+H]^+$ calcd. 283.1658, found: 283.1656; IR (ATR) 3360, 2978, 2875, 1957, 1727, 1369, 1292, 1105, 845, 734 cm^{-1}; HPLC (DAICEL CHIRALPAK IF-3®–IF®, hexane:*i*-PrOH = 99:1, 0.7 mL/min, 205 nm), minor diastereomer: tR = 37.2 min (major), 40.5 min (minor), major diastereomer: tR = 43.5 min (major), 69.0 min (minor).

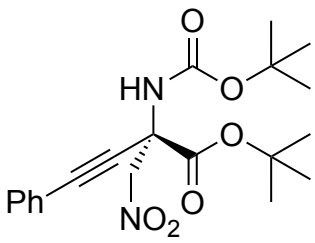
***tert*-Butyl (*S*)-[1-benzyl-3-(nitromethyl)-2-oxoindolin-3-yl]carbamate (4ja):**



To a suspension of **3b** (2.7 mg, 0.0055 mmol) and MS 4A (5.0 mg) in toluene (0.25 mL) were added 1.0 M toluene solution of Et_2Zn (5.0 μL, 0.005 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. *tert*-Butyl (1-benzyl-2-oxoindolin-3-ylidene)carbamate (**1j**: 16.8 mg, 0.05 mmol) and nitromethane (**2a**; 13.4 μL, 0.25 mmol) were added at 10 °C. After stirred at 10 °C for 168 h, the reaction mixture was purified by silica-gel column chromatography using hexane/AcOEt (4/1 to 2/1) as a mixed eluent to give (*S*)-**4ja** (15.9 mg, 0.040 mmol) in 80% yield with 90% ee.

Yellow solid; $[\alpha]_D^{25}$ +17.2 (c 0.63, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.5 Hz, 1H), 7.34–7.19 (m, 7H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 5.91 (br, 1H), 5.04–4.80 (m, 3H), 4.61 (d, *J* = 12.3 Hz, 1H), 1.32 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 153.7, 142.4, 135.0, 130.0, 128.9, 127.9, 127.3, 125.8, 124.5, 123.5, 110.0, 81.3, 77.8, 59.9, 44.5, 28.1; HPLC (DAICEL CHIRALPAK AD-H®, hexane:*i*-PrOH = 80:20, 2 mL/min, 40 °C, 254 nm), tR = 7.5 min (major), 13.6 min (minor).
Spectroscopic data of ^{1}H and ^{13}C NMR were identical to that reported in reference 13. The absolute stereochemistry was found to be *S* by comparison with the optical rotation reported in the literature 13.

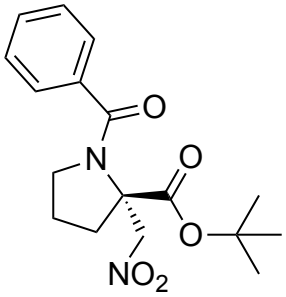
***tert*-Butyl (*S*)-2-[(*tert*-butoxycarbonyl)amino]-2-(nitromethyl)-4-phenylbut-3-ynoate (4ka):**



To a suspension of **3b** (2.7 mg, 0.0055 mmol) and MS 4A (5.0 mg) in toluene (0.25 mL) were 1.0 M toluene solution of Et_2Zn (5.0 μL, 0.005 mmol) and the reaction mixture was stirred under argon at room temperature for 1 h. **1k** (16.5 mg, 0.05 mmol) and nitromethane (**2a**; 13.4 μL, 0.25 mmol) were added at room temperature. After stirred at room temperature for 24 h, the reaction mixture was purified by silica-gel column chromatography using hexane/AcOEt (19/1 to 9/1) as a mixed eluent to give (*S*)-**4ka** (16.6 mg, 0.043 mmol) in 85% yield with 66% ee.

White solid; M.p. 88.0-89.0 °C; $[\alpha]_D^{25}$ +17.0 (c 0.19, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.44–7.40 (m, 2H), 7.36–7.28 (m, 3H), 5.84 (br, 1H), 5.48 (d, *J* = 13.5 Hz, 1H), 5.11 (d, *J* = 13.5 Hz, 1H), 5.11 (br, 1H), 1.55 (s, 9H), 1.46 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.4, 154.3, 131.7, 129.7, 128.9, 120.9, 86.1, 83.4, 82.9, 79.7, 78.7, 56.5, 28.1, 27.3; HRMS (ESI) m/z for $C_{20}H_{26}N_2O_6Na$ $[M+Na]^+$ calcd. 413.1689, found: 413.1689; IR (ATR) 3343, 2978, 2933, 1707, 1554, 1504, 1285, 1149, 1056, 760 cm^{-1}; HPLC (DAICEL CHIRALPAK IF®) hexane:^{i}PrOH =99:1, 1.0 mL/min, 40 °C, 240 nm, tR = 10.4 min (minor), 13.9 min (major).

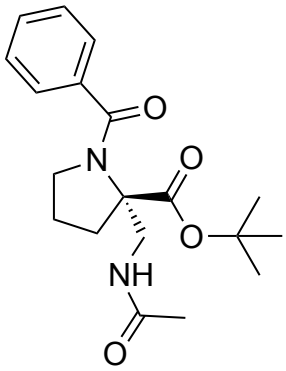
***tert*-Butyl (*S*)-1-benzoyl-2-(nitromethyl)pyrrolidine 2-carboxylate (5):**



To a solution of (*S*)-**4e** (91% ee; 115.1 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) were added triethylamine (138.6 μL, 1.0 mmol) and benzoyl chloride (105.4 μL, 0.75 mmol) at 0 °C under argon. After stirred at room temperature for 48 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 4/1) as a mixed eluent to give (*S*)-**5** (152.1 mg, 0.46 mmol) in 91% yield with 91% ee.

Colorless oil; $[\alpha]_D^{25}$ –26.2 (c 0.77, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.53–7.47 (m, 2H), 7.46–7.38 (m, 3H), 5.52 (d, *J* = 11.7 Hz, 1H), 4.94 (d, *J* = 11.7 Hz, 1H), 3.61–3.47 (m, 2H), 2.58–2.48 (m, 1H), 2.30–2.22 (m, 1H), 2.14–1.99 (m, 1H), 1.90–1.80 (m, 1H), 1.51 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 169.5, 136.0, 130.4, 128.4, 126.9, 83.1, 75.7, 67.3, 51.3, 33.9, 27.8, 23.9; HRMS (ESI) m/z for $C_{17}H_{22}N_2O_5Na$ $[M+Na]^+$ calcd. 357.1426, found: 357.1418; IR (ATR) 2976, 2961, 2927, 1729, 1614, 1561, 1406, 1370, 1250, 1146 cm^{-1}; HPLC (DAICEL CHIRALPAK IG®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 40 °C, 225 nm), tR = 10.4 min (minor), 16.1 min (major).

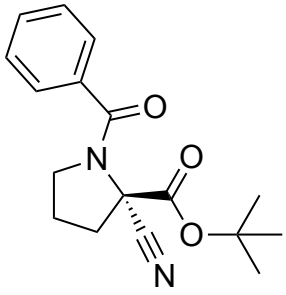
***tert*-Butyl (*S*)-2-(acetamidomethyl)-1-benzoylpyrrolidine-2-carboxylate (6):**



To a solution of (*S*)-**5** (91% ee; 33.4 mg, 0.1 mmol) in acetic acid (2 mL) was added zinc (130.8 mg, 2.0 mmol) at room temperature under argon. After stirred at room temperature for 24 h, the reaction was quenched with sat. $NaHCO_3$ aq. (10 mL) and the reaction mixture was extracted with $CHCl_3$ (10 mL × 3). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using CH_2Cl_2/MeOH (19/1 to 9/1) as a mixed eluent to give the corresponding primary amine, to which were added CH_2Cl_2 (1 mL), triethylamine (27.7 μL, 0.2 mmol), and acetic anhydrate (14.2 μL, 0.15 mmol) at 0 ºC under argon. After stirred at room temperature for 6 h, the reaction was quenched with sat. $NaHCO_3$ aq. (5 mL) and the reaction mixture was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (1/1) as a mixed eluent to give (*S*)-**6** (28.5 mg, 0.082 mmol) in 82% yield with 91% ee.

Colorless oil; $[\alpha]_D^{25}$ +19.7 (c 0.11, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46–7.38 (m, 5H), 6.85 (br, 1H), 3.94–3.81 (m, 2H), 3.58–3.53 (m, 2H), 2.16–2.11 (m, 2H), 2.00 (s, 3H), 1.98–1.90 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 170.6, 170.3, 136.7, 130.0, 128.4, 126.5, 81.9, 69.2, 51.5, 43.5, 35.0, 28.0, 24.1, 23.5; HRMS (ESI) m/z for $C_{19}H_{26}N_2O_4Na$ $[M+Na]^+$ calcd. 369.1790, found: 369.1806; IR (ATR) 3306, 2977, 2927, 2855, 1727, 1631, 1410, 1368, 1264, 1150 cm^{-1}; HPLC (DAICEL CHIRALPAK IG®, hexane:*i*-PrOH = 80:20, 0.7 mL/min, 220 nm), tR = 50.4 min (minor), 67.5 min (major).

***tert*-Butyl (*S*)-1-benzoyl-2-cyanopyrrolidine 2-carboxylate (7):**

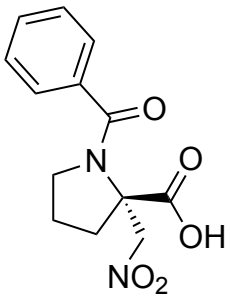


To a solution of tin(II) chloride (37.9 mg, 0.2 mmol), thiophenol (61.2 μL, 0.6 mmol), and triethylamine (83.2 μL, 0.6 mmol) in ethanol (1 mL) was added (*S*)-**5** (91% ee; 33.4 mg, 0.1 mmol) at room temperature under argon. After stirred at room temperature for 1 h, the reaction was quenched with 1M HCl aq. (1 mL) at 0 ºC and the reaction mixture was extracted with CH_2Cl_2 (5 mL × 2). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (4/1 to 1/1) as a mixed eluent to give the corresponding oxime, to which were added THF (1 mL), triethylamine (69.3 μL, 0.5 mmol), and thionyl chloride (10.9 μL, 0.15 mmol) at 0 ºC under argon. After stirred at room temperature for 3 h, the reaction was quenched with sat. $NaHCO_3$ aq. (5 mL) and extracted with AcOEt (5

mL × 2). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 4/1) as a mixed eluent to give (*S*)-**7** (19.2 mg, 0.064 mmol) in 64% yield with 91% ee.

Colorless oil; $[\alpha]_D^{25}$ +53.4 (c 0.11, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.61–7.50 (m, 2H), 7.48–7.39 (m, 3H), 3.79–3.65 (m, 2H), 2.73–2.65 (m, 1H), 2.45–2.35 (m, 1H), 2.22–2.12 (m, 2H), 1.55 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 165.3, 134.6, 131.0, 128.4, 127.4, 117.4, 84.8, 63.0, 50.4, 37.4, 27.7, 25.3; HRMS (ESI) m/z for $C_{17}H_{20}N_2O_3Na$ $[M+Na]^+$ calcd. 323.1372, found: 323.1377; IR (ATR) 2985, 2906, 1743, 1632, 1393, 1369, 1287, 1151, 1130, 842 cm^{-1}; HPLC (DAICEL CHIRALPAK IG®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 40 °C, 254 nm), tR = 15.5 min (minor), 16.7 min (major).

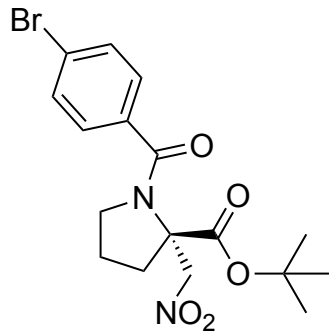
(*S*)-1-Benzoyl-2-(nitromethyl)pyrrolidine-2-carboxylic acid (8):



To a solution of (*S*)-**5** (91% ee; 33.4 mg, 0.1 mmol) in $CHCl_3$ (1 mL) was added 4.0 M 1,4-dioxane solution of HCl (250.0 μL, 1.0 mmol) at room temperature under argon. After stirred at 50 °C for 6 h, the reaction was cooled down to room temperature and the reaction mixture was concentrated under reduced pressure to remove HCl. The residue was extracted with CH_2Cl_2 (5 mL × 2) and sat. $NaHCO_3$ aq. (5 mL). The aqueous layers were acidified with 1.0 M HCl aq. (10 mL) and extracted with CH_2Cl_2 (5 mL × 2). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to give (*S*)-**8** (25.1 mg, 0.090 mmol) in 90% yield with 91% ee.

White solid; $[\alpha]_D^{25}$ –34.5 (c 0.17, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.66–7.64 (m, 2H), 7.48–7.42 (m, 3H), 5.56 (d, *J* = 12.0 Hz, 1H), 4.99 (d, *J* = 12.0 Hz, 1H), 4.13 (br, 1H), 3.66–3.55 (m, 2H), 2.58–2.52 (m, 1H), 2.47–2.41 (m, 1H), 2.21–2.11 (m, 1H), 1.93–1.87 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 171.2, 135.0, 130.9, 128.5, 127.3, 75.4, 66.8, 51.9, 33.7, 23.9; HRMS (ESI) m/z for $C_{13}H_{14}N_2O_5Na$ $[M+Na]^+$ calcd. 301.0800, found: 301.0806; IR (ATR) 2956, 1732, 1592, 1572, 1544, 1454, 1436, 1379, 1218, 795 cm^{-1}; HPLC (DAICEL CHIRALPAK IG®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 40 °C, 220 nm), tR = 11.6 min (minor), 14.7 min (major).

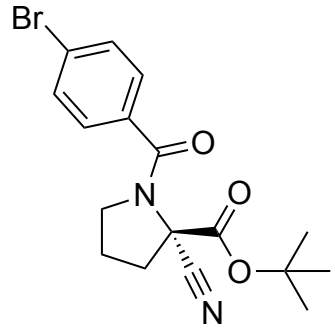
***tert*-Butyl (*S*)-1-(4-bromobenzoyl)-2-(nitromethyl)pyrrolidine-2-carboxylate (9):**



To a solution of (*S*)-**4e** (91% ee; 23.0 mg, 0.1 mmol) in CH_2Cl_2 (1 mL) were added triethylamine (27.7 μL, 0.2 mmol) and 4-bromobenzoyl chloride (32.9mg, 0.15 mmol) at 0 °C under argon. After stirred at room temperature for 48 h, the reaction was quenched with sat. $NaHCO_3$ aq. (5 mL) and the reaction mixture was extracted with CH_2Cl_2 (5 mL × 2). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 4/1) as a mixed eluent to give (*S*)-**9** (37.6 mg, 0.091 mmol) in 91% yield with 90% ee. The further recrystallization led to increase enantiomeric excess of (*S*)-**9** into 96% ee, however, the enantio-rich product was oily and the obtained solid was racemic.

Colorless oil; $[\alpha]_D^{25}$ +35.1 (c 0.06, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 5.49 (d, *J* = 11.7 Hz, 1H), 4.92 (d, *J* = 11.7 Hz, 1H), 3.58–3.45 (m, 2H), 2.56–2.46 (m, 1H), 2.30–2.22 (m, 1H), 2.15–2.00 (m, 1H), 1.91–1.80 (m, 1H), 1.50 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2, 168.8, 134.8, 131.7, 128.6, 124.9, 83.2, 75.6, 67.4, 51.3, 33.9, 27.9, 23.9; HRMS (ESI) m/z for $C_{17}H_{21}BrN_2O_5Na$ $[M+Na]^+$ calcd. 435.0532, found: 435.0528; IR (ATR) 2985, 2906, 1745, 1633, 1395, 1369, 1287, 1152, 1130, 730 cm^{-1}; HPLC (DAICEL CHIRALPAK IG®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 40 °C, 235 nm), tR = 15.2 min (miner), 23.2 min (major).

***tert*-Butyl (*S*)-1-(4-bromobenzoyl)-2-cyanopyrrolidine-2-carboxylate (10):**



To a solution of tin(II) chloride (18.9 mg, 0.1 mmol), thiophenol (30.6 μL, 0.3 mmol), and triethylamine (41.6 μL, 0.3 mmol) in ethanol (0.5 mL) was added (*S*)-**9** (96% ee; 20.7 mg, 0.05 mmol) at room temperature under argon. After stirred at room temperature for 1 h, the reaction was quenched with 1M HCl aq. (0.5 mL) at 0 °C and the reaction mixture was extracted with CH_2Cl_2 (5 mL × 2). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography using hexane/AcOEt (4/1 to 1/1) as a mixed eluent to give the corresponding oxime (13.9 mg, 0.035 mmol) in 70% yield. To the obtained oxime (11.9 mg, 0.03 mmol) were added THF (0.5 mL), triethylamine (20.8 μL, 0.15 mmol), and thionyl chloride (3.3 μL, 0.045 mmol) at 0 °C under argon. After stirred at room temperature for 3 h, the reaction was quenched with sat. $NaHCO_3$ aq. (5 mL) and extracted with AcOEt (5 mL × 2). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure.

The residue was purified by silica-gel column chromatography using hexane/AcOEt (7/1 to 4/1) as a mixed eluent to give (*S*)-**10** (10.0 mg, 0.026 mmol) in 88% yield (62 % yield; over 2 step) with 95% ee.

White solid; M.p. 145.5–146.5 °C; $[\alpha]_D^{25}$ –15.6 (c 0.21, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 3.77–3.62 (m, 2H), 2.73–2.65 (m, 1H), 2.44–2.34 (m, 1H), 2.22–2.13 (m, 2H), 1.55 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 168.0, 150.0, 135.0, 131.5, 128.6, 124.5, 82.7, 68.7, 50.9, 34.3, 27.9, 24.5; HRMS (ESI) m/z for $C_{17}H_{19}BrN_2O_3Na$ $[M+Na]^+$ calcd. 401.0477, found: 401.0475; IR (ATR) 2976, 2928, 1740, 1629, 1402, 1385, 1367, 1295, 1150, 845 cm^{-1}; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 90:10, 1.0 mL/min, 40 °C, 235 nm), tR = 19.1 min (major), 22.8 min (minor).

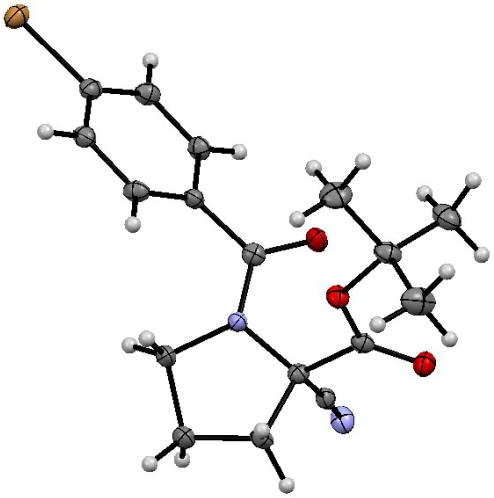
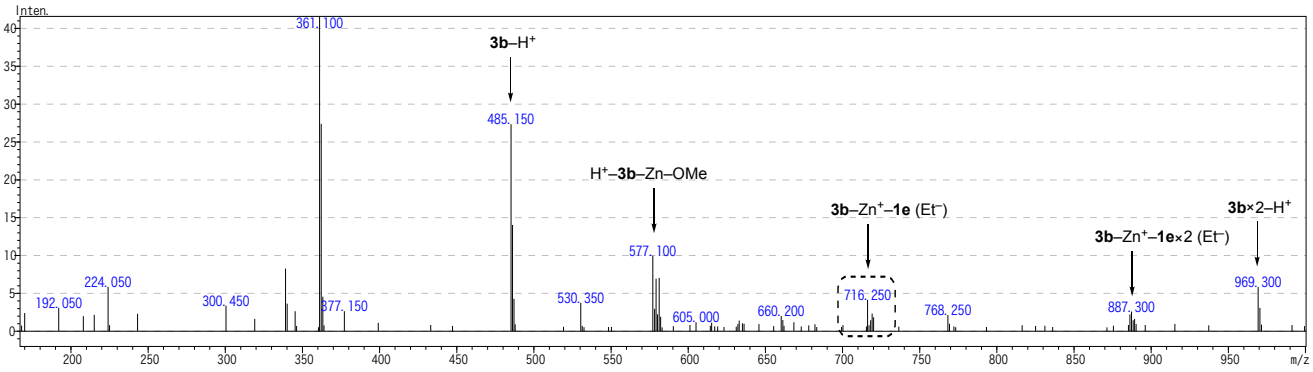


Figure S1. X-ray crystallography analysis for (*S*)-**10** (CCDC No. 2100064).

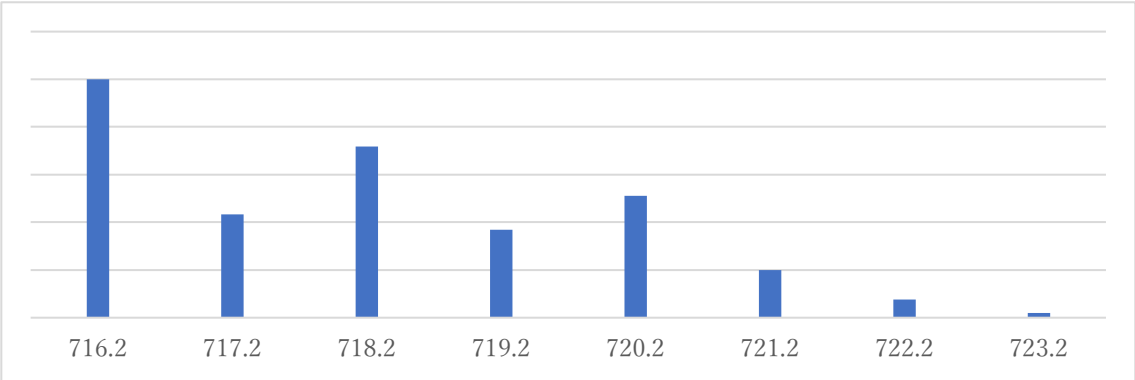
7. ESI Mass Spectra for Complexes:

In order to clarify the assumed reaction mechanism (Figure 2-A), the ESI-Mass spectroscopic analysis was carried out. Consequently, the complex **B**, which is formed during the reaction using **1e**, Et_2Zn, and **3b** in a 1:1:1 ratio in toluene was detected by the ESI-Mass spectroscopic analysis.

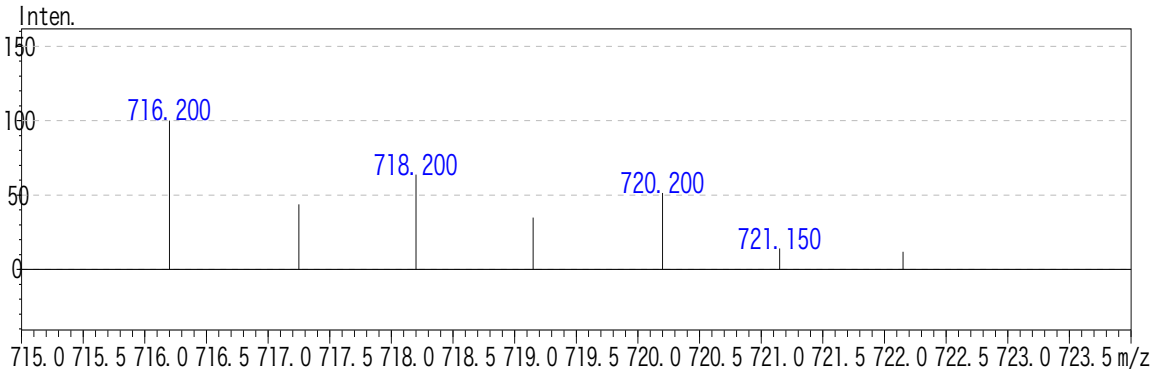
The ESI-Mass spectroscopic analysis of complex **B**



(a) Theoretical peaks about complex **B**



(b) Major peaks about complex B



8. MO Calculations:

The calculation was performed using Gaussian 16 revision C.01. Geometry optimizations were performed using B3LYP-D3 functional with 6-31G(d) basis set. After optimization of structures, frequency calculations were performed at the same level of the theory to confirm that the obtained structures were a transition state (one imaginary frequency). Single point energy calculations for the optimized geometry were performed using M06 functional with 6-311G (d,p) basis set for all the atoms in SMD solvation model (toluene). The calculation results for TS-*S* and TS-*R* were shown in Figure S1. The relative energies of the optimized structures were depicted. As a result, the TS-*S* was most stable complex.

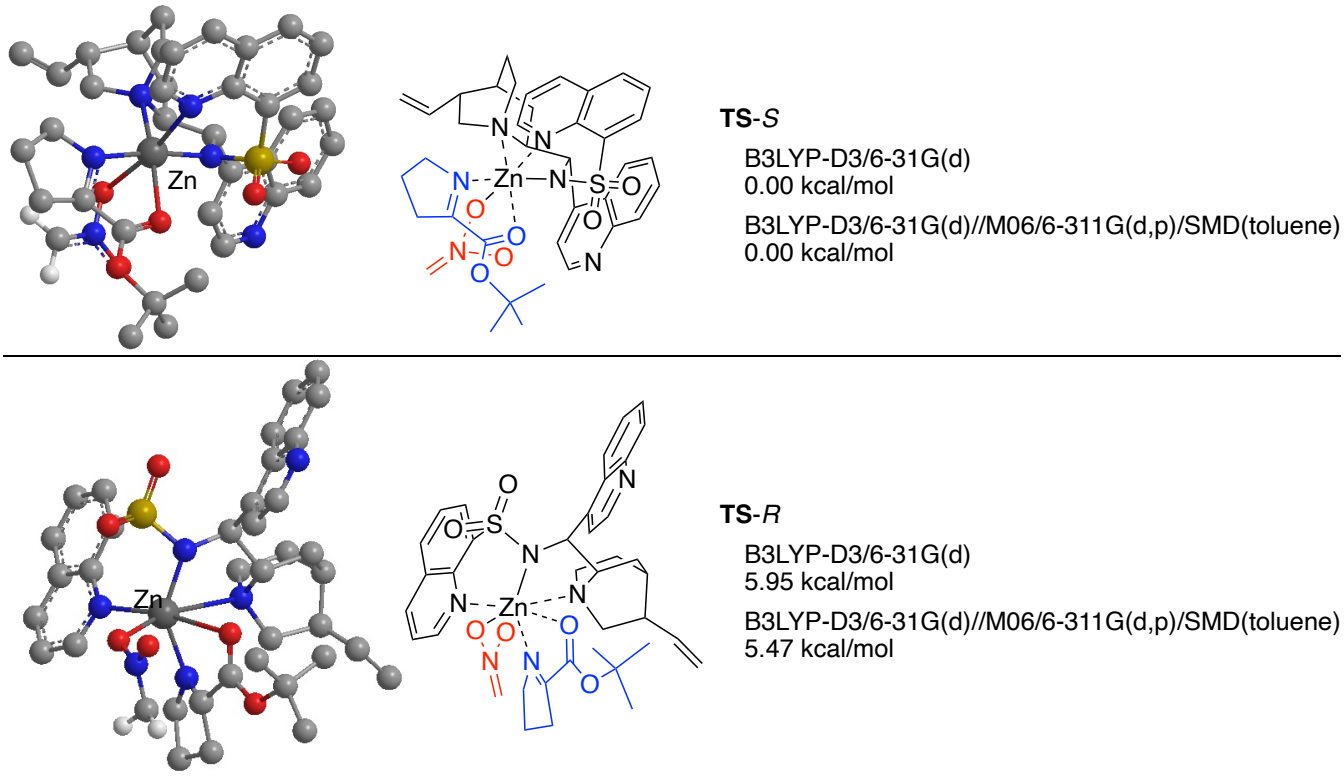


Figure S1. MO calculation for the complex among **1e**, **2a** and **3b**/Et_2Zn

Optimized structure for transition states

TS-*S*

B3LYP-D3/6-31G(d) free energy: -4431.76604002 (a.u.)

Number of imaginary frequencies: 1 (-214.3137)

B3LYP-D3/6-31G(d)// M06/6-311G(d,p)/SMD(toluene) single point energy: -4430.81740090 (a.u.)

C	-4.104142	-1.235798	-1.229683
C	-4.708629	-2.445976	-1.715112
N	-4.039367	-3.631083	-1.813047
C	-2.772992	-3.634532	-1.447653
C	-2.081431	-2.511022	-0.943032
C	-2.735953	-1.302213	-0.813287
C	-1.985586	-0.119453	-0.188750
C	-1.817861	-0.395622	1.331550
C	-4.904280	-0.058352	-1.207864
C	-6.070676	-2.434675	-2.120186
H	-2.244860	-4.583335	-1.541197
H	-1.407114	2.256988	0.966701
N	-0.650029	0.083242	-0.763311
H	-2.591279	0.787288	-0.304363
C	-3.157657	-0.306516	2.117769
N	-0.785520	0.506589	1.946160
H	-1.394500	-1.395928	1.428444
C	-0.536035	0.047978	3.337120
C	-1.816315	0.128987	4.236724
C	-2.973757	0.624956	3.329213
C	-1.276384	1.909172	1.992525
C	-2.596862	2.023730	2.807284
H	-3.480605	-1.303541	2.433587
H	-3.960353	0.086634	1.483846
H	-0.154230	-0.973159	3.277863
H	0.259227	0.674411	3.753535
H	-1.662097	0.889932	5.013615
C	-2.102567	-1.176588	4.928890
H	-3.900060	0.674252	3.911732
H	-1.037023	-2.612082	-0.663593
H	-0.479352	2.515698	2.435897
H	-2.477329	2.721940	3.644711
C	-6.220654	-0.079372	-1.611922
C	-6.815293	-1.280101	-2.066596
H	-6.805291	0.836828	-1.591758
H	-4.468842	0.883045	-0.891653
H	-6.487531	-3.372081	-2.475444
H	-7.855488	-1.282478	-2.381793
S	-0.585136	0.868203	-2.174930
H	-3.405277	2.415321	2.178351
O	-1.840116	0.704696	-2.930879
H	-2.206441	-2.051932	4.285970

C	-2.221845	-1.328889	6.248795
H	-2.117635	-0.489003	6.933612
H	-2.429862	-2.296554	6.697281
C	-0.528784	2.653781	-1.786864
C	0.480477	3.225256	-0.952787
C	0.571929	4.656152	-0.885040
C	-0.369413	5.462732	-1.577390
H	-0.283735	6.544137	-1.505400
C	-1.361541	4.879432	-2.327141
H	-2.084993	5.493145	-2.856099
C	-1.425580	3.471096	-2.442862
H	-2.172653	3.002850	-3.075003
O	0.700993	0.609873	-2.833142
N	1.333972	2.427730	-0.233182
C	2.312166	3.005402	0.444839
C	2.514774	4.399982	0.520070
C	1.624056	5.222723	-0.125292
H	2.973075	2.325206	0.973877
H	3.344745	4.795832	1.096537
H	1.715277	6.305043	-0.071188
C	3.427369	-1.080513	-0.472614
O	2.360411	-0.843700	-1.026384
O	4.515070	-1.576527	-1.040183
C	4.540810	-1.927821	-2.496491
C	5.976994	-2.420650	-2.675884
H	6.694924	-1.632005	-2.427281
H	6.175034	-3.286175	-2.035261
H	6.137878	-2.718068	-3.717003
Zn	0.898561	0.116944	0.439966
C	4.273342	-0.672606	-3.331174
H	4.964807	0.129862	-3.049133
H	4.446378	-0.908127	-4.387365
H	3.246163	-0.320046	-3.219654
C	3.564698	-0.803271	0.989285
C	4.874203	-0.775556	1.767285
C	2.991431	0.312440	2.873236
C	4.528001	0.150587	2.961961
H	5.670798	-0.367041	1.136367
H	5.200729	-1.770740	2.078181
H	2.648830	1.312983	3.158648
H	2.476334	-0.406267	3.527931
H	5.019149	1.122459	2.845057
H	4.846695	-0.261473	3.923662
N	2.654387	0.032460	1.474072
N	1.635175	-2.835591	0.915074
O	0.787940	-2.010996	1.416903
O	1.386451	-3.479013	-0.120113
C	2.886735	-2.847197	1.486528
H	3.548579	-3.608412	1.090855
H	2.885746	-2.652410	2.550984

C	3.529581	-3.042065	-2.771331
H	3.695021	-3.891753	-2.101510
H	2.504019	-2.694649	-2.644089
H	3.658199	-3.387953	-3.803241

TS-*R*

B3LYP-D3/6-31G(d) free energy: -4431.75654715 (a.u.)

Number of imaginary frequencies: 1 (-241.6639)

B3LYP-D3/6-31G(d)// M06/6-311G(d,p)/SMD(toluene) single point energy: -4430.80868134 (a.u.)

C	-3.413350	-2.342207	-0.828695
C	-3.601583	-3.516065	-1.636452
N	-2.613630	-4.068404	-2.399326
C	-1.444511	-3.462098	-2.389081
C	-1.144408	-2.313754	-1.623101
C	-2.108479	-1.747708	-0.814189
C	-1.745255	-0.540957	0.063730
C	-0.912782	-0.993497	1.289985
C	-4.539390	-1.846592	-0.111586
C	-4.871869	-4.152312	-1.664788
H	-0.668418	-3.899122	-3.018120
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N	-1.009930	0.493763	-0.686651
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N	-0.538592	0.153670	2.157784
H	0.033336	-1.382620	0.900433
C	0.410539	-0.327203	3.173980
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C	-1.650224	-1.669561	3.613836
C	-1.713145	0.720573	2.849647
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H	-2.655537	-2.257441	1.801537
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H	-4.965995	-5.038633	-2.284625
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H	-3.469805	-0.516336	3.349048
O	-3.308564	0.981936	-1.705483
H	0.842698	-3.161078	3.311639
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C	-2.077150	3.027210	-0.631364
C	-0.926369	3.800888	-0.300600
C	-1.117868	5.128447	0.201128
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H	-2.557489	6.601939	0.864901
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C	-3.337766	3.521199	-0.374575
H	-4.192751	2.918922	-0.663561
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N	0.333676	3.295552	-0.494991
C	1.370327	4.110624	-0.370045
C	1.268303	5.453079	0.047748
C	0.026470	5.943730	0.375599
H	2.334846	3.676437	-0.611151
H	2.162565	6.062141	0.127567
H	-0.096821	6.959097	0.744567
C	2.998702	-1.181887	-0.386016
O	1.872810	-1.325505	-0.836929
O	3.982236	-2.077681	-0.400050
C	3.828738	-3.422278	-1.025878
C	5.206033	-4.045046	-0.791362
H	5.987354	-3.454976	-1.280986
H	5.431870	-4.101476	0.278482
H	5.229676	-5.058641	-1.204133
Zn	0.814147	1.143163	-0.514725
C	3.539203	-3.268877	-2.520083
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H	3.567396	-4.257808	-2.991464
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C	3.410336	0.110509	0.261840
C	4.611548	0.203028	1.194159
C	2.897769	1.819069	1.711685
C	4.425475	1.605511	1.796168
H	5.569573	0.048496	0.693984
H	4.515956	-0.577420	1.960913
H	2.630391	2.858411	1.496923
H	2.406618	1.560153	2.657998
H	4.952873	2.351532	1.190441
H	4.806556	1.686790	2.818119
N	2.410733	0.902404	0.664236
C	2.739778	-4.206940	-0.289558
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H	2.727011	-5.238228	-0.658749
C	4.217934	0.875554	-1.529511
H	4.455157	1.858106	-1.143657
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N	3.106177	0.852123	-2.353027
O	2.967838	-0.012472	-3.226176
O	2.157384	1.676935	-2.058340

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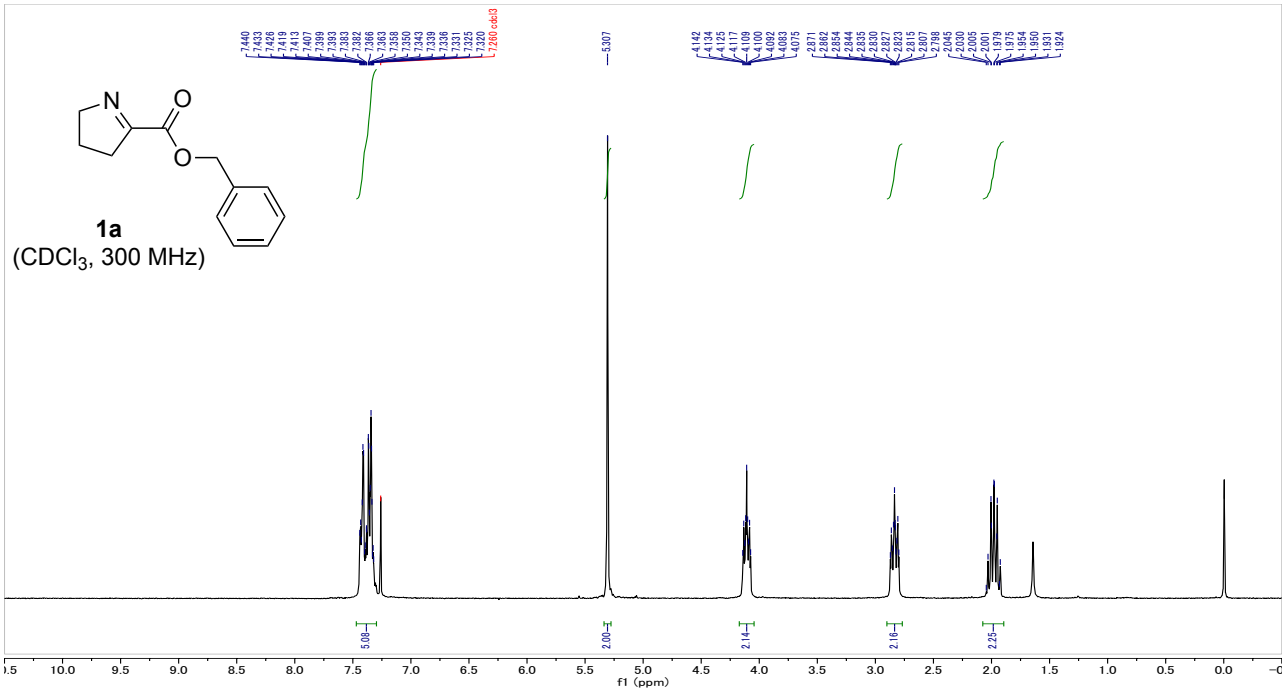
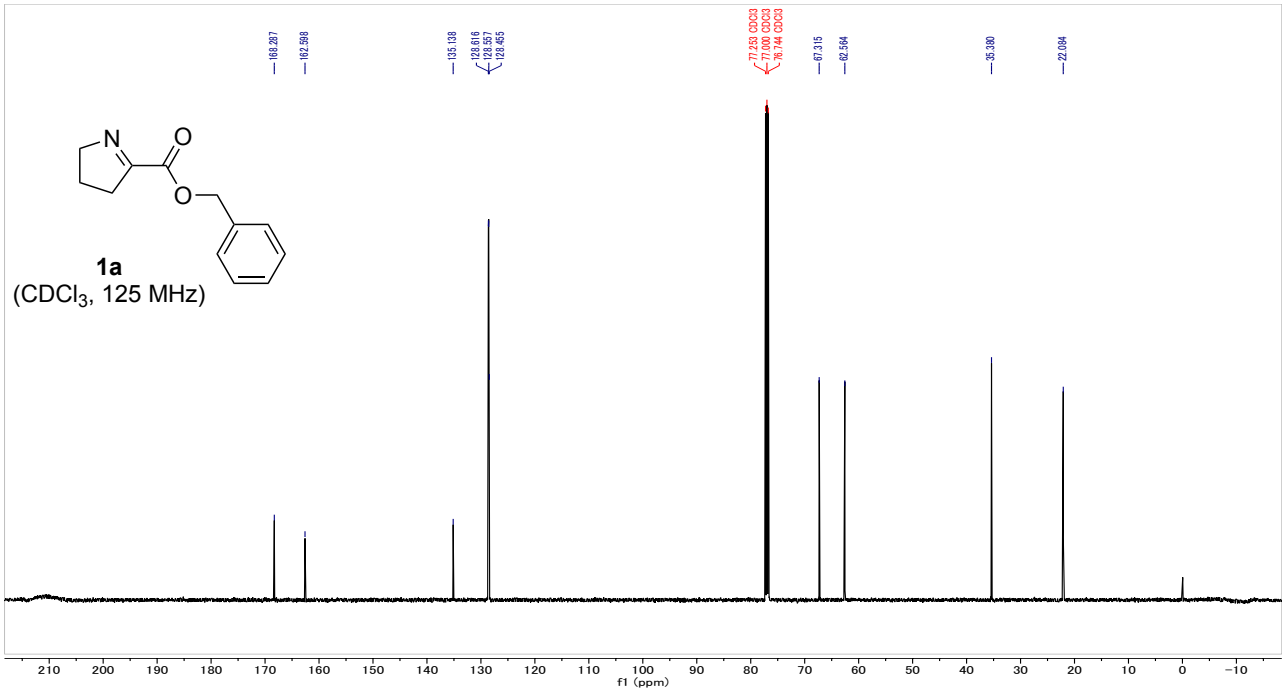
10. ^{1}H, ^{13}C NMR Spectra:

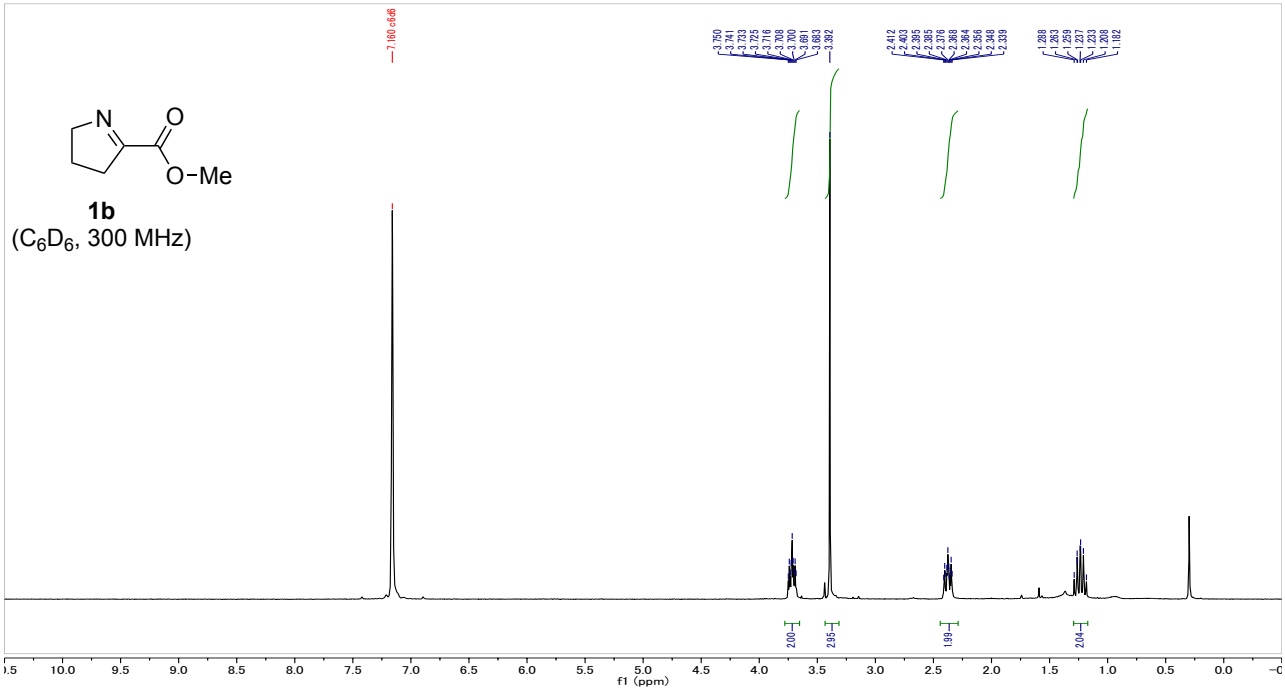
^{1}H NMR of benzyl 1-pyrroline 2-carboxylate (**1a**)



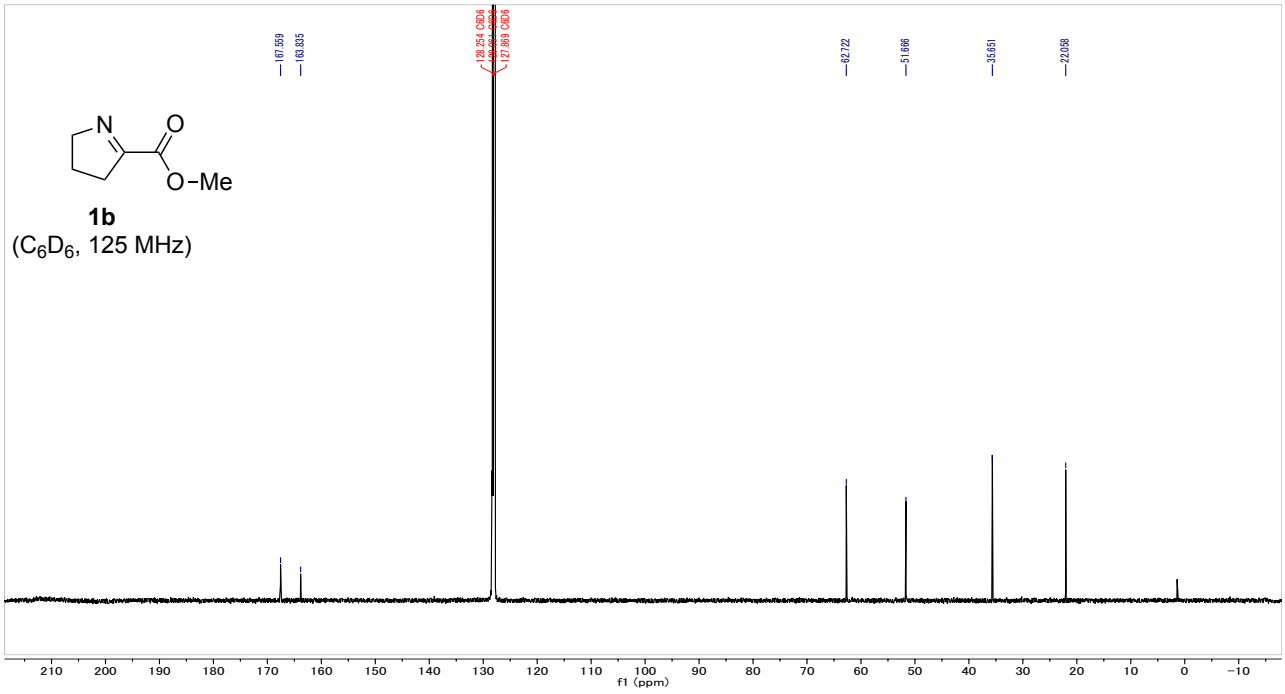
^{13}C NMR of benzyl 1-pyrroline 2-carboxylate (**1a**)



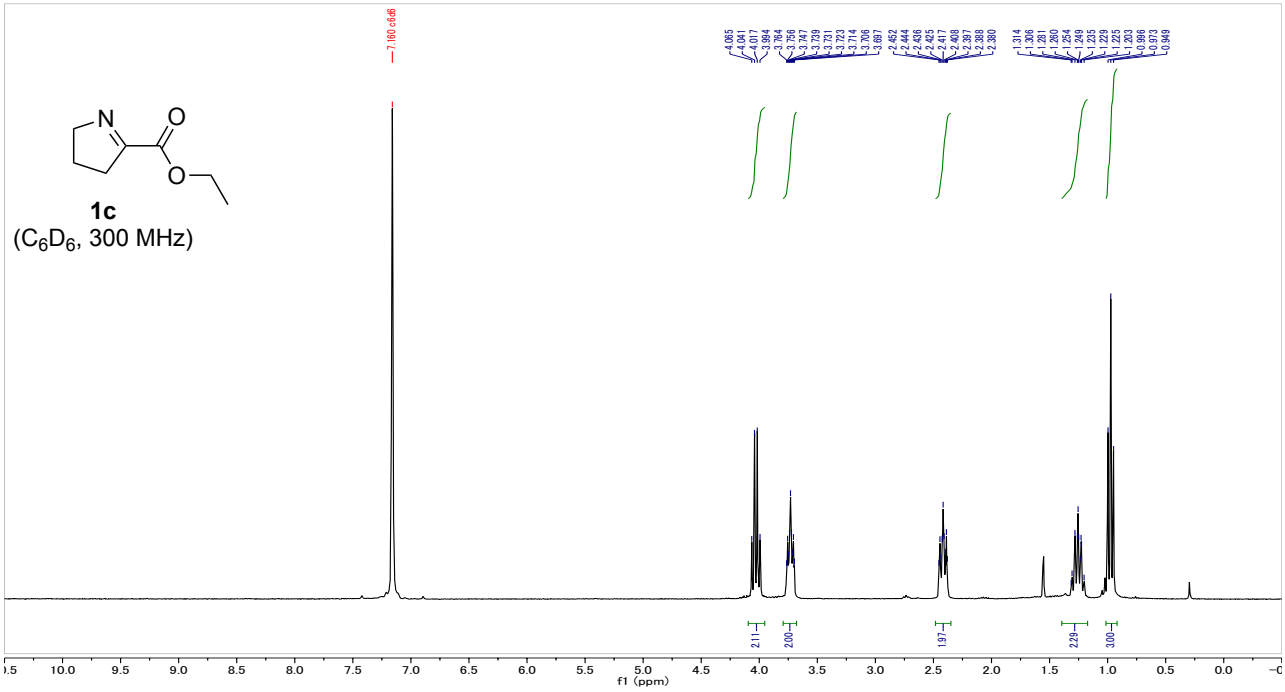
^{1}H NMR of methyl 1-pyrroline 2-carboxylate (**1b**)



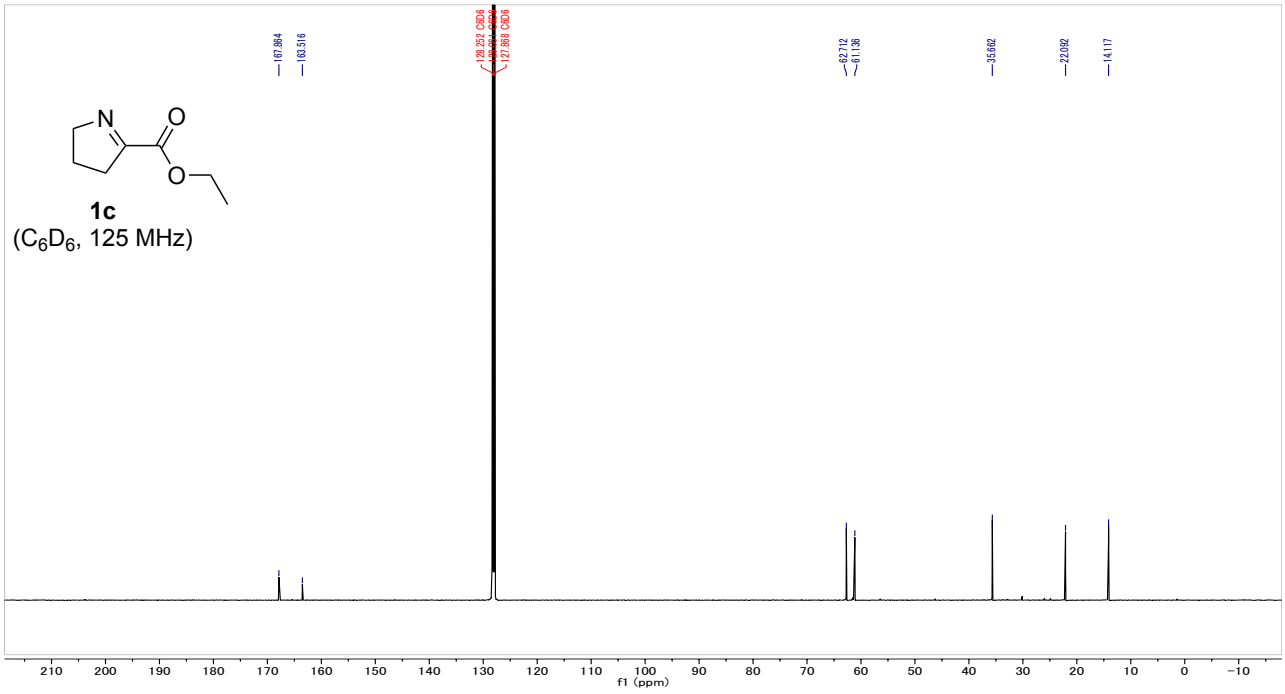
^{13}C NMR of methyl 1-pyrroline 2-carboxylate (**1b**)



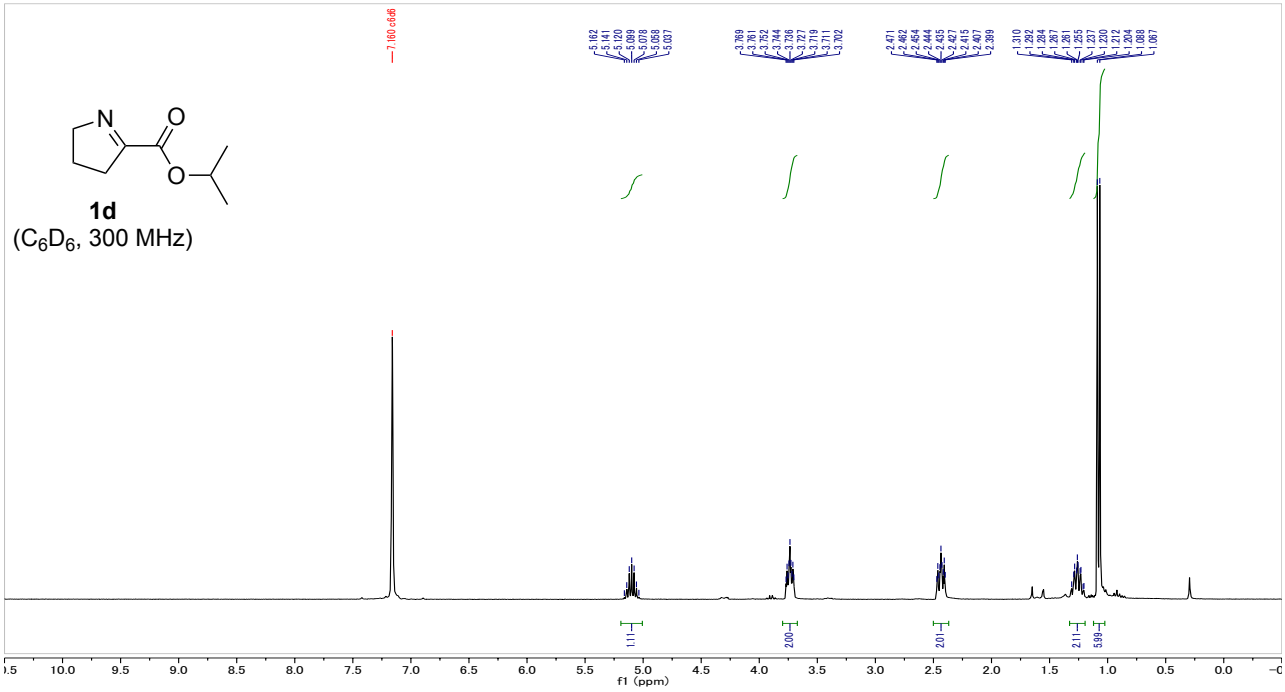
^{1}H NMR of ethyl 1-pyrroline 2-carboxylate (**1c**)



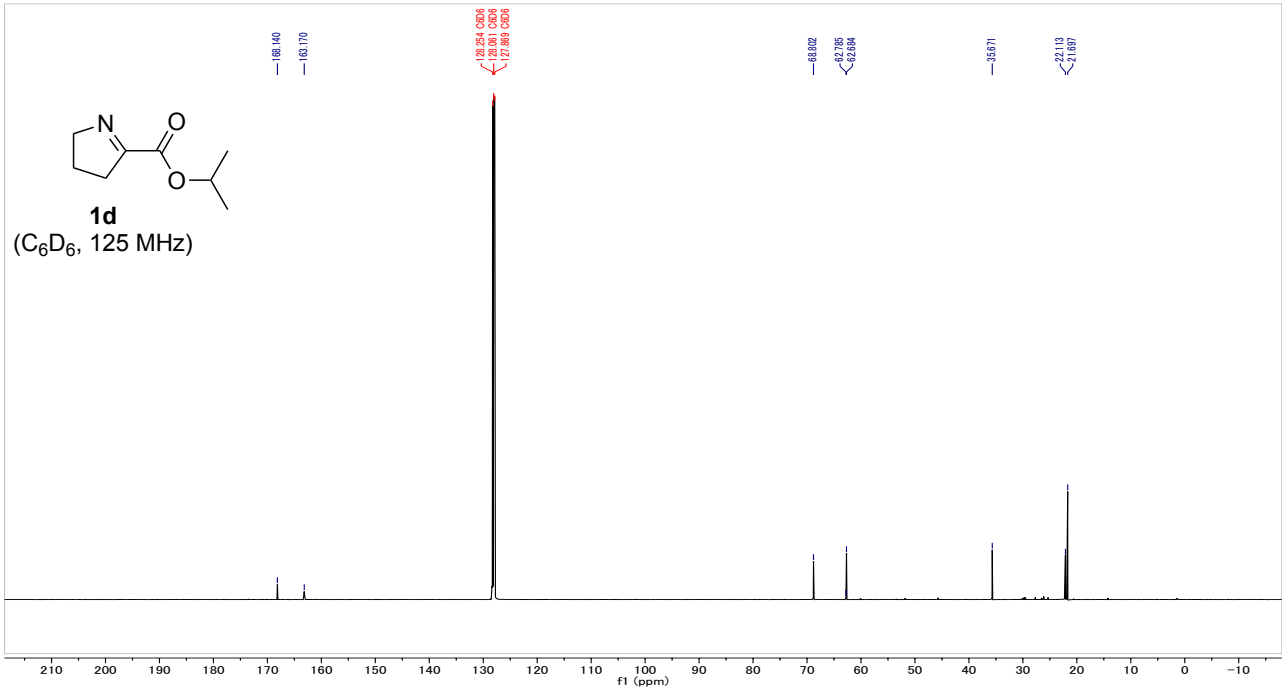
^{13}C NMR of ethyl 1-pyrroline 2-carboxylate (**1c**)



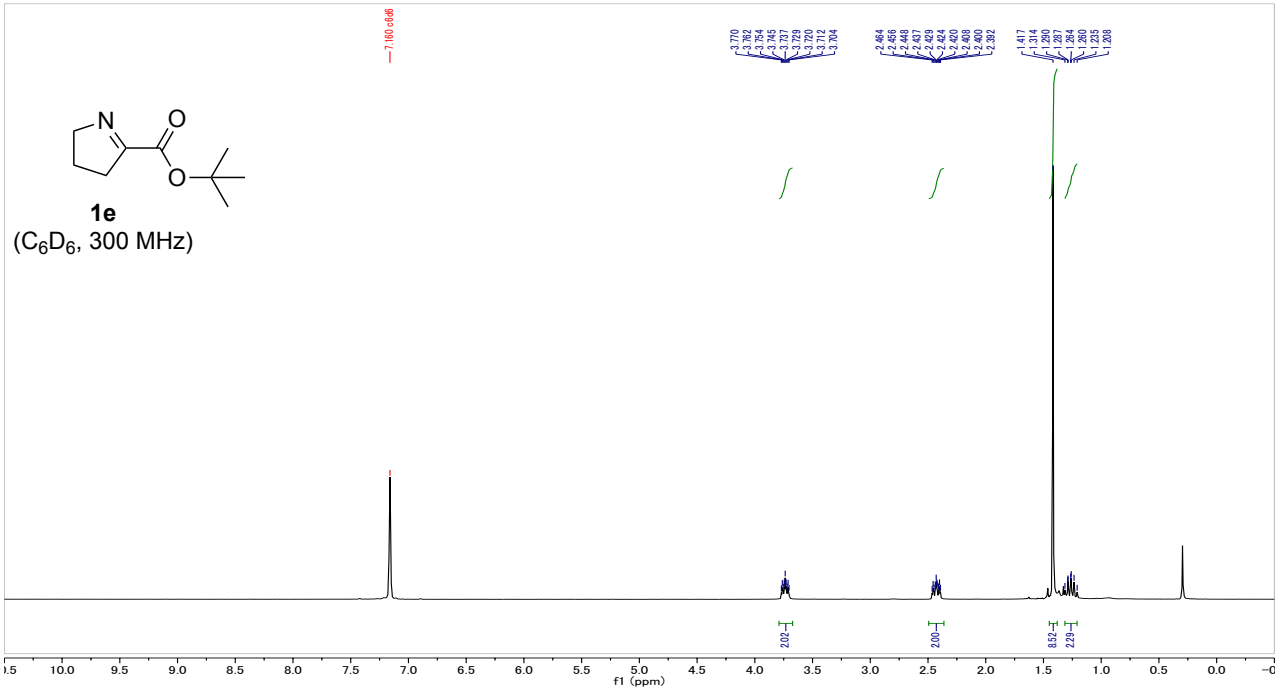
^{1}H NMR of *iso*-propyl 1-pyrroline 2-carboxylate (**1d**)



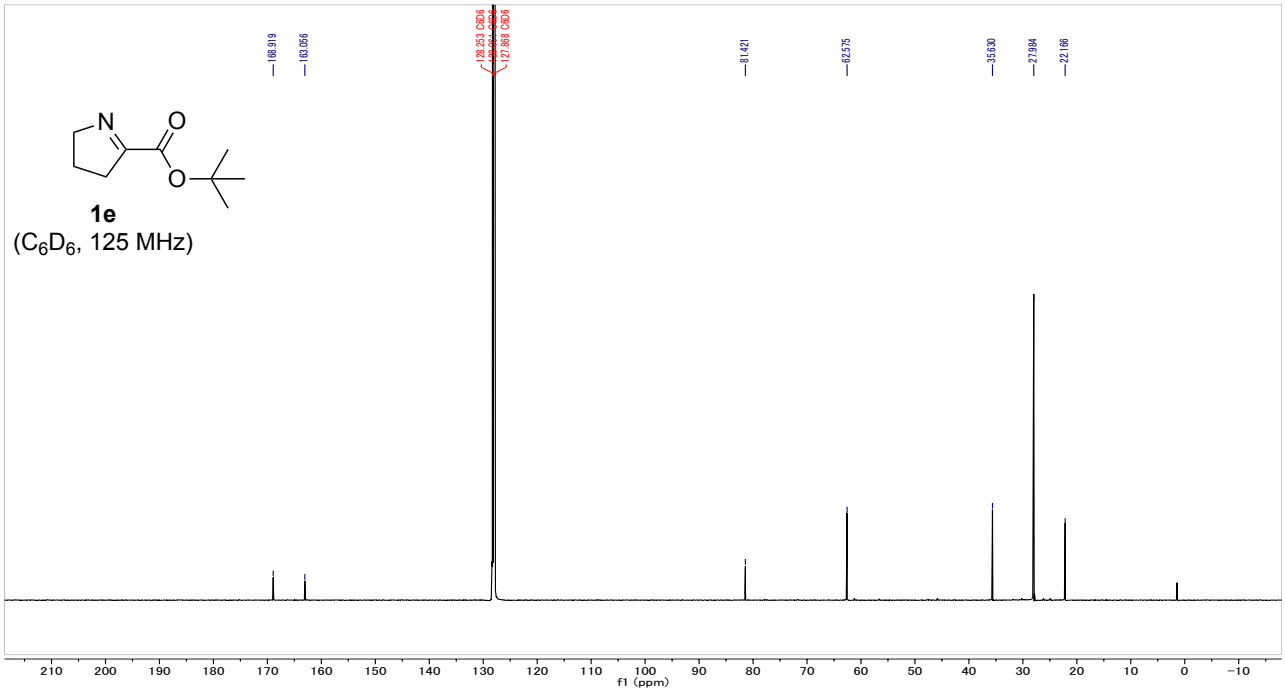
^{13}C NMR of *iso*-propyl 1-pyrroline 2-carboxylate (**1d**)



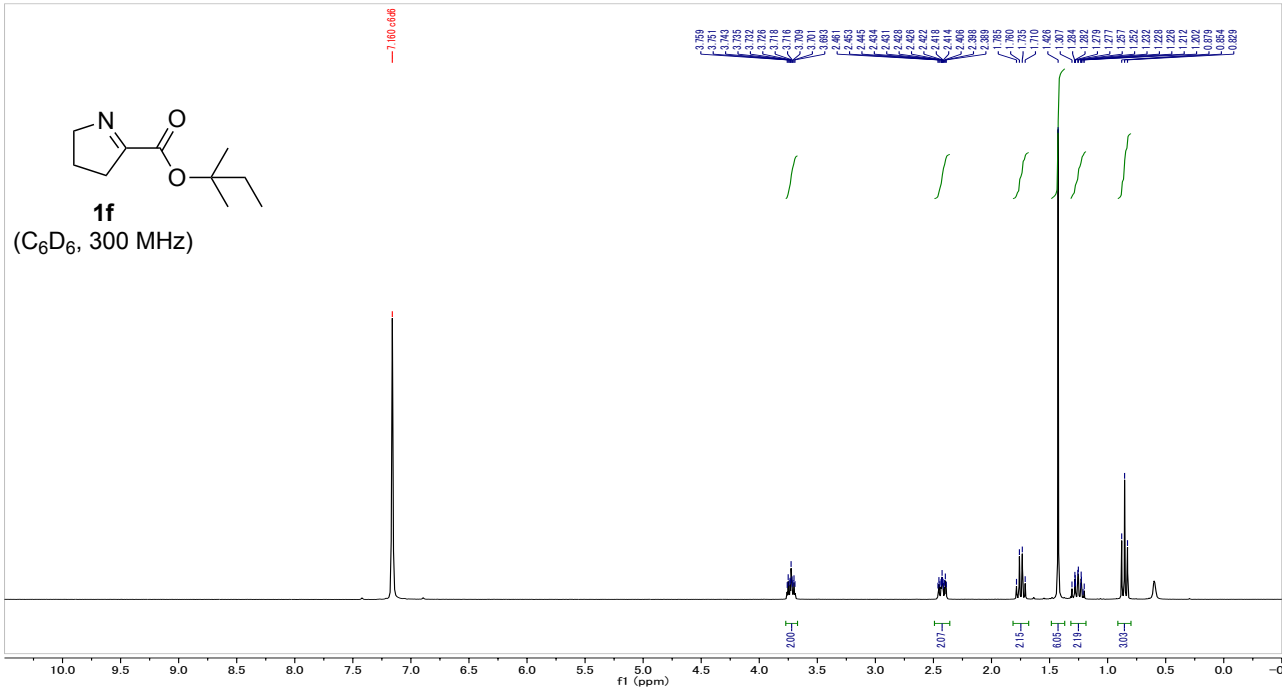
^{1}H NMR of *tert*-butyl 1-pyrroline 2-carboxylate (**1e**)



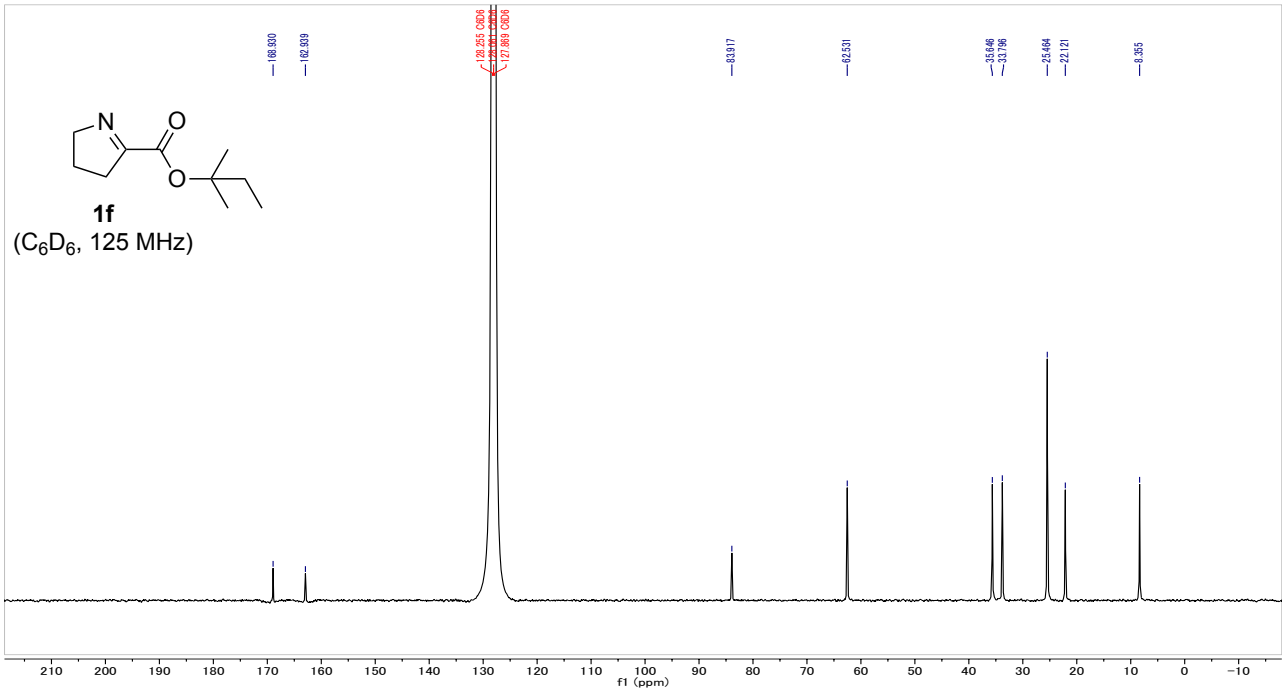
^{13}C NMR of *tert*-butyl 1-pyrroline 2-carboxylate (**1e**)



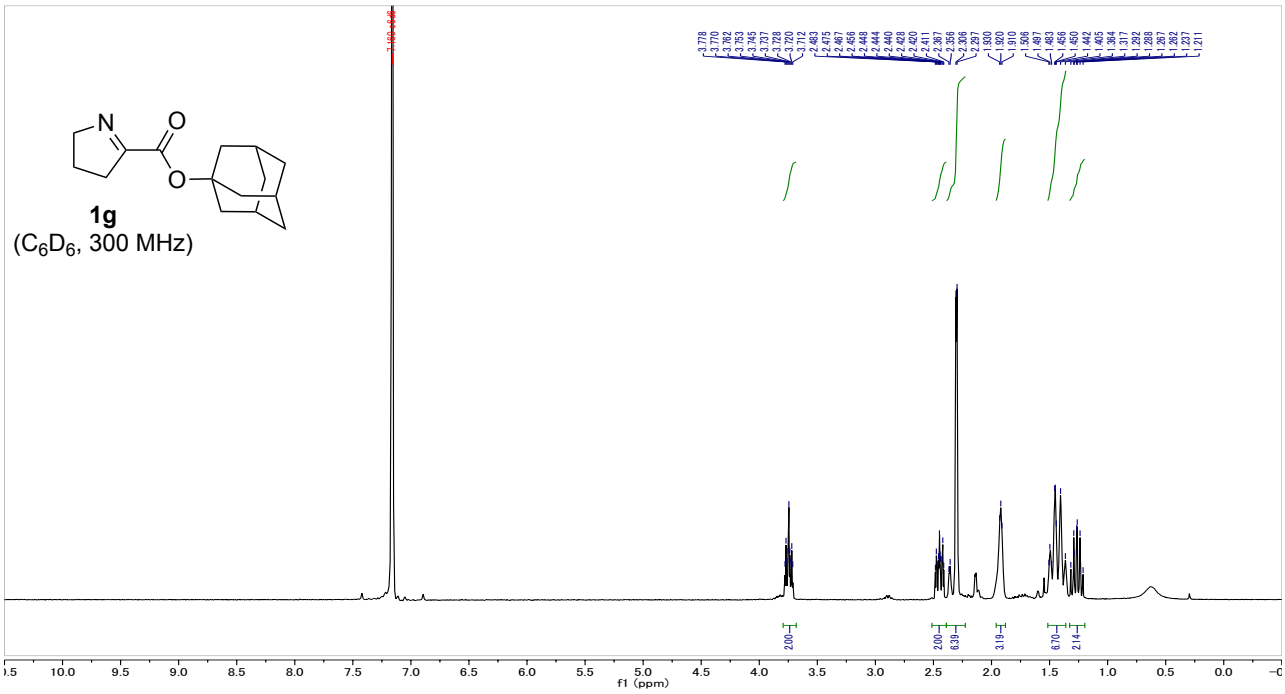
^{1}H NMR of *tert*-pentyl 1-pyrroline 2-carboxylate (**1f**)



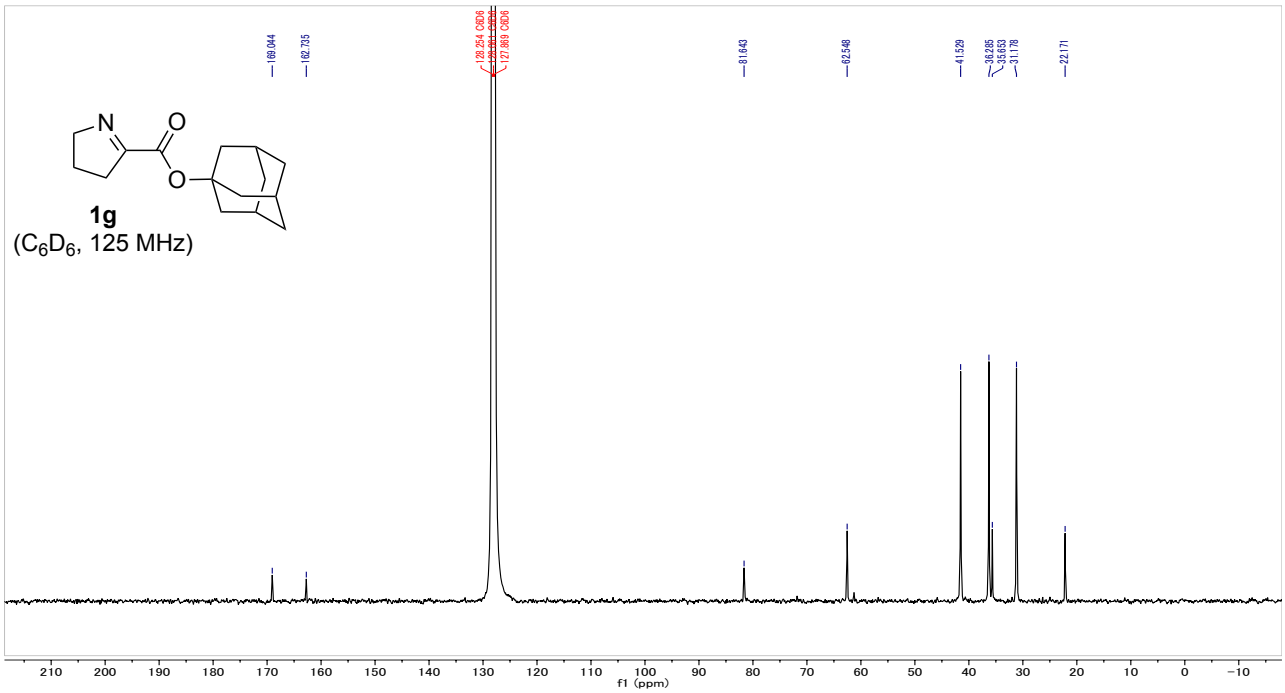
^{13}C NMR of *tert*-pentyl 1-pyrroline 2-carboxylate (**1f**)



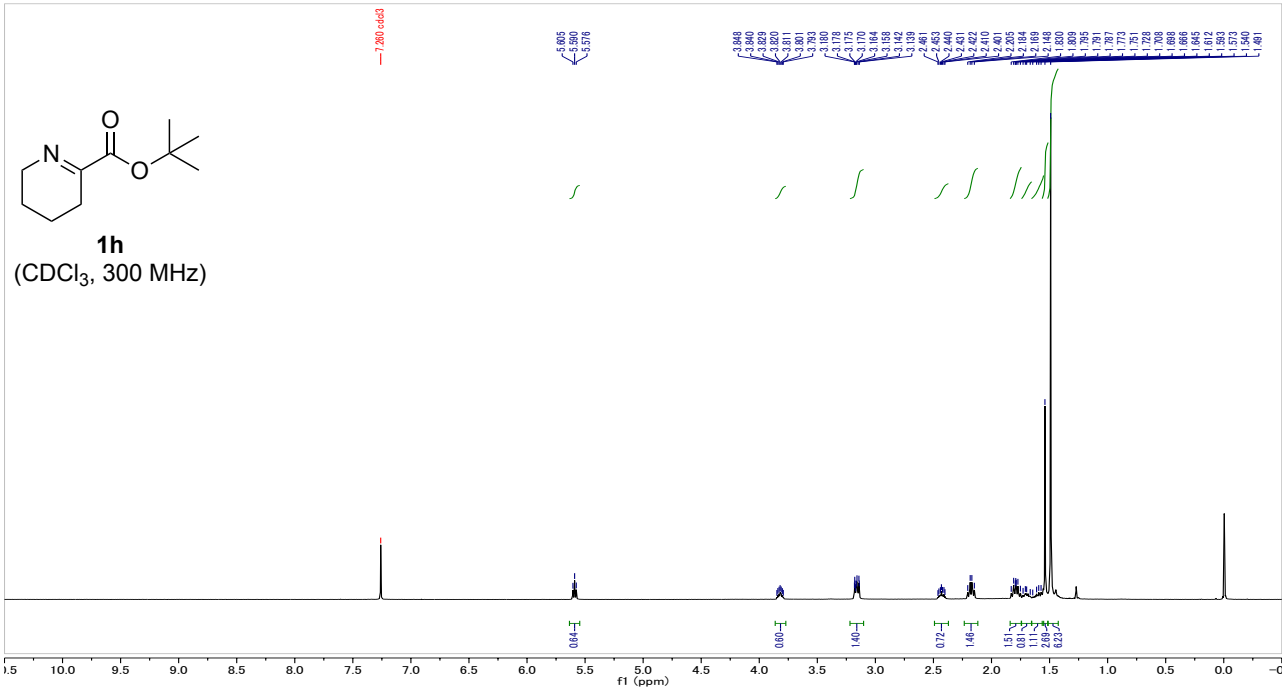
^{1}H NMR of adamanta-1-yl 1-pyrroline 2-carboxylate (**1g**)



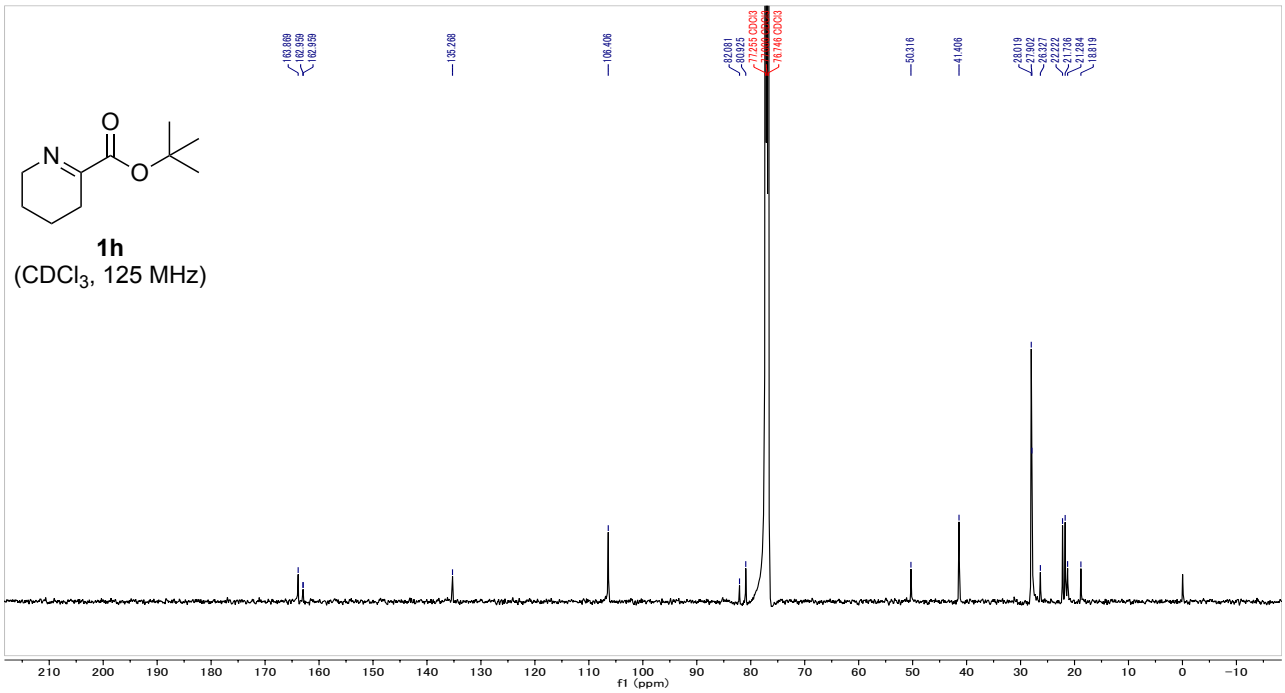
^{13}C NMR of adamanta-1-yl 1-pyrroline 2-carboxylate (**1g**)



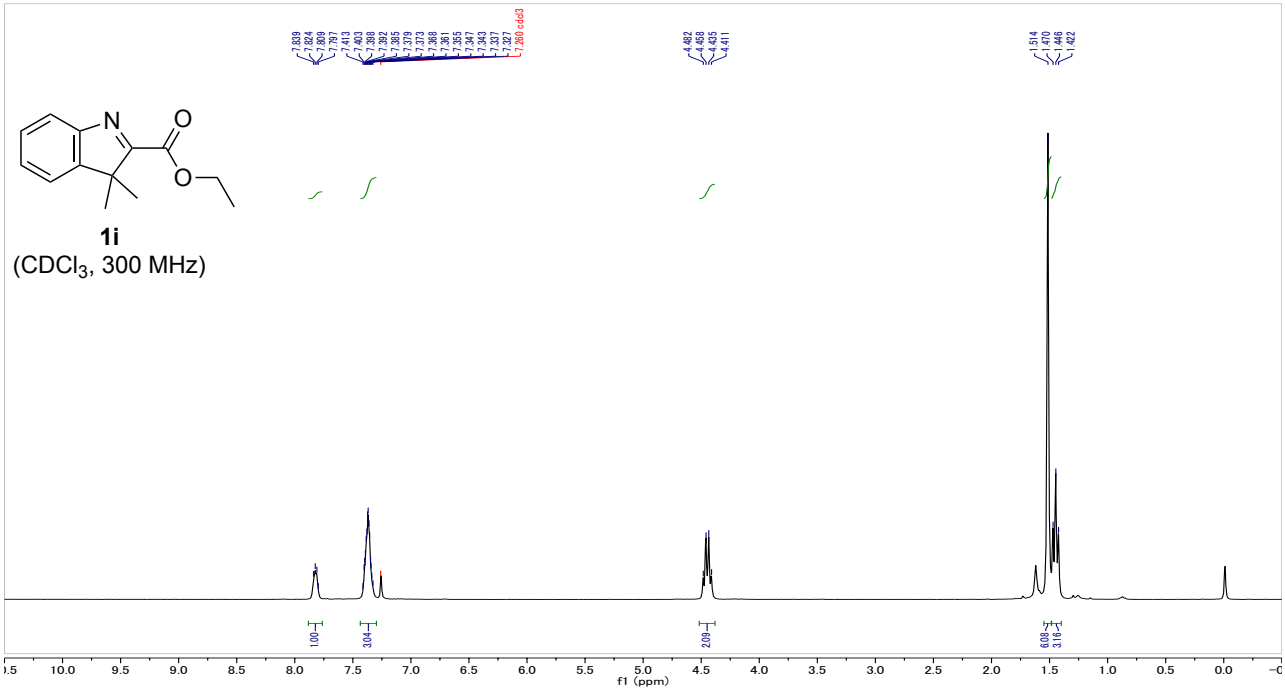
^{1}H NMR of *tert*-butyl-3,4,5,6-tetrahydropyridine 2-carboxylate (**1h**)



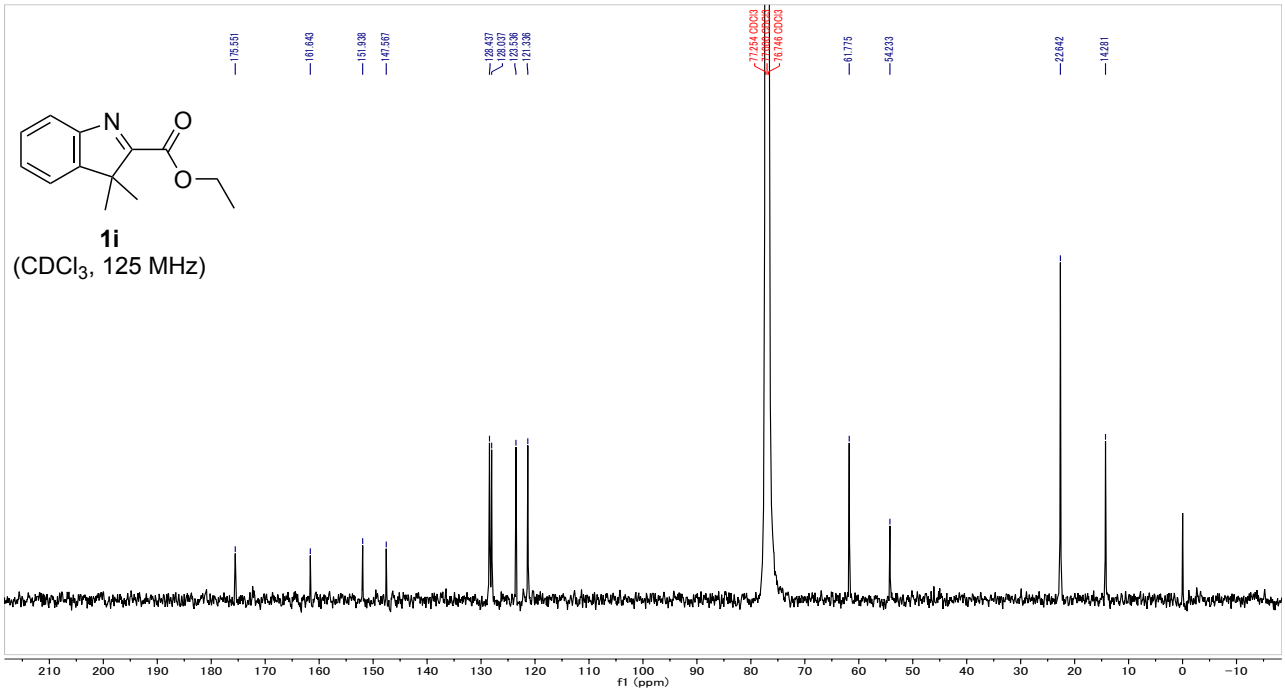
^{13}C NMR of *tert*-butyl-3,4,5,6-tetrahydropyridine 2-carboxylate (**1h**)



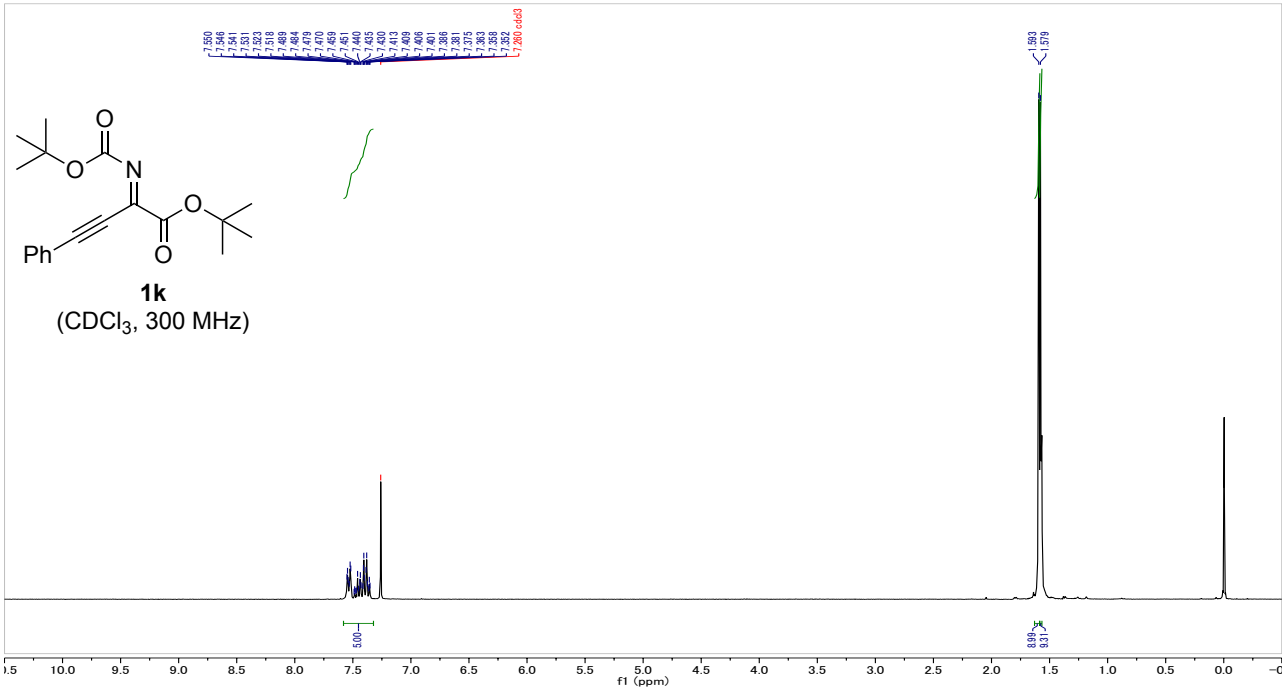
^{1}H NMR of ethyl 3,3-dimethyl-3*H*-indole-2-carboxylate (**1i**)



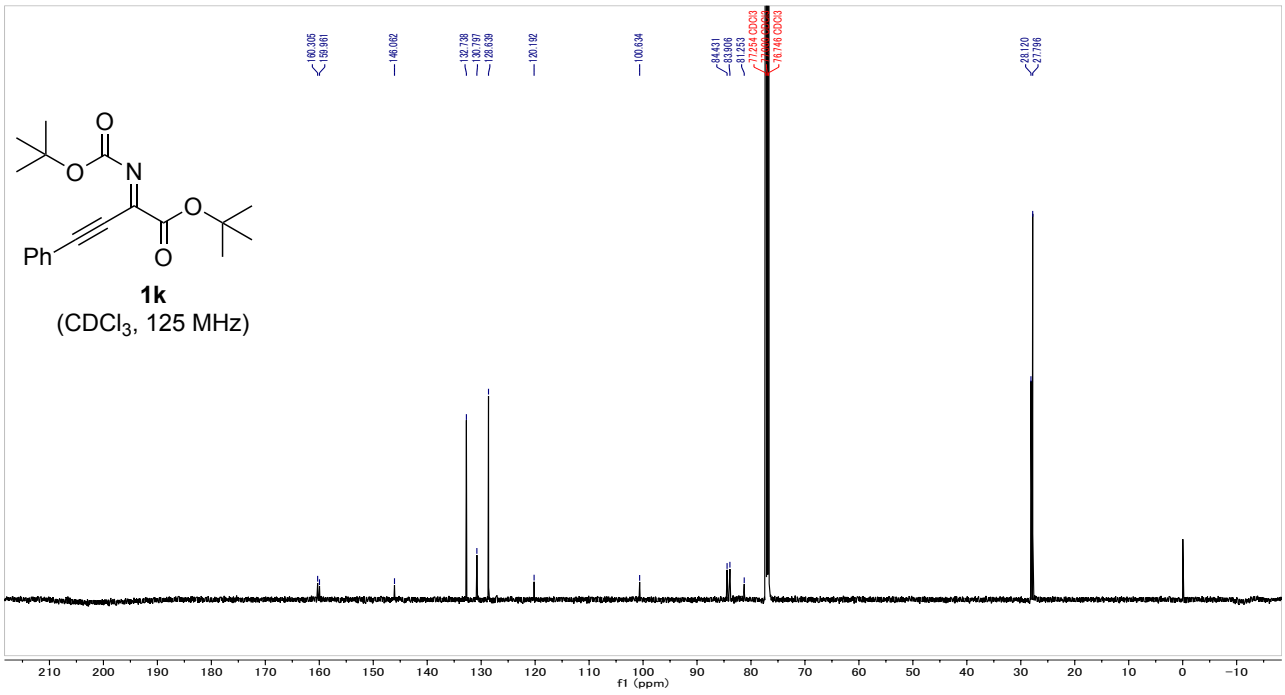
^{13}C NMR of ethyl 3,3-dimethyl-3*H*-indole-2-carboxylate (**1i**)



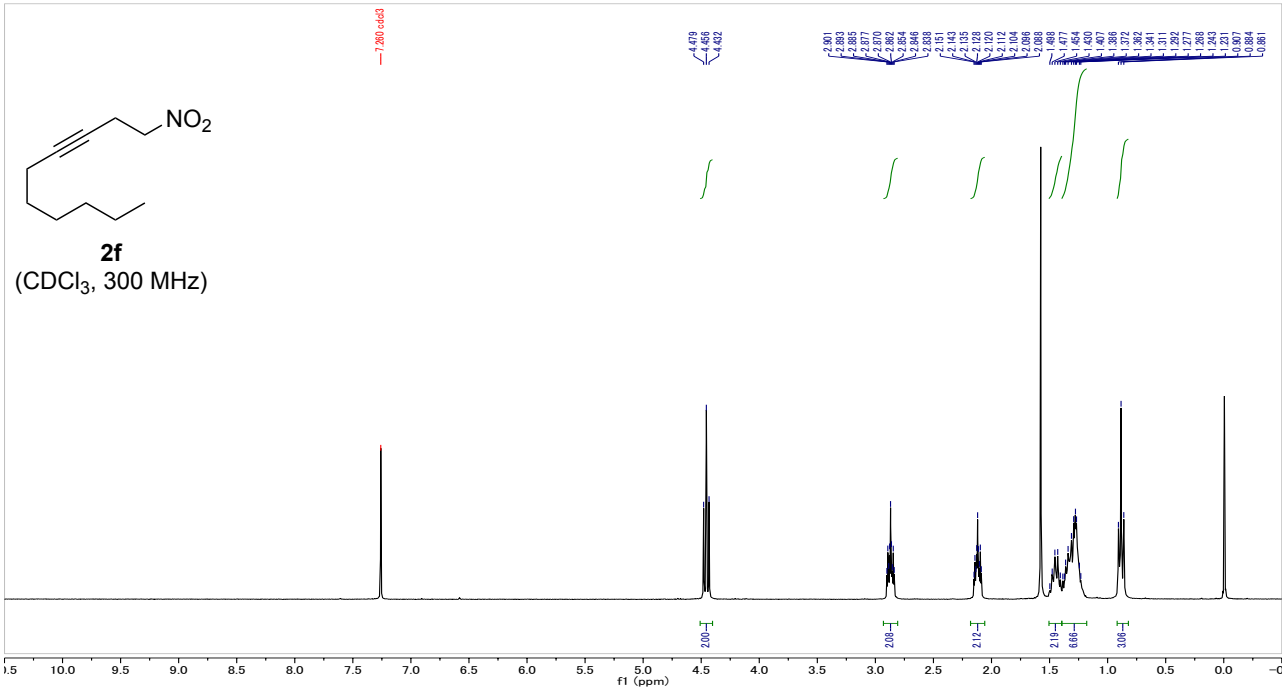
^{1}H NMR of *tert*-butyl 2-[(*tert*-butoxycarbonyl)imino]-4-phenylbut-3-ynoate (**1k**)



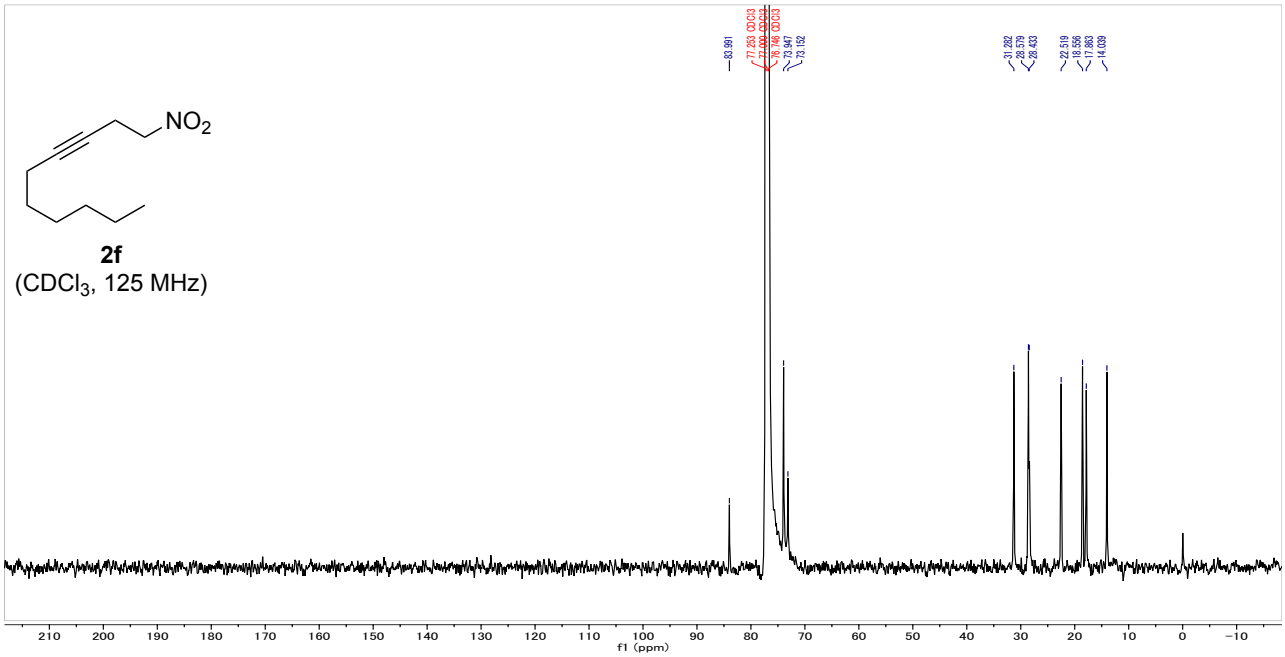
^{13}C NMR of *tert*-butyl 2-[(*tert*-butoxycarbonyl)imino]-4-phenylbut-3-ynoate (**1k**)



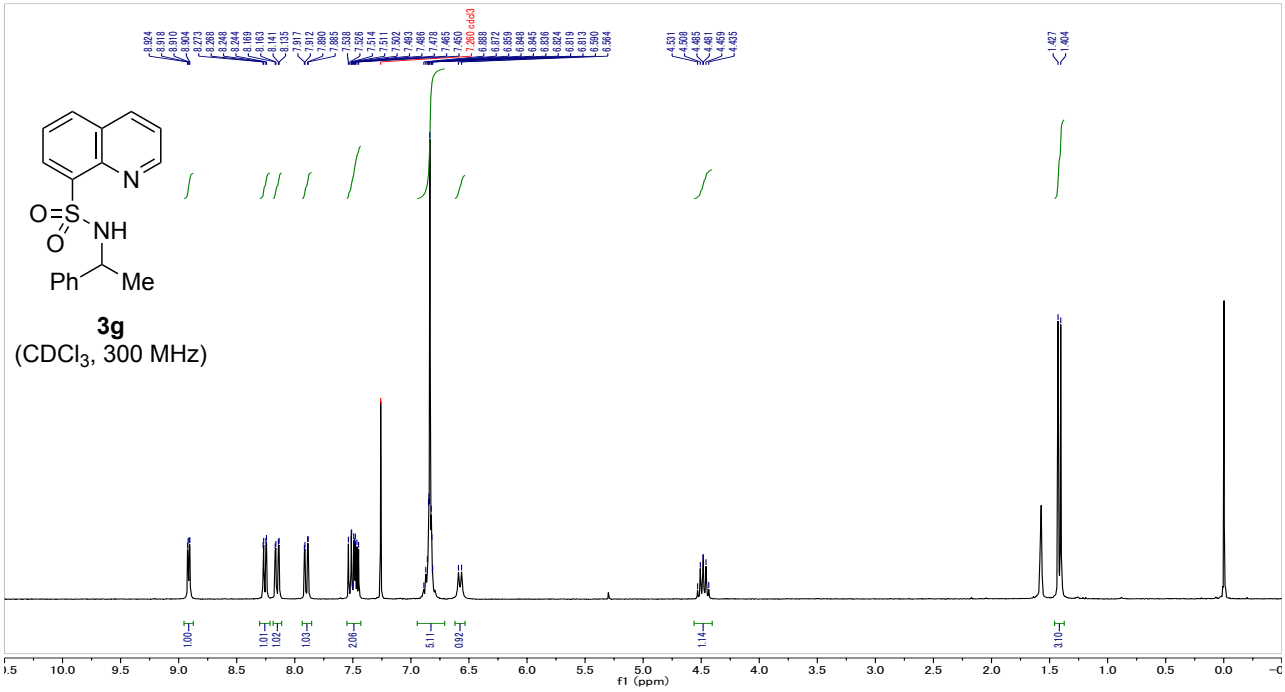
^{1}H NMR of 1-nitrodec-3-yne (**2f**)



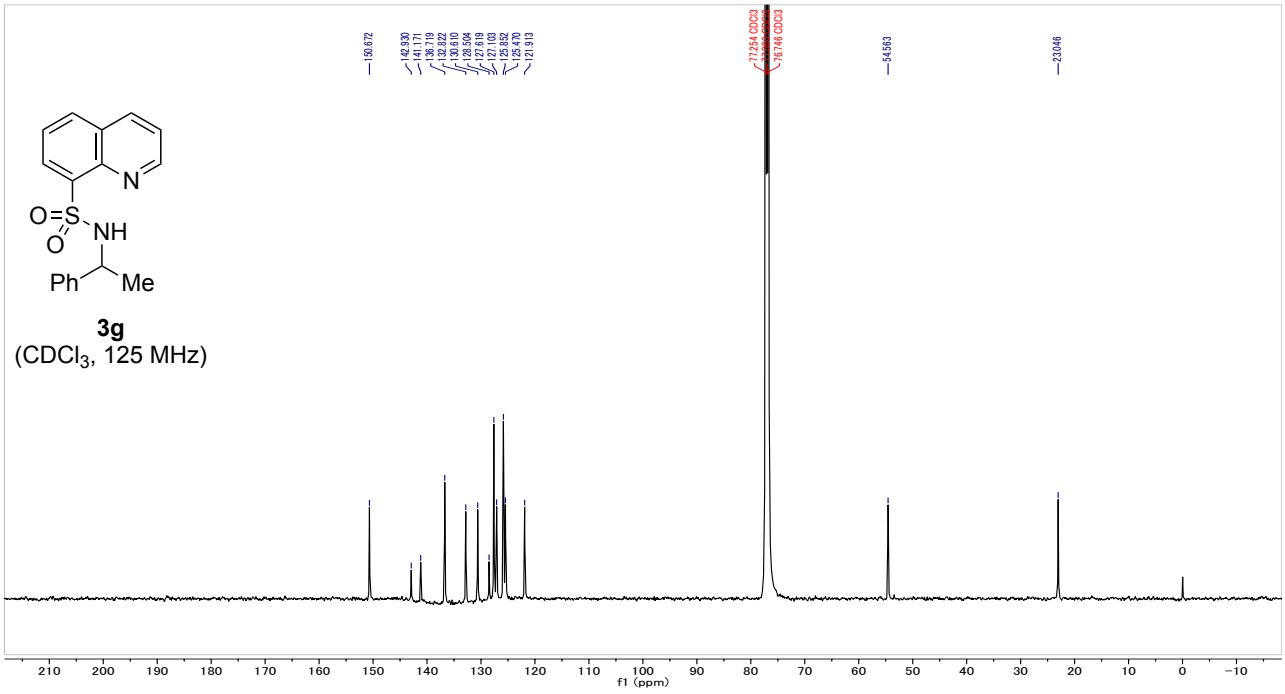
^{13}C NMR of 1-nitrodec-3-yne (**2f**)



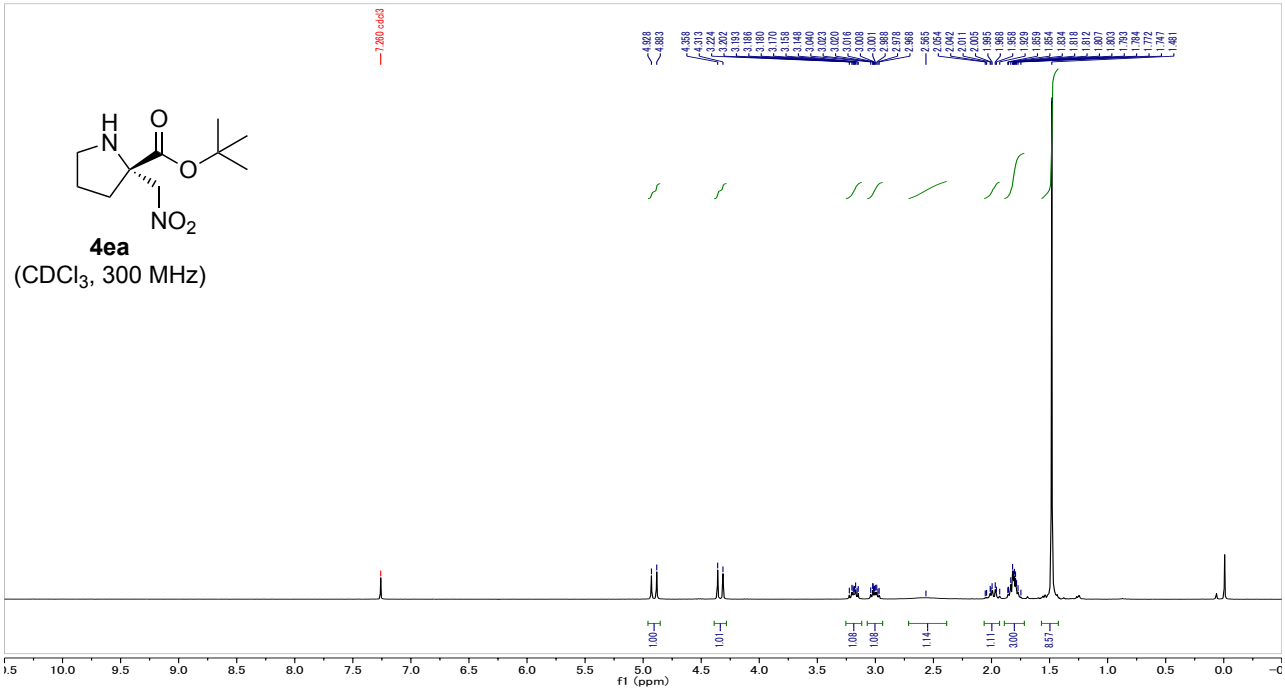
^{1}H NMR of *N*-(1-phenylethyl)quinoline-8-sulfonamide (**3g**)



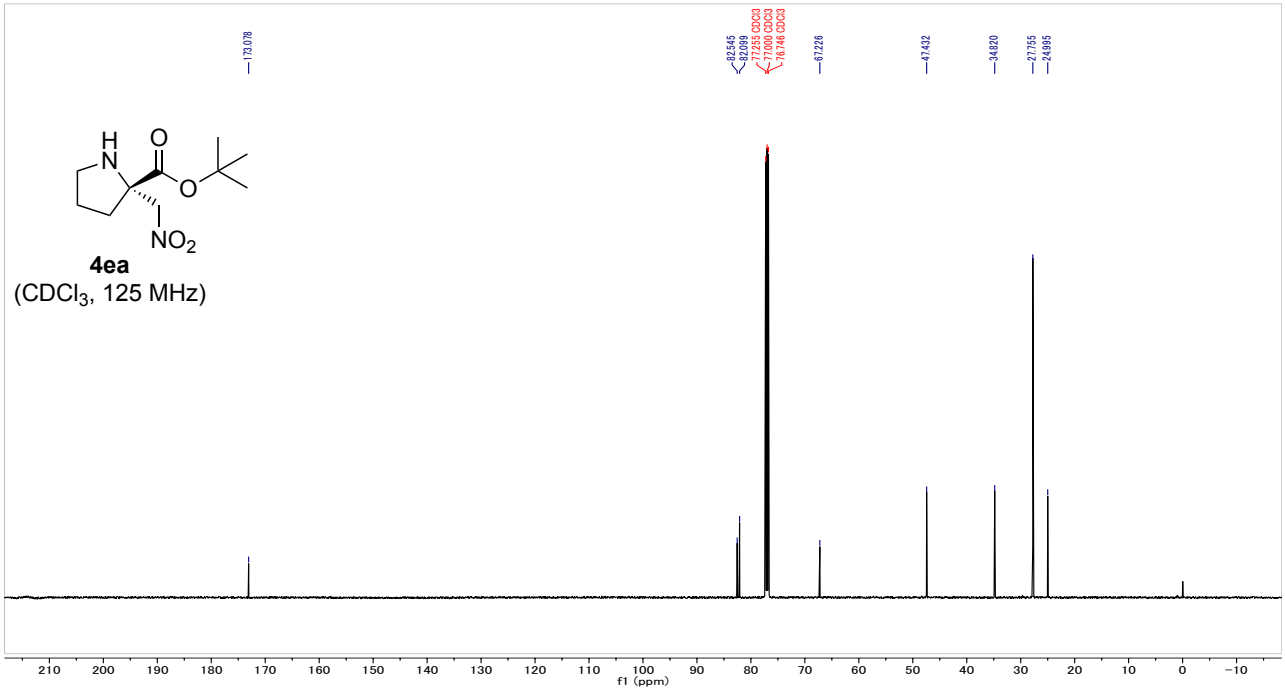
^{13}C NMR of *N*-(1-phenylethyl)quinoline-8-sulfonamide (**3g**)



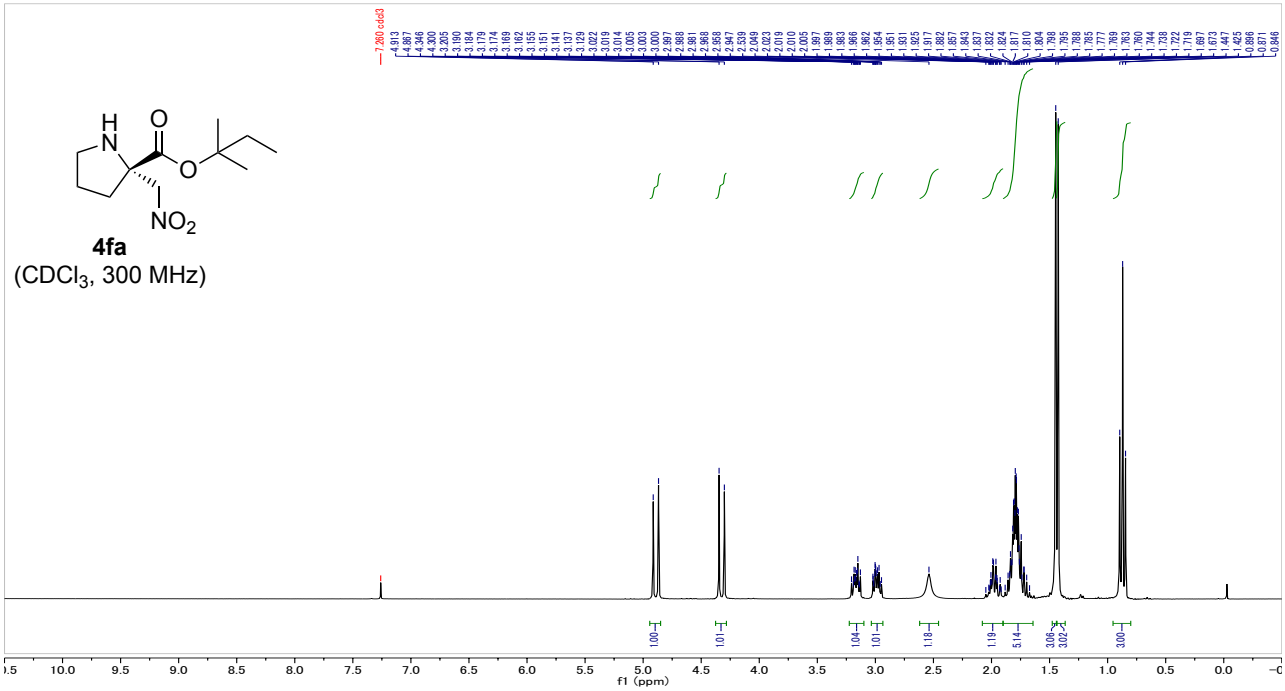
^{1}H NMR of *tert*-butyl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**4ea**]



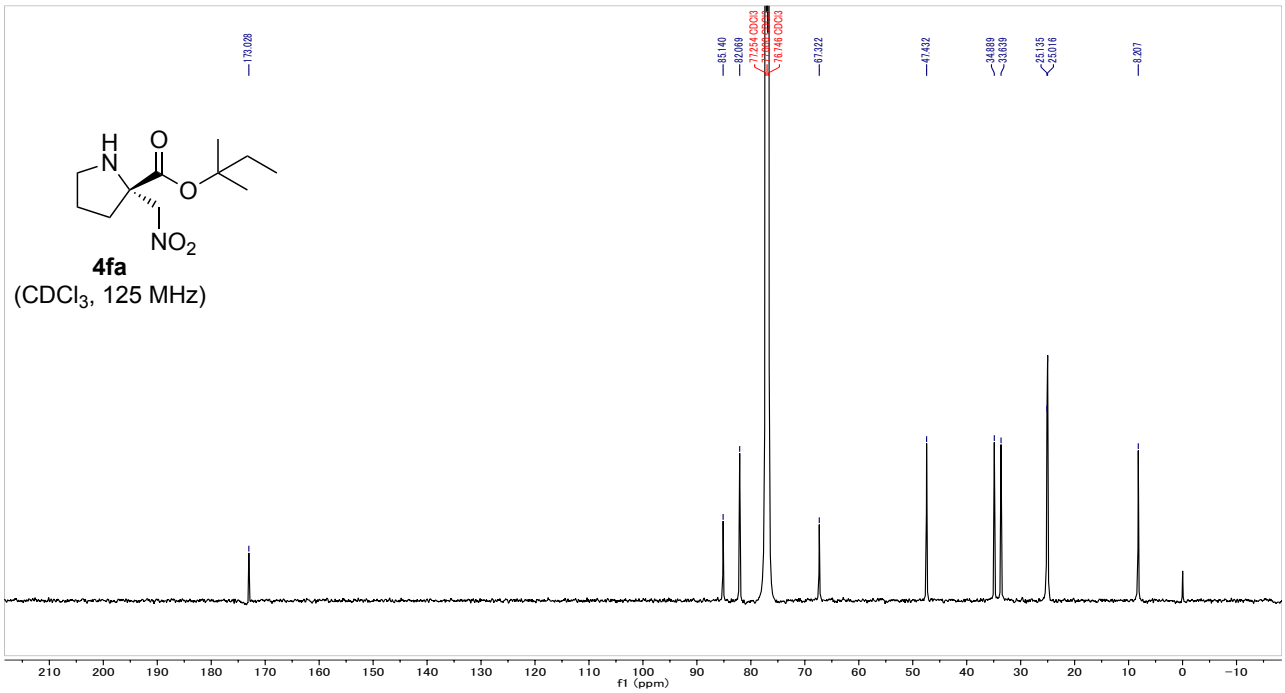
^{13}C NMR of *tert*-butyl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**4ea**]



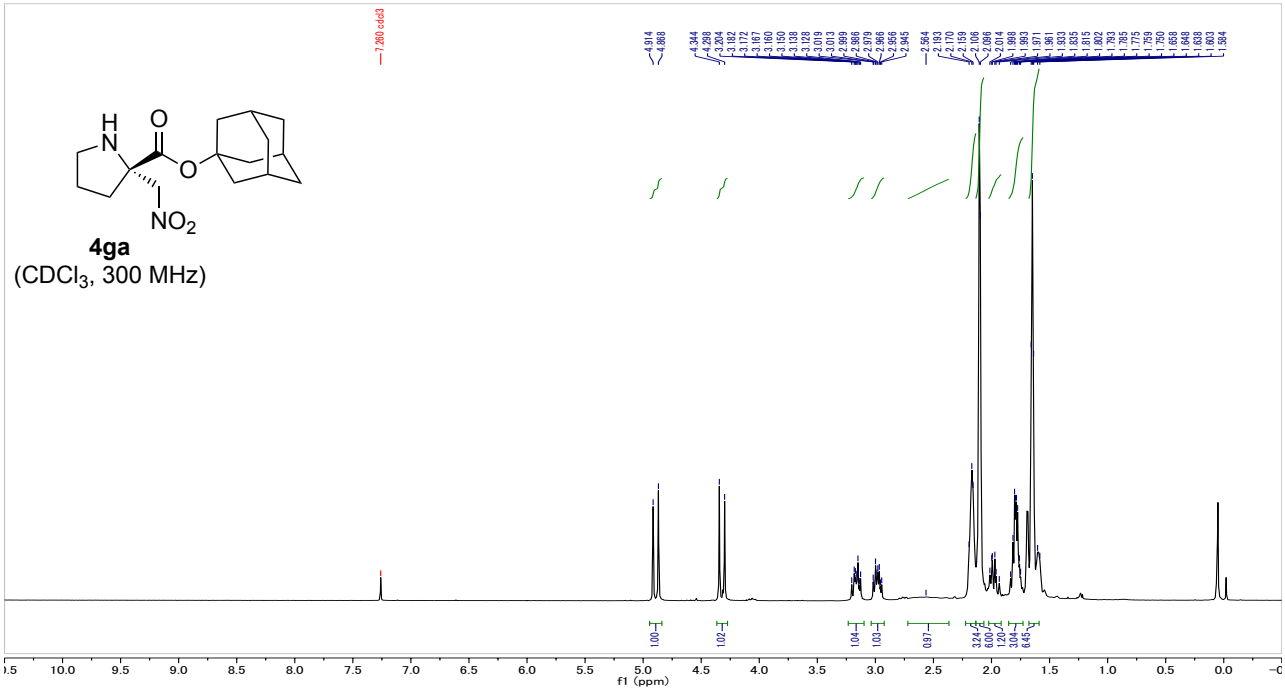
^{1}H NMR of *tert*-pentyl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**4fa**]



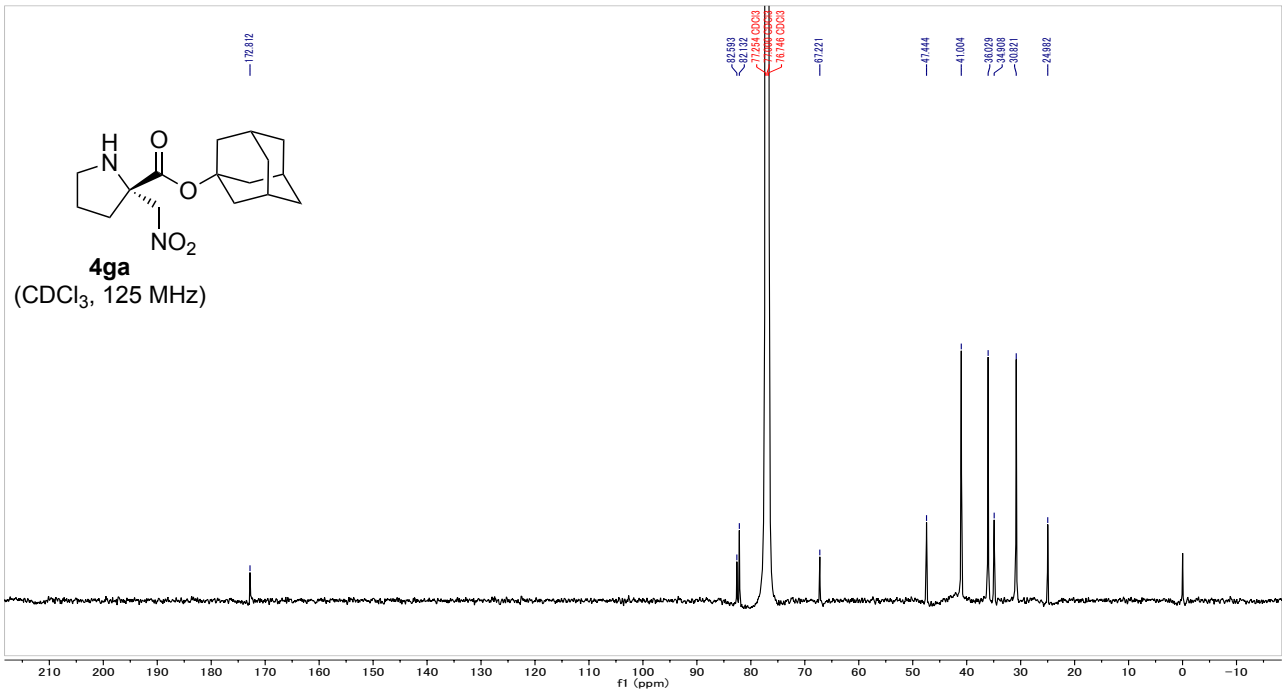
^{13}C NMR of *tert*-pentyl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**4fa**]



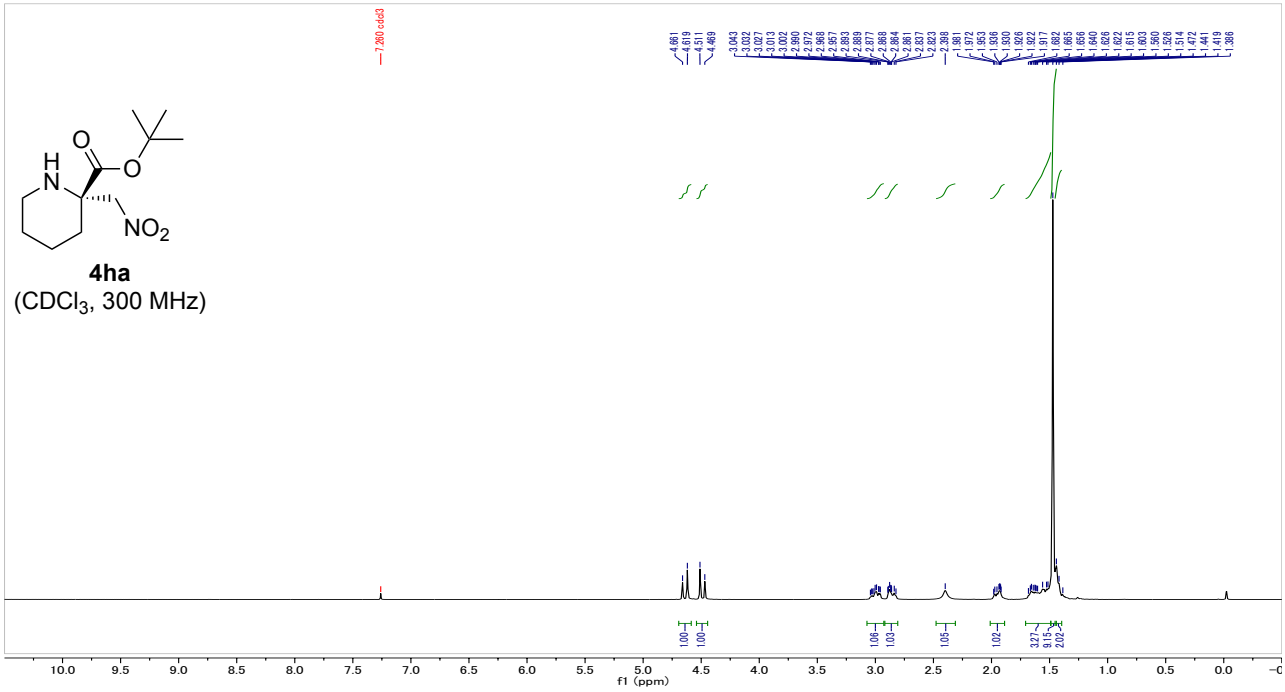
^{1}H NMR of adamanta-1-yl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**4ga**]



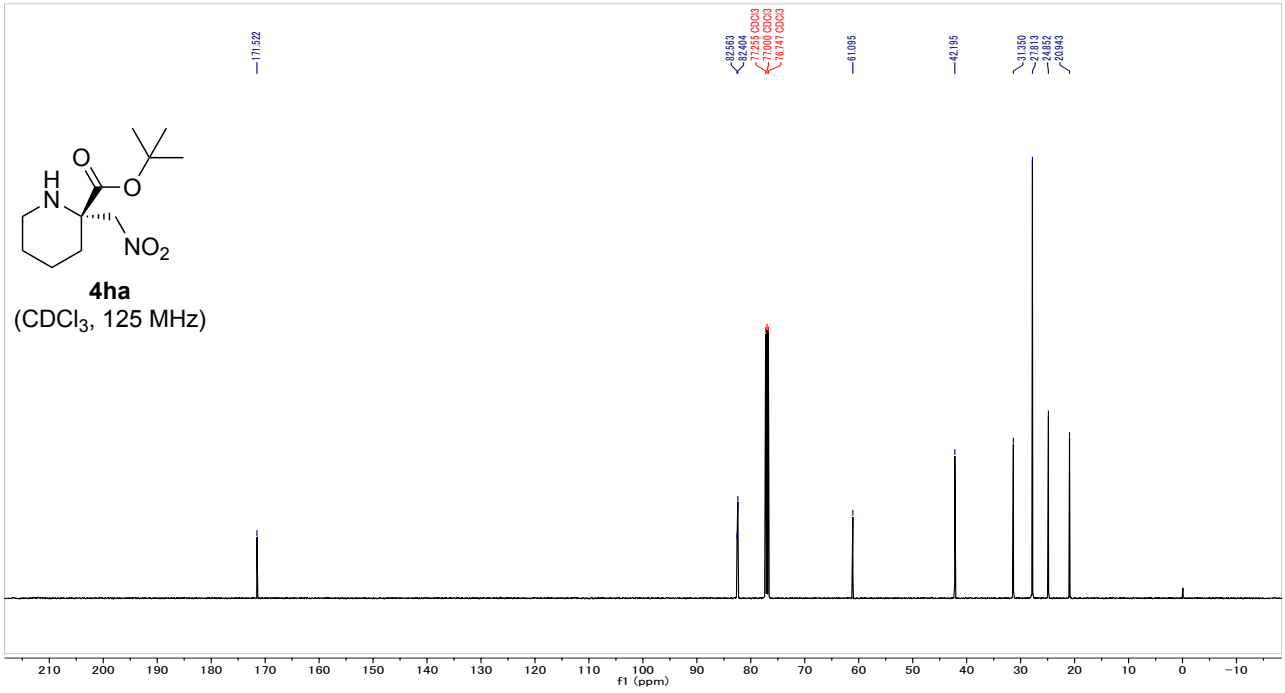
^{13}C NMR of adamanta-1-yl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**4ga**]



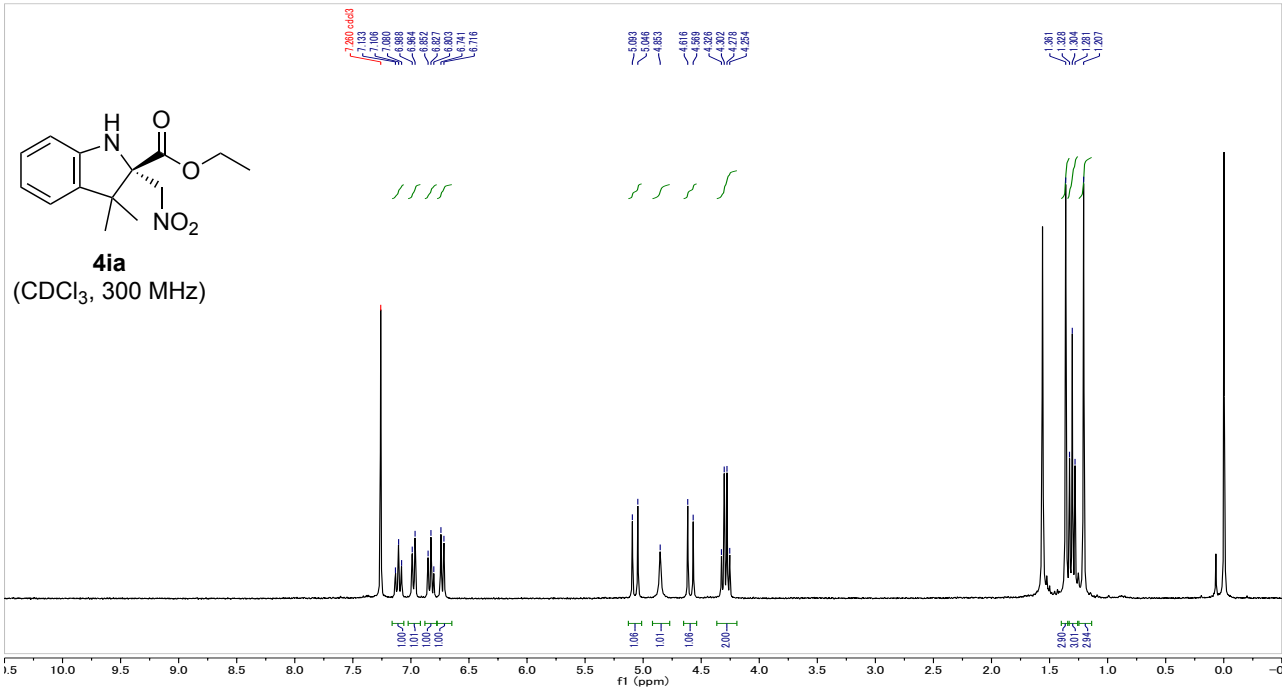
^{1}H NMR of *tert*-butyl (*S*)-2-(nitromethyl)piperidine 2-carboxylate [(*S*)-**4ha**]



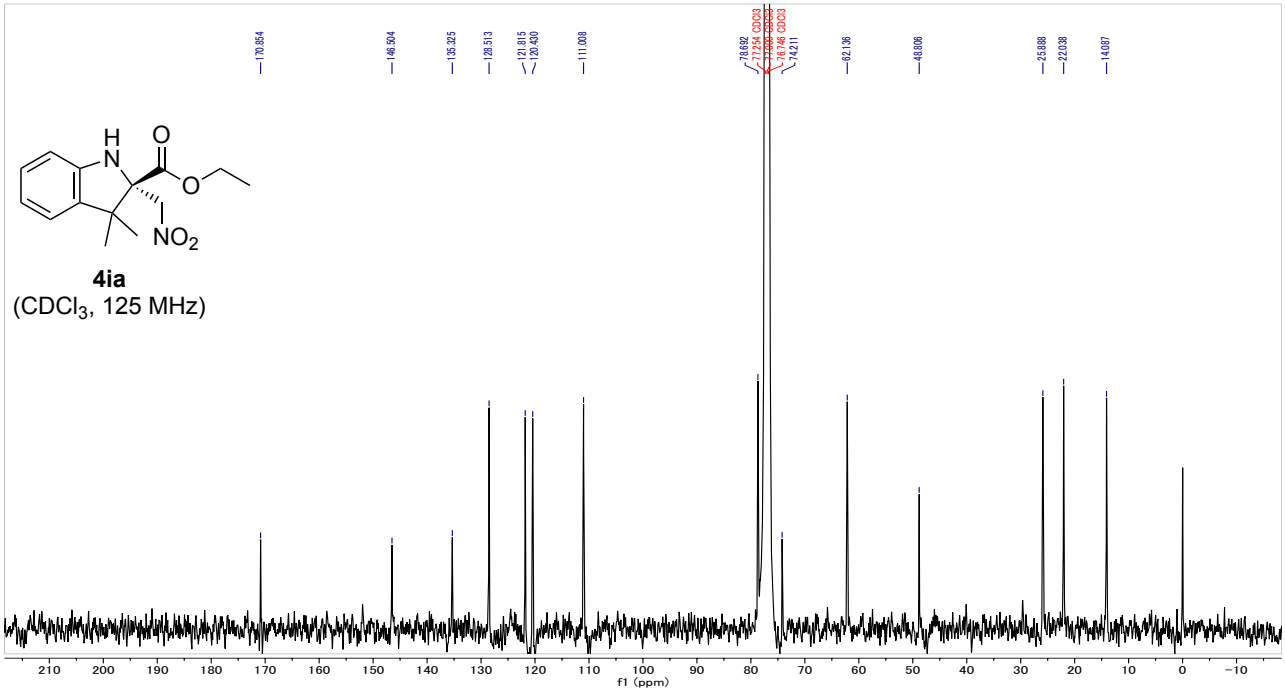
^{13}C NMR of *tert*-butyl (*S*)-2-(nitromethyl)piperidine 2-carboxylate [(*S*)-**4ha**]



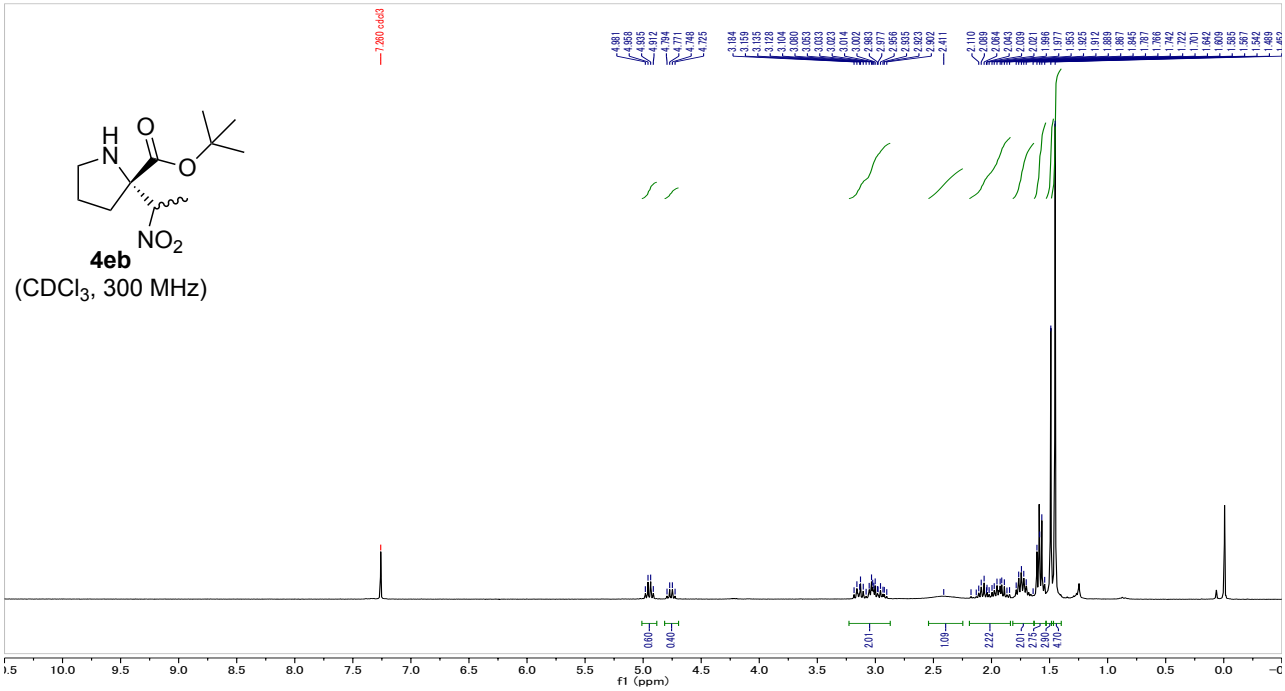
^{1}H NMR of ethyl (*S*)-3,3-dimethyl-2-(nitromethyl)indoline-2-carboxylate [(*S*)-**4ia**]



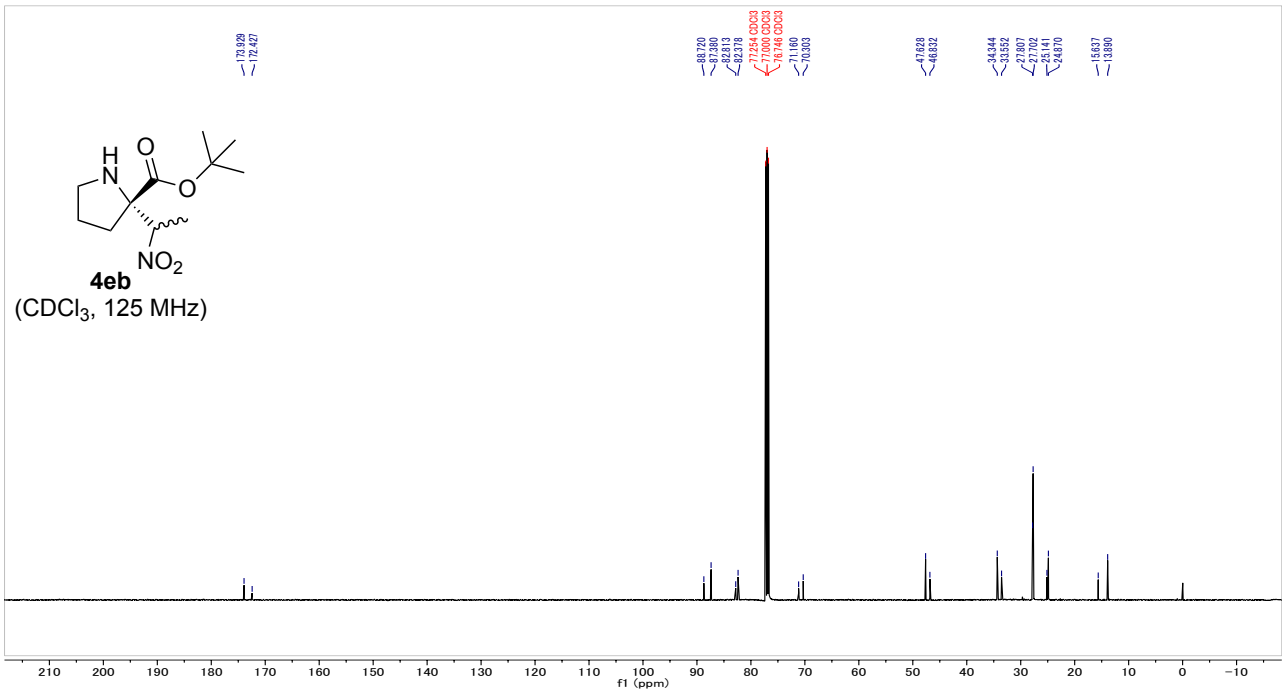
^{13}C NMR of ethyl (*S*)-3,3-dimethyl-2-(nitromethyl)indoline-2-carboxylate [(*S*)-**4ia**]



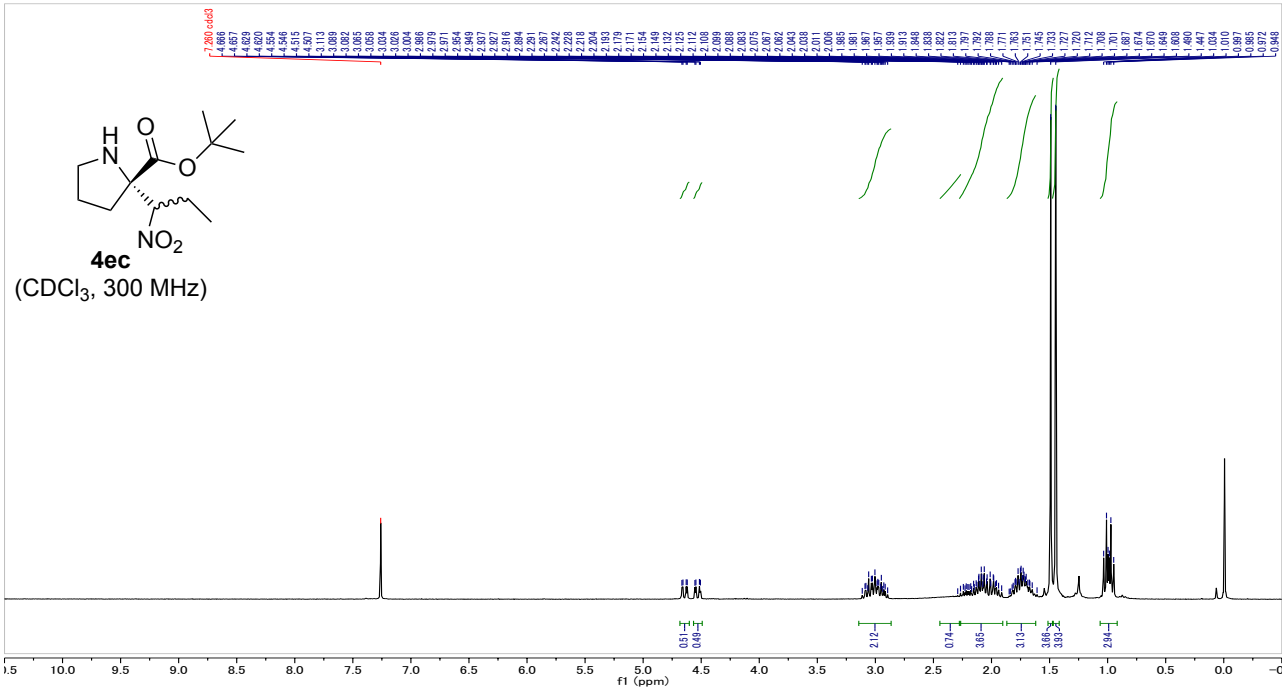
^{1}H NMR of *tert*-butyl 2-(nitroethyl)pyrrolidine 2-carboxylate [(*S*)-**4eb**]



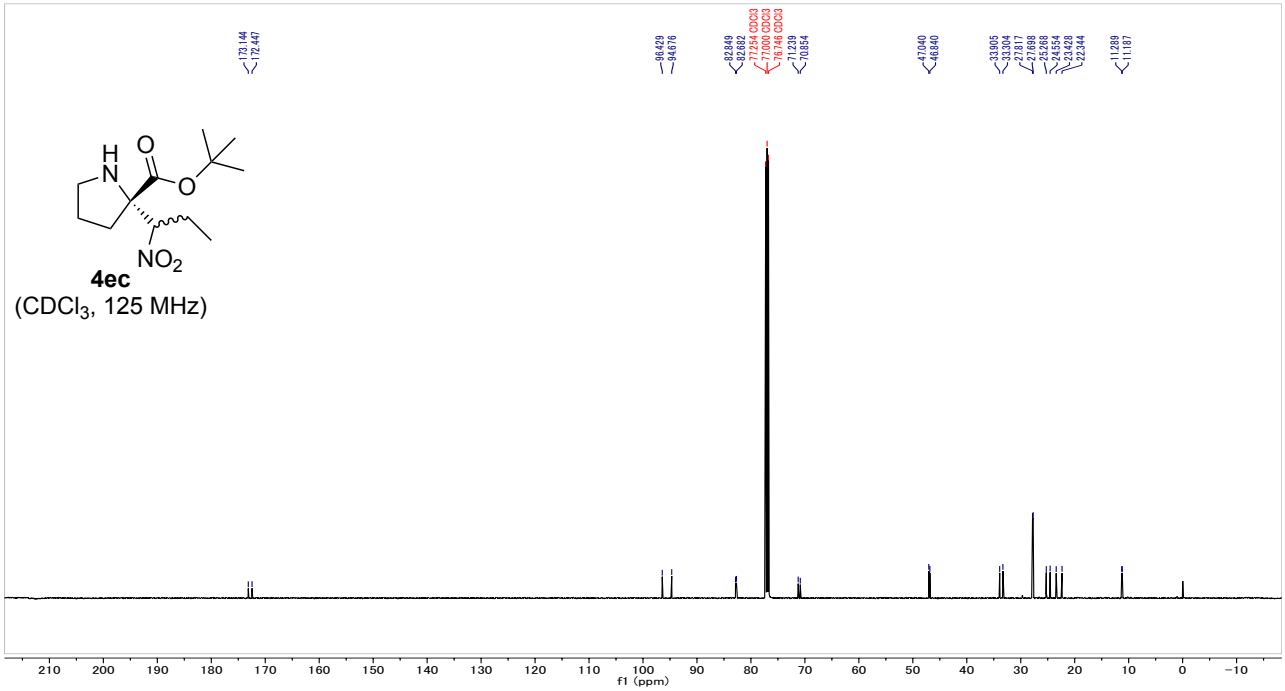
^{13}C NMR of *tert*-butyl 2-(nitroethyl)pyrrolidine 2-carboxylate [(*S*)-**4eb**]



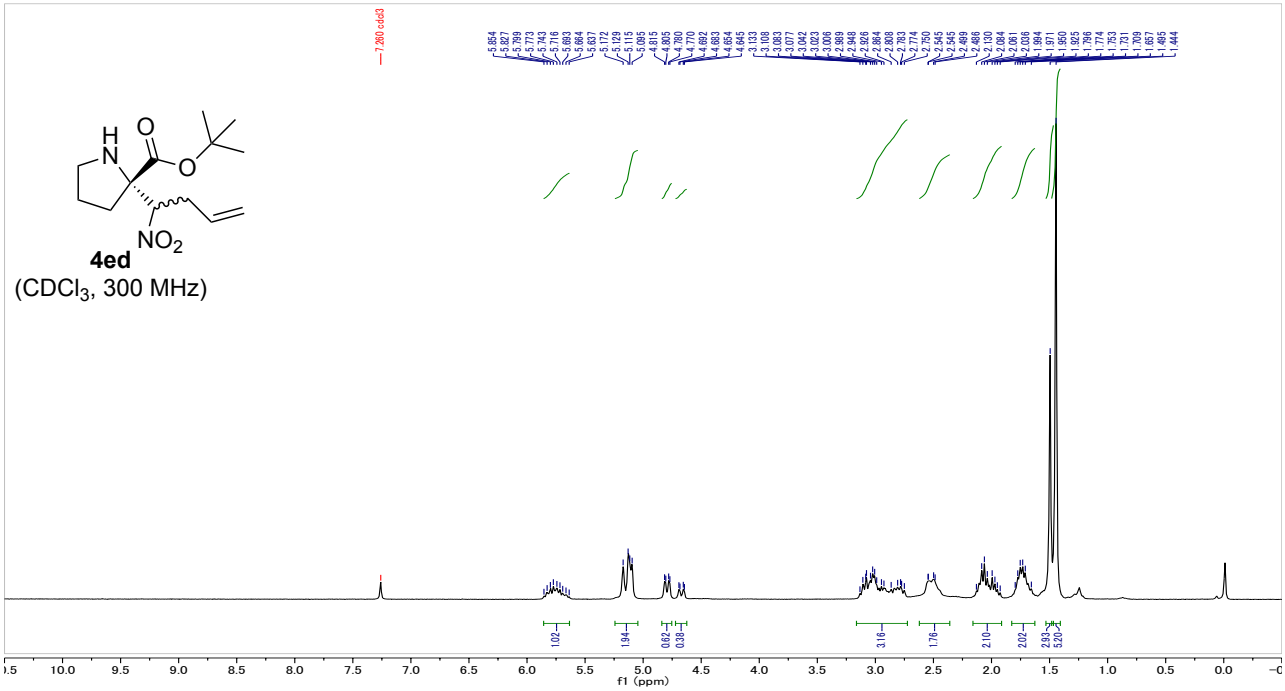
^{1}H NMR of *tert*-butyl 2-(1-nitropropyl)pyrrolidine 2-carboxylate [(*S*)-**4ec**]



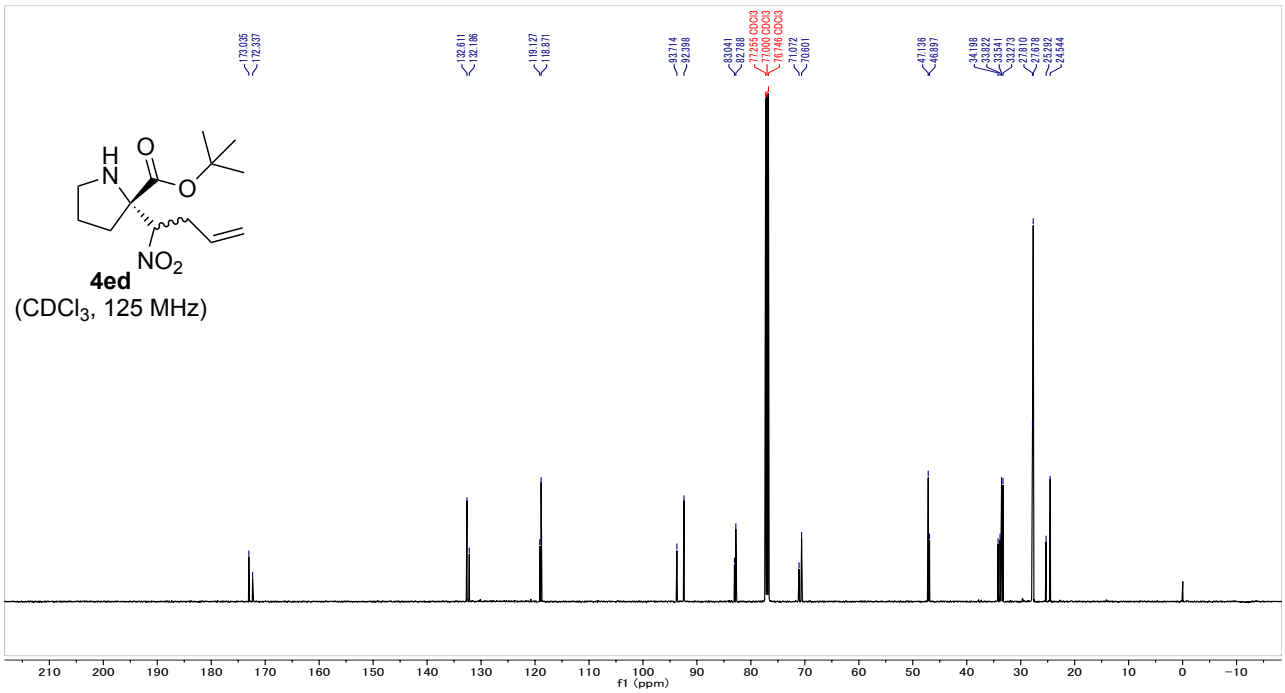
^{13}C NMR of *tert*-butyl 2-(1-nitropropyl)pyrrolidine 2-carboxylate [(*S*)-**4ec**]



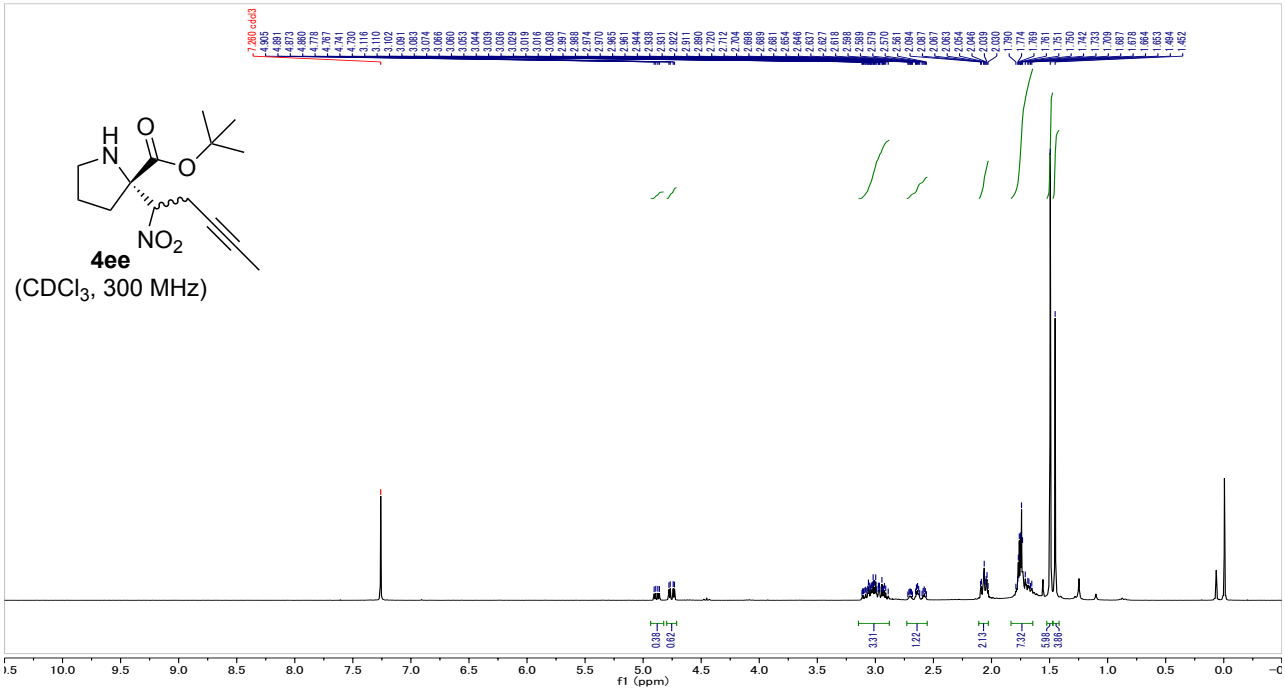
^{1}H NMR of *tert*-butyl (*S*)-2-(1-nitrobut-3-en-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4ed**]



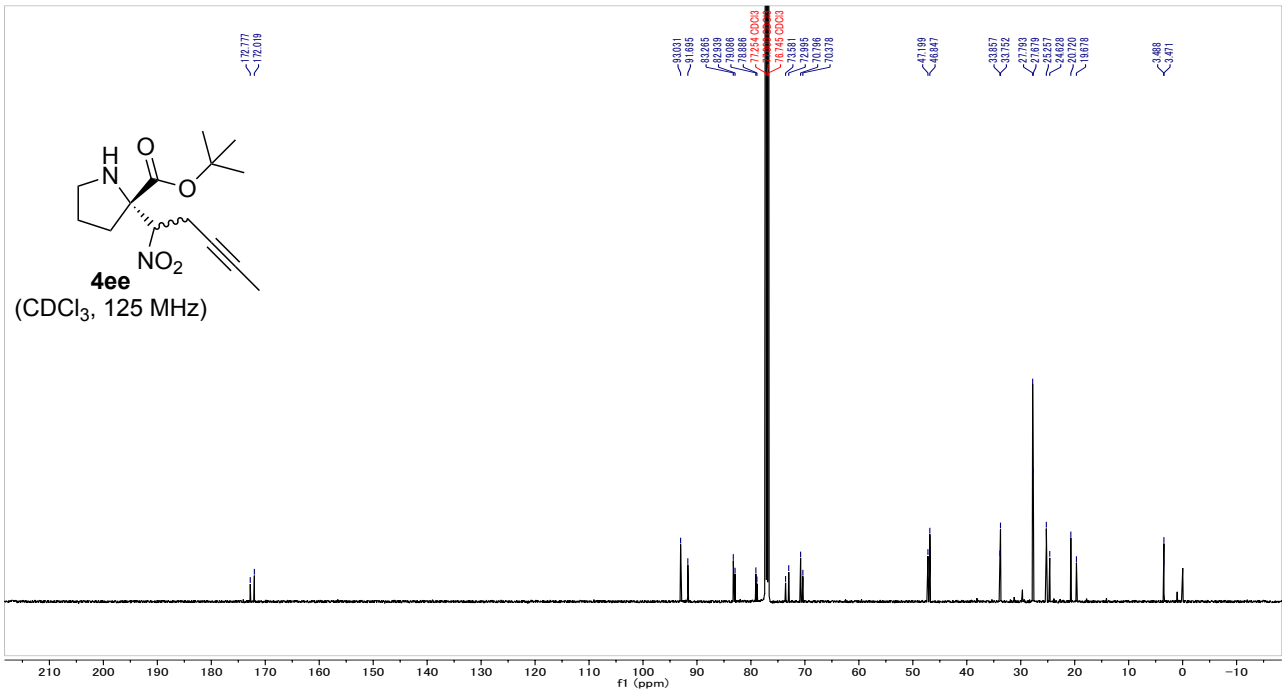
^{13}C NMR of *tert*-butyl (*S*)-2-(1-nitrobut-3-en-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4ed**]



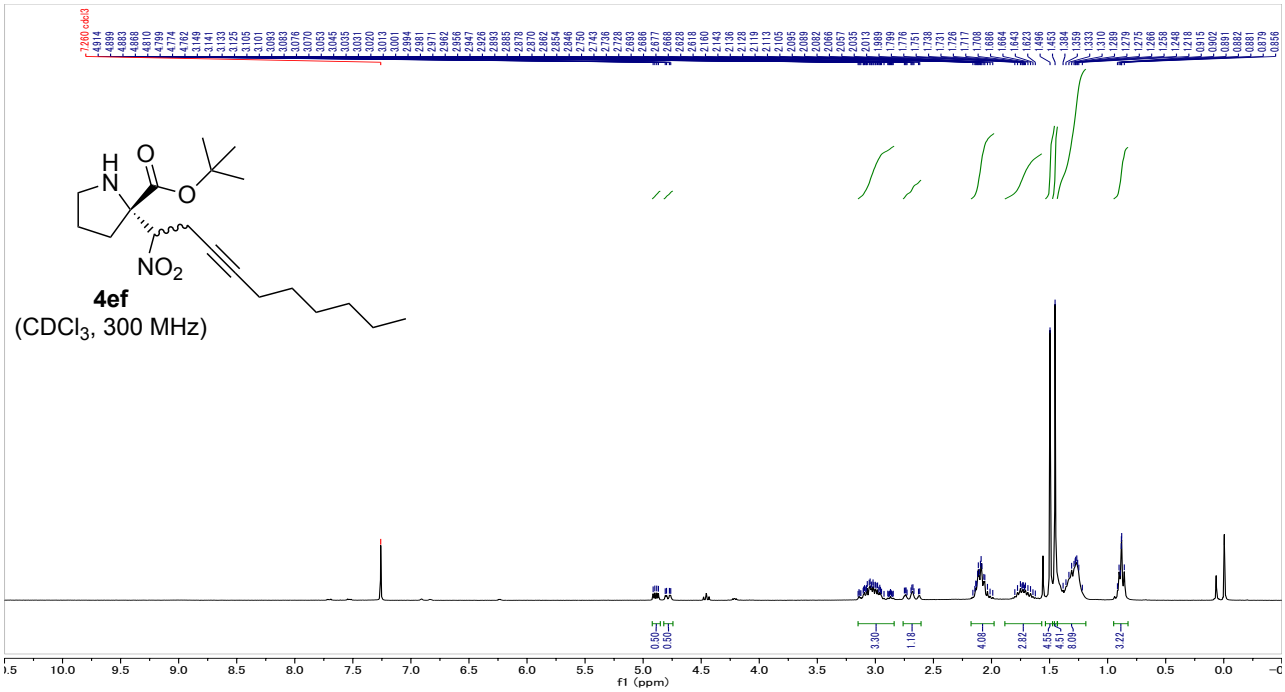
^{1}H NMR of *tert*-butyl (*S*)-2-(1-nitropent-3-yn-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4ee**]



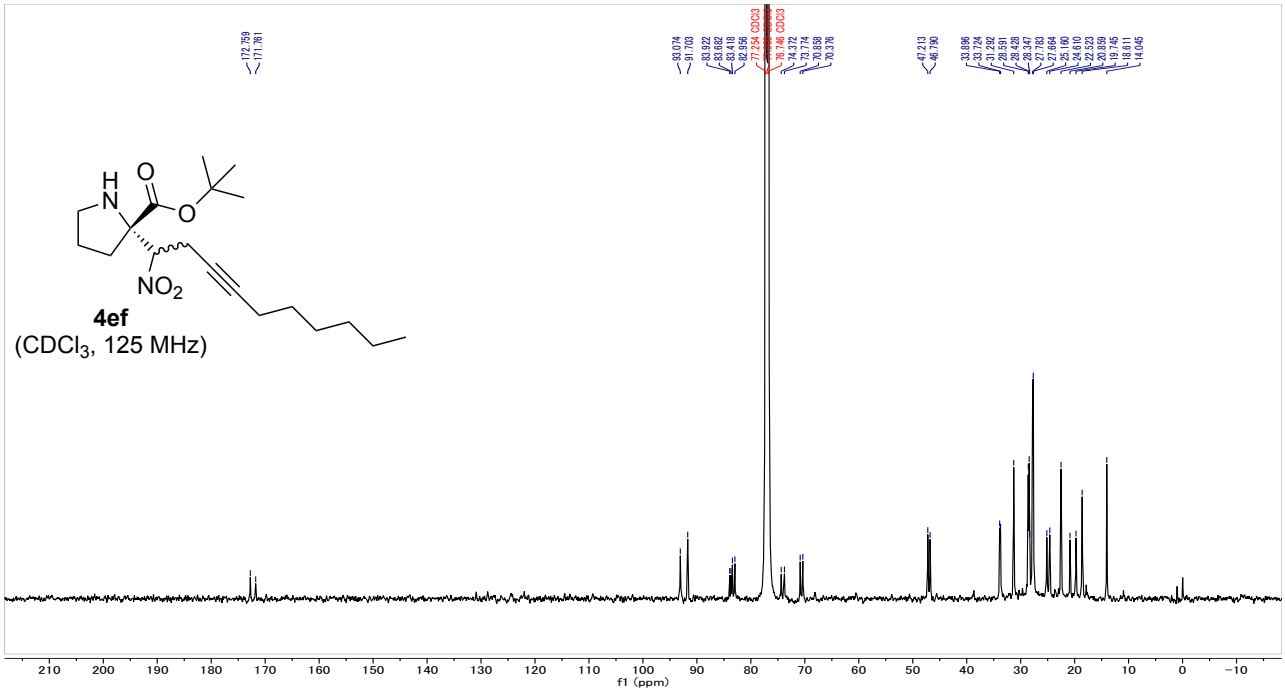
^{13}C NMR of *tert*-butyl (*S*)-2-(1-nitropent-3-yn-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4ee**]



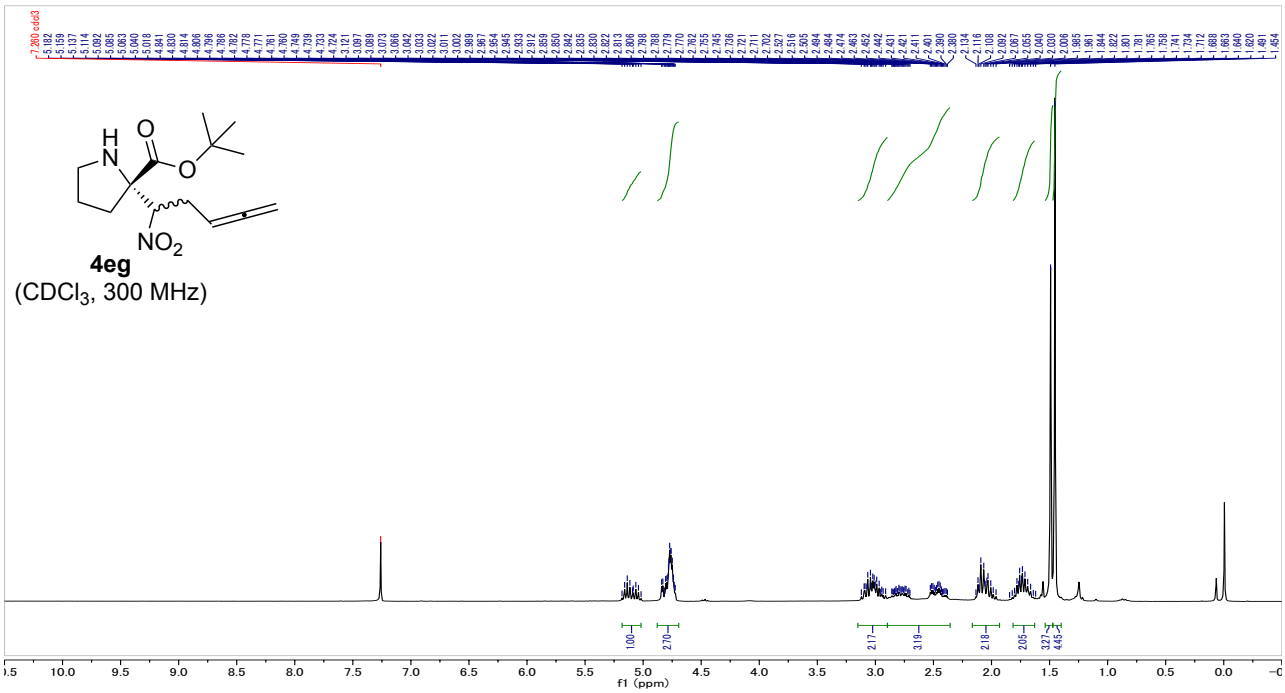
^{1}H NMR of *tert*-butyl (*S*)-2-(1-nitrodec-3-yn-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4ef**]



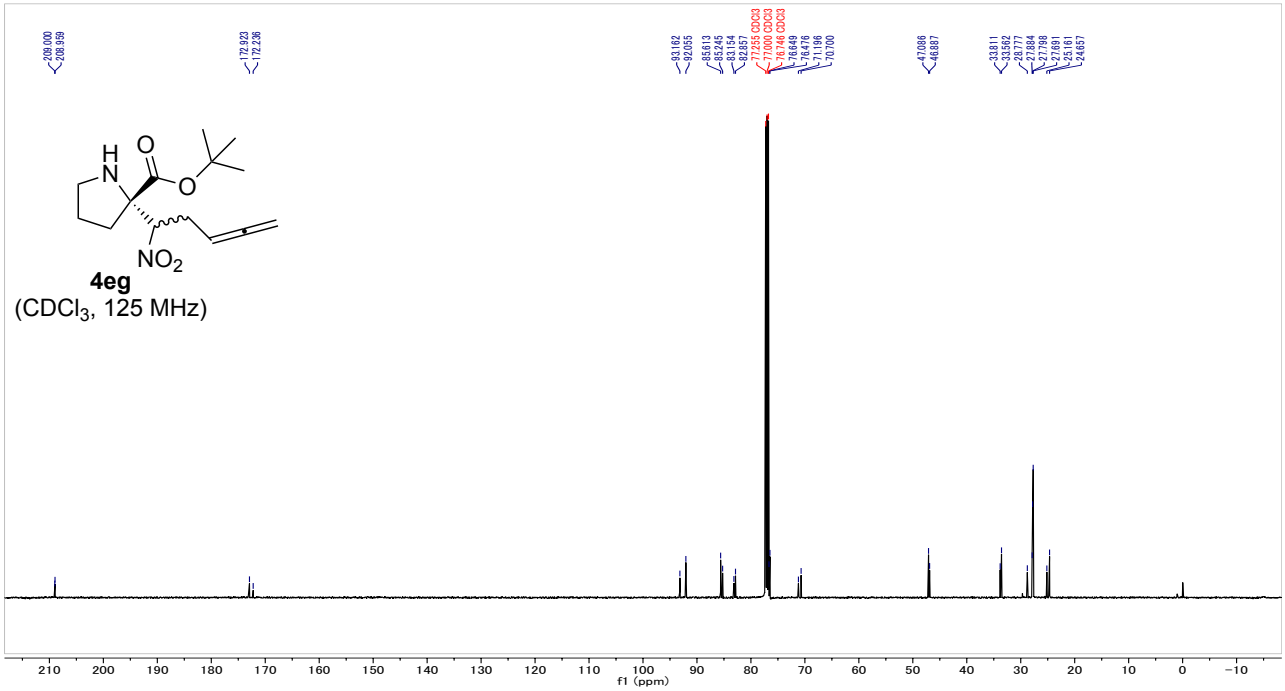
^{13}C NMR of *tert*-butyl (*S*)-2-(1-nitrodec-3-yn-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4ef**]



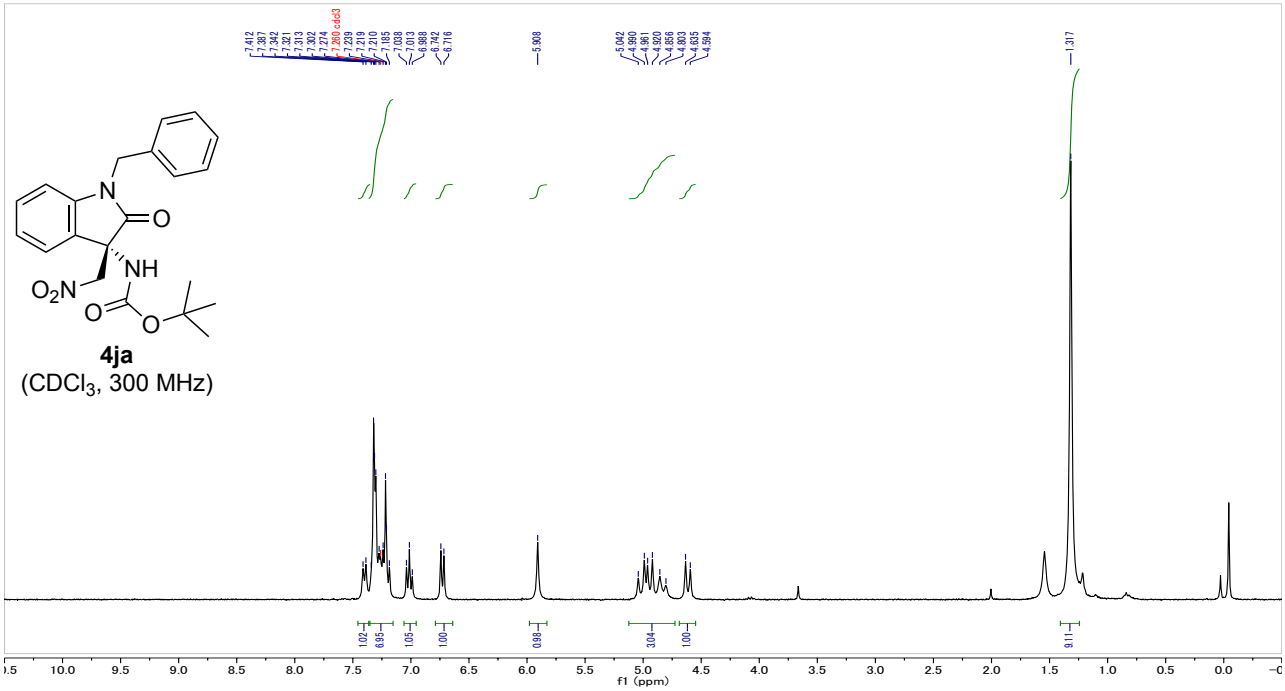
^{1}H NMR of *tert*-butyl (*S*)-2-(1-nitropenta-3,4-dien-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4eg**]



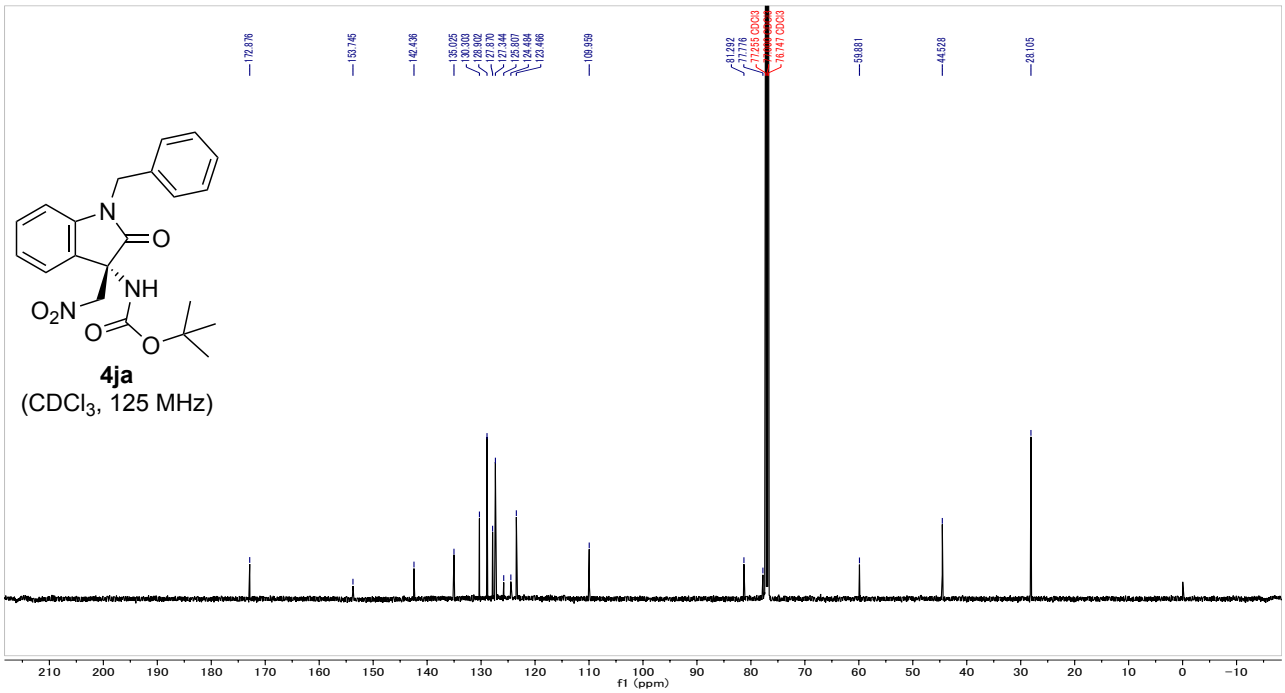
^{13}C NMR of *tert*-butyl (*S*)-2-(1-nitropenta-3,4-dien-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4eg**]



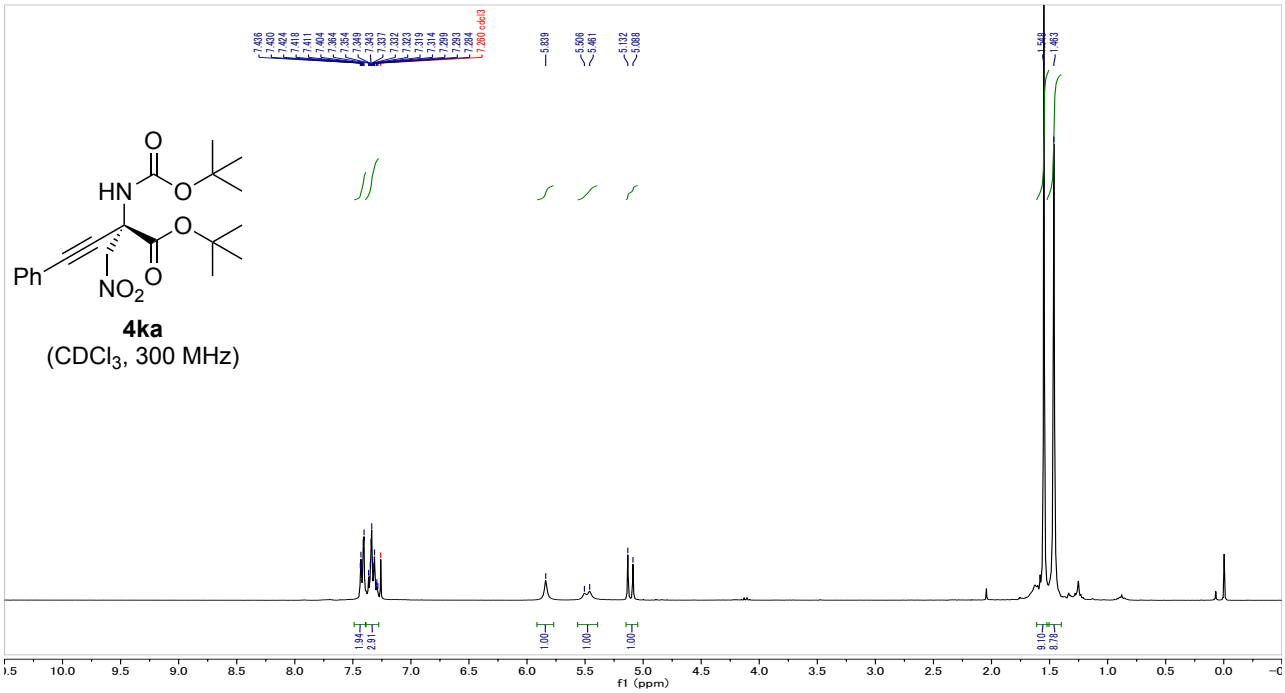
^{1}H NMR of *tert*-butyl (*S*)-1-benzyl-3-(nitromethyl)-2-oxoindolin-3-yl]carbamate [(*S*)-**4ja**]



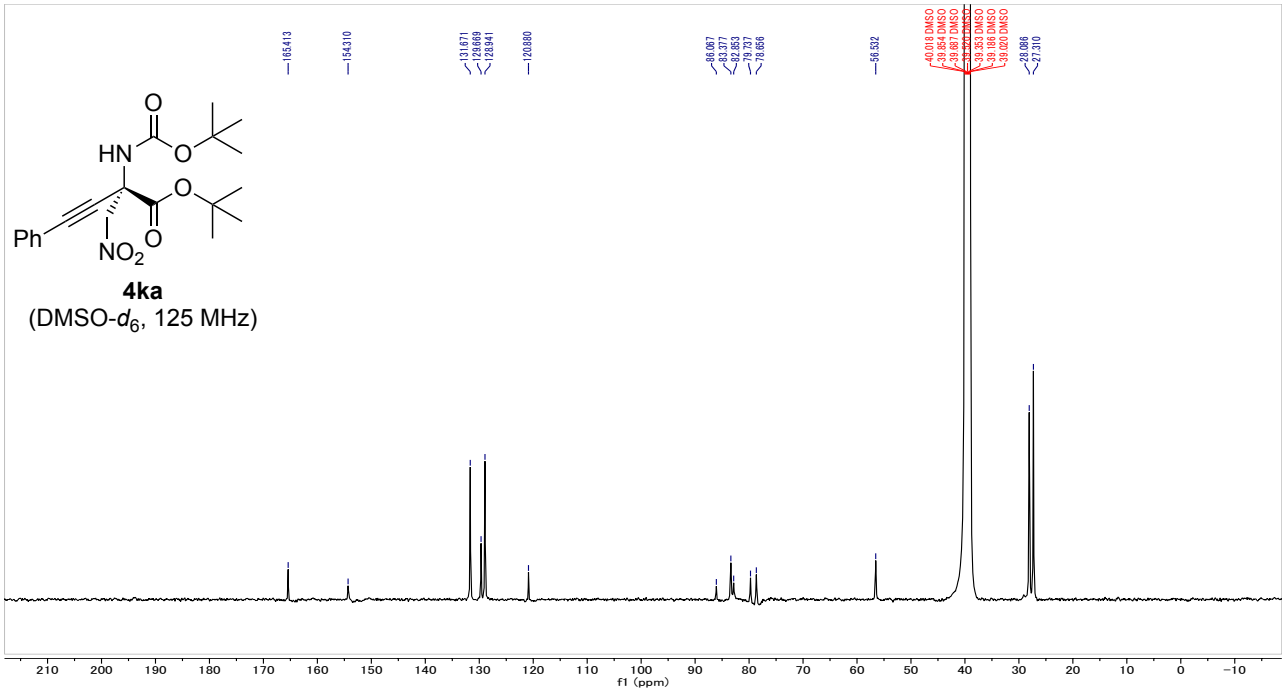
^{13}C NMR of *tert*-butyl (*S*)-1-benzyl-3-(nitromethyl)-2-oxoindolin-3-yl]carbamate [(*S*)-**4ja**]



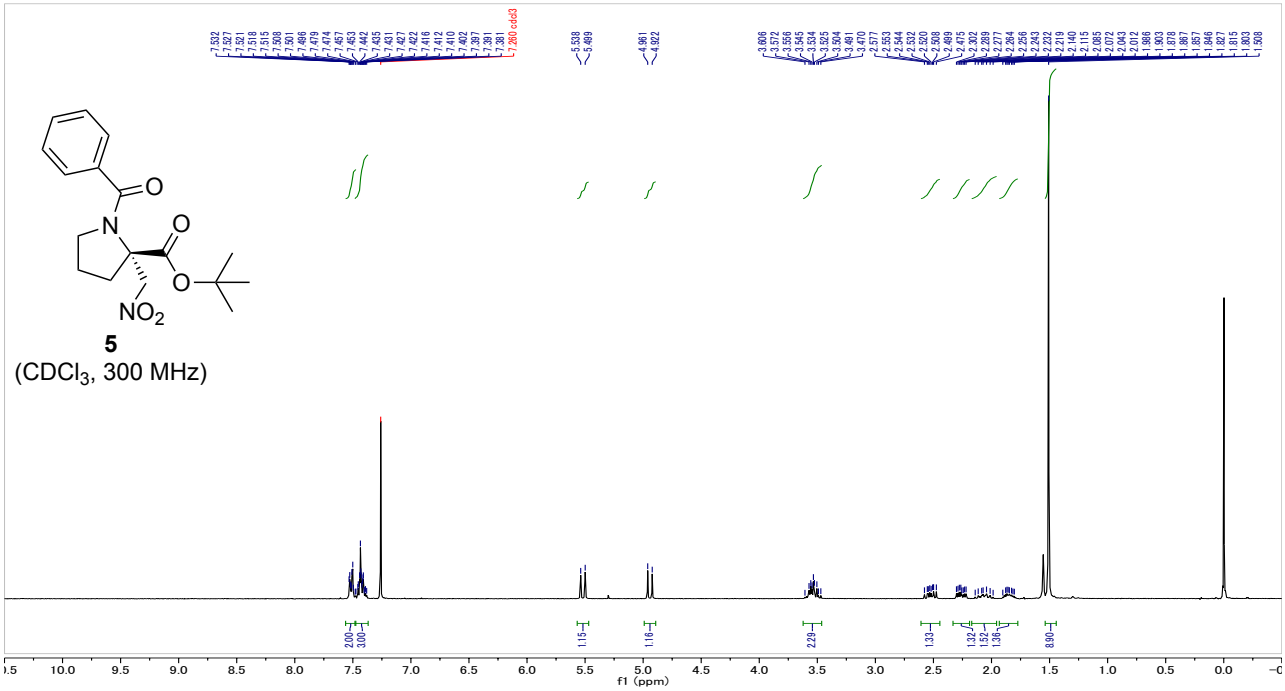
^{1}H NMR of *tert*-butyl (*S*)-2-[(*tert*-butoxycarbonyl)amino]-2-(nitromethyl)-4-phenylbut-3-ynoate [(*S*)-**4ka**]



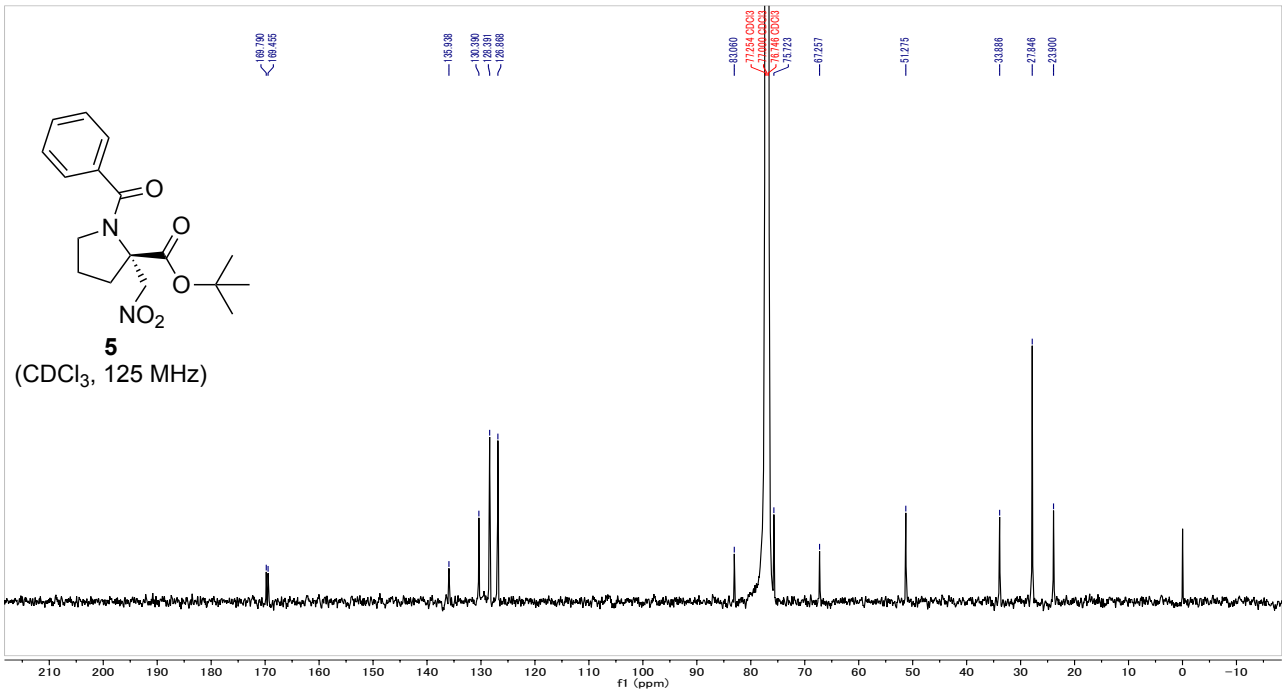
^{13}C NMR of *tert*-butyl (*S*)-2-[(*tert*-butoxycarbonyl)amino]-2-(nitromethyl)-4-phenylbut-3-ynoate [(*S*)-**4ka**]



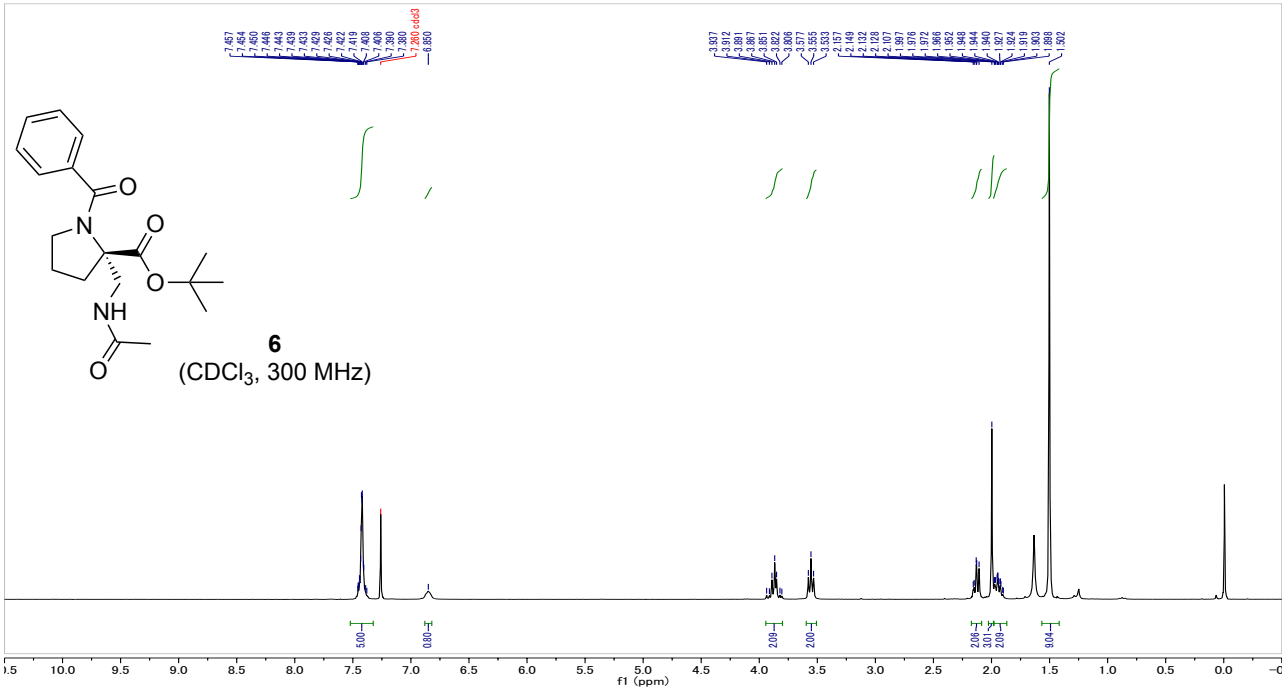
^{1}H NMR of *tert*-butyl (*S*)-1-benzoyl-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**5**]



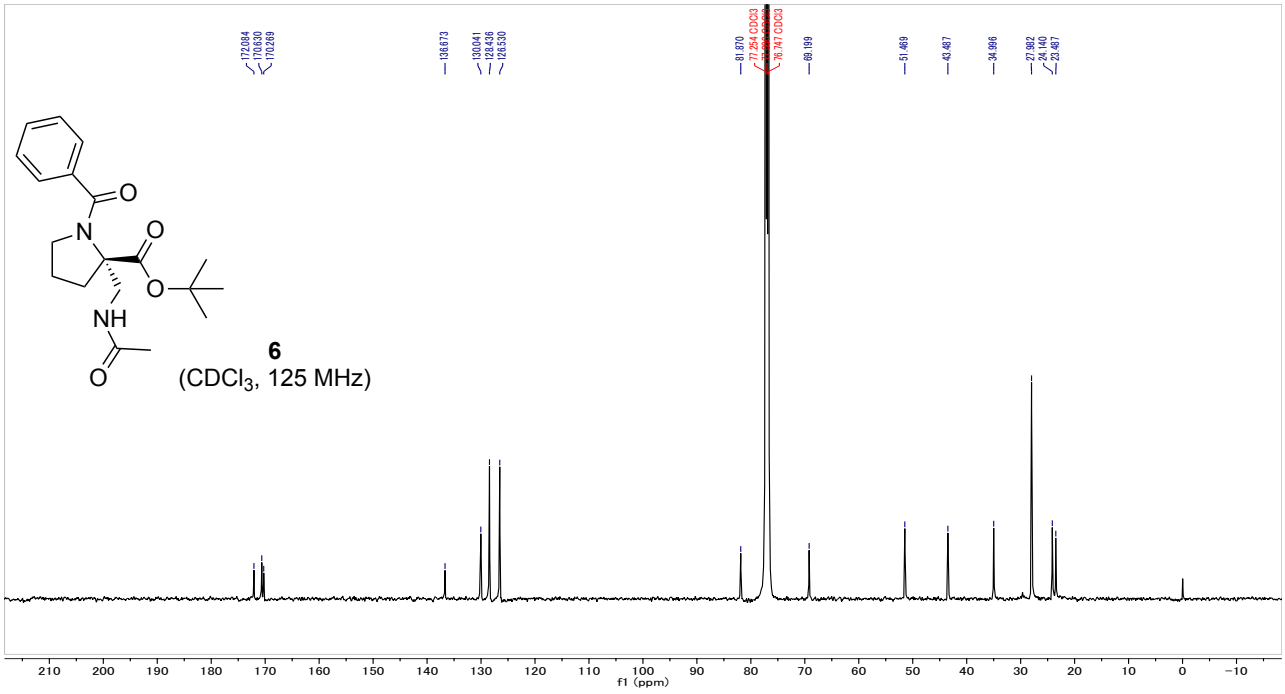
^{13}C NMR of *tert*-butyl (*S*)-1-benzoyl-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**5**]



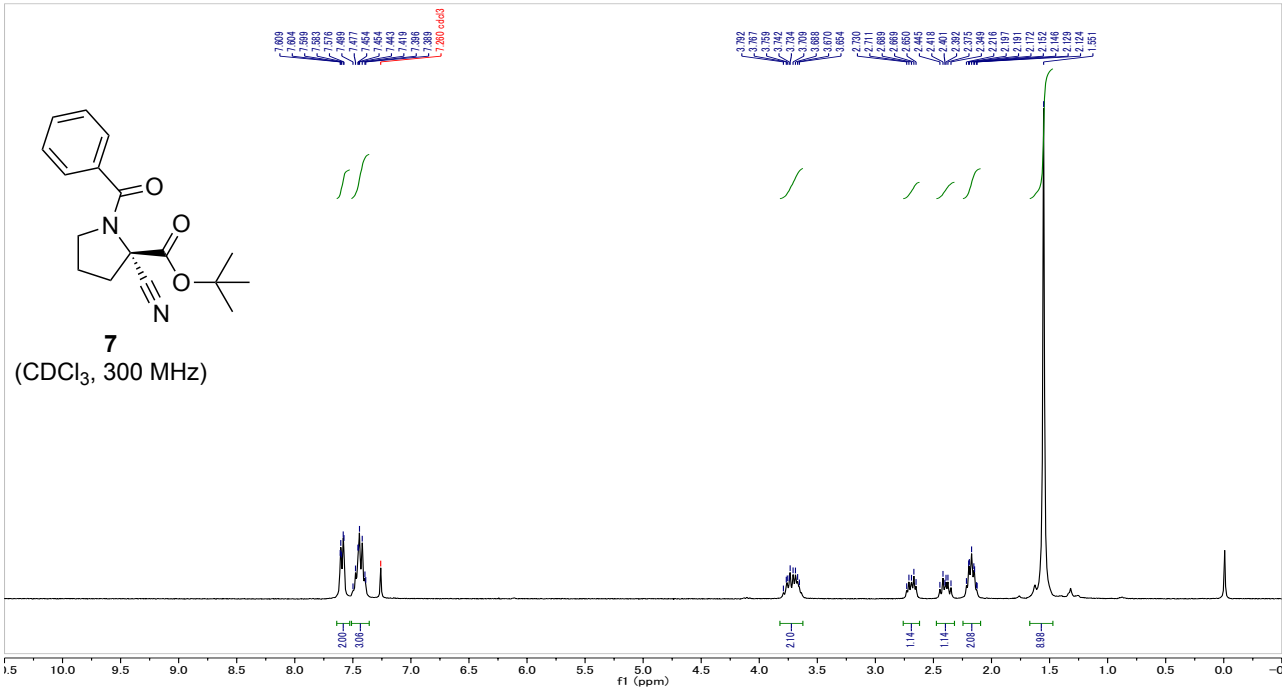
^{1}H NMR of *tert*-butyl (*S*)-2-(acetamidomethyl)-1-benzoylpyrrolidine-2-carboxylate [(*S*)-**6**]



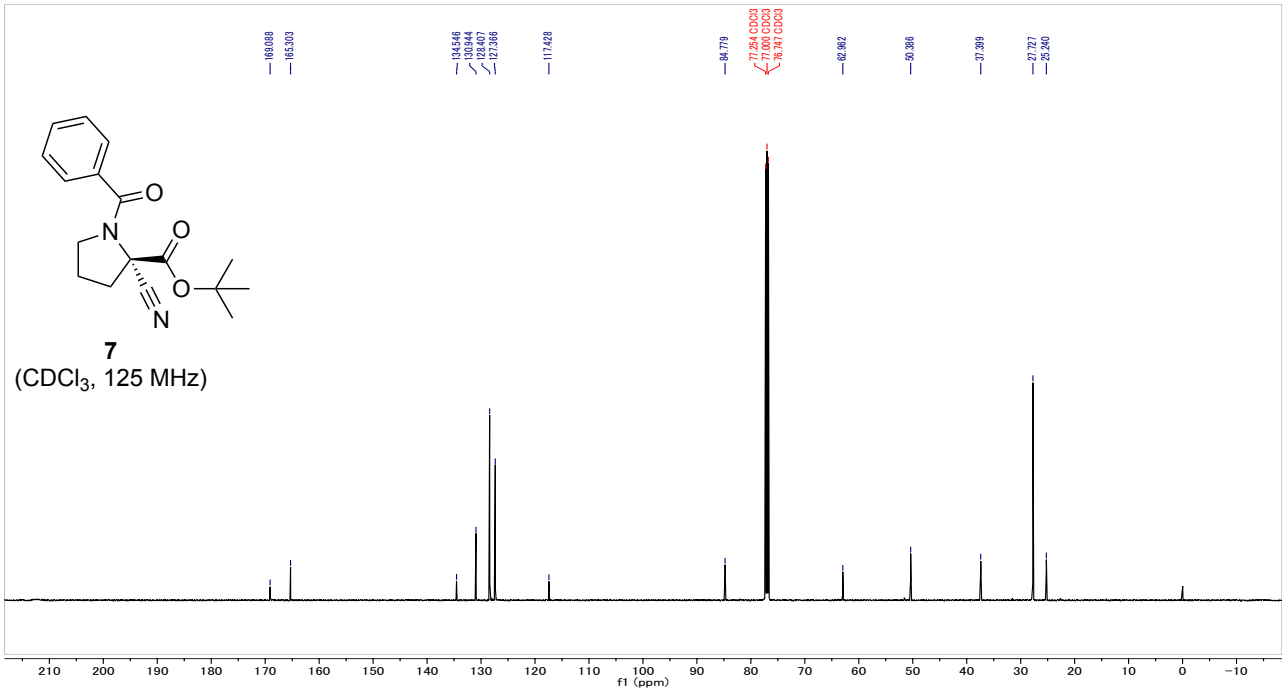
^{13}C NMR of *tert*-butyl (*S*)-2-(acetamidomethyl)-1-benzoylpyrrolidine-2-carboxylate [(*S*)-**6**]



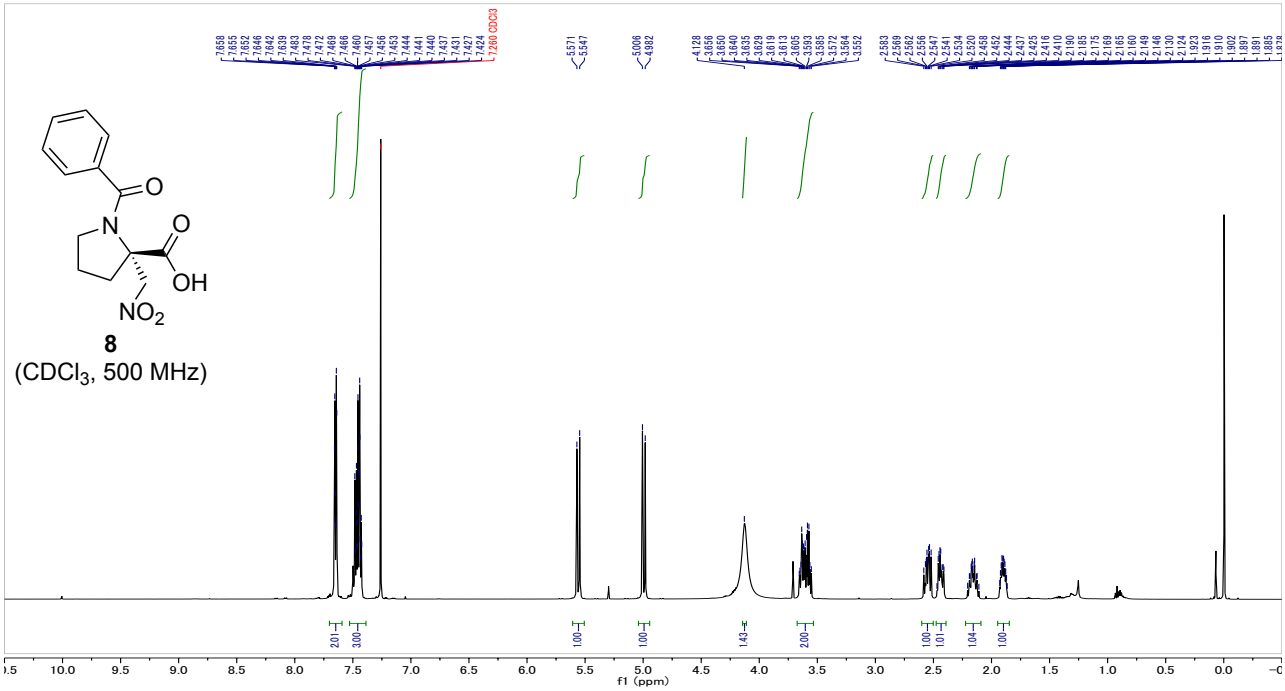
^{1}H NMR of *tert*-butyl (*S*)-1-benzoyl-2-cyanopyrrolidine 2-carboxylate [(*S*)-**7**]



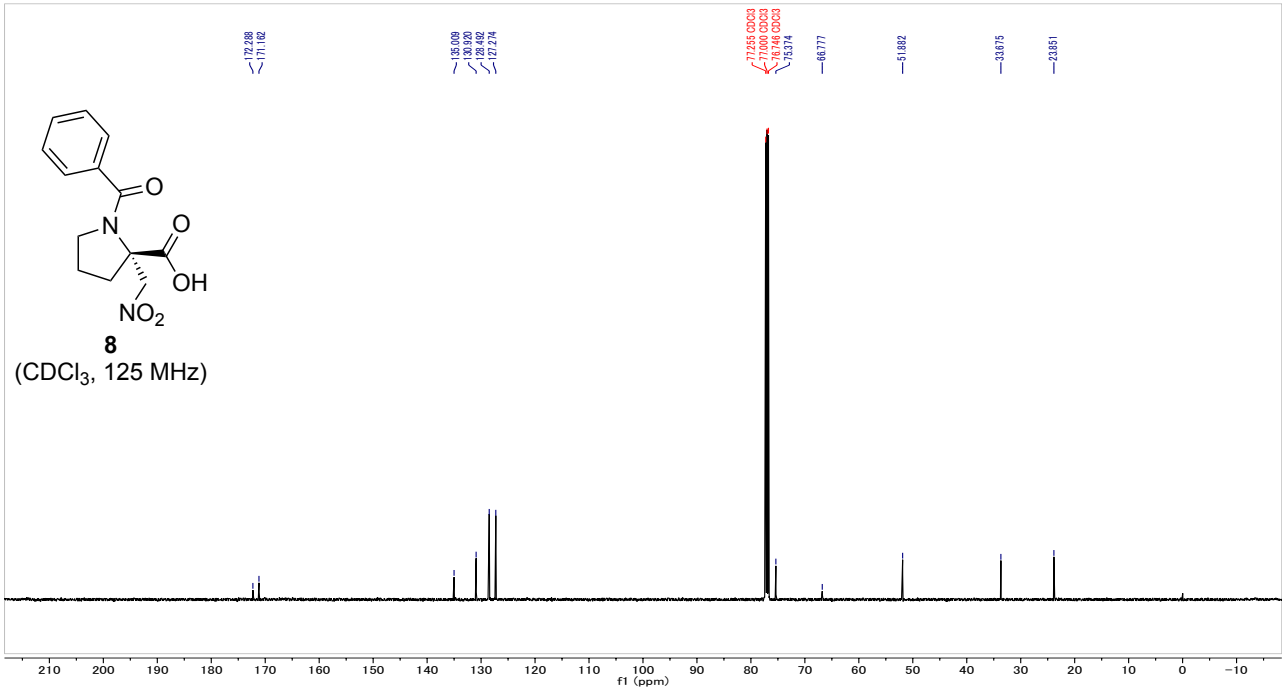
^{13}C NMR of *tert*-butyl (*S*)-1-benzoyl-2-cyanopyrrolidine 2-carboxylate [(*S*)-**7**]



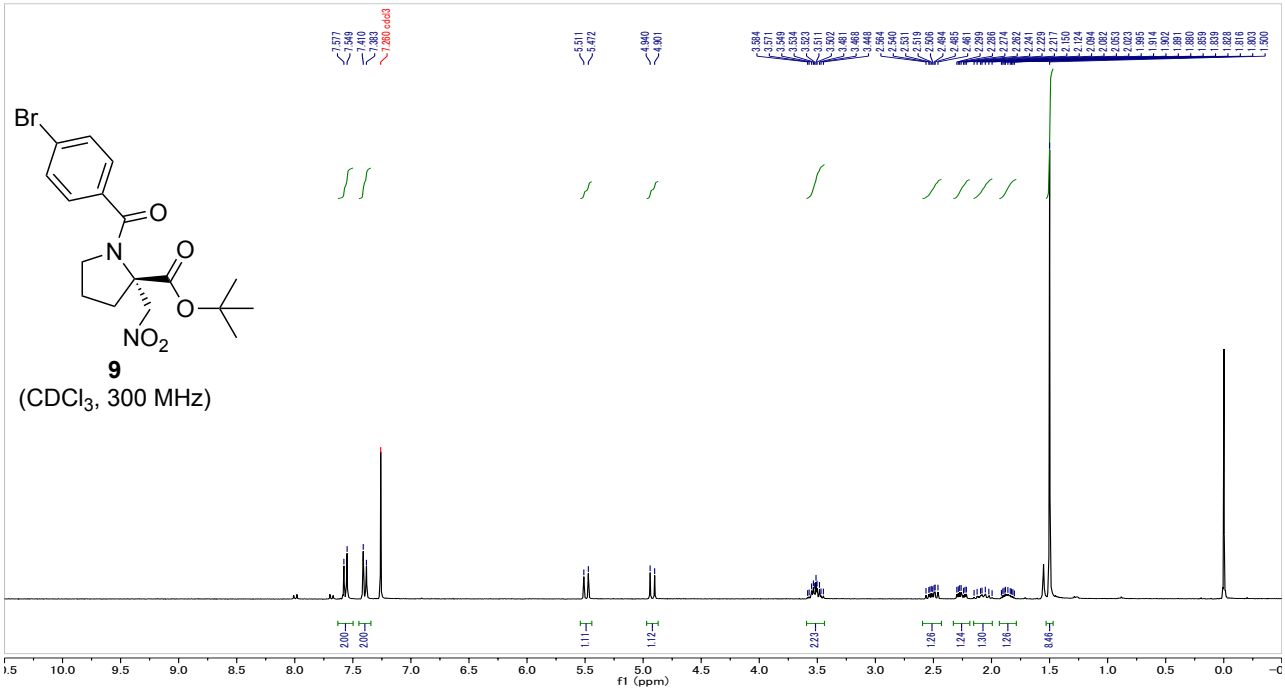
^{1}H NMR of 1-benzoyl-2-(nitromethyl)pyrrolidine-2-carboxylic acid [(*S*)-**8**]



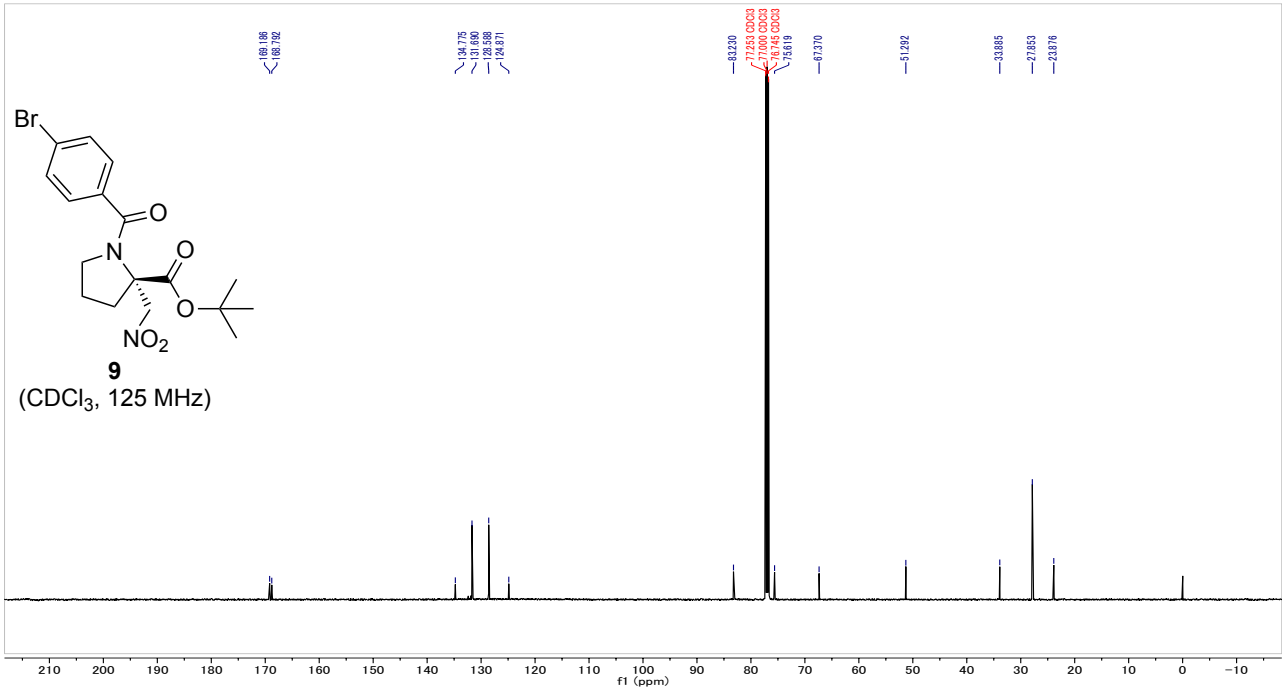
^{13}C NMR of 1-benzoyl-2-(nitromethyl)pyrrolidine-2-carboxylic acid [(*S*)-**8**]



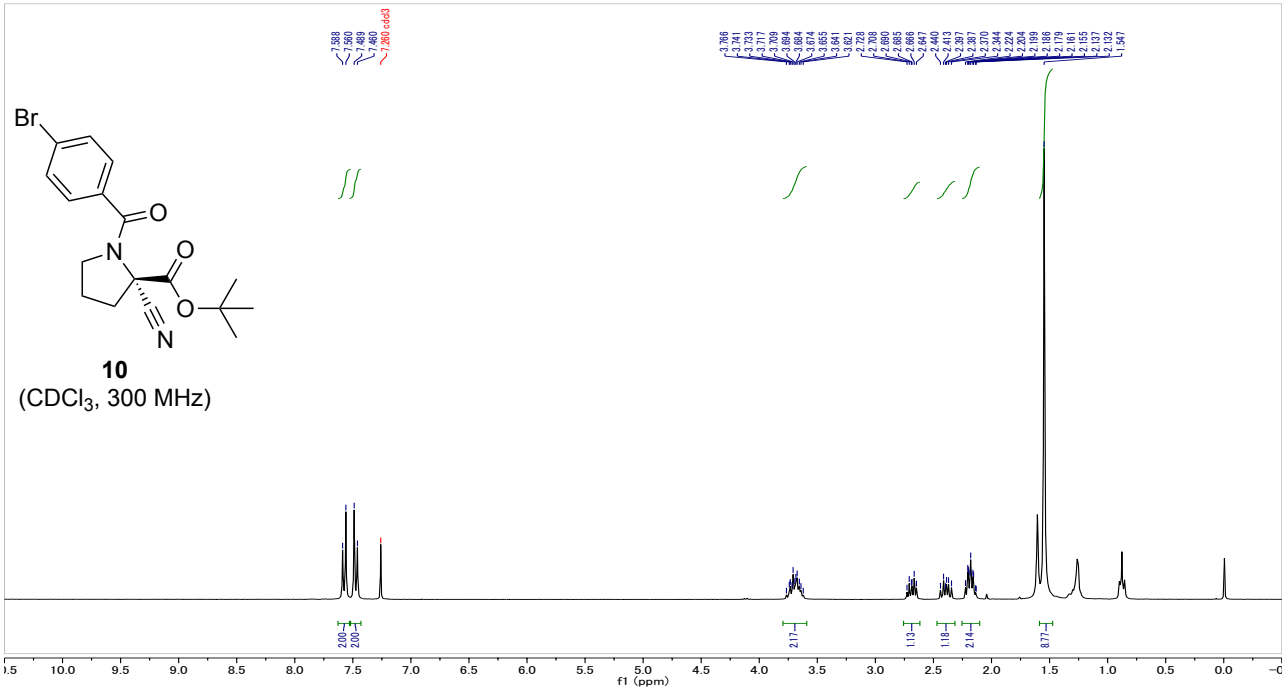
^{1}H NMR of *tert*-butyl (*S*)-1-(4-bromobenzoyl)-2-(nitromethyl)pyrrolidine-2-carboxylate [(*S*)-**9**]



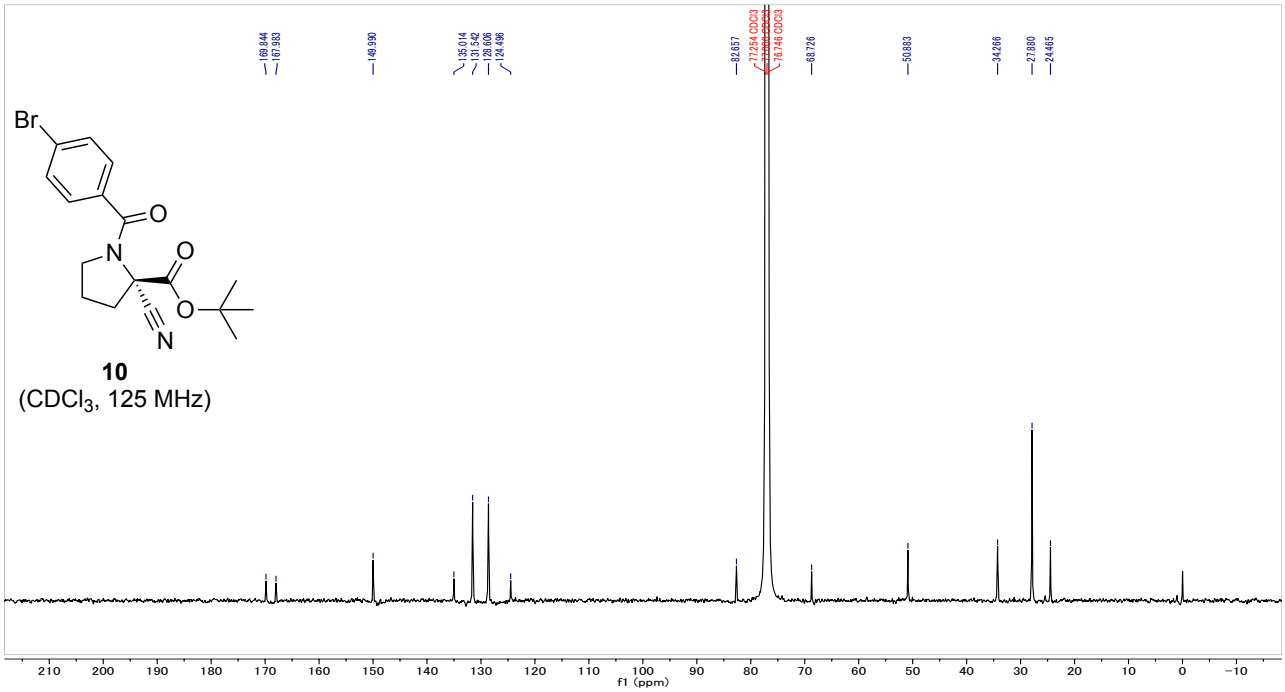
^{13}C NMR of *tert*-butyl (*S*)-1-(4-bromobenzoyl)-2-(nitromethyl)pyrrolidine-2-carboxylate [(*S*)-**9**]



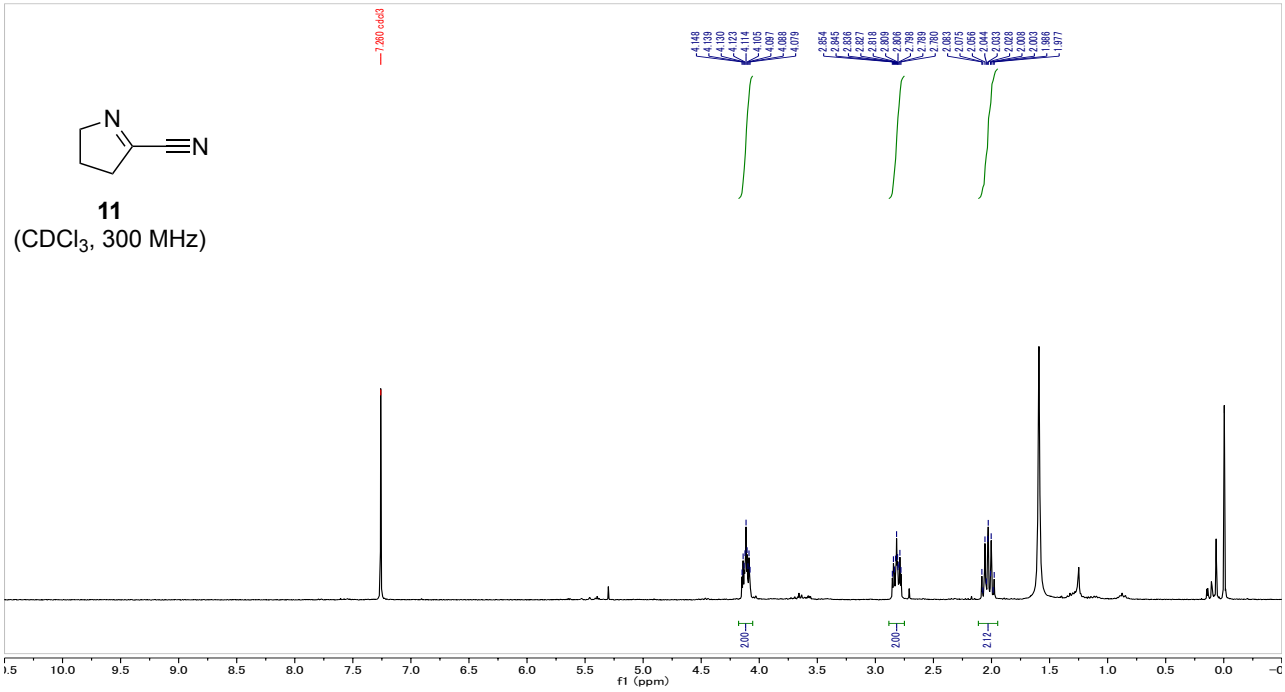
^{1}H NMR of *tert*-butyl (*S*)-1-(4-bromobenzoyl)-2-cyanopyrrolidine-2-carboxylate [(*S*)-**10**]



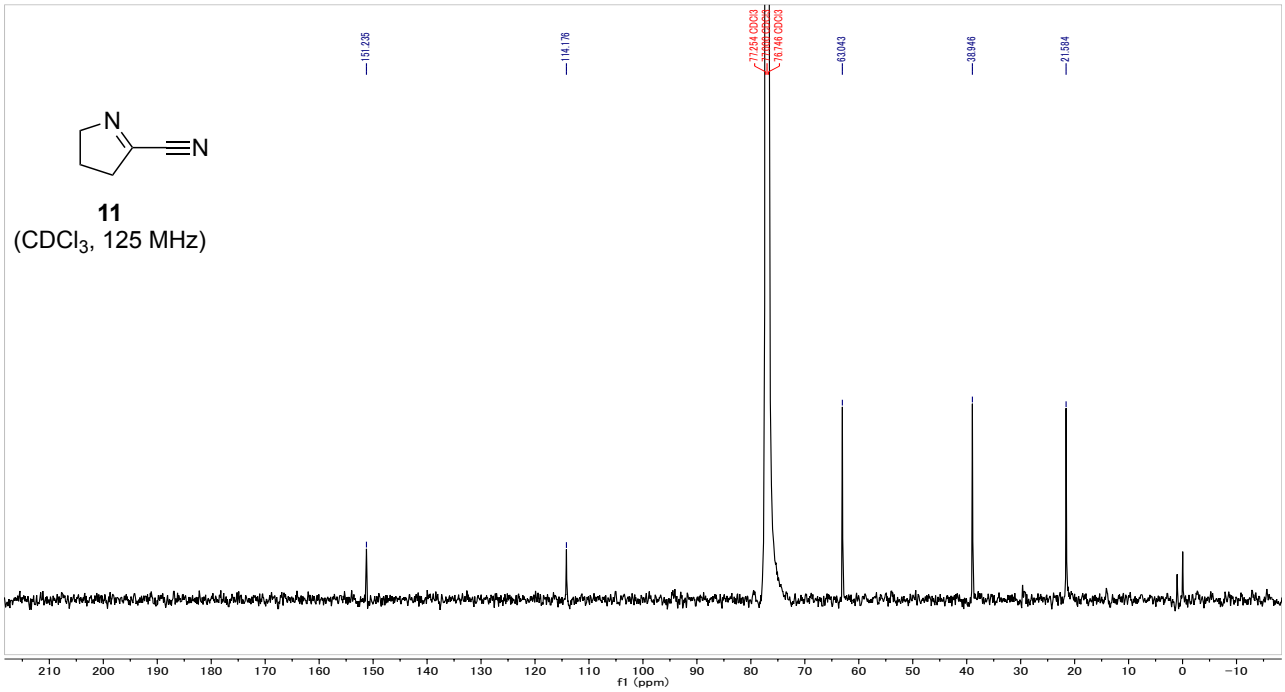
^{13}C NMR of *tert*-butyl (*S*)-1-(4-bromobenzoyl)-2-cyanopyrrolidine-2-carboxylate [(*S*)-**10**]



^{1}H NMR of 2-cyano-1-pyrroline (**11**)

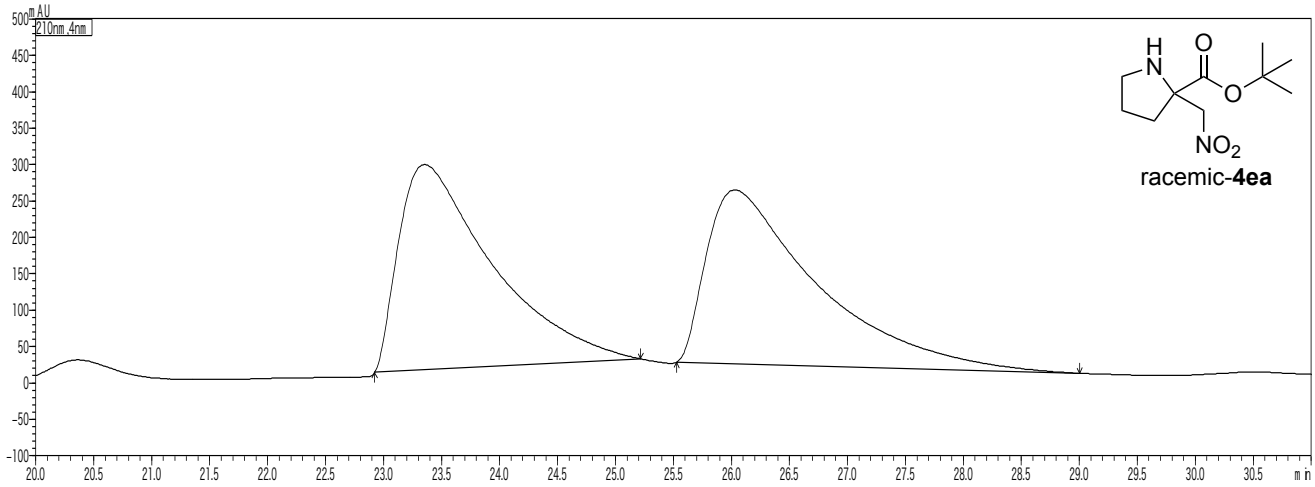


^{13}C NMR of 2-cyano-1-pyrroline (**11**)

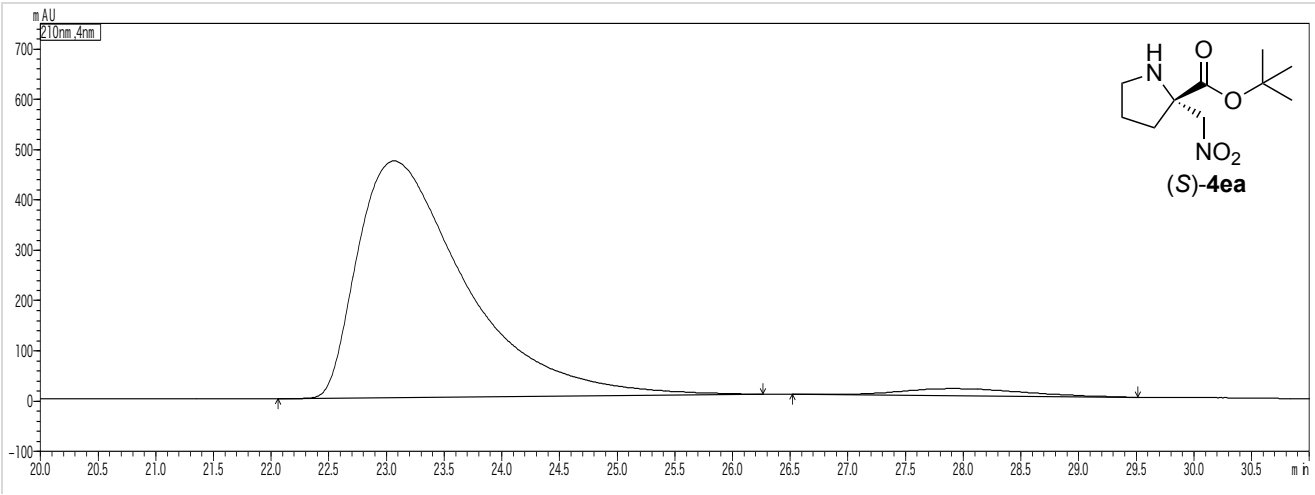


11. HPLC Charts:

HPLC of *tert*-butyl 2-(nitromethyl)pyrrolidine 2-carboxylate [racemic-**4ea**]



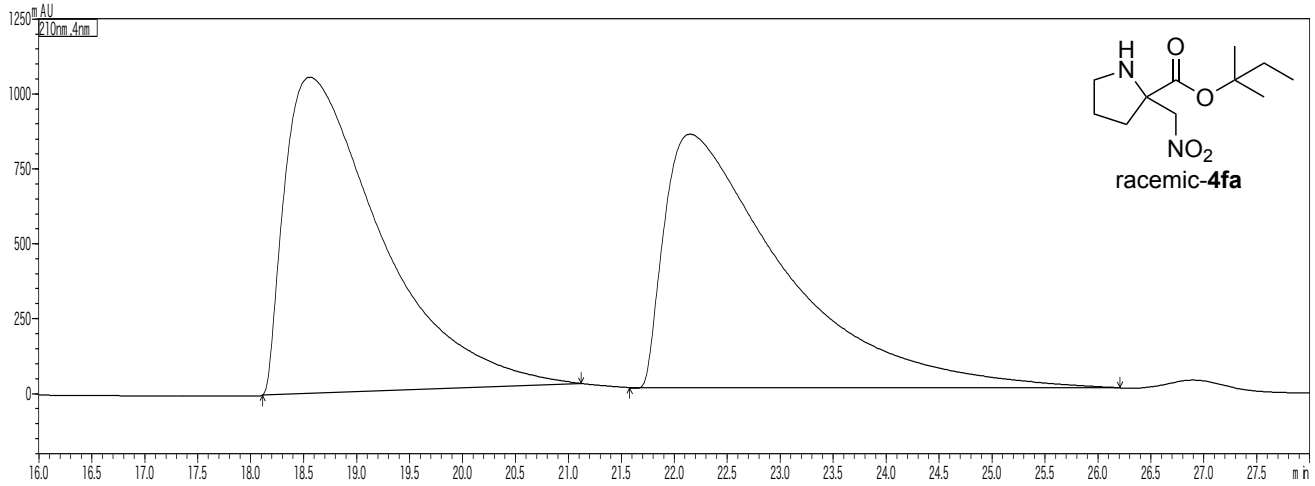
HPLC of *tert*-butyl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**4ea**]



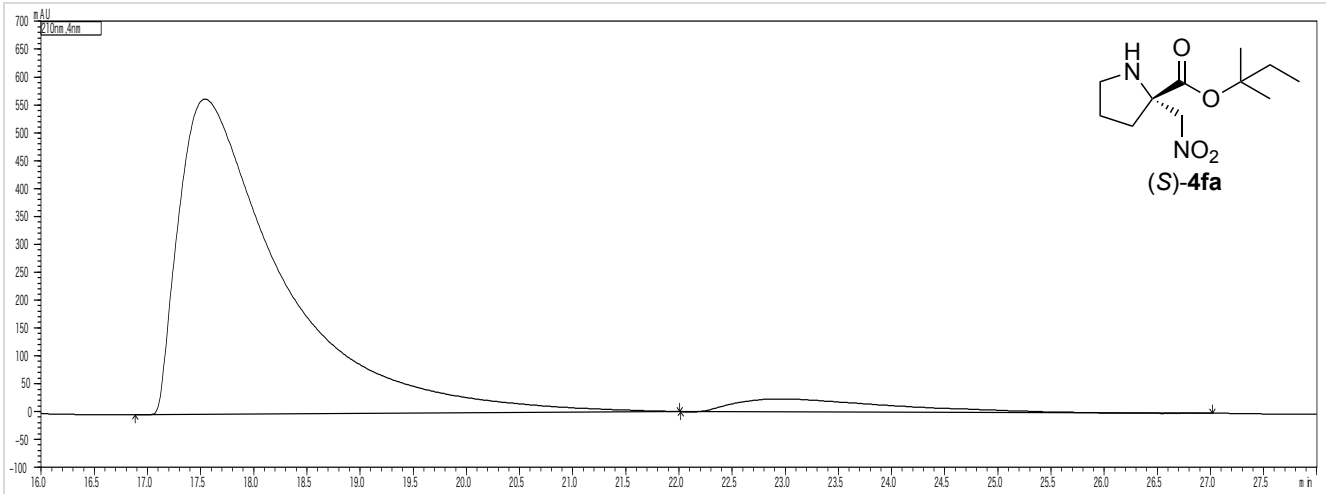
racemic-**4ea**		
Peak	tR (min)	Area (%)
1	23.4	50.2
2	26.0	49.8

(*S*)-**4ea**		
Peak	tR (min)	Area (%)
1	23.1	97.0
2	27.9	3.0

HPLC of *tert*-pentyl 2-(nitromethyl)pyrrolidine 2-carboxylate [racemic-**4fa**]



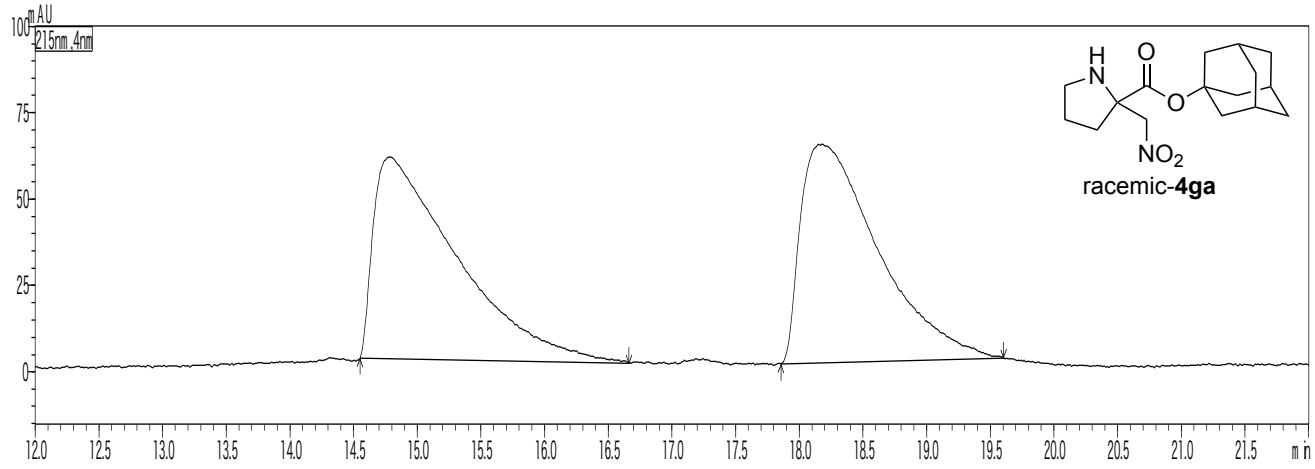
HPLC of pentyl-1-yl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**4fa**]



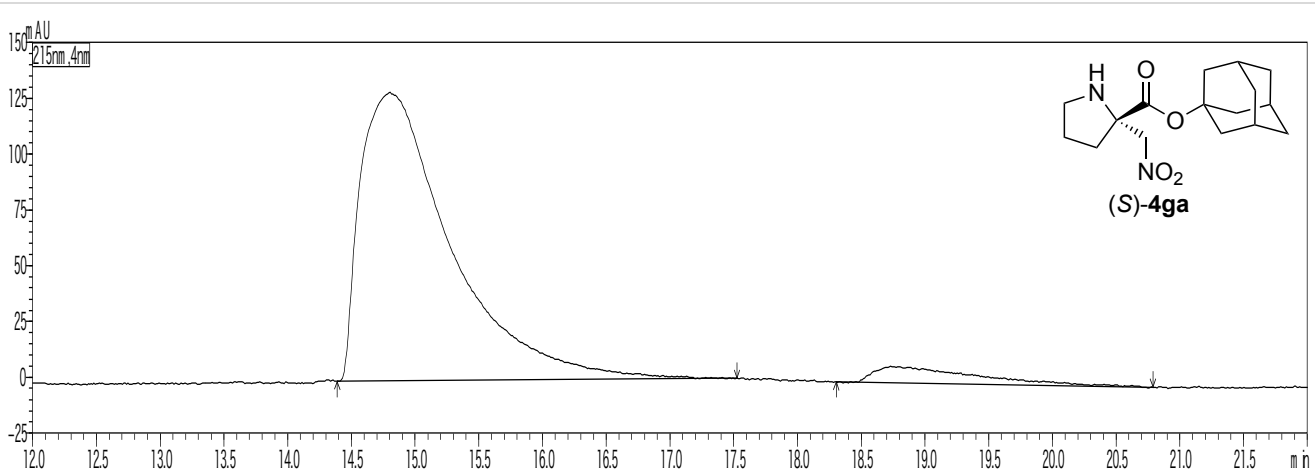
racemic-**4fa**		
Peak	tR (min)	Area (%)
1	18.6	50.2
2	22.1	49.8

(*S*)-**4fa**		
Peak	tR (min)	Area (%)
1	17.5	94.1
2	23.0	5.9

HPLC of adamanta-1-yl 2-(nitromethyl)pyrrolidine 2-carboxylate [racemic-**4ga**]



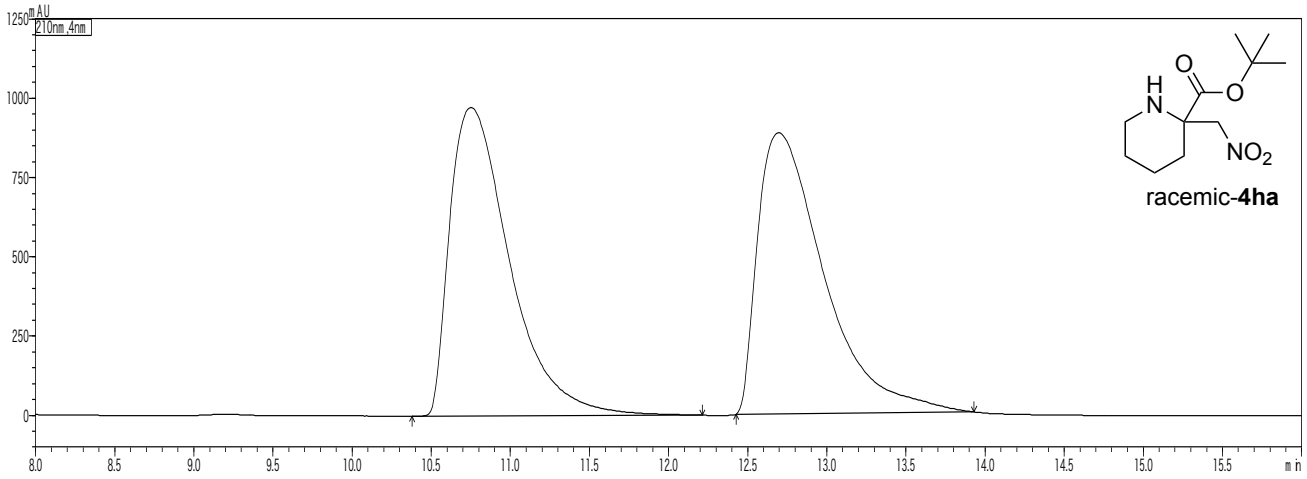
HPLC of adamanta-1-yl (*S*)-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**4ga**]



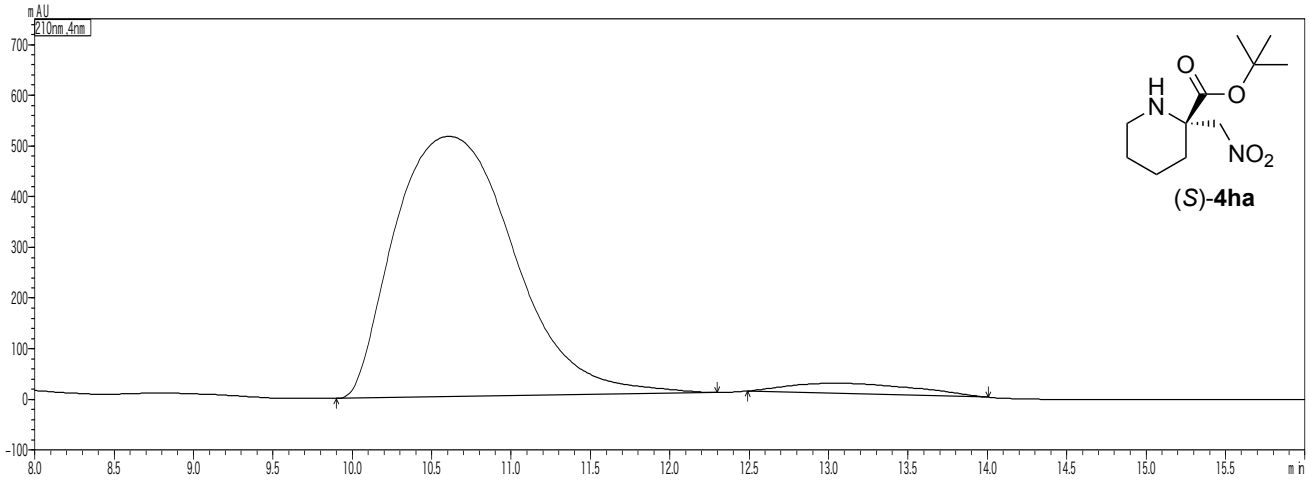
racemic-**4ga**		
Peak	tR (min)	Area (%)
1	14.8	50.0
2	18.2	50.0

(*S*)-**4ga**		
Peak	tR (min)	Area (%)
1	14.8	94.0
2	18.7	6.0

HPLC of *tert*-butyl 2-(nitromethyl)piperidine 2-carboxylate [racemic-**4ha**]



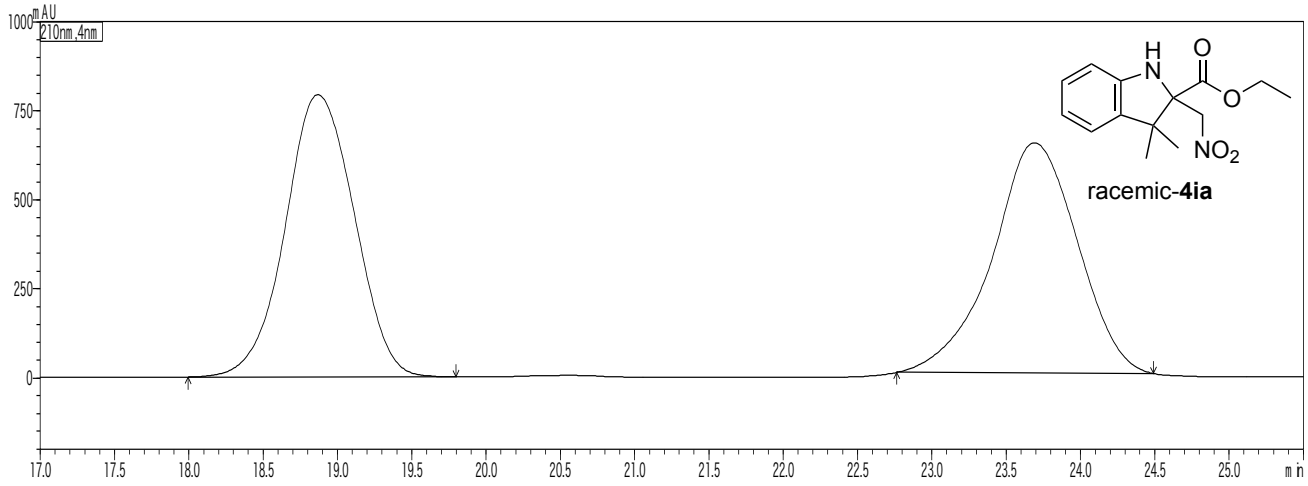
HPLC of *tert*-butyl (*S*)-2-(nitromethyl)piperidine 2-carboxylate [(*S*)-**4ha**]



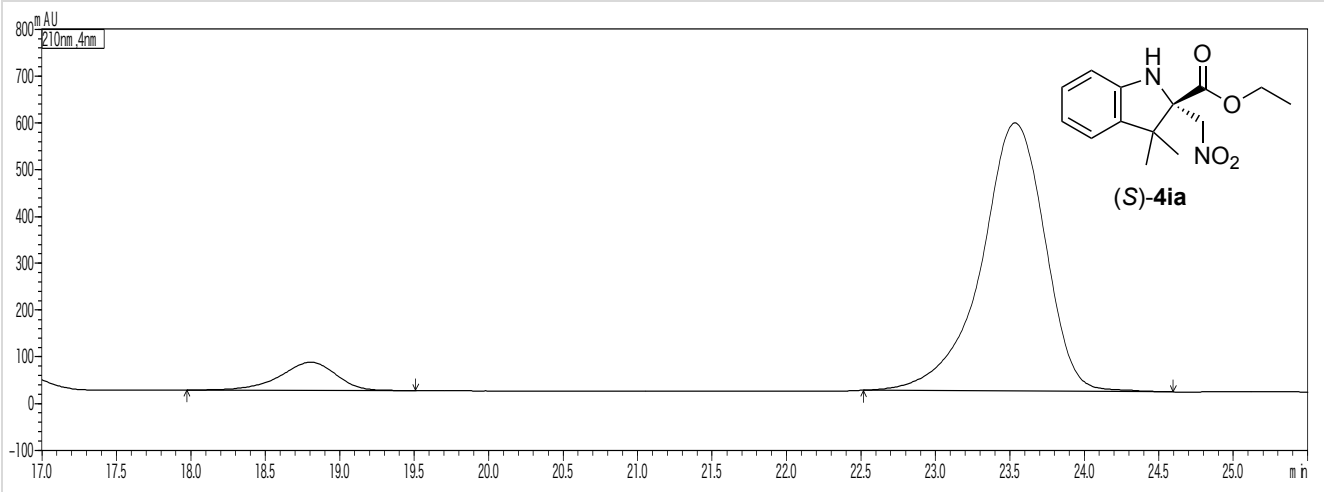
racemic-**4ha**		
Peak	tR (min)	Area (%)
1	10.8	49.8
2	12.7	50.2

(*S*)-**4ha**		
Peak	tR (min)	Area (%)
1	10.6	96.0
2	13.1	4.0

HPLC of ethyl 3,3-dimethyl-2-(nitromethyl)indoline-2-carboxylate [racemic-**4ia**]



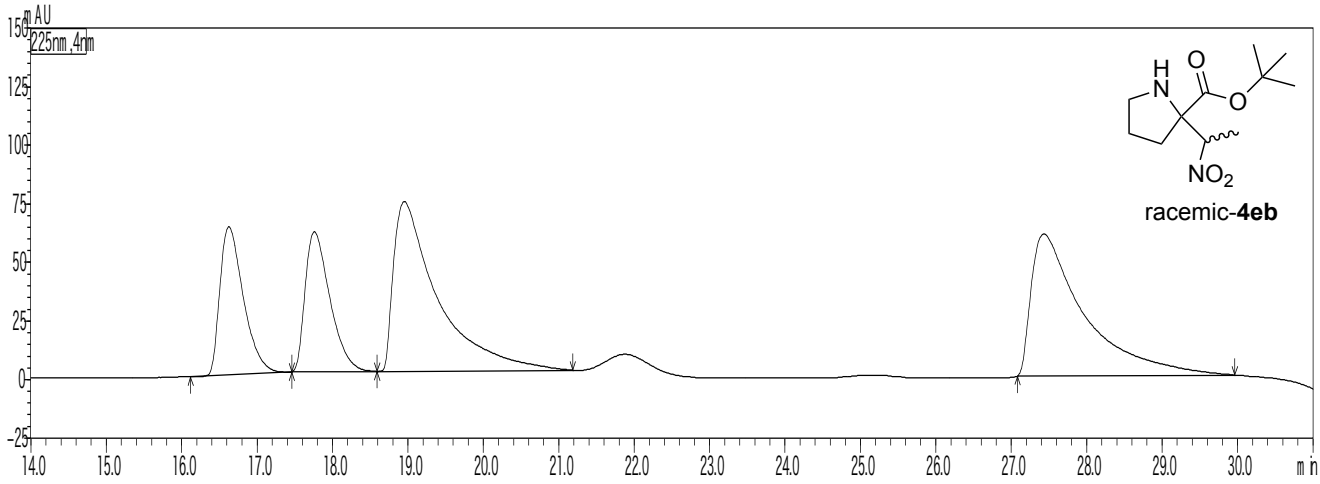
HPLC of ethyl (*S*)-3,3-dimethyl-2-(nitromethyl)indoline-2-carboxylate [(*S*)-**4ia**]



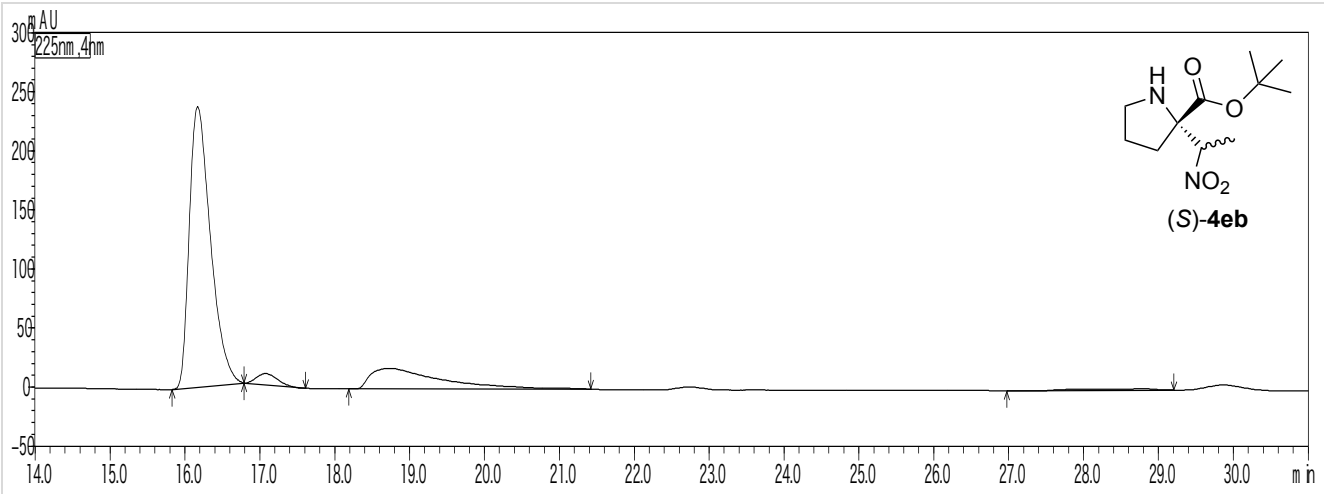
racemic-**4ia**		
Peak	tR (min)	Area (%)
1	18.9	49.8
2	23.7	50.2

(*S*)-**4ia**		
Peak	tR (min)	Area (%)
1	18.8	8.5
2	23.5	91.5

HPLC of *tert*-butyl 2-(nitroethyl)pyrrolidine 2-carboxylate [racemic-**4eb**]



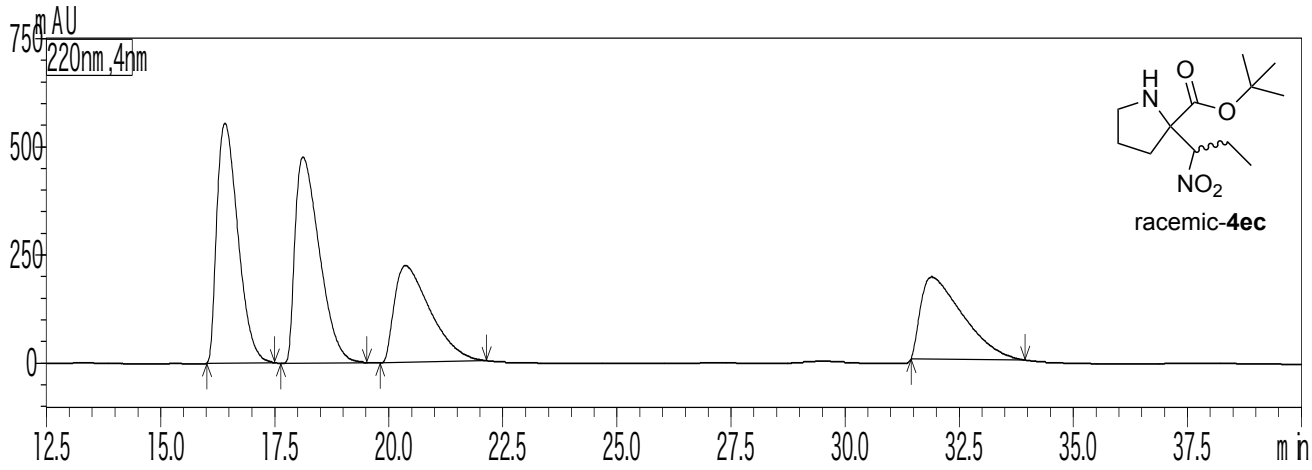
HPLC of *tert*-butyl 2-(nitroethyl)pyrrolidine 2-carboxylate [(*S*)-**4eb**]



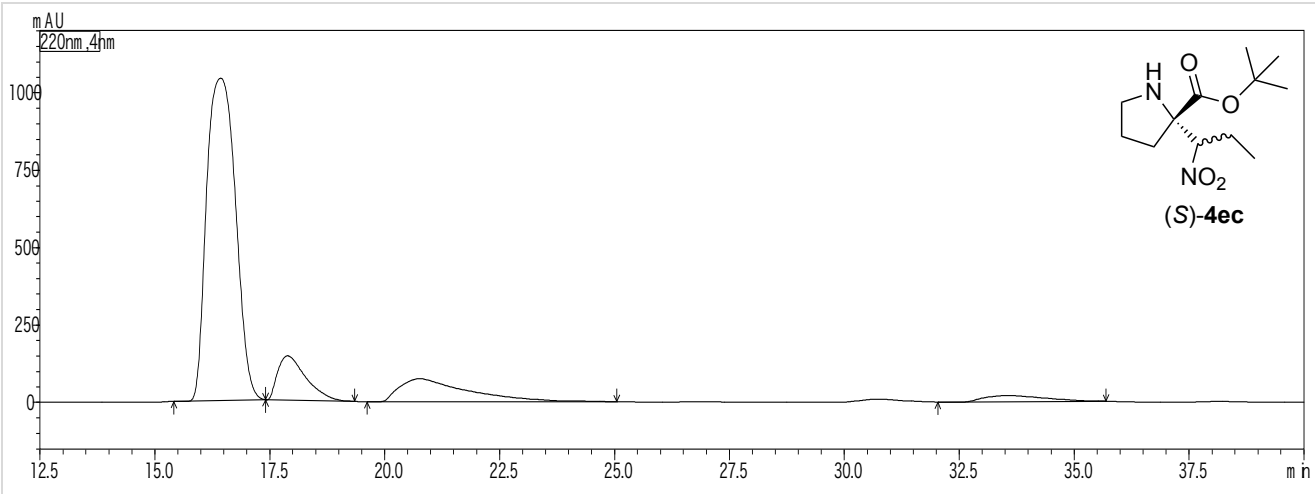
racemic-**4eb**		
Peak	tR (min)	Area (%)
1	16.6	15.8
2	17.8	15.8
3	19.0	34.2
4	27.4	34.3

(*S*)-**4eb**		
Peak	tR (min)	Area (%)
1	16.2	76.1
2	17.0	3.0
3	18.7	19.2
4	28.8	1.6

HPLC of *tert*-butyl 2-(1-nitropropyl)pyrrolidine 2-carboxylate [racemic-**4ec**]



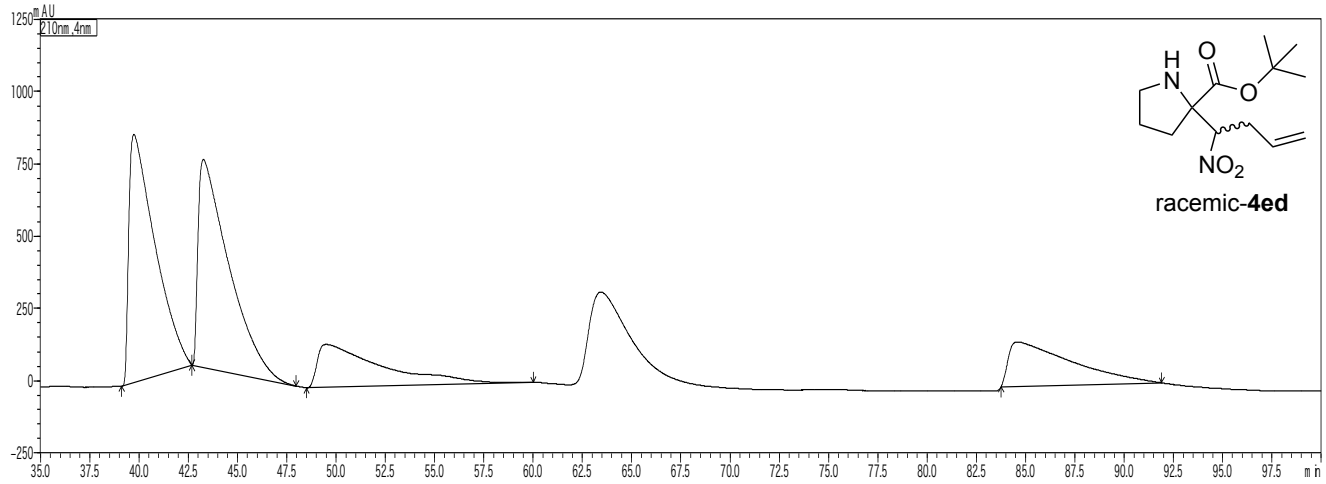
HPLC of *tert*-butyl 2-(1-nitropropyl)pyrrolidine 2-carboxylate [(*S*)-**4ec**]



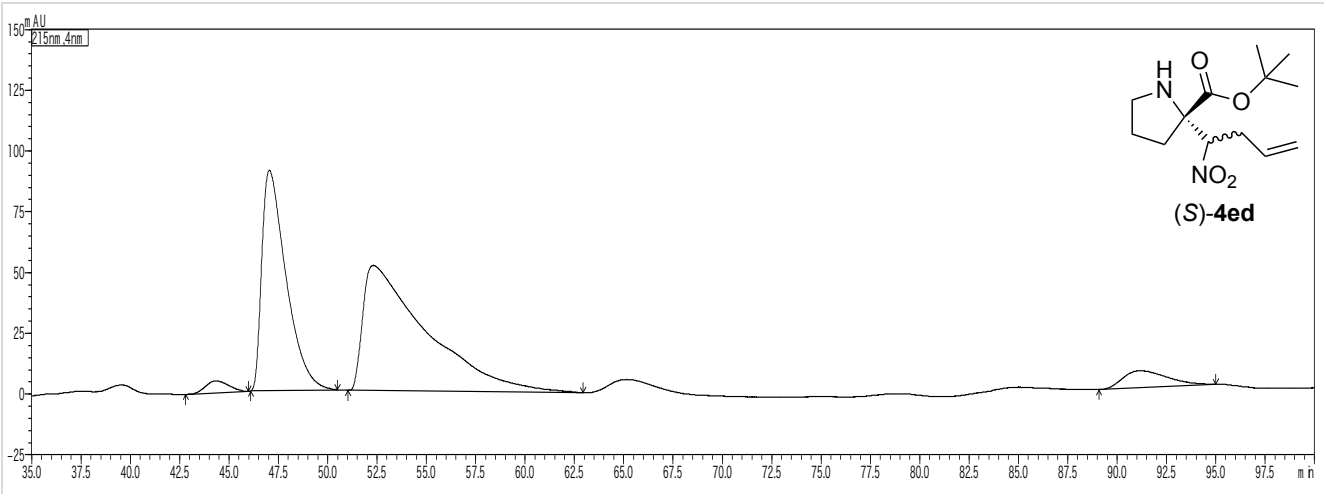
racemic-**4ec**		
Peak	tR (min)	Area (%)
1	16.4	29.6
2	18.1	29.5
3	20.4	20.5
4	31.9	20.4

(*S*)-**4ec**		
Peak	tR (min)	Area (%)
1	16.4	74.5
2	17.9	10.1
3	20.8	12.5
4	33.6	2.9

HPLC of *tert*-butyl 2-(1-nitrobut-3-en-1-yl)pyrrolidine 2-carboxylate [racemic-**4ed**]



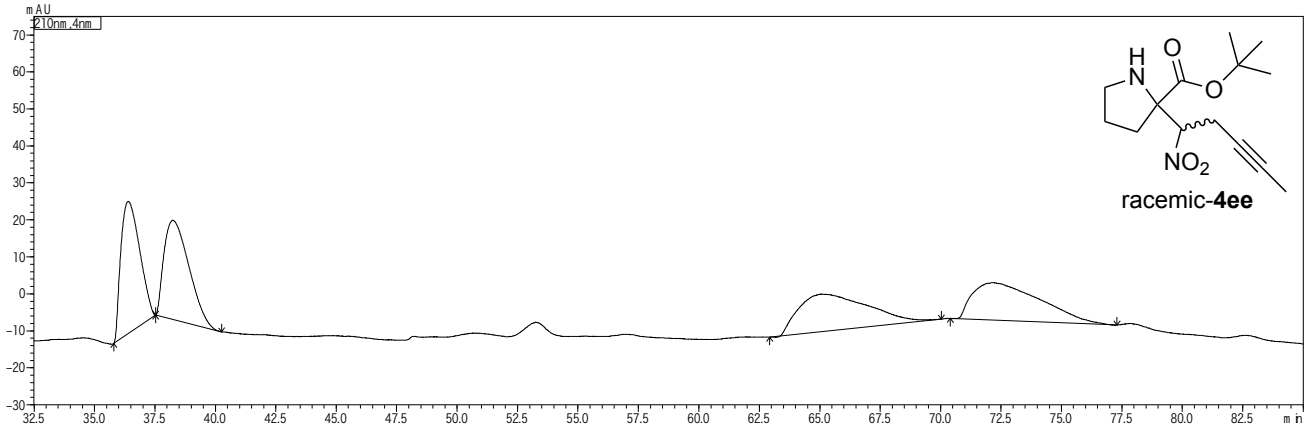
HPLC of *tert*-butyl (*S*)-2-(1-nitrobut-3-en-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4ed**]



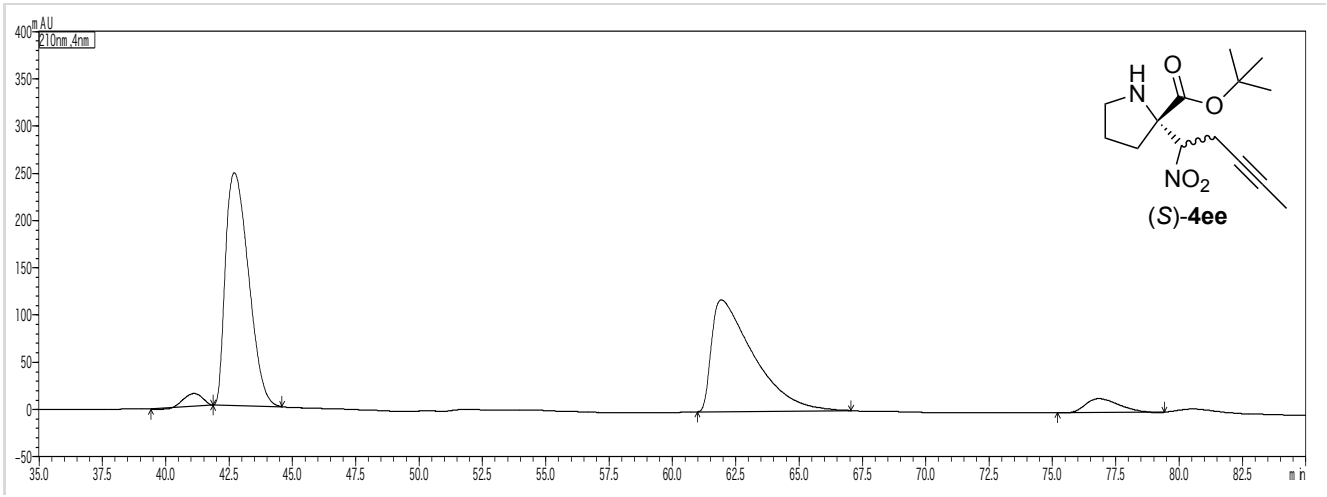
racemic-**4ed**		
Peak	tR (min)	Area (%)
1	39.7	35.1
2	43.3	34.8
3	49.5	15.0
4	84.6	15.1

(*S*)-**4ed**		
Peak	tR (min)	Area (%)
1	44.3	1.9
2	47.0	37.3
3	52.3	55.5
4	91.2	5.3

HPLC of *tert*-butyl 2-(1-nitropent-3-yn-1-yl)pyrrolidine 2-carboxylate [racemic-**4ee**]



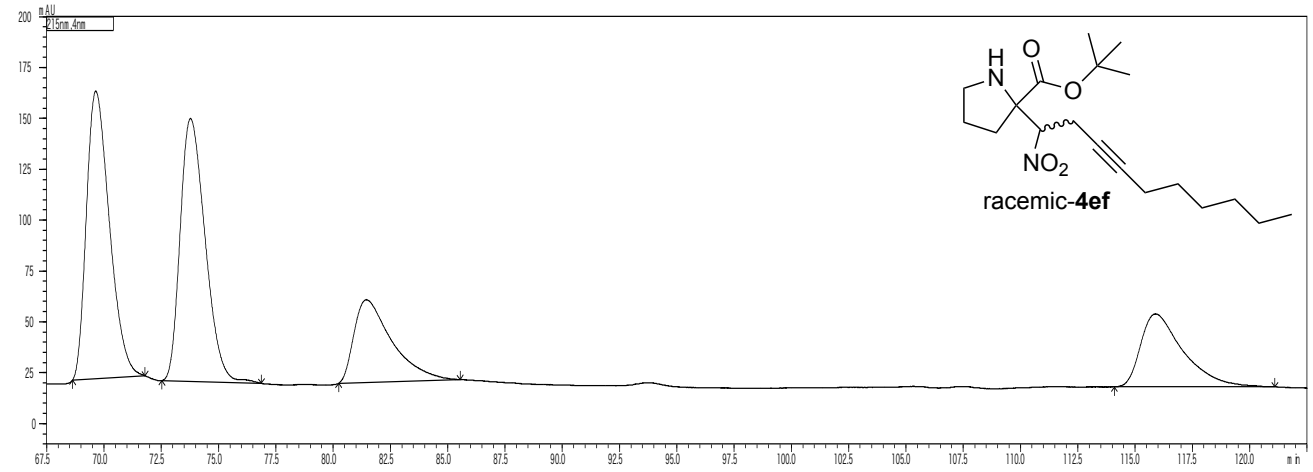
HPLC of *tert*-butyl (*S*)-2-(1-nitropent-3-yn-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4ee**]



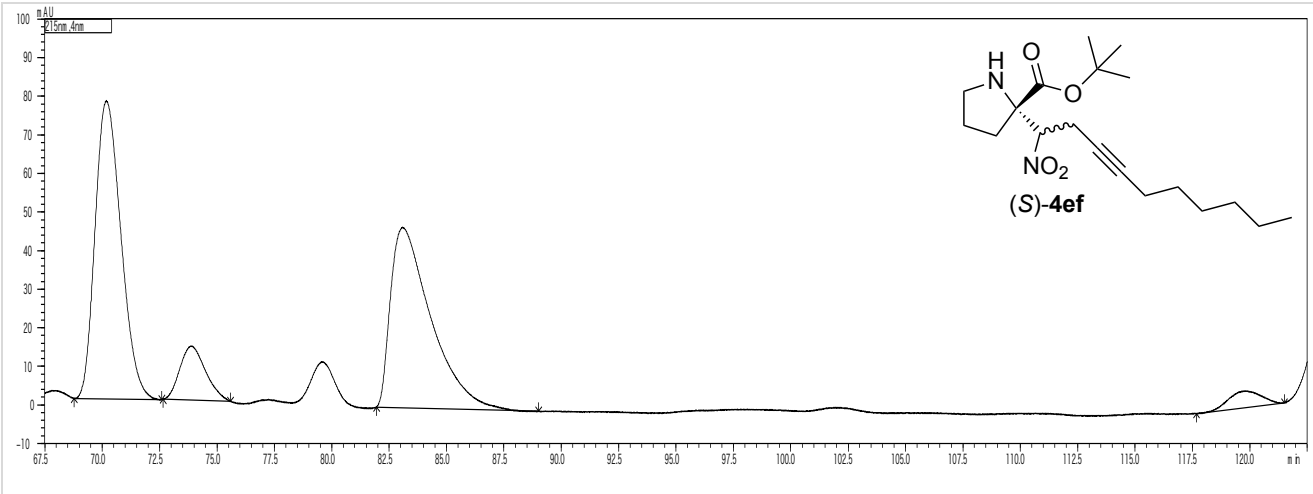
racemic-**4ee**		
Peak	tR (min)	Area (%)
1	36.4	24.7
2	38.2	24.8
3	65.0	25.2
4	72.1	25.3

(*S*)-**4ee**		
Peak	tR (min)	Area (%)
1	41.1	2.2
2	42.7	49.9
3	61.9	43.6
4	76.8	4.3

HPLC of *tert*-butyl 2-(1-nitrodec-3-yn-1-yl)pyrrolidine 2-carboxylate [racemic-**4ef**]



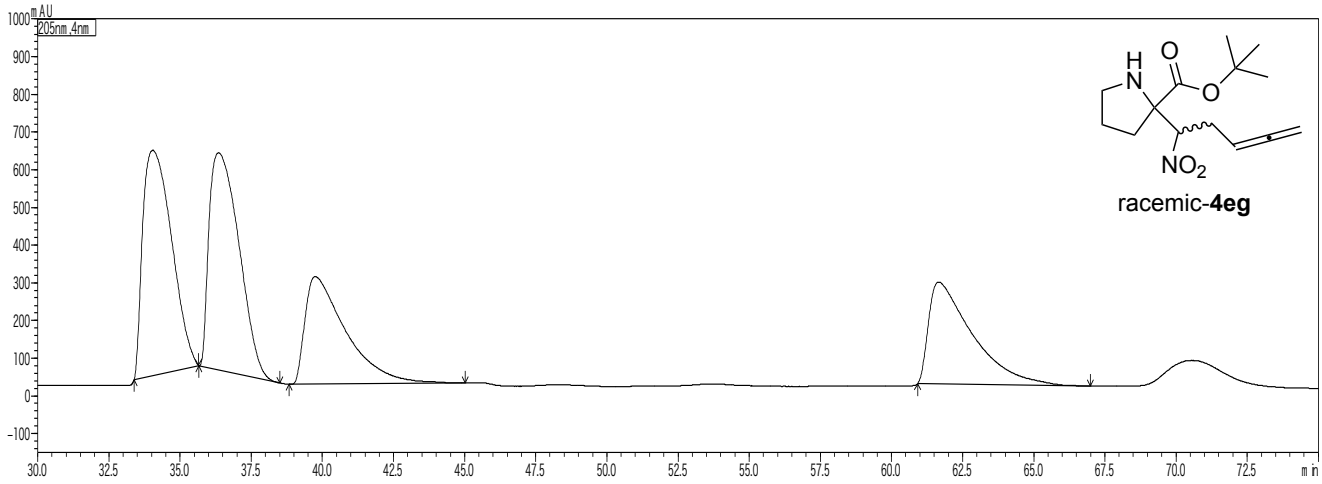
HPLC of *tert*-butyl (*S*)-2-(1-nitrodec-3-yn-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4ef**]



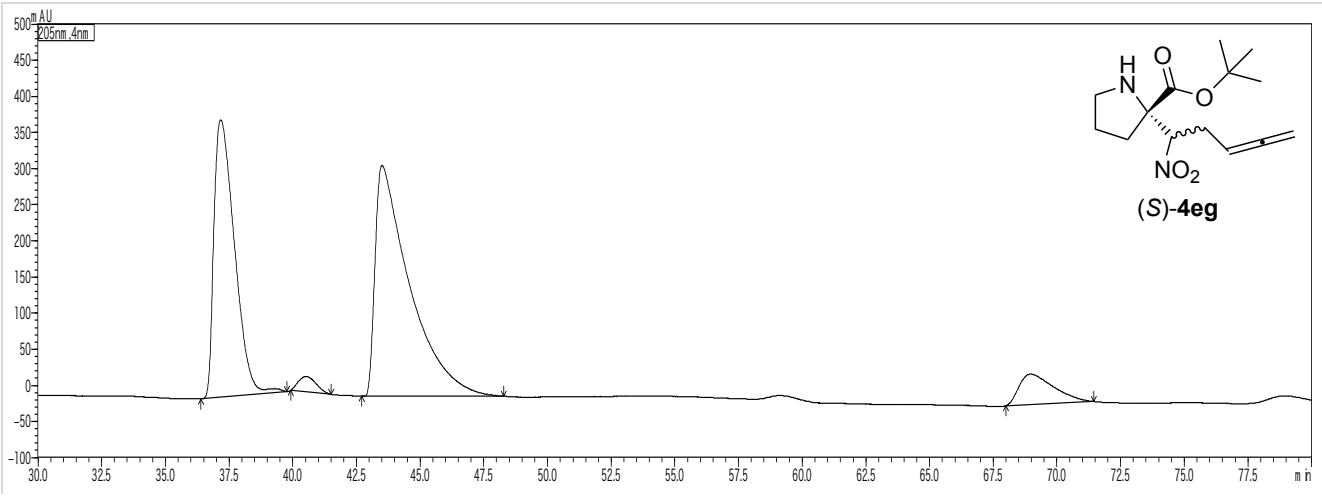
racemic-**4ef**		
Peak	tR (min)	Area (%)
1	69.6	33.8
2	73.8	33.6
3	81.5	16.3
4	115.9	16.3

(*S*)-**4ef**		
Peak	tR (min)	Area (%)
1	70.2	45.6
2	73.9	8.2
3	83.1	43.0
4	119.8	3.2

HPLC of *tert*-butyl 2-(1-nitropenta-3,4-dien-1-yl)pyrrolidine 2-carboxylate [racemic-**4eg**]



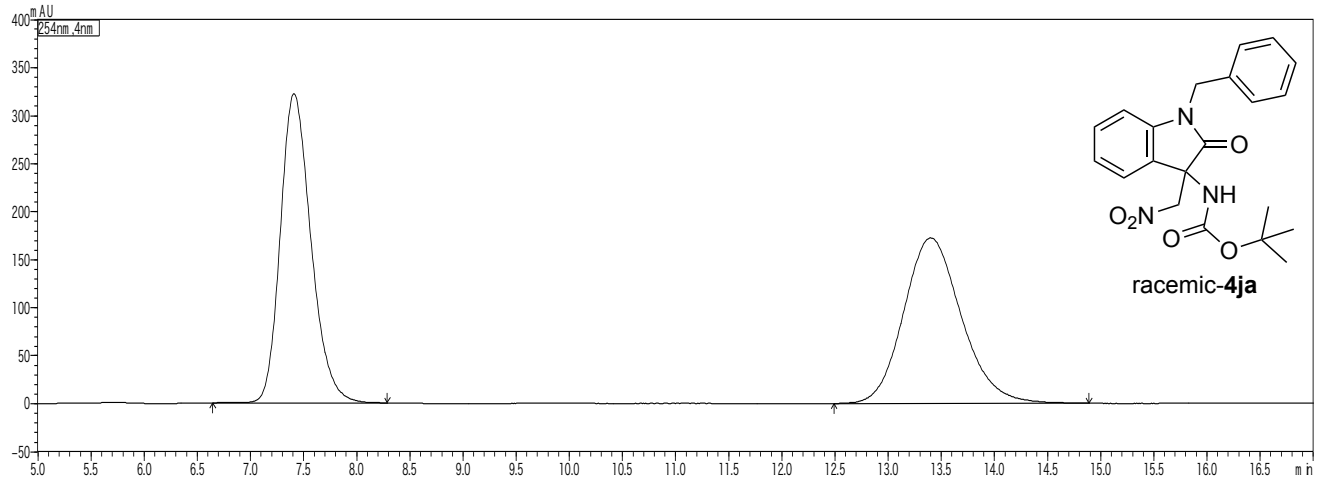
HPLC of *tert*-butyl (*S*)-2-(1-nitropenta-3,4-dien-1-yl)pyrrolidine 2-carboxylate [(*S*)-**4eg**]



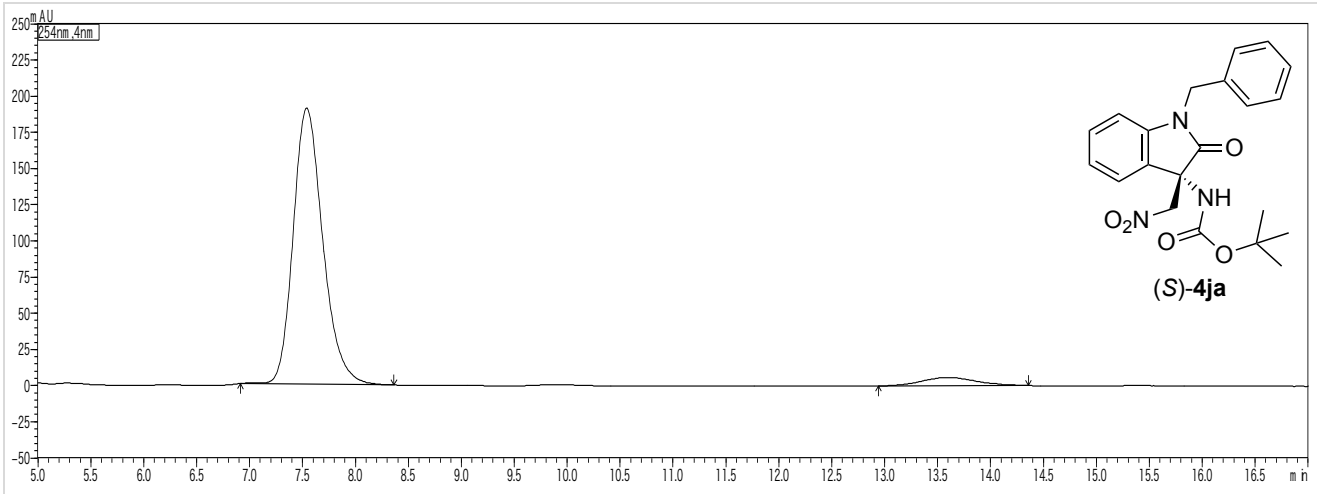
racemic-**4eg**		
Peak	tR (min)	Area (%)
1	34.0	29.8
2	36.4	29.7
3	39.8	20.1
4	61.7	20.4

(*S*)-**4eg**		
Peak	tR (min)	Area (%)
1	37.2	38.1
2	40.5	1.8
3	43.5	53.1
4	69.0	7.0

HPLC of *tert*-butyl 1-benzyl-3-(nitromethyl)-2-oxoindolin-3-yl]carbamate [racemic-**4ja**]



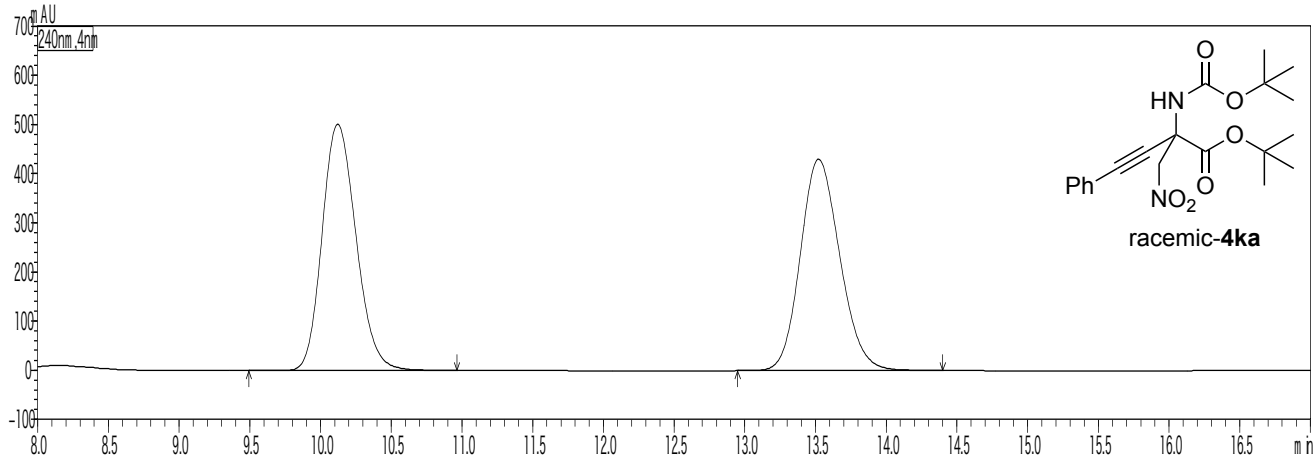
HPLC of *tert*-butyl (*S*)-1-benzyl-3-(nitromethyl)-2-oxoindolin-3-yl]carbamate [(*S*)-**4ja**]



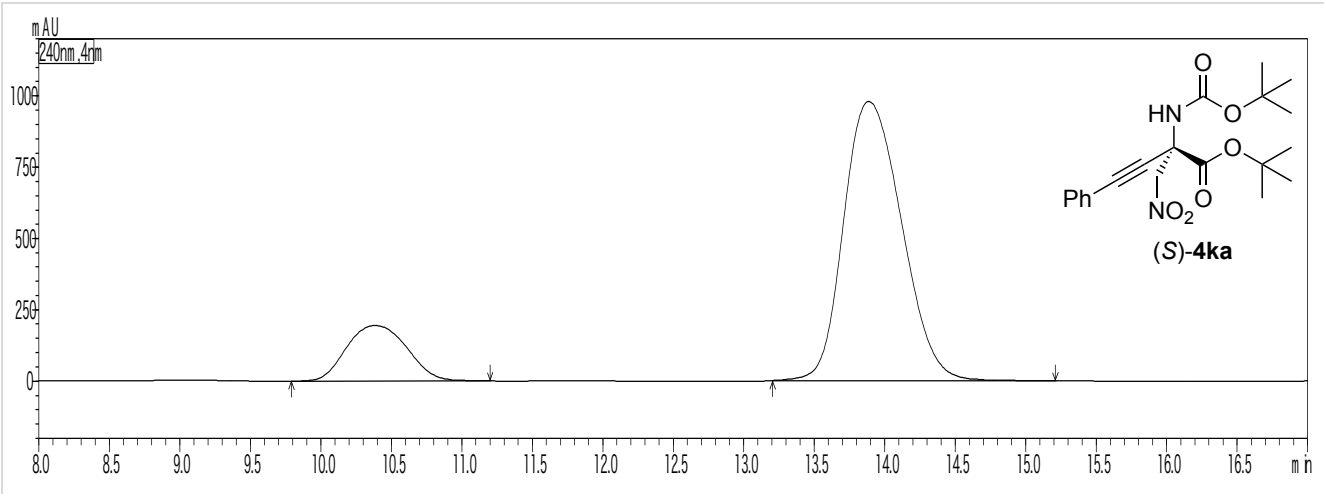
racemic-**4ja**		
Peak	tR (min)	Area (%)
1	7.4	49.9
2	13.4	50.1

(*S*)-**4ja**		
Peak	tR (min)	Area (%)
1	7.5	94.9
2	13.6	5.1

HPLC of *tert*-butyl 2-[(*tert*-butoxycarbonyl)amino]-2-(nitromethyl)-4-phenylbut-3-ynoate [racemic-**4ka**]



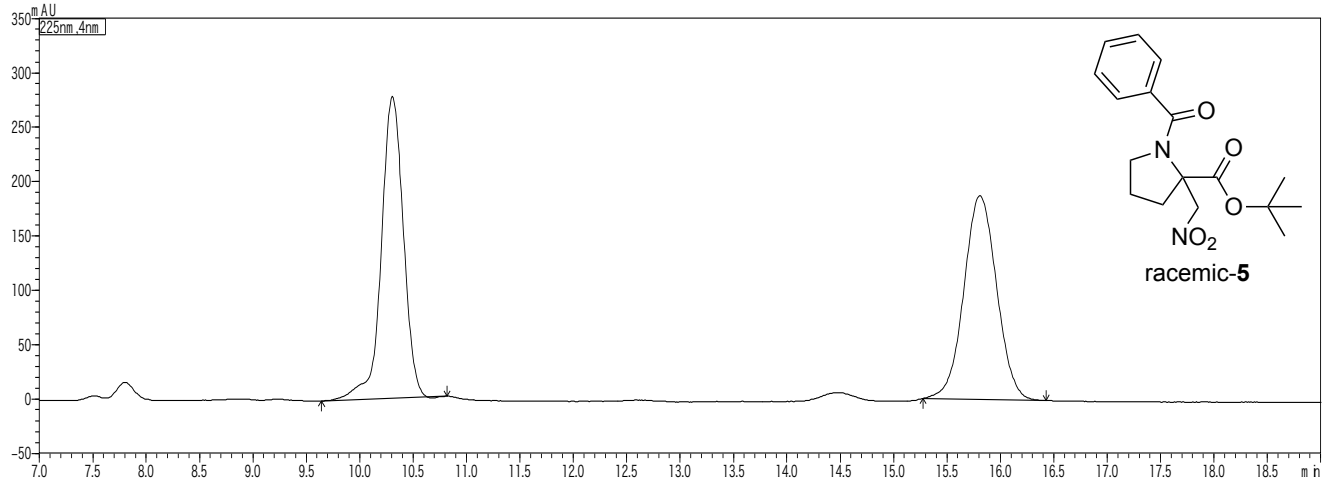
HPLC of *tert*-butyl (*S*)-2-[(*tert*-butoxycarbonyl)amino]-2-(nitromethyl)-4-phenylbut-3-ynoate [(*S*)-**4ka**]



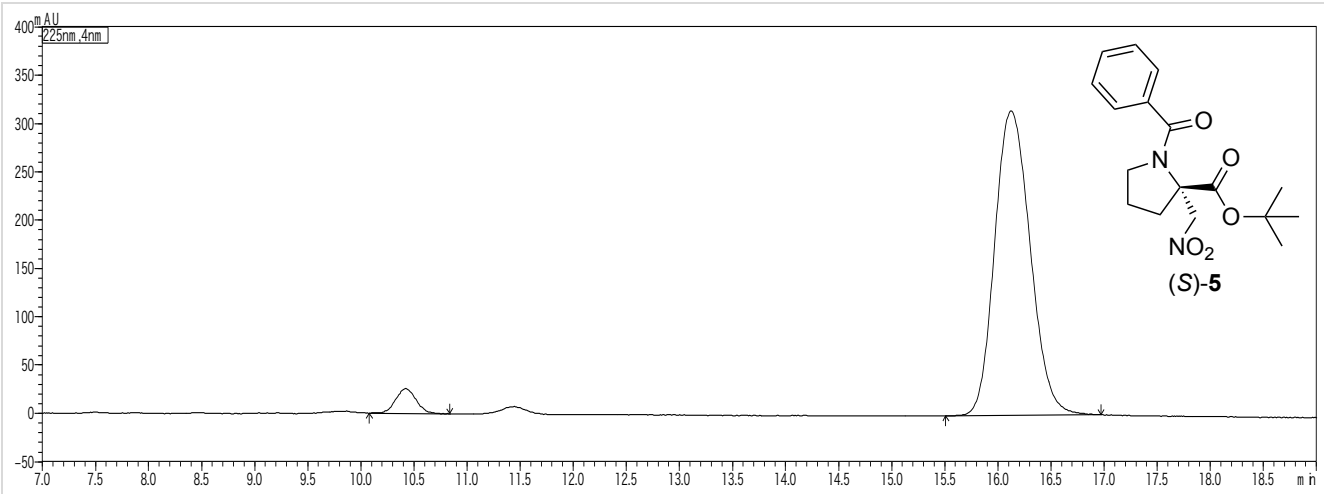
racemic-**4ka**		
Peak	tR (min)	Area (%)
1	10.1	50.0
2	13.5	50.0

(*S*)-**4ka**		
Peak	tR (min)	Area (%)
1	10.4	17.2
2	13.9	82.8

HPLC of *tert*-butyl 1-benzoyl-2-(nitromethyl)pyrrolidine 2-carboxylate [racemic-**5**]



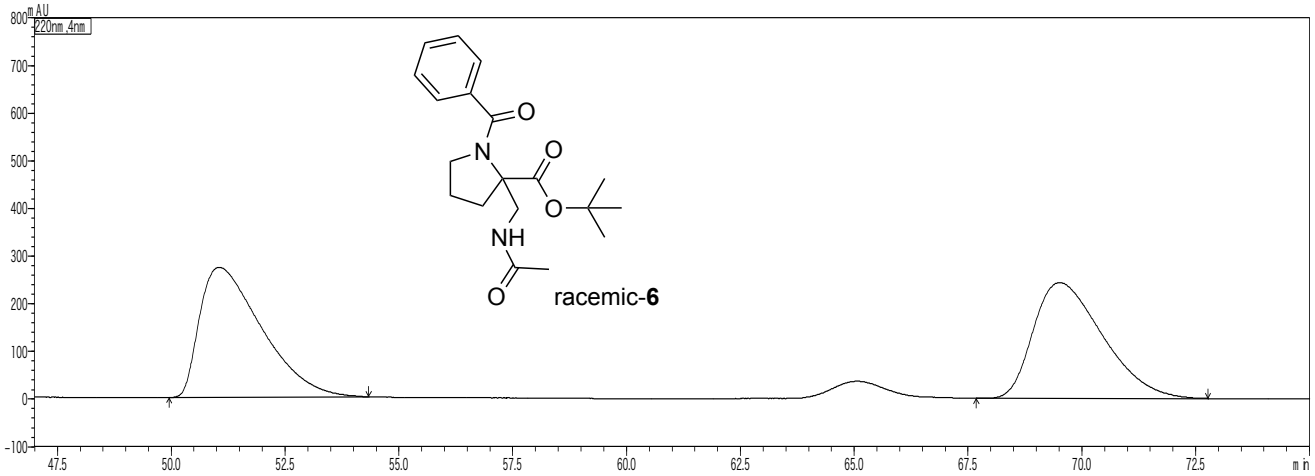
HPLC of *tert*-butyl (*S*)-1-benzoyl-2-(nitromethyl)pyrrolidine 2-carboxylate [(*S*)-**5**]



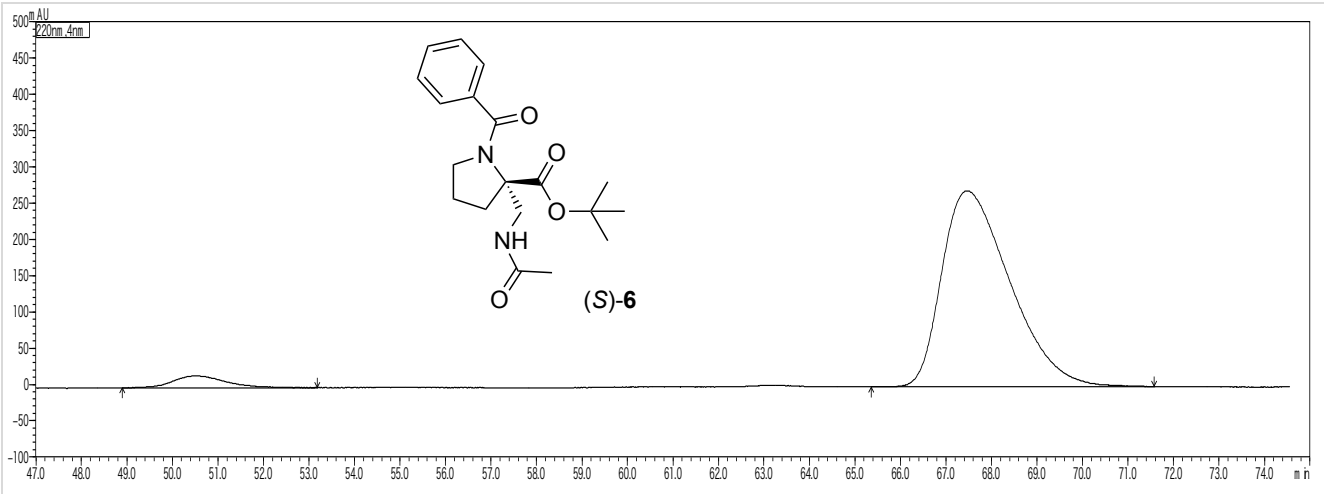
racemic-**5**		
Peak	tR (min)	Area (%)
1	10.3	49.9
2	15.8	50.1

(*S*)-**5**		
Peak	tR (min)	Area (%)
1	10.4	4.5
2	16.1	95.5

HPLC of *tert*-butyl 2-(acetamidomethyl)-1-benzoylpyrrolidine-2-carboxylate [racemic-**6**]



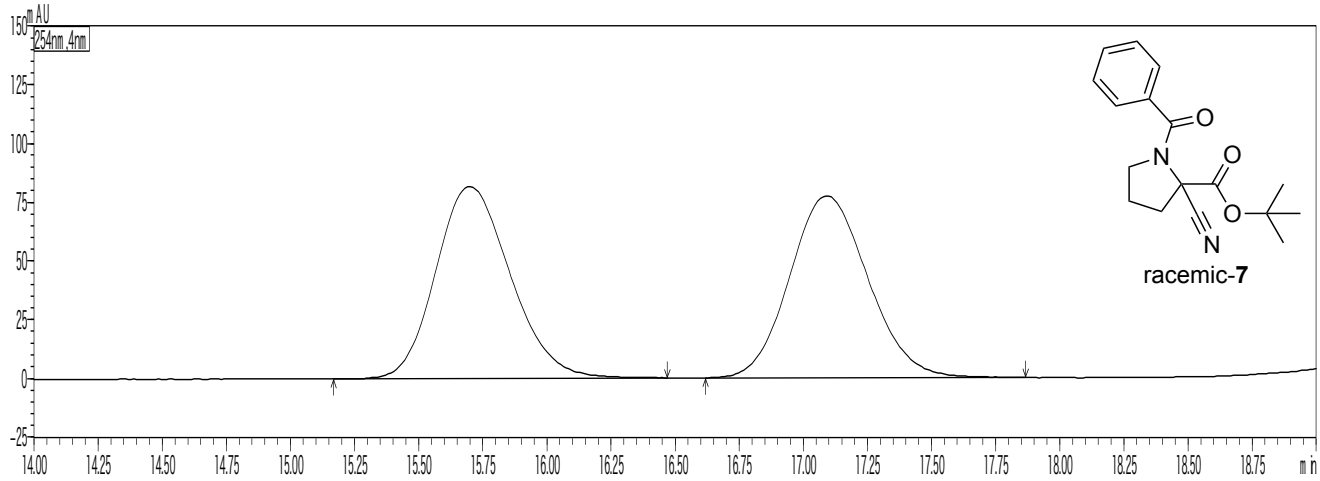
HPLC of *tert*-butyl (*S*)-2-(acetamidomethyl)-1-benzoylpyrrolidine-2-carboxylate [(*S*)-**6**]



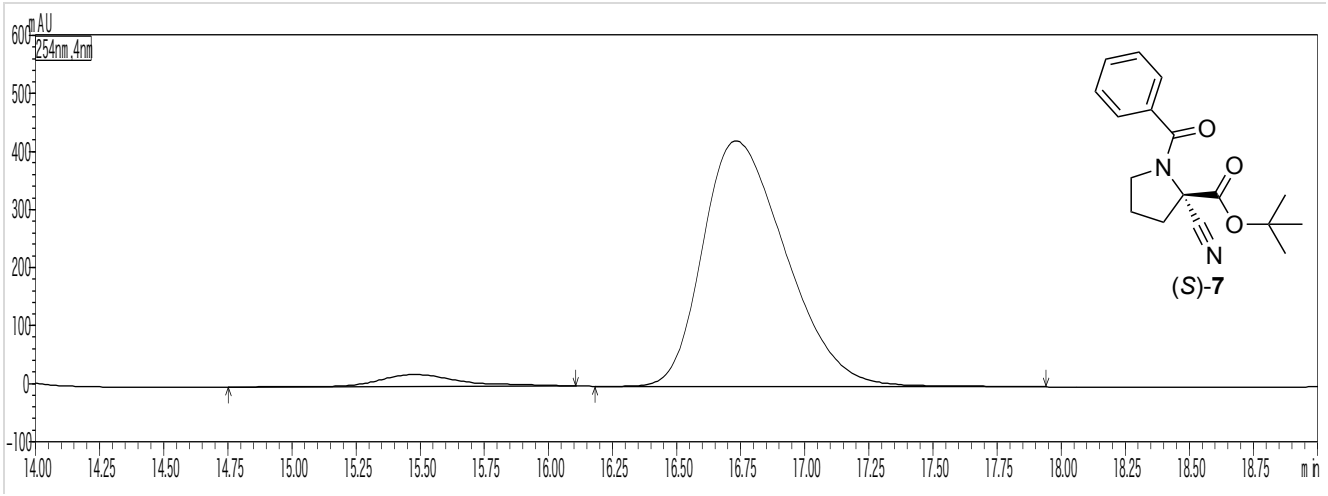
racemic-**6**		
Peak	tR (min)	Area (%)
1	51.1	50.1
2	69.5	49.9

(*S*)-**6**		
Peak	tR (min)	Area (%)
1	50.4	4.4
2	67.5	95.6

HPLC of *tert*-butyl 1-benzoyl-2-cyanopyrrolidine 2-carboxylate [racemic-**7**]



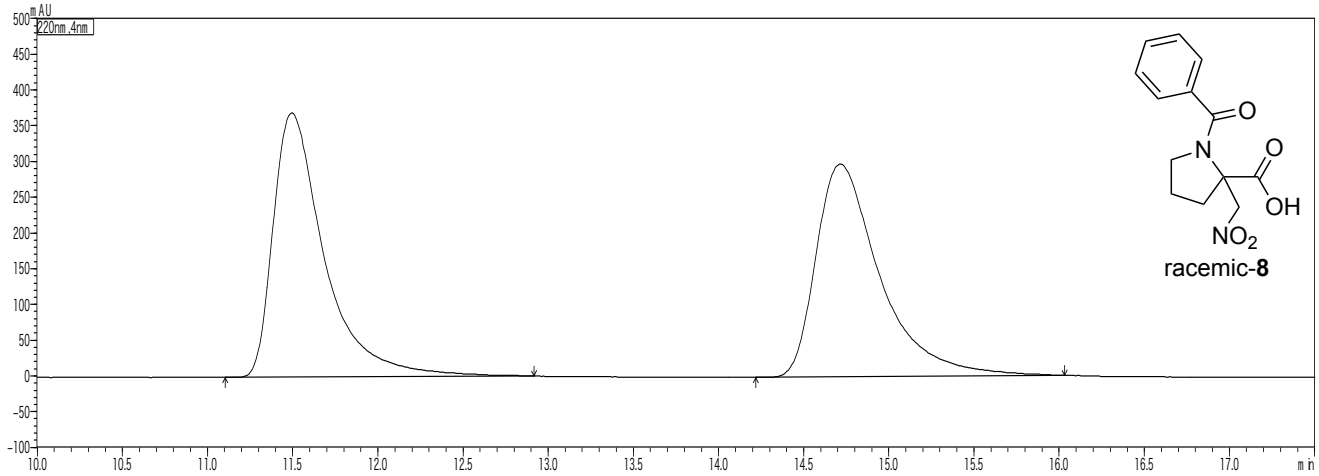
HPLC of *tert*-butyl (*S*)-1-benzoyl-2-cyanopyrrolidine 2-carboxylate [(*S*)-**7**]



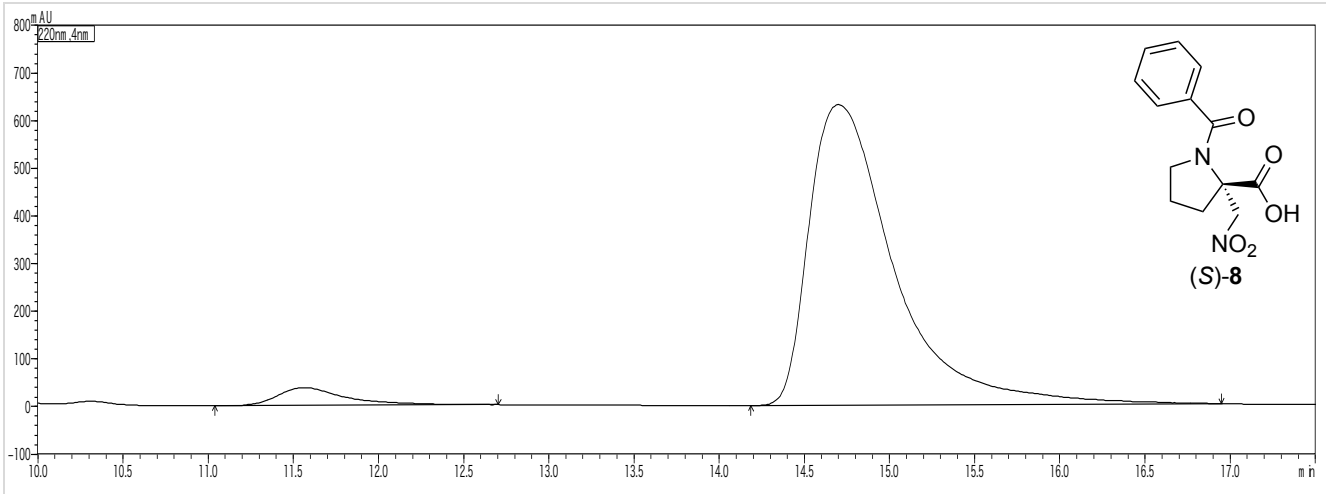
racemic-**7**		
Peak	tR (min)	Area (%)
1	15.7	50.1
2	17.1	49.9

(*S*)-**7**		
Peak	tR (min)	Area (%)
1	15.5	4.4
2	16.7	95.6

HPLC of 1-benzoyl-2-(nitromethyl)pyrrolidine-2-carboxylic acid [racemic-**8**]



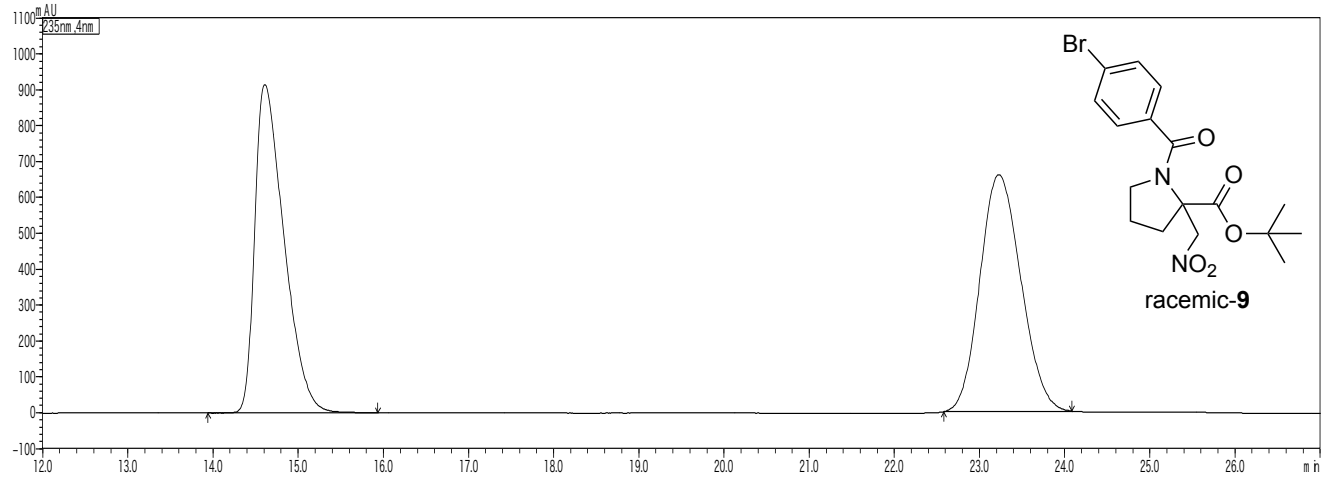
HPLC of (*S*)-1-benzoyl-2-(nitromethyl)pyrrolidine-2-carboxylic acid [(*S*)-**8**]



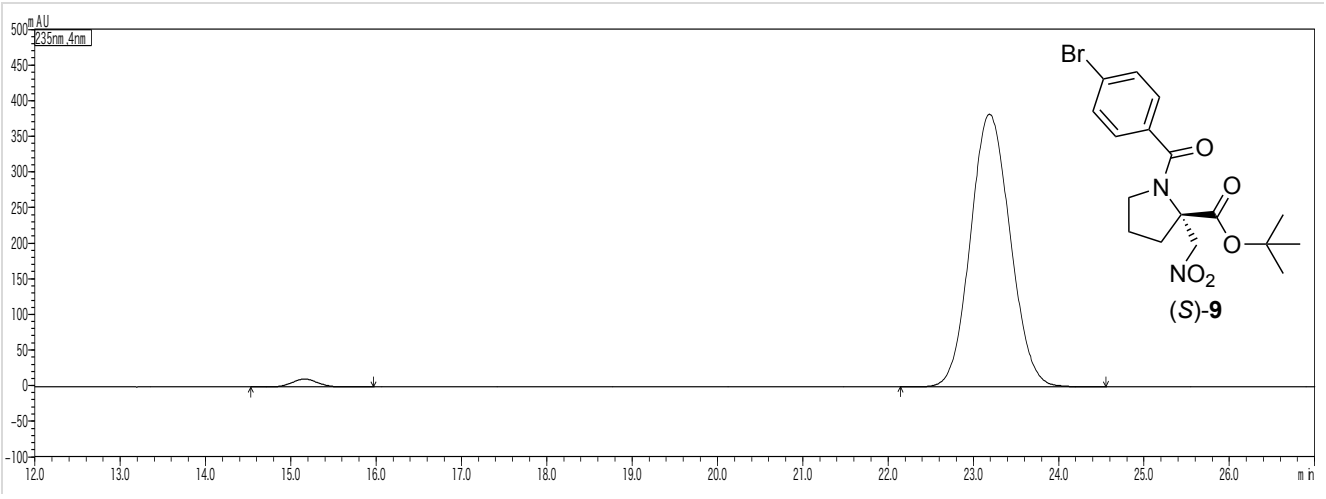
racemic-**8**		
Peak	tR (min)	Area (%)
1	11.5	49.8
2	14.7	50.2

(*S*)-**8**		
Peak	tR (min)	Area (%)
1	11.6	4.5
2	14.7	95.5

HPLC of *tert*-butyl 1-(4-bromobenzoyl)-2-(nitromethyl)pyrrolidine-2-carboxylate [racemic-**9**]



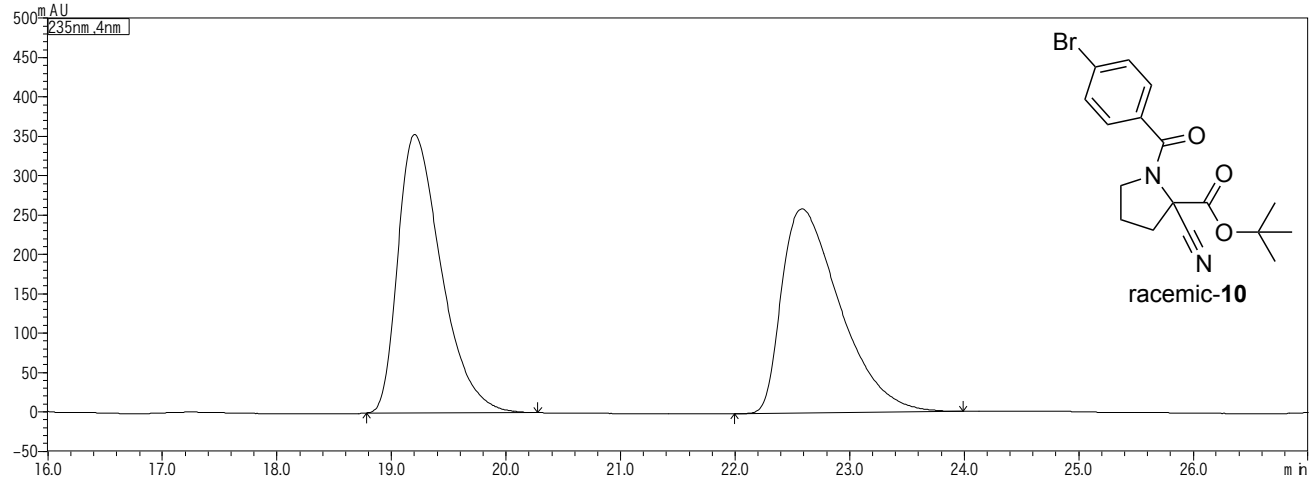
HPLC of *tert*-butyl (*S*)-1-(4-bromobenzoyl)-2-(nitromethyl)pyrrolidine-2-carboxylate [(*S*)-**9**]



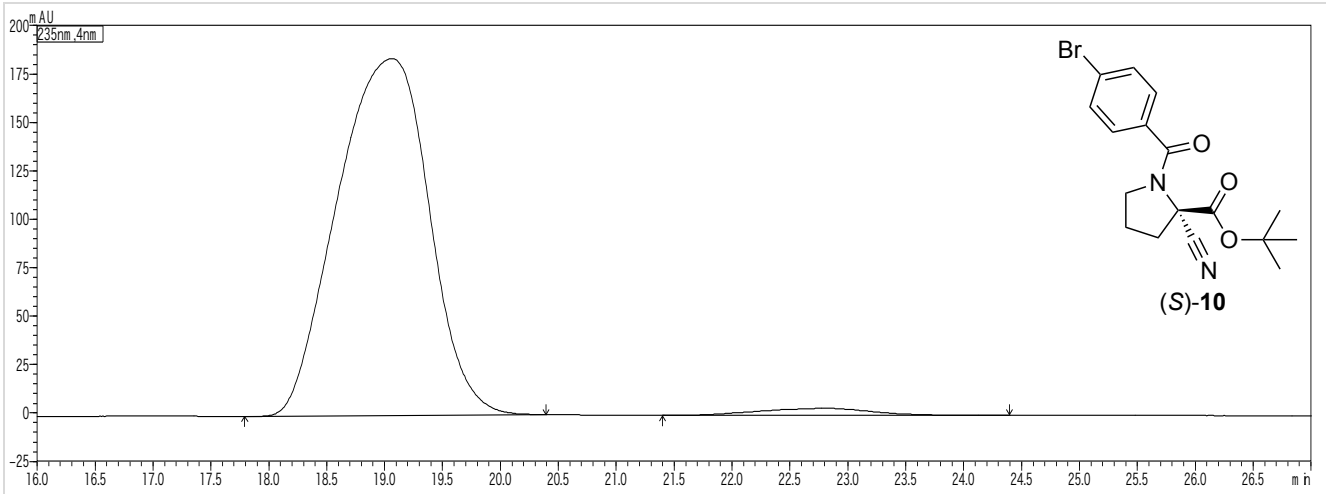
racemic-**9**		
Peak	tR (min)	Area (%)
1	14.6	49.8
2	23.2	50.2

(*S*)-**9**		
Peak	tR (min)	Area (%)
1	15.2	1.9
2	23.2	98.1

HPLC of *tert*-butyl 1-(4-bromobenzoyl)-2-cyanopyrrolidine-2-carboxylate [racemic-**10**]



HPLC of *tert*-butyl (*S*)-1-(4-bromobenzoyl)-2-cyanopyrrolidine-2-carboxylate [(*S*)-**10**]



racemic-**10**		
Peak	tR (min)	Area (%)
1	19.2	50.2
2	22.6	49.8

(*S*)-**10**		
Peak	tR (min)	Area (%)
1	19.1	97.7
2	22.8	2.3