
Supplementary information

Stereoretentive decarbonylative C(sp^3)–C(sp^3) cross-coupling

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Stereoretentive decarbonylative C(sp³)-C(sp³) cross-coupling

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1. Materials and methods

1.1 Materials

Metals

Nickel(II) bromide ethylene glycol dimethyl ether ($\text{NiBr}_2 \cdot \text{dme}$, 97%) was purchased from Millipore Sigma, stored in a N_2 -filled glovebox, and used as received. Manganese powder (-140 + 325 mesh, 99.6%) was purchased from Alfa Aesar, stored in a N_2 -filled glovebox.

Ligands

Ligands **L5-L8** were synthesized according to literature procedures¹. All other ligands were purchased from commercial suppliers and used without purification.

Solvents

Tetrahydrofuran (THF) and dichloromethane (DCM) were purified by passage through activated alumina and molecular sieves in a solvent purification system (Inert Corporation) and stored in a N_2 -filled glovebox. *N,N*-dimethylisobutylamide (DMIB) and other amide solvents were purchased from Millipore Sigma, stored in a N_2 -filled glovebox, and used as received.

Alkyl iodides

All alkyl iodides were synthesized according to literature procedures or purchased from commercial suppliers and used without purification.

Other reagents

4-(Dimethylamino)pyridine (DMAP, 99%) was purchased from Alfa Aesar. 2,2'-Dipyridyl carbonate was purchased from ChemImpex International and used without further purification.

1.2 Methods

NMR Spectroscopy

^1H -NMR and proton-decoupled ^{13}C -NMR ($^{13}\text{C}\{^1\text{H}\}$) spectra were acquired on a 500 MHz Avance spectrometer equipped with a DCH cryoprobe (Bruker) and 400 MHz Avance spectrometer equipped with a BBFO probe (Bruker), proton-decoupled ^{19}F -NMR ($^{19}\text{F}\{^1\text{H}\}$) spectra were acquired on a 400 MHz Avance spectrometer equipped with a BBFO probe (Bruker). NMR chemical shifts are reported in ppm and are referenced to CDCl_3 at 7.26 ppm (^1H NMR) and 77.16 ppm ($^{13}\text{C}\{^1\text{H}\}$ NMR), or C_6D_6 at 7.16 ppm (^1H NMR) and 128.06 ppm ($^{13}\text{C}\{^1\text{H}\}$ NMR) ppm and are noted as such. Coupling constants (J) are reported in Hertz.

Gas Chromatography

GC analyses were performed on an Agilent 7890A GC equipped with dual DB-5 columns (20 m × 180 μm × 0.18 μm), dual FID detectors, and hydrogen as the carrier gas. A sample volume of 1 μL was injected at a temperature of 300 °C and a 100:1 split ratio. The initial inlet pressure was 20.3 psi but varied as the column flow was held constant at 1.8 mL/min for the duration of the run. The initial oven temperature of 50 °C was held for 0.46 min followed by a temperature ramp of 65 °C/min up to 300 °C. The total run time was 5.0 min and the FID temperature was 325 °C.

Supercritical Fluid Chromatography Mass Spectrometry (SFC/MS)

SFC/MS analyses were performed on a Waters Acquity UPC² equipped with Acquity UPC² PDA (λ = 190-410 nm) and Acquity QDa Detector. The eluent was mixtures of CO₂/MeOH or CO₂/*i*-PrOH. Daicel Dcpack SFC columns were used for separations: IA-3/IF-3/IC-3 (3 mm ID × 150 mm L, 3 μm PS), MeOH in scCO₂ (v = 0.8 mL/min) or *i*-PrOH in scCO₂ (v = 0.6 mL/min), 40 °C, 2200 psi; SFC-B (4.6 mm ID × 150 mm L, 5 μm PS), MeOH in scCO₂, v = 2 mL/min, 40 °C, 1500 psi.

High-Performance Liquid Chromatography (HPLC)

HPLC analyses were performed with isolated materials on a Waters e2695 separations module with 2998 PDA detector and Daicel Chiralpak columns, HPLC grade *i*-PrOH and hexanes were used as mobile phase.

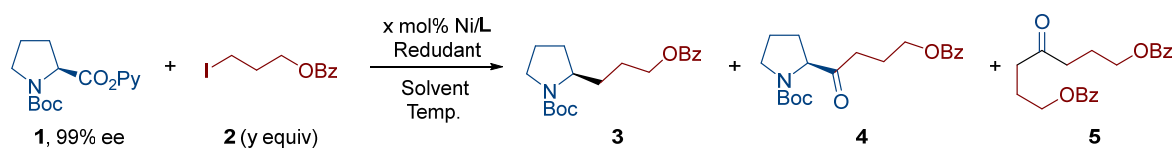
Chromatography

Chromatography was performed on silica gel (EMD, silica gel 60, particle size 0.040-0.063 mm) using standard flash techniques, on a Biotage Isolera One (detection at 254 nm and 280 nm, on Sfar Duo columns). Products were visualized by UV, PMA stain, or fractions were analyzed by SFC/MS with Daicel Dcpack SFC-B columns.

High Resolution Mass Spectrometry

Mass spectrometry data was collected on a Thermo Q Exactive Plus (thermofisher.com) via flow injection with electrospray ionization or via ASAP-MS (asap-ms.com) by the chemistry mass spectrometry facility at the University of Wisconsin – Madison. The purchase of the Thermo Q Exactive Plus in 2015 was funded by NIH (National Institutes of Health) Award 1S10 OD020022 to the Department of Chemistry.

2. Optimization of stereoretentive decarbonylative cross coupling



Procedure for condition optimization

In an N₂ filled glovebox, to a vial (4 mL) containing a PTFE-coated stirbar was added the appropriate Ni salt, ligand, and solvent (0.5 mL). This mixture was stirred at rt for 10 min. To this vial was added the pyridyl ester, alkyl iodide, and reductant. The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was heated and stirred (800 RPM). After the specified reaction time, the vial was removed from the hotplate, and allowed to cool to rt, 1,3,5-trimethoxybenzene (TMB) was added as internal standard for GC analysis and the mixture was diluted with ethyl acetate (3 mL). A portion (0.2 mL) of the resulting mixture was passed through a pad of silica gel, and the pad was washed with ethyl acetate (5 mL). The filtration was analyzed by GC (calibrated GC yield vs 1,3,5-trimethoxybenzene as internal standard) and SFC (e.r. vs the corresponding racemic samples as references). e.r. = enantiomeric ratio; e.e. = $[(\% \text{ of major enantiomer}) - (\% \text{ of minor enantiomer})] / [(\% \text{ major enantiomer}) + (\% \text{ minor enantiomer})]$; e.s. = $[(\text{e.e. of product}) / (\text{e.e. of starting material})] \times 100\%$.

Table S1. Summary of optimization

$\text{1, 0.2 mmol, 99.5:0.5 e.r.} + \text{2, 2.5 equiv} \xrightarrow[\text{THF:DMIB (10:1), 40 } ^\circ\text{C, 6 h}]{\text{NiBr}_2\cdot\text{dme (20 mol\%), L5 (20 mol\%), Mn (3.0 equiv)}}$

Entry	Deviations from above reaction conditions	yield (%)	e.r.
1	None	77	98:2
2	1.5 equiv of 2	49	91.5:18.5
3	THF as solvent	30	97:3
4	DMA instead of DMIB	24	92.5:7.5
5	60 °C	50	98:2
6	Zn instead of Mn	26	87.5:22.5
7	TDAE instead of Mn	0	nd
8	20 mol% NiBr₂·dme, 24 mol% ^tBuPyPz	80 (78% isolated)	99:1
9	10 mol% NiBr ₂ ·dme, 12 mol% ^t BuPyPz	66	98:2
10	no Mn	0	nd
11	no ligand	10	60:40
12	no NiBr ₂ ·dme	0	nd

Table S2. Effect of ligands

$\text{1, 0.2 mmol, 99.5:0.5 e.r.} + \text{2 (2.5 equiv)} \xrightarrow[\text{THF:DMIB (10:1), 40 } ^\circ\text{C, 6 h}]{\text{NiBr}_2\cdot\text{dme (20 mol\%), ligand (24 mol\%), Mn (3.0 equiv)}}$

L1, trace 1 remains unreactive	L2, 21%, 86:14 e.r. 73% e.s., 60% 1 recovery	L3, 42%, 98:2 e.r. 97% e.s., with 10% 4	L4, 51%, 97:3 e.r. 95% e.s., with 4% 4
L5, 80%, 99:1 e.r. 99% e.s., with 3% 4	L6, 57%, 96.5:3.5 e.r. 94% e.s., with 3% 4	L7, 64%, 96.5:3.5 e.r. 94% e.s., with 4% 4	L8, 53%, 94.5:5.5 e.r. 90% e.s., with 5% 4

Table S3. Effect of reductants

1, 0.2 mmol
99.5:0.5 e.r.
2 (2.5 equiv)

3 **4**

entry	reductant	3 (%)	e.r. of 3 (%)	4 (%)
1	Zn	26	82.5:17.5	3
2	Mn	77	98:2	3
3	TDAE	0	nd	0
4	TMS-pyrazine ^a	12	nd	0
5	no reductant	0	nd	0

^a1,4-bis(trimethylsilyl)-1,4-dihydropyrazine.

Table S4. Effect of Solvent

1, 0.2 mmol
99.5:0.5 e.r.
2 (2.5 equiv)

3 **4**

entry	solvent	3 (%)	e.r. of 3 (%)	4 (%)
1	THF:DMA (25:1)	48	87.5:12.5	4
2	THF:DMTFA (25:1)	34	85:15	-
3	THF:DMB (25:1)	37	95:5	3
4	THF:DMIB (25:1)	47	98:2	5
5	THF:DMIB (10:1)	77	98:2	3
6	THF:DMIB (5:1)	58	96:4	3
7	THF only	30	97:3	8

DMTFA

DMB

DMIB

Table S5. Effect of varying the equivalents of alkyl iodide

1, 0.2 mmol
99.5:0.5 e.r.
2 (x equiv)

NiBr₂·dme (20 mol%)
L5 (20 mol%)
 Mn (3.0 equiv)
 THF:DMIB (10:1)
 40 °C, 6 h

3 + **4**

entry	x equiv of 2	3 (%)	e.r. of 3 (%)	4 (%)
1	1.5	42	91.5:8.5	4
2	2.5	77	98:2	3
3	3.0	78	98:2	3

Table S6. Effect of temperature

1, 0.2 mmol
99.5:0.5 e.r.
2 (2.5 equiv)

NiBr₂·dme (20 mol%)
L5 (20 mol%)
 Mn (3.0 equiv)
 THF:DMIB (10:1)
 temp., 6 h

3 + **4**

entry	temp. (°C)	3 (%)	e.r. of 3 (%)	4 (%)
1	30	15	91:9	5
2	40	77	98:2	3
3	50	66	97.5:2.5	4
4	60	50	98:2	5

Table S7. Effect of catalyst loading

1, 0.2 mmol
99.5:0.5 e.r.
2 (2.5 equiv)

NiBr₂·dme (x mol%)
L5 (y mol%)
 Mn (3.0 equiv)
 THF:DMIB (10:1)
 40 °C, 6 h

3 + **4**

entry	x	y	3 (%)	e.r. of 3 (%)	4 (%)
1	20	20	77	98:2	4
2	15	15	73	97.5:2.5	5
3	10	10	65	97.5:2.5	3
4	10	12	66	98:2	5
5 ^a	20	24	80 (78% isolated)	99:1	3
6	20	30	71	99:1	3

^a1,7-diphenylheptan-4-one **5** was observed as CO trapping product in 65% isolated yield.

Table S8. Comparison of different radical precursors

radical precursor				
standard condition	78%, 99:1 e.r. 99% e.s.	12%, 96:4 e.r. 93% e.s.	39%, 94.5:5.5 e.r. 90% e.s.	trace
optimized condition (deviation from above)	as above	58%, 92:8 e.r. 85% e.s. (with 1.0 equiv of NaI)	23%, 98:2 e.r. ^a 97% e.s. (with DMIB as solvent)	15%, 75:25 e.r. ^a 51% e.s. (with DMIB as solvent)

^aNMR yield using 1,3,5-trimethoxybenzene as internal standard

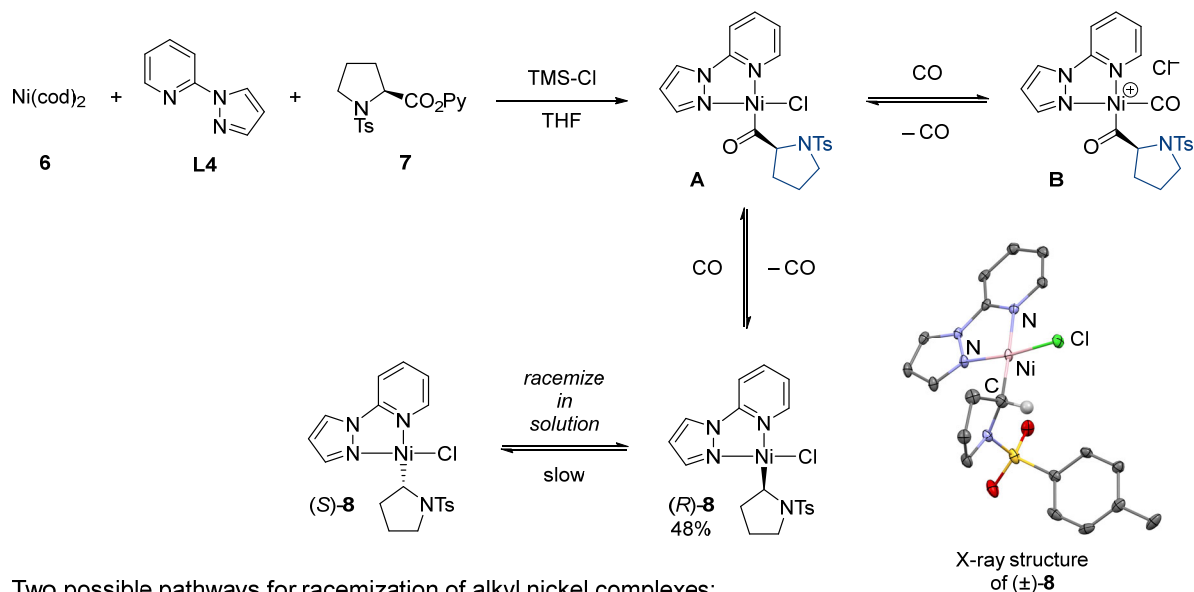
Table S9. Optimization of cross-coupling with α -hydroxy acid derivatives

entry	L	solvent	isolated yield (%)	e.r.
1	L4	THF:DMIB (20:1)	65	99.5:0.5
2	L5	THF:DMIB (20:1)	66	99.5:0.5
3	L7	THF:DMIB (20:1)	58	99.5:0.5
4	L8	THF:DMIB (20:1)	63	99.5:0.5
5 ^a	L5	THF	58	99.5:0.5
6	L5	THF:DMIB (10:1)	55	99.5:0.5

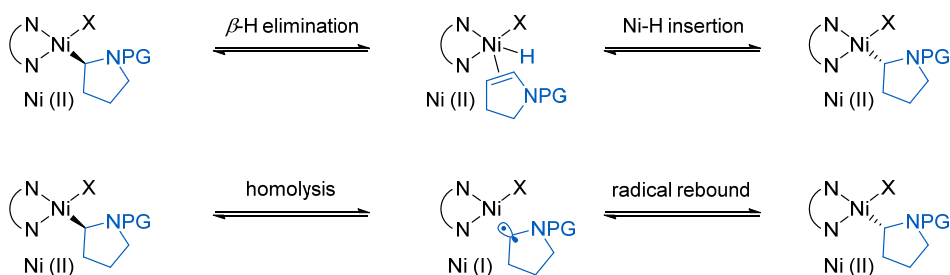
Dmc, dimethylcarbamylyl. ^aReaction time was 24 h.

3. Mechanism investigation

3.1 Stoichiometric oxidative addition and decarbonylation



Two possible pathways for racemization of alkyl nickel complexes:



In an N_2 filled glovebox, Ni(cod)_2 (55.0 mg, 0.2 mmol) and **L4** (29.0 mg, 0.2 mmol) were dissolved in THF (3 mL) in a 20 mL vial containing a PTFE-coated stirbar. The resulting deep blue (**L4**) Ni(cod) solution was stirred for 5 min at rt and cooled to 0 °C. To another 20 mL vial was added pyridyl ester **7** (79.3 mg, 0.2 mmol), THF (2 mL), and TMSCl (21.7 mg, 0.2 mmol). The resulting mixture was added to the solution of (**L4**) Ni(cod) in the vial at 0 °C. The solution was stirred at rt for 5 min. The resulting red mixture was filtered, and the filtrate was collected in a 20 mL vial as a red solution. To the red solution was added pentane (5 mL), red precipitates were formed and removed by filtration (10-micron PE fritted filter), the red solid and filtrate were collected separately in two vials.

The red solid (23.9 mg) was washed by pentane (3×5 mL) and dried under reduced pressure. NMR analysis indicates that complex **8** and **A** were in ~1:1 ratio. ^1H NMR of complex **A** (500 MHz, C_6D_6) δ 8.40 (d, J = 5.3 Hz, 1H), 7.86 (d, J = 7.8 Hz, 2H), 7.71 – 7.63 (m, 1H), 7.63 – 7.55 (m, 1H), 7.25 – 7.20 (m, 1H), 7.07 – 6.98 (m, 1H), 6.74 (d, J = 8.0 Hz, 2H), 6.32 – 6.24 (m, 1H), 5.81 – 5.67 (m, 1H), 5.46 (dd, J = 9.0, 3.6 Hz, 1H), 3.83 – 3.76 (m, 1H), 3.27 – 3.15 (m, 1H), 2.90 – 2.66 (m, 1H), 1.85 (s, 3H), 1.82 – 1.70 (m, 1H), 1.53

(dt, $J = 12.9, 5.7$ Hz, 1H), 1.17 – 1.09 (m, 1H).

To the filtrate was added pentane (10 mL), yellow precipitates were rapidly formed and filtered. At this time, the solids were washed with pentane (3×10 mL) before they were dried under vacuum to give the desired product complex **8** as yellow solid (45.0 mg, 48% yield). **¹H NMR of complex 8** (500 MHz, C₆D₆) δ 8.81 (d, $J = 5.4$ Hz, 1H), 8.29 (d, $J = 7.8$ Hz, 2H), 8.02 – 7.98 (m, 1H), 7.98 – 7.96 (m, 1H), 7.27 – 7.20 (m, 2H), 6.91 (d, $J = 7.8$ Hz, 2H), 6.19 – 6.12 (m, 1H), 5.95 – 5.81 (m, 1H), 3.82 – 3.71 (m, 1H), 3.41 – 3.28 (m, 1H), 3.12 – 2.97 (m, 1H), 2.19 – 2.06 (m, 1H), 1.89 (s, 3H), 1.85 – 1.80 (m, 1H), 1.58 – 1.43 (m, 1H), 1.18 – 1.05 (m, 1H). **¹³C{¹H} NMR** (126 MHz, C₆D₆) δ 148.7, 145.8, 142.8, 141.1, 140.2, 134.3, 129.6, 128.8, 128.7, 121.5, 110.3, 109.5, 49.0, 37.8, 34.7, 24.4, 21.2. Further purification of **complex A** by recrystallization was unsuccessful. QNMR revealed ~90% purity for **complex A**. The major impurity was identified as acyl nickel **complex B** (~10%, see ¹³CO insertion experiment for further evidence). **¹H NMR of complex B** (500 MHz, C₆D₆) δ 8.49 (d, $J = 5.4$ Hz, 1H), 7.88 (d, $J = 7.9$ Hz, 2H), 7.76 – 7.69 (m, 1H), 7.27 – 7.21 (m, 1H), 7.15 – 7.10 (m, 1H), 6.79 – 6.75 (m, 1H), 6.74 (d, $J = 8.2$ Hz, 2H), 6.28 – 6.22 (m, 1H), 5.75 – 5.66 (m, 1H), 5.51 (dd, $J = 9.0, 3.7$ Hz, 1H), 3.92 – 3.79 (m, 1H), 3.27 – 3.18 (m, 1H), 2.82 – 2.74 (m, 1H), 1.85 (s, 3H), 1.80 – 1.74 (m, 1H), 1.53 – 1.49 (m, 1H), 1.28 – 1.17 (m, 1H).

These results indicate that complex **8**, **A**, and **B** were formed by the oxidative addition of 2-pyridyl ester **7** with Ni(cod)₂, the decarbonylation and CO reinsertion are reversible at room temperature.

Growing single crystals of (R)-**8** in Et₂O/pentane at -30 °C resulted in the formation of orange single crystals suitable for X-ray diffraction analysis. (R)-**8** and (S)-**8** were found in 1:1 ratio by X-ray diffraction analysis. This data indicates that complex (R)-**8** could slowly racemize in the solution when growing the crystals, such process might be attributed to the reversible β -hydride elimination-insertion or homolysis-radical rebound mechanisms. Further mechanistic investigations appear to rule out radical pathways and provide clear evidence for reversible β -hydride elimination and alkene coordination.

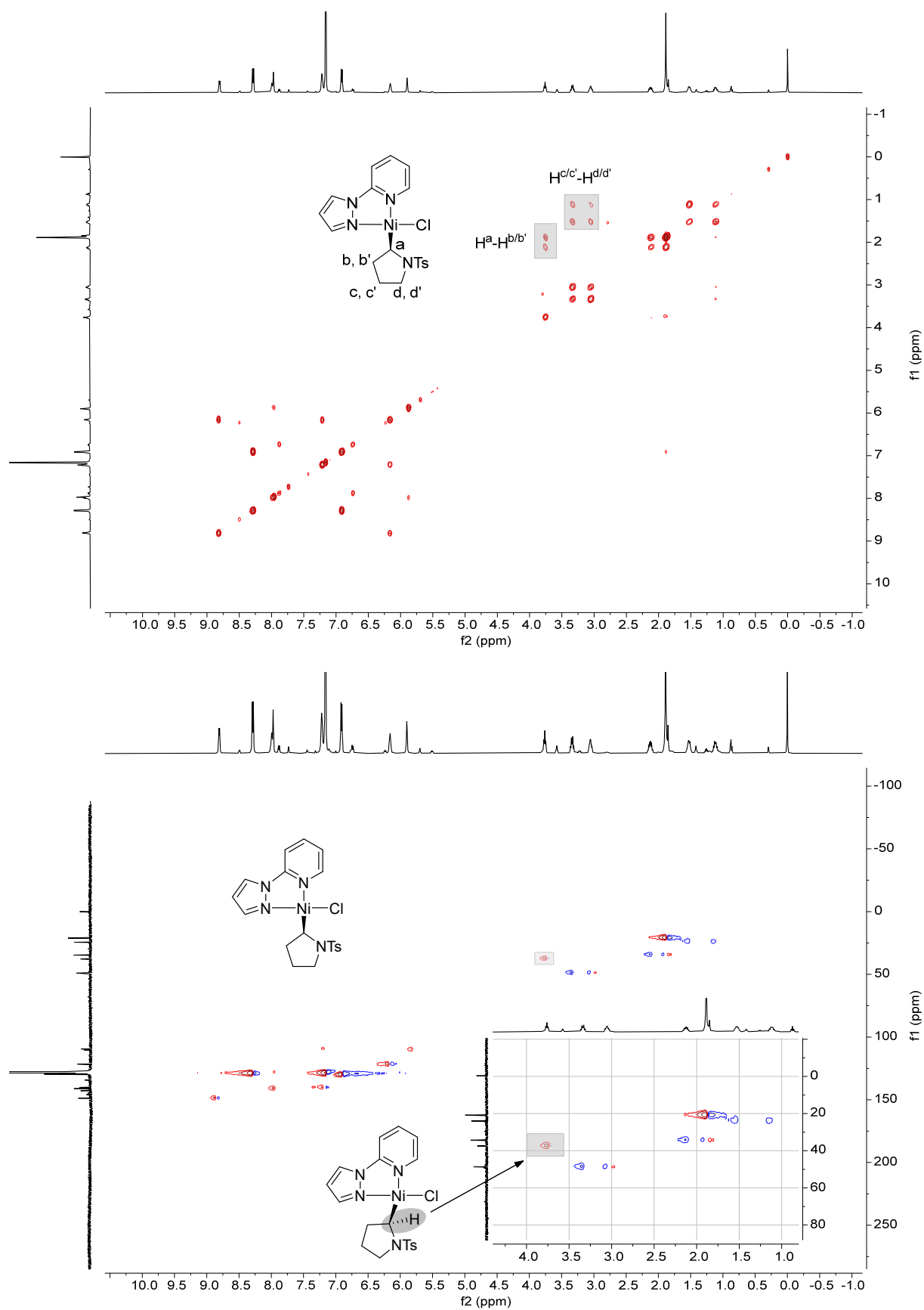


Fig. S2. COSY and HSQC spectra for complex 8.

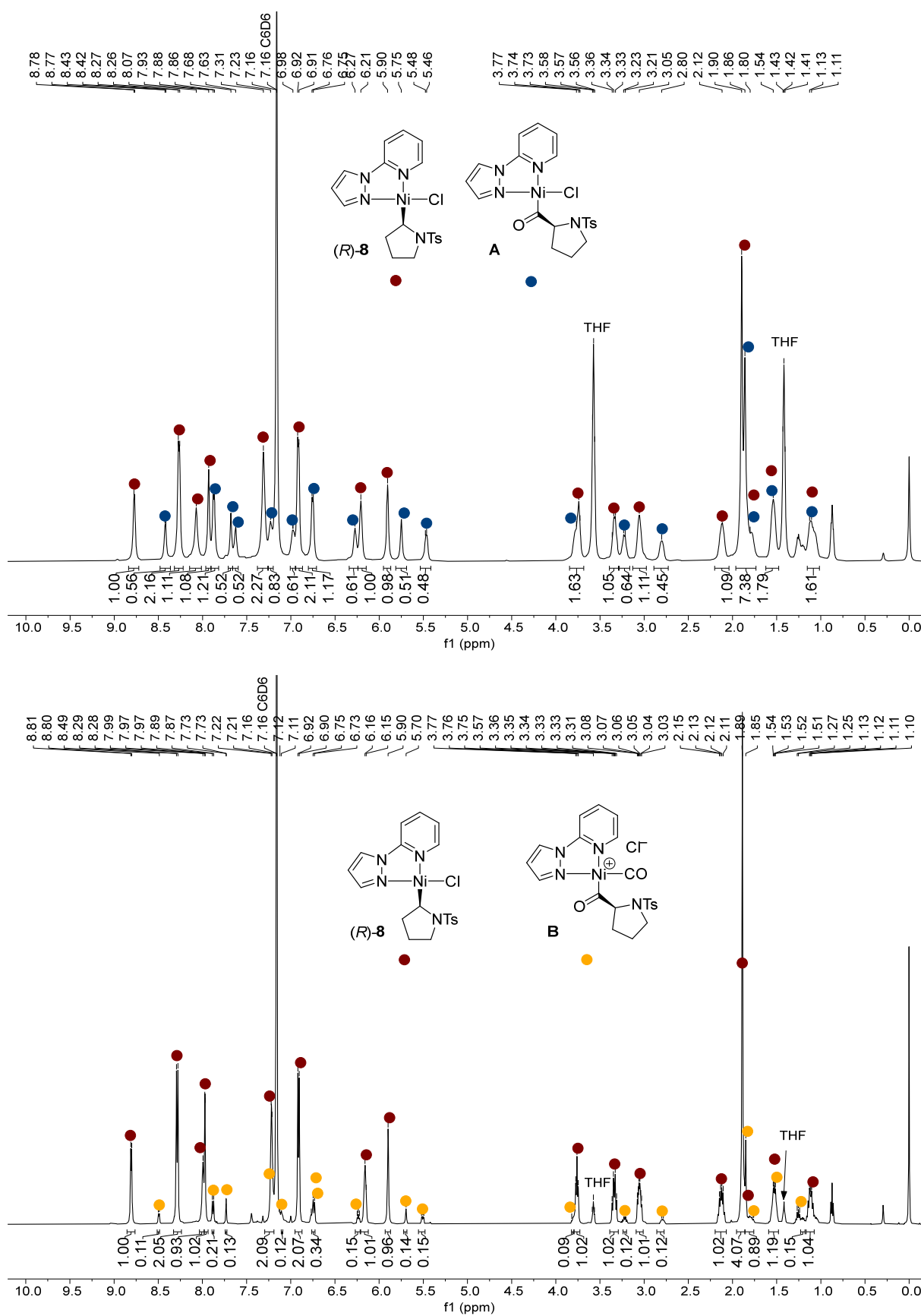
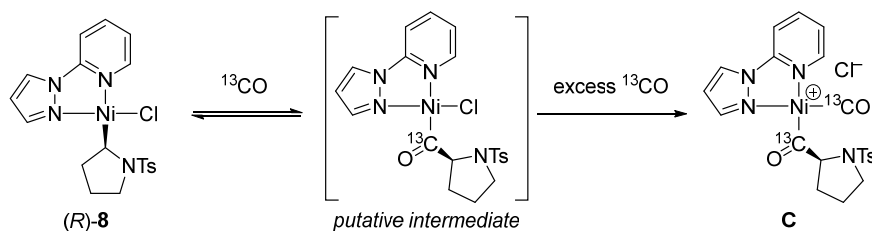


Fig. S3. ^1H NMR (500 MHz, C_6D_6) spectra for mixtures containing **complex 8**, **A** and **B**.

3.2 ^{13}C O insertion equilibrium



In a nitrogen-filled glovebox, a screw-cap NMR tube was charged with **(R)-8** (4.6 mg, 10 μmol , 1.0 equiv) and C_6D_6 (0.4 mL). The tube was sealed with a rubber septum, and the initial NMR spectra were recorded. Then ^{13}CO (1 mL, ~ 40 μmol , ~ 4.0 equiv) was injected into the tube with a microsyringe. The tube was occasionally shaken, and the reaction was occasionally monitored by NMR. The ^1H NMR spectrum showed full conversion of complex **8** after 5 min. The $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum showed new peaks at 247.4 and 191.8 ppm, corresponding to the Ni-acyl and Ni- ^{13}C O on ^{13}C -labeled Ni-acyl **complex C**, respectively. ^1H NMR (500 MHz, C_6D_6) δ 8.56 – 8.30 (m, 1H), 7.87 (d, $J = 7.8$ Hz, 2H), 7.73 (s, 1H), 7.30 (s, 1H), 7.10 (s, 3H), 6.74 (d, $J = 7.9$ Hz, 2H), 6.65 (s, 1H), 6.22 (d, $J = 7.6$ Hz, 1H), 5.73 (s, 1H), 5.58 – 5.41 (m, 1H), 3.78 (s, 1H), 3.32 – 3.12 (m, 1H), 2.77 (s, 1H), 1.85 (s, 3H), 1.79 (s, 1H), 1.53 (s, 1H), 1.06 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, C_6D_6) δ 247.4, 191.8, 147.1, 146.0, 144.5, 142.7, 140.4, 136.9, 129.7, 121.7, 110.7, 109.5, 67.8 (d, $J = 16.9$ Hz), 49.6, 29.9, 24.6, 21.1. The NMR spectra matched with the impurity **B** found in a stoichiometric oxidative addition reaction. Together with the stoichiometric decarbonylative oxidative addition experiments, this data reveals that decarbonylation of acyl nickel complexes and CO coordination-insertion of alkyl nickel complexes are fast and reversible.

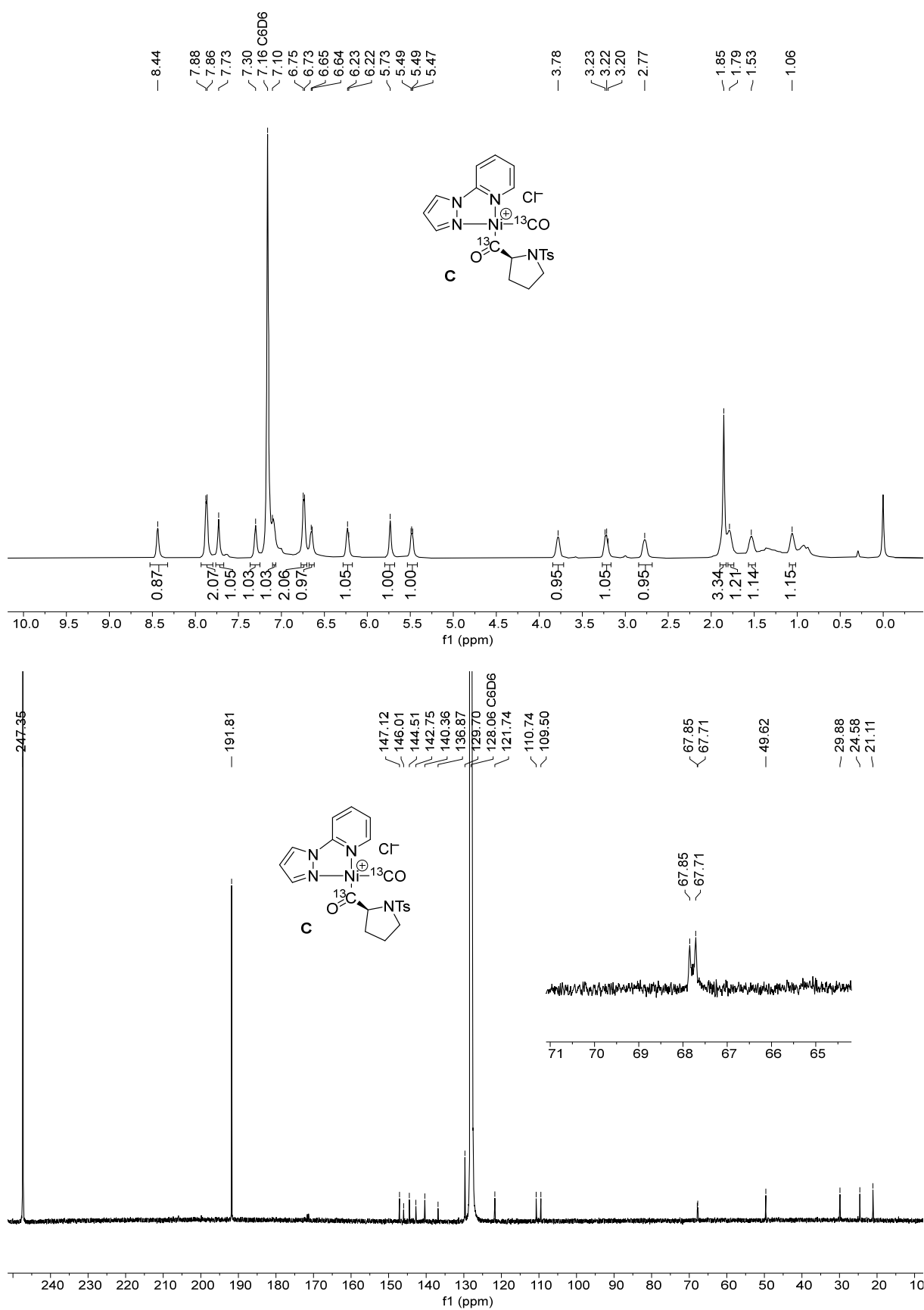
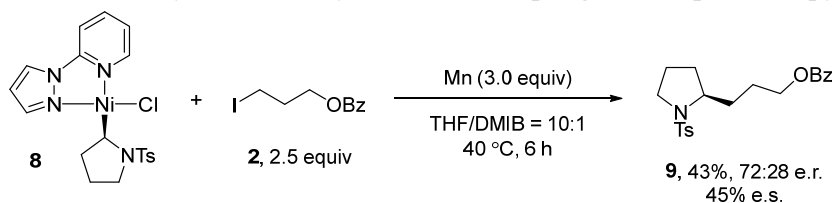


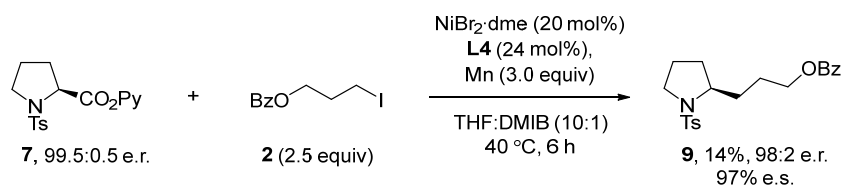
Fig. S4. ¹H NMR (500 MHz, C₆D₆) and ¹³C{¹H} NMR (125 MHz, C₆D₆) spectra for **complex C**.

3.3 Comparison of the stoichiometric and catalytic decarbonylative cross coupling

3.3.1 Stoichiometric and catalytic decarbonylative cross coupling of N-Ts proline 2-pyridyl ester

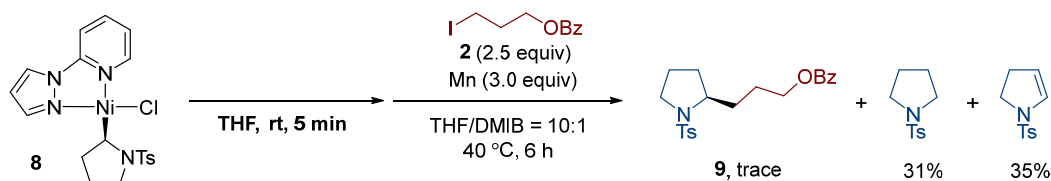


Stoichiometric cross coupling of 8 with 2: In a nitrogen-filled glovebox, a 4 mL vial was charged with **8** (46.4 mg, 0.1 mmol, 1.0 equiv), **2** (72.5 mg, 0.25 mmol, 2.5 equiv), Mn (16.5 mg, 0.3 mmol, 3.0 equiv), THF/DMIB (10:1, 0.5 mL), and a PTFE-coated stirbar. The vial was sealed tightly with a screw cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 °C for 6 h. After the specified reaction time, the reaction mixture was removed from the hotplate, and allowed to cool to rt, diluted with ethyl acetate (4 mL), and passed through a pad of silica gel. The vial and pad were washed with ethyl acetate (4 mL). The filtrate was concentrated in vacuo. The crude product was analyzed by NMR and SFC with 1,3,5-trimethoxybenzene as internal standard, β -hydride eliminated, protonated, and cross-coupling products were detected. The filtrate was concentrated in vacuo and purified by column chromatography to give the desired product **9** in 43% isolated yield (72:28 e.r., 45% e.s.).



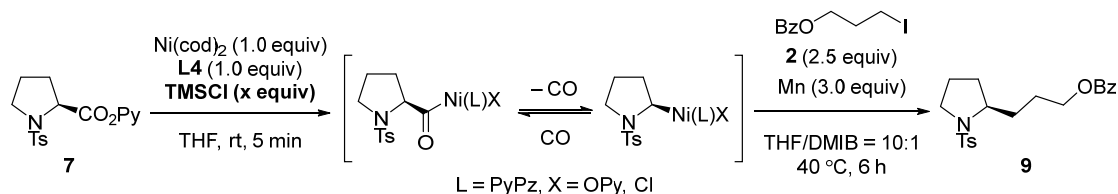
Catalytic decarbonylative cross coupling of 7 with 2: In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added $\text{NiBr}_2 \cdot \text{dme}$ (6.2 mg, 0.02 mmol), **L4** (3.5 mg, 0.024 mmol), and THF/DMIB (10:1, 0.5 mL). This mixture was stirred at rt for 10 min. To this vial was added **7** (34.6 mg, 0.1 mmol, 1.0 equiv), **2** (72.5 mg, 0.25 mmol, 2.5 equiv), and Mn (16.5 mg, 0.3 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 °C for 6 h. After the specified reaction time, the reaction mixture was removed from the hotplate, and was allowed to cool to rt, diluted with ethyl acetate (2 mL), and passed through a pad of silica gel. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired product **9** in 14% isolated yield (98:2 e.r., 97% e.s.).

3.3.2 Observation of the decomposition of complex **8**



In a nitrogen-filled glovebox, a 4 mL vial was charged with **8** (46.4 mg, 0.1 mmol, 1.0 equiv), THF (0.5 mL), and a PTFE-coated stirbar, the resulting mixture was stirred at rt for 5 min. After that, to the mixture was added **2** (72.5 mg, 0.25 mmol, 2.5 equiv), Mn (16.5 mg, 0.3 mmol, 3.0 equiv), and DMIB (50 μ L). The vial was sealed tightly with a screw cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 $^{\circ}$ C for 6 h. After the specified reaction time, the reaction mixture was removed from the hotplate, and allowed to cool to rt, diluted with ethyl acetate (4 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (4 mL). The crude mixture was analyzed by SFC, β -hydride eliminated and protonated side products were detected. The filtrate was concentrated in vacuo. The residue was analyzed by NMR with 1,3,5-trimethoxybenzene as internal standard, protonated and β -hydride eliminated side products were detected in 31% and 35% yield, respectively. Only trace amount of **9** was detected by NMR.

3.3.3 X-type ligand effect of stoichiometric cross coupling of N-Ts proline 2-pyridyl ester

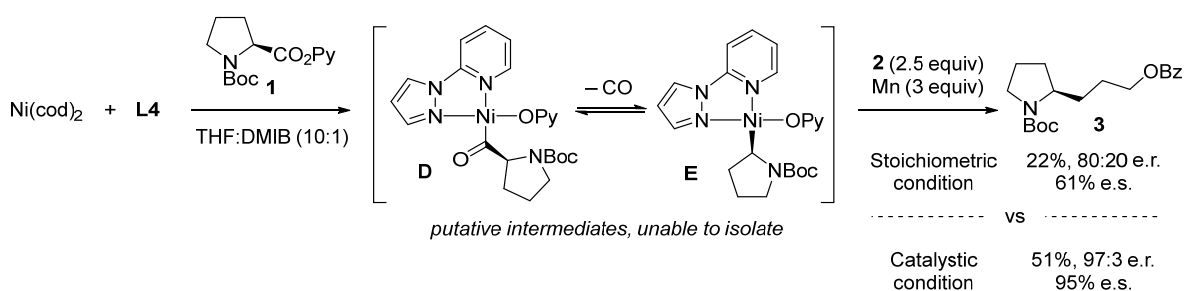


Entry	x equiv of TMSCl	yield (%)	e.r.	e.s.
1	0	13	97.5:2.5	97
2	1.0	10	79.5:20.5	60

Step-wise stoichiometric decarbonylative cross coupling with or without TMSCl: In an N_2 filled glovebox, $Ni(cod)_2$ (55.0 mg, 0.2 mmol) and **L4** (29.0 mg, 0.2 mmol) were dissolved in THF (1 mL) in a 4 mL vial containing a PTFE-coated stirbar. The resulting deep blue (**L4**) $Ni(cod)$ solution was stirred for 5 min at rt and cooled to 0 $^{\circ}$ C. To this vial was added pyridyl ester **7** (69.3 mg, 0.2 mmol) and TMSCl (21.7 mg, 0.2 mmol, for the condition with 1.0 equiv of TMSCl, entry 2 only). The resulting solution was stirred at rt for 5 min before adding **2** (145 mg, 0.5 mmol, 2.5 equiv), Mn (33 mg, 0.6 mmol, 3.0 equiv), and DMIB (100 μ L). The vial was sealed tightly with a screw cap fitted with a PTFE septum before being removed from

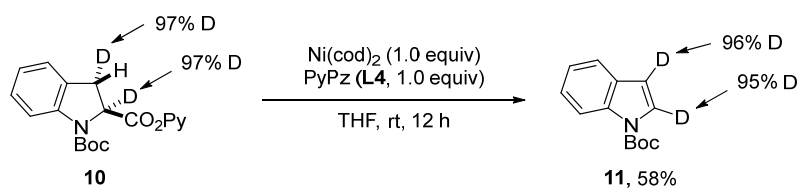
the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 °C for 6 h. After the specified reaction time, the reaction mixture was removed from the hotplate, and allowed to cool to rt, diluted with ethyl acetate (4 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (4 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired product **9**. The reaction without TMSCl formed compound **9** in 13% yield (97.5:2.5 e.r., 97% e.s.); the reaction with 1.0 equiv of TMSCl formed compound **9** in 10% yield (79.5:20.5 e.r., 60% e.s.). This data indicates that Cl anion greatly affects the enantiospecificity of stoichiometric decarbonylative cross coupling.

3.3.4 Stoichiometric and catalytic decarbonylative cross coupling of N-Boc proline 2-pyridyl ester



Step-wise stoichiometric decarbonylative cross coupling of **1 with **2**:** In an N₂ filled glovebox, Ni(cod)₂ (55.0 mg, 0.2 mmol) and **L4** (29.0 mg, 0.2 mmol) were dissolved in THF (1 mL) in a 4 mL vial containing a PTFE-coated stirbar. The resulting deep blue (**L4**)Ni(cod) solution was stirred for 5 min at rt and cooled to 0 °C. To this vial was added pyridyl ester **1** (58.4 mg, 0.2 mmol). The resulting solution was stirred at rt for 5 min before adding **2** (145 mg, 0.5 mmol, 2.5 equiv), Mn (33 mg, 0.6 mmol, 3.0 equiv), and DMIB (100 μL). The vial was sealed tightly with a screw cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 °C for 6 h. After the specified reaction time, and allowed to cool to rt, 1,3,5-trimethoxybenzene (TMB) was added as internal standard for GC analysis and the mixture was diluted with ethyl acetate (3 mL). A portion (0.2 mL) of the resulting mixture was passed through a pad of silica gel to remove excess Mn and insoluble salts, and the pad was washed with ethyl acetate (5 mL). The filtration was analyzed by GC (calibrated GC yield vs 1,3,5-trimethoxybenzene as internal standard) and SFC (e.r. vs the corresponding racemic samples as references), giving the desired product **3** in 22% GC yield (80:20 e.r., 61% e.s.). Ketone **4** was observed as the major side product in 27% GC yield. In comparison, the corresponding catalytic condition (c.f. **Table S2**) gave the desired product **3** in 51% GC yield (97:3 e.r., 95% e.s.).

3.4 β -hydride elimination of deuterium-labeled 2-pyridyl ester



β -hydride elimination under the stoichiometric condition: In an N_2 filled glovebox, Ni(cod)_2 (55.0 mg, 0.2 mmol) and **L4** (29.0 mg, 0.2 mmol) were dissolved in THF (2 mL) in a 4 mL vial containing a PTFE-coated stirbar. To this vial was added pyridyl ester **10** (68.4 mg, 0.2 mmol). The vial was sealed tightly with a screw cap fitted with a PTFE septum, and the solution was stirred at rt for 12 h. After that, the mixture was diluted with ethyl acetate (2 mL) and passed through a pad of silica gel. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the product *tert*-butyl 1H-indole-1-carboxylate-2,3-*d*₂ (**11**) (colorless oil, 25.2 mg, 58% yield). ^1H NMR (500 MHz, CDCl_3) δ 8.24 – 8.09 (m, 1H), 7.62 (s, 0.05H), 7.60 – 7.54 (m, 1H), 7.36 – 7.29 (m, 1H), 7.28 – 7.21 (m, 1H), 6.58 (s, 0.04H), 1.69 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 149.9, 135.3, 130.6, 125.7 (t, $J_{\text{CD}} = 27.5$ Hz), 124.3, 122.7, 121.0, 115.3, 107.0 (t, $J_{\text{CD}} = 26.6$ Hz), 83.7, 28.3.

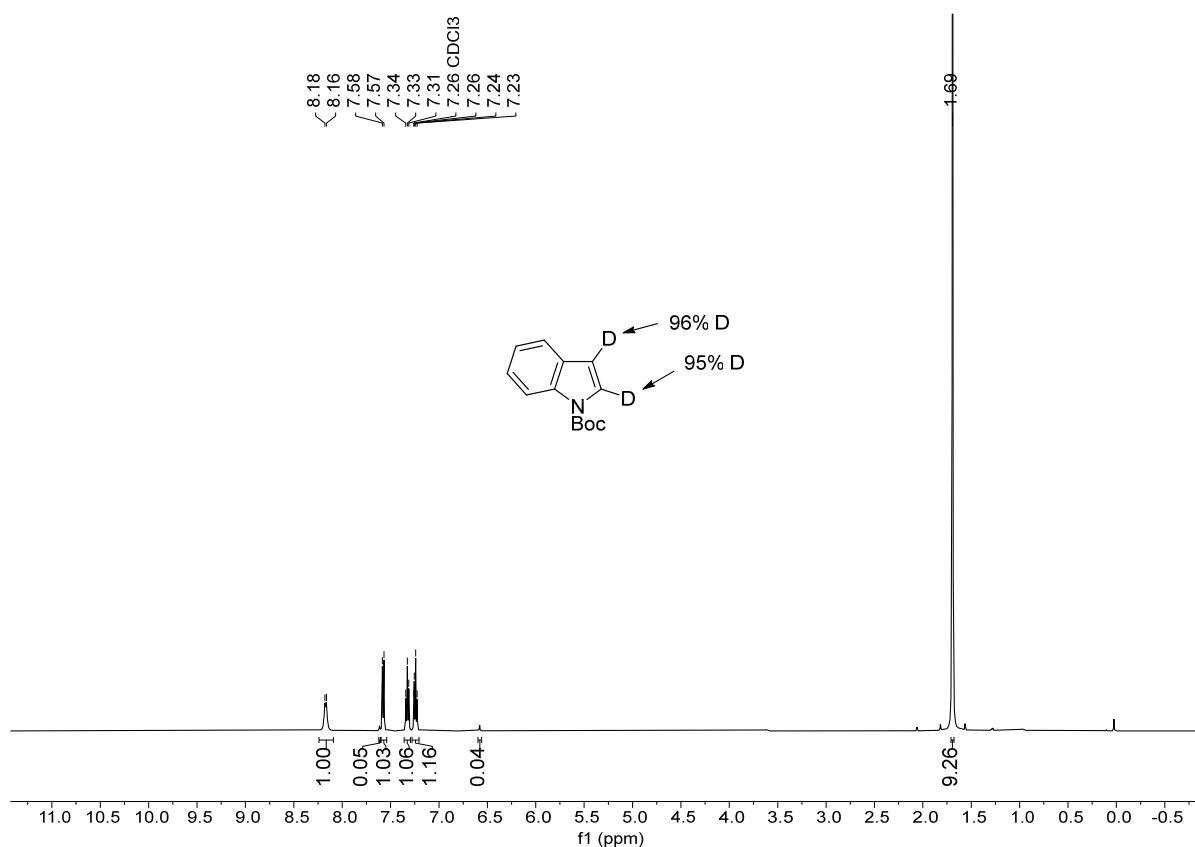


Fig. S5. ^1H NMR (500 MHz, CDCl_3) spectrum of **11**

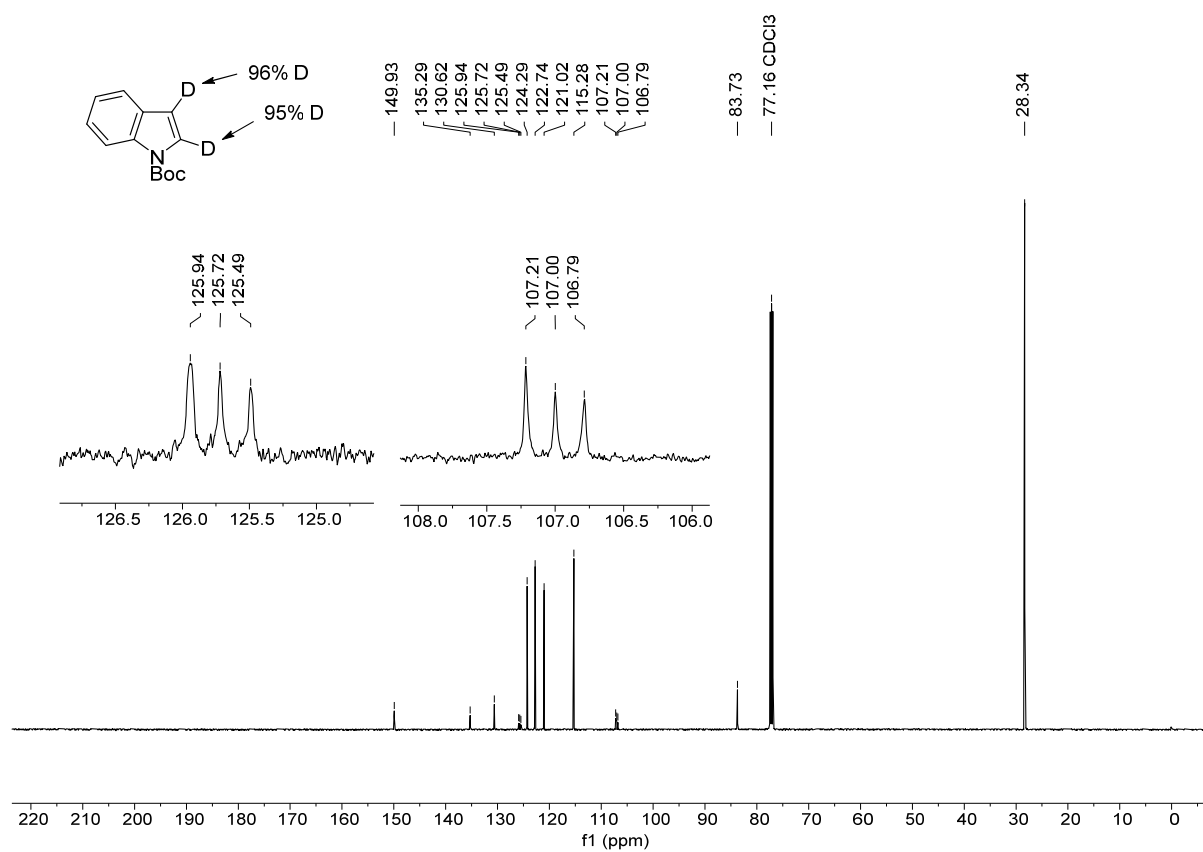
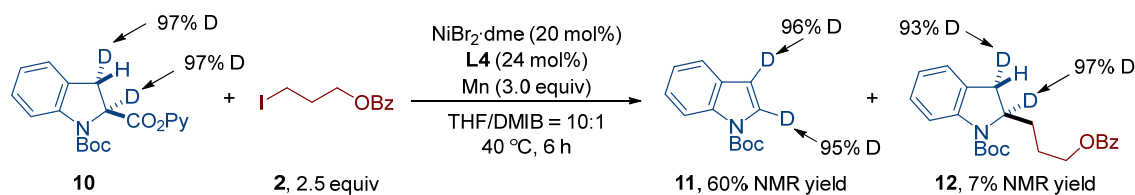


Fig. S6. $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) spectrum of **11**



β-hydride elimination under the catalytic conditions In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added NiBr₂·dme (12.4 mg, 0.04 mmol, 20 mol%), L4 (7.0 mg, 0.048 mmol, 24 mol%), and THF/DMIB (10:1, 0.5 mL). This mixture was stirred at rt for 10 min. To this vial was added **10** (68.4 mg, 0.2 mmol, 1.0 equiv), **2** (145.0 mg, 0.5 mmol, 2.5 equiv), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum and stirred (800 RPM) at 40 °C for 6 h. After the specified reaction time, the reaction mixture was removed from the hotplate, and was allowed to cool to rt, diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired product **11** in 60% NMR yield (39.1 mg, colorless oil, mixture with propyl benzoate as impurity), and cross-coupling product **12** in 7% NMR yield (6.4 mg, colorless oil, mixture with 4-oxoheptane-1,7-diyl dibenzoate (**5**) as impurity). NMR yields were corrected by integration ratio. **tert-butyl (2R,3S)-2-(3-(benzoyloxy)propyl)indoline-1-carboxylate-2,3-*d*2 (12)**. ¹H NMR (500 MHz, CDCl₃) δ 8.09 – 7.97 (m, 2H), 7.80 – 7.40 (br, 1H, overlapped), 7.60 – 7.50 (m, 1H), 7.48 – 7.38 (m, 2H), 7.22 – 7.06 (m, 2H), 6.99 – 6.90 (m, 1H), 4.62 – 4.42 (m, 0.03H), 4.33 (t, *J* = 6.2 Hz, 2H), 3.39 – 3.27 (m, 0.07H), 2.81 – 2.68 (m, 1H), 1.94 – 1.87 (m, 1H), 1.86 – 1.71 (m, 3H), 1.55 (s, 9H). HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₃H₂₆D₂NO₄⁺: 384.2138, found: 384.2131.

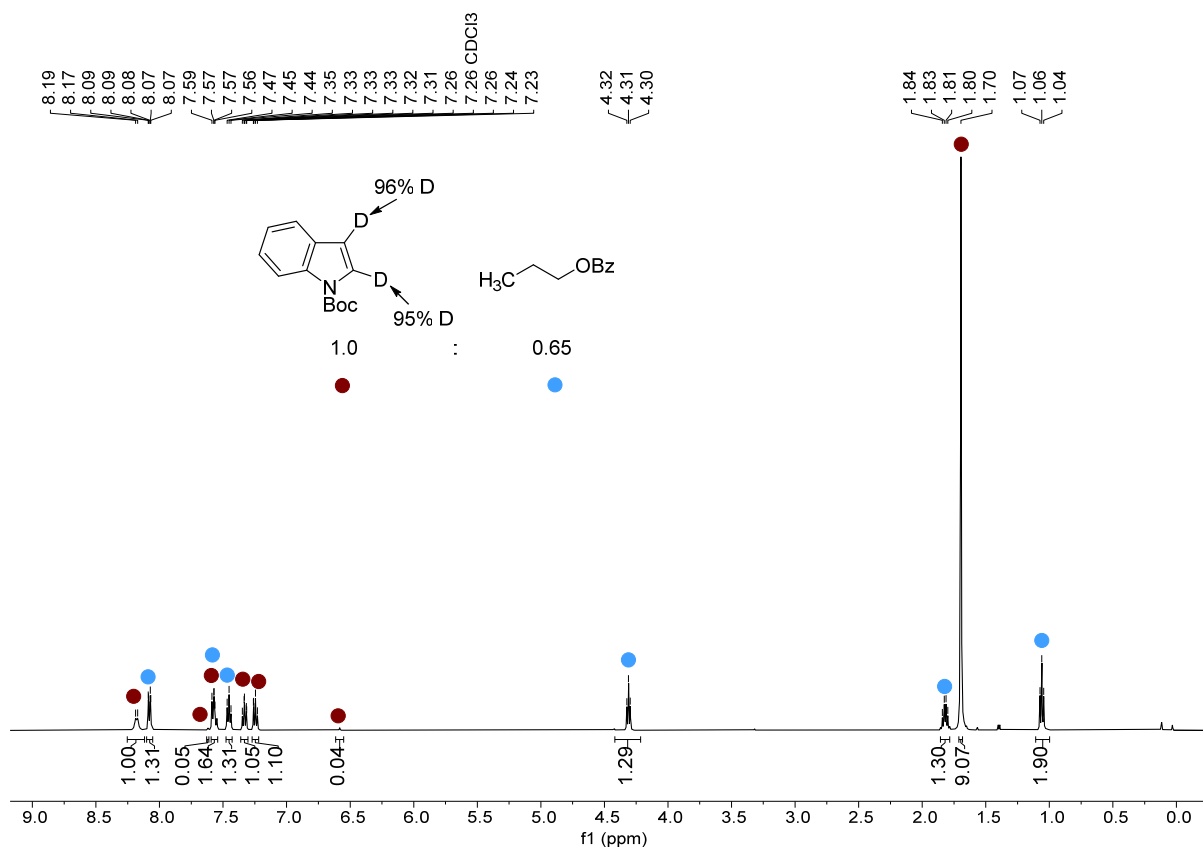


Fig. S7. ¹H NMR (500 MHz, CDCl₃) spectrum of **11** with propyl benzoate as impurity

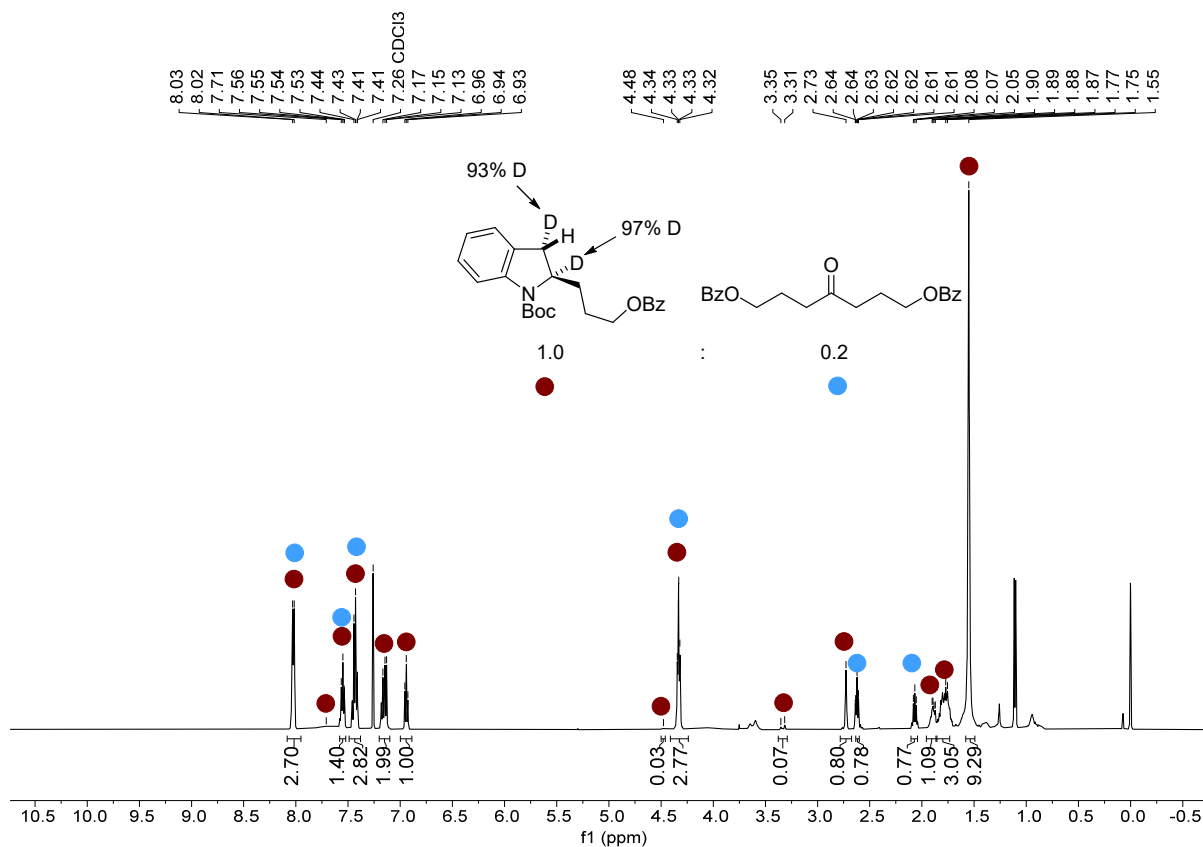
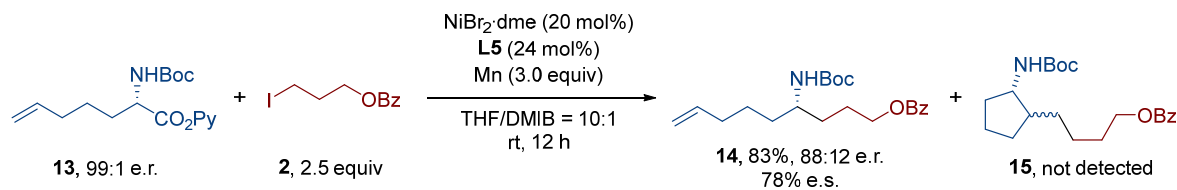


Fig. S8. ¹H NMR (500 MHz, CDCl₃) spectrum of **12** with 4-oxoheptane-1,7-diyl dibenzoate (**5**)

3.5 Radical clock experiments

3.5.1 Catalytic radical clock experiments



In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added $\text{NiBr}_2 \cdot \text{dme}$ (12.4 mg, 0.04 mmol, 20 mol%), **L5** (9.6 mg, 0.048 mmol, 24 mol%), and THF/DMIB (10:1, 0.5 mL). This mixture was stirred at rt for 10 min. To this vial was added 2-pyridyl ester **13** (64.1 mg, 0.2 mmol, 1.0 equiv), alkyl iodides **2** (145.0 mg, 0.5 mmol, 2.5 equiv), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The reaction mixture was stirred (800 RPM) at rt for 12 h. After the specified reaction time, the reaction mixture was diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the direct cross-coupling products **14** in 83% isolated yield. All the coupling products were collected, no radical cyclization products were detected, see Section 3.5.3 for proposed mechanism. (*S*)-4-((*tert*-butoxycarbonyl)amino)non-8-en-1-yl benzoate (**14**) (colorless oil, 60.0 mg, 83% yield, 88:12 e.r., 78% e.s.). ^1H NMR (500 MHz, CDCl_3) δ 8.08 – 8.03 (m, 2H), 7.61 – 7.53 (m, 1H), 7.50 – 7.41 (m, 2H), 5.86 – 5.73 (m, 1H), 5.09 – 4.99 (m, 1H), 4.99 – 4.92 (m, 1H), 4.45 – 4.07 (m, 1H), 4.34 (t, J = 6.6 Hz, 2H) 3.72 – 3.44 (m, 1H), 2.14 – 2.01 (m, 2H), 1.93 – 1.76 (m, 2H), 1.71 – 1.61 (m, 1H), 1.53 – 1.35 (m, 5H), 1.46 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 166.7, 155.8, 138.6, 133.0, 130.5, 129.7, 128.4, 114.8, 79.1, 65.0, 50.4, 35.2, 33.7, 32.3, 28.5, 25.5, 25.3. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{21}\text{H}_{32}\text{NO}_4^+$: 362.2326, found: 362.2319. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO_2 , v = 0.6 mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (minor) = 7.060 min (12%), tR (major) = 7.280 min (88%).

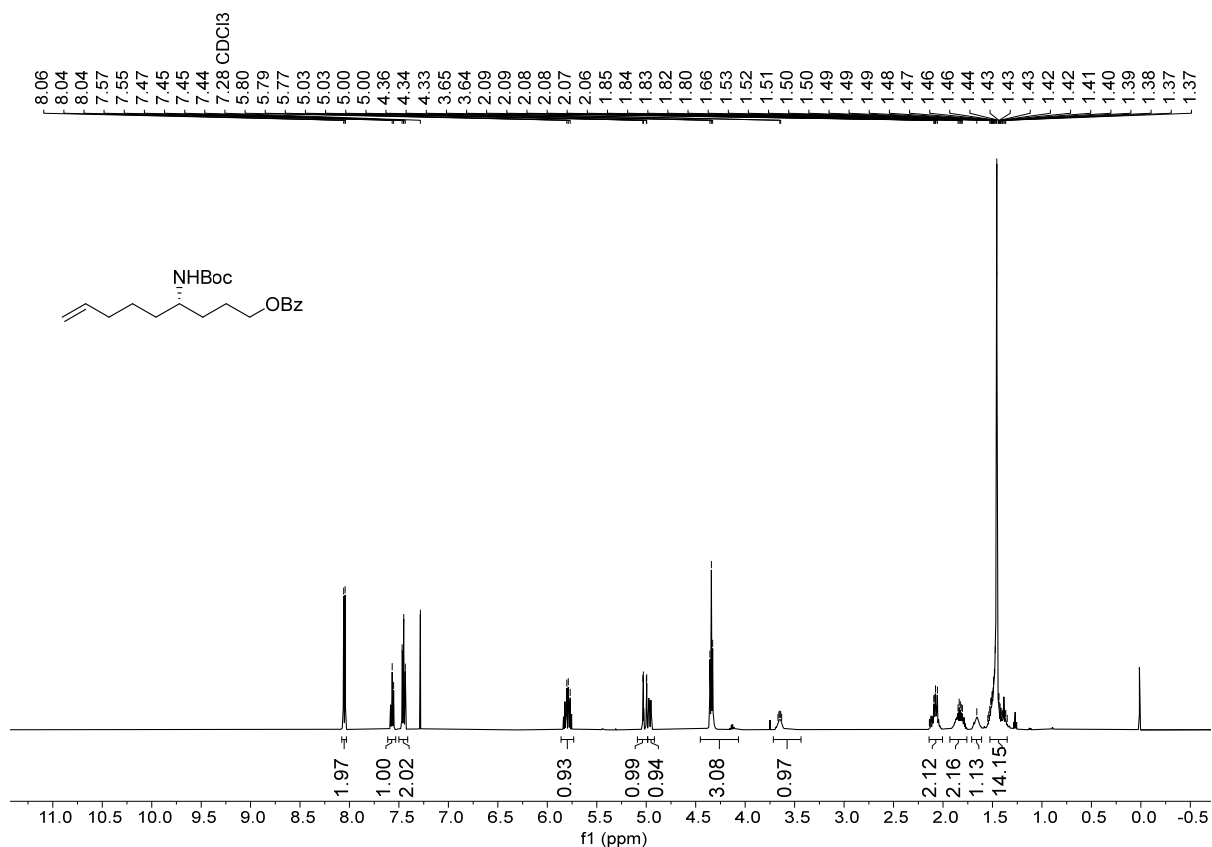


Fig. S9. ¹H NMR (500 MHz, CDCl₃) spectrum of **14**

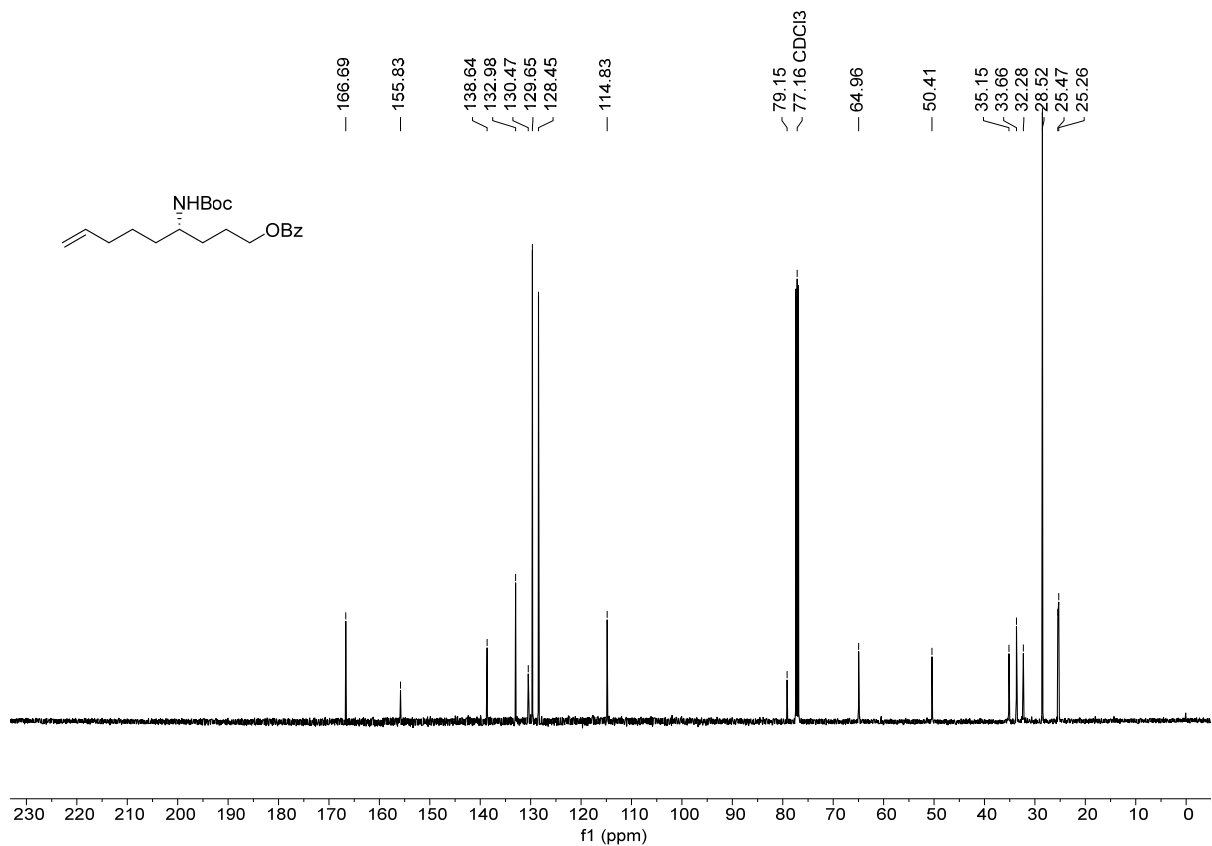
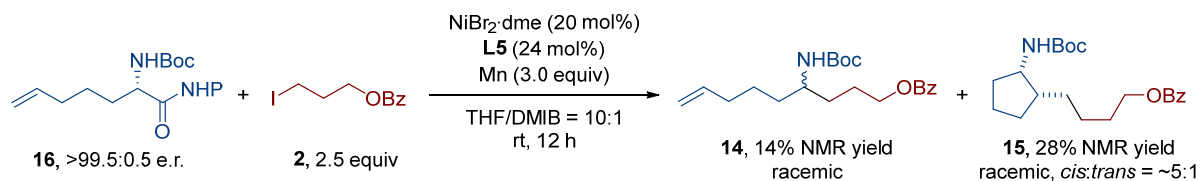


Fig. S10. ¹³C{¹H} NMR (125 MHz, CDCl₃) spectrum of **14**



Catalytic reaction: In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added $\text{NiBr}_2 \cdot \text{dme}$ (12.4 mg, 0.04 mmol, 20 mol%), **L5** (9.6 mg, 0.048 mmol, 24 mol%), and THF/DMIB (10:1, 0.5 mL). This mixture was stirred at rt for 10 min. To this vial was added NHP ester **16** (77.6 mg, 0.2 mmol, 1.0 equiv, >99.5:0.5 e.r.), alkyl iodides **2** (145.0 mg, 0.5 mmol, 2.5 equiv), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The reaction mixture was stirred (800 RPM) at rt for 12 h. After that, the reaction mixture was diluted with EtOAc (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography (hexane/EtOAc). The combined mixture of **14** and **15** was collected and analyzed by NMR and SFC. The NMR analysis indicated that cross-coupling products **14** and radical cyclization product **15** were formed in 1:2 ratio. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO_2 , $v = 0.6 \text{ mL/min}$, 40 $^\circ\text{C}$, 2200 psi, t_R (**14**) = 7.096 min (19.1%), 7.322 min (19.8%); t_R (*cis*-**15**) = 8.914 min (25.2%), 9.177 min (24.4%); t_R (*trans*-**15**) = 9.509 min (5.7%), 10.127 min (5.9%). **Further purification of 15:** The mixture of **14** and **15** was dissolved with acetone (5 mL) and transferred to a 20 mL vial charged with a PTFE-coated stirbar and KMnO_4 (50 mg). The resulting mixture was stirred at rt for 2 h. After that, the reaction mixture was diluted with ethyl acetate (5 mL), and passed through a pad of silica gel. The vial and pad were washed with EtOAc (10 mL). The filtrate was concentrated in vacuo. The residue was further purified by column chromatography to give the cyclization product **15** as colorless oil (22.0 mg, 28% NMR yield, *cis:trans* = 5:1, with ~2% of **14** as impurity). The ratio of diastereomers refers to the characteristic peaks (δ 4.0 ppm for *cis*-1,2-disubstituted cyclopentyl, δ 3.5 ppm for *trans*-1,2-disubstituted cyclopentyl, see Section 3.5.3 for proposed mechanism)^{2,3}. The NMR yields were corrected by integration ratio. **4-(2-((*tert*-butoxycarbonyl)amino)cyclopentyl)butyl benzoate (15)** ^1H NMR (500 MHz, CDCl_3) δ 8.17 – 7.95 (m, 2H), 7.67 – 7.51 (m, 1H), 7.47 – 7.39 (m, 2H), 4.44 – 4.25 (m, 1H), 4.31 (t, $J = 6.7 \text{ Hz}$, 2H), 4.04 (br, 0.83H, *cis* isomer), 3.56 (br, 0.17H, *trans* isomer), 2.12 – 1.73 (m, 5H), 1.72 – 1.57 (m, 2H), 1.54 – 1.47 (m, 4H) 1.44 (s, 9H), 1.33 – 1.17 (m, 2H). HRMS (ESI) m/z ($\text{M}+\text{H}$)⁺ calcd for $\text{C}_{21}\text{H}_{32}\text{NO}_4$ ⁺: 362.2326, found: 362.2319.

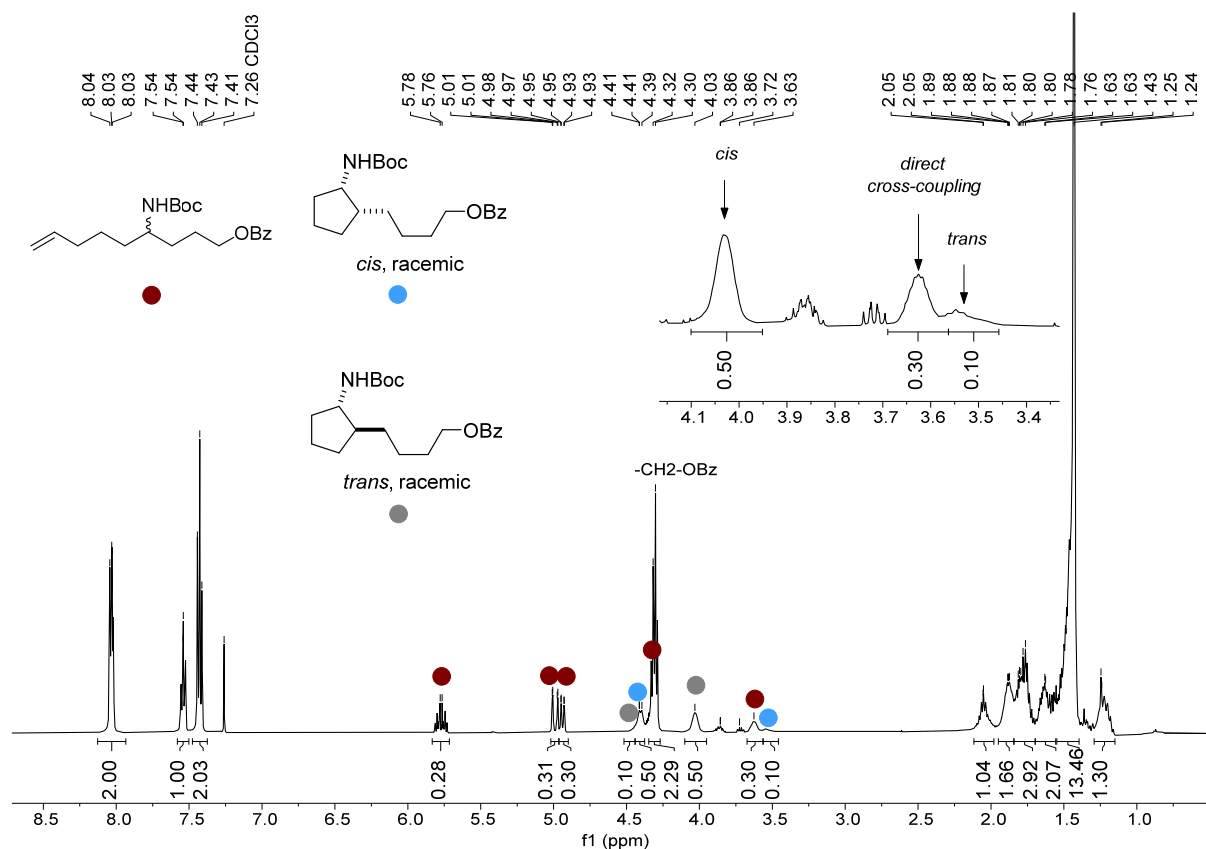


Fig. S11. ¹H NMR (500 MHz, CDCl₃) spectrum of mixture of **14** and **15**

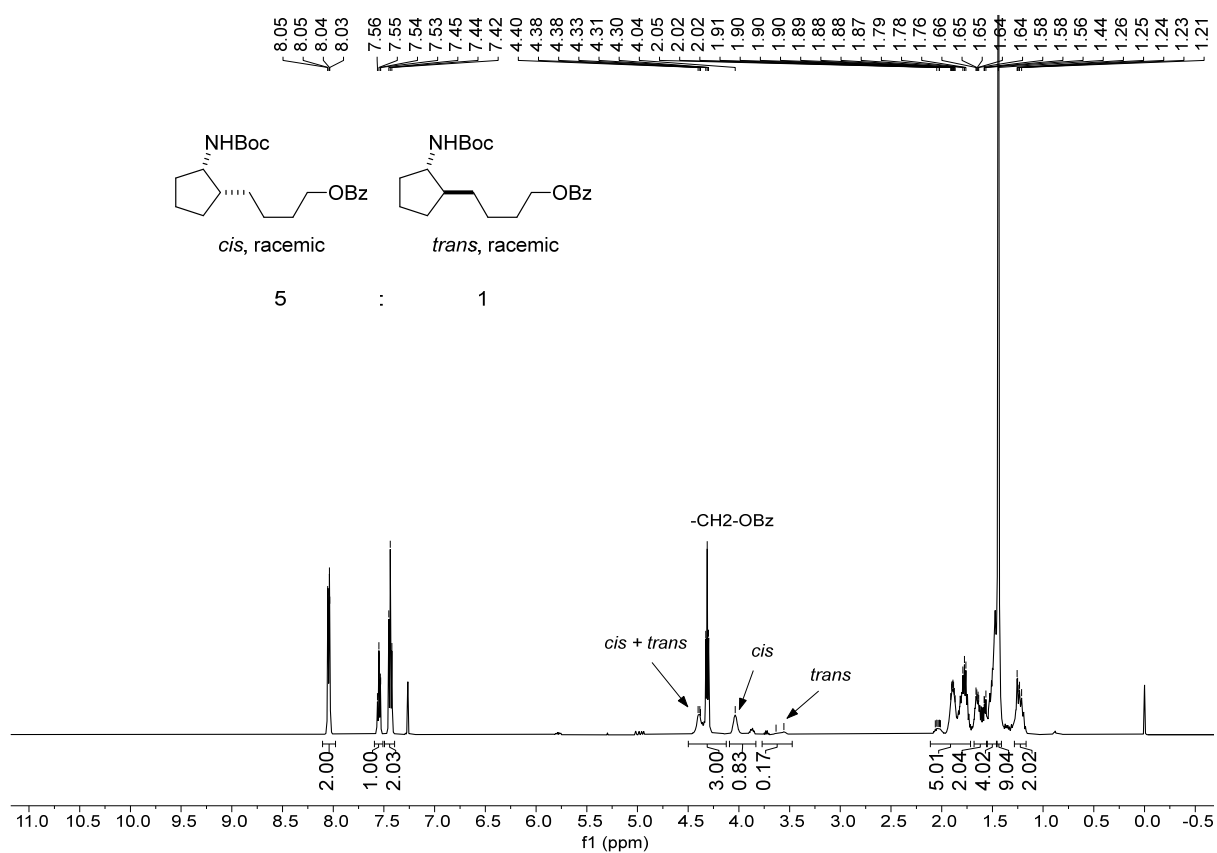
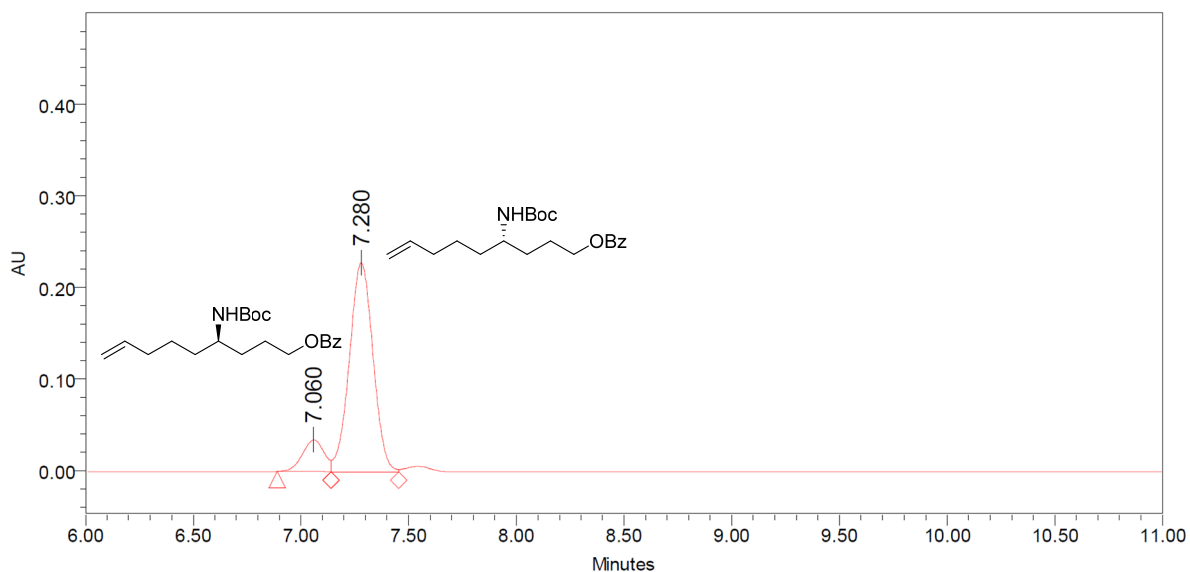
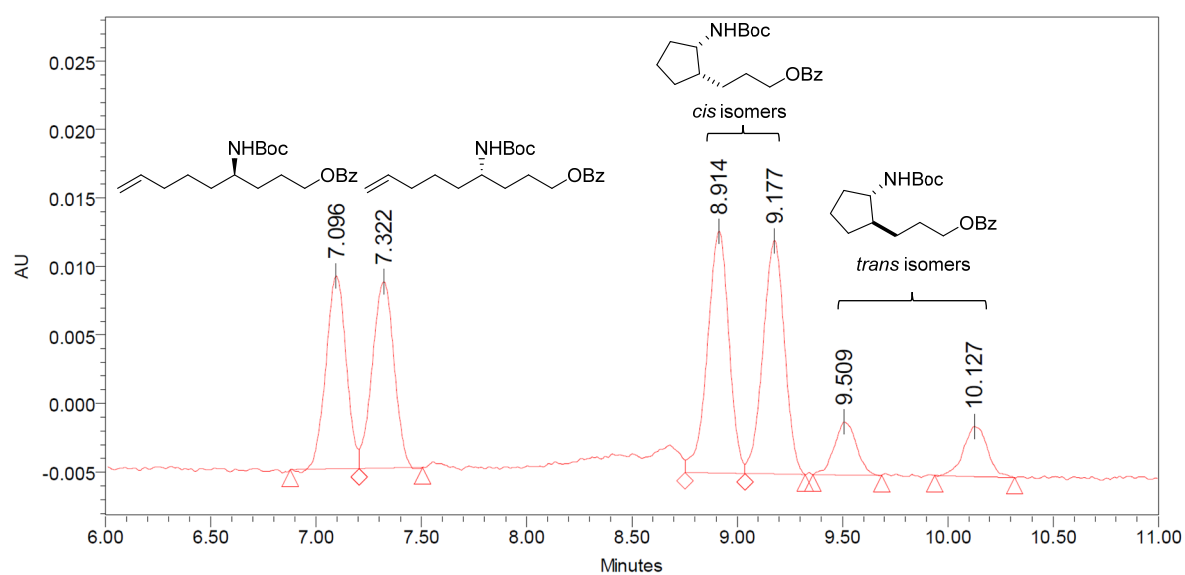


Fig. S12. ¹H NMR (500 MHz, CDCl₃) spectrum of **15**



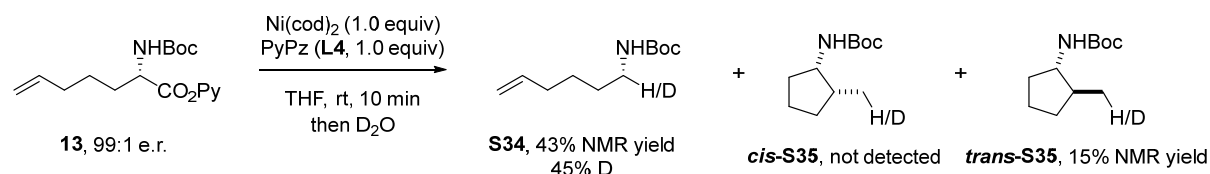
	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 225.8 nm (PDA Spectrum (190-410)nm)	7.060	34374	238801	12.07
2	PDA Spectrum PDA 225.8 nm (PDA Spectrum (190-410)nm)	7.280	227922	1740165	87.93



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 225.8 nm (PDA Spectrum (190-410)nm)	7.096	14083	94853	19.08
2	PDA Spectrum PDA 225.8 nm (PDA Spectrum (190-410)nm)	7.322	13611	98216	19.75
3	PDA Spectrum PDA 225.8 nm (PDA Spectrum (190-410)nm)	8.914	17649	125301	25.20
4	PDA Spectrum PDA 225.8 nm (PDA Spectrum (190-410)nm)	9.177	17049	121400	24.41
5	PDA Spectrum PDA 225.8 nm (PDA Spectrum (190-410)nm)	9.509	3884	28412	5.71
6	PDA Spectrum PDA 225.8 nm (PDA Spectrum (190-410)nm)	10.127	3669	29066	5.85

Fig. S13. SFC analysis of **14** and **15**

3.5.2 Stoichiometric radical clock experiments



In an N₂ filled glovebox, Ni(cod)₂ (55.0 mg, 0.2 mmol, 1.0 equiv) and **L4** (29.0 mg, 0.2 mmol, 1.0 equiv) were dissolved in THF (2 mL) in a 4 mL vial containing a PTFE-coated stirbar. To this vial was added pyridyl ester **13** (64.1 mg, 0.2 mmol, 1.0 equiv). The resulting solution was stirred at rt for 10 min before adding D₂O (0.2 mL, 10 mmol, 50 equiv). 1,3,5-trimethoxybenzene was added as internal standard and the mixture was diluted with EtOAc (2 mL) and passed through a pad of silica gel. The vial and pad were washed with EtOAc (2 mL). The filtrate was concentrated in vacuo. The residue was analyzed by NMR. Protonated and deuterated product **S34** were observed in 43% NMR yield with 45% deuterium incorporation. The cyclization product *trans*-**S35** was observed in 15% NMR yield, but the *cis*- isomer was not detected. The NMR data matched reported spectra². The *trans* diastereoselectivity indicates a Ni-C insertion mechanism, which distinguishes this reaction from radical pathways, see Section 3.5.3 for proposed mechanism.

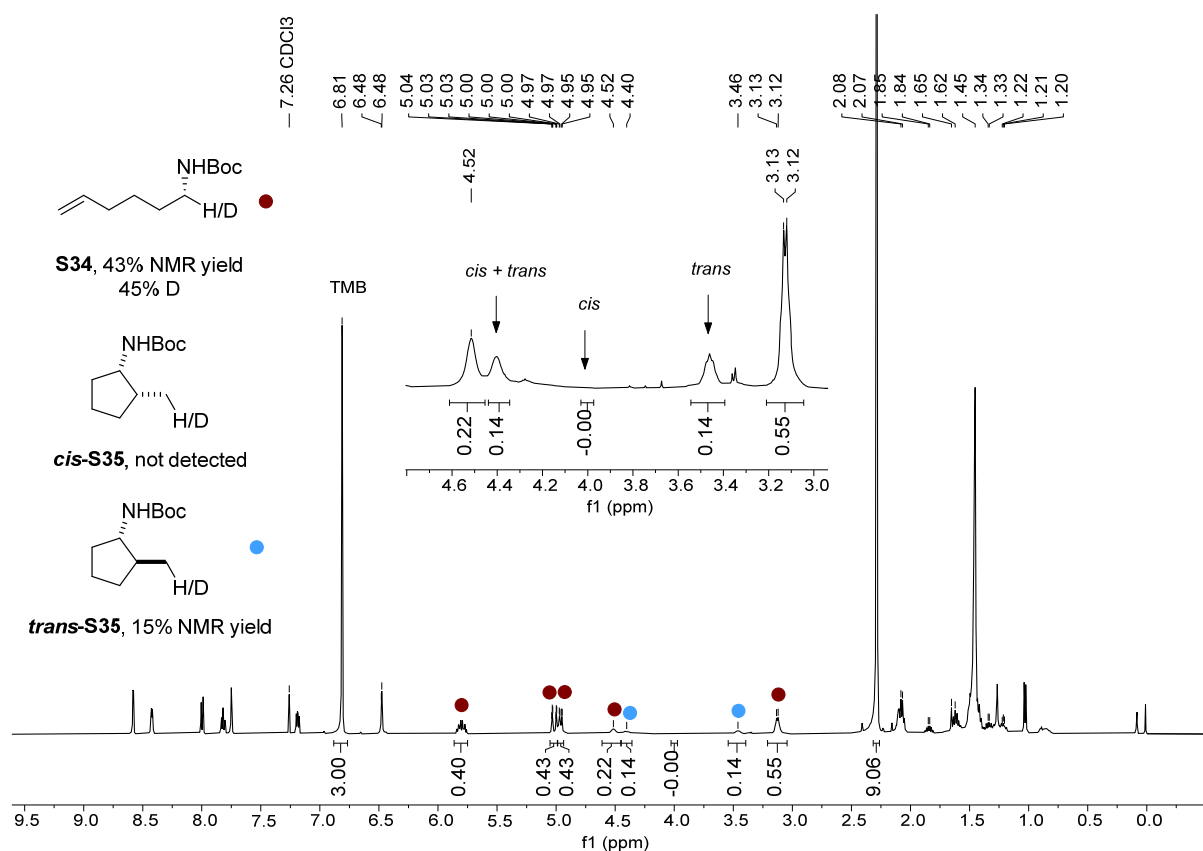
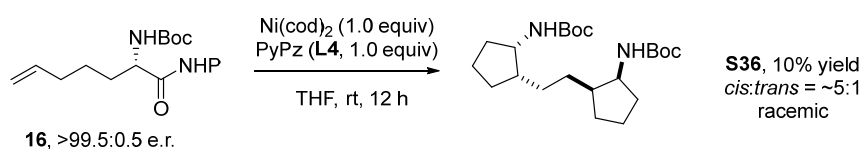


Fig. S14. NMR analysis of **S34** and **S35**



In an N₂ filled glovebox, Ni(cod)₂ (27.5 mg, 0.1 mmol, 1.0 equiv) and **L4** (14.5 mg, 0.1 mmol, 1.0 equiv) were dissolved in THF (1 mL) in a 4 mL vial containing a PTFE-coated stirbar. To this vial was added NHP ester **16** (38.8 mg, 0.1 mmol, 1.0 equiv). The resulting solution was stirred at rt for 12 h. The mixture was diluted with ethyl acetate (2 mL) and passed through a pad of silica gel to remove the nickel salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the dimerization products **S36** in 10% isolated yield (3.8 mg, colorless oil). The product contains mixture of diastereomers, the ratio of *cis:trans* = ~5:1 refers to the characteristic peaks (δ 4.0 ppm for *cis*-1,2-disubstituted cyclopentyl, δ 3.5 ppm for *trans*-1,2-disubstituted cyclopentyl)^{2,3}. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₂H₄₁N₂O₄⁺: 397.3061, found: 397.3056. This comparison experiment showed that the NHP ester formed *cis*-cyclization product by radical pathway, see Section 3.5.3 for proposed mechanism.

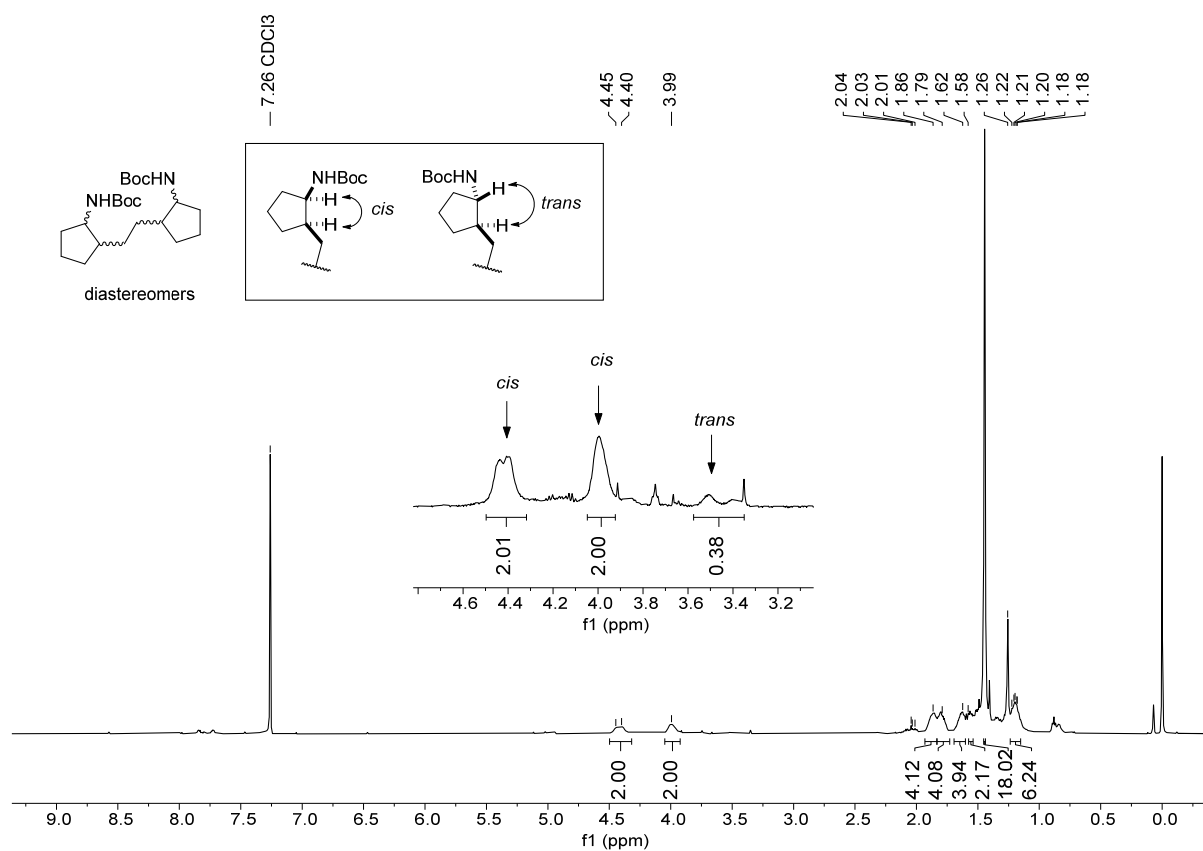
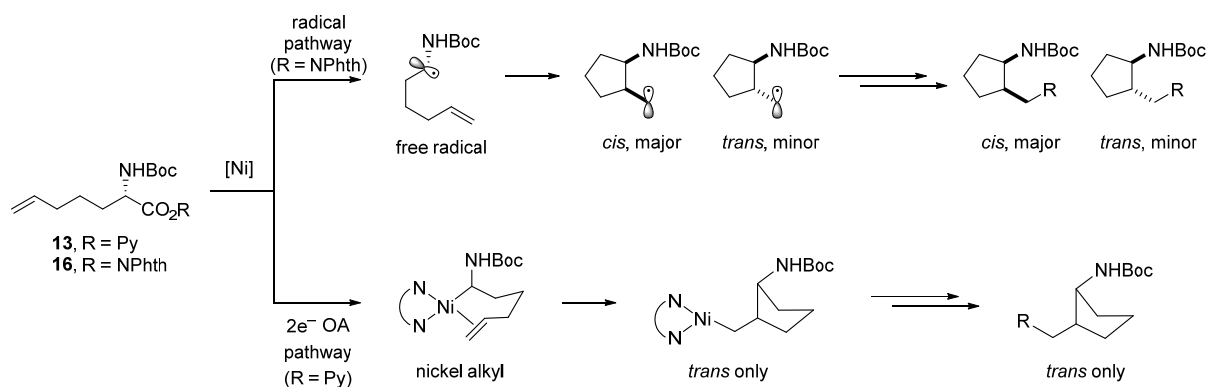


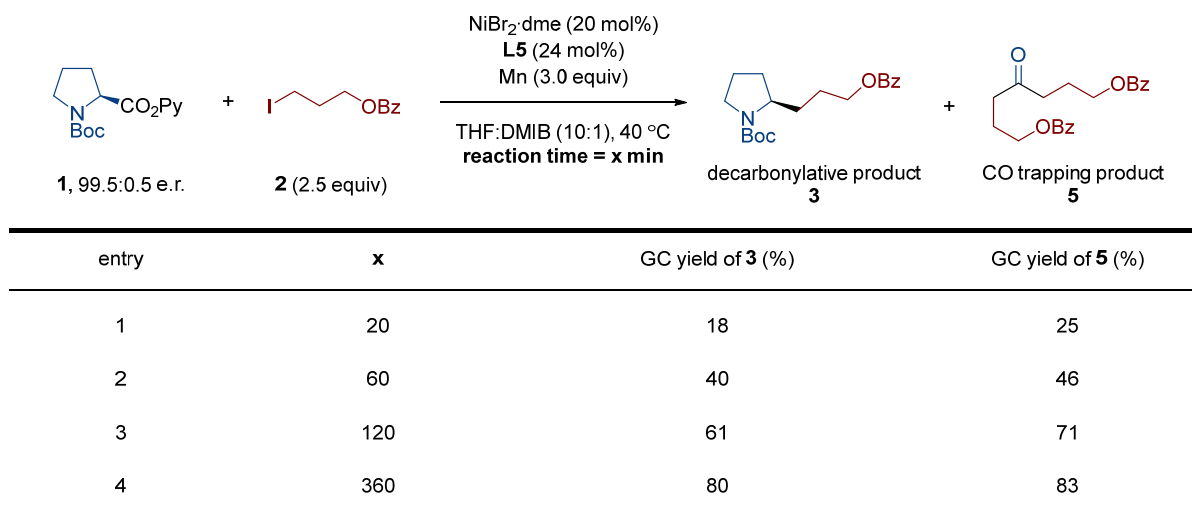
Fig. S15. NMR analysis of **S36**

3.5.3 Proposed mechanism for the radical clock experiments



Under both stoichiometric and catalytic conditions, reactions with NHP ester formed radical cyclization product with *cis*- products as the major diastereomer. This is consistent with the fact that the cyclization of 1-substituted hex-5-enyl radicals afford mainly *cis*-disubstituted products^{4,5}. In sharp contrast, the reactions with 2-pyridyl esters resulted in no radical cyclization product. Moreover, the cyclization with 2-pyridyl esters under the stoichiometric condition formed the *trans*-diastereomer stereoselectively. This data supports a classic organometallic migratory insertion mechanism: the oxidative addition and decarbonylation sequence forms the key nickel alkyl species, which could coordinate with the terminal alkene, the subsequent insertion of Ni-C to alkene affords the *trans*-disubstituted product stereoselectively⁶⁻⁸. These results clearly exclude the possibility of potential reversible nickel-carbon homolysis to form a carbon-centered radical.

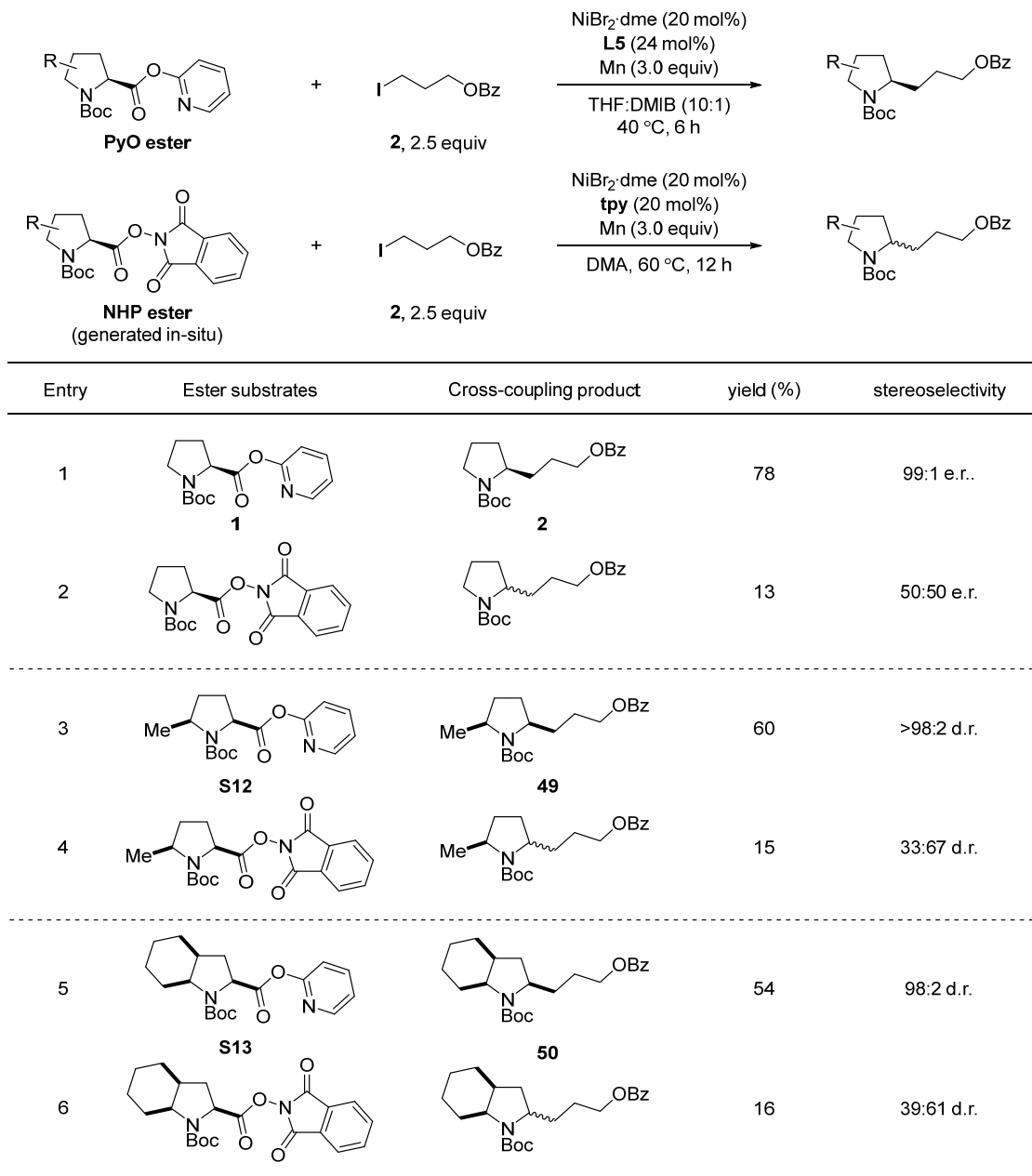
3.6 Data establishing concurrent formation of product and CO trapping product



In a nitrogen-filled glovebox, to 4 mL vials containing PTFE-coated stirbars was added NiBr₂·dme (12.4 mg, 0.04 mmol, 20 mol%), **L5** (9.6 mg, 0.048 mmol, 24 mol%), Mn (0.6 mmol, 3.0 equiv), and THF/DMIB (10:1, 0.5 mL), respectively. The mixture was stirred at rt for 10 min. To these vials were added **1** (58.4 mg, 0.2 mmol, 1.0 equiv), **2** (145 mg, 0.5 mmol, 2.5 equiv). The vials were closed with threaded caps fitted with a PTFE septum before being removed from the glovebox. The vials were placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 °C. The reaction mixture was allowed to cool to rt after listed reaction time, diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). 1,3,5-trimethoxybenzene (0.1 mmol) was added as internal standard for GC analysis. The residue was purified by column chromatography, **4-oxoheptane-1,7-diyl dibenzoate (5)** was isolated as a white solid (entry 4, 46.0 mg, 65%). ¹H NMR (500 MHz, CDCl₃) δ 8.02 – 7.99 (m, 4H), 7.57 – 7.51 (m, 2H), 7.45 – 7.39 (m, 4H), 4.33 (t, *J* = 6.3 Hz, 4H), 2.60 (t, *J* = 7.2 Hz, 4H), 2.15 – 2.00 (m, 4H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 208.7, 166.6, 133.1, 130.3, 129.7, 128.5, 64.2, 39.3, 23.0. The NMR data matched reported spectra⁹. Based on GC analysis, the yields of CO trapping product **5** (vs **1** as limiting reagent) increases in proportion to the formation of decarbonylative product **3**.

3.7 Comparison of decarbonylation with decarboxylation

3.7.1 Decarbonylative cross coupling *versus* decarboxylative cross coupling of NHP esters with alkyl iodides

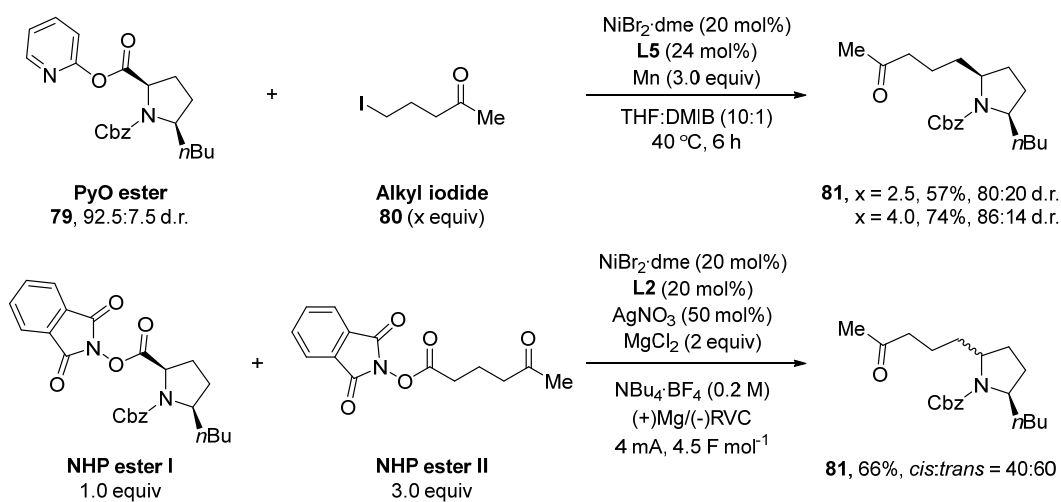


Decarbonylative cross coupling of 2-pyridyl esters following general procedure A (see section S5 for detail).

Decarboxylative cross coupling of NHP esters with alkyl iodides following a modified procedure in previously reported literature¹⁰: In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added NiBr₂·dme (12.4 mg, 0.04 mmol, 20 mol%), tpy (**L1**, 9.3 mg, 0.04 mmol, 20 mol%), and DMA (1 mL). This mixture was stirred at rt for 2 h. To this vial was added the listed NHP ester (0.2 mmol, 1.0 equiv), **2** (145.0 mg, 0.5 mmol, 2.5 equiv), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a

threaded cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 60 °C for 12 h. After the specified reaction time, the reaction mixture was allowed to cool to rt, diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired products.

3.7.2 Decarbonylative cross-coupling *versus* doubly decarboxylative cross coupling



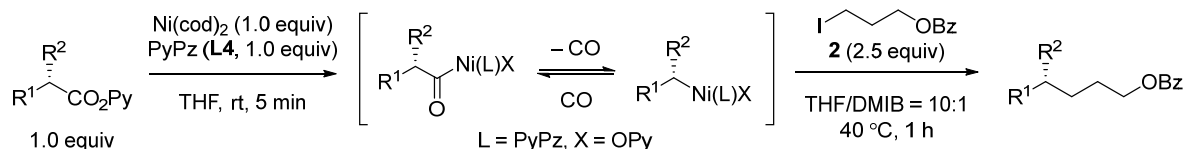
Decarbonylative cross coupling following general procedure A (see section S5 and S7 for detail). In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added NiBr₂·dme (12.4 mg, 0.04 mmol, 20 mol%), L5 (9.6 mg, 0.048 mmol, 24 mol%), and THF/DMIB (10:1, 0.5 mL). This mixture was stirred at rt for 10 min. To this vial was added 2-pyridyl ester (0.2 mmol, 1.0 equiv), 80 (0.5 or 0.8 mmol, 2.5 or 4.0 equiv), and Mn (0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 °C for 6 h. After the specified reaction time, the reaction mixture was removed from the hotplate, and was allowed to cool to rt, diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired products. Result of **doubly decarboxylative cross coupling** of NHP esters was based on the reported literature¹¹.

3.8 Mechanistic investigations into stereoablation

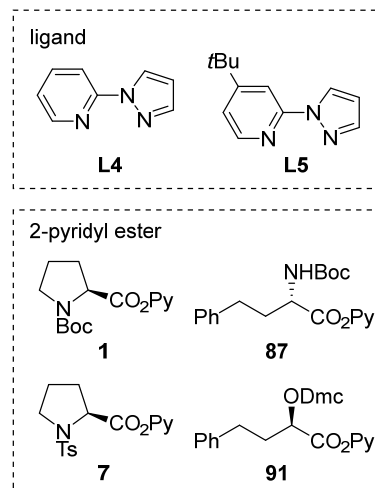
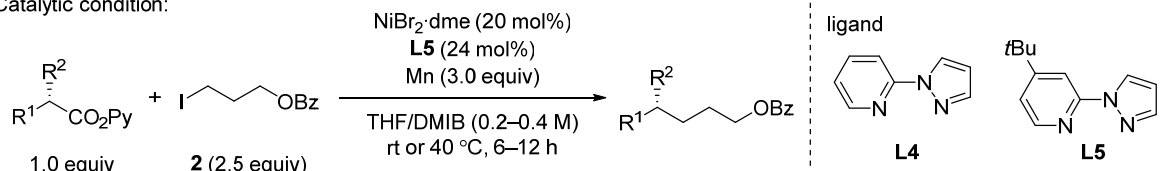
3.8.1 Experimental evidence on stereoablation

Table S10. Comparison experiments of stoichiometric and catalytic cross-coupling

Stoichiometric condition:



Catalytic condition:



entry	2-pyridyl ester	stoichiometric			catalytic		
		yield (%)	e.r.	e.s. (%)	yield (%)	e.r.	e.s. (%)
1	1	28	78:22	57	78	99:1	99
2	7	9	98:2	97	14	98:2	97
3	87	35	53:47	7	69	96.5:3.5	94
4	91	40	99:1	98	65	99.5:0.5	>99

Stoichiometric decarbonylative cross coupling followed a modified procedure without Mn: In an N₂ filled glovebox, Ni(cod)₂ (55.0 mg, 0.2 mmol, 1.0 equiv) and **L4** (29.0 mg, 0.2 mmol, 1.0 equiv) were dissolved in THF (1 mL) in a 4 mL vial containing a PTFE-coated stirbar. The resulting deep blue (**L4**)Ni(cod) solution was stirred for 5 min at rt. To this vial was added 2-pyridyl esters (0.2 mmol, 1.0 equiv). The resulting solution was stirred at rt for 5 min before adding **2** (145 mg, 0.5 mmol, 2.5 equiv) and DMIB (100 μL). The vial was sealed tightly with a screw cap fitted with a PTFE septum before being placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 °C for 1 h. The reaction mixture was allowed to cool to rt after listed reaction time, diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). 1,3,5-trimethoxybenzene was dissolved as internal standard for chiral SFC analysis. The filtrate was concentrated in vacuo. The residue was analyzed by NMR. Note: Mn was not used in these stoichiometric reactions to avoid the influence of Mn salts and the potential reduction of nickel alkyl species.

Data analysis and proposed mechanism: The stoichiometric reactions will have very fast oxidative addition/decarbonylation, but radical generation is not enhanced at the same rate, resulting in more time for the alkylnickel species to isomerize and decompose. As such, β-hydride elimination and reduction products (Alkyl-H) were observed in all these reactions. The stoichiometric reaction of *N*-Boc proline 2-pyridyl ester

(1) resulted in the product with lower e.s. than the catalytic reaction (**Table S10**, entry 1). This can be attributed to radical formation (and, thus, radical capture) being faster under catalytic conditions, resulting in less racemization/decomposition. In contrast, both the stoichiometric and catalytic reactions of *N*-Ts proline 2-pyridyl ester (**7**) formed the product in low yield with high e.s. (**Table S10**, entry 2). We attribute this to slow Ni-H reinsertion to the corresponding β -hydride elimination alkene side product. Acyclic amino acids are also prone to β -hydride elimination, but the Ni-H reinsertion is faster, resulting in racemization under stoichiometric conditions (slow radical capture) but stereoretention under catalytic conditions (fast radical capture, **Table S10**, entry 3). Finally, the Ni-H reinsertion to the *O*-vinyl carbamate generated from α -oxygenated acid 2-pyridyl ester **91** is slow, thus resulting in no loss of stereochemistry under both stoichiometric and catalytic conditions (**Table S10**, entry 4). Our proposed mechanism appears below, and additional experimental evidence is provided in the following sections.

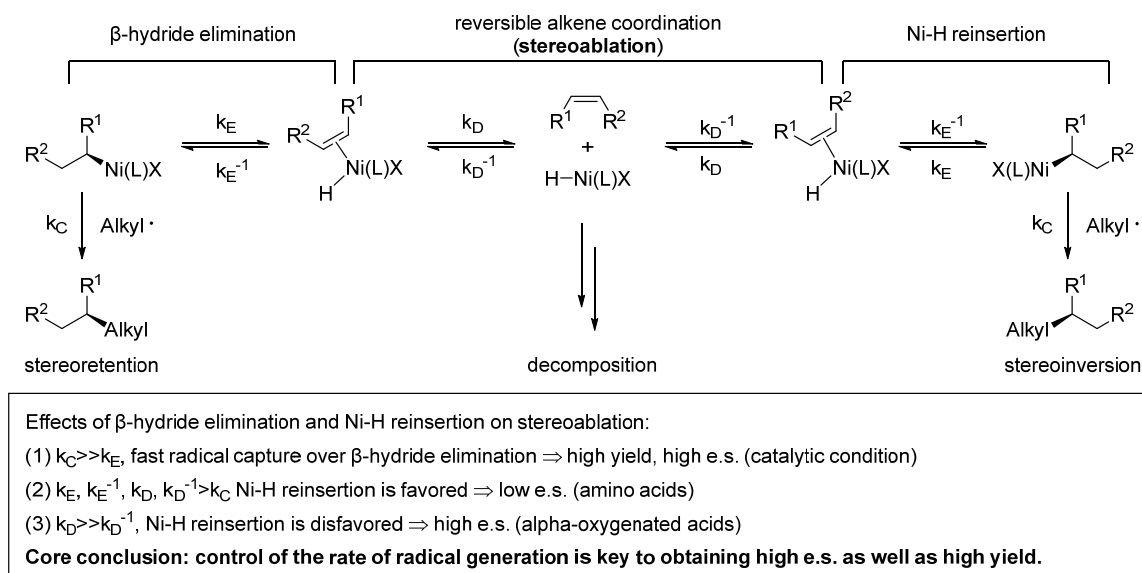
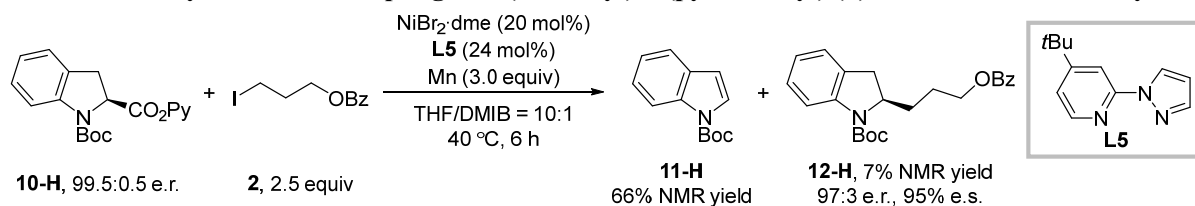


Fig. S16. Proposed mechanism of stereoablation

3.8.2 Decarbonylative cross-coupling of 1-(*tert*-butyl) 2-(pyridin-2-yl) (*S*)-indoline-1,2-dicarboxylate



In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added $\text{NiBr}_2\cdot\text{dme}$ (12.4 mg, 0.04 mmol, 20 mol%), **L5** (9.6 mg, 0.048 mmol, 24 mol%), and THF/DMIB (10:1, 0.5 mL). This mixture was stirred at rt for 10 min. To this vial was added **10-H** (68.1 mg, 0.2 mmol, 1.0 equiv), **2** (145.0 mg, 0.5 mmol, 2.5 equiv), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum and stirred (800 RPM) at 40 °C for 6 h. After the specified reaction time, the reaction mixture was removed from the hotplate, and was allowed to cool to rt, diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired product **11-H** in 66% NMR yield (40.8 mg, colorless oil, mixture with propyl benzoate as impurity), and cross-coupling product **12-H** in 7% NMR yield (6.3 mg, colorless oil, mixture with 4-oxoheptane-1,7-diyl dibenzoate (**5**) as impurity). NMR yields were corrected by integration ratio. *tert*-butyl 1H-indole-1-carboxylate (**11-H**) ^1H NMR (500 MHz, CDCl_3) δ 8.20 – 8.14 (m, 1H), 7.62 (d, J = 3.8 Hz, 1H), 7.60 – 7.52 (m, 1H), 7.36 – 7.29 (m, 1H), 7.28 – 7.21 (m, 1H), 6.58 (d, J = 3.8 Hz, 1H), 1.69 (s, 9H). *tert*-butyl (*R*)-2-(3-(benzyloxy)propyl)indoline-1-carboxylate (**12-H**) ^1H NMR (500 MHz, CDCl_3) δ 8.12 – 7.99 (m, 2H), 7.89 – 7.66 (m, 1H), 7.75 – 7.45 (br, 1H, overlapped), 7.47 – 7.38 (m, 2H), 7.22 – 7.06 (m, 2H), 7.01 – 6.87 (m, 1H), 4.62 – 4.42 (m, 1H), 4.33 (t, J = 6.3 Hz, 2H), 3.39 – 3.27 (m, 1H), 2.80 – 2.70 (m, 1H), 1.95 – 1.87 (m, 1H), 1.86 – 1.71 (m, 3H), 1.55 (s, 9H). HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{23}\text{H}_{28}\text{NO}_4$: 382.2013, found: 382.2007. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 20% MeOH in scCO_2 , tR (minor) = 7.996 min (3.0%), tR (major) = 8.274 min (97.0%).

Compound **10-H** was prone to β -hydride elimination, but the cross-coupling product **12-H** was formed in high e.s., indicating that a fast β -hydride elimination but slow Ni-H reinsertion process would result in low yield but high enantiospecificity

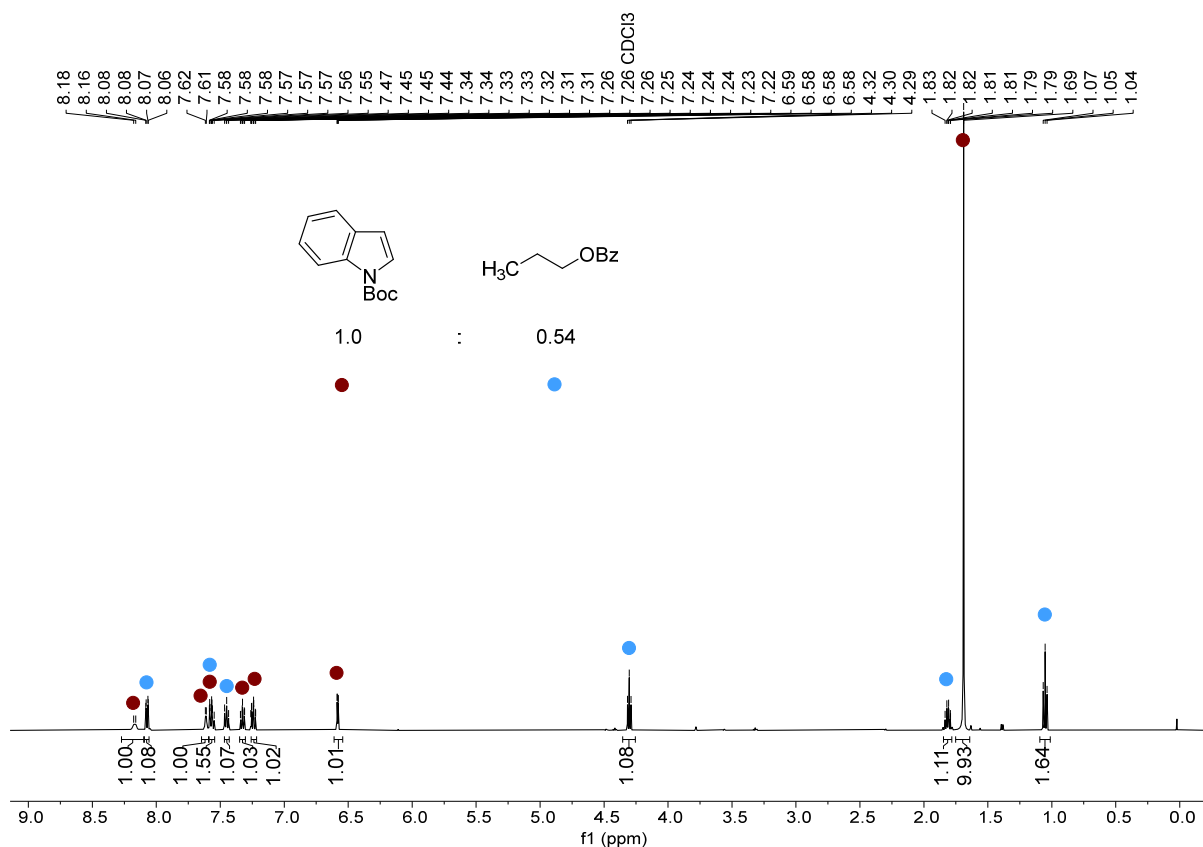


Fig. S17. NMR analysis of 11-H

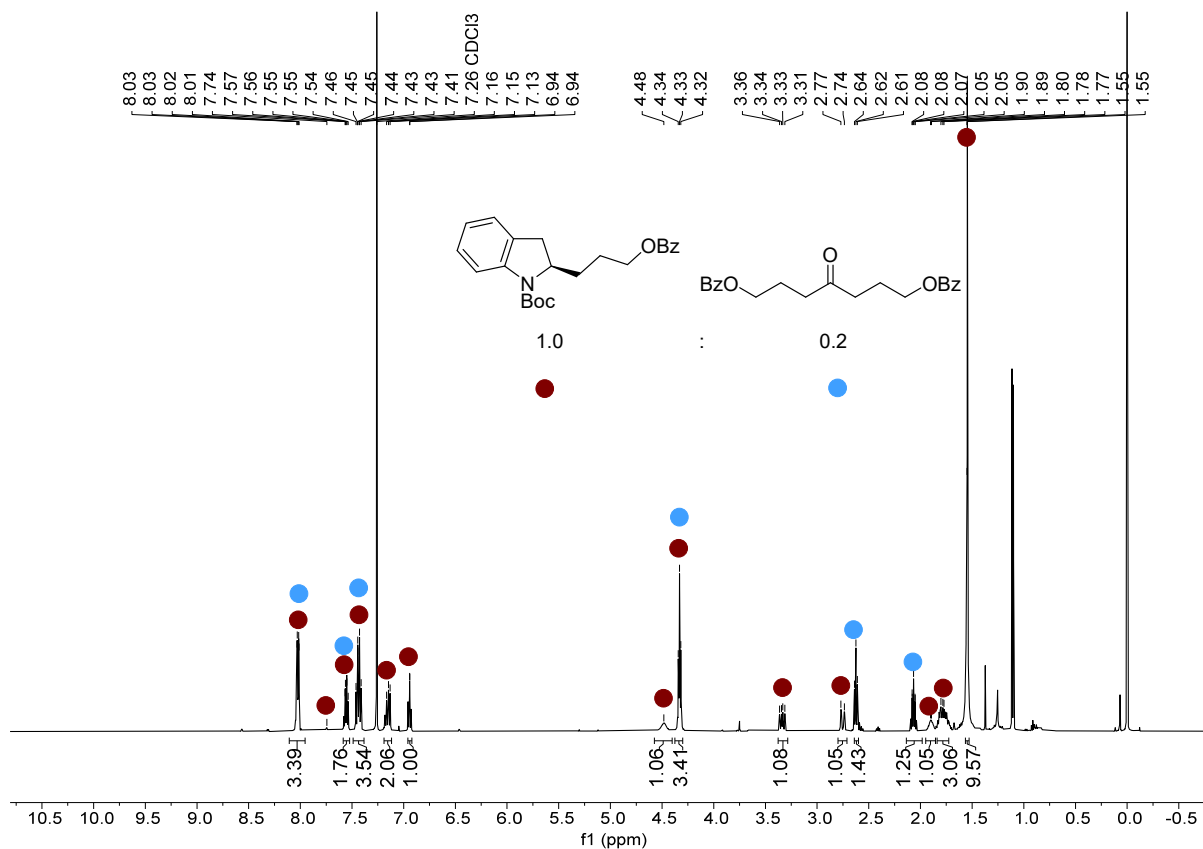
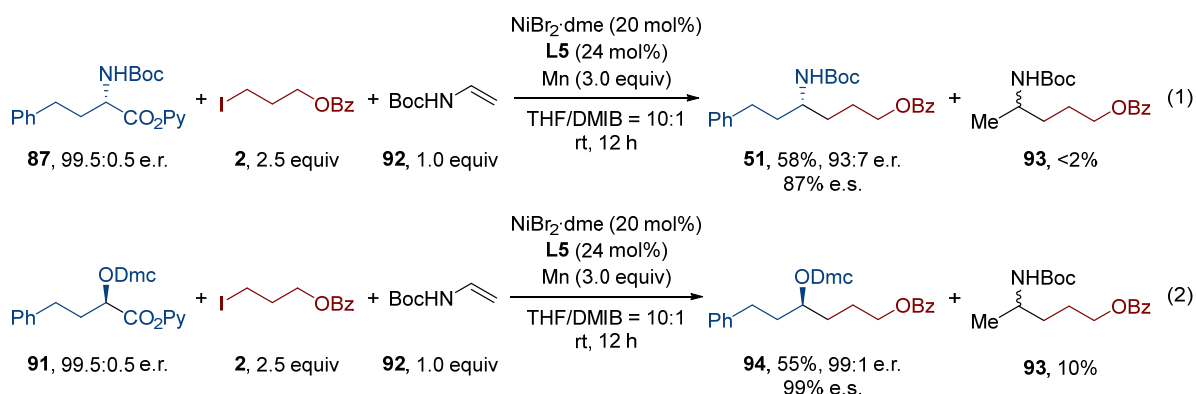


Fig. S18. NMR analysis of 12-H

3.8.3 Competition experiment of Ni-H reinsertion



Comparison of acyclic amino acid 2-pyridyl ester with α -oxygenated acid 2-pyridyl ester: In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added $\text{NiBr}_2\cdot\text{dme}$ (12.4 mg, 0.04 mmol, 20 mol%), **L5** (9.6 mg, 0.048 mmol, 24 mol%), and THF/DMIB (10:1, 1 mL). This mixture was stirred at rt for 10 min. To this vial was added 2-pyridyl ester **87** or **91** (0.2 mmol, 1.0 equiv), alkyl iodides **2** (145.0 mg, 0.5 mmol, 2.5 equiv), *tert*-butyl vinylcarbamate **92** (28.6 mg, 0.2 mmol, 1.0 equiv), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The reaction mixture was stirred (800 RPM) at rt for 12 h. After the specified reaction time, the reaction mixture was diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was combined and concentrated in vacuo. The residue was analyzed by NMR and chiral SFC with 1,3,5-trimethoxybenzene as internal standard and purified by column chromatography. NMR yields are shown.

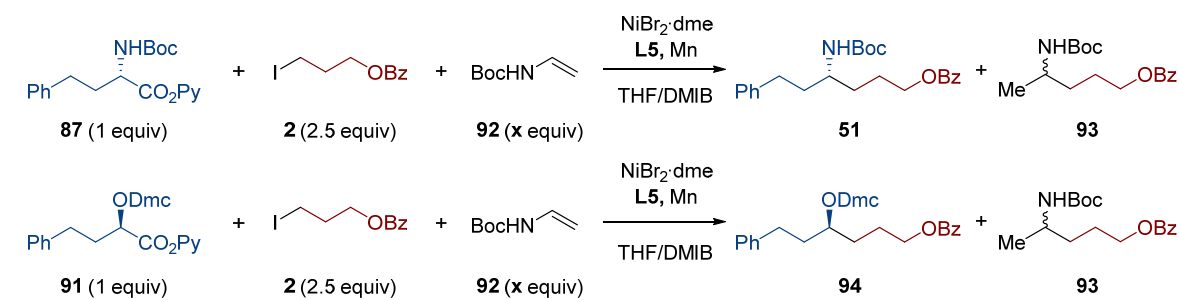
(S)-4-((*tert*-butoxycarbonyl)amino)pentyl benzoate (93) ^1H NMR (500 MHz, CDCl_3) δ 8.06 – 8.01 (m, 2H), 7.58 – 7.52 (m, 1H), 7.47 – 7.40 (m, 2H), 4.33 (t, J = 6.3 Hz, 2H), 4.46 – 4.04 (m, 1H), 3.72 (s, 1H), 1.90 – 1.73 (m, 2H), 1.61 – 1.51 (m, 2H), 1.44 (s, 9H), 1.15 (d, J = 6.6 Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 166.7, 155.5, 133.0, 130.5, 129.7, 128.5, 79.3, 64.9, 46.5, 34.0, 28.6, 25.6, 21.5. HRMS (ESI) m/z ($\text{M}+\text{H}^+$) calcd for $\text{C}_{17}\text{H}_{26}\text{NO}_4^+$: 308.1856, found: 308.1853.

(R)-4-((dimethylcarbamoyl)oxy)-6-phenylhexyl benzoate (94) ^1H NMR (500 MHz, CDCl_3) δ 8.06 – 8.02 (m, 2H), 7.60 – 7.52 (m, 1H), 7.47 – 7.41 (m, 2H), 7.30 – 7.25 (m, 2H), 7.21 – 7.15 (m, 3H), 4.96 – 4.88 (m, 1H), 4.33 (t, J = 6.4 Hz, 2H), 2.91 (s, 3H), 2.89 (s, 3H), 2.75 – 2.61 (m, 2H), 2.02 – 1.92 (m, 1H), 1.92 – 1.80 (m, 3H), 1.80 – 1.73 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 166.7, 156.6, 141.9, 133.0, 130.5, 129.7, 128.5, 128.5, 128.4, 126.0, 74.4, 64.9, 36.6, 36.3, 35.9, 31.9, 31.1, 24.8. HRMS (ESI) m/z ($\text{M}+\text{H}^+$) calcd for $\text{C}_{22}\text{H}_{18}\text{NO}_4^+$: 370.2013, found: 370.2006. SFC analysis: Daicel Chiralpak IA-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 1%

to 3% MeOH in scCO₂, tR (minor) = 7.671 min (1%), tR (major) = 8.065 min (99%).

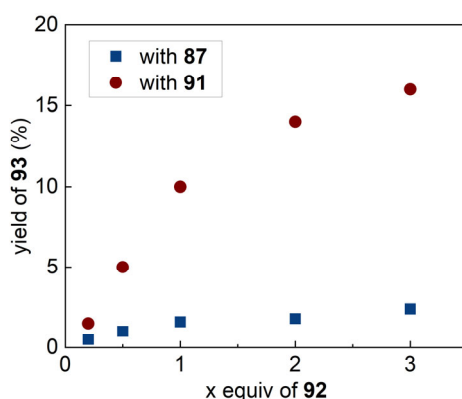
Only a <2% yield of Ni-H reinsertion product **93** was detected in the reaction with **87** (eq 1), but a 10% yield of **93** was observed from the reaction with **91** (eq 2). This data is consistent with the hypothesis that β -hydride elimination is possible for both substrates, but Ni-H reinsertion of acyclic *N*-alkenyl carbamate (β -hydride elimination product of acyclic amino acid derivatives) is more favorable than *O*-alkenyl carbamate (β -hydride elimination product of α -oxygenated acid 2-pyridyl ester).

A series of competition experiments using different concentrations of *O*-*tert*-butyl *N*-vinylcarbamate (**92**) were conducted (Fig. S19) and in both cases an increase in crossover product **93** was observed with additional **92**. Corrected SFC yields with 1,3,5-TMB as internal standard are shown. As the amount of **92** added was increased from 0.2 equiv to 3.0 equiv, the yield of **93** increased from 0.5% to 2.4% in the reactions with **87**. In the reactions with **91**, As the amount of **92** added was increased from 0.2 equiv to 3.0 equiv, the yield of **93** increased from 1.5% to 16%. These results indicate that β -hydride elimination is possible for both amino acid and α -oxygenated acid 2-pyridyl esters, but the β -hydride elimination product of the former exhibits slower dissociation and/or faster Ni-H reinsertion than the latter with alkenyl carbamate moieties.



entry	x	reaction with 87				reaction with 91			
		yield (%) of 93	yield (%) of 51	e.r.	e.s. (%)	yield (%) of 93	yield (%) of 94	e.r.	e.s. (%)
1	0.2	0.5	57	93.5:6.5	88	1.5	56	99.5:0.5	99
2	0.5	1	58	93:7	87	5	53	99.5:0.5	99
3	1	1.6	58	93:7	87	10	55	99.5:0.5	99
4	2	1.8	56	93:7	87	14	54	99.5:0.5	99
5	3	2.4	54	92.5:7.5	86	16	52	99.5:0.5	99

Condition: 2-pyridyl ester (0.2 mmol, 1.0 equiv), alkyl iodide (2.5 equiv) NiBr₂·dme (20 mol%), **L5** (24 mol%), Mn (3.0 equiv), THF/DMIB (10:1, 0.2 M), rt, 12 h. SFC yield using 1,3,5-trimethoxybenzene as internal standard are shown.



Proposed mechanism:

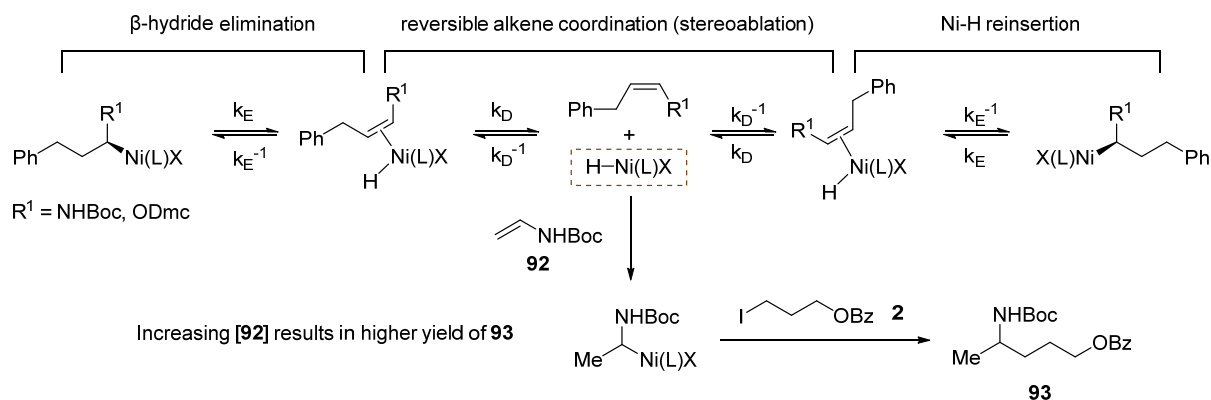
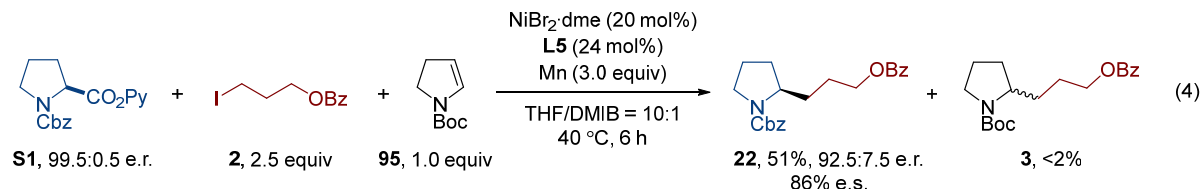
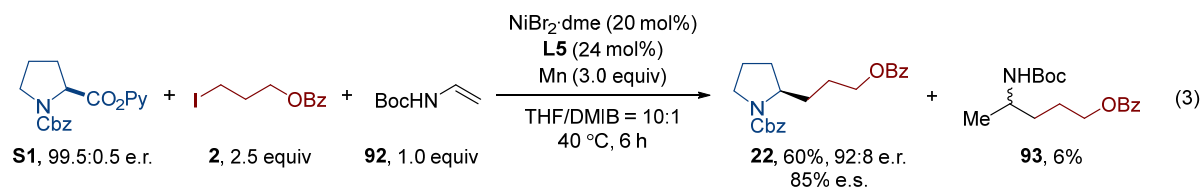
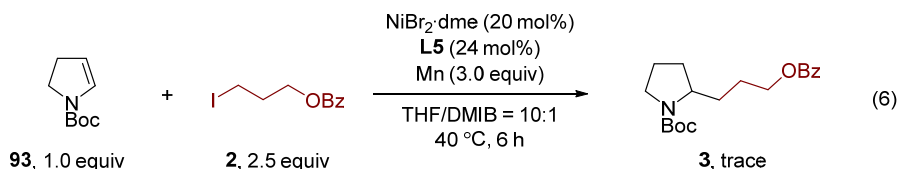
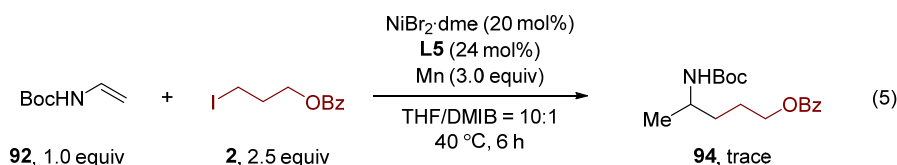


Fig. S19. Competition experiment of Ni-H reinsertion with different concentrations of *tert*-butyl vinylcarbamate



Comparison of *N*-vinyl carbamate with *N*-Cbz-2-pyrroline: In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added NiBr₂·dme (12.4 mg, 0.04 mmol, 20 mol%), **L5** (9.6 mg, 0.048 mmol, 24 mol%), and THF/DMIB (10:1, 1 mL). This mixture was stirred at rt for 10 min. To this vial was added 2-pyridyl ester **S1** (65.3 mg, 0.2 mmol, 1.0 equiv), alkyl iodides **2** (145.0 mg, 0.5 mmol, 2.5 equiv), *tert*-butyl vinylcarbamate **92** (28.6 mg, 0.2 mmol, 1.0 equiv) or *N*-Boc 2-pyrrolines **95** (33.8 mg, 0.2 mmol, 1.0 equiv), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The reaction mixture was stirred (800 RPM) at 40 °C for 6 h. After the specified reaction time, the reaction mixture was diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was analyzed by NMR and chiral SFC with 1,3,5-trimethoxybenzene as internal standard and purified by column chromatography. NMR yields are shown. The yield of crossover product **93** (eq 3) was higher than cross-over product **3** (eq 4), indicating that dissociation of substrate and Ni-H reinsertion of **92** (β -hydride elimination product of acyclic amino acid derivatives) is more favorable than **95** (β -hydride elimination product of proline derivatives).



Control experiments: In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added NiBr₂·dme (12.4 mg, 0.04 mmol, 20 mol%), **L5** (9.6 mg, 0.048 mmol, 24 mol%), and THF/DMIB (10:1, 1 mL). This mixture was stirred at rt for 10 min. To this vial was added alkyl iodides **2** (145.0 mg, 0.5 mmol,

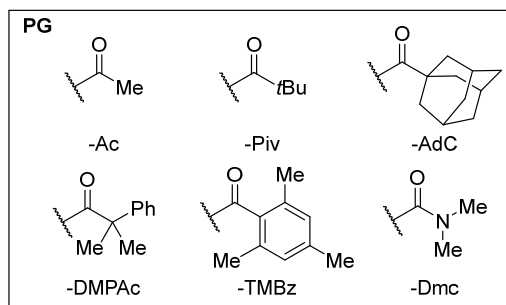
2.5 equiv), *tert*-butyl vinylcarbamate **92** (28.6 mg, 0.2 mmol, 1.0 equiv, eq 5) or N-Boc 2-pyrrolines **93** (33.8 mg, 0.2 mmol, 1.0 equiv, eq 6), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The reaction mixture was stirred (800 RPM) at 40 °C for 6 h. After the specified reaction time, the reaction mixture was diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was analyzed by NMR and chiral SFC with 1,3,5-trimethoxybenzene as internal standard, NMR yields are shown.

In both reactions (eq 5 and eq 6), the coupling products **94** and **3** were formed in trace yield, the major product was dimerization of alkyl iodide (hexane-1,6-diyl dibenzoate).

3.8.4 Protecting group effect on α -oxygenated acid 2-pyridyl esters in cross-coupling

Table S11. Protecting group effect of α -oxygenated acid derivatives

entry	PG	yield (%)	e.r.
1	Ac	33	99:1
2	Piv	35	98:2
3	AdC	42	99.5:0.5
4	DMPAc	35	>99.5:0.5
5	TMBz	30	99:1
6	Dmc	58	>99.5:0.5



In a nitrogen-filled glovebox, to a vial (4 mL) containing a PTFE-coated stirbar was added NiBr₂·dme (12.4 mg, 0.04 mmol, 20 mol%), **L5** (9.6 mg, 0.048 mmol, 24 mol%), and THF (1 mL). This mixture was stirred at rt for 10 min. To this vial was added 2-pyridyl esters (0.2 mmol, 1.0 equiv), 2-(3-iodopropyl)isoindoline-1,3-dione (157.5 mg, 0.5 mmol, 2.5 equiv), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 °C for 48 h. After the specified reaction time, the mixture was diluted with ethyl acetate (2 mL) and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired products. Isolated yields are shown. All α -oxygenated acid 2-pyridyl esters with different protecting groups provided high e.s. with variable yields.

4. Synthesis and characterization of starting materials

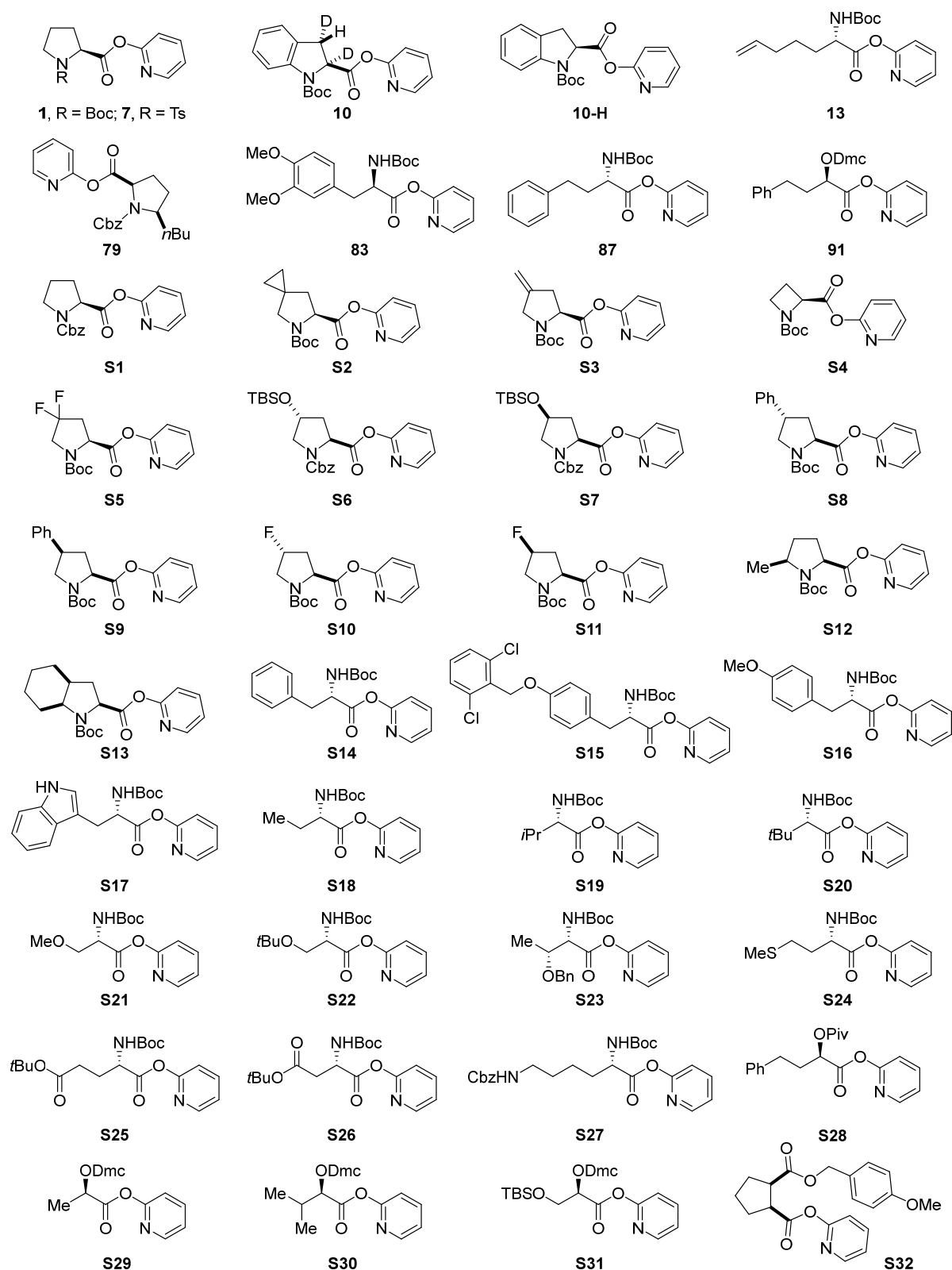
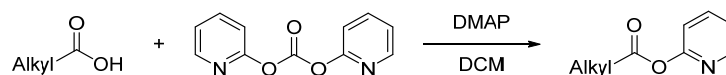


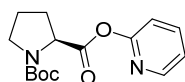
Fig. S20. Pyridyl esters used in this study.

S5 and **S6** were synthesized following the reported literature¹². All other pyridyl esters were synthesized by reactions of the corresponding carboxylic acids with di(pyridin-2-yl) carbonate following general procedure.

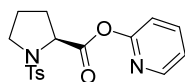
General Procedure for synthesis of pyridyl esters



A round-bottom flask was charged with carboxylic acid (1.0 equiv), di(pyridin-2-yl) carbonate (1.2 equiv), *N,N*-dimethylaminopyridine (DMAP) (0.2 equiv), and DCM (resulting in a 1.0 M solution of carboxylic acid). The mixture was stirred vigorously with a magnetic stirbar for 30 min at rt. The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel eluting with hexanes/EtOAc to afford the pyridyl esters. Note that the ester products may contain small amounts of *N*-acylpyridinone as side products. Similar products have been reported in the literature¹³, the ratio depends upon the substrate.

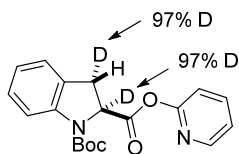


1-(*tert*-butyl) 2-(pyridin-2-yl) (S)-pyrrolidine-1,2-dicarboxylate (1) (10 mmol scale, colorless oil, 2.1 g, 72% yield, 99.5:0.5 e.r.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.40 – 8.31 (m, 1H), 7.79 – 7.69 (m, 1H), 7.22 – 7.15 (m, 1H), 7.14 – 7.00 (m, 1H), 4.48 (m, 1H), 3.62 – 3.52 (m, 1H), 3.50 – 3.38 (m, 1H), 2.41 – 2.28 (m, 1H), 2.27 – 2.18 (m, 1H), 2.08 – 2.00 (m, 1H), 1.96 – 1.85 (m, 1H), 1.44 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 171.3, 171.3, 158.1, 157.9, 154.6, 153.8, 148.8, 148.5, 139.6, 122.2, 122.1, 116.7, 116.1, 80.4, 80.1, 59.3, 59.2, 46.8, 46.5, 31.0, 29.9, 28.5, 28.5, 24.6, 23.8. HRMS (ESI) *m/z* (M+Na)⁺ calcd for C₁₅H₂₀N₂NaO₄⁺: 315.1315, found: 315.1311. [α]_D²⁰ = -72.8 (c 1.6, CHCl₃). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO₂, *v* = 0.6 mL/min, 40 °C, 2200 psi, tR (major) = 6.700 min (99.5%), tR (minor) = 7.285 min (0.5%).



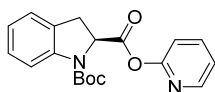
Pyridin-2-yl tosyl-L-prolinate (7) ¹H NMR (500 MHz, CDCl₃) (10 mmol scale, white solid, 2.3 g, 66% yield, 99.5:0.5 e.r.). δ 8.43 – 8.38 (m, 1H), 7.86 – 7.78 (m, 6H), 7.37 – 7.31 (m, 2H), 7.27 – 7.23 (m, 1H), 7.22 – 7.18 (m, 1H), 4.50 – 4.45 (m, 1H), 3.63 – 3.54 (m, 1H), 3.39 – 3.30 (m, 1H), 2.43 (s, 3H), 2.34 – 2.26 (m, 1H), 2.25 – 2.17 (m, 1H), 2.15 – 2.05 (m, 1H), 1.88 – 1.77 (m, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 170.4, 157.8, 148.5, 143.9, 139.7, 134.9, 129.9, 127.6, 122.4, 116.6, 60.6, 48.7, 31.0, 24.9, 21.6. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₁₇H₁₈N₂O₄S⁺: 347.1060, found: 347.1054. [α]_D²⁰ = -50.4 (c 1.0, CHCl₃). m.p. (°C): 86-87. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to

40% *i*-PrOH in scCO₂, *v* = 0.6 mL/min, 40 °C, 2200 psi, *t*_R (major) = 12.194 min (99.5%), *t*_R (minor) = 13.314 min (0.5%).



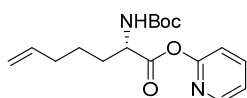
1-(*tert*-butyl) 2-(pyridin-2-yl) indoline-1,2-dicarboxylate-2,3-*d*₂ (10, *cis*-deuterium substituted isomer)

A 25 mL round bottom flask was charged with a magnetic stirbar, 1-(*tert*-butyl) 2-methyl 1H-indole-1,2-dicarboxylate (1.0 g, 3.6 mmol, 1.0 equiv), 5 wt% Pd/C (200 mg), and EtOD (10 mL). The mixture was evacuated and refilled with D₂ before it was stirred for 12 h at rt under an atmosphere of D₂ (balloon). After the reaction was complete until judged by TLC, the mixture was diluted with ethyl acetate (10 mL) and passed through a pad of silica gel. The pad was washed with ethyl acetate (10 mL). The filtrate was concentrated under reduced pressure in a 100 mL round bottom flask. The residue was dissolved in THF (5 mL) and the vessel was charged with a magnetic stirbar, LiOH (120 mg, 5 mmol), and H₂O (5 mL). The mixture was stirred vigorously at rt for 4 h. At this time, the mixture was acidified with 1 N HCl (20 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL), the combined organic layer was dried over MgSO₄, and concentrated under reduced pressure. The resulting residue was used directly in the general procedure for pyridyl ester synthesis to afford the title compound as a white solid (0.91 g, 74% yield, racemic). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.43 – 8.35 (m, 1H), 8.02 – 7.42 (m, 1H), 7.86 – 7.71 (m, 1H), 7.25 – 7.18 (m, 2H), 7.17 – 7.03 (m, 2H), 6.99 – 6.95 (m, 1H), 5.11 (m, 0.03H), 3.65 (m, 0.03H), 3.40 (s, 1H, *w*_{1/2} = 5.3 Hz at 24 °C), 1.64 – 1.54 (m, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 169.9, 157.8, 152.8, 151.6, 148.8, 142.7, 141.7, 139.7, 128.7, 128.2, 128.1, 127.6, 125.1, 124.6, 122.8, 122.4, 116.5, 116.0, 114.8, 82.7, 81.9, 60.2 (t, *J*_{CD} = 26.3 Hz), 32.3 (t, *J*_{CD} = 24.8 Hz, major rotamer), 31.7 (t, *J*_{CD} = 25.0 Hz, minor rotamer), 28.4. HRMS (ESI) *m/z* (M+NH₄)⁺ calcd for C₁₉H₂₂D₂N₂O₄⁺: 360.1887, found: 360.1887. m.p. (°C): 87-91.

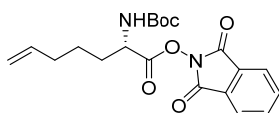


1-(*tert*-butyl) 2-(pyridin-2-yl) (*S*)-indoline-1,2-dicarboxylate (10-H) (1 mmol scale, white solid, 0.28 g, 82% yield, 99.5:0.5 e.r.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.48 – 8.25 (m, 1H), 8.02 – 7.44 (m, 1H), 7.77 (t, *J* = 7.8 Hz, 1H), 7.23 – 7.17 (m, 2H), 7.16 – 7.05 (m, 2H), 6.99 – 6.94 (m, 1H), 5.23 – 5.01 (m,

1H), 3.72 – 3.56 (m, 1H), 3.41 (dd, $J = 16.7, 4.9$ Hz, 1H), 1.65 – 1.53 (m, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 169.9, 157.7, 152.8, 151.6, 148.8, 148.5, 142.6, 141.6, 139.7, 128.7, 128.1, 128.0, 127.7, 125.0, 124.5, 122.8, 122.4, 116.5, 116.0, 114.8, 82.7, 81.9, 60.5, 32.7, 31.8, 28.4. HRMS (ESI) m/z ($\text{M}+\text{Na}^+$) calcd for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{NaO}_4^+$: 363.1315, found: 363.1307. $[\alpha]^{20} = -48.5$ (c 1.0, CHCl_3). M.P. ($^\circ\text{C}$): 87-91. SFC analysis: Daicel Chiralpak IA-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 $^\circ\text{C}$, 2200 psi, t_R (minor) = 2.167 min ($< 0.5\%$), t_R (major) = 2.296 min ($> 99.5\%$).

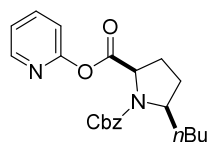


pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)hept-6-enoate (13) (1.5 mmol scale, colorless oil, 0.33 g, 69% yield, 99:1 e.r.). ^1H NMR (500 MHz, CDCl_3) δ 8.41 – 8.37 (m, 1H), 7.83 – 7.71 (m, 1H), 7.23 (dd, $J = 7.3, 4.9$ Hz, 1H), 7.10 (d, $J = 8.2$ Hz, 1H), 5.88 – 5.68 (m, 1H), 5.13 – 4.89 (m, 3H), 4.63 – 4.33 (m, 1H), 2.19 – 2.09 (m, 2H), 2.06 – 2.00 (m, 1H), 1.87 – 1.77 (m, 1H), 1.64 – 1.55 (m, 2H), 1.46 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 171.3, 157.8, 155.5, 148.7, 139.7, 138.0, 122.4, 116.4, 115.4, 80.2, 53.8, 33.3, 32.0, 28.4, 24.8. HRMS (ESI) m/z ($\text{M}+\text{H}^+$) calcd for $\text{C}_{17}\text{H}_{25}\text{N}_2\text{O}_4^+$: 321.1809, found: 321.1806. $[\alpha]^{20} = -7.5$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% MeOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, t_R (minor) = 4.346 min (1.0%), t_R (major) = 4.773 min (99.0%).

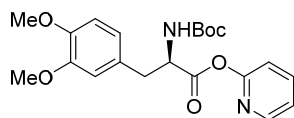


1,3-dioxoisindolin-2-yl (S)-2-((tert-butoxycarbonyl)amino)hept-6-enoate (16) A 100 mL round-bottom flask was charged with (S)-2-((tert-butoxycarbonyl)amino)hept-6-enoic acid (316 mg, 1.3 mmol, 1.0 equiv), 2-hydroxyisindoline-1,3-dione (303 mg, 1.3 mmol, 1.0 equiv), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (273 mg, 1.43 mmol, 1.1 equiv), N,N -dimethylaminopyridine (DMAP) (16 mg, 0.13 mmol, 0.1 equiv), and DCM (10 mL). The mixture was stirred vigorously with a magnetic stirbar for 6 h at rt. The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel eluting with hexanes/EtOAc to afford the NHP ester (1.3 mmol scale, colorless oil, 0.41 g, 81% yield, $>99.5:0.5$ e.r.). ^1H NMR (500 MHz, CDCl_3) δ 7.92 – 7.85 (m, 2H), 7.82 – 7.76 (m, 2H), 5.90 – 5.73 (m, 1H), 5.16 – 4.88 (m, 3H), 4.81 – 4.63 (m, 1H), 2.25 – 2.08 (m, 2H), 2.08 –

1.95 (m, 1H), 1.93 – 1.81 (m, 1H), 1.66 – 1.59 (m, 2H), 1.47 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 169.6, 161.6, 155.0, 137.9, 135.0, 129.0, 124.2, 115.5, 80.7, 52.0, 33.2, 32.5, 28.4, 24.3. HRMS (ESI) m/z ($\text{M}+\text{H}^+$) calcd for $\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}_6^+$: 389.1703, found: 389.1707. $[\alpha]^{20} = -8.6$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 88-91. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 1% to 10% MeOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (minor) = 8.481 min (< 0.5%), tR (major) = 9.805 min (> 99.5%).

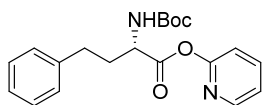


1-benzyl 2-(pyridin-2-yl) (2R,5R)-5-butylpyrrolidine-1,2-dicarboxylate (79) (10 mmol scale, colorless oil, 2.6 g, 68% yield, 92.5:7.5 d.r.). Diastereomeric ratio (d.r.) was determined by SFC analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.42 – 8.32 (m, 1H), 7.81 – 7.72 (m, 0.5H), 7.68 – 7.61 (m, 0.5H), 7.40 – 7.27 (m, 5H), 7.23 – 7.17 (m, 1H), 7.16 (d, $J = 8.2$ Hz, 0.5H), 6.61 (d, $J = 8.3$ Hz, 0.5H), 5.25 – 5.10 (m, 2H), 4.69 – 4.55 (m, 1H), 4.07 – 3.91 (m, 1H), 2.44 – 2.35 (m, 1H), 2.32 – 2.22 (m, 1H), 2.09 – 1.78 (m, 3H), 1.54 – 1.43 (m, 1H), 1.38 – 1.22 (m, 4H), 0.95 – 0.79 (m, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 171.4, 171.3, 158.0, 157.8, 155.2, 154.3, 148.6, 148.5, 139.6, 139.5, 136.7, 128.6, 128.5, 128.1, 128.1, 128.0, 122.2, 116.7, 116.2, 67.3, 67.2, 60.4, 59.9, 59.7, 58.9, 34.2, 33.7, 30.2, 29.5, 29.2, 28.7, 28.2, 22.8, 22.6, 14.2, 14.1. HRMS (ESI) m/z ($\text{M}+\text{H}^+$) calcd for $\text{C}_{22}\text{H}_{27}\text{N}_2\text{O}_4^+$: 383.1965 found: 383.1962. $[\alpha]^{20} = -34.8$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 20% *i*-PrOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 12.062 min (92.5%), tR (minor) = 11.489 min (7.5%).

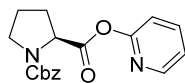


pyridin-2-yl (R)-2-((tert-butoxycarbonyl)amino)-3-(3,4-dimethoxyphenyl)propanoate (83) (2 mmol scale, white solid, 595 mg, 74% yield, 97.5:2.5 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.41 – 8.37 (m, 1H), 7.82 – 7.76 (m, 1H), 7.28 – 7.21 (m, 1H), 7.04 (d, $J = 8.1$ Hz, 1H), 6.91 – 6.86 (m, 1H), 6.84 – 6.79 (m, 2H), 5.06 – 4.96 (m, 1H), 4.90 – 4.78 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.31 – 3.20 (m, 2H), 1.43 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 170.4, 157.8, 155.3, 149.2, 148.7, 148.4, 139.8, 128.1, 122.5, 121.8, 116.5, 112.8, 111.4, 80.3, 56.0 (2C, overlapped), 54.7, 37.7, 28.4. HRMS (ESI) m/z ($\text{M}+\text{Na}^+$) calcd for $\text{C}_{21}\text{H}_{26}\text{N}_2\text{NaO}_6^+$: 425.1683, found: 425.1677. $[\alpha]^{20} = -21.3$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 89-93. SFC

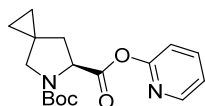
analysis: Daicel Chiralpak IF-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO₂, *v* = 0.6 mL/min, 40 °C, 2200 psi, tR (major) = 7.144 min (97.5%), tR (minor) = 7.659 min (2.5%).



pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)-4-phenylbutanoate (87) (10 mmol scale, white solid, 2.3 g, 65% yield, 99.5:0.5 e.r.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.44 – 8.36 (m, 1H), 7.85 – 7.75 (m, 1H), 7.33 – 7.28 (m, 2H), 7.26 – 7.18 (m, 4H), 7.07 (d, *J* = 8.1 Hz, 1H), 5.25 – 4.87 (m, 1H), 4.69 – 4.33 (m, 1H), 2.90 – 2.76 (m, 2H), 2.40 – 2.33 (m, 1H), 2.19 – 2.07 (m, 1H), 1.47 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 171.2, 157.8, 155.5, 148.8, 140.8, 139.7, 128.7, 128.6, 126.4, 122.5, 116.4, 80.3, 53.7, 34.4, 31.9, 28.5. HRMS (ESI) *m/z* (M+Na)⁺ calcd for C₂₀H₂₄N₂NaO₄⁺: 379.1628, found: 379.1626. [α]_D²⁰ = +8.5 (c 1.0, CHCl₃). m.p. (°C): 84-87. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 30% *i*-PrOH in scCO₂, *v* = 0.6 mL/min, λ = 255.4 nm, 40 °C, 2200 psi, tR (major) = 6.948 min (99.5%), tR (minor) = 6.283 min (0.5%).

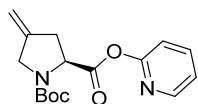


1-benzyl 2-(pyridin-2-yl) (S)-pyrrolidine-1,2-dicarboxylate (S1) (10 mmol scale, colorless oil, 2.2 g, 67% yield, 99.5:0.5 e.r.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.41 – 8.34 (m, 1H), 7.81 – 7.73 (m, 0.5H), 7.69 – 7.60 (m, 0.5H), 7.40 – 7.36 (m, 2H), 7.35 – 7.28 (m, 3H), 7.23 – 7.17 (m, 1H), 7.17 – 7.11 (m, 0.5H), 6.62 – 6.56 (m, 0.5H), 5.30 – 5.08 (m, 2H), 4.65 – 4.54 (m, 1H), 3.74 – 3.64 (m, 1H), 3.62 – 3.51 (m, 1H), 2.45 – 2.35 (m, 1H), 2.35 – 2.26 (m, 1H), 2.14 – 2.05 (m, 1H), 2.02 – 1.90 (m, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 171.0, 170.9, 157.9, 157.7, 155.1, 154.3, 148.6, 148.5, 139.6, 139.6, 136.8, 136.6, 128.6, 128.6, 128.3, 128.1, 128.1, 127.9, 122.3, 116.7, 116.2, 67.4, 67.2, 59.6, 59.1, 47.2, 46.7, 31.0, 30.0, 24.6, 23.7. HRMS (ESI) *m/z* (M+Na)⁺ calcd for C₁₈H₁₈N₂NaO₄⁺: 349.1159, found: 349.1156. [α]_D²⁰ = -53.7 (c 1.2, CHCl₃). SFC analysis: Daicel Chiralpak IF-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO₂, *v* = 0.6 mL/min, λ = 255.4 nm, 40 °C, 2200 psi, tR (major) = 14.240 min (99.5%), tR (minor) = 16.378 min (0.5%).

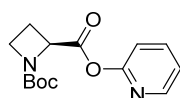


5-(tert-butyl) 6-(pyridin-2-yl) (S)-5-azaspiro[2.4]heptane-5,6-dicarboxylate (S2) (5 mmol scale,

colorless oil, 1.1 g, 69% yield, 99.5:0.5 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.41 – 8.33 (m, 1H), 7.81 – 7.71 (m, 1H), 7.23 – 7.17 (m, 1H), 7.16 (d, J = 8.1 Hz, 0.5H), 7.06 (d, J = 8.1 Hz, 0.5H), 4.68 (dd, J = 8.5, 4.4 Hz, 0.5H), 4.62 (dd, J = 8.5, 4.2 Hz, 0.5H), 3.49 – 3.36 (m, 2H), 2.41 (dd, J = 12.9, 8.6 Hz, 0.5H), 2.34 (dd, J = 12.9, 8.5 Hz, 0.5H), 2.17 – 2.05 (m, 1H), 1.47 (s, 4.5H), 1.45 (s, 4.5H), 0.73 – 0.53 (m, 4H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 171.0, 170.8, 158.1, 158.0, 154.5, 153.8, 148.8, 148.5, 139.5, 139.5, 122.2, 122.1, 116.7, 116.0, 80.4, 80.1, 59.8, 59.6, 54.3, 53.8, 39.1, 38.1, 28.5, 28.5, 21.0, 20.3, 12.2, 12.1, 9.4, 9.2. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{17}\text{H}_{22}\text{N}_2\text{NaO}_4^+$: 341.1472, found: 341.1466. $[\alpha]^{20} = -37.9$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , v = 0.6 mL/min, λ = 255.4 nm, 40 $^\circ\text{C}$, 2200 psi, t_R (major) = 5.803 min (99.5%), t_R (minor) = 6.199 min (0.5%).

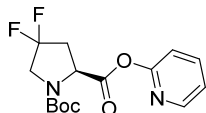


1-(*tert*-butyl) 2-(pyridin-2-yl) (S)-4-methylenepyrrolidine-1,2-dicarboxylate (S3) (10 mmol scale, colorless oil, 1.9 g, 63% yield, 99.5:0.5 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.41 – 8.32 (m, 1H), 7.82 – 7.71 (m, 1H), 7.24 – 7.16 (m, 1H), 7.13 (d, J = 8.1 Hz, 0.5H), 7.04 (d, J = 8.1 Hz, 0.5H), 5.08 – 4.96 (m, 2H), 4.70 (dd, J = 9.5, 3.6 Hz, 0.5H), 4.63 (dd, J = 9.6, 3.4 Hz, 0.5H), 4.17 – 4.05 (m, 2H), 3.15 – 3.01 (m, 1H), 2.92 – 2.86 (m, 1H), 1.46 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 170.7, 170.6, 157.9, 157.7, 154.5, 153.7, 148.8, 148.5, 143.0, 141.9, 139.6, 139.6, 122.3, 122.2, 116.6, 116.0, 108.6, 108.4, 80.7, 80.5, 59.2, 58.9, 51.0, 50.7, 36.7, 35.8, 28.4, 28.4. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{NaO}_4^+$: 327.1315, found: 327.1309. $[\alpha]^{20} = -30.1$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IF-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , v = 0.6 mL/min, 40 $^\circ\text{C}$, 2200 psi, t_R (major) = 8.448 min (99.5%), t_R (minor) = 9.943 min (0.5%).

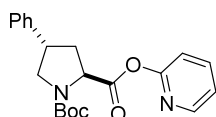


1-(*tert*-butyl) 2-(pyridin-2-yl) (S)-azetidine-1,2-dicarboxylate (S4) (10 mmol scale, white solid, 1.7 g, 61% yield, 99:1 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.44 – 8.37 (m, 1H), 7.83 – 7.77 (m, 1H), 7.25 – 7.21 (m, 1H), 7.18 – 7.08 (m, 1H), 4.85 (dd, J = 9.2, 5.3 Hz, 1H), 4.15 – 4.06 (m, 1H), 4.01 – 3.92 (m, 1H), 2.69 – 2.58 (m, 1H), 2.49 – 2.38 (m, 1H), 1.44 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 169.4, 157.6, 155.2, 148.6, 139.6, 122.3, 116.2, 80.3, 60.4, 47.3, 28.3, 20.3. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd

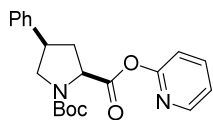
for $C_{14}H_{18}N_2NaO_4^+$: 301.1159, found: 301.1153. $[\alpha]^{20} = -82.0$ (c 1.6, $CHCl_3$). m.p. ($^{\circ}C$): 71-73. SFC analysis: Daicel Chiralpak IF-3 (3 mm ID $\times$ 150 mm L, 3 μ m PS), gradient from 3% to 20% *i*-PrOH in $scCO_2$, $v = 0.6$ mL/min, 40 $^{\circ}C$, 2200 psi, tR (major) = 5.285 min (99%), tR (minor) = 4.907 min (1%).



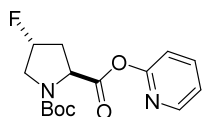
1-(*tert*-butyl) 2-(pyridin-2-yl) (S)-4,4-difluoropyrrolidine-1,2-dicarboxylate (S5) (10 mmol scale, colorless oil, 2.1 g, 64% yield, 99.5:0.5 e.r.). 1H NMR (500 MHz, $CDCl_3$, two rotamers in 1:1 ratio) δ 8.43 – 8.32 (m, 1H), 7.83 – 7.74 (m, 1H), 7.26 – 7.18 (m, 1H), 7.14 (d, $J = 8.2$ Hz, 0.5H), 7.06 (d, $J = 8.2$ Hz, 0.5H), 4.80 – 4.66 (m, 1H), 3.92 – 3.80 (m, 2H), 2.91 – 2.77 (m, 1H), 2.78 – 2.65 (m, 1H), 1.46 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, two rotamers) δ 169.1, 169.0, 157.6, 157.5, 153.8, 153.0, 148.8, 148.6, 139.8, 139.7, 126.1 (t, $J_{CF} = 249.1$ Hz), 125.5 (t, $J_{CF} = 249.0$ Hz), 122.6, 122.5, 116.4, 115.9, 81.8, 81.5, 57.3, 56.9, 53.3 (t, $J_{CF} = 31.9$ Hz), 52.8 (t, $J_{CF} = 32.0$ Hz), 38.5 (t, $J_{CF} = 25.8$ Hz), 37.6 (t, $J_{CF} = 25.7$ Hz), 28.3, 28.2. $^{19}F\{^1H\}$ NMR (377 MHz, $CDCl_3$, two rotamers in 1:1 ratio) δ -98.5 (d, $J_{FF} = 234.1$ Hz, 0.5F, rotamer a), -99.7 (d, $J_{FF} = 234.1$ Hz, 0.5F, rotamer a), -99.5 (d, $J_{FF} = 234.3$ Hz, 0.5F, rotamer b), -100.2 (d, $J_{FF} = 234.3$ Hz, 0.5F, rotamer b). HRMS (ESI) m/z ($M+Na$) $^+$ calcd for $C_{14}H_{18}F_2N_2NaO_4^+$: 351.1127, found: 351.1120. $[\alpha]^{20} = -28.8$ (c 1.1, $CHCl_3$). SFC analysis: Daicel Chiralpak IF-3 (3 mm ID $\times$ 150 mm L, 3 μ m PS), gradient from 3% to 40% *i*-PrOH in $scCO_2$, $v = 0.6$ mL/min, 40 $^{\circ}C$, 2200 psi, tR (major) = 4.419 min (99.5%), tR (minor) = 6.148 min (0.5%).



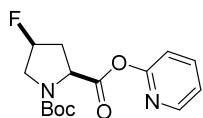
1-(*tert*-butyl) 2-(pyridin-2-yl) (2S,4S)-4-phenylpyrrolidine-1,2-dicarboxylate (S8) (1.7 mmol scale, colorless oil, 304 mg, 49% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. 1H NMR (500 MHz, $CDCl_3$, two rotamers) δ 8.42 (m, 1H), 7.84 – 7.77 (m, 1H), 7.36 – 7.31 (m, 2H), 7.27 – 7.26 (m, 1H), 7.26 – 7.23 (m, 3H), 7.20 (d, $J = 8.1$ Hz, 0.5H), 7.10 (d, $J = 8.1$ Hz, 0.5H), 4.80 – 4.73 (m, 0.5H), 4.71 – 4.65 (m, 0.5H), 4.14 – 4.08 (m, 0.5H), 4.07 – 4.00 (m, 0.5H), 3.73 – 3.64 (m, 1H), 3.54 – 3.48 (m, 0.5H), 3.46 – 3.40 (m, 0.5H), 2.68 – 2.62 (m, 1H), 2.50 (m, 1H), 1.50 (s, 4.5H), 1.49 (s, 4.5H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, two rotamers) δ 171.0, 171.0, 158.1, 157.9, 154.5, 153.7, 148.8, 148.5, 140.4, 140.3, 139.7, 128.8, 127.2, 122.4, 122.3, 116.7, 116.1, 80.7, 80.4, 59.5, 59.3, 53.3, 52.6, 42.6, 41.6, 37.9, 36.8, 28.5, 28.5. HRMS (ESI) m/z ($M+Na$) $^+$ calcd for $C_{24}H_{24}N_2NaO_4^+$: 391.1628, found: 391.1619.



1-(*tert*-butyl) 2-(pyridin-2-yl) (2S,4R)-4-phenylpyrrolidine-1,2-dicarboxylate (S9) (0.85 mmol scale, colorless oil, 202 mg, 65% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.43 – 8.38 (m, 1H), 7.84 – 7.75 (m, 1H), 7.35 – 7.31 (m, 2H), 7.30 – 7.27 (m, 3H), 7.25 – 7.20 (m, 1H), 7.22 (d, J = 7.3 Hz, 0.5H), 7.09 (d, J = 8.2 Hz, 0.5H), 4.68 – 4.54 (m, 1H), 4.19 – 4.14 (m, 0.5H), 4.05 – 3.96 (m, 0.5H), 3.56 – 3.39 (m, 2H), 2.93 – 2.78 (m, 1H), 2.44 – 2.29 (m, 1H), 1.50 (s, 4.5H), 1.49 (s, 4.5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 171.0, 171.0, 158.1, 157.9, 154.4, 153.6, 148.8, 148.5, 139.6, 139.4, 128.9, 128.8, 127.4, 127.4, 127.3, 122.3, 122.2, 116.9, 116.1, 80.9, 80.5, 59.8, 59.7, 53.4, 52.7, 44.1, 43.2, 38.2, 37.1, 28.5, 28.5. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{24}\text{H}_{24}\text{N}_2\text{NaO}_4^+$: 391.1628, found: 391.1622.

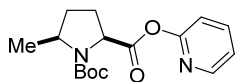


1-(*tert*-butyl) 2-(pyridin-2-yl) (2S,4R)-4-fluoropyrrolidine-1,2-dicarboxylate (S10) (10 mmol scale, white solid, 1.6 g, 52% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.40 – 8.32 (m, 1H), 7.77 (m, 1H), 7.25 – 7.19 (m, 1H), 7.19 – 7.15 (m, 0.5H), 7.09 – 7.04 (m, 0.5H), 5.35 – 5.26 (m, 0.5H), 5.25 – 5.14 (m, 0.5H), 4.75 – 4.58 (m, 1H), 4.03 – 3.78 (m, 1H), 3.73 – 3.55 (m, 1H), 2.83 – 2.64 (m, 1H), 2.48 – 2.22 (m, 1H), 1.46 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 170.6, 157.8, 157.6, 154.3, 153.6, 148.8, 148.4, 139.7, 122.4, 122.3, 116.7, 115.9, 91.97 (d, J_{CF} = 178.8 Hz), 90.38 (d, J_{CF} = 179.4 Hz), 81.2, 80.9, 77.4, 76.9, 57.9, 57.8, 53.40 (d, J_{CF} = 22.7 Hz), 53.14 (d, J_{CF} = 22.6 Hz), 37.65 (d, J_{CF} = 22.8 Hz), 36.59 (d, J_{CF} = 22.8 Hz), 28.4, 28.4. $^{19}\text{F}\{^1\text{H}\}$ NMR (377 MHz, CDCl_3 , two rotamers) δ -176.6, -177.4. m.p. ($^\circ\text{C}$): 106-107. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{15}\text{H}_{20}\text{FN}_2\text{O}_4^+$: 311.1402, found: 311.1392.

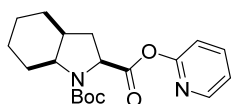


1-(*tert*-butyl) 2-(pyridin-2-yl) (2S,4S)-4-fluoropyrrolidine-1,2-dicarboxylate (S11) (10 mmol scale, white solid, 1.7 g, 55% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.40 – 8.35 (m, 1H), 7.80 – 7.70 (m, 1H), 7.23 – 7.16 (m, 1H), 7.15 – 7.11 (m, 0.5H), 7.09 – 7.03 (m, 0.5H), 5.34 – 5.29 (m, 0.5H), 5.24 – 5.20 (m, 0.5H), 4.78 (d, J = 9.8

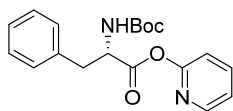
Hz, 0.5H), 4.69 (d, $J = 9.8$ Hz, 0.5H), 3.86 (m, 1H), 3.78 – 3.61 (m, 1H), 2.80 – 2.67 (m, 1H), 2.59 – 2.37 (m, 1H), 1.46 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 169.9, 169.6, 157.9, 157.8, 154.0, 153.7, 148.7, 148.6, 139.6, 139.5, 122.3, 122.2, 116.5, 116.2, 92.25 (d, $J_{\text{CF}} = 177.7$ Hz), 91.35 (d, $J_{\text{CF}} = 177.1$ Hz), 80.9, 80.7, 57.8, 57.6, 53.34 (d, $J_{\text{CF}} = 24.3$ Hz), 53.07 (d, $J_{\text{CF}} = 24.1$ Hz), 37.61 (d, $J_{\text{CF}} = 22.1$ Hz), 36.63 (d, $J_{\text{CF}} = 21.9$ Hz), 28.4, 28.3. $^{19}\text{F}\{^1\text{H}\}$ NMR (377 MHz, CDCl_3 , two rotamers) δ -172.5, -172.7. m.p. ($^{\circ}\text{C}$): 111–113. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^{+}$ calcd for $\text{C}_{15}\text{H}_{20}\text{FN}_2\text{O}_4^{+}$: 311.1402, found: 311.1390.



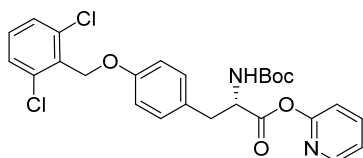
1-(*tert*-butyl) 2-(pyridin-2-yl) (2S,5S)-5-methylpyrrolidine-1,2-dicarboxylate (S12) (4 mmol scale, colorless oil, 0.86 g, 70% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.42 – 8.33 (m, 1H), 7.81 – 7.71 (m, 1H), 7.24 – 7.17 (m, 1H), 7.16 (d, $J = 8.7$ Hz, 0.5H), 7.07 (d, $J = 8.1$ Hz, 0.5H), 4.58 – 4.49 (m, 0.5H), 4.49 – 4.43 (m, 0.5H), 4.11 – 4.06 (m, 0.5H), 4.00 – 3.93 (m, 0.5H), 2.39 – 2.30 (m, 1H), 2.28 – 2.21 (m, 1H), 2.13 – 2.04 (m, 1H), 1.74 – 1.67 (m, 1H), 1.45 (s, 9H), 1.33 – 1.29 (m, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 171.6, 158.2, 158.0, 154.4, 153.5, 148.8, 148.5, 139.5, 122.2, 122.1, 116.7, 116.1, 80.3, 80.0, 60.3, 54.4, 54.3, 32.6, 31.9, 29.0, 28.5, 28.3, 28.1, 20.6, 20.0. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^{+}$ calcd for $\text{C}_{16}\text{H}_{23}\text{N}_2\text{O}_4^{+}$: 307.1652, found: 307.1647.



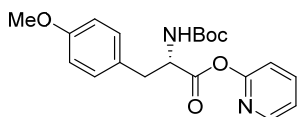
1-(*tert*-butyl) 2-(pyridin-2-yl) (2S,3aS,7aS)-octahydro-1H-indole-1,2-dicarboxylate (S13) (5 mmol scale, white solid, 1.4 g, 81% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.44 – 8.36 (m, 1H), 7.83 – 7.73 (m, 1H), 7.25 – 7.17 (m, 0.5H), 7.20 (d, $J = 8.3$ Hz, 1H), 7.10 (d, $J = 8.1$ Hz, 0.5H), 4.52 – 4.41 (m, 1H), 3.94 – 3.85 (m, 0.5H), 3.82 – 3.71 (m, 0.5H), 2.45 – 2.30 (m, 1H), 2.32 – 2.21 (m, 2H), 2.25 – 1.96 (m, 2H), 1.80 – 1.72 (m, 1H), 1.71 – 1.63 (m, 2H), 1.51 – 1.49 (m, 1H), 1.46 (s, 9H), 1.35 – 1.28 (m, 1H), 1.21 – 1.11 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 171.7, 171.6, 158.3, 158.0, 154.3, 153.4, 148.8, 148.5, 142.0, 139.6, 134.4, 122.2, 122.1, 120.6, 116.9, 116.1, 107.4, 80.3, 79.9, 59.5, 59.3, 57.6, 57.4, 37.4, 36.7, 32.8, 31.6, 28.6, 28.5, 28.0, 27.7, 26.1, 26.0, 23.9, 23.8, 20.7, 20.6. m.p. ($^{\circ}\text{C}$): 118–120. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^{+}$ calcd for $\text{C}_{19}\text{H}_{26}\text{N}_2\text{NaO}_4^{+}$: 369.1785, found: 369.1778.



pyridin-2-yl (tert-butoxycarbonyl)-L-phenylalaninate (S14) (10 mmol scale, waxy solid, 2.5 g, 73% yield, 96:4 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.41 – 8.35 (m, 1H), 7.77 – 7.71 (m, 1H), 7.31 – 7.28 (m, 2H), 7.25 – 7.12 (m, 4H), 6.98 (d, J = 8.1 Hz, 1H), 5.06 (m, 1H), 4.89 – 4.62 (m, 1H), 3.35 – 3.26 (m, 1H), 3.25 – 3.17 (m, 1H), 1.39 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 170.2, 157.7, 155.2, 148.7, 139.7, 135.8, 129.6, 128.8, 127.3, 122.4, 116.4, 80.2, 54.7, 38.1, 28.4. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{19}\text{H}_{22}\text{N}_2\text{NaO}_4^+$: 365.1472, found: 365.1470. $[\alpha]^{20} = +20.1$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , v = 0.6 mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 8.389 min (96%), tR (minor) = 8.847 min (4%).

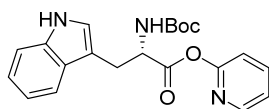


pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-((2,6-dichlorobenzyl)oxy)phenyl)-propanoate (S15) (5 mmol scale, white solid, 1.6 g, 62% yield, 96:4 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.44 – 8.38 (m, 1H), 7.82 – 7.75 (m, 1H), 7.35 (d, J = 8.1 Hz, 2H), 7.27 – 7.20 (m, 4H), 7.03 (d, J = 8.1 Hz, 1H), 6.99 (d, J = 8.6 Hz, 2H), 5.25 (s, 2H), 5.12 – 4.99 (m, 1H), 4.90 – 4.62 (m, 1H), 3.33 – 3.18 (m, 2H), 1.43 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 170.3, 158.2, 157.7, 155.3, 148.7, 139.7, 137.1, 132.2, 130.7, 130.5, 128.6, 128.6, 128.4, 122.4, 116.4, 115.3, 80.2, 65.3, 54.8, 37.3, 28.4. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{26}\text{H}_{26}\text{Cl}_2\text{N}_2\text{NaO}_5^+$: 539.1111, found: 539.1104. $[\alpha]^{20} = +21.1$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 140-143. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , v = 0.6 mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 13.598 min (96%), tR (minor) = 13.339 min (4%).

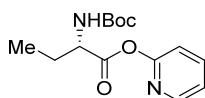


pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-methoxyphenyl)propanoate (S16) (5 mmol scale, white solid, 1.35 g, 72% yield, 99:1 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.42 (dd, J = 5.0, 2.0 Hz, 1H), 7.81 – 7.76 (m, 1H), 7.24 (dd, J = 7.3, 4.9 Hz, 1H), 7.23 – 7.17 (m, 2H), 7.04 (d, J = 8.2 Hz, 1H), 6.90 – 6.83 (m, 2H), 5.06 – 4.94 (m, 1H), 4.88 – 4.73 (m, 1H), 3.79 (s, 3H), 3.32 – 3.17 (m, 2H), 1.43 (s,

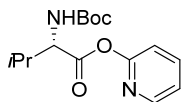
9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 170.4, 159.0, 157.8, 155.3, 148.8, 139.7, 130.7, 127.7, 122.5, 116.4, 114.3, 80.2, 55.4, 54.9, 37.3, 28.4. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{20}\text{H}_{24}\text{N}_2\text{NaO}_5^+$: 395.1577, found: 395.1572. $[\alpha]^{20} = +18.8$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 90-93. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 9.222 min (99%), tR (minor) = 10.488 min (1%).



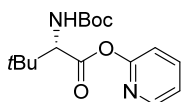
pyridin-2-yl (tert-butoxycarbonyl)-L-tryptophanate (S17) (5 mmol scale, white solid, 1.3 g, 68% yield, 97:3 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.58 (s, 1H), 8.43 – 8.35 (m, 1H), 7.76 – 7.67 (m, 1H), 7.65 (d, $J = 7.8$ Hz, 1H), 7.32 (d, $J = 8.1$ Hz, 1H), 7.22 – 7.15 (m, 3H), 7.15 – 7.07 (m, 1H), 6.92 (d, $J = 8.1$ Hz, 1H), 5.26 – 5.13 (m, 1H), 5.02 – 4.84 (m, 1H), 3.54 – 3.40 (m, 2H), 1.44 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 170.7, 157.8, 155.5, 148.5, 139.7, 136.3, 127.8, 123.5, 122.4, 122.1, 119.6, 118.8, 116.5, 111.4, 109.5, 80.2, 54.8, 28.4, 27.7. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{21}\text{H}_{23}\text{N}_3\text{NaO}_4^+$: 404.1581, found: 404.1579. $[\alpha]^{20} = -18.9$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 42-45. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 7.490 min (97%), tR (minor) = 7.684 min (3%).



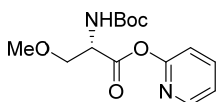
pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)butanoate (S18) (10 mmol scale, waxy solid, 2.0 g, 71% yield, 98.5:1.5 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.43 – 8.31 (m, 1H), 7.87 – 7.68 (m, 1H), 7.23 – 7.18 (m, 1H), 7.07 (d, $J = 8.2$ Hz, 1H), 5.30 – 4.76 (m, 1H), 4.67 – 4.14 (m, 1H), 2.14 – 1.95 (m, 1H), 1.95 – 1.77 (m, 1H), 1.43 (s, 9H), 1.05 (t, $J = 7.5$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 171.2, 157.8, 155.5, 148.7, 139.7, 122.4, 116.4, 80.1, 54.9, 28.4, 25.8, 9.8. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{14}\text{H}_{20}\text{N}_2\text{NaO}_4^+$: 303.1315, found: 303.1310. $[\alpha]^{20} = -14.3$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 25% *i*-PrOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 5.281 min (98.5%), tR (minor) = 5.581 min (1.5%).



pyridin-2-yl (tert-butoxycarbonyl)-L-valinate (S19) (10 mmol scale, colorless oil, 2.3 g, 78% yield, 99:1 e.r.). ^1H NMR (500 MHz, CDCl_3) δ 8.49 – 8.33 (m, 1H), 7.82 – 7.74 (m, 1H), 7.25 – 7.22 (m, 1H), 7.09 (d, J = 8.1 Hz, 1H), 5.18 – 4.72 (m, 1H), 4.55 – 4.29 (m, 1H), 2.45 – 2.31 (m, 1H), 1.47 (s, 9H), 1.11 (d, J = 6.9 Hz, 3H), 1.05 (d, J = 6.9 Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 170.9, 157.9, 155.8, 148.8, 139.7, 122.4, 116.4, 80.2, 58.9, 31.5, 28.5, 19.3, 17.7. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{15}\text{H}_{22}\text{N}_2\text{NaO}_4^+$: 317.1472, found: 317.1466. $[\alpha]^{20} = -7.9$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , v = 0.6 mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 6.403 min (99%), tR (minor) = 5.970 min (1%).

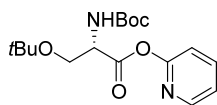


pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)-3,3-dimethylbutanoate (S20) (10 mmol scale, waxy solid, 2.5 g, 81% yield, 99:1 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.43 – 8.36 (m, 1H), 7.82 – 7.74 (m, 1H), 7.25 – 7.20 (m, 1H), 7.08 (d, J = 8.1 Hz, 1H), 5.31 – 4.84 (m, 1H), 4.47 – 4.11 (m, 1H), 1.46 (s, 9H), 1.13 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 170.4, 157.9, 155.7, 148.8, 139.6, 122.4, 116.5, 80.1, 62.0, 35.2, 28.5, 26.8. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{16}\text{H}_{24}\text{N}_2\text{NaO}_4^+$: 331.1628, found: 331.1622. $[\alpha]^{20} = -8.7$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , v = 0.6 mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 6.065 min (99%), tR (minor) = 5.166 min (1%).

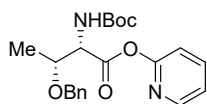


pyridin-2-yl N-(tert-butoxycarbonyl)-O-methyl-L-serinate (S21) (10 mmol scale, waxy solid, 2.5 g, 84% yield, 90.5:9.5 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.44 – 8.36 (m, 1H), 7.84 – 7.74 (m, 1H), 7.25 – 7.22 (m, 1H), 7.12 (d, J = 8.2 Hz, 1H), 5.52 – 5.38 (m, 1H), 4.75 – 4.53 (m, 1H), 4.03 (dd, J = 9.6, 2.9 Hz, 1H), 3.74 (dd, J = 9.9, 3.4 Hz, 1H), 3.42 (s, 3H), 1.46 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 169.2, 157.8, 155.6, 148.7, 139.7, 122.4, 116.4, 80.3, 72.5, 59.6, 54.4, 28.4. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{14}\text{H}_{20}\text{N}_2\text{NaO}_5^+$: 319.1264, found: 319.1259. $[\alpha]^{20} = -6.3$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , v =

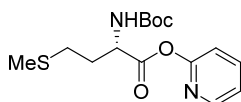
0.6 mL/min, 40 °C, 2200 psi, tR (major) = 9.187 min (90.5%), tR (minor) = 10.863 min (9.5%).



pyridin-2-yl N-(tert-butoxycarbonyl)-O-(tert-butyl)-L-serinate (S22) (10 mmol scale, waxy solid, 2.8 g, 83% yield, 90:10 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.43 – 8.34 (m, 1H), 7.84 – 7.73 (m, 1H), 7.25 – 7.20 (m, 1H), 7.12 (d, J = 8.9 Hz, 1H), 5.51 – 5.13 (m, 1H), 4.77 – 4.43 (m, 1H), 4.03 (dd, J = 9.0, 3.1 Hz, 1H), 3.70 (dd, J = 9.3, 3.0 Hz, 1H), 1.47 (s, 9H), 1.20 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 169.5, 158.0, 155.7, 148.7, 139.5, 122.3, 116.4, 80.2, 73.8, 62.3, 54.7, 28.5, 27.5. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{17}\text{H}_{26}\text{N}_2\text{NaO}_5^+$: 361.1734, found: 361.1728. $[\alpha]^{20} = -6.2$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , v = 0.6 mL/min, 40 °C, 2200 psi, tR (major) = 7.074 min (90%), tR (minor) = 9.678 min (10%).

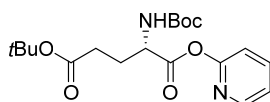


pyridin-2-yl O-benzyl-N-(tert-butoxycarbonyl)-L-threoninate (S23) (10 mmol scale, colorless oil, 3.1 g, 80% yield, 95.5:4.5 d.r.). Diastereomeric ratio (d.r.) was determined by SFC analysis. ^1H NMR (400 MHz, CDCl_3 , two rotamers) δ 8.42 – 8.38 (m, 1H), 7.79 – 7.70 (m, 1H), 7.38 – 7.27 (m, 5H), 7.26 – 7.17 (m, 1H), 7.01 (d, J = 8.2 Hz, 1H), 5.47 – 5.09 (m, 1H), 4.65 (d, J = 11.5 Hz, 1H), 4.61 (dd, J = 9.7, 2.4 Hz, 1H), 4.54 (d, J = 11.5 Hz, 1H), 4.45 – 4.36 (m, 1H), 1.46 (s, 9H), 1.34 (d, J = 6.3 Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , two rotamers) δ 169.6, 157.9, 156.2, 148.7, 139.6, 138.0, 128.5, 128.0, 127.9, 122.3, 116.4, 80.2, 74.8, 71.4, 58.7, 28.4, 16.6. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{N}_2\text{NaO}_5^+$: 409.1734, found: 409.1728. $[\alpha]^{20} = -12.5$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , v = 0.6 mL/min, 40 °C, 2200 psi, tR (major) = 5.605 min (95.5%), tR (minor) = 5.855 min (4.5%).

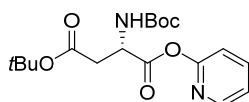


pyridin-2-yl (tert-butoxycarbonyl)-L-methioninate (S24) (10 mmol scale, waxy solid, 1.9 g, 58% yield, 99:1 e.r.). ^1H NMR (400 MHz, CDCl_3 , two rotamers) δ 8.43 – 8.37 (m, 1H), 7.85 – 7.76 (m, 1H), 7.26 – 7.21 (m, 1H), 7.11 (d, J = 8.1 Hz, 1H), 5.31 – 4.91 (m, 1H), 4.85 – 4.39 (m, 1H), 2.77 – 2.60 (m, 2H), 2.44 – 2.27

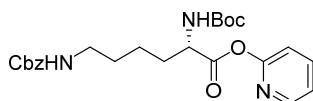
(m, 1H), 2.20 – 2.06 (m, 4H), 1.45 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , two rotamers) δ 170.8, 157.7, 155.5, 148.8, 139.8, 122.5, 116.4, 80.4, 53.1, 31.9, 30.1, 28.4, 15.6. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{15}\text{H}_{22}\text{N}_2\text{NaO}_4\text{S}^+$: 349.1192, found: 349.1187. $[\alpha]^{20} = -11.6$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IF-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 8.209 min (99%), tR (minor) = 9.620 min (1%).



5-(*tert*-butyl) 1-(pyridin-2-yl) (tert-butoxycarbonyl)-L-glutamate (S25) (10 mmol scale, colorless oil, 3.2 g, 84% yield, 99:1 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.43 – 8.37 (m, 1H), 7.84 – 7.74 (m, 1H), 7.26 – 7.21 (m, 1H), 7.11 (d, $J = 8.1$ Hz, 1H), 5.27 – 4.87 (m, 1H), 4.69 – 4.35 (m, 1H), 2.52 – 2.40 (m, 2H), 2.39 – 2.28 (m, 1H), 2.20 – 2.07 (m, 1H), 1.45 (s, 18H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 172.1, 170.8, 157.8, 155.6, 148.7, 139.7, 122.5, 116.4, 81.0, 80.3, 53.6, 31.8, 28.4, 28.2, 27.5. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{19}\text{H}_{28}\text{N}_2\text{NaO}_6^+$: 403.1840, found: 403.1834. $[\alpha]^{20} = -4.9$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IF-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 8.066 min (99%), tR (minor) = 8.456 min (1%).

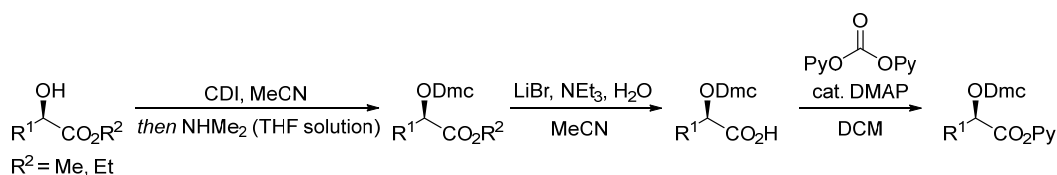


4-(*tert*-butyl) 1-(pyridin-2-yl) (tert-butoxycarbonyl)-L-aspartate (S26) (10 mmol scale, waxy solid, 3.0 g, 82% yield, 93.5:6.5 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.43 – 8.35 (m, 1H), 7.83 – 7.75 (m, 1H), 7.25 – 7.21 (m, 1H), 7.12 (d, $J = 8.1$ Hz, 1H), 5.66 – 5.11 (m, 1H), 4.94 – 4.57 (m, 1H), 3.08 (dd, $J = 16.9, 5.1$ Hz, 1H), 2.89 (dd, $J = 16.9, 4.5$ Hz, 1H), 1.46 (s, 18H, overlapped). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 170.3, 169.9, 157.9, 155.5, 148.7, 139.7, 122.4, 116.4, 82.1, 80.4, 50.6, 38.2, 28.5, 28.2. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{18}\text{H}_{27}\text{N}_2\text{O}_6^+$: 367.1864, found: 367.1852. $[\alpha]^{20} = -5.5$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 7.098 min (93.5%), tR (minor) = 9.669 min (6.5%).

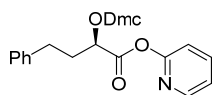


pyridin-2-yl N6-((benzyloxy)carbonyl)-N2-(tert-butoxycarbonyl)-L-lysinate (S27) (10 mmol scale, colorless oil, 3.6 g, 79% yield, 99:1 e.r.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.28 – 8.23 (m, 1H), 7.72 – 7.65 (m, 1H), 7.25 – 7.19 (m, 5H), 7.12 – 7.06 (m, 1H), 7.00 (d, J = 8.1 Hz, 1H), 5.35 – 5.25 (m, 1H), 5.22 – 5.15 (m, 1H), 5.00 (s, 2H), 4.51 – 4.41 (m, 1H), 3.34 – 2.98 (m, 3H), 1.98 – 1.86 (m, 1H), 1.84 – 1.74 (m, 1H), 1.57 – 1.41 (m, 4H), 1.36 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 171.2, 157.7, 156.7, 155.6, 148.7, 139.7, 136.8, 128.6, 128.2, 128.1, 122.4, 116.4, 80.2, 66.7, 53.6, 40.3, 31.7, 29.1, 28.4, 22.1. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{24}\text{H}_{32}\text{N}_3\text{O}_6$ $^+$: 458.2286, found: 458.2279. $[\alpha]^{20} = -4.5$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% *i*-PrOH in scCO_2 , v = 0.6 mL/min, 40 $^\circ\text{C}$, 2200 psi, t_R (major) = 15.017 min (99%), t_R (minor) = 15.372 min (1%).

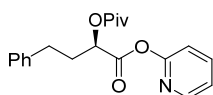
Synthesis of Dmc Protected Hydroxy Acid 2-pyridyl esters



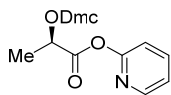
A 100 mL round bottom flask was charged with α -hydroxy ester (1.0 equiv, 10 mmol), carbonyl diimidazole (1.5 equiv, 15 mmol), and MeCN (20 mL). The mixture was stirred with a magnetic stirbar for 1 h at rt before dimethylamine (2.0 equiv, 20 mmol, 2.0 M solution in THF, 10 mL) was added dropwise to the flask. The mixture was stirred for an additional 30 min at rt before it was concentrated in vacuo. The residue was dissolved in DCM (40 mL), and the resulting solution was washed with 1 N HCl (3×10 mL). The aqueous layer was extracted with additional DCM (20 mL). The combined organic layers were dried over MgSO_4 and concentrated in vacuo. The residue was dissolved in MeCN (30 mL) and transferred to a 100 mL round bottom flask charged with a magnetic stirbar. To the resulting solution was added LiBr (10 equiv, 100 mmol), triethylamine (3.0 equiv, 30 mmol), and H_2O (3.0 equiv, 0.54 mL). The mixture was stirred vigorously at rt for 12 h. The reaction mixture was diluted with EtOAc (20 mL) and H_2O (20 mL), acidified with 1 N HCl (60 mL), and extracted with EtOAc (3×20 mL). The combined organic layers were dried over MgSO_4 and concentrated under reduced pressure. The residue was directly used in the general procedure for pyridyl ester synthesis.



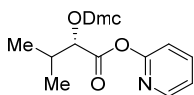
pyridin-2-yl (R)-2-((dimethylcarbamoyl)oxy)-4-phenylbutanoate (91) (10 mmol scale, white solid, 1.5 g, 46% yield, 99.5:0.5 e.r.). ^1H NMR (500 MHz, CDCl_3) δ 8.46 – 8.32 (m, 1H), 7.83 – 7.71 (m, 1H), 7.33 – 7.27 (m, 2H), 7.25 – 7.18 (m, 4H), 7.12 (d, J = 8.2 Hz, 1H), 5.18 (dd, J = 8.1, 4.9 Hz, 1H), 2.97 (s, 3H), 2.95 (s, 3H), 2.93 – 2.82 (m, 2H), 2.45 – 2.30 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 169.4, 157.7, 155.7, 148.6, 140.6, 139.6, 128.6, 128.6, 126.3, 122.3, 116.5, 72.6, 36.7, 36.1, 32.9, 31.6. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{NaO}_4^+$: 351.1315, found: 351.1311. $[\alpha]^{20} = 15.8$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 56–60. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 35% MeOH in scCO_2 , v = 0.6 mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 8.893 min (99.5%), tR (minor) = 9.272 min (0.5%).



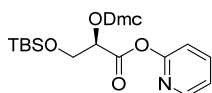
pyridin-2-yl (R)-4-phenyl-2-(pivaloyloxy)butanoate (S28). A 100 mL round bottom flask was charged with (R)-2-hydroxy-4-phenylbutanoic acid (1.8 g, 10 mmol, 1.0 equiv), pivaloyl chloride (1.2 g, 10 mmol, 1.0 equiv) and DCM (10 mL). The mixture was stirred with a magnetic stirbar for 2 days at rt. The reaction mixture was concentrated under reduced pressure, and to the residue in the same flask was added di(pyridin-2-yl) carbonate (2.59 g, 12 mmol, 1.2 equiv), *N,N*-dimethylaminopyridine (DMAP) (244 mg, 2 mmol, 0.2 equiv), and DCM (10 mL). The mixture was stirred vigorously with a magnetic stirbar for 30 min at rt. The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel eluting with hexanes/EtOAc to afford the product (white solid, 1.6 g, 47% yield, > 99.5:0.5 e.r.). ^1H NMR (500 MHz, CDCl_3) δ 8.45 – 8.33 (m, 1H), 7.83 – 7.72 (m, 1H), 7.34 – 7.28 (m, 2H), 7.25 – 7.20 (m, 4H), 7.08 (d, J = 8.1 Hz, 1H), 5.18 (dd, J = 7.8, 5.1 Hz, 1H), 2.97 – 2.87 (m, 1H), 2.87 – 2.77 (m, 1H), 2.48 – 2.35 (m, 2H), 1.30 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 178.1, 168.7, 157.6, 148.8, 140.4, 139.7, 128.7, 128.6, 126.5, 122.5, 116.4, 71.3, 38.9, 32.6, 31.5, 27.2. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{20}\text{H}_{23}\text{NNaO}_4^+$: 364.1519, found: 364.1515. m.p. ($^\circ\text{C}$): 46–48. $[\alpha]^{20} = 4.3$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 46–48. SFC analysis: Daicel Chiralpak IA-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 1% to 10% MeOH in scCO_2 , v = 0.8 mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (minor) = 2.419 min (< 0.5%), tR (major) = 2.773 min (> 99.5%).



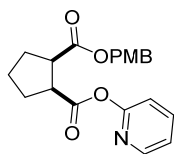
pyridin-2-yl (*R*)-2-((dimethylcarbamoyl)oxy)propanoate (S29) (5 mmol scale, colorless oil, 0.85 g, 71% yield, 99:1 e.r.). ^1H NMR (500 MHz, CDCl_3) δ 8.41 – 8.31 (m, 1H), 7.81 – 7.71 (m, 1H), 7.23 – 7.16 (m, 1H), 7.16 – 7.08 (m, 1H), 5.22 (q, J = 7.1 Hz, 1H), 2.96 (s, 3H), 2.92 (s, 3H), 1.66 (d, J = 7.1 Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 170.0, 157.7, 155.7, 148.6, 139.6, 122.3, 116.5, 69.5, 36.6, 36.1, 17.1. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{11}\text{H}_{15}\text{N}_2\text{O}_4$ $^+$: 239.1026, found: 239.1024. $[\alpha]^{20} = 2.1$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 20% MeOH in scCO_2 , v = 0.6 mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 10.263 min (99.0%), tR (minor) = 10.808 min (1.0%).



pyridin-2-yl (*S*)-2-((dimethylcarbamoyl)oxy)-3-methylbutanoate (S30) (10 mmol scale, pale yellow oil, 1.6 g, 60% yield, 97.5:2.5 e.r.). ^1H NMR (500 MHz, CDCl_3) δ 8.43 – 8.32 (m, 1H), 7.79 – 7.72 (m, 1H), 7.22 – 7.17 (m, 1H), 7.13 (d, J = 8.1 Hz, 1H), 4.98 (d, J = 4.5 Hz, 1H), 2.99 (s, 3H), 2.93 (s, 3H), 2.49 – 2.40 (m, 1H), 1.16 – 1.10 (m, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 169.1, 157.8, 156.0, 148.6, 139.5, 122.3, 116.6, 77.6, 36.6, 36.0, 30.5, 19.0, 17.6. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{N}_2\text{O}_4$ $^+$: 267.1339, found: 267.1334. $[\alpha]^{20} = -0.5$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IA-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% MeOH in scCO_2 , v = 0.8 mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 1.346 min (97.5%), tR (minor) = 1.564 min (2.5%).



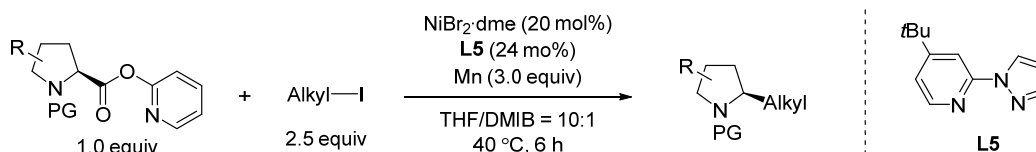
pyridin-2-yl (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-((dimethylcarbamoyl)oxy)propanoate (S31) (10 mmol scale, white solid, 2.1 g, 57% yield, 98.5:1.5 e.r.). ^1H NMR (500 MHz, CDCl_3) δ 8.43 – 8.34 (m, 1H), 7.77 (td, J = 7.8, 2.0 Hz, 1H), 7.24 – 7.18 (m, 1H), 7.14 (d, J = 8.1 Hz, 1H), 5.35 (dd, J = 5.5, 3.0 Hz, 1H), 4.23 (dd, J = 11.2, 5.4 Hz, 1H), 4.12 (dd, J = 11.2, 3.0 Hz, 1H), 3.01 (s, 3H), 2.95 (s, 3H), 0.90 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 167.4, 157.7, 155.7, 148.7, 139.5, 122.3, 116.5, 74.8, 63.1, 36.7, 36.2, 25.9, 18.4, -5.3, -5.3. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{17}\text{H}_{28}\text{N}_2\text{NaO}_5\text{Si}^+$: 391.1660, found: 391.1650. $[\alpha]^{20} = 1.4$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 52-54. SFC analysis: Daicel Chiralpak IA-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 1% to 10% MeOH in scCO_2 , v = 0.8 mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (minor) = 2.601 min (1.5%), tR (major) = 3.262 min (98.5%).



***cis*-1-(4-methoxybenzyl) 2-(pyridin-2-yl)-cyclopentane-1,2-dicarboxylate (S32)** A 100 mL round bottom flask was charged with a magnetic stirbar, cyclopentane-*cis*-1,2-dicarboxylic acid anhydride (1.40 g, 10 mmol, 1.0 equiv), 4-methoxybenzyl alcohol (PMB-OH, 1.38 g, 10 mmol, 1.0 equiv), pyridine (2.37 g, 30 mmol, 3.0 equiv), and DCM (10 mL). The mixture was stirred for 24 h at rt. The stirbar was removed and reaction mixture was concentrated under reduced pressure. To this residue was added a magnetic stirbar, di(pyridin-2-yl) carbonate (2.59 g, 12 mmol, 1.2 equiv), *N,N*-dimethylaminopyridine (DMAP) (244 mg, 2 mmol, 0.2 equiv), and DCM (10 mL). The mixture was stirred vigorously for 30 min at rt. The reaction mixture was then concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (hexanes/EtOAc). After concentration, the product was obtained as a colorless oil (1.3 g, 37% yield). ¹H NMR (500 MHz, CDCl₃) δ 8.38 – 8.33 (m, 1H), 7.72 – 7.65 (m, 1H), 7.29 – 7.23 (m, 2H), 7.20 – 7.15 (m, 1H), 6.93 – 6.88 (m, 1H), 6.83 – 6.80 (m, 2H), 5.07 (s, 2H), 3.77 (s, 3H), 3.34 – 3.20 (m, 2H), 2.27 – 2.18 (m, 1H), 2.14 – 2.00 (m, 3H), 1.96 – 1.87 (m, 1H), 1.73 – 1.65 (m, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 173.9, 172.0, 159.6, 157.9, 148.5, 139.3, 130.2, 128.1, 122.0, 116.7, 113.9, 66.5, 55.3, 47.2, 46.9, 29.3, 28.5, 23.9. HRMS (ESI) *m/z* (M+Na)⁺ calcd for C₂₀H₂₁NNaO₅⁺: 378.1312, found: 378.1302.

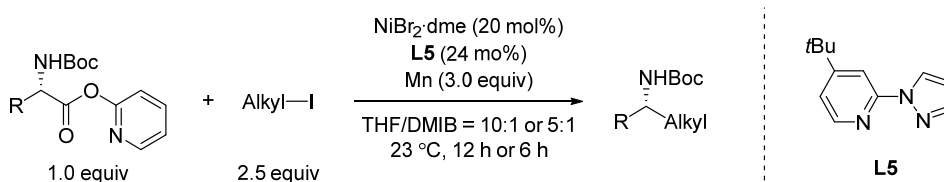
5. Characterization of cross-coupled products

General Procedure A (for proline derivatives)



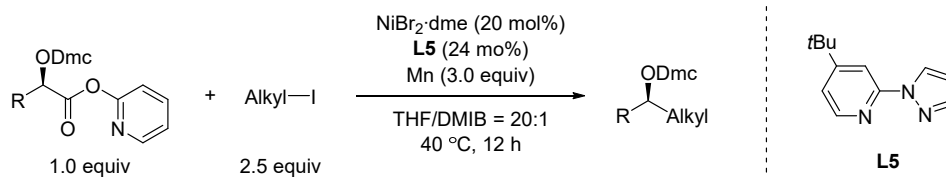
In a nitrogen-filled glovebox, to a vial (4 mL) containing a PTFE-coated stirbar was added NiBr₂·dme (0.04 mmol, 20 mol%), **L5** (0.048 mmol, 24 mol%), and THF/DMIB (10:1, 0.5 mL). This mixture was stirred at rt for 10 min. To this vial was added 2-pyridyl esters (0.2 mmol, 1.0 equiv), alkyl iodides (0.5 mmol, 2.5 equiv), and Mn (0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 °C for 6 h. After the specified reaction time, the reaction mixture was removed from the hot plate and allowed to cool to rt. The resulting mixture was diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salt. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired products.

General Procedure B (for acyclic amino acid derivatives)

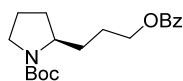


In a nitrogen-filled glovebox, to a vial (4 mL) containing a PTFE-coated stirbar was added NiBr₂·dme (0.04 mmol, 20 mol%), **L5** (0.048 mmol, 20 mol%), and THF/DMIB (10:1 or 5:1, 0.5 mL). This mixture was stirred at rt for 10 min. To this vial was added 2-pyridyl esters (0.2 mmol, 1.0 equiv), alkyl iodides (0.5 mmol, 2.5 equiv), and Mn (0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at rt for 6 h (THF:DMIB = 5:1) or 12 h (THF:DMIB = 10:1). After the specified reaction time, the mixture was diluted with ethyl acetate (2 mL) and passed through a pad of silica gel to remove excess Mn and insoluble salt. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired products.

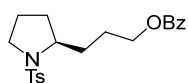
General Procedure C (for α -oxygenated acid derivatives)



In a nitrogen-filled glovebox, a vial (4 mL) containing a PTFE-coated stirbar was charged with $\text{NiBr}_2(\text{dme})$ (12.4 mg, 0.04 mmol, 20 mol%), **L5** (9.6 mg, 0.048 mmol, 24 mol%), and THF/DMIB (20:1, 1.0 mL). This mixture was stirred at rt for 10 min. To this mixture was added the 2-pyridyl ester (0.2 mmol, 1.0 equiv), alkyl iodide (0.5 mmol, 2.5 equiv), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The vial was placed on a hotplate in a reaction heating block, and the reaction mixture was stirred (800 RPM) at 40 °C for 12 h. After this time, the mixture was diluted with ethyl acetate (2 mL) and passed through a pad of silica gel to remove excess Mn and insoluble salts. The vial and pad were washed with additional ethyl acetate (2 mL). The combined filtrate was concentrated in vacuo and the residue was purified by column chromatography to afford the product.

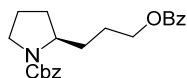


tert-butyl (S)-2-(3-(benzyloxy)propyl)pyrrolidine-1-carboxylate (3) (following general procedure A, colorless oil, 52.0 mg, 78% yield, 99:1 e.r., 99% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.06 – 8.00 (m, 2H), 7.58 – 7.52 (m, 1H), 7.46 – 7.40 (m, 2H), 4.38 – 4.24 (m, 2H), 3.90 – 3.74 (m, 1H), 3.48 – 3.28 (m, 2H), 2.01 – 1.91 (m, 1H), 1.90 – 1.72 (m, 5H), 1.68 – 1.63 (m, 1H), 1.51 – 1.47 (m, 1H), 1.44 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 154.8, 133.0, 130.5, 129.7, 128.5, 79.3, 65.1, 57.1, 46.7, 46.3, 31.5, 30.9, 30.2, 28.7, 25.8, 24.0, 23.2. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{19}\text{H}_{28}\text{NO}_4$: 334.2013, found: 334.2006. $[\alpha]^{20} = -48.5$ (c 1.0, CHCl_3). Chiral HPLC condition: Daicel chiral AS-H, isocratic 1% *i*-PrOH in hexanes, t_R (major) = 11.624 min (99%), t_R (minor) = 13.035 min (1%).

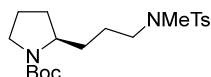


(S)-3-(1-tosylpyrrolidin-2-yl)propyl benzoate (9) (following general procedure A, waxy solid, 10.9 mg, 14% yield, 98:2 e.r., 97% e.s.). ^1H NMR (500 MHz, CDCl_3) δ 8.08 – 8.02 (m, 2H), 7.74 – 7.69 (m, 2H), 7.59 – 7.52 (m, 1H), 7.47 – 7.40 (m, 2H), 7.30 – 7.27 (m, 2H), 4.42 – 4.28 (m, 2H), 3.73 – 3.66 (m, 1H), 3.42 –

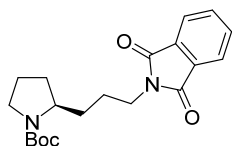
3.35 (m, 1H), 3.29 – 3.17 (m, 1H), 2.41 (s, 3H), 2.00 – 1.91 (m, 1H), 1.89 – 1.81 (m, 2H), 1.82 – 1.73 (m, 1H), 1.72 – 1.60 (m, 2H), 1.58 – 1.54 (m, 2H), 1.53 – 1.46 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 166.8, 143.4, 135.0, 133.0, 130.5, 129.8, 129.7, 128.5, 127.7, 64.9, 60.2, 49.1, 33.0, 31.0, 25.6, 24.3, 21.6. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{NO}_4\text{S}^+$: 388.1577, found: 388.1573. $[\alpha]^{20} = -28.4$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 11.152 min (98%), tR (minor) = 13.185 min (2%).



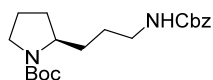
benzyl (S)-2-(3-(benzyloxy)propyl)pyrrolidine-1-carboxylate (22) (following general procedure A, colorless oil, 45.6 mg, 62% yield, 97.5:2.5 e.r., 96% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.17 – 7.90 (m, 2H), 7.58 – 7.51 (m, 1H), 7.47 – 7.39 (m, 2H), 7.39 – 7.27 (m, 5H), 5.18 – 5.07 (m, 2H), 4.46 – 4.17 (m, 2H), 4.03 – 3.83 (m, 1H), 3.56 – 3.35 (m, 2H), 2.04 – 1.65 (m, 7H), 1.58 – 1.45 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.6, 155.1, 137.2, 137.0, 132.9, 130.5, 130.4, 129.6, 128.5, 128.4, 127.9, 127.9, 66.8, 66.6, 65.0, 64.8, 57.7, 57.0, 46.7, 46.4, 31.3, 30.8, 30.7, 30.1, 25.7, 25.6, 23.9, 23.1. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{22}\text{H}_{26}\text{NO}_4^+$: 368.1856, found: 368.1850. $[\alpha]^{20} = -34.5$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 20% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 14.115 min (97.5%), tR (minor) = 14.851 min (2.5%).



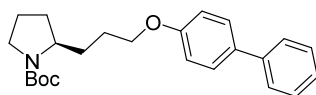
tert-butyl (S)-2-(3-((N,4-dimethylphenyl)sulfonamido)propyl)pyrrolidine-1-carboxylate (23) (following general procedure A, white solid, 41.4 mg, 52% yield, 99:1 e.r., 99% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.69 – 7.59 (m, 2H), 7.38 – 7.26 (m, 2H), 3.84 – 3.63 (m, 1H), 3.44 – 3.19 (m, 2H), 3.09 – 2.87 (m, 2H), 2.70 (s, 3H), 2.42 (s, 3H), 1.99 – 1.65 (m, 4H), 1.64 – 1.58 (m, 1H), 1.57 – 1.48 (m, 2H), 1.44 (s, 9H), 1.40 – 1.29 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 154.8, 143.4, 134.6, 129.8, 127.5, 79.3, 79.0, 57.0, 50.3, 46.6, 46.2, 34.9, 34.7, 31.9, 31.5, 31.0, 30.2, 28.7, 25.0, 24.5, 23.9, 23.2, 21.6. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{20}\text{H}_{33}\text{N}_2\text{O}_4\text{S}^+$: 397.2156, found: 397.2153. $[\alpha]^{20} = -34.0$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 40–41. Chiral HPLC condition: Daicel chiral IC, isocratic 5% *i*-PrOH in hexanes, tR (major) = 27.295 min (99%), tR (minor) = 24.665 min (1%).



tert-butyl (R)-2-(3-(1,3-dioxoisindolin-2-yl)propyl)pyrrolidine-1-carboxylate (24) (following general procedure A, colorless oil, 61.5 mg, 86% yield, 99.5:0.5 e.r., >99% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.87 – 7.75 (m, 2H), 7.72 – 7.61 (m, 2H), 3.84 – 3.56 (m, 3H), 3.41 – 3.20 (m, 2H), 1.96 – 1.84 (m, 1H), 1.85 – 1.50 (m, 6H), 1.45 – 1.26 (m, 10H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 168.4, 154.7, 134.0, 133.9, 132.2, 123.2, 123.2, 79.1, 79.0, 56.9, 46.6, 46.2, 38.0, 37.9, 32.1, 31.6, 30.8, 30.0, 28.6, 25.7, 25.5, 23.9, 23.2. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{20}\text{H}_{27}\text{N}_2\text{O}_4^+$: 359.1965, found: 359.1960. $[\alpha]^{20} = -22.8$ (c 1.0, CHCl_3). Chiral HPLC condition: Daicel chiral IC, isocratic 30% *i*-PrOH in hexanes, t_R (major) = 15.035 min (99.5%), t_R (minor) = 10.861 min (0.5%).

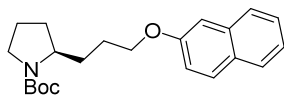


tert-butyl (R)-2-(3-(((benzyloxy)carbonyl)amino)propyl)pyrrolidine-1-carboxylate (25) (following general procedure A, colorless oil, 45.0 mg, 62% yield, 99:1 e.r., 99% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.40 – 7.26 (m, 5H), 5.28 – 4.67 (m, 3H), 3.88 – 3.58 (m, 1H), 3.43 – 3.10 (m, 4H), 1.93 – 1.65 (m, 4H), 1.64 – 1.56 (m, 1H), 1.55 – 1.45 (m, 2H), 1.45 (s, 9H), 1.37 – 1.22 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 156.5, 154.8, 136.8, 136.7, 128.6, 128.2, 128.1, 79.2, 79.1, 66.7, 66.5, 56.8, 46.6, 46.2, 41.1, 41.0, 31.9, 31.5, 30.8, 30.2, 28.6, 26.9, 26.7, 23.8, 23.1. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{20}\text{H}_{31}\text{N}_2\text{O}_4^+$: 363.2278, found: 363.2273. $[\alpha]^{20} = -18.4$ (c 1.0, CHCl_3). Chiral HPLC condition: Daicel chiral AS-H, isocratic 4% *i*-PrOH in hexanes, t_R (major) = 7.228 min (99%), t_R (minor) = 6.515 min (1%).

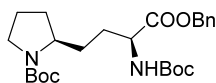


tert-butyl (S)-2-(3-([1,1'-biphenyl]-4-yloxy)propyl)pyrrolidine-1-carboxylate (26) (following general procedure A, white solid, 58.6 mg, 77% yield, 98.5:1.5 e.r., 98% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.58 – 7.54 (m, 2H), 7.54 – 7.50 (m, 2H), 7.44 – 7.39 (m, 2H), 7.33 – 7.28 (m, 1H), 6.99 – 6.93 (m, 2H), 4.09 – 3.95 (m, 2H), 3.91 – 3.77 (m, 1H), 3.49 – 3.26 (m, 2H), 2.03 – 1.77 (m, 6H), 1.74 – 1.65 (m, 1H), 1.58 – 1.50 (m, 1H), 1.48 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 158.7, 154.8, 141.0, 133.7, 128.8, 128.2, 126.8, 126.7, 114.9, 79.3, 79.0, 68.1, 68.0, 57.2, 46.7, 46.3, 31.4, 31.0, 30.8, 30.2, 28.7, 26.3, 23.9, 23.2. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{24}\text{H}_{32}\text{NO}_3^+$: 382.2377, found: 382.2373. $[\alpha]^{20} =$

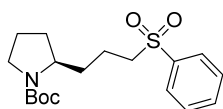
-18.9 (c 1.0, CHCl₃). m.p. (°C): 68-69. Chiral HPLC condition: Daicel chiral IC, isocratic 3% *i*-PrOH in hexanes, tR (major) = 21.770 min (98.5), tR (minor) = 19.962 min (1.5).



tert-butyl (S)-2-(3-(naphthalen-2-yloxy)propyl)pyrrolidine-1-carboxylate (27) (following general procedure A, white solid, 47.6 mg, 67% yield, 99:1 e.r., 99% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 7.78 – 7.75 (m, 1H), 7.75 – 7.69 (m, 2H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.35 – 7.31 (m, 1H), 7.16 – 7.11 (m, 2H), 4.20 – 4.02 (m, 2H), 3.96 – 3.76 (m, 1H), 3.53 – 3.26 (m, 2H), 2.02 – 1.79 (m, 6H), 1.76 – 1.66 (m, 1H), 1.64 – 1.52 (m, 1H), 1.49 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 157.1, 154.9, 134.7, 129.4, 129.0, 127.7, 126.8, 126.4, 123.6, 119.1, 106.7, 79.2, 68.0, 57.2, 46.7, 46.3, 31.5, 31.0, 30.8, 30.2, 28.7, 26.3, 23.9, 23.2. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₂H₃₀NO₃⁺: 356.2220, found: 356.2216. [α]_D²⁰ = -63.0 (c 1.5, CHCl₃). m.p. (°C): 76-78. Chiral HPLC condition: Daicel chiral IC, gradient from 1% to 3% *i*-PrOH in hexanes, tR (major) = 23.684 min (99%), tR (minor) = 22.878 min (1%).

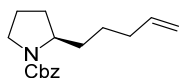


tert-butyl (S)-2-((S)-4-(benzyloxy)-3-((tert-butoxycarbonyl)amino)-4-oxobutyl)pyrrolidine-1-carboxylate (28) (following general procedure A, colorless oil, 60.7 mg, 66% yield, 99:1 d.r.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 7.41 – 7.26 (m, 5H), 5.37 – 4.96 (m, 3H), 4.42 – 4.02 (m, 1H), 3.87 – 3.56 (m, 1H), 3.44 – 3.27 (m, 1H), 3.26 – 3.18 (m, 1H), 1.90 – 1.57 (m, 6H), 1.54 – 1.46 (m, 1H), 1.43 (s, 9H), 1.42 (s, 9H), 1.29 – 1.19 (m, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 172.6, 155.6, 155.4, 154.8, 135.5, 128.7, 128.5, 79.9, 79.3, 67.1, 56.9, 53.6, 46.6, 46.2, 30.9, 30.3, 29.5, 28.7, 28.4, 23.8, 23.2. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₅H₃₉N₂O₆⁺: 463.2803, found: 463.2794. [α]_D²⁰ = -9.5 (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO₂, v = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 10.320 min (99%), tR (minor) = 10.694 min (1%).

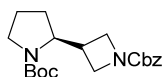


tert-butyl (S)-2-(3-(phenylsulfonyl)propyl)pyrrolidine-1-carboxylate (29) (following general procedure A, colorless oil, 40.2 mg, 57% yield, 95.5:4.5 e.r., 92% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 7.92 – 7.84 (m, 2H), 7.70 – 7.61 (m, 1H), 7.59 – 7.51 (m, 2H), 3.78 – 3.55 (m, 1H), 3.42 – 3.20 (m, 2H),

3.11 (q, J = 10.5 Hz, 2H), 1.94 – 1.84 (m, 1H), 1.81 – 1.73 (m, 3H), 1.70 – 1.62 (m, 2H), 1.61 – 1.53 (m, 1H), 1.40 (s, 9H), 1.39 – 1.33 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 154.8, 139.3, 133.8, 129.4, 128.2, 79.5, 79.2, 56.6, 56.3, 46.6, 46.2, 33.8, 32.9, 31.0, 30.0, 28.6, 23.9, 23.1, 19.8. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{18}\text{H}_{28}\text{NO}_4\text{S}^+$: 354.1734, found: 354.1728. $[\alpha]^{20} = -21.0$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IA-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 40% MeOH in scCO_2 , v = 0.8 mL/min, 40 $^\circ\text{C}$, 2200 psi, t_R (major) = 3.270 min (95.5%), t_R (minor) = 2.830 min (4.5%).



benzyl (R)-2-(pent-4-en-1-yl)pyrrolidine-1-carboxylate (30) (following general procedure A, colorless oil, 30.3 mg, 55% yield, 97:3 e.r., 95% e.s., with 7% 2-alkene side product). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.39 – 7.33 (m, 4H), 7.33 – 7.28 (m, 1H), 5.87 – 5.32 (m, 1H), 5.20 – 5.08 (m, 2H), 5.06 – 4.83 (m, 2H), 3.92 – 3.77 (m, 1H), 3.55 – 3.32 (m, 2H), 2.16 – 1.97 (m, 2H), 1.97 – 1.64 (m, 5H), 1.46 – 1.29 (m, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 155.2, 155.0, 138.9, 138.7, 137.4, 137.2, 128.6, 128.0, 128.0, 127.9, 114.7, 66.8, 66.5, 58.1, 57.4, 46.7, 46.4, 34.2, 33.9, 33.8, 33.6, 30.8, 30.0, 25.8, 25.7, 24.0, 23.2. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{17}\text{H}_{24}\text{NO}_2^+$: 274.1801, found: 274.1789. $[\alpha]^{20} = -73.5$ (c 1.6, CHCl_3). SFC analysis: Daicel Chiralpak IF-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 1% to 5% MeOH in scCO_2 , v = 0.8 mL/min, 40 $^\circ\text{C}$, 2200 psi, t_R (major) = 11.223 min (97%), t_R (minor) = 11.582 min (3%).

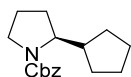


tert-butyl (S)-2-(1-((benzyloxy)carbonyl)azetidin-3-yl)pyrrolidine-1-carboxylate (31) (following general procedure A, colorless oil, 34.6 mg, 48% yield, 99.5:0.5 e.r., >99% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.37 – 7.32 (m, 4H), 7.32 – 7.28 (m, 1H), 5.09 (s, 2H), 4.16 – 3.90 (m, 4H), 3.80 – 3.66 (m, 1H), 3.58 – 3.34 (m, 1H), 3.31 – 3.23 (m, 1H), 2.96 – 2.62 (m, 1H), 2.05 – 1.90 (m, 1H), 1.88 – 1.76 (m, 2H), 1.65 – 1.57 (m, 1H), 1.45 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 156.6, 155.3, 155.1, 136.9, 128.6, 128.1, 128.1, 80.2, 79.6, 66.7, 59.2, 53.7, 52.8, 51.5, 47.3, 46.9, 33.7, 28.9, 28.6, 28.1, 23.9, 23.1. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{20}\text{H}_{29}\text{N}_2\text{O}_4^+$: 361.2122, found: 361.2115. $[\alpha]^{20} = -21.1$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO_2 , v = 0.8 mL/min, 40 $^\circ\text{C}$, 2200 psi, t_R (major) = 18.876 min (99.5%), t_R (minor) = 18.414 min (0.5%).

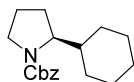


tert-butyl (S)-6-(1-((benzyloxy)carbonyl)pyrrolidin-2-yl)-2-azaspiro[3.3]heptane-2-carboxylate (32)

(following general procedure A, colorless oil, 39.7 mg, 50% yield, 99.5:0.5 e.r., >99% e.s.). ^1H NMR (400 MHz, CDCl_3 , two rotamers) δ 7.43 – 7.28 (m, 5H), 5.10 (d, J = 3.3 Hz, 2H), 3.93 – 3.72 (m, 4H), 3.71 – 3.58 (m, 1H), 3.56 – 3.39 (m, 1H), 3.39 – 3.31 (m, 1H), 2.30 – 1.96 (m, 4H), 1.81 (m, 4H), 1.63 – 1.51 (m, 1H), 1.42 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , two rotamers) δ 156.4, 155.9, 155.6, 137.2, 136.8, 128.6, 128.5, 128.2, 128.0, 127.9, 79.3, 67.1, 66.7, 61.7, 61.0, 47.0, 46.8, 37.1, 36.1, 34.4, 33.9, 33.7, 29.1, 28.5, 28.2, 23.9, 23.1. HRMS (ESI) m/z ($M+H$) $^+$ calcd for $\text{C}_{23}\text{H}_{33}\text{N}_2\text{O}_4$: 401.2435, found: 401.2426. $[\alpha]^{20} = -58.0$ (c 1.2, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 25% MeOH in scCO_2 , v = 0.8 mL/min, 40 $^\circ\text{C}$, 2200 psi, t_R (major) = 14.040 min (3%), t_R (minor) = 14.687 min (25%).

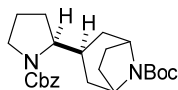


benzyl (S)-2-cyclopentylpyrrolidine-1-carboxylate (33) (following general procedure A, colorless oil, 25.4 mg, 46% yield, 97.5:2.5 e.r., 96% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.39 – 7.33 (m, 4H), 7.32 – 7.27 (m, 1H), 5.19 – 5.05 (m, 2H), 4.00 – 3.84 (m, 1H), 3.62 – 3.46 (m, 1H), 3.44 – 3.26 (m, 1H), 2.23 – 1.98 (m, 1H), 1.93 – 1.79 (m, 3H), 1.75 – 1.39 (m, 8H), 1.25 – 1.09 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 155.7, 137.4, 128.5, 128.1, 127.9, 66.8, 66.6, 61.5, 60.9, 46.6, 44.3, 30.0, 29.3, 28.8, 28.5, 25.4, 25.2, 24.0, 23.2. $[\alpha]^{20} = -76.5$ (c 1.5, CHCl_3). HRMS (ESI) m/z ($M+H$) $^+$ calcd for $\text{C}_{17}\text{H}_{24}\text{NO}_2$: 274.1802, found: 274.1797. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 10% MeOH in scCO_2 , v = 0.8 mL/min, 40 $^\circ\text{C}$, 2200 psi, t_R (major) = 8.568 min (97.5%), t_R (minor) = 8.810 min (2.5%).



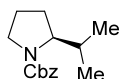
benzyl (S)-2-cyclohexylpyrrolidine-1-carboxylate (34) (following general procedure A, reaction temperature 60 $^\circ\text{C}$, colorless oil, 29.3 mg, 51% yield, 90.5:9.5 e.r., 82% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.40 – 7.32 (m, 4H), 7.32 – 7.28 (m, 1H), 5.24 – 5.14 (m, 1H), 5.14 – 5.00 (m, 1H), 3.84 – 3.70 (m, 1H), 3.63 – 3.46 (m, 1H), 3.36 – 3.23 (m, 1H), 1.83 – 1.76 (m, 4H), 1.75 – 1.69 (m, 2H), 1.68 – 1.53 (m, 4H), 1.24 – 1.05 (m, 3H), 1.05 – 0.86 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 155.6, 155.4, 137.4, 137.3, 128.5, 127.9, 66.7, 66.6, 62.7, 62.0, 47.2, 46.9, 41.5, 40.7, 30.2, 27.9, 27.5, 26.7,

26.7, 26.6, 26.4, 24.5, 23.8. HRMS (ESI) m/z ($M+H$)⁺ calcd for C₁₈H₂₆NO₂⁺: 288.1958, found: 288.1954. $[\alpha]^{20} = -44.3$ (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 10% MeOH in scCO₂, $v = 0.8$ mL/min, 40 °C, 2200 psi, tR (major) = 8.998 min (90.5%), tR (minor) = 9.251 min (9.5%).

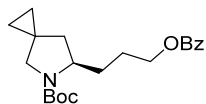


tert-butyl 3-((S)-1-((benzyloxy)carbonyl)pyrrolidin-2-yl)-8-azabicyclo[3.2.1]octane-8-carboxylate (35)

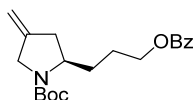
(following general procedure A, colorless oil, 52.8 mg, 64% yield, 94.5:5.5 e.r., 90% e.s., >98:2 d.r.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 7.38 – 7.33 (m, 4H), 7.33 – 7.28 (m, 1H), 5.31 – 5.12 (m, 1H), 5.12 – 4.98 (m, 1H), 4.31 – 4.19 (m, 1H), 4.19 – 4.04 (m, 1H), 3.85 – 3.70 (m, 1H), 3.64 – 3.48 (m, 1H), 3.31 – 3.21 (m, 1H), 2.68 – 2.18 (m, 1H), 1.94 – 1.74 (m, 5H), 1.70 – 1.63 (m, 2H), 1.50 (s, 3H), 1.46 (s, 9H), 1.36 – 1.28 (m, 2H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 155.3, 153.6, 137.2, 137.0, 128.6, 128.1, 128.0, 127.9, 79.1, 66.9, 66.6, 61.4, 60.8, 53.9, 53.8, 53.2, 53.0, 47.2, 47.0, 34.9, 34.0, 33.8, 31.6, 31.5, 31.0, 30.7, 28.6, 28.4, 27.8, 27.1, 26.4, 26.3, 24.5, 23.8. HRMS (ESI) m/z ($M+H$)⁺ calcd for C₂₄H₃₅N₂O₄⁺: 415.2591, found: 415.2584. $[\alpha]^{20} = -44.0$ (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 25% MeOH in scCO₂, $v = 0.8$ mL/min, 40 °C, 2200 psi, tR (major) = 13.505 min (94.5%), tR (minor) = 13.971 min (5.5%).



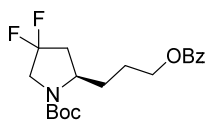
benzyl (S)-2-isopropylpyrrolidine-1-carboxylate (36) (following general procedure A, THF:DMIB = 20:1, colorless oil, 26.4 mg, 53% yield, 96:4 e.r., 93% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 7.44 – 7.28 (m, 5H), 5.20 – 5.05 (m, 2H), 3.84 – 3.72 (m, 1H), 3.68 – 3.50 (m, 1H), 3.43 – 3.14 (m, 1H), 2.34 – 2.01 (m, 1H), 1.86 – 1.73 (m, 4H), 0.95 – 0.83 (m, 3H), 0.83 – 0.69 (m, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 155.7, 155.4, 137.4, 137.2, 128.6, 127.9, 127.9, 66.8, 66.6, 63.2, 62.6, 47.4, 47.1, 30.9, 30.1, 26.7, 25.8, 24.5, 23.8, 19.6, 17.0, 16.9. HRMS (ESI) m/z ($M+H$)⁺ calcd for C₁₅H₂₂NO₂⁺: 248.1645, found: 248.1641. $[\alpha]^{20} = -72$ (c 1.5, CHCl₃). SFC analysis: Daicel Chiralpak OD-H (4.6 mm ID × 250 mm L, 5 μm PS), gradient from 1% to 20% MeOH in scCO₂, $v = 0.8$ mL/min, 40 °C, 2200 psi, tR (major) = 4.861 min (96%), tR (minor) = 5.054 min (4%).



tert-butyl (R)-6-(3-(benzyloxy)propyl)-5-azaspiro[2.4]heptane-5-carboxylate (37) (following general procedure A, colorless oil, 52.5 mg, 73% yield, 98:2 e.r., >99% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.09 – 8.00 (m, 2H), 7.58 – 7.51 (m, 1H), 7.45 – 7.40 (m, 2H), 4.39 – 4.27 (m, 2H), 4.08 – 3.87 (m, 1H), 3.54 – 3.33 (m, 1H), 3.13 – 2.99 (m, 1H), 2.25 – 2.07 (m, 1H), 2.02 – 1.87 (m, 1H), 1.81 – 1.73 (m, 2H), 1.73 – 1.66 (m, 1H), 1.44 (s, 9H), 1.39 (d, $J = 12.6$ Hz, 1H), 0.64 – 0.47 (m, 4H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 154.6, 133.0, 130.5, 129.6, 128.4, 79.3, 65.1, 58.1, 54.5, 53.9, 39.5, 38.7, 31.6, 31.0, 28.7, 25.9, 20.5, 19.8, 14.1, 7.8. $[\alpha]^{20} = -16.0$ (c 1.0, CHCl_3). HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{21}\text{H}_{30}\text{NO}_4$: 360.2169, found: 360.2166. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 10% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 10.123 min (98%), tR (minor) = 9.822 min (2%).

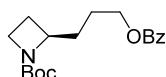


tert-butyl (R)-2-(3-(benzyloxy)propyl)-4-methylenepyrrolidine-1-carboxylate (38) (following general procedure A, colorless oil, 33.8 mg, 49% yield, 94:6 e.r., 88% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.07 – 7.97 (m, 2H), 7.58 – 7.50 (m, 1H), 7.48 – 7.37 (m, 2H), 5.05 – 4.92 (m, 2H), 4.38 – 4.25 (m, 2H), 4.15 – 3.96 (m, 2H), 3.88 – 3.74 (m, 1H), 2.83 – 2.62 (m, 1H), 2.33 – 2.20 (m, 1H), 1.79 – 1.66 (m, 3H), 1.57 – 1.48 (m, 1H), 1.45 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 154.3, 145.5, 144.6, 133.0, 130.4, 129.6, 128.4, 107.8, 107.5, 79.6, 64.9, 56.7, 50.5, 50.0, 37.9, 37.2, 31.3, 30.8, 28.6, 25.5. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{20}\text{H}_{28}\text{NO}_4$: 346.2013, found: 346.2008. $[\alpha]^{20} = -32.3$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), isocratic 5% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 18.762 min (94%), tR (minor) = 15.283 min (6%).

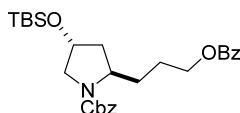


tert-butyl (R)-2-(3-(benzyloxy)propyl)-4,4-difluoropyrrolidine-1-carboxylate (39) (following general procedure A, colorless oil, 24.4 mg, 33% yield, 84:16 e.r., 69% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.05 – 8.01 (m, 2H), 7.57 – 7.52 (m, 1H), 7.47 – 7.41 (m, 2H), 4.43 – 4.28 (m, 2H), 4.20 – 3.98 (m, 1H), 3.98 – 3.70 (m, 1H), 3.67 – 3.57 (m, 1H), 2.59 – 2.42 (m, 1H), 2.21 – 2.09 (m, 1H), 2.07 – 1.89 (m,

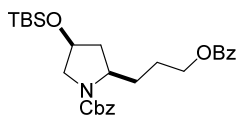
1H), 1.80 – 1.73 (m, 2H), 1.70 – 1.63 (m, 1H), 1.45 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 154.1, 133.1, 130.4, 129.7, 128.5, 127.5 ($J_{\text{CF}} = 243.5$ Hz), 80.6, 64.6, 55.8, 53.5 (br, rotamers), 39.2 (br, rotamers), 31.0 (br, rotamers), 28.5, 25.4. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , two rotamers) -95.83 (d, $J_{\text{FF-gem}} = 234.3$ Hz, 1F, two rotamers), -99.28 (d, $J_{\text{FF-gem}} = 233.3$, 1F, two rotamers). HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{19}\text{H}_{25}\text{F}_2\text{NNaO}_4^+$: 392.1644, found: 392.1638. $[\alpha]^{20} = -23.8$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 4.200 min (84%), tR (minor) = 4.442 min (16%).



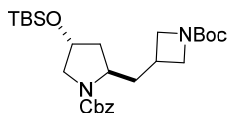
tert-butyl (R)-2-(3-(benzyloxy)propyl)azetidine-1-carboxylate (40) (following general procedure A, colorless oil, 20.1 mg, 31% yield, 97.5:2.5 e.r., 96% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.07 – 8.01 (m, 2H), 7.57 – 7.53 (m, 1H), 7.47 – 7.40 (m, 2H), 4.41 – 4.31 (m, 2H), 4.29 – 4.22 (m, 1H), 3.89 – 3.76 (m, 2H), 2.36 – 2.22 (m, 1H), 2.08 – 1.95 (m, 1H), 1.92 – 1.71 (m, 4H), 1.43 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 156.8, 133.0, 130.5, 129.7, 128.5, 79.4, 64.9, 61.8, 46.5, 32.3, 28.6, 24.4, 22.0. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{18}\text{H}_{26}\text{NO}_4^+$: 320.1856, found: 320.1853. $[\alpha]^{20} = -20.5$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IF-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 20% *i*-PrOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 5.853 min (97.5%), tR (minor) = 5.613 min (2.5%).



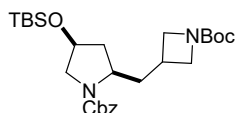
benzyl (2R,4R)-2-(3-(benzyloxy)propyl)-4-((tert-butyldimethylsilyl)oxy)pyrrolidine-1-carboxylate (41) (following general procedure A, colorless oil, 43.5 mg, 44% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.07 – 7.98 (m, 2H), 7.59 – 7.52 (m, 1H), 7.47 – 7.39 (m, 2H), 7.37 – 7.26 (m, 5H), 5.27 – 5.05 (m, 2H), 4.39 – 4.29 (m, 2H), 4.28 – 4.20 (m, 1H), 4.14 – 3.98 (m, 1H), 3.67 – 3.39 (m, 2H), 2.26 – 1.81 (m, 2H), 1.83 – 1.63 (m, 3H), 1.60 – 1.49 (m, 1H), 0.85 (s, 9H), 0.05 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 155.6, 137.1, 137.0, 133.0, 130.5, 130.4, 129.7, 128.6, 128.5, 128.0, 127.9, 70.4, 69.9, 66.9, 66.7, 65.1, 64.9, 56.5, 55.8, 55.3, 55.0, 40.9, 40.2, 31.7, 31.0, 25.8, 25.3, 25.1, 18.1, -4.7. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{28}\text{H}_{40}\text{NO}_5\text{Si}^+$: 498.2670, found: 498.2665. $[\alpha]^{20} = -32.1$ (c 1.0, CHCl_3).



benzyl (2R,4S)-2-(3-(benzyloxy)propyl)-4-((tert-butyldimethylsilyl)oxy)pyrrolidine-1-carboxylate (42) (following general procedure A, colorless oil, 47.2 mg, 47% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.08 – 7.99 (m, 2H), 7.58 – 7.51 (m, 1H), 7.42 (q, $J = 7.2$ Hz, 2H), 7.39 – 7.23 (m, 5H), 5.19 – 5.06 (m, 2H), 4.40 – 4.29 (m, 2H), 4.29 – 4.22 (m, 1H), 4.01 – 3.89 (m, 1H), 3.82 – 3.62 (m, 1H), 3.32 – 3.23 (m, 1H), 2.20 – 1.96 (m, 2H), 1.86 – 1.67 (m, 4H), 0.86 (s, 9H), 0.05 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 166.7, 155.1, 155.0, 137.1, 136.9, 133.0, 132.9, 130.5, 130.4, 129.7, 129.6, 128.6, 128.4, 128.4, 128.1, 128.0, 128.0, 71.2, 70.5, 67.0, 66.8, 65.2, 65.0, 57.5, 56.8, 55.3, 55.0, 39.5, 38.9, 31.7, 31.1, 25.9, 25.8, 25.7, 18.0, -4.7, -4.8. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{28}\text{H}_{40}\text{NO}_5\text{Si}^+$: 498.2670, found: 498.2669. $[\alpha]^{20} = -21.1$ (c 1.0, CHCl_3).

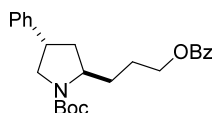


benzyl (2R,4R)-2-((1-(tert-butoxycarbonyl)azetidin-3-yl)methyl)-4-((tert-butyldimethylsilyl)oxy)pyrrolidine-1-carboxylate (43) (following general procedure A, colorless oil, 66.0 mg, 65% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.38 – 7.32 (m, 4H), 7.32 – 7.27 (m, 1H), 5.21 – 5.01 (m, 2H), 4.39 – 4.29 (m, 1H), 4.04 – 3.82 (m, 3H), 3.66 – 3.41 (m, 3H), 3.43 – 3.33 (m, 1H), 2.64 – 2.35 (m, 1H), 2.21 – 1.88 (m, 2H), 1.73 – 1.57 (m, 2H), 1.42 (s, 9H), 0.84 (s, 9H), 0.09 – 0.01 (m, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 156.4, 155.7, 137.0, 136.8, 128.6, 128.2, 128.0, 127.9, 79.2, 70.4, 69.9, 67.1, 66.8, 55.2, 54.9, 54.8, 54.7, 54.5, 41.1, 40.4, 40.2, 39.5, 28.5, 26.4, 26.2, 25.8, 18.0, -4.7, -4.8. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{27}\text{H}_{45}\text{N}_2\text{O}_5\text{Si}^+$: 505.3092, found: 505.3086. $[\alpha]^{20} = +12.7$ (c 1.0, CHCl_3).

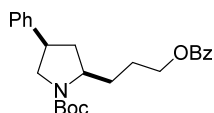


benzyl (2R,4S)-2-((1-(tert-butoxycarbonyl)azetidin-3-yl)methyl)-4-((tert-butyldimethylsilyl)oxy)pyrrolidine-1-carboxylate (44) (following general procedure A, colorless oil, 64.1 mg, 63% yield, 95:5 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.39 – 7.33 (m, 4H), 7.33 – 7.27 (m, 1H), 5.21 – 5.02 (m, 2H), 4.41 – 4.28 (m, 1H), 4.05 – 3.77

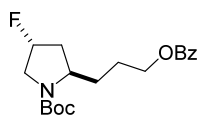
(m, 3H), 3.75 – 3.57 (m, 2H), 3.54 – 3.45 (m, 1H), 3.32 – 3.20 (m, 1H), 2.67 – 2.39 (m, 1H), 2.35 – 2.10 (m, 1H), 2.08 – 2.00 (m, 1H), 1.95 – 1.83 (m, 1H), 1.70 – 1.58 (m, 1H), 1.42 (s, 9H), 0.87 (s, 9H), 0.05 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 156.5, 156.4, 155.1, 155.0, 137.0, 136.7, 128.7, 128.6, 128.3, 128.1, 128.0, 79.2, 79.1, 71.4, 70.6, 67.2, 66.8, 56.0, 55.4, 55.4, 55.1, 54.7, 40.0, 39.8, 39.5, 39.1, 31.9, 28.8, 28.6, 26.6, 26.4, 25.9, 18.0, -4.7, -4.8. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{27}\text{H}_{45}\text{N}_2\text{O}_5\text{Si}^+$: 505.3092, found: 505.3088. $[\alpha]^{20} = -50.1$ (c 1.0, CHCl_3).



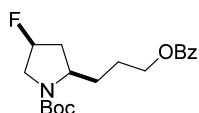
tert-butyl (2R,4S)-2-(3-(benzyloxy)propyl)-4-phenylpyrrolidine-1-carboxylate (45) (following general procedure A, colorless oil, 41.0 mg, 50% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.08 – 8.03 (m, 2H), 7.59 – 7.52 (m, 1H), 7.47 – 7.41 (m, 2H), 7.35 – 7.29 (m, 2H), 7.26 – 7.21 (m, 3H), 4.42 – 4.33 (m, 2H), 4.13 – 3.87 (m, 1H), 3.84 – 3.73 (m, 1H), 3.50 – 3.18 (m, 2H), 2.19 – 2.05 (m, 2H), 2.02 – 1.89 (m, 1H), 1.88 – 1.78 (m, 2H), 1.65 – 1.56 (m, 1H), 1.46 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 154.7, 141.5, 133.1, 133.0, 130.5, 130.4, 129.7, 128.7, 128.5, 127.3, 127.2, 126.9, 79.6, 79.4, 65.1, 65.0, 57.5, 53.5, 52.6, 42.2, 41.4, 38.5, 37.2, 31.8, 31.2, 28.6, 26.2. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{25}\text{H}_{32}\text{NO}_4^+$: 410.2326, found: 410.2321. $[\alpha]^{20} = -9.6$ (c 1.0, CHCl_3).



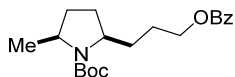
tert-butyl (2R,4R)-2-(3-(benzyloxy)propyl)-4-phenylpyrrolidine-1-carboxylate (46) (following general procedure A, colorless oil, 52.4 mg, 64% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.08 – 8.02 (m, 2H), 7.58 – 7.52 (m, 1H), 7.47 – 7.41 (m, 2H), 7.36 – 7.29 (m, 2H), 7.26 – 7.22 (m, 3H), 4.43 – 4.28 (m, 2H), 4.21 – 3.83 (m, 2H), 3.29 – 3.16 (m, 2H), 2.60 – 2.48 (m, 1H), 2.36 – 2.02 (m, 1H), 1.85 – 1.74 (m, 3H), 1.73 – 1.62 (m, 1H), 1.48 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 154.7, 140.7, 133.0, 132.9, 130.5, 130.4, 129.6, 128.7, 128.4, 127.2, 126.9, 79.6, 79.4, 65.1, 65.0, 57.6, 57.3, 53.6, 52.7, 43.3, 42.8, 40.0, 39.6, 32.1, 31.1, 28.6, 25.0, 24.8. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{25}\text{H}_{32}\text{NO}_4^+$: 410.2326, found: 410.2321. $[\alpha]^{20} = -26.3$ (c 1.0, CHCl_3).



tert-butyl (2R,4R)-2-(3-(benzyloxy)propyl)-4-fluoropyrrolidine-1-carboxylate (47) (following general procedure A, colorless oil, 47.6 mg, 68% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.06 – 8.00 (m, 2H), 7.60 – 7.51 (m, 1H), 7.47 – 7.40 (m, 2H), 5.22 – 5.00 (m, 1H), 4.39 – 4.27 (m, 2H), 4.11 – 3.77 (m, 2H), 3.45 – 3.28 (m, 1H), 2.50 – 2.34 (m, 1H), 2.20 – 1.95 (m, 1H), 1.86 – 1.67 (m, 3H), 1.63 – 1.50 (m, 1H), 1.45 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 154.9, 133.0, 130.4, 129.7, 128.5, 91.62 (d, $J_{\text{CF}} = 177.6$ Hz), 79.9, 64.9, 55.6, 55.5, 53.32 (d, $J_{\text{CF}} = 54.0$ Hz), 38.68 (d, $J_{\text{CF}} = 87.3$ Hz), 31.7, 31.0, 28.6, 24.9, 24.7. $^{19}\text{F}\{^1\text{H}\}$ NMR (377 MHz, CDCl_3 , two rotamers) δ -177.1, -177.8. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{19}\text{H}_{27}\text{FNO}_4$: 352.1919, found: 352.1922. $[\alpha]^{20} = -24.3$ (c 1.0, CHCl_3).



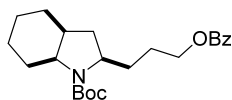
tert-butyl (2R,4S)-2-(3-(benzyloxy)propyl)-4-fluoropyrrolidine-1-carboxylate (48) (following general procedure A, colorless oil, 41.2 mg, 59% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.09 – 7.98 (m, 2H), 7.58 – 7.51 (m, 1H), 7.49 – 7.32 (m, 2H), 5.36 – 5.04 (m, 1H), 4.43 – 4.21 (m, 2H), 4.11 – 3.81 (m, 1H), 3.80 – 3.53 (m, 2H), 2.20 – 2.03 (m, 2H), 2.05 – 1.90 (m, 1H), 1.86 – 1.74 (m, 2H), 1.74 – 1.64 (m, 1H), 1.45 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 154.4, 133.0, 130.6, 129.7, 128.6, 128.5, 128.4, 93.14 (d, $J = 175.7$ Hz), 79.9, 64.9, 56.8, 53.32 (d, $J = 35.9$ Hz), 36.67 (d, $J = 93.4$ Hz), 31.6, 31.2, 28.6, 26.1. $^{19}\text{F}\{^1\text{H}\}$ NMR (377 MHz, CDCl_3 , two rotamers) δ -169.2, -169.5. HRMS (ESI) m/z ($\text{M}+\text{Na}$) $^+$ calcd for $\text{C}_{19}\text{H}_{26}\text{FNNaO}_4$: 374.1738, found: 374.1735. $[\alpha]^{20} = -8.7$ (c 1.0, CHCl_3).



tert-butyl (2S,5S)-2-(3-(benzyloxy)propyl)-5-methylpyrrolidine-1-carboxylate (49) (following general procedure A, colorless oil, 41.6 mg, 60% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.09 – 7.99 (m, 2H), 7.58 – 7.51 (m, 1H), 7.47 – 7.38 (m, 2H), 4.36 – 4.27 (m, 2H), 3.97 – 3.65 (m, 2H), 2.09 – 1.84 (m, 3H), 1.84 – 1.71 (m, 2H), 1.70 – 1.60 (m, 1H), 1.60 – 1.55 (m, 1H), 1.50 – 1.39 (m, 1H), 1.44 (s, 9H), 1.21 (d, $J = 6.2$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR

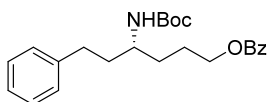
(126 MHz, CDCl₃, two rotamers) δ 166.7, 155.0, 133.0, 130.5, 129.6, 128.4, 79.1, 65.2, 58.3, 54.2, 32.5, 31.9, 29.6, 28.7, 25.9, 22.2. HRMS (ESI) m/z (M+H)⁺ calcd for C₂₀H₃₀NO₄⁺: 348.2169, found: 348.2165. $[\alpha]^{20} = +8.7$ (c 1.0, CHCl₃).

In comparison, cross coupling the corresponding NHP ester with alkyl iodide formed the desired product in 15% yield with 33:67 d.r. (diastereomeric ratio was determined by NMR analysis).



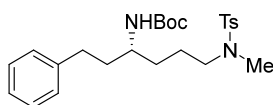
***tert*-butyl (2R,3aS,7aS)-2-(3-(benzyloxy)propyl)octahydro-1H-indole-1-carboxylate (50)** (following general procedure A, colorless oil, 41.7 mg, 54% yield, 98:2 d.r.). Diastereomeric ratio (d.r.) was determined by SFC analysis. ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.07 – 7.99 (m, 2H), 7.57 – 7.51 (m, 1H), 7.46 – 7.39 (m, 2H), 4.33 (t, J = 6.8 Hz, 2H), 3.91 – 3.63 (m, 2H), 2.42 – 2.11 (m, 2H), 2.04 – 1.84 (m, 2H), 1.82 – 1.69 (m, 4H), 1.67 – 1.55 (m, 2H), 1.51 – 1.37 (m, 2H), 1.43 (s, 9H), 1.33 – 1.21 (m, 1H), 1.18 – 1.04 (m, 2H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 166.7, 154.8, 132.9, 130.6, 129.7, 128.4, 78.9, 65.2, 57.8, 57.6, 36.2, 34.4, 33.8, 32.6, 29.5, 28.7, 26.2, 25.7, 24.3, 20.8. HRMS (ESI) m/z (M+H)⁺ calcd for C₂₃H₃₄NO₄⁺: 388.2482, found: 388.2477. $[\alpha]^{20} = -21.1$ (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μ m PS), gradient from 3% to 15% MeOH in scCO₂, v = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 12.174 min (98%), tR (minor) = 12.626 min (2%).

In comparison, cross coupling the corresponding NHP ester with alkyl iodide formed the desired product in 16% yield with 39:61 d.r. (Diastereomeric ratio was determined by SFC analysis).

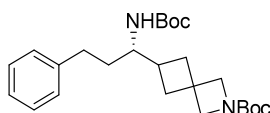


(S)-4-((*tert*-butoxycarbonyl)amino)-6-phenylhexyl benzoate (51) (following general procedure B, THF:DMIB = 10:1, reaction time = 12 h, white solid, 54.7 mg, 69% yield, 96.5:3.5 e.r., 94% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.07 – 8.01 (m, 2H), 7.58 – 7.53 (m, 1H), 7.47 – 7.40 (m, 2H), 7.31 – 7.25 (m, 2H), 7.22 – 7.13 (m, 3H), 4.40 – 4.03 (m, 1H), 4.32 (t, J = 6.5 Hz, 2H), 3.92 – 3.43 (m, 1H), 2.78 – 2.58 (m, 2H), 1.91 – 1.77 (m, 3H), 1.75 – 1.64 (m, 2H), 1.54 – 1.49 (m, 1H), 1.46 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 166.7, 155.8, 142.0, 133.0, 130.5, 129.7, 128.6, 128.5, 126.0, 79.3, 64.9, 50.5, 37.7, 32.5, 32.4, 28.6, 25.5. HRMS (ESI) m/z (M+H)⁺ calcd for C₂₄H₃₂NO₄⁺: 398.2326, found:

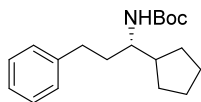
398.2320. $[\alpha]^{20} = +15.4$ (c 1.0, CHCl₃). m.p. (°C): 86-88. Chiral HPLC condition: Daicel chiral AS-H, 5% *i*-PrOH in hexanes, tR (major) = 8.770 min (96.5%), tR (minor) = 10.204 min (3.5%).



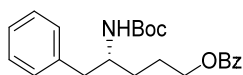
tert-butyl (S)-6-((N,4-dimethylphenyl)sulfonamido)-1-phenylhexan-3-ylcarbamate (53) (following general procedure B, THF:DMIB = 10:1, reaction time = 12 h, white solid, 50.4 mg, 55% yield, 96:4 e.r., 93% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 7.73 – 7.60 (m, 2H), 7.32 – 7.28 (m, 2H), 7.29 – 7.24 (m, 2H), 7.20 – 7.14 (m, 3H), 4.45 – 4.01 (m, 1H), 3.77 – 3.40 (m, 1H), 3.05 – 2.89 (m, 2H), 2.68 (s, 3H), 2.71 – 2.65 (m, 1H), 2.64 – 2.56 (m, 1H), 2.41 (s, 3H), 1.86 – 1.71 (m, 1H), 1.69 – 1.52 (m, 4H), 1.44 (s, 9H), 1.43 – 1.35 (m, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 155.9, 143.3, 142.0, 134.7, 129.7, 128.5, 128.5, 127.5, 126.0, 79.2, 50.4, 50.1, 37.9, 34.8, 32.8, 32.5, 28.5, 24.3, 21.6. HRMS (ESI) m/z (M+H)⁺ calcd for C₂₅H₃₇N₂O₄S⁺: 461.2469, found: 461.2462. $[\alpha]^{20} = +14.2$ (c 1.0, CHCl₃). m.p. (°C): 40-41. Chiral HPLC condition: Daicel chiral OD-H, gradient from 5% to 40% *i*-PrOH in hexanes, tR (major) = 13.835 min (96%), tR (minor) = 15.404 min (4%).



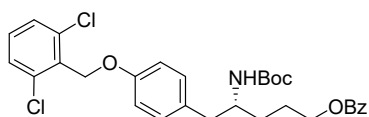
tert-butyl (S)-6-(1-((tert-butoxycarbonyl)amino)-3-phenylpropyl)-2-azaspiro[3.3]heptane-2-carboxylate (53) (following general procedure B, THF:DMIB = 5:1, reaction time = 6 h, colorless oil, 46.5 mg, 54% yield, 97:3 e.r., 95% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 7.32 – 7.24 (m, 2H), 7.21 – 7.13 (m, 3H), 4.30 – 3.97 (m, 1H), 3.89 (s, 2H), 3.82 – 3.76 (m, 1H), 3.76 – 3.71 (m, 1H), 3.64 – 3.27 (m, 1H), 2.79 – 2.63 (m, 1H), 2.63 – 2.53 (m, 1H), 2.21 – 2.05 (m, 3H), 2.00 – 1.92 (m, 1H), 1.87 – 1.80 (m, 1H), 1.75 – 1.68 (m, 1H), 1.46 (s, 9H), 1.44 – 1.43 (m, 1H), 1.42 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 156.4, 156.2, 142.0, 128.6, 128.5, 126.0, 79.4, 61.5, 54.7, 36.6, 36.3, 35.6, 35.2, 34.9, 33.8, 32.5, 28.5. HRMS (ESI) m/z (M+H)⁺ calcd for C₂₅H₃₉N₂O₄⁺: 431.2904, found: 431.2895. $[\alpha]^{20} = +12.4$ (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 10% MeOH in scCO₂, v = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 15.726 min (97%), tR (minor) = 16.809 min (3%).



tert-butyl (S)-(1-cyclopentyl-3-phenylpropyl)carbamate (54) (following general procedure B, THF:DMIB = 10:1, reaction time = 12 h, colorless oil, 27.0 mg, 45% yield, 77.5:22.5 e.r., 56% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 7.30 – 7.23 (m, 2H), 7.21 – 7.13 (m, 3H), 4.46 – 4.04 (m, 1H), 3.61 – 3.24 (m, 1H), 2.77 – 2.67 (m, 1H), 2.61 (m, 1H), 1.93 – 1.80 (m, 2H), 1.75 – 1.66 (m, 2H), 1.65 – 1.55 (m, 3H), 1.54 – 1.49 (m, 2H), 1.46 (s, 9H), 1.29 – 1.16 (m, 2H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 156.1, 142.5, 128.5, 128.5, 125.9, 79.0, 54.7, 45.5, 37.0, 32.6, 29.9, 28.9, 28.6, 25.7, 25.4. HRMS (ESI) m/z (M+Na)⁺ calcd for C₁₉H₂₉NNaO₂⁺: 326.2091, found: 326.2086. [α]²⁰ = +6.3 (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO₂, v = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 4.182 min (77.5%), tR (minor) = 4.425 min (22.5%).

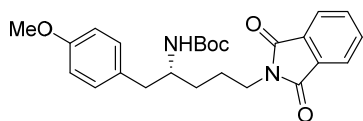


(R)-4-((tert-butoxycarbonyl)amino)-5-phenylpentyl benzoate (55) (following general procedure B, THF:DMIB = 5:1, reaction time = 6 h, white solid, 50.2 mg, 65% yield, 92.5:7.5 e.r., 92% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.06 – 7.94 (m, 2H), 7.58 – 7.53 (m, 1H), 7.47 – 7.39 (m, 2H), 7.30 – 7.25 (m, 2H), 7.23 – 7.16 (m, 3H), 4.49 – 4.21 (m, 3H), 4.04 – 3.62 (m, 1H), 2.89 – 2.71 (m, 2H), 1.96 – 1.85 (m, 1H), 1.85 – 1.75 (m, 1H), 1.73 – 1.63 (m, 1H), 1.50 – 1.42 (m, 1H), 1.41 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 166.6, 155.6, 138.1, 133.0, 130.5, 129.7, 129.6, 128.5, 128.4, 126.5, 79.3, 64.7, 51.5, 41.6, 30.8, 28.5, 25.6. HRMS (ESI) m/z (M+H)⁺ calcd for C₂₃H₃₀NO₄⁺: 384.2169, found: 384.2163. [α]²⁰ = +24.0 (c 1.0, CHCl₃). m.p. (°C): 88-91. Chiral HPLC condition: Daicel chiral AS-H, 4% *i*-PrOH in hexanes, tR (major) = 16.563 min (92.5%), tR (minor) = 13.958 min (7.5%).

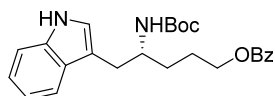


(R)-4-((tert-butoxycarbonyl)amino)-5-(4-((2,6-dichlorobenzyl)oxy)phenyl)pentyl benzoate (56) (following general procedure B, THF:DMIB = 5:1, reaction time = 6 h, white solid, 74.3 mg, 67% yield, 97.5:2.5 e.r., 98% e.s.). ¹H NMR (400 MHz, CDCl₃, two rotamers) δ 8.06 – 7.95 (m, 2H), 7.58 – 7.52 (m, 1H), 7.47 – 7.41 (m, 2H), 7.40 – 7.32 (m, 2H), 7.28 – 7.19 (m, 1H), 7.16 – 7.09 (m, 2H), 6.99 – 6.91 (m, 2H), 5.23 (s, 2H), 4.53 – 4.26 (m, 3H), 3.98 – 3.64 (m, 1H), 2.92 – 2.56 (m, 2H), 1.95 – 1.77 (m, 2H), 1.75

– 1.64 (m, 1H), 1.51 – 1.45 (m, 1H), 1.42 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , two rotamers) δ 166.6, 157.6, 155.6, 137.1, 133.0, 132.3, 130.7, 130.5, 130.5, 130.4, 129.6, 128.5, 128.4, 114.9, 79.2, 65.3, 64.7, 51.5, 40.6, 30.6, 28.5, 25.5. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{30}\text{H}_{34}\text{Cl}_2\text{NO}_5^+$: 558.1809, found: 558.1800. $[\alpha]^{20} = +36.9$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 112–114. Chiral HPLC condition: Daicel chiral IC, isocratic 20% *i*-PrOH in hexanes, tR (major) = 11.910 min (97.5%), tR (minor) = 9.889 min (2.5%). Growing single crystals of **50** in ethyl acetate/hexanes by slow diffusion at rt resulted in the formation of colorless single crystals suitable for X-ray diffraction analysis.

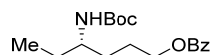


tert-butyl (R)-((5-(1,3-dioxoisindolin-2-yl)-1-(4-methoxyphenyl)pentan-2-yl)carbamate (57) (following general procedure B, THF:DMIB = 5:1, reaction time = 6 h, white solid, 62.8 mg, 72% yield, 97:3 e.r., 96% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.88 – 7.77 (m, 2H), 7.74 – 7.65 (m, 2H), 7.10 – 6.99 (m, 2H), 6.83 – 6.70 (m, 2H), 4.44 – 4.06 (m, 1H), 3.86 – 3.76 (m, 1H), 3.74 (s, 3H), 3.65 (t, $J = 7.1$ Hz, 2H), 2.75 – 2.61 (m, 2H), 1.82 – 1.74 (m, 1H), 1.74 – 1.63 (m, 1H), 1.59 – 1.46 (m, 1H), 1.37 (s, 9H), 1.36 – 1.26 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 168.4, 158.2, 155.5, 134.0, 132.2, 130.5, 130.1, 123.3, 113.9, 79.1, 55.3, 51.5, 40.5, 37.8, 31.4, 28.5, 25.4. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{25}\text{H}_{31}\text{N}_2\text{O}_5^+$: 439.2228, found: 439.2219. $[\alpha]^{20} = +36.1$ (c 1.0, CHCl_3). m.p. ($^\circ\text{C}$): 122–124. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), isocratic 10% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 $^\circ\text{C}$, 2200 psi, tR (major) = 2.860 min (97%), tR (minor) = 2.420 min (3%).

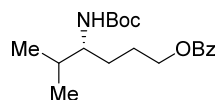


(R)-4-((tert-butoxycarbonyl)amino)-5-(1H-indol-3-yl)pentyl benzoate (58) (following general procedure B, THF:DMIB = 5:1, reaction time = 6 h, white solid, 69.0 mg, 82% yield, 95:5 e.r., 96% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.26 (s, 1H), 8.06 – 7.94 (m, 2H), 7.64 (d, $J = 7.9$ Hz, 1H), 7.59 – 7.51 (m, 1H), 7.47 – 7.38 (m, 2H), 7.39 – 7.30 (m, 1H), 7.23 – 7.16 (m, 1H), 7.16 – 7.08 (m, 1H), 7.00 (s, 1H), 4.60 – 4.37 (m, 1H), 4.30 (t, $J = 6.5$ Hz, 2H), 4.11 – 3.85 (m, 1H), 3.06 – 2.80 (m, 2H), 1.98 – 1.84 (m, 1H), 1.84 – 1.80 (m, 1H), 1.77 – 1.66 (m, 1H), 1.53 – 1.34 (m, 1H), 1.45 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 155.8, 136.3, 132.9, 130.5, 129.6, 128.4, 128.1, 122.8, 122.1, 119.5, 119.1, 112.0, 111.2, 79.2, 64.9, 50.9, 31.1, 30.9, 28.5, 25.7. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{25}\text{H}_{31}\text{N}_2\text{O}_4^+$: 423.2278,

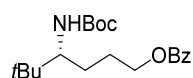
found: 423.2272. $[\alpha]^{20} = +18.9$ (c 1.0, CHCl_3). m.p. ($^{\circ}\text{C}$): 89-91. SFC analysis: Daicel Chiralpak IF-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 $^{\circ}\text{C}$, 2200 psi, tR (major) = 14.457 min (95%), tR (minor) = 14.901 min (5%).



(S)-4-((tert-butoxycarbonyl)amino)hexyl benzoate (59) (following general procedure B, THF:DMIB = 5:1, reaction time = 12 h, colorless oil, 44.9 mg, 70% yield, 94.5:5.5 e.r., 92% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.10 – 7.97 (m, 2H), 7.60 – 7.51 (m, 1H), 7.46 – 7.40 (m, 2H), 4.33 (t, $J = 6.5$ Hz, 2H), 4.31 – 4.17 (m, 1H), 3.62 – 3.42 (m, 1H), 1.90 – 1.72 (m, 2H), 1.70 – 1.59 (m, 1H), 1.59 – 1.50 (m, 1H), 1.44 (s, 9H), 1.42 – 1.28 (m, 2H), 0.92 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 155.9, 133.0, 130.6, 129.7, 128.5, 79.2, 65.0, 51.9, 31.8, 28.6, 28.5, 25.5, 10.4. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{18}\text{H}_{28}\text{NO}_4$: 322.2013, found: 322.2006. $[\alpha]^{20} = +24.1$ (c 1.0, CHCl_3). m.p. ($^{\circ}\text{C}$): 78-80. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 $^{\circ}\text{C}$, 2200 psi, tR (major) = 6.757 min (94.5%), tR (minor) = 7.017 min (5.5%).

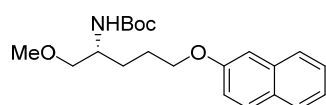


(R)-4-((tert-butoxycarbonyl)amino)-5-methylhexyl benzoate (60) (following general procedure B, THF:DMIB = 10:1, reaction time = 12 h, colorless oil, 56.3 mg, 84% yield, 92:8 e.r., 86% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 8.06 – 7.99 (m, 2H), 7.57 – 7.51 (m, 1H), 7.46 – 7.39 (m, 2H), 4.33 (t, $J = 6.5$ Hz, 2H), 4.33 (t, $J = 6.5$ Hz, 1H), 3.59 – 3.31 (m, 1H), 1.92 – 1.82 (m, 1H), 1.82 – 1.75 (m, 1H), 1.76 – 1.69 (m, 1H), 1.69 – 1.60 (m, 1H), 1.44 (s, 9H), 1.41 – 1.33 (m, 1H), 0.91 (d, $J = 6.8$ Hz, 3H), 0.88 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 166.7, 156.1, 133.0, 130.5, 129.7, 128.5, 79.1, 65.0, 55.5, 32.4, 29.3, 28.5, 25.9, 19.3, 17.7. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{19}\text{H}_{30}\text{NO}_4$: 336.2169, found: 336.2164. $[\alpha]^{20} = +21.3$ (c 1.0, CHCl_3). Chiral HPLC condition: Daicel chiral IC, 3% *i*-PrOH in hexanes, tR (major) = 32.921 min (92%), tR (minor) = 21.512 min (8%).

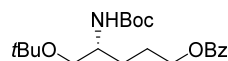


(R)-4-((tert-butoxycarbonyl)amino)-5,5-dimethylhexyl benzoate (61) (following general procedure B,

THF:DMIB = 10:1, reaction time = 12 h, colorless oil, 25.8 mg, 37% yield, 76.5:23.5 e.r., 54% e.s.). ¹H NMR (400 MHz, CDCl₃, two rotamers) δ 8.11 – 7.97 (m, 2H), 7.58 – 7.52 (m, 1H), 7.48 – 7.39 (m, 2H), 4.34 (t, *J* = 6.3 Hz, 2H), 4.31 – 4.02 (m, 1H), 3.51 – 3.16 (m, 1H), 1.98 – 1.83 (m, 1H), 1.83 – 1.74 (m, 2H), 1.44 (s, 9H), 1.24 – 1.14 (m, 1H), 0.90 (s, 9H). ¹³C{¹H} NMR (101 MHz, CDCl₃, two rotamers) δ 166.7, 156.4, 133.0, 130.6, 129.7, 128.5, 79.1, 65.0, 58.8, 34.9, 28.6, 28.5, 27.1, 26.5. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₀H₃₂NO₄⁺: 350.2326, found: 350.2320. [α]²⁰ = +9.8 (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IF-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO₂, v = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 9.187 min (76.5%), tR (minor) = 9.630 min (23.5%).

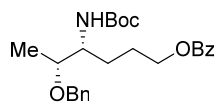


tert-butyl (R)-(1-methoxy-5-(naphthalen-2-yloxy)pentan-2-yl)carbamate (62) (following general procedure B, THF:DMIB = 5:1, reaction time = 6 h, waxy solid, 35.3 mg, 49% yield, 88:12 e.r., 94% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 7.78 – 7.74 (m, 1H), 7.74 – 7.69 (m, 2H), 7.46 – 7.40 (m, 1H), 7.36 – 7.30 (m, 1H), 7.18 – 7.08 (m, 2H), 4.91 – 4.31 (m, 1H), 4.15 – 4.03 (m, 2H), 3.86 – 3.72 (m, 1H), 3.48 – 3.39 (m, 2H), 3.36 (s, 3H), 1.99 – 1.84 (m, 2H), 1.85 – 1.75 (m, 1H), 1.74 – 1.62 (m, 1H), 1.45 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 157.1, 155.8, 134.7, 129.5, 129.1, 127.8, 126.9, 126.4, 123.6, 119.1, 106.8, 79.4, 74.8, 67.8, 59.3, 50.2, 29.1, 28.6, 26.1. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₁H₃₀NO₄⁺: 360.2169, found: 360.2165. [α]²⁰ = +16.6 (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 2% to 20% MeOH in scCO₂, v = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 9.187 min (88%), tR (minor) = 10.863 min (12%).

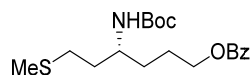


(R)-5-(tert-butoxy)-4-((tert-butoxycarbonyl)amino)pentyl benzoate (63) (following general procedure B, THF:DMIB = 5:1, reaction time = 6 h, colorless oil, 26.5 mg, 35% yield, 90:10 e.r., 99% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.07 – 8.01 (m, 2H), 7.58 – 7.52 (m, 1H), 7.48 – 7.39 (m, 2H), 4.86 – 4.69 (m, 1H), 4.43 – 4.24 (m, 2H), 3.81 – 3.50 (m, 1H), 3.43 – 3.30 (m, 2H), 1.88 – 1.77 (m, 2H), 1.75 – 1.67 (m, 1H), 1.65 – 1.58 (m, 1H), 1.44 (s, 9H), 1.15 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 166.8, 155.8, 133.0, 130.6, 129.7, 128.5, 79.2, 72.9, 65.1, 63.3, 50.6, 28.8, 28.6, 27.6, 25.7. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₁H₃₄NO₅⁺: 380.2432, found: 380.2426. [α]²⁰ = +17.1 (c 1.0, CHCl₃). SFC analysis:

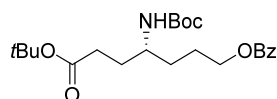
Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 1% to 5% MeOH in scCO₂, v = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 10.071 min (90%), tR (minor) = 10.434 min (10%).



(4R,5S)-5-(benzyloxy)-4-((tert-butoxycarbonyl)amino)hexyl benzoate (64) (following general procedure B, THF:DMIB = 5:1, reaction time = 12 h, colorless oil, 47.0 mg, 55% yield, 96:4 d.r.). ¹H NMR (400 MHz, CDCl₃, two rotamers) δ 8.07 – 7.98 (m, 2H), 7.61 – 7.51 (m, 1H), 7.47 – 7.39 (m, 2H), 7.34 – 7.25 (m, 5H), 4.76 (d, *J* = 9.8 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.38 (d, *J* = 11.5 Hz, 1H), 4.35 – 4.26 (m, 2H), 3.70 – 3.49 (m, 2H), 1.90 – 1.78 (m, 1H), 1.78 – 1.73 (m, 1H), 1.71 – 1.65 (m, 2H), 1.44 (s, 9H), 1.21 (d, *J* = 6.2 Hz, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃, two rotamers) δ 166.7, 156.4, 138.5, 133.0, 130.6, 129.7, 128.5, 128.5, 127.9, 127.8, 79.2, 75.6, 71.0, 65.0, 54.8, 29.7, 28.5, 25.8, 16.4. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₅H₃₄NO₅⁺: 428.2432, found: 428.2426. [α]_D²⁰ = +15.5 (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IA-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 1% to 5% MeOH in scCO₂, v = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 5.407 min (96%), tR (minor) = 5.918 min (4%).

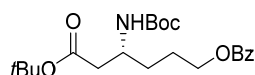


(R)-4-((tert-butoxycarbonyl)amino)-6-(methylthio)hexyl benzoate (65) (following general procedure B, THF:DMIB = 5:1, reaction time = 6 h, white solid, 50.7 mg, 69% yield, 92:8 e.r., 89% e.s.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.09 – 7.95 (m, 2H), 7.59 – 7.52 (m, 1H), 7.49 – 7.38 (m, 2H), 4.42 – 4.05 (m, 1H), 4.33 (t, *J* = 6.5 Hz, 2H), 3.82 – 3.55 (m, 1H), 2.59 – 2.46 (m, 2H), 2.09 (s, 3H), 1.92 – 1.74 (m, 3H), 1.69 – 1.59 (m, 2H), 1.55 – 1.49 (m, 1H), 1.43 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 166.7, 155.8, 133.0, 130.5, 129.7, 128.5, 79.4, 64.8, 50.1, 35.5, 32.2, 30.9, 28.5, 25.5, 15.8. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₁₉H₃₀NO₄S⁺: 368.1890, found: 368.1884. [α]_D²⁰ = +19.0 (c 1.0, CHCl₃). m.p. (°C): 57–58. SFC analysis: Daicel Chiralpak IF-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 20% MeOH in scCO₂, v = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 7.194 min (92%), tR (minor) = 7.470 min (8%).

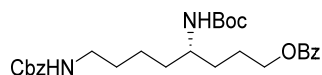


(R)-7-(tert-butoxy)-4-((tert-butoxycarbonyl)amino)-7-oxoheptyl benzoate (66) (following general

procedure B, used **L3** instead of **L5**, THF:DMIB = 5:1, reaction time = 12 h, colorless oil, 54.8 mg, 65% yield, 96.5:3.5 e.r., 95% e.s.) *versus* (following general procedure B, using **L5** as ligand, THF:DMIB = 10:1, reaction time = 12 h, 53.9 mg, colorless oil, 64% yield, 92:8 e.r.). ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.07 – 7.98 (m, 2H), 7.57 – 7.50 (m, 1H), 7.46 – 7.39 (m, 2H), 4.45 – 3.97 (m, 3H), 3.71 – 3.41 (m, 1H), 2.28 (t, *J* = 7.4 Hz, 2H), 1.93 – 1.73 (m, 3H), 1.68 – 1.57 (m, 2H), 1.54 – 1.47 (m, 1H), 1.43 (s, 9H), 1.42 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 173.0, 166.7, 155.8, 133.0, 130.5, 129.7, 128.4, 80.5, 79.2, 64.8, 50.4, 32.6, 32.4, 30.5, 28.5, 28.2, 25.5. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₃H₃₆NO₆⁺: 422.2537, found: 422.2530. [α]_D²⁰ = +24.5 (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 25% MeOH in scCO₂, *v* = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 7.019 min (96.5%), tR (minor) = 7.395 min (3.5%).

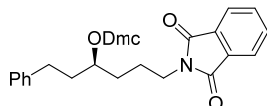


(R)-6-(tert-butoxy)-4-((tert-butoxycarbonyl)amino)-6-oxohexyl benzoate (67) (following general procedure B, THF:DMIB = 10:1, reaction time = 12 h, colorless oil, 43.2 mg, 53% yield, 86.5:13.5 e.r., 85% e.s.) ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.06 – 8.00 (m, 2H), 7.58 – 7.52 (m, 1H), 7.46 – 7.40 (m, 2H), 5.15 – 4.44 (m, 1H), 4.39 – 4.28 (m, 2H), 4.06 – 3.79 (m, 1H), 2.54 – 2.36 (m, 2H), 1.91 – 1.76 (m, 2H), 1.73 – 1.60 (m, 2H), 1.44 (s, 18H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 171.0, 166.7, 155.5, 133.0, 130.5, 129.7, 128.5, 81.2, 79.4, 64.8, 47.8, 40.7, 31.6, 28.5, 28.2, 25.8. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₂H₃₄NO₆⁺: 408.2381, found: 408.2376. [α]_D²⁰ = +22.3 (c 1.0, CHCl₃). Chiral HPLC condition: Daicel chiral IC, isocratic 20% *i*-PrOH in hexanes, tR (major) = 7.325 min (86.5%), tR (minor) = 11.080 min (13.5%).

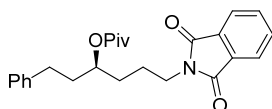


(S)-8-(((benzyloxy)carbonyl)amino)-4-((tert-butoxycarbonyl)amino)octyl benzoate (68) (following general procedure B, THF:DMIB = 10:1, reaction time = 12 h, 72.1 mg, white solid, 72% yield, 94.5:5.5 e.r., 91% e.s.) ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 8.07 – 7.99 (m, 2H), 7.58 – 7.51 (m, 1H), 7.47 – 7.40 (m, 2H), 7.37 – 7.32 (m, 4H), 7.32 – 7.28 (m, 1H), 5.08 (s, 2H), 4.91 – 4.55 (m, 1H), 4.39 – 4.01 (m, 3H), 3.71 – 3.40 (m, 1H), 3.26 – 3.08 (m, 2H), 1.87 – 1.75 (m, 2H), 1.66 – 1.58 (m, 1H), 1.54 – 1.31 (m, 7H), 1.43 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 166.7, 156.6, 156.0, 136.8, 133.0, 130.5, 129.7, 128.6, 128.5, 128.2, 128.2, 79.3, 66.7, 64.9, 50.3, 40.9, 35.4, 32.4, 29.8, 28.5, 25.5, 23.1. HRMS (ESI)

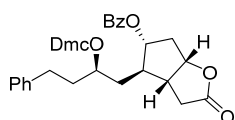
m/z ($M+H$)⁺ calcd for C₂₈H₃₉N₂O₆⁺: 499.2803, found: 499.2794. $[\alpha]^{20} = +13.7$ (c 1.0, CHCl₃). m.p. (°C): 70–71. Chiral HPLC condition: Daicel chiral AD, 20% *i*-PrOH in hexanes, tR (major) = 21.927 min (94.5%), tR (minor) = 19.449 min (5.5%).



(R)-6-(1,3-dioxoisindolin-2-yl)-1-phenylhexan-3-yl dimethylcarbamate (69) (following general procedure C, colorless oil, 52.4 mg, 66% yield, 99.5:0.5 e.r., >99% e.s.). ¹H NMR (500 MHz, CDCl₃) δ 7.88 – 7.78 (m, 2H), 7.74 – 7.64 (m, 2H), 7.26 – 7.21 (m, 2H), 7.15 (d, *J* = 7.6 Hz, 3H), 4.99 – 4.79 (m, 1H), 3.68 (d, *J* = 7.0 Hz, 2H), 2.93 – 2.80 (m, 6H), 2.71 – 2.56 (m, 2H), 1.97 – 1.80 (m, 2H), 1.78 – 1.69 (m, 2H), 1.68 – 1.58 (m, 2H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 168.4, 156.5, 141.9, 134.0, 132.2, 128.4, 128.4, 125.9, 123.2, 74.2, 38.0, 36.5, 36.2, 35.9, 31.9, 31.8, 24.5. $[\alpha]^{20} = -2.5$ (c 1.0, CHCl₃). HRMS (ESI) m/z ($M+H$)⁺ calcd for C₂₃H₂₇N₂O₄⁺: 395.1965, found: 395.1965. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 20% MeOH in scCO₂, *v* = 0.6 mL/min, 40 °C, 2200 psi, tR (major) = 14.016 min (> 99.5%), tR (minor) = 14.738 min (< 0.5%).

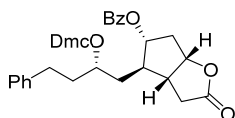


(R)-6-(1,3-dioxoisindolin-2-yl)-1-phenylhexan-3-yl pivalate (70) (following general procedure C, reaction was run in THF for 24 h, colorless oil, 30.2 mg, 37% yield, 98:2 e.r., 96% e.s.). ¹H NMR (500 MHz, CDCl₃) δ 7.88 – 7.81 (m, 2H), 7.75 – 7.67 (m, 2H), 7.28 – 7.23 (m, 2H), 7.19 – 7.10 (m, 3H), 5.02 – 4.89 (m, 1H), 3.72 – 3.65 (m, 2H), 2.68 – 2.51 (m, 2H), 1.93 – 1.79 (m, 2H), 1.75 – 1.67 (m, 2H), 1.67 – 1.59 (m, 2H), 1.21 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 178.3, 168.5, 141.7, 134.0, 132.3, 128.6, 128.4, 126.1, 123.4, 72.7, 39.0, 37.9, 36.1, 31.8, 31.5, 27.4, 24.5. $[\alpha]^{20} = -4.2$ (c 1.0, CHCl₃). HRMS (ESI) m/z ($M+NH_4$)⁺ calcd for C₂₅H₃₃N₂O₄⁺: 425.2435, found: 425.2434. SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO₂, *v* = 0.6 mL/min, 40 °C, 2200 psi, tR (major) = 7.769 min (98%), tR (minor) = 8.235 min (2%).



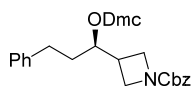
(3aR,4R,5R,6aS)-4-((R)-2-((dimethylcarbamoyl)oxy)-4-phenylbutyl)-2-oxohexahydro-2H-

cyclopenta[*b*]furan-5-yl benzoate (71) (following general procedure C, colorless oil, 52.9 mg, 57% yield, 99:1 d.r., 98% e.s.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ¹H NMR (500 MHz, CDCl₃) δ 8.04 – 7.92 (m, 2H), 7.59 – 7.49 (m, 1H), 7.47 – 7.40 (m, 2H), 7.30 – 7.22 (m, 2H), 7.22 – 7.13 (m, 3H), 5.29 – 5.20 (m, 1H), 5.11 – 5.06 (m, 1H), 5.01 – 4.93 (m, 1H), 2.92 (dd, *J* = 18.6, 10.9 Hz, 1H), 2.86 (s, 6H), 2.80 – 2.73 (m, 1H), 2.73 – 2.62 (m, 2H), 2.48 (dd, *J* = 18.7, 2.8 Hz, 1H), 2.40 – 2.28 (m, 2H), 2.24 – 2.16 (m, 1H), 2.02 – 1.78 (m, 3H), 1.47 – 1.38 (m, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 177.1, 166.0, 156.3, 141.5, 133.3, 129.8, 129.8, 128.6, 128.5, 128.4, 126.1, 84.7, 81.1, 72.3, 49.8, 43.3, 38.6, 38.0, 36.8, 36.6, 36.6, 35.9, 31.9. [α]²⁰ = -32.1 (c 1.0, CHCl₃). HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₇H₃₂NO₆⁺: 466.2224, found: 466.2225.



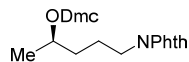
(3aR,4R,5R,6aS)-4-((S)-2-((dimethylcarbamoyl)oxy)-4-phenylbutyl)-2-oxohexahydro-2H-

cyclopenta[*b*]furan-5-yl benzoate (72) (following general procedure C, colorless oil, 57.8 mg, 62% yield, 98:2 d.r., 96% e.s.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ¹H NMR (500 MHz, CDCl₃) δ 8.03 – 7.95 (m, 2H), 7.58 – 7.51 (m, 1H), 7.47 – 7.41 (m, 2H), 7.30 – 7.22 (m, 2H), 7.20 – 7.12 (m, 3H), 5.23 – 5.18 (m, 1H), 5.12 – 5.03 (m, 1H), 4.85 – 4.75 (m, 1H), 2.91 (s, 3H), 2.88 (s, 3H), 2.85 – 2.69 (m, 3H), 2.67 – 2.58 (m, 1H), 2.41 – 2.26 (m, 3H), 2.19 – 2.11 (m, 1H), 2.02 – 1.93 (m, 1H), 1.93 – 1.85 (m, 1H), 1.77 – 1.70 (m, 1H), 1.68 – 1.60 (m, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 176.8, 166.1, 156.2, 141.4, 133.3, 129.8, 129.7, 128.6 (2C, overlapped), 128.5, 126.2, 84.5, 80.9, 73.1, 49.7, 43.2, 38.3, 37.9, 36.6, 36.1, 35.9 (2C overlapped), 31.8. [α]²⁰ = -26.7 (c 1.0, CHCl₃). HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₇H₃₂NO₆⁺: 466.2224, found: 466.2227.

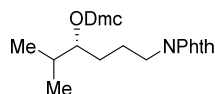


benzyl (R)-3-(1-((dimethylcarbamoyl)oxy)-3-phenylpropyl)azetidine-1-carboxylate (73) (following general procedure C, colorless oil, 34.1 mg, 43% yield, 99:1 e.r., 99% e.s.). ¹H NMR (500 MHz, CDCl₃) δ 7.34 – 7.27 (m, 5H), 7.25 – 7.22 (m, 2H), 7.18 – 7.11 (m, 3H), 5.08 – 5.02 (m, 2H), 5.02 – 4.96 (m, 1H), 4.02 – 3.91 (m, 3H), 3.78 – 3.69 (m, 1H), 2.88 (s, 3H), 2.84 – 2.72 (m, 4H), 2.68 – 2.55 (m, 2H), 1.91 – 1.80 (m, 1H), 1.80 – 1.70 (m, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 156.5, 156.4, 141.4, 136.9, 128.6, 128.4, 128.1, 128.1, 126.2, 74.3, 66.7, 51.1, 36.7, 35.9, 34.3, 33.1, 31.8. HRMS (ESI) *m/z* (M+H)⁺ calcd for

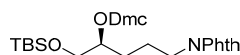
$C_{23}H_{29}N_2O_4^+$: 397.2122, found: 397.2115. $[\alpha]^{20} = -1.3$ (c 1.0, $CHCl_3$). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μ m PS), gradient from 3% to 40% MeOH in $scCO_2$, $v = 0.6$ mL/min, 40 $^\circ$ C, 2200 psi, tR (major) = 10.775 min (99.5%), tR (minor) = 11.078 min (0.5%).



(R)-5-(1,3-dioxoisindolin-2-yl)pentan-2-yl dimethylcarbamate (74) (following general procedure C, colorless oil, 46.3 mg, 76% yield, 99:1 e.r., 99% e.s.). 1H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.76 (m, 2H), 7.73 – 7.65 (m, 2H), 4.86 – 4.74 (m, 1H), 3.67 (t, $J = 7.1$ Hz, 2H), 2.85 (s, 6H), 1.80 – 1.66 (m, 2H), 1.65 – 1.50 (m, 2H), 1.19 (d, $J = 6.4$ Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.5, 156.4, 134.0, 132.2, 123.3, 71.2, 38.0, 36.4, 35.9, 33.6, 24.7, 20.5. HRMS (ESI) m/z ($M+H$) $^+$ calcd for $C_{16}H_{21}N_2O_4^+$: 305.1496, found: 305.1494. $[\alpha]^{20} = -8.4$ (c 1.0, $CHCl_3$). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μ m PS), gradient from 3% to 20% MeOH in $scCO_2$, $v = 0.6$ mL/min, 40 $^\circ$ C, 2200 psi, tR (minor) = 10.263 min (99.0%), tR (major) = 10.808 min (1.0%).

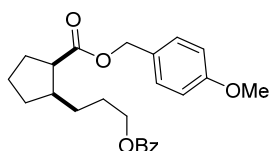


(R)-6-(1,3-dioxoisindolin-2-yl)-2-methylhexan-3-yl dimethylcarbamate (75) (following general procedure C, colorless oil, 25.9 mg, 39% yield, 97.5:2.5 e.r., 99% e.s.). 1H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.77 (m, 2H), 7.77 – 7.65 (m, 2H), 4.73 – 4.55 (m, 1H), 3.74 – 3.61 (m, 2H), 2.89 (s, 6H), 1.86 – 1.78 (m, 1H), 1.76 – 1.66 (m, 2H), 1.61 – 1.54 (m, 2H), 0.88 (d, $J = 6.8$ Hz, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.5, 156.9, 134.0, 132.3, 123.3, 78.8, 38.1, 36.6, 35.9, 31.7, 28.8, 25.0, 18.7, 17.8. HRMS (ESI) m/z ($M+H$) $^+$ calcd for $C_{18}H_{25}N_2O_4^+$: 333.1809, found: 333.1804. $[\alpha]^{20} = 3.6$ (c 1.0, $CHCl_3$). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μ m PS), gradient from 3% to 15% MeOH in $scCO_2$, $v = 0.6$ mL/min, 40 $^\circ$ C, 2200 psi, tR (minor) = 10.380 min (2.5%), tR (major) = 10.908 min (97.5%).



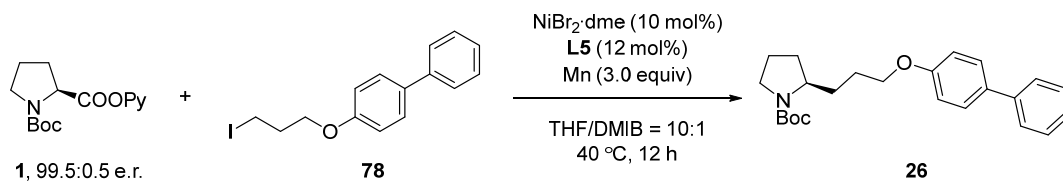
(S)-1-((tert-butyldimethylsilyl)oxy)-5-(1,3-dioxoisindolin-2-yl)pentan-2-yl dimethylcarbamate (76) (following general procedure C, colorless oil, 43.5 mg, 50% yield, 98.5:1.5 e.r., 99% e.s.). 1H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.78 (m, 2H), 7.78 – 7.64 (m, 2H), 4.84 – 4.69 (m, 1H), 3.70 (t, $J = 7.0$ Hz, 2H), 3.66 (dd, $J = 10.7, 4.8$ Hz, 1H), 3.61 (dd, $J = 10.7, 4.9$ Hz, 1H), 2.88 (s, 6H), 1.82 – 1.60 (m, 4H), 0.84 (s, 9H),

0.01 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 168.5, 156.4, 134.0, 132.3, 123.3, 74.8, 64.3, 38.1, 28.2, 25.9, 24.6, 18.3, -5.3, -5.4. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{22}\text{H}_{35}\text{N}_2\text{O}_5\text{Si}^+$: 435.2310, found: 435.2308. $[\alpha]^{20} = -6.4$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 20% MeOH in scCO_2 , $v = 0.6$ mL/min, 40 $^\circ\text{C}$, 2200 psi, t_R (major) = 7.345 min (98.5%), t_R (minor) = 7.668 min (1.5%).



***cis*-3-(2-(((4-methoxybenzyl)oxy)carbonyl)cyclopentyl)propyl benzoate (77)** (following general procedure C, reaction was run in THF, 60 $^\circ\text{C}$, colorless oil, 26.2 mg, 33% yield, >98:2 d.r.). Diastereomeric ratio (d.r.) was determined by NMR analysis. ^1H NMR (500 MHz, CDCl_3) δ 8.06 – 8.00 (m, 2H), 7.59 – 7.51 (m, 1H), 7.47 – 7.40 (m, 2H), 7.32 – 7.23 (m, 2H), 6.92 – 6.78 (m, 2H), 5.02 (q, $J = 12.0$ Hz, 2H), 4.19 (t, $J = 6.6$ Hz, 2H), 3.77 (s, 3H), 2.93 – 2.82 (m, 1H), 2.16 – 2.06 (m, 1H), 2.00 – 1.90 (m, 1H), 1.90 – 1.66 (m, 5H), 1.63 – 1.51 (m, 1H), 1.51 – 1.39 (m, 2H), 1.36 – 1.25 (m, 1H). ^{13}C NMR (126 MHz, CDCl_3) δ 175.5, 166.7, 159.7, 133.0, 130.6, 130.4, 129.7, 128.5, 128.4, 114.0, 65.9, 65.2, 55.4, 47.6, 43.8, 31.3, 28.6, 28.0, 27.7, 24.0. HRMS (ESI) m/z ($\text{M}+\text{NH}_4$) $^+$ calcd for $\text{C}_{24}\text{H}_{32}\text{NO}_5^+$: 414.2275, found: 414.2269.

6. Scale-up stereoretentive decarbonylative cross coupling



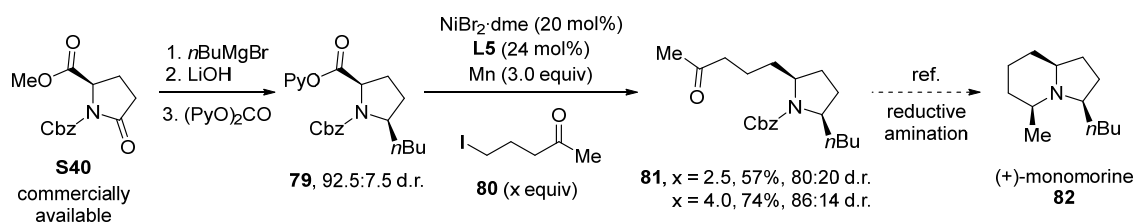
Procedure in 0.2 mmol scale with 10 mol% catalyst loading: In a nitrogen-filled glovebox, to a vial containing a PTFE-coated stirbar was added $\text{NiBr}_2 \cdot \text{dme}$ (12.4 mmol, 10 mol%), **L5** (9.6 mmol, 12 mol%), and THF/DMIB (10:1, 0.5 mL). This mixture was stirred at rt for 10 min. To this vial was added **1** (58.4 mg, 0.2 mmol, 1.0 equiv), **78** (169.0 mg, 8.5 mmol, 2.5 equiv), and Mn (33.0 mg, 0.6 mmol, 3.0 equiv). The vial was closed with a threaded cap fitted with a PTFE septum before being removed from the glovebox. The mixture was stirred (800 RPM) at 40 °C for 12 h. After the specified reaction time, the reaction mixture was removed from the hotplate, and was allowed to cool to rt, diluted with ethyl acetate (2 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salt. The vial and pad were washed with ethyl acetate (2 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired products **26** as white solid (58.5 mg, 77%, 97.5:2.5 e.r., 95% e.s.).

Procedure in 3.4 mmol scale with 10 mol% catalyst loading: In a nitrogen-filled glovebox, to a flask containing a PTFE-coated stirbar was added $\text{NiBr}_2 \cdot \text{dme}$ (104.9 mg, 0.34 mmol, 10 mol%), **L5** (82.5 mg, 0.41 mmol, 12 mol%), and THF/DMIB (10:1, 10 mL). This mixture was stirred at rt for 30 min. To this flask was added **1** (1.0 g, 3.4 mmol, 1.0 equiv), **78** (2.9 g, 8.5 mmol, 2.5 equiv), and Mn (561.0 mg, 0.6 mmol, 3.0 equiv). The flask was sealed with a rubber cap before being removed from the glovebox. The flask was placed in oil bath, and the reaction mixture was stirred (800 RPM) at 40 °C for 12 h. After the specified reaction time, the reaction mixture was removed from the oil bath, and was allowed to cool to rt, diluted with ethyl acetate (30 mL), and passed through a pad of silica gel to remove excess Mn and insoluble salt. The vial and pad were washed with ethyl acetate (30 mL). The filtrate was concentrated in vacuo. The residue was purified by column chromatography to give the desired products **26** as white solid (928 mg, 71%, 97.5:2.5 e.r., 95% e.s.).

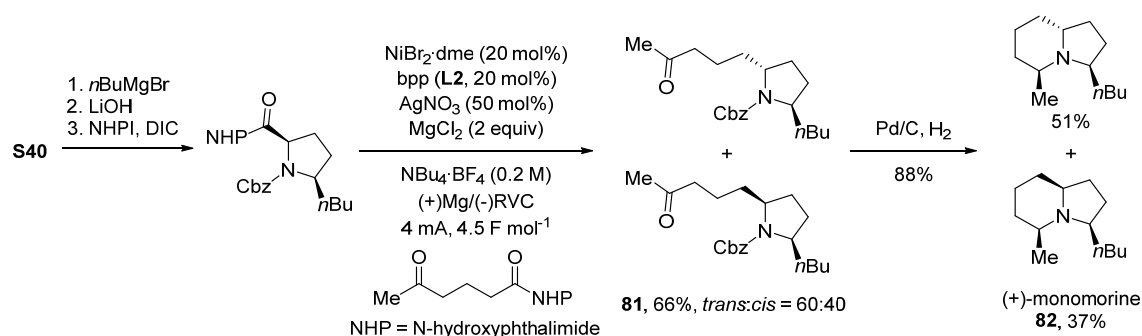
7. Synthesis of key intermediates for bioactive molecules

Synthesis of (+)-monomorine

This work



Route from selected literature

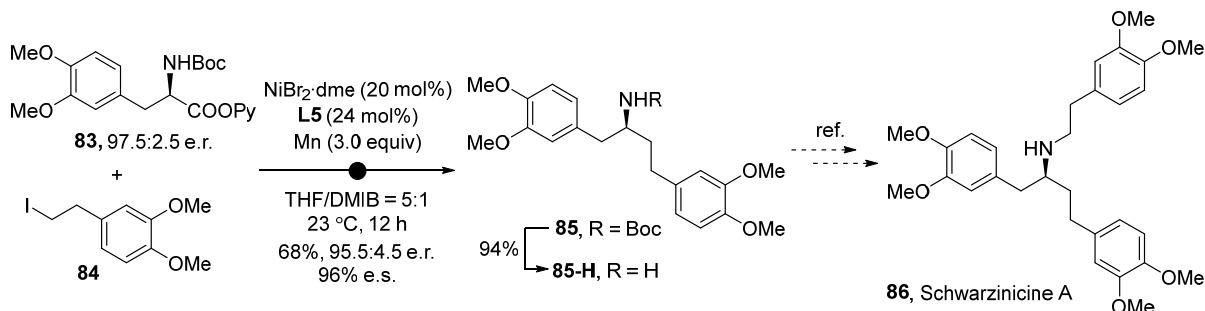


Synthesis of benzyl (2R,5S)-2-butyl-5-(4-oxopentyl)pyrrolidine-1-carboxylate (81) (Following general procedure A, using 4 equiv of alkyl iodide, 50.8 mg, colorless oil, 74% yield, 86:14 d.r.) *versus* (Following general procedure A, 39.5 mg, colorless oil, 57% yield, 80:20 d.r.). Diastereomeric ratio (d.r.) was determined by SFC analysis. ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 7.37 – 7.30 (m, 4H), 7.30 – 7.27 (m, 1H), 5.21 – 4.99 (m, 2H), 3.87 – 3.67 (m, 2H), 2.53 – 2.22 (m, 2H), 2.14 – 2.00 (m, 3H), 1.97 – 1.80 (m, 3H), 1.72 – 1.39 (m, 5H), 1.34 – 1.16 (m, 6H), 0.92 – 0.78 (m, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 209.1, 209.0, 208.8, 208.6, 155.5, 154.4, 154.2, 137.2, 128.5, 128.5, 128.2, 128.0, 127.9, 66.6, 66.5, 66.5, 59.2, 58.7, 58.6, 58.3, 58.1, 57.9, 57.4, 35.5, 35.1, 33.7, 33.6, 32.3, 32.1, 30.0, 29.9, 29.9, 29.8, 29.4, 29.0, 28.9, 28.9, 28.6, 27.7, 26.8, 26.7, 23.7, 22.7, 22.7, 22.6, 20.7, 20.5, 14.2, 14.1, 14.1. HRMS (ESI) *m/z* (M+H)⁺ calcd for C₂₁H₃₂NO₃⁺: 346.2377, found: 346.2371. [α]_D²⁰ = +10.1 (c 1.0, CHCl₃). SFC analysis: Daicel Chiralpak IC-3 (3 mm ID × 150 mm L, 3 μm PS), gradient from 3% to 15% MeOH in scCO₂, v = 0.8 mL/min, 40 °C, 2200 psi, tR (major) = 10.738 min (86%), tR (minor) = 11.382 min (14%).

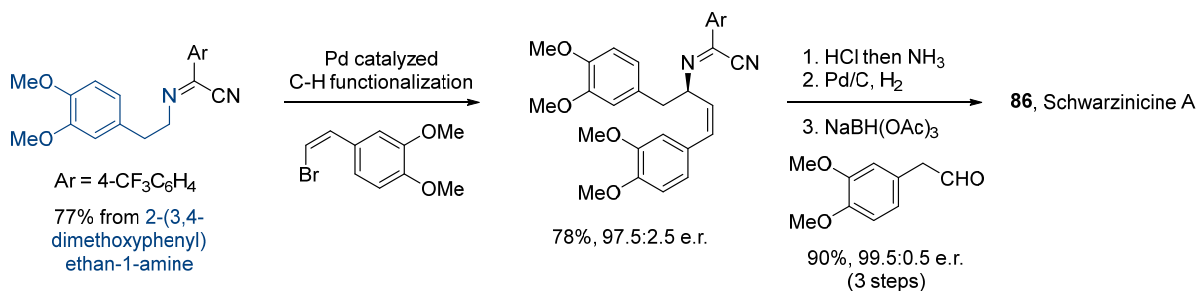
The literature route using an NHP ester provided **81** in 66% yield (1:1.5 *cis/trans*)¹¹.

Synthesis of Schwarzinicine A

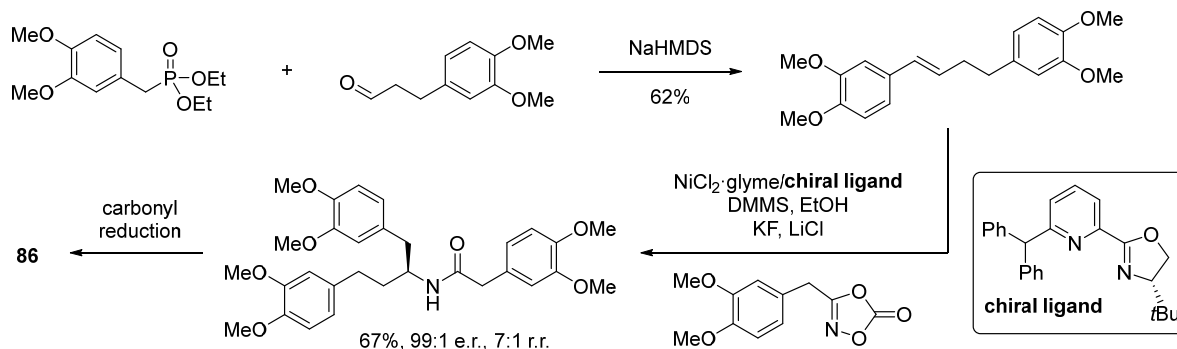
This work



Route A from selected literature



Route B from selected literature



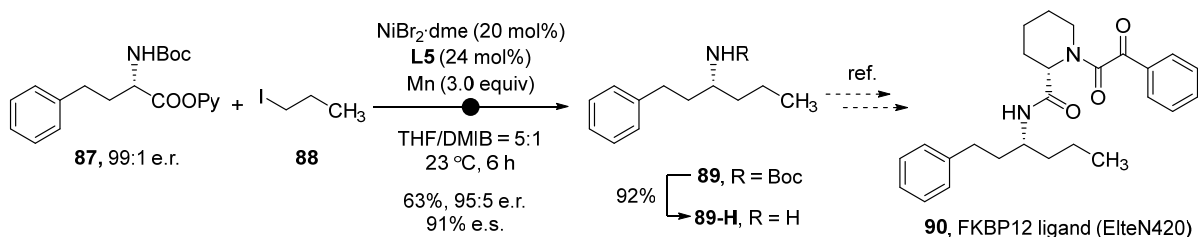
tert-butyl (S)-((1,4-bis(3,4-dimethoxyphenyl)butan-2-yl)carbamate (85) (following general procedure B, THF:DMIB = 5:1, reaction time = 12 h, 60.1 mg, white solid, 68% yield, 95.5:4.5 e.r., 96% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 6.82 – 6.74 (m, 2H), 6.71 – 6.62 (m, 4H), 4.42 – 4.03 (m, 1H), 3.91 – 3.80 (m, 1H), 3.84 (s, 12H), 2.79 – 2.61 (m, 3H), 2.61 – 2.52 (m, 1H), 1.86 – 1.71 (m, 1H), 1.62 – 1.51 (m, 1H), 1.42 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 155.6, 149.0, 148.9, 147.7, 147.3, 134.5, 130.7, 121.6, 120.3, 112.7, 112.0, 111.4, 111.3, 79.2, 56.0, 56.0, 55.9, 51.3, 41.2, 36.4, 32.1, 28.5. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{25}\text{H}_{35}\text{NNaO}_6^+$: 468.2357, found: 468.2354. $[\alpha]^{20} = +19.7$ (c 1.0, CHCl_3). m.p. (°C): 97-98. SFC analysis: Daicel Chiralpak IF-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 3% to 30% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 °C, 2200 psi, t_R (major) = 17.334 min (95.5%), t_R (minor) = 16.977 min (4.5%).

Synthesis of (S)-1,4-bis(3,4-dimethoxyphenyl)butan-2-amine (85-H) Boc-protected amine **75** was treated with TFA in DCM at rt for 4 h. The resulting mixture was quenched with an aqueous NaOH solution. The aqueous layer was extracted with DCM (3×5 mL). The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure in vacuo. The residue was purified by column chromatography to give the deprotected products **(S)-1-phenylhexan-3-amine (85-H)** as white solid at 94% yield. ¹H NMR (500 MHz, CDCl₃, two rotamers) δ 6.79 – 6.75 (m, 1H), 6.74 – 6.71 (m, 1H), 6.71 – 6.62 (m, 4H), 5.12 (br, 2H), 3.84 – 3.79 (m, 12H), 3.23 – 3.01 (m, 1H), 2.83 – 2.76 (m, 1H), 2.77 – 2.64 (m, 2H), 2.65 – 2.56 (m, 1H), 1.87 – 1.63 (m, 2H). ¹³C{¹H} NMR (126 MHz, CDCl₃, two rotamers) δ 149.1, 148.9, 147.9, 147.3, 133.8, 130.3, 121.3, 120.1, 112.4, 111.7, 111.4, 111.3, 55.9, 55.9 (2C, overlapped), 55.8, 52.4, 41.8, 36.9, 31.6. HRMS (ESI) m/z (M+H)⁺ calcd for C₂₀H₂₈NO₄⁺: 346.2013, found: 346.2008.

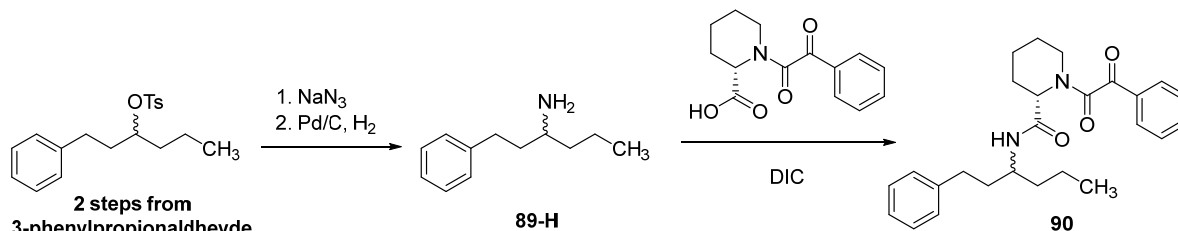
In route A, Pd-catalyzed enantioselective C-H activation afforded the chiral amine intermediate in 78% yield with 97.5:2.5 e.r., which further underwent deprotection to give the key intermediate **85-H**¹⁴. In route B, Ni-catalyzed enantioselective hydroamidation played a key role in synthesis of chiral amide intermediate on the path to **86**¹⁵.

Synthesis of FKBP12 ligand (ElteN420)

This work



Route from selected literature



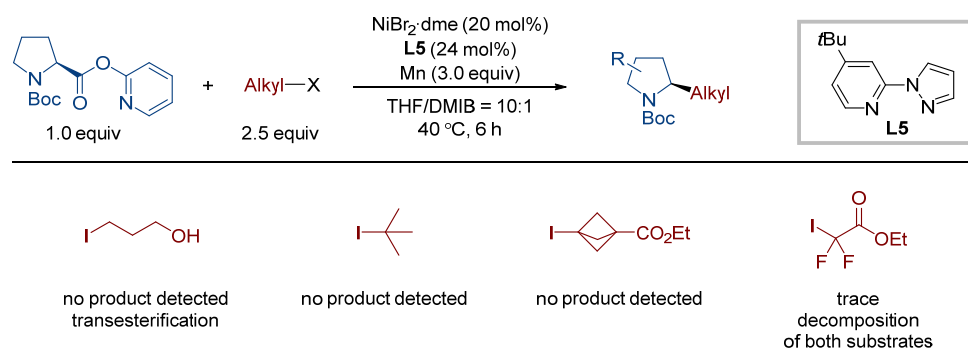
***tert*-butyl (R)-(1-phenylhexan-3-yl)carbamate (89)** (Following general procedure A, THF:DMIB = 5:1, reaction time = 6 h, 35.1 mg, colorless oil, 63% yield, 95:5 e.r., 91% e.s.). ^1H NMR (500 MHz, CDCl_3 , two rotamers) δ 7.31 – 7.25 (m, 2H), 7.22 – 7.13 (m, 3H), 4.44 – 3.96 (m, 1H), 3.73 – 3.37 (m, 1H), 2.79 – 2.56 (m, 2H), 1.84 – 1.72 (m, 1H), 1.70 – 1.58 (m, 1H), 1.51 – 1.44 (m, 1H), 1.46 (s, 9H), 1.41 – 1.31 (m, 3H), 0.97 – 0.88 (m, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 155.9, 142.3, 128.5, 128.5, 125.9, 79.0, 50.5, 38.1, 37.8, 32.5, 28.6, 19.2, 14.1. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{17}\text{H}_{28}\text{NO}_2^+$: 278.2115, found: 278.2110. $[\alpha]^{20} = +25.7$ (c 1.0, CHCl_3). SFC analysis: Daicel Chiralpak IF-3 (3 mm ID $\times$ 150 mm L, 3 μm PS), gradient from 1% to 5% MeOH in scCO_2 , $v = 0.8$ mL/min, 40 °C, 2200 psi, t_R (major) = 6.794 min (95%), t_R (minor) = 7.166 min (5%).

Synthesis of (R)-1-phenylhexan-3-amine (89-H) Boc-protected amine **75** was treated with TFA in DCM at rt for 4 h. The resulting mixture was quenched with an aqueous NaOH solution. The aqueous layer was extracted with DCM (3 $\times$ 5 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure in vacuo. The residue was analysed by NMR (92% NMR yield using TMB as internal standard) and purified by column chromatography to give the deprotected products as white solid. ^1H NMR (500 MHz, CDCl_3) δ 7.22 – 7.17 (m, 2H), 7.15 – 7.07 (m, 3H), 2.80 – 2.63 (m, 4H), 2.62 – 2.52 (m, 1H), 1.75 – 1.66 (m, 1H), 1.64 – 1.52 (m, 1H), 1.44 – 1.32 (m, 2H), 1.33 – 1.20 (m, 2H), 0.83 (t, $J = 6.8$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3 , two rotamers) δ 142.2, 128.5, 128.5, 125.9, 50.9, 39.6, 39.1, 32.5, 19.2, 14.2. HRMS (ESI) m/z ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{12}\text{H}_{20}\text{N}^+$: 178.1590, found: 178.1589.

In the original synthesis of ElteN420, the racemic key intermediate **89-H** was prepared from the corresponding aldehyde via grignard reaction, tosylation, nucleophilic substitution, and hydrogenation of the azido group¹⁶.

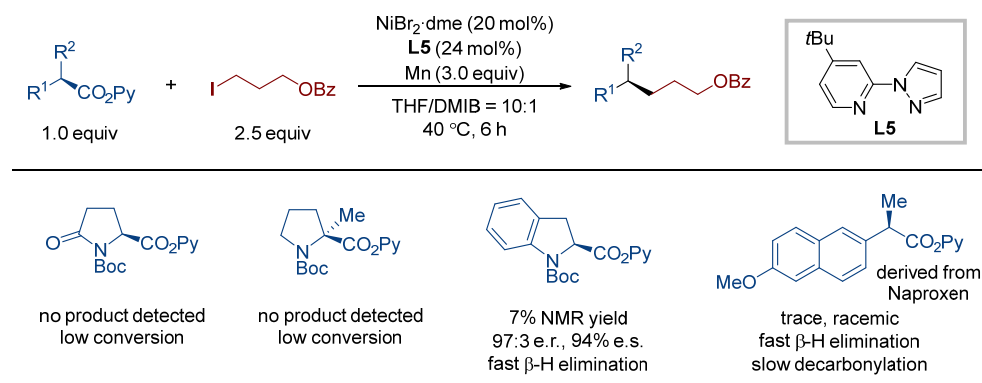
8. Examples of unsuccessful substrates

Table S12. Unsuccessful alkyl iodides



Among alkyl iodides tested, the alkyl iodides bearing a free alcohol resulted in no product formation due to transesterification to 2-pyridyl esters. *Tert*-Butyl iodide and Bicyclo[1.1.1]pentyl iodide are not suitable for decarbonylative cross-coupling under these conditions. Ethyl 2,2-difluoro-2-iodoacetate was also tested, however, only trace amount of cross-coupling product was detected, both substrates decomposed in the reaction.

Table S13. Unsuccessful 2-pyridyl esters



Among 2-pyridyl esters tested, a 2-pyrrolidone carboxylic acid ester was not tolerated. A α -tertiary acid (α -methyl proline) was found to be challenging because of slow oxidative addition and/or decarbonylation. A 2-pyridyl ester bearing an N-Boc indoline moiety provided low yield of cross-coupling product. β -hydride elimination was observed as the major side reaction (and we used this in our studies on decomposition pathways). A 2-pyridyl ester derived from Naproxen also resulted in a low yield of cross-coupling product due to fast β -hydride elimination and/or slow decarbonylation, giving the corresponding ketone and alkene compounds as the major side products.

9. Crystal structure and crystallographic data

X-ray analysis of complex 8 Form I (CCDC reference code: 2516892)

Data Collection

A red crystal with approximate dimensions 0.046 x 0.074 x 0.063 mm³ was selected under oil under ambient conditions and attached to the tip of a MiTeGen MicroMount©. The crystal was mounted in a stream of cold nitrogen at 100(1) K and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed on a Bruker D8 VENTURE PhotonIII four-circle diffractometer with Cu K α (λ = 1.54178 Å) radiation and the detector to crystal distance of 5.0 cm.

The initial cell constants were obtained from a 180° ϕ scan conducted at a 2θ = 50° angle with an exposure time of 2 seconds per frame. The reflections were successfully indexed by an automated indexing routine built into the APEX5 program. The final cell constants were calculated from a set of 7068 strong reflections from the actual data collection.

The data were collected by using a half sphere data collection routine to survey reciprocal space to the extent of a half sphere to a resolution of 0.78 Å. A total of 21855 data were harvested by collecting 30 sets of frames with 1.0° scans in ω and ϕ with exposure times of 1–36 sec per frame. These highly redundant datasets were corrected for Lorentz and polarization effects. The absorption correction was based on fitting a function to the empirical transmission surface as sampled by multiple equivalent measurements.

Structure Solution and Refinement

The diffraction data were consistent with the space groups $P\bar{1}$ and $P1$. The E -statistics strongly suggested the centrosymmetric space group $P\bar{1}$ which yielded chemically reasonable and computationally stable results of refinement.

A successful solution by direct methods provided most non-hydrogen atoms from the E -map. The remaining non-hydrogen atoms were located with an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined with anisotropic displacement coefficients. All hydrogen atoms were included in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients. The asymmetric unit contains one Ni(C₈H₇N₃)(C₁₁H₁₄NSO₂)Cl molecule.

Many crystals were screened, and the selected crystal proved to be a non-merohedral twin with an approximate second component contribution of 8%. The twin components are related by a 179.1° rotation

about the crystallographic a axis. The intensities from only the major domain were used, and the structure refinement was conducted as a single crystal.

The final least-squares refinement of 254 parameters against 4165 data resulted in residuals R (based on F^2 for $I \geq 2\sigma$) and wR (based on F^2 for all data) of 0.0483 and 0.1356, respectively. The final difference Fourier map contains a peak of residual electron density (ca. $1.09 \text{ e}/\text{\AA}^3$) in the vicinity of atom Ni1. This peak was in a chemically unreasonable position and was considered noise.

Summary

Crystal Data for $\text{C}_{19}\text{H}_{21}\text{ClN}_4\text{NiO}_2\text{S}$ ($M = 463.62 \text{ g/mol}$): triclinic, space group $P\bar{1}$ (no. 2), $a = 9.1793(10) \text{ \AA}$, $b = 9.7101(10) \text{ \AA}$, $c = 11.7843(12) \text{ \AA}$, $\alpha = 95.272(7)^\circ$, $\beta = 99.134(7)^\circ$, $\gamma = 104.780(7)^\circ$, $V = 993.04(18) \text{ \AA}^3$, $Z = 2$, $T = 100.00 \text{ K}$, $\mu(\text{Cu K}\alpha) = 3.825 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.551 \text{ g/cm}^3$, 7327 reflections measured ($7.672^\circ \leq 2\theta \leq 158.816^\circ$), 4165 unique ($R_{\text{int}} = 0.0247$, $R_{\text{sigma}} = 0.0364$) which were used in all calculations. The final R_1 was 0.0483 ($I > 2\sigma(I)$) and wR_2 was 0.1356 (all data).

Crystal structure and crystallographic data

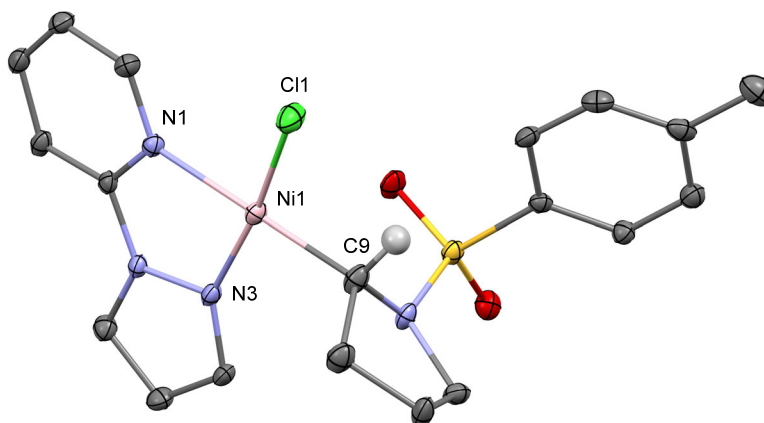


Fig. S21. Crystal structure of **8 Form I**. The compound crystallizes as a racemate, thus the enantiomer shown (C9-*R*) was chosen arbitrarily.

Table S14. Selected bond length angles for **8 Form I**.

Bond lengths	[Å]
Ni1–Cl1	2.1809(7)
Ni1–N1	2.003(2)
Ni1–N3	1.8906(19)
Ni1–C9	1.938(2)

Table S15. Selected angles for **8 Form I**

Angles	[°]
N1–Ni1–Cl1	94.02(6)
N3–Ni1–Cl1	175.19(6)
N3–Ni1–N1	81.35(8)
N3–Ni1–C9	95.03(9)
C9–Ni1–Cl1	89.46(7)
C9–Ni1–N1	173.76(9)

Tau-4 of the nickel complex **8 Form I**

$\tau_4 = \frac{360^\circ - (\alpha + \beta)}{141^\circ} = \frac{360^\circ - (175.19^\circ + 173.76^\circ)}{141^\circ} = 0.0784(8)$; τ_4 varies from 0 to 1, 0 for square planar, 1 for tetrahedral; α = bond angle (N3–Ni1–Cl1), β = bond angle (C9–Ni1–N1)¹⁷.

Table S16. Crystal data and structure refinement

Identification code	Weix30b
Empirical formula	$\text{Ni}(\text{C}_8\text{H}_7\text{N}_3)(\text{C}_{11}\text{H}_{14}\text{NSO}_2)\text{Cl}$
Formula weight	463.62
Temperature/K	100.00
Crystal system	triclinic
Space group	$P\bar{1}$
a/Å	9.1793(10)
b/Å	9.7101(10)
c/Å	11.7843(12)
$\alpha/^\circ$	95.272(7)
$\beta/^\circ$	99.134(7)
$\gamma/^\circ$	104.780(7)
Volume/Å ³	993.04(18)
Z	2
$\rho_{\text{calc}}/\text{g}/\text{cm}^3$	1.551
μ/mm^{-1}	3.825
F(000)	480.0
Crystal size/mm ³	$0.074 \times 0.063 \times 0.046$
Radiation	Cu K α ($\lambda = 1.54178$)
2 Θ range for data collection/ $^\circ$	7.672 to 158.816
Index ranges	$-11 \leq h \leq 11, -10 \leq k \leq 12, -14 \leq l \leq 14$
Reflections collected	21855
Independent reflections	4165 [$R_{\text{int}} = 0.0247, R_{\text{sigma}} = 0.0364$]
Data/restraints/parameters	4165/0/254
Goodness-of-fit on F ²	1.038
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0483, wR_2 = 0.1332$
Final R indexes [all data]	$R_1 = 0.0511, wR_2 = 0.1356$
Largest diff. peak/hole / e Å ⁻³	1.09/-0.35

X-ray analysis of complex 8 Form II (CCDC reference code: 2516891)

Data Collection

A red crystal with approximate dimensions 0.171 x 0.019 x 0.029 mm³ was selected under oil under ambient and attached to the tip of a MiTeGen MicroMount©. The crystal was mounted in a stream of cold nitrogen at 100(1) K and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed on a Bruker Quazar SMART APEXII diffractometer with Mo K α ($\lambda = 0.71073$ Å) radiation and the diffractometer to crystal distance of 5.0 cm.

The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 12 frames collected at intervals of 0.5° in a 6° range about ω with an exposure time of 10 seconds per frame. The reflections were successfully indexed by an automated indexing routine built into the APEX5 program. The final cell constants were calculated from a set of 4924 strong reflections from the actual data collection.

The data were collected by using a half sphere data collection routine to survey reciprocal space to the extent of a half sphere to a resolution of 0.80 Å. A total of 27753 data were harvested by collecting 4 sets of frames with 0.5° scans in ω and ϕ with exposure times of 191 sec per frame. These redundant datasets were corrected for Lorentz and polarization effects. The absorption correction was based on fitting a function to the empirical transmission surface as sampled by multiple equivalent measurements.

Structure Solution and Refinement

The diffraction data were consistent with the space groups $P\bar{1}$ and $P1$. The E -statistics strongly suggested the centrosymmetric space group $P\bar{1}$ which yielded chemically reasonable and computationally stable results of refinement.

A successful solution by direct methods provided most non-hydrogen atoms from the E -map. The remaining non-hydrogen atoms were located with an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined with anisotropic displacement coefficients. All hydrogen atoms were included in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients.

The asymmetric unit contains two Ni(C₈H₇N₃)(C₁₁H₁₄NSO₂)Cl molecules with similar geometries. A rigid bond restraint was applied to C17 and C18 to yield chemically reasonable anisotropic displacement coefficients. An idealized geometry constraint was applied to the C13–C18 aromatic six-membered ring to yield chemically reasonable carbon to carbon bond distances.

The final least-squares refinement of 495 parameters against 8036 data resulted in residuals R (based on F^2 for $I \geq 2\sigma$) and wR (based on F^2 for all data) of 0.0591 and 0.1464, respectively. The final difference Fourier map contains a peak of residual electron density (ca. $1.24 \text{ e}/\text{\AA}^3$) in the vicinity of atom Ni1a. This peak was in a chemically unreasonable position and was considered noise.

Summary

Crystal Data for $\text{C}_{19}\text{H}_{21}\text{ClN}_4\text{NiO}_2\text{S}$ ($M=463.62 \text{ g/mol}$): triclinic, space group $P\bar{1}$ (no. 2), $a = 7.704(4) \text{ \AA}$, $b = 13.687(8) \text{ \AA}$, $c = 19.250(10) \text{ \AA}$, $\alpha = 101.753(11)^\circ$, $\beta = 98.91(2)^\circ$, $\gamma = 91.516(14)^\circ$, $V = 1959.8(18) \text{ \AA}^3$, $Z = 4$, $T = 100.00 \text{ K}$, $\mu(\text{Mo K}\alpha) = 1.256 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.571 \text{ g/cm}^3$, 27753 reflections measured ($2.19^\circ \leq 2\Theta \leq 52.804^\circ$), 8036 unique ($R_{\text{int}} = 0.0815$, $R_{\text{sigma}} = 0.0839$) which were used in all calculations. The final R_1 was 0.0591 ($I > 2\sigma(I)$) and wR_2 was 0.1464 (all data).

Crystal structure and crystallographic data

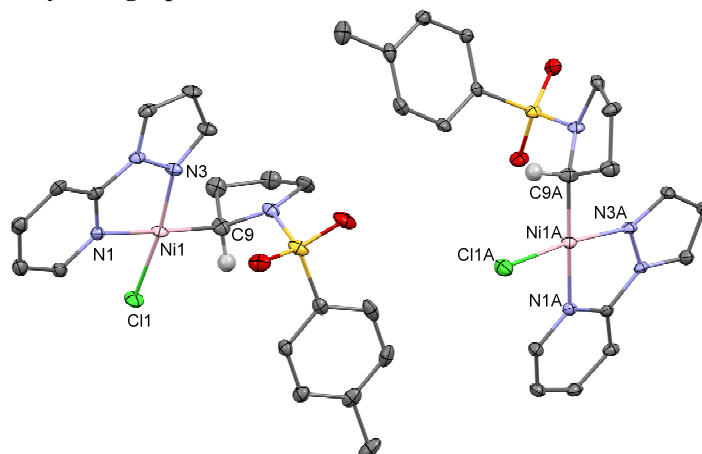


Fig. S22. Crystal structure of **8 Form II**. The compound crystallizes as a racemate, thus the enantiomers shown (C9–S and C9A–S) are chosen arbitrarily.

Table S17. Selected bond length angles for **8 Form II**.

Bond lengths	[Å]	Bond lengths	[Å]
Ni1–Cl1	2.1733(17)	Ni1A–Cl1A	2.1669(19)
Ni1–N1	1.999(4)	Ni1A–N1A	1.997(4)
Ni1–N3	1.886(4)	Ni1A–N3A	1.901(4)
Ni1–C9	1.937(6)	Ni1A–C9A	1.918(5)

Table S18. Selected angles for **8 Form II**

Angles	[°]	Angles	[°]
N1–Ni1–Cl1	93.45(12)	N1A–Ni1A–Cl1A	92.99(12)
N3–Ni1–Cl1	173.13(14)	N3A–Ni1A–Cl1A	173.08(12)
N3–Ni1–N1	81.70(17)	N3A–Ni1A–N1A	81.66(16)
N3–Ni1–C9	95.9(2)	N3A–Ni1A–C9A	96.4(2)
C9–Ni1–Cl1	88.94(17)	C9A–Ni1A–Cl1A	89.12(18)
C9–Ni1–N1	177.6(2)	C9A–Ni1A–N1A	176.85(19)

Tau-4 of the nickel complex **8 Form II**

$\tau_4 = \frac{360^\circ - (\alpha + \beta)}{141^\circ} = \frac{360^\circ - (173.13^\circ + 177.6^\circ)}{141^\circ} = 0.0657(17)$ and $\frac{360^\circ - (173.08^\circ + 176.85^\circ)}{141^\circ} = 0.0714(16)$; τ_4 varies from 0 to 1, 0 for square planar, 1 for tetrahedral; α = bond angle (N3–Ni1–Cl1 or N3A–Ni1A–Cl1A), β = bond angle (C9–Ni1–N1 and C9A–Ni1A–N1A)¹⁷.

Table S19. Crystal data and structure refinement

Identification code	Weix30
Empirical formula	Ni(C ₈ H ₇ N ₃)(C ₁₁ H ₁₄ NSO ₂)Cl
Formula weight	463.62
Temperature/K	100.00
Crystal system	triclinic
Space group	$P\bar{1}$
a/Å	7.704(4)
b/Å	13.687(8)
c/Å	19.250(10)
$\alpha/^\circ$	101.753(11)
$\beta/^\circ$	98.91(2)
$\gamma/^\circ$	91.516(14)
Volume/Å ³	1959.8(18)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.571
μ/mm^{-1}	1.256
F(000)	960.0
Crystal size/mm ³	0.171 × 0.029 × 0.019
Radiation	Mo K α (λ = 0.71073)
2 Θ range for data collection/ $^\circ$	2.19 to 52.804
Index ranges	-9 ≤ h ≤ 9, -16 ≤ k ≤ 17, -24 ≤ l ≤ 24
Reflections collected	27753
Independent reflections	8036 [R_{int} = 0.0815, R_{sigma} = 0.0839]
Data/restraints/parameters	8036/1/495
Goodness-of-fit on F ²	1.022
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0591, wR_2 = 0.1291
Final R indexes [all data]	R_1 = 0.1061, wR_2 = 0.1464
Largest diff. peak/hole / e Å ⁻³	1.24/-0.49

X-ray analysis of 56 (CCDC reference code: 2516893)

Data Collection

A colorless crystal with approximate dimensions $0.14 \times 0.05 \times 0.05 \text{ mm}^3$ was selected under oil under ambient conditions and attached to the tip of a MiTeGen MicroMount©. The crystal was mounted in a stream of cold nitrogen at 100(1) K and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed on a Bruker D8 VENTURE PhotonIII four-circle diffractometer with Cu K α ($\lambda = 1.54178 \text{ \AA}$) radiation and the detector to crystal distance of 5.0 cm.

The initial cell constants were obtained from a $180^\circ \phi$ scan conducted at a $2\theta = 50^\circ$ angle with the exposure time of 1 second per frame. The reflections were successfully indexed by an automated indexing routine built in the APEX6 program. The final cell constants were calculated from a set of 8009 strong reflections from the actual data collection.

The data were collected by using the hemisphere data collection routine to survey the reciprocal space to a resolution of $0.78 \text{ \AA}$. A total of 31133 data were harvested by collecting 34 sets of frames with 1.0° scans in ω and ϕ with an exposure time 1–4 sec per frame. These highly redundant datasets were corrected for Lorentz and polarization effects. The absorption correction was based on fitting a function to the empirical transmission surface as sampled by multiple equivalent measurements.

Structure Solution and Refinement

The systematic absences in the diffraction data were consistent for the space groups $P2_1$ and $P2_1/m$. The E -statistics strongly suggested the non-centrosymmetric space group $P2_1$ that yielded chemically reasonable and computationally stable results of refinement.

A successful solution by intrinsic phasing provided most non-hydrogen atoms from the E -map. The remaining non-hydrogen atoms were located in an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined with anisotropic displacement coefficients. All hydrogen atoms attached to carbon atoms were included in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients.

The absolute structure was established by resonant scattering effects. ***The absolute configuration of atom C15 is R.***

The final least-squares refinement of 350 parameters against 5929 data resulted in residuals R (based on F^2 for $I \geq 2\sigma$) and wR (based on F^2 for all data) of 0.0242 and 0.0632, respectively. The final difference Fourier

map was featureless.

Summary

Crystal Data for $C_{30}H_{33}NO_5Cl_2$ ($M=558.47$ g/mol): monoclinic, space group $P2_1$ (no. 4), $a = 5.2016(4)$ Å, $b = 9.6332(9)$ Å, $c = 27.856(3)$ Å, $\beta = 93.519(7)^\circ$, $V = 1393.2(2)$ Å³, $Z = 2$, $T = 100$ K, $\mu(\text{Cu K}\alpha) = 2.425$ mm⁻¹, $D_{\text{calc}} = 1.331$ g/cm³, 31133 reflections measured ($6.358^\circ \leq 2\Theta \leq 158.464^\circ$), 5929 unique ($R_{\text{int}} = 0.0322$, $R_{\text{sigma}} = 0.0244$) which were used in all calculations. The final R_1 was 0.0242 ($I > 2\sigma(I)$) and wR_2 was 0.0632 (all data).

Crystal structure and crystallographic data

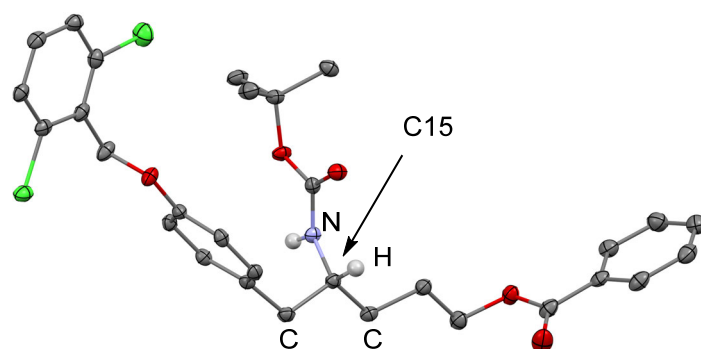


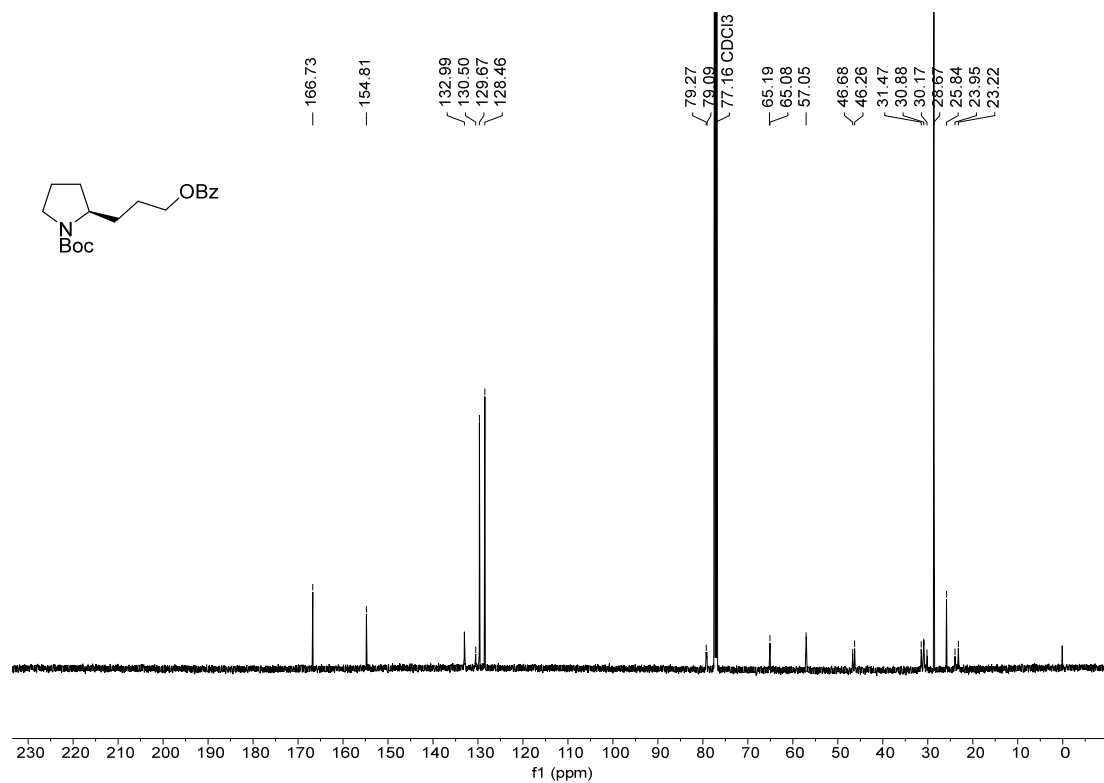
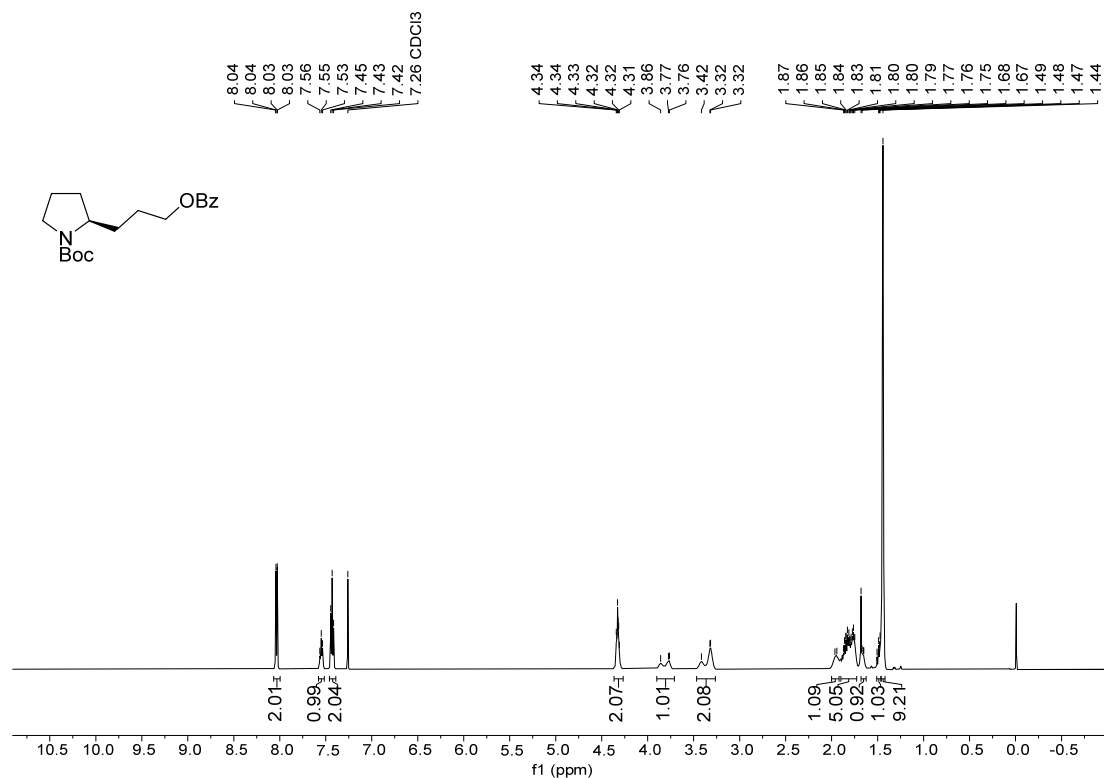
Fig. S23. Crystal structure of **56**

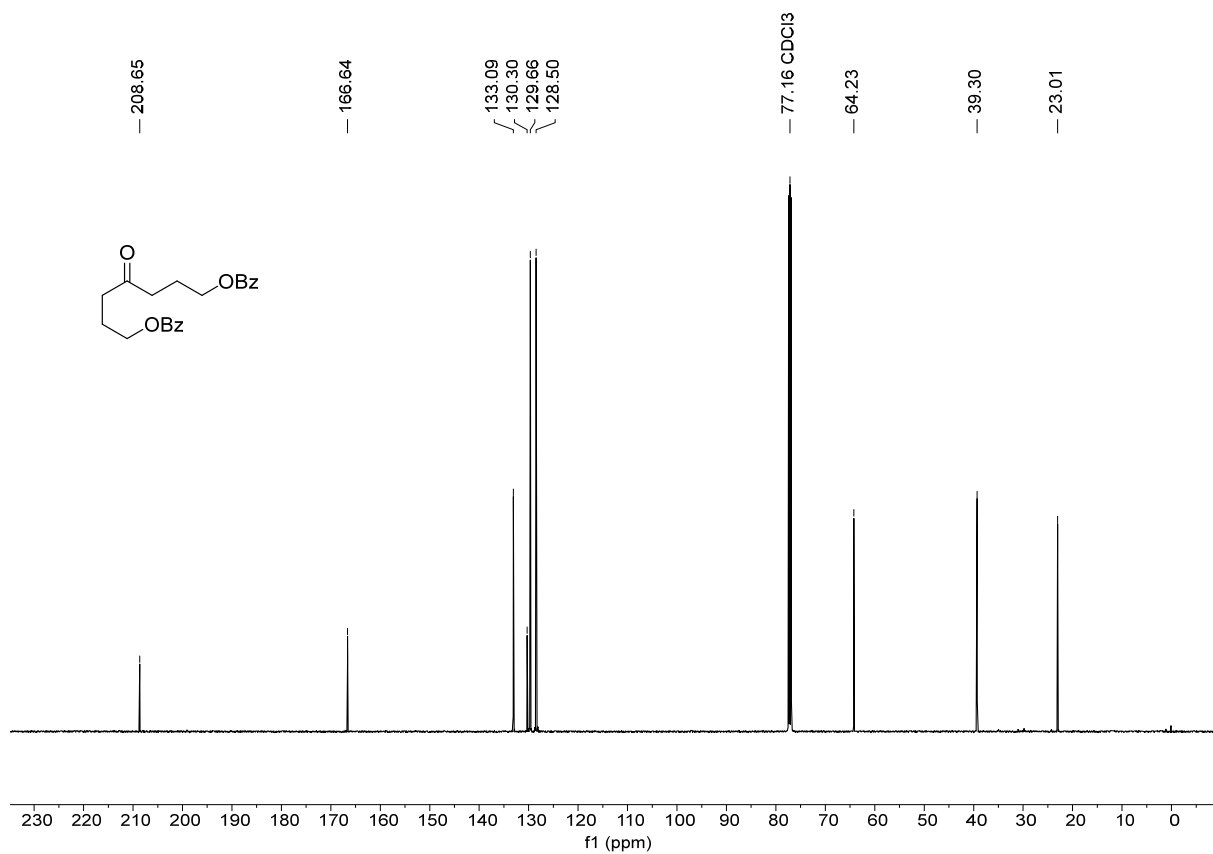
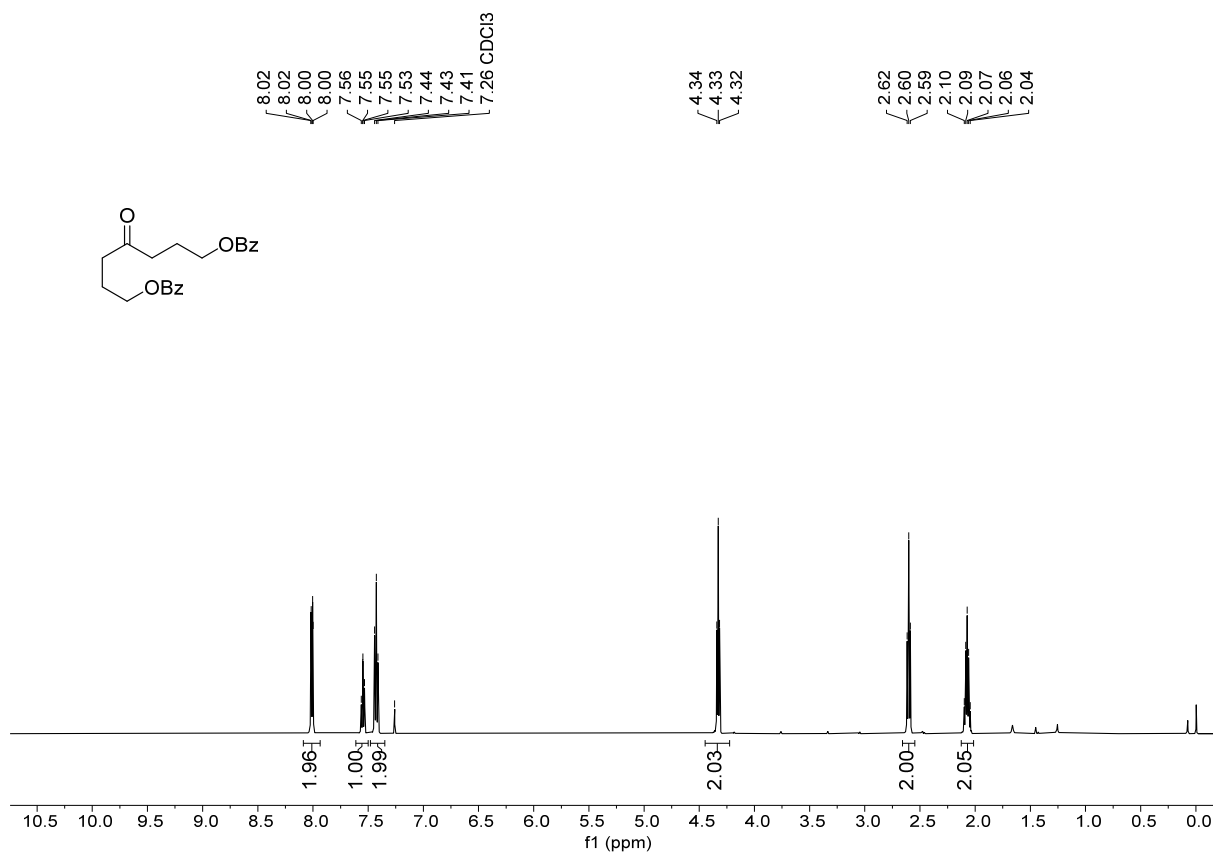
Table S20. Crystal data and structure refinement

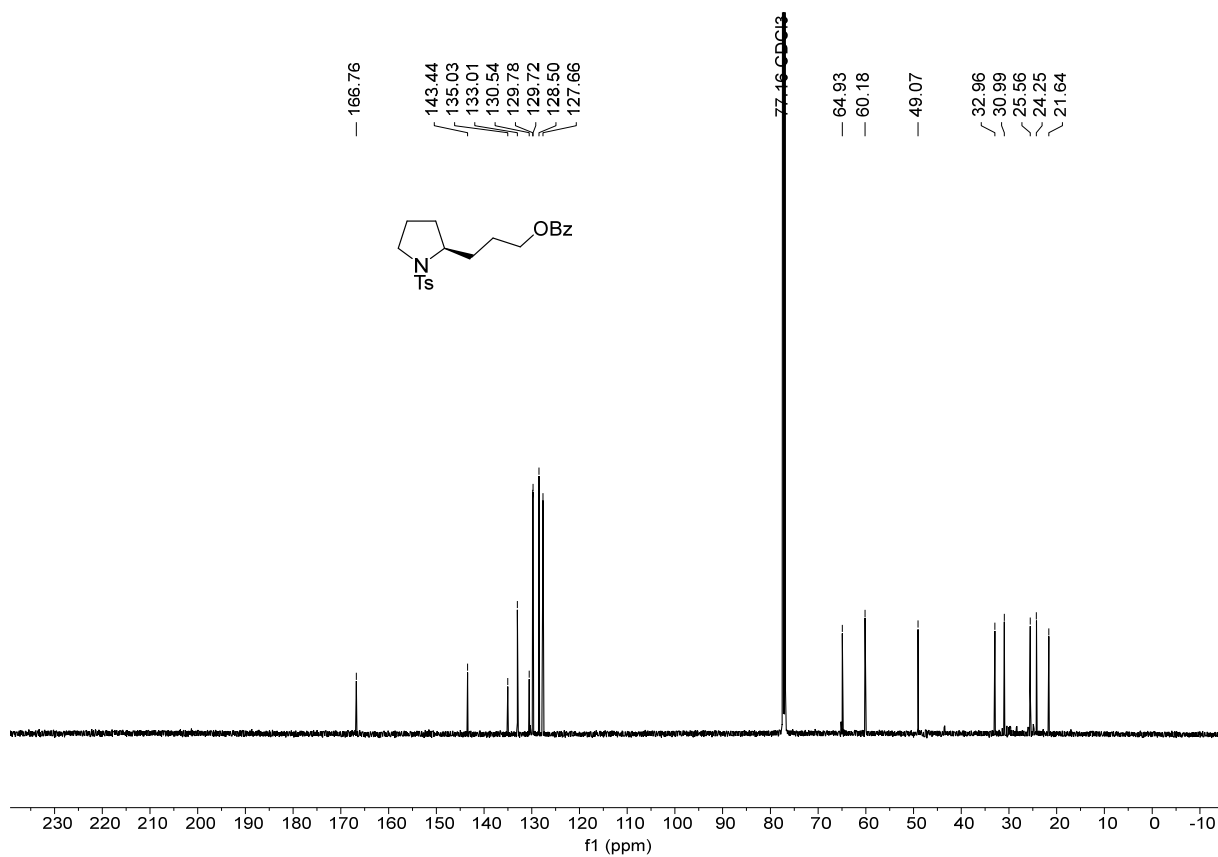
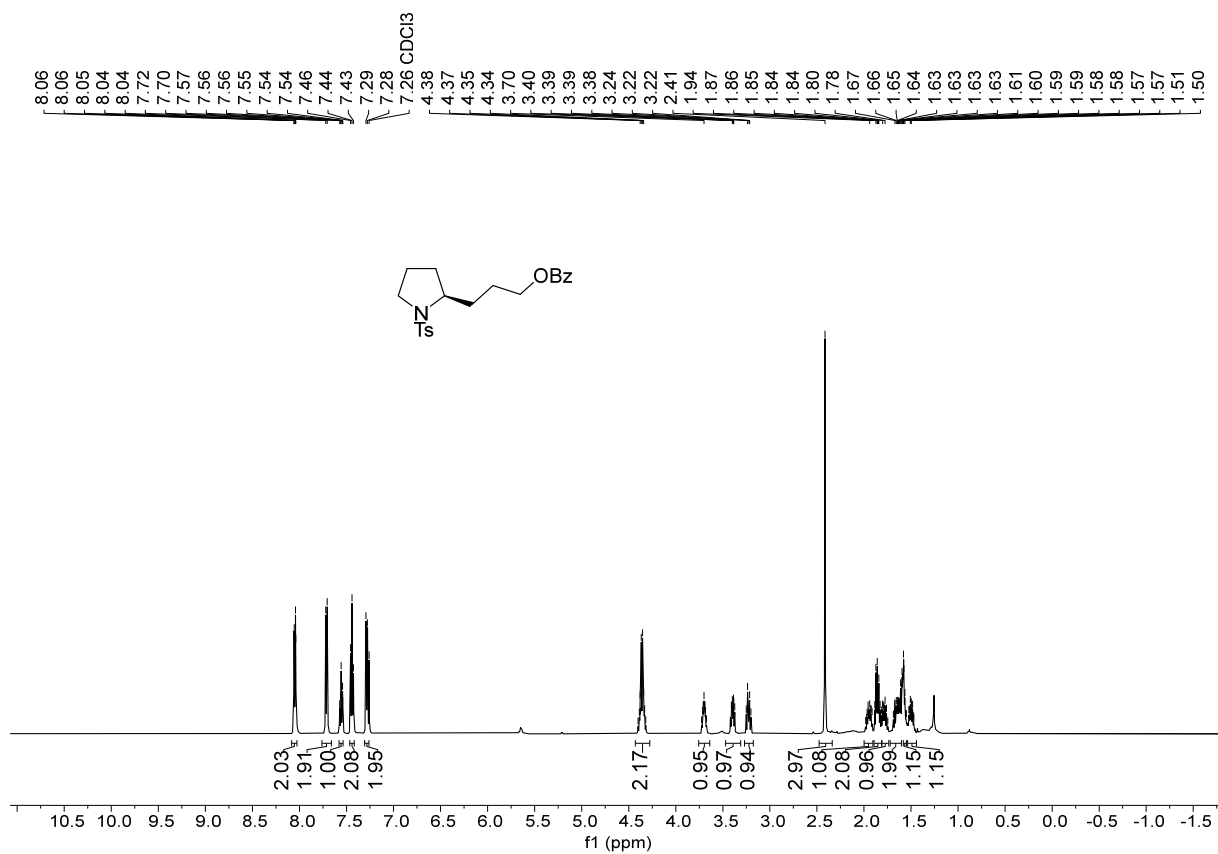
Identification code	Weix38
Empirical formula	C ₃₀ H ₃₃ NO ₅ Cl ₂
Formula weight	558.47
Temperature/K	100
Crystal system	monoclinic
Space group	P2 ₁
a/Å	5.2016(4)
b/Å	9.6332(9)
c/Å	27.856(3)
α /°	90
β /°	93.519(7)
γ /°	90
Volume/Å ³	1393.2(2)
Z	2
$\rho_{\text{calc}}/\text{cm}^3$	1.331
μ/mm^{-1}	2.425
F(000)	588.0
Crystal size/mm ³	0.14 × 0.05 × 0.05
Radiation	Cu K α (λ = 1.54178)
2 Θ range for data collection/°	6.358 to 158.464
Index ranges	-6 ≤ h ≤ 5, -12 ≤ k ≤ 12, -35 ≤ l ≤ 35
Reflections collected	31133
Independent reflections	5929 [R _{int} = 0.0322, R _{sigma} = 0.0244]
Data/restraints/parameters	5929/1/350
Goodness-of-fit on F ²	1.073
Final R indexes [I >= 2 σ (I)]	R ₁ = 0.0242, wR ₂ = 0.0630
Final R indexes [all data]	R ₁ = 0.0245, wR ₂ = 0.0632
Largest diff. peak/hole / e Å ⁻³	0.20/-0.17
Flack parameter	0.007(4)

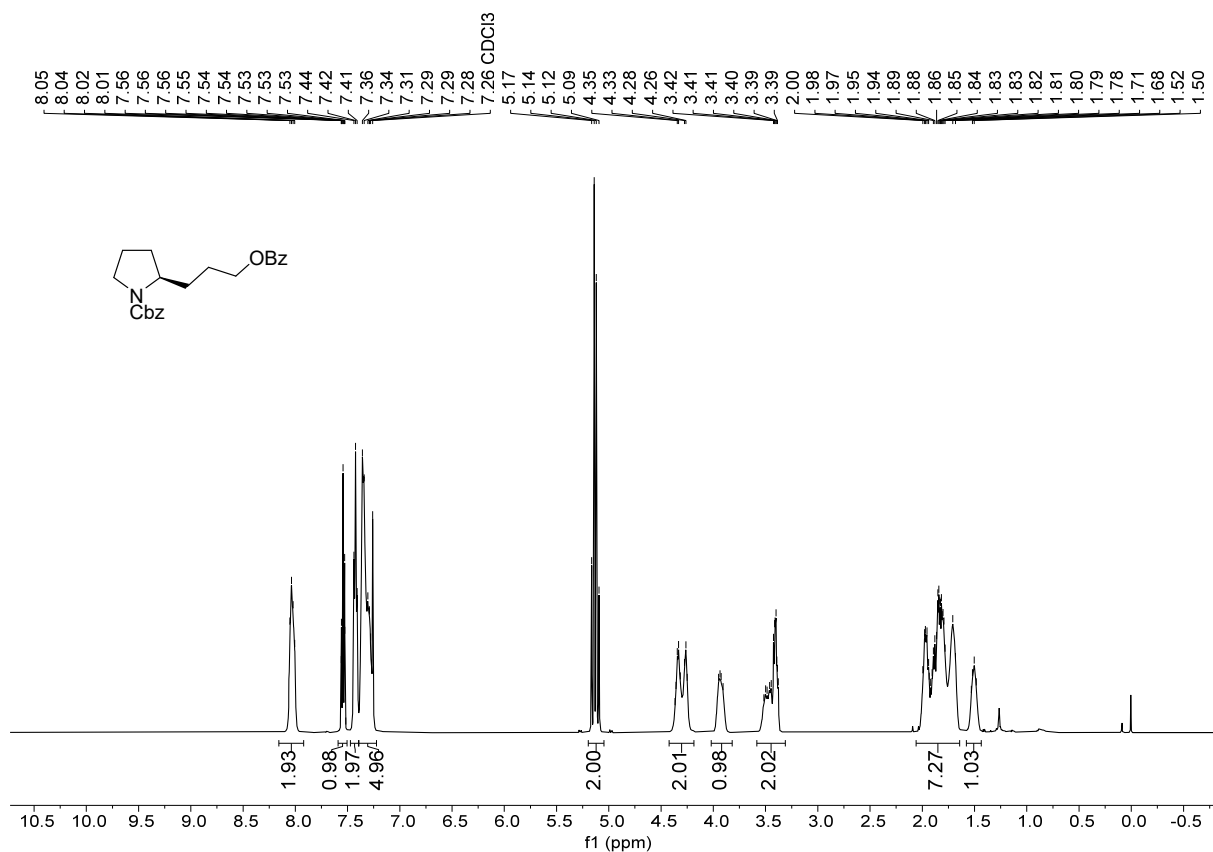
10. NMR spectra

10.1 NMR spectra of coupling products

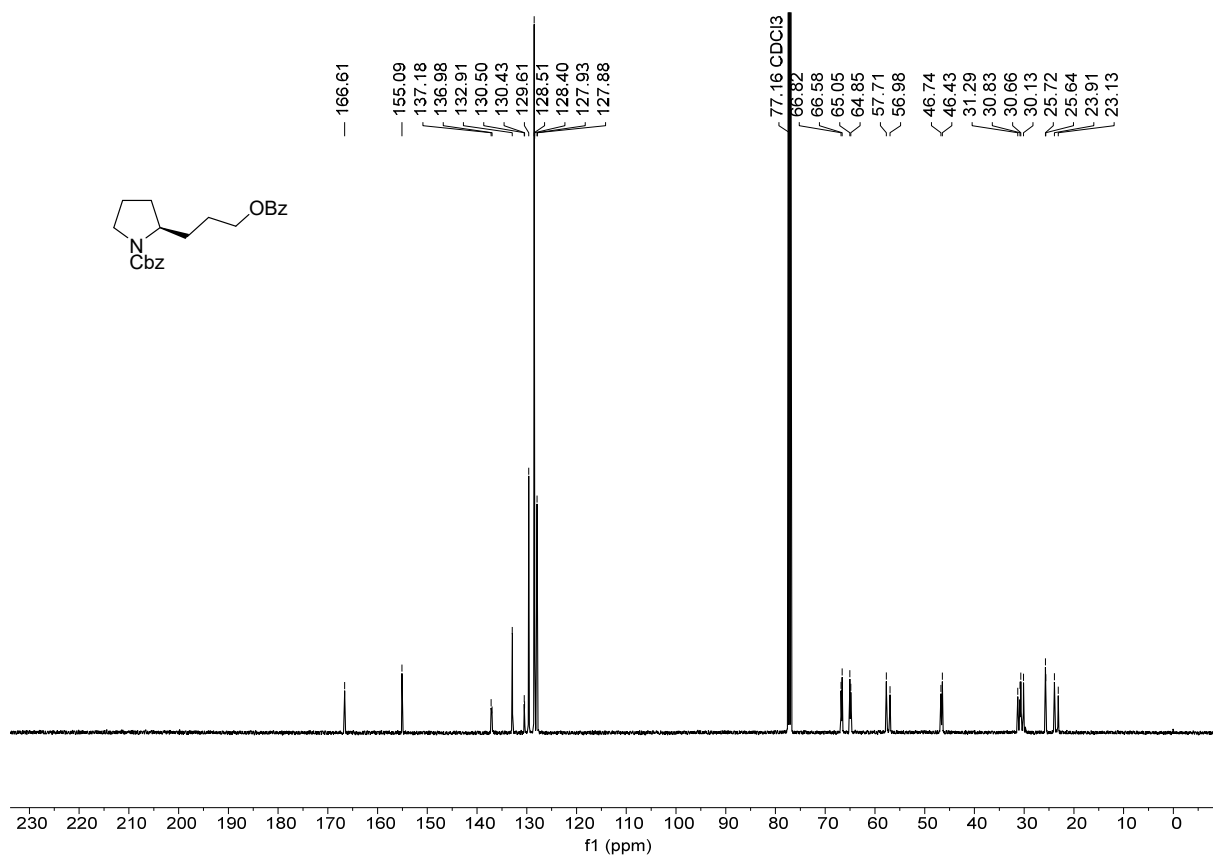




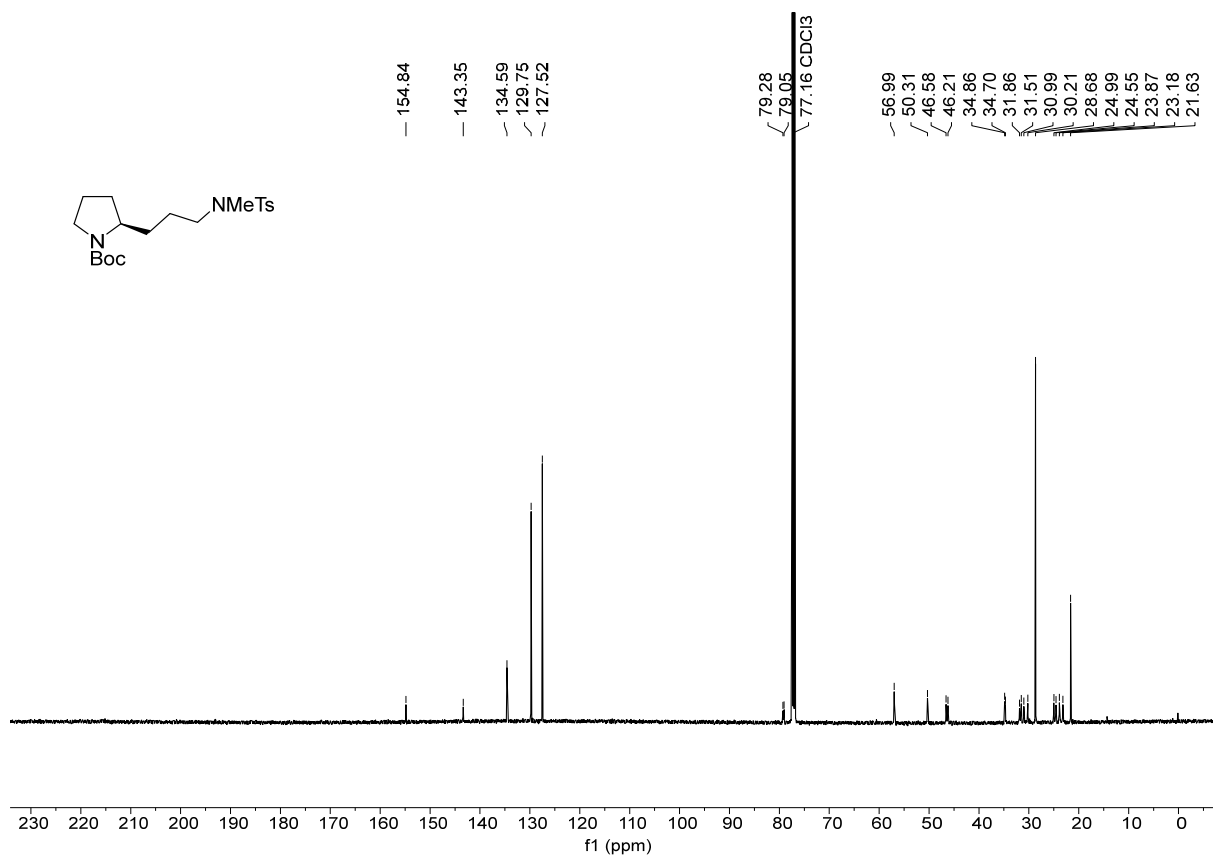
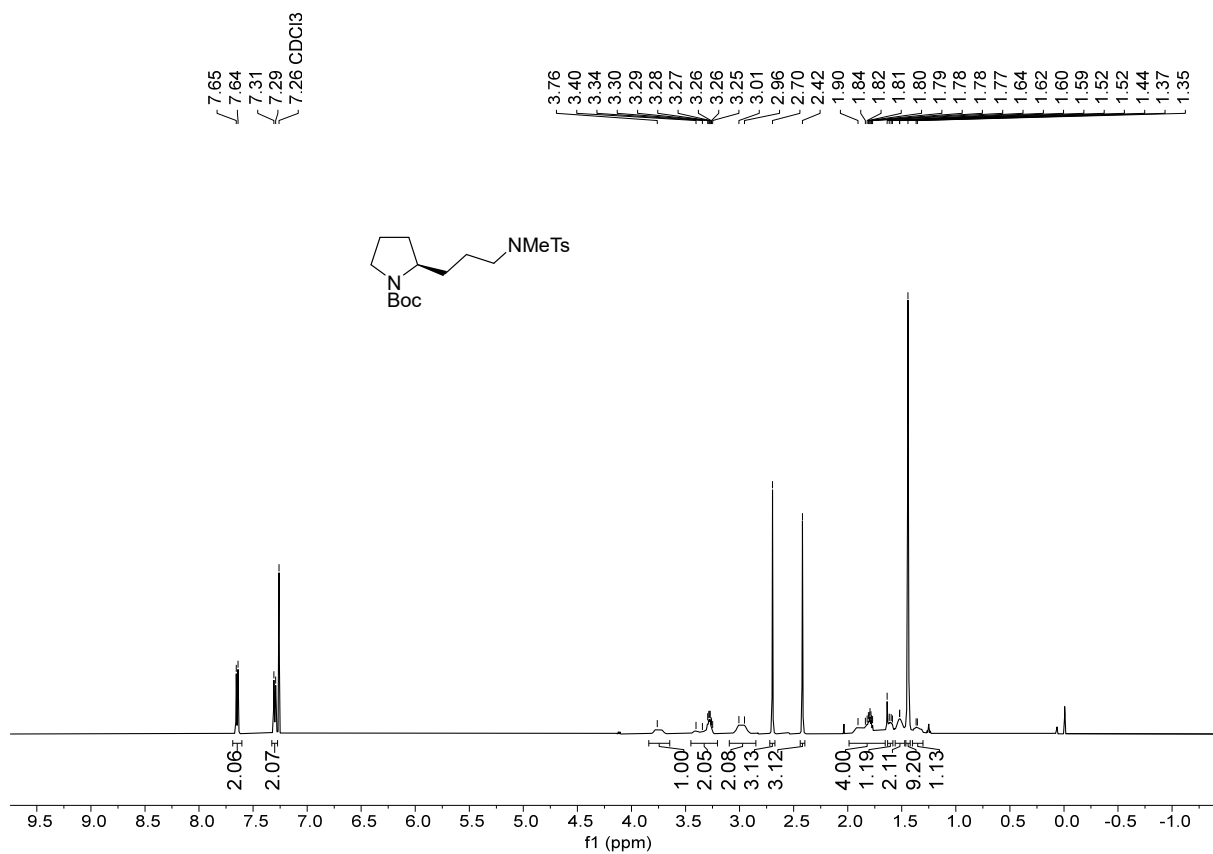


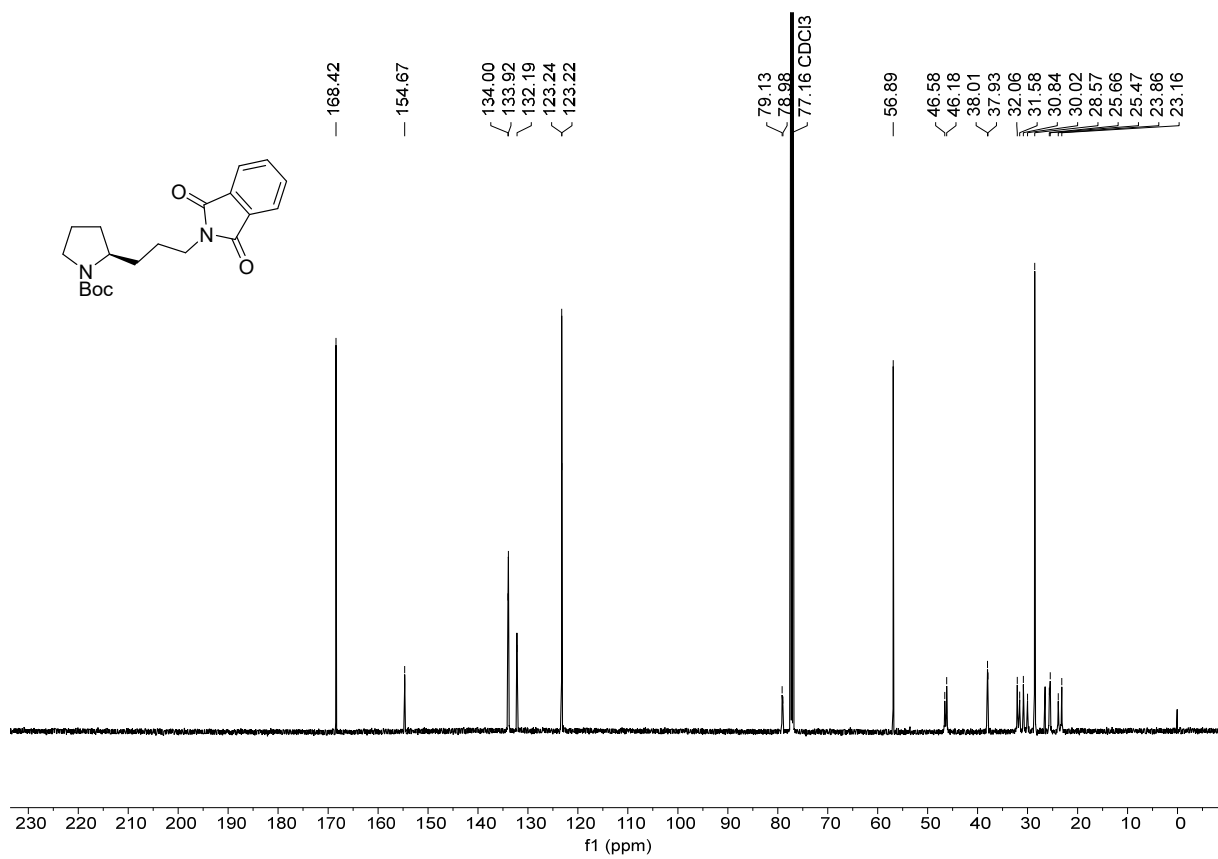
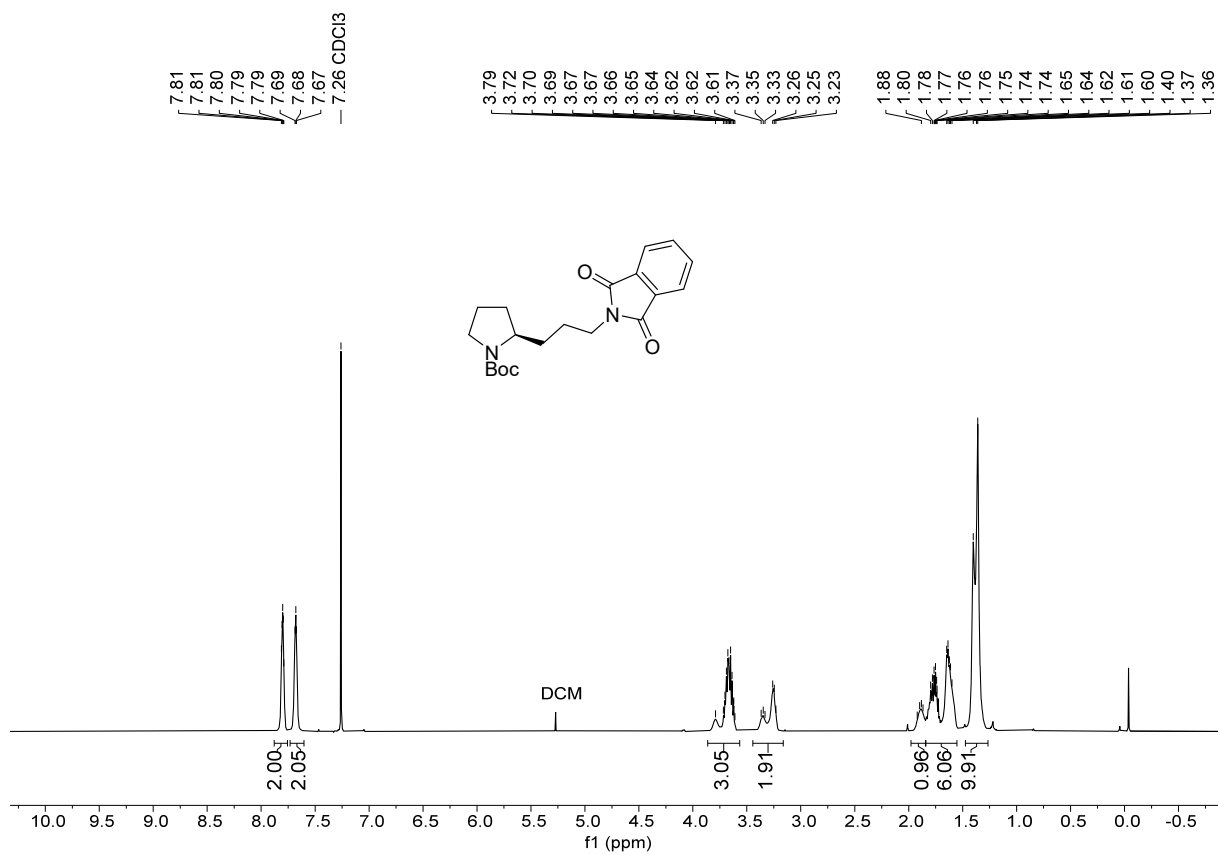


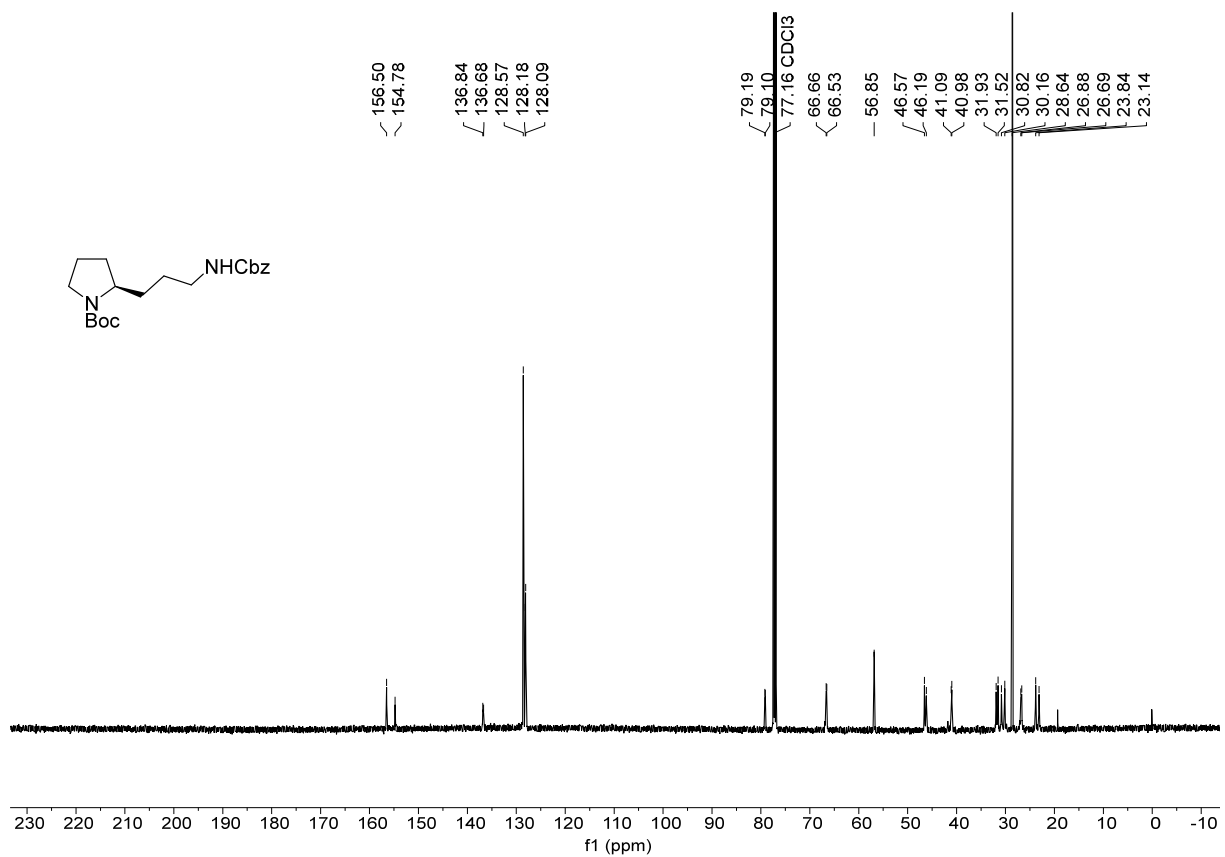
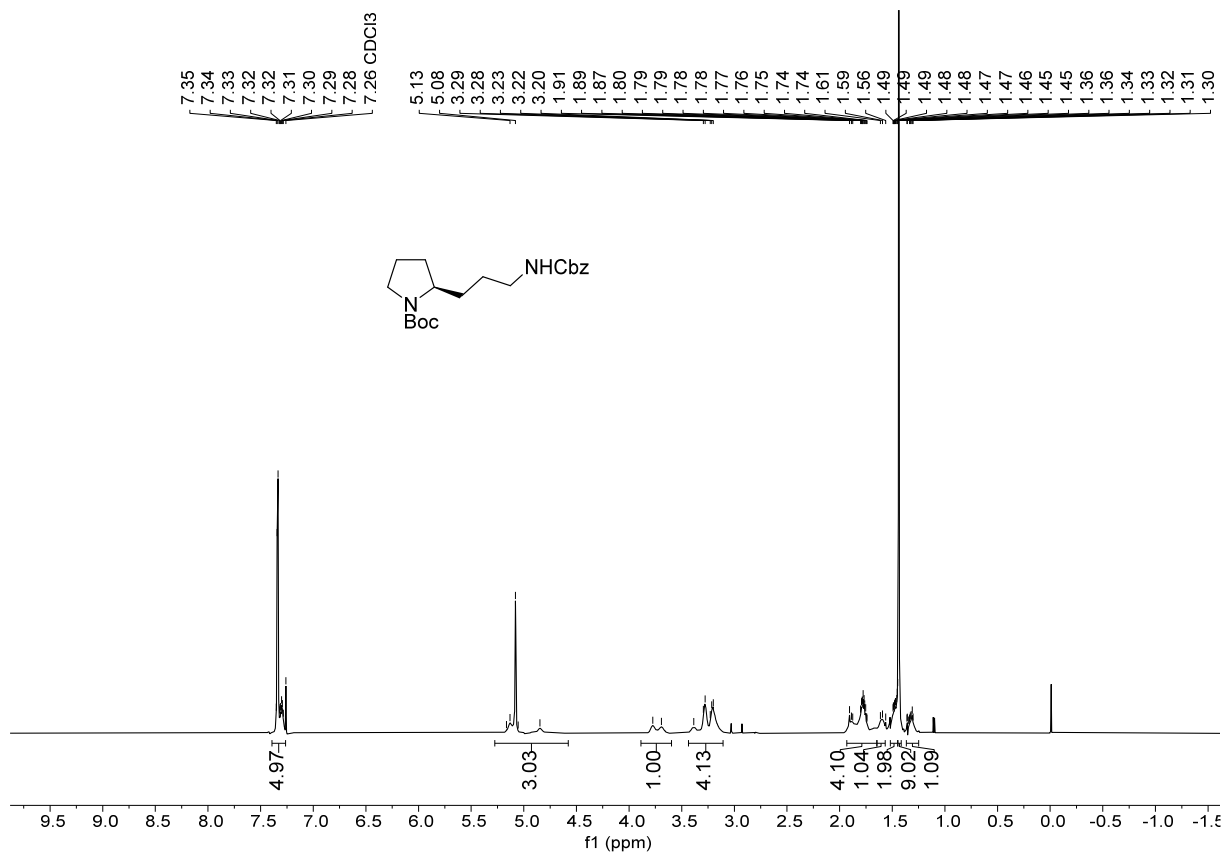
¹H NMR (500 MHz, CDCl₃) of 22

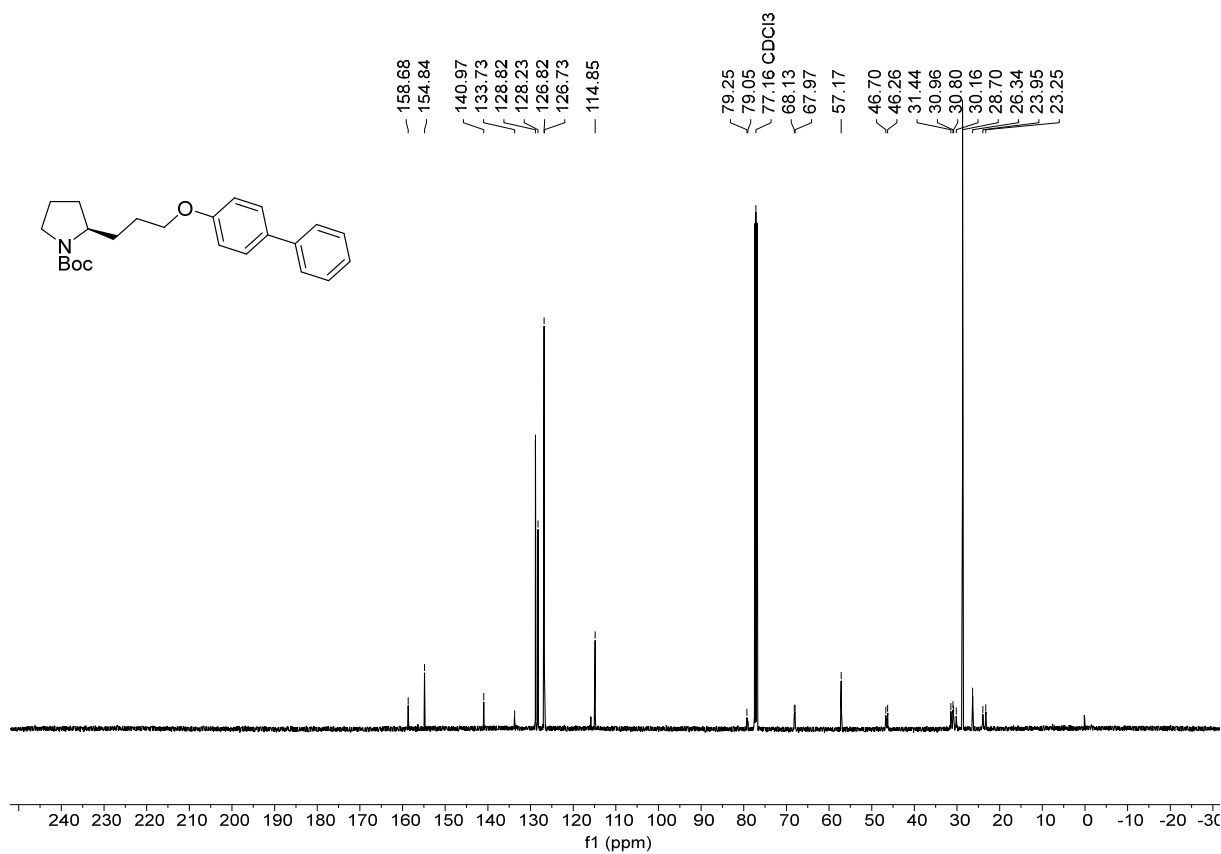
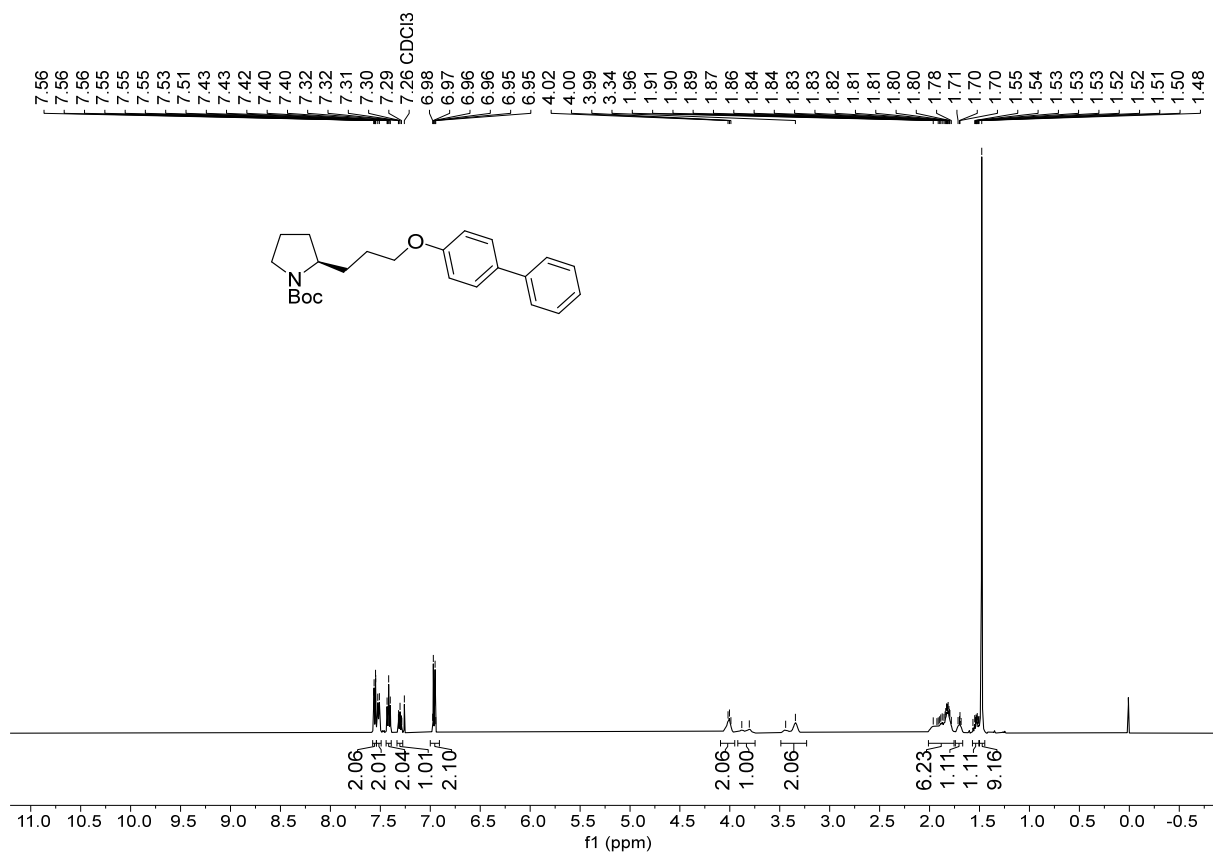


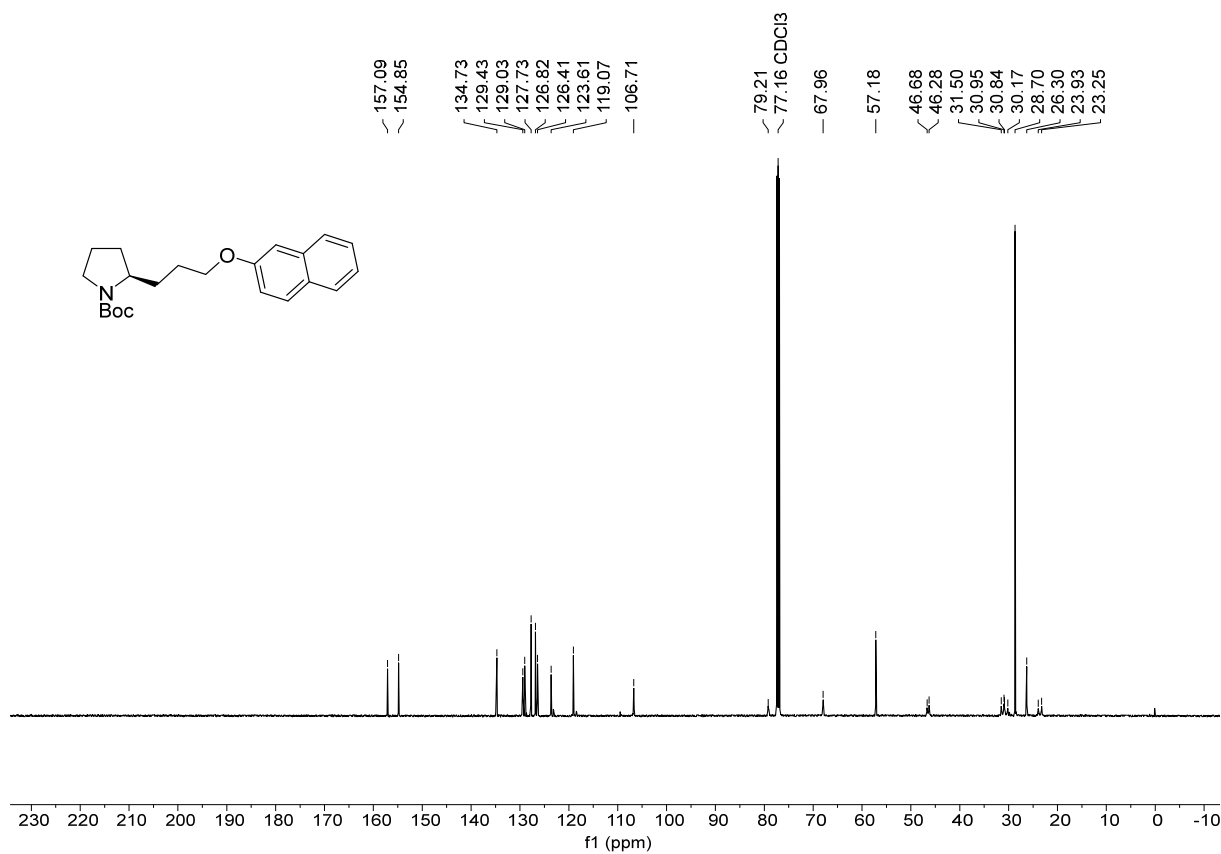
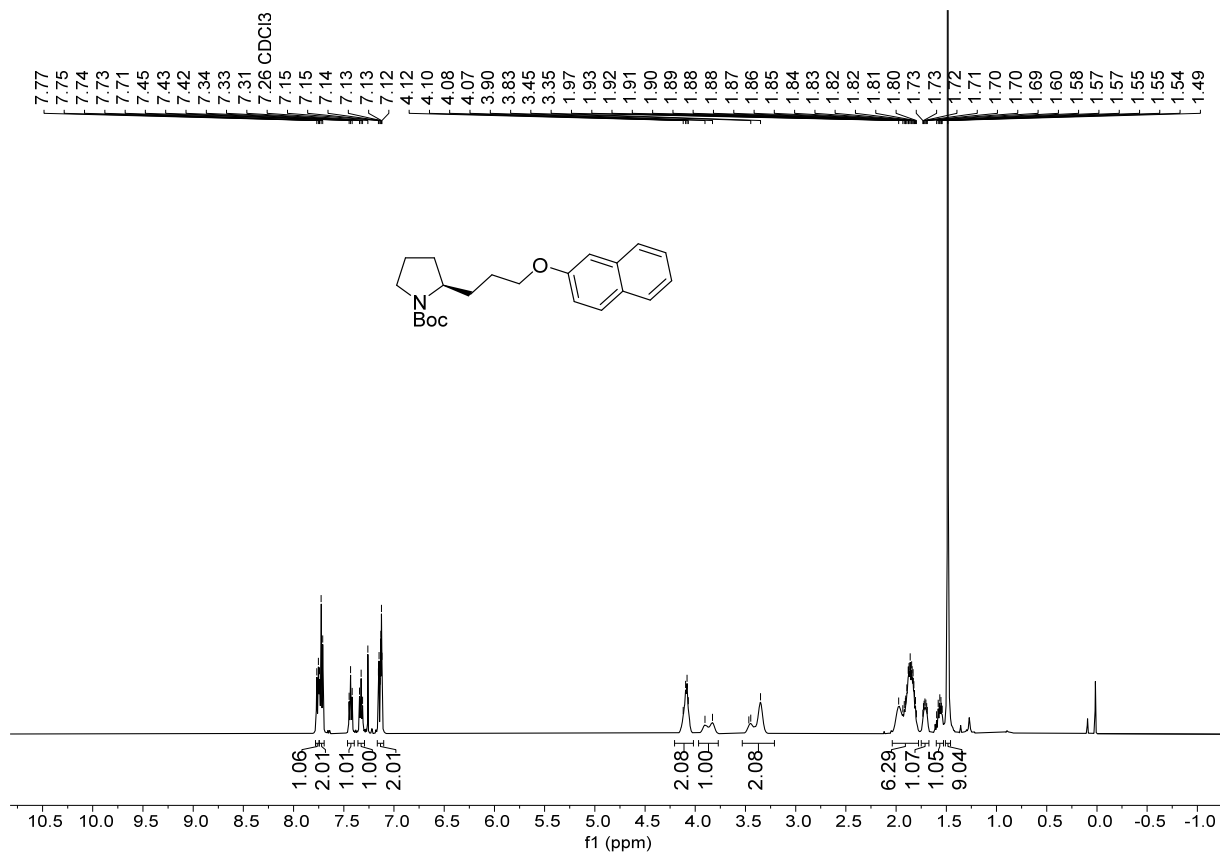
¹³C {¹H} NMR (125 MHz, CDCl₃) of 22

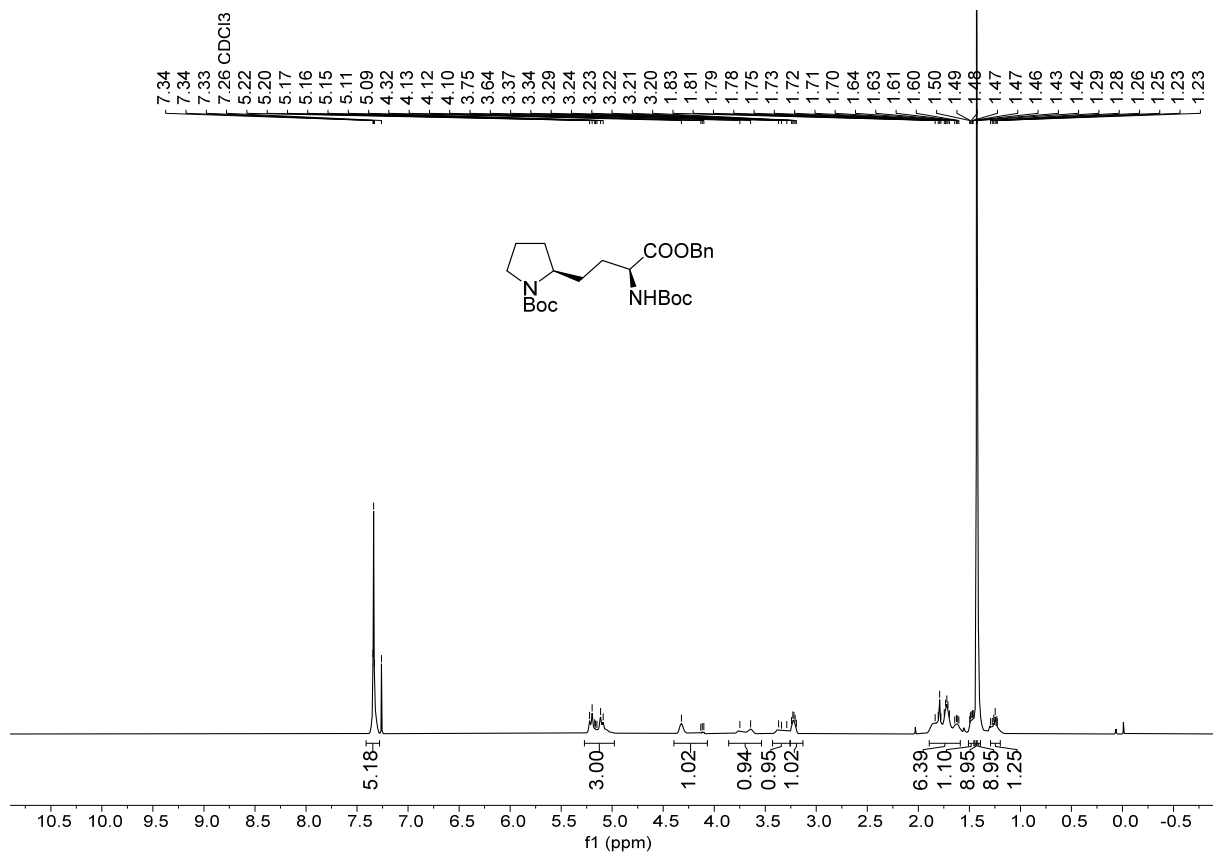




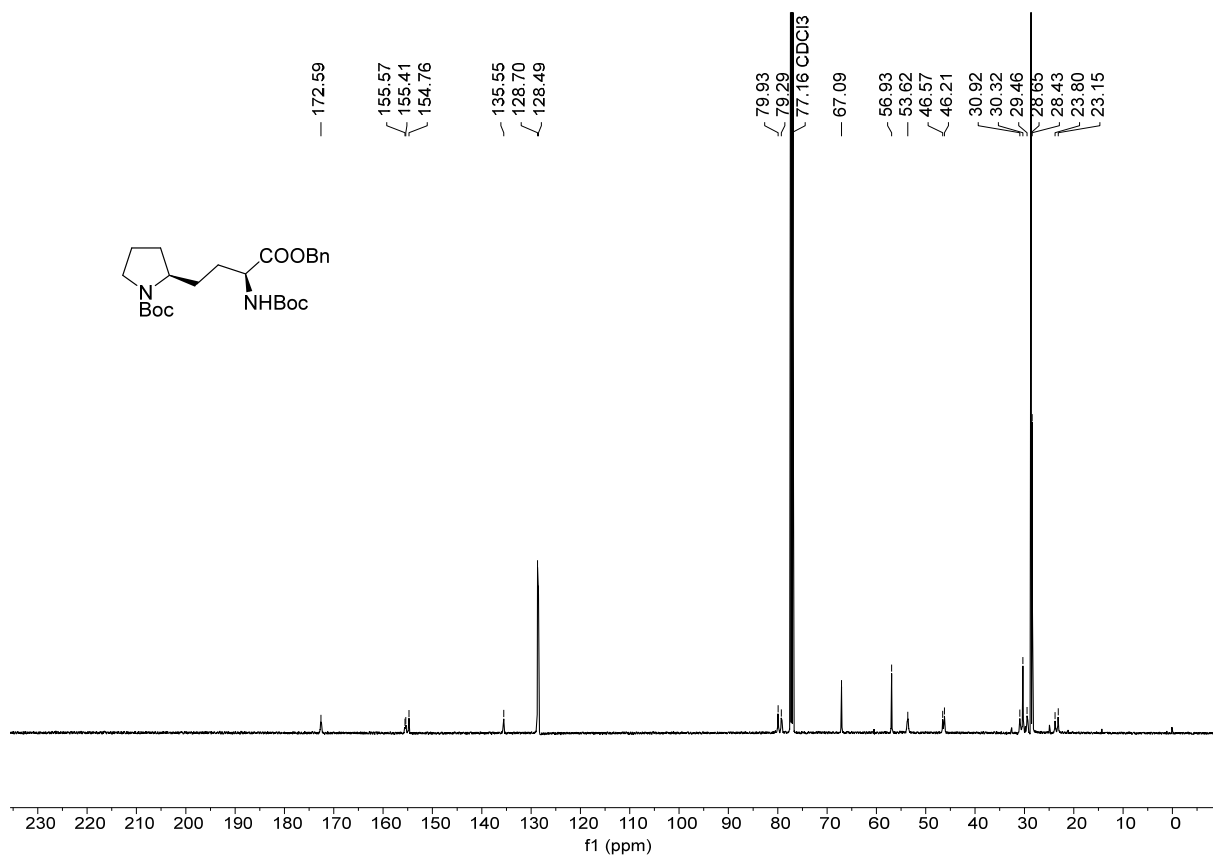




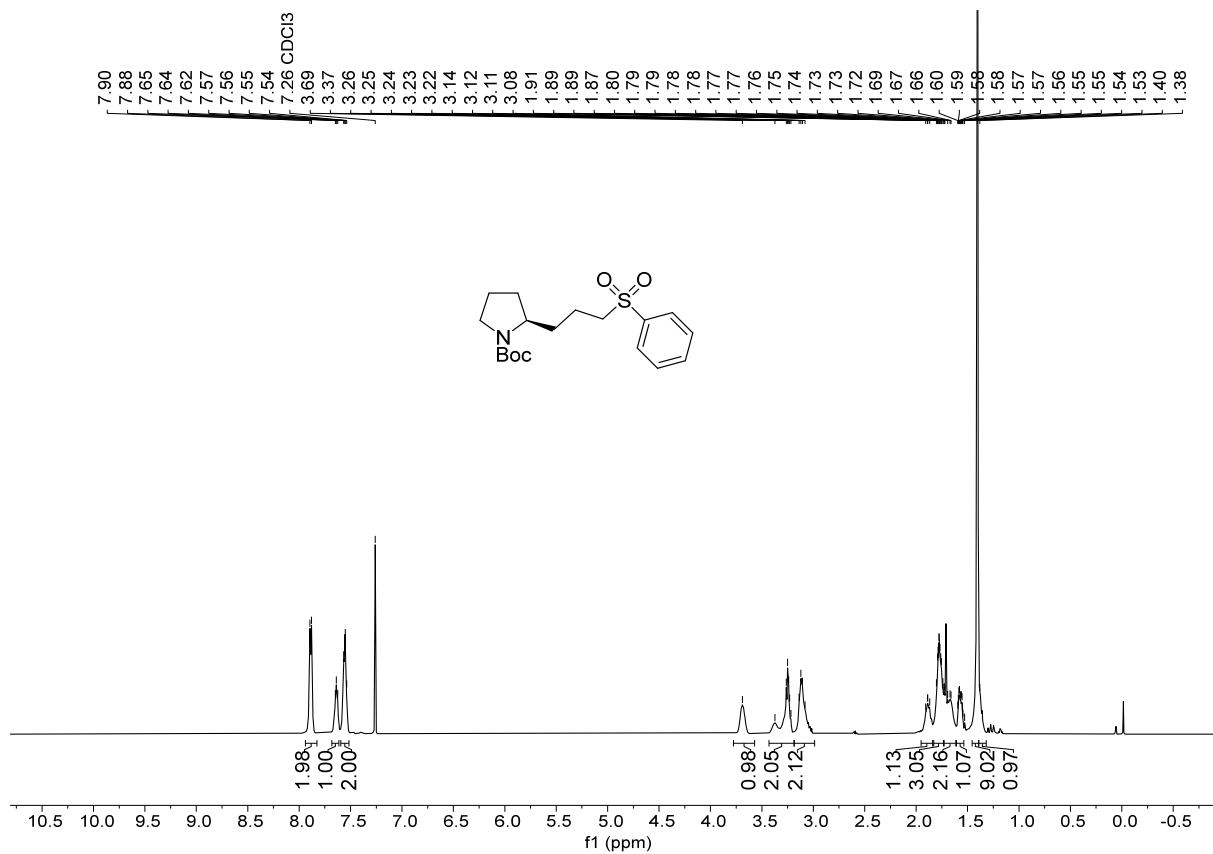




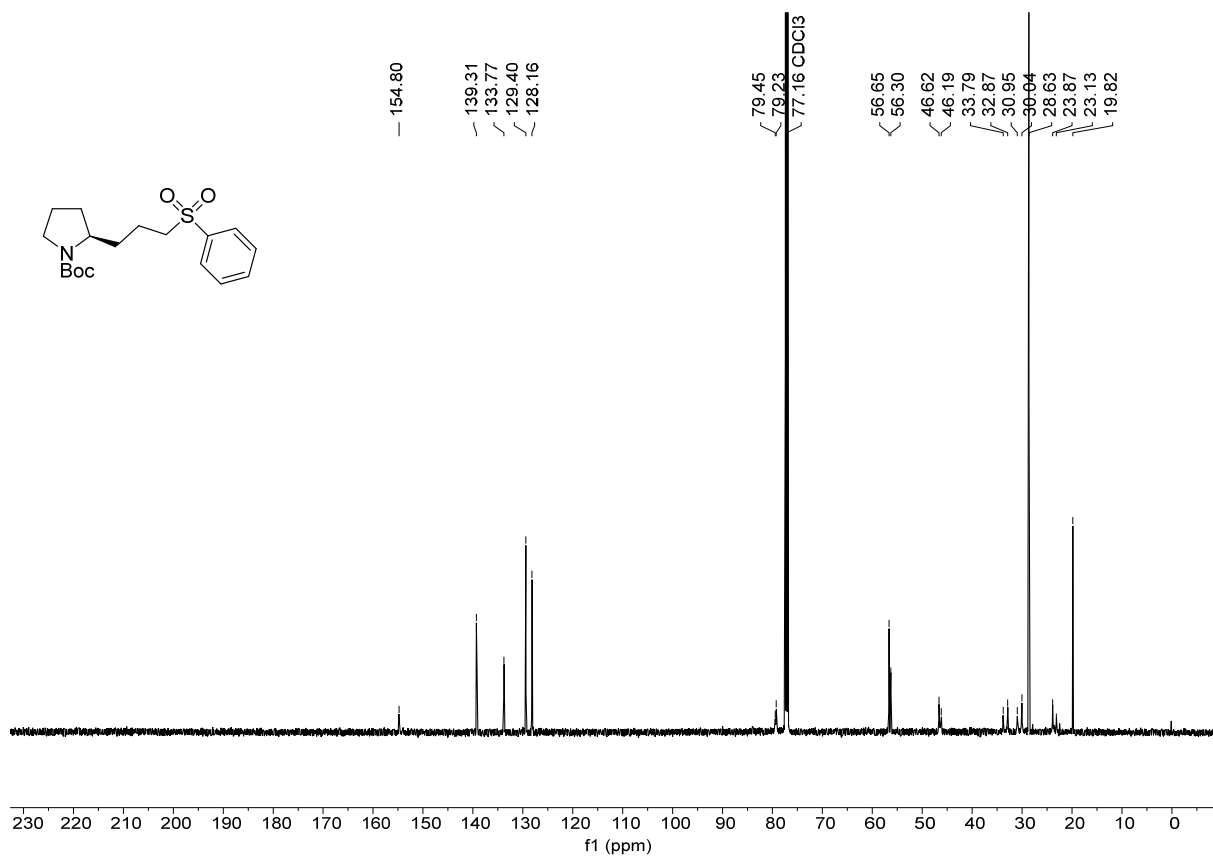
^1H NMR (500 MHz, CDCl_3) of **28**



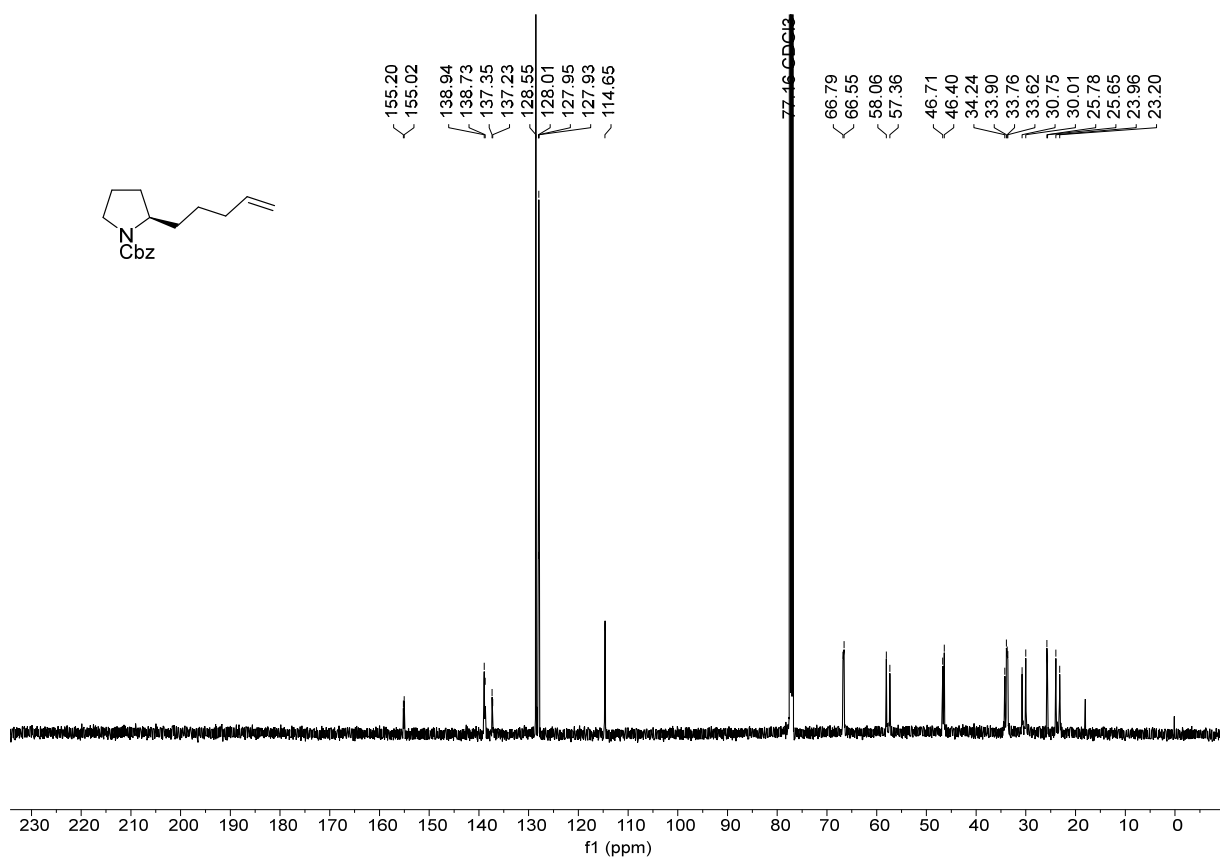
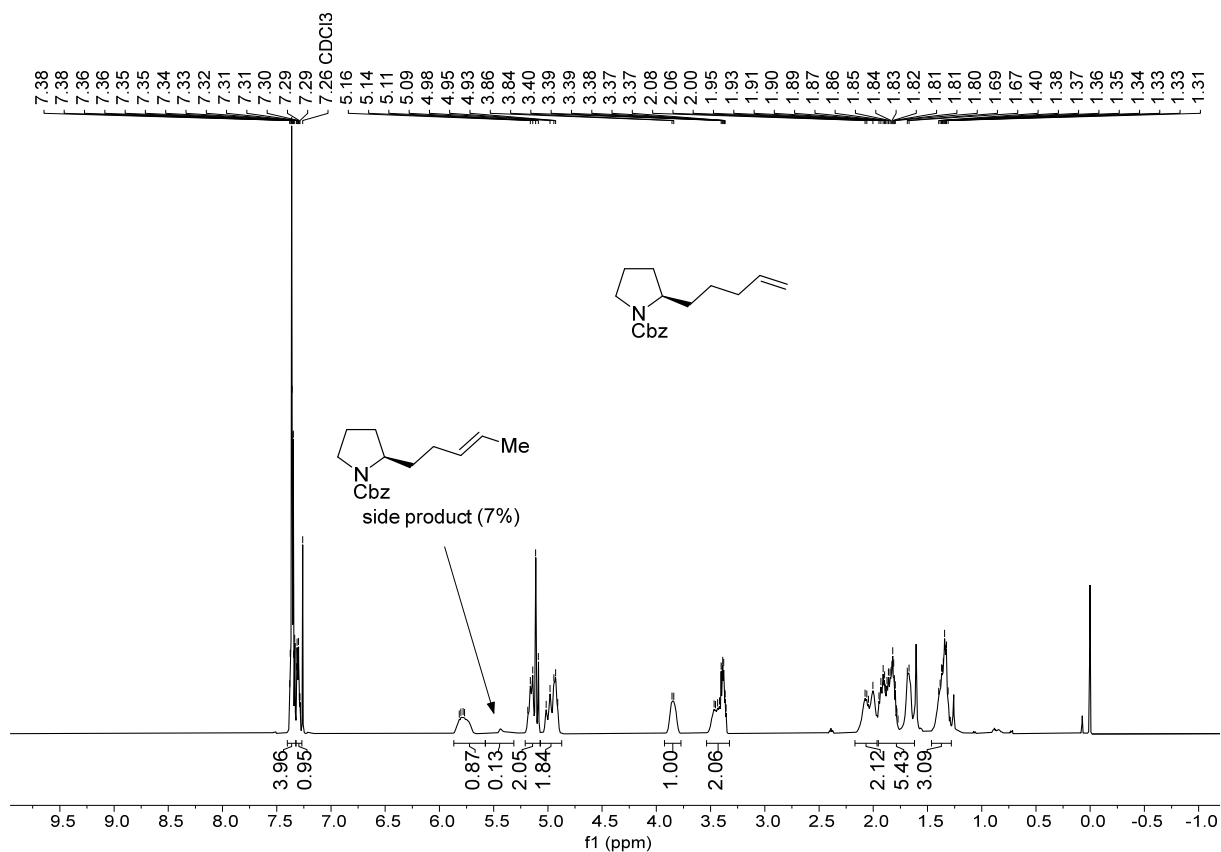
^{13}C NMR (125 MHz, CDCl_3) of **28**

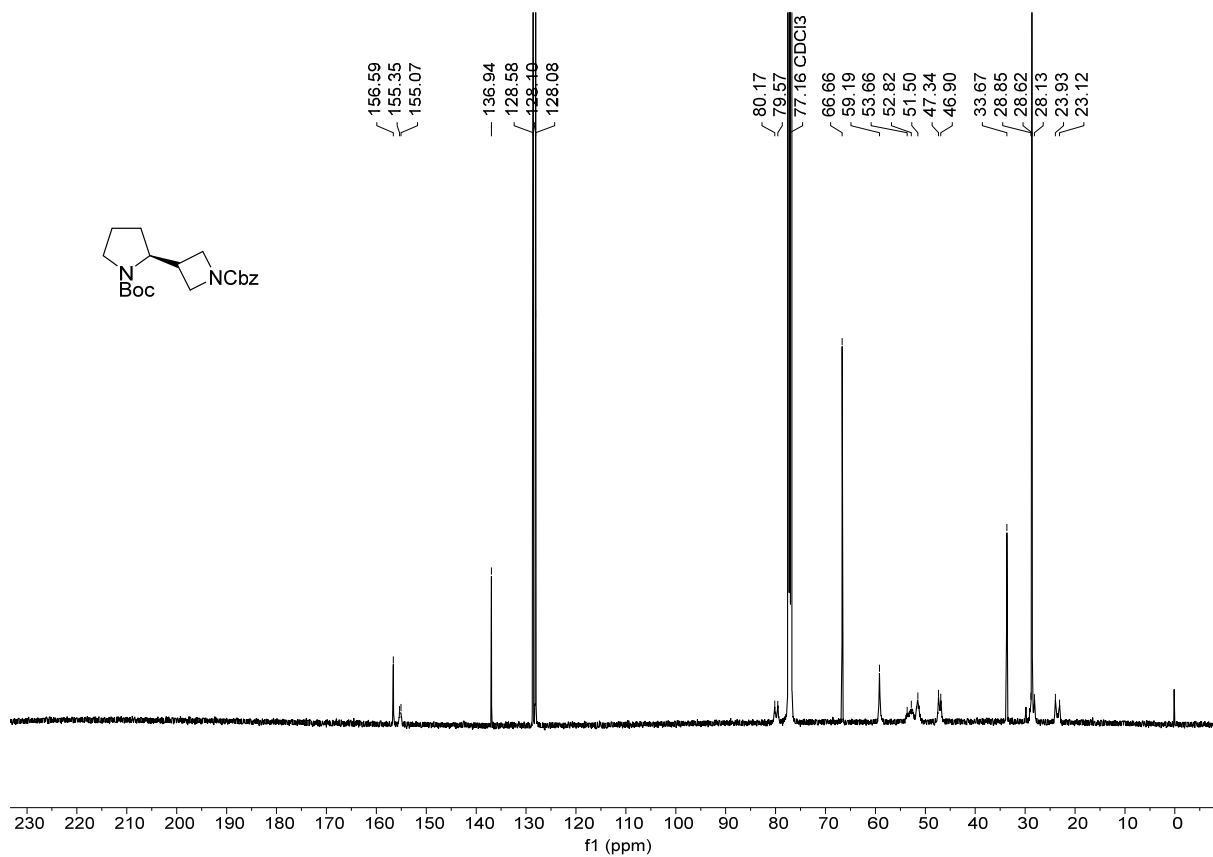
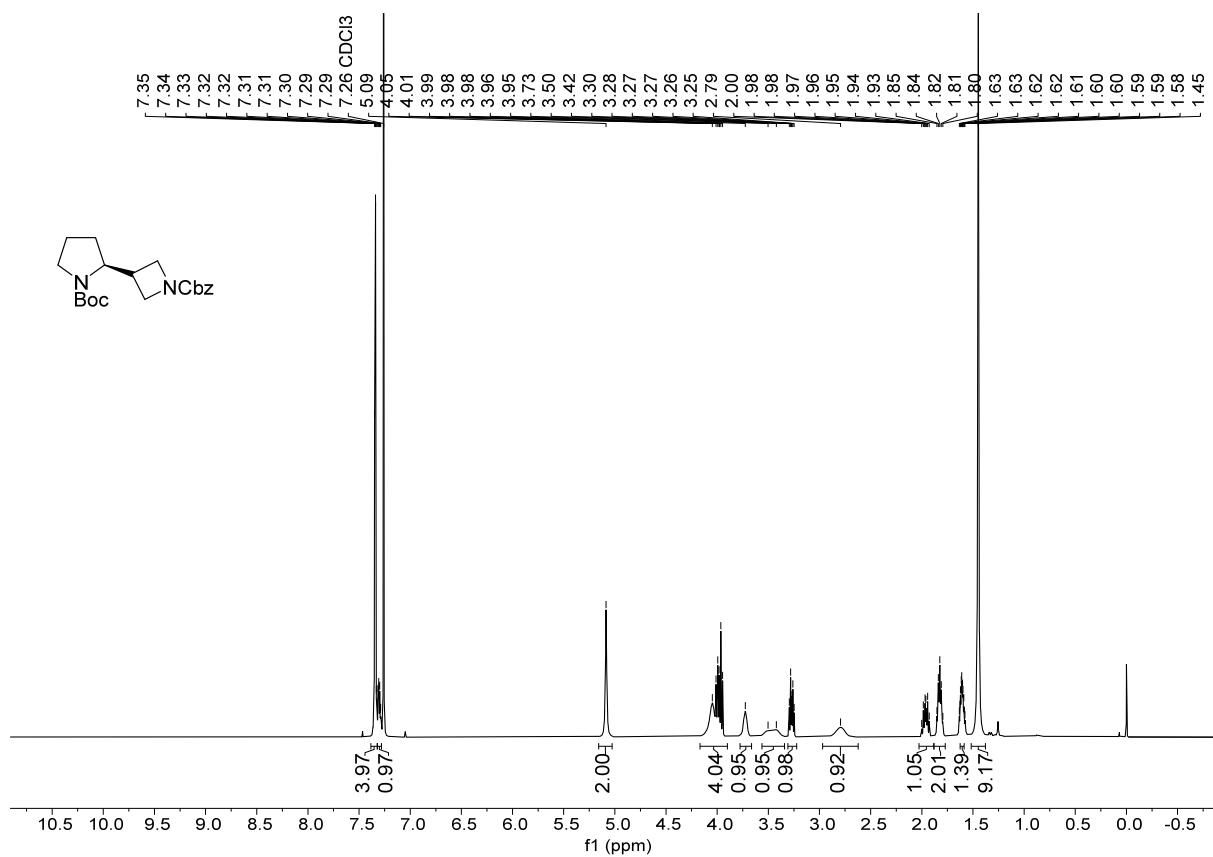


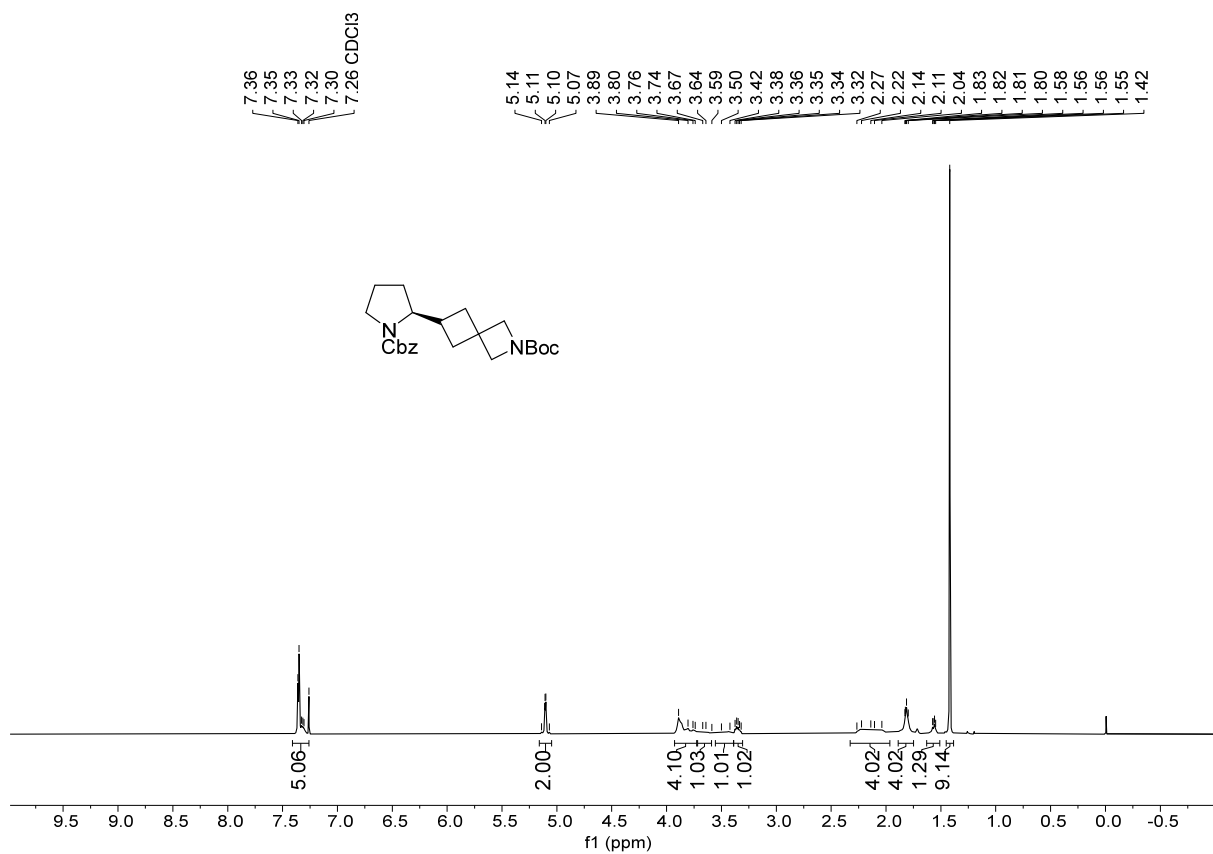
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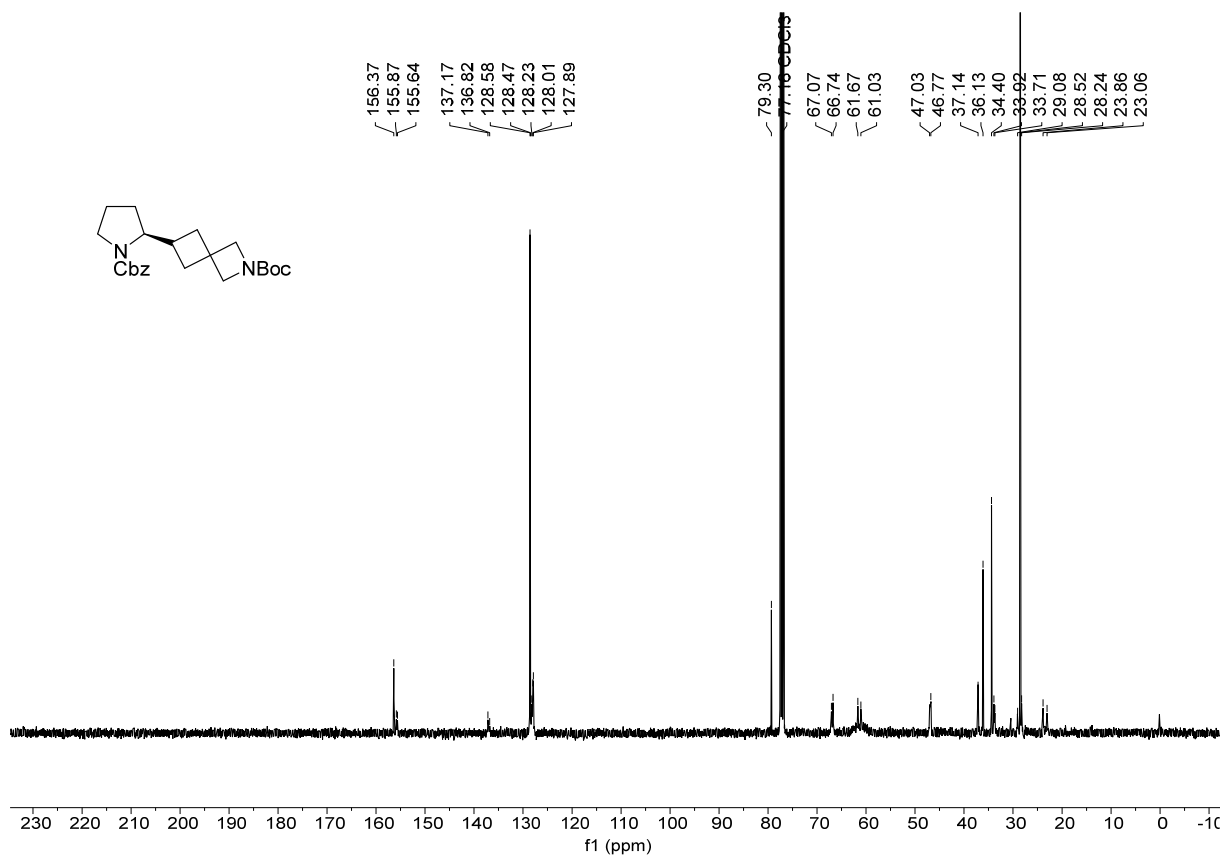
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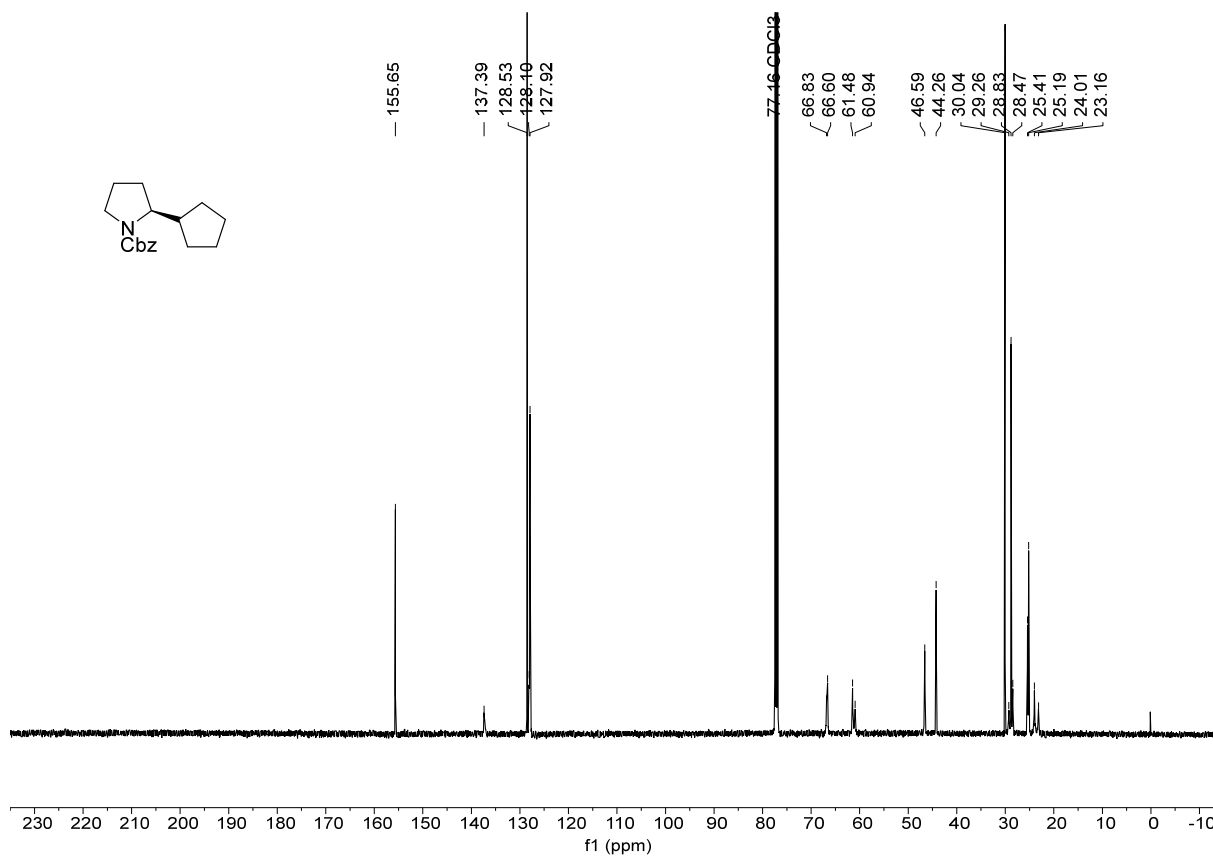
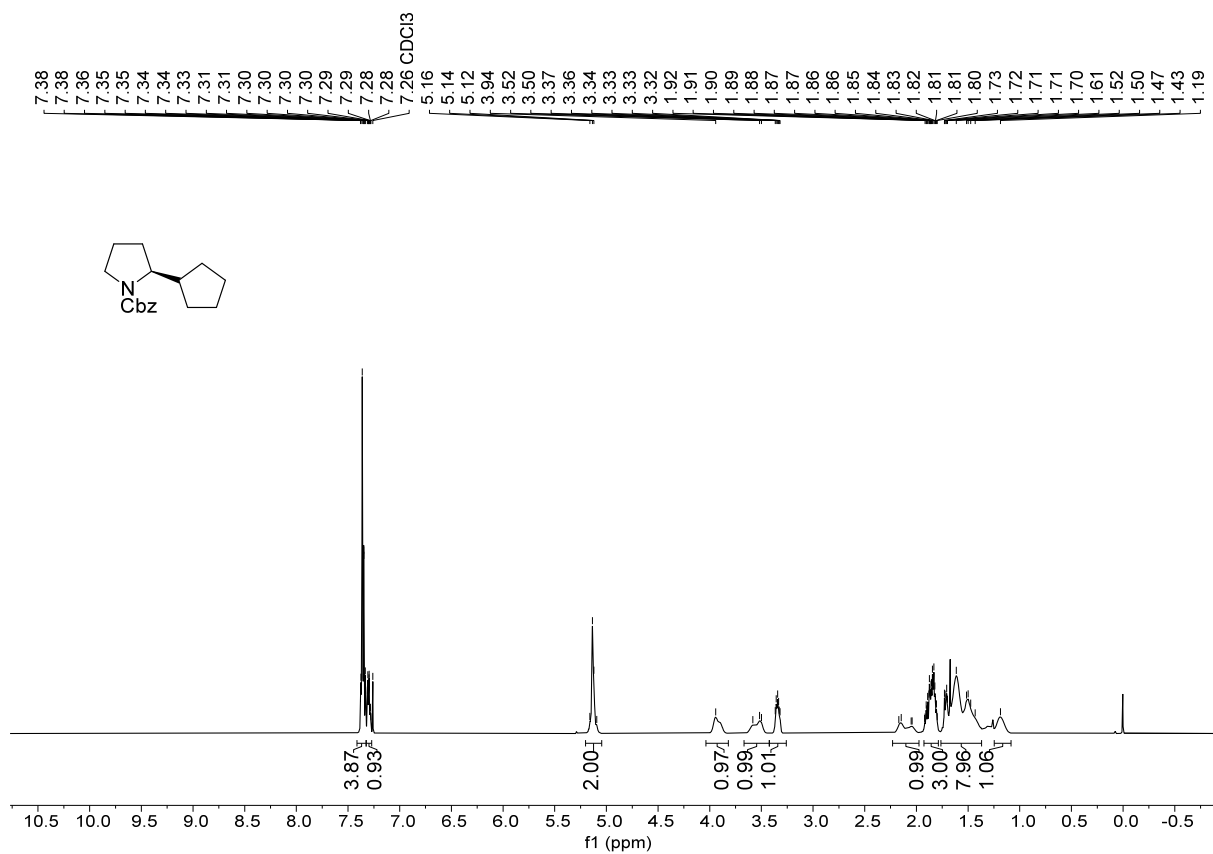


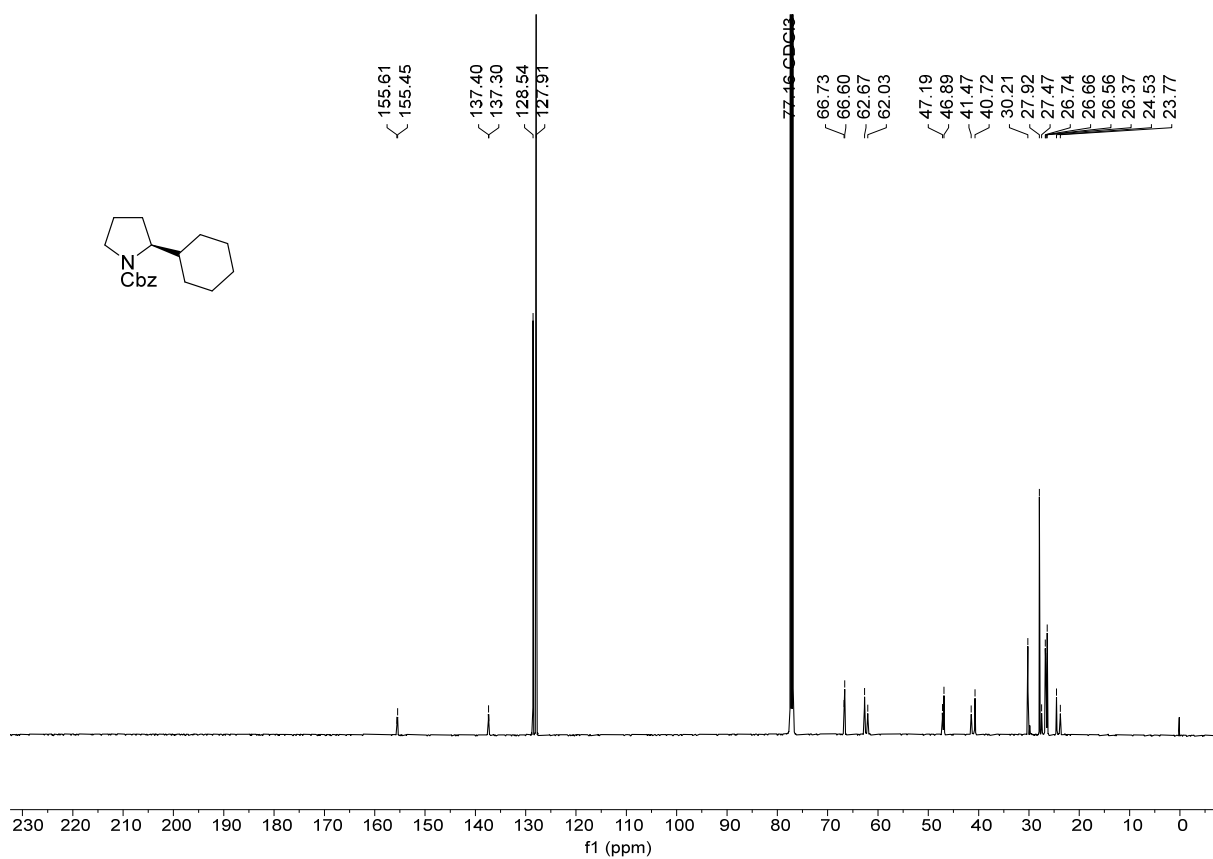
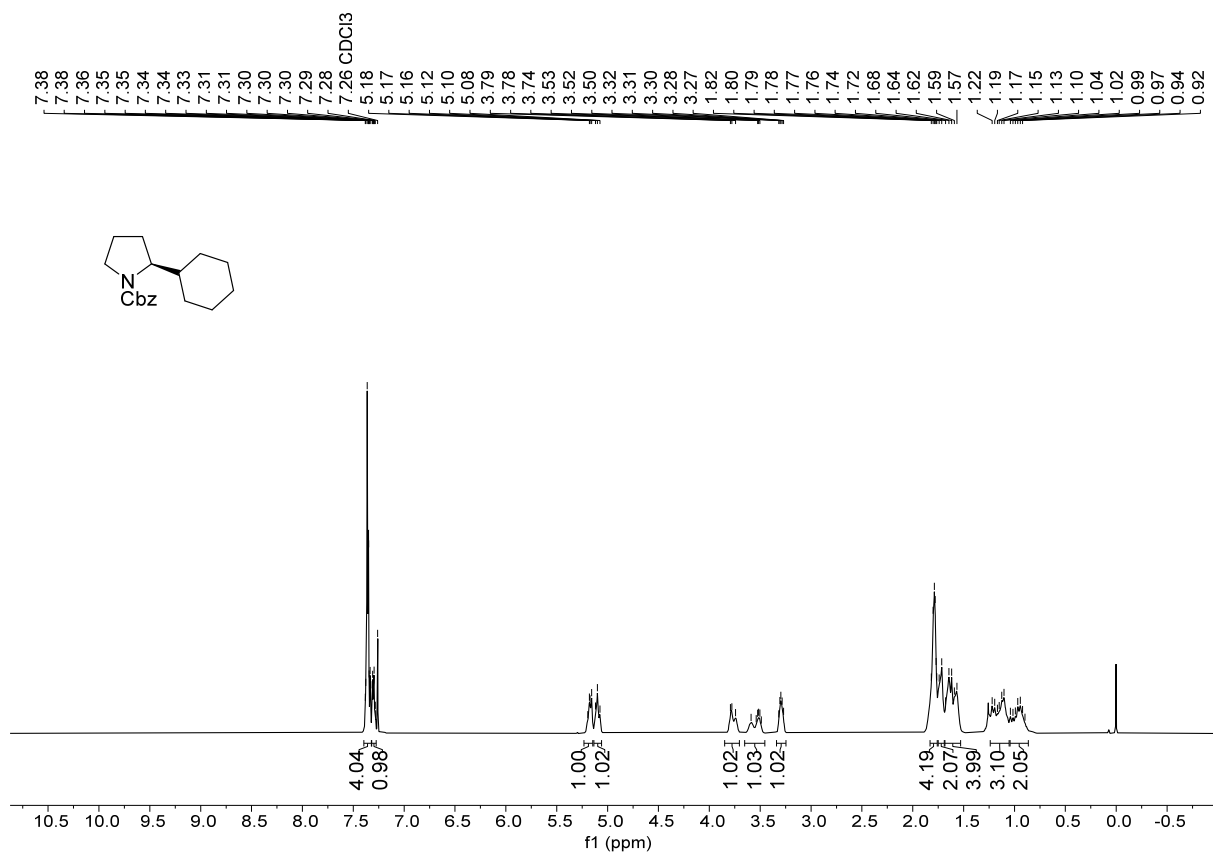


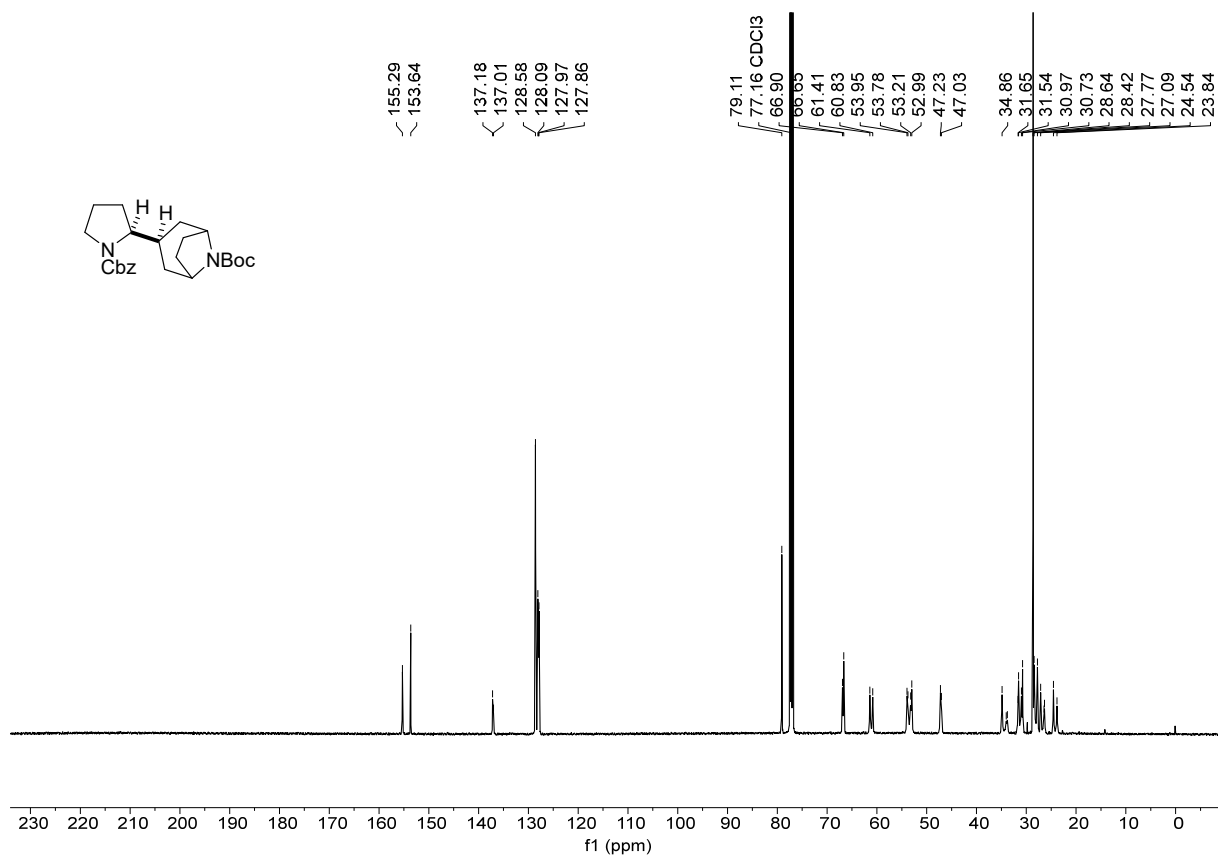
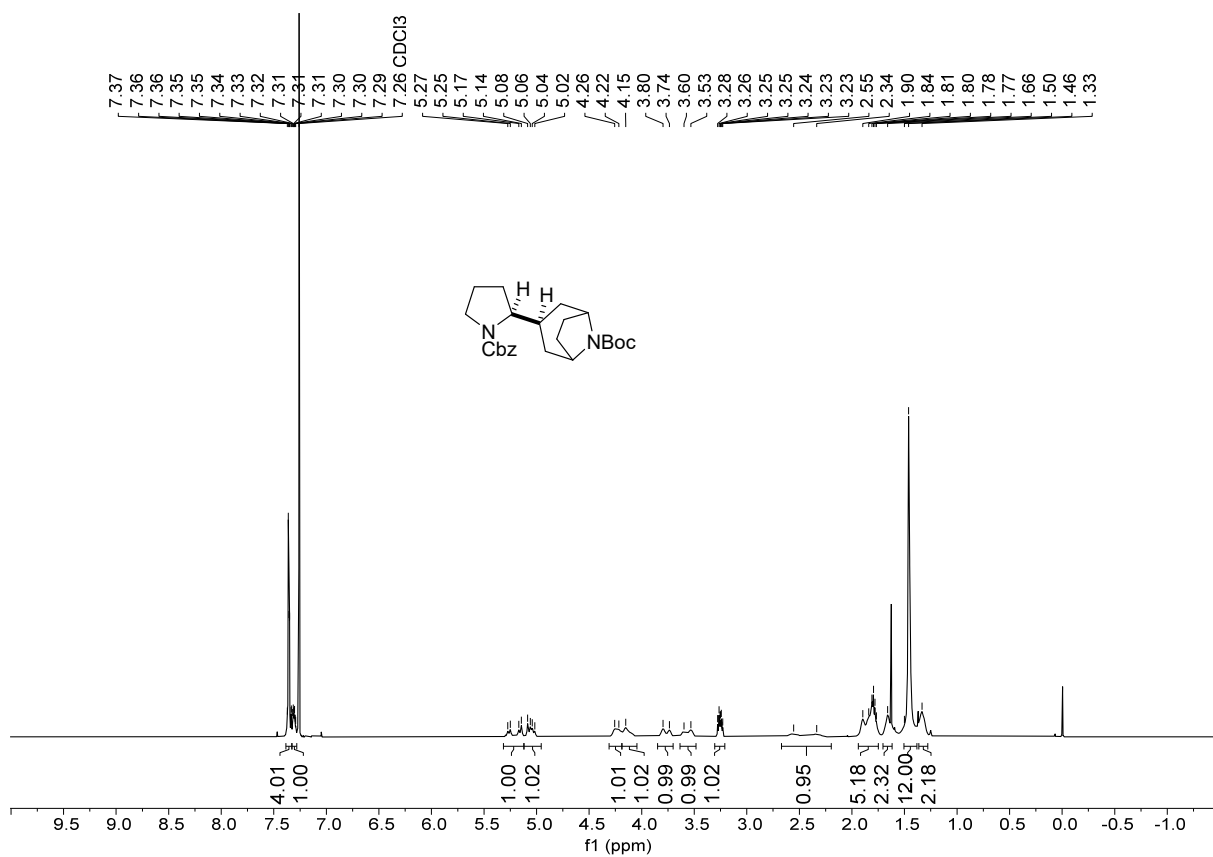
¹H NMR (500 MHz, CDCl₃) of **32**

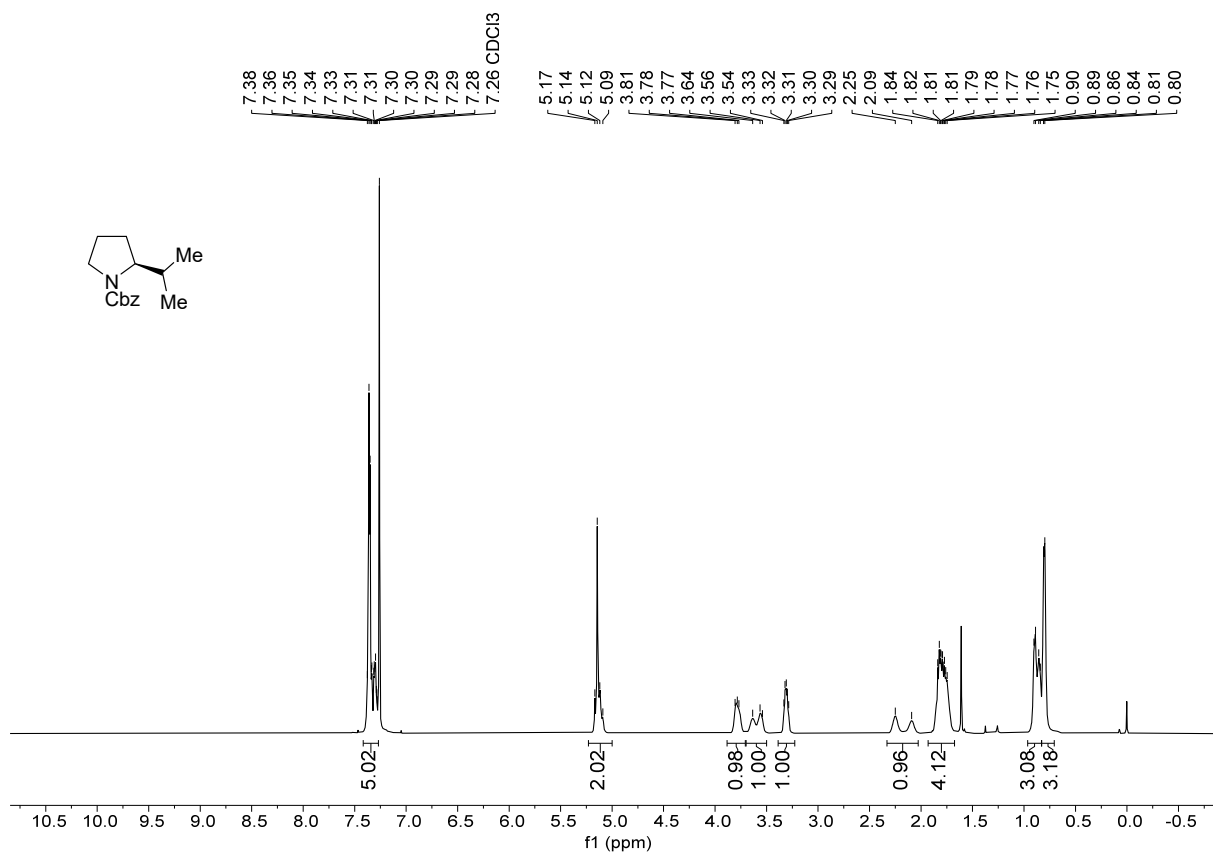


¹³C {¹H} NMR (125 MHz, CDCl₃) of **32**

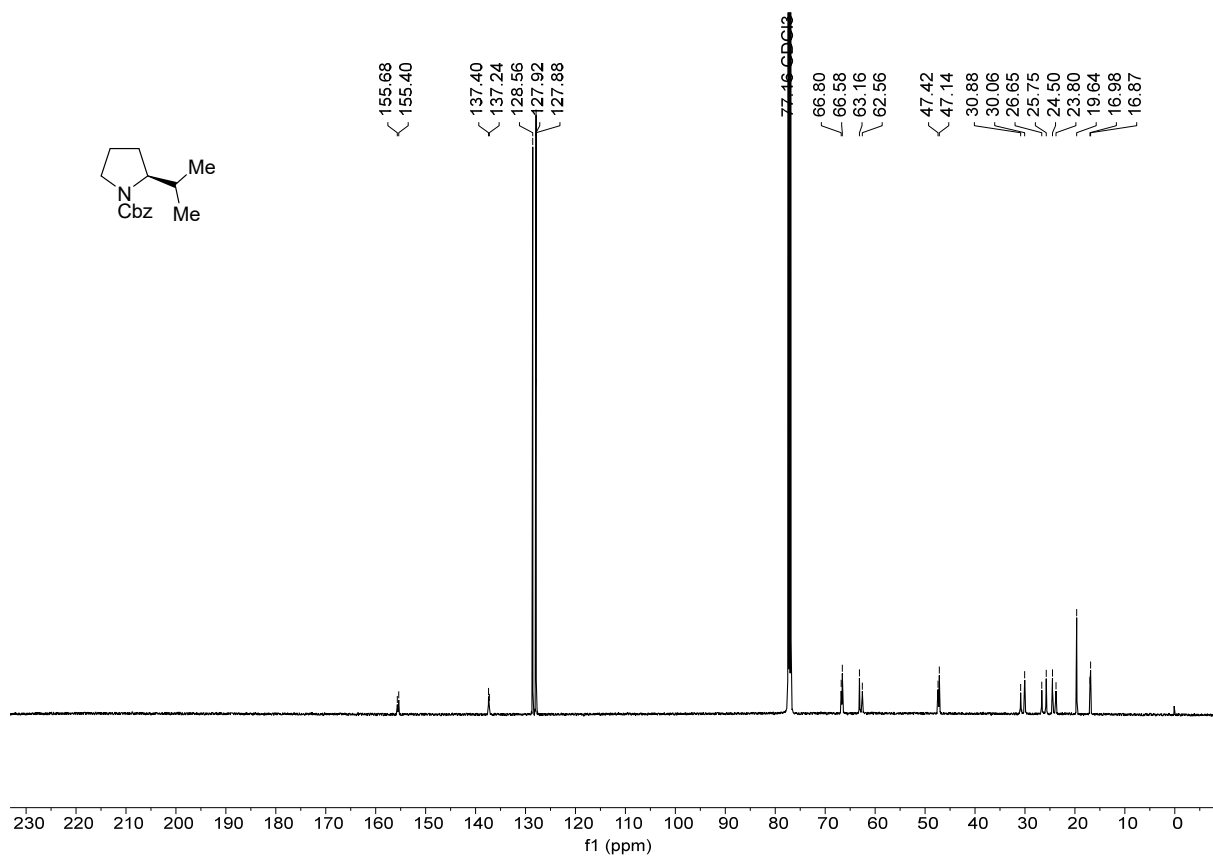




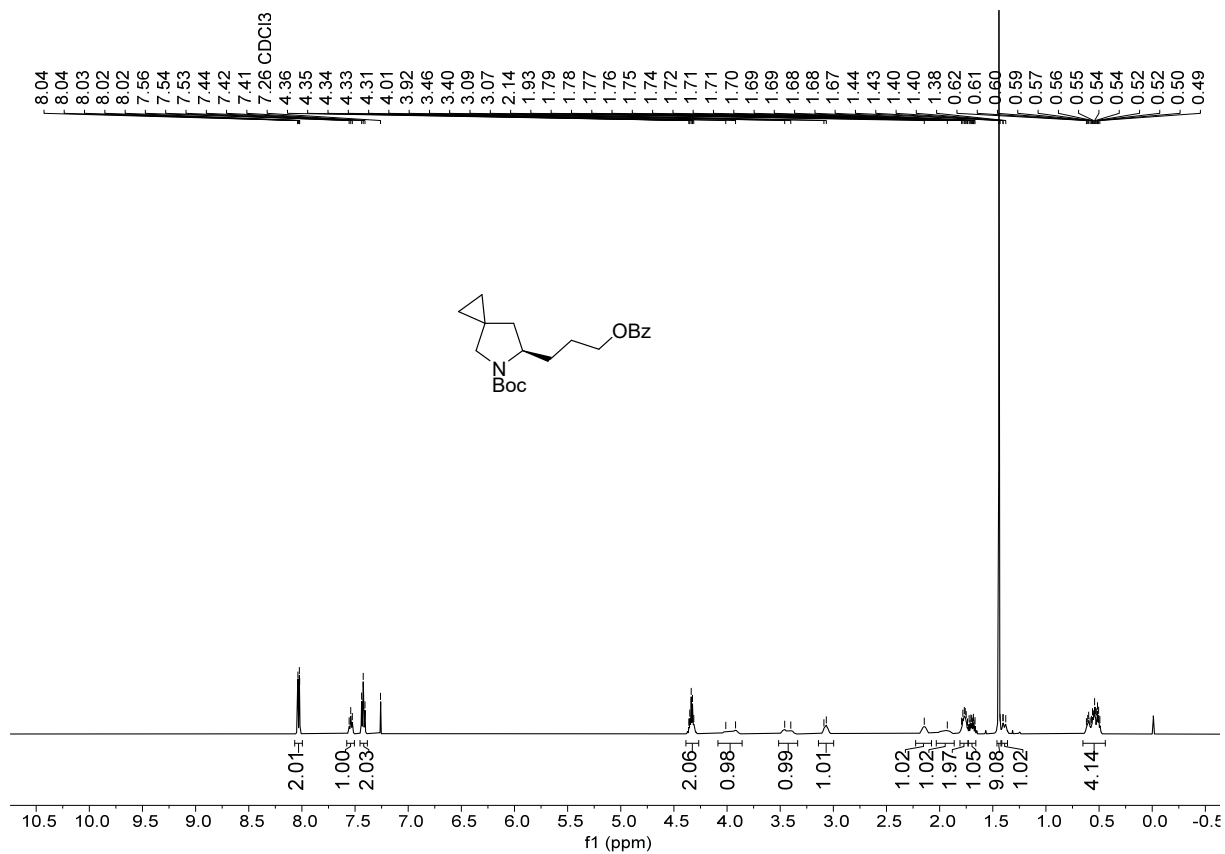




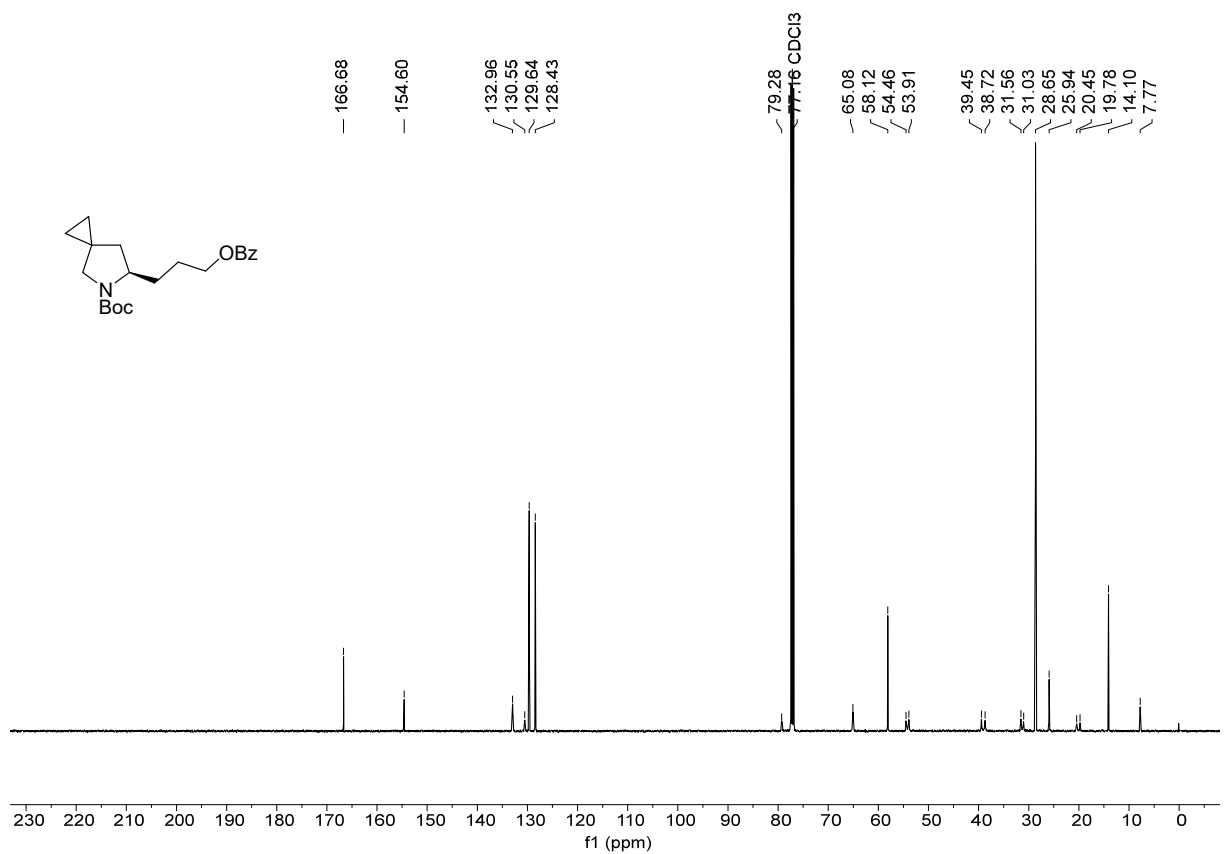
¹H NMR (500 MHz, CDCl₃) of **36**



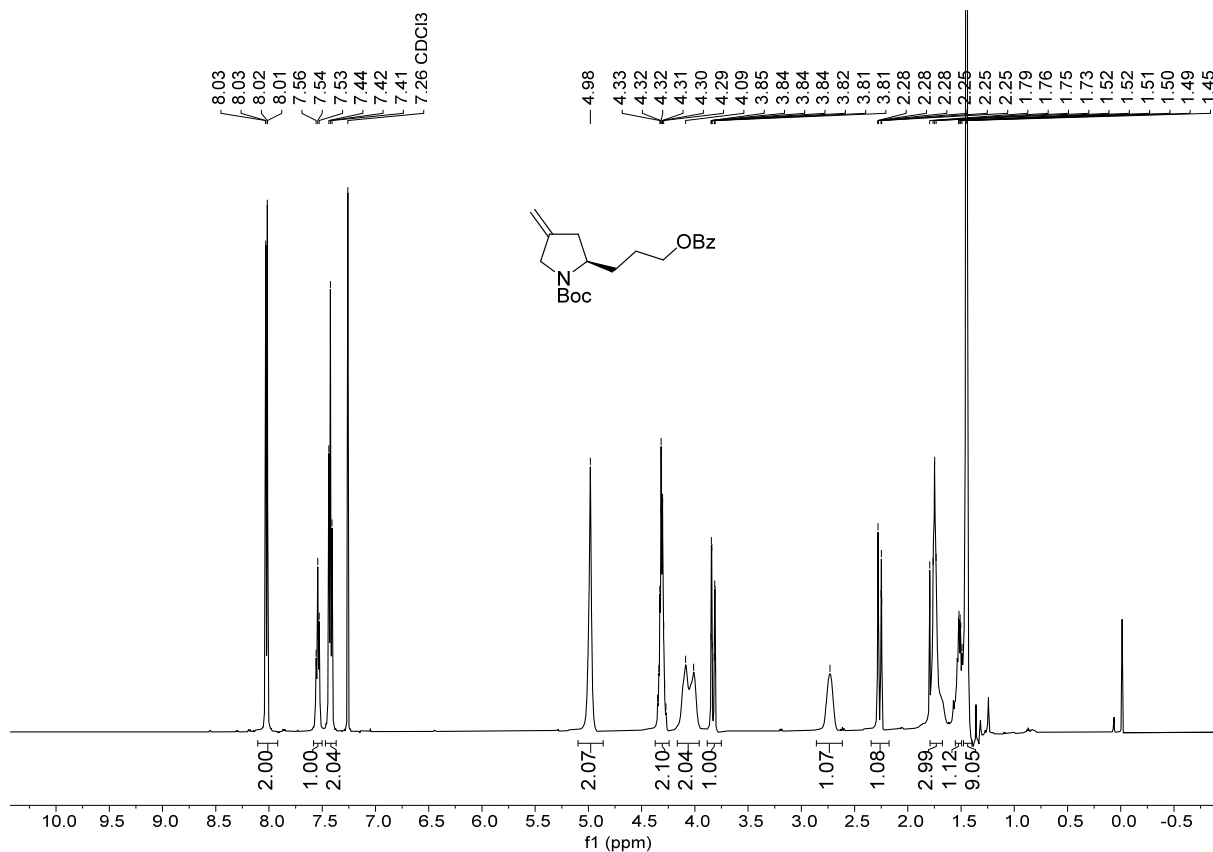
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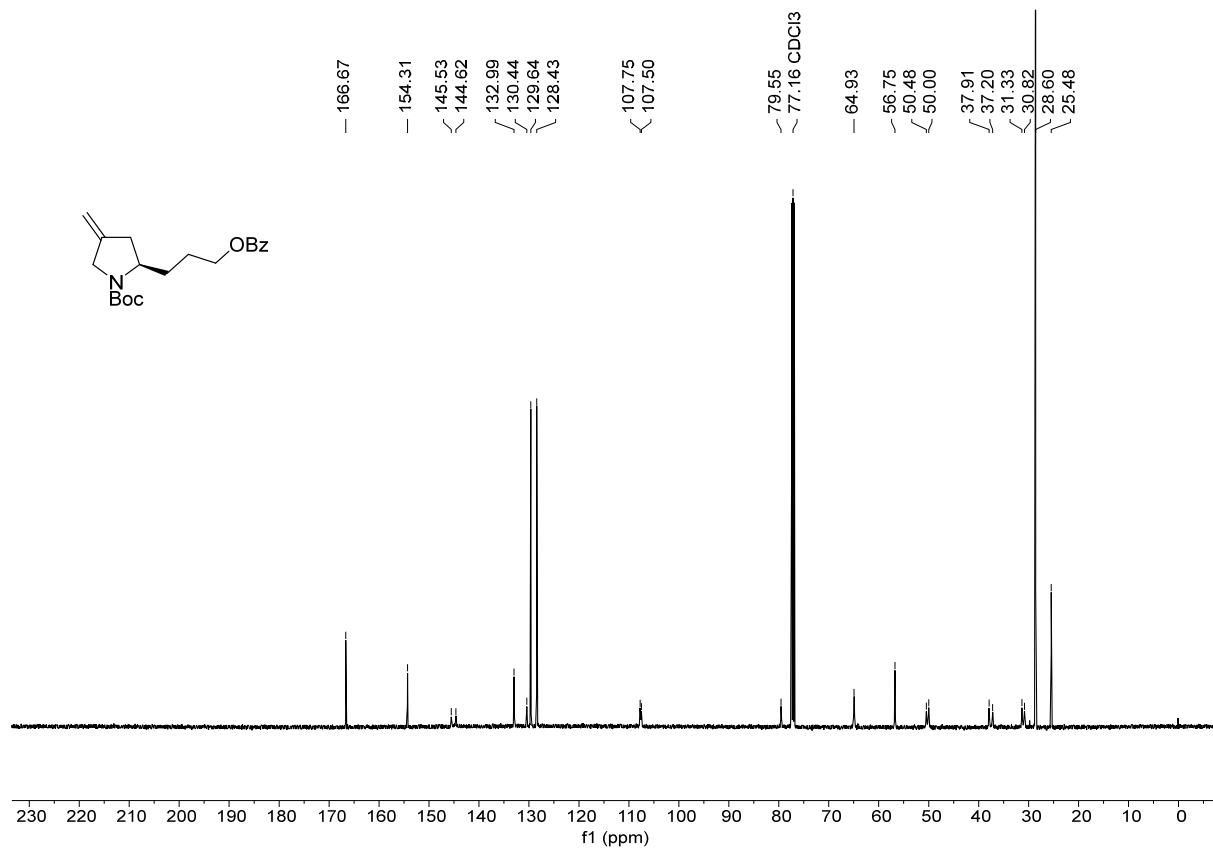
¹H NMR (500 MHz, CDCl₃) of 37



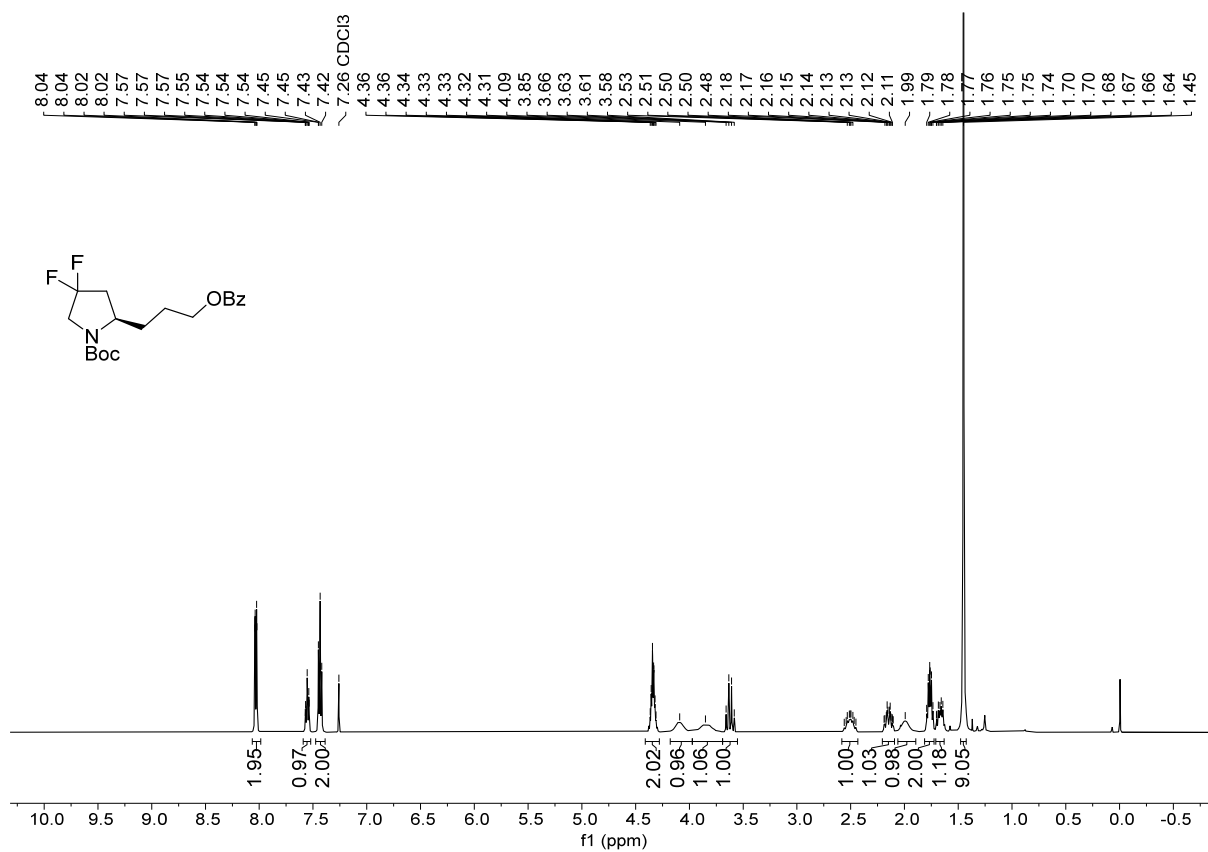
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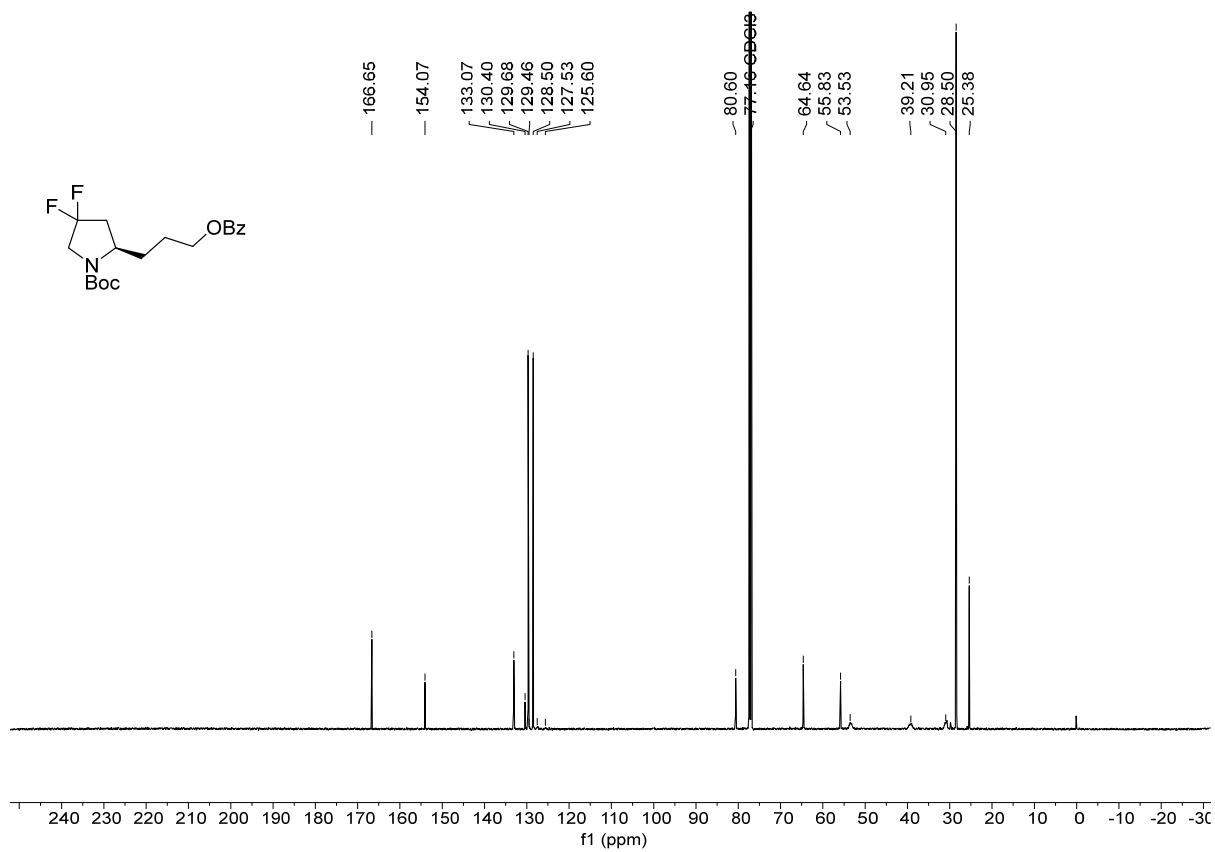
¹H NMR (500 MHz, CDCl₃) of **38**



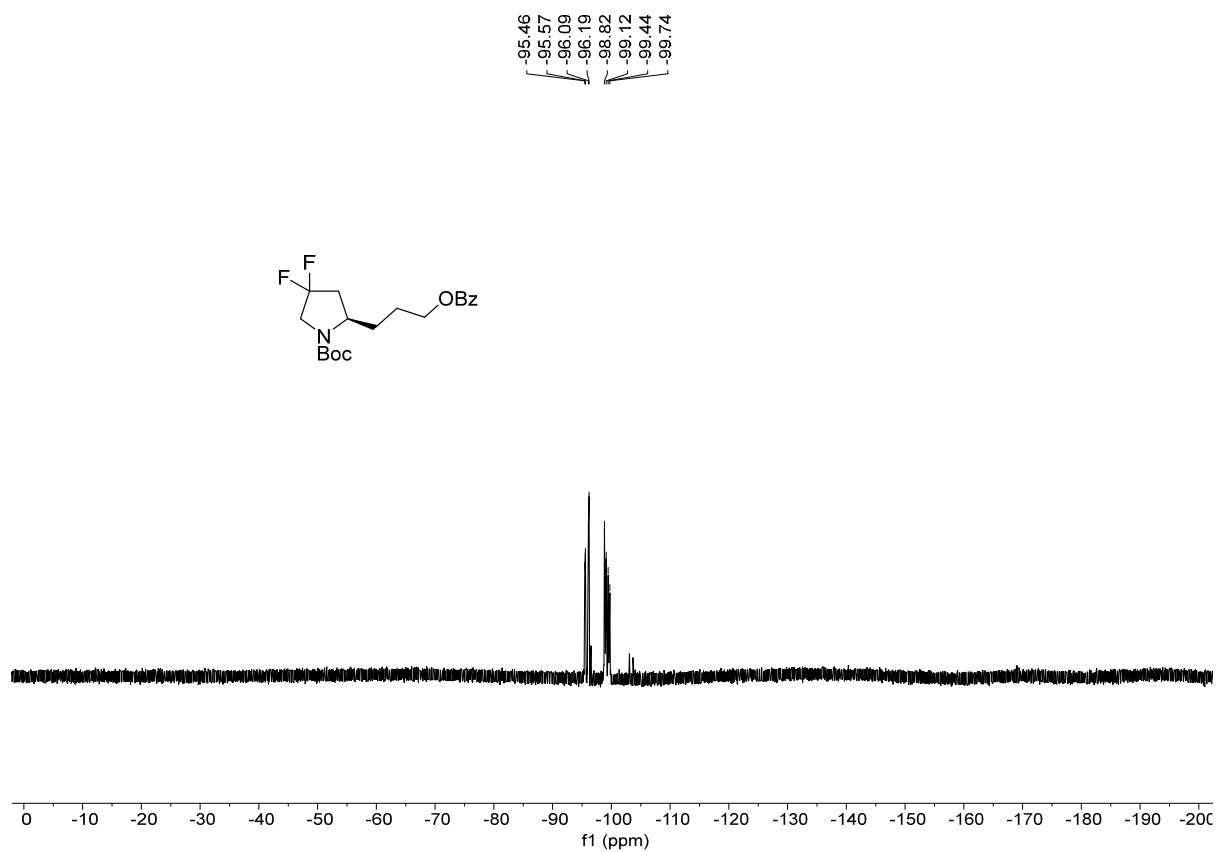
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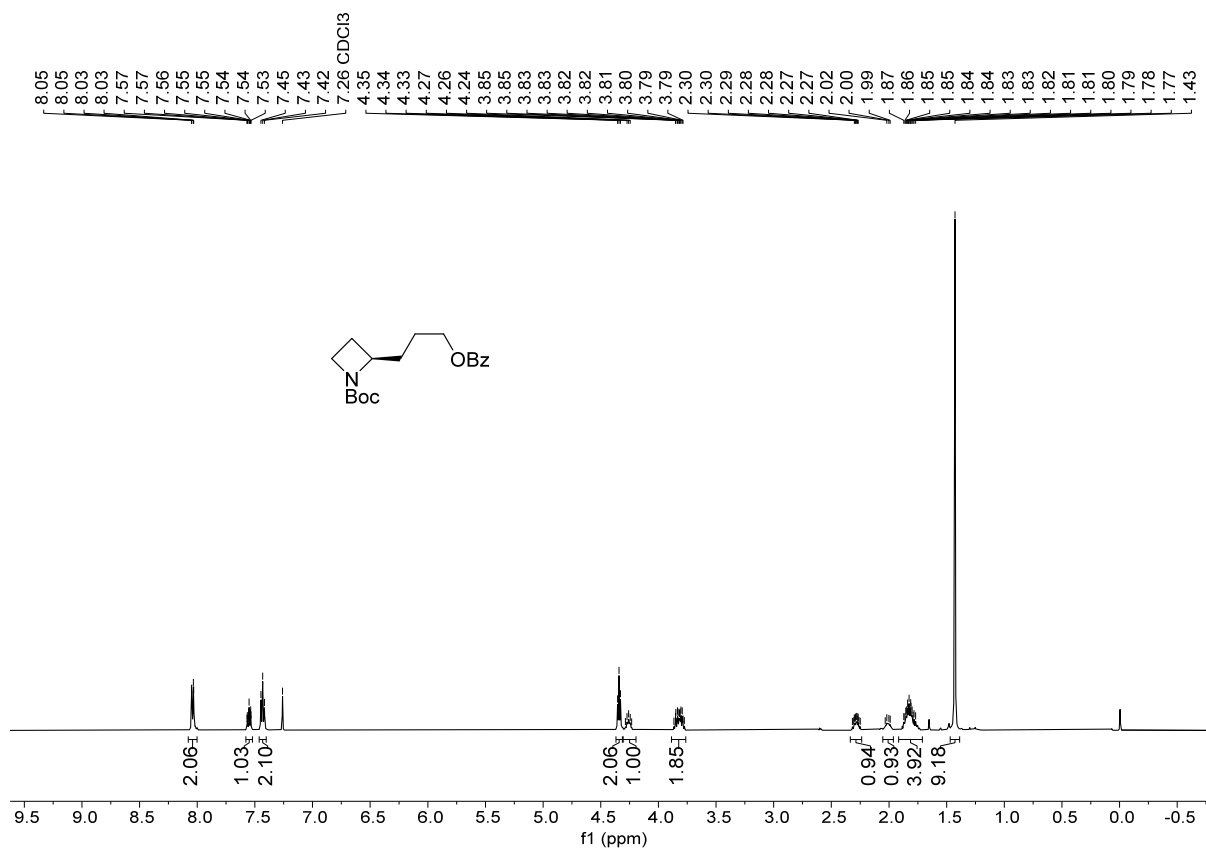
¹H NMR (500 MHz, CDCl₃) of **39**



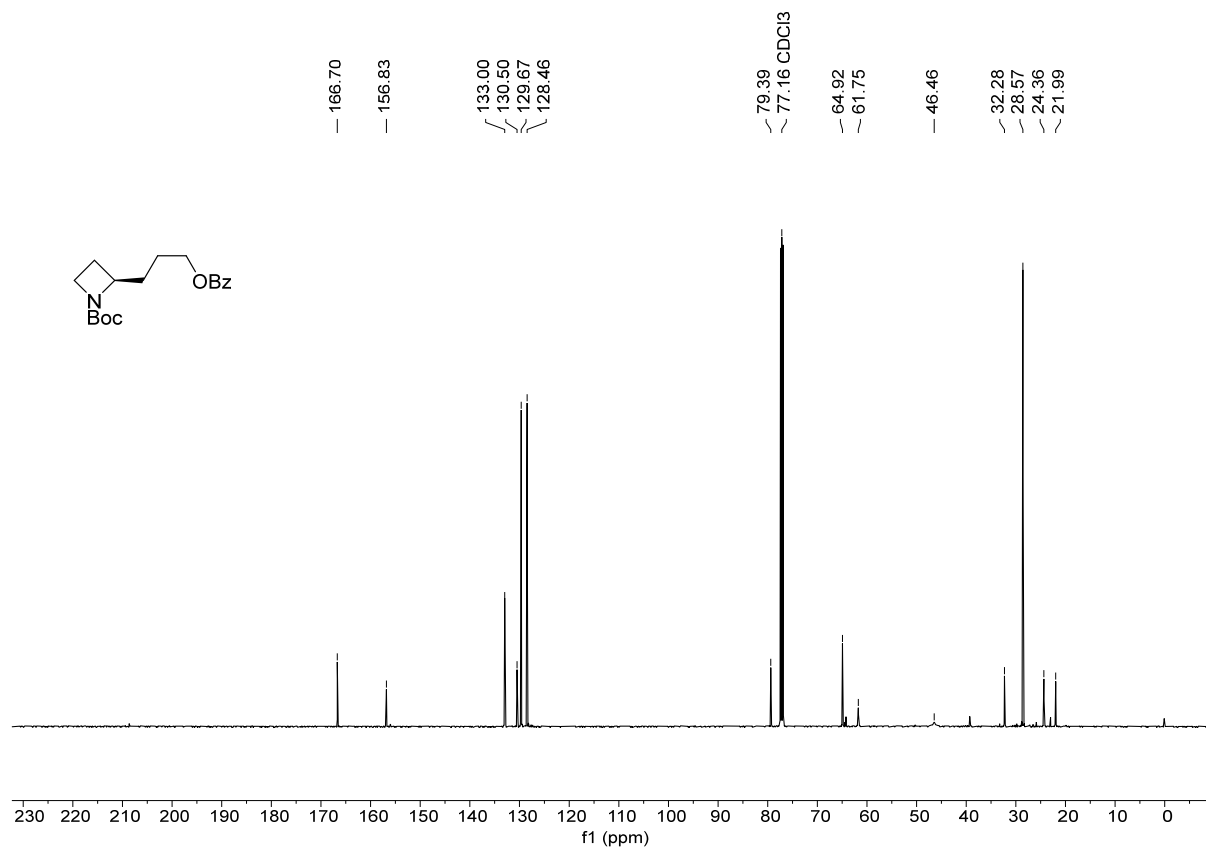
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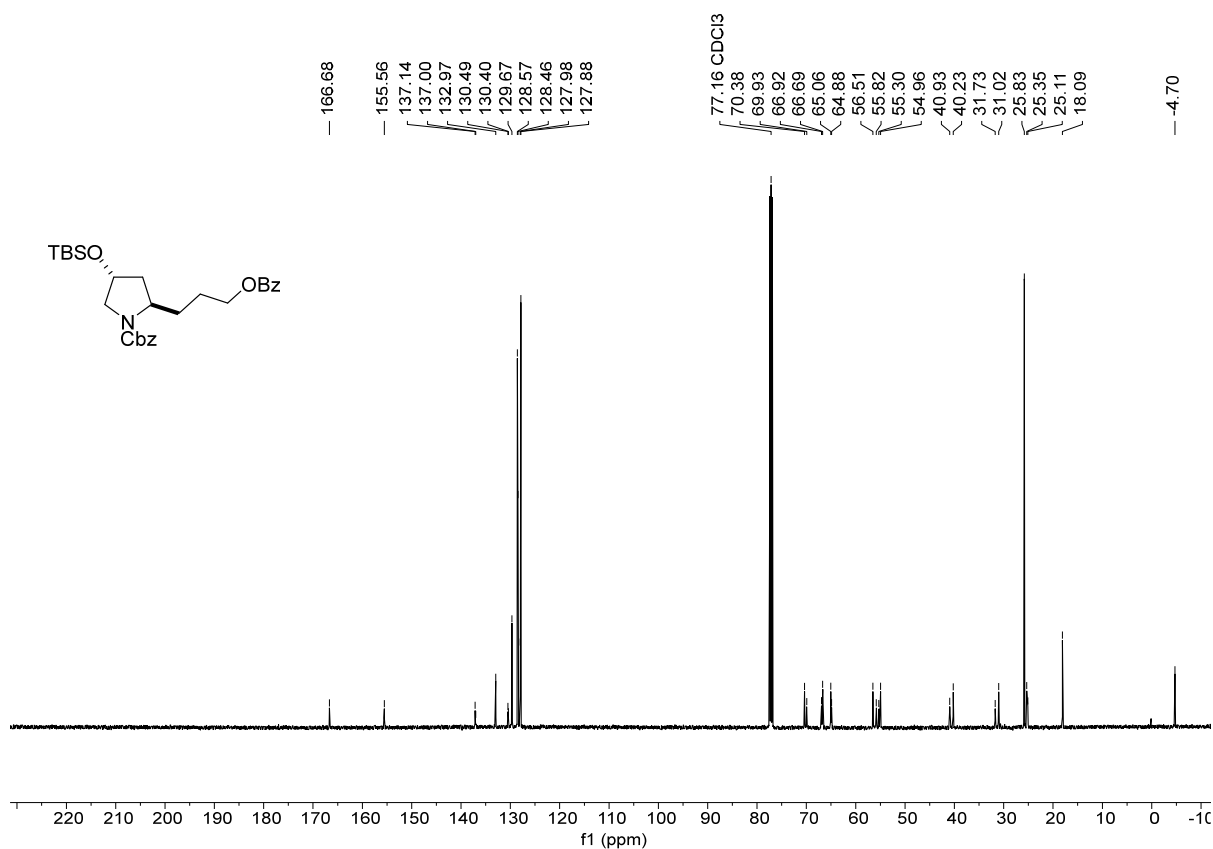
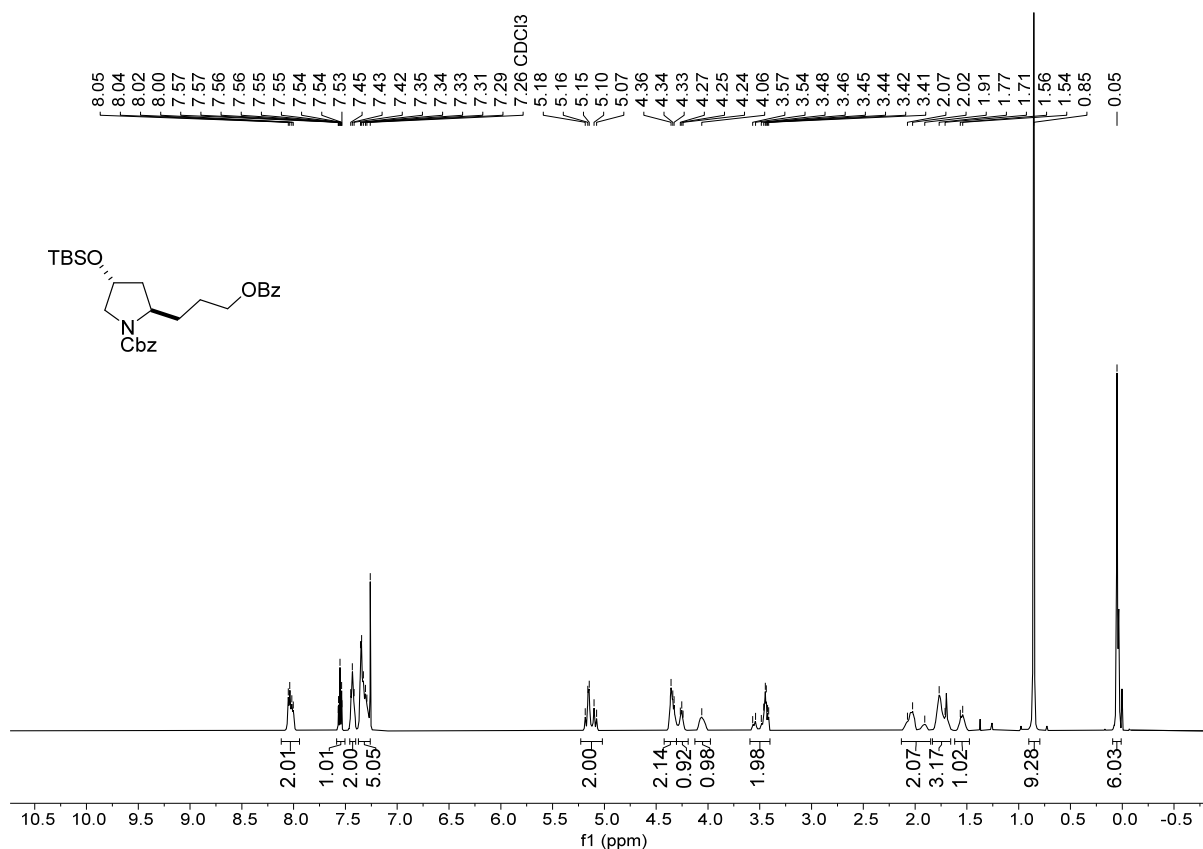
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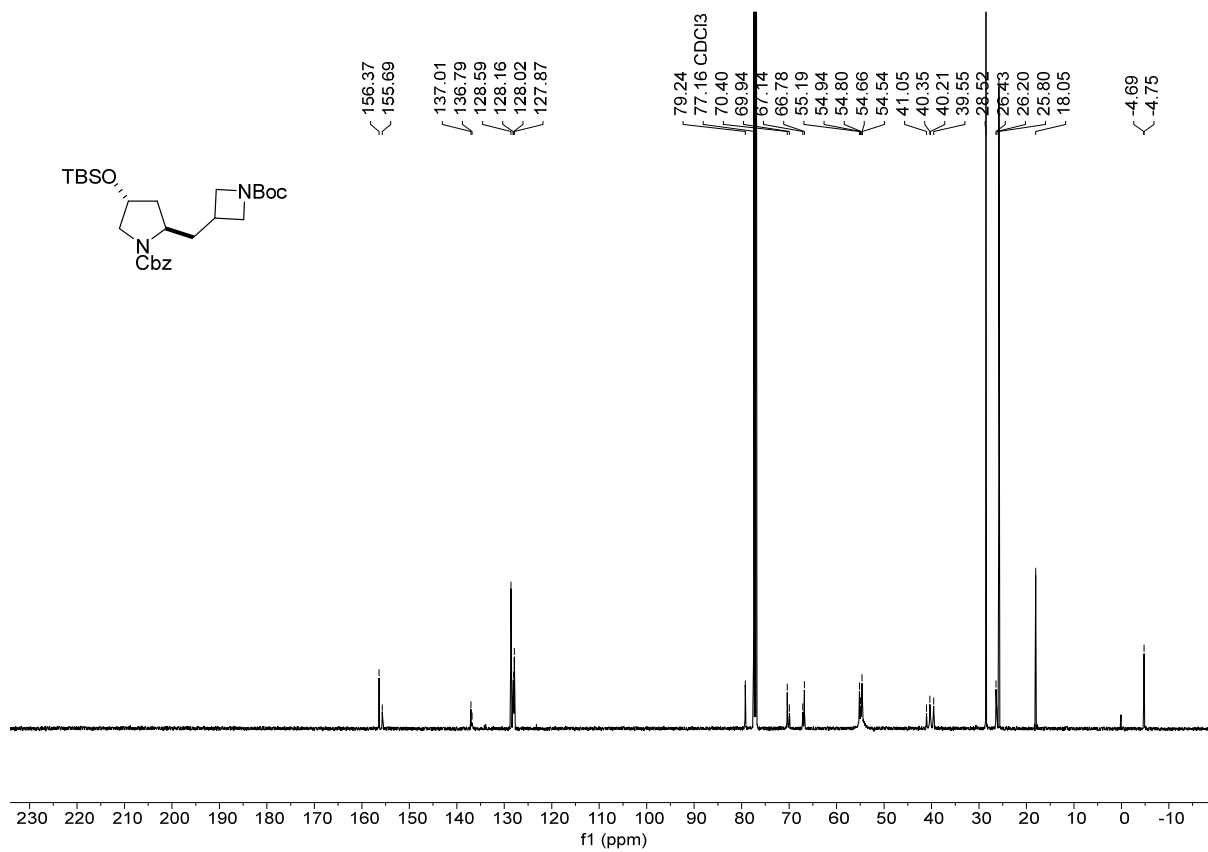
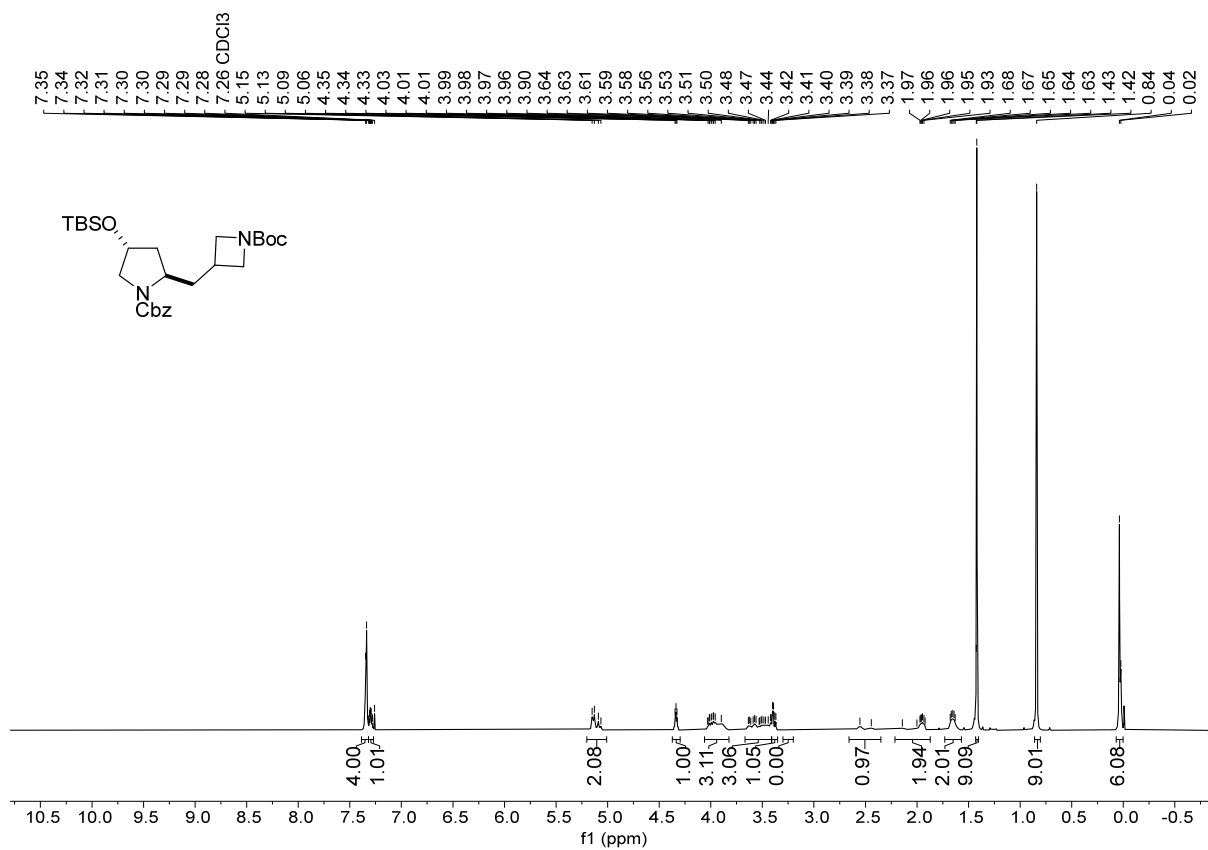


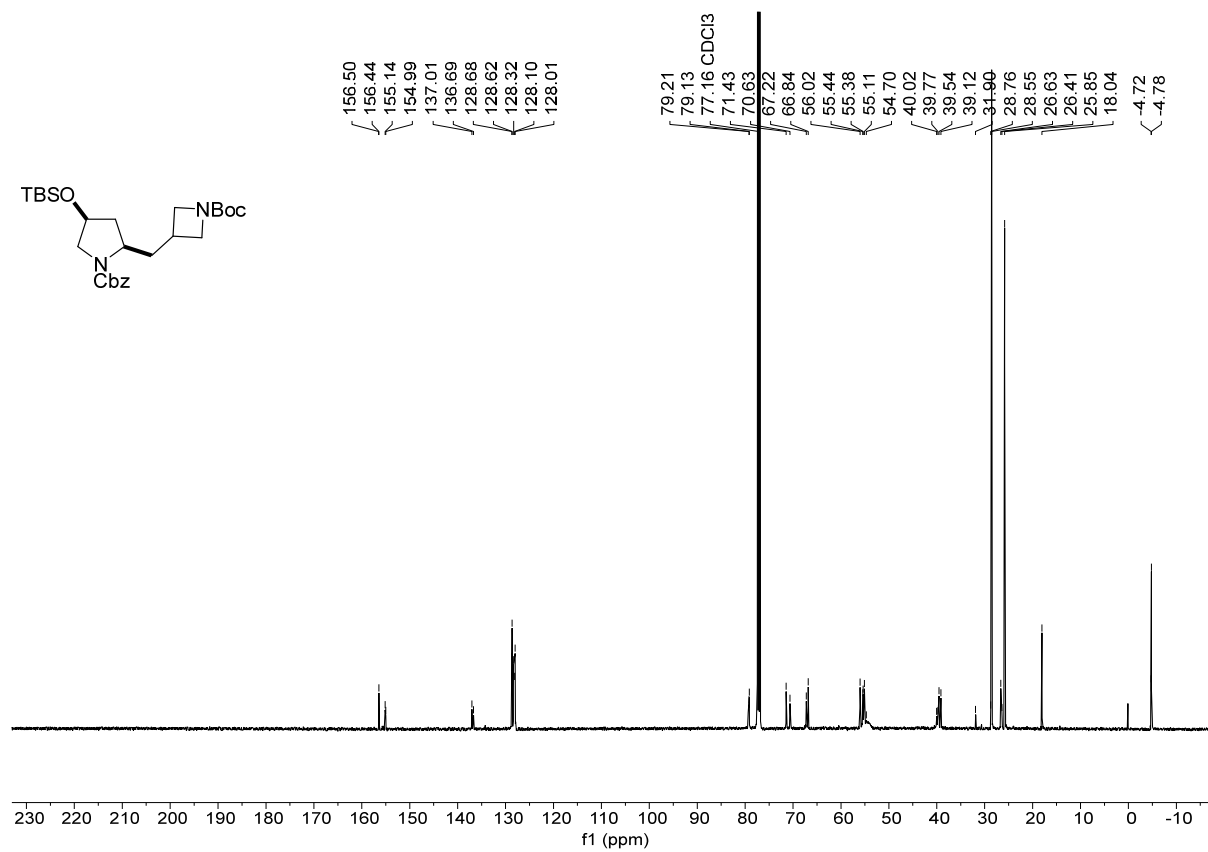
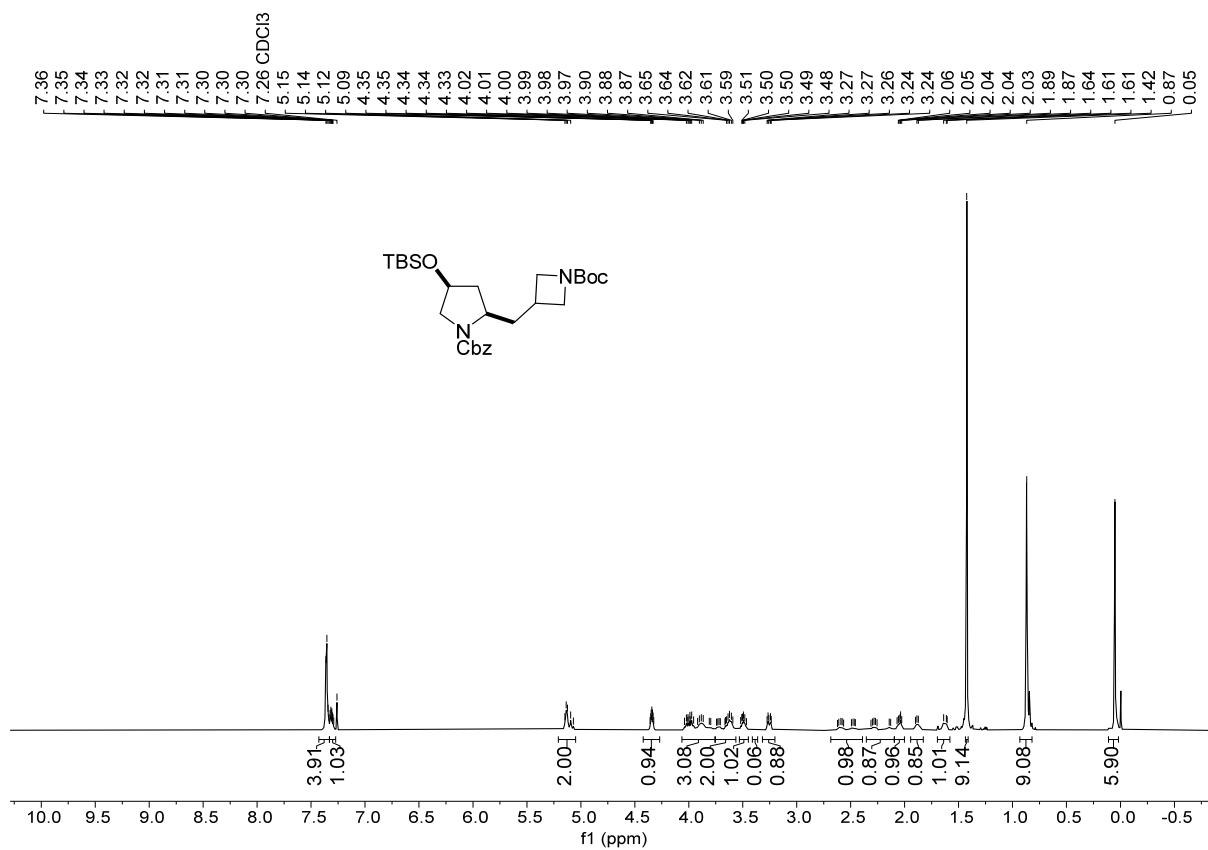
¹H NMR (500 MHz, CDCl₃) of **40**

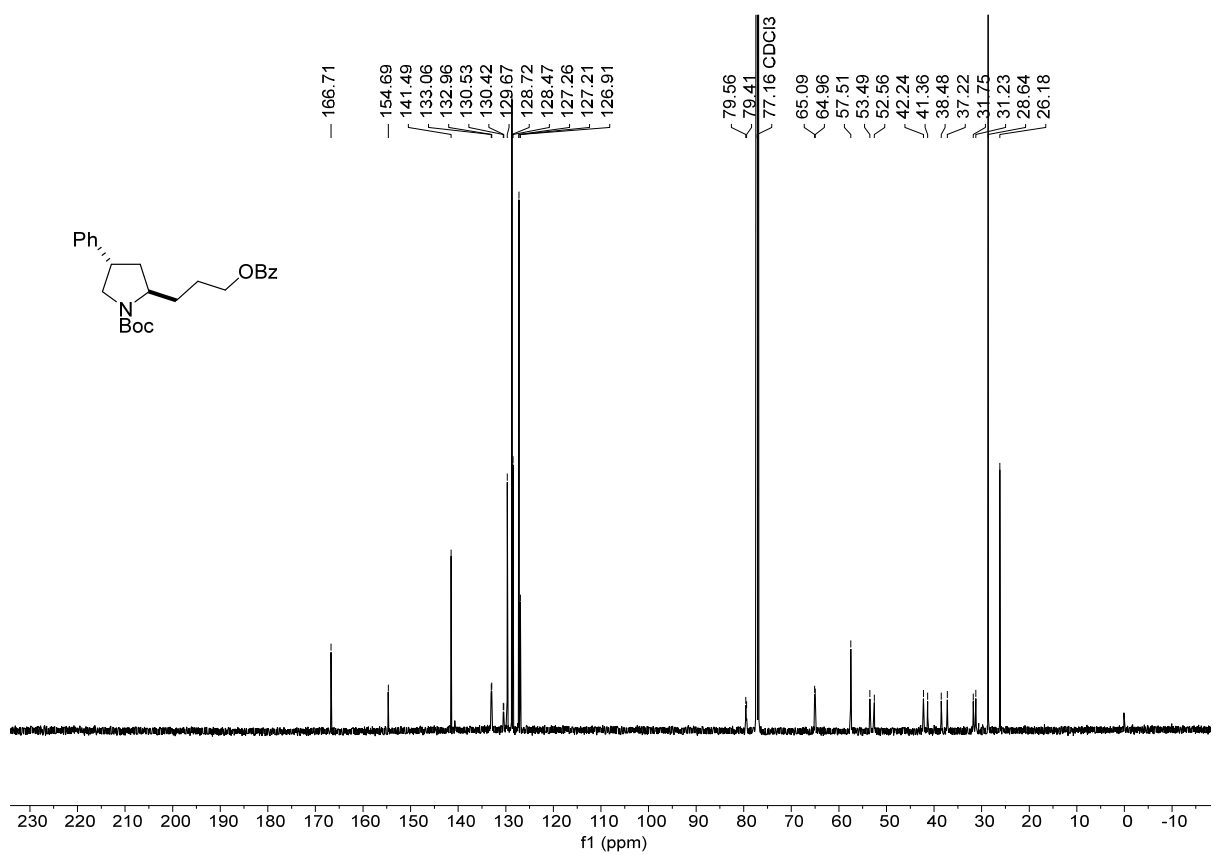
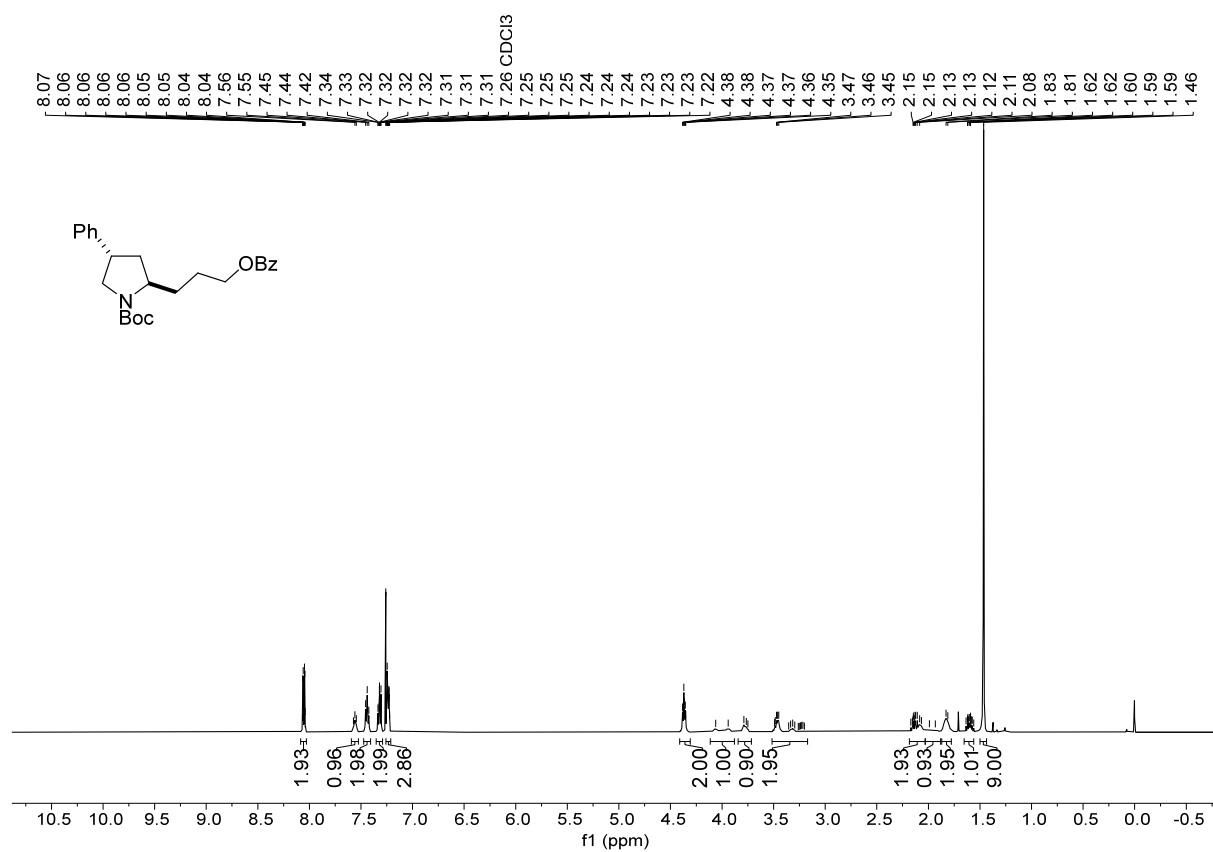


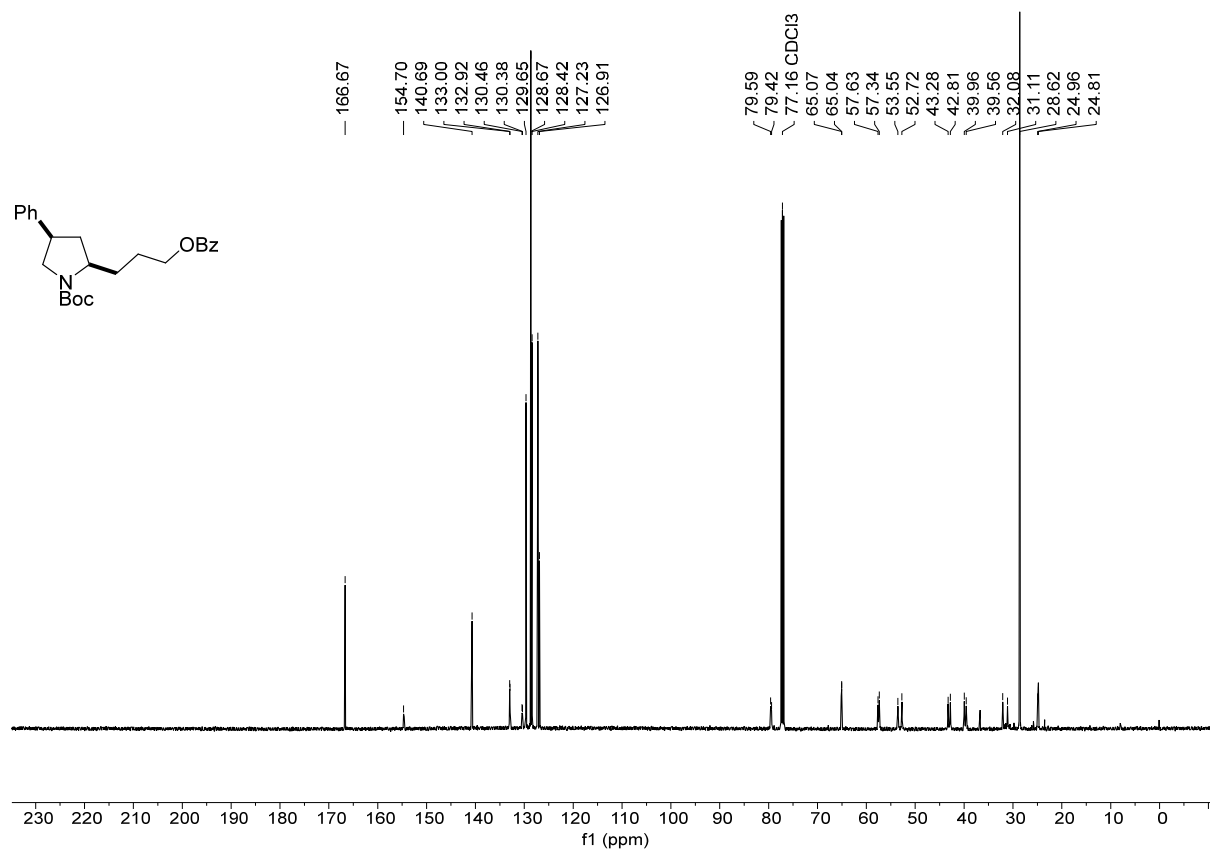
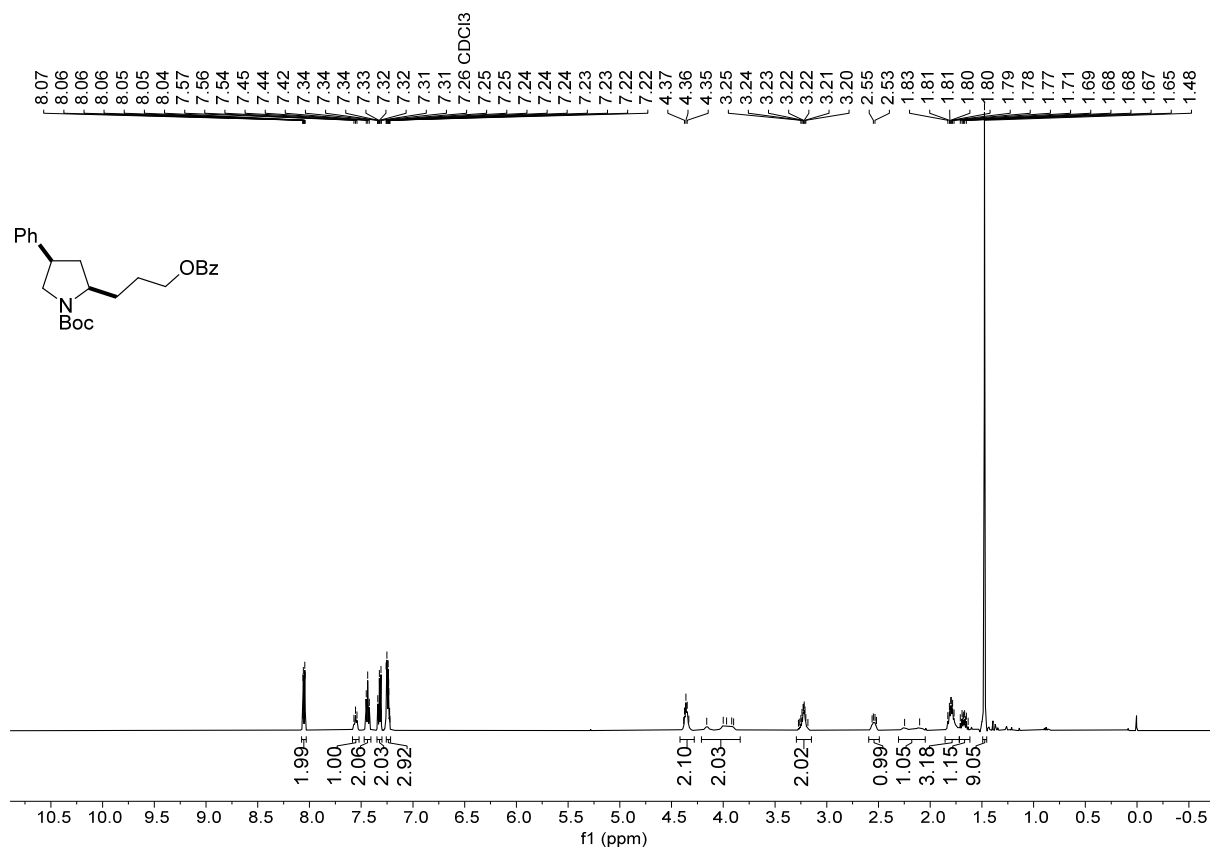
¹³C{¹H} NMR (125 MHz, CDCl₃) of **40**

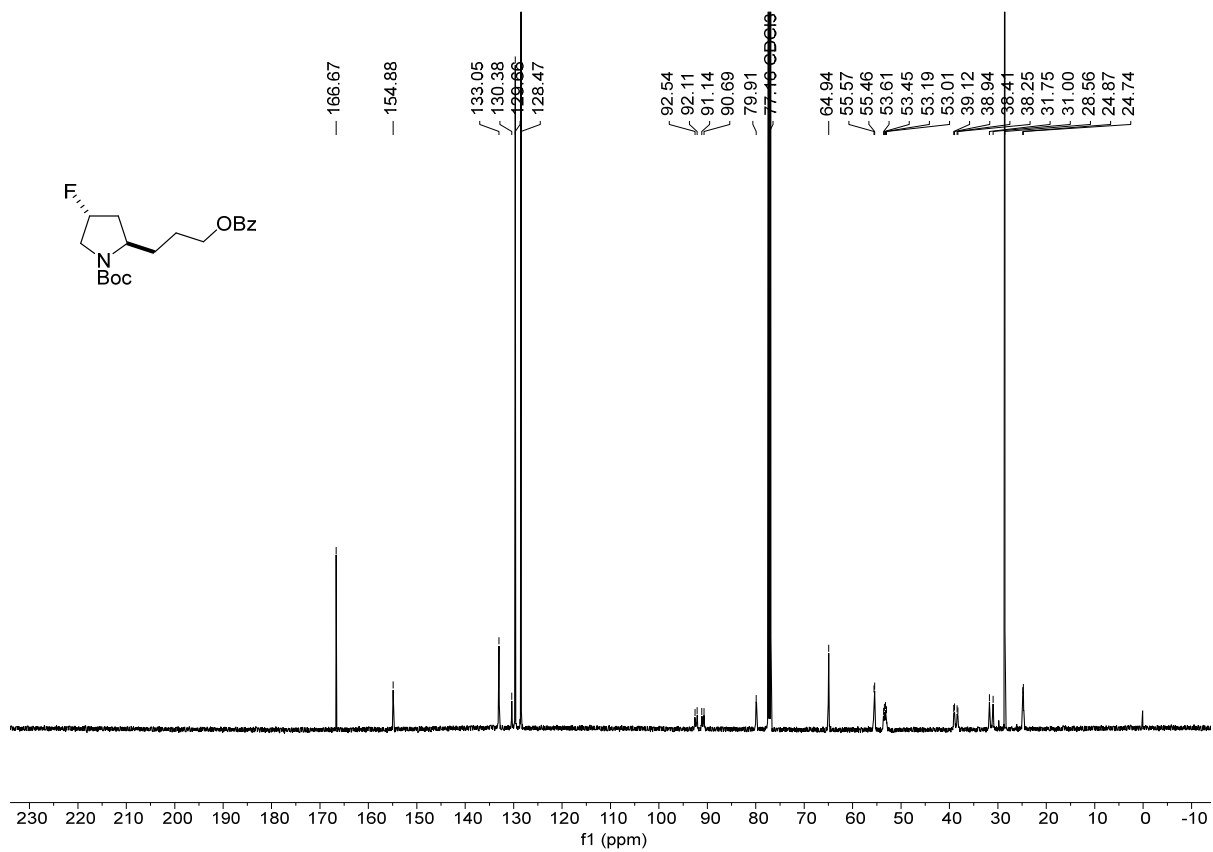
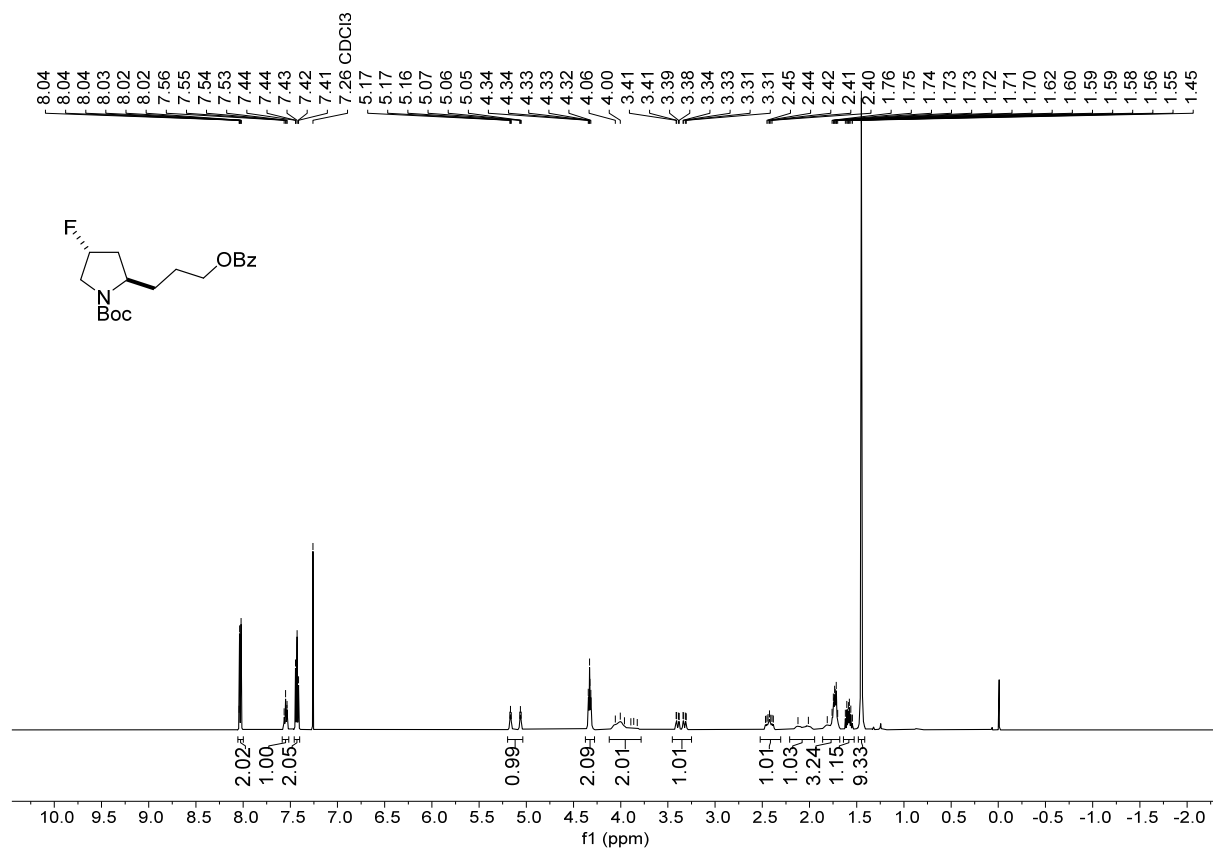


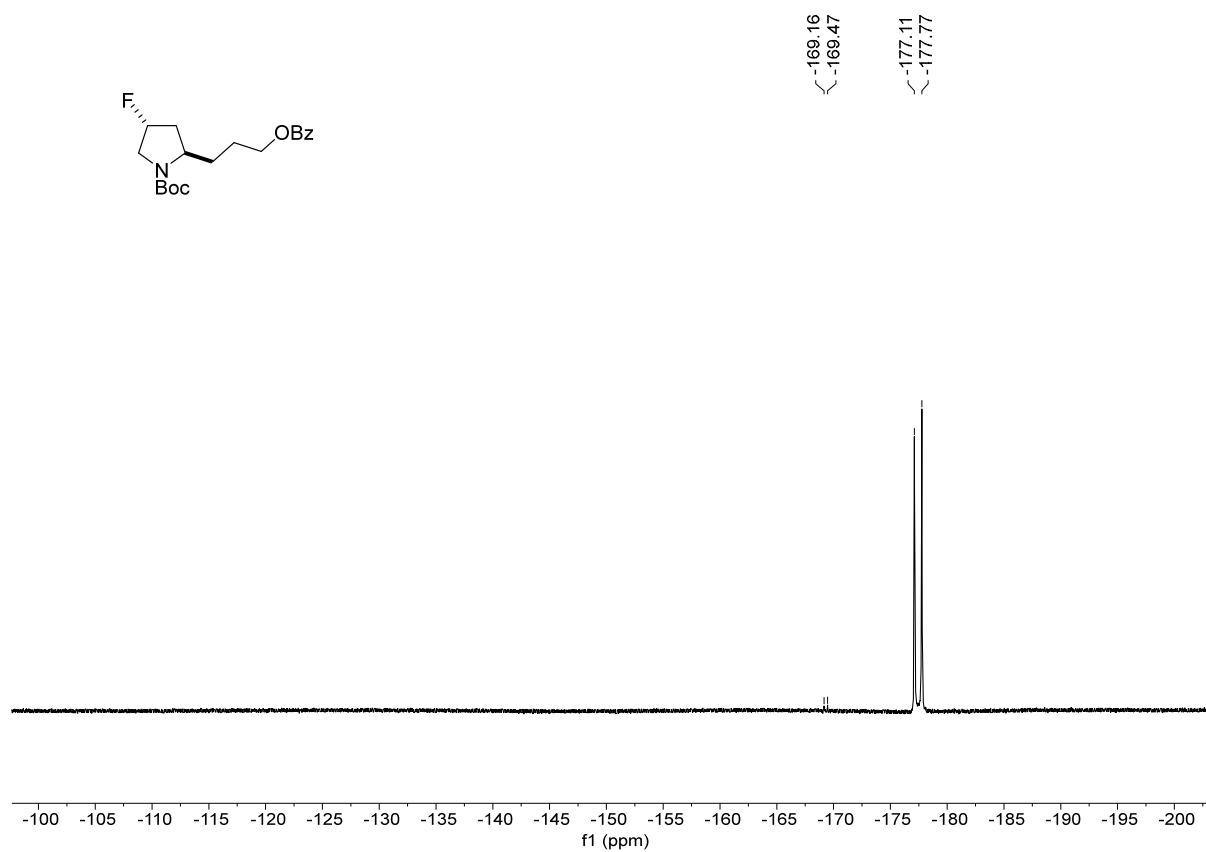




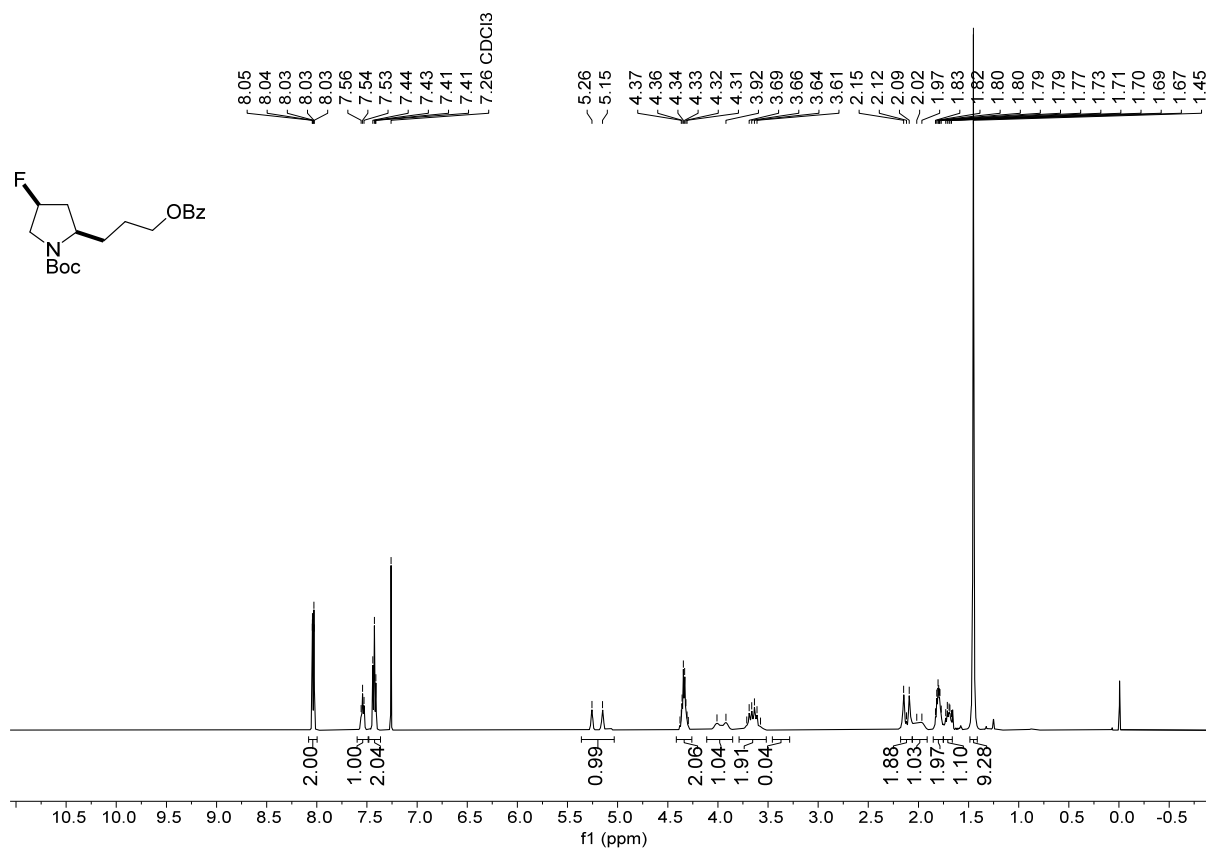




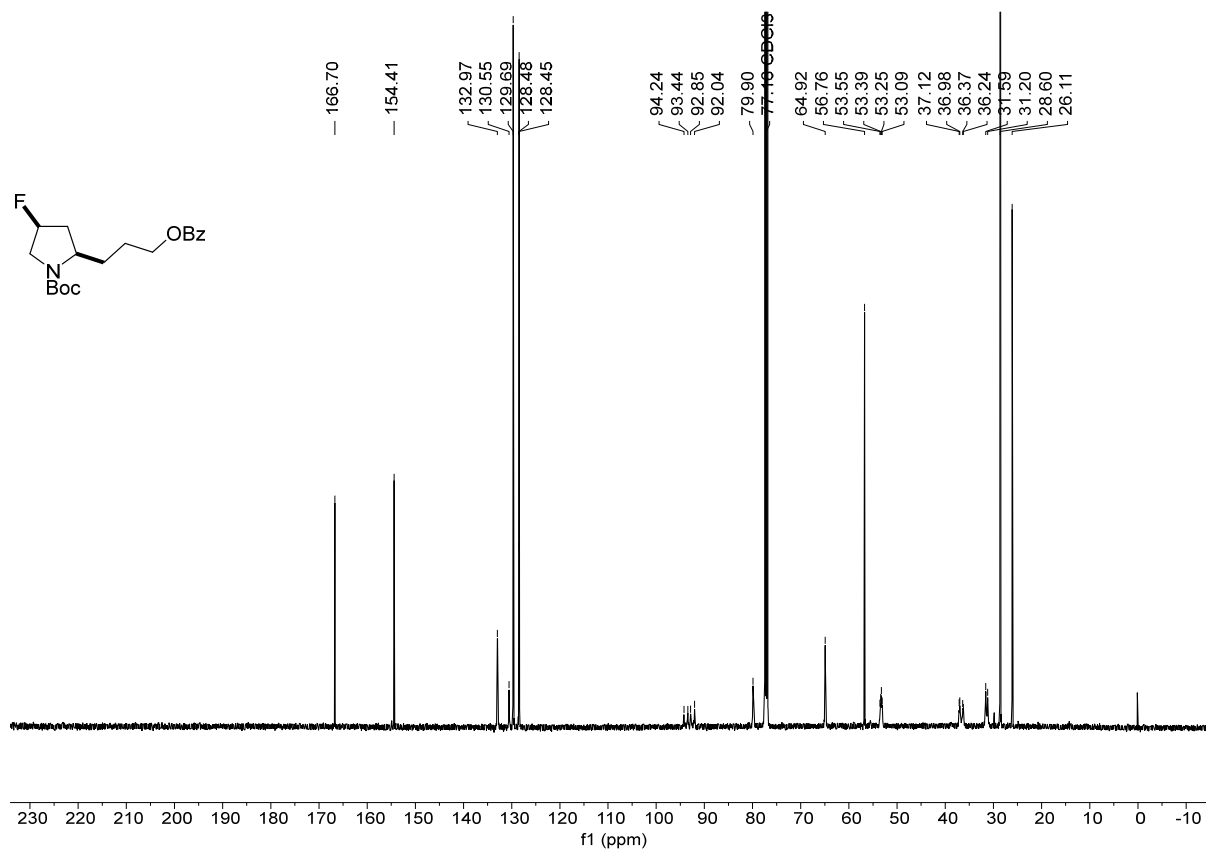




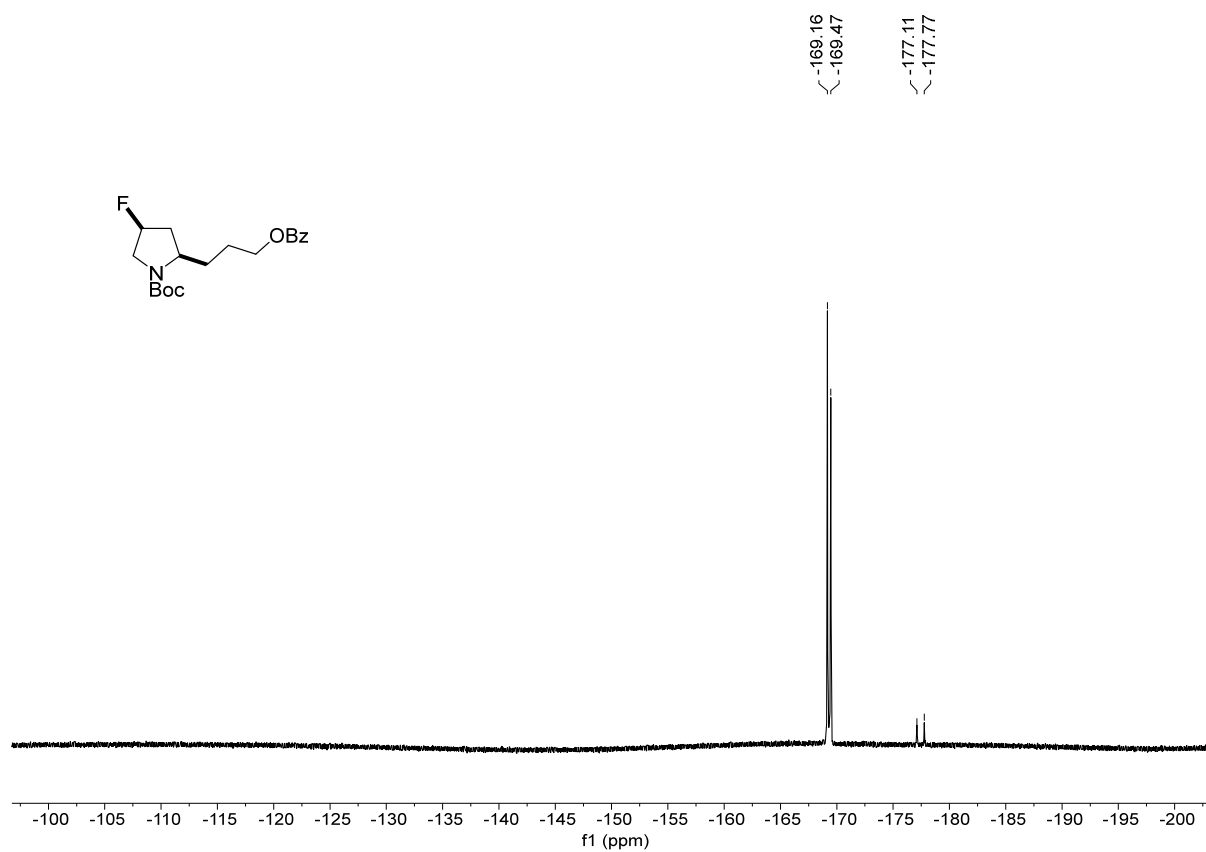
$^{19}\text{F}\{^1\text{H}\}$ NMR (377 MHz, CDCl_3) of **47**



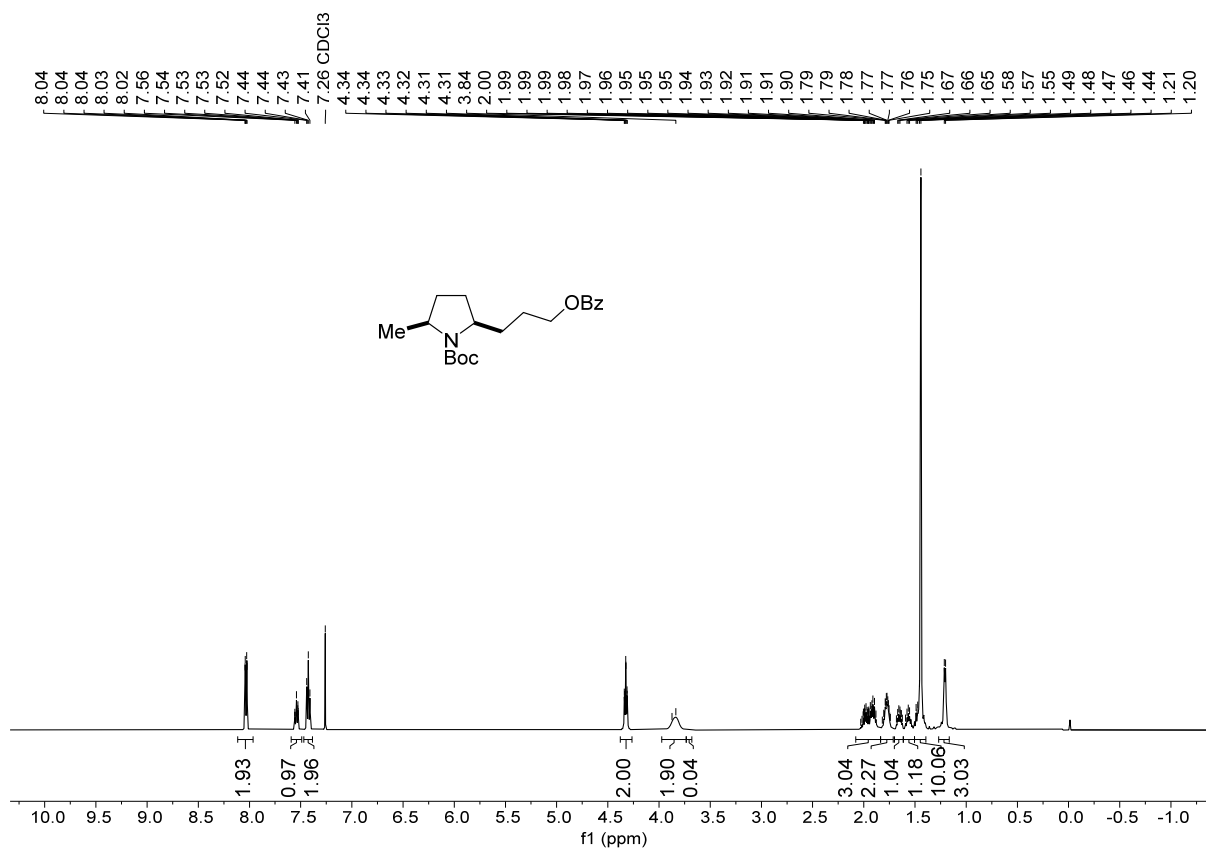
¹H NMR (500 MHz, CDCl₃) of **48**



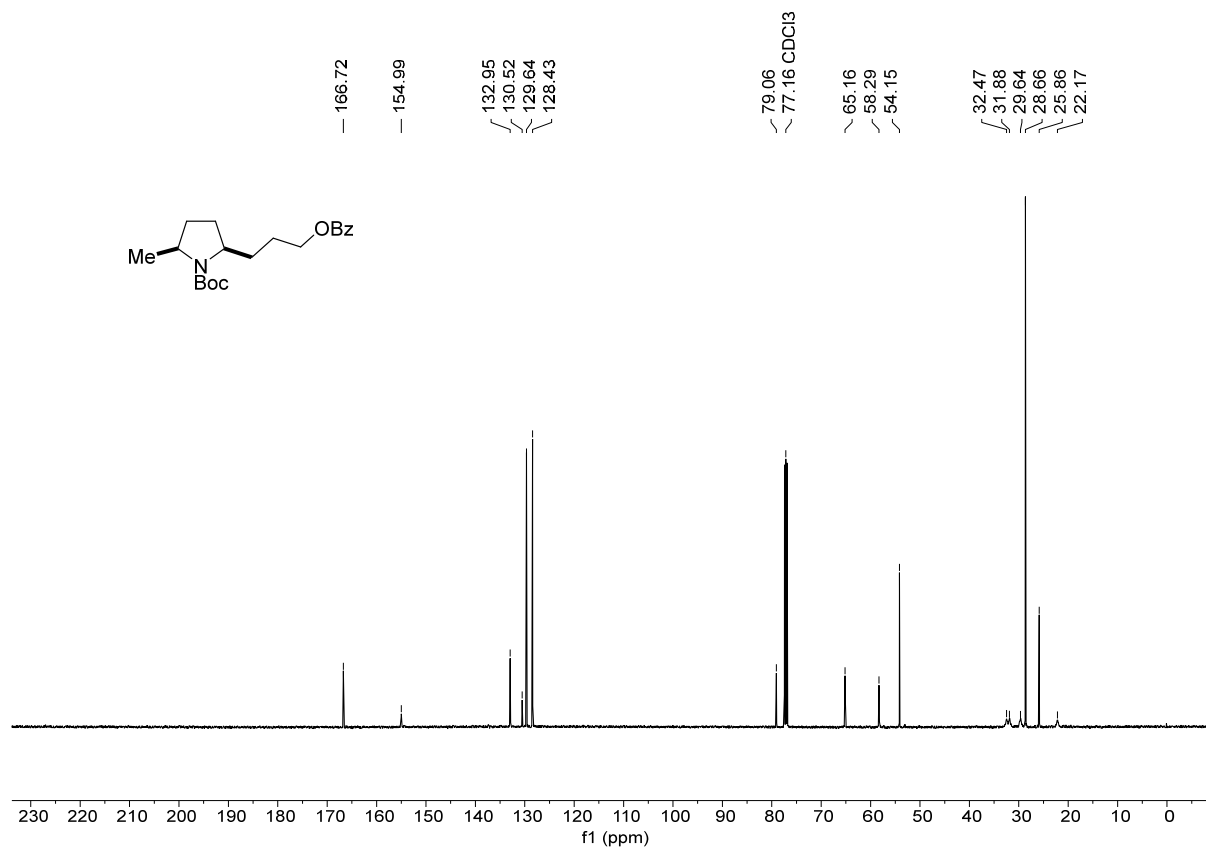
¹³C {¹H} NMR (125 MHz, CDCl₃) of **48**



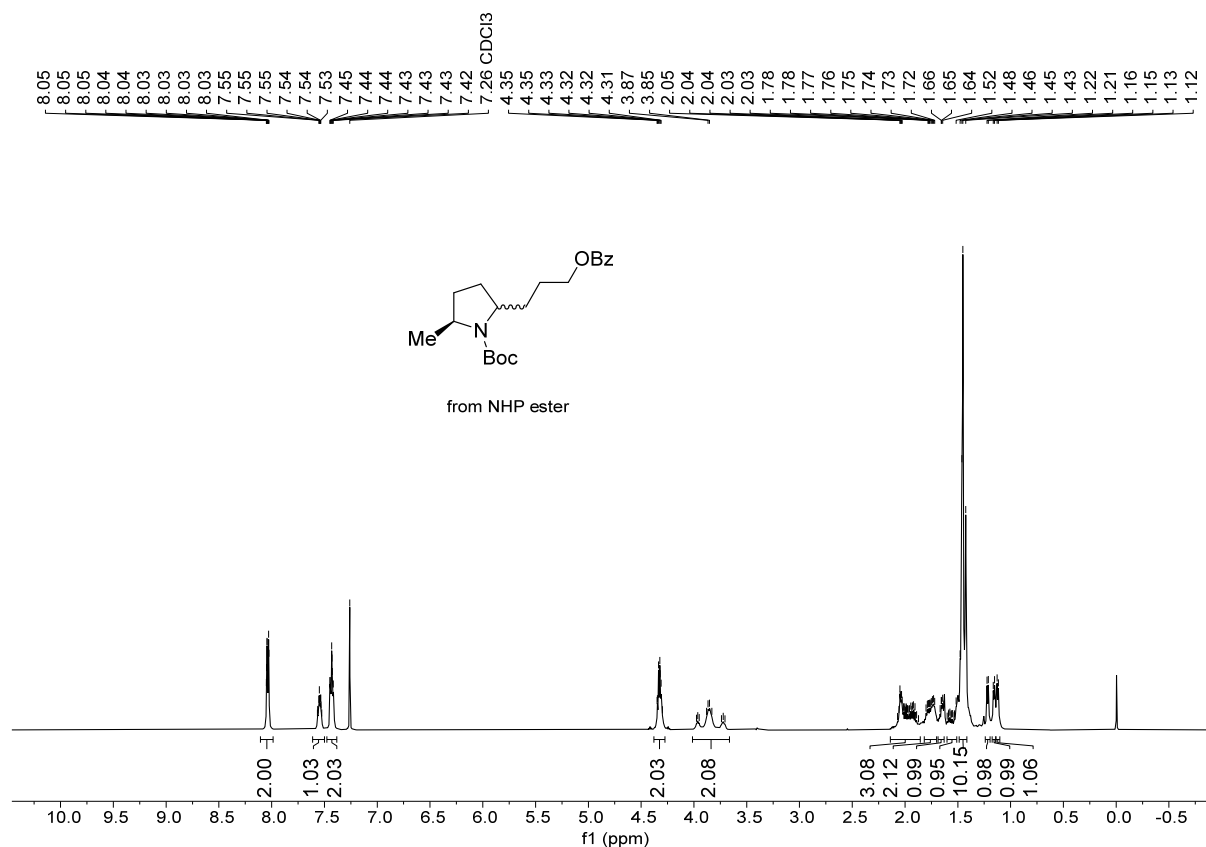
$^{19}\text{F}\{^1\text{H}\}$ NMR (377 MHz, CDCl_3) of **48**



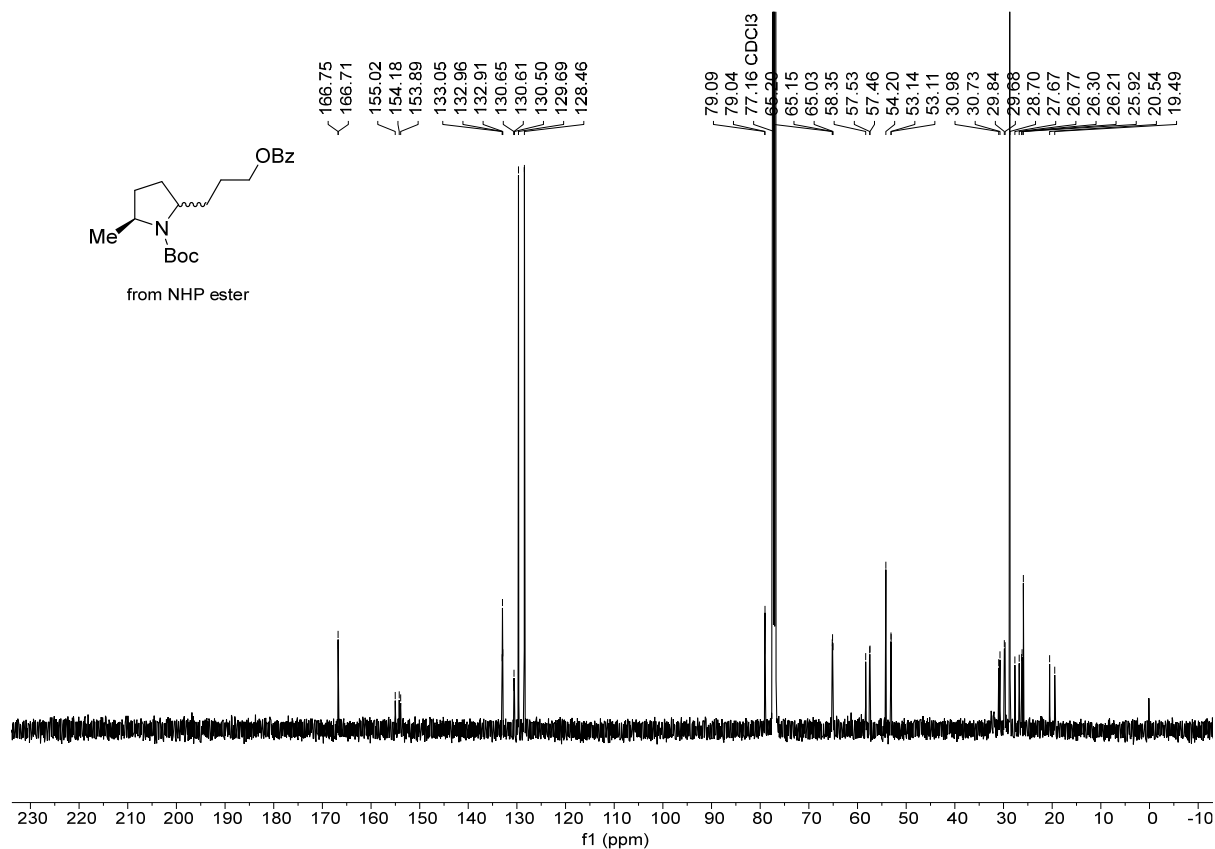
¹H NMR (500 MHz, CDCl₃) of **49**



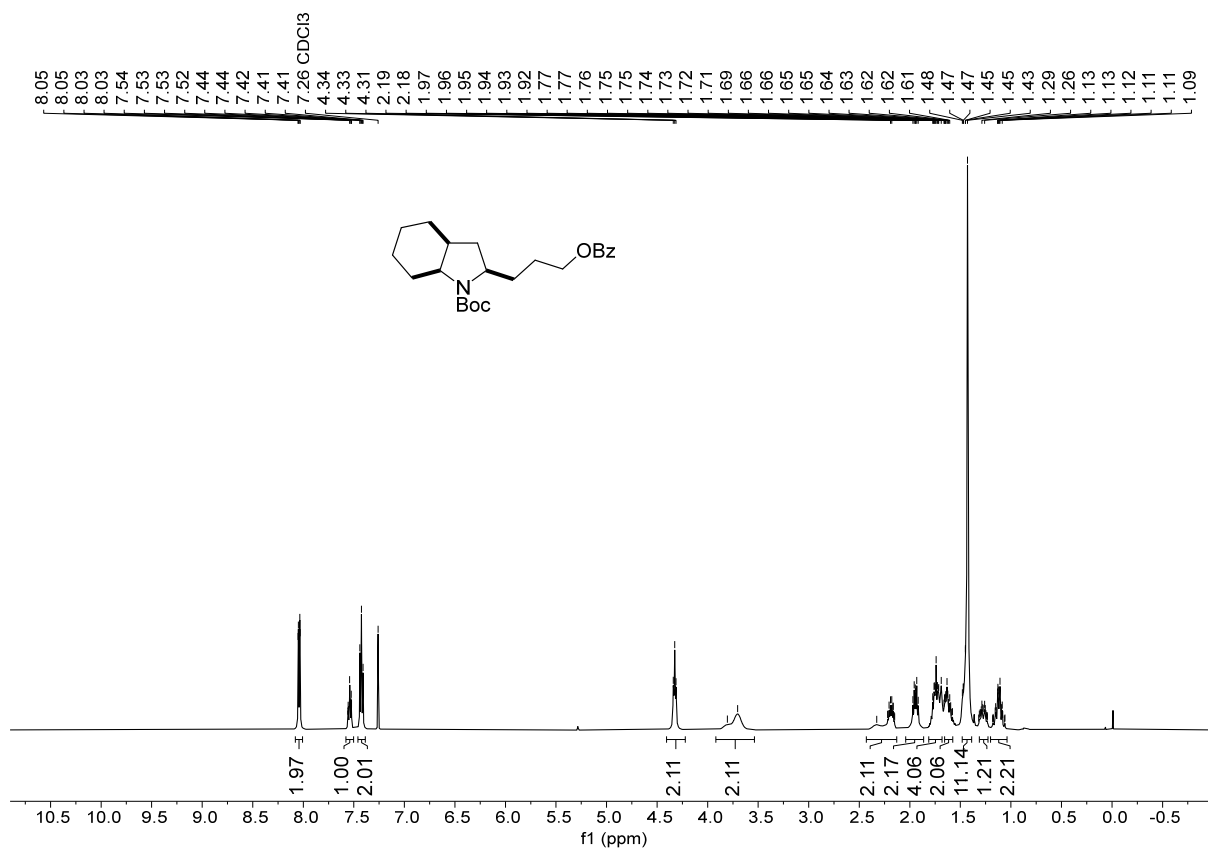
¹³C {¹H} NMR (125 MHz, CDCl₃) of **49**



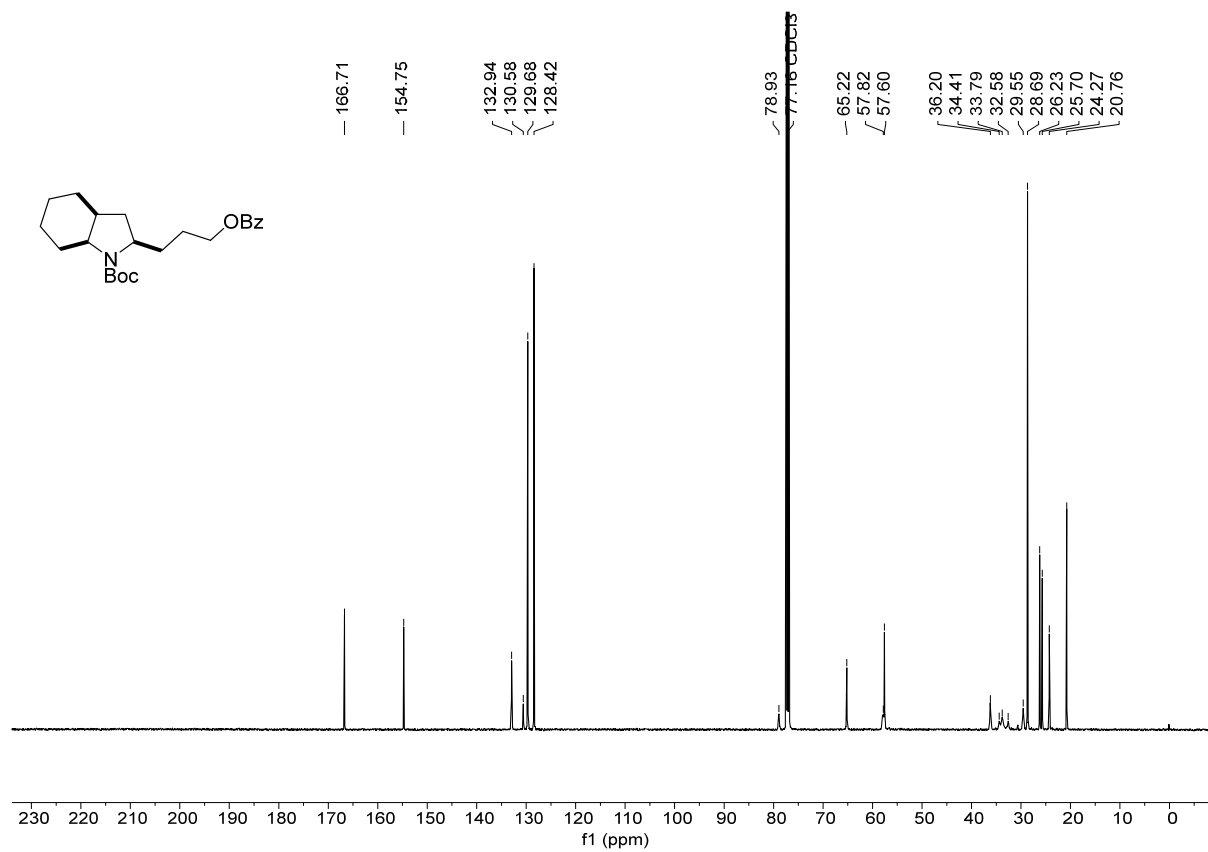
¹H NMR (500 MHz, CDCl₃) of **49** from decarboxylative cross coupling



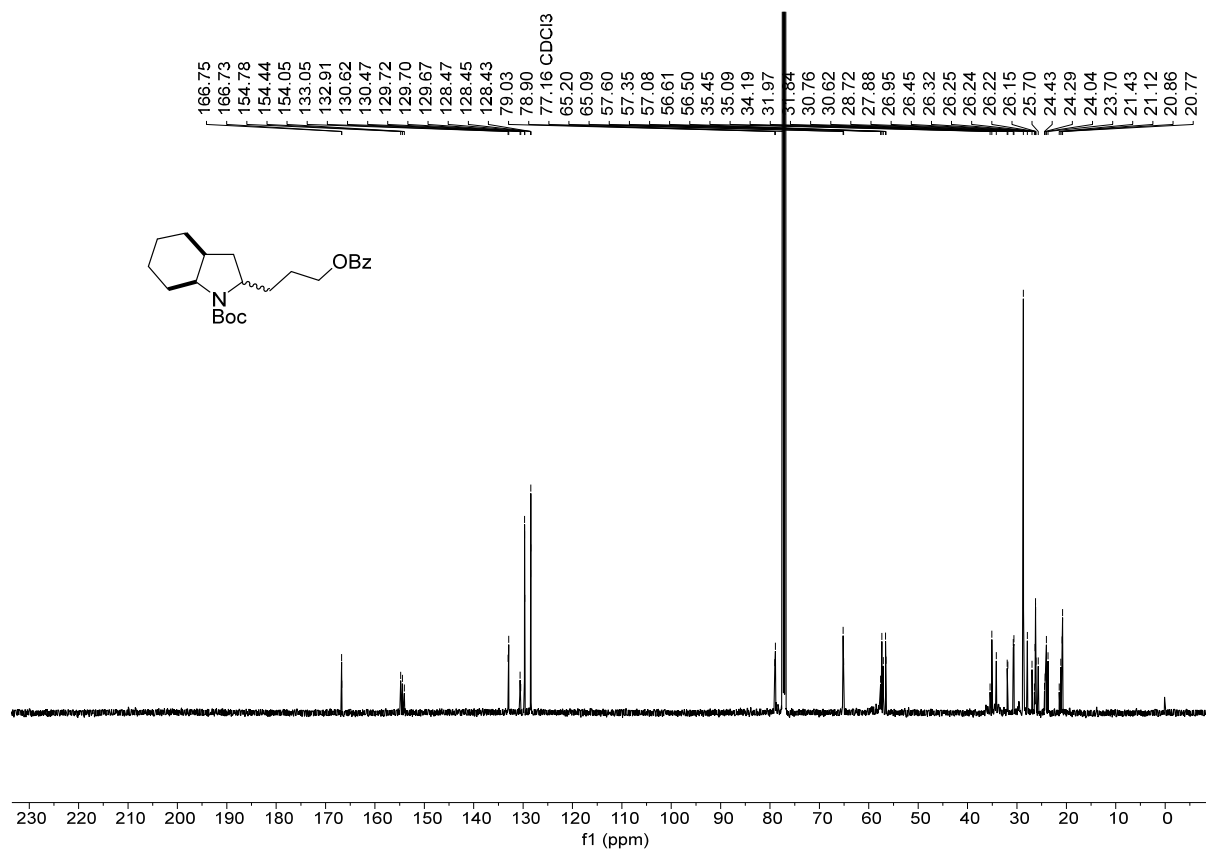
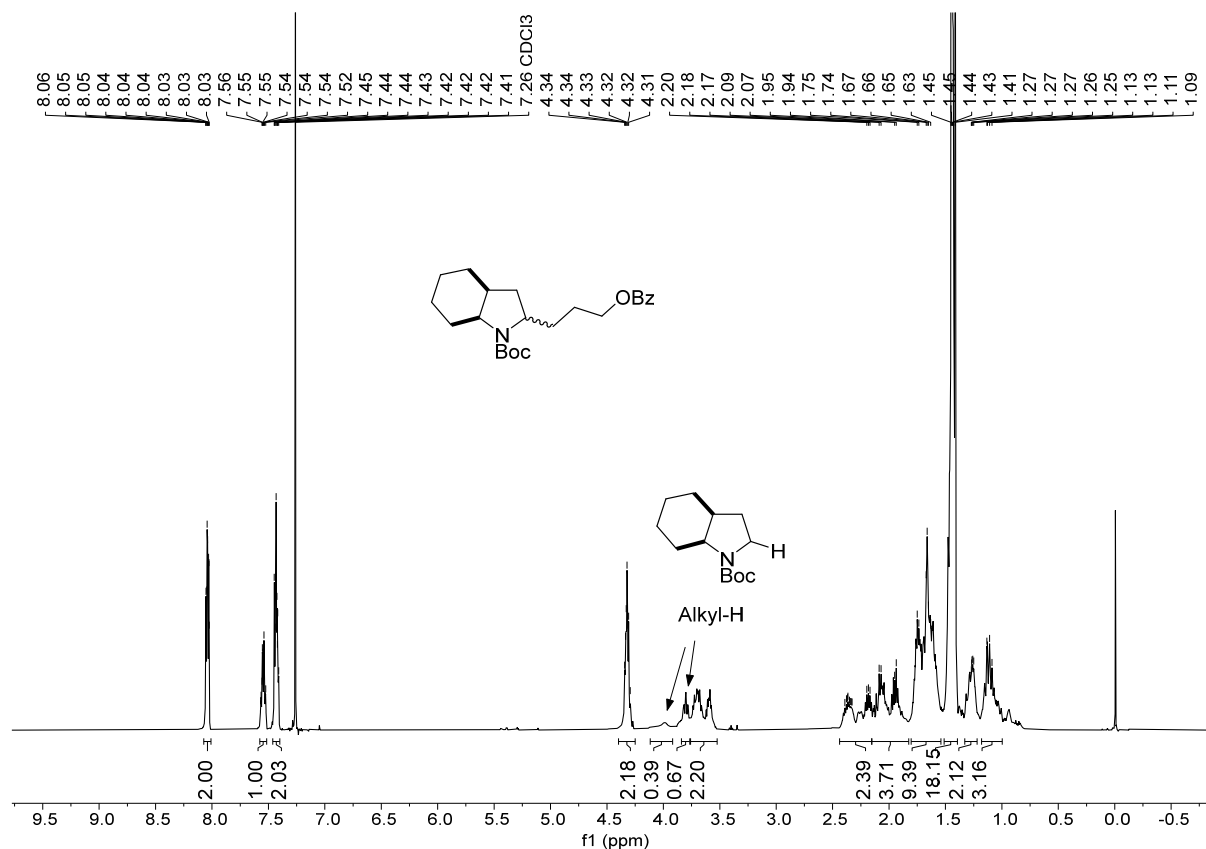
¹³C{¹H} NMR (125 MHz, CDCl₃) of **49** from decarboxylative cross coupling

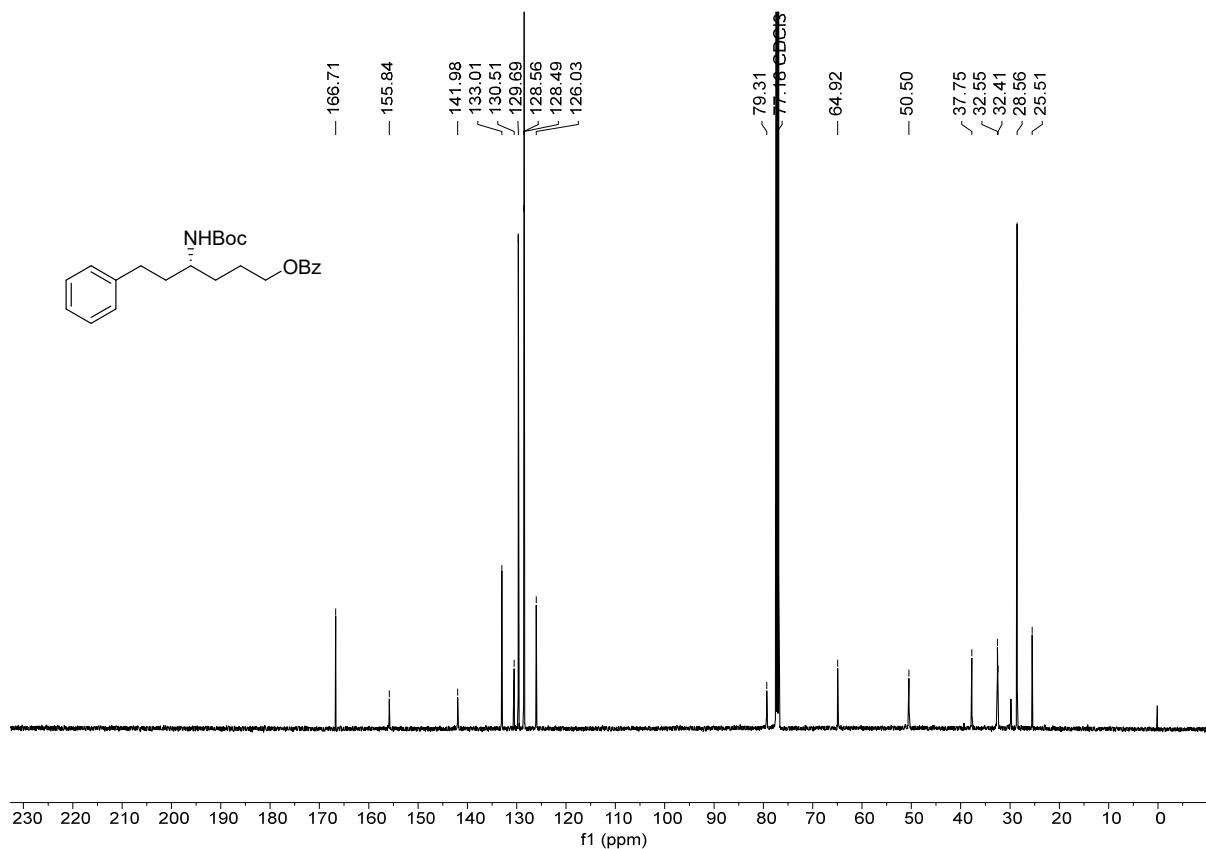
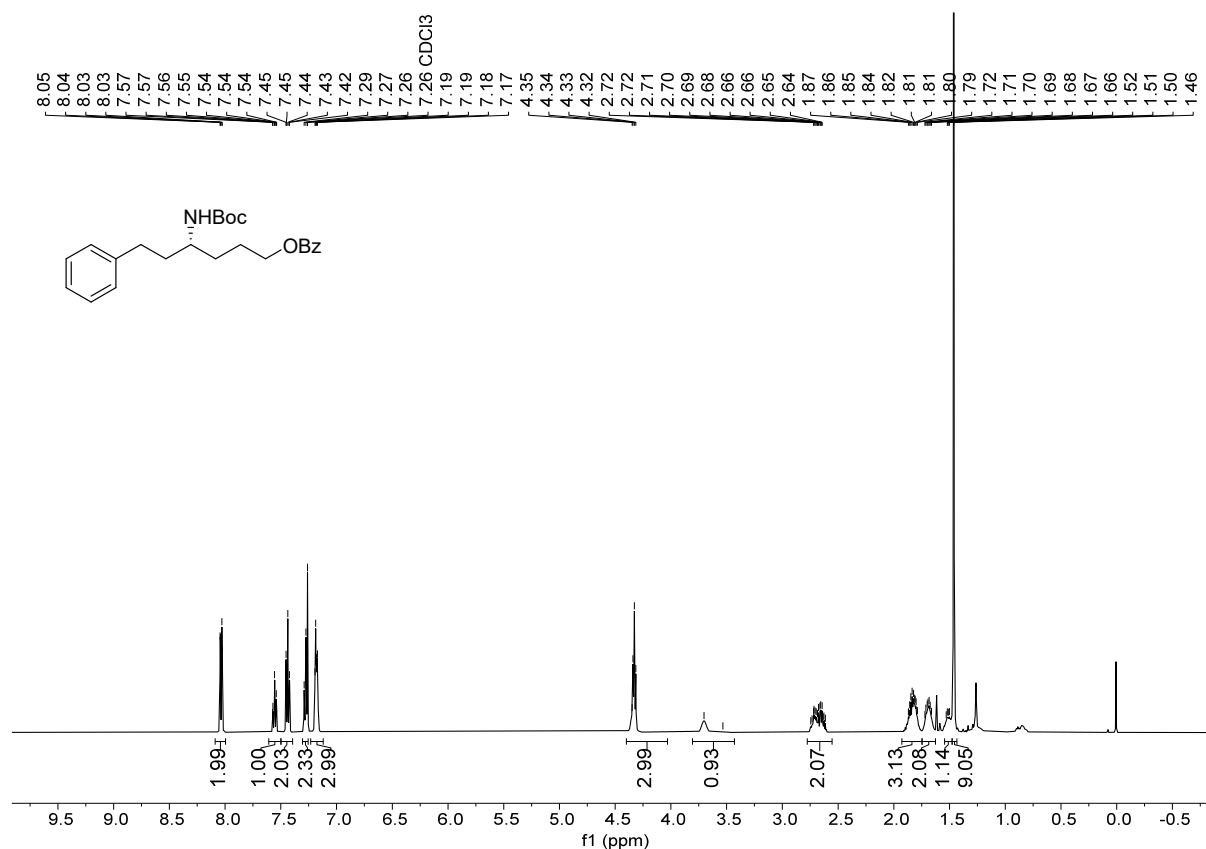


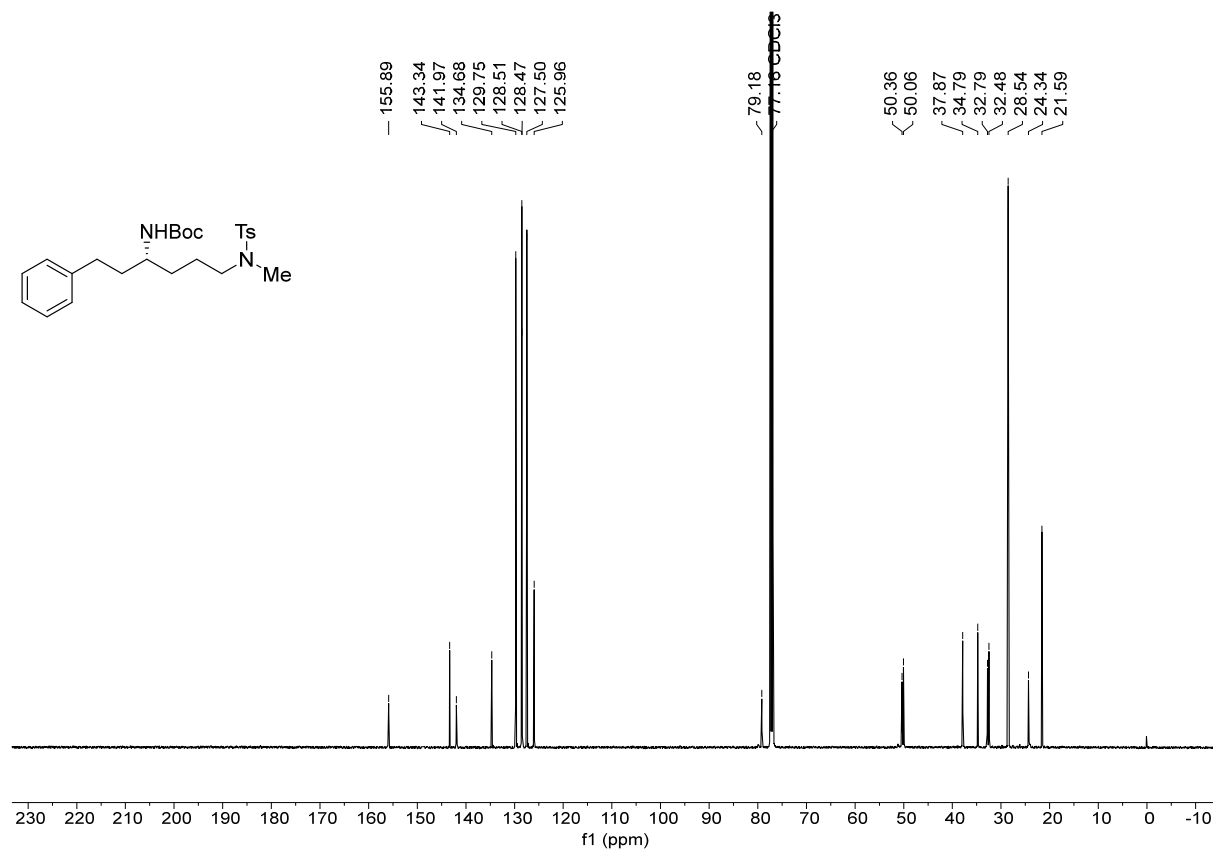
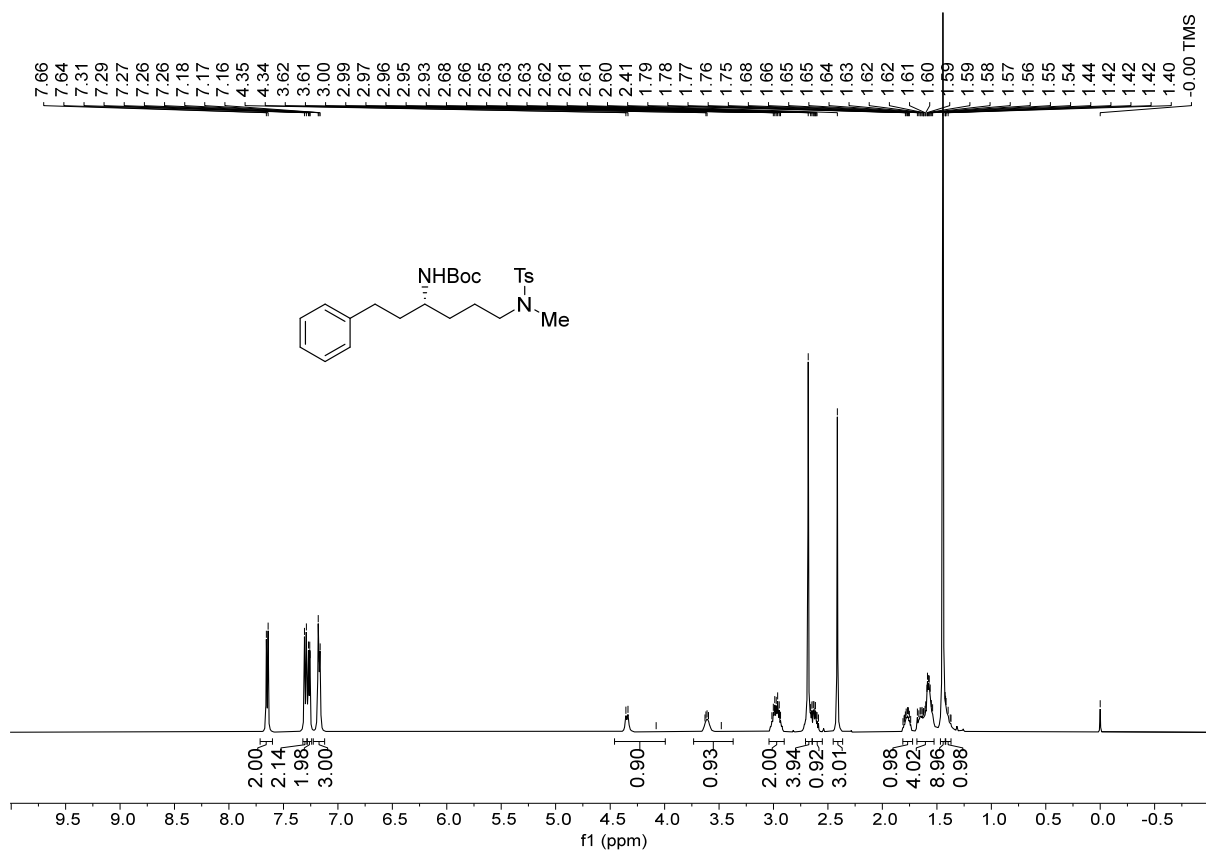
¹H NMR (500 MHz, CDCl₃) of **50**

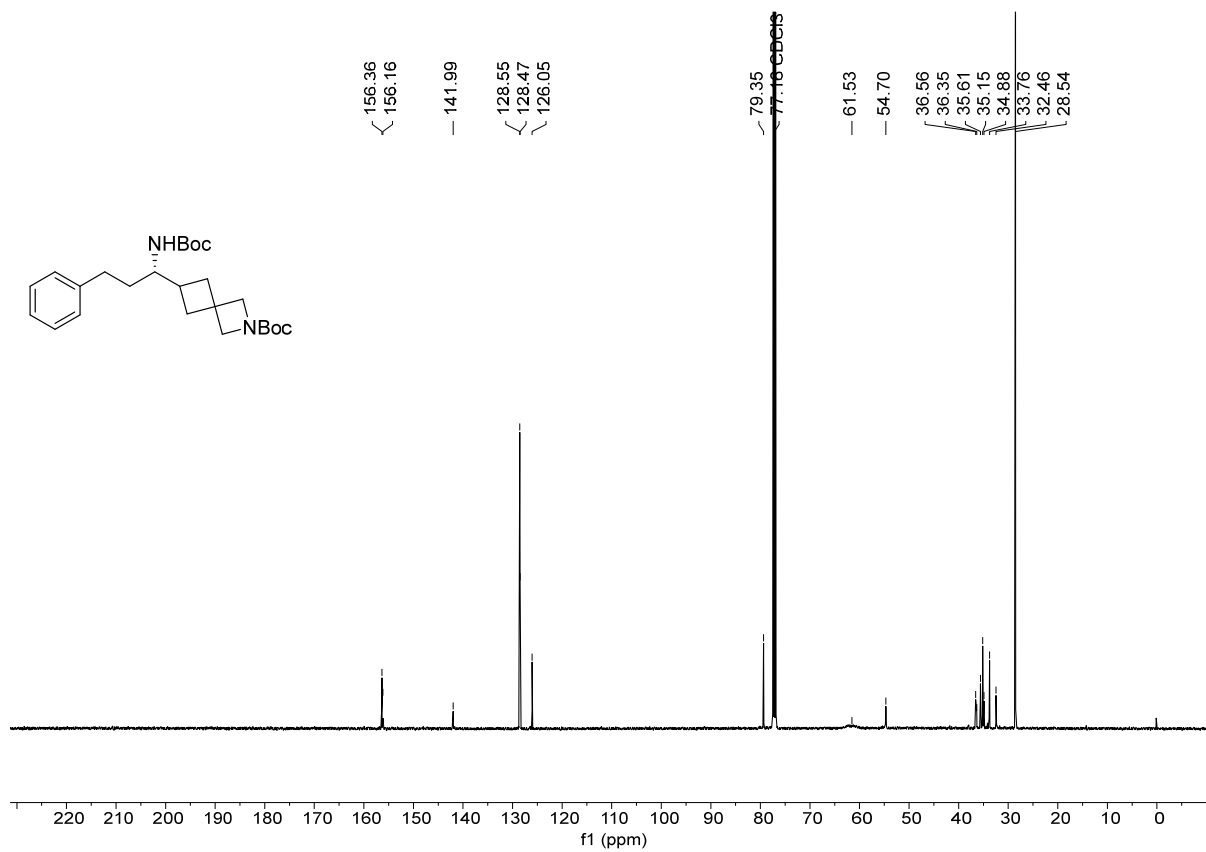
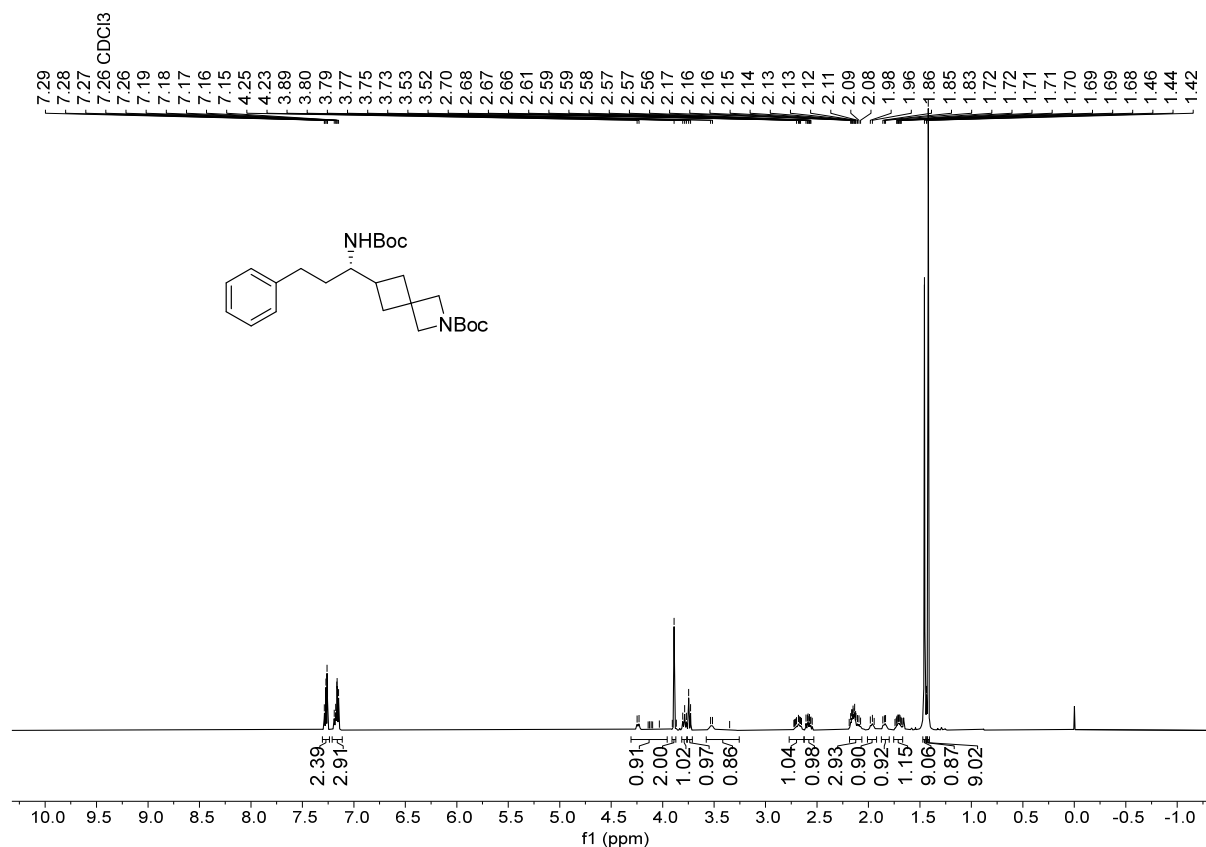


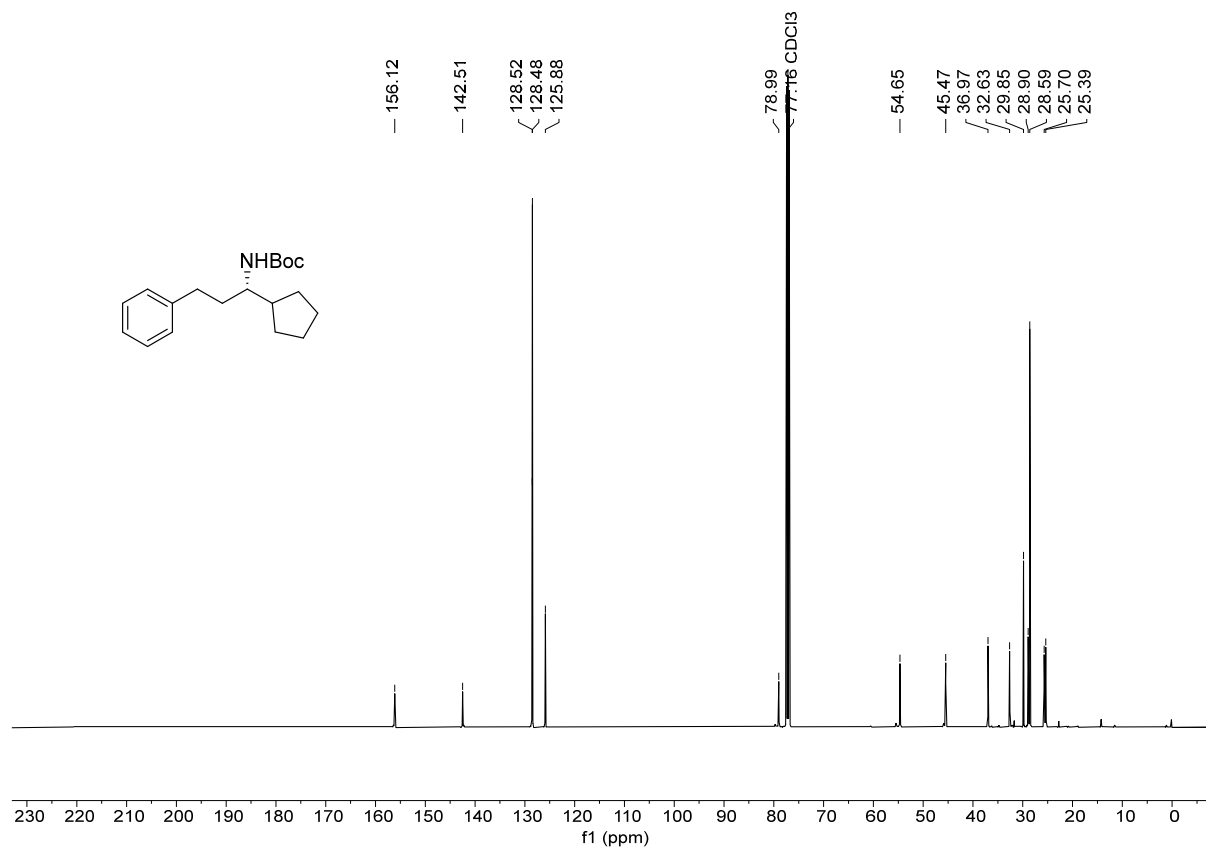
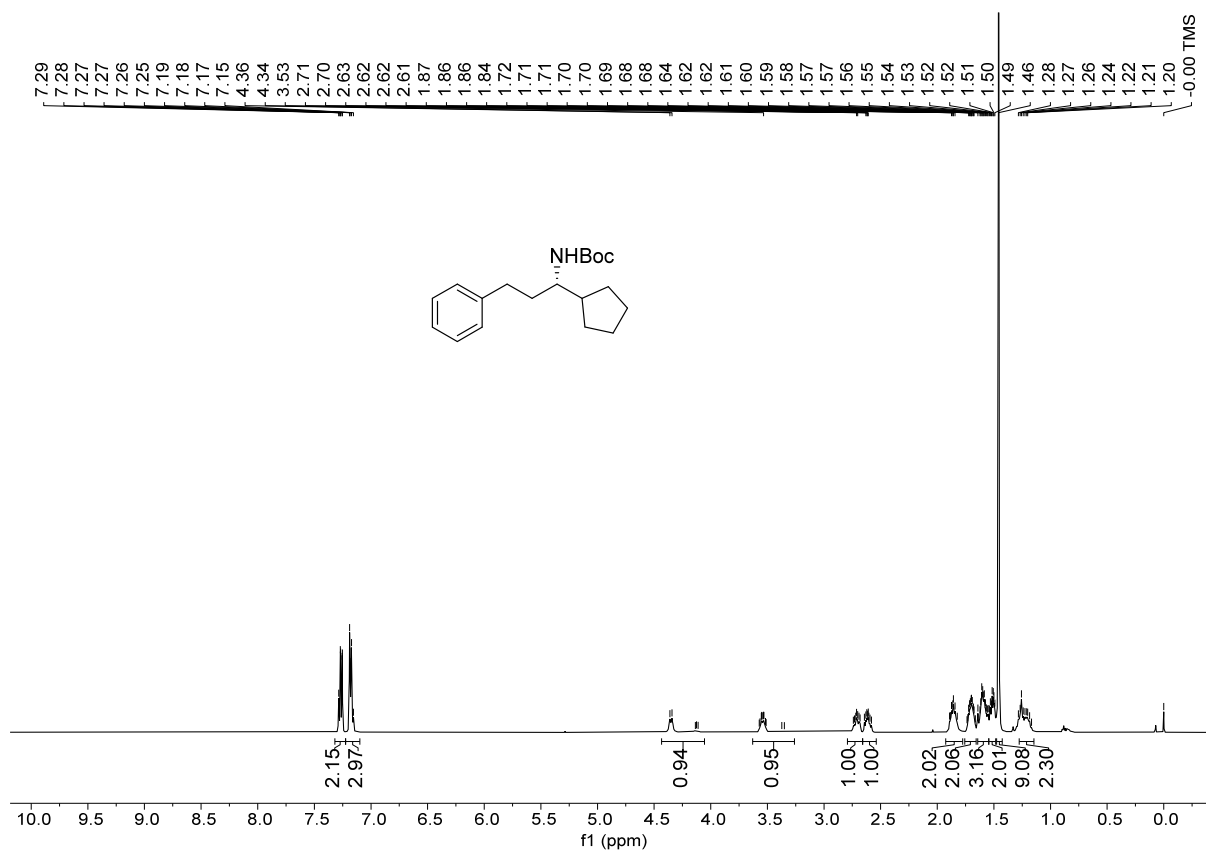
¹³C {¹H} NMR (125 MHz, CDCl₃) of **50**

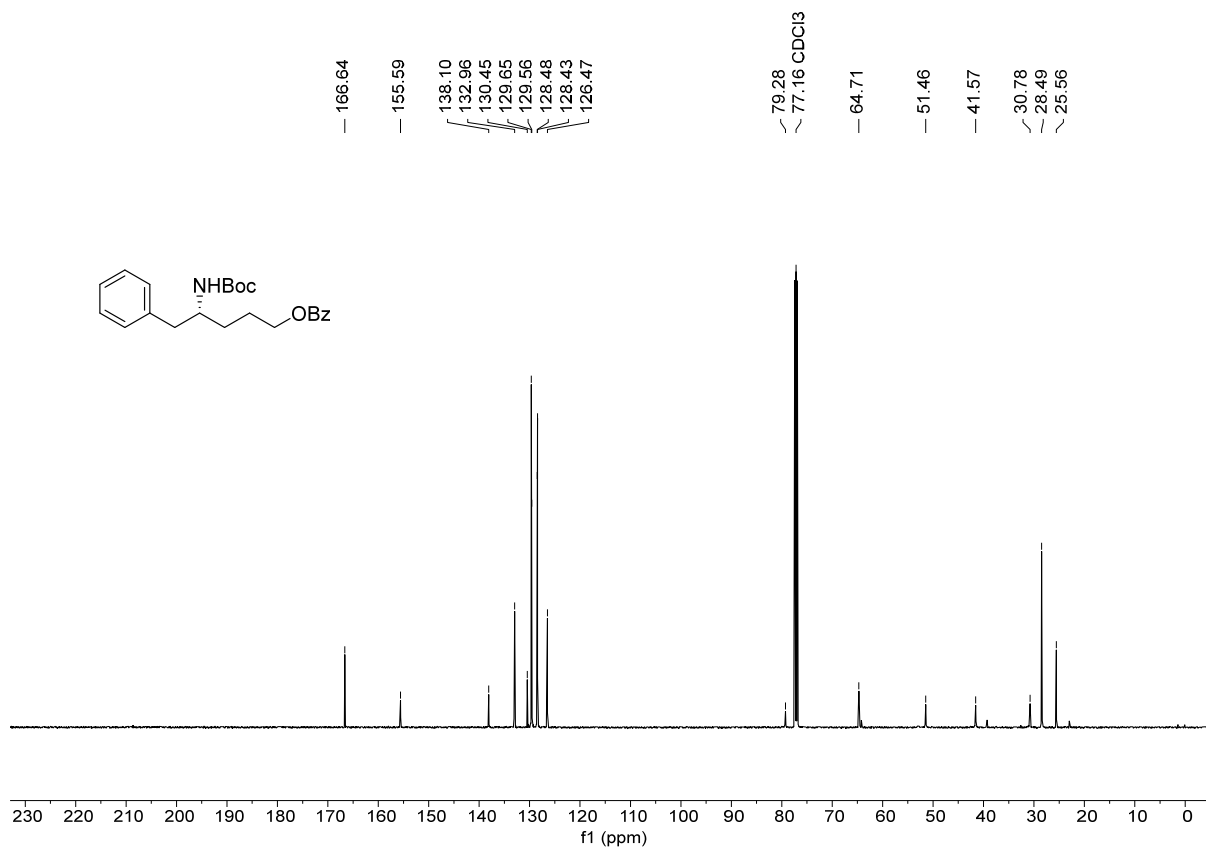
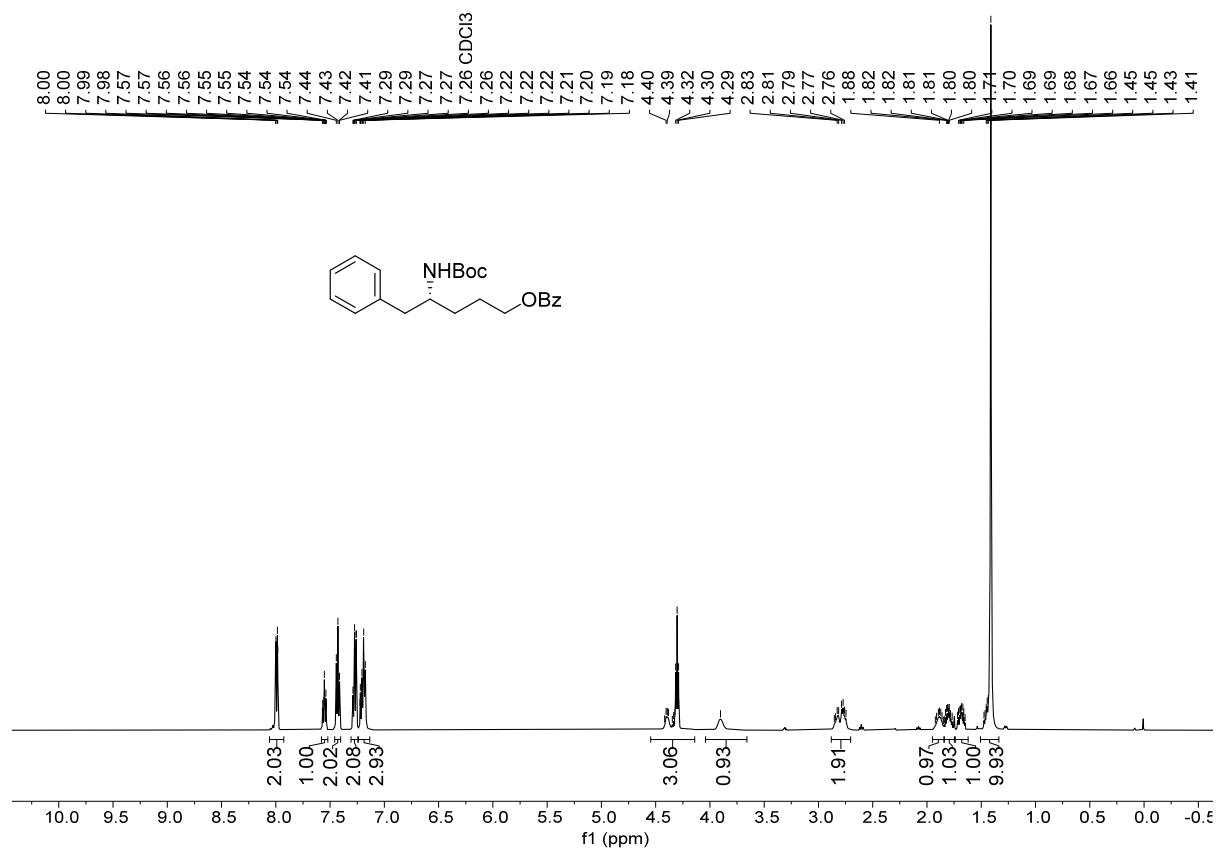


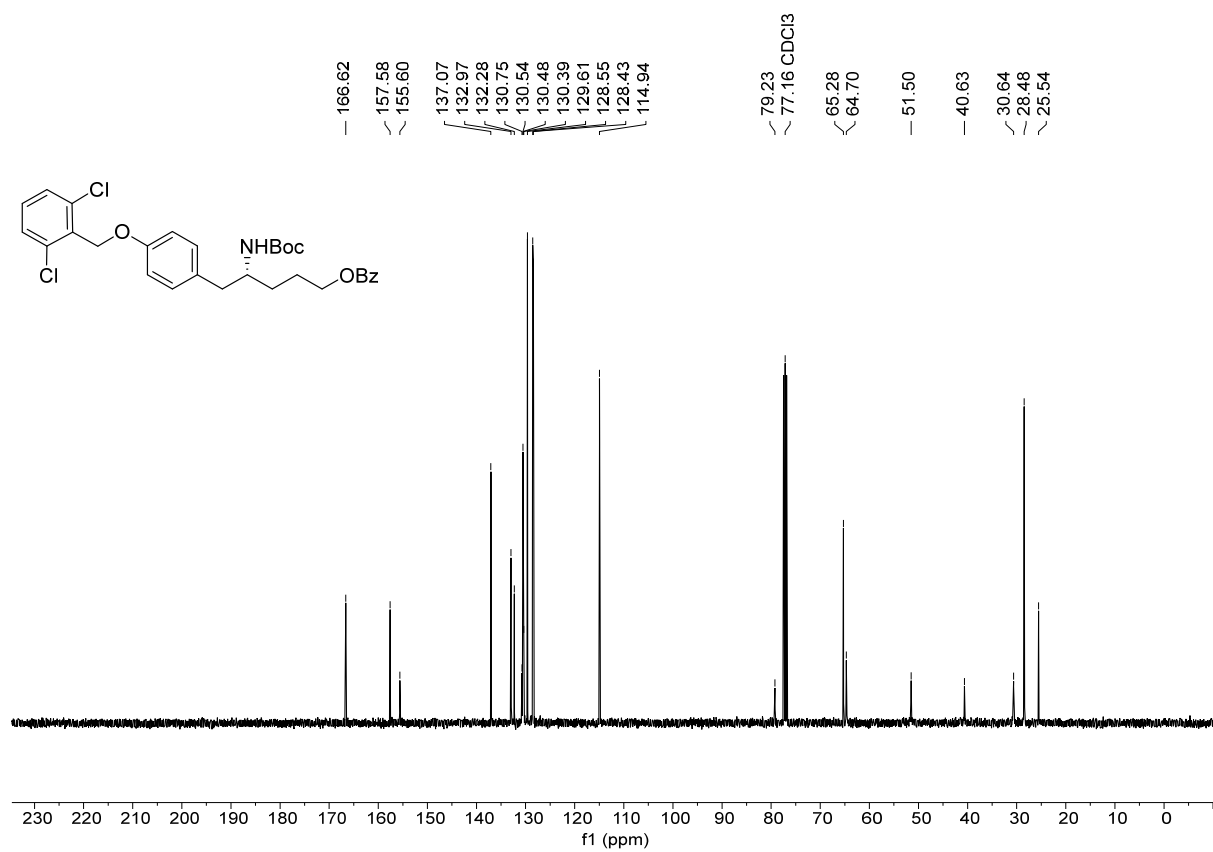
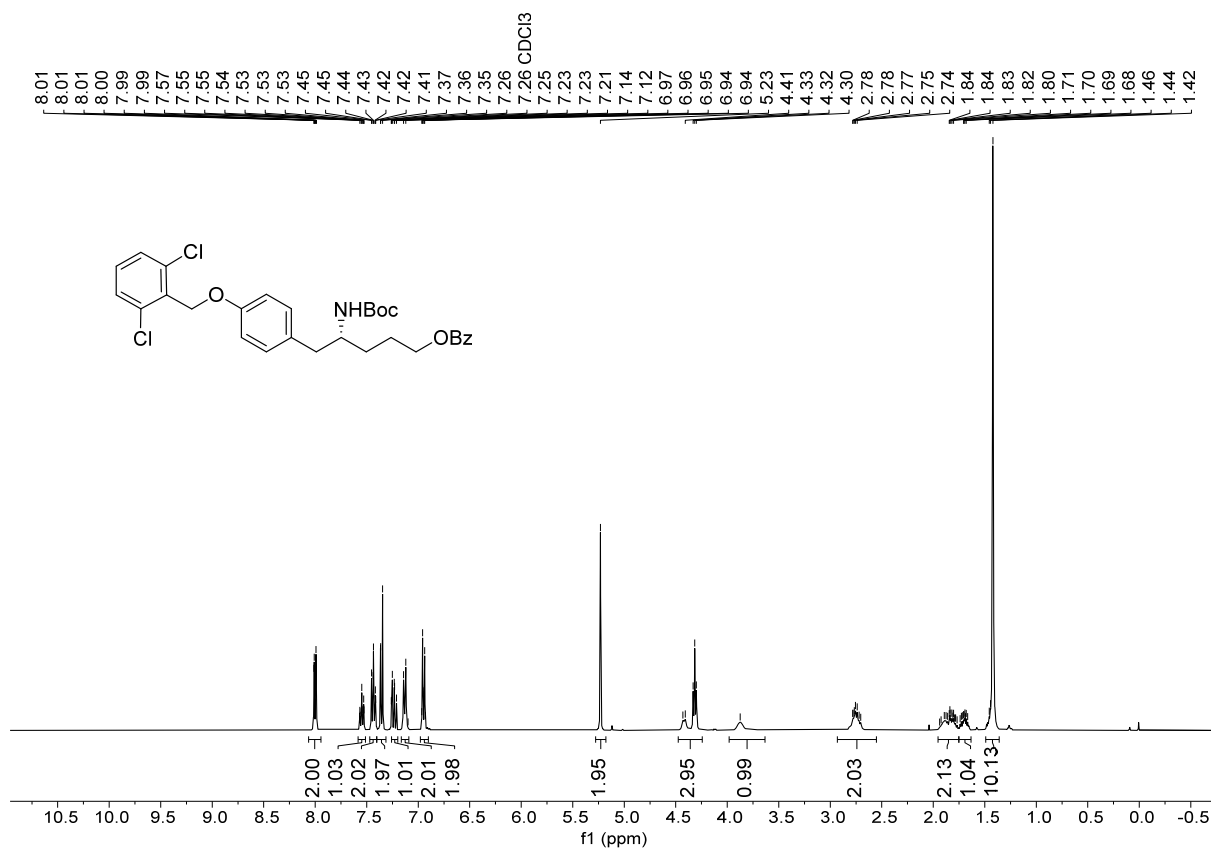


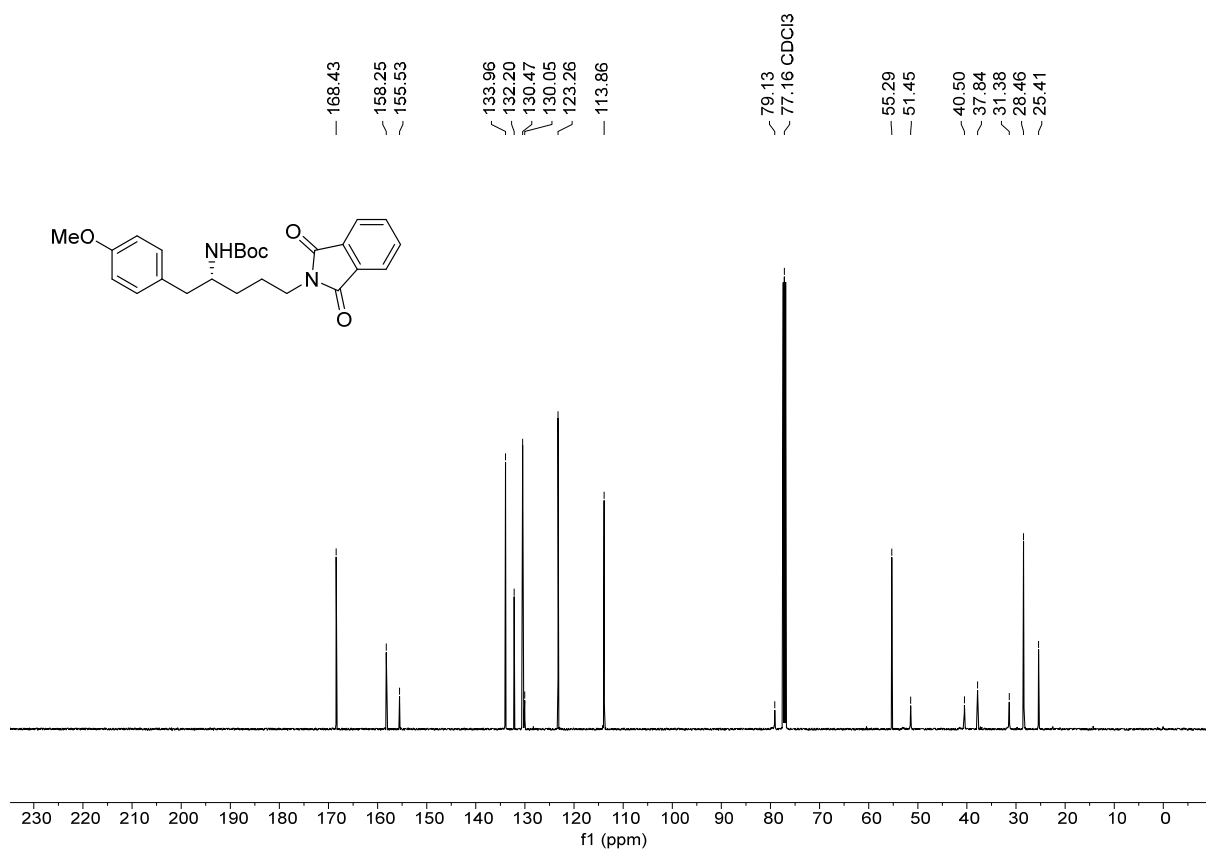
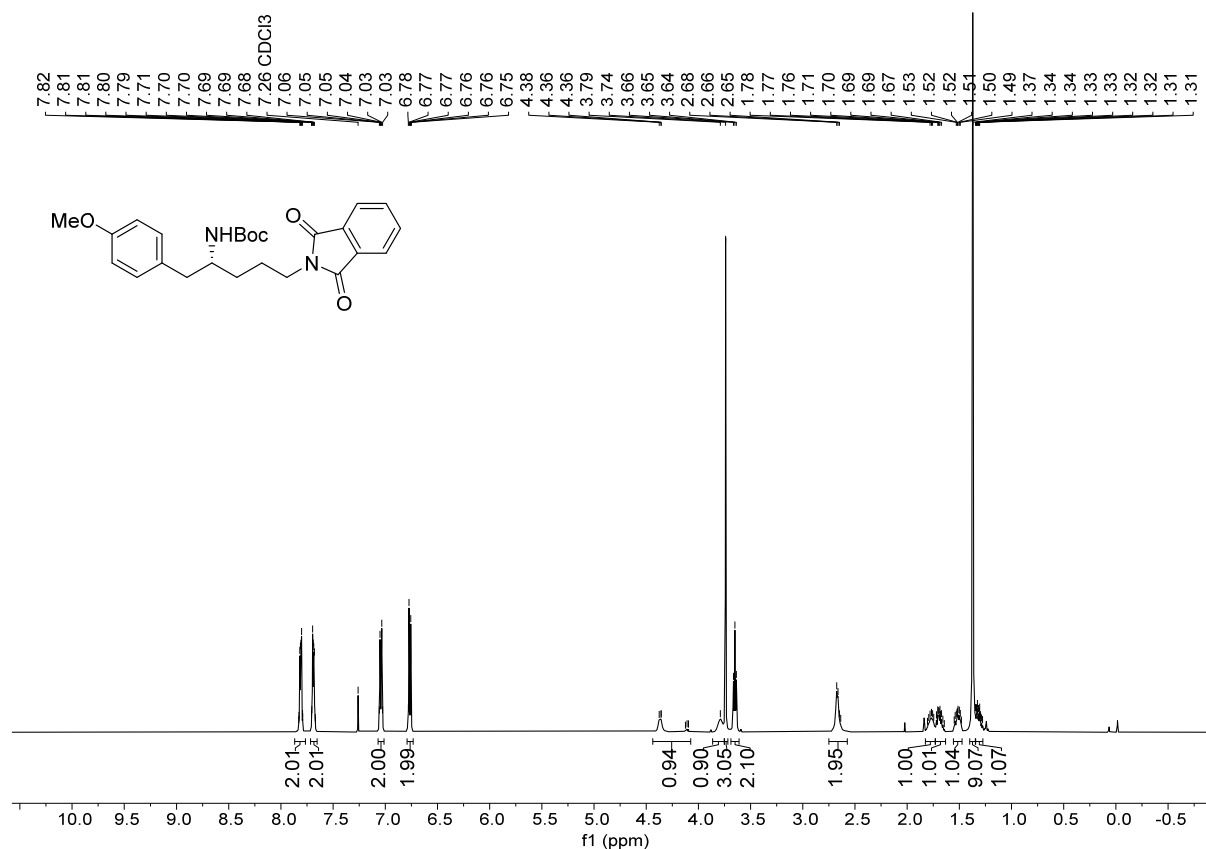


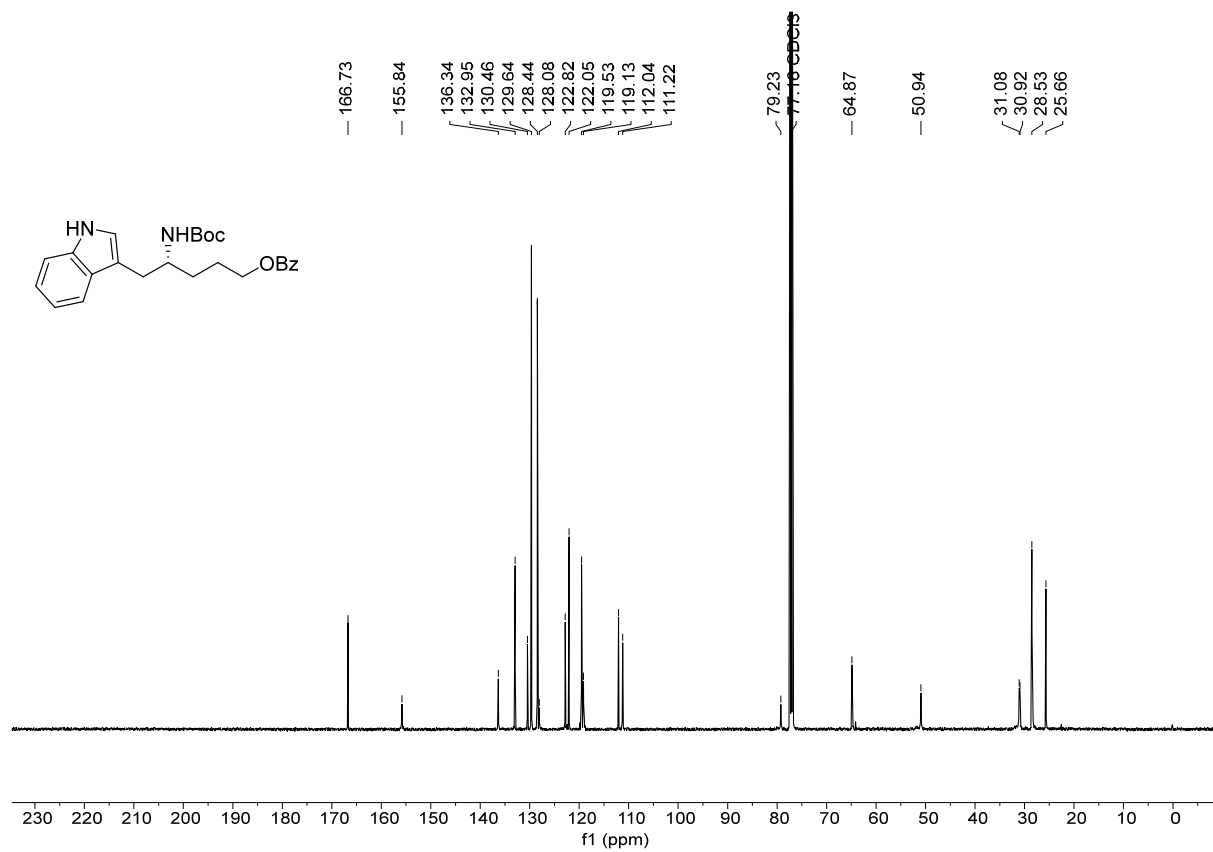
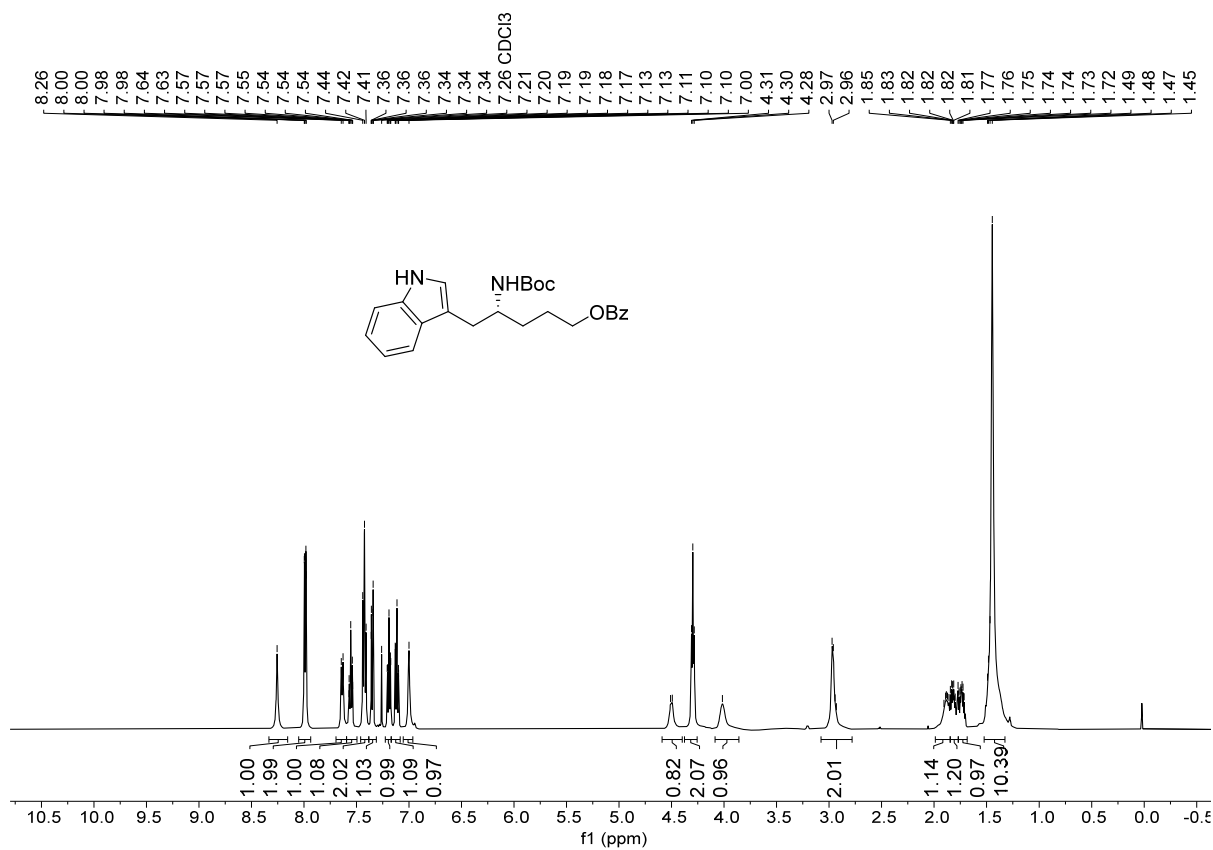


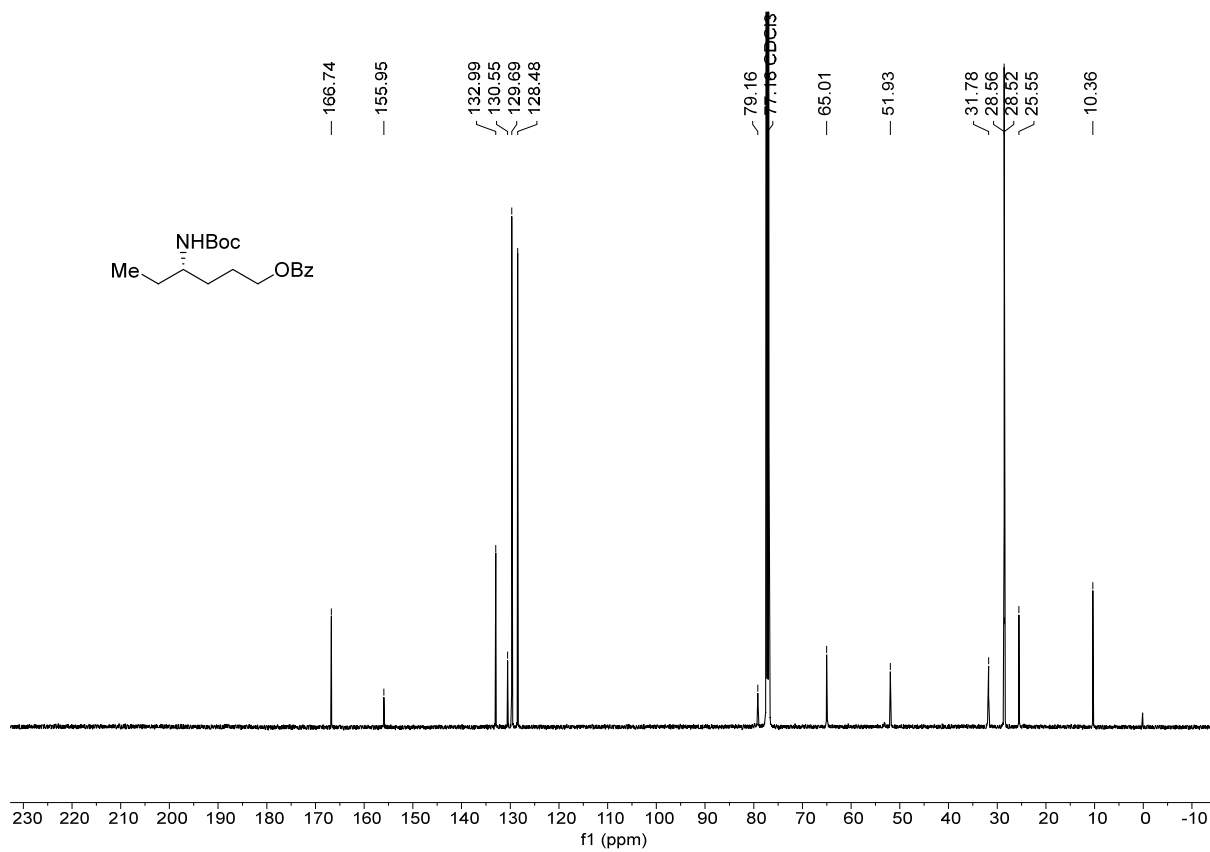
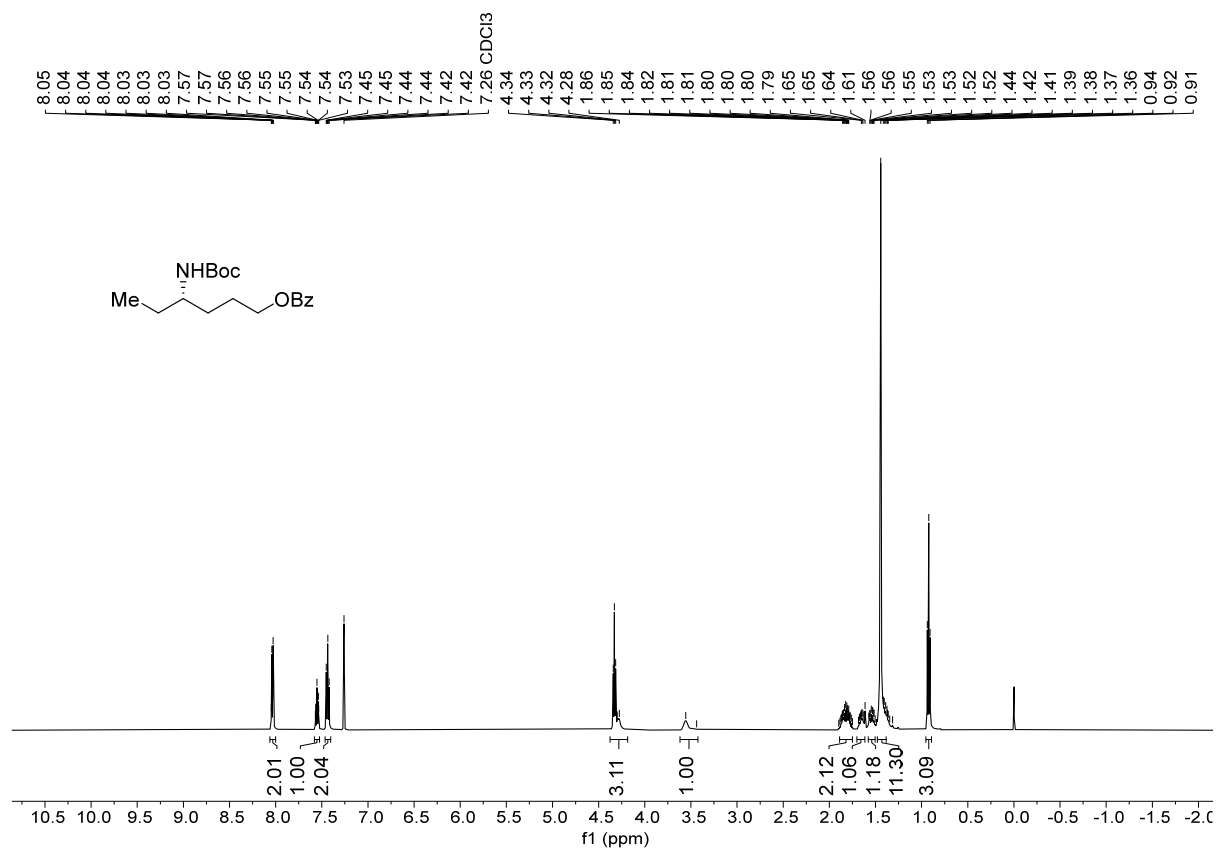


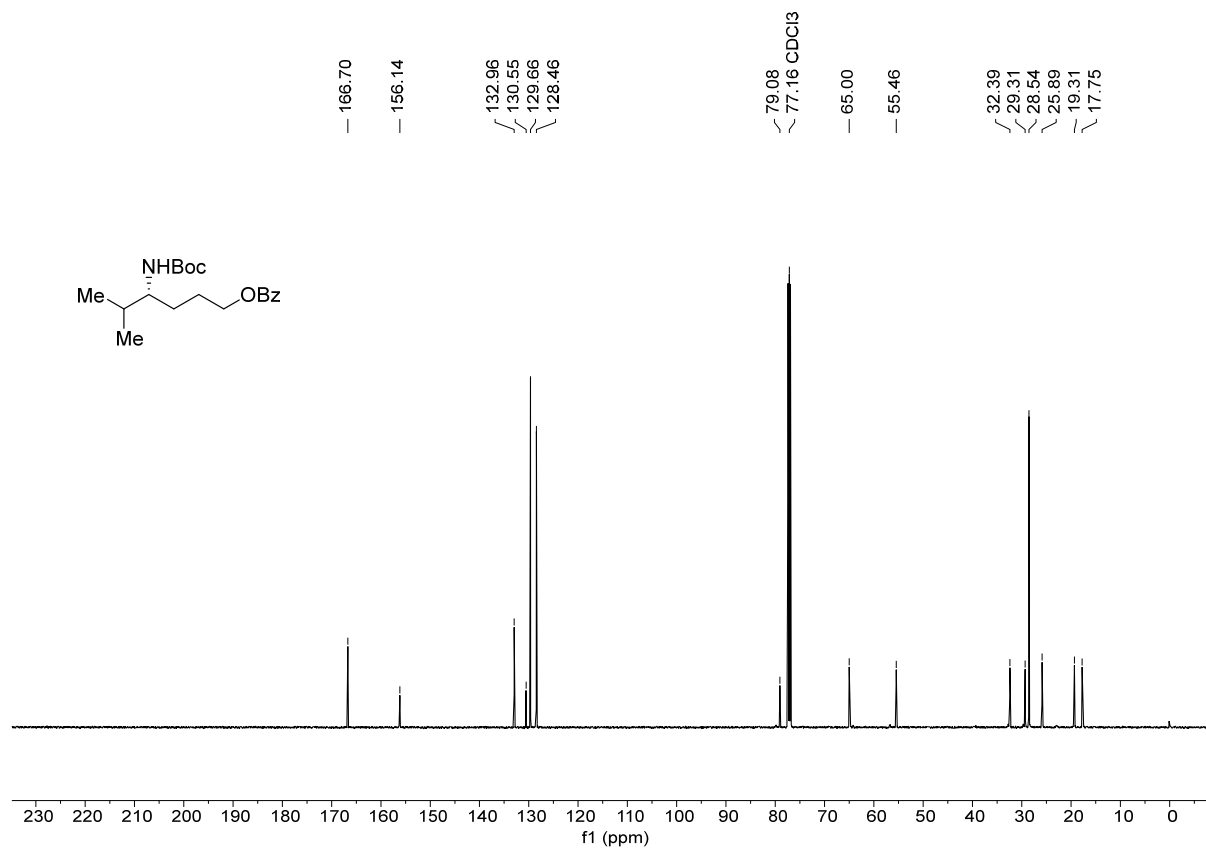
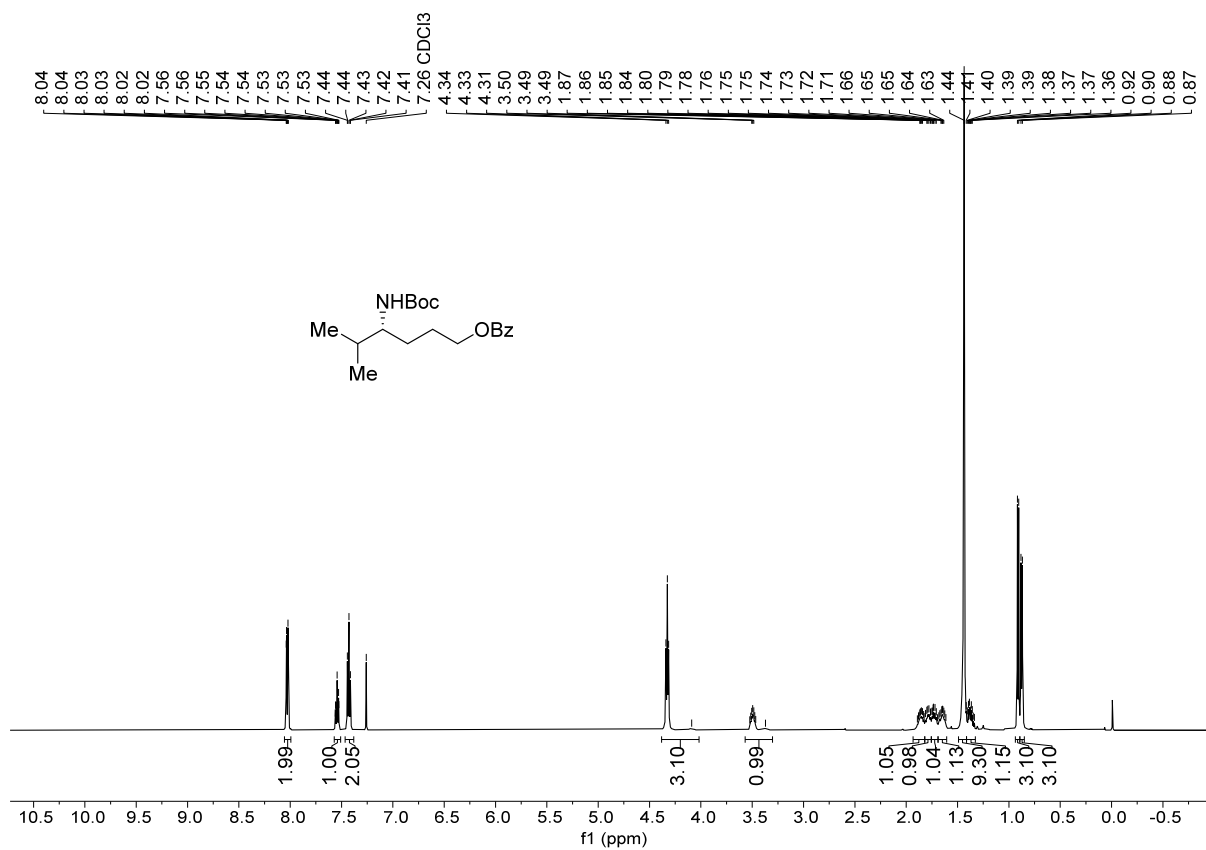


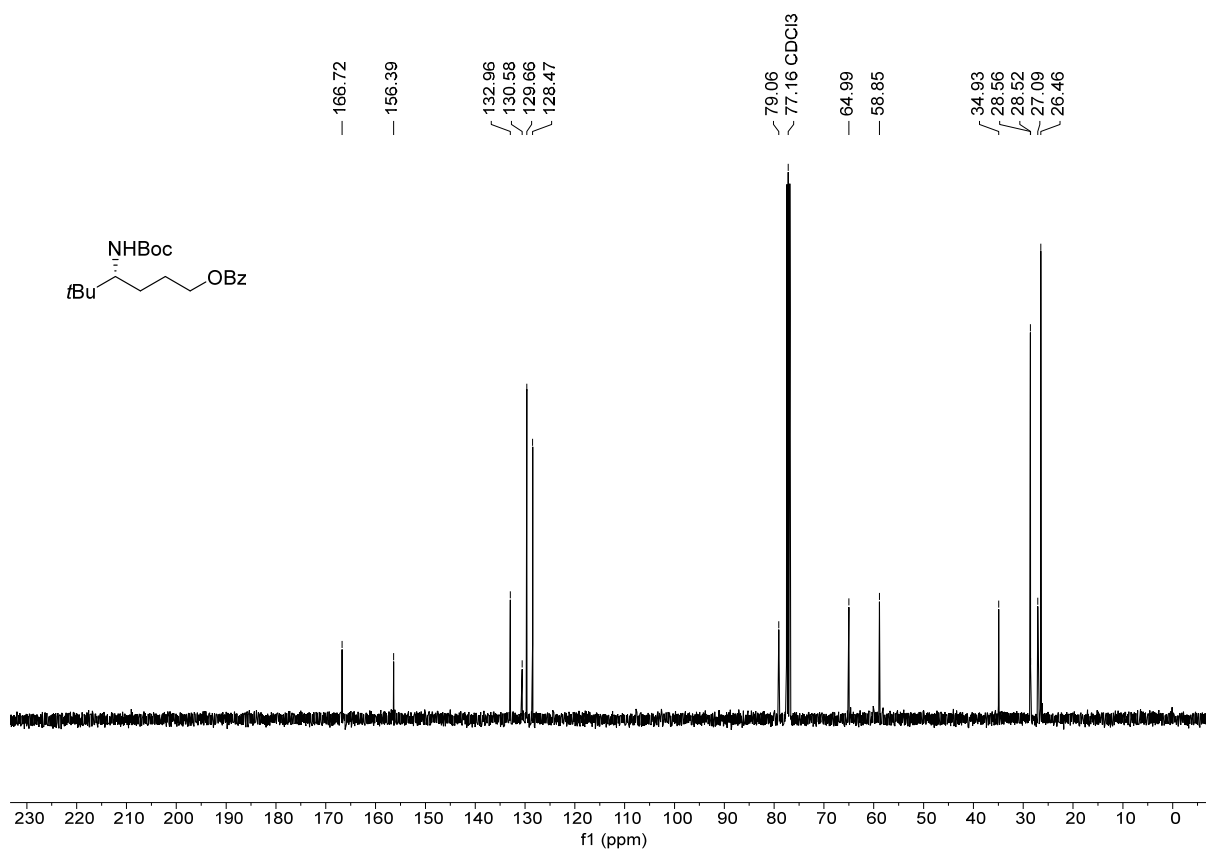
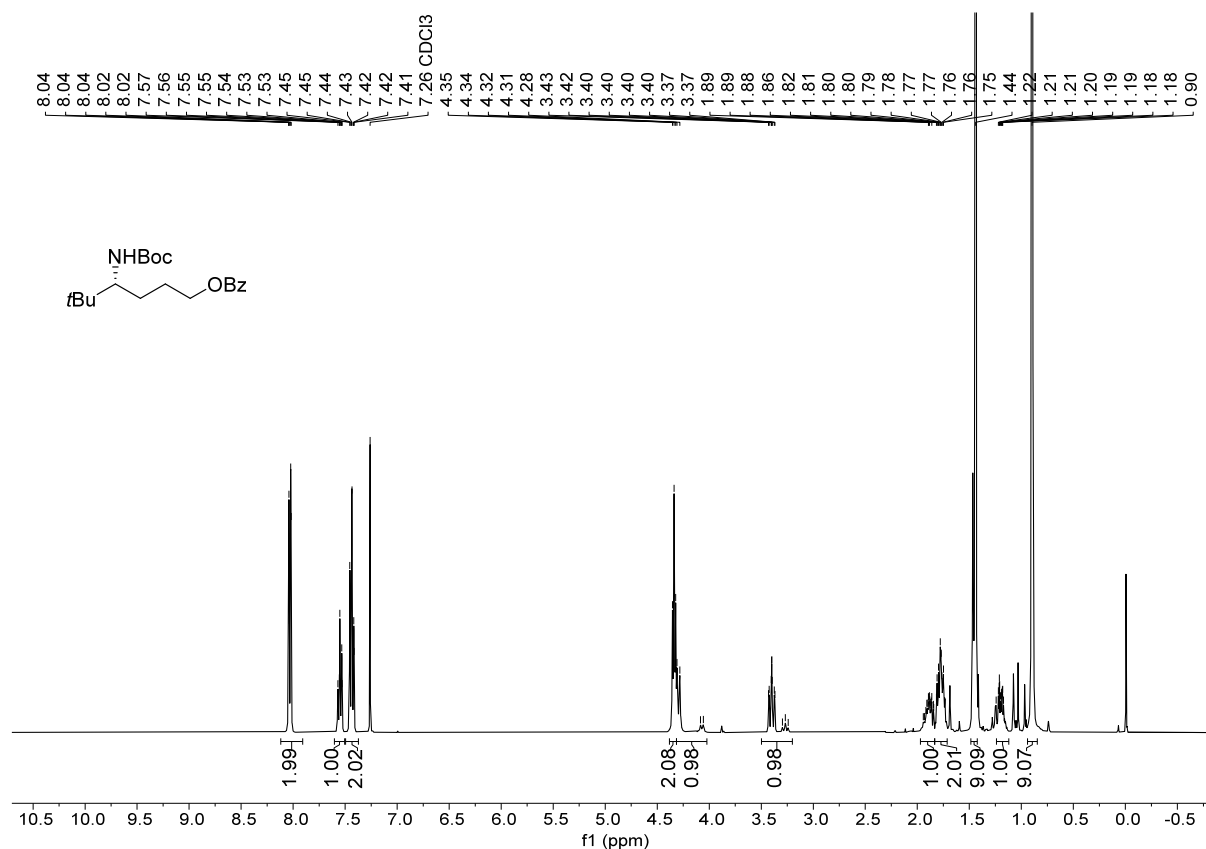


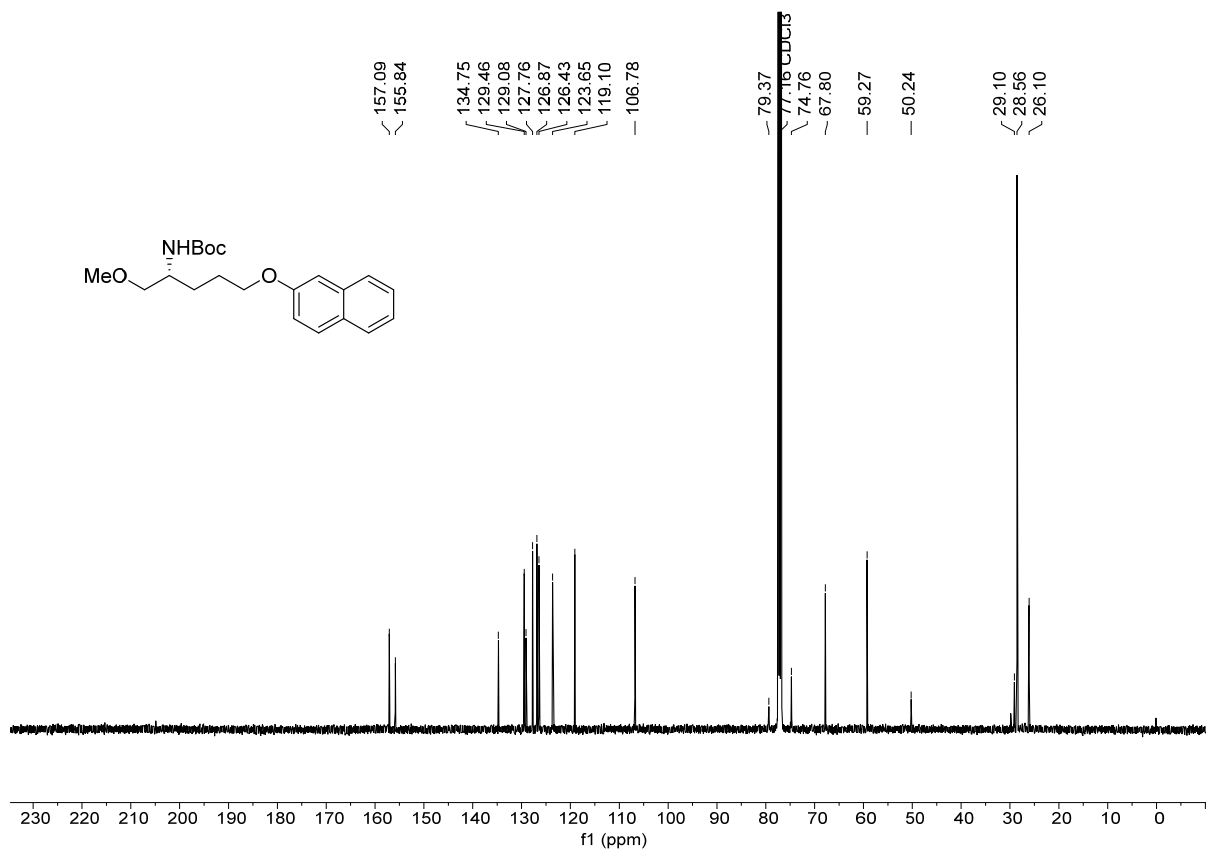
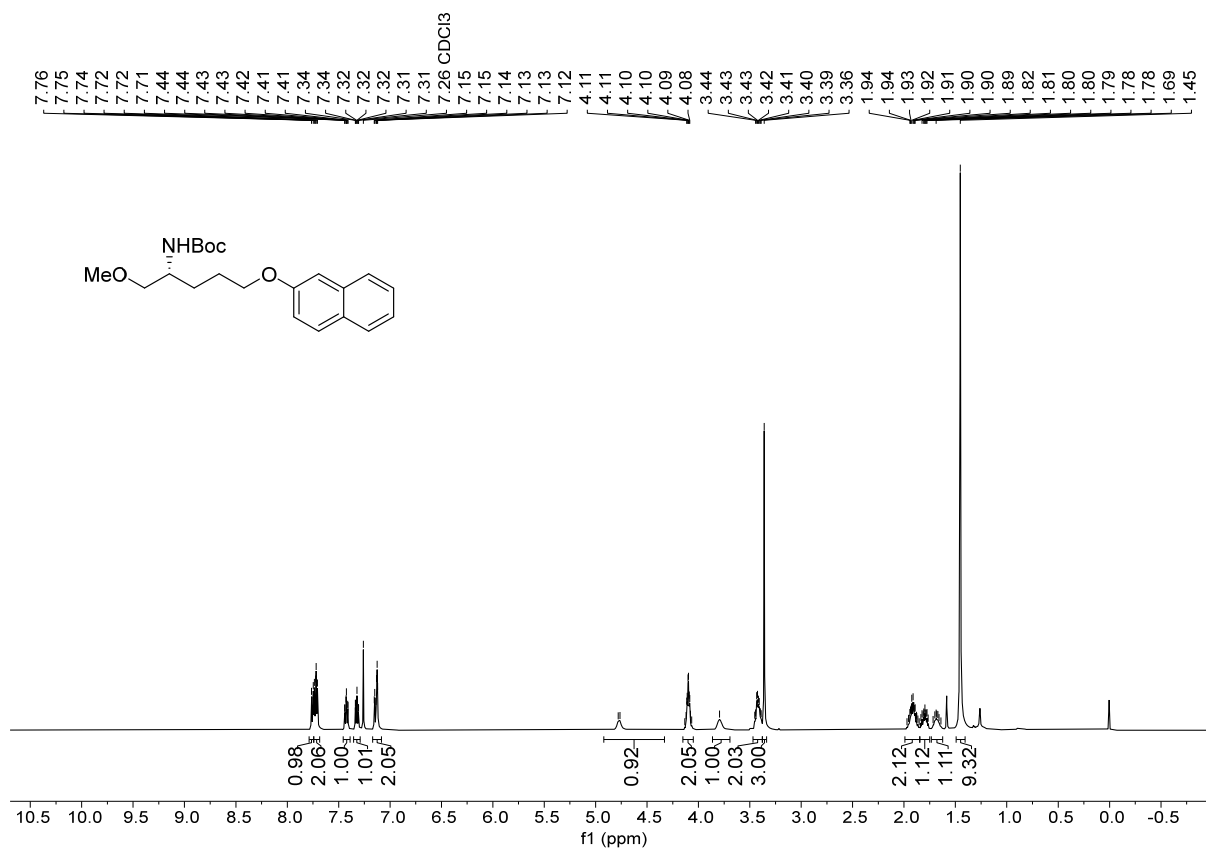


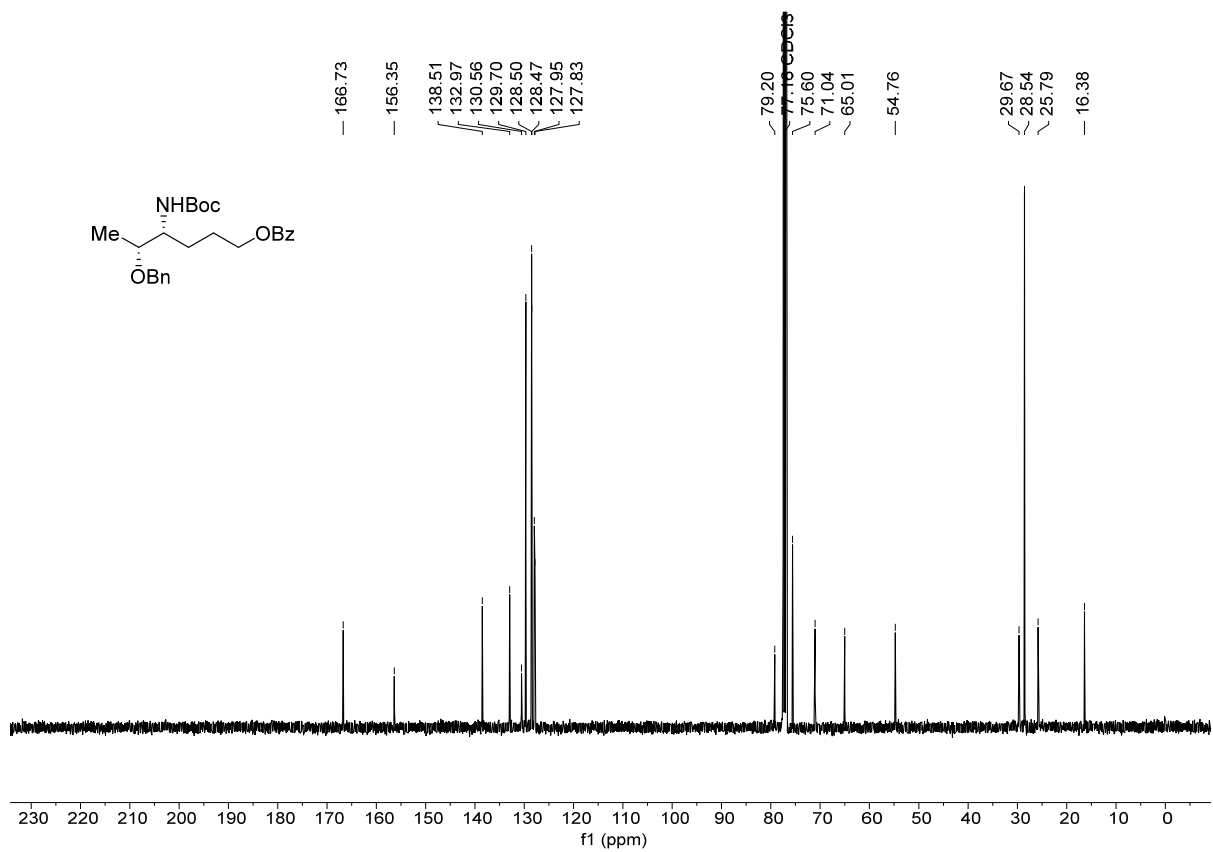
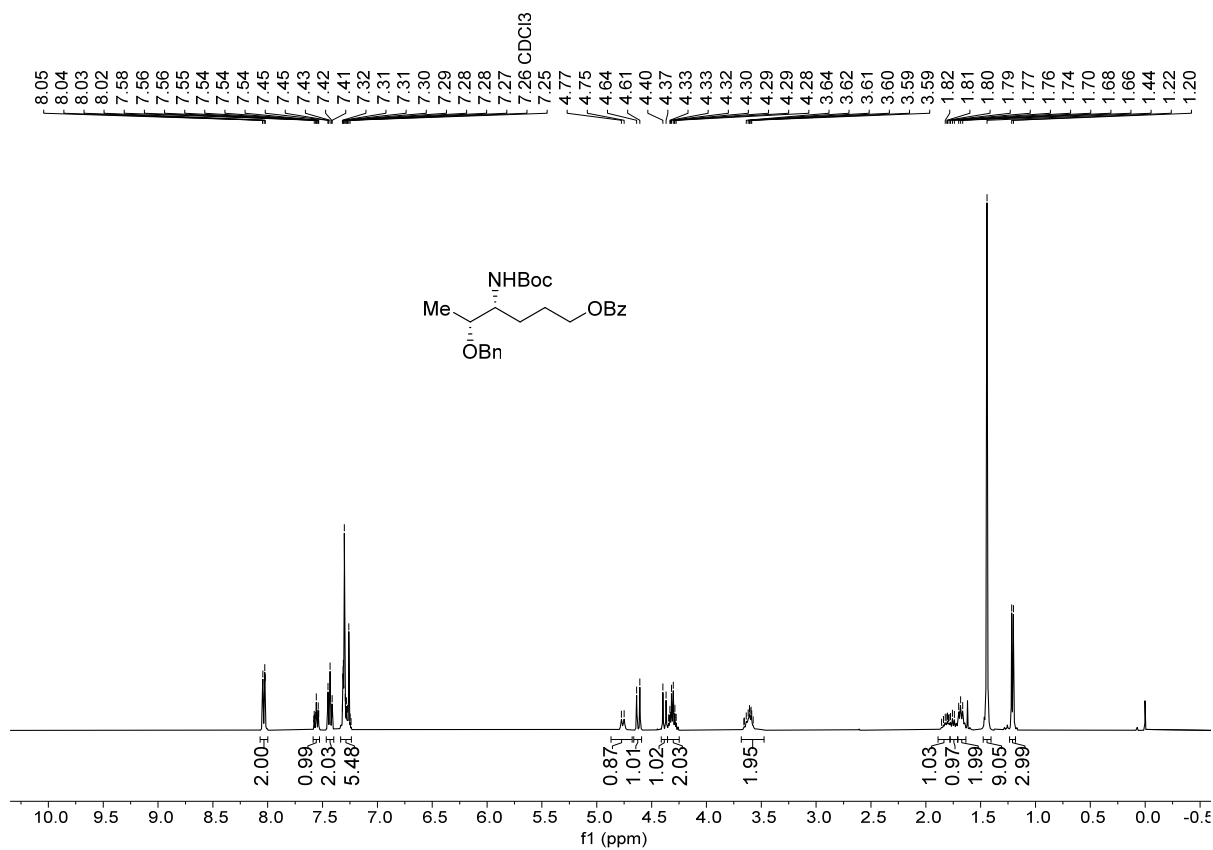


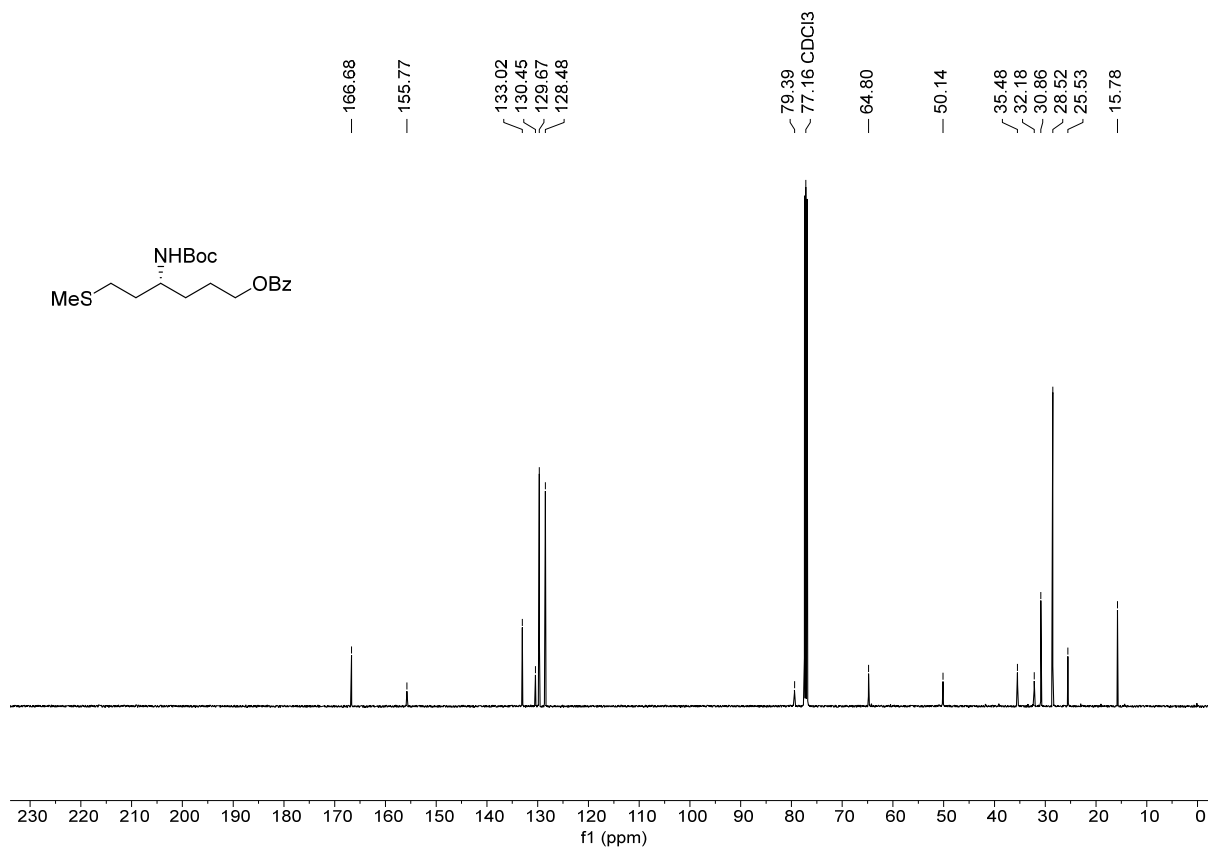
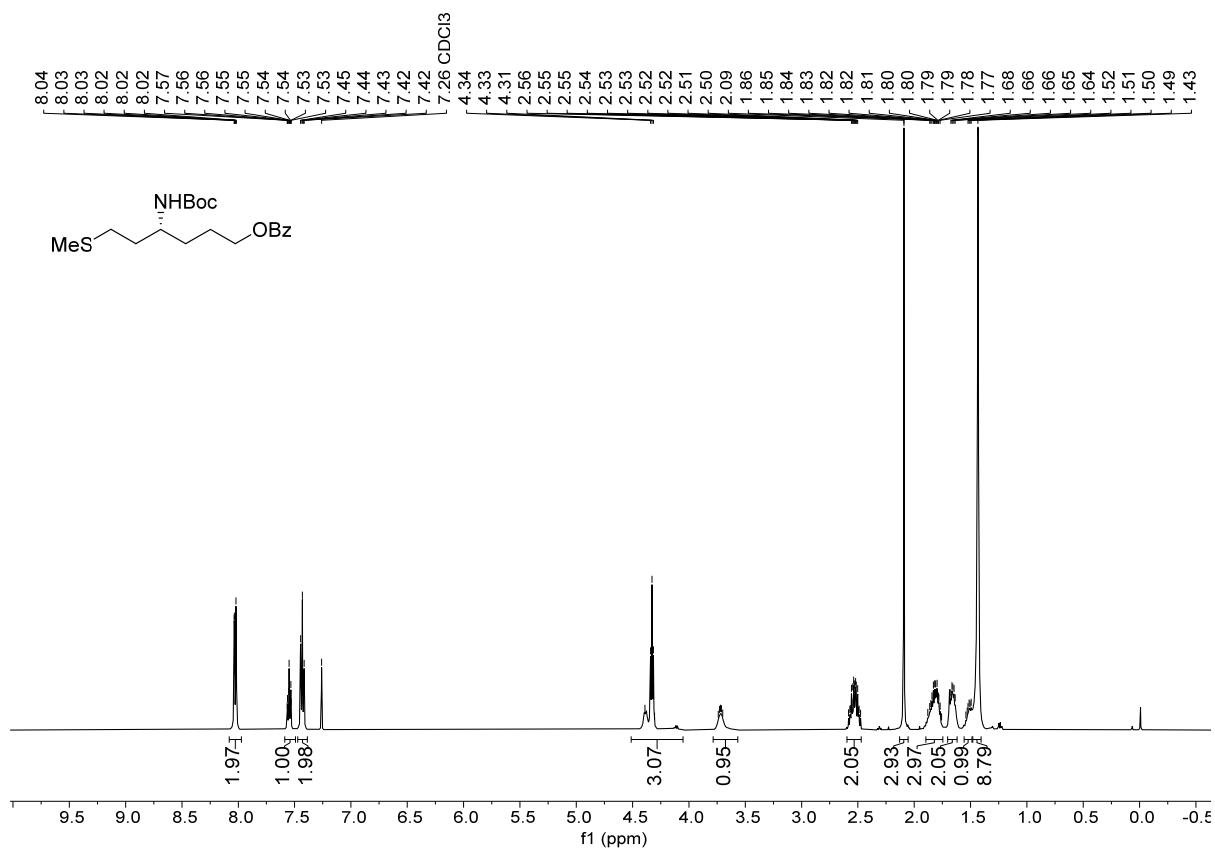


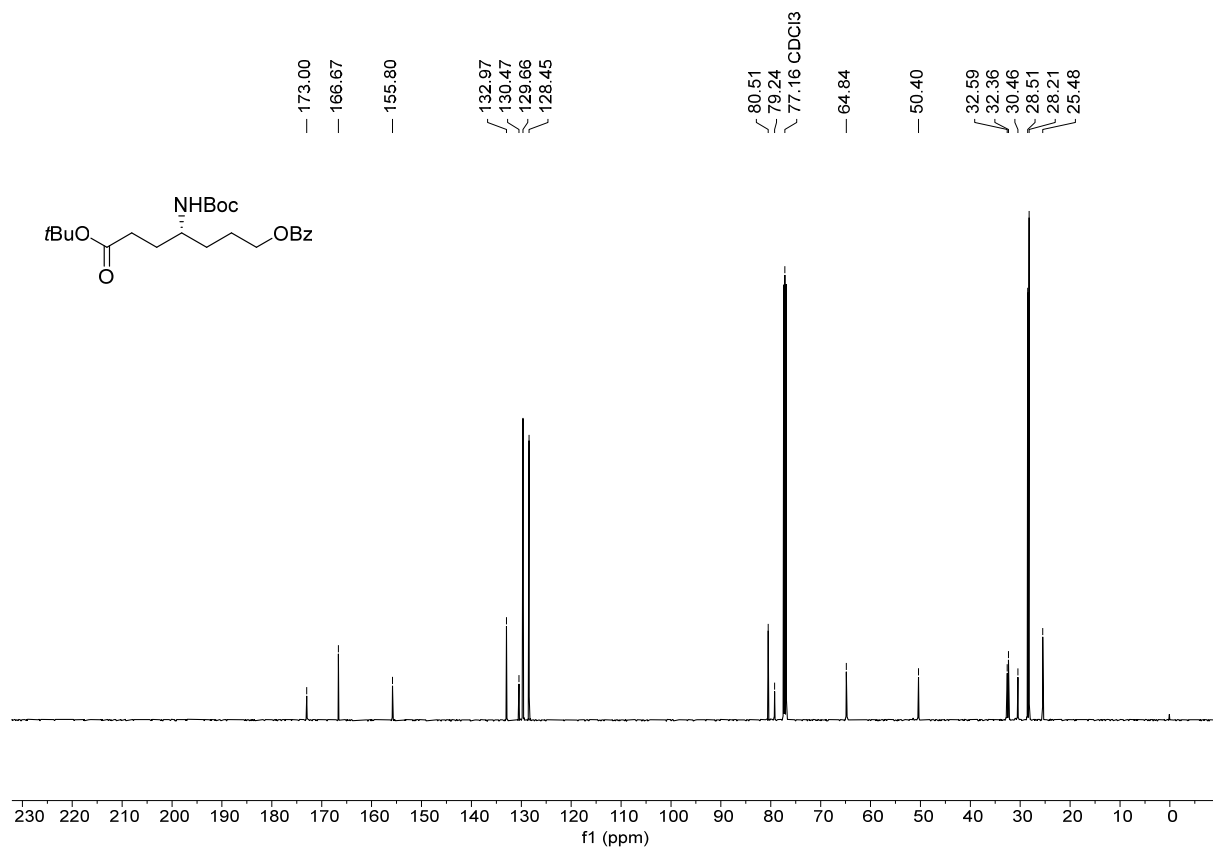
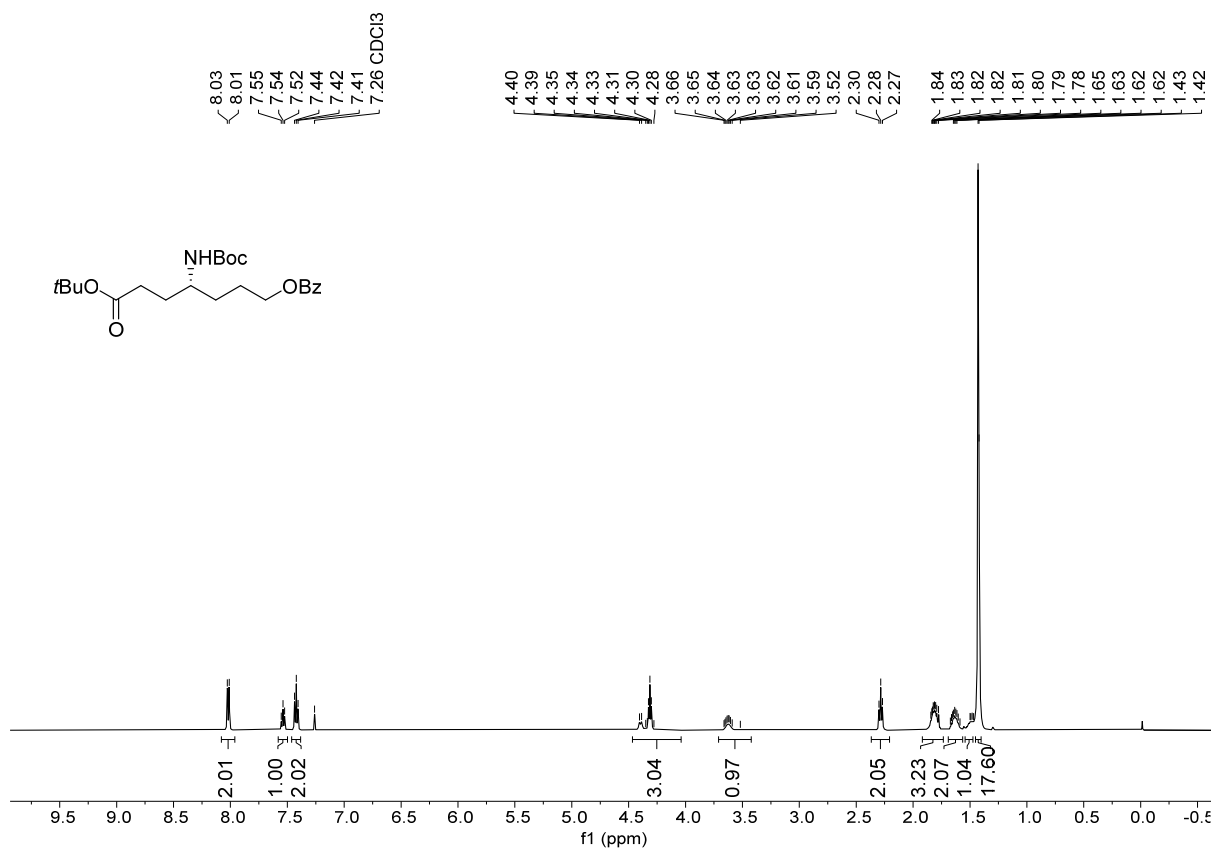


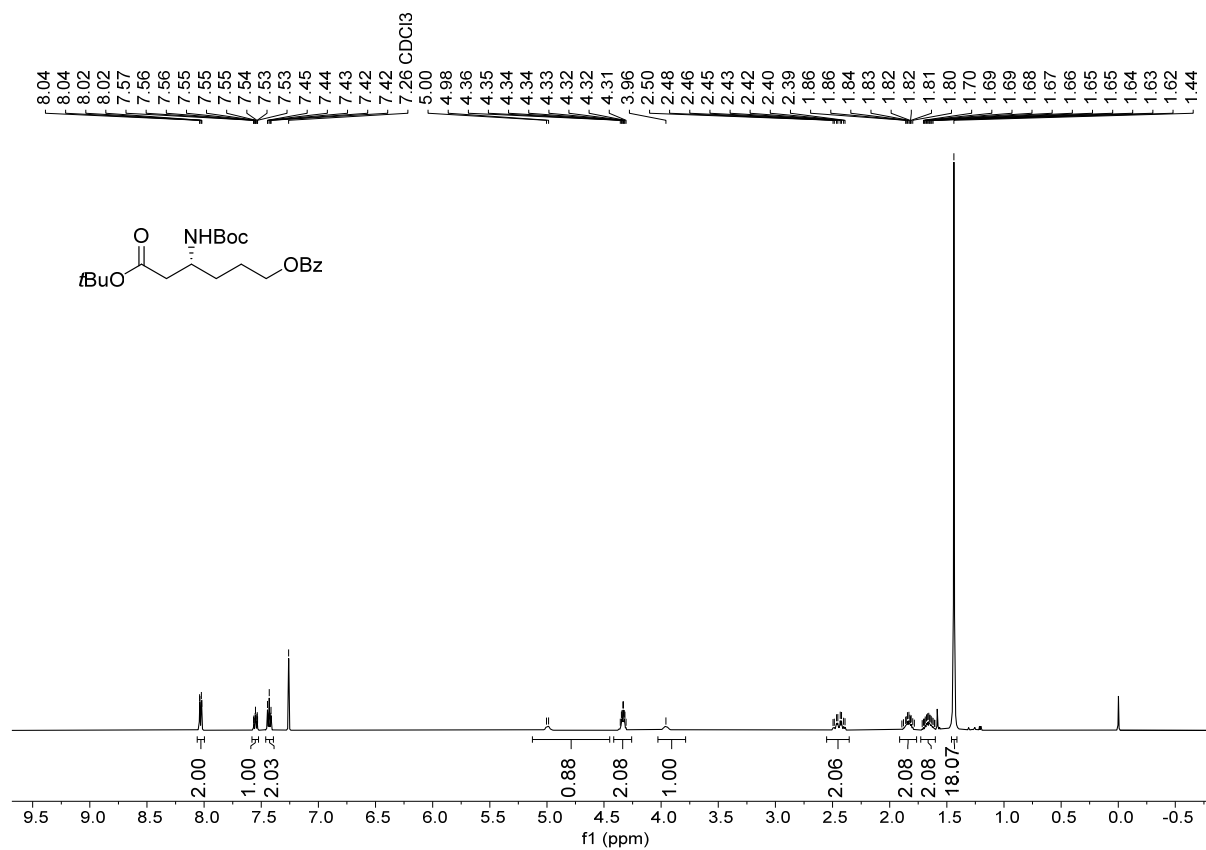




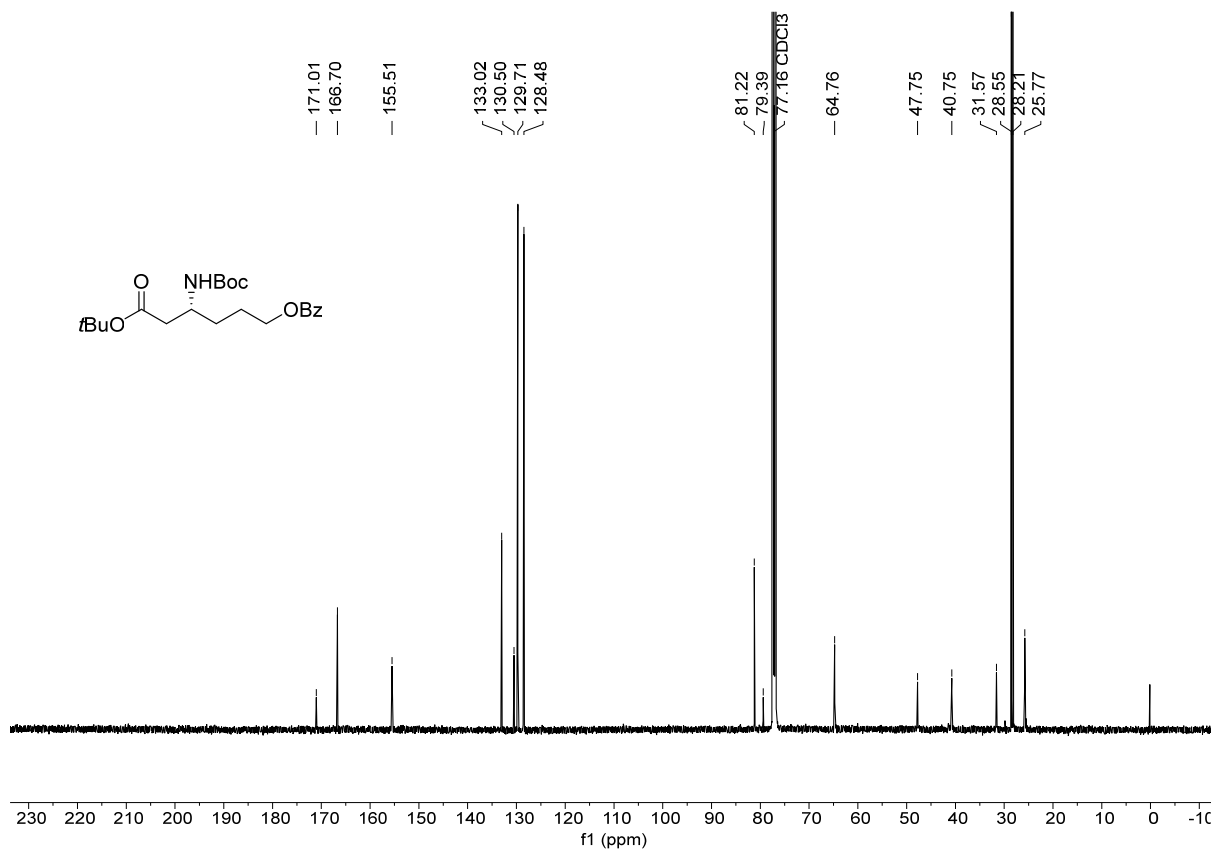




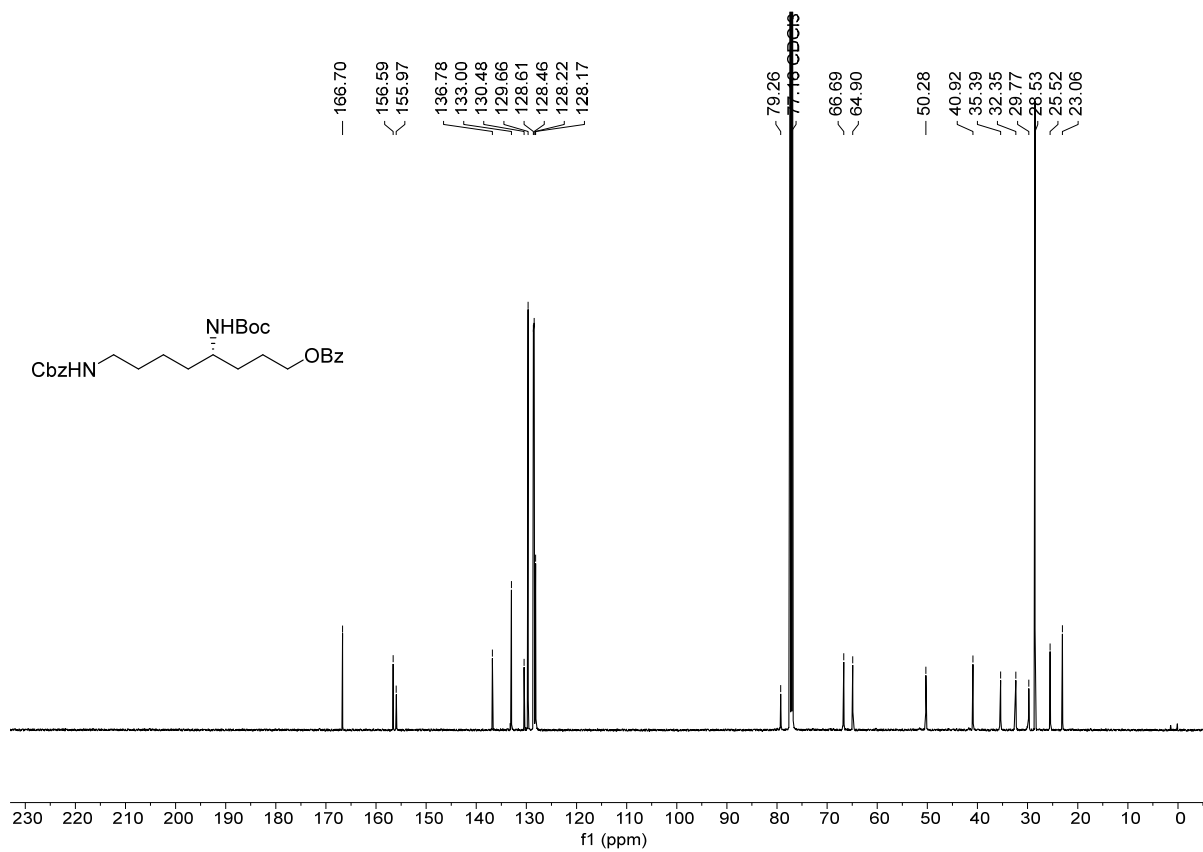
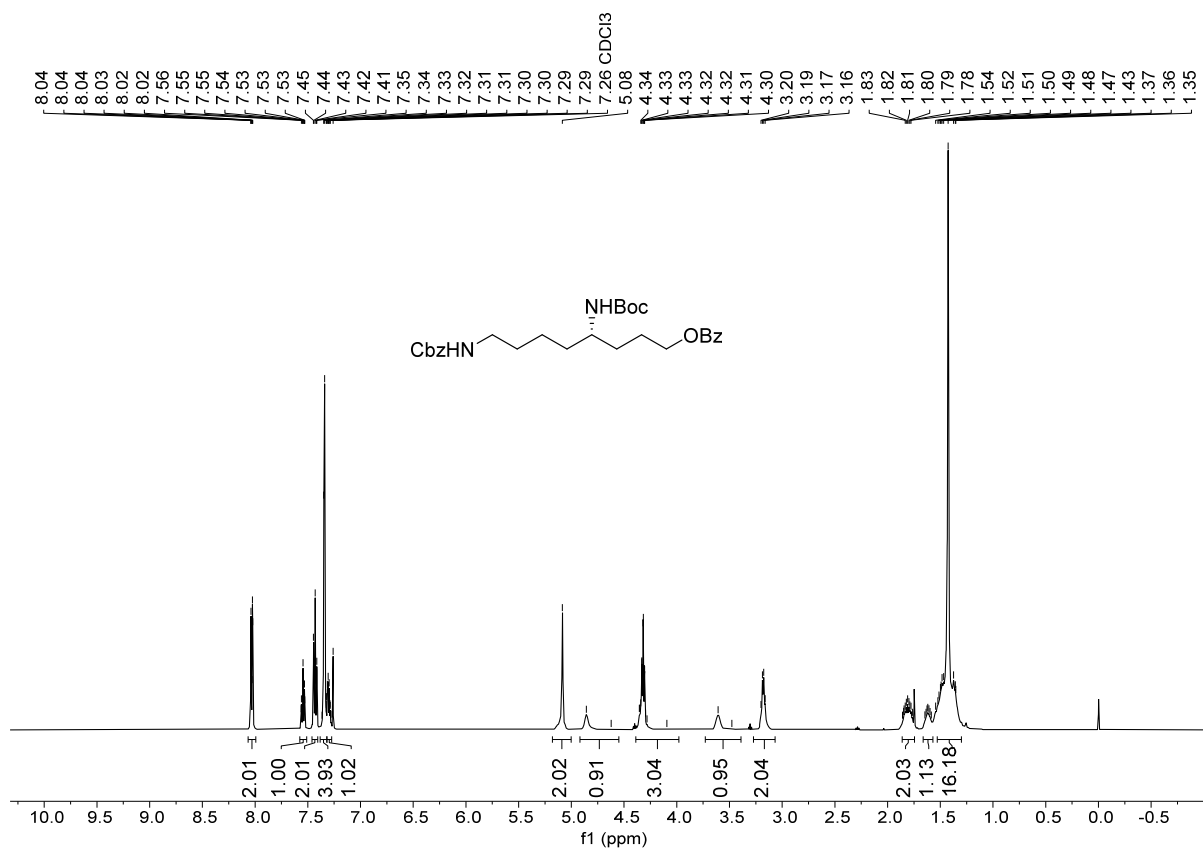


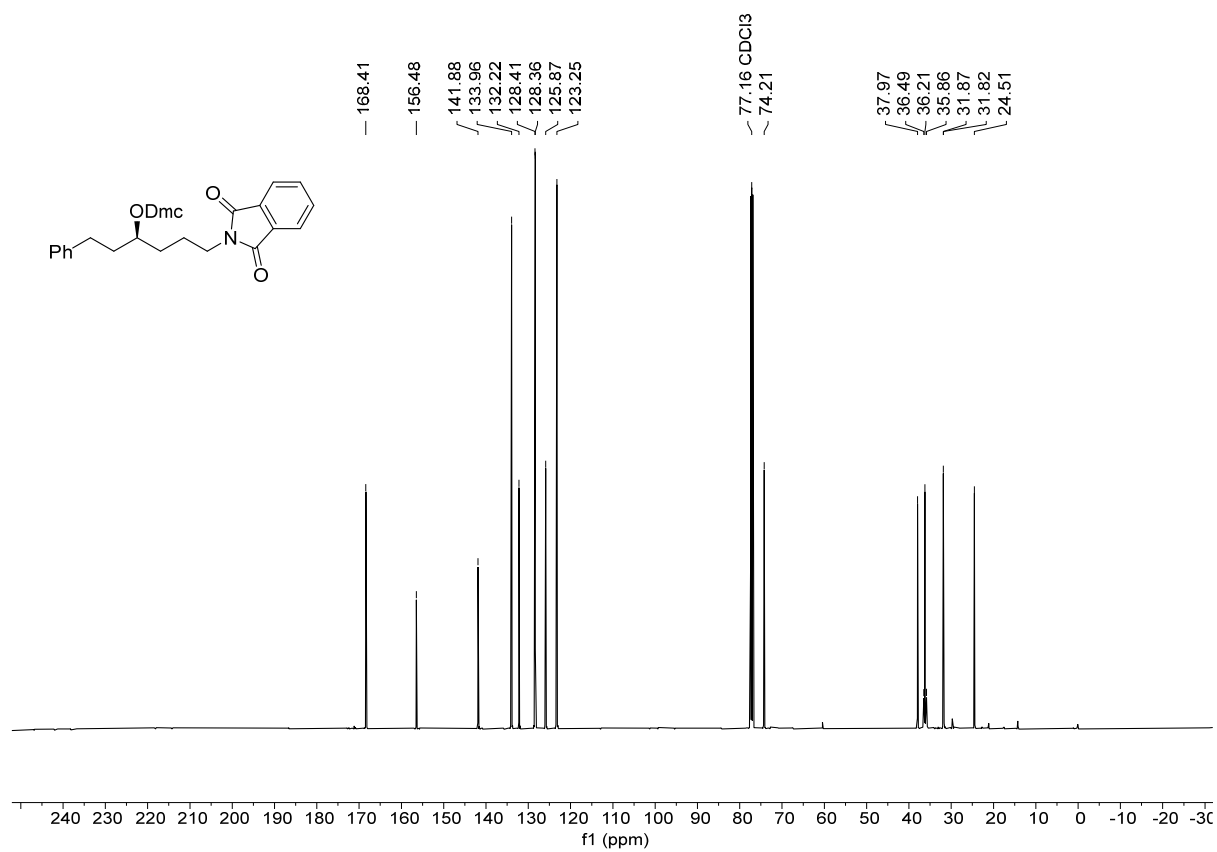
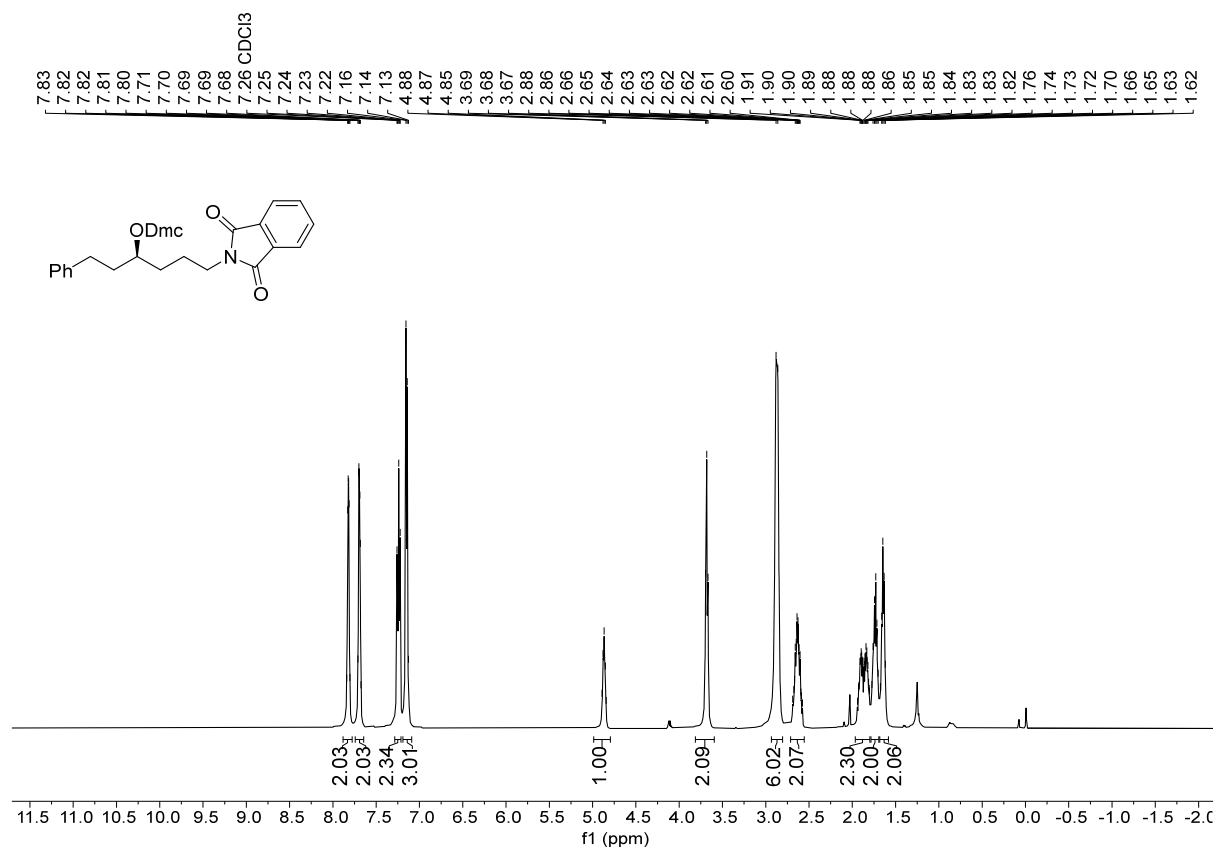


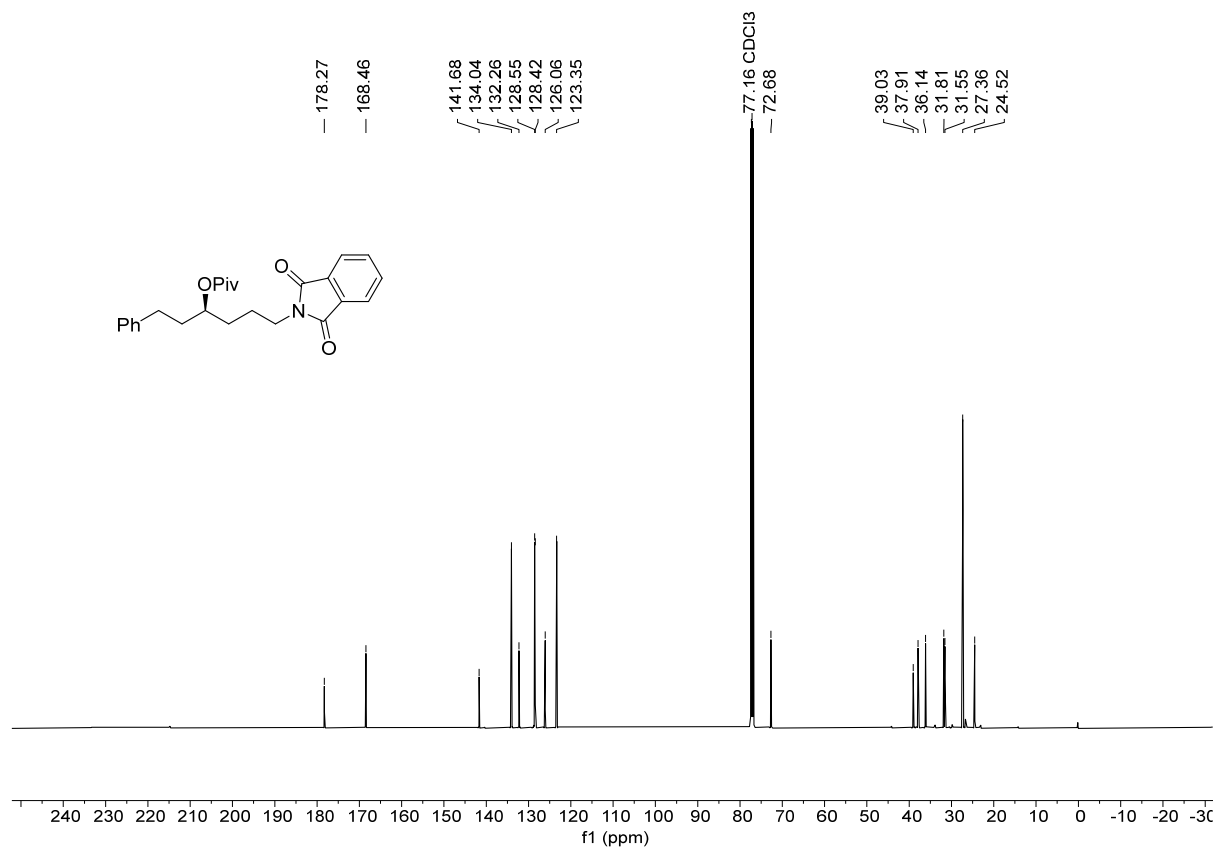
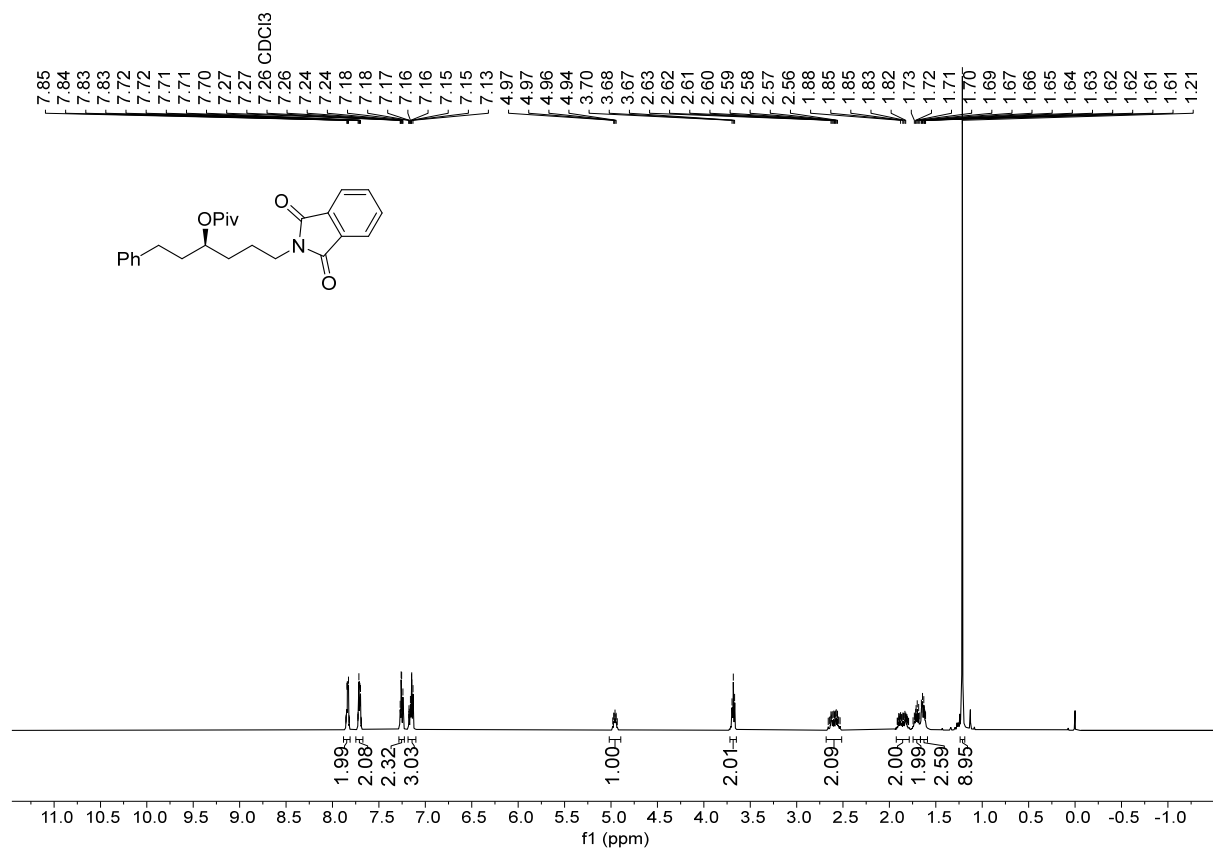
¹H NMR (500 MHz, CDCl₃) of **67**

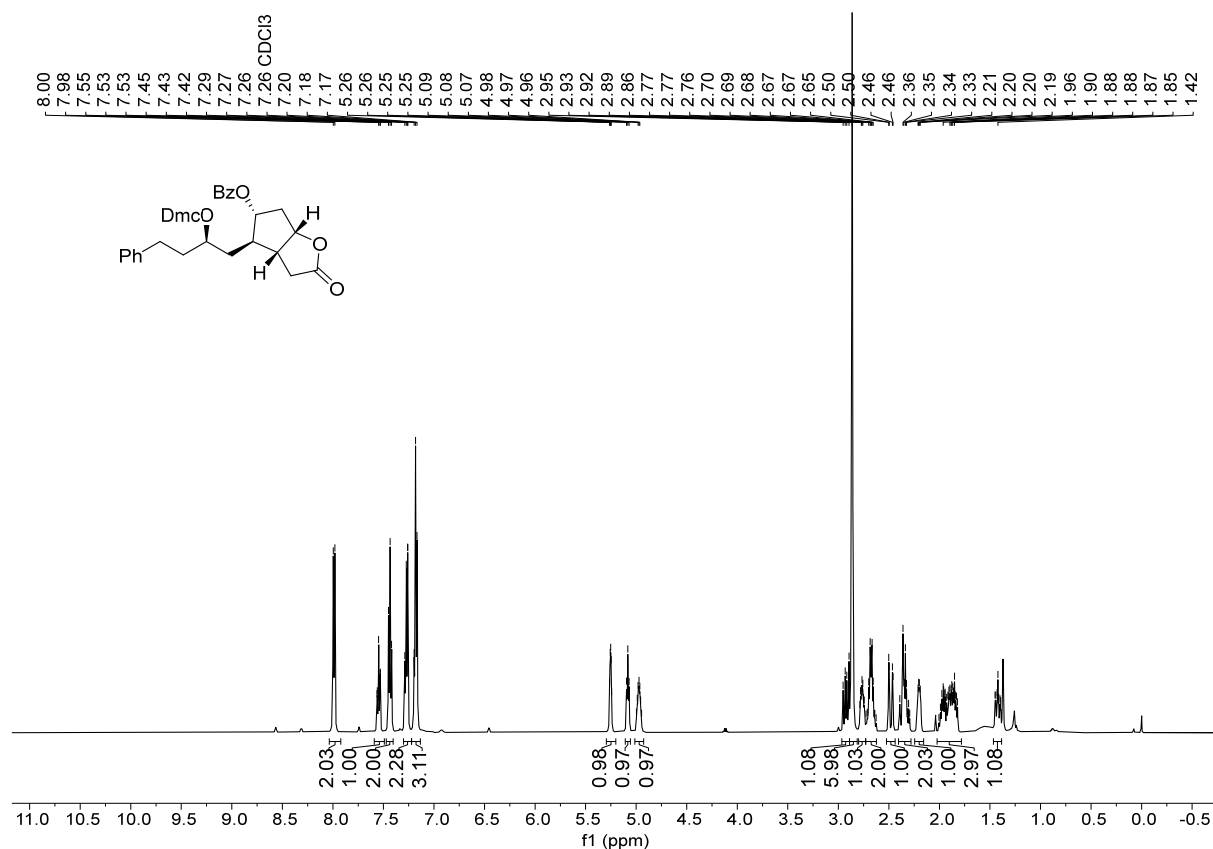


¹³C {¹H} NMR (125 MHz, CDCl₃) of **67**

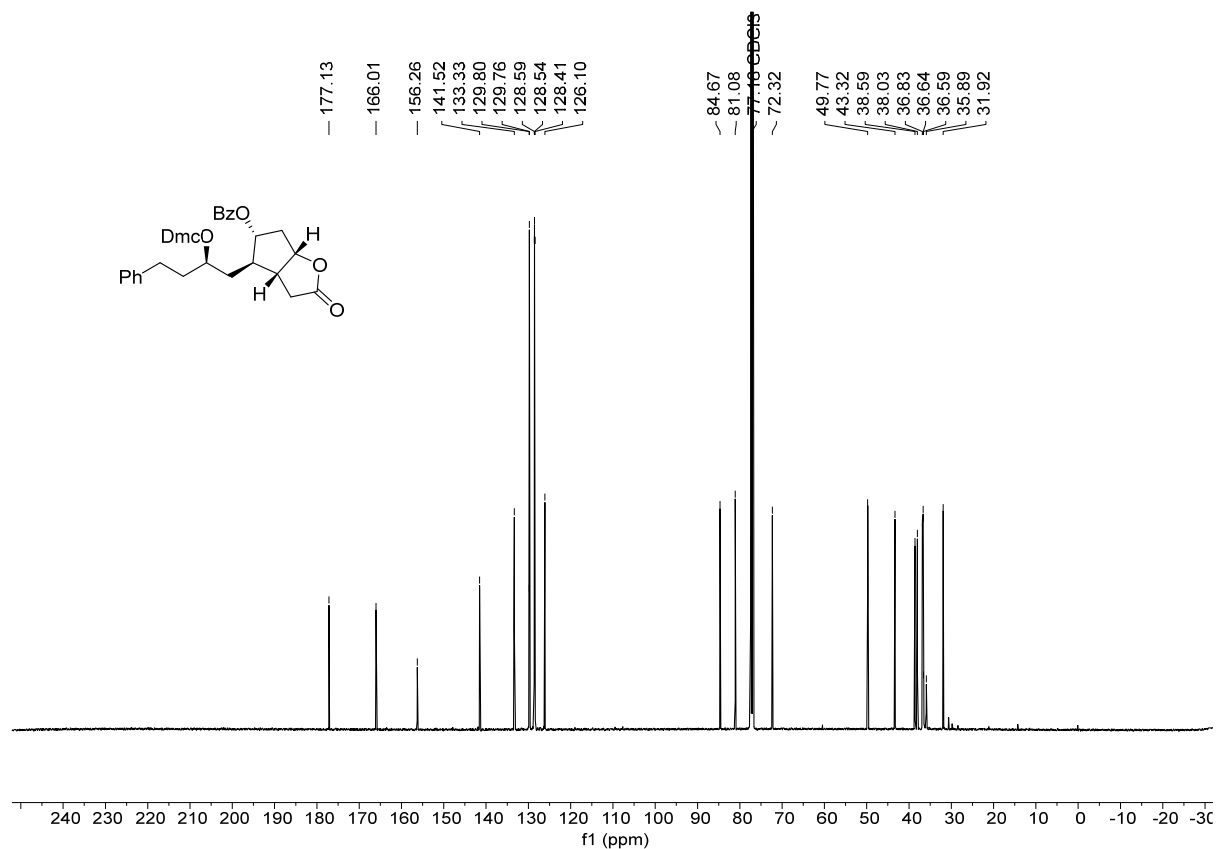




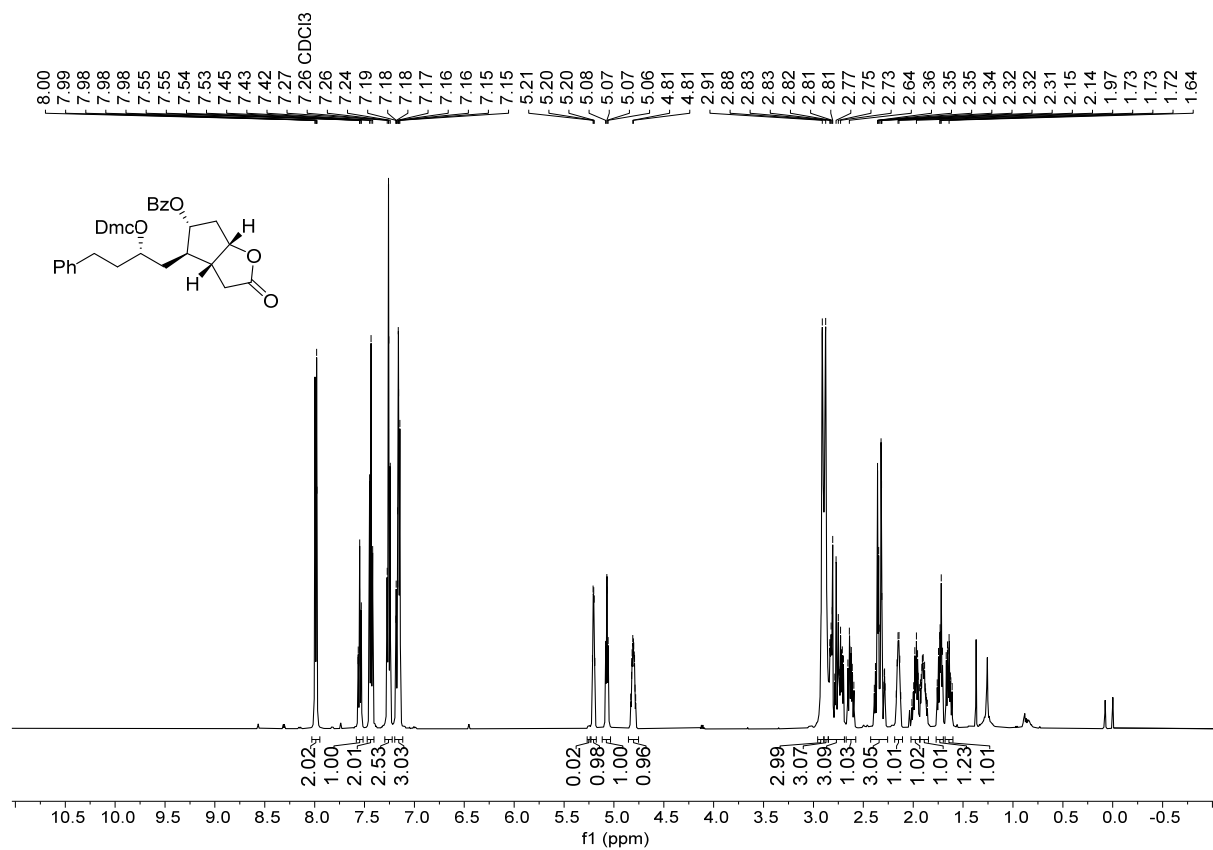




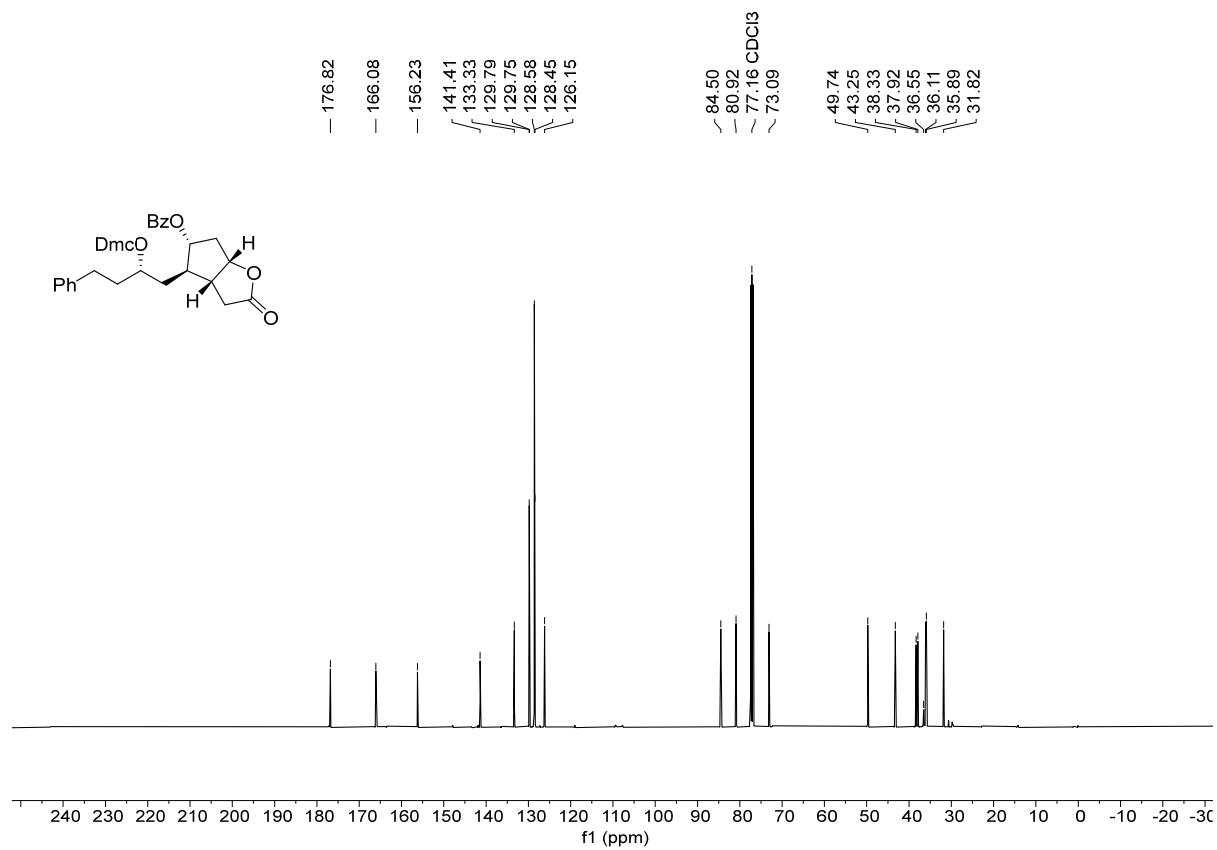
¹H NMR (500 MHz, CDCl₃) of **71**



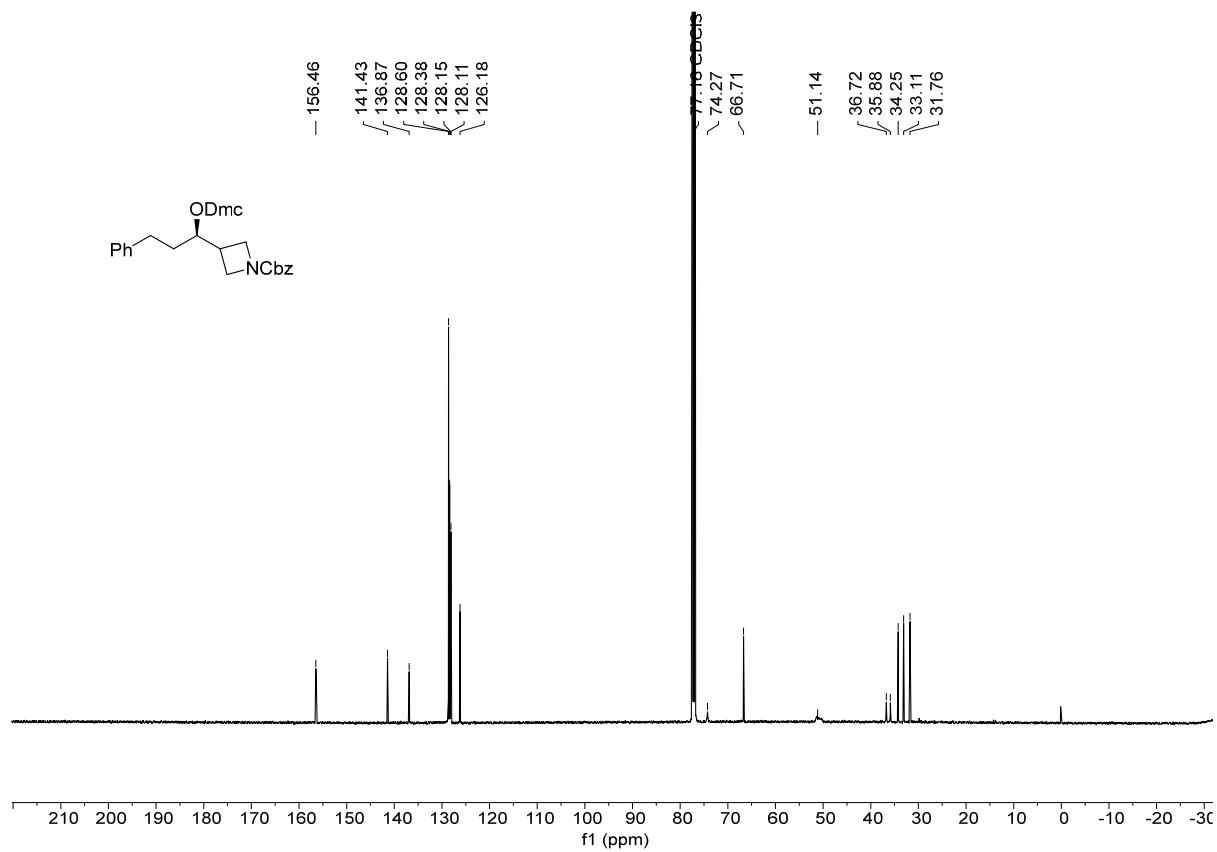
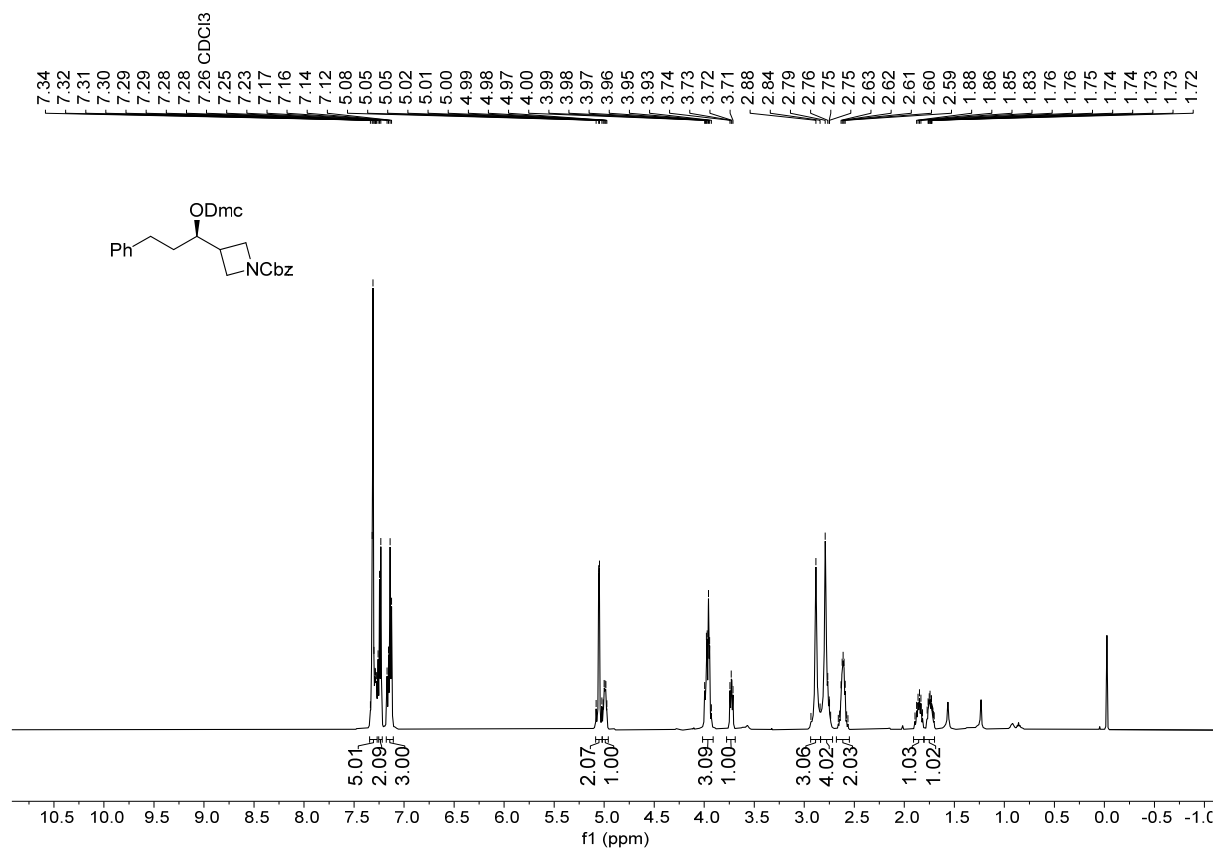
¹³C {¹H} NMR (125 MHz, CDCl₃) of **71**

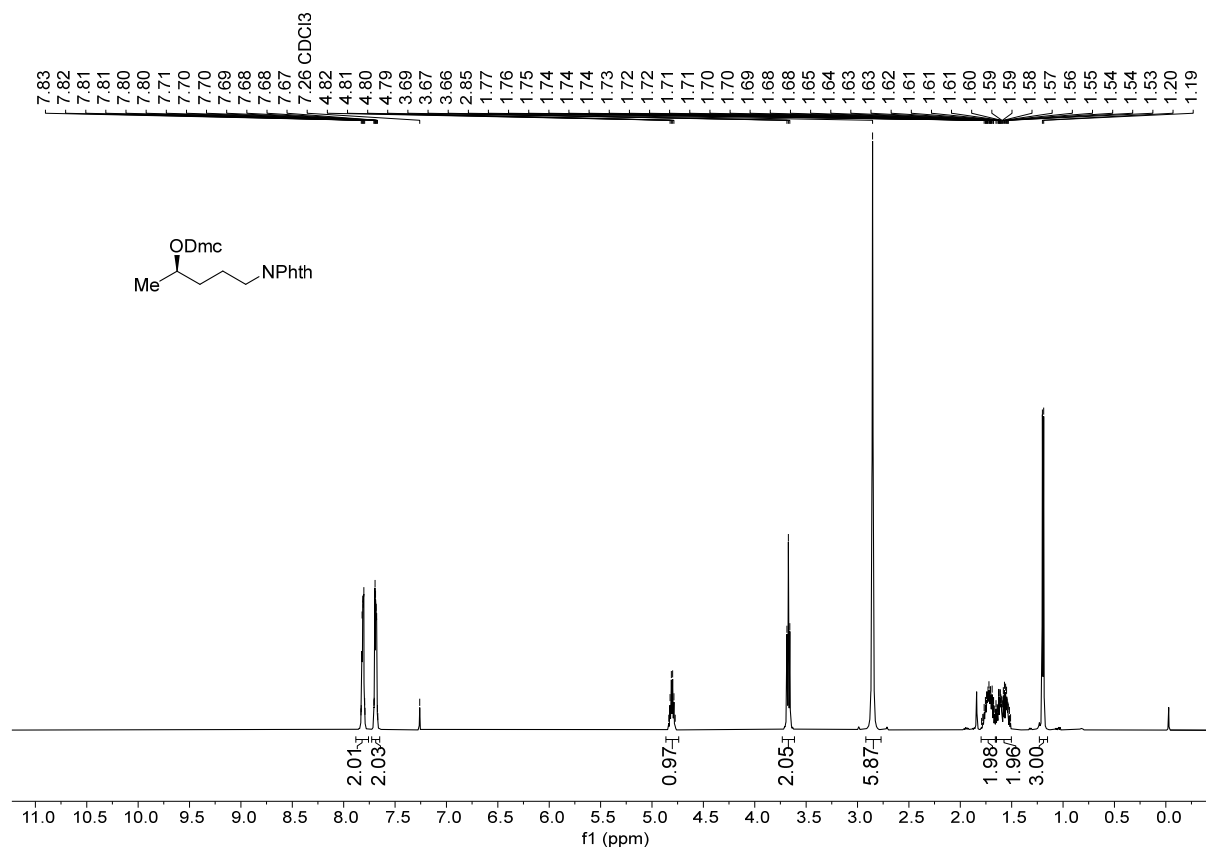


^1H NMR (500 MHz, CDCl_3) of **72**

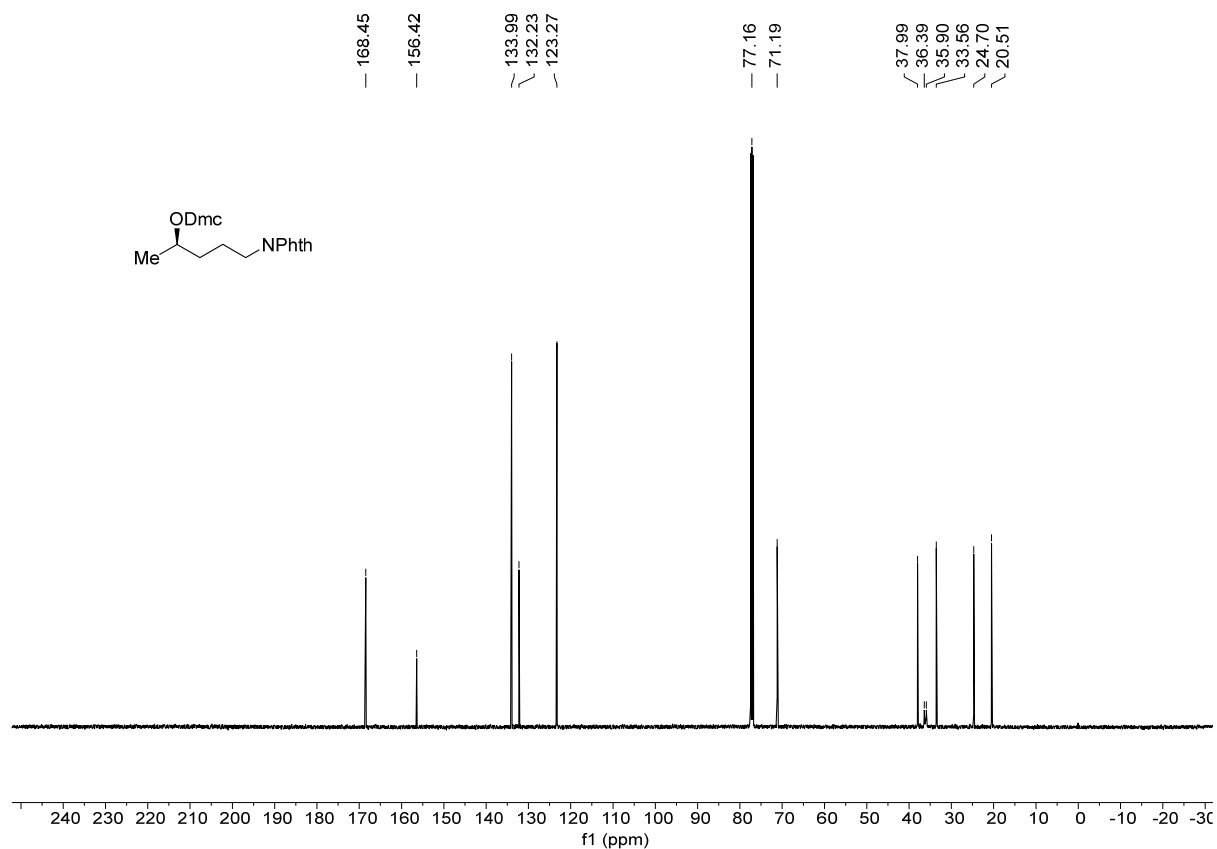


$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) of **72**

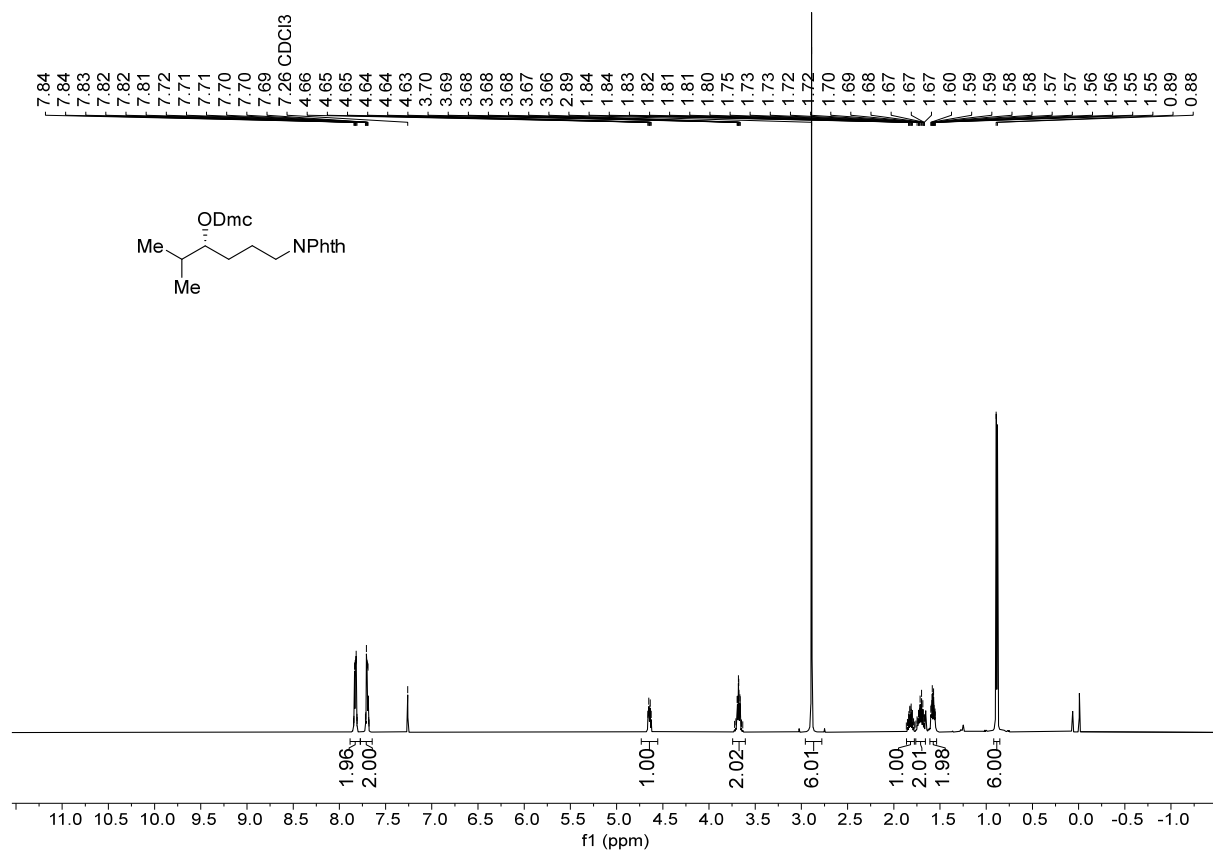




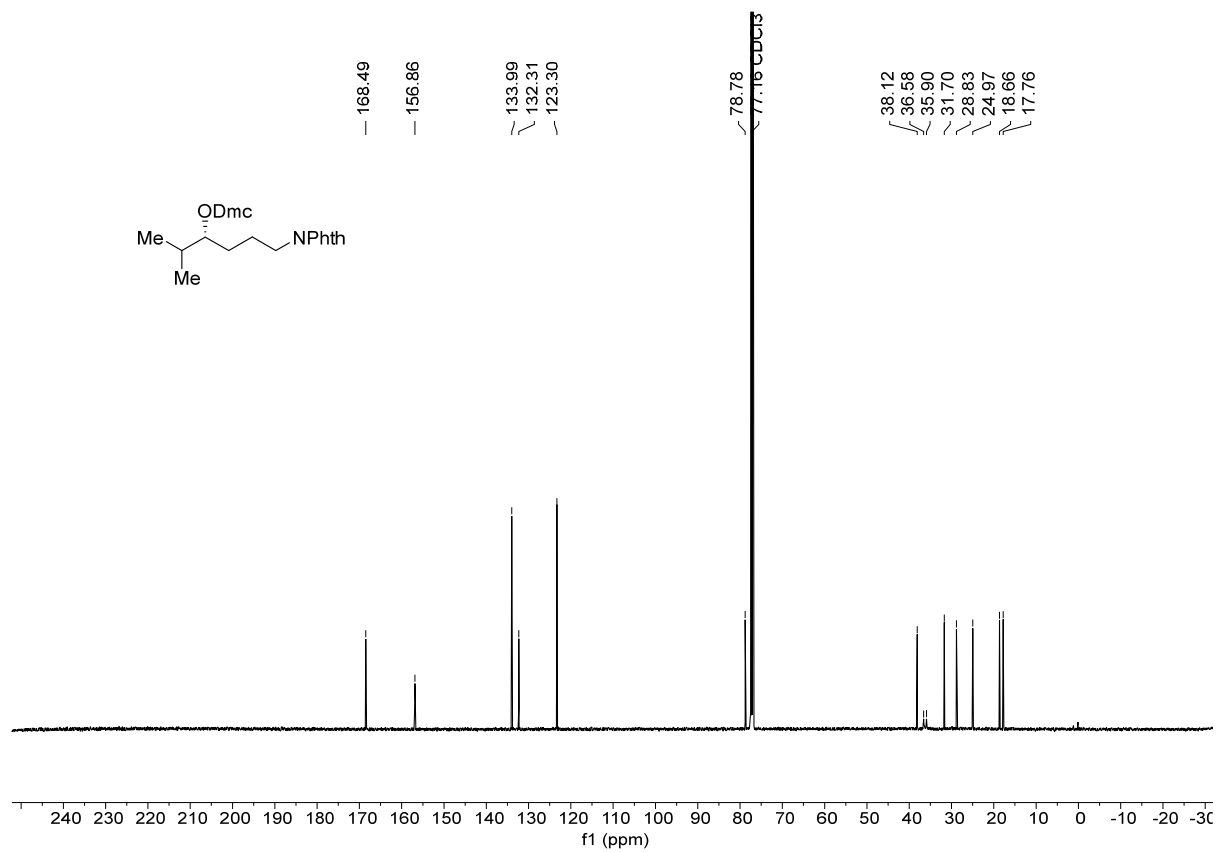
¹H NMR (500 MHz, CDCl₃) of **74**



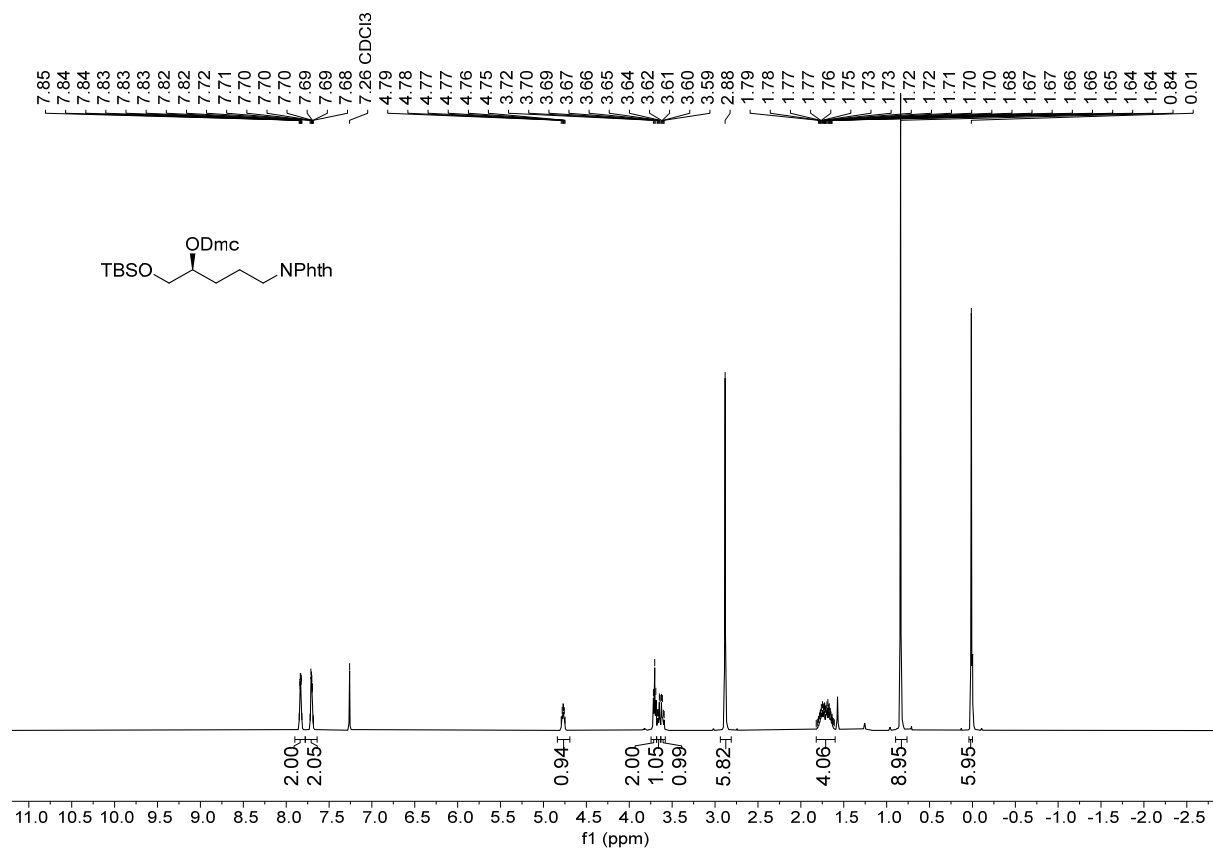
¹³C {¹H} NMR (125 MHz, CDCl₃) of **74**



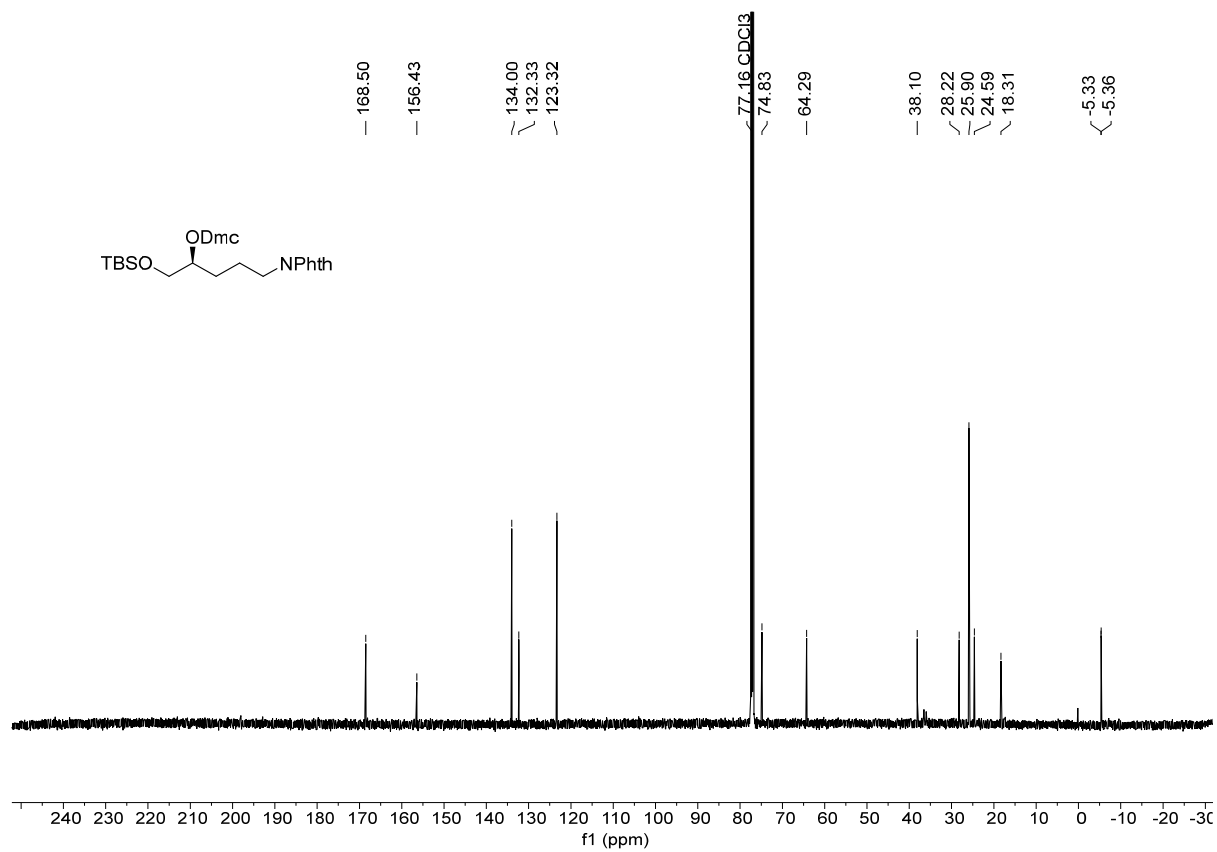
¹H NMR (500 MHz, CDCl₃) of **75**



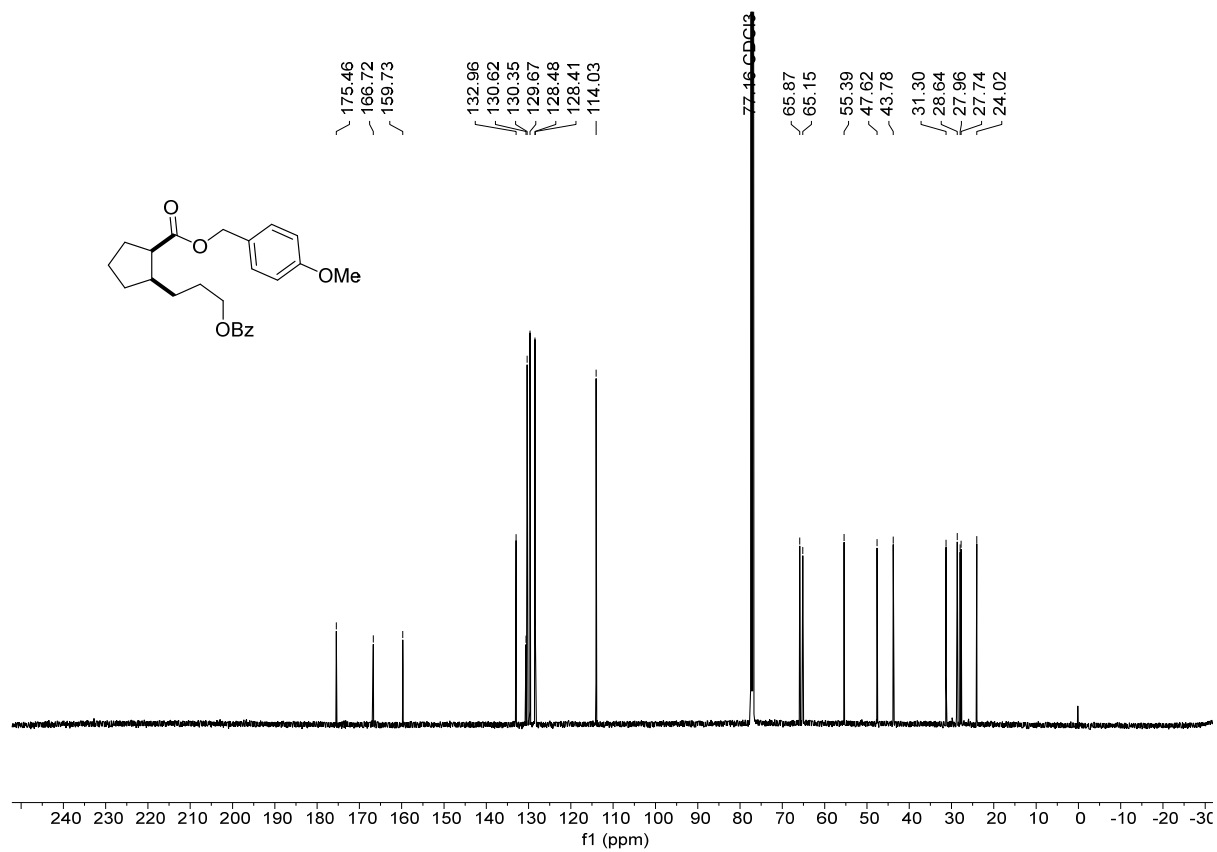
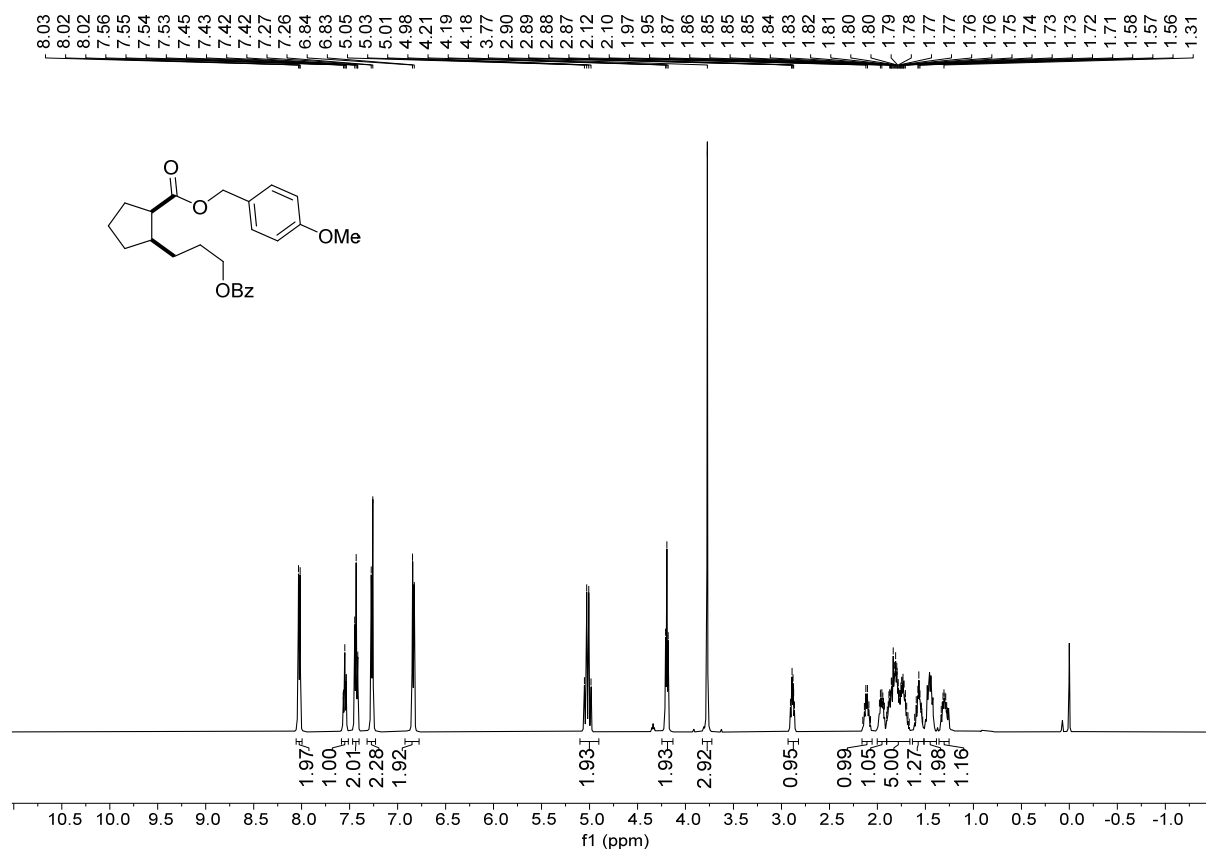
¹³C{¹H} NMR (125 MHz, CDCl₃) of **75**

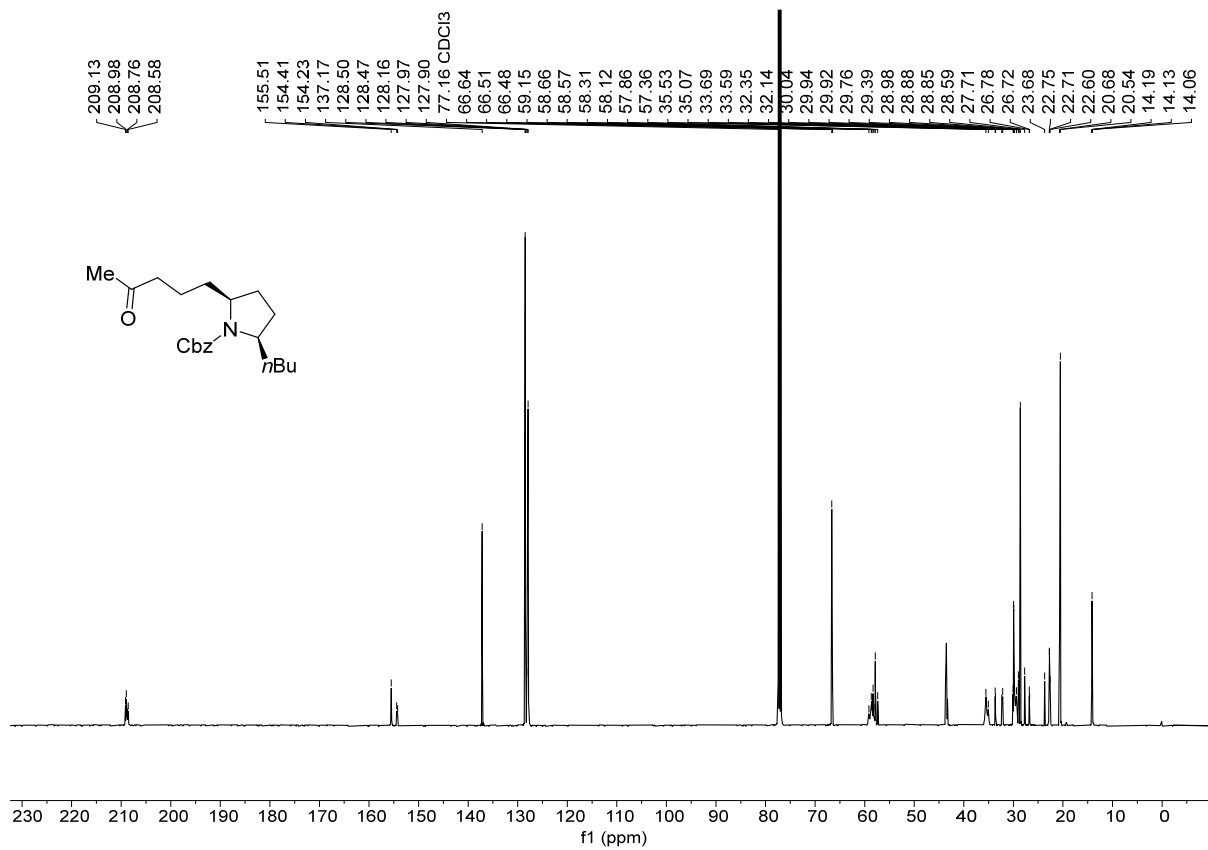
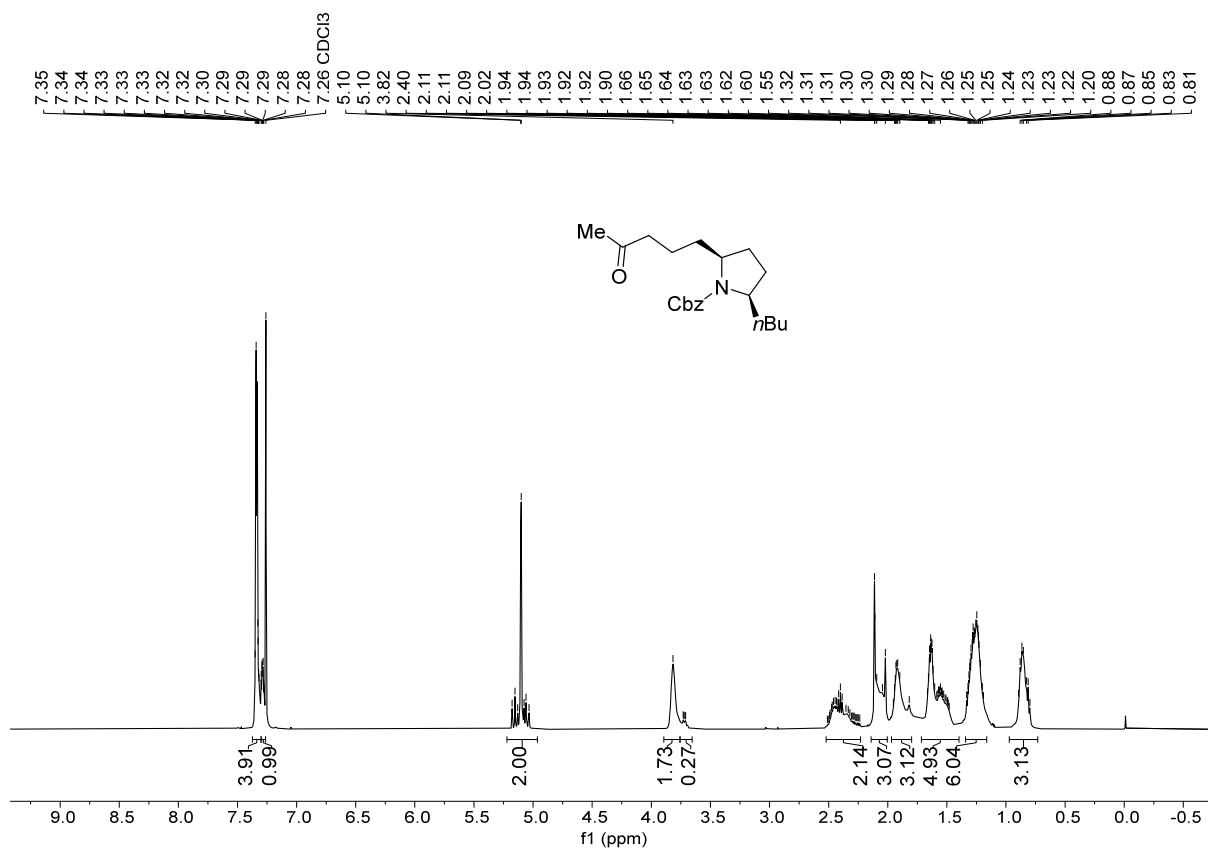


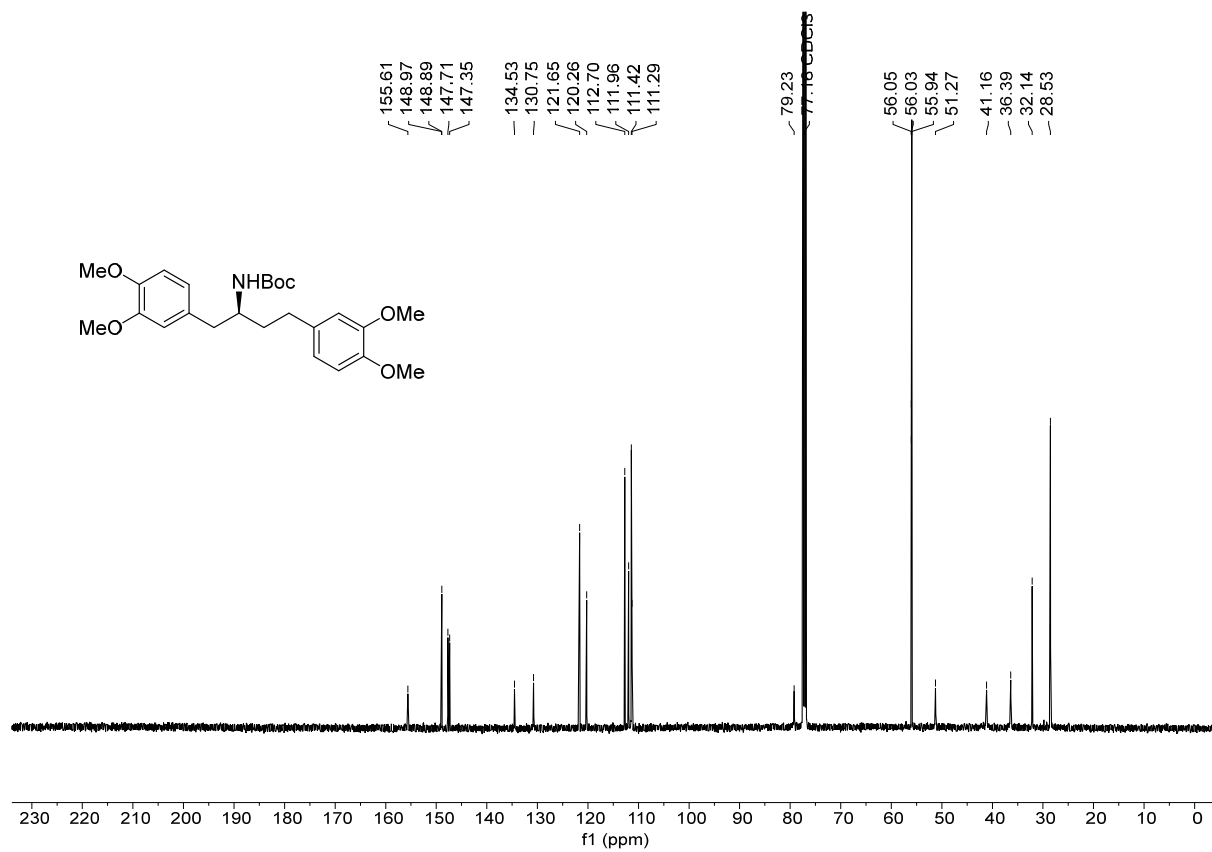
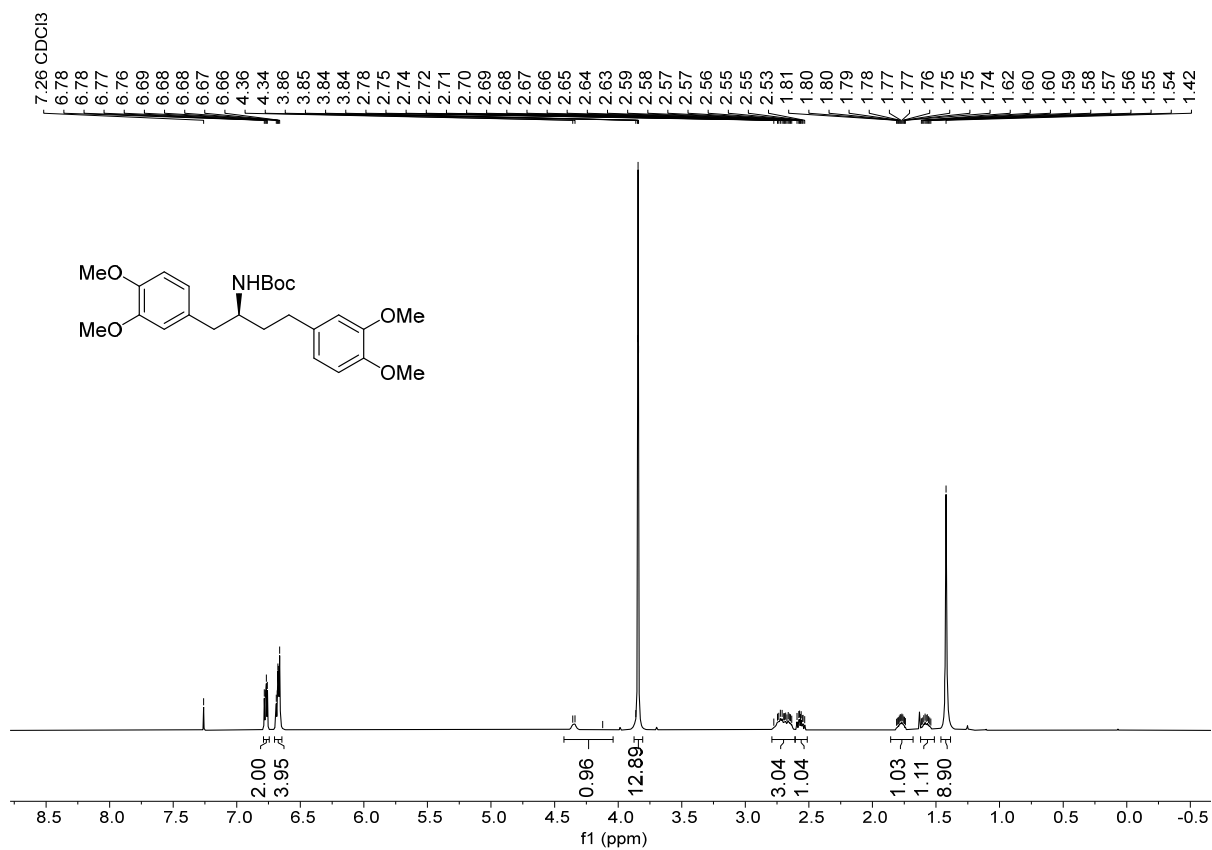
¹H NMR (500 MHz, CDCl₃) of **76**

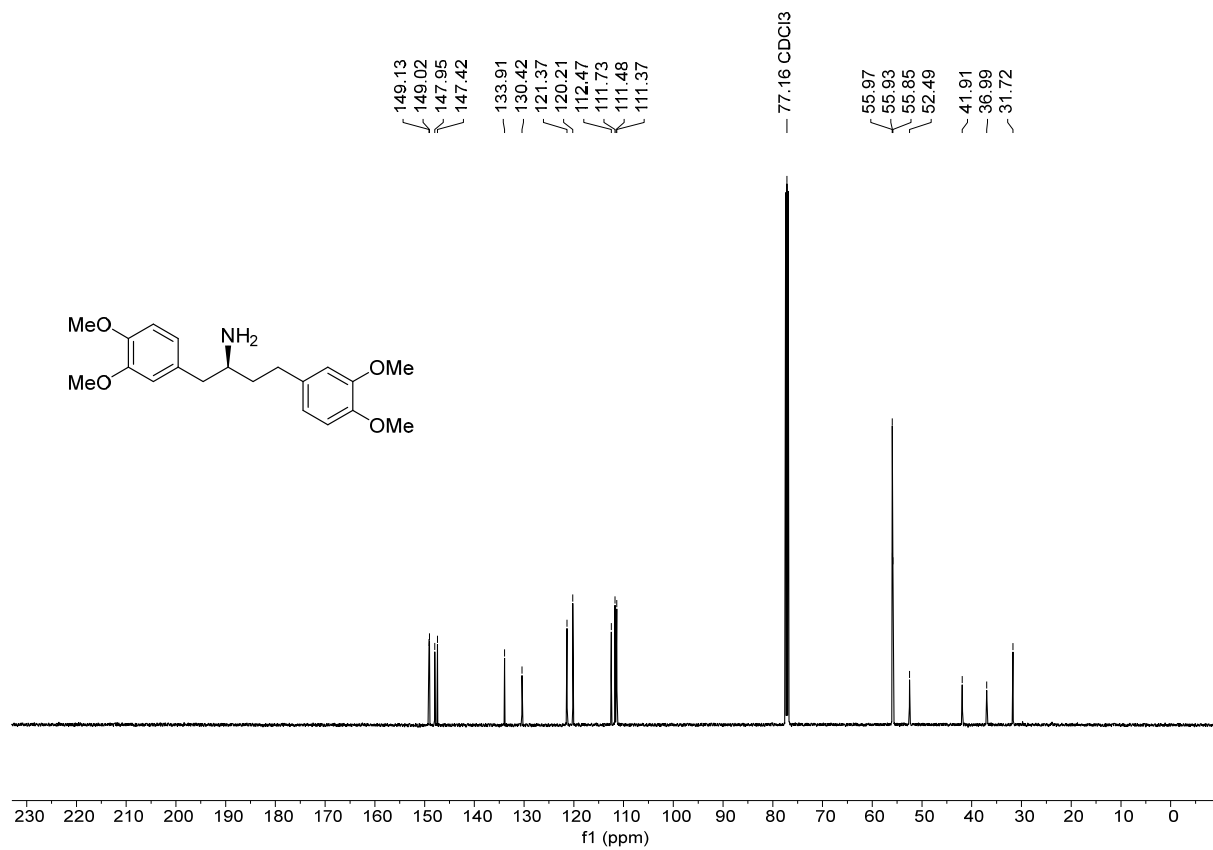
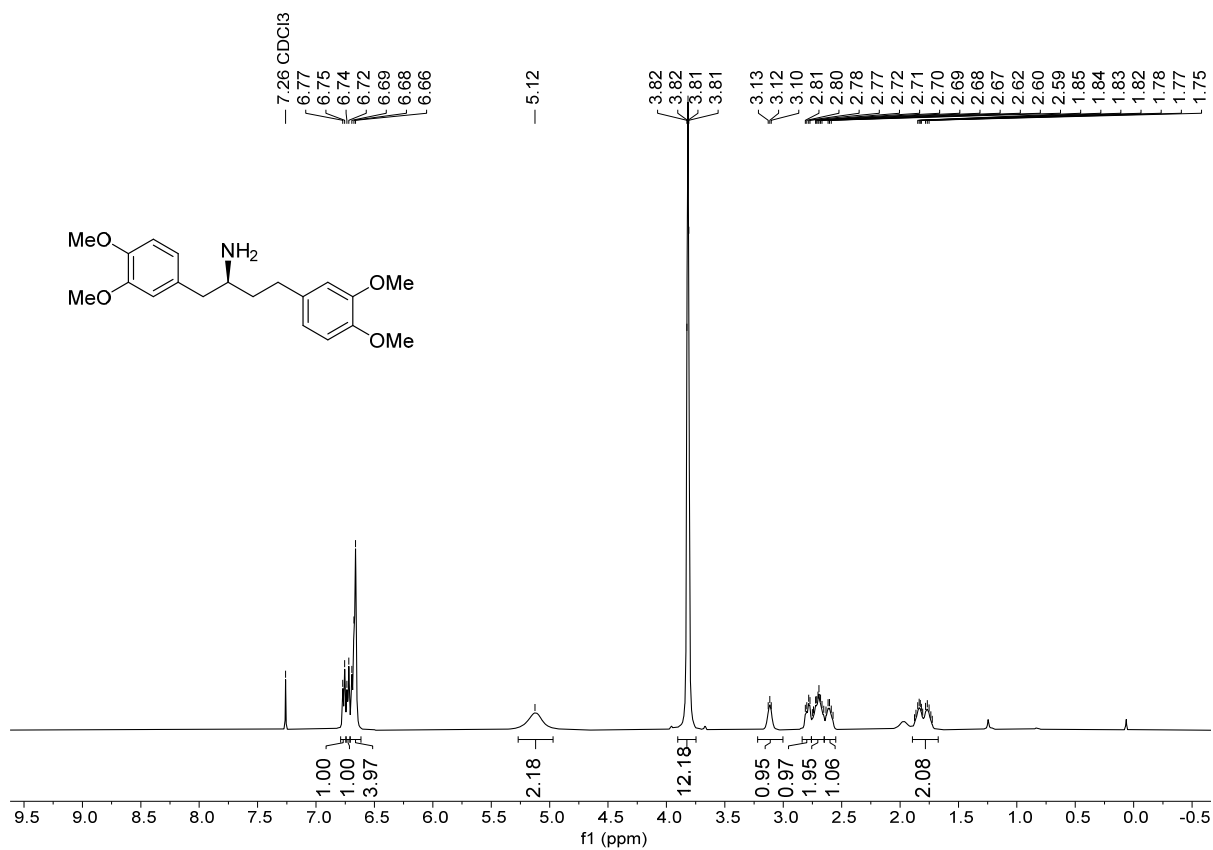


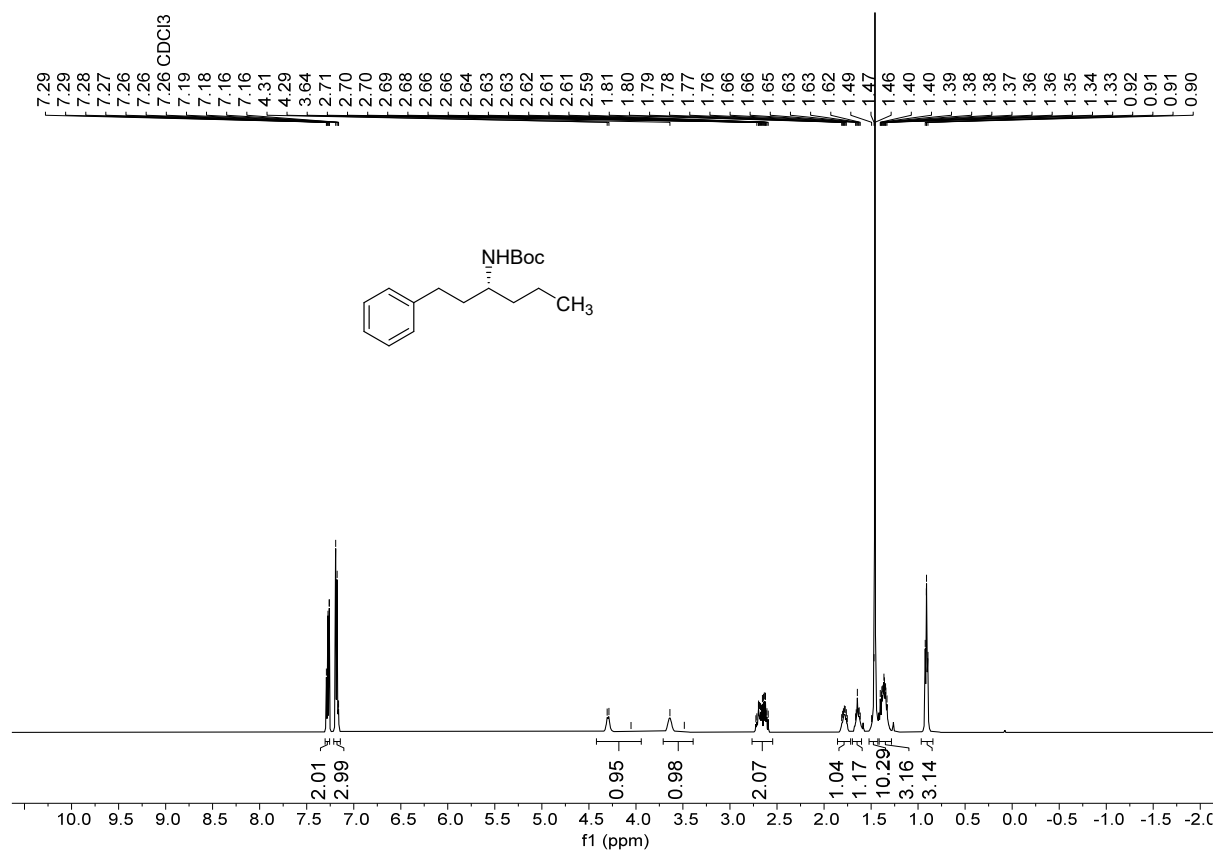
¹³C {¹H} NMR (125 MHz, CDCl₃) of **76**



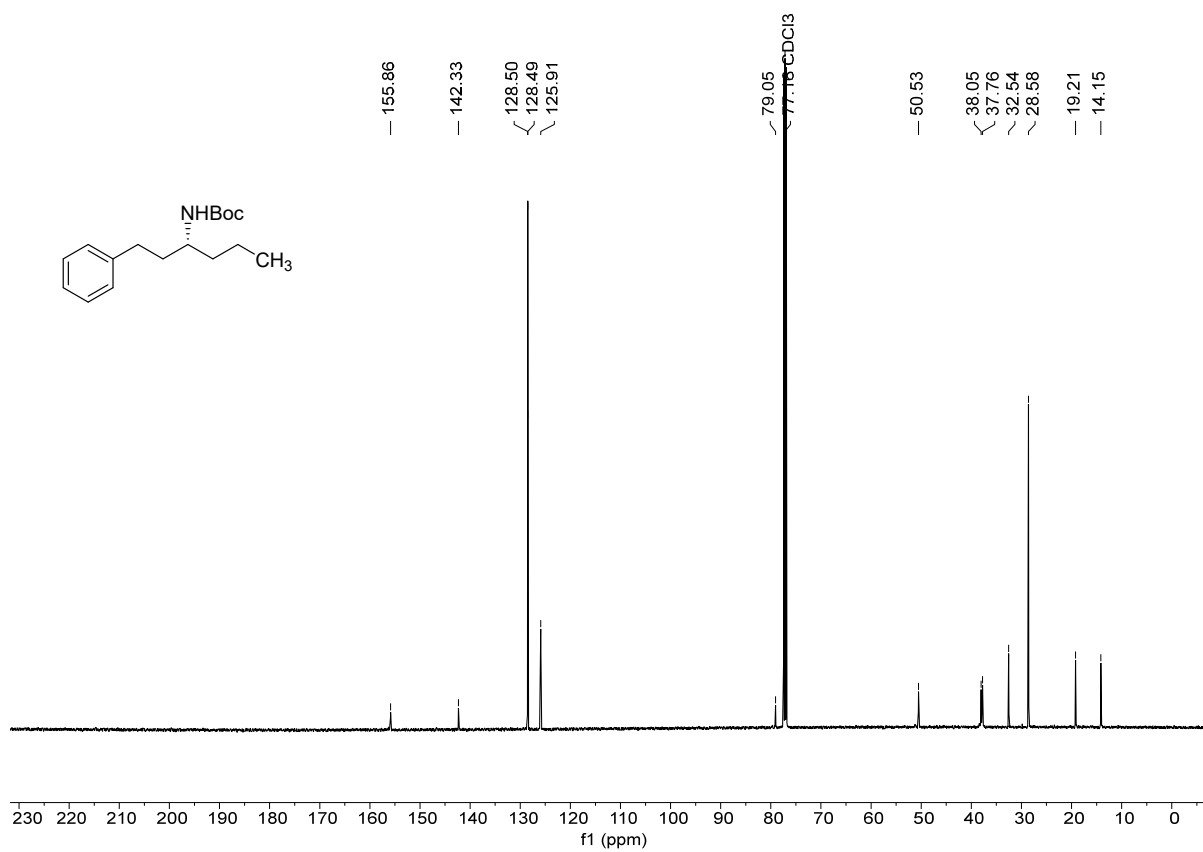




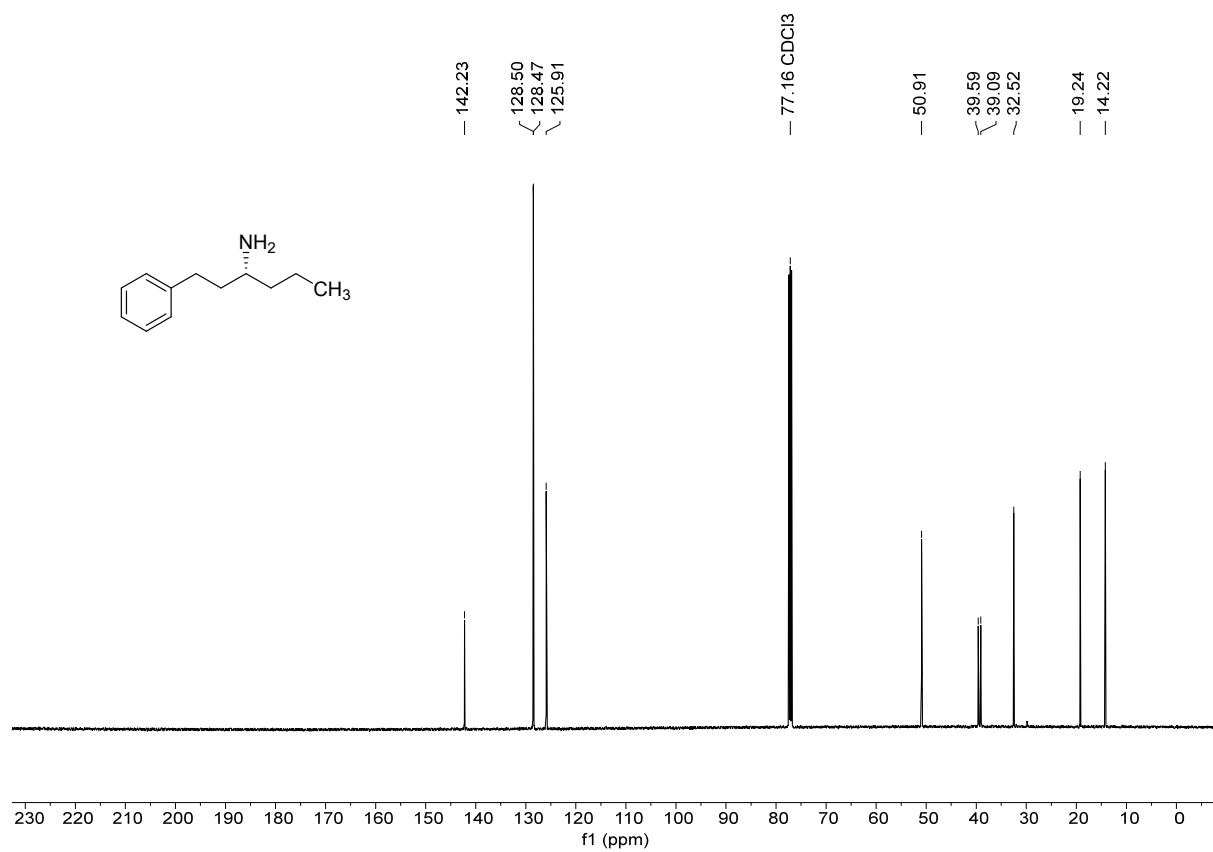
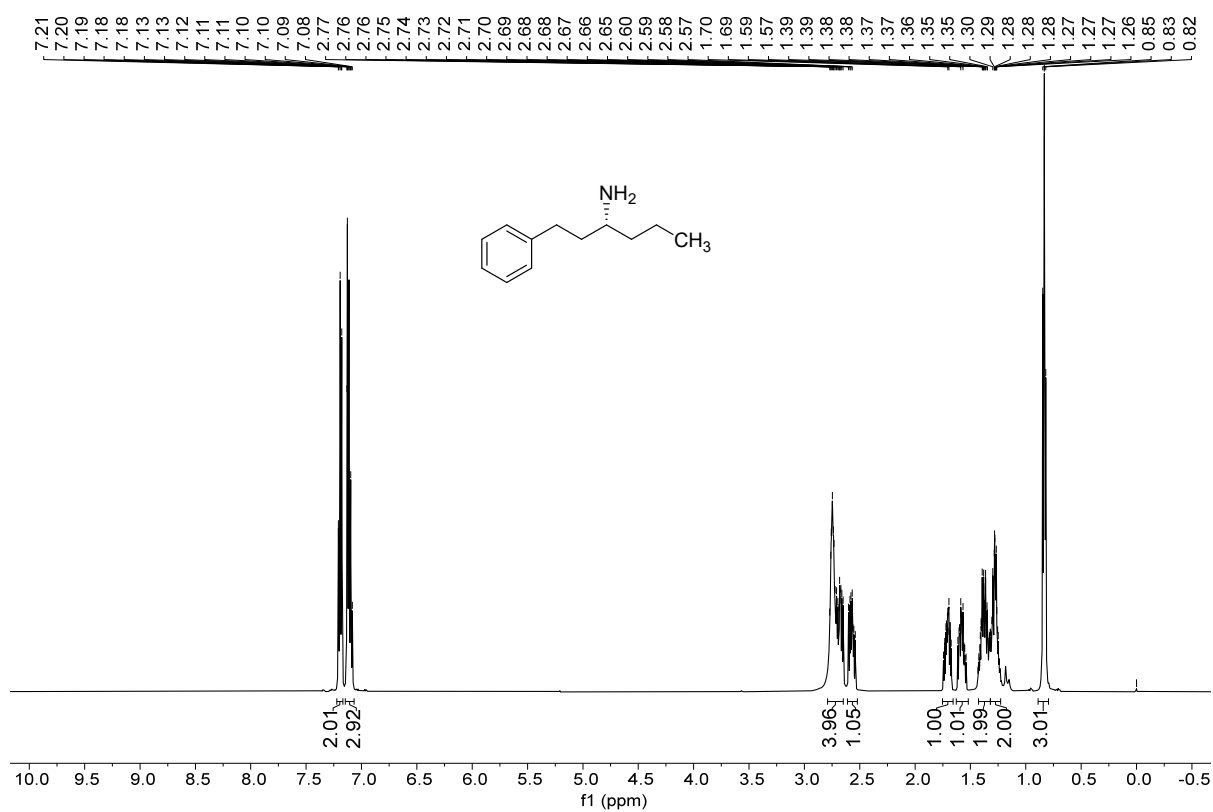


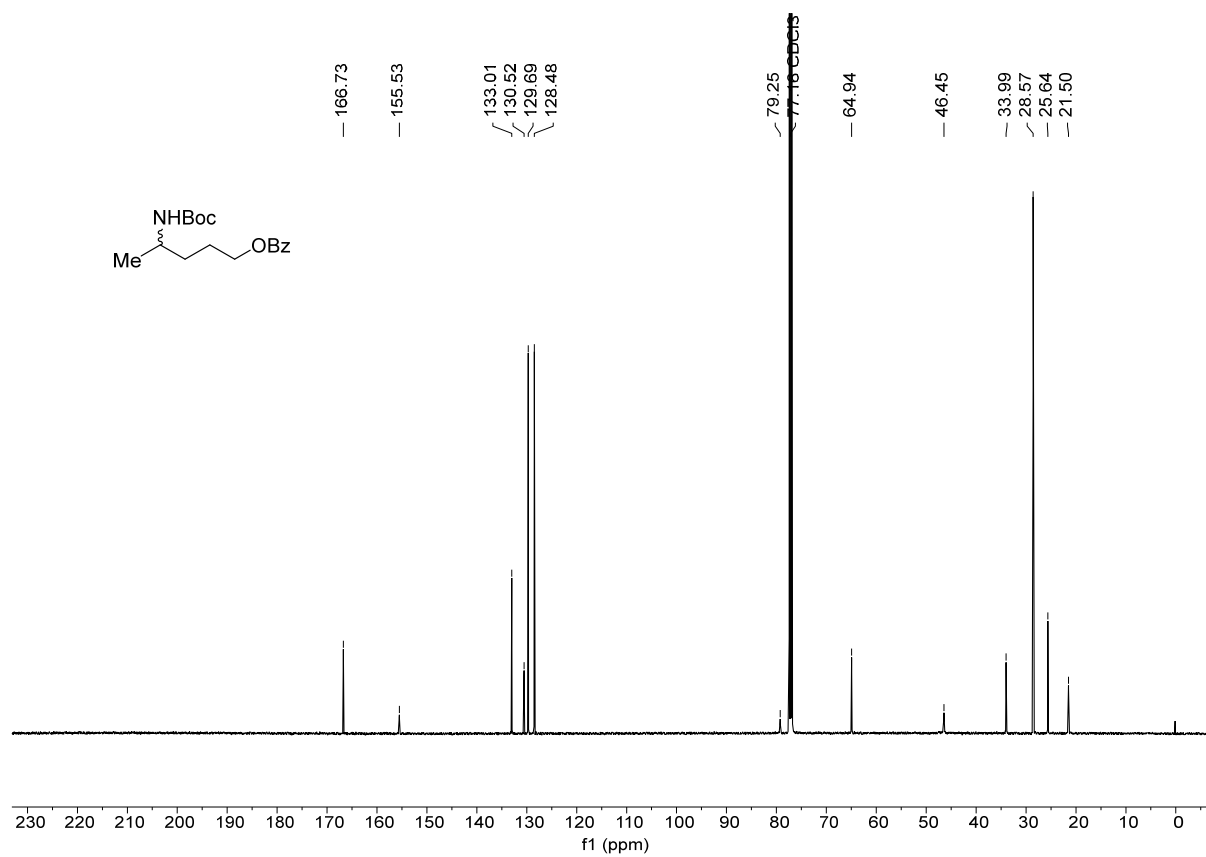
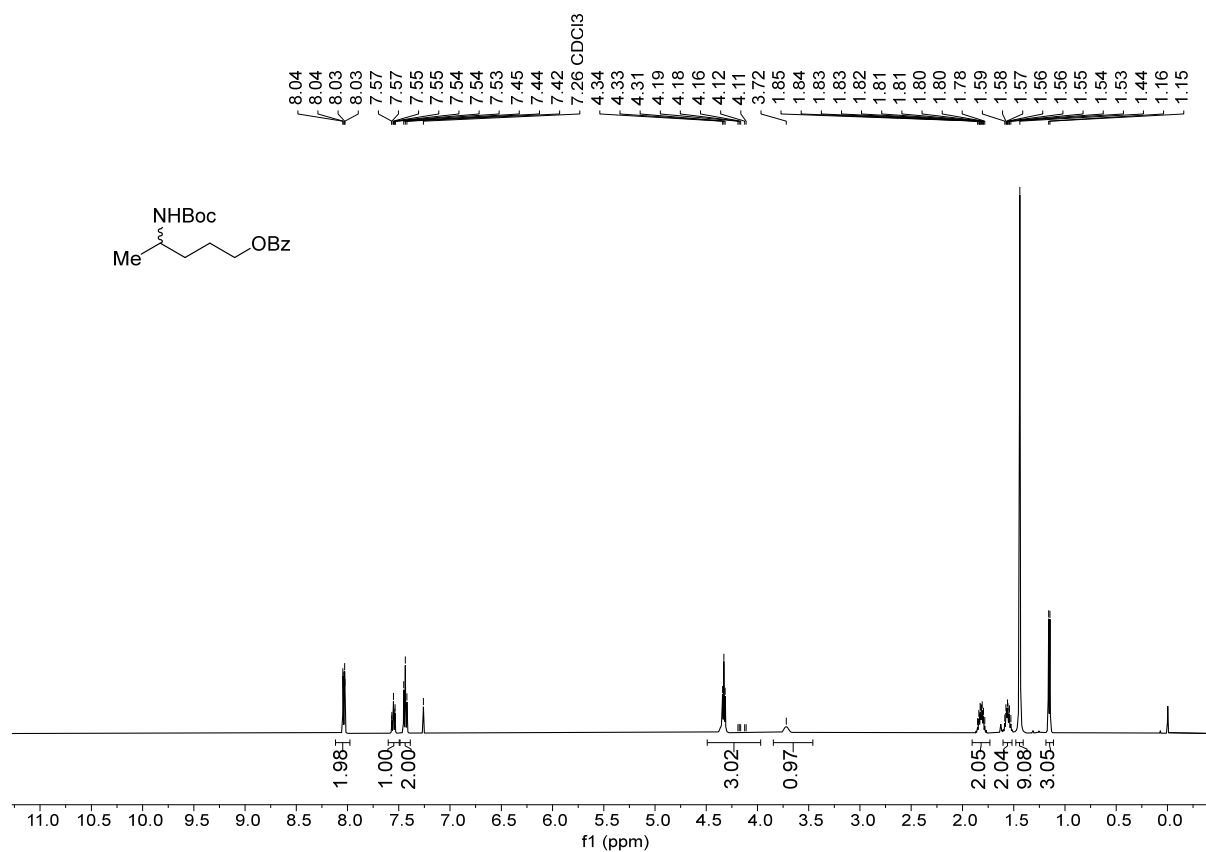


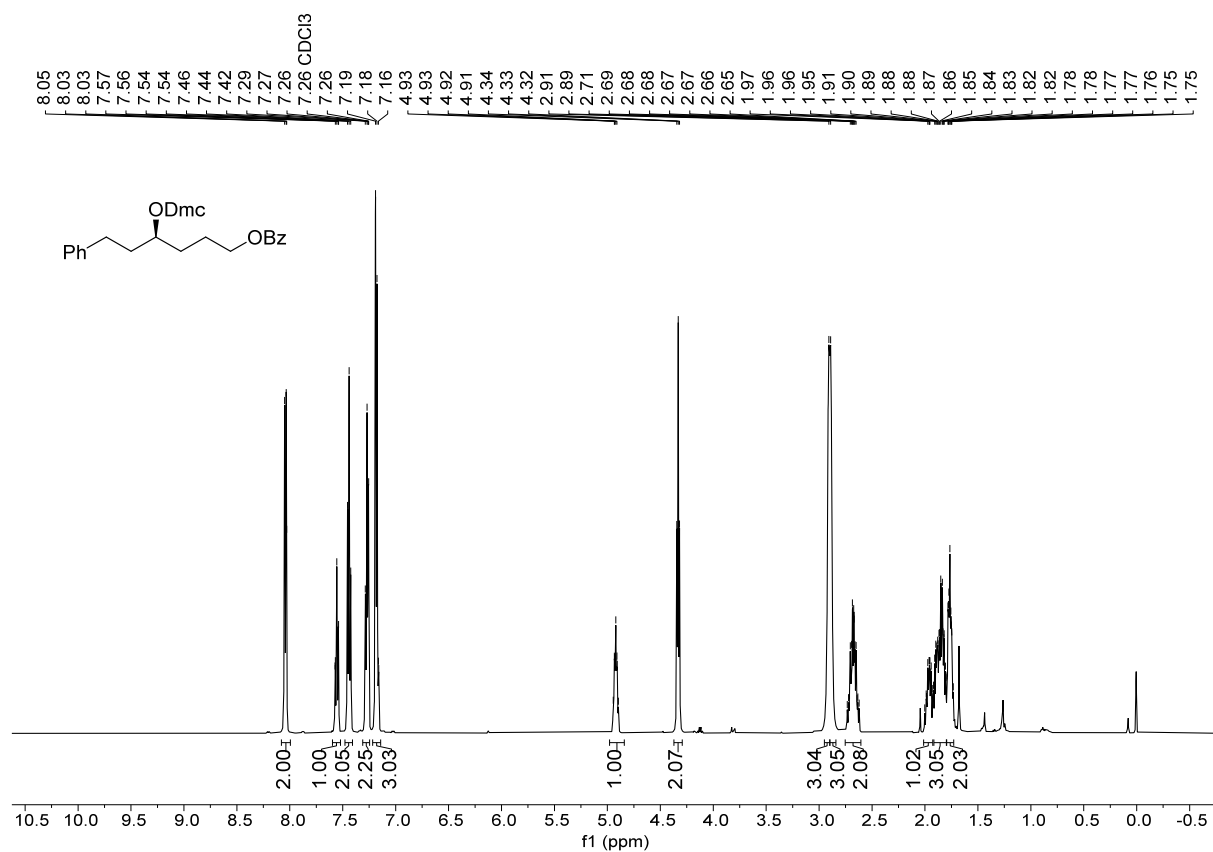
¹H NMR (500 MHz, CDCl₃) of **89**



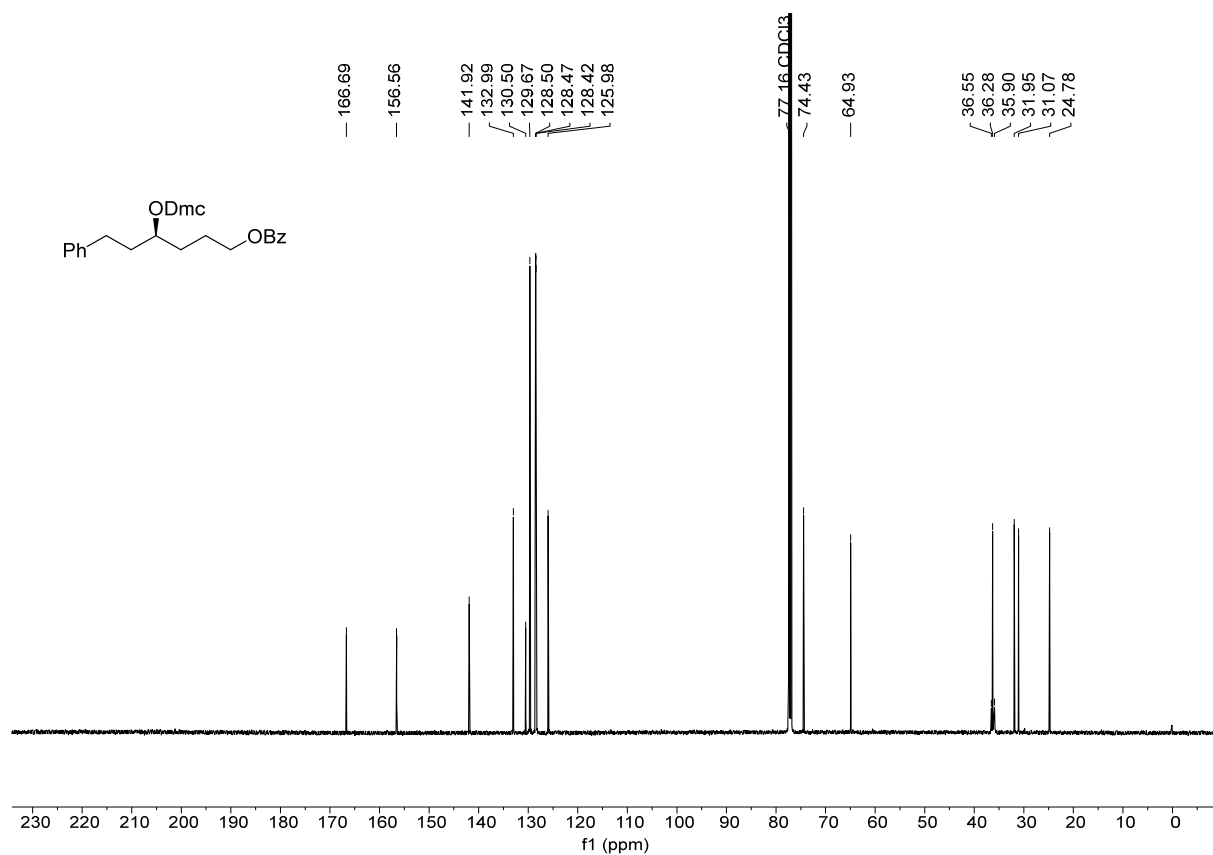
¹³C{¹H} NMR (125 MHz, CDCl₃) of **89**





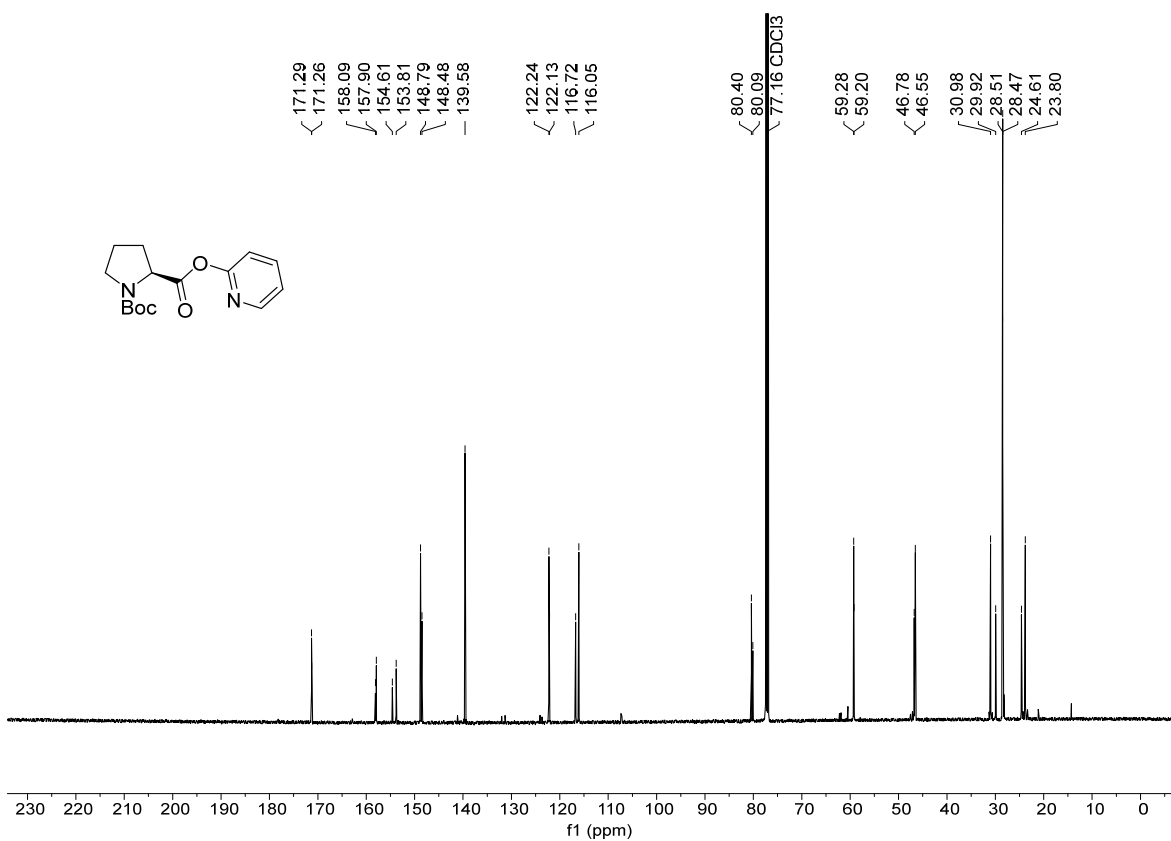
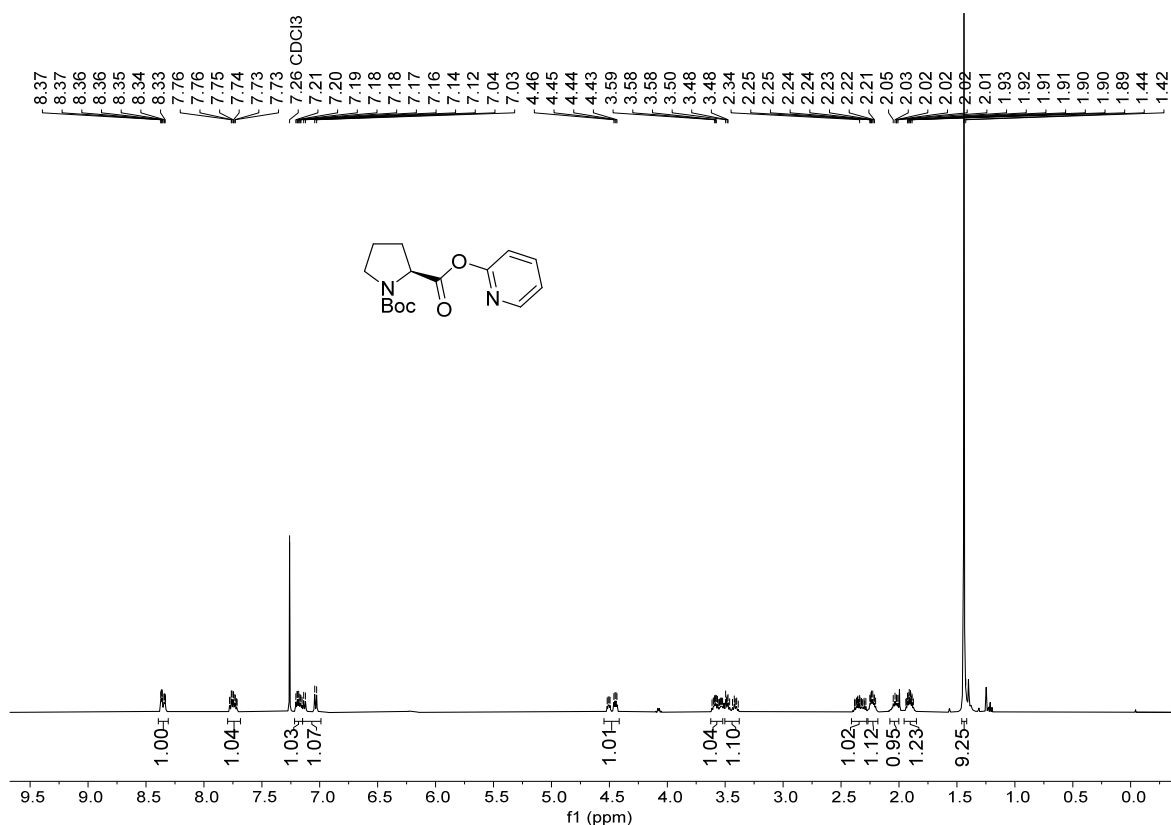


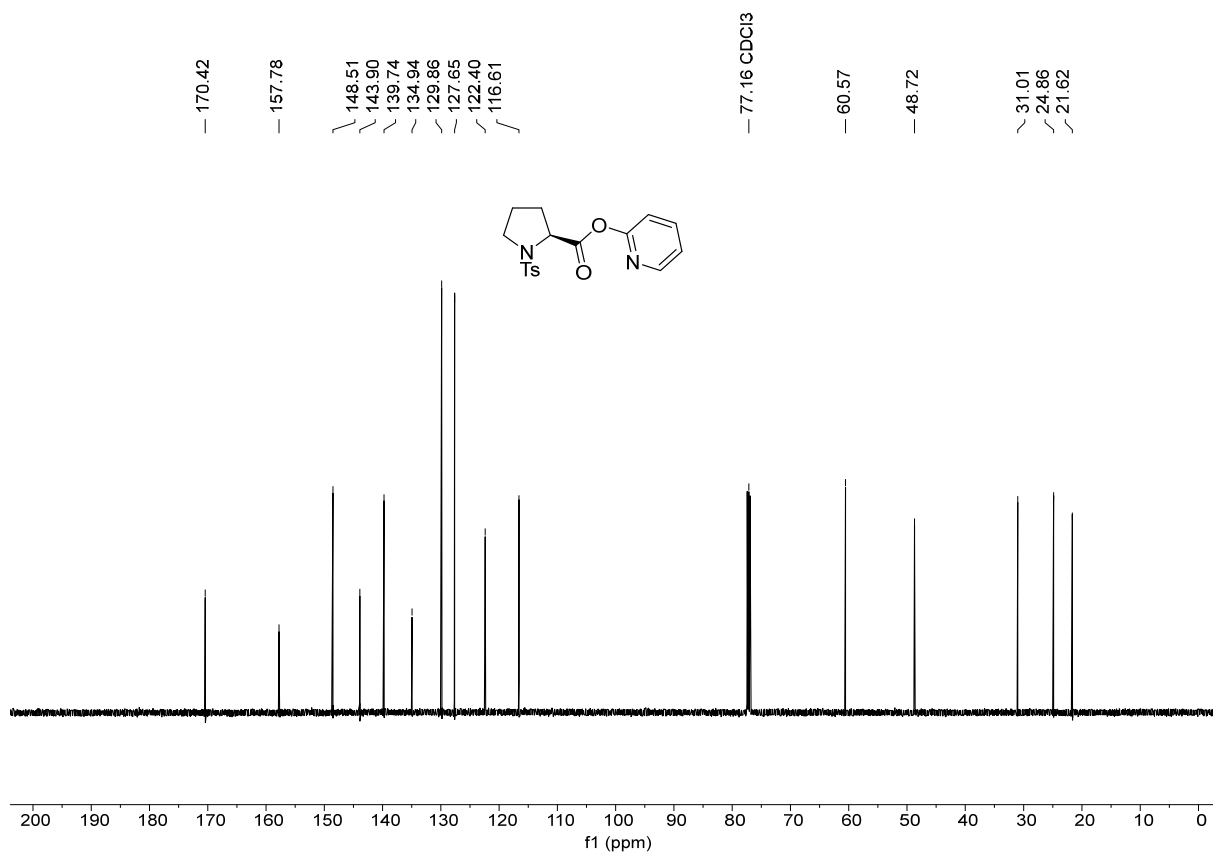
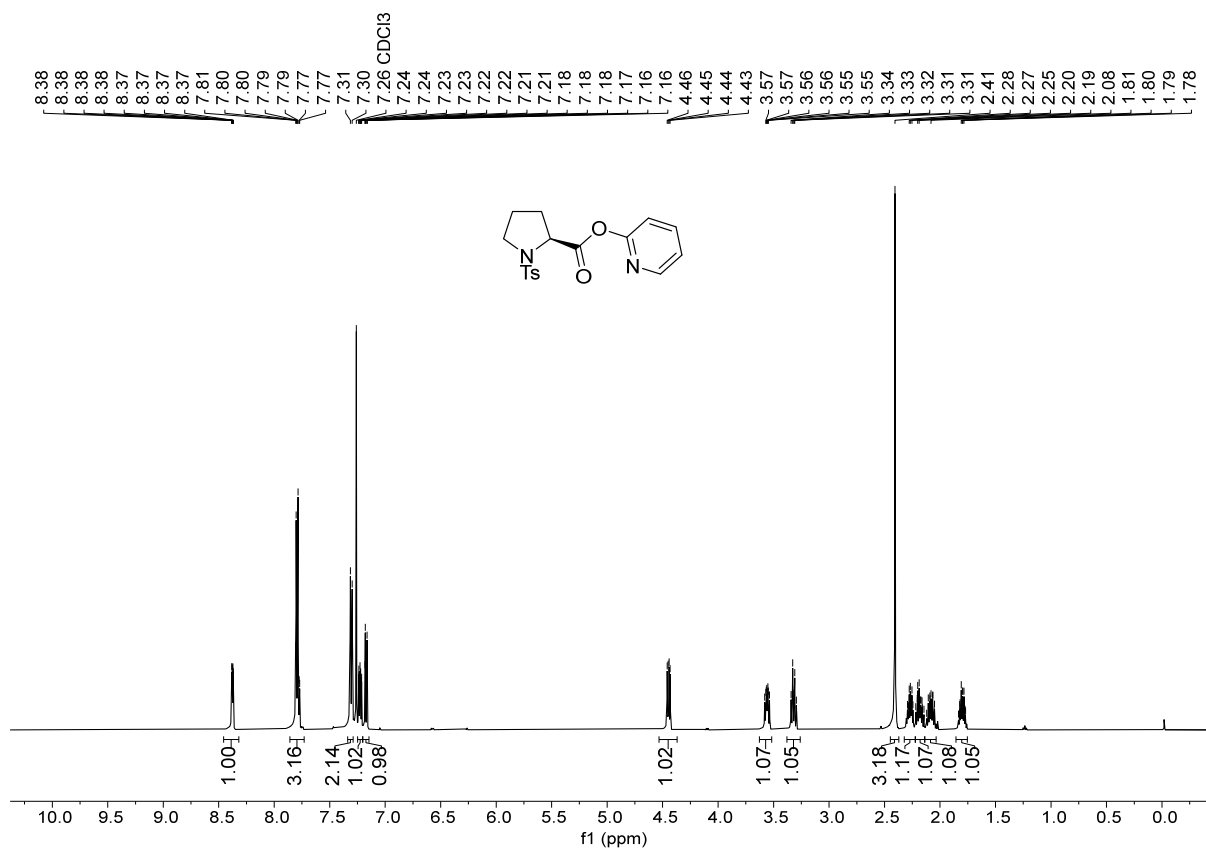
¹H NMR (500 MHz, CDCl₃) of **94**

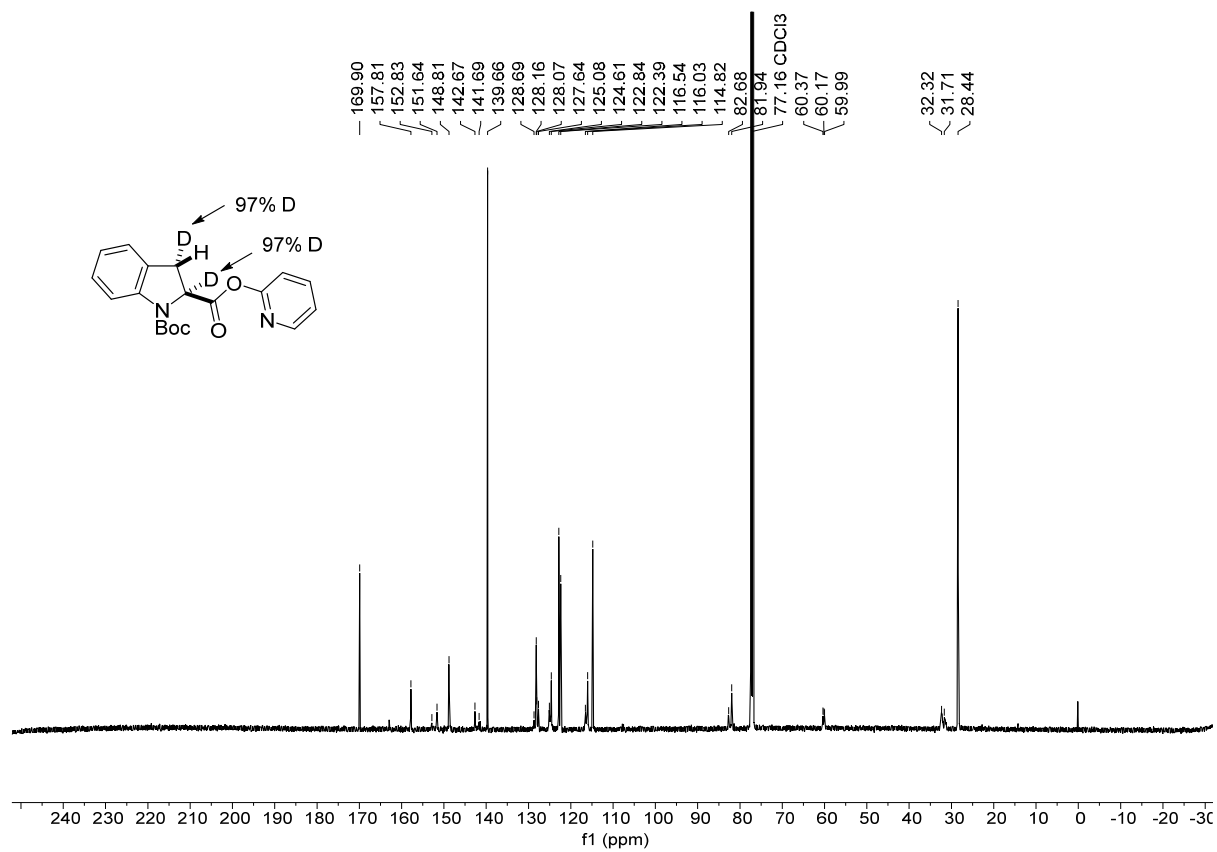
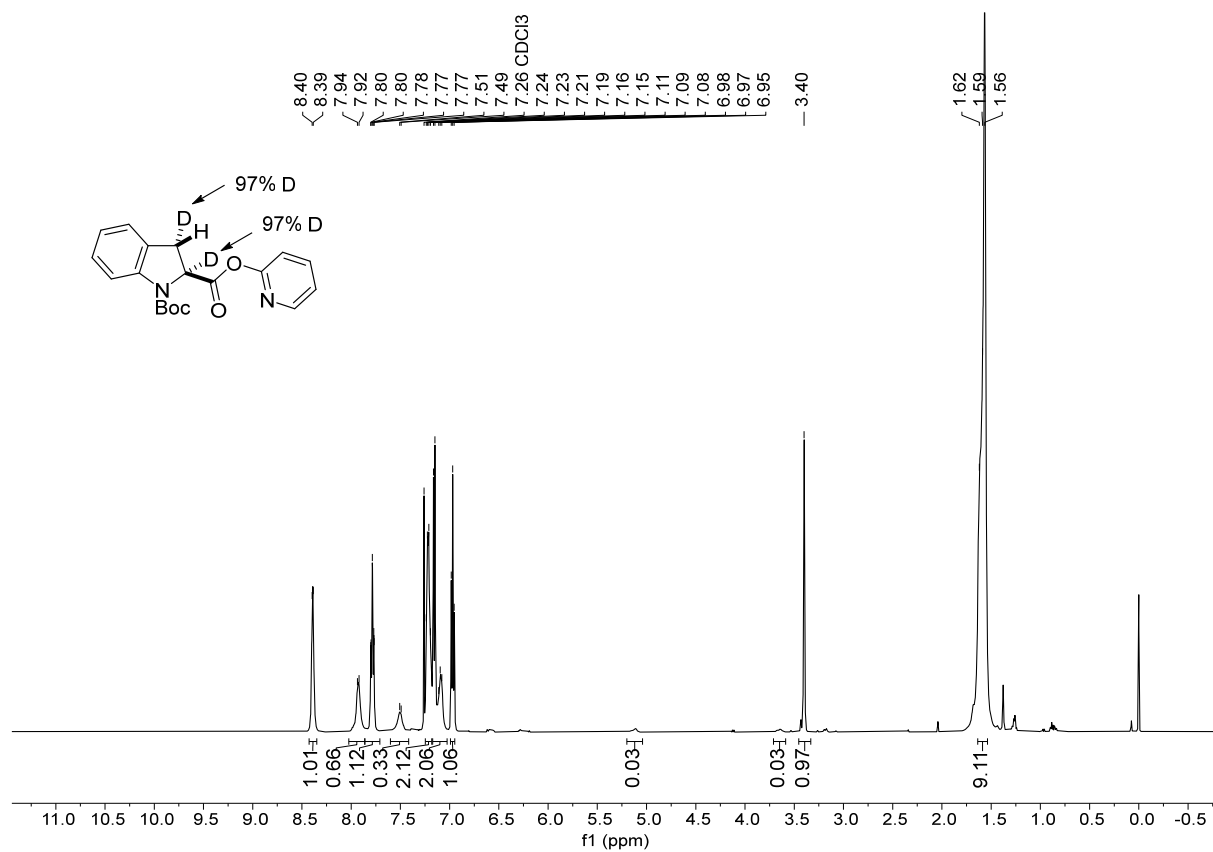


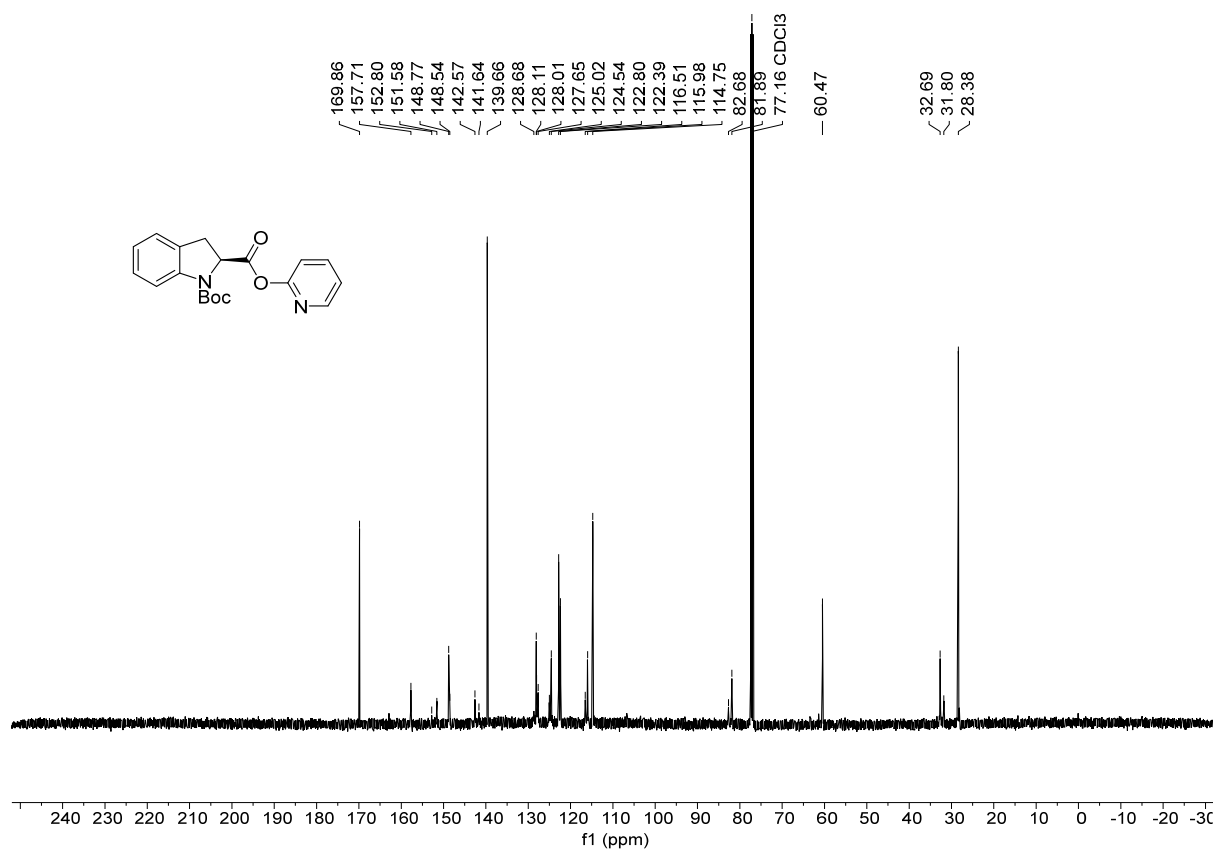
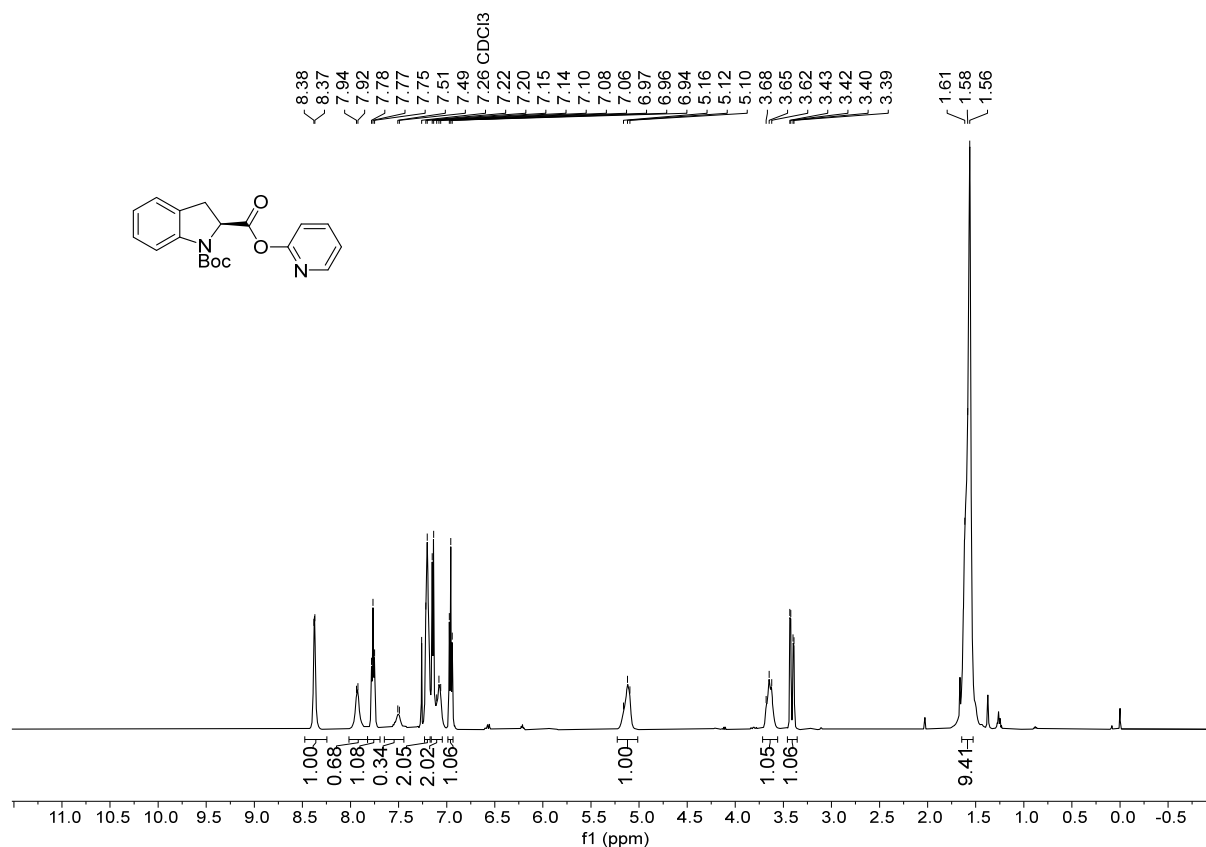
¹³C{¹H} NMR (125 MHz, CDCl₃) of **94**

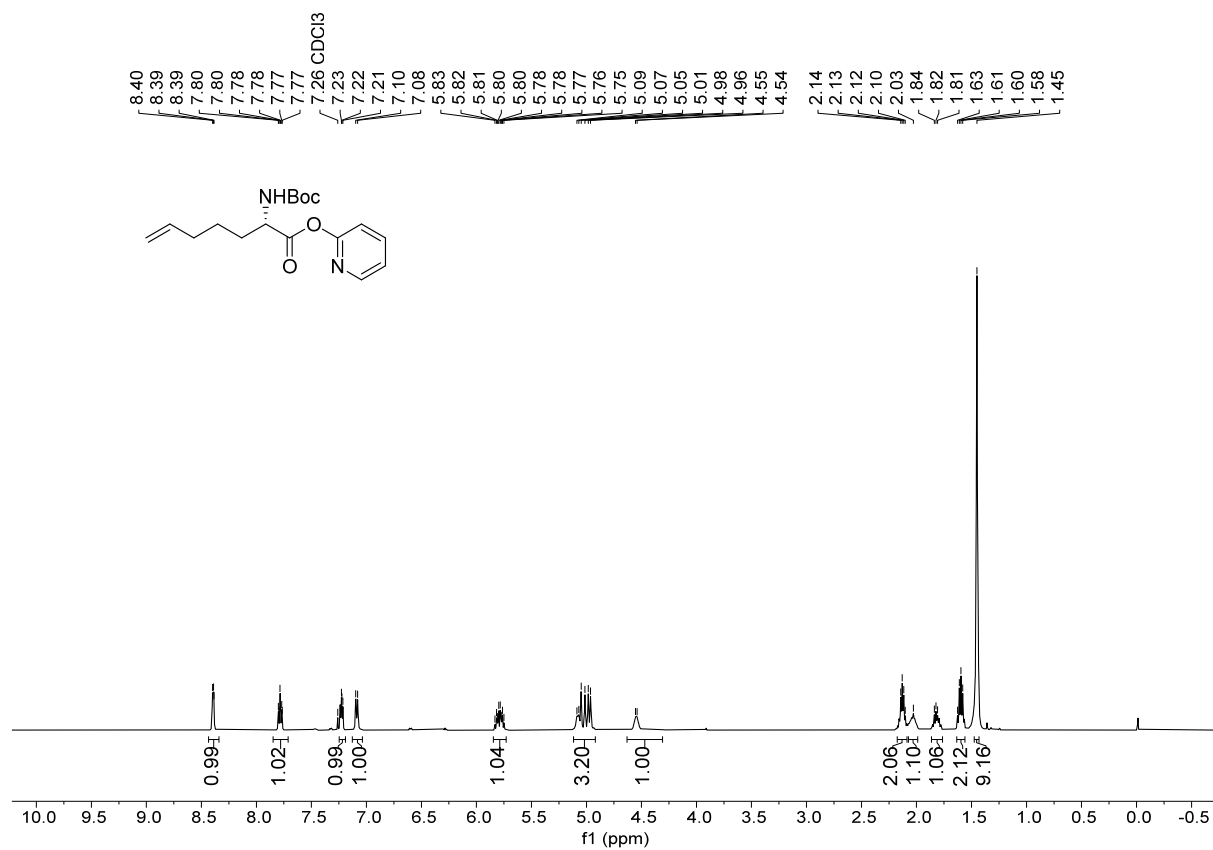
10.2 NMR spectra of starting materials



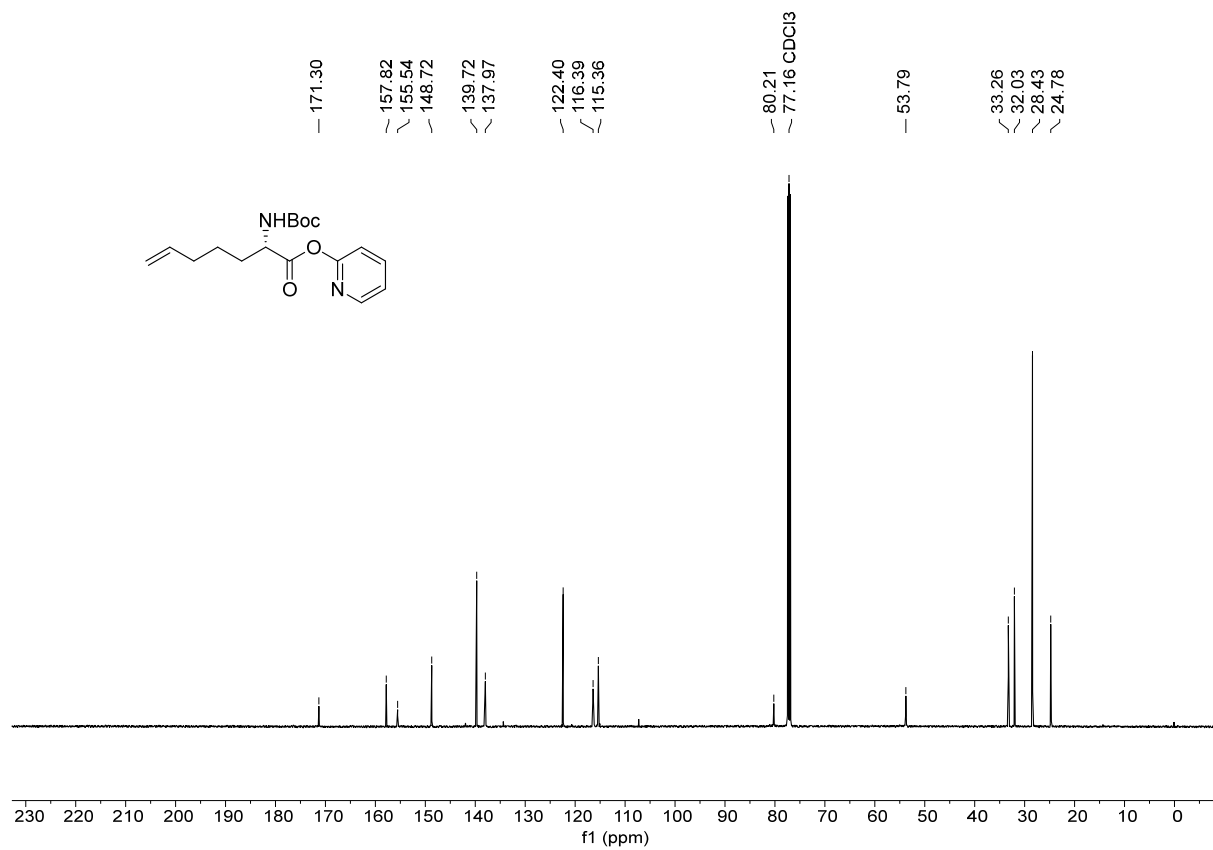




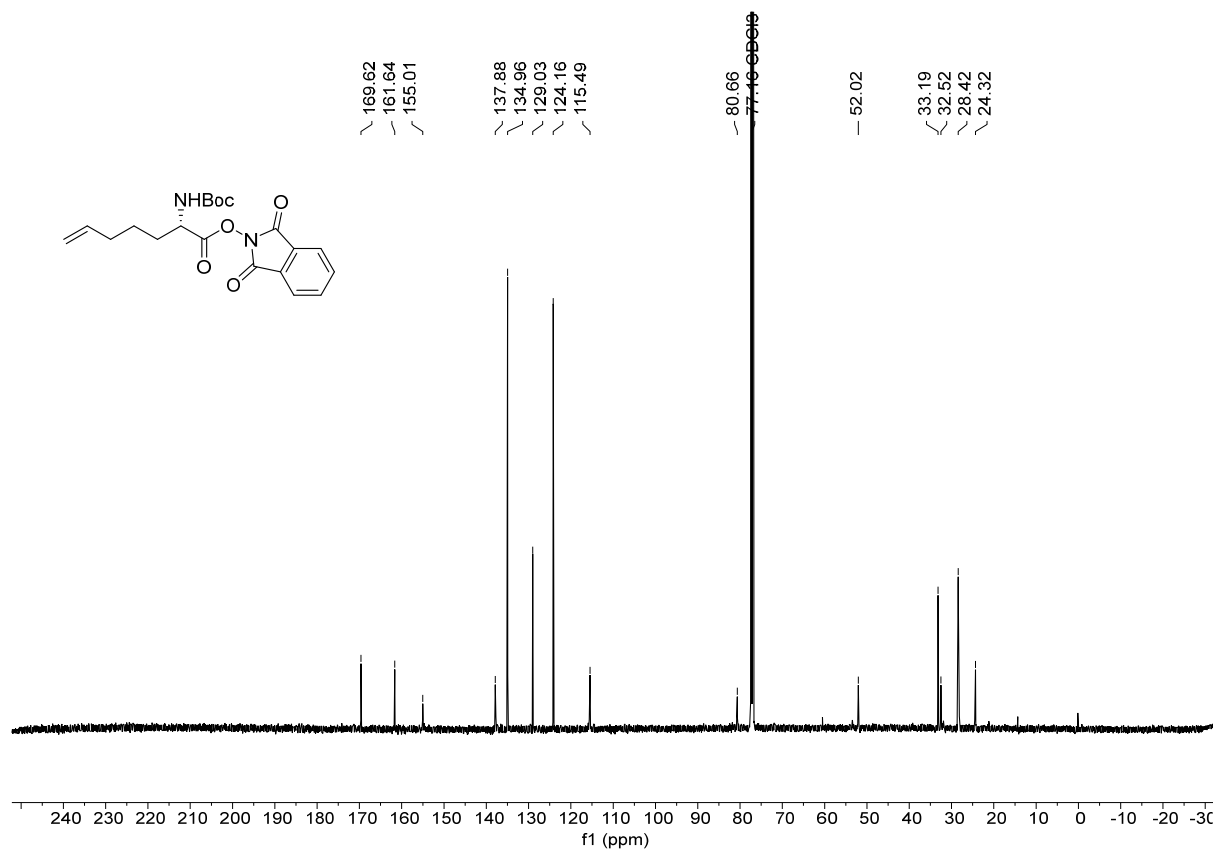
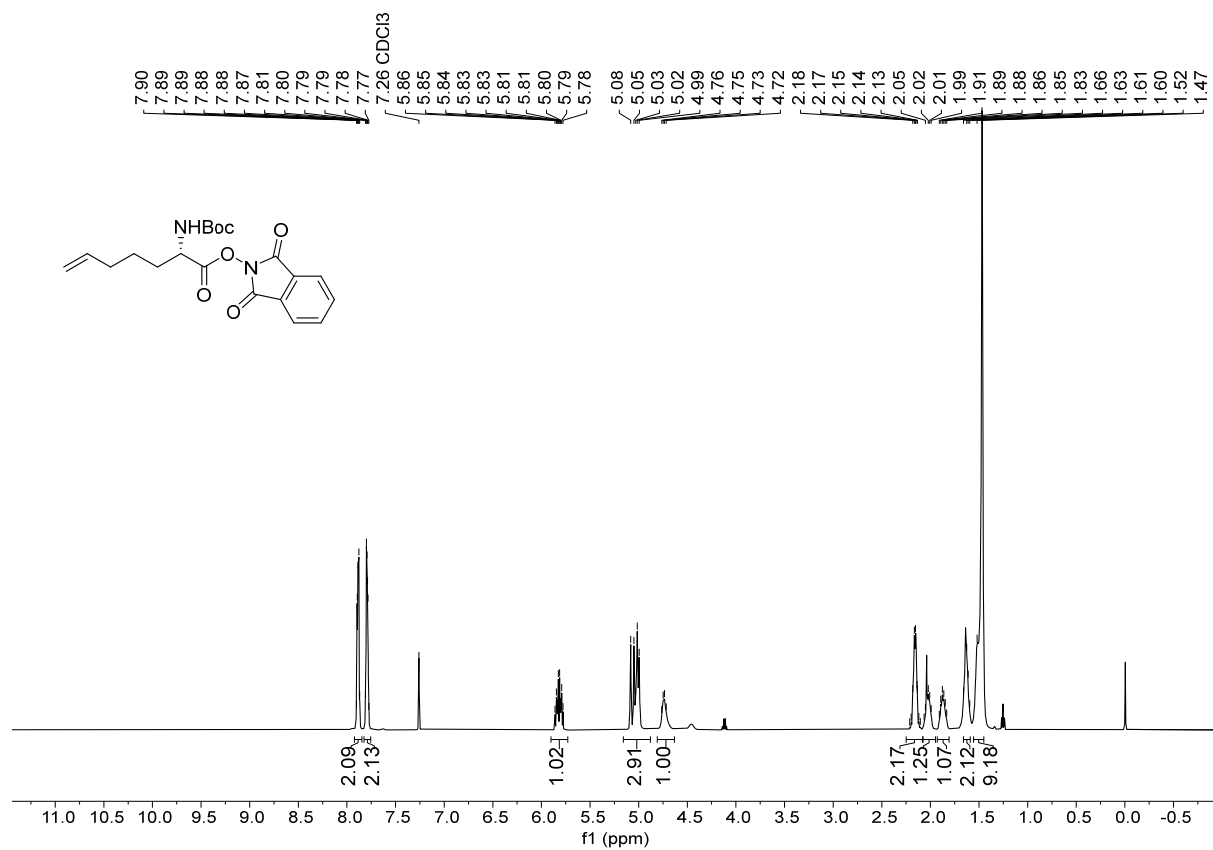


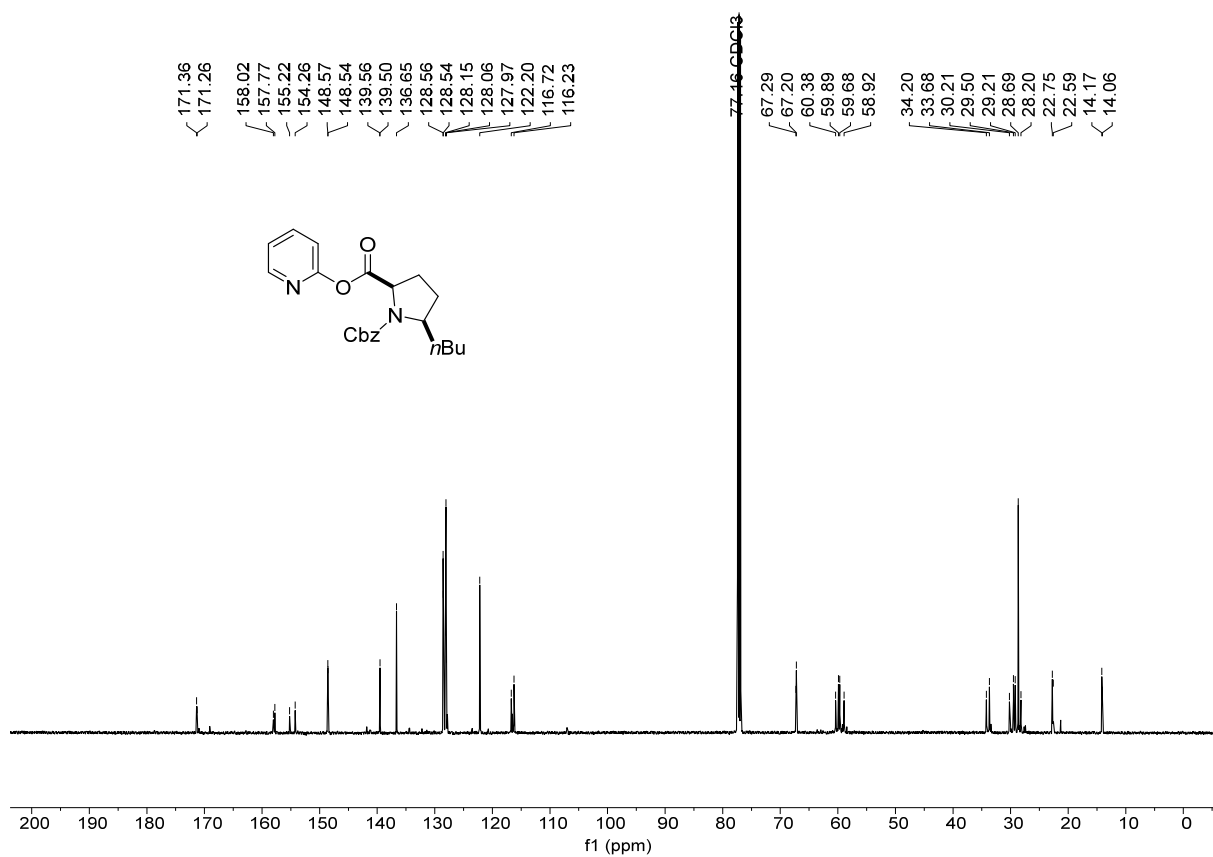
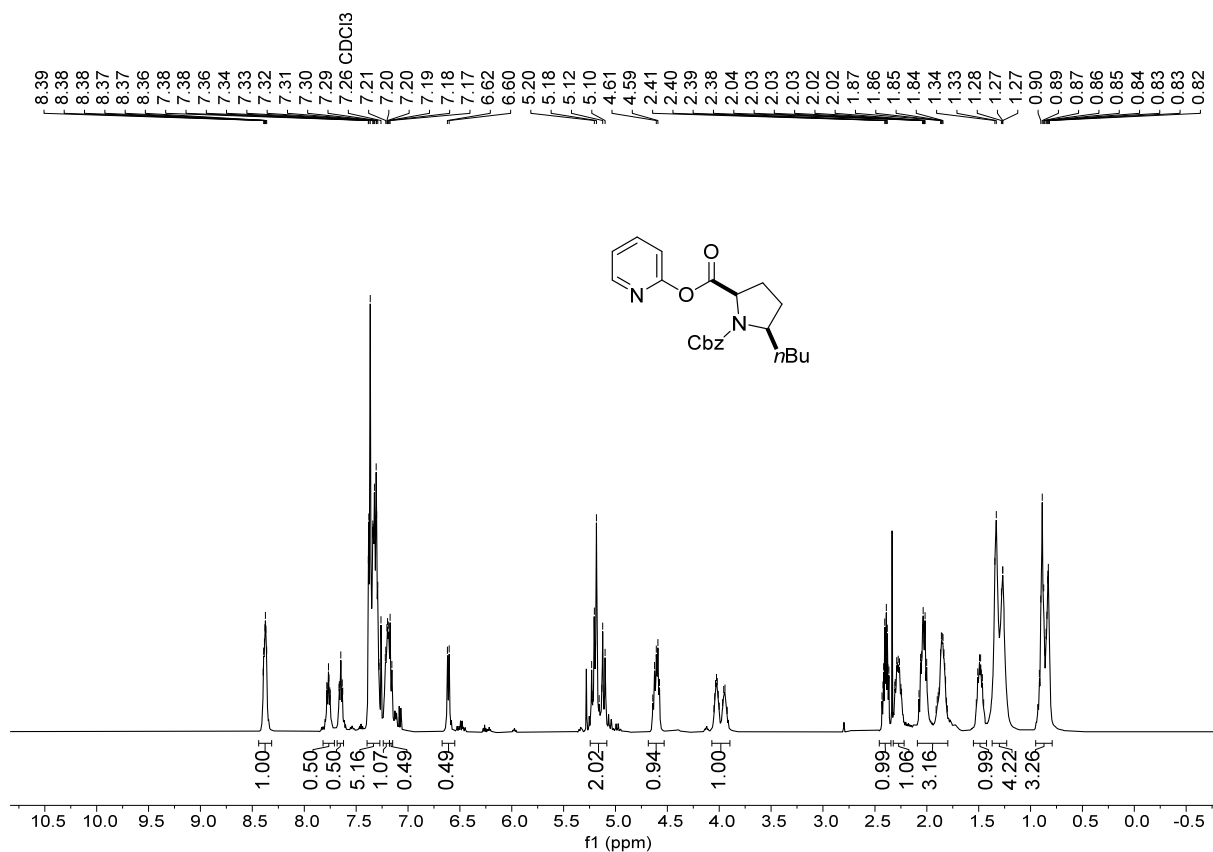


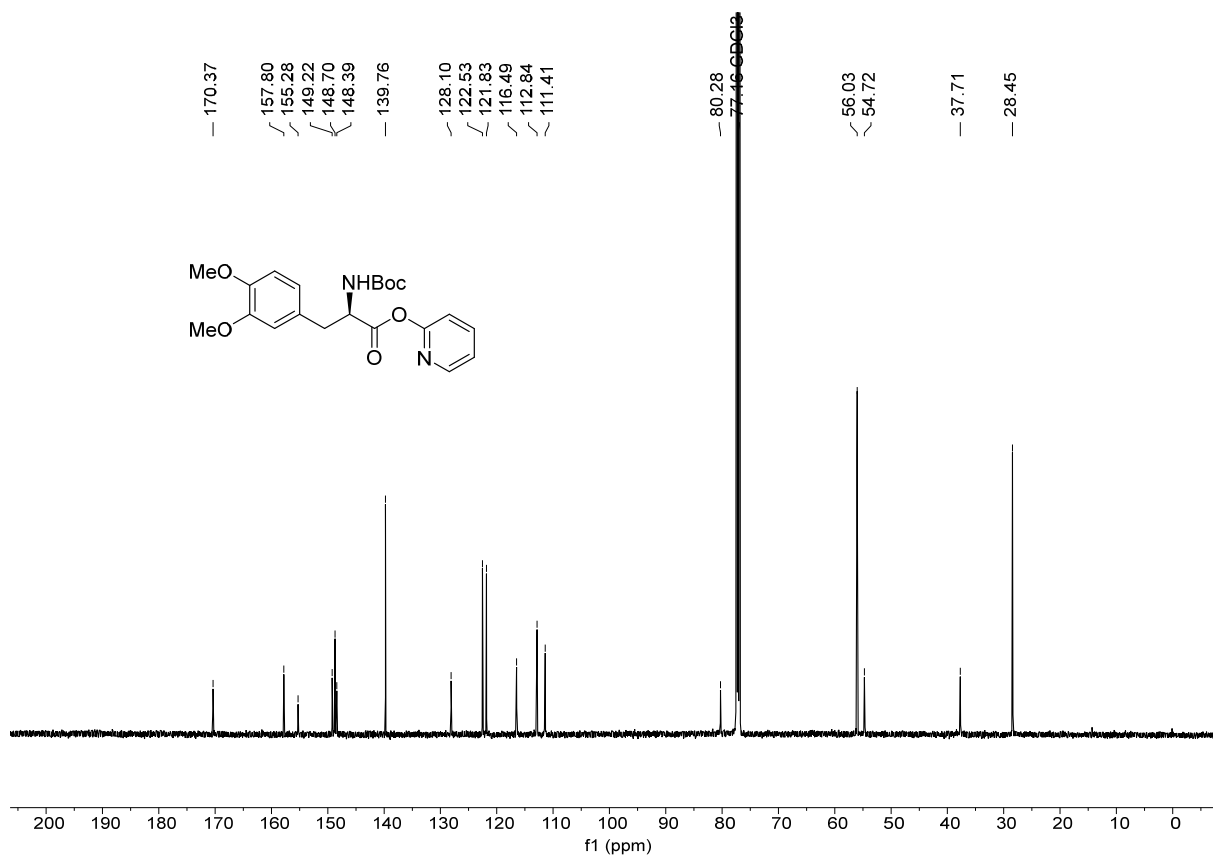
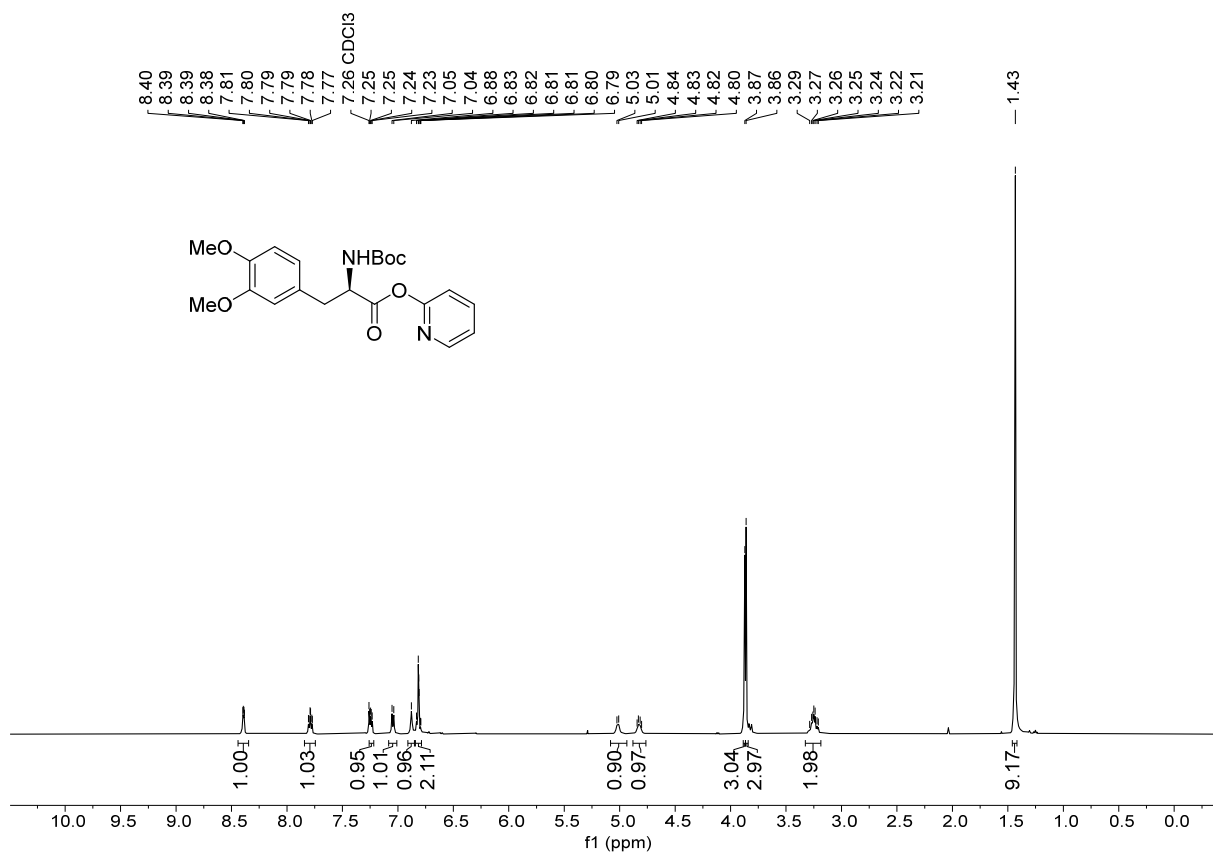
¹H NMR (500 MHz, CDCl₃) of **13**

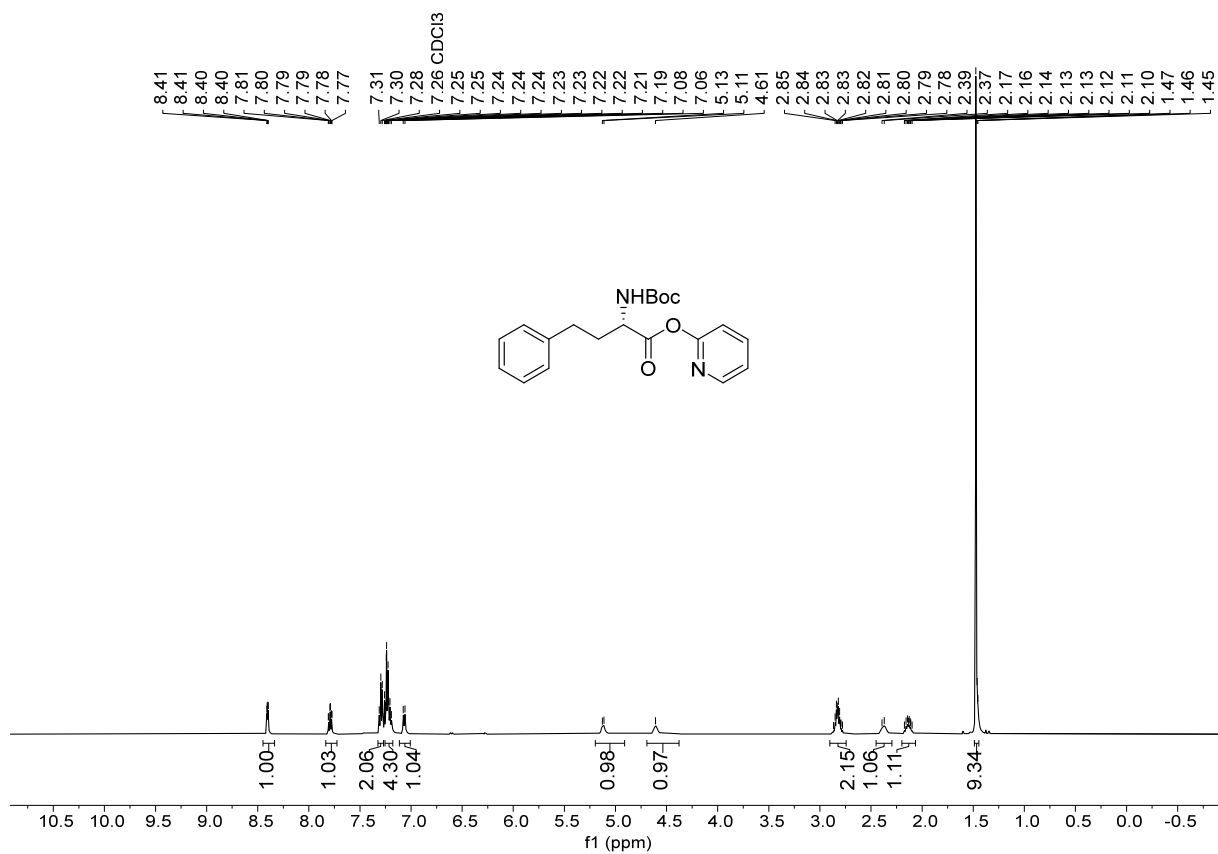


¹³C {¹H} NMR (125 MHz, CDCl₃) of **13**

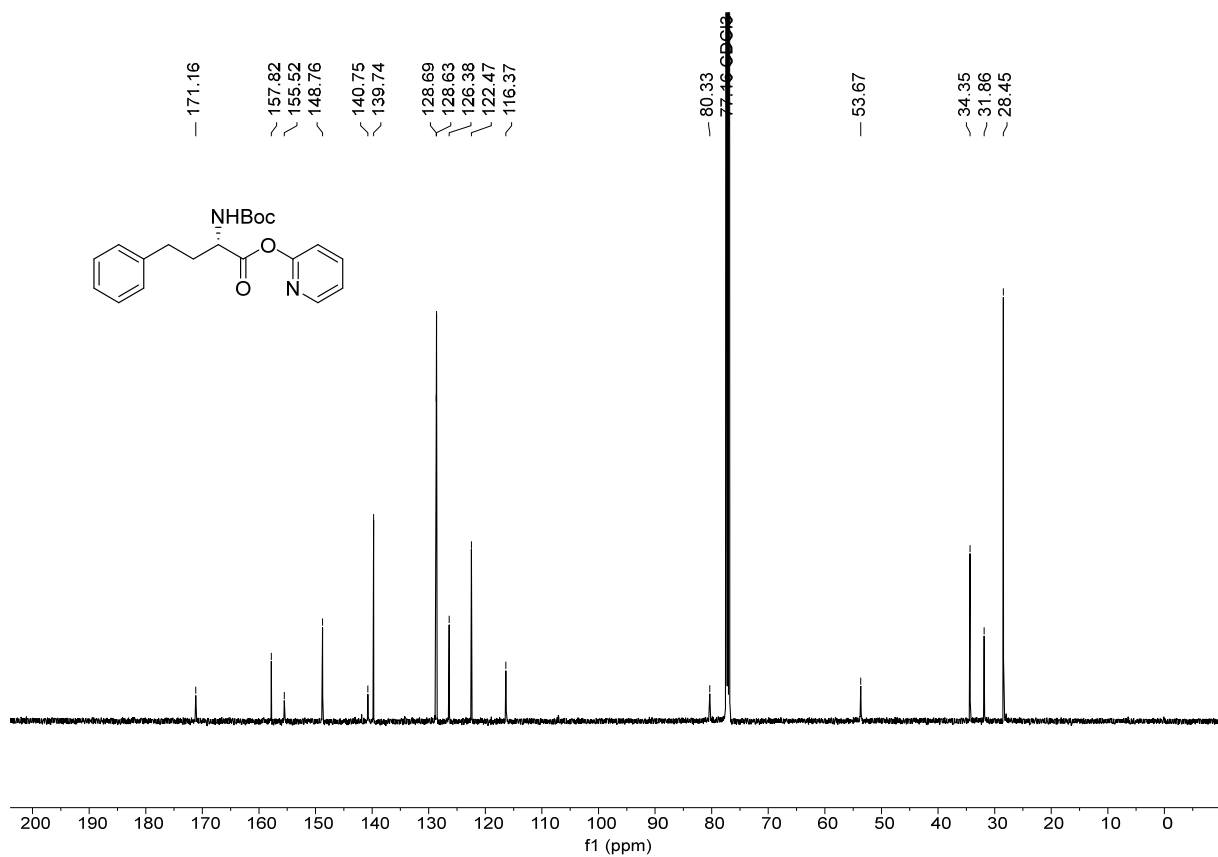




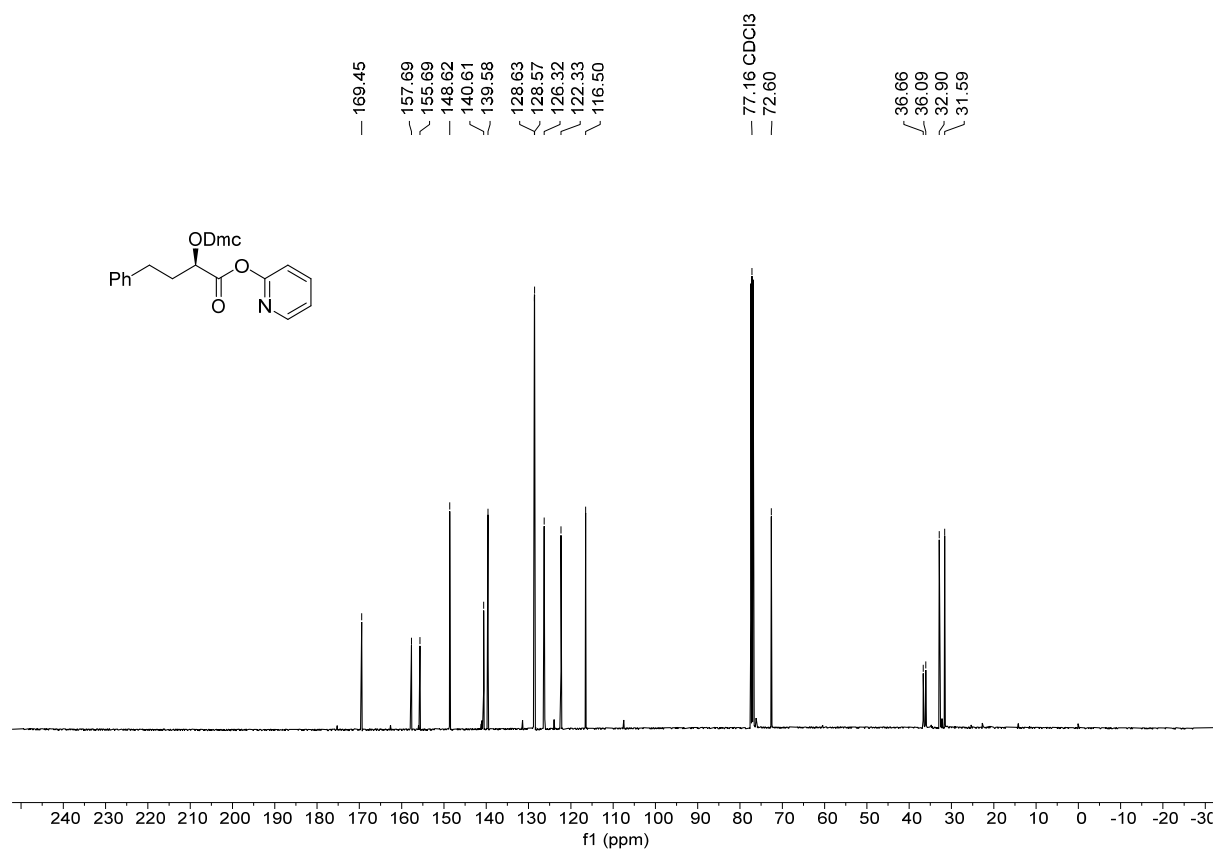
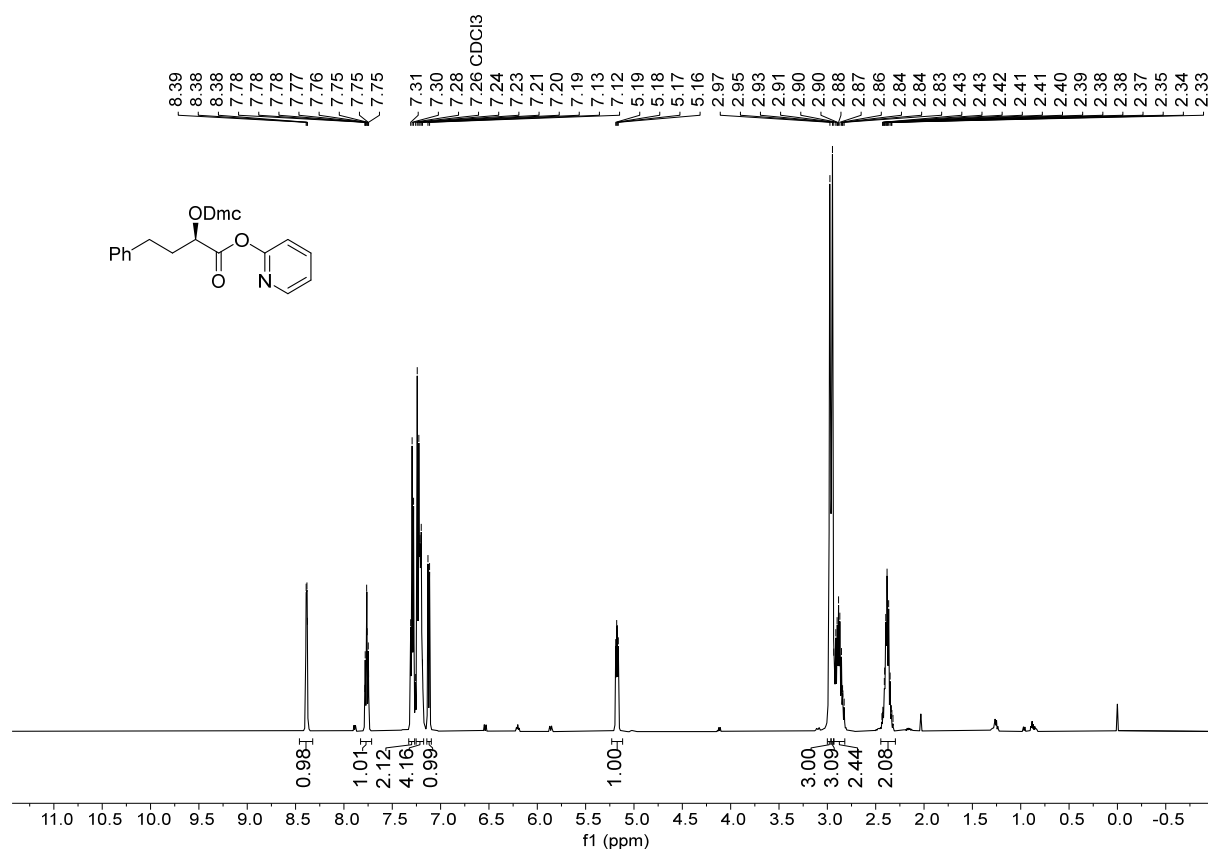


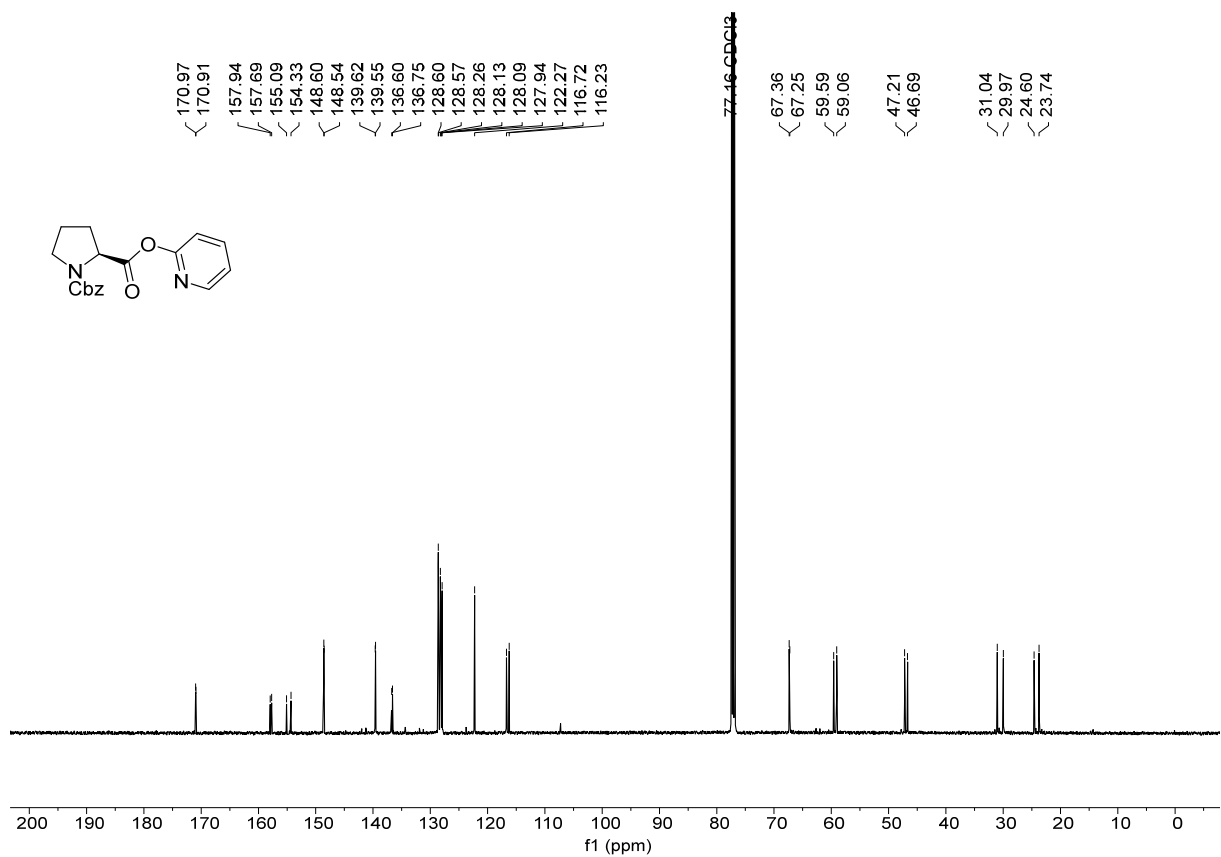
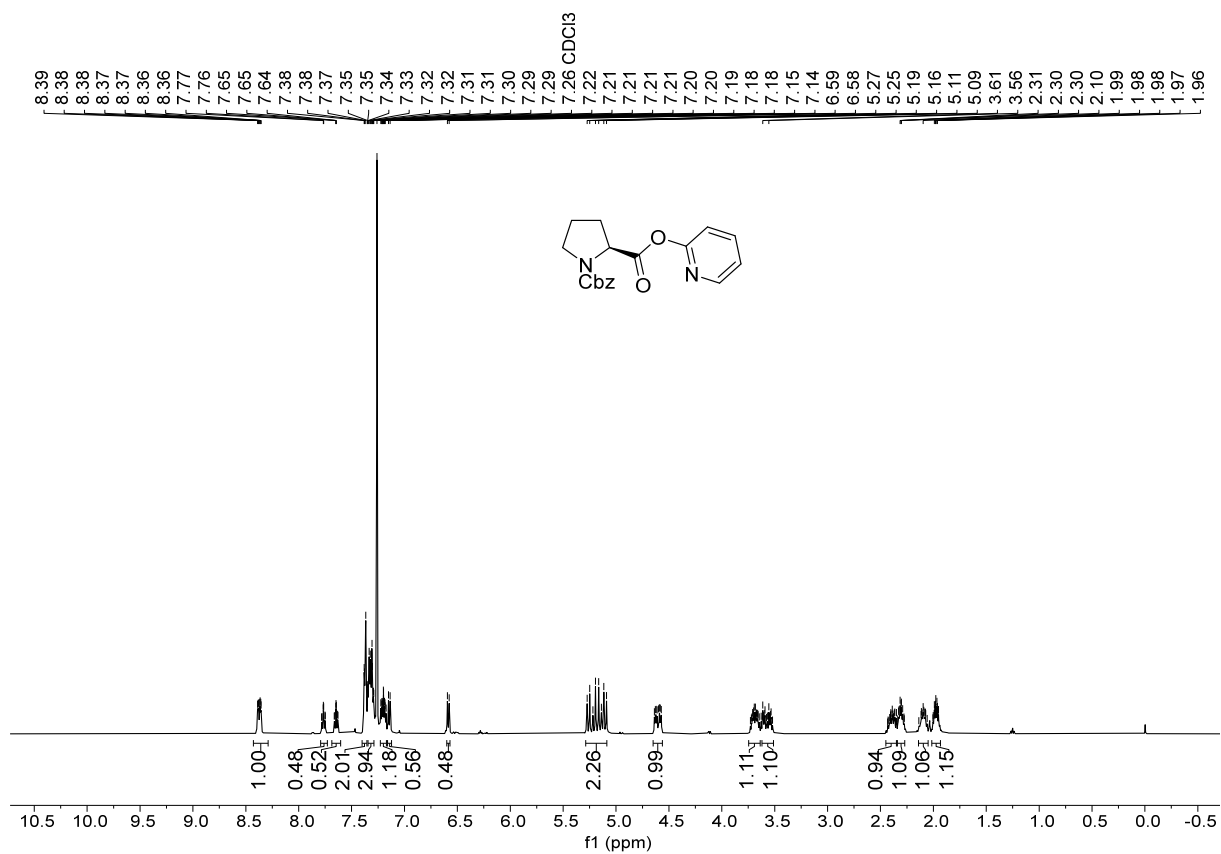


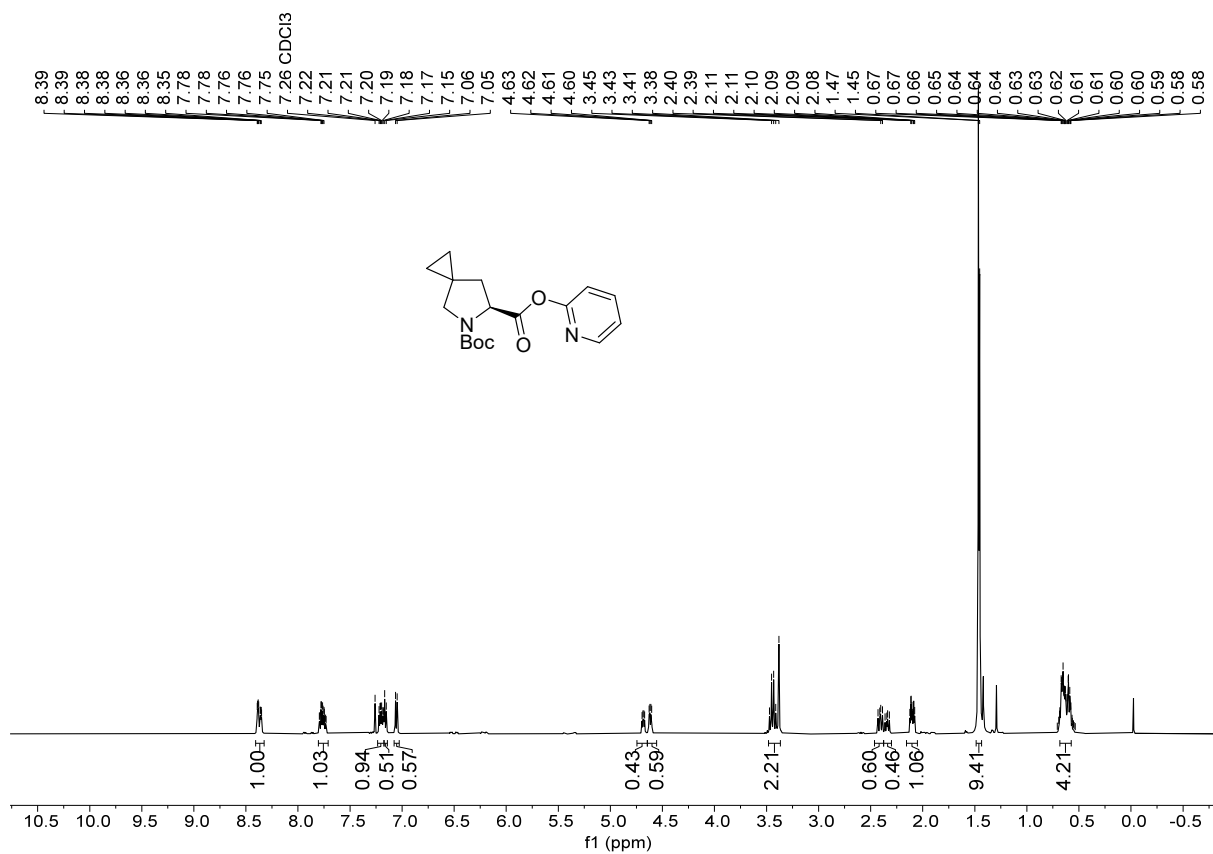
¹H NMR (500 MHz, CDCl₃) of **87**



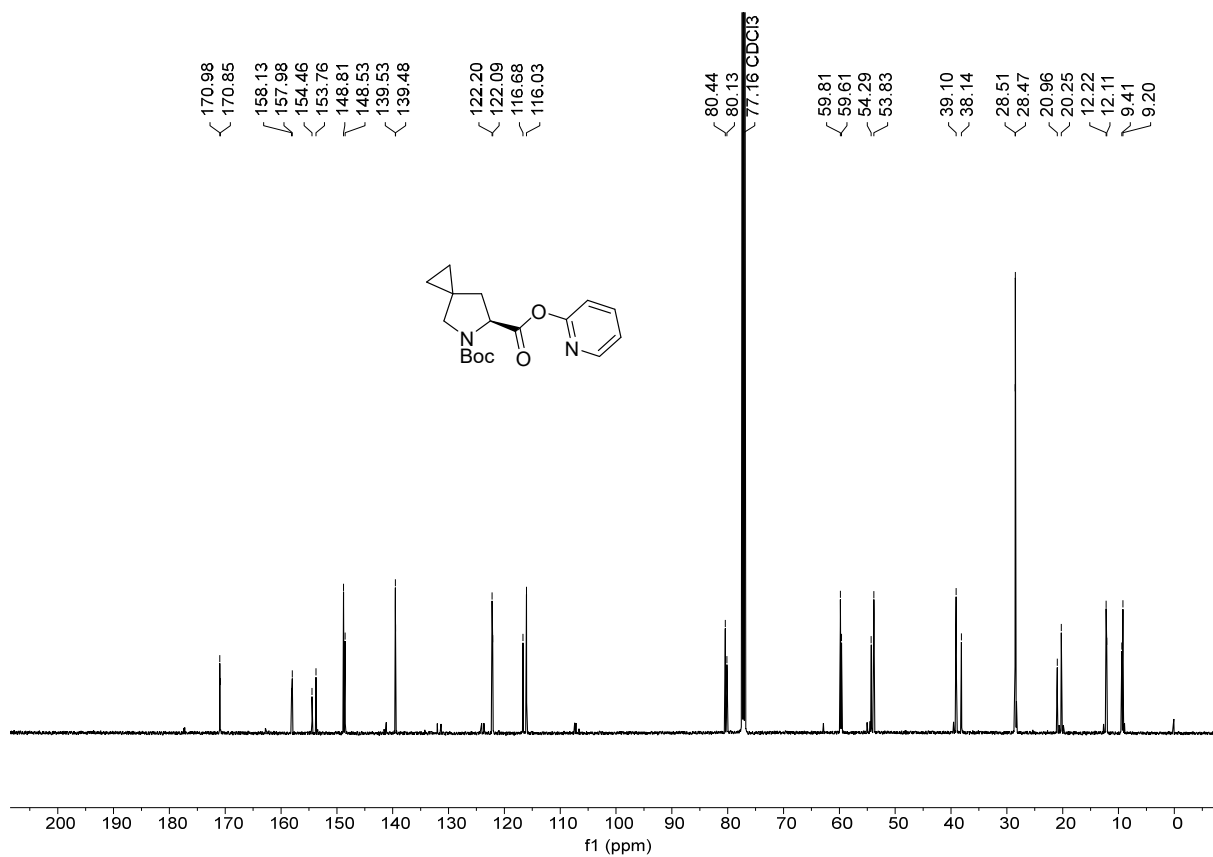
¹³C {¹H} NMR (125 MHz, CDCl₃) of **87**



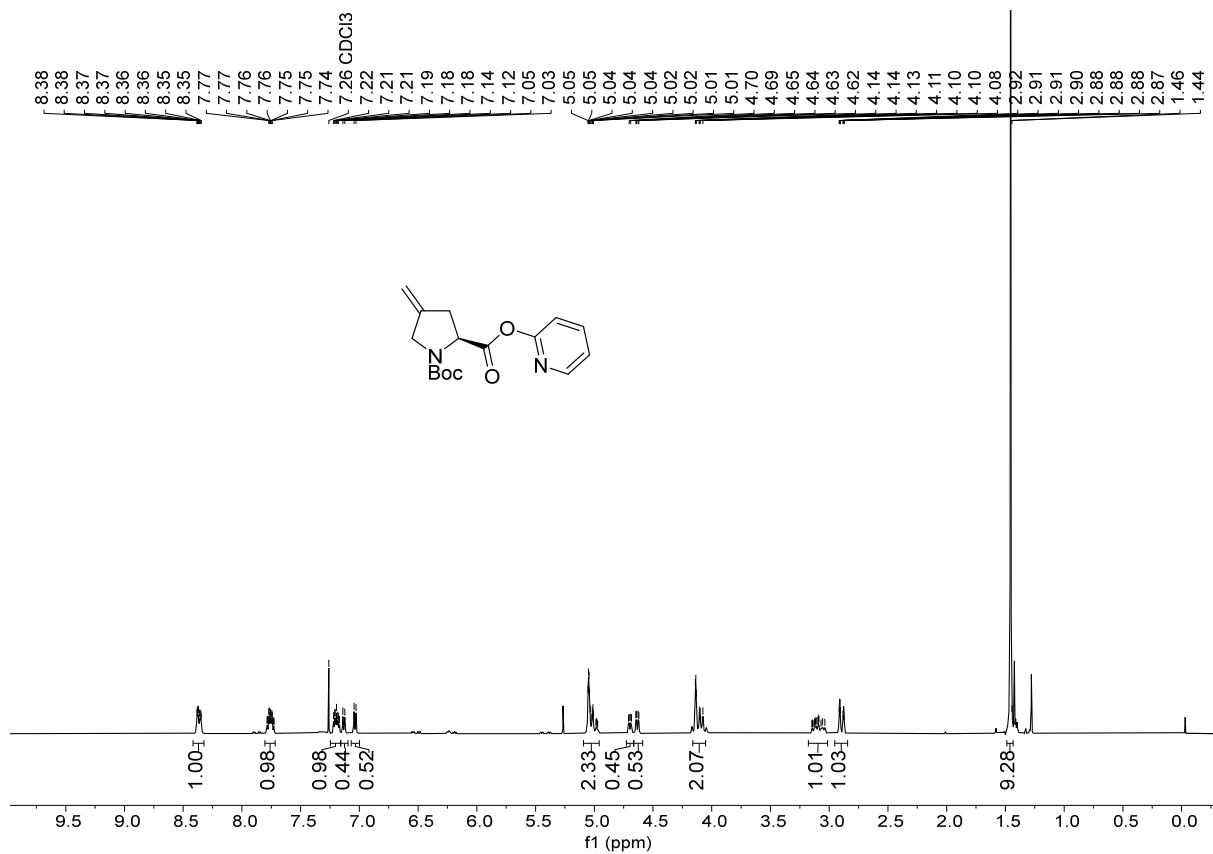




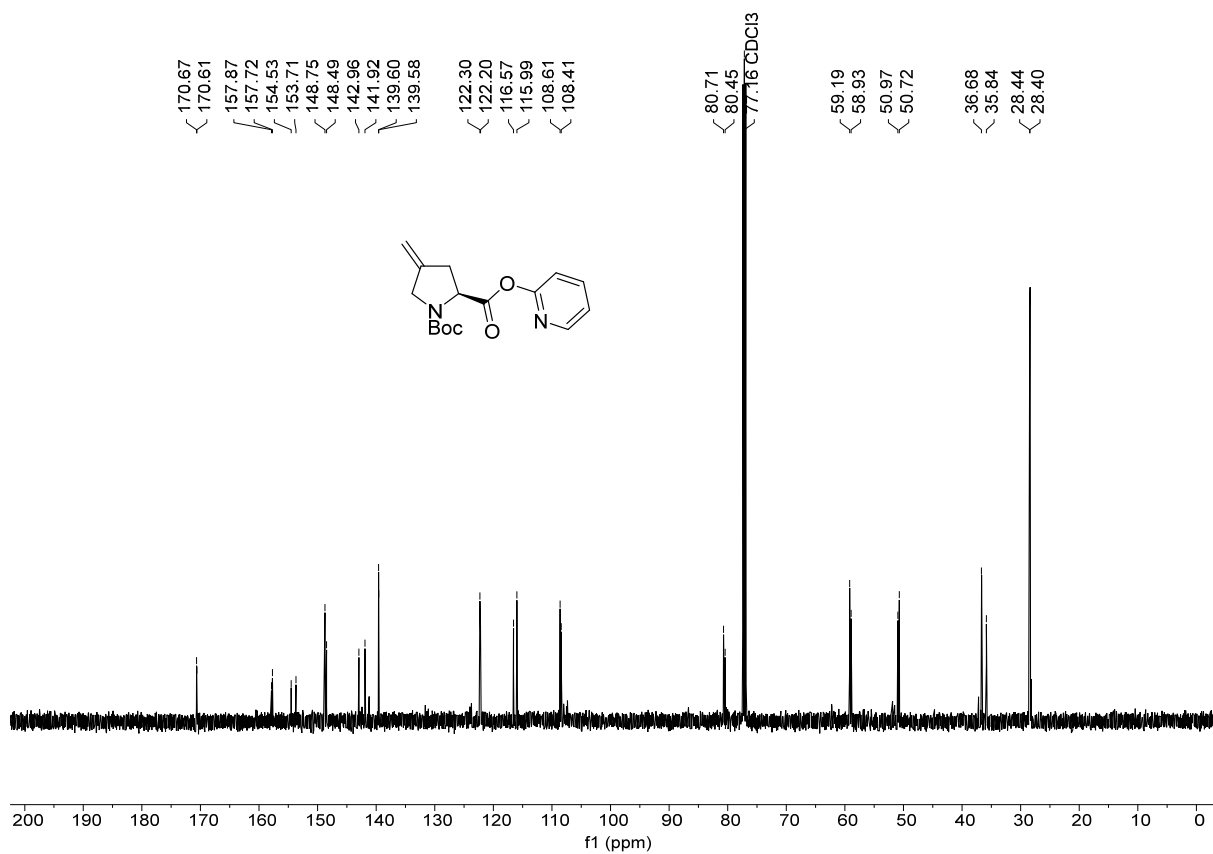
¹H NMR (500 MHz, CDCl₃) of S2



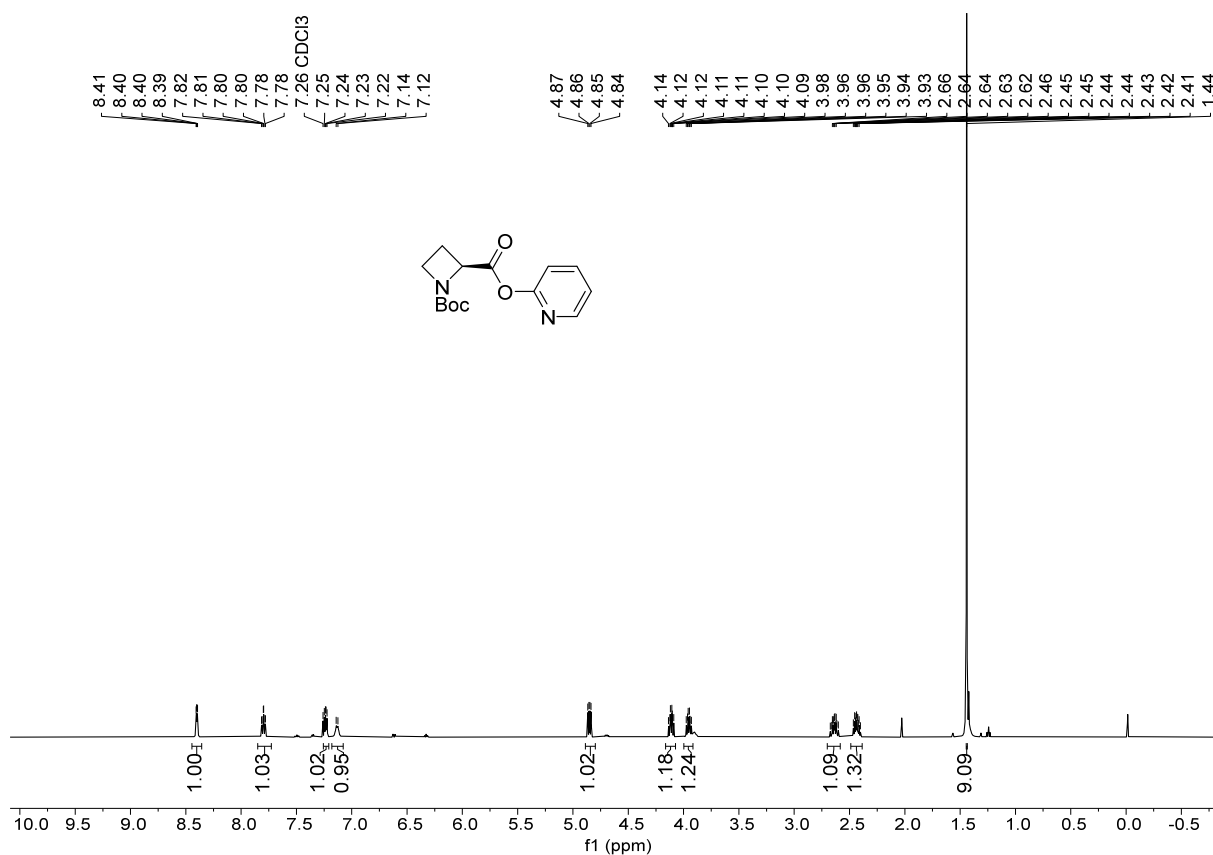
¹³C {¹H} NMR (125 MHz, CDCl₃) of S2



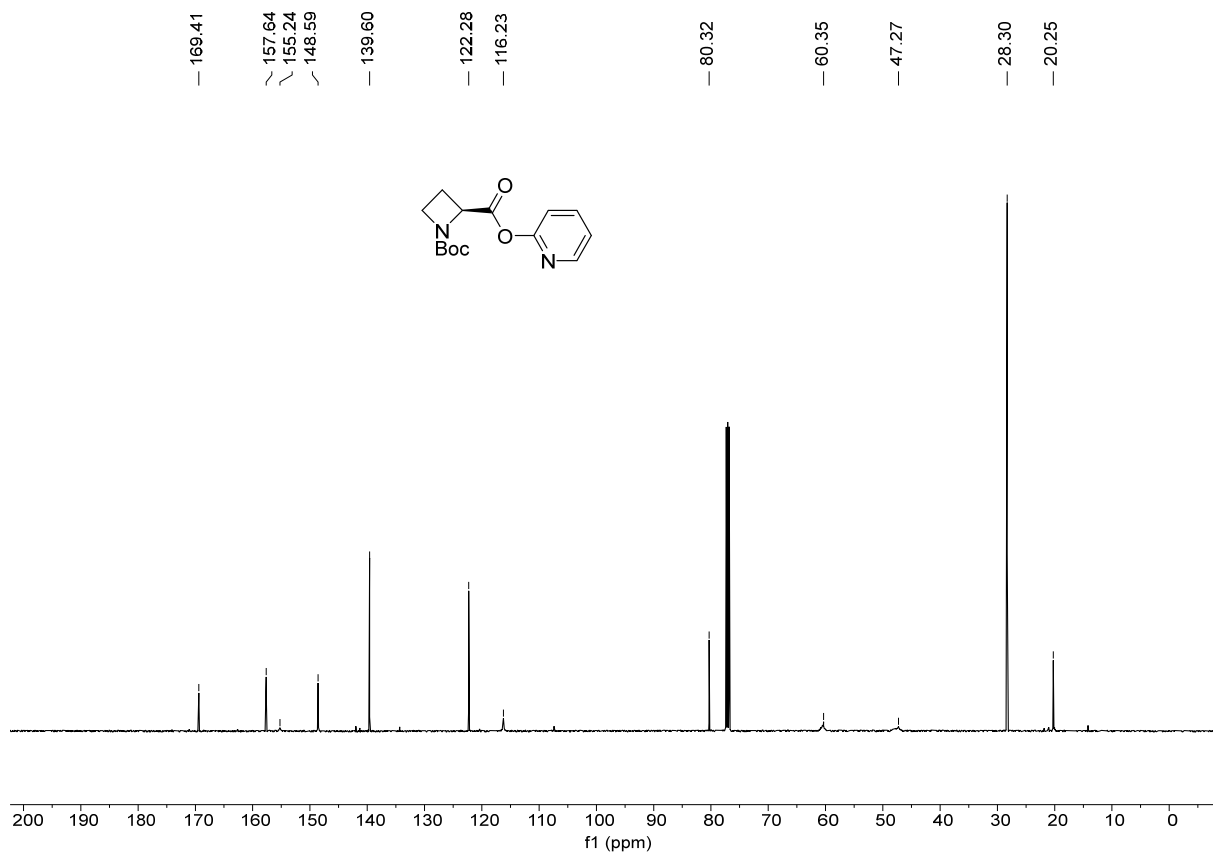
¹H NMR (500 MHz, CDCl₃) of S3



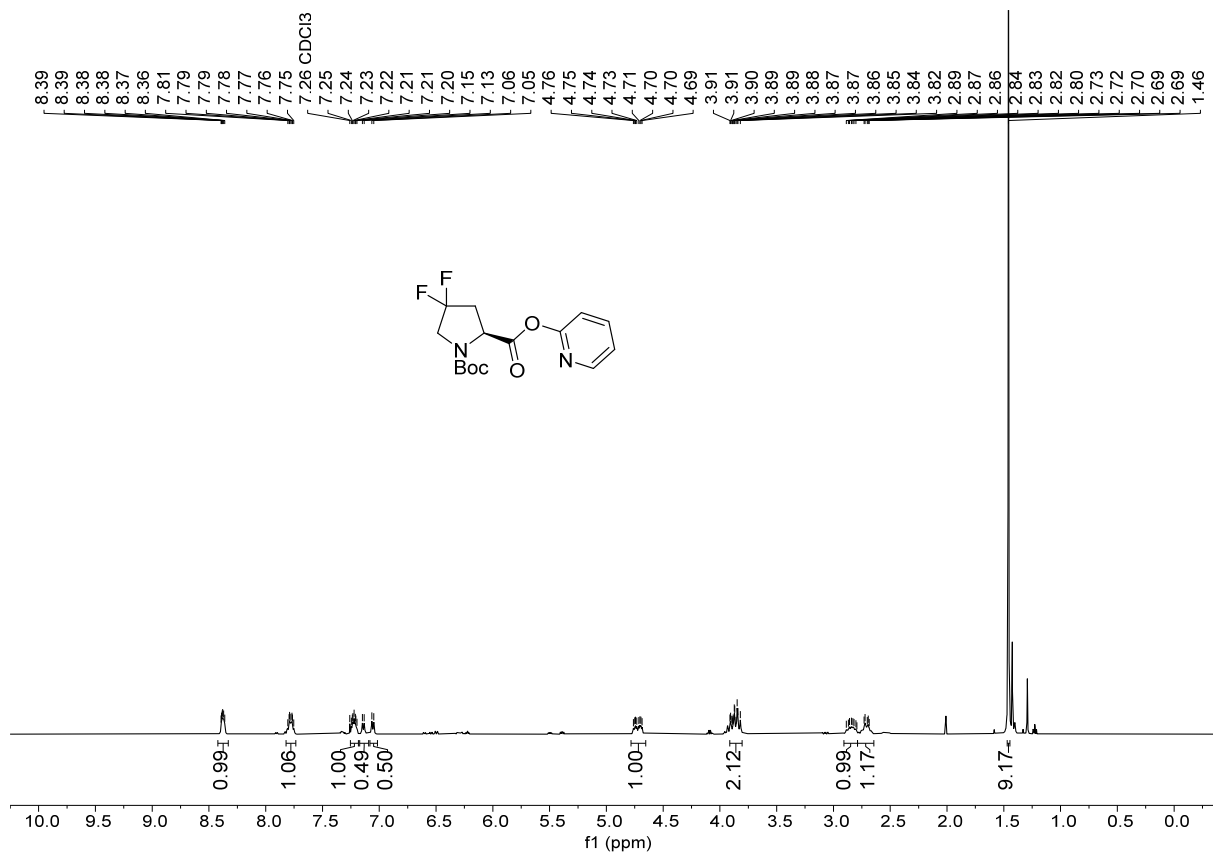
¹³C {¹H} NMR (125 MHz, CDCl₃) of S3



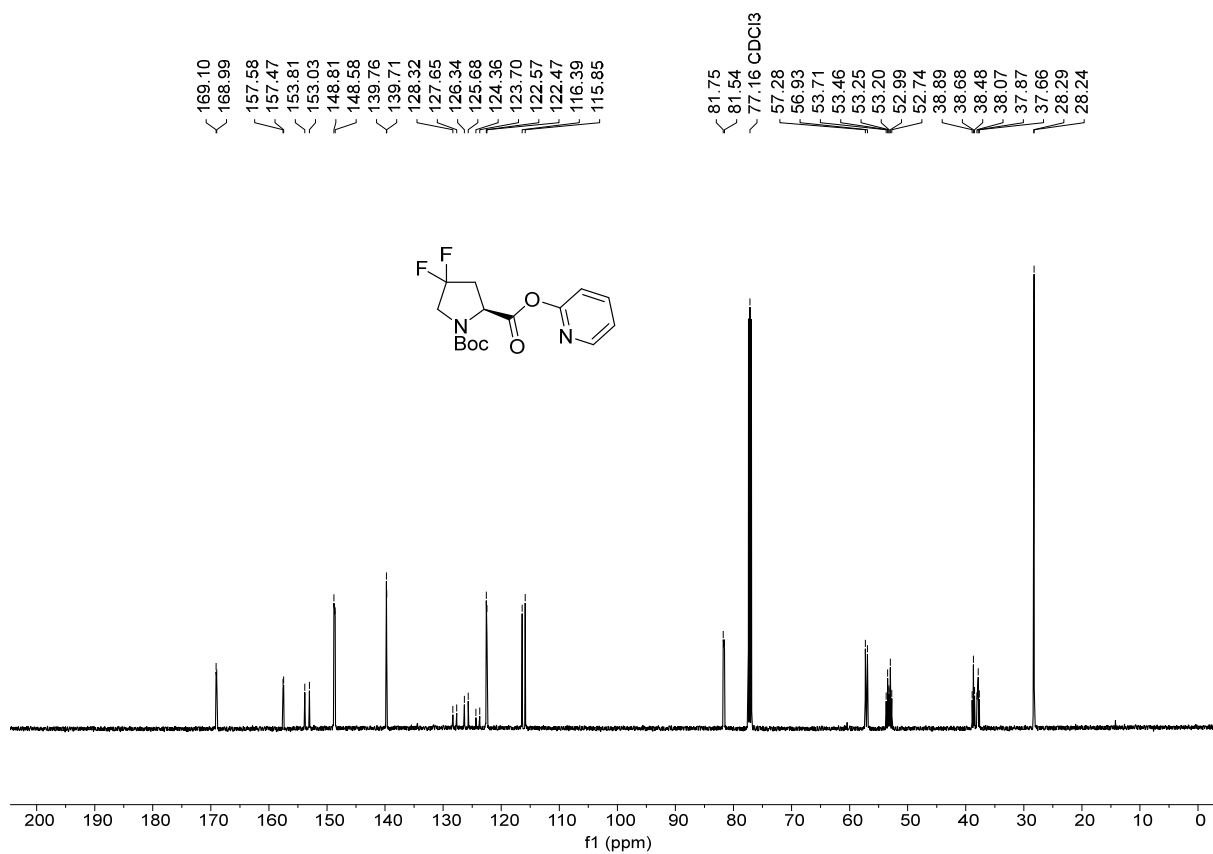
¹H NMR (500 MHz, CDCl₃) of S4



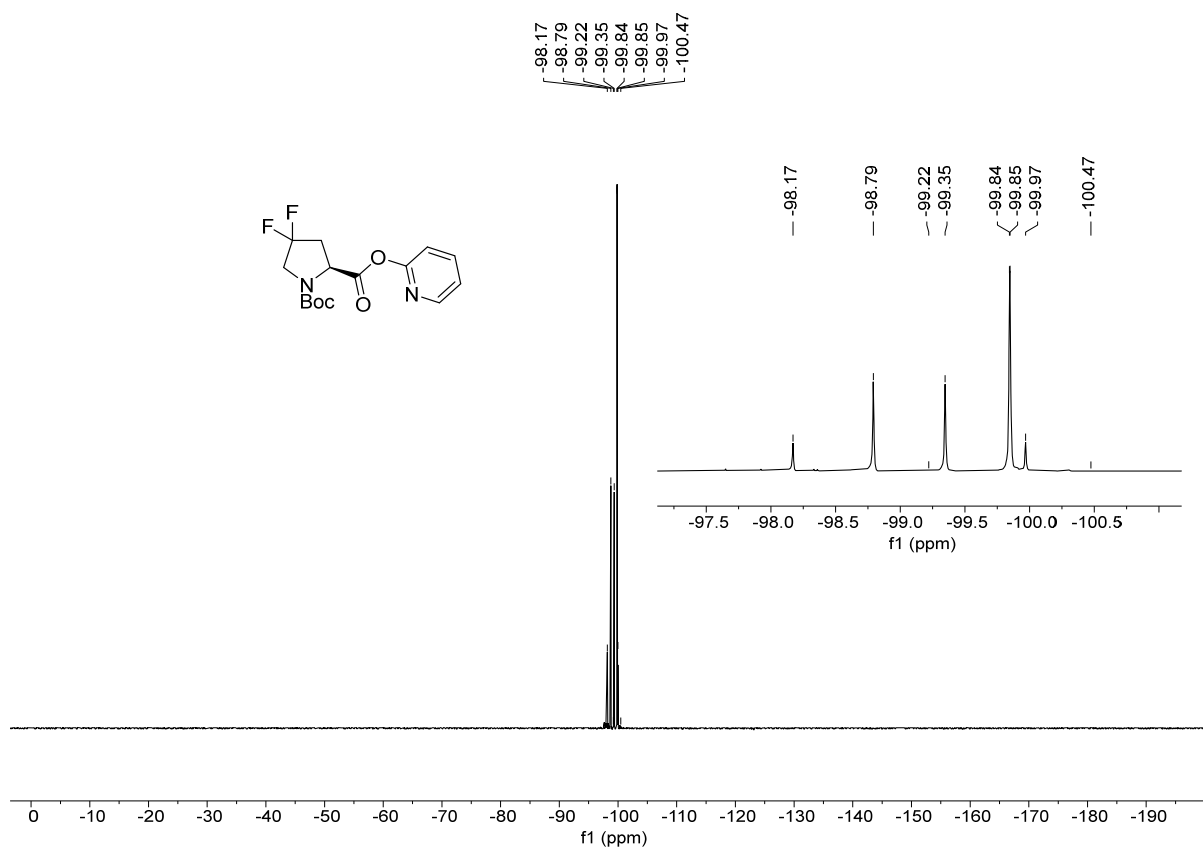
¹³C{¹H} NMR (125 MHz, CDCl₃) of S4

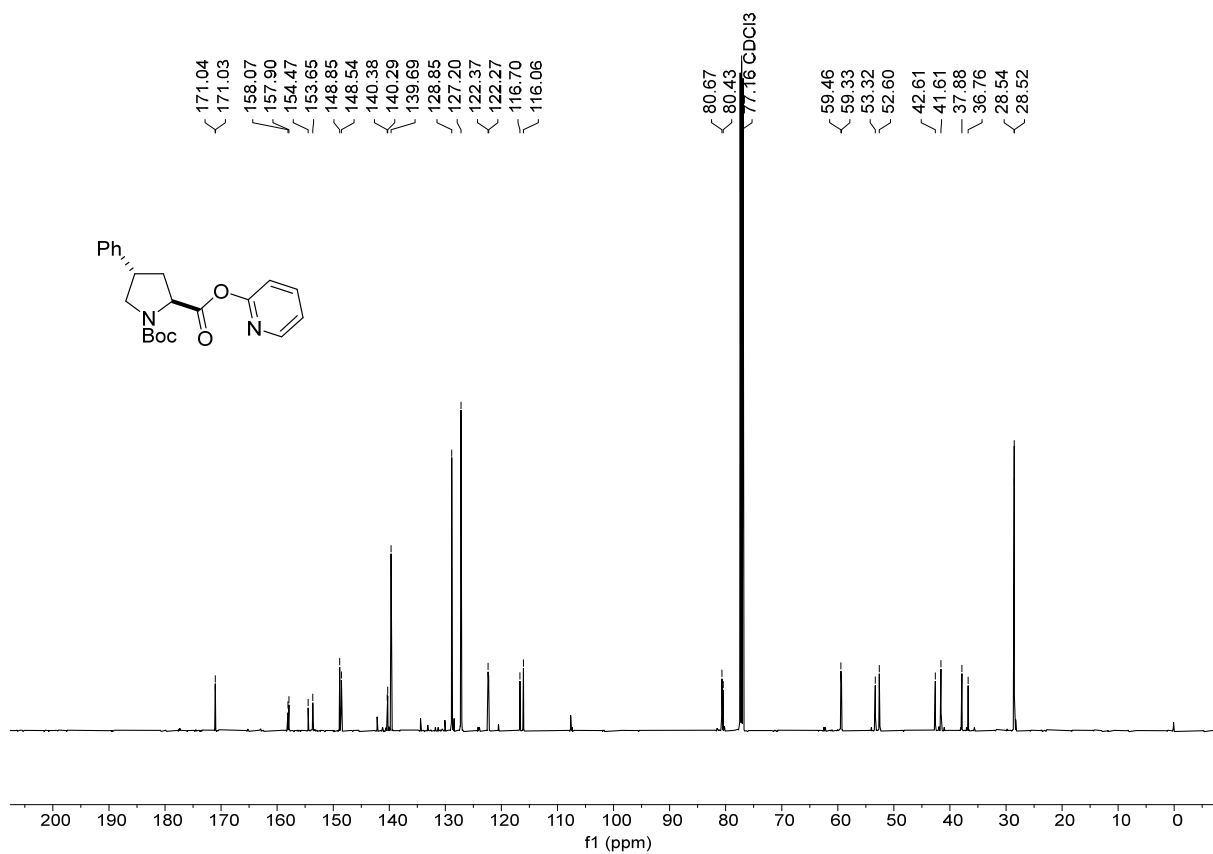
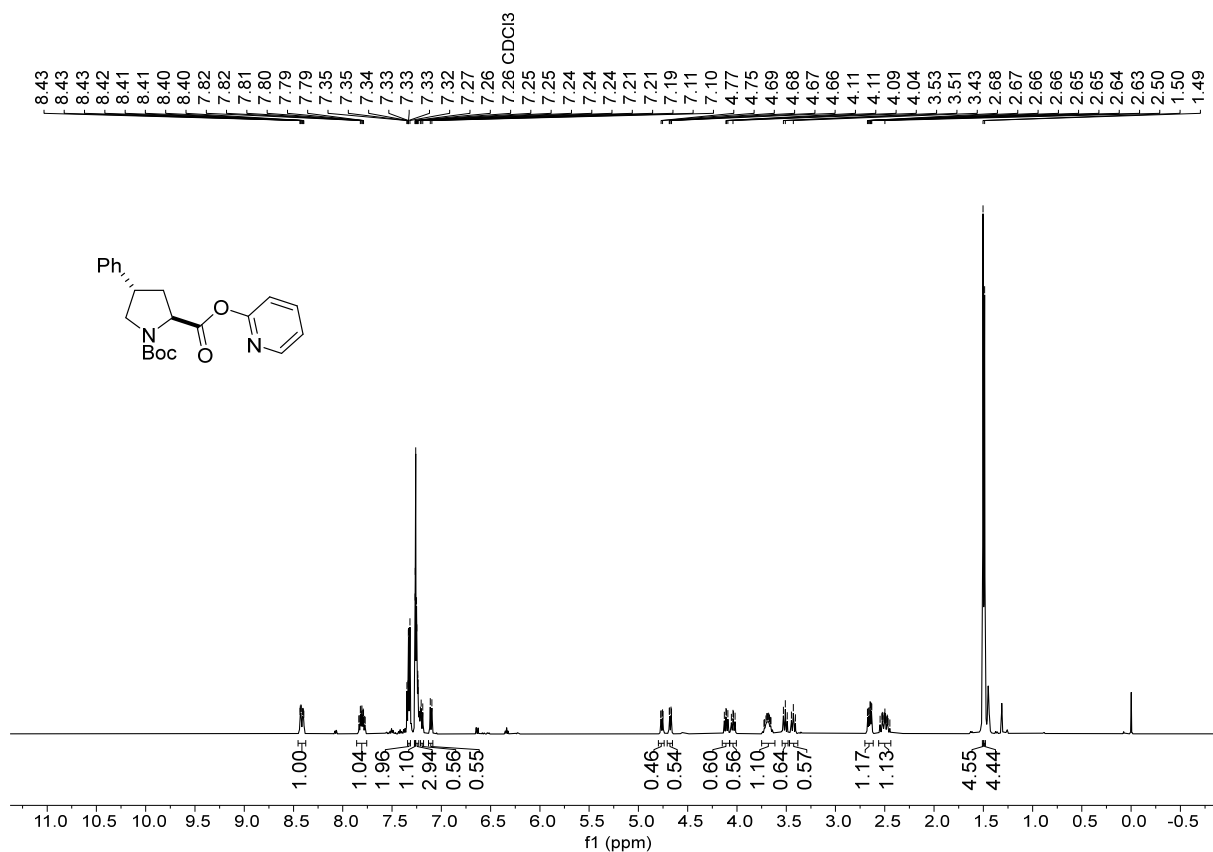


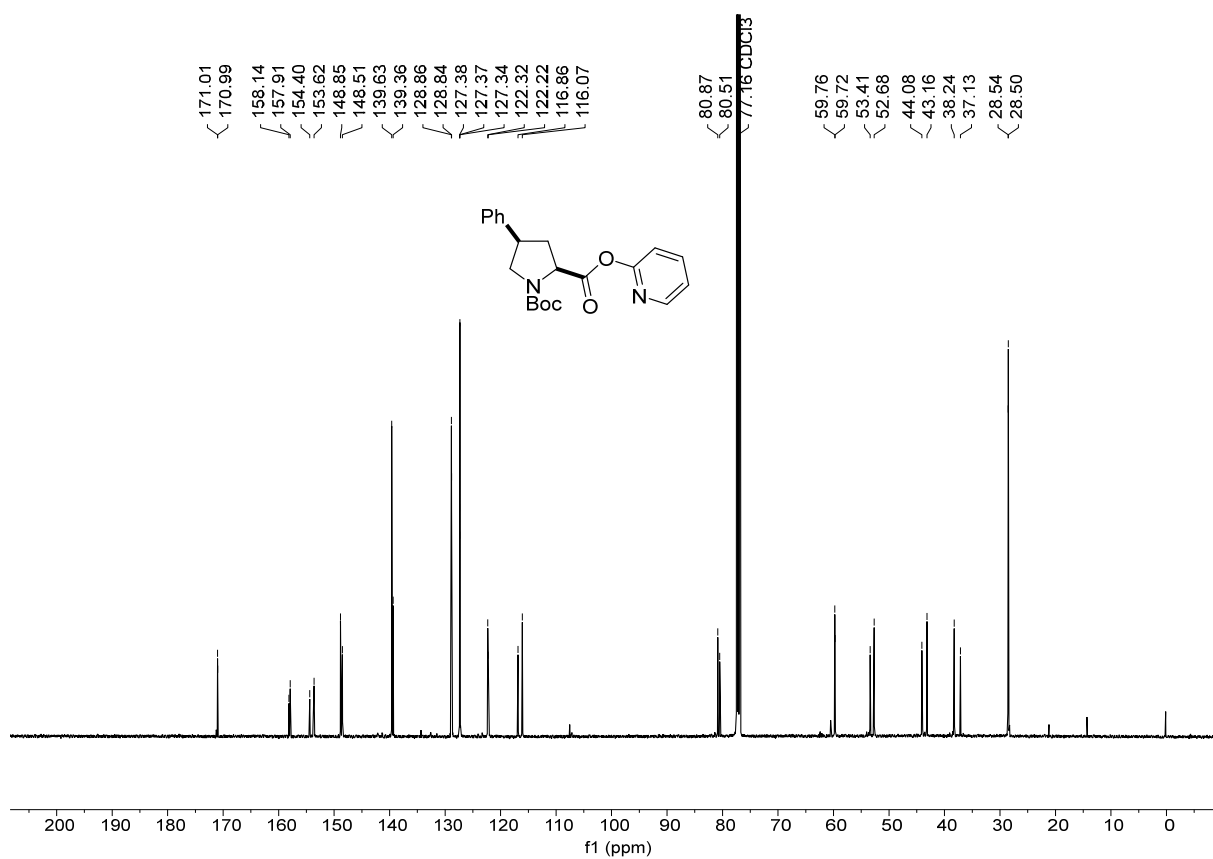
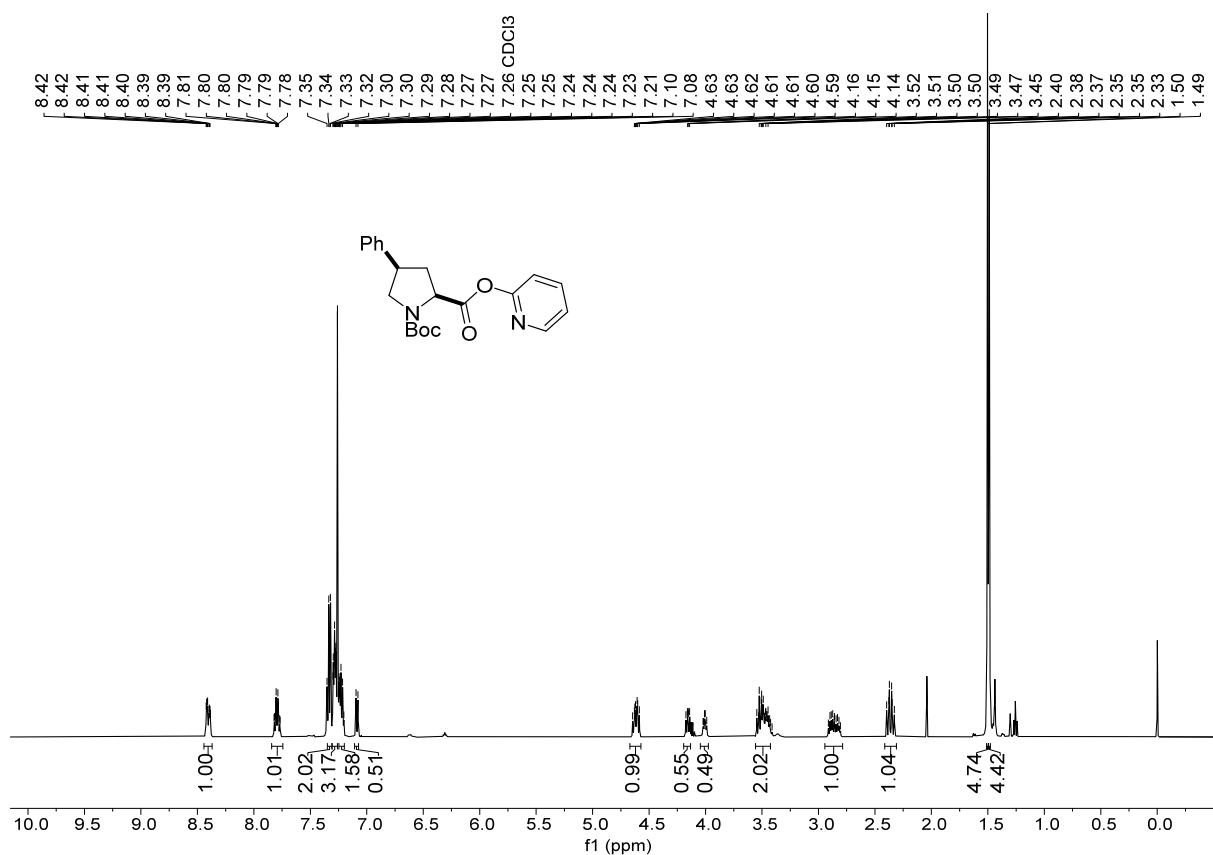
¹H NMR (500 MHz, CDCl₃) of **S5**

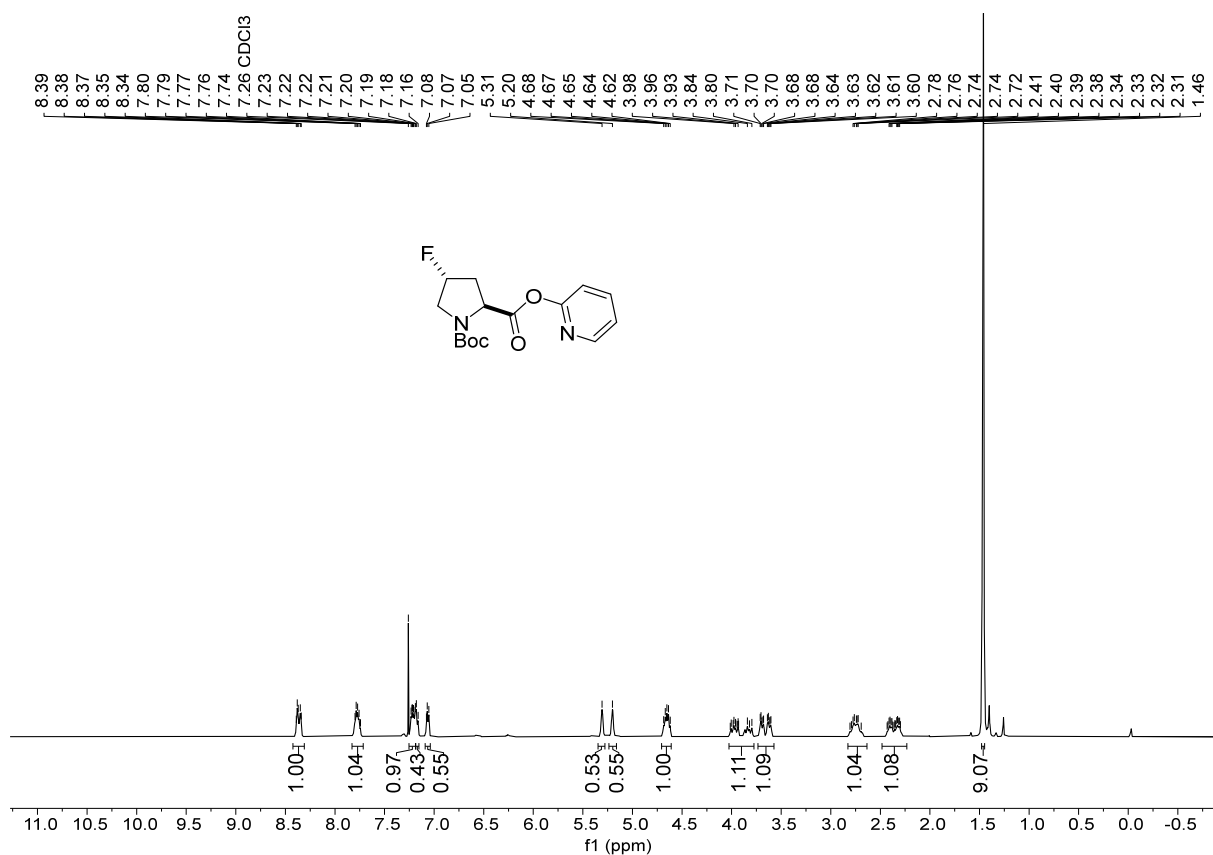


¹³C {¹H} NMR (125 MHz, CDCl₃) of **S5**

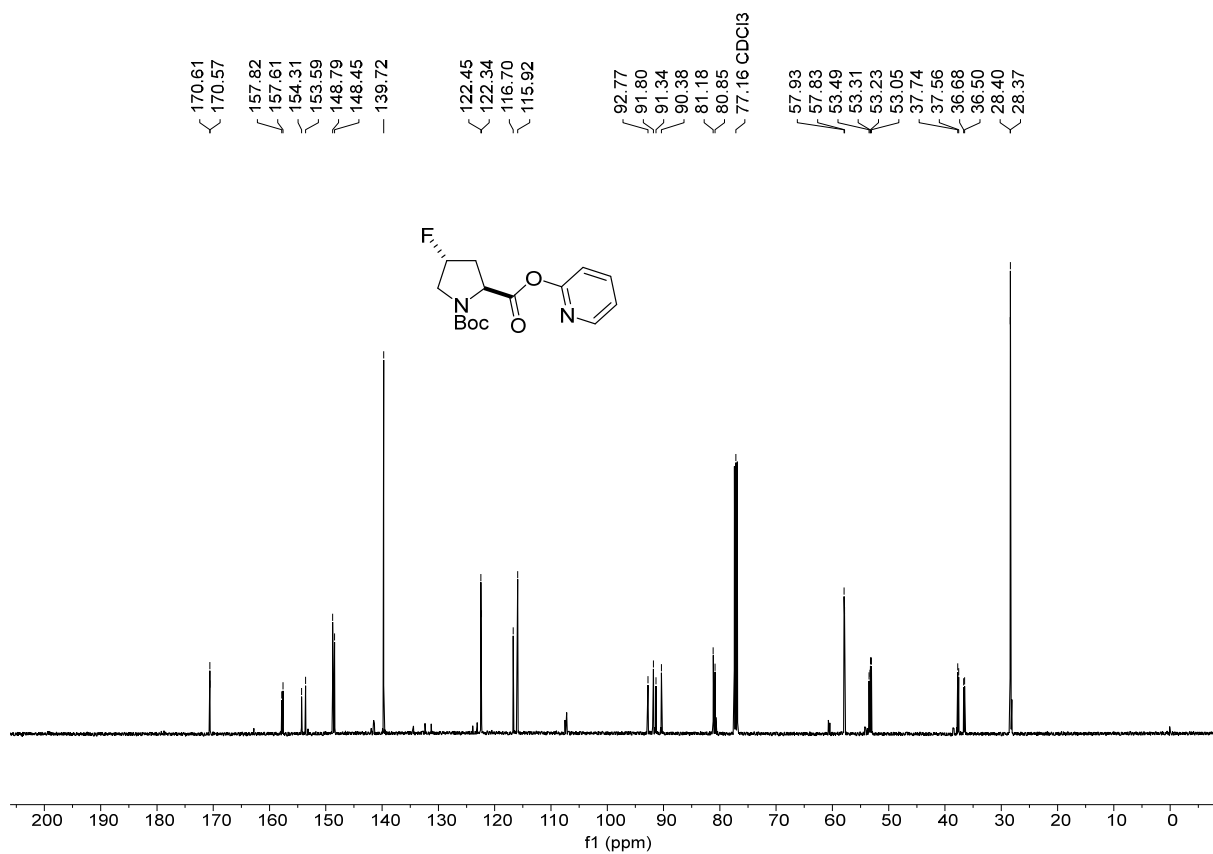




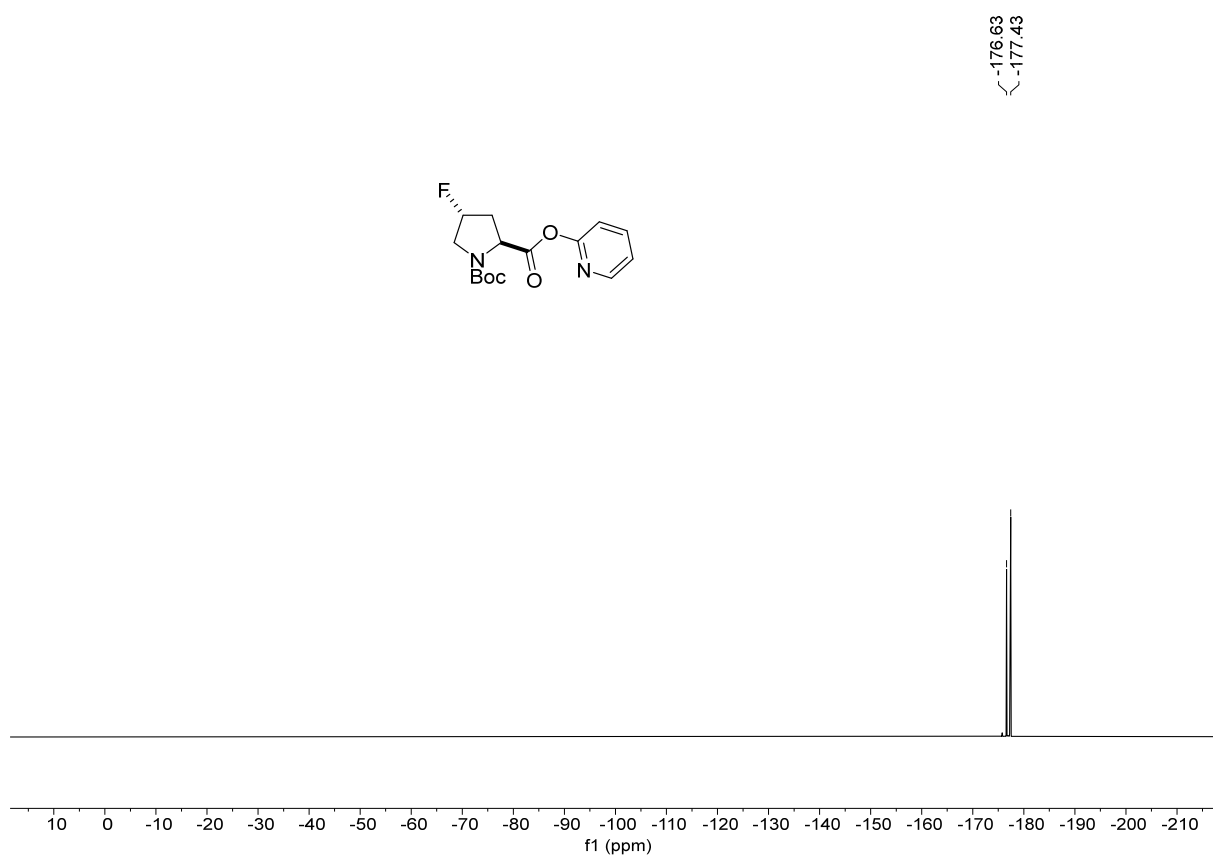




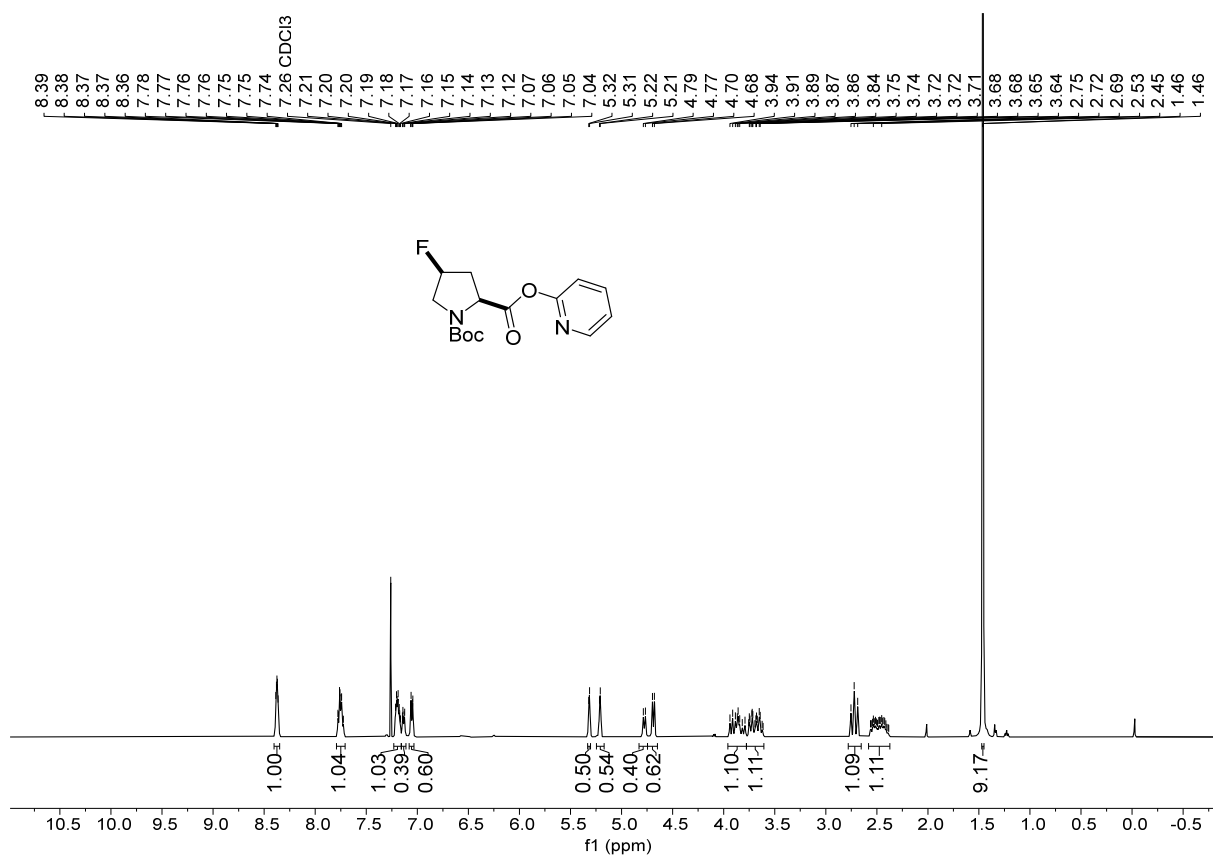
¹H NMR (500 MHz, CDCl₃) of S10



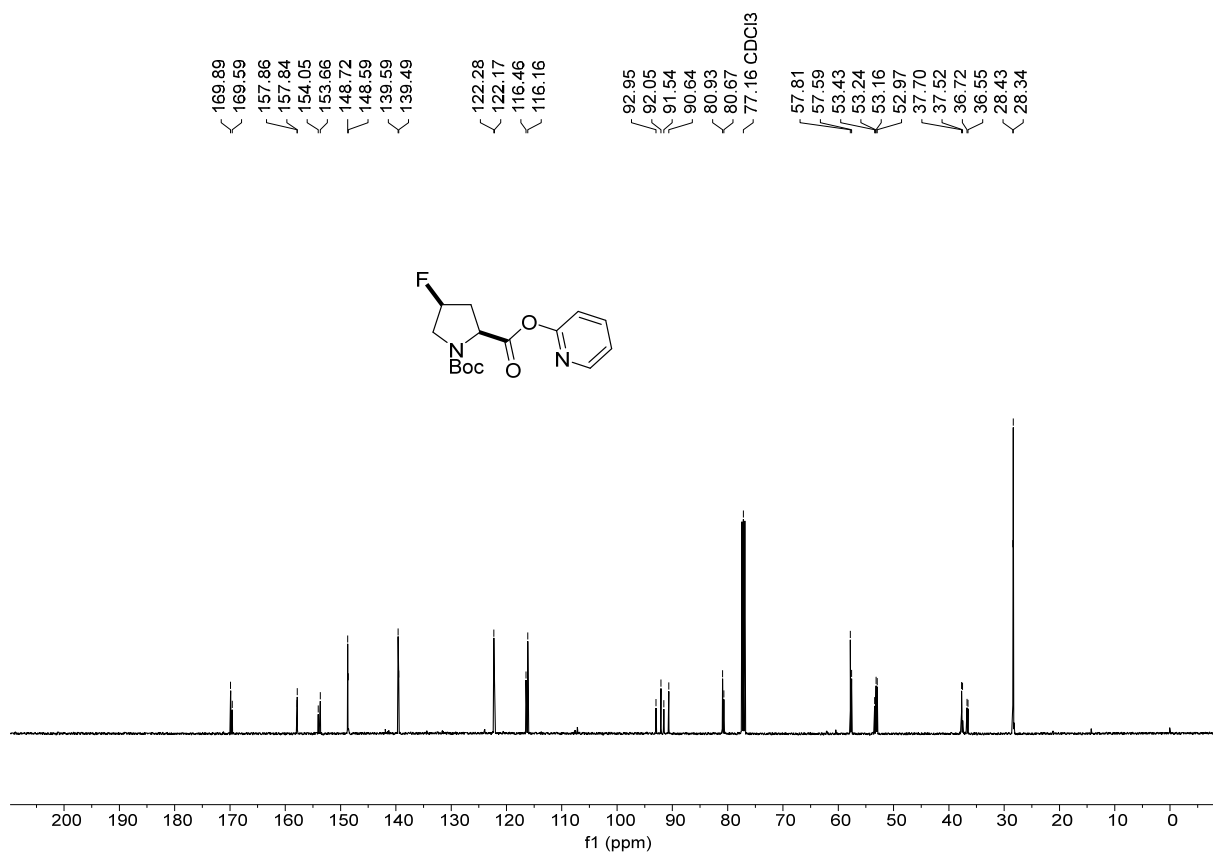
¹³C {¹H} NMR (125 MHz, CDCl₃) of S10



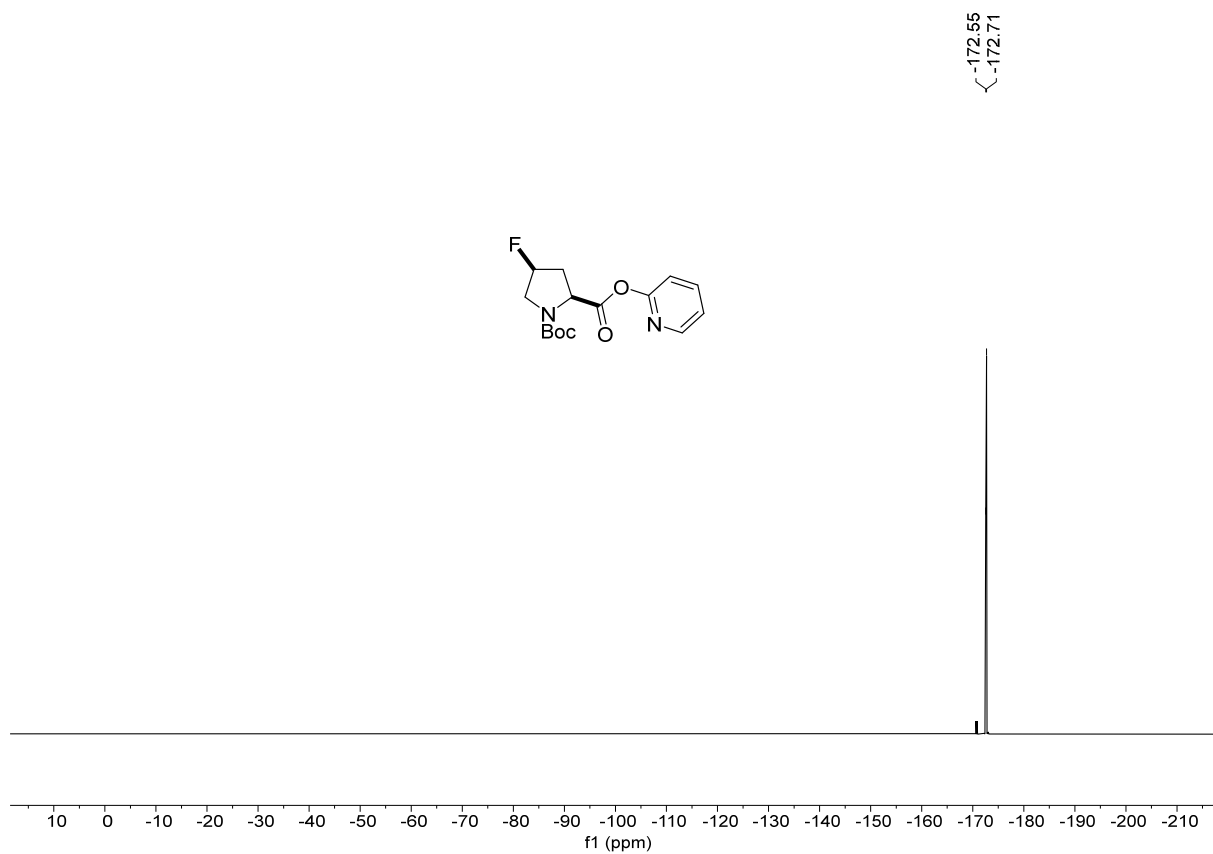
$^{19}\text{F}\{^1\text{H}\}$ NMR (377 MHz, CDCl_3) of S10



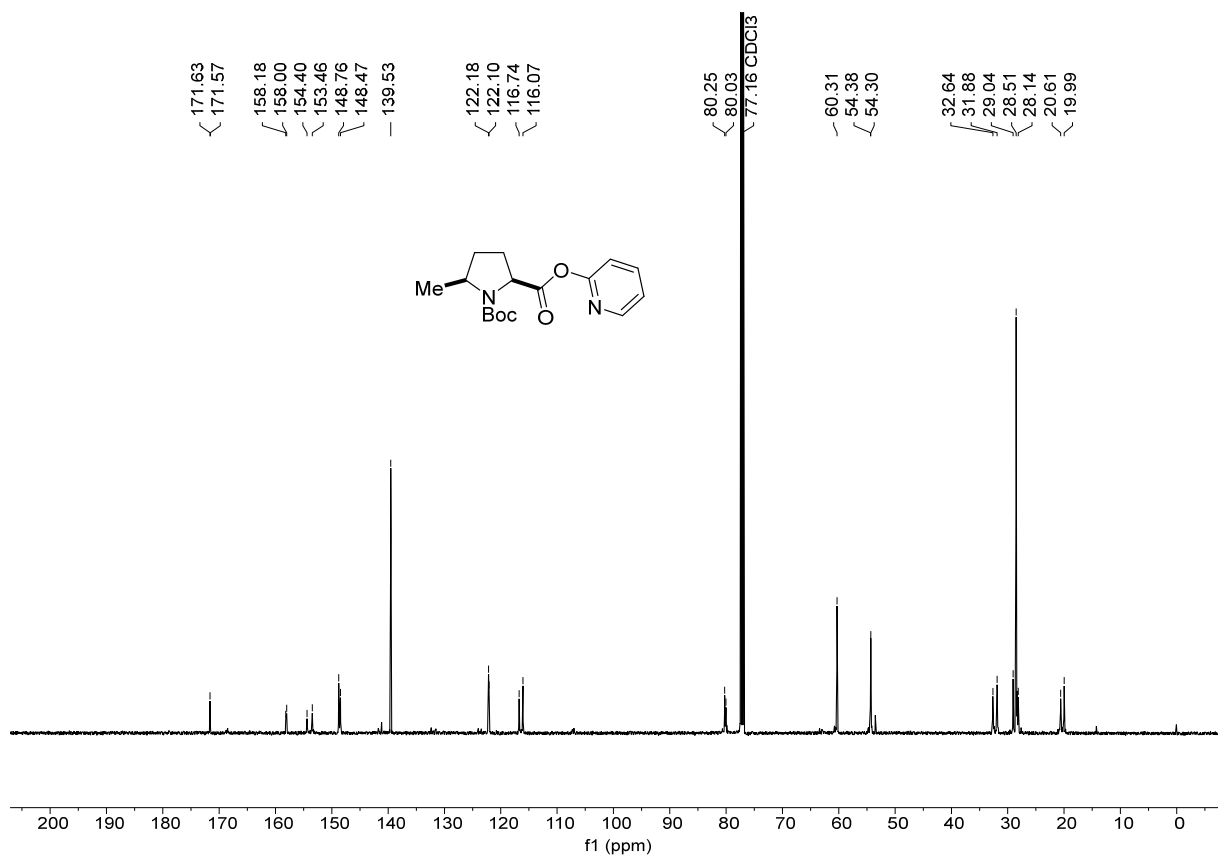
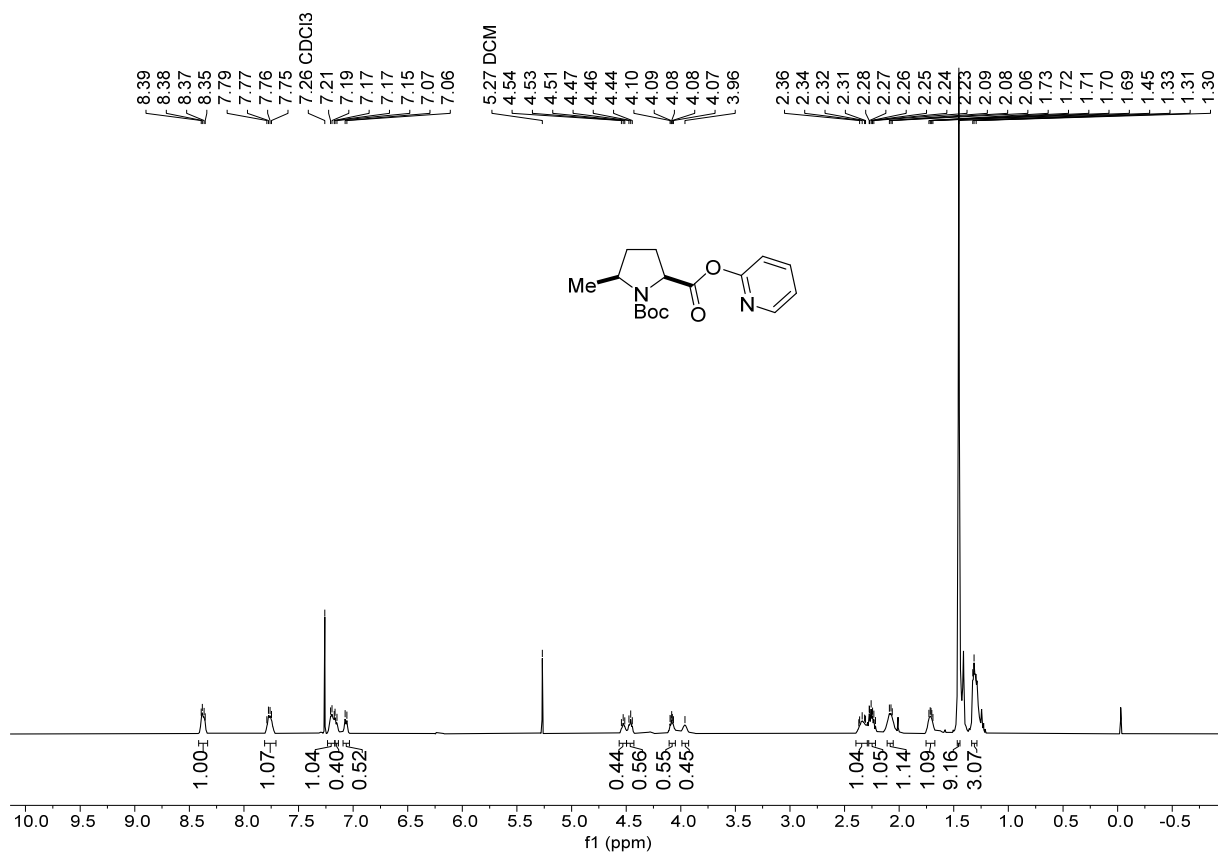
¹H NMR (500 MHz, CDCl₃) of S11

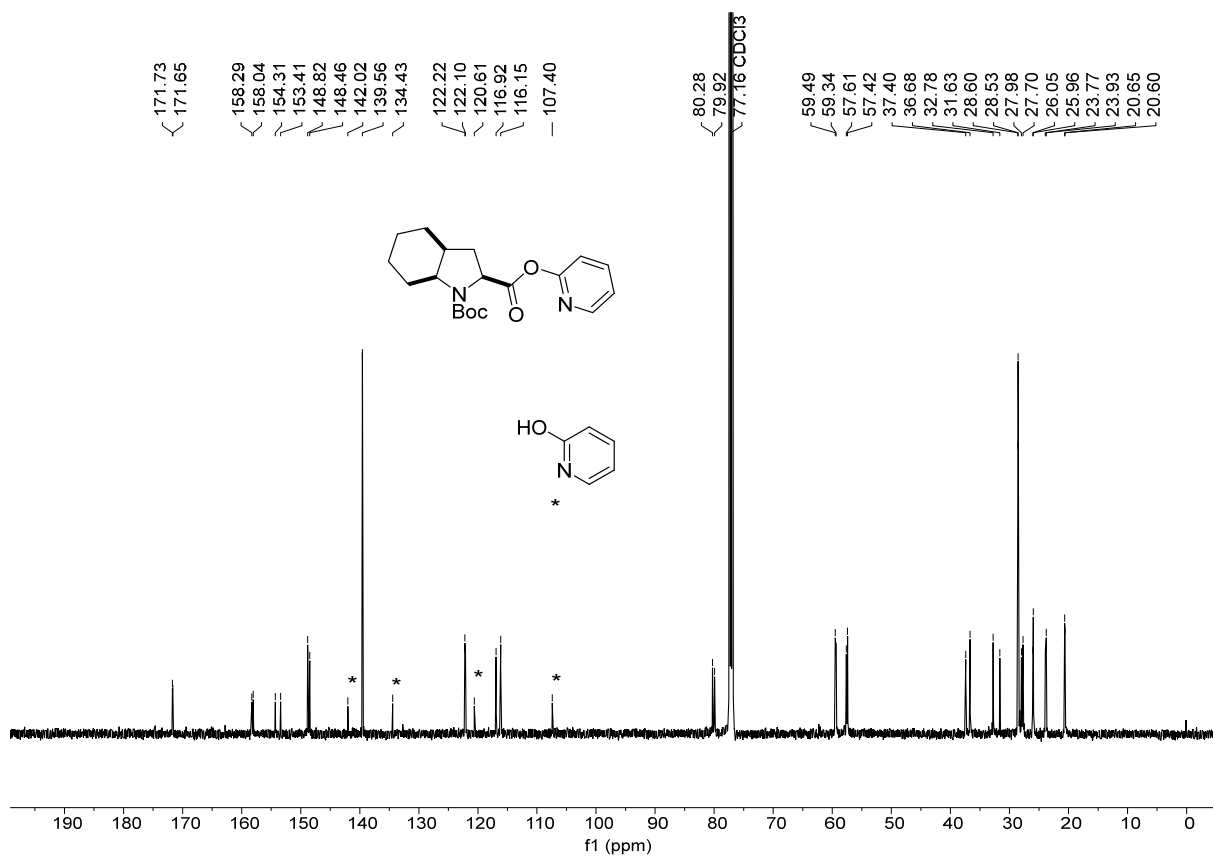
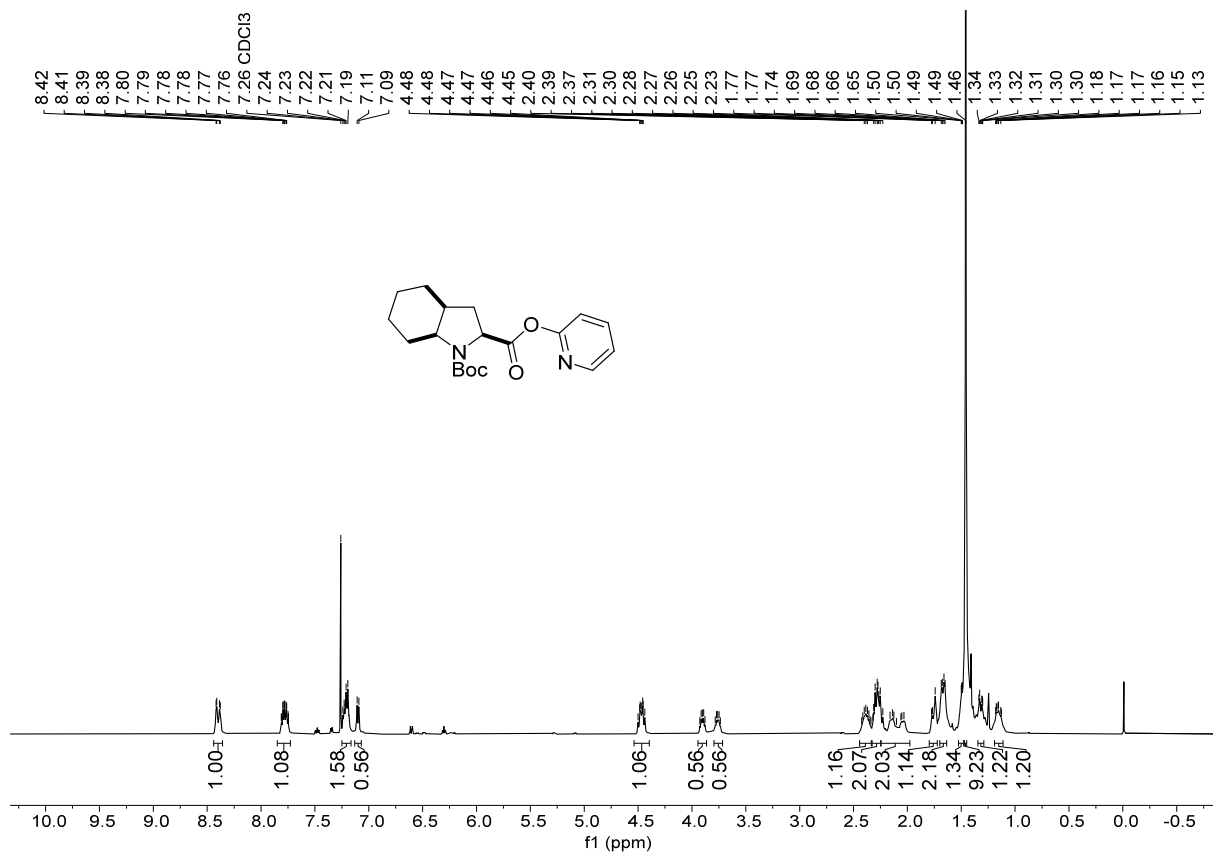


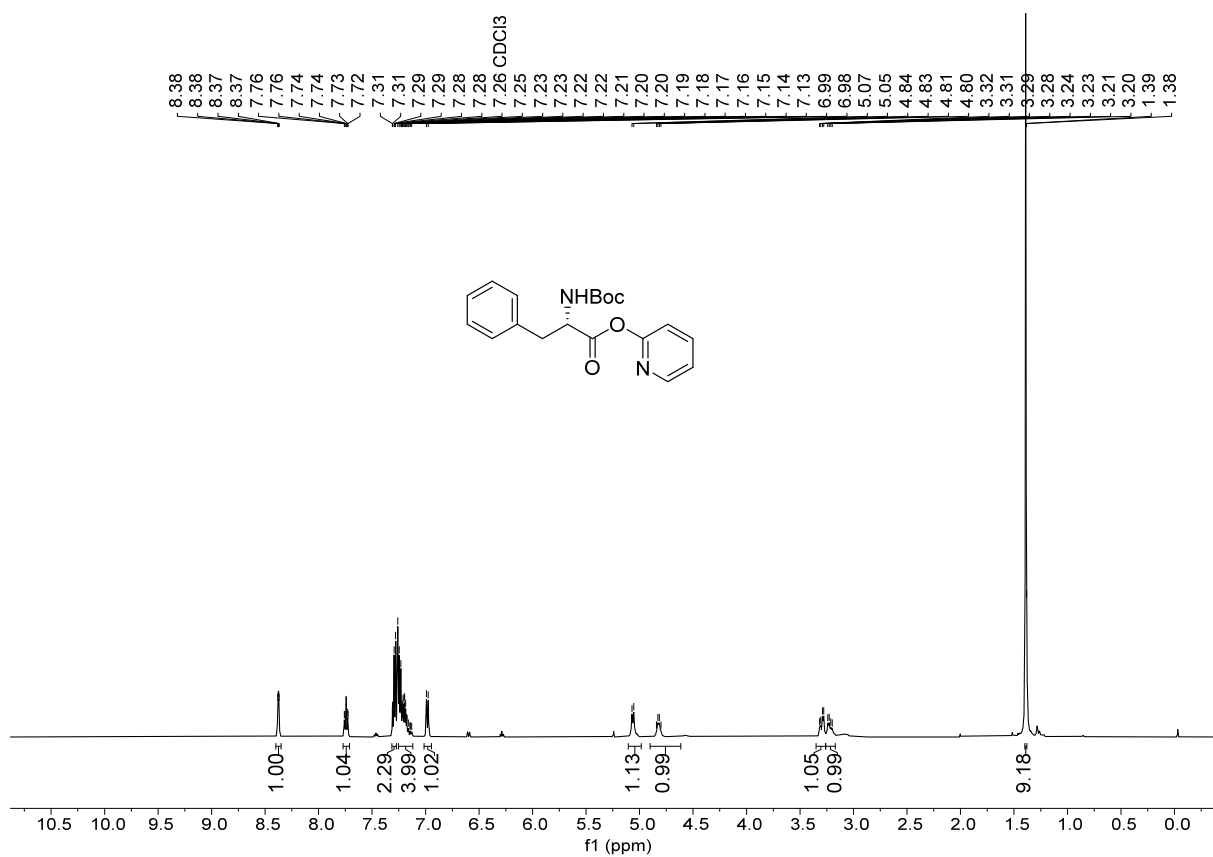
¹³C {¹H} NMR (125 MHz, CDCl₃) of S11



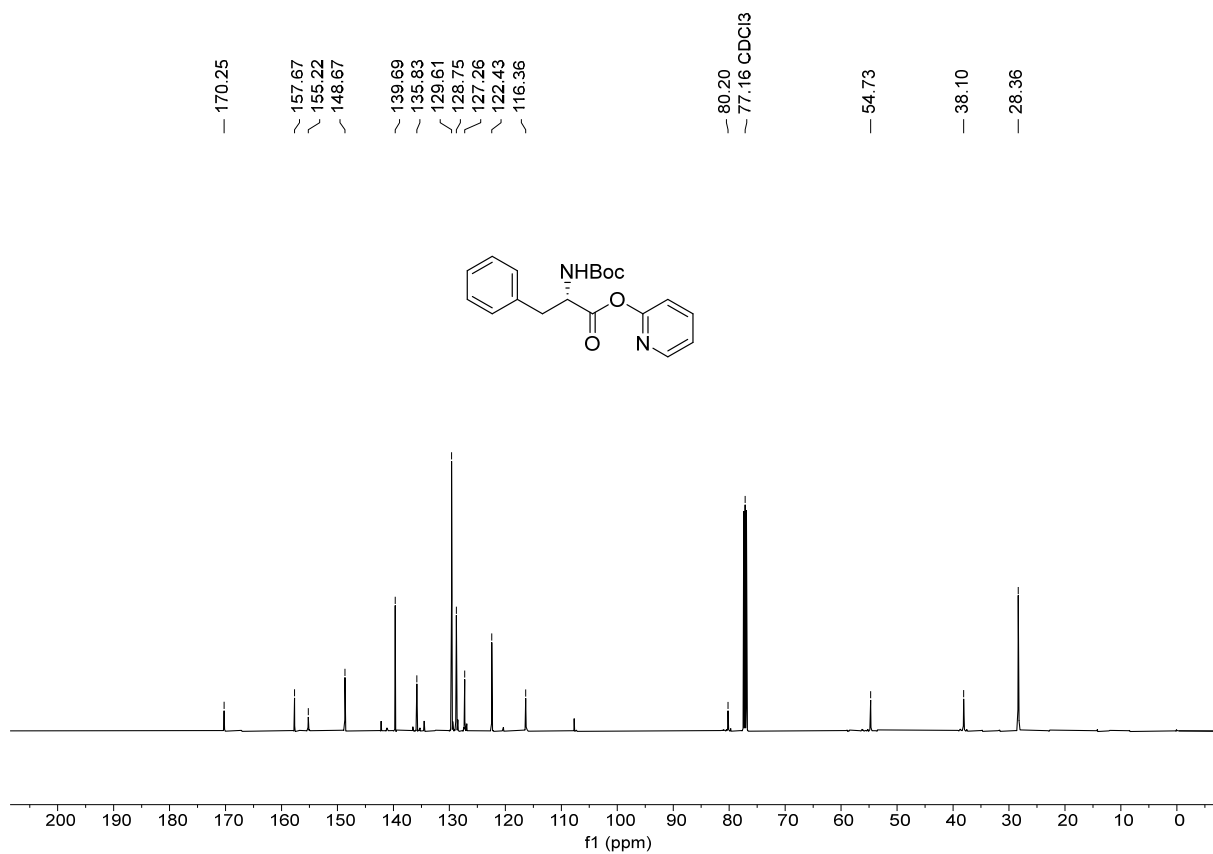
$^{19}\text{F}\{^1\text{H}\}$ NMR (377 MHz, CDCl_3) of **S11**



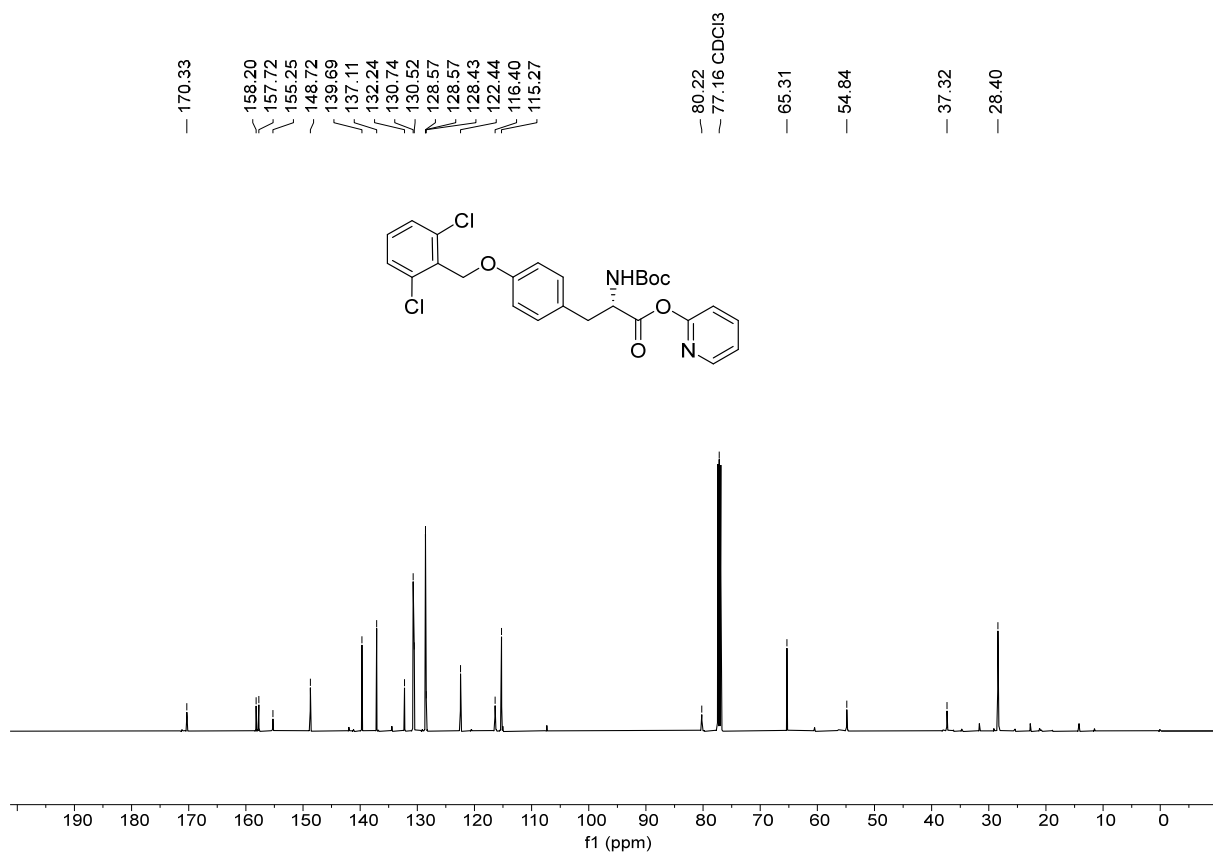
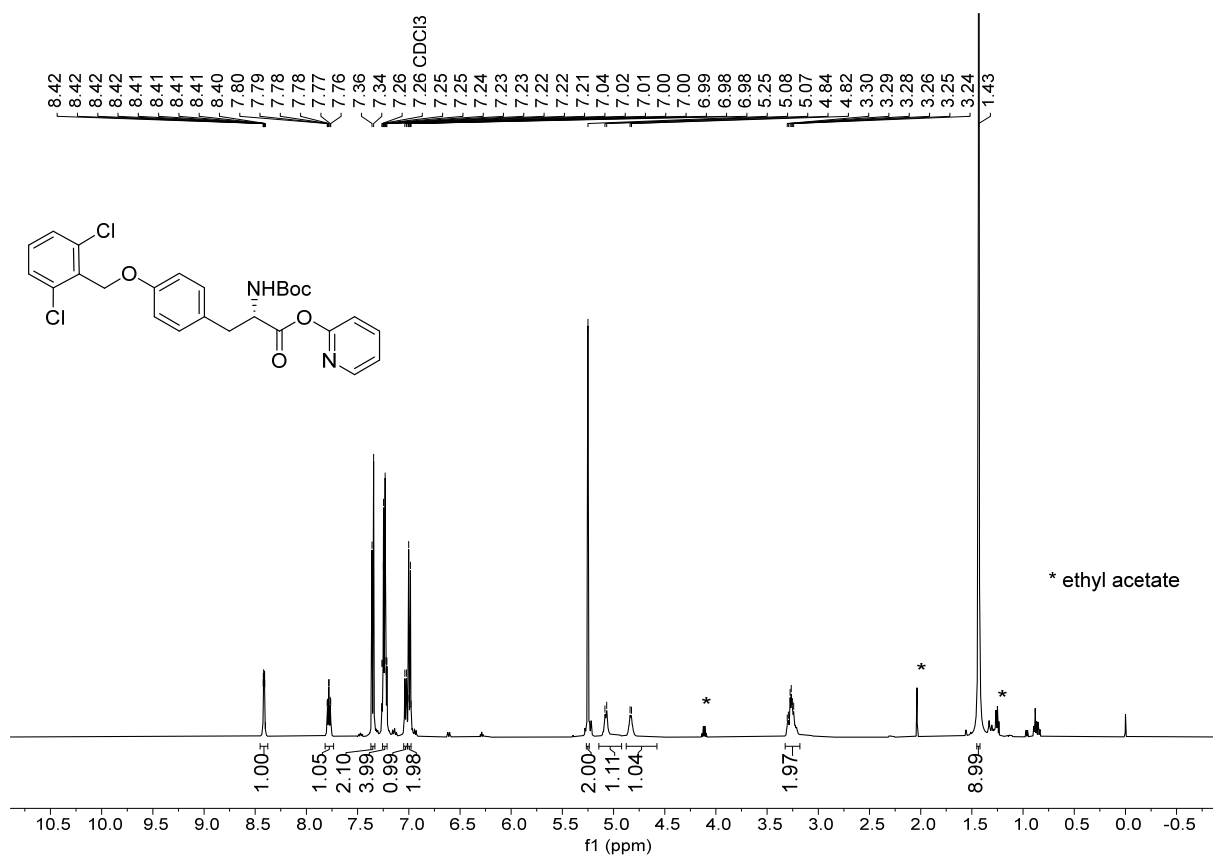


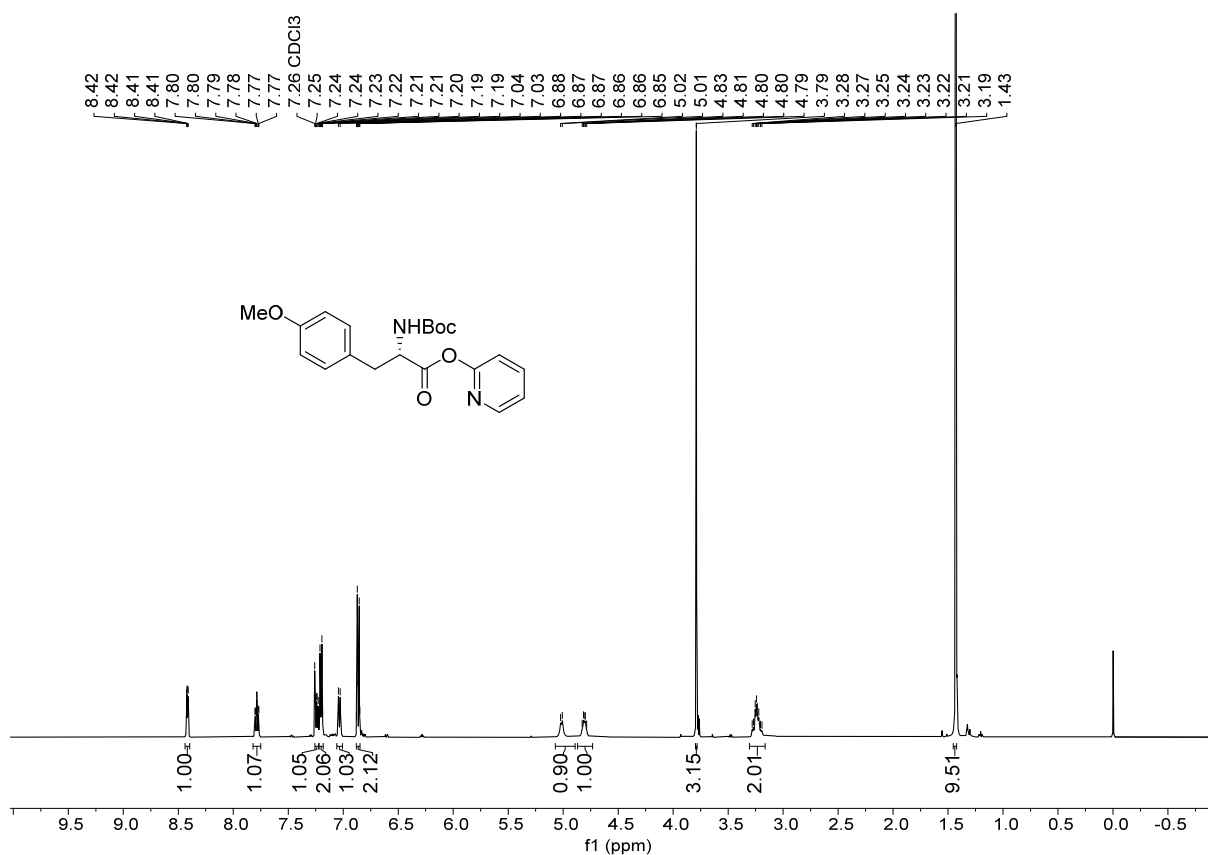


¹H NMR (500 MHz, CDCl₃) of S14

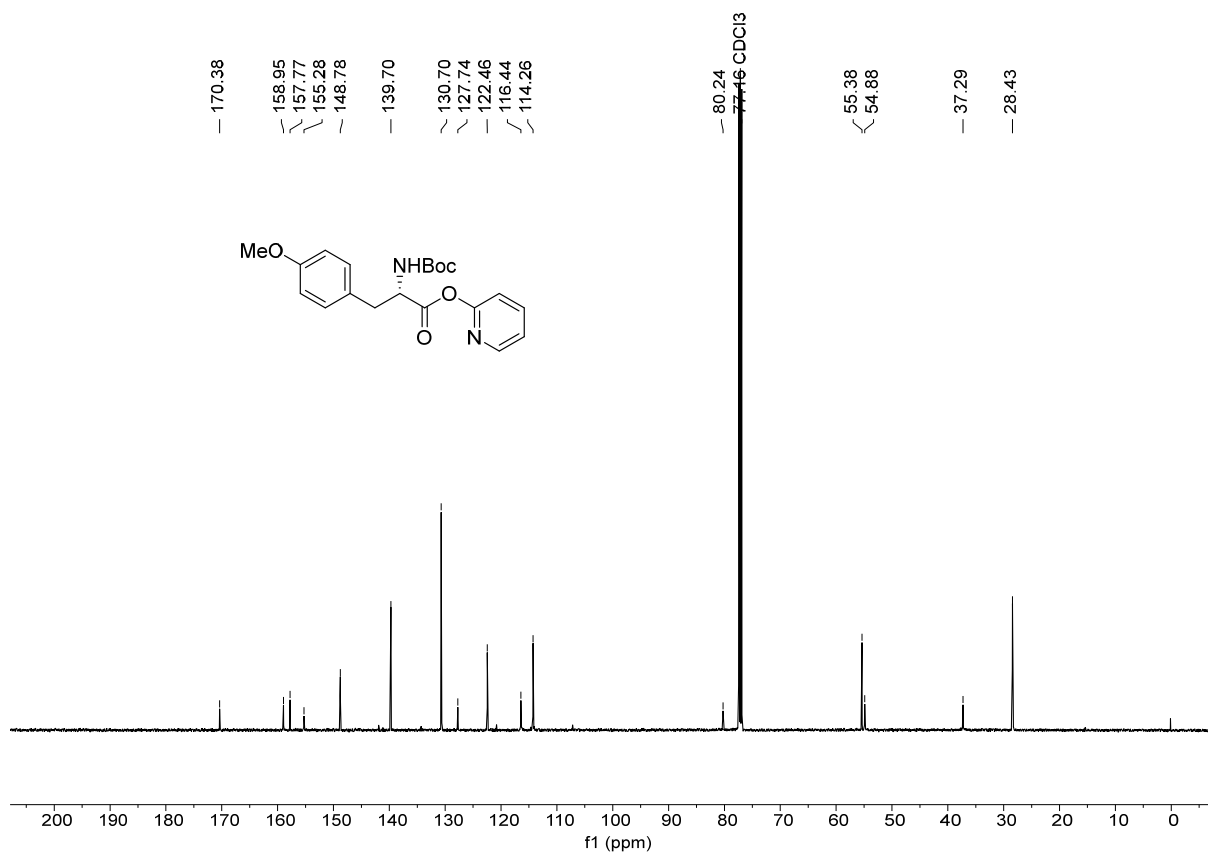


¹³C {¹H} NMR (125 MHz, CDCl₃) of S14

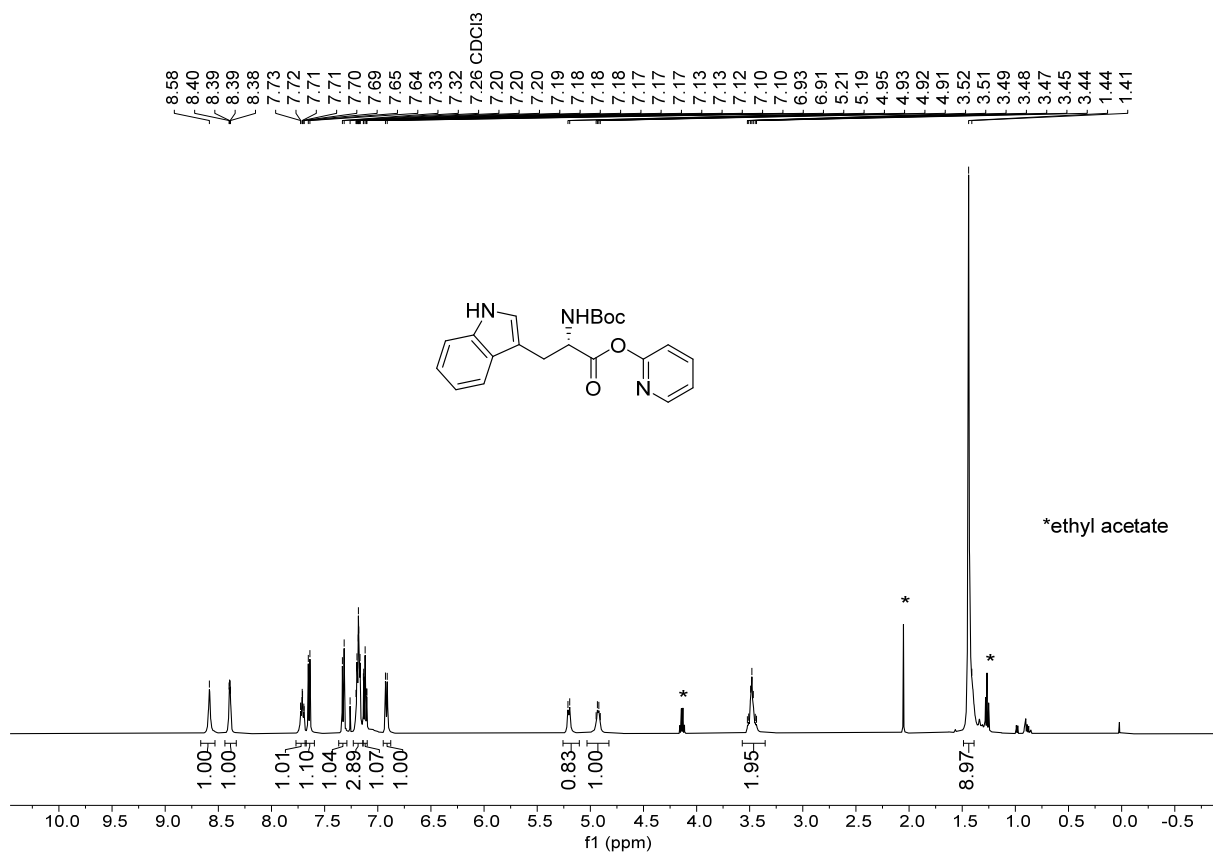




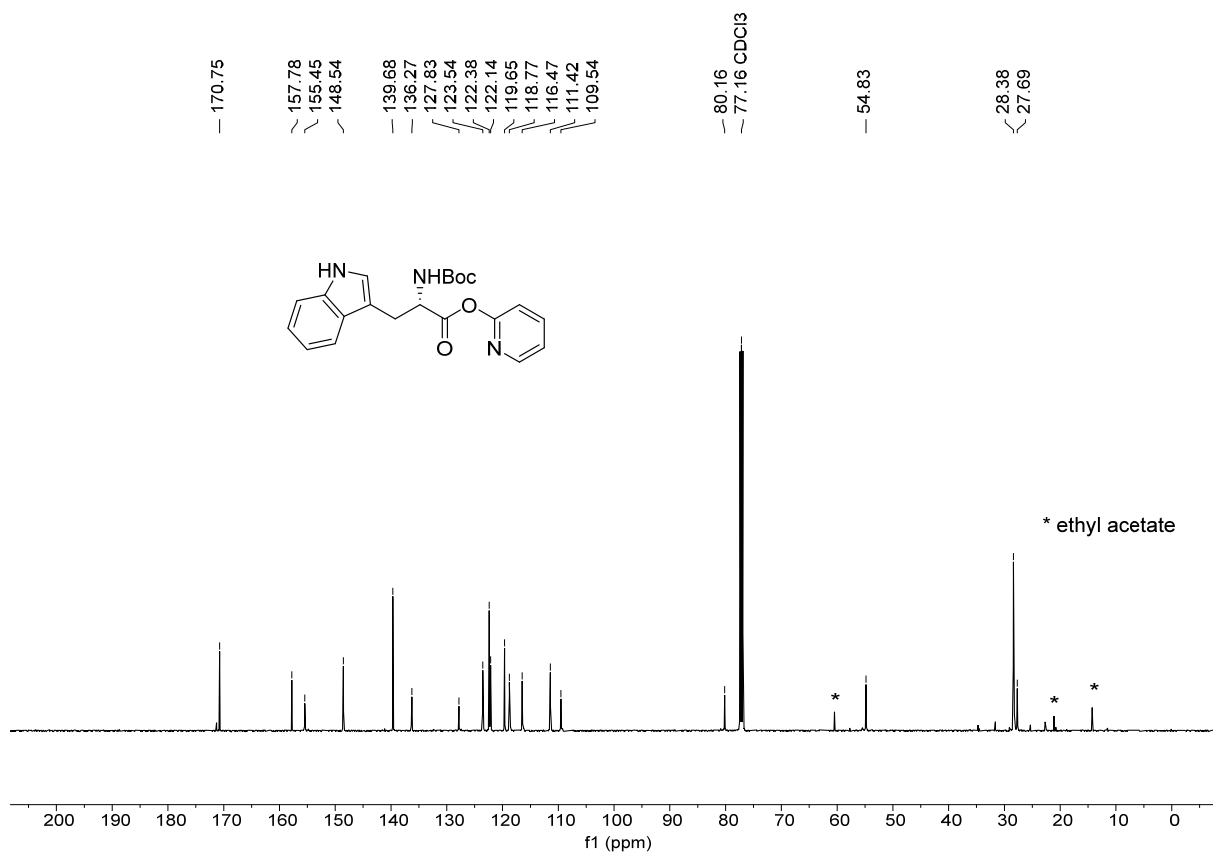
¹H NMR (500 MHz, CDCl₃) of S16



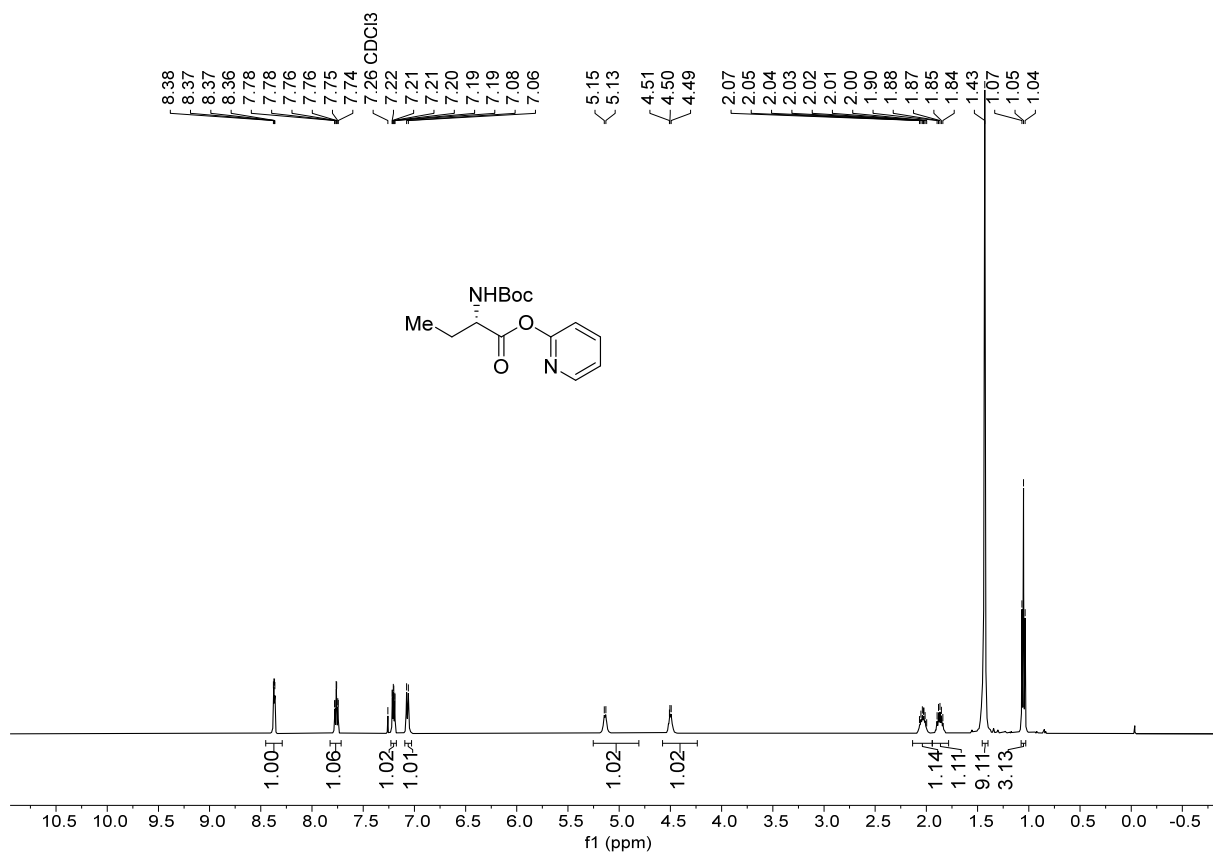
¹³C {¹H} NMR (125 MHz, CDCl₃) of S16



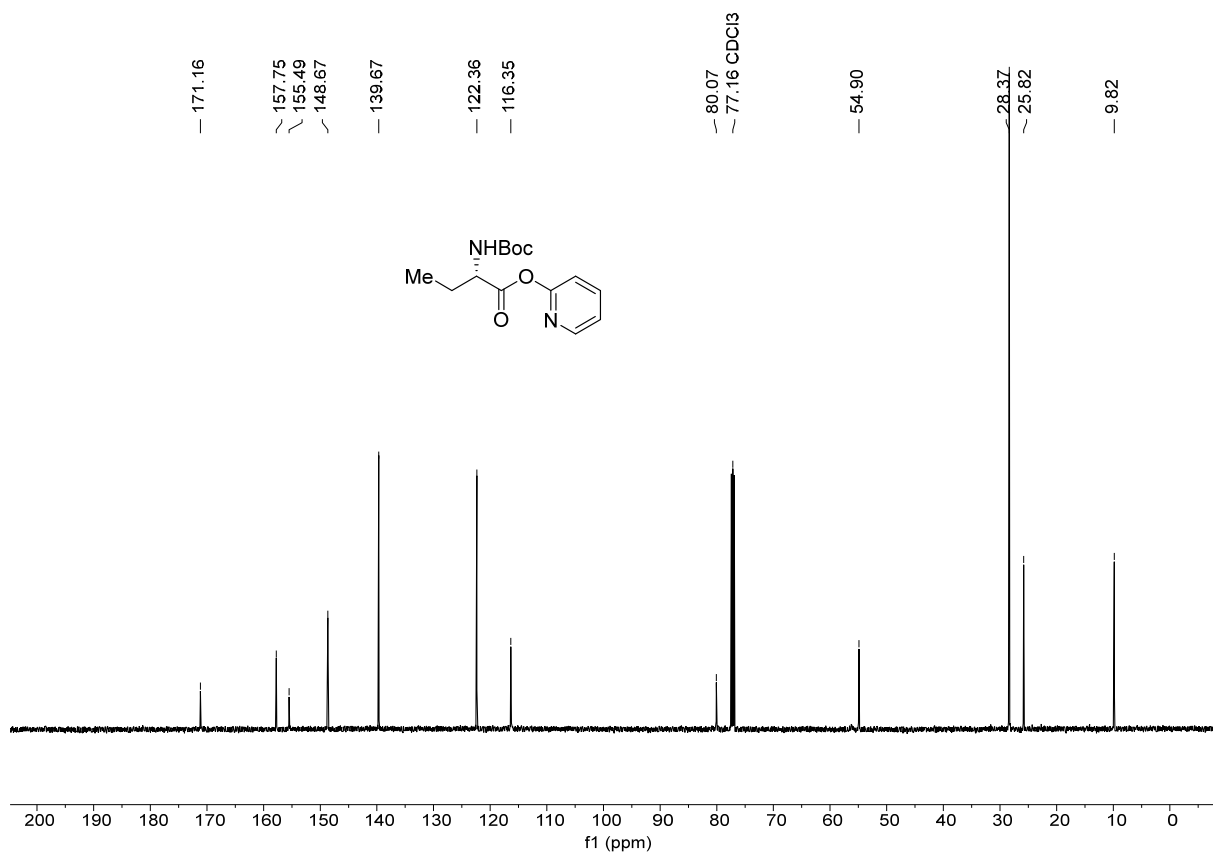
¹H NMR (500 MHz, CDCl₃) of S17



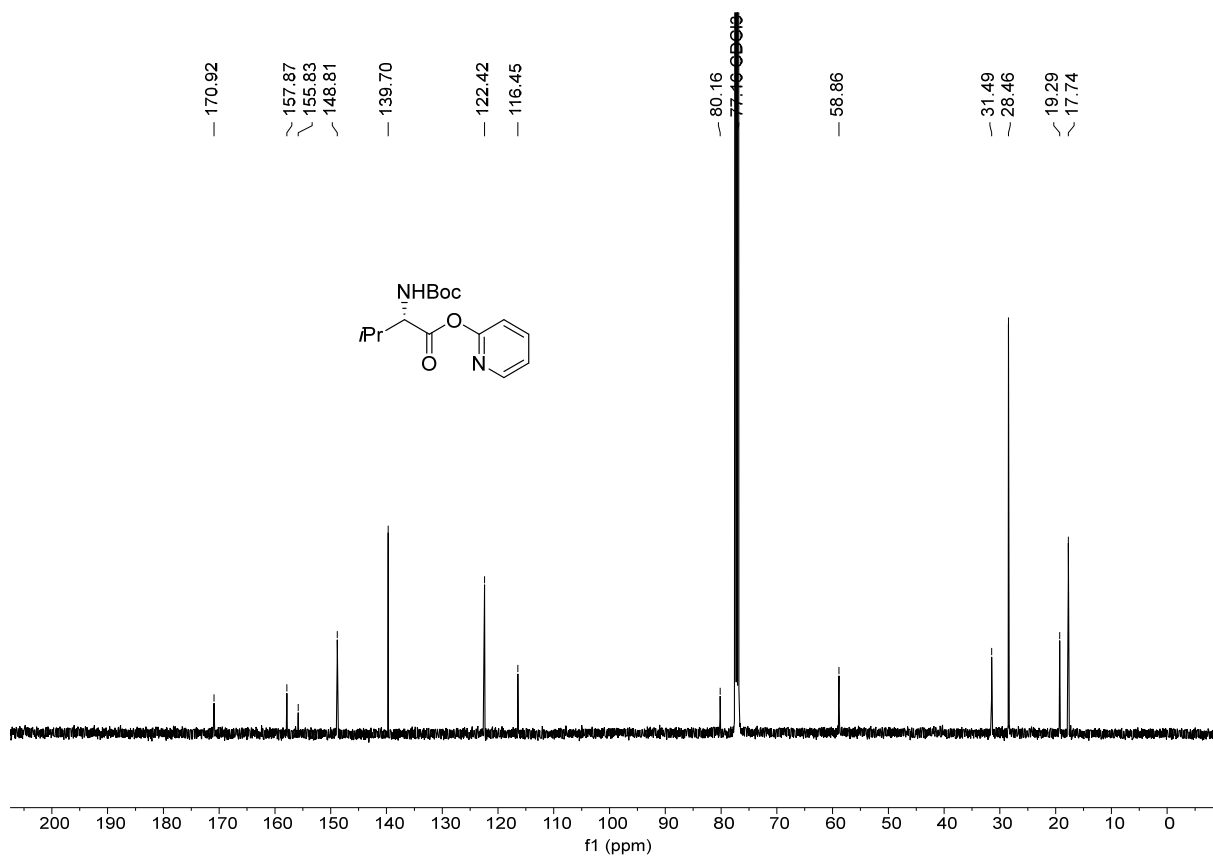
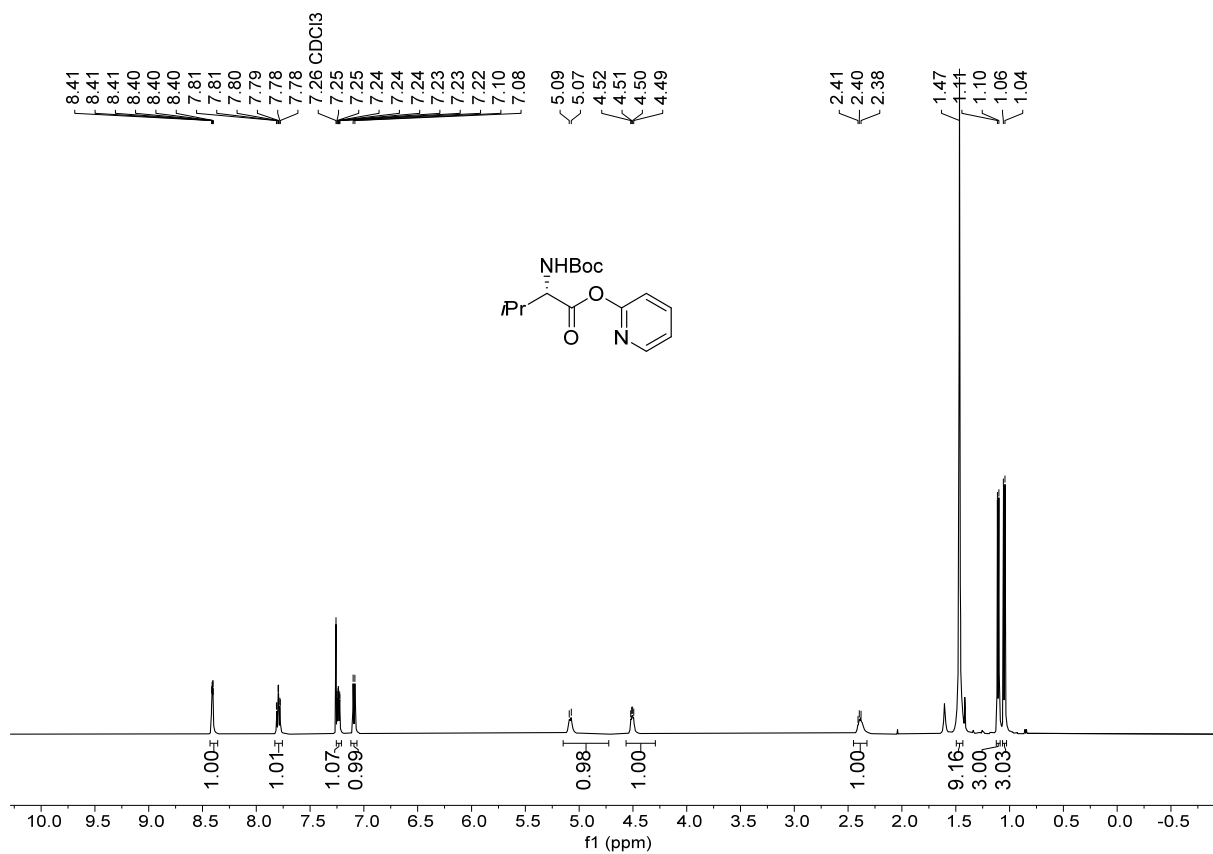
¹³C {¹H} NMR (125 MHz, CDCl₃) of S17

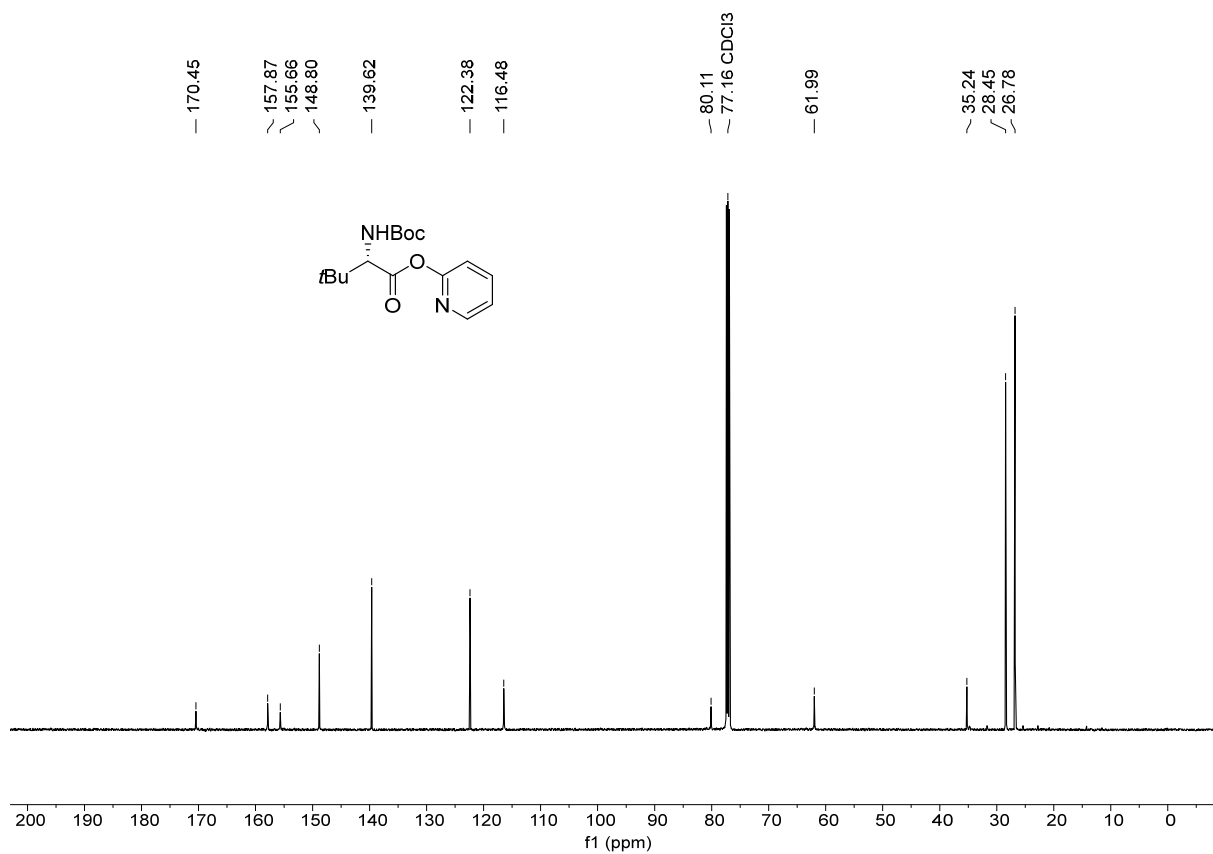
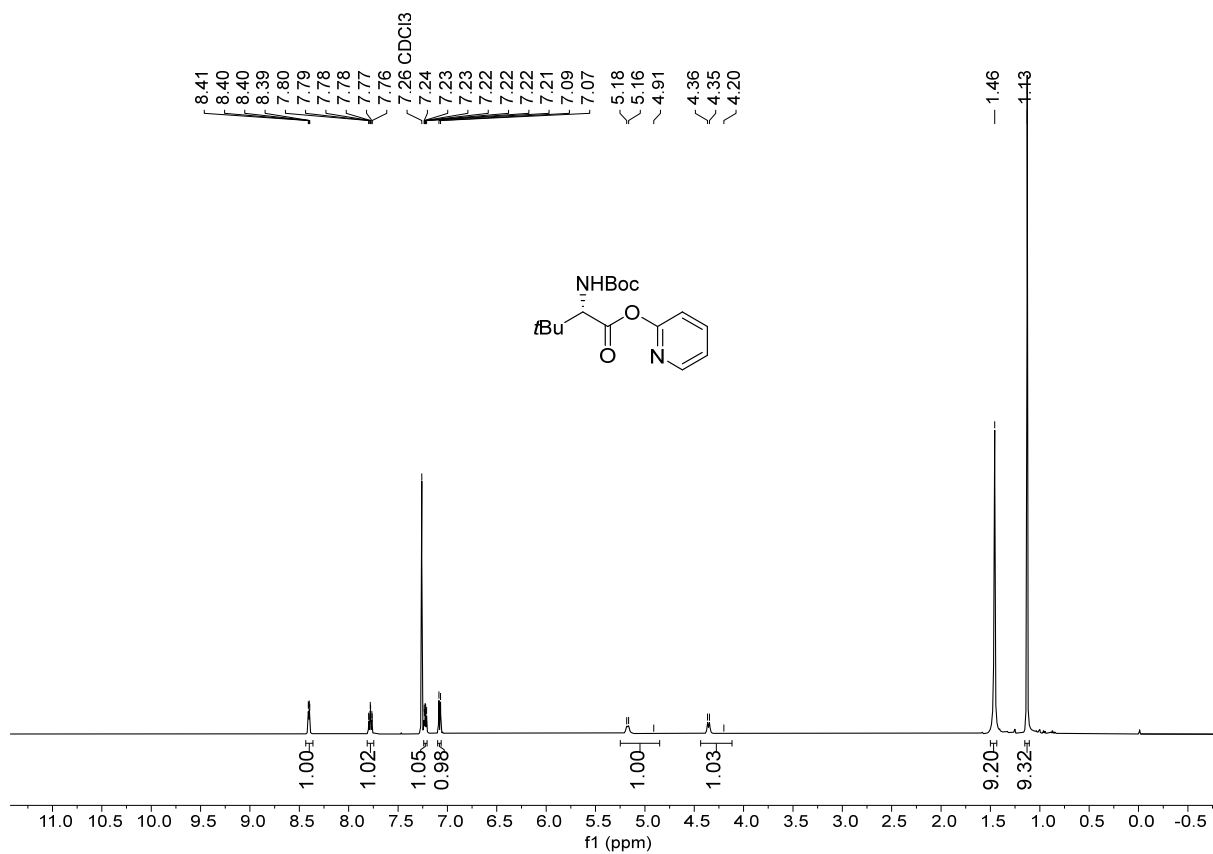


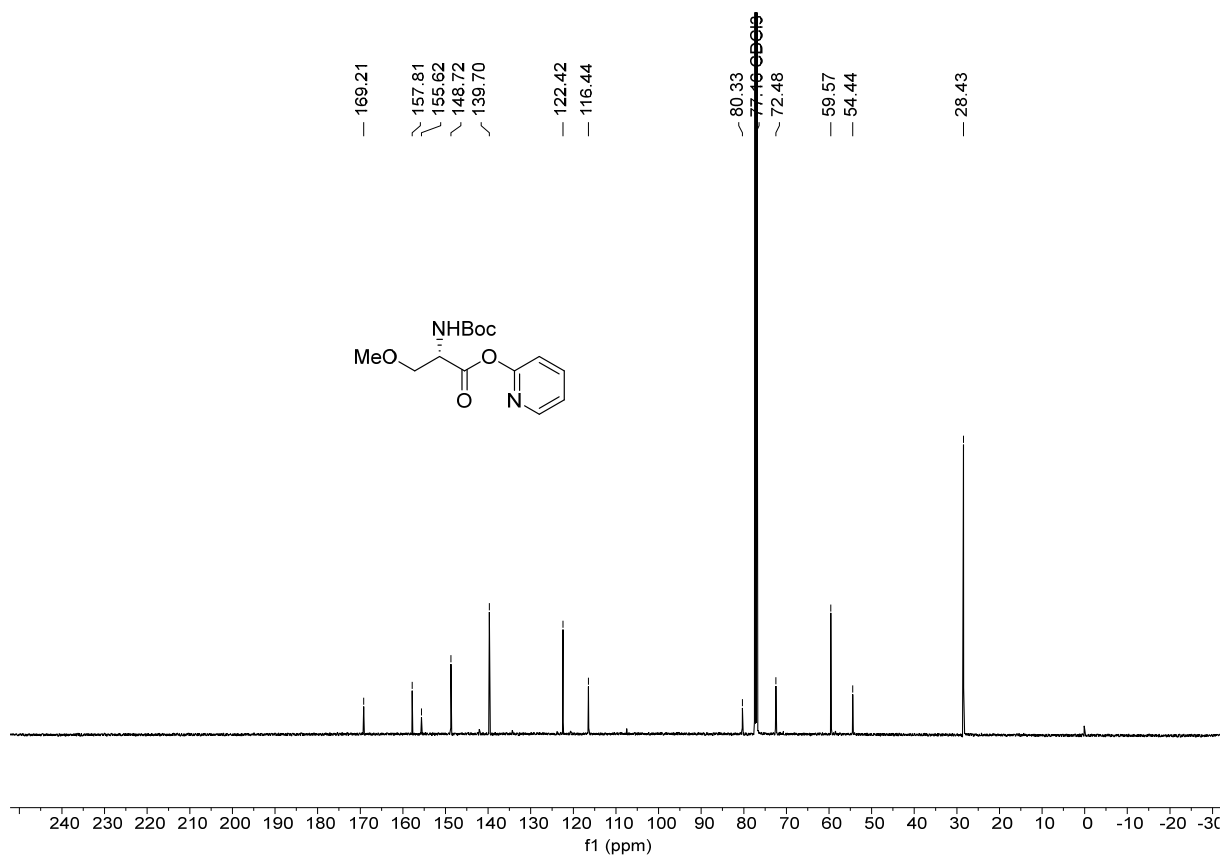
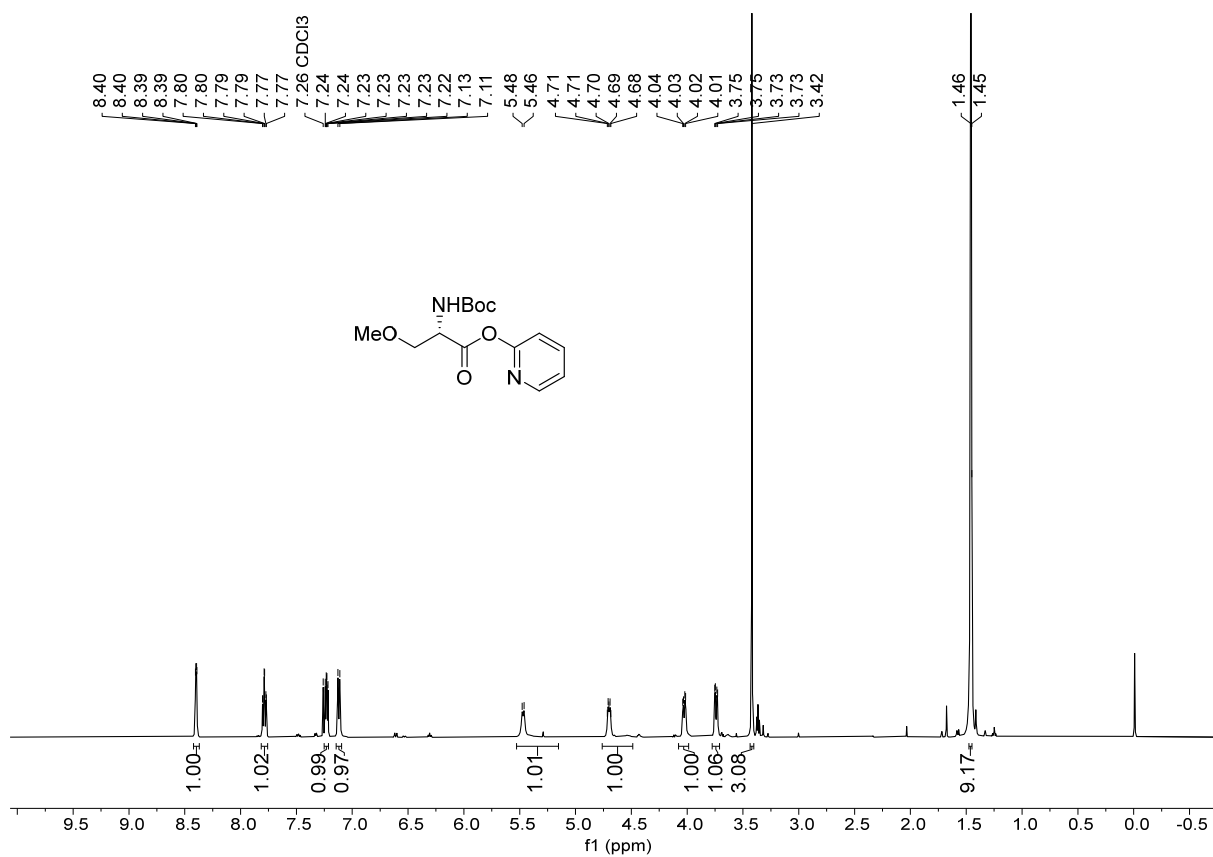
¹H NMR (500 MHz, CDCl₃) of S18

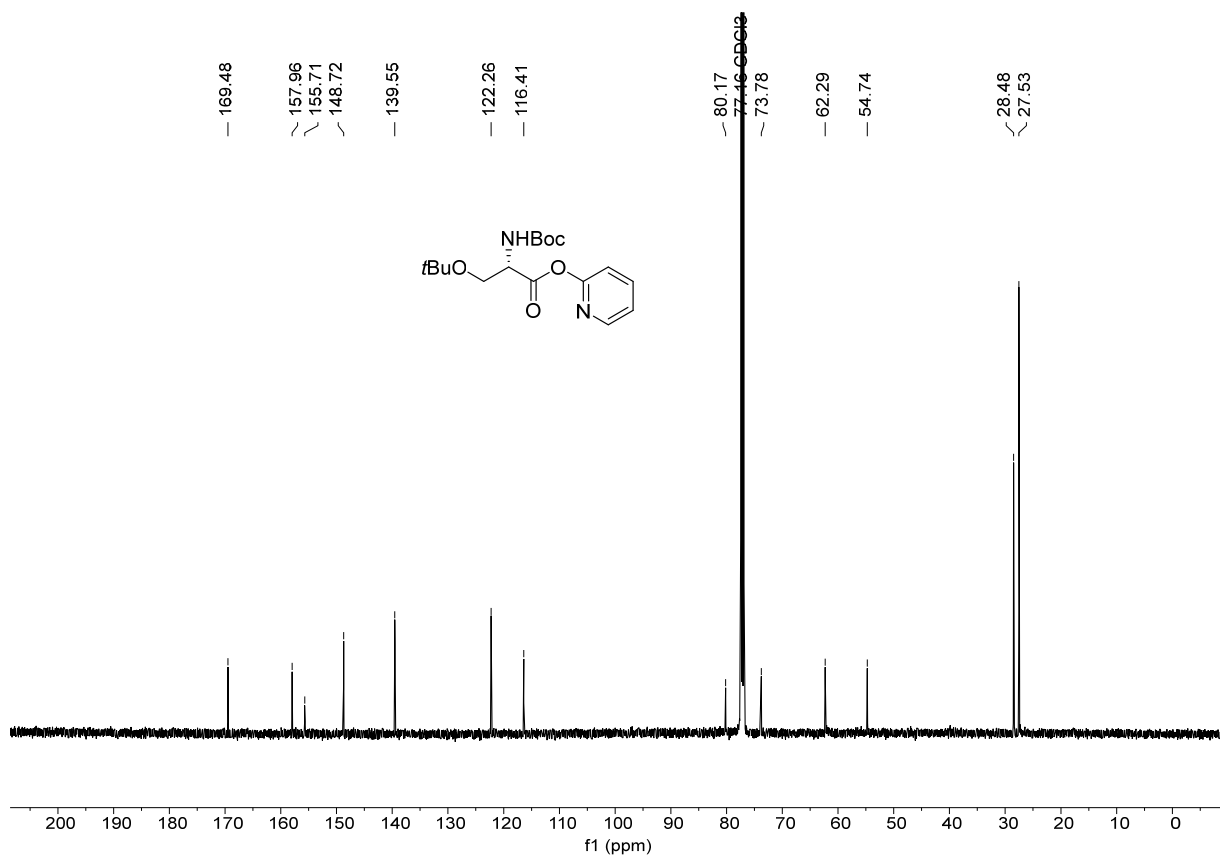
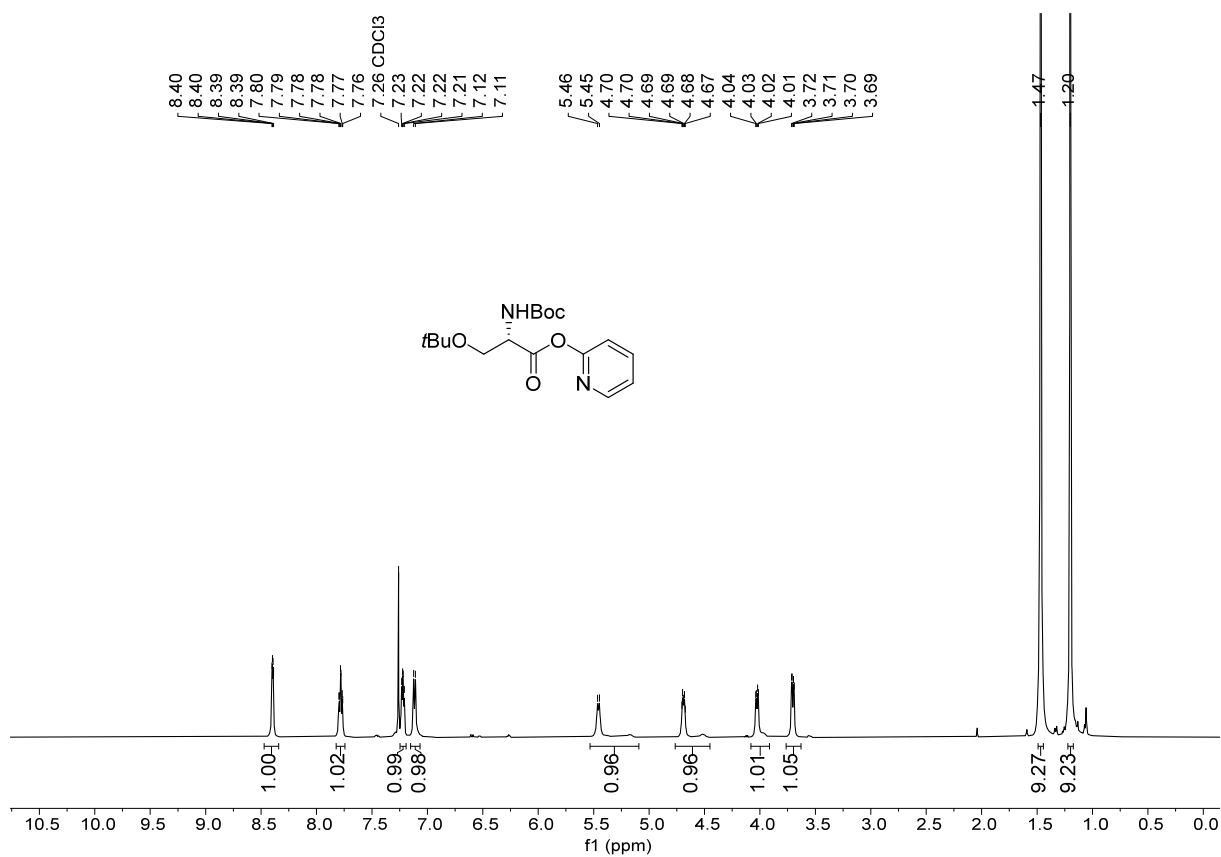


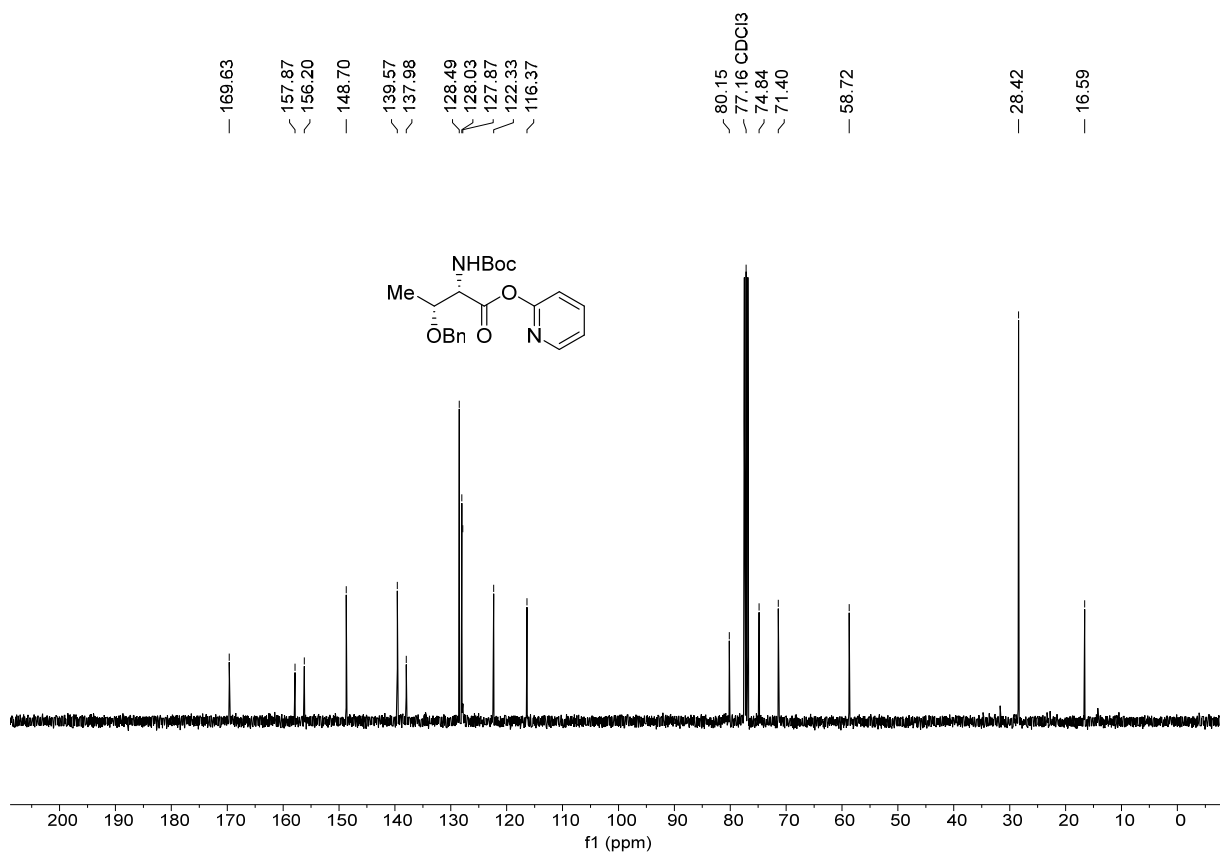
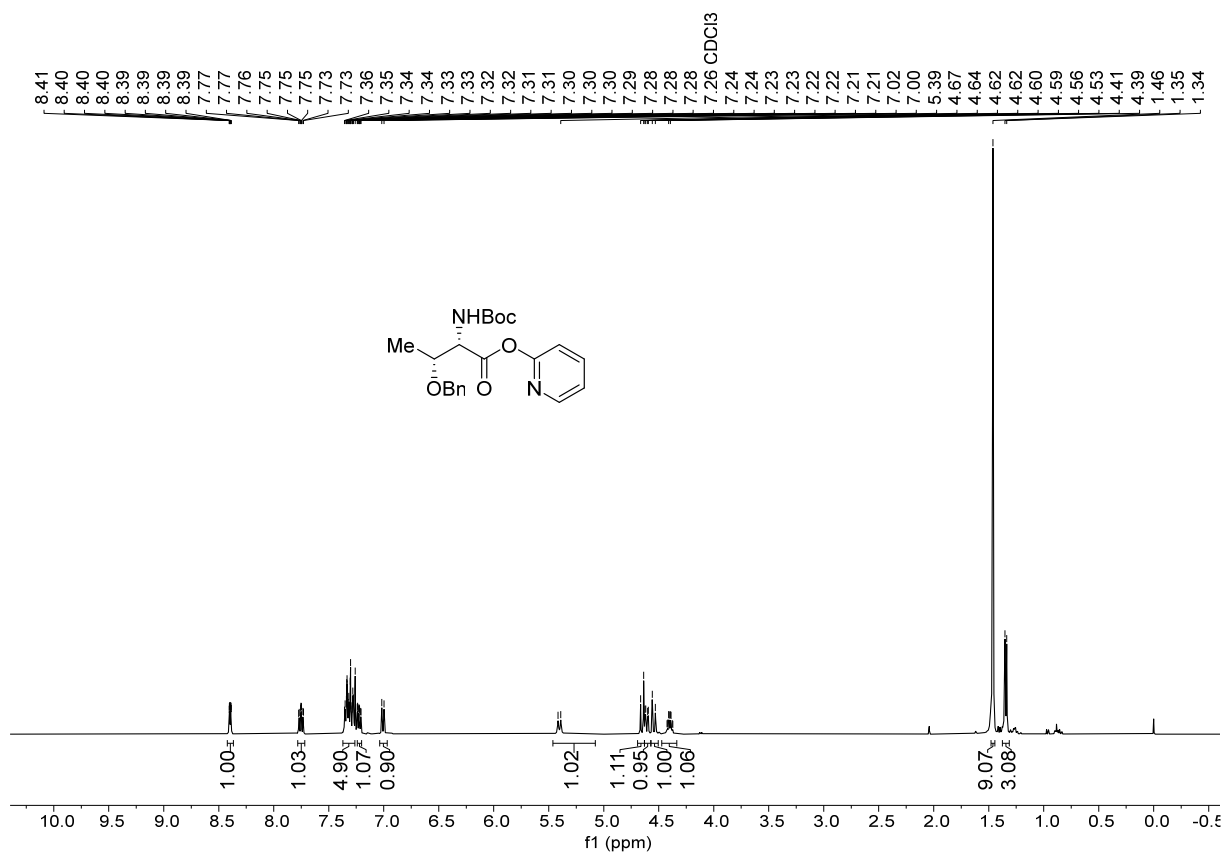
¹³C {¹H} NMR (125 MHz, CDCl₃) of S18

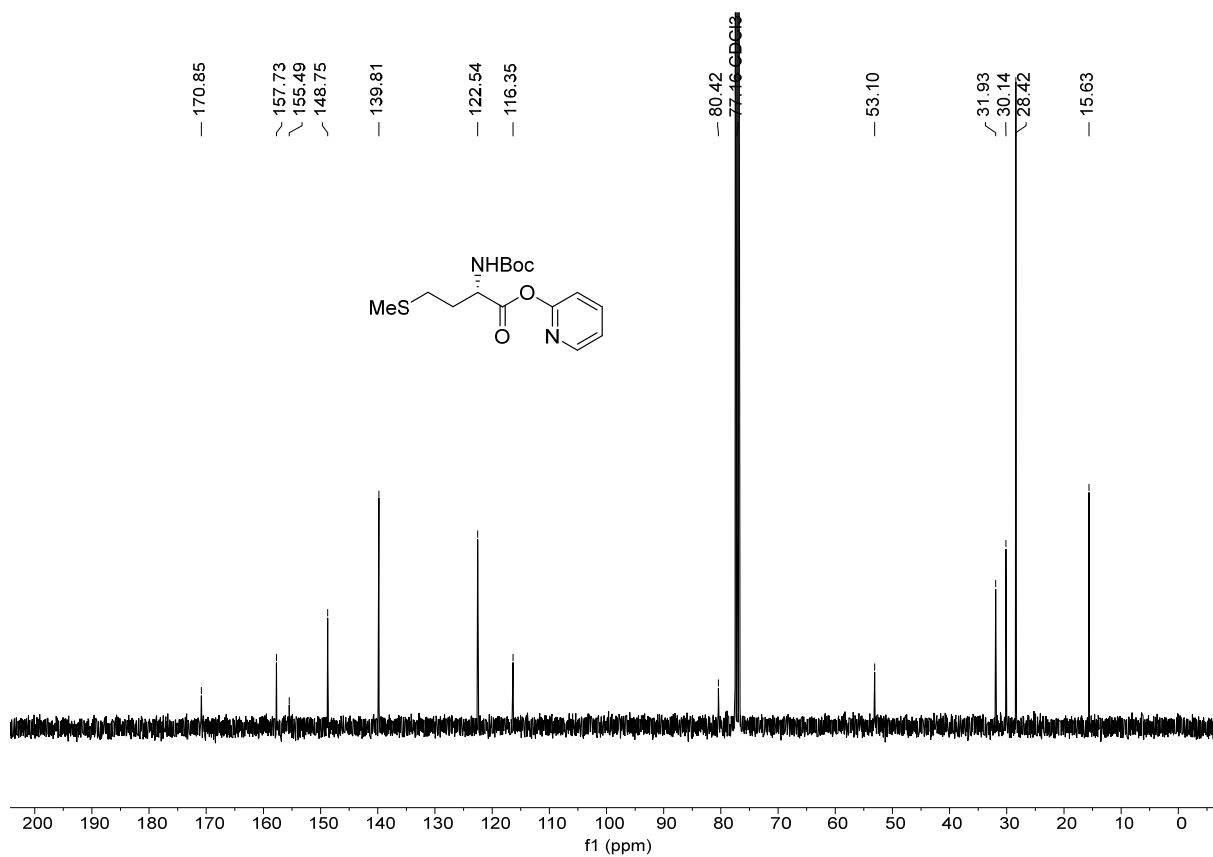
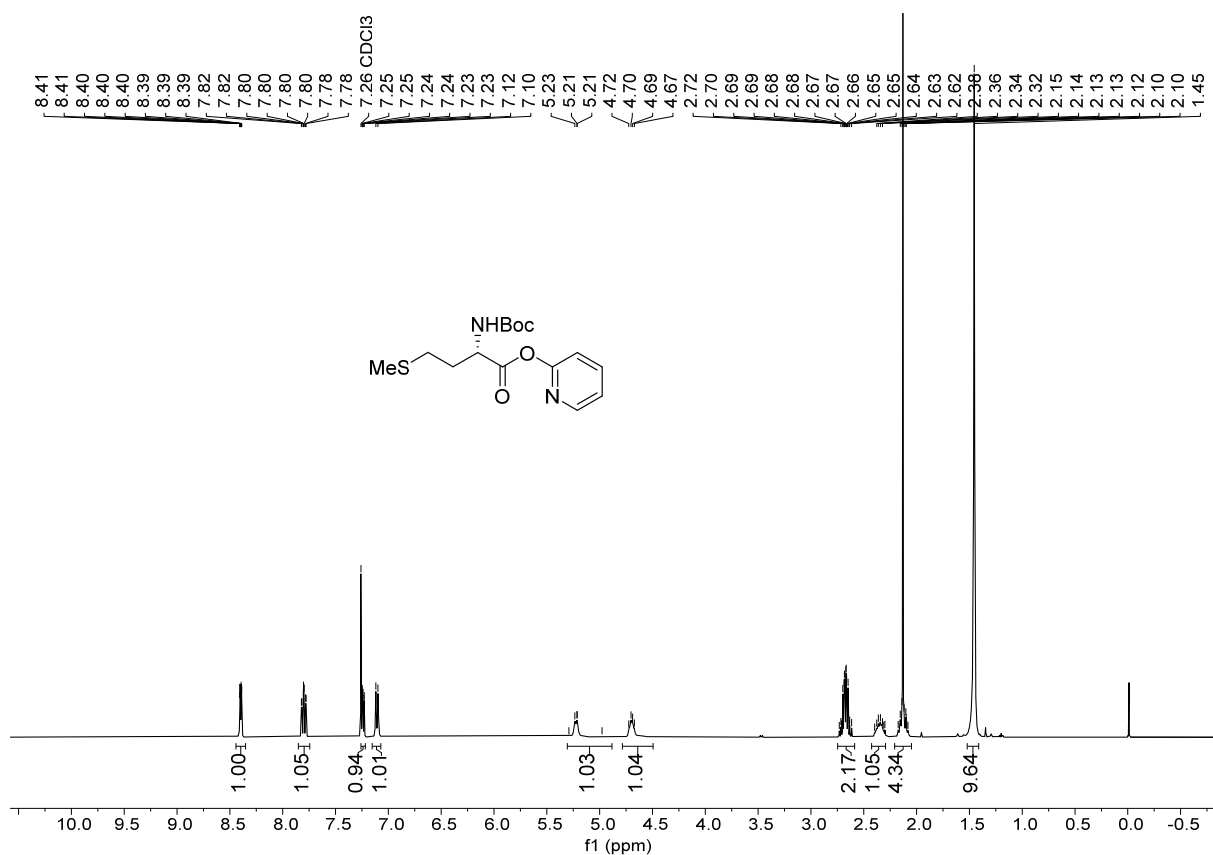


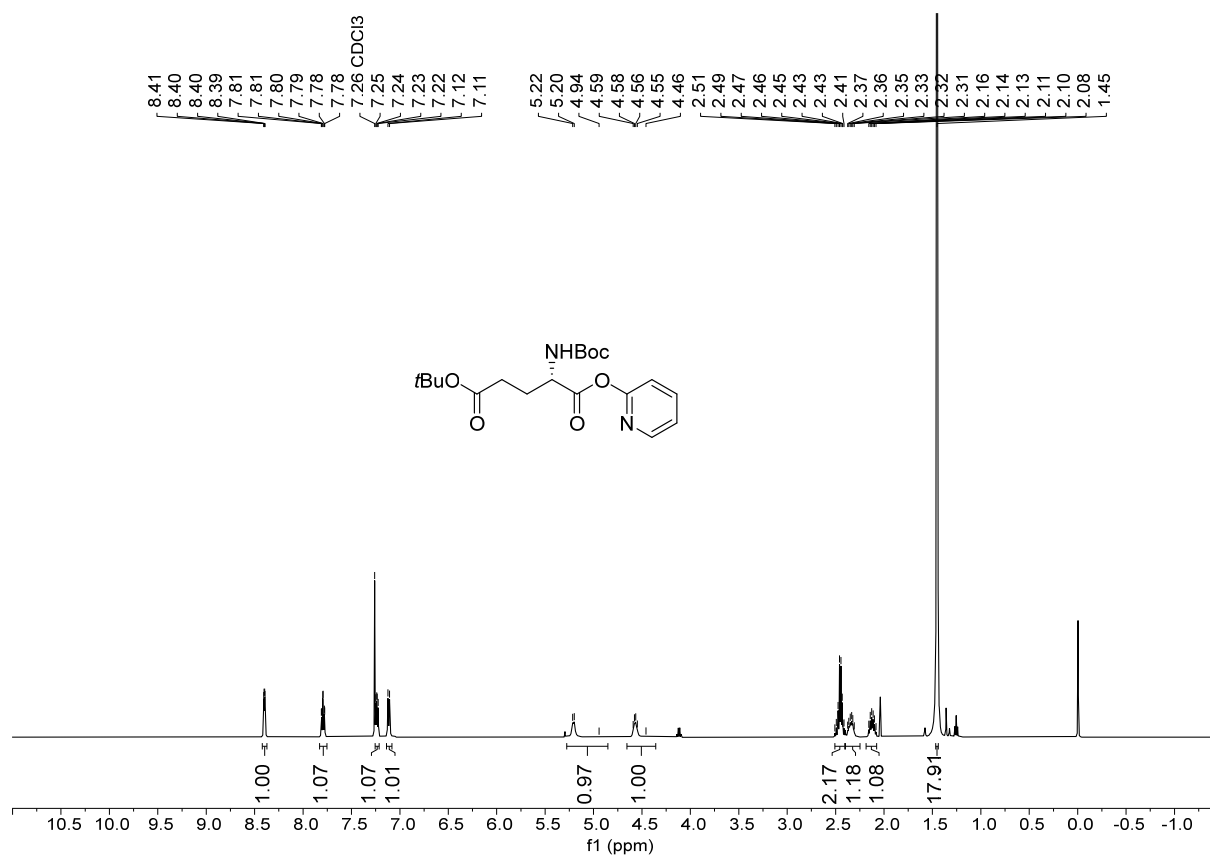




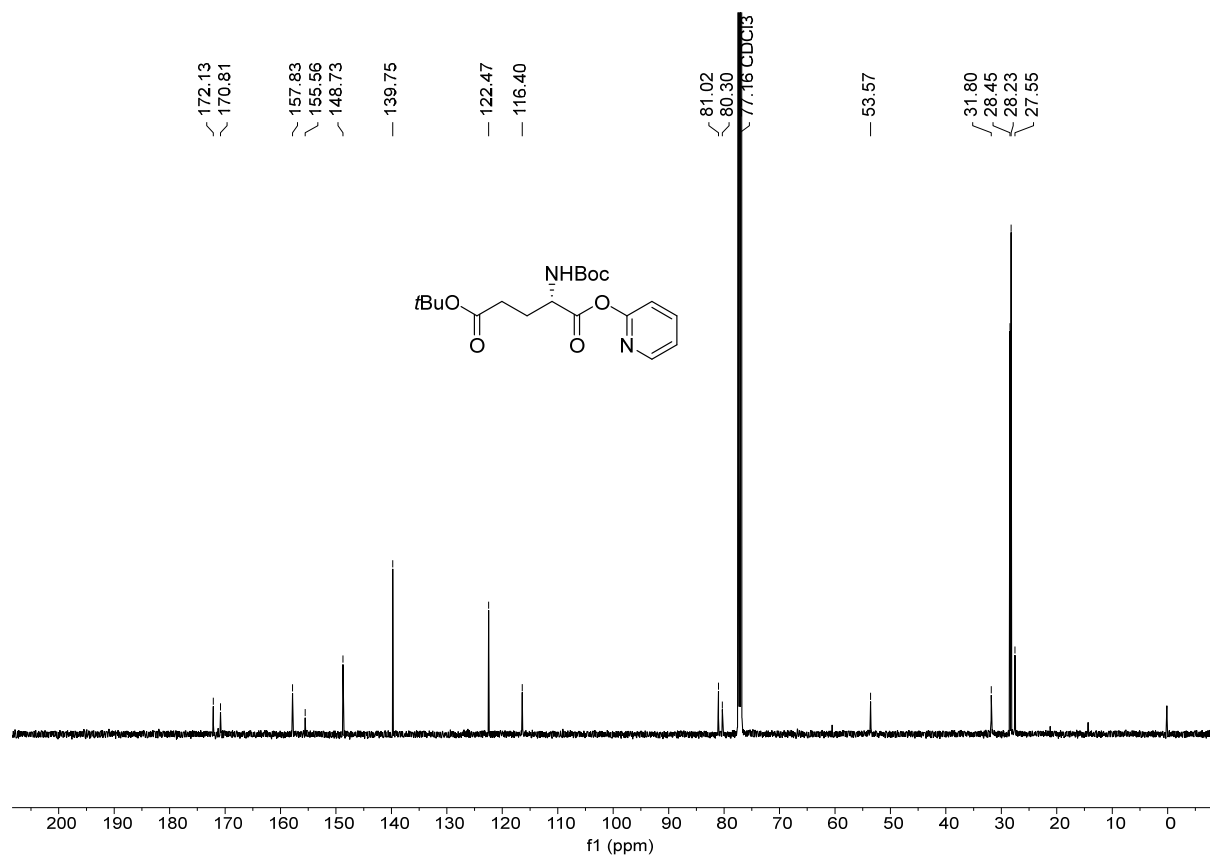




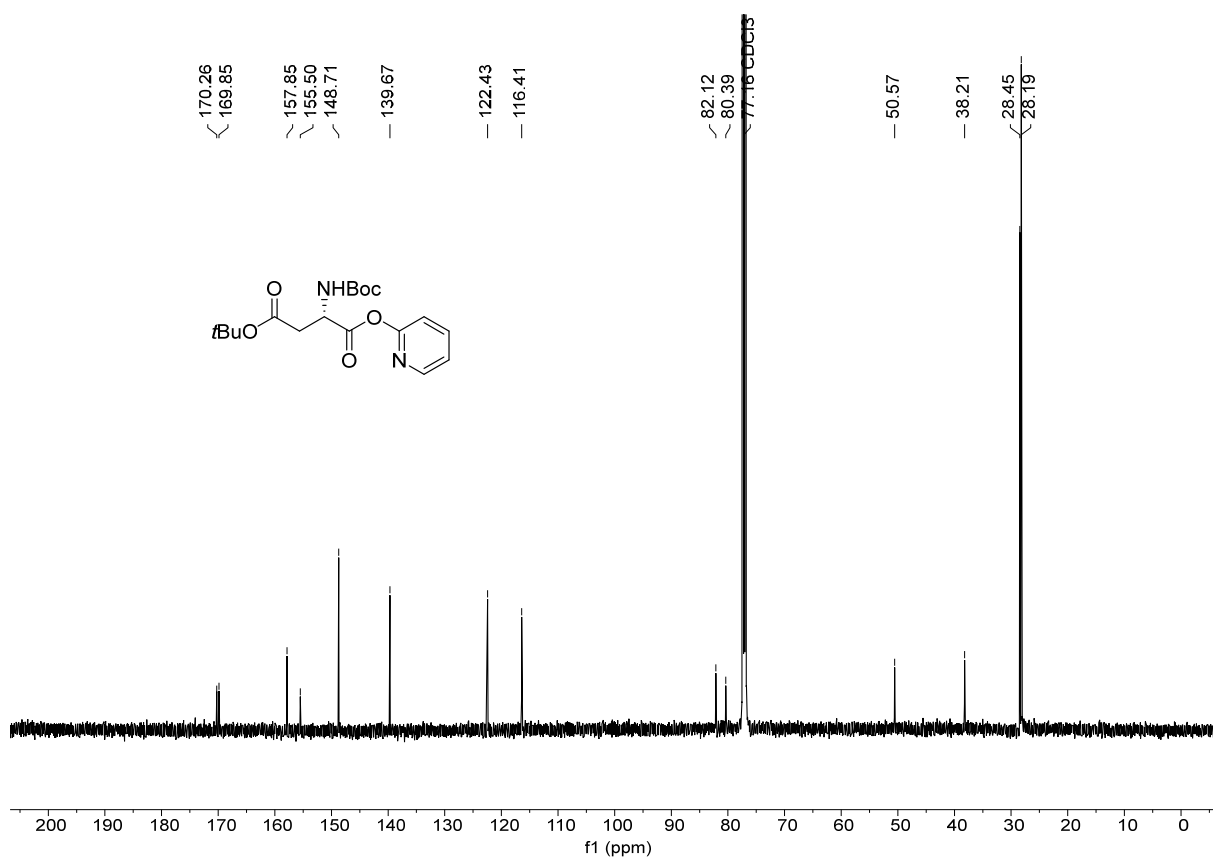
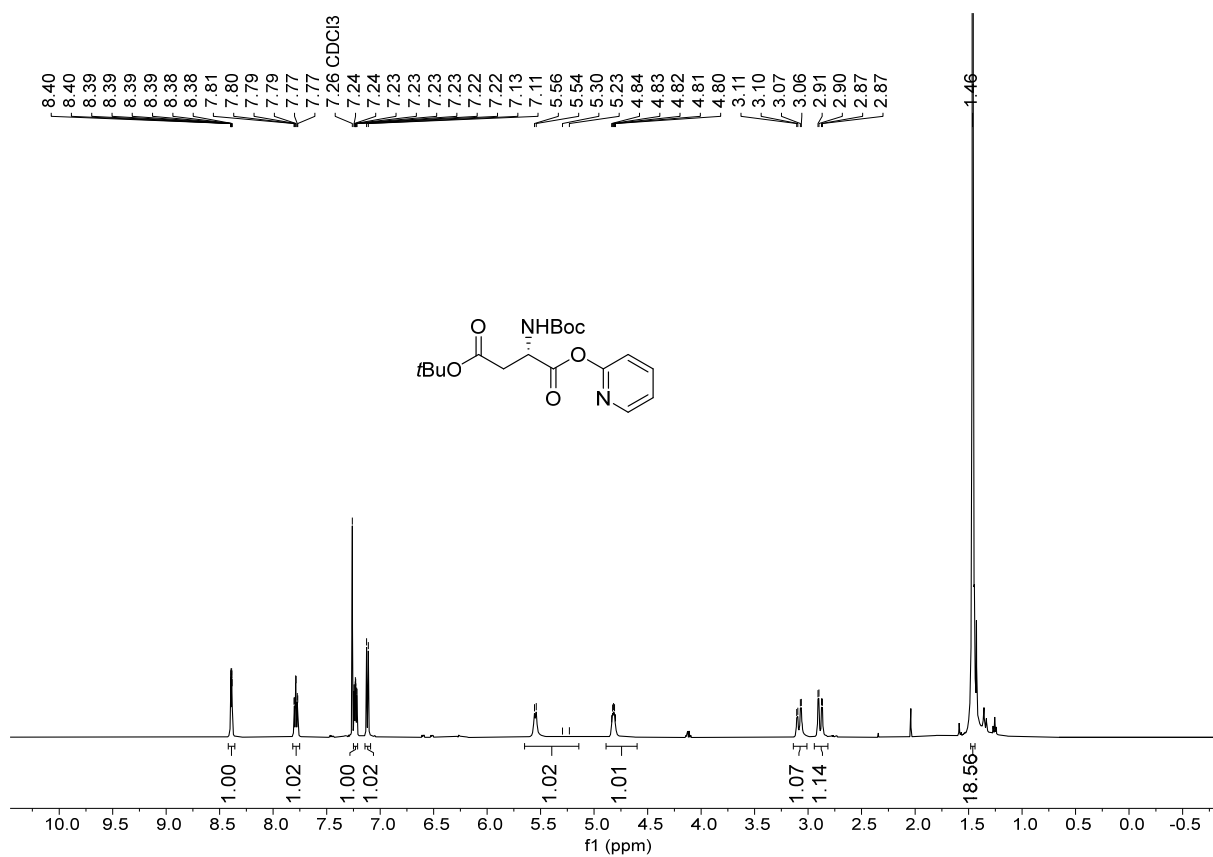


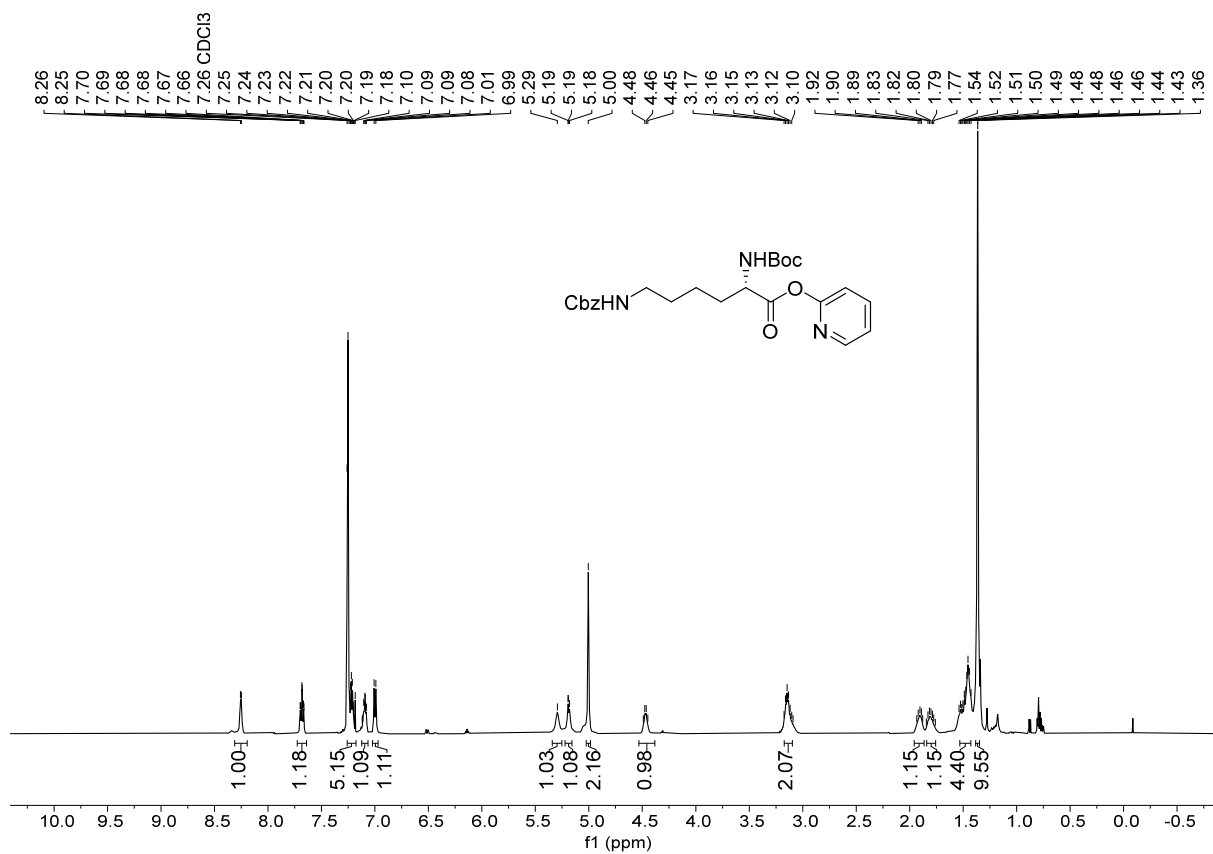


¹H NMR (500 MHz, CDCl₃) of S25

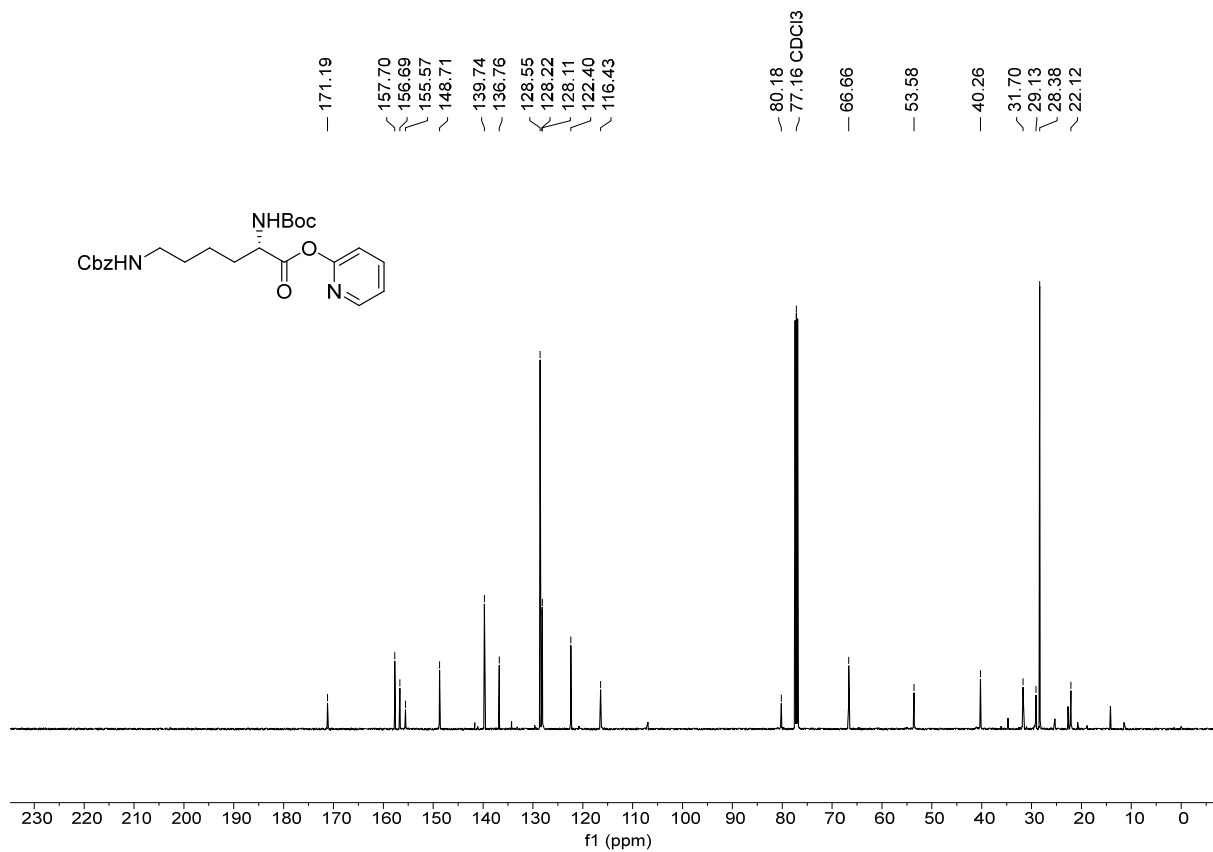


¹³C {¹H} NMR (125 MHz, CDCl₃) of S25

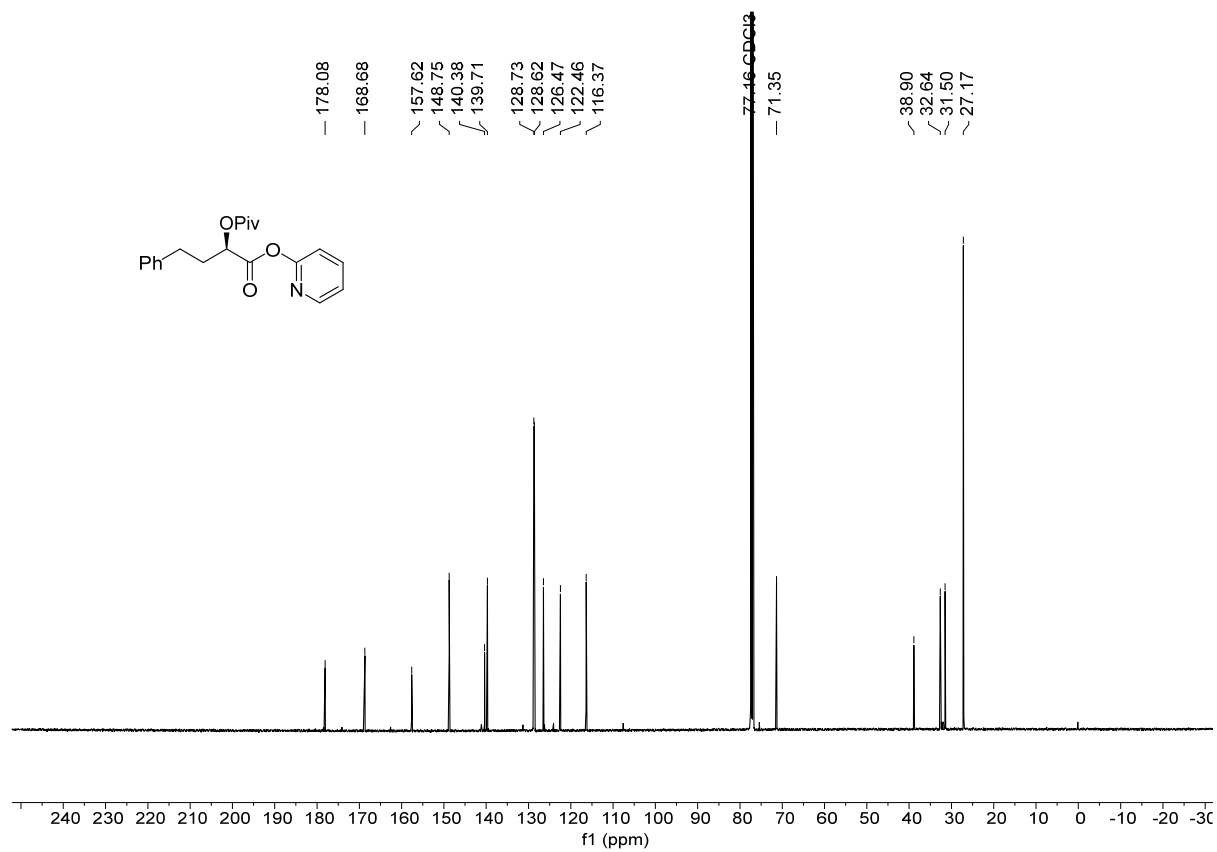
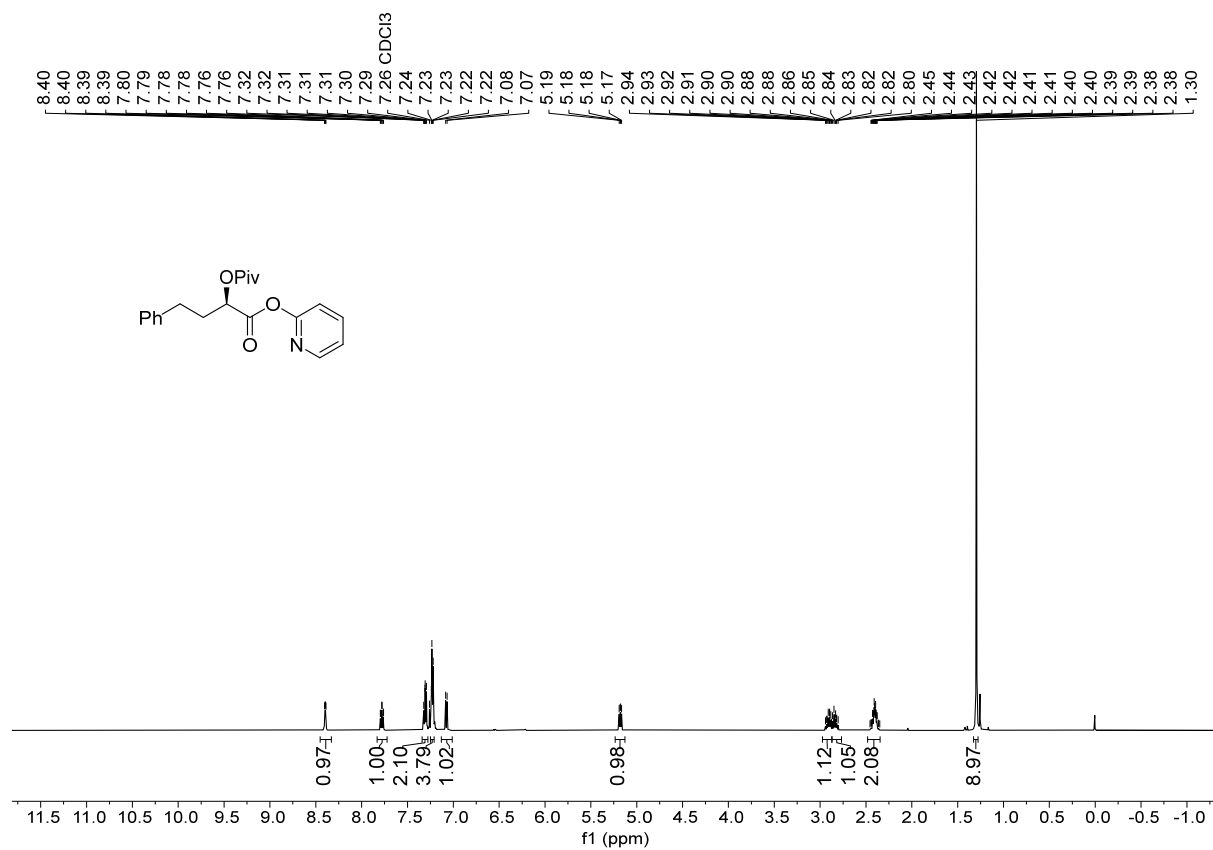


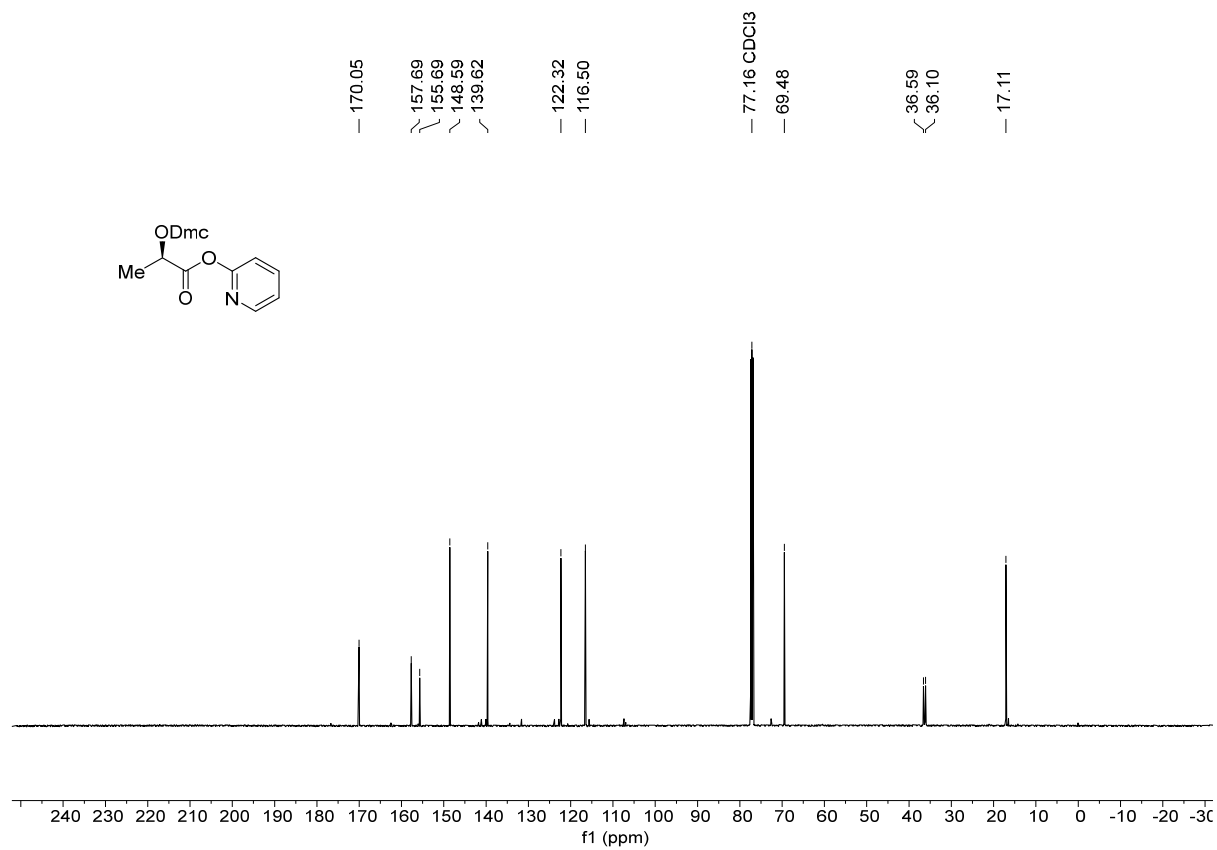
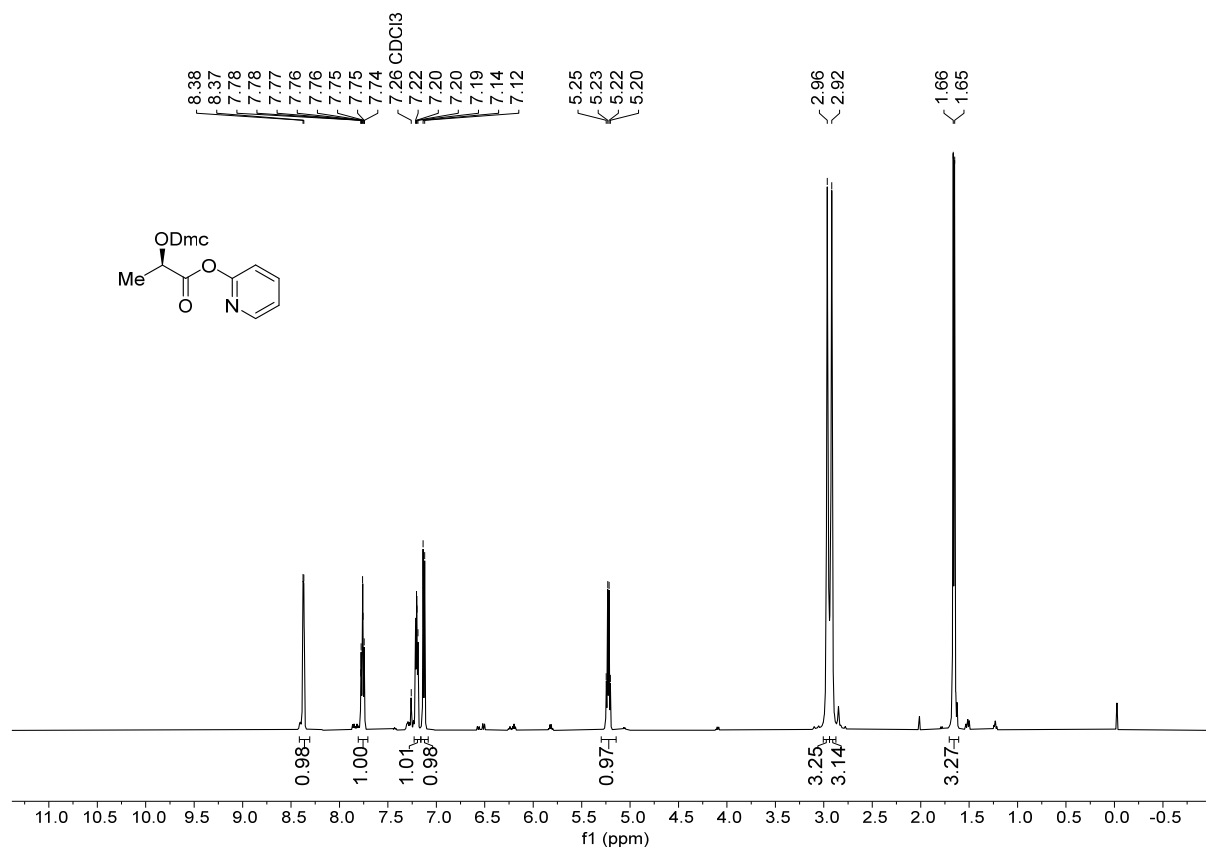


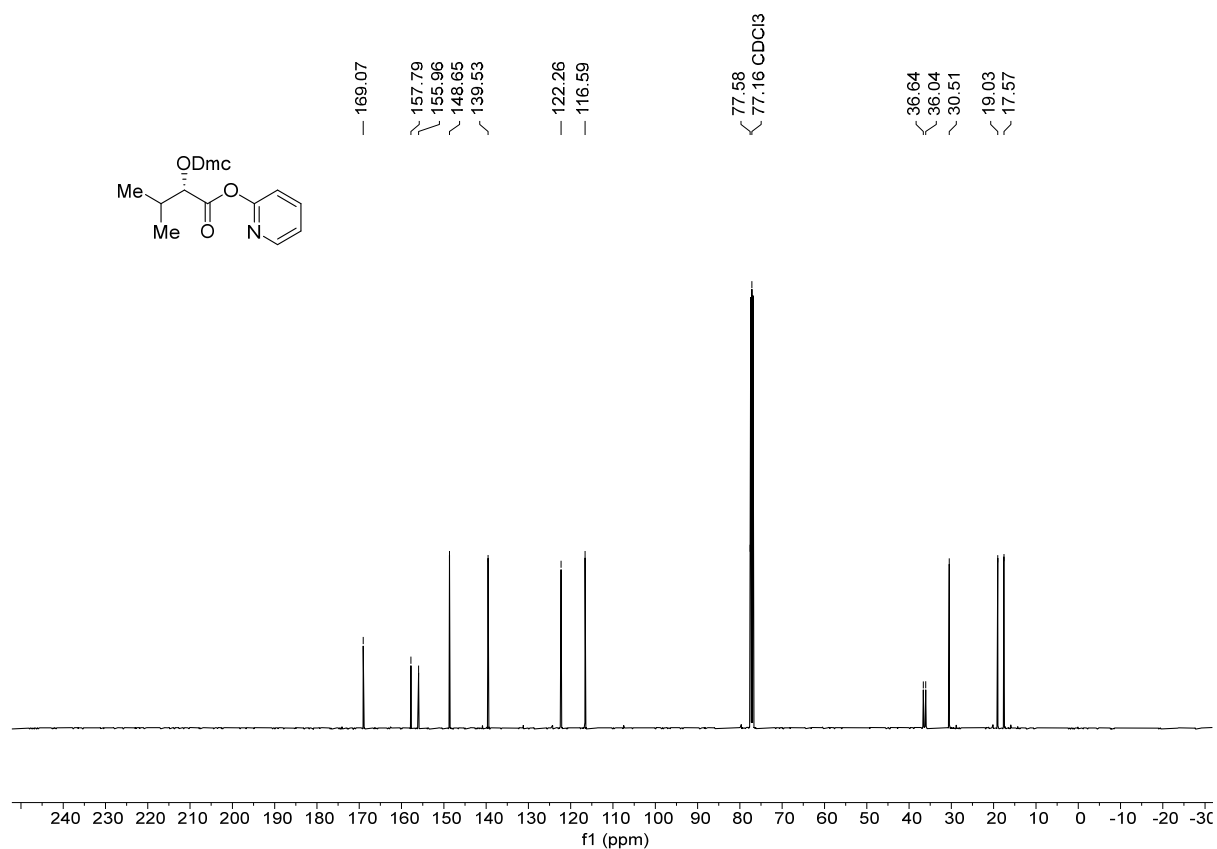
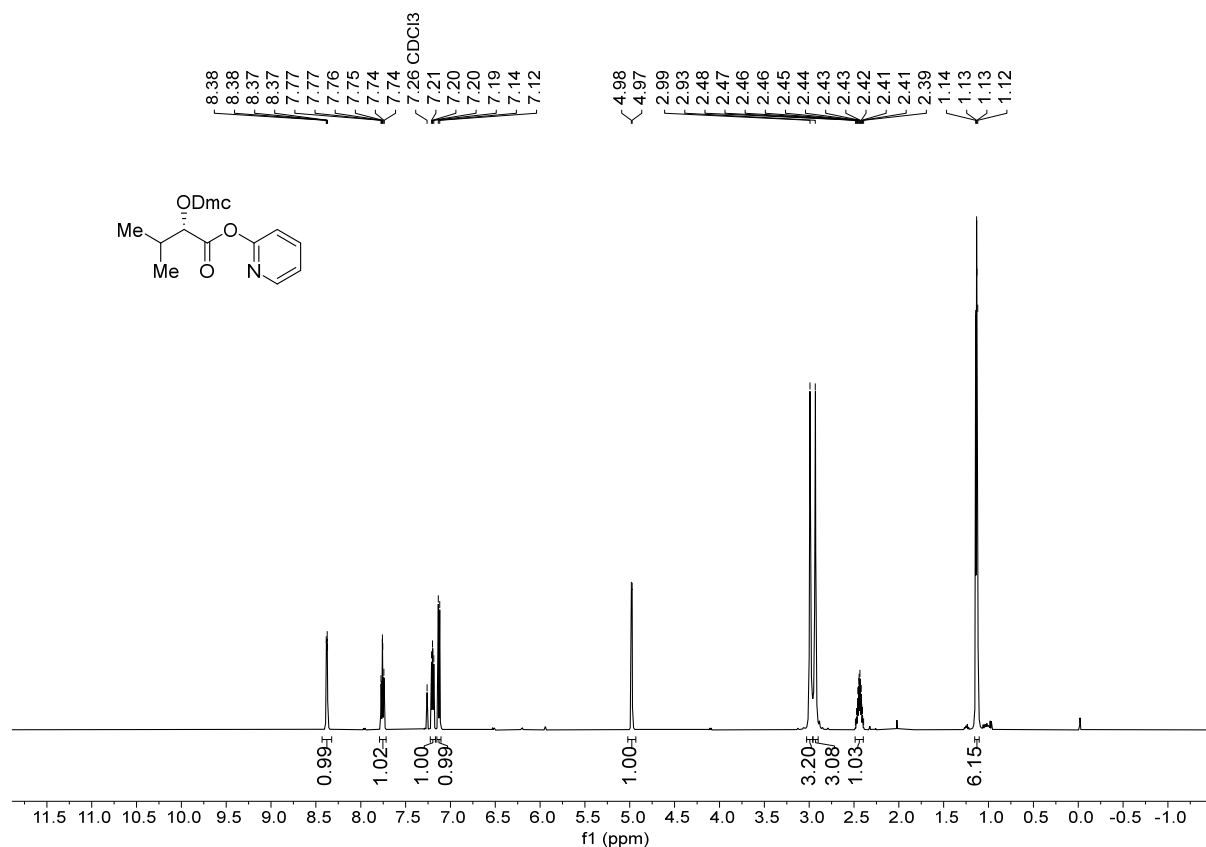
¹H NMR (500 MHz, CDCl₃) of S27

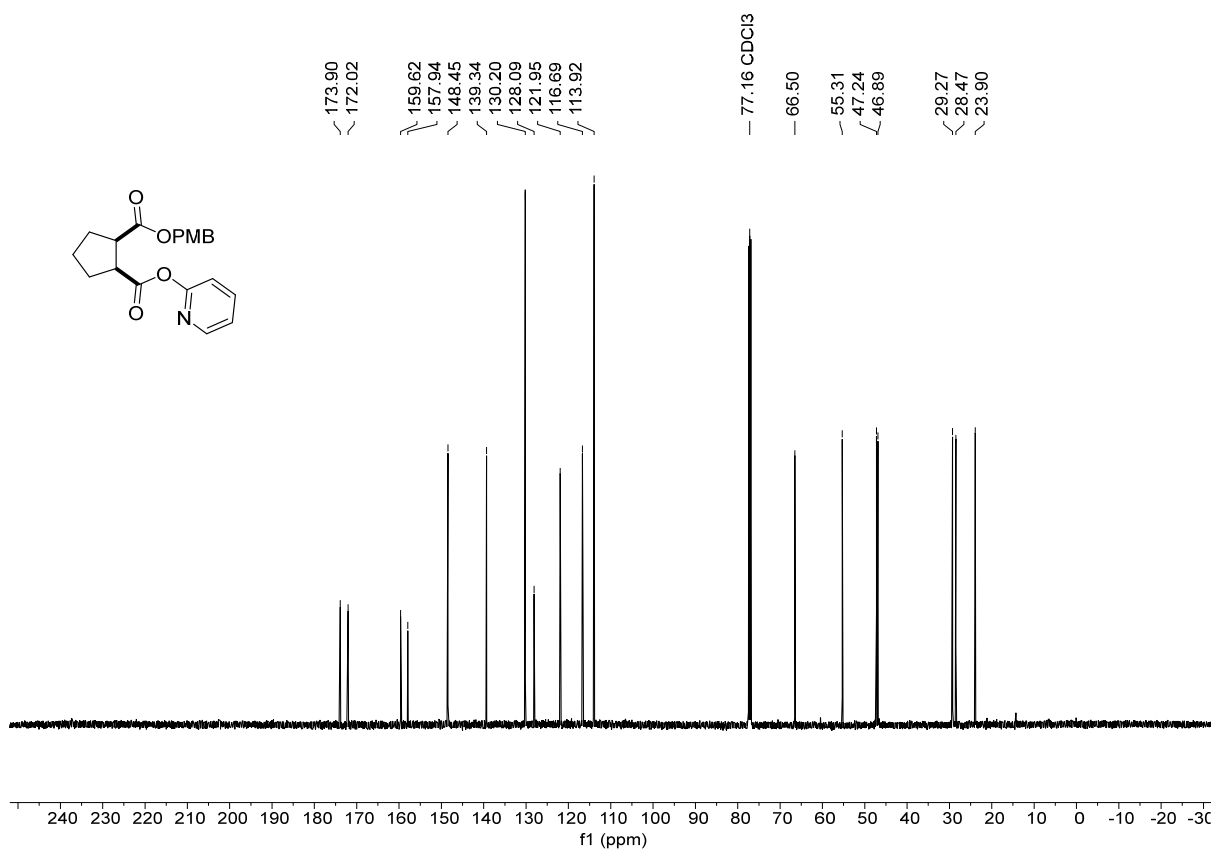
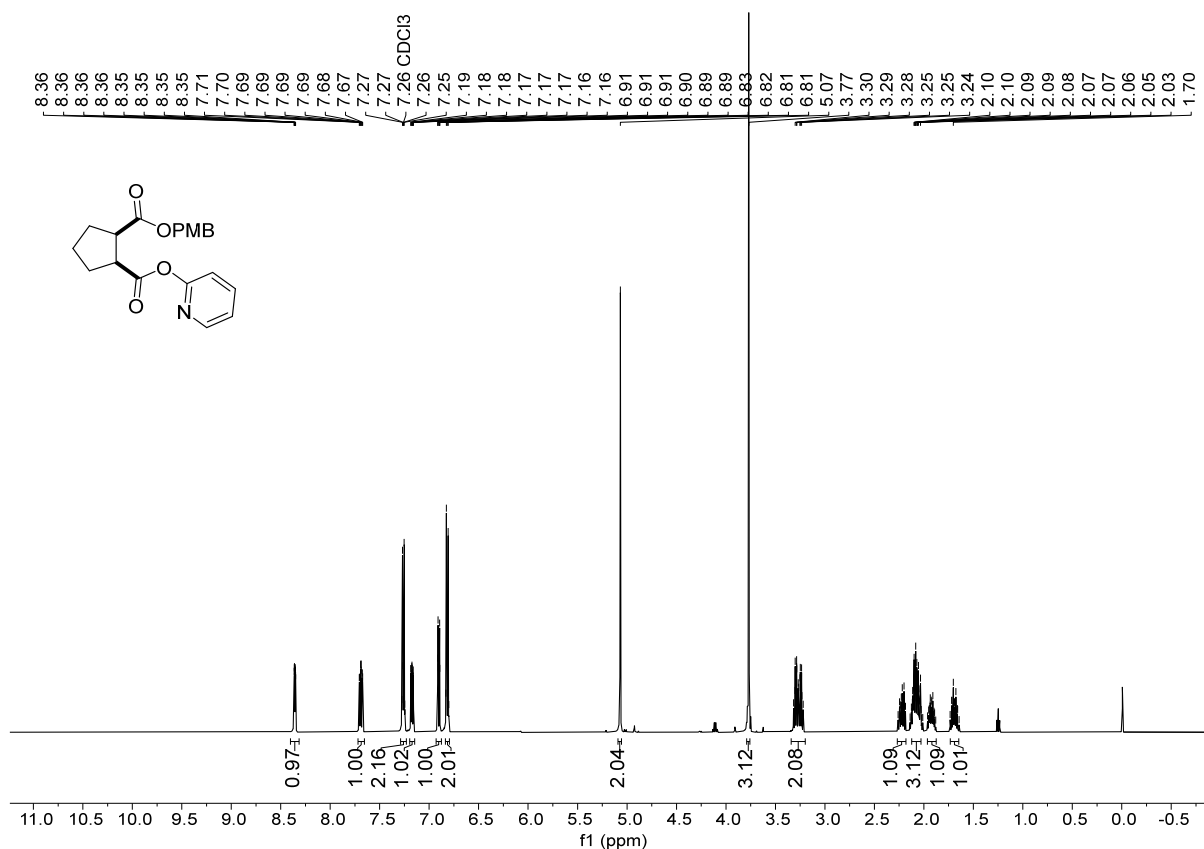


¹³C {¹H} NMR (125 MHz, CDCl₃) of S27



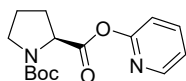




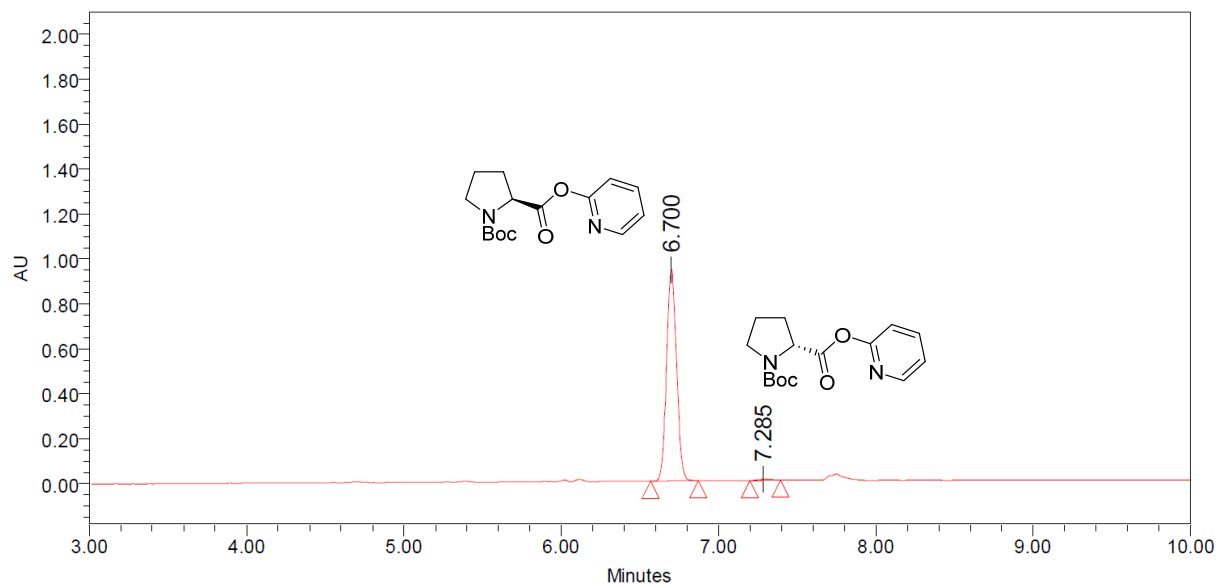


11. Chiral SFC and HPLC analysis

11.1 SFC analysis of starting materials

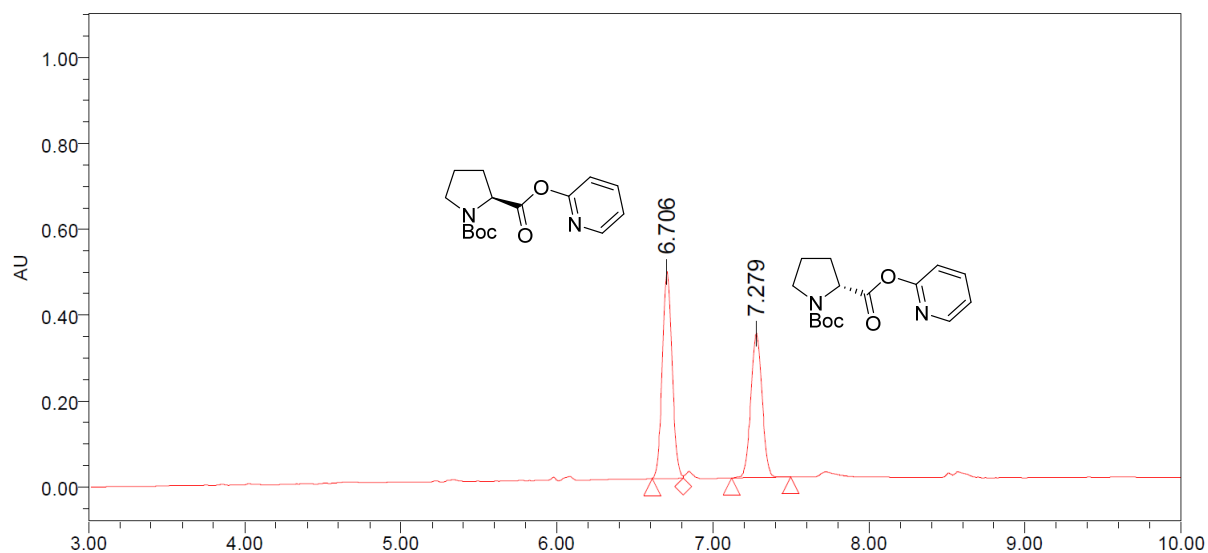


1-(tert-butyl) 2-(pyridin-2-yl) (S)-pyrrolidine-1,2-dicarboxylate (1)

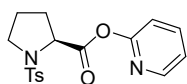


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 255.4 nm (PDA Spectrum (190-410)nm)	6.700	940025	4147392	99.28
2	PDA Spectrum PDA 255.4 nm (PDA Spectrum (190-410)nm)	7.285	5860	30145	0.72

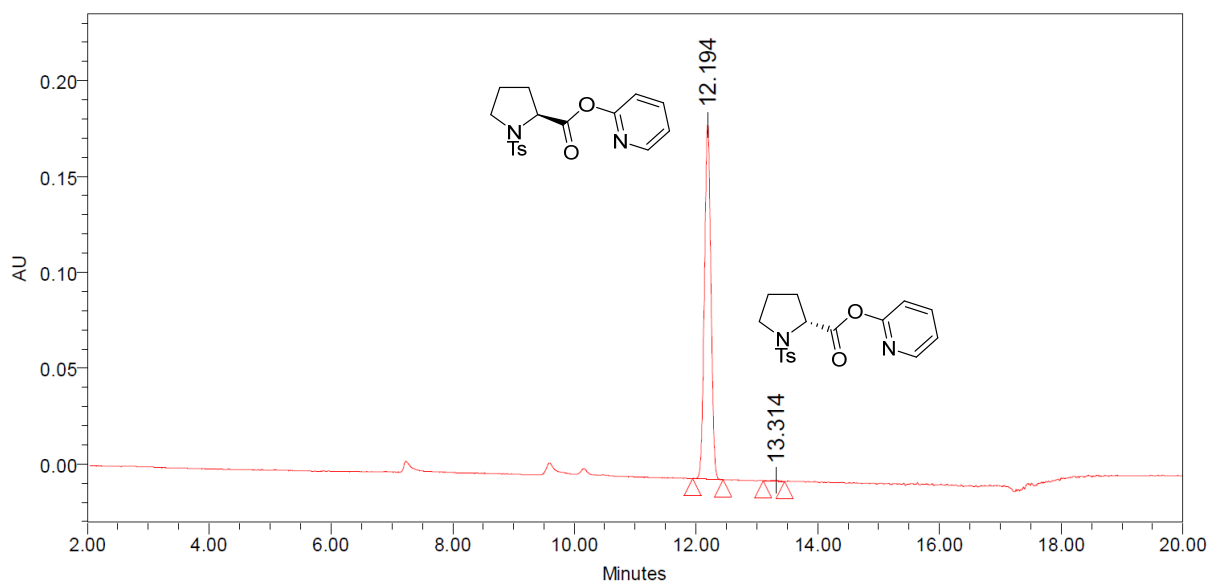
Racemic mixture standard



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	6.706	481924	2103088	55.49
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	7.279	335507	1686658	44.51

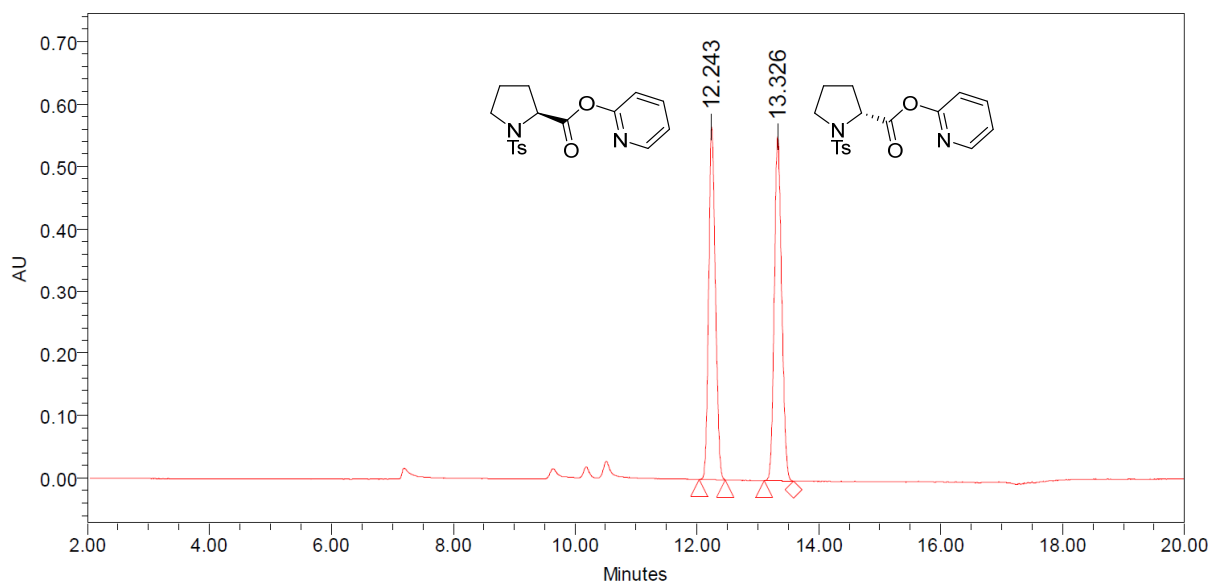


Pyridin-2-yl tosyl-L-prolinate (7)

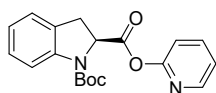


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	12.194	185018	1368308	99.75
2	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	13.314	476	3386	0.25

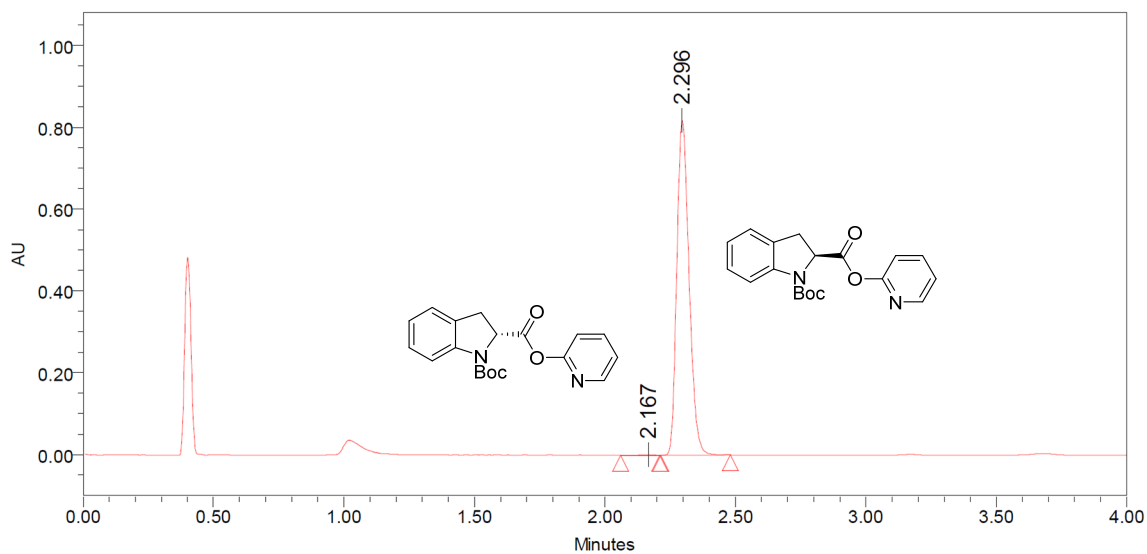
Racemate



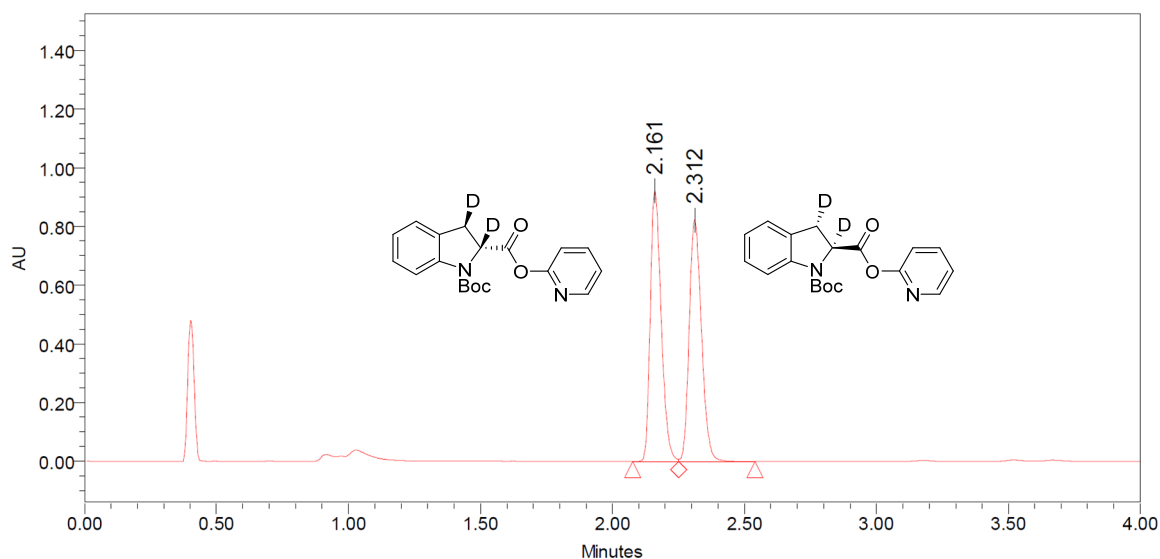
	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	12.243	566414	4301057	47.88
2	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	13.326	552636	4682672	52.12



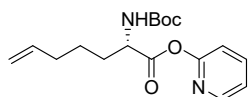
1-(*tert*-butyl) 2-(pyridin-2-yl) (*S*)-indoline-1,2-dicarboxylate (10-H)



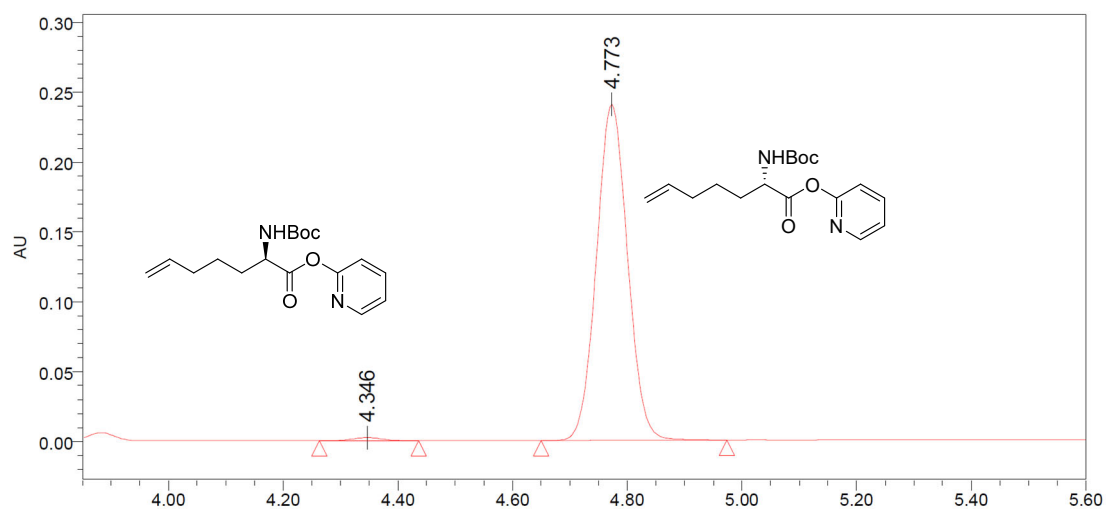
	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 240.0 nm (PDA Spectrum (190-410)nm)	2.167	1307	4420	0.17
2	PDA Spectrum PDA 240.0 nm (PDA Spectrum (190-410)nm)	2.296	818431	2674115	99.83



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 240.0 nm (PDA Spectrum (190-410)nm)	2.161	924797	2637302	49.82
2	PDA Spectrum PDA 240.0 nm (PDA Spectrum (190-410)nm)	2.312	825175	2655974	50.18

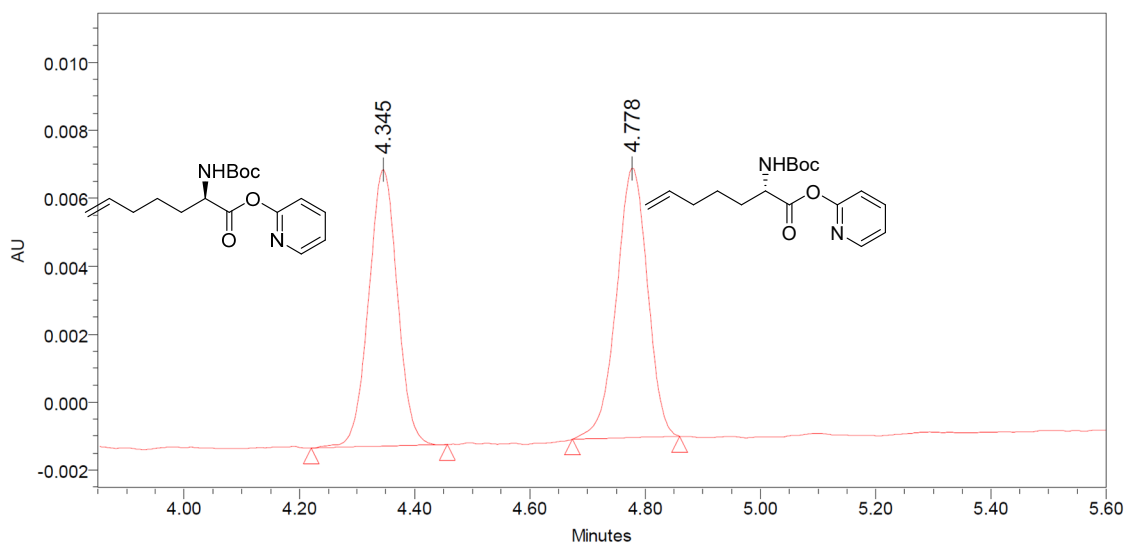


pyridin-2-yl (S)-2-((*tert*-butoxycarbonyl)amino)hept-6-enoate (13)

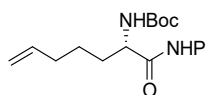


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	4.346	2154	7544	0.83
2	PDA Ch1 254nm@4.8nm -Compens.	4.773	240380	904588	99.17

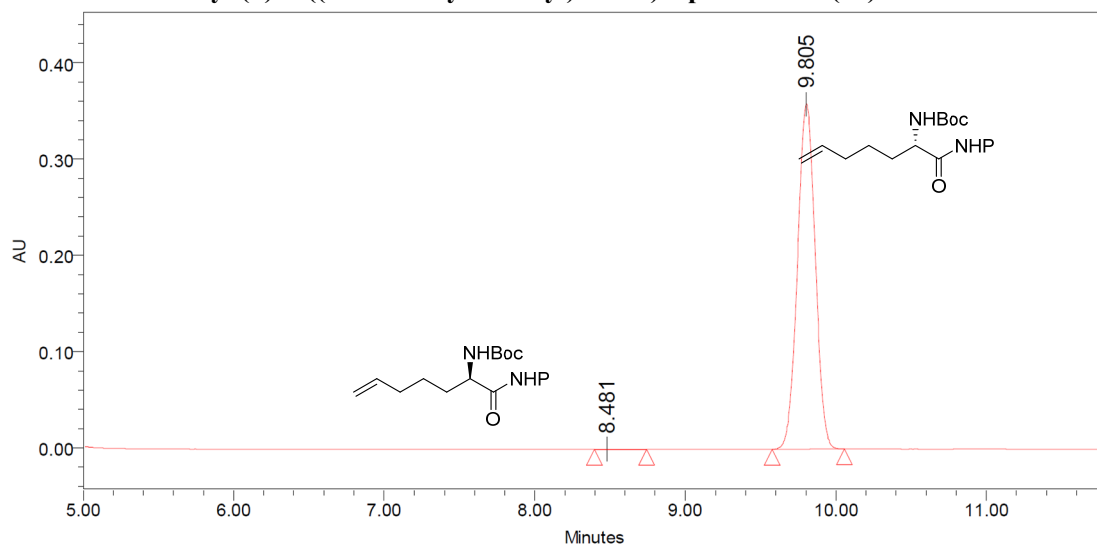
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	4.345	8151	28239	48.68
2	PDA Ch1 254nm@4.8nm -Compens.	4.778	7940	29775	51.32

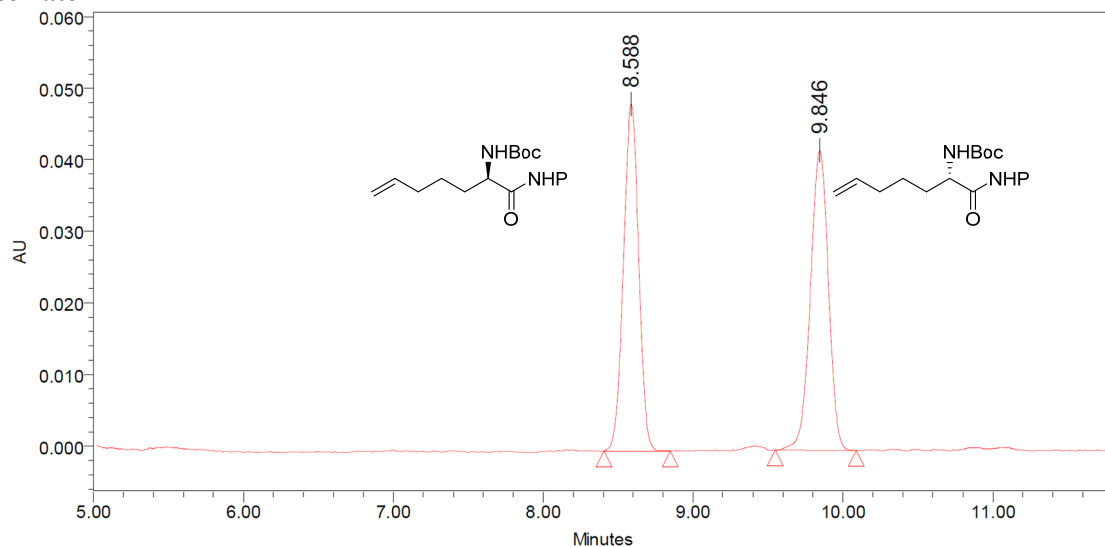


1,3-dioxoisindolin-2-yl (*S*)-2-((tert-butoxycarbonyl)amino)hept-6-enoate (16)

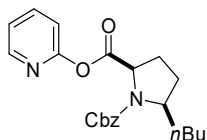


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	8.481	132	1319	0.04
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	9.805	358667	2939836	99.96

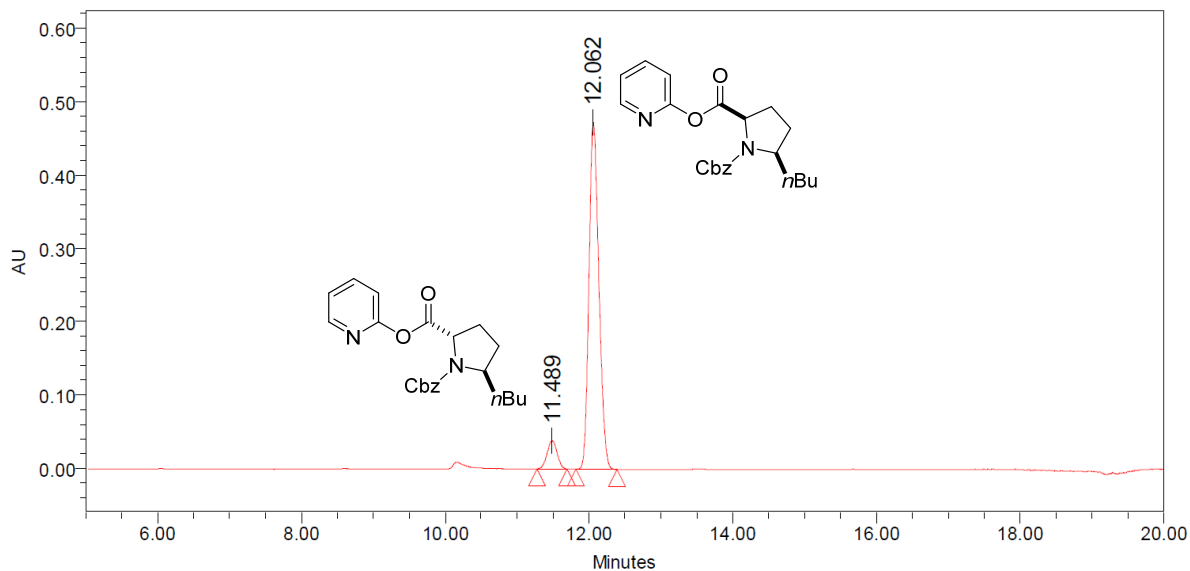
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	8.588	48490	341905	49.34
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	9.846	41952	350986	50.66

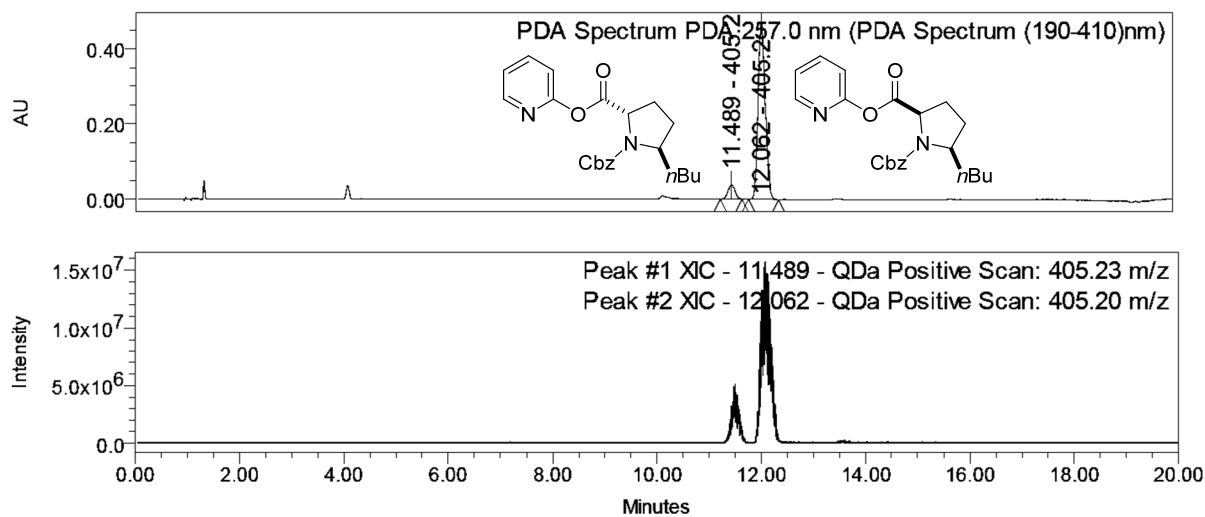


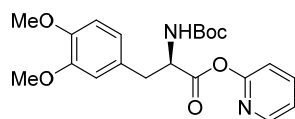
1-benzyl 2-(pyridin-2-yl) (2R,5R)-5-butylpyrrolidine-1,2-dicarboxylate (79)



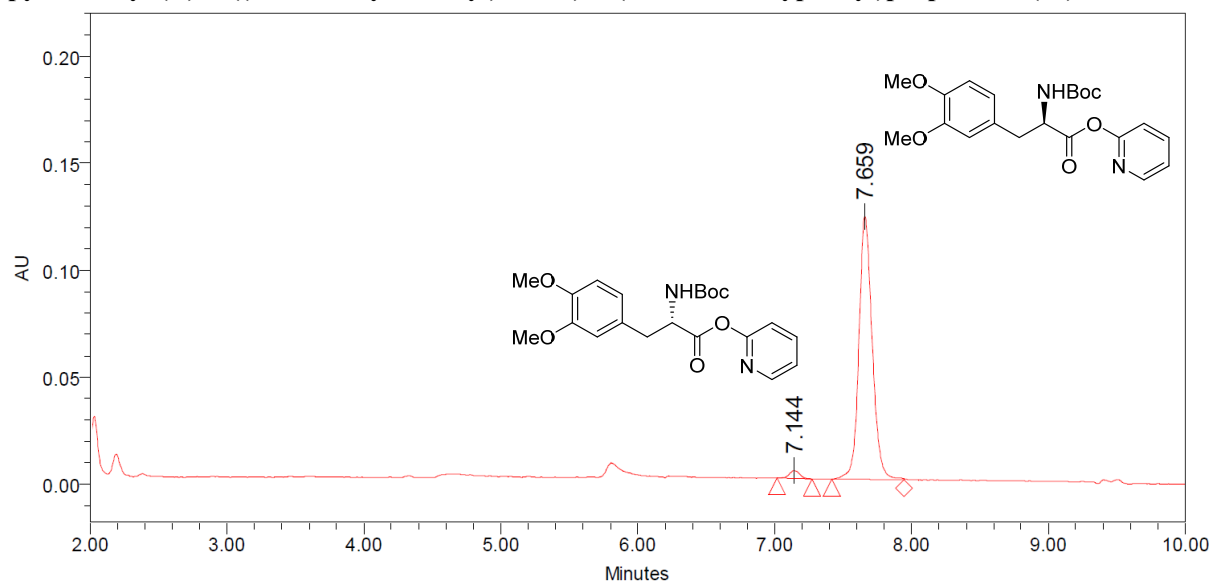
	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 257.0 nm (PDA Spectrum (190-410)nm)	11.489	38225	370441	7.52
2	PDA Spectrum PDA 257.0 nm (PDA Spectrum (190-410)nm)	12.062	473195	4555085	92.48

Mass analysis



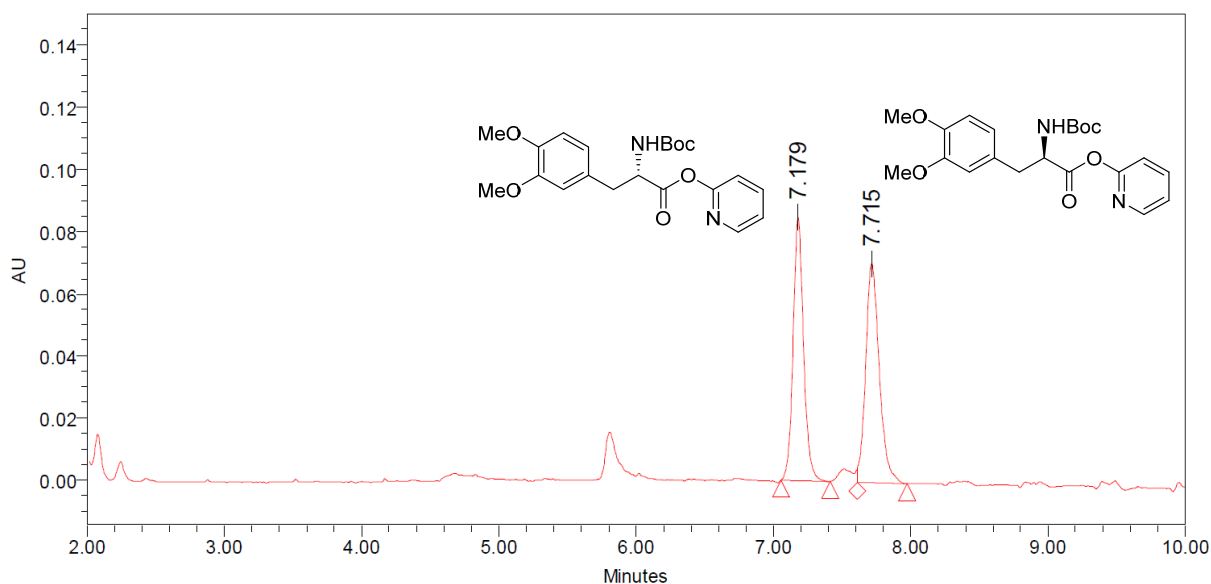


pyridin-2-yl (R)-2-((tert-butoxycarbonyl)amino)-3-(3,4-dimethoxyphenyl)propanoate (83)

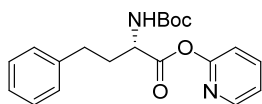


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 260.0 nm (PDA Spectrum (190-410)nm)	7.144	3770	19890	2.34
2	PDA Spectrum PDA 260.0 nm (PDA Spectrum (190-410)nm)	7.659	122889	829595	97.66

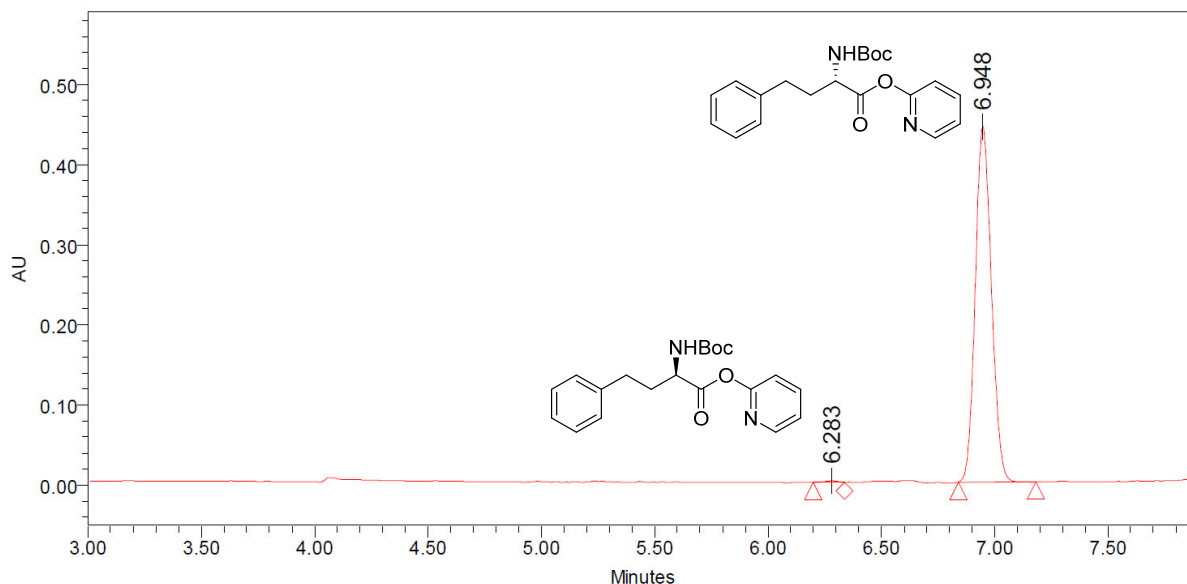
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 260.0 nm (PDA Spectrum (190-410)nm)	7.179	85159	450036	48.04
2	PDA Spectrum PDA 260.0 nm (PDA Spectrum (190-410)nm)	7.715	70658	486833	51.96

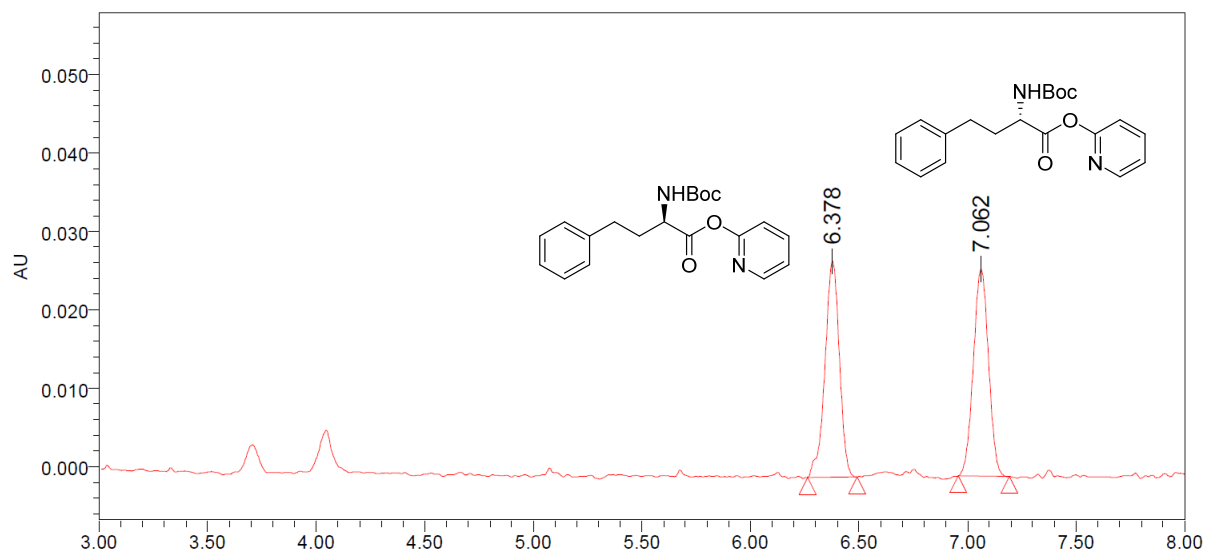


pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)-4-phenylbutanoate (87)

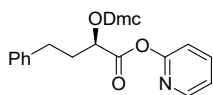


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	6.283	2293	9810	0.45
2	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	6.948	443766	2194475	99.55

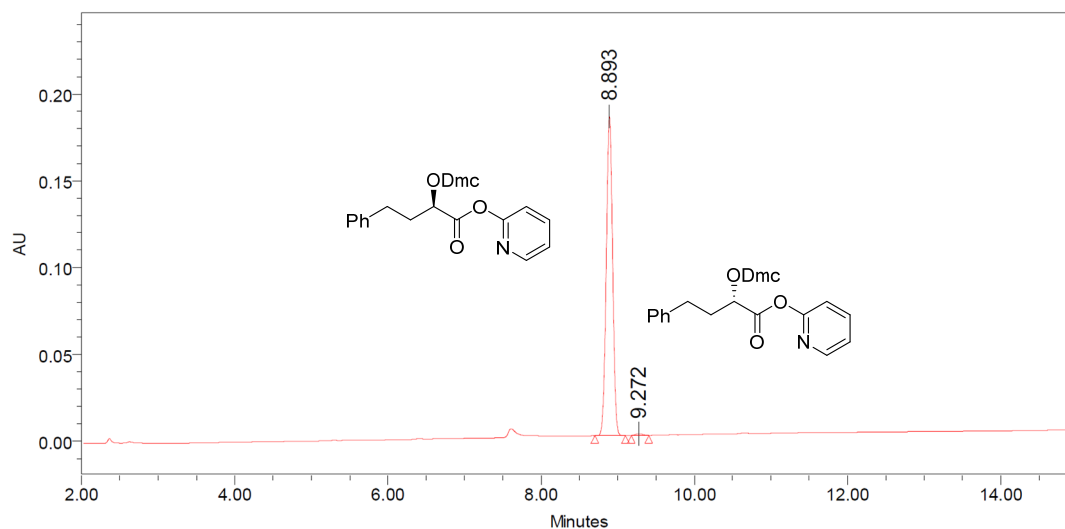
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	6.378	27531	127487	49.81
2	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	7.062	26391	128447	50.19

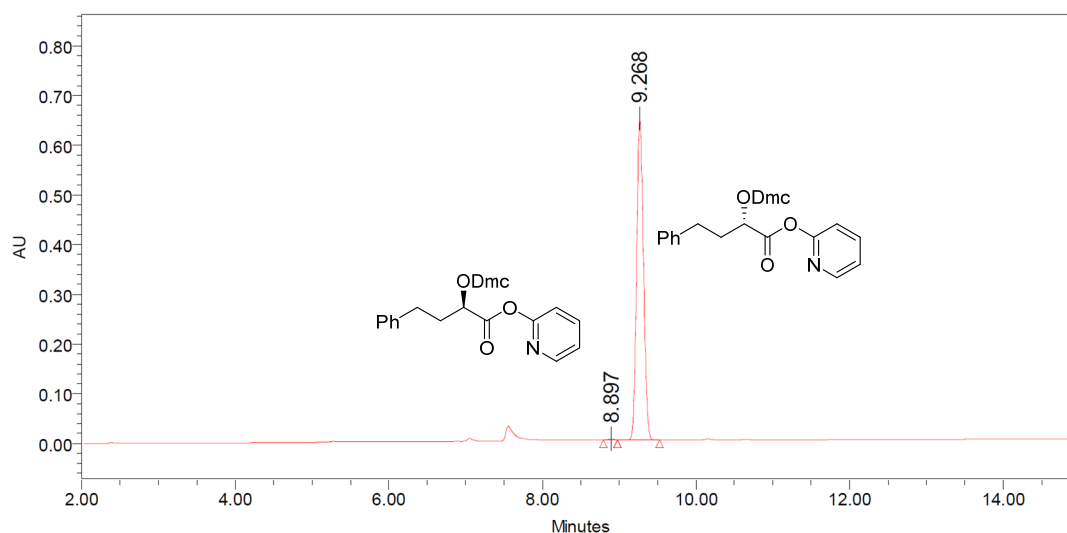


pyridin-2-yl (*R*)-2-((dimethylcarbamoyl)oxy)-4-phenylbutanoate (91)

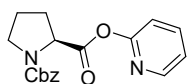


	Processed Channel Descr.	RT	Area	Height	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	8.893	1054988	184198	99.45
2	PDA Ch1 254nm@4.8nm -Compens.	9.272	5808	850	0.55

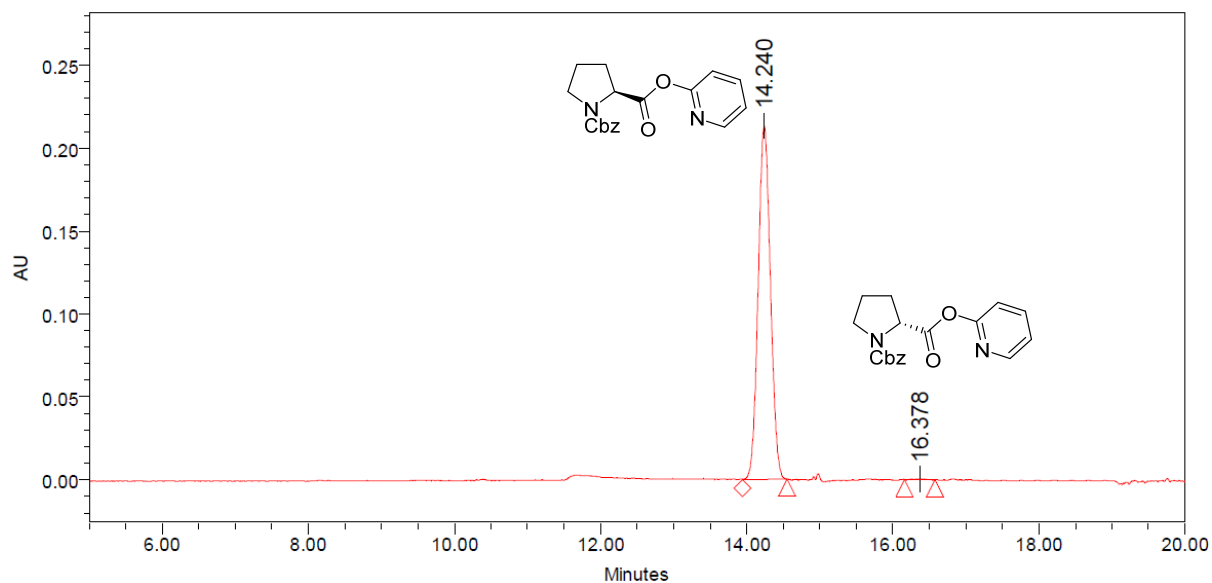
(*S*)-enantiomer



	Processed Channel Descr.	RT	Area	Height	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	8.897	14127	2535	0.35
2	PDA Ch1 254nm@4.8nm -Compens.	9.268	4022283	647756	99.65

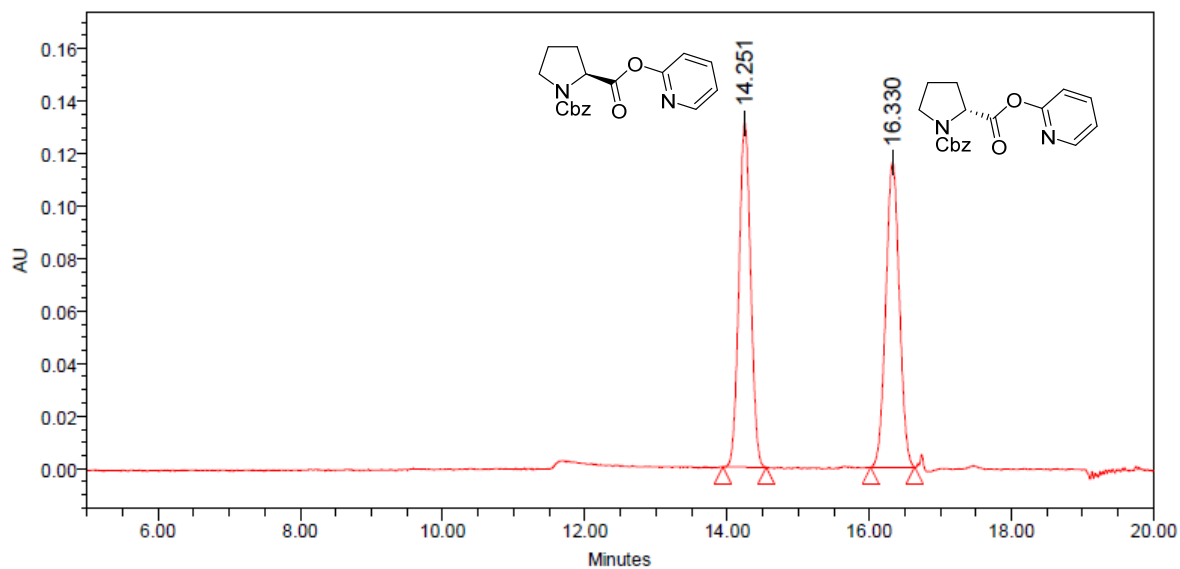


1-benzyl 2-(pyridin-2-yl) (S)-pyrrolidine-1,2-dicarboxylate (S1)

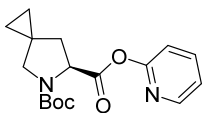


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 261.8 nm (PDA Spectrum (190-410)nm)	14.240	213290	2505991	99.83
2	PDA Spectrum PDA 261.8 nm (PDA Spectrum (190-410)nm)	16.378	441	4169	0.17

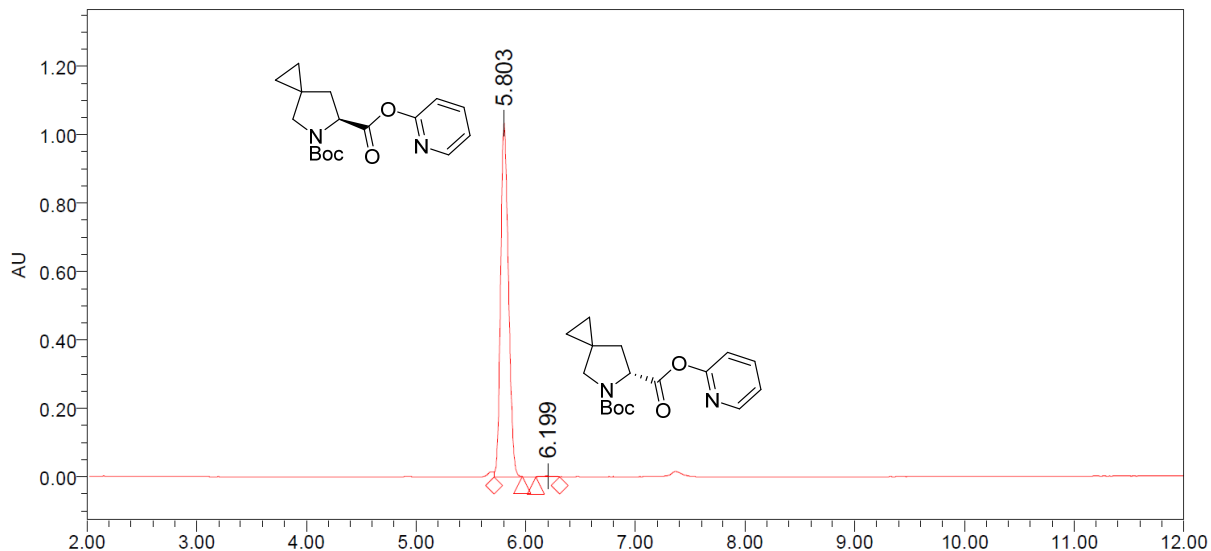
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 261.8 nm (PDA Spectrum (190-410)nm)	14.251	131075	1519108	49.51
2	PDA Spectrum PDA 261.8 nm (PDA Spectrum (190-410)nm)	16.330	116109	1548889	50.49

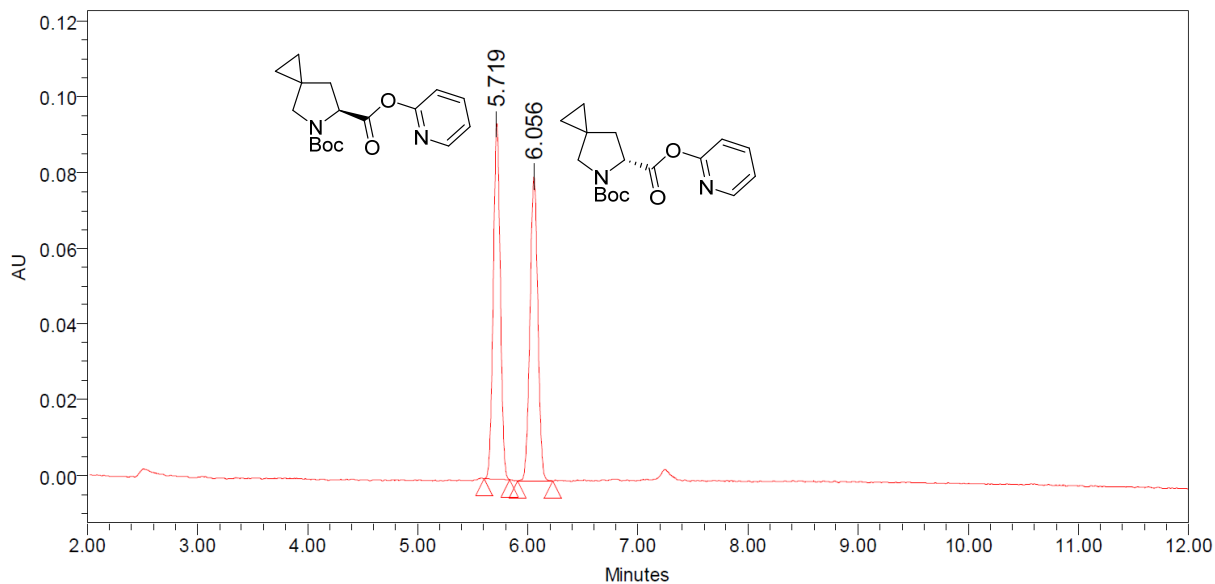


5-(tert-butyl) 6-(pyridin-2-yl) (S)-5-azaspiro[2.4]heptane-5,6-dicarboxylate (S2)

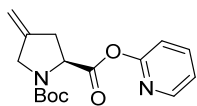


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	5.803	1034143	5138424	99.79
2	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	6.199	1833	10868	0.21

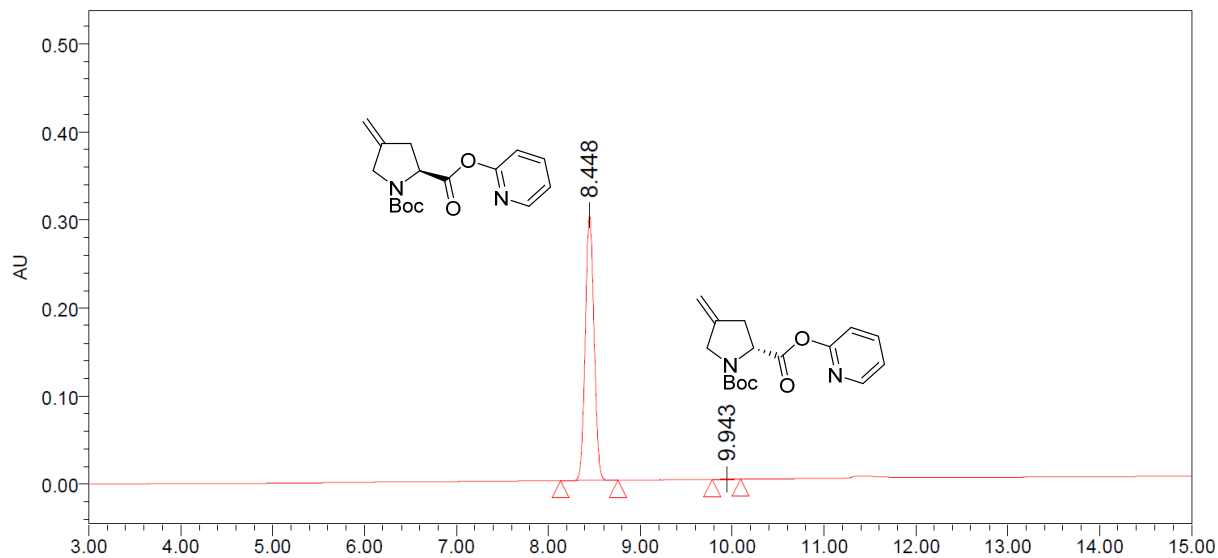
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	5.719	93896	416911	51.02
2	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	6.056	80425	400227	48.98

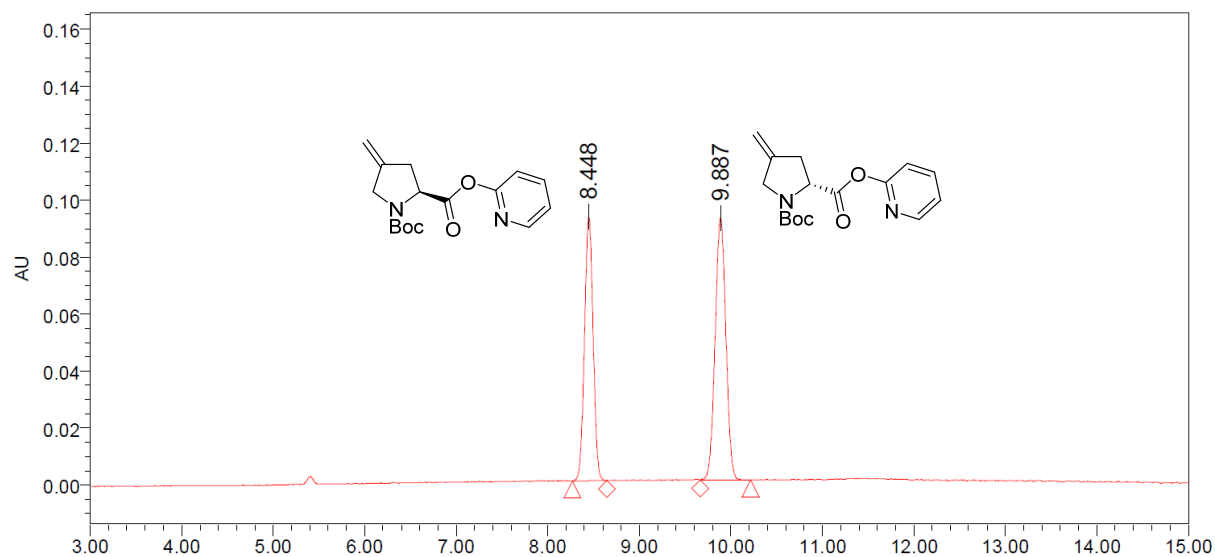


1-(tert-butyl) 2-(pyridin-2-yl) (S)-4-methylenepyrrolidine-1,2-dicarboxylate (S3)

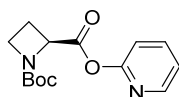


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	8.448	301201	1998848	99.93
2	PDA Ch1 254nm@4.8nm -Compens.	9.943	164	1316	0.07

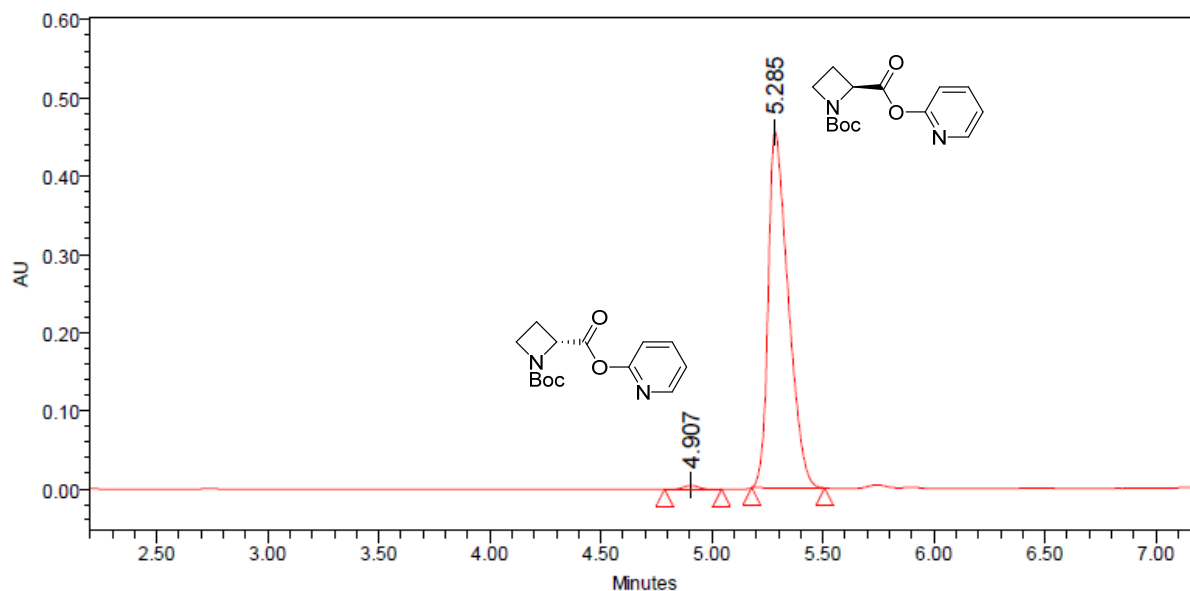
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 254.0 nm (PDA Spectrum (190-410)nm)	8.448	92684	607688	44.77
2	PDA Spectrum PDA 254.0 nm (PDA Spectrum (190-410)nm)	9.887	91814	749561	55.23

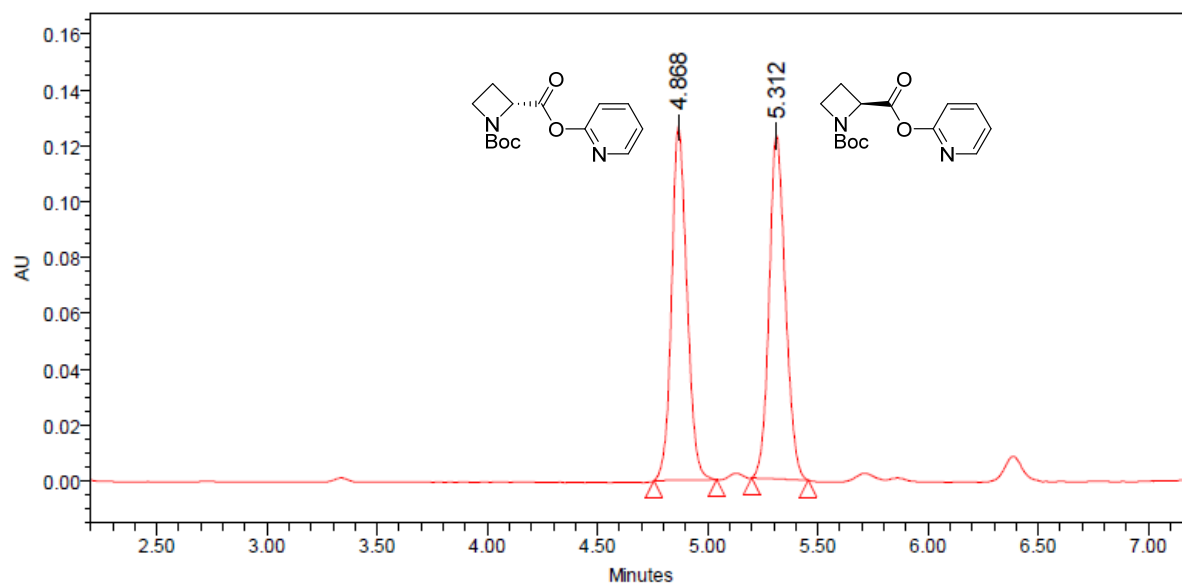


1-(tert-butyl) 2-(pyridin-2-yl) (S)-azetidine-1,2-dicarboxylate (S4)

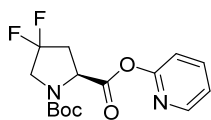


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	4.907	4768	21402	0.75
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	5.285	455374	2844839	99.25

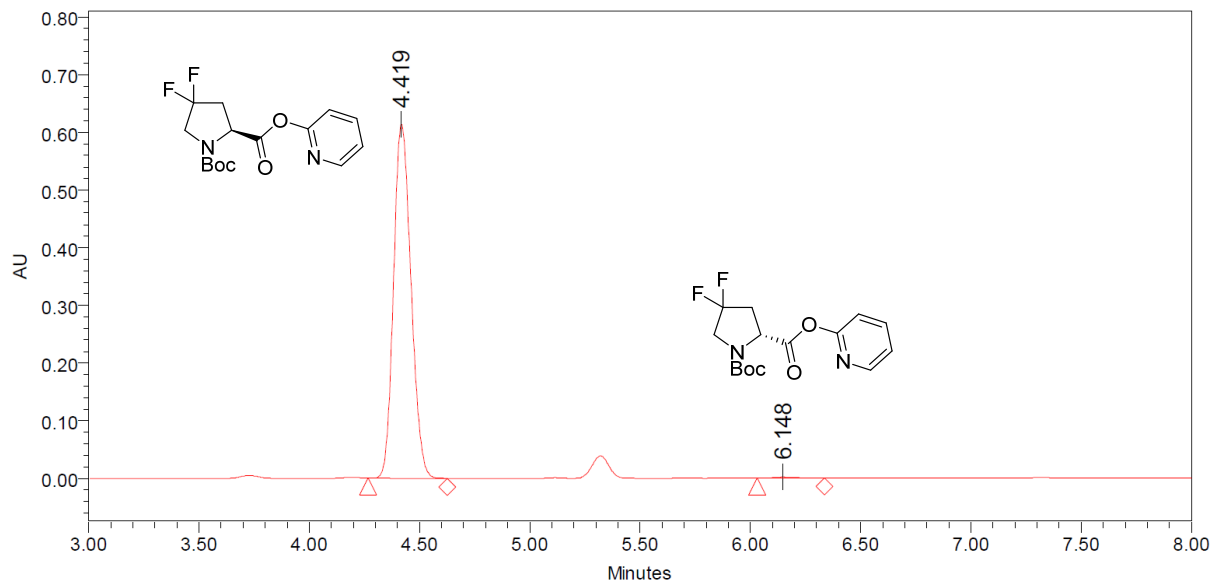
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	4.868	126420	613215	49.23
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	5.312	122910	632281	50.77

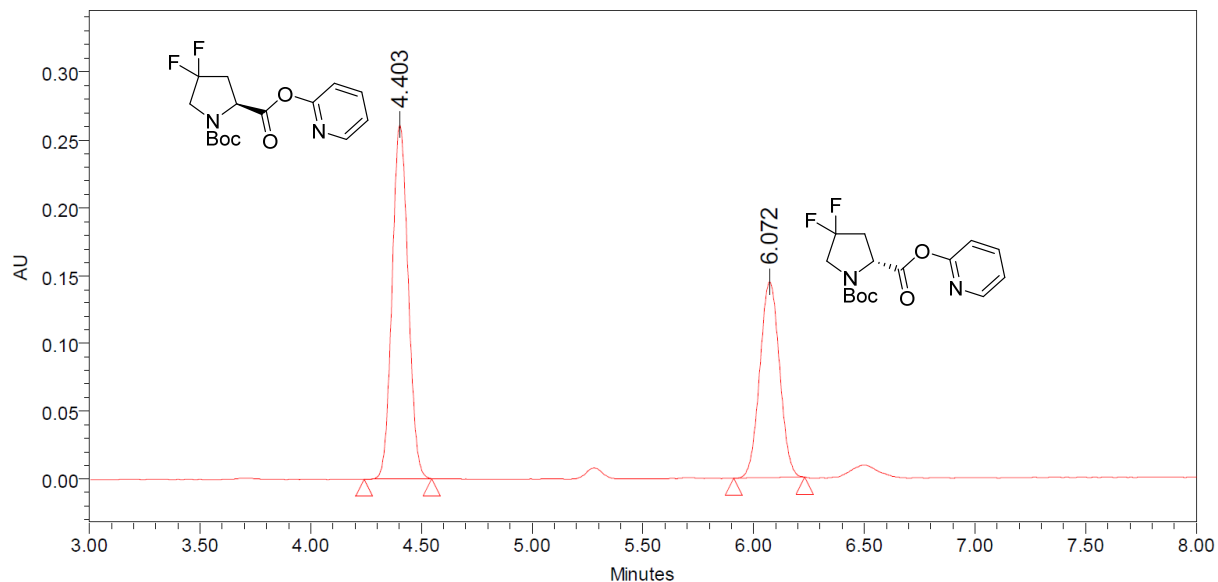


1-(tert-butyl) 2-(pyridin-2-yl) (S)-4,4-difluoropyrrolidine-1,2-dicarboxylate (S5)

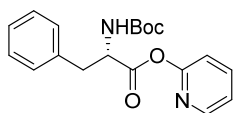


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	4.419	613855	3366275	99.55
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	6.148	1974	15162	0.45

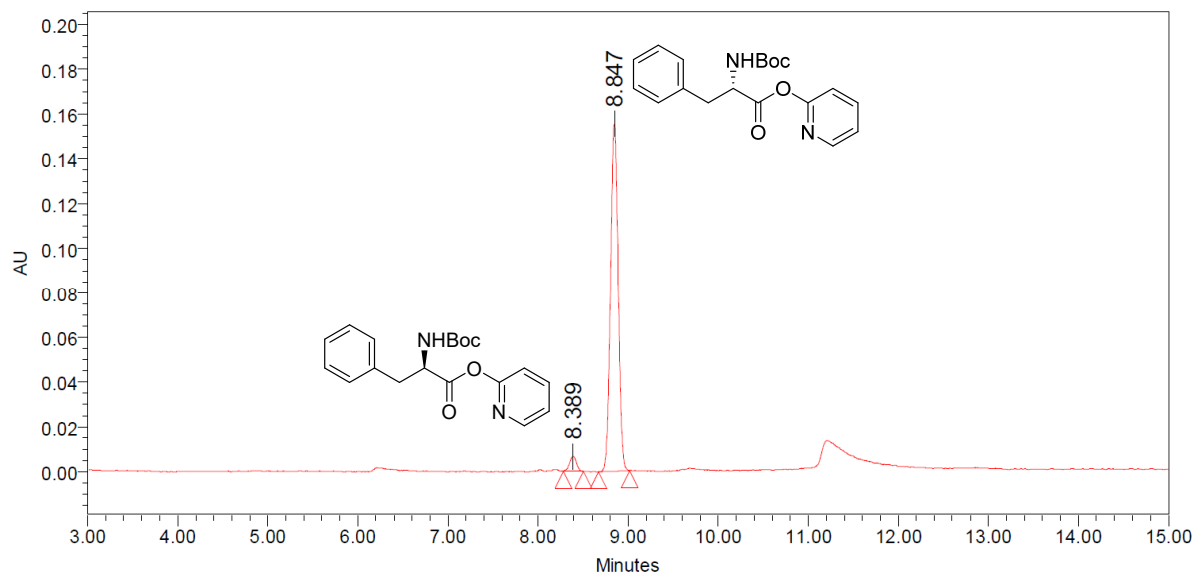
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	4.403	261106	1317071	59.55
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	6.072	144773	894542	40.45

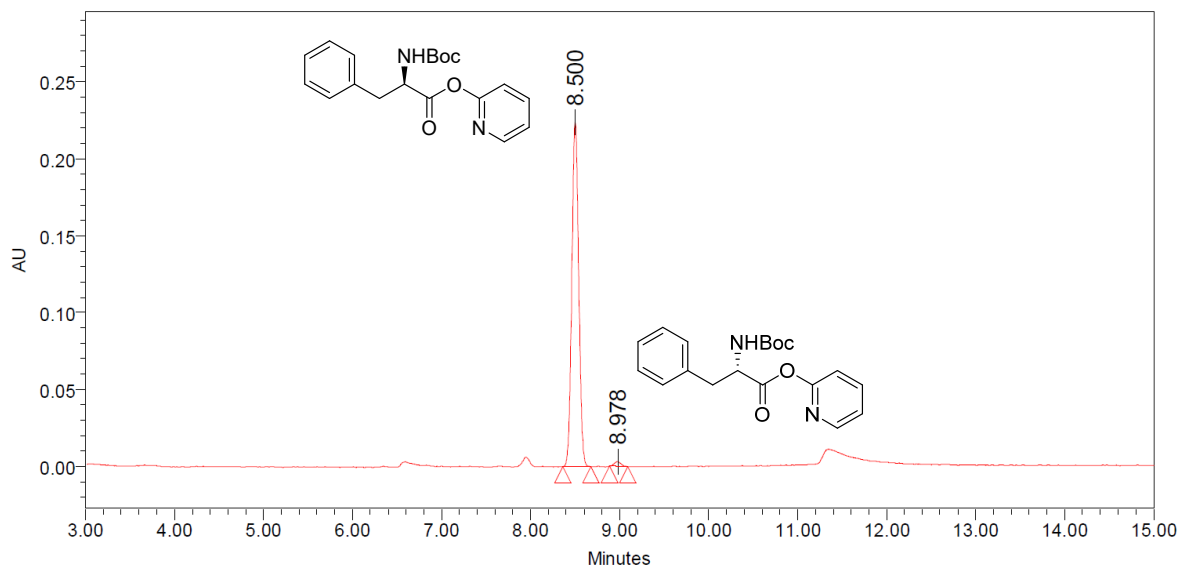


pyridin-2-yl (tert-butoxycarbonyl)-L-phenylalaninate (S14)

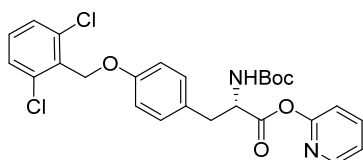


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 258.0 nm (PDA Spectrum (190-410)nm)	8.389	6687	35939	3.78
2	PDA Spectrum PDA 258.0 nm (PDA Spectrum (190-410)nm)	8.847	155506	914838	96.22

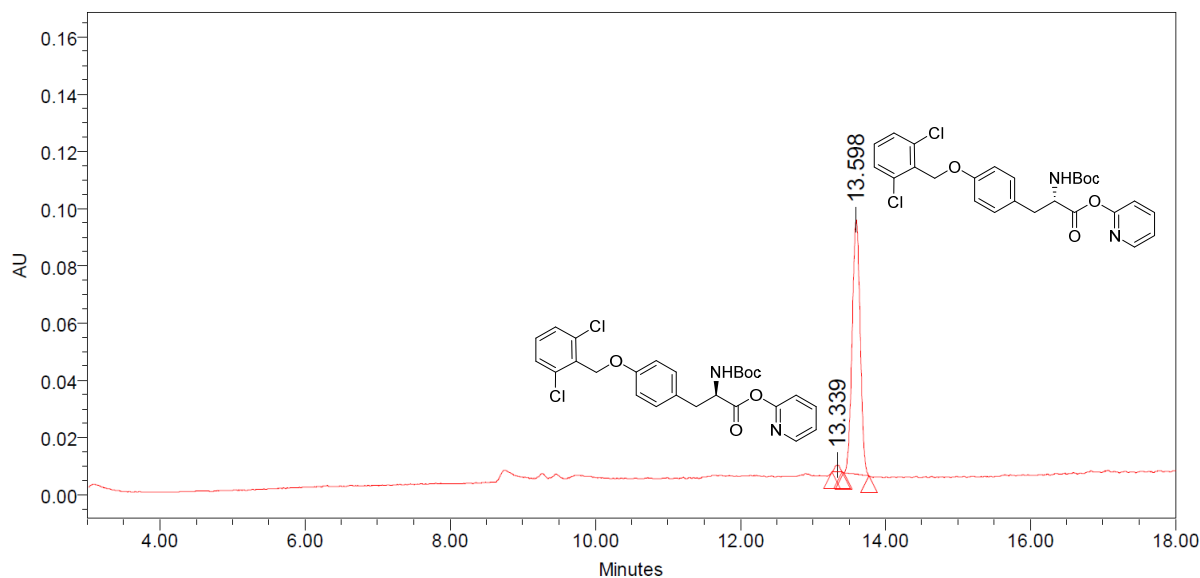
pyridin-2-yl (tert-butoxycarbonyl)-D-phenylalaninate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 258.0 nm (PDA Spectrum (190-410)nm)	8.500	223627	1204163	98.64
2	PDA Spectrum PDA 258.0 nm (PDA Spectrum (190-410)nm)	8.978	3060	16651	1.36

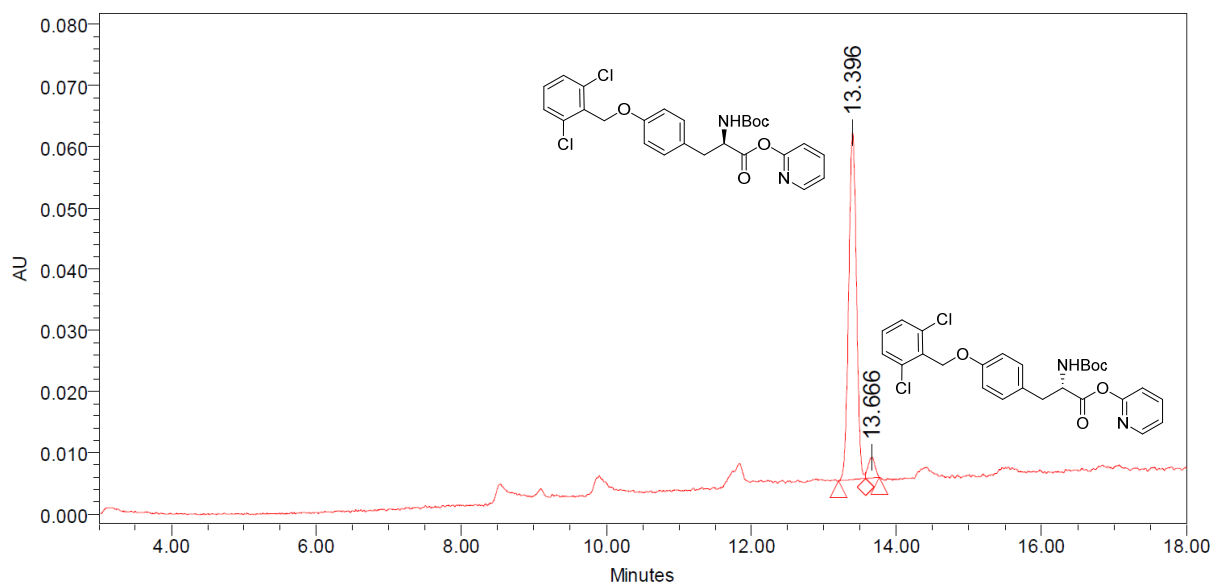


pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-((2,6-dichlorobenzyl)oxy)phenyl)-propanoate
(S15)

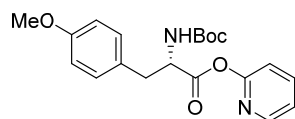


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 243.0 nm (PDA Spectrum (190-410)nm)	13.339	2392	11683	1.68
2	PDA Spectrum PDA 243.0 nm (PDA Spectrum (190-410)nm)	13.598	89006	684032	98.32

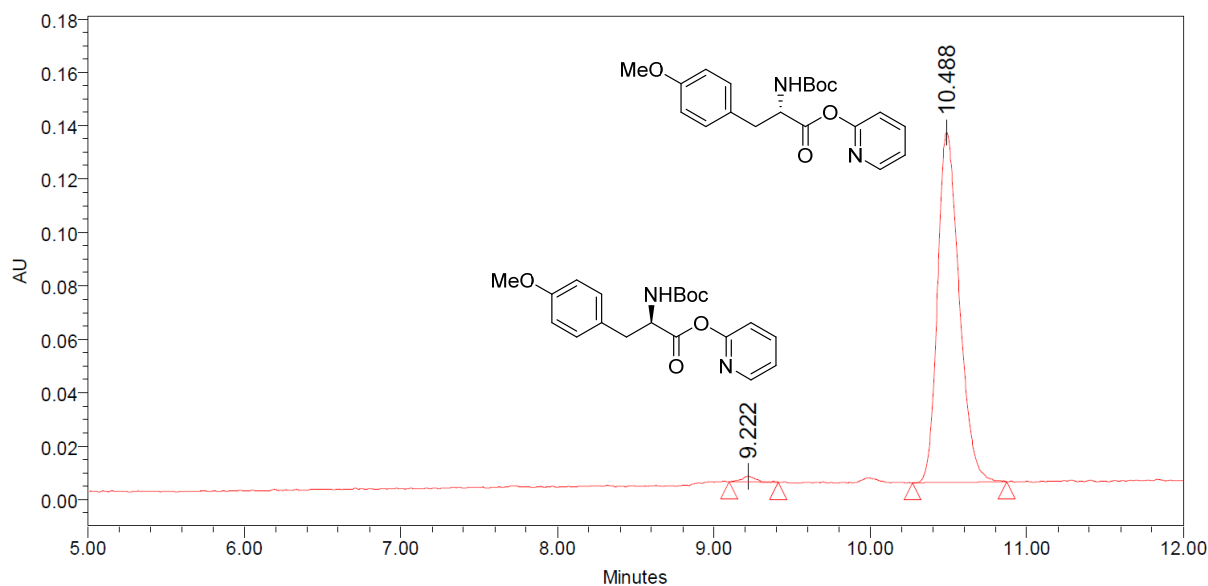
(R)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 243.0 nm (PDA Spectrum (190-410)nm)	13.396	56695	423817	95.06
2	PDA Spectrum PDA 243.0 nm (PDA Spectrum (190-410)nm)	13.666	3401	22003	4.94

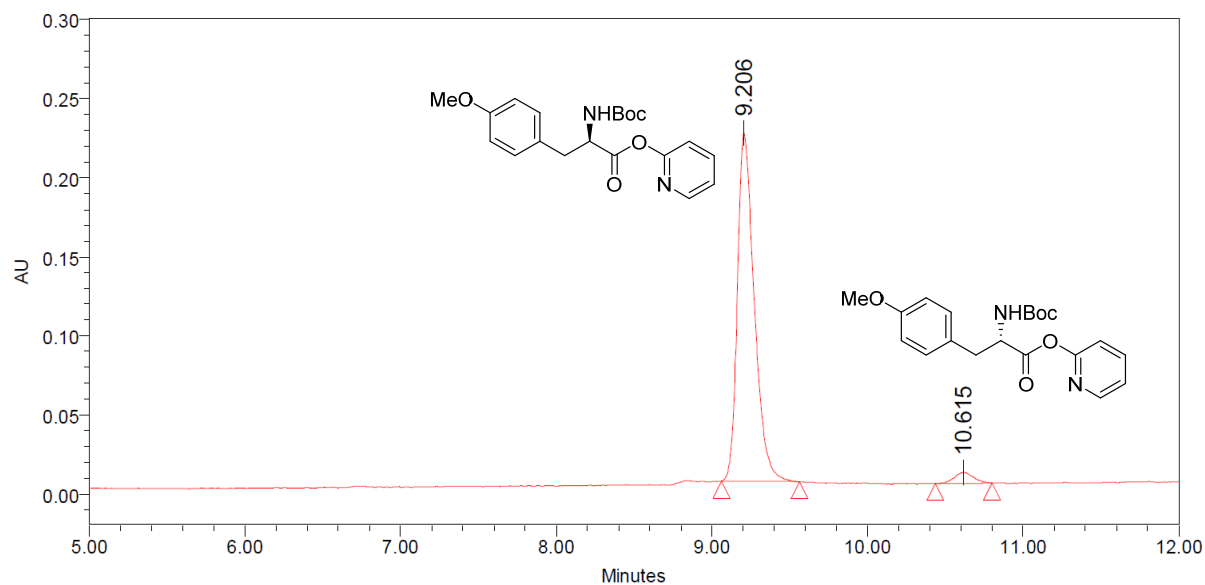


pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-methoxyphenyl)propanoate (S16)

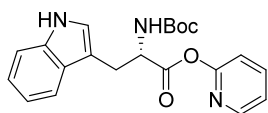


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 244.0 nm (PDA Spectrum (190-410)nm)	9.222	2123	13843	1.08
2	PDA Spectrum PDA 244.0 nm (PDA Spectrum (190-410)nm)	10.488	131148	1262937	98.92

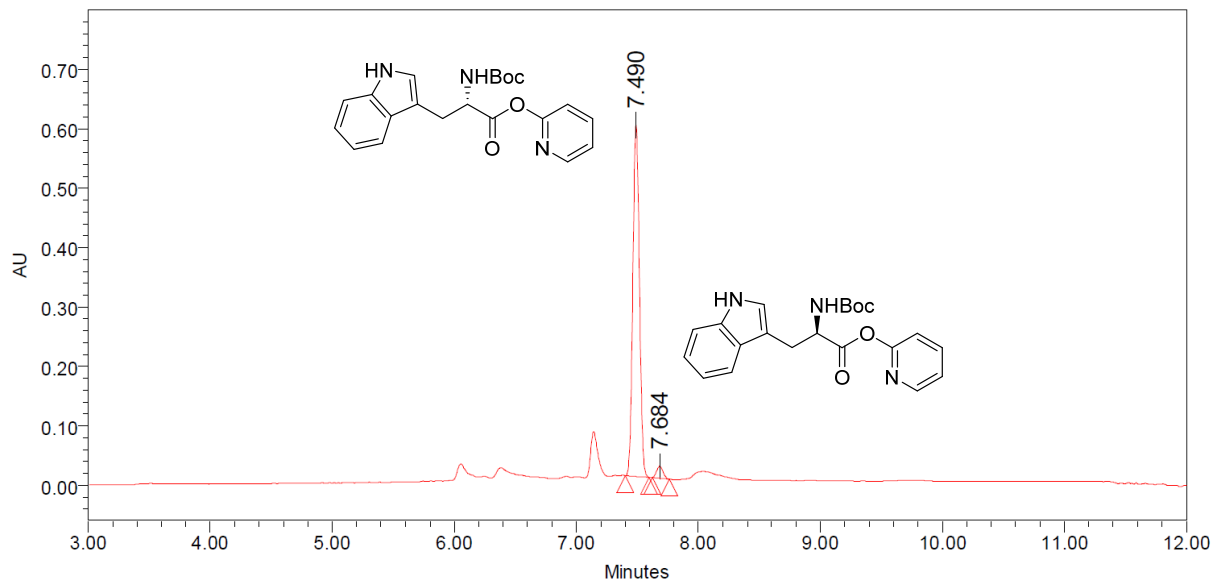
(R)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 244.0 nm (PDA Spectrum (190-410)nm)	9.206	220242	1653338	96.45
2	PDA Spectrum PDA 244.0 nm (PDA Spectrum (190-410)nm)	10.615	7007	60803	3.55

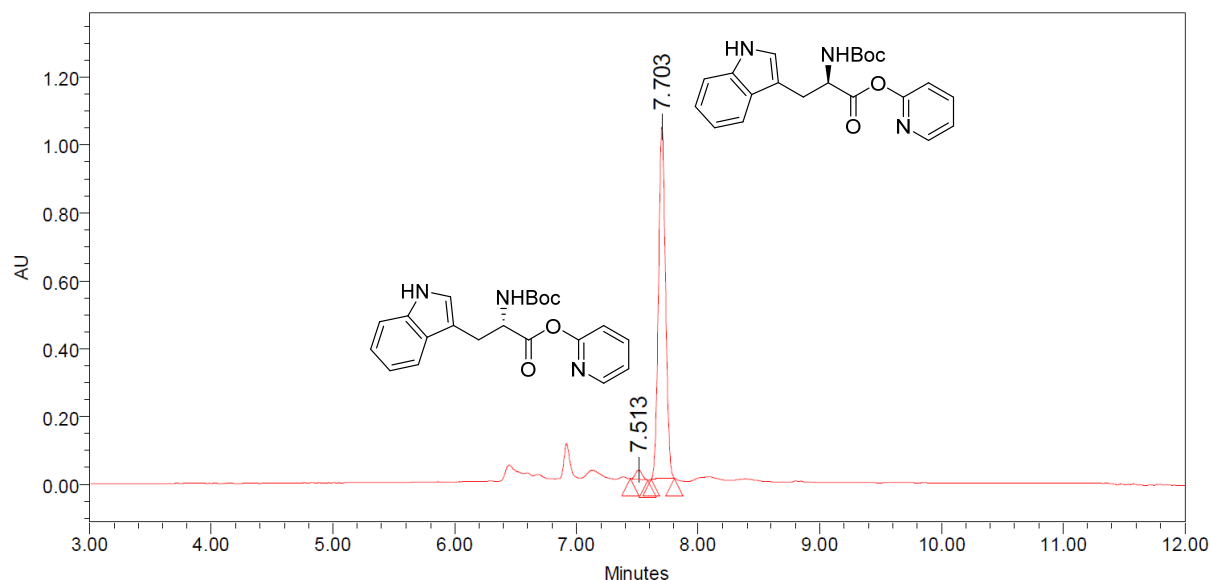


pyridin-2-yl (tert-butoxycarbonyl)-L-tryptophanate (S17)

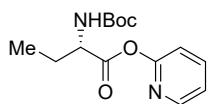


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	7.490	591288	2208193	96.74
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	7.684	20158	74374	3.26

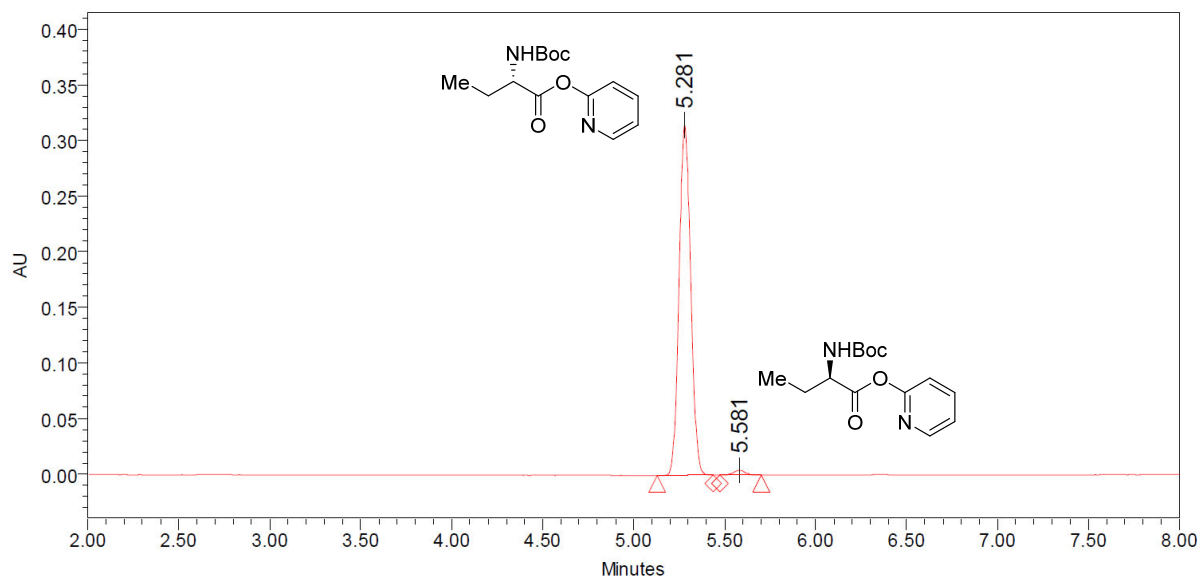
(D)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	7.513	27702	102155	2.38
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	7.703	1036234	4191179	97.62

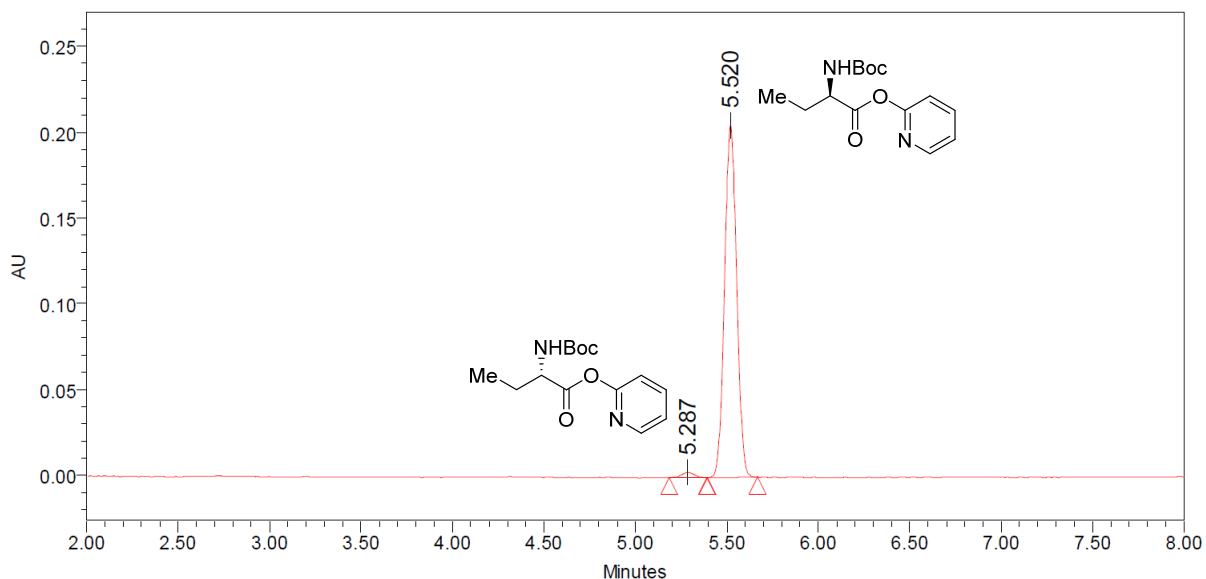


pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)butanoate (S18)

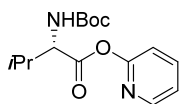


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 257.0 nm (PDA Spectrum (190-410)nm)	5.281	315316	1395212	98.55
2	PDA Spectrum PDA 257.0 nm (PDA Spectrum (190-410)nm)	5.581	4319	20571	1.45

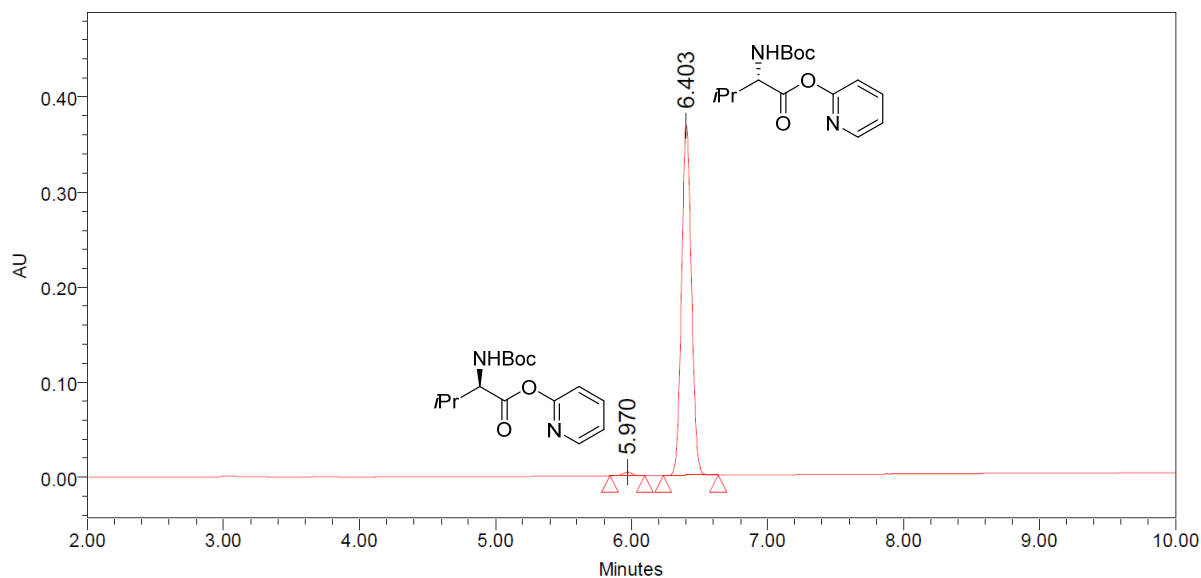
(R)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 257.0 nm (PDA Spectrum (190-410)nm)	5.287	2982	13949	1.46
2	PDA Spectrum PDA 257.0 nm (PDA Spectrum (190-410)nm)	5.520	205236	941239	98.54

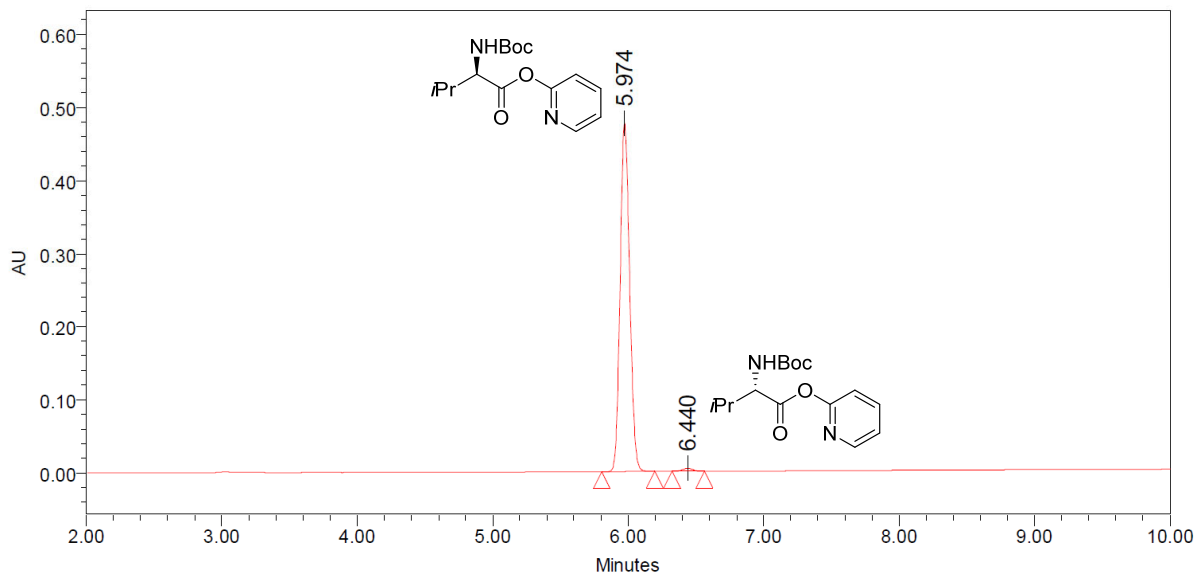


pyridin-2-yl (tert-butoxycarbonyl)-L-valinate (S19)

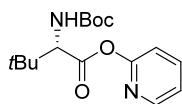


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	5.970	3596	17075	0.91
2	PDA Ch1 254nm@4.8nm -Compens.	6.403	367814	1862272	99.09

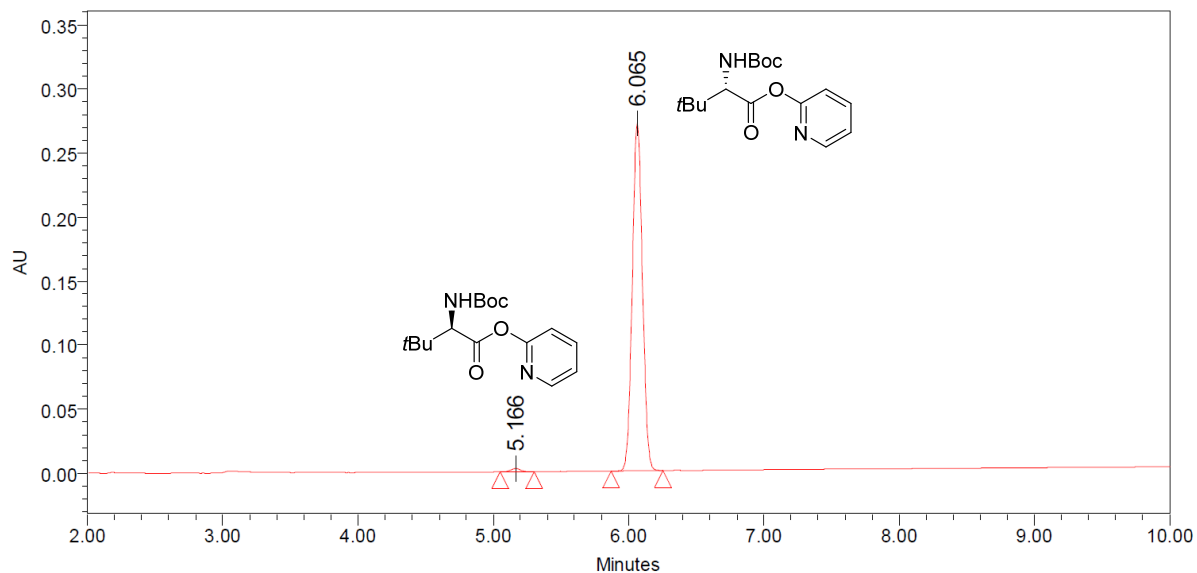
(D)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	5.974	476796	2323498	99.16
2	PDA Ch1 254nm@4.8nm -Compens.	6.440	4015	19699	0.84

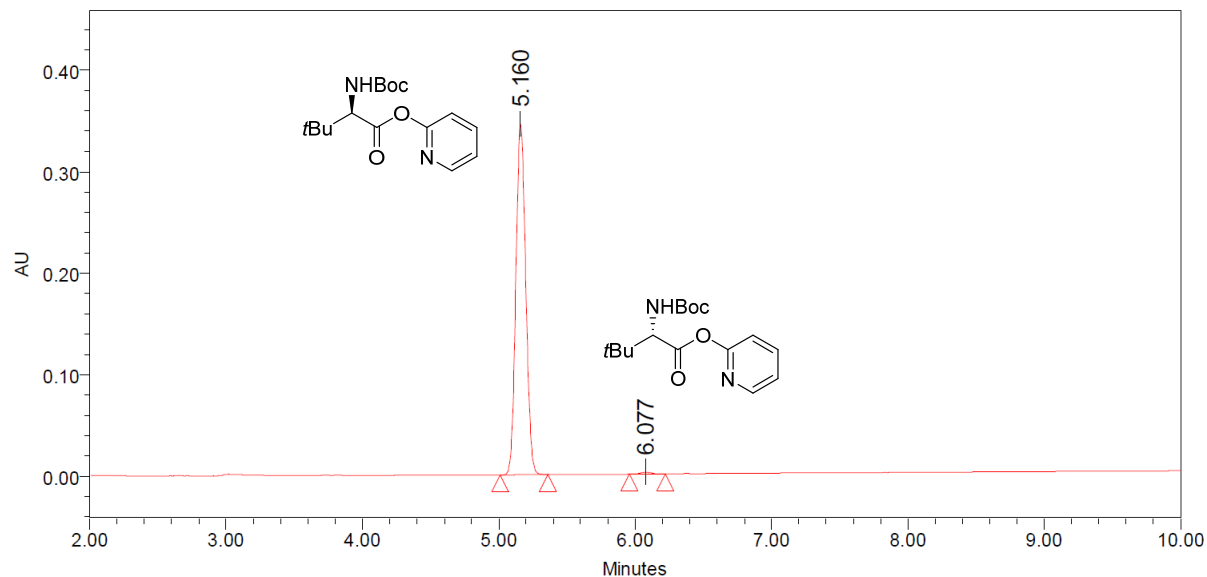


pyridin-2-yl (S)-2-((tert-butoxycarbonyl)amino)-3,3-dimethylbutanoate (S20)

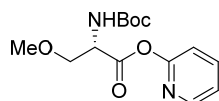


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	5.166	2543	12764	0.90
2	PDA Ch1 254nm@4.8nm -Compens.	6.065	271421	1411922	99.10

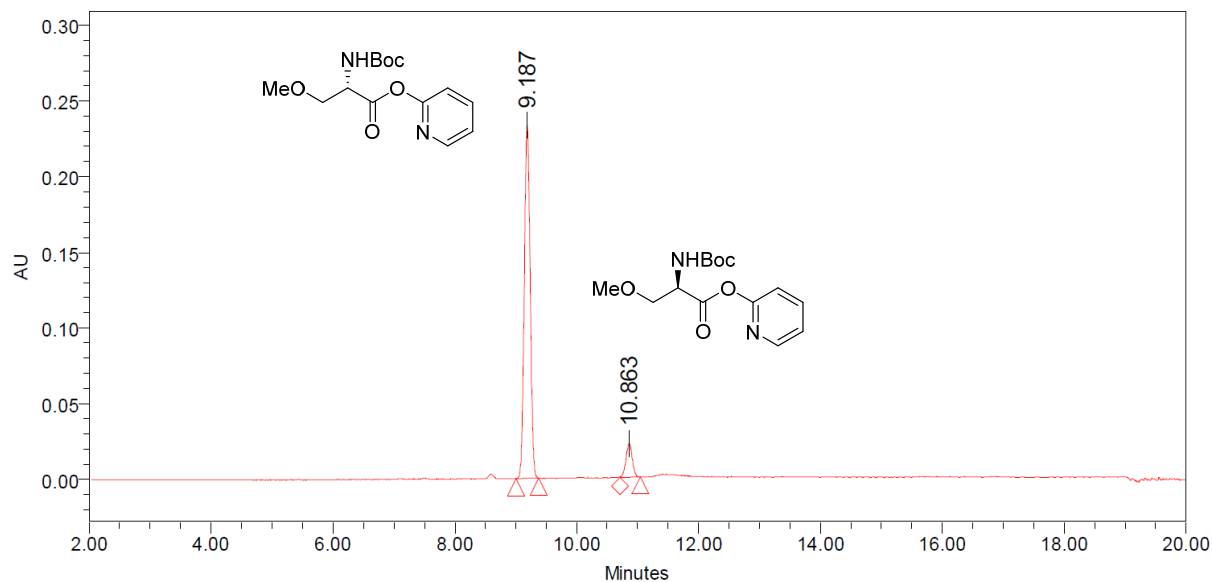
(R)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	5.160	346069	1735954	99.47
2	PDA Ch1 254nm@4.8nm -Compens.	6.077	1793	9336	0.53

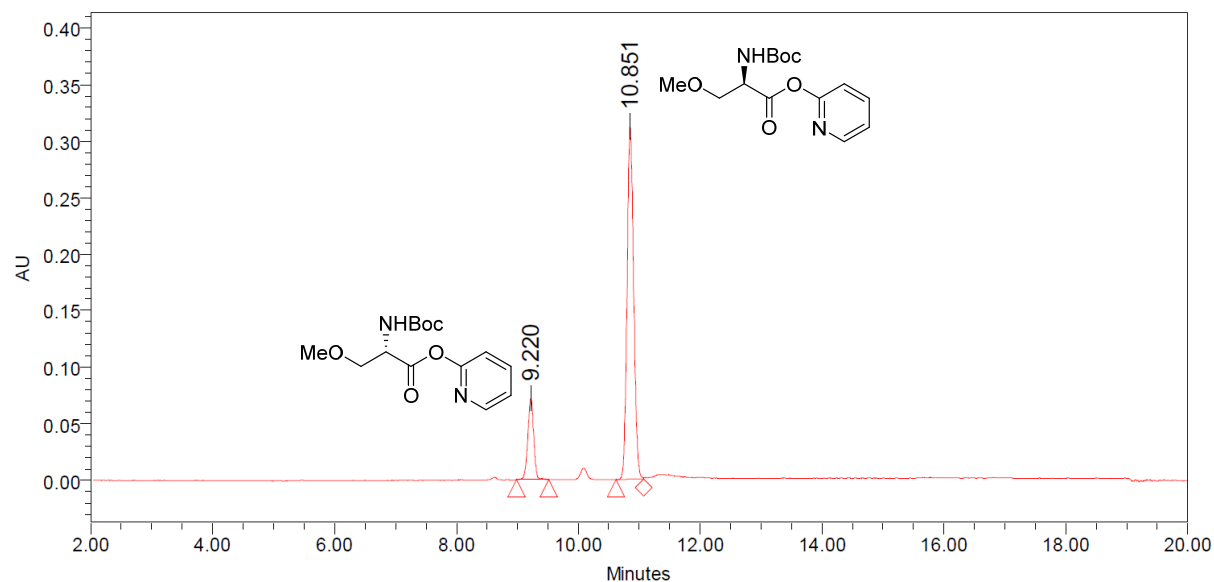


pyridin-2-yl N-(tert-butoxycarbonyl)-O-methyl-L-serinate (S21)

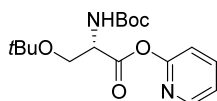


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	9.187	233296	1532971	90.43
2	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	10.863	22264	162141	9.57

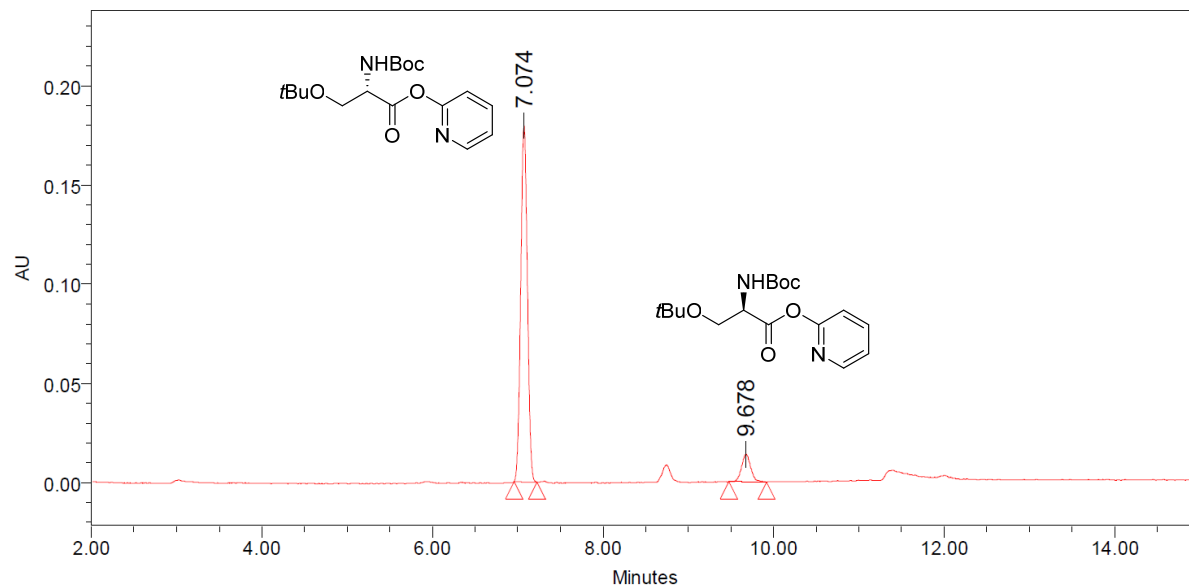
(D)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	9.220	71736	480460	16.96
2	PDA Spectrum PDA 255.0 nm (PDA Spectrum (190-410)nm)	10.851	311869	2352839	83.04

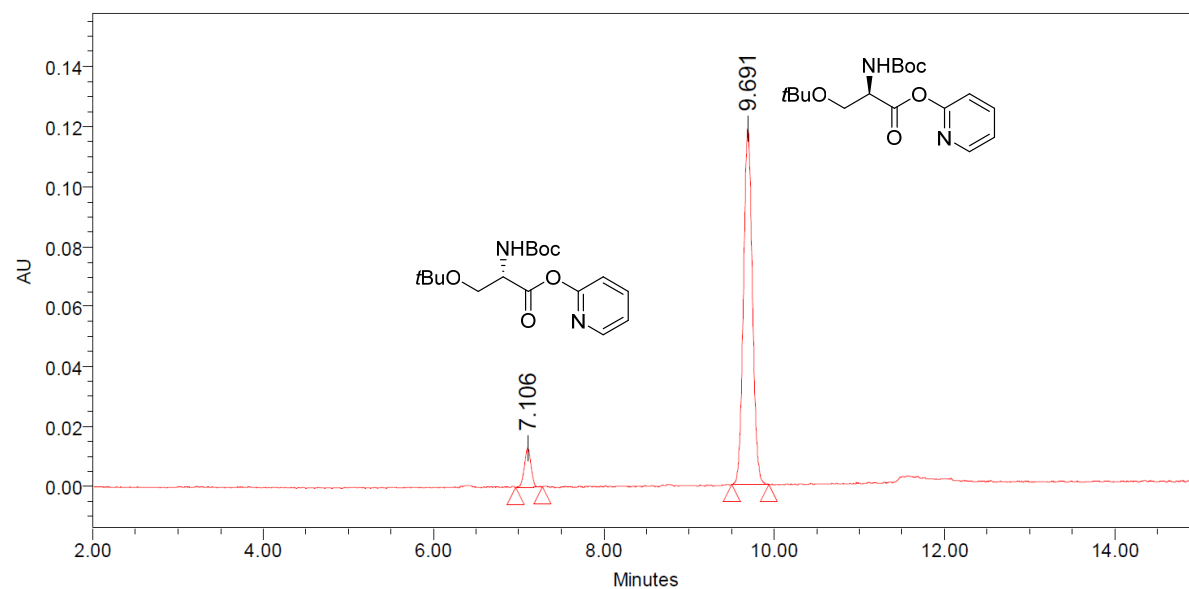


pyridin-2-yl N-(tert-butoxycarbonyl)-O-(tert-butyl)-L-serinate (S22)

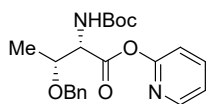


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 256.0 nm (PDA Spectrum (190-410)nm)	7.074	179844	972382	90.20
2	PDA Spectrum PDA 256.0 nm (PDA Spectrum (190-410)nm)	9.678	13928	105689	9.80

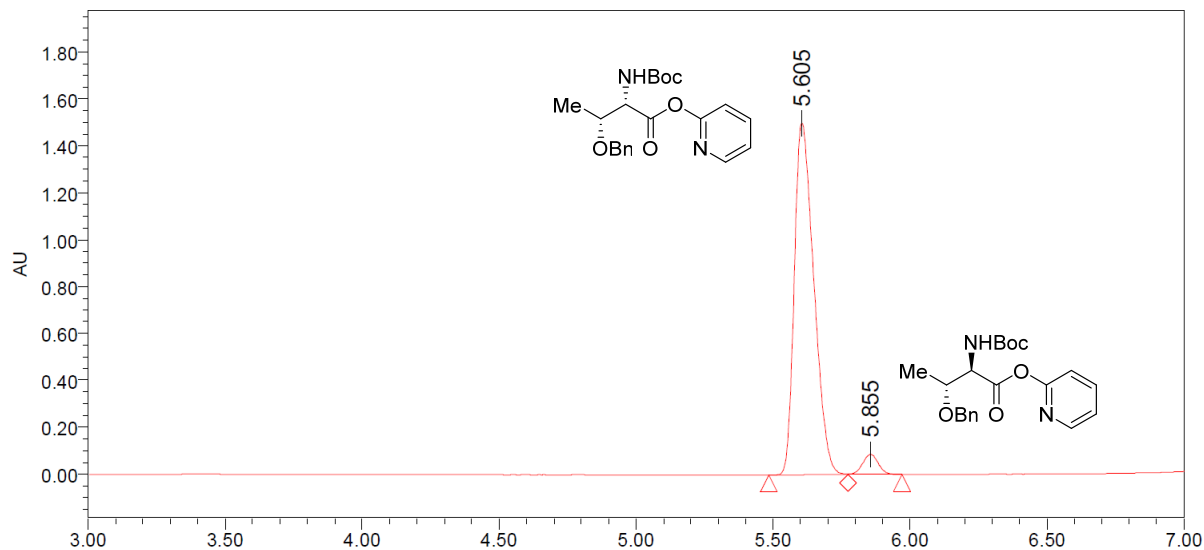
(D)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 256.0 nm (PDA Spectrum (190-410)nm)	7.106	12960	70090	7.45
2	PDA Spectrum PDA 256.0 nm (PDA Spectrum (190-410)nm)	9.691	118782	871213	92.55

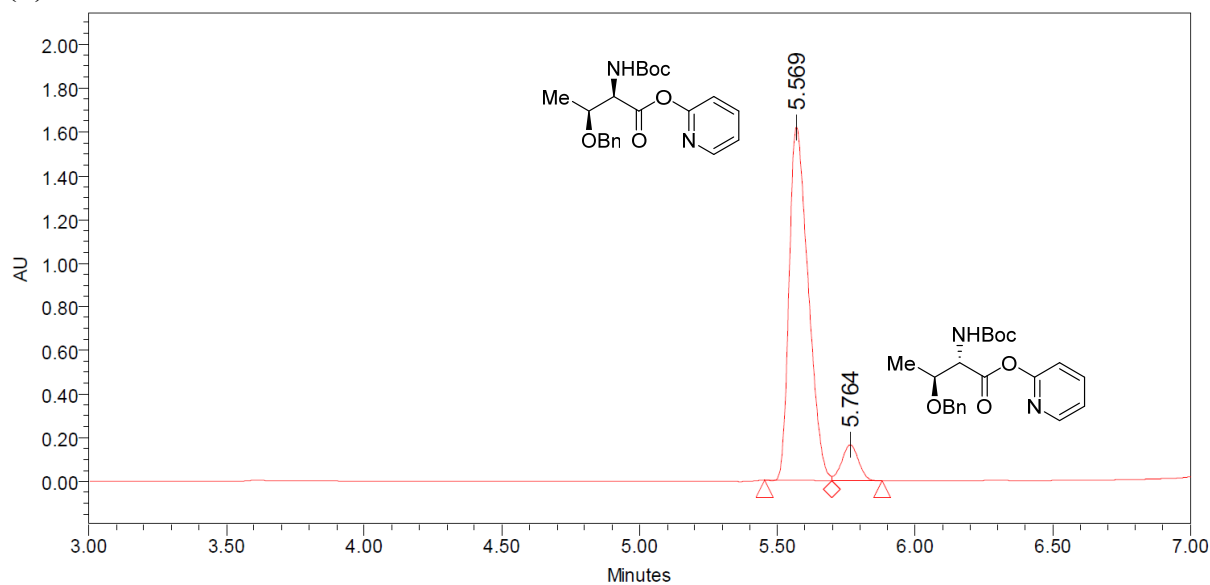


pyridin-2-yl O-benzyl-N-(tert-butoxycarbonyl)-L-threoninate (S23)

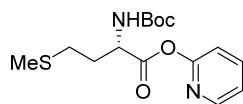


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 260.1 nm (PDA Spectrum (190-410)nm)	5.605	1501469	7422434	95.60
2	PDA Spectrum PDA 260.1 nm (PDA Spectrum (190-410)nm)	5.855	86065	341821	4.40

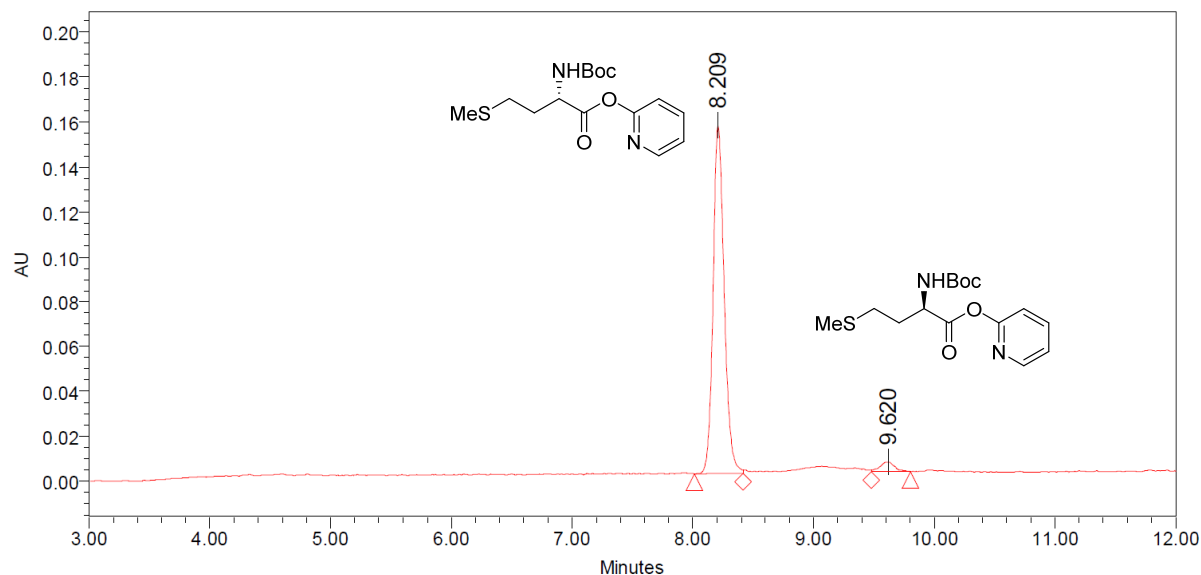
(L)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 260.1 nm (PDA Spectrum (190-410)nm)	5.569	1618542	7813528	91.84
2	PDA Spectrum PDA 260.1 nm (PDA Spectrum (190-410)nm)	5.764	163716	694673	8.16

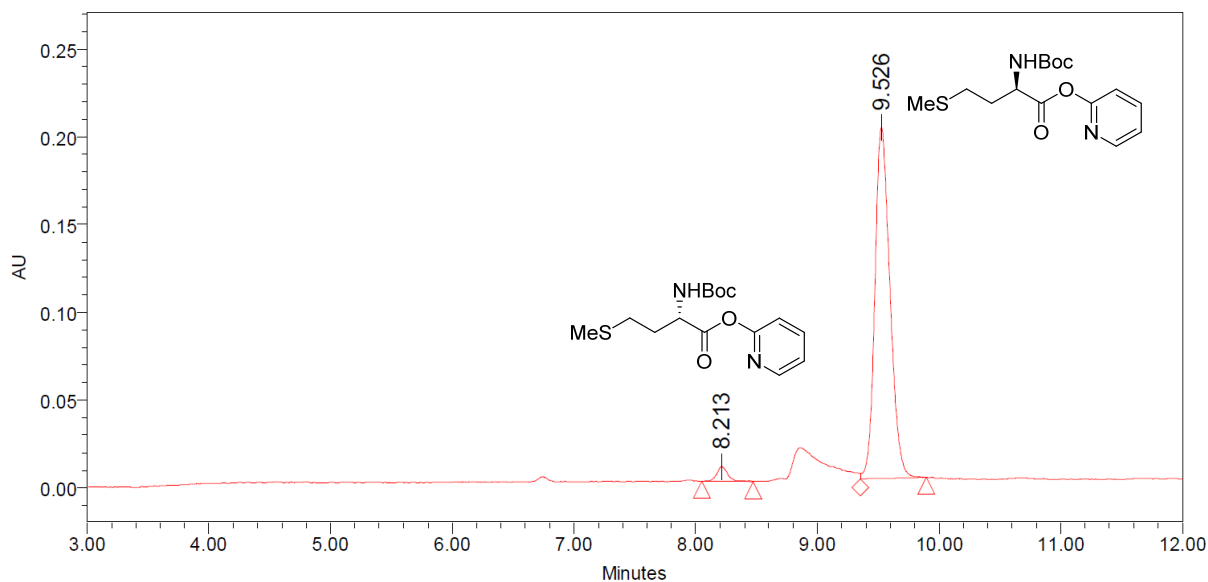


pyridin-2-yl (tert-butoxycarbonyl)-L-methioninate (S24)

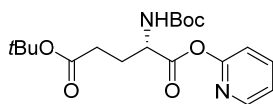


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 258.0 nm (PDA Spectrum (190-410)nm)	8.209	154990	991236	96.46
2	PDA Spectrum PDA 258.0 nm (PDA Spectrum (190-410)nm)	9.620	4263	36337	3.54

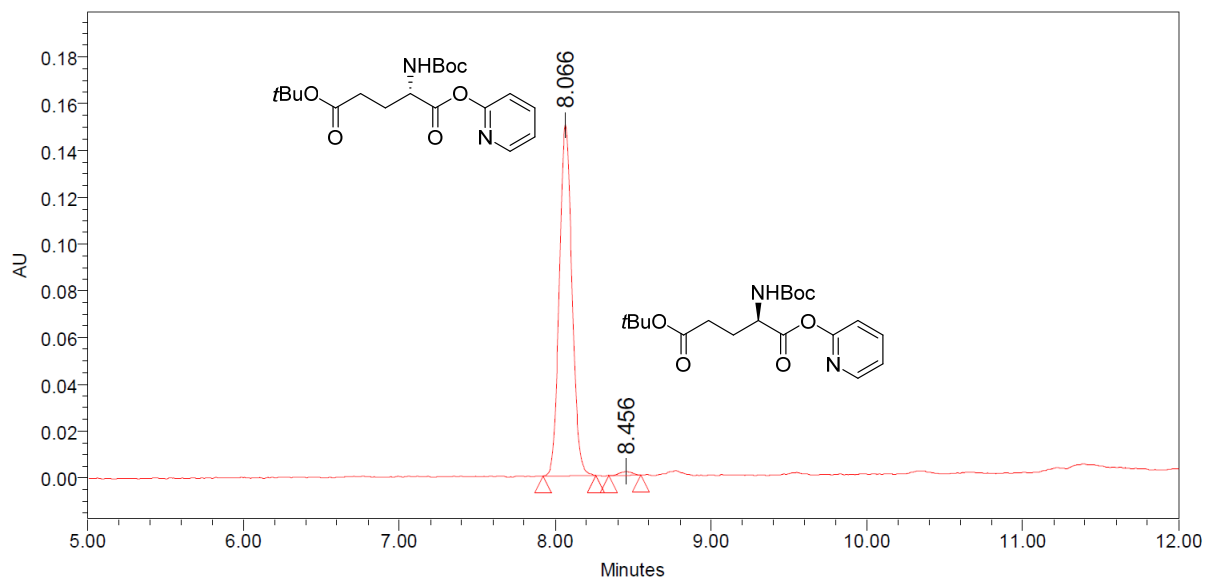
(D)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 258.0 nm (PDA Spectrum (190-410)nm)	8.213	8392	53516	3.01
2	PDA Spectrum PDA 258.0 nm (PDA Spectrum (190-410)nm)	9.526	200054	1721743	96.99

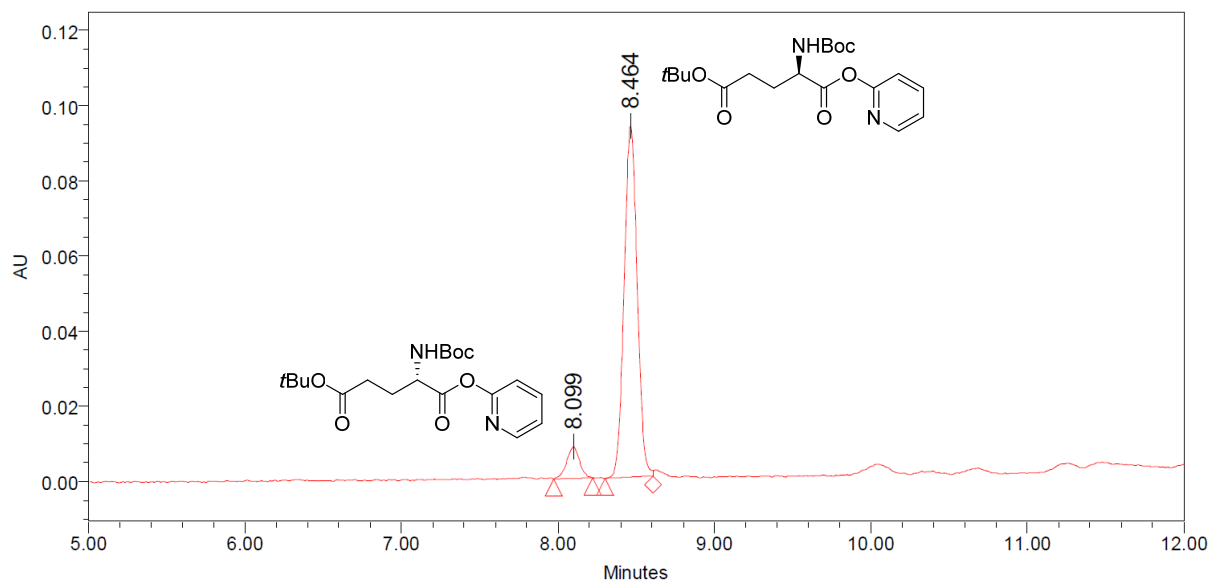


5-(tert-butyl) 1-(pyridin-2-yl) (tert-butoxycarbonyl)-L-glutamate (S25)

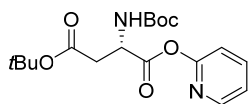


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	8.066	150142	850405	98.97
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	8.456	1689	8820	1.03

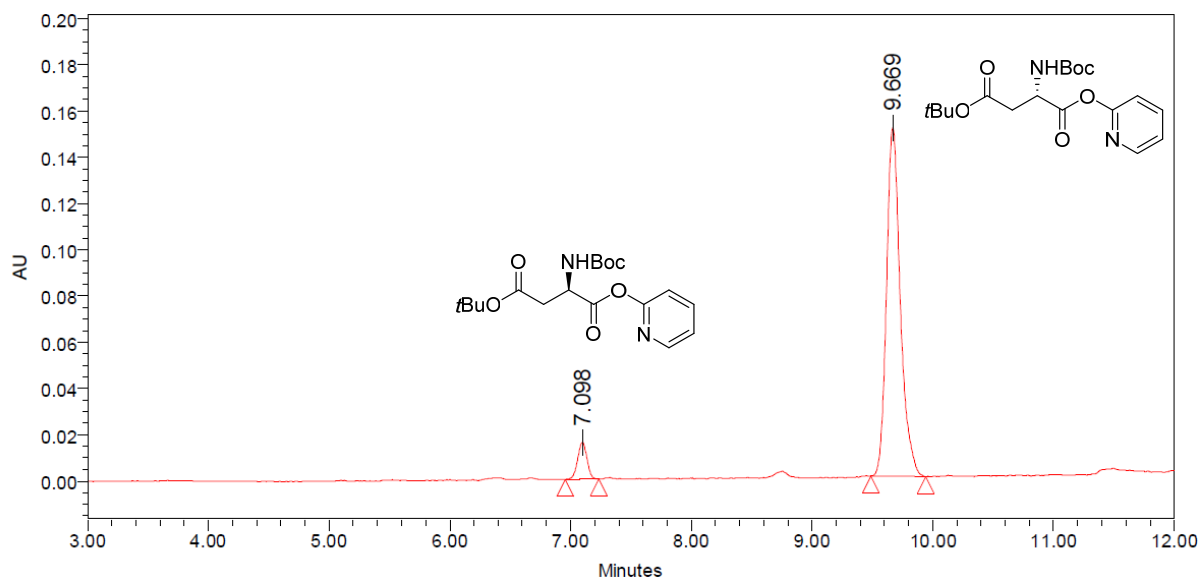
(D)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	8.099	8421	47939	8.14
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	8.464	93384	540987	91.86

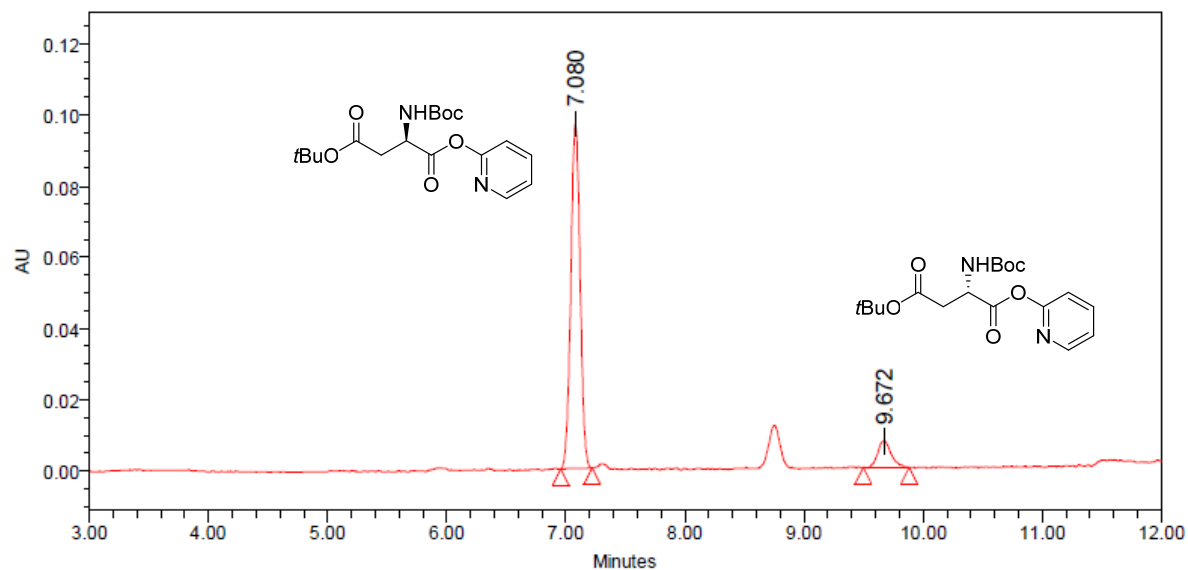


4-(tert-butyl) 1-(pyridin-2-yl) (tert-butoxycarbonyl)-L-aspartate (S26)

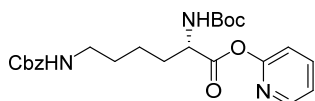


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	7.098	15843	85826	6.68
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	9.669	150899	1198235	93.32

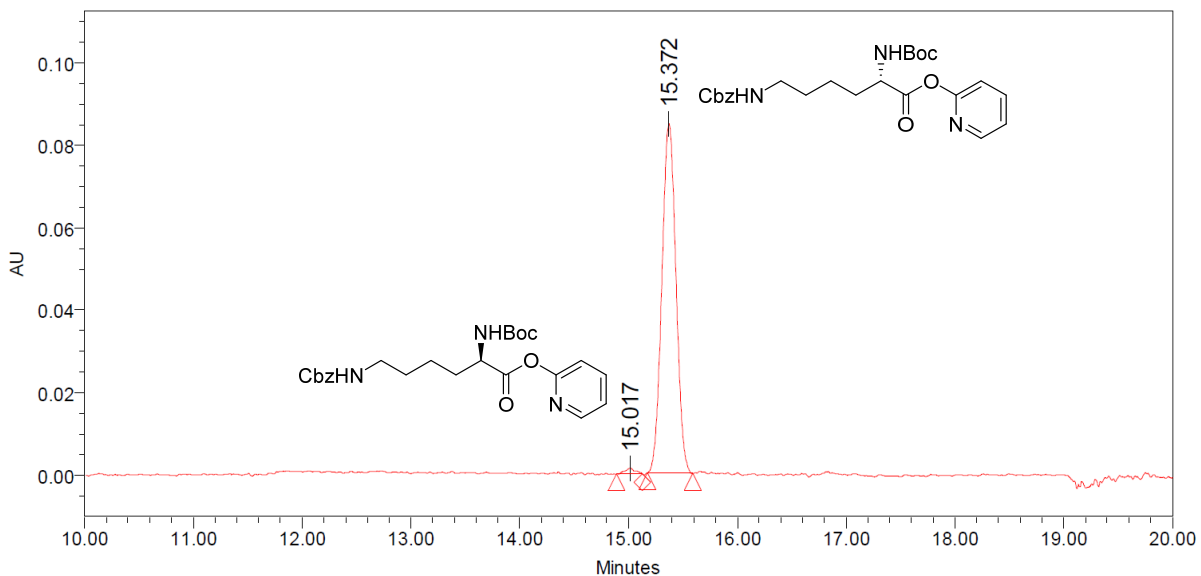
(D)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	7.080	96978	524909	89.81
2	PDA Spectrum PDA 250.0 nm (PDA Spectrum (190-410)nm)	9.672	7504	59535	10.19

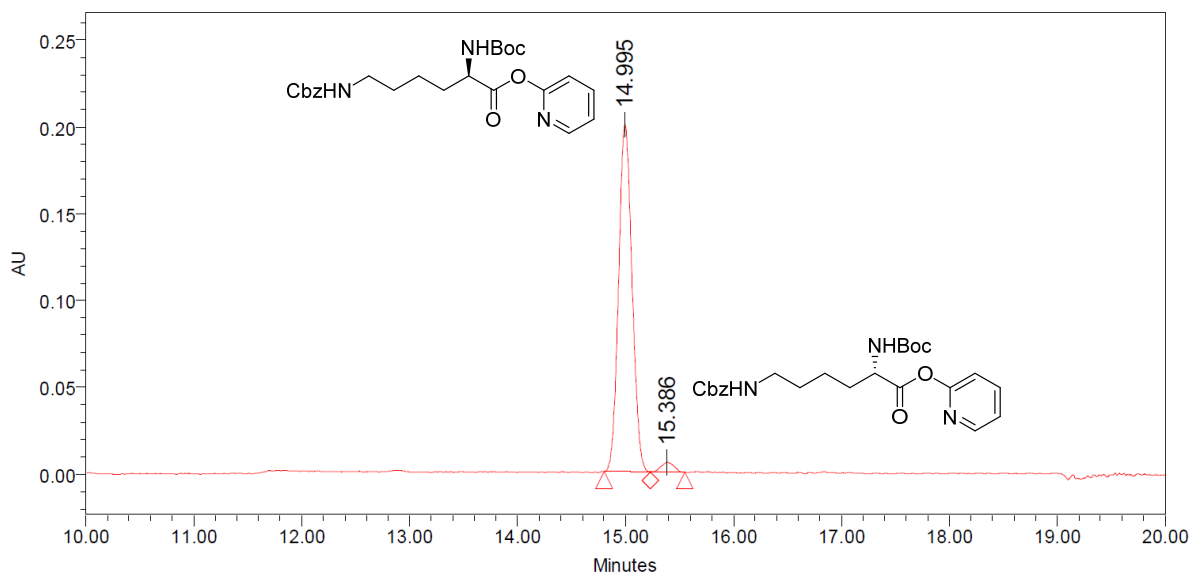


pyridin-2-yl N6-((benzyloxy)carbonyl)-N2-(tert-butoxycarbonyl)-L-lysinate (S27)

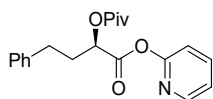


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 260.0 nm (PDA Spectrum (190-410)nm)	15.017	1364	9256	1.20
2	PDA Spectrum PDA 260.0 nm (PDA Spectrum (190-410)nm)	15.372	84600	760954	98.80

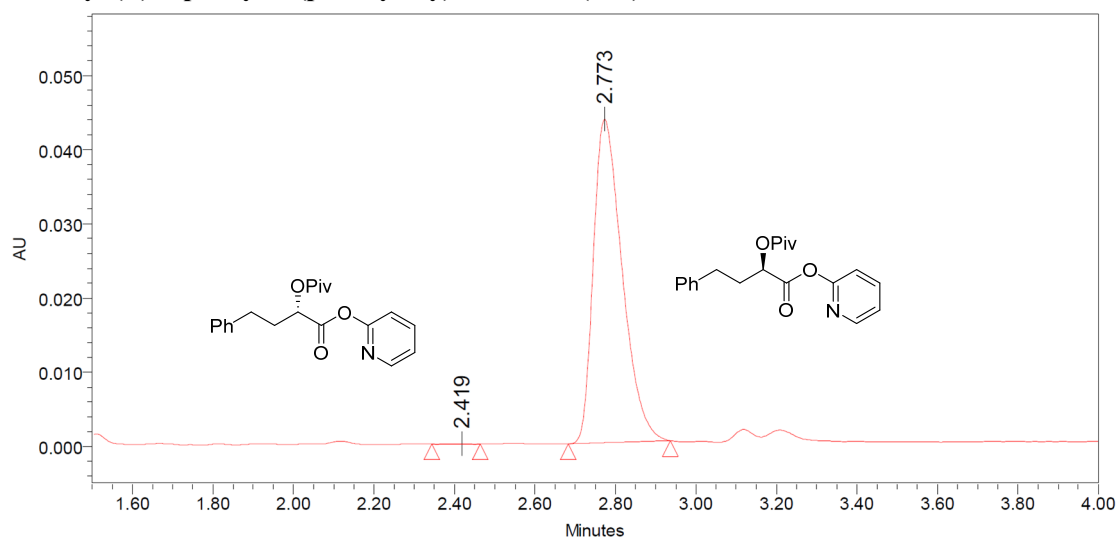
(D)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 260.0 nm (PDA Spectrum (190-410)nm)	14.995	199843	1732263	97.36
2	PDA Spectrum PDA 260.0 nm (PDA Spectrum (190-410)nm)	15.386	5736	47016	2.64

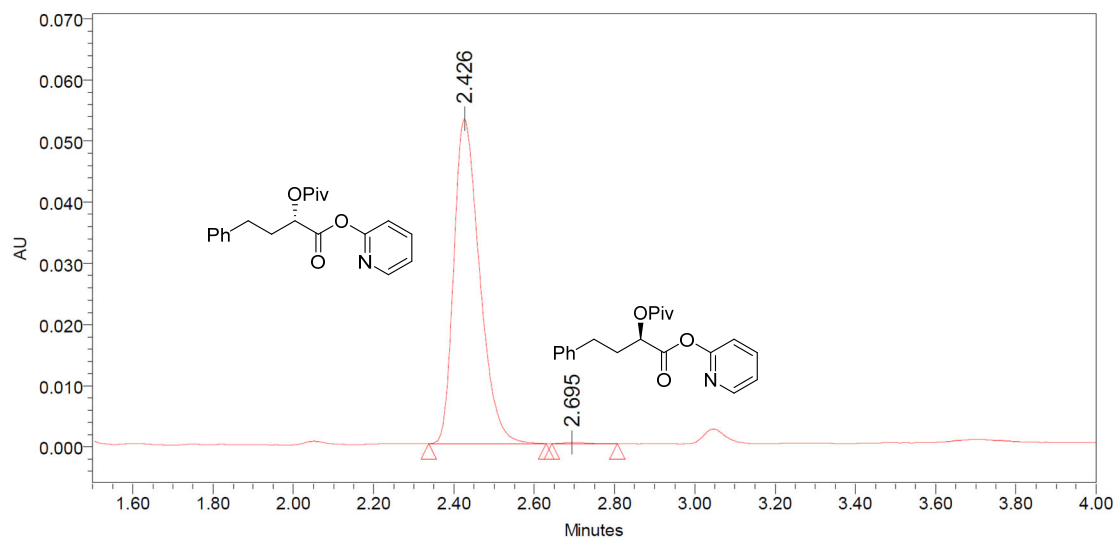


pyridin-2-yl (*R*)-4-phenyl-2-(pivaloyloxy)butanoate (S28)

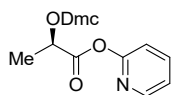


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch2 254nm@4.8nm -Compens.	2.419	38	125	0.06
2	PDA Ch2 254nm@4.8nm -Compens.	2.773	43622	215870	99.94

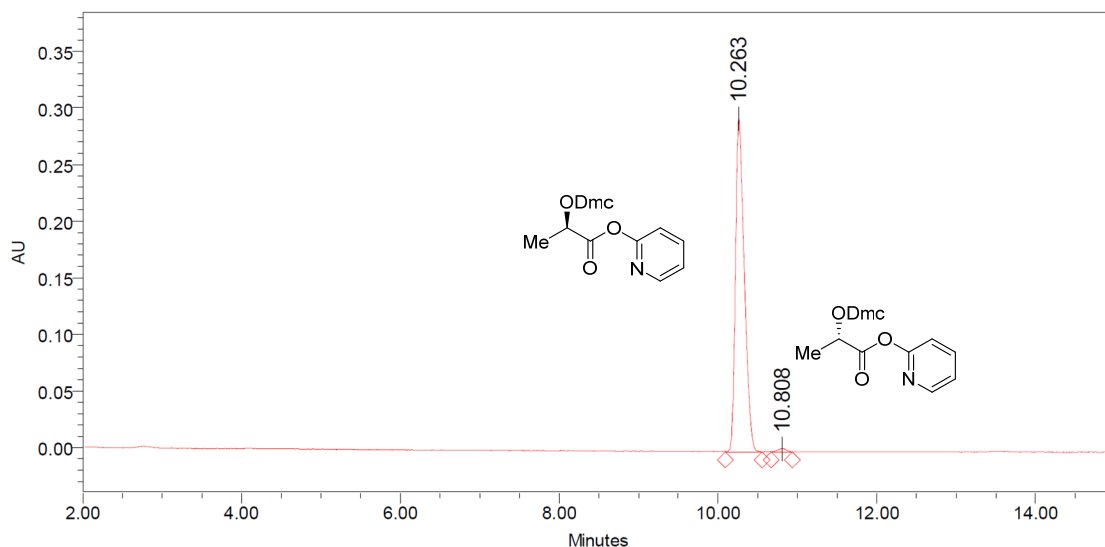
(*S*)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch2 254nm@4.8nm -Compens.	2.426	53094	235802	99.66
2	PDA Ch2 254nm@4.8nm -Compens.	2.695	186	806	0.34

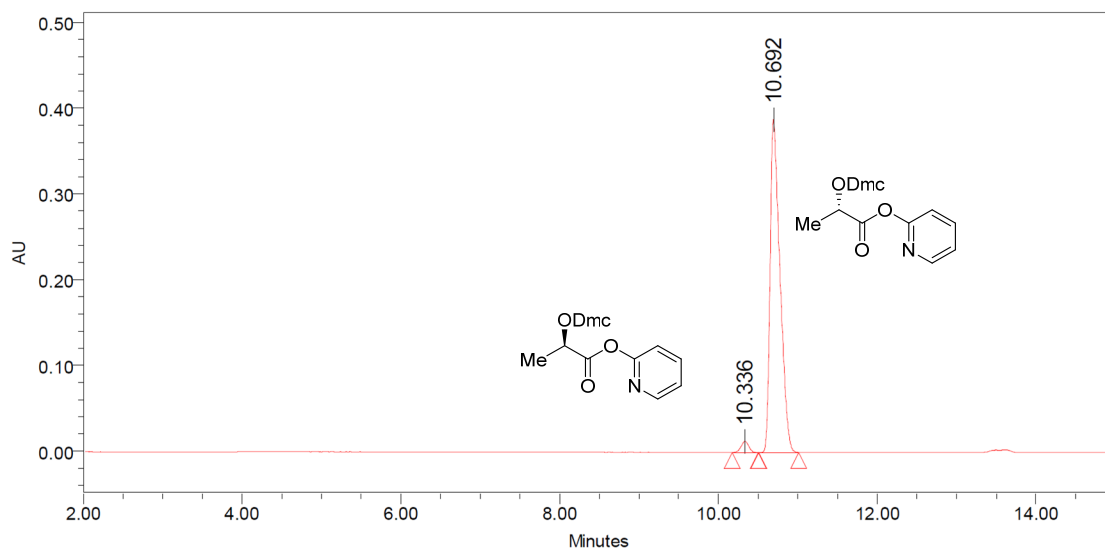


pyridin-2-yl (*R*)-2-((dimethylcarbamoyl)oxy)propanoate (S29)

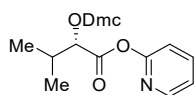


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 291.0 nm (PDA Spectrum (190-410)nm)	10.263	294302	2281083	99.10
2	PDA Spectrum PDA 291.0 nm (PDA Spectrum (190-410)nm)	10.808	2683	20695	0.90

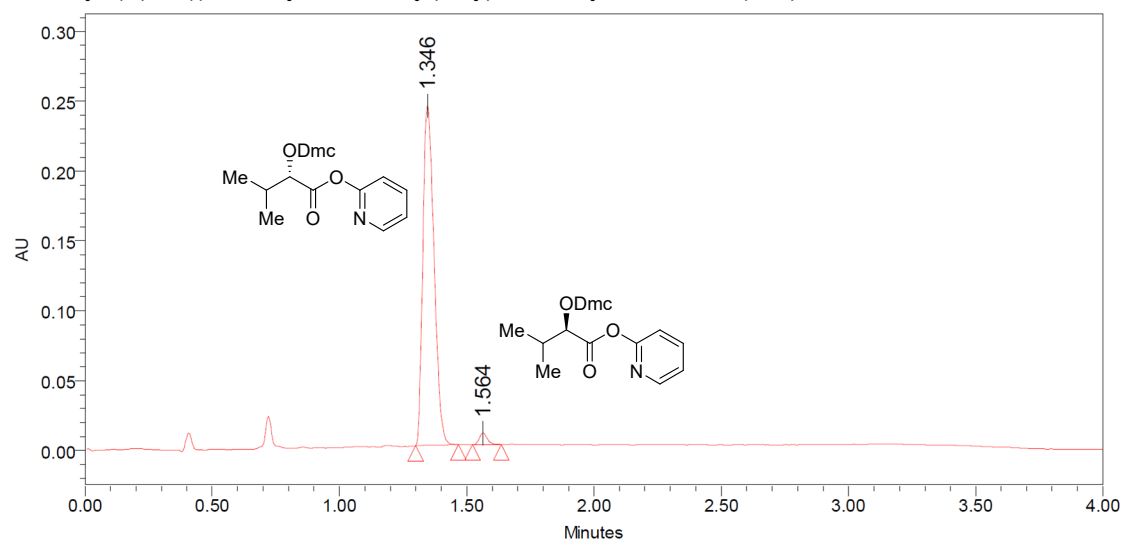
(*S*)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 291.0 nm (PDA Spectrum (190-410)nm)	10.336	12739	84734	2.46
2	PDA Spectrum PDA 291.0 nm (PDA Spectrum (190-410)nm)	10.692	388441	3366157	97.54

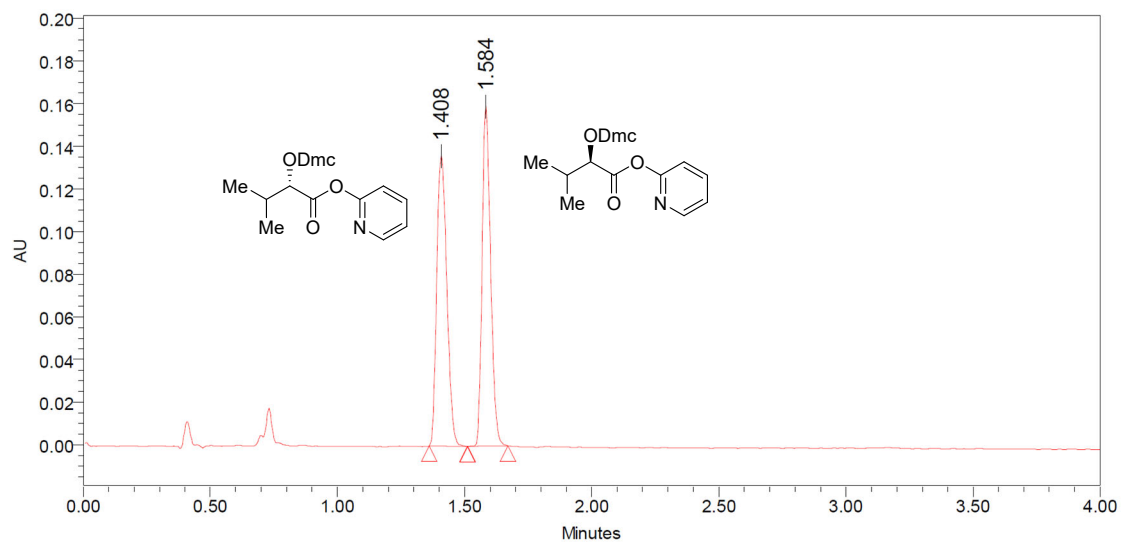


pyridin-2-yl (*R*)-2-((dimethylcarbamoyl)oxy)-3-methylbutanoate (S30)

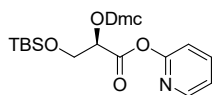


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 254.0 nm (PDA Spectrum (190-410)nm)	1.346	243559	743824	97.66
2	PDA Spectrum PDA 254.0 nm (PDA Spectrum (190-410)nm)	1.564	8250	17804	2.34

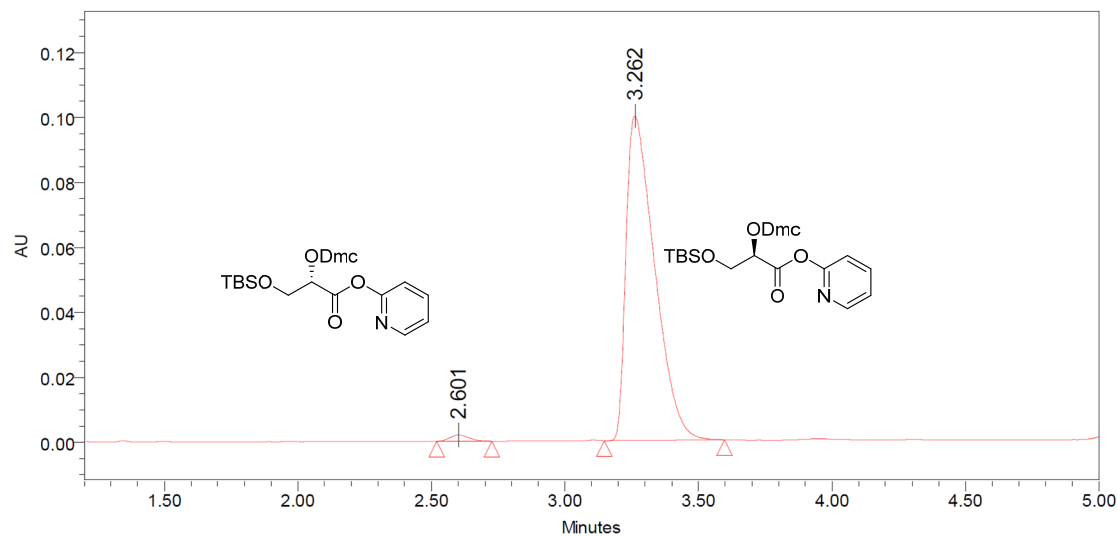
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 254.0 nm (PDA Spectrum (190-410)nm)	1.408	136413	374265	50.27
2	PDA Spectrum PDA 254.0 nm (PDA Spectrum (190-410)nm)	1.584	159403	370297	49.73

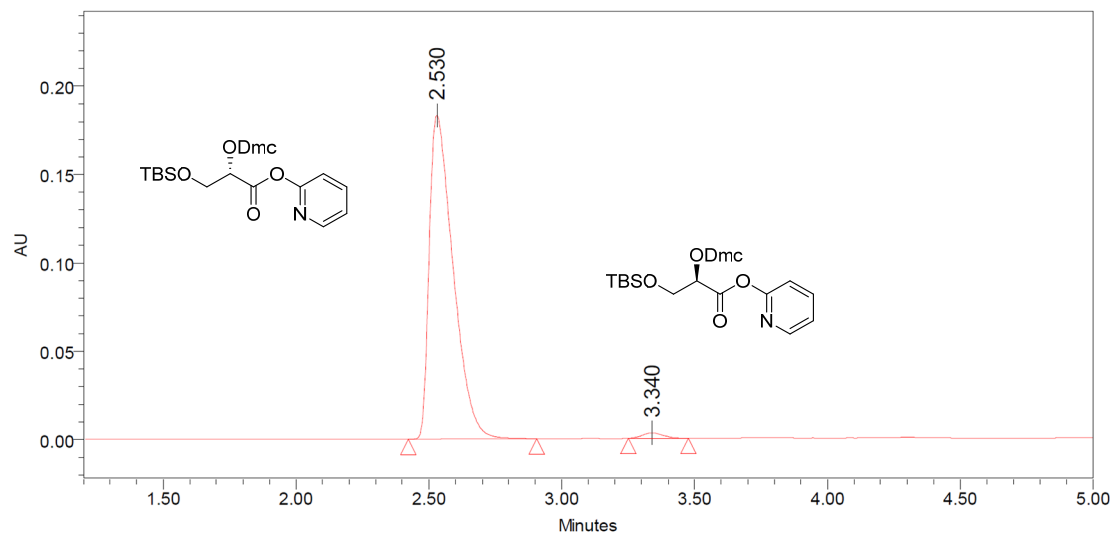


pyridin-2-yl (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-((dimethylcarbamoyl)oxy)propanoate (S31)



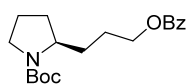
	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch2 254nm@4.8nm -Compens.	2.601	1964	9832	1.30
2	PDA Ch2 254nm@4.8nm -Compens.	3.262	99924	744076	98.70

(*S*)-enantiomer

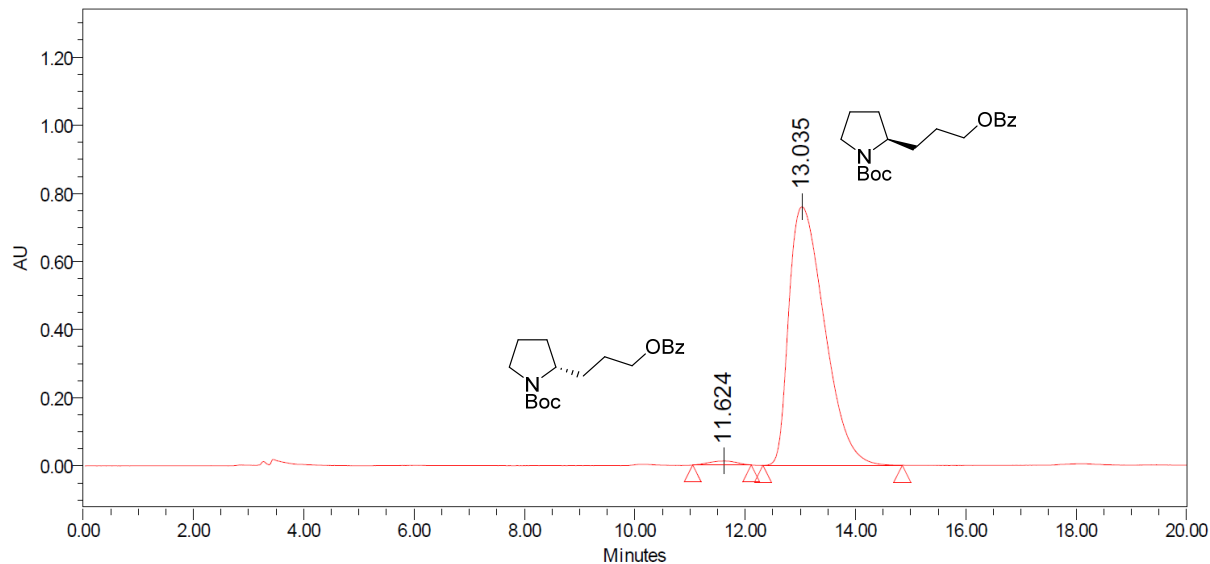


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch2 254nm@4.8nm -Compens.	2.530	183088	1139530	98.56
2	PDA Ch2 254nm@4.8nm -Compens.	3.340	2998	16683	1.44

11.2 SFC analysis of cross-coupling products

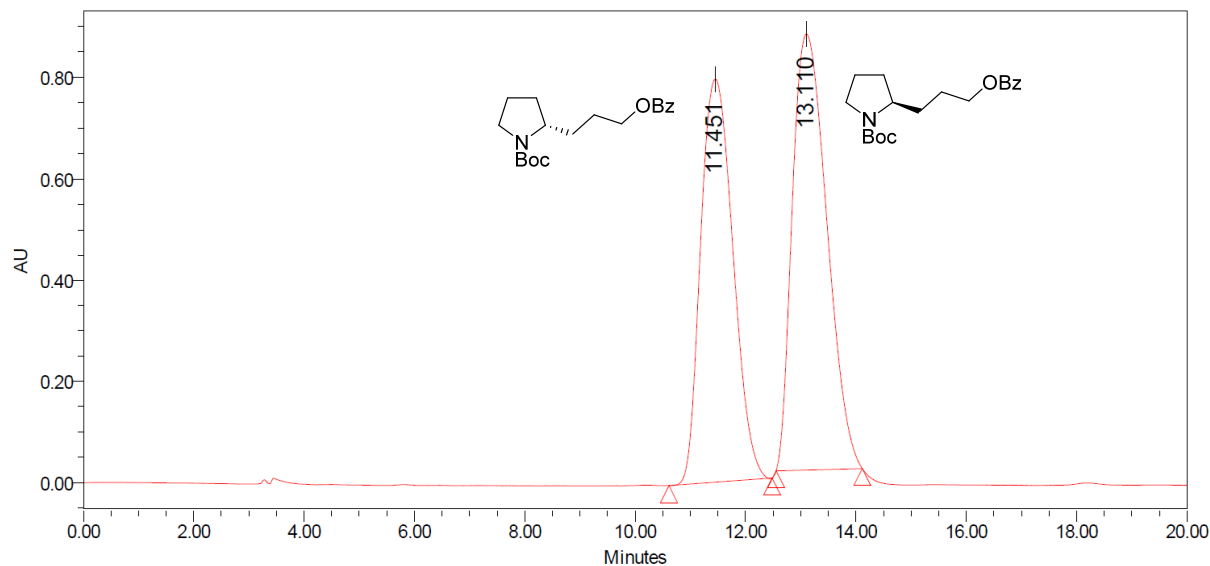


tert-butyl (S)-2-(3-(benzyloxy)propyl)pyrrolidine-1-carboxylate (3)

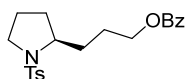


	RT	Area	Height	% Area
1	11.624	406914	11939	1.18
2	13.035	34092835	759645	98.82

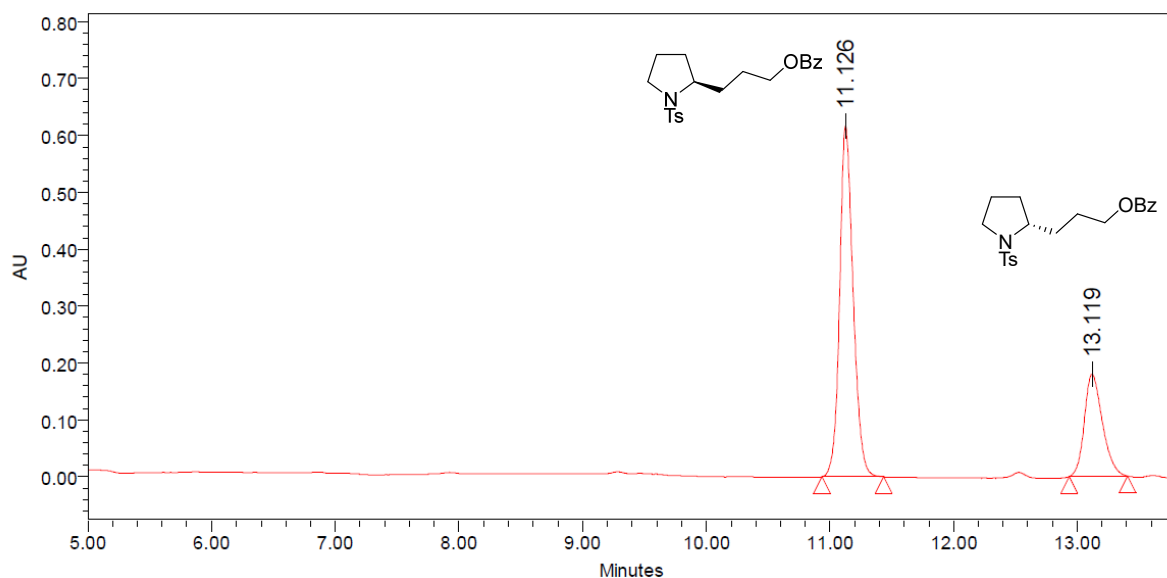
Racemic mixture



	RT	Area	Height	% Area
1	11.451	32432082	795409	46.43
2	13.110	37418480	860720	53.57

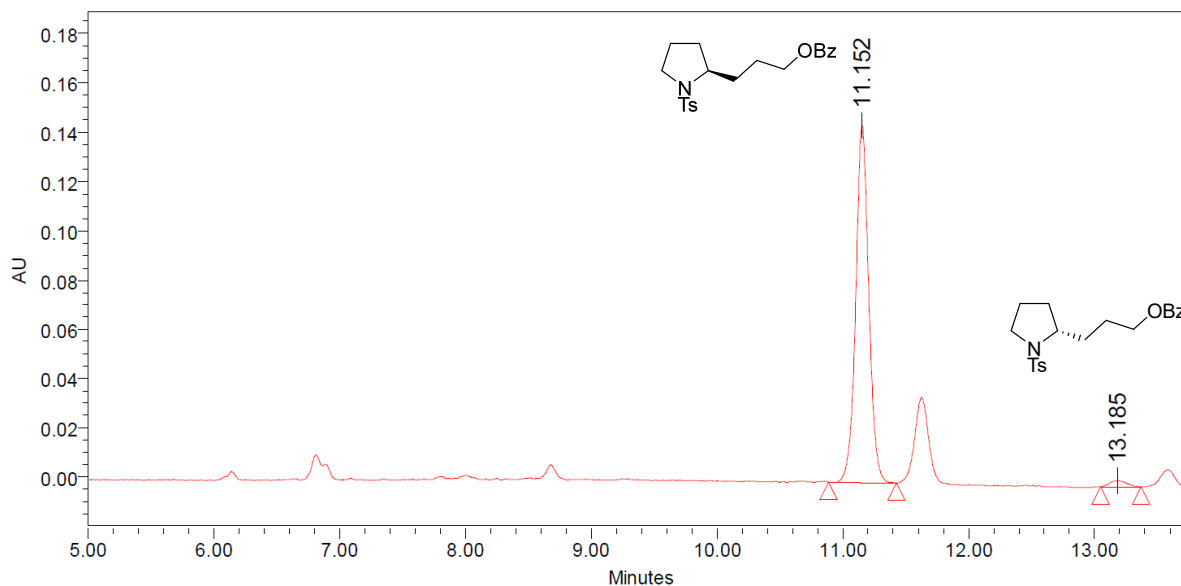


(S)-3-(1-tosylpyrrolidin-2-yl)propyl benzoate (9) from stoichiometric reaction



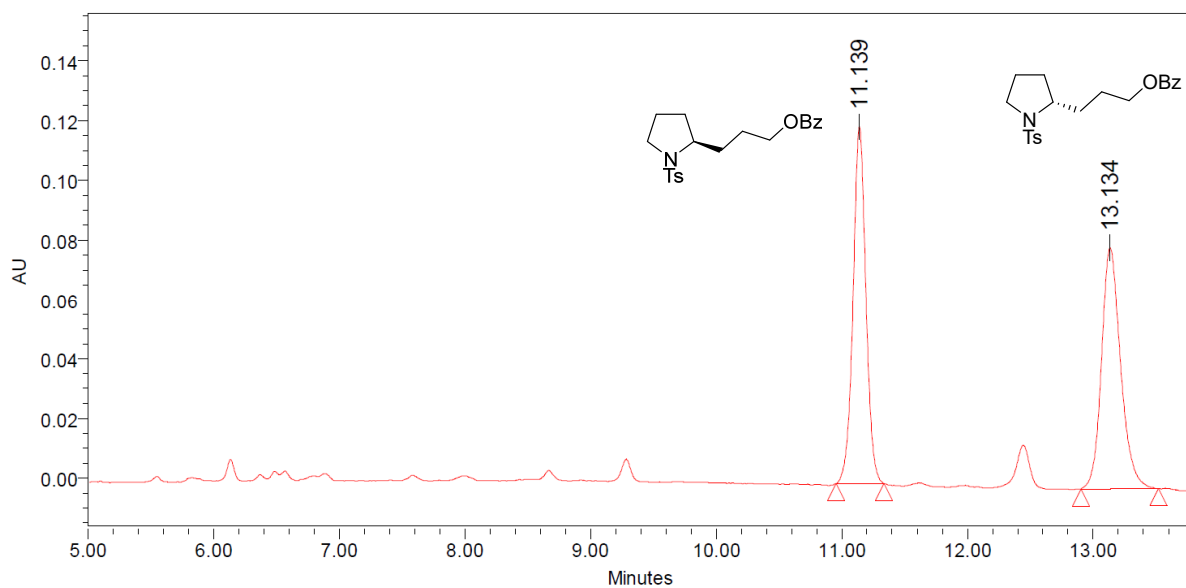
	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 228.9 nm (PDA Spectrum (190-410)nm)	11.126	617306	4686259	72.05
2	PDA Spectrum PDA 228.9 nm (PDA Spectrum (190-410)nm)	13.119	179130	1817701	27.95

(S)-3-(1-tosylpyrrolidin-2-yl)propyl benzoate (9) from catalytic reaction

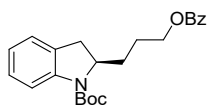


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 228.9 nm (PDA Spectrum (190-410)nm)	11.152	145139	1050493	97.83
2	PDA Spectrum PDA 228.9 nm (PDA Spectrum (190-410)nm)	13.185	2518	23308	2.17

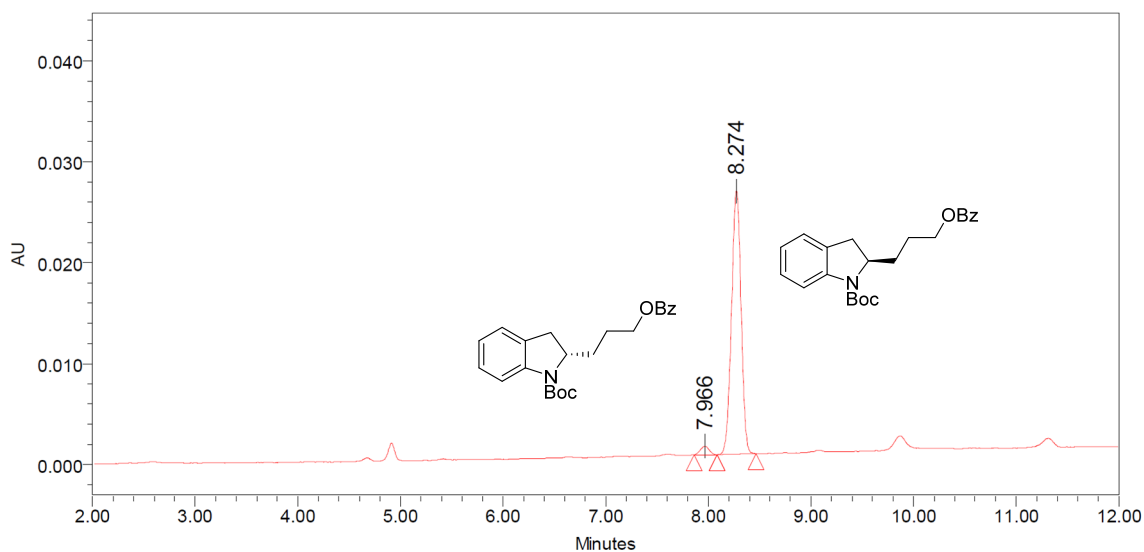
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 228.9 nm (PDA Spectrum (190-410)nm)	11.139	119788	854578	50.00
2	PDA Spectrum PDA 228.9 nm (PDA Spectrum (190-410)nm)	13.134	81119	854648	50.00

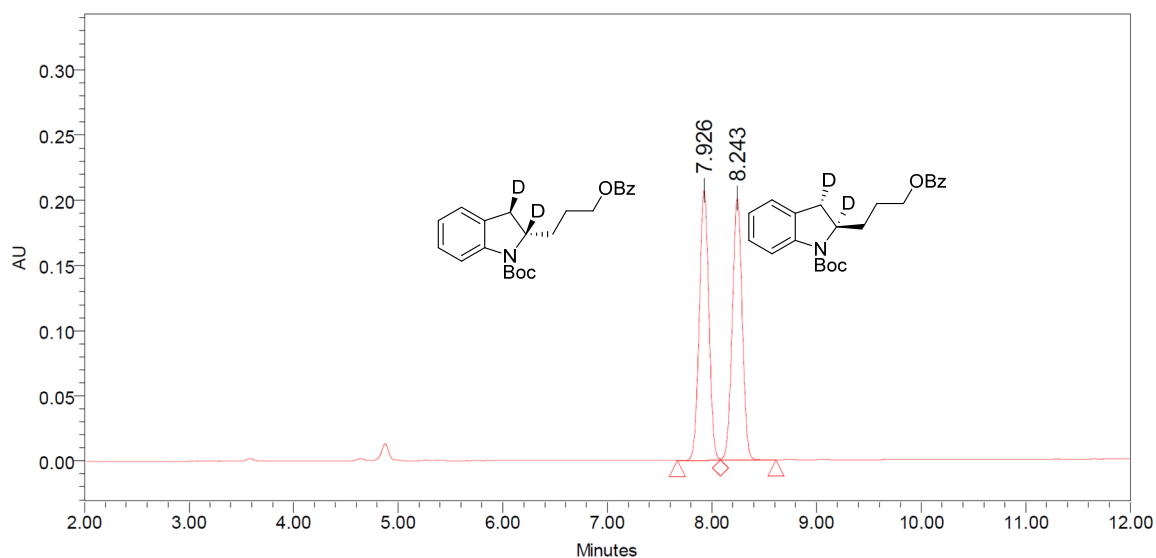


***tert*-butyl (*R*)-2-(3-(benzyloxy)propyl)indoline-1-carboxylate (12-H)**

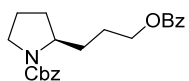


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	7.966	845	4956	2.85
2	PDA Ch1 254nm@4.8nm -Compens.	8.274	26098	168853	97.15

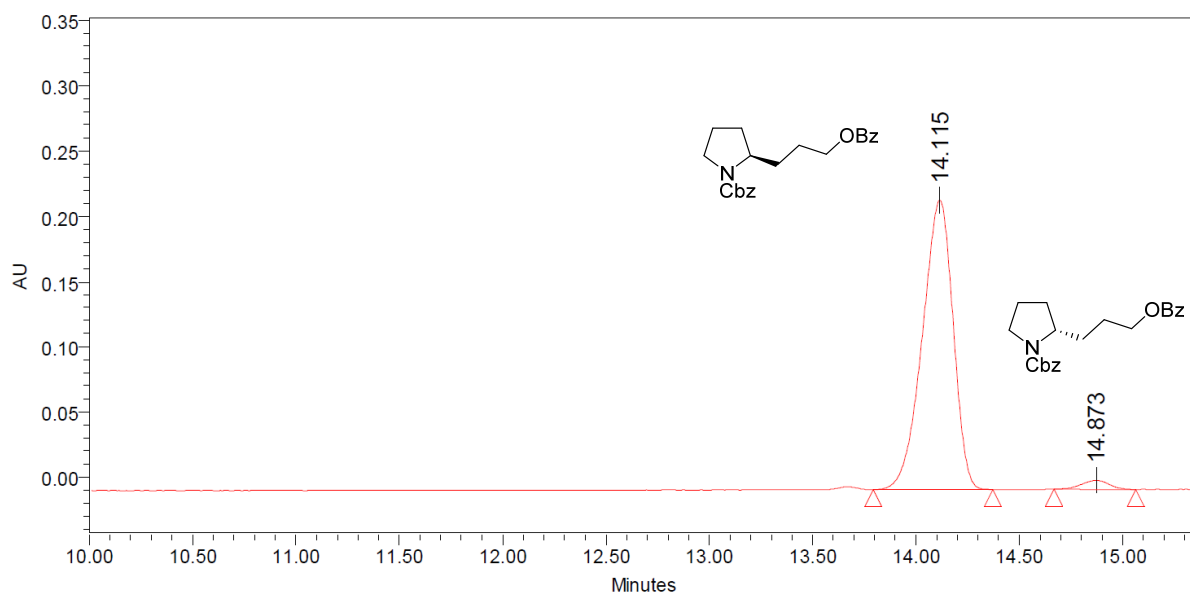
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Ch1 254nm@4.8nm -Compens.	7.926	206895	1312095	49.88
2	PDA Ch1 254nm@4.8nm -Compens.	8.243	200798	1318192	50.12

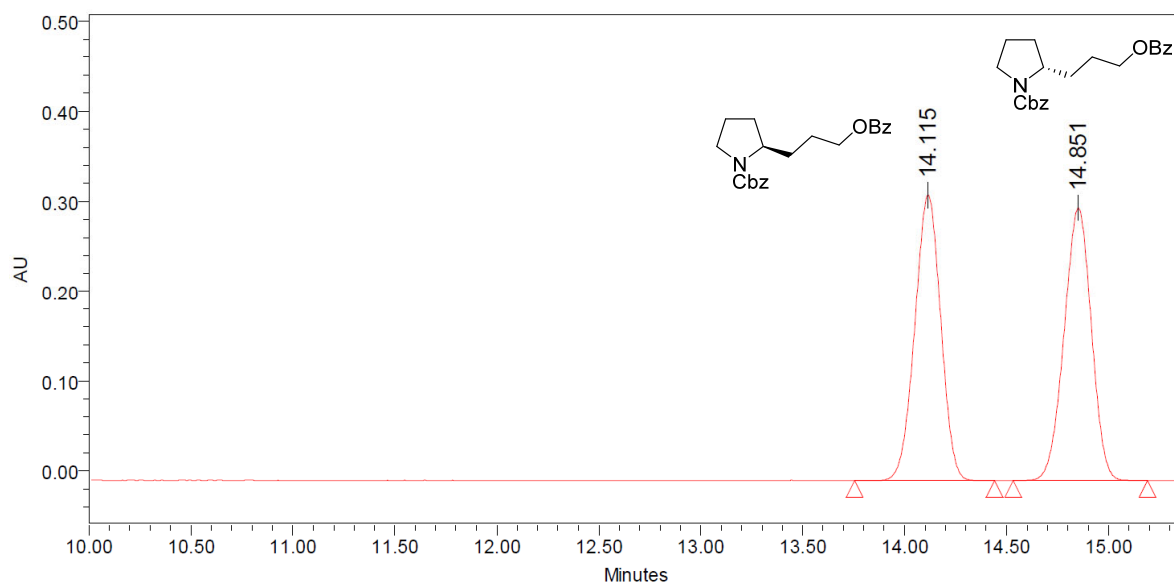


benzyl (S)-2-(3-(benzyloxy)propyl)pyrrolidine-1-carboxylate (22)

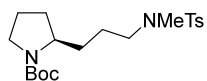


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 226.0 nm (PDA Spectrum (190-410)nm)	14.115	222127	2298686	97.33
2	PDA Spectrum PDA 226.0 nm (PDA Spectrum (190-410)nm)	14.873	6817	63038	2.67

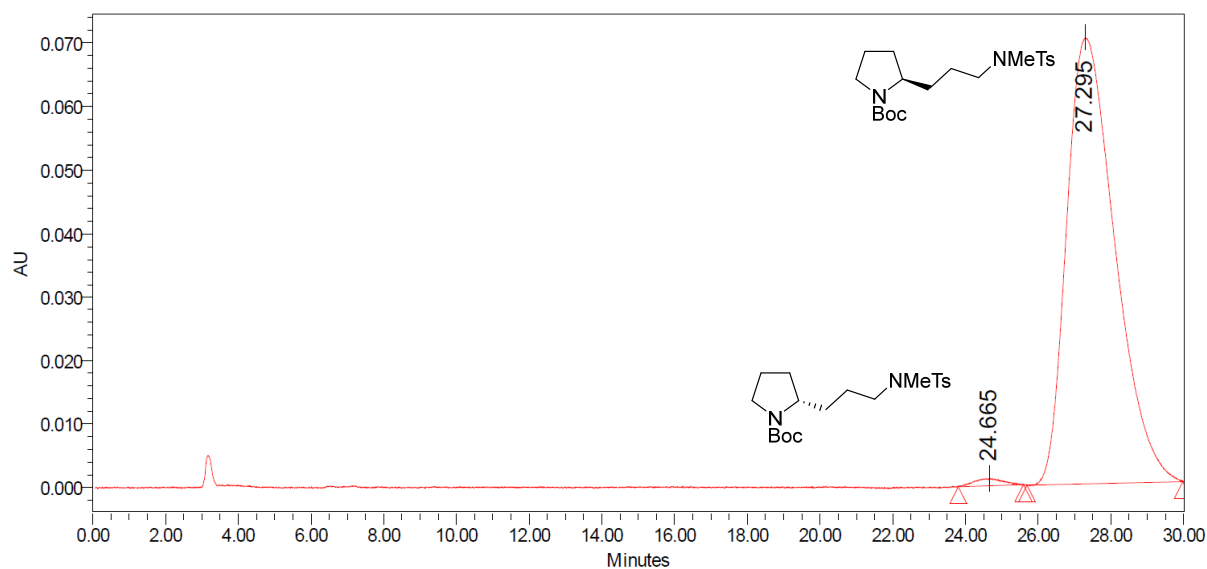
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 226.0 nm (PDA Spectrum (190-410)nm)	14.115	317660	2811471	49.99
2	PDA Spectrum PDA 226.0 nm (PDA Spectrum (190-410)nm)	14.851	303362	2812841	50.01

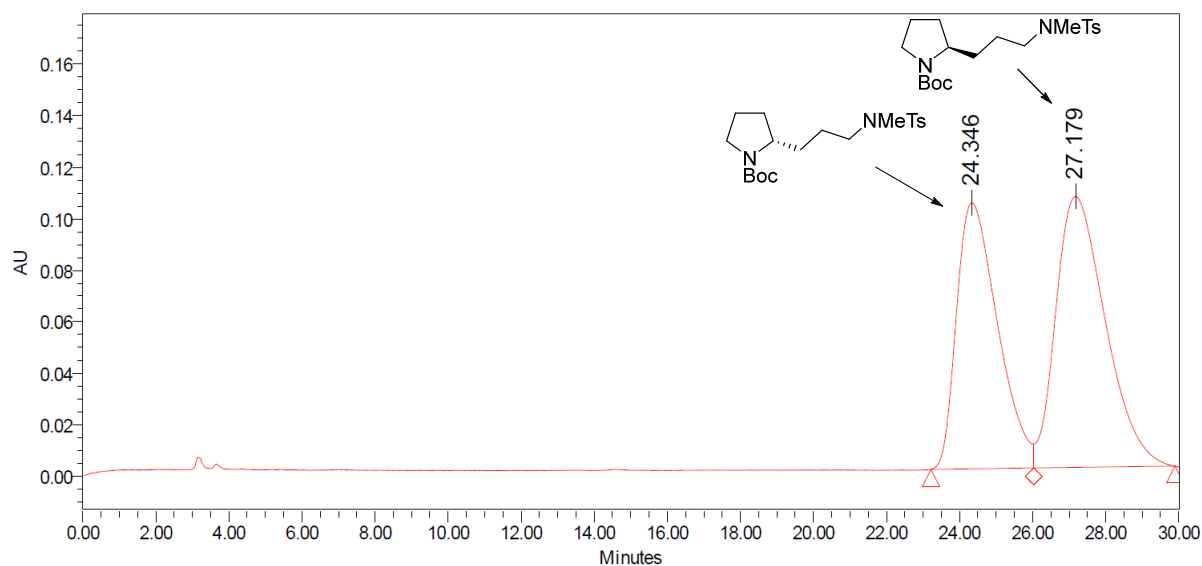


tert-butyl (S)-2-(3-((N,4-dimethylphenyl)sulfonamido)propyl)pyrrolidine-1-carboxylate (23).

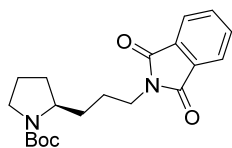


	RT	Area	Height	% Area
1	24.665	62501	1176	0.96
2	27.295	6476476	70284	99.04

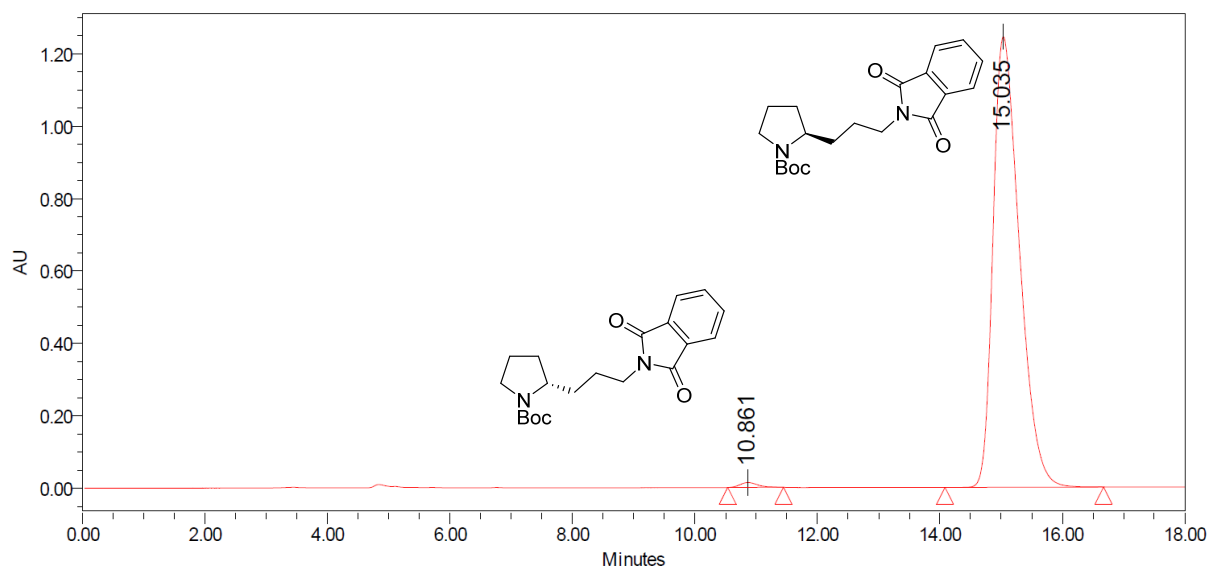
Racemic mixture



	RT	Area	Height	% Area
1	24.346	8063285	103510	44.83
2	27.179	9922987	105384	55.17

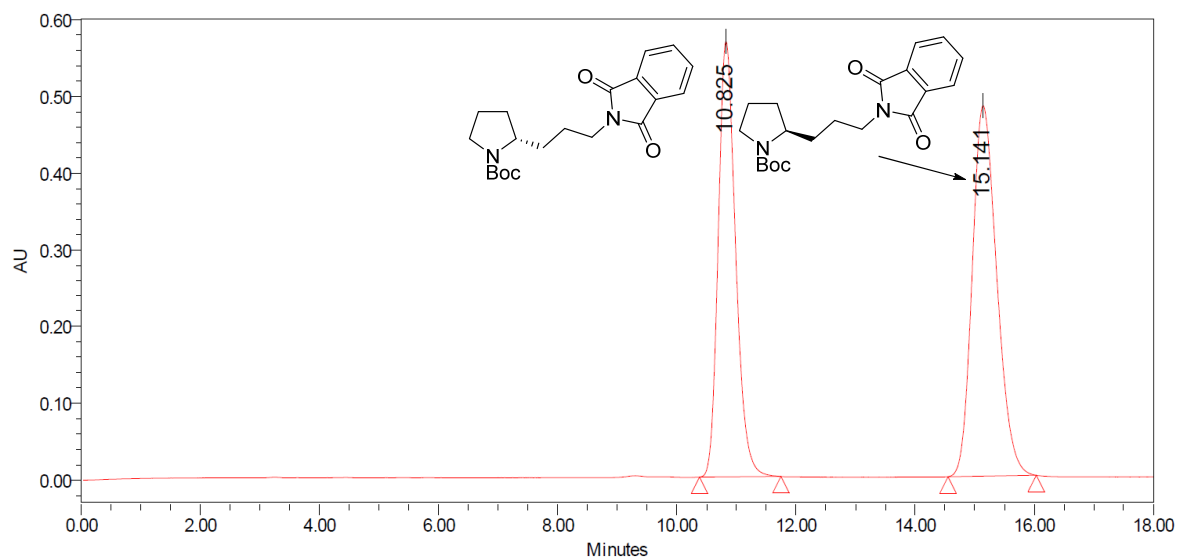


tert-butyl (R)-2-(3-(1,3-dioxisoindolin-2-yl)propyl)pyrrolidine-1-carboxylate (24)

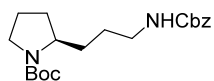


	RT	Area	Height	% Area
1	10.861	269309	13303	0.72
2	15.035	37132442	1243953	99.28

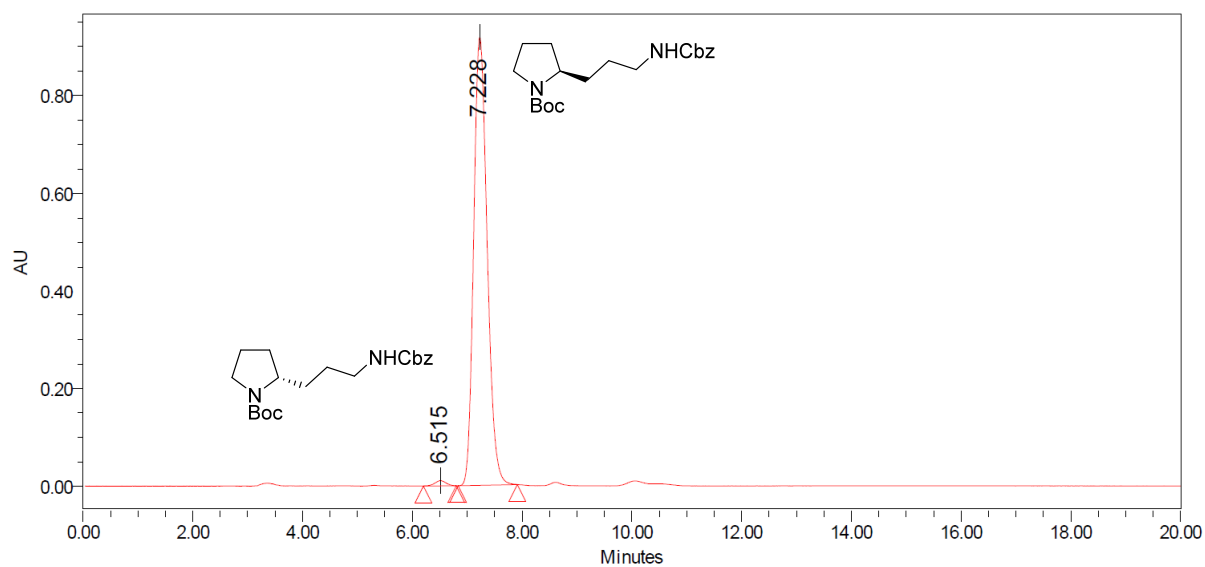
Racemic mixture



	RT	Area	Height	% Area
1	10.825	11491928	567539	45.43
2	15.141	13806154	482931	54.57

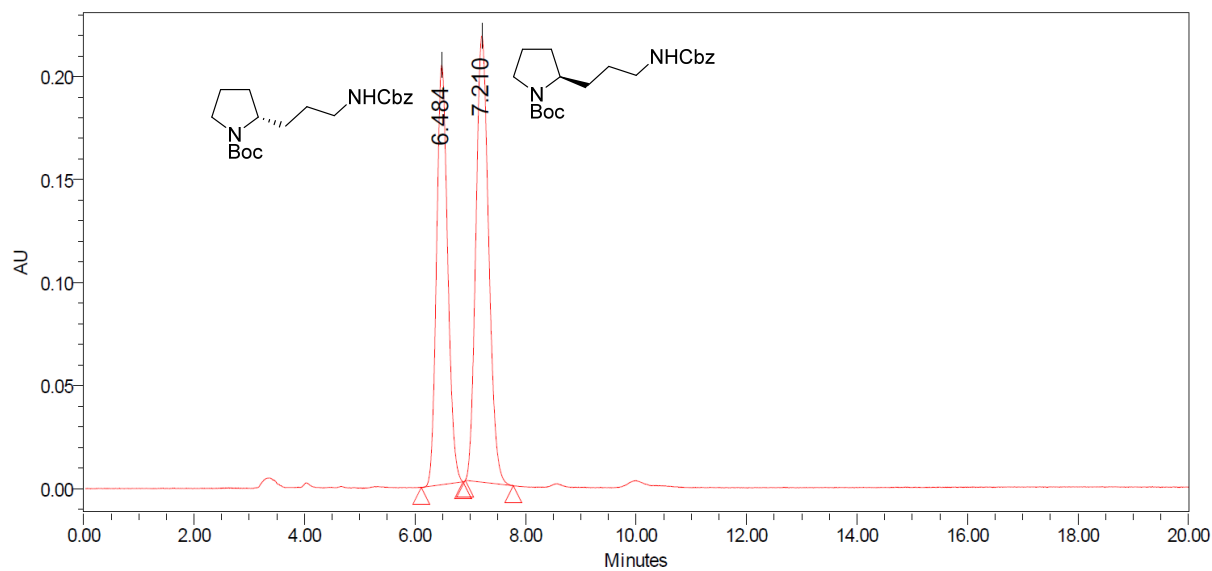


tert-butyl (R)-2-(3-(((benzyloxy)carbonyl)amino)propyl)pyrrolidine-1-carboxylate (25)

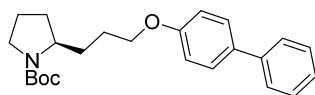


	RT	Area	Height	% Area
1	6.515	150404	10641	0.95
2	7.228	15654166	917295	99.05

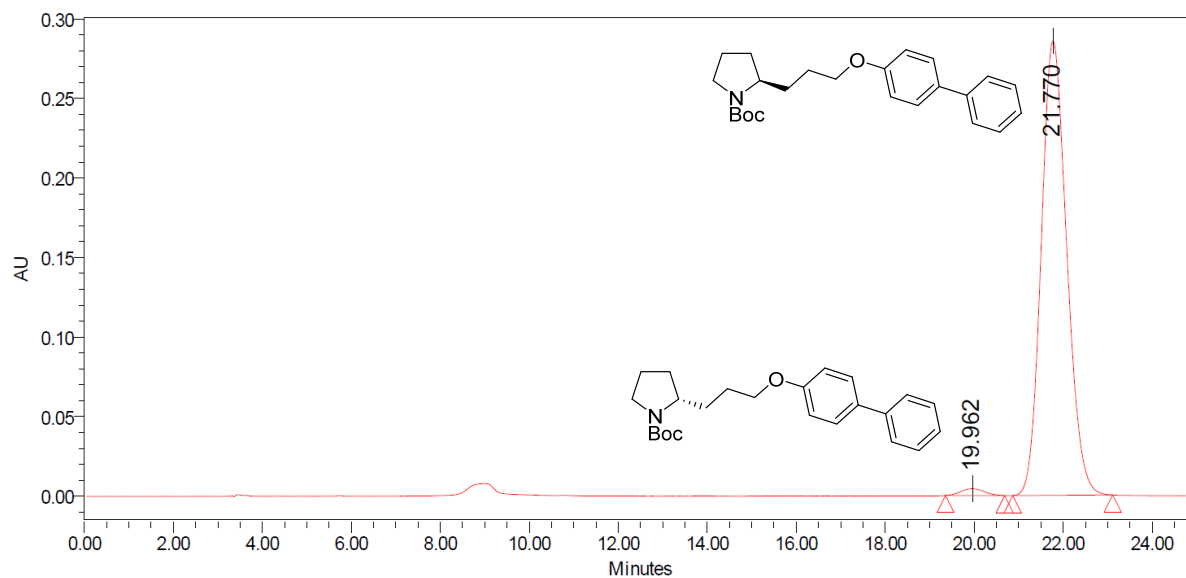
Racemic mixture



	RT	Area	Height	% Area
1	6.484	2854813	203848	45.00
2	7.210	3488676	216601	55.00

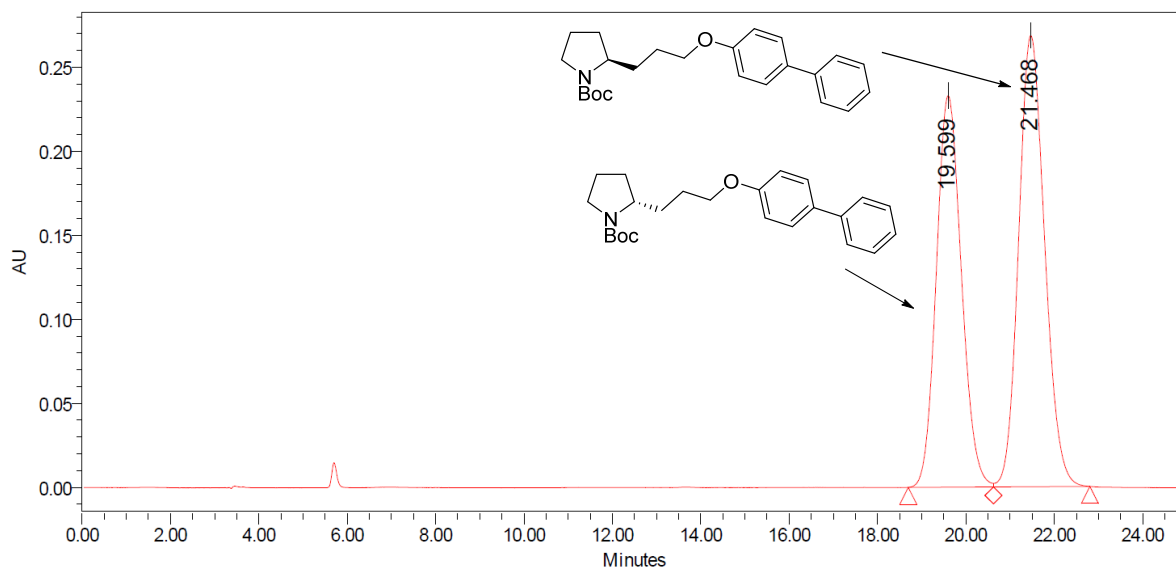


tert-butyl (S)-2-(3-([1,1'-biphenyl]-4-yloxy)propyl)pyrrolidine-1-carboxylate (26)

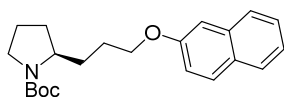


	RT	Area	Height	% Area
1	19.962	158470	4331	1.38
2	21.770	11345336	285566	98.62

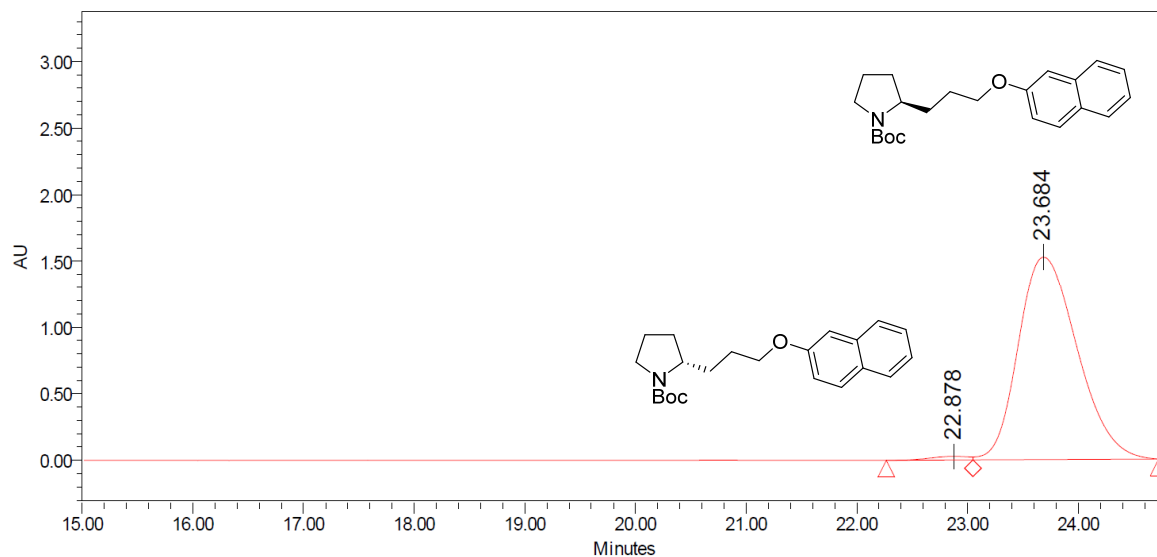
Racemic mixture



	RT	Area	Height	% Area
1	19.599	9183608	232975	45.56
2	21.468	10971486	268514	54.44

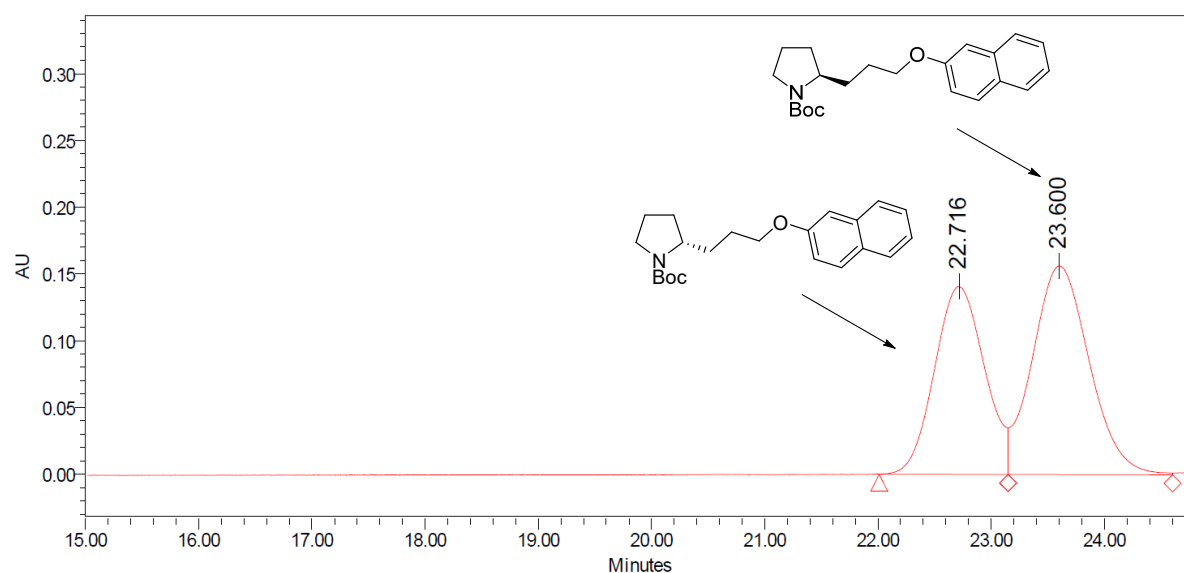


tert-butyl (S)-2-(3-(naphthalen-2-yloxy)propyl)pyrrolidine-1-carboxylate (27)

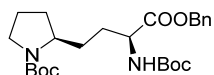


	RT	Area	Height	% Area
1	22.878	678120	28147	1.19
2	23.684	56297848	1526631	98.81

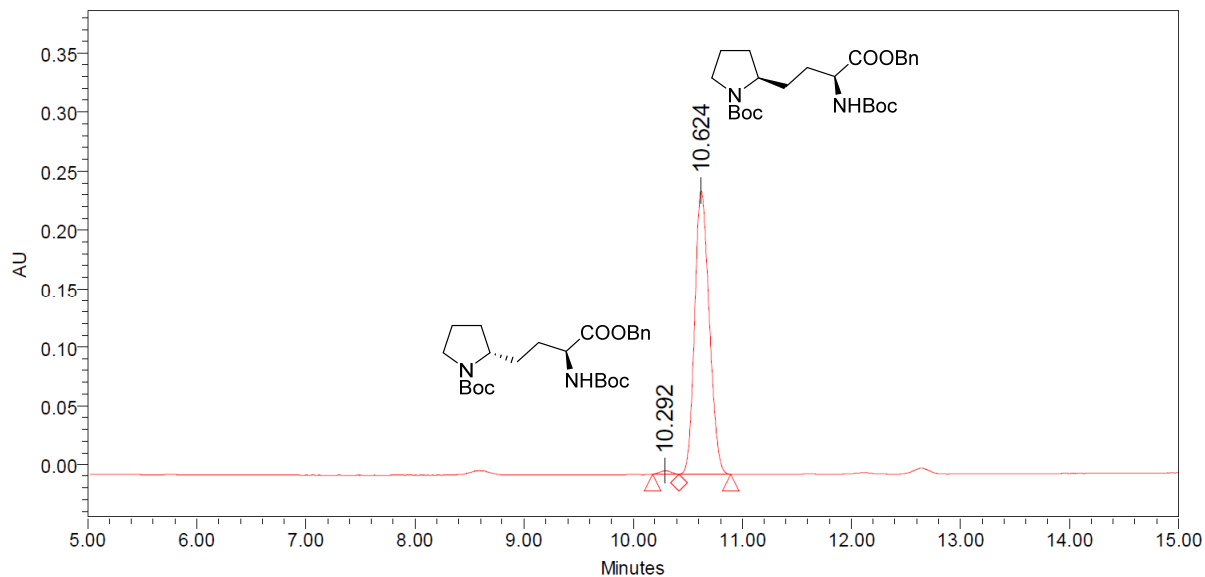
Racemic mixture



	RT	Area	Height	% Area
1	22.716	4322143	140789	44.19
2	23.600	5459510	156148	55.81

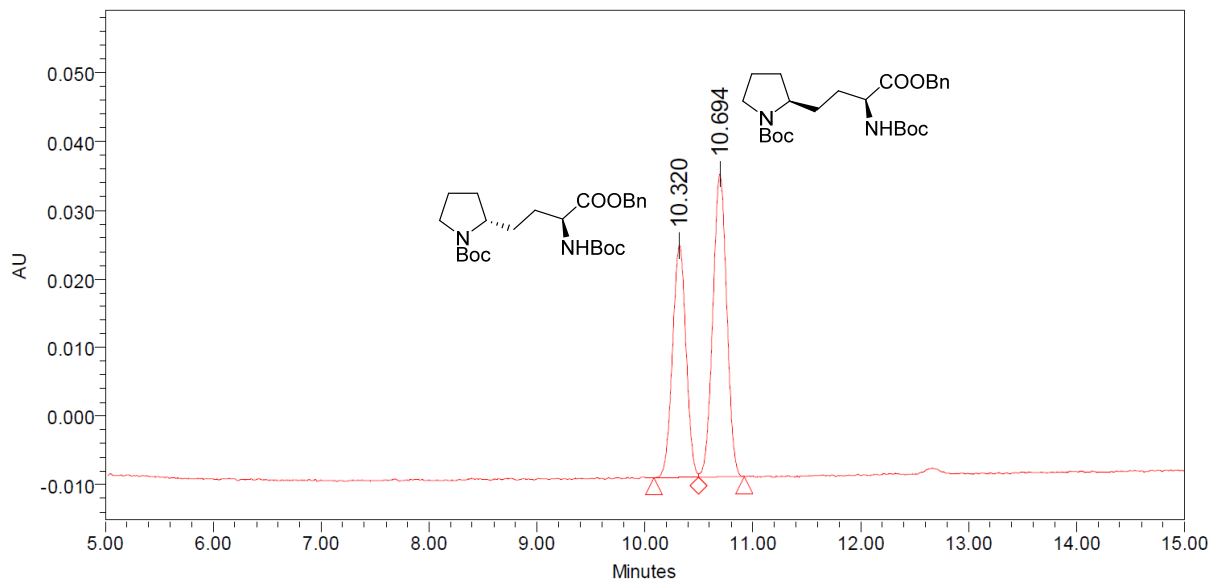


tert-butyl (S)-2-((S)-4-(benzyloxy)-3-((tert-butoxycarbonyl)amino)-4-oxobutyl)pyrrolidine-1-carboxylate (28)

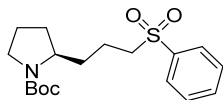


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 216.0 nm (PDA Spectrum (190-410)nm)	10.292	2886	21181	0.93
2	PDA Spectrum PDA 216.0 nm (PDA Spectrum (190-410)nm)	10.624	241942	2247534	99.07

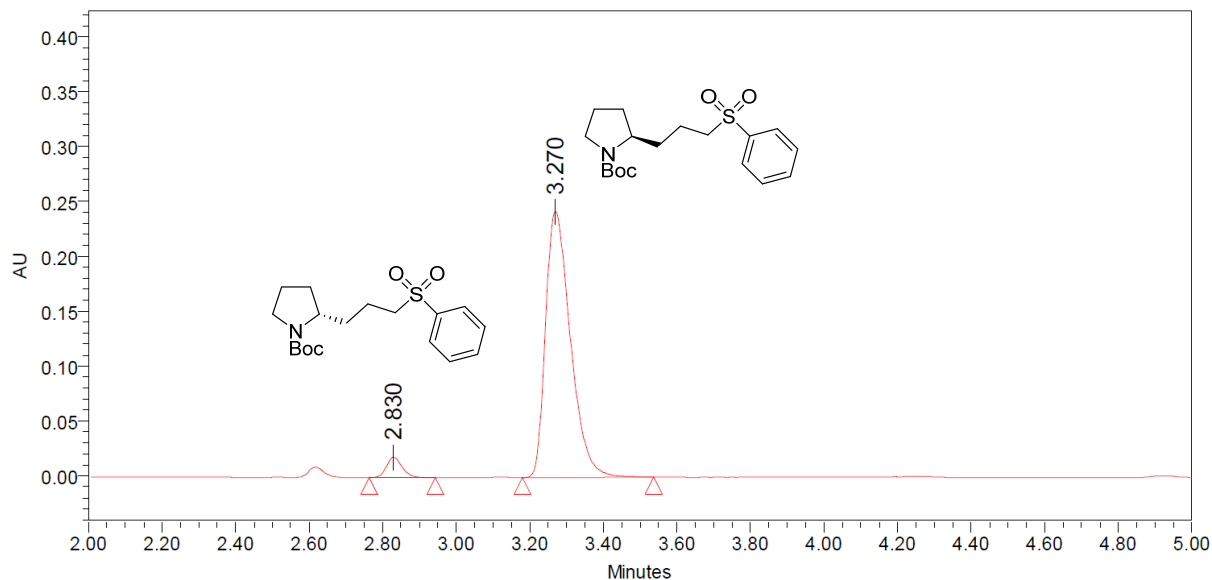
Mixture of diastereomers



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 216.0 nm (PDA Spectrum (190-410)nm)	10.320	33908	296060	42.82
2	PDA Spectrum PDA 216.0 nm (PDA Spectrum (190-410)nm)	10.694	44132	395370	57.18

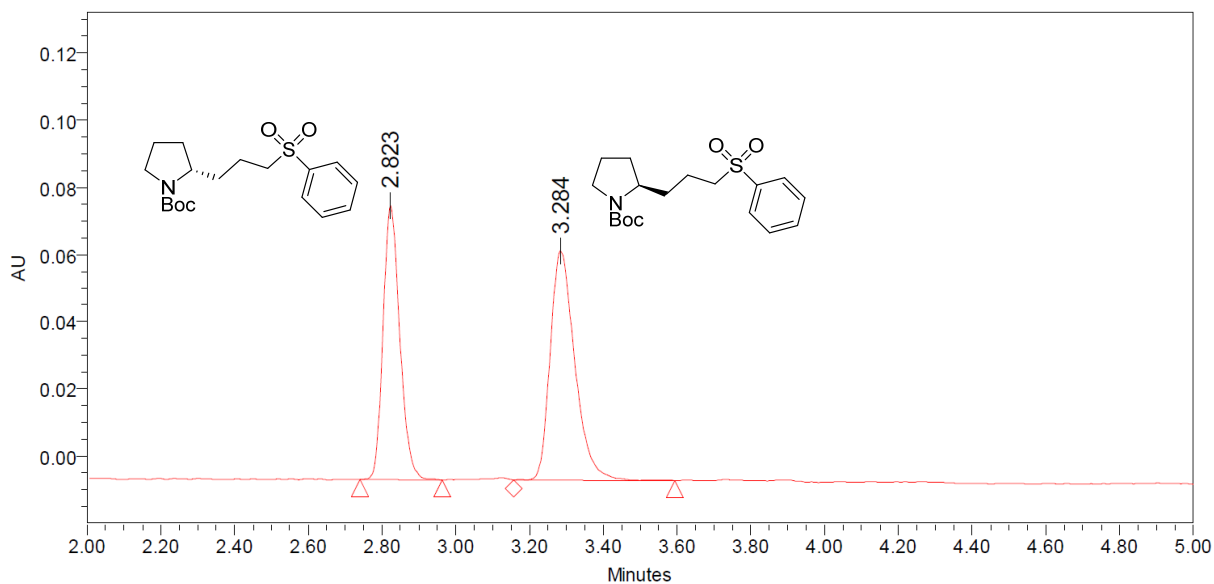


tert-butyl (S)-2-(3-(phenylsulfonyl)propyl)pyrrolidine-1-carboxylate (29)

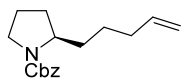


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 217.4 nm (PDA Spectrum (190-410)nm)	2.830	18489	54723	4.59
2	PDA Spectrum PDA 217.4 nm (PDA Spectrum (190-410)nm)	3.270	242187	1138628	95.41

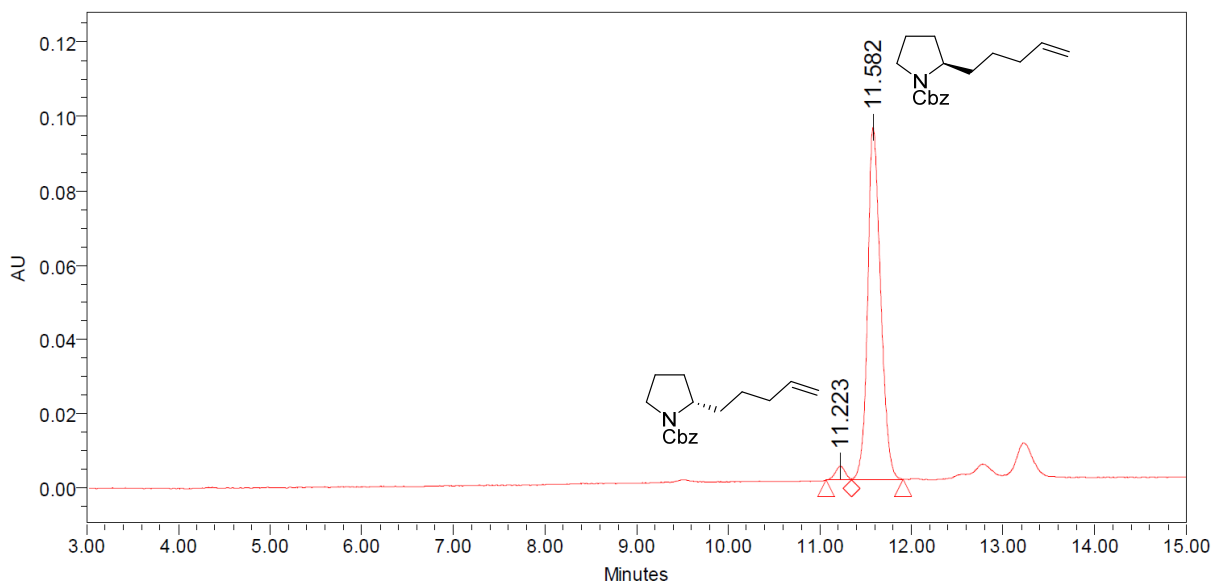
Racemic mixture



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 217.4 nm (PDA Spectrum (190-410)nm)	2.823	81730	257725	44.72
2	PDA Spectrum PDA 217.4 nm (PDA Spectrum (190-410)nm)	3.284	68441	318540	55.28

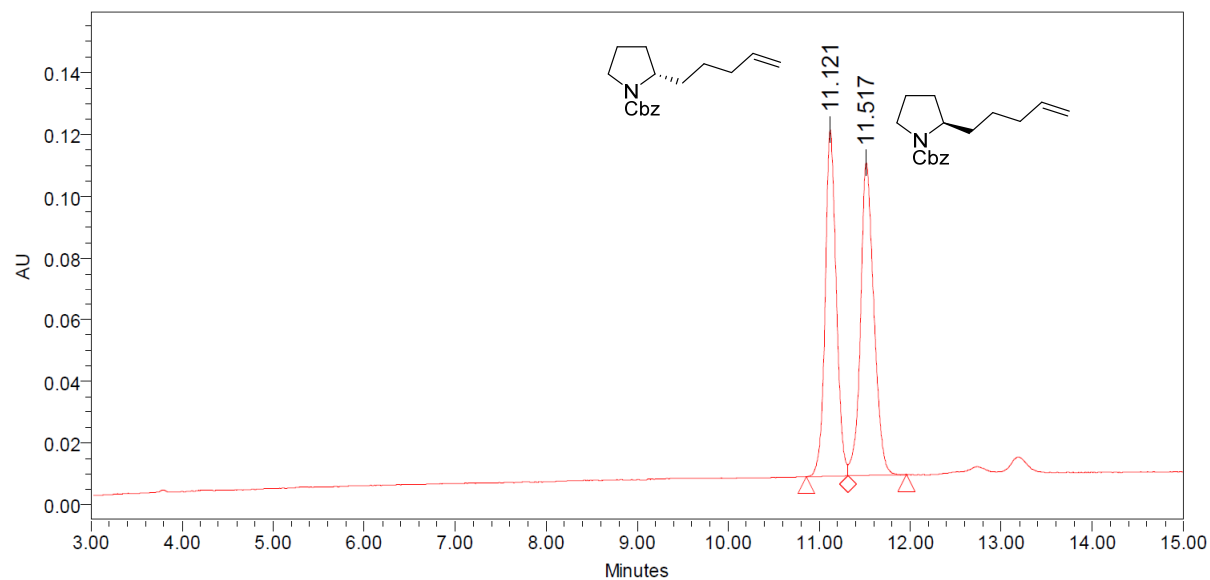


benzyl (R)-2-(pent-4-en-1-yl)pyrrolidine-1-carboxylate (30)

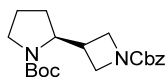


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 214.5 nm (PDA Spectrum (190-410)nm)	11.223	3710	27928	2.90
2	PDA Spectrum PDA 214.5 nm (PDA Spectrum (190-410)nm)	11.582	94966	934079	97.10

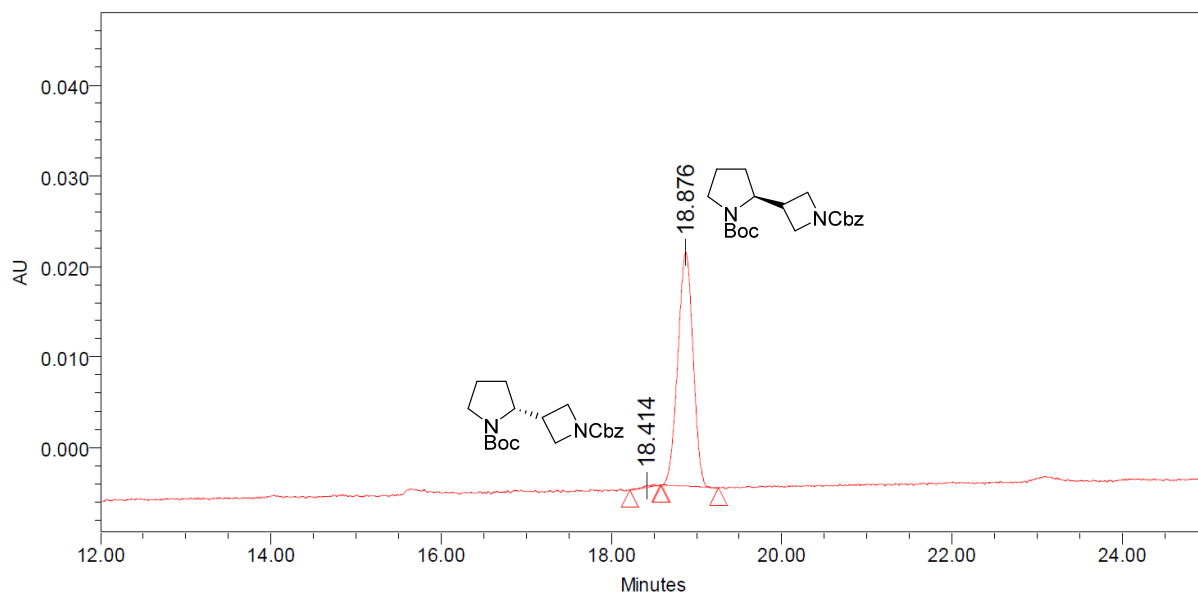
Racemic mixture



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 214.5 nm (PDA Spectrum (190-410)nm)	11.121	112319	950043	47.90
2	PDA Spectrum PDA 214.5 nm (PDA Spectrum (190-410)nm)	11.517	101399	1033411	52.10

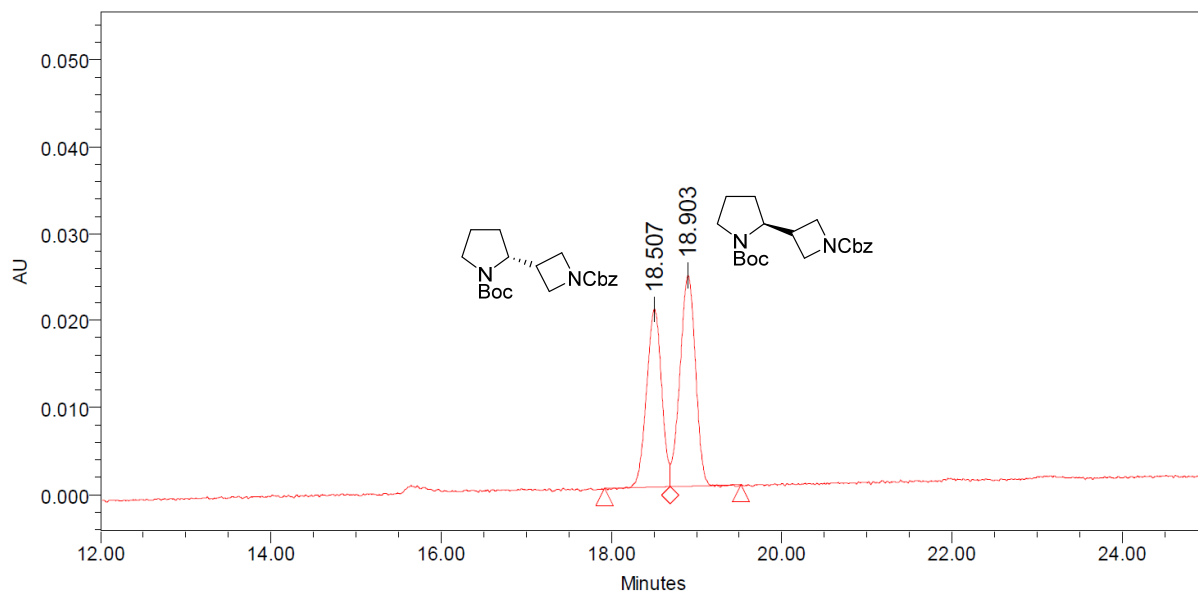


tert-butyl (S)-2-(1-((benzyloxy)carbonyl)azetidin-3-yl)pyrrolidine-1-carboxylate (31)

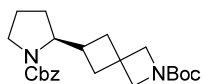


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 216.0 nm (PDA Spectrum (190-410)nm)	18.414	212	1874	0.58
2	PDA Spectrum PDA 216.0 nm (PDA Spectrum (190-410)nm)	18.876	25801	319554	99.42

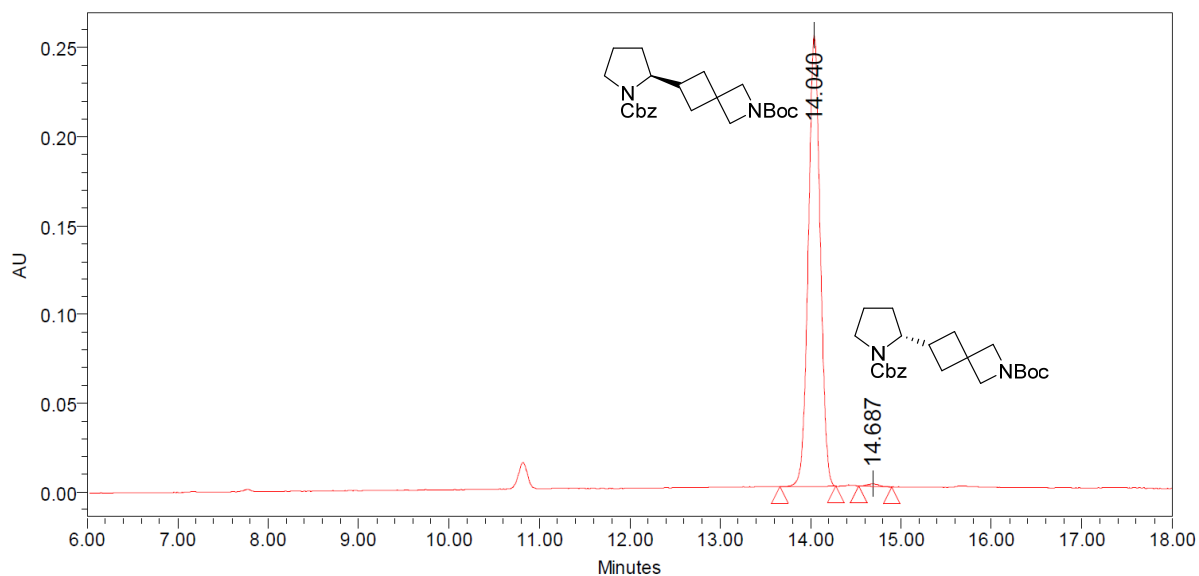
Racemic mixture



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	18.507	20396	251038	44.97
2	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	18.903	24264	307206	55.03

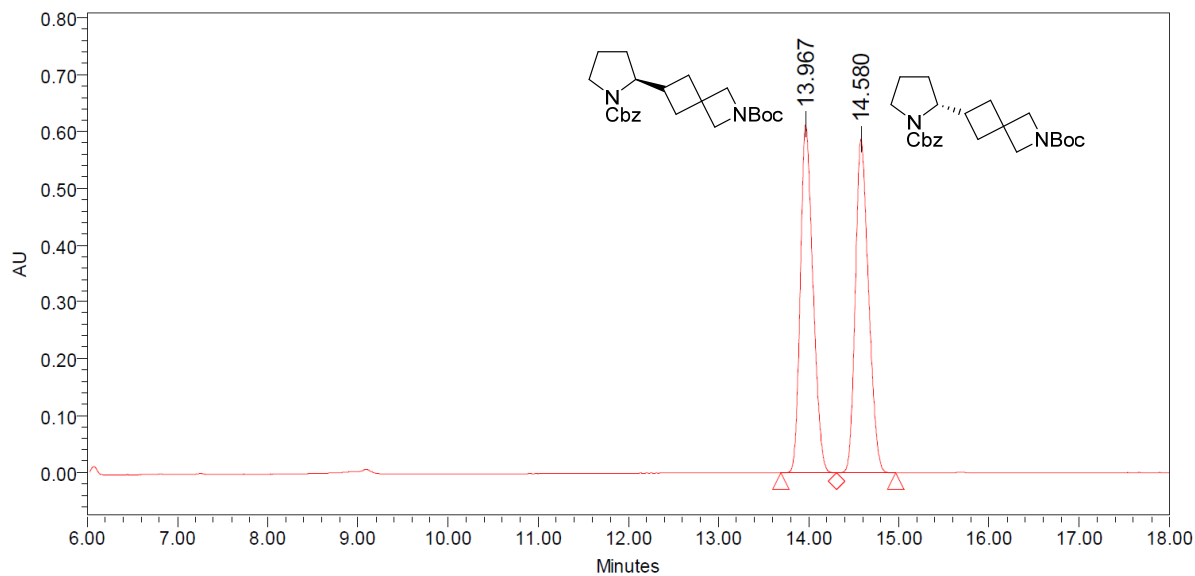


tert-butyl (S)-6-(1-((benzyloxy)carbonyl)pyrrolidin-2-yl)-2-azaspiro[3.3]heptane-2-carboxylate (32)

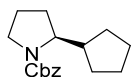


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	14.040	253709	2331145	99.46
2	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	14.687	1546	12619	0.54

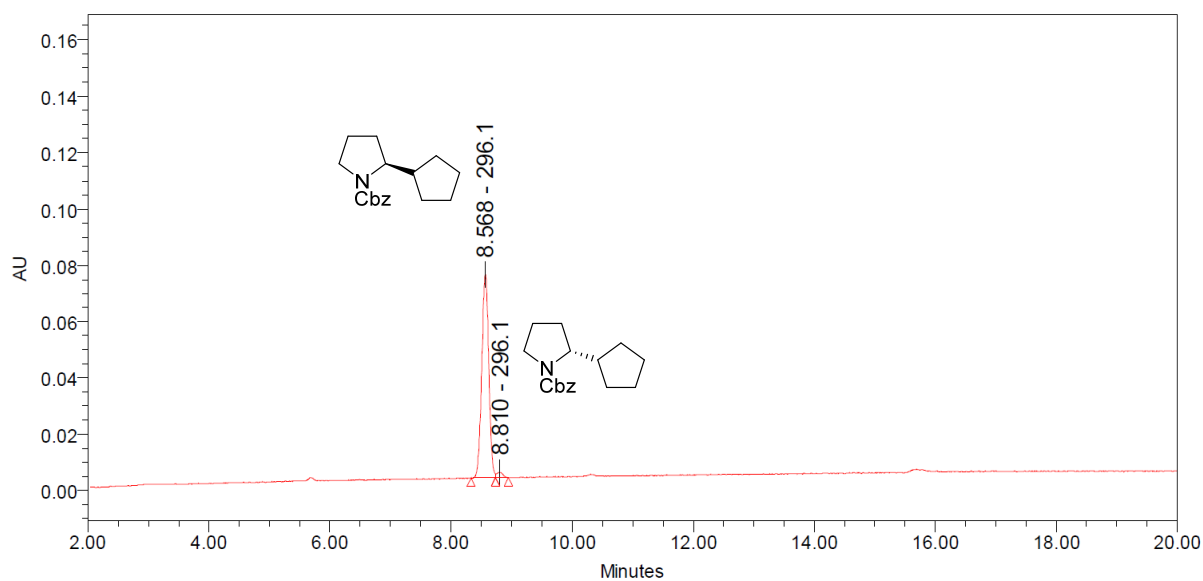
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	13.967	612873	5937634	49.94
2	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	14.580	586860	5951986	50.06

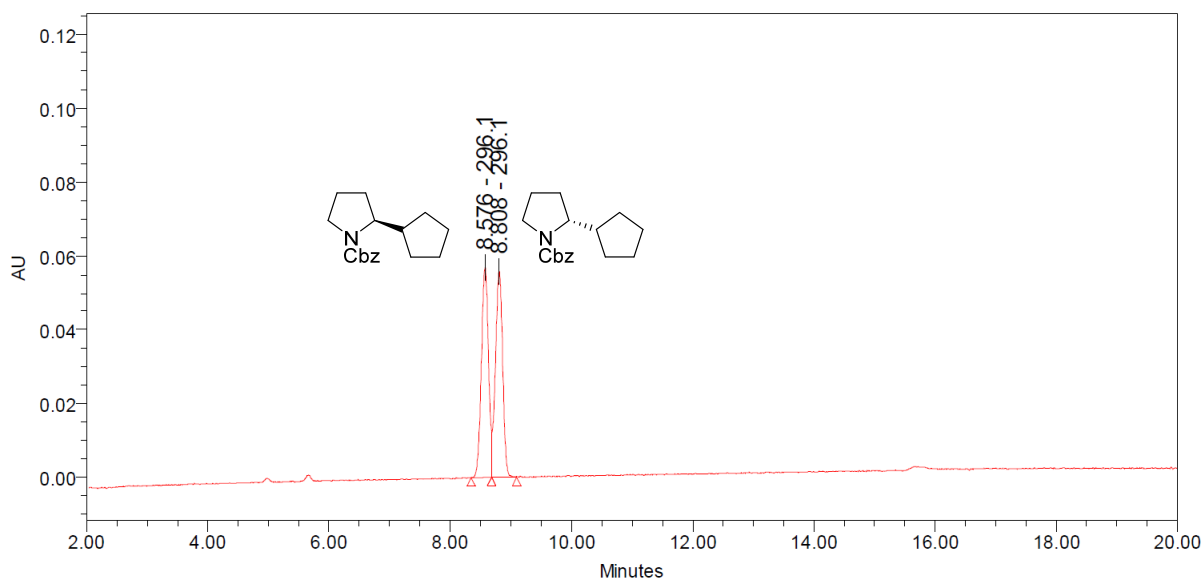


benzyl (S)-2-cyclopentylpyrrolidine-1-carboxylate (33)

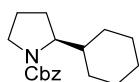


	RT	Area	Height	% Area
1	8.568	585675	72448	97.73
2	8.810	13631	1854	2.27

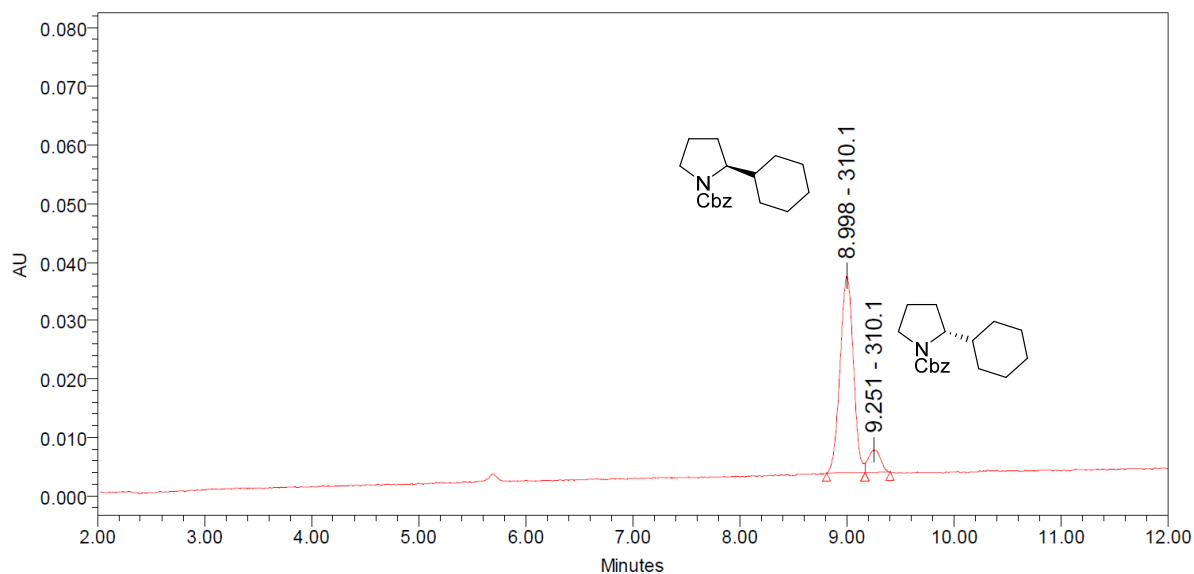
Racemate



	RT	Area	Height	% Area
1	8.576	468377	57154	49.94
2	8.808	469519	56126	50.06

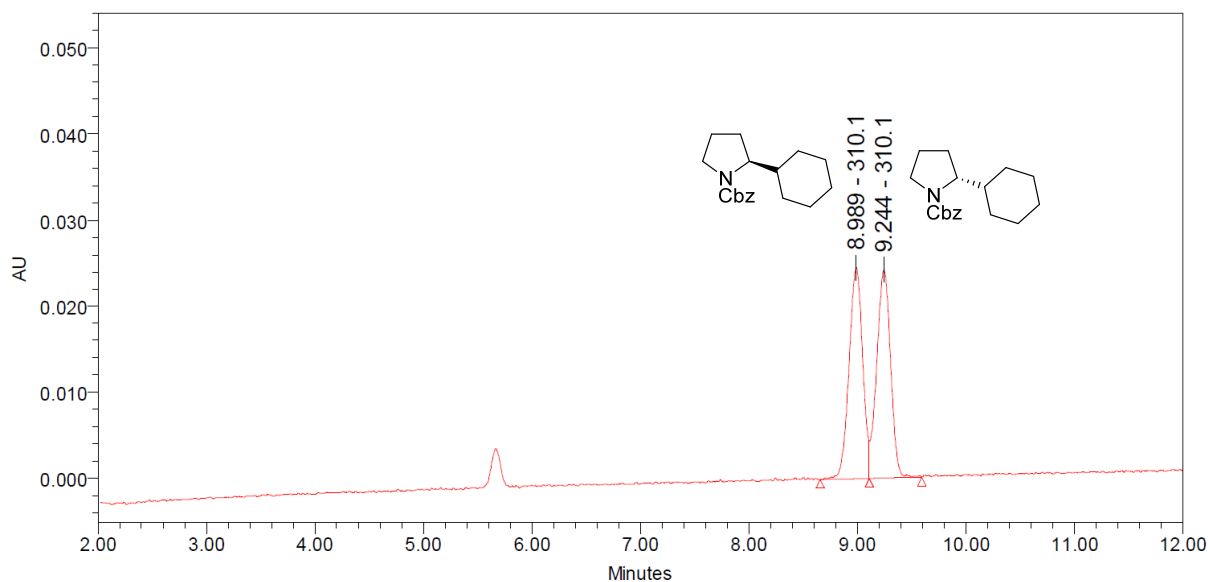


benzyl (S)-2-cyclohexylpyrrolidine-1-carboxylate (34)

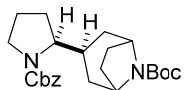


	RT	Area	Height	% Area
1	8.998	290333	33789	90.57
2	9.251	30219	3812	9.43

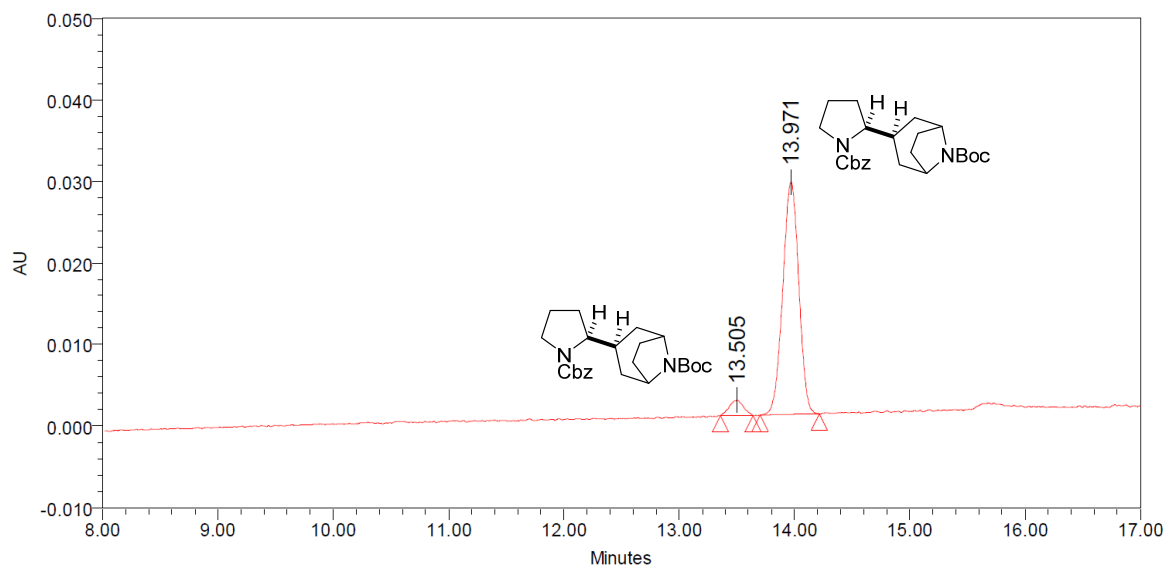
Racemate



	RT	Area	Height	% Area
1	8.989	215507	24613	50.04
2	9.244	215181	24292	49.96

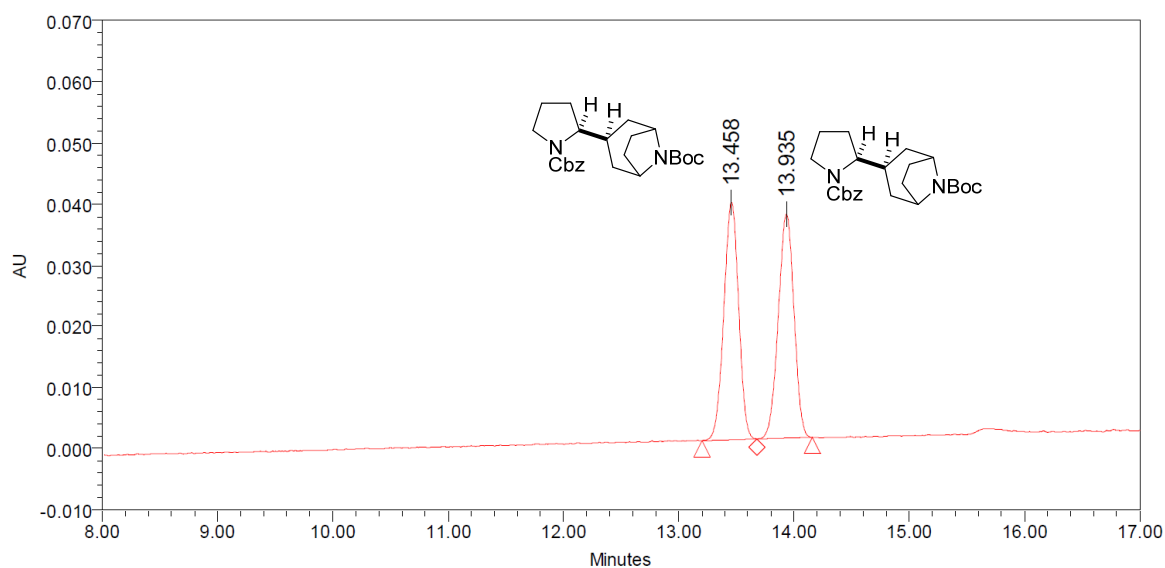


tert-butyl 3-((S)-1-((benzyloxy)carbonyl)pyrrolidin-2-yl)-8-azabicyclo[3.2.1]octane-8-carboxylate (35)

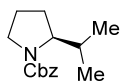


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 217.0 nm (PDA Spectrum (190-410)nm)	13.505	1888	16010	5.51
2	PDA Spectrum PDA 217.0 nm (PDA Spectrum (190-410)nm)	13.971	28548	274666	94.49

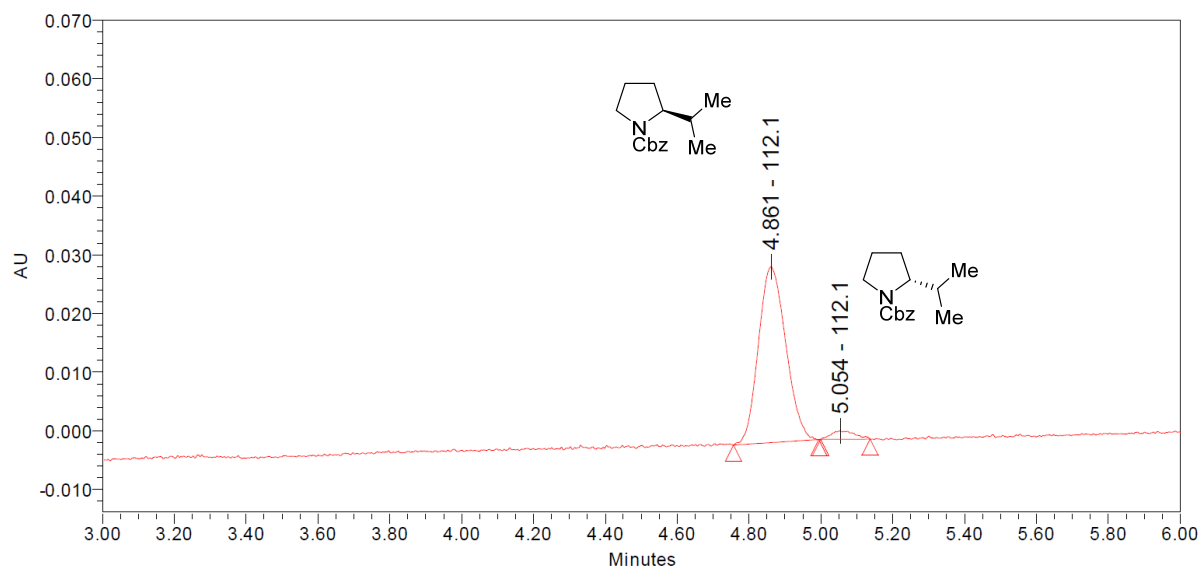
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	13.458	38950	347796	50.05
2	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	13.935	36762	347036	49.95

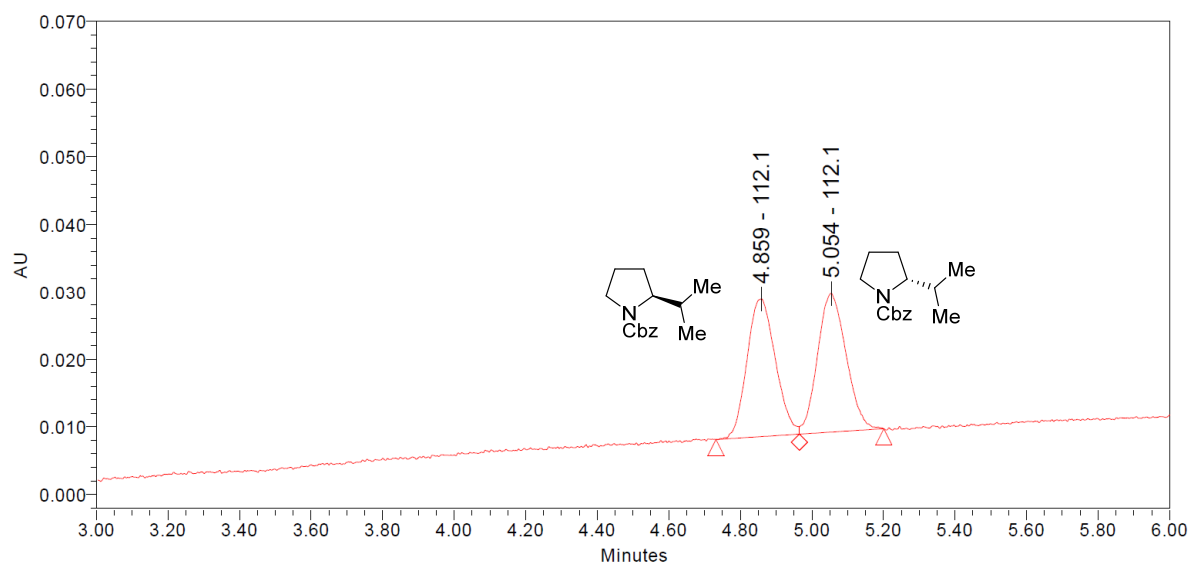


benzyl (S)-2-isopropylpyrrolidine-1-carboxylate (36)

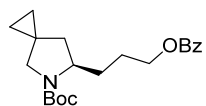


	RT	Height (μV)	Area	% Area
1	4.861	30009	158759	96.01
2	5.054	1414	6599	3.99

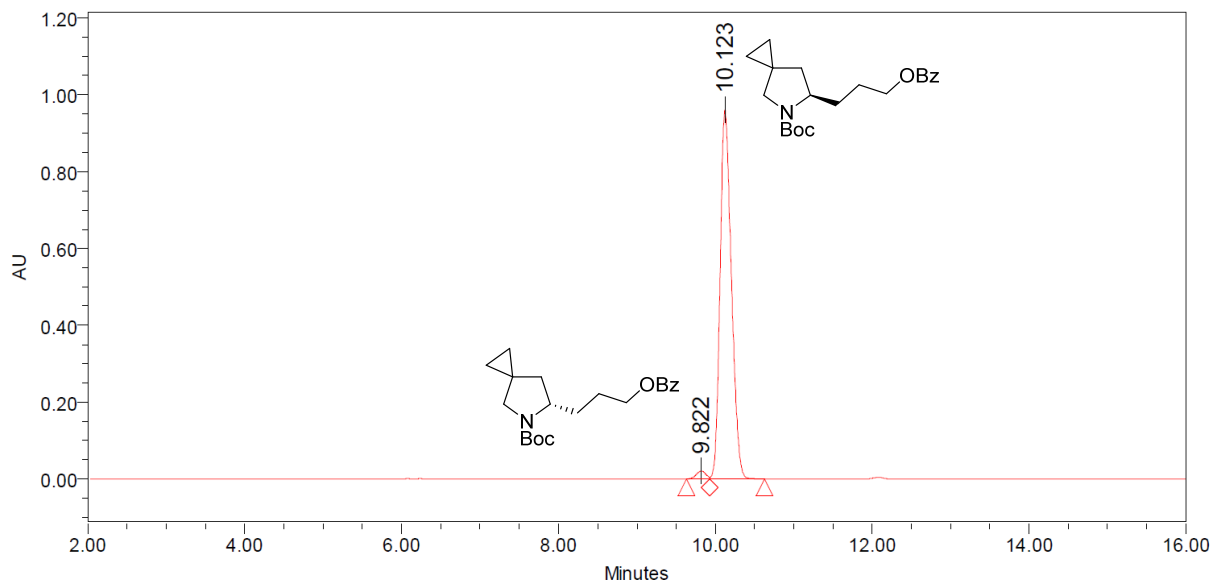
Racemate



	RT	Height (μV)	Area	% Area
1	4.859	20396	112553	49.70
2	5.054	20537	113931	50.30

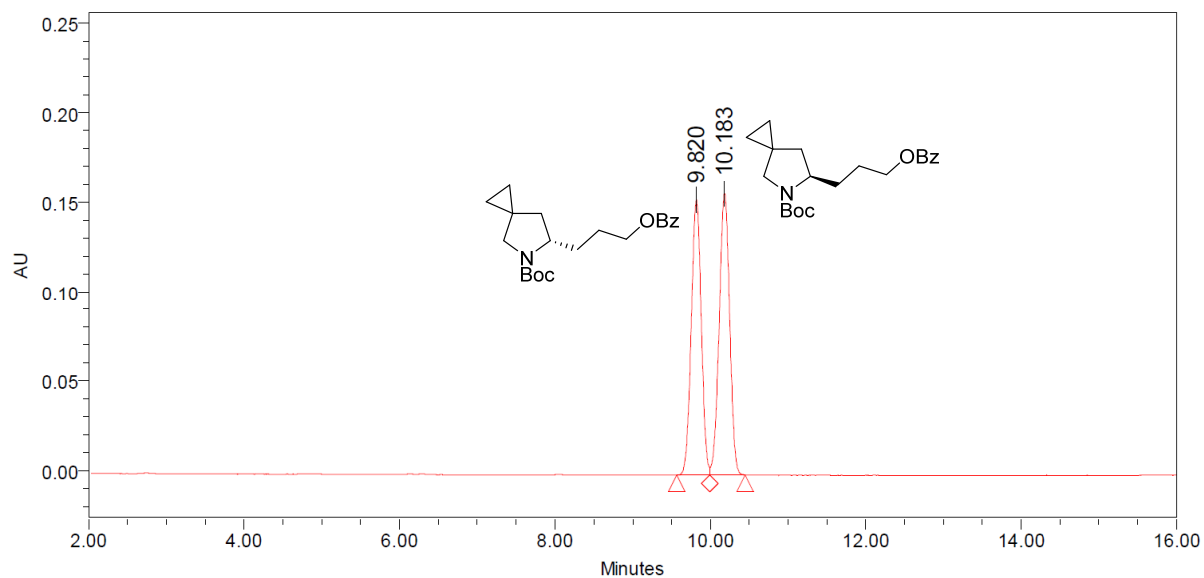


tert-butyl (R)-6-(3-(benzyloxy)propyl)-5-azaspiro[2.4]heptane-5-carboxylate (37)

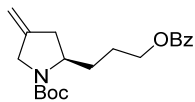


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 226.0 nm (PDA Spectrum (190-410)nm)	9.822	20773	176434	1.80
2	PDA Spectrum PDA 226.0 nm (PDA Spectrum (190-410)nm)	10.123	960620	9615176	98.20

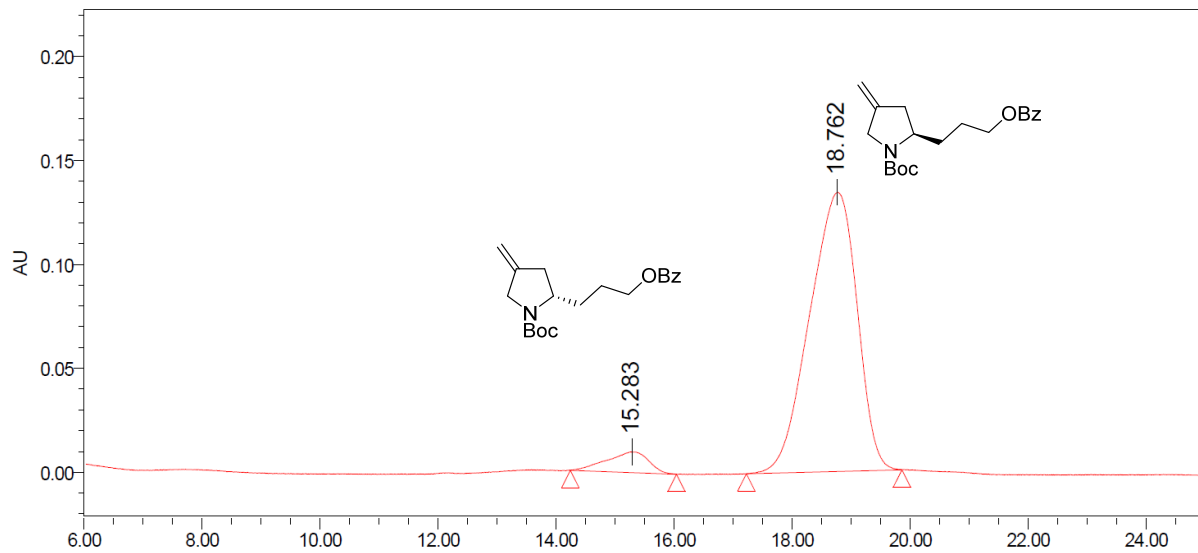
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 226.0 nm (PDA Spectrum (190-410)nm)	9.820	153991	1378111	48.33
2	PDA Spectrum PDA 226.0 nm (PDA Spectrum (190-410)nm)	10.183	157534	1473377	51.67

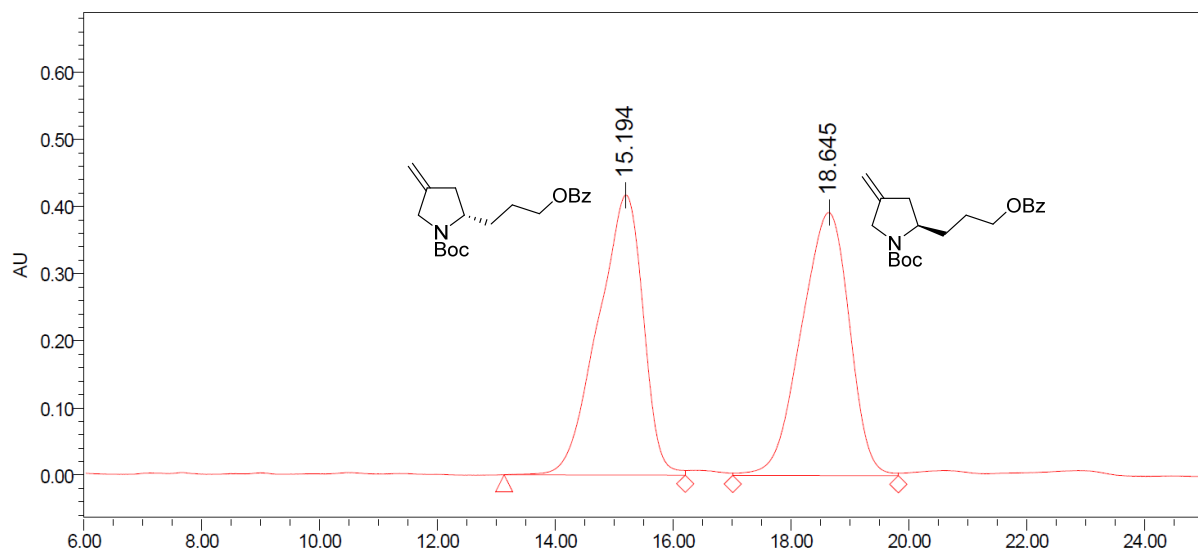


tert-butyl (R)-2-(3-(benzyloxy)propyl)-4-methylenepyrrolidine-1-carboxylate (38)

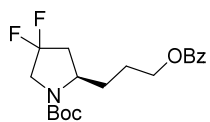


	RT	Area	Height	% Area
1	15.283	493814	10038	6.17
2	18.762	7509712	134393	93.83

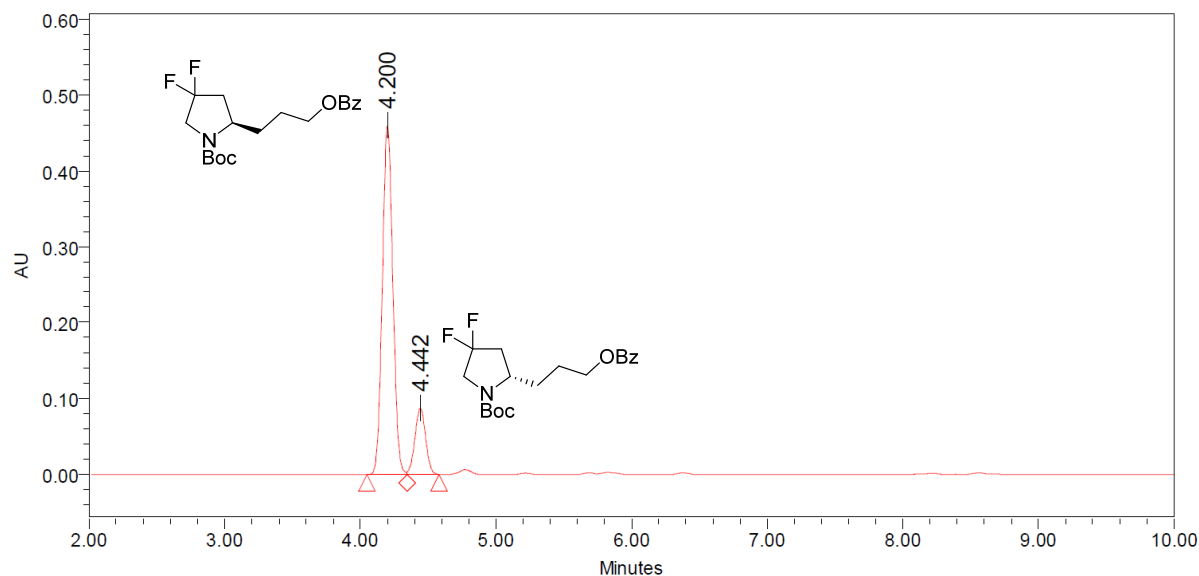
Racemate



	RT	Area	Height	% Area
1	15.194	22237081	417213	49.95
2	18.645	22280926	391860	50.05

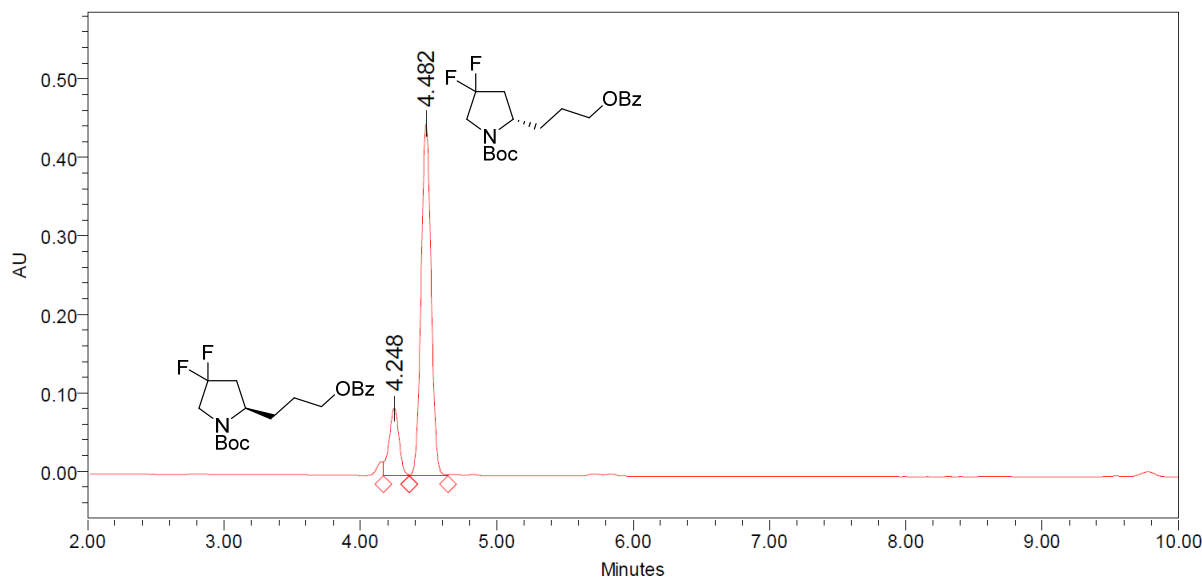


tert-butyl (R)-2-(3-(benzyloxy)propyl)-4,4-difluoropyrrolidine-1-carboxylate (39)

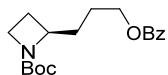


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-410)nm)	4.200	460134	2470255	83.84
2	PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-410)nm)	4.442	86858	476300	16.16

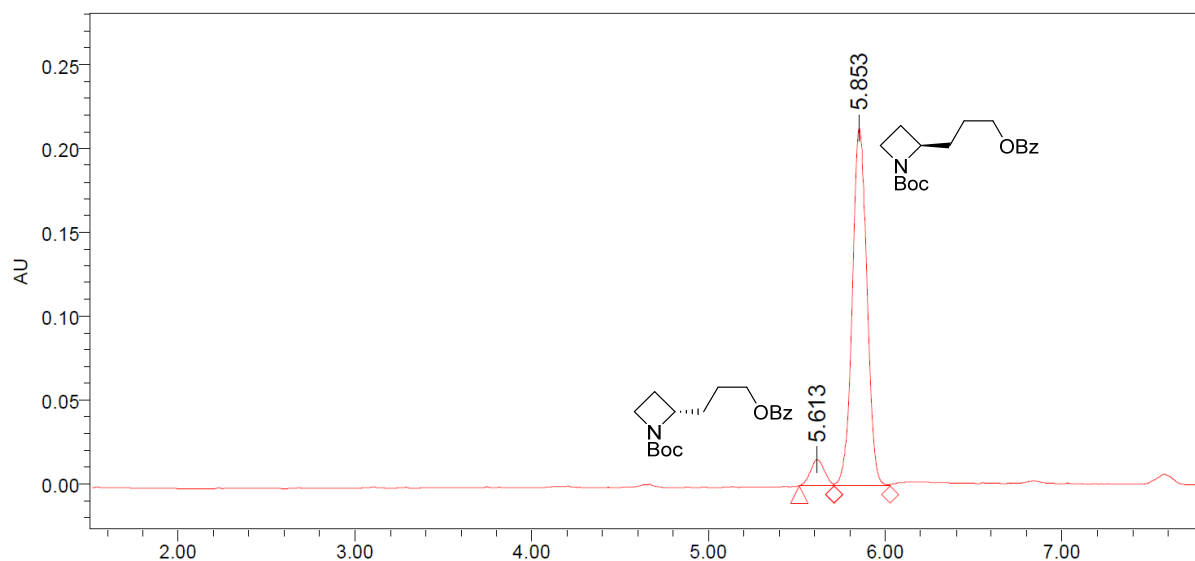
(S)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-410)nm)	4.248	85596	430337	15.90
2	PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-410)nm)	4.482	448897	2276273	84.10

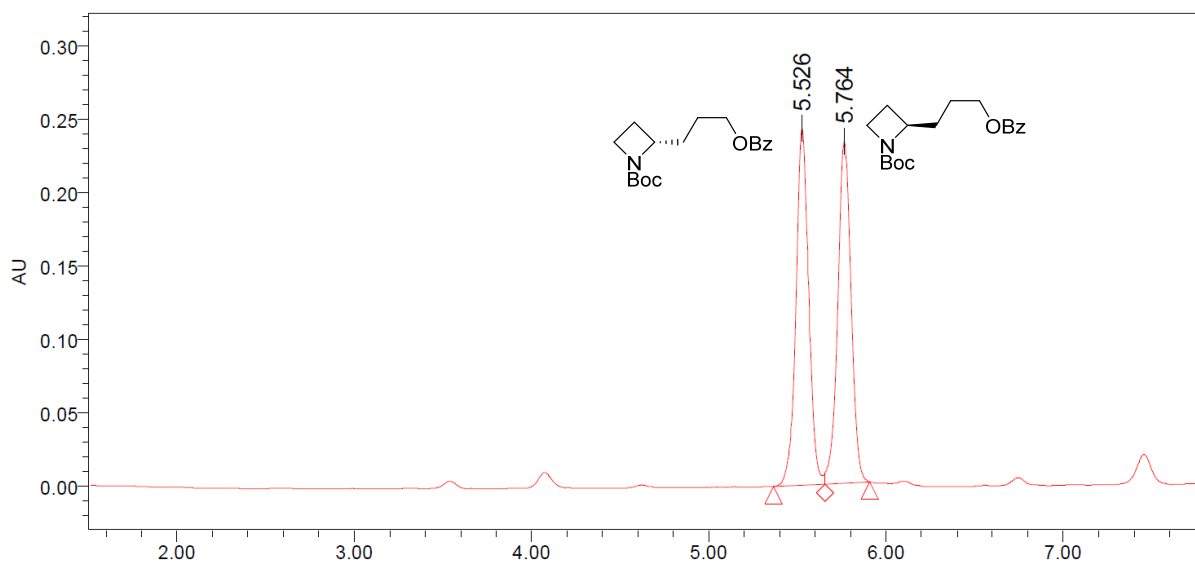


tert-butyl (R)-2-(3-(benzyloxy)propyl)azetidine-1-carboxylate (40)

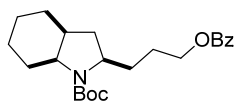


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 218.0 nm (PDA Spectrum (190-410)nm)	5.613	15568	86886	6.60
2	PDA Spectrum PDA 218.0 nm (PDA Spectrum (190-410)nm)	5.853	213427	1230197	93.40

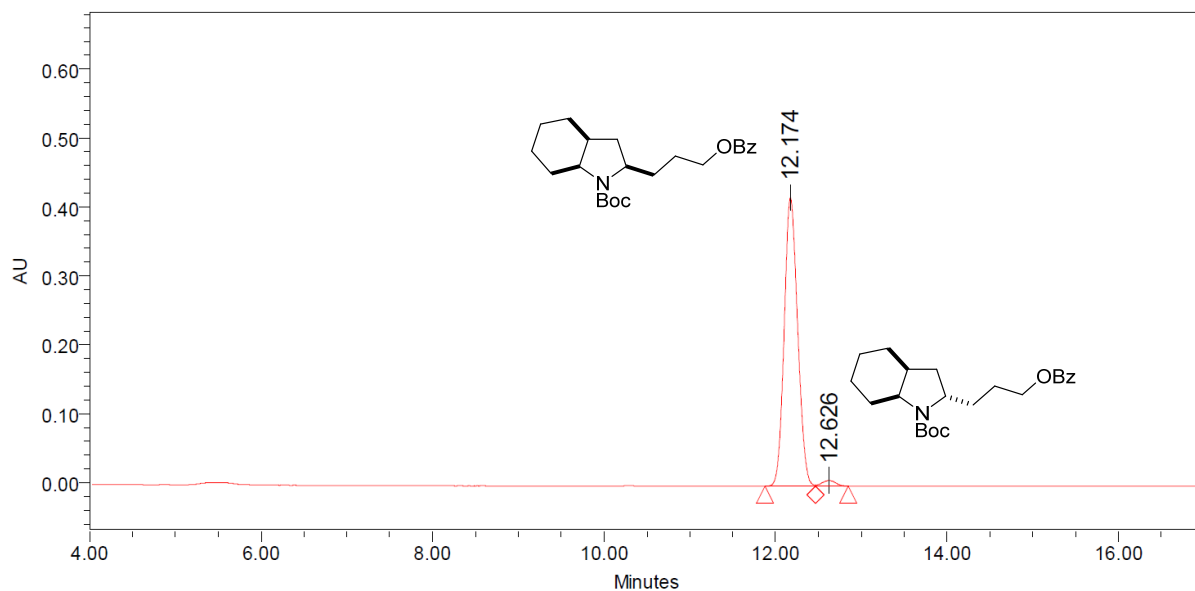
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 218.0 nm (PDA Spectrum (190-410)nm)	5.526	243011	1221856	50.25
2	PDA Spectrum PDA 218.0 nm (PDA Spectrum (190-410)nm)	5.764	232926	1209503	49.75

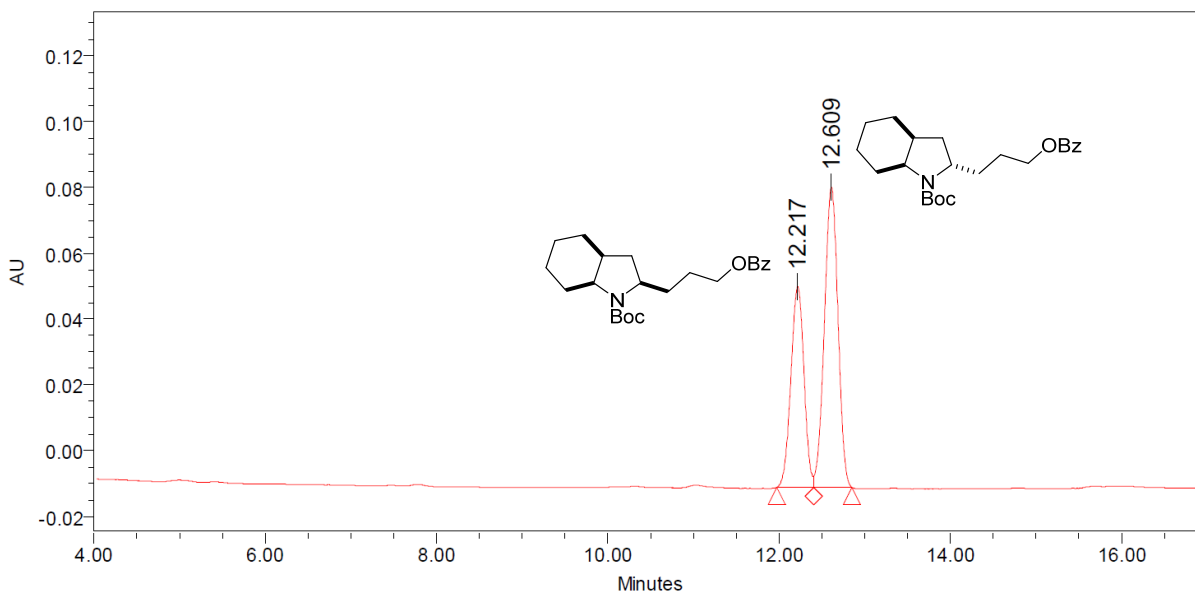


tert-butyl (2R,3aS,7aS)-2-(3-(benzyloxy)propyl)octahydro-1H-indole-1-carboxylate (50)

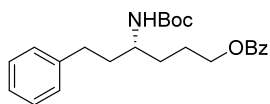


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 230.5 nm (PDA Spectrum (190-410)nm)	12.174	418719	4544557	98.02
2	PDA Spectrum PDA 230.5 nm (PDA Spectrum (190-410)nm)	12.626	8317	91746	1.98

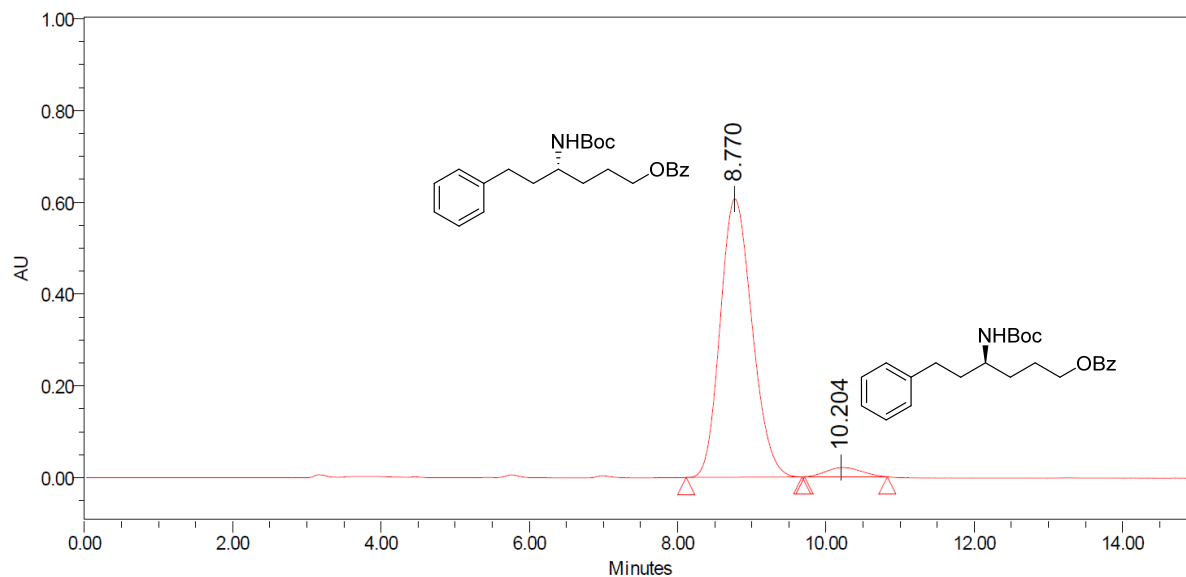
Mixture of diastereomers (from dual radical cross coupling of the corresponding NHP ester with alkyl iodide)



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 230.5 nm (PDA Spectrum (190-410)nm)	12.217	61098	645421	38.99
2	PDA Spectrum PDA 230.5 nm (PDA Spectrum (190-410)nm)	12.609	91316	1009758	61.01

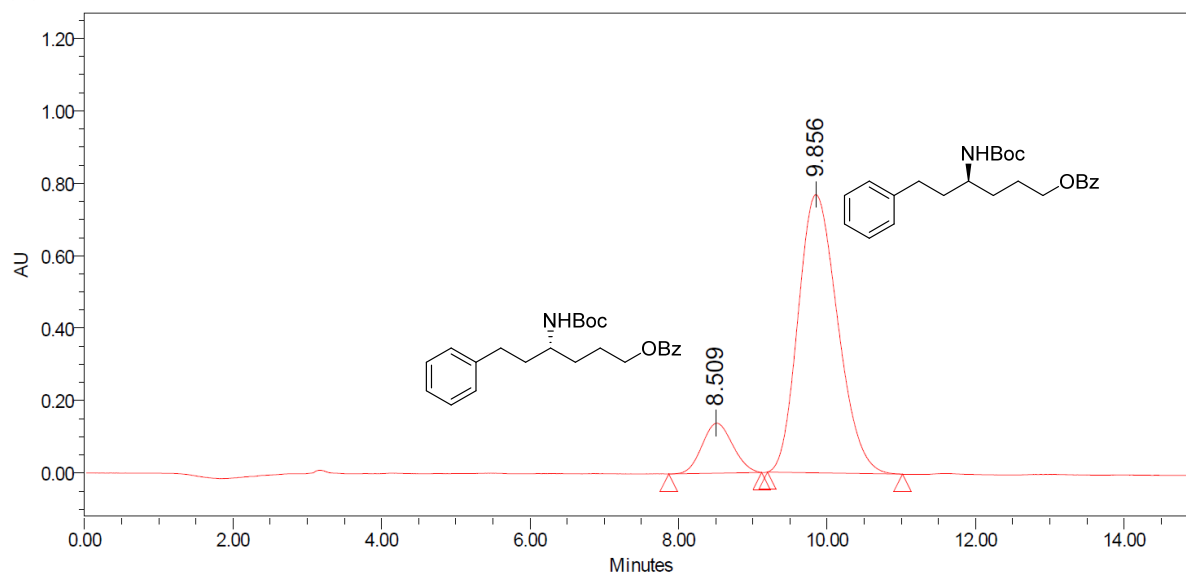


(S)-4-((tert-butoxycarbonyl)amino)-6-phenylhexyl benzoate (51)

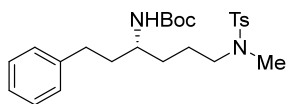


	RT	Area	Height	% Area
1	8.770	18119866	606668	96.41
2	10.204	674588	20273	3.59

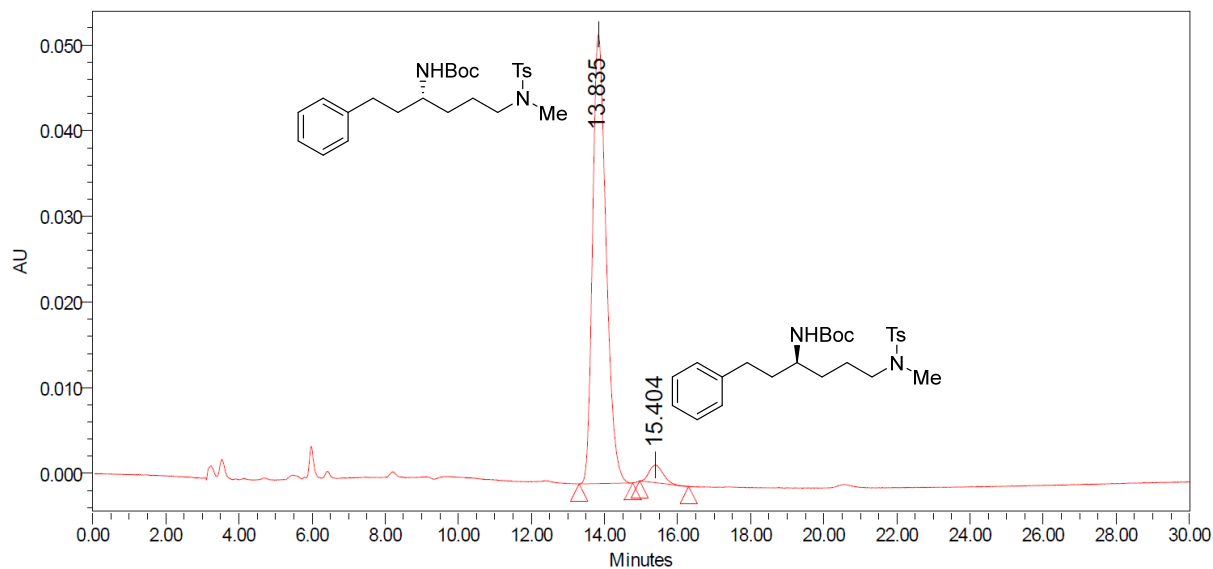
(R)-enantiomer



	RT	Area	Height	% Area
1	8.509	3956165	138118	12.32
2	9.856	28151322	765153	87.68

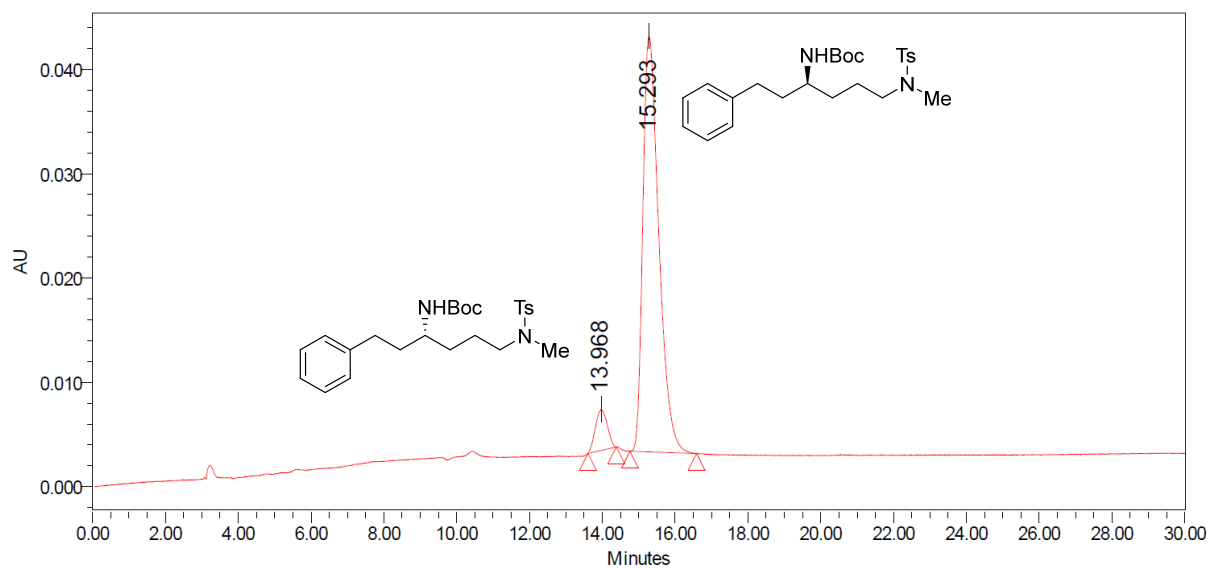


tert-butyl (S)-(6-((N,4-dimethylphenyl)sulfonamido)-1-phenylhexan-3-yl)carbamate (52)

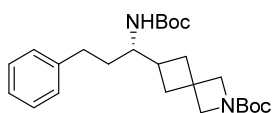


	RT	Area	Height	% Area
1	13.835	1344016	52401	96.04
2	15.404	55361	2089	3.96

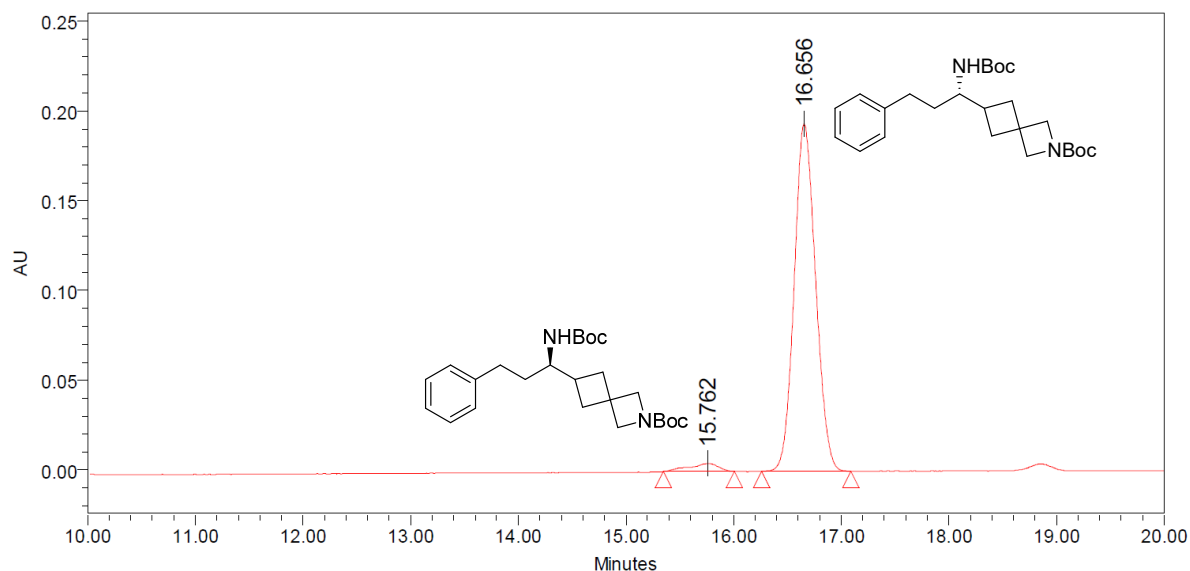
(R)-enantiomer



	RT	Area	Height	% Area
1	13.968	88272	3935	6.80
2	15.293	1210682	39837	93.20

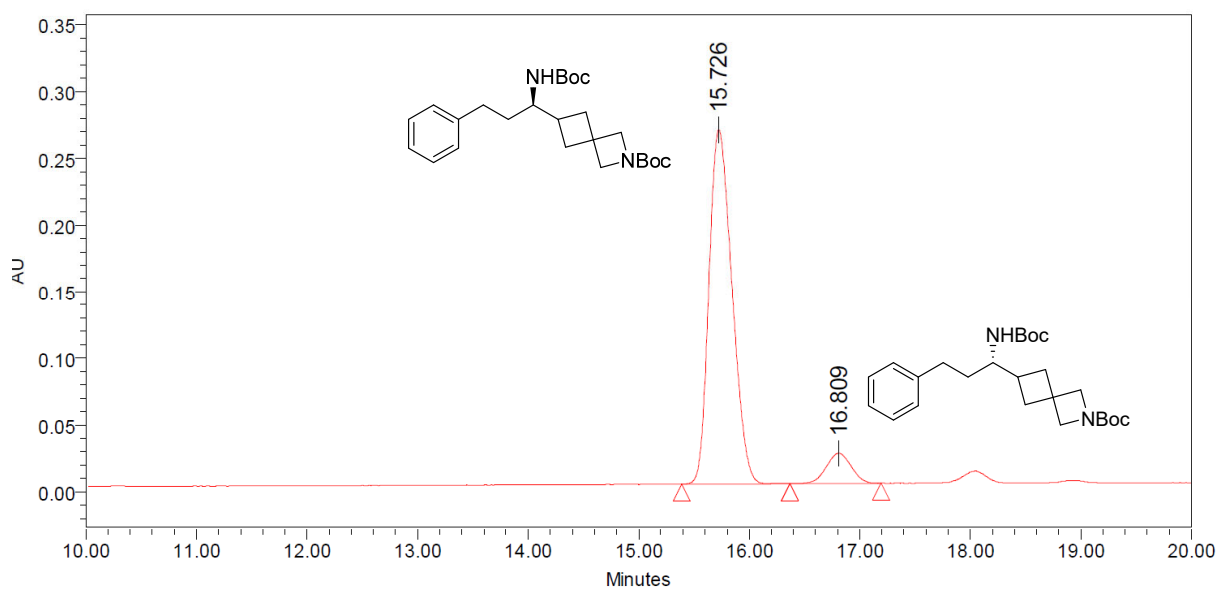


tertbutyl (S)-6-(1-(tert-butoxycarbonyl)amino)-3-phenylpropyl)-2-azaspiro[3.3]heptane-2-carboxylate (53)

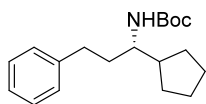


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	15.762	4481	84963	3.07
2	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	16.656	193638	2678633	96.93

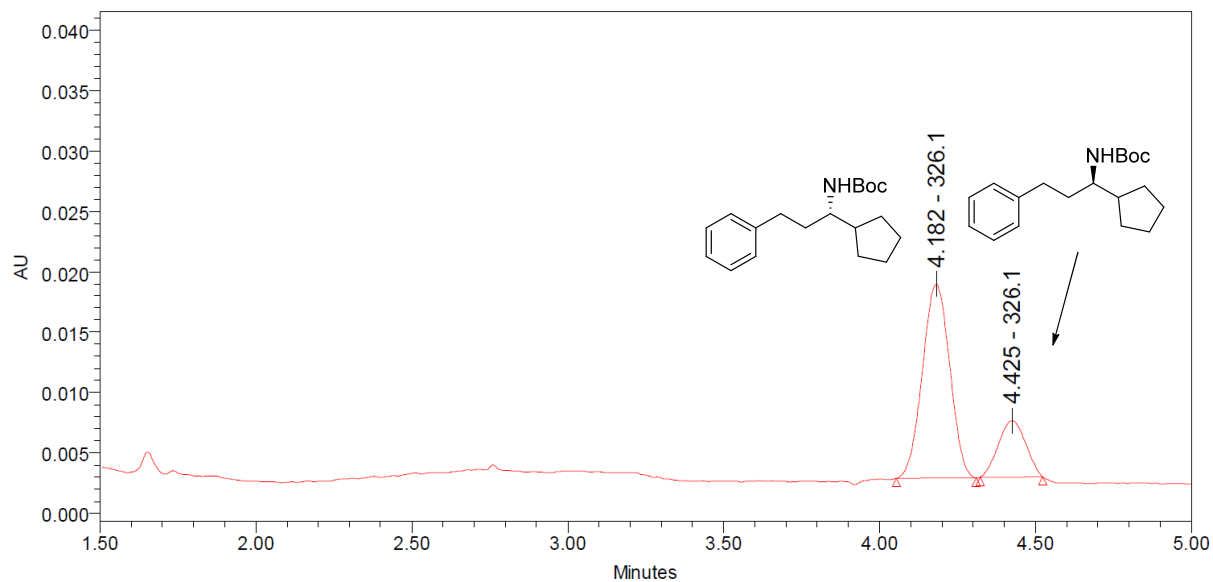
(R)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	15.726	265410	3835246	91.57
2	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	16.809	22440	353010	8.43

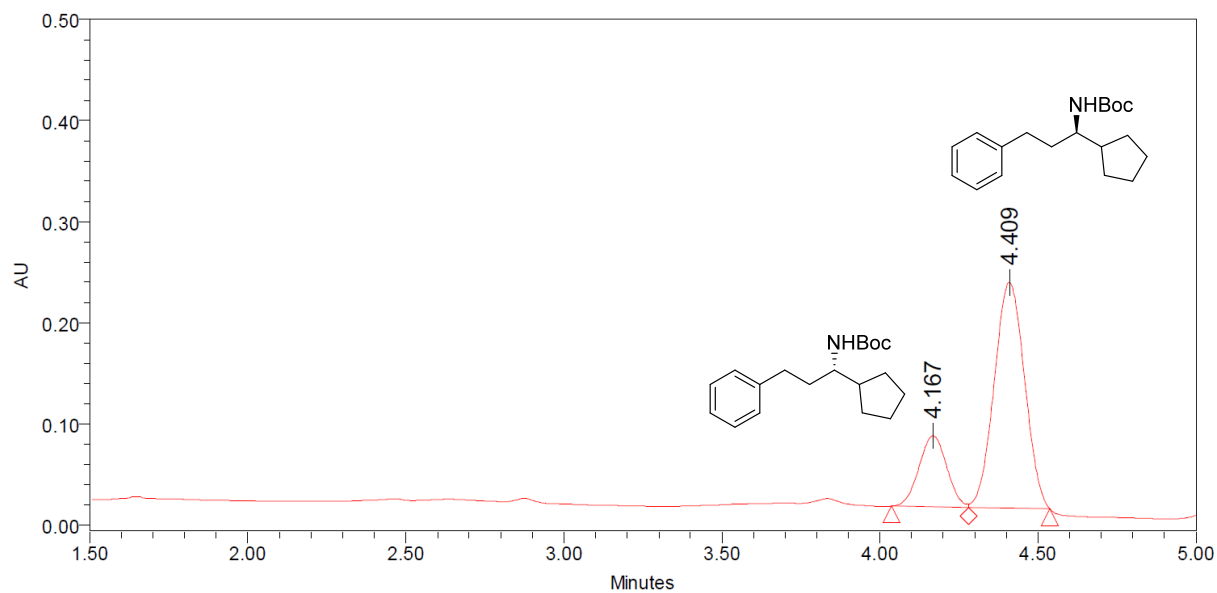


tert-butyl (S)-(1-cyclopentyl-3-phenylpropyl)carbamate (54)

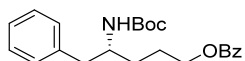


	Processed Channel Descr.	RT	Area	Height	% Area
1	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	4.182	97545	16097	77.56
2	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	4.425	28229	4646	22.44

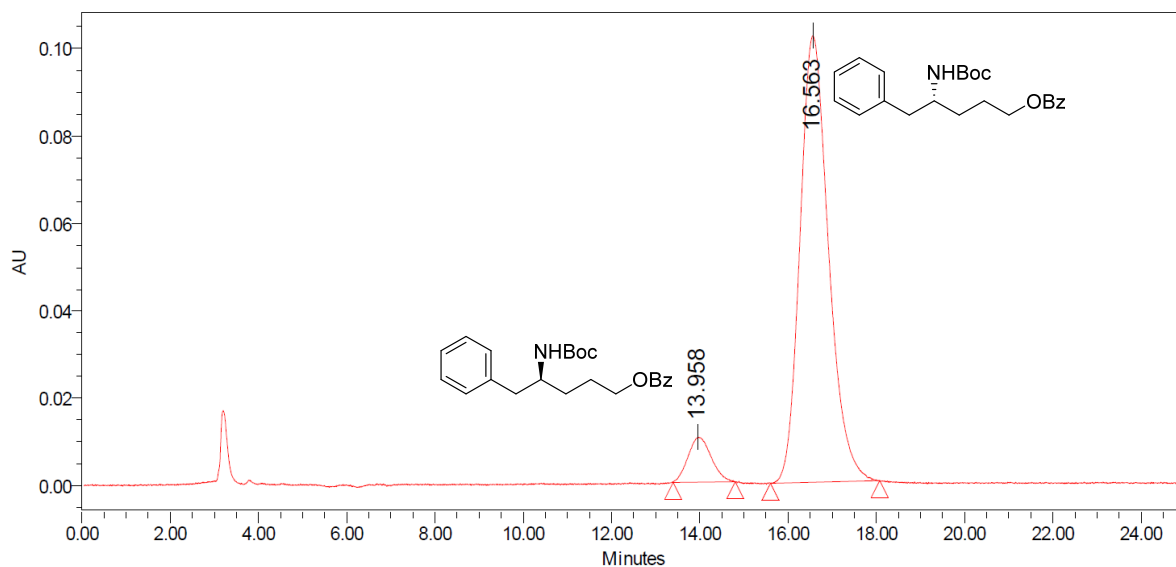
(R)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	4.167	70323	428441	22.32
2	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	4.409	223321	1490694	77.68

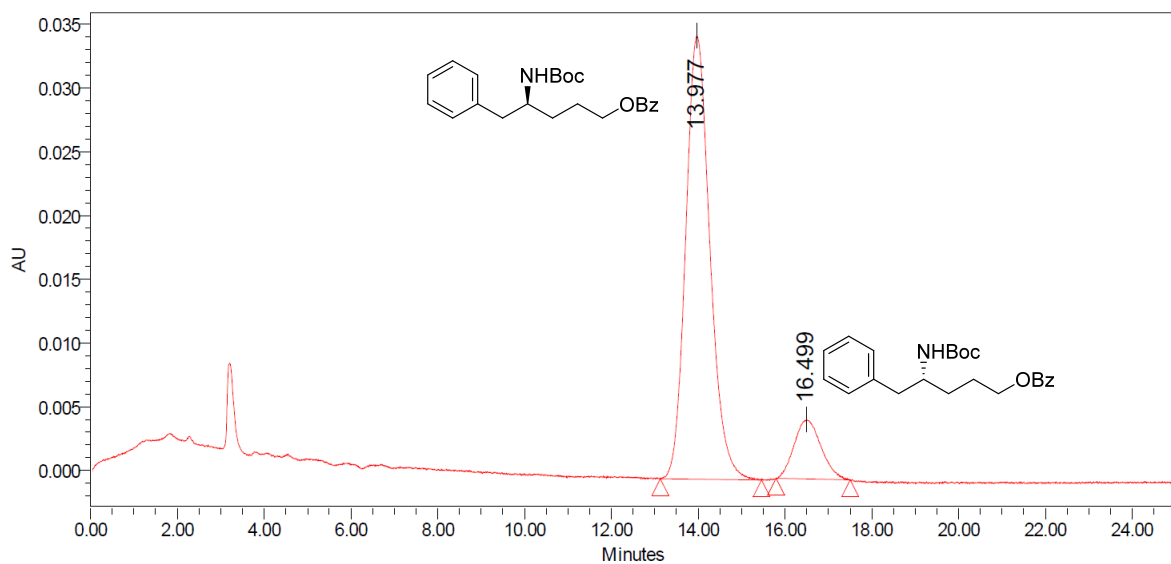


(R)-4-((tert-butoxycarbonyl)amino)-5-phenylpentyl benzoate (55)

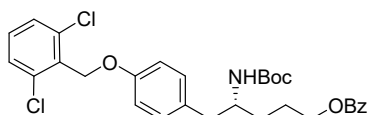


	RT	Area	Height	% Area
1	13.958	376807	10376	7.59
2	16.563	4589074	102159	92.41

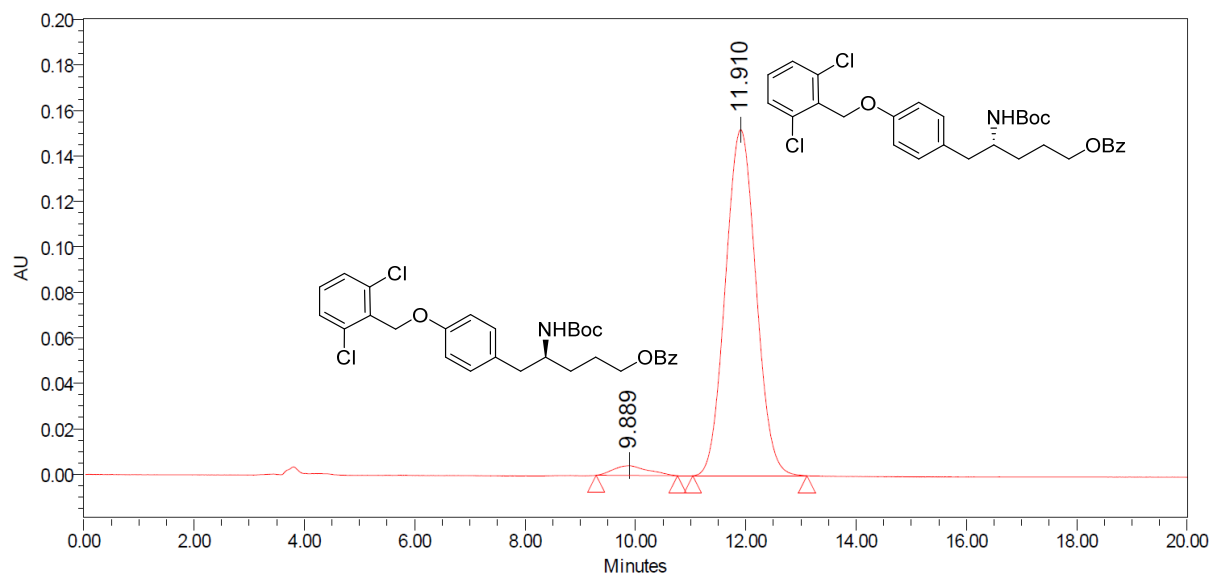
(S)-enantiomer



	RT	Area	Height	% Area
1	13.977	1347186	34798	87.09
2	16.499	199769	4661	12.91

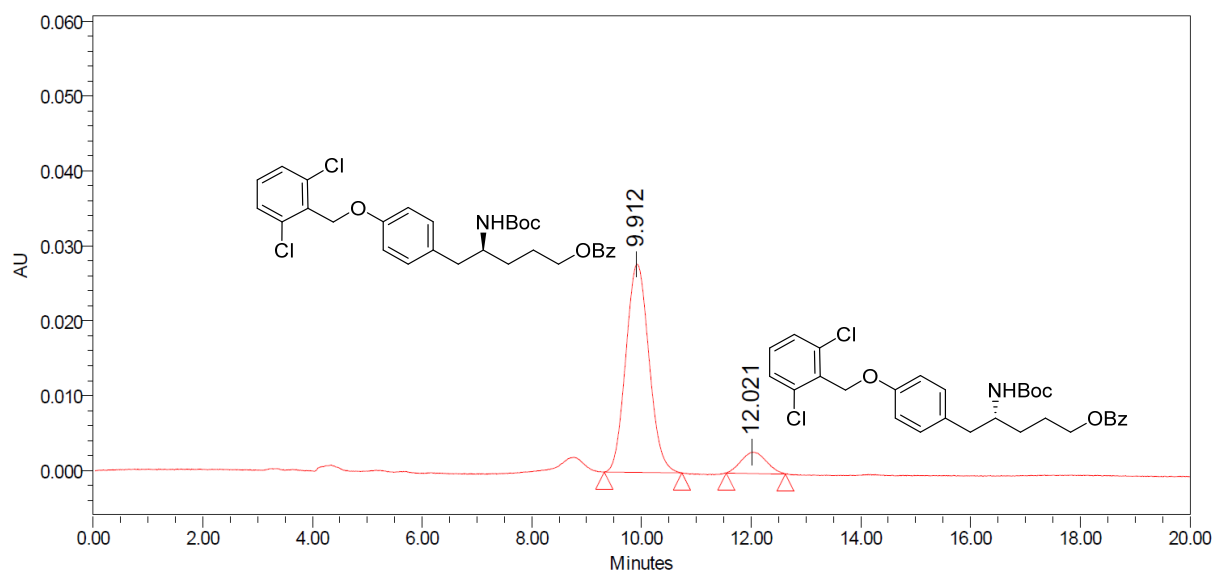


(R)-4-((tert-butoxycarbonyl)amino)-5-(4-((2,6-dichlorobenzyl)oxy)phenyl)pentyl benzoate (56)

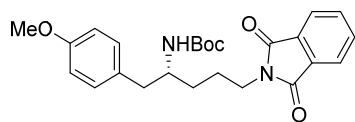


	RT	Area	Height	% Area
1	9.889	154477	3901	2.55
2	11.910	5891640	152380	97.45

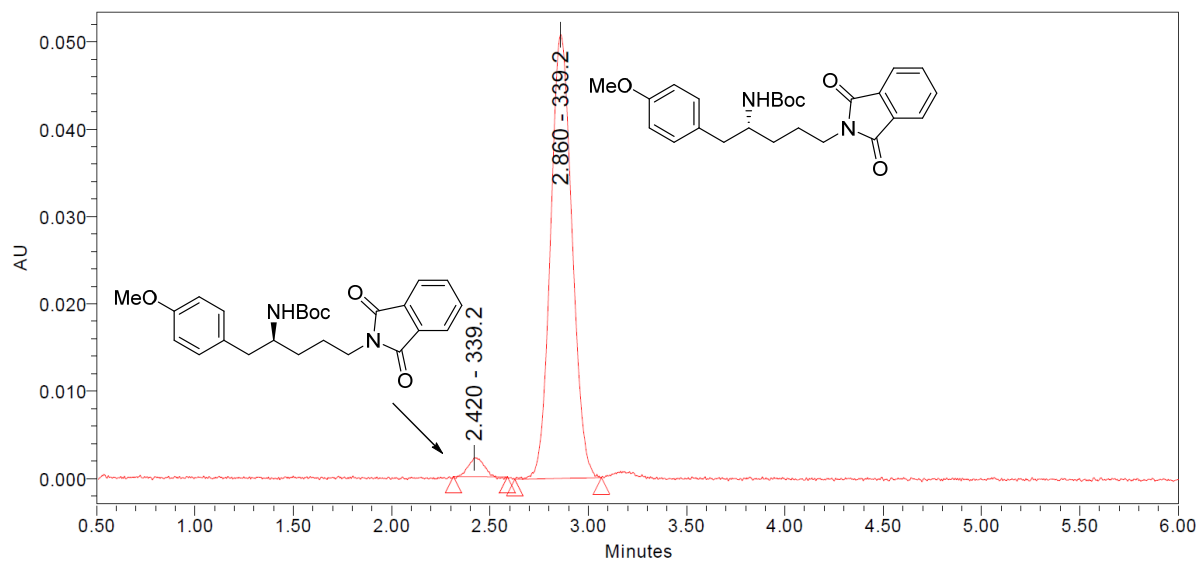
(S)-enantiomer



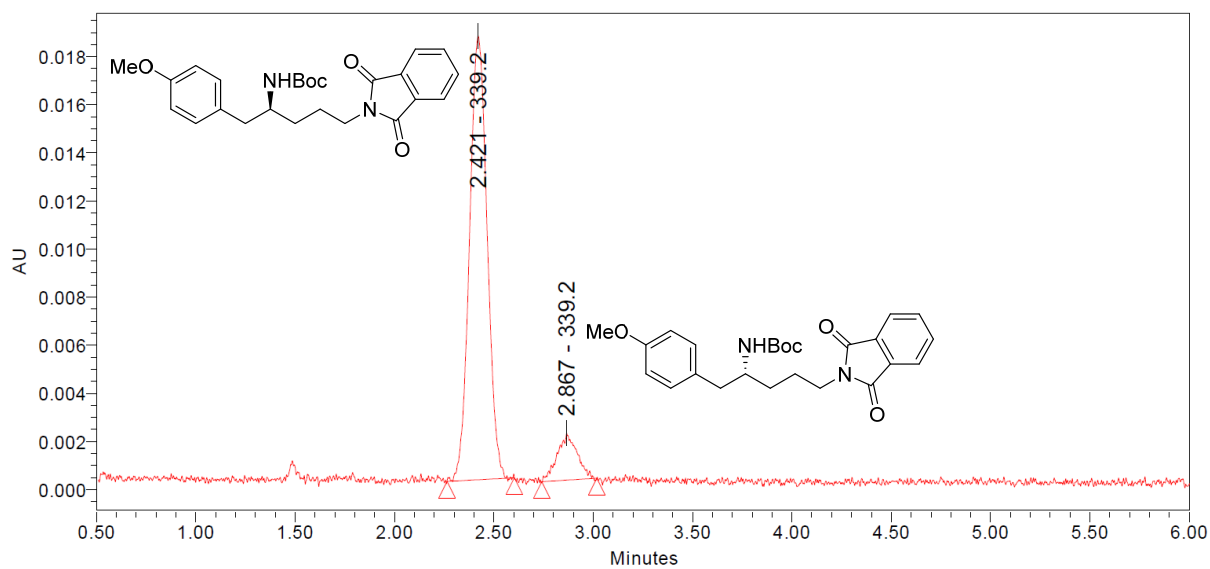
	RT	Area	Height	% Area
1	9.912	817344	27814	89.89
2	12.021	91917	2861	10.11

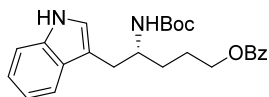


tert-butyl (R)-(5-(1,3-dioxisoindolin-2-yl)-1-(4-methoxyphenyl)pentan-2-yl)carbamate (57)

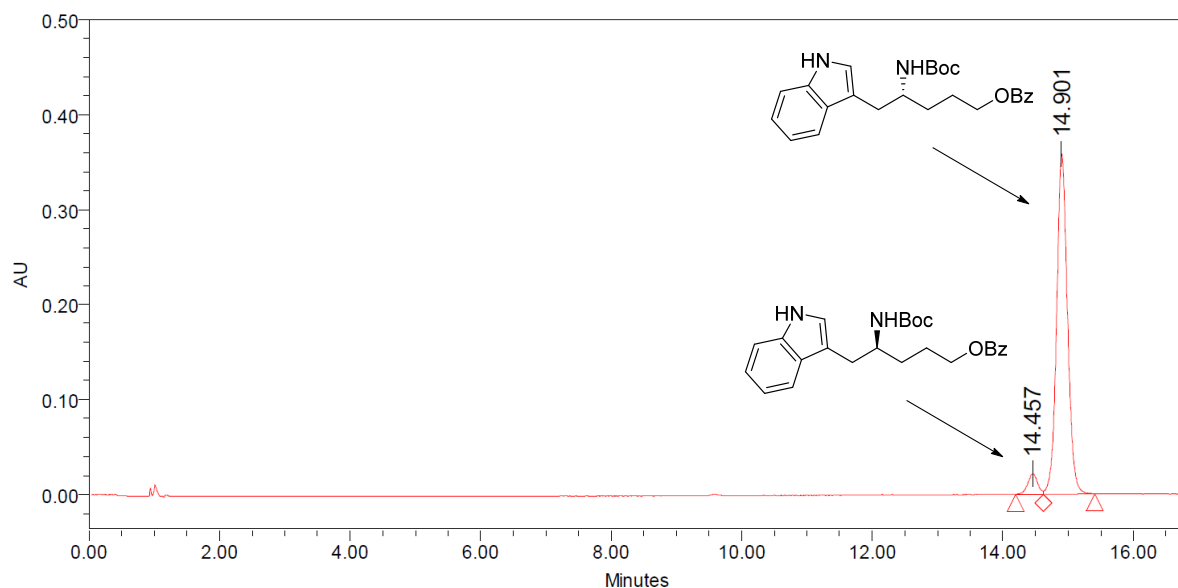


(S)-enantiomer



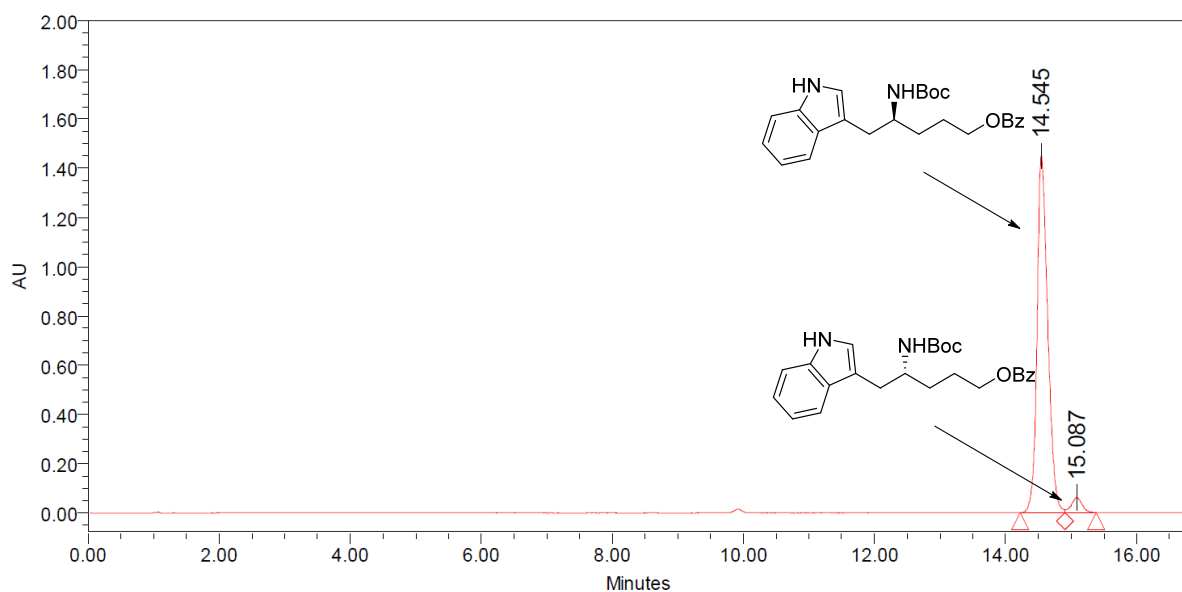


(R)-4-((tert-butoxycarbonyl)amino)-5-(1H-indol-3-yl)pentyl benzoate (58)

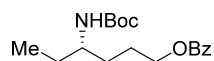


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	14.457	21597	227034	5.20
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	14.901	358267	4136467	94.80

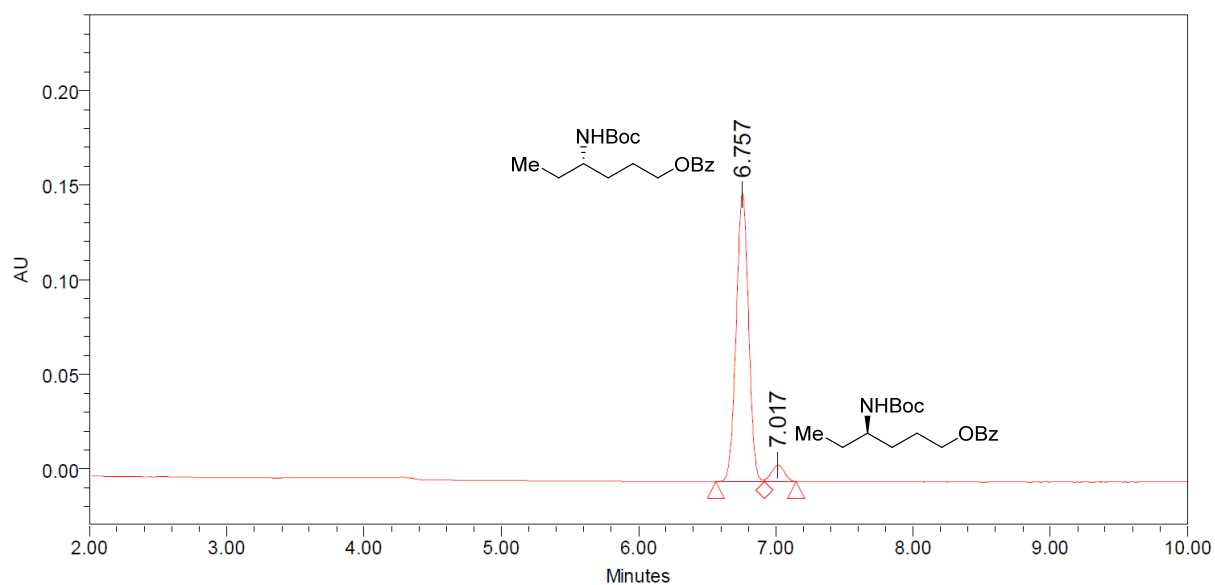
(S)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	14.545	1449640	16390800	95.95
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	15.087	60827	692082	4.05

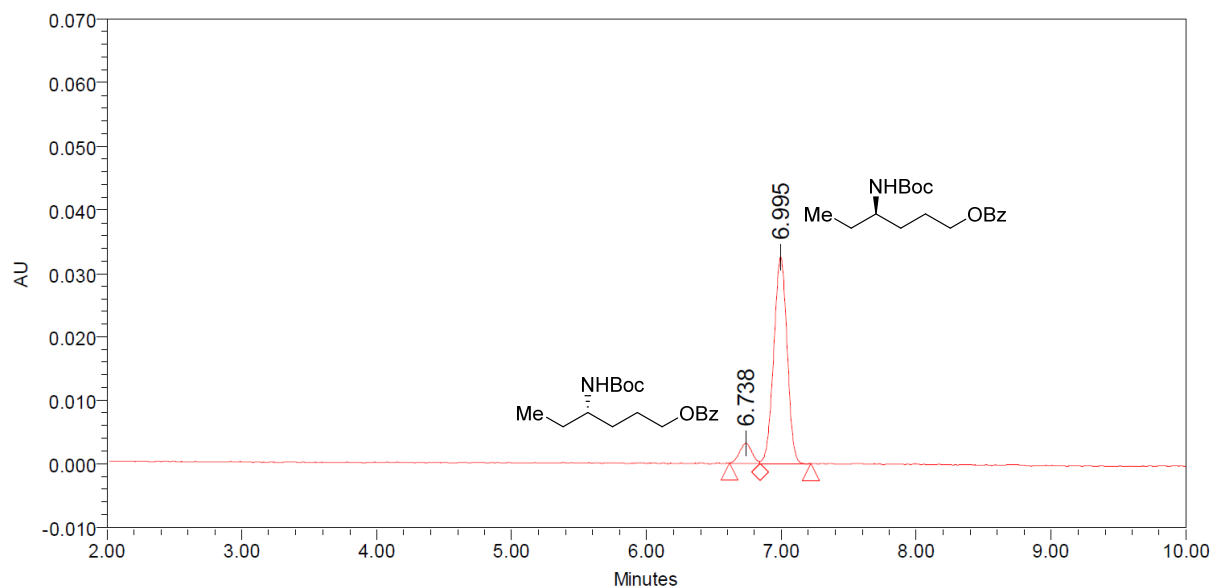


(S)-4-((tert-butoxycarbonyl)amino)hexyl benzoate (59)

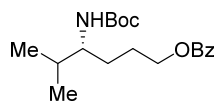


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 226.1 nm (PDA Spectrum (190-410)nm)	6.757	151891	953270	94.46
2	PDA Spectrum PDA 226.1 nm (PDA Spectrum (190-410)nm)	7.017	8556	55898	5.54

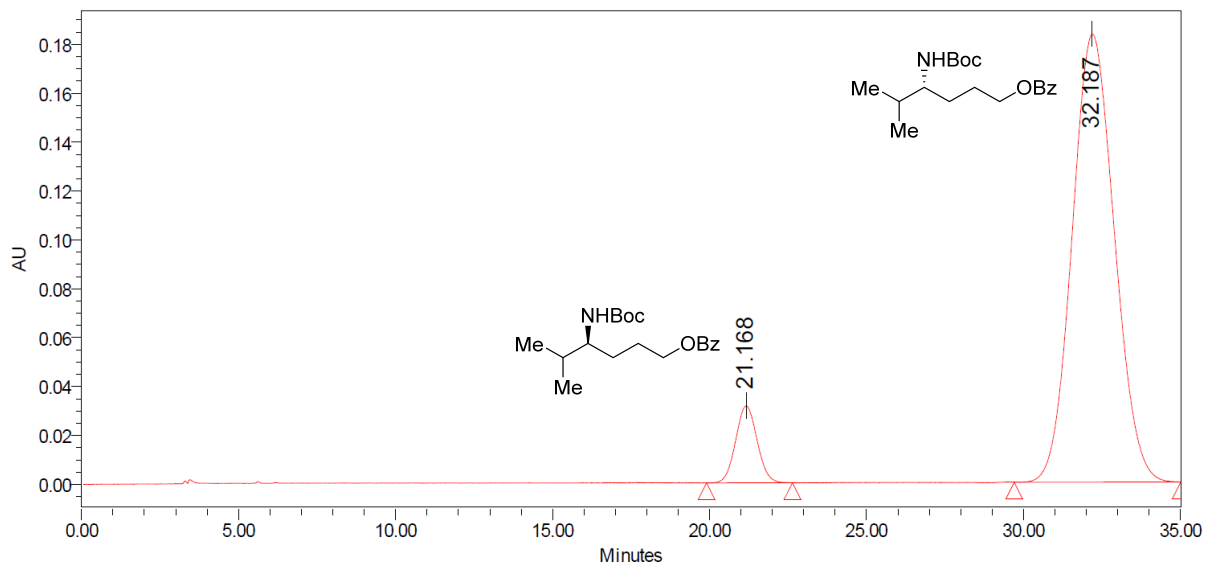
(R)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 226.1 nm (PDA Spectrum (190-410)nm)	6.738	3179	20033	8.19
2	PDA Spectrum PDA 226.1 nm (PDA Spectrum (190-410)nm)	6.995	32616	224432	91.81

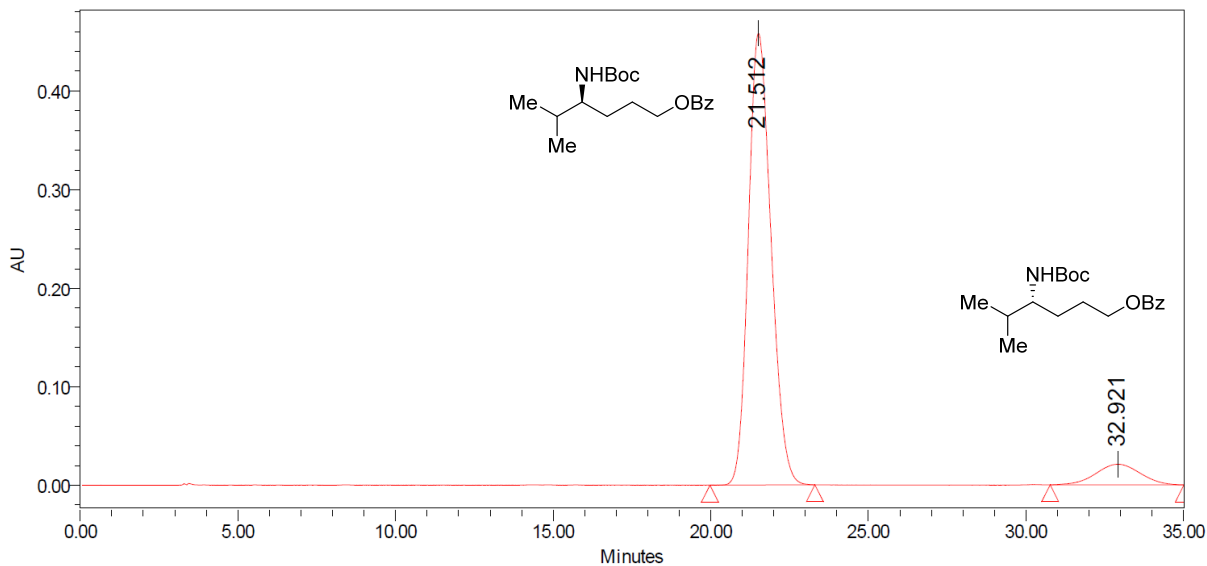


(R)-4-((tert-butoxycarbonyl)amino)-5-methylhexyl benzoate (60)

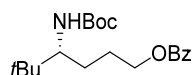


	RT	Area	Height	% Area
1	21.168	1494760	31521	8.02
2	32.187	17136208	183392	91.98

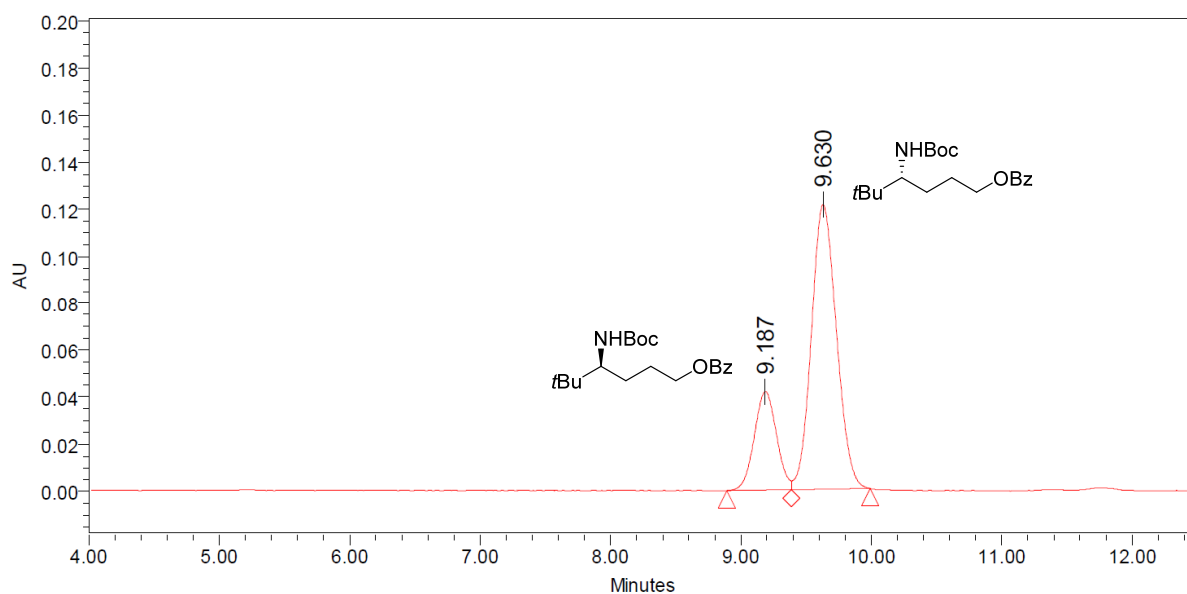
(S)-enantiomer



	RT	Area	Height	% Area
1	21.512	22920023	458077	91.78
2	32.921	2053251	21000	8.22

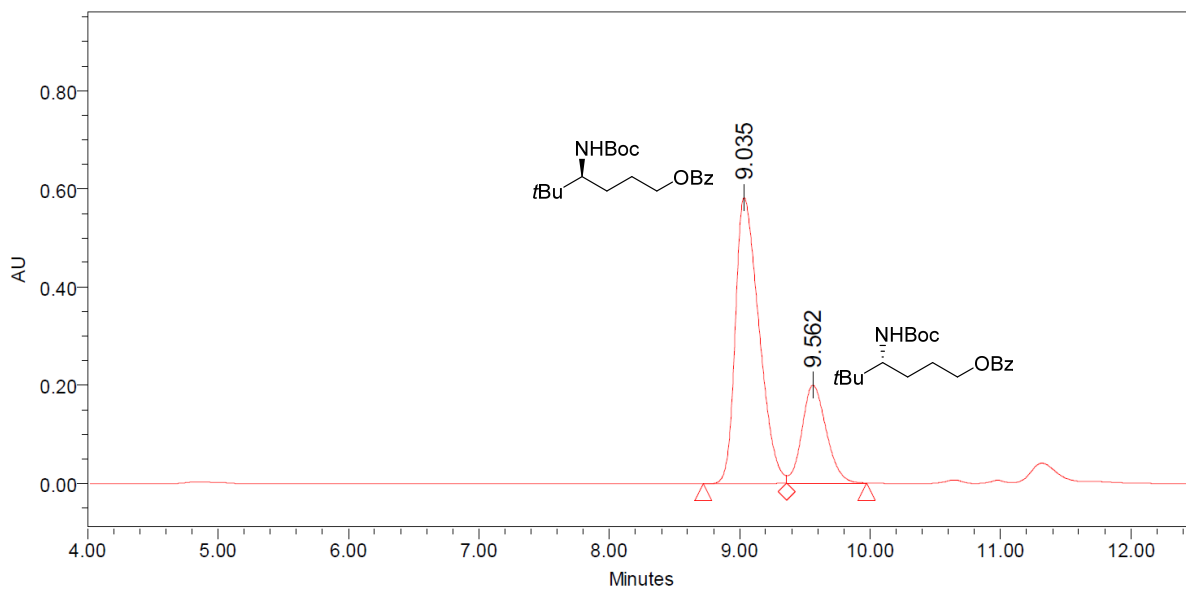


(R)-4-((tert-butoxycarbonyl)amino)-5,5-dimethylhexyl benzoate (61)

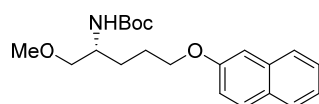


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 228.0 nm (PDA Spectrum (190-410)nm)	9.187	41672	494137	23.43
2	PDA Spectrum PDA 228.0 nm (PDA Spectrum (190-410)nm)	9.630	121022	1614421	76.57

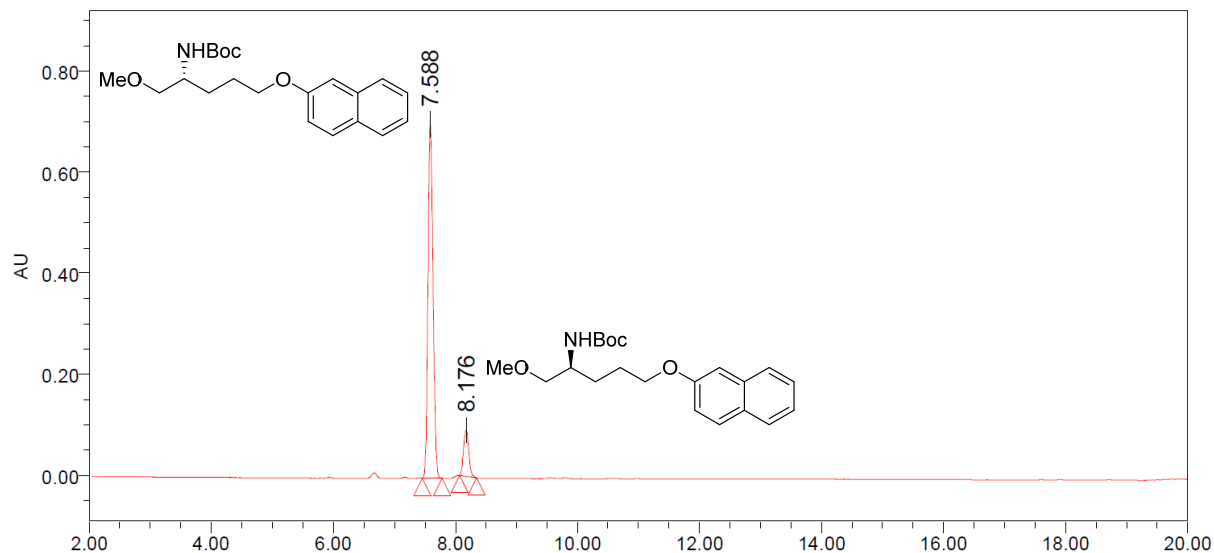
(S)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 228.0 nm (PDA Spectrum (190-410)nm)	9.035	581814	7334021	74.04
2	PDA Spectrum PDA 228.0 nm (PDA Spectrum (190-410)nm)	9.562	199383	2571825	25.96

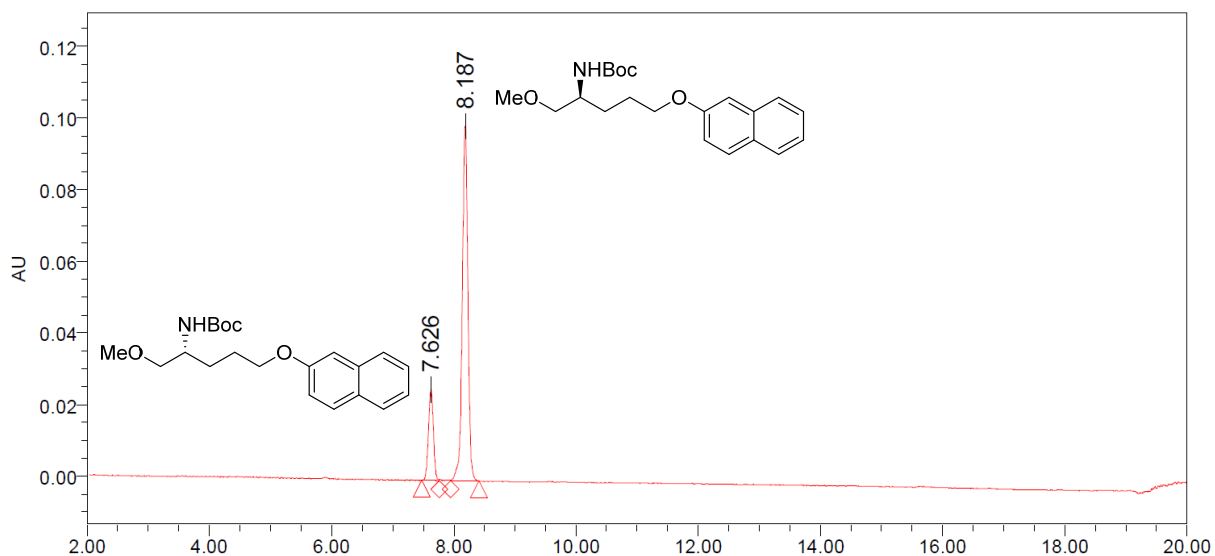


tert-butyl (R)-(1-methoxy-5-(naphthalen-2-yloxy)pentan-2-yl)carbamate (62)

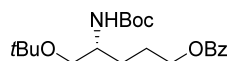


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 268.0 nm (PDA Spectrum (190-410)nm)	7.588	701195	3989888	88.01
2	PDA Spectrum PDA 268.0 nm (PDA Spectrum (190-410)nm)	8.176	92220	543776	11.99

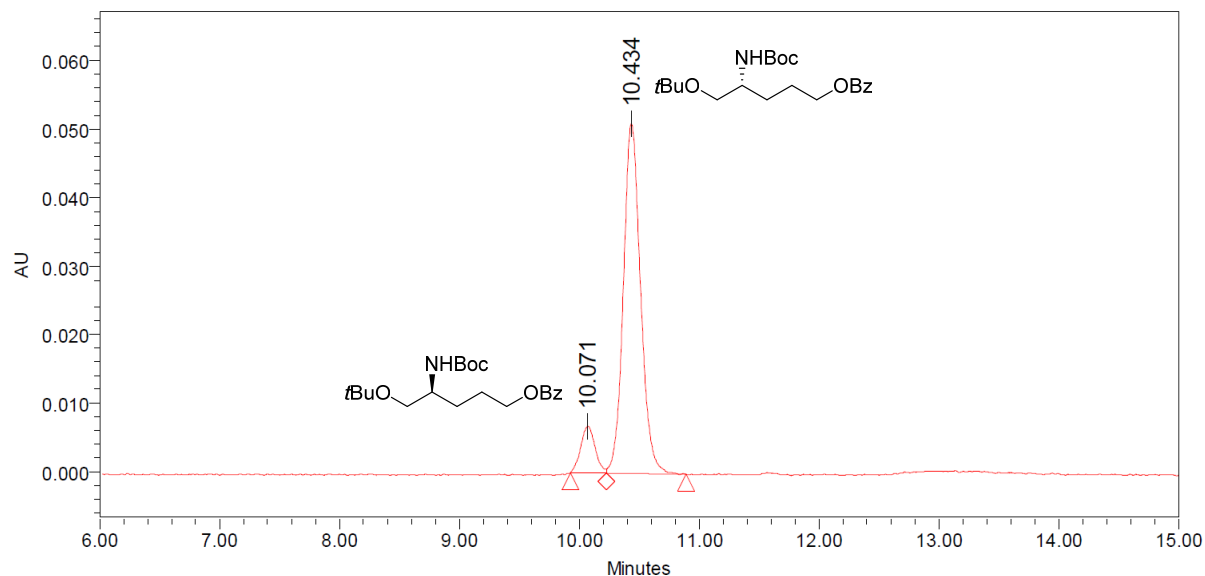
(S)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 268.0 nm (PDA Spectrum (190-410)nm)	7.626	25318	139605	18.20
2	PDA Spectrum PDA 268.0 nm (PDA Spectrum (190-410)nm)	8.187	99004	627617	81.80

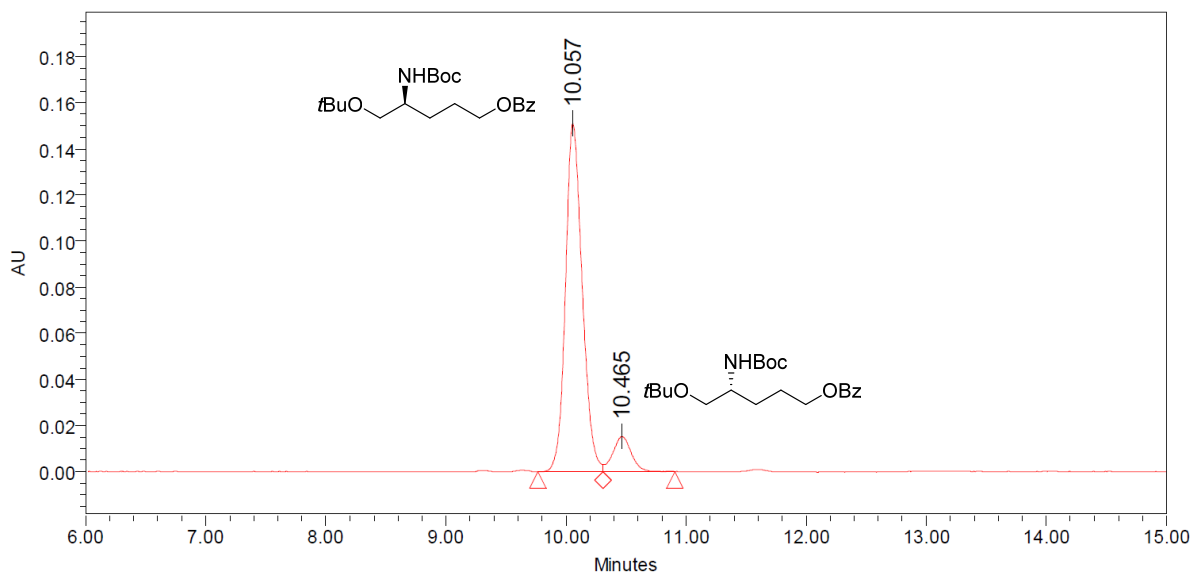


(R)-5-(tert-butoxy)-4-((tert-butoxycarbonyl)amino)pentyl benzoate (63)

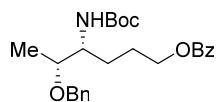


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 230.5 nm (PDA Spectrum (190-410)nm)	10.071	6813	56860	10.04
2	PDA Spectrum PDA 230.5 nm (PDA Spectrum (190-410)nm)	10.434	51083	509542	89.96

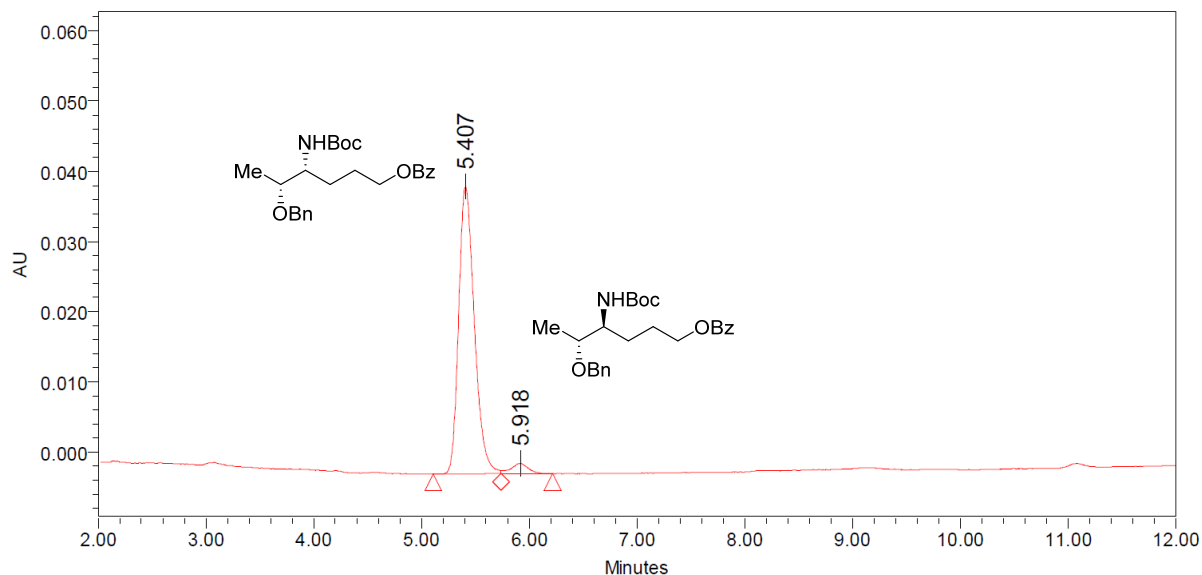
(S)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 230.5 nm (PDA Spectrum (190-410)nm)	10.057	150941	1459877	90.05
2	PDA Spectrum PDA 230.5 nm (PDA Spectrum (190-410)nm)	10.465	15136	161298	9.95

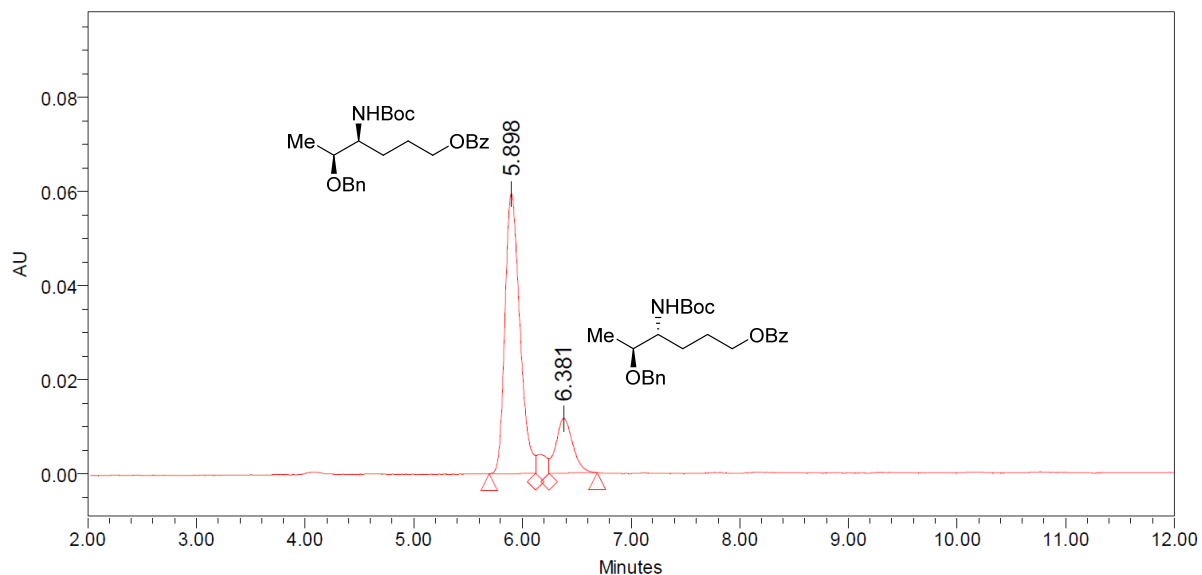


(4R,5S)-5-(benzyloxy)-4-((tert-butoxycarbonyl)amino)hexyl benzoate (64)

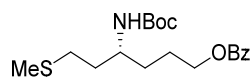


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	5.407	40914	412719	96.26
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	5.918	1444	16049	3.74

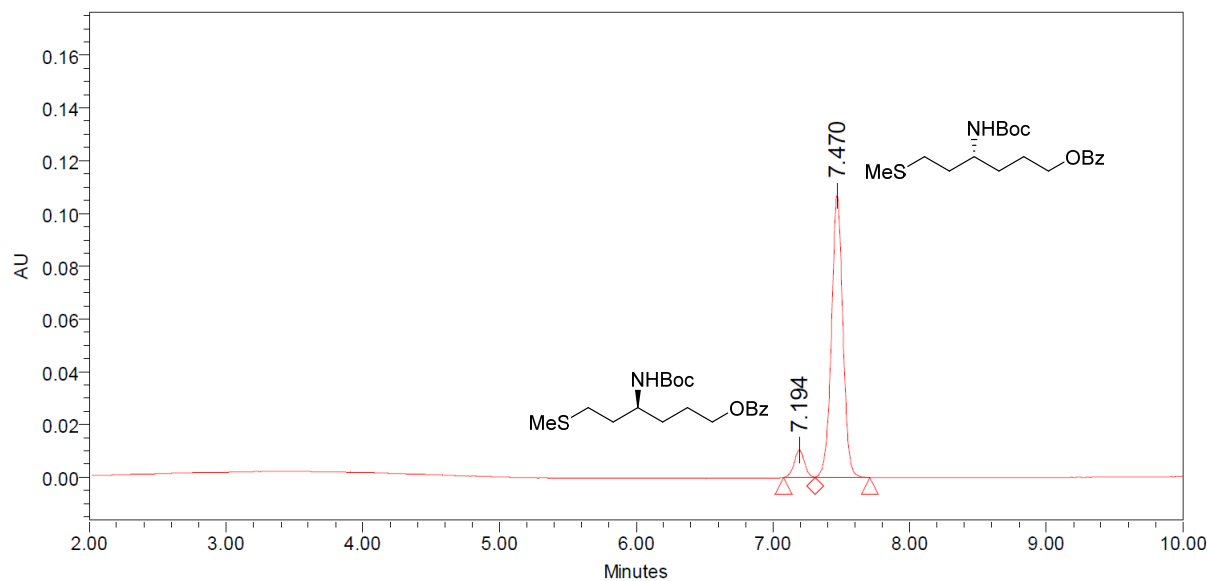
Mixture of diastereomers



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	5.898	59474	567941	82.04
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	6.381	11603	124328	17.96

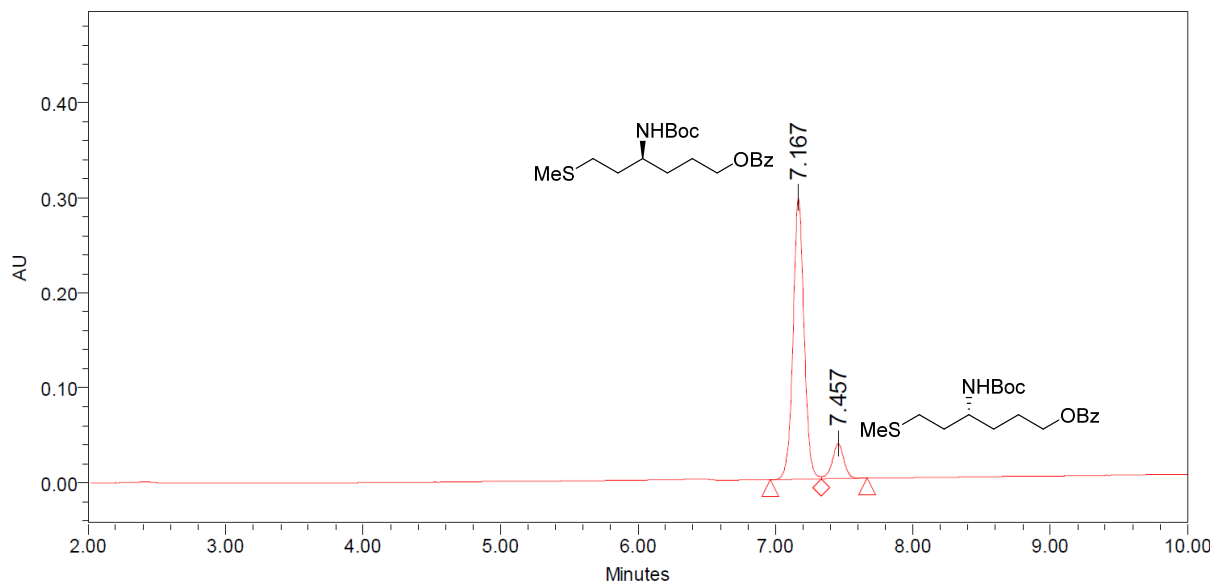


(R)-4-((tert-butoxycarbonyl)amino)-6-(methylthio)hexyl benzoate (65)

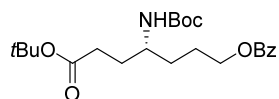


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 230.0 nm (PDA Spectrum (190-410)nm)	7.194	10402	55109	8.14
2	PDA Spectrum PDA 230.0 nm (PDA Spectrum (190-410)nm)	7.470	106951	622150	91.86

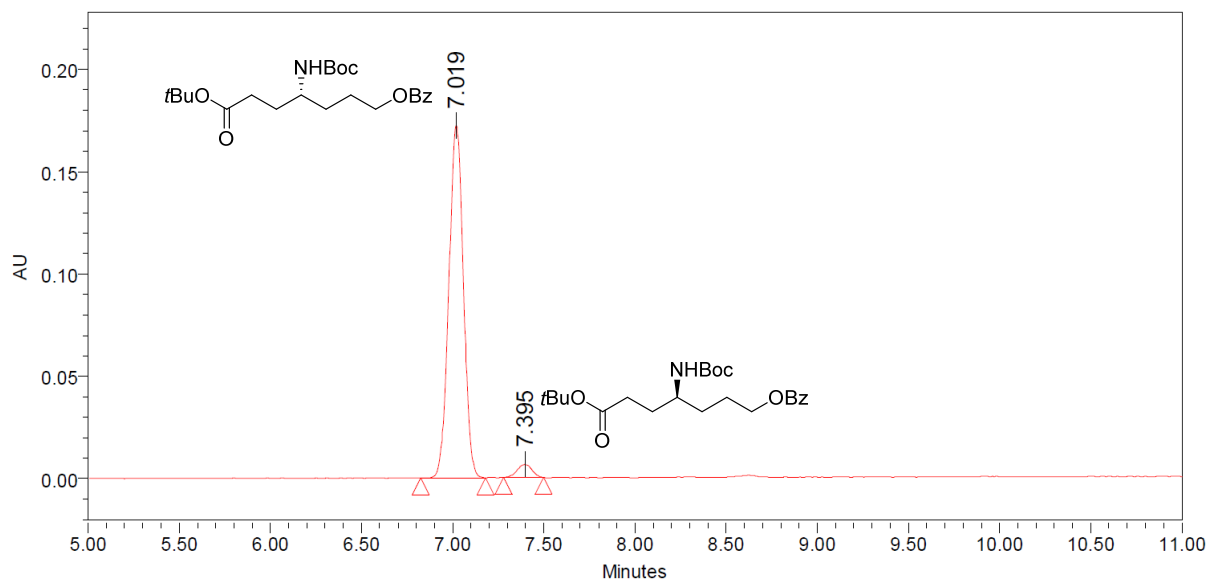
(S)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 230.0 nm (PDA Spectrum (190-410)nm)	7.167	297047	1651125	88.42
2	PDA Spectrum PDA 230.0 nm (PDA Spectrum (190-410)nm)	7.457	36919	216245	11.58

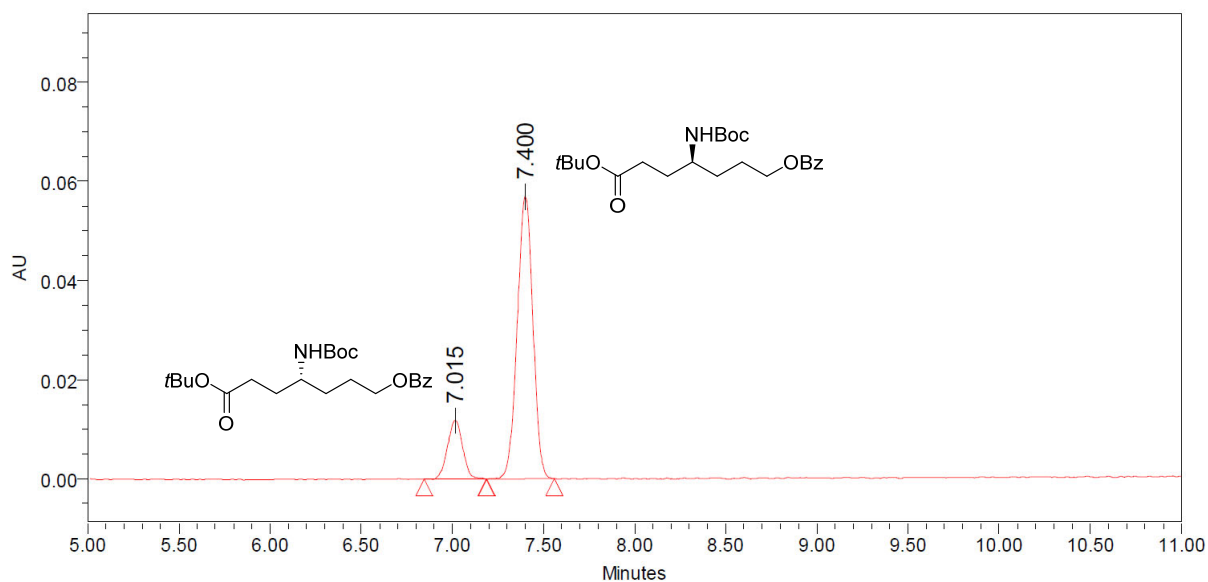


(R)-7-(tert-butoxy)-4-((tert-butoxycarbonyl)amino)-7-oxoheptyl benzoate (66)

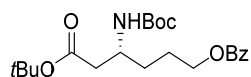


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 224.0 nm (PDA Spectrum (190-410)nm)	7.019	172309	956800	96.42
2	PDA Spectrum PDA 224.0 nm (PDA Spectrum (190-410)nm)	7.395	6284	35499	3.58

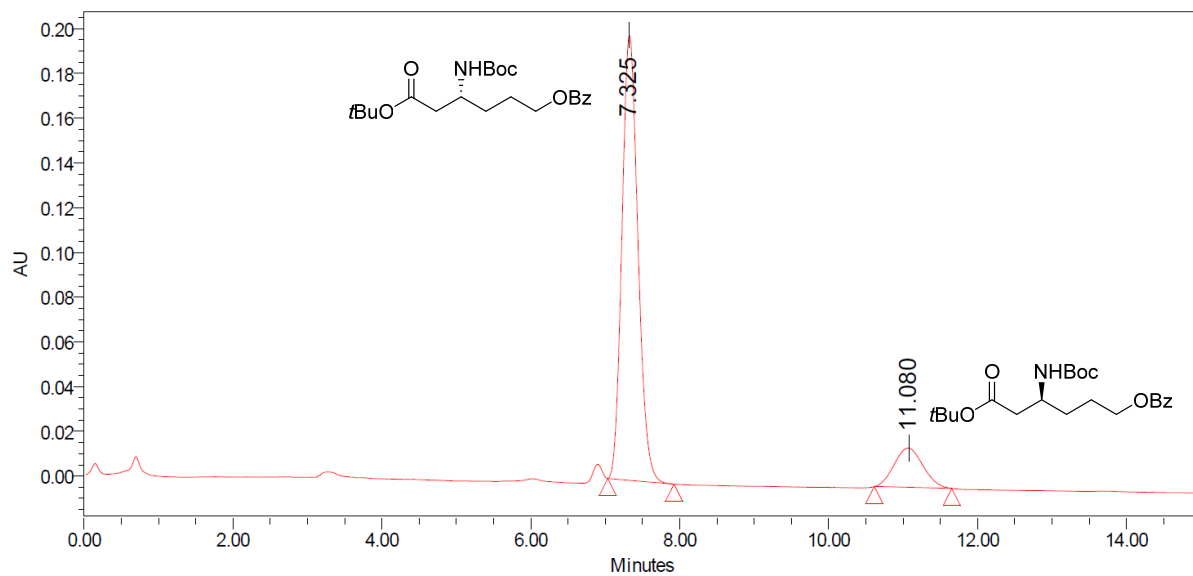
(S)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 224.0 nm (PDA Spectrum (190-410)nm)	7.015	11850	68961	16.81
2	PDA Spectrum PDA 224.0 nm (PDA Spectrum (190-410)nm)	7.400	56951	341284	83.19

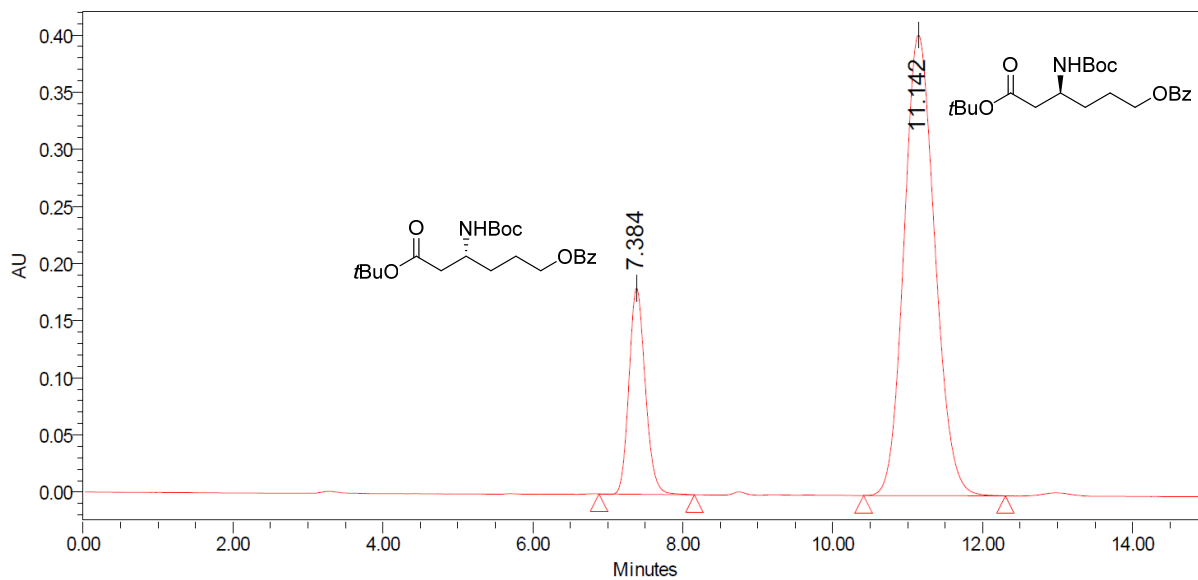


(R)-6-(tert-butoxy)-4-((tert-butoxycarbonyl)amino)-6-oxohexyl benzoate (67)

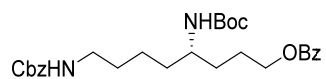


	RT	Area	Height	% Area
1	7.325	2973315	199056	86.30
2	11.080	472145	17516	13.70

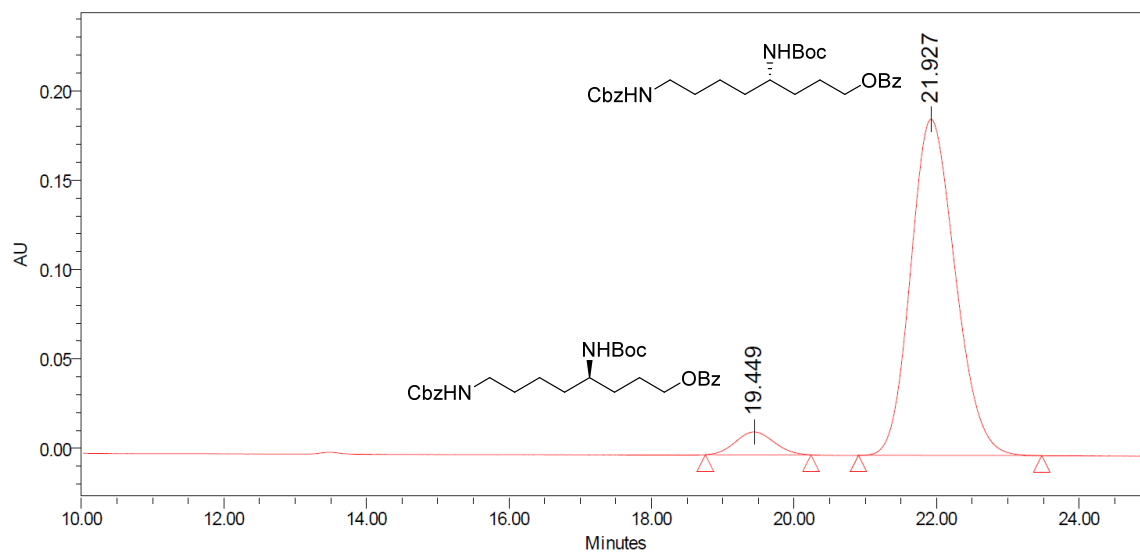
(S)-enantiomer



	RT	Area	Height	% Area
1	7.384	2727696	180423	19.10
2	11.142	11555081	403062	80.90

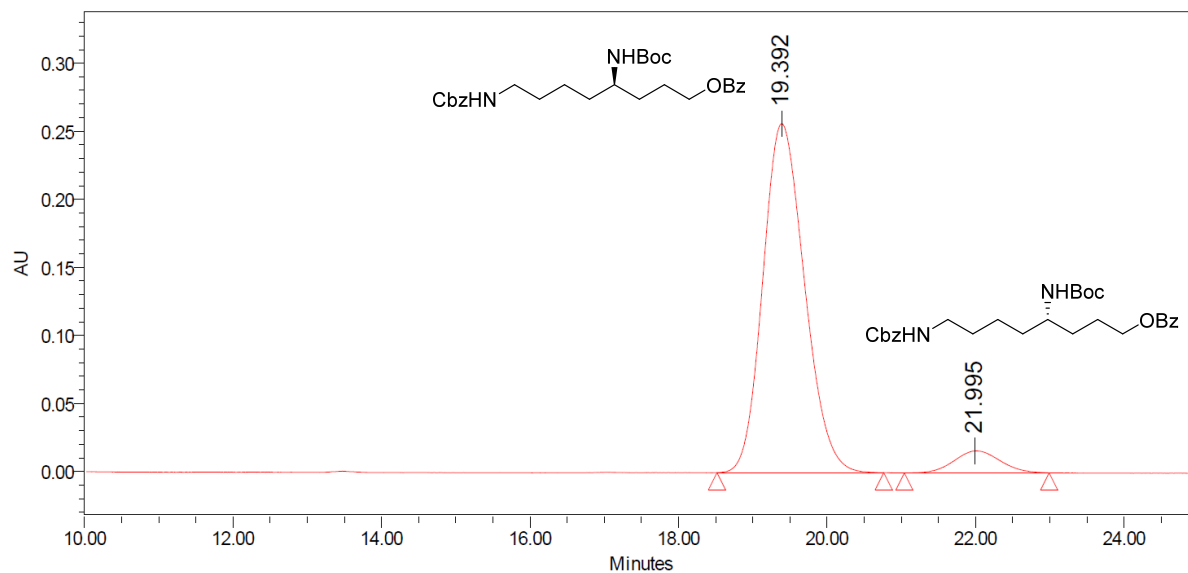


(S)-8-(((benzyloxy)carbonyl)amino)-4-((tert-butoxycarbonyl)amino)octyl benzoate (68)

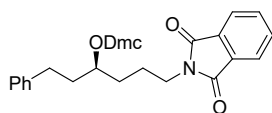


	RT	Area	Height	% Area
1	19.449	478543	12789	5.54
2	21.927	8164419	188032	94.46

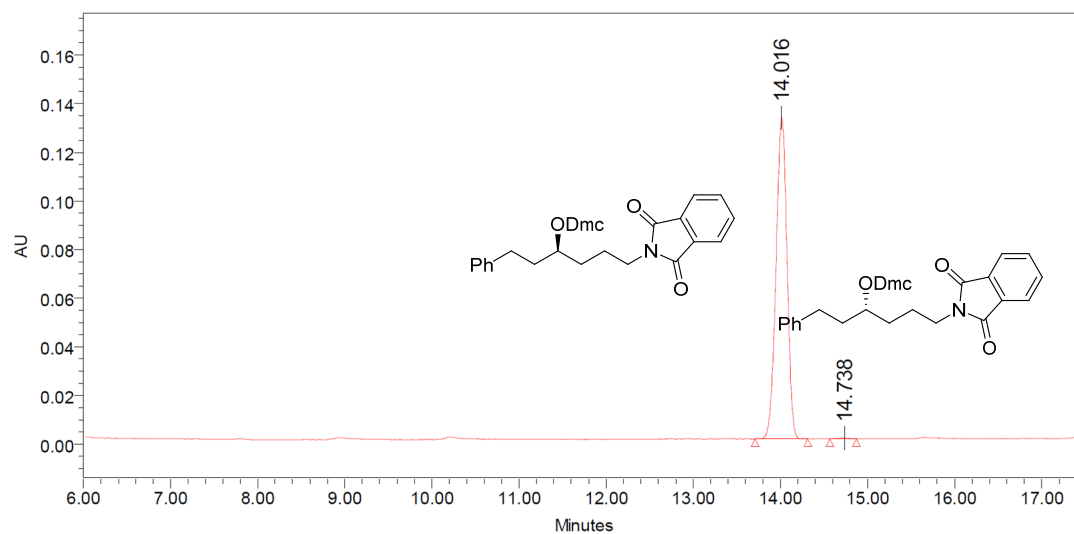
(R)-enantiomer



	RT	Area	Height	% Area
1	19.392	9986782	256513	93.50
2	21.995	694433	16216	6.50

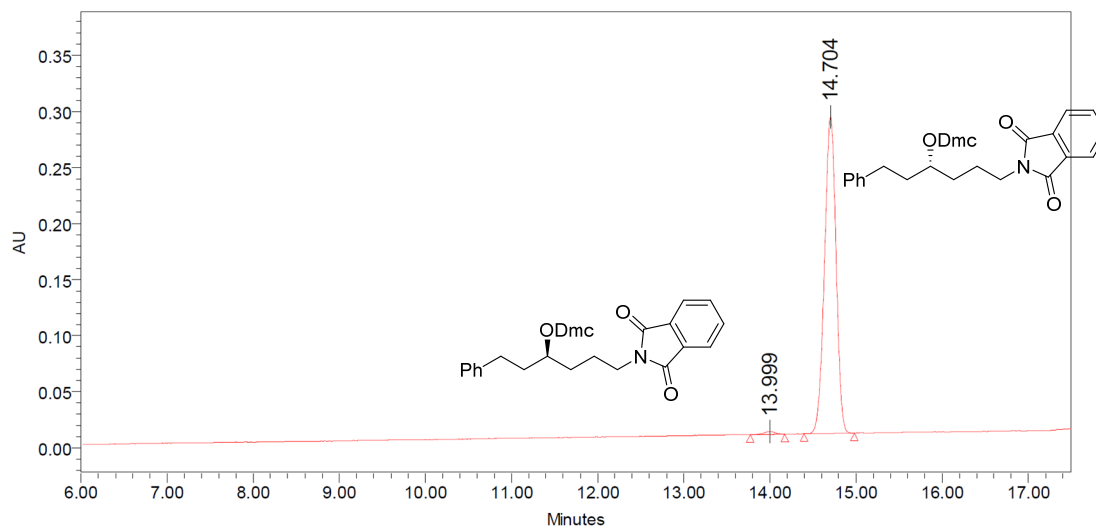


(R)-6-(1,3-dioxoisindolin-2-yl)-1-phenylhexan-3-yl dimethylcarbamate (69)

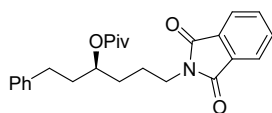


	Processed Channel Descr.	RT	Area	Height	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	14.016	1158691	132143	99.70
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	14.738	3460	374	0.30

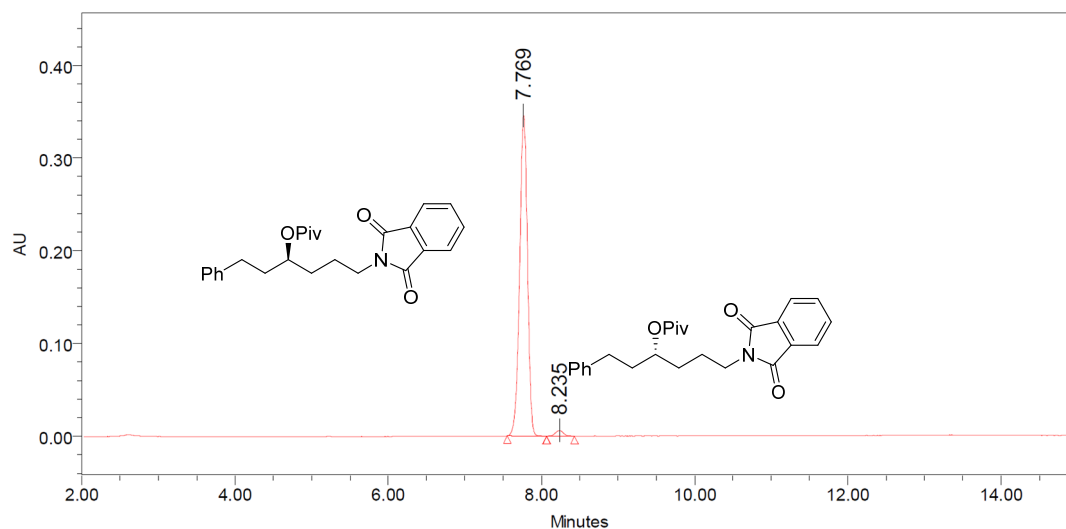
(S)-enantiomer



	Processed Channel Descr.	RT	Area	Height	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	13.999	24124	2645	0.91
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	14.704	2628440	282528	99.09

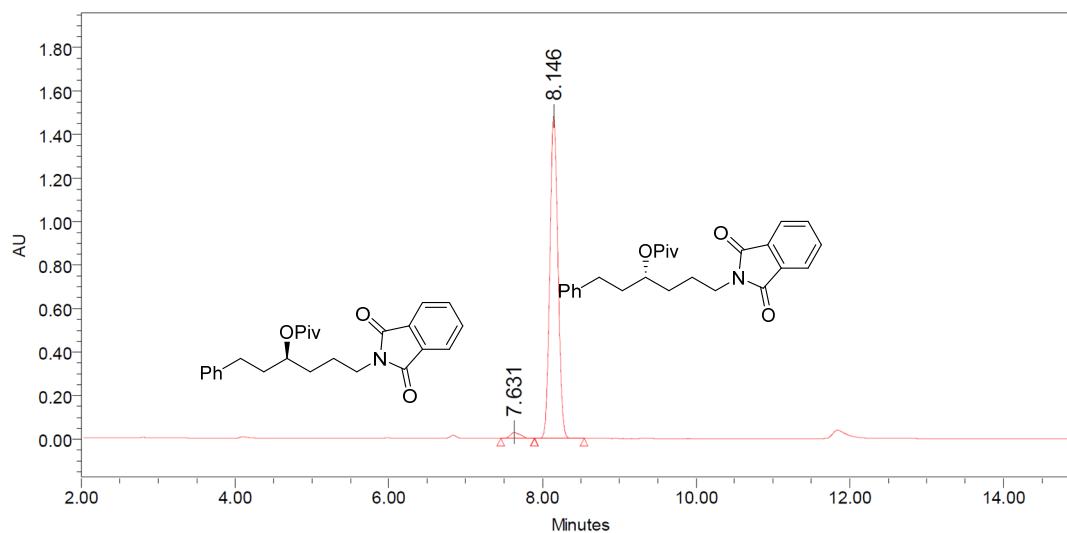


(R)-6-(1,3-dioxoisindolin-2-yl)-1-phenylhexan-3-yl pivalate (70)

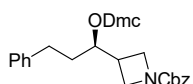


	Processed Channel Descr.	RT	Area	Height	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	7.769	2465847	345621	98.21
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	8.235	45065	6183	1.79

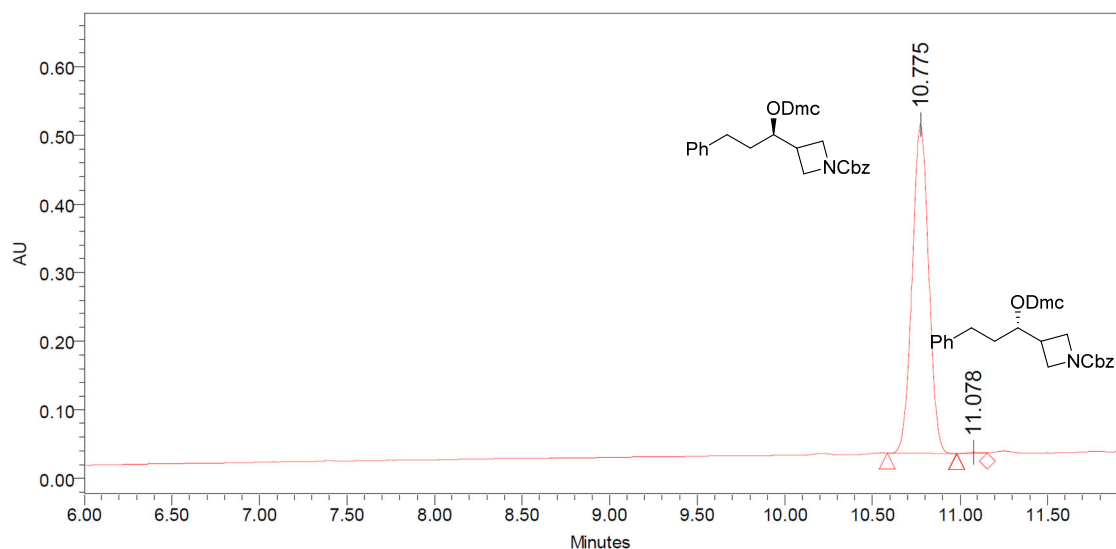
(S)-enantiomer



	Processed Channel Descr.	RT	Area	Height	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	7.631	260650	27950	2.35
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	8.146	10846222	1481224	97.65

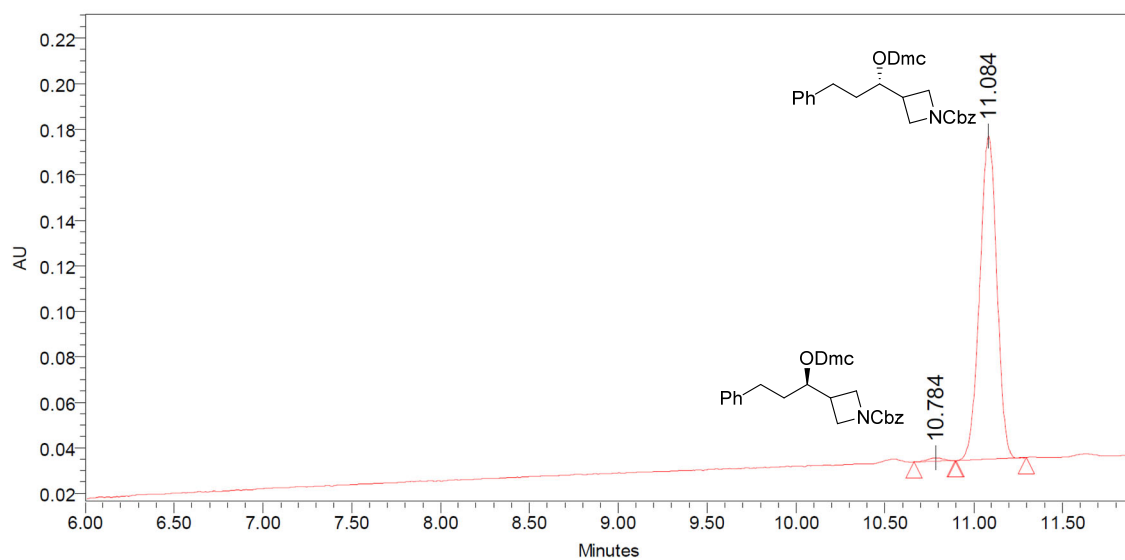


benzyl (*R*)-3-(1-((dimethylcarbamoyl)oxy)-3-phenylpropyl)azetidine-1-carboxylate (73)



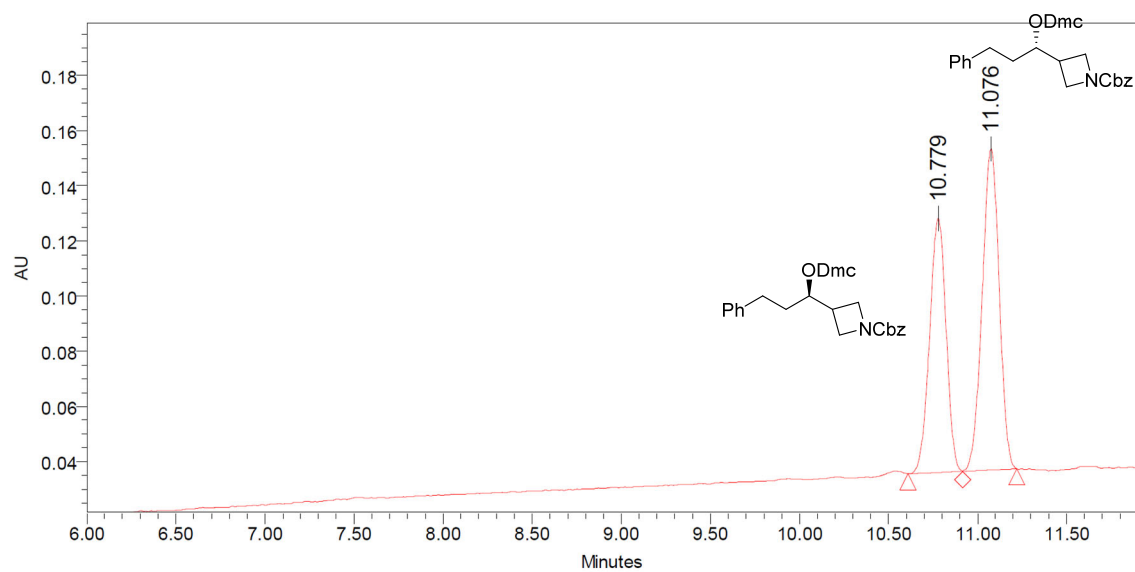
	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	10.775	479616	3139796	99.72
2	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	11.078	1426	8792	0.28

(*S*)-enantiomer

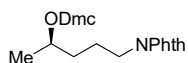


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	10.784	1495	9017	0.94
2	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	11.084	142090	952229	99.06

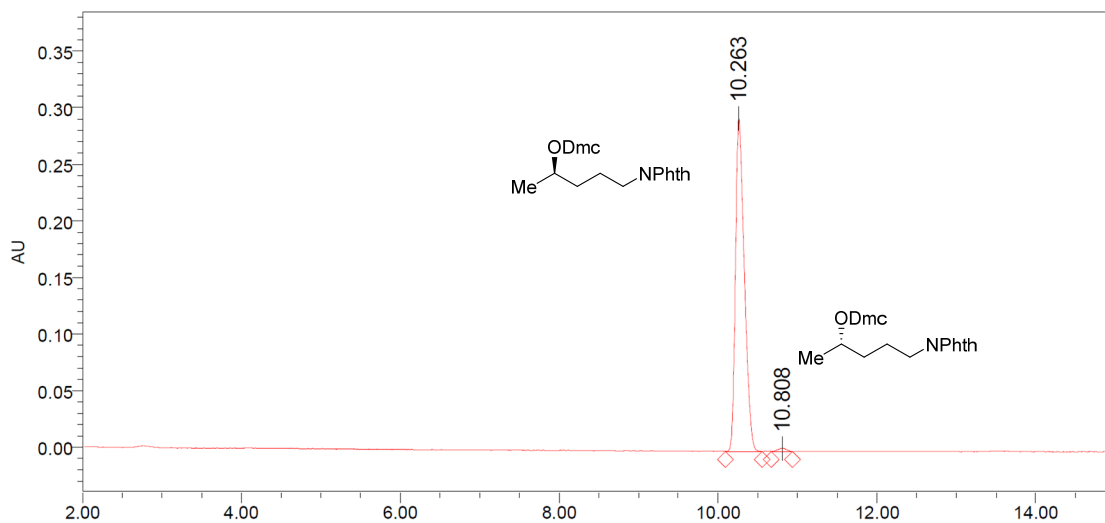
Racemic mixture



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	10.779	92235	592965	43.37
2	PDA Spectrum PDA 214.0 nm (PDA Spectrum (190-410)nm)	11.076	116505	774271	56.63

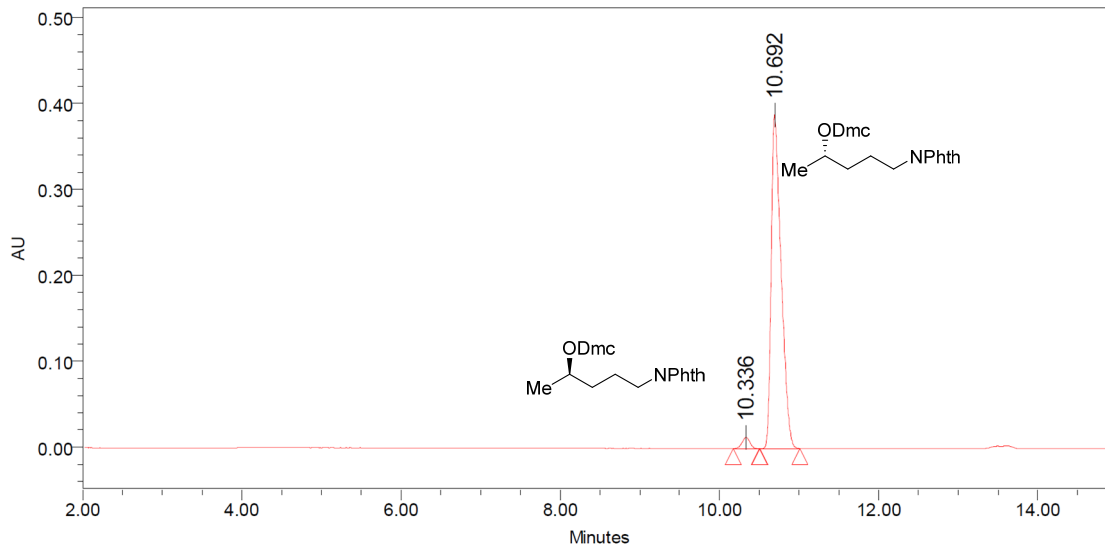


(R)-5-(1,3-dioxoisindolin-2-yl)pentan-2-yl dimethylcarbamate (74)

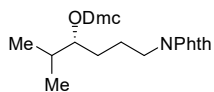


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 291.0 nm (PDA Spectrum (190-410)nm)	10.263	294302	2281083	99.10
2	PDA Spectrum PDA 291.0 nm (PDA Spectrum (190-410)nm)	10.808	2683	20695	0.90

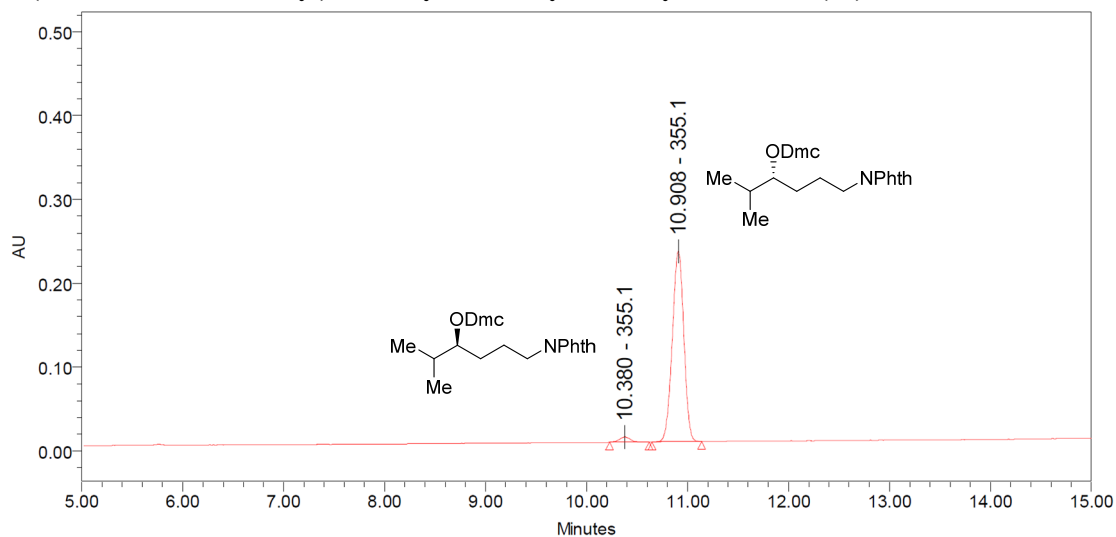
(S)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 291.0 nm (PDA Spectrum (190-410)nm)	10.336	12739	84734	2.46
2	PDA Spectrum PDA 291.0 nm (PDA Spectrum (190-410)nm)	10.692	388441	3366157	97.54

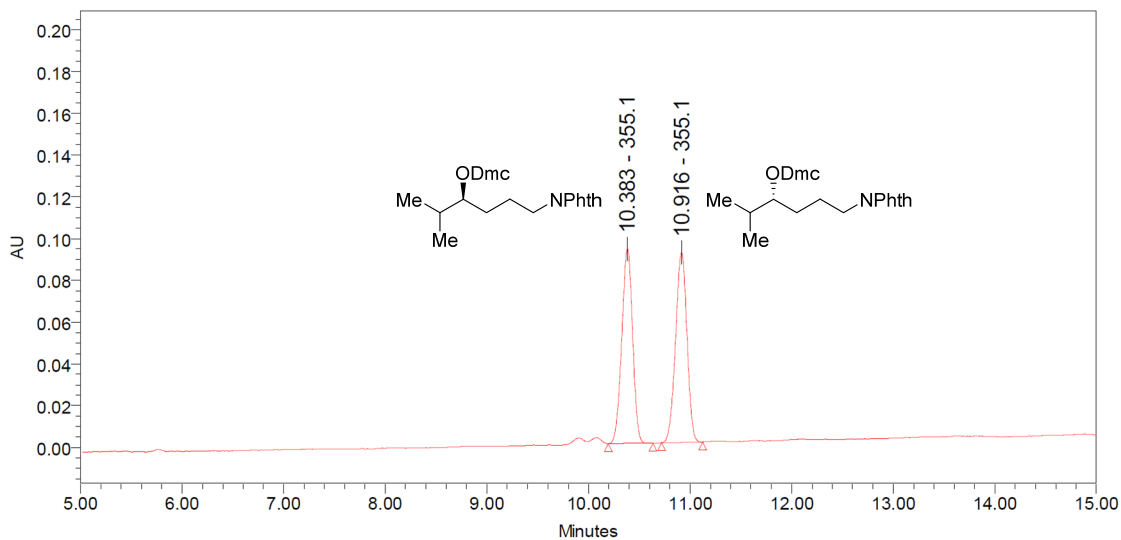


(S)-6-(1,3-dioxoisindolin-2-yl)-2-methylhexan-3-yl dimethylcarbamate (75)

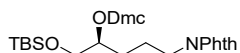


	Processed Channel Descr.	RT	Area	Height	% Area
1	PDA Spectrum PDA 218.0 nm (PDA Spectrum (190-410)nm)	10.380	45478	6091	2.46
2	PDA Spectrum PDA 218.0 nm (PDA Spectrum (190-410)nm)	10.908	1801400	227426	97.54

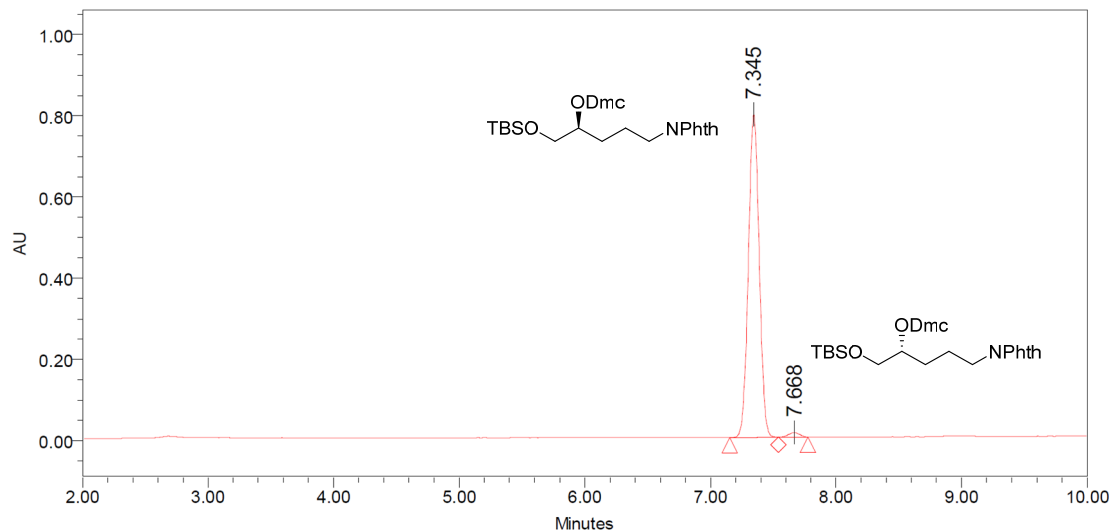
Racemate



	Processed Channel Descr.	RT	Area	Height	% Area
1	PDA Spectrum PDA 218.0 nm (PDA Spectrum (190-410)nm)	10.383	691583	93216	49.32
2	PDA Spectrum PDA 218.0 nm (PDA Spectrum (190-410)nm)	10.916	710605	90995	50.68

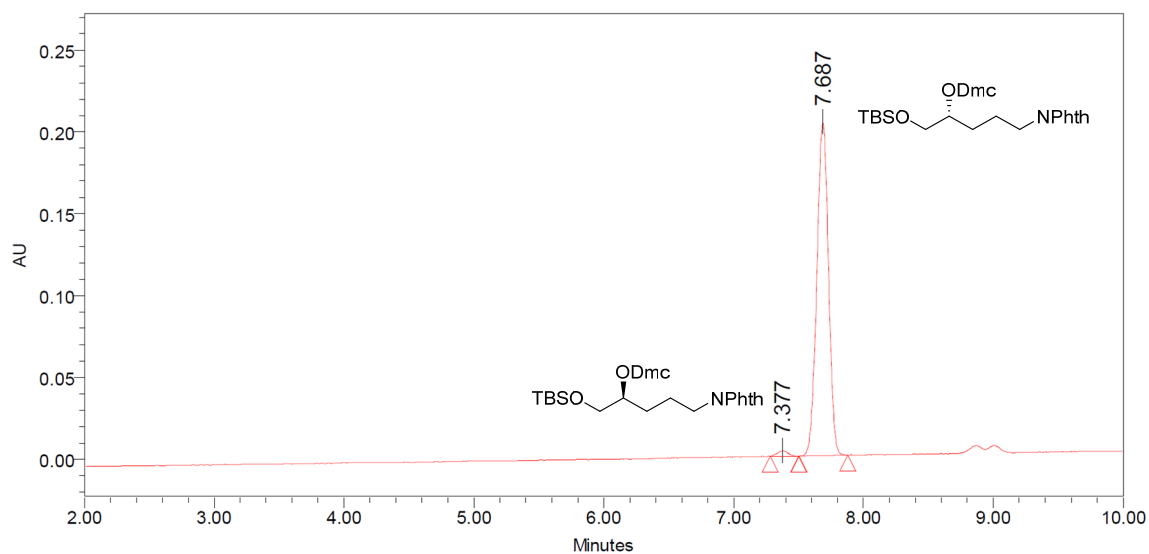


(S)-1-((*tert*-butyldimethylsilyl)oxy)-5-(1,3-dioxoisindolin-2-yl)pentan-2-yl dimethylcarbamate (76)

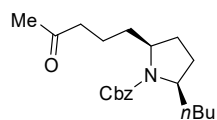


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	7.345	795406	4771410	98.62
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	7.668	10912	66603	1.38

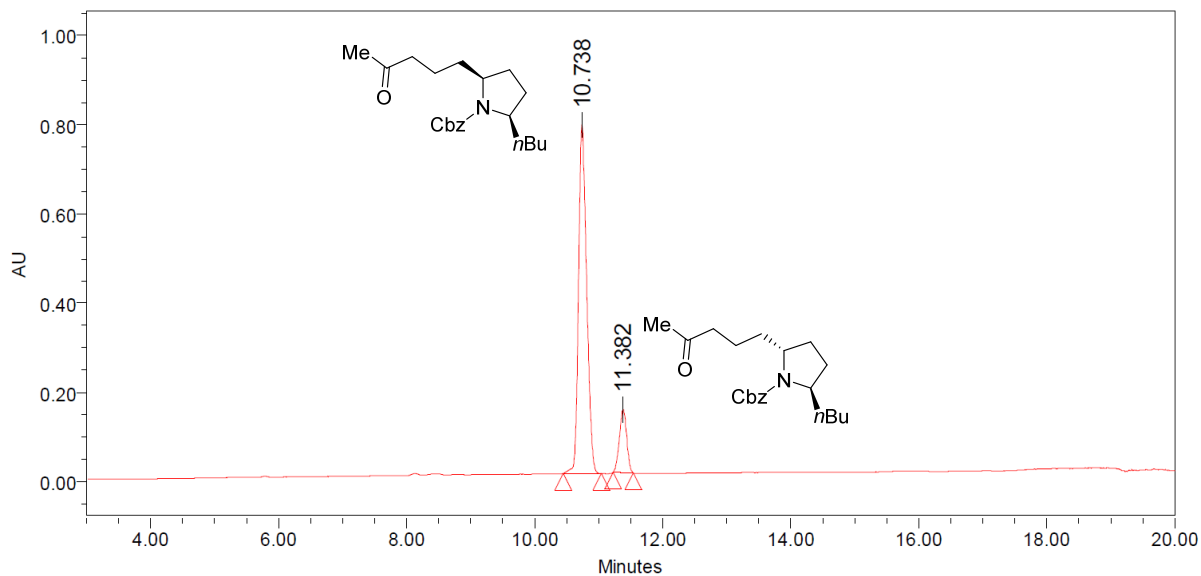
(R)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	7.377	3216	18296	1.42
2	PDA Spectrum PDA 220.0 nm (PDA Spectrum (190-410)nm)	7.687	203906	1267037	98.58

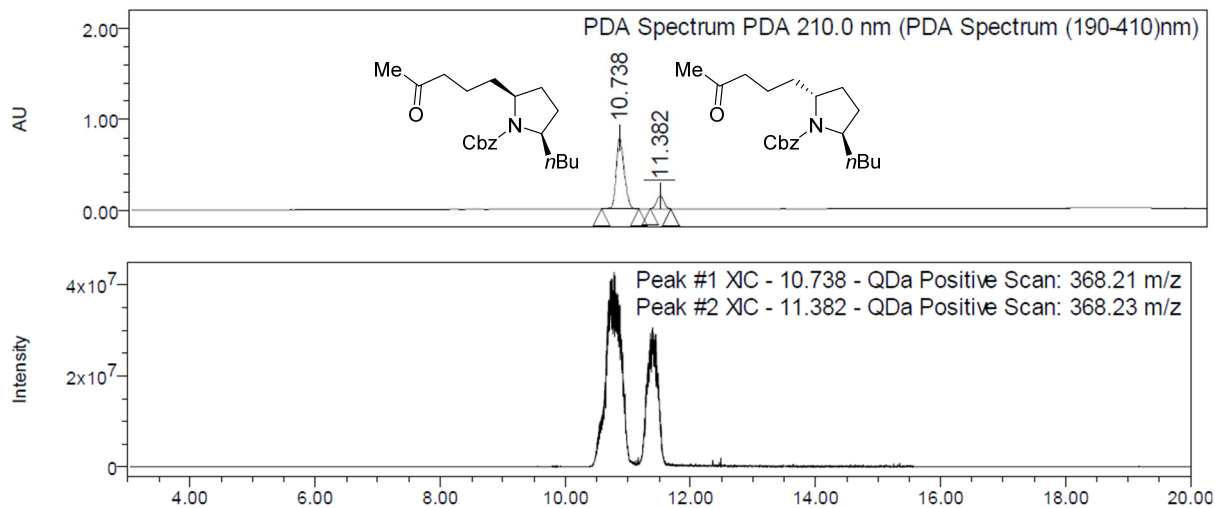


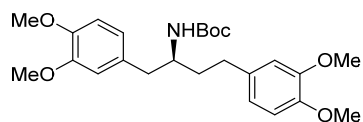
benzyl (2R,5S)-2-butyl-5-(4-oxopentyl)pyrrolidine-1-carboxylate (81)



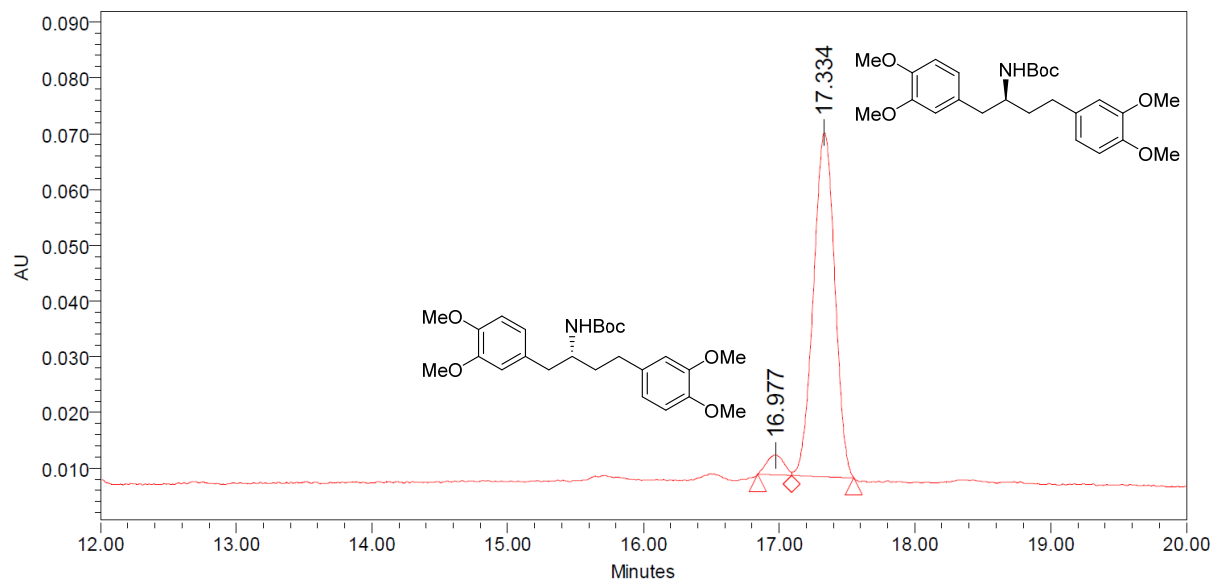
	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 210.0 nm (PDA Spectrum (190-410)nm)	10.738	781883	6853941	85.90
2	PDA Spectrum PDA 210.0 nm (PDA Spectrum (190-410)nm)	11.382	141271	1124604	14.10

Mass analysis



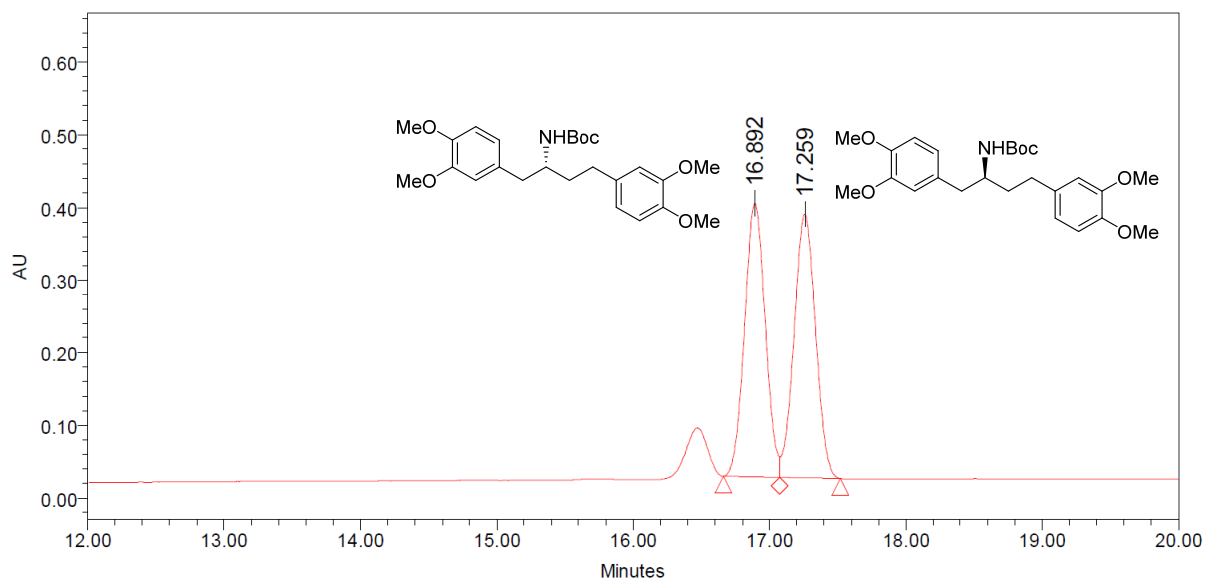


tert-butyl (S)-(1,4-bis(3,4-dimethoxyphenyl)butan-2-yl)carbamate (85)

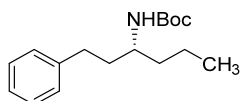


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	16.977	3527	31244	4.43
2	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	17.334	61762	673371	95.57

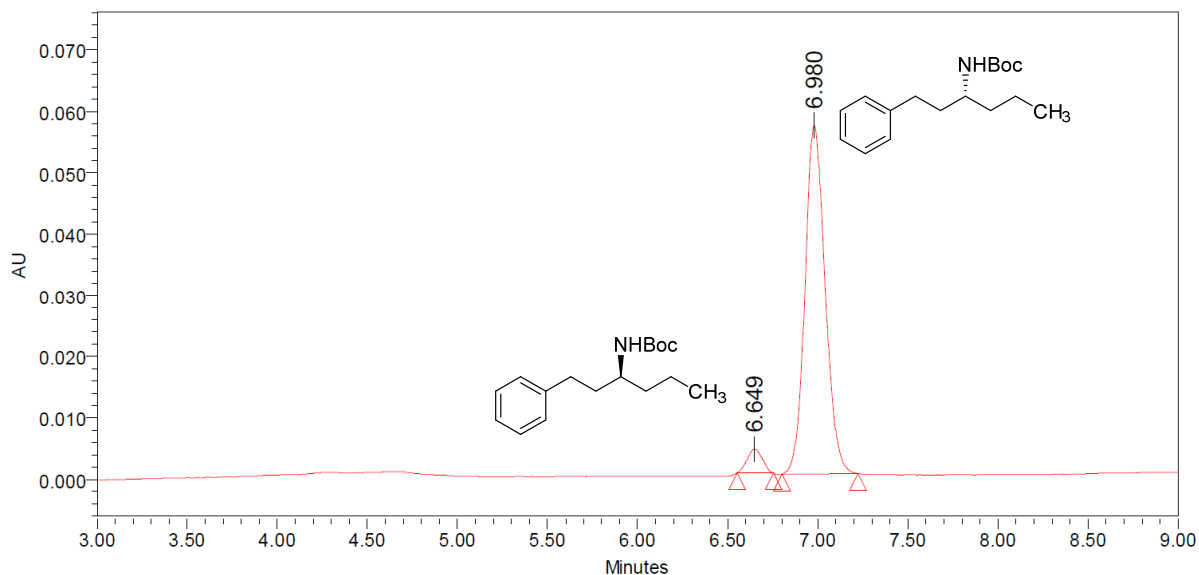
Racemate



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 210.0 nm (PDA Spectrum (190-410)nm)	16.892	377038	3965639	49.99
2	PDA Spectrum PDA 210.0 nm (PDA Spectrum (190-410)nm)	17.259	363035	3967681	50.01

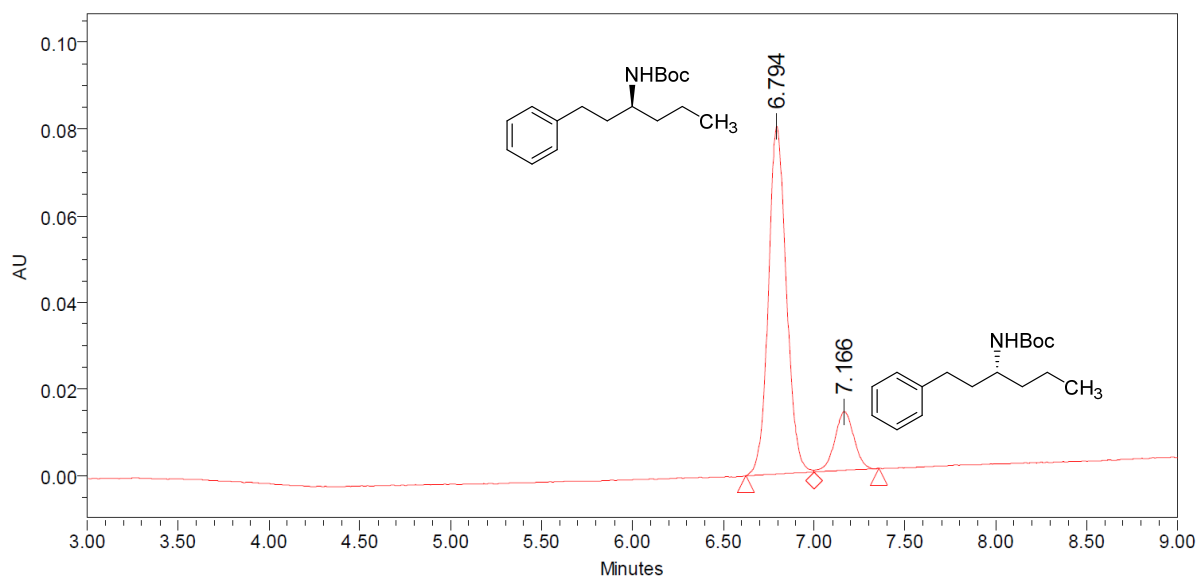


tert-butyl (R)-(1-phenylhexan-3-yl)carbamate (89)

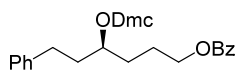


	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	6.649	3857	22941	4.93
2	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	6.980	56855	441956	95.07

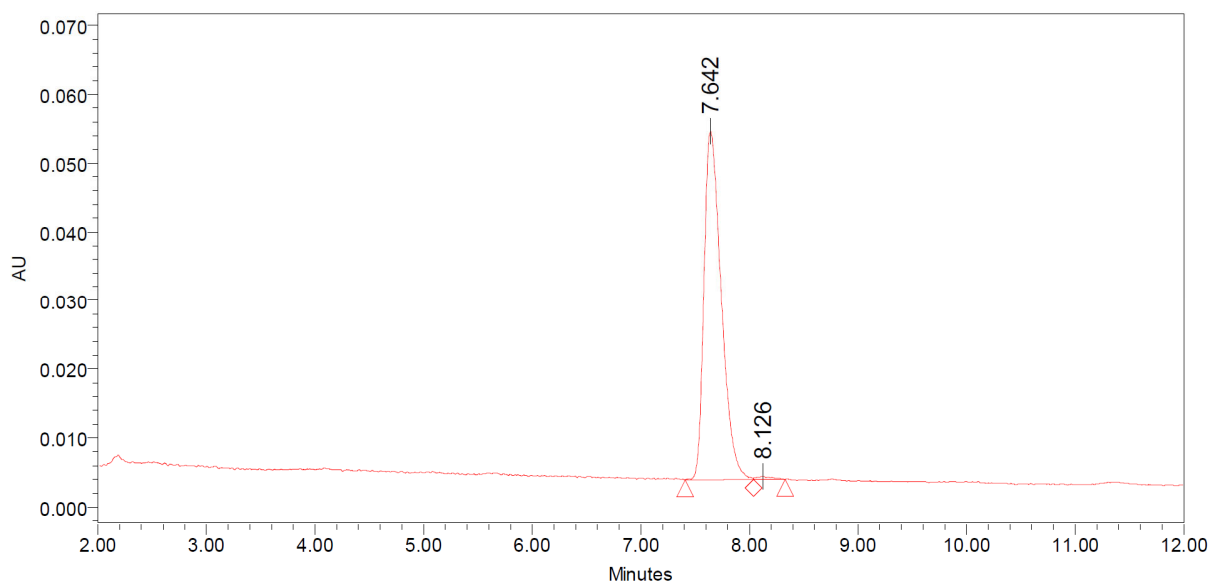
(R)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	6.794	80294	552622	84.80
2	PDA Spectrum PDA 215.0 nm (PDA Spectrum (190-410)nm)	7.166	13488	99043	15.20

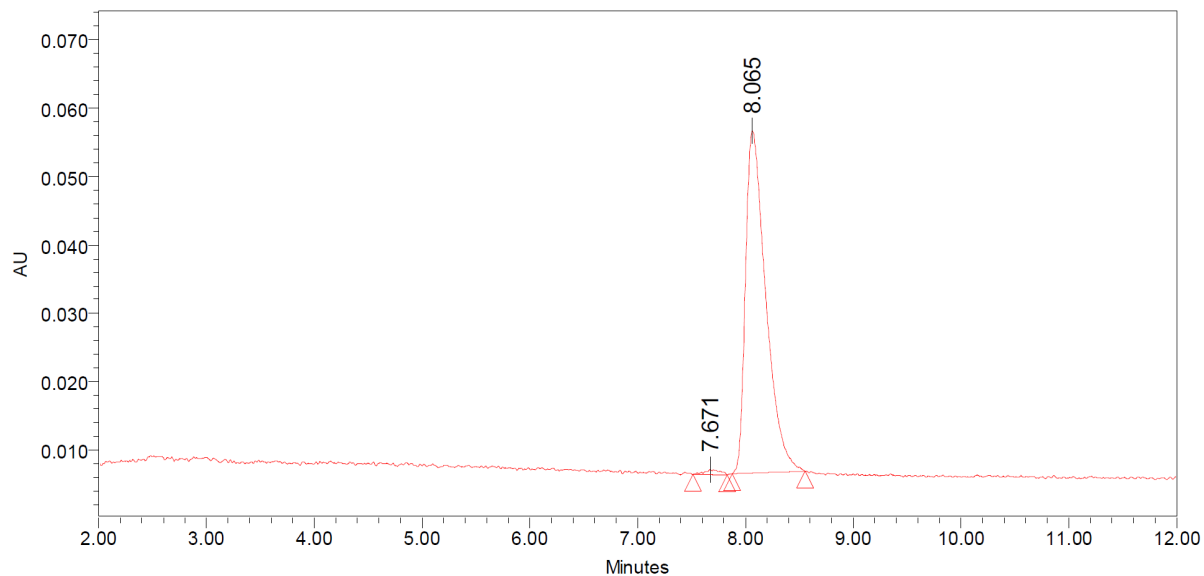


(R)-4-((dimethylcarbamoyl)oxy)-6-phenylhexyl benzoate (94)



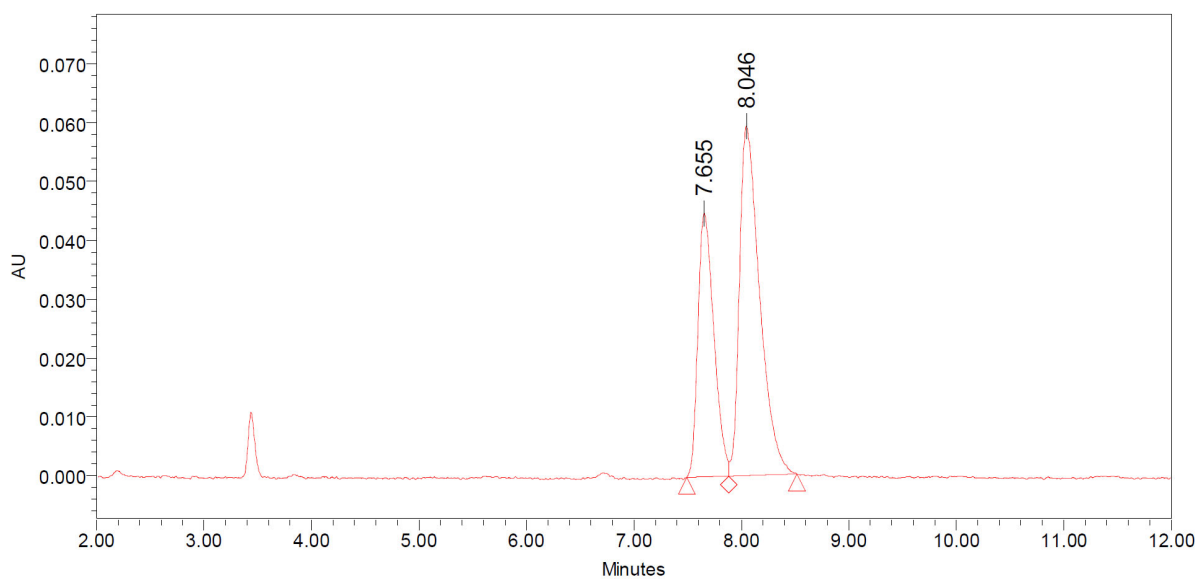
	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-410)nm)	7.642	50665	558342	99.21
2	PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-410)nm)	8.126	467	4451	0.79

(S)-enantiomer



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-410)nm)	7.671	763	7337	1.11
2	PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-410)nm)	8.065	50038	654770	98.89

mixture of (R)- and (S)- enantiomers



	Processed Channel	Retention Time (min)	Height	Area	% Area
1	PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-410)nm)	7.655	44774	461103	37.29
2	PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-410)nm)	8.046	59372	775341	62.71

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