

Supporting Information

Quinim: a New Ligand Scaffold Enabled Nickel-Catalyzed Enantioselective Synthesis of α -Alkylated γ -Lactam

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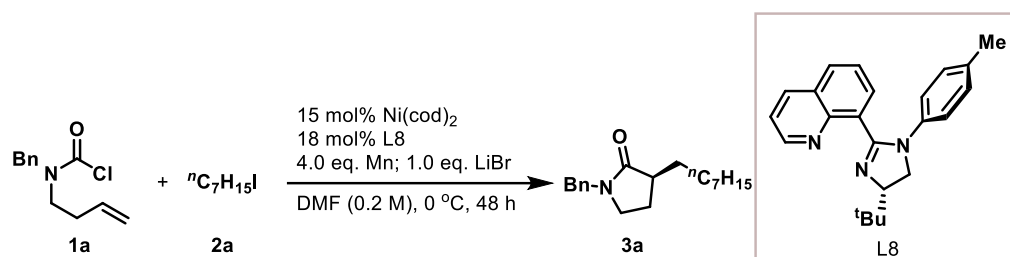
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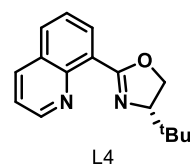
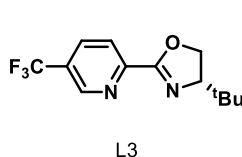
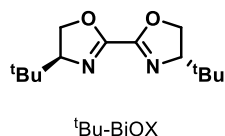
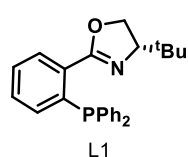
General information

All reactions were carried out under nitrogen atmosphere and anhydrous conditions unless otherwise indicated. All manipulations of air- sensitive or moisture-sensitive compounds were performed in a glovebox under an atmosphere of nitrogen. Unless otherwise noted, all catalytic reactions were run in dried glassware. Toluene and THF were distilled from sodium/benzophenone. DCM was distilled over CaH₂. Ni(cod)₂ (CAS 1295-35-8) was purchased from Sinocompound. Manganese powder (7439-96-5, 325 mesh) was purchased from Alfa Aesar; LiBr (7550-35-8) and C₇H₁₅I (4282-40-0) were purchased from Adamas. *N,N*-Dimethylformamide (DMF, CAS 68-12-2) was purchased from Adamas (99.8%, SafeDry, with molecular sieves, Water ≤ 50 ppm (by K.F.), SafeSeal); Other commercial reagents were purchased from Bidepharm, Energy Chemical, 9dingchem, Adamas-beta China and were used as received. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.20 mm Huanghai silica gel plates (HSGF 254) using UV light as the visualizing agent and Iodine and KMnO₄ with heat as the developing agents. All new compounds were characterized by means of GC, ¹H-NMR, ¹³C-NMR, and HR-MS. GC analysis was performed on Agilent Technologies 7820A GC system. GC runs were performed with the following method: GC; HP-5 column; inlet temperature 100 °C; column temperature 100 °C for 1 min, then 50 °C/min to 280 °C, then 280 °C for 6 min. HPLC was performed on SHIMADZU LC-2030 Plus and SIL-20A. Optical rotations were recorded on digital automatic polarimeter (WZZ-2S). X-ray analysis was performed on Bruker D8 Venture diffractometer. NMR spectra were recorded using a Bruker AVANCE III 400 MHz NMR spectrometer and can be found at the end of the paper. High-resolution mass spectra (HRMS) were recorded on a Waters GCT Premier mass spectrometer using EI-TOF (electron ionization-time of flight), Agilent Technologies 7250 GCQTOF (EI), and JEOL AccuTOF LC-plus 4G (ESI). All ¹H-NMR data are reported in δ units, parts per million (ppm), and were calibrated relative to the signals for residual chloroform (7.26 ppm) in deuteriochloroform (CDCl₃). All ¹³C-NMR data are reported in ppm relative to CDCl₃ (77.16 ppm) and were obtained with ¹H decoupling. The following abbreviations or combinations thereof were used to explain the multiplicities: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sept = septet, m = multiplet.

Variations from the standard condition



Entry	deviation from above	1a (%) ^b	3a (%) ^b	e.r. (%) ^c
1	none	0	92	97:3
2	no LiBr	0	85	95.5:4.5
3	Zn instead of Mn	0	16	83.5:16.5
4	2.0 eq. ⁿ C ₇ H ₁₅ I; 3.0 eq. Mn	3	73	92.5:7.5
5	10 mol% Cat.; 12 mol% L8	21	52	94.5:5.5
6	Ni(ClO ₄) ₂ ·6H ₂ O instead of Ni(cod) ₂	6	70	97:3
7	ⁿ C ₇ H ₁₅ Br	0	0	-
8	L1	55	0	-
9	^t Bu-Biox	44	0	-
10	L3	34	12	84.5:15.5
11	L4	0	68	77:23



^aReaction conditions: **1a** (0.1 mmol), **2a** (3.0 equiv., 0.3 mmol), Ni(cod)₂ (15 mol%, 0.015 mmol), ligand (18 mol%, 0.018 mmol), Mn (4.0 equiv., 0.4 mmol), LiBr (1.0 equiv., 0.1 mmol), solvent (0.5 mL) under 0 °C for 48 h. ^bCorrected GC yield. ^cDetermined by HPLC-analysis on a chiral stationary phase.

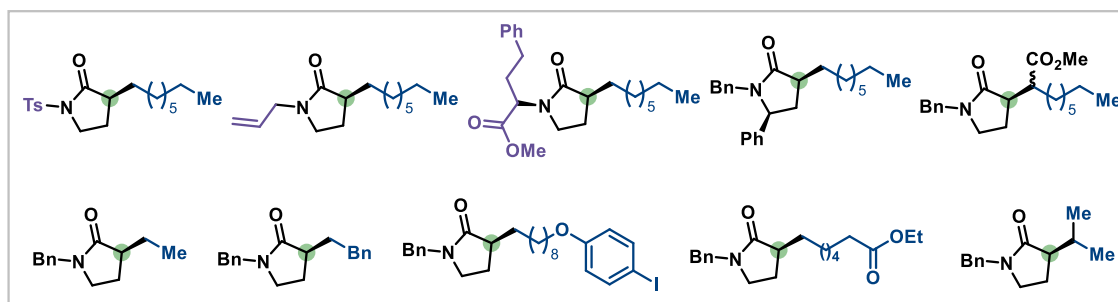


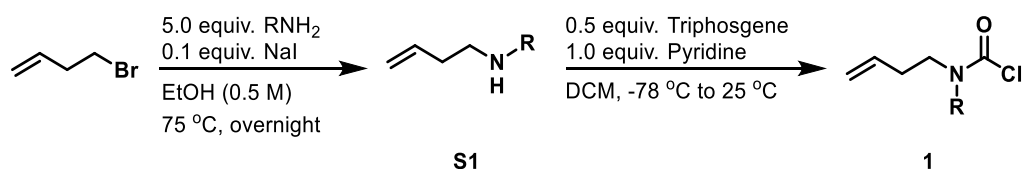
Figure S1. The failed substrate scope

Experimental procedures and characterization data for substrates

Compounds **1a**,¹ **2g**,² **2h**,³ **2k**,⁴ **2m**,⁵ **2q**,⁶ **2s**⁶ were synthesized according to the published procedures.

General procedure for carbamoyl chloride synthesis:

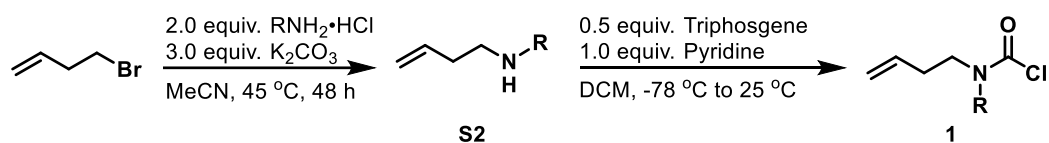
General procedure A for carbamoyl chloride synthesis



To a solution of amine (5.0 equiv.) and 4-bromo-1-butene (1.0 equiv.) in EtOH (0.5M) was added NaI (0.1 equiv.). The mixture was stirred in reflux overnight. Then the solvent was removed *in vacuo*, DCM followed by KOH (1.0 M, 2 mL/mmol) were added, and the two-phase mixture was separated. The organic phase was washed with water and brine, dried over Na₂SO₄, filtered, and evaporated *in vacuo*. The residue was purified by flash chromatography (PE/EtOAc = 5/1) to give **S1** as a yellow oil.

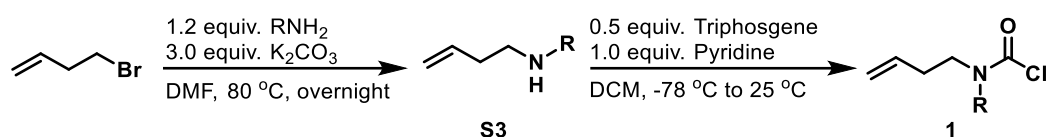
To a solution of **S1** (1.0 equiv.) in DCM was added pyridine (1.0 equiv.) and triphosgene (0.5 equiv.) in sequence at -78 °C. The mixture was then allowed to warm to room temperature. The reaction was quenched with 1 M HCl when the starting material was consumed, extracted with DCM, dried over Na₂SO₄. After removing the solvent, the residue was purified by column chromatography to give substrate **1**.

General procedure B for carbamoyl chloride synthesis



This procedure was performed according to the known literature.⁷ To a solution of amine hydrochloride (2.0 equiv.) in acetonitrile (0.33 M) was added K₂CO₃ (3.0 equiv.). The mixture was stirred for 1 h at room temperature, then 4-bromo-1-butene (1.0 equiv.) was added, and the mixture was stirred at 45 °C for 48 h. The insoluble material was filtered off and the filtrate concentrated under reduced pressure. DCM and H₂O were added, the two-phase mixture was separated, and the aqueous phase was extracted twice with DCM. The combined organic phases were dried over Na₂SO₄, filtered, and evaporated *in vacuo*. The residue was purified by flash chromatography (PE/EtOAc = 5/1) to give **S2**. Procedure of carbamoyl chloride is consistent with procedure A.

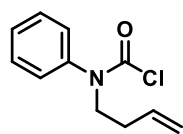
General procedure C for carbamoyl chloride synthesis



This procedure was performed according to the published literature.⁸ A round-bottomed flask equipped with a stirring bar was charged with alkylamine (1.2 equiv.), K₂CO₃ (2 equiv.), and dry DMF (0.33 M). Homoallyl bromide (1.0 equiv.) was slowly added to the mixture and heated to 80 °C. When the starting material was consumed as monitored by TLC, the reaction mixture was cooled to room temperature, diluted with ethyl acetate and washed with H₂O for three times. The combined organic layers were then dried over anhydrous Na₂SO₄, filtered, concentrated. The residue was purified by flash chromatography (PE/EtOAc = 5/1) to give **S3**. Procedure of carbamoyl chloride is consistent with procedure A.

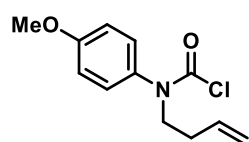
Characterization data for carbamoyl chloride substrates:

But-3-en-1-yl(phenyl)carbamic chloride (**1t**)



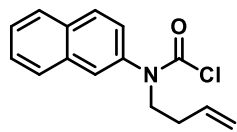
General procedure A was followed with aniline on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 20/1) afforded **1t** as yellow oil (585 mg, 56% over 2 steps); *R_f* = 0.58 (PE/EtOAc = 20/1); ¹H NMR (400 MHz, CDCl₃): δ 7.46–7.38 (m, *J* = 8.4 Hz, 3H), 7.23 (d, *J* = 7.2 Hz, 2H), 5.80–5.70 (m, 1H), 5.14–5.07 (m, 2H), 3.81 (t, *J* = 7.6 Hz, 2H), 2.39–2.33 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 149.3, 141.8, 134.2, 129.7, 128.8, 128.6, 117.8, 52.3, 32.0; HRMS (EI): Calcd for C₁₁H₁₂ClNO: 209.0607; found: 209.0599.

But-3-en-1-yl(4-methoxyphenyl)carbamic chloride (**1u**)



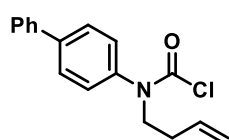
General procedure A was followed with 4-methoxyaniline on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 20/1) afforded **1u** as yellow oil (674 mg, 56% over 2 steps); *R_f* = 0.32 (PE/EtOAc = 10/1); ¹H NMR (400 MHz, CDCl₃): δ 7.13 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 9.2 Hz, 2H), 5.75 (ddt, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.12–5.08 (m, 2H), 3.84 (s, 3H), 3.77 (t, *J* = 7.2 Hz, 2H), 2.37–2.32 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 159.6, 149.8, 134.7, 134.4, 129.6, 117.7, 114.8, 55.6, 52.4, 32.0; HRMS (EI): Calcd for C₁₂H₁₄ClNO₂: 239.0713; found: 239.0712.

But-3-en-1-yl(naphthalen-2-yl)carbamic chloride (1v)



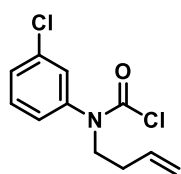
General procedure A was followed with naphthalen-2-amine on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 20/1) afforded **1v** as a yellow oil (279 mg, 22% over 2 steps); R_f = 0.46 (PE/EtOAc = 20/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.92–7.85 (m, 3H), 7.72 (s, 1H), 7.57–7.55 (m, 2H), 7.32 (d, J = 8.8 Hz, 1H), 5.76 (ddt, J = 17.2, 10.4, 6.8 Hz, 1H), 5.15–5.10 (m, 2H), 3.90 (t, J = 7.2 Hz, 2H), 2.43–2.38 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 149.5, 139.1, 134.3, 133.5, 132.9, 129.7, 128.2, 128.0, 127.4, 127.3, 127.1, 126.2, 117.9, 52.5, 32.1; **HRMS (EI)**: Calcd for $\text{C}_{15}\text{H}_{14}\text{ClNO}$: 259.0764; found: 259.0765.

[1,1'-Biphenyl]-4-yl(but-3-en-1-yl)carbamic chloride (1w)



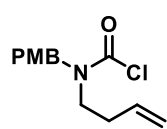
General procedure A was followed with [1,1'-biphenyl]-4-amine on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 20/1) afforded **1w** as yellow solid (257 mg, 18% over 2 steps); R_f = 0.52 (PE/EtOAc = 20/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.65 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 7.6 Hz, 2H), 7.47 (t, J = 8.0 Hz, 2H), 7.39 (t, J = 7.2 Hz, 1H), 7.30 (d, J = 8.0 Hz, 2H), 5.83–5.73 (m, 1H), 5.16–5.11 (m, 2H), 3.85 (t, J = 7.2 Hz, 2H), 2.43–2.38 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 149.3, 141.7, 140.9, 139.9, 134.2, 129.0, 128.9, 128.3, 128.0, 127.3, 117.8, 52.3, 32.0; **HRMS (EI)**: Calcd for $\text{C}_{17}\text{H}_{16}\text{ClNO}$: 285.0920; found: 285.0919.

But-3-en-1-yl(3-chlorophenyl)carbamic chloride (1x)



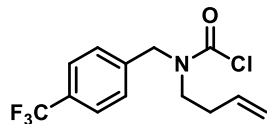
General procedure A was followed with 3-chloroaniline on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1x** as a colorless oil (174 mg, 14% over 2 steps); R_f = 0.60 (PE/EtOAc = 20/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.30–7.29 (m, 2H), 7.18 (s, 1H), 7.07–7.06 (m, 1H), 5.71–5.61 (m, 1H), 5.05–5.01 (m, 2H), 3.79–3.72 (m, 2H), 2.30–2.25 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 148.8, 142.7, 135.0, 133.9, 130.6, 129.1, 128.9, 127.0, 118.0, 52.2, 31.9; **HRMS (EI)**: Calcd for $\text{C}_{11}\text{H}_{11}\text{Cl}_2\text{NO}$: 243.0218; found: 243.0215.

But-3-en-1-yl(4-methoxybenzyl)carbamic chloride (**1y**)



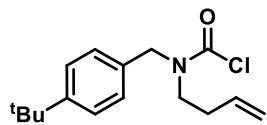
General procedure A was followed with (4-methoxyphenyl)methanamine on 3.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1y** as a colorless oil (452 mg, 60% over 2 steps); Product was isolated as a 1:1 mixture of rotamers; R_f = 0.53 (PE/EtOAc = 10/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.20 (t, J = 8.4 Hz, 2H), 6.89 (t, J = 8.8 Hz, 2H), 5.79–5.67 (m, 1H), 5.11–5.05 (m, 2H), 4.65 (s, 1H), 4.52 (s, 1H), 3.80 (s, 3H), 3.43 (t, J = 7.6 Hz, 1H), 3.38 (t, J = 7.6 Hz, 1H), 2.37–2.29 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 159.6, 159.5, 150.2, 134.3, 129.7, 127.9, 117.9, 114.3, 55.4, 54.1, 52.2, 49.5, 48.5, 32.5, 31.6; **HRMS (EI)**: Calcd for $\text{C}_{13}\text{H}_{16}\text{ClNO}_2$: 253.0870; found: 253.0871.

But-3-en-1-yl(4-(trifluoromethyl)benzyl)carbamic chloride (**1z**)



General procedure A was followed with (4-(trifluoromethyl)phenyl)methanamine on 4 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1z** as a colorless oil (615 mg, 53% over 2 steps); Product was isolated as a 1:1 mixture of rotamers. ^1H and ^{13}C NMR data listed is for the major rotamer. R_f = 0.56 (PE/EtOAc = 20/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.64–7.60 (m, 2H), 7.40–7.38 (m, 2H), 5.80–5.68 (m, 1H), 5.12–5.07 (m, 2H), 4.78 (s, 1H), 4.64 (s, 1H), 3.49 (t, J = 7.2 Hz, 1H), 3.43 (t, J = 7.2 Hz, 1H), 2.41–2.34 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 150.4, 149.5, 139.9, 134.0, 133.6, 130.3 (q, $J_{\text{C-F}}$ = 32.4 Hz), 127.3, 125.9 (q, $J_{\text{C-F}}$ = 3.5 Hz), 124.0 (q, $J_{\text{C-F}}$ = 270.6 Hz), 118.1, 117.9, 54.2, 52.3, 50.2, 49.2, 32.6, 31.7. $^{19}\text{F NMR}$ (376 MHz, CDCl_3): -62.6; **HRMS (EI)**: Calcd for $\text{C}_{13}\text{H}_{13}\text{ClF}_3\text{NO}$: 291.0638; found: 291.0632.

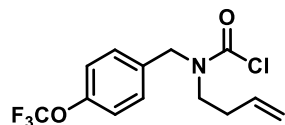
But-3-en-1-yl(4-(tert-butyl)benzyl)carbamic chloride (**1aa**)



General procedure A was followed with (4-(tert-butyl)phenyl)methanamine on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1aa** as a yellow oil (1.01 g, 72% over 2 steps); Product was isolated as a 1:1 mixture of rotamers. R_f = 0.64 (PE/EtOAc = 20/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.39 (d, J = 8.4 Hz, 2H), 7.23–7.19 (m, 2H), 5.81–5.69 (m, 1H), 5.12–5.06 (m, 2H), 4.70 (s, 1H), 4.56 (s, 1H), 3.46 (t, J = 7.2 Hz, 1H), 3.41 (t, J = 7.2 Hz, 1H), 2.40–2.33 (m, 2H), 1.33 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 151.3, 150.2, 149.6, 134.3, 134.0, 132.7,

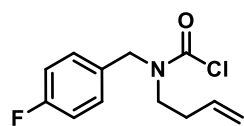
132.5, 128.0, 127.0, 125.9, 125.9, 117.9, 117.7, 54.3, 52.3, 49.7, 48.7, 34.7, 32.6, 31.7, 31.4; **HRMS (EI)**: Calcd for C₁₆H₂₂ClNO: 279.1390; found: 279.1393.

But-3-en-1-yl(4-(trifluoromethoxy)benzyl)carbamic chloride (**1ab**)



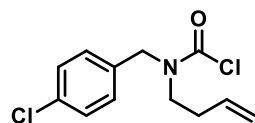
General procedure A was followed with (4-(trifluoromethoxy)phenyl)methanamine on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1ab** as a yellow oil (791 mg, 52% over 2 steps); Product was isolated as a 1:1 mixture of rotamers. **R_f** = 0.62 (PE/EtOAc = 20/1); **¹H NMR** (400 MHz, CDCl₃): δ 7.32–7.29 (m, 2H), 7.24–7.19 (m, 2H), 5.80–5.68 (m, 1H), 5.11–5.06 (m, 2H), 4.72 (s, 1H), 4.58 (s, 1H), 3.47 (t, *J* = 7.2 Hz, 1H), 3.41 (t, *J* = 7.2 Hz, 1H), 2.40–2.33 (m, 2H); **¹³C NMR** (100 MHz, CDCl₃): δ 150.4, 149.5, 149.1, 134.6, 134.4, 134.1, 133.8, 129.6, 128.6, 121.6, 121.5, 120.5 (q, *J*_{C-F} = 255.7 Hz), 118.2, 118.0, 54.0, 52.0, 50.0, 49.0, 32.6, 31.7; **¹⁹F NMR** (376 MHz, CDCl₃): -57.9; **HRMS (EI)**: Calcd for C₁₃H₁₃ClF₃NO₂: 307.0587; found: 307.0586.

But-3-en-1-yl(4-fluorobenzyl)carbamic chloride (**1ac**)



General procedure A was followed with (4-fluorophenyl)methanamine on 5 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1ac** as a colorless oil (560 mg, 46% over 2 steps); Product was isolated as a 1:1 mixture of rotamers. **R_f** = 0.55 (PE/EtOAc = 20/1); **¹H NMR** (400 MHz, CDCl₃): δ 7.28–7.23 (m, 2H), 7.09–7.02 (m, 2H), 5.79–5.67 (m, 1H), 5.11–5.06 (m, 2H), 4.68 (s, 1H), 4.55 (s, 1H), 3.45 (t, *J* = 7.2 Hz, 1H), 3.39 (t, *J* = 7.2 Hz, 1H), 2.38–2.31 (m, 2H); **¹³C NMR** (100 MHz, CDCl₃): 162.5 (d, *J*_{C-F} = 245.5 Hz), 150.2, 149.3, 134.0, 133.7, 131.5 (d, *J*_{C-F} = 3.2 Hz), 131.2 (d, *J*_{C-F} = 3.2 Hz), 129.9 (d, *J*_{C-F} = 8.3 Hz), 128.9 (d, *J*_{C-F} = 8.1 Hz), 118.0, 117.7, 115.9 (d, *J*_{C-F} = 21.8 Hz), 115.8 (d, *J*_{C-F} = 21.6 Hz), 53.9, 51.9, 49.7, 48.7, 32.5, 31.5; **¹⁹F NMR** (376 MHz, CDCl₃): -113.7–113.8 (m); **HRMS (EI)**: Calcd for C₁₂H₁₃ClFNO: 241.0664; found: 241.0658.

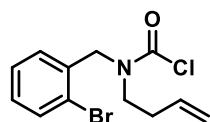
But-3-en-1-yl(4-chlorobenzyl)carbamic chloride (**1ad**)



General procedure A was followed with (4-chlorophenyl)methanamine on 4 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1ad** as a colorless oil (530 mg, 52% over 2 steps); Product was isolated as a 1:1 mixture

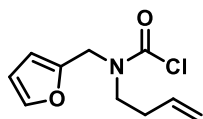
of rotamers; R_f = 0.57 (PE/EtOAc = 20/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.43–7.39 (m, 2H), 7.30–7.26 (m, 2H), 5.86–5.74 (m, 1H), 5.18–5.13 (m, 2H), 4.75 (s, 1H), 4.61 (s, 1H), 3.52 (t, J = 7.6 Hz, 1H), 3.47 (t, J = 7.2 Hz, 1H), 2.46–2.38 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 150.3, 149.5, 134.1, 129.5, 129.2, 129.1, 128.5, 118.1, 117.9, 54.0, 52.1, 49.9, 49.0, 32.6, 31.7; **HRMS (EI)**: Calcd for $\text{C}_{12}\text{H}_{13}\text{Cl}_2\text{NO}$: 257.0374; found: 257.0376.

(2-Bromophenyl)(but-3-en-1-yl)carbamic chloride (**1ae**)



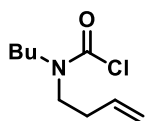
General procedure A was followed with (2-bromophenyl)methanamine on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 20/1) afforded **1ae** as a yellow oil (616 mg, 42% over 2 steps); Product was isolated as a 1:1 mixture of rotamers. R_f = 0.55 (PE/EtOAc = 20/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.55 (t, J = 7.2 Hz, 1H), 7.35–7.13 (m, 3H), 5.79–5.68 (m, 1H), 5.12–5.06 (m, 2H), 4.76 (s, 1H), 4.69 (s, 1H), 3.47 (t, J = 7.6 Hz, 1H), 3.42 (t, J = 7.6 Hz, 1H), 2.40–2.35 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 149.9, 149.7, 134.6, 134.5, 133.9, 133.6, 133.0, 133.0, 129.5, 129.3, 129.1, 127.9, 127.9, 127.6, 123.4, 122.7, 117.9, 117.8, 54.5, 52.2, 49.9, 49.1, 32.5, 31.6; **HRMS (EI)**: $[\text{M}-\text{Br}]^+$ Calcd for $\text{C}_{12}\text{H}_{13}\text{ClNO}^+$: 222.0686; found: 222.0686.

But-3-en-1-yl(furan-2-ylmethyl)carbamic chloride (**1af**)



General procedure A was followed with furan-2-ylmethanamine on 4.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1af** as a colorless oil (464 mg, 54% over 2 steps); R_f = 0.38 (PE/EtOAc = 20/1); Product was isolated as a 1:1 mixture of rotamers; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.39 (d, J = 4.0 Hz, 1H), 6.35–6.33 (m, 2H), 5.79–5.68 (m, 1H), 5.11–5.05 (m, 2H), 4.64 (s, 1H), 4.54 (s, 1H), 3.53 (t, J = 7.6 Hz, 1H), 3.47 (t, J = 7.6 Hz, 1H), 2.36–2.29 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 149.8, 149.2, 149.2, 142.9, 142.9, 134.2, 133.9, 117.9, 117.7, 110.8, 110.7, 109.9, 109.1, 50.1, 49.1, 47.9, 45.5, 32.6, 31.7; **HRMS (EI)**: Calcd for $\text{C}_{10}\text{H}_{12}\text{ClNO}_2$: 213.0557; found: 213.0558.

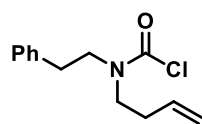
But-3-en-1-yl(butyl)carbamic chloride (**1ag**)



General procedure A was followed with butan-1-amine on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 20/1) afforded **1ag** as a yellow oil (179 mg, 19% over 2 steps); R_f = 0.56

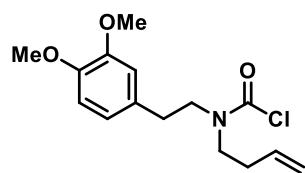
(PE/EtOAc = 20/1); Product was isolated as a 1:1 mixture of rotamers; **¹H NMR** (400 MHz, CDCl₃): δ 5.82–5.70 (m, 1H), 5.15–5.06 (m, 2H), 3.49–3.32 (m, 4H), 2.42–2.34 (m, 2H), 1.65–1.55 (m, 2H), 1.38–1.27 (m, 2H), 0.95 (t, *J* = 7.6 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 149.3, 149.1, 134.4, 134.0, 117.9, 117.7, 51.4, 50.7, 50.0, 49.4, 33.0, 32.0, 30.6, 29.6, 20.0, 20.0, 13.9, 13.8. **HRMS (EI)**: Calcd for C₉H₁₆ClNO: 189.0920; found: 189.0919.

But-3-en-1-yl(phenethyl)carbamic chloride (**1ah**)



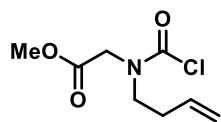
General procedure A was followed with 2-phenylethan-1-amine on 4.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1ah** as a colorless oil (287 mg, 30 % over 2 steps); *R_f* = 0.52 (PE/EtOAc = 20/1); Product was isolated as a 1:1 mixture of rotamers; **¹H NMR** (400 MHz, CDCl₃): δ 7.35–7.21 (m, 5H), 5.79–5.69 (m, 1H), 5.12–5.07 (m, 2H), 3.63 (t, *J* = 7.6 Hz, 1H), 3.57 (t, *J* = 7.2 Hz, 1H), 3.38–3.33 (m, 2H), 2.97–2.91 (m, 2H), 2.38–2.31 (m, 2H); **¹³C NMR** (100 MHz, CDCl₃): δ 149.2, 138.1, 137.7, 134.2, 133.9, 128.9, 128.9, 128.8, 127.0, 126.8, 118.0, 117.8, 53.2, 52.1, 51.4, 49.9, 35.1, 33.7, 32.9, 32.0; **HRMS (EI)**: [M-Cl]⁺ Calcd for C₁₃H₁₆NO: 202.1232; found: 202.1222.

But-3-en-1-yl(3,4-dimethoxyphenethyl)carbamic chloride (**1ai**)



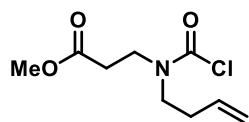
General procedure A was followed with 2-(3,4-dimethoxyphenyl)ethan-1-amine on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1ai** as a yellow oil (757 mg, 51% over 2 steps). Product was isolated as a 1:1 mixture of rotamers. *R_f* = 0.43 (PE/EtOAc = 5/1); **¹H NMR** (400 MHz, CDCl₃): δ 6.81 (dd, *J* = 8.0, 2.8 Hz, 1H), 6.75–6.70 (m, 2H), 5.78–5.67 (m, 1H), 5.11–5.05 (m, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 3.60 (t, *J* = 7.6 Hz, 1H), 3.53 (t, *J* = 7.2 Hz, 1H), 3.35–3.31 (m, 2H), 2.90–2.84 (m, 2H), 2.34–2.30 (m, 2H); **¹³C NMR** (100 MHz, CDCl₃): δ 149.2, 149.1, 148.1, 147.9, 134.3, 133.9, 130.6, 130.3, 120.9, 120.8, 118.0, 117.8, 112.1, 112.0, 111.5, 111.4, 56.0, 53.4, 52.3, 51.5, 50.0, 34.7, 33.3, 32.9, 32.0; **HRMS (EI)**: [M-Cl]⁺ Calcd for C₁₅H₂₀NO₃: 262.1443; found: 262.1435.

Methyl N-(but-3-en-1-yl)-N-(chlorocarbonyl)glycinate (**1aj**)



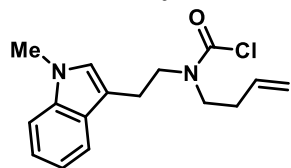
General procedure B was followed with methyl glycinate hydrochloride on 8.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 20/1) afforded **1aj** as a colorless oil (727 mg, 44% over 2 steps). Product was isolated as a 1:1 mixture of rotamers. R_f = 0.34 (PE/EtOAc = 20/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 5.80–5.67 (m, 1H), 5.14–5.05 (m, 2H), 4.16 (s, 1H), 4.07 (s, 1H), 3.77 (s, 3H), 3.57 (t, J = 7.2 Hz, 1H), 3.49 (t, J = 7.2 Hz, 1H), 2.41–2.32 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 168.6, 168.3, 150.4, 149.6, 134.0, 133.7, 118.2, 117.9, 52.7, 52.6, 52.5, 51.8, 50.7, 50.4, 32.6, 31.8; **HRMS (EI)**: Calcd for $\text{C}_8\text{H}_{12}\text{ClNO}_3$: 205.0506; found: 205.0508.

Methyl 3-(but-3-en-1-yl(chlorocarbonyl)amino)propanoate (**1ak**)



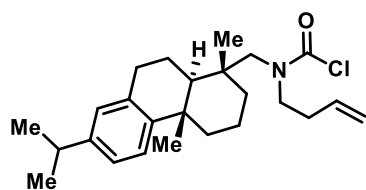
General procedure B was followed with methyl 3-aminopropanoate hydrochloride on 4.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1ak** as a colorless oil (604 mg, 69% over 2 steps); Product was isolated as a 1:1 mixture of rotamers. R_f = 0.29 (PE/EtOAc = 10/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 5.81–5.69 (m, 1H), 5.14–5.07 (m, 2H), 3.74–3.69 (m, 4H), 3.61 (t, J = 7.2 Hz, 1H), 3.55 (t, J = 7.2 Hz, 1H), 3.44 (t, J = 7.2 Hz, 1H), 2.70–2.65 (m, 2H), 2.41–2.33 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 171.8, 171.4, 149.5, 149.1, 134.1, 133.8, 118.2, 118.0, 52.2, 52.1, 51.6, 49.9, 47.1, 46.2, 33.5, 33.0, 32.2, 32.0; **HRMS (EI)**: [M-COCl] Calcd for $\text{C}_8\text{H}_{14}\text{NO}_2$: 156.1025; found: 156.1026.

But-3-en-1-yl(2-(1-methyl-1H-indol-3-yl)ethyl)carbamic chloride (**1al**)



General procedure C was followed with 2-(1-methyl-1H-indol-3-yl)ethan-1-amine⁹ on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **1al** as a yellow oil (100 mg, 7% over 2 steps); R_f = 0.6 (PE/EtOAc = 5/1); Product was isolated as a 1:1 mixture of rotamers. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.63–7.60 (m, 1H), 7.33–7.30 (m, 1H), 7.27–7.22 (m, 1H), 7.16–7.12 (m, 1H), 6.90 (s, 1H), 5.78–5.68 (m, 1H), 5.10–5.06 (m, 1H), 3.77 (s, 3H), 3.70–3.60 (m, 2H), 3.43–3.38 (m, 2H), 3.12–3.06 (m, 2H), 2.38–2.33 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 149.2, 149.1, 137.1, 137.0, 134.2, 133.9, 127.6, 127.5, 126.9, 121.9, 121.8, 119.2, 119.1, 118.7, 118.6, 117.9, 117.7, 110.6, 110.3, 110.2, 109.5, 109.4, 52.4, 51.3, 51.3, 49.8, 48.1, 32.9, 32.7, 32.0, 24.6, 23.3; **HRMS (EI)**: [M-HCl]⁺ Calcd for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}$: 254.1414; found: 254.1418.

Cabamoyl chloride (**1am**)

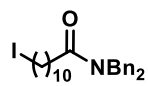


General procedure A was followed with ((1R,4aS,10aR)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methanamine hydrochloride on 5.0 mmol and purification by flash column chromatography on silica gel (PE/EA = 50/1) afforded **1am** as a colorless oil (179.9 mg, 10% over 2 steps); R_f = 0.49 (PE/EtOAc = 50/1); ^1H NMR (400 MHz, CDCl_3): δ 7.16 (d, J = 8.0 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 6.90 (s, 1H), 5.81–5.70 (m, 1H), 5.15–5.09 (m, 2H), 3.79–3.59 (m, 1H), 3.43–3.12 (m, 3H), 2.98–2.79 (m, 3H), 2.43–2.28 (m, 3H), 1.90–1.69 (m, 4H), 1.47–1.34 (m, 4H), 1.29–1.22 (m, 9H), 0.98 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 150.7, 147.3, 145.9, 134.6, 134.0, 127.1, 124.0, 118.0, 59.9, 53.1, 45.3, 40.6, 38.2, 37.8, 37.5, 33.6, 32.8, 30.0, 26.0, 24.1, 24.1, 19.6, 18.9, 18.6; HRMS (EI): $[\text{M}-\text{COCl}]$ Calcd for $\text{C}_{21}\text{H}_{30}\text{N}$: 401.2485; found: 401.2492.

General procedure for alkyl iodide synthesis

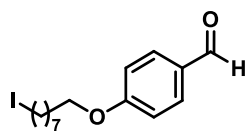
A mixture of alkyl bromide (1.0 equiv.) and NaI (2.0 equiv.) in acetone (0.5 M) was refluxed overnight under N_2 atmosphere. The reaction mixture was filtered, and washed with acetone. The combined filtrate was concentrated under reduced pressure. The residue was diluted with DCM and successively washed with H_2O and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography to give the corresponding alkyl iodides.

N,N-Dibenzyl-11-iodoundecanamide (**2l**)



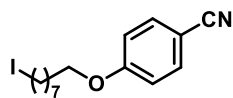
Typical iodination procedure was followed on 10.0 mmol to give **2l** as a yellow solid (4.84 g, 99%); R_f = 0.61 (PE/EtOAc = 3/1); ^1H NMR (400 MHz, CDCl_3): δ 7.37 (t, J = 7.2 Hz, 2H), 7.31–7.26 (m, 4H), 7.21 (d, J = 7.2 Hz, 2H), 7.15 (d, J = 7.2 Hz, 2H), 4.60 (s, 2H), 4.45 (s, 2H), 3.18 (t, J = 7.2 Hz, 2H), 2.41 (t, J = 7.6 Hz, 2H), 1.81 (quin, J = 7.2 Hz, 2H), 1.71 (quin, J = 7.2 Hz, 2H), 1.39–1.27 (m, 12H); ^{13}C NMR (100 MHz, CDCl_3): δ 173.9, 137.7, 136.8, 129.1, 128.7, 128.4, 127.7, 127.5, 126.5, 50.1, 48.2, 33.7, 33.4, 30.6, 29.5, 29.5, 28.6, 25.6, 7.4; HRMS (ESI): $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{25}\text{H}_{35}\text{NOI}^+$: 492.1758; found: 492.1746.

4-((8-Iodooctyl)oxy)benzaldehyde (2n)



To a solution of salicylaldehyde (6.0 mmol) in acetone (12 mL) was added K_2CO_3 (1.5 equiv.). After stirring at room temperature for 1 h, 1,8-dibromooctane (2.0 equiv.) was then added and the mixture was stirred overnight. The reaction mixture was filtered and concentrated. The crude residue was purified by silica gel column to give 4-((8-bromooctyl)oxy)benzaldehyde. Typical iodination procedure was followed and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **2n** as a white solid (1.48 g, 69% over 2 steps); R_f = 0.55 (PE/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 9.88 (s, 1H), 7.83 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 4.04 (t, J = 6.4 Hz, 2H), 3.19 (t, J = 7.2 Hz, 2H), 1.87–1.78 (m, 4H), 1.50–1.37 (m, 8H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.9, 164.4, 132.1, 130.0, 114.9, 68.5, 33.6, 30.5, 29.3, 29.2, 28.6, 26.0, 7.3; **HRMS (EI)**: Calcd for $\text{C}_{15}\text{H}_{21}\text{IO}_2$: 360.0586; found: 360.0592.

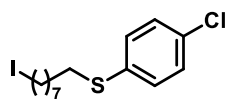
4-((8-Iodooctyl)oxy)benzonitrile (2o)



To a solution of 4-hydroxybenzonitrile (6.0 mmol) in acetone (12 mL) was added K_2CO_3 (1.5 equiv.). After stirring at room temperature for 1 h, 1,8-dibromooctane (2.0 equiv.) was then added and the mixture was stirred overnight. The reaction mixture was filtered and concentrated. The crude residue was purified by silica gel column to give 4-((8-bromooctyl)oxy)benzonitrile. Typical iodination procedure was followed and purification by flash column chromatography on silica gel (PE/EA = 10/1) afforded **2o** as a yellow oil (978 mg, 46% over 2 steps); R_f = 0.52 (PE/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 7.57 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 3.99 (t, J = 6.4 Hz, 2H), 3.19 (t, J = 7.2 Hz, 2H), 1.86–1.76 (m, 4H), 1.49–1.34 (m, 8H); ^{13}C NMR (100 MHz, CDCl_3): δ 162.5, 134.1, 119.5, 115.3, 103.8, 68.4, 33.6, 30.5, 29.2, 29.1, 28.5, 26.0, 7.4; **HRMS (ESI)**: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{15}\text{H}_{20}\text{NOINa}^+$: 380.0482; found: 380.0481.

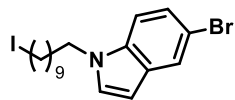
(4-Chlorophenyl)(8-iodooctyl)sulfane (2p)

To a solution of 4-chlorobenzenethiol (3.0 mmol) in acetone (6 mL) was added K_2CO_3 (1.5 equiv.). After stirring at room temperature for 1 h, 1,8-dibromooctane (2.0 equiv.) was then added and the mixture was stirred overnight. The reaction mixture was filtered



and concentrated. The crude residue was purified by silica gel column to afford (8-bromooctyl)(4-chlorophenyl)sulfane. Typical iodination procedure was followed and purification by flash column chromatography on silica gel (PE/EA = 50/1) afforded **2p** as a yellow oil (849 mg, 74% over 2 steps); R_f = 0.65 (PE/EtOAc = 50/1) **¹H NMR** (400 MHz, CDCl₃): δ 7.24 (s, 4H), 3.20–3.16 (m, 2H), 2.88 (t, J = 7.2 Hz, 2H), 1.84–1.78 (m, 2H), 1.66–1.56 (m, 2H), 1.42–1.28 (m, 8H); **¹³C NMR** (100 MHz, CDCl₃): δ 135.6, 131.7, 130.3, 129.0, 33.9, 33.6, 30.5, 29.1, 29.0, 28.7, 28.5, 7.4; **HRMS (EI)**: Calcd for C₁₄H₂₀ClSI: 382.0024; found: 382.0013.

5-Bromo-1-(10-iododecyl)-1H-indole (**2r**)

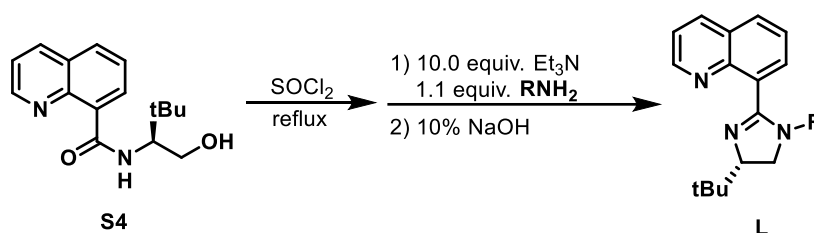


To a solution of 5-bromo-indole (5.0 mmol) in acetone (10 mL) was added K₂CO₃ (1.5 equiv.). After stirring at room temperature for 1 h, 1,10-dibromodecane (2.0 equiv.) was then added and the mixture was stirred overnight. The reaction mixture was filtered and concentrated. The crude residue was purified by silica gel column to give 5-bromo-1-(10-bromodecyl)-1H-indole. Typical iodination procedure was followed and purification by flash column chromatography on silica gel (PE/EA = 20/1) afforded **2r** as a yellow oil (850 mg, 37% over 2 steps); R_f = 0.42 (PE/EtOAc = 20/1). **¹H NMR** (400 MHz, CDCl₃): δ 7.81 (d, J = 1.6 Hz, 1H), 7.36–7.33 (m, 1H), 7.28–7.25 (m, 1H), 7.16–7.14 (m, 1H), 6.49 (d, J = 3.2 Hz, 1H), 4.15 (t, J = 7.2 Hz, 2H), 3.25 (t, J = 7.2 Hz, 2H), 1.91–1.83 (m, 4H), 1.45–1.32 (m, 12H); **¹³C NMR** (100 MHz, CDCl₃): δ 134.7, 130.3, 129.1, 124.2, 123.5, 112.6, 110.9, 100.6, 46.7, 33.6, 30.6, 30.3, 29.4, 29.4, 29.3, 28.6, 27.0, 7.5. **HRMS (EI)**: Calcd for C₁₈H₂₅BrIN: 461.0215; found: 461.0210.

Experimental procedures and characterization data for ligand synthesis

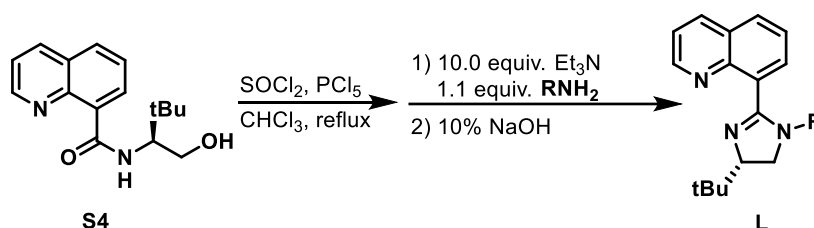
Ligands **L4**,¹⁰ **L5**,¹⁰ **L6**,¹¹ **L7**¹² were synthesized according to the reported literatures.

General procedure D for synthesis of chiral quinoline-imidazole ligands



A solution of **S4**¹⁰ (1.0 equiv.) in SOCl_2 (1.0 M) was refluxed for 12 h. After cooling to room temperature, excess thionyl chloride was then evaporated. The residue was dissolved in dry diethyl ether and to this solution was added dry triethylamine (10.0 equiv.), followed by amine (1.1 equiv.). After stirring for 12 h at room temperature, 10% NaOH (20 mL/mmol) was added, the aqueous portion was extracted with dichloromethane and the organic layer was washed with brine, dried over Na_2SO_4 , and evaporated. The crude product was purified by flash silica gel column chromatography eluting with EA-DCM/MeOH = 10/1 to give corresponding ligand.

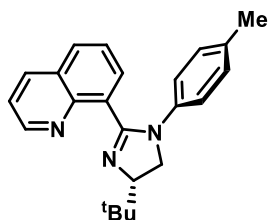
General procedure E for synthesis of chiral quinoline-imidazole ligands



A solution of **S4** (1.0 equiv.) in chloroform (0.1 M) and thionyl chloride (6.0 equiv.) was refluxed for 2 h (completion was confirmed by TLC) to form the chloropicolinamide. Phosphorus pentachloride (2.1 equiv.) was added, and the resulting suspension was refluxed for another 6 h (reaction completion was monitored by TLC). The solution was cooled to 0 °C and a solution of aniline (2.2 equiv.) in triethylamine (7.3 equiv.) and chloroform (0.1 M) was added via syringe. The solution was stirred at r.t. for 2 h and then refluxed for 12 h. The chloroform was removed *in vacuo* and 20% NaOH (20 mL/mmol) was added to the crude product. The aqueous was extracted with dichloromethane. The combined organic layer was washed with brine, and dried over anhydrous Na_2SO_4 . After filtration and concentration under reduced pressure, the crude

material was purified by flash column chromatography on silica gel with EA/MeOH = 10/1 to give the corresponding ligand.

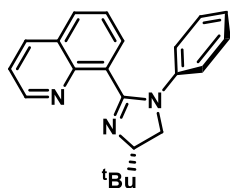
(S)-8-(4-(tert-butyl)-1-(p-tolyl)-4,5-dihydro-1H-imidazol-2-yl)quinoline (L8)



General procedure D was followed with *p*-toluidine on 1.5 mmol and purification by flash column chromatography on silica gel (EA to DCM/MeOH = 10/1) to afforded **L8** as a pale yellow solid (320 mg, 62%); R_f = 0.25 (DCM/MeOH = 10/1).

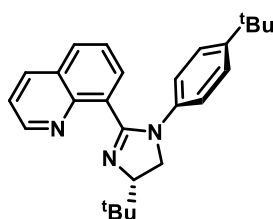
^1H NMR (400 MHz, CDCl_3): δ 8.80 (dd, J = 4.0, 2.0 Hz, 1H), 8.06 (dd, J = 8.0, 2.0 Hz, 1H), 7.86–7.81 (m, 2H), 7.52 (dd, J = 8.0, 7.2 Hz, 1H), 7.29 (dd, J = 8.0, 4.0 Hz, 1H), 6.70 (d, J = 8.4 Hz, 2H), 6.56 (d, J = 8.4 Hz, 2H), 4.21–4.14 (m, 2H), 3.91–3.83 (m, 1H), 2.08 (s, 3H), 1.08 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 160.7, 150.7, 146.2, 139.3, 135.9, 132.6, 131.9, 130.8, 129.7, 129.0, 128.2, 126.2, 121.3, 120.3, 73.6, 53.3, 34.6, 26.2, 20.6; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{26}\text{N}_3^+$: 344.2121; found: 344.2122.

(S)-8-(4-(tert-butyl)-1-phenyl-4,5-dihydro-1H-imidazol-2-yl)quinoline (L9)



General procedure D was followed with aniline on 0.2 mmol and purification by flash column chromatography on silica gel (EA to DCM/MeOH = 10/1) to afforded **L9** as a pale yellow solid (43.8 mg, 66%); R_f = 0.38 (DCM/MeOH = 10/1). ^1H NMR (400 MHz, CDCl_3): δ 8.74 (dd, J = 4.0, 1.6 Hz, 1H), 8.07 (dd, J = 8.4, 1.6 Hz, 1H), 7.95 (d, J = 6.4 Hz, 1H), 7.87 (d, J = 8.4, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.29 (dd, J = 8.0, 4.0 Hz, 1H), 6.92 (t, J = 8.0 Hz, 2H), 6.77 (d, J = 7.2 Hz, 1H), 6.67 (d, J = 8.0 Hz, 2H), 4.31–4.19 (m, 2H), 3.96 (t, J = 7.6 Hz, 1H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 161.2, 150.8, 145.9, 141.0, 136.0, 131.3, 130.4, 128.5, 128.2, 126.3, 123.1, 121.5, 120.5, 72.3, 53.2, 34.6, 26.1; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{22}\text{H}_{24}\text{N}_3^+$: 330.1965; found: 330.1967.

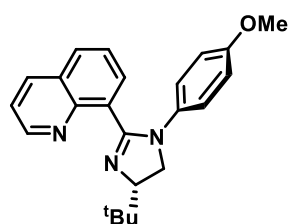
(S)-8-(4-(tert-butyl)-1-(4-(tert-butyl)phenyl)-4,5-dihydro-1H-imidazol-2-yl)quinoline (L10)



General procedure E was followed with cyclohexylamine on 0.2 mmol and purification by flash column chromatography on silica gel (PE/EA = 1/1-DCM/MeOH = 10/1) to afforded **L10** as a white solid (55.9 mg, 73%); R_f = 0.35 (DCM/MeOH =

10/1). **¹H NMR** (400 MHz, CDCl₃): δ 8.76 (dd, *J* = 4.4, 2.0 Hz, 1H), 8.08 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.92 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.87 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.30 (dd, *J* = 8.4, 4.4 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.60 (d, *J* = 8.8 Hz, 2H), 4.30–4.18 (m, 2H), 3.95 (dd, *J* = 8.8, 7.2 Hz, 1H), 1.11 (s, 9H), 1.10 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃): δ 161.4, 150.8, 146.2, 146.0, 138.1, 136.0, 131.3, 130.5, 128.3, 126.2, 125.4, 121.5, 120.1, 71.8, 53.3, 34.6, 34.2, 31.3, 26.0; **HRMS (ESI)**: [M+H]⁺ Calcd for C₂₆H₃₂N₃⁺: 386.2591; found: 386.2584.

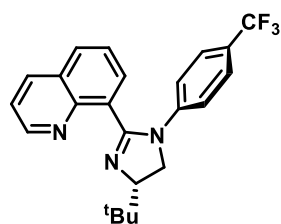
(S)-8-(4-(tert-butyl)-1-(4-methoxyphenyl)-4,5-dihydro-1H-imidazol-2-yl)quinoline (L11)



General procedure E was followed with cyclohexylamine on 0.2 mmol and purification by flash column chromatography on silica gel (PE/EA = 1/1-DCM/MeOH = 10/1) to afford **L11** as a white solid (30.0 mg, 42%); *R_f* = 0.32 (DCM/MeOH = 10/1). **¹H NMR** (400 MHz, CDCl₃): δ 8.80 (dd, *J* = 4.0, 1.6 Hz,

1H), 8.05 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.88 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.81 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.52 (dd, *J* = 8.0, 7.2 Hz, 1H), 7.30 (dd, *J* = 8.4, 4.4 Hz, 1H), 6.71 (d, *J* = 8.8 Hz, 2H), 6.46 (d, *J* = 9.2 Hz, 2H), 4.23–4.16 (m, 2H), 3.89–3.84 (m, 1H), 3.59 (s, 9H), 1.09 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃): δ 161.9, 155.9, 150.7, 146.0, 136.0, 134.9, 131.3, 131.1, 130.0, 128.2, 126.1, 123.4, 121.4, 113.7, 73.0, 55.4, 54.3, 34.6, 26.1; **HRMS (ESI)**: [M+H]⁺ Calcd for C₂₃H₂₆N₃O⁺: 360.2070; found: 360.2066.

(S)-8-(4-(tert-butyl)-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazol-2-yl)quinoline (L12)

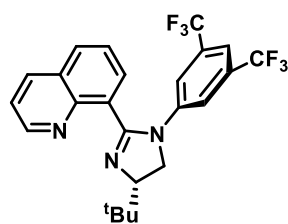


General procedure E was followed with 4-(trifluoromethyl)aniline on 0.2 mmol and purification by flash column chromatography on silica gel (PE/EA = 1/1-DCM/MeOH = 10/1) to afford **L12** as a white solid (54.6 mg, 69%); *R_f* = 0.36 (DCM/MeOH = 10/1). **¹H NMR** (400

MHz, CDCl₃): δ 8.72 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.10 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.31 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.11 (d, *J* = 8.4, 2H), 6.58 (d, *J* = 8.4 Hz, 2H), 4.19–4.15 (m, 2H), 3.97–3.93 (m, 1H), 1.08 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃): δ 159.3, 150.9, 146.0, 144.2, 136.0, 132.2, 130.7, 130.2, 128.4, 126.4, 125.6 (q, *J_{C-F}* = 3.7 Hz), 122.9 (q, *J_{C-F}* = 33.3 Hz), 121.7, 117.7, 73.5, 52.2, 34.5, 26.1; **¹⁹F NMR** (376 MHz, CDCl₃): -61.8; **HRMS (ESI)**: [M+H]⁺ Calcd for

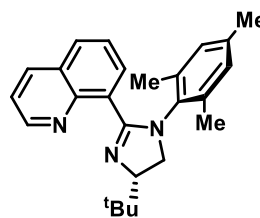
$C_{23}H_{23}N_3F_3^+$: 398.1839; found: 398.1835.

(S)-8-(1-(3,5-bis(trifluoromethyl)phenyl)-4-(tert-butyl)-4,5-dihydro-1H-imidazol-2-yl)quinoline (L13)



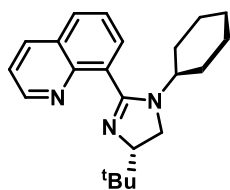
General procedure E was followed with 3,5-bis(trifluoromethyl)aniline on 0.2 mmol and purification by flash column chromatography on silica gel (PE/EA = 1/1-DCM/MeOH = 10/1) to afford **L13** as a white solid (39.2 mg, 42%); R_f = 0.38 (DCM/MeOH = 10/1); 1H NMR (400 MHz, $CDCl_3$): δ 8.62 (dd, J = 4.0, 1.6 Hz, 1H), 8.10 (dd, J = 8.4, 1.6 Hz, 1H), 7.97 (dd, J = 7.2, 1.6 Hz, 1H), 7.93 (dd, J = 8.4, 1.6 Hz, 1H), 7.62 (dd, J = 8.0, 7.2 Hz, 1H), 7.28 (dd, J = 8.4, 4.0 Hz, 1H), 7.11 (s, 1H), 6.85 (s, 2H), 4.23–4.19 (m, 2H), 3.94–3.91 (m, 1H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.0, 150.7, 145.6, 142.4, 135.9, 131.4 (q, J_{C-F} = 32.8 Hz), 131.3, 130.9, 130.5, 128.3, 126.4, 122.9 (q, J_{C-F} = 271.2 Hz), 121.6, 117.3, 113.9 (q, J_{C-F} = 3.6 Hz), 73.8, 51.7, 34.4, 26.1; ^{19}F NMR (376 MHz, $CDCl_3$): -63.5; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{24}H_{22}N_3F_6^+$: 466.1712; found: 466.1722.

(S)-8-(4-(tert-butyl)-1-mesityl-4,5-dihydro-1H-imidazol-2-yl)quinoline (L14)



General procedure D was followed with 2,4,6-trimethylaniline on 0.5 mmol and purification by flash column chromatography on silica gel (PE/EA = 1/1 to DCM/MeOH = 10/1) to afford **L14** as a white solid (160.2 mg, 86%); R_f = 0.48 (DCM/MeOH = 10/1). 1H NMR (400 MHz, $CDCl_3$): δ 8.82 (dd, J = 4.0, 1.2 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 7.6 Hz, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.28–7.25 (m, 1H), 6.60 (s, 1H), 6.55 (s, 1H), 4.31 (t, J = 10.8 Hz, 1H), 3.89–3.84 (m, 1H), 3.71 (t, J = 9.6 Hz, 1H), 2.41 (s, 3H), 2.25 (s, 3H), 2.03 (s, 3H), 1.12 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 149.9, 146.0, 137.5, 136.7, 136.5, 135.8, 135.3, 131.1, 130.7, 130.0, 129.1, 129.1, 127.9, 125.6, 121.2, 73.8, 53.0, 34.6, 26.4, 20.8, 18.7, 18.6. **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{25}H_{30}N_3^+$: 372.2434; found: 372.2430.

(S)-8-(4-(tert-butyl)-1-cyclohexyl-4,5-dihydro-1H-imidazol-2-yl)quinoline (L15)



General procedure E was followed with cyclohexylamine on 0.2 mmol and purification by flash column chromatography on silica gel (PE/EA = 1/1 to DCM/MeOH = 10/1) to afford **L15** as a white solid (24.1 mg, 36%); R_f = 0.35 (DCM/MeOH = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 8.94 (dd, J = 4.4, 1.6 Hz, 1H), 8.16 (dd, J = 8.0, 1.6 Hz, 1H), 7.88 (dd, J = 8.4, 1.2 Hz, 1H), 7.81 (dd, J = 7.2, 1.2 Hz, 1H), 7.57 (dd, J = 8.0, 7.6 Hz, 1H), 7.40 (dd, J = 8.0, 4.0 Hz, 1H), 4.02 (dd, J = 11.2, 8.8 Hz, 1H), 3.65 (dd, J = 11.2, 9.6 Hz, 1H), 3.42 (t, J = 9.2 Hz, 1H), 2.80–2.72 (m, 1H), 1.88–1.85 (m, 1H), 1.65–1.39 (m, 7H), 1.01 (s, 9H), 0.98–0.76 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 164.0, 150.9, 146.3, 136.2, 131.0, 129.7, 128.2, 126.3, 121.5, 72.7, 55.0, 45.4, 34.8, 31.5, 30.4, 26.1, 25.7, 25.5. HRMS (ESI): $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{22}\text{H}_{30}\text{N}_3^+$: 336.2434; found: 336.2432.

Experimental procedures and characterization data for products

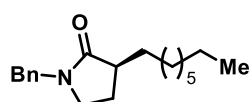
General procedure for asymmetric synthesis of 3-alkylated γ -lactam via Ni-catalyzed reductive cross coupling:

To a dried 8-mL vial were added ligand (18 mol%), Mn (4.0 equiv.) and carbamoyl chloride (1.0 equiv.) (if solid). Then the vial was transferred into glovebox. LiBr (1.0 equiv.), Ni(cod)₂ (15 mol%), DMF (0.2 M), carbamoyl chloride (1.0 equiv.) (if liquid) and alkyl halide (3.0 equiv.) were added in sequence inside the glovebox. The vial was then taken out from the glovebox, sealed with parafilm, put into cryogenic bath (0 °C) and stirred for needed time. After completion, the reaction mixture was quenched with H₂O, filtered through a pad of celite and extracted with EA for three times. The resulted filtrate was separated. The combined organic phase was washed with brine and concentrated under reduced pressure to yield the crude product, which was purified by silica gel flash column chromatography to afford products **3**.

Comments: The reaction is extremely sensitive to air (oxygen), the set up reaction on the glovebox is essential to maintain the reaction in the air-free condition. Meanwhile, the author suggests that avoid of the monitor reaction by TLC or GC-MS during the reaction. Thereby, if different substrates are performed with this methodology, 72 h is the recommended reaction time.

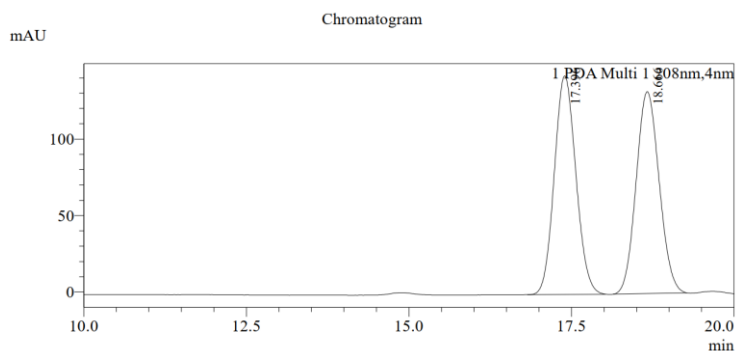
Characterization data for products:

(S)-1-benzyl-3-octylpyrrolidin-2-one (**3a**)



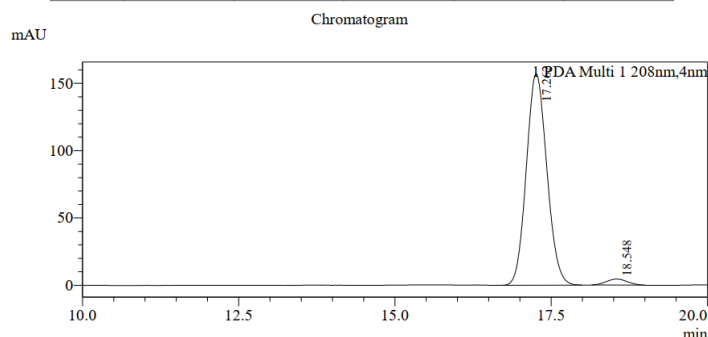
General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3a** as a pale yellow oil (49.4 mg, 86%); *R*_f = 0.20 (PE/EtOAc = 5/1); [α]_D²⁰ = +9.60 (c=1.00, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.34–7.21 (m, 5H), 4.45 (abq, *J* = 14.8 Hz, 2H), 3.18–3.14 (m, 2H), 2.46–2.40 (m, 1H), 2.19–2.12 (m, 1H), 1.93–1.91 (m, 1H), 1.69–1.58 (m, 1H), 1.36–1.27 (m, 13H), 0.88 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 176.9, 136.8, 128.7, 128.2, 127.5, 46.7, 44.9, 42.0, 31.9, 31.5, 29.6, 29.6, 29.3, 27.3, 24.8, 22.7, 14.2; **HRMS (ESI)**: [M+H]⁺ Calcd for C₁₉H₃₀NO⁺: 288.2322; found: 288.2328.

HPLC (Chiralpak IC): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 208 nm, *t*_R = 17.262 min (major), *t*_R = 18.548 min (minor); 97:3 e.r.



Peak Table

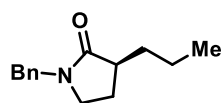
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	17.396	18.027	142792	3302530	50.377
2	18.666	19.275	132024	3253068	49.623
Total			274816	6555598	100.000



Peak Table

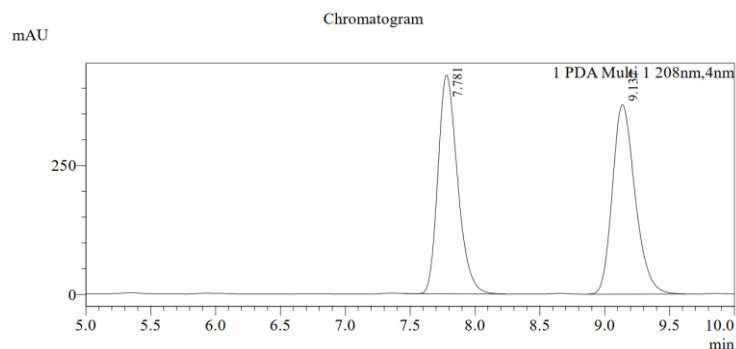
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	17.262	17.995	156974	3595562	97.203
2	18.548	18.997	4439	103456	2.797
Total			161413	3699018	100.000

(S)-1-benzyl-3-propylpyrrolidin-2-one (**3b**)



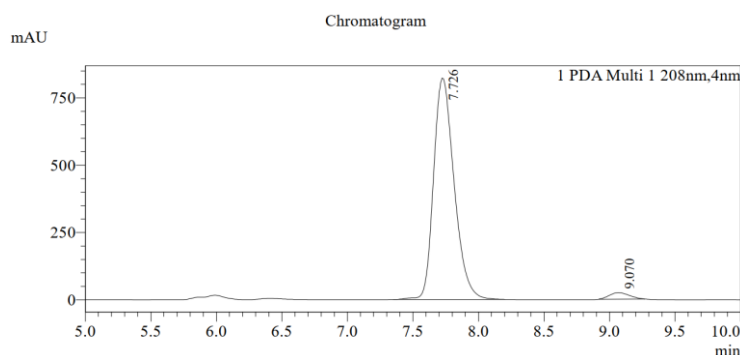
General procedure was followed on 0.2 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3b** as a pale yellow oil (37.5 mg, 86%); R_f = 0.20 (PE/EtOAc = 5/1); $[\alpha]_D^{20}$ = + 5.60 (c = 2.80, CHCl_3). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.33–7.20 (m, 5H), 4.44 (abq, J = 14.4 Hz, 2H), 3.18–3.14 (m, 2H), 2.48–2.41 (m, 1H), 2.19–2.10 (m, 1H), 1.92–1.84 (m, 1H), 1.67–1.58 (m, 1H), 1.45–1.30 (m, 3H), 0.94 (t, J = 7.2 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 177.0, 136.8, 128.7, 128.2, 127.6, 46.7, 45.0, 41.8, 33.6, 24.9, 20.5, 14.1; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{20}\text{NO}^+$: 218.1539; found: 218.1539.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 208 nm, t_R = 7.726 min (major), t_R = 9.070 min (minor); 97.5:2.5 e.r.



Peak Table

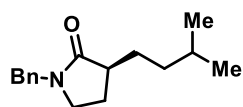
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.781	8.235	423271	4450534	49.841
2	9.137	9.621	366729	4478916	50.159
Total			790001	8929450	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.726	8.203	821989	8962191	97.297
2	9.070	9.269	23922	248992	2.703
Total			845911	9211184	100.000

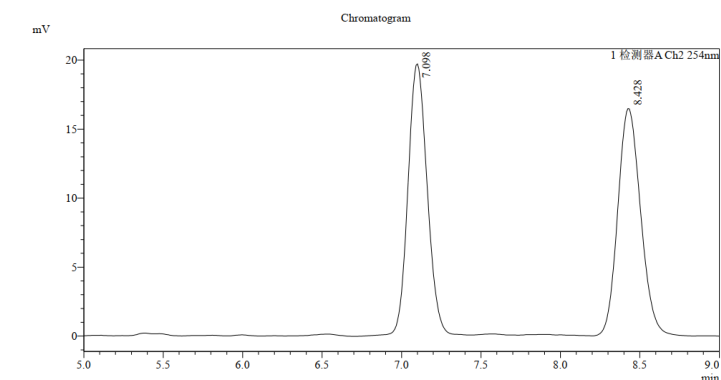
(S)-1-benzyl-3-isopentylpyrrolidin-2-one (**3c**)



General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3c** as a pale yellow oil (20.0 mg, 41%); R_f = 0.48 (PE/EtOAc = 3/1); $[\alpha]_D^{25}$ = + 5.87 (c = 1.50, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.34–7.21 (m, 5H), 4.45 (abq, J = 14.8 Hz, 2H) 3.20–3.12 (m, 2H), 2.45–2.37 (m, 1H), 2.19–2.11 (m, 1H), 1.97–1.88 (m, 1H), 1.67–1.51 (m, 2H), 1.40–1.30 (m, 1H), 1.26–1.20 (m, 2H), 0.90 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 177.0, 136.8, 128.7, 128.2, 127.6, 46.8, 45.0, 42.3, 36.5, 29.4, 28.2, 24.9, 22.8, 22.6; **HRMS (ESI)**: $[M+Na]^+$ Calcd for C₁₆H₂₃NONa⁺: 268.1672; found: 268.1680.

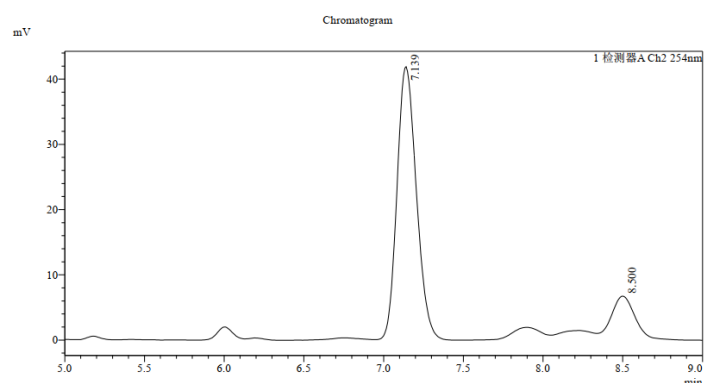
HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254

nm, t_R = 7.139 min (major), t_R = 8.500 min (minor); 90.5:9.5 e.r.



检测器A Ch2 254nm

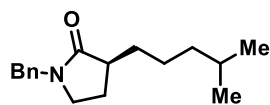
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.098	164892	19670	49.961		M	
2	8.428	165147	16476	50.039		M	
总计		330039	36146				



检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.139	352975	41856	90.374		M	
2	8.500	37596	4863	9.626		M	
总计		390570	46719				

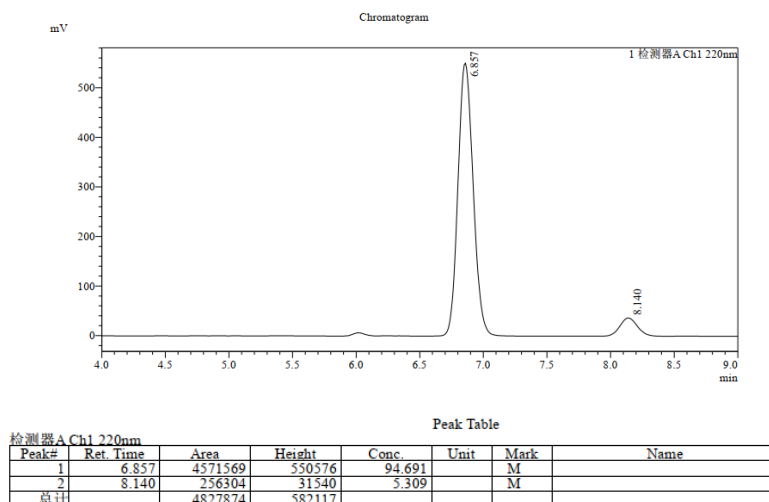
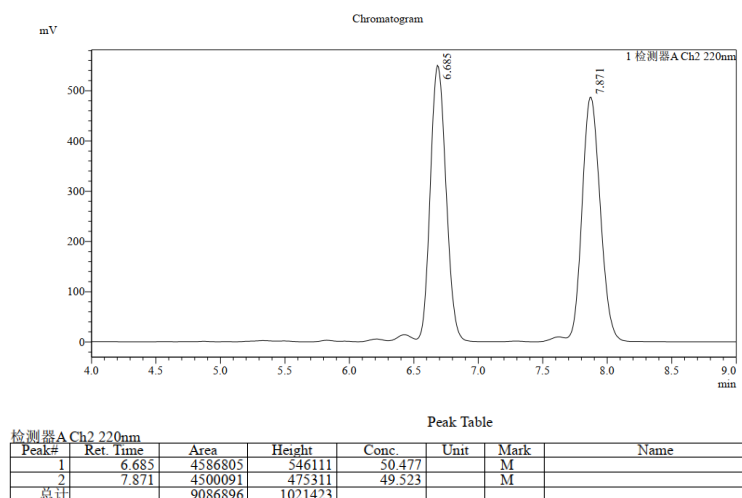
(S)-1-benzyl-3-(4-methylpentyl)pyrrolidin-2-one (**3d**)



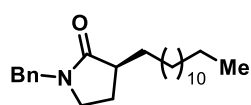
General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3d** as a pale yellow oil (44.0 mg, 85%); R_f = 0.50 (PE/EtOAc = 3/1); $[\alpha]_D^{25}$ = +3.57 (c = 3.70, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ 7.33–7.20 (m, 5H), 4.44 (abq, J = 14.8 Hz, 2H), 3.18–3.14 (m, 2H), 2.48–2.40 (m, 1H), 2.19–2.11 (m, 1H), 1.93–1.81 (m, 1H), 1.68–1.58 (m, 1H), 1.54 (sept, J = 6.8 Hz, 1H), 1.41–1.30 (m, 3H), 1.25–1.17 (m, 2H), 0.86 (d, J = 6.4 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.0, 136.8, 128.7, 128.2, 127.6, 46.7, 45.0, 42.1, 38.9, 31.7, 27.9, 25.0, 24.9, 22.7, 22.6.; **HRMS (ESI)**: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{25}\text{NO}^+$: 282.1828; found: 282.1833.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 90/10, flow rate 1.0 mL/min, λ = 220

nm, t_R = 6.857 min (major), t_R = 8.140 min (minor); 94.5:5.5 e.r.



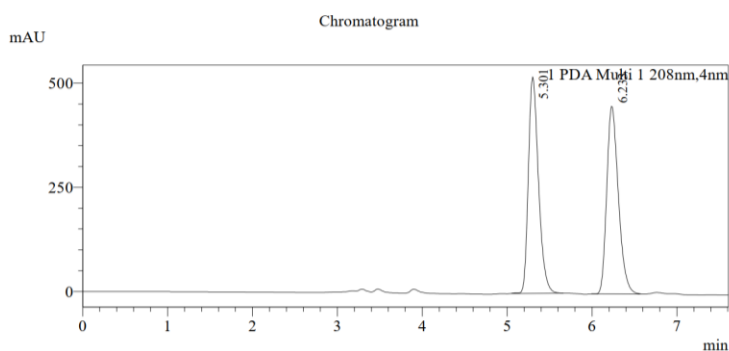
(S)-1-benzyl-3-tridecylpyrrolidin-2-one (**3e**)



General procedure was followed on 0.2 mmol scale with a reaction time of 63 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3e** as a pale yellow solid (61.8 mg, 86%); R_f = 0.40 (PE/EtOAc = 5/1); $[\alpha]_D^{20}$ = -69.40 (c = 1.00, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃): δ 7.34–7.21 (m, 5H), 4.45 (abq, J = 14.4 Hz, 2H), 3.18–3.14 (m, 2H), 2.47–2.40 (m, 1H), 2.19–2.11 (m, 1H), 1.93–1.89 (m, 1H), 1.68–1.58 (m, 1H), 1.37–1.25 (m, 23H), 0.88 (t, J = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 177.0, 136.8, 128.7, 128.2, 127.6, 46.8, 45.0, 42.1, 32.0, 31.5, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 27.3, 24.9, 22.8, 14.2; **HRMS (ESI)**: $[M+H]^+$ Calcd for C₂₄H₄₀NO⁺: 358.3104; found: 358.3100.

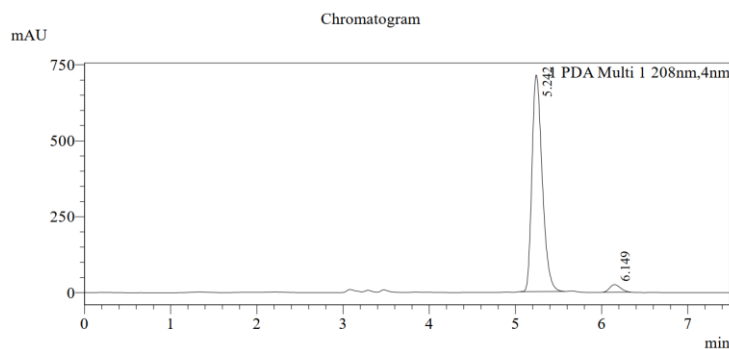
HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 208

nm, t_R = 5.242 min (major), t_R = 6.149 min (minor); 96.5:3.5 e.r.



Peak Table

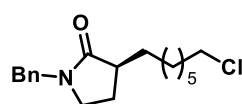
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.301	5.664	518549	4306625	50.025
2	6.233	6.624	450531	4302370	49.975
Total			969080	8608996	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.242	5.568	712288	5930635	96.480
2	6.149	6.336	24802	216353	3.520
Total			737090	6146988	100.000

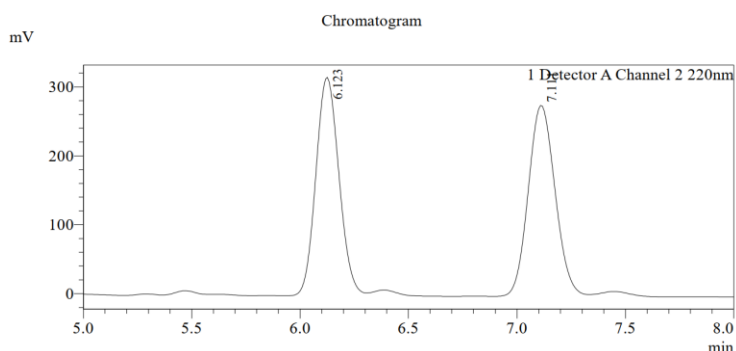
(S)-1-benzyl-3-(7-chloroheptyl)pyrrolidin-2-one (**3f**)



General procedure was followed on 0.2 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3f** as a pale yellow oil (49.9 mg, 81%); R_f = 0.19 (PE/EtOAc = 5/1); $[\alpha]_D^{25}$ = + 6.40 (c = 4.00, CHCl_3). **^1H NMR** (400 MHz, CDCl_3): δ 7.33–7.21 (m, 5H), 4.48 (abq, J = 14.4 Hz, 2H), 3.52 (t, J = 6.8 Hz, 2H), 3.20–3.12 (m, 2H), 2.46–2.40 (m, 1H), 2.19–2.11 (m, 1H), 1.92–1.89 (m, 1H), 1.76 (quin, J = 6.8 Hz, 2H), 1.68–1.58 (m, 1H), 1.44–1.35 (m, 9H); **^{13}C NMR** (100 MHz, CDCl_3): δ 176.8, 136.8, 128.7, 128.1, 127.5, 46.7, 45.2, 44.9, 42.0, 32.7, 31.4, 29.4, 28.8, 27.1, 26.9, 24.9; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for

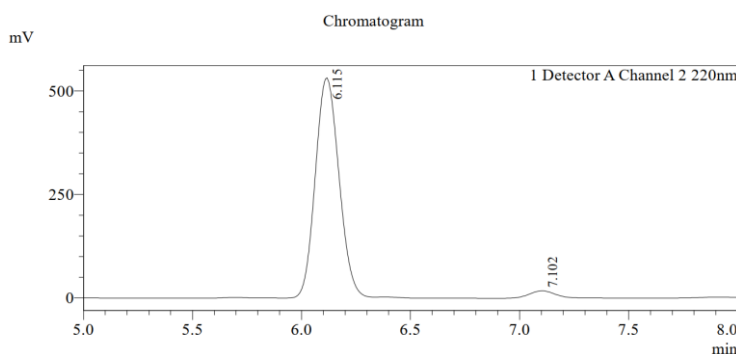
$C_{18}H_{27}NOCl^+$: 308.1776; found: 308.1772

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 220 nm, t_R = 6.115 min (major), t_R = 7.102 min (minor); 96.5:3.5 er.



Peak Table

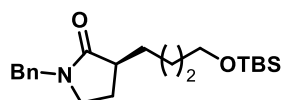
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	6.123	6.642	317225	2426446	49.674
2	7.111	7.675	277153	2458294	50.326
Total			594379	4884740	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	6.115	6.592	531564	4037019	96.520
2	7.102	7.358	17567	145560	3.480
Total			549131	4182579	100.000

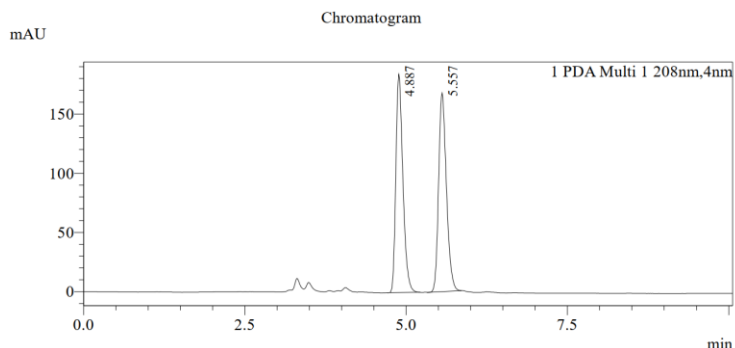
(S)-1-benzyl-3-(4-((tert-butyldimethylsilyl)oxy)butyl)pyrrolidin-2-one (3g)



General procedure was followed on 0.2 mmol scale with a reaction time of 42 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3g** as a pale yellow oil (57.0 mg, 79%); R_f = 0.38 (PE/EtOAc = 5/1); $[\alpha]_D^{20}$ = +5.00 (c = 5.10, $CHCl_3$). **1H NMR** (400 MHz, $CDCl_3$): δ 7.34–7.21 (m, 5H), 4.45 (abq, J = 14.8 Hz, 2H), 3.62 (t, J = 6.4 Hz, 2H), 3.18–3.12 (m, 2H), 2.48–2.41 (m, 1H), 2.20–2.12 (m, 1H), 1.96–1.89 (m, 1H), 1.68–1.52 (m, 3H), 1.46–1.34 (m, 3H), 0.89 (s, 9H), -0.05 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 176.8, 136.8, 128.7, 128.1, 127.5, 63.0,

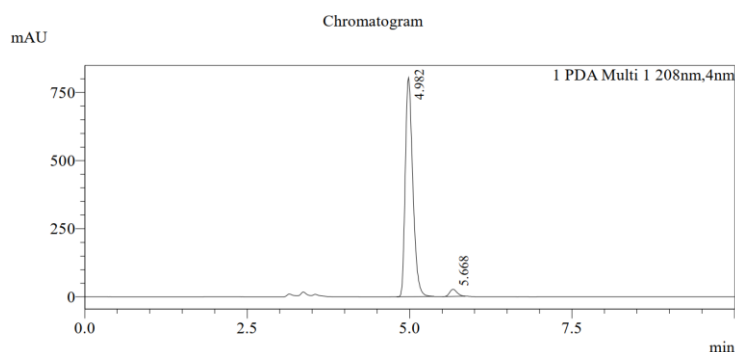
46.7, 44.9, 42.0, 32.8, 31.2, 26.0, 24.8, 23.6, 18.4, -5.2; **HRMS (ESI):** $[M+Na]^+$ Calcd for $C_{21}H_{35}NNaO_2Si^+$: 384.2329; found: 384.2325.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 208 nm, t_R = 4.982 min (major), t_R = 5.668 min (minor); 97:3 e.r.



Peak Table

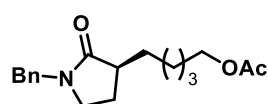
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	4.887	5.216	184201	1401769	49.849
2	5.557	5.856	167608	1410245	50.151
Total			351809	2812014	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	4.982	5.376	803844	6497728	96.889
2	5.668	5.856	26193	208621	3.111
Total			830037	6706349	100.000

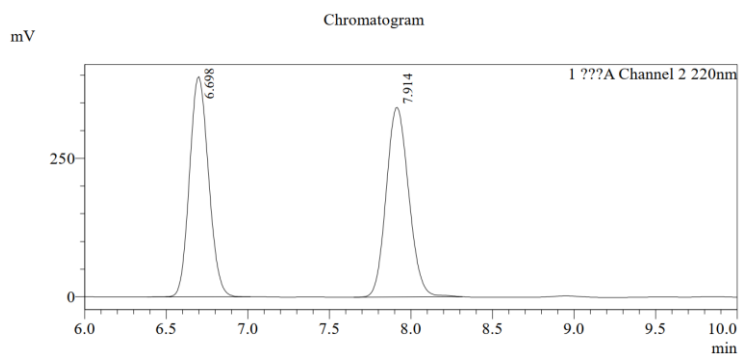
(S)-5-(1-benzyl-2-oxopyrrolidin-3-yl)pentyl acetate (**3h**)



General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3h** as a colorless oil (52.7 mg, 87%); R_f = 0.18 (PE/EtOAc = 3/1); $[\alpha]_D^{20}$ = +1.50 (c = 3.90, $CHCl_3$). **1H NMR** (400 MHz, $CDCl_3$): δ 7.33–7.20 (m, 5H), 4.44 (abq, J = 14.8 Hz, 2H), 4.05 (t, J = 6.8 Hz, 2H), 3.19–3.15 (m, 2H), 2.48–2.41 (m, 1H), 2.20–2.11 (m, 1H), 2.04 (s, 3H), 1.93–1.87 (m, 1H), 1.67–1.60 (m, 3H), 1.39–1.33 (m, 5H);

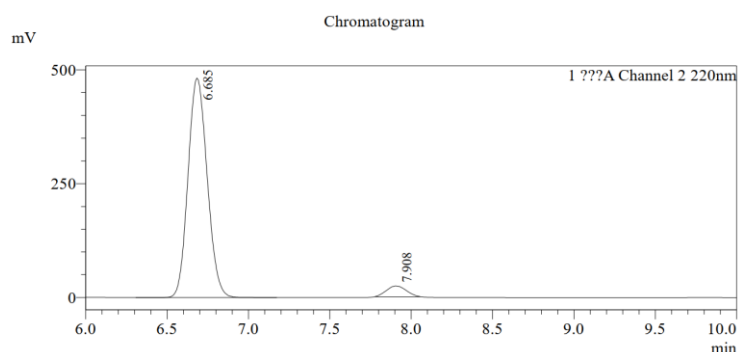
^{13}C NMR (100 MHz, CDCl_3): δ 176.7, 171.3, 136.7, 128.7, 128.1, 127.5, 64.5, 46.7, 44.9, 41.9, 31.3, 28.5, 26.8, 25.9, 24.8, 21.1.; **HRMS (ESI)**: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_3\text{Na}^+$: 326.1727; found: 326.1717;

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 220 nm, t_{R} = 6.685 min (major), t_{R} = 7.908 min (minor). 95:5 e.r.



Peak Table

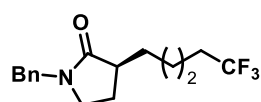
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	6.698	7.017	397220	3232849	49.498
2	7.914	8.317	342220	3298357	50.502
Total			739440	6531206	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	6.685	7.175	481994	3959255	95.226
2	7.908	8.058	23641	198485	4.774
Total			505635	4157740	100.000

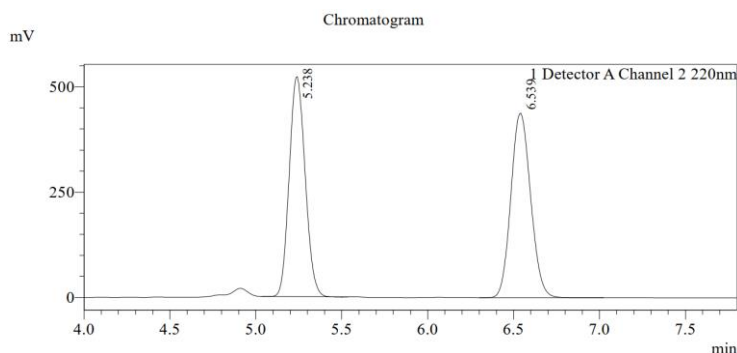
(S)-1-benzyl-3-(5,5,5-trifluoropentyl)pyrrolidin-2-one (**3i**)



General procedure was followed on 0.2 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3i** as a pale yellow oil (38.5 mg, 64%); R_f = 0.29 (PE/EtOAc = 3/1); $[\alpha]_{\text{D}}^{25}$ = +2.80 (c = 2.43, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ 7.33–7.20 (m, 5H), 4.44 (abq, J = 14.4 Hz, 2H), 3.19–3.16 (m, 2H), 2.48–2.40 (m, 1H), 2.20–2.02 (m, 3H), 1.94–1.87

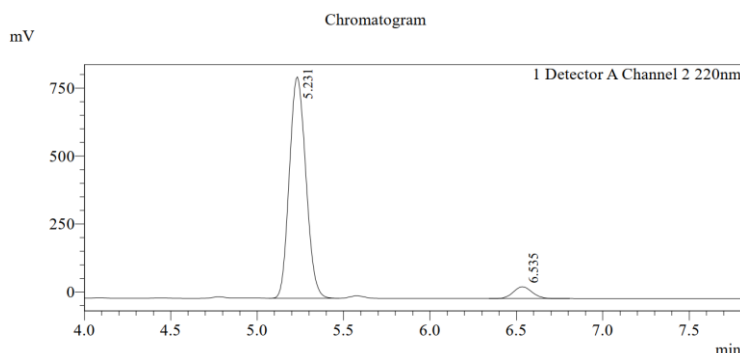
(m, 1H), 1.67–1.56 (m, 3H), 1.50–1.37 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.4, 136.7, 128.8, 128.2, 127.6, 127.3 (q, $J_{\text{C-F}} = 274.5$ Hz), 46.8, 44.9, 41.7, 33.7 (q, $J_{\text{C-F}} = 28.3$ Hz), 31.1, 26.3, 24.9, 22.0 (q, $J_{\text{C-F}} = 2.8$ Hz); ^{19}F NMR (376 MHz, CDCl_3): -66.3 (t, $J = 10.9$ Hz); **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{21}\text{NOF}_3^+$: 300.1570; found: 300.1566.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, $\lambda = 220$ nm, $t_{\text{R}} = 5.231$ min (major), $t_{\text{R}} = 6.535$ min (minor); 94:6 e.r.



Peak Table

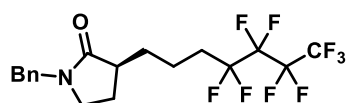
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.238	5.575	521819	3367669	49.062
2	6.539	7.025	438001	3496501	50.938
Total			959820	6864170	100.000



Peak Table

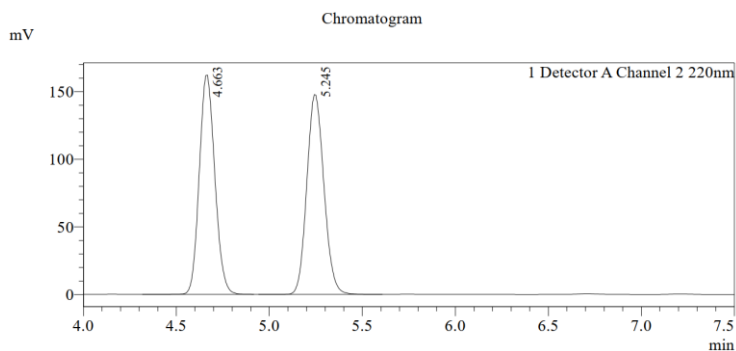
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.231	5.475	813718	5417631	94.222
2	6.535	6.808	43541	332235	5.778
Total			857260	5749866	100.000

(S)-1-benzyl-3-(4,4,5,5,6,6,6-heptafluorohexyl)pyrrolidin-2-one (**3j**)



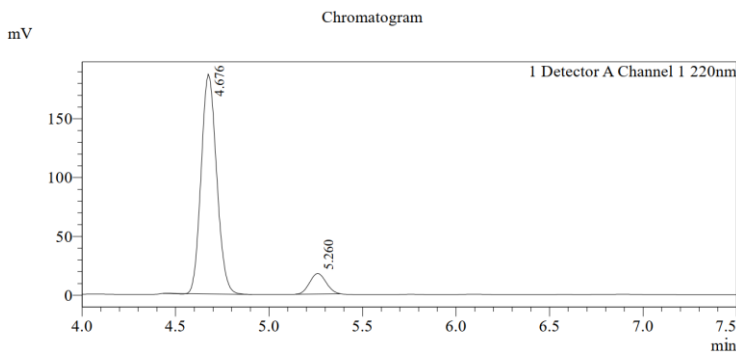
General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours at 5 °C. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3j** as a colorless oil (30.4 mg, 35%); $R_f = 0.41$ (PE/EtOAc =

3/1); $[\alpha]_D^{25} = + 5.20$ ($c = 2.00$, CHCl_3). **^1H NMR** (400 MHz, CDCl_3): δ 7.35–7.21 (m, 5H), 4.45 (abq, $J = 14.8$ Hz, 2H), 3.20 (dd, $J = 8.4, 5.2$ Hz, 1H), 2.52–2.44 (m, 1H), 2.24–2.05 (m, 3H), 2.00–1.93 (m, 1H), 1.75–1.61 (m, 3H), 1.55–1.45 (m, 1H); **^{13}C NMR** (100 MHz, CDCl_3): δ 176.0, 136.6, 128.8, 128.2, 127.7, 46.9, 44.9, 41.7, 31.0, 30.9 (t, $J_{\text{C-F}} = 22.5$ Hz), 24.8, 18.1 (t, $J_{\text{C-F}} = 3.0$ Hz); **^{19}F NMR** (376 MHz, CDCl_3): -81.0–81.1 (m, 3F), -114.5–114.6 (m, 2F), -124.4–124.5 (m, 2F), -126.0–126.1 (m, 2F); **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{18}\text{F}_9\text{NO}^+$: 436.1317; found: 436.1307; **HPLC** (Chiralpak AD-H): n -Hexane/ i -PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 220$ nm, $t_R = 4.676$ min (major), $t_R = 5.260$ min (minor); 91:9 e.r.



Peak Table

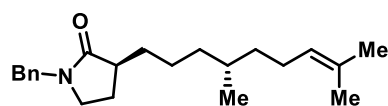
Detector A Channel 2 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	4.663	4.917	161655	941680	49.888
2	5.245	5.608	147543	945916	50.112
Total			309197	1887597	100.000



Peak Table

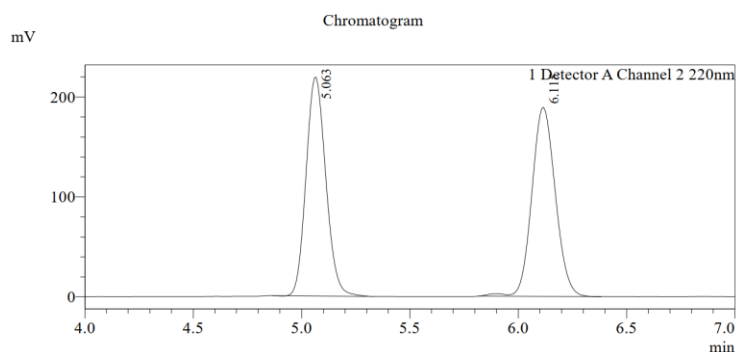
Detector A Channel 1 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	4.676	4.908	186797	1078687	90.930
2	5.260	5.383	17538	107593	9.070
Total			204335	1186279	100.000

(S)-1-benzyl-3-((R)-4,8-dimethylnon-7-en-1-yl)pyrrolidin-2-one (3k)



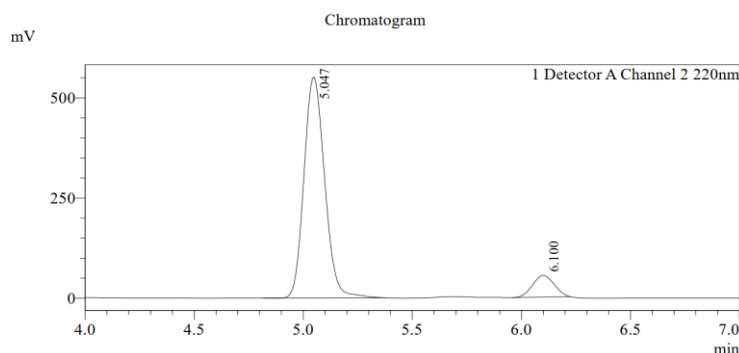
General procedure was followed on 0.2 mmol scale with a reaction time of 84 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3k** as a pale yellow oil (40.4 mg, 62%); R_f = 0.56 (PE/EtOAc = 3/1); $[\alpha]_D^{25}$ = + 11.00 (c = 2.28, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ 7.33–7.21 (m, 5H), 5.09 (t, J = 7.2 Hz, 1H), 4.45 (abq, J = 14.8 Hz, 1H), 3.18–3.15 (m, 2H), 2.48–2.41 (m, 1H), 2.19–2.11 (m, 1H), 2.04–1.84 (m, 3H), 1.68 (s, 3H), 1.66–1.62 (m, 1H), 1.60 (s, 3H), 1.44–1.28 (m, 6H), 1.18–1.08 (m, 2H), 0.86 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.0, 136.8, 131.1, 128.7, 128.2, 127.6, 125.1, 46.8, 45.0, 42.1, 37.3, 36.9, 32.4, 31.8, 25.8, 25.7, 24.9, 24.7, 19.6, 17.7; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{22}\text{H}_{34}\text{NO}^+$: 328.2635; found: 328.2625.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 90/10, flow rate 1.0 mL/min, λ = 220 nm, t_R = 5.047 min (major), t_R = 6.100 min (minor); 90.5:9.5 d.r.



Peak Table

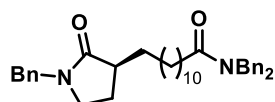
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.063	5.333	219012	1391728	49.303
2	6.115	6.383	189384	1431074	50.697
Total			408396	2822802	100.000



Peak Table

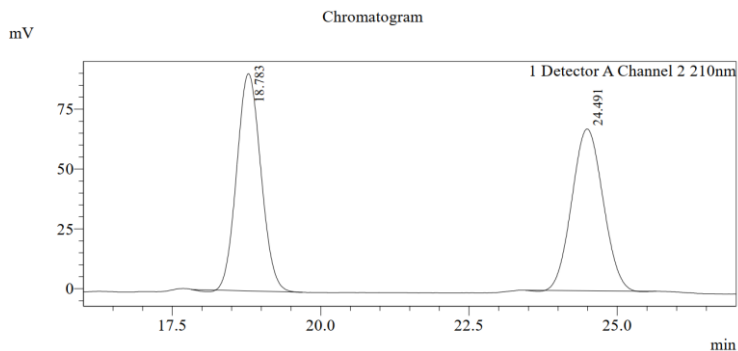
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.047	5.383	551079	3633217	90.655
2	6.100	6.225	54160	374542	9.345
Total			605240	4007760	100.000

(S)-N,N-dibenzyl-12-(1-benzyl-2-oxopyrrolidin-3-yl)dodecanamide (3l)



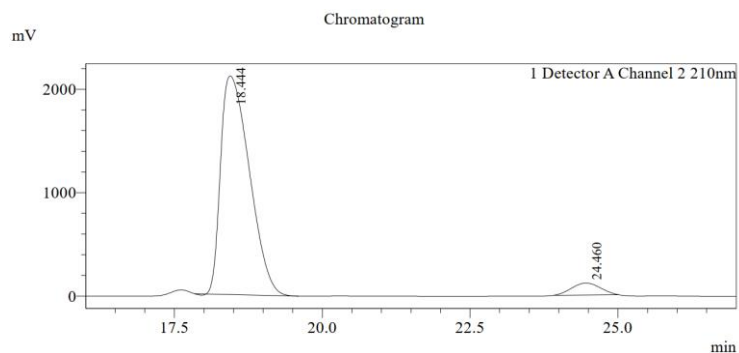
General procedure was followed on 0.2 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3l** as a pale yellow oil (90.6 mg, 82%). R_f = 0.23 (PE/EtOAc = 3/1); $[\alpha]_D^{25}$ = +2.00 (c = 4.56, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ 7.37–7.19 (m, 13H), 7.15 (d, J = 7.2 Hz, 2H), 4.59 (s, 2H), 4.43 (abq, J = 14.4 Hz, 2H), 4.43 (s, 2H), 3.18–3.10 (m, 2H), 2.40 (t, J = 7.2 Hz, 2H), 2.18–2.09 (m, 1H), 1.92–1.84 (m, 1H), 1.73–1.66 (m, 2H), 1.64–1.57 (m, 1H), 1.37–1.24 (m, 18H); ^{13}C NMR (100 MHz, CDCl_3): δ 13C NMR (101 MHz, CDCl_3) δ 176.9, 173.8, 137.6, 136.8, 136.7, 129.0, 128.7, 128.6, 128.3, 128.1, 127.6, 127.5, 127.4, 126.4, 49.9, 48.1, 46.7, 44.9, 42.0, 33.3, 31.4, 29.6, 29.6, 29.5, 29.5, 27.3, 25.5, 24.8; **HRMS (ESI)**: $[M+H]^+$ Calcd for $\text{C}_{37}\text{H}_{49}\text{N}_2\text{O}_2^+$: 553.3789; found: 553.3788.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 80/20, flow rate 1.0 mL/min, λ = 210 nm, t_R = 18.444 (major), t_R = 24.460 min (minor); 95:5 e.r.



Peak Table

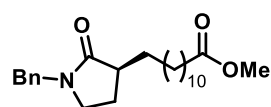
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	18.783	19.692	90768	2566978	50.897
2	24.491	25.658	67651	2476459	49.103
Total			158420	5043437	100.000



Peak Table

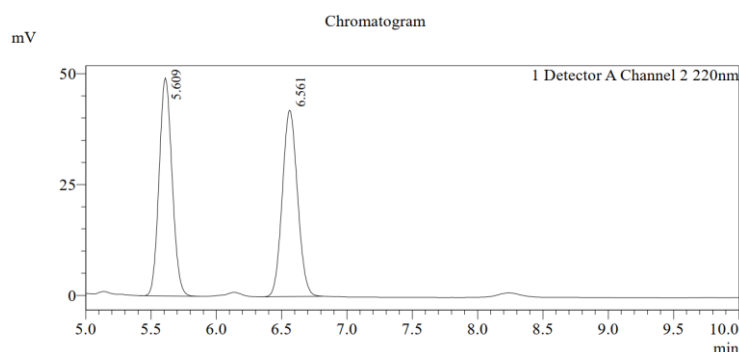
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	18.444	19.600	2114113	71560701	94.830
2	24.460	25.008	116194	3901690	5.170
Total			2230307	75462391	100.000

Methyl (S)-12-(1-benzyl-2-oxopyrrolidin-3-yl)dodecanoate (**3m**)

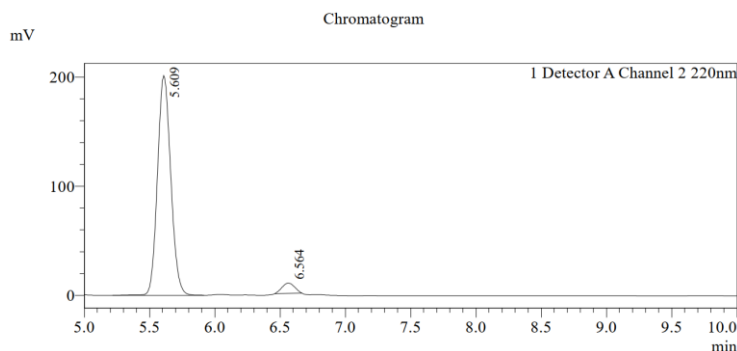


General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3m** as a colorless oil (42.5 mg, 55%); R_f = 0.48 (PE/EtOAc = 3/1); $[\alpha]_D^{25}$ = +3.48 (c = 3.10, CHCl_3). **^1H NMR** (400 MHz, CDCl_3): δ 7.33–7.21(m, 5H), 4.44 (abq, J = 14.4 Hz, 2H), 3.67 (s, 3H), 3.18–3.15 (m, 2H), 2.46–2.40 (m, 1H), 2.30 (t, J = 7.6 Hz, 2H), 2.19–2.11 (m, 1H), 1.93–1.89 (m, 1H), 1.68–1.59 (m, 3H), 1.37–1.26 (m, 17H); **^{13}C NMR** (100 MHz, CDCl_3): δ 177.0, 174.5, 136.8, 128.7, 128.2, 127.6, 51.5, 46.7, 45.0, 42.0, 34.2, 31.5, 29.6, 29.6, 29.5, 29.3, 29.2, 27.3, 25.0, 24.9; **HRMS (ESI)**: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{24}\text{H}_{37}\text{NO}_3\text{Na}^+$: 410.2666; found: 410.2667.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 80/20, flow rate 1.0 mL/min, λ = 220 nm, t_R = 5.609 min (major), t_R = 6.564 min (minor); 95.5:4.5 er.

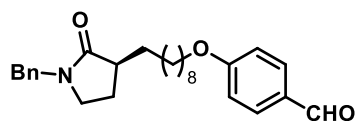


Peak Table					
Detector A Channel 2 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.609	5.883	49168	340441	50.004
2	6.561	6.817	42013	340382	49.996
Total			91180	680823	100.000



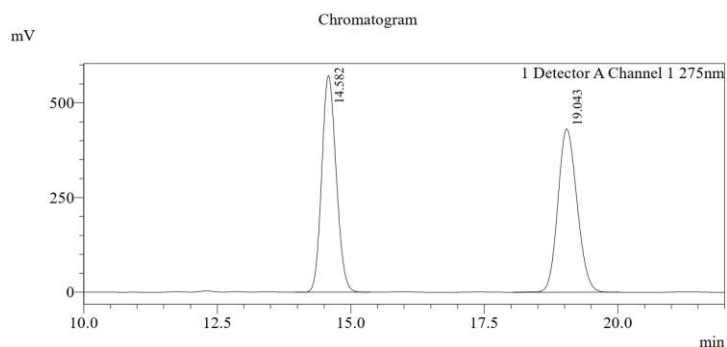
Peak Table					
Detector A Channel 2 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.609	5.917	201436	1426931	95.731
2	6.564	6.667	9454	63629	4.269
Total			210890	1490560	100.000

(S)-4-((9-(1-benzyl-2-oxopyrrolidin-3-yl)nonyl)oxy)benzaldehyde (**3n**)



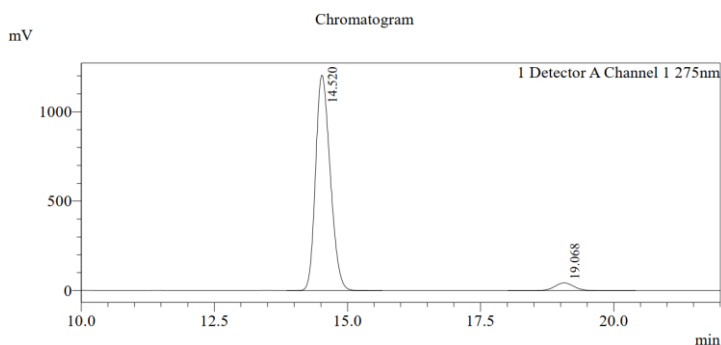
General procedure was followed on 0.2 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3n** as a pale yellow oil (59.2 mg, 70%). R_f = 0.21 (PE/EtOAc = 5/1); $[\alpha]_D^{25}$ = + 3.20 (c = 2.90, CHCl_3). **^1H NMR** (400 MHz, CDCl_3): δ 9.85 (s, 1H), 7.80 (d, J = 8.8 Hz, 2H), 7.32–7.19 (m, 5H), 6.97 (d, J = 8.8 Hz, 2H), 4.43 (abq, J = 14.8 Hz, 2H), 4.01 (t, J = 6.4 Hz, 2H), 3.17–3.13 (m, 2H), 2.45–2.38 (m, 1H), 2.17–2.10 (m, 1H), 1.91–1.88 (m, 1H), 1.79 (quin, J = 6.8 Hz, 2H), 1.61 (dq, J = 8.4, 12.8 Hz, 1H), 1.46–1.41 (m, 2H), 1.36–1.24 (m, 11H); **^{13}C NMR** (100 MHz, CDCl_3): δ 190.9, 176.9, 164.3, 136.8, 132.1, 129.8, 128.7, 128.2, 127.6, 114.8, 68.5, 46.7, 45.0, 42.0, 31.4, 29.6, 29.5, 29.5, 29.4, 29.1, 27.3, 26.0, 24.9; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{36}\text{NO}_3^+$: 422.2690; found: 422.2691.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 80/20, flow rate 1.0 mL/min, λ = 275 nm, t_R = 14.520 min (major), t_R = 19.068 min (minor); 95.5:4.5 e.r.



Peak Table

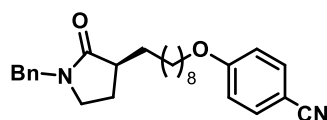
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	14.582	15.375	571784	10792554	49.972
2	19.043	20.025	430964	10804454	50.028
Total			1002748	21597008	100.000



Peak Table

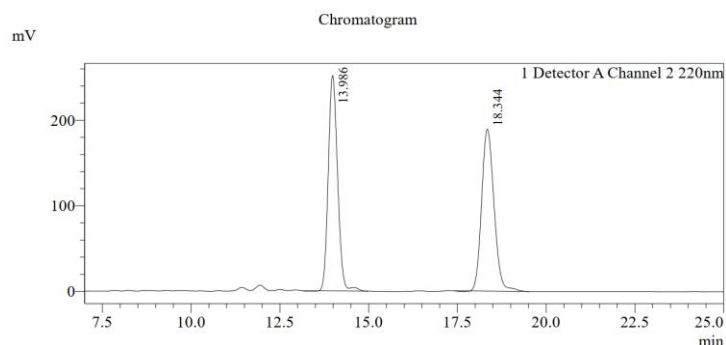
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	14.520	15.658	1204705	23087780	95.623
2	19.068	20.408	42508	1056738	4.377
Total			1247213	24144518	100.000

(S)-4-((9-(1-benzyl-2-oxopyrrolidin-3-yl)nonyl)oxy)benzonitrile (3o)



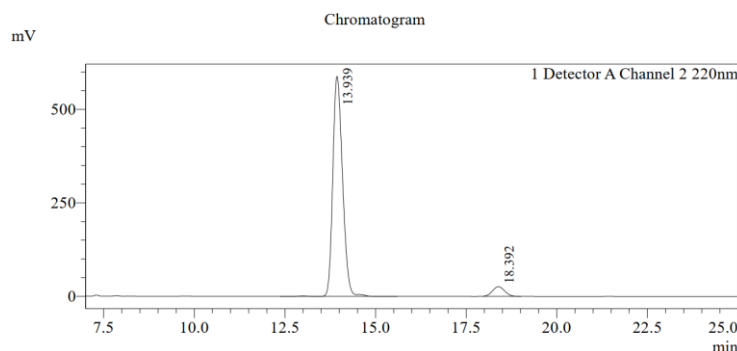
General procedure was followed on 0.2 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3o** as a pale yellow oil (73.1 mg, 87%); R_f = 0.21 (PE/EtOAc = 3/1); $[\alpha]_D^{25}$ = + 1.00 (c = 5.30, CHCl_3). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.55 (d, J = 8.8 Hz, 2H), 7.32–7.20 (m, 5H), 6.92 (d, J = 8.8 Hz, 2H), 4.43 (abq, J = 14.4 Hz, 2H), 3.97 (t, J = 6.4 Hz, 2H), 3.17–3.14 (m, 2H), 2.43–2.39 (m, 1H), 2.18–2.10 (m, 1H), 1.91–1.88 (m, 1H), 1.78 (quin, J = 6.8 Hz, 2H), 1.62 (dq, J = 8.4, 12.8 Hz, 1H), 1.43–1.30 (m, 13H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 176.9, 162.5, 136.7, 134.0, 128.7, 128.1, 127.5, 119.4, 115.2, 103.6, 68.4, 46.7, 44.9, 42.0, 31.4, 29.6, 29.5, 29.4, 29.3, 29.0, 27.2, 25.9, 24.8; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{35}\text{N}_2\text{O}_2^+$: 419.2693; found: 419.2697.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 220 nm, t_R = 13.939 min (major), t_R = 18.392 min (minor); 95:5 e.r.



Peak Table

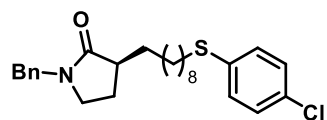
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	13.986	14.992	251948	4616124	50.019
2	18.344	19.517	189345	4612616	49.981
Total			441293	9228740	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	13.939	15.608	588084	11000638	94.817
2	18.392	19.017	25732	601281	5.183
Total			613815	11601919	100.000

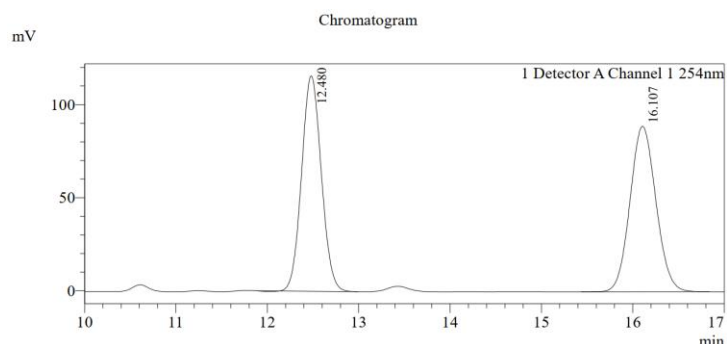
(S)-1-benzyl-3-(9-((4-chlorophenyl)thio)nonyl)pyrrolidin-2-one (3p)



General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3p** as a pale yellow oil (66.9 mg, 76%); R_f = 0.25 (PE/EtOAc = 5/1); $[\alpha]_D^{25}$ = + 3.10 (c = 3.35, CHCl_3). **^1H NMR** (400 MHz, CDCl_3): δ 7.33–7.21 (m, 9H), 4.48 (d, J = 14.4 Hz, 1H), 4.41 (d, J = 14.8 Hz, 1H), 3.18–3.14 (m, 2H), 2.88 (t, J = 7.6 Hz, 2H), 2.46–2.39 (m, 1H), 2.18–2.10 (m, 1H), 1.92–1.81 (m, 1H), 1.67–1.58 (m, 3H), 1.39–1.27 (m, 14H); **^{13}C NMR** (100 MHz, CDCl_3): δ 176.9, 136.8, 135.7, 131.6, 130.2, 129.0, 128.7, 128.2, 127.6, 46.7, 45.0, 42.0, 33.9, 31.4, 29.6, 29.5, 29.2, 29.1, 28.8, 27.3,

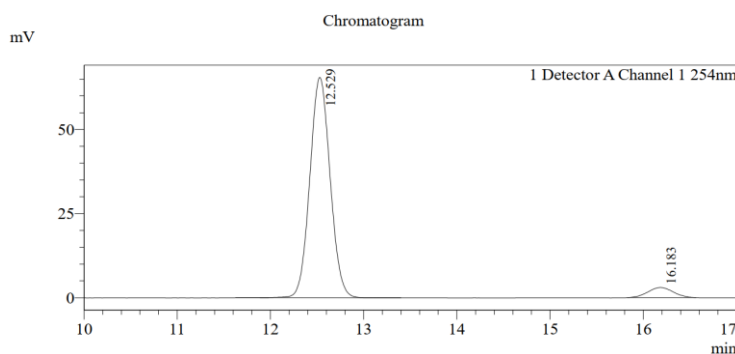
24.9; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{26}H_{35}NOSCl^+$: 444.2122; found: 444.2123.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, t_R = 12.529 min (major), t_R = 16.183 min (minor); 94.5:5.5 e.r.



Peak Table

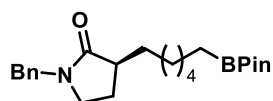
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	12.480	12.992	115693	1735130	49.750
2	16.107	16.842	88883	1752555	50.250
Total			204576	3487685	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	12.529	13.400	65477	991561	94.592
2	16.183	16.567	3000	56693	5.408
Total			68477	1048253	100.000

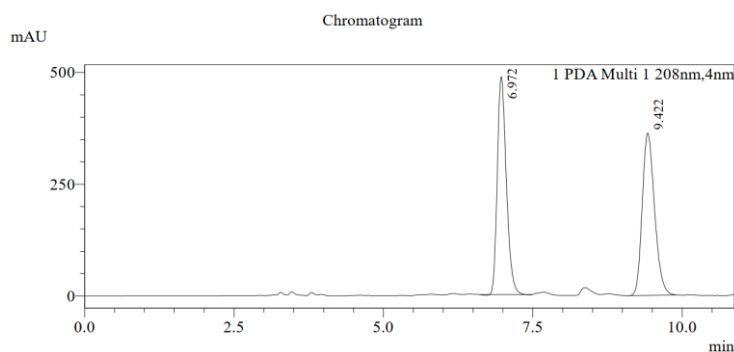
(S)-1-benzyl-3-(6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)pyrrolidin-2-one (3q)



General procedure was followed on 0.2 mmol scale with a reaction time of 46 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3q** as a colorless oil (48.3 mg, 63%). R_f = 0.30 (PE/EtOAc = 3/1); $[\alpha]_D^{25}$ = +0.73 (c = 3.85, $CHCl_3$). **1H NMR** (400 MHz, $CDCl_3$): δ 7.34–7.21 (m, 5H), 4.44 (abq, J = 14.4 Hz, 2H), 3.20–3.12 (m, 2H), 2.45–2.39 (m, 1H), 2.19–2.10 (m, 1H), 1.92–1.88 (m, 1H), 1.63 (dq, J = 12.4, 8.4 Hz, 1H), 1.42–1.28 (m, 9H), 1.24 (s, 12H), 0.77 (t, J = 7.6

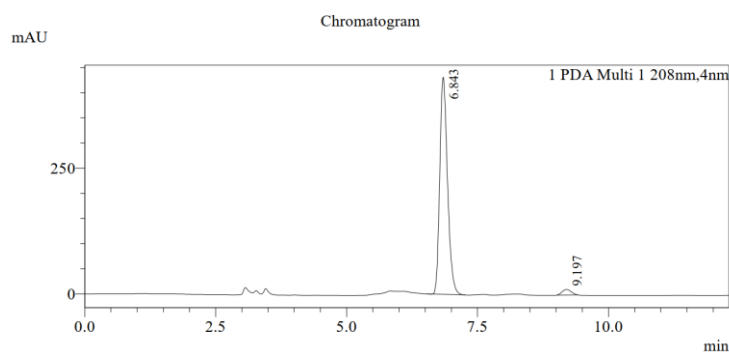
Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.9, 136.8, 128.7, 128.1, 127.5, 82.9, 46.7, 44.9, 42.0, 32.4, 31.4, 29.4, 27.2, 24.9, 24.8, 24.0; **HRMS (ESI)**: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{36}\text{BNO}_3\text{Na}^+$: 408.2681; found: 408.2679.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 208 nm, t_{R} = 6.843 min (major), t_{R} = 9.197 min (minor); 97:3 e.r.



Peak Table

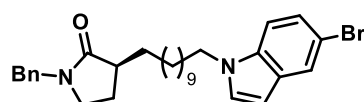
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	6.972	7.488	487148	5134303	49.638
2	9.422	9.909	363176	5209167	50.362
Total			850324	10343470	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	6.843	7.264	431742	4443052	97.039
2	9.197	9.419	11246	135558	2.961
Total			442988	4578610	100.000

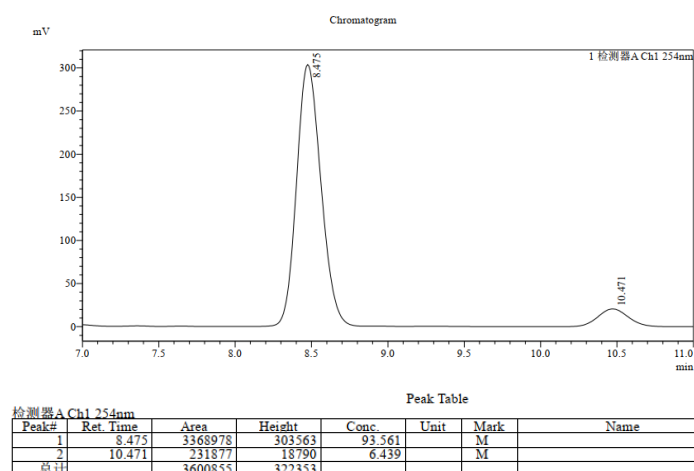
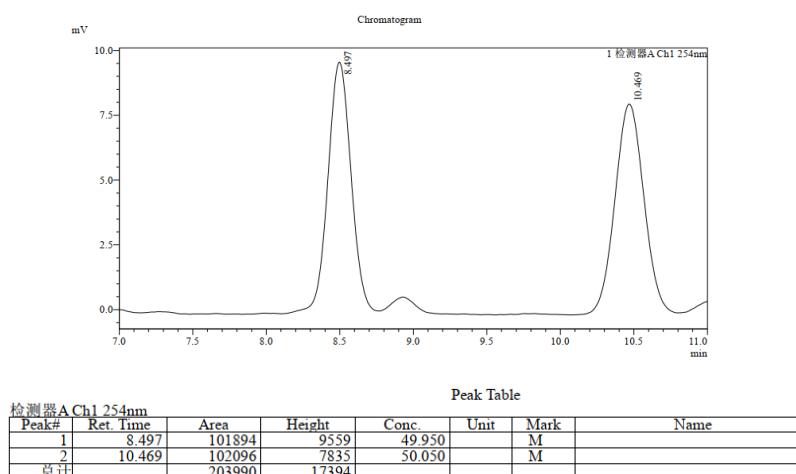
(S)-1-benzyl-3-(11-(5-bromo-1H-indol-1-yl)undecyl)pyrrolidin-2-one (3r)



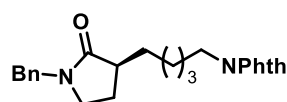
General procedure was followed on 0.2 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3r** as a pale yellow oil (46.5 mg, 44%). R_f = 0.36 (PE/EtOAc = 3/1); $[\alpha]_{\text{D}}^{25}$ = + 8.38 (c = 2.10, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ 7.73 (d, J = 1.2 Hz, 1H), 7.33–7.18 (m, 7H), 7.08 (d, J = 3.2 Hz, 1H), 6.41 (d, J = 3.2 Hz, 1H), 4.44

(abq, $J = 14.4$ Hz, 2H), 4.07 (t, $J = 7.2$ Hz, 1H), 3.17–3.14 (m, 2H), 2.46–2.39 (m, 1H), 2.18–2.10 (m, 1H), 1.92–1.89 (m, 1H), 1.83–1.78 (m, 2H), 1.62 (dq, $J = 12.8, 8.4$ Hz, 1H), 1.34–1.23 (m, 17H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.0, 136.8, 134.7, 130.3, 129.1, 128.7, 128.2, 127.6, 124.2, 123.4, 112.5, 110.9, 100.6, 46.8, 46.7, 45.0, 42.1, 31.5, 30.3, 29.6, 29.6, 29.6, 29.6, 29.5, 29.3, 27.3, 27.0, 24.9. **HRMS (ESI):** $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{30}\text{H}_{40}\text{N}_2\text{OBr}^+$: 523.2319; found: 523.2308.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 80/20, flow rate 1.0 mL/min, $\lambda = 245$ nm, $t_{\text{R}} = 8.475$ min (major), $t_{\text{R}} = 10.471$ min (minor); 93.5:6.5 e.r.



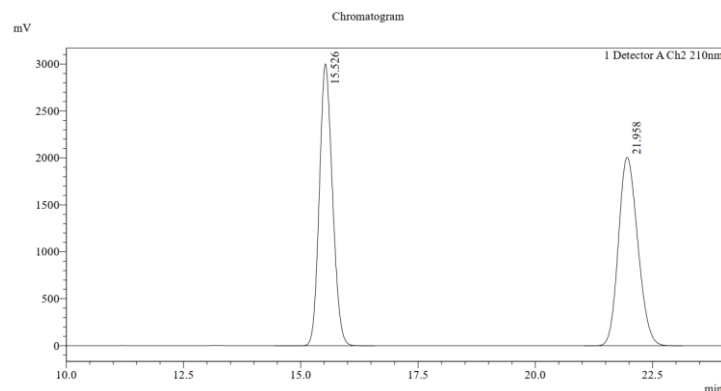
(S)-2-(5-(1-benzyl-2-oxopyrrolidin-3-yl)pentyl)isoindoline-1,3-dione (**3s**)



General procedure was followed on 0.2 mmol scale with a reaction time of 42 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3s** as a colorless oil (70.4 mg, 90%); $R_f = 0.42$ (PE/EtOAc = 1/1); $[\alpha]_{\text{D}}^{20} = +1.50$ ($c = 6.20$, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ 7.86–7.81 (m, 2H), 7.73–7.69 (m, 2H), 7.34–7.25 (m, 3H), 7.24–7.21 (m, 2H), 4.44 (abq, $J = 14.8$ Hz, 2H), 3.68 (t, J

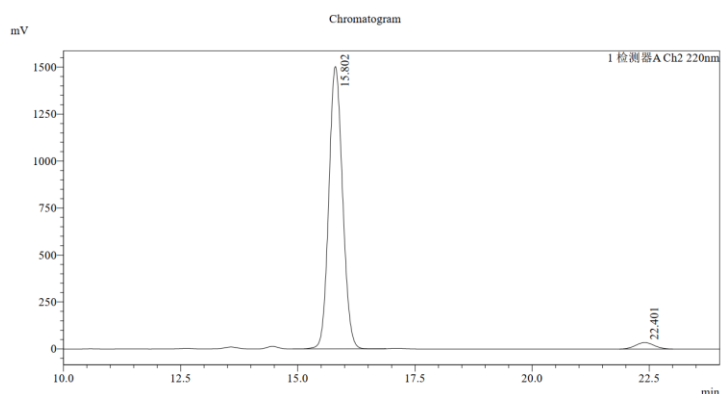
= 7.2 Hz, 2H), 3.20–3.13 (m, 2H), 2.47–2.41 (m, 1H), 2.20–2.12 (m, 1H), 1.92–1.86 (m, 1H), 1.74–1.58 (m, 3H), 1.47–1.33 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.6, 168.4, 136.6, 133.9, 132.1, 128.6, 128.0, 127.4, 123.1, 46.6, 44.8, 41.8, 37.8, 31.2, 28.4, 26.7, 26.7, 24.7; **HRMS (ESI)**: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{24}\text{H}_{26}\text{N}_2\text{O}_3\text{Na}^+$: 413.1836; found: 413.1835.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 220 nm, t_{R} = 15.802 min (major), t_{R} = 22.401 min (minor); 97:3 e.r.



Peak Table

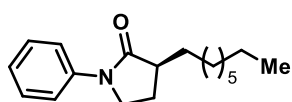
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	15.526	58299286	3003058	50.280		M	
2	21.958	57650247	2007321	49.720		M	
总计		115949533	5010379				



Peak Table

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	15.802	30575490	1502822	96.993		M	
2	22.401	947906	34179	3.007		M	
总计		31523396	1537001				

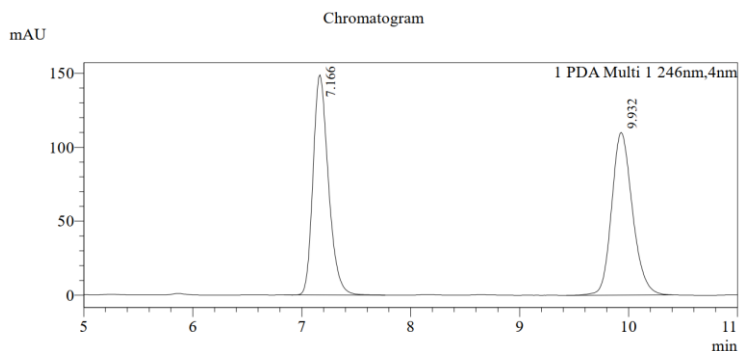
(S)-3-octyl-1-phenylpyrrolidin-2-one (3t)



General procedure was followed on 0.2 mmol scale with a reaction time of 52 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3t** as a pale yellow oil (28.8 mg, 53%). R_f = 0.25 (PE/EtOAc = 10/1); $[\alpha]_{\text{D}}^{20}$ = +3.90 (c = 2.21, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ 7.63 (d, J = 7.6 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.13 (t, J = 7.2 Hz, 1H), 3.79–3.76 (m, 2H), 2.62–2.55 (m, 1H),

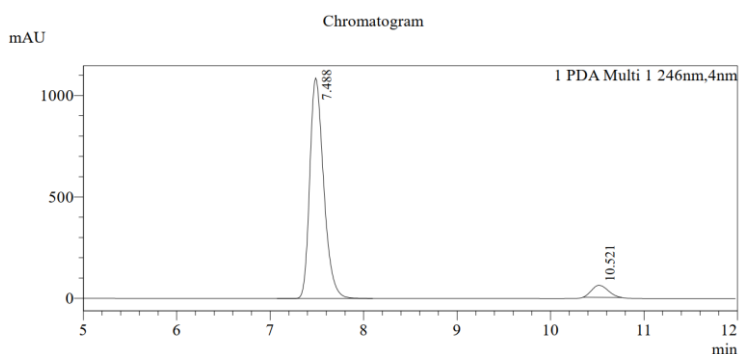
2.36–2.28 (m, 1H), 2.00–1.93 (m, 1H), 1.84–1.75 (m, 1H), 1.46–1.28 (m, 13H), 0.88 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.3, 139.8, 128.9, 124.4, 119.8, 46.9, 43.6, 32.0, 31.4, 29.7, 29.6, 29.4, 27.4, 24.9, 22.8, 14.2; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{28}\text{NO}^+$: 274.2165; found: 274.2167.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 246$ nm, $t_{\text{R}} = 7.488$ (major), $t_{\text{R}} = 10.521$ min (minor); 94:6 e.r.



Peak Table

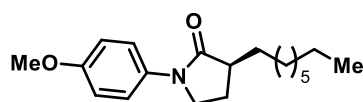
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.166	7.765	148804	1457555	49.965
2	9.932	10.411	109959	1459609	50.035
Total			258763	2917163	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.488	8.096	1086915	11226755	93.909
2	10.521	10.763	59709	728145	6.091
Total			1146624	11954899	100.000

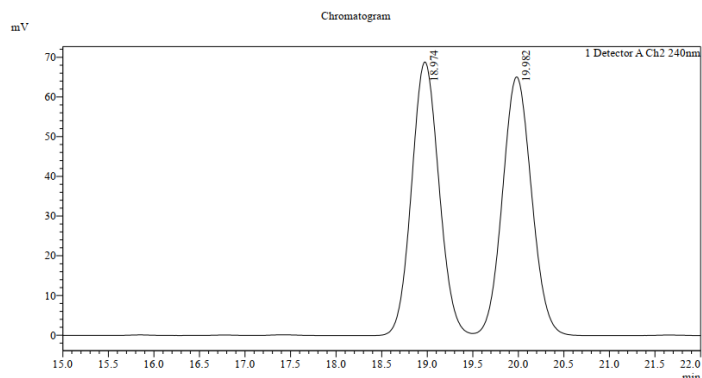
(S)-1-(4-methoxyphenyl)-3-octylpyrrolidin-2-one (**3u**)



General procedure was followed on 0.2 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3u** as a colorless oil (40.4 mg, 67%); $R_f = 0.34$ (PE/EtOAc = 5/1); $[\alpha]_{\text{D}}^{20} = +10.4$ ($c = 1.00$, CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3): δ 7.52 (d, $J = 8.8$

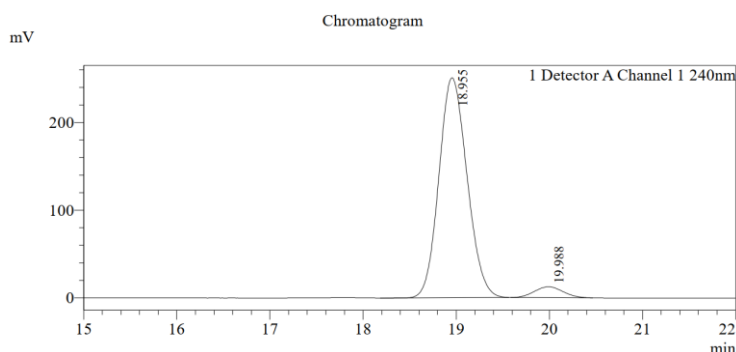
Hz, 2H), 6.89 (d, $J = 9.2$ Hz, 2H), 3.79 (s, 3H), 3.75–3.71 (m, 2H), 2.60–2.52 (m, 1H), 2.34–2.26 (m, 1H), 1.98–1.89 (m, 1H), 1.83–1.74 (m, 1H), 1.45–1.27 (m, 13H), 0.88 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.9, 156.5, 133.1, 121.6, 114.1, 55.6, 47.3, 43.4, 32.0, 31.4, 29.7, 29.6, 29.4, 27.4, 25.0, 22.8, 14.2; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{19}\text{H}_{30}\text{NO}_2^+$: 304.2271; found: 304.2270.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 95/5, flow rate 1.0 mL/min, $\lambda = 240$ nm, $t_{\text{R}} = 18.955$ min (major), $t_{\text{R}} = 19.988$ min (minor); 95:5 e.r.



Peak Table

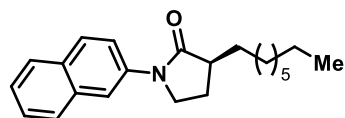
Peak#	Ret. Time	Area	Height	Conc	Unit	Mark	Name
1	18.974	1418615	68547	49.992		M	
2	19.982	1419096	64732	50.008		M	
总计		2837711	133278				



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	18.955	19.567	250709	5269929	95.199
2	19.988	20.467	12429	265753	4.801
Total			263138	5535682	100.000

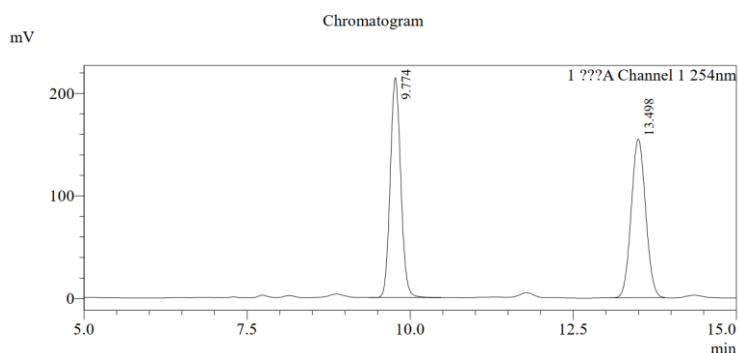
(S)-1-(naphthalen-2-yl)-3-octylpyrrolidin-2-one (**3v**)



General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3v** as a colorless oil (42.5 mg, 66%). $R_f = 0.21$ (PE/EtOAc = 10/1); $[\alpha]_{\text{D}}^{20} = +9.00$ ($c = 1.00$, CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3): δ 8.00 (d, $J =$

8.8 Hz, 1H), 7.89 (s, 1H), 7.84–7.79 (m, 3H), 7.48–7.39 (m, 2H), 3.89–3.86 (m, 2H), 2.67–2.59 (m, 1H), 2.39–2.32 (m, 1H), 2.03–1.97 (m, 1H), 1.88–1.78 (m, 1H), 1.51–1.29 (m, 13H), 0.90 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.5, 137.5, 133.6, 130.7, 128.6, 127.8, 127.6, 126.4, 125.2, 119.8, 116.6, 47.1, 43.7, 32.0, 31.4, 29.7, 29.6, 29.41, 27.4, 25.0, 22.8, 14.2; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{22}\text{H}_{30}\text{NO}^+$: 324.2322; found: 324.2317.

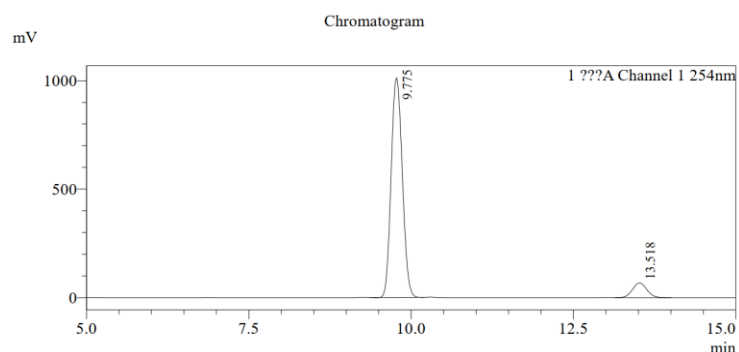
HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 254$ nm, $t_{\text{R}} = 9.775$ min (major), $t_{\text{R}} = 13.518$ min (minor); 92:8 e.r.



Peak Table

???A Channel 1 254nm

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	9.774	10.475	214234	2409241	50.233
2	13.498	13.908	154838	2386858	49.767
Total			369072	4796099	100.000

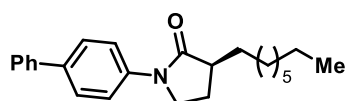


Peak Table

???A Channel 1 254nm

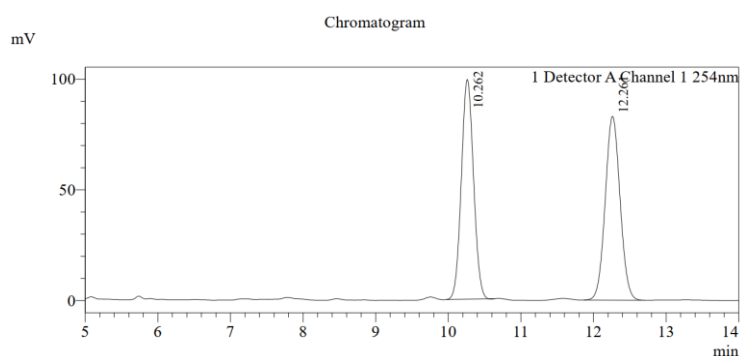
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	9.775	10.233	1011124	12083602	92.077
2	13.518	14.008	67800	1039741	7.923
Total			1078924	13123343	100.000

(S)-1-([1,1'-biphenyl]-4-yl)-3-octylpyrrolidin-2-one (**3w**)



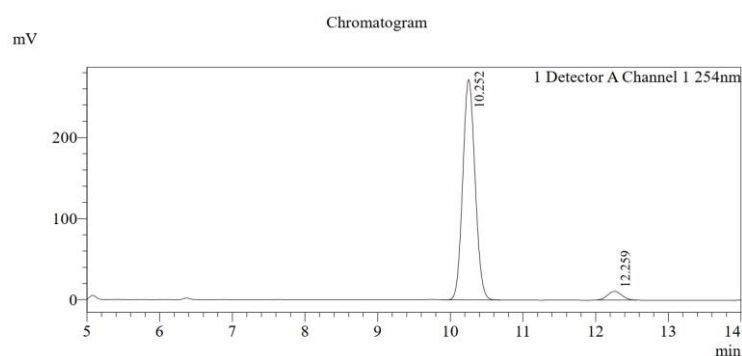
General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel,

PE/EtOAc = 5/1) to afford **3w** as a colorless oil (51.7 mg, 74%); R_f = 0.18 (PE/EtOAc = 10/1); $[\alpha]_D^{20}$ = +20.6 (c =1.00, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃): δ 7.73 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 7.2 Hz, 2H), 7.44 (t, J = 8.0 Hz, 2H), 7.33 (d, J = 7.6 Hz, 1H), 3.81 (dd, J = 8.4, 5.2 Hz, 2H), 2.65–2.57 (m, 1H), 2.38–2.30 (m, 1H), 2.02–1.96 (m, 1H), 1.87–1.77 (m, 1H), 1.52–1.29 (m, 13H), 0.90 (t, J = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 176.4, 140.6, 139.0, 137.1, 128.9, 127.5, 127.2, 127.0, 120.0, 46.9, 43.6, 32.0, 31.4, 29.7, 29.6, 29.4, 27.3, 24.9, 22.8, 14.2; **HRMS (ESI)**: $[M+H]^+$ Calcd for C₂₄H₃₂NO⁺: 350.2478; found: 350.2474. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, t_R = 10.252 min (major), t_R = 12.259 min (minor); 95.5:4.5 e.r.



Peak Table

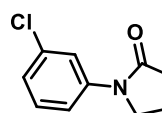
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	10.262	10.642	99161	1158390	49.519
2	12.261	12.708	83023	1180871	50.481
Total			182184	2339261	100.000



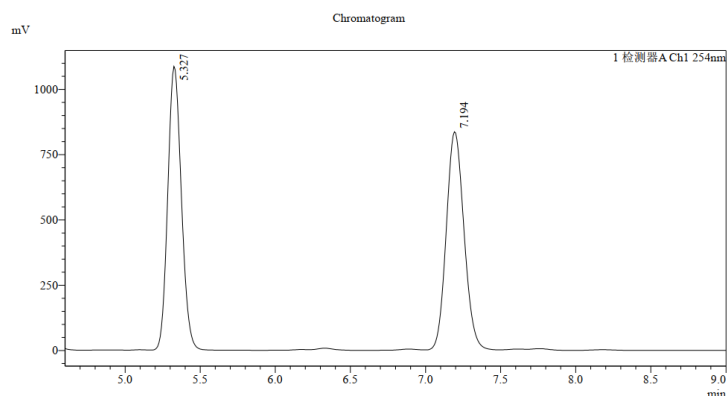
Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	10.252	10.692	271668	3205033	95.611
2	12.259	12.567	10724	147118	4.389
Total			282392	3352151	100.000

(S)-1-(3-chlorophenyl)-3-octylpyrrolidin-2-one (3x)

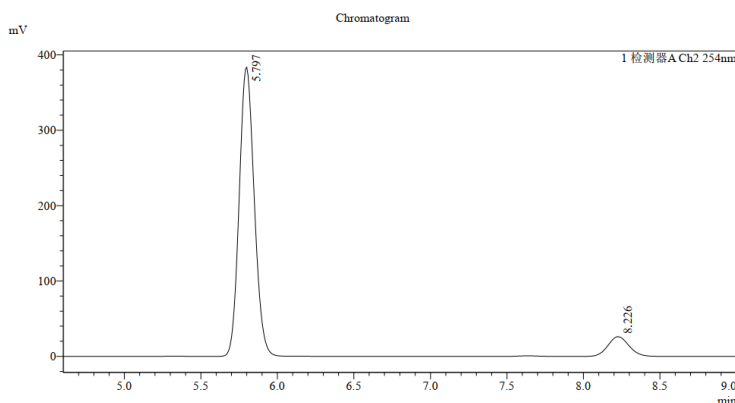


General procedure was followed on 0.2 mmol scale with a reaction time of 107 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3x** as a colorless oil (24.3 mg, 40%). R_f = 0.26 (PE/EtOAc = 30/1); $[\alpha]_D^{25}$ = +4.60 (c = 2.00, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ 7.70 (t, J = 2.0 Hz, 1H), 7.56–7.54 (m, 1H), 7.27 (t, J = 8.0 Hz, 1H), 7.11–7.08 (m, 1H), 3.74 (dd, J = 8.4, 5.2 Hz, 2H), 2.62–2.55 (m, 1H), 2.37–2.30 (m, 1H), 1.98–1.91 (m, 1H), 1.84–1.75 (m, 1H), 1.49–1.27 (m, 13H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.5, 140.9, 134.6, 129.9, 124.3, 119.7, 117.6, 46.8, 43.6, 32.0, 31.3, 29.7, 29.6, 29.4, 27.3, 24.8, 22.8, 14.2; **HRMS (EI)**: Calcd for $\text{C}_{18}\text{H}_{26}\text{ClNO}$: 307.1703; found: 307.1706. **HPLC** (Chiralpak AD-H): n -Hexane/ i -PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, t_R = 5.797 min (major), t_R = 8.226 min (minor); 93:7 e.r.



检测器A Ch1 254nm

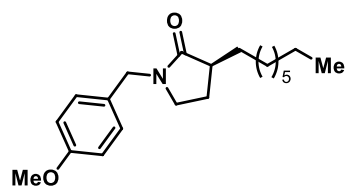
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.327	6817248	1085535	50.231		M	
2	7.194	6754502	830850	49.769		M	
总计		13571750	1916385				



检测器A Ch2 254nm

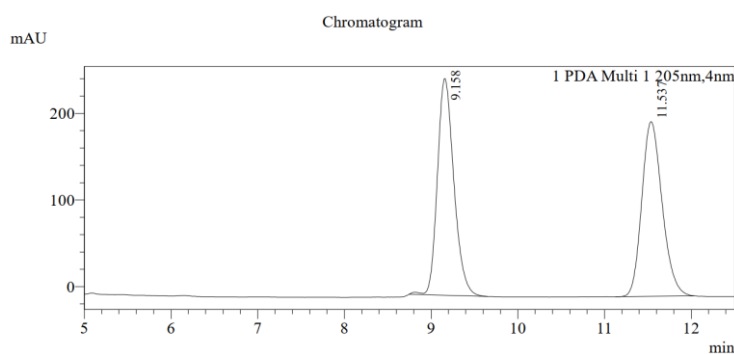
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.797	2625294	383638	92.897		M	
2	8.226	200719	23705	7.103		M	
总计		2826013	407343				

(S)-1-(4-methoxybenzyl)-3-octylpyrrolidin-2-one (3y)



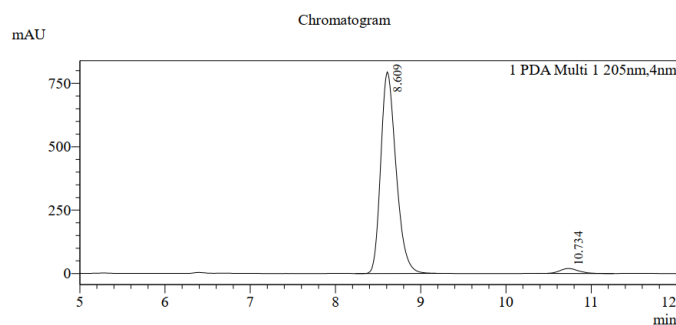
General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3y** as a colorless oil (52.9 mg, 83%). R_f = 0.38 (PE/EtOAc = 3/1); $[\alpha]_D^{25}$ = +4.60 (c = 2.00, CHCl_3). **^1H NMR** (400 MHz, CDCl_3): δ 7.15 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 8.4 Hz, 2H), 4.38 (abq, J = 14.4 Hz, 2H), 3.78 (s, 3H), 3.16–3.12 (m, 2H), 2.45–2.37 (m, 1H), 2.18–2.09 (m, 1H), 1.91–1.86 (m, 1H), 1.61 (dq, J = 12.8, 8.4 Hz, 1H), 1.33–1.25 (m, 13H), 0.87 (t, J = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl_3): δ 176.8, 159.1, 129.6, 129.0, 114.1, 55.4, 46.2, 44.9, 42.2, 32.0, 31.5, 29.7, 29.6, 29.4, 27.3, 24.9, 22.8, 14.2; **HRMS (ESI)**: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{31}\text{NO}_2\text{Na}^+$: 340.2247; found: 340.2242.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 90/10, flow rate 1.0 mL/min, λ = 205 nm, t_R = 8.609 min (major), t_R = 10.734 min (minor); 97:3 er.



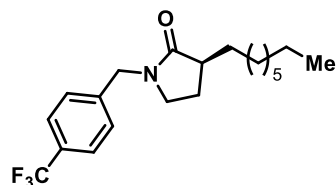
Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	9.158	9.653	250178	3312572	50.167
2	11.537	12.032	201706	3290542	49.833
Total			451883	6603114	100.000



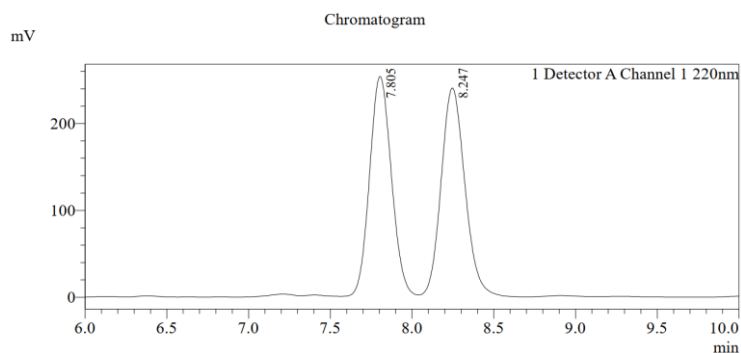
Peak Table					
PDA Ch1 205nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	8.609	9.237	794396	9923858	97.110
2	10.734	11.264	19444	295291	2.890
Total			813841	10219148	100.000

(S)-3-octyl-1-(4-(trifluoromethyl)benzyl)pyrrolidin-2-one (3z)

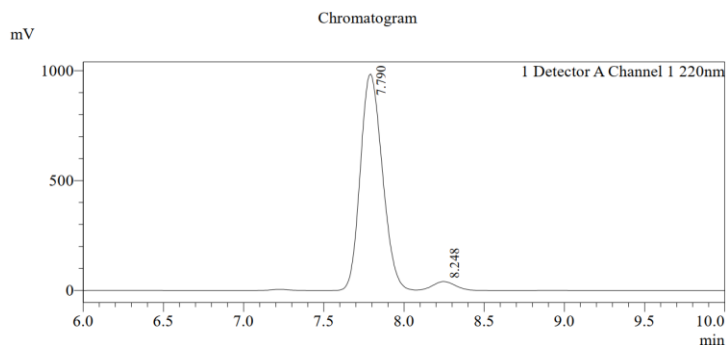


General procedure was followed on 0.2 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3z** as a pale yellow oil (58.3 mg, 82%). R_f = 0.50 (PE/EtOAc = 3/1); $[\alpha]_D^{25}$ = +3.95 (c = 2.43, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.56 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 4.48 (abq, J = 14.8 Hz), 3.17 (dd, J = 8.4, 5.6 Hz, 1H), 2.47–2.40 (m, 1H), 2.22–2.14 (m, 1H), 1.92–1.89 (m, 1H), 1.65 (dq, J = 12.8, 8.4 Hz, 1H), 1.35–1.25 (m, 13H), 0.86 (t, J = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 177.2, 141.0, 129.9 (q, J_{C-F} = 32.3 Hz), 128.4, 125.7 (q, J_{C-F} = 14.8 Hz), 124.2 (q, J_{C-F} = 270.2 Hz), 46.4, 45.1, 41.9, 32.0, 31.4, 29.7, 29.6, 29.4, 27.3, 24.9, 22.8, 14.2. **¹⁹F NMR** (376 MHz, CDCl₃): -62.5; **HRMS (EI)**: Calcd for C₂₀H₂₈F₃NO: 355.2123; found: 355.2121.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm, t_R = 7.790 min (major), t_R = 8.248 min (minor); 96:4 e.r.



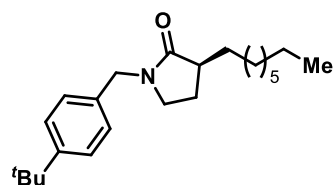
Peak Table					
Detector A Channel 1 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.805	8.033	252281	2328165	49.266
2	8.247	8.725	238926	2397562	50.734
Total			491208	4725727	100.000



Peak Table

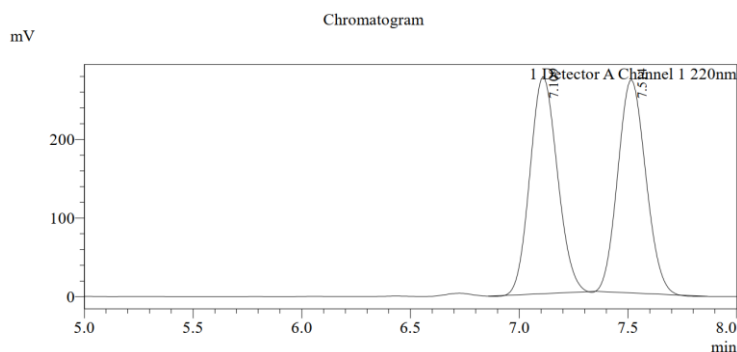
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.790	8.058	982430	9369133	96.239
2	8.248	8.575	39081	366108	3.761
Total			1021511	9735241	100.000

(S)-1-(4-(tert-butyl)benzyl)-3-octylpyrrolidin-2-one (3aa)

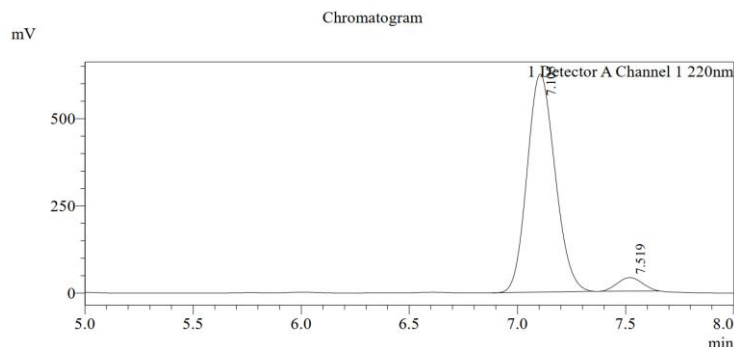


General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3aa** as a pale yellow oil (60.8 mg, 88%); R_f = 0.50 (PE/EtOAc = 3/1); $[\alpha]_D^{20}$ = +5.80 (c = 1.00, CH_2Cl_2). **^1H NMR** (400 MHz, CDCl_3): δ 7.33 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 4.41 (abq, J = 14.8 Hz, 2H), 3.19–3.15 (m, 2H), 2.45–2.39 (m, 1H), 2.18–2.10 (m, 1H), 1.93–1.89 (m, 1H), 1.67–1.58 (m, 1H), 1.45–1.26 (m, 22H), 0.87 (t, J = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl_3): δ 176.9, 150.4, 133.7, 127.9, 125.6, 46.4, 45.0, 42.1, 34.6, 32.0, 31.5, 31.4, 29.7, 29.6, 29.4, 27.30, 24.83, 22.75, 14.2; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{38}\text{NO}^+$: 344.2948; found: 344.2943.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm, t_R = 7.105 min (major), t_R = 7.519 min (minor); 94.5:5.5 e.r.

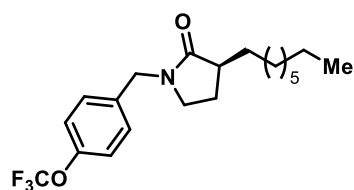


Peak Table					
Detector A Channel 1 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.109	7.350	275965	2430889	50.068
2	7.514	7.867	270901	2424255	49.932
Total			546866	4855144	100.000



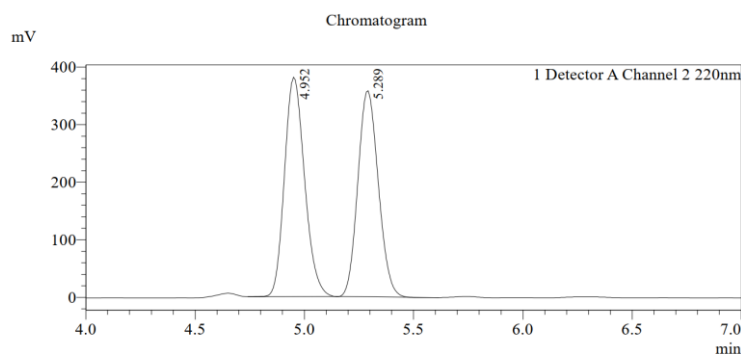
Peak Table					
Detector A Channel 1 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.105	7.350	624881	5641325	94.715
2	7.519	7.658	38932	314761	5.285
Total			663812	5956086	100.000

(S)-3-octyl-1-(4-(trifluoromethoxy)benzyl)pyrrolidin-2-one (**3ab**)



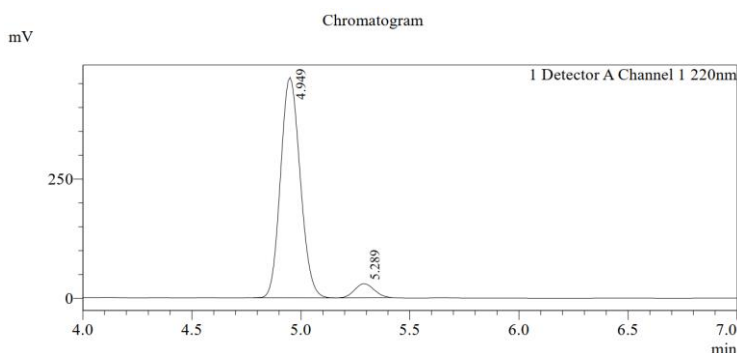
General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 3/1) to afford **3ab** as a pale yellow oil (62.7 mg, 84%). $[\alpha]_D^{20} = +2.00$ ($c=1.00$, CHCl_3). $R_f = 0.38$ (PE/EtOAc = 3/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.24 (d, $J = 8.4$ Hz, 2H), 7.15 (d, $J = 8.4$ Hz, 2H), 4.46 (abq, $J = 14.8$ Hz, 2H), 3.18–3.15 (m, 2H), 2.45–2.39 (m, 1H), 2.20–2.12 (m, 1H), 1.91–1.88 (m, 1H), 1.69–1.59 (m, 1H) 1.34–1.25 (m, 13H), 0.86 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 177.1, 148.7, 135.6, 129.5, 121.3, 120.5 (q, $J_{C-F} = 255.5$ Hz), 46.0, 45.0, 41.9, 32.0, 31.4, 29.7, 29.6, 29.4, 27.3, 24.9, 22.8, 14.2; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): -57.9; **HRMS (ESI)**: $[M+H]^+$ Calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_2\text{F}_3^+$: 372.2145; found: 372.2142.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 220$ nm, $t_R = 4.949$ min (major), $t_R = 5.289$ min (minor); 94:6 e.r.



Peak Table

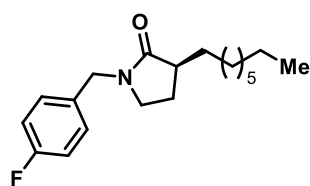
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	4.952	5.158	381003	2422416	50.956
2	5.289	5.617	357662	2331537	49.044
Total			738665	4753953	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	4.949	5.167	462141	2871111	94.026
2	5.289	5.417	29381	182411	5.974
Total			491522	3053522	100.000

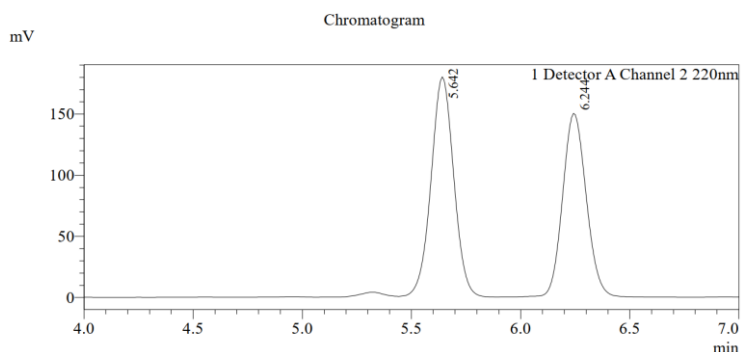
(S)-1-(4-fluorobenzyl)-3-octylpyrrolidin-2-one (**3ac**)



General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3ac** as a pale yellow oil (48.9 mg, 80%); R_f = 0.38 (PE/EtOAc = 3/1); $[\alpha]_D^{20}$ = +3.80 (c = 3.50, CHCl_3). **^1H NMR** (400 MHz, CDCl_3): δ 7.20–7.16 (m, 2H), 7.00–6.96 (m, 2H), 4.40 (abq, J = 14.8 Hz, 2H), 3.17–3.13 (m, 2H), 2.44–2.38 (m, 1H), 2.18–2.10 (m, 1H), 1.90–1.87 (m, 1H), 1.62 (dq, J = 12.8, 8.2 Hz, 1H), 1.33–1.25 (m, 13H), 0.86 (t, J = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl_3): δ 177.0, 162.3 (d, $J_{\text{C-F}}$ = 244.1 Hz), 132.6 (d, $J_{\text{C-F}}$ = 3.4 Hz), 129.9 (d, $J_{\text{C-F}}$ = 8.0 Hz), 115.6 (d, $J_{\text{C-F}}$ = 21.4 Hz), 46.0, 44.9, 42.0, 32.0, 31.4, 29.7, 29.6, 29.4, 27.3, 24.8, 22.8, 14.2; **^{19}F NMR** (376 MHz, CDCl_3): -5.34–-5.35 (m). **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for

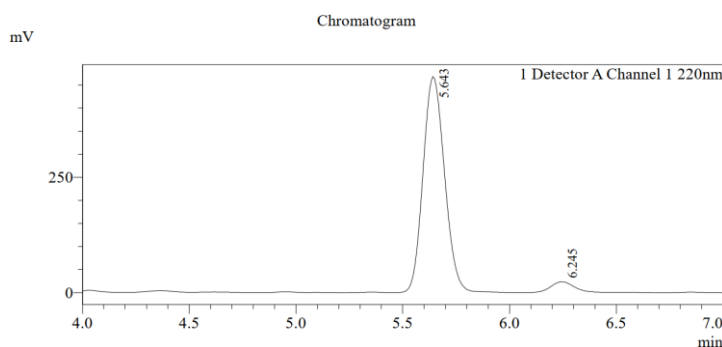
C₁₉H₂₉NOF⁺: 306.2228; found: 306.2225.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 220 nm, *t_R* = 5.643 min (major), *t_R* = 6.245 min (minor); 95.5:4.5 e.r.



Peak Table

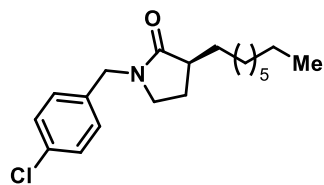
Detector A Channel 2 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.642	5.775	170856	1147916	50.691
2	6.244	6.475	149609	1116606	49.309
Total			320465	2264522	100.000



Peak Table

Detector A Channel 1 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.643	5.975	467629	3275314	95.664
2	6.245	6.383	21706	148471	4.336
Total			489335	3423786	100.000

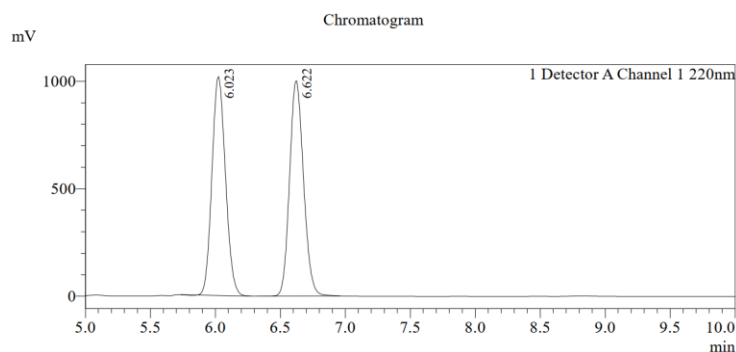
(S)-1-(4-chlorobenzyl)-3-octylpyrrolidin-2-one (**3ad**)



General procedure was followed on 0.2 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3ad** as a pale yellow oil (54.3 mg, 84%). *R_f* = 0.5 (PE/EtOAc = 3/1); $[\alpha]_D^{25}$ = +2.17 (*c* = 3.23, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.19 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 4.32 (abq, *J* = 14.4 Hz, 2H), 3.08–3.05 (m, 2H), 2.36–2.30 (m, 1H), 2.11–2.03 (m, 1H), 1.82–1.79 (m, 1H), 1.55 (dq, *J* = 12.8, 8.8 Hz, 1H), 1.25–1.17 (m, 13H), 0.78 (t, *J* = 6.8 Hz, 3H); **¹³C NMR** (100 MHz,

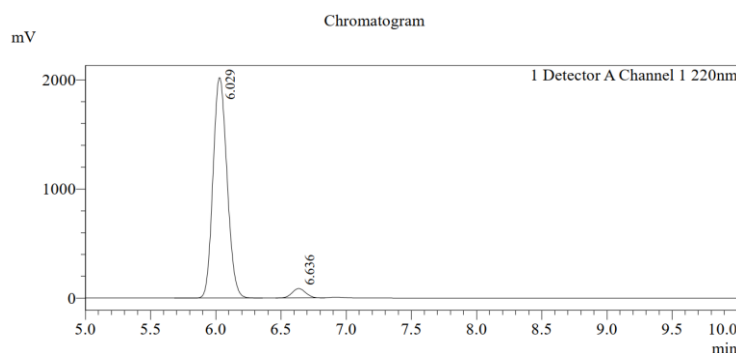
CDCl₃): δ 177.0, 135.4, 133.4, 129.6, 128.9, 46.1, 44.9, 41.9, 31.9, 31.4, 29.6, 29.6, 29.4, 27.3, 24.9, 22.8, 14.2; **HRMS (ESI)**: [M+H]⁺ Calcd for C₁₉H₂₉NOCl⁺: 322.1932; found: 322.1930.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 220 nm, *t*_R = 6.029 min (major), *t*_R = 6.636 min (minor); 96:4 e.r.



Peak Table

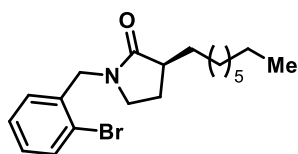
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	6.023	6.283	1017445	7373162	49.613
2	6.622	6.958	1000602	7488135	50.387
Total			2018047	14861297	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	6.029	6.358	2017109	15091425	96.067
2	6.636	6.842	85808	617902	3.933
Total			2102917	15709327	100.000

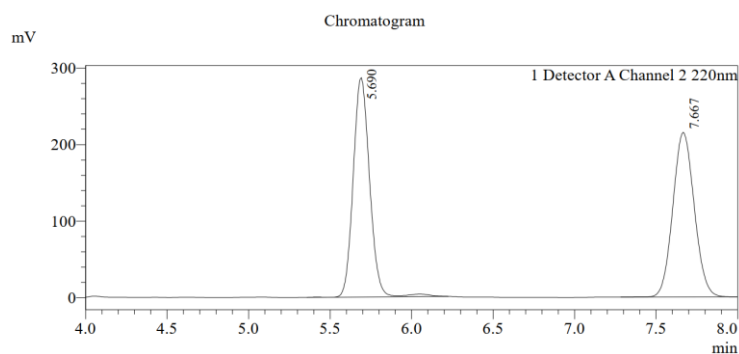
(S)-1-(2-bromobenzyl)-3-octylpyrrolidin-2-one (**3ae**)



General procedure was followed on 0.2 mmol scale with a reaction time of 57 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3ae** as a pale yellow oil (45.4 mg, 62%); *R*_f = 0.5 (PE/EtOAc = 5/1); [α]_D²⁰ = +3.40 (*c* = 3.16, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.55 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.28 (td, *J* = 7.2, 0.8 Hz, 1H), 7.22 (dd, *J* = 7.6, 1.2 Hz,

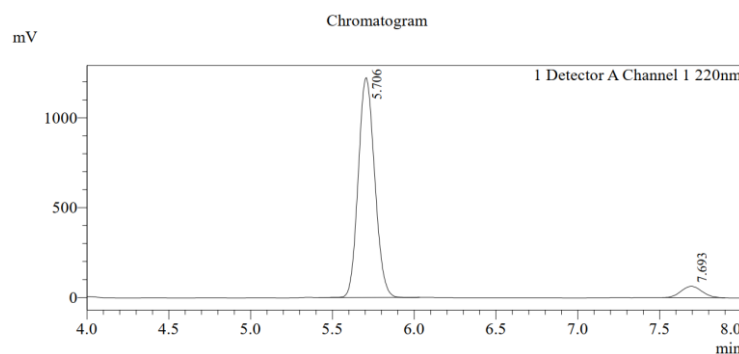
1H), 7.14 (td, $J = 7.2, 1.2$ Hz, 1H), 4.59 (abq, $J = 15.2$ Hz, 2H), 3.26–3.18 (m, 2H), 2.48–2.42 (m, 1H), 2.23–2.15 (m, 1H), 1.94–1.90 (m, 1H), 1.67 (dq, $J = 12.8, 8.4$ Hz, 1H), 1.37–1.27 (m, 13H), 0.88 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.2, 135.9, 133.0, 129.8, 129.2, 127.9, 123.8, 46.6, 45.3, 41.9, 32.0, 31.4, 29.7, 29.6, 29.4, 27.3, 25.0, 22.8, 14.2; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{19}\text{H}_{29}\text{NOBr}^+$: 366.1427; found: 366.1422.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 220$ nm, $t_{\text{R}} = 5.706$ min (major), $t_{\text{R}} = 7.693$ min (minor); 94:6 e.r.



Peak Table

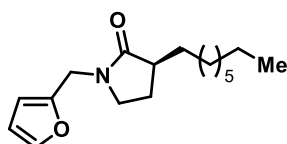
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.690	6.225	286321	2014108	50.633
2	7.667	8.083	215007	1963765	49.367
Total			501328	3977873	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.706	6.033	1222439	8557765	93.791
2	7.693	7.900	63524	566528	6.209
Total			1285964	9124292	100.000

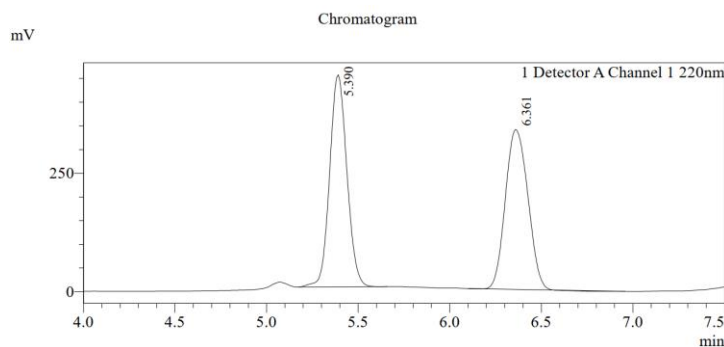
(S)-1-(furan-2-ylmethyl)-3-octylpyrrolidin-2-one (3af)



General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1)

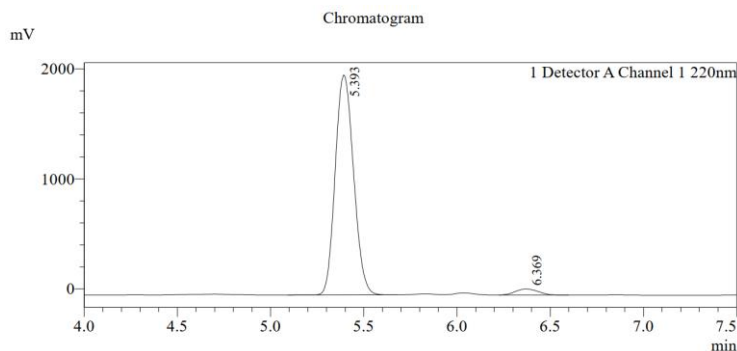
to afford **3af** as a pale yellow oil (46.7 mg, 84%); R_f = 0.38 (PE/EtOAc = 3/1); $[\alpha]_D^{20}$ = +5.00 (c=1.00, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃): δ 7.33 (s, 1H), 6.29 (s, 1H), 6.20 (d, J = 2.8 Hz, 1H), 4.43 (s, 2H), 3.29–3.19 (m, 2H), 2.41–2.35 (m, 1H), 2.19–2.10 (m, 1H), 1.88–1.84 (m, 1H), 1.67–1.58 (m, 1H), 1.31–1.24 (m, 13H), 0.86 (t, J = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 176.8, 150.5, 142.4, 110.5, 108.3, 45.3, 42.0, 39.5, 32.0, 31.4, 29.7, 29.6, 29.4, 27.3, 24.9, 22.8, 14.3; **HRMS (ESI)**: $[M+Na]^+$ Calcd for C₁₇H₂₇NO₂Na⁺: 300.1934; found: 300.1927.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 220 nm, t_R = 5.393 min (major), t_R = 6.369 min (minor); 96.5:3.5 e.r.



Peak Table

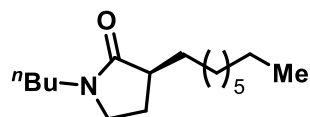
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.390	5.658	447248	2937132	50.468
2	6.361	6.958	337798	2882615	49.532
Total			785045	5819747	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.393	5.683	2000626	13721034	96.716
2	6.369	6.600	54791	465882	3.284
Total			2055417	14186916	100.000

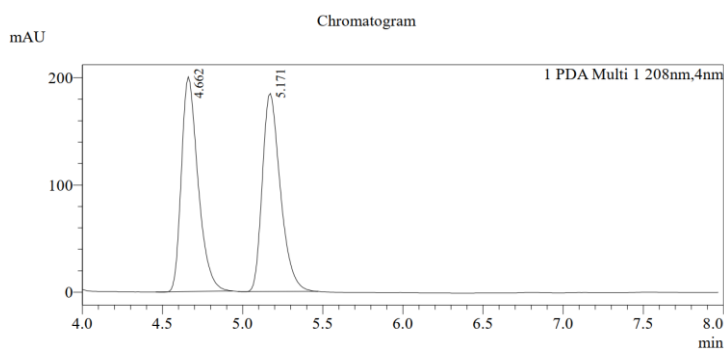
(S)-1-butyl-3-octylpyrrolidin-2-one (3ag)



General procedure was followed on 0.2 mmol scale with a reaction time of 52 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1)

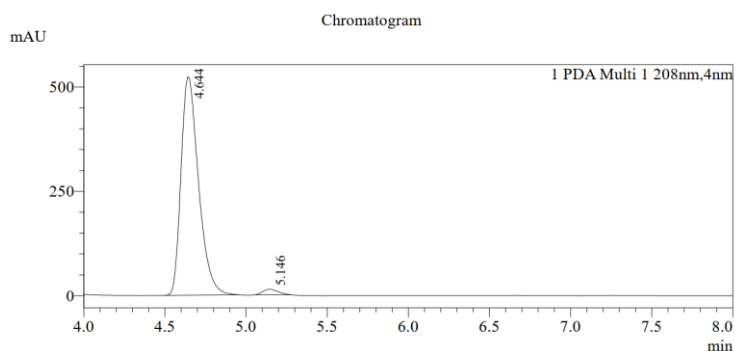
to afford **3ag** as a pale yellow oil (40.9 mg, 81%); R_f = 0.29 (PE/EtOAc = 5/1); $[\alpha]_D^{20}$ = +9.20 (c =3.35, CHCl_3). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 3.30–3.18 (m, 4H), 2.36–2.34 (m, 1H), 2.19–2.11 (m, 1H), 1.90–1.78 (m, 1H), 1.62 (dq, J = 12.4, 8.4 Hz, 1H), 1.49–1.42 (m, 2H), 1.32–1.23 (m, 15H), 0.90 (t, J = 7.2 Hz, 3H), 0.85 (t, J = 6.8 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 176.8, 45.4, 42.4, 42.2, 32.0, 31.5, 29.7, 29.6, 29.5, 29.4, 27.4, 25.0, 22.8, 20.1, 14.2, 13.9; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{32}\text{NO}^+$: 254.2478; found: 254.2483.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 90/10, flow rate 1.0 mL/min, λ = 208 nm, t_R = 4.644 min (major), t_R = 5.146 min (minor); 98:2 e.r.



Peak Table

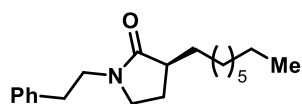
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	4.662	4.939	200366	1450432	50.040
2	5.171	5.472	184720	1448120	49.960
Total			385087	2898552	100.000



Peak Table

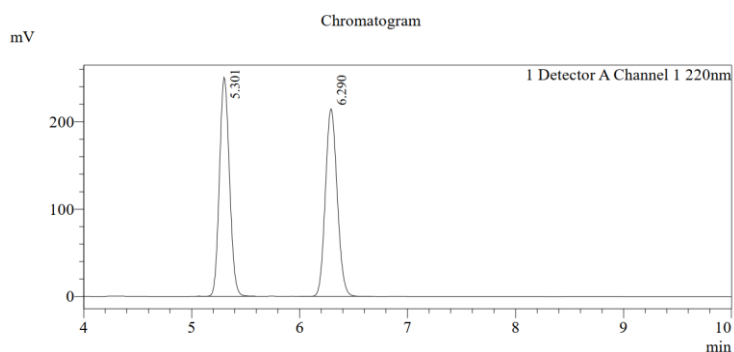
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	4.644	4.960	522905	3928353	97.817
2	5.146	5.280	13239	87653	2.183
Total			536144	4016006	100.000

(S)-3-octyl-1-phenethylpyrrolidin-2-one (3ah)



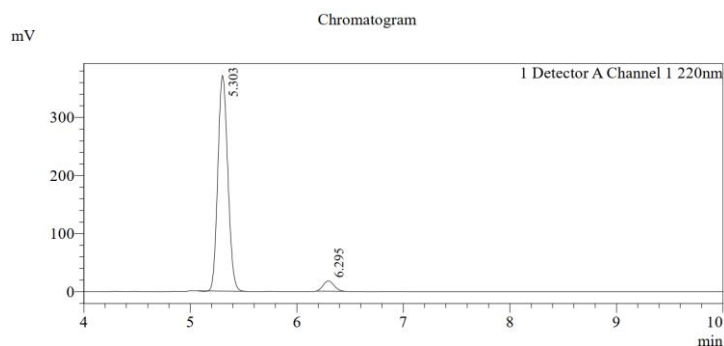
General procedure was followed on 0.21 mmol scale with a reaction time of 60 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3ah** as a pale yellow oil (54.5 mg, 85%); R_f = 0.43 (PE/EtOAc = 3/1); $[\alpha]_D^{20}$ = -5.80 (c = 1.00, CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3): δ 7.30–7.26 (m, 2H), 7.21–7.19 (m, 3H), 3.61–3.53 (m, 1H), 3.50–3.43 (m, 1H), 3.16–3.11 (m, 2H), 2.83 (t, J = 7.2 Hz, 2H), 2.36–2.30 (m, 1H), 2.13–2.05 (m, 1H), 1.88–1.73 (m, 1H), 1.56 (dq, J = 12.8, 8.4 Hz, 1H), 1.33–1.26 (m, 13H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.9, 138.9, 128.8, 128.6, 126.5, 46.0, 44.1, 42.0, 33.9, 31.9, 31.4, 29.7, 29.6, 29.4, 27.2, 25.1, 22.7, 14.2; **HRMS (ESI)**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{32}\text{NO}^+$: 302.2478; found: 302.2475.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 90/10, flow rate 1.0 mL/min, λ = 220 nm, t_R = 5.303 min (major), t_R = 6.295 min (minor); 95:5 e.r.



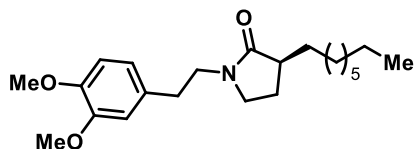
Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.301	5.592	250367	1614585	49.729
2	6.290	6.667	214611	1632214	50.271
Total			464978	3246799	100.000

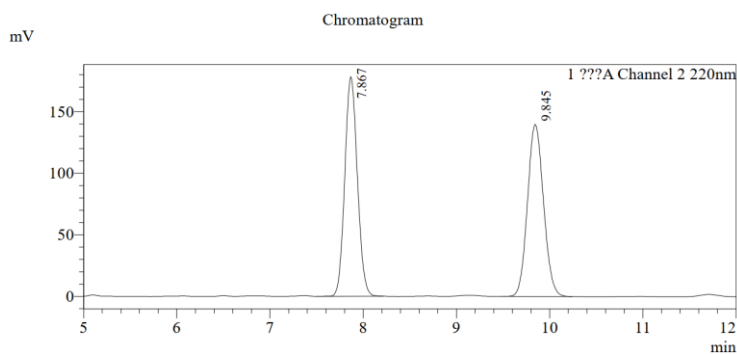


Peak Table					
Detector A Channel 1 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.303	5.525	371230	2417020	95.134
2	6.295	6.450	17546	123620	4.866
Total			388776	2540639	100.000

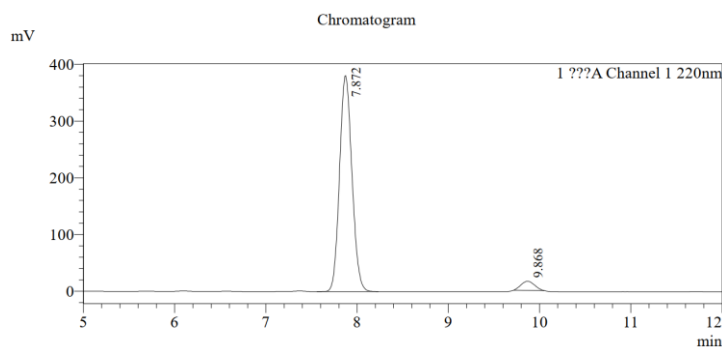
(S)-1-(3,4-dimethoxyphenethyl)-3-octylpyrrolidin-2-one (3ai)



General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3ai** as a colorless oil (42.5 mg, 59%). $R_f = 0.20$ (PE/EtOAc = 3/1); $[\alpha]_D^{20} = -3.00$ ($c = 2.70$, CHCl_3). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 6.78–6.71 (m, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 3.57–3.41 (m, 2H), 3.16–3.13 (m, 2H), 2.76 (t, $J = 7.2$ Hz, 2H), 2.35–2.29 (m, 1H), 2.13–2.04 (m, 1H), 1.81–1.79 (m, 1H), 1.60–1.51 (m, 1H), 1.27–1.24 (m, 13H), 0.86 (t, $J = 6.8$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 176.9, 148.9, 147.6, 131.4, 120.7, 111.9, 111.3, 55.9, 46.0, 44.2, 42.1, 33.4, 31.9, 31.4, 29.7, 29.6, 29.4, 27.3, 25.1, 22.7, 14.2; **HRMS (ESI)**: $[M+H]^+$ Calcd for $\text{C}_{22}\text{H}_{36}\text{NO}_3^+$: 362.2690; found: 362.2689. **HPLC** (Chiralpak AD-H): n -Hexane/ i -PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 220$ nm, $t_R = 7.872$ min (major), $t_R = 9.868$ min (minor); 95.5:4.5 e.r.



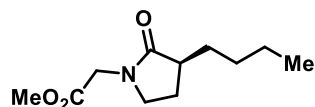
Peak Table					
???A Channel 2 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.867	8.217	178369	1673018	50.005
2	9.845	10.242	139803	1672683	49.995
Total			318172	3345701	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.872	8.233	380491	3597720	95.563
2	9.868	10.050	16170	167026	4.437
Total			396661	3764746	100.000

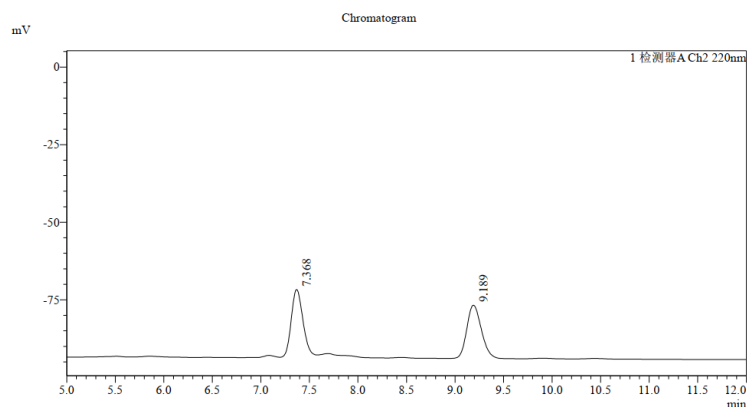
Methyl (S)-2-(3-butyl-2-oxopyrrolidin-1-yl)acetate (**3aj**)



General procedure was followed on 0.2 mmol scale with a reaction time of 38 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1)

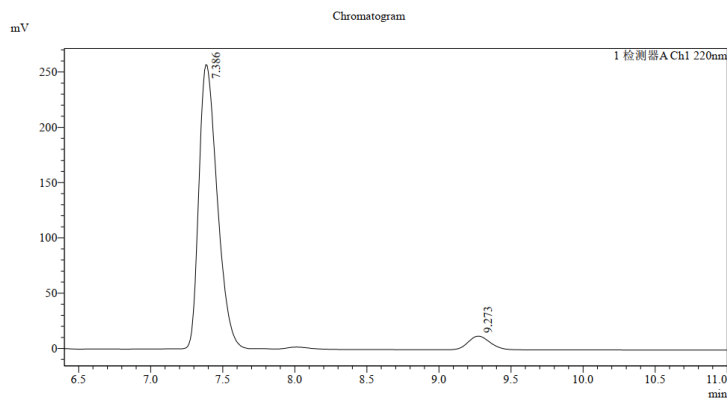
to afford **3aj** as a pale yellow oil (30.1 mg, 70%); R_f = 0.43 (PE/EtOAc = 2/1); $[\alpha]_D^{25}$ = +13.37 (c = 1.91, CHCl_3). **^1H NMR** (400 MHz, CDCl_3): δ 4.03 (abq, J = 17.6 Hz, 2H), 3.69 (s, 3H), 3.42–3.32 (m, 2H), 2.43–2.37 (m, 1H), 2.24–2.16 (m, 1H), 1.86–1.83 (m, 1H), 1.75–1.66 (m, 1H), 1.38–1.22 (m, 5H), 0.87 (t, J = 6.4 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl_3): δ 177.7, 169.3, 52.2, 46.1, 44.1, 41.4, 30.9, 29.4, 25.0, 22.7, 14.1.; **HRMS (ESI)**: Calcd for $\text{C}_{11}\text{H}_{19}\text{NO}_3$: 213.1365; found: 213.1363.

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 90/10, flow rate 1.0 mL/min, λ = 220 nm, t_R = 7.386 min (major), t_R = 9.273 min (minor); 95.5:4.5 er.



Peak Table

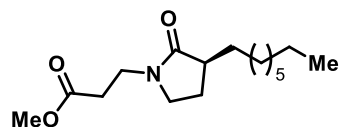
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.368	174553	21441	49.405		M	
2	9.189	178754	17178	50.595		M	
总计		353307	38618				



Peak Table

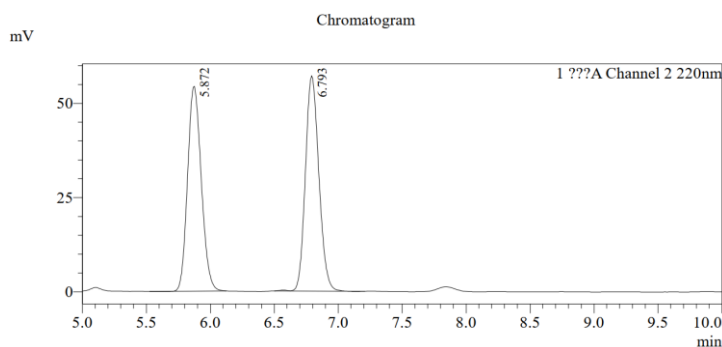
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.386	2270560	257009	95.576		M	
2	9.273	105095	11219	4.424		M	
总计		2375655	268228				

Methyl (S)-3-(3-octyl-2-oxopyrrolidin-1-yl)propanoate (**3ak**)



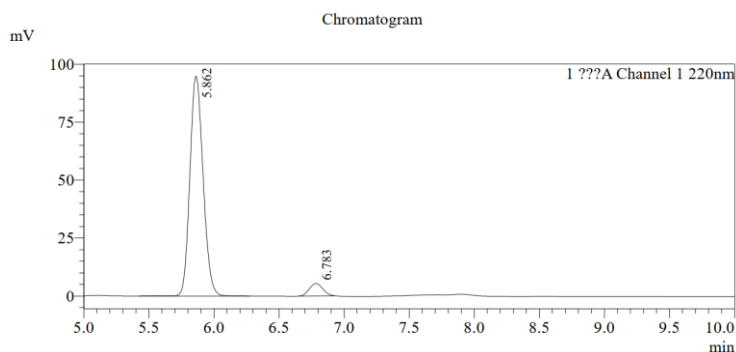
General procedure was followed on 0.2 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3ak** as a colorless oil (40.9 mg, 72%). $[\alpha]_D^{20} = +9.80$ (c=1.00, CH₂Cl₂). $R_f = 0.29$ (PE/EtOAc = 3/1); ¹H NMR (400 MHz, CDCl₃): δ 3.66 (s, 3H), 3.55 (t, $J = 7.2$ Hz, 2H), 3.32–3.28 (m, 2H), 2.54 (t, $J = 6.8$ Hz, 2H), 2.37–2.30 (m, 1H), 2.19–2.11 (m, 1H), 1.83–1.81 (m, 1H), 1.67–1.58 (m, 1H), 1.28–1.23 (m, 13H), 0.85 (t, $J = 7.2$ Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 177.1, 172.3, 51.9, 46.1, 41.9, 38.8, 32.6, 31.9, 31.3, 29.6, 29.6, 29.4, 27.3, 25.2, 22.7, 14.2; HRMS (ESI): $[M+Na]^+$ Calcd for C₁₆H₂₉NO₃Na⁺: 306.2040; found: 306.2038.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 220$ nm, $t_R = 5.862$ min (major), $t_R = 6.783$ min (minor); 94.5:5.5 e.r.



Peak Table

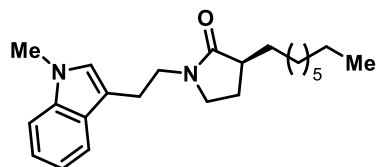
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.872	6.125	54300	405145	49.228
2	6.793	7.208	57052	417847	50.772
Total			111352	822993	100.000



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	5.862	6.275	94764	671141	94.523
2	6.783	6.933	5405	38890	5.477
Total			100170	710031	100.000

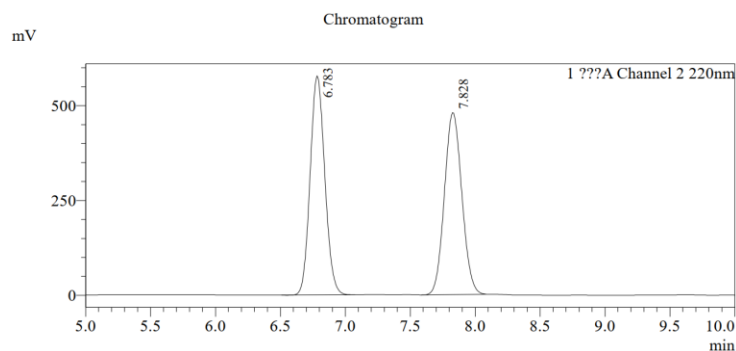
(S)-1-(2-(1-methyl-1H-indol-3-yl)ethyl)-3-octylpyrrolidin-2-one (3aI)



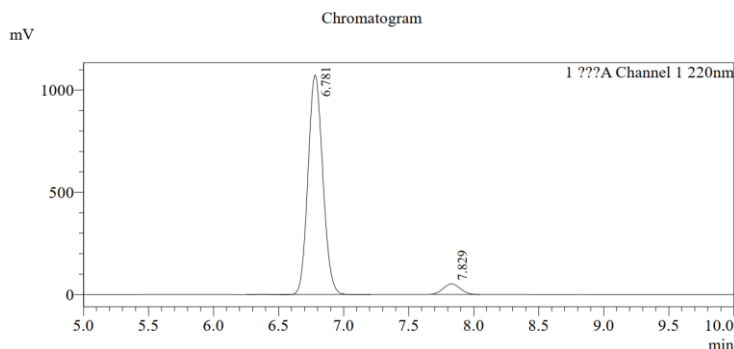
General procedure was followed on 0.19 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford **3aI** as a pale yellow oil

(49.5mg, 73%). $[\alpha]_D^{20} = -2.00$ ($c = 4.20$, CHCl_3). $R_f = 0.43$ (PE/EtOAc = 3/1); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.62 (d, $J = 8.0$ Hz, 1H), 7.29 (d, $J = 8.0$ Hz, 1H), 7.23 (t, $J = 7.2$ Hz, 1H), 7.12 (t, $J = 7.2$ Hz, 1H), 6.92 (s, 1H), 3.74 (s, 3H), 3.68–3.56 (m, 2H), 3.23 (dd, $J = 8.4, 5.6$ Hz, 2H), 2.99 (t, $J = 7.2$ Hz, 2H), 2.41–2.34 (m, 1H), 2.15–2.05 (m, 1H), 1.90–1.86 (m, 1H), 1.62–1.53 (m, 1H), 1.31–1.28 (m, 13H), 0.89 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 176.9, 137.0, 127.9, 126.7, 121.6, 118.8, 111.5, 109.3, 45.9, 43.2, 42.2, 32.7, 32.0, 31.4, 29.7, 29.6, 29.4, 27.3, 25.0, 23.3, 22.8, 14.2; **HRMS (ESI)**: $[M+H]^+$ Calcd for $\text{C}_{23}\text{H}_{35}\text{N}_2\text{O}^+$: 355.2744; found: 355.2734.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 220$ nm, $t_R = 6.781$ min (major), $t_R = 7.829$ min (minor); 95:5 e.r.

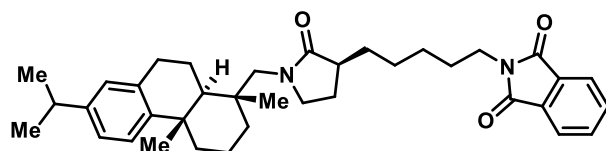


Peak Table					
???A Channel 2 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	6.783	7.075	577876	4549631	50.297
2	7.828	8.083	479756	4495956	49.703
Total			1057632	9045587	100.000



Peak Table					
???A Channel 1 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	6.781	7.208	1073517	8499333	94.751
2	7.829	8.050	51294	470887	5.249
Total			1124811	8970220	100.000

2-(5-((S)-1-(((1R,4aS,10aR)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)-2-oxopyrrolidin-3-yl)pentyl)isoindoline-1,3-dione (3am)

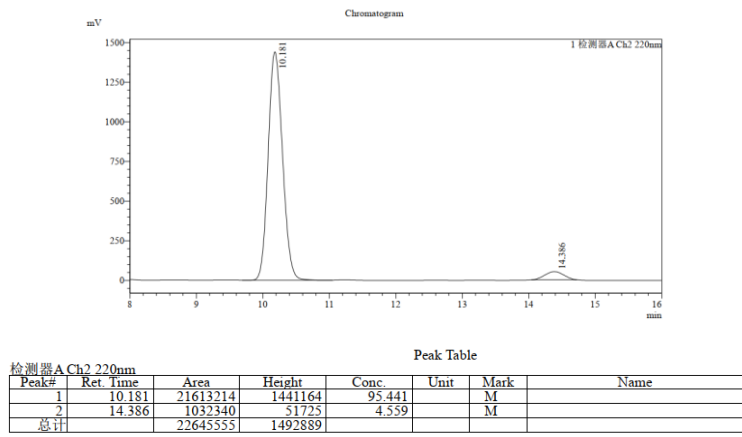
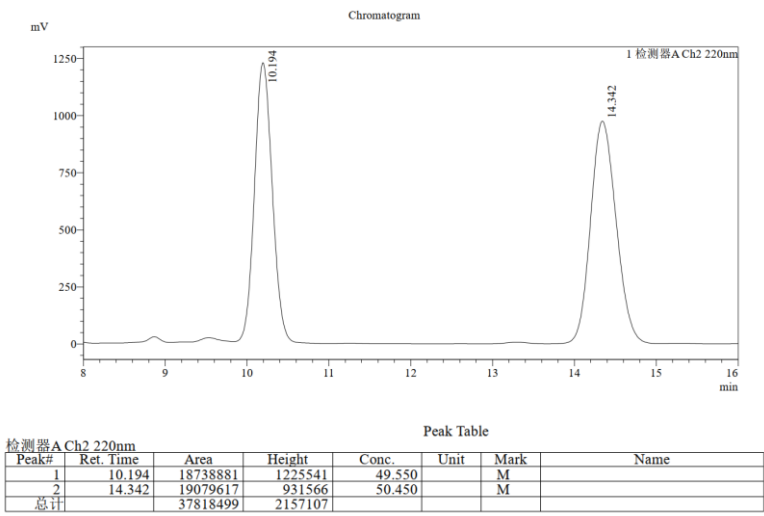


General procedure was followed on 0.16 mmol scale with a reaction time of 72 hours. The reaction mixture was purified by flash column

chromatography (silica gel, PE/DCM = 1/1) to afford **3am** as a colorless oil (55.1 mg, 61%). R_f = 0.35 (PE/DCM = 1/1); $[\alpha]_D^{25}$ = +5.90 (c = 5.00, CHCl_3). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.82 (dd, J = 5.6, 3.2 Hz, 2H), 7.69 (dd, J = 5.6, 3.2 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 6.89 (s, 1H), 3.66 (dd, J = 7.2 Hz, 2H), 3.40–3.30 (m, 2H), 3.16 (d, J = 13.6 Hz, 1H), 3.08 (d, J = 13.6 Hz, 1H), 2.95–2.78 (m, 3H), 2.35–2.24 (m, 2H), 2.15–2.07 (m, 1H), 2.01–1.96 (m, 1H), 1.86–1.80 (m, 1H), 1.77–1.58 (m, 6H), 1.47–1.32 (m, 9H), 1.22–1.19 (m, 9H), 0.94 (s, 3H), 0.88 (t, J = 6.8 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 178.3, 168.5, 147.3, 145.5, 134.8, 133.9, 132.2, 127.0, 124.1, 123.8, 123.2, 55.2, 49.6, 45.6, 41.5, 39.3, 38.3, 37.9, 37.6, 37.4, 33.4, 31.4, 30.3, 28.5, 26.8, 25.8, 25.4, 24.1, 24.0, 19.2, 19.2, 18.7; **HRMS (ESI)**: Calcd for $\text{C}_{37}\text{H}_{48}\text{N}_2\text{O}_3$: 568.3665; found: 568.3666.

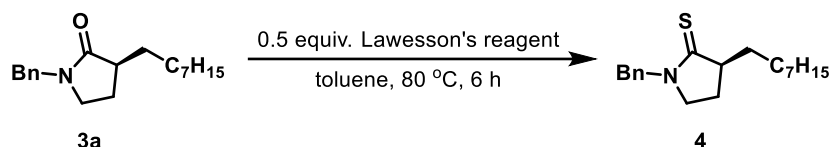
HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 80/20, flow rate 1.0 mL/min, λ = 220

nm, t_R = 10.181 min (major), t_R = 14.386 min (minor); 95.5:4.5 e.r.



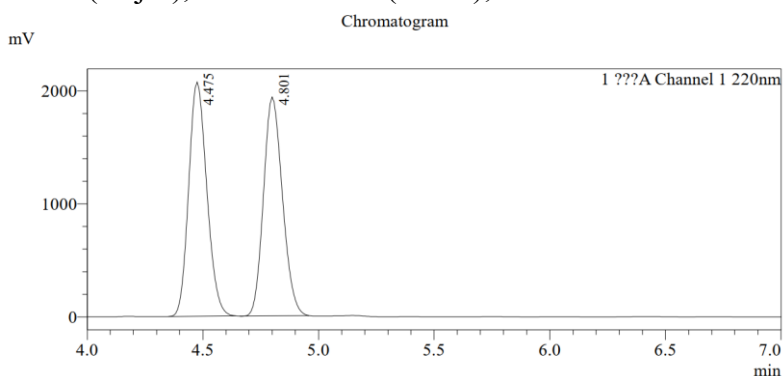
Experimental procedures and characterization data for derivatization

i) Thiation for amides



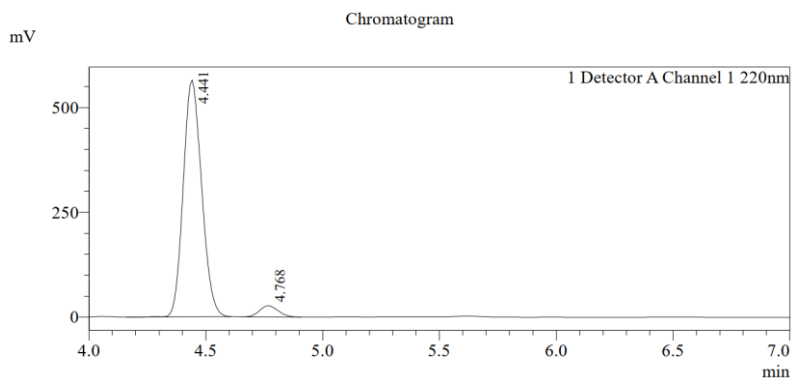
To a reaction vial was added **3a** (28.7 mg, 0.1 mmol) under air. Subsequently, Lawesson's reagent (20 mg, 0.05 mmol) and anhydrous toluene (0.5 mL) was added under nitrogen atmosphere, and the reaction was stirred at 80 °C for 6 h. After completion, H₂O was added and the reaction mixture was extracted with EtOAc for three times, and concentrated under reduced pressure. The residue was purified by flash chromatography to afford the desired product **4** (29.7 mg, 98%). $[\alpha]_{\text{D}}^{25} = +27.00$ (c = 0.40, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.36–7.26 (m, 5H), 5.01 (abq, $J = 14.4$ Hz, 2H), 3.53–3.42 (m, 2H), 2.91–2.84 (m, 1H), 2.26–2.17 (m, 2H), 1.72–1.63 (m, 1H), 1.47–1.27 (m, 13H), 0.88 (t, $J = 7.2$ Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 206.0, 135.4, 128.9, 128.4, 128.1, 54.2, 52.3, 51.8, 34.4, 32.0, 29.7, 29.7, 29.4, 27.2, 26.0, 22.8, 14.2. **HRMS (ESI)**: $[M+H]^+$ Calcd for C₁₉H₃₀NS⁺: 304.2094; found: 304.2097.

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 220$ nm, $t_{\text{R}} = 4.441$ min (major), $t_{\text{R}} = 4.768$ min (minor); 95.5:4.5 er.



Peak Table

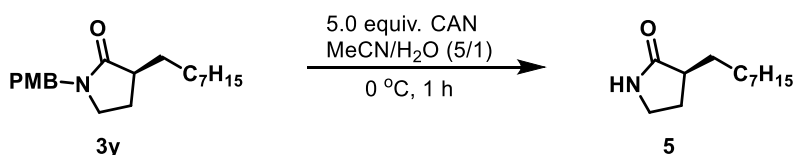
???A Channel 1 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	4.475	4.642	2072895	11191308	50.299
2	4.801	4.958	1936957	11058308	49.701
Total			4009852	22249616	100.000



Peak Table

Detector A Channel 1 220nm					
Peak#	Ret. Time	Peak End	Height	Area	Area%
1	4.441	4.608	564145	3071771	95.340
2	4.768	4.908	26834	150138	4.660
Total			590979	3221908	100.000

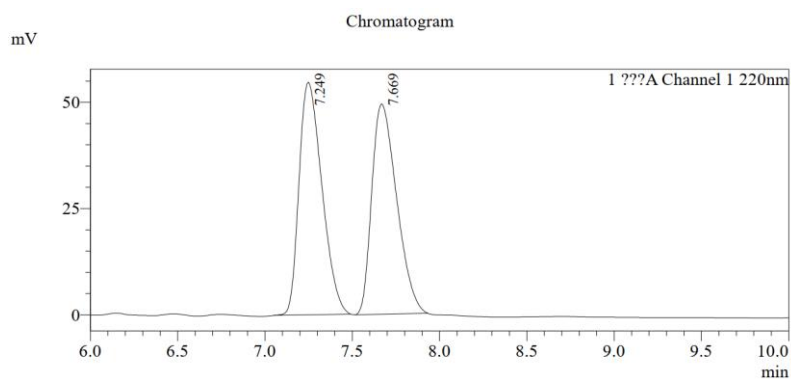
ii) Deprotection of γ -lactam



To a solution of **3y** (31.7 mg, 0.1 mmol) in dry acetonitrile (2.0 mL) and H₂O (0.4 mL) was added cerium ammonium nitrate (274 mg, 0.5 mmol) at 0 °C. After it was stirred for 1 h at 0 °C (TLC monitored), the reaction mixture was warmed to room temperature, and the organic layer was separated. The aqueous phase was washed with EtOAc for three times. The combined organic layer was dried over Na₂SO₄. The crude product was purified by column chromatography on silica gel (PE/EtOAc (1% Et₃N) = 1/2) to give **5** (16.6 mg, 84%) as a white solid: *R_f* = 0.42 (PE/EtOAc = 2/1); [α]_D²⁵ = +93.00 (c=0.12, CHCl₃).

¹H NMR (400 MHz, CDCl₃): δ 7.31 (s, 1H), 3.31–3.22 (m, 2H), 2.32–2.17 (m, 2H), 1.81–1.65 (m, 2H), 1.28–1.21 (m, 13H), 0.82 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 181.4, 41.2, 40.6, 31.9, 30.9, 29.6, 29.5, 29.3, 27.5, 27.4, 22.7, 14.1; **HRMS (ESI)**: [M+H]⁺ Calcd for C₁₂H₂₄NO⁺: 198.1852; found: 198.1855.

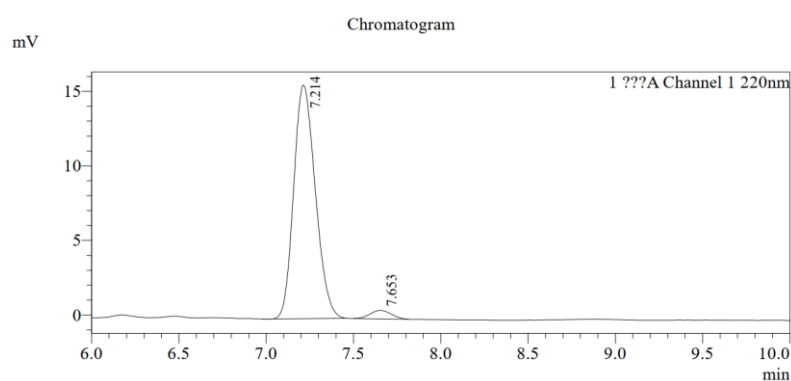
HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm, *t_R* = 7.214 min (major), *t_R* = 7.653 min (minor); 96.5:3.5 er.



Peak Table

???A Channel 1 220nm

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.249	7.492	54702	499868	50.422
2	7.669	7.933	49481	491511	49.578
Total			104183	991379	100.000

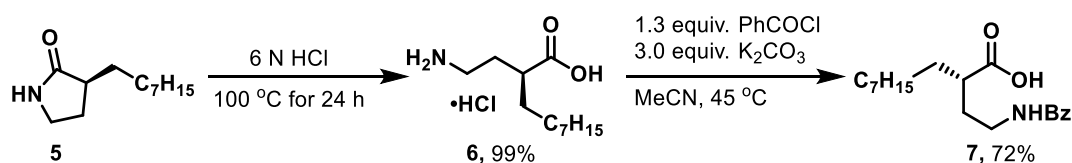


Peak Table

???A Channel 1 220nm

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	7.214	7.467	15656	135122	96.602
2	7.653	7.817	564	4753	3.398
Total			16219	139876	100.000

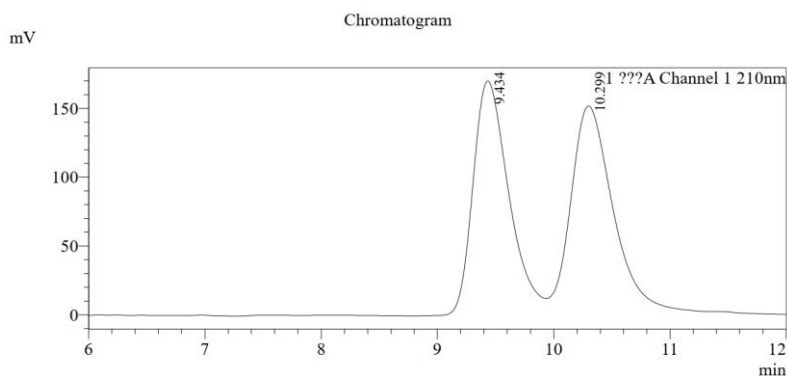
iii) Ring opening to access γ -amino acid derivative



A solution of **5** (19.7 mg, 0.1 mmol) in 0.6 mL of 6 N HCl was heated to 100 °C for 12 h. After cooled to rt, the solvent was removed under reduced pressure. Ethyl acetate (1 mL) was added, then the mixture was suspended by sonication and stirred at rt for 1 h. The white solid product **6** was obtained by filtration with MeOH washing in quantitative yield (25.0 mg). **¹H NMR** (400 MHz, CD₃OD): δ 2.88 (t, J = 8.0 Hz, 2H),

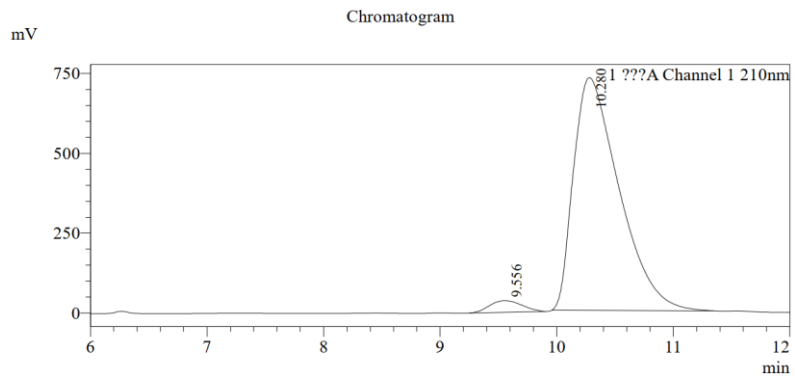
2.38 (m, 1H), 1.92–1.83 (m, 1H), 1.75–1.73 (m, 1H), 1.59–1.58 (m, 1H), 1.49–1.45 (m, 1H), 1.23 (m, 12H), 0.83 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ 178.4, 43.9, 39.0, 33.2, 33.0, 30.6, 30.5, 30.3, 28.1, 23.7, 14.4; **HRMS (ESI)**: $[\text{M-HCl}+\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{26}\text{NO}^+$: 216.1958; found: 216.1961.

To a solution of **6** (0.04 mmol, 1.0 equiv.) in acetonitrile (1 mL) was added K_2CO_3 (0.12 mmol, 3.0 equiv.). The mixture was stirred for 1 h at room temperature, then benzoyl chloride (0.052 mmol, 1.3 equiv.) was added, and the stirring continued at 45 °C for 12 h. H_2O was added and the pH of the reaction mixture was adjusted ($\text{pH} < 1$) with HCl. the two-phase mixture was separated, and the aqueous phase was extracted with EtOAc for several times. The combined organic phases were dried over Na_2SO_4 , filtered, and evaporated *in vacuo*. The residue was purified by flash chromatography (PE/EtOAc = 2/1) to give **7** (9.2 mg, 72%). $[\alpha]_{\text{D}}^{25} = +25.65$ ($c = 0.92$, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ 7.77 (d, $J = 7.2$ Hz, 2H), 7.51 (t, $J = 7.2$ Hz, 1H), 7.43 (t, $J = 7.2$ Hz, 2H), 6.52 (s, 1H), 3.60–3.47 (m, 2H), 2.51–2.44 (m, 1H), 1.95–1.81 (m, 2H), 1.76–1.67 (m, 1H), 1.52–1.43 (m, 1H), 1.33–1.24 (m, 12H), 0.87 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 179.8, 168.3, 134.2, 131.9, 128.8, 127.1, 43.4, 38.6, 32.5, 32.4, 32.0, 29.7, 29.5, 29.4, 27.4, 22.8, 14.2.; **HRMS (ESI)**: Calcd for $\text{C}_{19}\text{H}_{29}\text{NO}_3$: 319.2147; found: 319.2144. **HPLC** (Chiralpak AD-H): *n*-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, $\lambda = 210$ nm, $t_{\text{R}} = 9.556$ min (minor), $t_{\text{R}} = 10.280$ min (major); 3.5:96.5 er.



Peak Table

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	9.433	9.892	54431	1083243	49.914
2	10.298	10.950	47196	1086990	50.086
Total			101626	2170233	100.000



Peak Table

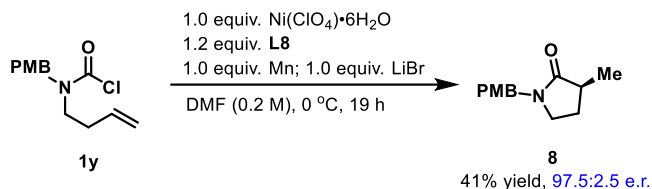
???A Channel 2 254nm

Peak#	Ret. Time	Peak End	Height	Area	Area%
1	9.566	9.917	11833	221565	3.270
2	10.280	11.383	238787	6554506	96.730
Total			250620	6776071	100.000

Mechanism Study

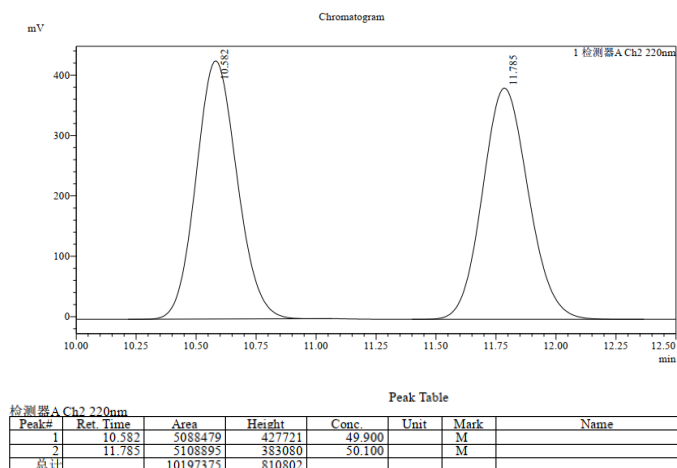
a) Stoichiometric reaction of the carbamoyl chloride **1y** with nickle catalyst

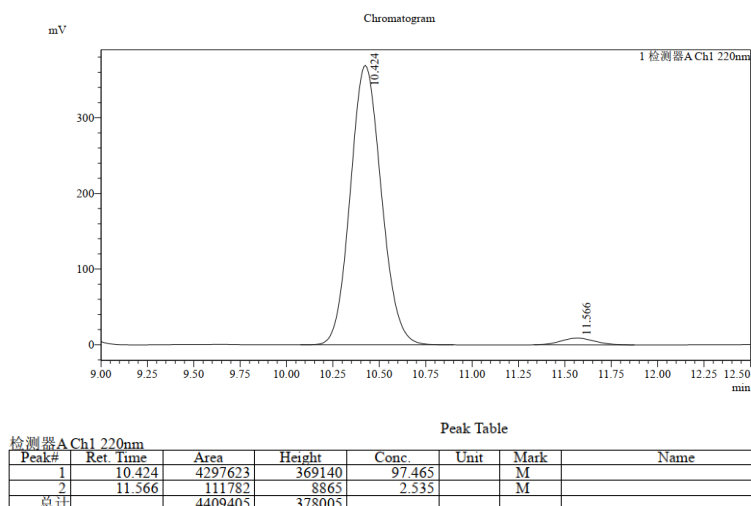
i) Stoichiometric $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ was employed as the nickel source



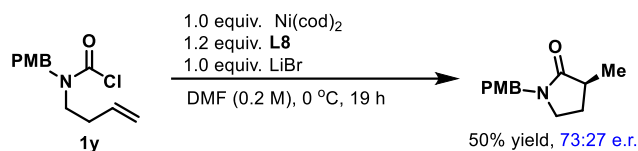
To a dried 8-mL vial were added $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (18.3 mg, 0.05 mmol, 1.0 equiv.), Quinim **L8** (20.6 mg, 0.06 mmol, 1.2 equiv.), and Mn (2.8 mg, 0.05 mmol, 1.0 equiv.). Then the vial was transferred into glovebox. LiBr (4.4 mg, 0.05 mmol, 1.0 equiv.) and DMF (0.5 mL, 0.2 M) were added in sequence, followed by carbamoyl chloride **1y** (12.7 mg, 0.05 mmol, 1.0 equiv.). The vial was then taken out from the glovebox, sealed with parafilm, put into the cryogenic bath (0 °C) and stirred for 19 h. After completion, the reaction mixture was quenched with sat. aq. NH_4Cl and H_2O , filtered through a pad of celite, and extracted with EtOAc for three times. The combined organic phase was washed with brine and concentrated under reduced pressure to yield the crude product, which was purified by silica gel flash column chromatography to afford products **8** (4.5 mg, 41%). **¹H NMR** (400 MHz, CDCl_3): δ 7.14 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 4.37 (abq, J = 14.4 Hz, 2H), 3.78 (s, 3H), 3.17–3.09 (m, 2H), 2.53–2.44 (m, 1H), 2.22–2.14 (m, 1H), 1.61–1.51 (m, 1H), 1.21 (d, J = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl_3): δ 177.3, 159.1, 129.5, 128.9, 114.1, 55.3, 46.2, 44.6, 36.9, 27.1, 16.5; **HRMS (EI)**: Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_2$: 219.1259; found: 219.1261

HPLC (Chiralpak AD-H): n -Hexane/ i -PrOH = 90/10, flow rate 1.0 mL/min, λ = 220 nm, t_R = 10.424 min (major), t_R = 11.566 min (minor); 97.5:2.5 e.r.

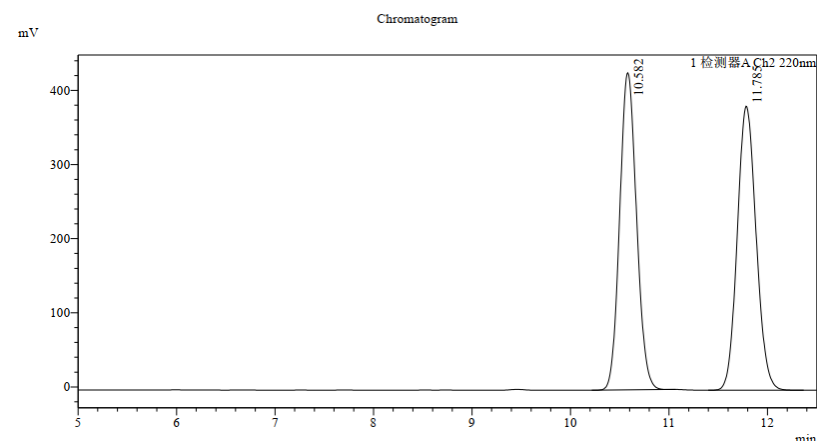




ii) Stoichiometric Ni(cod)₂ was employed as the nickel source



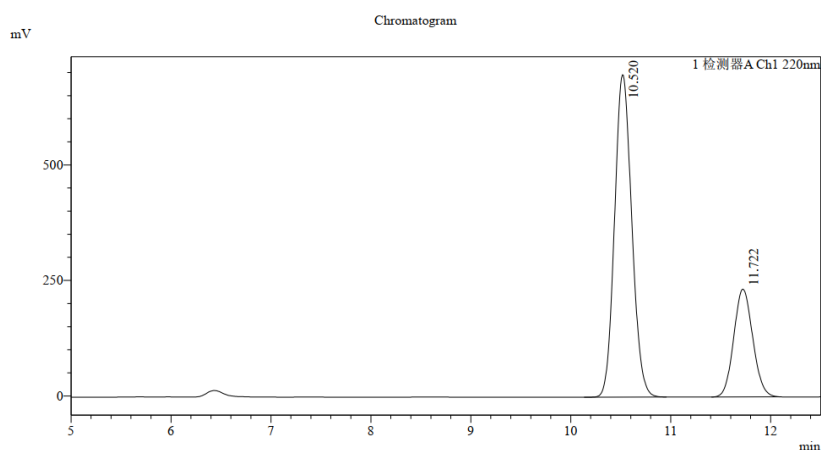
To a dried 8-mL vial were added Quinim L8 (20.6 mg, 0.06 mmol, 1.2 equiv.). Then the vial was transferred into glovebox. Ni(cod)₂ (13.8 mg, 0.05 mmol, 1.0 equiv.), LiBr (4.4 mg, 0.05 mmol, 1.0 equiv.) and DMF (0.5 mL, 0.2 M) were added in sequence, followed by carbamoyl chloride (12.7 mg, 0.05 mmol, 1.0 equiv.). The vial was then quickly taken out from the glovebox, sealed with parafilm, put into the cryogenic bath (0 °C) and stirred for 19 h. After completion, the reaction mixture was quenched with sat. aq. NH₄Cl and H₂O, filtered through a pad of celite, and extracted with EtOAc for three times. The combined organic phase was washed with brine and concentrated under reduced pressure to yield the crude product, which was purified by silica gel flash column chromatography to afford products **8** (5.5 mg, 50%). **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 210 nm, t_R = 10.520 min (major), t_R = 11.722 min (minor); 73:27 e.r.



检测器A Ch2 220nm

Peak Table

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.582	5088479	427721	49.900		M	
2	11.785	5108895	383080	50.100		M	
总计		10197375	810802				



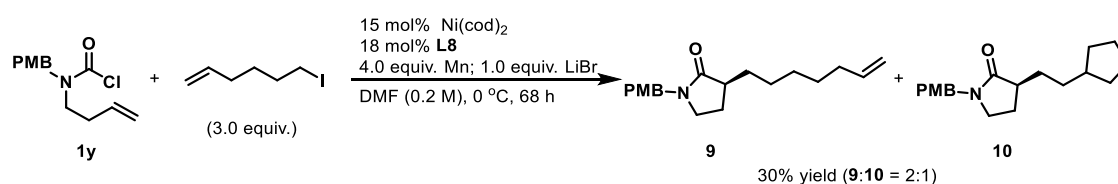
检测器A Ch1 220nm

Peak Table

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.520	8360340	697775	73.008		M	
2	11.722	3090975	233453	26.992		M	
总计		11451315	931228				

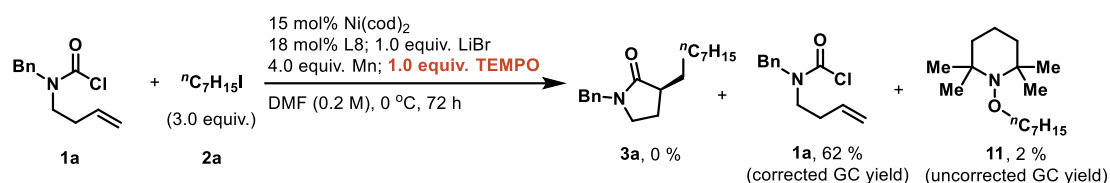
Comments: When 1.0 equiv of $\text{Ni}(\text{cod})_2$ was employed as the nickel source, the *e.r.* of the desired product **8** was dropped down to the 73:27, presumably due to 2 equivalent of COD in the reaction which serve as a ligand on the nickel center to diminish the enantioselectivity. When 1.0 equivalent Mn powder was used as the reductant to reduce the $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ *in situ* to the $\text{Ni}(0)$ species, the reductive cyclized product **8** was isolated with high *e.r.* (97.5:2.5) that is similar to the *e.r.* (97:3) of the reductive coupling product **3y** in catalytic reaction of substrate **1y** with primary alkyl iodide.

b) Radical cyclization of the carbamoyl chloride **1y** with 6-iodohex-1-ene



To a dried 8-mL vial were added ligand (6.2 mg, 0.018 mmol, 18 mol%), Mn (22 mg, 0.4 mmol, 4.0 equiv.). Then the vial was transferred into glovebox. LiBr (8.7 mg, 0.1 mmol, 1.0 equiv.), Ni(cod)₂ (4.2 mg, 0.015 mmol, 15 mol%), DMF (0.5 mL, 0.2 M), carbamoyl chloride **1y** (25.4 mg, 0.1 mmol, 1.0 equiv.) and alkyl halide (63 mg, 0.3 mmol, 3.0 equiv.) were added in sequence inside the glovebox. The vial was then taken out from the glovebox, sealed with parafilm, put into the cryogenic bath (0 °C) and stirred for 68 h. After completion, the reaction mixture was quenched with H₂O, filtered through a pad of celite and extracted with EtOAc for three times. The combined organic phase was washed with brine and concentrated under reduced pressure to yield the crude product, which was purified by silica gel flash column chromatography to afford product **9** and **10** as an inseparable mixture (9.1 mg, 30%). ¹³C NMR data listed is for the major product **9**. ¹H NMR (400 MHz, CDCl₃): δ 7.15 (d, *J* = 8.4 Hz, 3H), 6.85 (d, *J* = 8.8 Hz, 3H), 5.80 (ddt, *J* = 16.8, 10.4, 6.8 Hz, 1 H), 5.01–4.91 (m, 2H), 4.38 (abq, *J* = 14.4 Hz, 3H), 3.79 (s, 4.5H), 3.17–3.13 (m, 3H), 2.46–2.38 (m, 1.5 H), 2.18–2.09 (m, 1.5H), 2.06–2.01 (m, 2H), 1.91–1.88 (m, 1.5H), 1.76–1.74 (m, 1.5H), 1.66–1.56 (m, 3.5H), 1.52–1.47 (m, 1H), 1.43–1.33 (m, 8H); ¹³C NMR (100 MHz, CDCl₃): δ 176.8, 159.1, 139.2, 129.6, 128.9, 114.4, 114.1, 55.4, 46.2, 44.9, 42.2, 33.8, 31.4, 29.1, 28.9, 27.1, 24.9. The formation of mixture of **9** and **10** revealed that the reaction proceeded in a SET pathway.

c) Radical trap reaction



To a dried 8-mL vial were added ligand **L8** (6.2 mg, 0.018 mmol, 18 mol%), Mn (22 mg, 0.4 mmol, 4.0 equiv.) and TEMPO (15.6 mg, 0.1 mmol, 1.0 equiv.). Then the vial was transferred into glovebox. LiBr (8.7 mg, 0.1 mmol, 1.0 equiv.), Ni(cod)₂ (4.2 mg, 0.015 mmol, 15 mol%), DMF (0.5 mL, 0.2 M), carbamoyl chloride **1a** (22.3 mg, 0.1 mmol, 1.0 equiv.) and **2a** (49 μL, 0.3 mmol, 3.0 equiv.) were added in sequence inside the glovebox. The vial was then taken out from the glovebox, sealed with parafilm, put into the cryogenic bath (0 °C) and stirred for 72 h. The reaction mixture was quenched with H₂O, extracted with EtOAc, and GC analysis was conducted by using an aliquot of the resulting organic phase, dodecane was used as the internal standard. The reductive cross-coupling reaction was completely inhibited by the addition of TEMPO, which indicated that the reaction might proceed via a radical process. **1a** was largely remained in 62% GC yield and **3a** was not observed by either TLC or GC analysis. The trace amount of TEMPO-adduct **11** could be observed at GC and confirmed by GC-MS.

Crystallographic Data for Compound 3s

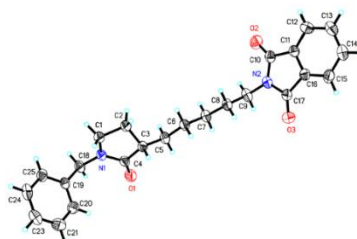


Fig. S1 Crystal data and structure refinement for **3s** (CCDC 2007665)

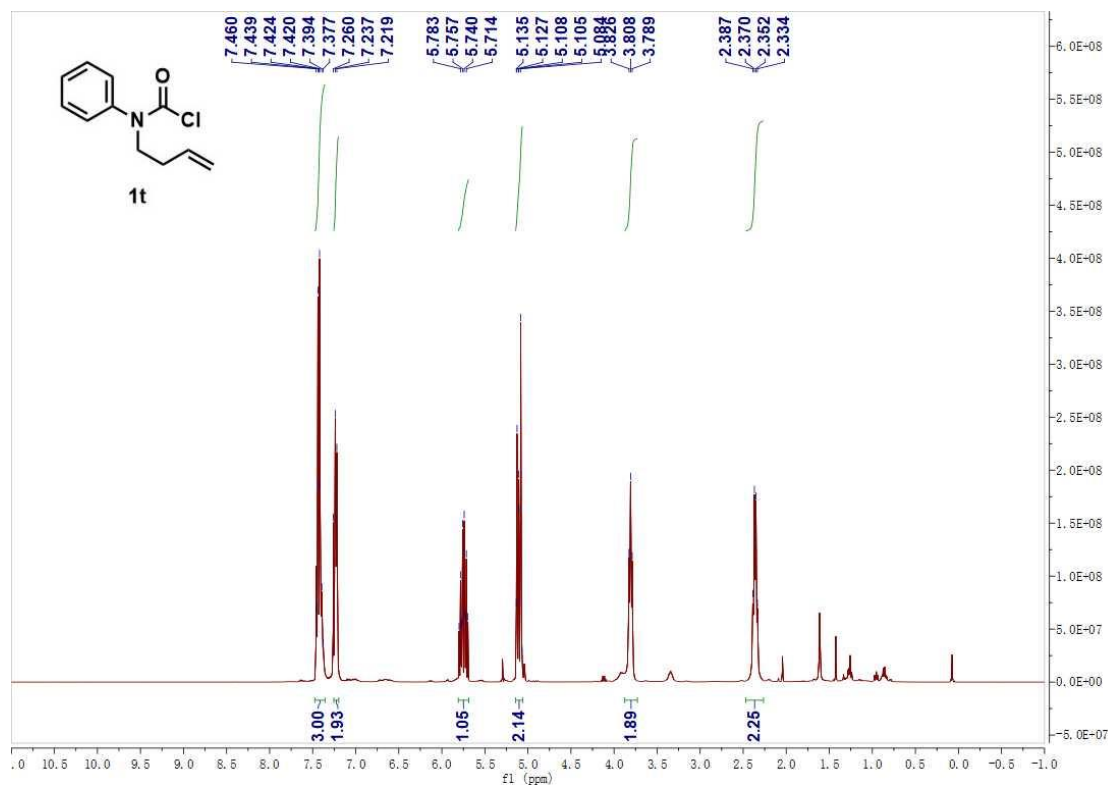
Empirical formula	$C_{24}H_{26}N_2O_3$	
Formula weight	390.47	
Temperature	293(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P 1	
Unit cell dimensions	$a = 4.78730(10)$ Å	$\alpha = 95.705(2)^\circ$
	$b = 6.1826(2)$ Å	$\beta = 97.548(2)^\circ$
	$c = 17.9738(4)$ Å	$\gamma = 95.863(2)^\circ$
Volume	$521.17(2)$ Å ³	
Z	1	
Density (calculated)	1.244 Mg/m ³	
Absorption coefficient	0.659 mm ⁻¹	
F(000)	208	
Crystal size	0.200 x 0.140 x 0.100 mm ³	
Theta range for data collection	12.912 to 72.235 °	
Index ranges	-5 ≤ h ≤ 5, -7 ≤ k ≤ 7, -22 ≤ l ≤ 22	
Reflections collected	13683	
Independent reflections	3795 [R(int) = 0.0378]	
Completeness to theta = 67.679 °	95.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7533 and 0.5433	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3795 / 3 / 263	
Goodness-of-fit on F ²	1.039	
Final R indices [I > 2σ(I)]	R1 = 0.0334, wR2 = 0.0915	
R indices (all data)	R1 = 0.0339, wR2 = 0.0923	
Absolute structure parameter	0.09(8)	
Extinction coefficient	0.12(3)	
Largest diff. peak and hole	0.099 and -0.081 e.Å ⁻³	

References

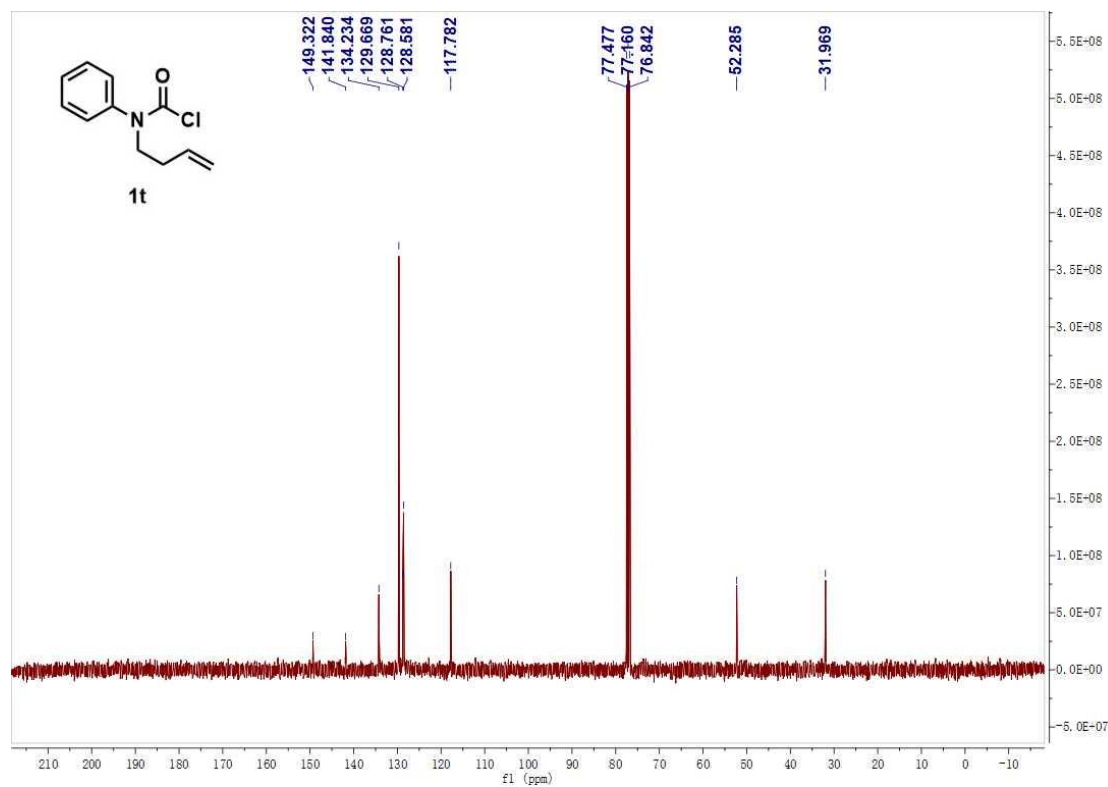
1. Grainger R. S.; Innocenti P. *Angew. Chem. Int. Ed.* **2004**, *43*, 3445
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11. Fryzuk, M. D.; Jafarpour, L.; Rettig, S. J. *Tetrahedron: Asymmetry*, **1998**, *9*, 3191.
12. Wu, X.-Y.; Shen, Y.-Y.; Ma, B.; Zhou, Q.-L.; Chan A. S. C. *Journal of Molecular Catalysis A: Chemical*, **2000**, *157*, 59.

NMR Spectra

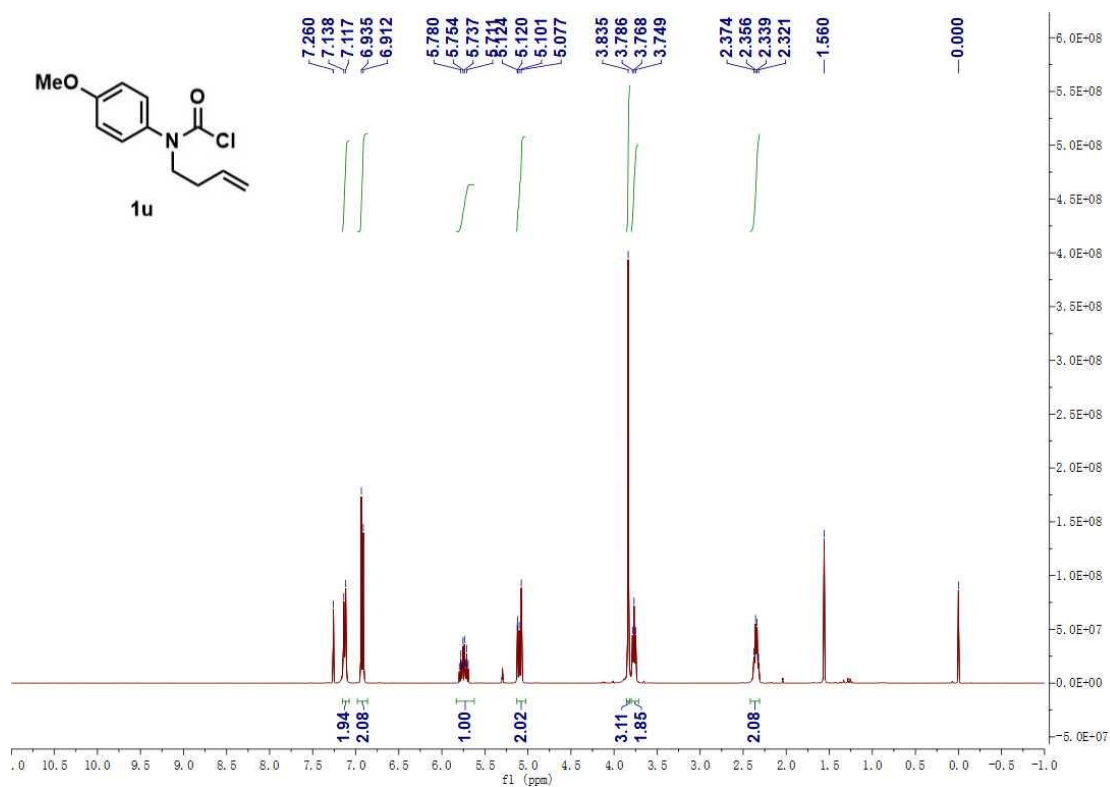
^1H NMR-spectrum (400 MHz, CDCl_3) of **1t**



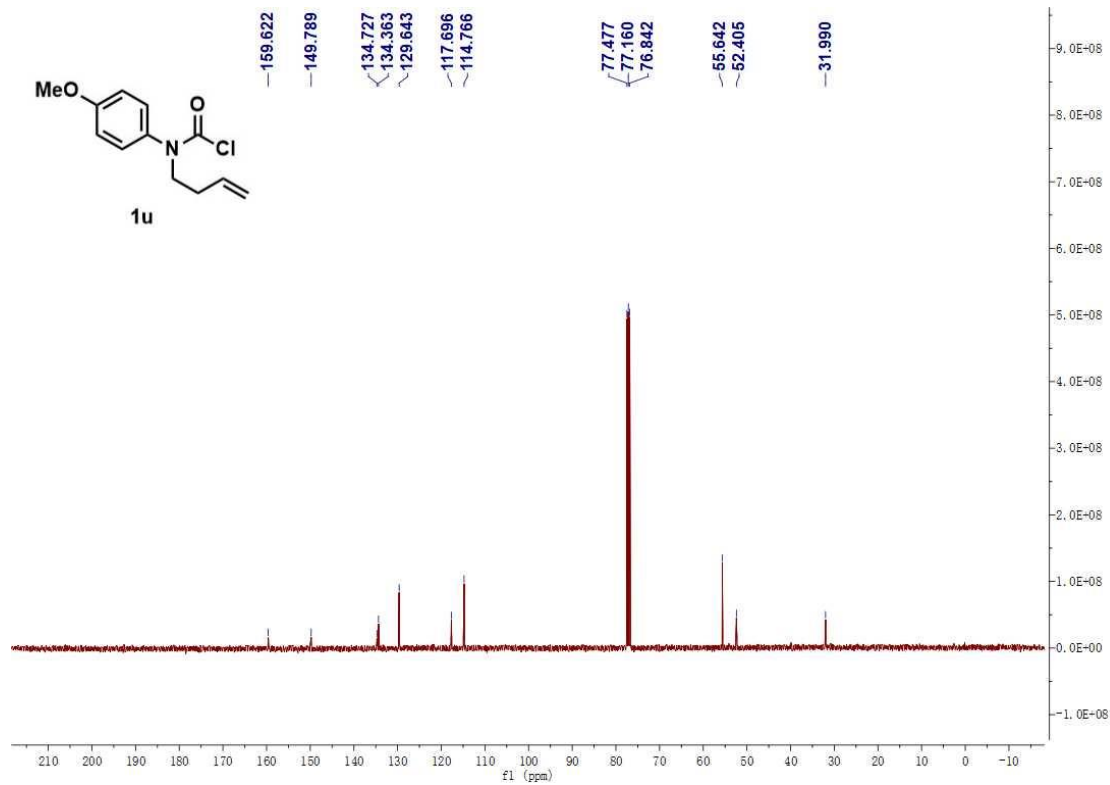
^{13}C NMR-spectrum (100 MHz, CDCl_3) of **1t**



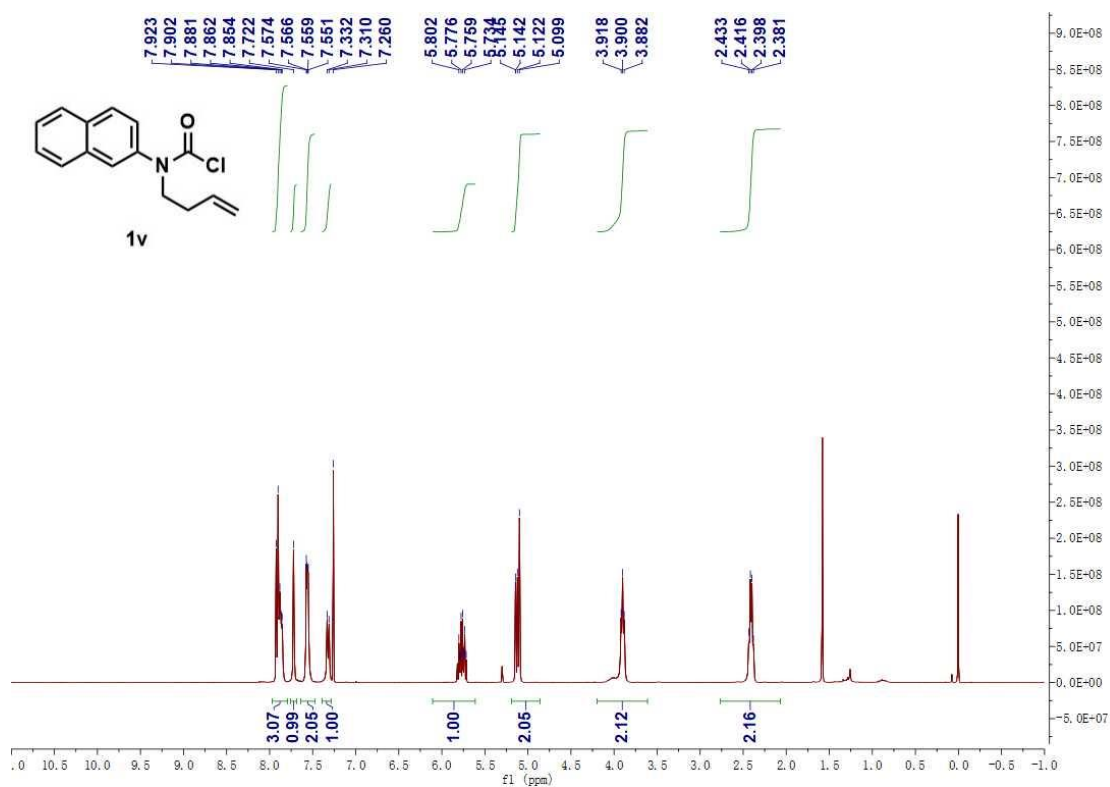
^1H NMR-spectrum (400 MHz, CDCl_3) of **1u**



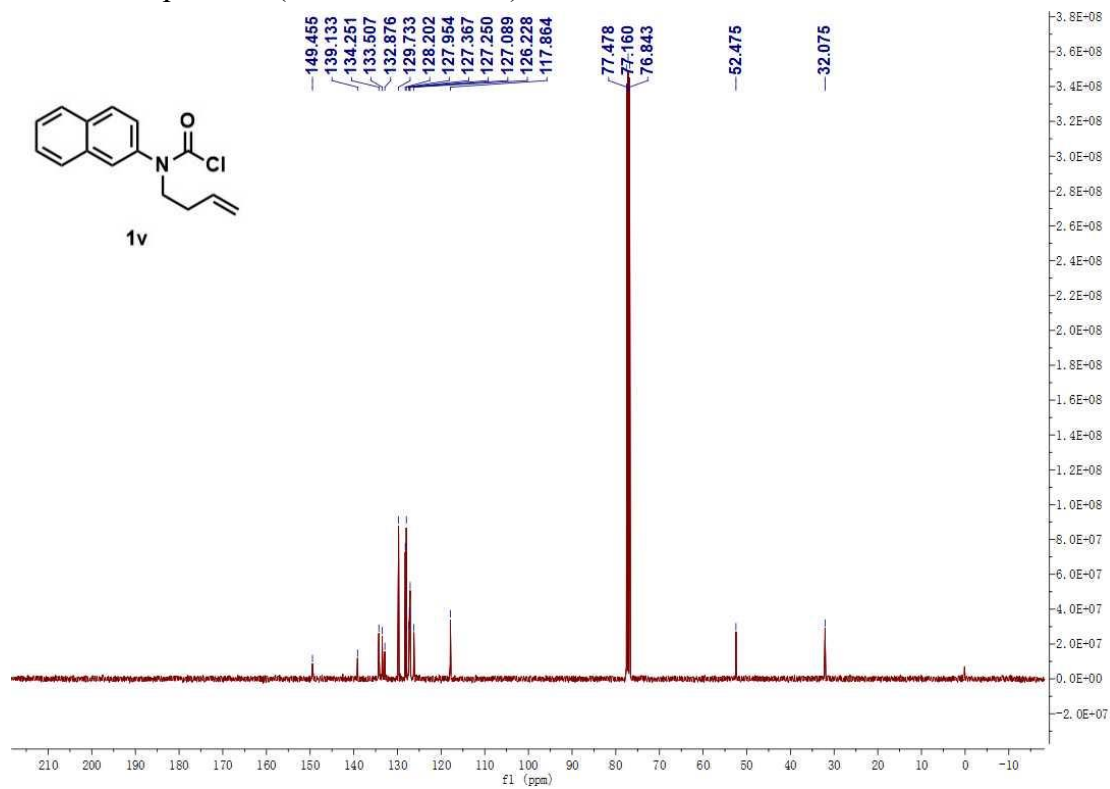
^{13}C NMR-spectrum (100 MHz, CDCl_3) of **1u**



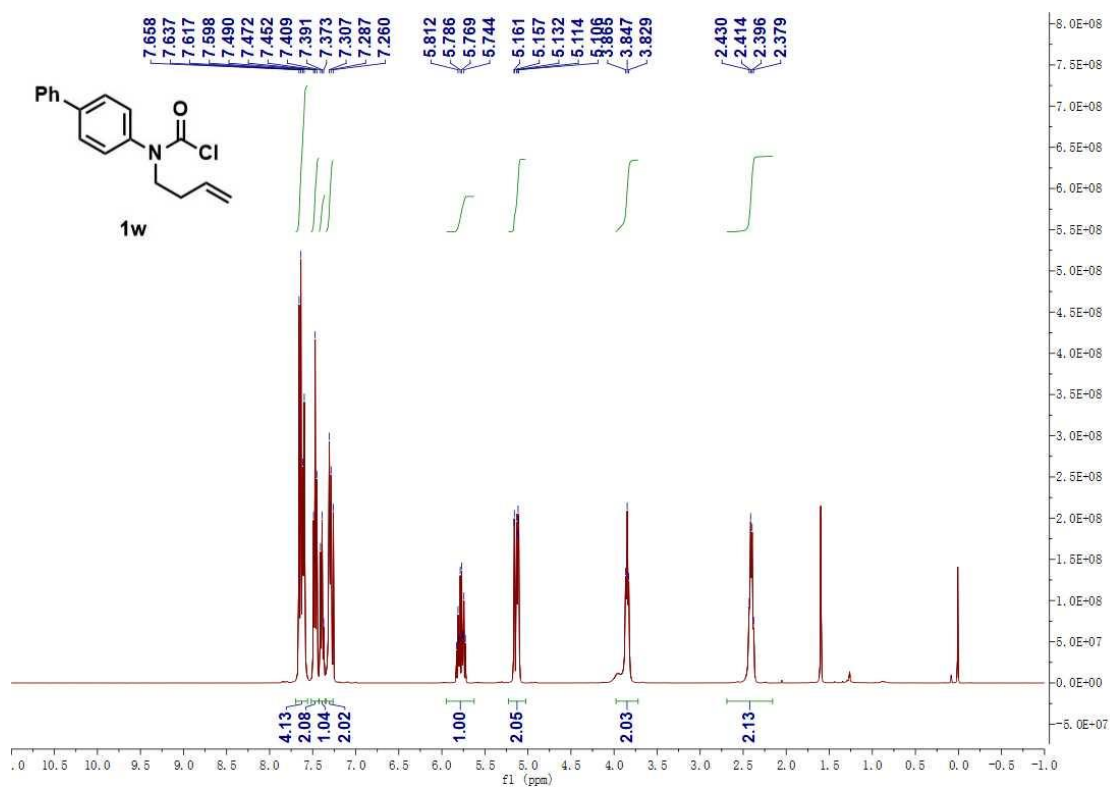
¹H NMR-spectrum (400 MHz, CDCl₃) of **1v**



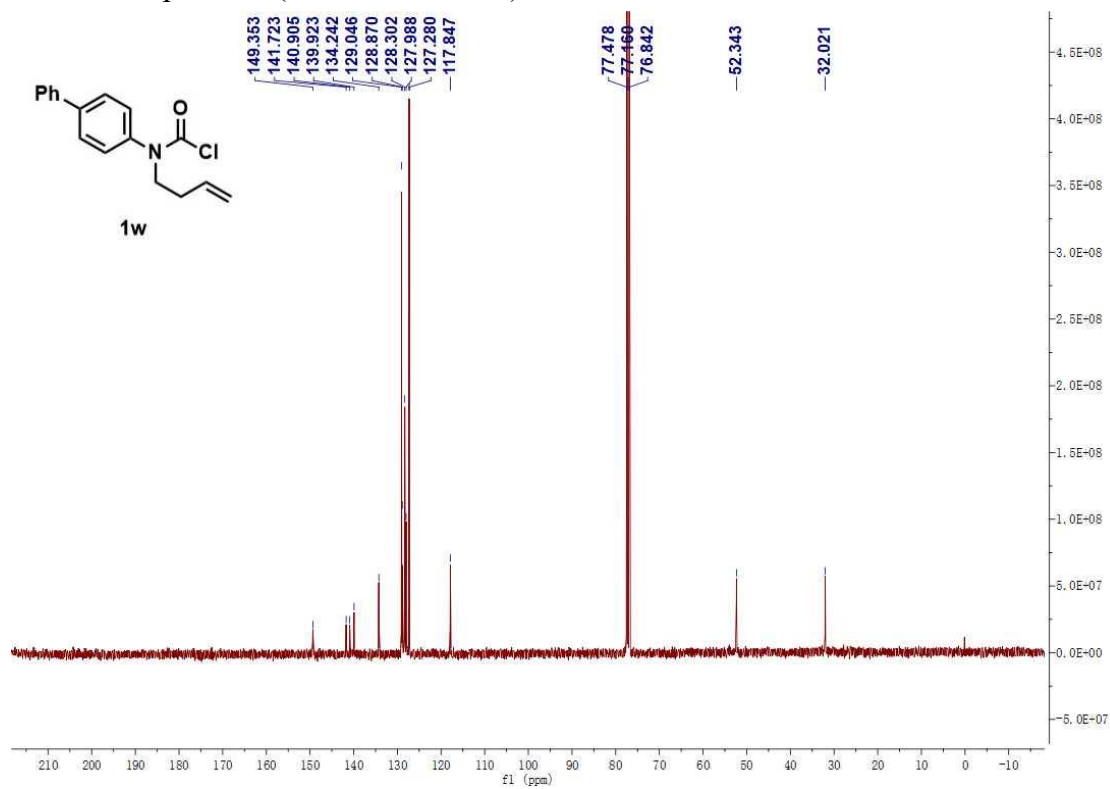
¹³C NMR-spectrum (100 MHz, CDCl₃) of **1v**



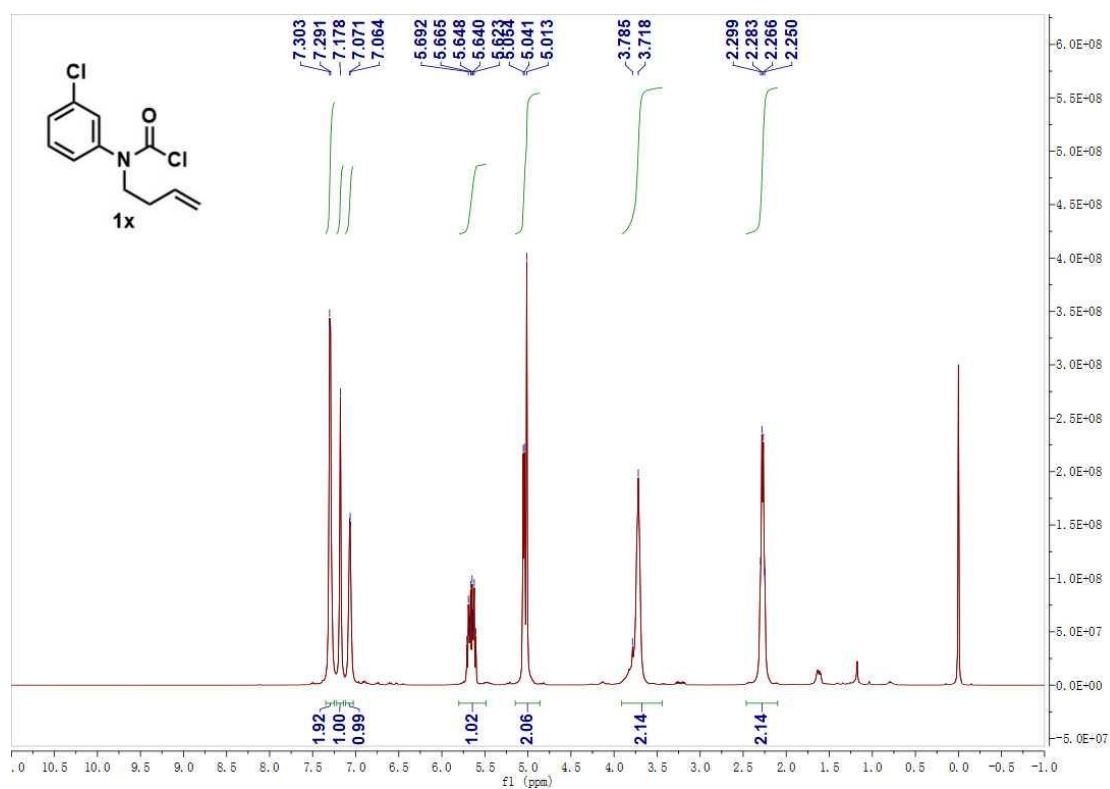
¹H NMR-spectrum (400 MHz, CDCl₃) of **1w**



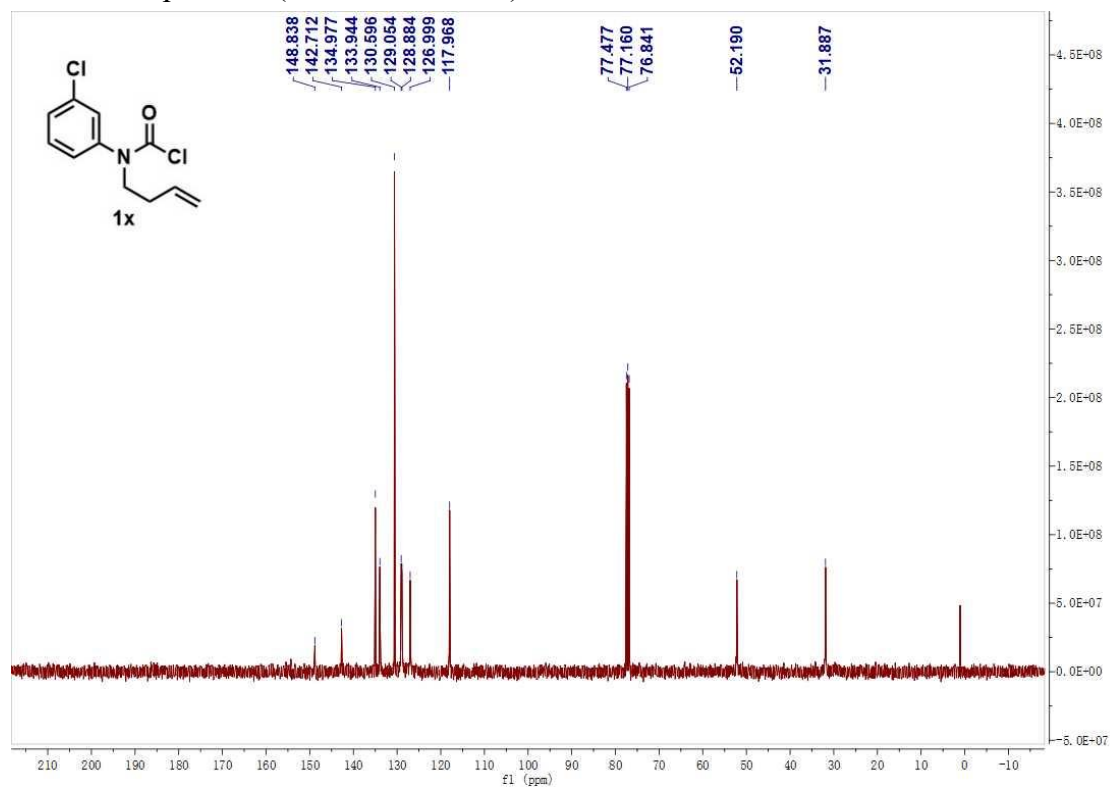
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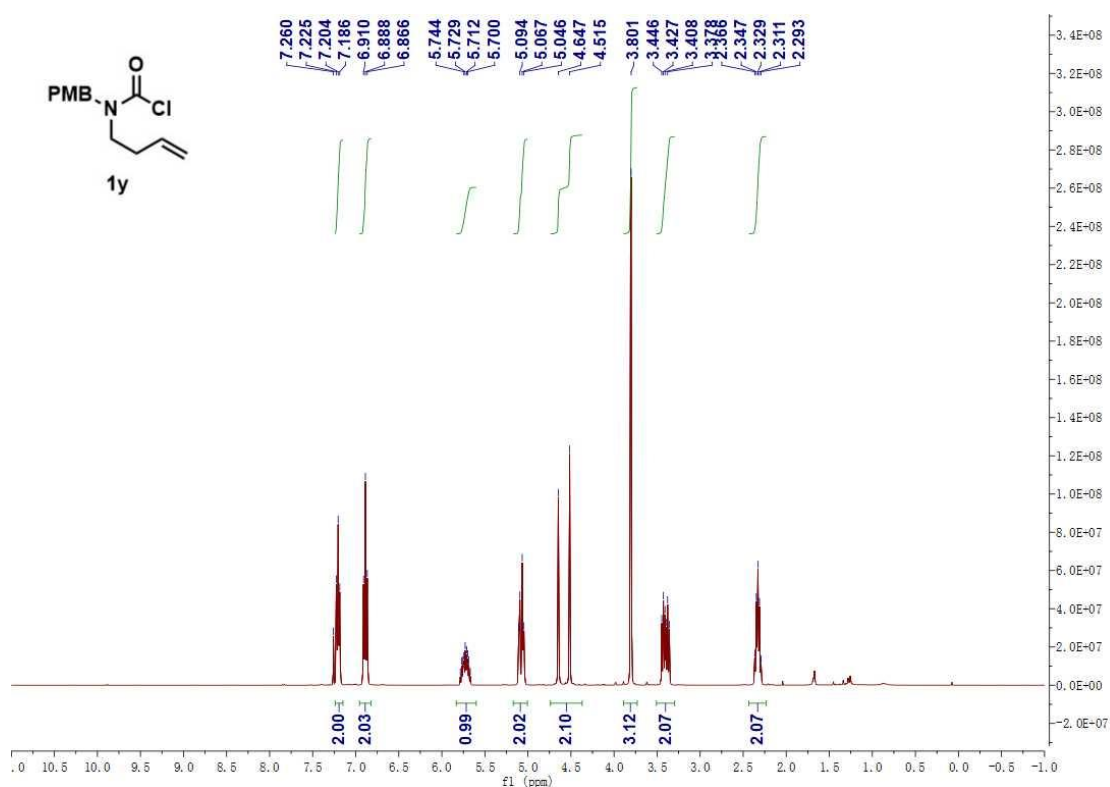
^1H NMR-spectrum (400 MHz, CDCl_3) of **1x**



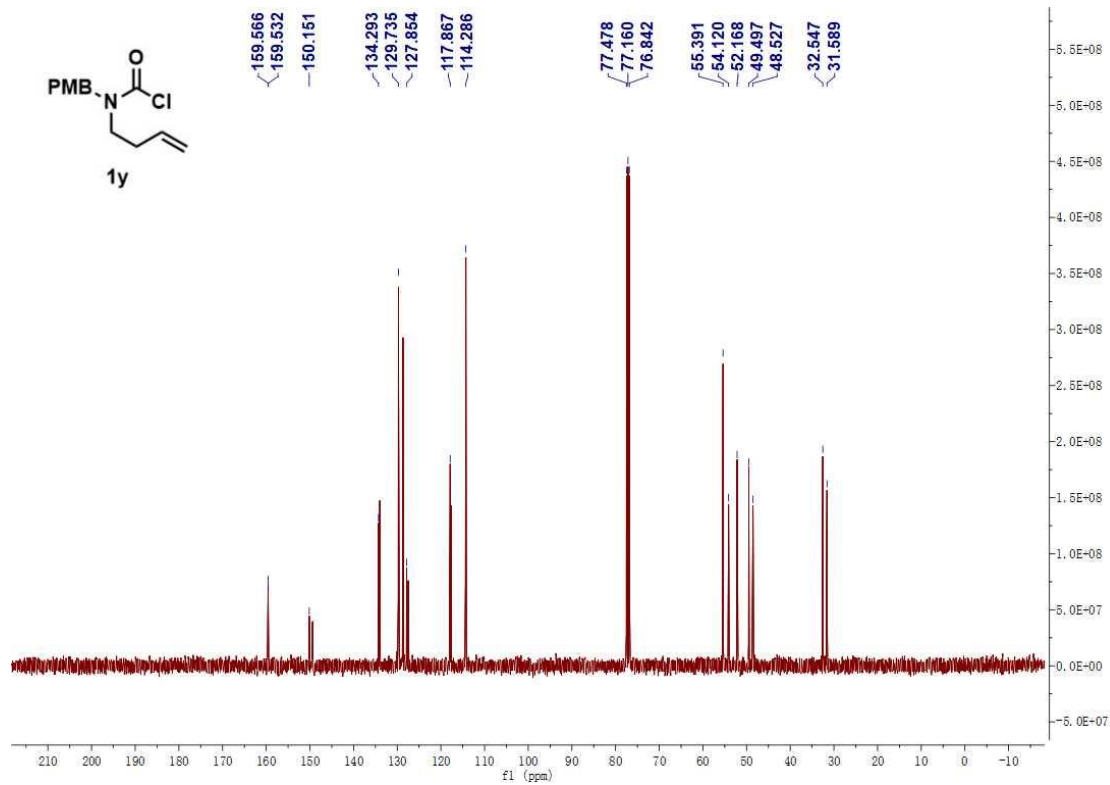
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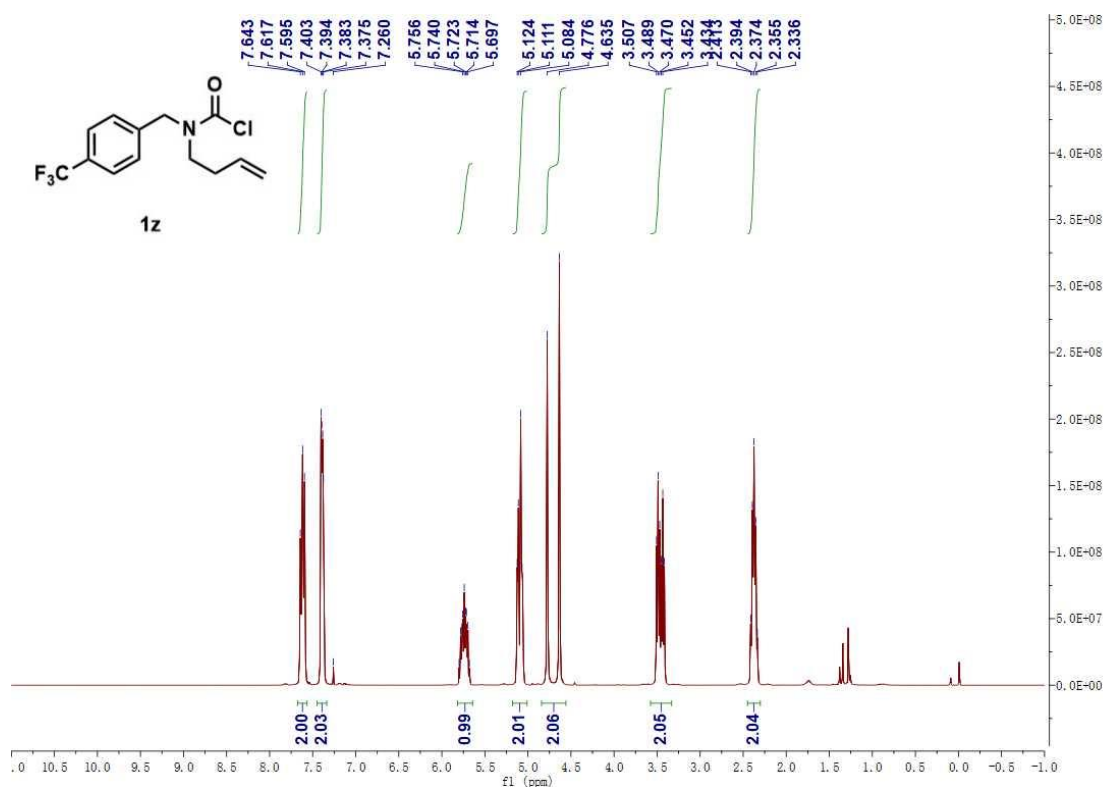
^1H NMR-spectrum (400 MHz, CDCl_3) of **1y**



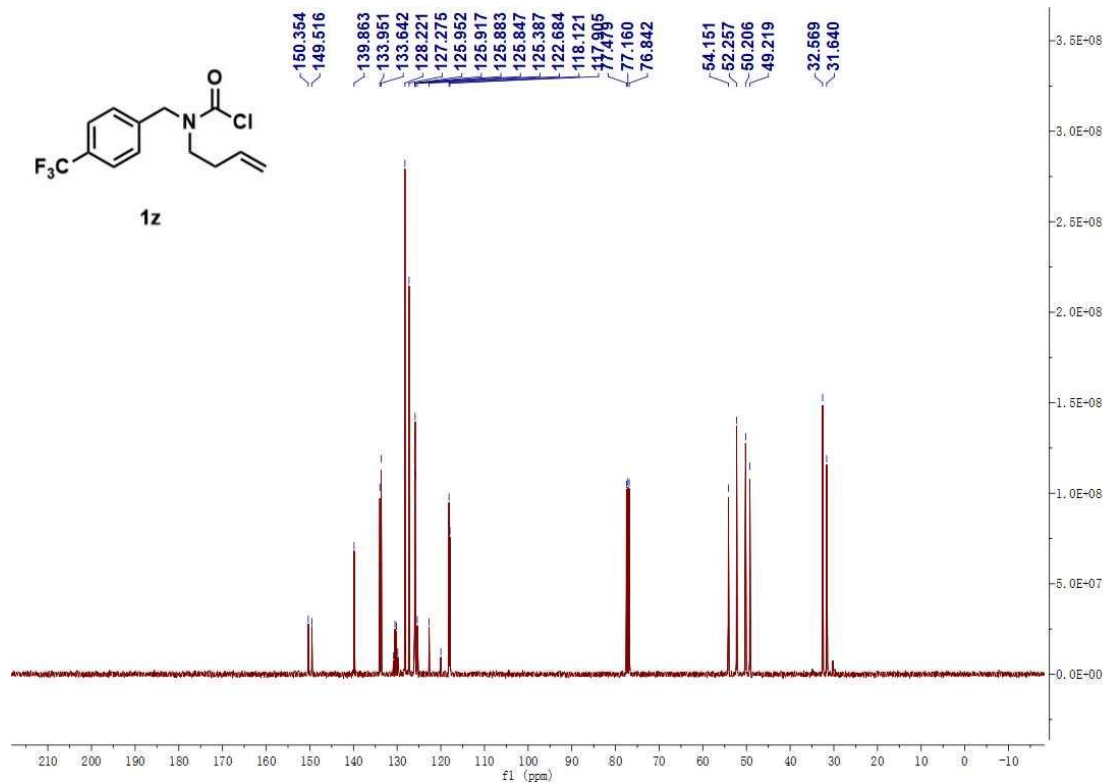
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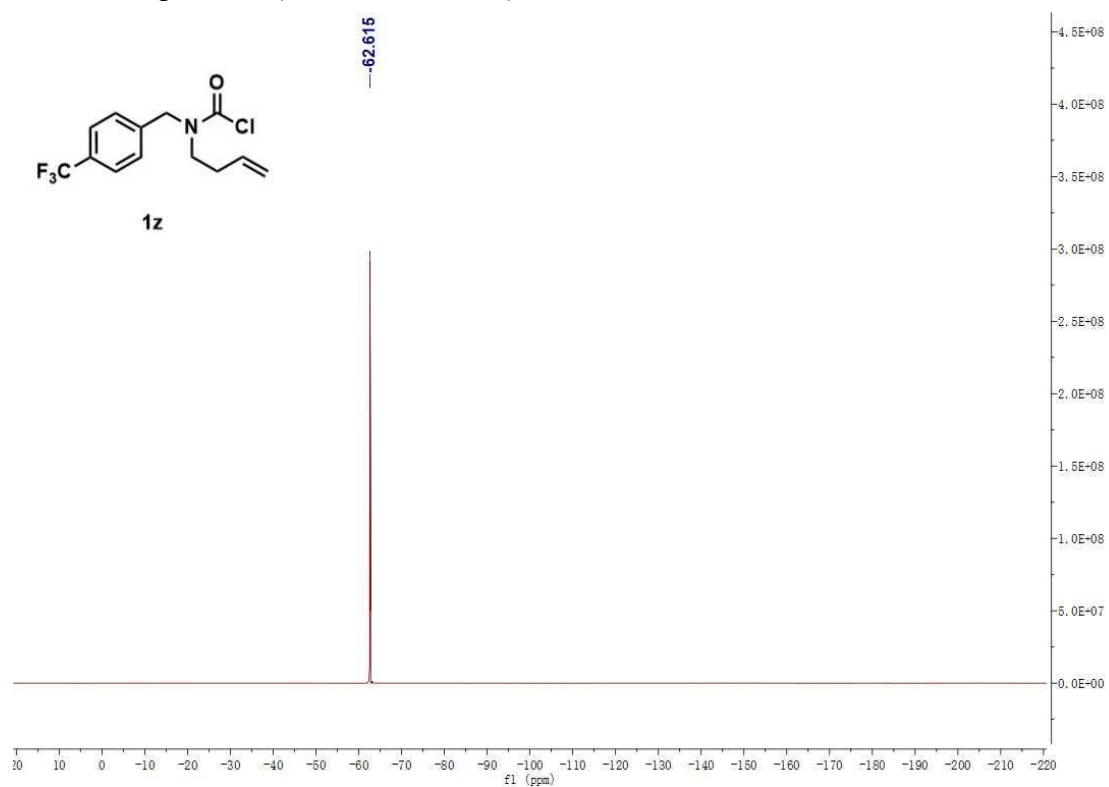
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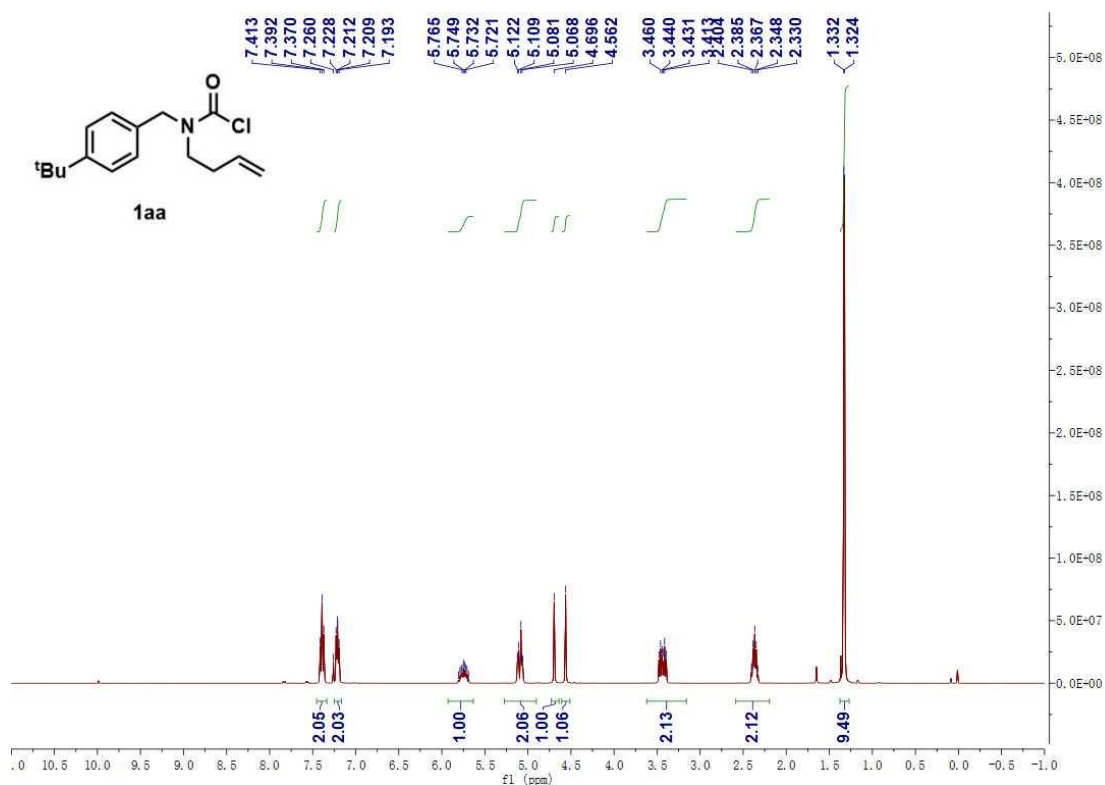
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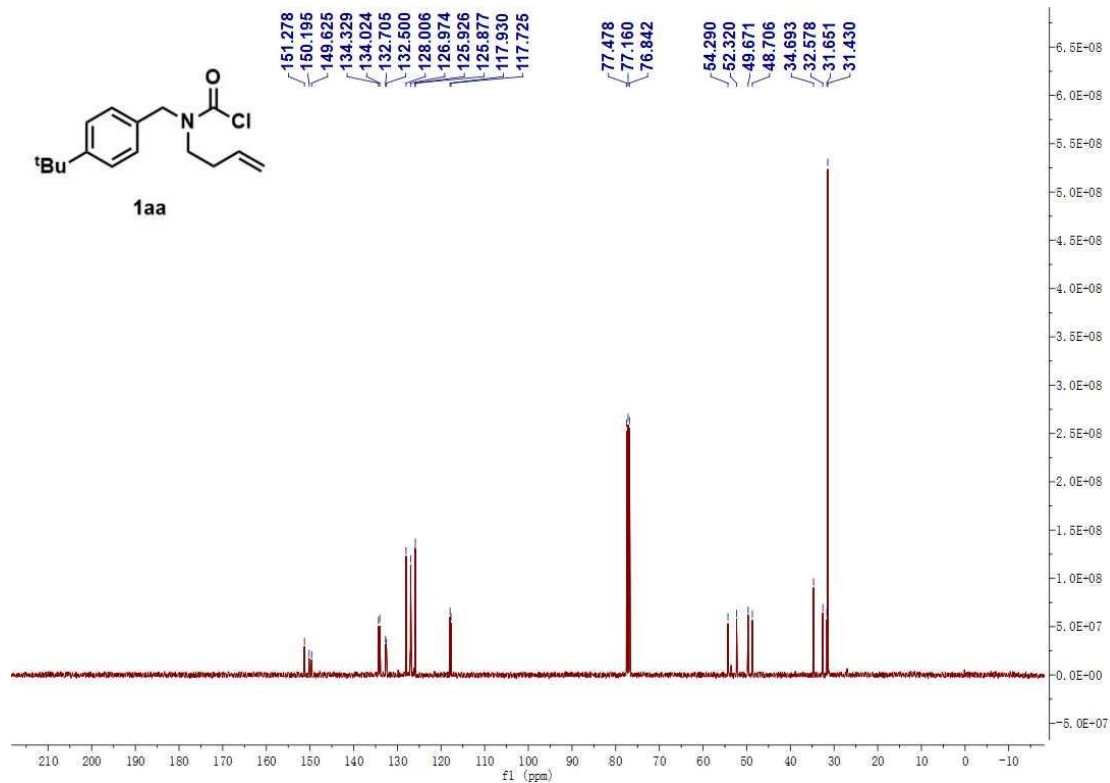
^{19}F NMR-spectrum (376 MHz, CDCl_3) of **1z**



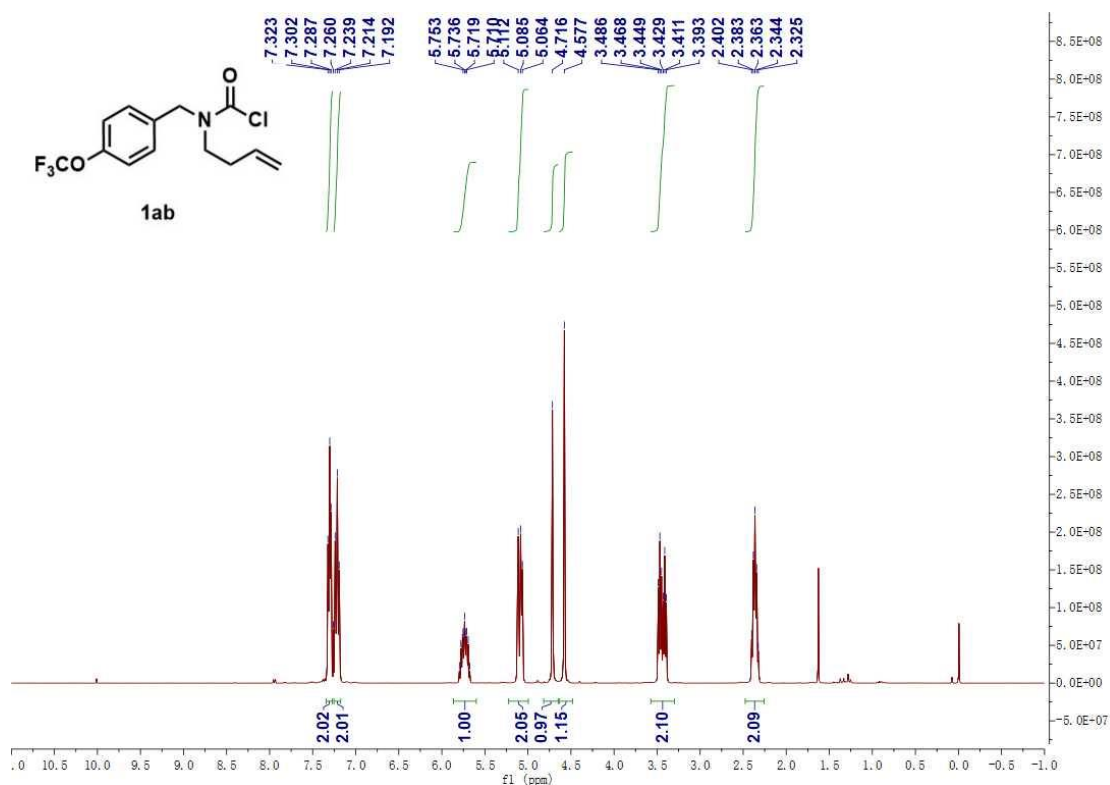
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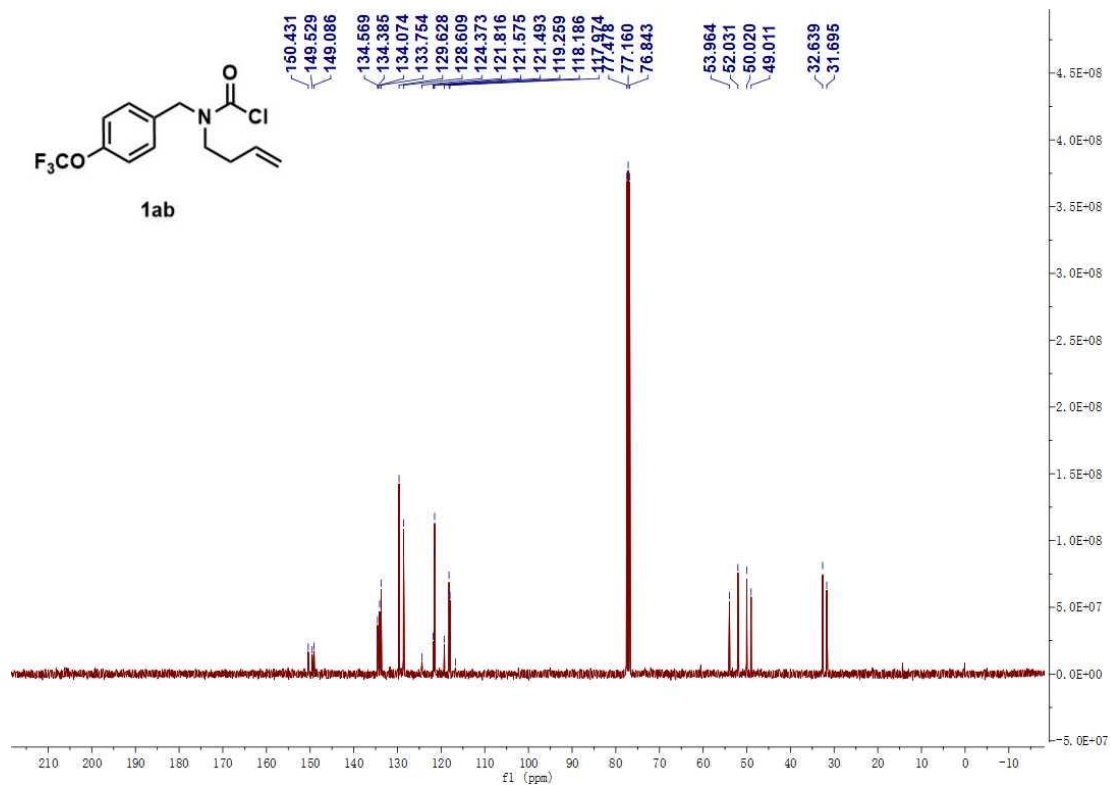
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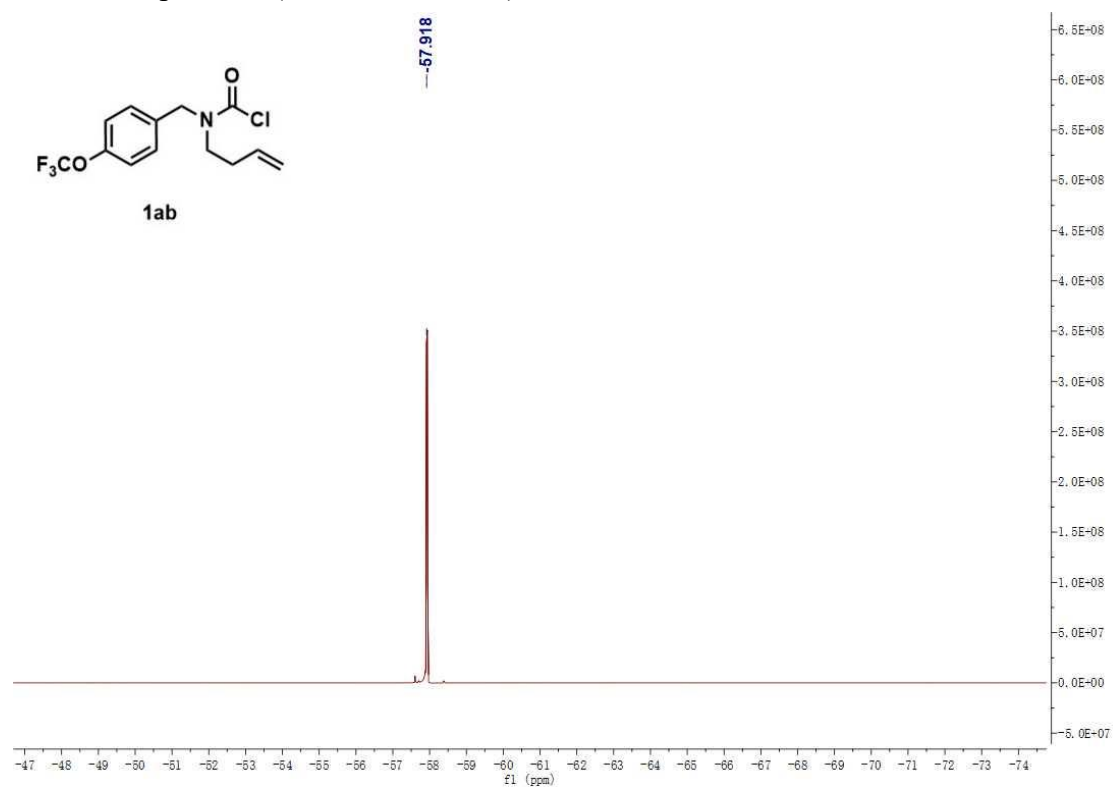
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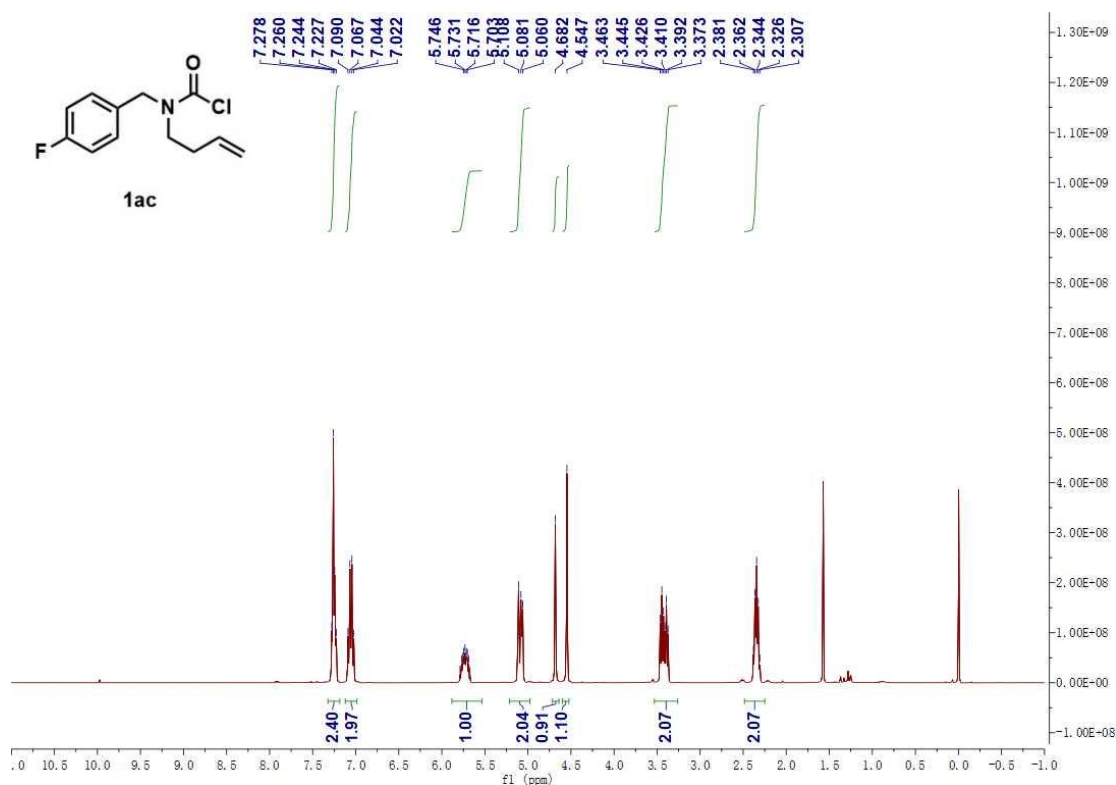
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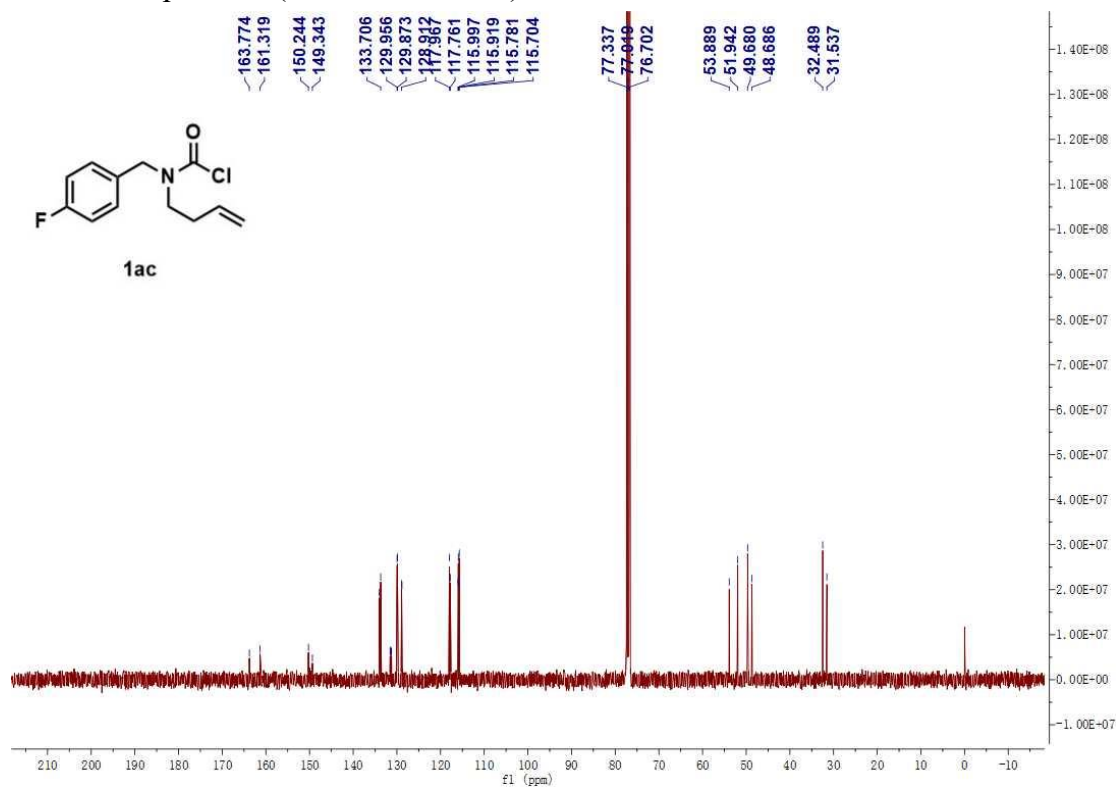
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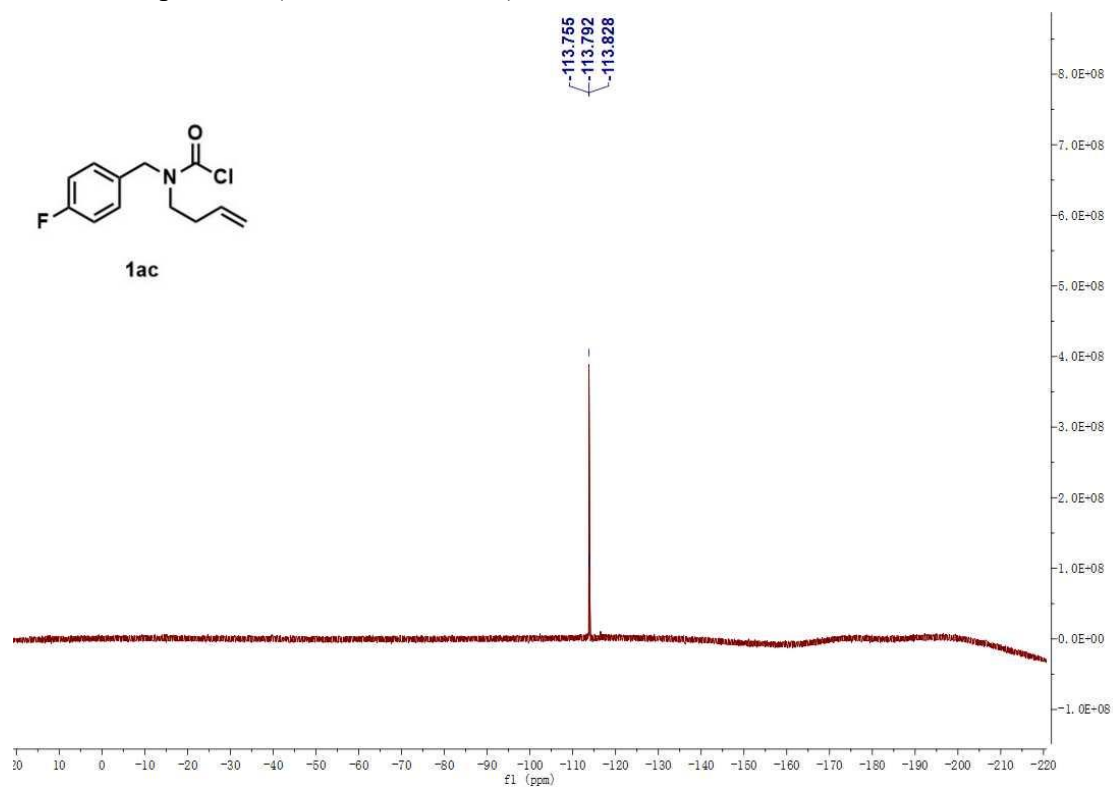
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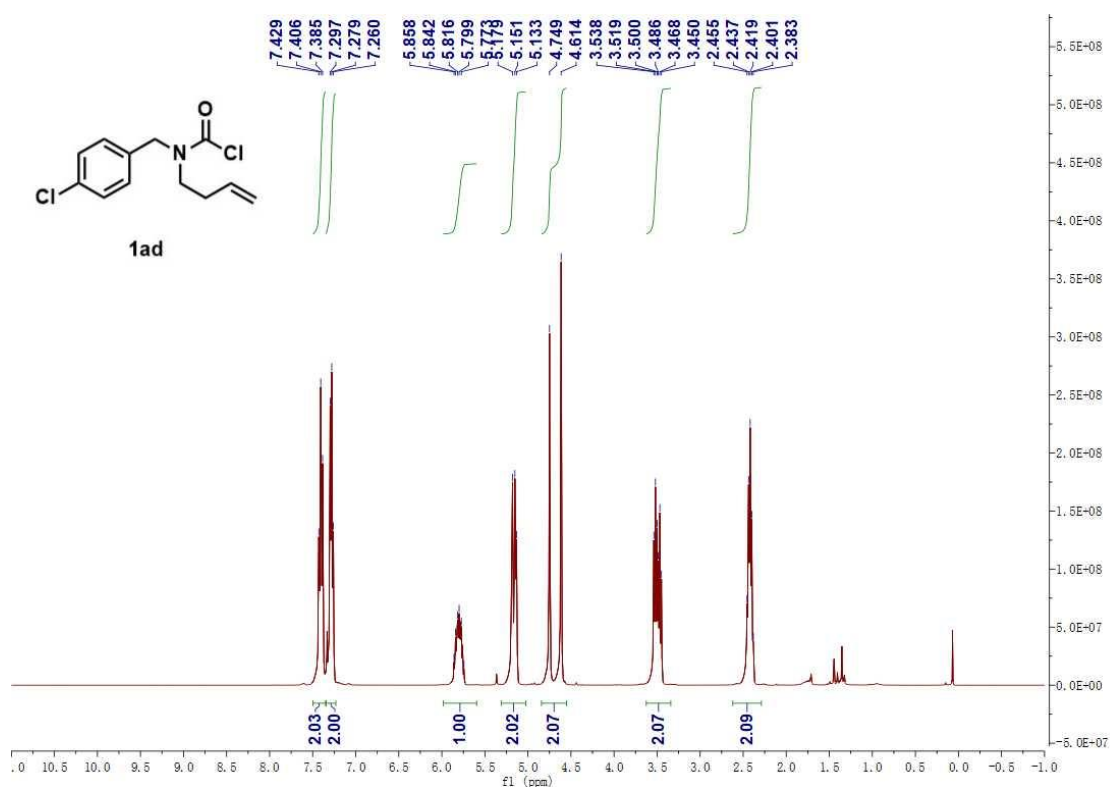
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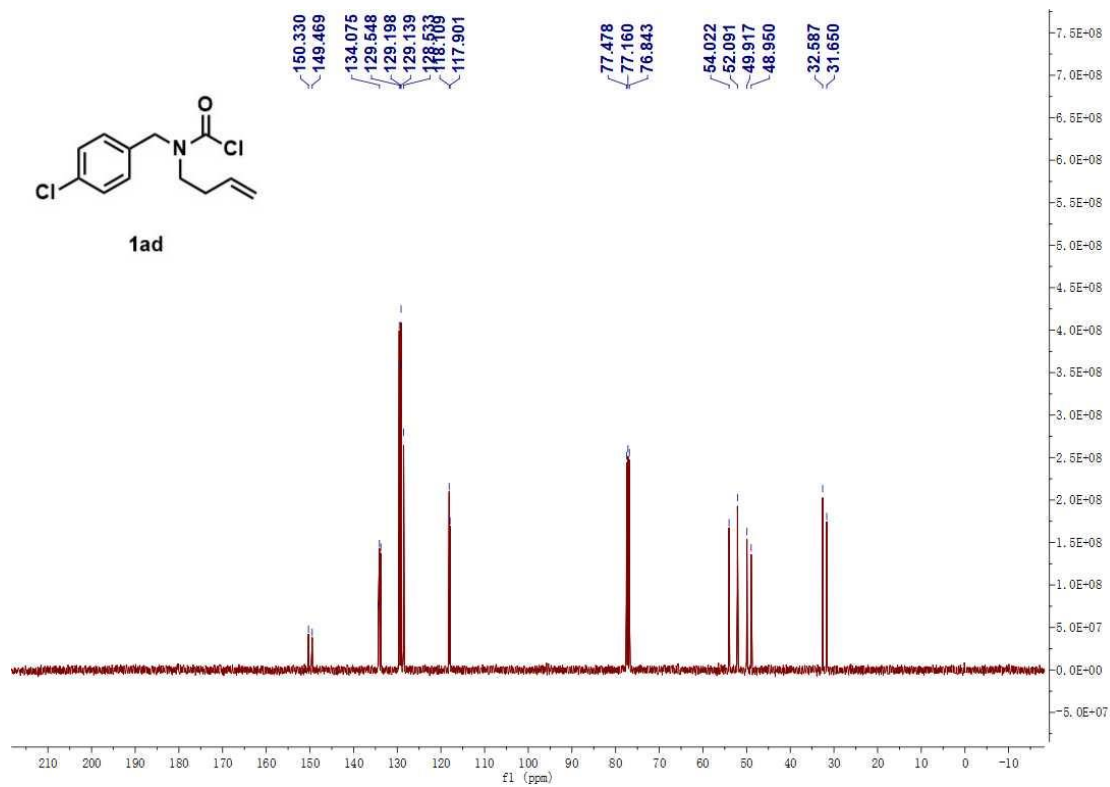
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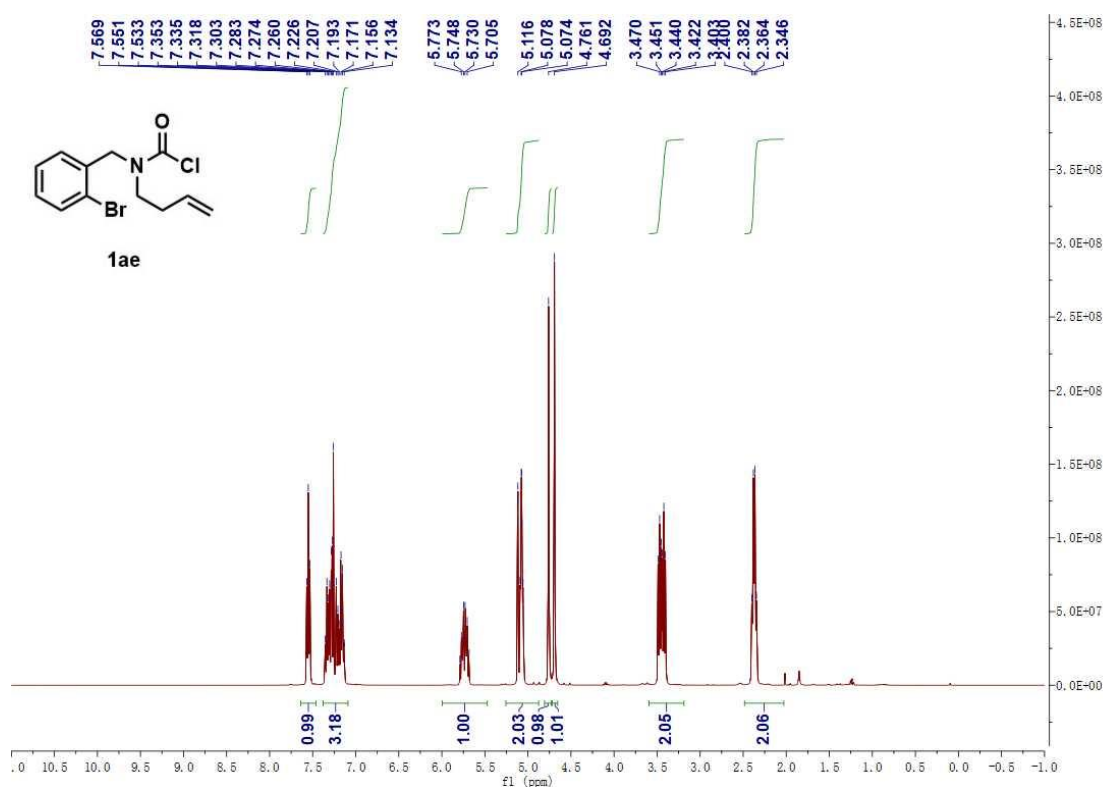
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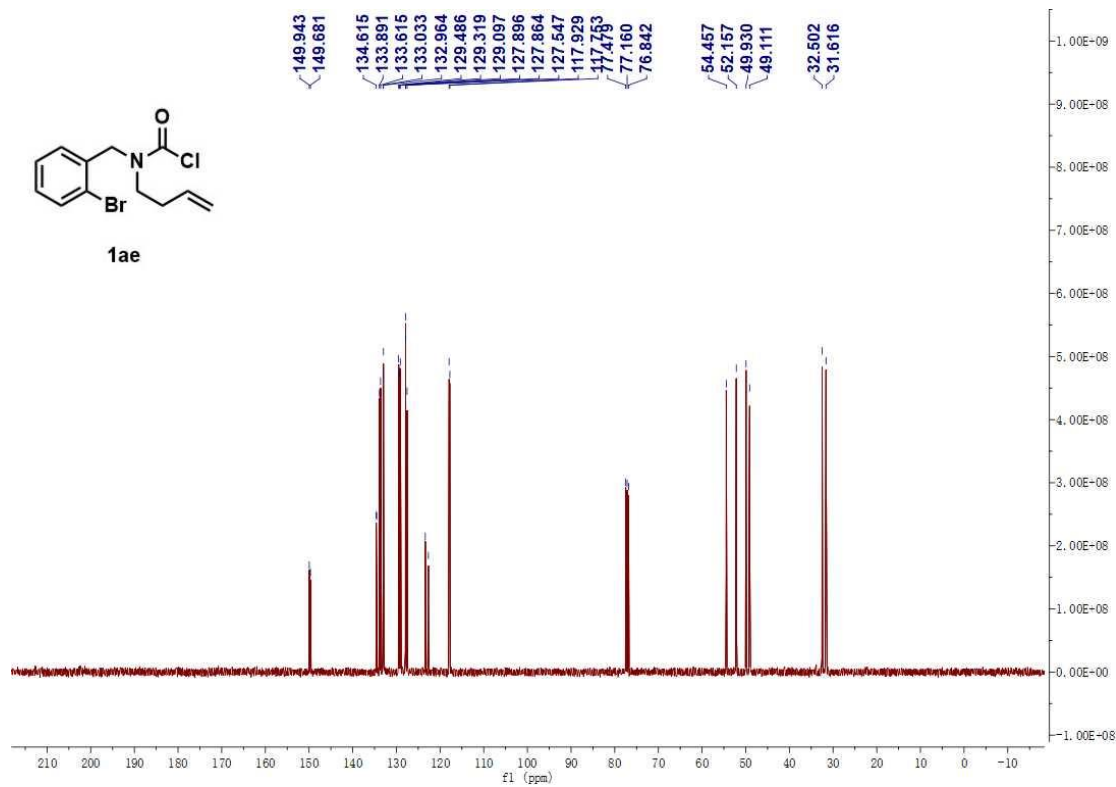
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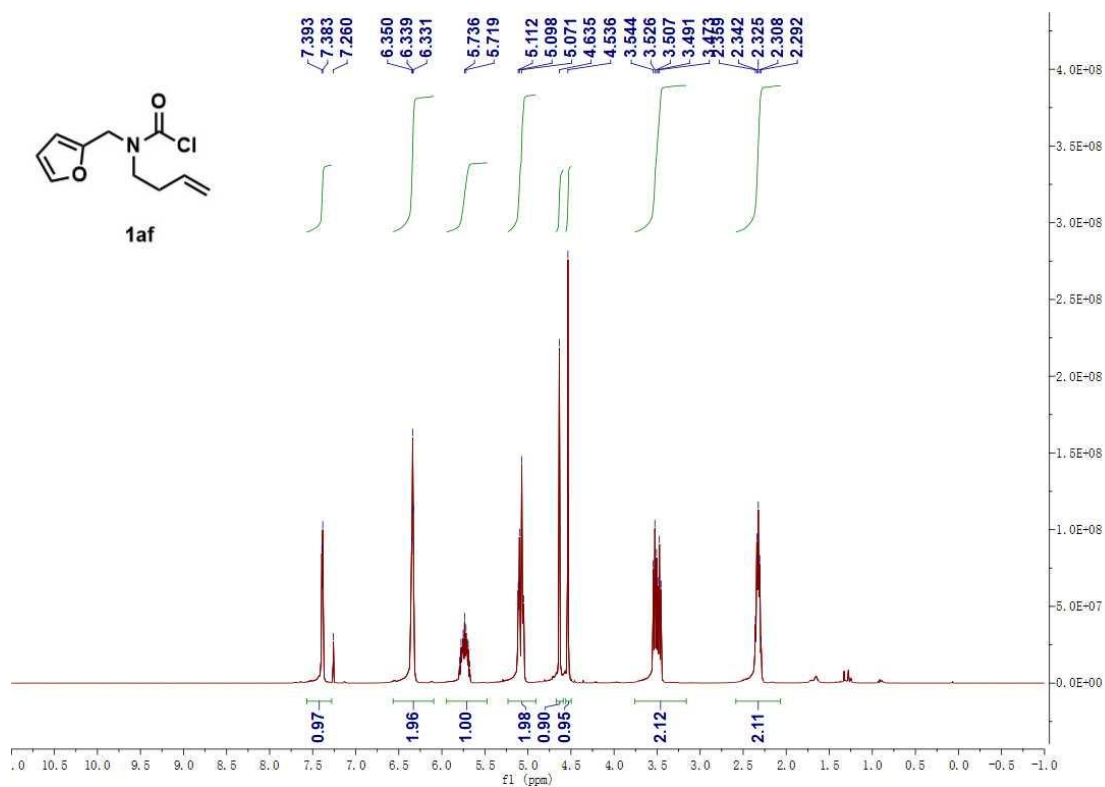
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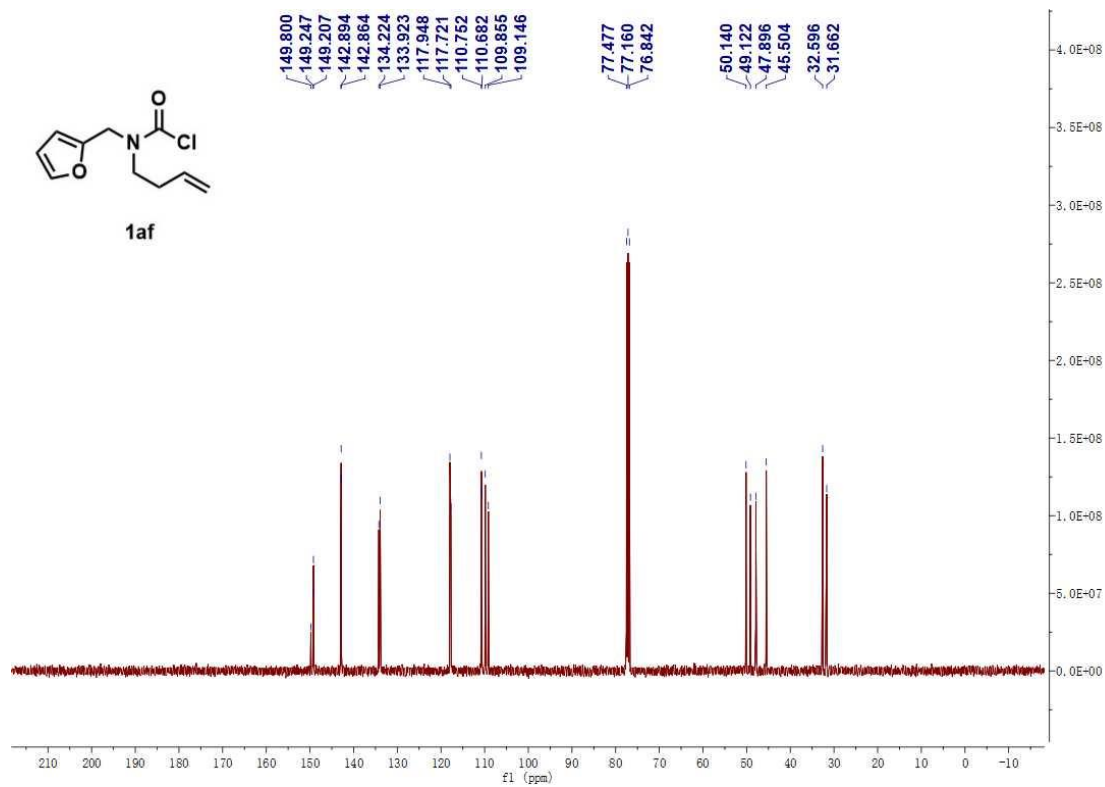
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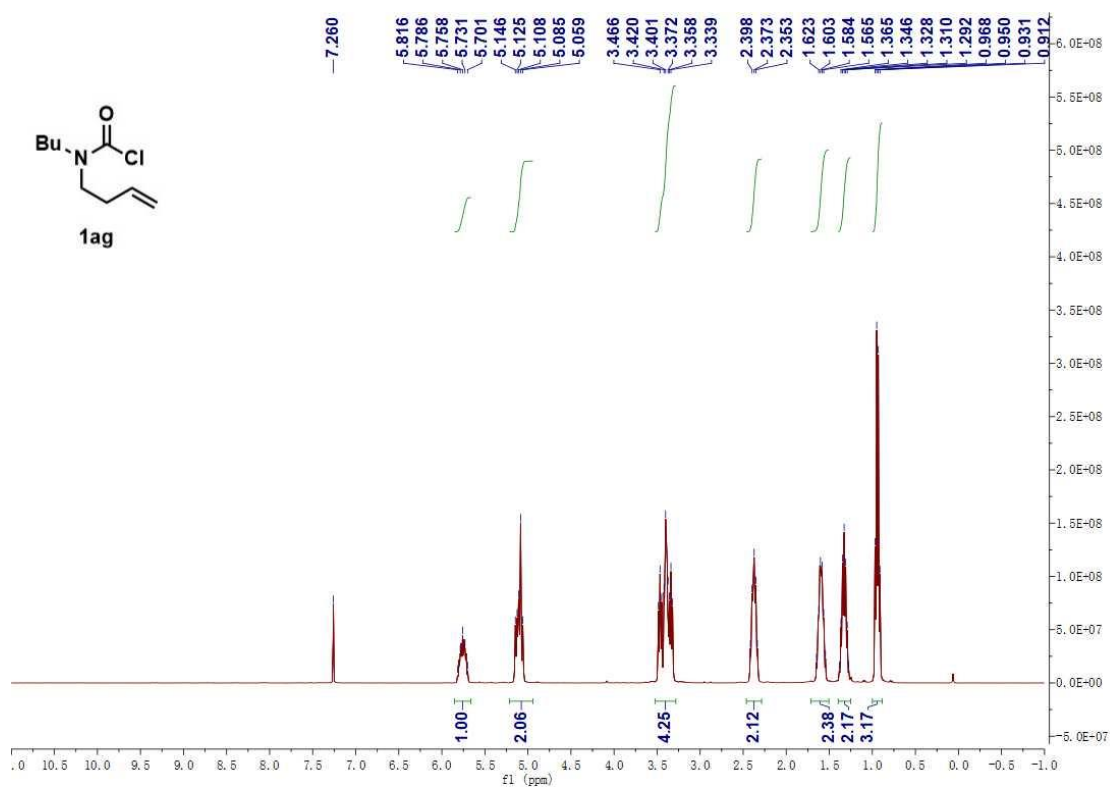
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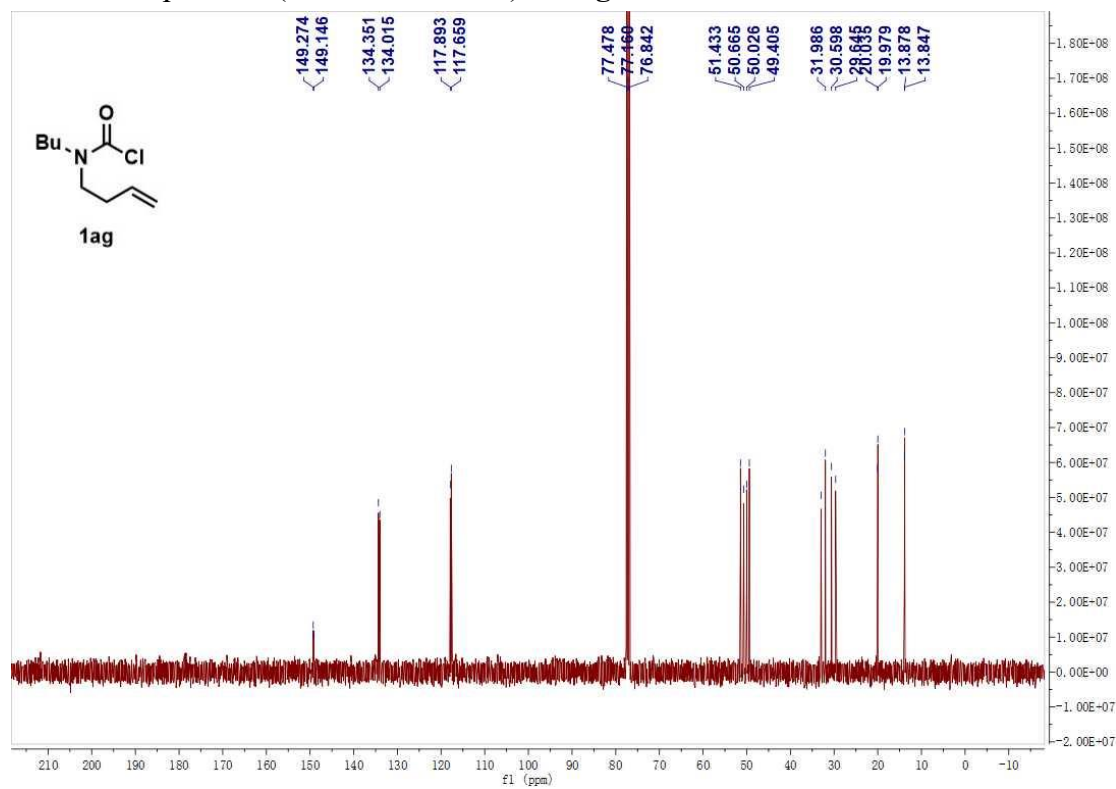
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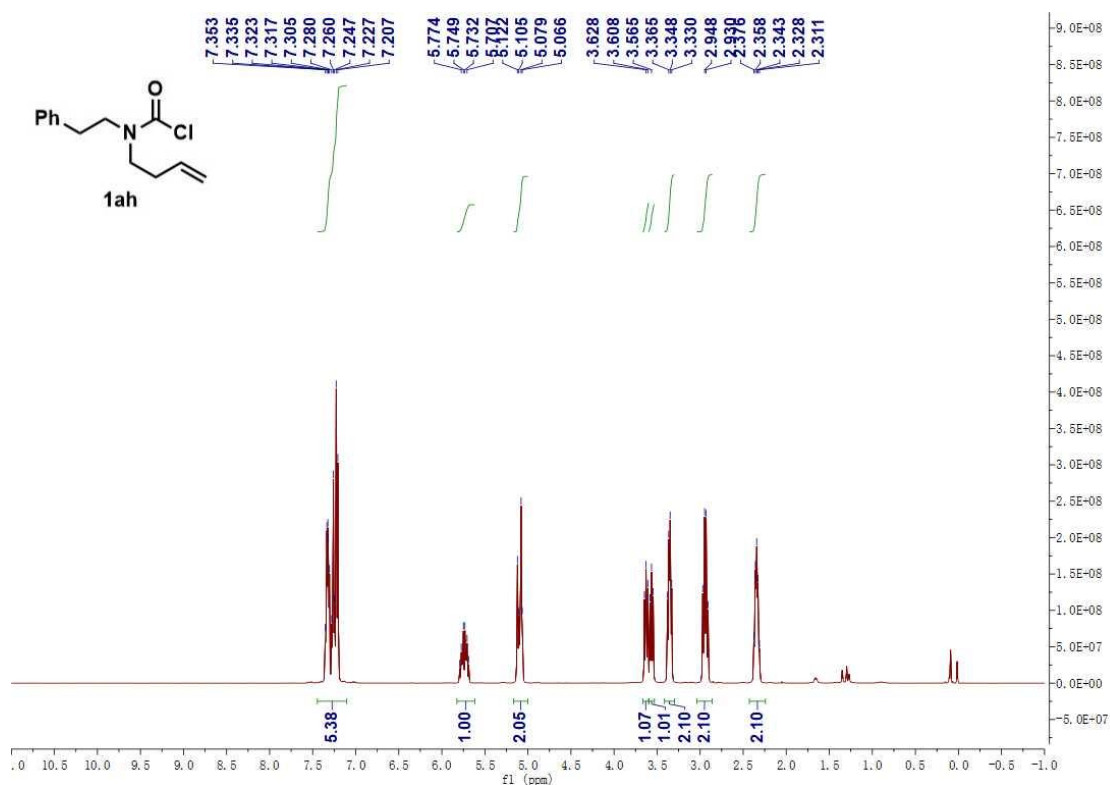
^1H NMR-spectrum (400 MHz, CDCl_3) of **1ag**



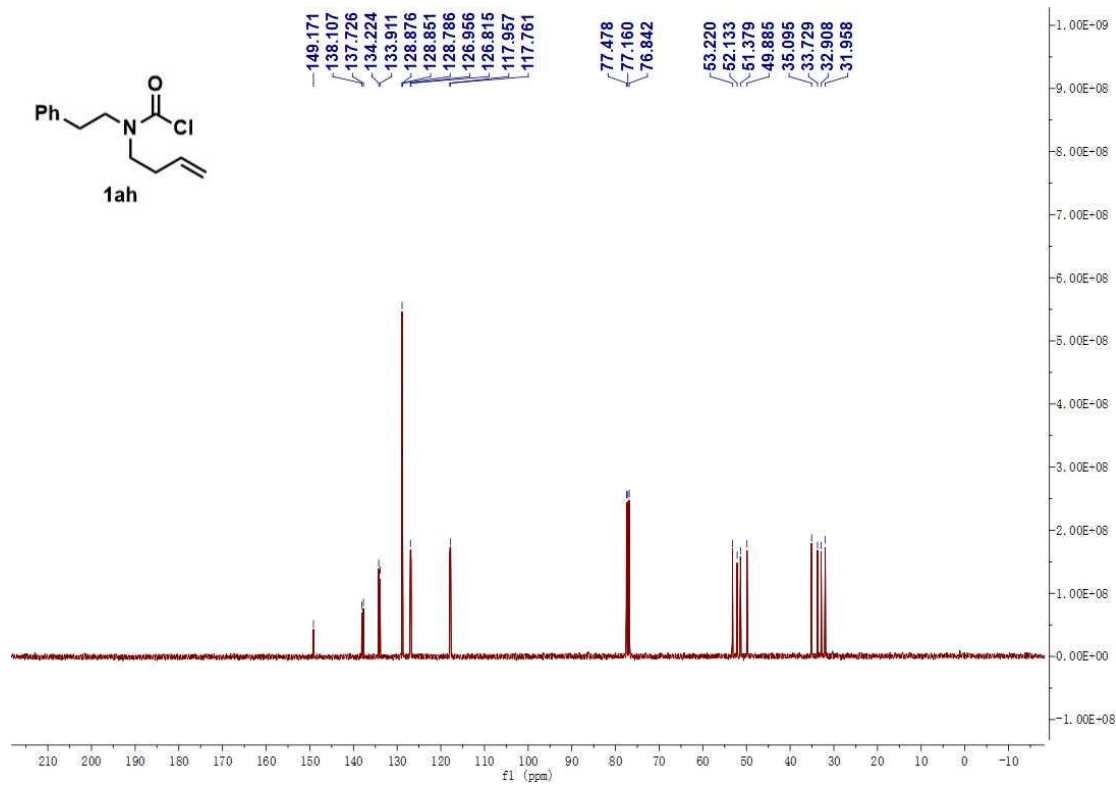
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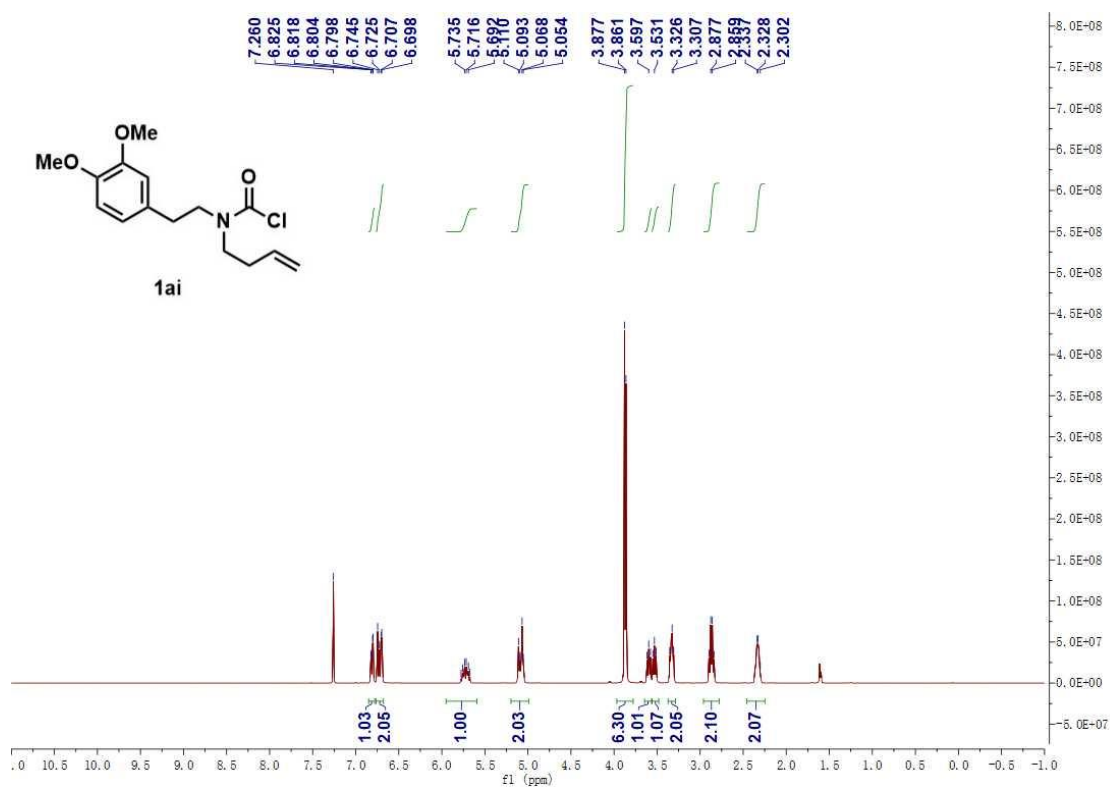
¹H NMR-spectrum (400 MHz, CDCl₃) of **1ah**



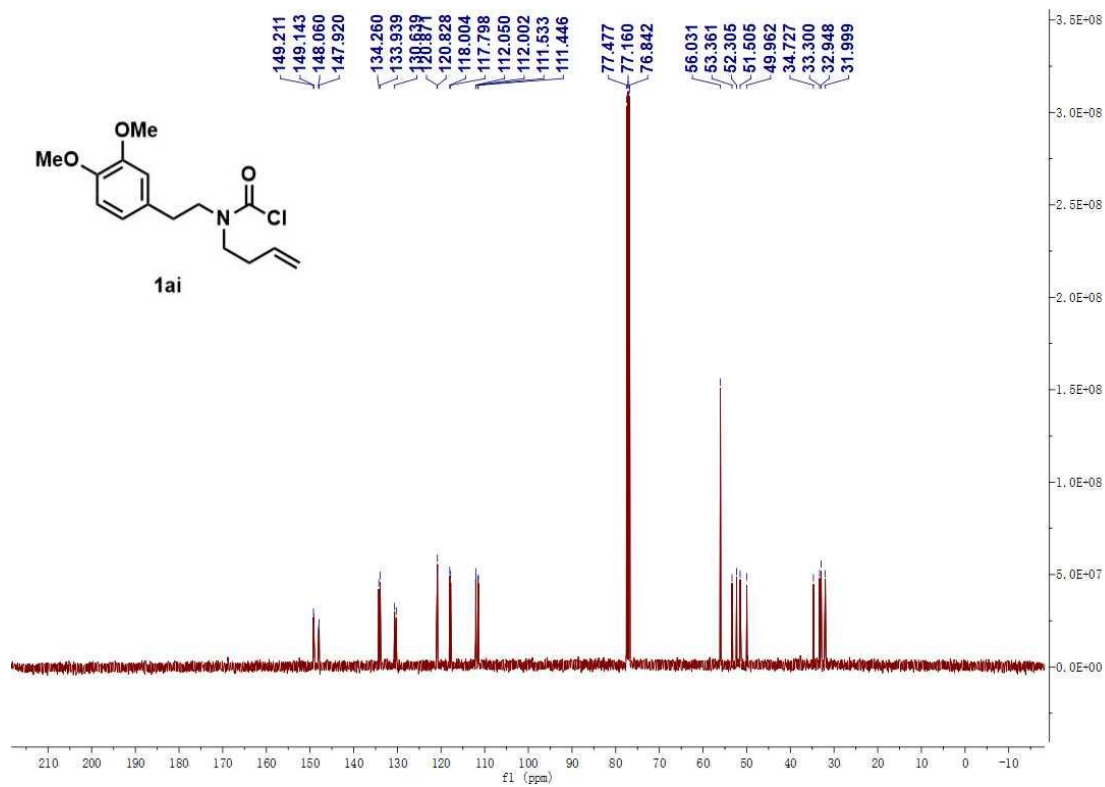
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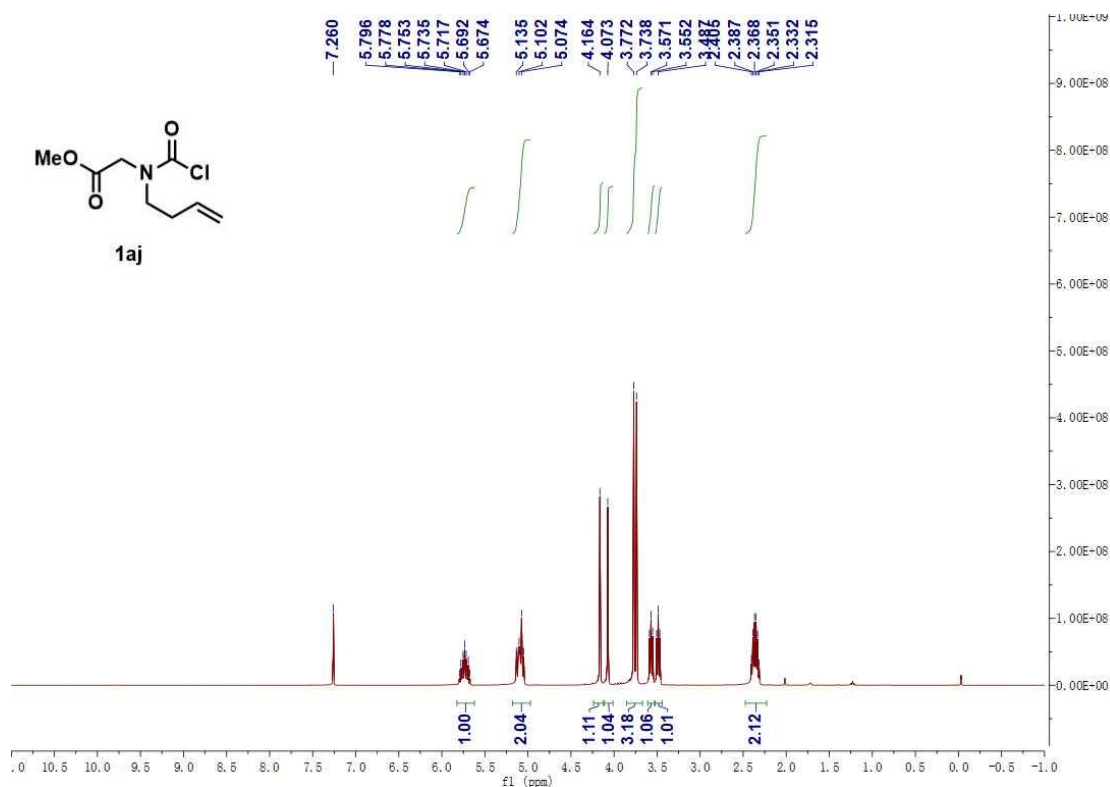
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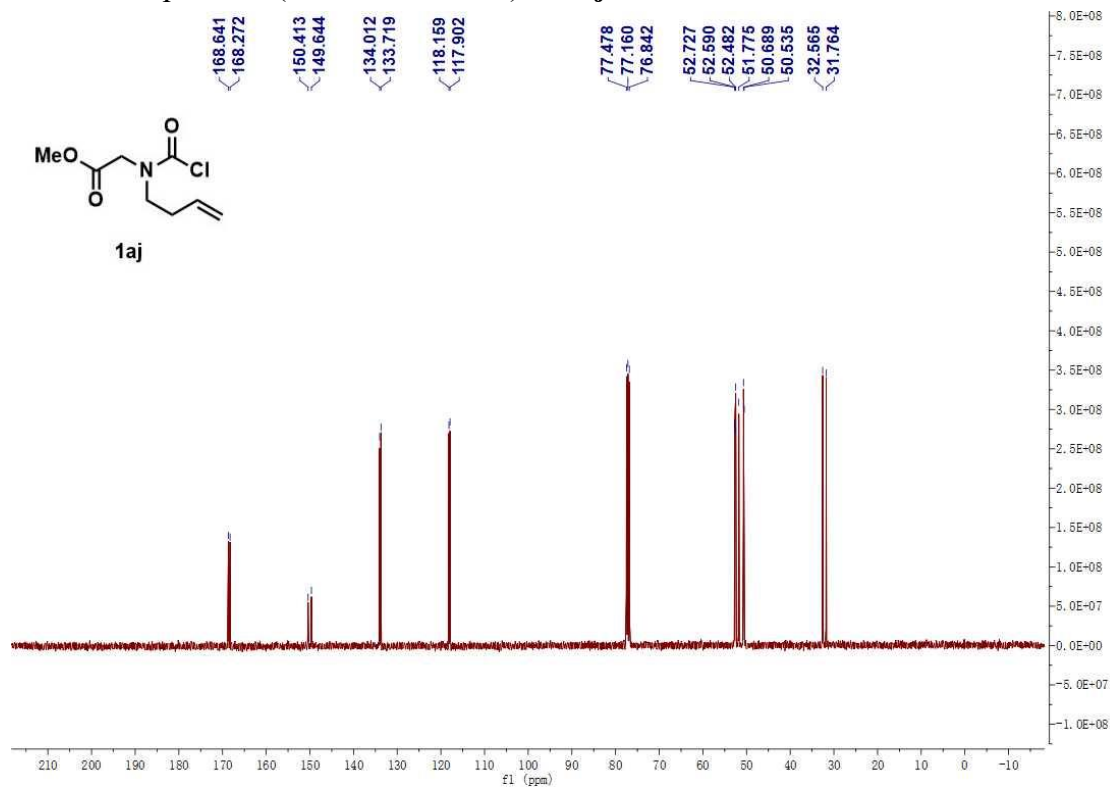
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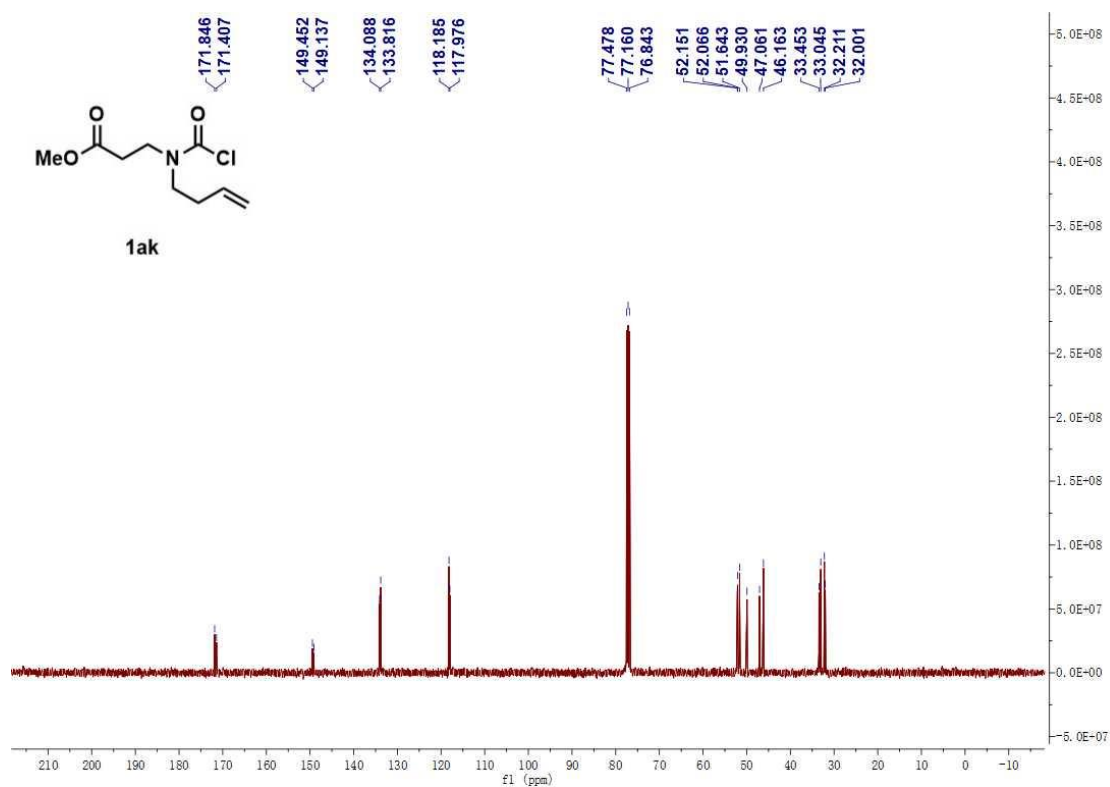
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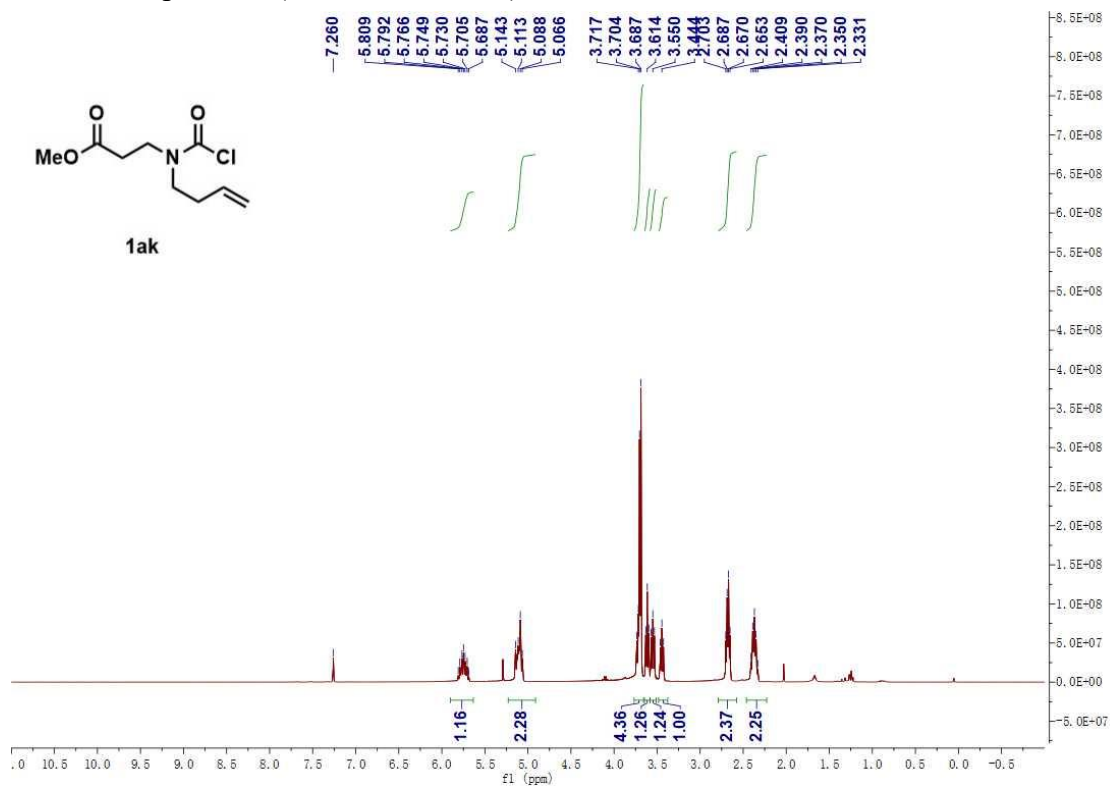
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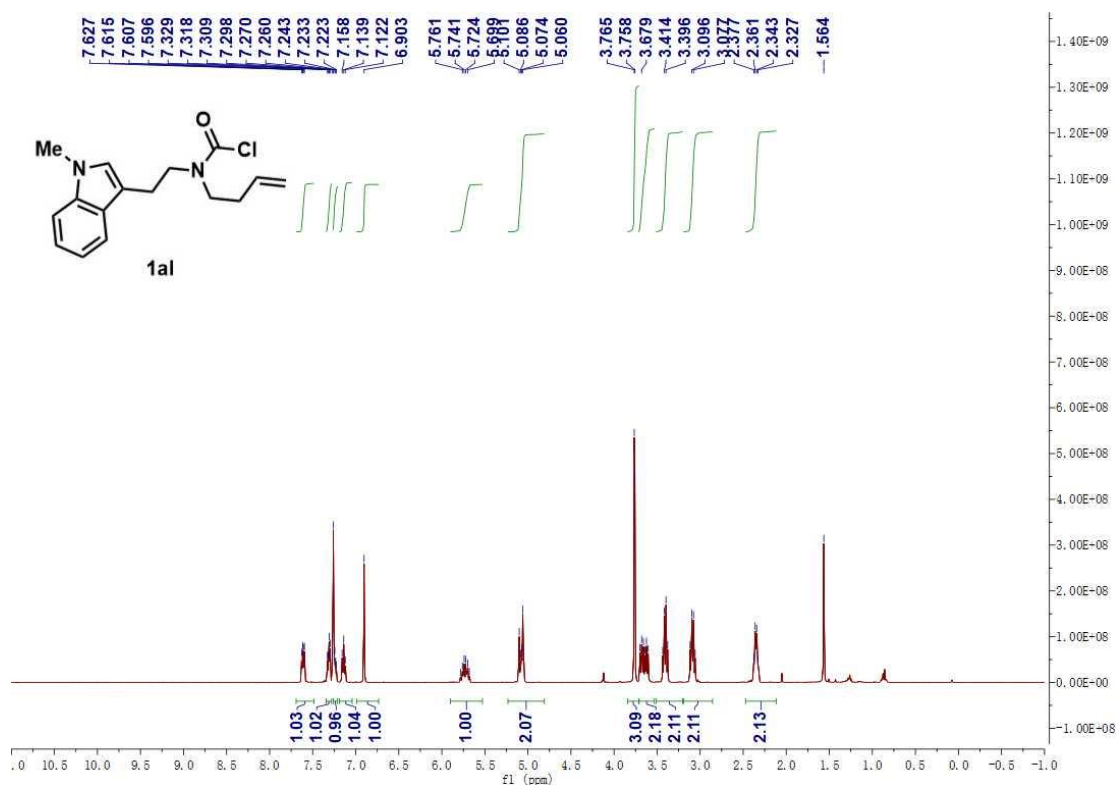
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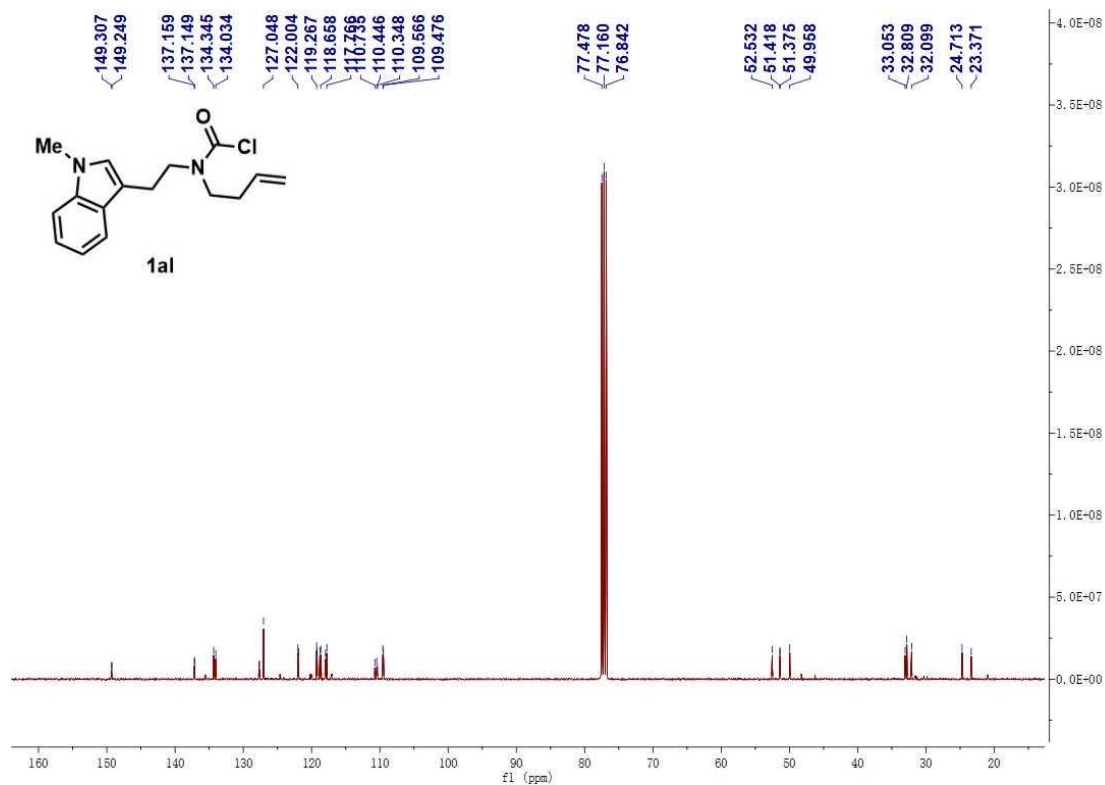
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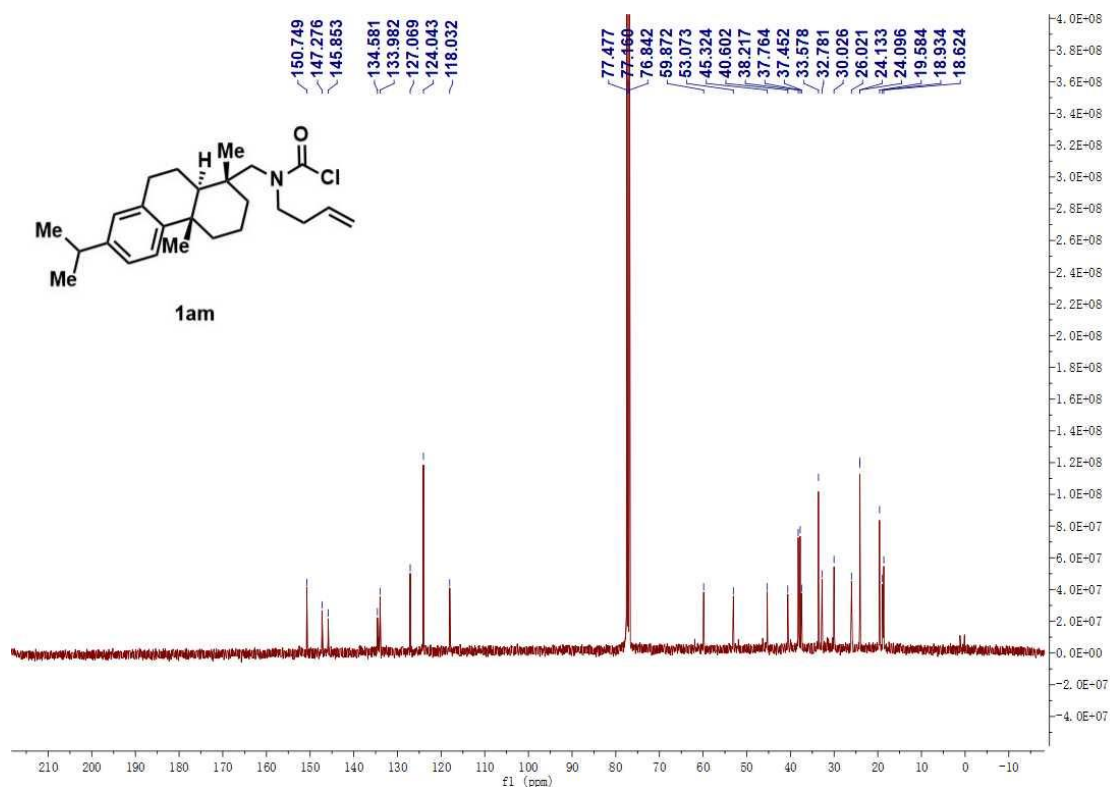
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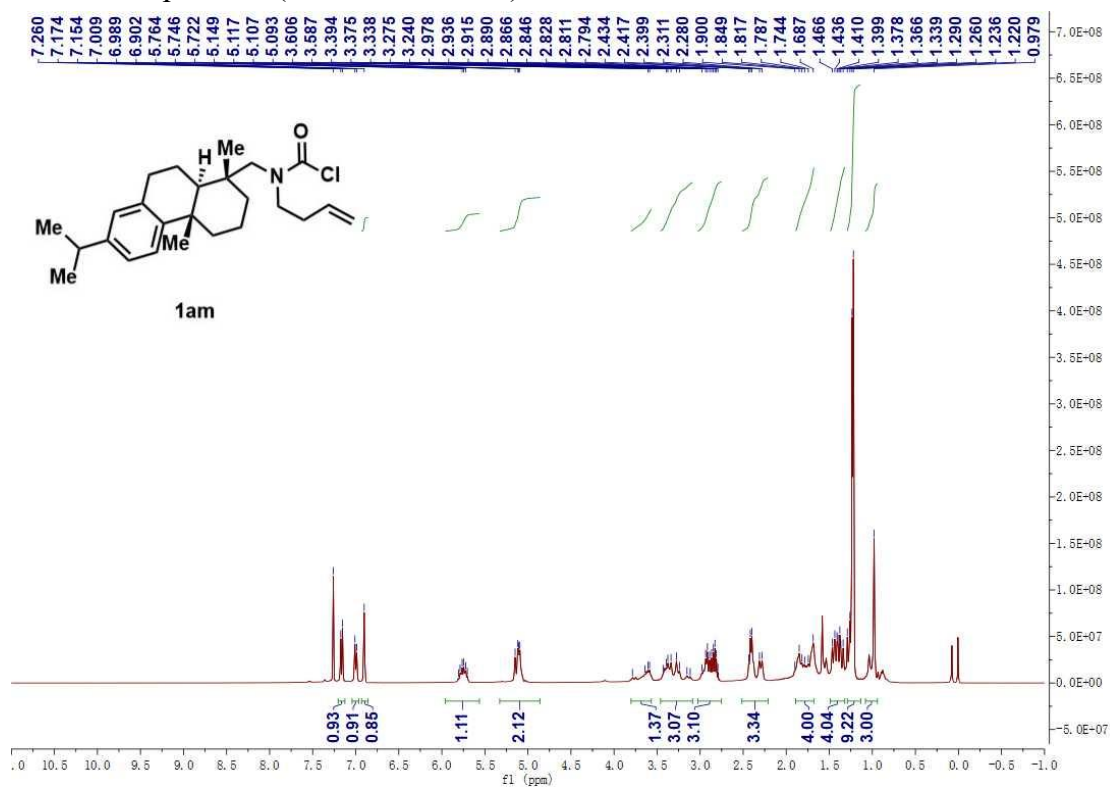
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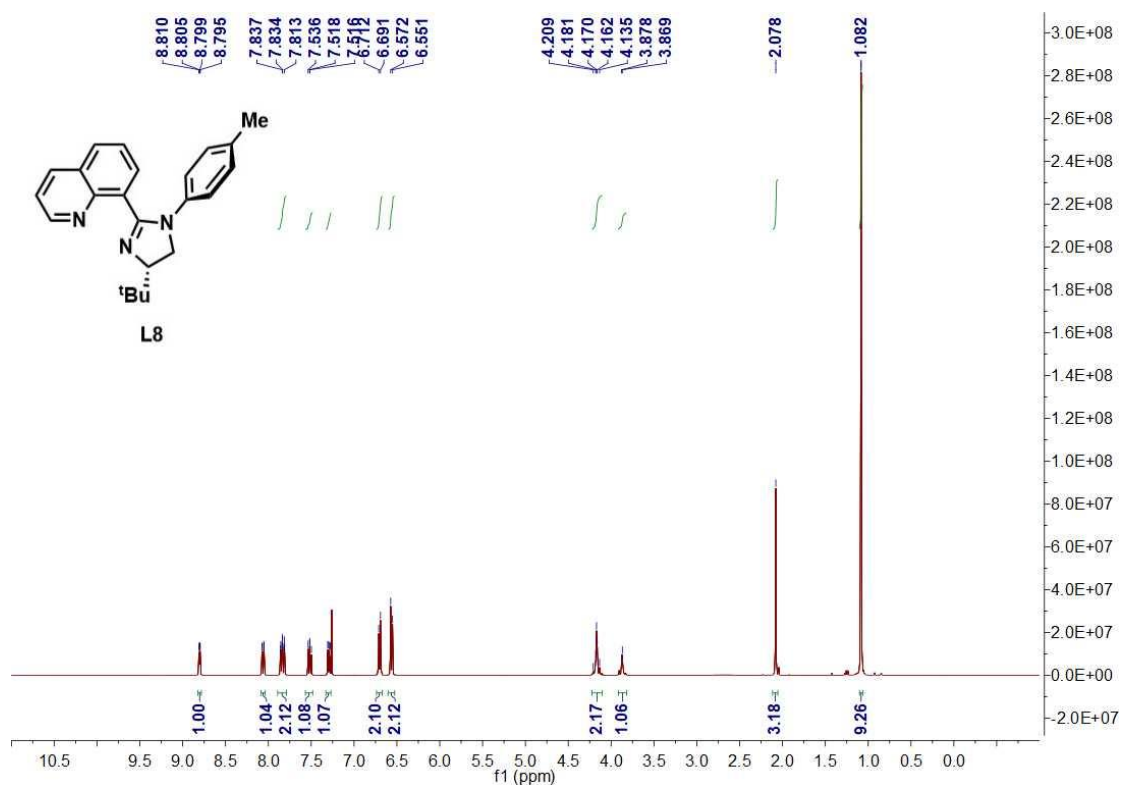
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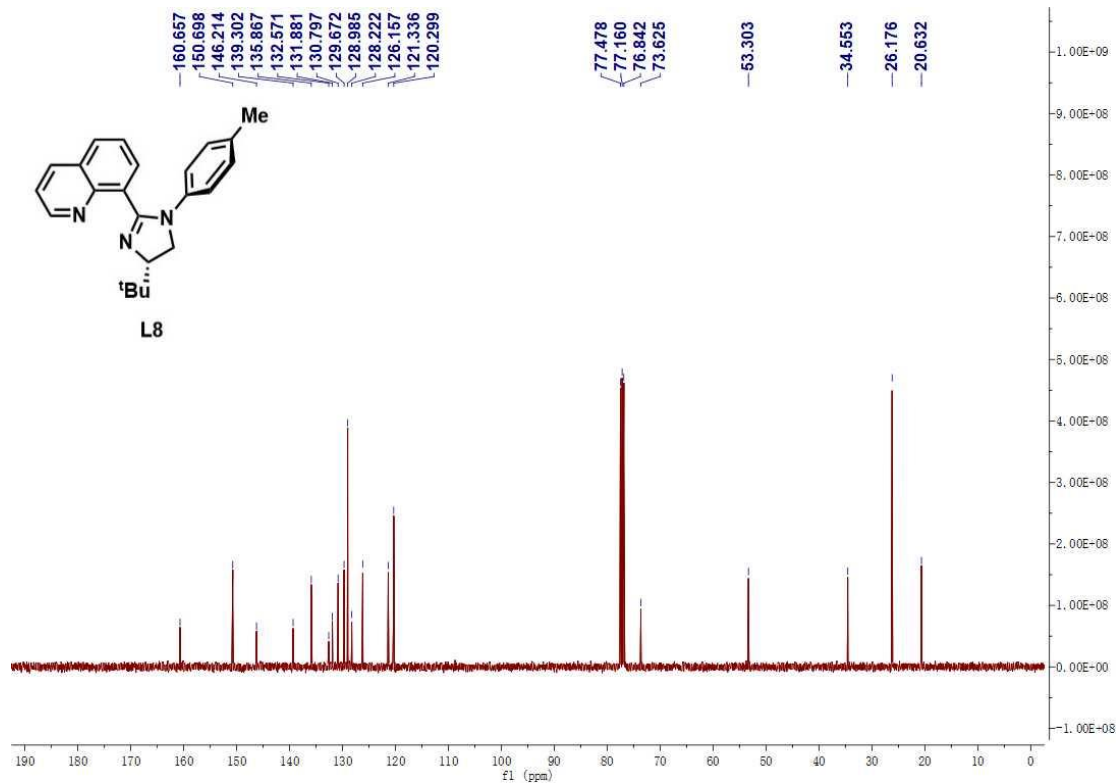
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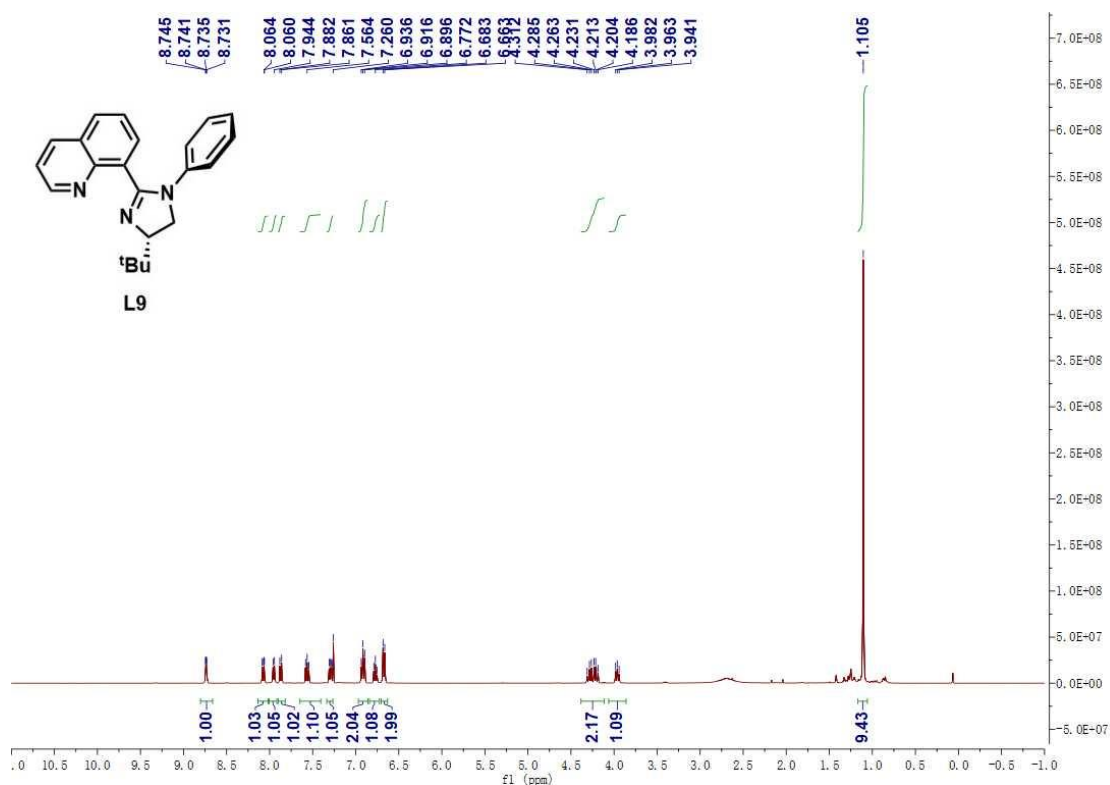
¹H NMR-spectrum (400 MHz, CDCl₃) of **L8**



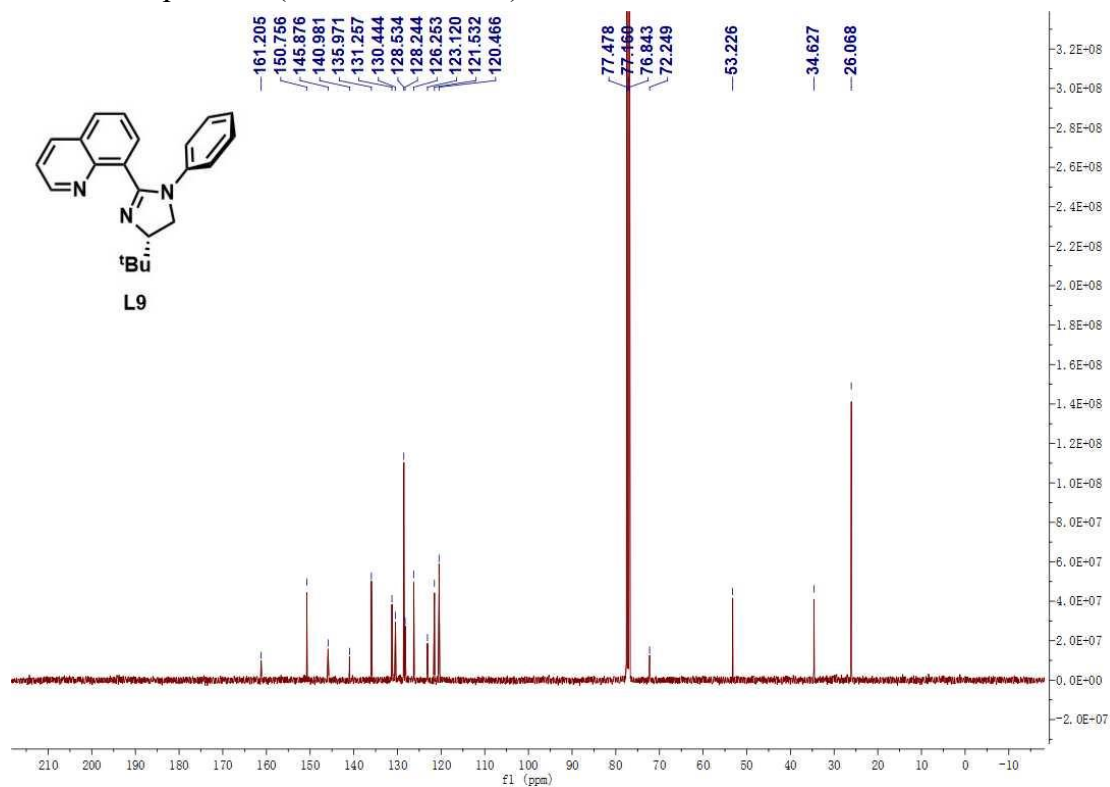
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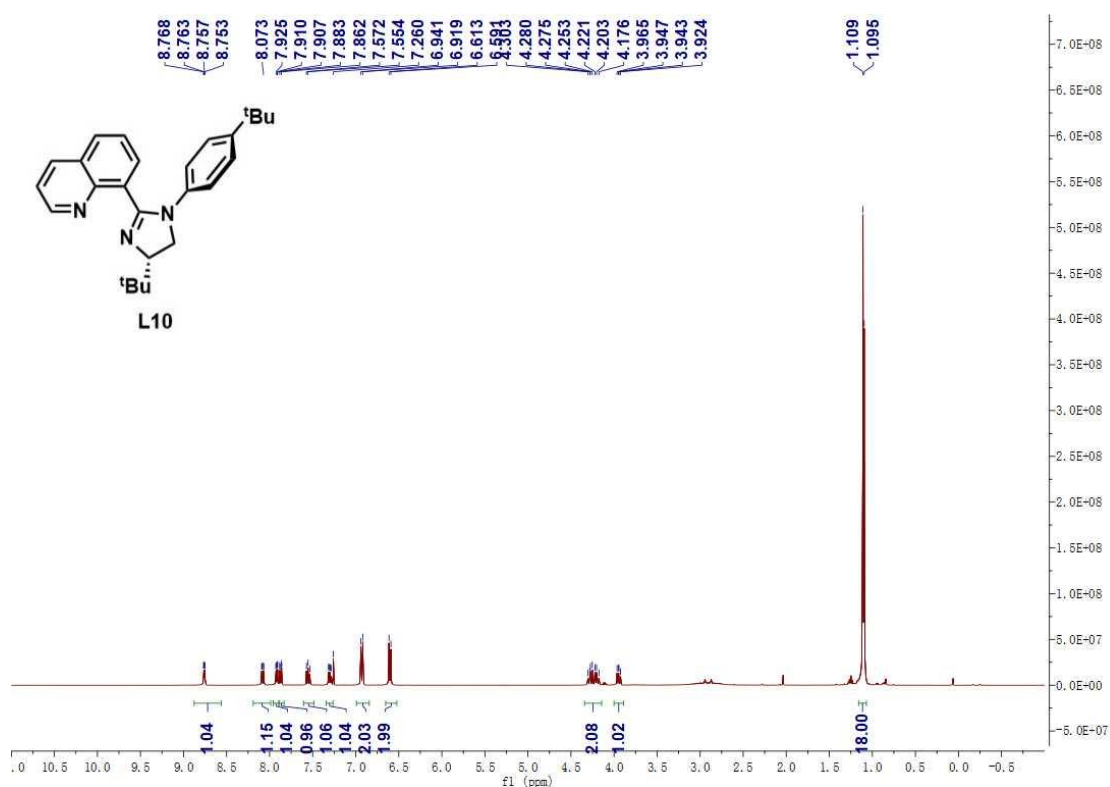
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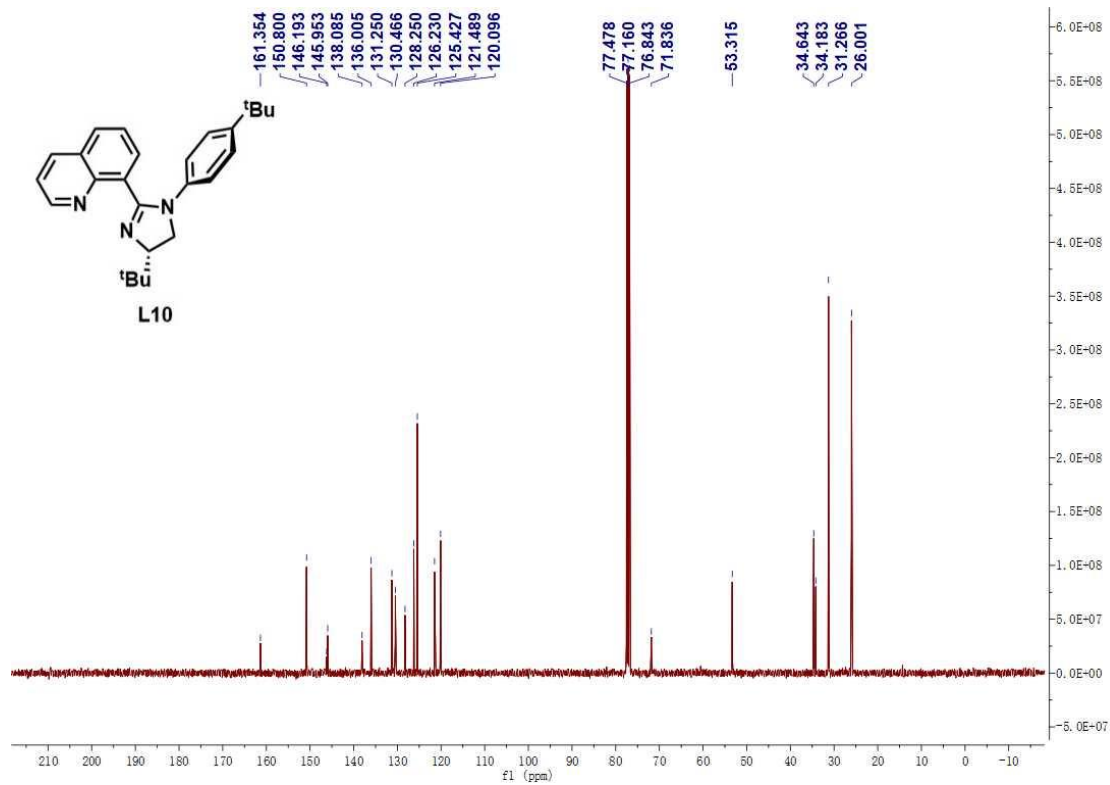
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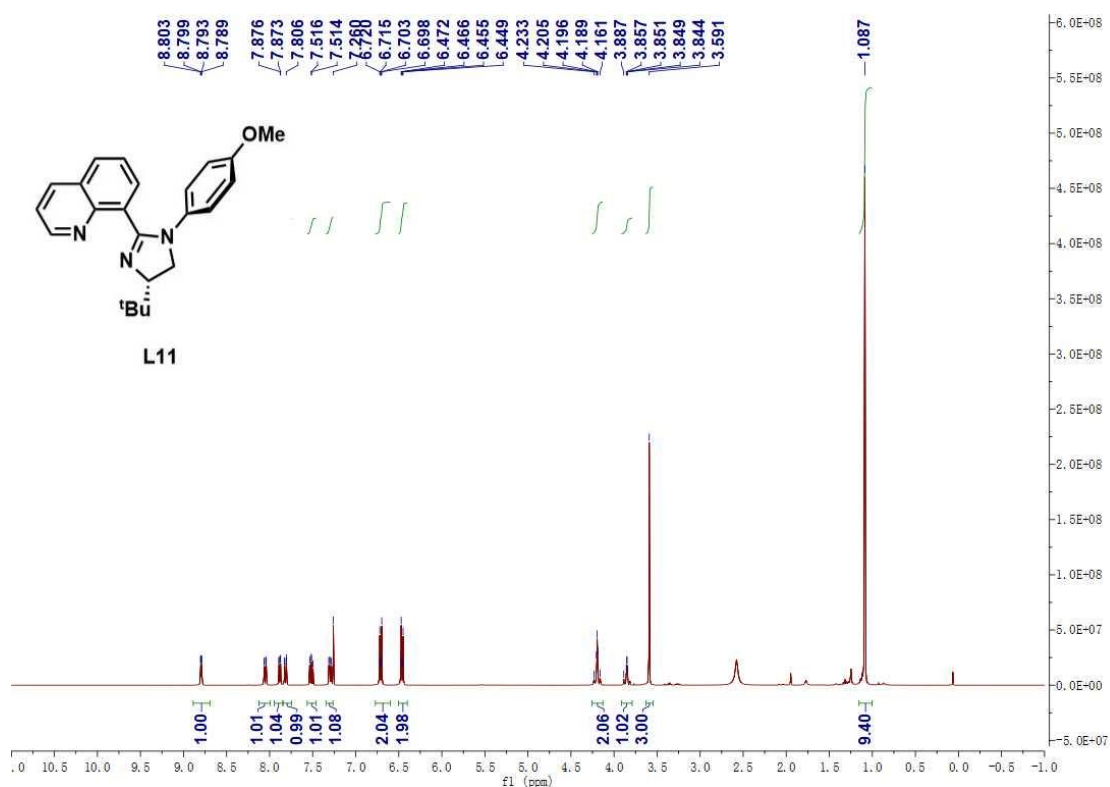
¹H NMR-spectrum (400 MHz, CDCl₃) of L10



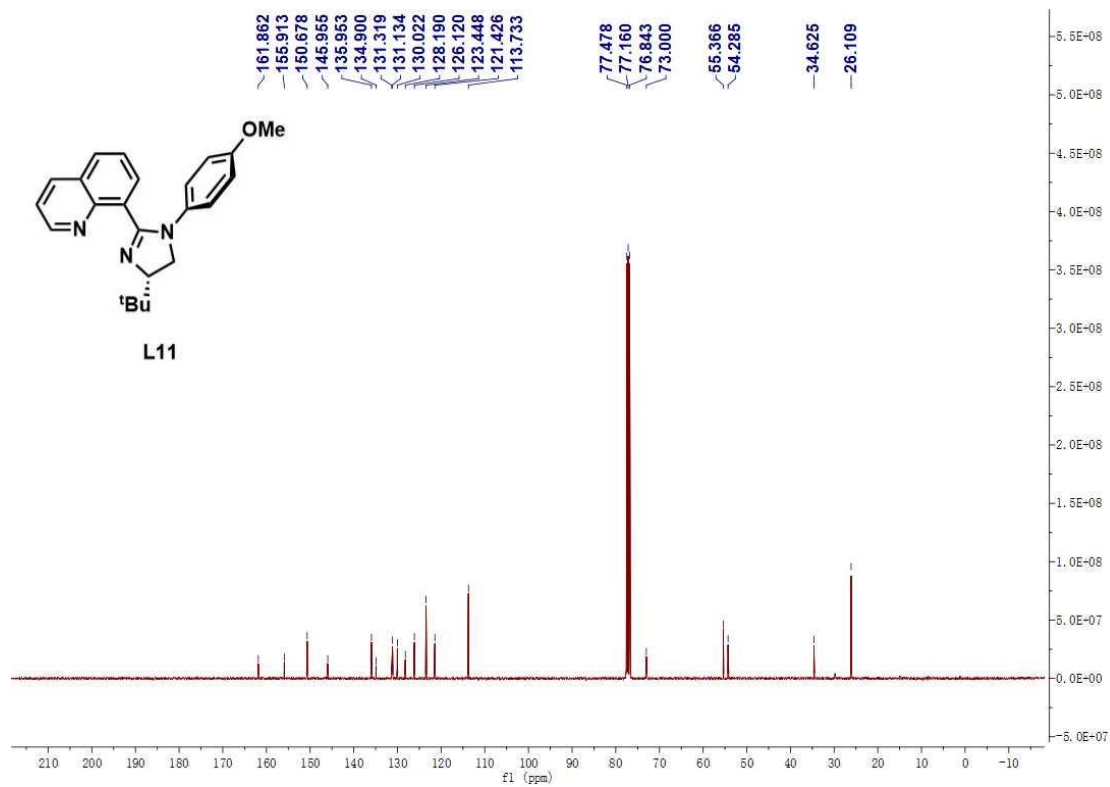
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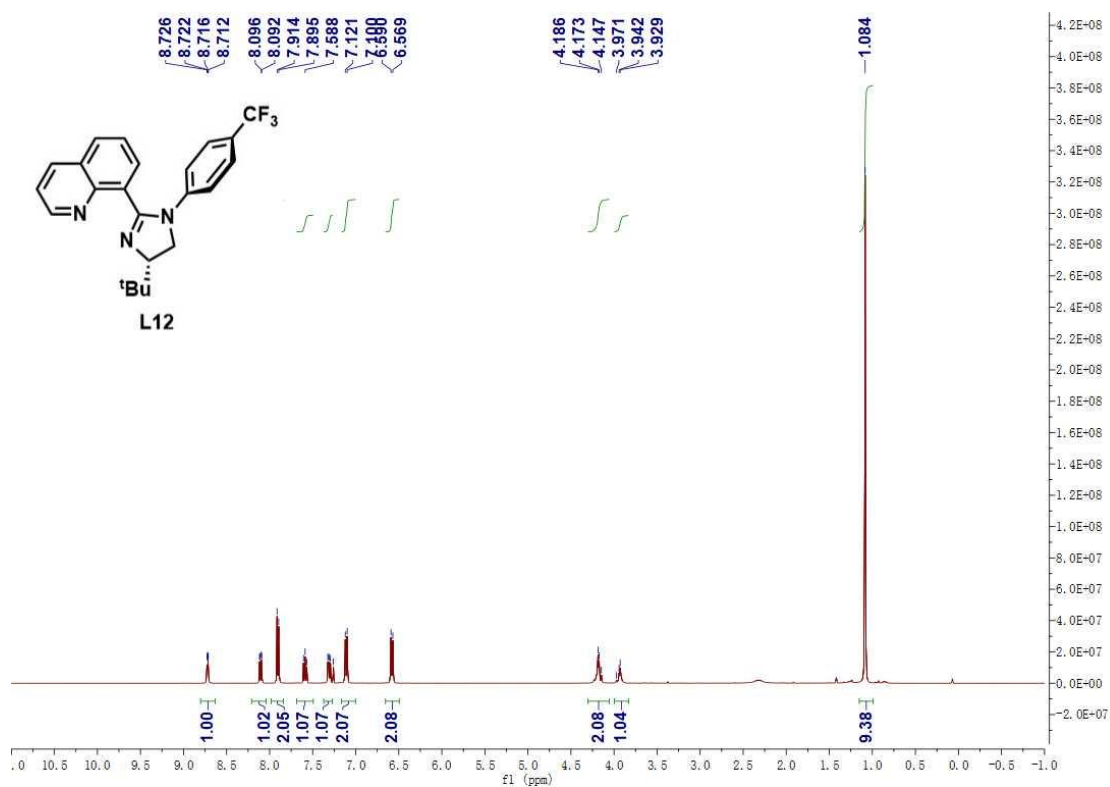
¹H NMR-spectrum (400 MHz, CDCl₃) of L11



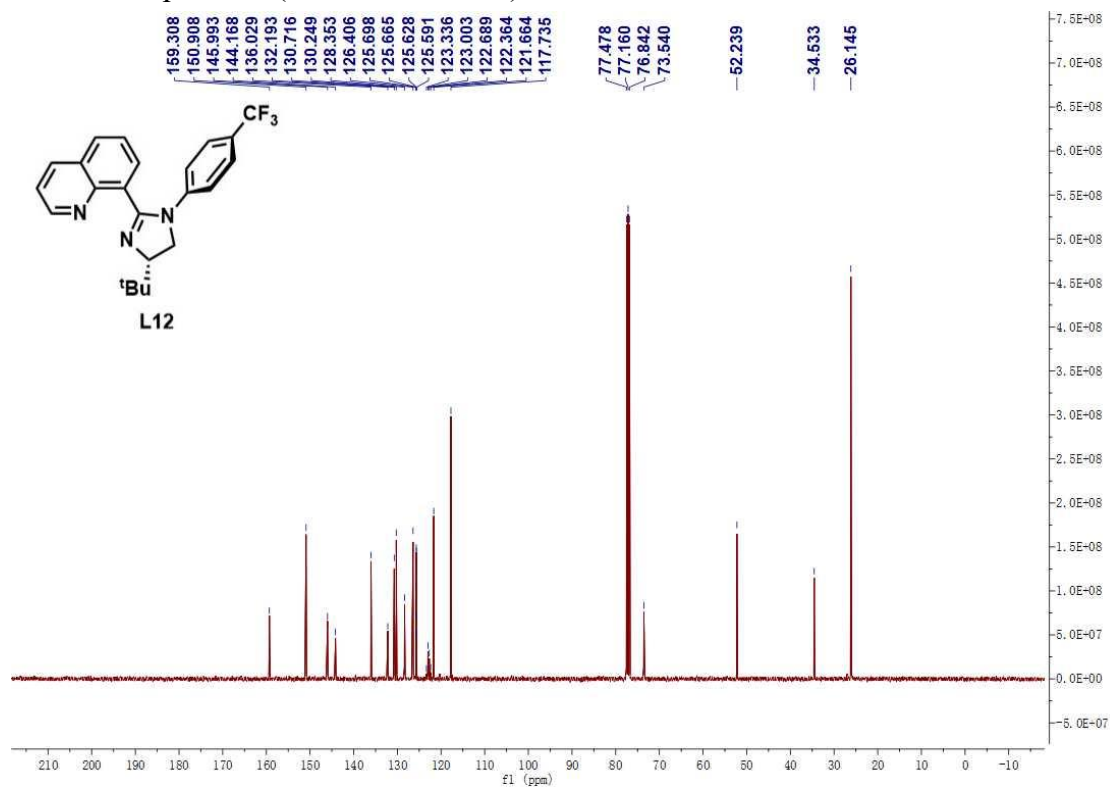
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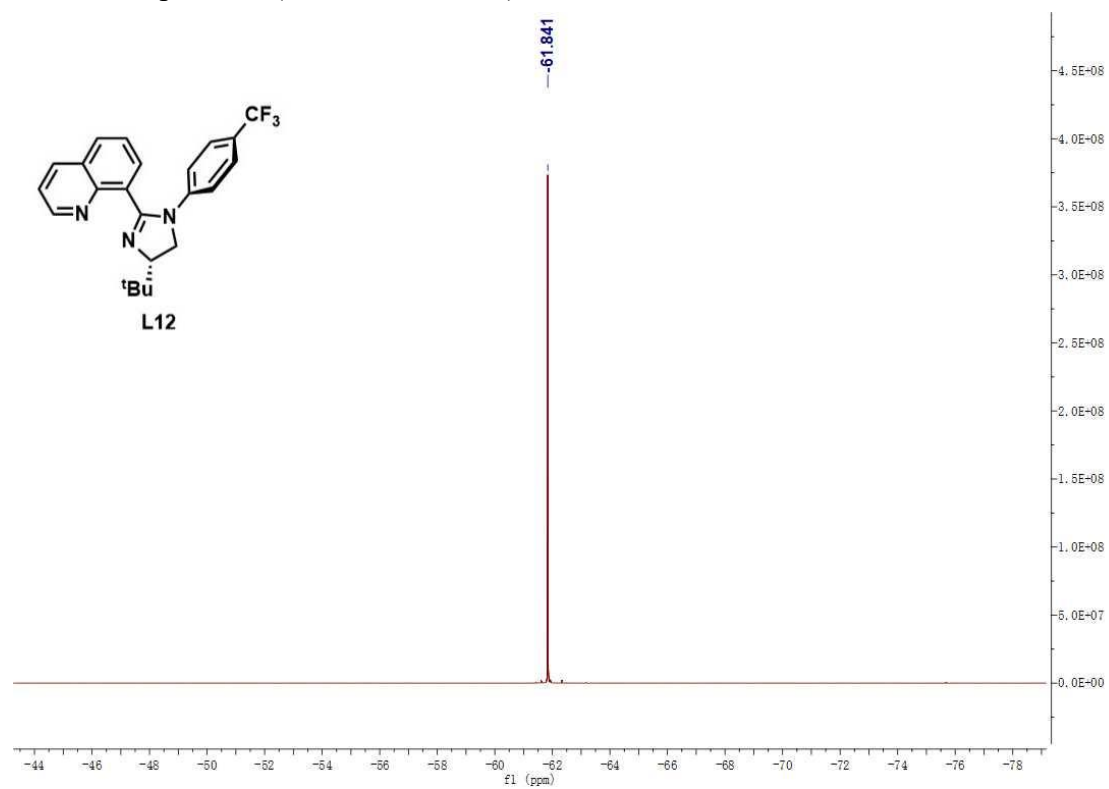
¹H NMR-spectrum (400 MHz, CDCl₃) of L12



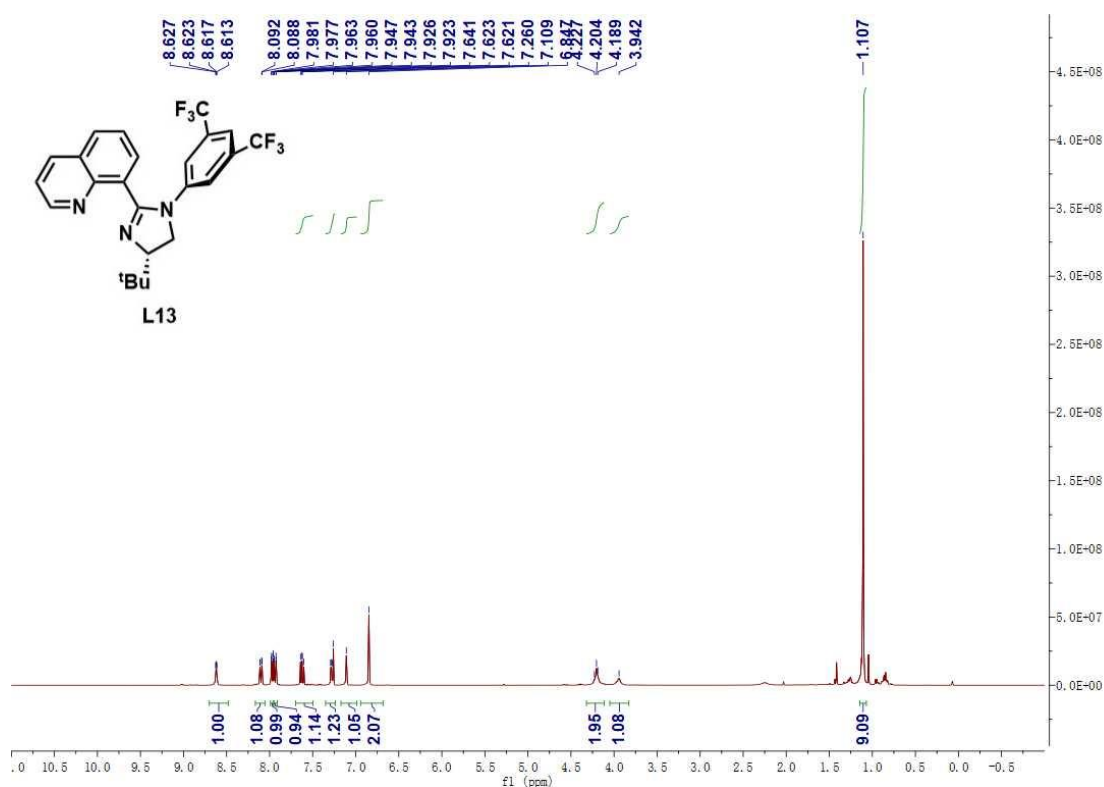
¹³C NMR-spectrum (100 MHz, CDCl₃) of L12



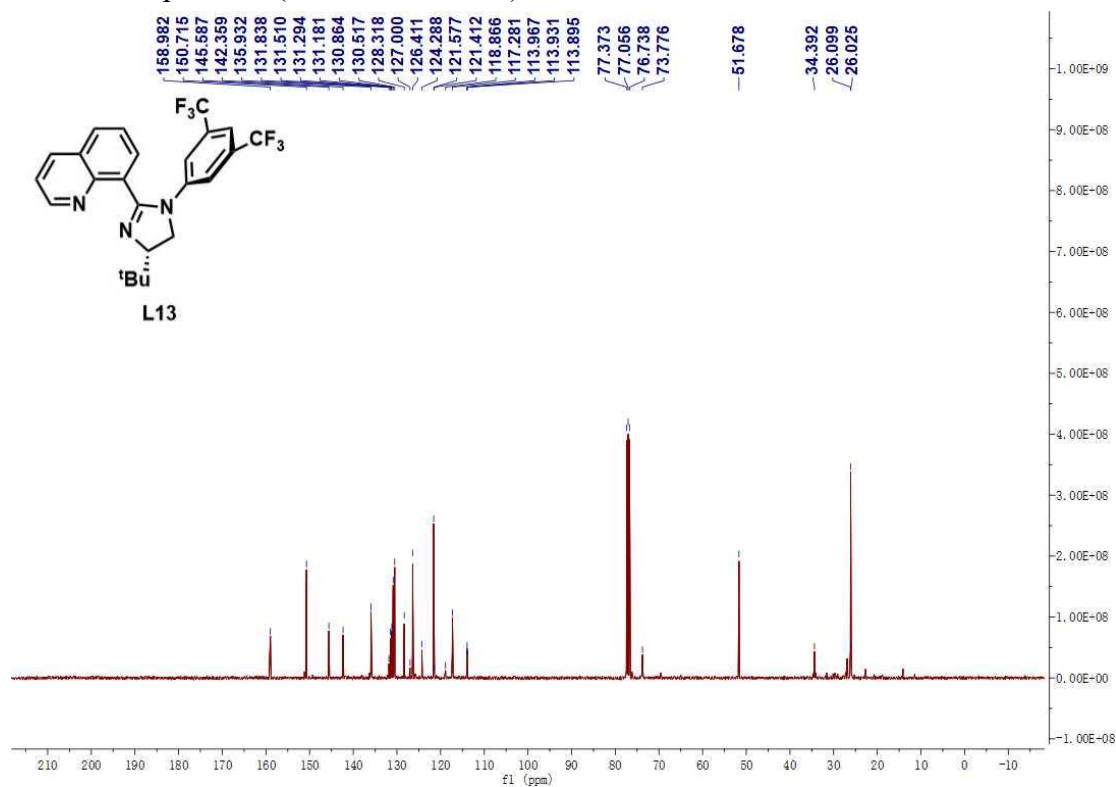
^{19}F NMR-spectrum (376 MHz, CDCl_3) of L12



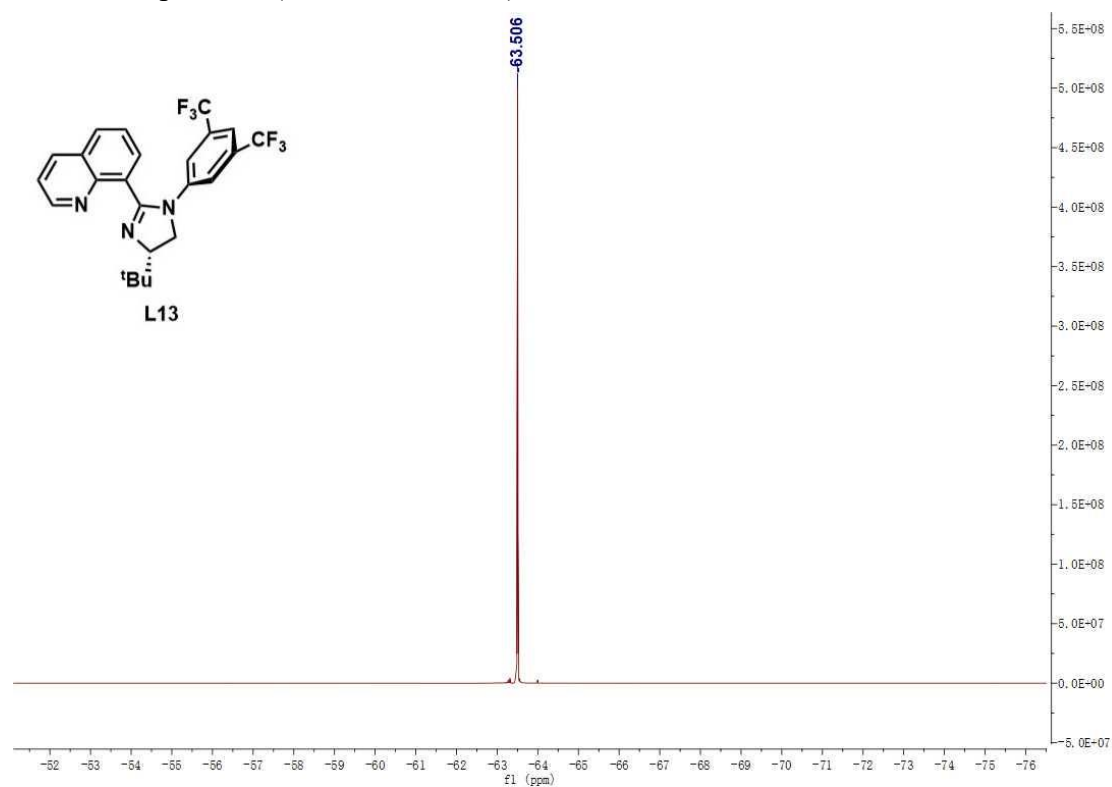
¹H NMR-spectrum (400 MHz, CDCl₃) of L13



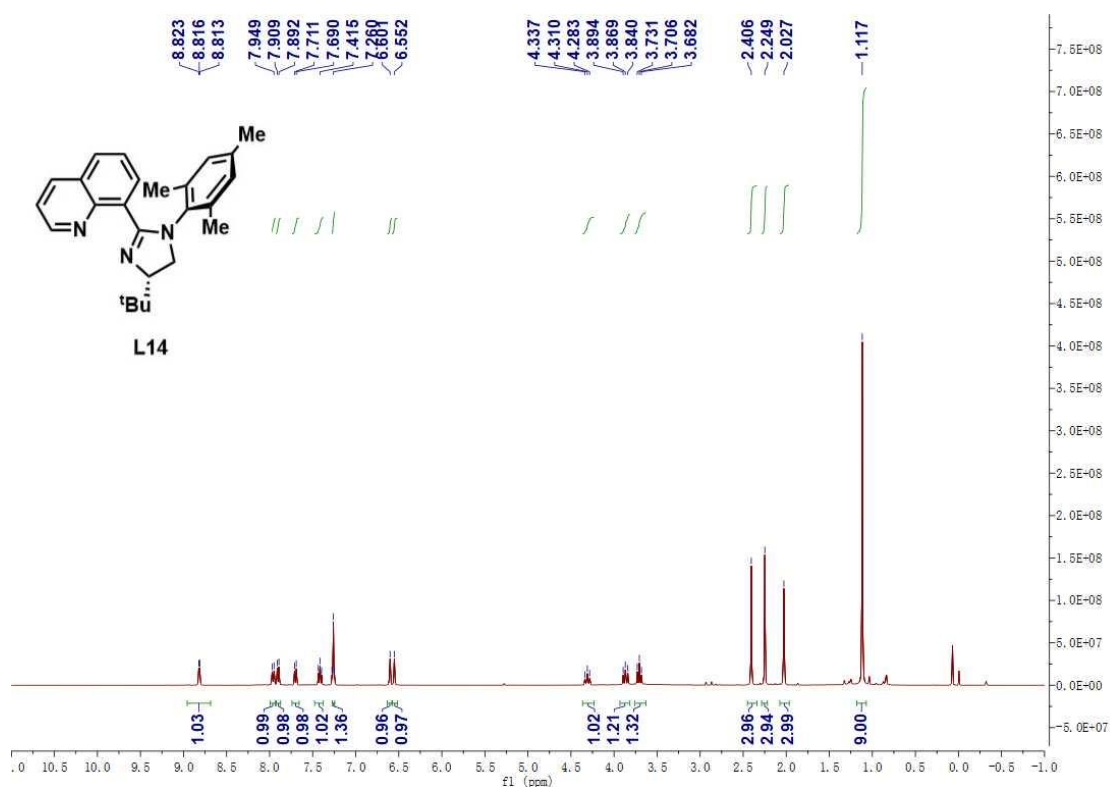
¹³C NMR-spectrum (100 MHz, CDCl₃) of L13



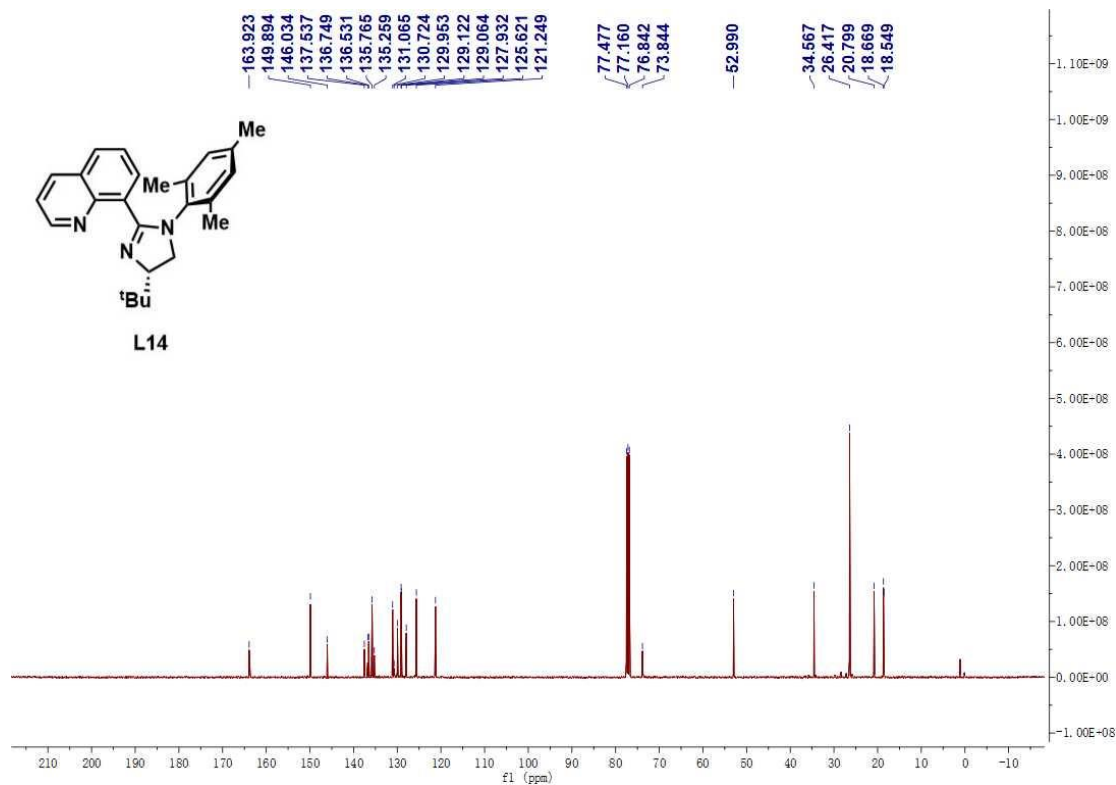
^{19}F NMR-spectrum (376 MHz, CDCl_3) of L13



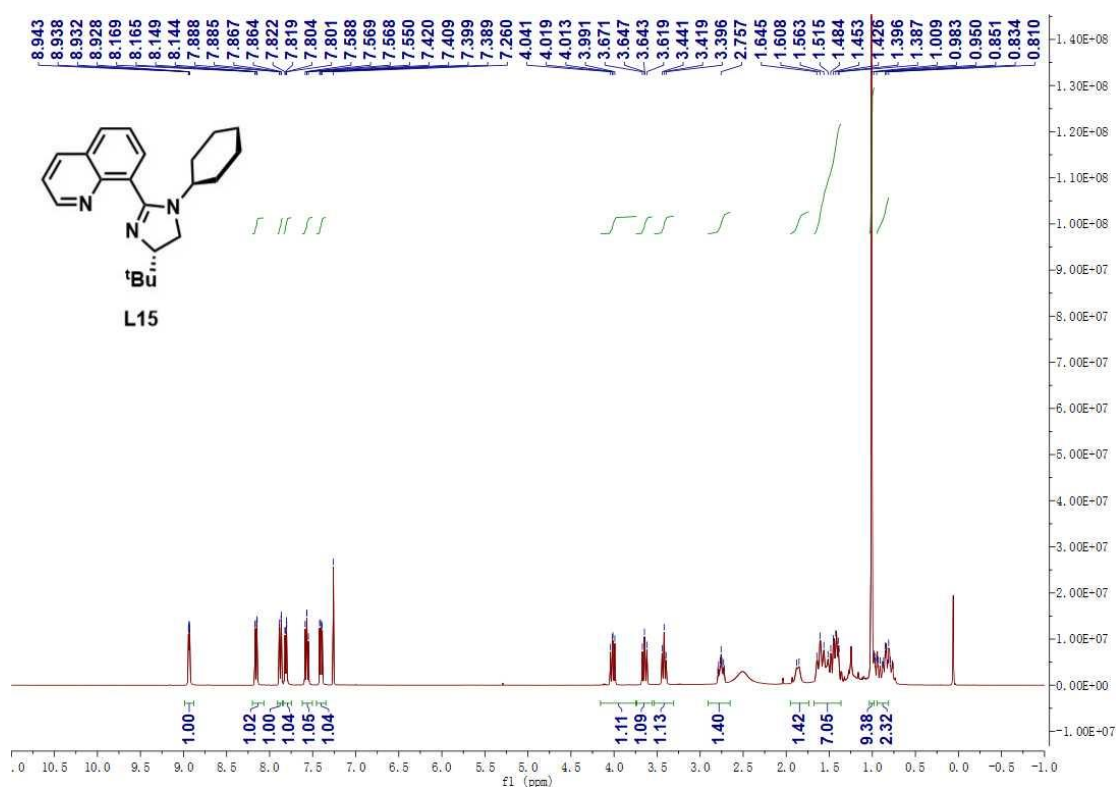
¹H NMR-spectrum (400 MHz, CDCl₃) of L14



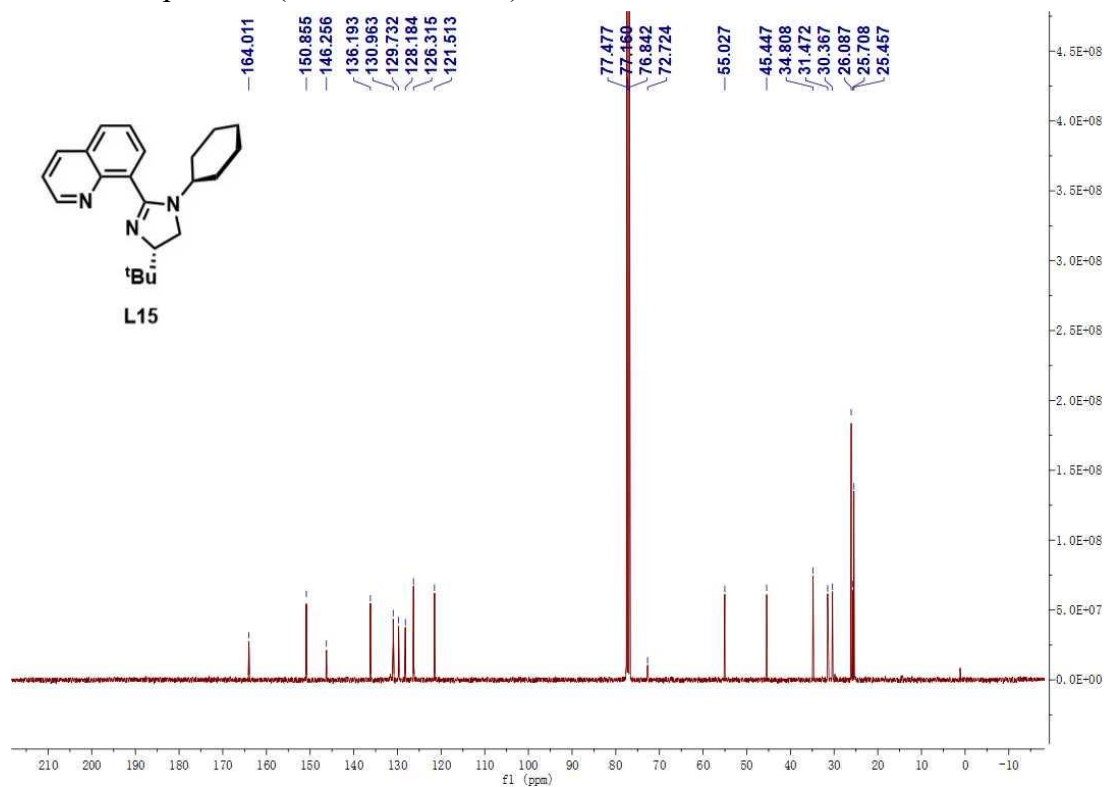
¹³C NMR-spectrum (100 MHz, CDCl₃) of L14



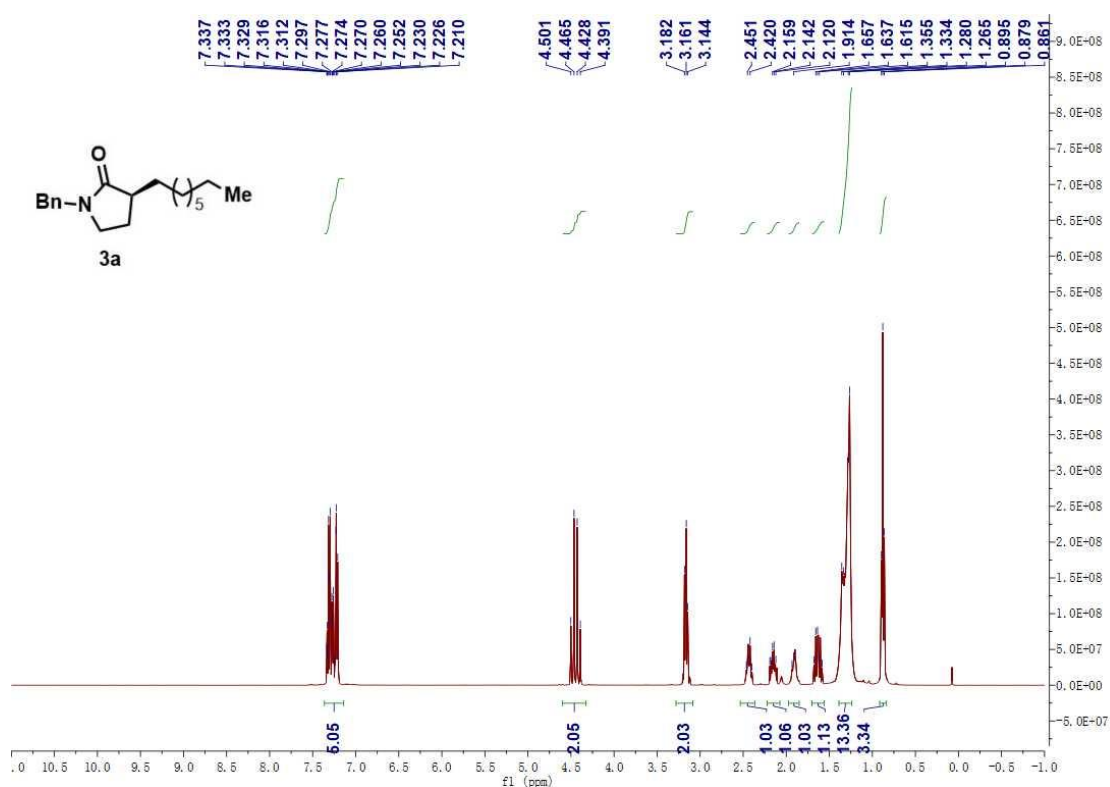
¹H NMR-spectrum (400 MHz, CDCl₃) of L15



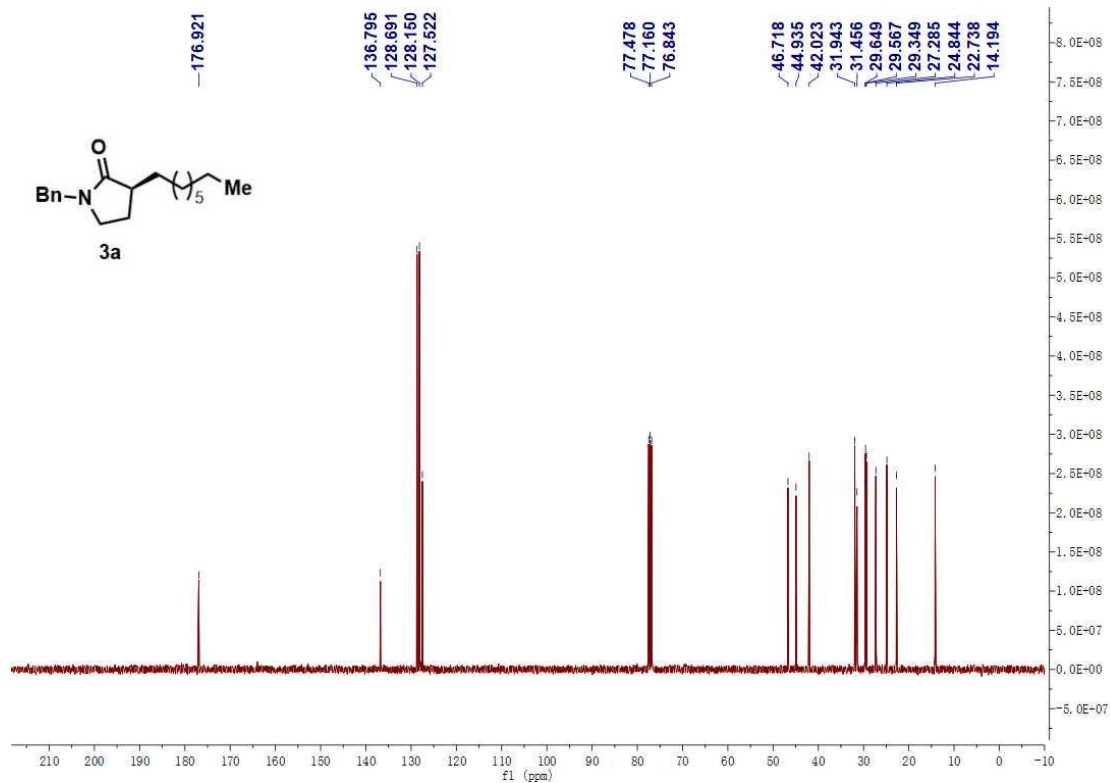
¹³C NMR-spectrum (100 MHz, CDCl₃) of L15



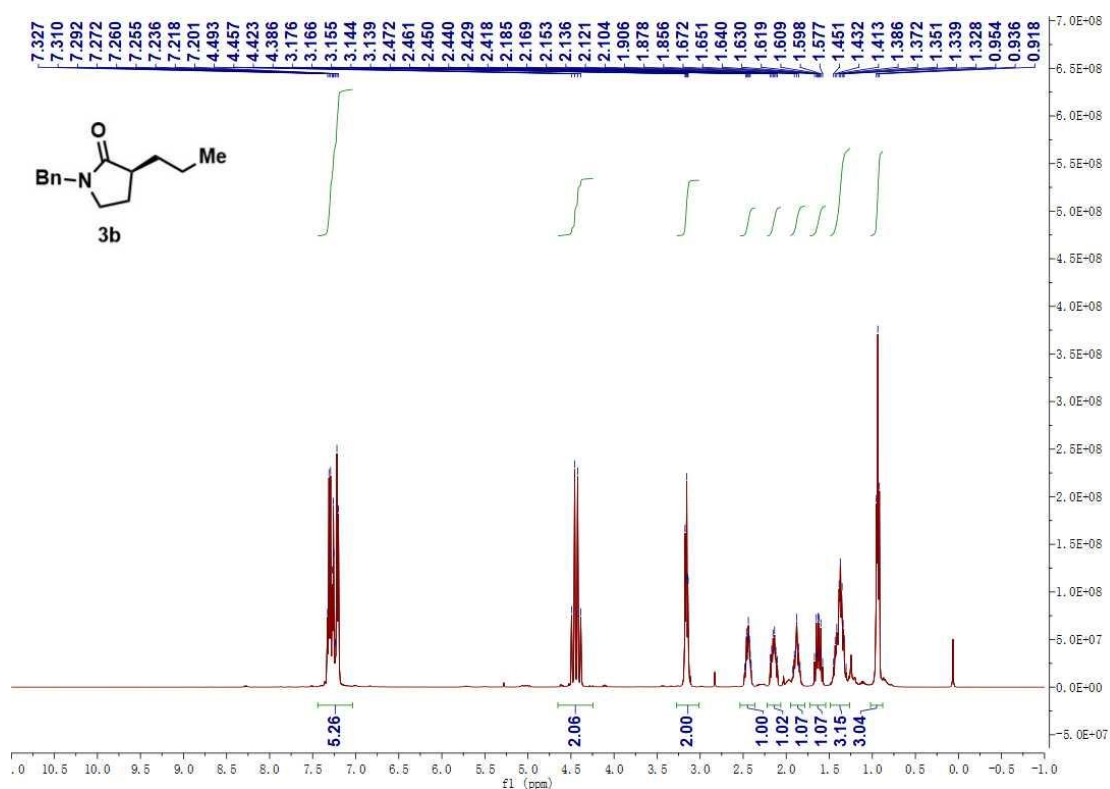
¹H NMR-spectrum (400 MHz, CDCl₃) of **3a**



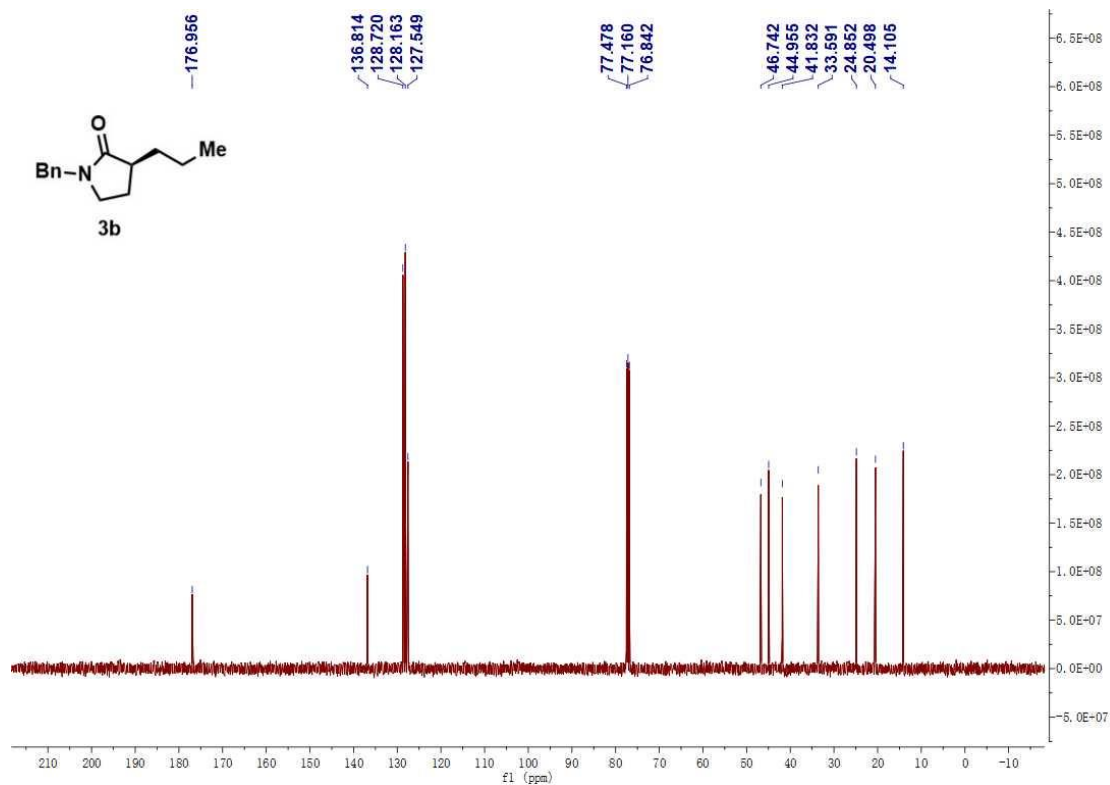
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3a**



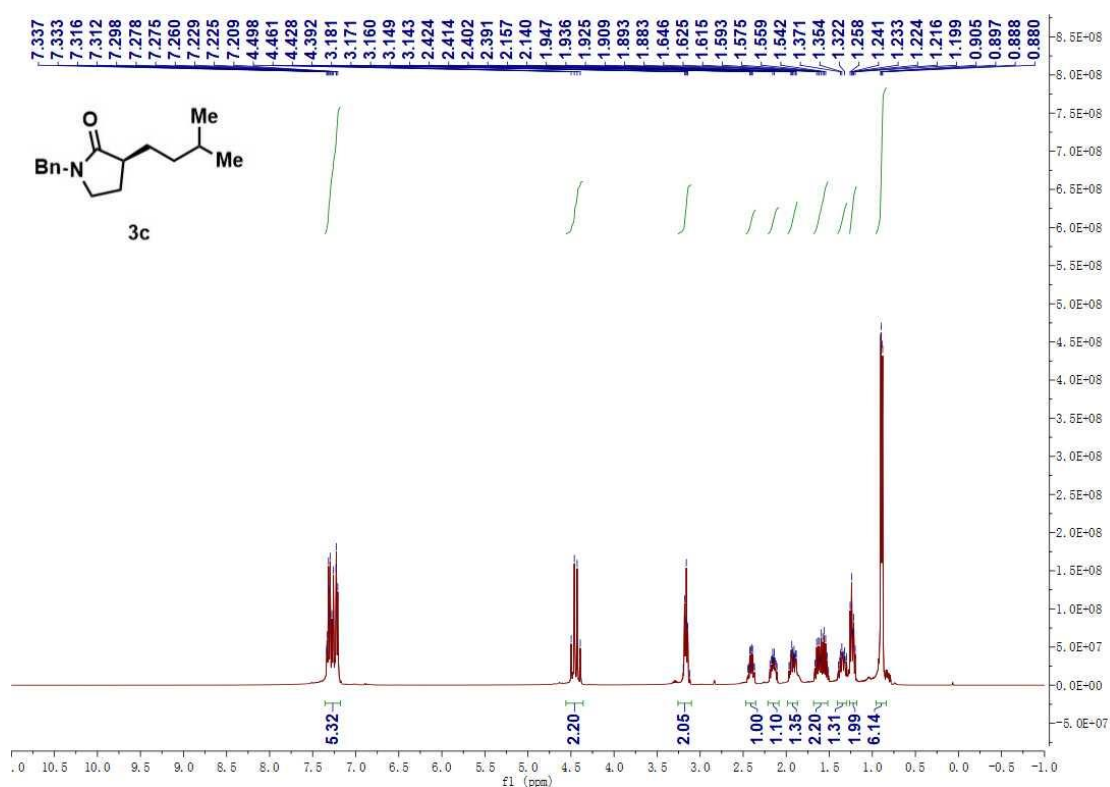
¹H NMR-spectrum (400 MHz, CDCl₃) of **3b**



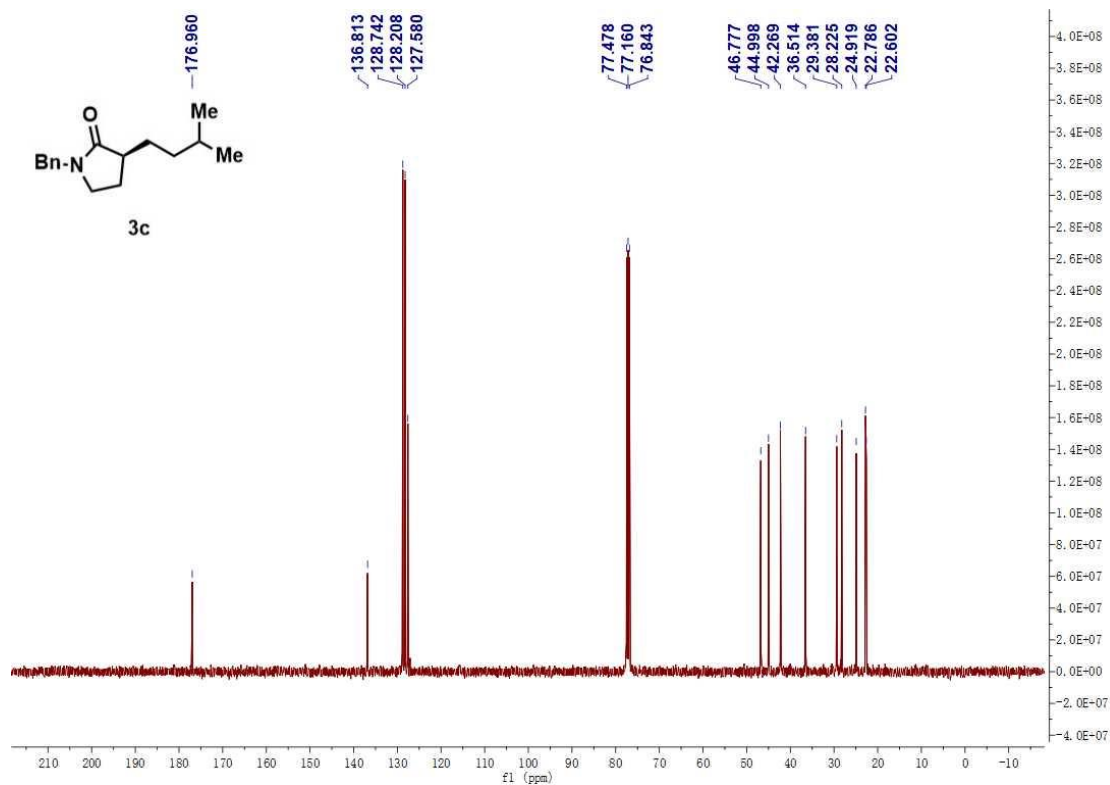
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3b**



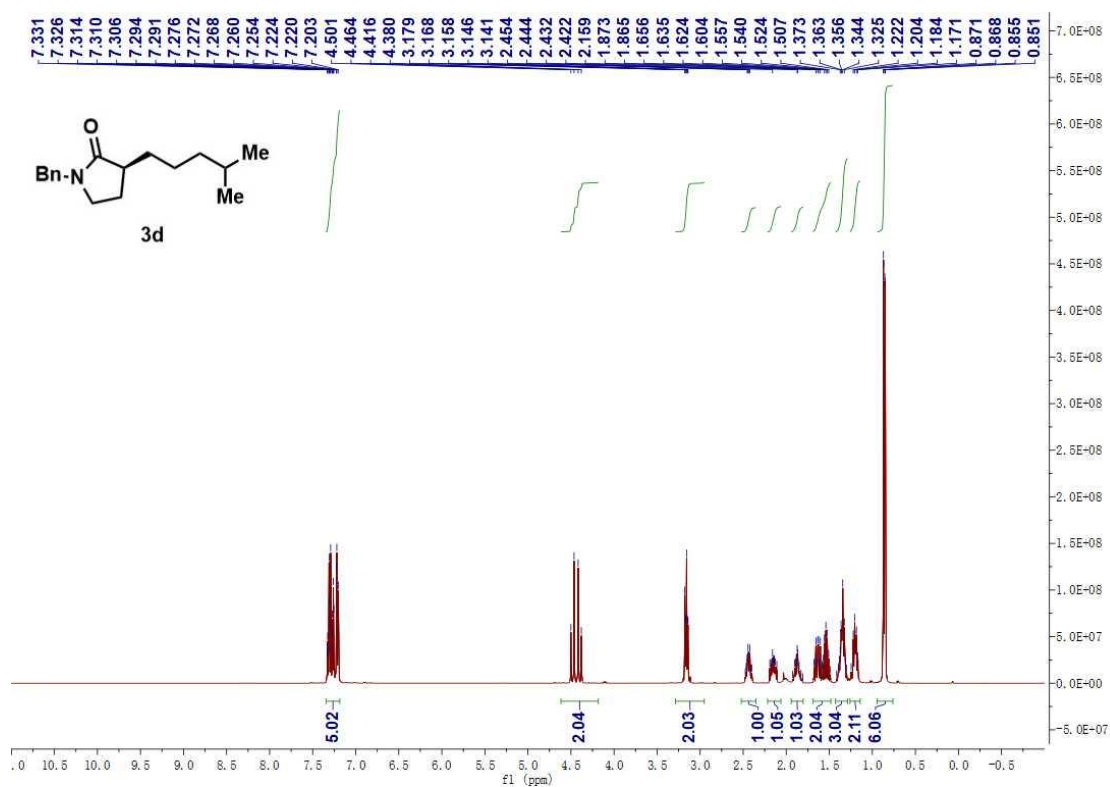
¹H NMR-spectrum (400 MHz, CDCl₃) of **3c**



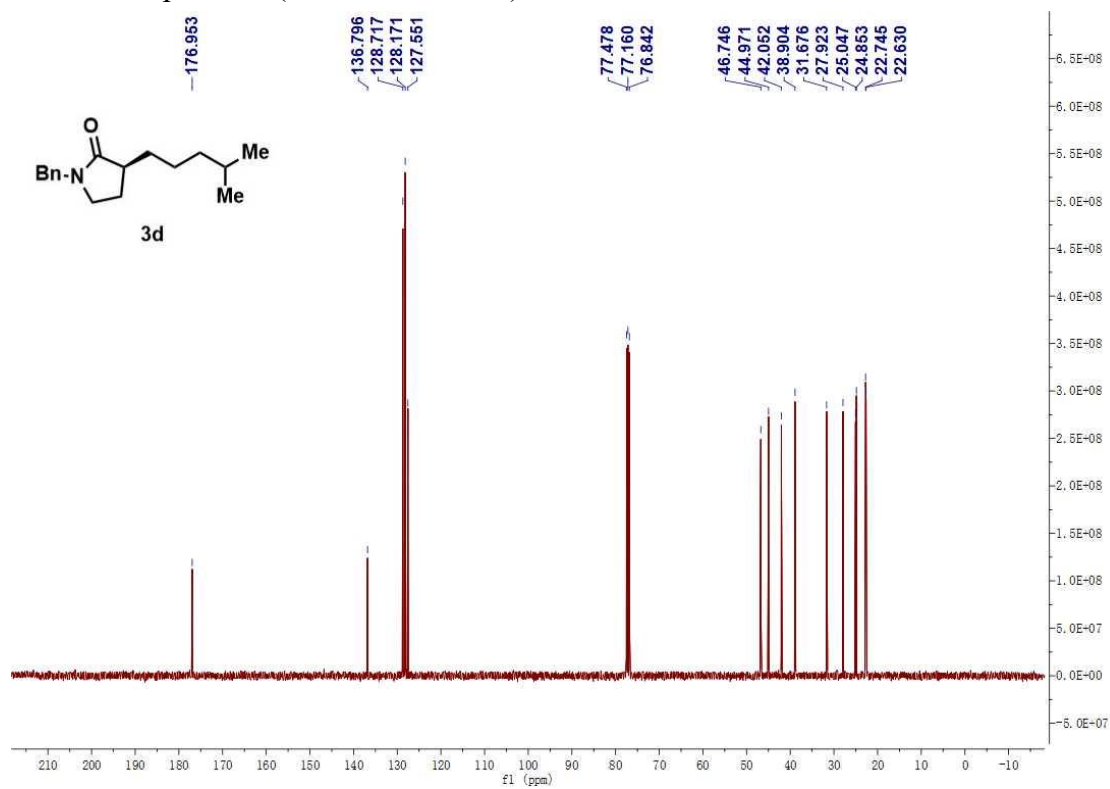
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3c**



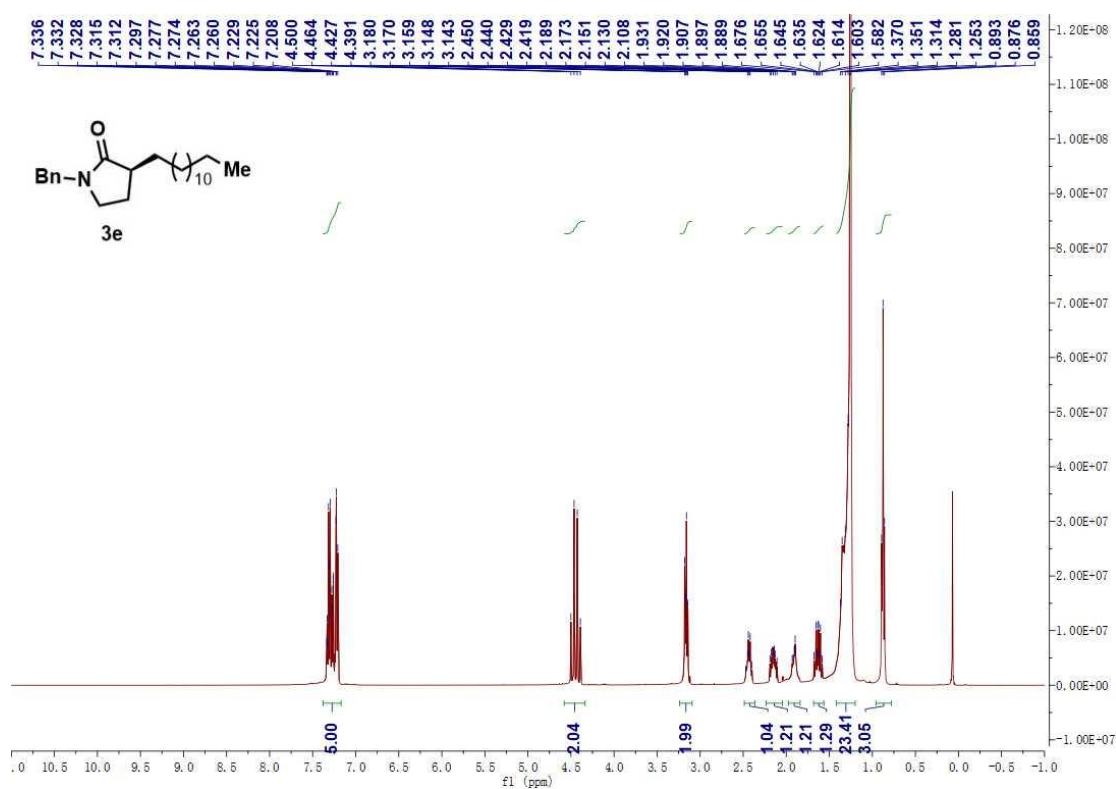
¹H NMR-spectrum (400 MHz, CDCl₃) of **3d**



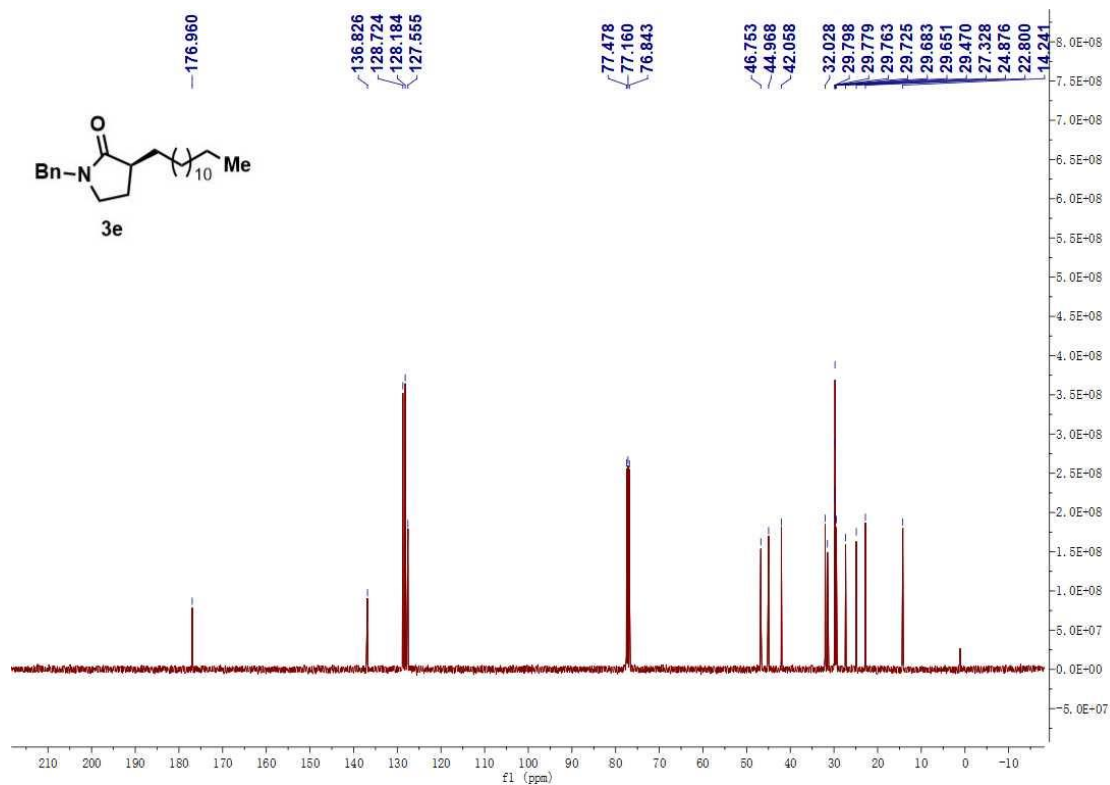
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3d**



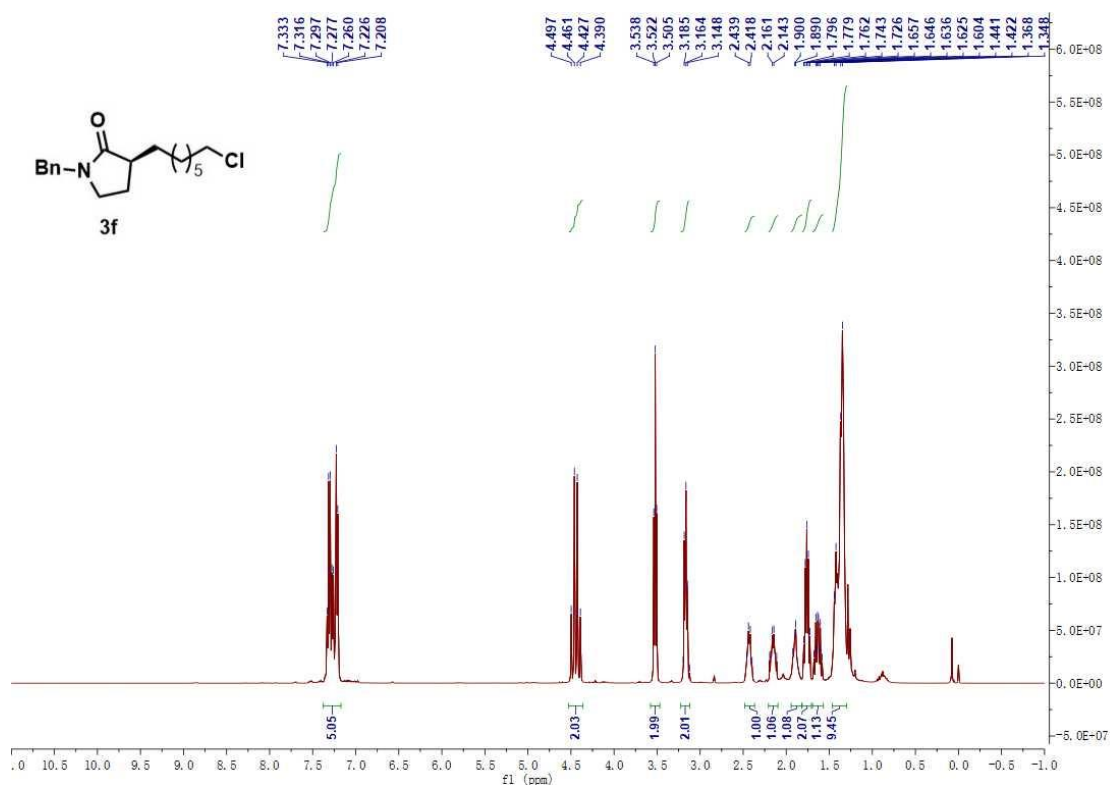
^1H NMR-spectrum (400 MHz, CDCl_3) of **3e**



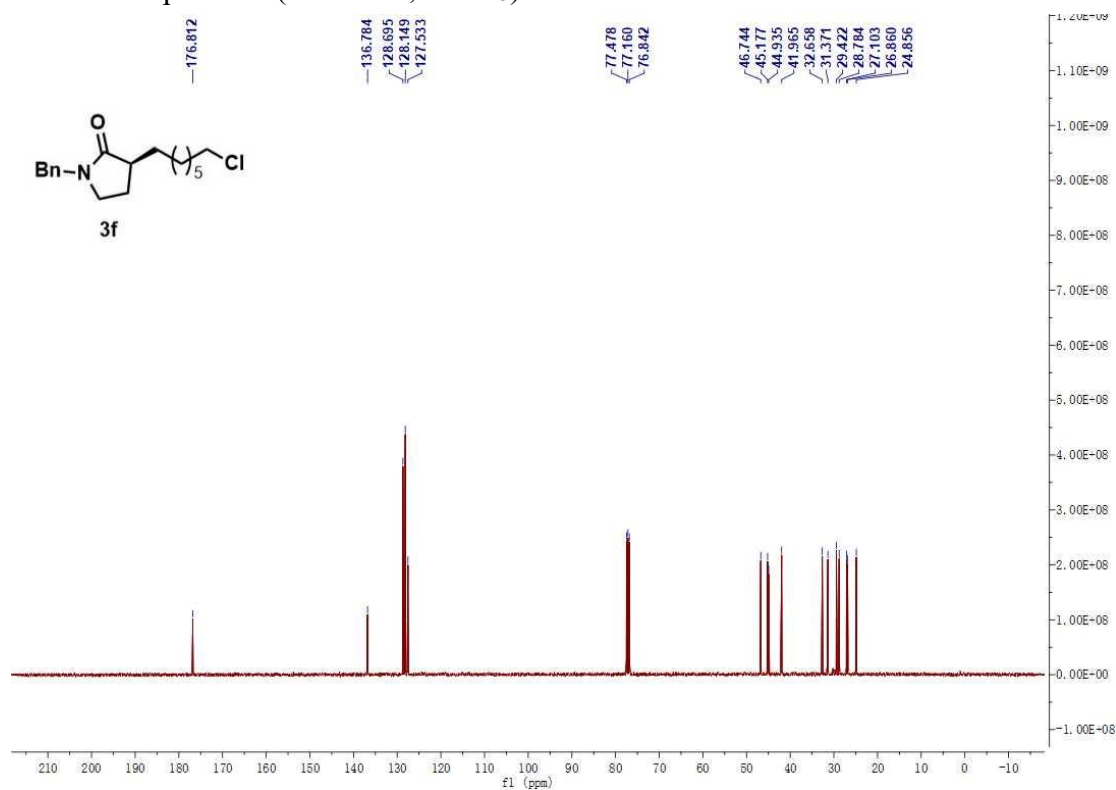
^{13}C NMR-spectrum (100 MHz, CDCl_3) of **3e**



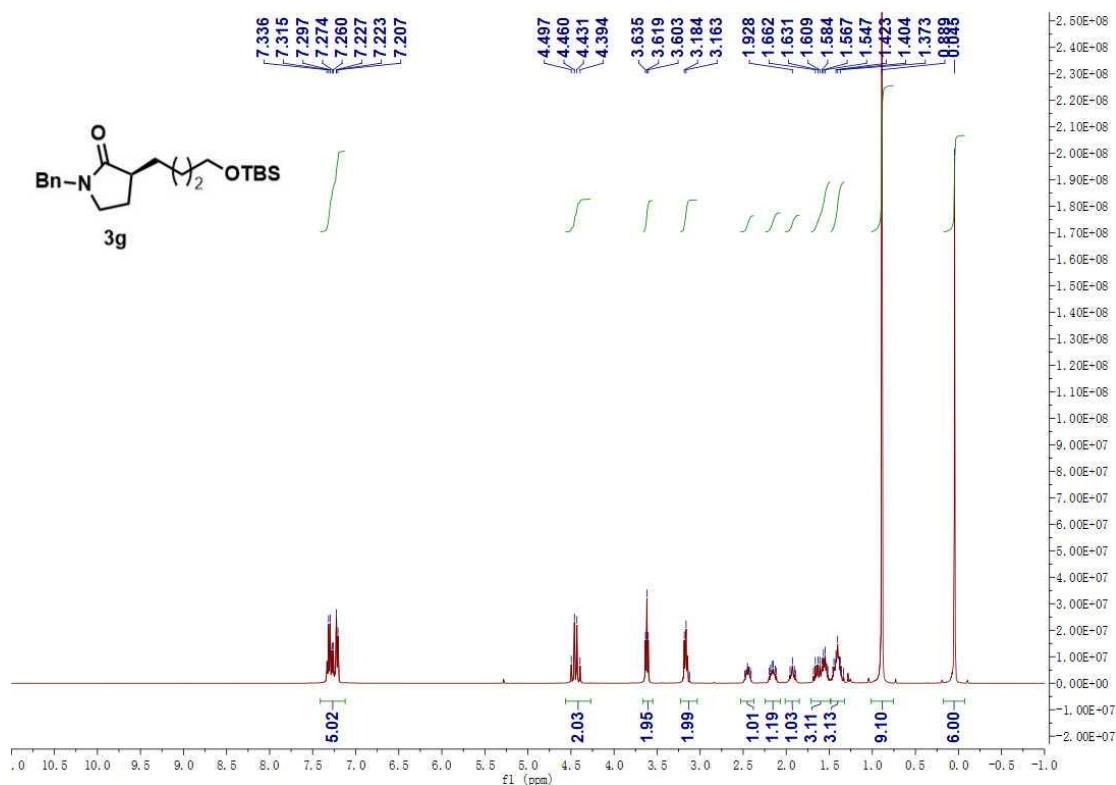
¹H NMR-spectrum (400 MHz, CDCl₃) of **3f**



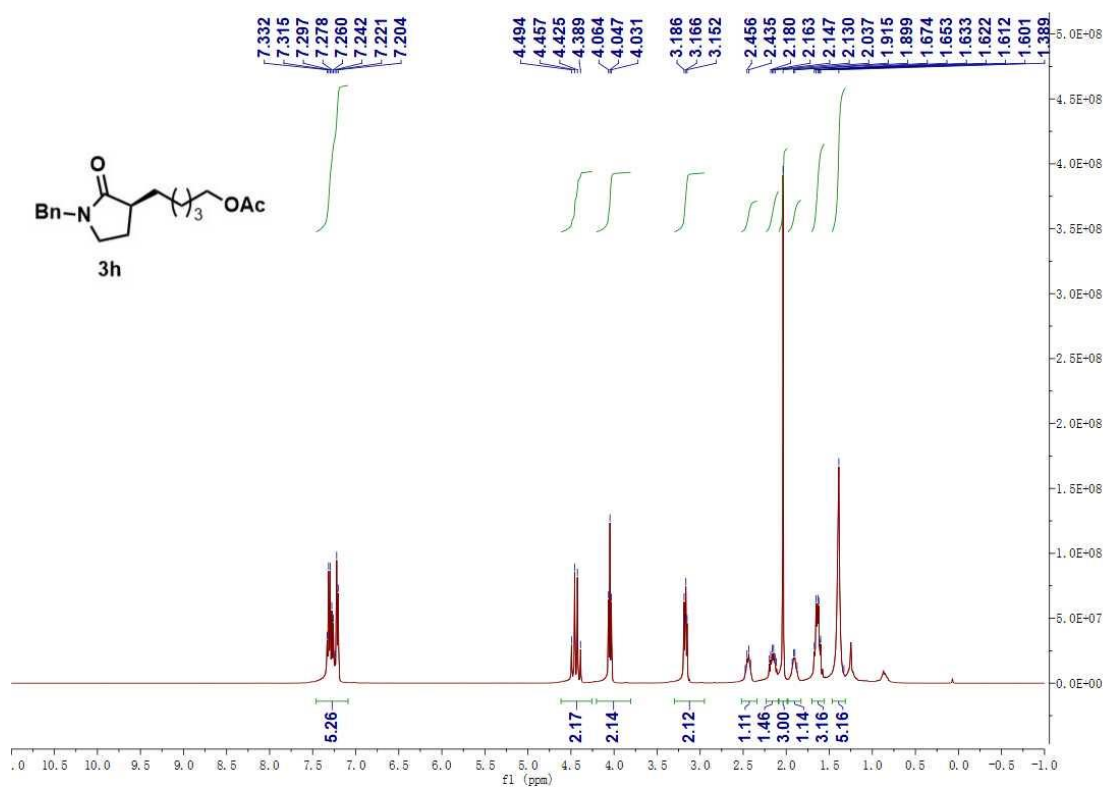
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3f**



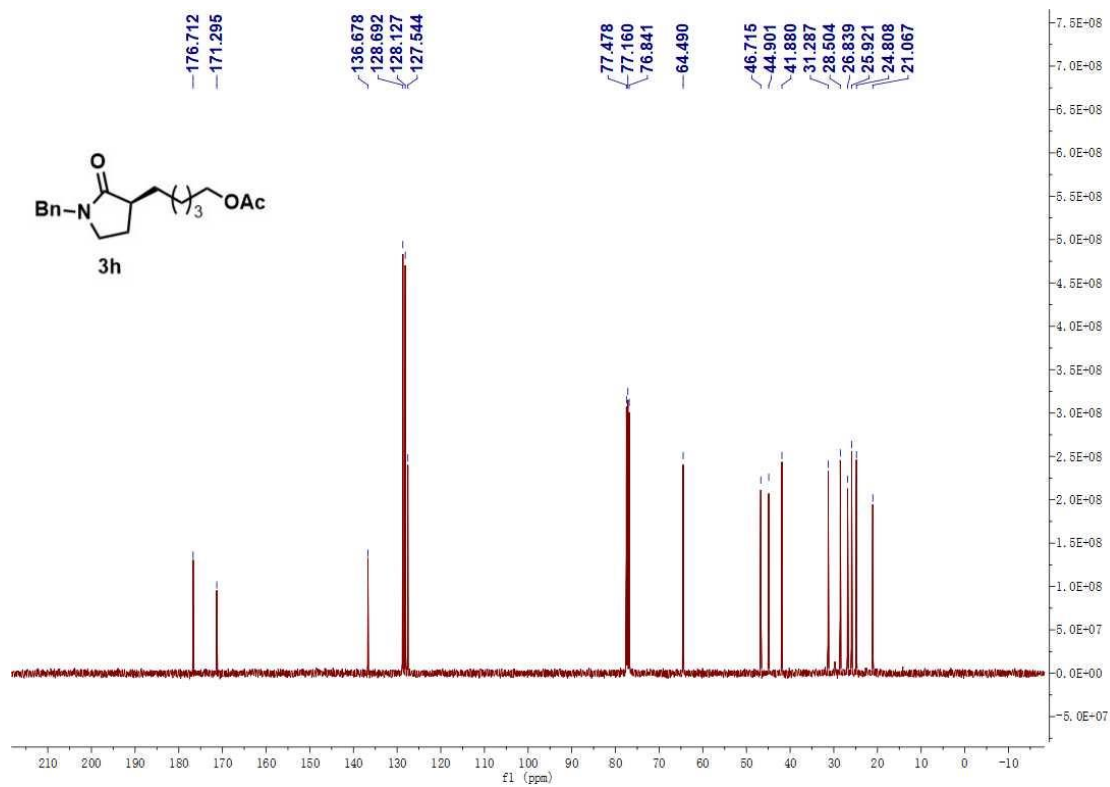
^1H NMR-spectrum (400 MHz, CDCl_3) of **3g**



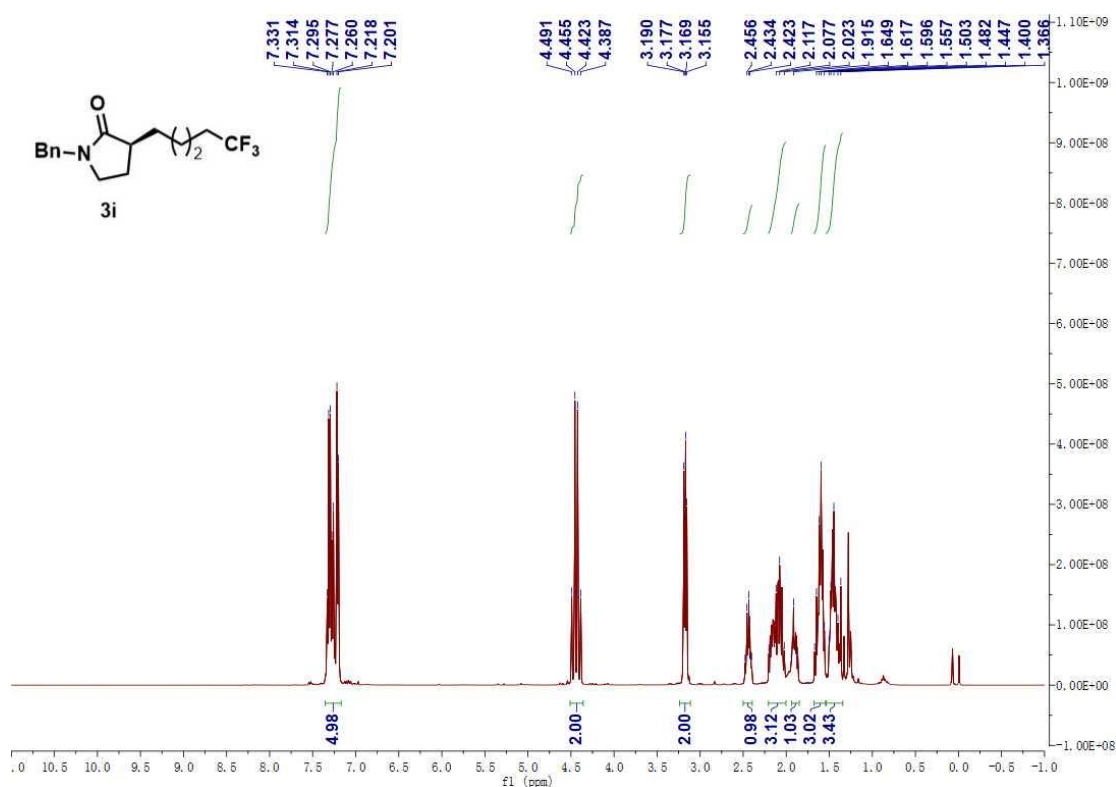
¹H NMR-spectrum (400 MHz, CDCl₃) of **3h**



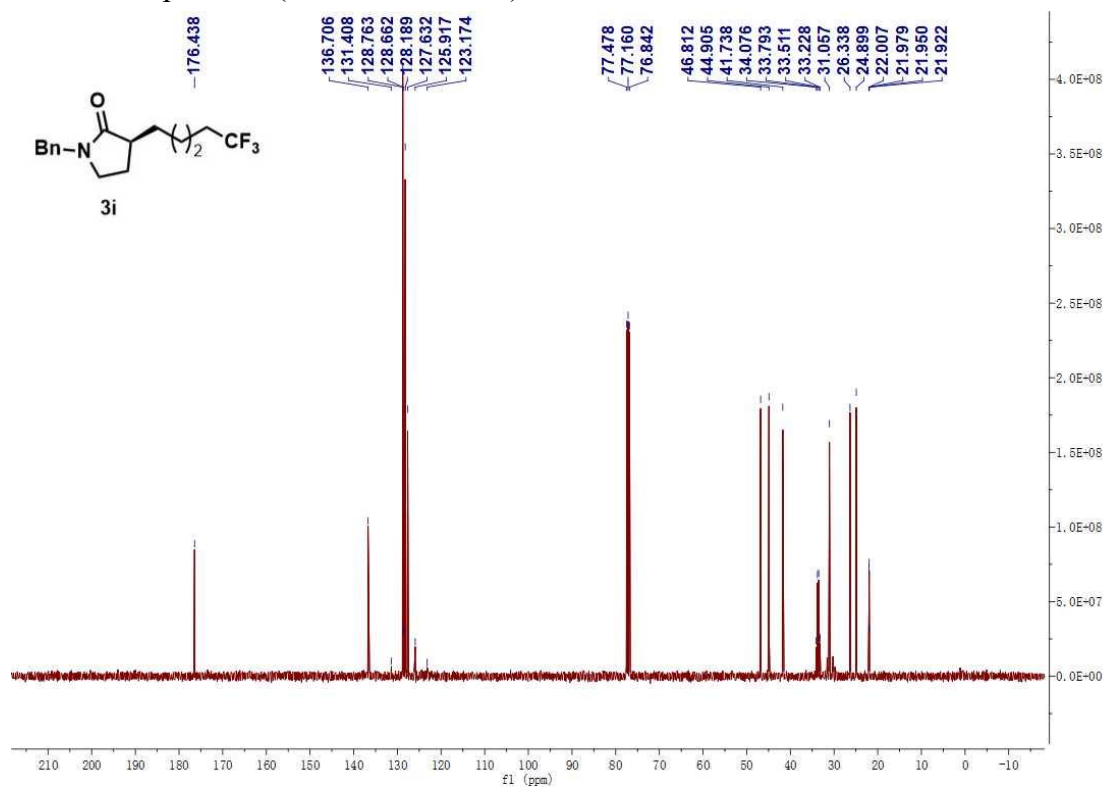
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3h**



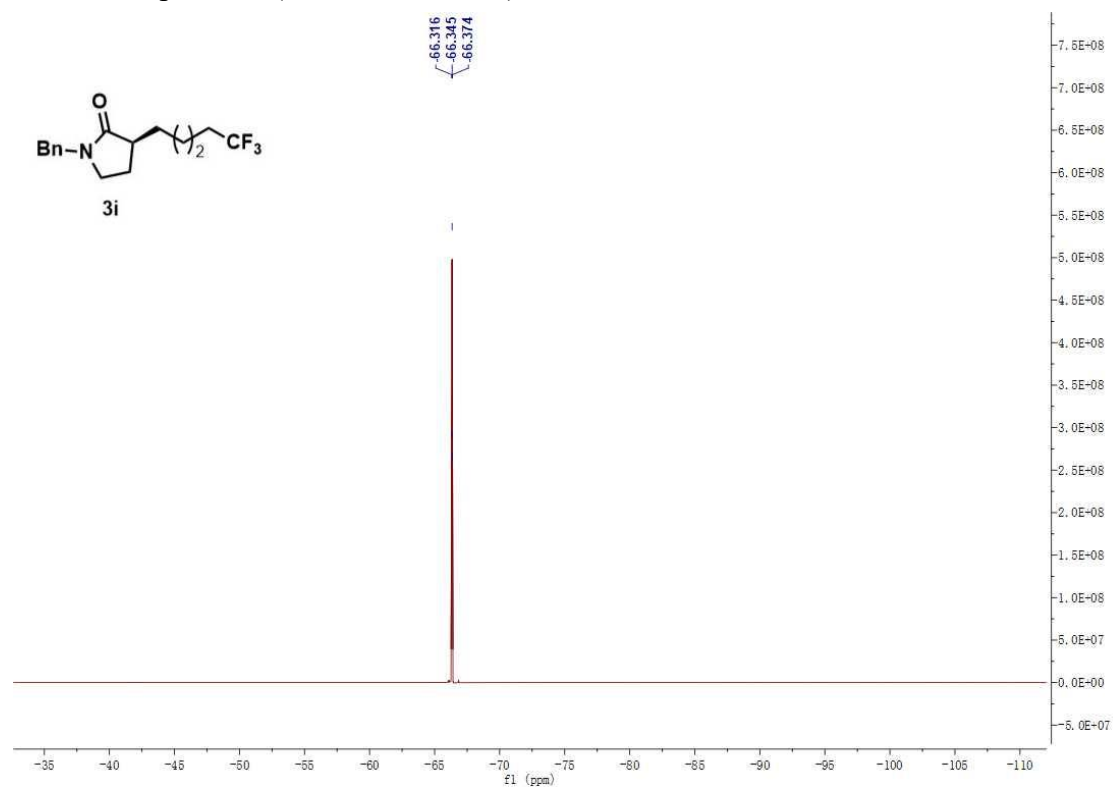
¹H NMR-spectrum (400 MHz, CDCl₃) of **3i**



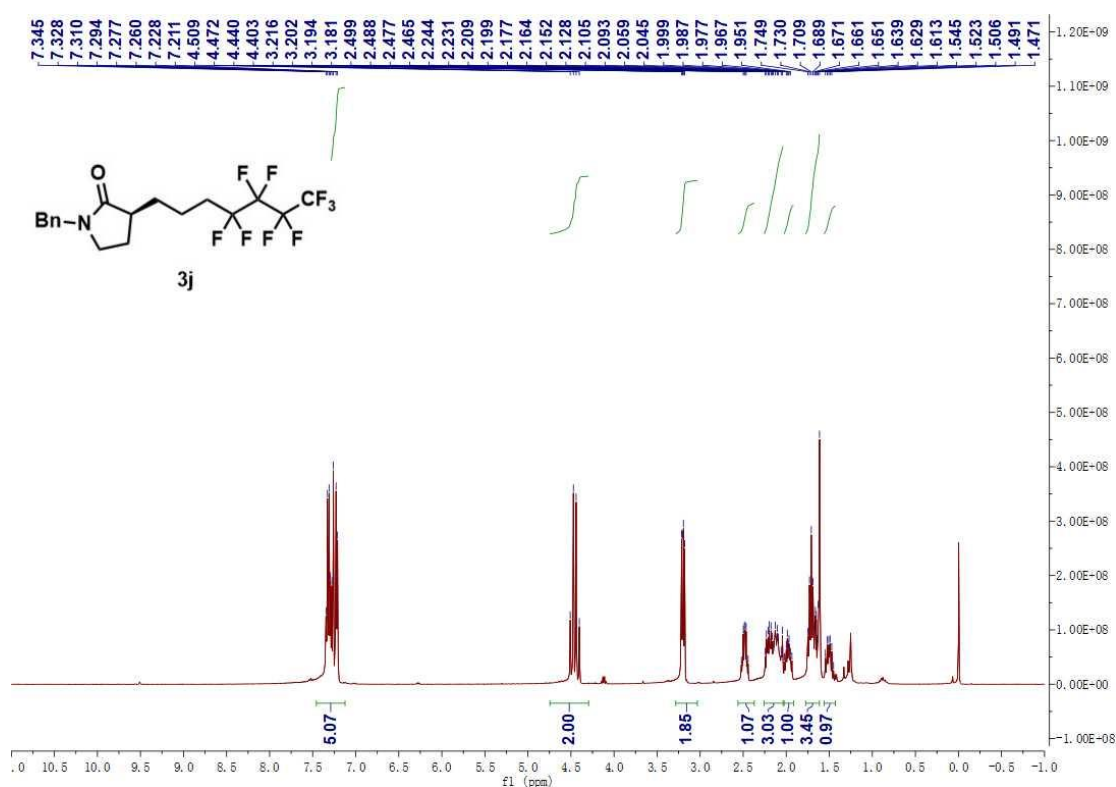
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3i**



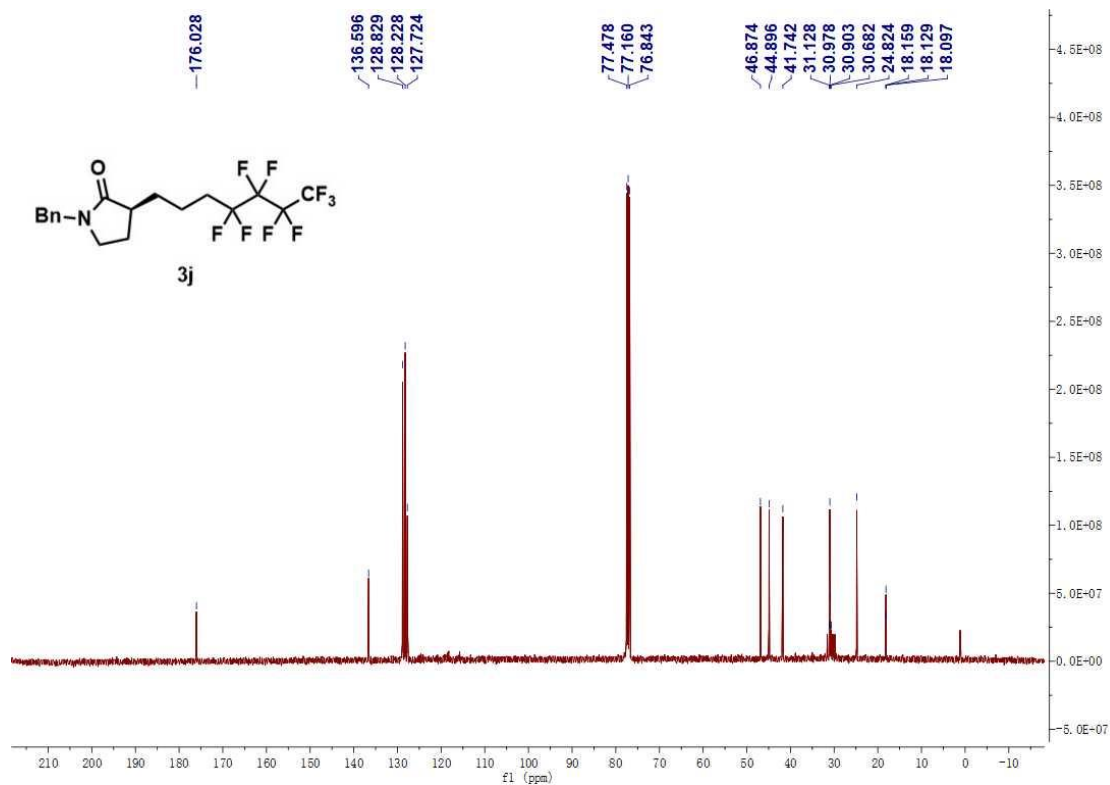
¹⁹F NMR-spectrum (376 MHz, CDCl₃) of **3i**



¹H NMR-spectrum (400 MHz, CDCl₃) of **3j**



¹³C NMR-spectrum (100 MHz, CDCl₃) of **3j**



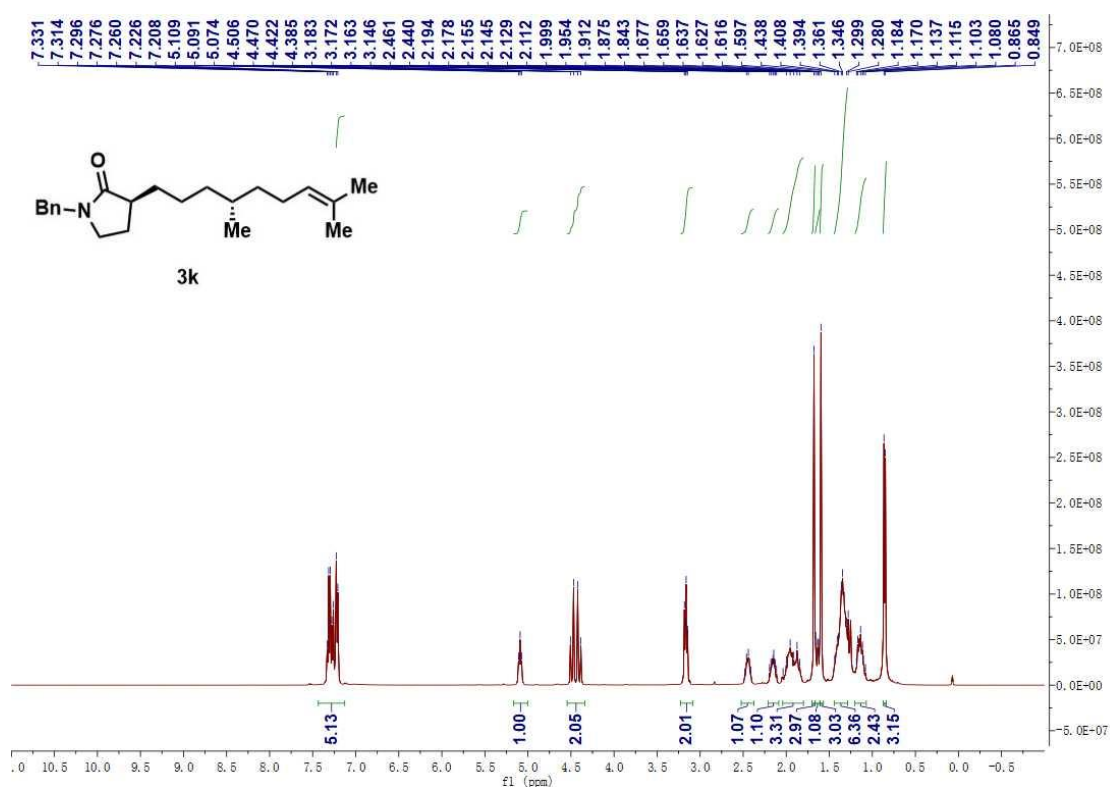
C1CC(=O)N(C1)C/C=C/C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)F

3j

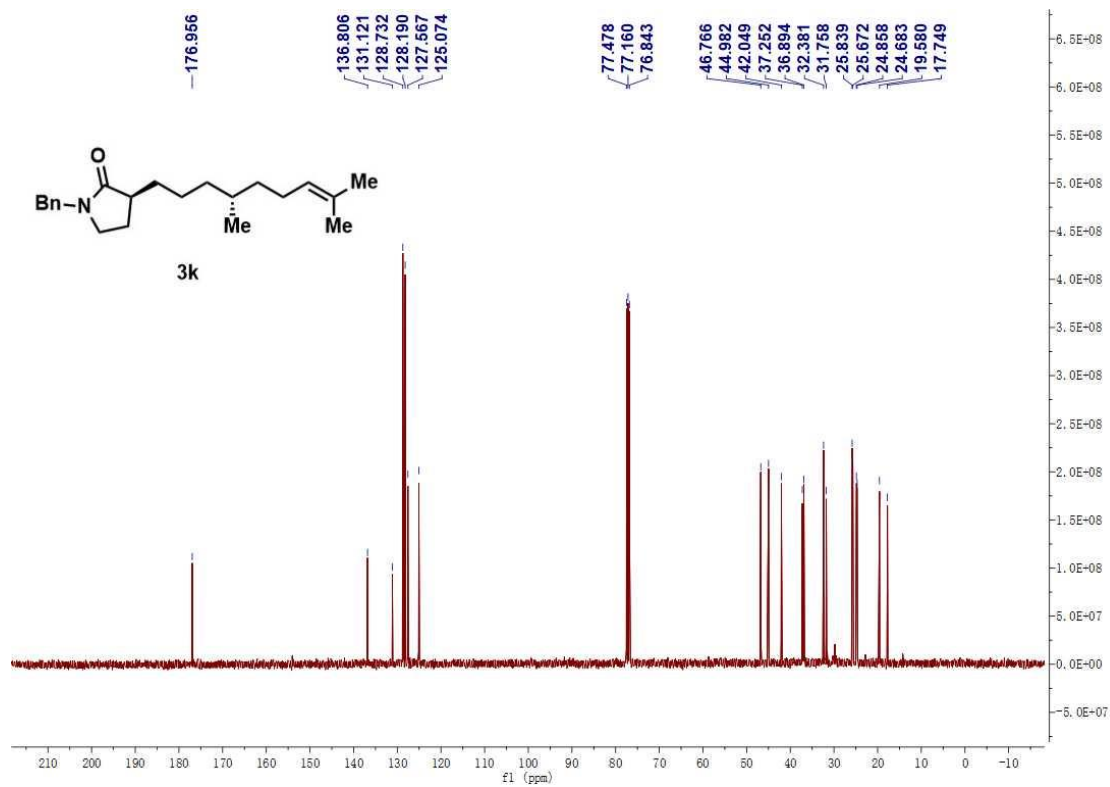
13C NMR spectrum (ppm):

Chemical Shift (ppm)	Integration
-81.016, -81.042, -81.067, -81.074	3.00
-114.468, -114.511, -114.550, -114.592, -114.636	2.48
-124.400, -124.477	2.28
-124.503, -126.034, -126.065, -126.087, -126.100, -126.119	2.14

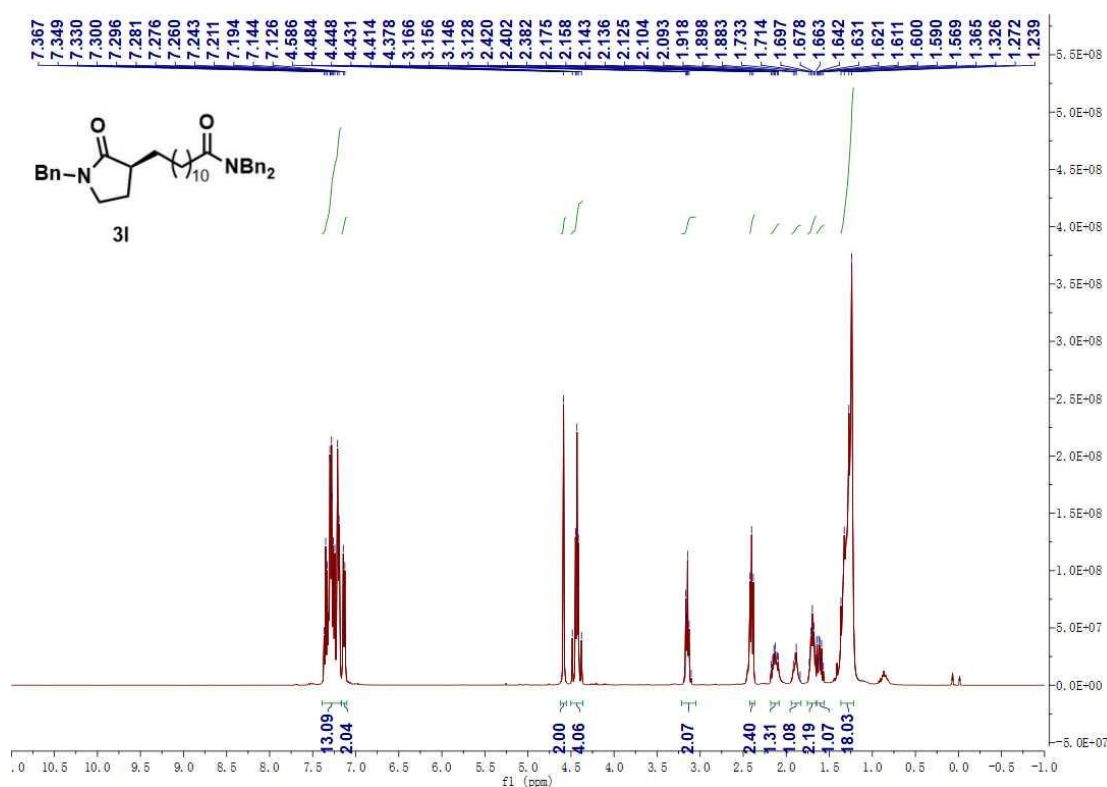
¹H NMR-spectrum (400 MHz, CDCl₃) of **3k**



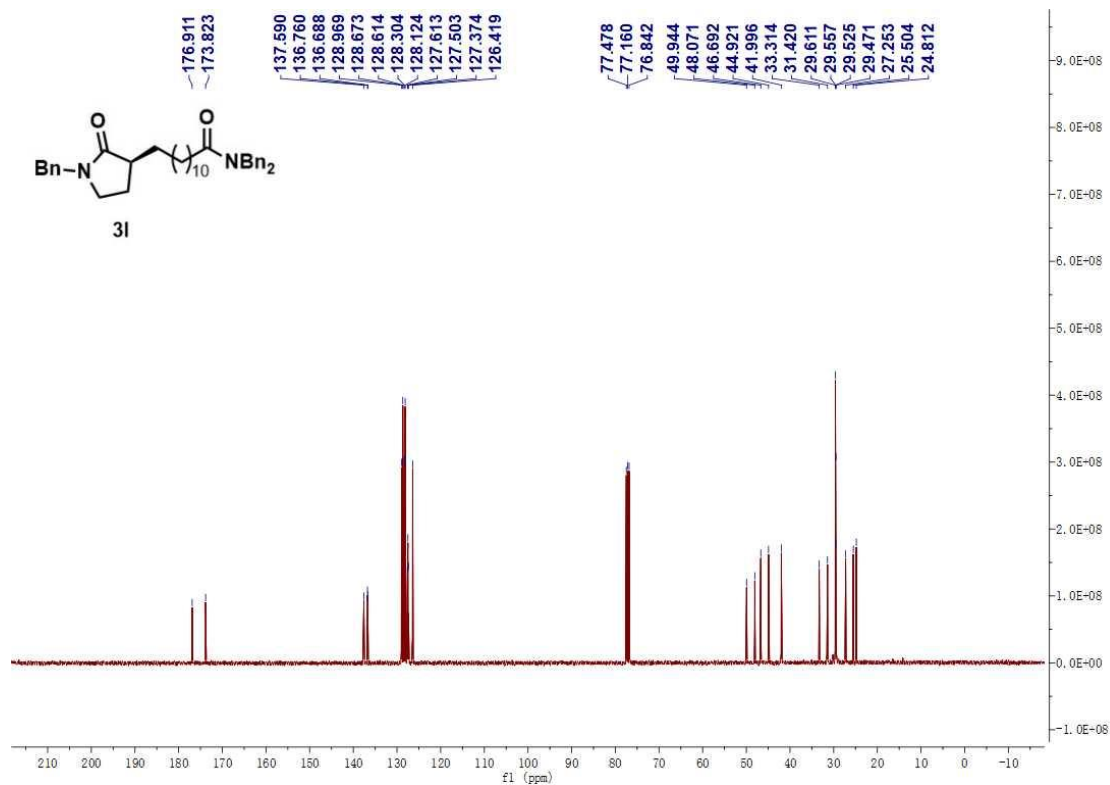
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3k**



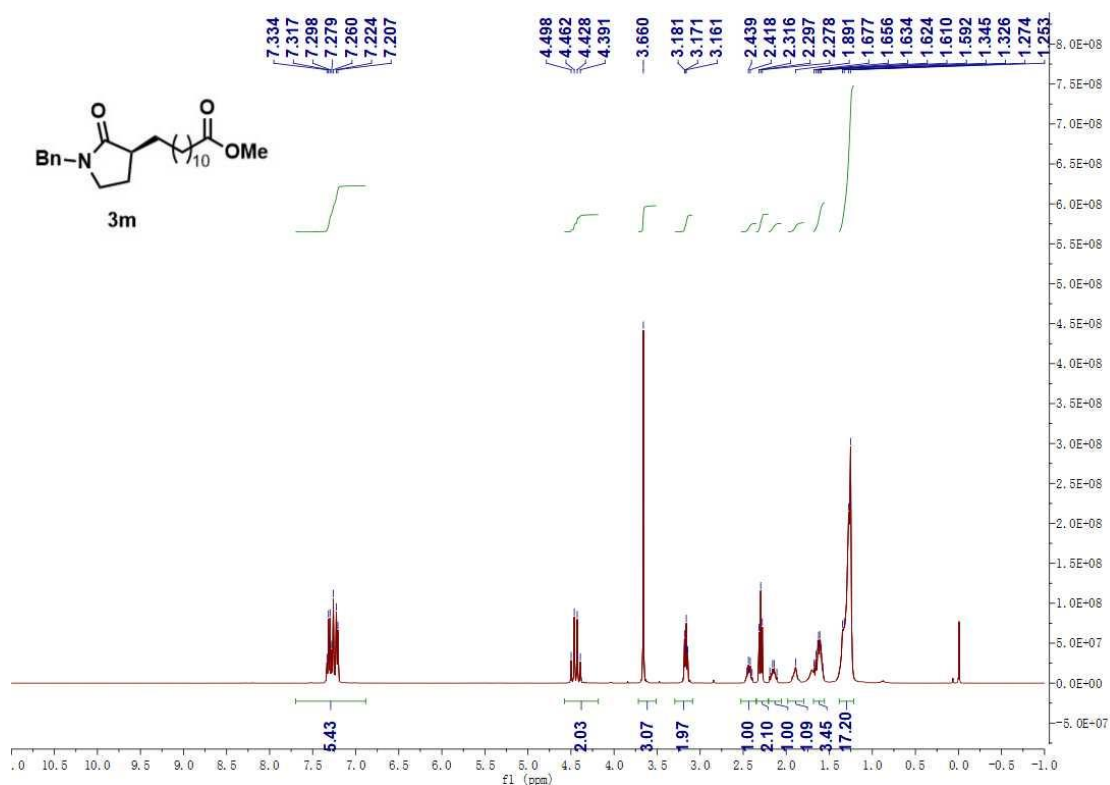
¹H NMR-spectrum (400 MHz, CDCl₃) of **3I**



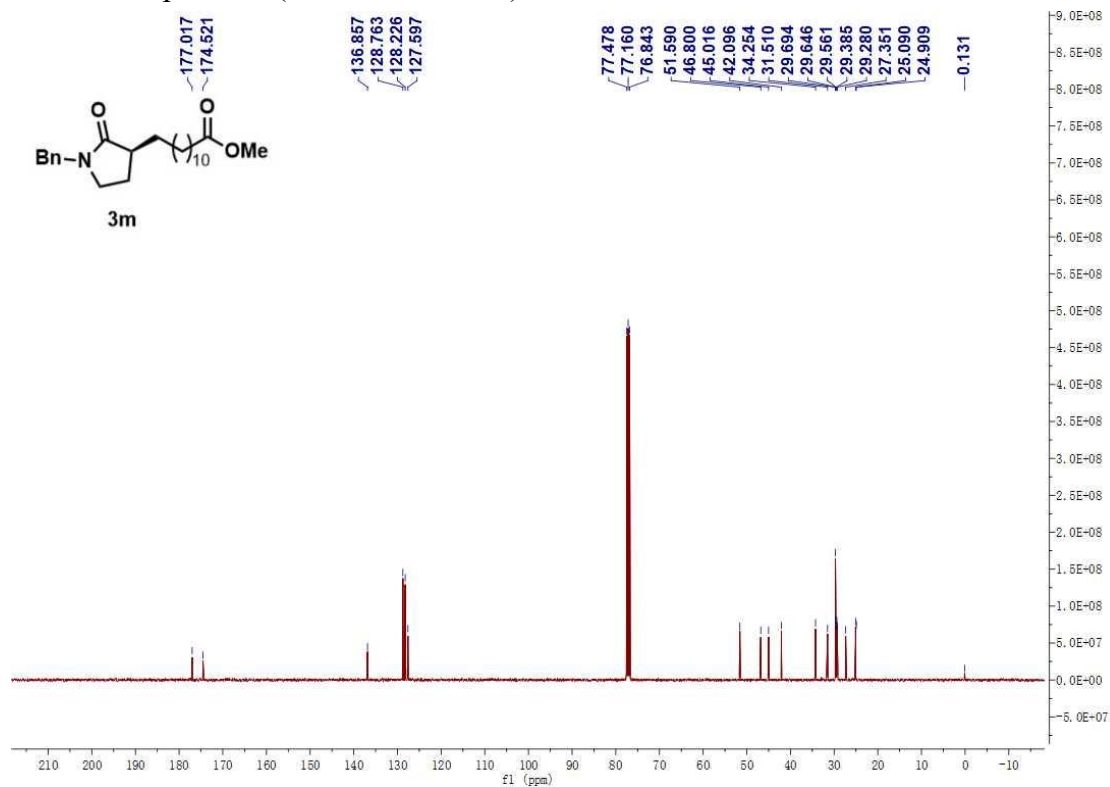
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3I**



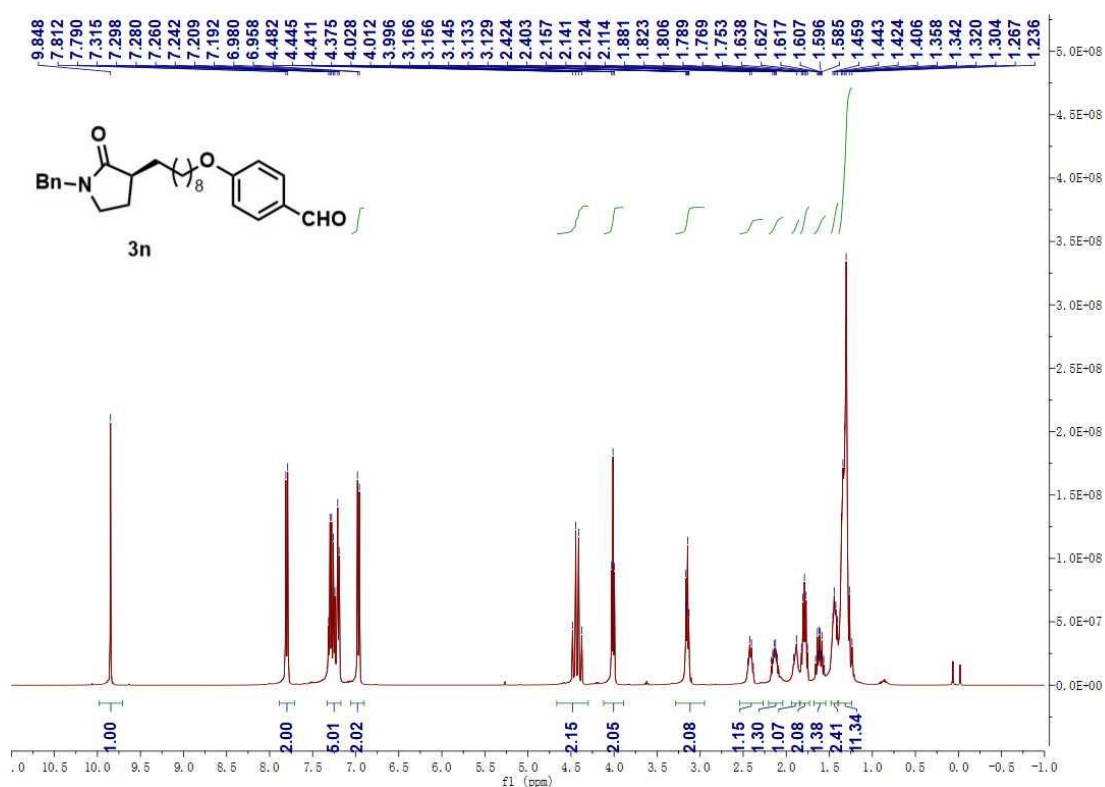
¹H NMR-spectrum (400 MHz, CDCl₃) of **3m**



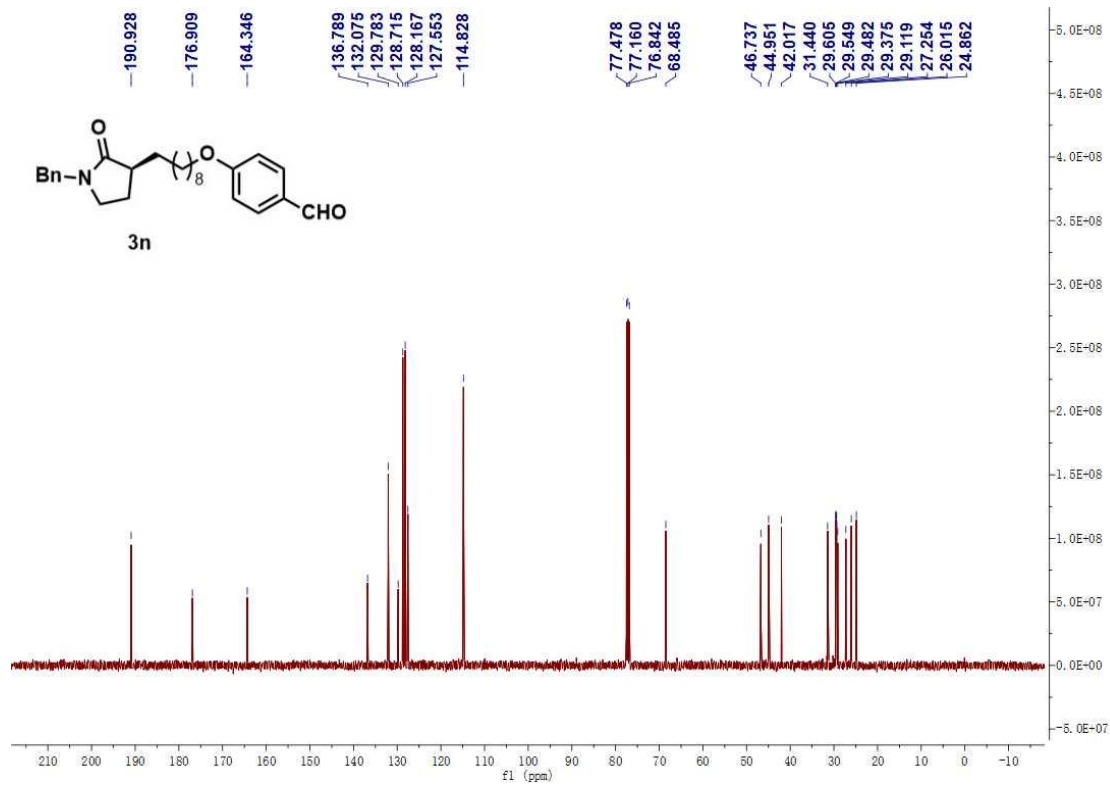
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3m**



¹H NMR-spectrum (400 MHz, CDCl₃) of **3n**

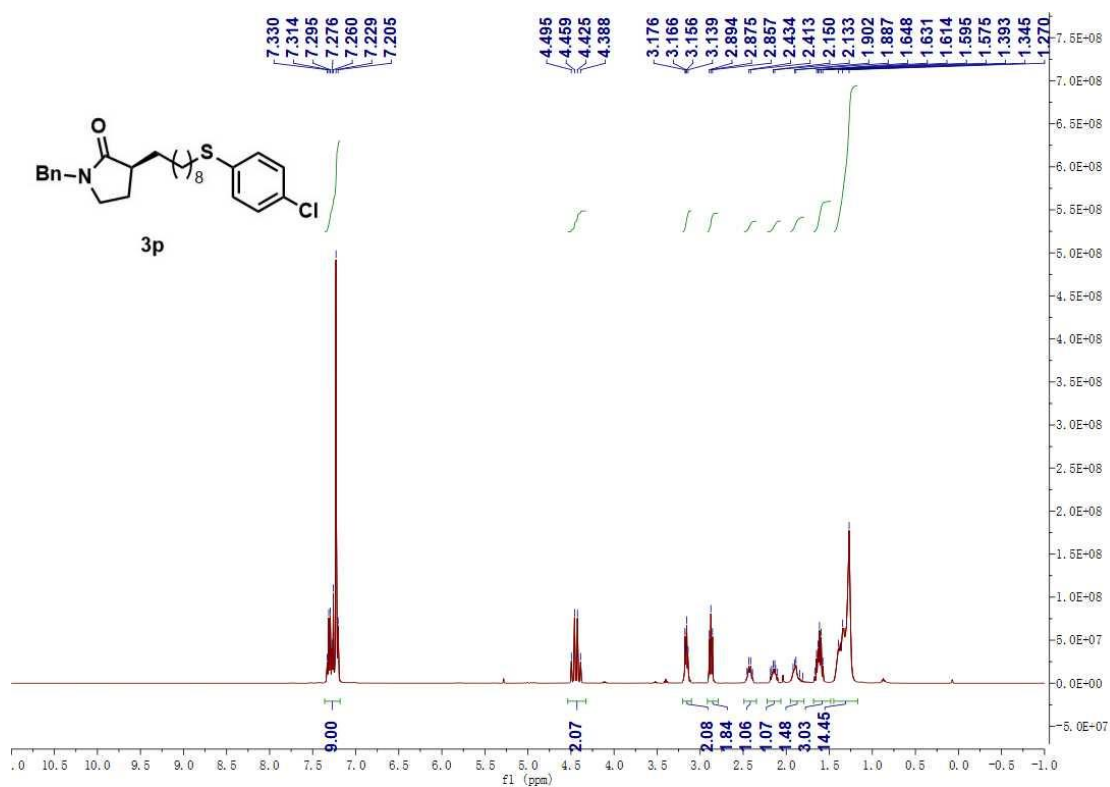


¹³C NMR-spectrum (100 MHz, CDCl₃) of **3n**

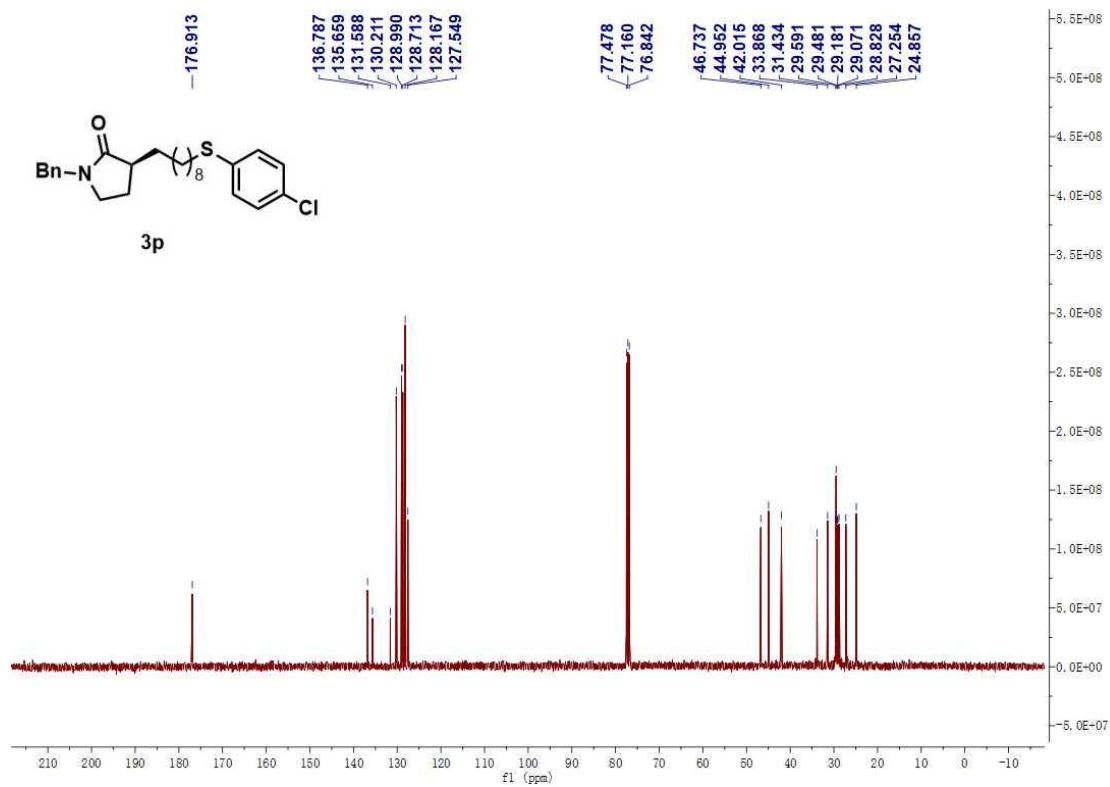


Chemical structure of **30** is shown. The ¹³C NMR spectrum (CDCl₃) shows peaks at 176.875, 162.499, 136.738, 133.984, 128.679, 128.123, 127.519, 119.406, 115.225, 103.588, 77.478, 77.160, 76.842, 68.437, 46.696, 44.921, 41.975, 31.391, 29.556, 29.497, 29.424, 29.312, 29.000, 27.200, 25.944, and 24.820 ppm.

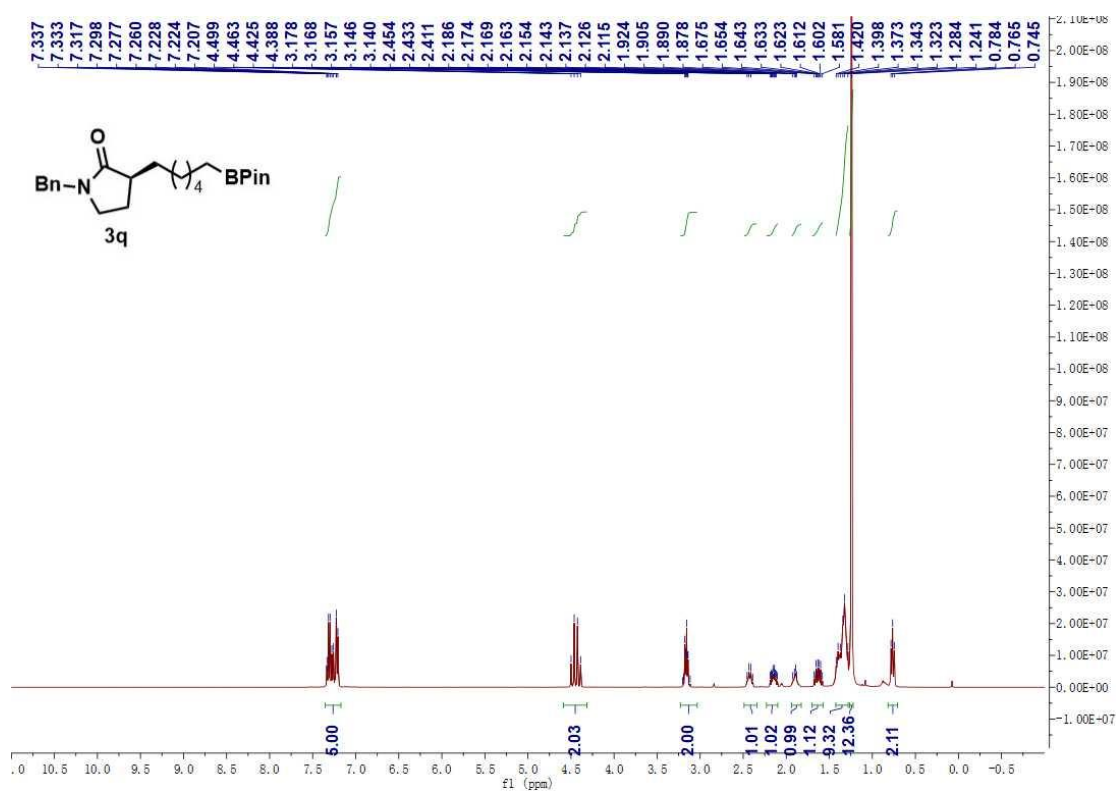
¹H NMR-spectrum (400 MHz, CDCl₃) of **3p**



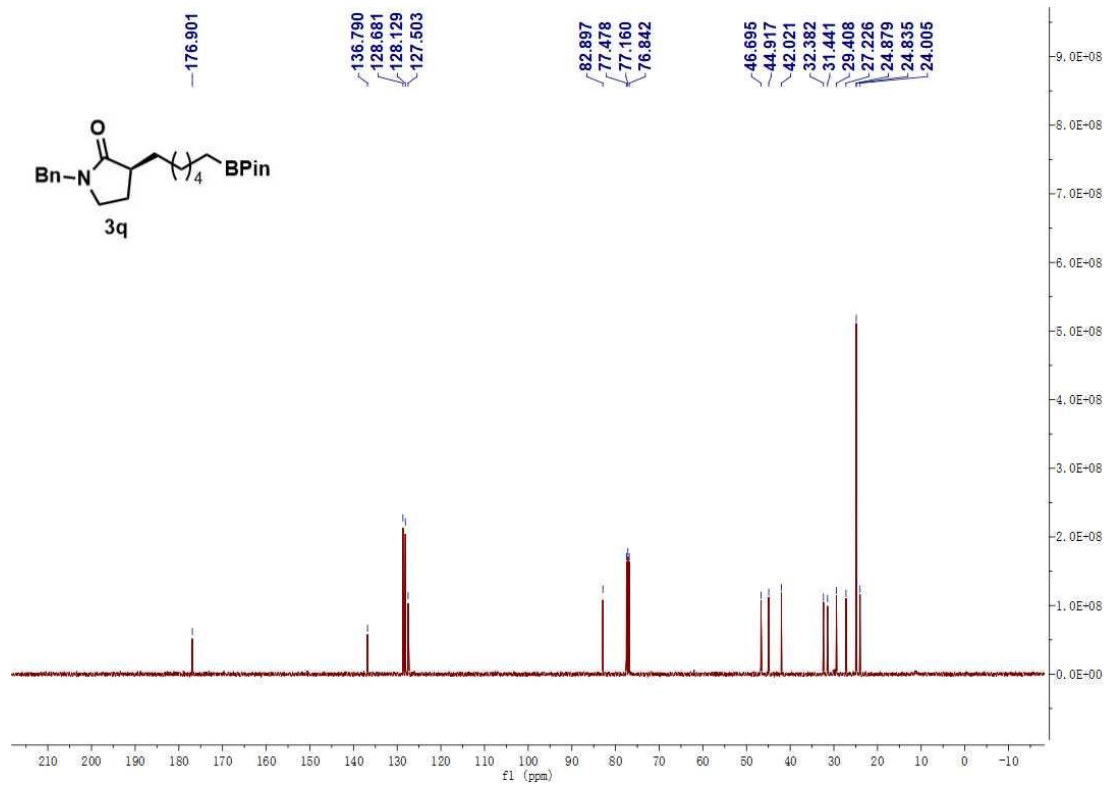
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3p**



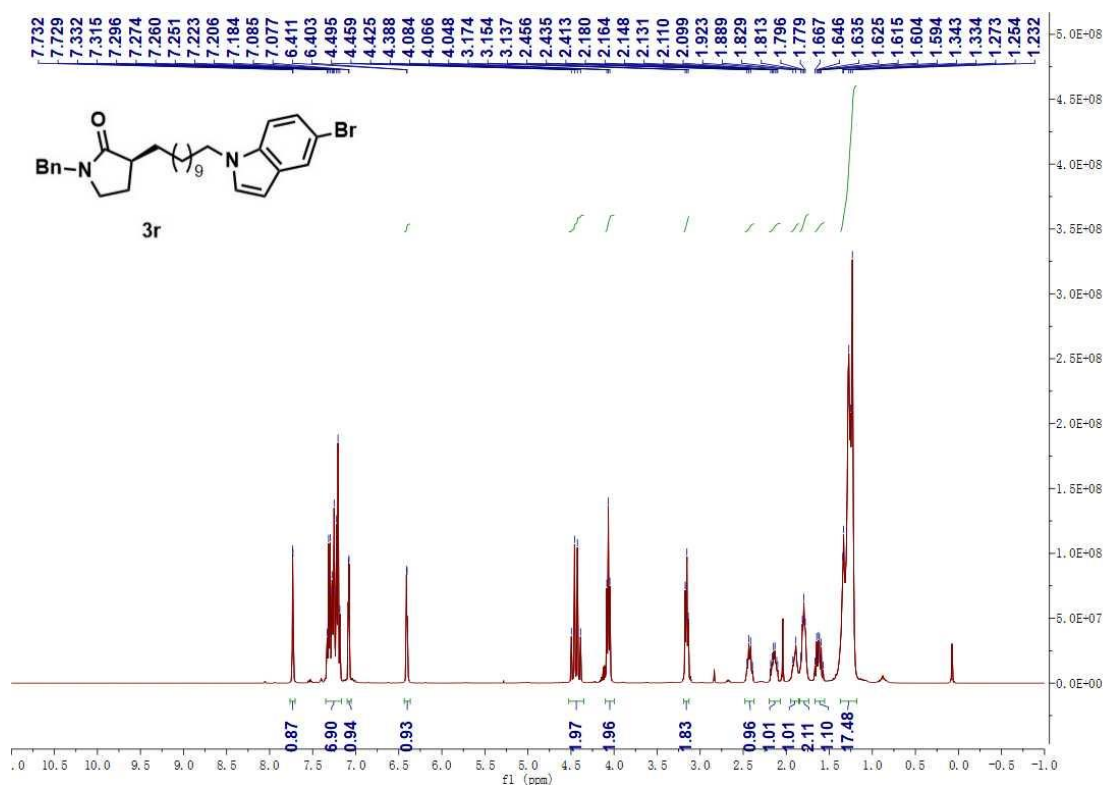
¹H NMR-spectrum (400 MHz, CDCl₃) of **3q**



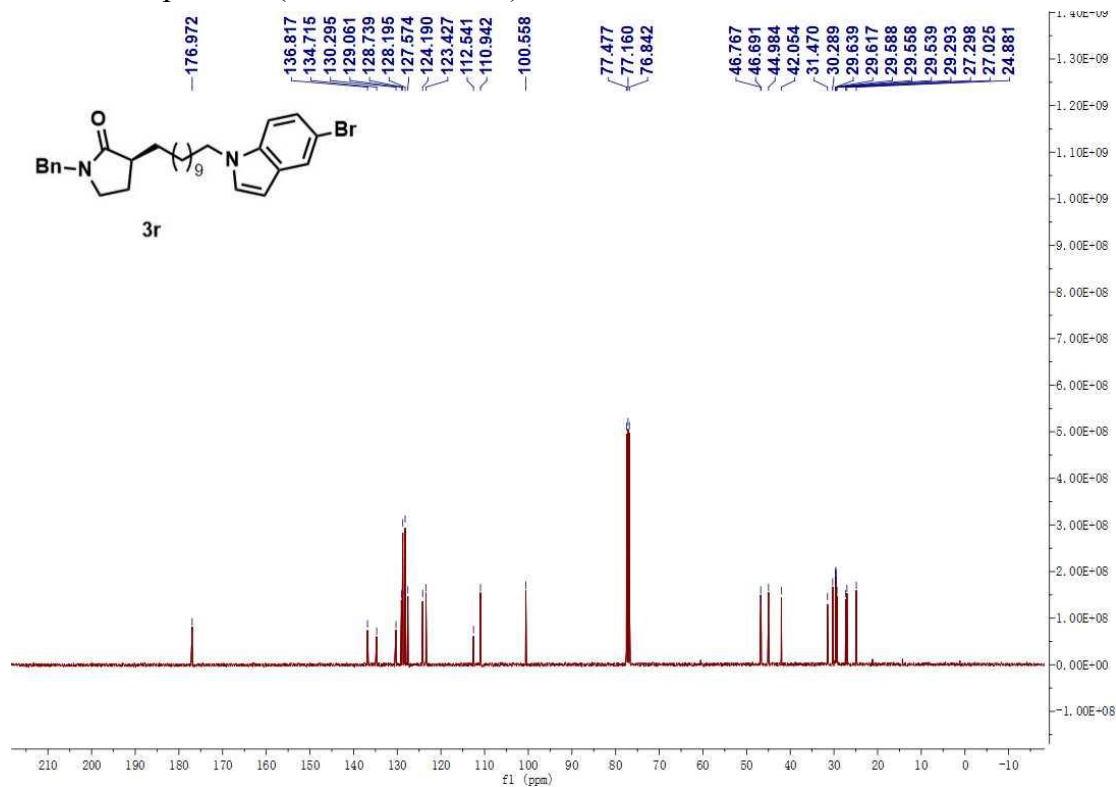
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3q**



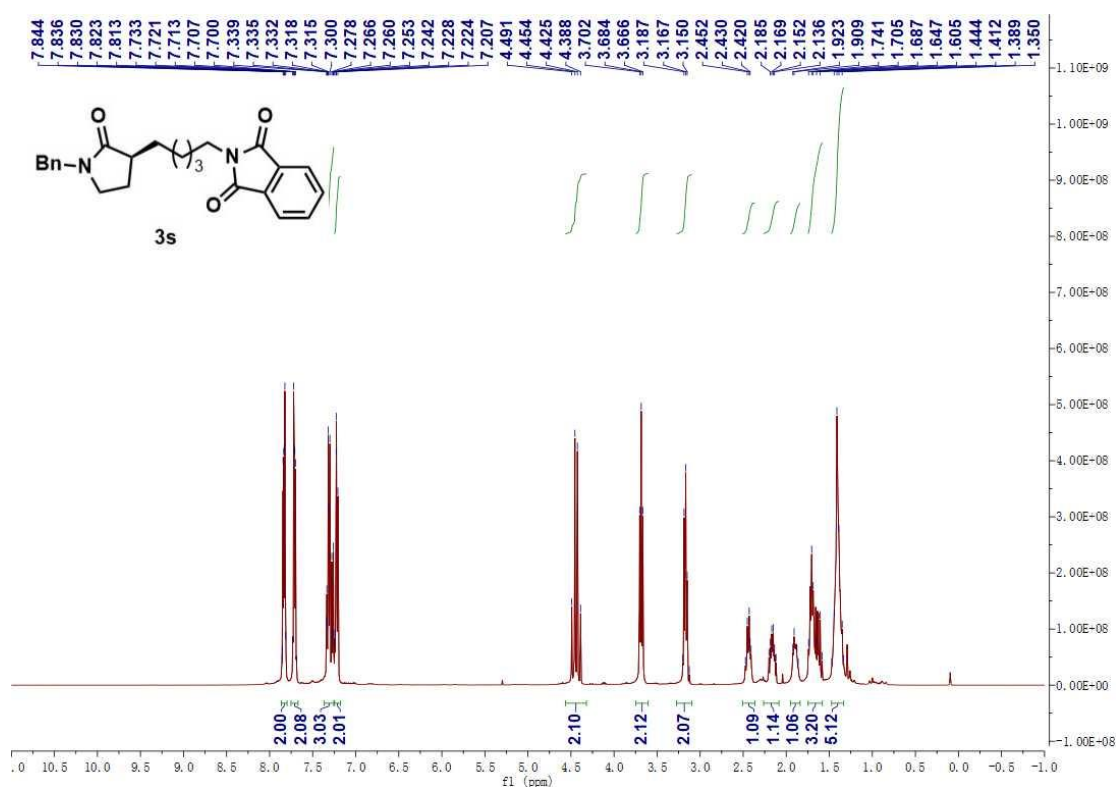
¹H NMR-spectrum (400 MHz, CDCl₃) of **3r**



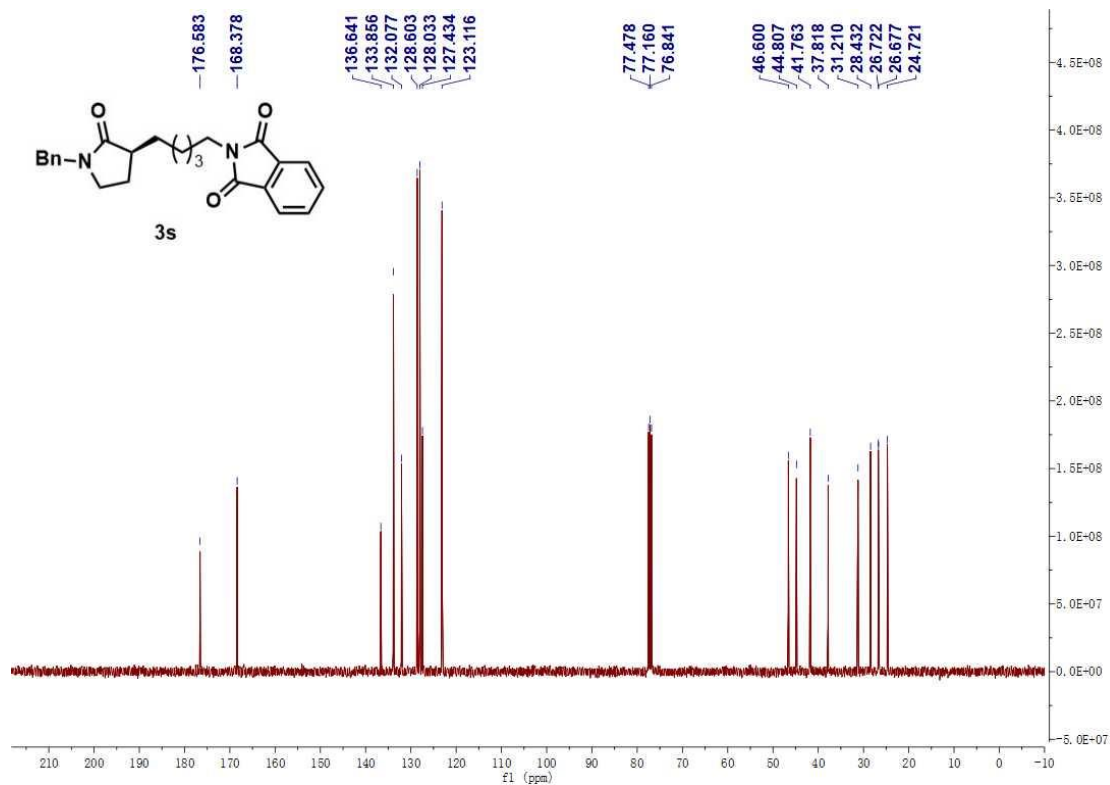
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3r**



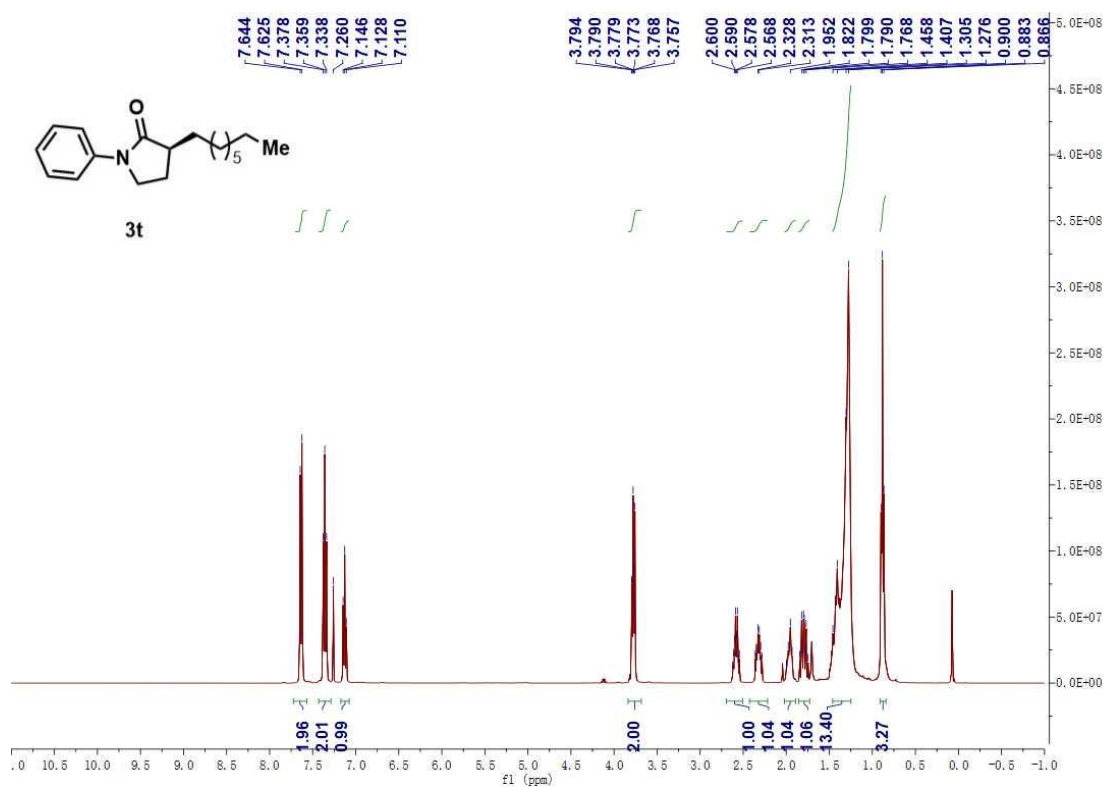
¹H NMR-spectrum (400 MHz, CDCl₃) of **3s**



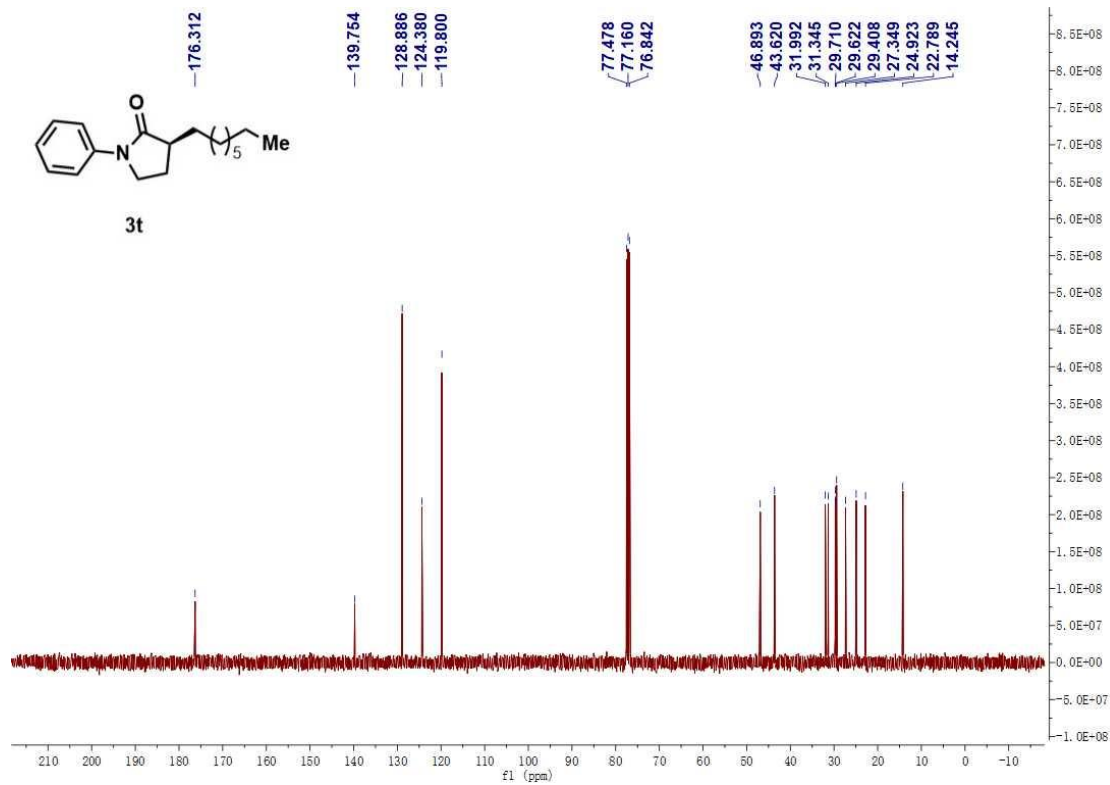
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3s**



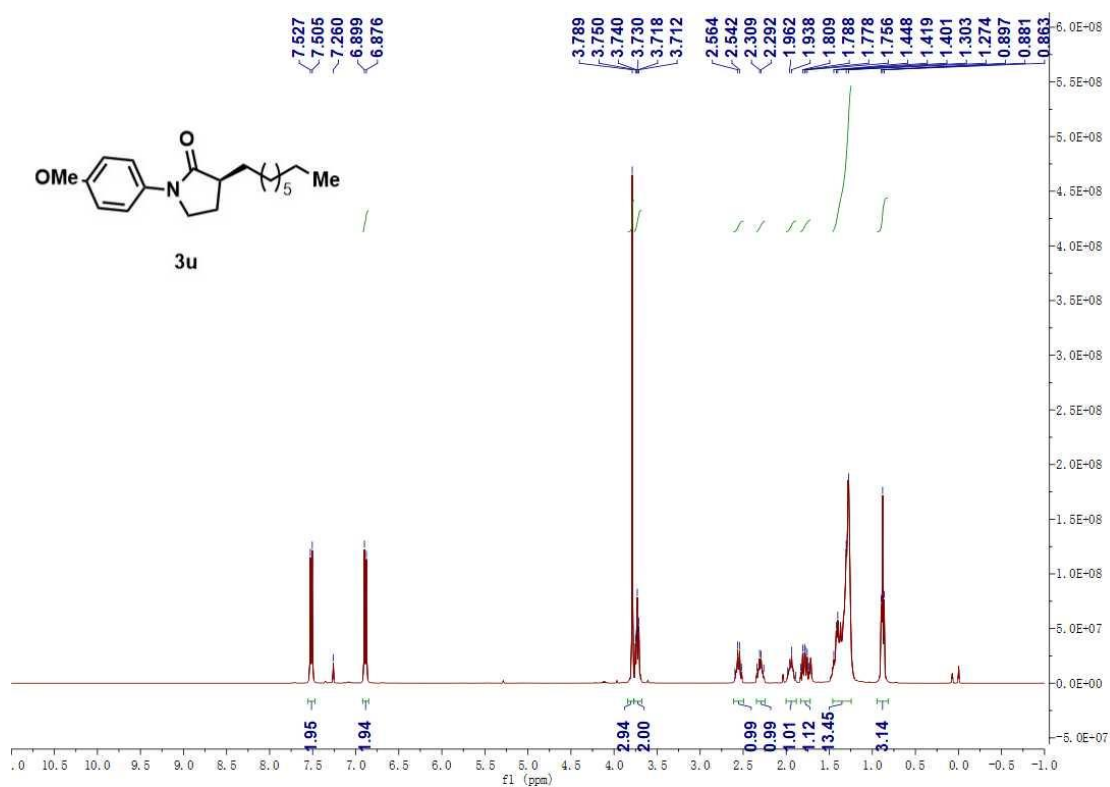
¹H NMR-spectrum (400 MHz, CDCl₃) of **3t**



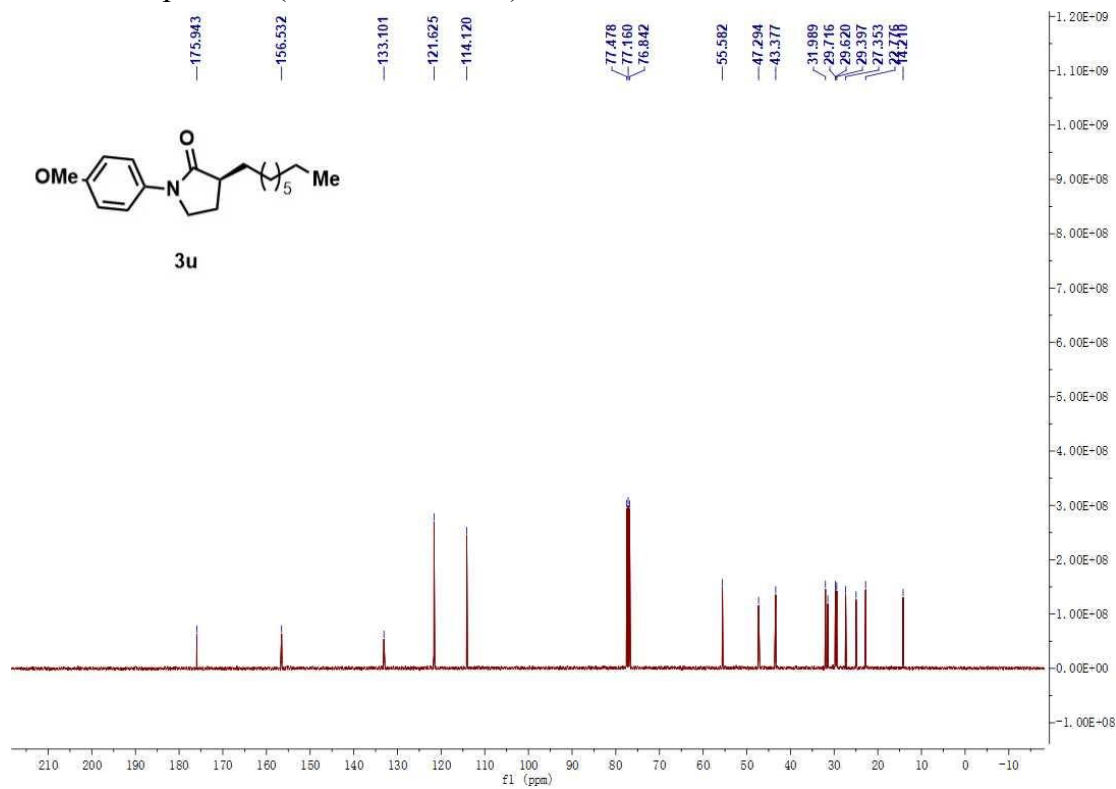
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3t**



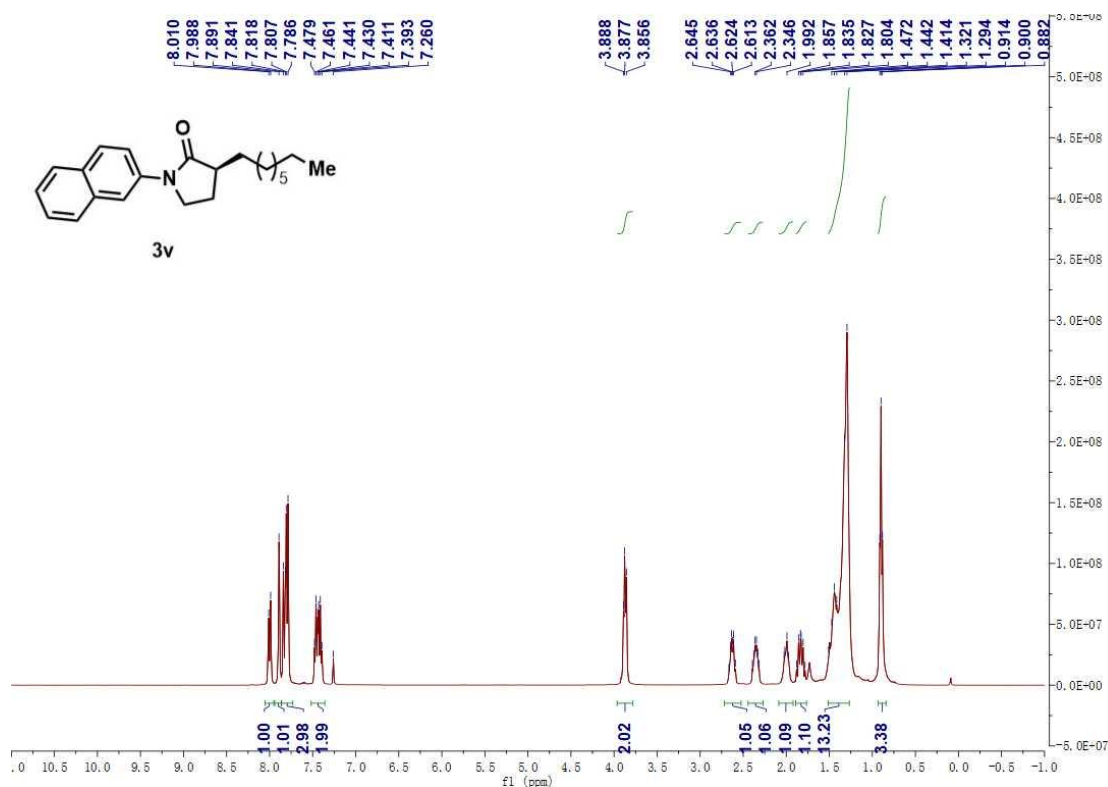
¹H NMR-spectrum (400 MHz, CDCl₃) of **3u**



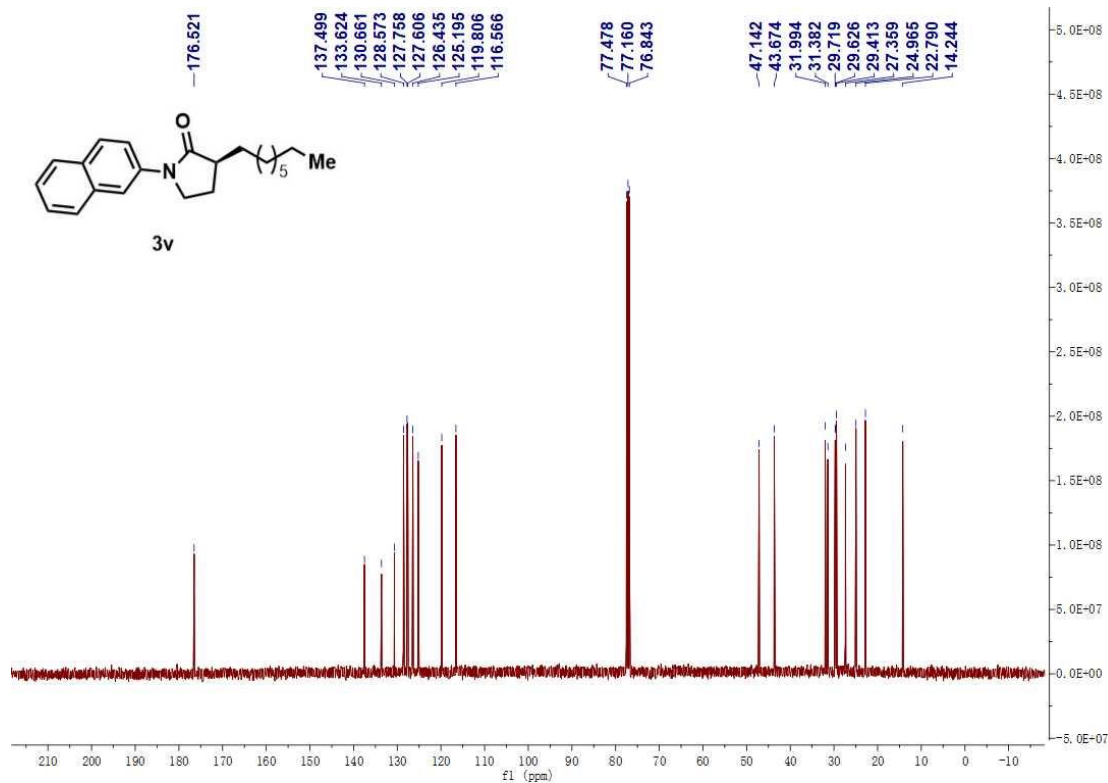
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3u**



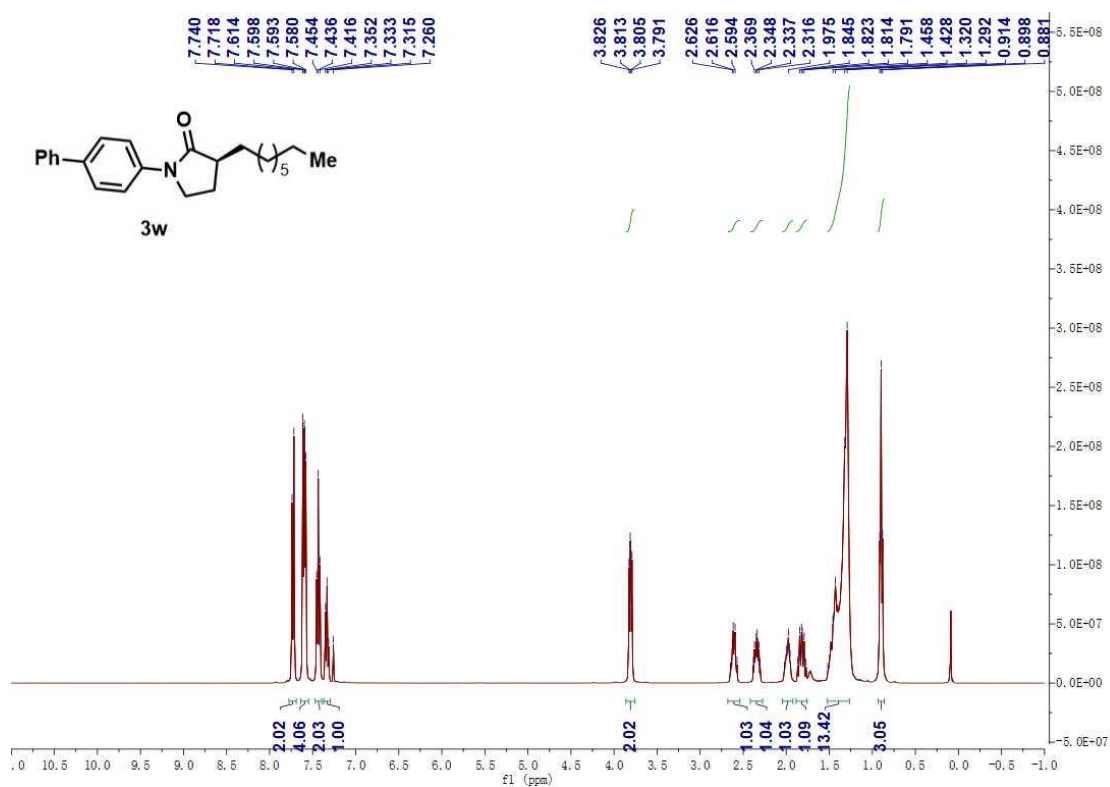
¹H NMR-spectrum (400 MHz, CDCl₃) of **3v**



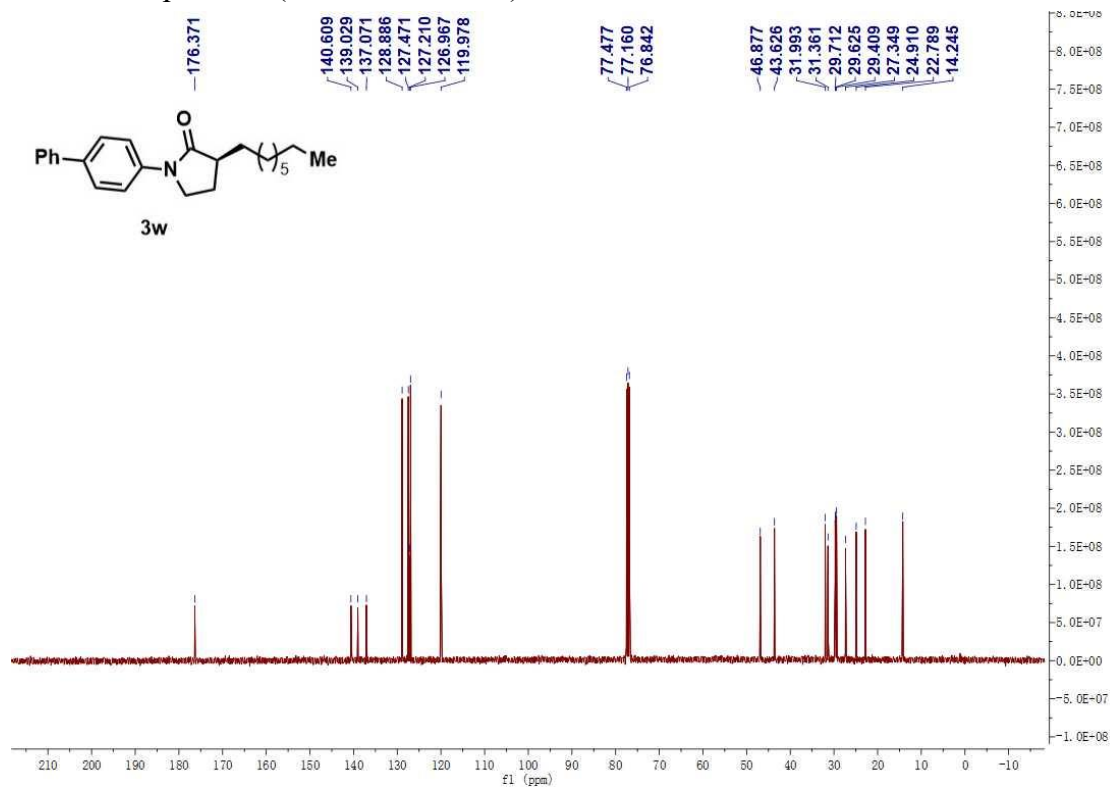
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3v**



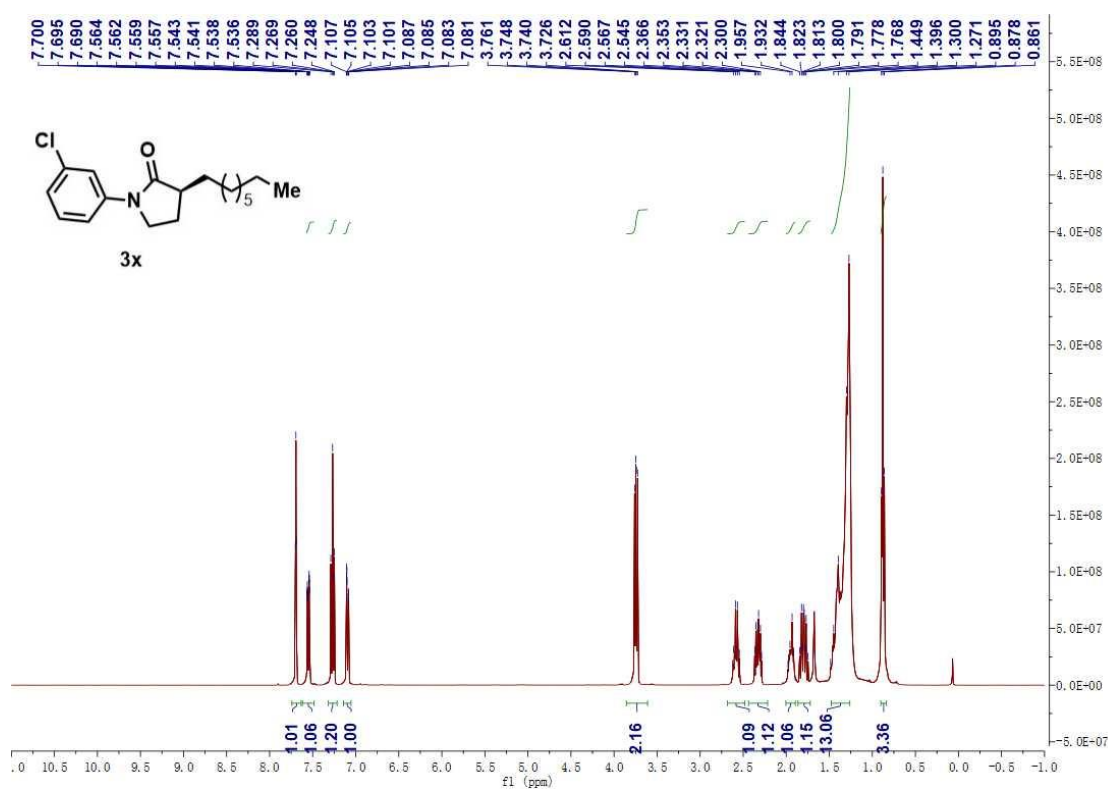
¹H NMR-spectrum (400 MHz, CDCl₃) of **3w**



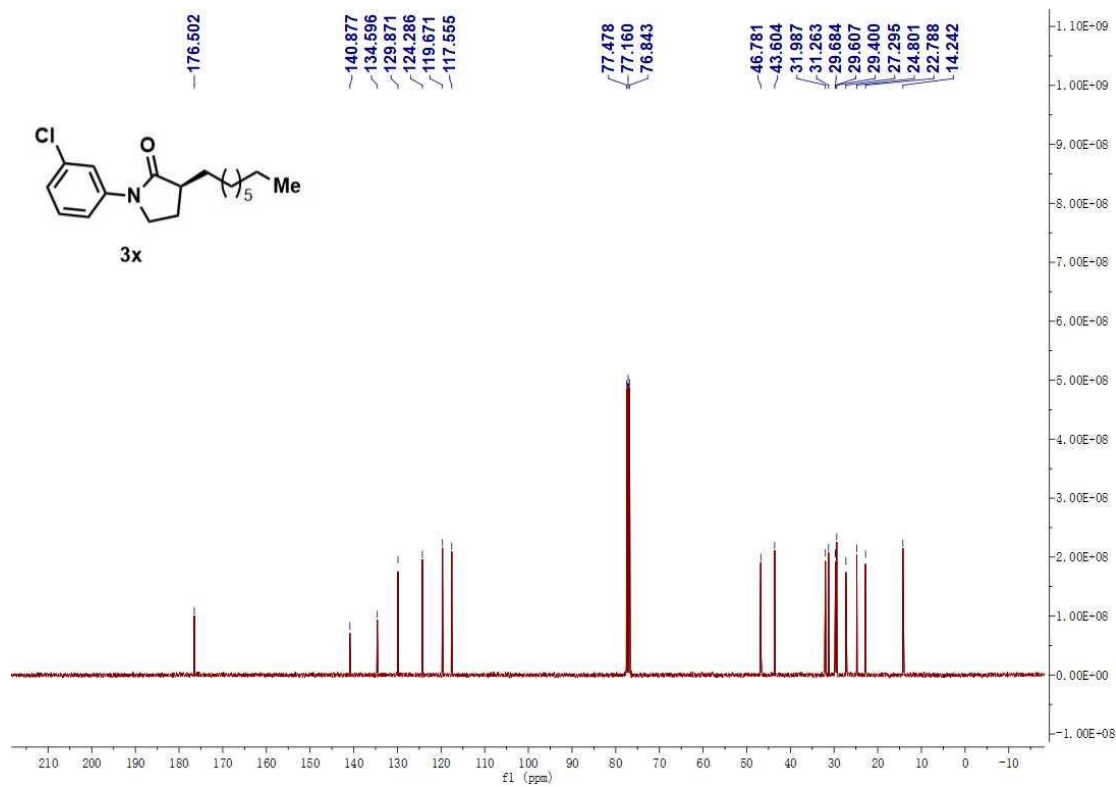
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3w**



¹H NMR-spectrum (400 MHz, CDCl₃) of **3x**



¹³C NMR-spectrum (100 MHz, CDCl₃) of **3x**



Chemical structure of **3y** is shown above the spectrum. The spectrum displays peaks corresponding to the structure, with chemical shifts (ppm) labeled above the peaks and integration values labeled below the baseline.

Chemical shifts (ppm) labeled above the peaks:

- 7.260, 7.158, 7.137, 6.849, 6.828
- 4.425, 4.388, 4.362, 4.326, 3.784
- 3.159, 3.149, 3.138
- 2.417, 2.395, 2.138, 2.120, 1.879, 1.632, 1.611, 1.600, 1.579, 1.326, 1.310, 1.268, 1.253, 0.886, 0.870, 0.852

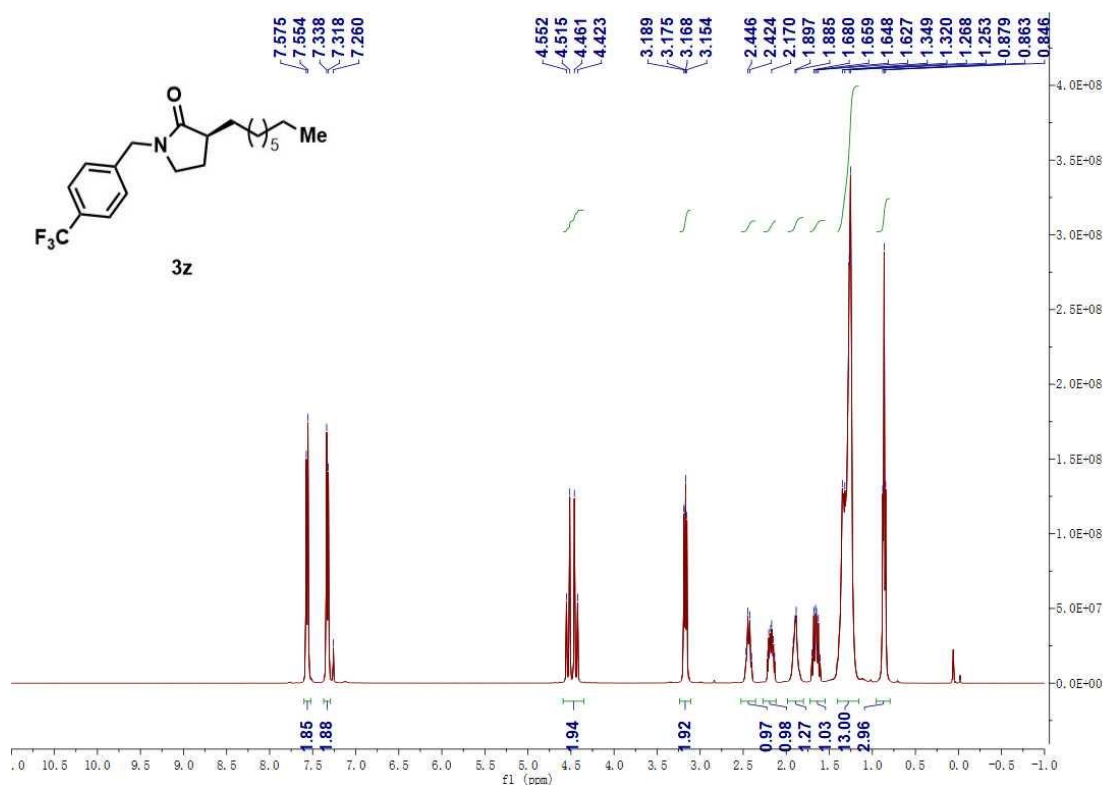
Integration values labeled below the baseline:

- 2.00, 1.99
- 2.02, 3.02
- 2.02
- 1.02, 1.04, 1.10, 1.13, 1.37, 3.29

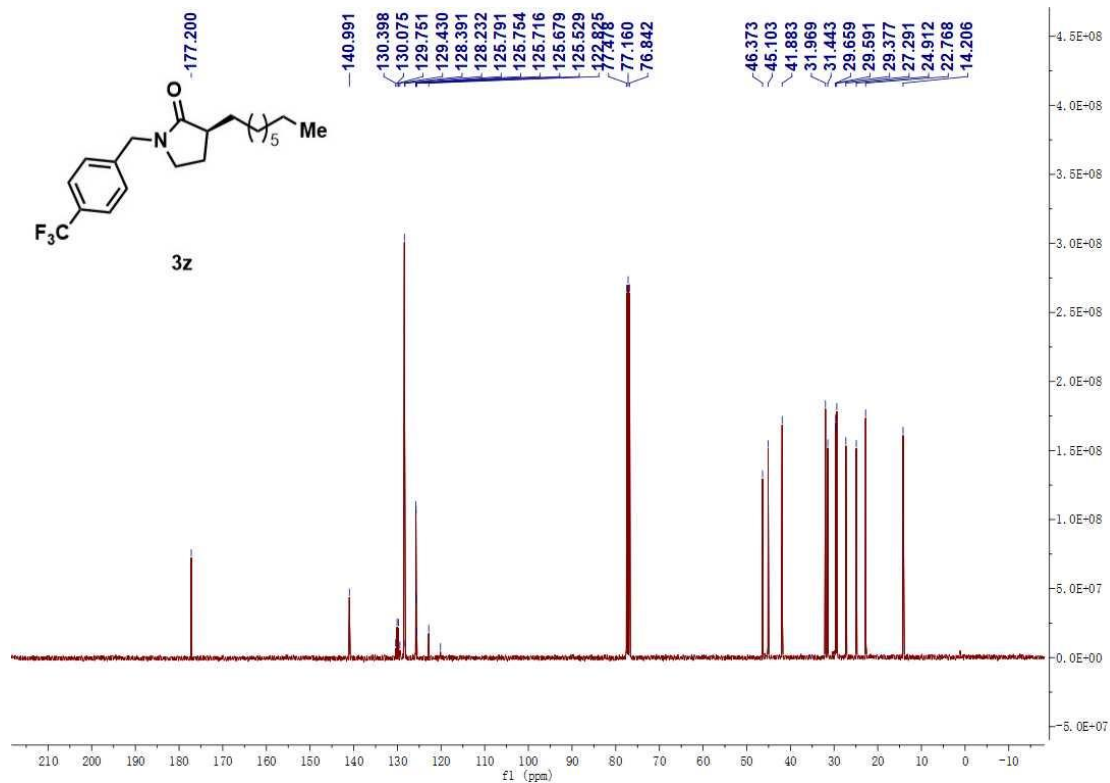
Chemical structure of **3y** is shown above the spectrum. The spectrum displays the following chemical shifts (ppm):

- 176.845
- 159.087
- 129.561
- 128.955
- 114.077
- 77.477
- 77.160
- 76.842
- 55.370
- 46.156
- 44.861
- 42.162
- 31.988
- 31.496
- 29.694
- 29.613
- 29.395
- 27.333
- 24.858
- 22.783
- 14.239

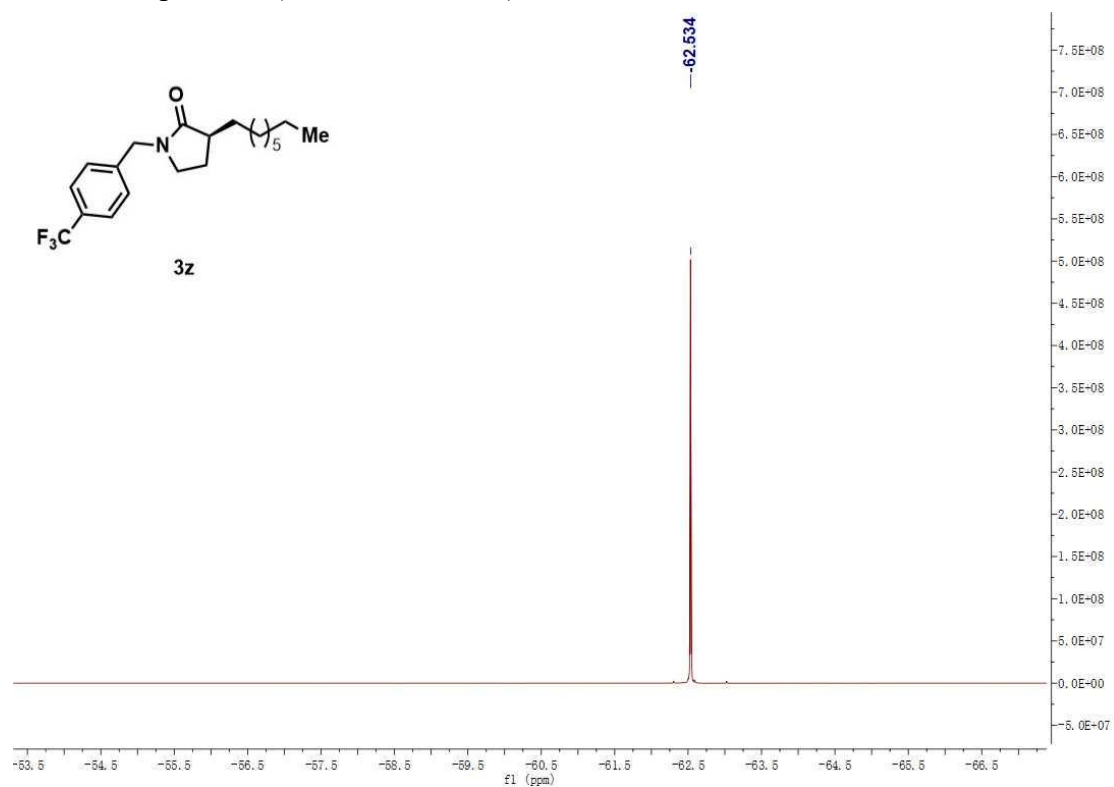
¹H NMR-spectrum (400 MHz, CDCl₃) of **3z**



¹³C NMR-spectrum (100 MHz, CDCl₃) of **3z**



¹⁹F NMR-spectrum (376 MHz, CDCl₃) of **3z**



3aa

CCCCC[C@H]1CCCN(C1Cc2ccc(C(C)(C)C)cc2)C(=O)

¹H NMR spectrum (CDCl₃) of compound **3aa**. The x-axis represents the chemical shift in ppm (f1), ranging from -1.0 to 11.0. The y-axis represents the intensity, ranging from -2.0E+07 to 4.0E+08. The spectrum shows several peaks corresponding to the structure of **3aa**.

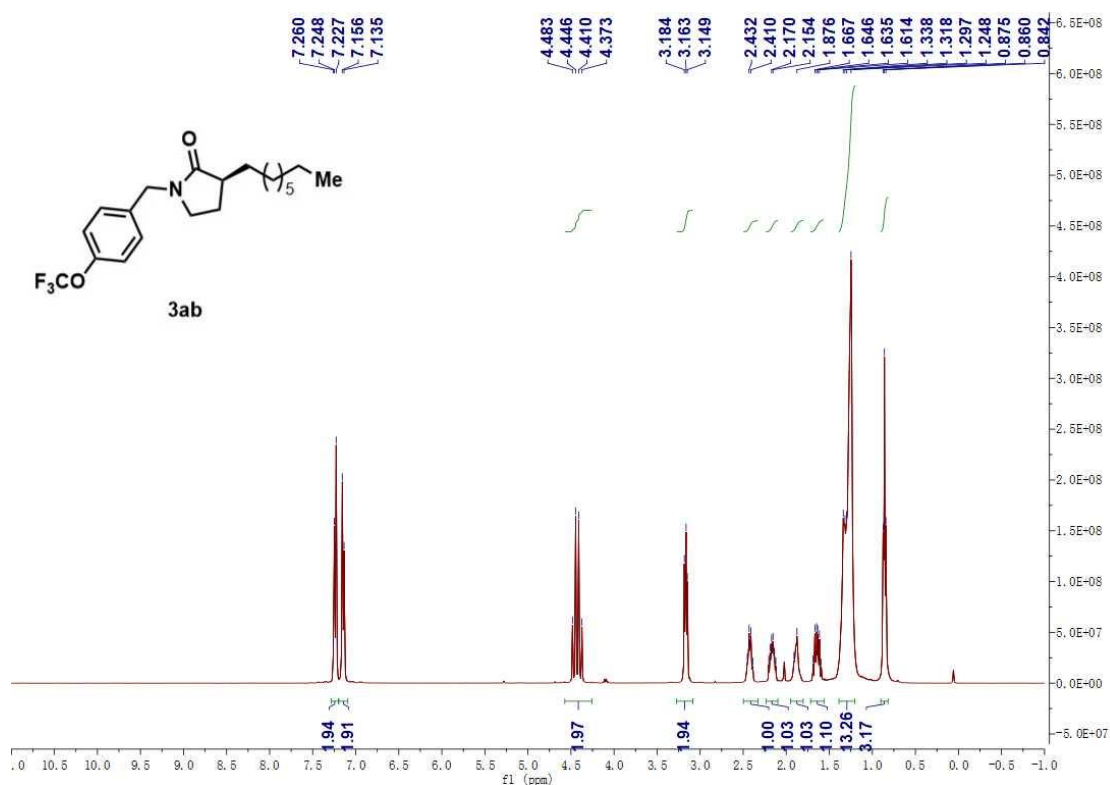
Chemical structure of **3aa** is shown above the spectrum. The structure is a 4-tert-butylbenzyl group attached to the nitrogen of a 2-(5-methylpentyl)pyrrolidine-1-one.

Key peaks and integrations are labeled:

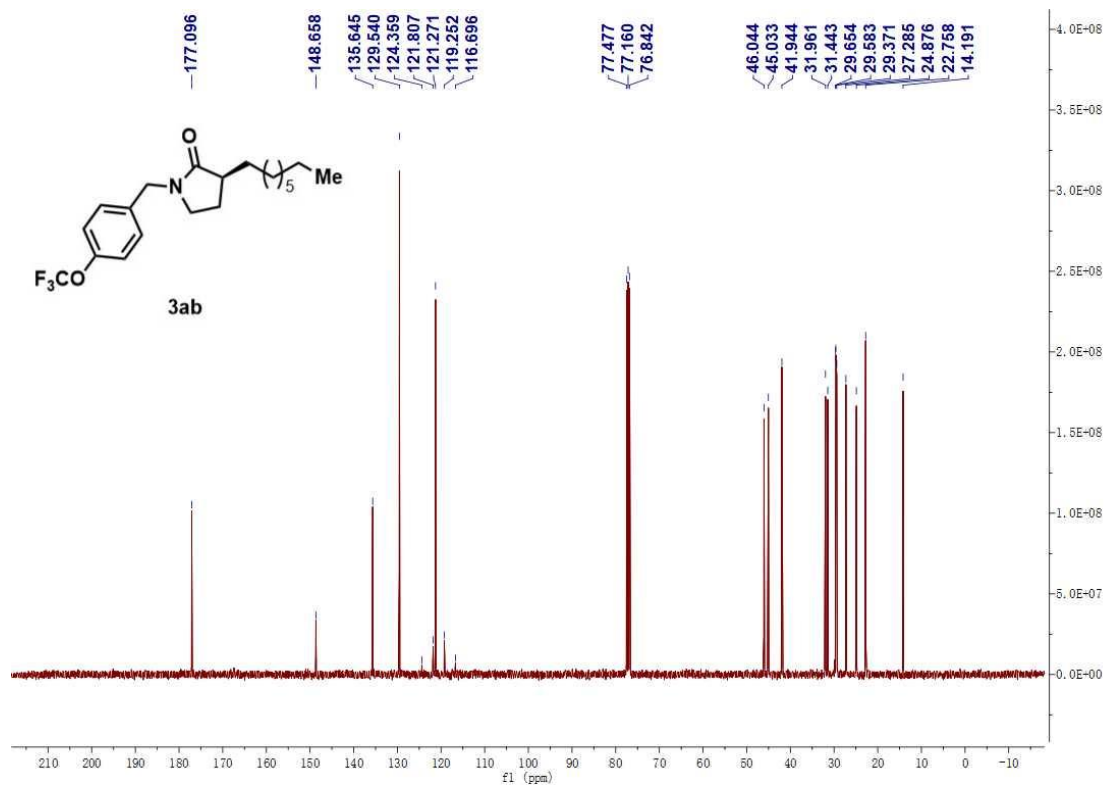
- Aromatic protons (7.3 ppm): Integration 1.93, 1.93.
- Aliphatic protons (4.4-4.5 ppm): Integration 2.03.
- Aliphatic protons (3.1-3.2 ppm): Integration 2.00.
- Aliphatic protons (1.6-2.5 ppm): Integration 1.00, 1.06, 1.05, 1.19, 22.20, 3.16.
- Aliphatic protons (1.4 ppm): Integration 22.20.

Figure S10. ¹³C NMR spectrum of compound **3aa** in CDCl₃. The chemical structure of **3aa** is shown in the top left corner. The spectrum displays peaks corresponding to the carbons in the molecule, with the following chemical shifts (ppm) labeled: 176.864, 150.422, 133.711, 127.898, 125.576, 77.478, 77.160, 76.842, 46.347, 44.995, 42.077, 34.561, 31.954, 31.483, 31.413, 29.664, 29.583, 29.362, 27.301, 24.830, 22.748, and 14.205. The x-axis represents the chemical shift in ppm, ranging from -10 to 210.

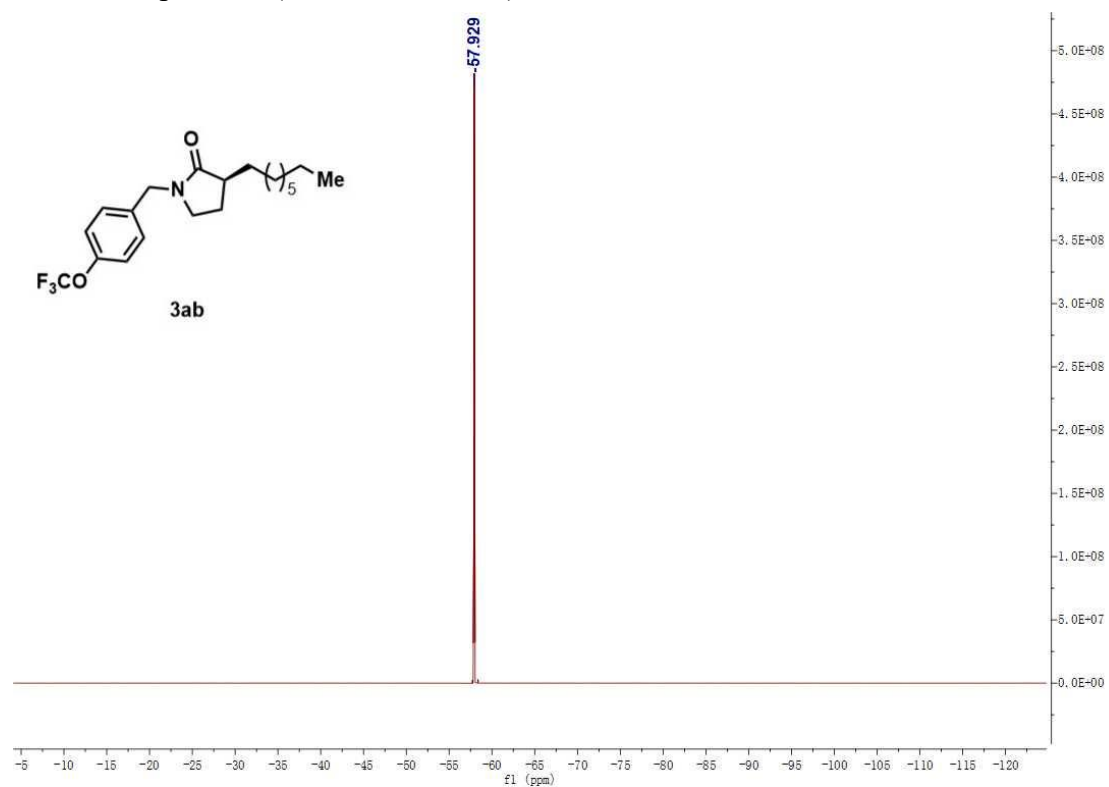
¹H NMR-spectrum (400 MHz, CDCl₃) of **3ab**



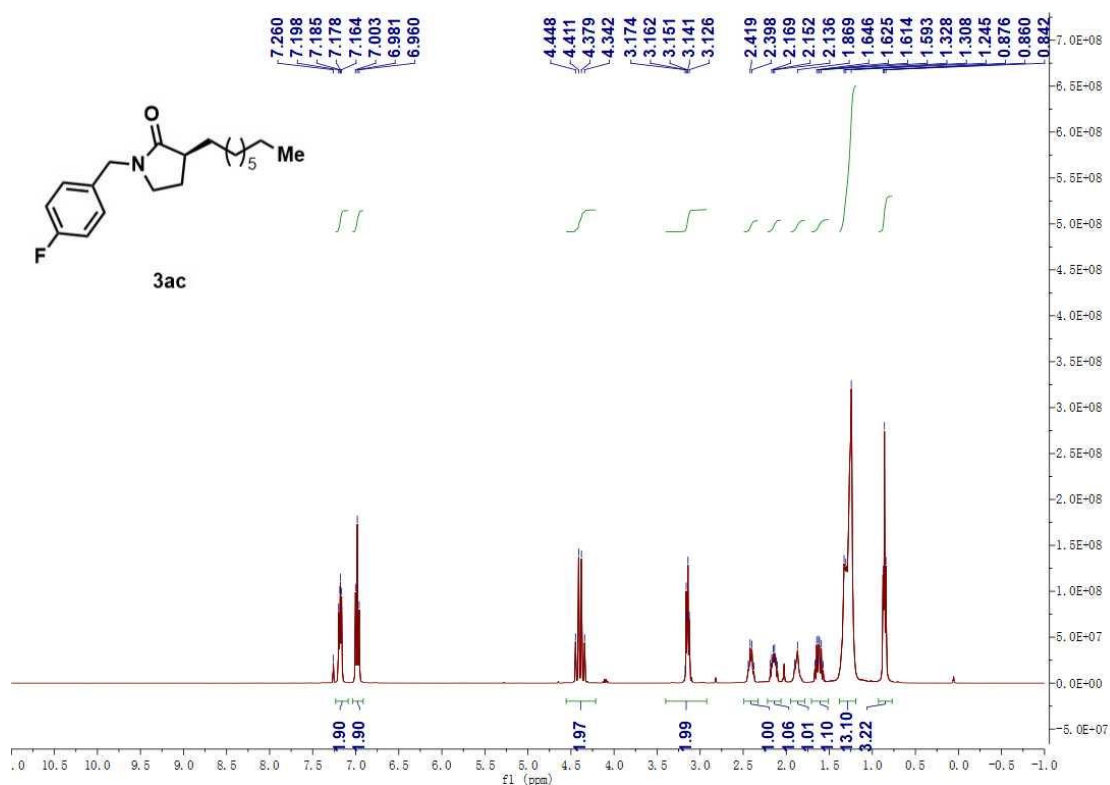
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3ab**



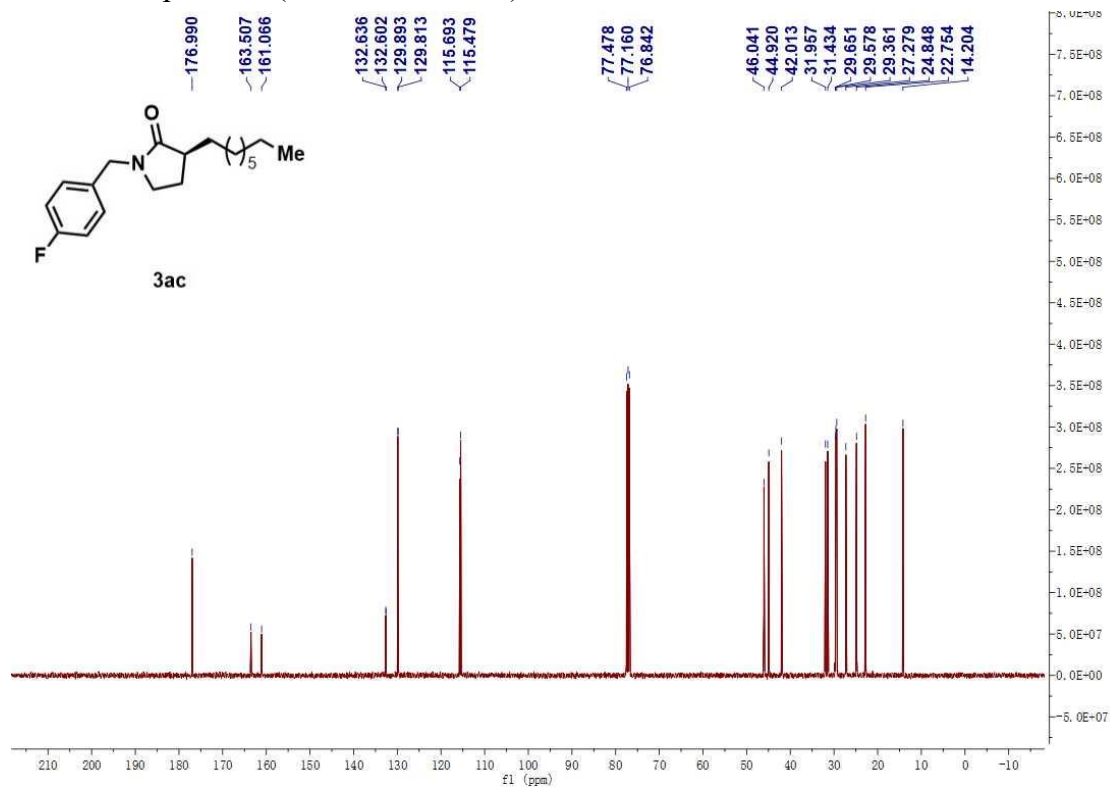
¹⁹F NMR-spectrum (376 MHz, CDCl₃) of **3ab**



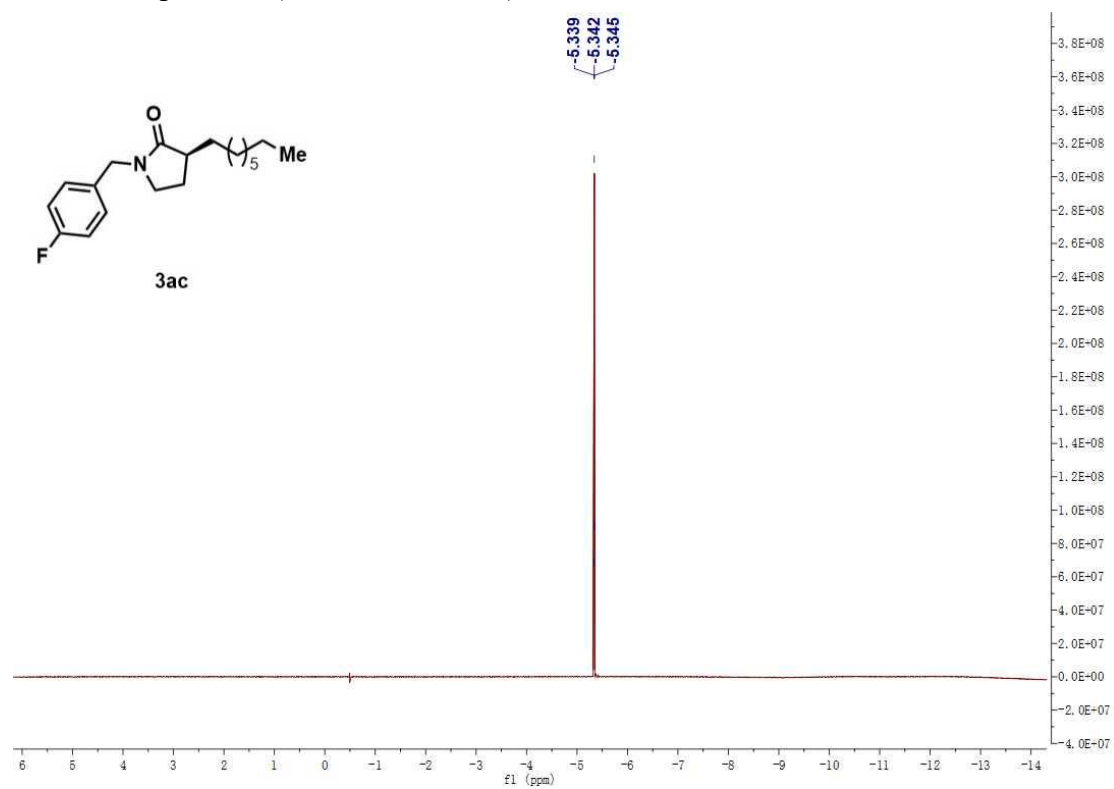
¹H NMR-spectrum (400 MHz, CDCl₃) of **3ac**



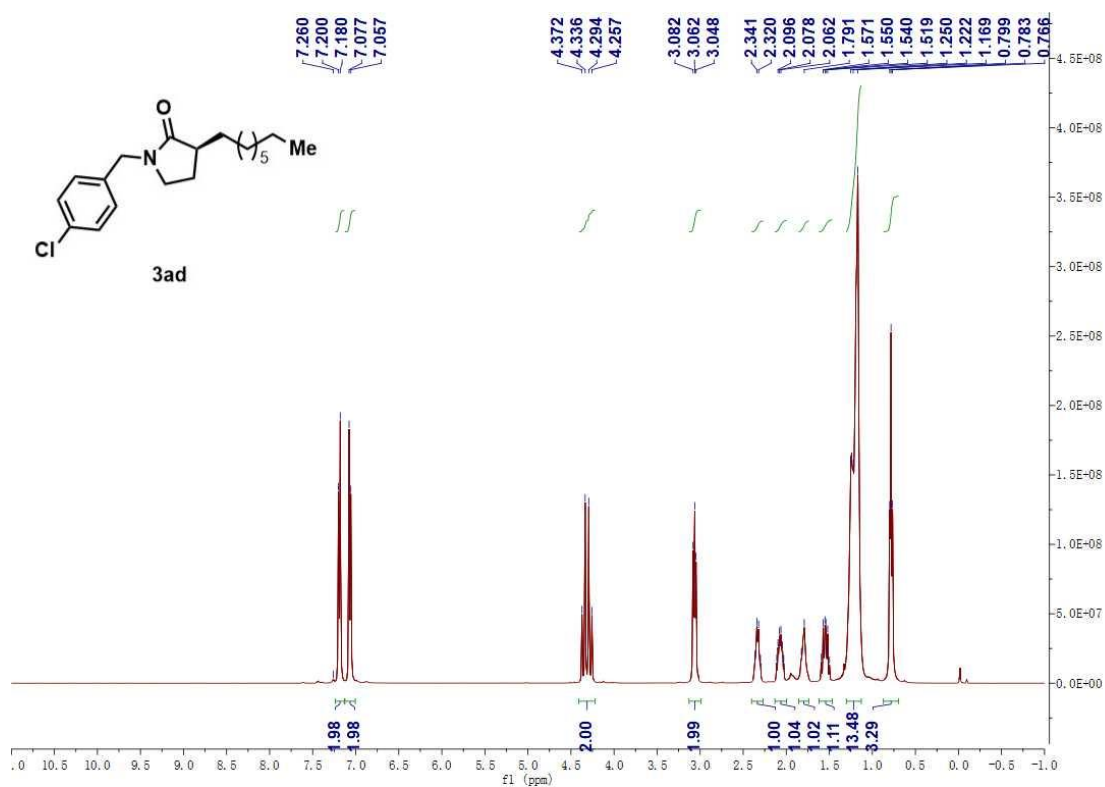
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3ac**



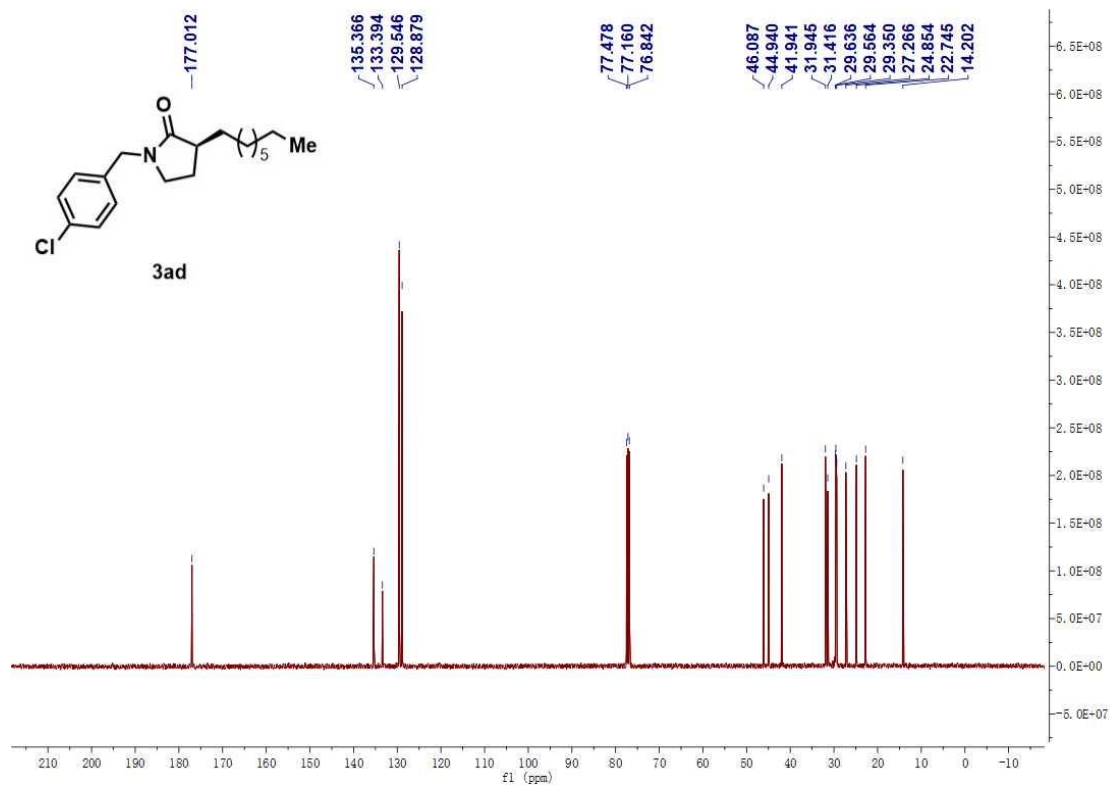
¹⁹F NMR-spectrum (376 MHz, CDCl₃) of **3ac**



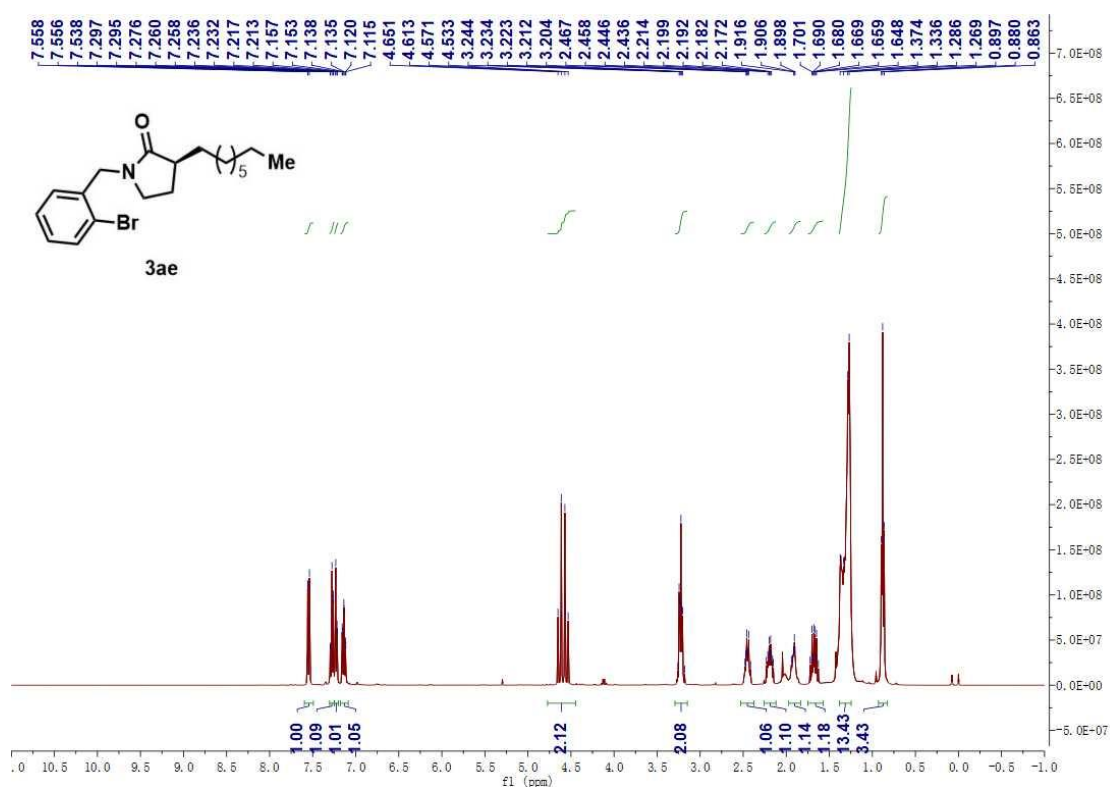
¹H NMR-spectrum (400 MHz, CDCl₃) of **3ad**



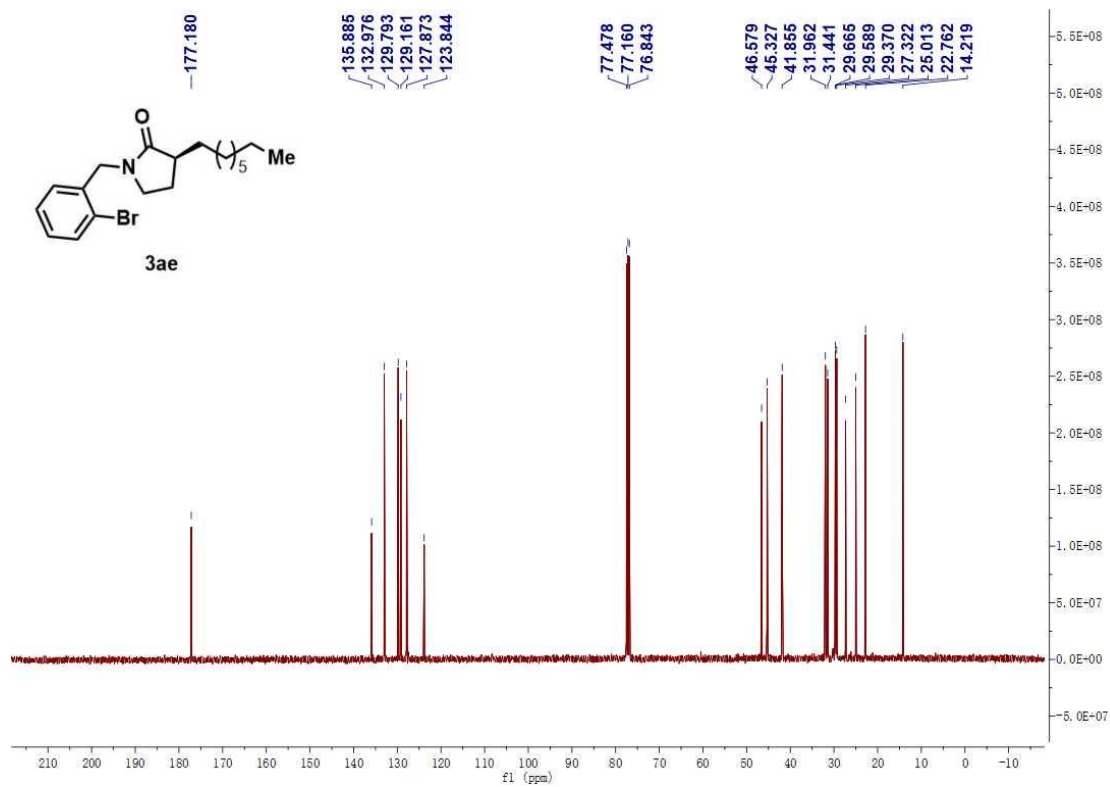
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3ad**



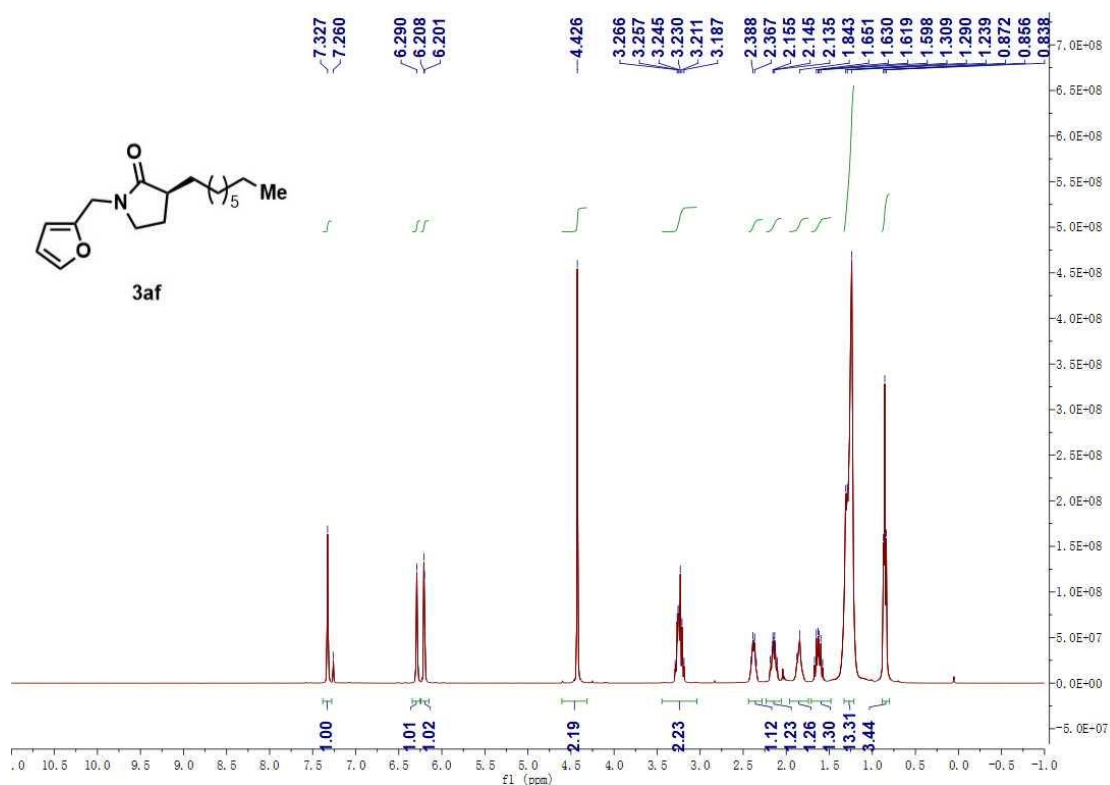
¹H NMR-spectrum (400 MHz, CDCl₃) of **3ae**



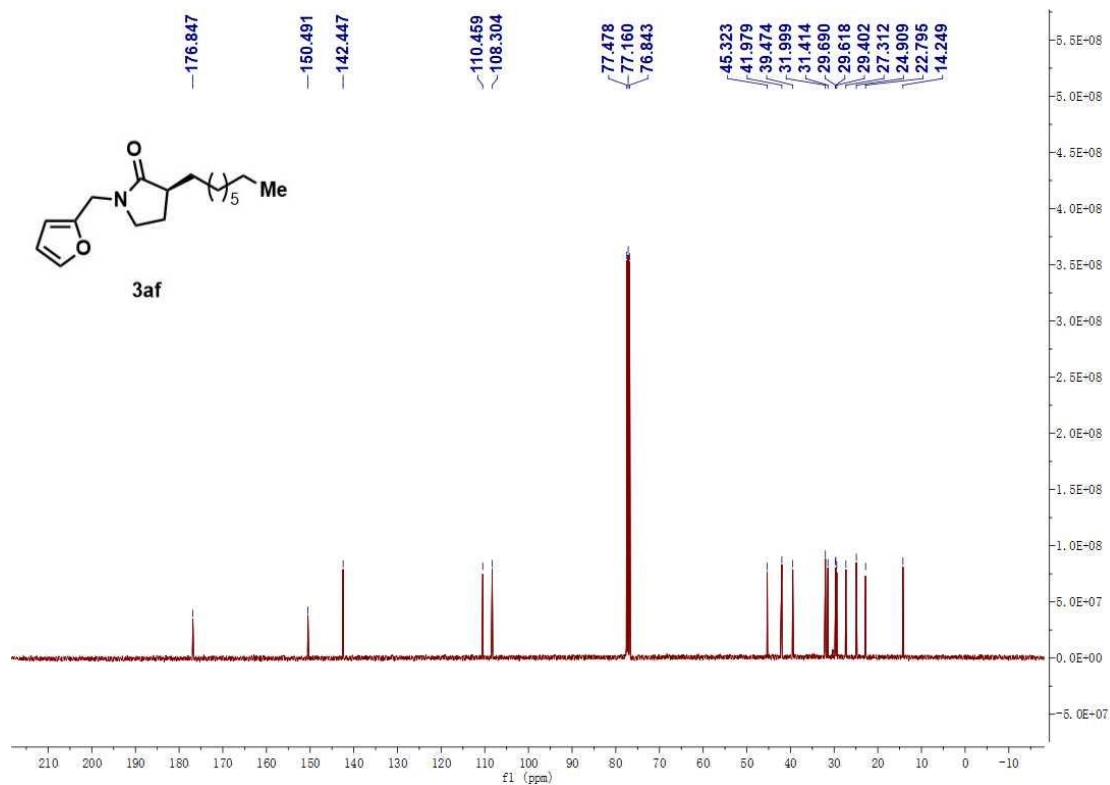
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3ae**



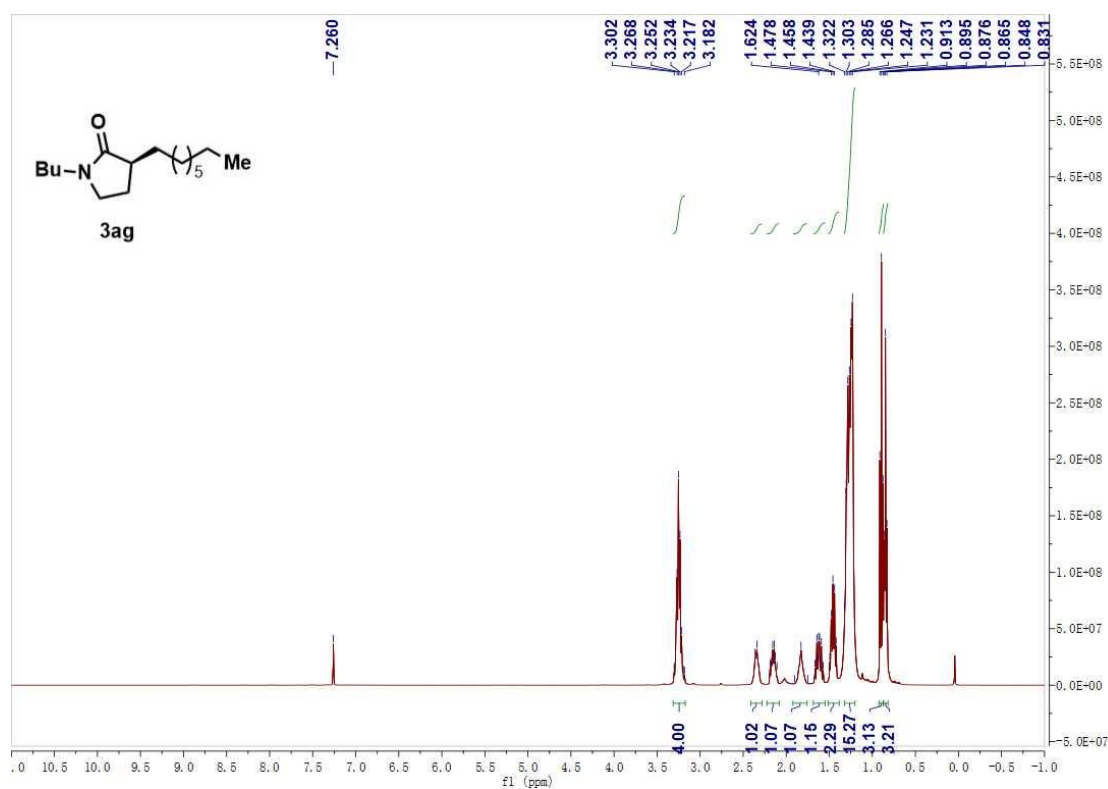
¹H NMR-spectrum (400 MHz, CDCl₃) of **3af**



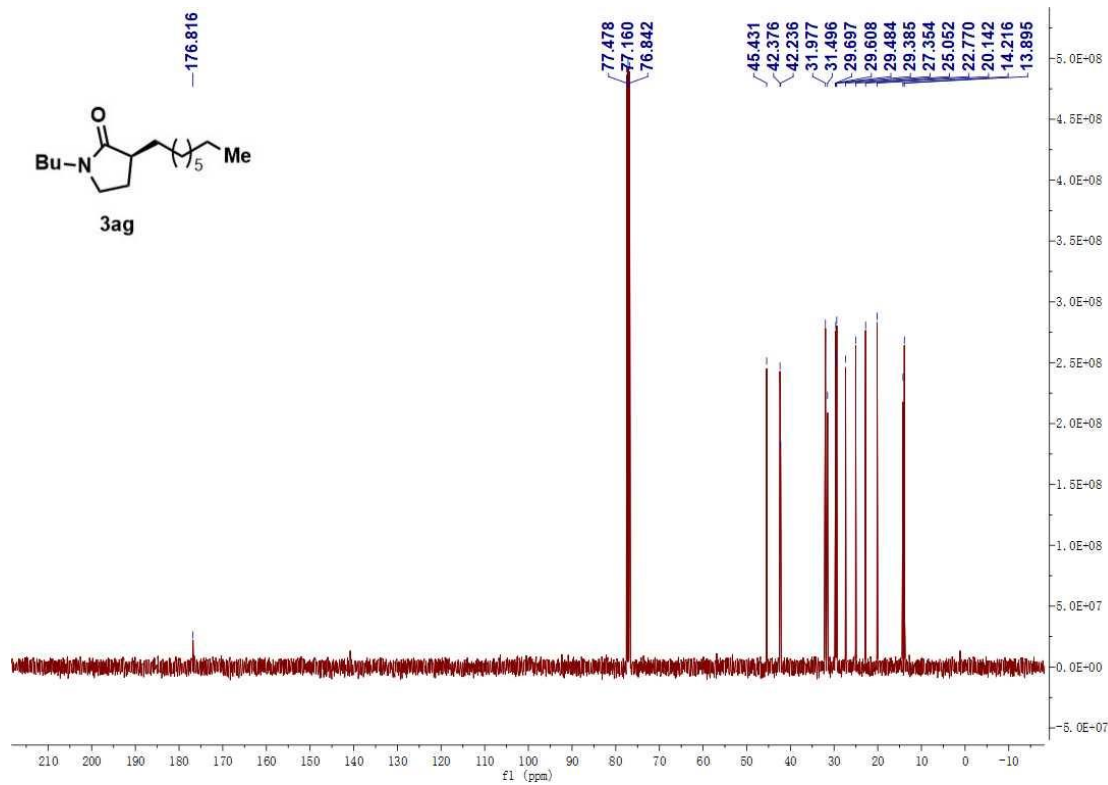
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3af**



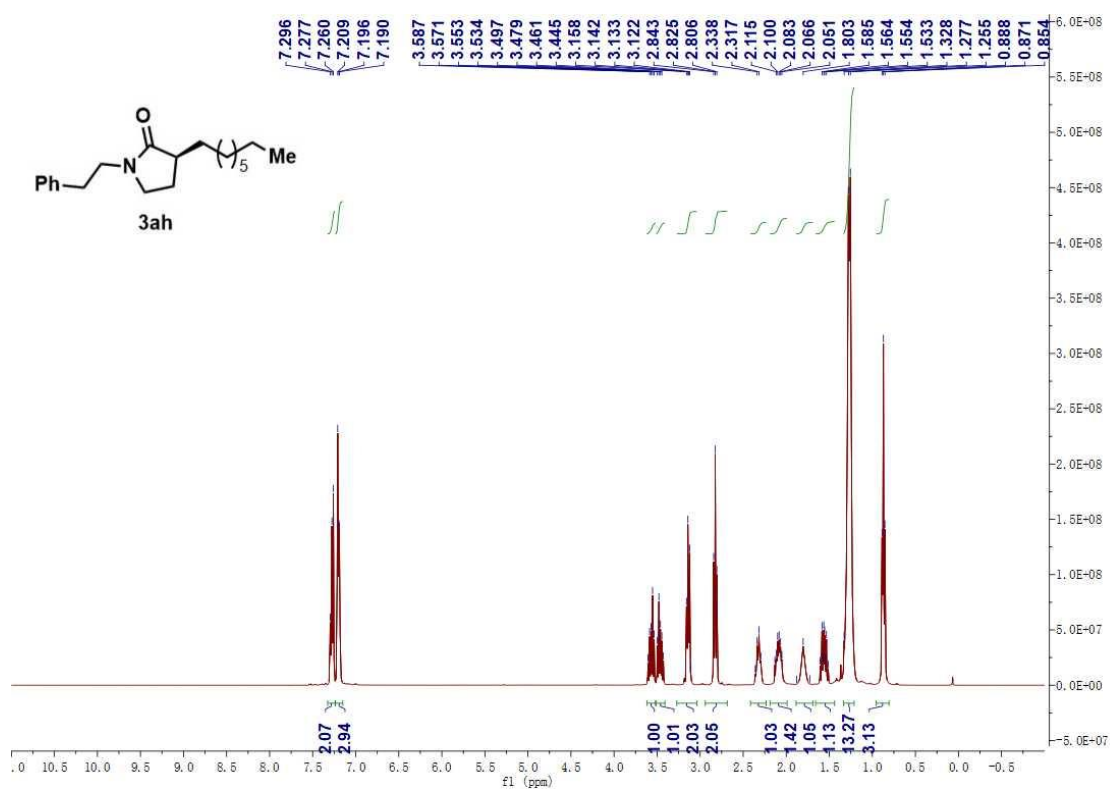
^1H NMR-spectrum (400 MHz, CDCl_3) of **3ag**



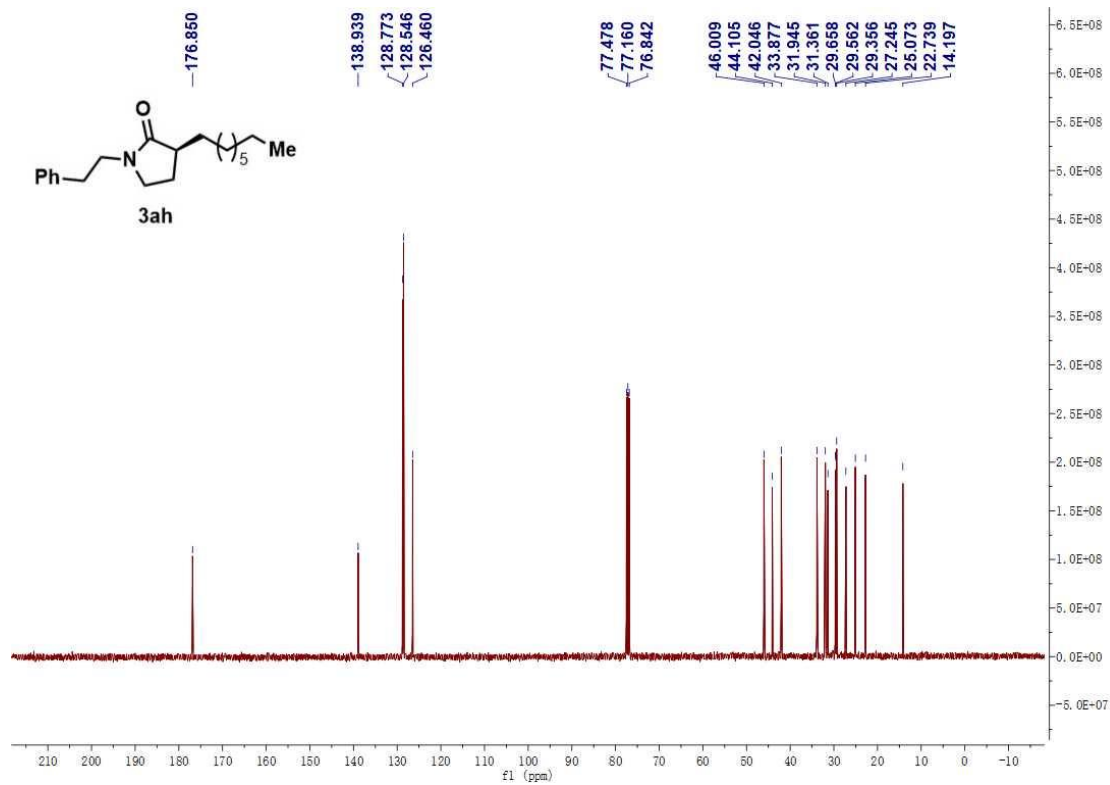
^{13}C NMR-spectrum (100 MHz, CDCl_3) of **3ag**



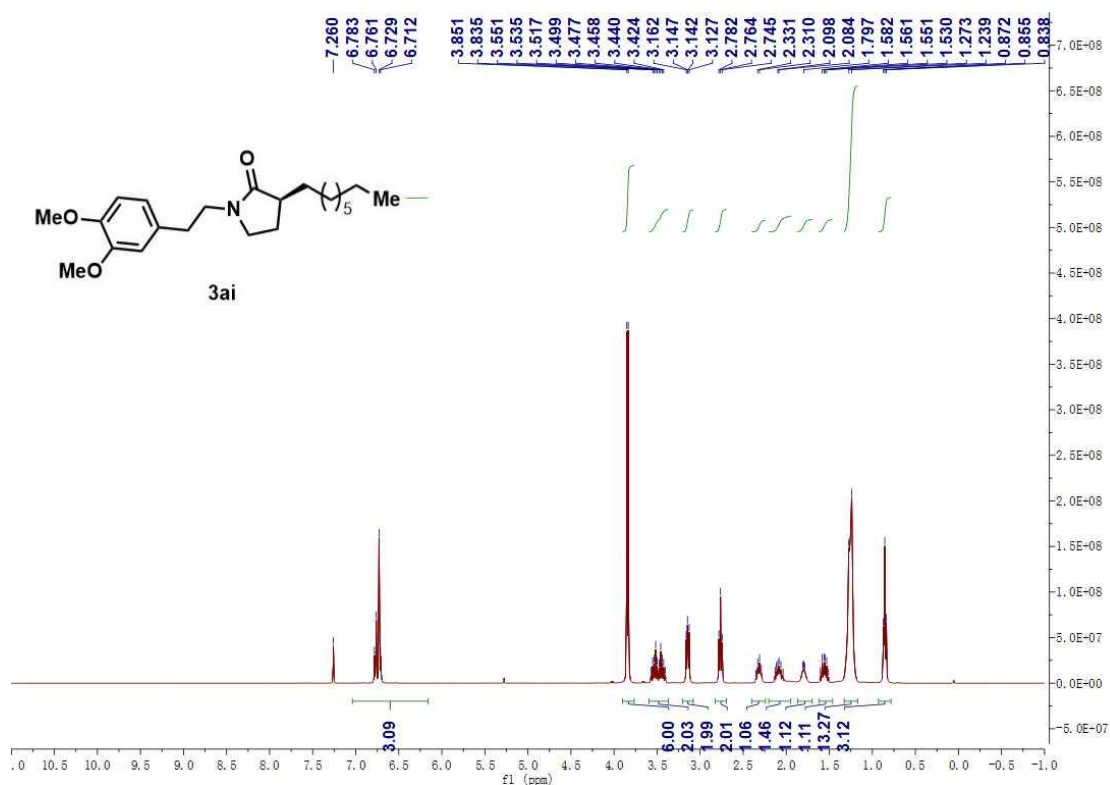
¹H NMR-spectrum (400 MHz, CDCl₃) of **3ah**



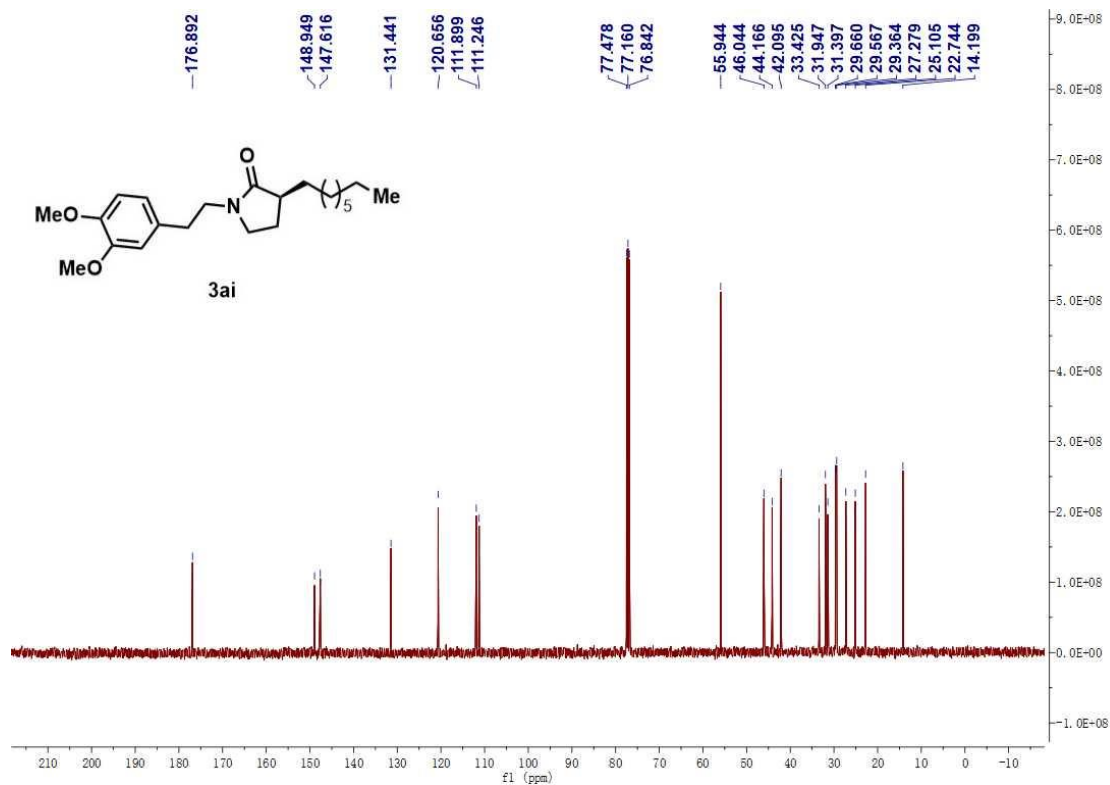
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3ah**



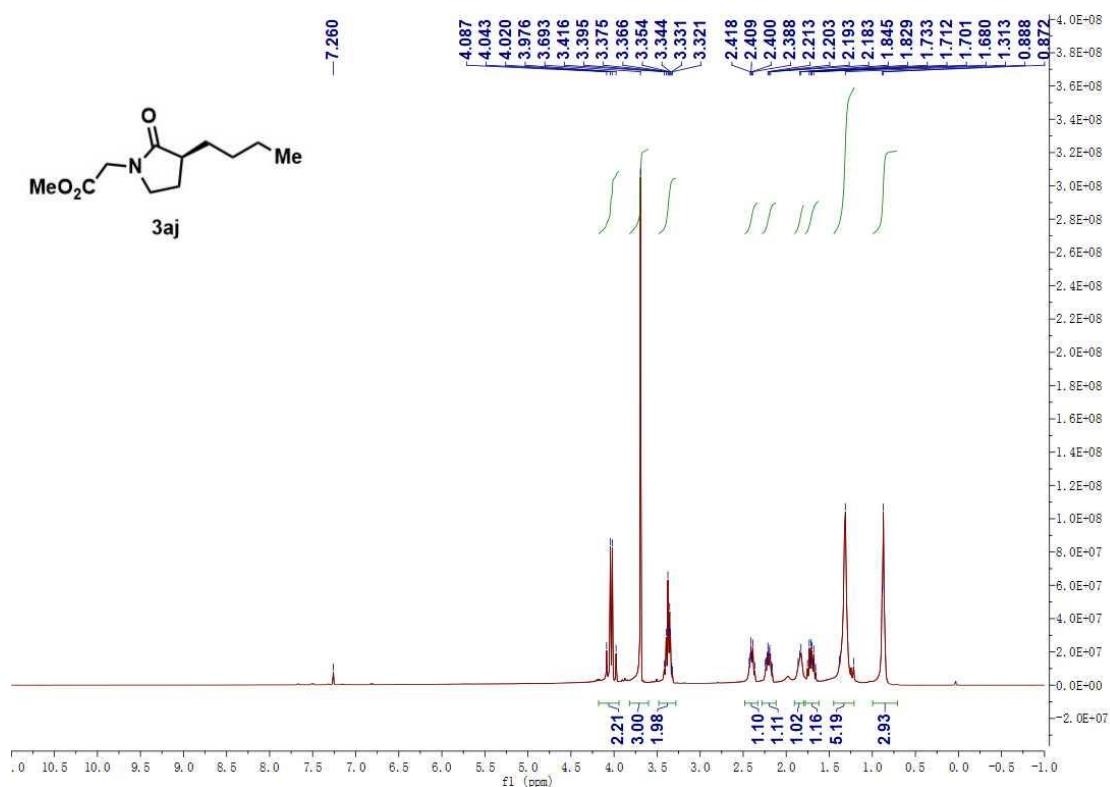
¹H NMR-spectrum (400 MHz, CDCl₃) of **3ai**



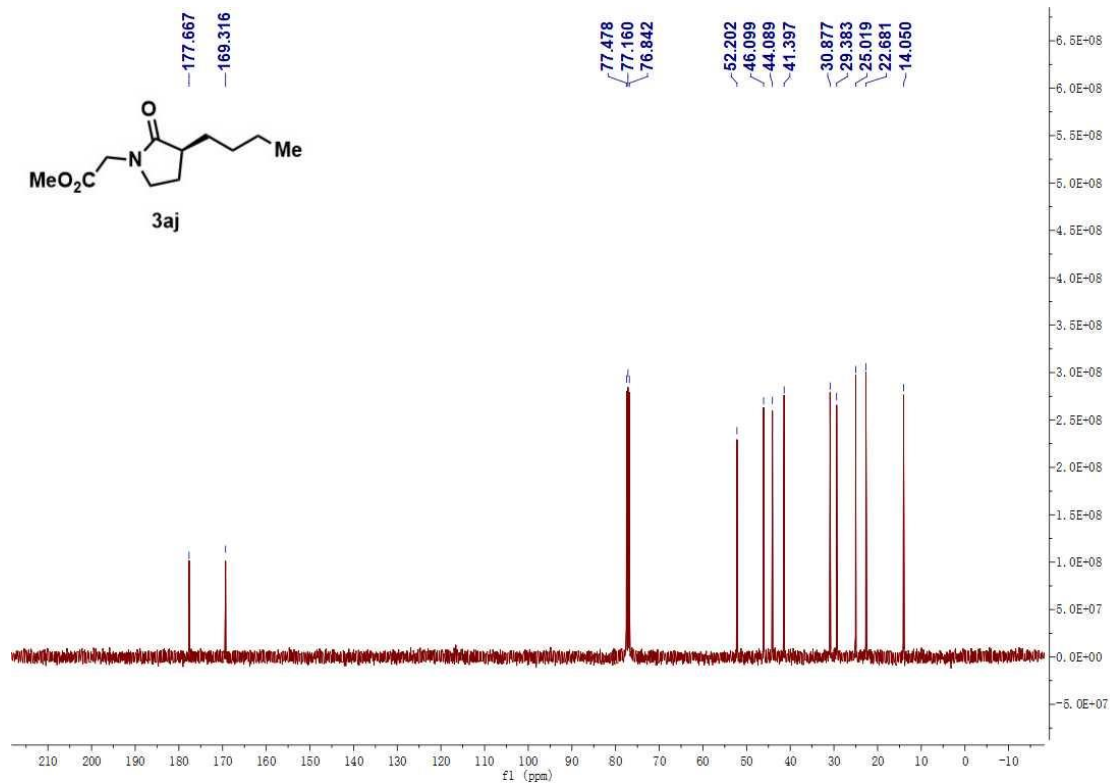
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3ai**



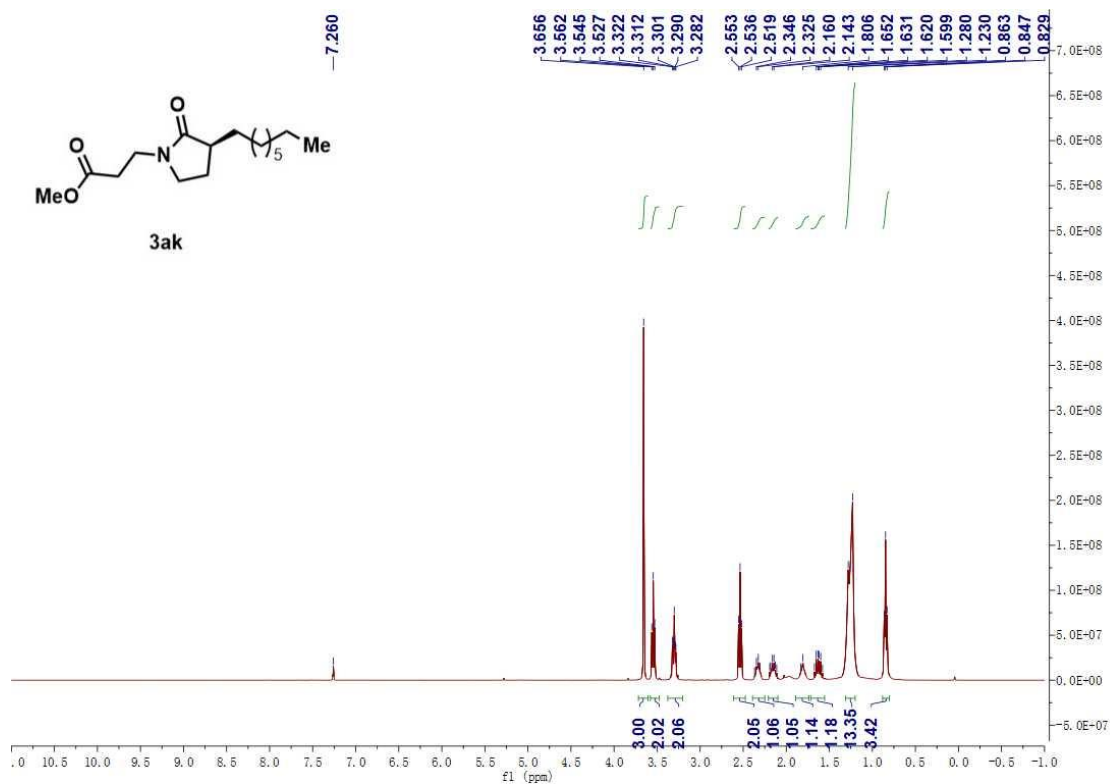
¹H NMR-spectrum (400 MHz, CDCl₃) of **3aj**



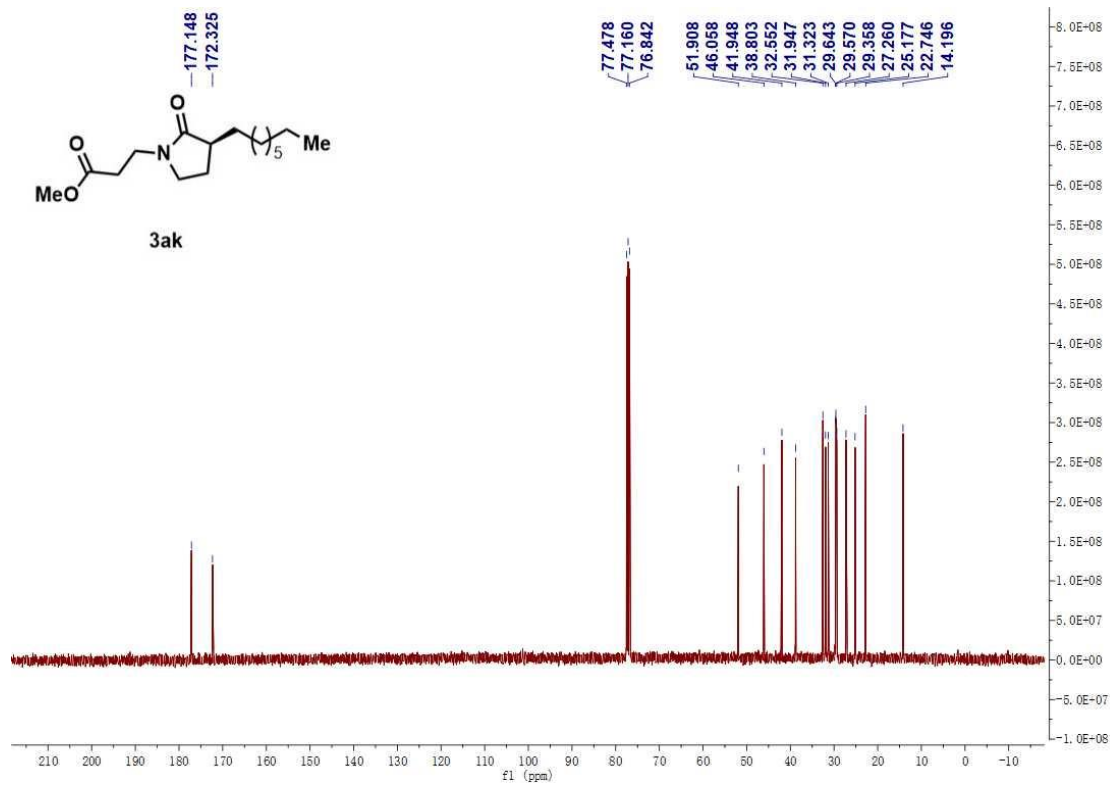
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3aj**



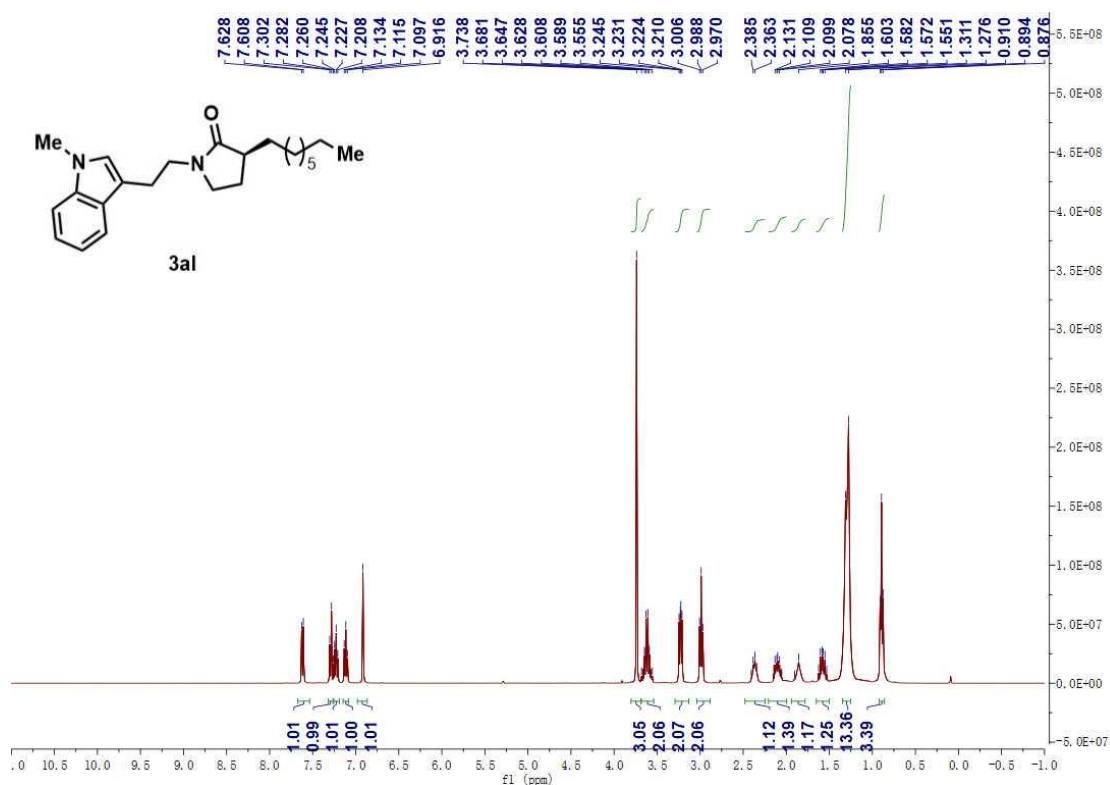
^1H NMR-spectrum (400 MHz, CDCl_3) of **3ak**



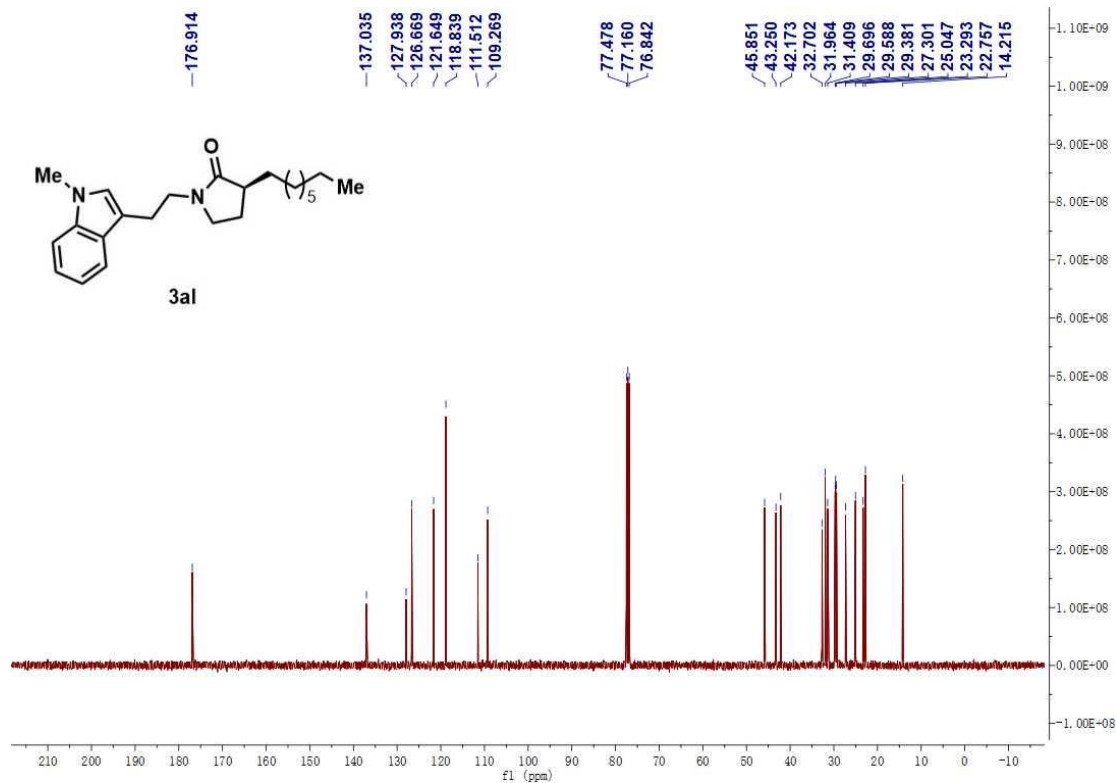
^{13}C NMR-spectrum (100 MHz, CDCl_3) of **3ak**



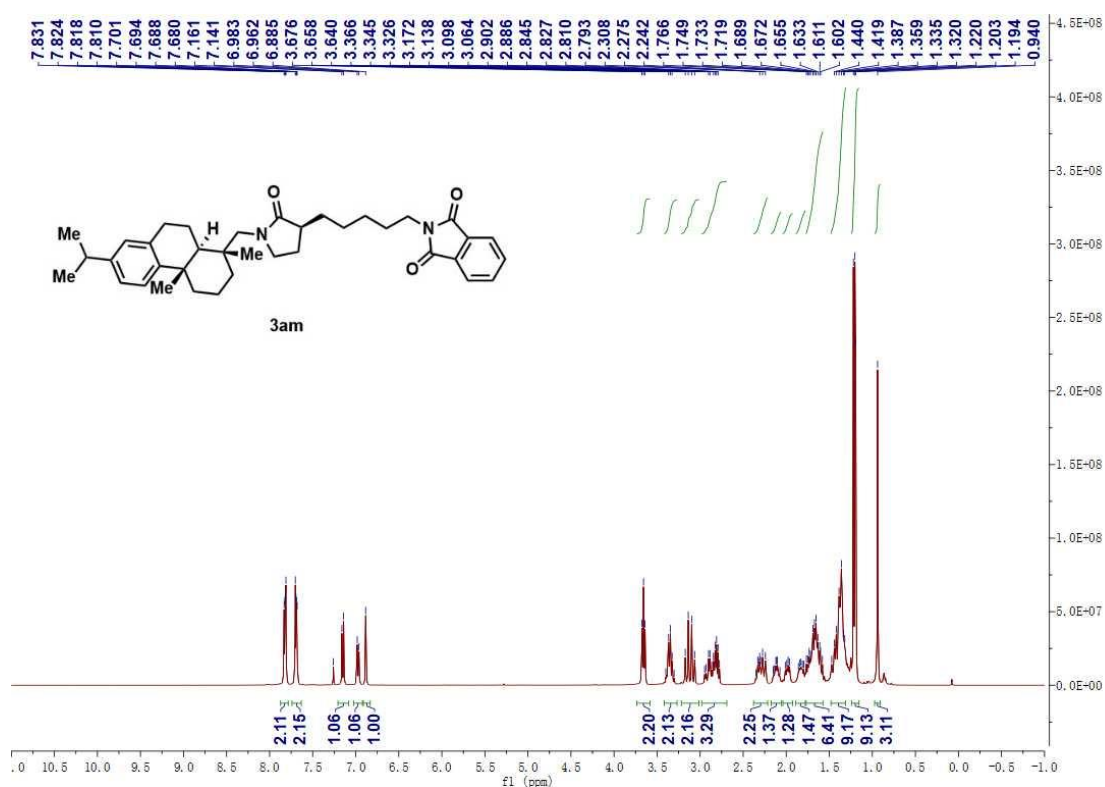
¹H NMR-spectrum (400 MHz, CDCl₃) of **3al**



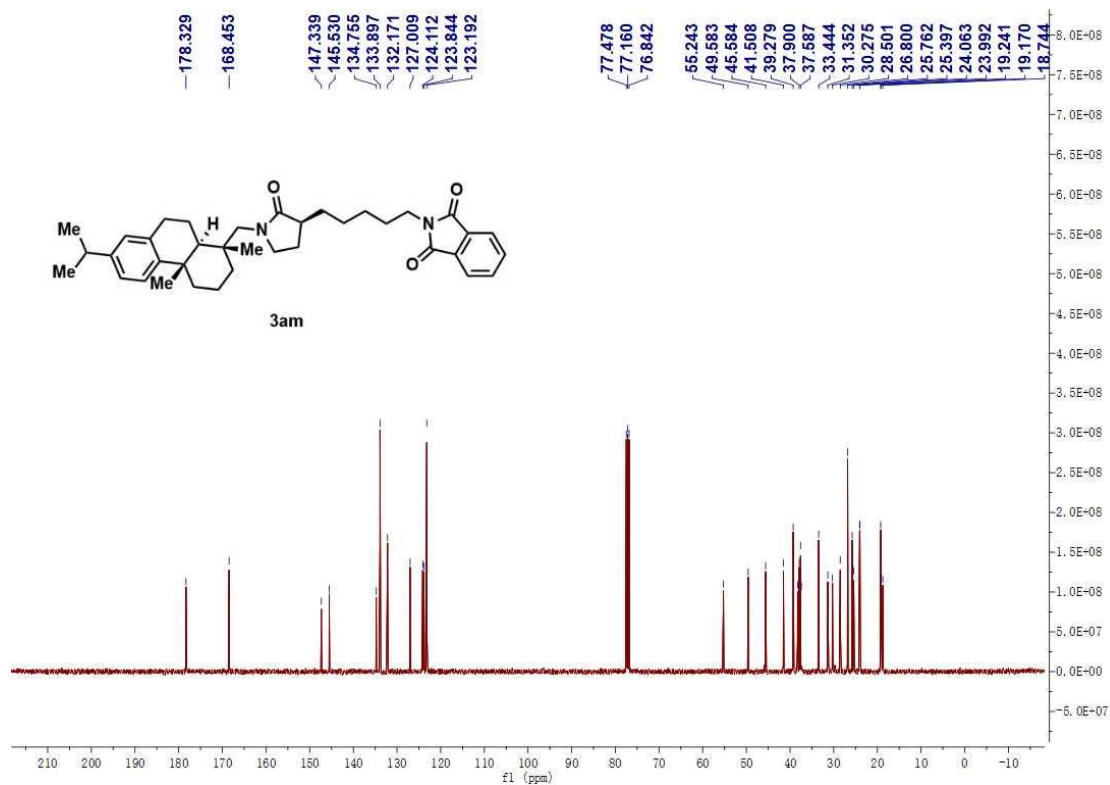
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3al**



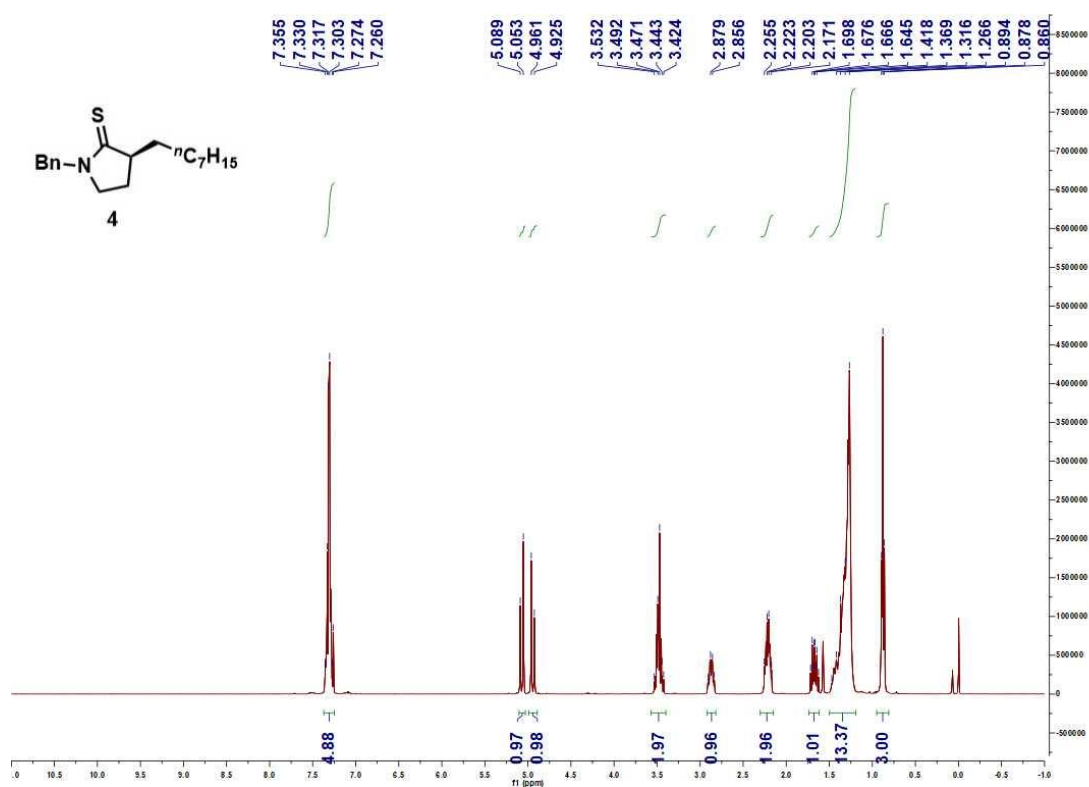
¹H NMR-spectrum (400 MHz, CDCl₃) of **3am**



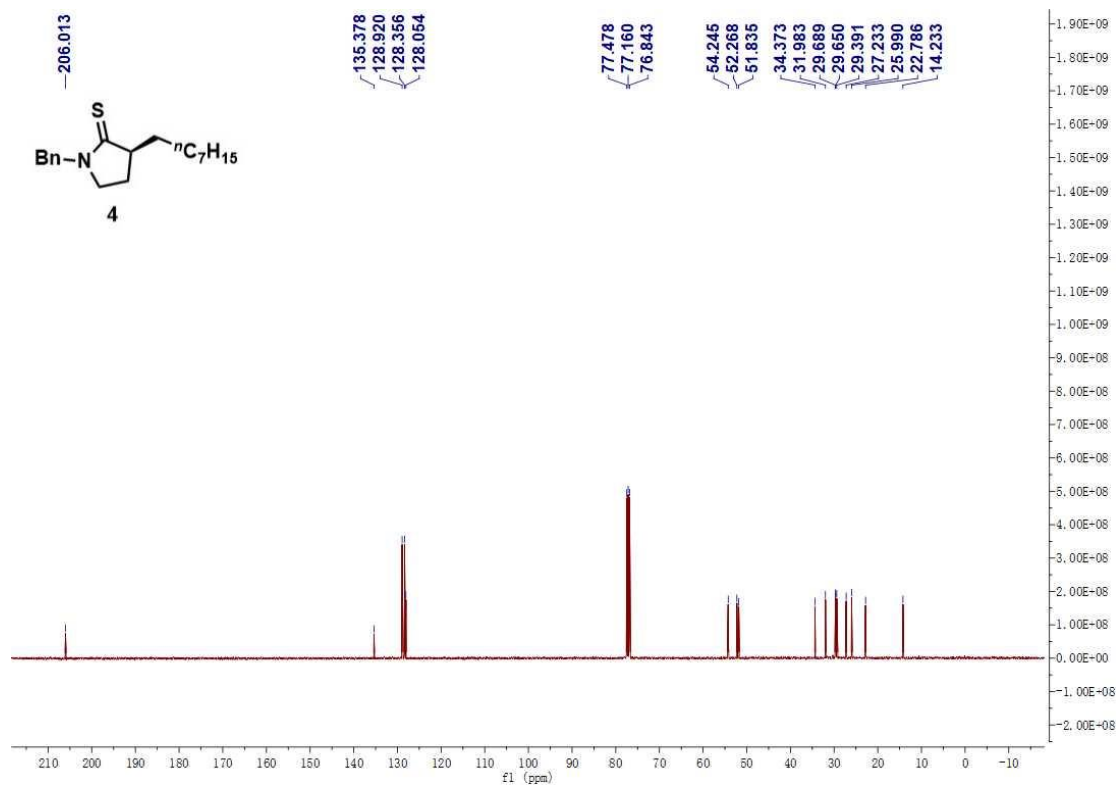
¹³C NMR-spectrum (100 MHz, CDCl₃) of **3am**



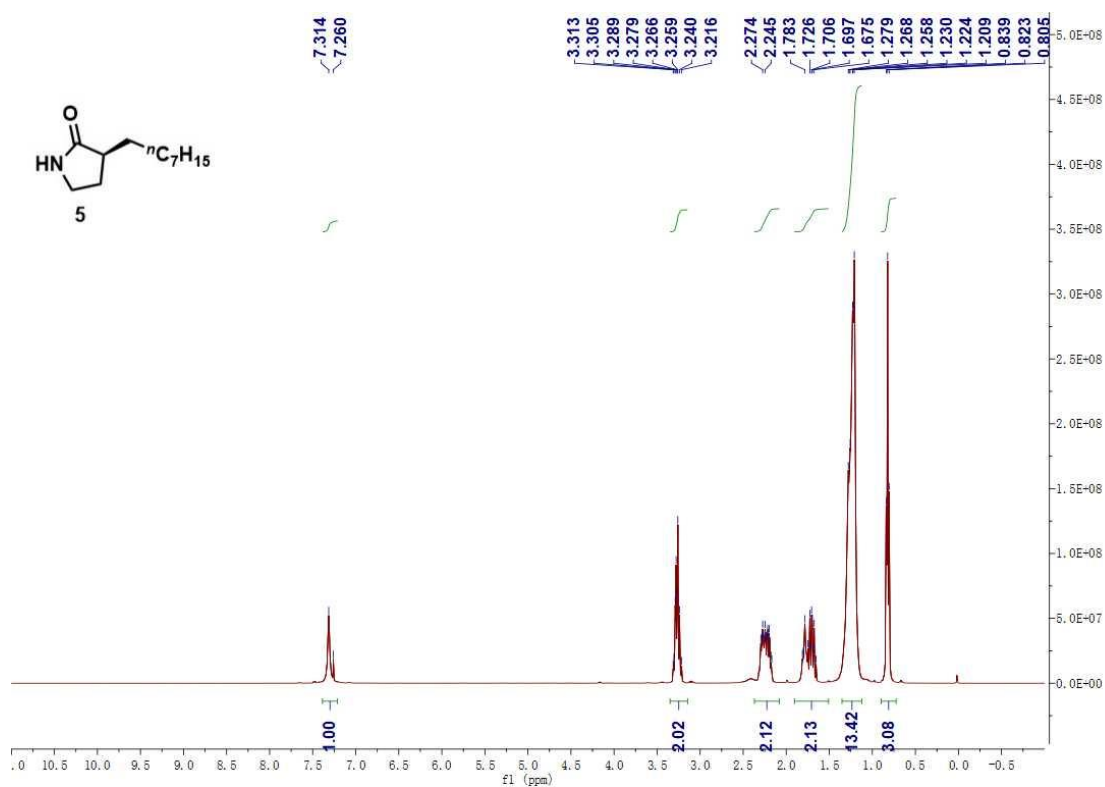
¹H NMR-spectrum (400 MHz, CDCl₃) of **4**



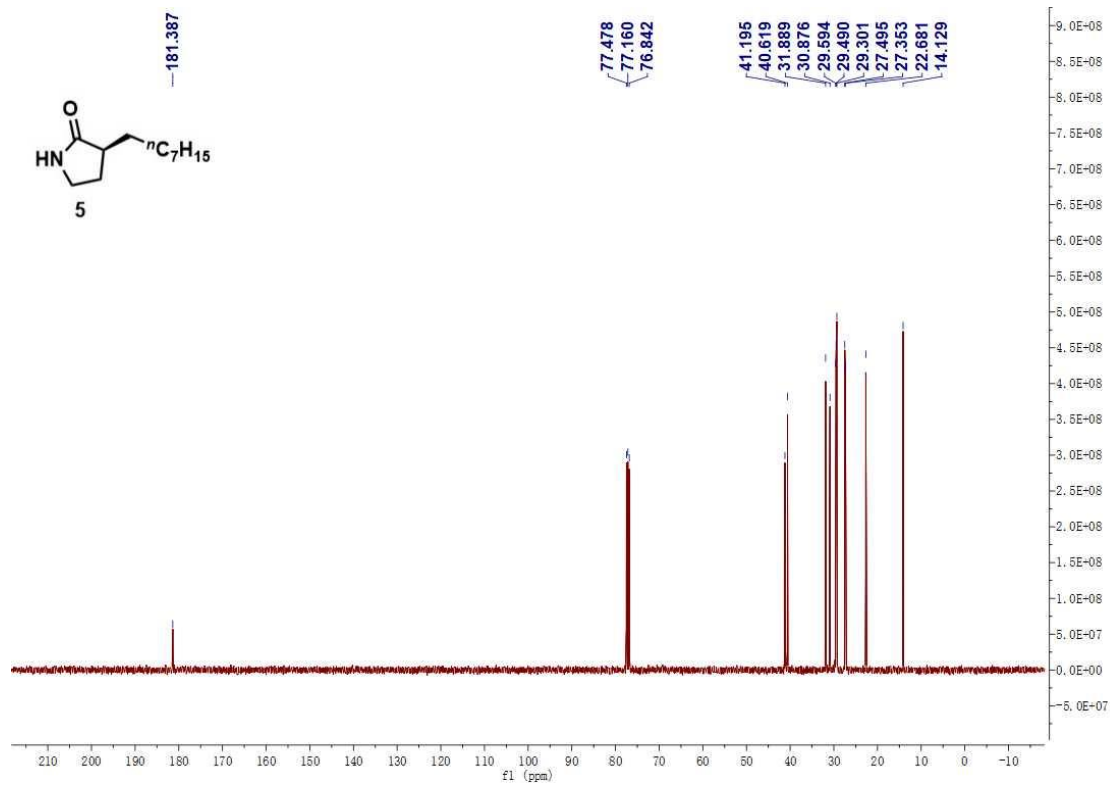
¹³C NMR-spectrum (100 MHz, CDCl₃) of **4**



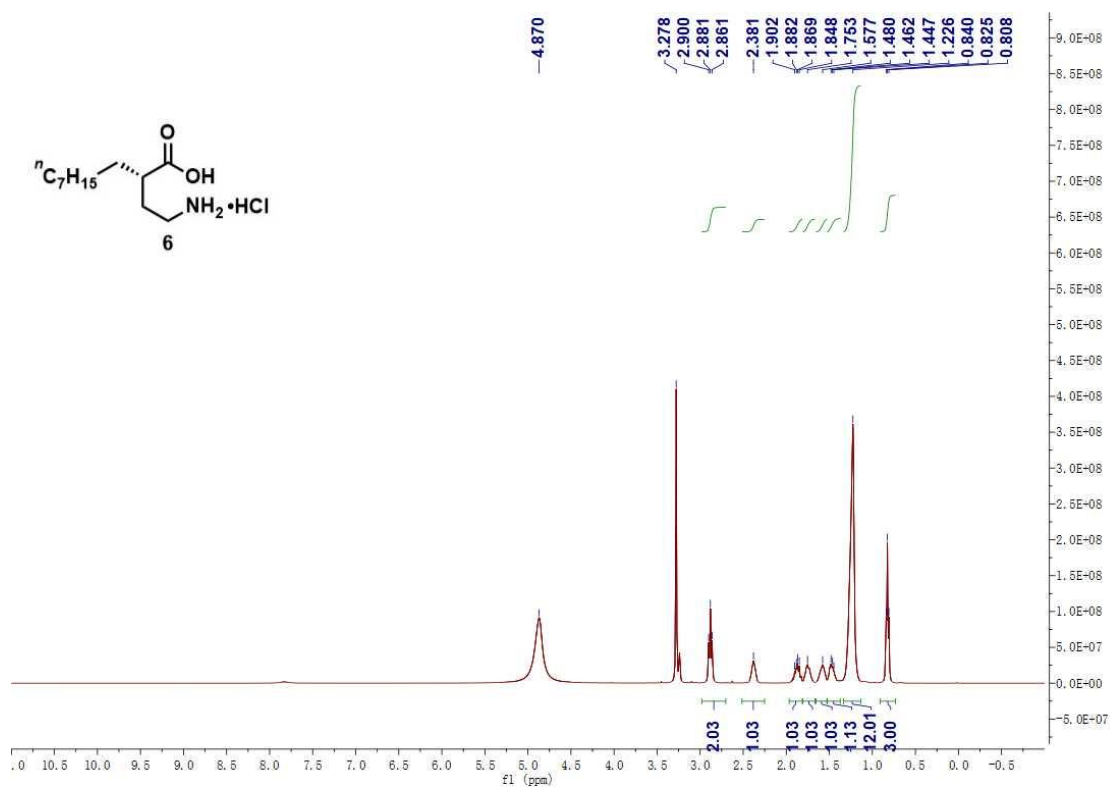
^1H NMR-spectrum (400 MHz, CDCl_3) of **5**



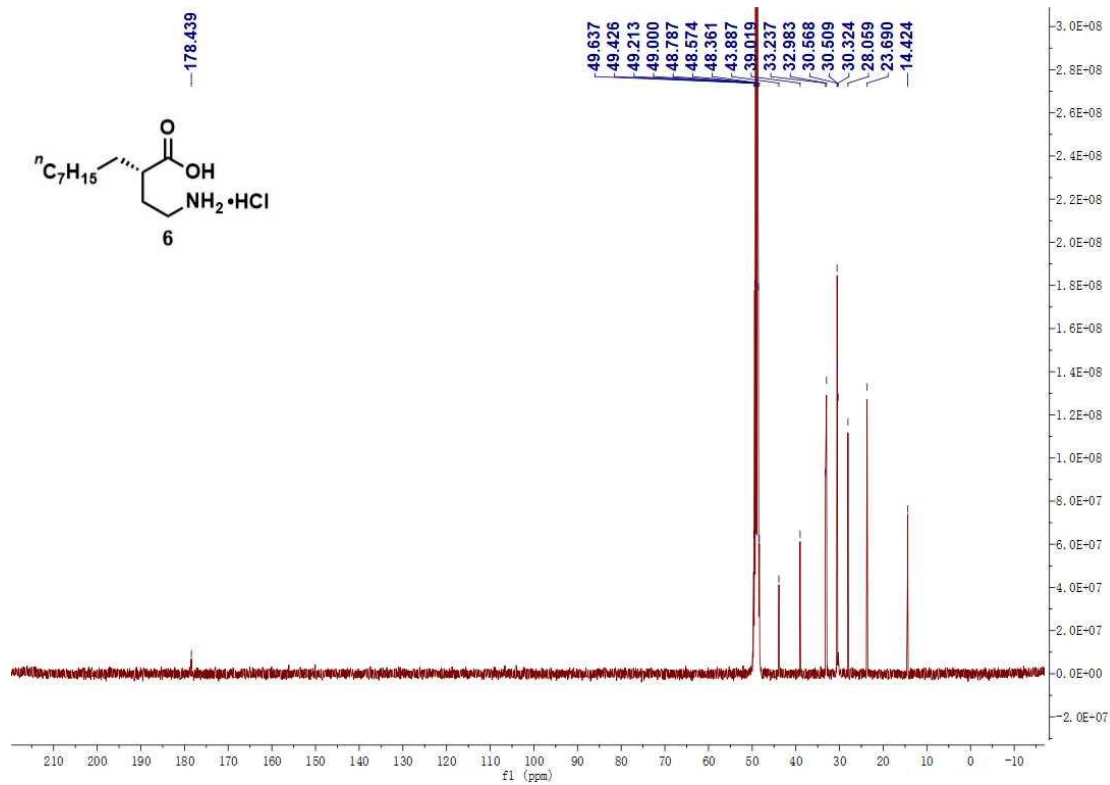
^{13}C NMR-spectrum (100 MHz, CDCl_3) of **5**



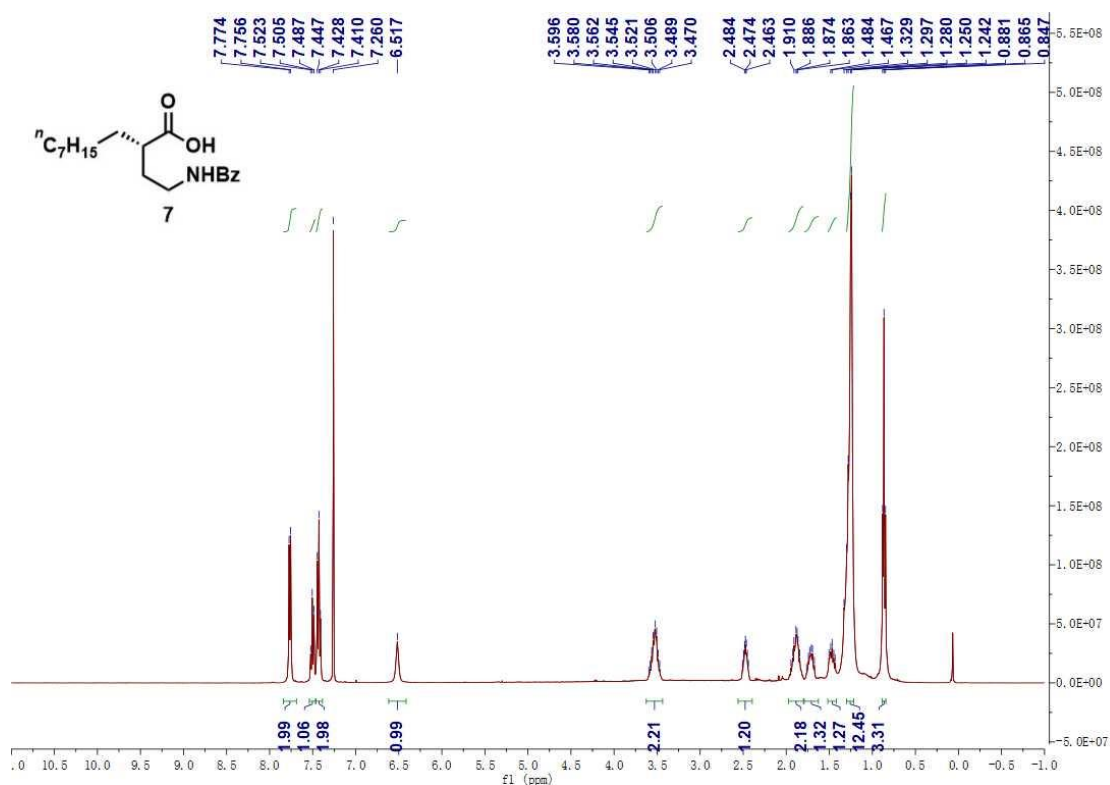
^1H NMR-spectrum (400 MHz, CDCl_3) of **6**



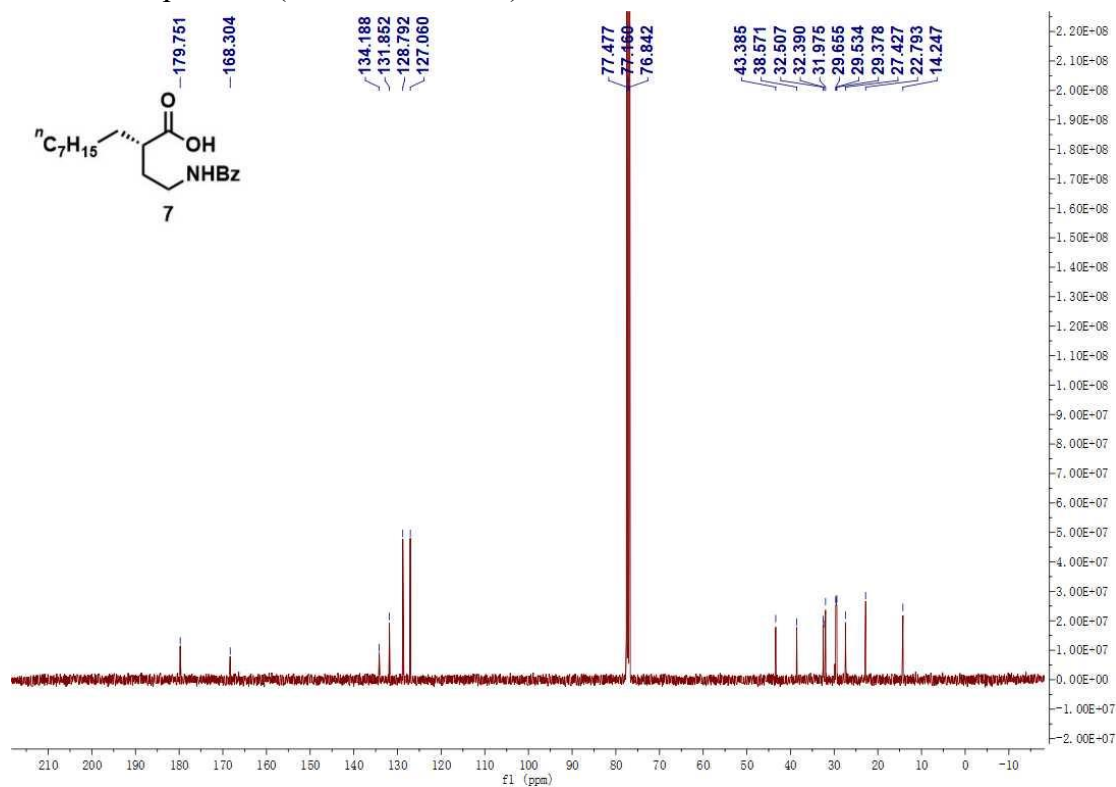
^{13}C NMR-spectrum (100 MHz, CDCl_3) of **6**



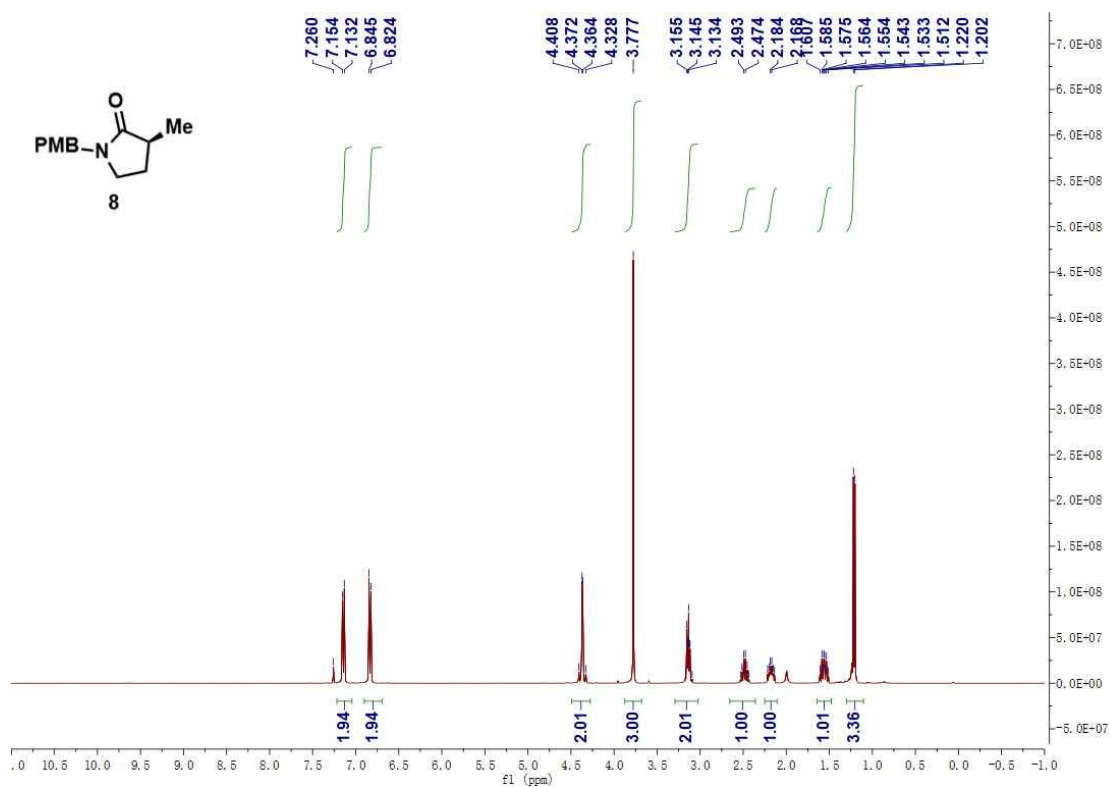
^1H NMR-spectrum (400 MHz, CDCl_3) of 7



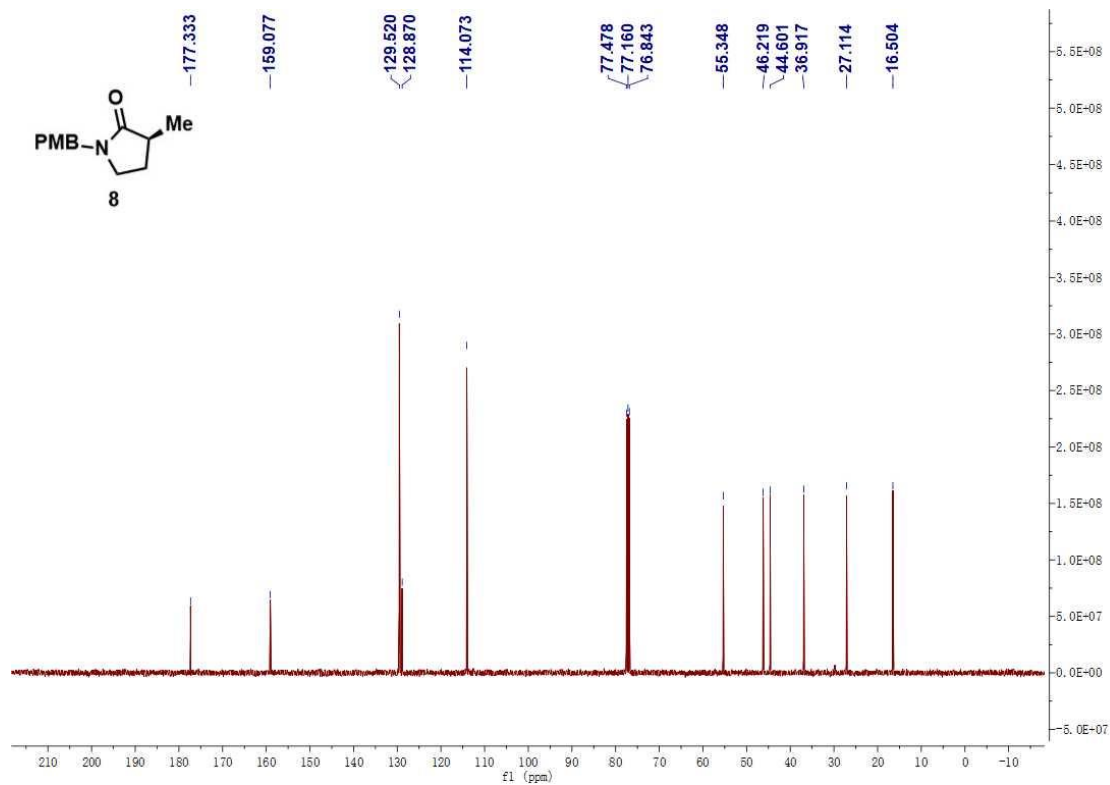
^{13}C NMR-spectrum (100 MHz, CDCl_3) of 7



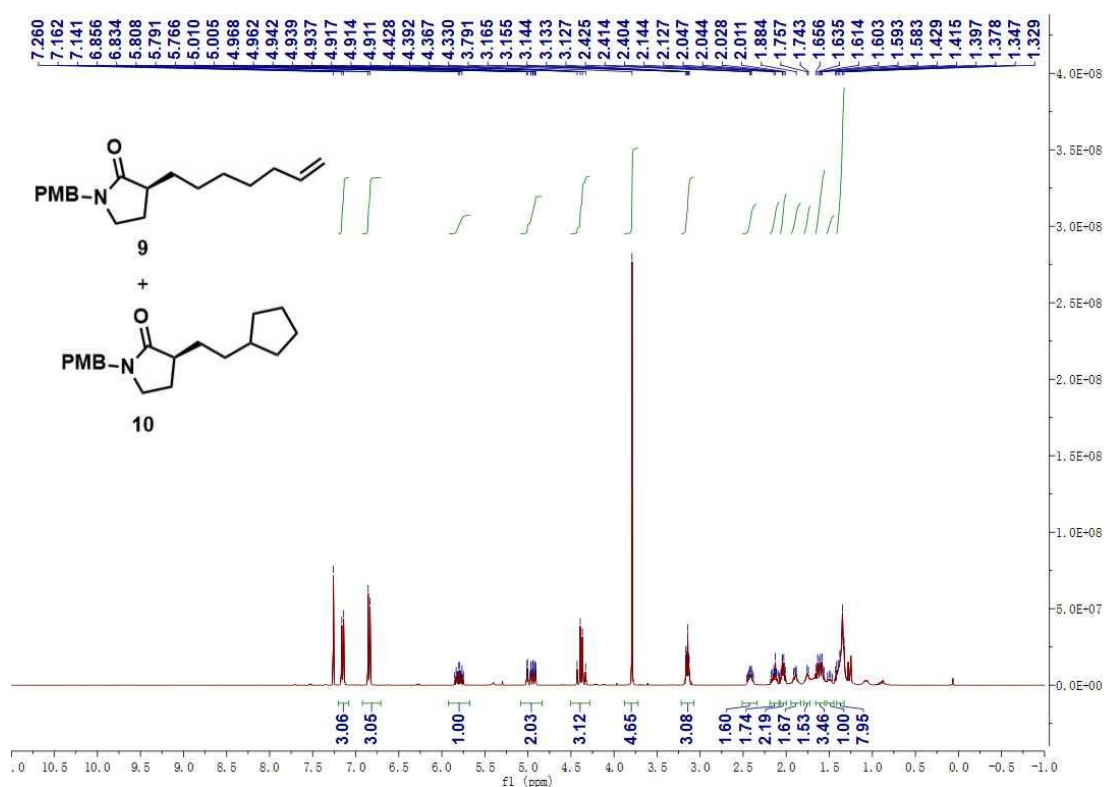
¹H NMR-spectrum (400 MHz, CDCl₃) of **8**



¹³C NMR-spectrum (100 MHz, CDCl₃) of **8**



¹H NMR-spectrum (400 MHz, CDCl₃) of **9** and **10**



¹³C NMR-spectrum (100 MHz, CDCl₃) of **9** and **10**

