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Supporting Information

# Enantioselective Copper(I)/Chiral Phosphoric Acid Catalyzed Intramolecular Amination of Allylic and Benzylic C–H Bonds

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anie_201911742_sm_miscellaneous_information.pdf

# Supporting Information

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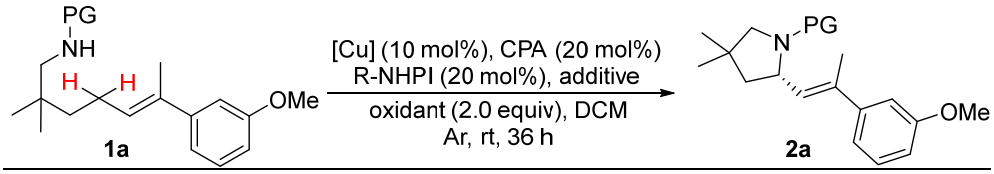
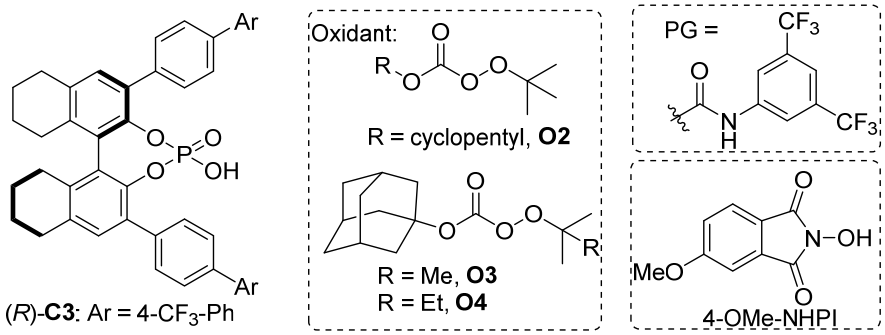
**Table S1 Optimization of reaction conditions of enantioselective allylic C−H bond amination**[a]

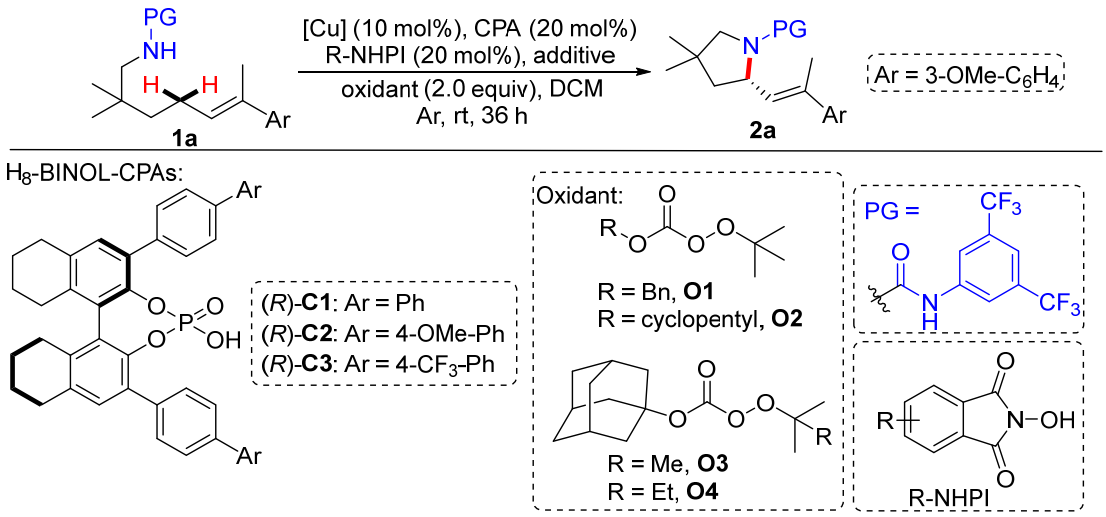



| entry | [Cu] | CPA | R-NHPI | oxidant | additive | yield(%)[b] | er[c] |
|---|---|---|---|---|---|---|---|
| 1 | CuTc | (*R*)-**C1** | --- | **O2**, **O1** *etc* | --- | 0 | N.A. |
| 2 | CuTc | (*R*)-**C1** | NHPI | **O2** | --- | 64 | 60:40 |
| 3 | CuTc | (*R*)-**C1** | 4-Me-NHPI | **O2** | --- | 50 | 71:29 |
| 4 | CuTc | (*R*)-**C1** | 4-OMe-NHPI | **O2** | --- | 72 | 75:25 |
| 5 | CuTc | (*R*)-**C2** | 4-OMe-NHPI | **O2** | --- | 78 | 69:31 |
| 6 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O2** | --- | 72 | 87:13 |
| 7 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O1** | --- | 79 | 88:12 |
| 8 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | --- | 82 | 86:14 |
| 9 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O4** | --- | 60(75) | 86:14 |
| 10 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 77 | 87:13 |
| 11[d] | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 65 | 90:10 |
| 12[d] | CuOAc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 76[h] | 93:7 |
| 13[d,e] | CuOAc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 70 | 93:7 |
| 14[f] | CuOAc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 60(90) | 93:7 |
| 15[f] | CuOAc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | --- | 45(70) | 83:17 |
| 16[d] | --- | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 0 | N.A. |
| 17[d] | CuOAc | (*R*)-**C3**[g] | 4-OMe-NHPI | **O3** | --- | 76[h] | 95:5 |

[a] Reaction was performed on a 0.025 mmol scale. [b] Ratio was determined by crude $^1$H NMR using 1,3,5-trimethoxybenzene as internal standard. [c]er value was determined by HPLC. [d] Reaction temperature was 10 °C, 72 h. [e] 30% mol (*R*)-**C3** were added. [f] Reaction temperature was 0 °C.[g]15% mol of [(R)-$C_3$]$_2$Zn was used. [h] Isolated yield. Reaction conversion was shown in parentheses. CuTc = Copper thiophene-2-carboxylate. N.A. = not available.

**Table S2 Detailed screening of reaction conditions of enantioselective allylic C−H bond amination.**

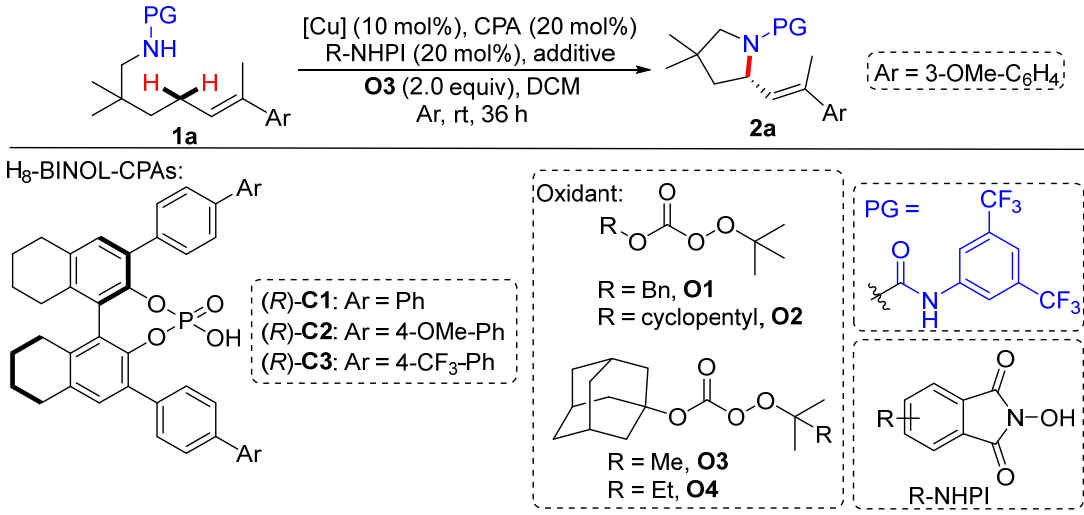



| entry | [Cu] | CPA | R-NHPI | oxidant | additive | yield(%)[b] | er[c] |
|---|---|---|---|---|---|---|---|
| 1 | CuTc | (*R*)-**C1** | --- | **O2**, **O1**, LPO, DTBP, PIDA, *etc.* | --- | 0 | N.A. |
| 2 | CuTc | (*R*)-**C1** | NHPI | **O2** | --- | 64 | 60:40 |
| 3 | CuTc | (*R*)-**C1** | 4-Me-NHPI | **O2** | --- | 50 | 71:29 |
| 4 | CuTc | (*R*)-**C1** | 4-OMe-NHPI | **O2** | --- | 72 | 75:25 |
| 5 | CuTc | (*R*)-**C2** | 4-OMe-NHPI | **O2** | --- | 78 | 69:31 |
| 6 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O2** | --- | 72 | 87:13 |
| 7 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O1** | --- | 79 | 88:12 |
| 8 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | --- | 82 | 86:14 |
| 9 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O4** | --- | 60(75) | 86:14 |
| 10 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | CaO(1.5) | 69 | 84:16 |
| 11 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | MgO(1.5) | 63 | 90:10 |
| 12 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 77 | 87:13 |
| 13[d] | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | MgO(1.5) | 65 | 83:17 |
| 14[d] | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 75 | 90:10 |
| 15[d] | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.0) | 70 | 91:9 |
| 16[d] | CuTc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(0.5) | 62(85) | 92:8 |
| 17[d] | CuOAc | (*R*)-**C3** | 4-OMe-NHPI(10%) | **O3** | ZnO(1.5) | 40(60) | 91:9 |
| 18[d] | CuOAc | (*R*)-**C3** | 4-OMe-NHPI(30%) | **O3** | ZnO(1.5) | 63(90) | 91:9 |
| 19[d] | CuOAc | --- | 4-OMe-NHPI | **O3** | ZnO(1.5) | 25(50) | N.A. |
| 20[d] | CuOAc | --- | 4-OMe-NHPI | **O3** | --- | 18(40) | N.A. |
| 21[d] | CuOAc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 76 | 93:7 |
| 22[e] | CuOAc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 60(90) | 93:7 |
| 23[d] | CuOAc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 70 | 93:7 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | (30%) | | | | | |
| 24[d] | CuOAc | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 60(90) | 93:7 |
| 25[d] | --- | (*R*)-**C3** | 4-OMe-NHPI | **O3** | ZnO(1.5) | 0 | N.A. |
| 26[d] | CuOAc | (*R*)-**C3**[f] (15%) | 4-OMe-NHPI | **O3** | --- | 76 | 95:5 |
| 27[d] | CuOAc | (*R*)-**C3**[f] (20%) | 4-OMe-NHPI | **O3** | --- | 74 | 95:5 |
| 28[d] | CuOAc | (*R*)-**C3**[f] (10%) | 4-OMe-NHPI | **O3** | --- | 74 | 93:7 |

[a] Reaction was performed on a 0.025 mmol scale. [b] Ratio was determined by crude $^1$H NMR using 1,3,5-trimethoxybenzene as internal standard. [c]er value was determined by HPLC. [d] Reaction temperature was 10 °C, 72 h. [e] Reaction temperature was 0 °C. [f] (*R*)-**C3** was pre-treated with 0.5 equiv. of $ZnEt_2$. [g] Isolated yield. Reaction conversion was shown in parentheses. N.A. = not available.

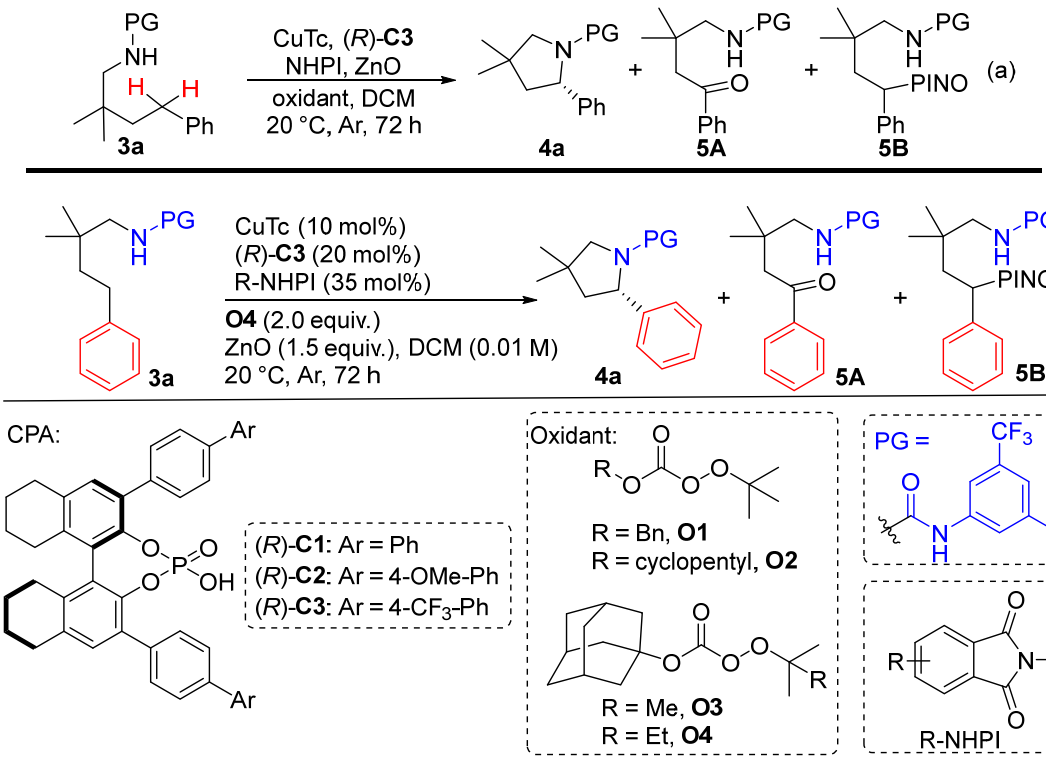
**Table S3 Reaction conditions screening of enantioselective allylic C−H bond amination**




| entry | [Cu] | CPA | R-NHPI | additive | yield(%)[b] | er[c] |
|---|---|---|---|---|---|---|
| 1 | CuTc | (*R*)-**C3** | 4-OMe-NHPI | ZnO(1.5) | 65 | 91:9 |
| 2 | CuCN | (*R*)-**C3** | 4-OMe-NHPI | ZnO(1.5) | 30(50) | 80:20 |
| 3 | CuBr | (*R*)-**C3** | 4-OMe-NHPI | ZnO(1.5) | 78 | 89:11 |
| 4 | CuCl | (*R*)-**C3** | 4-OMe-NHPI | ZnO(1.5) | 72 | 90:10 |
| 5 | $Cu_2S$ | (*R*)-**C3** | 4-OMe-NHPI | ZnO(1.5) | 28(40) | 72:28 |
| 6 | CuOAc | (*R*)-**C3** | 4-OMe-NHPI | ZnO(1.5) | 76 | 93:7 |
| 7[c] | CuOAc(15%) | (*R*)-**C3**(30%) | 4-OMe-NHPI | ZnO(1.5) | 68(90) | 90:10 |
| 8[d] | CuOAc(5%) | (*R*)-**C3**(10%) | 4-OMe-NHPI | ZnO(1.5) | 62(80) | 92:8 |
| 9[d] | CuOAc(5%) | (*R*)-**C3**(15%) | 4-OMe-NHPI | ZnO(1.5) | 60(78) | 85:15 |
| 10[d] | CuOAc(10%) | (*R*)-**C3**(10%) | 4-OMe-NHPI | ZnO(1.5) | 60(78) | 90:10 |
| 11[d] | CuOAc(10%) | (*R*)-**C3**(15%) | 4-OMe-NHPI | ZnO(1.5) | 60(80) | 87:13 |
| 12[d] | CuOAc(15%) | (*R*)-**C3**(10%) | 4-OMe-NHPI | ZnO(1.5) | 61(81) | 82:18 |
| 13[d] | CuOAc(10%) | (*R*)-**C3**(25%) | 4-OMe-NHPI | ZnO(1.5) | 60(80) | 92:8 |

[a] Reaction was performed on a 0.025 mmol scale. [b] Ratio was determined by crude $^1$H NMR using 1,3,5-trimethoxybenzene as internal standard. [c] -5 °C. [d] 0 °C. Reaction conversion was shown in parentheses. N.A. = not available.

**Table S4 Optimization of reaction conditions of enantioselective benzylic C−H bond amination[a]**




| entry | Variation from standard conditions | Conv. (%) | Yield of **2a**/(**5A**/**5B**)[b] | ee (%)[c] |
|---|---|---|---|---|
| 1 | without 4-OMe-NHPI | <5% | trace(-/-) | N.A. |
| 2 | NHPI instead of 4-OMe-NHPI | 40 | 1/2.8 | 87 |
| 3 | 4-Me-NHPI instead of 4-OMe-NHPI | 42 | 1/2.0 | 92 |
| 4 | 3-F-NHPI instead of 4-OMe-NHPI | 50 | 1/1.5 | 70 |
| 5 | **O1** instead of **O4** | 40 | 30(6/4) | 70 |
| 6 | **O2** instead of **O4** | 42 | 33(4/2) | 85 |
| 7 | **O3** instead of **O4** | 43 | 34(6/4) | 81 |
| 8 | without (*R*)-**C3** | 20 | 10(4/5) | N.A. |
| 9 | (*R*)-**C1** instead of (*R*)-**C3** | 30 | 24(2/3) | 84 |
| 10 | (*R*)-**C2** instead of (*R*)-**C3** | 34 | 27(4/-) | 81 |
| 11 | none | 35 | 30(2/-) | 94 |
| 12 | without ZnO | 20 | 15(3/-) | 86 |
| 13[d] | $(CPA)_2Zn$ instead of (*R*)-**C3** and ZnO | 30 | 22(2/-) | 98 |
| 14 | without CuTc | <5% | trace(-/-) | N.A. |
| 15[e] | 4-OMe-NHPI (1.0 equiv), **O4** (3.0 equiv) | 55 | 40(-/-)(67[f]) | 90 |
| 16[d,g] | 4-OMe-NHPI (1.0 equiv), **O4** (3.0 equiv) | 50 | 38(3/4)(76[f]) | 88 |

[a] Reaction was performed on a 0.025 mmol scale. [b] Ratio was determined by crude $^1$H NMR using 1,3,5-trimethoxybenzene as internal standard. [c]ee value on HPLC. [d] Zinc phosphate (20 mol%) was used. [e] (*R*)-**C3** (5 mol%) was added at 12 h and 36 h respectively and $NaSbF_6$ (1.0 equiv) was added.

Reaction was performed on a 0.1 mmol scale and reaction time was 7 days. [f]Isolated yield in parentheses was based on recovered starting material. [g] (*R*)-**C3** (5 mol%) was added at 18 h and 40 h respectively. Reaction was performed on a 0.1 mmol scale and reaction time was 7 days. N.A. = not available.

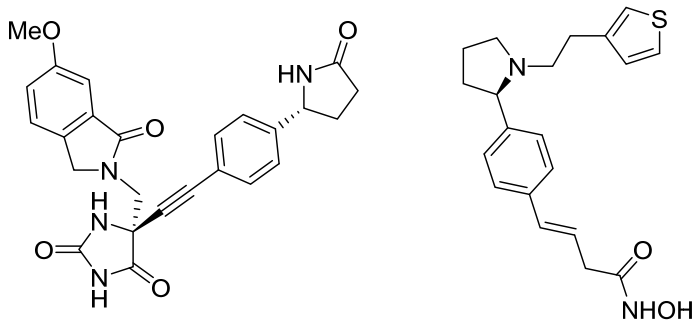
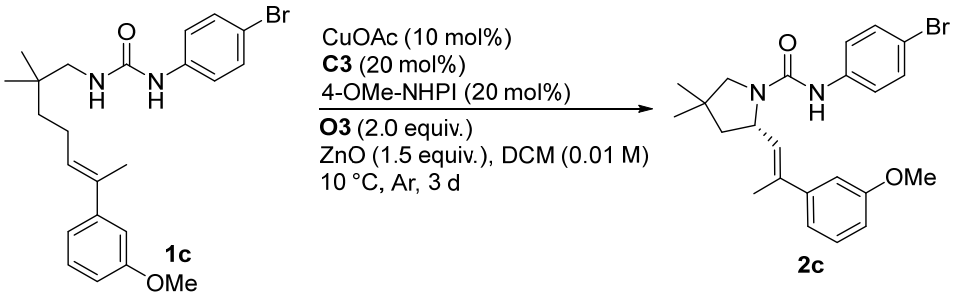



**Figure S1** Bioactive molecules containing chiral α-aryl pyrrolidines with olefin or alkyne functional groups at para position




| ee of **C3** (%) | 1st run ee **2c** (%) | 2nd run ee **2c** (%) | 3rd ee **2c** (%) | average (%) |
|---|---|---|---|---|
| 0 | -3.1 | -1.0 | 4.3 | 0.07 |
| 20(*R*) | 25.9 | 26.6 | 27.0 | 26.5 |
| 40(*R*) | 55.3 | 51.9 | 53.0 | 53.4 |
| 60(*R*) | 66.5 | 66.4 | 63.0 | 65.3 |
| 80(*R*) | 77.0 | 75.7 | 76.0 | 76.2 |
| 99(*R*) | 86.0 | 86.0 | 86.0 | 86.0 |

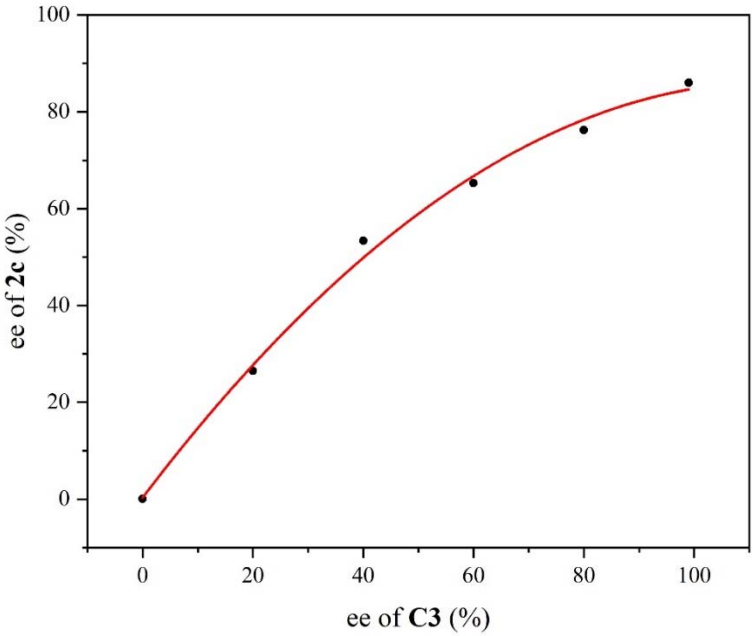
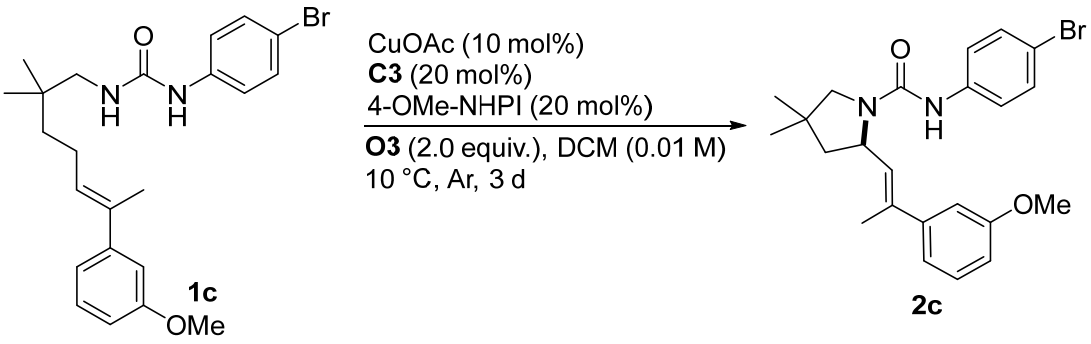



**Figure S2 Non-linear effect experiments in the presence of ZnO**




| ee of **C3** (%) | 1st run ee **2c** (%) | 2nd run ee **2c** (%) | average (%) |
|---|---|---|---|
| 0 | 6 | 8 | 7 |
| 20(*R*) | 17 | 20 | 18.5 |
| 40(*R*) | 33 | 30 | 31.5 |
| 60(*R*) | 37 | 39 | 38 |
| 80(*R*) | 55 | 53 | 54 |
| 99(*R*) | 66 | 68 | 67 |

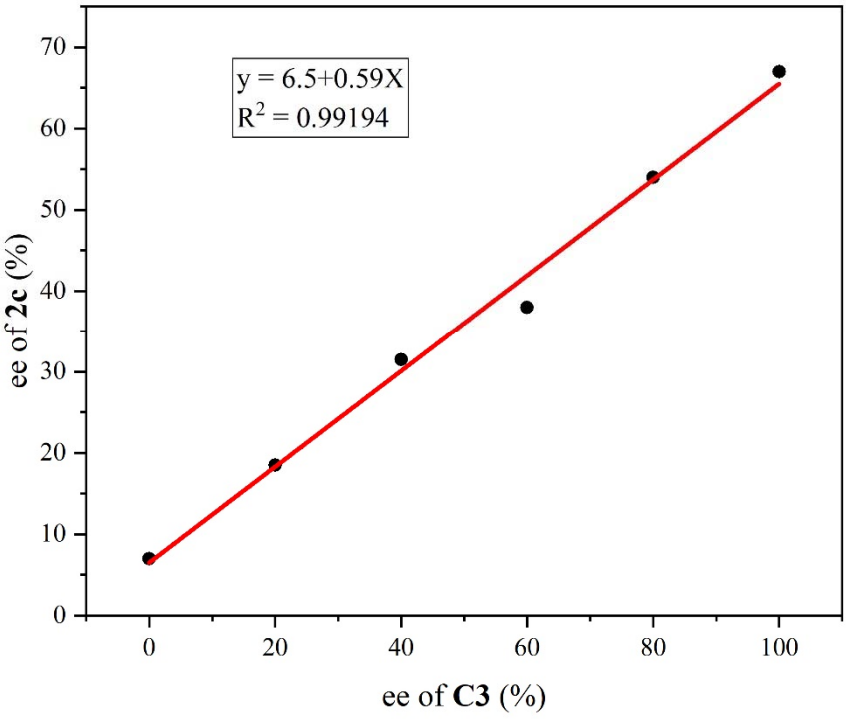
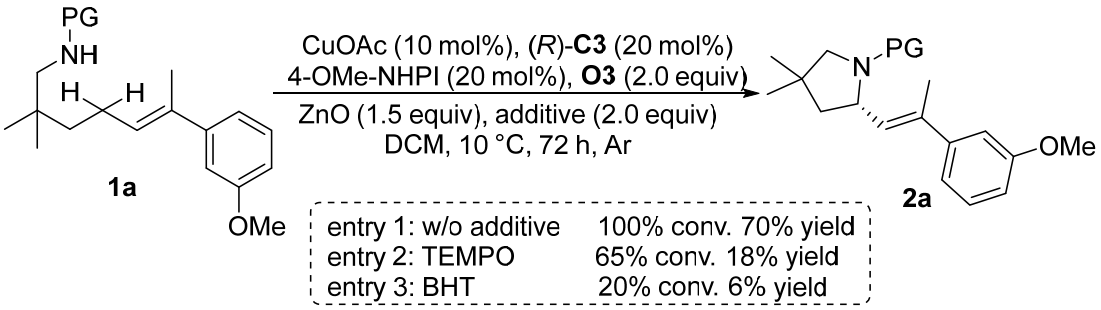
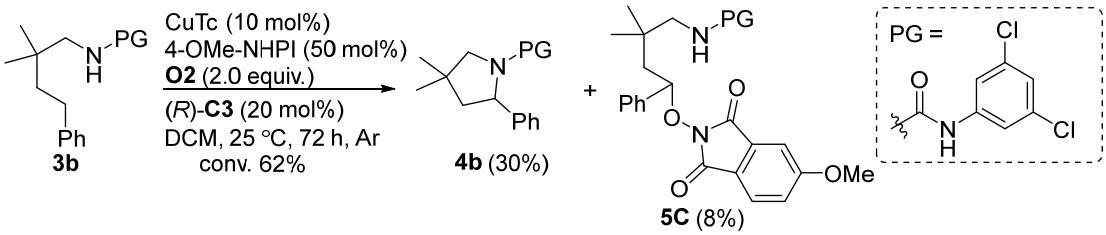


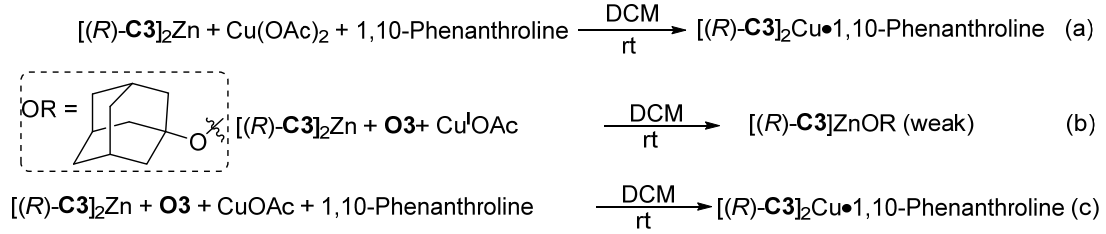

**Figure S3 Linear effect experiments without ZnO**




**Scheme S1 Control experiments with radical inhibitors**

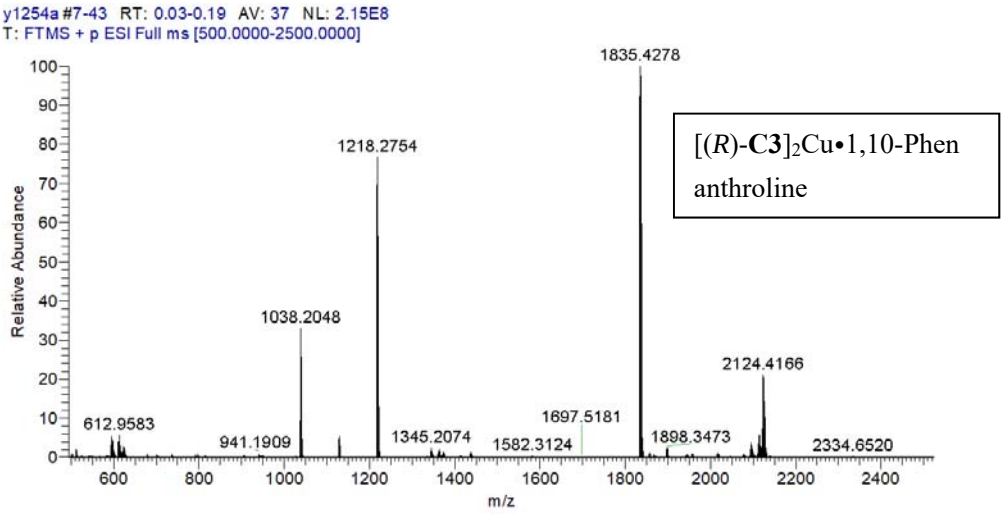



**Scheme S2 Benzylic C–H amination of 3b**

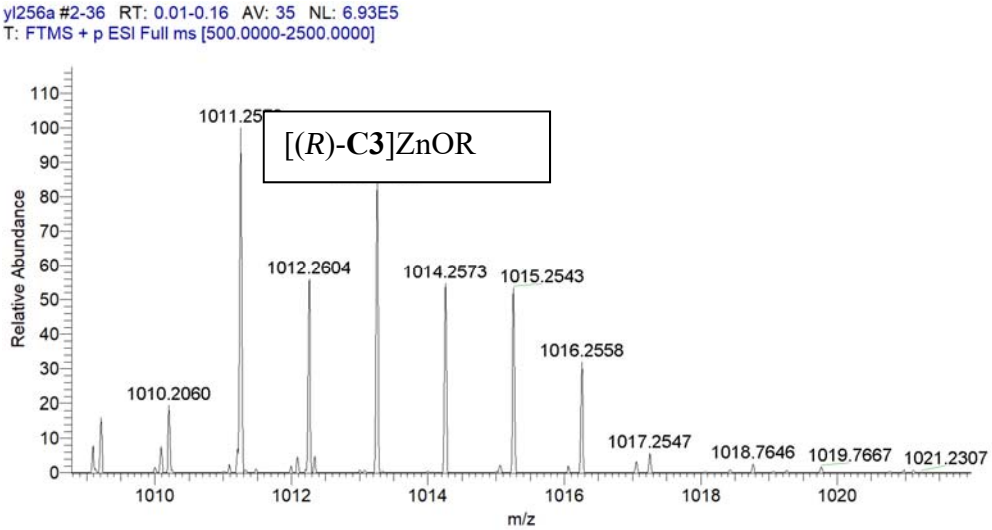



**Scheme S3 Transmetallation between Cu(II) and $(CPA)_2Zn$**

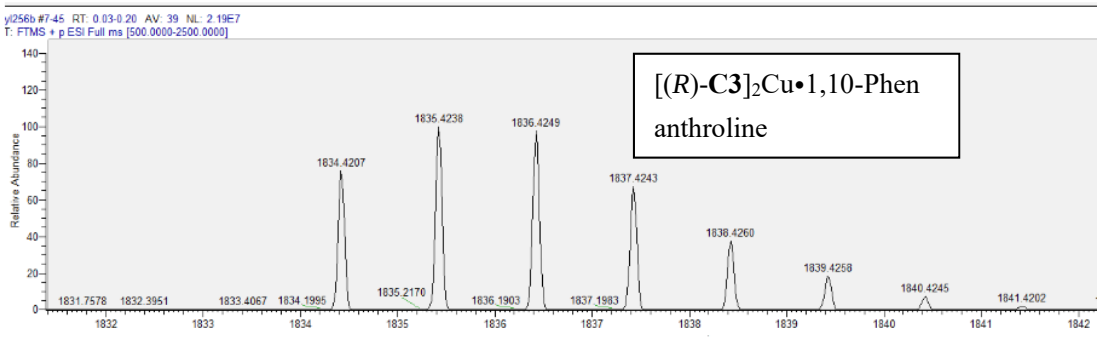
**Scheme S3-a**: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added [(*R*)-**C3**]$_2$Zn (6.23 mg, 1.5 equiv.), $Cu(OAc)_2$ (0.46 mg 1.0 equiv.) and 1,10-Phenanthroline (0.54 mg, 1.2 equiv.). The tube was evacuated and backfilled with argon for three times, then dry DCM (0.5 mL) was added *via* syringe. The tube was stirred at rt overnight. The reaction mixture was evaporated and the sample was analyzed by ESI-MS. The following peaks were observed: **HRMS** (ESI) m/z calcd. for $C_{104}H_{77}F_{12}N_2O_8P_2Cu$ $[M+H]^+$ 1834.4254, found 1834.4246.




**Scheme S3-b**: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added [(*R*)-**C3**]$_2$Zn (8.3 mg, 1.5 equiv.), CuOAc (0.62 mg 1.5 equiv.) and **O3** (0.9 mg, 1.0 equiv.). The tube was evacuated and backfilled with argon for three times, then dry DCM (0.5 mL) was added *via* syringe. The tube was stirred at rt for 3 h. The reaction mixture was evaporated and the sample was analyzed by ESI-MS. The following peaks were observed: **HRMS** (ESI) m/z calcd. for $C_{56}H_{50}F_6O_5PZn$ $[M+H]^+$ 1011.2586, found 1011.2570 (weak).



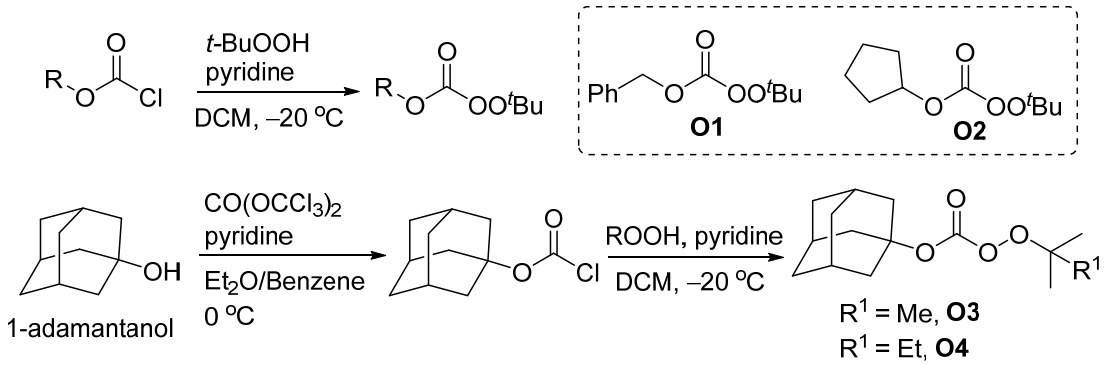

**Scheme S3-c**: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added [(*R*)-**C3**]$_2$Zn (8.3 mg, 1.5 equiv.), CuOAc (0.62 mg 1.5 equiv.), **O3** (0.9 mg, 1.0 equiv.) and 1,10-Phenanthroline (1.5 mg, 2.5 equiv.). The tube was evacuated and backfilled with argon for three times, then dry DCM (0.5 mL) was added *via* syringe. The tube was stirred at rt for 3 h. The reaction mixture was evaporated and the sample was analyzed by ESI-MS. The following peaks were observed: **HRMS** (ESI) m/z calcd. for $C_{104}H_{77}F_{12}N_2O_8P_2Cu$ $[M+H]^+$ 1834.4254, found 1834.4214.


yl256b #7-45 RT: 0.03-0.20 AV: 39 NL: 2.19E7
T: FTMS + p ESI Full ms [500.0000-2500.0000]
[(R)-C3]2Cu•1,10-Phenanthroline
Relative Abundance
1834.4207
1835.4238
1836.4249
1837.4243
1838.4260
1839.4258
1840.4245
1841.4202
1831.7578
1832.3951
1833.4067
1834.1995
1835.2170
1836.1903
1837.1983

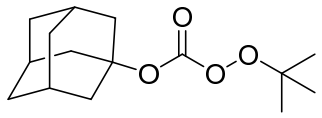
## General information

All reactions were carried out under argon (Ar) atmosphere using Schlenk techniques with magnetic stirring. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. CuTc and CuOAc were purchased from TCL. Chiral phosphoric acids (CPAs) were purchased from Daicel Chiral Technologies (China). Dichloromethane was purchased anhydrous from JK and transferred under an argon atmosphere. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F254 plates. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 0.040-0.063 mm). Visualization on TLC was achieved by use of UV light (254 nm) or iodine. NMR spectra were recorded on a Bruker DPX 400 spectrometer at 400 MHz for $^{1}$H NMR, 100 MHz for $^{13}$C NMR and 376 MHz for $^{19}$F NMR in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Data for $^{1}$H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quarter; m, multiplet), coupling constant (Hz), integration. Data for $^{13}$C NMR are reported in terms of chemical shift (δ, ppm). $^{19}$F NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer [$CFCl_3$ as an external reference (0 ppm)]. HMRS were obtained on a Bruker Apex IV RTMS. The blue LEDs were directly got from the supermarket.

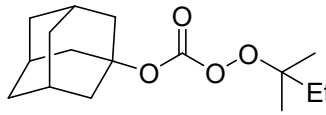
## General procedure for the synthesis of oxidant:




**O1** and **O2** were prepared directly from the corresponding benzyl carbonochloridate and cyclopentyl carbonochloridate in 80% and 85% yields, respectively according to reference[1] and the data are consistent with those reported in the literature.
**O3** and **O4** were prepared from 1-adamantanol via two steps according to reference[2].

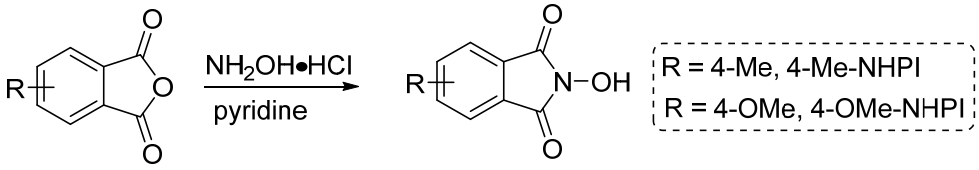


**O3**, 70% yield from 1-adamantanol, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 2.25 – 2.17 (m, 3H), 2.14 (d, *J* = 3.2 Hz, 6H), 1.67 (t, *J* = 3.1 Hz, 6H), 1.32 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 152.4, 84.3, 83.5, 41.0, 35.9, 31.0, 25.9. **HRMS** (ESI) m/z calcd. for $C_{15}H_{24}NaO_4$ $[M+H]^+$ 291.1563, found 291.1567.



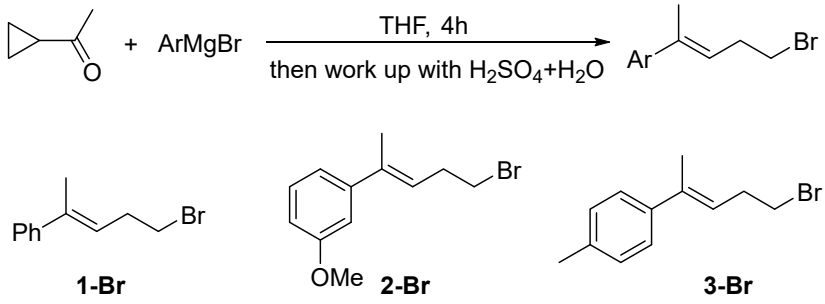
**O4**, 60% yield from 1-adamantanol, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 2.21 (s, 3H), 2.16 – 2.09 (m, 6H), 1.70 – 1.58 (m, 8H), 1.26 (s, 6H), 0.96 – 0.89 (m, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 152.4, 85.9, 84.3, 47.7, 41.0, 35.9, 31.1, 23.5, 8.2. **HRMS** (ESI) m/z calcd. for $C_{16}H_{26}NaO_4$ $[M+H]^+$ 305.1723, found 305.1721.

**General procedure for the synthesis of R-NHPI.**




4-Me-NHPI and 4-OMe-NHPI were prepared directly from the corresponding 5-methylisobenzofuran-1,3-dione and 5-methoxyisobenzofuran-1,3-dione in 85% and 82% yields, respectively according to reference[3]. Data are consistent with those reported in the literature.

**General procedure for the synthesis of homoallylic bromide.**



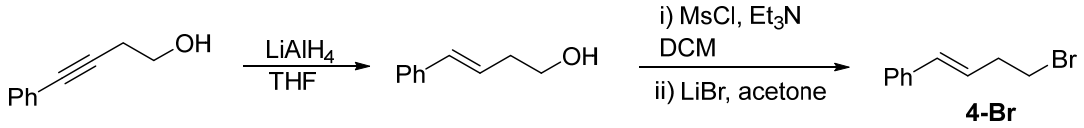

Tri-substituted homoallylic bromides (**1-Br** to **3-Br**) were prepared according to reference[4].

A flame-dried 50-mL Schlenk flask was evacuated and flushed three times with nitrogen, and then charged with (3-methoxyphenyl)magnesium bromide (60 mmol, 1.0 M in THF, generated in situ from 1-bromo-3-methoxybenzene and magnesium). The solution was cooled to 0 ºC, after which a solution of 1-cyclopropylethanone (4.26 mg, 50 mmol, 1 equiv) was added. The resulting solution was warmed up to room temperature and stirred for 4 h. The mixture was cooled to 0 ºC, and then a mixture of $H_2SO_4$ and $H_2O$ ($H_2SO_4$:$H_2O$ = 1:1, v/v, 16 mL) was added. The resulting mixture was stirred for 30 min at room temperature and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine, dried over $Na_2SO_4$, and concentrated

*in vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: PE) to afford the final product **2-Br** (10.4 g, 68% yield).

**1-Br** and **3-Br** were prepared according to the similar procedure in 62% and 71% yields, respectively.

Di-substituted homoallylic bromides **4-Br** was prepared according to procedure reported in the reference[5].

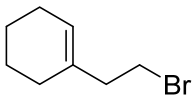



**4-Br**

To a three necked flask, THF (60 mL) and $LiAlH_4$ (3.8 g, 100 mmol) were added. This solution was cooled at 0 °C, and 4-phenylbut-3-yn-1-ol (2.92 g, 20 mmol) in THF (10 mL) was dropped to the mixture over 15 min. After refluxing for 18 h, the reaction mixture was quenched with 1N NaOH (10 mL) at 0 °C. This mixture was filtered, and the filtrate was dried ($MgSO_4$). The solvent was evaporated, and the residue was purified by column chromatography (eluent: hexane/ethyl acetate = 80:20) to give the alcohol product (2.84 g, 96%).

To an ice cooled solution of above alcohol (9.1 mmol) and $Et_3N$ (1.9 mL, 13.7 mmol) in dry DCM (20 ml) was added methanesulfonyl chloride (0.8 mL, 10 mmol) *via* syringe at 0 ºC under argon atmosphere. The mixture was stirred for 45 min at 0 ºC before the reaction was quenched with $H_2O$. The organic materials were washed with saturated $NaHCO_3$ aqueous solution, then extracted twice with DCM. The combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo after filtration.

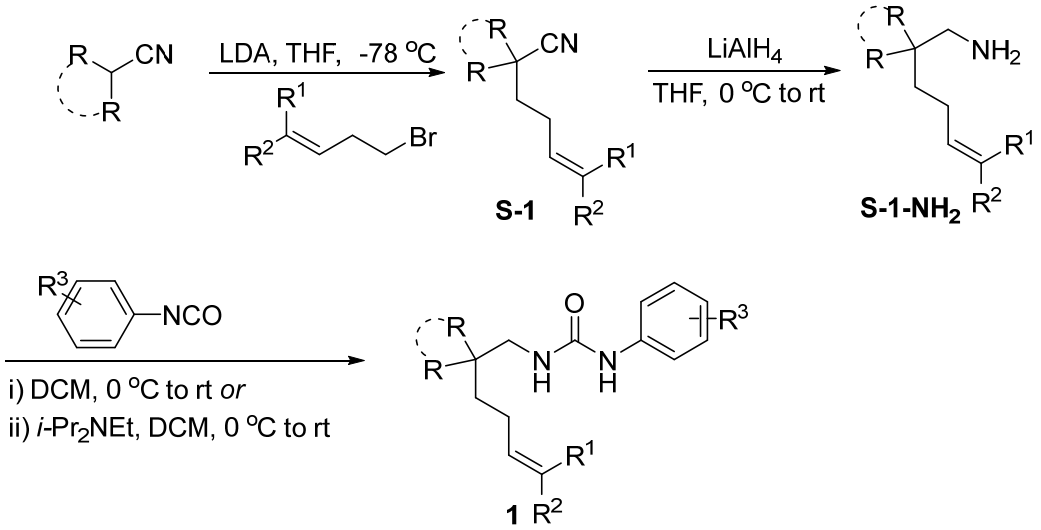
The resulting crude material was dissolved in acetone (40 mL) before addition of lithium bromide (3.6 g, 41 mmol) at 0 ºC. The mixture was stirred at 50 ºC for 5 h. The reaction was then cooled to room temperature and acetone was removed under reduced pressure. The resulting residue was diluted with $H_2O$ and the organic materials were extracted thrice with ethyl acetate. The combined organic extracts were dried over $Na_2SO_4$ and concentrated in vacuo after filtration. The resulting residue was purified by flash column chromatography (petroleum ether/ ethyl acetate =100/1-30/1) to give the **4-Br** (1.63 g, 7.7 mmol) in 80% overall isolated yield in 2 steps.




**5-Br**

**5-Br** was prepared according to reference and the data are consistent with those reported in the literature[6].

**General procedure for the synthesis of alkenyl urea substrates 1.**




To a two-neck round bottom flask containing diisopropylamine (2.0 mL, 13.3 mmol) in dry THF (15 mL) cooled to –78 °C was added dropwise *n*-BuLi (5.6 mL, 2.4 M, 13.3 mmol). The solution was stirred at –78 °C for 30 min. A solution of isobutyronitrile (1.0 mL, 11.1 mmol) was added dropwise and the solution was stirred at –78 °C for further 30 min. To the reaction mixture was added dropwise a solution of homoallylic bromide (12.2 mmol) in dry THF (5.0 mL). Upon completion of the addition, the reaction was allowed to warm to room temperature and stirred overnight. The reaction was quenched by adding saturated aqueous $NH_4Cl$ (20 mL), and the mixture was extracted three times with $Et_2O$. The combined organic extracts were washed with water and brine. After drying with $MgSO_4$ and removal of the solvents under reduced pressure, the resulting crude material was purified by flash column chromatography to yield the corresponding products **S-1**[7].

The following reduction of **S-1** by $LiAlH_4$ and reaction with aryl isocyanate were performed according to procedures reported in the reference[8].

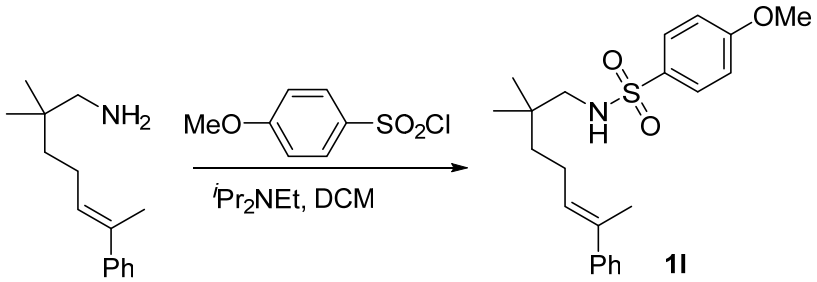
**Reduction of S-1:** To a suspension solution of $LiAlH_4$ (10.0 mmol) in anhydrous THF (20.0 mL) was slowly added **S-1** (5.0 mmol) in dry THF (5.0 mL) in ice-bath under Argon. Then the mixture was warmed to room temperature, and stirred for an additional 2 hours. The reaction mixture was quenched by slow, sequential addition of water (0.5 mL) in $Na_2SO_4$ (4.0 g) at 0 °C. The reaction mixture was warmed to room temperature, stirred for an additional 30 minutes, filtered and concentrated *in vacuo* to afford corresponding products **S-1-NH$_2$**, which was directly used in the next reaction without further purification.

**Synthesis of urea substrate 1a.** To a stirred solution of **S-1a-NH$_2$** (2.0 mmol) in dry DCM (5.0 mL) was slowly added 1-isocyanato-3,5-bis(trifluoromethyl)-benzene (2.0 mmol) at 0 °C. Then, the reaction mixture was stirred for an additional 15 min at 0 °C. After complete conversion (monitored by TLC), the crude mixture was directly purified by silica gel column chromatography and dried under reduced pressure to afford **1a** (0.60 g, 60%) as a white powder.

**Synthesis of urea substrates 1b**. 1,2-dichloro-4-isocyanatobenzene (2.0 mmol) was slowly added to a stirred solution of **S-2a-NH$_2$** (2.0 mmol) (2.0 mmol) and ethyldiisopropylamine (*i*-$Pr_2$NEt, 2.0 mmol) in dry DCM (5.0 mL) at 0 °C. The reaction

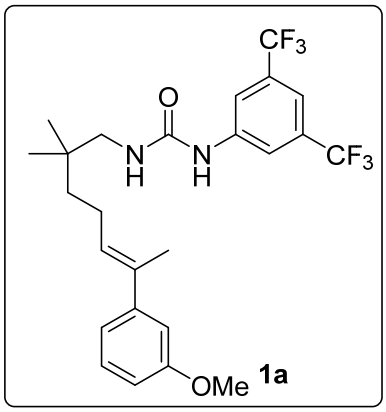
mixture was stirred for an additional 15 min at 0 °C. After complete conversion (monitored by TLC), the crude mixture was directly purified by silica gel column chromatography to give urea substrate **1b** (0.48 g, 55%).

**Procedure for the synthesis of substrate 1l.**



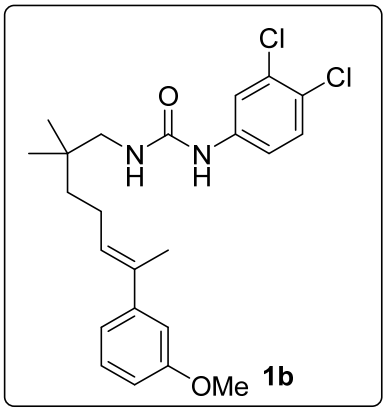

A flame-dried 25-mL round-bottom flask was charged with (*E*)-2,2-dimethyl-6-phenylhept-5-en-1-amine (392 mg, 1.8 mmol) and $^{i}Pr_2NEt$ (0.62 mL, 3.6 mmol) in DCM (8.0 mL), 4-methoxybenzenesulfonyl chloride (447 mg, 2.16 mmol) was added. The resulting mixture was stirred at rt overnight, and the reaction mixture was quenched with saturated $NaHCO_3$ aqueous solution, then extracted twice with DCM. The combined organic extracts was washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo after filtration. The crude mixture was directly purified by silica gel column chromatography to give substrate **1l** (419 mg, 60% yield).

**(*E*)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(6-(3-methoxyphenyl)-2,2-dimethylhept-5-en-1-yl)urea**



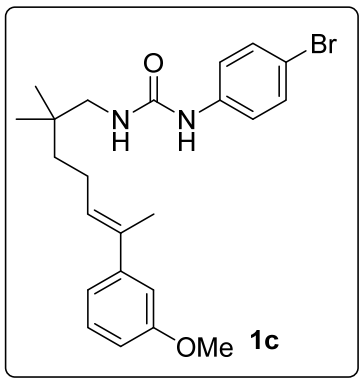

**1a**, 60% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)** δ 7.78 (s, 1H), 7.73 (d, *J* = 1.5 Hz, 2H), 7.41 (t, *J* = 1.4 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 6.92 (ddd, *J* = 7.7, 1.8, 0.9 Hz, 1H), 6.87 (dd, *J* = 2.6, 1.7 Hz, 1H), 6.76 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 5.68 (tq, *J* = 7.2, 1.4 Hz, 1H), 5.58 (t, *J* = 6.1 Hz, 1H), 3.79 (s, 3H), 3.12 (d, *J* = 6.0 Hz, 2H), 2.11 (dd, *J* = 10.7, 6.1 Hz, 2H), 1.96 (d, *J* = 1.3 Hz, 3H), 1.34 – 1.27 (m, 2H), 0.90 (s, 6H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 159.4, 155.7, 145.3, 140.5, 134.6, 132.2 (q, $J_{C-F}$ = 33.1 Hz), 129.2, 128.4, 123.1 (q, $J_{C-F}$ = 271.0 Hz), 118.5, 118.2, 115.9 –115.7 (m, 1C), 111.7, 111.6, 55.2, 50.1, 39.4, 34.4, 24.7, 23.3, 15.7.
**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.27.
**HRMS** (ESI) m/z calcd. for $C_{25}H_{29}F_6N_2O_2$ $[M+H]^+$ 503.2133, found 503.2137.

**(*E*)-1-(3,4-dichlorophenyl)-3-(6-(3-methoxyphenyl)-2,2-dimethylhept-5-en-1-yl)urea**



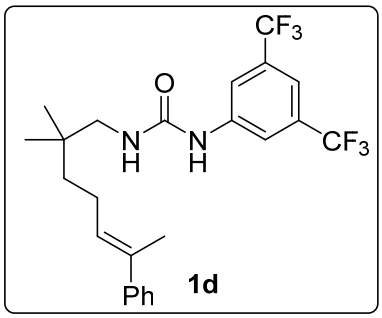

**1b**, 55% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.19 (s, 1H), 7.43 (d, *J* = 2.4 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 8.8 Hz, 1H), 6.94 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.91 (dt, *J* = 8.0, 1.2 Hz, 1H), 6.86 (t, *J* = 2.0 Hz, 1H), 6.74 (ddd, *J* = 8.2, 2.4, 0.8 Hz, 1H), 6.05 (t, *J* = 6.0 Hz, 1H), 5.66 (td, *J* = 7.2, 1.6 Hz, 1H), 3.77 (s, 3H), 3.06 (d, *J* = 6.0 Hz, 2H), 2.11 – 2.05 (m, 2H), 1.95 (d, *J* = 1.2 Hz, 3H), 1.31 – 1.26 (m, 2H), 0.86 (s, 6H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 159.5, 156.7, 145.3, 138.6, 134.6, 132.6, 130.3, 129.2, 128.5, 125.9, 121.2, 118.9, 118.2, 111.7, 111.7, 55.2, 50.1, 39.5, 34.5, 24.8, 23.4, 15.8.
**HRMS** (ESI) m/z calcd. for $C_{23}H_{29}Cl_2N_2O_2$ $[M+H]^+$ 435.1601, found 435.1599.

**(*E*)-1-(4-bromophenyl)-3-(6-(3-methoxyphenyl)-2,2-dimethylhept-5-en-1-yl)urea**



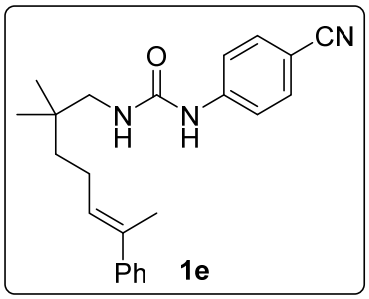

**1c**, 65% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.85 (s, 1H), 7.27 – 7.22 (m, 2H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.11 – 7.09 (m, 2H), 6.91 (ddd, *J* = 7.8, 1.8, 1.0 Hz, 1H), 6.87 (dd, *J* = 2.8, 1.6 Hz, 1H), 6.75 (ddd, *J* = 8.0, 2.4, 0.8 Hz, 1H), 5.82 (t, *J* = 6.0 Hz, 1H), 5.69 –5.65 (m, 1H), 3.78 (s, 3H), 3.04 (d, *J* = 6.0 Hz, 2H), 2.11 – 2.04 (m, 2H), 1.94 (d, *J* = 1.6 Hz, 3H), 1.31 – 1.21 (m, 2H), 0.84 (s, 6H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 159.5, 156.7, 145.4, 138.2, 134.5, 131.9, 129.2, 128.6, 121.4, 118.2, 115.5, 111.7, 111.6, 55.3, 50.0, 39.5, 34.5, 24.8, 23.4, 15.8.
**HRMS** (ESI) m/z calcd. for $C_{23}H_{30}BrN_2O_2$ $[M+H]^+$ 445.1485, found 445.1483.

**(*E*)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-6-phenylhept-5-en-1-yl)urea**



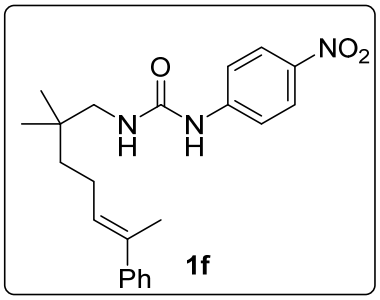

**1d**, 62% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.26 (s, 1H), 7.73 (s, 2H), 7.41 (s, 1H), 7.36 – 7.26 (m, 4H), 7.25 – 7.19 (m, 1H), 5.95 (t, *J* = 6.0 Hz, 1H), 5.71 – 5.67 (m, 1H), 3.15 (d, *J* = 6.0 Hz, 2H), 2.22 – 2.06 (m, 2H), 2.00 (d, *J* = 1.3 Hz, 3H), 1.42 – 1.29 (m, 2H), 0.92 (s, 6H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 156.2, 143.7, 140.4, 134.8, 132.2 (q, $J_{C\text{-}F}$ = 33.1 Hz), 128.2, 128.0, 126.6, 125.5, 123.1 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.5, 115.8, 50.2, 39.6, 34.4, 24.6, 23.3, 15.6.
**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.31.
**HRMS** (ESI) m/z calcd. for $C_{24}H_{27}F_6N_2O$ $[M+H]^+$ 473.2028, found 473.2030.

**(*E*)-1-(4-cyanophenyl)-3-(2,2-dimethyl-6-phenylhept-5-en-1-yl)urea**



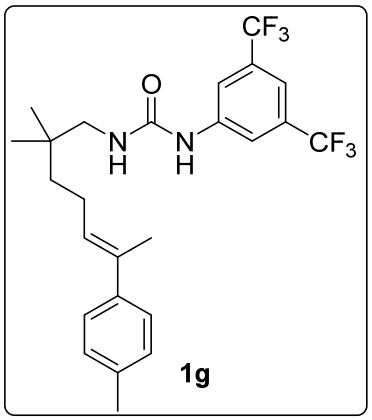

**1e**, 55% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.05 (s, 1H), 7.43 (s, 4H), 7.33 – 7.22 (m, 4H), 7.21 – 7.14 (m, 1H), 5.77 (t, *J* = 6.0 Hz, 1H), 5.67 – 5.64 (m, 1H), 3.12 (d, *J* = 6.0 Hz, 2H), 2.13 – 2.11 (m, 2H), 1.97 (d, *J* = 1.3 Hz, 3H), 1.38 – 1.27 (m, 2H), 0.91 (s, 6H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 155.7, 144.1, 143.7, 134.8, 133.3, 128.2, 128.1, 126.7, 125.5, 119.7, 118.3, 104.1, 49.9, 39.5, 34.5, 24.9, 23.4, 15.7.
**HRMS** (ESI) m/z calcd. for $C_{23}H_{28}N_3O$ $[M+H]^+$ 362.2232, found 362.2228.

**(*E*)-1-(2,2-dimethyl-6-phenylhept-5-en-1-yl)-3-(4-nitrophenyl)urea**



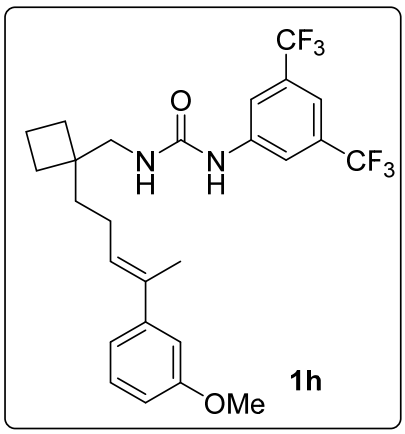

**1f**, 50% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.11 (d, *J* = 9.2 Hz, 2H), 8.05 (s, 1H), 7.53 (d, *J* = 9.2 Hz, 2H), 7.36 – 7.27 (m, 4H), 7.24 – 7.17 (m, 1H), 5.77 (t, *J* = 6.1 Hz, 1H), 5.73 – 5.68 (m, 1H), 3.19 (d, *J* = 6.1 Hz, 2H), 2.20 – 2.14 (m, 2H), 2.01 (d, *J* = 1.2 Hz, 3H), 1.42 – 1.34 (m, 2H), 0.96 (s, 6H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 155.3, 146.1, 143.6, 141.7, 134.8, 128.2, 128.1, 126.6, 125.5, 125.4, 117.7, 50.1, 39.4, 34.5, 24.9, 23.4, 15.7.
**HRMS** (ESI) m/z calcd. for $C_{22}H_{28}N_3O_2$ $[M+H]^+$ 382.2131, found 382.2127.

**(*E*)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-6-(p-tolyl)hept-5-en-1-yl)urea**




**1g**, 58% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.86 (s 2H), 7.50 (s, 1H), 7.28 – 7.26 (m, 3H), 7.14 – 7.11 (m, 2H), 6.82 (s, 1H), 5.74 – 5.70 (m, 1H), 4.90 (t, *J* = 6.1 Hz, 1H), 3.18 (d, *J* = 6.2 Hz, 2H), 2.35 (s, 3H), 2.22 – 2.17 (m, 2H), 2.03 (d, *J* = 1.2 Hz, 3H), 1.43 – 1.34 (m, 2H), 0.98 (s, 6H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 155.7, 140.8, 140.5, 136.3, 134.6, 132.2 (q, $J_{C\text{-}F}$ = 33.1 Hz), 128.9, 127.3, 125.3, 123.2 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.5, 115.8, 50.1, 39.6, 34.4, 24.7, 23.3, 21.0, 15.6.
**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.13.
**HRMS** (ESI) m/z calcd. for $C_{25}H_{29}F_6N_2O$ $[M+H]^+$ 487.2184, found 487.2186.

**(*E*)-1-(3,5-bis(trifluoromethyl)phenyl)-3-((1-(4-(3-methoxyphenyl)pent-3-en-1-yl)cyclobutyl)methyl)urea**



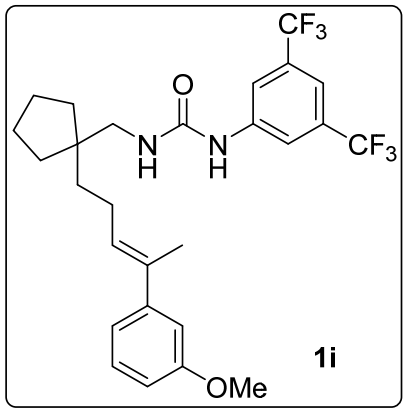

**1h**, 65% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.00 (s, 1H), 7.74 (s, 2H), 7.42 (s, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 6.95 – 6.92 (m, 1H), 6.90 – 6.89 (m, 1H), 6.80 – 6.77 (m, 1H), 5.82 – 5.61 (m, 2H), 3.81 (s, 3H), 3.38 (d, *J* = 5.6 Hz, 2H), 2.18 – 2.08 (m, 2H), 1.99 (s, 3H), 1.94 – 1.74 (m, 6H), 1.62 – 1.53 (m, 2H).

**$^{13}$C NMR (101 MHz, $CDCl_3$) δ** 159.4, 156.0, 145.3, 140.5, 134.8, 132.1 (q, $J_{C\text{-}F}$ = 33.1 Hz), 129.2, 128.1, 123.1 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.4, 118.2, 115.7, 111.7, 111.6, 55.2, 46.3, 41.7, 37.2, 29.1, 23.4, 15.7, 15.1.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.25.

**HRMS** (ESI) m/z calcd. for $C_{26}H_{29}F_6N_2O_2$ $[M+H]^+$ 515.2133, found 515.2134.

**(*E*)-1-(3,5-bis(trifluoromethyl)phenyl)-3-((1-(4-(3-methoxyphenyl)pent-3-en-1-yl)cyclopentyl)methyl)urea**



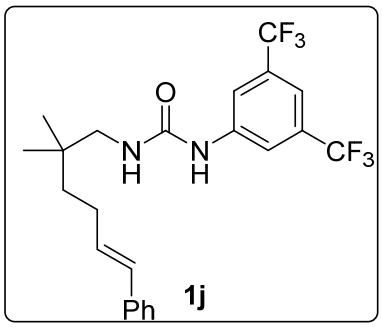

**1i**, 62% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.41 (s, 1H), 7.66 (s, 2H), 7.35 (s, 1H), 7.17 (t, *J* = 7.9 Hz, 1H), 6.90 – 6.87 (m, 1H), 6.85 (t, *J* = 2.1 Hz, 1H), 6.75 – 6.73 (m, 1H), 6.06 (t, *J* = 5.9 Hz, 1H), 5.68 – 5.64 (m, 1H), 3.77 (s, 3H), 3.22 (d, *J* = 5.5 Hz, 2H), 2.15 – 2.07 (m, 2H), 1.93 (s, 3H), 1.58 – 1.55 (m, 4H), 1.44 – 1.36 (m, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 159.4, 156.5, 145.3, 140.4, 134.7, 132.1 (q, $J_{C\text{-}F}$ = 33.1 Hz), 129.1, 128.2, 123.1 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.5, 118.2, 115.8, 111.7, 111.6, 55.2, 46.7, 45.8, 37.4, 35.5, 25.0, 24.1, 15.6.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.32.

**HRMS** (ESI) m/z calcd. for $C_{27}H_{31}F_6N_2O_2$ $[M+H]^+$ 529.2290, found 529.2295.

**(*E*)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-6-phenylhex-5-en-1-yl)urea**

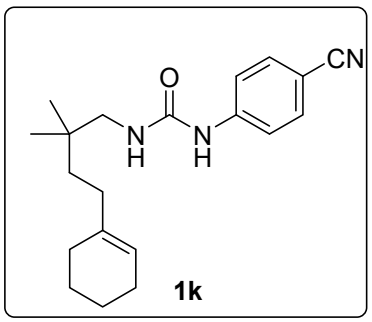



**1j**, 50% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.83 (s, 2H), 7.46 (s, 1H), 7.33 – 7.26 (m, 4H), 7.21 – 7.19 (m, 1H), 7.13 (s, 1H), 6.42 – 6.33 (dt, *J* = 16.0, 1.6 Hz, 1H), 6.18 (dt, *J* = 16.0, 6.7 Hz, 1H), 5.08 (t, *J* = 6.2 Hz, 1H), 3.15 (d, *J* = 6.1 Hz, 2H), 2.24 – 2.13 (m, 2H), 1.42 – 1.36 (m, 2H), 0.94 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 154.9, 140.6, 137.6, 132.2 (q, $J_{C\text{-}F}$ = 33.1 Hz), 130.8, 129.8, 128.6, 127.0, 125.9, 123.2 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.4, 115.8, 50.0, 39.3, 34.4, 27.6, 24.9. **$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.08.

**HRMS** (ESI) m/z calcd. for $C_{23}H_{25}F_6N_2O$ $[M+H]^+$ 459.1866, found 459.1863.

**1-(4-cyanophenyl)-3-(4-(cyclohex-1-en-1-yl)-2,2-dimethylbutyl)urea**



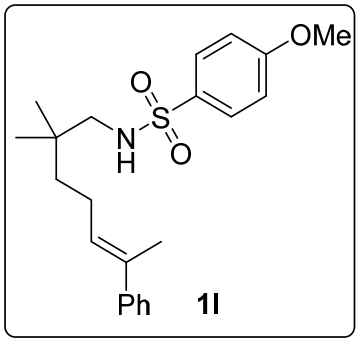
**1k**

**1k**, 45% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.75 (s, 1H), 7.58 – 7.37 (m, 4H), 5.51 (t, *J* = 6.0 Hz, 1H), 5.36 – 5.33 (m, 1H), 3.09 (d, *J* = 6.0 Hz, 2H), 1.99 – 1.82 (m, 6H), 1.64 – 1.43 (m, 4H), 1.36 – 1.23 (m, 2H), 0.88 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 155.4, 143.9, 137.9, 133.3, 120.6, 119.5, 118.4, 104.4, 49.9, 37.9, 34.2, 32.2, 28.6, 25.2, 24.9, 23.1, 22.5.

**HRMS** (ESI) m/z calcd. for $C_{20}H_{28}N_3O$ $[M+H]^+$ 326.2232, found 326.2230.

**(*E*)-N-(2,2-dimethyl-6-phenylhept-5-en-1-yl)-4-methoxybenzenesulfonamide**



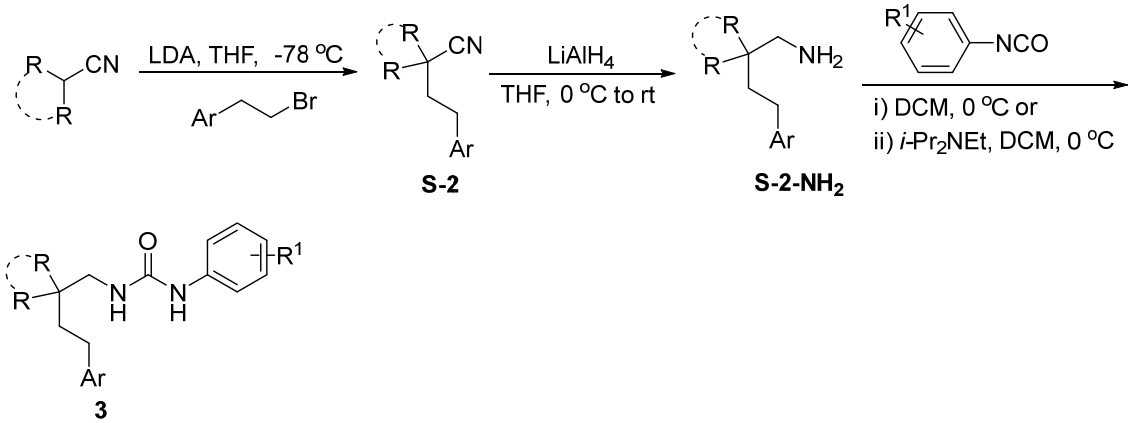
**1l**

**1l**, 75% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.81 (d, *J* = 8.9 Hz, 2H), 7.36 – 7.25 (m, 5H), 7.22 – 7.16 (m, 1H), 6.93 (d, *J* = 8.9 Hz, 2H), 5.66 (td, *J* = 7.1, 1.4 Hz, 1H), 5.13 – 5.06 (m, 1H), 3.79 (s, 3H), 2.70 (d, *J* = 6.8 Hz, 2H), 2.12 – 2.02 (m, 2H), 1.98 (d, *J* = 1.3 Hz, 3H), 1.36 – 1.27 (m, 2H), 0.89 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 162.8, 143.8, 134.6, 131.6, 129.2, 128.4, 128.2, 126.5, 125.6, 114.3, 55.6, 52.9, 39.1, 33.9, 25.0, 23.3, 15.8.

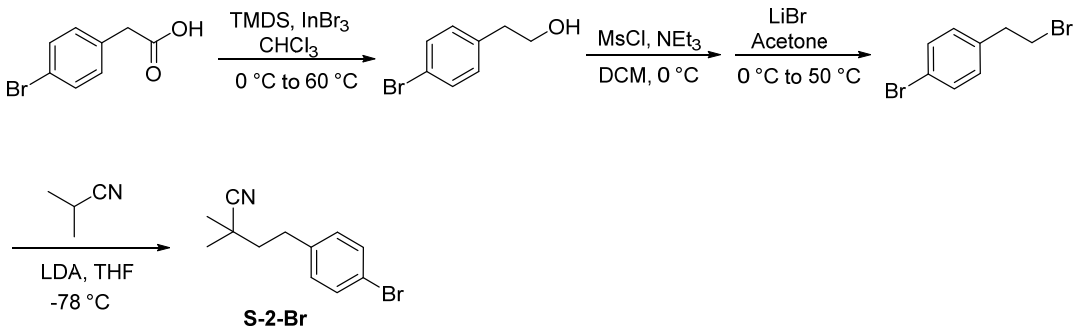
**HRMS** (ESI) m/z calcd. for $C_{22}H_{30}NO_3S$ $[M+H]^+$ 388.1946, found 388.1944.

**General procedure for the synthesis of benzyl urea substrates 3.**




**S-2** were synthesized from homobenzylic bromides according to the similar procedures reported in the reference[7,8]. Benzyl urea substrates **3** were prepared from **S-2** through $LiAlH_4$ reduction and reaction with different aryl isocynates with the similar procedures for the synthesis of substrates **1**.

**General procedure for the synthesis of homobenzylic bromide S-2-Br.**[9]



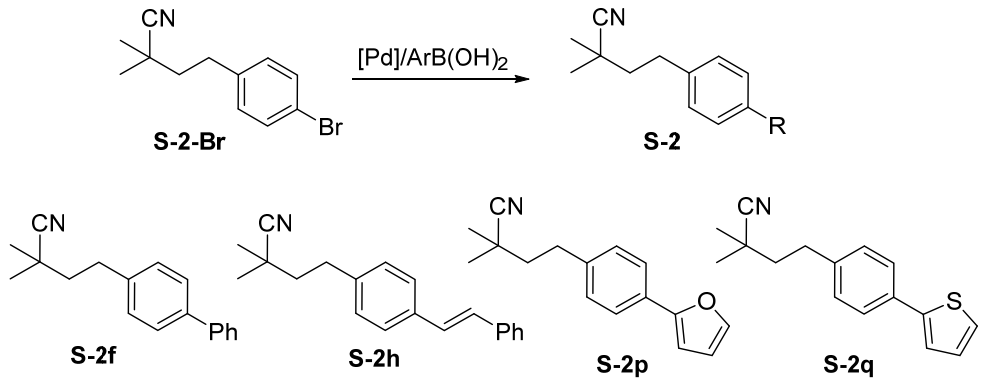

To a two-neck round bottom flask equipped with a magnetic stir bar was added 2-(4-bromophenyl)acetic acid (10.8 g, 50 mmol) and $InBr_3$ (886.7 mg, 5 mmol%), $CHCl_3$ (50 mL) was successively added under argon atmosphere. Then 1,1,3,3-Tetramethyldisiloxane (TMDS) (17.7 mL, 100 mmol) was dropwise added at 0 ºC under argon atmosphere for 5 min. The mixture was stirred at 60 °C ca. 2h. Then, the reaction was quenched with $H_2O$ at 0 ºC and the organic layer was dried with anhydrous $Na_2SO4$ and evaporated under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/ ethyl acetate =10/1-2/1) to afford the 2-(4-bromophenyl)ethan-1-ol (5.5 g, 27.5 mmol) in 55% isolated yields.

To an ice cooled solution of above alcohol and $Et_3N$ (5.7 mL, 41.3 mmol) in dry DCM (80 ml) was added methanesulfonyl chloride (2.3 mL, 41.3 mmol) *via* syringe at 0 ºC under argon atmosphere. The mixture was stirred for 45 min at 0 ºC before the reaction was quenched with $H_2O$. The organic materials were washed with saturated $NaHCO_3$ aqueous solution, then extracted twice with DCM. The combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo after filtration.

The resulting crude material was dissolved in acetone (80 mL) before addition of lithium bromide (10.8 g, 123.8 mmol) at 0 ºC. The mixture was stirred at 50 ºC overnight. The reaction was then cooled to room temperature and acetone was removed under reduced pressure. The resulting residue was diluted with $H_2O$ and the organic materials were extracted thrice with ethyl acetate. The combined organic extracts were dried over $Na_2SO_4$ and concentrated in vacuo after filtration. The resulting residue was purified by flash column chromatography (petroleum ether/ ethyl acetate =100/1-30/1) to give the 1-bromo-4-(2-bromoethyl)benzene (7.0 g, 26.7 mmol) in 97% overall isolated yield in 2 steps.

**S-2-Br** (3.52g, 70% yield) was synthesized from isobutyronitrile (20 mmol) and 1-bromo-4-(2-bromoethyl)benzene (21 mmol) under LDA conditions with the similar procedure mentioned above.

**General procedure for the synthesis of S-2f, S-2h, S-2p and S-2q.**



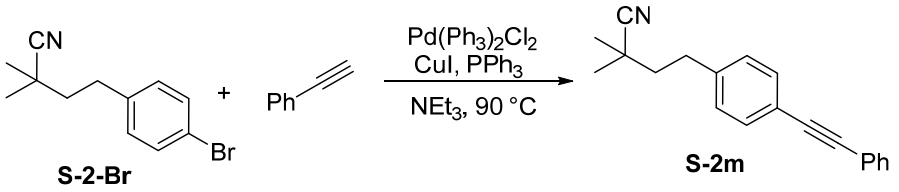

**S-2f**, **S-2h**, **S-2p** and **S-2q** were prepared from **S-2-Br** with different $ArB(OH)_2$ under palladium catalysis.

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **S-2-Br** (1.52 g, 6.0 mmol), phenylboronic acid (0.88 g, 7.2 mmol), $Pd(PPh_3)_4$ (350 mg, 5 mol%) and $Na_2CO_3$ (2.6 g, 24 mmol). The tube was evacuated and backfilled with argon for three times, then toluene (15.0 mL) and water (15.0 mL) were added *via* syringe. The tube was stirred at 80 °C overnight. After completion, the reaction mixture was diluted with ethyl acetate (30 mL) and filtered through celite. The filtrate was washed with water and brine. After drying with $MgSO_4$ and removal of the solvents under reduced pressure, the resulting crude material was purified by flash column chromatography to yield 1.27 g of 4-([1,1'-biphenyl]-4-yl)-2,2-dimethylbutanenitrile **S-2f** in 85% isolated yield.

**S-2h** (90% yield) was prepared from **S-2-Br** and correspond (*E*)-styrylboronic acid with the similar procedure.

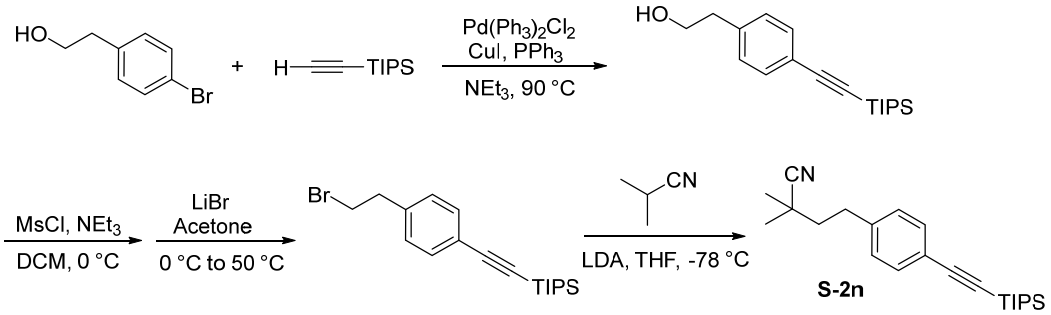
To a flame-dried Schlenk tube equipped with a magnetic stir bar was added **S-2-Br** (1.3 g, 5 mmol), and furan-2-ylboronic acid (1.4 g, 12.5 mmol) or thiophen-2-ylboronic acid (1.6 g, 12.5 mmol) were dissolved in dimethoxyethane (DME) (20 mL) under argon atmosphere. Then 2 M aq $K_2CO_3$ (1.25 mL, 12.5 mmol) was successively added and the mixture was degassed for 10 min. Finally, $Pd(PPh_3)_4$ (578.0 mg, 10 mmol%) was added under argon atmosphere and the mixture was stirred at 85 °C overnight. The resulting mixture was cooled to ambient temperature and diluted with $H_2O$ and the organic materials were extracted thrice with ethyl acetate. The combined organic extracts were dried over $Na_2SO_4$ and concentrated in vacuo after filtration. The resulting residue was purified by flash chromatography (petroleum ether/ ethyl acetate =100/1–50/1) to give the 4-(4-(furan-2-yl)phenyl)-2,2-dimethylbutanenitrile **S-2p** (1.0 g, 4.2 mmol) or 2,2-dimethyl-4-(4-(thiophen-2-yl)phenyl)butanenitrile **S-2q** (1.23 g, 4.8 mmol) in 84% and 96% isolated yields respectively.

**General procedure for the synthesis of alkynylated starting materials:**
**Procedure for the synthesis of S-2m**




To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **S-2-Br** (1.26 g, 5.0 mmol), CuI (53 mg 5.5 mol%), $Pd(PPh_3)_2Cl_2$ (176 mg, 5 mol%) and $PPh_3$ (132 mg, 10 mol%). The tube was evacuated and backfilled with argon for three times, then ethynylbenzene (0.7 mL, 6.0 mmol) and dry $Et_3N$ (12.0 mL) were added *via* syringe. The tube was stirred at 90 °C overnight. After completion, the reaction mixture was diluted with ethyl acetate (30 mL) and filtered through celite. The filtrate was washed with water and brine. After drying with $MgSO_4$ and removal of the solvents under reduced pressure, the resulting crude material was purified by flash column chromatography to yield 1.35 g of 2,2-dimethyl-4-(4-(phenylethynyl)phenyl)butanenitrile **S-2m** in 99% isolated yield.

**Procedure for the synthesis of S-2n.**

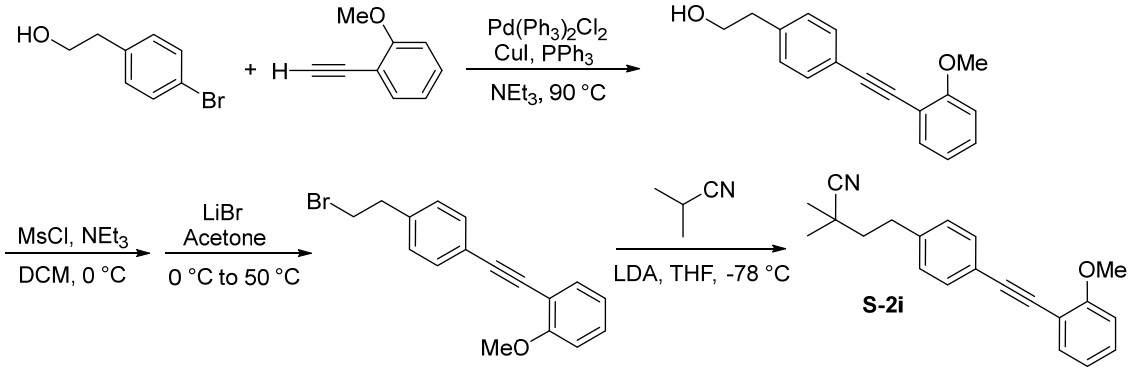



To a round bottom flask equipped with a magnetic stir bar was added 2-(4-bromophenyl)ethan-1-ol (3.0 g, 15 mmol), $Pd(PPh_3)_2Cl_2$ (526.4 mg, 5 mmol%) , CuI (157.1 mg, 5.5 mmol%) and $PPh_3$ (393.4 mg, 10 mmol%). The flask was evacuated and backfilled with argon for three times. Then anhydrous $Et_3N$ (30 mL) was added *via* syringe under argon atmosphere. Finally, ethynyltriisopropylsilane was dropwise added under argon atmosphere and the mixture was stirred for 60 h at 90 ºC. The crude reaction mixture was then filtered through a short celite/$SiO_2$ pad, and neutralized by using saturated $NH_4Cl$ aqueous solution (50 mL x 2). The aqueous phase was extracted with ethyl acetate (30 mL x 3), and the combined organic phases were washed with brine (20 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure to give the desired crude products. Purification by flash column chromatography (petroleum ether/ ethyl acetate =30/1–10/1) to give the 2-(4-((triisopropylsilyl)ethynyl)phenyl)ethan-1-ol (2.5 g, 8.4 mmol) in 56% isolated yields. To an ice cooled solution of above propargylic alcohol and $Et_3N$ (1.8 mL, 12.6 mmol) in dry DCM (25 ml) was added methanesulfonyl chloride (0.7 mL, 12.6 mmol) *via* syringe at 0 ºC under argon atmosphere. The mixture was stirred for 45 min at 0 ºC before the reaction was quenched with $H_2O$. The organic materials were washed with saturated $NaHCO_3$ aqueous solution, then extracted twice with DCM. The combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo

after filtration.

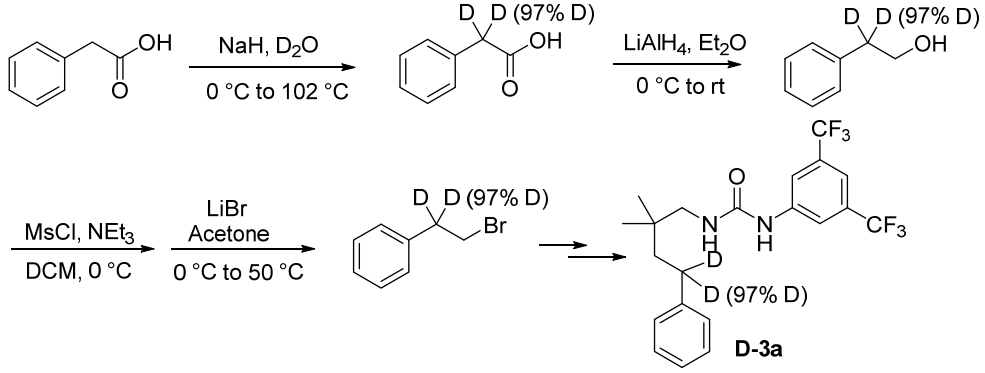
The resulting crude material including mesylate was then, without purification, dissolved in acetone (25 mL) before addition of lithium bromide (3.3 g, 37.8 mmol) at 0 ºC. The mixture was stirred at 50 ºC overnight. The reaction was then cooled to room temperature and acetone was removed under reduced pressure. The resulting residue was diluted with $H_2O$ and the organic materials were extracted thrice with ethyl acetate. The combined organic extracts were dried over $Na_2SO_4$ and concentrated in vacuo after filtration. The resulting residue was purified by flash column chromatography (petroleum ether/ ethyl acetate =100/1–30/1) to give the ((4-(2-bromoethyl)phenyl)ethynyl)triisopropylsilane (3.0 g, 8.2 mmol) in 98% overall isolated yield in 2 steps.

**S-2n** was prepared from ((4-(2-bromoethyl)phenyl)ethynyl)triisopropylsilane and isobutyronitrile under LDA conditions with the similar procedure shown above in 70% yield.




**S-2i** was prepared from 2-(4-bromophenyl)ethan-1-ol and corresponding 1-ethynyl-2-methoxybenzene in 45% yield over three steps.

**General procedure for the synthesis of D-3a.**



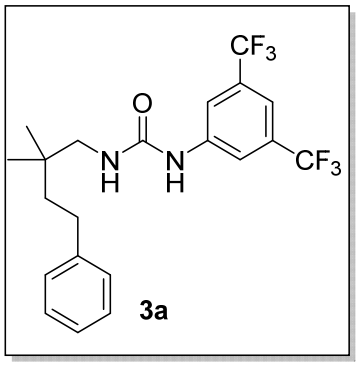

In a three-neck 100 mL round bottom flask equipped with a magnetic stir bar, reflux condenser, and rubber septum, NaH (1.7 g, 42 mmol) was added slowly to $D_2O$ (12 mL) at 0 ºC under argon atmosphere. Phenylacetic acid (4.1 g, 30 mmol) was added, and the mixture was heated at reflux at 100 °C for 4 days under argon. The reaction mixture was acidified with 4 N HCI to a pH of 4 and extracted thrice with DCM. The combined organic extracts were dried with $Na_2SO_4$, filtered, and concentrated to give a quantitative yield of phenylacetic acid with 93% deuterium incorporation in the benzylic position. This procedure was repeated to give 97% deuterated product.

To a stirred ice-cooled suspension of lithium aluminum hydride (1.1 g, 36 mmol)in 80 mL of anhydrous diethyl ether was dropwise added of the preceding acid (4.1 g, 30 mmol) in 20 mL of anhydrous diethyl ether. The hydride mixture was stirred at room temperature overnight. Excess hydride was quenched by adding 8 mL of 10% aqueous NaOH. The mixture was filtered and organic layer was washed with brine, extracted with EtOAc. The combined organic extracts were dried with $Na_2SO_4$, filtered, and concentrated to give the 2-phenylethan-2,2-*d*$_2$-1-ol (3.4 g, 27.5 mmol, 97% deuterium incorporation) in 92% yield.

(2-bromoethyl-1,1-*d*$_2$)benzene was prepared from 2-phenylethan-2,2-*d*$_2$-1-ol with the similar procedures for the synthesis of 1-bromo-4-(2-bromoethyl)benzene.

**D-3a** was prepared from (2-bromoethyl-1,1-*d*$_2$)benzene with the similar procedure mentioned above.

**1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-phenylbutyl)urea**



3a

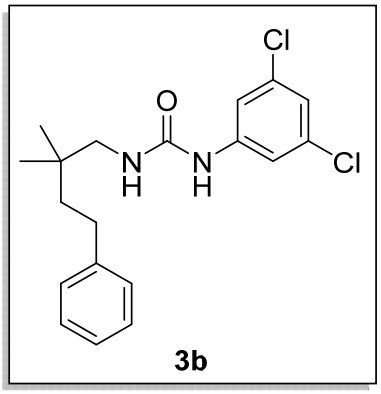
**3a**, 72% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 8.50 (s, 1H), 7.62 (s, 2H), 7.36 (s, 1H), 7.19 (t, *J* = 7.3 Hz, 2H), 7.13 – 7.09 (m, 1H), 7.06 (d, *J* = 6.8 Hz, 2H), 6.16 (t, *J* = 6.1 Hz, 1H), 3.08 (d, *J* = 6.0 Hz, 2H), 2.51 – 2.46 (m, 2H), 1.46 – 1.42 (m, 2H), 0.88 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 156.6, 142.4, 140.3, 132.2 (q, $J_{C\text{-}F}$ = 33.1 Hz), 128.4, 128.1, 125.8, 123.0 (q, $J_{C\text{-}F}$ = 271.1 Hz), 118.7 – 118.6 (m, 1C), 115.9 – 115.8 (m, 1C), 50.1, 42.0, 34.5, 30.4, 24.5.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.06.

**HRMS** (ESI) m/z calcd. for $C_{21}H_{23}F_6N_2O$ $[M+H]^+$ 433.1709, found 433.1703.

**1-(3,5-dichlorophenyl)-3-(2,2-dimethyl-4-phenylbutyl)urea**



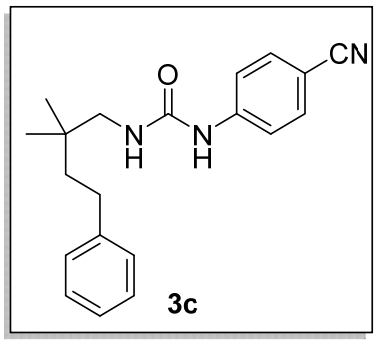
3b

**3b**, 56% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.61 (s, 1H), 7.25 – 7.21 (m, 2H), 7.16 – 7.14 (m, 3H), 7.12 – 7.10 (m, 2H), 6.92 (t, *J* = 1.8 Hz, 1H), 5.62 (t, *J* = 6.2 Hz, 1H), 3.08 (d, *J* = 6.1 Hz, 2H), 2.54 – 2.50 (m, 2H), 1.47 – 1.43 (m, 2H), 0.90 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 155.9, 142.7, 140.9, 135.1, 128.4, 128.2, 125.8, 122.7, 117.6, 50.0, 42.0, 34.6, 30.4, 24.8.

**HRMS** (ESI) m/z calcd. for $C_{19}H_{23}Cl_2N_2O$ $[M+H]^+$ 365.1182, found 365.1177.

**11-(4-cyanophenyl)-3-(2,2-dimethyl-4-phenylbutyl)urea**

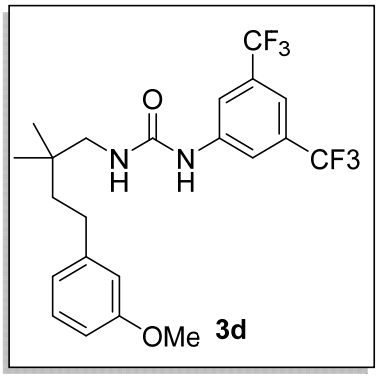



**3c**, 52% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)**: δ 7.66 (s, 1H), 7.44 (s, 4H), 7.25 – 7.21 (m, 2H), 7.17 – 7.11 (m, 3H), 5.48 (t, *J* = 6.0 Hz, 1H), 3.13 (d, *J* = 6.0 Hz, 2H), 2.56 – 2.52 (m, 2H), 1.51 – 1.46 (m, 2H), 0.93 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 155.9, 144.1, 142.6, 133.3, 128.5, 128.2, 125.9, 119.7, 118.4, 104.1, 49.9, 41.9, 34.6, 30.5, 24.9.

**HRMS** (ESI) m/z calcd. for $C_{20}H_{24}N_3O$ $[M+H]^+$ 322.1914, found 322.1909.

**1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-(3-methoxyphenyl)-2,2-dimethylbutyl) urea**



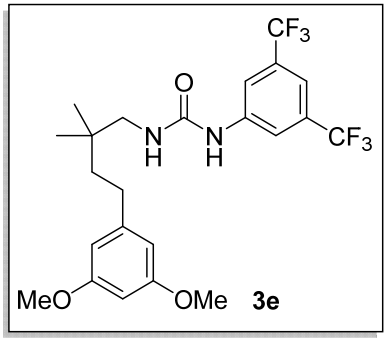

**3d**, 66% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)**: δ 7.72 -7.65 (m, 3H), 7.42 – 7.41 (m, 1H), 7.16 (t, *J* = 7.8 Hz, 1H), 6.73 – 6.68 (m, 3H), 5.47 (t, *J* = 6.1 Hz, 1H), 3.78 (s, 3H), 3.10 (d, *J* = 6.0 Hz, 2H), 2.53 – 2.48 (m, 2H), 1.46 – 1.41 (m, 2H), 0.91 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 159.6, 156.3, 144.3, 140.4, 132.1 (q, $J_{C\text{-}F}$ = 33.1 Hz), 129.4, 122.8 (q, $J_{C\text{-}F}$ = 271.1 Hz), 120.7, 118.6 - 118.5 (m, 1C), 115.7(8) – 115.7(4) (m, 1C), 114.3, 110.8, 55.1, 50.1, 41.9, 34.5, 30.4, 24.5.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.30.

**HRMS** (ESI) m/z calcd. for $C_{22}H_{25}F_6N_2O_2$ $[M+H]^+$ 463.1815, found 463.1808

**1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-(3,5-dimethoxyphenyl)-2,2-dimethylbutyl )urea**



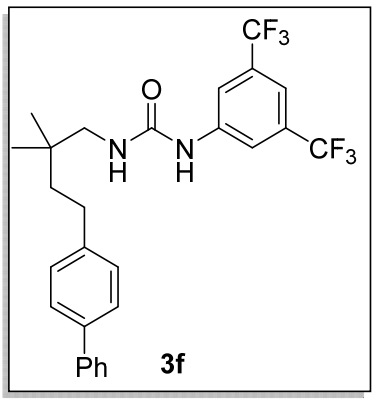

**3e**, 70% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)**: δ 8.05 (s, 1H), 7.71 (s, 2H), 7.39 (s, 1H), 6.30 – 6.27 (m, 3H), 5.72 (t, *J* = 6.1 Hz, 1H), 3.72 (s, 6H), 3.09 (d, *J* = 6.0 Hz, 2H), 2.48 – 2.44 (m, 2H), 1.45 – 1.40 (m, 2H), 0.89 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 160.8, 156.1, 145.2, 140.5, 132.1 (q, $J_{C\text{-}F}$ = 33.1 Hz), 123.1 (q, $J_{C\text{-}F}$ = 271.1 Hz), 118.5 – 118.4 (m, 1C), 115.8 – 115.7 (m, 1C), 106.5, 97.5, 55.2, 50.0, 41.7, 34.5, 30.7, 24.5.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.28.

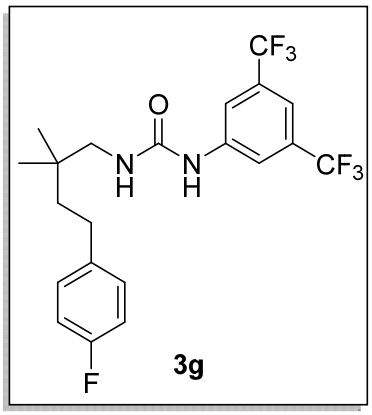
**HRMS** (ESI) m/z calcd. for $C_{23}H_{27}F_6N_2O_3$ $[M+H]^+$ 493.1920, found 493.1915.

**1-(4-([1,1'-biphenyl]-4-yl)-2,2-dimethylbutyl)-3-(3,5-bis(trifluoromethyl)phenyl) urea**



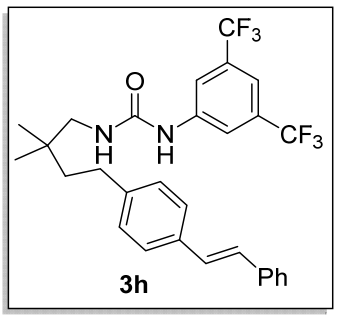

**3f**, 70% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)**: δ 7.80 (s, 2H), 7.56 – 7.53 (m, 2H), 7.50 – 7.40 (m, 5H), 7.34 – 7.30 (m, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.17 (s, 1H), 5.11(t, *J* = 6.2 Hz, 1H), 3.17 (d, *J* = 6.1 Hz, 2H), 2.63 – 2.59 (m, 2H), 1.56 – 1.52 (m, 2H), 0.97 (s, 6H).
**$^{13}$C NMR (101 MHz, Acetone-*d*6)**: δ155.1, 142.8, 142.6, 140.9, 138.3, 131.5 (q, $J_{C-F}$ = 33.1 Hz), 128.9, 128.8, 127.0, 126.8, 126.6, 123.7 (q, $J_{C-F}$ = 271.1 Hz), 117.5 – 117.4 (m, 1C), 113.9 – 113.7 (m, 1C), 48.9, 41.9, 34.6, 29.9, 24.5.
**$^{19}$F NMR (376 MHz, Acetone-*d*6)** δ -63.58.
**HRMS** (ESI) m/z calcd. for $C_{27}H_{27}F_6N_2O$ $[M+H]^+$ 509.2022, found 509.2018.

**1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-(4-fluorophenyl)-2,2-dimethylbutyl)urea**



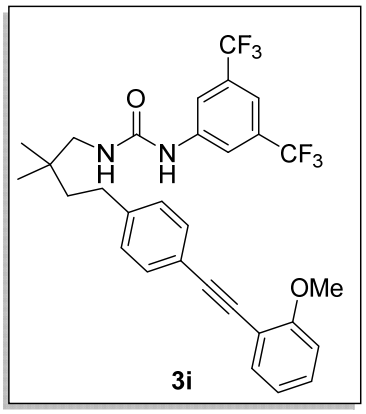

**3g**, 62% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)**: δ 7.84 (s, 2H), 7.49 (s, 1H), 7.13 – 7.09 (m, 2H), 6.96 – 6.91 (m, 2H), 6.86 (s, 1H), 4.90 (t, *J* = 6.2 Hz, 1H), 3.17 (d, *J* = 6.2 Hz, 2H), 2.59 – 2.55 (m, 2H), 1.51 – 1.47 (m, 2H), 0.97 (s, 6H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 161.2 (d, $J_{C-F}$ = 241.9 Hz), 156.6, 140.3, 138.0 (d, $J_{C-F}$ = 3.5 Hz), 132.2 (q, $J_{C-F}$ = 33.1 Hz), 129.4 (d, $J_{C-F}$ = 7.8 Hz), 123.0 (q, $J_{C-F}$ = 271.1 Hz), 118.6 – 118.5 (m, 1C), 115.9 – 115.8 (m, 1C), 115.1 (d, $J_{C-F}$ = 21.0 Hz), 50.1, 42.1, 34.4, 29.5, 24.5.
**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.10, -117.75.
**HRMS** (ESI) m/z calcd. for $C_{21}H_{22}F_7N_2O$ $[M+H]^+$ 451.1615, found 154.1609.

**(*E*)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-(4-styrylphenyl)butyl) urea**




**3h**, 70% yield, **$^{1}$H NMR (400 MHz, Acetone-$d_6$)**: δ 8.58 (s, 1H), 8.17 (m, 2H), 7.59 – 7.57 (m, 2H), 7.53 – 7.49 (m, 3H), 7.38 – 7.34 (m, 2H), 7.26 – 7.22 (m, 3H), 7.20 (d, *J* = 4.6 Hz, 2H), 6.18 (t, *J* = 6.6 Hz, 1H), 3.21 (d, *J* = 6.3 Hz, 2H), 2.69 – 2.64 (m, 2H), 1.58 – 1.53 (m, 2H), 1.00 (s, 6H).
**$^{13}$C NMR (101 MHz, Acetone-$d_6$)**: δ 155.1, 143.0, 142.8, 137.6, 134.9, 131.5 (q, $J_{C-F}$ = 33.3 Hz), 128.7, 128.6, 128.5, 127.6, 127.3, 126.5, 126.4, 123.6 (q, $J_{C-F}$ = 270.3 Hz), 117.5 – 117.4 (m, 1C), 113.9 – 113.7 (m, 1C), 48.9, 41.8, 34.6, 30.1, 24.5.
**$^{19}$F NMR (376 MHz, Acetone-$d_6$)**: δ -63.55.
**HRMS** (ESI) m/z calcd. for $C_{29}H_{29}F_6N_2O$ $[M+H]^+$ 535.2179, found 535.2179.

**1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-(4-((2-methoxyphenyl)ethynyl)phenyl)-2,2-dimethylbutyl)urea**



3i

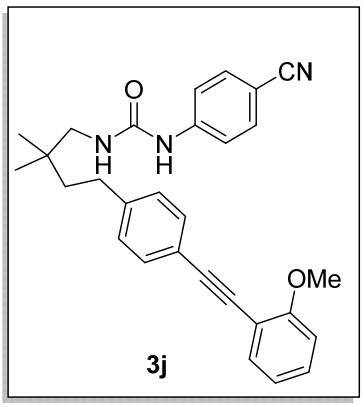
**3i**, 52% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)**: δ 7.77 - 7.71 (m, 3H), 7.49 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.41 – 7.38 (m, 3H), 7.34 – 7.29 (m, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.97 – 6.90 (m, 2H), 5.53 – 5.48 (m, 1H), 3.89 (s, 3H), 3.08 (d, *J* = 6.0 Hz, 2H), 2.53 – 2.49 (m, 2H), 1.42 – 1.38 (m, 2H), 0.90 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 159.7, 156.2, 143.0, 140.4, 133.7, 132.2 (q, $J_{C\text{-}F}$ = 33.1 Hz), 131.7, 129.9, 128.2, 123.1 (q, $J_{C\text{-}F}$ = 271.1 Hz), 120.8, 120.7, 118.4, 115.8 – 115.6 (m, 1C), 112.4, 110.8, 93.7, 85.3, 55.8, 50.1, 41.5, 34.5, 30.3, 24.5.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.14.

**HRMS** (ESI) m/z calcd. for $C_{30}H_{29}F_6N_2O_2$ $[M+H]^+$ 563.2128, found 563.2123.

**1-(4-cyanophenyl)-3-(4-(4-((2-methoxyphenyl)ethynyl)phenyl)-2,2-dimethylbutyl) urea**



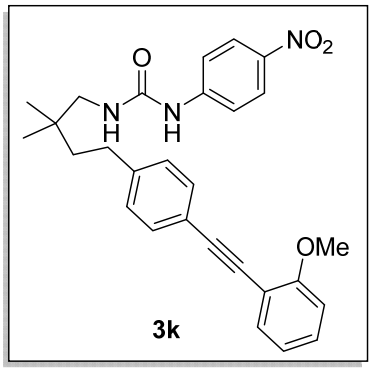
3j

**3j**, 54% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)**: δ 8.00 (s, 1H), 7.48 – 7.37 (m, 7H), 7.31 – 7.27 (m, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.95 - 6.87 (m, 2H), 5.65 (t, *J* = 6.4 Hz, 1H), 3.87 (s, 3H), 3.08 (d, *J* = 6.0 Hz, 2H), 2.53 – 2.48 (m, 2H), 1.44 – 1.40 (m, 2H), 0.90 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 159.7, 155.5, 144.1, 143.1, 133.6, 133.3, 131.7, 129.9, 128.3, 120.8, 119.7, 118.3, 112.4, 110.9, 104.1, 93.7, 85.4, 55.9, 49.8, 41.5, 34.6, 30.4, 24.9.

**HRMS** (ESI) m/z calcd. for $C_{29}H_{30}N_3O_2$ $[M+H]^+$ 452.2333, found 452.2327.

**1-(4-(4-((2-methoxyphenyl)ethynyl)phenyl)-2,2-dimethylbutyl)-3-(4-nitrophenyl) urea**



3k

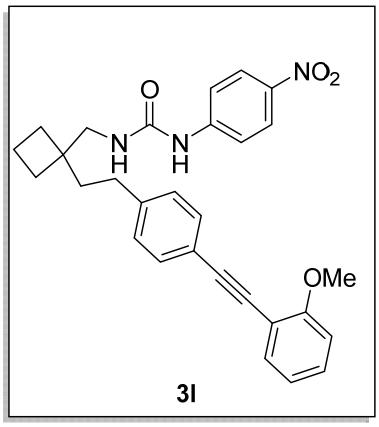
**3k**, 50% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)**: δ 8.07 (d, *J* = 9.2 Hz, 2H), 7.59 (s, 1H), 7.52 – 7.48 (m, 3H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.33 – 7.29 (m, 1H), 7.08 (d, *J* = 8.1 Hz, 2H), 6.97 - 6.90 (m, 2H), 5.27 (t, *J* = 6.1 Hz, 1H), 3.91 (s, 3H), 3.13 (d, *J* = 6.1 Hz, 2H), 2.57 – 2.53 (m, 2H), 1.46 – 1.42 (m, 2H), 0.94 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 159.6, 154.9, 145.9, 143.2, 141.7, 133.7, 131.7, 129.9, 128.3, 125.3, 120.9, 120.7, 117.6, 112.4, 111.0, 93.7, 85.3, 56.0, 50.0, 41.4, 34.6, 30.4, 24.8.

**HRMS** (ESI) m/z calcd. for $C_{28}H_{30}N_3O_4$ $[M+H]^+$ 472.2231, found 472.2227.

**1-(4-(4-((2-methoxyphenyl)ethynyl)phenyl)cyclobutyl)methyl)-3-(4-nitrophenyl)**

**urea**

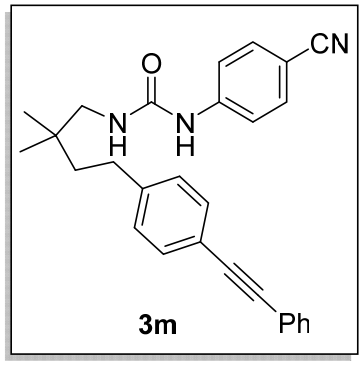



**3l**, 62% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 8.15 (s, 1H), 8.07 (d, *J* = 9.2 Hz, 2H), 7.54 (d, *J* = 9.2 Hz, 2H), 7.47 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.29 (ddd, *J* = 8.4, 7.5, 1.7 Hz, 1H), 7.07 (d, *J* = 8.2 Hz, 2H), 6.93 (td, *J* = 7.5, 1.0 Hz, 1H), 6.89 (dd, *J* = 8.4, 1.0 Hz, 1H), 5.72 (t, *J* = 5.8 Hz, 1H), 3.88 (s, 3H), 3.38 (d, *J* = 5.7 Hz, 2H), 2.57 – 2.44 (m, 2H), 1.94 – 1.82 (m, 2H), 1.76 (t, *J* = 7.5 Hz, 4H), 1.72 – 1.59 (m, 2H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 159.6, 155.0, 145.9, 142.9, 141.8, 133.7, 131.7, 129.9, 128.3, 125.3, 120.8, 120.7, 117.5, 112.4, 110.9, 93.7, 85.3, 55.9, 46.2, 41.8, 39.1, 30.3, 29.2, 15.1.

**HRMS** (ESI) m/z calcd. for $C_{29}H_{30}N_3O_4$ $[M+H]^+$ 484.2231, found 484.2228.

**1-(4-cyanophenyl)-3-(2,2-dimethyl-4-(4-(phenylethynyl)phenyl)butyl)urea**

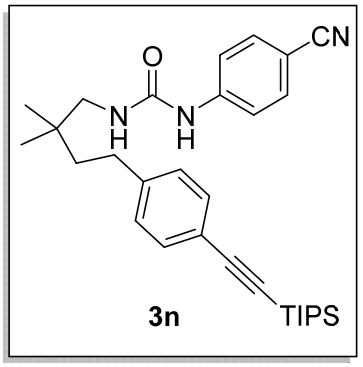



**3m**, 57% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.69 (s, 1H), 7.51 – 7.49 (m, 2H), 7.44 (s, 4H), 7.39 (d, *J* = 7.8 Hz, 2H), 7.34 – 7.31 (m, 3H), 7.09 (d, *J* = 7.8 Hz, 2H), 5.49 (t, *J* = 6.0 Hz, 1H), 3.11 (d, *J* = 6.1 Hz, 2H), 2.56 – 2.52 (m, 2H), 1.48 – 1.44 (m, 2H), 0.92 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 155.3, 143.9, 143.1, 133.3, 131.7, 131.6, 128.4, 128.3, 128.2, 123.3, 120.7, 119.6, 118.4, 104.3, 89.4, 89.1, 49.8, 41.6, 34.6, 30.5, 24.9.

**HRMS** (ESI) m/z calcd. for $C_{28}H_{28}N_3O$ $[M+H]^+$ 422.2227, found 422.2220.

**1-(4-cyanophenyl)-3-(2,2-dimethyl-4-(4-((triisopropylsilyl)ethynyl)phenyl)butyl) urea**

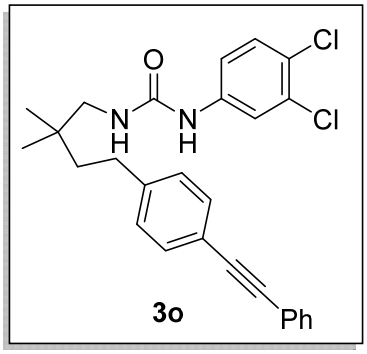



**3n**, 58% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.48 (q, *J* = 8.8 Hz, 4H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.33 (s, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 5.24 (t, *J* = 6.0 Hz, 1H), 3.13 (d, *J* = 6.0 Hz, 2H), 2.57 – 2.53 (m, 2H), 1.48 – 1.44 (m, 2H), 1.12 (s, 21H), 0.94 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 155.0, 143.7, 143.2, 133.3, 132.1, 128.2, 121.0, 119.4, 118.4, 107.1, 104.6, 90.0, 49.8, 41.7, 34.6, 30.5, 24.9, 18.7, 11.3.

**HRMS** (ESI) m/z calcd. for $C_{31}H_{44}N_3OSi$ $[M+H]^+$ 502.3254, found 502.3251.

**1-(3,4-dichlorophenyl)-3-(2,2-dimethyl-4-(4-(phenylethynyl)phenyl)butyl)urea**

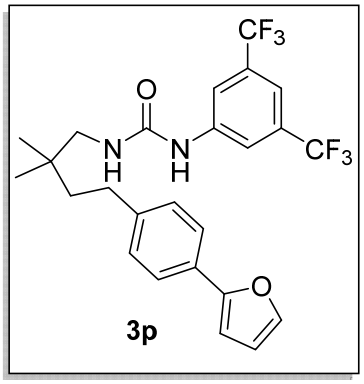



**3o**, 60% yield, **$^{1}$H NMR (400 MHz, Acetone-*d*$_6$)** δ 8.20 (s, 1H), 8.00 (d, *J* = 2.4 Hz, 1H), 7.62 – 7.53 (m, 2H), 7.50 – 7.39 (m, 6H), 7.35 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.34 – 7.29 (m, 2H), 6.04 (t, *J* = 6.3 Hz, 1H), 3.21 (d, *J* = 6.4 Hz, 2H), 2.77 – 2.67 (m, 2H), 1.63 – 1.51 (m, 2H), 1.02 (s, 6H).

**$^{13}$C NMR (101 MHz, Acetone)** δ 155.1, 144.3, 141.0, 131.7, 131.4, 131.3, 130.3, 128.7, 128.6, 128.3, 123.4, 123.2, 120.3, 119.2, 117.7, 89.4, 88.5, 48.7, 41.6, 34.6, 30.3, 24.5.

**HRMS** (ESI) m/z calcd. for $C_{27}H_{27}Cl_2N_2O$ $[M+H]^+$ 465.1495, found 465.1496.

**1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-(4-(furan-2-yl)phenyl)-2,2-dimethylbutyl) urea**



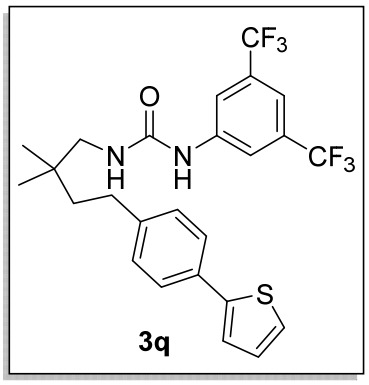

**3p**, 65% yield, **$^{1}$H NMR (400 MHz, Acetone-*d*$_6$)**: δ 8.56 (s, 1H), 8.17 (s, 2H), 7.62 (s, 1H), 7.60 – 7.59 (m, 2H), 7.53 (s, 1H), 7.28 (d, *J* = 7.9 Hz, 2H), 6.76 (d, *J* = 3.4 Hz, 1H), 6.53 – 6.52 (m, 1H), 6.17 (s, 1H), 3.21 (d, *J* = 6.3 Hz, 2H), 2.70 – 2.65 (m, 2H), 1.58 – 1.54 (m, 2H), 1.00 (s, 6H).

**$^{13}$C NMR (101 MHz, Acetone)**: δ 155.1, 154.0, 142.8, 142.7, 142.0, 131.5 (q, $J_{C\text{-}F}$ = 32.6 Hz), 128.7, 128.5, 123.6 (q, $J_{C\text{-}F}$ = 271.0 Hz), 123.5, 117.5, 113.8, 111.6, 104.5, 48.9, 41.8, 34.6, 30.1, 24.5.

**$^{19}$F NMR (376 MHz, Acetone)**: δ -63.59.

**HRMS** (ESI) m/z calcd. for $C_{25}H_{25}F_6N_2O_2$ $[M+H]^+$ 499.1820, found 499.1821.

**1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-(4-(thiophen-2-yl)phenyl) butyl)urea**



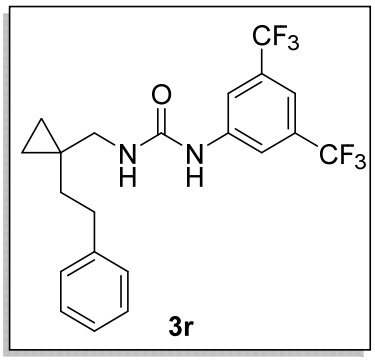

**3q**, 66% yield, **$^{1}$H NMR (400 MHz, CDCl$_3$)**: δ 8.26 (s, 1H), 7.65 (s, 2H), 7.43 (d, *J* = 7.8 Hz, 2H), 7.37 (s, 1H), 7.22 -7.19 (m, 2H), 7.07 – 7.01 (m, 3H), 5.95 (t, *J* = 6.1 Hz, 1H), 3.09 (d, *J* = 5.9 Hz, 2H), 2.51 – 2.46 (m, 2H), 1.47 – 1.42 (m, 2H), 0.88 (s, 6H).

**$^{13}$C NMR (101 MHz, CDCl$_3$)**: δ 156.3, 144.2, 141.9, 140.3, 132.2 (q, $J_{C\text{-}F}$ = 33.0 Hz), 132.1, 128.7, 128.0, 125.9, 124.4, 123.0 (q, $J_{C\text{-}F}$ = 270.9 Hz), 122.7, 118.6, 115.9, 50.1, 41.9, 34.5, 30.1, 24.6.

**$^{19}$F NMR (376 MHz, CDCl$_3$)**: δ -63.27.

**HRMS** (ESI) m/z calcd. for $C_{25}H_{25}F_6N_2OS$ $[M+H]^+$ 515.1592, found 515.1592.

**1-(3,5-bis(trifluoromethyl)phenyl)-3-((1-phenethylcyclopropyl)methyl)urea**



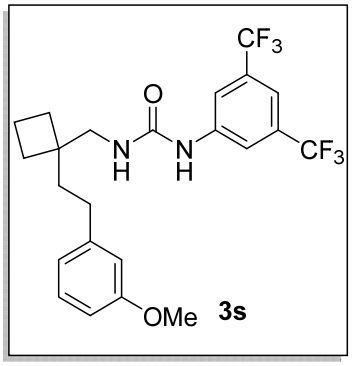

**3r**, 54% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)**: δ 7.76 (s, 1H), 7.72 (s, 2H), 7.40 (s, 1H), 7.22 - 7.18 (m, 2H), 7.14 – 7.13 (m, 1H), 7.10- 7.08 (m, 2H), 5.57 (t, *J* = 5.5 Hz, 1H), 3.20 (d, *J* = 5.4 Hz, 2H), 2.67 – 2.63 (m, 2H), 1.58 – 1.54 (m, 2H), 0.38 – 0.31 (m, 4H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 156.5, 141.8, 140.3, 132.2 (q, $J_{C-F}$ = 33.1 Hz), 128.4, 128.1, 125.9, 123.1 (q, $J_{C-F}$ = 271.1 Hz), 118.7, 115.9, 46.0, 36.7, 33.0, 20.0, 10.6.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.36.

**HRMS** (ESI) m/z calcd. for $C_{21}H_{21}F_6N_2O$ $[M+H]^+$ 431.1553, found 431.1549.

**1-(3,5-bis(trifluoromethyl)phenyl)-3-((1-(3-methoxyphenethyl)cyclobutyl)methyl) urea**



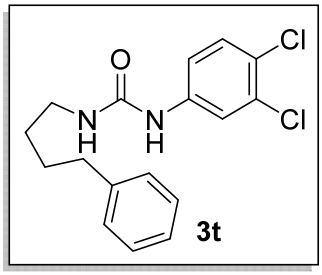

**3s**, 63% yield, **$^{1}$H NMR (400 MHz, $CDCl_3$)**: δ 8.09 (s, 1H), 7.67 (s, 2H), 7.38 (s, 1H), 7.14 – 7.10 (m, 1H), 6.70 – 6.66 (m, 3H), 5.80 (t, *J* = 5.5 Hz, 1H), 3.73 (s, 3H), 3.33 (d, *J* = 5.7 Hz, 2H), 2.48 – 2.44 (m, 2H), 1.86 – 1.78 (m, 2H), 1.75 -1.70 (m, 4H), 1.69 – 1.65 (m, 2H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 159.6, 156.8, 143.9, 140.4, 132.2 (q, $J_{C-F}$ = 33.1 Hz), 129.4, 123.1 (q, $J_{C-F}$ = 271.1 Hz), 120.6, 118.7, 115.8, 114.3, 110.8, 55.0, 46.3, 41.8, 39.3, 30.4, 29.0, 15.0.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.31.

**HRMS** (ESI) m/z calcd. for $C_{23}H_{25}F_6N_2O_2$ $[M+H]^+$ 475.1815, found 475.1813.

**1-(3,4-dichlorophenyl)-3-(4-phenylbutyl)urea**

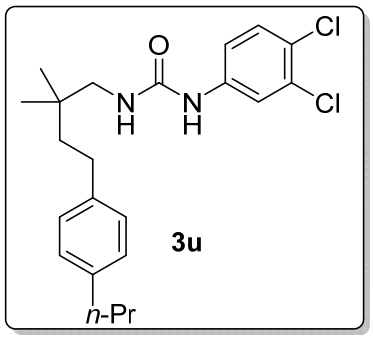



**3t**, 52% yield, **$^{1}$H NMR (400 MHz, Chloroform-*d*)** δ 7.44 (d, *J* = 2.4 Hz, 1H), 7.27 – 7.24 (m, 3H), 7.20 – 7.04 (m, 5H), 5.20 (t, *J* = 5.7 Hz, 1H), 3.21 – 3.16 (m, 2H), 2.58 (t, *J* = 7.6 Hz, 2H), 1.63 – 1.56 (m, 2H), 1.52 – 1.46 (m, 2H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 155.5, 142.0, 138.4, 132.7, 130.5, 128.4, 126.2, 125.9, 121.4, 119.0, 40.2, 35.5, 29.6, 28.6.

**HRMS** (ESI) m/z calcd. for $C_{17}H_{19}Cl_2N_2O$ $[M+H]^+$ 337.0869, found 337.0867.

**1-(3,4-dichlorophenyl)-3-(2,2-dimethyl-4-(4-propylphenyl)butyl)urea**

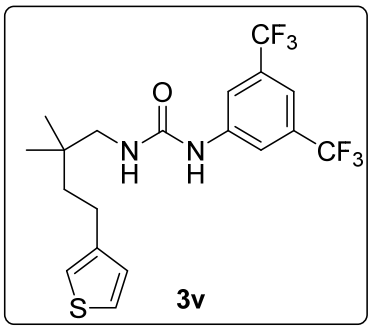



**3u**, 64% yield, **$^1$H NMR (400 MHz, Chloroform-d):** δ 8.28 (s, 1H), 7.39 (d, J = 2.5 Hz, 1H), 7.09 (d, J = 8.6 Hz, 1H), 7.00 (q, J = 8.1 Hz, 4H), 6.88 (dd, J = 8.7, 2.5 Hz, 1H), 6.14 (t, J = 6.2 Hz, 1H), 3.04 (d, J = 5.9 Hz, 2H), 2.56 – 2.38 (m, 4H), 1.57 (dt, J = 14.7, 7.4 Hz, 2H), 1.47 – 1.37 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H), 0.85 (s, 6H).

**$^{13}$C NMR (101 MHz, Chloroform-d)**: δ 157.1, 140.2, 139.8, 138.6, 132.6, 130.4, 128.6, 128.1, 126.1, 121.5, 119.1, 50.1, 42.2, 37.8, 34.7, 30.1, 24.9, 24.8, 14.1.

**HRMS** (ESI) m/z calcd. for $C_{22}H_{29}Cl_2N_2O$ $[M+H]^+$ 407.1651, found 407.1650.

**1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-(thiophen-3-yl)butyl)urea**



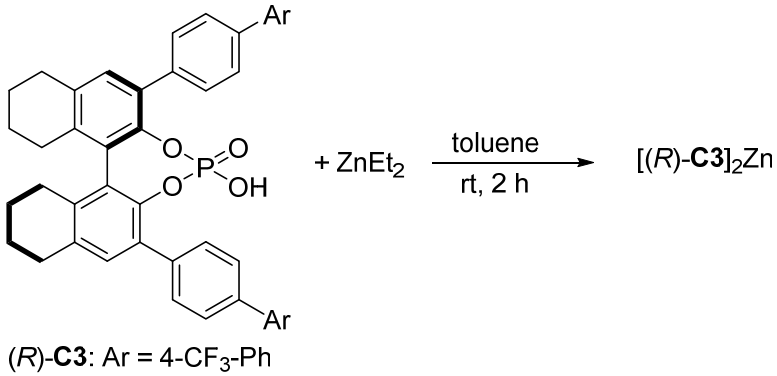

**3v**, 62% yield, **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.30 (s, 1H), 7.64 (s, 2H), 7.37 (s, 1H), 7.16 (dd, *J* = 4.7, 3.2 Hz, 1H), 6.88 – 6.78 (m, 2H), 6.01 (t, *J* = 6.1 Hz, 1H), 3.09 (d, *J* = 6.0 Hz, 2H), 2.61 – 2.46 (m, 2H), 1.57 – 1.42 (m, 2H), 0.89 (s, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 156.4, 142.6, 140.2, 132.2 (q, $J_{C\text{-}F}$ = 33.1 Hz), 128.0, 125.4, 123.0 (q, $J_{C\text{-}F}$ = 271.0 Hz), 119.6, 118.7, 116.0, 50.1, 40.5, 34.4, 24.7, 24.6.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.33.

**HRMS** (ESI) m/z calcd. for $C_{19}H_{21}F_6N_2OS$ $[M+H]^+$ 439.1279, found 439.1276.

## Procedure for the synthesis of [(*R*)-C3]$_2$Zn.

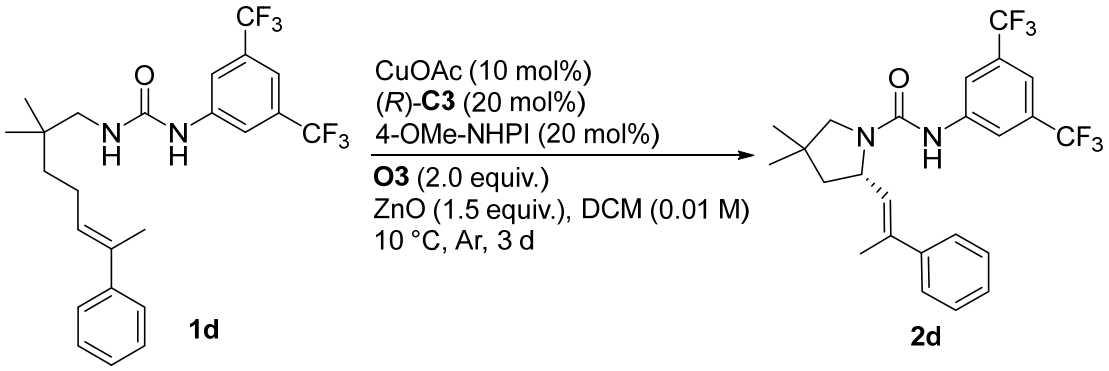



To a flame-dried round bottom flask equipped with a magnetic stir bar was added (*R*)-**C3** (160 mg, 0.2 mmol) and dry toluene (2 mL) was then added *via* syringe. $ZnEt_2$ (100 μL, 1.0 M in hexane solution) was added slowly *via* syringe under Ar. The resulting mixture was stirred at room temperature for 2 h. The solvent was removed under reduced pressure to afford 140 mg [(*R*)-**C3**]$_2$Zn as brown crystal.

[(*R*)-**C3**]$_2$Zn

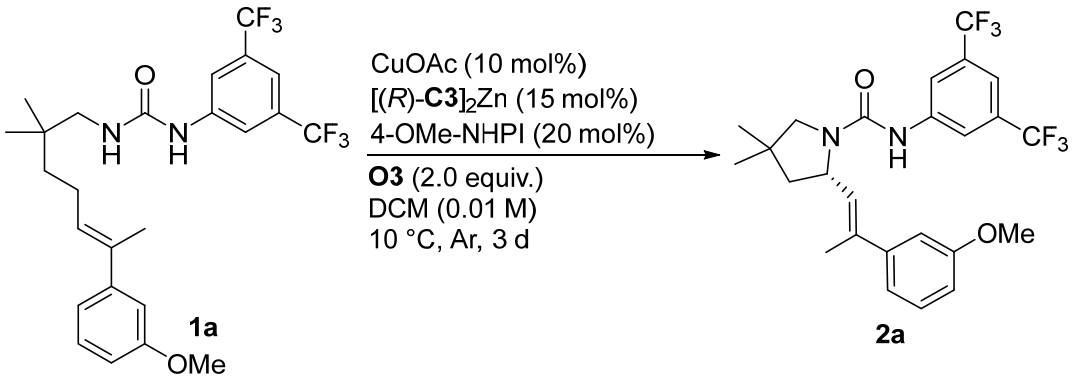
**$^{1}$H NMR (400 MHz, DMSO-$d_6$)** δ 7.95 (dd, *J* = 8.4, 3.0 Hz, 16H), 7.80 (d, *J* = 8.0 Hz, 8H), 7.75 (d, *J* = 8.0 Hz, 8H), 7.18 (s, 4H), 2.93 – 2.76 (m, 8H), 2.70 – 2.59 (m, 4H), 2.21 – 2.14 (m, 4H), 1.81 – 1.73 (m, 12H), 1.58 – 1.53 (m, 4H).
**$^{13}$C NMR (101 MHz, DMSO)** δ 145.3, 145.2, 144.4, 138.5, 137.2, 136.9, 133.7, 130.9, 130.8, 130.7, 128.5, 128.1 (q, *J* = 31.6 Hz), 127.74, 127.01, 126.2–126.1 (m, 1C), 124.7 (q, $J_{C\text{-}F}$ = 271.0 Hz), 29.0, 27.9, 22.7, 22.6.
**$^{19}$F NMR (376 MHz, DMSO)** δ -60.85.
**$^{31}$P NMR (162 MHz, DMSO)** δ 0.02.
**HRMS** (ESI) m/z calcd. for $C_{92}H_{69}F_{12}O_8P_2Zn$ $[M+H]^+$ 1655.3562, found 1655.3566.

## General procedure for enantioselective radical allylic C−H amination under conditions A:



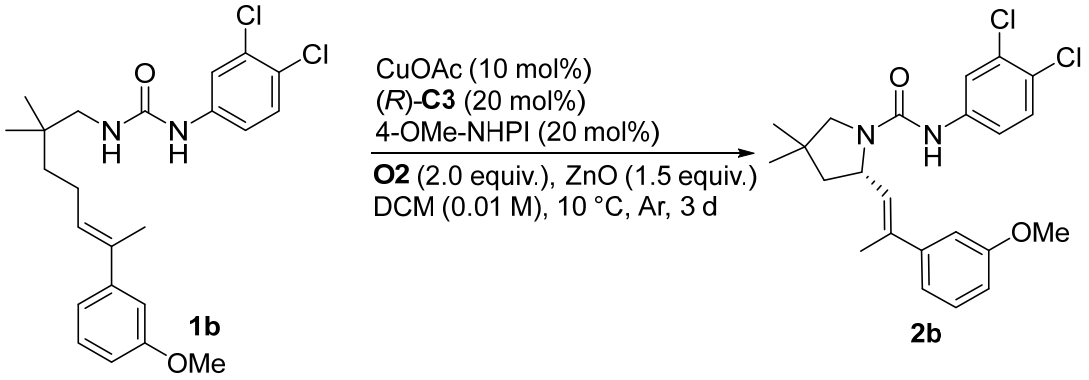

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **1d** (47.5 0.1 mmol), CuOAc (1.24 mg 10 mol%), (*R*)-**C3** (16 mg, 20 mol%), 4-OMe-NHPI (4.0 mg, 20 mol%), and ZnO (12 mg, 0.15 mmol). The tube was evacuated and backfilled with argon for three times, the **O3** (48 μL, 0.2 mmol) and dry DCM (10.0 mL) was added *via* syringe. The tube was stirred at 10 °C for 3 days. After completion, the solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (petroleum ether/ ethyl acetate =20/1−10/1) to give the corresponding product **2d** (35.8 mg) in 76% isolated yield.

## General procedure for enantioselective radical allylic C−H amination under conditions B:



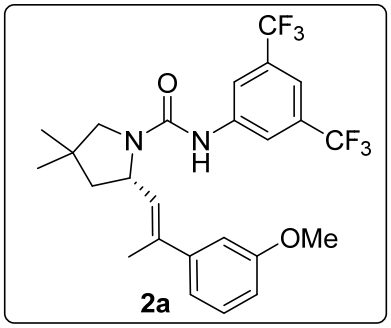

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **1a** (50.5 mg, 0.1 mmol), CuOAc (1.24 mg 10 mol%), [(*R*)-**C3**]$_2$Zn (25 mg, 15 mol%) and 4-OMe-NHPI (4.0 mg, 20 mol%). The tube was evacuated and backfilled with argon for three times, the **O3** (48 μL, 0.2 mmol) and dry DCM (10.0 mL) was added *via* syringe. The tube was stirred at 10 °C for 3 days. After completion, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (petroleum ether/ ethyl acetate =20/1-10/1) to give the corresponding product **2a** (38 mg) in 76% isolated yield.

## Procedure for enantioselective radical allylic C−H amination of 1b.




To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **1d** (47.5 0.1 mmol), CuOAc (1.24 mg 10 mol%), (*R*)-**C3** (16 mg, 20 mol%), 4-OMe-NHPI (4.0 mg, 20 mol%), and ZnO (12 mg, 0.15 mmol). The tube was evacuated and backfilled with argon for three times, the **O2** (36 μL, 0.2 mmol) and dry DCM (10.0 mL) was added *via* syringe. The tube was stirred at 10 °C for 3 days. After completion, the solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (petroleum ether/ ethyl acetate =20/1−10/1) to give the corresponding product **2b** (38 mg) in 88% isolated yield.

**(*S*)(*E*)-N-(3,5-bis(trifluoromethyl)phenyl)-2-(2-(3-methoxyphenyl)prop-1-en-1-yl)-4,4-dimethylpyrrolidine-1-carboxamide**




**2a**, 76% yield, $[\alpha]_D^{27} = -75.8$ (*c* 1.04, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.79 (s, 2H), 7.47 (s, 1H), 7.35 – 7.28 (m, 1H), 7.07 – 6.99 (m, 2H), 6.95 (t, *J* = 2.1 Hz, 1H), 6.89 (ddd, *J* = 8.2, 2.6, 1.2 Hz, 1H), 5.89 (dd, *J* = 9.0, 1.2 Hz, 1H), 4.75 (td, *J* = 9.0, 7.1 Hz, 1H), 3.84 (s, 3H), 3.67 (d, *J* = 10.6 Hz, 1H), 3.26 (d, *J* = 10.6 Hz, 1H), 2.28 (d, *J* = 1.2 Hz, 3H), 2.11 (ddd, *J* = 12.7, 7.1, 1.6 Hz, 1H), 1.75 (dd, *J* = 12.7, 9.1 Hz, 1H), 1.21 (s, 3H), 1.17 (s, 3H).

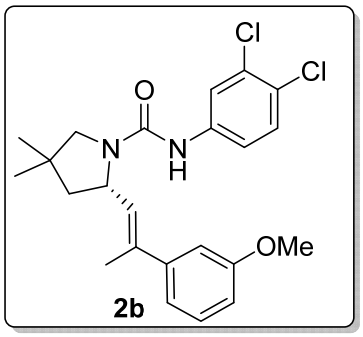
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ (one C signal was overlapped) 159.8, 153.8, 143.4, 140.8, 138.4, 132.1 (q, $J_{C\text{-}F}$ = 33.1 Hz), 129.7, 123.2 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.6 – 118.5 (m, 1C), 118.1, 115.8 – 115.6 (m, 1C), 113.2, 111.7, 59.1, 55.8, 55.3, 47.6, 36.7, 26.3(0), 26.2(7), 16.3.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.07.

**HRMS** (ESI) m/z calcd. for $C_{25}H_{27}F_6N_2O_2$ $[M+H]^+$ 501.1977, found 501.1976.

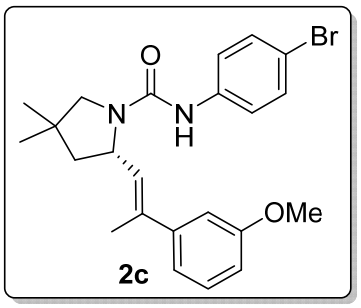
**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(minor) = 10.1 min, t(major) = 14.5 min, 95:5 er.

**(*S*)(*E*)-N-(3,4-dichlorophenyl)-2-(2-(3-methoxyphenyl)prop-1-en-1-yl)-4,4-dimethylpyrrolidine-1-carboxamide**



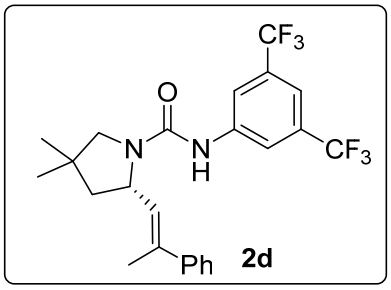

**2b**, 88% yield, $[\alpha]_D^{27}$= –106.6 (*c* 0.62, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-d)** δ 7.59 (d, *J* = 2.5 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.04 – 6.97 (m, 2H), 6.92 (t, *J* = 2.0 Hz, 1H), 6.86 (ddd, *J* = 8.2, 2.4, 0.8 Hz, 1H), 6.67 (s, 1H), 5.85 (dq, *J* = 8.8, 1.3 Hz, 1H), 4.68 (td, *J* = 9.0, 7.2 Hz, 1H), 3.82 (s, 3H), 3.66 – 3.63 (m, 1H), 3.21 (d, *J* = 10.6 Hz, 1H), 2.23 (d, *J* = 1.2 Hz, 3H), 2.06 (ddd, *J* = 12.6, 7.1, 1.5 Hz, 1H), 1.69 (dd, *J* = 12.7, 9.0 Hz, 1H), 1.17 (s, 3H), 1.13 (s, 3H).
**$^{13}$C NMR (101 MHz, CDCl3)** δ 159.8, 154.0, 143.5, 138.9, 137.9, 132.6, 130.3, 129.9, 129.6, 125.4, 120.5, 118.2, 118.1, 113.1, 111.8, 59.1, 55.6, 55.3, 47.6, 36.7, 26.3, 26.2, 16.2.
**HRMS** (ESI) m/z calcd. for $C_{23}H_{27}Cl_2N_2O_2$ $[M+H]^+$ 433.1444, found 433.1441.
**HPLC condition:** Chiralcel AD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(minor) =24.0 min, t(major) = 28.6 min, 94:6 er.

**(*S*)(*E*)-N-(4-bromophenyl)-2-(2-(3-methoxyphenyl)prop-1-en-1-yl)-4,4-dimethylpyrrolidine-1-carboxamide**




**2c**, 80% yield, $[\alpha]_D^{27}$= –78.05 (*c* 0.54, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.34 – 7.29 (m, 2H), 7.28 – 7.25 (m, 1H), 7.23 – 7.13 (m, 2H), 7.00 (ddd, *J* = 7.6, 2.0, 0.8 Hz, 1H), 6.92 (t, *J* = 2.1 Hz, 1H), 6.85 (ddd, *J* = 8.0, 2.4, 0.8 Hz, 1H), 6.65 (s, 1H), 5.86 (dq, *J* = 8.8, 1.2 Hz, 1H), 4.68 (td, *J* = 9.0, 7.2 Hz, 1H), 3.81 (s, 3H), 3.65 (dd, *J* = 10.4, 1.6 Hz, 1H), 3.21 (d, *J* = 10.4 Hz, 1H), 2.23 (d, *J* = 1.3 Hz, 3H), 2.05 (ddd, *J* = 12.7, 7.2, 1.6 Hz, 1H), 1.70 – 1.64 (m, 1H), 1.17 (s, 3H), 1.13 (s, 3H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ (one C signal was overlapped) 159.8, 154.3, 143.6, 138.5, 137.7, 131.8, 130.1, 129.6, 120.4, 118.2, 114.8, 113.0, 111.9, 59.1, 55.5, 55.3, 47.7, 36.6, 26.3, 16.2.
**HRMS** (ESI) m/z calcd. for $C_{23}H_{28}BrN_2O_2$ $[M+H]^+$ 443.1329, found 443.1325.
**HPLC condition:** Chiralcel AD-3, *i*-PrOH/*n*-hexane = 85/15, flow rate 0.8 mL/min. λ = 260 nm, t(minor) =16.6 min, t(major) = 22.0 min, 94:6 er.

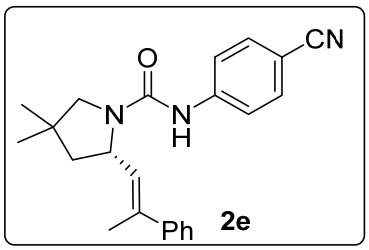
**(*S*)(*E*)-N-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(2-phenylprop-1-en-1-yl)pyrrolidine-1-carboxamide**




**2d**, 76% yield, $[\alpha]_D^{27}$= –23.88 (*c* 0.1, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.76 (s, 2H), 7.48 – 7.29 (m, 6H), 7.01 (s, 1H), 5.86 (dd, *J* = 9.0, 1.4 Hz, 1H), 4.73 (td, *J* = 9.0, 7.1 Hz, 1H), 3.66 (dd, *J* = 10.6, 1.6 Hz, 1H), 3.23 (d, *J* = 10.7 Hz, 1H), 2.28 (d, *J* = 1.4 Hz, 3H), 2.09 (ddd, *J* = 12.6, 7.1, 1.6 Hz, 1H), 1.73 (dd, *J* = 12.7, 9.1 Hz, 1H), 1.19 (s, 3H), 1.15 (s, 3H).

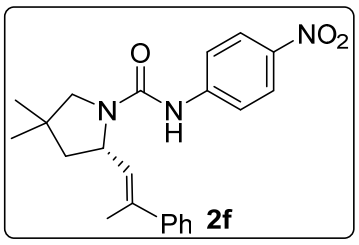
**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 153.8, 141.9, 140.8, 132.1 (q, $J_{C-F}$ = 33.1 Hz), 129.6, 128.7, 128.1, 127.3, 125.7, 123.2 (q, $J_{C-F}$ = 271.0 Hz), 118.5 – 118.4 (m, 1C), 115.8 – 115.6 (m, 1C), 59.2, 55.8, 47.6, 36.7, 26.3(2), 26.2(9), 16.3.
$^{19}$F NMR (376 MHz, $CDCl_3$) δ -63.09.
**HRMS** (ESI) m/z calcd. for $C_{24}H_{25}F_6N_2O$ $[M+H]^+$ 471.1871, found 471.1875.
**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.4 mL/min. λ = 254 nm, t(minor) = 11.9 min, t(major) = 14.8 min, 93:7 er.

**(*S*)(*E*)-N-(4-cyanophenyl)-4,4-dimethyl-2-(2-phenylprop-1-en-1-yl)pyrrolidine-1-carboxamide**



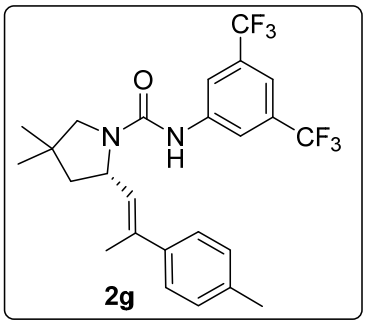

**2e**, 78% yield, $[\alpha]_D^{27}$ = −137.1 (*c* 0.5, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.53 – 7.45 (m, 2H), 7.44 – 7.31 (m, 7H), 6.97 (s, 1H), 5.86 (dd, *J* = 9.1, 1.4 Hz, 1H), 4.72 (td, *J* = 9.0, 7.1 Hz, 1H), 3.67 (dd, *J* = 10.8, 1.6 Hz, 1H), 3.22 (d, *J* = 10.7 Hz, 1H), 2.27 (d, *J* = 1.6 Hz, 3H), 2.07 (ddd, *J* = 12.7, 7.1, 1.6 Hz, 1H), 1.71 (dd, *J* = 12.7, 9.1 Hz, 1H), 1.17 (s, 3H), 1.14 (s, 3H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 153.7, 143.6, 141.8, 138.4, 133.3, 129.5, 128.7, 128.1, 125.7, 119.3, 118.4, 105.0, 59.1, 55.7, 47.6, 36.7, 26.4, 26.3, 16.2.
**HRMS** (ESI) m/z calcd. for $C_{23}H_{26}N_3O$ $[M+H]^+$ 360.2076, found 360.2071.
**HPLC condition:** Chiralcel AD-3, *i*-PrOH/*n*-hexane = 85/15, flow rate 0.8 mL/min. λ = 254 nm, t(minor) = 15.3 min, t(major) = 24.6 min, 92.5:7.5 er.

**(*S*)(*E*)-4,4-dimethyl-N-(4-nitrophenyl)-2-(2-phenylprop-1-en-1-yl)pyrrolidine-1-carboxamide**



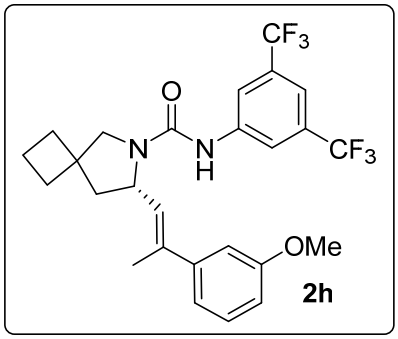

**2f**, 62% yield, $[\alpha]_D^{27}$ = −14.7 (*c* 0.1, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.11 (d, *J* = 8.8 Hz, 2H), 7.44 – 7.32 (m, 7H), 7.11 (s, 1H), 5.88 (d, *J* = 9.1 Hz, 1H), 4.73 (q, *J* = 8.5 Hz, 1H), 3.68 (d, *J* = 10.7 Hz, 1H), 3.24 (d, *J* = 10.8 Hz, 1H), 2.29 (s, 3H), 2.09 (dd, *J* = 12.7, 7.0 Hz, 1H), 1.73 (dd, *J* = 12.7, 9.1 Hz, 2H), 1.19 (s, 3H), 1.15 (s, 3H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 153.5, 145.5, 142.2, 141.7, 138.6, 129.4, 128.7, 128.2, 125.7, 125.2, 117.7, 59.2, 55.8, 47.7, 36.6, 26.3(0), 26.2(9), 16.2.
**HRMS** (ESI) m/z calcd. for $C_{22}H_{26}N_3O_3$ $[M+H]^+$ 380.1974, found 380.1974.
**HPLC condition:** Chiralcel AD-3, *i*-PrOH/*n*-hexane = 85/15, flow rate 0.8 mL/min. λ = 254 nm, t(minor) = 16.0 min, t(major) = 25.8 min, 91:9 er.

**(*S*)(*E*)-N-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(2-(p-tolyl)prop-1-en-1-yl)pyrrolidine-1-carboxamide**



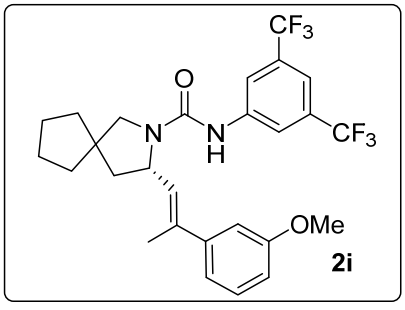

**2g**, 81% yield, $[\alpha]_D^{27}$ = –78.6 (*c* 0.6, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.75 (s, 2H), 7.44 (s, 1H), 7.36 – 7.28 (m, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.06 (s, 1H), 5.89 – 5.77 (m, 1H), 4.72 (td, *J* = 9.1, 7.0 Hz, 1H), 3.66 (dd, *J* = 10.8, 1.6 Hz, 1H), 3.23 (d, *J* = 10.7 Hz, 1H), 2.36 (s, 3H), 2.26 (d, *J* = 1.3 Hz, 3H), 2.08 (ddd, *J* = 12.6, 7.1, 1.6 Hz, 1H), 1.72 (dd, *J* = 12.8, 9.1 Hz, 1H), 1.18 (s, 3H), 1.14 (s, 3H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 153.9, 140.8, 138.9, 138.5, 138.1, 132.1 (q, $J_{C\text{-}F}$ = 33.1 Hz), 129.4, 128.7, 125.5, 123.2 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.5 – 118.4 (m, 1C), 115.7 – 115.5 (m, 1C), 59.1, 55.8, 47.7, 36.6, 26.3(0), 26.2(8), 21.1, 16.2.
**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.07.
**HRMS** (ESI) m/z calcd. for $C_{25}H_{27}F_6N_2O$ $[M+H]^+$ 485.2028, found 485.2028.
**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.4 mL/min. λ = 254 nm, t(minor) = 10.4 min, t(major) = 13.0 min, 92:8 er.

**(*S*)(*E*)-N-(3,5-bis(trifluoromethyl)phenyl)-7-(2-(3-methoxyphenyl)prop-1-en-1-yl)-6-azaspiro[3.4]octane-6-carboxamide**




**2h**, 80% yield, $[\alpha]_D^{27}$ = –80.6 (*c* 0.8, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.76 (s, 2H), 7.45 (s, 1H), 7.29 (t, *J* = 8.0 Hz, 1H), 6.99 (ddd, *J* = 7.8, 1.8, 0.9 Hz, 1H), 6.94 (s, 1H), 6.93 – 6.92 (m, 1H), 6.86 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 5.84 (dd, *J* = 9.1, 1.4 Hz, 1H), 4.64 (dt, *J* = 9.1, 7.2 Hz, 1H), 3.82 (s, 3H), 3.81 (d, *J* = 10.7 Hz, 1H), 3.50 (d, *J* = 10.7 Hz, 1H), 2.34 (ddd, *J* = 12.6, 7.2, 1.1 Hz, 1H), 2.25 (d, *J* = 1.3 Hz, 3H), 2.16 – 1.87 (m, 7H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 159.8, 153.8, 143.4, 140.8, 138.2, 132.1 (q, $J_{C\text{-}F}$ = 33.1 Hz), 129.7, 129.5, 123.2 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.5 – 118.4 (m, 1C), 118.1, 115.7 – 115.6 (m, 1C), 113.2, 111.8, 57.9, 55.6, 55.3, 45.8, 43.4, 32.4, 30.6, 16.3, 16.1.
**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.08.
**HRMS** (ESI) m/z calcd. for $C_{26}H_{27}F_6N_2O_2$ $[M+H]^+$ 513.1977, found 513.1980.
**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(minor) = 13.0 min, t(major) = 16.0 min, 94:6 er.

**(*S*)(*E*)-N-(3,5-bis(trifluoromethyl)phenyl)-3-(2-(3-methoxyphenyl)prop-1-en-1-yl)-2-azaspiro[4.4]nonane-2-carboxamide**




**2i**, 84% yield, $[\alpha]_D^{27}$ = –60.3 (*c* 0.8, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.77 (s, 2H), 7.45 (s, 1H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.04 – 6.97 (m, 2H), 6.93 (t, *J* = 2.1 Hz, 1H), 6.87 (ddd, *J* = 8.2, 2.5, 0.9 Hz, 1H), 5.88 (dd, *J* = 9.1, 1.4 Hz, 1H), 4.66 (td, *J* = 8.6, 7.1 Hz, 1H), 3.82 (s, 3H), 3.69 (d, *J* = 10.6 Hz, 1H), 3.33 (d, *J* = 10.6 Hz, 1H), 2.26 (d, *J* = 1.4

Hz, 3H), 2.19 (ddd, *J* = 12.5, 7.1, 1.4 Hz, 1H), 1.86 (dd, *J* = 12.5, 8.4 Hz, 1H), 1.77 – 1.49 (m, 8H).

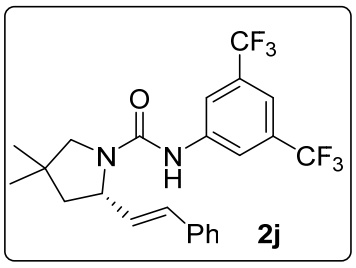
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 159.8, 153.8, 143.4, 140.8, 138.4, 132.1 (q, $J_{C\text{-}F}$ = 33.1 Hz), 129.8, 129.7, 123.2 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.5 – 118.4 (m, 1C), 118.1, 115.7 – 115.6 (m, 1C), 113.2, 111.7, 57.9, 56.2, 55.3, 47.8, 45.9, 37.5, 36.3, 24.9, 24.8, 16.3.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.08.

**HRMS** (ESI) m/z calcd. for $C_{27}H_{29}F_6N_2O_2$ $[M+H]^+$ 527.2133, found 527.2136.

**HPLC condition**: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(minor) = 10.9 min, t(major) = 15.1 min, 90:10 er.

**(*S*)(*E*)-N-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-styrylpyrrolidine-1-carboxamide**




**2j**, 54% yield, $[\alpha]_D^{27}$ = –50.9 (*c* 0.5, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.79 (s, 2H), 7.48 – 7.42 (m, 3H), 7.42 – 7.37 (m, 2H), 7.37 – 7.31 (m, 1H), 7.11 (s, 1H), 6.83 (d, *J* = 16.0 Hz, 1H), 6.27 (dd, *J* = 16.0, 8.4 Hz, 1H), 4.52 (q, *J* = 8.0 Hz, 1H), 3.71 (d, *J* = 10.6 Hz, 1H), 3.27 (d, *J* = 10.6 Hz, 1H), 2.12 (ddd, *J* = 12.8, 7.2, 1.6 Hz, 1H), 1.82 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.22 (s, 3H), 1.15 (s, 3H).

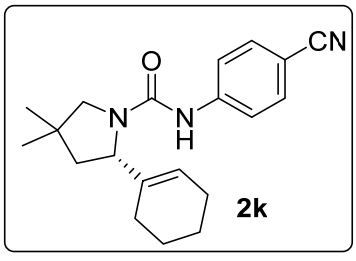
**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 154.0, 140.6, 135.3, 132.6, 132.4, 131.9 (q, $J_{C\text{-}F}$ = 33.1 Hz), 129.0, 128.7, 126.5, 123.2 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.6 – 118.5 (m, 1C), 115.8 – 115.7 (m, 1C), 60.1, 59.4, 48.2, 36.8, 26.3, 26.2.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.09.

**HRMS** (ESI) m/z calcd. for $C_{23}H_{23}F_6N_2O$ $[M+H]^+$ 457.1709, found 457.1708.

**HPLC condition**: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 13.3 min, t(minor) = 20.8 min, 90:10 er.

**(*S*)-*N*-(4-cyanophenyl)-2-(cyclohex-1-en-1-yl)-4,4-dimethylpyrrolidine-1-carboxamide**




**2k**, 25% yield (40% conversion), $[\alpha]_D^{27}$ = 14.4 (*c* 0.14, $CHCl_3$). **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.55 (d, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.25 (s, 1H), 6.02 (t, *J* = 1.7 Hz, 1H), 4.27 (dd, *J* = 9.9, 7.1 Hz, 1H), 3.76 (dd, *J* = 10.9, 1.8 Hz, 1H), 3.08 (d, *J* = 10.9 Hz, 1H), 2.20 – 2.17 (m, 2H), 1.99 – 1.96 (m, 2H), 1.90 – 1.85 (m, 1H), 1.82 – 1.75 (m, 1H), 1.73 – 1.58 (m, 4H), 1.16 (s, 3H), 1.09 (s, 3H).

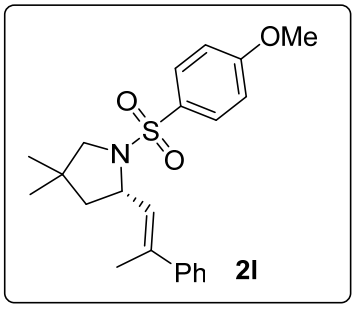
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 153.8, 143.7, 139.5, 133.3, 126.4, 119.3, 118.2, 104.9, 63.9, 59.5, 46.1, 36.2, 26.1, 25.8, 25.3, 22.4(2), 22.4(1), 22.3.

**HRMS** (ESI) m/z calcd. for $C_{20}H_{26}N_3O$ $[M+H]^+$ 324.2076, found 324.2074.

**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane =97/3, flow rate 0.3 mL/min. λ = 254 nm, t(major) =60.8 min, t(minor) = 69.5 min, 76:24 er.

**(*S*)(*E*)-1-((4-methoxyphenyl)sulfonyl)-4,4-dimethyl-2-(2-phenylprop-1-en-1-**

**yl)pyrrolidine**



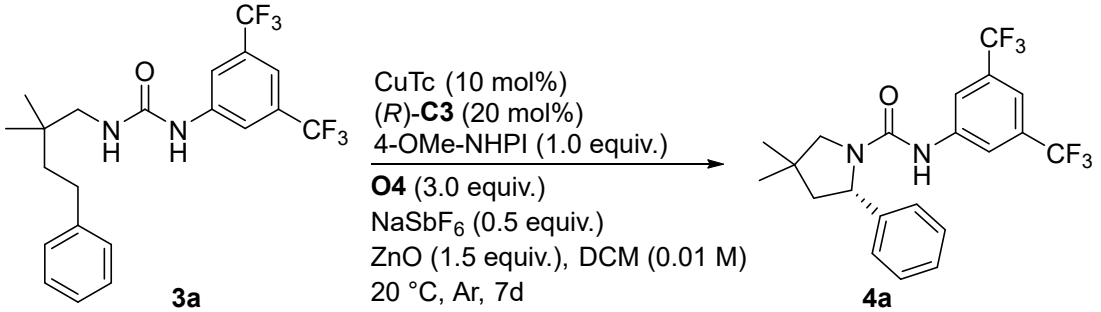
**2l**

**2l**, 35% yield (75% conversion), $[\alpha]_D^{27}$ = –30.9 (*c* 0.2, $CHCl_3$). **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.75 (d, J = 8.3 Hz, 2H), 7.44 – 7.10 (m, 5H), 6.91 (d, J = 8.4 Hz, 2H), 5.66 (d, J = 8.6 Hz, 1H), 4.54 (q, J = 8.3 Hz, 1H), 3.83 (s, 3H), 3.32 (d, J = 10.0 Hz, 1H), 3.23 (d, J = 10.0 Hz, 1H), 2.10 (s, 3H), 1.91 (dd, J = 12.7, 7.6 Hz, 1H), 1.57 (dd, J = 12.6, 8.7 Hz, 1H), 1.12 (s, 3H), 0.92 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 162.6, 142.9, 134.9, 131.2, 129.8, 129.5, 128.1, 127.0, 125.8, 113.9, 61.1, 58.0, 55.5, 47.7, 37.6, 26.6, 26.2, 16.0.

**HRMS** (ESI) m/z calcd. for $C_{22}H_{28}NO_3S$ $[M+H]^+$ 386.1790, found 386.1786.

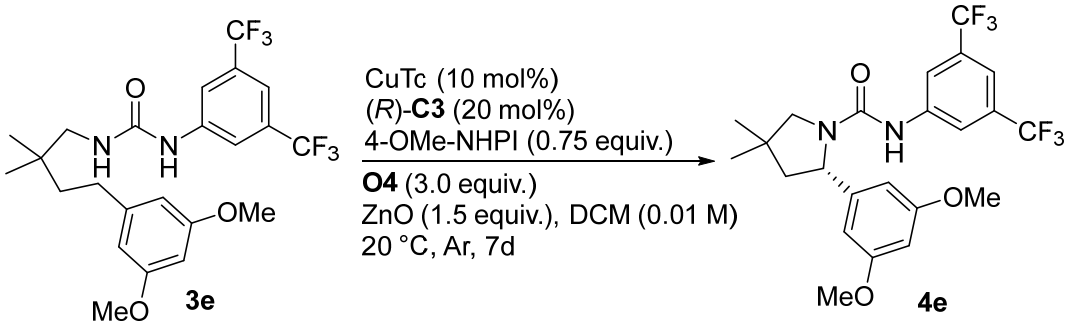
**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 16.0 min, t(minor) = 18.4 min, 87:13 er.

## General procedure for enantioselective radical benzylic C−H amination:



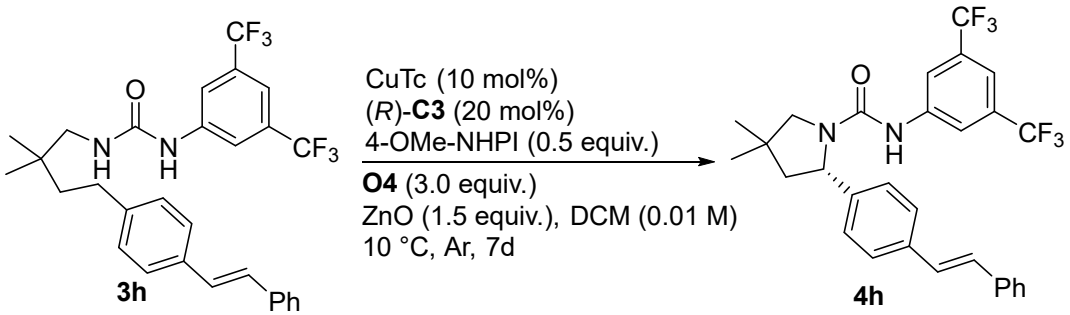

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **3a** (43.2 mg, 0.1 mmol), CuTc (1.9 mg 10 mol%), (*R*)-**C3** (16 mg, 20 mol%), 4-OMe-NHPI (19 mg, 0.1 mmol), ZnO (12 mg, 0.15 mmol) and $NaSbF_6$ (13 mg, 0.05 mmol). The tube was evacuated and backfilled with argon for three times, the **O4** (72 μL, 0.3 mmol) and dry DCM (10.0 mL) was added *via* syringe. The tube was stirred at 20 °C and (*R*)-**C3** (4 mg, 5 mol%) was added after 12 h and 24 h, respectively. After 7 days, the reaction stopped and the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (petroleum ether/ ethyl acetate =20/1-10/1) to give the corresponding product **4a** in 38% isolated yield with 55% conversion (67% yield based on recovered starting material).

## Procedure for enantioselective radical benzylic C−H amination of 3e.



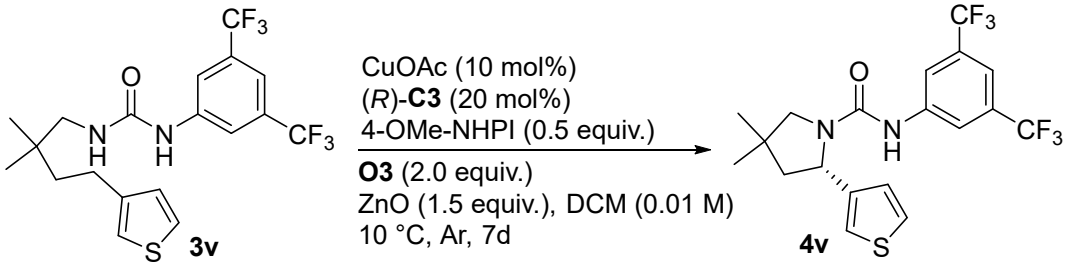

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **3e** (49.3 mg, 0.1 mmol), CuTc (1.9 mg 10 mol%), (*R*)-**C3** (16 mg, 20 mol%), 4-OMe-NHPI (14.3 mg, 0.075 mmol), and ZnO (12 mg, 0.15 mmol). The tube was evacuated and backfilled with argon for three times, the **O4** (72 μL, 0.3 mmol) and dry DCM (10.0 mL) was added *via* syringe. The tube was stirred at 10 °C and (*R*)-**C3** (4 mg, 5 mol%) was added after 12 h and 24 h, respectively. After 7 days, the reaction stopped and the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (petroleum ether/ ethyl acetate =20/1-10/1) to give the corresponding product **4e** in 40% isolated yield with 53% conversion (76% yield based on recovered starting material).

## Procedure for enantioselective radical benzylic C−H amination of 3h.



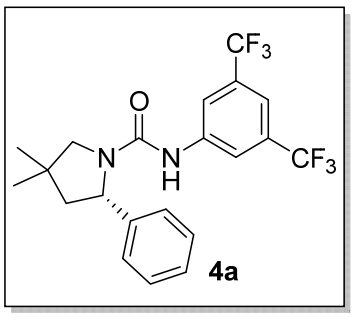

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **3h** (53.5 mg, 0.1 mmol), CuTc (1.9 mg 10 mol%), (*R*)-**C3** (16 mg, 20 mol%), 4-OMe-NHPI (9.5 mg, 0.05 mmol), and ZnO (12 mg, 0.15 mmol). The tube was evacuated and backfilled with argon for three times, the **O4** (72 μL, 0.3 mmol) and dry DCM (10.0 mL) was added *via* syringe. The tube was stirred at 10 °C and (*R*)-**C3** (4 mg, 5 mol%) was added after 12 h and 24 h, respectively. After 7 days, the reaction stopped and the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (petroleum ether/ ethyl acetate =20/1-10/1) to give the corresponding product **4h** in 44% isolated yield with 60% conversion (73% yield based on recovered starting material).

## Procedure for enantioselective radical benzylic C−H amination of 3v.




To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **3v** (43.8 mg, 0.1 mmol), CuOAc (1.24 mg 10 mol%), (*R*)-**C3** (16 mg, 20 mol%), 4-OMe-NHPI (9.5 mg, 0.05 mmol), and ZnO (12 mg, 0.15 mmol). The tube was evacuated and backfilled with argon for three times, the **O3** (48 μL, 0.2 mmol) and dry DCM (10.0 mL) was added *via* syringe. The tube was stirred at 10 °C and (*R*)-**C3** (4 mg, 5 mol%) was added after 12 h and 24 h, respectively. After 7 days, the reaction stopped and the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (petroleum ether/ ethyl acetate =20/1-10/1) to give the corresponding product **4v** in 51% isolated yield with 71% conversion (72% yield based on recovered starting material).

**(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-phenylpyrrolidine-1-carboxamide**




**4a**, 69% yield based on recovered starting material, $[\alpha]_D^{27}$ = –63.1 (*c* 0.5, $CHCl_3$).

**$^1$H NMR (400 MHz, $CDCl_3$)**: δ 7.53 (s, 2H), 7.47-7.37 (m, 6H), 6.29 (s, 1H), 4.86 (dd, *J* = 9.2, 7.2 Hz, 1H), 3.85 (d, *J* = 10.4 Hz, 1H), 3.40 (d, *J* = 10.8 Hz, 1H), 2.28 (ddd, *J* = 12.7, 7.0, 1.5 Hz, 1H), 1.84 (dd, *J* = 12.4, 10.0 Hz, 1H), 1.19 (s, 3H), 1.18 (s, 3H).

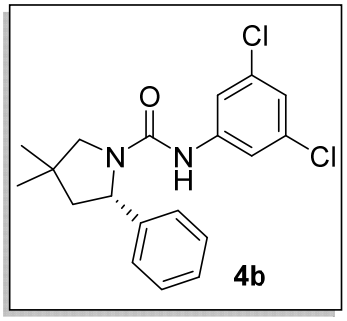
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 153.6, 142.1, 140.5, 131.9 (q, $J_{C\text{-}F}$ = 33.3 Hz), 129.7, 128.6, 125.9, 123.1(q, $J_{C\text{-}F}$ = 271.0 Hz), 118.7 – 118.6 (m, 1C), 116.0 – 115.8 (m, 1C), 61.7, 60.3, 52.0, 37.3, 26.1, 25.9.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.09.

**HRMS** (ESI) m/z calcd. for $C_{21}H_{21}F_6N_2O$ $[M+H]^+$ 431.1553, found 431.1549.

**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 10.6 min, t(minor) = 16.4 min, 95:5 er.

**(*S*)-*N*-(3,5-dichlorophenyl)-4,4-dimethyl-2-phenylpyrrolidine-1-carboxamide**

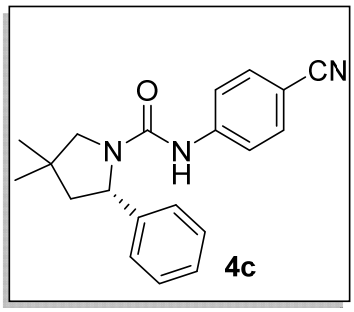



**4b**, 84% yield based on recovered starting material, $[\alpha]_D^{27}$ = –31.7 (*c* 0.1, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.45 – 7.41 (m, 2H), 7.38 – 7.34 (m, 3H), 7.02 (s, 2H), 6.90 (t, *J* = 2.0 Hz, 1H), 6.04 (s, 1H), 4.80 (dd, *J* = 9.6, 6.8 Hz, 1H), 3.84 (d, *J* = 10.8 Hz, 1H), 3.37 (d, *J* = 10.8 Hz, 1H), 2.25 (ddd, *J* = 12.9, 7.0, 1.7 Hz, 1H), 1.81 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.17 (s, 3H), 1.15 (s, 3H).

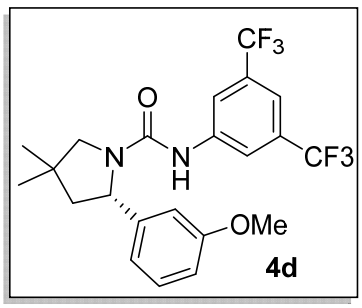
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 153.6, 142.2, 140.9, 134.8, 129.7, 128.5, 125.9, 122.5, 117.1, 61.7, 60.2, 52.1, 37.3, 26.1, 25.9.
**HRMS** (ESI) m/z calcd. for $C_{19}H_{21}Cl_2N_2O$ $[M+H]^+$ 363.1025, found 363.1022.
**HPLC condition:** Chiralcel IA, *i*-PrOH/*n*-hexane = 90/10, flow rate 1.0 mL/min. λ = 254 nm, t(major) = 6.8 min, t(minor) = 12.7 min, 91:9 er.

**(*S*)-*N*-(4-cyanophenyl)-4,4-dimethyl-2-phenylpyrrolidine-1-carboxamide**



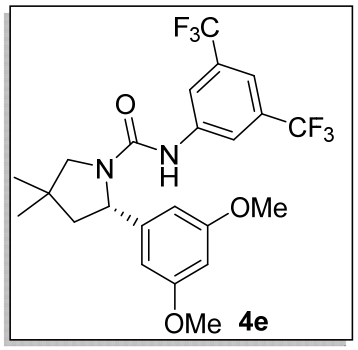

**4c**, 72% yield based on recovered starting material, $[\alpha]_D^{27}$ = –77.8 (*c* 0.5, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.46 – 7.41 (m, 4H), 7.38 – 7.34 (m, 3H), 7.15 (d, *J* = 8.4 Hz, 2H), 6.25 (s, 1H), 4.83 (dd, *J* = 9.8, 7.0 Hz, 1H), 3.87 (d, *J* = 10.8 Hz, 1H), 3.38 (d, *J* = 10.8 Hz, 1H), 2.26 (ddd, *J* = 12.8, 7.0, 1.8 Hz, 1H), 1.83 (dd, *J* = 12.8, 10.0 Hz, 1H), 1.18 (s, 3H), 1.17 (s, 3H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 153.5, 143.2, 142.1, 133.1, 129.7, 128.6, 126.0, 119.2, 118.5, 105.1, 61.8, 60.2, 52.1, 37.2, 26.1, 25.9.
**HRMS** (ESI) m/z calcd. for $C_{20}H_{22}N_3O$ $[M+H]^+$ 320.1757, found 320.1756.
**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 85/15, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 16.1 min, t(minor) = 20.8 min, 92:8 er.

**(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(3-methoxyphenyl)-4,4-dimethylpyrro lidine-1-carboxamide**




**4d**, 61% yield based on recovered starting material, $[\alpha]_D^{27}$ = –44.5 (*c* 0.6, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.57 (s, 2H), 7.42 (s, 1H), 7.39 – 7.34 (m, 1H), 6.97 – 6.95 (m, 1H), 6.91 – 6.88 (m, 2H), 6.36 (s, 1H), 4.82 (dd, *J* = 9.6, 7.2 Hz, 1H), 3.85 – 3.82 (m, 4H), 3.38 (d, *J* = 10.4 Hz, 1H), 2.27 (ddd, *J* = 12.8, 7.0, 1.7 Hz, 1H), 1.84 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.18 (s, 3H), 1.16 (s, 3H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 160.6, 153.6, 143.8, 140.5,131.9 (q, $J_{C\text{-}F}$ = 33.1 Hz), 130.8, 123.2 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.7 – 118.6 (m, 1C), 118.0, 115.9 – 115.8 (m, 1C), 113.5, 111.9, 61.6, 60.2, 55.3, 51.8, 37.3, 26.1, 25.9.
**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.07.
**HRMS** (ESI) m/z calcd. for $C_{22}H_{23}F_6N_2O_2$ $[M+H]^+$ 461.1658, found 461.1655.
**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 15.1 min, t(minor) = 29.9 min, 95:5 er.

**(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(3,5-dimethoxyphenyl)-4,4-dimethyl pyrrolidine-1-carboxamide**




**4e**, 76% yield based on recovered starting material,$[\alpha]_D^{27}$= –18.4 (*c* 0.2, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.61 (s, 2H), 7.42 (s, 1H), 6.50 (d, *J* = 2.0 Hz, 2H), 6.47 (s, 1H), 6.43 (t, *J* = 2.0 Hz, 1H), 4.78 (dd, *J* = 9.6, 7.2 Hz, 1H), 3.85 – 3.80 (m, 7H), 3.36 (d, *J* = 10.4 Hz, 1H), 2.25 (ddd, *J* = 12.8, 7.0, 1.7 Hz, 1H), 1.84 (dd, *J* = 12.8, 10.0 Hz, 1H), 1.18 (s, 3H), 1.15 (s, 3H).

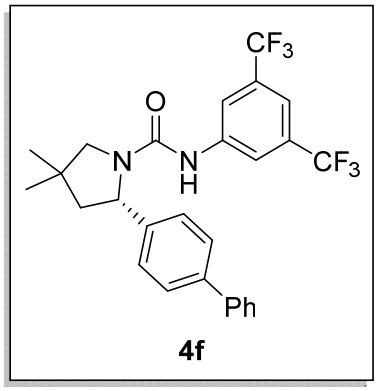
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 161.9, 153.8, 144.7, 140.6, 132.0 (q, $J_{C\text{-}F}$ = 33.1 Hz), 123.2 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.7 – 118.6 (m, 1C), 115.9 – 115.7 (m, 1C), 103.9, 99.5, 61.8, 60.2, 55.4, 51.5, 37.3, 26.1, 25.8.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.07.

**HRMS** (ESI) m/z calcd. for $C_{23}H_{25}F_6N_2O_3$ $[M+H]^+$ 491.1764, found 491.1762.

**HPLC condition:** Chiralcel AD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.8 mL/min. λ = 254 nm, t(major) = 7.3 min, t(minor) = 13.3 min, 94.5:5.5 er.

**(*S*)-2-([1,1'-biphenyl]-4-yl)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl pyrrolidine-1-carboxamide**




**4f**, 64% yield based on recovered starting material, $[\alpha]_D^{27}$= –74.5 (*c* 0.8, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.66 – 7.57 (m, 6H), 7.47 – 7.41 (m, 5H), 7.39 – 7.35 (m, 1H), 6.40 (s, 1H), 4.93 (t, *J* = 8.2 Hz, 1H), 3.84 (d, *J* = 10.4 Hz, 1H), 3.44 (d, *J* = 10.4 Hz, 1H), 2.31 (ddd, *J* = 12.8, 7.0, 1.7 Hz, 1H), 1.87 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.20 (s, 3H), 1.19 (s, 3H).

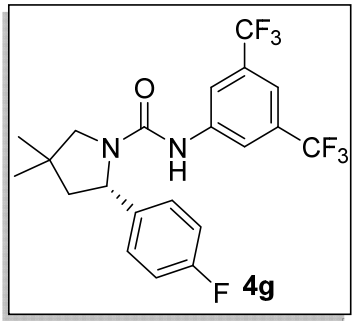
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 153.6, 141.5, 141.1, 140.5, 140.2, 132.0 (q, $J_{C\text{-}F}$ = 33.1 Hz), 128.9, 128.3, 127.6, 127.1, 126.3, 123.1 (q, $J_{C\text{-}F}$ = 271.3 Hz), 118.7 – 118.6 (m, 1C), 115.9 – 115.8 (m, 1C), 61.4, 60.3, 51.8, 37.5, 26.1, 25.9.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.04.

**HRMS** (ESI) m/z calcd. for $C_{27}H_{25}F_6N_2O$ $[M+H]^+$ 507.1866, found 507.1866.

**HPLC condition:** Chiralcel AD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 10.5 min, t(minor) = 12.8 min, 94:6 er.

**(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(4-fluorophenyl)-4,4-dimethylpyro lidine-1-carboxamide**




**4g**, 80% yield based on recovered starting material, $[\alpha]_D^{27}$= –61.1 (*c* 0.6, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.64 (s, 2H), 7.44 (s, 1H), 7.35 – 7.31 (m, 2H), 7.11 (t, *J* = 8.6 Hz, 2H), 6.32 (s, 1H), 4.90 (dd, *J* = 8.8, 7.2 Hz, 1H), 3.78 (d, *J* = 10.8 Hz, 1H), 3.40 (d, *J* = 10.6 Hz, 1H), 2.26 (ddd, *J* = 12.8, 7.0, 1.7 Hz, 1H), 1.77 (dd, *J* = 12.8, 9.6 Hz, 2H), 1.18 (s, 3H), 1.17 (s, 3H).

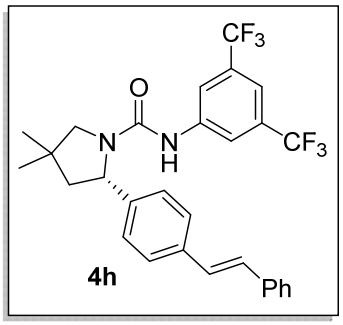
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 162.4 (q, $J_{C\text{-}F}$ = 246.1 Hz), 153.5, 140.3, 138.0, 132.0 (q, $J_{C\text{-}F}$ = 33.1 Hz), 127.4 (d, $J_{C\text{-}F}$ = 8.1 Hz), 123.2 (q, $J_{C\text{-}F}$ = 271.2 Hz), 118.7 – 118.6 (m, 1C), 116.5 (d, $J_{C\text{-}F}$ = 21.5 Hz), 116.0 – 115.9 (m, 1C), 61.0, 60.3, 51.8, 37.6, 26.1, 25.9.

**$^{19}$F NMR (565 MHz, DMSO-$d_6$, 80 °C)** δ -61.80, -116.86.

**HRMS** (ESI) m/z calcd. for $C_{21}H_{20}F_7N_2O$ $[M+H]^+$ 449.1458, found 449.1454.

**HPLC condition:** Chiralcel IA, *i*-PrOH/*n*-hexane = 98/2, flow rate 0.4 mL/min. λ = 254 nm, t(major) = 26.9 min, t(minor) = 31.6 min, 94:6 er.

**(*S*)-(*E*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(4-styrylphenyl) pyrrolidine-1-carboxamide**




**4h**, 73% yield based on recovered starting material, $[\alpha]_D^{27}$= –85 (*c* 1.4, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.60 – 7.56 (m, 4H), 7.53 – 7.51 (m, 2H), 7.41 (s, 1H), 7.39 – 7.34 (m, 4H), 7.30 – 7.27 (m, 1H), 7.11 (d, *J* = 2.0 Hz, 2H), 6.36 (s, 1H), 4.91 – 4.86 (m, 1H), 3.84 (d, *J* = 10.4 Hz, 1H), 3.42 (d, *J* = 10.5 Hz, 1H), 2.28 (ddd, *J* = 12.8, 7.1, 1.6 Hz, 1H), 1.83 (dd, *J* = 12.8, 9.7 Hz, 1H), 1.19 (s, 3H), 1.18 (s, 3H).

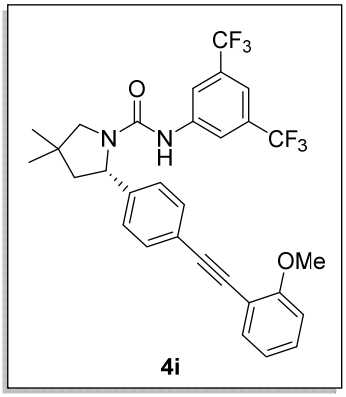
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 153.6, 140.4, 137.0, 135.2, 132.0 (q, $J_{C\text{-}F}$ = 32.9 Hz), 129.6, 128.7, 127.9, 127.7, 127.6, 126.6, 126.2, 124.3, 123.1 (q, $J_{C\text{-}F}$ = 271.1 Hz), 119.1 -118.7 (m, 1C), 116.0 - 115.8 (m, 1C), 61.5, 60.3, 51.8, 37.4, 26.1, 25.9.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.04.

**HRMS** (ESI) m/z calcd. for $C_{29}H_{27}F_6N_2O$ $[M+H]^+$ 533.2028, found 533.2028.

**HPLC condition:** Chiralcel IA, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 15.5 min, t(minor) = 18.7 min, 96:4 er.

**(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(4-((2-methoxyphenyl)ethynyl)phenyl)-4,4-dimethylpyrrolidine-1-carboxamide**



4i

**4i**, 70% yield based on recovered starting material, $[\alpha]_D^{27}$= –43 (*c* 1.0, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.65 (s, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.49 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.43 (s, 1H), 7.28 (d, *J* = 8.1 Hz, 3H), 6.96 – 6.90 (m, 2H), 6.32 (s, 1H), 4.92 – 4.88 (m, 1H), 3.91 (s, 3H), 3.83 – 3.81 (m, 1H), 3.41 (d, *J* = 10.4 Hz, 1H), 2.28 (ddd, *J* = 12.8, 7.2, 1.7 Hz, 1H), 1.82 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.20 (s, 3H), 1.19 (s, 3H).

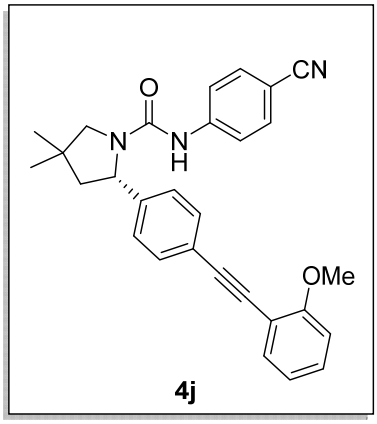
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 160.0, 153.6, 142.1, 140.4, 133.6, 132.8, 132.0 (q, $J_{C\text{-}F}$ = 33.1 Hz), 130.0, 125.7, 123.8, 123.1 (q, $J_{C\text{-}F}$ = 271.1 Hz), 120.5, 119.1 – 118.7 (m, 1C), 116.0 – 115.9 (m, 1C), 112.2, 110.8, 92.6, 86.6, 61.5, 60.3, 55.8, 51.7, 37.6, 26.1, 25.9.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -63.0.

**HRMS** (ESI) m/z calcd. for $C_{30}H_{27}F_6N_2O_2$ $[M+H]^+$ 561.1977, found 561.1978.

**HPLC condition:** Chiralcel IA, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 17.7 min, t(minor) = 22.0 min, 96:4 er.

**(*S*)-*N*-(4-cyanophenyl)-2-(4-((2-methoxyphenyl)ethynyl)phenyl)-4,4-dimethyl pyrrolidine-1-carboxame**



4j

**4j**, 74% yield based on recovered starting material, $[\alpha]_D^{27}$= –154.6 (*c* 0.6, $CHCl_3$).

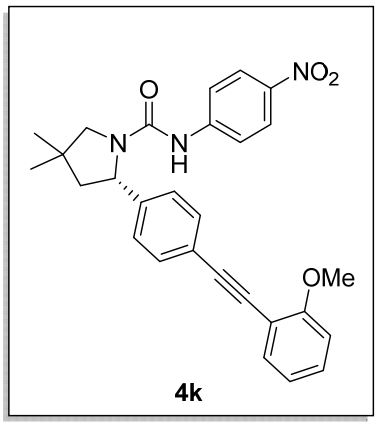
**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.50 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.35 – 7.31 (m, 3H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.97 – 6.91 (m, 2H), 6.23 (s, 1H), 4.85 (dd, *J* = 9.6, 7.0 Hz, 1H), 3.92 (s, 3H), 3.86 (d, *J* = 10.8 Hz, 1H), 3.39 (d, *J* = 10.4 Hz, 1H), 2.27 (ddd, *J* = 12.9, 7.0, 1.6 Hz, 1H), 1.81 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.18 (s, 3H), 1.17 (s, 3H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 156.0, 153.4, 143.1, 142.0, 133.6, 133.1, 132.9, 130.1, 125.9, 123.9, 120.6, 119.2, 118.6, 112.0, 110.7, 105.3, 92.6, 86.8, 61.6, 60.2, 55.9, 51.9, 37.4, 26.1, 25.9.

**HRMS** (ESI) m/z calcd. for $C_{29}H_{28}N_3O_2$ $[M+H]^+$ 450.2176, found 450.2175.

**HPLC condition:** Chiralcel AD-H, *i*-PrOH/*n*-hexane = 75/25, flow rate 1.0 mL/min. λ = 230 nm, t(minor) = 13.7 min, t(major) = 24.9 min, 97:3 er.

**(*S*)-2-(4-((2-methoxyphenyl)ethynyl)phenyl)-4,4-dimethyl-*N*-(4-nitrophenyl) pyrrolidine-1-carboxamde**




**4k**, 69% yield based on recovered starting material, $[\alpha]_D^{27}$= –180 (*c* 1.3, $CHCl_3$).

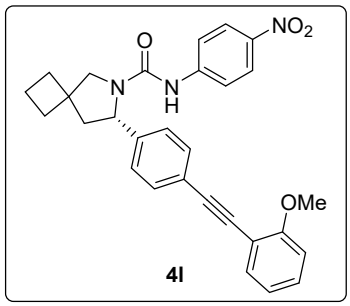
**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 8.09 – 8.05 (m, 2H), 7.63 – 7.61 (m, 2H), 7.50 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.36 – 7.31 (m, 3H), 7.24 (d, *J* = 10.5 Hz, 2H), 6.97 – 6.91 (m, 2H), 6.38 (s, 1H), 4.87 (dd, *J* = 9.6, 7.0 Hz, 1H), 3.92 (s, 3H), 3.86 (d, *J* = 10.8 Hz, 1H), 3.40 (d, *J* = 10.8 Hz, 1H), 2.28 (ddd, *J* = 12.8, 7.1, 1.7 Hz, 1H), 1.82 (dd, *J* = 12.8, 9.7 Hz, 1H), 1.19 (s, 3H), 1.17 (s, 3H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 160.0, 153.2, 145.0, 142.4, 141.9, 133.6, 132.9, 130.1, 125.9, 125.1, 124.0, 120.6, 117.9, 112.0, 110.7, 92.5, 86.8, 61.6, 60.3, 55.9, 51.9, 37.4, 26.1, 25.9.

**HRMS** (ESI) m/z calcd. for $C_{28}H_{28}N_3O_4$ $[M+H]^+$ 470.2074, found 470.2075.

**HPLC condition**: Chiralcel IA, *i*-PrOH/*n*-hexane = 85/15, flow rate 1.0 mL/min. λ = 280 nm, t(minor) = 26.6 min, t(major) = 31.7 min, 96.5:3.5 er.

**(*S*)-7-(4-((2-methoxyphenyl)ethynyl)phenyl)-N-(4-nitrophenyl)-6-azaspiro [3.4]octane-6-carboxamide**




**4l**, 68% yield based on recovered starting material, $[\alpha]_D^{27}$= –123.3 (*c* 0.4, $CHCl_3$).

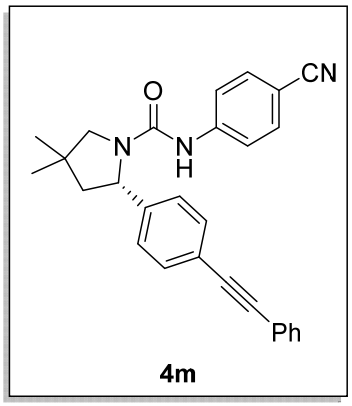
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.08 (d, *J* = 9.2 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.52 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.40 – 7.32 (m, 3H), 7.28 (d, *J* = 5.6 Hz, 2H), 7.02 – 6.89 (m, 2H), 6.40 (s, 1H), 4.84 (t, *J* = 7.3 Hz, 1H), 4.01 (d, *J* = 10.8 Hz, 1H), 3.94 (s, 3H), 3.68 (d, *J* = 10.7 Hz, 1H), 2.56 (dd, *J* = 12.6, 7.3 Hz, 1H), 2.18 – 1.85 (m, 7H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 156.0, 153.3, 145.0, 142.4, 141.5, 133.6, 132.7, 130.1, 125.9, 125.0, 123.8, 120.6, 118.0, 112.0, 110.7, 92.6, 86.8, 61.2, 59.0, 55.9, 49.3, 43.7, 32.6, 30.4, 16.1.

**HRMS** (ESI) m/z calcd. for $C_{29}H_{28}N_3O_4$ $[M+H]^+$ 480.2080, found 480.2081.

**HPLC condition:** Chiralcel AD-H, *i*-PrOH/*n*-hexane = 70/30, flow rate 1.0 mL/min. λ = 280 nm, t(minor) = 18.3 min, t(major) = 27.0 min, 96:4 er.

**(*S*)-*N*-(4-cyanophenyl)-4,4-dimethyl-2-(4-(phenylethynyl)phenyl)pyrrolidine-1-carboxamide**




**4m**, 80% yield based on recovered starting material, $[\alpha]_D^{27}$= –107 (*c* 1.1, $CHCl_3$).

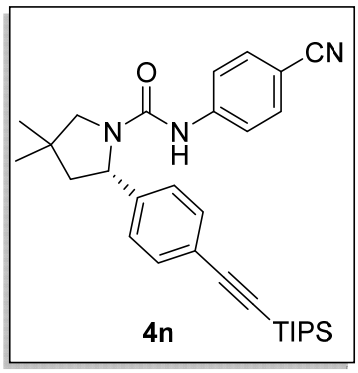
**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.58 (d, *J* = 8.4 Hz, 2H), 7.54 – 7.52 (m, 2H), 7.46 – 7.43 (m, 2H), 7.37 – 7.33 (m, 5H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.28 (s, 1H), 4.88 (dd, *J* = 9.6, 7.2 Hz, 1H), 3.82 (d, *J* = 10.4 Hz, 1H), 3.39 (d, *J* = 10.4 Hz, 1H), 2.26 (ddd, *J* = 12.8, 7.1, 1.7 Hz, 1H), 1.80 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.17 (s, 3H), 1.16 (s, 3H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 153.4, 143.1, 142.3, 133.1, 132.7, 131.6, 128.6, 128.4, 125.9, 123.4, 122.9, 119.2, 118.6, 105.3, 90.3, 88.6, 61.5, 60.3, 51.7, 37.5, 26.1, 25.9.

**HRMS** (ESI) m/z calcd. for $C_{28}H_{26}N_3O$ $[M+H]^+$ 420.2070, found 420.2067.

**HPLC condition:** Chiralcel IA, *i*-PrOH/*n*-hexane = 80/20, flow rate 1.0 mL/min. λ = 254 nm, t(minor) = 11.8 min, t(major) = 15.4 min, 97:3 er.

**(*S*)-*N*-(4-cyanophenyl)-4,4-dimethyl-2-(4-((triisopropylsilyl)ethynyl)phenyl) pyrrolidine-1-carboxamide**




**4n**, 81% yield based on recovered starting material, $[\alpha]_D^{27}$= –116 (*c* 0.6, $CHCl_3$).

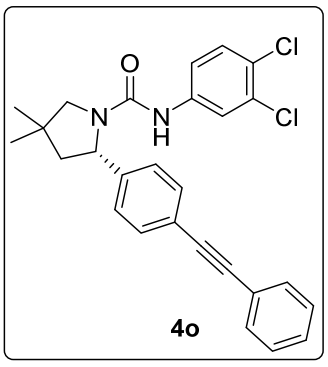
**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.52 (d, *J* = 7.6 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.24 (s, 1H), 4.85 (dd, *J* = 9.5, 7.0 Hz, 1H), 3.82 (d, *J* = 10.6 Hz, 1H), 3.38 (d, *J* = 10.6 Hz, 1H), 2.27 – 2.22 (m, 1H), 1.75 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.16 (s, 3H), 1.15 (s, 3H), 1.13 (s, 21H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 153.4, 143.1, 142.4, 133.2, 133.1, 128.4, 125.7, 119.2, 118.6, 106.2, 105.3, 91.8, 61.5, 60.2, 51.8, 37.5, 26.1, 25.9, 18.7, 11.3.

**HRMS** (ESI) m/z calcd. for $C_{31}H_{42}N_3OSi$ $[M+H]^+$ 500.3097, found 500.3095.

**HPLC condition:** Chiralcel IA, *i*-PrOH/*n*-hexane = 80/20, flow rate 1.0 mL/min. λ = 254 nm, t(minor) = 5.7 min, t(major) = 9.1 min, 95.5:4.5 er.

**(*S*)-*N*-(3,4-dichlorophenyl)-4,4-dimethyl-2-(4-(phenylethynyl)phenyl)pyrrolidine-1-carboxamide**

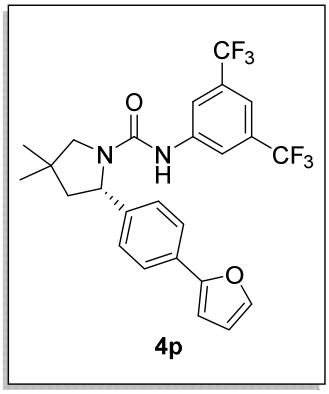



**4o**, 75% yield based on recovered starting material, $[\alpha]_D^{27}$= –79 (*c* 0.2, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.65 – 7.52 (m, 4H), 7.46 (d, *J* = 2.6 Hz, 1H), 7.42 – 7.31 (m, 5H), 7.23 (d, *J* = 8.8 Hz, 1H), 6.99 – 6.82 (m, 1H), 6.05 (s, 1H), 4.88 (t, *J* = 8.2 Hz, 1H), 3.83 (d, *J* = 10.4 Hz, 1H), 3.40 (d, *J* = 10.4 Hz, 1H), 2.28 (dd, *J* = 12.8, 7.1 Hz, 1H), 1.80 (dd, *J* = 12.8, 9.5 Hz, 1H), 1.19 (s, 3H), 1.18 (s, 3H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 153.8, 142.5, 138.4, 132.7, 132.5, 131.6, 130.2, 128.5, 128.4, 125.9, 125.8, 123.3, 123.0, 120.7, 118.3, 90.1, 88.7, 61.4, 60.3, 51.7, 37.6, 26.2, 25.9.
**HRMS** (ESI) m/z calcd. for $C_{27}H_{25}Cl_2N_2O$ $[M+H]^+$ 463.1338, found 463.1338.
**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 1.0 mL/min. λ = 254 nm, t(major) = 17.9 min, t(minor) = 28.4 min, 95:5 er.

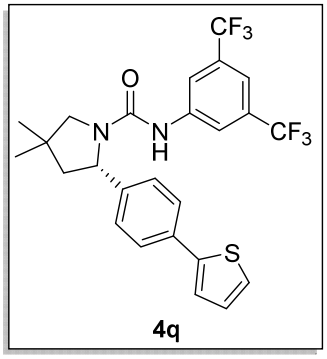
**(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(4-(furan-2-yl)phenyl)-4,4-dimethyl pyrrolidine-1-carboxamide**



4p

**4p**, 65% yield based on recovered starting material, $[\alpha]_D^{27}$ = –52.2 (*c* 0.7, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.73 (d, *J* = 8.0 Hz, 2H), 7.62 (s, 2H), 7.48 (s, 1H), 7.41 – 7.37 (m, 3H), 6.68 (d, *J* = 3.3 Hz, 1H), 6.48 (t, *J* = 2.5 Hz, 1H), 6.34 (s, 1H), 4.89 (dd, *J* = 9.5, 7.1 Hz, 1H), 3.84 (d, *J* = 10.5 Hz, 1H), 3.41 (d, *J* = 10.5 Hz, 1H), 2.28 (dd, *J* = 12.8, 7.1 Hz, 1H), 1.83 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.19 (s, 3H), 1.17 (s, 3H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 153.6, 153.1, 142.4, 140.9, 140.4, 132.0 (q, $J_{C-F}$ = 32.8 Hz), 131.1, 126.2, 124.9, 123.1 (q, $J_{C-F}$ =271.0 Hz), 118.7 – 118.6 (m, 1C), 115.9 – 115.8 (m, 1C), 111.8, 105.6, 61.5, 60.3, 51.8, 37.5, 26.1, 25.9.
**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.05.
**HRMS** (ESI) m/z calcd. for $C_{25}H_{23}F_6N_2O_2$ $[M+H]^+$ 497.1664, found 497.1667.
**HPLC condition:** Chiralcel ID, *i*-PrOH/*n*-hexane = 96/4, flow rate 0.4 mL/min. λ = 254 nm, t(major) = 16.1 min, t(minor) = 20.3 min, 91:9 er.

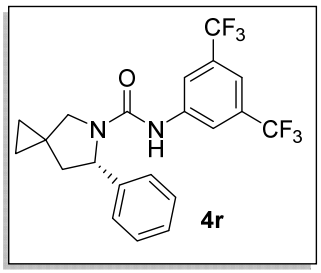
**(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(4-(thiophen-2-yl)phenyl) pyrrolidine-1-carboxamide**



4q

**4q**, 66% yield based on recovered starting material, $[\alpha]_D^{27}$ = –71 (*c* 1.1, $CHCl_3$).
**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.67 – 7.64 (m, 4H), 7.42 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.31 (dd, *J* = 9.0, 4.4 Hz, 2H), 7.09 (t, *J* = 4.4 Hz, 1H), 6.38 (s, 1H), 4.91 (t, *J* = 8.3 Hz, 1H), 3.82 (d, *J* = 10.4 Hz, 1H), 3.42 (d, *J* = 10.4 Hz, 1H), 2.29 (dd, *J* = 12.9, 7.1 Hz, 1H), 1.83 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.19 (s, 3H), 1.18 (s, 3H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 153.6, 143.4, 141.2, 140.4, 134.6, 132.0 (q, $J_{C-F}$ = 33.1 Hz), 128.1, 127.0, 126.3, 125.3, 123.5, 123.1 (q, $J_{C-F}$ = 270.9 Hz), 118.8 – 118.7 (m, 1C), 115.9 – 115.8 (m, 1C), 61.4, 60.3, 51.7, 37.6, 26.1, 25.9.
**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.03.
**HRMS** (ESI) m/z calcd. for $C_{25}H_{23}F_6N_2OS$ $[M+H]^+$ 514.1435, found 514.1439.
**HPLC condition**: Chiralcel ID, *i*-PrOH/*n*-hexane = 96/4, flow rate 0.4 mL/min. λ = 254 nm, t(major) = 16.6 min, t(minor) = 20.9 min, 94:6 er.

**(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-6-phenyl-5-azaspiro[2.4]heptane-5-carboxamide**




**4r**, 60% yield based on recovered starting material, $[\alpha]_D^{27}$= –17 (*c* 0.3, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.59 (s, 2H), 7.46 – 7.42 (m, 5H), 7.39 – 7.36 (m, 1H), 6.30 (s, 1H), 4.99 (dd, *J* = 7.9, 4.9 Hz, 1H), 3.79 (d, *J* = 10.3 Hz, 1H), 3.63 (d, *J* = 10.3 Hz, 1H), 2.50 (dd, *J* = 12.6, 7.9 Hz, 1H), 1.89 (dd, *J* = 12.6, 4.9 Hz, 1H), 0.76 – 0.67 (m, 2H), 0.62 – 0.58 (m, 1H), 0.55 – 0.51 (m, 1H).

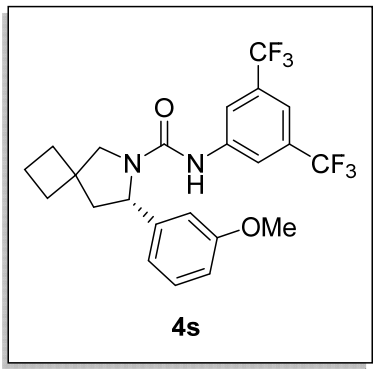
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 153.3, 142.0, 140.4, 132.0 (q, $J_{C\text{-}F}$ = 33.1 Hz), 129.5, 128.4, 126.0, 123.2 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.7 – 118.6 (m, 1C), 116.0 – 115.8 (m, 1C), 62.3, 55.3, 45.0, 19.8, 11.8, 9.0.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.07.

**HRMS** (ESI) m/z calcd. for $C_{21}H_{19}F_6N_2O$ $[M+H]^+$ 429.1396, found 429.1391.

**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 12.3 min, t(minor) = 16.0 min, 95:5 er.

**(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-7-(3-methoxyphenyl)-6-azaspiro[3.4] octane-6-carboxamide**




**4s**, 69% yield based on recovered starting material, $[\alpha]_D^{27}$= –61 (*c* 0.25, $CHCl_3$).

**$^1$H NMR (400 MHz, Chloroform-*d*)**: δ 7.58 (s, 2H), 7.42 – 7.41 (m, 1H), 7.37 – 7.33 (m, 1H), 6.95 – 6.92 (m, 1H), 6.90 – 6.87 (m, 2H), 6.36 (s, 1H), 4.76 (t, *J* = 7.2 Hz, 1H), 3.98 (d, *J* = 10.7 Hz, 1H), 3.82 (s, 3H), 3.63 (d, *J* = 10.6 Hz, 1H), 2.53 (ddd, *J* = 12.6, 7.3, 1.2 Hz, 1H), 2.13 – 1.89 (m, 7H).

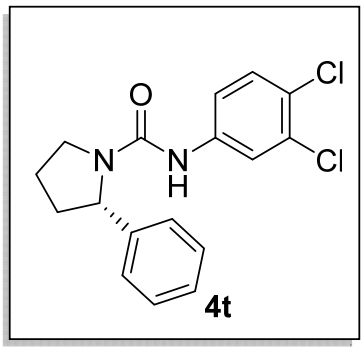
**$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 160.5, 153.7, 143.5, 140.5, 131.9 (q, $J_{C\text{-}F}$ = 33.1 Hz), 130.7, 123.1 (q, $J_{C\text{-}F}$ = 271.0 Hz), 118.7 – 118.6 (m, 1C), 118.0, 115.9 – 115.7 (m, 1C), 113.4, 111.8, 61.2, 59.9, 55.3, 49.3, 43.6, 32.8, 30.2, 16.1.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.07.

**HRMS** (ESI) m/z calcd. for $C_{23}H_{23}F_6N_2O_2$ $[M+H]^+$ 473.1664, found 473.1661.

**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 14.0 min, t(minor) = 20.3 min, 92:8 er.

**(*S*)-N-(3,4-dichlorophenyl)-2-phenylpyrrolidine-1-carboxamide**




**4t**, 37% yield based on recovered starting material, $[\alpha]_D^{27}$ = 43 (*c* 0.1, $CHCl_3$).

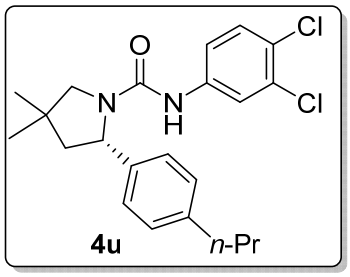
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.40 (d, *J* = 7.5 Hz, 2H), 7.39 – 7.29 (m, 4H), 7.20 (d, *J* = 8.8 Hz, 1H), 6.92 (d, *J* = 8.8 Hz, 1H), 6.04 (s, 1H), 4.84 (d, *J* = 8.0 Hz, 1H), 3.85 – 3.71 (m, 2H), 2.05 – 2.44 (m, 1H), 2.04 – 1.90 (m, 3H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 153.7, 142.2, 138.6, 132.4, 130.1, 129.4, 128.4, 126.9, 125.8, 120.7, 118.4, 61.5, 47.6, 26.3, 23.2.

**HRMS** (ESI) m/z calcd. for $C_{17}H_{17}Cl_2N_2O$ $[M+H]^+$ 335.0712, found 335.0710.

**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.6 mL/min. λ = 254 nm, t(minor) = 46.2 min, t(minor) = 53.8 min, 92.5:7.5 er.

**(*S*)-N-(3,4-dichlorophenyl)-4,4-dimethyl-2-(4-propylphenyl)pyrrolidine-1-carboxamide**




**4u**, 67% yield based on recovered starting material, $[\alpha]_D^{27}$ = –70 (*c* 1.0, $CHCl_3$).

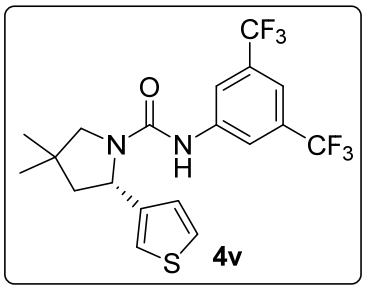
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.29 – 7.20 (m, 5H), 7.17 (d, *J* = 8.8 Hz, 1H), 6.82 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.06 (s, 1H), 4.76 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.83 (d, *J* = 10.4 Hz, 1H), 3.35 (d, *J* = 10.8 Hz, 1H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.22 (ddd, *J* = 12.8, 6.8, 1.6 Hz, 1H), 1.81 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.65 (q, *J* = 7.6 Hz, 2H), 1.16 (s, 3H), 1.15 (s, 3H), 0.94 (t, *J* = 7.2 Hz, 3H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 153.9, 143.2, 139.3, 138.7, 132.3, 130.1, 129.7, 125.9, 125.4, 120.5, 118.2, 61.5, 60.1, 52.2, 37.6, 37.1, 26.1, 25.9, 24.5, 13.8.

**HRMS** (ESI) m/z calcd. for $C_{22}H_{27}Cl_2N_2O$ $[M+H]^+$ 405.1495, found 405.1495.

**HPLC condition:** Chiralcel AD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 32.7 min, t(minor) = 37.9 min, 90.5:9.5 er.

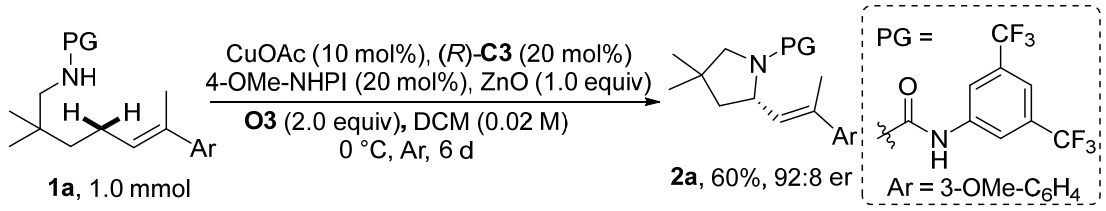
**(*S*)-N-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(thiophen-3-yl)pyrrolidine-1-carboxamide**




**4v**, 72% yield based on recovered starting material, $[\alpha]_D^{27}$ = –11 (*c* 0.4, $CHCl_3$) **$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.58 (s, 2H), 7.46 (dd, *J* = 5.1, 2.9 Hz, 1H), 7.43 (s, 1H), 7.34 (dd, *J* = 3.0, 1.4 Hz, 1H), 7.07 (dd, *J* = 5.0, 1.4 Hz, 1H), 6.50 (s, 1H), 4.99 (dd, *J* = 9.5, 7.0 Hz, 1H), 3.79 (d, *J* = 10.6 Hz, 1H), 3.36 (d, *J* = 10.6 Hz, 1H), 2.23 (ddd, *J* = 12.7, 7.1, 1.7 Hz, 1H), 1.89 (dd, *J* = 12.7, 9.5 Hz, 1H), 1.18 (s, 3H), 1.15 (s, 3H).

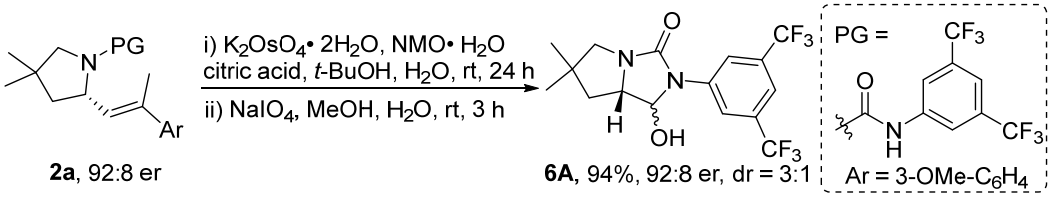
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 152.7, 142.5, 139.5, 131.0 (q, $J_{C-F}$ = 33.1 Hz), 127.8, 124.3, 122.1 (q, $J_{C-F}$ = 271 Hz), 120.5, 117.7 – 117.6 (m, 1C), 114.8 – 114.7 (m, 1C), 58.7, 56.3, 49.7, 36.0, 25.1, 24.9.
**HRMS** (ESI) m/z calcd. for $C_{19}H_{19}F_6N_2OS$ $[M+H]^+$ 437.1122, found 437.1121.
**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 9.3 min, t(minor) = 12.4 min, 68:32 er.

## Preparative scale enantioselective radical allylic C−H amination under conditions A:




To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **1a** (502 mg, 1.0 mmol), CuOAc (12.4 mg 10 mol%), (*R*)-**C3** (160 mg, 20 mol%), 4-OMe-NHPI (40 mg, 20 mol%) and ZnO (80 mg, 1.0 mmol). The tube was evacuated and backfilled with argon for three times, the **O3** (480 μL, 2.0 mmol) and dry DCM (50.0 mL) was added *via* syringe. The tube was stirred at 10 °C for 3 days. After completion, the reaction mixture was filtered through celite and the filtrate was evaporated under reduced pressure, and the residue was purified by flash chromatography (petroleum ether/ ethyl acetate =20/1−10/1) to give the corresponding product **2a** (300 mg) in 60% isolated yield with 92:8 er.

## Versatile transformation[10]

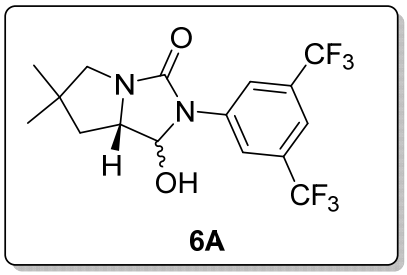



To a flame-dried Schlenk tube equipped with a magnetic stir bar was added **2a** (50.0 mg, 0.1 mmol). Then *t*-BuOH (1.0 mL) and deionized water (1.0 mL) was added while vigorous stirring followed by the addition of citric acid (38.5 mg, 0.2 mmol). Then $K_2OsO_4 \cdot 2H_2O$ (1.5 mg, 4 mol%) and $NMO \cdot H_2O$ (17.5 mg, 0.15 mmol) were sequentially added and the resulting mixture was vigorously stirred in air at rt for ca. 24 h. The resulting mixture was evaporated under reduced pressure until most of the *t*-BuOH had been removed. Then the mixture was diluted with HCl (1 M) solution and EtOAc and the separated aqueous layer was extracted with EtOAc. The combined organic layer was dried over anhydrous $Na_2SO_4$, filtered through a cotton plug and evaporated under reduced pressure. The residue thus obtained was used directly for the

next step without purification.

To a solution of the crude product obtained above in MeOH (1.5 mL) was added deionized $H_2O$ (0.5 mL) and $NaIO_4$ (42.8 mg, 0.2 mmol) sequentially. the resulting mixture was vigorously stirred in air at rt for ca. 3 h. Then the reaction mixture was repetitively diluted with MeCN and evaporated under reduced pressure until a dried residue was obtained. This residue was mixed with EtOAc and the resulting mixture was sonicated until all the solid was well dispersed in EtOAc. The suspension thus obtained was filtered through a celite pad and the filtrate was evaporated under reduced pressure, and the residue was purified by flash column chromatography (petroleum ether/ ethyl acetate =20/1-8/1) to give the corresponding product **6A** (36.0 mg) in 94% isolated yield.

**2-(3,5-bis(trifluoromethyl)phenyl)-1-hydroxy-6,6-dimethylhexahydro-3H-pyrrolo[1,2-c]imidazol-3-one**



**6A**

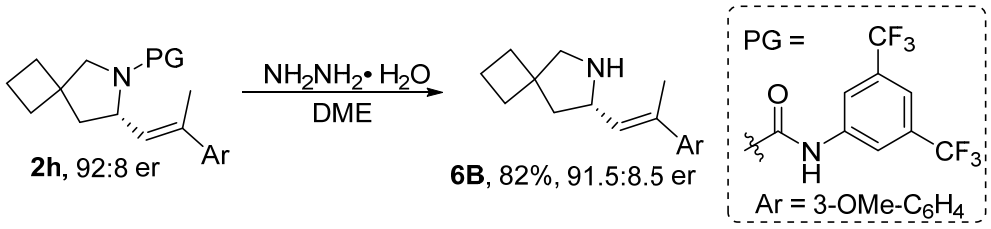
**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.21 (s, 2H), 7.55 (s, 1H), *5.59 (dd, J = 5.2 Hz, 0.2H)*, 5.44 (d, *J* = 9.1 Hz, 0.8H), *5.14 (d, J = 12.0 Hz, 0.2H)*, 4.22 – 4.19 (m, 1H), 3.74 (dd, *J* = 10.5, 6.2 Hz, 0.8H), 3.40 (d, *J* = 11.4 Hz, 0.8H), 2.76 (d, *J* = 11.4 Hz, 1H), *2.56 (d, J = 10.0 Hz, 0.2H)*, 1.88 (dd, *J* = 6.4 Hz, 0.8H), *1.80 (d, J = 11.5 Hz, 0.2H)*, *1.58 (dd, J = 6.0 Hz, 0.2H)*, 1.31 (d, *J* = 11.5 Hz, 0.8H), 1.09 (d, *J* = 13.1 Hz, 6H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 160.1, *156.6*, 141.1, *139.8*, 132.1 (q, *J* = 33.0 Hz, 1C), 123.1 (q, *J* = 271.1 Hz, 1C), 118.9(7) -118.9(2) (m, 1C), *117.4*, 117.0 - 116.8(m, 1C), *115.6*, 83.3, *82.0*, 66.0, *60.2*, 59.3, *56.3*, 43.6, *42.0*, 40.4, *37.8*, 28.5, 27.7, *27.3*, *26.2*. (The italics data represents minor diasteromer).

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -62.92 (minor), -62.99 (major).

**HRMS** (ESI) m/z calcd. for $C_{16}H_{17}F_6N_2O_2$ $[M+H]^+$ 383.1189, found 383.1186.

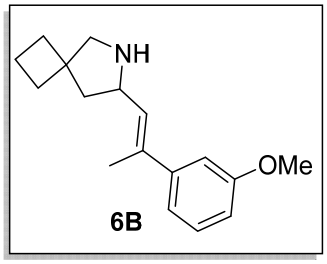
**HPLC condition:** Chiralcel IA, *i*-PrOH/*n*-hexane = 96/4, flow rate 0.4 mL/min. λ = 254 nm, minor diasteromer: t(minor) = 15.3 min, t(major) = 17.4 min, 92:8 er; major diasteromer: t(minor) = 20.0 min, t(major) = 21.8 min, 92:8 er.




To a flam-dried Schlenk tube equipped with a magnetic stir bar was charged with **2h** (25.6 mg, 0.05 mmol), hydrazine hydrate (30 μL, 0.5 mmol) and 1,2-Dimethoxyethane (2.0 mL). The sealed tube was then stirred at 80 °C for 96 h. Upon completion (monitored by TLC), the reaction mixture was cooled down to temperature. Then the crude product was concentrated *in vacuo* and purified by flash column chromatography using dichloromethane/methanol (50/1) as the eluent to give **6B** (10.6 mg) in 82%

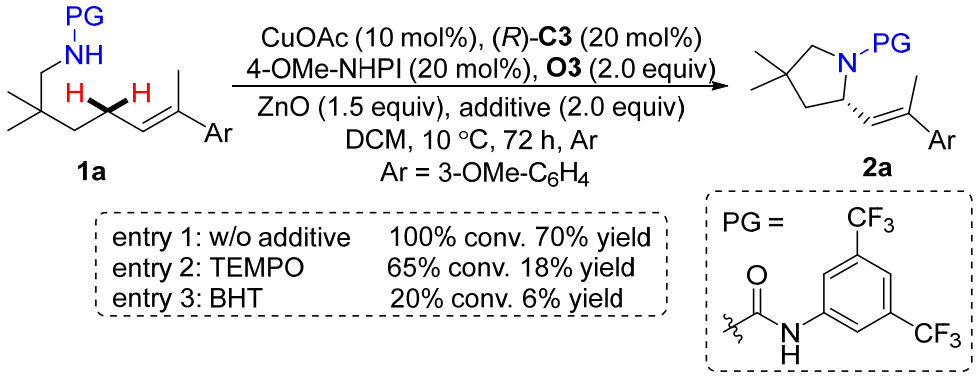
isolated yield.

**(*E*)-7-(2-(3-methoxyphenyl)prop-1-en-1-yl)-6-azaspiro[3.4]octane**

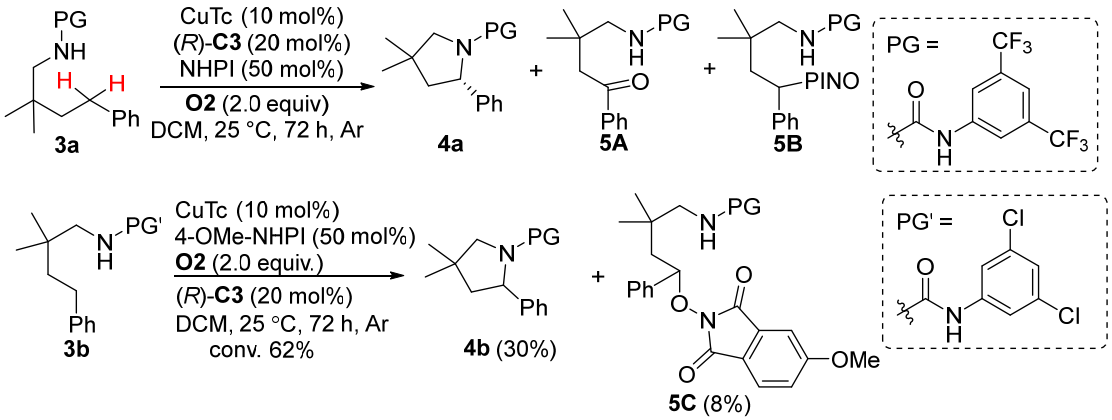



**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.20 (t, *J* = 7.9 Hz, 1H), 7.01 – 6.98 (m, 2H), 6.82 – 6.79 (m, 1H), 6.05 – 5.97 (m, 1H), 4.51 – 4.45 (m, 1H), 3.81 (s, 3H), 3.66 (brs, 1H), 3.22 (s, 2H), 2.25 (dd, J = 12.8, 6.4 Hz, 1H), 2.10 (d, *J* = 1.2 Hz, 3H), 2.07 – 1.94 (m, 5H), 1.91 – 1.83 (m, 2H).
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 159.6, 143.3, 141.8, 129.3, 122.0, 118.5, 113.6, 111.7, 56.9, 55.3, 54.9, 45.0, 44.3, 33.5, 29.9, 16.6, 16.0.
**HRMS** (ESI) m/z calcd. for $C_{17}H_{24}NO$ $[M+H]^+$ 258.1852, found 258.1848.
**HPLC condition:** Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.5 mL/min. λ = 254 nm, t(minor) = 24.7 min, t(major) = 36.4 min, 91.5:8.5 er.

## Mechanistic studies:




To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **1a** (50.5 0.1 mmol), CuOAc (1.24 mg 10 mol%), (*R*)-**C3** (16.0 mg, 20 mol%), 4-OMe-NHPI (4.0 mg, 20 mol%), ZnO (12.0 mg, 0.15 mmol) and additive (0.2 mmol). The tube was evacuated and backfilled with argon for three times, the **O3** (48 μL, 0.2 mmol) and dry DCM (8.0 mL) was added *via* syringe. The tube was stirred at 10 °C for 3 days. The solvent was removed under reduced pressure, and the conversion and yield were determined by crude $^1$H NMR using 1,3,5-trimethoxybenzene as internal standard.

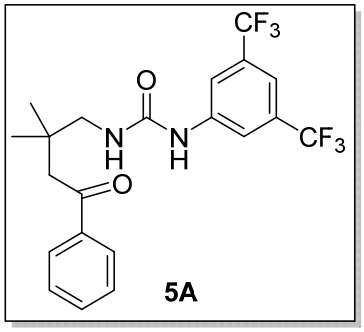



To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **3a** (43.2 mg, 0.1 mmol), CuTc (1.9 mg 10 mol%), (*R*)-**C3** (16.0 mg, 20 mol%) and NHPI (8.2 mg, 50 mol%). The tube was evacuated and backfilled with argon for three times, the **O2** (54 μL, 0.3 mmol) and dry DCM (8.0 mL) was added *via* syringe. The tube was stirred at rt for 3 days. The reaction stopped and the solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (petroleum ether/ethyl acetate =20/1-10/1) to give the corresponding product **4a** in 34% isolated yield with 65% conversion along with the detection of byproducts **5A** and **5B**.

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **3b** (36.5 0.1 mmol), CuTc (1.9 mg 10 mol%), (*R*)-**C3** (16.0 mg, 20 mol%), and 4-OMe-NHPI (9.8 mg, 50 mol%). The tube was evacuated and backfilled with argon for three times, the **O2** (36 μL, 0.2 mmol) and dry DCM (8.0 mL) was added *via* syringe. The tube was stirred at rt for 3 days. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (petroleum ether/ethyl acetate =20/1-10/1) to give the corresponding product **4b** in 30% isolated yield with 62% conversion along with the detection of byproducts **5C** (4.5 mg, 8%).

**1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-oxo-4-phenylbutyl)urea**

**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.95 (d, *J* = 7.7 Hz, 2H), 7.90 (s, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.42 (s, 1H), 6.05 (s, 1H), 3.28 (d, *J* = 6.7 Hz, 2H), 2.94 (s, 2H), 1.04 (s, 6H).

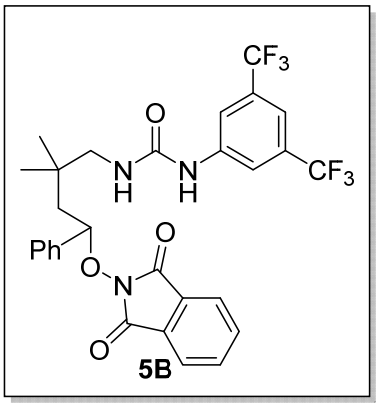



**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 202.9, 155.9, 141.1, 137.6, 133.9, 132.0 (q, $J_{C-F}$ = 33.1 Hz), 128.8, 128.5, 123.3 (q, $J_{C-F}$ = 271.1 Hz), 118.5, 115.5, 49.7, 36.1, 29.72, 26.5.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -63.11.

**HRMS** (ESI) m/z calcd. for $C_{21}H_{21}F_6N_2O_2$ $[M+H]^+$ 447.1507, found 447.1504.

**1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-((1,3-dioxoisoindolin-2-yl)oxy)-2,2-dimethyl-4-phenylbutyl)urea.**



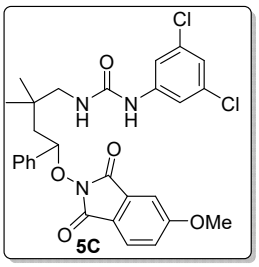

**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.02 (s, 2H), 7.97 (s, 1H), 7.73 (s, 4H), 7.46 (s, 1H), 7.43 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.35 – 7.29 (m, 3H), 6.33 (s, 1H), 5.57 (dd, *J* = 9.1, 1.7 Hz, 1H), 3.57 (dd, *J* = 14.0, 7.1 Hz, 1H), 3.36 (dd, *J* = 14.2, 5.9 Hz, 1H), 2.42 (dd, *J* = 15.8, 9.1 Hz, 1H), 1.76 (dd, *J* = 15.8, 1.7 Hz, 1H), 1.15 (s, 3H), 1.08 (s, 3H).

**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 164.2, 155.4, 141.4, 138.5, 134.9, 132.0 (q, $J_{C\text{-}F}$ = 33.1 Hz), 129.5, 128.5, 128.2, 128.1, 123.7, 123.4 (q, $J_{C\text{-}F}$ = 271.1 Hz), 118.1, 115.0, 87.0, 48.9, 46.9, 34.8, 28.6, 24.4.

**$^{19}$F NMR (376 MHz, $CDCl_3$)**: δ -62.99.

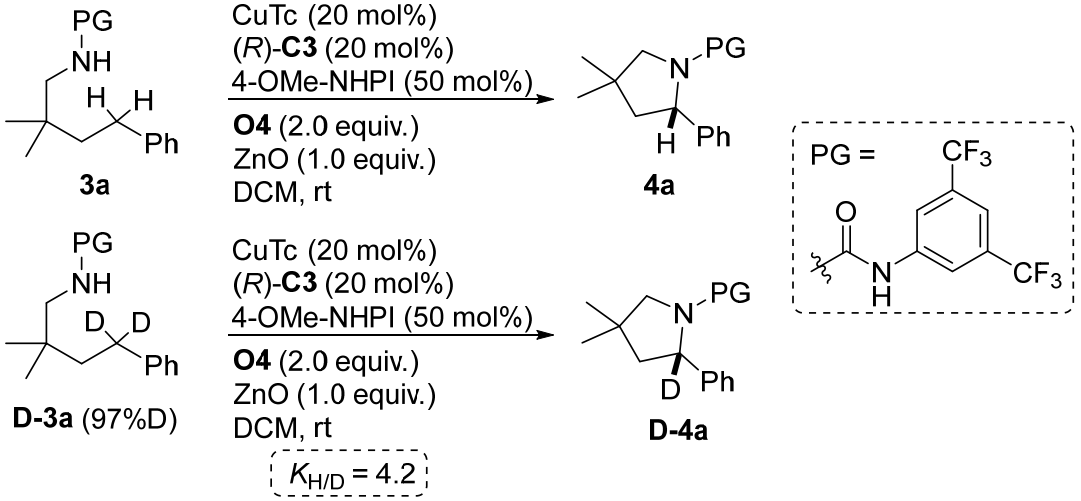
**HRMS** (ESI) m/z calcd. for $C_{29}H_{26}F_6N_3O_4$ $[M+H]^+$ 594.1828, found 594.1827.

**1-(3,5-dichlorophenyl)-3-(4-((5-methoxy-1,3-dioxoisoindolin-2-yl)oxy)-2,2-dimethyl-4-phenylbutyl)urea**



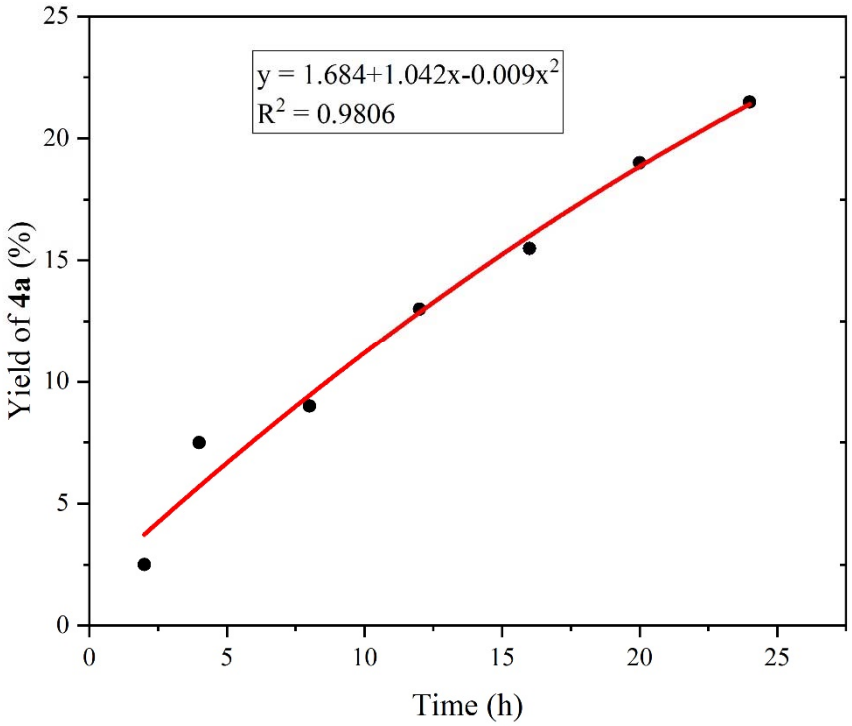

**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.66 (d, *J* = 8.3 Hz, 1H), 7.49 (d, *J* = 1.6 Hz, 2H), 7.47 (s, 1H), 7.42 – 7.40 (m, 2H), 7.31 – 7.29 (m, 3H), 7.19 (d, *J* = 2.4 Hz, 1H), 7.14 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.96 (t, *J* = 2.0 Hz, 1H), 6.26 (s, 1H), 5.57 – 5.47 (m, 1H), 3.90 (s, 3H), 3.56 (dd, *J* = 14.0, 7.6 Hz, 1H), 3.26 (dd, *J* = 14.4, 5.2 Hz, 1H), 2.39 (dd, *J* = 16.0, 9.2 Hz, 1H), 1.74 (d, *J* = 12.0 Hz, 1H), 1.11 (s, 3H), 1.06 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 165.3, 164.5, 163.9, 155.2, 141.9, 138.7, 134.9, 130.8, 129.4, 128.4, 128.2, 125.7, 121.8, 120.0, 119.7, 116.8, 109.1, 86.9, 56.2, 48.8, 47.4, 34.8, 28.9, 24.3.

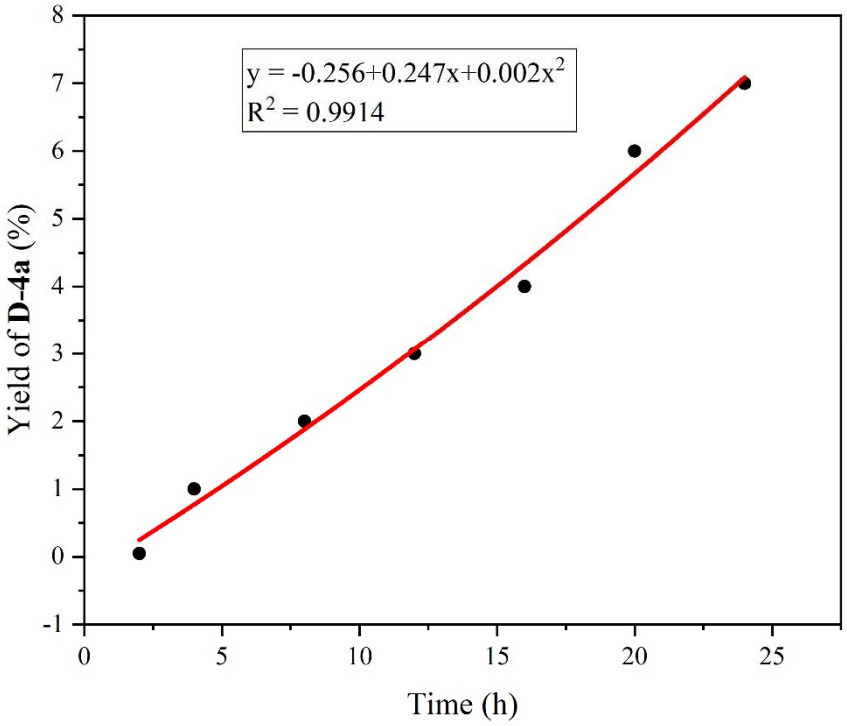
**HRMS** (ESI) m/z calcd. for $C_{28}H_{28}Cl_2N_3O_5$ $[M+H]^+$ 556.1401, found 556.1404.



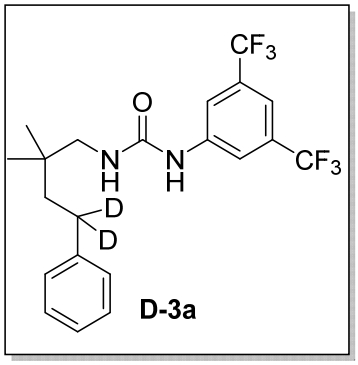

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **3a** (43.3 mg, 0.1 mmol) or **D-3a** (43.5 mg, 0.1 mmol), CuTc (3.8 mg 20 mol%), (*R*)-**C3** (16 mg,

20 mol%), 4-OMe-NHPI (10 mg, 50 mol%) and ZnO (8.0 mg, 0.1 mmol). The tube were evacuated and backfilled with argon for three times, the **O4** (48 μL, 0.2 mmol) and dry DCM (6.0 mL) was added *via* syringe. The tube was stirred at rt and the yield of **4a** and **D-4a** were determined by crude $^1$H NMR using 1,3,5-trimethoxybenzene as internal standard at different times to determine the intermolecular KIE value.






**1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-phenylbutyl-4,4-d$_2$)urea**



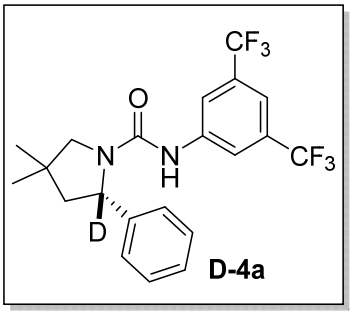

**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 8.49 (s, 1H), 7.68 (s, 2H), 7.41 (s, 1H), 7.34 – 7.01 (m, 5H), 6.15 (t, *J* = 6.4 Hz, 1H), 3.13 (d, *J* = 6.0 Hz, 2H), 2.52 (t, *J* = 8.8 Hz, 0.07 H), 1.48 (s, 2H), 0.93 (s, 6H).

**$^{13}$C NMR (101 MHz, CDCl$_3$)** δ 156.5, 142.4, 140.3, 132.1 (q, $J_{C\text{-}F}$ = 33.1 Hz), 128.4, 128.1, 125.0, 123.0 (q, $J_{C\text{-}F}$ = 271.1 Hz), 118.6, 115.9, 50.1, 41.9, 34.5, 24.6.

**$^{19}$F NMR (376 MHz, CDCl$_3$)**: δ -63.35.

**HRMS** (ESI) m/z calcd. for $C_{21}H_{21}D_2F_6N_2O$ $[M+H]^+$ 435.1835, found 435.1832.

**(S)-N-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-phenylpyrrolidine-2-d-1-carboxamide**

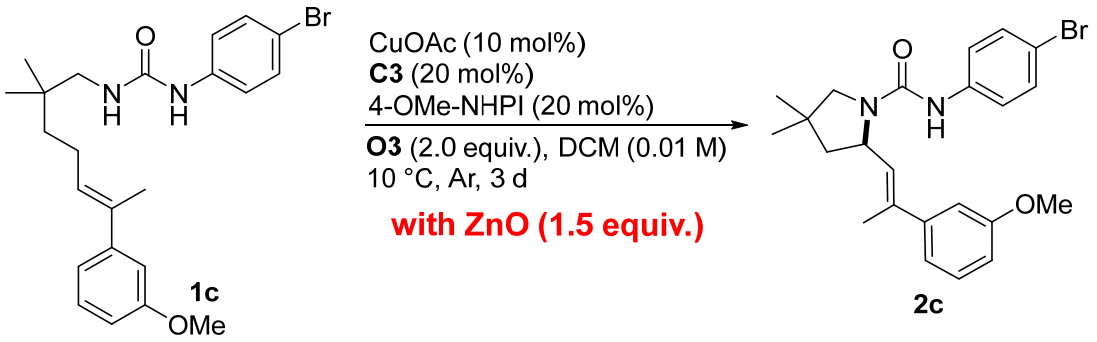



**$^1$H NMR (400 MHz, Chloroform-*d*)** δ 7.53 (s, 2H), 7.49 – 7.33 (m, 6H), 6.28 (s, 1H), 3.85 (d, *J* = 10.4 Hz, 1H), 3.40 (d, *J* = 10.4 Hz, 1H), 2.27 (dd, *J* = 12.4, 1.8 Hz, 1H), 1.84 (d, *J* = 12.4 Hz, 1H), 1.18 (s, 3H), 1.17 (s, 3H)

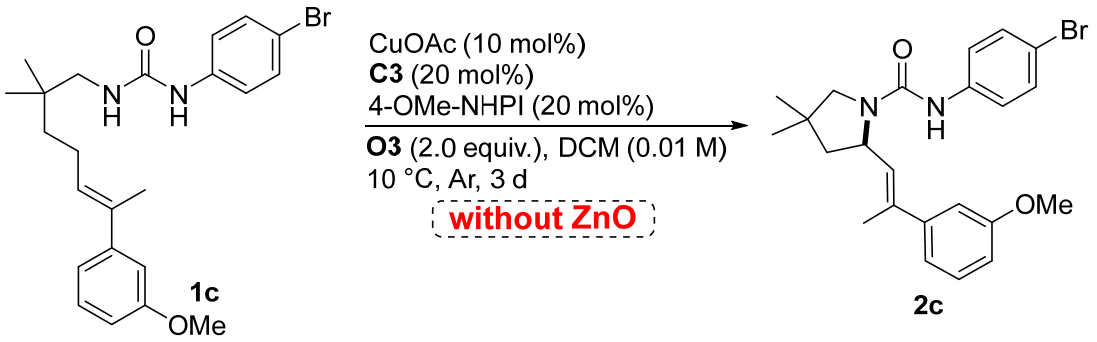
**$^{13}$C NMR (101 MHz, CDCl$_3$)** δ 153.6, 142.0, 140.5, 131.9 (q, $J_{C\text{-}F}$ = 33.3 Hz), 129.7, 128.6, 125.9, 123.1(q, $J_{C\text{-}F}$ = 271.0 Hz), 118.7 – 118.6 (m, 1C), 115.9 – 115.7 (m, 1C), 61.3 (t, $J_{C\text{-}D}$ = 21.3 Hz), 60.3, 51.9, 37.3, 26.1, 25.9.

**HRMS** (ESI) m/z calcd. for $C_{21}H_{20}DF_6N_2O$ $[M+H]^+$ 432.1615, found 432.1613.

**Non-linear effect experiments:**




To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **1c** (22.0 mg, 0.05 mmol), CuOAc (0.62 mg 10 mol%), **C3** (8.0 mg, 20 mol%), 4-OMe-NHPI (2.0 mg, 20 mol%) and ZnO (6.0 mg, 0.075 mmol). The tube was evacuated and backfilled with argon for three times, the **O3** (24 μL, 0.1 mmol) and dry DCM (5.0 mL) was added *via* syringe. The tube was stirred at 10 °C for 3 days. After completion, the reaction mixture was filtered through a pad of celite. The filtrate was used to collect the ee value by HPLC analysis on a Chiral column.

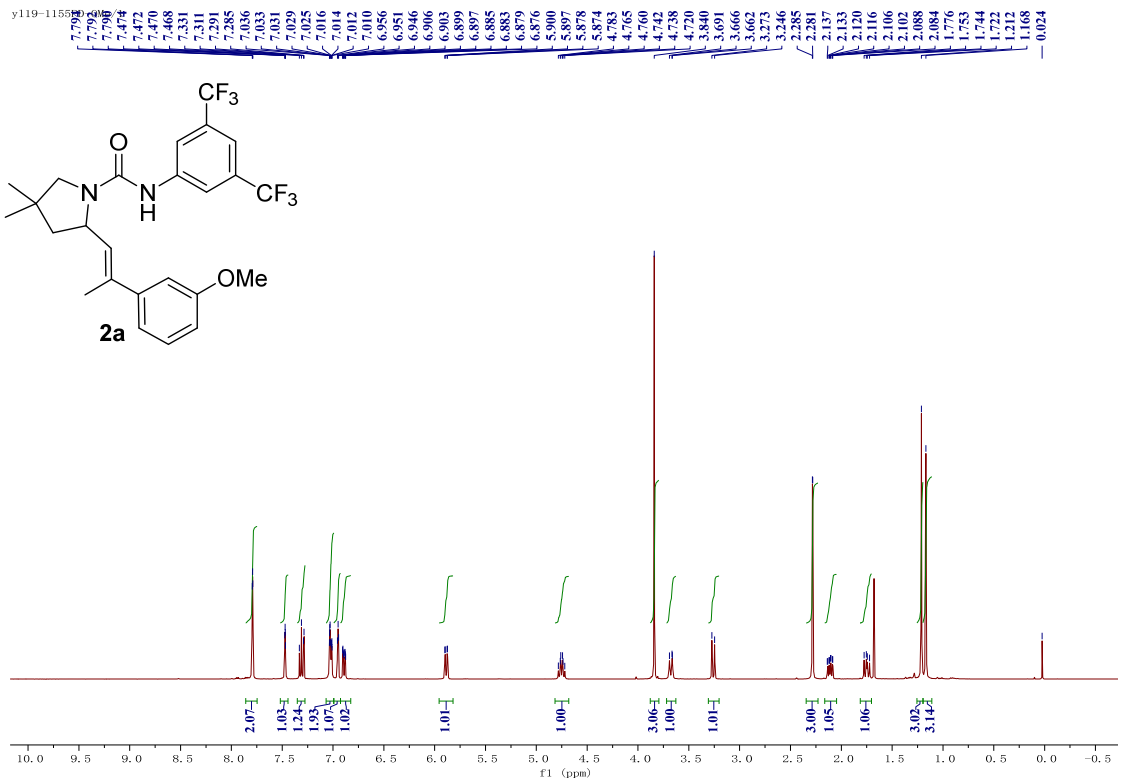



To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **1c** (22.0 mg, 0.05 mmol), CuOAc (0.62 mg 10 mol%), **C3** (8.0 mg, 20 mol%), and 4-OMe-NHPI (2.0 mg, 20 mol%). The tube was evacuated and backfilled with argon for three times, the **O3** (24 μL, 0.1 mmol) and dry DCM (5.0 mL) was added *via* syringe. The tube was stirred at 10 °C for 3 days. After completion, the reaction mixture was filtered through a pad of celite. The filtrate was used to collect the ee value by HPLC analysis on a Chiral column.

## References:

(1) N. Zhu, J. Zhao, H. Bao, *Chem. Sci.*, **2017**, *8*, 2081.
(2) S. Paria, Q.-K. Kang, M. Hatanaka, K. Maruoka, *ACS Catal.* **2019**, *9*, 78.
(3) I. B. Krylov, M. O. Kompanets, K. V. Novikova, I. O. Opeida, O. V. Kushch, B. N. Shelimov, G. I. Nikishin, D. O. Levitsky, A. O. Terent'ev, *J. Phys. Chem. A* **2016**, *120*, 68.
(4) X. Liu, Y. Liang, J. Ji, J. Luo, X. Zhao, *J. Am. Chem. Soc.* **2018**, *140*, 4782.
(5) (a) Y. Kita, T. Yata, Y. Nishimoto, M. Yasuda, *J. Org. Chem.* **2018**, *83*, 740. (b) M. E. Jung, S. Angelica, D. C. D'Amico, *J. Org. Chem.* **1997**, *62*, 9182.
(6) A. Kaga, Y. L. Tnay, S. Chiba, *Org. Lett.* **2016**, *18*, 3506.
(7) X. Peng, B. Meng, K. Tong, H. Hirao, S. Chiba, *Angew. Chem. Int. Ed.* **2014**, *53*, 1959.
(8) J.-S. Lin, X.-Y. Dong, T.-T. Li, N.-C. Jiang, B. Tan, X.-Y. Liu, *J. Am. Chem. Soc.* **2016**, *138*, 9357.
(9) N. Sakai, K. Kawana, R. Ikeda, Y. Nakaike, T. Konakahara, *Eur. J. Org. Chem.* **2011**, 3178.
(10) Q.-S. Gu, D. Yang, *Angew. Chem. Int. Ed*. **2017**, *56*, 5886; *Angew. Chem.* **2017**, *129*, 5980.

# NMR Spectra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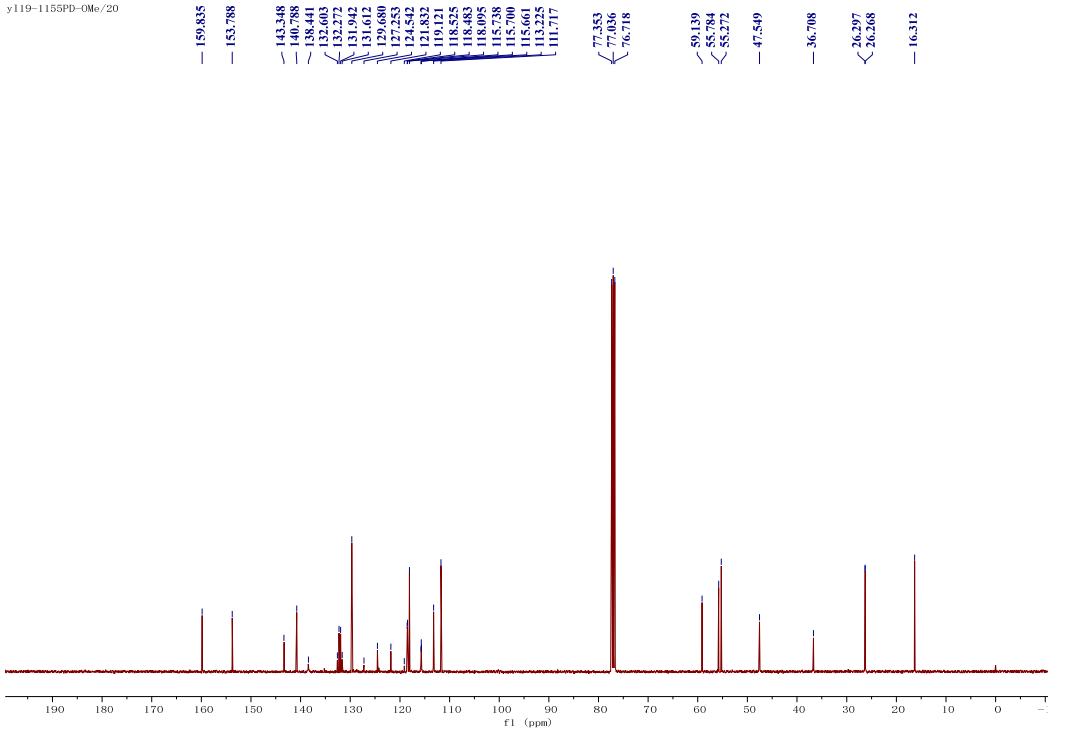
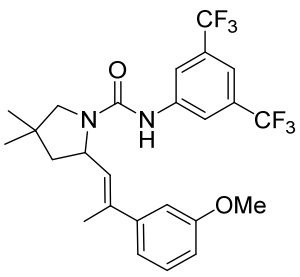
O
N
N
H
CF3
OMe
2a
f1 (ppm)

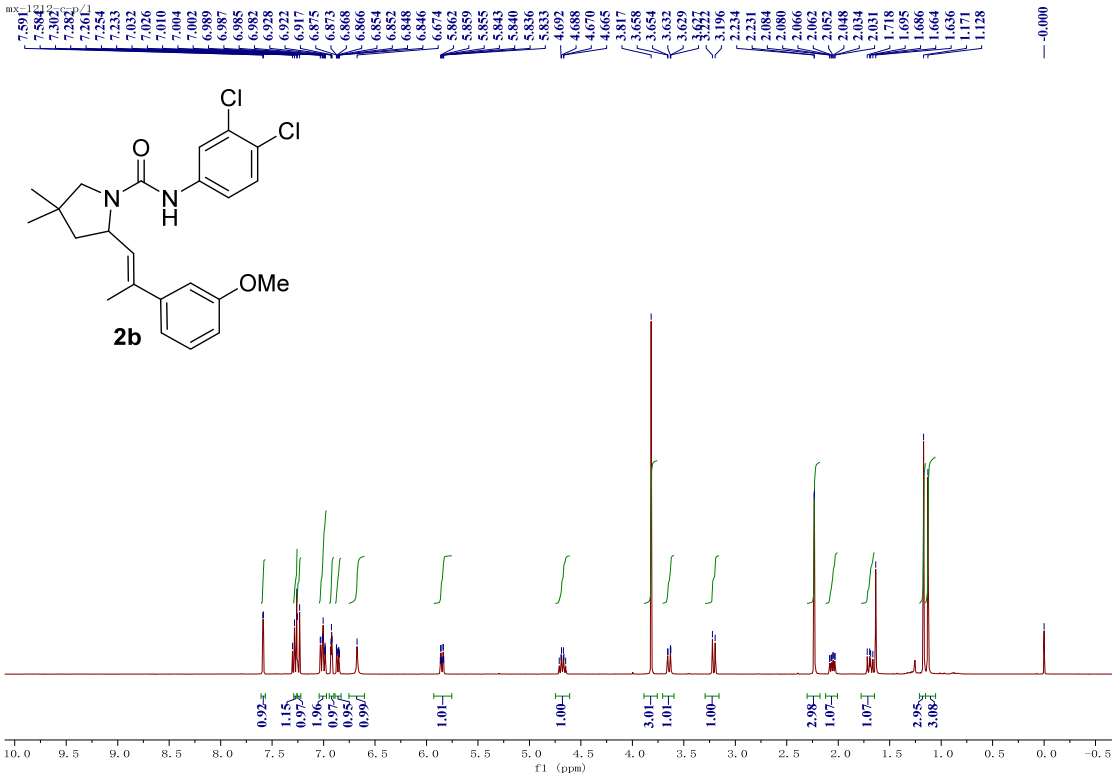

y119-1155PD-OMe/20
f1 (ppm)

y119-1155PD-OMe/19




**2a**







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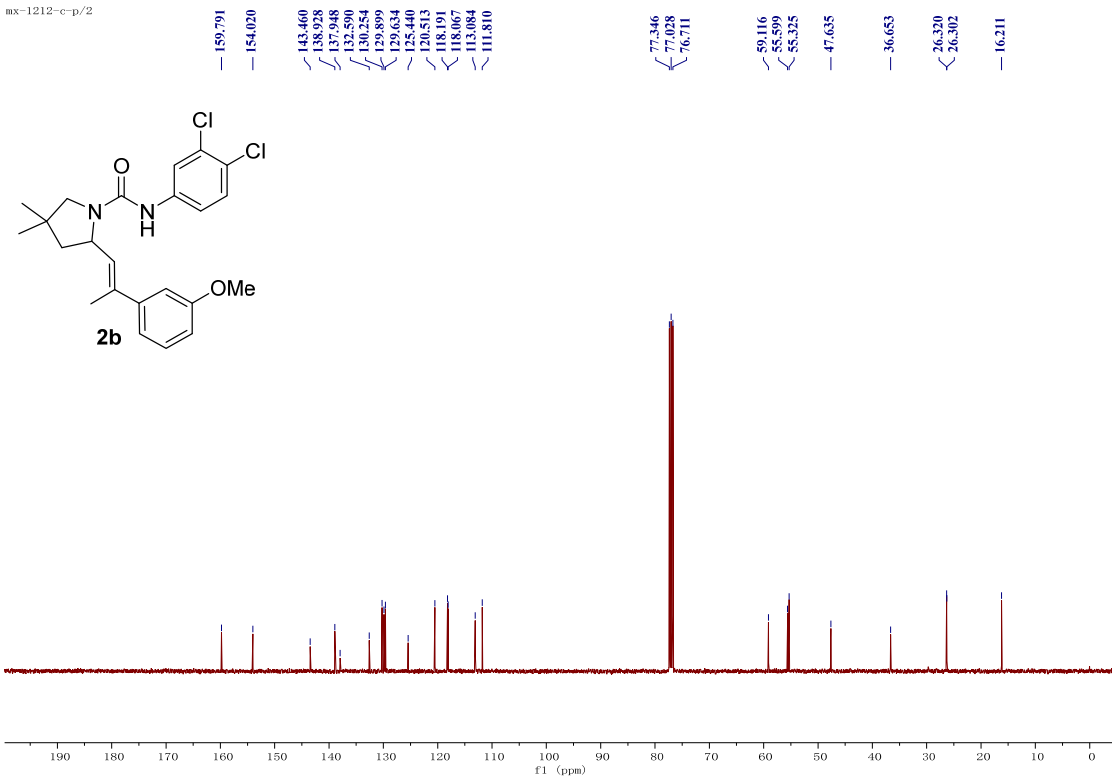
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N
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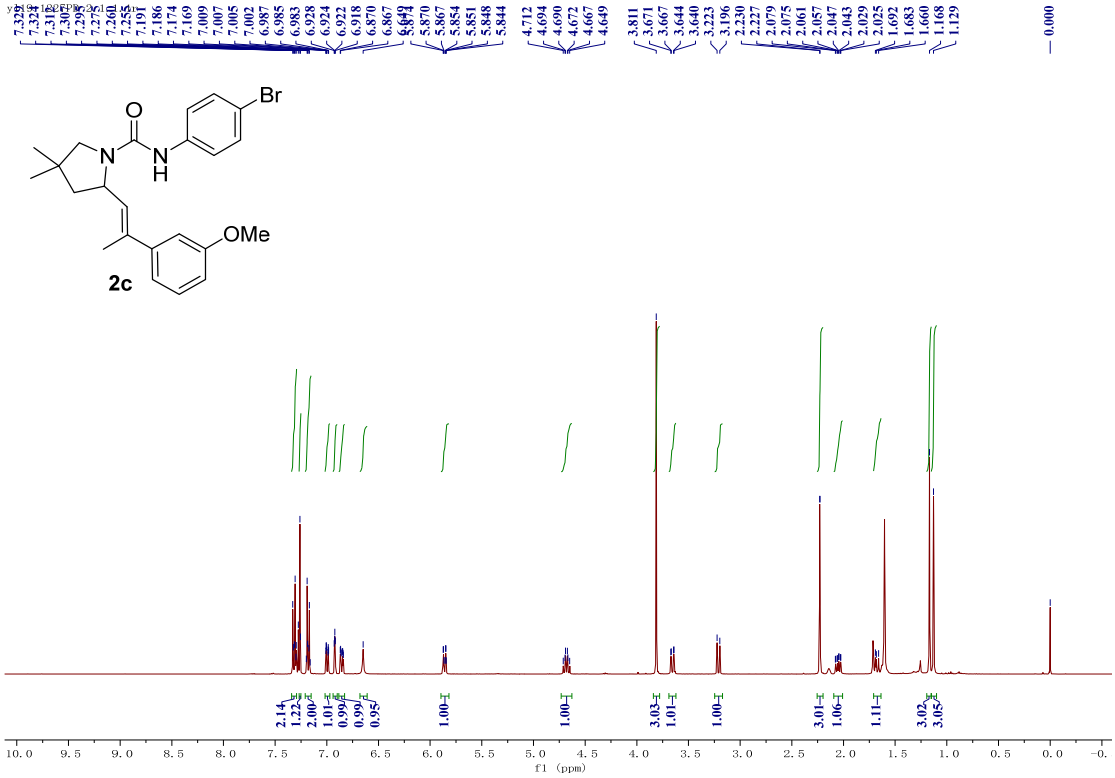
2b
f1 (ppm)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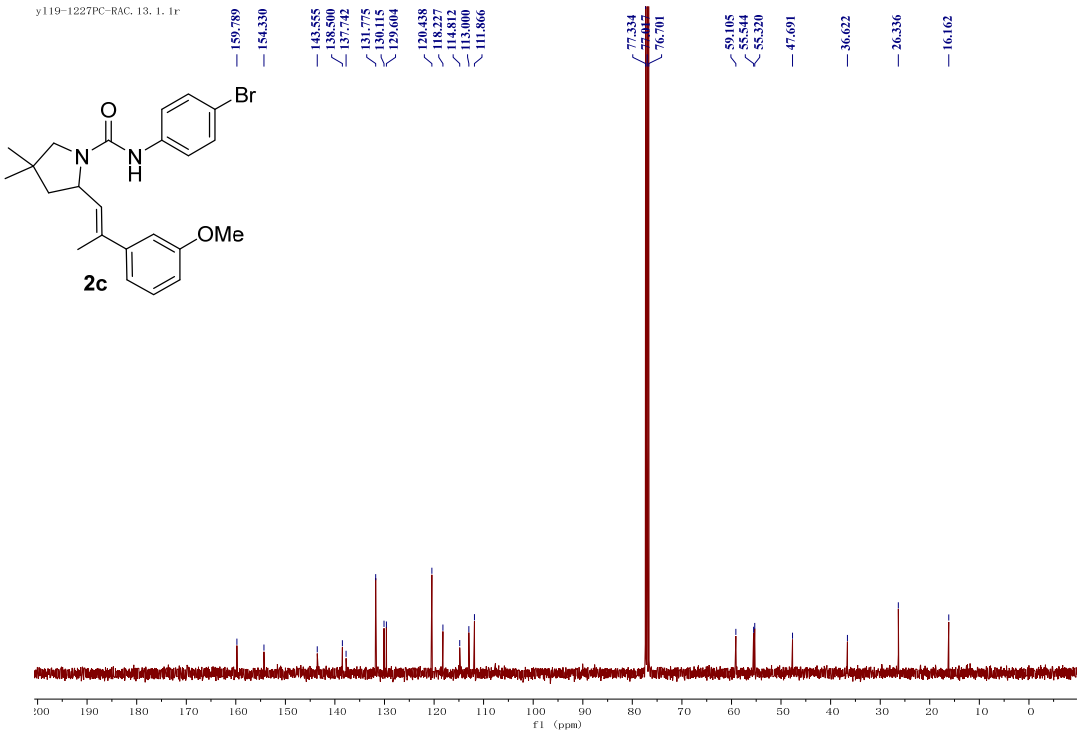
f1 (ppm)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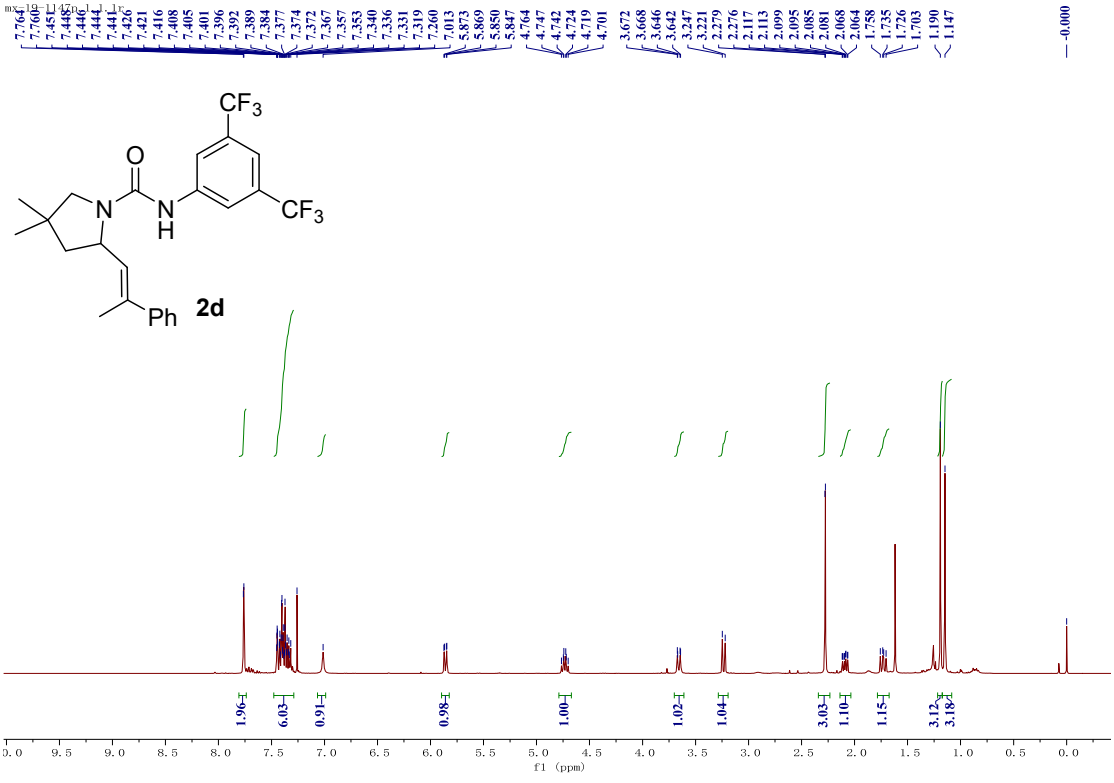
f1 (ppm)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N
H
CF3
Ph
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0.91
0.98
1.00
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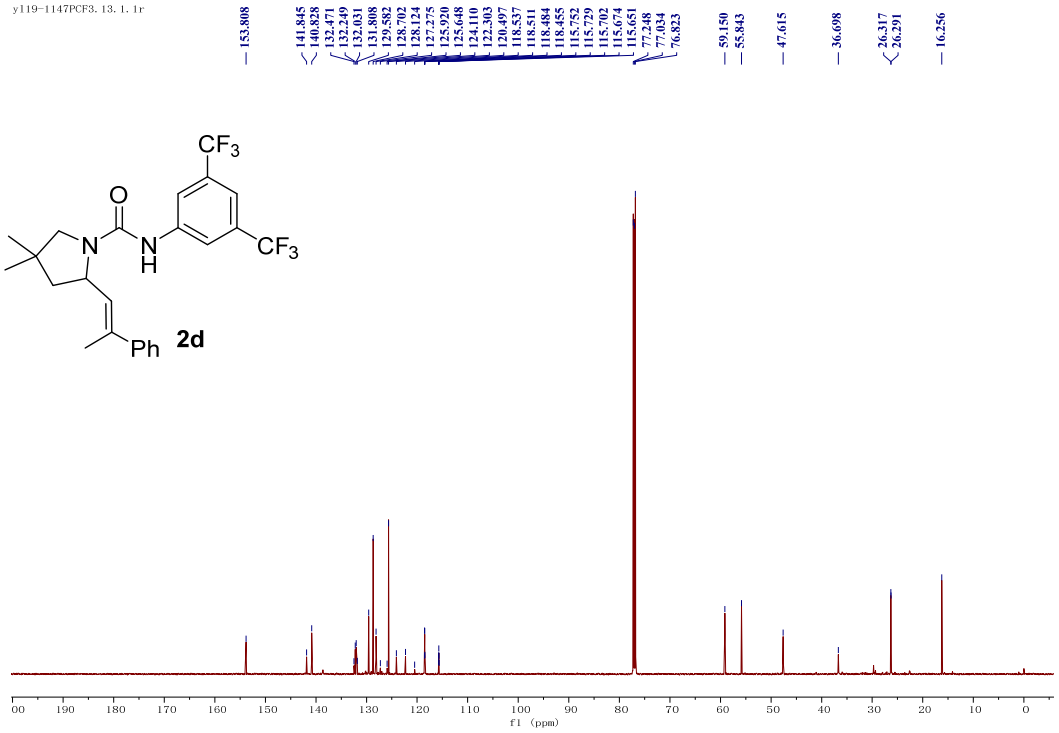
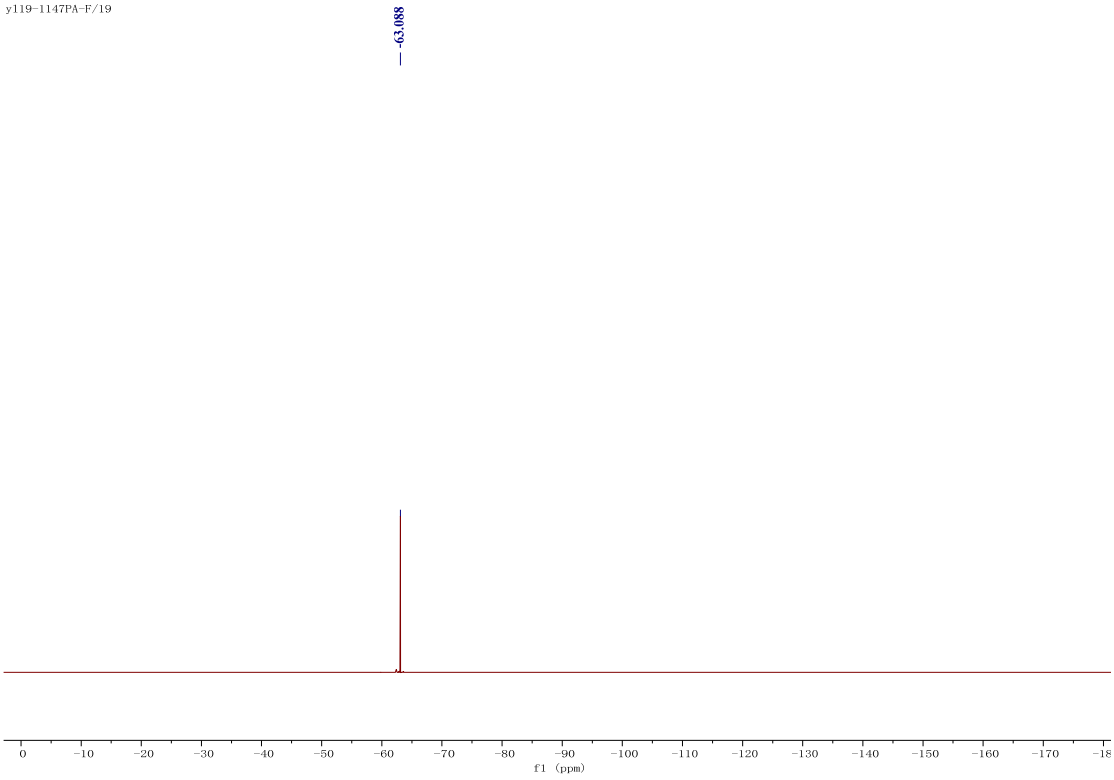
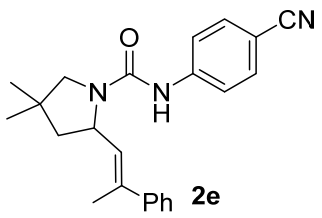
f1 (ppm)

y119-1147PCF3. 13. 1. 1r

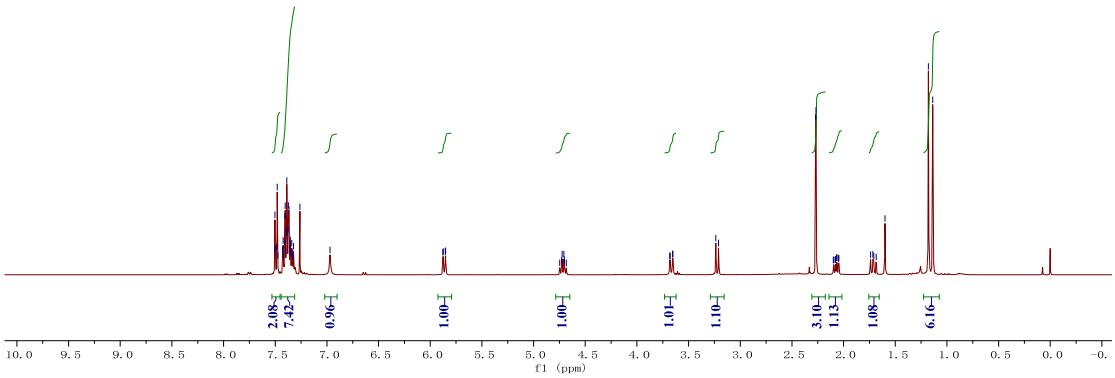


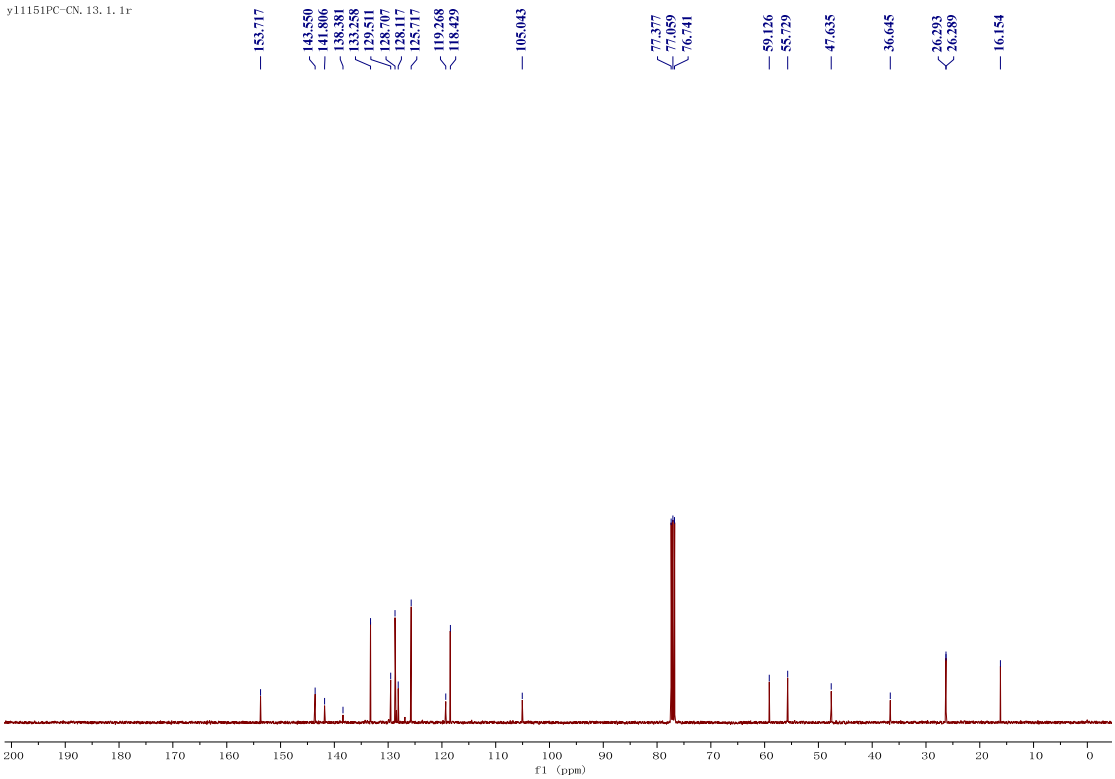

y119-1147PA-F/19

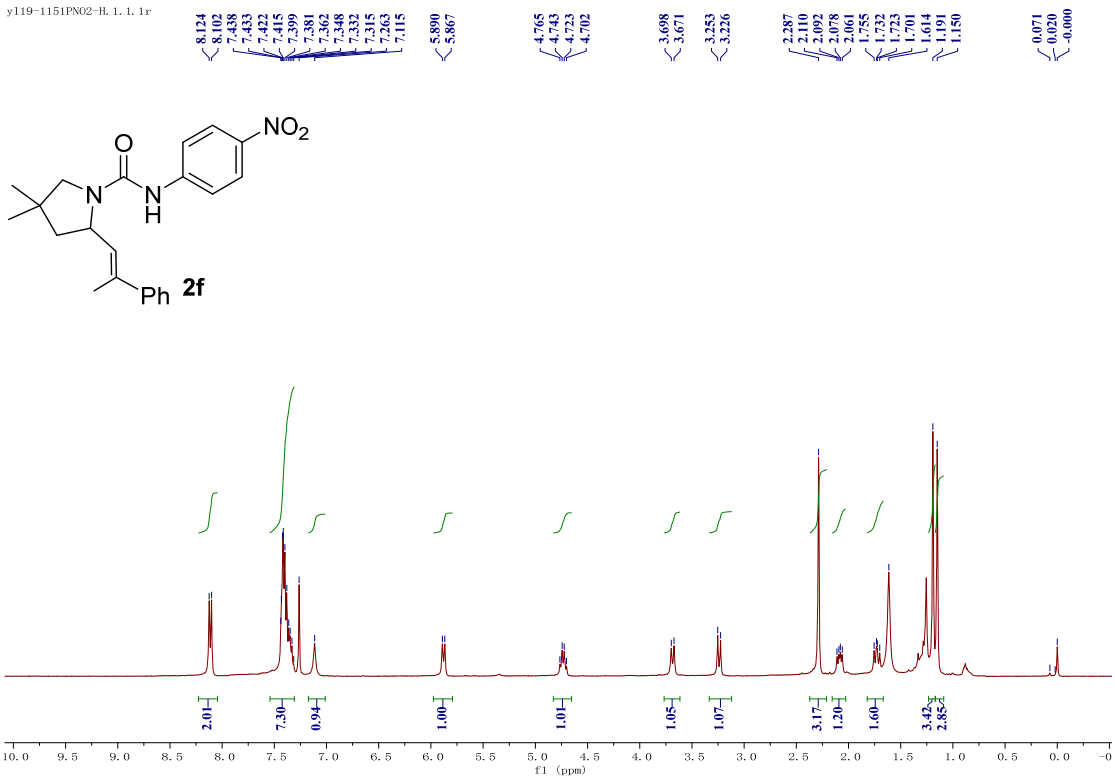


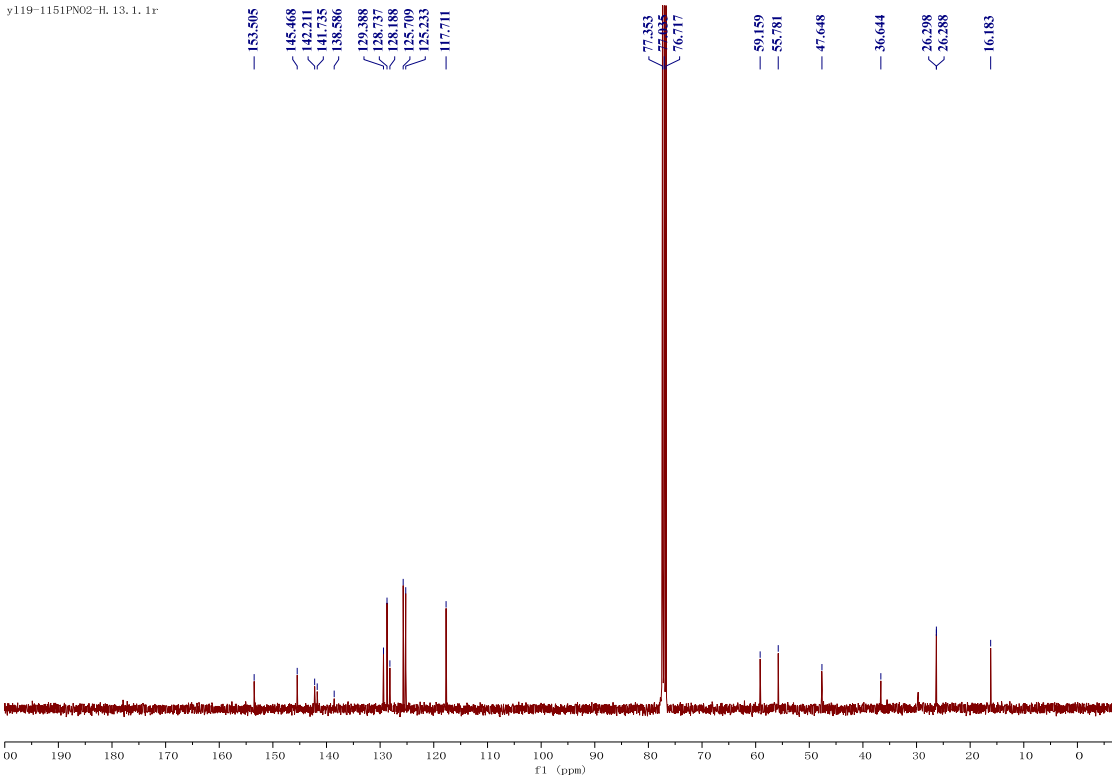

CN
O
N
N
H
Ph

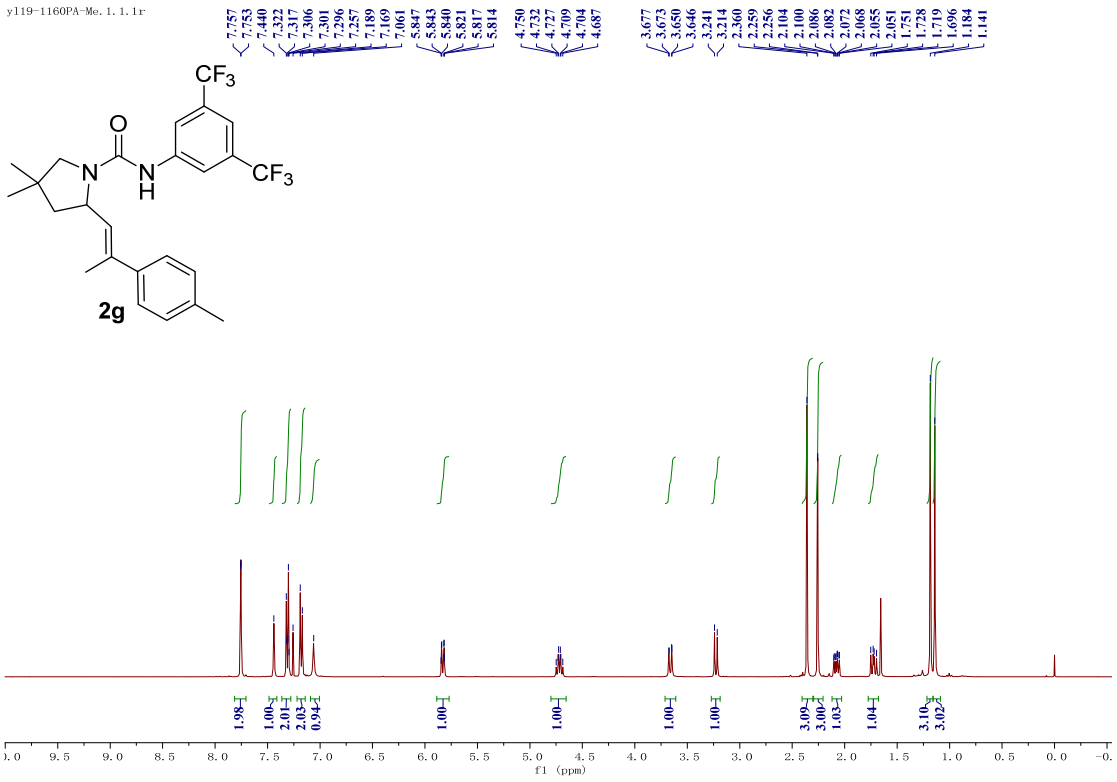
**2e**

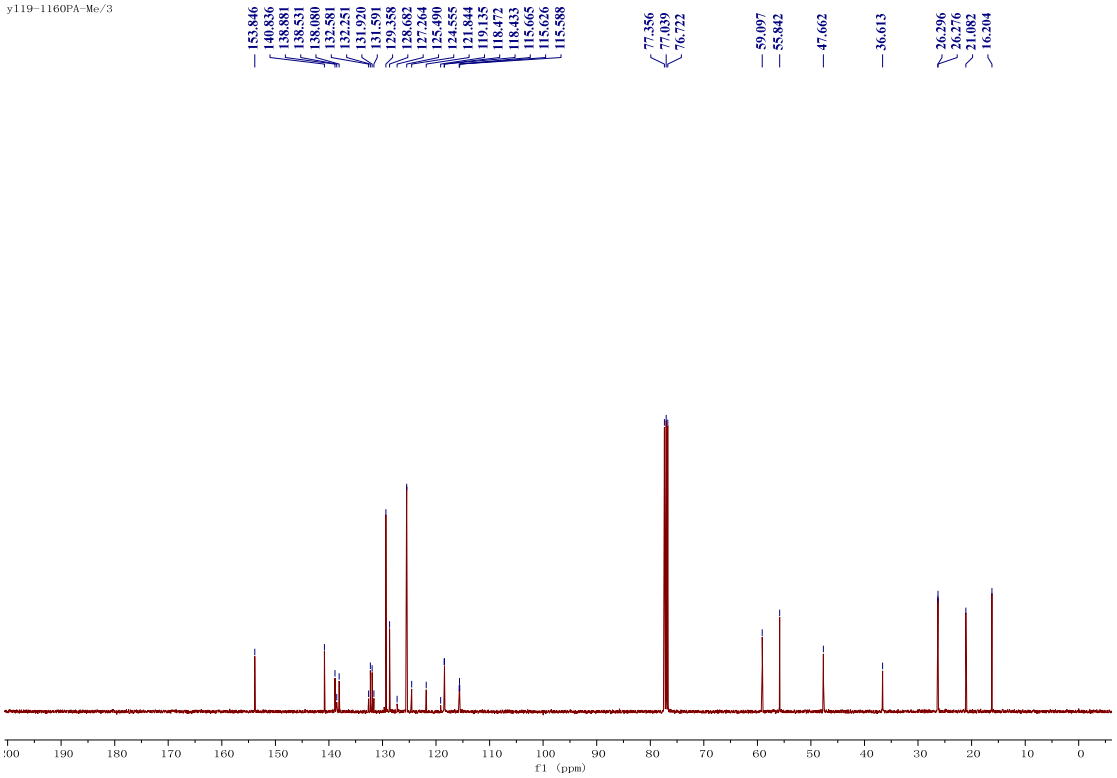

2.08
7.42
0.96
1.00
1.00
1.01
1.10
3.10
1.13
1.08
6.16
f1 (ppm)

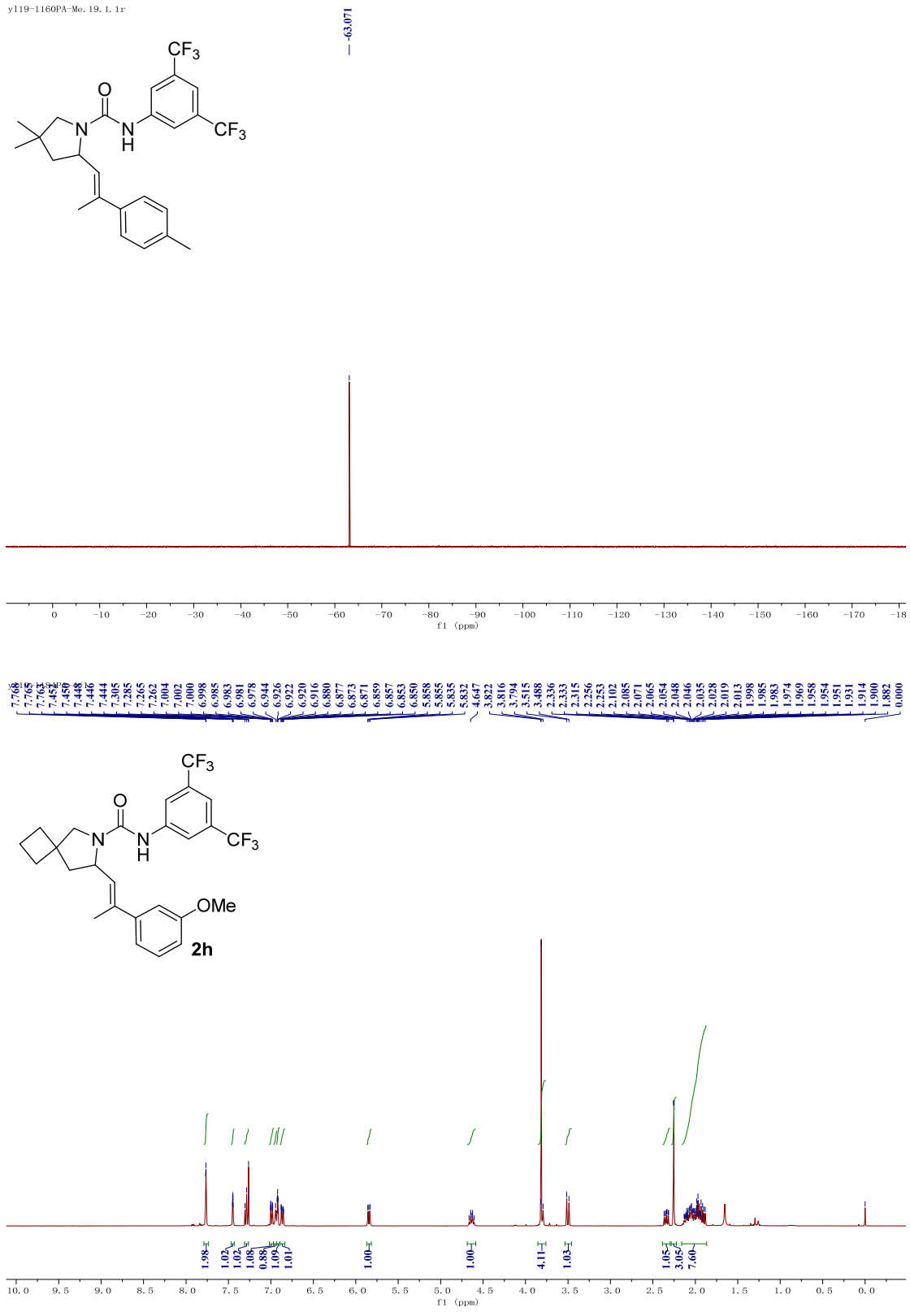

f1 (ppm)


y119-1151PN02-H.1.1.1r
8.124
8.102
7.438
7.433
7.422
7.415
7.399
7.381
7.362
7.348
7.332
7.315
7.263
7.115
5.890
5.867
4.765
4.743
4.723
4.702
3.698
3.671
3.253
3.226
2.287
2.110
2.092
2.078
2.061
1.755
1.732
1.723
1.701
1.614
1.191
1.150
0.071
0.020
-0.000
NO2
O
N
N
H
Ph
2f
2.01
7.30
0.94
1.00
1.01
1.05
1.07
3.17
1.20
1.60
3.42
2.85
f1 (ppm)


y119-1151PN02-H.13.1.1r
153.505
145.468
142.211
141.735
138.586
129.388
128.737
128.188
125.709
125.233
117.711
77.353
77.035
76.717
59.159
55.781
47.648
36.644
26.298
26.288
16.183
f1 (ppm)

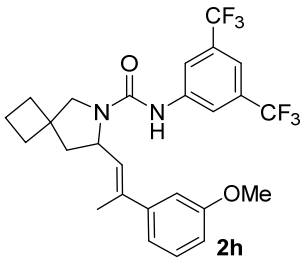

y119-1160PA-Me. 1. 1. 1r
7.757
7.753
7.440
7.322
7.317
7.306
7.301
7.296
7.257
7.189
7.169
7.061
5.847
5.843
5.840
5.821
5.817
5.814
4.750
4.732
4.727
4.709
4.704
4.687
3.677
3.673
3.650
3.646
3.241
3.214
2.360
2.259
2.256
2.104
2.100
2.086
2.082
2.072
2.068
2.055
2.051
1.751
1.728
1.719
1.696
1.184
1.141
CF3
O
N
N
H
CF3
2g
1.98
1.00
2.01
2.03
0.94
1.00
1.00
1.00
1.00
3.09
3.00
1.03
1.04
3.10
3.02
f1 (ppm)


y119-1160PA-Me/3
153.846
140.836
138.881
138.531
138.080
132.581
132.251
131.920
131.591
129.358
128.682
127.264
125.490
124.555
121.844
119.135
118.472
118.433
115.665
115.626
115.588
77.356
77.039
76.722
59.097
55.842
47.662
36.613
26.296
26.276
21.082
16.204
f1 (ppm)

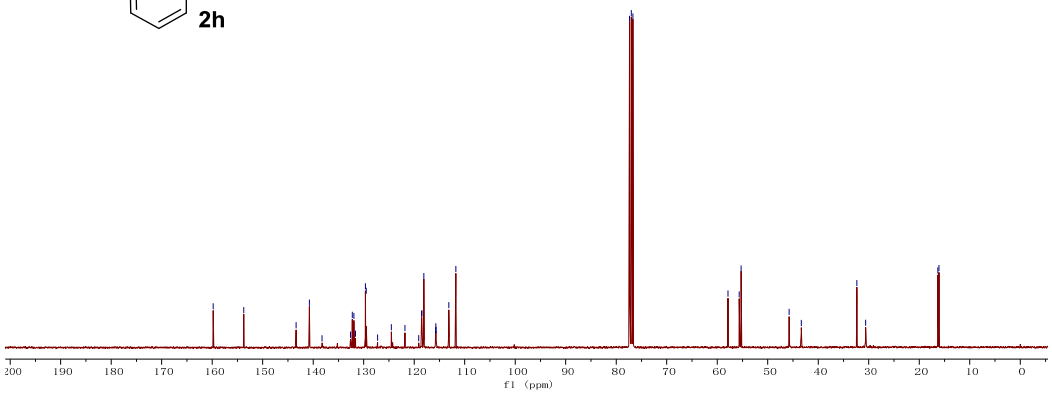

y119-1160PA-Me.19.1.1r
-63.071
CF3
O
N
N
H
CF3
f1 (ppm)
CF3
O
N
N
H
CF3
OMe
2h
1.98
1.02
1.02
1.08
0.88
1.09
1.01
1.00
1.00
4.11
1.03
1.05
3.05
7.60
f1 (ppm)

y119-1184PA-4/13

159.821
153.750
143.376
140.758
138.242
132.604
132.273
131.942
131.612
129.672
129.510
127.250
124.541
121.829
119.120
118.526
118.486
118.097
115.749
115.711
115.672
113.162
111.746
77.348
77.030
76.712
57.880
55.641
55.267
45.752
43.346
32.348
30.605
16.301
16.105

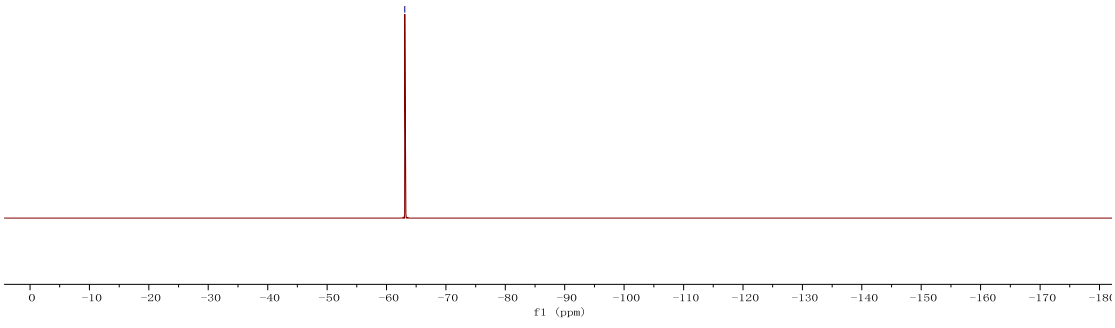


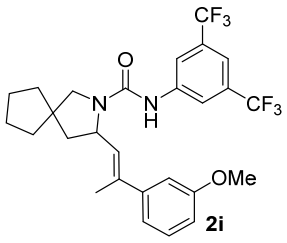

**2h**



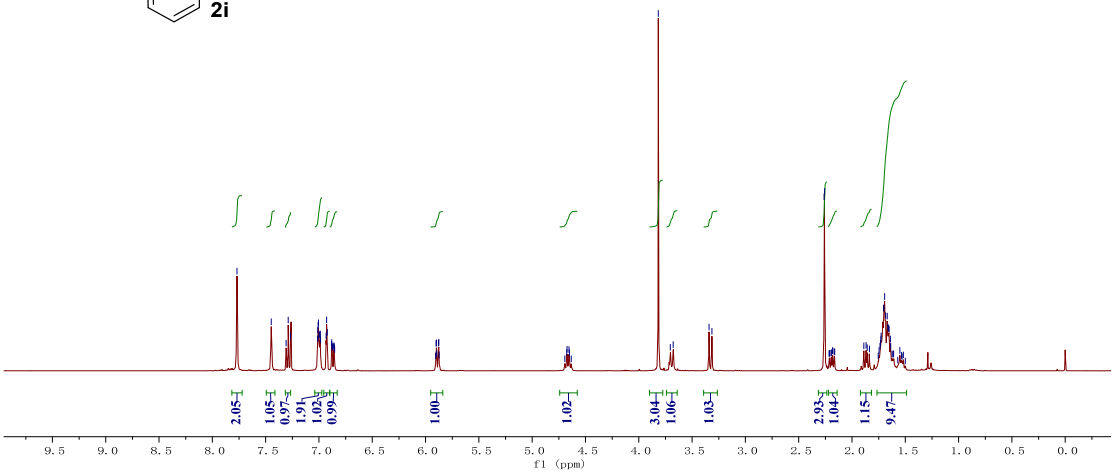

y119-1184PA-4/19

-63.079

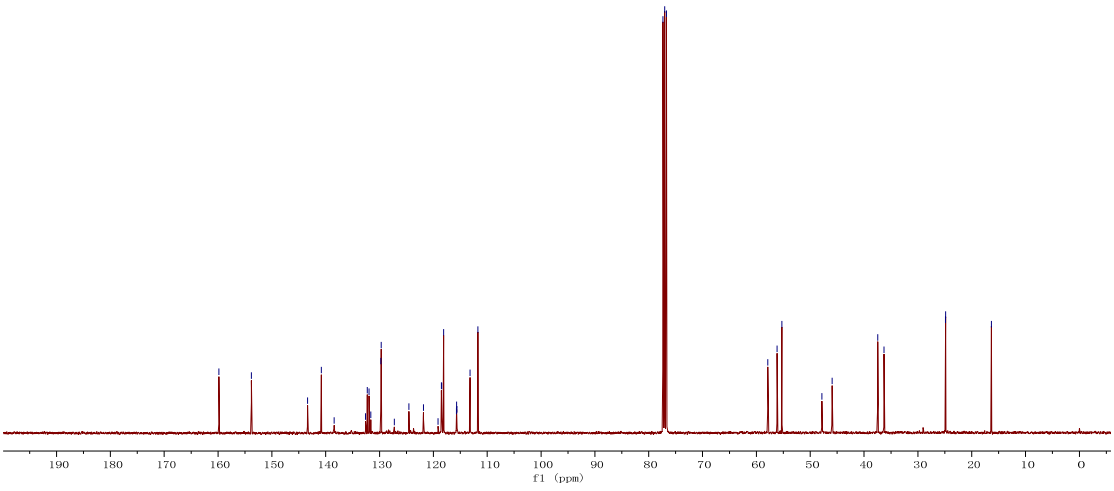



CF3
O
N
N
H
CF3
OMe

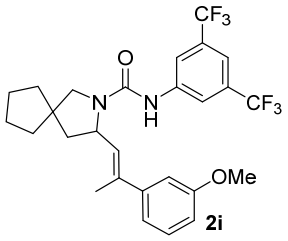
**2i**


2.05
1.05
0.97
1.91
1.02
0.99
1.00
1.02
3.04
1.06
1.03
2.93
1.04
1.15
9.47
f1 (ppm)


y119-1184PC-5/13


f1 (ppm)

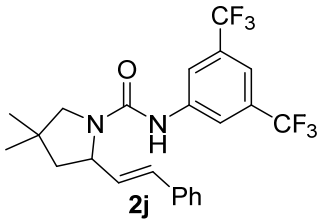
y119-1184PC-5/19



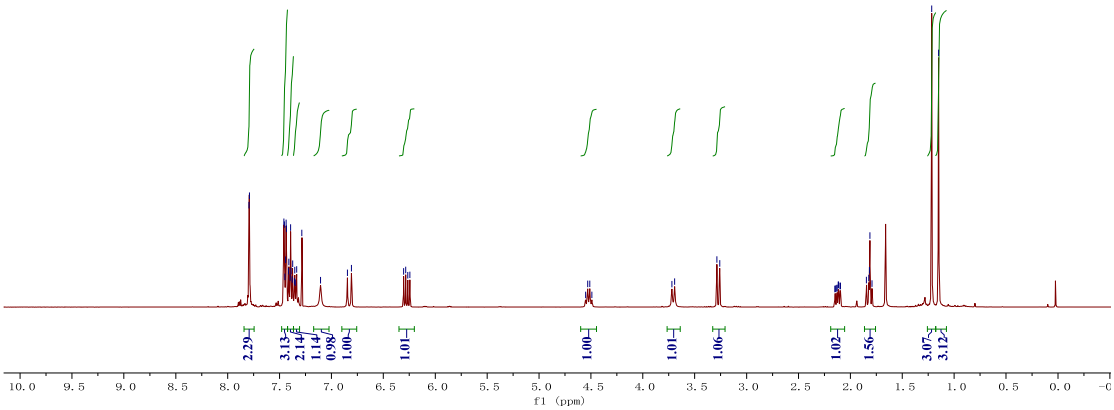

**2i**

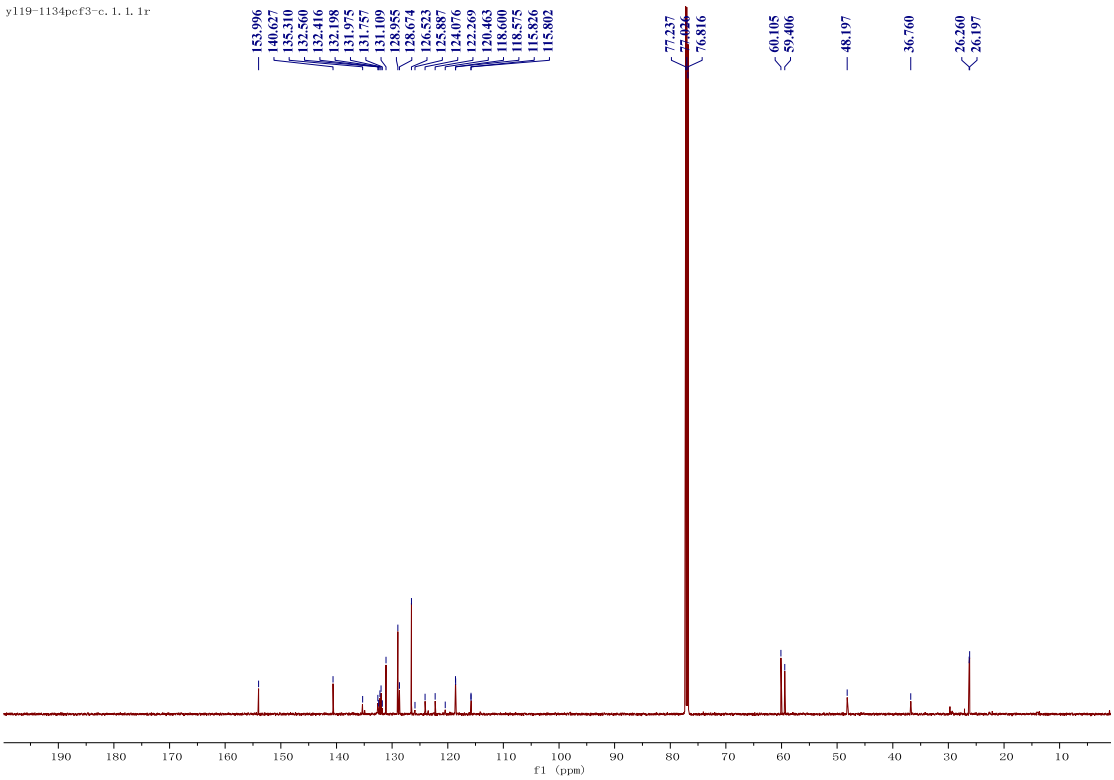


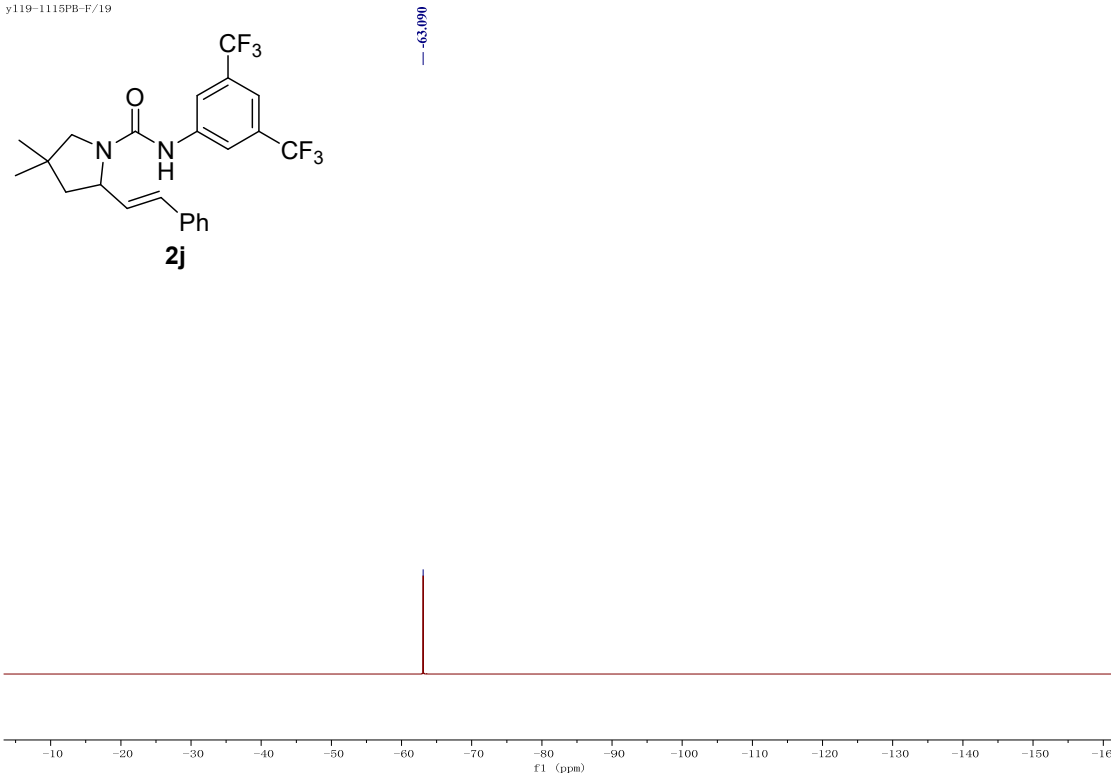




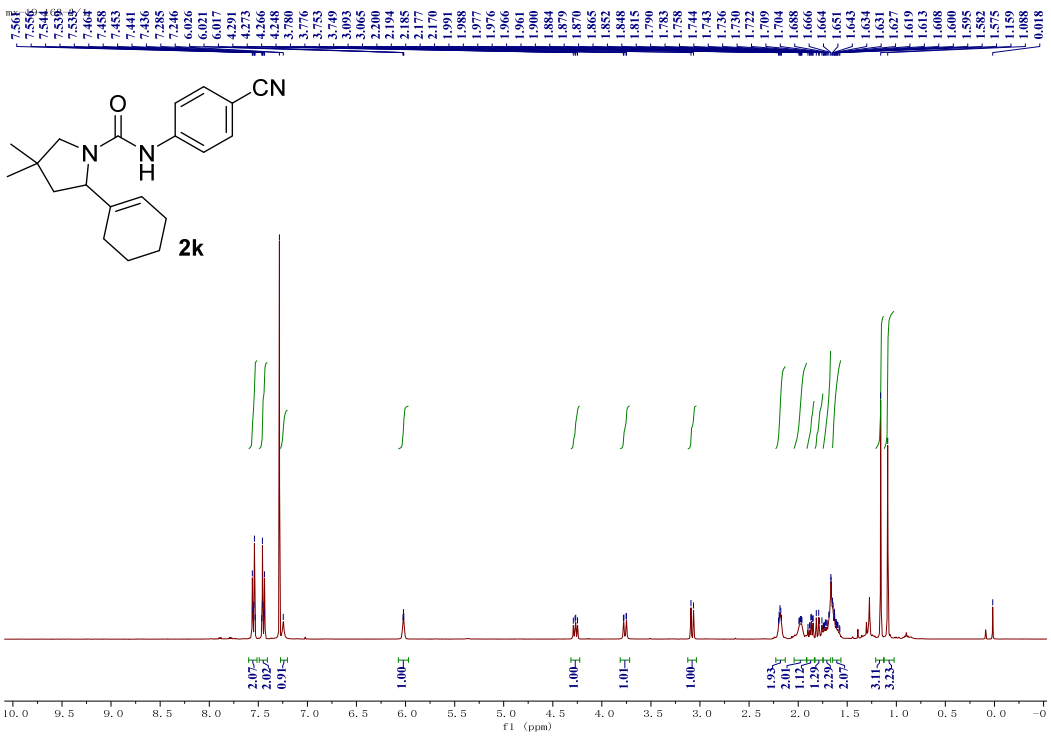

**2j**

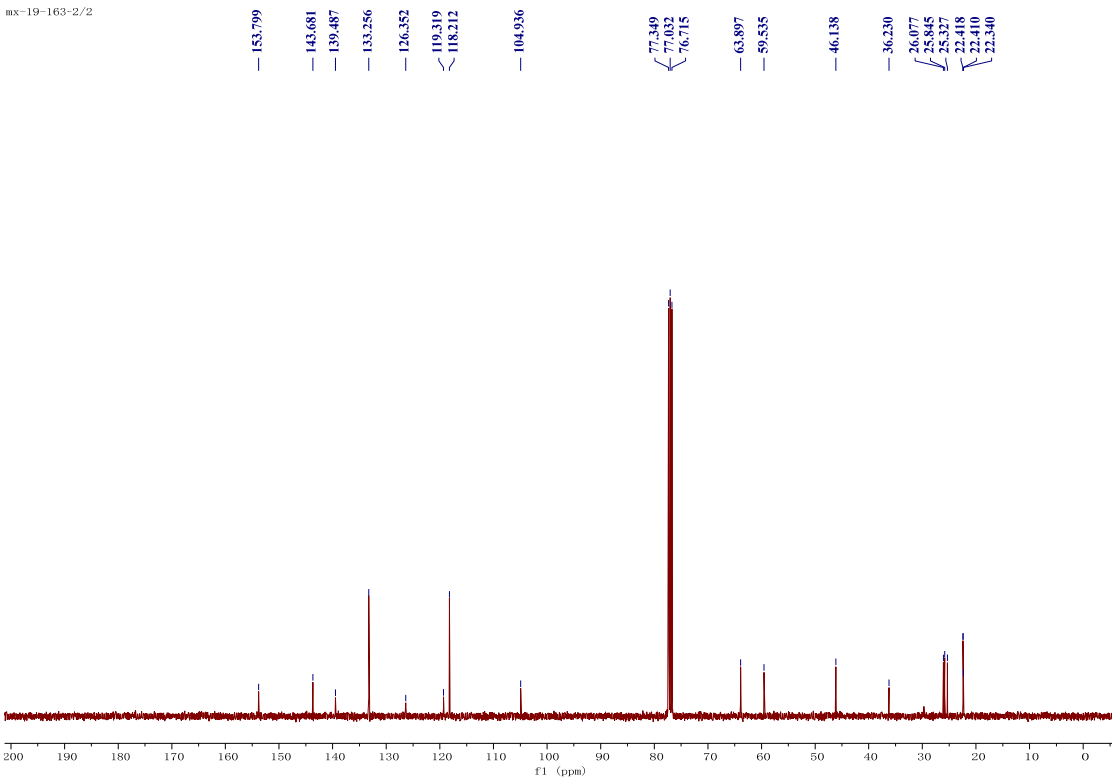


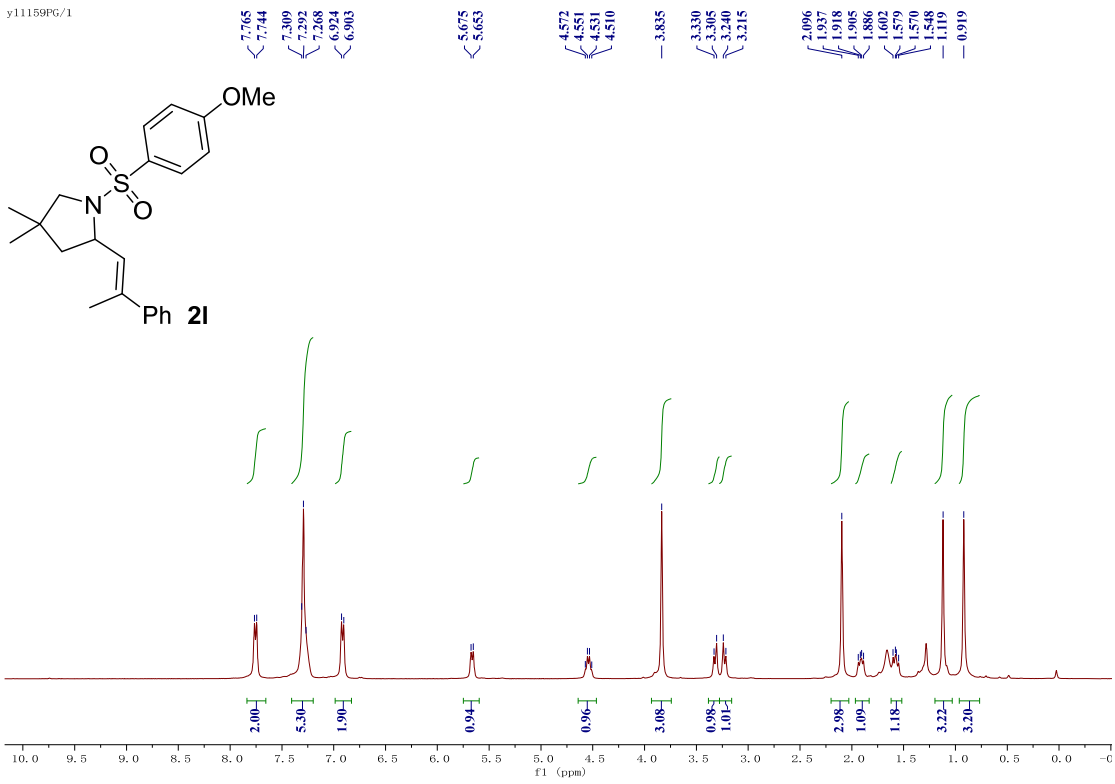

y119-1134pcf3-c.1.1.1r
153.996
140.627
135.310
132.560
132.416
132.198
131.975
131.757
131.109
128.955
128.674
126.523
125.887
124.076
122.269
120.463
118.600
118.575
115.826
115.802
77.237
77.036
76.816
60.105
59.406
48.197
36.760
26.260
26.197
f1 (ppm)

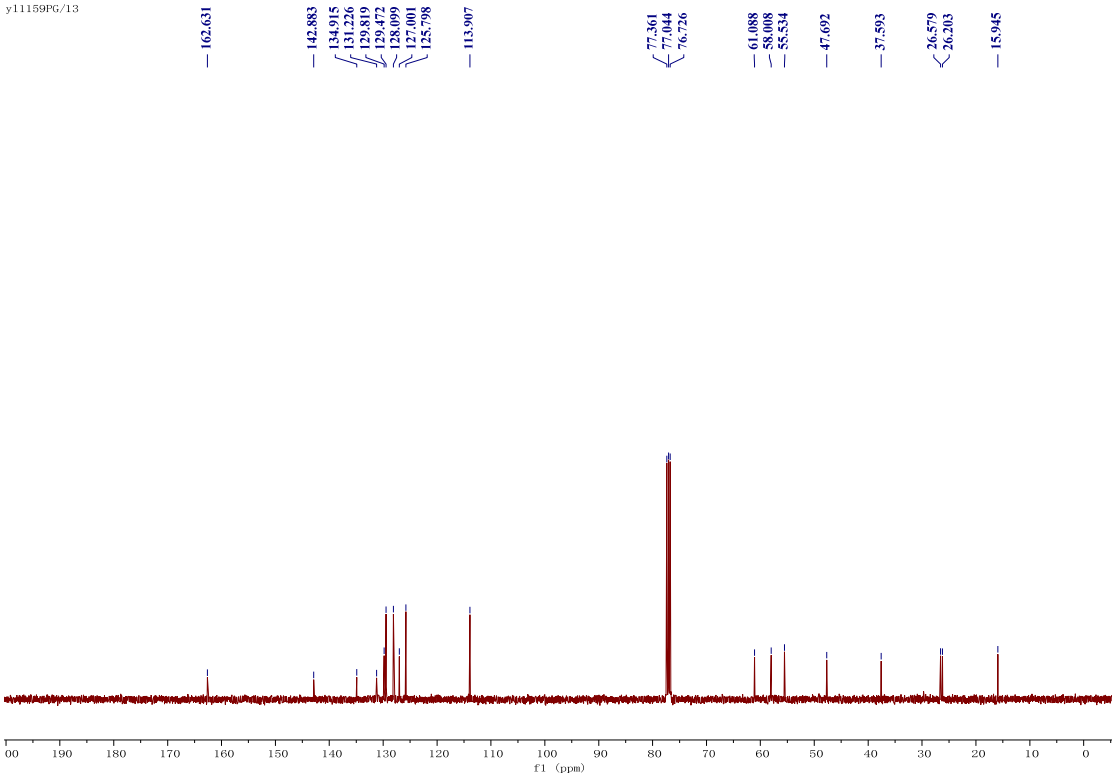

y119-1115PB-F/19
-63.090
CF3
O
N
H
N
CF3
Ph
f1 (ppm)

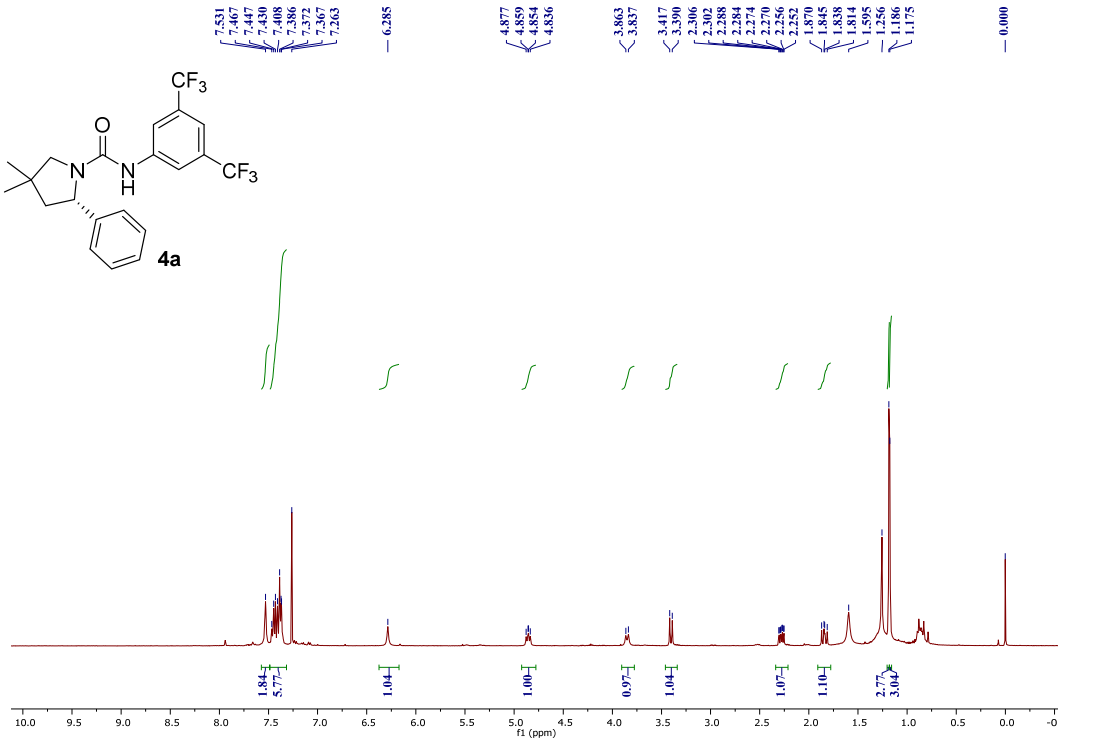
**2j**

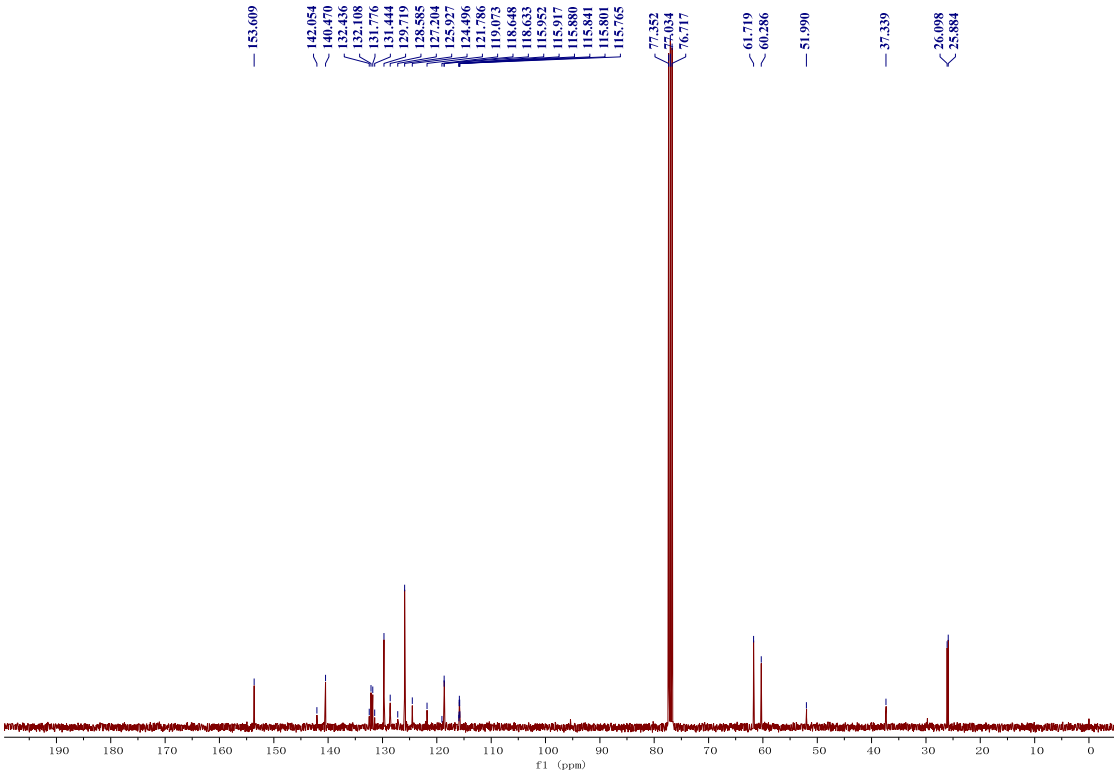

7.561
7.556
7.544
7.539
7.536
7.535
7.464
7.458
7.453
7.441
7.436
7.285
7.246
6.026
6.021
6.017
4.291
4.273
4.266
4.248
3.780
3.776
3.753
3.749
3.093
3.065
2.200
2.194
2.185
2.177
2.170
1.991
1.988
1.977
1.976
1.966
1.961
1.900
1.884
1.879
1.870
1.865
1.852
1.848
1.815
1.790
1.783
1.758
1.744
1.743
1.736
1.730
1.722
1.709
1.704
1.688
1.666
1.664
1.651
1.643
1.634
1.631
1.627
1.619
1.613
1.608
1.600
1.595
1.582
1.575
1.159
1.088
0.018
O
N
N
H
CN
2k
2.07
2.02
0.91
1.00
1.00
1.01
1.00
1.93
2.01
1.12
1.29
2.29
2.07
3.11
3.23
f1 (ppm)

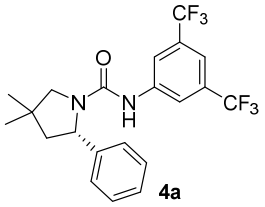

mx-19-163-2/2
153.799
143.681
139.487
133.256
126.352
119.319
118.212
104.936
77.349
77.032
76.715
63.897
59.535
46.138
36.230
26.077
25.845
25.327
22.418
22.410
22.340
f1 (ppm)


y11159PG/1
7.765
7.744
7.309
7.292
7.268
6.924
6.903
5.675
5.653
4.572
4.551
4.531
4.510
3.835
3.330
3.305
3.240
3.215
2.096
1.937
1.918
1.905
1.886
1.602
1.579
1.570
1.548
1.119
0.919
OMe
O
S
O
N
Ph
2l
2.00
5.30
1.90
0.94
0.96
3.08
0.98
1.01
2.98
1.09
1.18
3.22
3.20
f1 (ppm)


y11159PG/13
162.631
142.883
134.915
131.226
129.819
129.472
128.099
127.001
125.798
113.907
77.361
77.044
76.726
61.088
58.008
55.534
47.692
37.593
26.579
26.203
15.945
f1 (ppm)

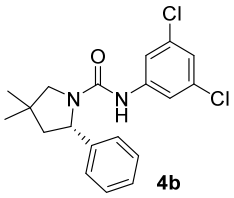

7.531
7.467
7.447
7.430
7.408
7.386
7.372
7.367
7.263
6.285
4.877
4.859
4.854
4.836
3.863
3.837
3.417
3.390
2.306
2.302
2.288
2.284
2.274
2.270
2.256
2.252
1.870
1.845
1.838
1.814
1.595
1.256
1.186
1.175
0.000
CF3
CF3
O
N
N
H
4a
1.84
5.77
1.04
1.00
0.97
1.04
1.07
1.10
2.77
3.04
f1 (ppm)


153.609
142.054
140.470
132.436
132.108
131.776
131.444
129.719
128.585
127.204
125.927
124.496
121.786
119.073
118.648
118.633
115.952
115.917
115.880
115.841
115.801
115.765
77.352
77.034
76.717
61.719
60.286
51.990
37.339
26.098
25.884
f1 (ppm)


CF3
O
N
H
N
CF3

4a


-63.089
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -2
f1 (ppm)


Cl
O
N
H
N
Cl

4b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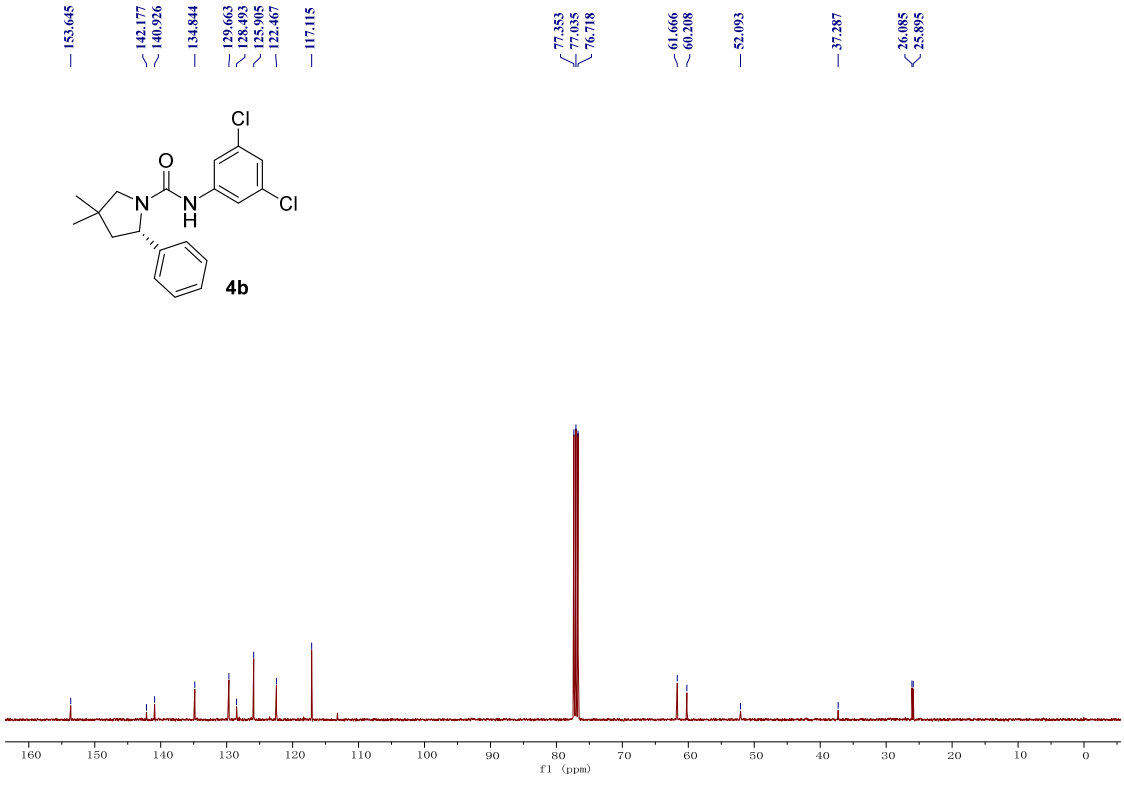
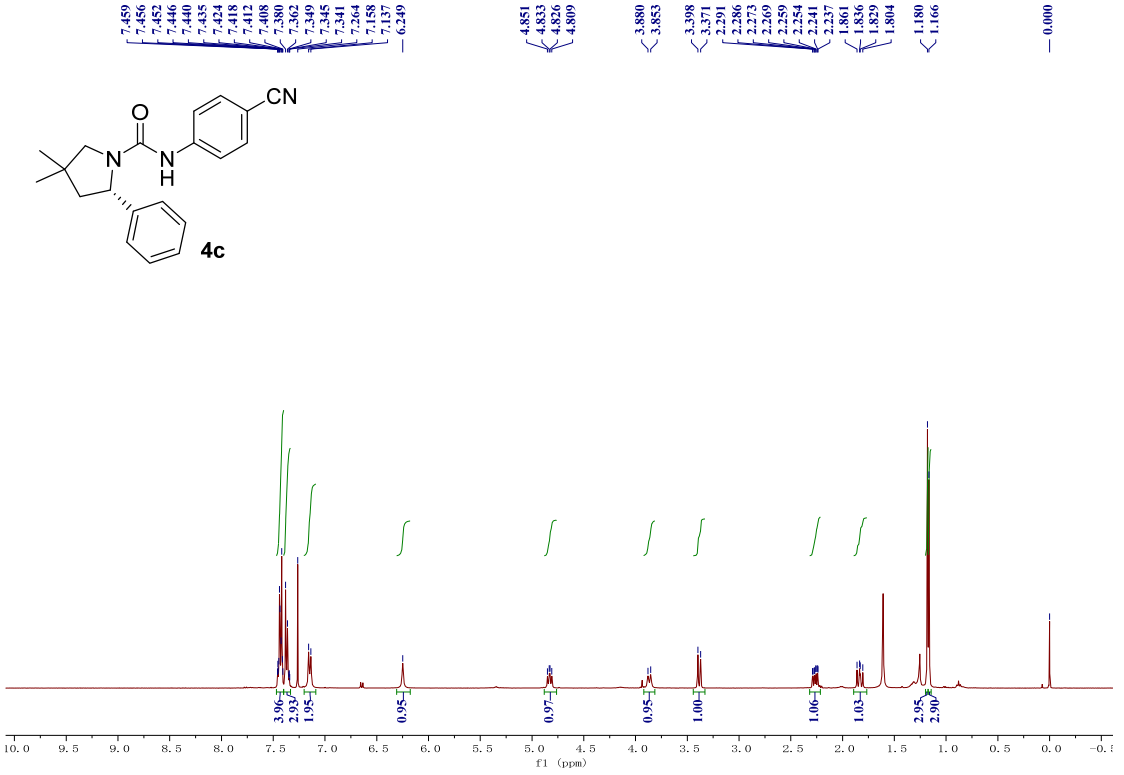
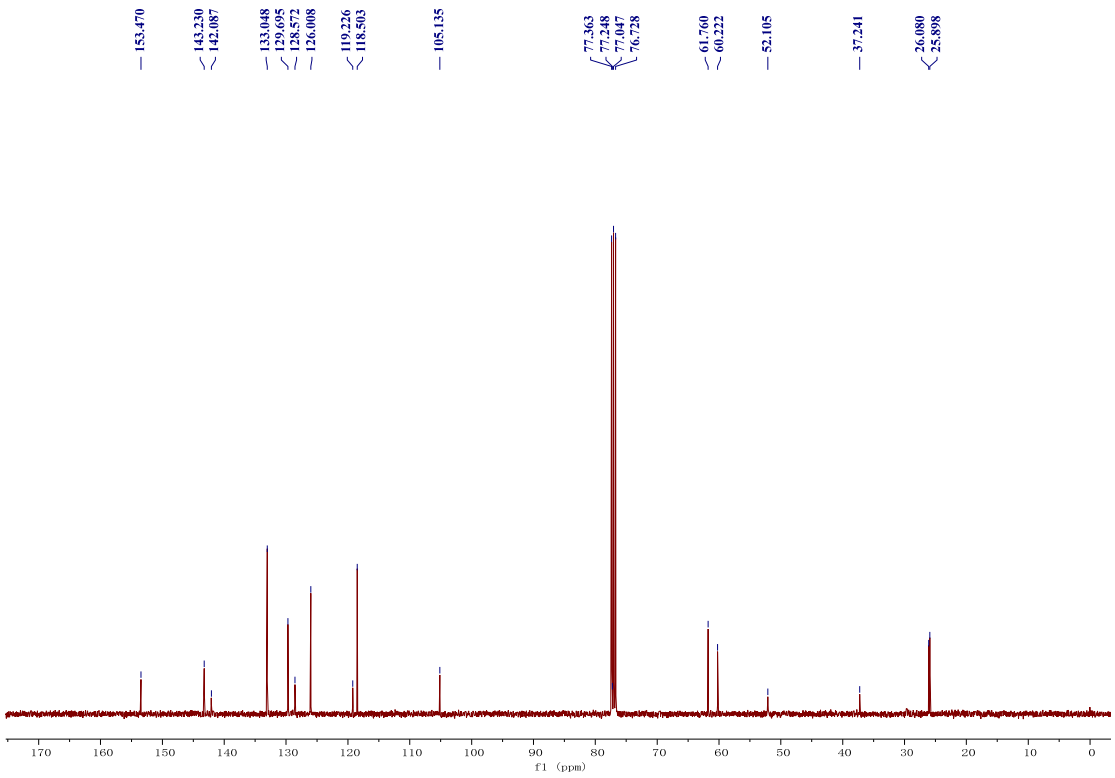
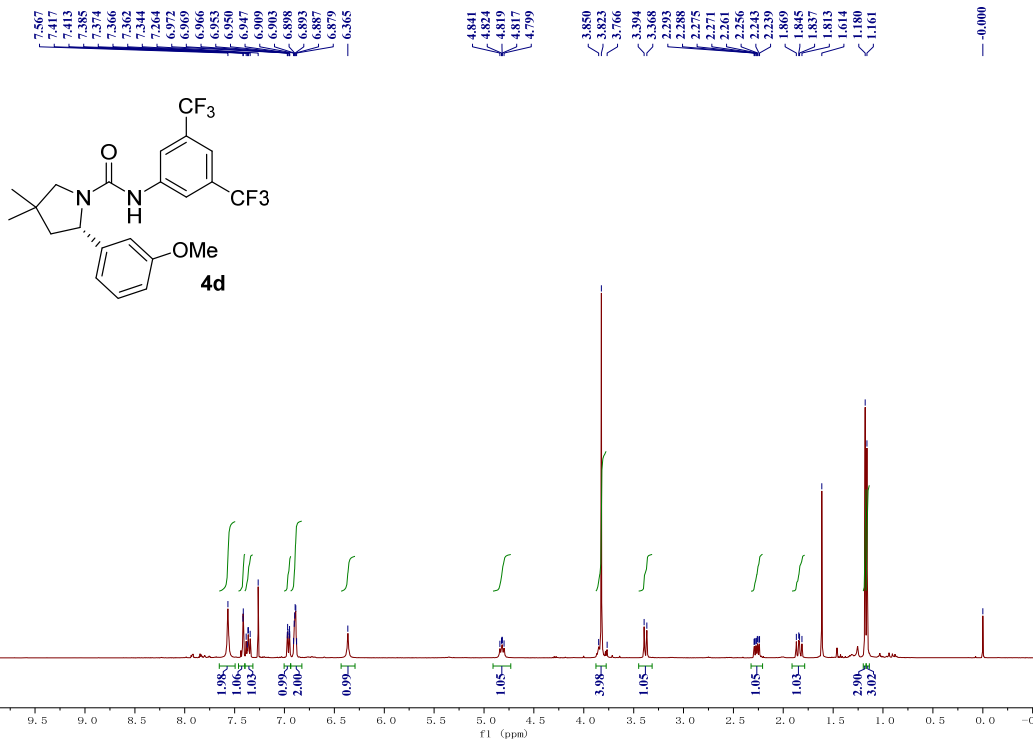
7.437
7.432
7.414
7.375
7.360
7.355
7.339
7.262
7.022
7.018
6.908
6.904
6.899
6.044
4.825
4.808
4.801
4.784
3.851
3.824
3.380
3.353
2.277
2.272
2.259
2.255
2.245
2.241
2.227
2.223
1.837
1.813
1.805
1.792
1.781
1.168
1.154
-0.000
1.97
3.10
1.82
0.92
0.98
0.99
1.13
1.00
1.05
1.29
2.88
3.01
f1 (ppm)


153.645
142.177
140.926
134.844
129.663
128.493
125.905
122.467
117.115
77.353
77.035
76.718
61.666
60.208
52.093
37.287
26.085
25.895
Cl
O
N
N
H
Cl
4b
f1 (ppm)


7.459
7.456
7.452
7.446
7.440
7.435
7.424
7.418
7.412
7.408
7.380
7.362
7.349
7.345
7.341
7.264
7.158
7.137
6.249
4.851
4.833
4.826
4.809
3.880
3.853
3.398
3.371
2.291
2.286
2.273
2.269
2.259
2.254
2.241
2.237
1.861
1.836
1.829
1.804
1.180
1.166
0.000
O
N
N
H
CN
4c
3.96
2.93
1.95
0.95
0.97
0.95
1.00
1.06
1.03
2.95
2.90
f1 (ppm)


153.470
143.230
142.087
133.048
129.695
128.572
126.008
119.226
118.503
105.135
77.363
77.248
77.047
76.728
61.760
60.222
52.105
37.241
26.080
25.898
f1 (ppm)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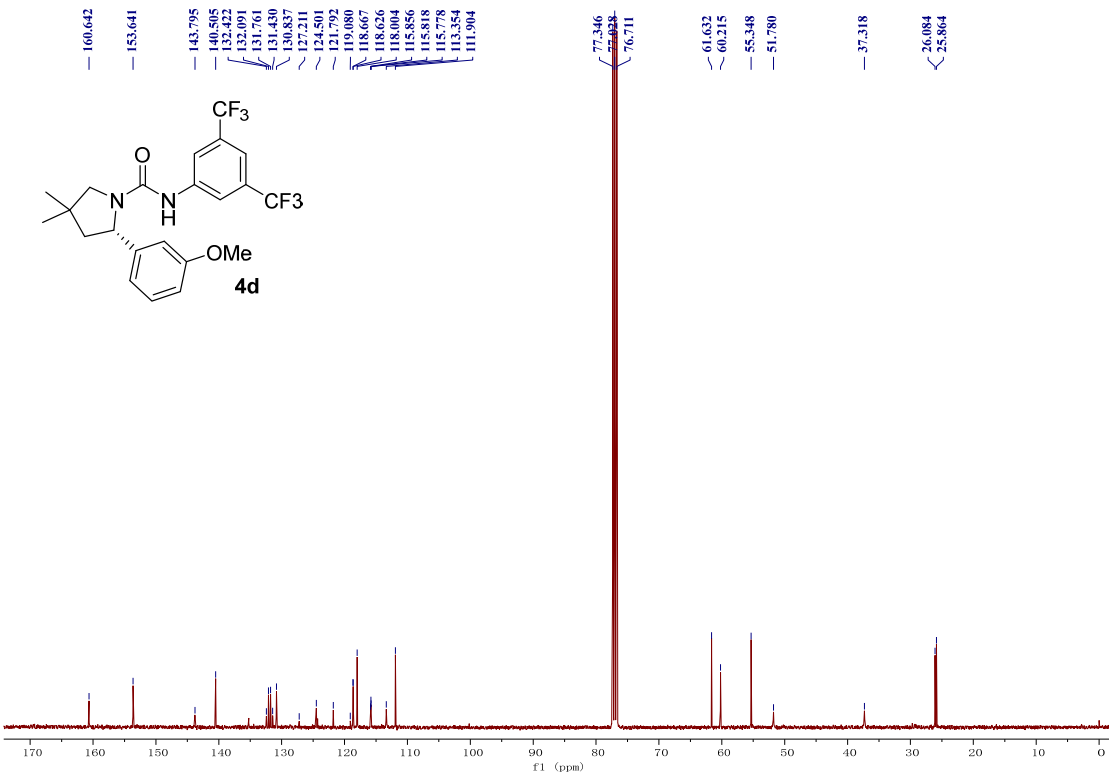
7.417
7.413
7.385
7.374
7.366
7.362
7.344
7.264
6.972
6.969
6.966
6.953
6.950
6.947
6.909
6.903
6.898
6.893
6.887
6.879
6.365
4.841
4.824
4.819
4.817
4.799
3.850
3.823
3.766
3.394
3.368
2.293
2.288
2.275
2.271
2.261
2.256
2.243
2.239
1.869
1.845
1.837
1.813
1.614
1.180
1.161
-0.000
CF3
O
N
N
H
CF3
OMe
4d
1.98
1.06
1.03
0.99
2.00
0.99
1.05
3.98
1.05
1.05
1.03
2.90
3.02
f1 (ppm)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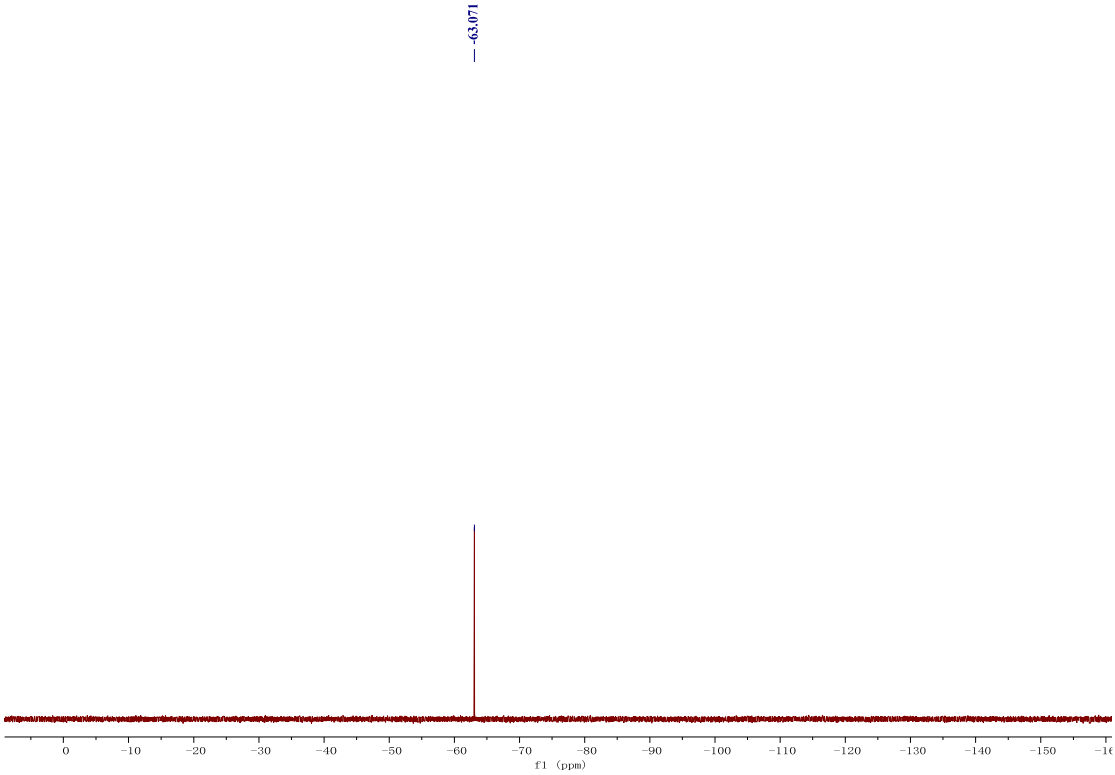
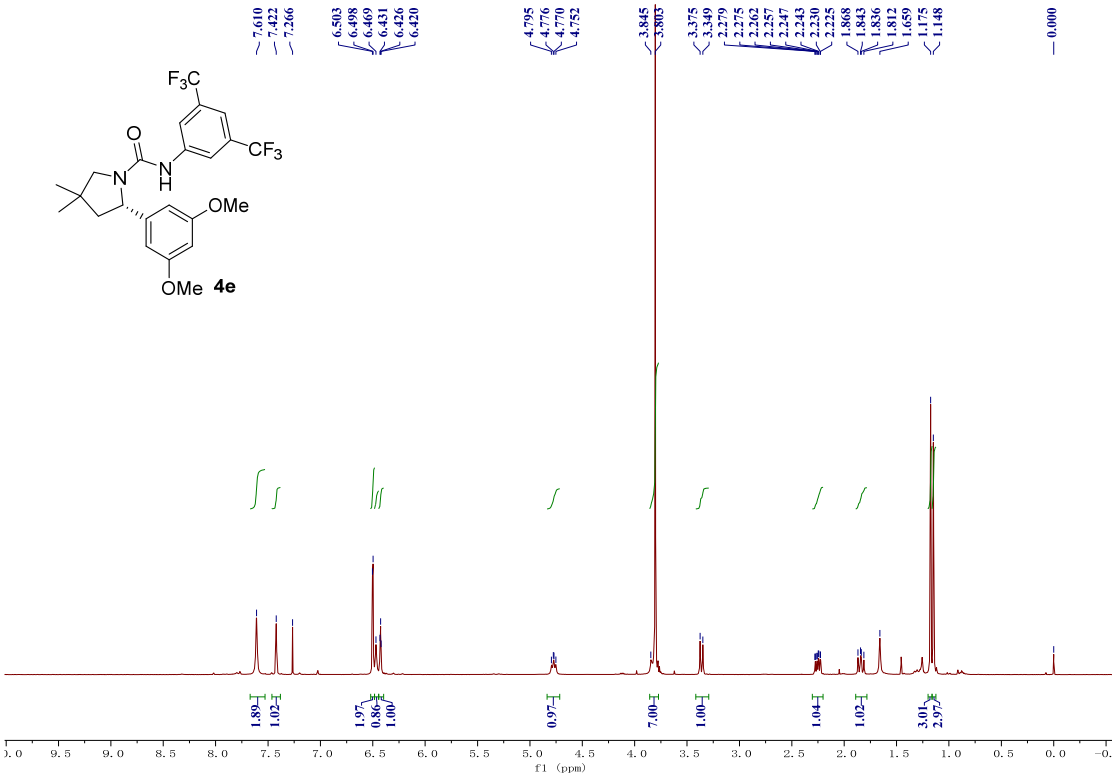
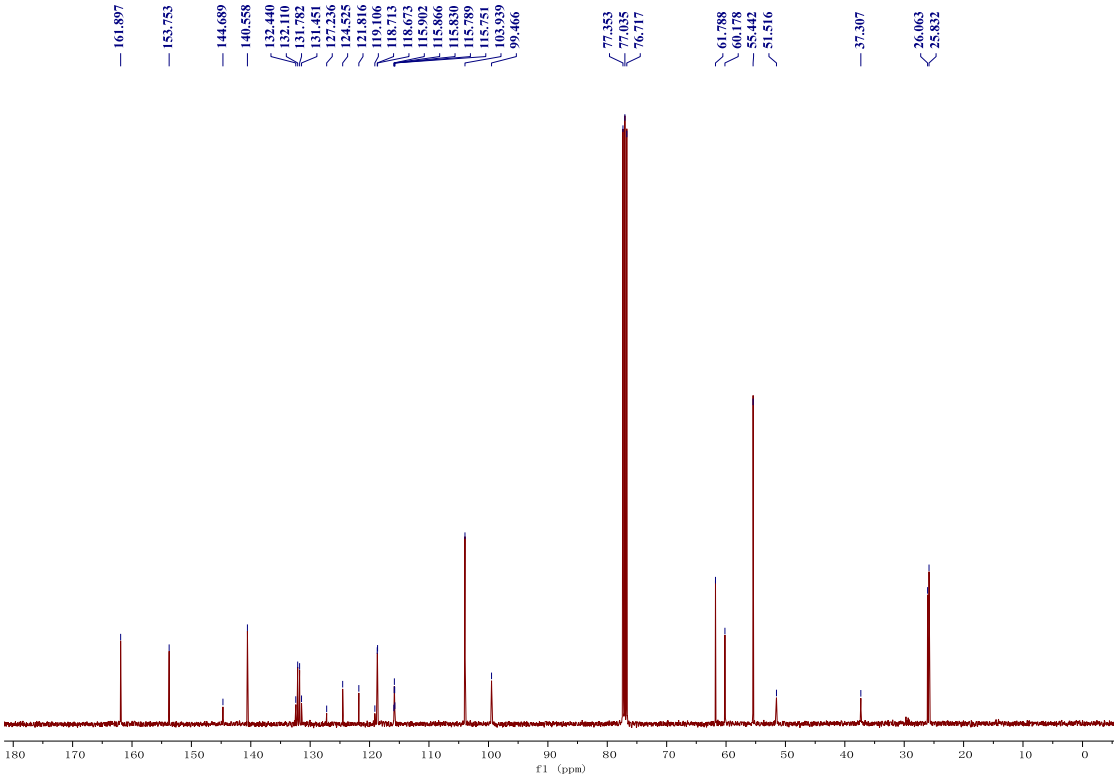
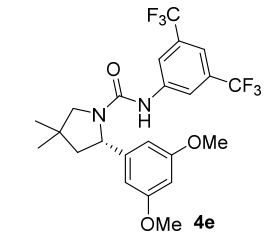
153.641
143.795
140.505
132.422
132.091
131.761
131.430
130.837
127.211
124.501
121.792
119.080
118.667
118.626
118.004
115.856
115.818
115.778
113.354
111.904
77.346
77.028
76.711
61.632
60.215
55.348
51.780
37.318
26.084
25.864
CF3
O
N
N
H
CF3
OMe
4d
f1 (ppm)


-63.071
f1 (ppm)

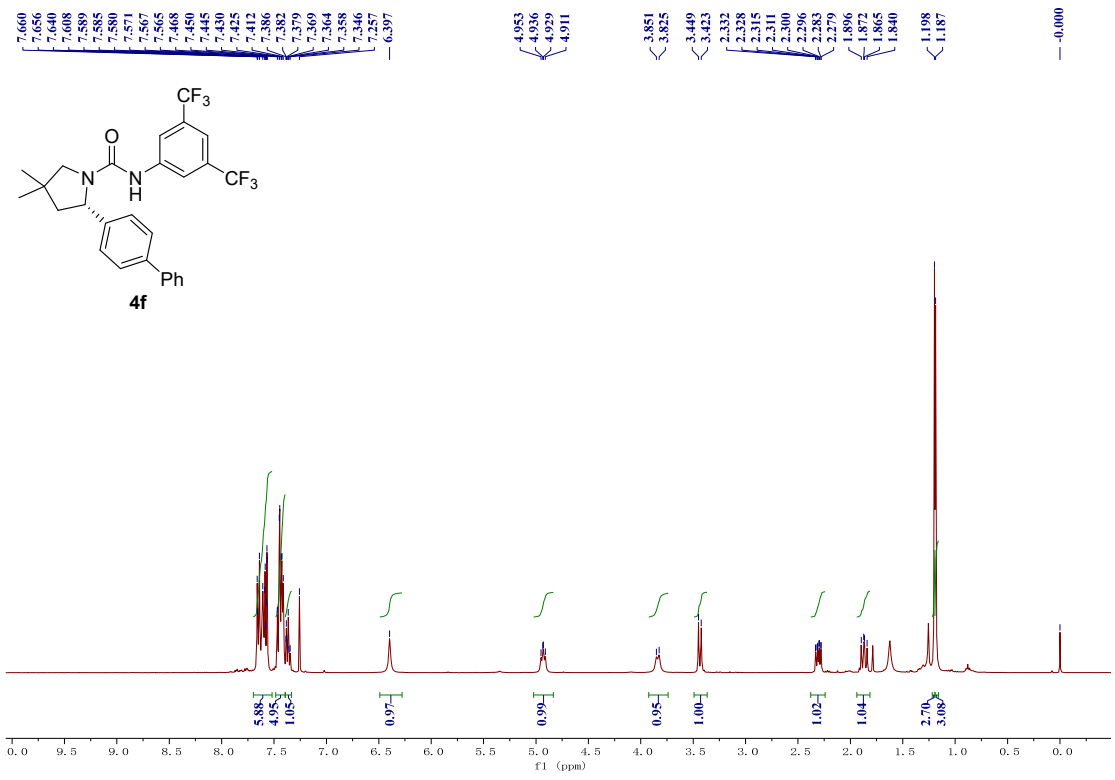

7.610
7.422
7.266
6.503
6.498
6.469
6.431
6.426
6.420
4.795
4.776
4.770
4.752
3.845
3.803
3.375
3.349
2.279
2.275
2.262
2.257
2.247
2.243
2.230
2.225
1.868
1.843
1.836
1.812
1.659
1.175
1.148
0.000
1.89
1.02
1.97
0.86
1.00
0.97
7.00
1.00
1.04
1.02
3.01
2.97
f1 (ppm)


161.897
153.753
144.689
140.558
132.440
132.110
131.782
131.451
127.236
124.525
121.816
119.106
118.713
118.673
115.902
115.866
115.830
115.789
115.751
103.939
99.466
77.353
77.035
76.717
61.788
60.178
55.442
51.516
37.307
26.063
25.832
f1 (ppm)


F3C
O
N
H
CF3
N
OMe
OMe

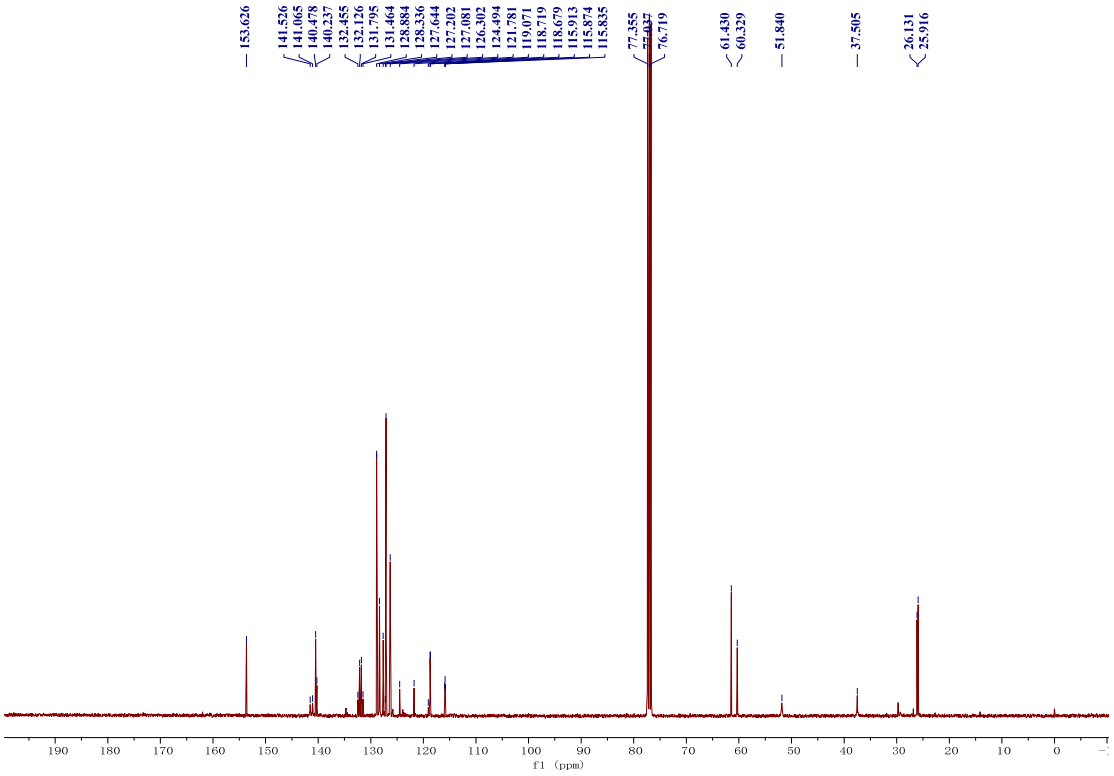
**4e**

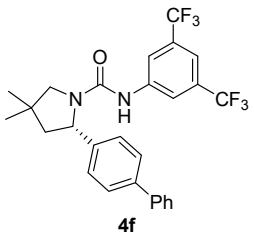

-63.071
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)


7.660
7.656
7.640
7.608
7.589
7.585
7.580
7.571
7.567
7.565
7.468
7.450
7.445
7.430
7.425
7.412
7.386
7.382
7.379
7.369
7.364
7.358
7.346
7.257
6.397
4.953
4.936
4.929
4.911
3.851
3.825
3.449
3.423
2.332
2.328
2.315
2.311
2.300
2.296
2.283
2.279
1.896
1.872
1.865
1.840
1.198
1.187
-0.000
5.88
4.95
1.05
0.97
0.99
0.95
1.00
1.02
1.04
2.70
3.08
f1 (ppm)


CF3
O
N
H
CF3
Ph

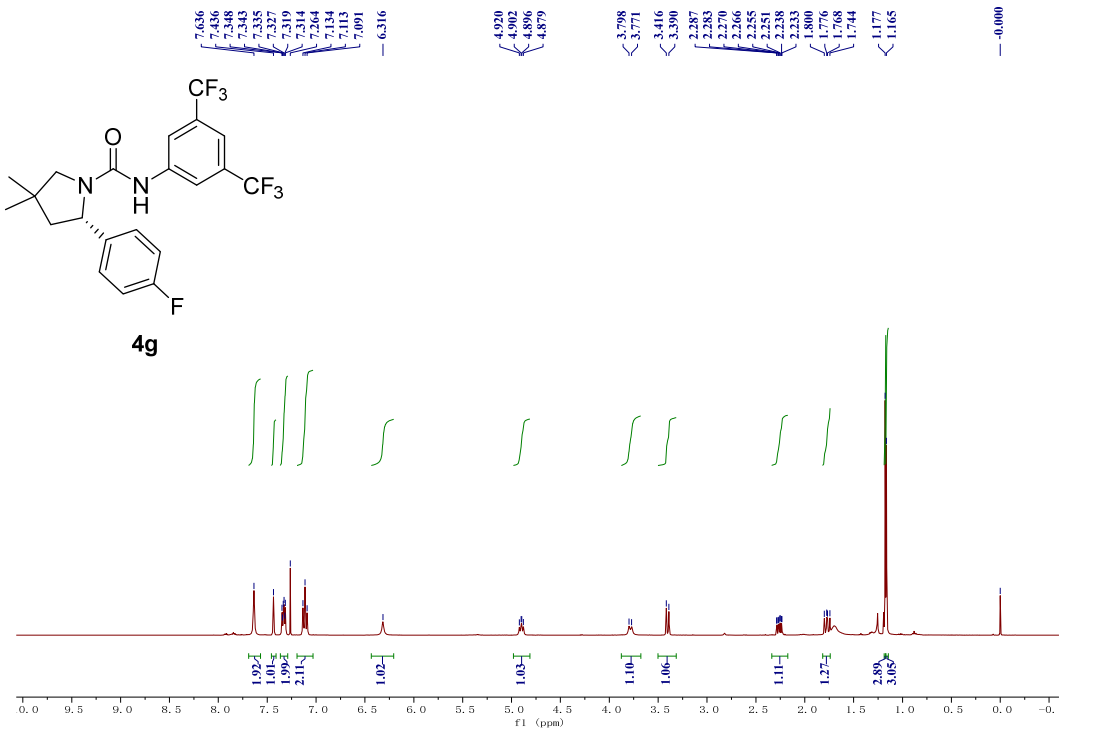
**4f**


153.626
141.526
141.065
140.478
140.237
132.455
132.126
131.795
131.464
128.884
128.336
127.644
127.202
127.081
126.302
124.494
121.781
119.071
118.719
118.679
115.913
115.874
115.835
77.355
77.037
76.719
61.430
60.329
51.840
37.505
26.131
25.916
f1 (ppm)


CF3
O
N
N
H
CF3
Ph

**4f**


-63.038
f1 (ppm)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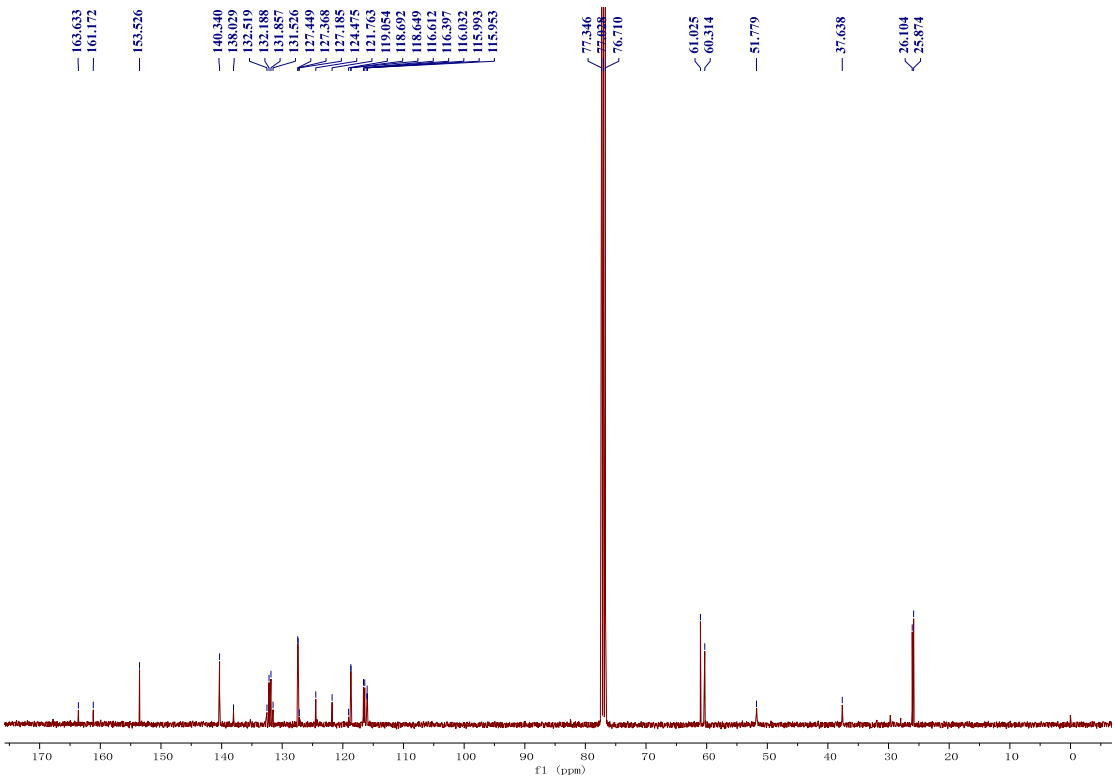
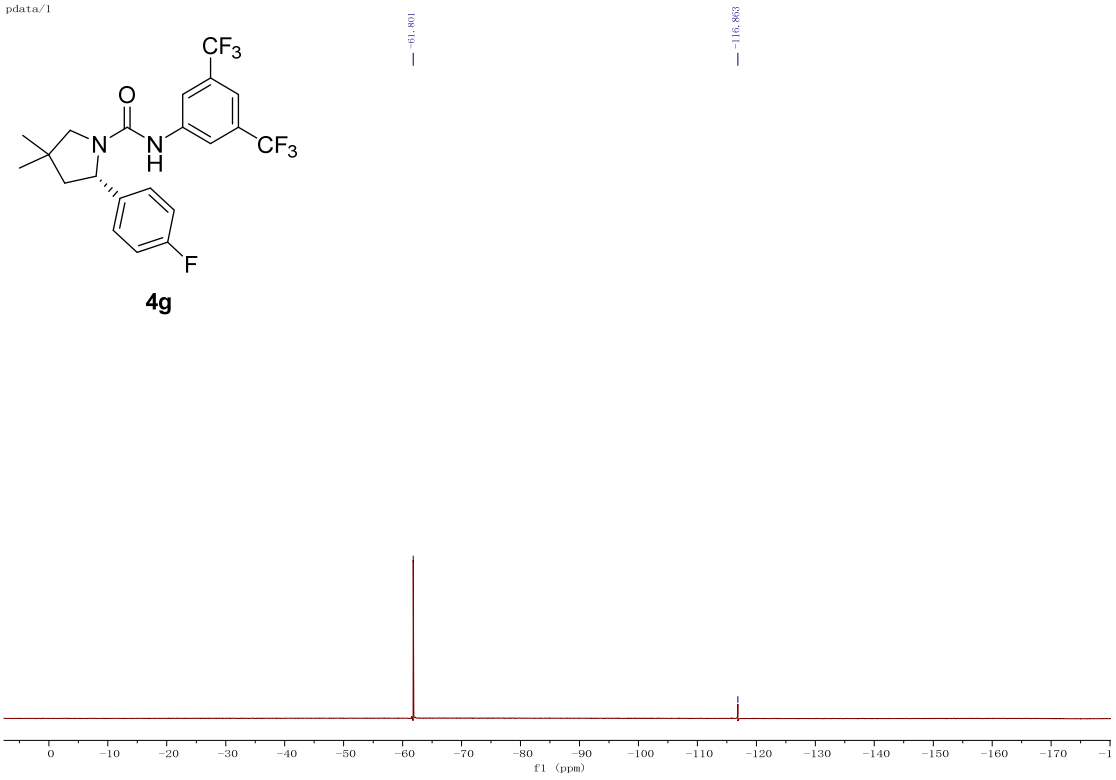
7.436
7.348
7.343
7.335
7.327
7.319
7.314
7.264
7.134
7.113
7.091
6.316
4.920
4.902
4.896
4.879
3.798
3.771
3.416
3.390
2.287
2.283
2.270
2.266
2.255
2.251
2.238
2.233
1.800
1.776
1.768
1.744
1.177
1.165
-0.000
CF3
CF3
O
N
N
H
F
4g
1.92
1.01
1.99
2.11
1.02
1.03
1.10
1.06
1.11
1.27
2.89
3.05
f1 (ppm)


163.633
161.172
153.526
140.340
138.029
132.519
132.188
131.857
131.526
127.449
127.368
127.185
124.475
121.763
119.054
118.692
118.649
116.612
116.397
116.032
115.993
115.953
77.346
77.038
76.710
61.025
60.314
51.779
37.638
26.104
25.874
f1 (ppm)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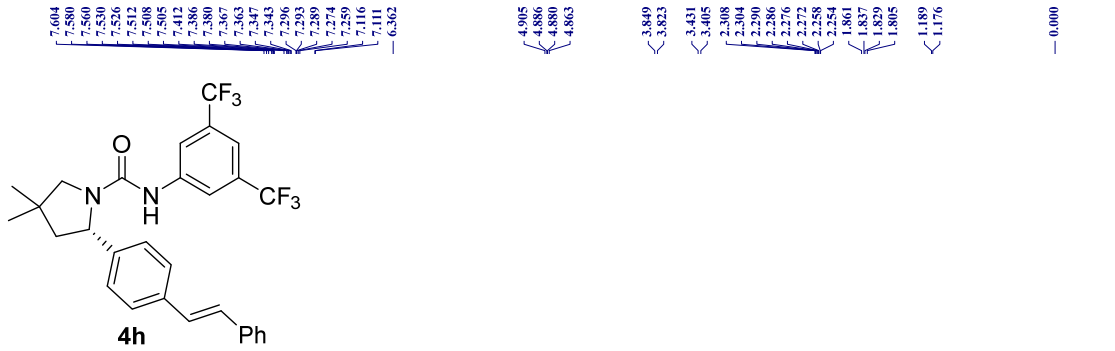
-116.863
CF3
O
N
N
H
CF3
F
4g
f1 (ppm)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7.560
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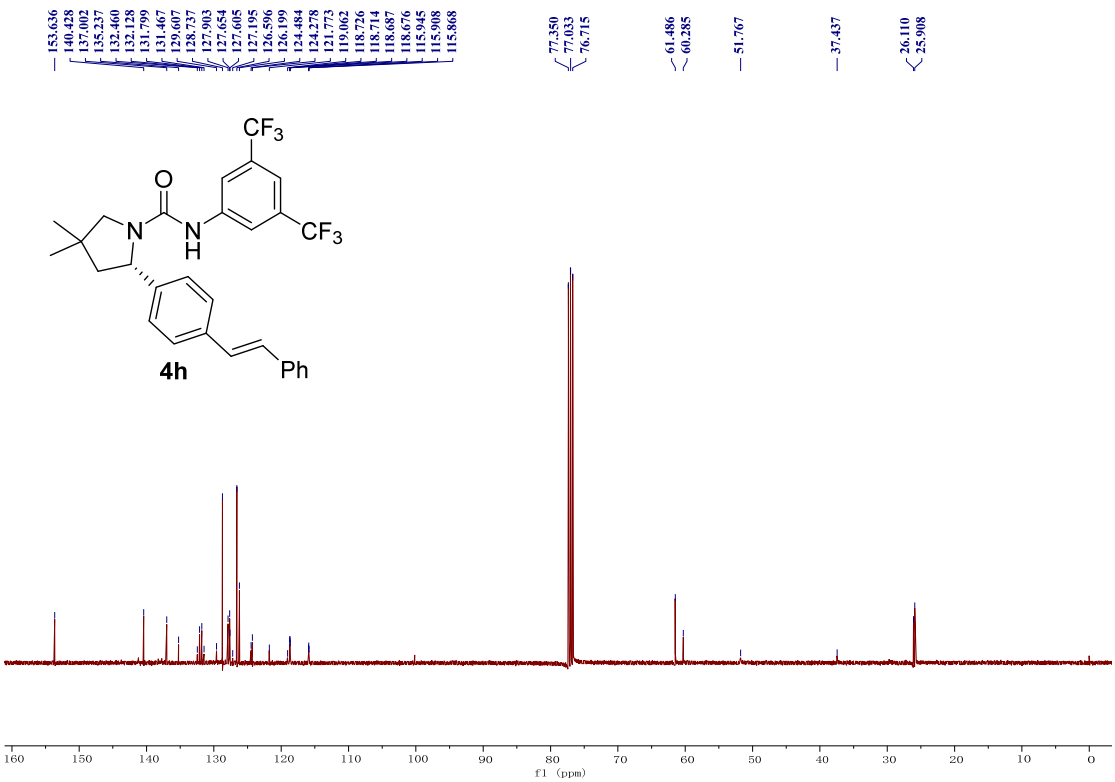
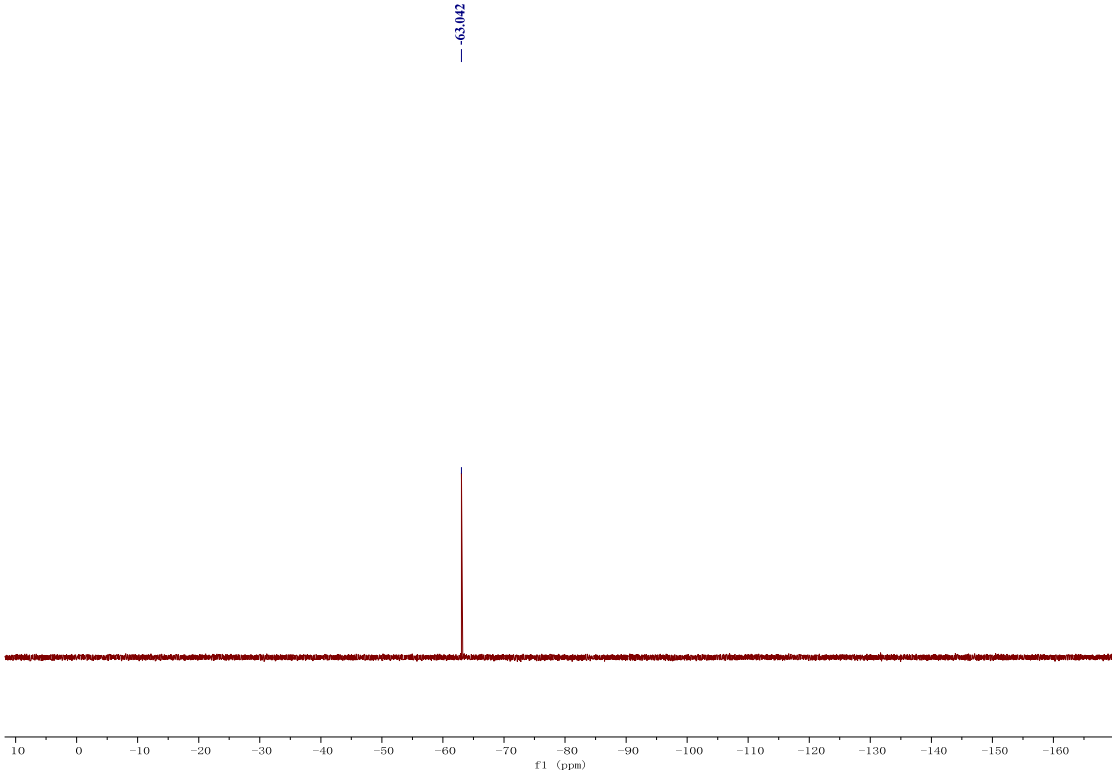
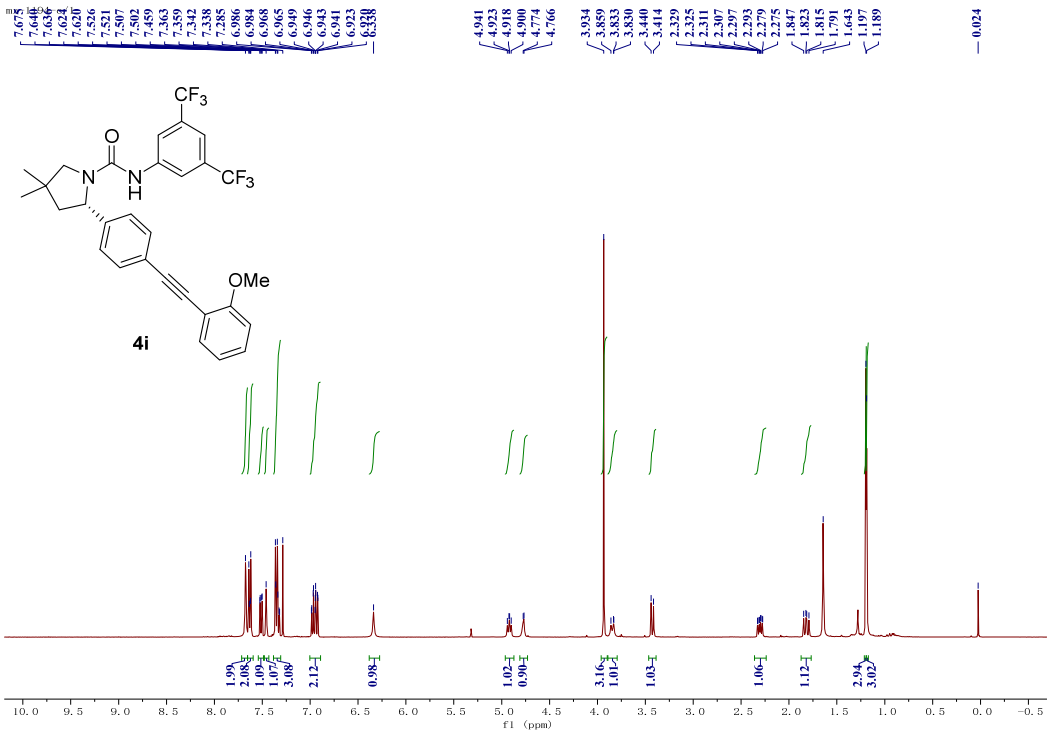
7.526
7.512
7.508
7.505
7.412
7.386
7.380
7.367
7.363
7.347
7.343
7.296
7.293
7.289
7.274
7.259
7.116
7.111
6.362
4.905
4.886
4.880
4.863
3.849
3.823
3.431
3.405
2.308
2.304
2.290
2.286
2.276
2.272
2.258
2.254
1.861
1.837
1.829
1.805
1.189
1.176
0.000


CF3
O
N
N
H
CF3
4h
Ph
3.99
2.16
1.06
4.10
1.01
1.92
1.01
1.00
1.11
1.08
1.16
1.14
2.94
3.01
f1 (ppm)


153.636
140.428
137.002
135.237
132.460
132.128
131.799
131.467
129.607
128.737
127.903
127.654
127.605
127.195
126.596
126.199
124.484
124.278
121.773
119.062
118.726
118.714
118.687
118.676
115.945
115.908
115.868
77.350
77.033
76.715
61.486
60.285
51.767
37.437
26.110
25.908
CF3
O
N
N
H
CF3
4h
Ph
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-63.042
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)


7.675
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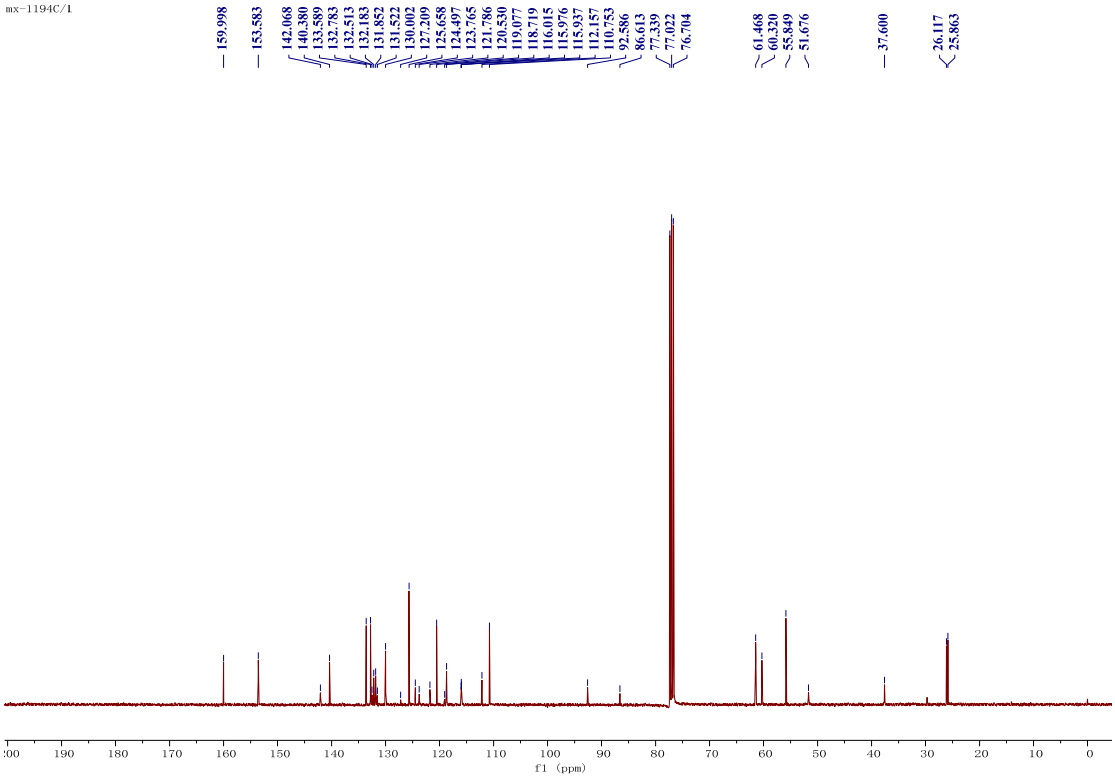
7.636
7.624
7.620
7.526
7.521
7.507
7.502
7.459
7.363
7.359
7.342
7.338
7.285
6.986
6.984
6.968
6.965
6.949
6.946
6.943
6.941
6.923
4.941
4.923
4.918
4.900
4.774
4.766
3.934
3.859
3.833
3.830
3.440
3.414
2.329
2.325
2.311
2.307
2.297
2.293
2.279
2.275
1.847
1.823
1.815
1.791
1.643
1.197
1.189
0.024
CF3
O
N
H
N
CF3
OMe
4i
1.99
2.08
1.09
1.07
3.08
2.12
0.98
1.02
0.90
3.16
1.01
1.03
1.06
1.12
2.94
3.02
f1 (ppm)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140.380
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132.783
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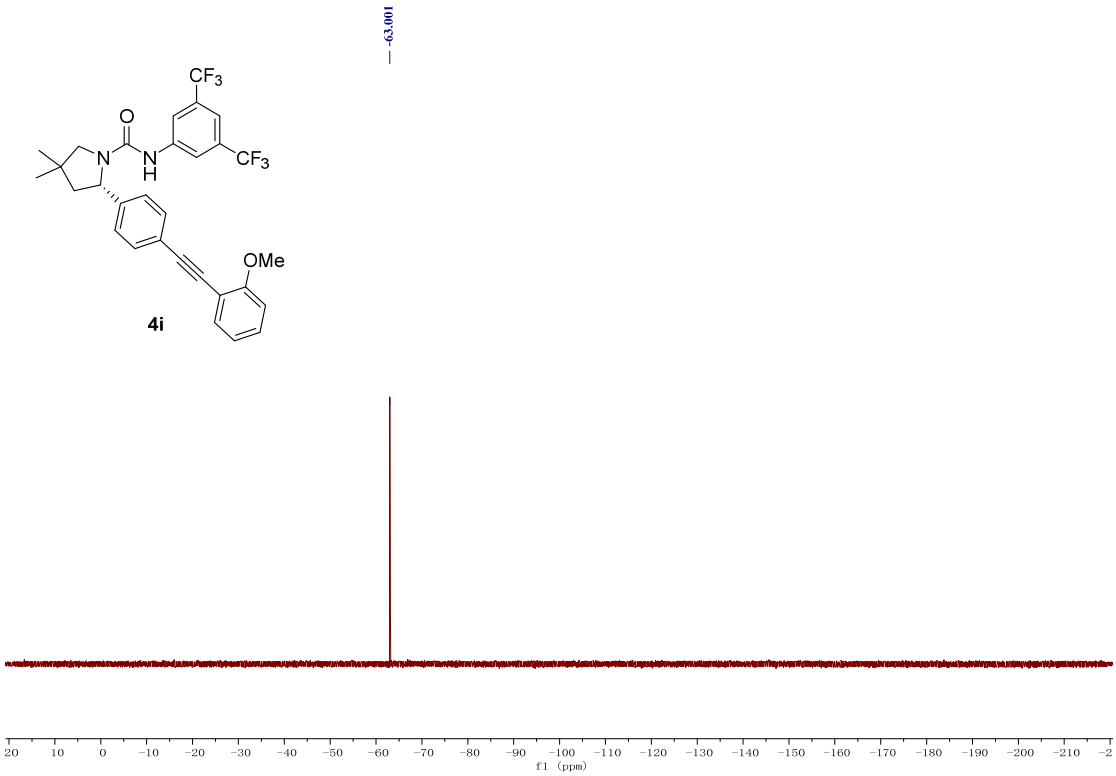
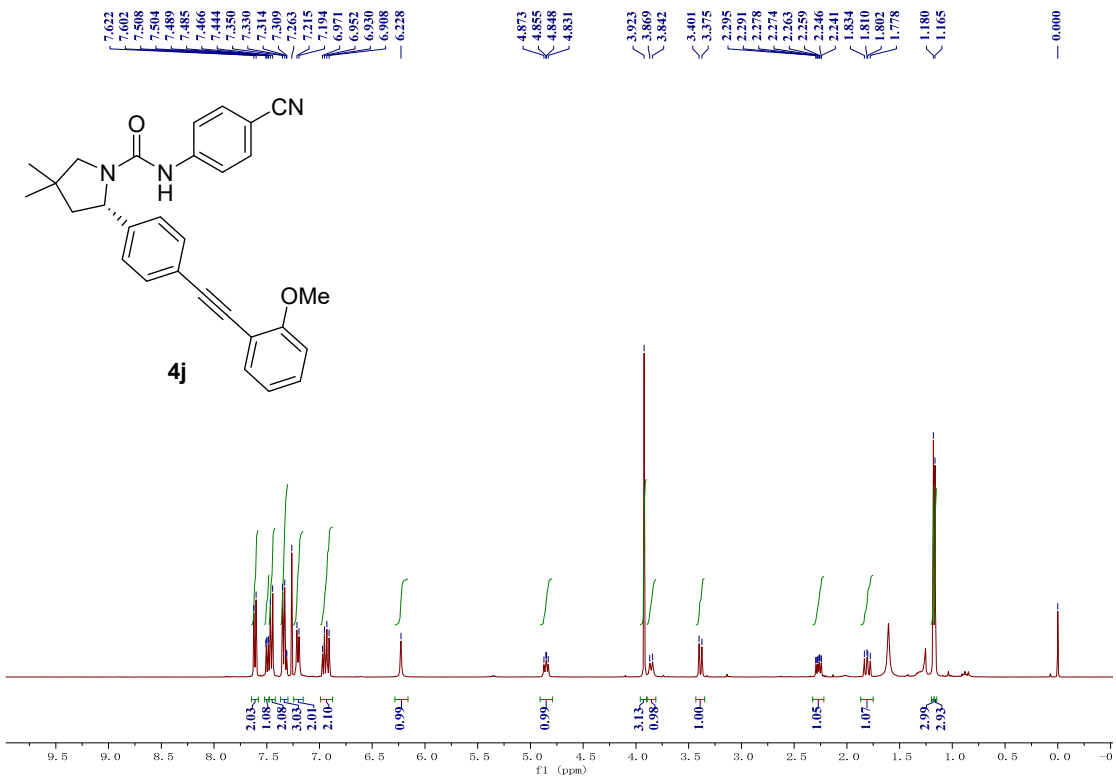
132.183
131.852
131.522
130.002
127.209
125.658
124.497
123.765
121.786
120.530
119.077
118.719
116.015
115.976
115.937
112.157
110.753
92.586
86.613
77.339
77.022
76.704
61.468
60.320
55.849
51.676
37.600
26.117
25.863
f1 (ppm)


-63.001
CF3
O
N
H
N
CF3
OMe
4i
f1 (ppm)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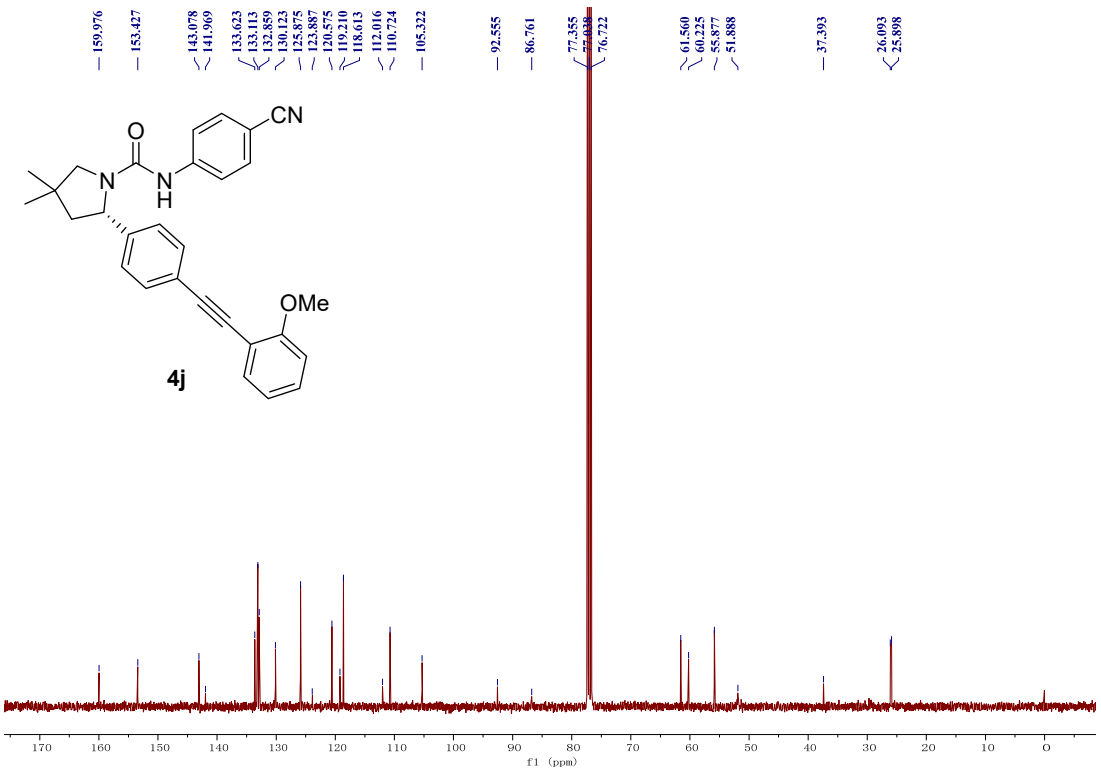
7.504
7.489
7.485
7.466
7.444
7.350
7.330
7.314
7.309
7.263
7.215
7.194
6.971
6.952
6.930
6.908
6.228
4.873
4.855
4.848
4.831
3.923
3.869
3.842
3.401
3.375
2.295
2.291
2.278
2.274
2.263
2.259
2.246
2.241
1.834
1.810
1.802
1.778
1.180
1.165
0.000
CN
O
N
H
OMe
4j
2.03
1.08
2.08
3.03
2.01
2.10
0.99
0.99
3.13
0.98
1.00
1.05
1.07
2.99
2.93
f1 (ppm)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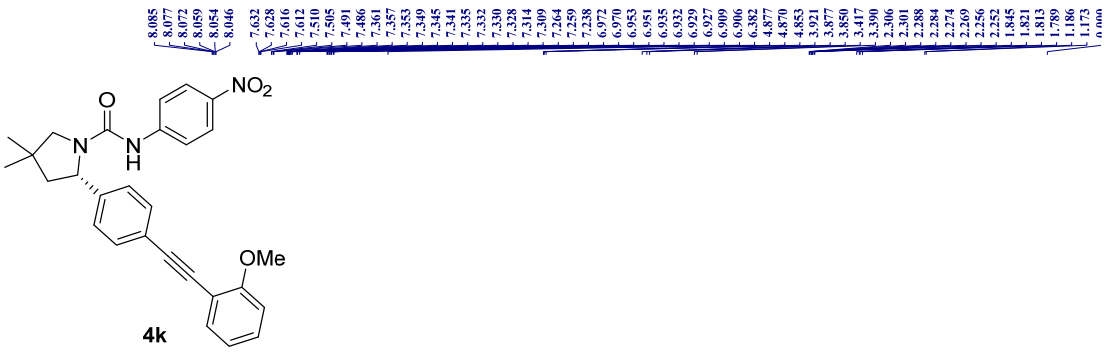
143.078
141.969
133.623
133.113
132.859
130.123
125.875
123.887
120.575
119.210
118.613
112.016
110.724
105.322
92.555
86.761
77.355
77.038
76.722
61.560
60.225
55.877
51.888
37.393
26.093
25.898
CN
O
N
N
H
OMe
4j
f1 (ppm)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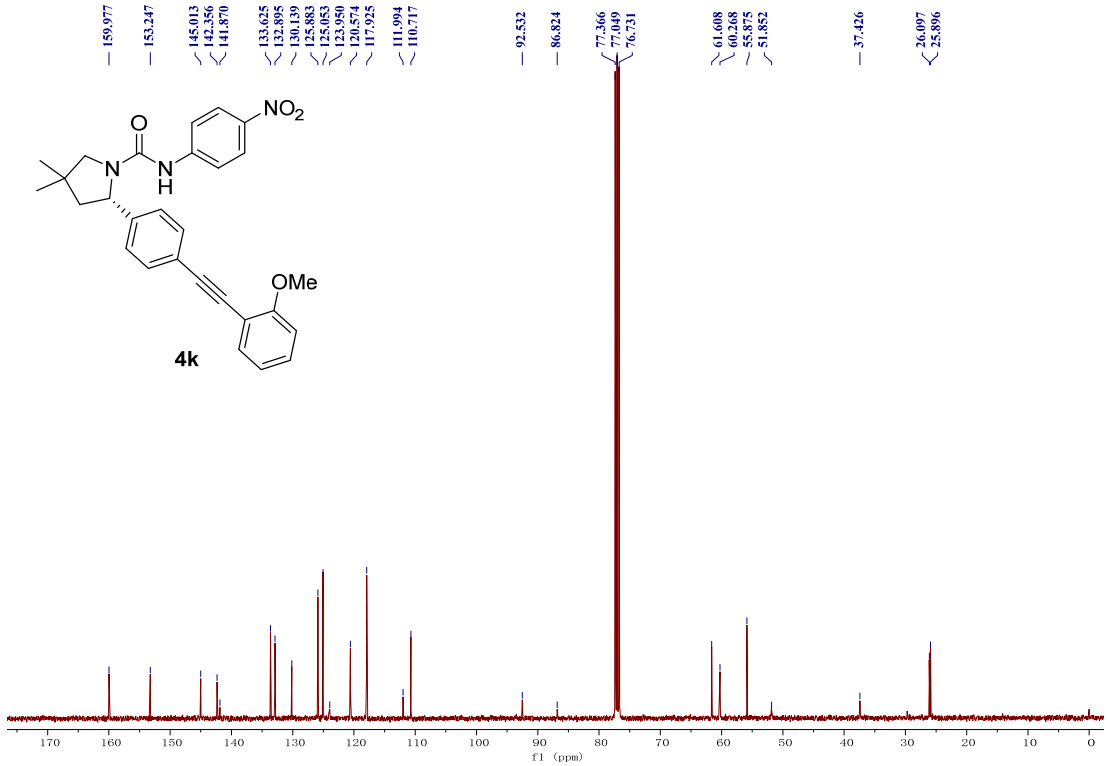
8.072
8.059
8.054
8.046
7.632
7.628
7.616
7.612
7.510
7.505
7.491
7.486
7.361
7.357
7.353
7.349
7.345
7.341
7.335
7.332
7.330
7.328
7.314
7.309
7.264
7.259
7.238
6.972
6.970
6.953
6.951
6.935
6.932
6.929
6.927
6.909
6.906
6.382
4.877
4.870
4.853
3.921
3.877
3.850
3.417
3.390
2.306
2.301
2.288
2.284
2.274
2.269
2.256
2.252
1.845
1.821
1.813
1.789
1.186
1.173
NO2
O
N
N
H
OMe
4k
2.06
2.04
1.13
3.08
2.00
2.08
0.96
1.00
3.06
0.96
1.01
1.04
1.05
2.81
2.91
f1 (ppm)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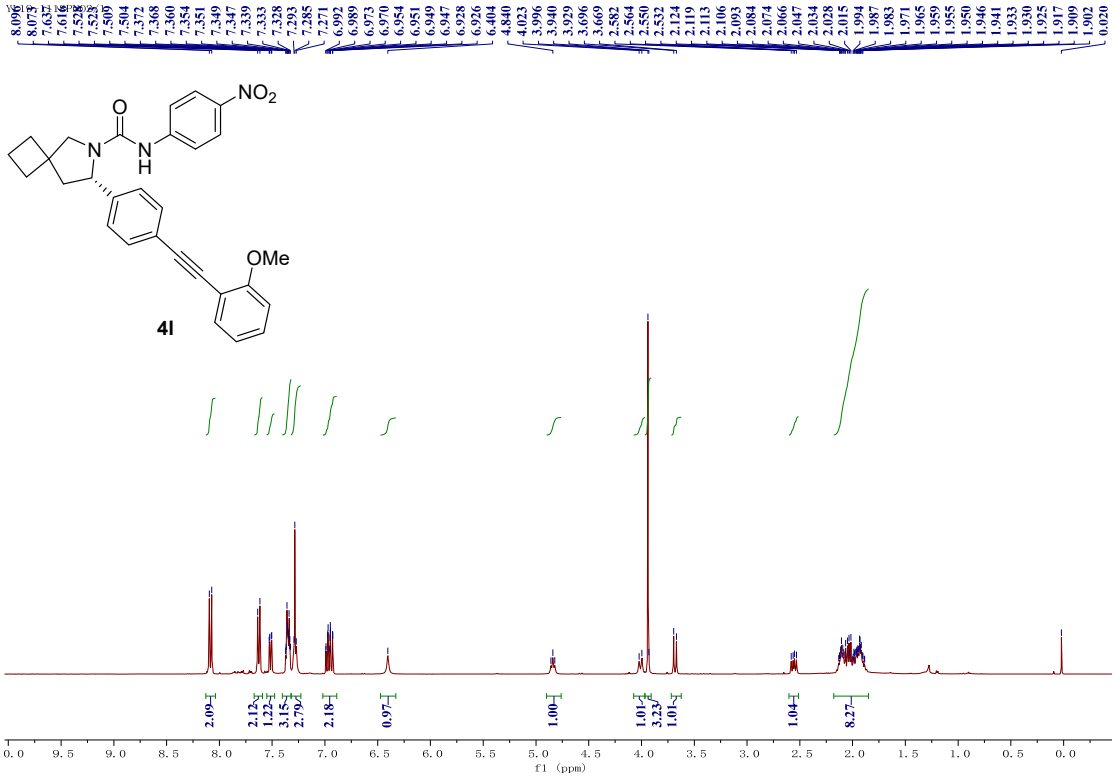
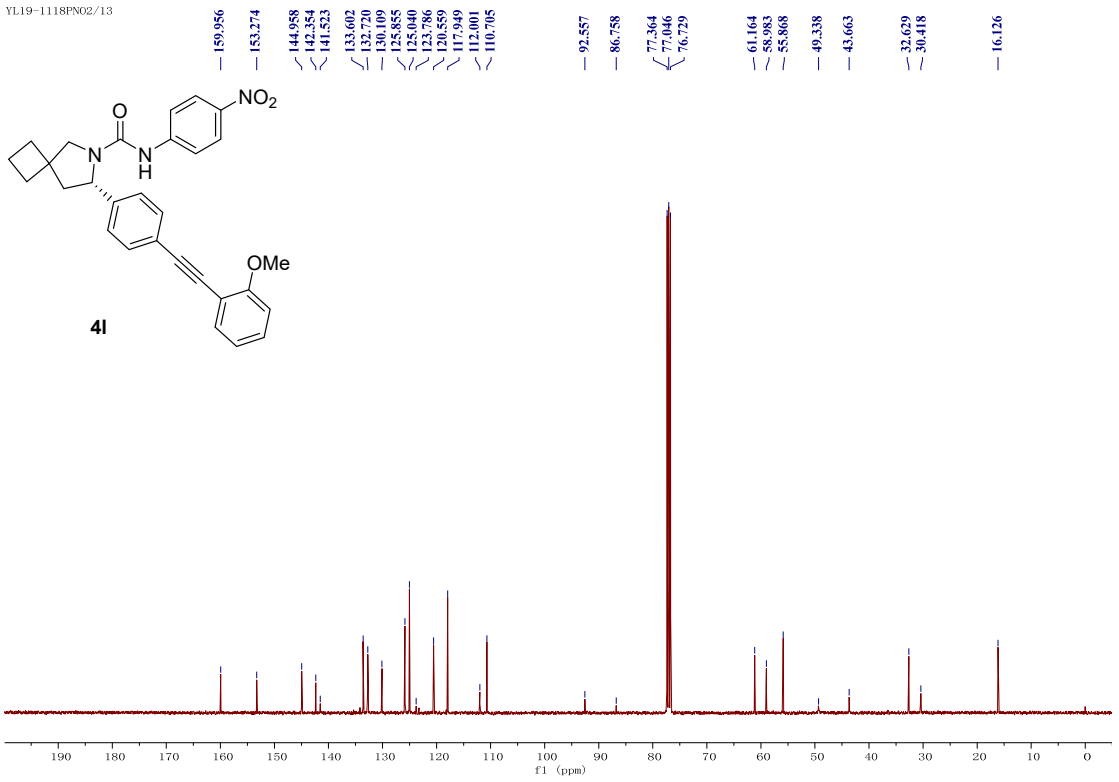
133.625
132.895
130.139
125.883
125.053
123.950
120.574
117.925
111.994
110.717
92.532
86.824
77.366
77.049
76.731
61.608
60.268
55.875
51.852
37.426
26.097
25.896
NO2
O
N
N
H
OMe
4k
f1 (ppm)


NO2
O
N
N
H
OMe
4l
2.09
2.12
1.22
3.15
2.79
2.18
0.97
1.00
1.01
3.23
1.01
1.04
8.27
f1 (ppm)


YL19-1118PN02/13
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141.523
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130.109
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120.559
117.949
112.001
110.705
92.557
86.758
77.364
77.046
76.729
61.164
58.983
55.868
49.338
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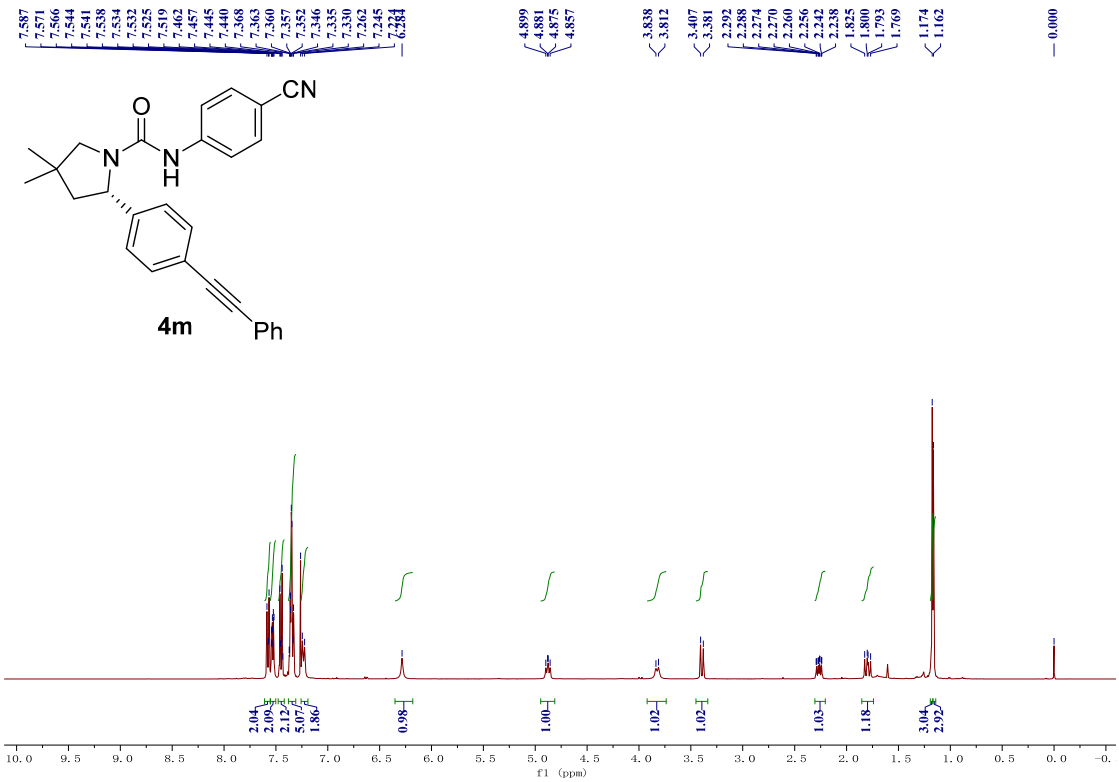
32.629
30.418
16.126
NO2
O
N
N
H
OMe
4l
f1 (ppm)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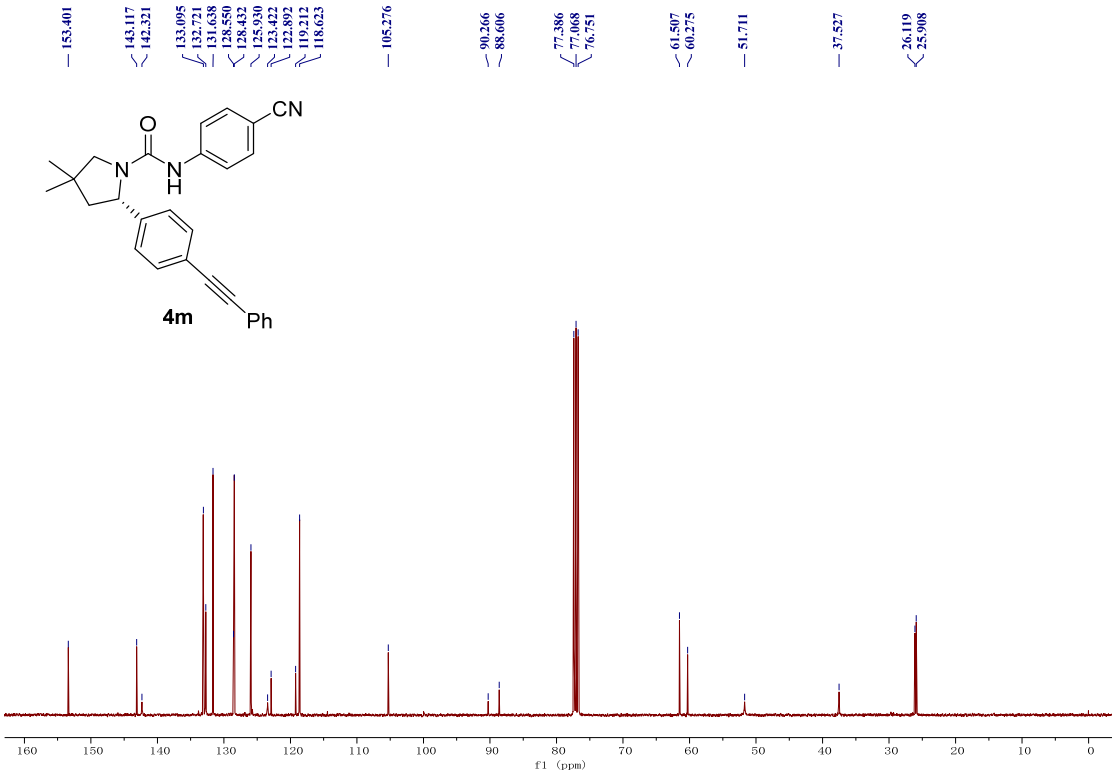
7.571
7.566
7.544
7.541
7.538
7.534
7.532
7.525
7.519
7.462
7.457
7.445
7.440
7.368
7.363
7.360
7.357
7.352
7.346
7.335
7.330
7.262
7.245
7.224
6.284
4.899
4.881
4.875
4.857
3.838
3.812
3.407
3.381
2.292
2.288
2.274
2.270
2.260
2.256
2.242
2.238
1.825
1.800
1.793
1.769
1.174
1.162
0.000
CN
O
N
N
H
4m
Ph
2.04
2.09
2.12
5.07
1.86
0.98
1.00
1.02
1.02
1.03
1.18
3.04
2.92
f1 (ppm)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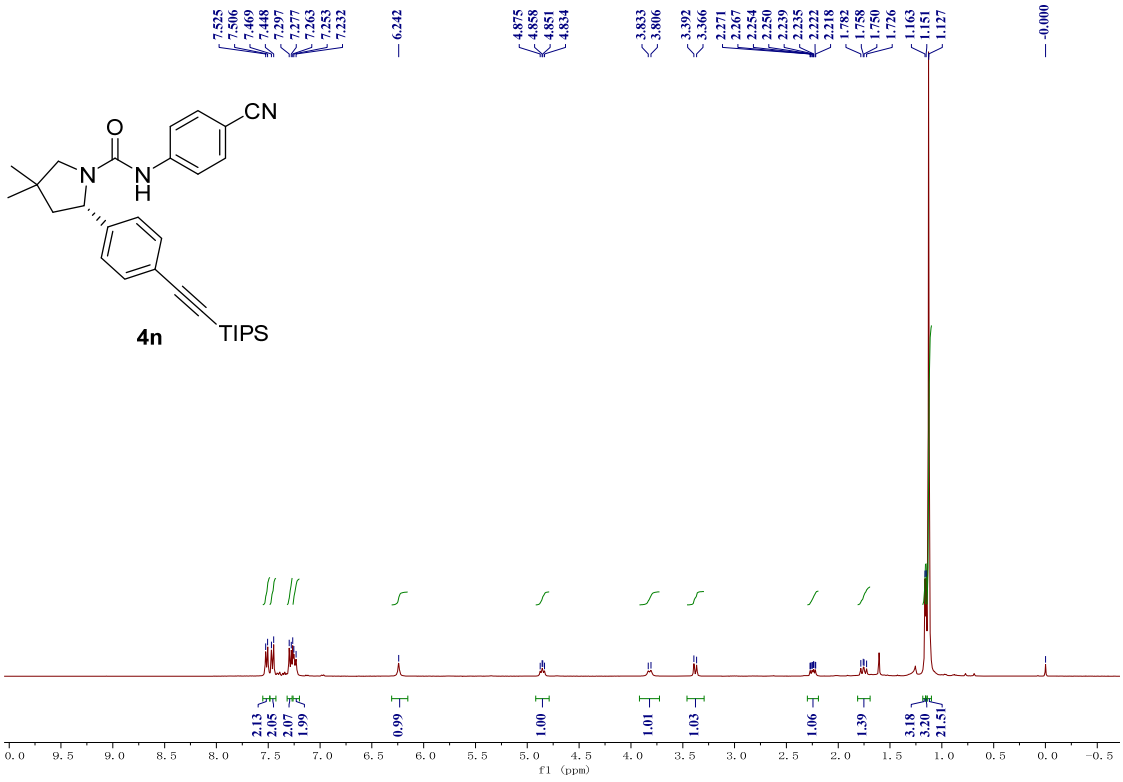
143.117
142.321
133.095
132.721
131.638
128.550
128.432
125.930
123.422
122.892
119.212
118.623
105.276
90.266
88.606
77.386
77.068
76.751
61.507
60.275
51.711
37.527
26.119
25.908
CN
O
N
N
H
Ph
4m
f1 (ppm)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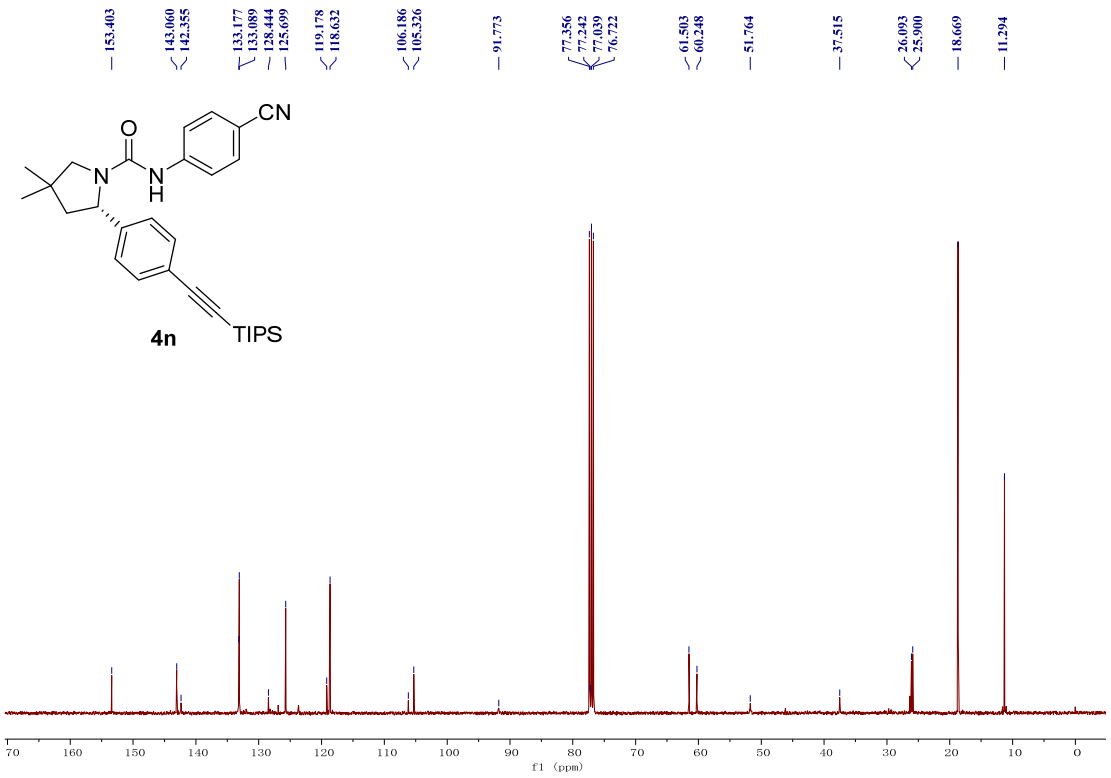
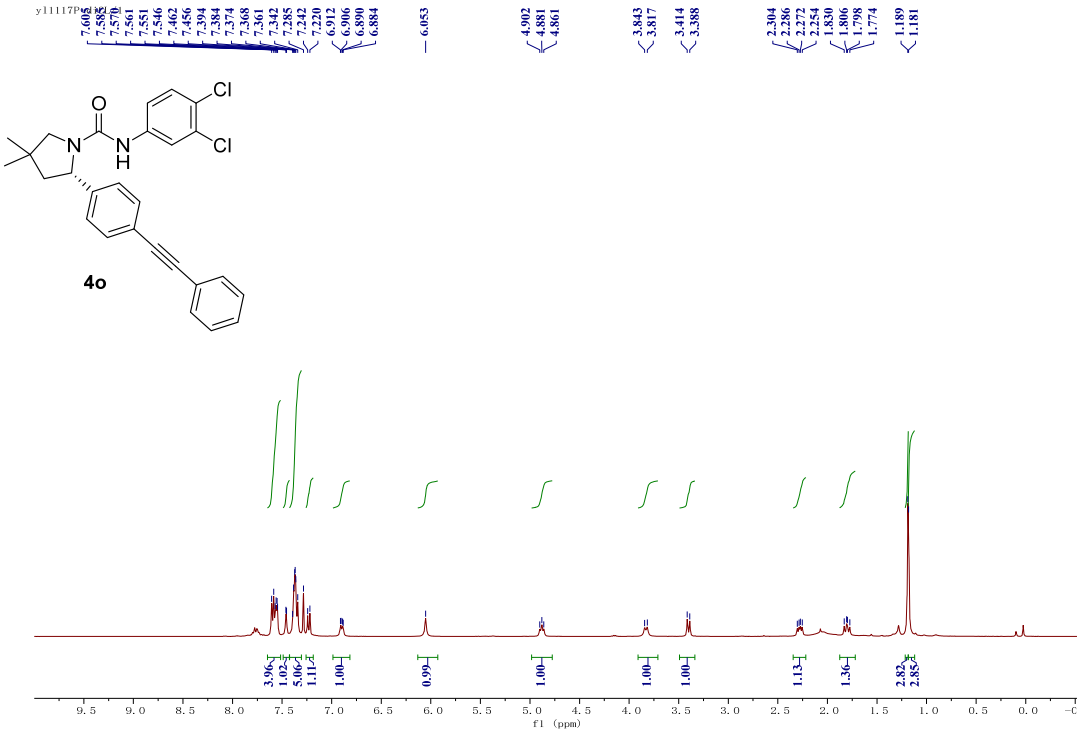
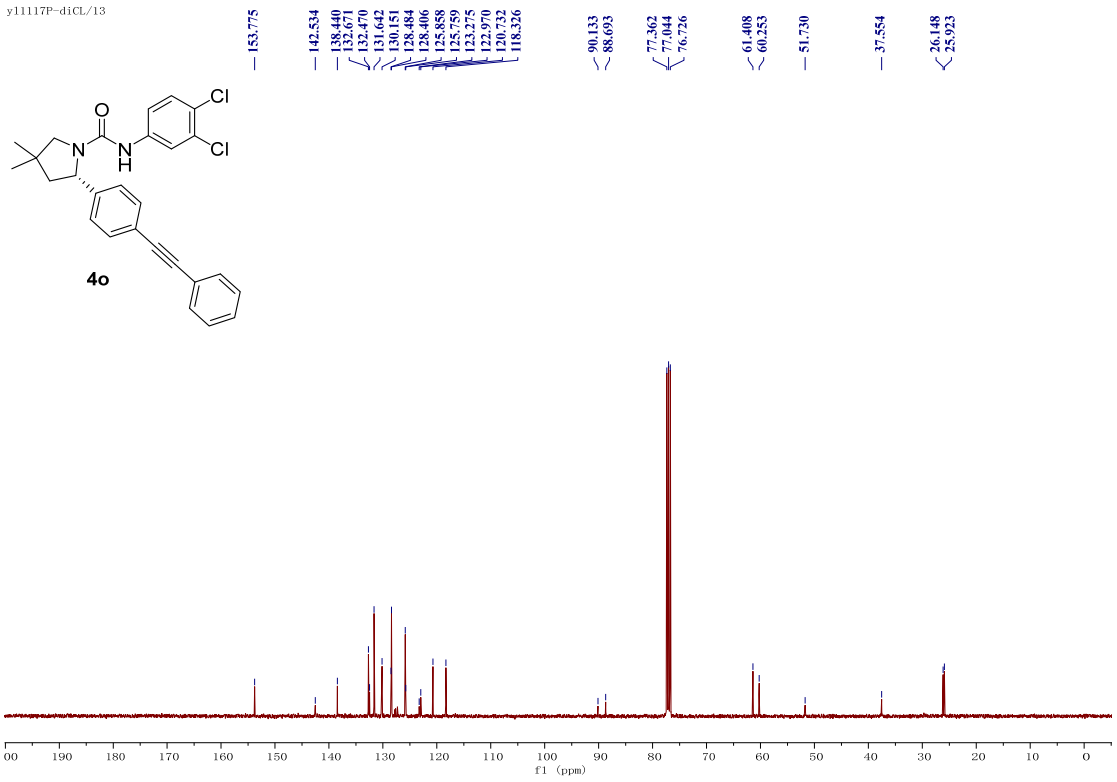
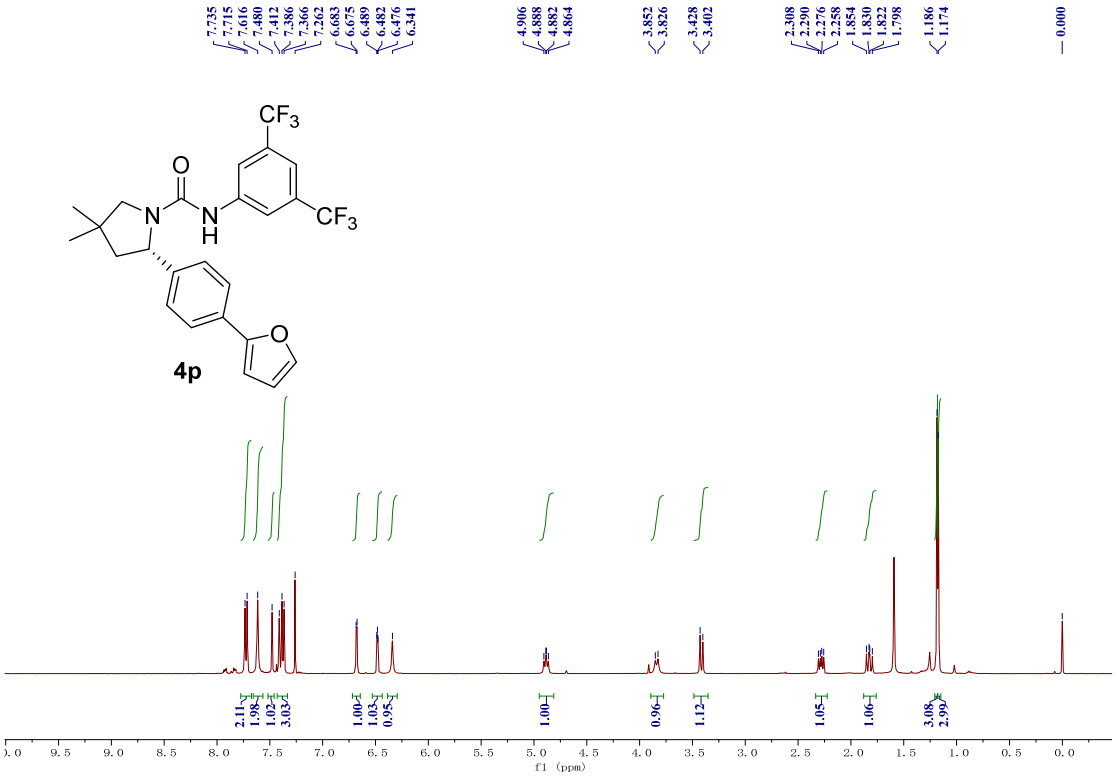
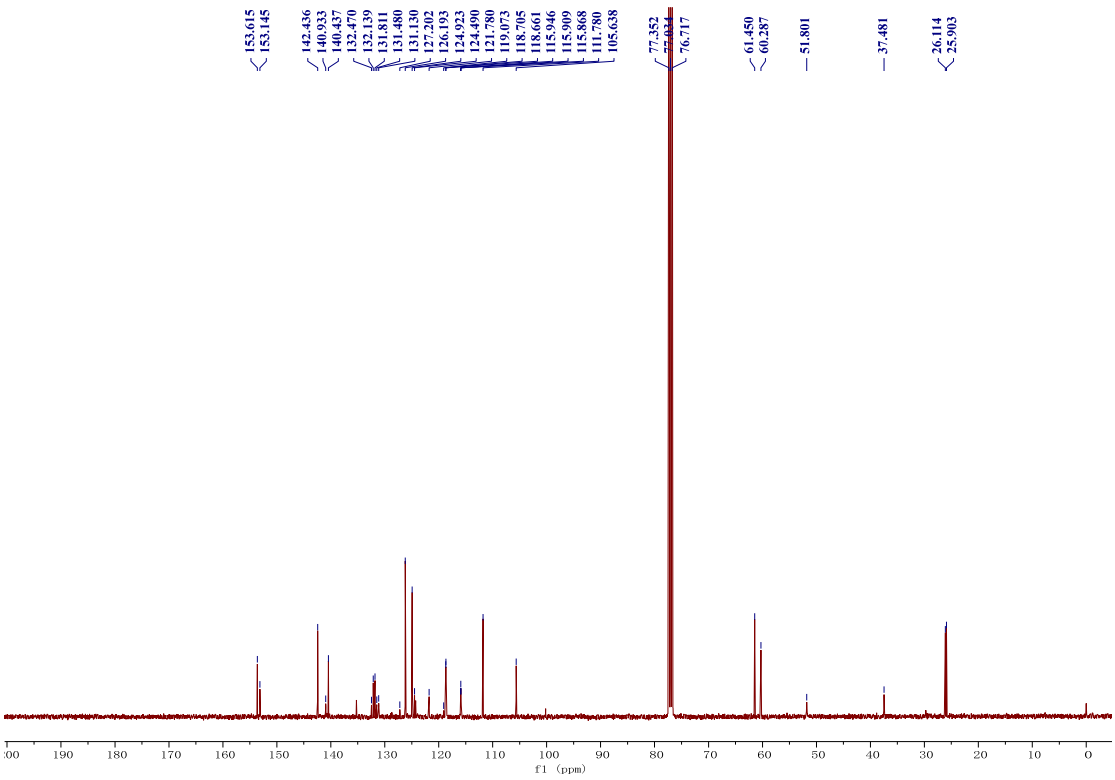
7.506
7.469
7.448
7.297
7.277
7.263
7.253
7.232
6.242
4.875
4.858
4.851
4.834
3.833
3.806
3.392
3.366
2.271
2.267
2.254
2.250
2.239
2.235
2.222
2.218
1.782
1.758
1.750
1.726
1.163
1.151
1.127
-0.000
CN
O
N
N
H
TIPS
4n
2.13
2.05
2.07
1.99
0.99
1.00
1.01
1.03
1.06
1.39
3.18
3.20
21.51
f1 (ppm)

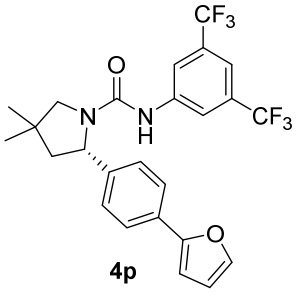

153.403
143.060
142.355
133.177
133.089
128.444
125.699
119.178
118.632
106.186
105.326
91.773
77.356
77.242
77.039
76.722
61.503
60.248
51.764
37.515
26.093
25.900
18.669
11.294
CN
O
N
N
H
TIPS
4n
f1 (ppm)


7.602
7.582
7.570
7.561
7.551
7.546
7.462
7.456
7.394
7.384
7.374
7.368
7.361
7.342
7.285
7.242
7.220
6.912
6.906
6.890
6.884
6.053
4.902
4.881
4.861
3.843
3.817
3.414
3.388
2.304
2.286
2.272
2.254
1.830
1.806
1.798
1.774
1.189
1.181
Cl
Cl
O
N
N
H
4o
3.96
1.02
5.06
1.11
1.00
0.99
1.00
1.00
1.00
1.13
1.36
2.82
2.85
f1 (ppm)


y11117P-diCL/13
153.775
142.534
138.440
132.671
132.470
131.642
130.151
128.484
128.406
125.858
125.759
123.275
122.970
120.732
118.326
90.133
88.693
77.362
77.044
76.726
61.408
60.253
51.730
37.554
26.148
25.923
Cl
Cl
O
N
H
4o
f1 (ppm)

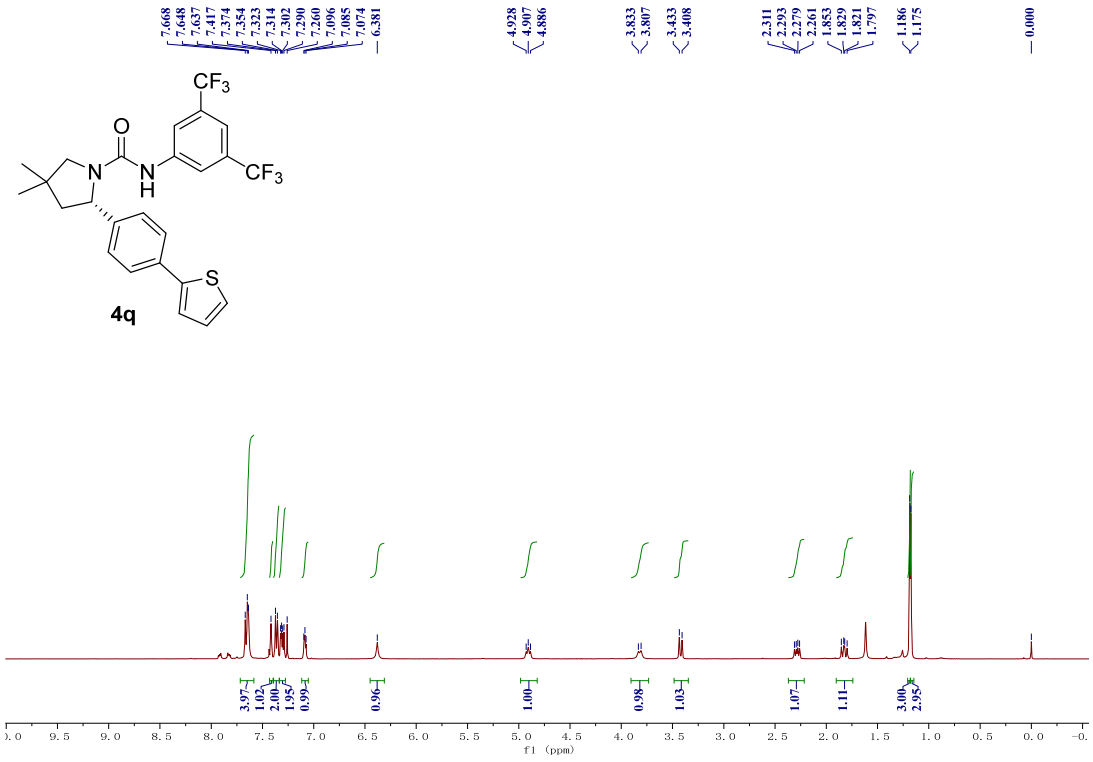

7.735
7.715
7.616
7.480
7.412
7.386
7.366
7.262
6.683
6.675
6.489
6.482
6.476
6.341
4.906
4.888
4.882
4.864
3.852
3.826
3.428
3.402
2.308
2.290
2.276
2.258
1.854
1.830
1.822
1.798
1.186
1.174
0.000
CF3
CF3
O
N
H
O
4p
2.11
1.98
1.02
3.03
1.00
1.03
0.95
1.00
0.96
1.12
1.05
1.06
3.08
2.99
f1 (ppm)


153.615
153.145
142.436
140.933
140.437
132.470
132.139
131.811
131.480
131.130
127.202
126.193
124.923
124.490
121.780
119.073
118.705
118.661
115.946
115.909
115.868
111.780
105.638
77.352
77.034
76.717
61.450
60.287
51.801
37.481
26.114
25.903
f1 (ppm)


CF3
O
N
H
CF3
O

**4p**


-63.050
f1 (ppm)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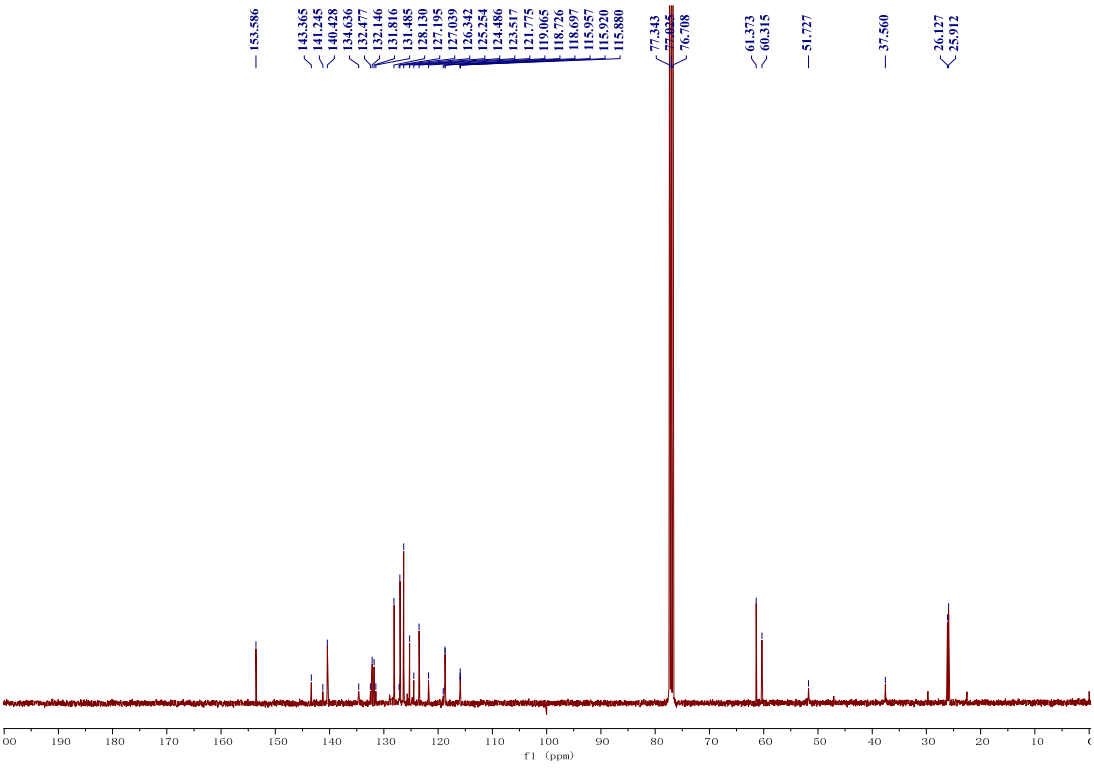
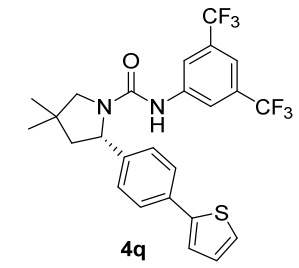
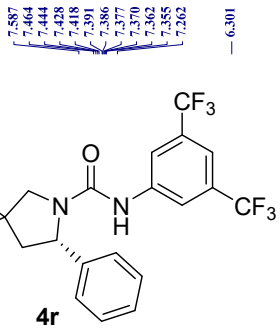
7.637
7.417
7.374
7.354
7.323
7.314
7.302
7.290
7.260
7.096
7.085
7.074
6.381
4.928
4.907
4.886
3.833
3.807
3.433
3.408
2.311
2.293
2.279
2.261
1.853
1.829
1.821
1.797
1.186
1.175
0.000
CF3
CF3
O
N
N
H
S
4q
3.97
1.02
2.00
1.95
0.99
0.96
1.00
0.98
1.03
1.07
1.11
3.00
2.95
f1 (ppm)


153.586
143.365
141.245
140.428
134.636
132.477
132.146
131.816
131.485
128.130
127.195
127.039
126.342
125.254
124.486
123.517
121.775
119.065
118.726
118.697
115.957
115.920
115.880
77.343
77.035
76.708
61.373
60.315
51.727
37.560
26.127
25.912
f1 (ppm)


CF3
O
N
N
H
CF3
S

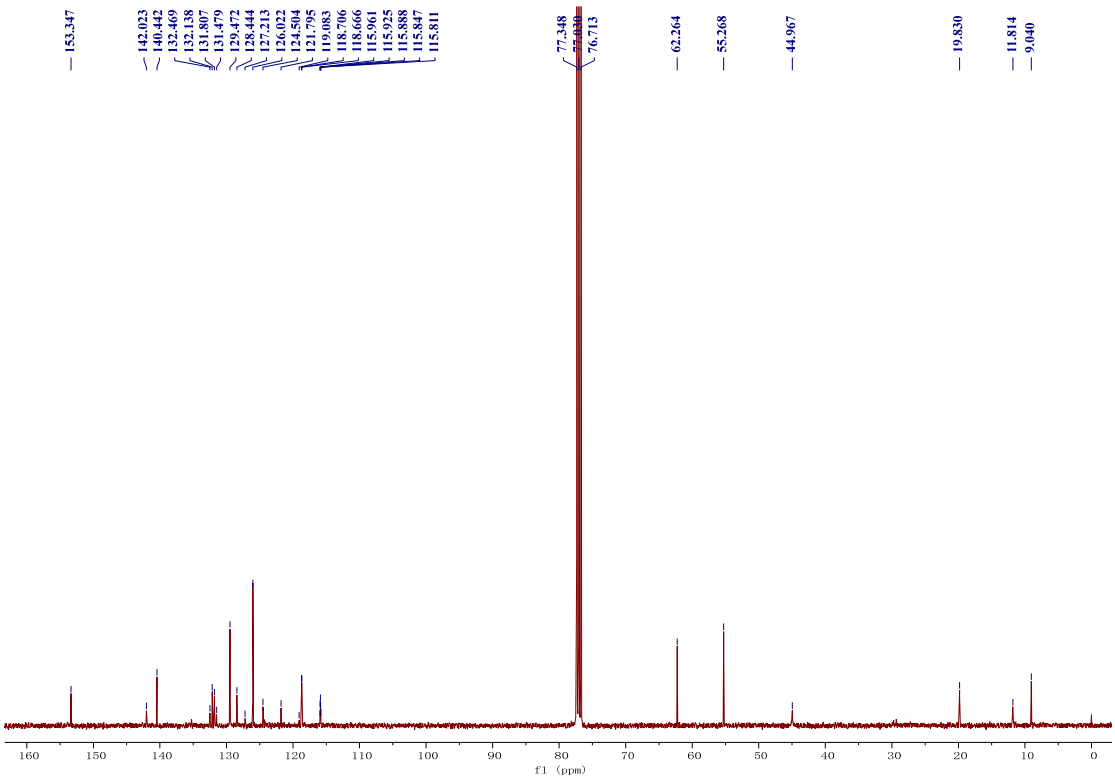
4q


-63.031
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)


CF3
O
N
N
H
CF3

4r


7.587
7.464
7.444
7.428
7.418
7.391
7.386
7.377
7.370
7.362
7.355
7.262
6.301
5.009
4.997
4.989
4.977
3.802
3.777
3.646
3.620
2.522
2.503
2.491
2.471
1.913
1.900
1.881
1.869
1.595
0.758
0.749
0.746
0.735
0.726
0.722
0.715
0.705
0.694
0.682
0.670
0.622
0.612
0.601
0.589
0.578
0.553
0.544
0.541
0.531
0.527
0.520
0.517
0.510
0.000
1.88
4.93
1.06
0.95
0.93
1.00
0.99
1.01
1.00
2.01
0.98
0.97
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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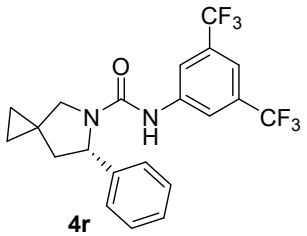
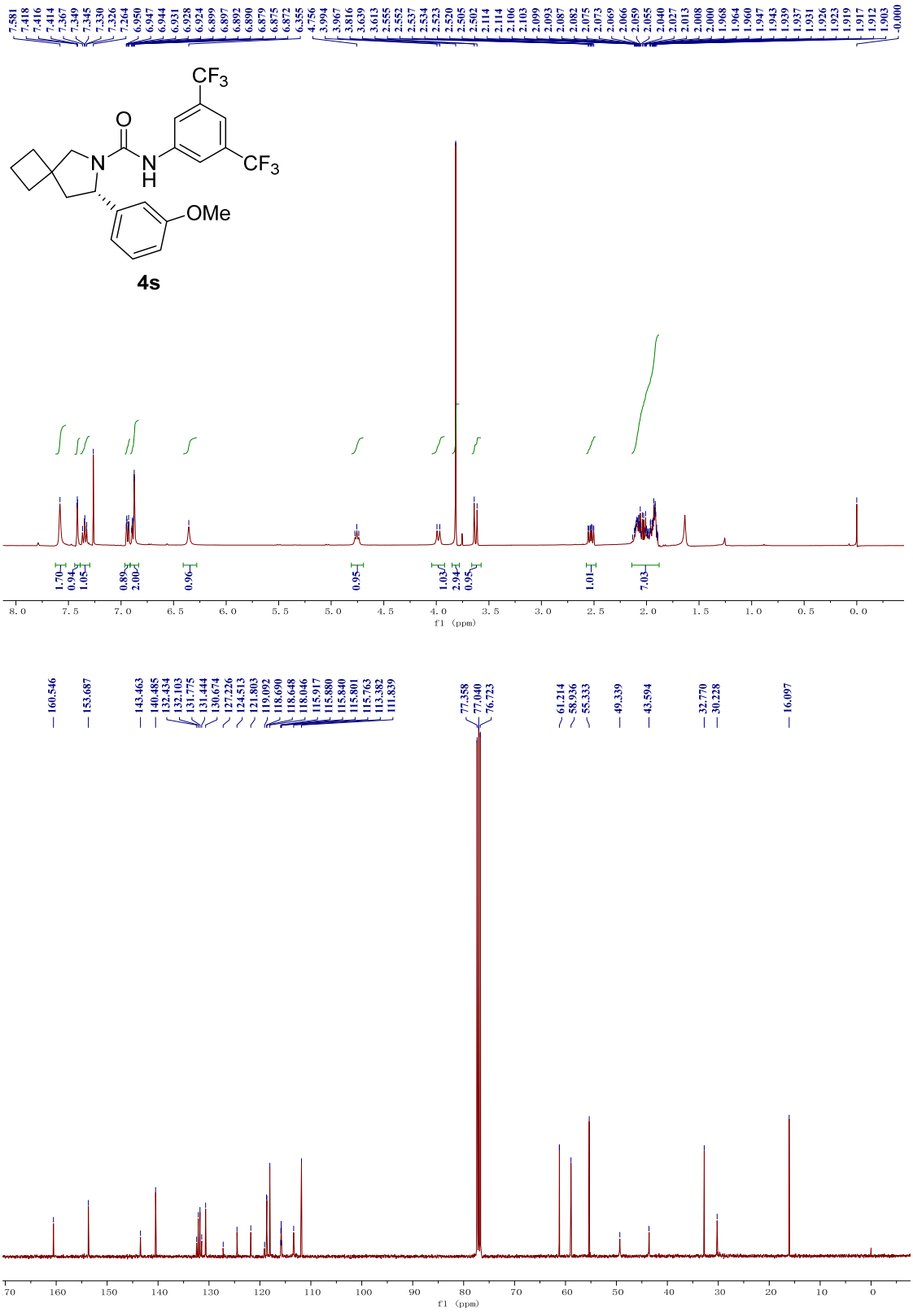
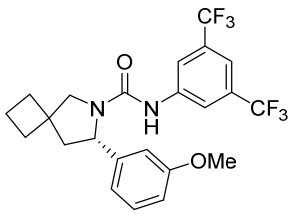
132.138
131.807
131.479
129.472
128.444
127.213
126.022
124.504
121.795
119.083
118.706
118.666
115.961
115.925
115.888
115.847
115.811
77.348
77.030
76.713
62.264
55.268
44.967
19.830
11.814
9.040
f1 (ppm)


CF3
O
N
N
H
CF3

**4r**


-63.072
f1 (ppm)


7.581 7.418 7.416 7.414 7.367 7.349 7.345 7.330 7.326 7.264 6.950 6.947 6.944 6.931 6.928 6.924 6.899 6.897 6.892 6.890 6.879 6.875 6.872 6.355 4.756 3.994 3.967 3.816 3.639 3.613 2.555 2.552 2.537 2.534 2.523 2.520 2.505 2.502 2.114 2.106 2.103 2.099 2.093 2.087 2.082 2.075 2.073 2.069 2.066 2.059 2.055 2.040 2.027 2.013 2.008 2.000 1.968 1.964 1.960 1.947 1.943 1.939 1.937 1.931 1.926 1.923 1.919 1.917 1.912 1.903 -0.000
CF3
O
N
N
H
CF3
OMe
4s
1.70 0.94 1.05 0.89 2.00 0.96 0.95 1.03 2.94 0.95 1.01 7.03
f1 (ppm)
160.546 153.687 143.463 140.485 132.434 132.103 131.775 131.444 130.674 127.226 124.513 121.803 119.092 118.690 118.648 118.046 115.917 115.880 115.840 115.801 115.763 113.382 111.839
77.358 77.040 76.723
61.214 58.936 55.333 49.339 43.594 32.770 30.228 16.097
f1 (ppm)


CF3
O
N
N
H
CF3
OMe

**4s**


-63.073
f1 (ppm)


ty19-3-79-439-P/1
7.429
7.411
7.392
7.370
7.356
7.338
7.317
7.297
7.273
7.262
7.257
7.213
7.191
6.934
6.912
6.038
4.851
4.831
3.848
3.831
3.820
3.805
3.788
3.765
3.751
3.734
3.720
3.707
2.497
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2.462
2.443
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2.000
1.989
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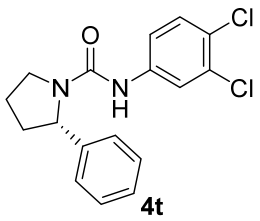
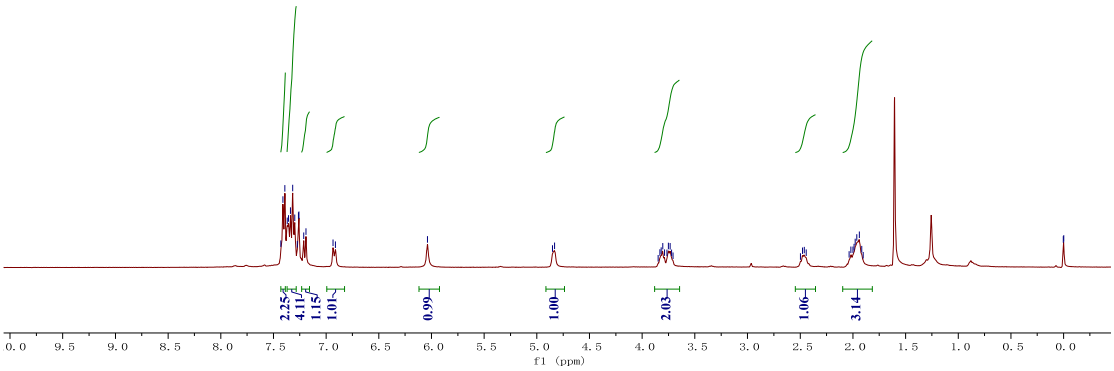
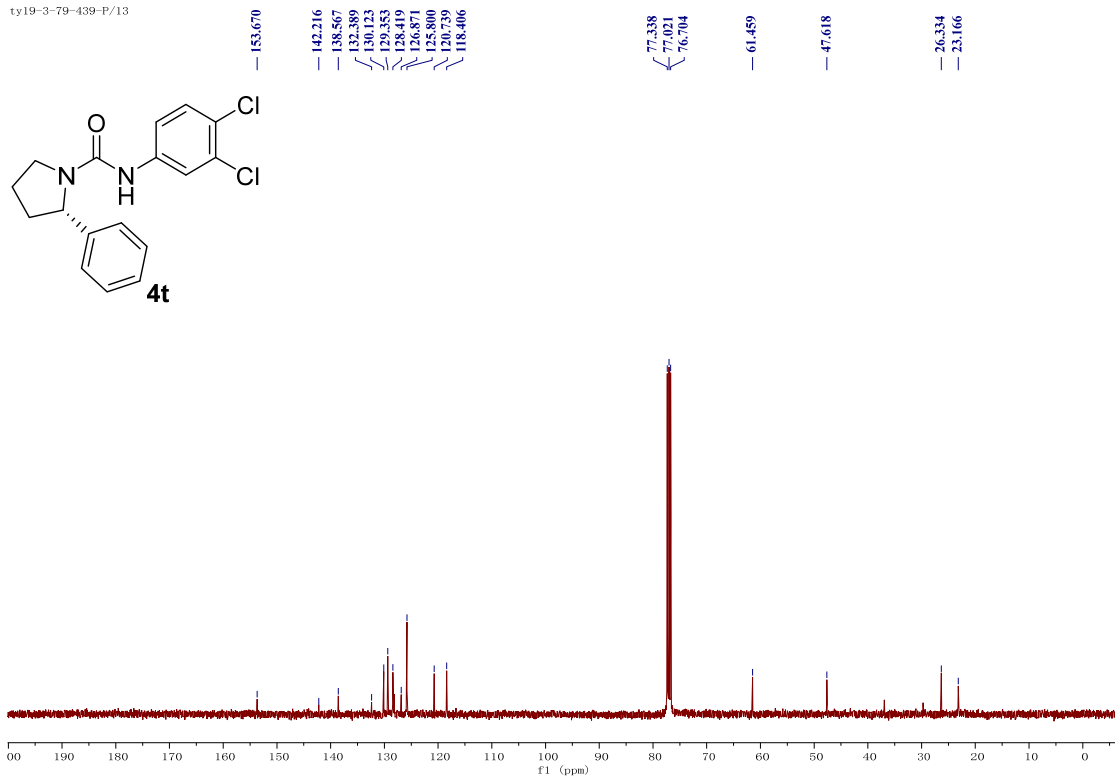
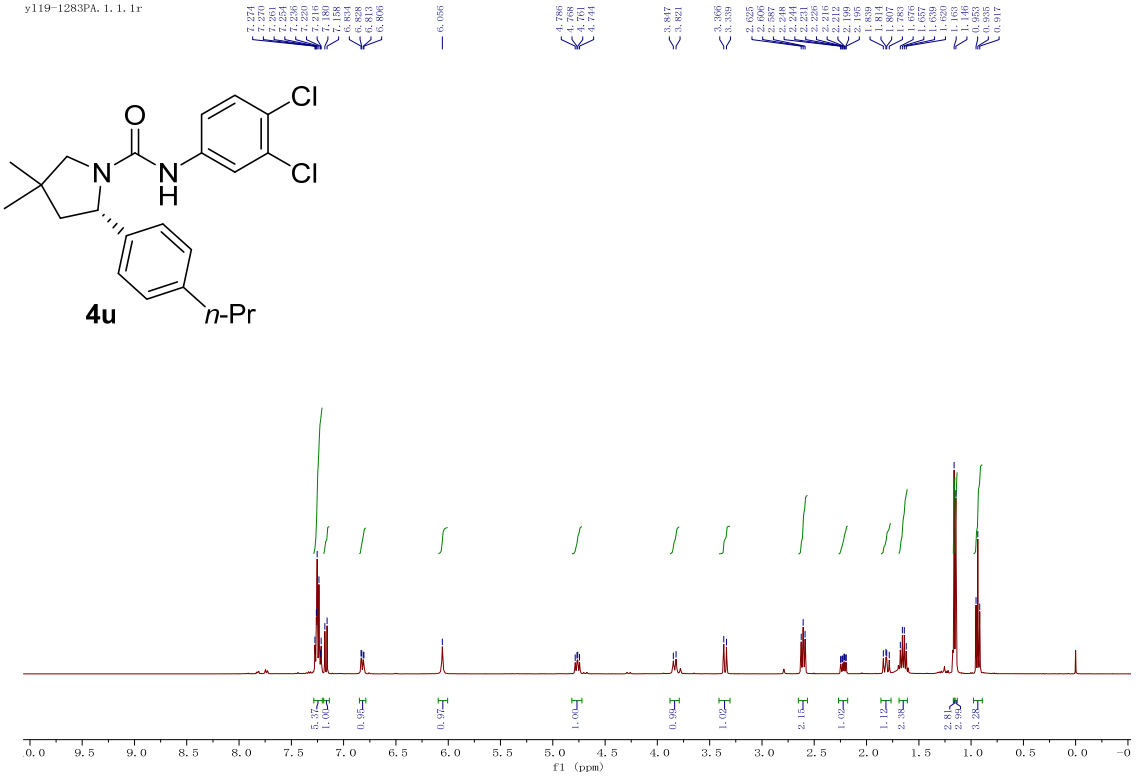
1.962
1.939
1.916
1.902
0.003
-0.001

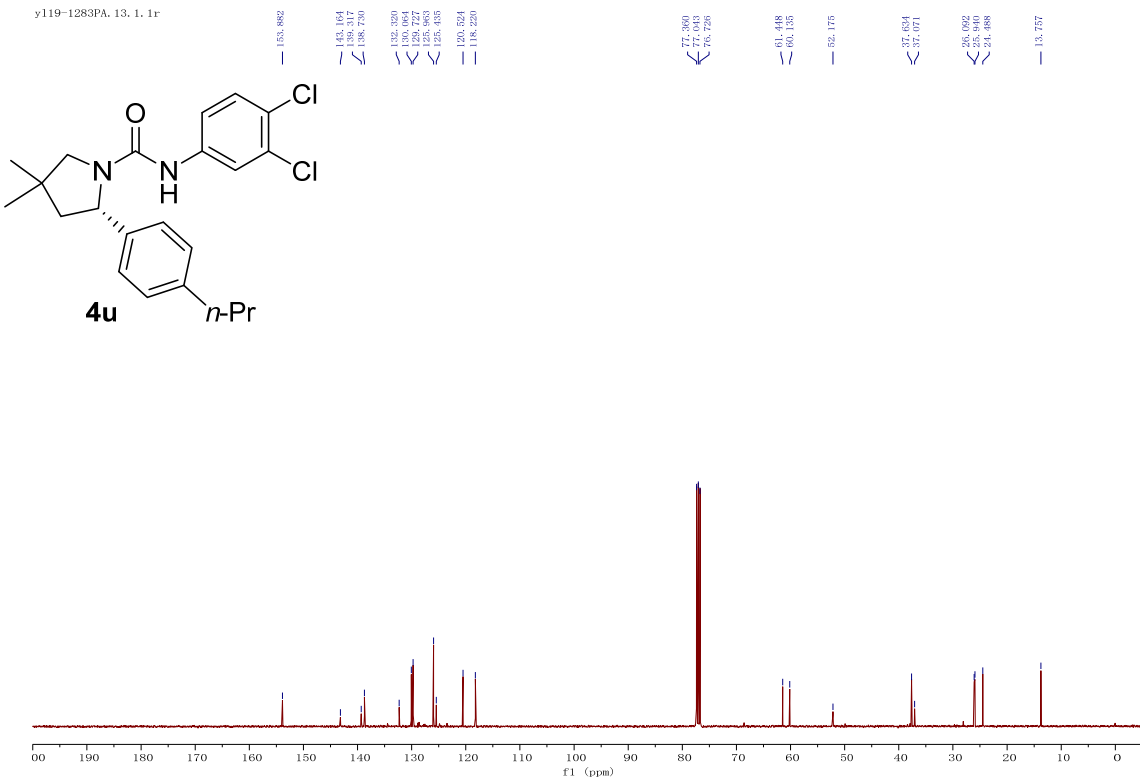

O
N
N
H
Cl
Cl

**4t**


2.25
4.11
1.15
1.01
0.99
1.00
2.03
1.06
3.14
f1 (ppm)


ty19-3-79-439-P/13
153.670
142.216
138.567
132.389
130.123
129.353
128.419
126.871
125.800
120.739
118.406
77.338
77.021
76.704
61.459
47.618
26.334
23.166
Cl
Cl
O
N
N
H
4t
f1 (ppm)


y119-1283PA.1.1.1r
Cl
Cl
O
N
N
H
4u
n-Pr
f1 (ppm)


y119-1283PA.13.1.1r
153.882
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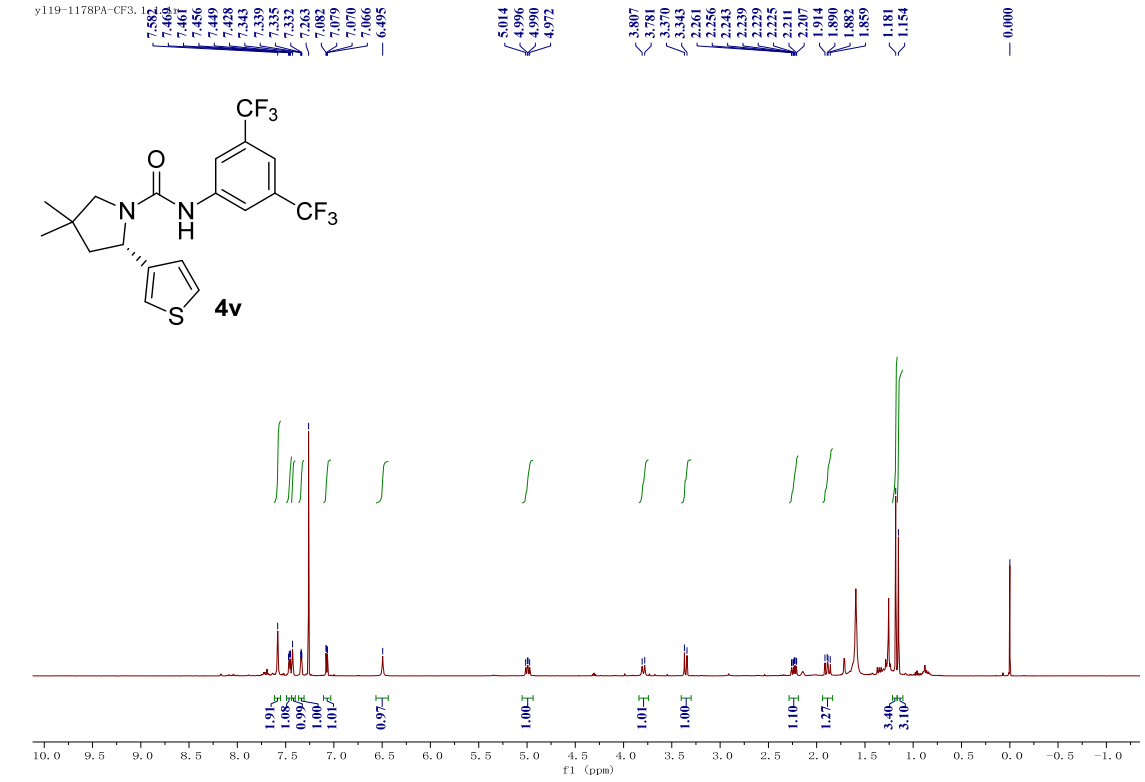
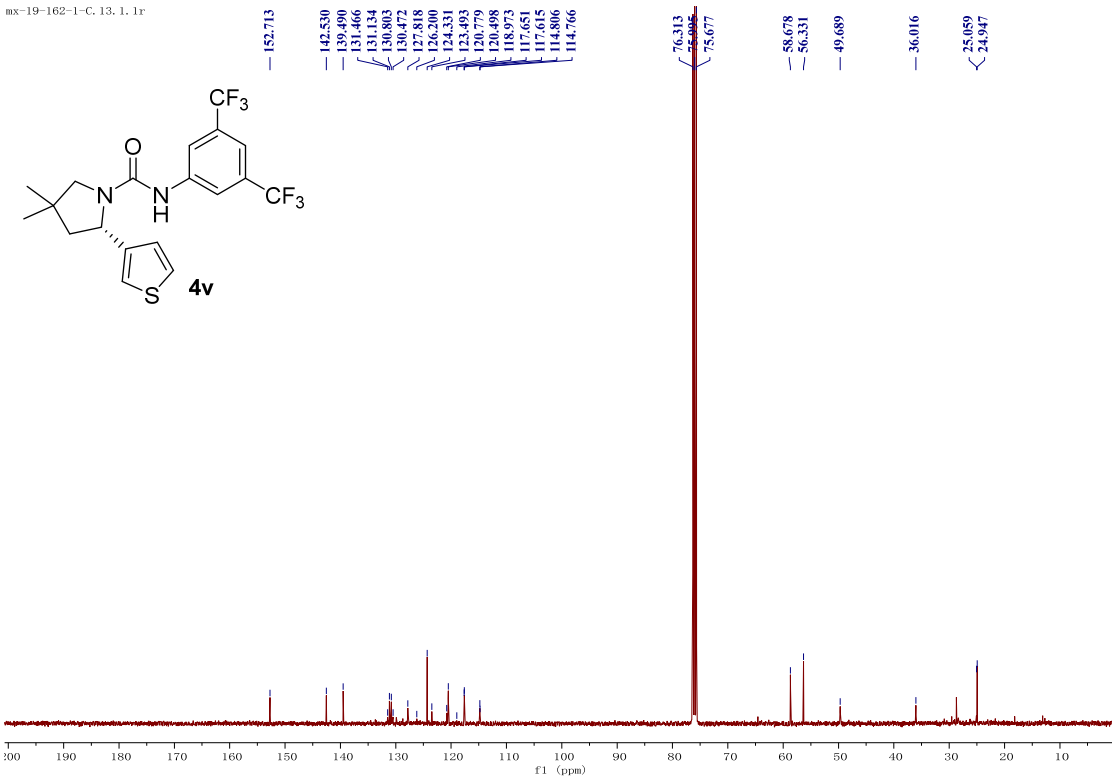
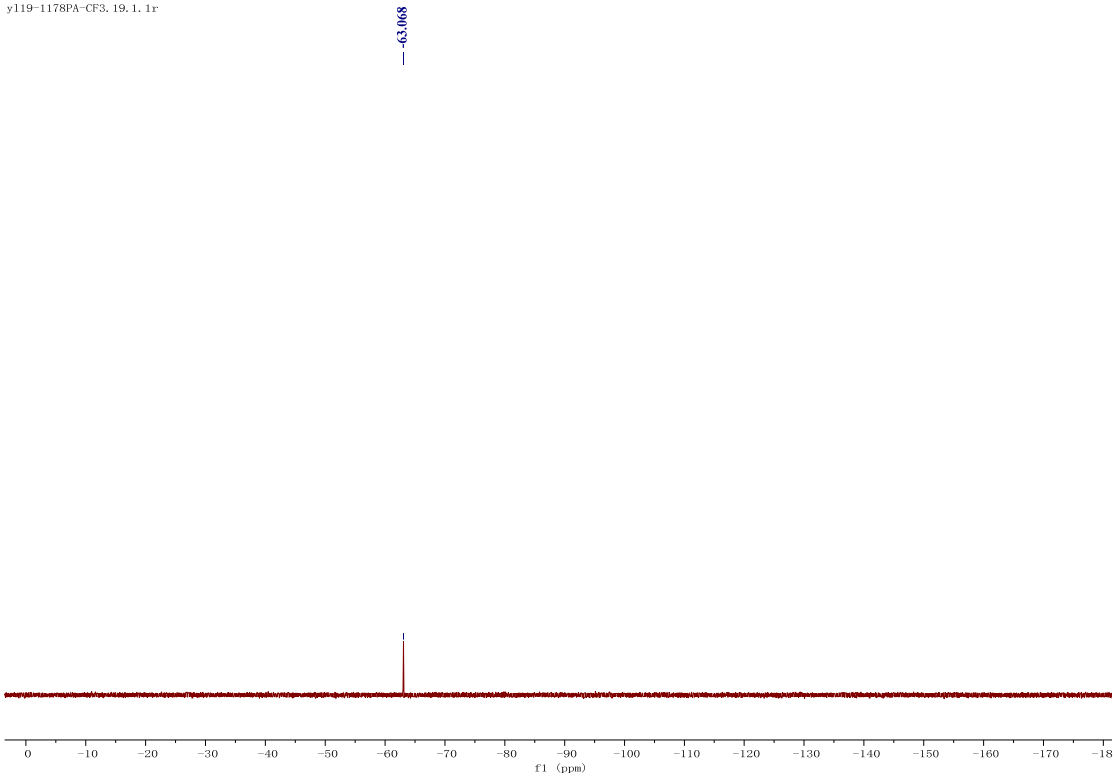
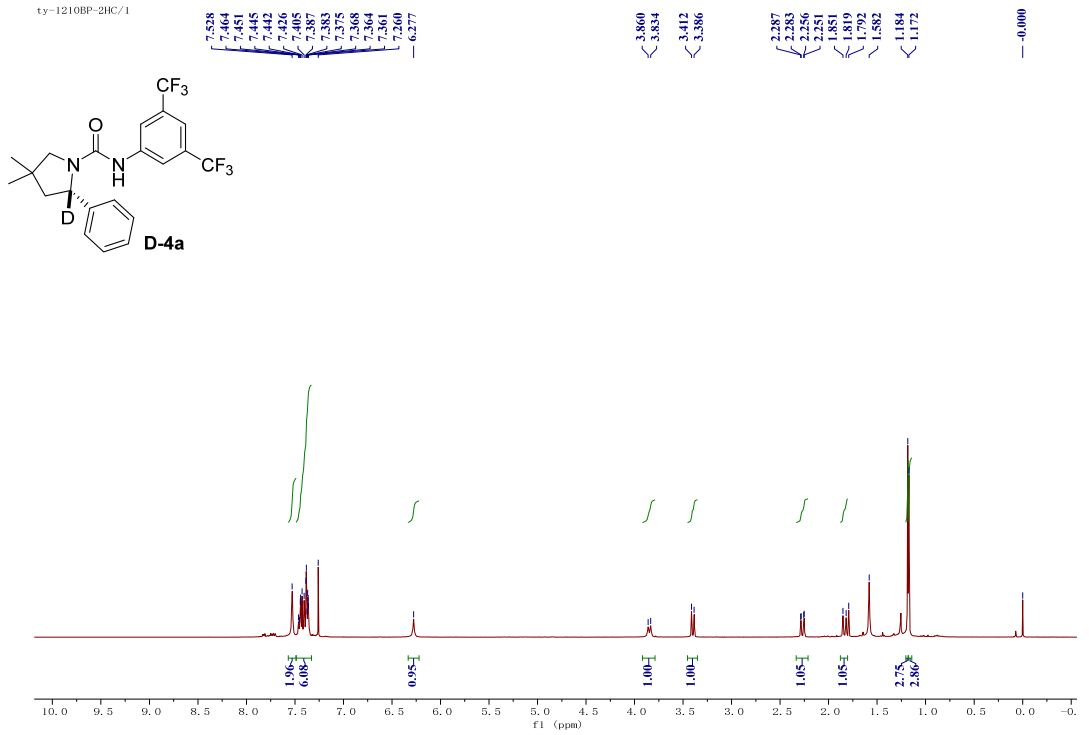
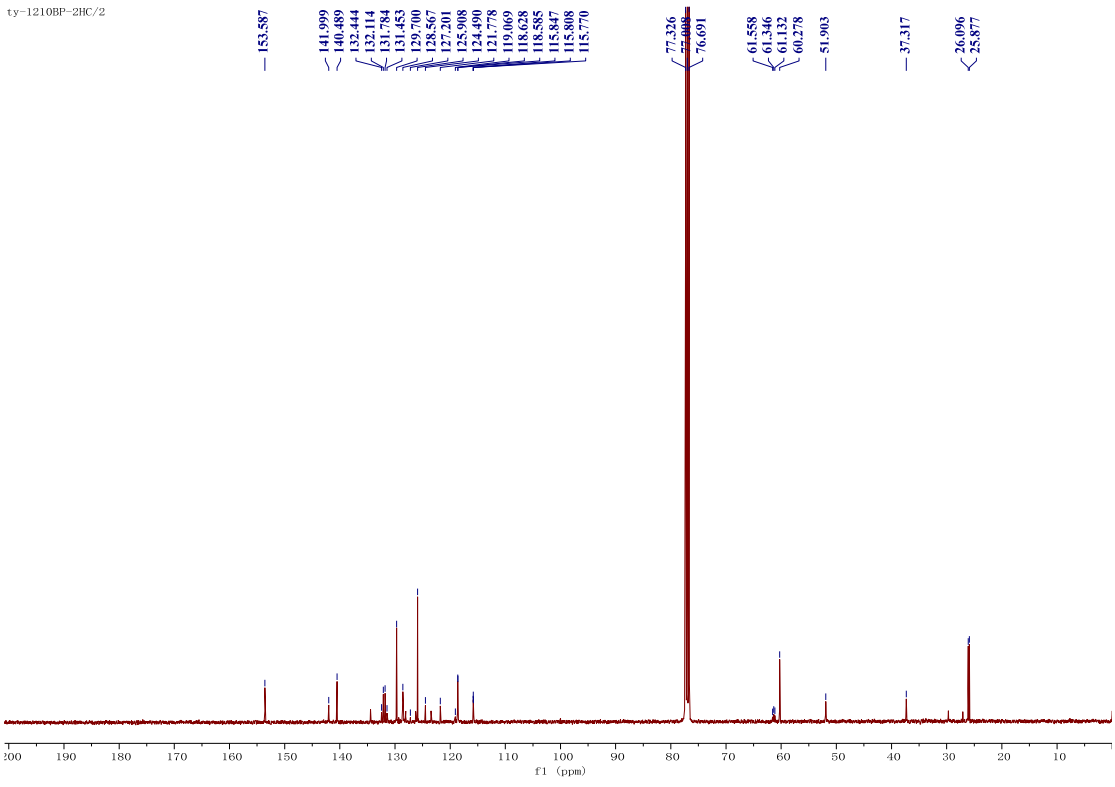
138.517
138.730
132.359
130.064
129.727
125.963
125.435
120.524
118.220
77.360
77.043
76.726
61.448
60.135
52.175
37.634
37.071
26.092
25.940
24.488
13.737
O
N
N
H
Cl
Cl
4u
n-Pr
f1 (ppm)

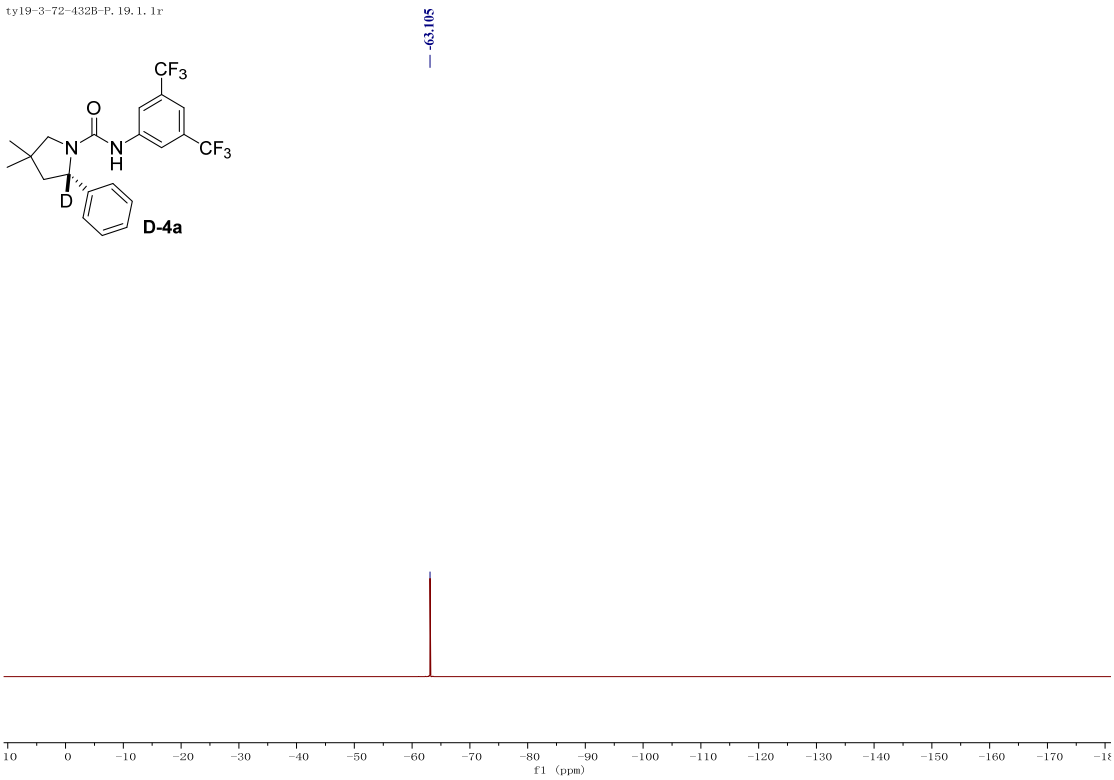

y119-1178PA-CF3.1.1r
7.582
7.469
7.467
7.456
7.449
7.428
7.343
7.339
7.335
7.332
7.263
7.082
7.079
7.070
7.066
6.495
5.014
4.996
4.990
4.972
3.807
3.781
3.370
3.343
2.261
2.256
2.243
2.239
2.229
2.225
2.211
2.207
1.914
1.890
1.882
1.859
1.181
1.154
0.000
CF3
CF3
O
N
N
H
S
4v
1.91
1.08
0.99
1.00
1.01
0.97
1.00
1.01
1.00
1.10
1.27
3.40
3.10
f1 (ppm)

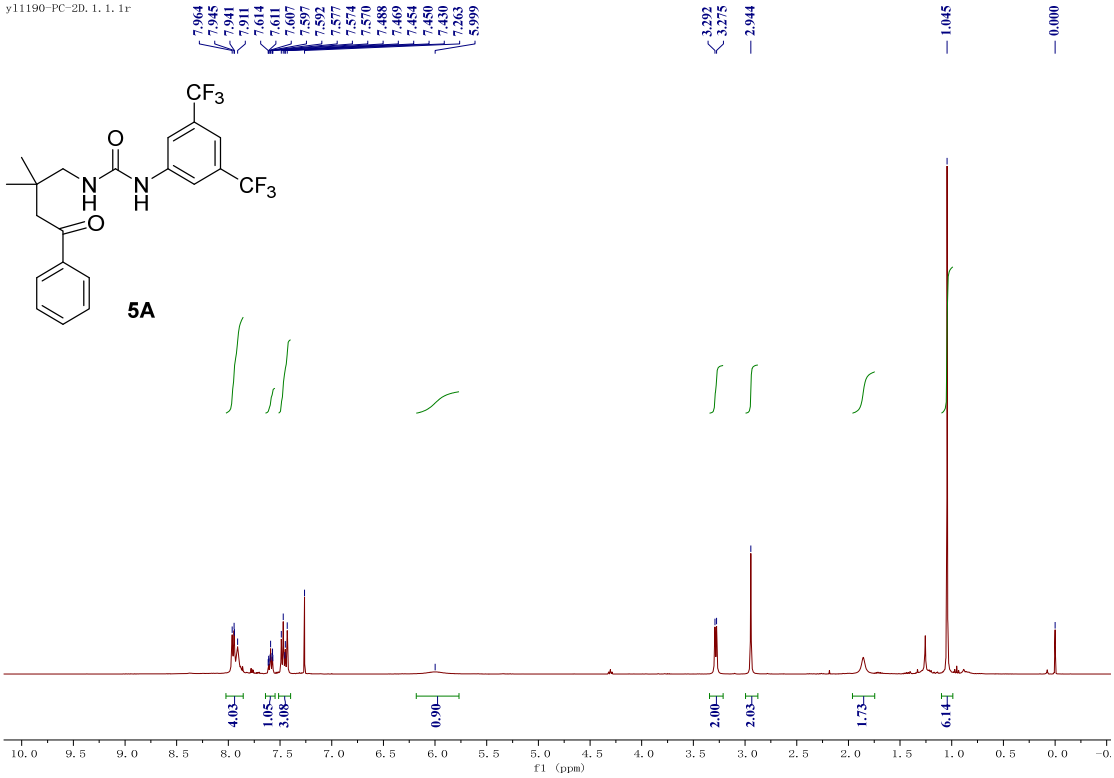

mx-19-162-1-C.13.1.1r
152.713
142.530
139.490
131.466
131.134
130.803
130.472
127.818
126.200
124.331
123.493
120.779
120.498
118.973
117.651
117.615
114.806
114.766
76.313
75.995
75.677
59.678
56.331
49.689
36.016
25.059
24.947
CF3
CF3
O
N
N
H
S
4v
f1 (ppm)

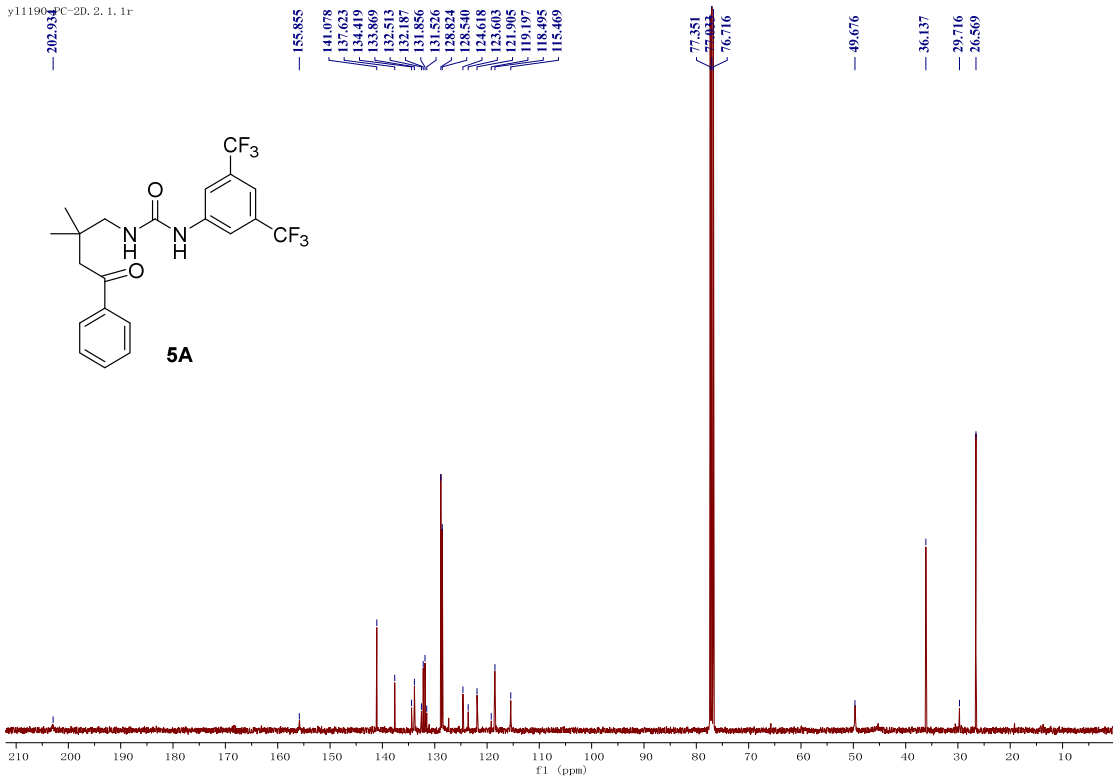

y119-1178PA-CF3.19.1.1r
-63.068
f1 (ppm)

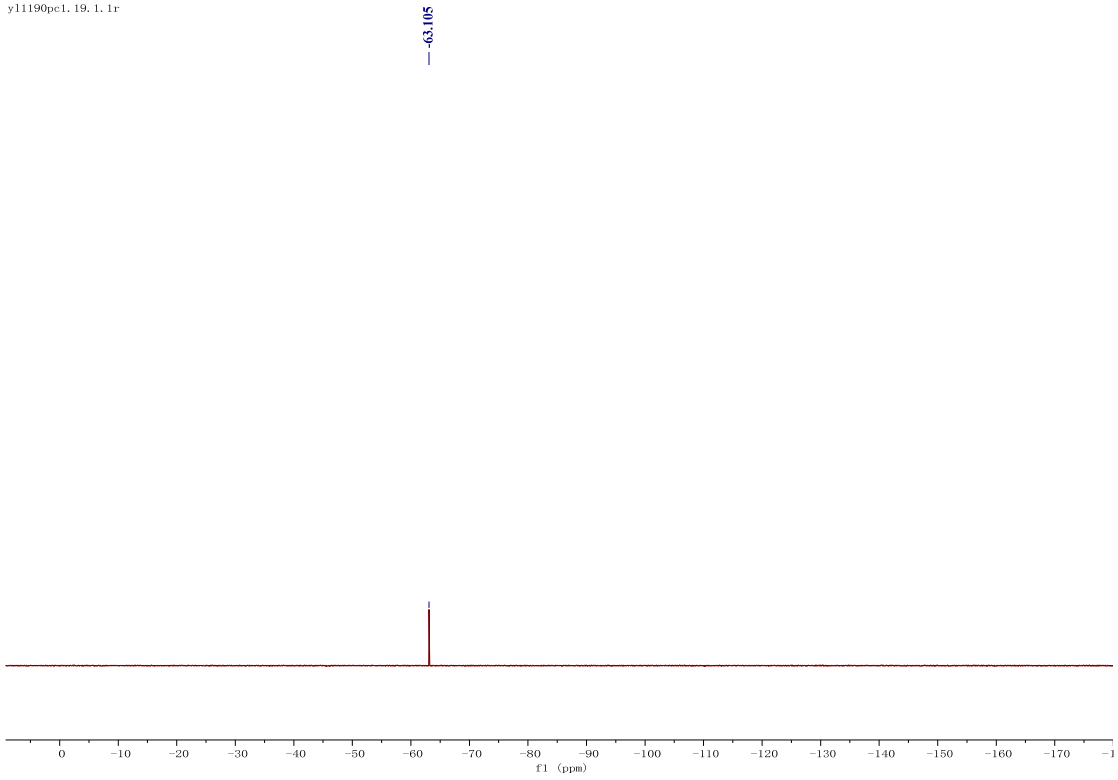

ty-1210BP-2HC/1
7.528
7.464
7.451
7.445
7.442
7.426
7.405
7.387
7.383
7.375
7.368
7.364
7.361
7.260
6.277
3.860
3.834
3.412
3.386
2.287
2.283
2.256
2.251
1.851
1.819
1.792
1.582
1.184
1.172
-0.000
CF3
O
N
H
N
CF3
D
D-4a
1.96
6.08
0.98
1.00
1.00
1.05
1.05
2.75
2.86
f1 (ppm)

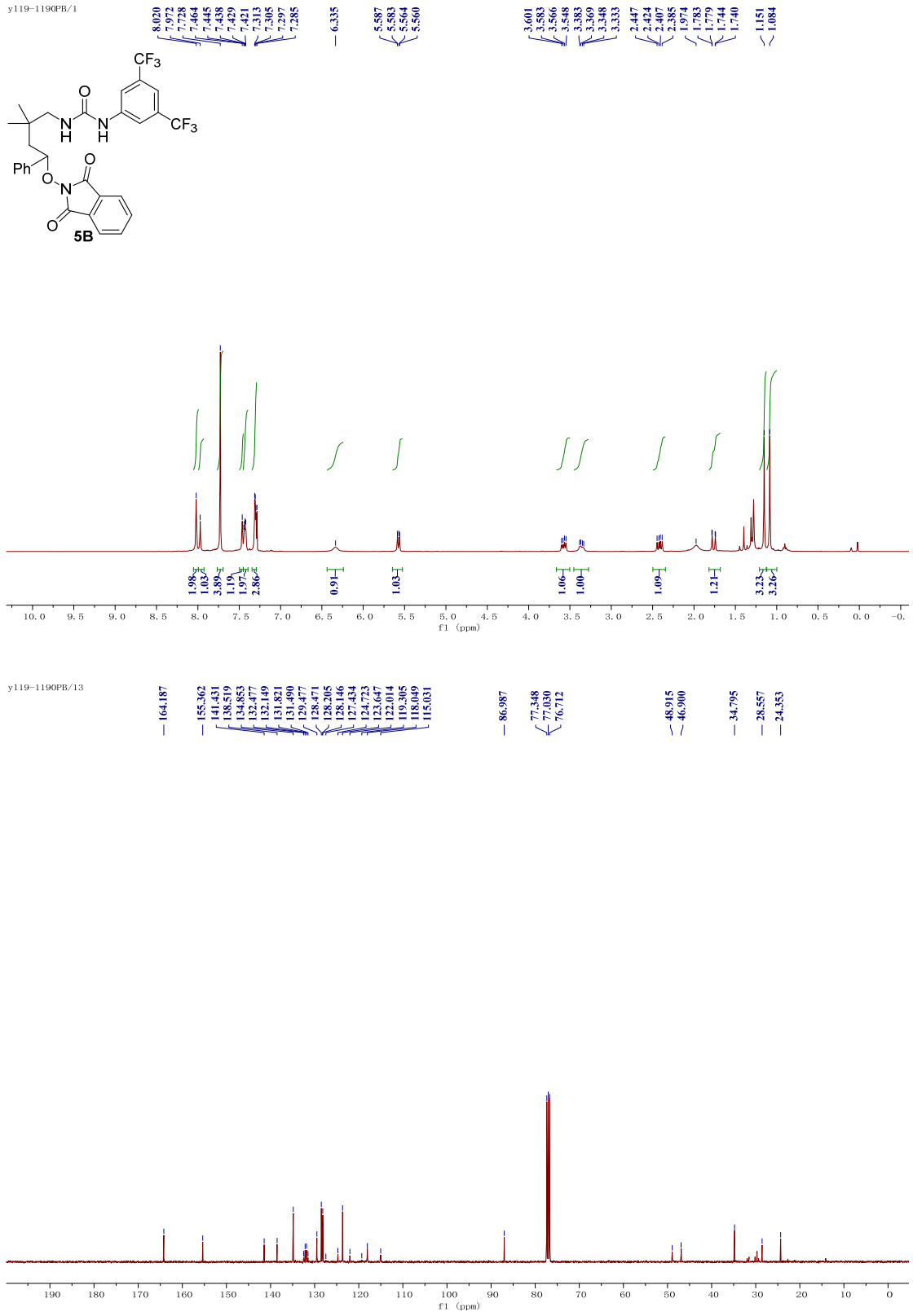

ty-1210BP-2HC/2
153.587
141.999
140.489
132.444
132.114
131.784
131.453
129.700
128.567
127.201
125.908
124.490
121.778
119.069
118.628
118.585
115.847
115.808
115.770
77.326
77.008
76.691
61.558
61.346
61.132
60.278
51.903
37.317
26.096
25.877
f1 (ppm)


ty19-3-72-432B-P.19.1.1r
-63.105
D-4a
f1 (ppm)

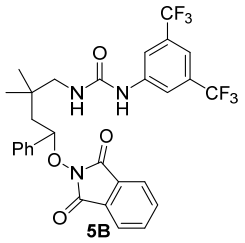

y11190-PC-2D.1.1.1r
7.964
7.945
7.941
7.911
7.614
7.611
7.607
7.597
7.592
7.577
7.574
7.570
7.488
7.469
7.454
7.450
7.430
7.263
5.999
3.292
3.275
2.944
1.045
0.000
5A
4.03
1.05
3.08
0.90
2.00
2.03
1.73
6.14
f1 (ppm)


y11190pc-2D. 2. 1. 1r
202.934
155.855
141.078
137.623
134.419
133.869
132.513
132.187
131.856
131.526
128.824
128.540
124.618
123.603
121.905
119.197
118.495
115.469
77.351
77.032
76.716
49.676
36.137
29.716
26.569
CF3
CF3
O
N
H
N
H
O
5A
f1 (ppm)


y11190pc1. 19. 1. 1r
-63.105
f1 (ppm)


y119-1190PB/1
8.020
7.972
7.728
7.464
7.445
7.438
7.429
7.421
7.313
7.305
7.297
7.285
6.335
5.587
5.583
5.564
5.560
3.601
3.583
3.566
3.548
3.383
3.369
3.348
3.333
2.447
2.424
2.407
2.385
1.974
1.783
1.779
1.744
1.740
1.151
1.084
CF3
CF3
O
N
H
N
H
Ph
O
N
O
O
5B
1.98
1.03
3.89
1.19
1.97
2.86
0.91
1.03
1.06
1.00
1.09
1.21
3.23
3.26
f1 (ppm)
y119-1190PB/13
164.187
155.362
141.431
138.519
134.853
132.477
132.149
131.821
131.490
129.477
128.471
128.205
128.146
127.434
124.723
123.647
122.014
119.305
118.049
115.031
86.987
77.348
77.030
76.712
48.915
46.900
34.795
28.557
24.353
f1 (ppm)

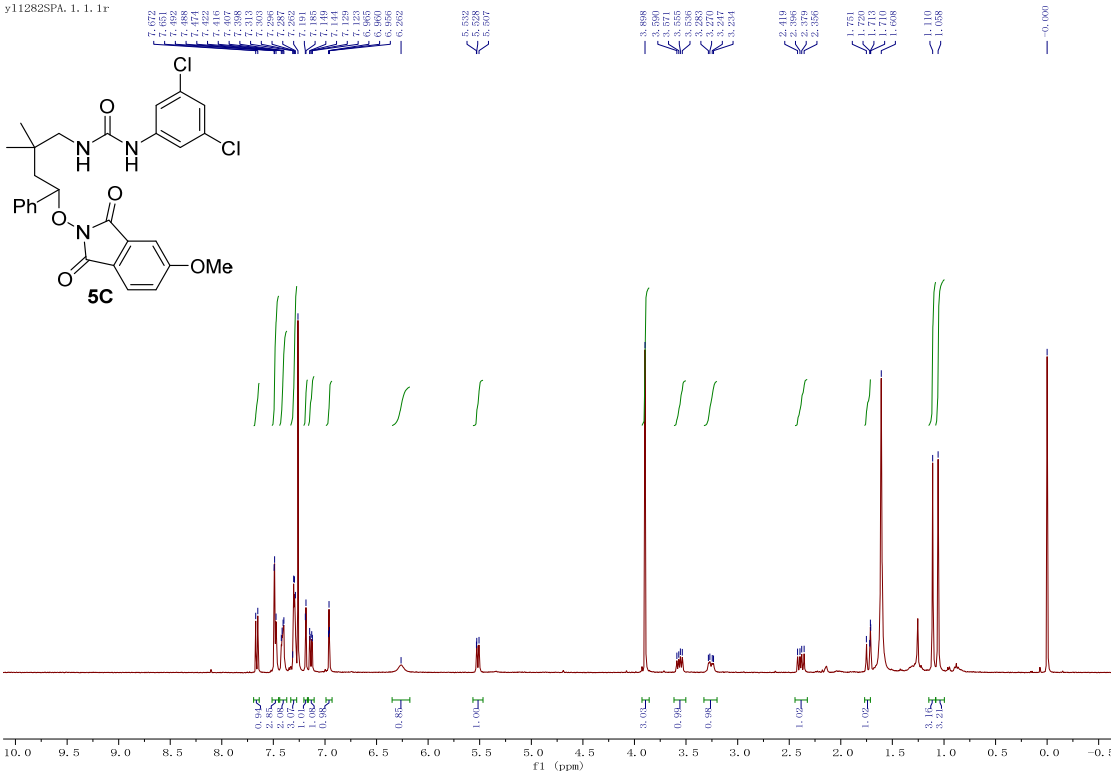
y119-1190PB/19



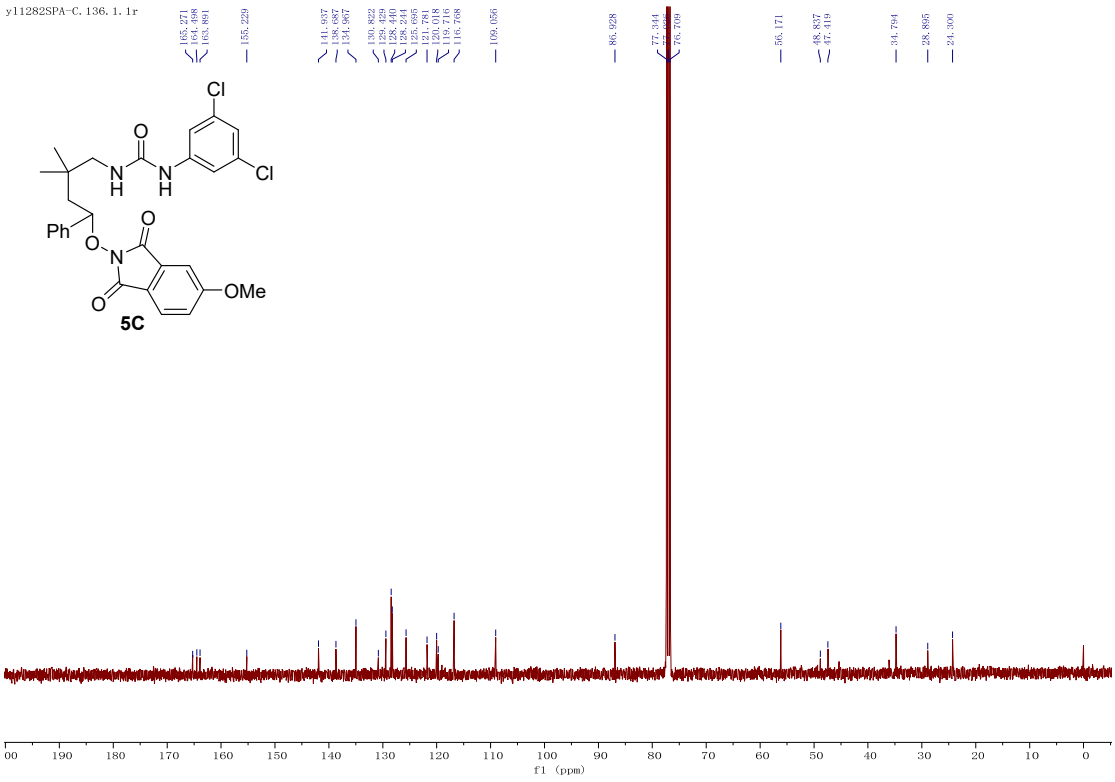

5B

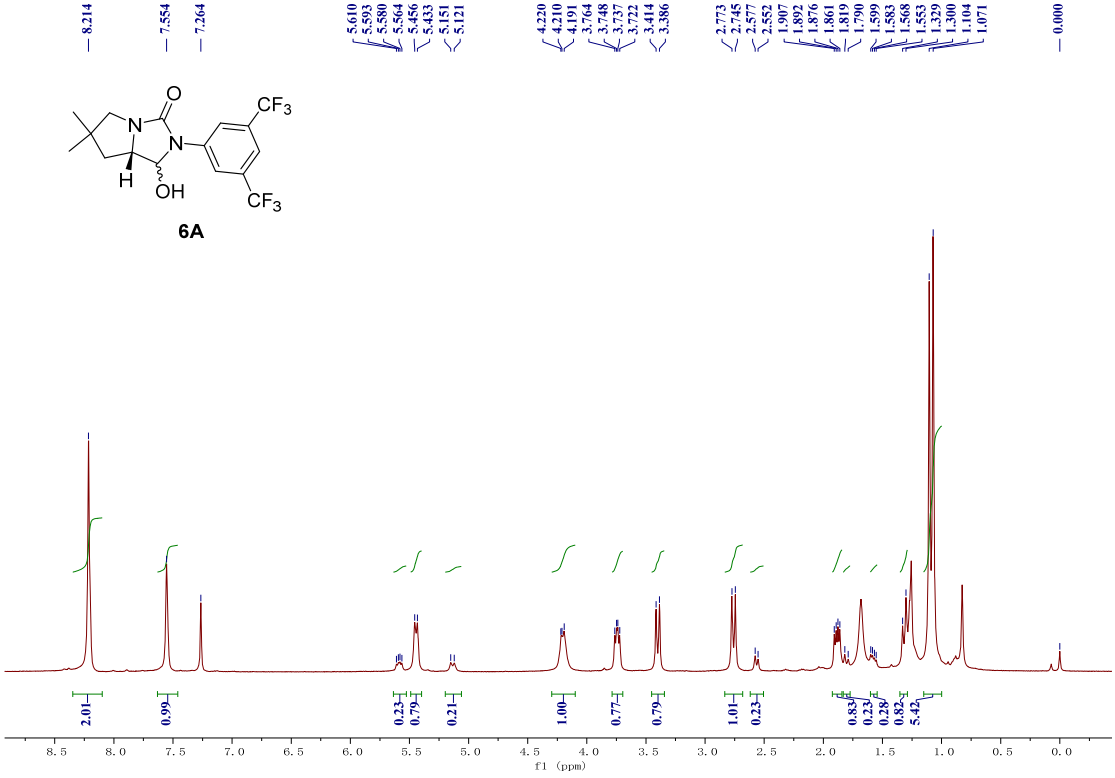


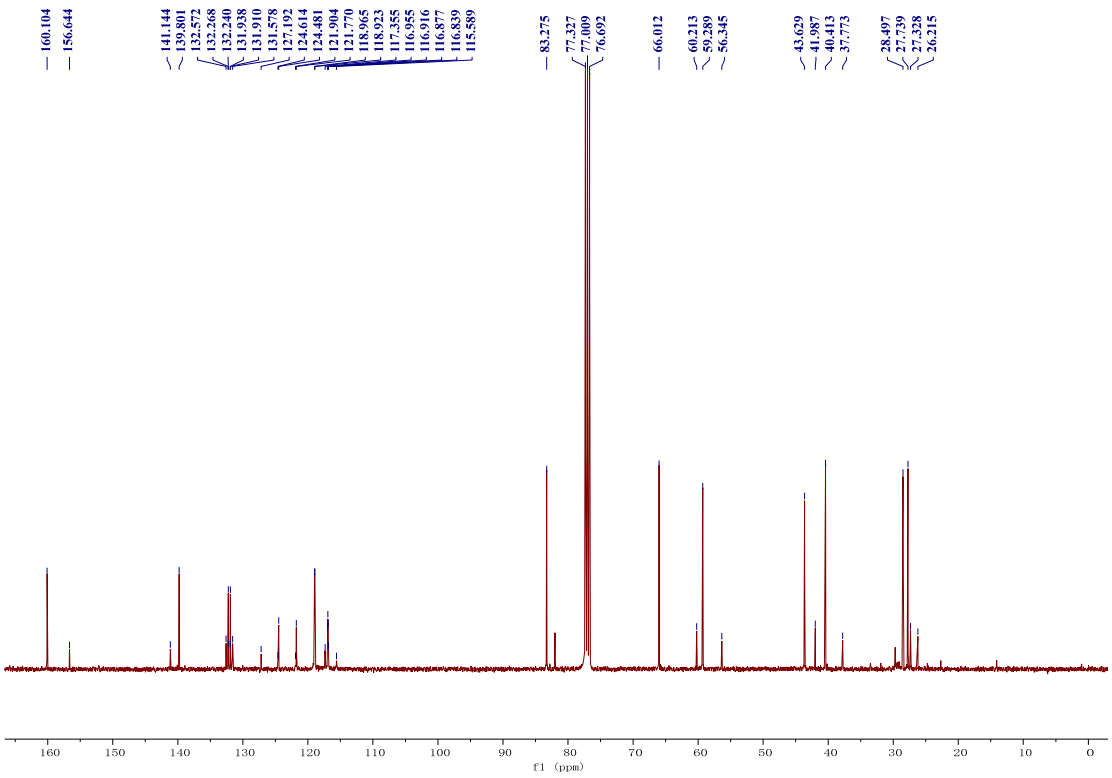

y11282SPA. 1. 1. 1r

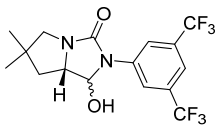



5C


y11282SPA-C.136.1.1r
165.271
164.498
163.891
155.229
141.937
138.687
134.967
130.822
129.429
128.440
128.244
125.695
121.781
120.018
119.716
116.768
109.056
86.928
77.344
77.088
76.769
56.171
48.857
47.410
34.794
28.895
24.300
Cl
Cl
O
N
H
N
H
Ph
O
O
N
O
O
OMe
5C
f1 (ppm)

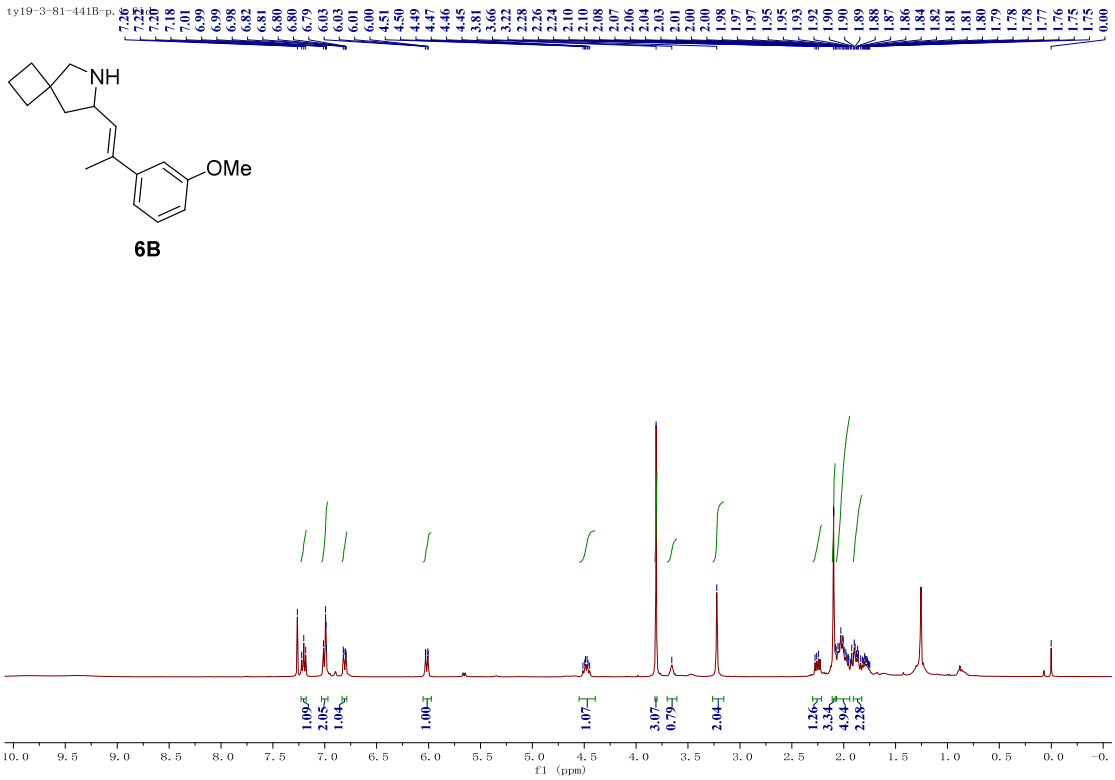

8.214
7.554
7.264
5.610
5.593
5.580
5.564
5.456
5.433
5.151
5.121
4.220
4.210
4.191
3.764
3.748
3.737
3.722
3.414
3.386
2.773
2.745
2.577
2.552
1.907
1.892
1.876
1.861
1.819
1.790
1.599
1.583
1.568
1.553
1.329
1.300
1.104
1.071
0.000
O
N
N
H
OH
CF3
CF3
6A
2.01
0.99
0.23
0.79
0.21
1.00
0.77
0.79
1.01
0.23
0.83
0.23
0.28
0.82
5.42
f1 (ppm)

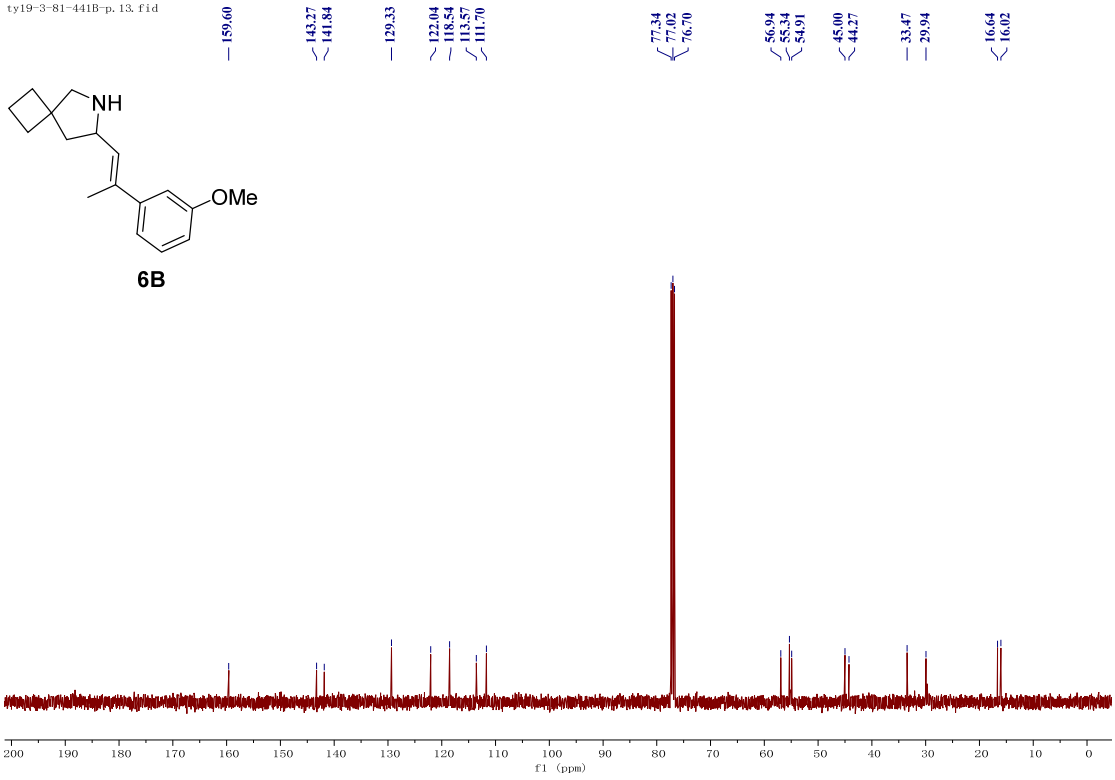

160.104
156.644
141.144
139.801
132.572
132.268
132.240
131.938
131.910
131.578
127.192
124.614
124.481
121.904
121.770
118.965
118.923
117.355
116.955
116.916
116.877
116.839
115.589
83.275
77.327
77.009
76.692
66.012
60.213
59.289
56.345
43.629
41.987
40.413
37.773
28.497
27.739
27.328
26.215
f1 (ppm)

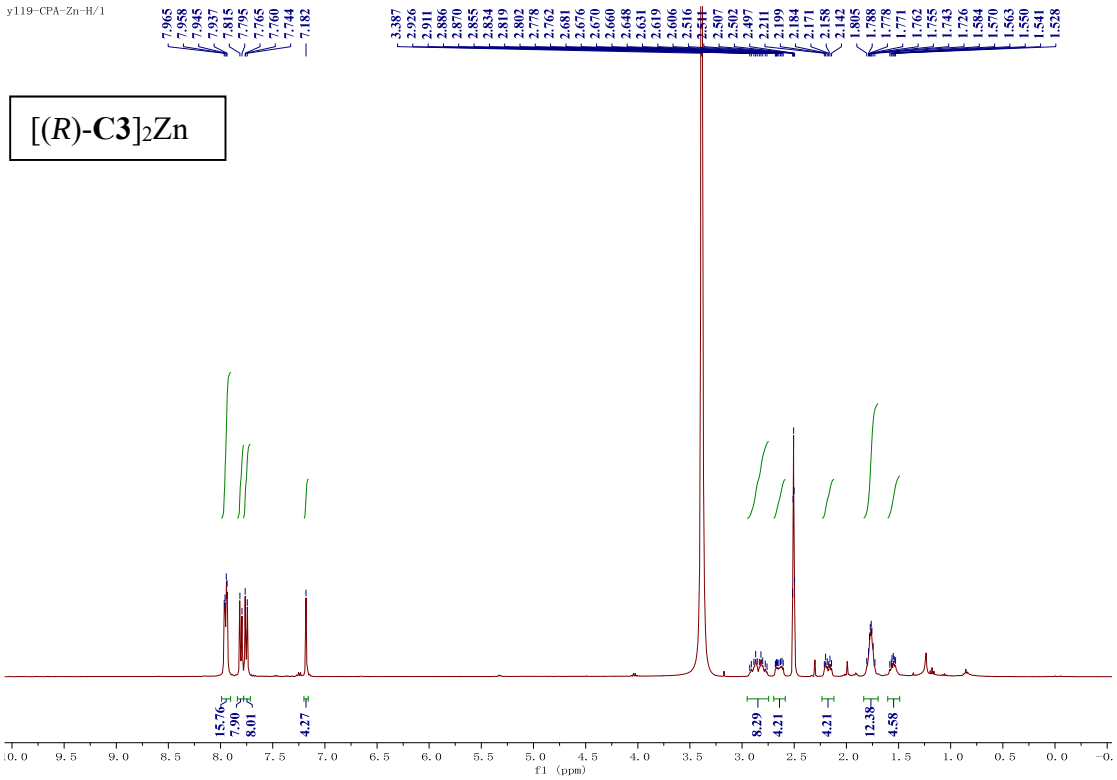

O
N
N
H
OH
CF3
CF3

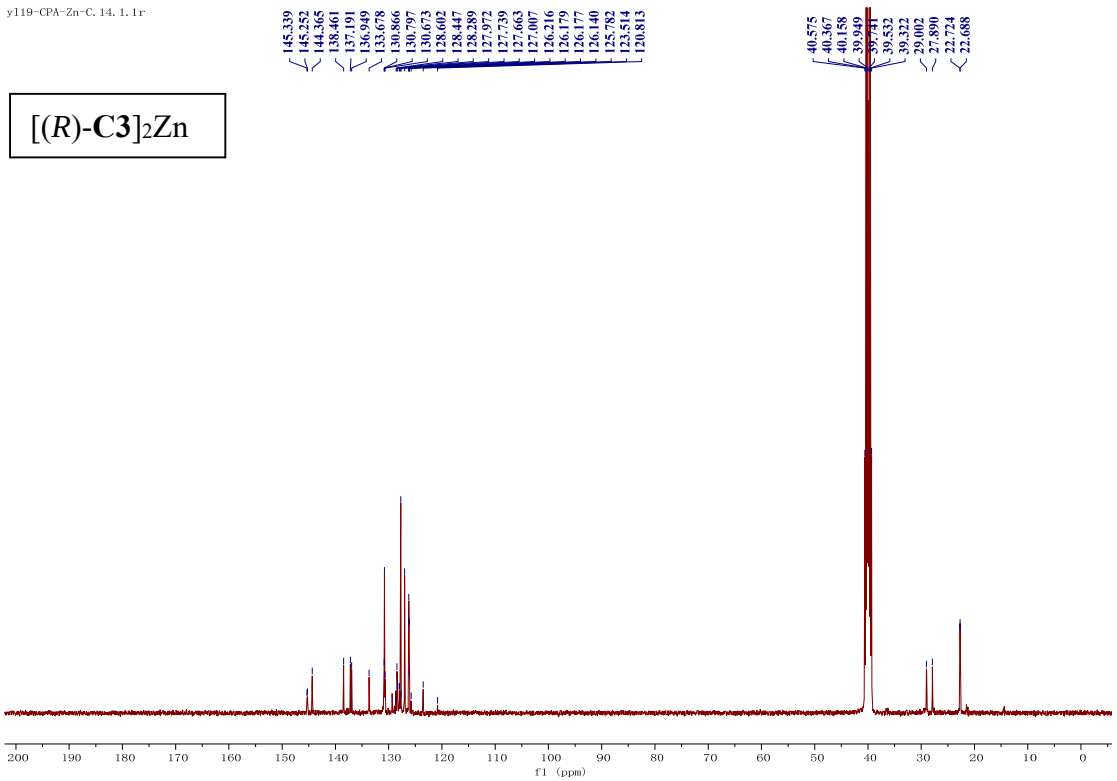
**6A**


-62.917
-62.988
f1 (ppm)


ty19-3-81-441B-p.
NH
OMe
6B
1.09
2.05
1.04
1.00
1.07
3.07
0.79
2.04
1.26
3.34
4.94
2.28
f1 (ppm)


ty19-3-81-441B-p.13.fid
159.60
143.27
141.84
129.33
122.04
118.54
113.57
111.70
77.34
77.02
76.70
56.94
55.34
54.91
45.00
44.27
33.47
29.94
16.64
16.02
NH
OMe
6B
f1 (ppm)

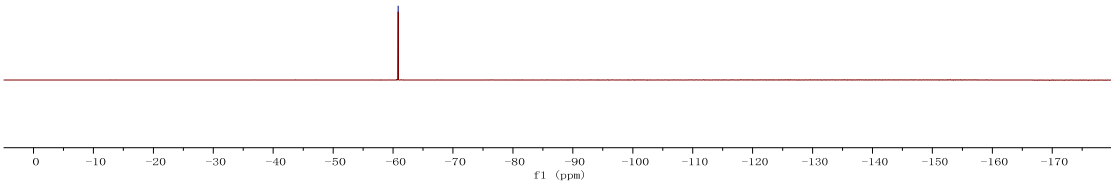

y119-CPA-Zn-H/1
[(R)-C3]2Zn
f1 (ppm)


y119-CPA-Zn-C. 14. 1. 1r
[(R)-C3]2Zn
f1 (ppm)

y119-CPA-Zn-H/19

-60.853

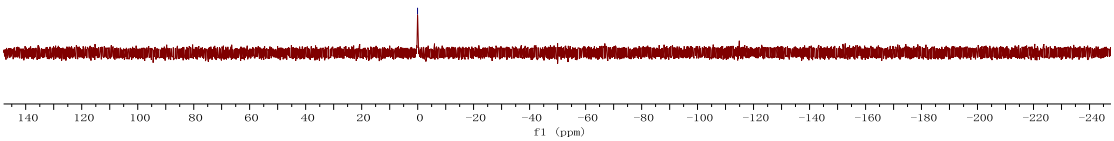
[(*R*)-**C3**]$_2$Zn



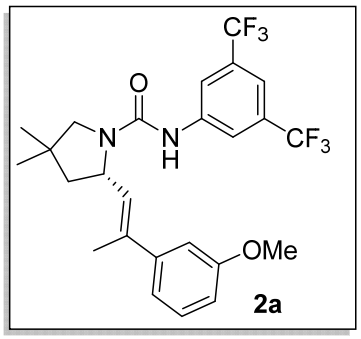

y119-CPA-Zn-H/31

0.023

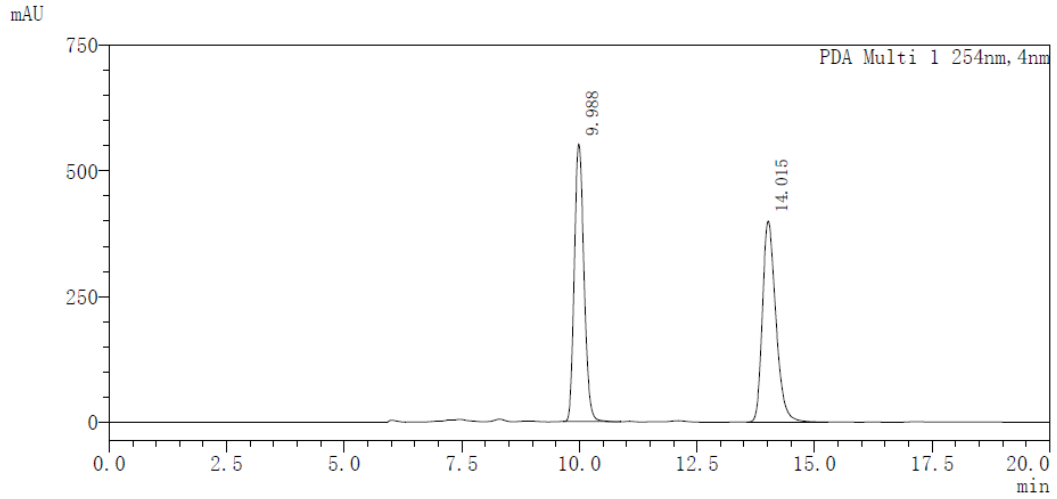
[(*R*)-**C3**]$_2$Zn



# HPLC Spectra

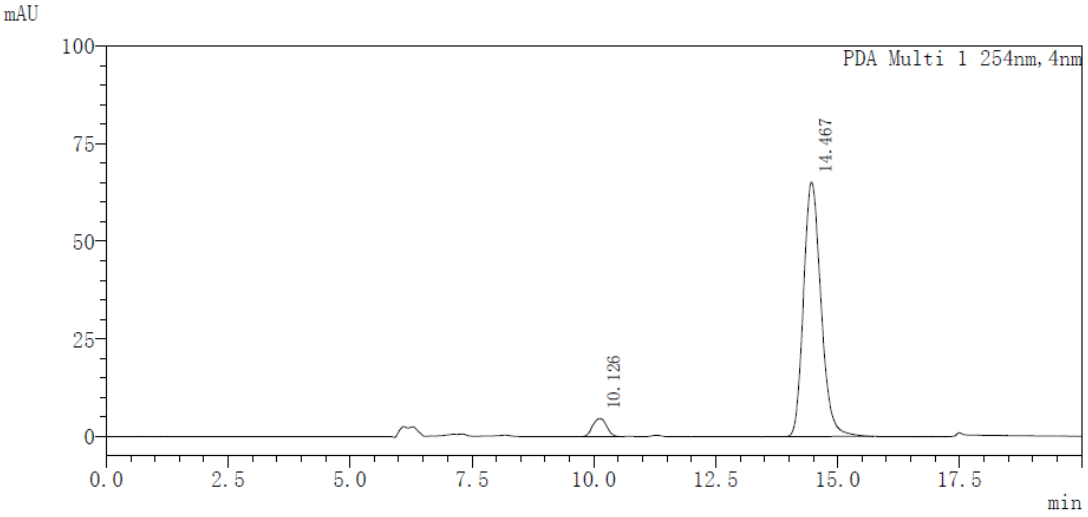



**2a**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(minor) = 10.1 min, t(major) = 14.5 min, 95:5 er.



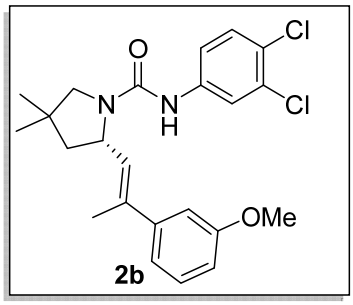

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 9.988 | 551868 | 7912441 | 49.932 |
| 14.015 | 399549 | 7934126 | 50.068 |

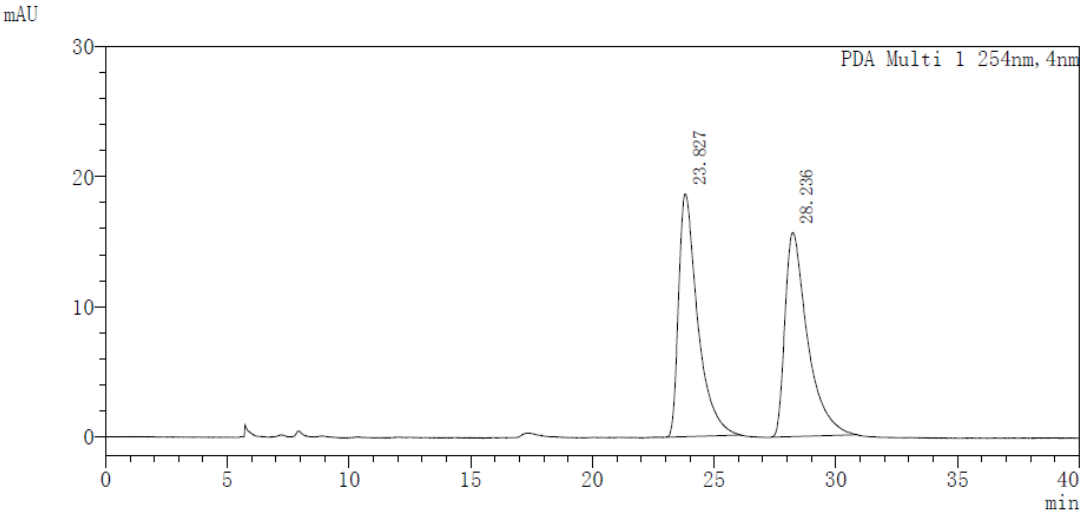



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 10.126 | 4580 | 90626 | 5.277 |
| 14.467 | 65224 | 1626735 | 94.723 |

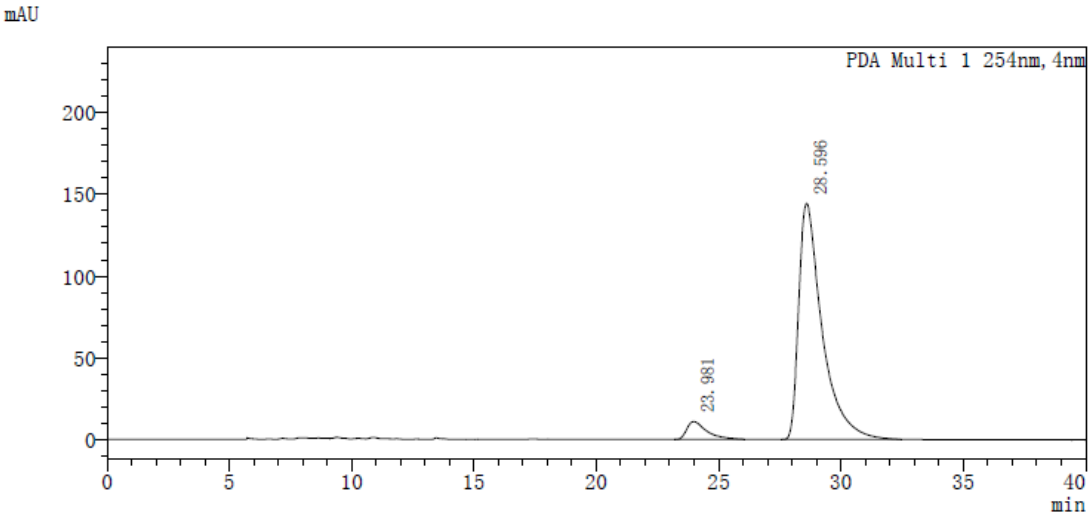



**2b**, HPLC condition: Chiralcel AD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(minor) =24.0 min, t(major) = 28.6 min, 94:6 er.



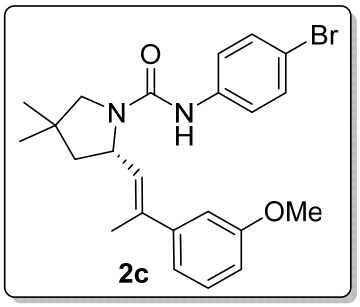

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 23.827 | 18669 | 1020088 | 50.165 |
| 28.236 | 15684 | 1013372 | 49.835 |

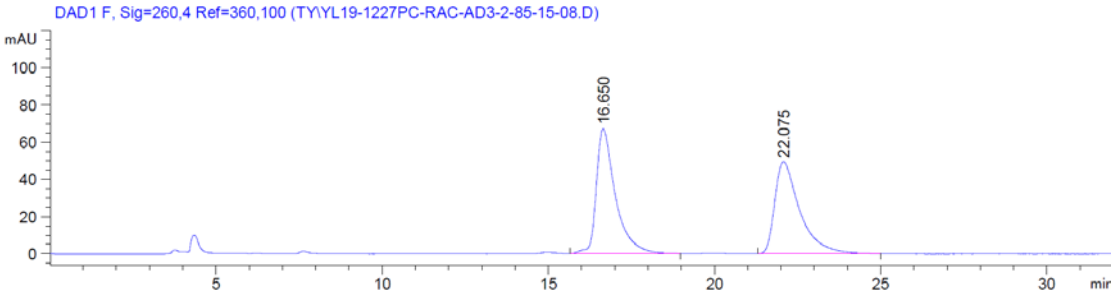



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 23.981 | 10910 | 606642 | 5.939 |
| 28.596 | 144406 | 9608206 | 94.061 |

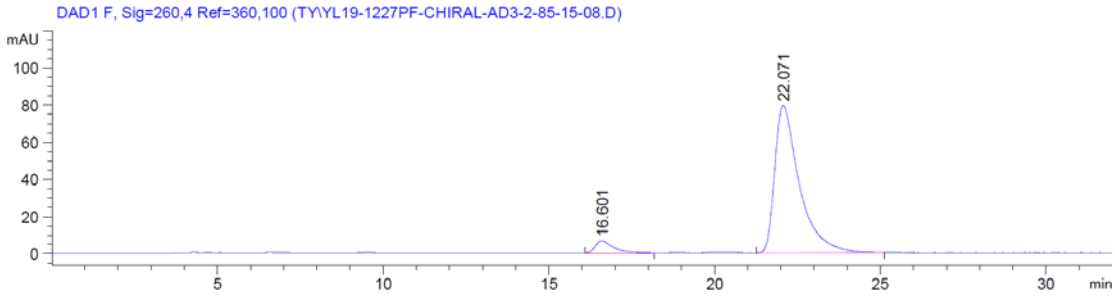



**2c**, HPLC condition: Chiralcel AD-3, *i*-PrOH/*n*-hexane = 85/15, flow rate 0.8 mL/min. λ = 260 nm, t(minor) =16.6 min, t(major) = 22.0 min, 94:6 er.



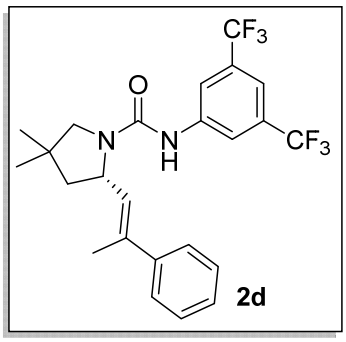

Signal 6: DAD1 F, Sig=260,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.650 | BB | 0.5759 | 2674.39111 | 66.97305 | 50.8674 |
| 2 | 22.075 | BB | 0.7511 | 2583.17969 | 49.32016 | 49.1326 |

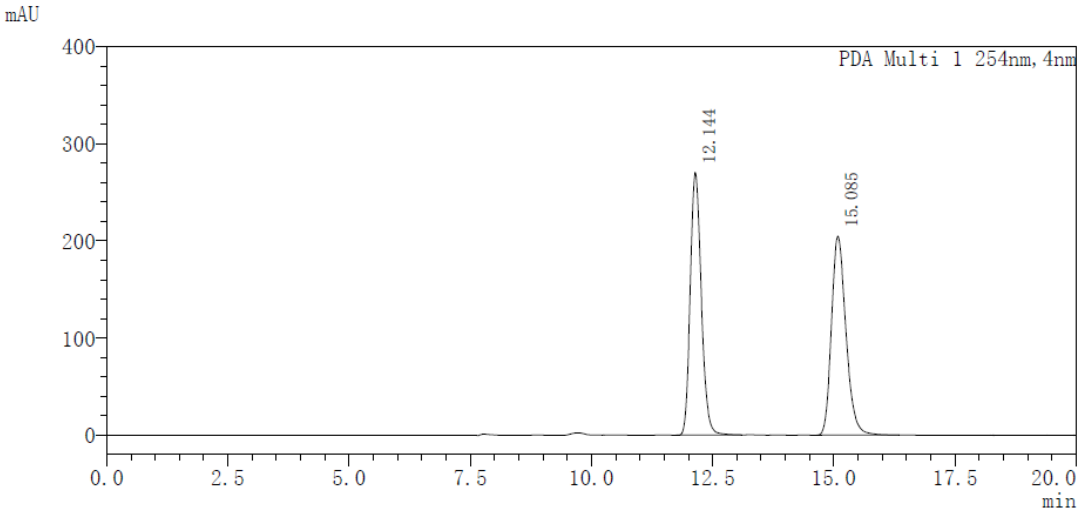



Signal 6: DAD1 F, Sig=260,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.601 | BB | 0.4759 | 244.58809 | 6.51709 | 5.6232 |
| 2 | 22.071 | BB | 0.7397 | 4105.05469 | 79.32757 | 94.3768 |

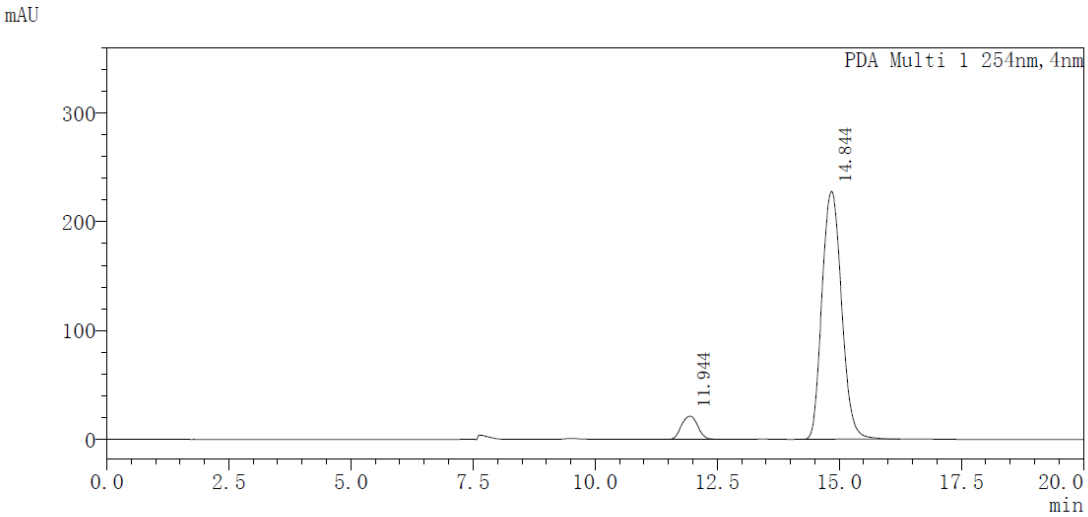



**2d**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.4 mL/min. λ = 254 nm, t(minor) = 11.9 min, t(major) = 14.8 min, 93:7 er.



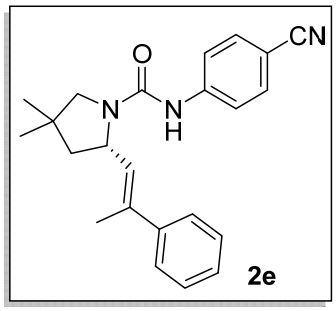

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 12.144 | 270121 | 4283335 | 50.161 |
| 15.085 | 204525 | 4255854 | 49.839 |

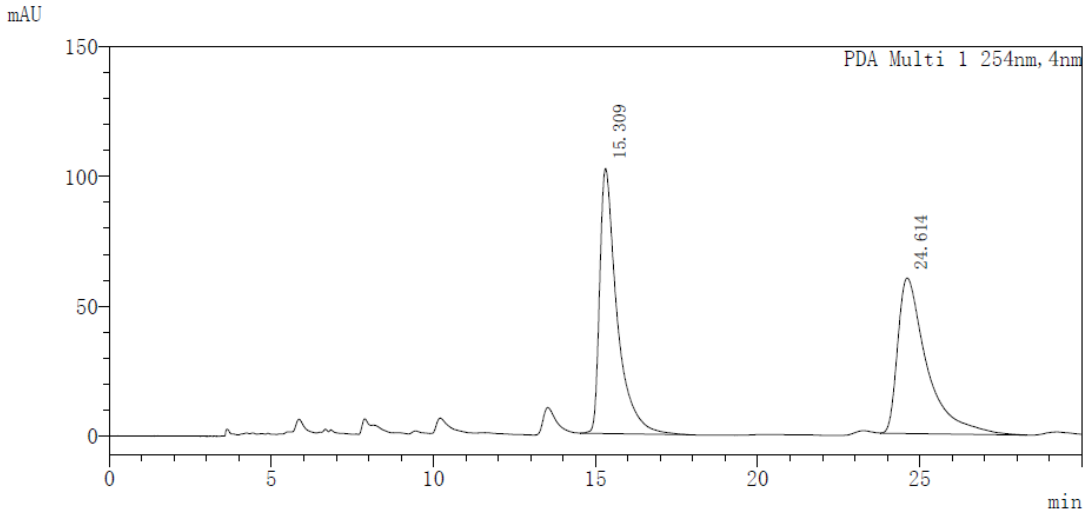



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 11.944 | 21135 | 489675 | 7.123 |
| 14.844 | 227950 | 6385142 | 92.877 |

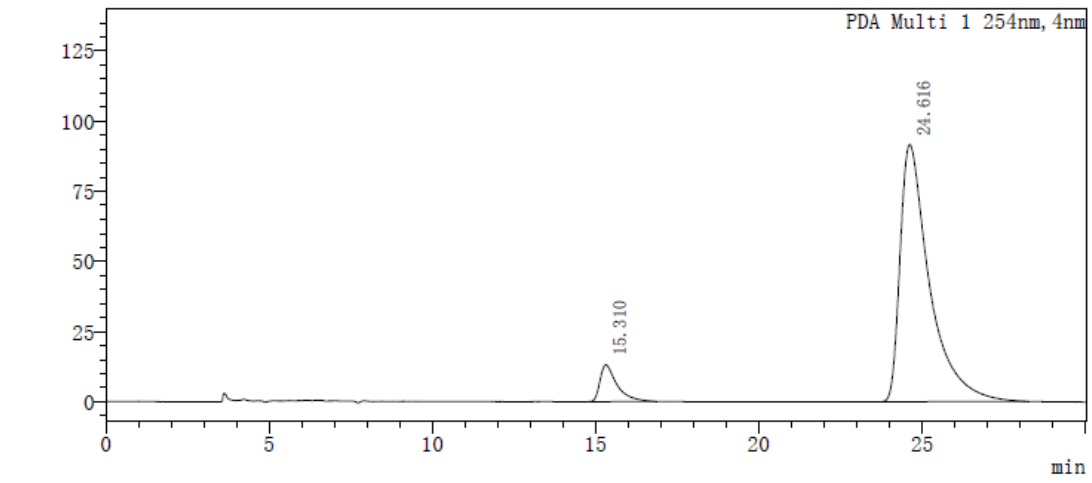



**2e**, HPLC condition: Chiralcel AD-3, *i*-PrOH/*n*-hexane = 85/15, flow rate 0.8 mL/min. λ = 254 nm, t(minor) = 15.3 min, t(major) = 24.6 min, 92.5:7.5 er.



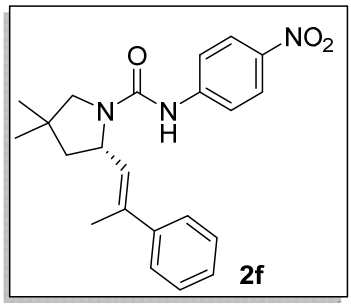

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 15.309 | 102170 | 3809712 | 50.487 |
| 24.614 | 59873 | 3736153 | 49.513 |

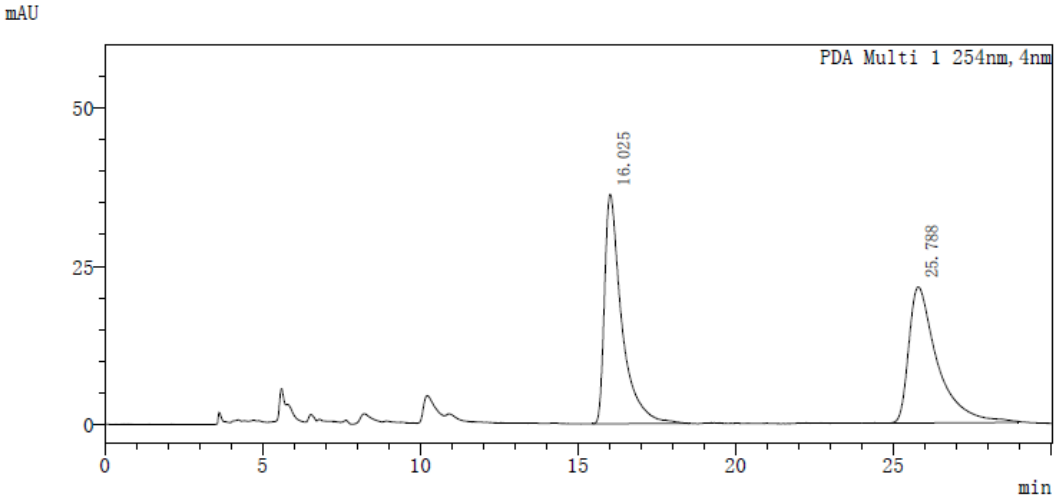



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 15.310 | 13097 | 472478 | 7.600 |
| 24.616 | 91729 | 5744280 | 92.400 |

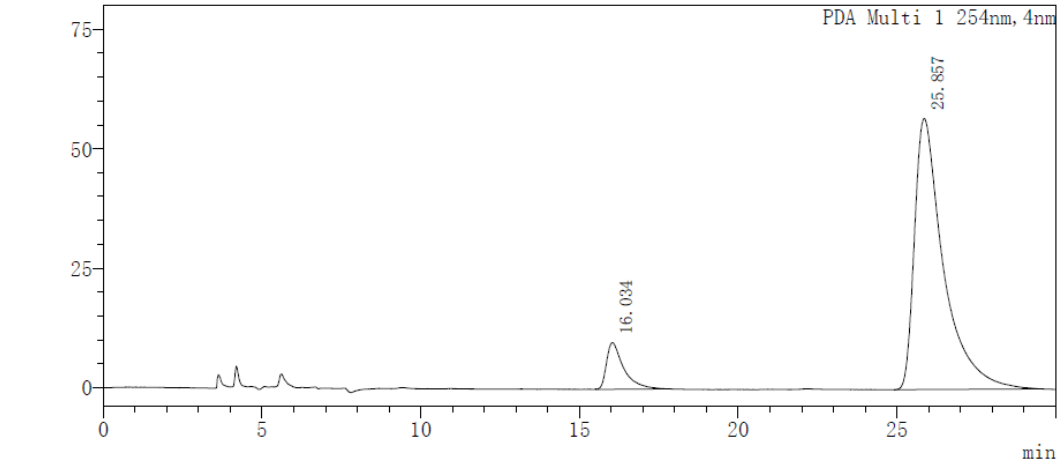



**2f**, HPLC condition: Chiralcel AD-3, *i*-PrOH/*n*-hexane = 85/15, flow rate 0.8 mL/min. λ = 254 nm, t(minor) = 16.0 min, t(major) = 25.8 min, 91:9 er.



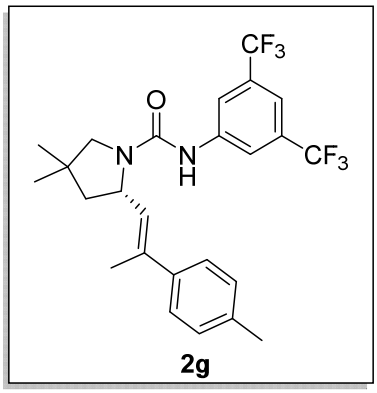

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 16.025 | 36284 | 1378016 | 50.265 |
| 25.788 | 21530 | 1363481 | 49.735 |

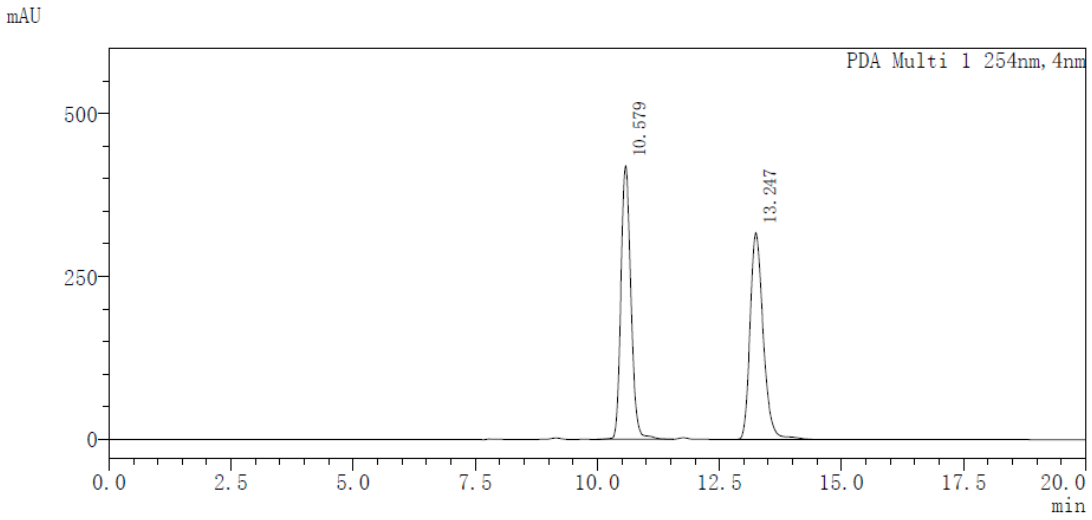



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 16.034 | 9756 | 364084 | 9.178 |
| 25.857 | 56719 | 3602745 | 90.822 |

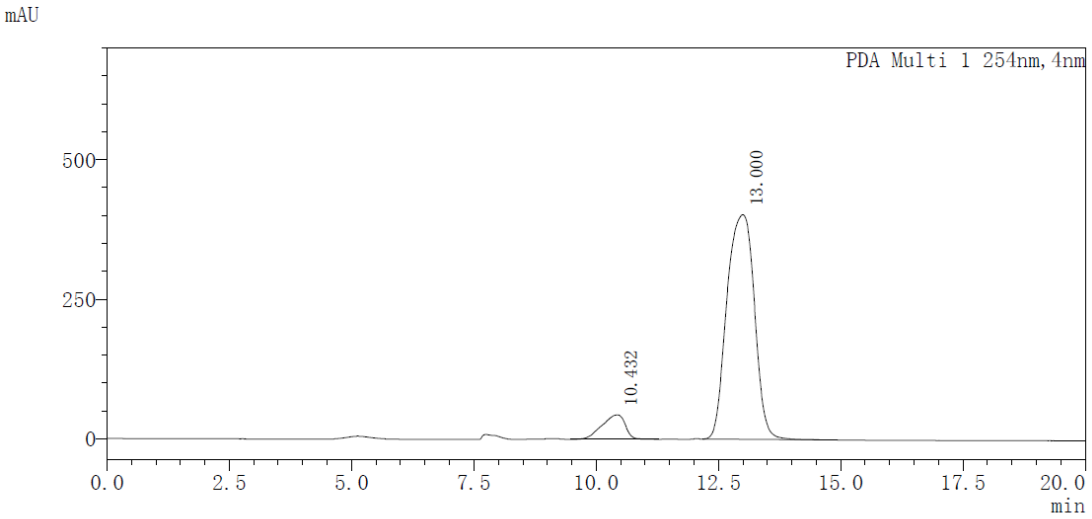



**2g**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.4 mL/min. λ = 254 nm, t(minor) = 10.4 min, t(major) = 13.0 min, 92:8 er.



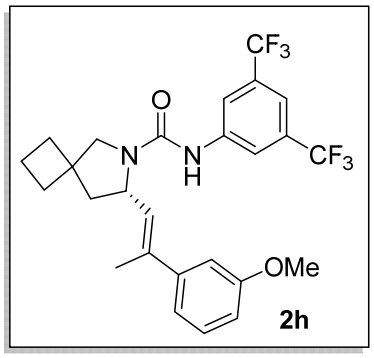

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 10.579 | 419006 | 5964992 | 50.055 |
| 13.247 | 317383 | 5951905 | 49.945 |

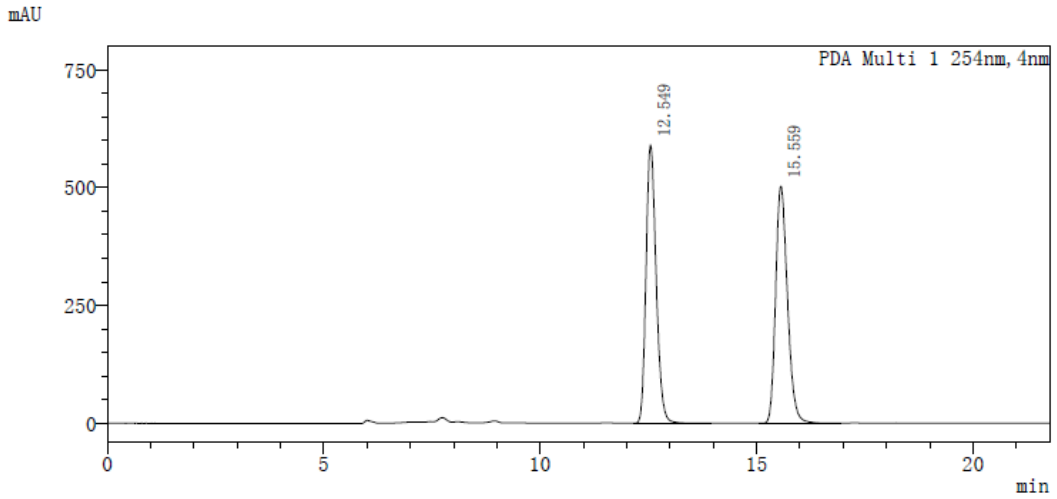



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 10.432 | 43717 | 1445224 | 8.393 |
| 13.000 | 402421 | 15773169 | 91.607 |

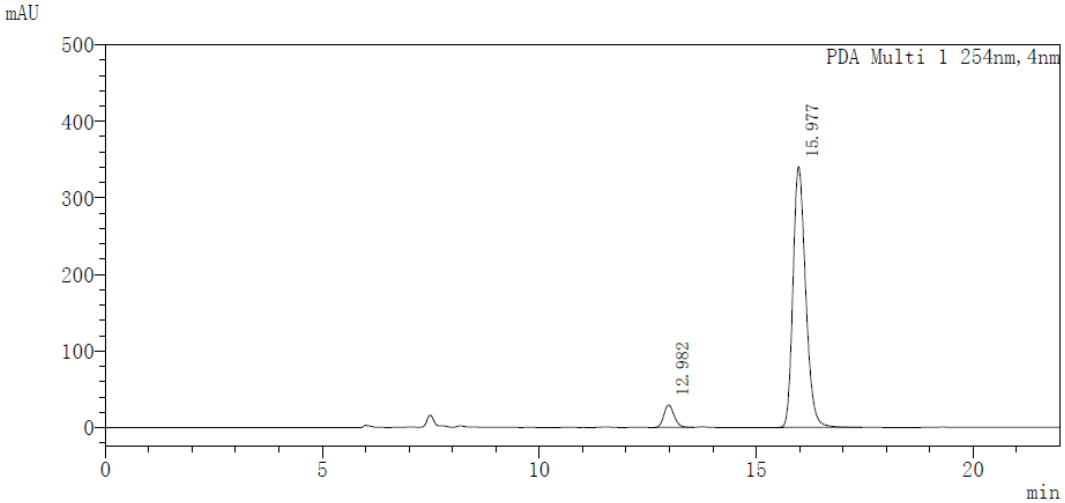



**2h**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(minor) = 13.0 min, t(major) = 16.0 min, 94:6 er



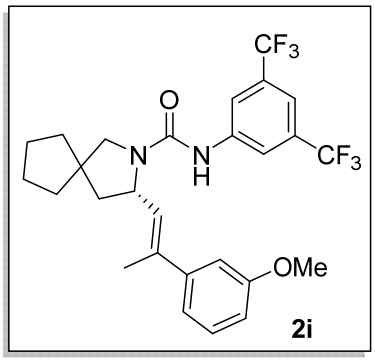

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 12.549 | 590215 | 9578797 | 50.009 |
| 15.559 | 502707 | 9575438 | 49.991 |

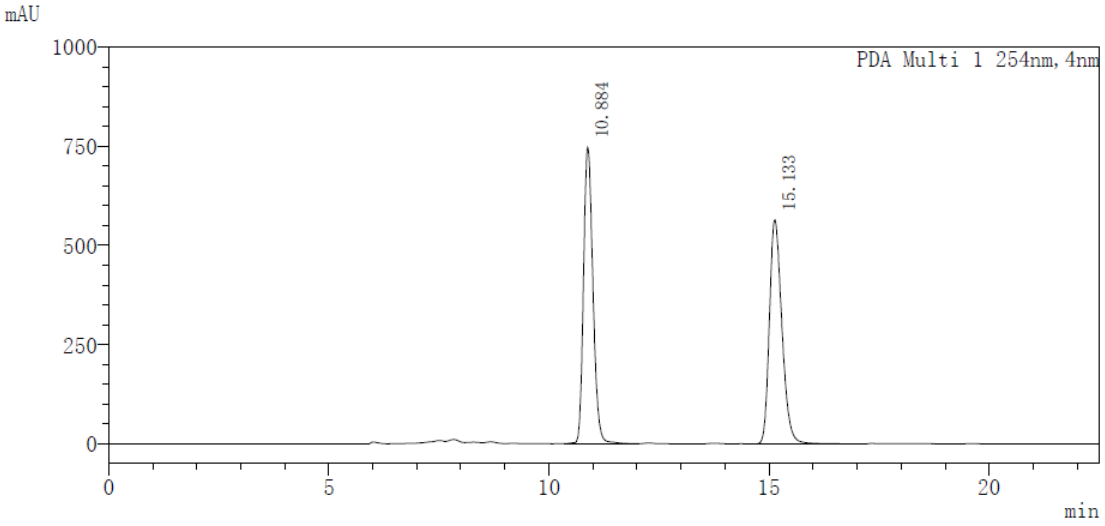



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 12.982 | 29280 | 475354 | 6.439 |
| 15.977 | 340541 | 6907414 | 93.561 |

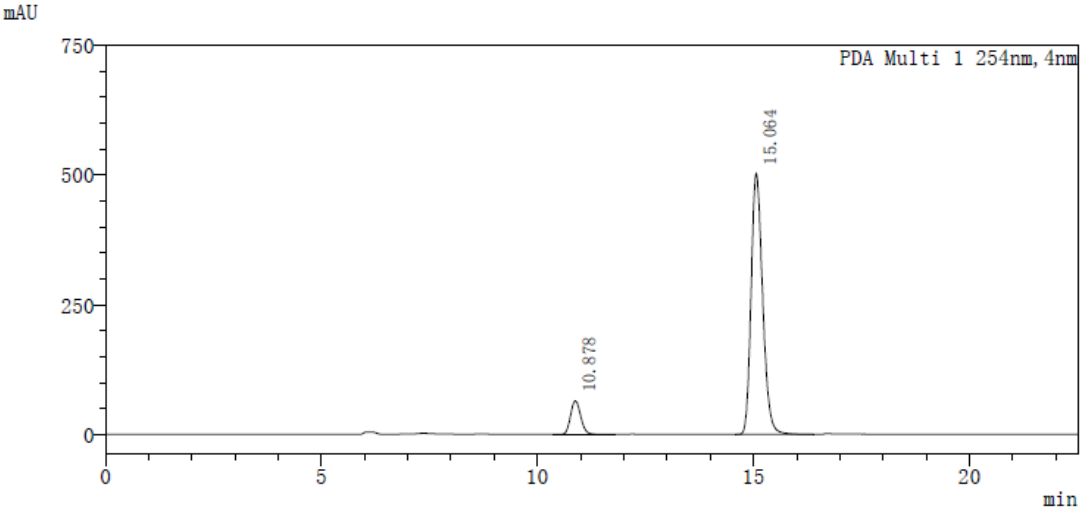



**2i**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(minor) = 10.9 min, t(major) = 15.1 min, 90:10 er.



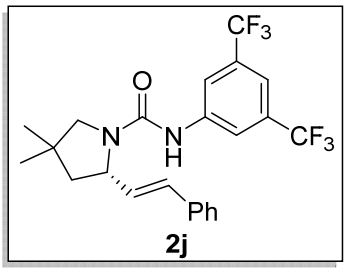

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 10.884 | 747002 | 11107427 | 49.933 |
| 15.133 | 564227 | 11137028 | 50.067 |

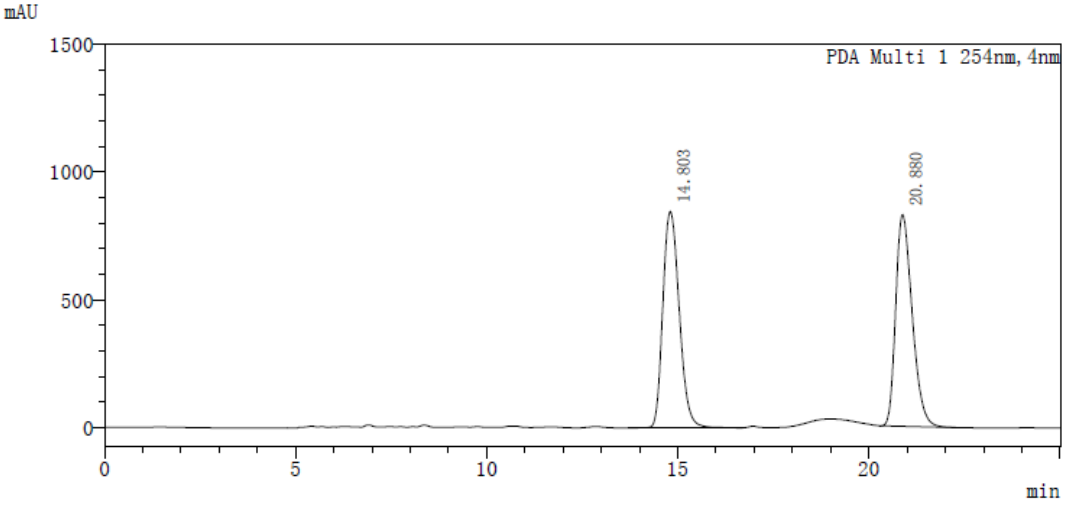



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 10.878 | 64442 | 1061501 | 10.217 |
| 15.064 | 502860 | 9328300 | 89.783 |

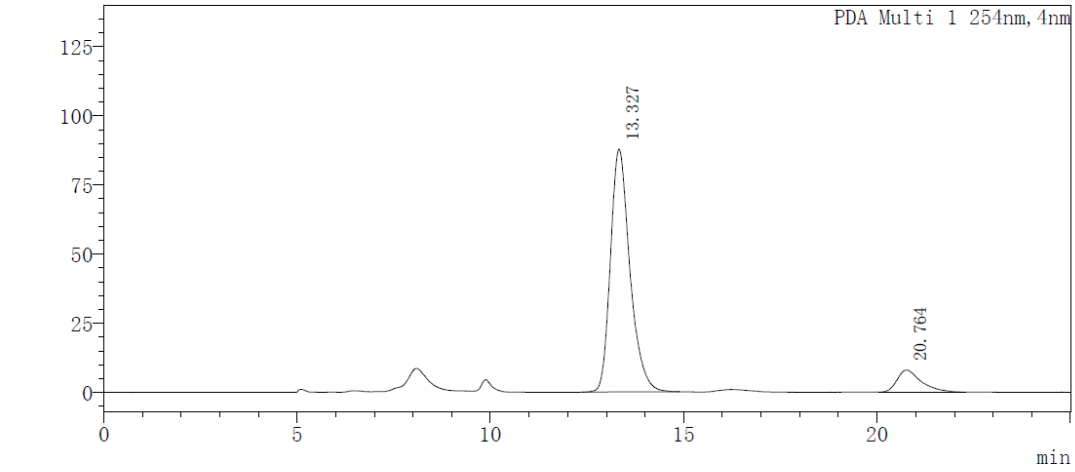



**2j**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 13.3 min, t(minor) = 20.8 min, 90:10 er.



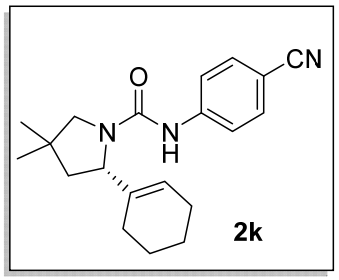

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 14.803 | 847099 | 25327353 | 50.445 |
| 20.880 | 828426 | 24880442 | 49.555 |

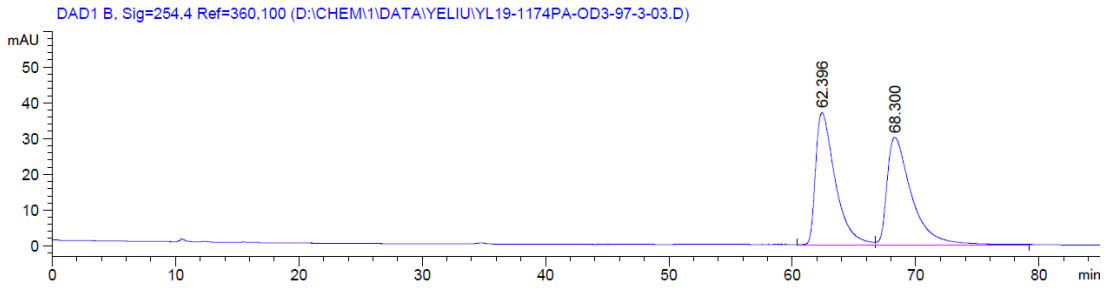



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 13.327 | 87825 | 3077339 | 89.993 |
| 20.764 | 7960 | 342186 | 10.007 |

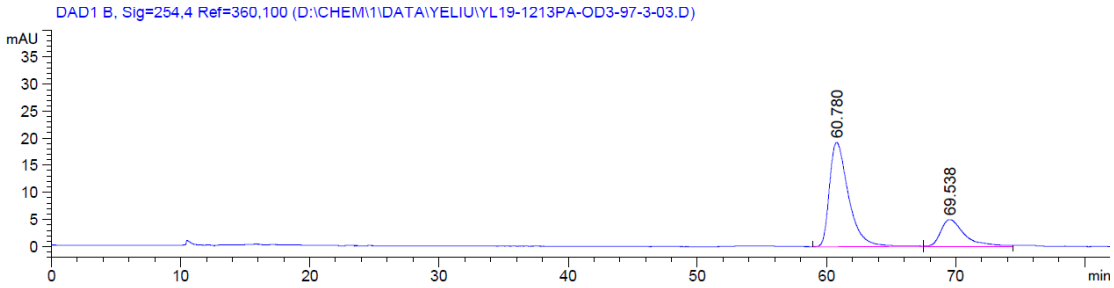



**2k**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane =97/3, flow rate 0.3 mL/min. λ = 254 nm, t(major) =60.8 min, t(minor) = 69.5 min, 76:24 er.



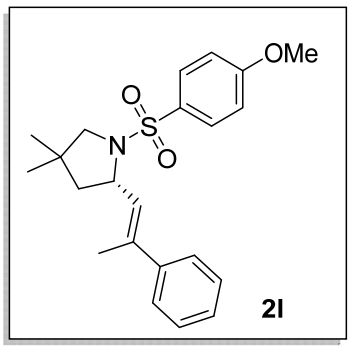

Signal 2: DAD1 B, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 62.396 | BV | 1.6440 | 4048.45679 | 36.89947 | 49.6989 |
| 2 | 68.300 | VB | 2.0164 | 4097.51758 | 30.02031 | 50.3011 |

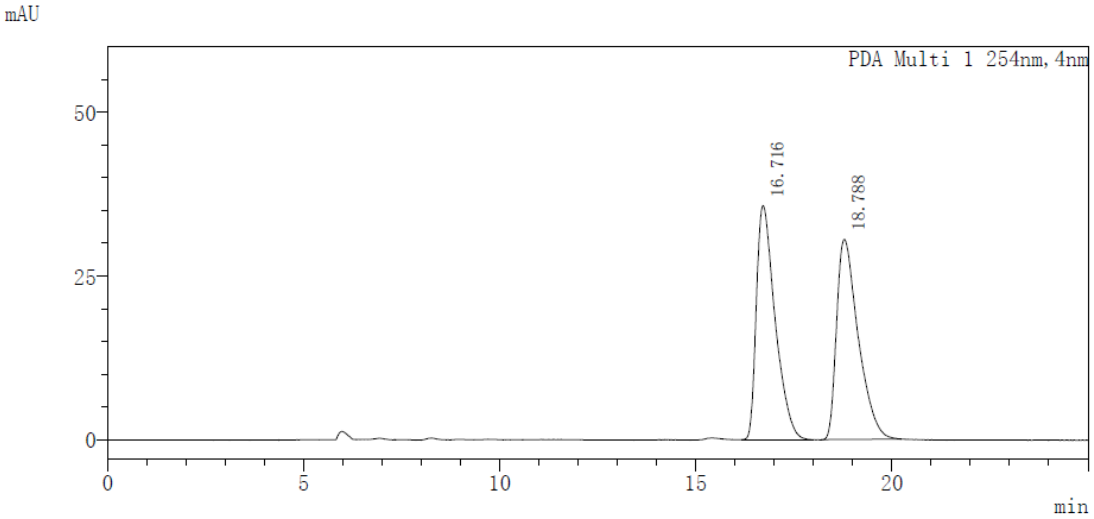



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 60.780 | BV | 1.5394 | 1974.55103 | 19.27051 | 75.5991 |
| 2 | 69.538 | VV | 1.8411 | 637.32129 | 4.96671 | 24.4009 |

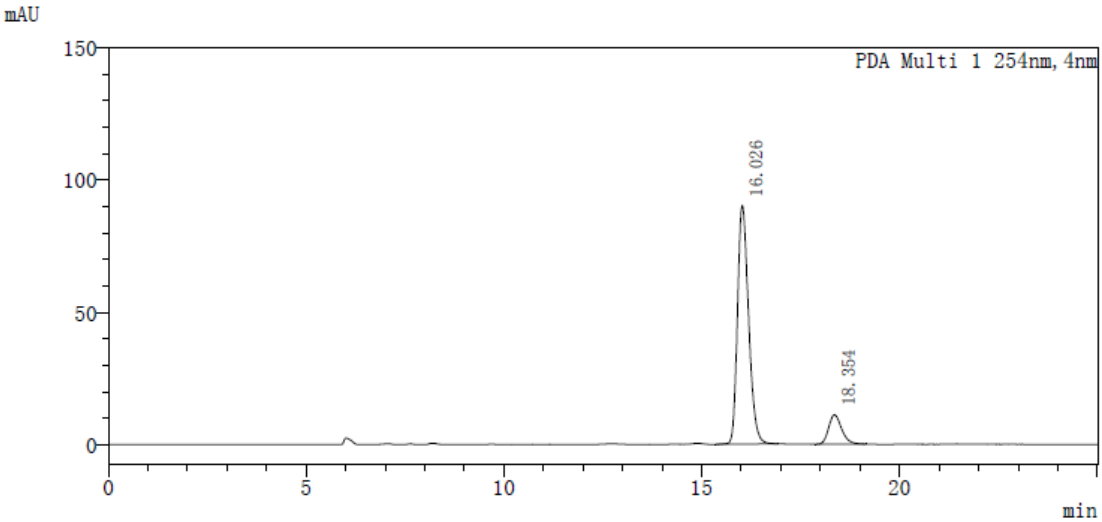



**2l**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 16.0 min, t(minor) = 18.4 min, 87:13 er.



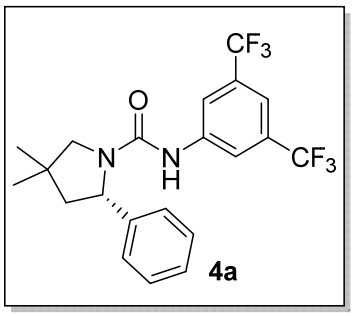

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 16.716 | 35676 | 1186252 | 50.294 |
| 18.788 | 30549 | 1172386 | 49.706 |

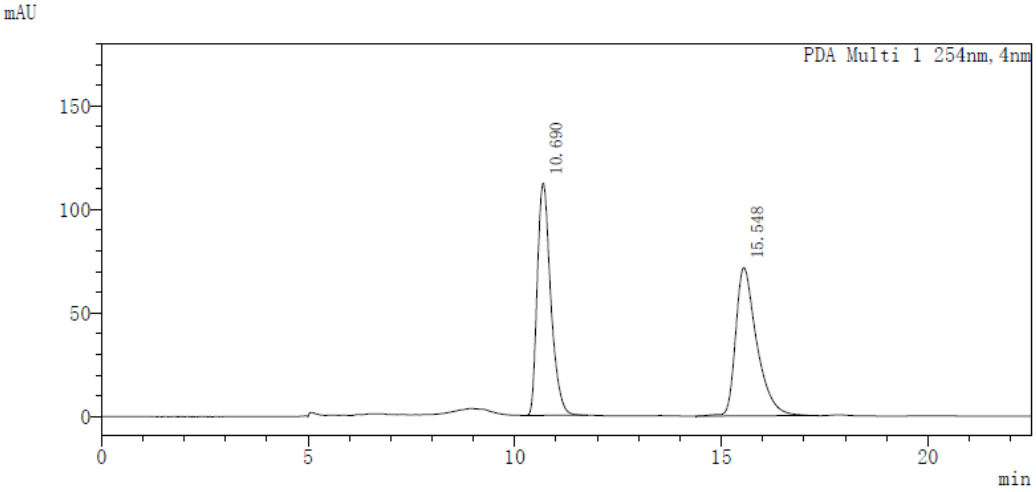



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 16.026 | 90181 | 1761082 | 87.395 |
| 18.354 | 11106 | 253992 | 12.605 |

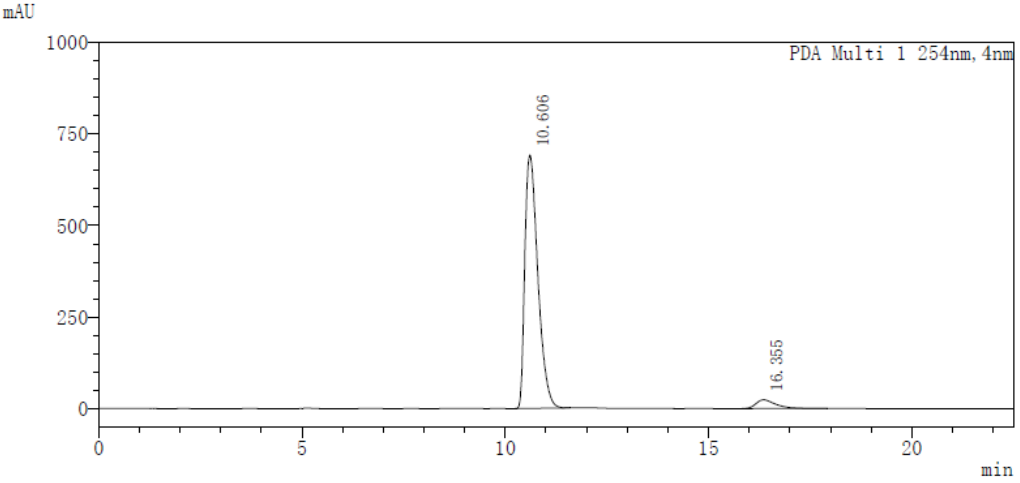



**4a** HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 10.6 min, t(minor) = 16.4 min, 95:5 er.



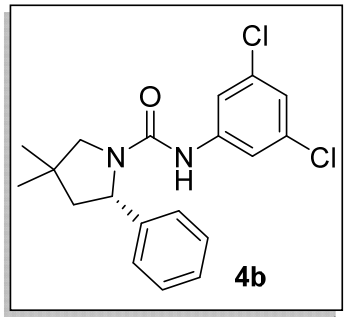

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 10.690 | 112186 | 2541789 | 49.895 |
| 15.548 | 71624 | 2552516 | 50.105 |

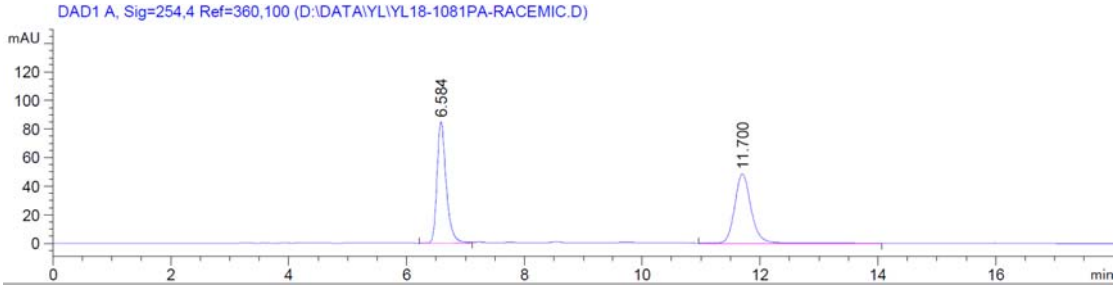



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 10.606 | 691696 | 15377548 | 95.047 |
| 16.355 | 23674 | 801387 | 4.953 |

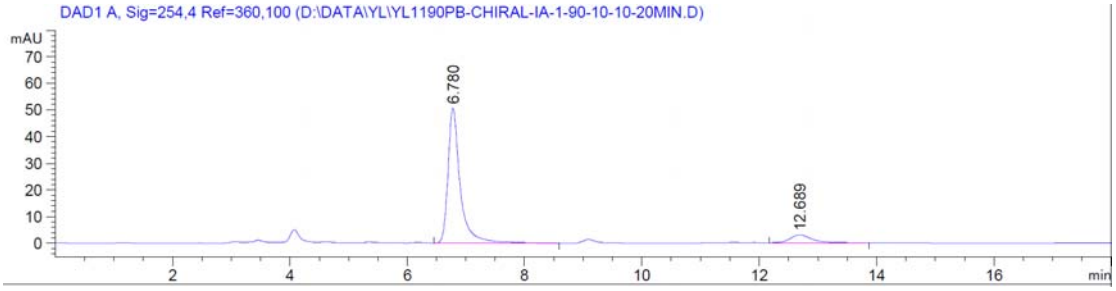



**4b**, HPLC condition: Chiralcel IA, *i*-PrOH/*n*-hexane = 90/10, flow rate 1.0 mL/min. λ = 254 nm, t(major) = 6.8 min, t(minor) = 12.7 min, 91:9 er.



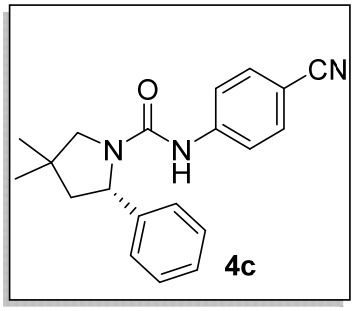

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.584 | BV | 0.1622 | 921.12390 | 85.15656 | 49.8263 |
| 2 | 11.700 | BV | 0.2945 | 927.54657 | 48.63167 | 50.1737 |

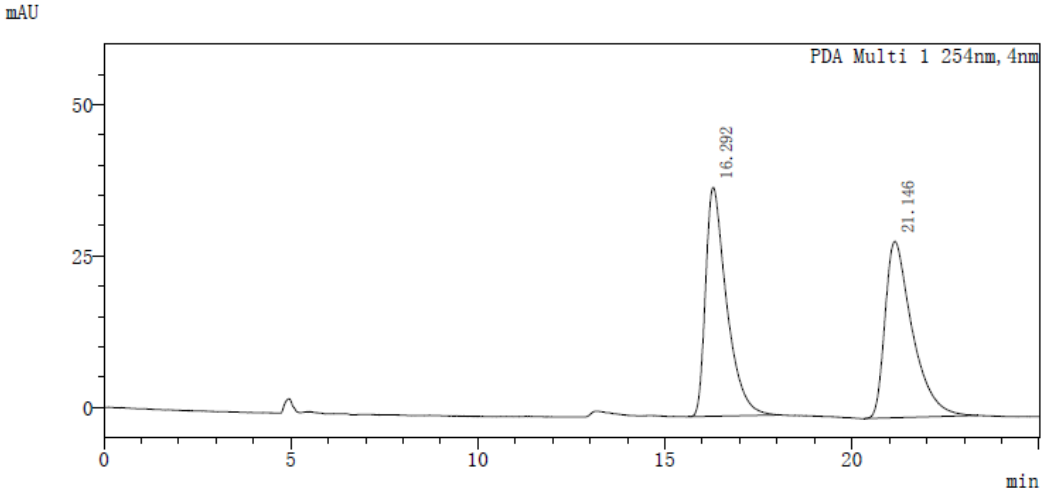



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.780 | BB | 0.2119 | 736.43317 | 50.55672 | 90.8121 |
| 2 | 12.689 | BB | 0.3787 | 74.50823 | 2.93006 | 9.1879 |

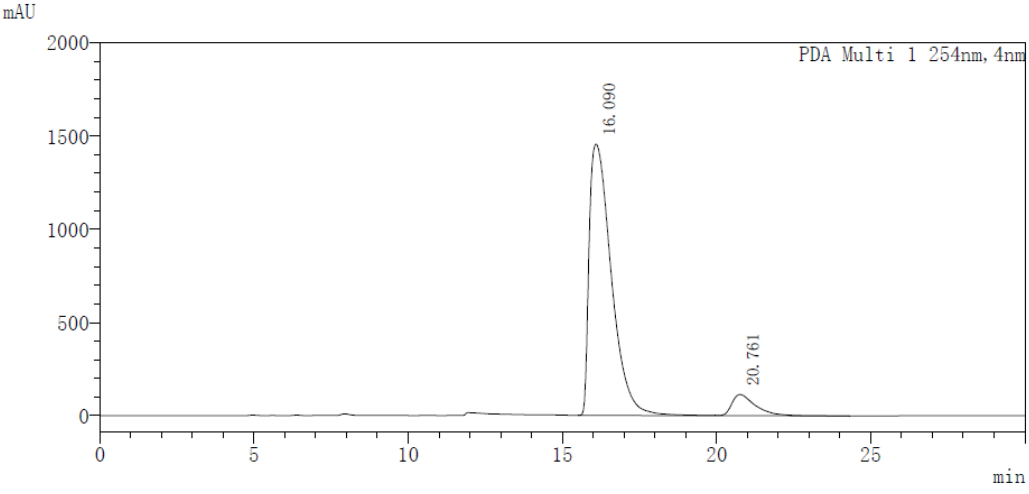



**4c**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 85/15, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 16.1 min, t(minor) = 20.8 min, 92:8 er.



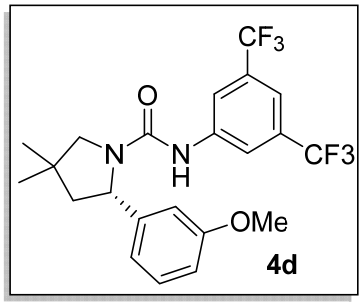

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 16.292 | 37797 | 1483007 | 50.054 |
| 21.146 | 29106 | 1479782 | 49.946 |

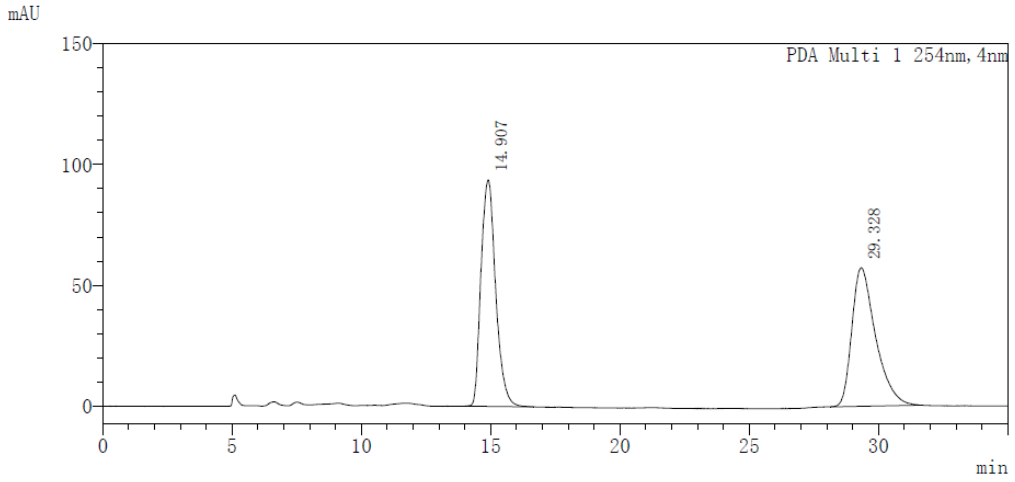



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 16.090 | 1454650 | 72641019 | 92.326 |
| 20.761 | 113867 | 6037824 | 7.674 |

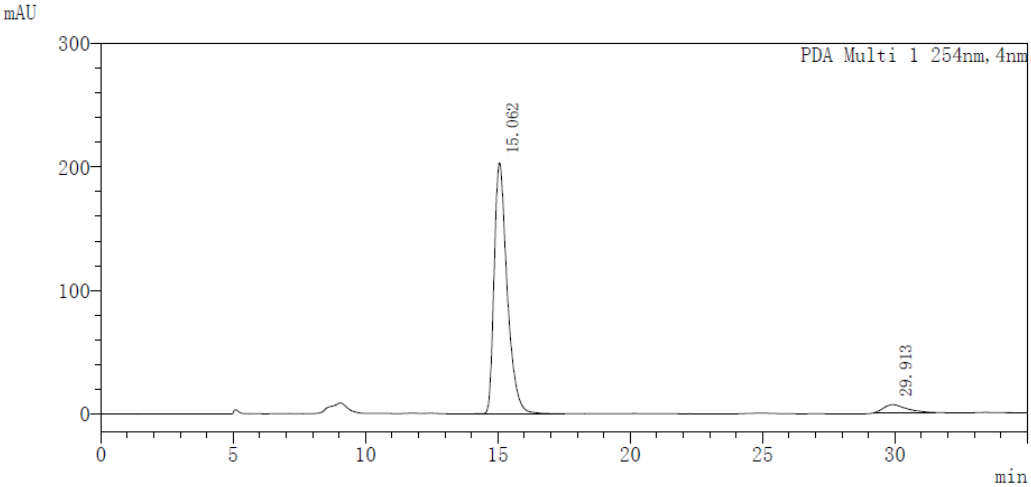



**4d**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 15.1 min, t(minor) = 29.9 min, 95:5 er.



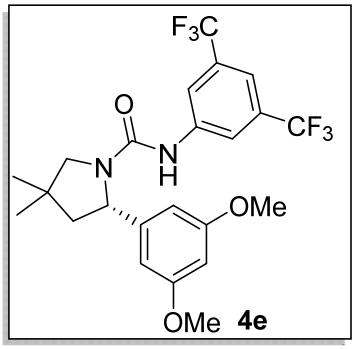

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 14.907 | 93793 | 3702332 | 50.281 |
| 29.328 | 57269 | 3660976 | 49.719 |

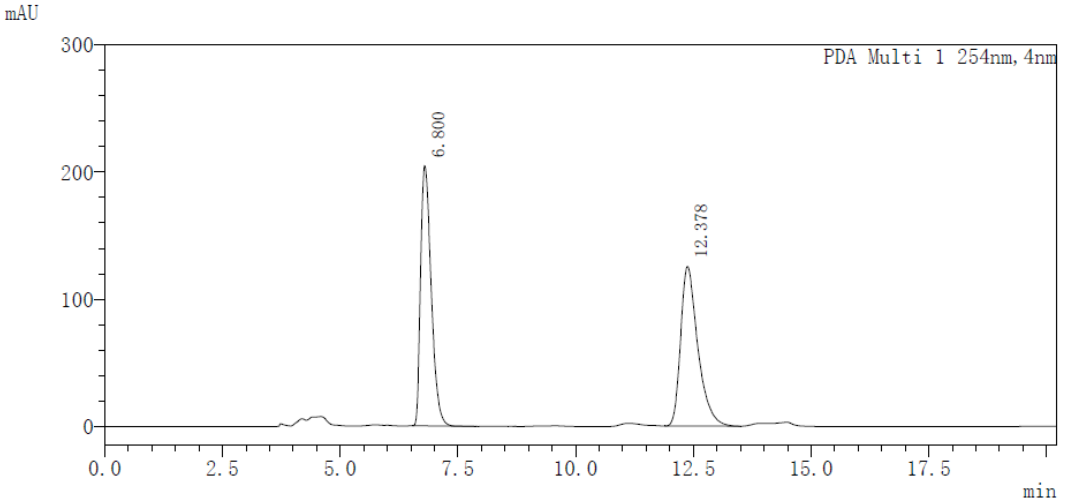



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 15.062 | 203424 | 6978598 | 94.896 |
| 29.913 | 6254 | 375356 | 5.104 |

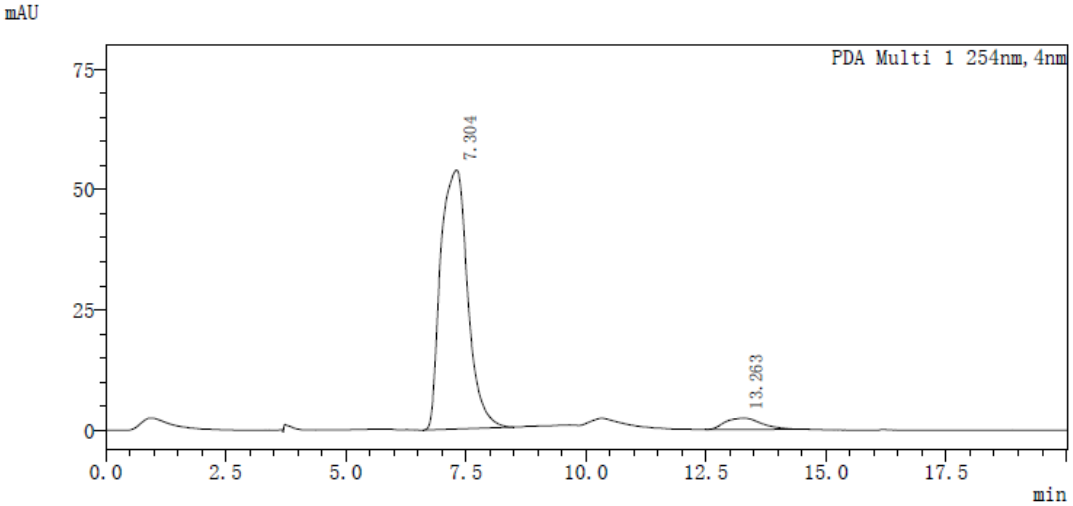



**4e**, HPLC condition: Chiralcel AD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.8 mL/min. λ = 254 nm, t(major) = 7.3 min, t(minor) = 13.3 min, 94.5:5.5 er.



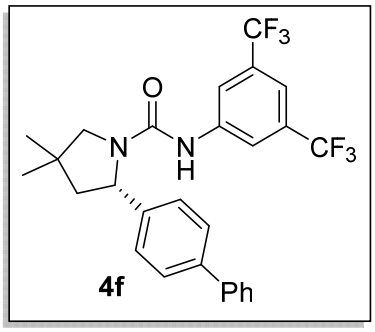

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 6.800 | 204358 | 3206130 | 50.140 |
| 12.378 | 125410 | 3188207 | 49.860 |

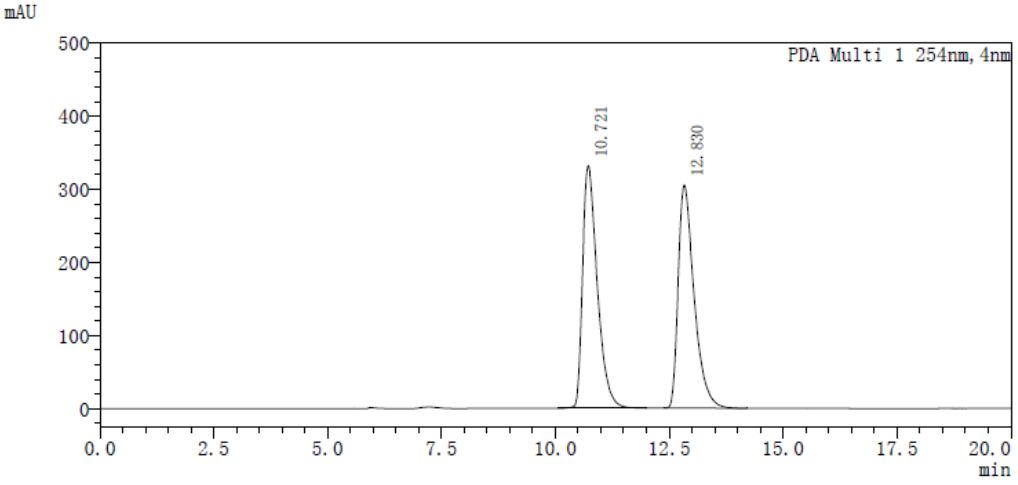



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 7.304 | 53747 | 2099902 | 94.469 |
| 13.263 | 2339 | 122941 | 5.531 |

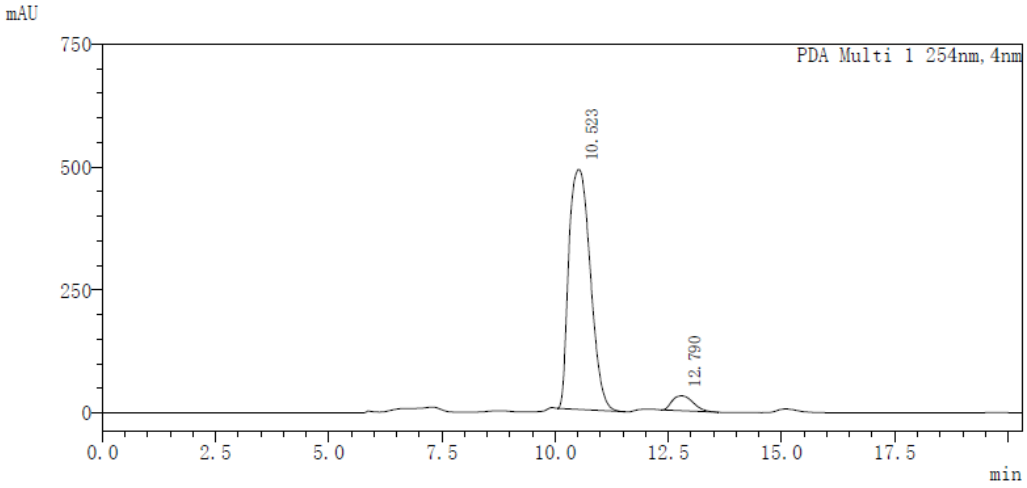



**4f**, HPLC condition: Chiralcel AD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 10.5 min, t(minor) = 12.8 min, 94:6 er.



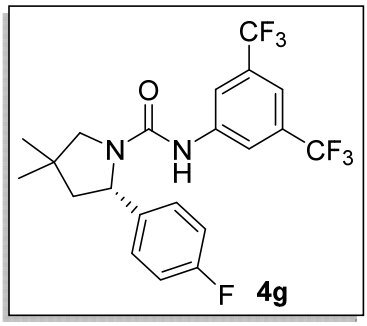

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 10.721 | 331349 | 7427921 | 50.066 |
| 12.830 | 305030 | 7408255 | 49.934 |

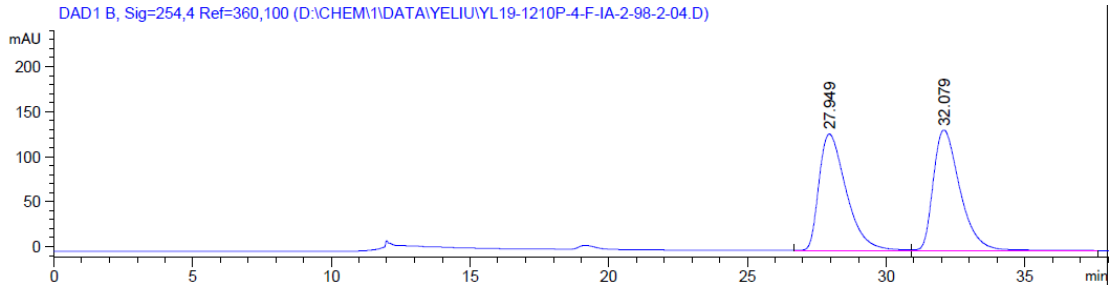



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 10.523 | 488697 | 16144737 | 94.266 |
| 12.790 | 30295 | 982065 | 5.734 |

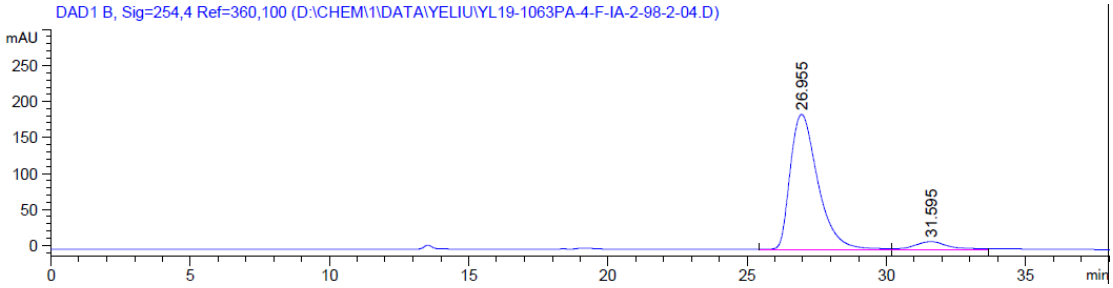



**4g**, HPLC condition: Chiralcel IA, *i*-PrOH/*n*-hexane = 98/2, flow rate 0.4 mL/min. λ = 254 nm, t(major) = 26.9 min, t(minor) = 31.6 min, 94:6 er.



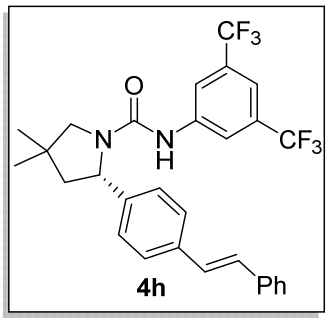

Signal 2: DAD1 B, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 27.949 | BV | 1.0432 | 8822.51660 | 129.43439 | 49.6936 |
| 2 | 32.079 | VB | 1.0300 | 8931.31934 | 133.92444 | 50.3064 |

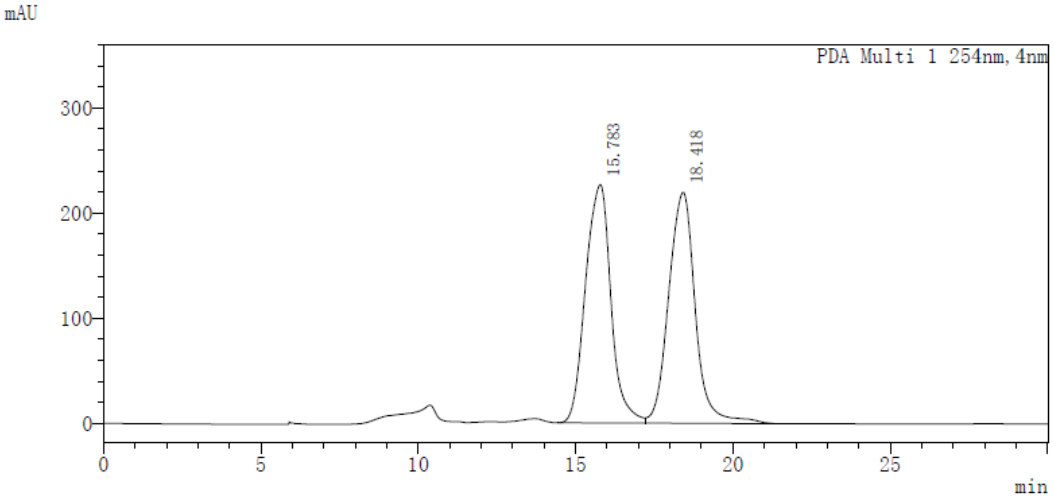



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 26.955 | BV | 1.0656 | 1.28801e4 | 187.45976 | 93.6796 |
| 2 | 31.595 | VV | 1.2307 | 868.99628 | 10.80079 | 6.3204 |

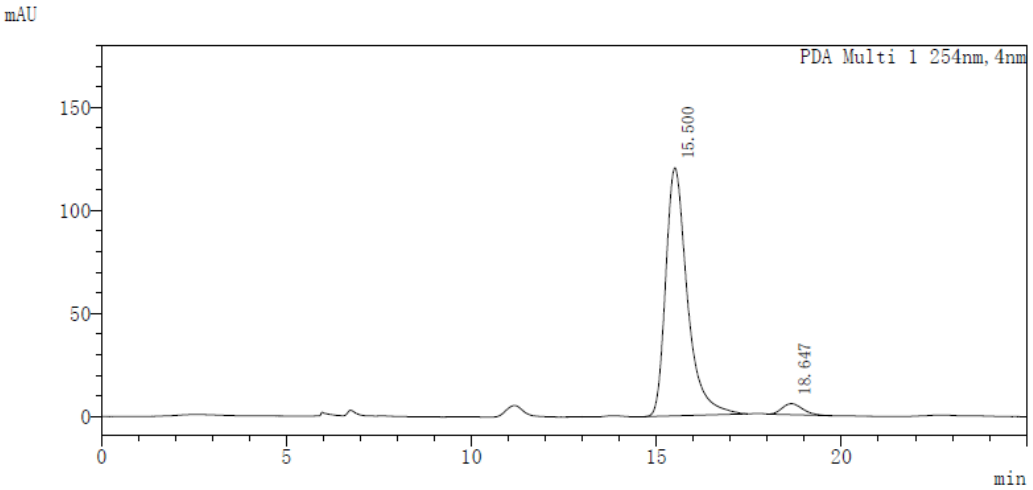



**4h**, HPLC condition: Chiralcel IA, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 15.5 min, t(minor) = 18.7 min, 96:4 er.



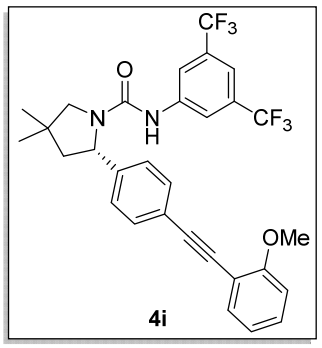

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 15.783 | 226572 | 12749093 | 49.604 |
| 18.418 | 219687 | 12952506 | 50.396 |

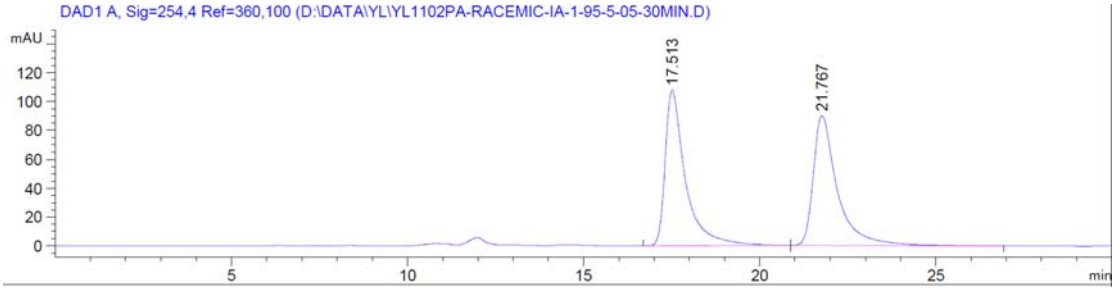



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 15.500 | 120368 | 4900510 | 95.935 |
| 18.647 | 5398 | 207632 | 4.065 |

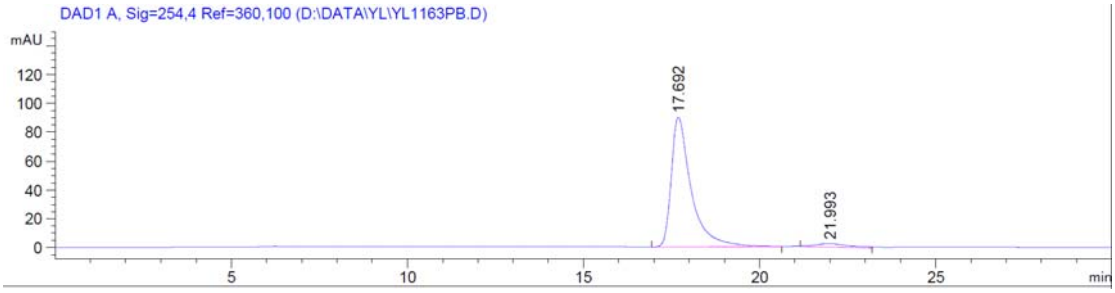



**4i,** HPLC condition: Chiralcel IA, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 17.7 min, t(minor) = 22.0 min, 96:4 er.

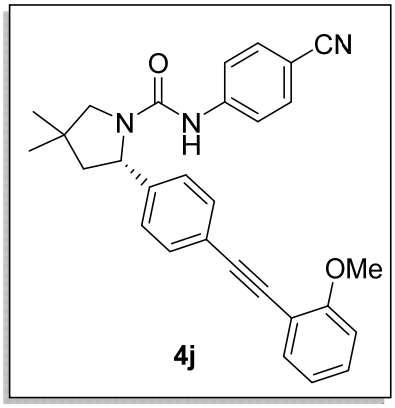



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

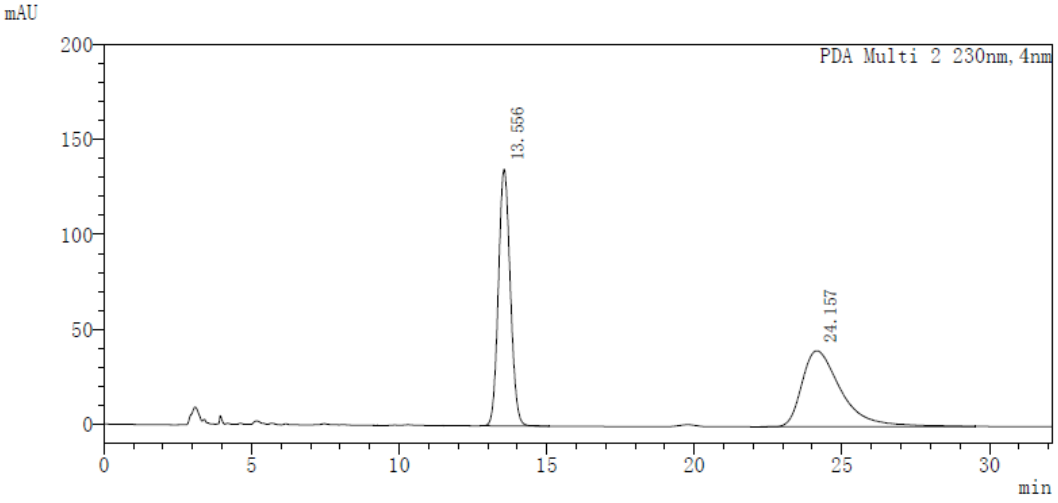
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 17.513 | BB | 0.5812 | 4318.60498 | 107.83671 | 50.0836 |
| 2 | 21.767 | BB | 0.6964 | 4304.19434 | 89.93429 | 49.9164 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 17.692 | BB | 0.5762 | 3540.71045 | 89.76898 | 95.6155 |
| 2 | 21.993 | MM R | 1.0766 | 162.36003 | 2.51339 | 4.3845 |

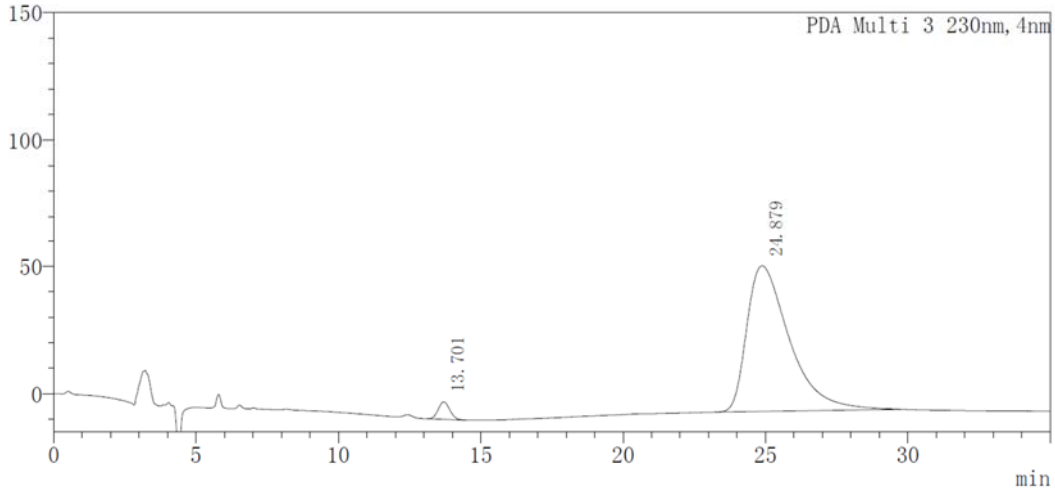



**4j,** HPLC condition: Chiralcel AD-H, *i*-PrOH/*n*-hexane = 75/25, flow rate 1.0 mL/min. λ = 230 nm, t(minor) = 13.7 min, t(major) = 24.9 min, 97:3 er.



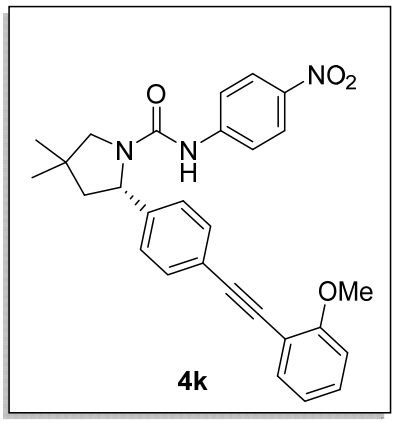

PDA Ch2 230nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 13.556 | 135331 | 3785004 | 50.477 |
| 24.157 | 40084 | 3713483 | 49.523 |

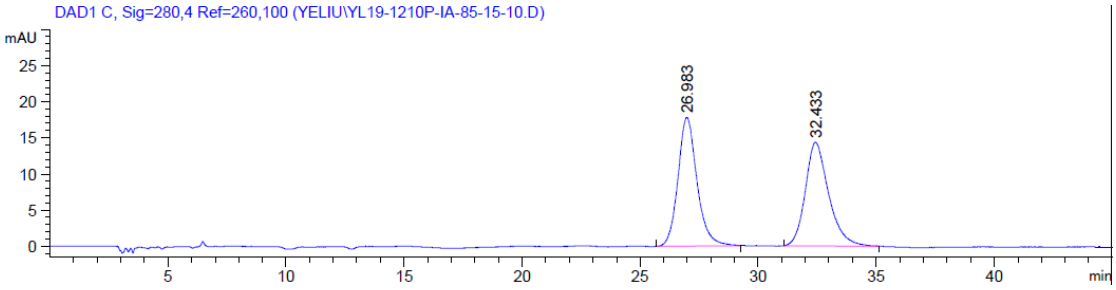



PDA Ch3 230nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 13.701 | 6884 | 195130 | 3.171 |
| 24.879 | 57149 | 5958344 | 96.829 |

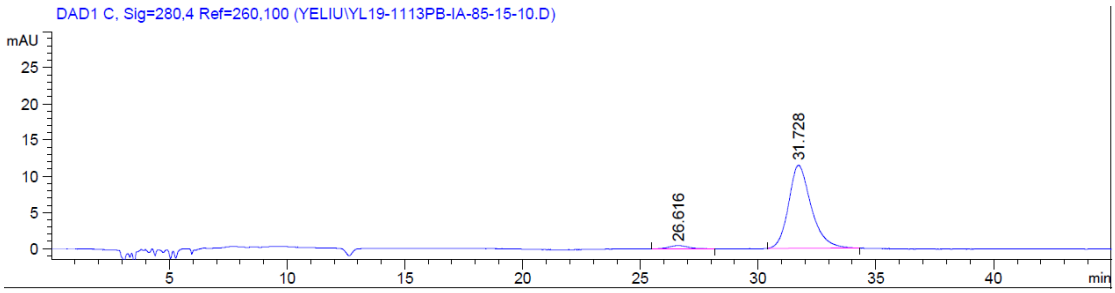



**4k**, HPLC condition: Chiralcel IA, *i*-PrOH/*n*-hexane = 85/15, flow rate 1.0 mL/min. λ = 280 nm, t(minor) = 26.6 min, t(major) = 31.7 min, 96.5:3.5 er.



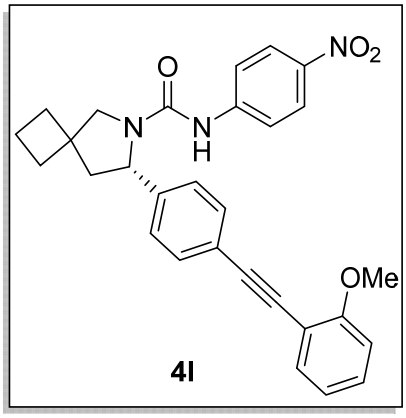

Signal 3: DAD1 C, Sig=280,4 Ref=260,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 26.983 | BB | 0.7927 | 997.63281 | 17.83261 | 50.2570 |
| 2 | 32.433 | BB | 0.9233 | 987.43036 | 14.34117 | 49.7430 |



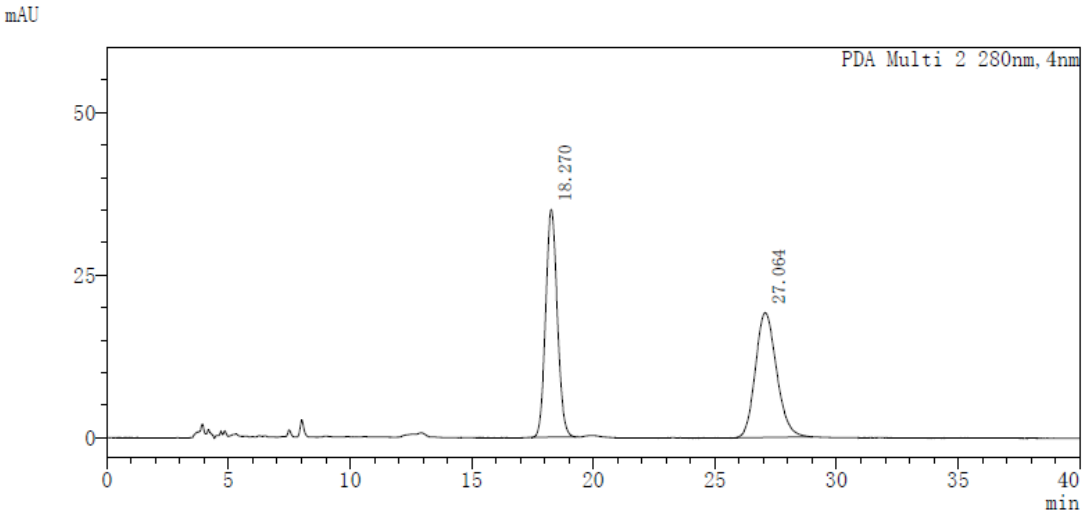

Signal 3: DAD1 C, Sig=280,4 Ref=260,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 26.616 | MM R | 0.9846 | 28.43053 | 4.81239e-1 | 3.5692 |
| 2 | 31.728 | BB | 0.9004 | 768.11865 | 11.48307 | 96.4308 |



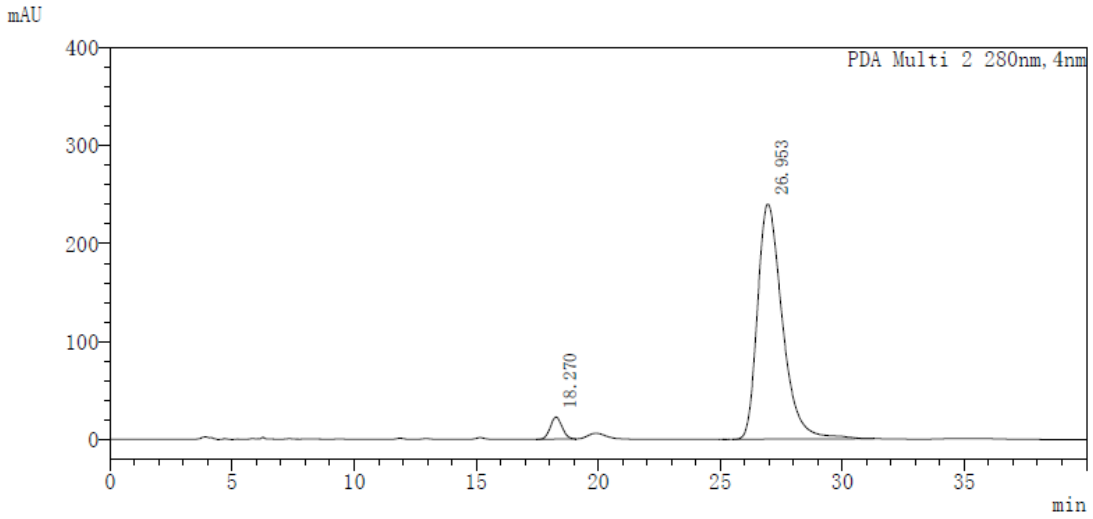

**4l**

**4l**, HPLC condition: Chiralcel AD-H, *i*-PrOH/*n*-hexane = 70/30, flow rate 1.0 mL/min. λ = 280 nm, t(minor) = 18.3 min, t(major) = 27.0 min, 96:4 er.



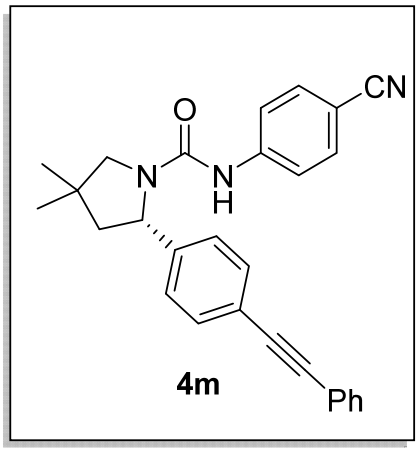

PDA Ch2 280nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 18.270 | 35020 | 1165926 | 50.036 |
| 27.064 | 19208 | 1164237 | 49.964 |

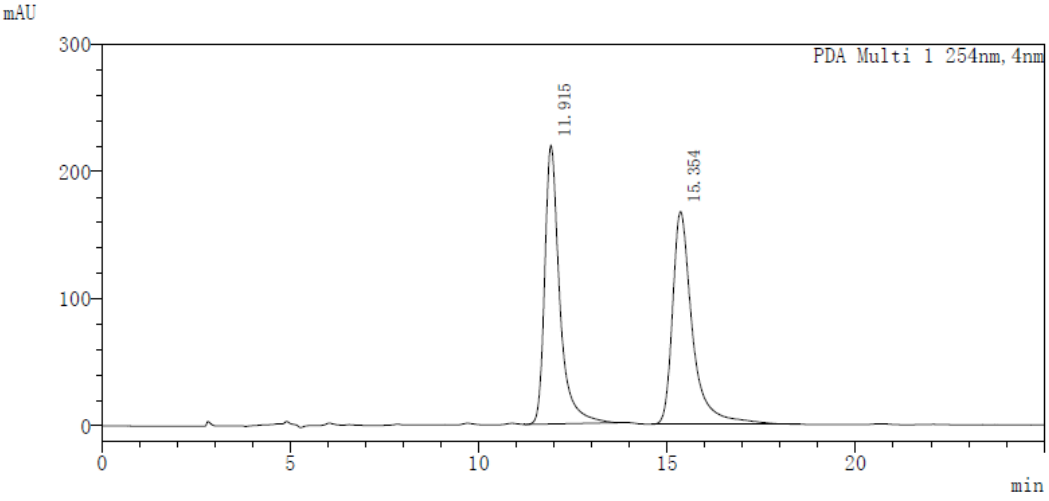



PDA Ch2 280nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 18.270 | 22468 | 750124 | 4.211 |
| 26.953 | 240264 | 17062663 | 95.789 |

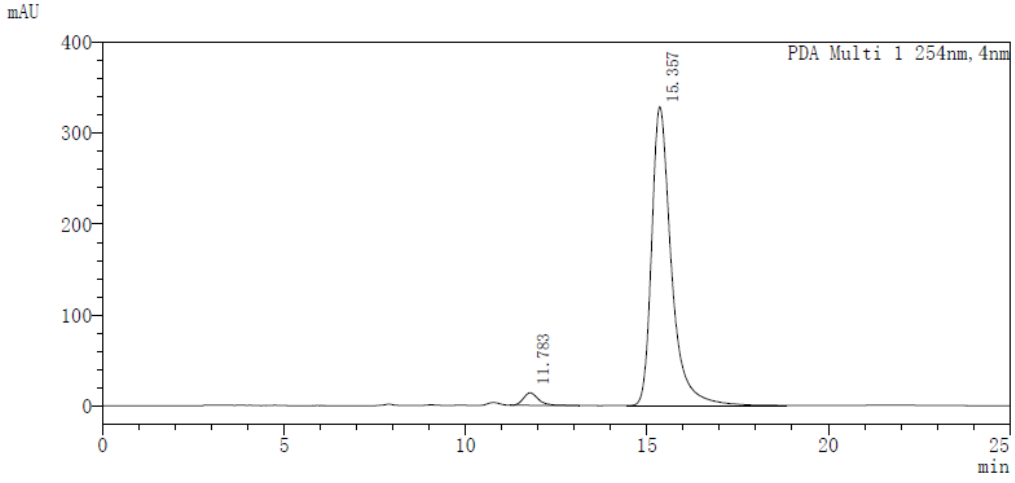



**4m,** HPLC condition: Chiralcel IA, *i*-PrOH/*n*-hexane = 80/20, flow rate 1.0 mL/min. λ = 254 nm, t(minor) = 11.8 min, t(major) = 15.4 min, 97:3 er.



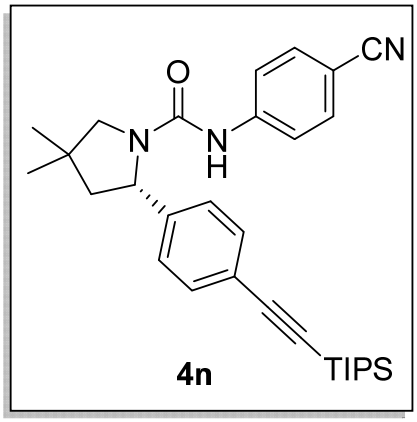

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 11.915 | 219037 | 6048885 | 49.485 |
| 15.354 | 167353 | 6174746 | 50.515 |

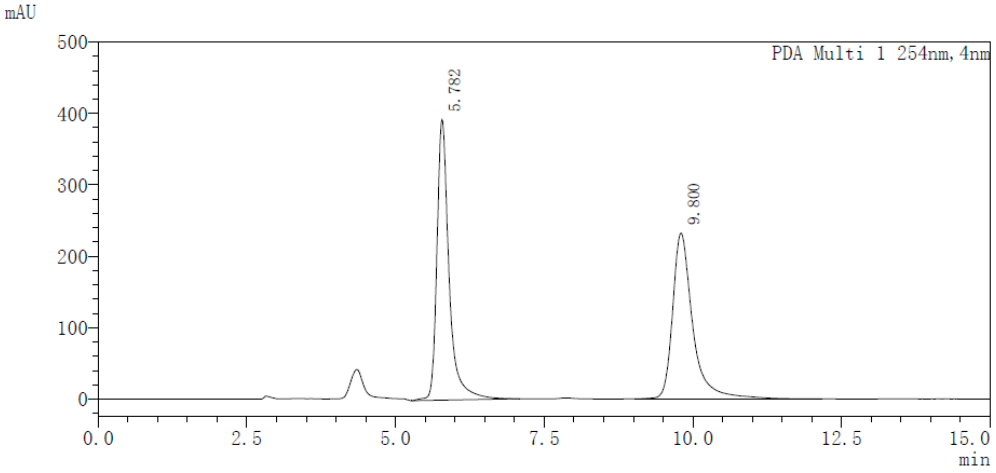



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 11.783 | 13672 | 393224 | 3.069 |
| 15.357 | 328811 | 12418723 | 96.931 |

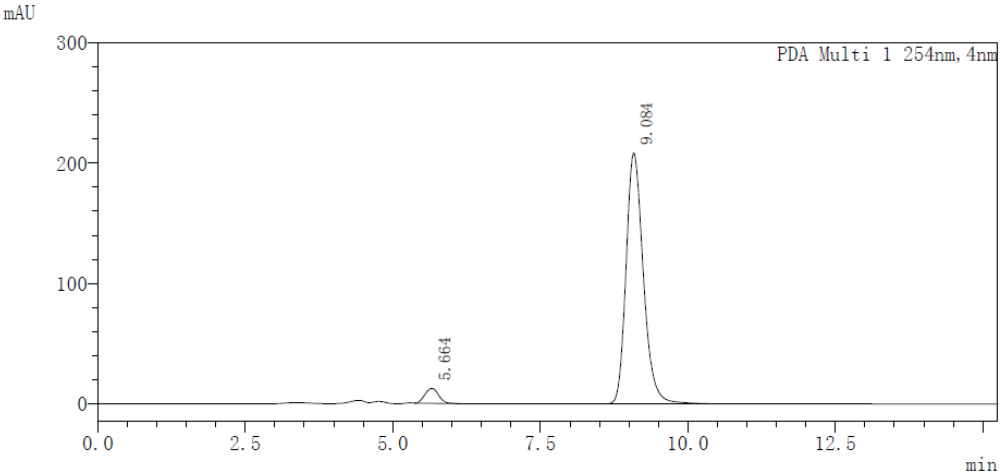



**4n,** HPLC condition: Chiralcel IA, *i*-PrOH/*n*-hexane = 80/20, flow rate 1.0 mL/min. λ = 254 nm, t(minor) = 5.7 min, t(major) = 9.1 min, 95.5:4.5 er.



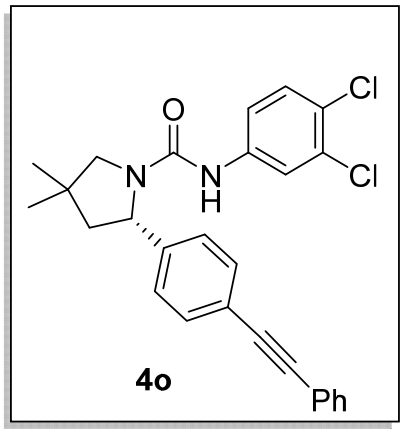

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 5.782 | 393104 | 5594260 | 50.624 |
| 9.800 | 231990 | 5456325 | 49.376 |

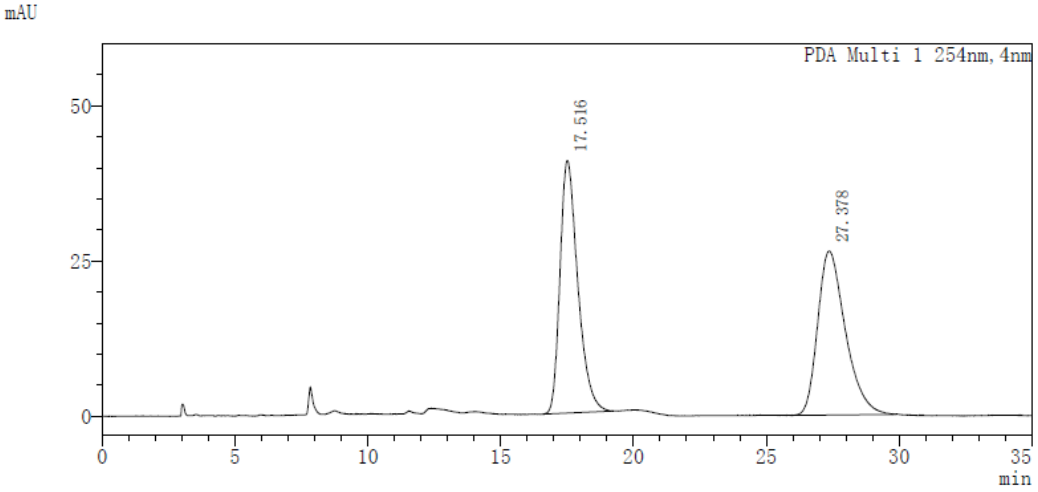



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 5.664 | 12402 | 200522 | 4.508 |
| 9.084 | 208508 | 4247369 | 95.492 |

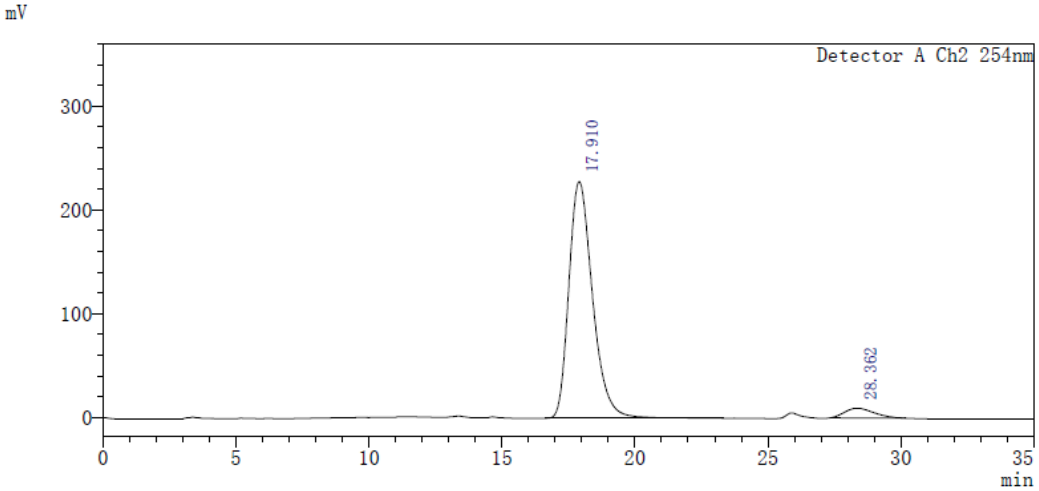



**4o**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 1.0 mL/min. λ = 254 nm, t(major) = 17.9 min, t(minor) = 28.4 min, 95:5 er.



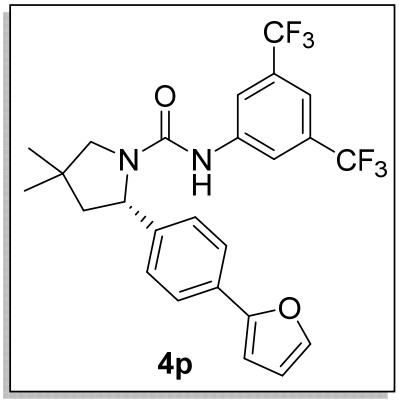

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 17.516 | 40688 | 1901659 | 49.805 |
| 27.378 | 26408 | 1916512 | 50.195 |

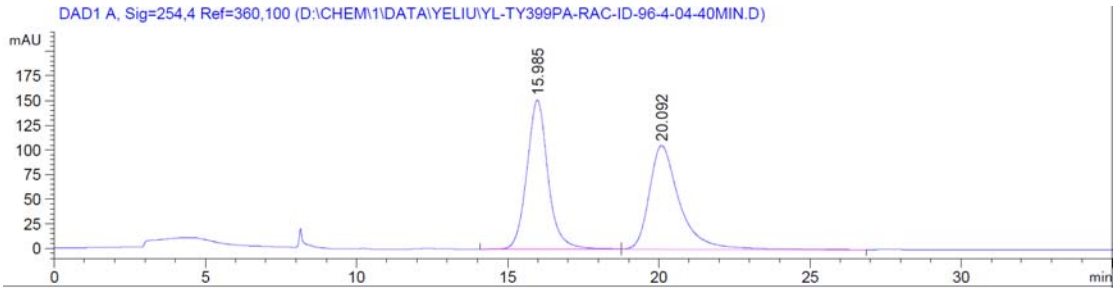



Detector A Ch2 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 17.910 | 228130 | 14163127 | 95.182 |
| 28.362 | 9371 | 716900 | 4.818 |

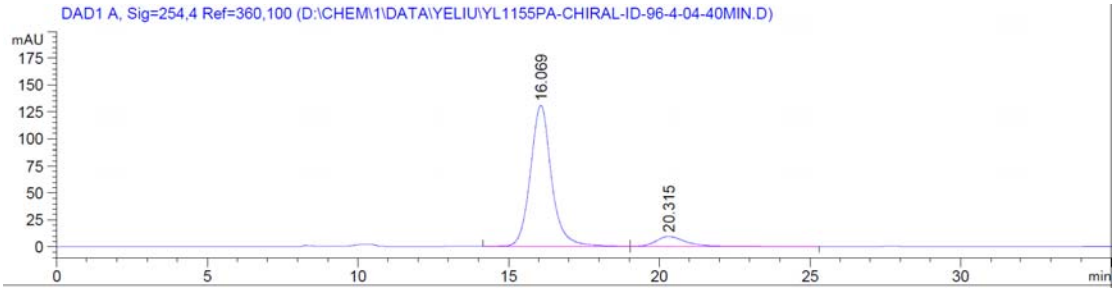



**4p,** HPLC condition: Chiralcel ID, *i*-PrOH/*n*-hexane = 96/4, flow rate 0.4 mL/min. λ = 254 nm, t(major) = 16.1 min, t(minor) = 20.3 min, 91:9 er.



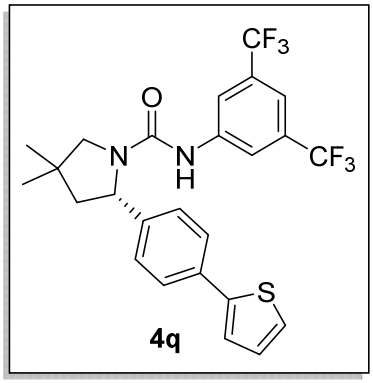

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 15.985 | BV | 0.7424 | 7464.87451 | 151.61041 | 50.2034 |
| 2 | 20.092 | VV | 1.0427 | 7404.38623 | 105.50870 | 49.7966 |

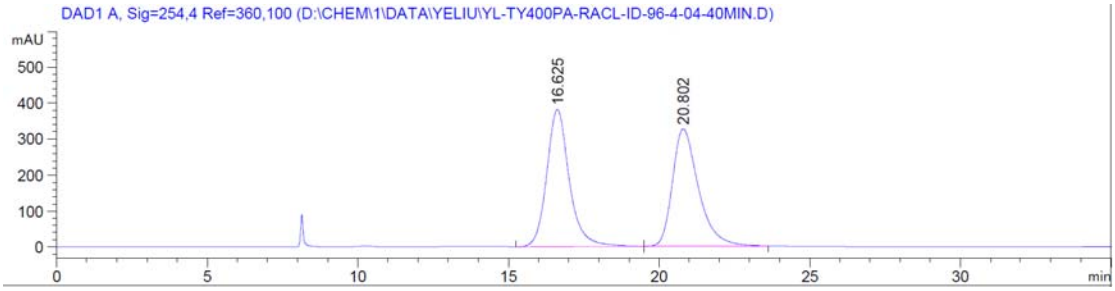



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.069 | VV | 0.7419 | 6442.18652 | 130.95869 | 90.6113 |
| 2 | 20.315 | VB | 1.0597 | 667.50903 | 9.31883 | 9.3887 |

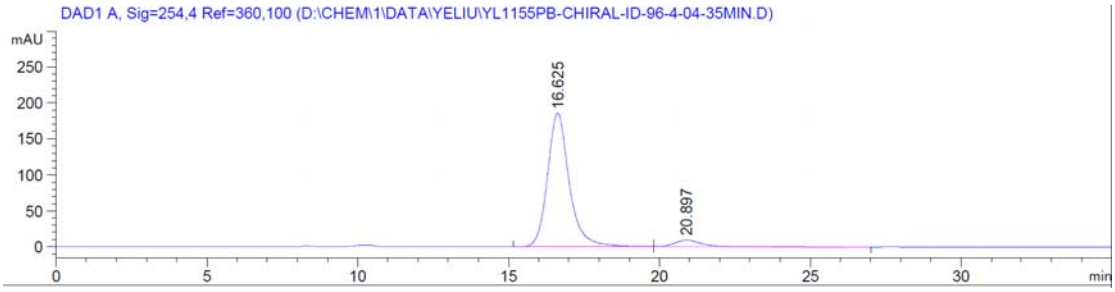



**4q,** HPLC condition: Chiralcel ID, *i*-PrOH/*n*-hexane = 96/4, flow rate 0.4 mL/min. λ = 254 nm, t(major) = 16.6 min, t(minor) = 20.9 min, 94:6 er.



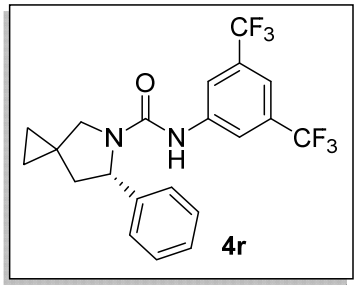

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.625 | BB | 0.7900 | 1.99101e4 | 380.80334 | 50.0914 |
| 2 | 20.802 | BV | 0.9230 | 1.98374e4 | 325.52408 | 49.9086 |

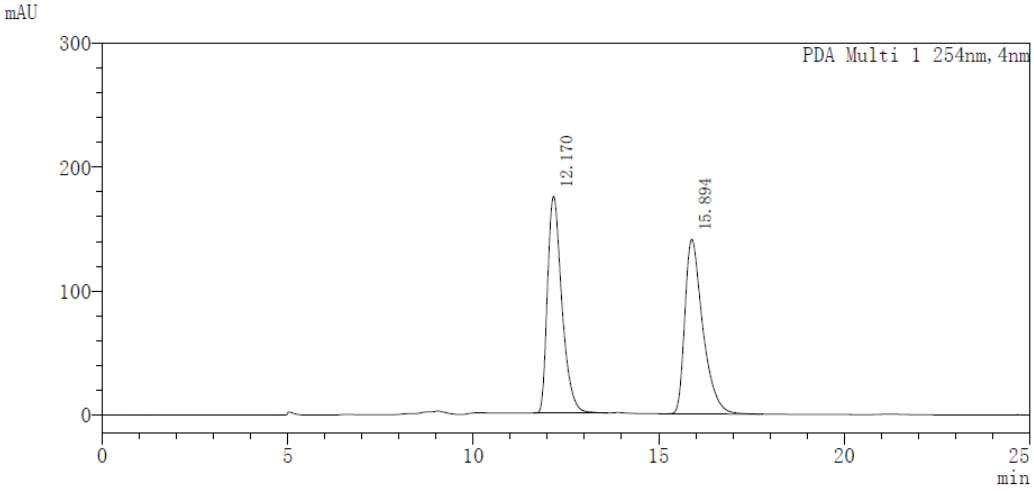



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.625 | VV | 0.7628 | 9390.16211 | 185.41672 | 93.5521 |
| 2 | 20.897 | VV | 1.0119 | 647.19409 | 9.43900 | 6.4479 |

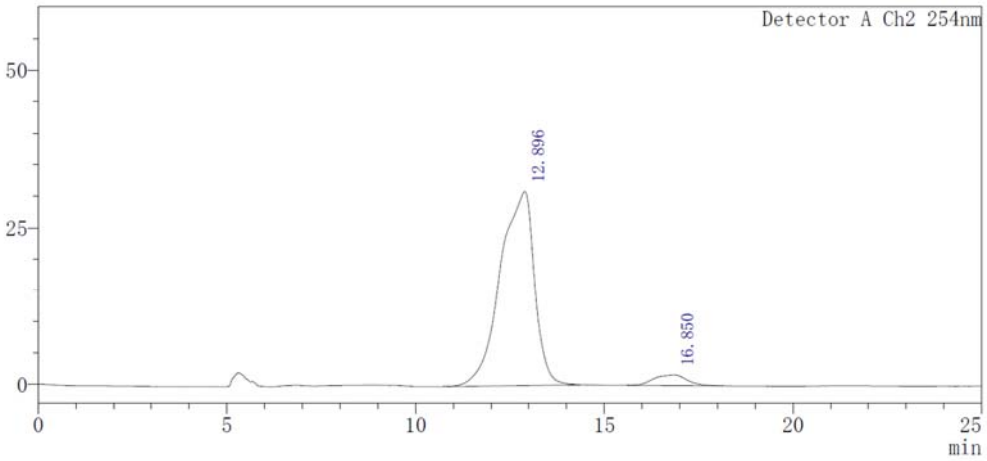



**4r,** HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 12.3 min, t(minor) = 16.0 min, 95:5 er.



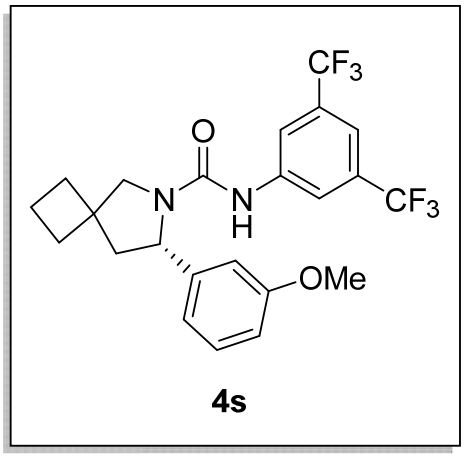

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 12.170 | 175127 | 4732898 | 50.005 |
| 15.894 | 140909 | 4732023 | 49.995 |



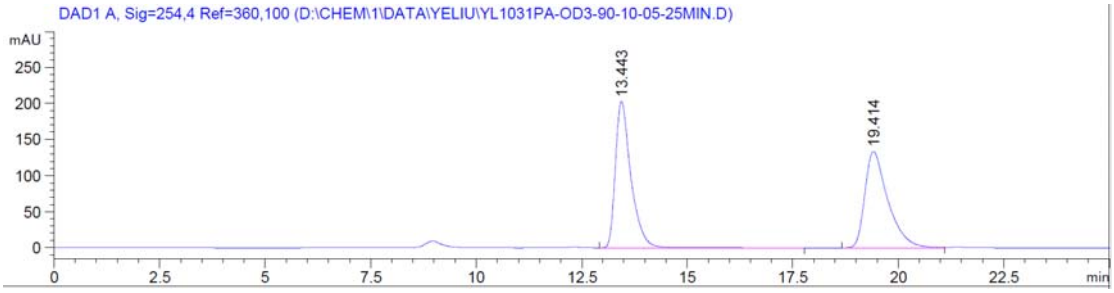

Detector A Ch2 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 12.896 | 30962 | 1959794 | 94.906 |
| 16.850 | 1705 | 105187 | 5.094 |
| | | | 100.000 |



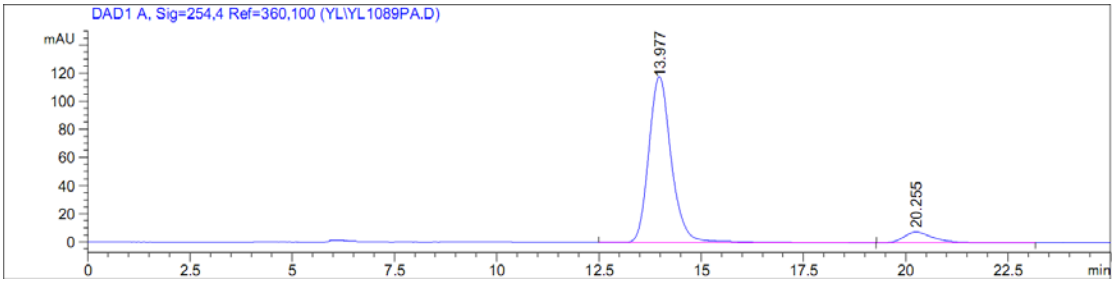

**4s**

**4s,** HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 14.0 min, t(minor) = 20.3 min, 92:8 er.



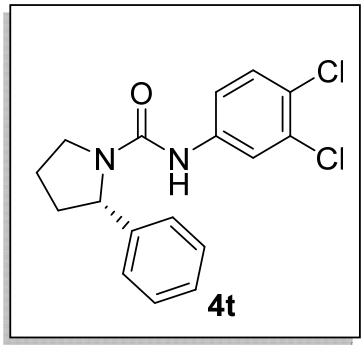

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 13.443 | BB | 0.3836 | 5213.37646 | 202.99559 | 50.5273 |
| 2 | 19.414 | BV | 0.5641 | 5104.55713 | 134.09773 | 49.4727 |

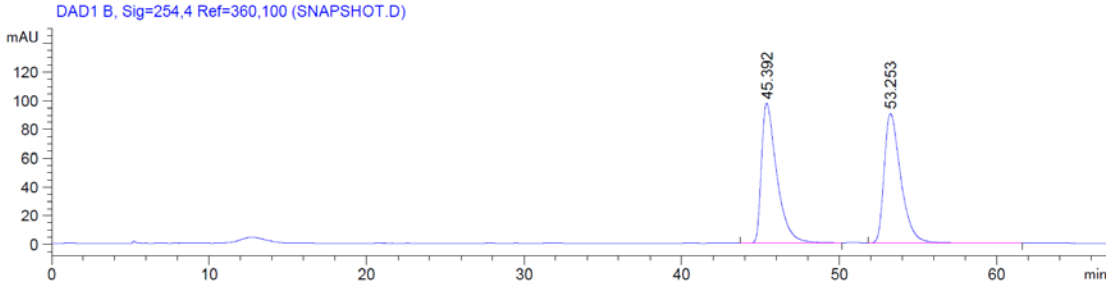



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 13.977 | BB | 0.5836 | 4529.45410 | 118.05036 | 92.2677 |
| 2 | 20.255 | BB | 0.7440 | 379.58371 | 7.68792 | 7.7323 |

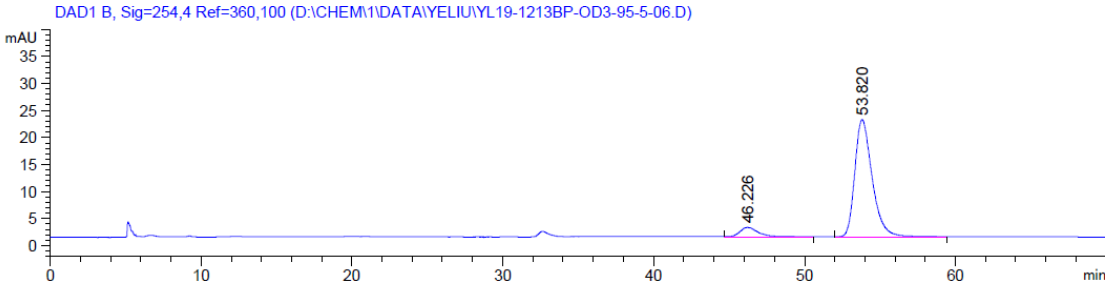



**4t**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.6 mL/min. λ = 254 nm, t(minor) = 46.2 min, t(minor) = 53.8 min, 92.5:7.5 er.



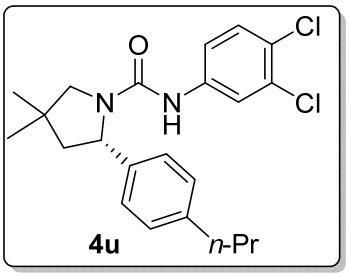

Signal 2: DAD1 B, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 45.392 | BV | 1.0204 | 6656.81152 | 97.03388 | 49.9147 |
| 2 | 53.253 | VB | 1.1202 | 6679.56201 | 90.17438 | 50.0853 |

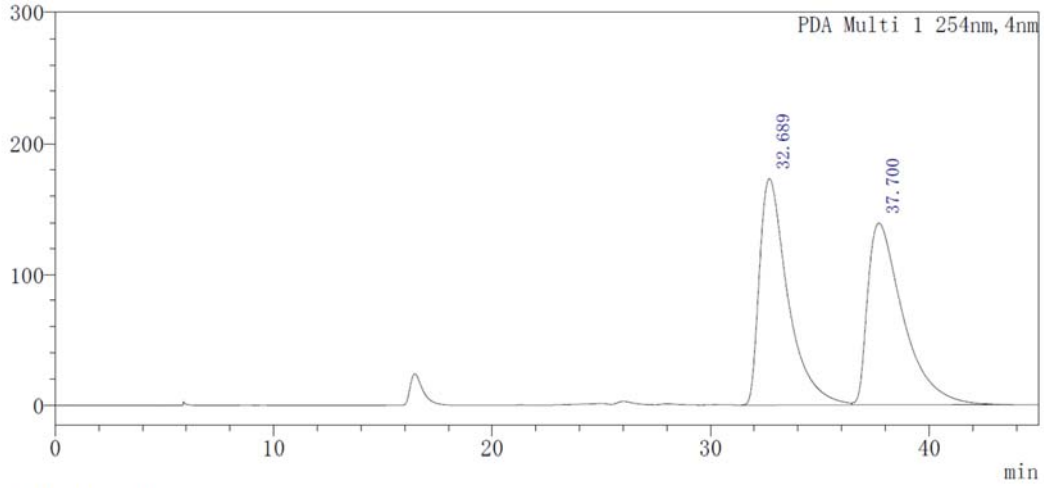



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 46.226 | VB | 1.2391 | 142.26128 | 1.71622 | 7.5970 |
| 2 | 53.820 | BV | 1.2158 | 1730.33655 | 21.66531 | 92.4030 |

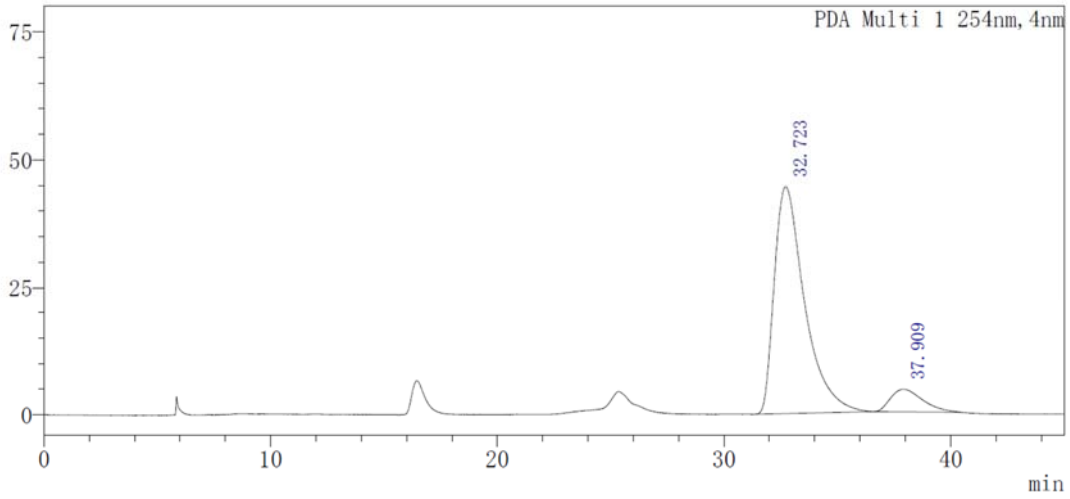



**4u**, Chiralcel AD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.5 mL/min. λ = 254 nm, t(major) = 32.7 min, t(minor) = 37.9 min, 90.5:9.5 er.



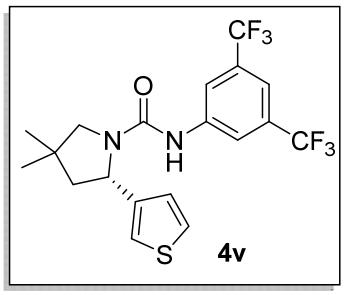

PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 32.689 | 173127 | 15669415 | 50.005 |
| 37.700 | 139152 | 15666086 | 49.995 |

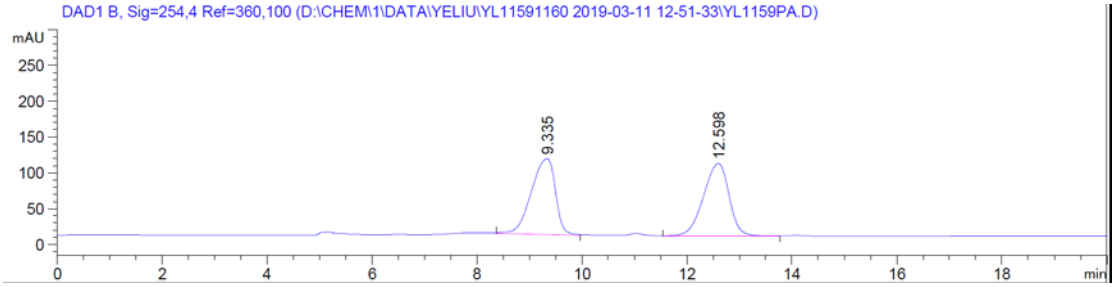



PDA Ch1 254nm

| T | Hight | Area | Area% |
|---|---|---|---|
| 32.723 | 44533 | 4131630 | 90.585 |
| 37.909 | 4403 | 429427 | 9.415 |

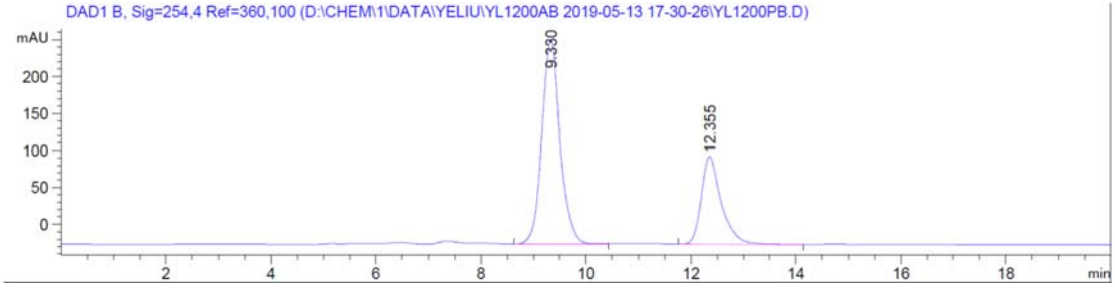



**4v**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 90/10, flow rate 0.6 mL/min. λ = 254 nm, t(major) = 9.3 min, t(minor) = 12.4 min, 68:32 er.



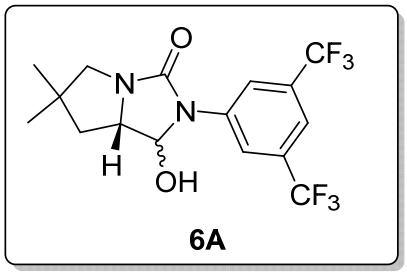

Signal 2: DAD1 B, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.335 | MM R | 0.5372 | 3416.96558 | 106.00591 | 50.0680 |
| 2 | 12.598 | BB | 0.5299 | 3407.68457 | 100.92472 | 49.9320 |



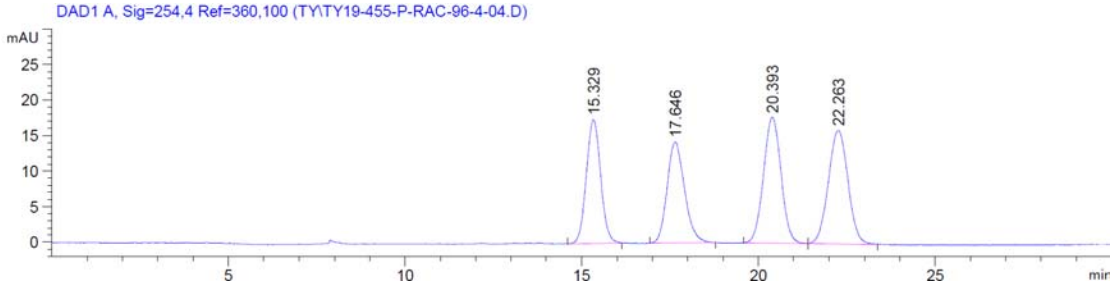

Signal 2: DAD1 B, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.330 | BV | 0.3698 | 6680.89697 | 276.60239 | 68.1099 |
| 2 | 12.355 | BB | 0.3880 | 3128.09131 | 118.48897 | 31.8901 |



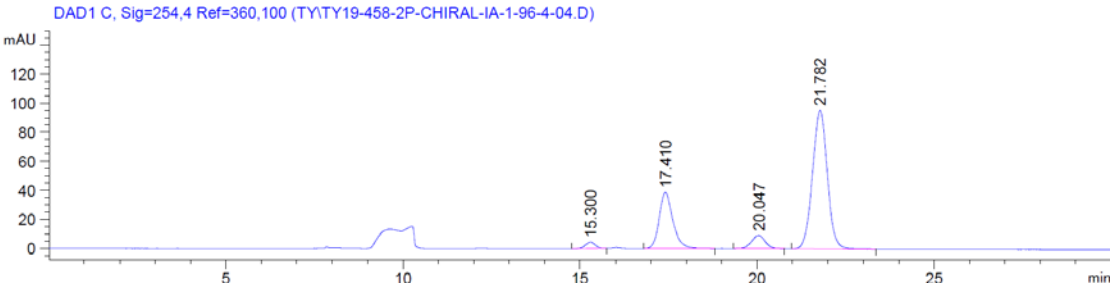

**6A**

**6A**, HPLC condition: Chiralcel IA, *i*-PrOH/*n*-hexane = 96/4, flow rate 0.4 mL/min. λ = 254 nm, minor diasteromer: t(minor) = 15.3 min, t(major) = 17.4 min, 92:8 er; major diasteromer: t(minor) = 20.0 min, t(major) = 21.8 min, 92:8 er.



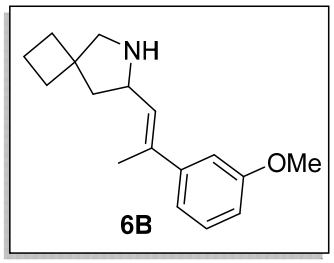

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 15.329 | BB | 0.4334 | 491.75681 | 17.41818 | 22.2807 |
| 2 | 17.646 | BB | 0.5091 | 488.25284 | 14.20116 | 22.1220 |
| 3 | 20.393 | BB | 0.5078 | 611.56238 | 17.75667 | 27.7089 |
| 4 | 22.263 | BB | 0.5565 | 615.52234 | 16.01059 | 27.8884 |

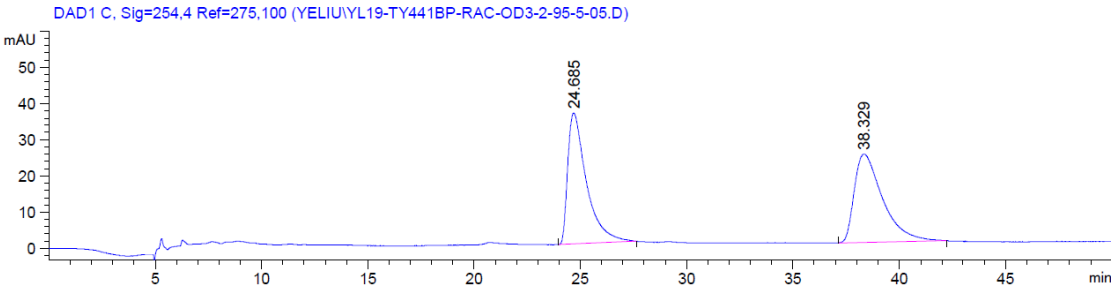



Signal 3: DAD1 C, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 15.300 | BB | 0.2831 | 89.68925 | 4.56707 | 2.1531 |
| 2 | 17.410 | BB | 0.4009 | 1044.49670 | 38.69160 | 25.0743 |
| 3 | 20.047 | BB | 0.3910 | 244.10229 | 9.15821 | 5.8600 |
| 4 | 21.782 | BB | 0.4484 | 2787.31519 | 95.53551 | 66.9126 |

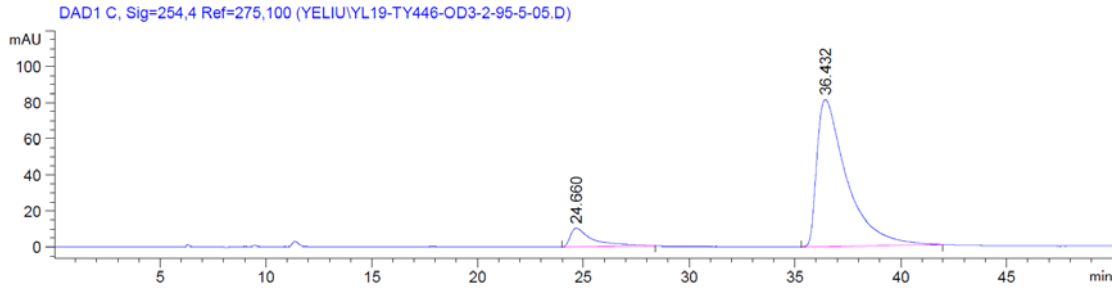



**6B**, HPLC condition: Chiralcel OD-3, *i*-PrOH/*n*-hexane = 95/5, flow rate 0.5 mL/min. λ = 254 nm, t(minor) = 24.7 min, t(major) = 36.4 min, 91.5:8.5 ee.




Signal 3: DAD1 C, Sig=254,4 Ref=275,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 24.685 | BB | 0.8860 | 2212.98999 | 36.16180 | 49.4496 |
| 2 | 38.329 | BB | 1.1661 | 2262.25659 | 24.39159 | 50.5504 |




Signal 3: DAD1 C, Sig=254,4 Ref=275,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 24.660 | BB | 0.9421 | 747.91583 | 10.31248 | 8.5299 |
| 2 | 36.432 | BB | 1.3472 | 8020.20410 | 81.56428 | 91.4701 |