Facile synthesis of novel spiroheterocycles *via* diastereoselective aziridination of cyclic enones

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Supporting Information

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1. General Information

General Procedures. All reactions were performed in oven-dried or flame-dried reaction vessels, modified Schlenk flasks, or round-bottom flasks. The flasks were fitted with Teflon screw caps and reactions were conducted under an atmosphere of argon if needed. Gas-tight syringes with stainless steel needles were used to transfer air- and moisture-sensitive liquids. All moisture and/or air sensitive solid compounds were manipulated inside normal desiccators. Flash column chromatography was performed using silica gel (40–63 μm, 230–400 mesh).

Analytical thin layer chromatography (TLC) was performed on silica gel 60 F_{254} aluminum plates (Merck) containing a 254 nm fluorescent indicator. TLC plates were visualized by exposure to short wave ultraviolet light (254 nm) and to a solution of $KMnO_4$ (1 g of $KMnO_4$, 6 g of K_2CO_3 and 0.1 g of KOH in 100 mL of H_2O) or vanillin (2 g of vanillin and 4 mL of concentrated H_2SO_4 in 100 mL of EtOH) followed by heating.

Organic solutions were concentrated at 30-50 ℃ on rotary evaporators at ~10 torr followed by drying on vacuum pump at ~1 torr. Reaction temperatures are reported as the temperature of the bath surrounding the vessel unless otherwise stated.

Materials. Commercial reagents and solvents were were obtained from Adamas-beta, Aldrich Chemical Co., Alfa Aesar, Macklin and Energy Chemical and used as received with the following exceptions: THF and toluene were purified by refluxing over Na-benzophenone under positive argon pressure followed by distillation. [1] The enone substrates were prepared according to literature procedure. [2]

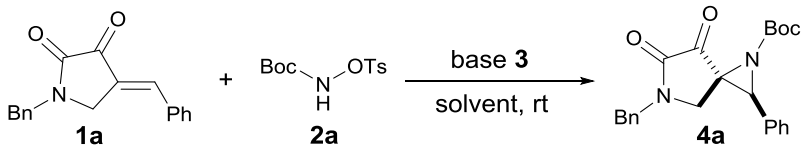
Instrumentation.

•Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with Bruker AV 300 MHz or 400 MHz spectrometer. Proton chemical shifts are reported in parts per million (δ scale), and are referenced using residual protium in the NMR solvents ($CDCl_3$: δ 7.26 ($CHCl_3$) and δ 2.50 (DMSO-d_6)). Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad singlet), coupling constant(s) (Hz), integration].

•Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with Bruker AV 300 MHz or 400 MHz spectrometers. Carbon chemical shifts are reported in parts per million (δ scale), and are referenced using the carbon resonances of the solvent (δ 77.16 ($CHCl_3$), 39.52 (DMSO)). Data are reported as follows: chemical shift [multiplicity (if not singlet), assignment (Cq = fully substituted carbon)].

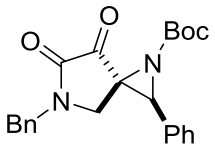
•High resolution mass spectra (HRMS) were recorded on a Waters SYNAPT G2 using an electrospray (ESI) ionization source.

2. Procedure for the Optimization of the Reaction Conditions



A dried glass tube was charged with 1-benzyl-4-benzylidenepyrrolidine-2,3-dione **1a** (0.1 mmol, 27.7 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.15 mmol, 43.1 mg) in an indicated solvent (0.1 M, 1 mL). Then Base **3** (base loading shown in Table 1 in the paper) was added to the reaction mixture, and the reaction was stirred at room temperature overnight. When the reaction was complete, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel eluting with petroleum ether/ethyl acetate (6:1 to 4:1) to afford the corresponding spiroaziridine product **4a**, which was further characterized by ^{1}H-NMR, ^{13}C-HMR and HRMS analysis.

tert-butyl-5-benzyl-6,7-dioxo-2-phenyl-1,5-diazaspiro[2.4]heptane-1-carboxylate 4a



4a

Prepared according to the general procedure using 1-benzyl-4-benzylidenepyrrolidine-2,3-dione **1a** (0.1 mmol, 27.7 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.15 mmol, 43.1 mg). After the reaction was complete, purification of the crude product via column chromatography delivered **4a** as a white solid with 93% yield.

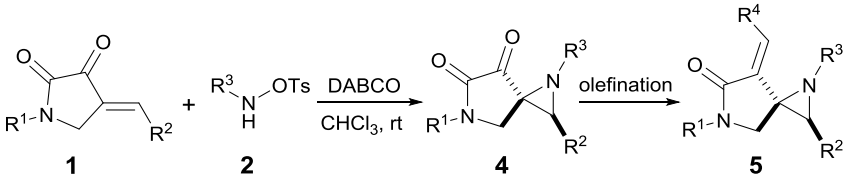
NMR and HRMS data for the product **4a***:*

^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 7.41 – 7.18 (m, 10H), 4.75 (d, *J* = 14.7 Hz, 1H), 4.54 (d, *J* = 14.7 Hz, 1H), 4.10 (s, 1H), 3.52 (d, *J* = 11.7 Hz, 1H), 3.11 (d, *J* = 11.7 Hz, 1H), 1.39 (s, 9H).

^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 192.8, 158.5, 157.2, 135.2, 133.1, 128.7, 128.6, 128.5, 127.8, 127.7, 127.2, 82.3, 50.5, 48.8, 47.0, 44.3, 27.5.

HRMS (ESI): *m/z* calculated for $C_{23}H_{24}N_2O_4Na^+$: 415.1634, found: 415.1633.

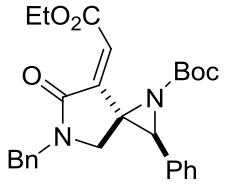
3. General Procedure for the Synthesis of spiroaziridines products 4 and 5



A dried glass tube was charged with pyrrolidine-2,3-dione **1** (0.2 mmol) and **2** (0.3 mmol) in 2 mL of $CHCl_3$, DABCO (0.3 mmol, 33.7 mg) was added then. The reaction was sealed with a Teflon cap and stirred at room temperature overnight. When the reaction was complete, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 6:1 to 4:1) to afford the corresponding spiroaziridine products 4, which was used for the next step.

A glass tube was charged with *t*-BuOK (1.0 equiv.) and $(EtO)_2POCH_2CO_2Et$ (ethyl 2-(diethoxyphosphoryl)acetate) (1.0 equiv.) in 1 mL of anhydrous THF, and the reaction was stirred at 0 ^oC for about 20 minutes, then the spiroaziridines **4** was added to the reaction mixture and stirred at room temperature for about 1 hour until the reaction was complete. The reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 6:1 to 5:1) to afford the corresponding desired products **5**.

tert-butyl-5-benzyl-7-(2-ethoxy-2-oxoethylidene)-6-oxo-2-phenyl-1,5-diazaspiro[2.4]heptane-1-carboxylate 5a:



5a

Prepared according to the general procedure using 1-benzyl-4-benzylidenepyrrolidine-2,3-dione **1a** (0.2 mmol, 55.4 mg) and *tert*-butyl(tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4a** as a white solid with 93% yield. The isolated yield of the HWE transformation was determined to be 91% yield.

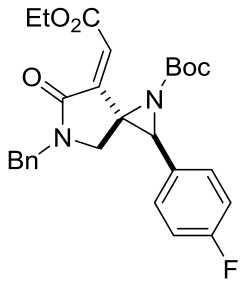
NMR and HRMS data for the product **5a**:

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.34 – 7.23 (m, 8H), 7.17 – 7.14 (m, 2H), 5.94 (s, 1H), 4.80 (d, *J* = 15.2 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.24 (d, *J* = 15.2 Hz, 1H), 3.93 (s, 1H), 3.24 (d, *J* = 11.2 Hz, 1H), 2.90 (d, *J* = 11.2 Hz, 1H), 1.52 (s, 9H), 1.37 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.9, 163.7, 158.1, 135.3, 134.8, 133.5, 128.9, 128.8, 128.5, 127.9, 127.0, 121.6, 83.4, 61.9, 49.6, 48.4, 48.1, 46.7, 28.1, 14.2.

HRMS (ESI): *m/z* calculated for $C_{27}H_{30}N_2O_5Na^+$: 485.2052, found: 485.2051.

tert-butyl-5-benzyl-7-(2-ethoxy-2-oxoethylidene)-2-(4-fluorophenyl)-6-oxo-1,5-diazaspiro[2.4] heptane -1-carboxylate 5b



5b

Prepared according to the general procedure using 1-benzyl-4-(4-fluorobenzylidene) pyrrolidine-2,3-dione **1b** (0.2 mmol, 59.0 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4b** as a white solid with 87% yield. The isolated yield of the HWE transformation was determined to be 88% yield.

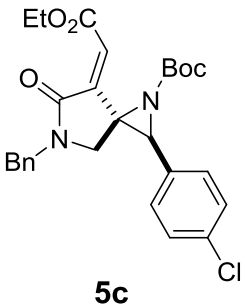
NMR and HRMS data for the product **5b***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.32 – 7.26 (m, 3H), 7.24 – 7.19 (m, 2H), 7.16 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.00 (t, *J* = 8.6 Hz, 2H), 5.93 (s, 1H), 4.77 (d, *J* = 14.8 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.28 (d, *J* = 14.8 Hz, 1H), 3.90 (s, 1H), 3.21 (d, *J* = 11.2 Hz, 1H), 2.87 (d, *J* = 11.2 Hz, 1H), 1.52 (s, 9H), 1.37 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.8, 163.6, 158.0, 135.3, 134.6, 129.3, 128.9, 128.7, 128.0, 121.7, 115.9, 115.7, 83.6, 61.9, 48.9, 48.2, 48.1, 46.8, 28.1, 14.2.

HRMS (ESI): *m/z* calculated for $C_{27}H_{29}FN_2O_5Na^+$: 503.1958, found: 503.1961.

tert-butyl-5-benzyl-2-(4-chlorophenyl)-7-(2-ethoxy-2-oxoethylidene)-6-oxo-1,5-diazaspiro[2.4] heptane-1-carboxylate 5c



5c

Prepared according to the general procedure using 1-benzyl-4-(4-chlorobenzylidene) pyrrolidine-2,3-dione **1c** (0.2 mmol, 62.4 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude

product via column chromatography delivered **4c** as a white solid with 89% yield. The isolated yield of the HWE transformation was determined to be 91% yield.

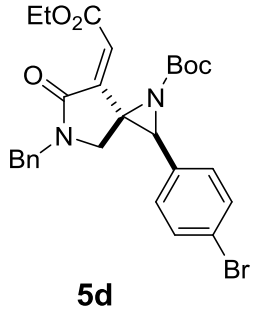
NMR and HRMS data for the product **5c***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.32 – 7.26 (m, 5H), 7.20 – 7.14 (m, 4H), 5.94 (s, 1H), 4.78 (d, *J* = 14.8 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.26 (d, *J* = 14.8 Hz, 1H), 4.26 (d, *J* = 14.8 Hz, 1H), 3.20 (d, *J* = 11.2 Hz, 1H), 2.86 (d, *J* = 11.2 Hz, 1H), 1.52 (s, 9H), 1.37 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.7, 163.5, 157.9, 135.2, 134.5, 132.1, 129.1, 129.0, 128.9, 128.3, 128.0, 127.9, 121.8, 83.6, 61.9, 48.8, 48.2, 48.1, 46.7, 28.0, 14.1.

HRMS (ESI): *m/z* calculated for $C_{27}H_{29}ClN_2O_5Na^+$: 519.1663, found: 519.1663.

tert-butyl-5-benzyl-2-(4-bromophenyl)-7-(2-ethoxy-2-oxoethylidene)-6-oxo-1,5-diazaspiro[2.4] heptane-1-carboxylate 5d



5d

Prepared according to the general procedure using 1-benzyl-4-(4-bromobenzylidene) pyrrolidine-2,3-dione **1d** (0.2 mmol, 71.2 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4d** as a white solid with 88% yield. The isolated yield of the HWE transformation was determined to be 89% yield.

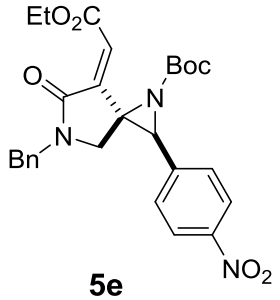
NMR and HRMS data for the product **5d**:

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.47 – 7.42 (m, 2H), 7.31 – 7.25 (m, 3H), 7.18 – 7.10 (m, 4H), 5.93 (s, 1H), 4.78 (d, *J* = 15.2 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.26 (d, *J* = 14.8Hz, 1H), 3.88 (s, 1H), 3.20 (d, *J* = 11.2 Hz, 1H), 2.86 (d, *J* = 11.2 Hz, 1H), 1.52 (s, 9H), 1.36 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.7, 163.6, 157.9, 135.3, 134.5, 132.6, 132.0, 129.0, 128.7, 128.0, 122.7, 121.8, 83.7, 61.9, 48.9, 48.3, 48.1, 46.8, 28.1, 14.2.

HRMS (ESI): *m/z* calculated for $C_{27}H_{29}BrN_2O_5Na^+$: 563.1158, found: 563.1158.

tert-butyl-5-benzyl-7-(2-ethoxy-2-oxoethylidene)-2-(4-nitrophenyl)-6-oxo-1,5-diazaspiro[2.4] heptane-1-carboxylate 5e



5e

Prepared according to the general procedure using 1-benzyl-4-(4-nitrobenzylidene) pyrrolidine-2,3-dione **1e** (0.2 mmol, 64.4 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4e** as a white solid with 89% yield. The isolated yield of the HWE transformation was determined to be 90% yield.

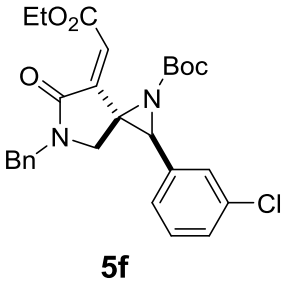
NMR and HRMS data for the product **5e***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.21 – 8.17 (m, 2H), 7.47 – 7.42 (m, 2H), 7.32 – 7.26 (m, 3H), 7.18 – 7.12 (m, 2H), 5.98 (s, 1H), 4.74 (d, *J* = 14.8 Hz, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 4.30 (d, *J* = 15.2 Hz, 1H), 4.01 (s, 1H), 3.23 (d, *J* = 11.2 Hz, 1H), 2.81 (d, *J* = 11.2 Hz, 1H), 1.53 (s, 9H), 1.37 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.5, 163.3, 157.6, 148.1, 140.8, 135.1, 134.0, 129.1, 129.0, 128.1, 128.0, 124.1, 122.3, 84.1, 62.0, 48.6, 48.5, 48.2, 46.8, 28.0, 14.2.

HRMS (ESI): *m/z* calculated for $C_{27}H_{29}N_3O_7Na^+$: 530.1903, found: 530.1905.

tert-butyl-5-benzyl-2-(3-chlorophenyl)-7-(2-ethoxy-2-oxoethylidene)-6-oxo-1,5-diazaspiro[2.4] heptane-1-carboxylate 5f



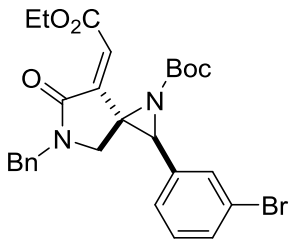
5f

Prepared according to the general procedure using 1-benzyl-4-(3-chlorobenzylidene) pyrrolidine-2,3-dione **1f** (0.2 mmol, 62.4 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4f** as a white solid with 85% yield. The isolated yield of the HWE transformation was determined to be 89% yield.

NMR and HRMS data for the product **5f**:

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.33 – 7.23 (m, 6H), 7.18 – 7.12 (m, 3H), 5.94 (s, 1H), 4.78 (d, *J* = 15.2 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.27 (d, *J* = 15.2 Hz, 1H), 3.91 (s, 1H), 3.23 (d, *J* = 11.2 Hz, 1H), 2.89 (d, *J* = 11.2 Hz, 1H), 1.52 (s, 9H), 1.37 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.6, 163.5, 157.8, 135.6, 135.2, 134.8, 134.4, 130.1, 128.9, 128.7, 127.9, 127.8, 126.9, 125.3, 121.8, 83.6, 61.8, 48.6, 48.2, 48.2, 46.7, 28.0, 14.1.
HRMS (ESI): *m/z* calculated for $C_{27}H_{29}ClN_2O_5Na^+$: 519.1663, found: 519.1664.

tert-butyl-5-benzyl-2-(3-bromophenyl)-7-(2-ethoxy-2-oxoethylidene)-6-oxo-1,5-diazaspiro[2.4] heptane-1-carboxylate 5g



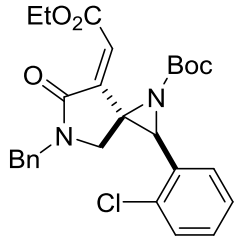
5g

Prepared according to the general procedure using 1-benzyl-4-(3-bromobenzylidene) pyrrolidine-2,3-dione **1g** (0.2 mmol, 71.2 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4g** as a white solid with 87% yield. The isolated yield of the HWE transformation was determined to be 91% yield.

NMR and HRMS data for the product **5g***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.44 – 7.39 (m, 2H), 7.33 – 7.25 (m, 3H), 7.21 – 7.13 (m, 4H), 5.93 (s, 1H), 4.78 (d, *J* = 15.2 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.28 (d, *J* = 15.2 Hz, 1H), 3.90 (s, 1H), 3.23 (d, *J* = 11.2 Hz, 1H), 2.89 (d, *J* = 11.2 Hz, 1H), 1.52 (s, 9H), 1.37 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.7, 163.5, 157.8, 135.9, 135.2, 134.4, 131.7, 130.4, 129.8, 128.9, 128.0, 127.9, 125.8, 123.0, 121.9, 83.7, 61.9, 48.6, 48.3, 48.2, 46.7, 28.0, 14.1.
HRMS (ESI): *m/z* calculated for $C_{27}H_{29}BrN_2O_5Na^+$: 563.1158, found: 563.1160.

tert-butyl-5-benzyl-2-(2-chlorophenyl)-7-(2-ethoxy-2-oxoethylidene)-6-oxo-1,5-diazaspiro[2.4] heptane-1-carboxylate 5h



5h

Prepared according to the general procedure using 1-benzyl-4-(2-chlorobenzylidene) pyrrolidine-2,3-dione **1h** (0.2 mmol, 62.4 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4h** as a white solid with 81% yield. The isolated yield of the HWE transformation was determined to be 84% yield.

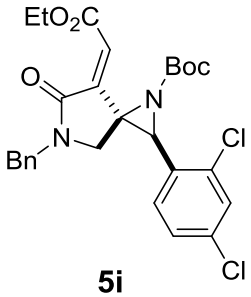
NMR and HRMS data for the product **5h***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.35 – 7.18 (m, 7H), 7.17 – 7.14 (m, 2H), 6.00 (s, 1H), 4.79 (d, *J* = 15.2 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.28 (d, *J* = 15.2 Hz, 1H), 4.08 (s, 1H), 3.07 (d, *J* = 11.2 Hz, 1H), 2.85 (d, *J* = 11.2 Hz, 1H), 1.54 (s, 9H), 1.37 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.5, 163.6, 158.1, 135.3, 134.3, 133.9, 131.8, 129.7, 129.2, 128.8, 128.5, 127.8, 127.7, 127.0, 122.0, 83.5, 61.7, 48.4, 48.0, 47.5, 46.5, 28.0, 14.1.

HRMS (ESI): *m/z* calculated for $C_{27}H_{29}ClN_2O_5Na^+$: 519.1663, found: 519.1665.

tert-butyl-5-benzyl-2-(2,4-dichlorophenyl)-7-(2-ethoxy-2-oxoethylidene)-6-oxo-1,5-diazaspiro[2.4] heptane-1-carboxylate 5i



5i

Prepared according to the general procedure using 1-benzyl-4-(2,4-dichlorobenzylidene) pyrrolidine-2,3-dione **1i** (0.2 mmol, 69.2 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4i** as a white solid with 86% yield. The isolated yield of the HWE transformation was determined to be 89% yield.

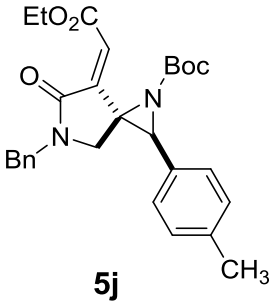
NMR and HRMS data for the product **5i***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.35 (d, *J* = 2.0 Hz, 1H), 7.31 – 7.25 (m, 4H), 7.20 – 7.15 (m, 3H), 6.00 (s, 1H), 4.78 (d, *J* = 15.2 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.29 (d, *J* = 15.2 Hz, 1H), 4.03 (s, 1H), 3.06 (d, *J* = 11.2 Hz, 1H), 2.83 (d, *J* = 11.2 Hz, 1H), 1.53 (s, 9H), 1.36 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.3, 163.4, 157.8, 135.1, 135.0, 134.5, 134.0, 130.6, 129.4, 129.1, 128.8, 127.8, 127.7, 127.4, 122.1, 83.6, 61.7, 48.3, 48.0, 46.8, 46.5, 27.9, 14.1.

HRMS (ESI): *m/z* calculated for $C_{27}H_{28}Cl_2N_2O_5Na^+$: 553.1273, found: 553.1270.

tert-butyl-5-benzyl-7-(2-ethoxy-2-oxoethylidene)-6-oxo-2-(*p*-tolyl)-1,5-diazaspiro[2.4]heptane-1-carboxylate 5j



5j

Prepared according to the general procedure using 1-benzyl-4-(4-methylbenzylidene) pyrrolidine-2,3-dione **1j** (0.2 mmol, 58.2 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4j** as a white solid with 90% yield. The isolated yield of the HWE transformation was determined to be 89% yield.

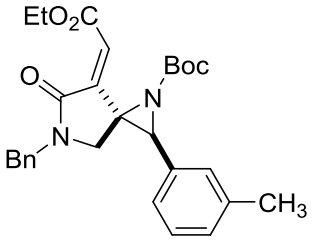
NMR and HRMS data for the product **5j***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.25 – 7.16 (m, 3H), 7.10 – 7.03 (m, 6H), 5.85 (s, 1H), 4.74 (d, *J* = 15.2 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 4.15 (d, *J* = 15.2 Hz, 1H), 3.82 (s, 1H), 3.16 (d, *J* = 11.2 Hz, 1H), 3.16 (d, *J* = 11.2 Hz, 1H), 2.25 (s, 3H), 1.45 (s, 9H), 1.29 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.9, 163.8, 158.2, 138.3, 135.4, 134.9, 130.5, 129.4, 128.9, 127.9, 126.9, 121.5, 83.3, 61.8, 49.5, 48.4, 48.0, 46.7, 28.1, 21.3, 14.2.

HRMS (ESI): *m/z* calculated for $C_{28}H_{32}N_2O_5Na^+$: 499.2209, found: 499.2209.

tert-butyl-5-benzyl-7-(2-ethoxy-2-oxoethylidene)-6-oxo-2-(*m*-tolyl)-1,5-diazaspiro[2.4]heptane-1-carboxylate 5k



5k

Prepared according to the general procedure using 1-benzyl-4-(3-methylbenzylidene) pyrrolidine-2,3-dione **1k** (0.2 mmol, 58.2 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4k** as a white solid with 88% yield. The isolated yield of the HWE transformation was determined to be 90% yield.

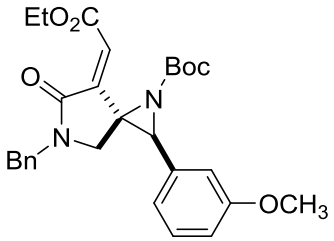
NMR and HRMS data for the product **5k***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.18 – 7.10 (m, 3H), 7.08 – 6.99 (m, 3H), 6.97 – 6.87 (m, 3H), 5.79 (s, 1H), 4.66 (d, *J* = 15.2 Hz, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 4.09 (d, *J* = 15.2 Hz, 1H), 3.76 (s, 1H), 3.09 (d, *J* = 11.2 Hz, 1H), 2.77 (d, *J* = 11.2 Hz, 1H), 2.16 (s, 3H), 1.38 (s, 9H), 1.22 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.8, 163.7, 158.2, 138.5, 135.4, 134.9, 133.4, 129.3, 129.1, 128.9, 128.6, 127.9, 127.6, 124.0, 121.6, 83.3, 61.8, 49.6, 48.4, 48.0, 46.7, 28.1, 21.5, 14.1.

HRMS (ESI): *m/z* calculated for $C_{28}H_{32}N_2O_5Na^+$: 499.2209, found: 499.2207.

tert-butyl-5-benzyl-7-(2-ethoxy-2-oxoethylidene)-2-(3-methoxyphenyl)-6-oxo-1,5-diazaspiro[2.4] heptane-1-carboxylate 5l



5l

Prepared according to the general procedure using 1-benzyl-4-(3-methoxybenzylidene) pyrrolidine-2,3-dione **1l** (0.2 mmol, 61.5 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4l** as a white solid with 84% yield. The isolated yield of the HWE transformation was determined to be 89% yield.

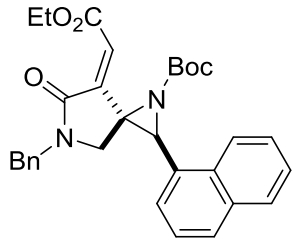
NMR and HRMS data for the product **5l***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.32 – 7.14 (m, 6H), 6.85 – 6.76 (m, 3H), 5.94 (s, 1H), 4.80 (d, *J* = 14.8 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.24 (d, *J* = 15.2 Hz, 1H), 3.91 (s, 1H), 3.77 (s, 3H), 3.23 (d, *J* = 11.2 Hz, 1H), 2.92 (d, *J* = 11.2 Hz, 1H), 1.52 (s, 9H), 1.37 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.8, 163.7, 159.9, 158.0, 135.3, 135.1, 134.8, 129.9, 128.9, 127.9, 121.6, 119.2, 114.4, 112.0, 83.4, 61.8, 55.4, 49.5, 48.4, 48.0, 46.7, 28.0, 14.1.

HR-MS (ESI): *m/z* calculated for $C_{28}H_{32}N_2O_6Na^+$: 515.2158, found:515.2164.

tert-butyl-5-benzyl-7-(2-ethoxy-2-oxoethylidene)-2-(naphthalen-1-yl)-6-oxo-1,5-diazaspiro[2.4] heptane-1-carboxylate 5m



5m

Prepared according to the general procedure using 1-benzyl-4-(naphthalen-1-ylmethylene) pyrrolidine-2,3-dione **1m** (0.2 mmol, 65.5 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4m** as a white solid with 80% yield. The isolated yield of the HWE transformation was determined to be 87% yield.

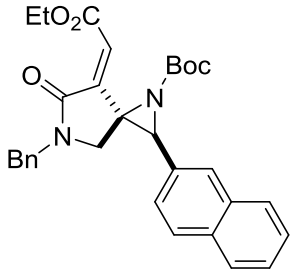
NMR and HRMS data for the product **5m***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.82 – 7.69 (m, 3H), 7.50 – 7.41 (m, 3H), 7.33 – 7.30 (m ,1H), 7.09 – 7.03 (m, 3H), 6.96 – 6.90 (m, 2H), 6.04 (s, 1H), 4.63 (d, *J* = 15.2 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 4.30 (s, 1H), 4.07 (d, *J* = 15.2 Hz, 1H), 3.00 (d, *J* = 11.2 Hz, 1H), 2.60 (d, *J* = 11.2 Hz, 1H), 1.49 (s, 9H), 1.32 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.7, 163.7, 158.5, 135.1, 134.9, 133.4, 131.3, 129.6, 128.9, 128.7, 127.7, 127.6, 127.2, 126.4, 125.5, 125.0, 122.7, 121.8, 83.4, 61.9, 48.4, 48.1, 48.1, 46.5, 28.1, 14.2.

HRMS (ESI): *m/z* calculated for $C_{31}H_{32}N_2O_5Na^+$: 535.2209, found: 535.2208.

tert-butyl-5-benzyl-7-(2-ethoxy-2-oxoethylidene)-2-(naphthalen-2-yl)-6-oxo-1,5-diazaspiro[2.4] heptane-1-carboxylate 5n



5n

Prepared according to the general procedure using 1-benzyl-4-(naphthalen-2-ylmethylene) pyrrolidine-2,3-dione **1n** (0.2 mmol, 65.5 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4n** as a white solid with 86% yield. The isolated yield of the HWE transformation was determined to be 90% yield.

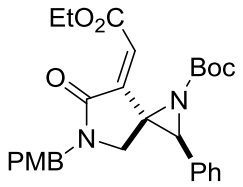
NMR and HRMS data for the product **5n***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.76 – 7.66 (m, 4H), 7.43 – 7.39 (m, 2H), 7.29 – 7.25 (m, 1H), 7.20 – 7.16 (m, 3H), 7.06 (dd, *J* = 7.6, 2.0 Hz, 2H), 5.92 (s, 1H), 4.73 (d, *J* = 15.2Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 2H), 4.11 (d, *J* = 15.2Hz, 1H), 4.03 (s, 1H), 3.19 (d, *J* = 11.2 Hz, 1H), 2.82 (d, *J* = 11.2 Hz, 1H), 1.48 (s, 9H), 1.31 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.8, 163.7, 158.2, 135.3, 134.8, 133.3, 133.2, 131.0, 128.9, 128.7, 128.1, 127.9, 126.7, 126.5, 126.2, 124.5, 121.7, 83.5, 61.9, 49.7, 48.5, 48.4, 46.8, 28.1, 28.0, 14.2.

HRMS (ESI): *m/z* calculated for $C_{31}H_{32}N_2O_5Na^+$: 535.2209, found: 535.2206.

tert-butyl-7-(2-ethoxy-2-oxoethylidene)-5-(4-methoxybenzyl)-6-oxo-2-phenyl-1,5-diazaspiro[2.4] heptane-1-carboxylate 5o



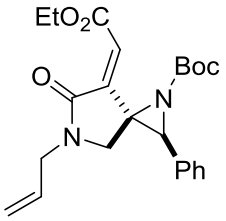
5o

Prepared according to the general procedure using 4-benzylidene-1-(4-methoxybenzyl) pyrrolidine-2,3-dione **1o** (0.2 mmol, 61.4 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4o** as a white solid with 89% yield. The isolated yield of the HWE transformation was determined to be 91% yield.

NMR and HRMS data for the product **5o***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.35 – 7.21 (m, 5H), 7.10 – 7.06 (m, 2H), 6.83 – 6.78 (m, 2H), 5.93 (s, 1H), 4.71 (d, *J* = 14.8 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.19 (d, *J* = 14.8 Hz, 1H), 3.92 (s, 1H), 3.77 (s, 3H), 3.21 (d, *J* = 11.2 Hz, 1H), 2.87 (d, *J* = 11.2 Hz, 1H), 1.52 (s, 9H), 1.37 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.8, 163.5, 159.3, 158.1, 134.9, 133.5, 129.3, 128.7, 128.4, 127.3, 126.9, 121.4, 114.2, 83.3, 61.8, 55.3, 49.5, 48.1, 46.1, 28.0, 14.1.
HRMS (ESI): *m/z* calculated for $C_{28}H_{32}N_2O_6Na^+$: 515.2158, found: 515.2159.

tert-butyl-5-allyl-7-(2-ethoxy-2-oxoethylidene)-6-oxo-2-phenyl-1,5-diazaspiro[2.4]heptane-1-carboxylate 5p

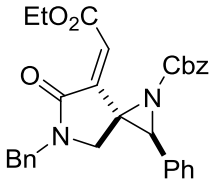


5p

Prepared according to the general procedure using 1-allyl-4-benzylidenepyrrolidine-2,3-dione **1p** (0.2 mmol, 61.4 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4p** as a white solid with 80% yield. The isolated yield of the HWE transformation was determined to be 81% yield.

NMR and HRMS data for the product **5p***:*
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.40 – 7.28 (m, 5H), 5.91 (s, 1H)，5.74 – 5.56 (m, 1H)，5.20 – 5.09 (m, 2H)，4.35 (d, *J* = 7.2 Hz, 2H)，4.09(m, 1H), 3.94 (s, 1H), 3.80 (m, 1H), 3.34 (d, *J* = 11.2 Hz, 1H), 2.93 (d, *J* = 11.2 Hz, 1H), 1.52 (s, 9H), 1.35 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.9, 163.4, 158.2, 134.7, 133.6, 131.2, 128.8, 128.6, 127.0, 121.4, 118.7, 83.5, 61.8, 49.9, 48.4, 48.1, 45.4, 28.1, 14.1.
HRMS (ESI): *m/z* calculated for $C_{23}H_{28}N_2O_5Na^+$: 435.1896, found: 435.1898.

benzyl-5-benzyl-7-(2-ethoxy-2-oxoethylidene)-6-oxo-2-phenyl-1,5-diazaspiro[2.4]heptane-1-carboxylate 5q



5q

Prepared according to the general procedure using 1-benzyl-4-benzylidenepyrrolidine-2,3-dione **1q** (0.2 mmol, 55.4 mg) and benzyl (tosyloxy)carbamate **2b** (0.3 mmol, 96.3 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4q** as a white solid with 90% yield. The isolated yield of the HWE transformation was determined to be 91% yield.

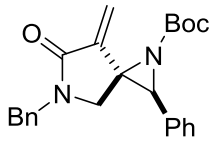
NMR and HRMS data for the product **5q***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.45 – 7.27 (m, 8H), 7.23 – 7.13 (m, 5H), 7.09 – 7.04 (m, 2H), 5.82 (s, 1H), 5.27 (d, *J* = 11.6 Hz, 1H), 5.10 (d, *J* = 11.6Hz, 1H),4.69 (d, *J* = 14.8 Hz, 1H), 4.36 (m, 2H), 4.24 (d, *J* = 14.8 Hz, 1H), 3.99 (s, 1H), 3.24 (d, *J* = 11.2 Hz, 1H), 2.88 (d, *J* = 11.2 Hz, 1H), 1.36 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.6, 163.4, 159.3, 135.1, 135.0, 134.7, 132.9, 129.1, 128.8, 128.7, 128.6, 127.8, 126.9, 121.3, 69.2, 61.8, 50.3, 48.3, 47.9, 46.7, 14.1.

HRMS (ESI): *m/z* calculated for $C_{30}H_{28}N_2O_5Na^+$: 519.1896, found: 519.1899.

tert-butyl-5-benzyl-7-methylene-6-oxo-2-phenyl-1,5-diazaspiro[2.4]heptane-1-carboxylate 5r



5r

Prepared according to the general procedure using 1-benzyl-4-benzylidenepyrrolidine-2,3-dione **1r** (0.2 mmol, 55.4 mg) and *tert*-butyl (tosyloxy)carbamate **2a** (0.3 mmol, 86.2 mg) in 2 mL of $CHCl_3$. After the reaction was complete, purification of the crude product via column chromatography delivered **4r** as a white solid with 93% yield. The isolated yield of the Wittig transformation was determined to be 81% yield.

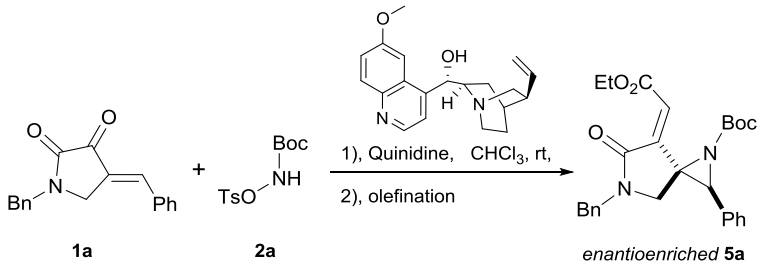
NMR and HRMS data for the product **5r***:*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.33 – 7.22 (m, 8H), 7.19 – 7.15 (m, 2H), 6.21 (s, 1H), 5.26 (s, 1H), 4.84 (d, *J* = 15.2 Hz, 1H), 4.27 (d, *J* = 15.2 Hz, 1H), 3.94 (s, 1H), 3.25 (d, *J* = 11.2 Hz, 1H), 2.91 (d, *J* = 11.2 Hz, 1H), 1.46 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.9, 158.4, 137.4, 135.7, 134.0, 128.9, 128.7, 128.3, 127.9, 127.8, 127.5, 127.0, 115.5, 82.7, 49.6, 48.9, 48.3, 46.8, 28.2.

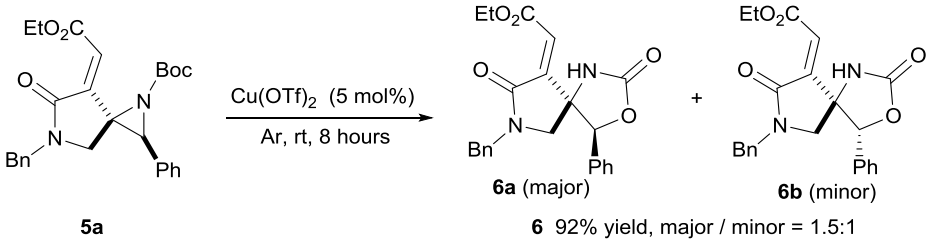
HRMS (ESI): *m/z* calculated for $C_{24}H_{26}N_2O_3Na^+$: 413.1841, found: 413.1836.

4. Procedure for the Asymmetric Synthesis of Chiral 5a



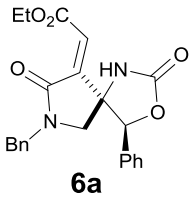
A dried glass tube was charged with 1-benzyl-4-benzylidenepyrrolidine-2,3-dione **1a** (0.2 mmol, 55.4mg), *tert*-butyl (tosyloxy)carbamate 2a (0.3 mmol, 86.2 mg) and quinidine (0.24 mmol, 77.9 mg) in 2 mL of $CHCl_3$, the reaction was sealed with a Teflon cap and stirred at room temperature overnight. After the reaction was complete, purification of the crude product via column chromatography delivered the enantioenriched **4a**. The isolated yield of the final product **5a** was determined to be 82% yield for 2 steps. The diastereomeric ratio was determined to be >95:5 by ^{1}H NMR spectroscopy of the crude reaction mixture. The enantiomeric excess of the product **5a** was determined to be 70% ee by chiral HPLC analysis on Chiralpak OD-H column (15% 2-propanol/*n*-hexane, 1 mL/min), UV 270 nm, t_{major} = 10.00 min, t_{minor} = 15.98 min; $[\alpha]_D^{20}$ = +40.0 (*c* = 4.0 in CH_2Cl_2).

5. Procedure for Synthetic Transformations of 5a



A dried glass tube was charged with **5a** (92.5 mg, 0.2 mmol), $Cu(OTf)_2$ (3.6 mg, 0.01 mmol), which were dissolved in 1 mL of dichloromethane (DCM) under argon, and the reaction was sealed with a Teflon cap and stirred at room temperature for about 8 hours. When the reaction was complete, the reaction mixture was directly purified by flash chromatography on silica gel eluting with petroleum ether/ethyl acetate (5:1 to 3:1) to afford the corresponding **6** as white solid in 92% yield with 1.5:1 d.r. The diastereoisomer could be sepreated by flash chromatography on silica gel, and further characterized by ^{1}H-NMR, ^{13}C-NMR and HRMS analysis, respectively. The corresponding data is listed as follows:

ethyl (Z)-2-(7-benzyl-2,8-dioxo-4-phenyl-3-oxa-1,7-diazaspiro[4.4]nonan-9-ylidene)acetate 6



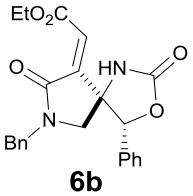
6a

NMR and HRMS data for the product **6a** *(major):*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.37 – 7.28 (m, 3H), 7.27 – 7.18 (m, 3H), 7.18 – 7.13 (m, 2H), 7.00 – 6.88 (m, 2H), 6.67 (s, 1H), 5.89 (s, 1H), 4.97 (s, 1H), 4.44 – 4.31 (m, 3H), 4.00 (d, *J* = 14.8 Hz, 1H), 3.16 (d, *J* = 11.2 Hz, 1H), 2.99 (d, *J* = 11.2 Hz, 1H), 1.38 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.5, 162.6, 157.5, 140.0, 134.5, 134.4, 129.6, 129.3, 128.9, 128.2, 127.9, 126.5, 126.3, 82.9, 65.8, 62.0, 51.1, 46.6, 14.1.

HRMS (ESI): *m/z* calculated for $C_{23}H_{22}N_2O_5Na^+$: 429.1426, found: 429.1429.



6b

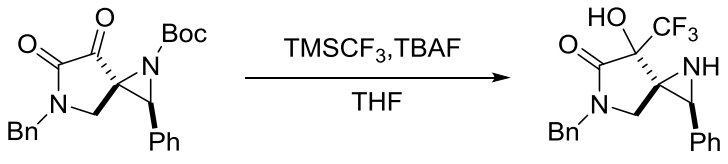
NMR and HRMS data for the product **6b** *(minor):*

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.40 – 7.36 (m, 3H), 7.33 – 7.25 (m, 3H), 7.25 – 7.20 (m, 2H), 7.18 – 7.13 (m, 2H), 5.64 (s, 1H), 5.25 (s, 1H), 4.93 (s, 1H), 4.88 (d, *J* = 15.2 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.23 (d, *J* = 15.2 Hz, 1H), 3.58 (d, *J* = 19.6, 1H), 3.28 (d, *J* = 19.6Hz, 1H), 1.36 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 166.9, 166.3, 156.3, 149.8, 136.7, 136.6, 135.5, 128.7, 128.5, 127.8, 126.8, 126.7, 126.5, 70.5, 61.7, 57.2, 49.8, 45.1, 13.1.

HRMS (ESI): *m/z* calculated for $C_{23}H_{22}N_2O_5Na^+$: 429.1426, found: 429.1425.

6. Procedure for Trifluoromethylation of Spiroaziridine Product **4a**

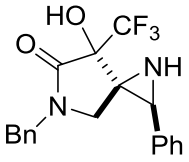


4a **7**

A dried glass tube was charged with **4a** (78.5 mg, 0.2 mmol), $TMSCF_3$ (36 mg, 0.25 mmol), 1 M TBAF/THF (20 uL) which were dissolved in 1 mL of anhydrous THF under argon, and the reaction was sealed with a Teflon cap and stirred at room temperature for about 3 hours. Then the reaction was cooled to 0 ^oC and quenched with 20 mL of 20% hydrochloric

acid. The reaction was stirred at room temperature for about 2 hours. Then the organic material was extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4, then concentrated under reduced pressure and purified by flash chromatography on silica gel eluting with petroleum ether/ethyl acetate (5:1 to 2:1) to afford the corresponding **7** as white solid in 85% yield, and further characterized by ^{1}H-NMR, ^{13}C-NMR and HRMS analysis, respectively.

5-benzyl-7-hydroxy-2-phenyl-7-(trifluoromethyl)-1,5-diazaspiro[2.4]heptan-6-one 7



7

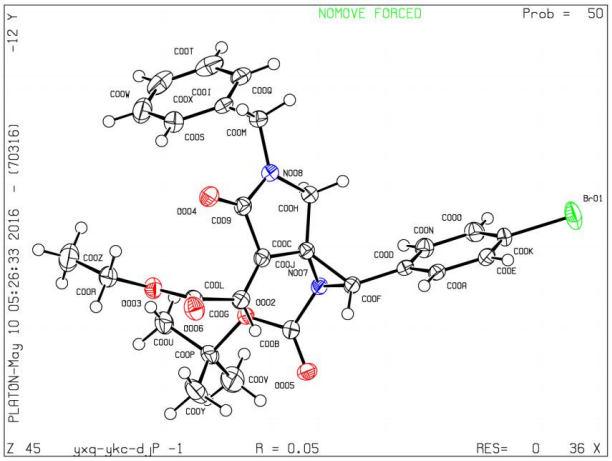
NMR and HRMS data for the product **7**

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm): 8.74 (s, 1H), 7.94 (s, 1H), 7.44 – 7.36 (m, 3H), 7.31 – 7.18 (m, 5H), 7.09 – 7.04 (m, 2H), 5.69 (s, 1H), 4.33 (d, *J* = 15.2 Hz, 1H), 4.19 (d, *J* = 15.2 Hz, 1H), 2.90 (d, *J* = 11.2 Hz, 1H), 2.75 (d, *J* = 11.2 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm): 165.3, 157.0, 135.1, 135.1, 129.4, 128.9, 128.6, 127.6, 127.6, 126.4, 78.3$_{CF3}$ (*J* = 27 Hz), 78.0$_{CF3}$, 77.8$_{CF3}$, 77.5$_{CF3}$, 77.3, 67.2, 51.6, 46.2.

HRMS (ESI): *m/z* calculated for $C_{19}H_{17}F_3N_2O_2H^+$: 363.1320, found: 363.1323.

7. Crystal data and structure refinement for the representative product 5d



Identification code	**5d**
Empirical formula	$C_{27}H_{29}BrN_2O_5$
Formula weight	541.43
Temperature/K	150(40)
Crystal system	triclinic
Space group	P-1

a/Å	9.8013(3)
b/Å	11.1877(5)
c/Å	13.1188(6)
α/°	99.051(4)
β/°	106.017(3)
γ/°	106.133(4)
Volume/$Å^3$	1284.88(10)
Z	2
$\rho_{calc}g/cm^3$	1.399
μ/mm^{-1}	2.508
F(000)	560.0
Crystal size/mm^3	0.75 × 0.4 × 0.3
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.506 to 134.144
Index ranges	$-11 \leq h \leq 8$, $-13 \leq k \leq 13$, $-15 \leq l \leq 15$
Reflections collected	13582
Independent reflections	4589 [R_{int} = 0.0366, R_{sigma} = 0.0306]
Data/restraints/parameters	4589/0/320
Goodness-of-fit on F^2	1.056
Final R indexes [I>=2σ (I)]	R_1 = 0.0504, wR_2 = 0.1316
Final R indexes [all data]	R_1 = 0.0520, wR_2 = 0.1341
Largest diff. peak/hole / e $Å^{-3}$	1.00/-0.46

8. Procedure for *in vitro* minimum inhibitory concentration assay

- Motivation of this study: We were inspired by the SAP core structure of the products, which has already been demonstrated to show antibacterial activity [3]. Moreover, spiro-frameworks with lactam functionalities are widely existed in the skeleton of many clinically used antibiotics such as cephalosporins. Therefore, we expected the synthesized novel spiroaziridines with γ-lactam functionalities would also have potential antibacterial bioactivity.

- Detailed work procedure: The minimum inhibitory concentration (MIC) of each compound was determined using a standard broth microdilution assay.[4] The procedure is that MIC data was determined by a microdilution method, following the National Committee for Clinical Laboratory Standards (NCCLS) (now called the Clinical Laboratory Standards Institute [CLSI]) The stock solutions of test compounds were diluted to give a serial, 2-fold

series, yielding final chemical concentrations that ranged from 128 to 8μg/mL. The MIC was defined as the lowest concentration of the chemical that inhibited the development of visible bacterial growth after an incubation for 16 h at 37^{o}C.

9. References and notes

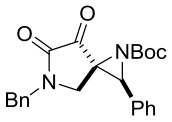
[1] a) E. Krell, *Handbook of Laboratory Distillation*, Elseriver Publishing Company, Amsterdam-London-New York, **1963**; b) M. J. Rosengart, *The Technique of Distillation and Rectification in the Laboratory*, VEB Verlag Technik, Berlin, **1954**; c) H. Stage *Columns for laboratory distillation*, *Angew. Chem.*, **1947**, *B19*, 175.

[2] P. L. Southwick, E. F. Barnas, *J. Org. Chem.*, **1962**, *27*, 98.

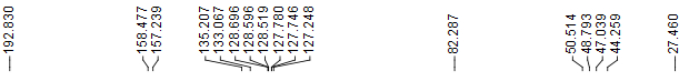
[3] M. Kidwai, S. Saxena, M. K. R. Khan, S. S. Thukral, *Bioorg. Med. Chem. Lett.*, **2005**, *15*, 4295.

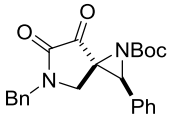
[4] L. Ouyang, Y. Huang, Y. Zhao, G. He, Y. Xie, J. Liu, J. He, B. Liu, Y. Wei, *Bioorg. Med.Chem. Lett.*, **2012**, *22*, 3044.

10. NMR and HPLC spectra of the spiroaziridines 4a and 5

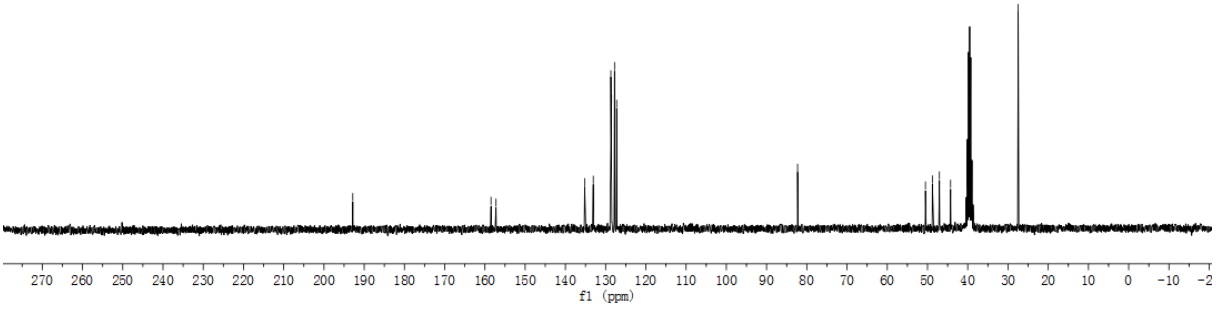


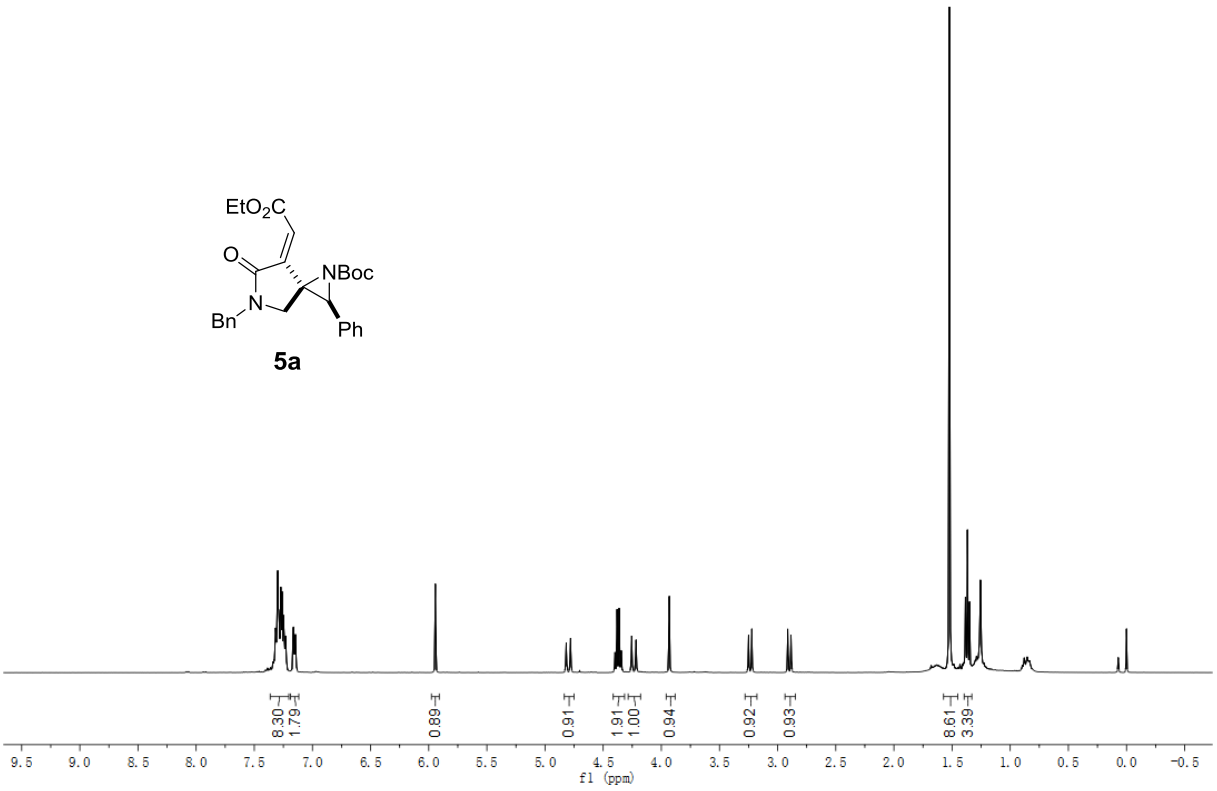
4a

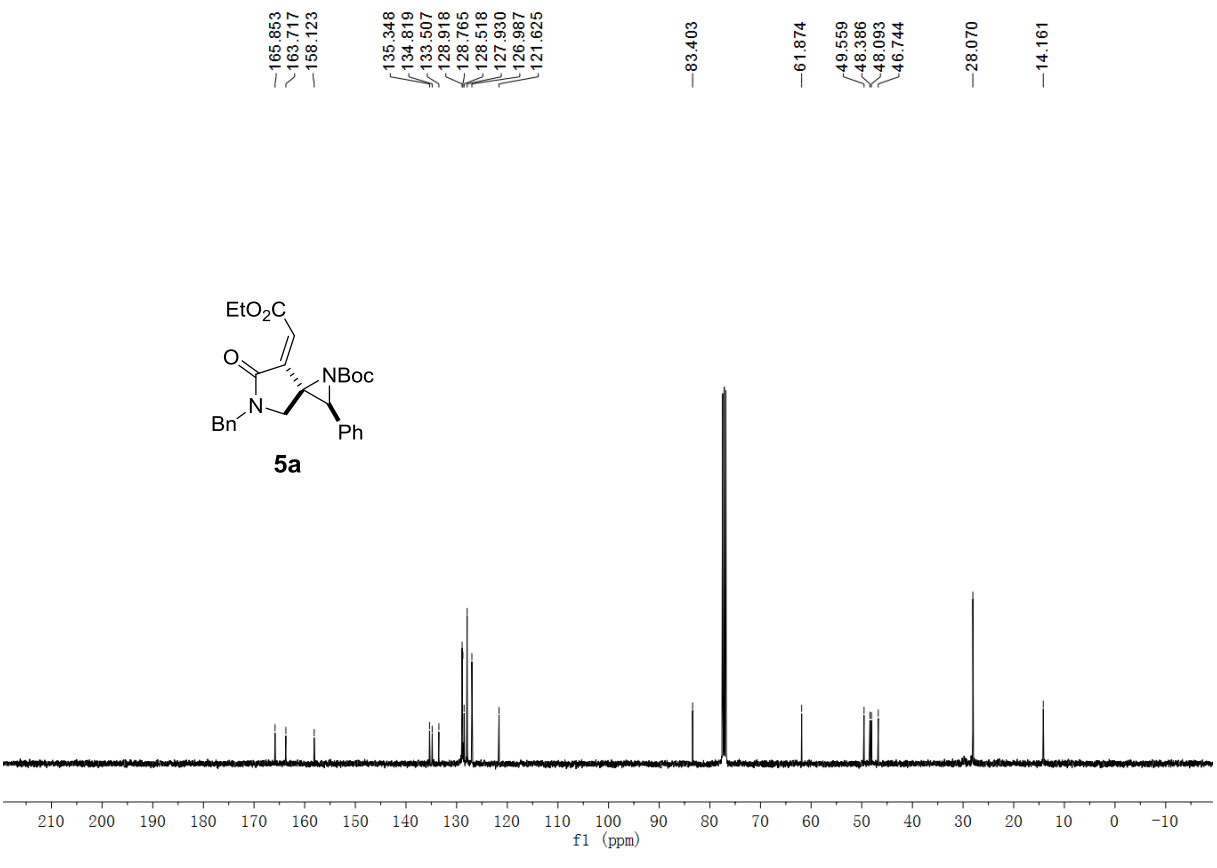




4a




EtO2C
O
NBoc
N
Bn
Ph
5a
8.30
1.79
0.89
0.91
1.91
1.00
0.94
0.92
0.93
8.61
3.39
f1 (ppm)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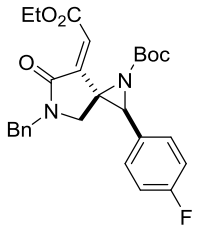
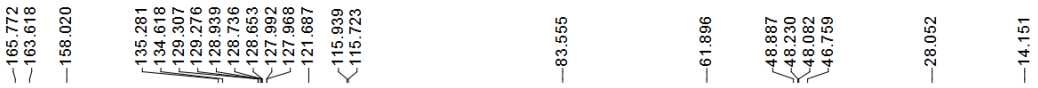
163.717
158.123
135.348
134.819
133.507
128.918
128.765
128.518
127.930
126.987
121.625
83.403
61.874
49.559
48.386
48.093
46.744
28.070
14.161
EtO2C
O
NBoc
N
Bn
Ph
5a
f1 (ppm)


EtO2C
O
Boc
N
Bn
N
F

5b

3.39
2.18
1.88
2.03
0.95
0.98
2.02
1.00
0.97
0.97
0.98
8.93
3.08
f1 (ppm)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163.618
158.020
135.281
134.618
129.307
129.276
128.939
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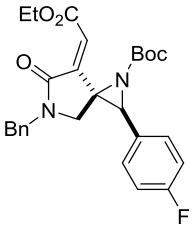
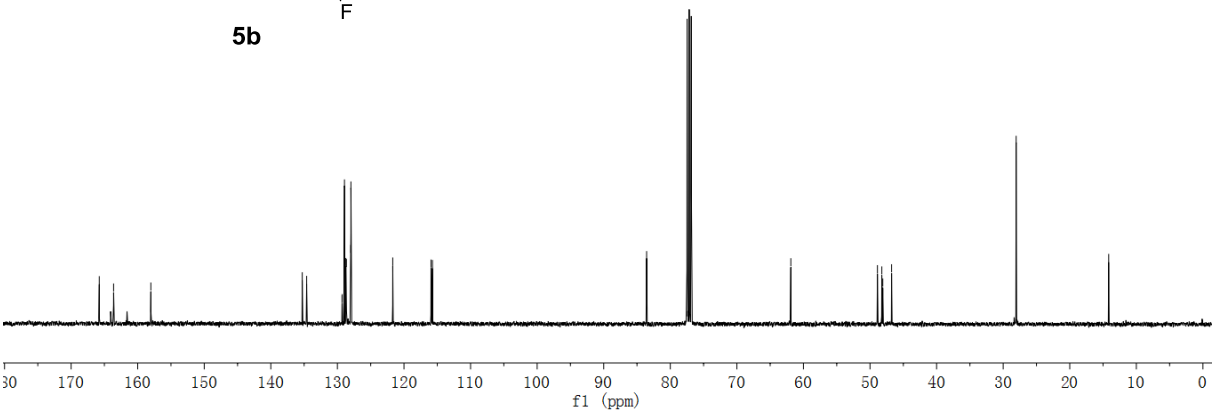
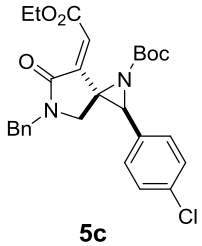
128.653
127.992
127.968
121.687
115.939
115.723
83.555
61.896
48.887
48.230
48.082
46.759
28.052
14.151


EtO2C
O
Boc
N
Bn
N
F

5b


f1 (ppm)


EtO2C
O
Boc
N
N
Bn
Cl

5c

5.33
3.89
0.96
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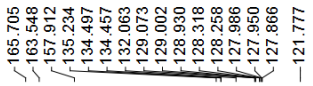
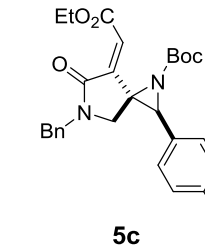
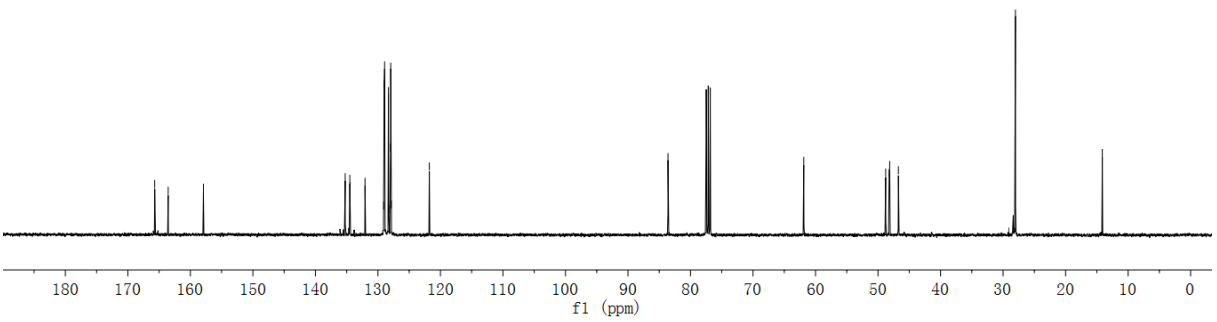
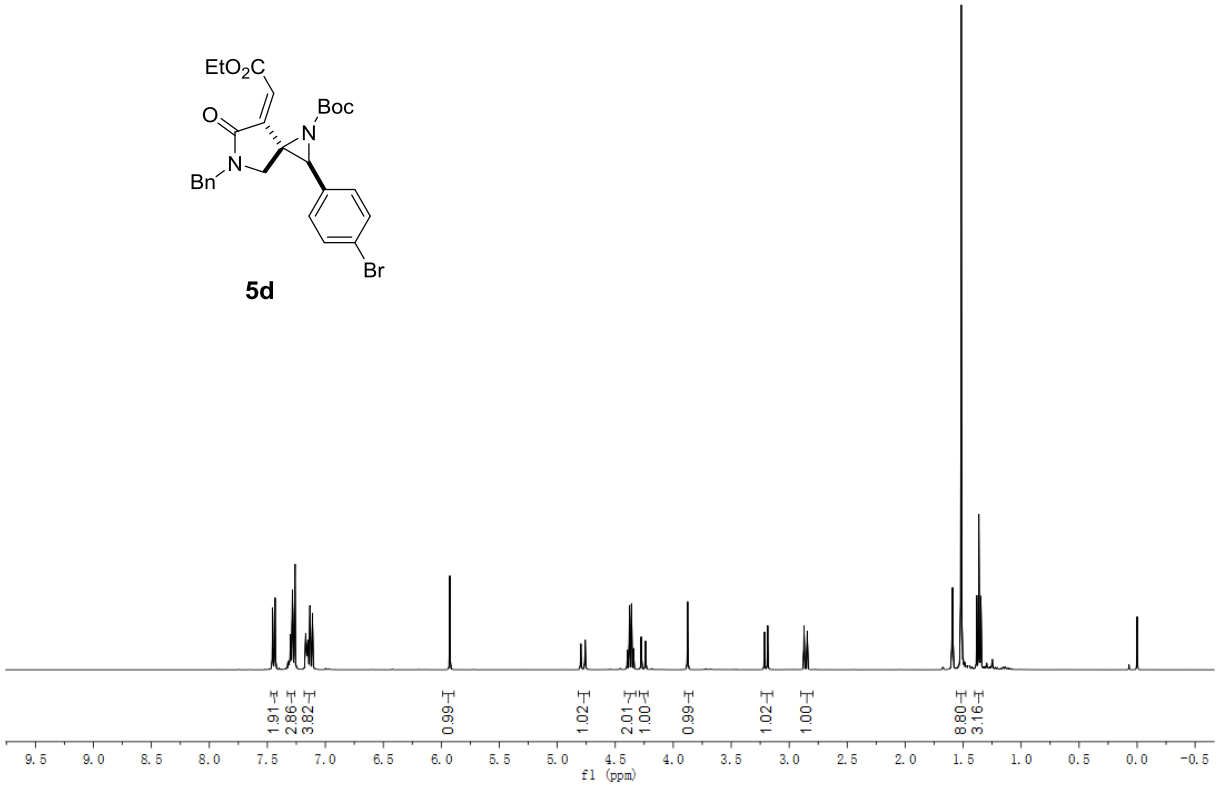
1.00
0.97
0.98
0.97
8.69
3.21
f1 (ppm)


165.705
163.548
157.912
135.234
134.497
134.457
132.063
129.073
129.002
128.930
128.318
128.258
127.986
127.950
127.866
121.777
83.597
61.879
48.781
48.225
48.133
46.739
28.021
14.126


EtO2C
O
Boc
N
N
Bn
Cl

5c


f1 (ppm)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O
Boc
N
N
Bn
Br
5d
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2.86
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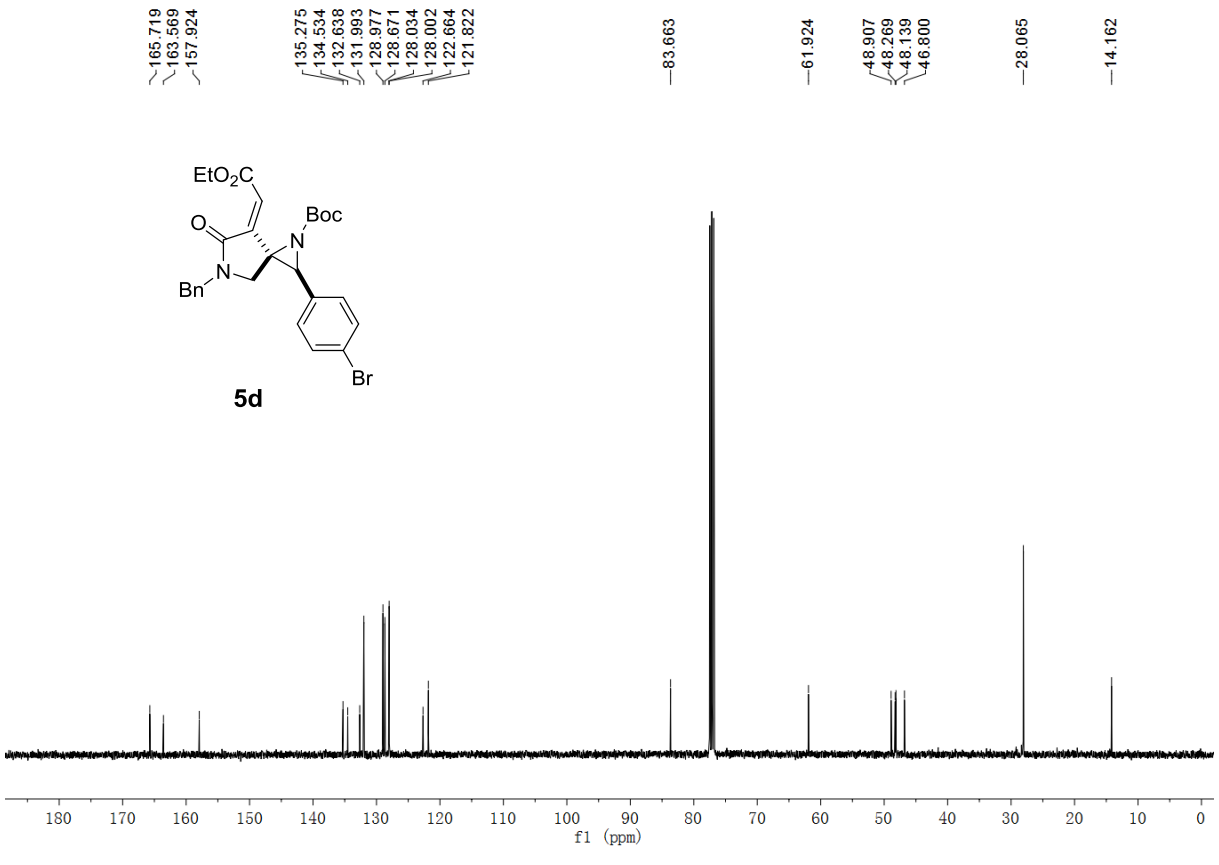
1.02
2.01
1.00
0.99
1.02
1.00
8.80
3.16
f1 (ppm)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163.569
157.924
135.275
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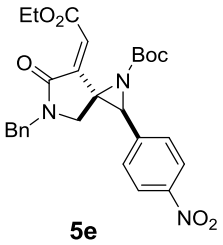
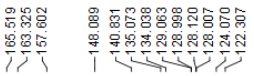
132.638
131.993
128.977
128.671
128.034
128.002
122.664
121.822
83.663
61.924
48.907
48.269
48.139
46.800
28.065
14.162
EtO2C
O
Boc
N
N
Bn
Br
5d
f1 (ppm)


EtO2C
O
Boc
N
N
Bn
NO2

5e

1.94
1.94
3.48
1.80
0.92
0.96
1.93
1.00
0.93
0.98
0.94
8.67
3.42
f1 (ppm)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163.325
157.602
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134.038
129.063
128.998
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48.464
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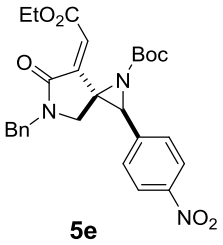
28.024
14.140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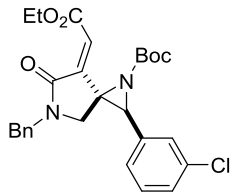
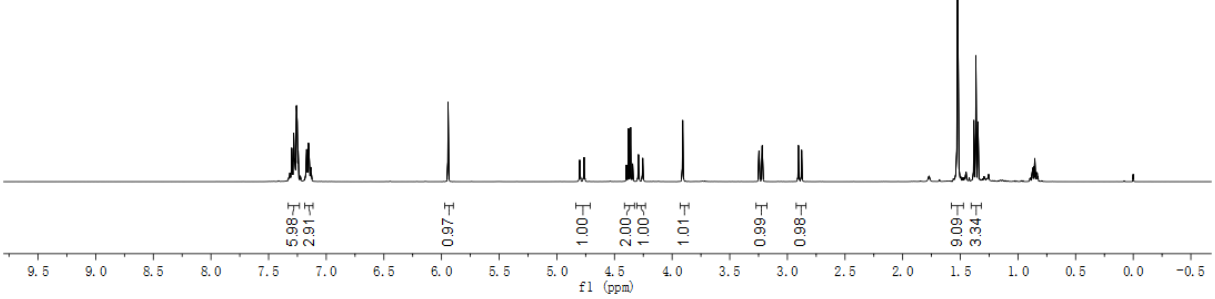
O
Boc
N
N
Bn
NO2

5e

f1 (ppm)


EtO2C
O
Boc
N
N
Bn
Cl

5f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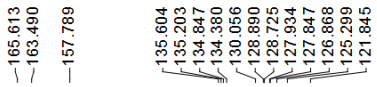
0.97
1.00
2.00
1.00
1.01
0.99
0.98
9.09
3.34
f1 (ppm)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135.203
134.847
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130.056
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128.725
127.934
127.847
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46.667
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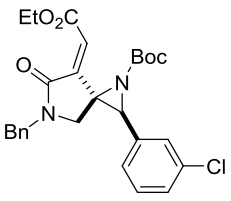
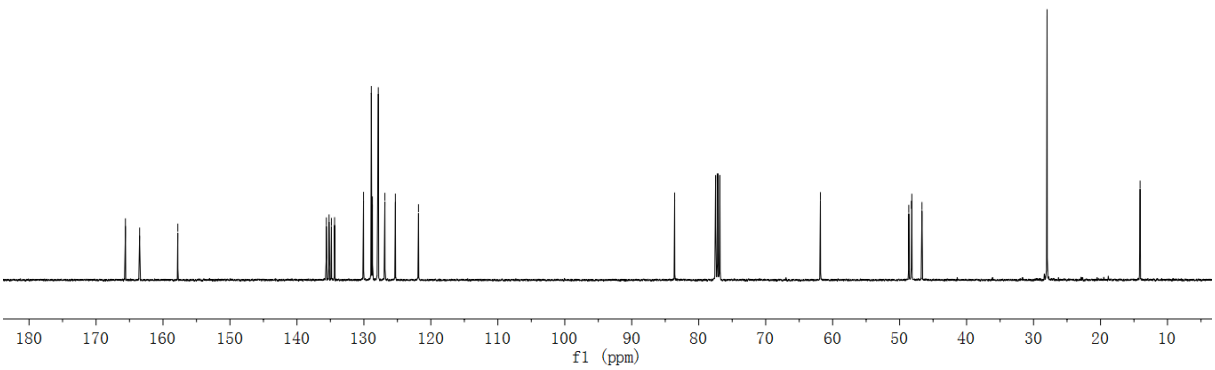
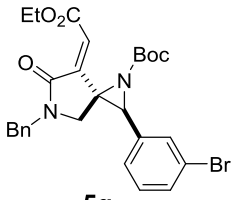
14.089


EtO2C
O
Boc
N
N
Bn
Cl

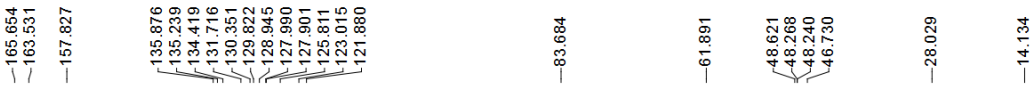
5f


f1 (ppm)


EtO2C
O
Boc
N
N
Bn
Br

5g

1.98
3.01
4.02
0.97
0.99
2.13
1.03
1.00
1.00
0.98
9.09
3.44
f1 (ppm)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125.811
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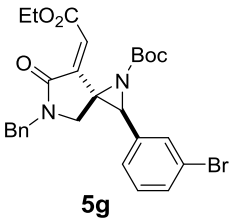
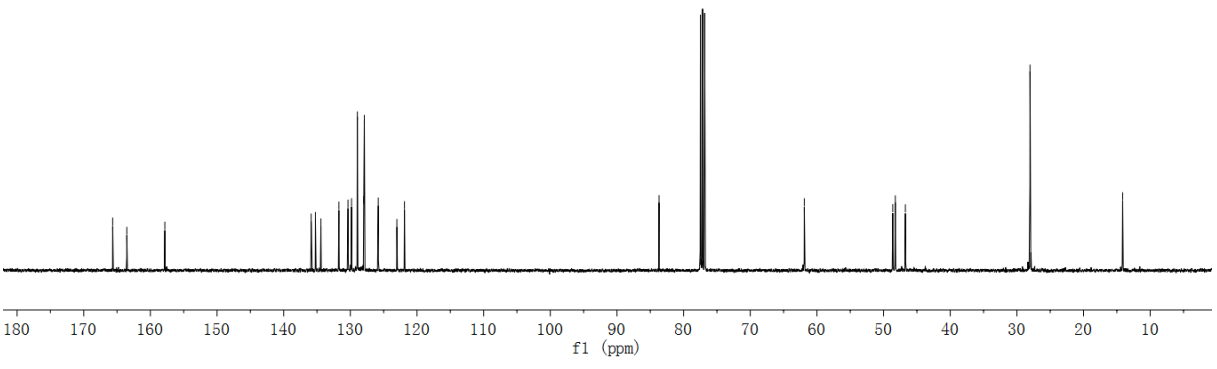
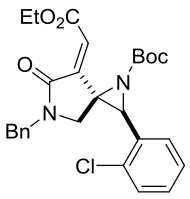
28.029
14.134


EtO2C
O
Boc
N
N
Bn
Br

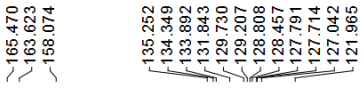
5g

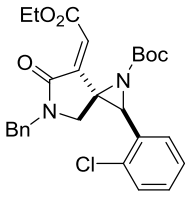

f1 (ppm)


EtO2C
O
Boc
N
N
Bn
Cl

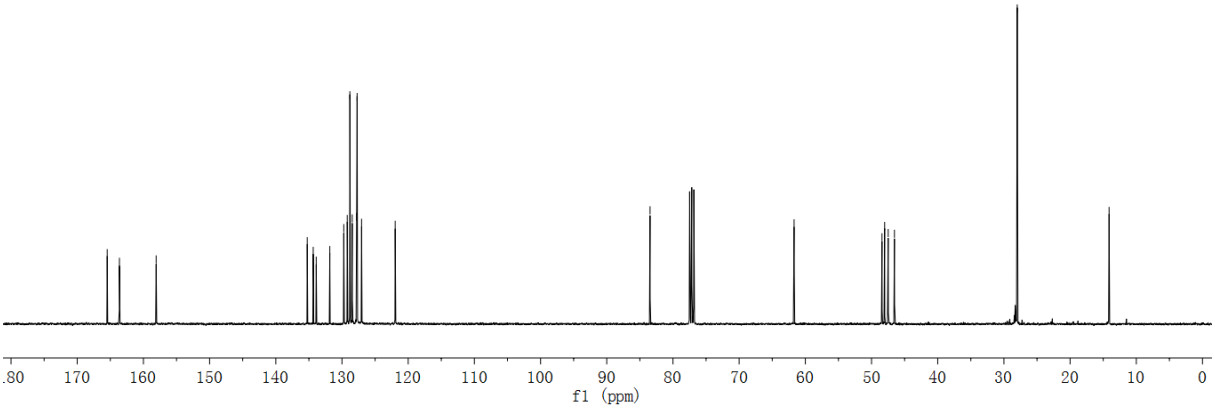
5h

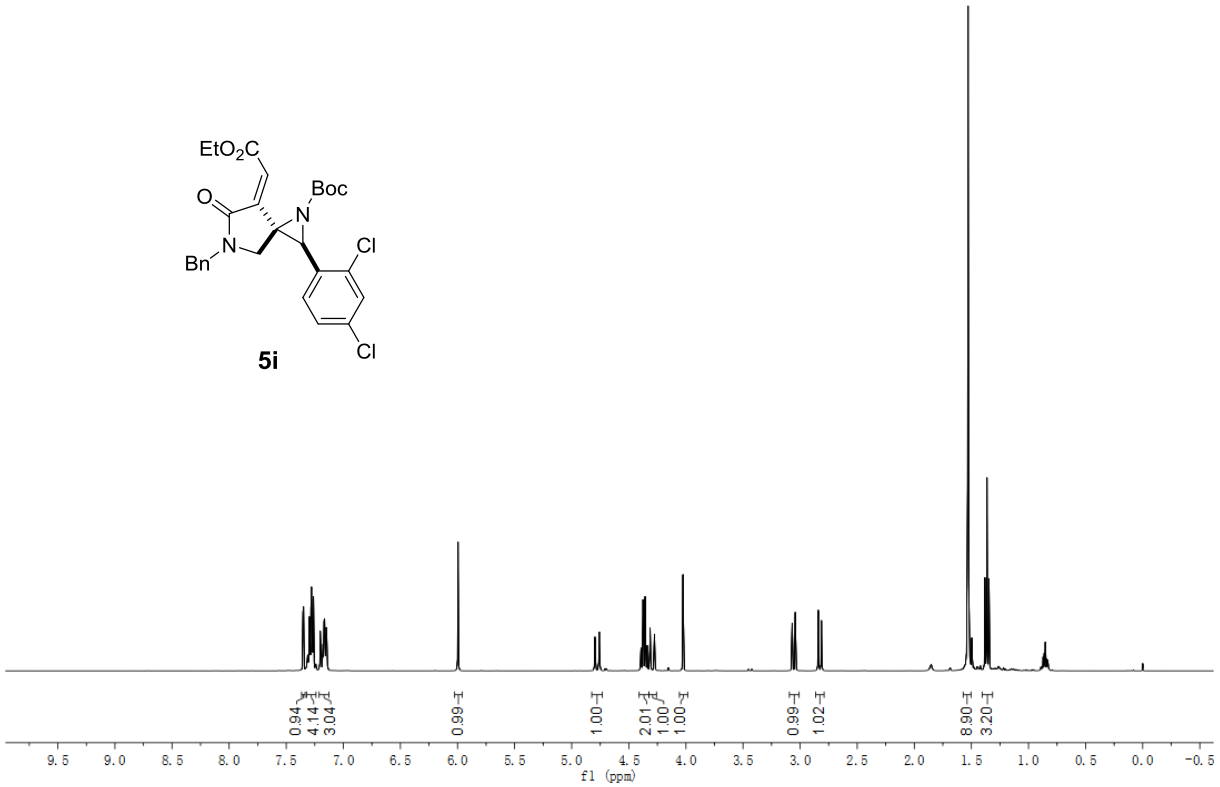
7.04
1.97
0.98
0.99
1.98
1.01
0.98
0.98
0.99
8.78
3.12
f1 (ppm)

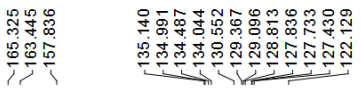

165.470
163.623
158.074
135.252
134.349
133.892
131.843
129.730
129.207
128.808
128.457
127.791
127.714
127.042
121.965
83.463
61.701
48.422
48.019
47.482
46.540
27.989
14.111

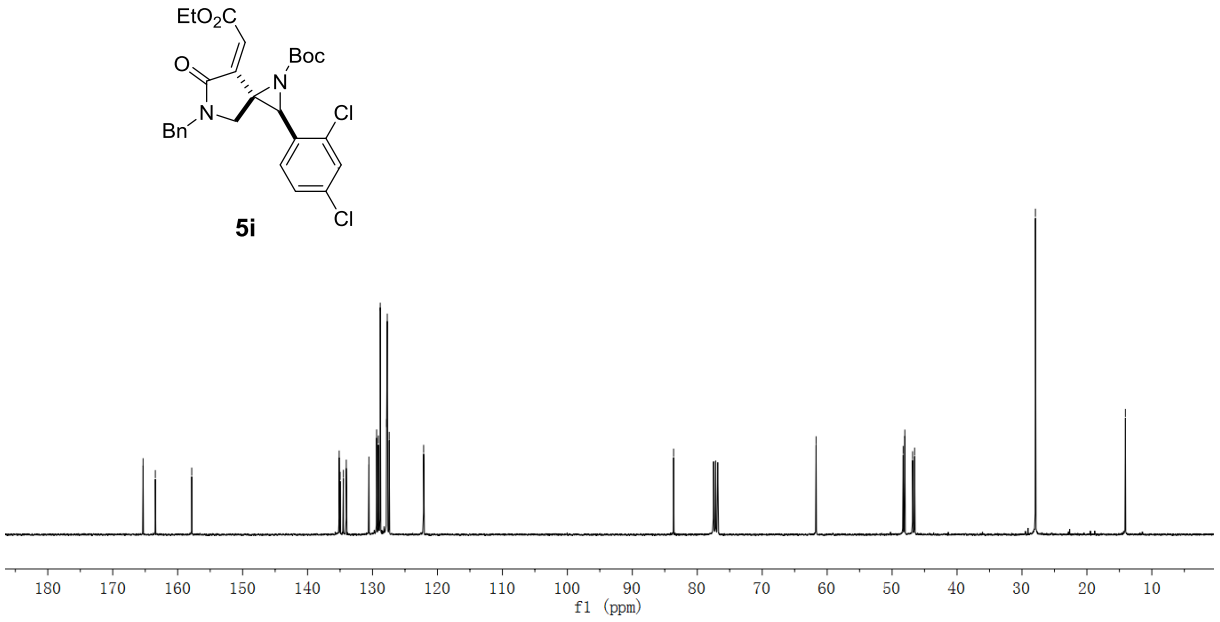

EtO2C
O
Boc
N
N
Bn
Cl

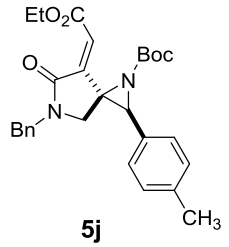
5h


f1 (ppm)

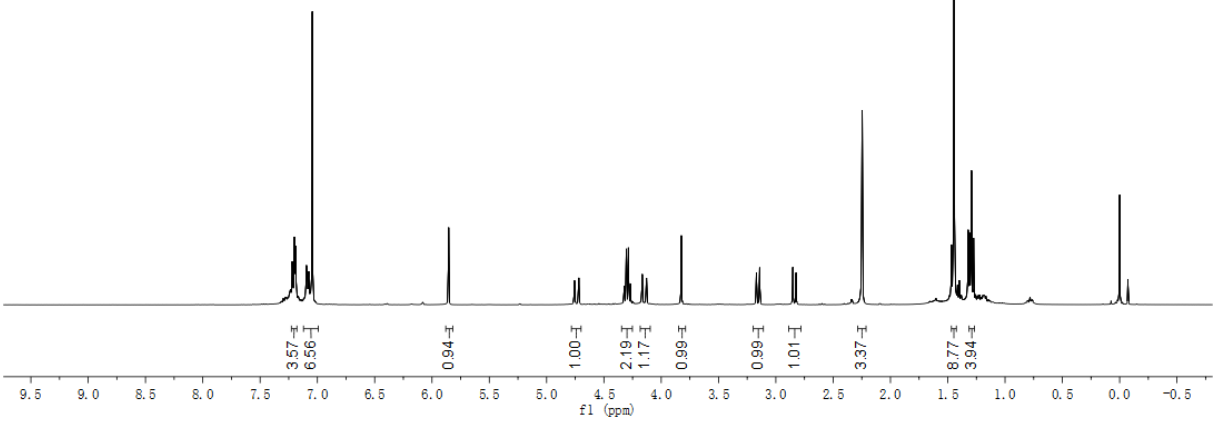

EtO2C
O
Boc
N
N
Bn
Cl
Cl
5i
0.94
4.14
3.04
0.99
1.00
2.01
1.00
0.99
1.02
8.90
3.20
f1 (ppm)

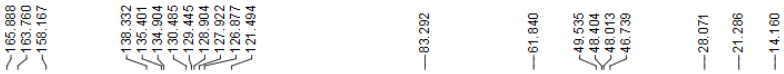

165.325
163.445
157.836
135.140
134.991
134.487
134.044
130.552
129.367
129.096
128.813
127.836
127.733
127.430
122.129
83.639
61.699
48.290
48.033
46.837
46.527
27.930
14.071

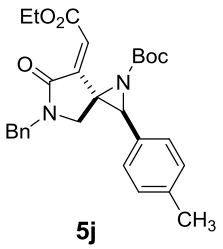

EtO2C
O
Boc
N
N
Bn
Cl
Cl
5i
f1 (ppm)


EtO2C
O
Boc
N
N
Bn
CH3

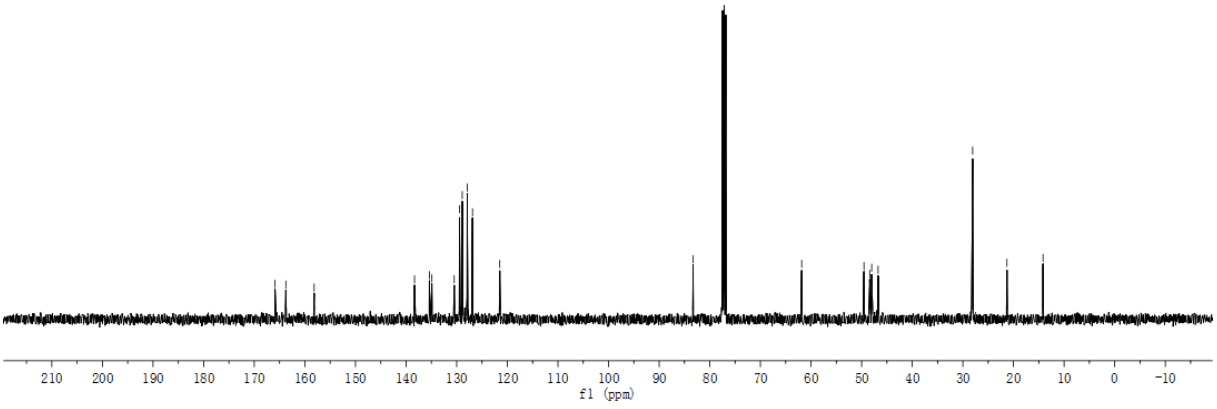
5j

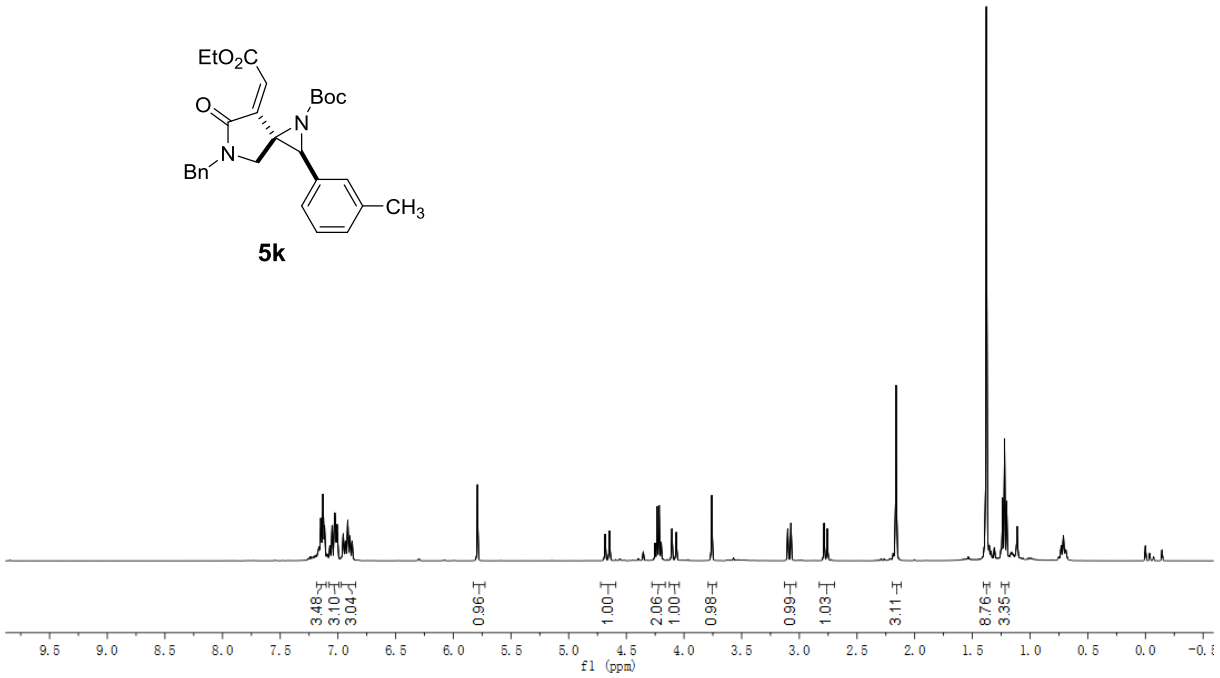

3.57
6.56
0.94
1.00
2.19
1.17
0.99
0.99
1.01
3.37
8.77
3.94
f1 (ppm)

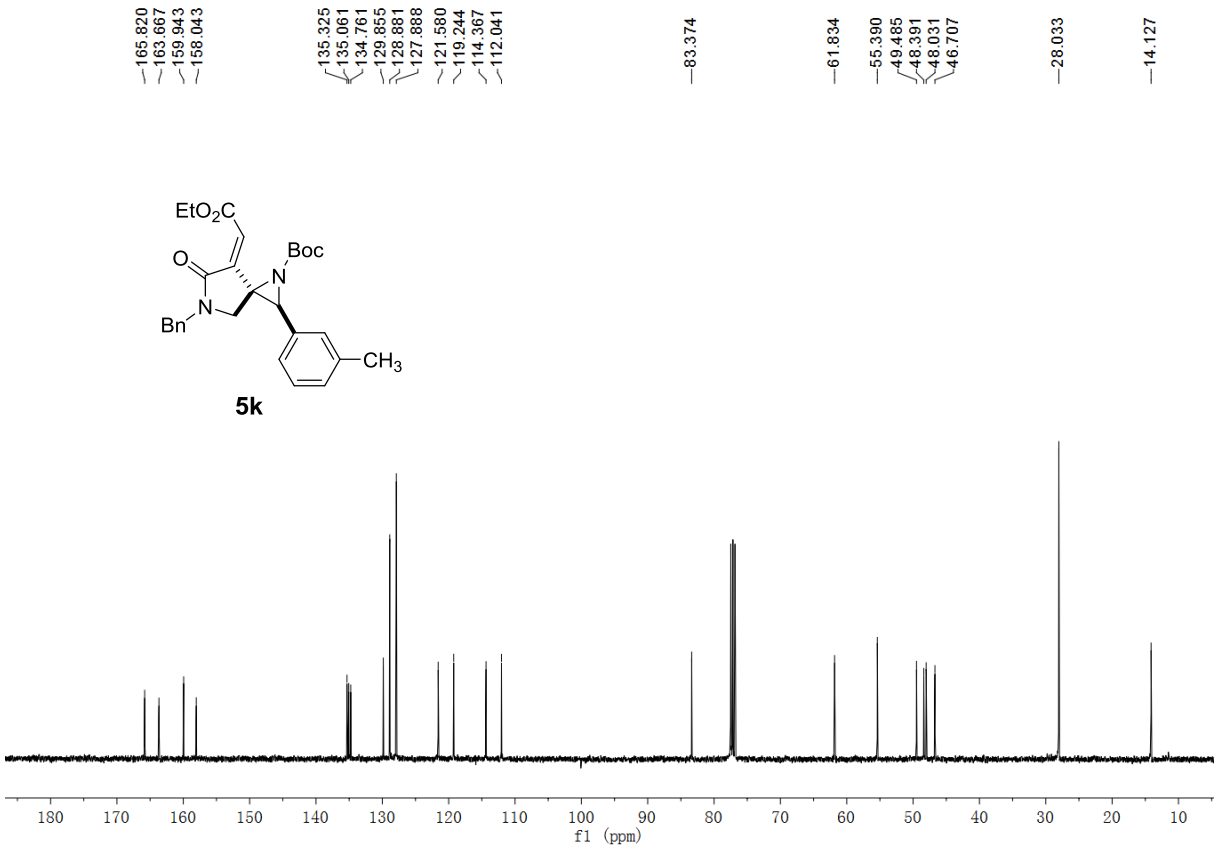

165.888
163.760
158.167
138.332
135.401
134.904
130.485
129.445
128.904
127.922
126.877
121.494
83.292
61.840
49.535
48.404
48.013
46.739
28.071
21.286
14.160

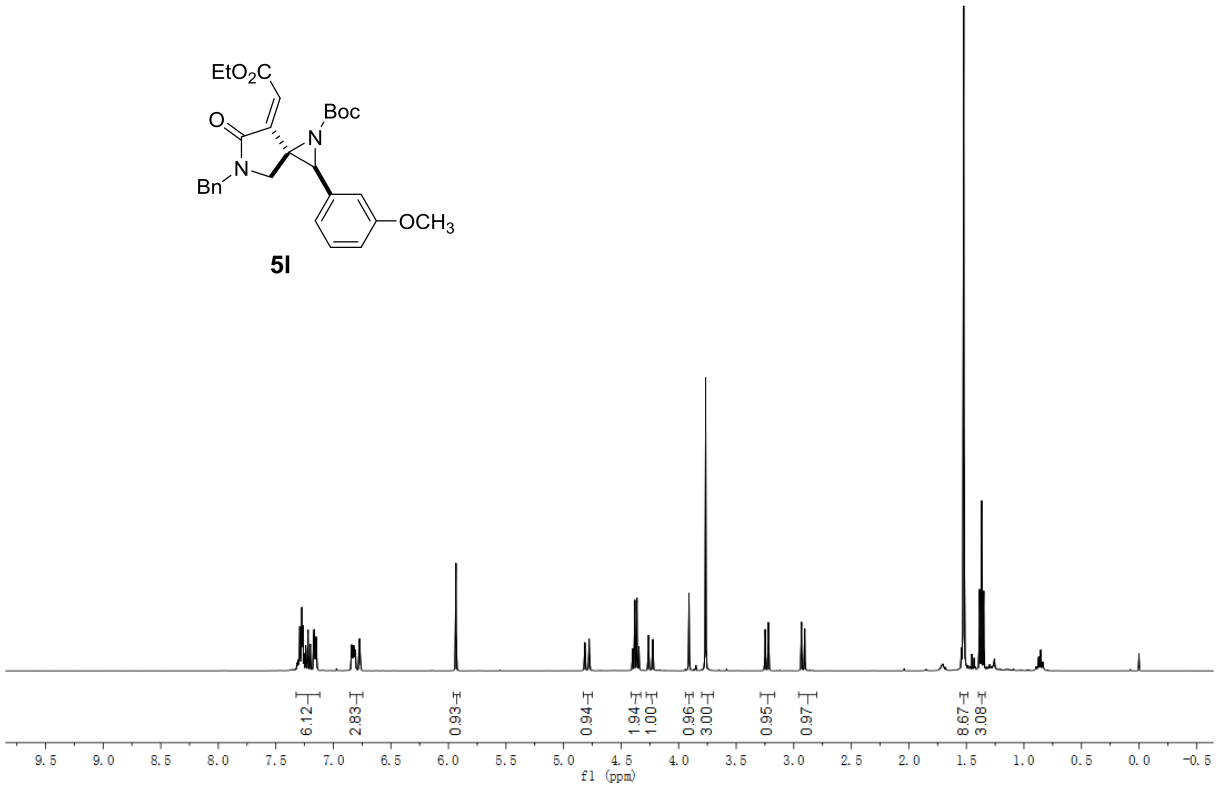

EtO2C
O
Boc
N
N
Bn
CH3

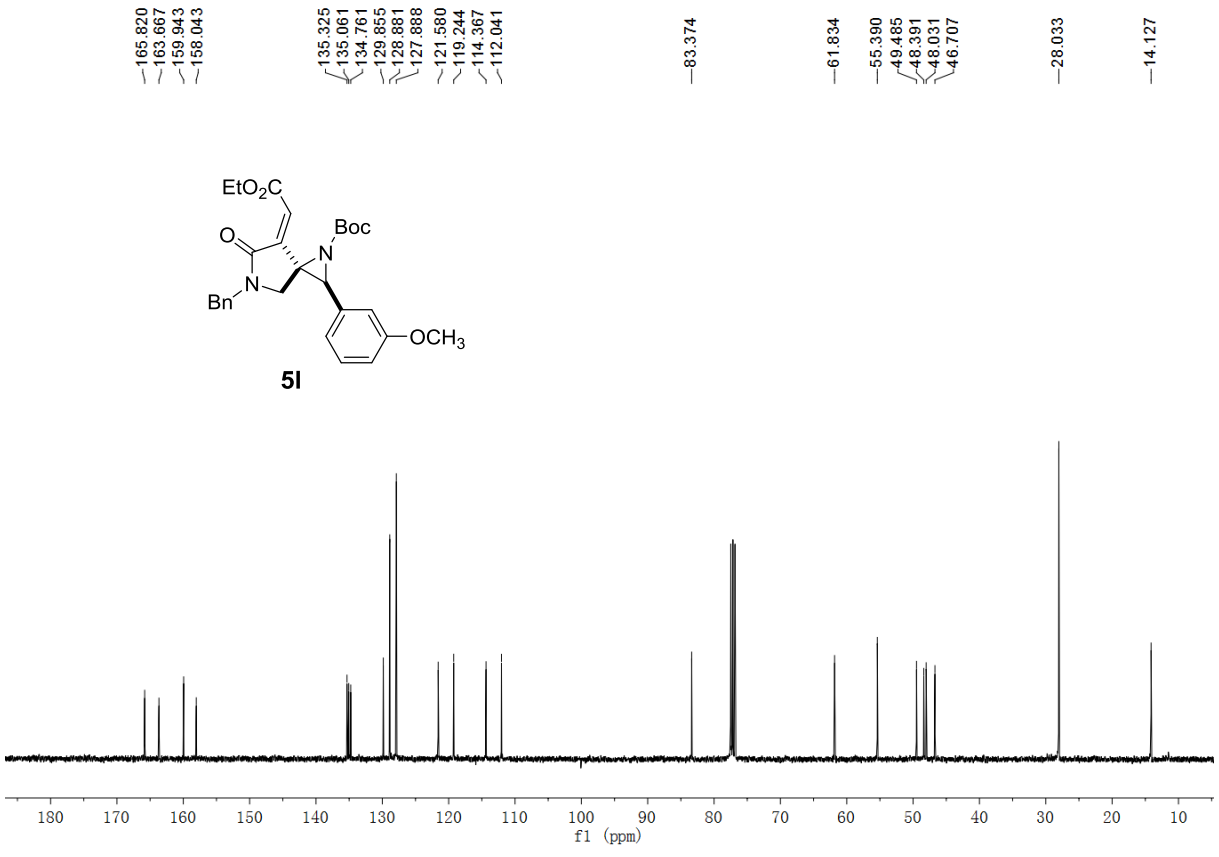
5j

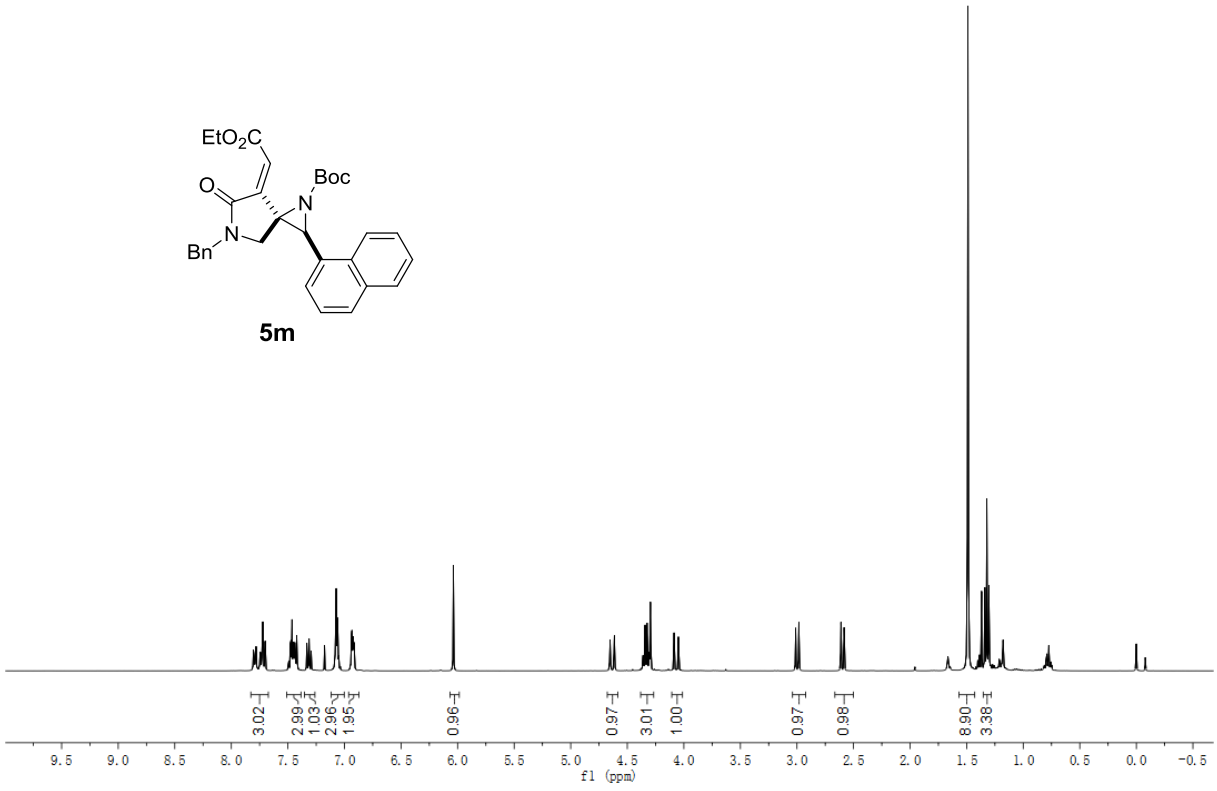

f1 (ppm)

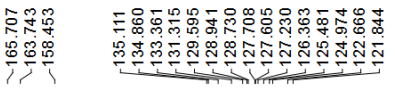

EtO2C
O
Boc
N
Bn
N
CH3
5k
3.48
3.10
3.04
0.96
1.00
2.06
1.00
0.98
0.99
1.03
3.11
8.76
3.35
f1 (ppm)


165.820
163.667
159.943
158.043
135.325
135.061
134.761
129.855
128.881
127.888
121.580
119.244
114.367
112.041
83.374
61.834
55.390
49.485
48.391
48.031
46.707
28.033
14.127
EtO2C
O
Boc
N
Bn
N
CH3
5k
f1 (ppm)


EtO2C
Boc
O
N
Bn
OCH3
5l
6.12
2.83
0.93
0.94
1.94
1.00
0.96
3.00
0.95
0.97
8.67
3.08
f1 (ppm)


165.820
163.667
159.943
158.043
135.325
135.061
134.761
129.855
128.881
127.888
121.580
119.244
114.367
112.041
83.374
61.834
55.390
49.485
48.391
48.031
46.707
28.033
14.127
EtO2C
Boc
O
N
Bn
OCH3
5l
f1 (ppm)


EtO2C
O
Boc
N
Bn
N
5m
3.02
2.99
1.03
2.96
1.95
0.96
0.97
3.01
1.00
0.97
0.98
8.90
3.38
f1 (ppm)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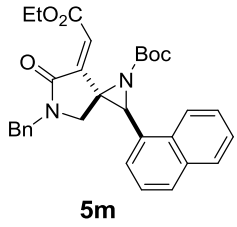
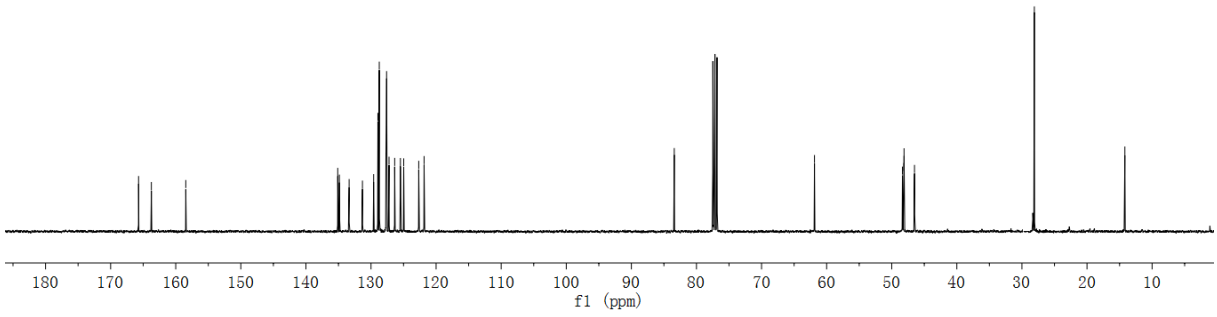
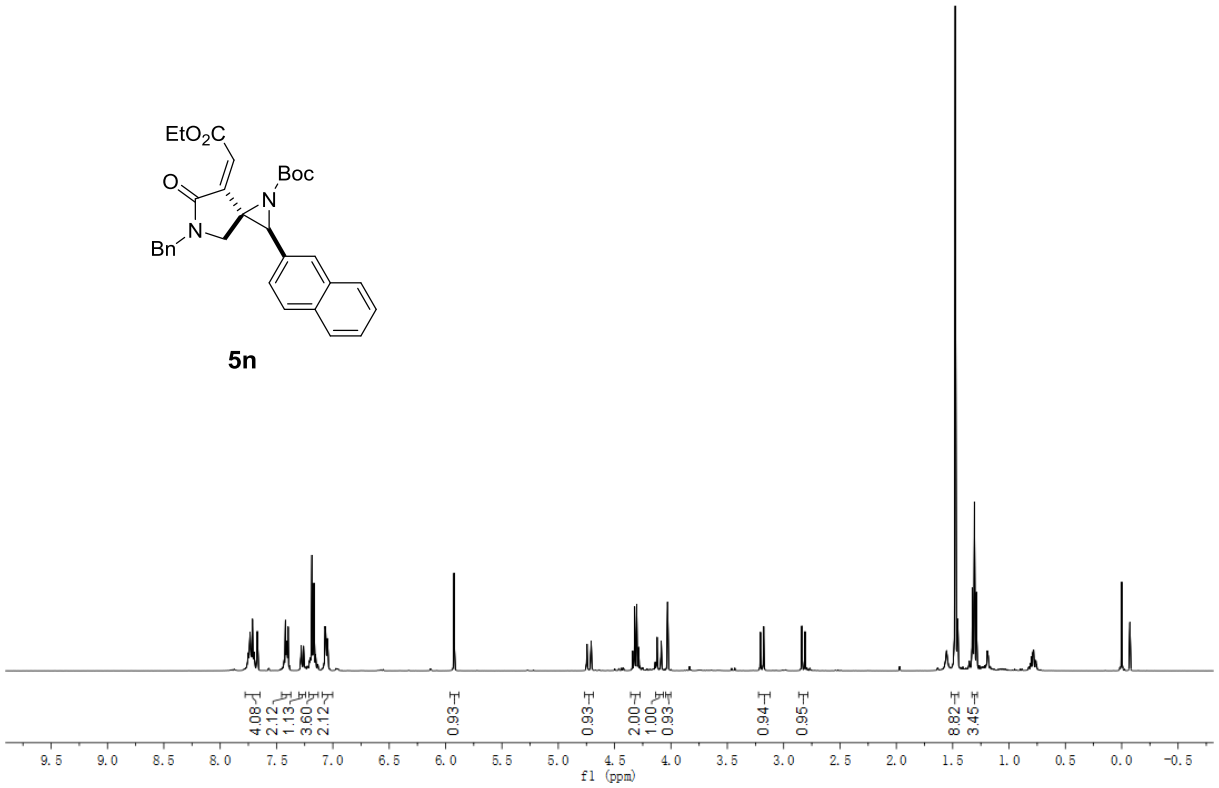
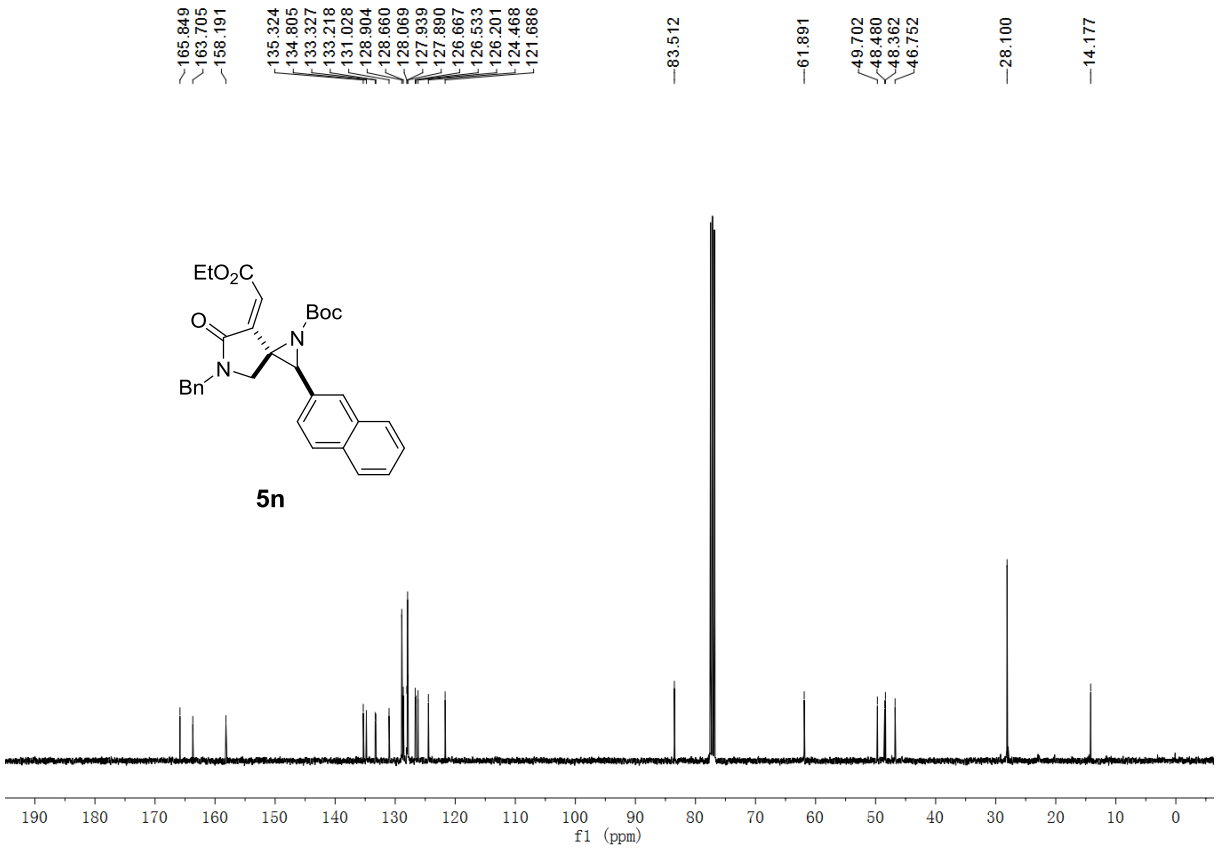
163.743
158.453
135.111
134.860
133.361
131.315
129.595
128.941
128.730
127.708
127.605
127.230
126.363
125.481
124.974
122.666
121.844
83.409
61.871
48.356
48.141
48.107
46.504
28.091
14.184


EtO2C
O
Boc
N
Bn
N
5m


f1 (ppm)


EtO2C
O
Boc
N
Bn
N
5n
4.08
2.12
1.13
3.60
2.12
0.93
0.93
2.00
1.00
0.93
0.94
0.95
8.82
3.45
f1 (ppm)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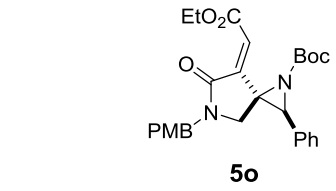
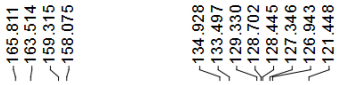
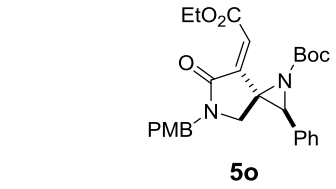
158.191
135.324
134.805
133.327
133.218
131.028
128.904
128.660
128.069
127.939
127.890
126.667
126.533
126.201
124.468
121.686
83.512
61.891
49.702
48.480
48.362
46.752
28.100
14.177
EtO2C
O
Boc
N
Bn
N
5n
f1 (ppm)


EtO2C
O
Boc
N
N
PMB
Ph

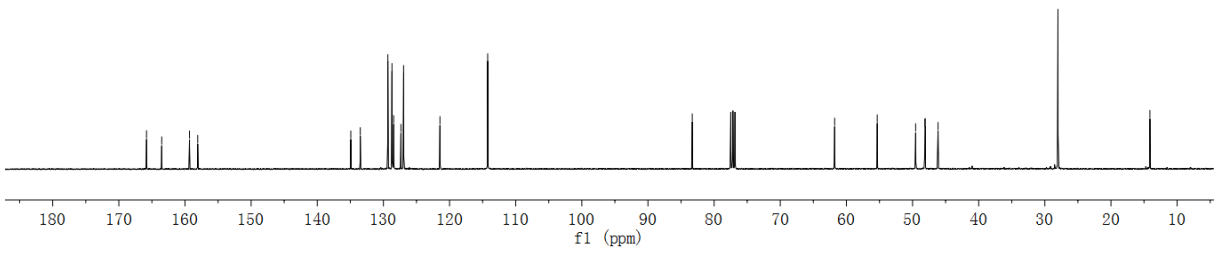
5o

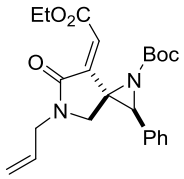
5.09
1.91
1.95
0.94
0.95
1.93
1.00
0.95
3.04
0.94
0.97
8.79
3.34
f1 (ppm)


165.811
163.514
159.315
158.075
134.928
133.497
129.330
128.702
128.445
127.346
126.943
121.448
114.234
83.305
61.777
55.339
49.532
48.145
48.075
46.145
28.015
14.110


EtO2C
O
Boc
N
N
PMB
Ph

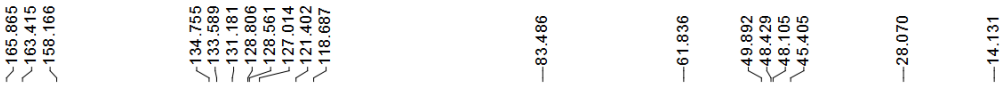
5o


f1 (ppm)


EtO2C
O
Boc
N
N
Ph

5p

5.27
0.94
0.98
1.93
1.94
0.99
1.09
1.00
0.97
0.97
8.47
2.97
f1 (ppm)


165.865
163.415
158.166
134.755
133.589
131.181
128.806
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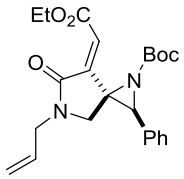
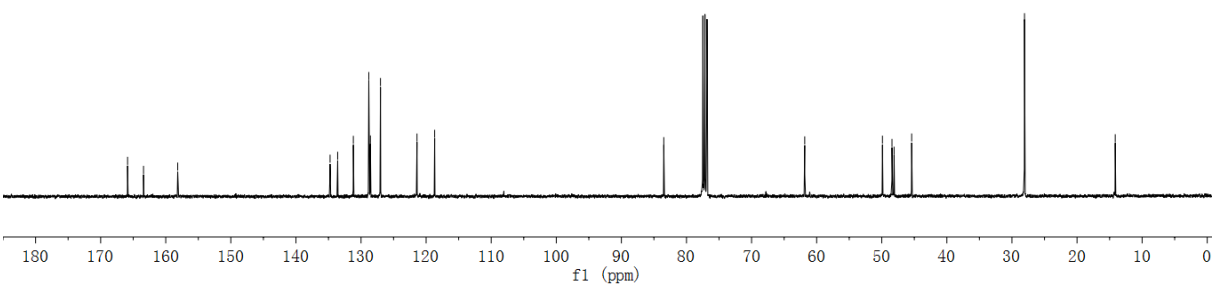
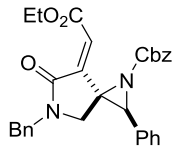
127.014
121.402
118.687
83.486
61.836
49.892
48.429
48.105
45.405
28.070
14.131

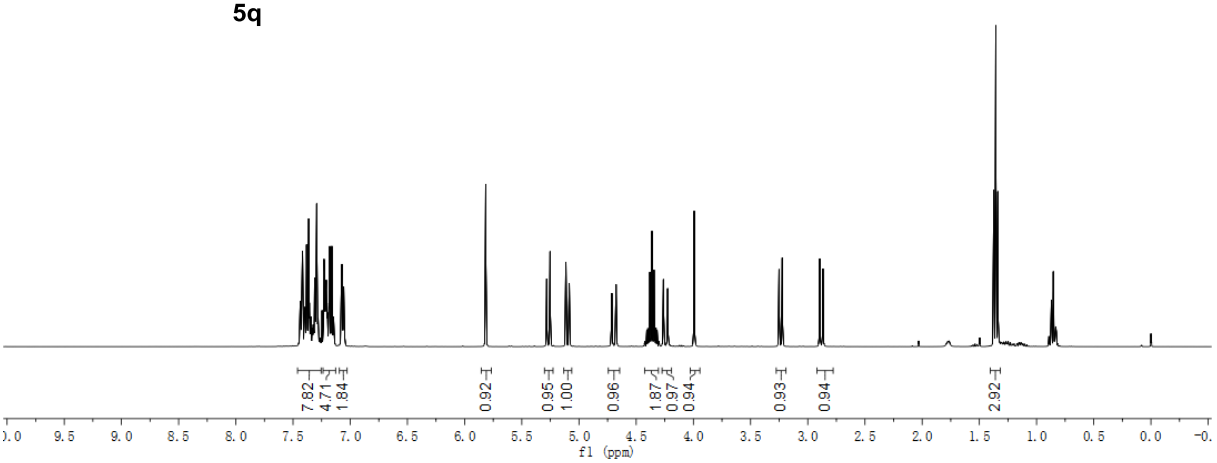

EtO2C
O
Boc
N
N
Ph

5p

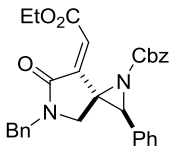

f1 (ppm)


EtO2C
O
Cbz
N
N
Bn
Ph

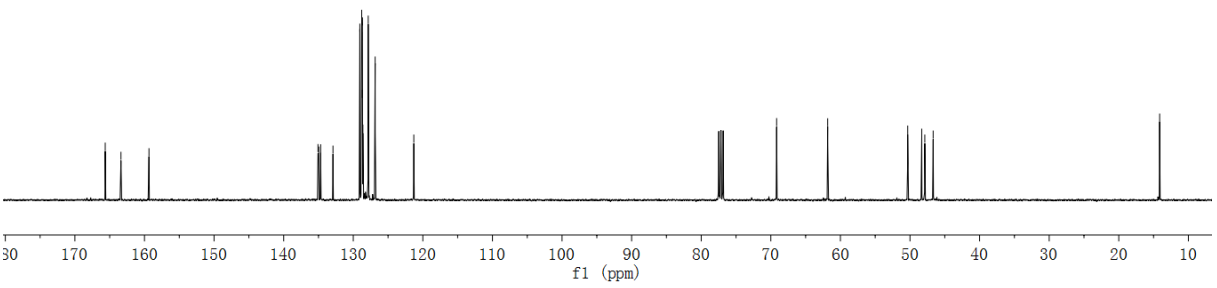
5q

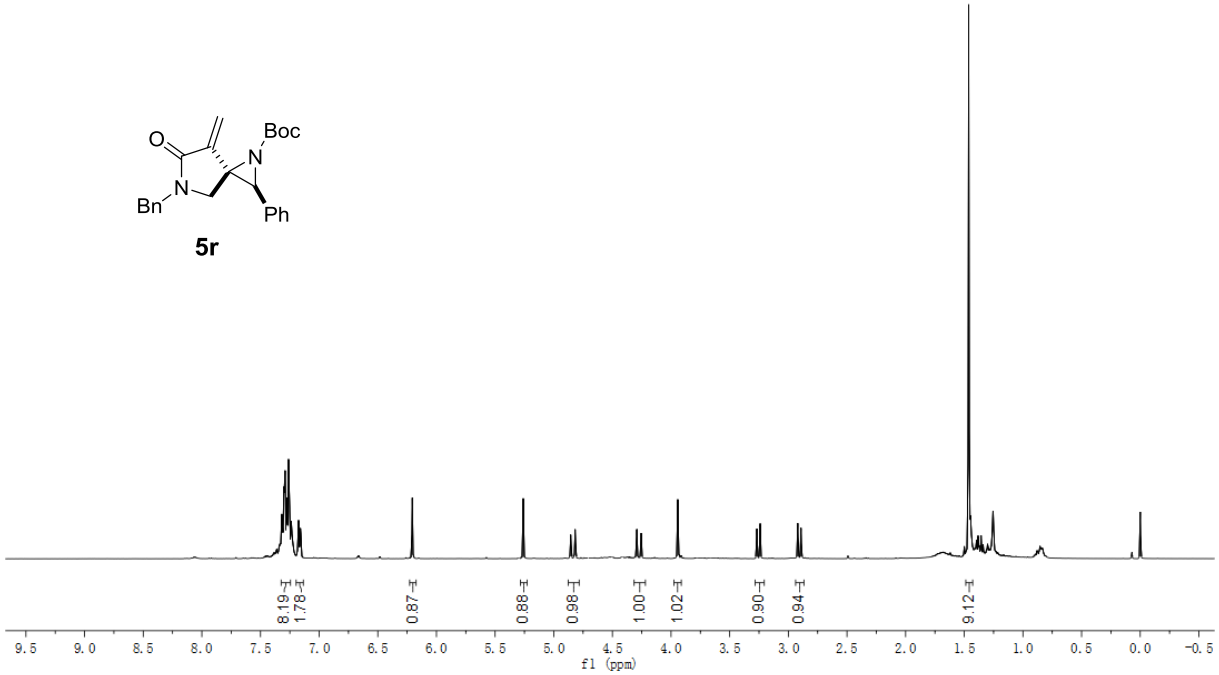

7.82
4.71
1.84
0.92
0.95
1.00
0.96
1.87
0.97
0.94
0.93
0.94
2.92
f1 (ppm)

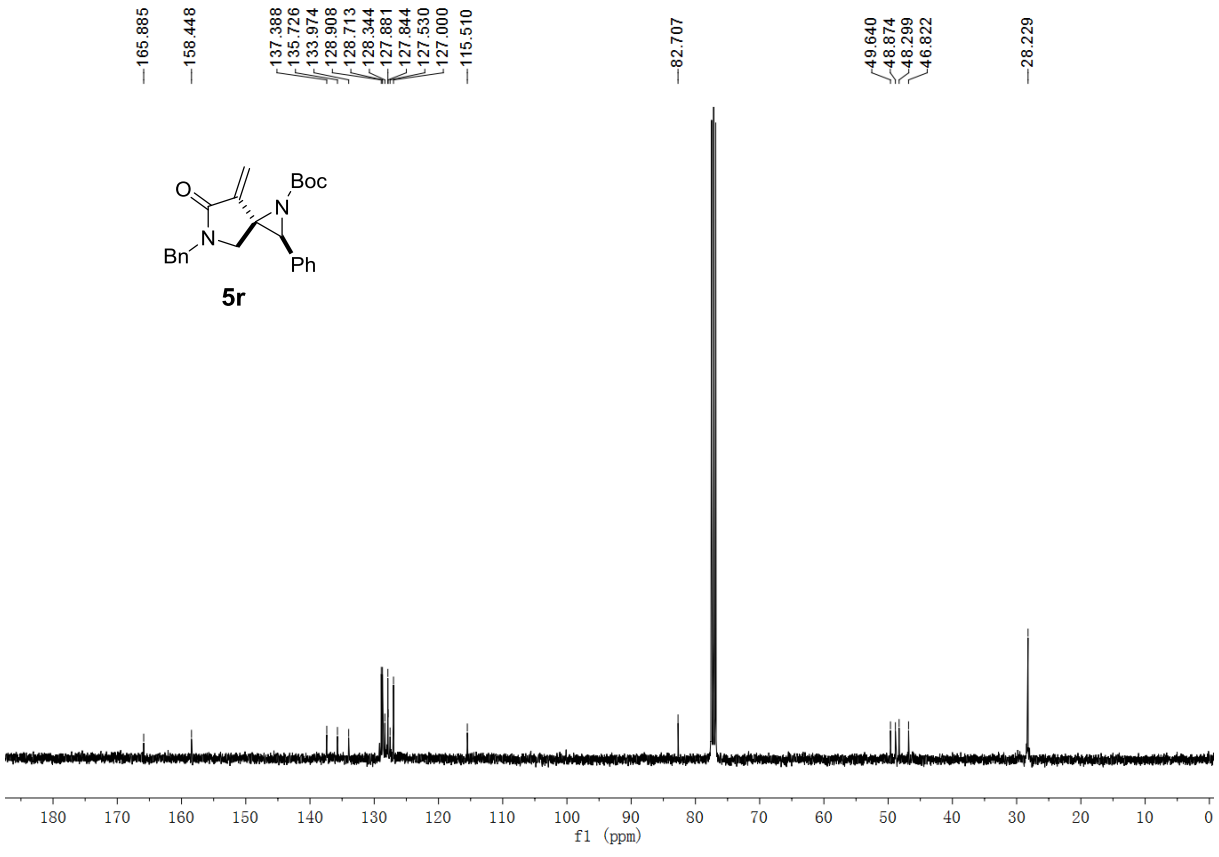

165.640
163.381
159.354
135.069
134.955
134.684
132.914
129.053
128.788
128.764
128.712
128.686
128.616
127.849
127.813
126.855
121.299
69.164
61.831
50.327
48.313
47.873
46.671
14.126

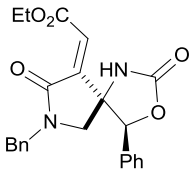

EtO2C
O
Cbz
N
N
Bn
Ph

5q

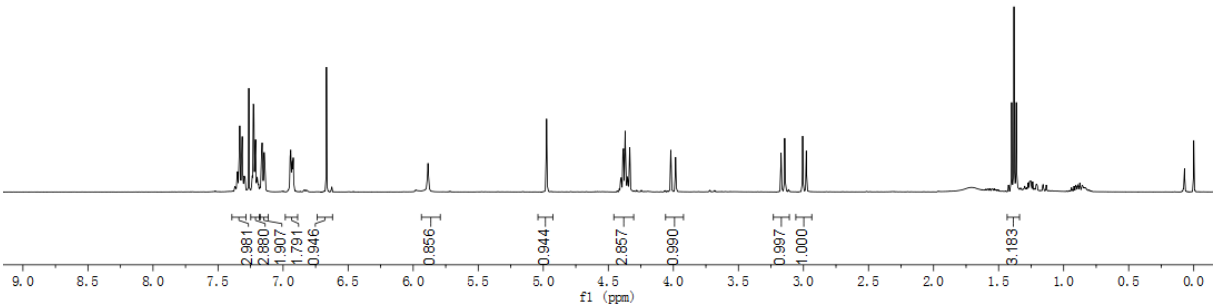

f1 (ppm)

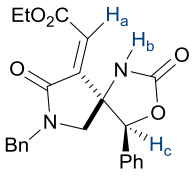

Boc
N
O
N
Bn
Ph
5r
8.19
1.78
0.87
0.88
0.98
1.00
1.02
0.90
0.94
9.12
f1 (ppm)


165.885
158.448
137.388
135.726
133.974
128.908
128.713
128.344
127.881
127.844
127.530
127.000
115.510
82.707
49.640
48.874
48.299
46.822
28.229
Boc
N
O
N
Bn
Ph
5r
f1 (ppm)

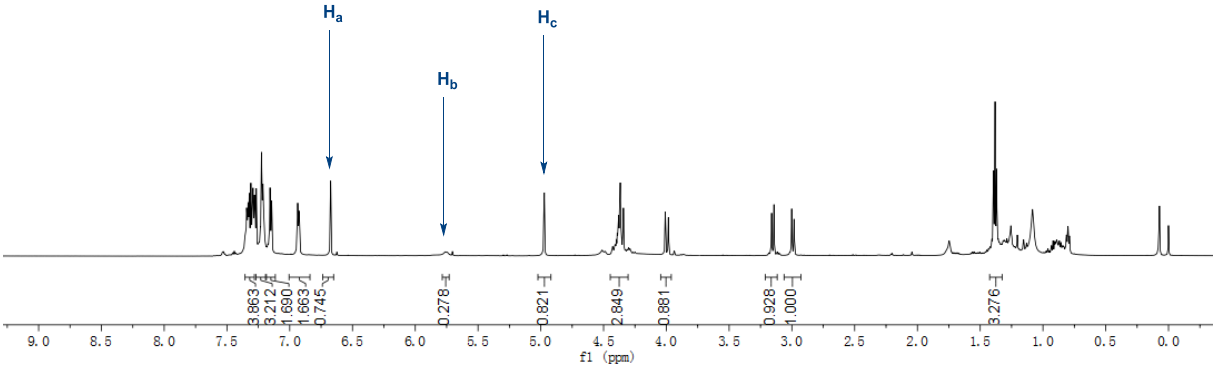


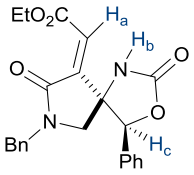
6a (major)



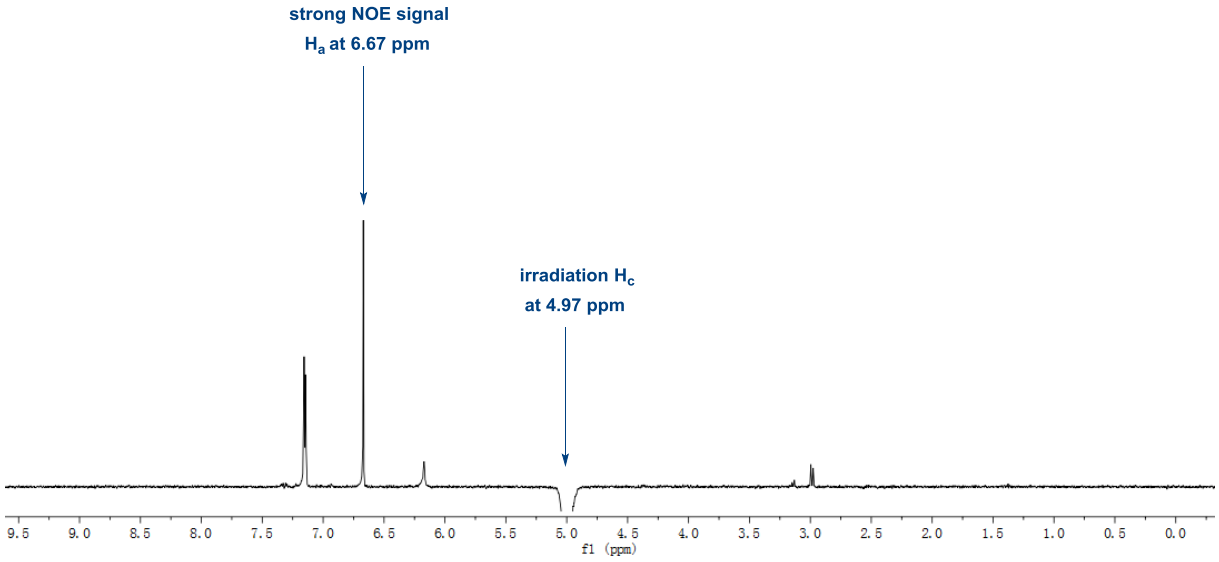


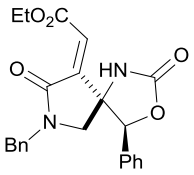
6a (major) + D_2O



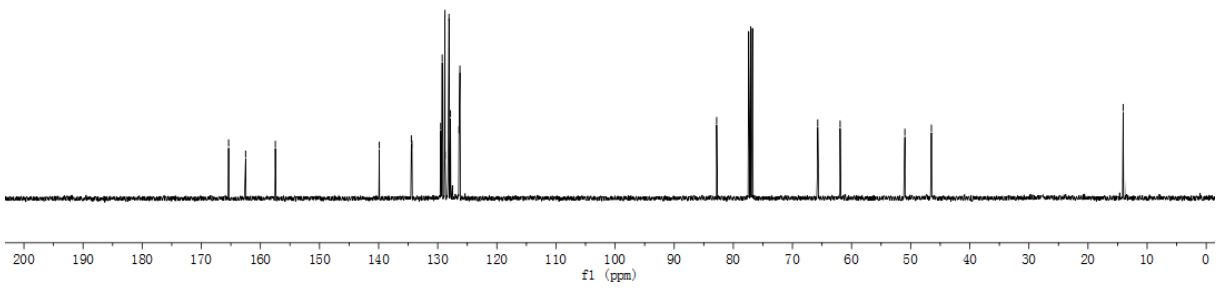


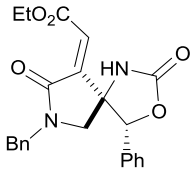
6a (major): NOEDS



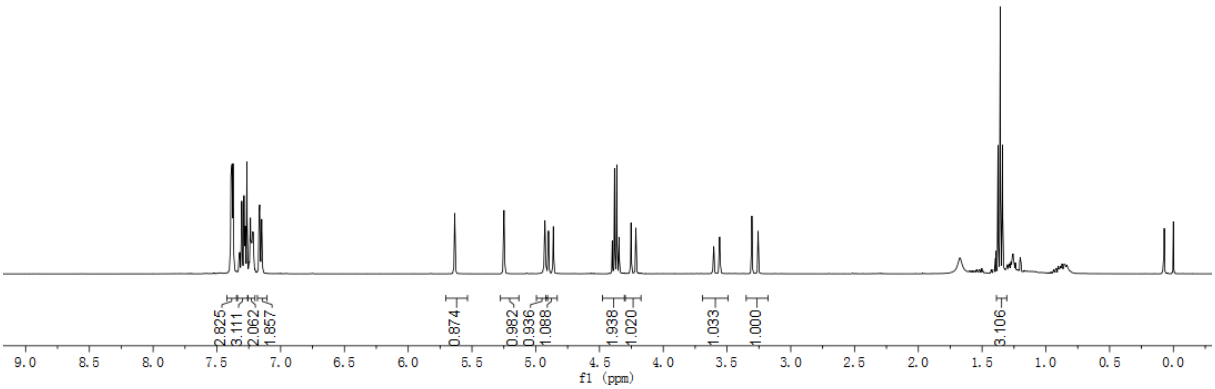


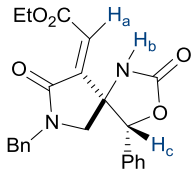
6a (major)



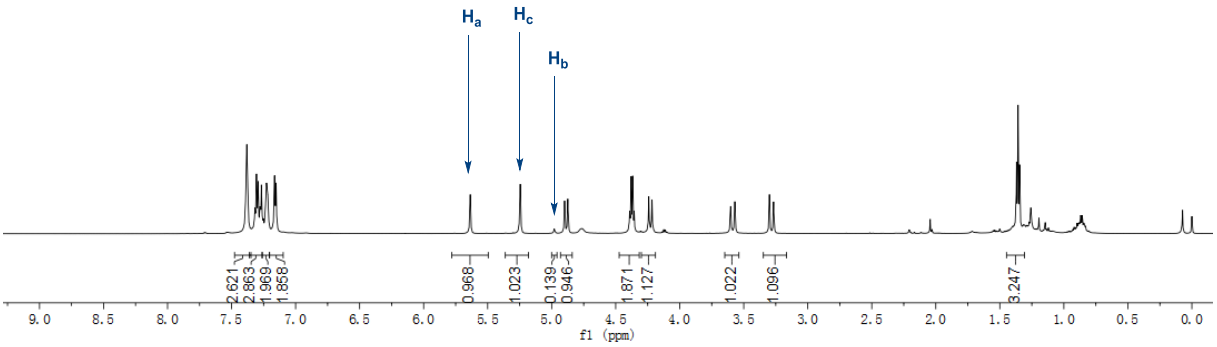


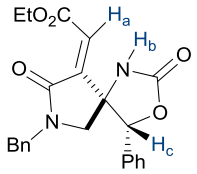
6b (minor)



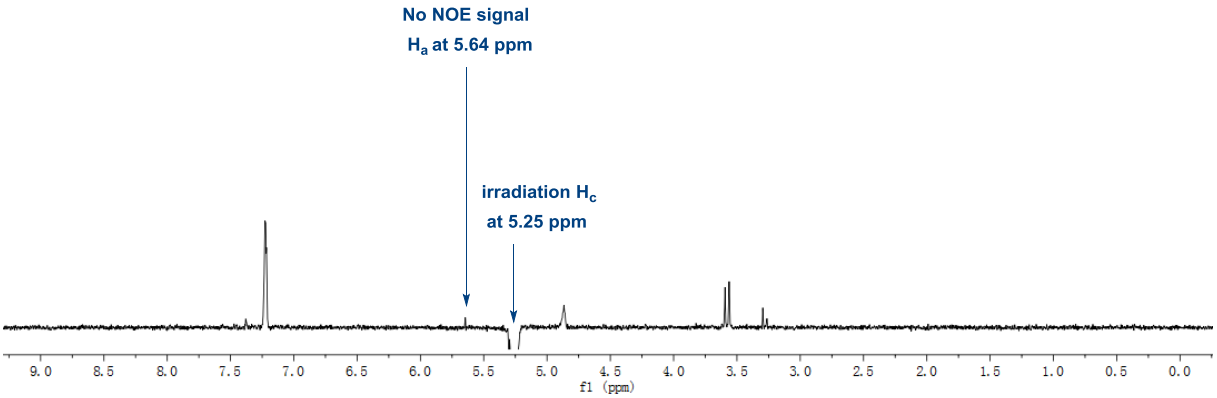


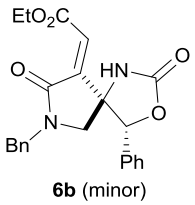
6b (minor) + D_2O



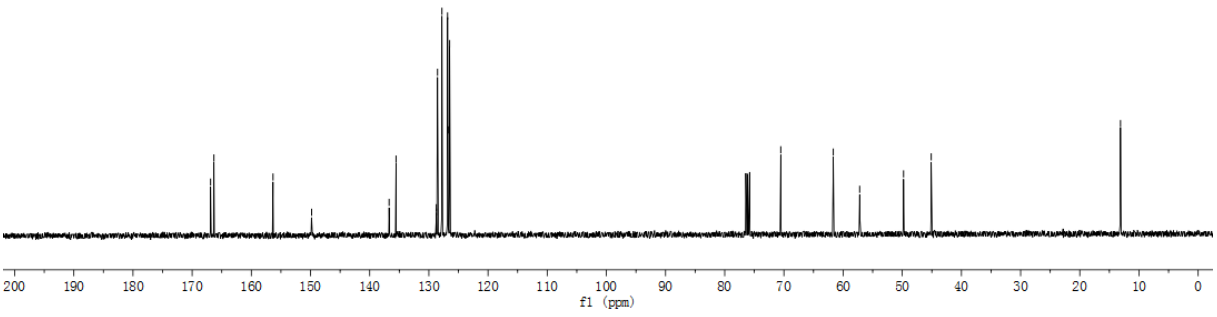


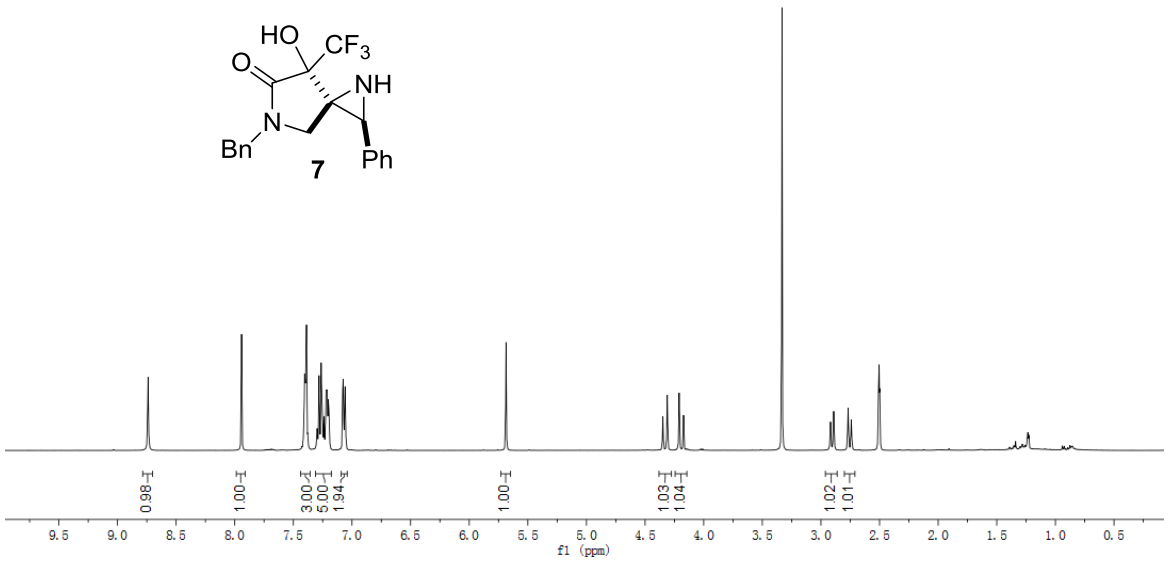
6b (minor): NOEDS

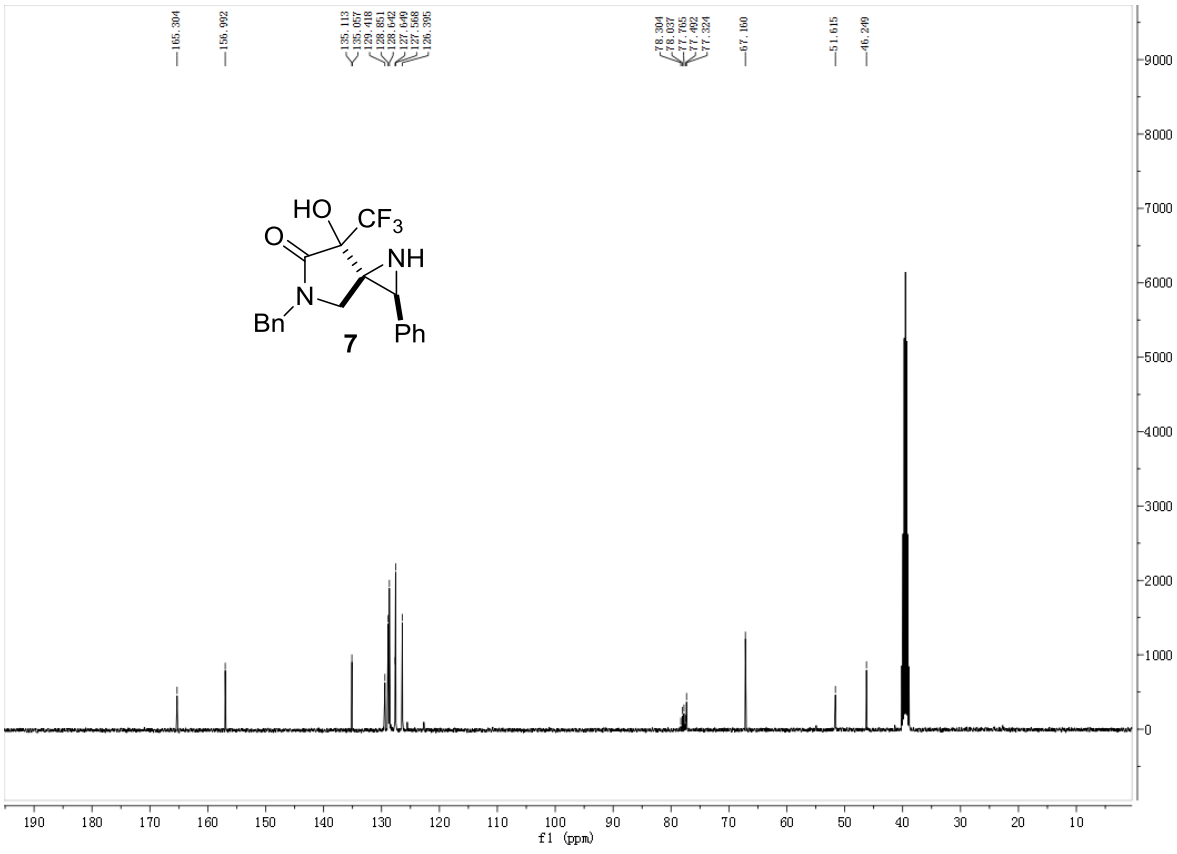


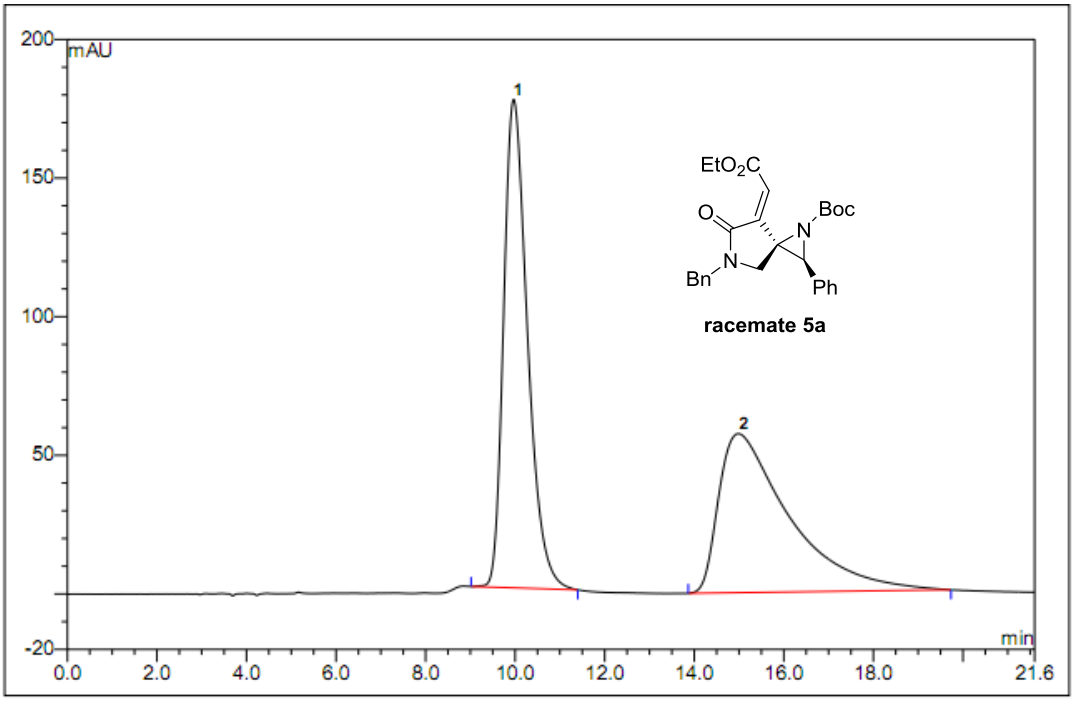


6b (minor)

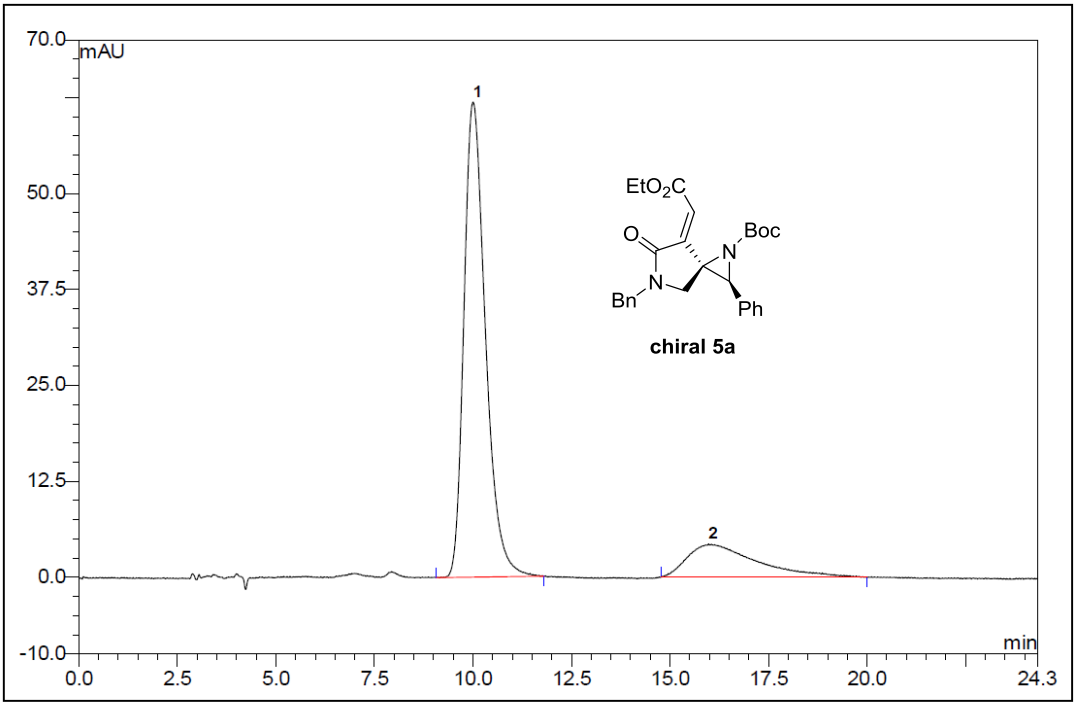



HO
CF3
O
NH
N
Bn
Ph
7
0.98
1.00
3.00
5.00
1.94
1.00
1.03
1.04
1.02
1.01
f1 (ppm)


165.304
156.992
135.113
135.057
129.418
128.851
128.642
127.649
127.568
126.395
78.304
78.037
77.765
77.492
77.224
67.160
51.615
46.249
HO
CF3
O
NH
N
Bn
Ph
7
f1 (ppm)



No.	Ret.Time min	Height mAU	Area mAU*min	Rel.Area %
1	9.97	176.158	108.537	51.00
2	15.00	57.352	104.287	49.00
Total:		233.510	212.824	100.00



No.	Ret.Time min	Height mAU	Area mAU*min	Rel.Area %
1	10.00	61.899	39.131	84.86
2	15.98	4.049	6.985	15.14
Total:		65.948	46.116	100.00