Catalytic Asymmetric [3 + 2] Cycloaddition of Pyrazolone-Derived MBH Carbonate: Highly Stereoselective Construction of Bispiro [Pyrazolone-Dihydropyrrole-Oxindole] Skeleton

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Supporting Information

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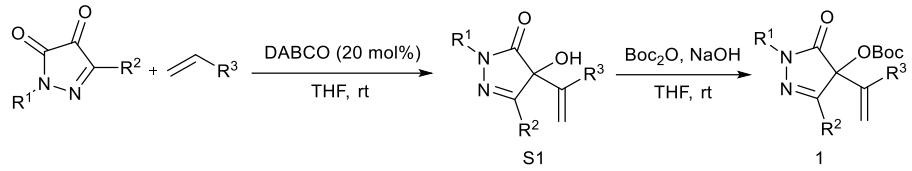
1. General information

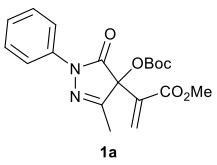
High Performance Liquid Chromatography (HPLC) was analyzed by chiral column in comparison with authentic racemates, using a Daicel Chiralpak OD-H or IA Column (250 x 4.6 mm). UV detection was performed at 270 nm. Nuclear magnetic resonance (NMR) spectra were recorded in DMSO-d_6 and $CDCl_3$ on JEOL 600 or 700 NMR instrument. Proton chemical shifts are reported in parts per million (δ scale). The ^1H NMR chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as standard. The ^{13}C NMR chemical shifts were given by using DMSO-d_6 or $CDCl_3$ as the internal standard (DMSO-d_6: δ = 39.52 ppm, $CDCl_3$: δ = 77.05 ppm). ^{19}F NMR chemical shifts were given by using 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]. High-resolution mass spectra (HRMS) were obtained using Agilent P/N G1969-90010 or Waters/Acquity UPLC-Synapt G2HDMS. High-resolution mass spectra were reported for the molecular ion $[M+Na]^+$ or $[M+H]^+$. X-ray diffraction experiment was carried out on an Agilent Gemini and the data obtained were deposited at the Cambridge Crystallographic Data Centre. UV detection was performed at 254 nm. Column chromatography was performed on silica gel (300-400 mesh) using an eluent of ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates; products were visualized using UV light. Optical rotation values were measured with instruments operating at λ = 589 nm, corresponding to the sodium D line at 25 ºC. All reagents and solvents were obtained from commercial sources and used without further purification. MBH Carbonate of Pyrazolinone **1a**[1] and 3-((tert-butoxycarbonyl)imino)-2-oxoindoline-1-carboxylate **2a**[2] were prepared according to the literature procedures. Oil baths were used as the heat source. Melting points were recorded on BUCHI Melting Point M-565 instrument.

2. Synthesis of substrates 1.



To a stirred solution of pyrazoledione (1.0 mmol) and corresponding acrylate (5.0 mmol) was added DABCO (23.0 mg, 0.21mmol), and the mixture was stirred at room temperature. After completion, the mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (EtOAc/petroleum ether = 1/5) to give the product S1. Boc_2O (0.46 mL, 2.0 mmol) was added to a stirred solution of S1 (1.0 mmol) and NaOH (80 mg, 2.0 mmol) in THF (5.0 mL) at 0 °C, and the mixture was stirred at room temperature. After completion (monitored by TLC), the reaction was quenched with water and extracted with EtOAc. The combined organic phases were dried over Na_2SO_4, and the solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/10) to give the product 1[1].

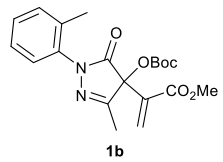
methyl 2-(4-((tert-butoxycarbonyl)oxy)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1a).



1a

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (dt, *J* = 7.8, 1.2 Hz, 1H), 7.60 – 7.32 (m, 2H), 7.18 (tt, *J* = 7.2, 1.2 Hz, 2H), 6.69 (s, 1H), 6.51 (s, 1H), 3.68 (s, 3H), 2.04 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 163.4, 153.7, 149.7, 138.1, 133.1, 131.4, 128.9, 125.2, 119.0, 84.9, 81.7, 52.6, 27.6, 13.0. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{22}N_2O_6$ 397.1370; Found 397.1369.

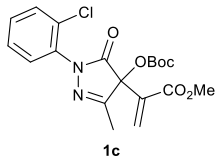
methyl 2-(4-((tert-butoxycarbonyl)oxy)-3-methyl-5-oxo-1-(o-tolyl)-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1b).



1b

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 – 7.40 (m, 1H), 7.32 – 7.17 (m, 3H), 6.68 (s, 1H), 6.52 (s, 1H), 3.77 (s, 3H), 2.39 (s, 3H), 2.02 (s, 3H), 1.49 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.7, 163.5, 153.5, 149.9, 136.1, 135.8, 133.1, 131.2, 131.1, 128.3, 126.4, 126.3, 84.6, 80.8, 52.5, 27.6, 18.1, 13.1. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{24}N_2O_6$ 411.1527; Found 411.1526.

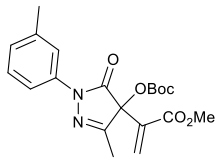
methyl 2-(4-((tert-butoxycarbonyl)oxy)-1-(2-chlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1c).



1c

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (dd, J = 8.4, 1.8 Hz, 1H), 7.48 (dd, J = 8.4, 1.8 Hz, 1H), 7.34 (td, J = 7.8, 1.8 Hz, 1H), 7.29 (td, J = 7.8, 1.8 Hz, 1H), 6.68 (s, 1H), 6.49 (s, 1H), 3.78 (s, 3H), 2.05 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.9, 163.6, 154.6, 150.1, 135.0, 132.9, 131.54, 131.51, 130.5, 129.4, 128.2, 127.5, 84.7, 80.8, 52.6, 27.6, 13.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{21}ClN_2O_6$ 431.0980; Found 431.0980.

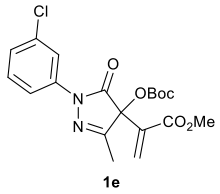
methyl 2-(4-((tert-butoxycarbonyl)oxy)-3-methyl-5-oxo-1-(m-tolyl)-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1d).



1d

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.74 – 7.64 (m, 2H), 7.28 (t, J = 7.7 Hz, 1H), δ 7.01 – 6.99 (m, 1H), 6.68 (s, 1H), 6.51 (s, 1H), 3.68 (s, 3H), 2.38 (s, 3H), 2.04 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 168.0, 163.4, 153.6, 149.6, 138.7, 137.9, 133.1, 131.3, 128.7, 126.0, 119.4, 116.1, 84.8, 81.7, 52.5, 27.6, 21.6, 12.9. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{24}N_2O_6$ 411.1527; Found 411.1531.

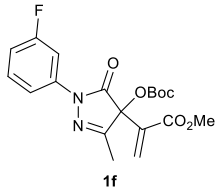
methyl 2-(4-((tert-butoxycarbonyl)oxy)-1-(3-chlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1e).



1e

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (t, J = 1.8 Hz, 1H), 7.85 (ddd, J = 8.4, 2.4, 1.2 Hz, 1H), 7.32 (t, J = 8.4 Hz, 1H), 7.17 – 7.13 (m, 1H), 6.70 (s, 1H), 6.53 (s, 1H), 3.69 (s, 3H), 2.03 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.2, 163.4, 154.1, 149.7, 139.1, 134.7, 132.9, 131.6, 130.0, 125.0, 118.7, 116.5, 85.1, 81.6, 52.6, 27.6, 12.9. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{21}ClN_2O_6$ 431.0980; Found 431.0979.

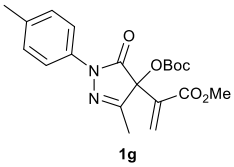
methyl 2-(4-((tert-butoxycarbonyl)oxy)-1-(3-fluorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1f).



1f

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (ddd, J = 8.4, 2.4, 1.2 Hz, 1H), 7.69 (dt, J = 10.8, 1.8 Hz, 1H), 7.36 – 7.32 (m, 1H), 6.89 – 6.85 (m, 1H), 6.70 (s, 1H), 6.53 (s, 1H), 3.68 (s, 3H), 2.03 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.2, 163.4, 162.2 (d, J_{CF} = 242.8 Hz), 153.9, 149.7, 139.5 (d, J_{CF} = 11.1 Hz), 132.9, 131.5, 130.2 (d, J_{CF} = 9.2 Hz), 113.9 (d, J_{CF} = 3.0 Hz), 111.8 (d, J_{CF} = 21.0 Hz), 106.2 (d, J_{CF} = 27.0 Hz), 85.1, 81.7, 52.6, 27.6, 12.9. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{21}FN_2O_6$ 415.1276; Found 415.1276.

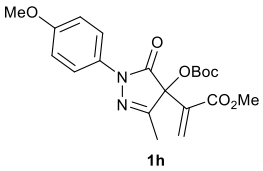
methyl 2-(4-((tert-butoxycarbonyl)oxy)-3-methyl-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1g).



1g

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 – 7.61 (m, 2H), 7.23 – 7.14 (m, 2H), 6.68 (s, 1H), 6.50 (s, 1H), 3.68 (s, 3H), 2.34 (s, 3H), 2.03 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 163.5, 153.6, 149.7, 135.7, 134.9, 133.2, 131.3, 129.5, 119.1, 84.8, 81.7, 52.6, 27.6, 21.1, 13.0. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{24}N_2O_6$ 411.1527; Found 411.1526.

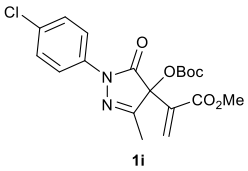
methyl 2-(4-((tert-butoxycarbonyl)oxy)-1-(4-methoxyphenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1h).



1h

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 – 7.70 (m, 2H), 6.93 (dd, *J* = 9.0, 3.0 Hz, 2H), 6.67 (s, 1H), 6.50 (s, 1H), 3.81 (s, 3H), 3.69 (s, 3H), 2.02 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 163.5, 157.3, 153.6, 149.7, 133.1, 131.5, 131.3, 121.2, 114.2, 84.8, 81.6, 55.6, 52.6, 27.6, 13.0. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{24}N_2O_7$ 427.1476; Found 427.1475.

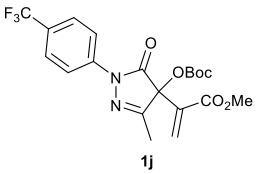
methyl 2-(4-((tert-butoxycarbonyl)oxy)-1-(4-chlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1i).



1i

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, *J* = 9.0 Hz, 2H), 7.36 (d, *J* = 9.0 Hz, 2H), 6.69 (s, 1H), 6.52 (s, 1H), 3.68 (s, 3H), 2.03 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 163.4, 154.0, 149.7, 136.7, 132.9, 131.5, 130.2, 128.9, 120.0, 85.1, 81.6, 52.6, 27.6, 12.9. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{21}ClN_2O_6$ 431.0980; Found 431.0984.

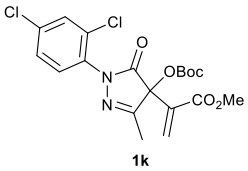
methyl 2-(4-((tert-butoxycarbonyl)oxy)-3-methyl-5-oxo-1-(4-(trifluoromethyl)-phenyl)-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1j).



1j

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 – 8.02 (m, 2H), 7.66 – 7.64 (m, 2H), 6.71 (s, 1H), 6.55 (s, 1H), 3.68 (s, 3H), 2.05 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.5, 163.4, 154.2, 149.7, 140.8, 132.9, 131.6, 126.7 (d, J_{CF} = 32.1 Hz), 126.2 (d, J_{CF} = 4.1 Hz), 125.2 (d, J_{CF} = 270.0 Hz), 118.1, 85.2, 81.6, 52.6, 27.6, 12.9. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{21}F_3N_2O_6$ 465.1244; Found 465.1249.

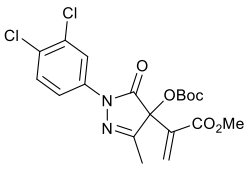
methyl 2-(4-((tert-butoxycarbonyl)oxy)-1-(2,4-dichlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1k).



1k

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.52 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 2.1 Hz, 1H), 7.32 (dd, J = 8.4, 2.1 Hz, 1H), 6.69 (s, 1H), 6.50 (s, 1H), 3.78 (s, 3H), 2.04 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 168.9, 163.4, 154.6, 150.0, 134.4, 133.7, 132.7, 132.3, 131.5, 130.2, 128.9, 127.7, 84.8, 80.5, 52.5, 27.6, 13.21, 13.20. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{20}Cl_2N_2O_6$ 465.0591; Found 465.0599.

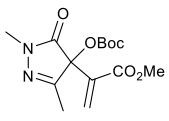
methyl 2-(4-((tert-butoxycarbonyl)oxy)-1-(3,4-dichlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1l).



1l

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 – 8.03 (m, 1H), 7.85 – 7.83 (m, 1H), 7.52 – 7.34 (m, 1H), 6.70 (s, 1H), 6.54 (s, 1H), 3.69 (s, 3H), 2.03 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.2, 163.4, 154.3, 149.7, 137.4, 132.9, 132.8, 131.7, 130.5, 128.2, 120.1, 117.6, 85.2, 81.5, 52.7, 27.6, 12.9. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{20}Cl_2N_2O_6$ 465.0591; Found 465.0585.

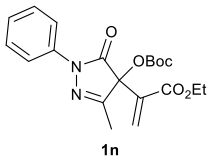
methyl 2-(4-((tert-butoxycarbonyl)oxy)-1,3-dimethyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1m).



1m

^{1}H NMR (700 MHz, $CDCl_3$) δ 6.62 (s, 1H), 6.44 (s, 1H), 3.73 (s, 3H), 3.37 (s, 3H), 1.93 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.8, 163.4, 153.1, 149.6, 132.9, 131.0, 84.5, 80.6, 52.4, 31.9, 27.6, 12.9. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{20}N_2O_6$ 335.1214; Found 335.1211.

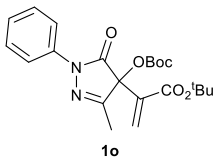
ethyl 2-(4-((tert-butoxycarbonyl)oxy)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1n).



1n

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.94 – 7.84 (m, 2H), 7.43 – 7.36 (m, 2H), 7.17 (tt, *J* = 7.7, 1.4 Hz, 1H), 6.69 (s, 1H), 6.49 (s, 1H), 4.12 (qd, *J* = 7.0, 2.1 Hz, 2H), 2.04 (s, 3H), 1.44 (s, 9H), 1.14 (t, *J* = 7.7 Hz, 3H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 168.1, 162.9, 153.7, 149.6, 138.1, 133.3, 131.1, 128.9, 125.0, 118.7, 84.8, 81.7, 61.7, 27.5, 13.9, 12.9. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{24}N_2O_6$ 411.1527; Found 411.1527.

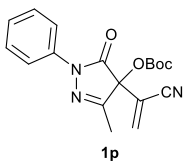
tert-butyl 2-(4-((tert-butoxycarbonyl)oxy)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1o).



1o

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 – 7.89 (m, 2H), 7.41 – 7.38 (m, 2H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.58 (s, 1H), 6.38 (s, 1H), 2.05 (s, 3H), 1.43 (s, 9H), 1.35 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.2, 162.4, 154.1, 149.8, 138.3, 134.6, 130.2, 128.9, 124.9, 118.7, 84.7, 83.1, 81.8, 27.9, 27.6, 13.1. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{28}N_2O_6$ 439.1840; Found 439.1846.

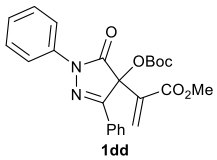
tert-butyl (4-(1-cyanovinyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1H-pyrazol-4-yl) carbonate (1p).



1p

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.4 Hz, 2H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.28 – 7.22 (m, 1H), 6.43 (s, 1H), 6.36 (s, 1H), 2.19(s, 3H), 1.47 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.4, 154.7, 149.9, 137.5, 135.4, 129.1, 126.1, 119.4, 115.9, 114.0, 86.1, 81.6, 27.6, 13.3. HRMS(ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{19}N_3O_4$ 364.1268, Found: 364.1270.

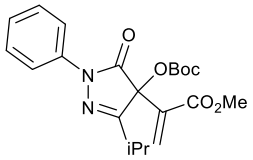
tert-butyl 2-(4-((tert-butoxycarbonyl)oxy)-5-oxo-1,3-diphenyl-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1dd).



1dd

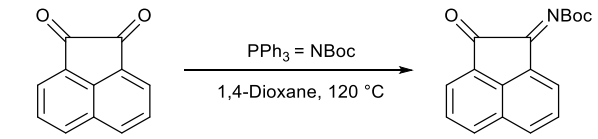
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 – 7.92 (m, 2H), 7.92 – 7.76 (m, 2H), 7.55 – 7.43 (m, 2H), 7.42 – 7.33 (m, 3H), 7.23 (tt, *J* = 7.2, 1.2 Hz, 1H), 6.73 (s, 1H), 6.73 (s, 1H), 3.60 (s, 3H), 1.35 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.2, 163.5, 151.5, 149.6, 138.2, 134.6, 130.7, 130.6, 129.4, 128.9, 128.9, 126.4, 125.5, 119.3, 85.0, 81.2, 52.5, 27.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{24}N_2O_6$ 459.1527; Found 459.1524.

methyl 2-(4-((tert-butoxycarbonyl)oxy)-3-isopropyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)acrylate (1ee).



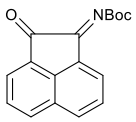
1ee

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.01 – 7.71 (m, 2H), 7.48 – 7.36 (m, 2H), 7.18 (tt, *J* = 7.7, 1.4 Hz, 1H), 6.67 (s, 1H), 6.55 (s, 1H), 3.67 (s, 3H), 2.68 – 2.62 (m, 1H), 1.44 (s, 9H), 1.32 – 1.12 (m, 6H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 168.2, 163.5, 159.9, 149.6, 138.1, 133.7, 130.7, 128.8, 125.1, 119.0, 84.6, 81.9, 52.5, 28.6, 27.5, 20.1, 20.0. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{26}N_2O_6$ 425.1683; Found 425.1682.



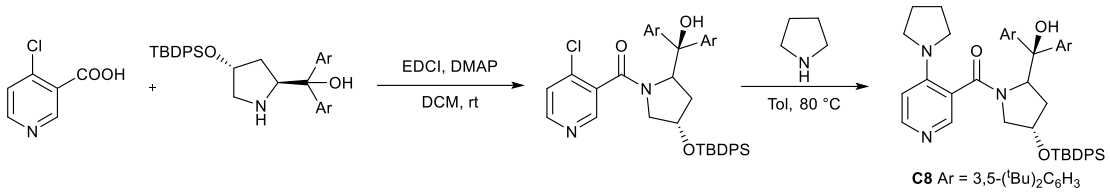
Acenaphthenequinone 9

To a solution of Acenaphthenequinone (1.0 g, 5.49 mmol) in 20.0 mL 1,4-Dioxane was added PPh_3 = NBoc (2.49 g, 6.59mmol). The mixture was stirred at 120 ℃ for 24 h. After completion, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel eluting with petroleum ether/ ethyl acetate (30:1) to afford the acenaphthenequinoneimine **9**.



^{1}H NMR (700 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 8.03 – 7.94 (m, 2H), 7.84 – 7.65 (m, 2H), 1.68 (s, 9H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 183.7, 161.1, 157.9, 144.3, 132.4, 130.5, 130.1, 129.4, 129.1, 128.7, 128.5, 122.4, 121.3, 83.4, 28.1. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{15}NO_3$ 304.0950; Found 304.0945.

3.General procedure for the preparation of new chiral DMAP-type catalysts.



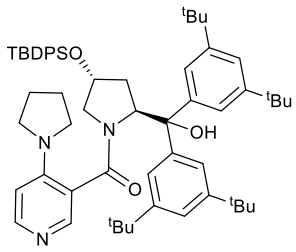
C8 Ar = 3,5-(^{t}Bu)$_2$C$_6$H$_3$

The newly developed catalyst **C8** was readily synthesized from chiral secondary amines and 4-chloronicotinic acid. To a solution of chiral secondary amines (1.69 g, 2.31 mmol) in 40.0 mL DCM was successively added 4-chloronicotinic acid (361.2 mg, 2.31 mmol), 1-Ethyl-3-(3-dimethyllaminopropyl)carbodiimide hydrochloride (EDCI, 884.6 mg, 4.62 mmol) and 4-Dimethylaminopyridine (DMAP, 28.2 mg, 0.23 mmol). The mixture was stirred at rt for 8 h before being quenched with water (20 mL). The phases were separated and the aqueous phase was extracted with DCM (2 × 10 mL). The combined organic phases were washed with brine (20 mL) before being dried (Na_2SO_4) and concentrated in vacuum. Purification by flash column chromatography on silica gel yielded the amide. To a solution of the amide (1.8 g, 2.06 mmol) in toluene (40 mL) was added pyrrolidine (206.9 μL, 2.48 mmol). Then, the mixture was stirred at 80 °C for 12 h. After completion, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel eluting with petroleum ether/ ethyl acetate (1:1) to afford the catalyst **C8**. The corresponding chiral secondary amines were prepared according to the literature procedure[3].

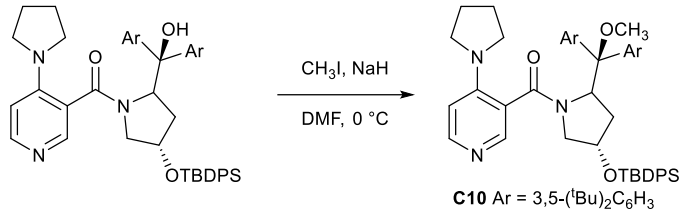
[1]. Z. H. Yang; P. Chen; Z. C. Chen; Z. Chen; W. Du; Y. C. Chen, *Angew. Chem. Int. Ed.*, 2021, **60** (25), 13913-13917.

[2]. M. Urban, M. Franc,a, M. Hofmanová, I. Císařováb and J. Veselý, *Org. Biomol. Chem.*, 2017, **15**, 9071-9076.

[3]. L. Caruana, F. Kniep, T. K. Johansen, P. H. Poulsen, K. A. Jørgensen, *J. Am. Chem. Soc.* 2014, **136**, 15929.

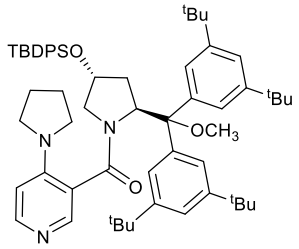


C8 was obtained as a white solid. 1.72g, 90% yield; $[\alpha]D^{20}$ = +17.8 (c = 0.06 in MeOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (d, *J* = 6.6 Hz, 1H), 7.77 (s, 1H), 7.49 – 7.42 (m, 2H), 7.38 (t, *J* = 1.8 Hz, 1H), 7.37 – 7.24 (m, 8H), 7.22 – 7.14 (m, 6H), 6.42 (s, 1H), 6.34 (d, *J* = 6.0 Hz, 1H), 5.41-5.38 (m, 1H), 4.09 (t, *J* = 3.6 Hz, 1H), 3.49-3.36 (m, 3H), 3.20 – 3.13 (m, 2H), 3.03 (dd, *J* = 12.0, 3.0 Hz, 1H), 2.16 (s, 1H), 2.09-2.01 (m, 1H), 1.95-1.87 (m, 1H), 1.83 – 1.74 (m, 2H), 1.32 – 1.25 (m, 1H), 1.19 (s, 18H), 1.17 (s, 18H), 0.94 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.4, 148.9, 148.8, 148.7, 147.8, 147.6, 142.4, 139.9, 134.5, 134.2, 132.3, 131.8, 129.1, 128.9, 126.9, 126.8, 121.6, 120.24, 120.20, 120.1, 114.9, 107.3, 81.4, 70.1, 68.9, 60.0, 48.2, 40.6, 33.9, 33.8, 30.6, 30.5, 25.9, 24.6, 18.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{59}H_{80}N_3O_3Si$ 906.5963, Found 906.5961.

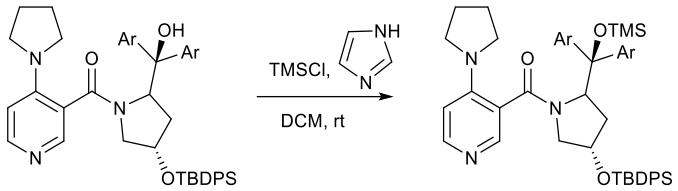


C10 Ar = 3,5-(^{t}Bu)$_2$C$_6$H$_3$

To a solution of **C8** (200.0 mg, 0.22 mmol) in DMF (2 mL) was added a solution of NaH (15.9 mg, 0.66 mmol) in DMF (1 mL) at 0 ℃. After 5 min, the mixture was added Iodomethane (16.5 μL, 0.26 mmol). The reaction was stirred at rt for 10 min before being quenched with water (1 mL). The mixture was extracted with EtOAc (2 × 5 mL). The combined organic phases were washed with brine (1 mL) and dried with Na_2SO_4. After concentrated in vacuum, the residue was purified by flash column chromatography on silica gel eluting with petroleum ether/ ethyl acetate (1:1) to afford **C10** as a white solid (180.0 mg, 89% yield).

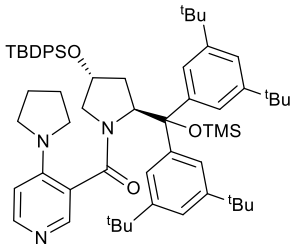


C10 was obtained as a white solid. 180.0 mg, 89% yield; $[\alpha]D^{20}$ = +19.4 (c =0.06 in MeOH). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.17 (d, *J* = 6.3 Hz, 1H), 7.73 (s, 1H), 7.49 – 7.48 (m, 2H), 7.37 – 7.34 (m, 3H), 7.34 – 7.27 (m, 6H), 7.25 – 7.18 (m, 2H), 7.13 (s, 1H), 7.09 (d, *J* = 2.1 Hz, 2H), 7.01 – 7.95 (m, 1H), 6.46 (d, *J* = 6.3 Hz, 1H), 6.01 (dd, *J* = 9.8, 3.5 Hz, 1H), 3.93 (t, *J* = 7.7 Hz, 1H), 3.53 – 3.48 (m, 2H), 3.33 – 3.31 (m, 1H), 3.28 – 3.25 (m, 2H), 2.96 (s, 3H), 2.39 – 2.29 (m, 2H), 1.91 – 1.84 (m, 2H), 1.71 – 1.65 (m, 2H), 1.25 (s, 18H), 1.19 (s, 18H), 0.94 (s, 9H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.8, 149.5, 149.4, 149.3, 140.4, 139.7, 135.7, 135.54, 135.46, 135.3, 133.5, 133.4, 129.8, 129.7, 127.70, 127.66, 124.0, 123.3, 121.2, 120.9, 117.1, 108.5, 87.2, 73.5, 60.2, 60.1, 52.2, 49.2, 41.4, 39.6, 34.84, 34.76, 31.5, 31.4, 26.9, 25.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{60}H_{81}N_3O_3Si$ 920.6120, Found 920.6124.



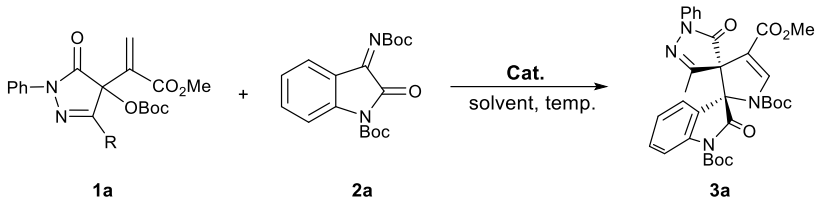
C11 Ar = 3,5-(^{t}Bu)$_2$C$_6$H$_3$

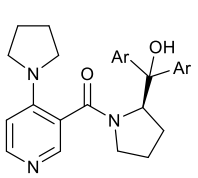
To a solution of **C8** (200.0 mg, 0.22 mmol) in DCM (2 mL) was added a solution of Imidazole (15.0 mg, 0.22 mmol) in DCM (1 mL) at room temperature, the mixture was added Chlorotrimethylsilane (33.6 μL, 0.26 mmol). The reaction was stirred at rt for 10 h before being quenched with water (1 mL). The mixture was extracted with DCM (2 × 5 mL). The combined organic phases were washed with brine (1 mL) and dried with Na_2SO_4. After concentrated in vacuum, the residue was purified by flash column chromatography on silica gel eluting with petroleum ether/ ethyl acetate (1:1) to afford **C11** as a white solid (195.0 mg, 90% yield).



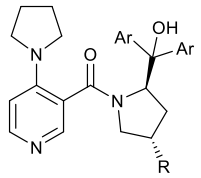
C11 was obtained as a white solid. 195.0 mg, 90% yield; $[\alpha]D^{20}$ = +18.1 (c = 0.06 in MeOH). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.10 (d, *J* = 6.3 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.46 – 7.42 (m, 2H), 7.42 – 7.37 (m, 1H), 7.39 – 7.34 (m, 1H), 7.36 – 7.31 (m, 3H), 7.29 – 7.28 (m, 2H), 7.27 – 7.25 (d, 2H), 7.17 (d, *J* = 1.4 Hz, 1H), 7.04 (s, 2H), 6.82 (s, 1H), 6.37 (d, *J* = 5.6 Hz, 1H), 5.86 (d, *J* = 8.4 Hz, 1H), 4.47 – 4.45 (m, 1H), 3.51 – 3.48 (m, 2H), 3.36 – 3.29 (m, 2H), 3.26 – 3.22 (m, 1H), 3.04 – 3.01 (m, 1H), 2.66 – 2.58 (m, 1H), 2.17 – 2.13 (m, 1H), 1.96 – 1.92 (m, 2H), 1.85 – 1.76 (m, 2H), 1.27 (s, 18H), 1.20 (s, 18H), 0.98 (s, 9H), -0.41 (s, 9H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 167.5, 147.9, 147.7, 147.5, 147.2, 141.5, 141.2, 134.1, 133.9, 132.2, 131.8, 128.4, 128.2, 126.22, 126.21, 121.9, 120.9, 119.9, 119.4, 115.9, 106.7, 83.8, 73.2, 62.9, 57.4, 47.1, 38.7, 33.4, 33.3, 30.0, 29.9, 25.4, 24.1, 17.4, -0.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{62}H_{87}N_3O_3Si_2$ 978.6359, Found 978.6324.

4. Optimization of the model reaction (Table S1)[a]

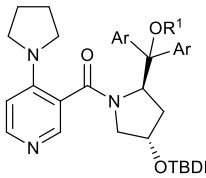




C1 Ar = C_6H_5
C2 Ar = 3,5-$(CH_3)_2C_6H_3$
C3 Ar = 3,5-$(^tBu)_2C_6H_3$
C4 Ar = 3,5-$(CF_3)_2C_6H_3$



C5 Ar = 3,5-$(CH_3)_2C_6H_3$, R = OH
C6 Ar = 3,5-$(^tBu)_2C_6H_3$, R = OH
C7 Ar = 3,5-$(CH_3)_2C_6H_3$, R = OTBDPS
C8 Ar = 3,5-$(^tBu)_2C_6H_3$, R = OTBDPS
C9 Ar = 3,5-$(^tBu)_2C_6H_3$, R^1 = $OSiPh_3$



C10 Ar = 3,5-$(^tBu)_2C_6H_3$, R^1 = CH_3
C11 Ar = 3,5-$(^tBu)_2C_6H_3$, R = TMS

Entry	R	Cat.	Solvent	T (°C)	t (h)	yield (%)[b]	*ee* (%)[c]	dr[d]
1	CH_3	PPh_3	CH_2Cl_2	rt	24	n.r.	-	-
2	CH_3	DABCO	CH_2Cl_2	rt	24	n.r.	-	-
3	CH_3	DMAP	CH_2Cl_2	rt	6	95	-	>20:1
4	CH_3	**C1**	CH_2Cl_2	rt	24	41	40	>20:1
5	CH_3	**C2**	CH_2Cl_2	rt	6	91	39	>20:1
6	CH_3	**C3**	CH_2Cl_2	rt	6	93	27	>20:1
7	CH_3	**C4**	CH_2Cl_2	rt	6	69	3	>20:1
8	CH_3	**C5**	CH_2Cl_2	rt	24	73	1	>20:1
9	CH_3	**C6**	CH_2Cl_2	rt	24	40	22	>20:1
10	CH_3	**C7**	CH_2Cl_2	rt	48	43	44	>20:1
11	CH_3	**C8**	CH_2Cl_2	rt	6	87	75	>20:1
12	CH_3	**C9**	CH_2Cl_2	rt	6	92	37	>20:1
13	CH_3	**C10**	CH_2Cl_2	rt	48	40	56	>20:1
14	CH_3	**C11**	CH_2Cl_2	rt	48	n.r.	n.r.	>20:1
15	CH_3	**C8**	Toluene	rt	4	98	83	>20:1
16	CH_3	**C8**	THF	rt	4	84	90	>20:1

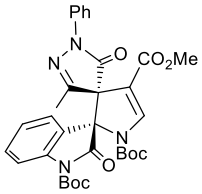
17	CH_3	**C8**	MeCN	rt	4	83	43	>20:1
18	CH_3	**C8**	EA	rt	4	86	80	>20:1
19	CH_3	**C8**	DCE	rt	4	90	86	>20:1
20	CH_3	**C8**	$CHCl_3$	rt	4	92	90	>20:1
21	CH_3	**C8**	$CHCl_3$	40	1	90	85	>20:1
22	CH_3	**C8**	$CHCl_3$	0	24	86	91	>20:1
23	CH_3	**C8**	$CHCl_3$	-10	48	88	92	>20:1
24	CH_3	**C8**	$CHCl_3$	-20	120	85	93	>20:1
25[e]	CH_3	**C8**	$CHCl_3$	rt	48	27	90	>20:1
26[f]	CH_3	**C8**	$CHCl_3$	rt	48	20	90	>20:1
27[g]	CH_3	**C8**	$CHCl_3$	rt	36	63	90	>20:1
28[h]	CH_3	**C8**	**$CHCl_3$**	**rt**	**24**	**89**	**90**	**>20:1**
29[i]	CH_3	**C8**	$CHCl_3$	rt	4	83	90	>20:1
30	*i*-Pr	**C8**	$CHCl_3$	rt	72	24	76	>20:1
31	Ph	**C8**	$CHCl_3$	rt	72	48	89	>20:1

Reaction conditions: [a] **1a** (0.12 mmol), **2a** (0.10 mmol), **Cat.** (20 mol%) in 1.0 mL DCM at room temperature; [b] Isolated yield after column chromatography; [c] Enantiomeric excess of major diastereoisomer was determined by HPLC using chiral stationary phase; [d] Determined by ^{1}H NMR. [e] 10 mol% **C8** in 1.0 mL $CHCl_3$; [f] 5 mol% **C8** in 1.0 mL $CHCl_3$; [g] 5 mol% **C8** in 0.25 mL $CHCl_3$; [h] 10 mol% **C8** in 0.5 mL $CHCl_3$; [i] 15 mol% **C8** in 0.75 mL $CHCl_3$.

5. General procedure for the asymmetric [2+3] annulation reaction.

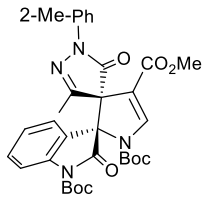
MBH Carbonate of pyrazolinone **1a** (0.12 mmol), 3-((tert-butoxycarbonyl)imino)-2-oxoindoline-1-carboxylate **2a** (0.10 mmol), and catalyst **C8** (9.1 mg, 0.01 mmol) were dissolved in $CHCl_3$ (0.5 mL), and the mixture was stirred at room temperature for 9-48 h. After completion of the reaction, the reaction mixture was concentrated and directly purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1 to 5/1) to afford the pure products **3a**.

1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3a).



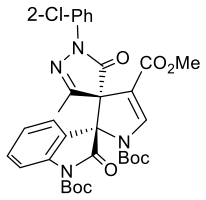
53.6 mg, 89% yield, white solid, mp 145.9 – 148.5 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 90% *ee*, $[\alpha]D^{20}$ = −91.2 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 °C) δ 8.22 (s, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.35 (dd, *J* = 7.2, 1.8 Hz, 2H), 7.33 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.20 (t, *J* = 7.8 Hz, 1H), 7.16 (td, *J* = 7.2, 1.8 Hz, 1H), 3.66 (s, 3H), 2.11 (s, 3H), 1.56 (s, 9H), 1.05 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 °C) δ 170.3, 169.2, 163.0, 156.5, 149.1, 148.2, 147.1, 139.2, 137.1, 131.4, 129.3, 126.1, 124.9, 119.4, 114.8, 107.9, 85.9, 84.8, 74.4, 52.4, 28.0, 27.5, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{34}N_4O_8$ 625.2269; Found 625.2270.

1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-3''-methyl-2,5''-dioxo-1''-(m-tolyl)-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3b).



51.8 mg, 84% yield, white solid, mp 88.1 – 89.3 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 84% *ee*, $[\alpha]D^{20}$ = -204.4 (c = 0.45, MeOH) . ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.20 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.25 (dd, *J* = 7.8, 7.2 Hz, 1H), 7.23 (d, *J* = 1.8 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.17 (td, *J* = 7.2, 1.8 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 3.71 (s, 3H), 2.08 (s, 3H), 1.75 (s, 3H), 1.58 (s, 9H), 1.04 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.3, 169.9, 163.0, 156.4, 148.3, 146.6, 139.2, 135.7, 135.5, 131.4, 131.2, 129.2, 126.9, 126.8, 126.5, 124.9, 114.7, 108.2, 85.8, 84.7, 74.5, 52.4, 28.1, 27.5, 17.3, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{36}N_4O_8$ 639.2425; Found 639.2425.

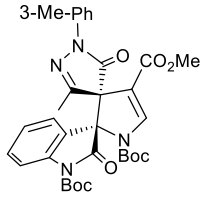
1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-1''-(2-chlorophenyl)-3''-methyl-2,5''-dioxo-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3c).



60.5 mg, 95% yield, white solid, mp 117.0 – 120.7 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 78% *ee*, $[\alpha]D^{20}$ = -128.9 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.21 (s, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.49 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.40 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.38 (d, *J* = 2.4 Hz, 1H), 7.36 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 7.00 (s, 1H), 3.71 (s, 3H), 2.11 (s, 3H), 1.58 (s, 9H), 1.06 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.0, 169.6, 162.9, 157.3, 149.0, 148.3, 146.5, 139.2, 134.4, 131.5, 131.4, 130.9, 130.5, 128.9, 128.4, 126.4, 124.9, 122.9, 114.8, 108.0, 85.6, 84.9, 74.9, 67.8, 52.4, 28.1, 27.5, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{33}ClN_4O_8$ 659.1879; Found 659.1878.

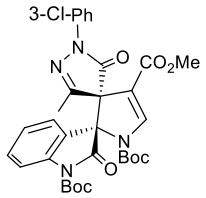
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-3''-methyl-2,5''-dioxo-1''-(m-tolyl)-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate

(3d).



52.4 mg, 85% yield, white solid, mp 149.2 – 152.8 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 90% *ee*, $[\alpha]D^{20}$ = -302.4 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 °C) δ 8.22 (s, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 8.4 Hz, 1H), 7.20 (td, *J* = 7.2, 1.8 Hz, 2H), 7.16 (d, *J* = 7.8 Hz, 2H), 6.98 (d, *J* = 7.8 Hz, 1H), 3.67 (s, 3H), 2.26 (s, 3H), 2.11 (s, 3H), 1.57 (s, 9H), 1.06 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 °C) δ 170.3, 169.2, 162.9, 156.4, 149.1, 148.2, 147.0, 139.2, 138.8, 137.1, 131.4, 129.1, 126.8, 126.1, 124.9, 119.9, 116.7, 114.7, 107.9, 85.9, 84.9, 74.4, 70.0, 52.4, 28.1, 27.5, 21.4, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{36}N_4O_8$ 639.2425; Found 639.2426.

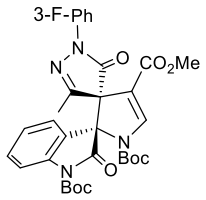
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-1''-(3-chlorophenyl)-3''-methyl-2,5''-dioxo-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3e).



55.4 mg, 87% yield, white solid, mp 149.2 – 151.8 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 91% *ee*, $[\alpha]D^{20}$ = -291.1 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 °C) δ 8.24 (s, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.42 – 7.40 (m, 2H), 7.39 – 7.35 (m, 2H), 7.22 (dt, *J* = 7.2, 1.8 Hz, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 3.67 (s, 3H), 2.13 (s, 3H), 1.56 (s, 9H), 1.06 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 °C) δ 170.3, 169.3, 162.9, 157.5, 148.9, 148.1, 147.2, 139.2, 138.3, 133.9, 131.5, 131.3, 126.0, 125.8, 124.9, 122.1, 118.4, 117.4, 114.8, 107.6, 85.9, 84.7, 74.6, 52.4, 28.0, 27.6, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{33}ClN_4O_8$ 659.1879; Found 659.1879.

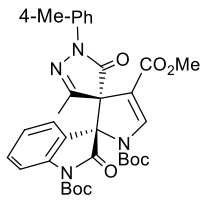
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-1''-(3-fluorophenyl)-3''-methyl-2,5''-dioxo-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-

tricarboxylate (3f).



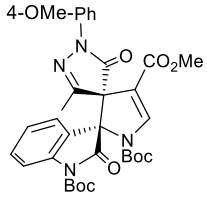
58.3 mg, 94% yield, white solid, mp 80.3 – 83.0 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 90% *ee*, $[\alpha]D^{20}$ = -397.8 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.24 (s, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.41 – 7.39 (m, 1H), 7.37 (dd, *J* = 8.4, 6.6 Hz, 1H), 7.28 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.21 (d, *J* = 1.8 Hz, 1H), 7.19 (dd, *J* = 5.4, 3 Hz, 1H), 6.99 (td, *J* = 8.4, 2.4 Hz, 1H), 3.67 (s, 3H), 2.13 (s, 3H). 1.56 (s, 9H), 1.06 (s, 9H). ^{19}F NMR (565 MHz, DMSO-d_6 60 ℃) δ -60.61. ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.1, 169.3, 163.3, 162.9, 161.7, 157.3, 148.1（d, J_{CF} = 139.4 Hz）, 147.2, 139.2, 138.5（d, J_{CF} = 10.9 Hz）, 131.5, 131.4（d, J_{CF} = 9.2 Hz）, 126.0, 124.9, 122.1, 114.8, 114.7（d, J_{CF} = 2.9 Hz）, 112.7（d, J_{CF} = 21.0 Hz）, 107.6, 105.9（d, J_{CF} = 26.7 Hz）, 85.9, 84.9, 74.5, 52.4, 28.0, 27.5, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{33}FN_4O_8$ 643.2175; Found 643.2173.

1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-3''-methyl-2,5''-dioxo-1''-(p-tolyl)-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3g).



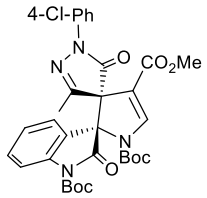
56.7 mg, 92% yield, white solid, mp 106.2 – 108.5 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 89% *ee*, $[\alpha]D^{20}$ = -448.9 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.21 (s, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.46 (t, *J* = 6.6 Hz, 1H), 7.40 (t, *J* = 8.4 Hz, 1H), 7.25 – 7.16 (m, 3H), 7.13 (d, *J* = 8.4 Hz, 1H), 3.66 (s, 3H), 2.25 (s, 3H), 2.10 (s, 3H), 1.56 (s, 9H), 1.05 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.3, 169.1, 163.0, 156.3, 149.2, 148.2, 147.0, 139.2, 135.5, 134.7, 131.4, 129.7, 126.1, 124.9, 122.3, 119.5, 114.7, 107.9, 85.9, 84.6, 74.4, 52.3, 28.1, 27.5, 20.9, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{36}N_4O_8$ 639.2425; Found 639.2429.

di-tert-butyl (3*R*,3'*R*)-4'-cyano-3''-methyl-2,5''-dioxo-1''-phenyl-3'',5''-dihydro-1'H-1''l4-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1'-dicarboxylate(3h).



61.4 mg, 97% yield, white solid, mp 110.2 – 112.1 °C; HPLC (Daicel Chiralpak IA, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 28.70 min (major), t_R = 79.70 min (minor); 92% *ee*, $[\alpha]D^{20}$ = -423.2 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.21 (s, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.41 (t, *J* = 8.4 Hz, 1H), 7.22 – 7.19 (m, 3H), 6.90 – 6.89 (m, 2H), 3.72 (s, 3H), 3.67 (s, 3H), 2.09 (s, 3H), 1.57 (s, 9H), 1.05 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.3, 169.0, 162.9, 157.7, 156.1, 149.1, 148.2, 147.0, 139.3, 131.4, 130.3, 126.1, 124.8, 121.6, 114.7, 114.6, 108.0, 85.8, 84.8, 74.4, 55.9, 52.3, 28.1, 27.5, 16.3. HRMS (ESI-TOF) m/z: [M+Na]+ Calcd for $C_{33}H_{37}N_4O_9$ 655.2375; Found 655.2380.

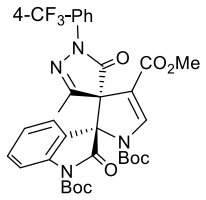
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-1''-(4-chlorophenyl)-3''-methyl-2,5''-dioxo-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3i).



59.9 mg, 94% yield, white solid, mp 130.8 – 133.9 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 90% *ee*, $[\alpha]D^{20}$ = -331.1 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.23 (s, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 7.2 Hz, 1H), 7.42 (d, *J* = 9.0 Hz, 2H), 7.39 (d, *J* = 2.4 Hz, 2H), 7.38 (d, *J* = 4.2 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 3.66 (s, 3H), 2.12 (s, 3H), 1.56 (s, 9H), 1.13 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 171.0, 169.2, 162.9, 157.1, 149.1, 148.2, 147.2, 139.2, 135.9, 131.5, 130.1, 129.4, 125.9, 124.9, 120.6, 118.7, 114.8, 107.7, 85.9, 84.9, 74.5, 52.4, 28.1, 27.5, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{33}ClN_4O_8$ 659.1879; Found 659.1875.

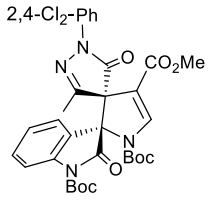
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-3''-methyl-2,5''-dioxo-1''-(4-(trifluoromethyl)phenyl)-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-

pyrazole]-1,1',4'-tricarboxylate (3j).



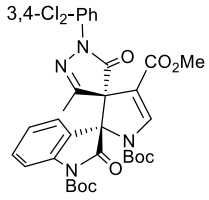
63.0 mg, 94% yield, white solid, mp 118.0 – 120.7 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 4.33 min (minor), t_R = 32.85 min (major); 92% *ee*, $[\alpha]D^{20}$ = -362.2 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.25 (s, 1H), 7.71 (d, *J* = 9.0 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 3H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 3.67 (s, 3H), 2.15 (s, 3H), 1.56 (s, 9H), 1.07 (s, 9H). ^{19}F NMR (565 MHz, DMSO- d_6 60 ℃) δ -111.06. ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.4, 169.5, 162.9, 157.8, 149.4, 148.1, 147.3, 140.2, 139.2, 131.6, 126.8 (q, J_{CF} = 3.9 Hz), 126.1, 125.9, 124.9, 123.6 (q, J_{CF} = 271.8 Hz), 118.7, 114.8, 107.6, 85.9, 85.0, 74.6, 52.5, 28.0, 27.6, 16.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{33}F_3N_4O_8$ 693.2143; Found 693.2144.

1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-1''-(2,4-dichlorophenyl)-3''-methyl-2,5''-dioxo-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3k).



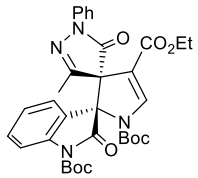
65.1 mg, 97% yield, white solid, mp 94.8 – 99.1 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 80% *ee*, $[\alpha]D^{20}$ = -153.3 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.22 (s, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 2.4 Hz, 1H), 7.47 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 3.71 (s, 3H), 2.11 (s, 3H), 1.58 (s, 9H), 1.06 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 169.9, 169.6, 162.9, 157.8, 148.9, 148.3, 146.5, 139.2, 134.6, 133.5, 132.4, 131.5, 130.1, 129.9, 128.8, 126.4, 124.9, 122.7, 114.8, 107.8, 85.6, 84.9, 74.9, 67.6, 52.4, 28.1, 27.5, 16.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{32}Cl_2N_4O_8$ 693.1489; Found 693.1484.

1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-1''-(3,4-dichlorophenyl)-3''-methyl-2,5''-dioxo-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3l).



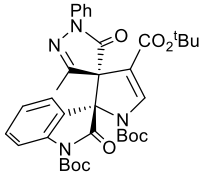
61.8 mg, 92% yield, white solid, mp 105.6 – 108.5 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 4.45 min (minor), t_R = 49.48 min (major); 93% *ee*, $[\alpha]D^{20}$ = -411.1 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.25 (s, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.45 (d, *J* = 2.4 Hz, 1H), 7.43 (d, *J* = 3.0 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 3.67 (s, 3H), 2.14 (s, 3H), 1.56 (s, 9H), 1.07 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.1, 169.4, 162.9, 162.2, 157.9, 149.1, 148.1, 147.3, 139.2, 136.8, 132.1, 131.6, 127.9, 125.9, 124.9, 122.3, 119.9, 118.7, 114.9, 107.5, 85.9, 84.7, 74.6, 52.4, 28.0, 27.5, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{32}Cl_2N_4O_8$ 693.1489; Found 693.1491.

1,1'-di-tert-butyl 4'-ethyl (3*R*,3'*R*)-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3n).



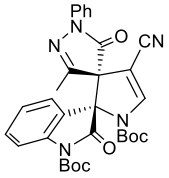
53.7 mg, 87% yield, white solid, mp 144.8 – 147.6 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 90% *ee*, $[\alpha]D^{20}$ = -42.2 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.20 (s, 1H), 7.67 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.47 (d, *J* = 7.2 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.37 – 7.27 (m, 4H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.16 (tt, *J* = 7.2, 1.8 Hz, 1H), 4.10 (dq, *J* = 6.6, 3.0 Hz, 2H), 2.12 (s, 3H), 1.57 (s, 9H), 1.14 (t, *J* = 7.2 Hz, 3H), 1.03 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.3, 169.3, 162.4, 156.6, 149.3, 148.2, 146.9, 139.2, 137.1, 131.4, 129.4, 126.1, 124.9, 122.4, 119.4, 114.8, 108.2, 85.9, 84.6, 74.5, 61.1, 28.1, 27.6, 16.3, 14.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{36}N_4O_8$ 639.2425; Found 639.2427.

tri-tert-butyl (3*R*,3'*R*)-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3o).



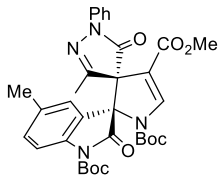
55.8 mg, 93% yield, white solid, mp 160.2 – 162.5 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 86% *ee*, $[\alpha]D^{20}$ = -326.7 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 °C) δ 8.12 (s, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 7.2 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.37-7.31 (m, 4H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.15 (t, *J* = 7.2 Hz, 1H), 2.13 (s, 3H), 1.56 (s, 9H), 1.31 (s, 9H), 1.03 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 °C) δ 170.2, 169.3, 161.5, 156.7, 149.3, 148.2, 146.6, 139.2, 137.2, 131.4, 129.4, 126.5, 126.0, 124.8, 119.2, 114.7, 109.3, 85.8, 84.8, 82.1, 74.6, 28.13, 28.06, 27.5, 16.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{35}H_{40}N_4O_8$ 667.2738; Found 667.2340.

di-tert-butyl (3*R*,3'*R*)-4'-cyano-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1'-dicarboxylate (3p).



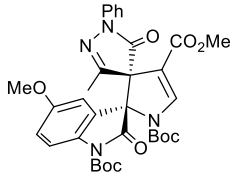
51.3 mg, 90% yield, white solid, mp 92.5 – 95.3 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 97% *ee*, $[\alpha]D^{20}$ = -402.2 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 °C) δ 8.78 (s, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.39 (dd, *J* = 9.0, 1.8 Hz, 2H), 7.37 (dd, *J* = 8.4, 6.6 Hz, 2H), 7.26 – 7.18 (m, 2H), 3.19 (s, 3H), 2.24 (s, 3H), 1.57 (s, 9H), 1.11 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 °C) δ 169.7, 167.9, 155.1, 152.9, 148.6, 148.1, 139.4, 136.6, 131.8, 129.6, 126.7, 126.2, 125.1, 119.5, 115.0, 113.5, 86.2, 85.4, 74.2, 28.0, 27.5, 16.2. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{31}H_{31}N_5O_6$ 592.2167; Found 592.2168.

1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-3'',5-dimethyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3r).



58.6 mg, 95% yield, white solid, mp 118.2 – 121.1 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 90% *ee*, $[\alpha]D^{20}$ = -302.8 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.21 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.36 (dd, *J* = 9.0, 1.8 Hz, 2H), 7.34 (dd, *J* = 9.0, 7.2 Hz, 2H), 7.27 (s, 1H), 7.20 – 7.17 (m, 1H), 7.16 (dt, *J* = 7.2, 1.8 Hz, 1H), 3.66 (s, 3H), 2.24 (s, 3H), 2.10 (s, 3H), 1.55 (s, 9H), 1.09 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.3, 169.2, 163.0, 156.5, 149.4, 148.2, 147.1, 137.1, 136.9, 134.3, 131.6, 129.3, 126.2, 126.1, 119.1, 118.7, 114.6, 107.8, 85.7, 84.7, 74.5, 52.4, 28.1, 27.6, 20.9, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{36}N_4O_8$ 639.2425; Found 639.2428.

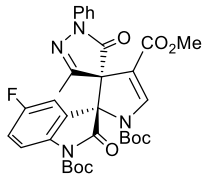
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-5-methoxy-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3s).



50.6 mg, 80% yield, white solid, mp 90.5 – 93.3 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): tR = 13.86 min (minor), tR = 20.33 min (major); 89% *ee*, $[\alpha]D^{20}$ = -331.1 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.21 (s, 1H), 7.59 (d, *J* = 9.0 Hz, 1H), 7.38 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.34 (dd, *J* = 9.0, 7.2 Hz, 2H), 7.18 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.02 (s, 1H), 6.96 (dd, *J* = 9.0, 2.4 Hz, 1H), 3.69 (s, 3H), 3.67 (s, 3H), 2.10 (s, 3H), 1.56 (s, 9H), 1.09 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.3, 169.3, 163.0, 156.8, 156.5, 149.3, 148.3, 147.2, 137.1, 132.4, 129.4, 126.1, 119.2, 116.7, 115.9, 112.1, 107.6, 85.6, 84.9, 74.5, 56.3, 52.4, 28.0, 27.6, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{36}N_4O_9$ 655.2374; Found 655.2373.

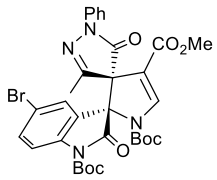
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-5-fluoro-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-

tricarboxylate (3t).



60.2 mg, 97% yield, white solid, mp 70.2 – 73.0 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 92% *ee*, $[\alpha]D^{20}$ = -315.6 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.21 (s, 1H), 7.69 (dd, *J* = 9.0, 4.8 Hz, 1H), 7.42 – 7.33 (m, 4H), 7.28 – 7.25(m, 2H), 7.19 (tt, *J* = 7.2, 1.8 Hz, 1H), 3.67 (s, 3H), 2.12 (s, 3H), 1.55 (s, 9H), 1.10 (s, 9H). ^{19}F NMR (565 MHz, DMSO-d_6, 60℃) δ -117.26. ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 169.8, 169.0, 162.9, 160.0（d, J_{CF} = 242.8 Hz）, 156.8, 148.9, 148.0, 147.0, 137.1, 135.3, 129.5, 129.4, 126.2, 119.2, 118.1（d, J_{CF} = 23.3 Hz）, 116.6（d, J_{CF} = 8.0 Hz）, 113.6（d, J_{CF} = 22.9 Hz）, 107.8, 86.1, 85.1, 74.2, 52.4, 28.0, 27.6, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{33}FN_4O_8$ 643.2175; Found 643.2178.

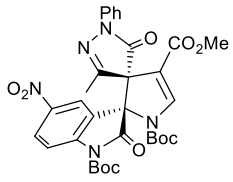
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-5-bromo-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3u).



62.7mg, 92% yield, white solid, mp 97.8 – 101.6 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 90% *ee*, $[\alpha]D^{20}$ = -131.1 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.22 (s, 1H), 7.61 (m, 2H), 7.50 – 7.28 (m, 4H), 7.20 (tt, *J* = 7.2, 1.8 Hz, 1H), 3.67 (s, 3H), 2.11 (s, 3H), 1.55 (s, 9H), 1.13 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 169.5, 169.1, 162.9, 156.6, 147.9, 147.1, 138.3, 137.0, 134.2, 129.5, 129.4, 128.6, 126.3, 119.3, 119.2, 117.0, 116.9, 107.8, 86.4, 85.3, 73.9, 71.1, 52.4, 28.0, 27.6, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{33}BrN_4O_8$ 703.1374; Found 703.1372.

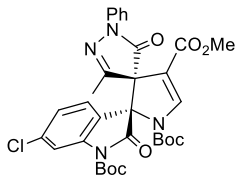
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-3''-methyl-5-nitro-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-

tricarboxylate (3v).



61.7 mg, 95% yield, white solid, mp 144.5 – 147.4 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 91% *ee*, $[\alpha]D^{20}$ = -348.9 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.39 – 8.29 (m, 2H), 8.27 (s, 1H), 7.90 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.32 (dd, *J* = 7.8, 1.8 Hz, 2H), 7.17 (tt, *J* = 7.2, 1.2 Hz 1H), 3.68 (s, 3H), 2.14 (s, 3H), 1.57 (s, 9H), 1.12 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 171.2, 168.8, 162.8, 156.8, 147.5, 147.1, 144.3, 144.1, 142.6, 136.9, 129.5, 127.7, 126.3, 121.1, 119.1, 118.9, 115.8, 111.2, 87.2, 85.8, 73.6, 52.5, 27.9, 27.6, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{33}N_5O_{10}$ 670.2120; Found 670.2122.

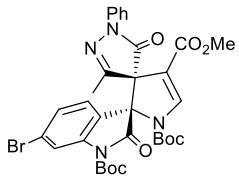
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-5-chloro-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3w).



61.8 mg, 97% yield, white solid, mp 66.8 − 67.9 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 91% *ee*, $[\alpha]D^{20}$ = -293.3 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.22 (s, 1H), 7.71 (d, *J* = 1.8 Hz, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.39 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.36 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.19 (td, *J* = 7.2, 1.2 Hz, 1H), 3.66 (s, 3H), 2.12 (s, 3H), 1.56 (s, 9H), 1.09 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 169.9, 169.0, 162.8, 156.6, 148.5, 146.9, 140.2, 137.1, 135.8, 133.2, 129.4, 127.7, 126.2, 124.9, 119.4, 118.7, 115.1, 107.9, 86.5, 85.0, 74.1, 52.4, 27.9, 27.6, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{33}ClN_4O_8$ 659.1879; Found 659.1871.

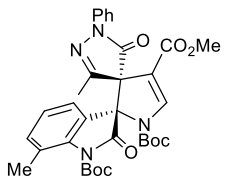
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-6-bromo-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-

tricarboxylate (3x).



62.0 mg, 91% yield, white solid, mp 118.2 – 121.1 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 91% *ee*, $[\alpha]D^{20}$ = -255.6 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.22 (s, 1H), 7.85 (d, *J* = 1.8Hz, 1H), 7.47 – 7.41 (m, 2H), 7.39 (dd, *J* = 8.4, 1.8Hz, 2H), 7.36 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.19 (tt, *J* = 7.2, 1.8 Hz, 1H), 3.66 (s, 3H), 2.11 (s, 3H), 1.56 (s, 9H), 1.13 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 169.8, 169.0, 162.8, 156.6, 149.0, 147.9, 146.9, 140.3, 137.0, 129.4, 127.8, 126.3, 124.1, 119.4, 118.7, 117.8, 107.9, 86.5, 85.2, 74.1, 52.4, 27.9, 27.6, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{33}BrN_4O_8$ 703.1374; Found 703.1373.

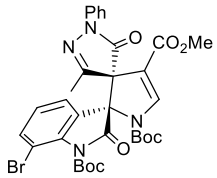
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-3'',7-dimethyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3y).



57.3 mg, 93% yield, white solid, mp 73.6 – 75.2 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 94% *ee*, $[\alpha]D^{20}$ = -418.9 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.20 (s, 1H), 7.37 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.33 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.16 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 3.66 (s, 3H), 2.12 (s, 3H), 2.11 (s, 9H), 1.53 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 171.3, 169.2, 163.0, 156.6, 149.2, 148.4, 146.9, 137.7, 137.2, 133.9, 129.3, 126.0, 124.7, 123.6, 123.3, 119.4, 118.7, 108.0, 86.3, 84.8, 74.9, 69.0, 52.3, 27.6, 27.5, 18.9, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{36}N_4O_8$ 639.2425; Found 639.2421.

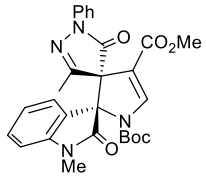
1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-7-bromo-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-

tricarboxylate (3z).



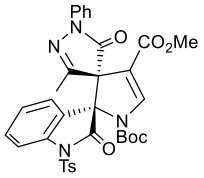
66.1 mg, 97% yield, white solid, mp 90.1 – 92.1 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 93% *ee*, $[\alpha]D^{20}$ = -304.4 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.21 (s, 1H), 7.61 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.47 (d, *J* = 7.2 Hz, 1H), 7.38 (dd, *J* = 9.0, 1.8 Hz, 2H), 7.35 (dd, *J* = 9.0, 7.2 Hz, 2H), 7.18 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 3.66 (s, 3H), 2.12 (s, 3H), 1.51 (s, 9H), 1.13 (s, 9H). ^{13}C NMR (150 MHz, DMSO-D_6, 60 ℃) δ 170.8, 168.9, 162.8, 156.8, 148.9, 146.8, 146.7, 137.8, 137.1, 135.7, 129.4, 126.4, 126.2, 125.4, 119.4, 108.1, 106.3, 86.9, 85.2, 75.1, 52.4, 27.6, 27.2, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{33}BrN_4O_8$ 703.1374; Found 703.1373.

1'-(tert-butyl) 4'-methyl (3*R*,3'*R*)-1,3''-dimethyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1',4'-dicarboxylate (3aa).



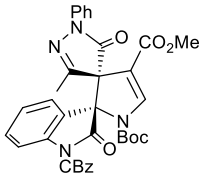
24.8 mg, 48% yield, yellow solid, mp 179.2 – 182.0 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 84% *ee*, $[\alpha]D^{20}$ = -348.9 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.18 (s, 1H), 7.41 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.34 (d, *J* = 1.8 Hz, 1H), 7.34 – 7.31 (m, 2H), 7.15 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.09 – 6.96 (m, 2H), 3.65 (s, 3H), 3.15 (s, 3H), 2.07 (s, 3H), 1.04 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 172.1, 169.7, 163.1, 157.1, 149.3, 147.1, 143.9, 138.7, 137.3, 131.1, 129.3, 125.9, 125.7, 122.9, 119.3, 111.1, 109.7, 108.3, 84.2, 74.2, 52.2, 27.6, 27.1, 16.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{28}H_{28}N_4O_6$ 539.1901; Found 539.1902.

1'-(tert-butyl) 4'-methyl (3*R*,3'*R*)-3''-methyl-2,5''-dioxo-1''-phenyl-1-tosyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1',4'-dicarboxylate (3bb).



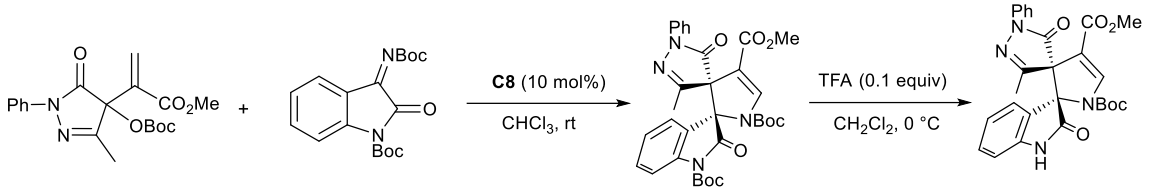
61.7 mg, 94% yield, white solid, mp 173.9 – 176.8 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 95% *ee*, $[\alpha]D^{20}$ = -324.4 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.18 (s, 1H), 7.98 (s, 2H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.47 – 7.41 (m, 4H), 7.38 – 7.30 (m, 4H), 7.26 – 7.09 (m, 2H), 3.66 (s, 3H), 2.36 (s, 3H), 2.11 (s, 3H), 0.66 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.5, 169.0, 162.8, 156.4, 146.7, 137.1, 133.9, 131.9, 130.8, 129.4, 128.4, 126.8, 126.2, 125.3, 122.7, 119.4, 113.3, 107.8, 84.1, 74.6, 52.4, 27.1, 21.6, 16.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{34}H_{32}N_4O_8$ 679.1833; Found 679.1835.

1'-(tert-butyl) 4'-methyl (3*R*,3'*R*)-3''-methyl-2,5''-dioxo-1-(2-oxo-2-phenyl-1l2-ethyl)-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1',4'-dicarboxylate (3cc).



60.5 mg, 95% yield, white solid, mp 110.2 – 114.0 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 91% *ee*, $[\alpha]D^{20}$ = -304.4 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.23 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.60 – 7.45 (m, 3H), 7.44 – 7.38 (m, 3H), 7.34 (m, 5H), 7.22 (t, *J* = 7.8 Hz, 1H), 7.16 (tt, *J* = 7.2, 1.2 Hz, 1H), 5.49 (s, 2H), 3.66 (s, 3H), 2.08 (s, 3H), 1.01 (s, 9H).. ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.1, 169.1, 162.9, 156.5, 149.8, 149.0, 146.9, 138.9, 137.1, 135.4, 131.5, 129.4, 129.1, 128.9, 128.4, 126.2, 126.1, 125.2, 122.5, 119.4, 114.9, 107.9, 85.0, 74.5, 68.8, 52.4, 27.5, 16.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{35}H_{32}N_4O_8$ 659.2112; Found 659.2115.

6. Gram-scale reaction and deprotection of product 3a



1a 1.3 g

2a 1.0 g

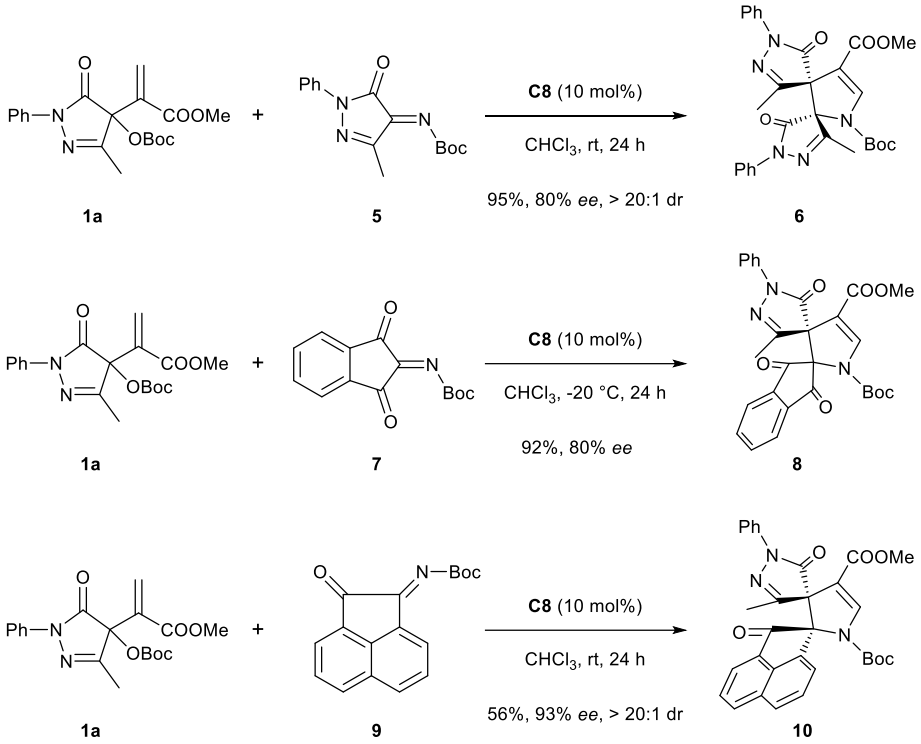
3a 1.56 g,
89%, 90% ee, > 20:1 dr

4a 1.16 g,
89%, 90% ee, > 20:1 dr

MBH Carbonate of pyrazolinone **1a** (1.3 g, 3.47 mmol), 3-((tert-butoxycarbonyl)imino)-2-oxoindoline-1-carboxylate **2a** (1.0 g, 2.89 mmol), and catalyst **C8** (262.3 mg, 0.29 mmol) were dissolved in $CHCl_3$ (5.0 mL), and the mixture was stirred at room temperature for 48 h. After completion of the reaction, the reaction mixture was concentrated and directly purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to afford the pure product **3a** (1.56 g, 89% yield, 90% *ee*, >20:1 dr) as a white solid.

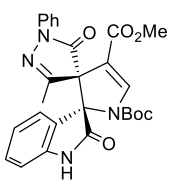
The compound **4a** were prepared by a modified reported procedure. The corresponding chiral compound **3a** (1.56 g, 2.59 mmol) was dissolved in 5.0 mL CH_2Cl_2 and add TFA (193.18 μL, 0.26 mmol) at 0 °C, then stirred for about 8 h at room temperature. The solution was concentrated when the reaction was completed under vacuum. The residue was then dissolved in dry ethyl acetate and washed with brine several times. The organic phase was dried over anhydrous $MgSO_4$ and concentrated under vacuum. The crude product was purified *via* flash chromatography (eluent: petroleum ether/ethyl acetate = 5/1 to 3/1) to give compound **4a**.

7. Structural diversity construction of product 3a



MBH Carbonate of Pyrazolinone **1a** (0.12 mmol), **5**, **7** and **9** (0.10 mmol), and catalyst **C8** (9.1 mg, 0.01 mmol) were dissolved in $CHCl_3$ (0.5 mL), and the mixture was stirred at room temperature for 24 h. After completion of the reaction, the reaction mixture was concentrated and directly purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1 to 5/1) to afford the pure products **6**, **8** and **10**.

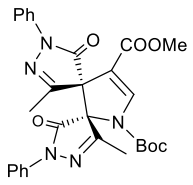
1'-(tert-butyl) 4'-methyl (3*R*,3'*R*)-3''-methyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1',4'-dicarboxylate (4a).



44.7 mg, 89% yield, yellow solid, mp 80.3 – 83.0 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 13.86 min (minor), t_R = 20.33 min (major); 90% *ee*, $[\alpha]D^{20}$ = -397.8 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 °C) δ 10.75 (s, 1H), 8.16 (s, 1H), 7.44 – 7.40 (dd, *J* = 9.0, 1.2 Hz, 2H), 7.34 – 7.31 (m, 3H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.15 (td, *J* = 7.2, 1.2 Hz, 1H), 6.93 (t, *J* = 8.4 Hz, 1H), 6.81 (d, *J* = 7.8

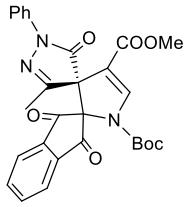
Hz, 1H), 3.65 (s, 3H), 2.13 (s, 3H), 1.11 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 173.6, 169.8, 163.2, 157.4, 149.4, 147.1, 142.6, 138.9, 137.4, 130.9, 129.3, 126.1, 125.8, 122.1, 119.2, 110.8, 108.1, 84.2, 74.7, 52.2, 27.6, 16.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{27}H_{26}N_4O_6$ 525.1745; Found 525.1754.

11-(tert-butyl) 13-methyl (5*R*,6*R*)-1,10-dimethyl-4,7-dioxo-3,8-diphenyl-2,3,8,9,11-pentaazadispiro[4.0.4^6.3^5]trideca-1,9,12-triene-11,13-dicarboxylate (6).



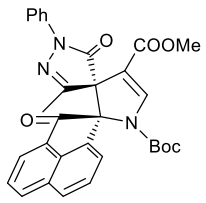
51.6 mg, 95% yield, white solid, mp 82.3 – 83.0 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 8.15 min (minor), t_R = 10.28 min (major); 80% *ee*, $[\alpha]D^{20}$ = -162.9 (c = 0.45, MeOH).^{1}H NMR (600 MHz, DMSO-d_6, 60℃) δ 8.15 (s, 1H), 7.65 – 7.59 (m, 4H), 7.43 – 7.38 (m, 4H), 7.23 – 7.20 (m, 2H), 3.68 (s, 3H), 2.26 (s, 3H), 2.21 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 168.5, 166.9, 162.4, 158.4, 144.8, 137.5, 137.4, 129.7, 129.6, 126.4, 126.3, 119.6, 119.2, 109.6, 86.1, 77.3, 52.6, 27.9, 16.4, 16.2. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{29}H_{29}N_5O_6$ 566.2016; Found 566.2010.

tert-butyl (*R*)-3''-methyl-4'-((methylperoxy)-l2-methyl)-1,3,5''-trioxo-1''-phenyl-1,1'',3,5''-tetrahydro-1'H-dispiro[indene-2,2'-pyrrole-3',4''-pyrazole]-1'-carboxylate (8).



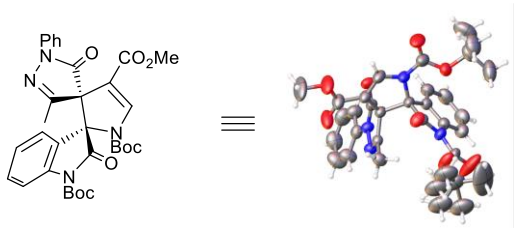
47.5 mg, 92% yield, white solid, mp 90.2 – 92.1 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 80:20, 1.0 mL/min, at 270 nm): t_R = 15.35 min (minor), t_R = 22.68 min (major); 80% *ee*, $[\alpha]D^{20}$ = -99.9 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 100 ℃) δ 8.15 (s, 1H), 8.03 – 8.01 (m, 3H), 7.97 – 7.94 (m, 1H), 7.30 – 7.26 (m, 2H), 7.24 – 7.22 (m, 2H), 7.16 – 7.13 (m, 1H), 3.64 (s, 3H), 2.15 (s, 3H), 1.47 (s, 4H), 1.05 (s, 5H). ^{13}C NMR (150 MHz, DMSO-d_6, 100 ℃) δ 167.9, 162.5, 157.7, 146.0, 140.4, 139.8, 138.5, 137.7, 137.2, 129.3, 126.3, 124.7, 124.3, 119.6, 108.2, 85.6, 78.7, 52.3, 27.5, 15.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{28}H_{25}N_3O_7$ 538.1590; Found 538.1588.

tert-butyl (1*S*,3'*R*)-3''-methyl-4'-((methylperoxy)-l2-methyl)-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H,2H-dispiro[acenaphthylene-1,2'-pyrrole-3',4''-pyrazole]-1'-carboxylate (10).



30.0 mg, 56% yield, white solid, mp 81.3 – 82.5 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 90:10, 1.0 mL/min, at 270 nm): t_R = 13.33 min (minor), t_R = 37.79 min (major); 93% *ee*, $[\alpha]D^{20}$ = -226.7 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.31 – 8.29 (m, 2H), 8.11 (d, *J* = 6.6 Hz, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.84 (t, *J* = 7.8 Hz, 1H), 7.76 – 7.71 (m, 2H), 7.26 – 7.25 (m, 4H), 7.11 – 7.08 (m, 1H), 3.67 (s, 3H), 2.05 (s, 3H), 0.60 (s, 9H). ^{13}C NMR (150 MHz, DMSO- d_6, 60 ℃) δ 196.8, 169.9, 163.2, 161.2, 156.9, 149.4, 147.4, 141.3, 137.2, 135.9, 133.7, 133.1, 130.5, 129.8, 129.31, 129.29, 128.9, 128.1, 126.9, 125.9, 123.5, 122.9, 119.5, 119.1, 107.9, 84.0, 78.3, 52.3, 27.2, 17.0. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{31}H_{27}N_3O_6$ 560.1792; Found 560.1786.

8. Single crystal X-ray diffraction analysis and crystal data



3a ≡ CCDC 2120377

To a 5 mL tube containing **3a** (20 mg) was added a 1:3 mixture of ethyl acetate and petroleum ether (2 mL). A clear solution was obtained through ultrasound treatment and was kept at room temperature for 1 day to get crystals of **3a**, which were characterized by single crystal X-ray diffraction. The data were collected by an Agilent Gemini. **3a** contains the supplementary crystallographic data for this paper. These data can be obtained fr*ee* of charge via www.ccdc.cam.ac.uk/data_request/cif

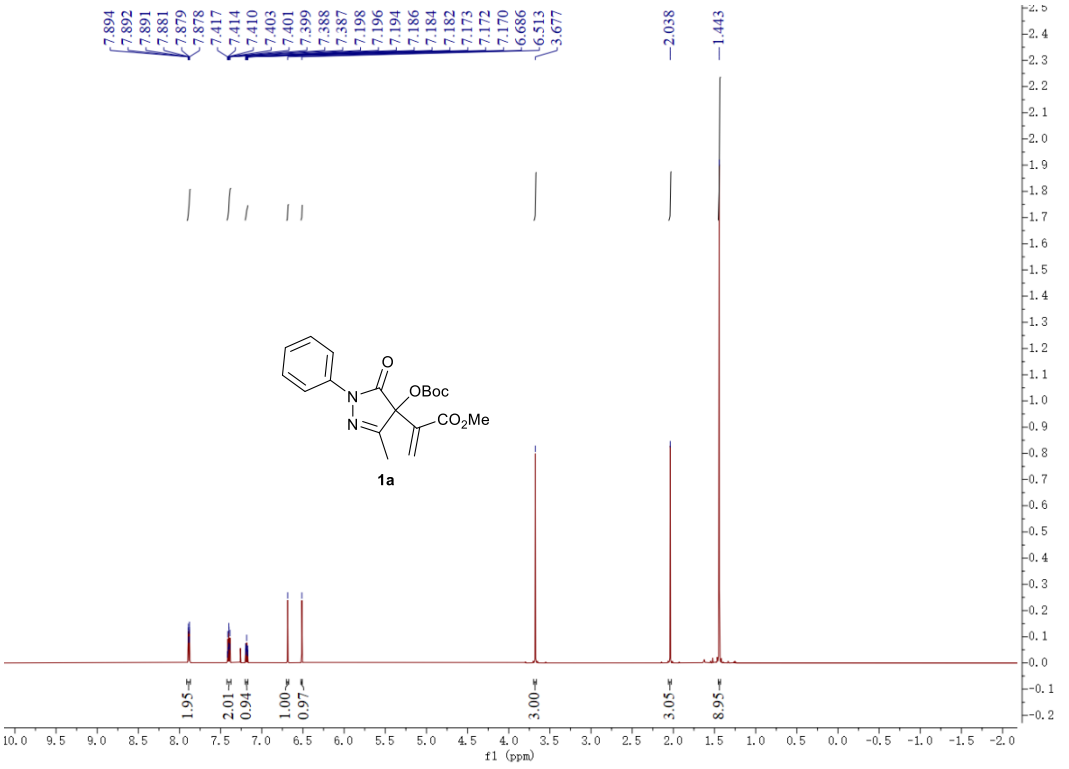
The ellipsoid contour percent probability level is 50%.

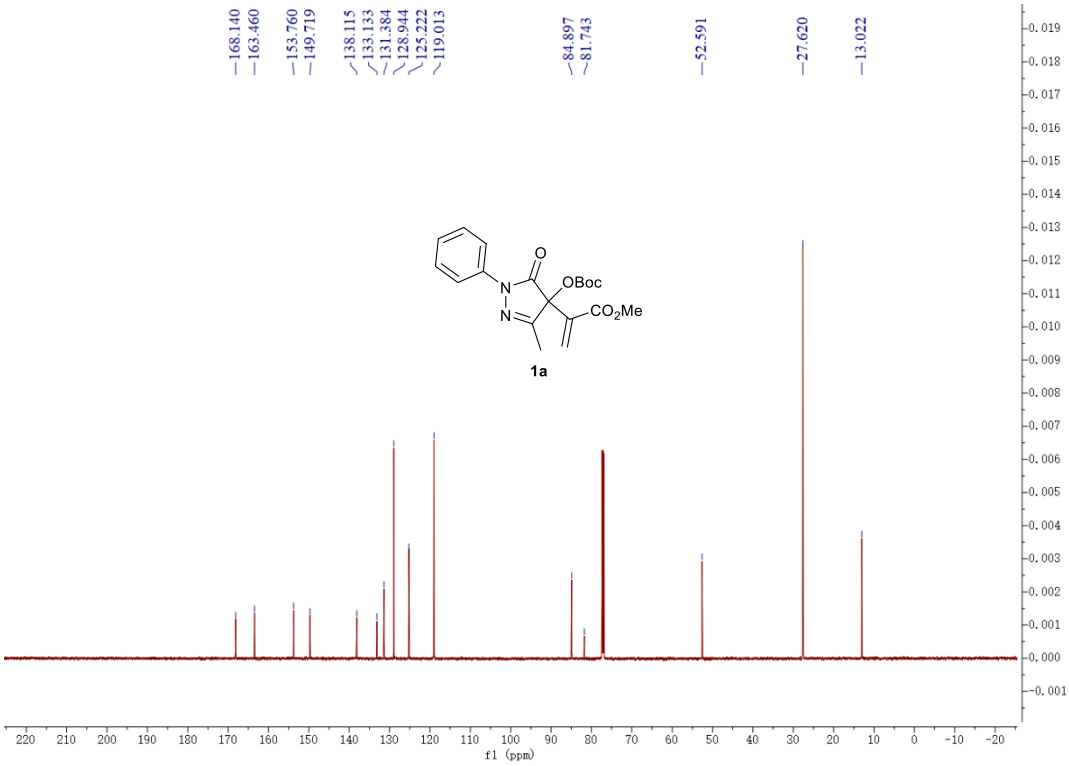
Empirical formula	$C_{32}H_{34}N_4O_8$
Formula weight	602.63
Temperature/K	293.15
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	9.4403(9)
b/Å	12.4980(11)
c/Å	27.612(2)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3257.8(5)
Z	4
ρ_{calc}g/cm^3	1.229

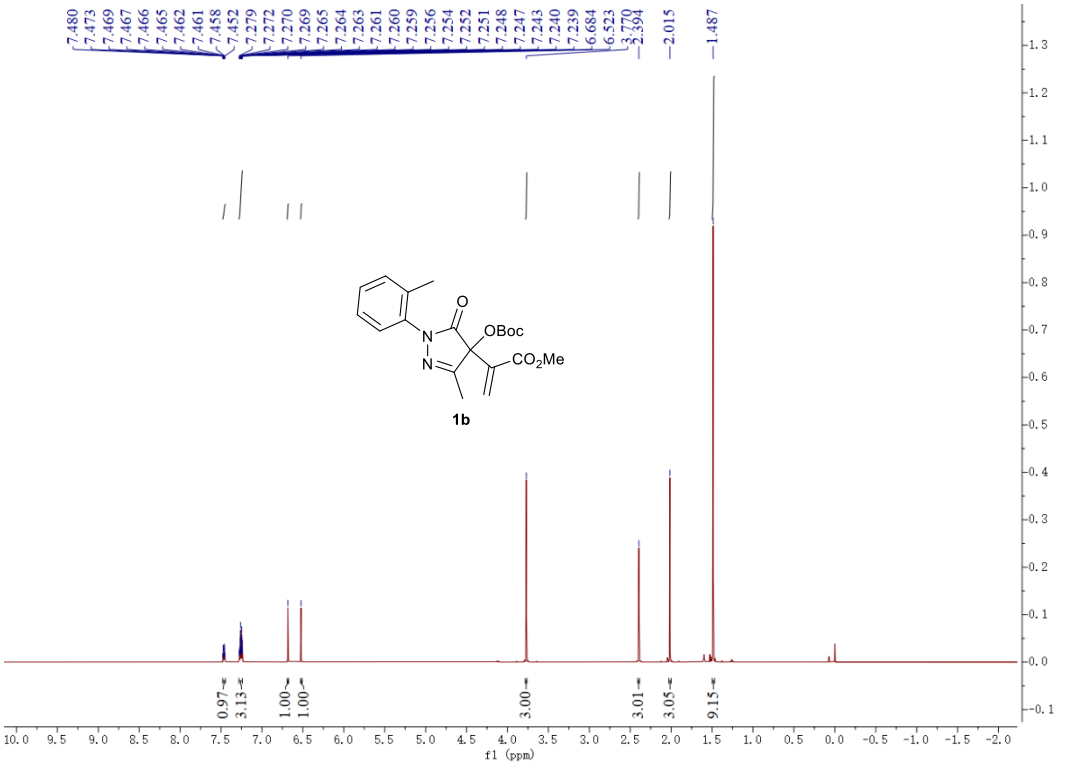
μ/mm^{-1}	0.089
F(000)	1272.0
Crystal size/mm^3	0.35 × 0.3 × 0.25
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.162 to 52.744
Index ranges	$-11 \leq h \leq 11$, $-15 \leq k \leq 15$, $-34 \leq l \leq 34$
Reflections collected	18292
Independent reflections	6617 [R_{int} = 0.0282, R_{sigma} = 0.0506]
Data/restraints/parameters	6617/2/408
Goodness-of-fit on F^2	1.011
Final R indexes [I>=2σ (I)]	R_1 = 0.0596, wR_2 = 0.1224
Final R indexes [all data]	R_1 = 0.0953, wR_2 = 0.1381
Largest diff. peak/hole / e $Å^{-3}$	0.33/-0.26
Flack parameter	-0.1(5)

9. NMR spectra and HPLC chromatograms

9.1 NMR spectra of substrates and catalysts



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7.248
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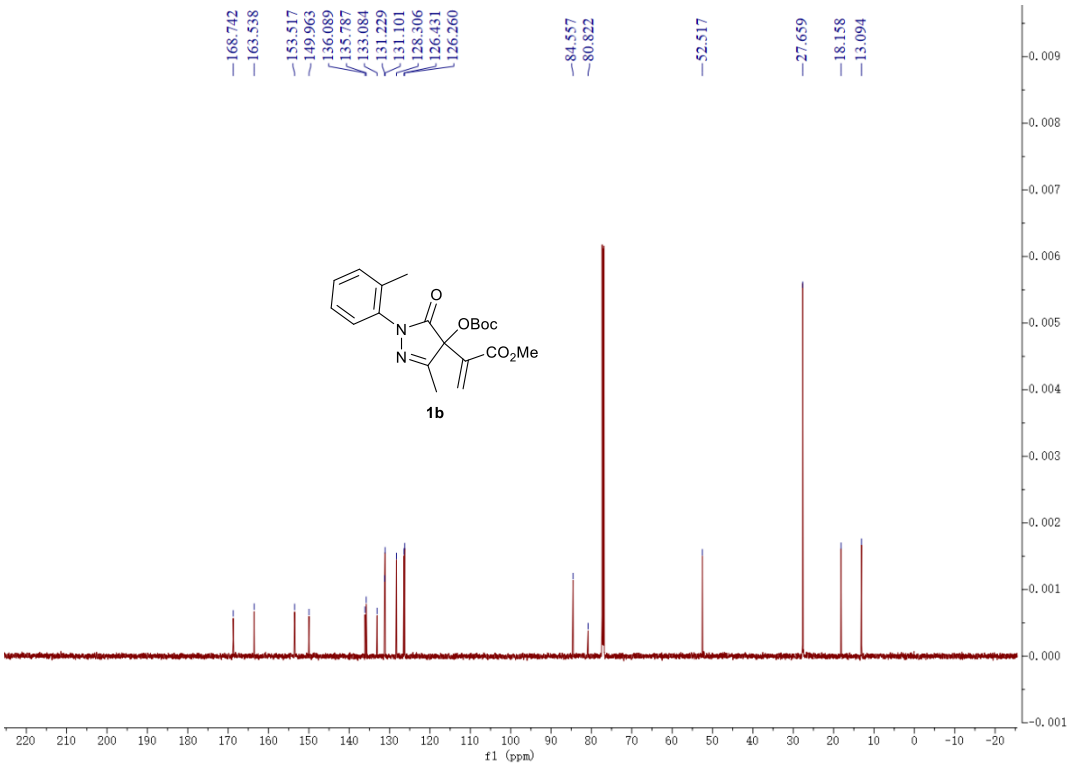
7.243
7.240
7.239
6.684
6.523
3.770
2.394
2.015
1.487
O
OBoc
N
N
CO2Me
1b
0.97
3.13
1.00
1.00
3.00
3.01
3.05
9.15
f1 (ppm)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153.517
149.963
136.089
135.787
133.084
131.229
131.101
128.306
126.431
126.260
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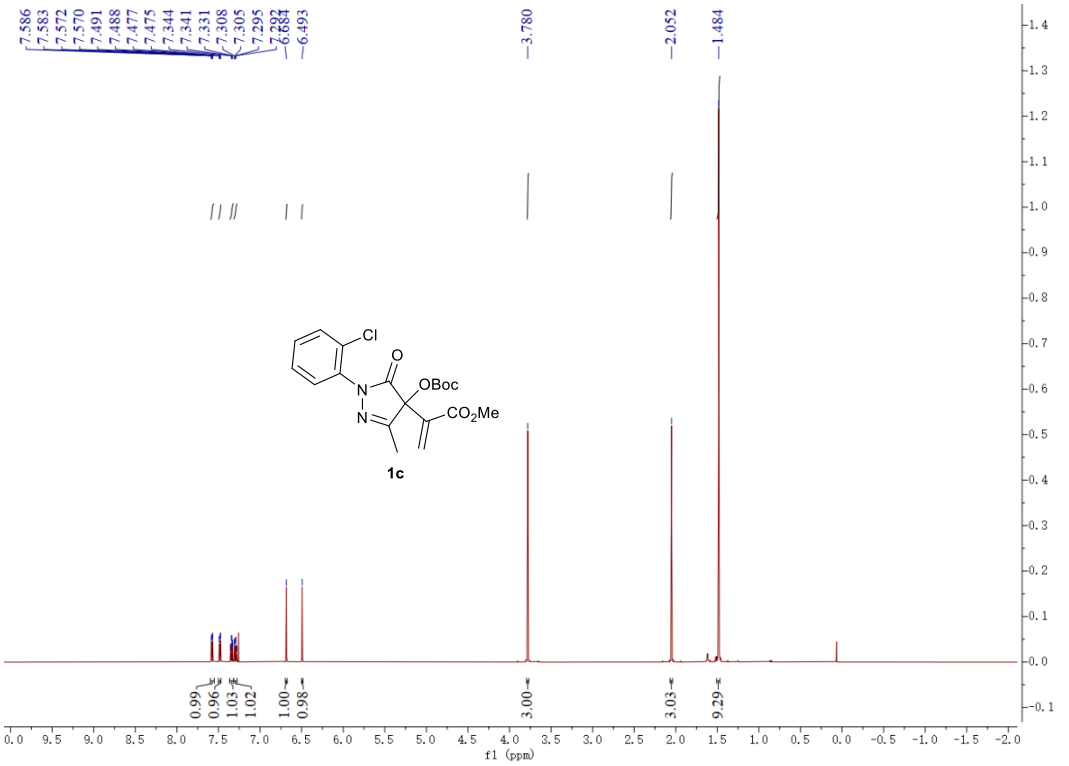
80.822
52.517
27.659
18.158
13.094
O
OBoc
N
N
CO2Me
1b
f1 (ppm)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7.572
7.570
7.491
7.488
7.477
7.475
7.344
7.341
7.331
7.308
7.305
7.295
7.282
6.684
6.493
3.780
2.052
1.484
Cl
O
N
N
OBoc
CO2Me
1c
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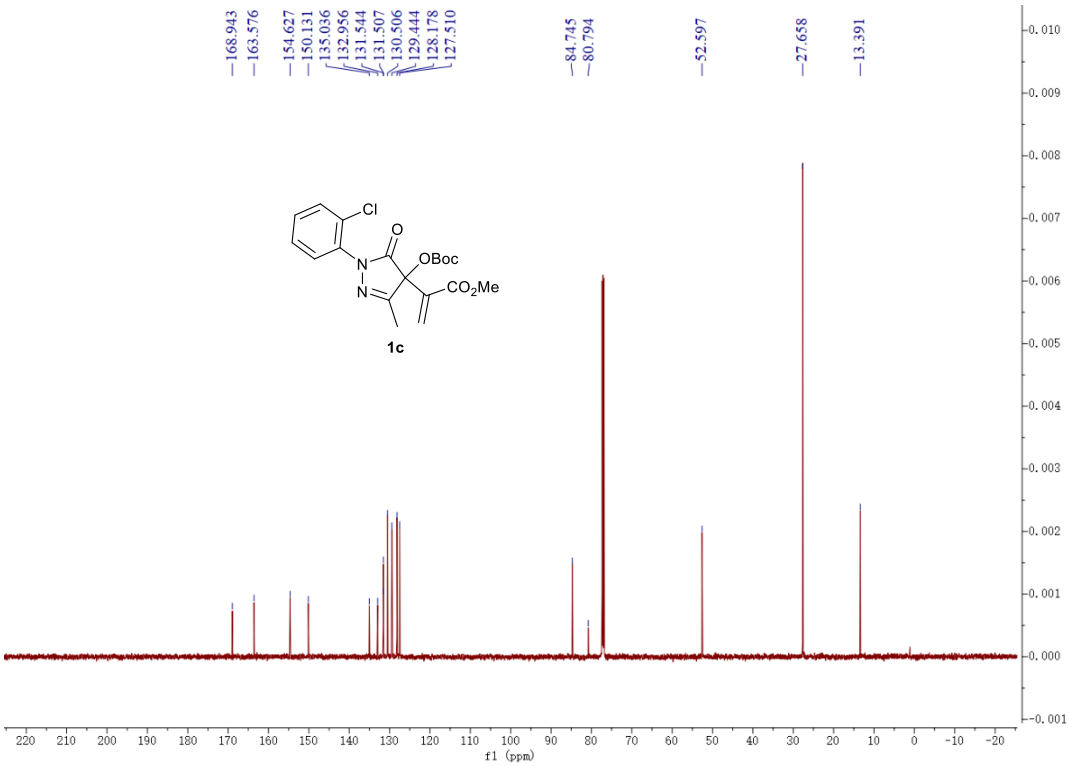
0.96
1.03
1.02
1.00
0.98
3.00
3.03
9.29
f1 (ppm)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131.507
130.506
129.444
128.178
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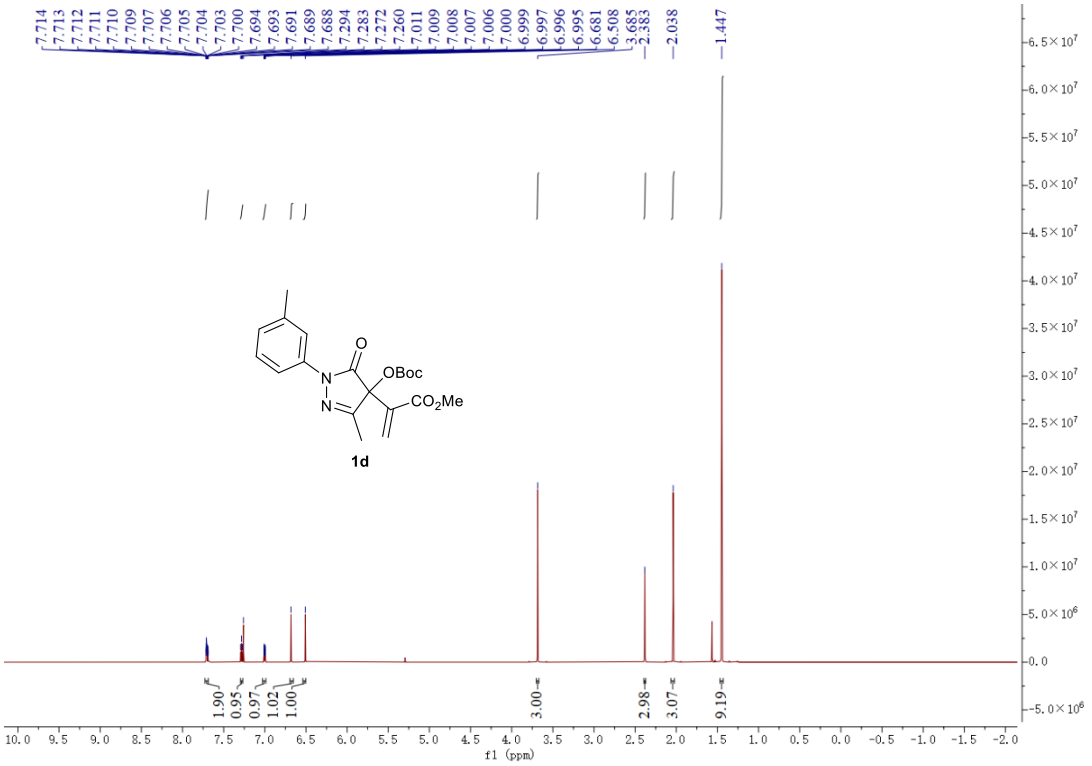
52.597
27.658
13.391
Cl
O
N
N
OBoc
CO2Me
1c
f1 (ppm)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7.712
7.711
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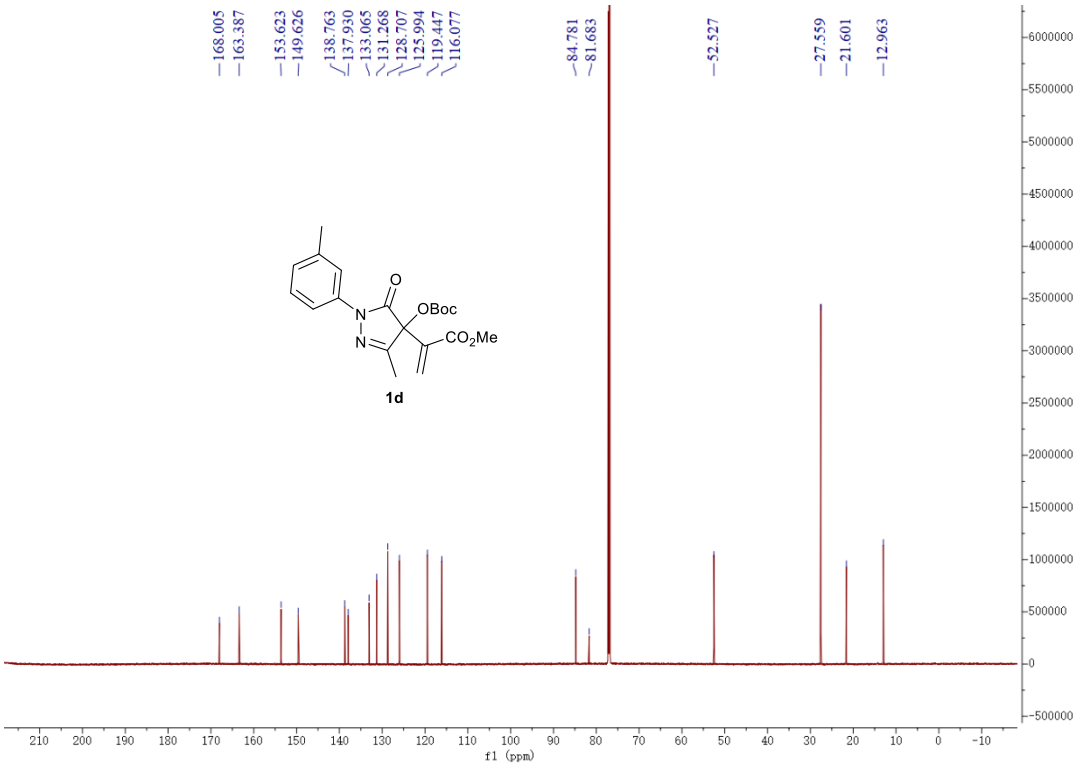
7.709
7.707
7.706
7.705
7.704
7.703
7.700
7.694
7.693
7.691
7.689
7.688
7.294
7.283
7.272
7.260
7.011
7.009
7.008
7.007
7.006
7.000
6.999
6.997
6.996
6.995
6.681
6.508
3.685
2.583
2.038
1.447
OBoc
CO2Me
1d
1.90
0.95
0.97
1.02
1.00
3.00
2.98
3.07
9.19
f1 (ppm)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137.930
133.065
131.268
128.707
125.994
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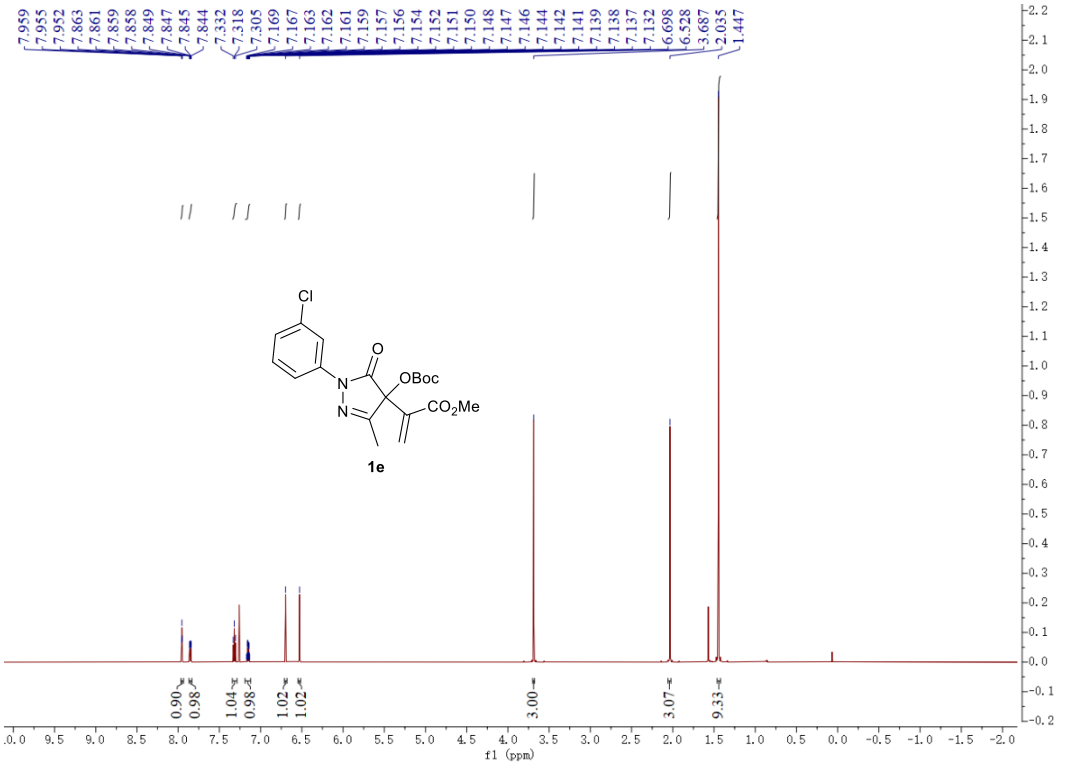
84.781
81.683
52.527
27.559
21.601
12.963
OBoc
CO2Me
1d
f1 (ppm)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7.861
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7.858
7.849
7.847
7.845
7.844
7.332
7.318
7.305
7.169
7.167
7.163
7.162
7.161
7.159
7.157
7.156
7.154
7.152
7.151
7.150
7.148
7.147
7.146
7.144
7.142
7.141
7.139
7.138
7.137
7.132
6.698
6.528
3.687
2.035
1.447
Cl
O
OBoc
N
N
CO2Me
1e
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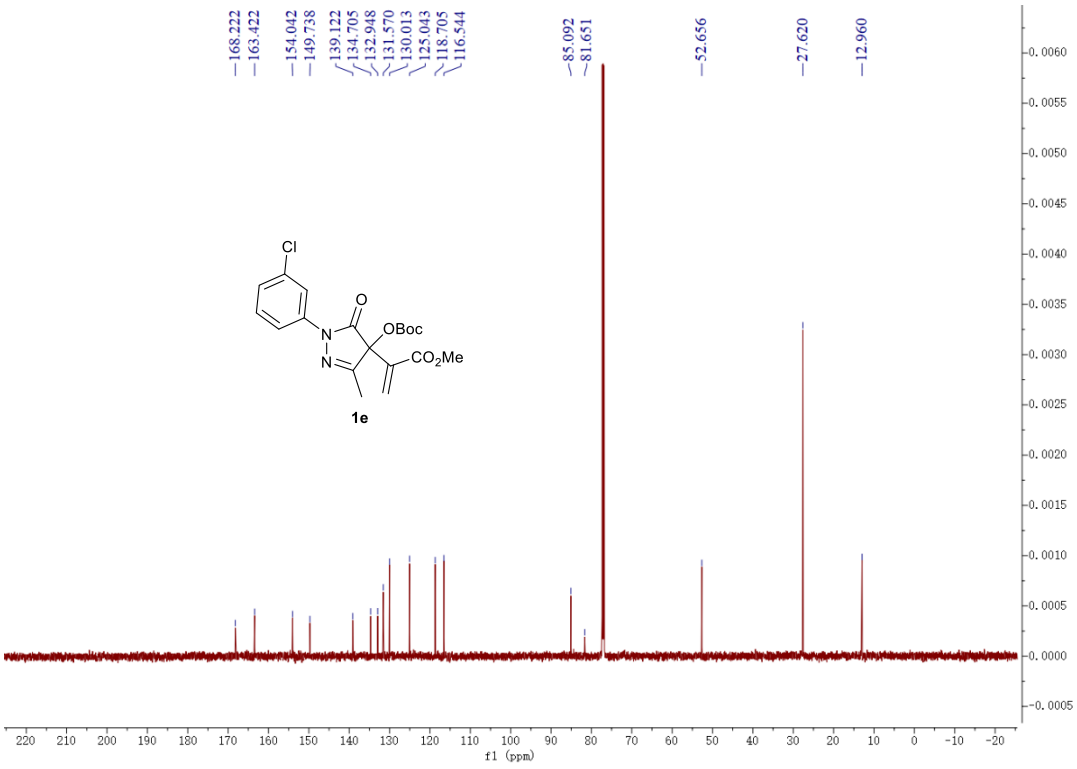
0.98
1.04
0.98
1.02
1.02
3.00
3.07
9.33
f1 (ppm)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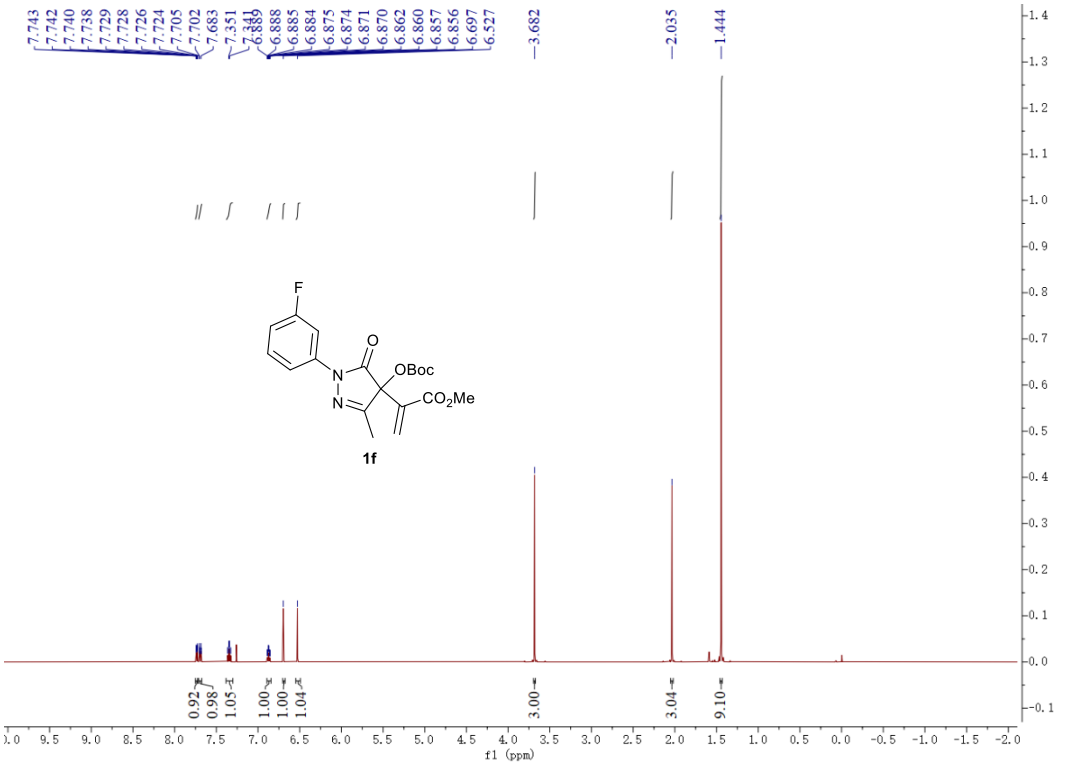
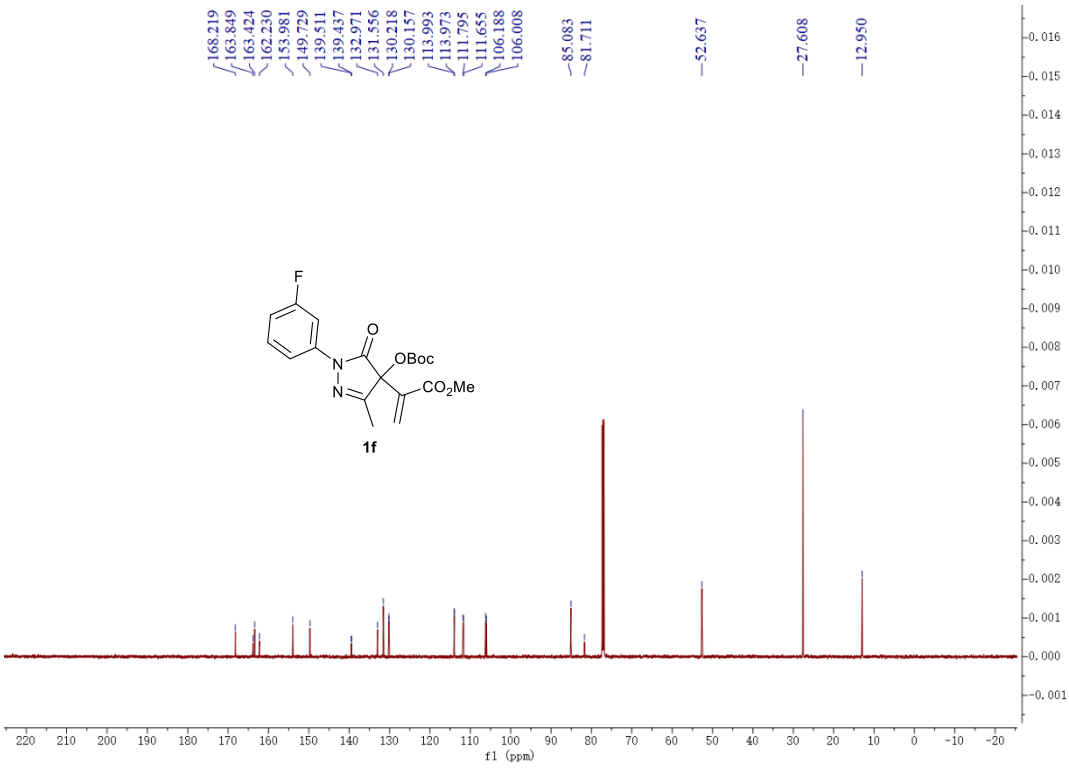
139.122
134.705
132.948
131.570
130.013
125.043
118.705
116.544
85.092
81.651
52.656
27.620
12.960
Cl
O
OBoc
N
N
CO2Me
1e
f1 (ppm)


7.743
7.742
7.740
7.738
7.729
7.728
7.726
7.724
7.705
7.702
7.683
7.351
6.888
6.885
6.884
6.875
6.874
6.871
6.870
6.862
6.860
6.857
6.856
6.697
6.527
3.682
2.035
1.444
F
O
OBoc
N
N
CO2Me
1f
0.92
0.98
1.05
1.00
1.00
1.04
3.00
3.04
9.10
f1 (ppm)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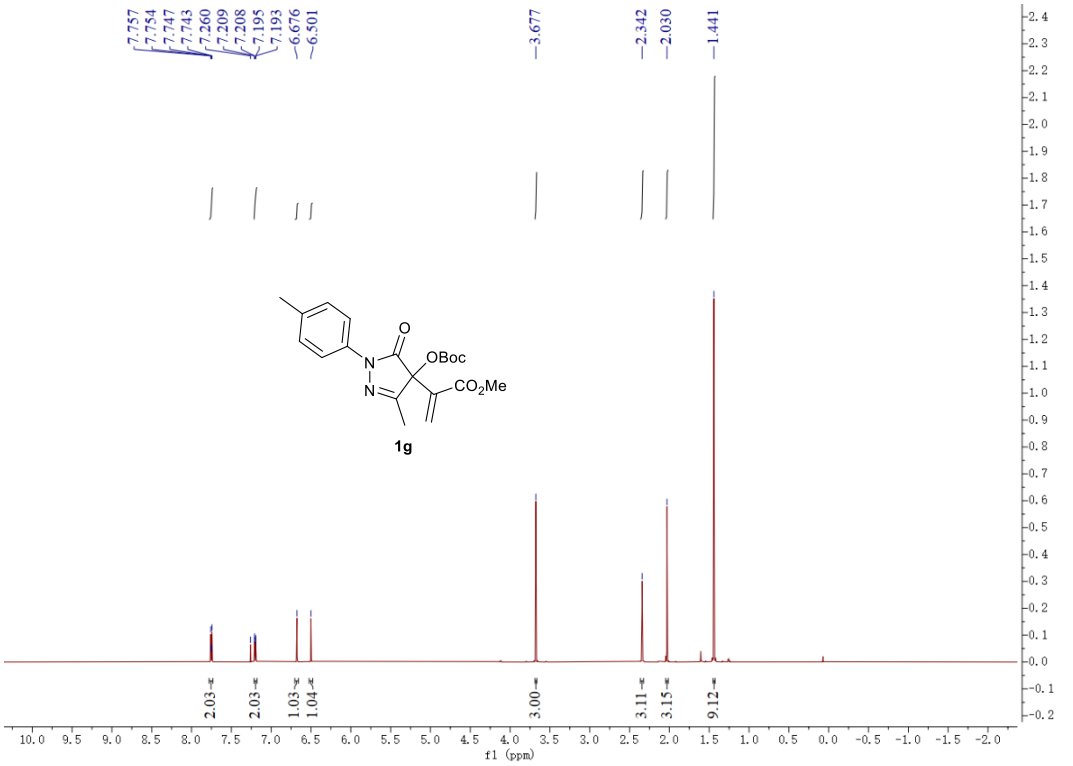
163.849
163.424
162.230
153.981
149.729
139.511
139.437
132.971
131.556
130.218
130.157
113.993
113.973
111.795
111.655
106.188
106.008
85.083
81.711
52.637
27.608
12.950
F
O
OBoc
N
N
CO2Me
1f
f1 (ppm)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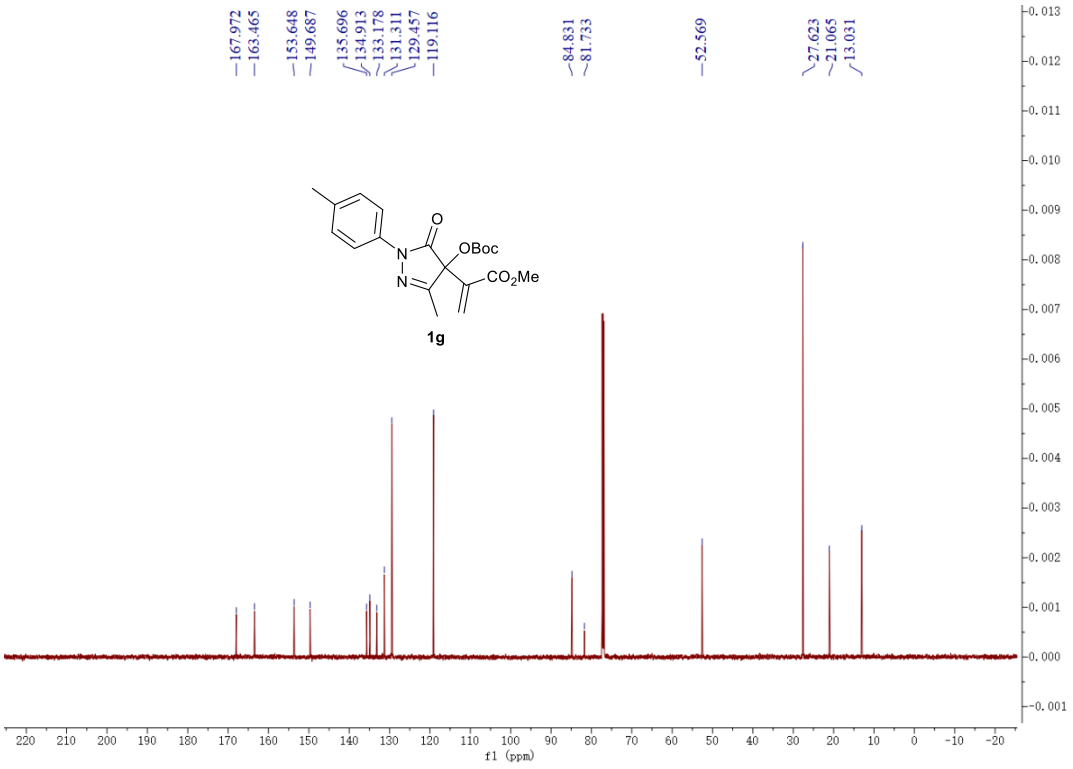
7.754
7.747
7.743
7.260
7.209
7.208
7.195
7.193
6.676
6.501
3.677
2.342
2.030
1.441
OBoc
CO2Me
1g
2.03
2.03
1.03
1.04
3.00
3.11
3.15
9.12
f1 (ppm)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153.648
149.687
135.696
134.913
133.178
131.311
129.457
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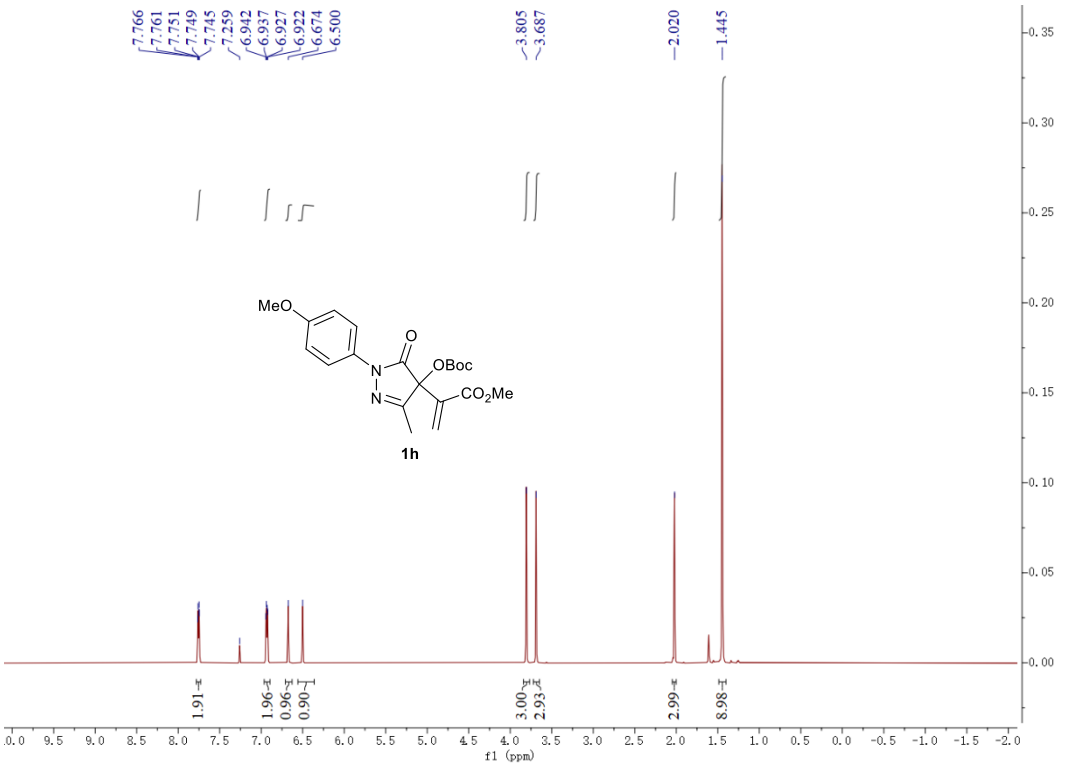
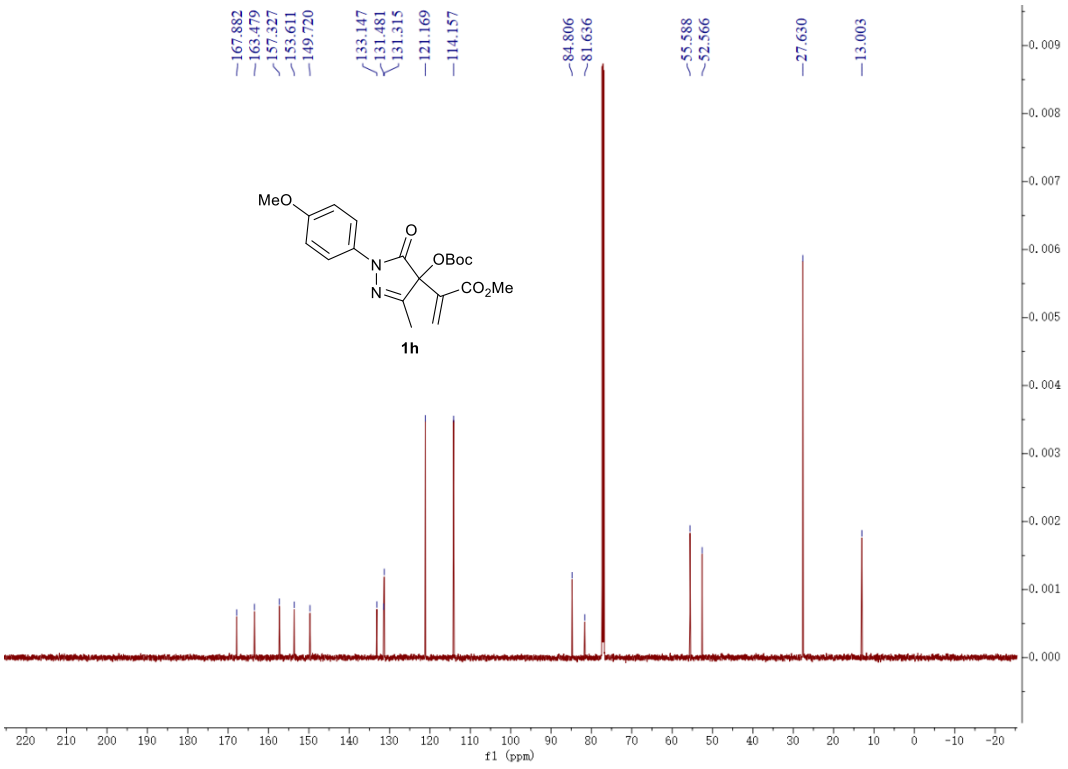
81.733
52.569
27.623
21.065
13.031
OBoc
CO2Me
1g
f1 (ppm)


7.766
7.761
7.751
7.749
7.745
7.259
6.942
6.937
6.927
6.922
6.674
6.500
3.805
3.687
2.020
1.445
MeO
O
N
N
OBoc
CO2Me
1h
1.91
1.96
0.96
0.90
3.00
2.93
2.99
8.98
f1 (ppm)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131.481
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121.169
114.157
84.806
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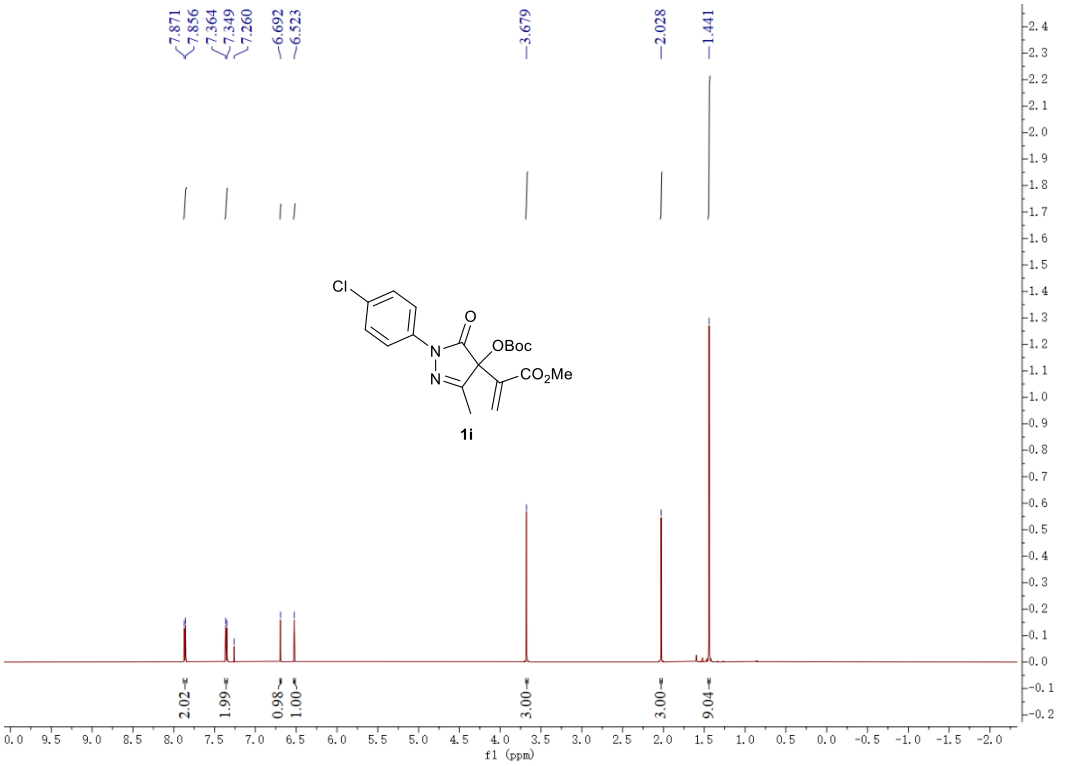
52.566
27.630
13.003
MeO
O
N
N
OBoc
CO2Me
1h
f1 (ppm)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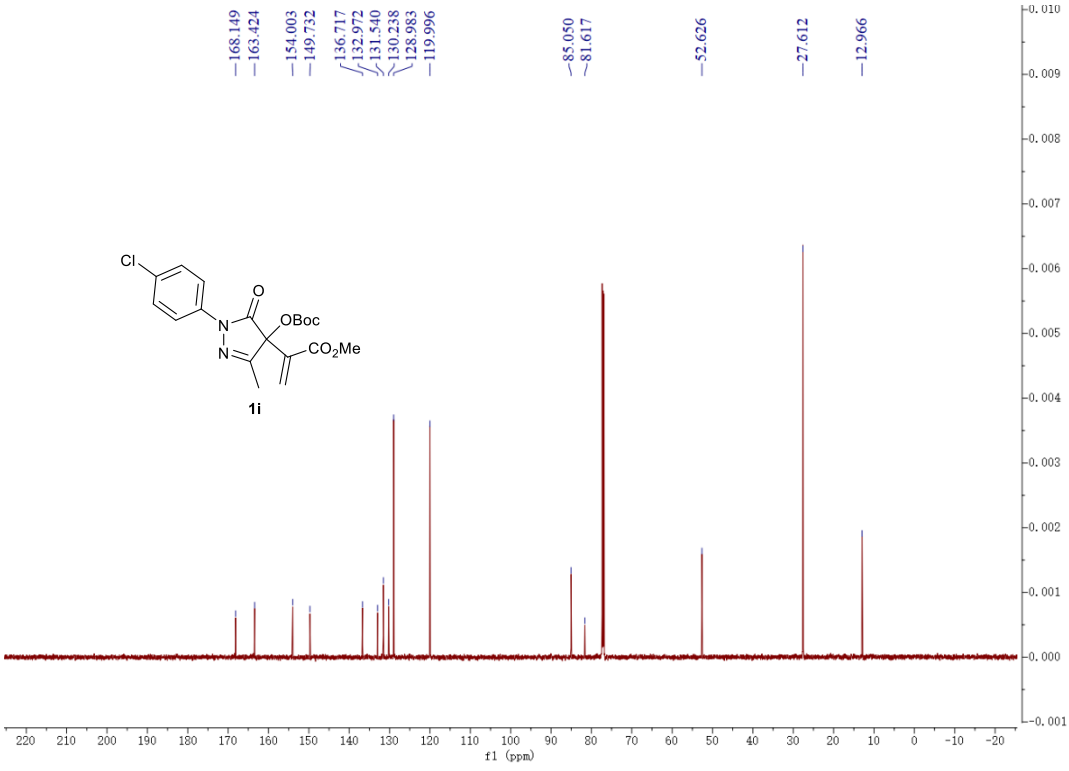
7.856
7.364
7.349
7.260
6.692
6.523
3.679
2.028
1.441
Cl
O
N
N
OBoc
CO2Me
1i
2.02
1.99
0.98
1.00
3.00
3.00
9.04
f1 (ppm)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154.003
149.732
136.717
132.972
131.540
130.238
128.983
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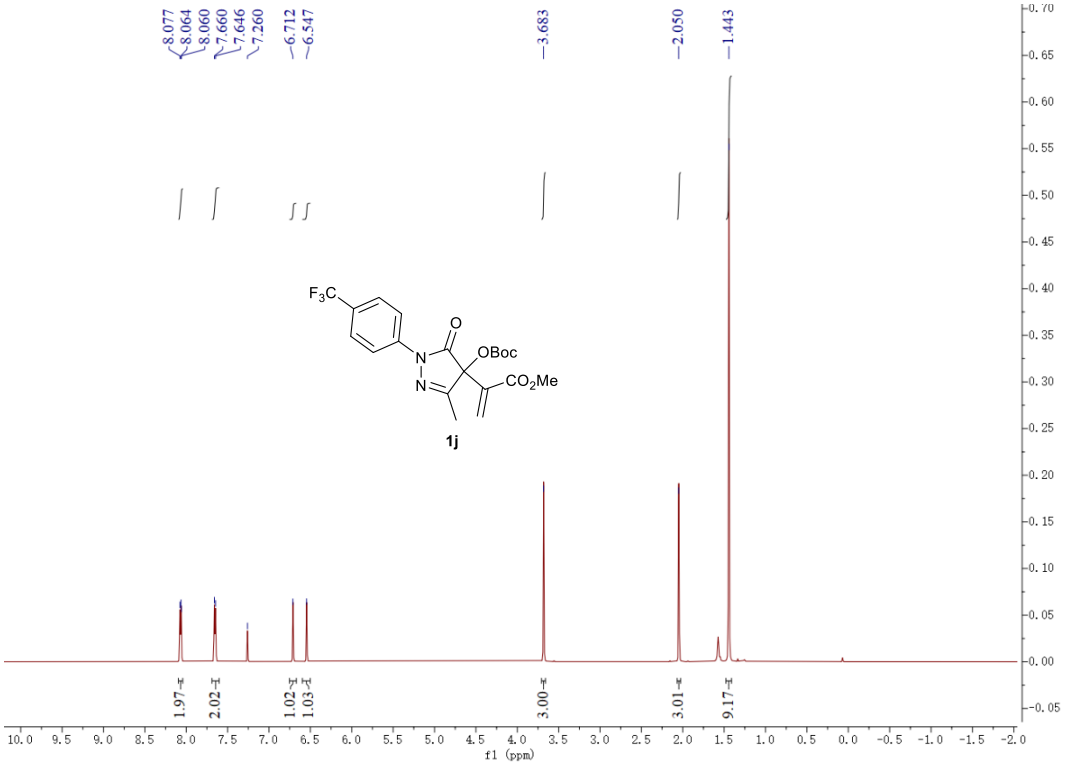
81.617
52.626
27.612
12.966
Cl
O
N
N
OBoc
CO2Me
1i
f1 (ppm)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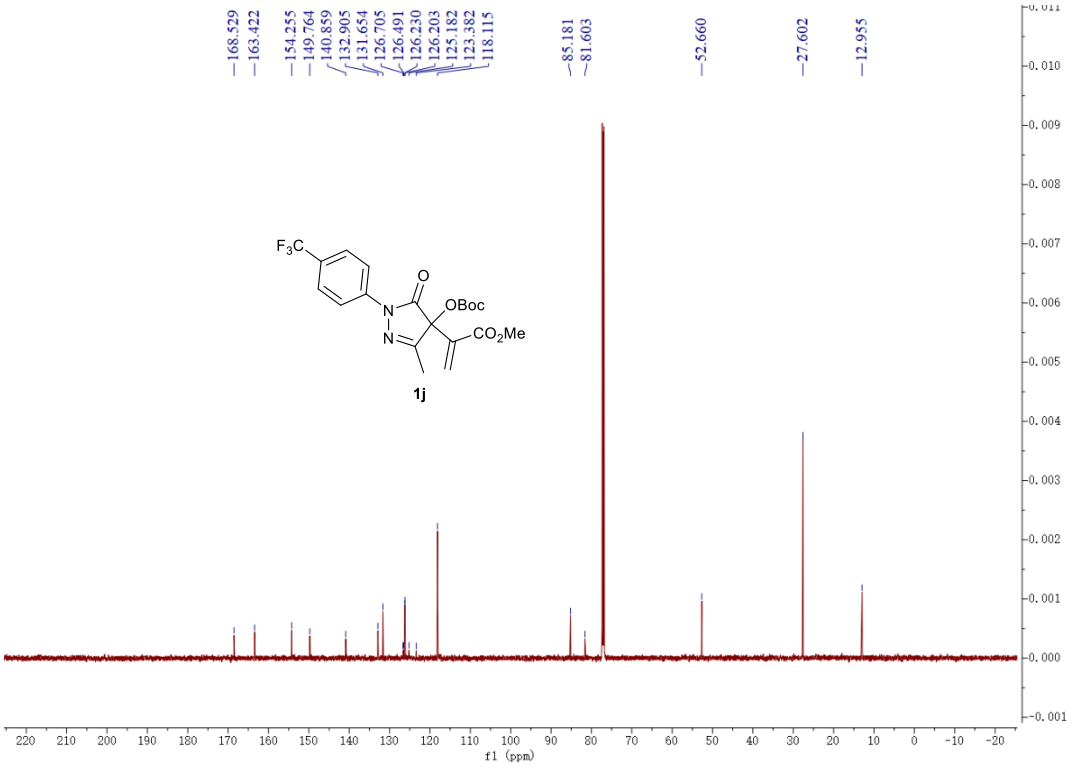
8.064
8.060
7.660
7.646
7.260
6.712
6.547
3.683
2.050
1.443
F3C
O
N
N
OBoc
CO2Me
1j
1.97
2.02
1.02
1.03
3.00
3.01
9.17
f1 (ppm)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126.705
126.491
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125.182
123.382
118.115
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52.660
27.602
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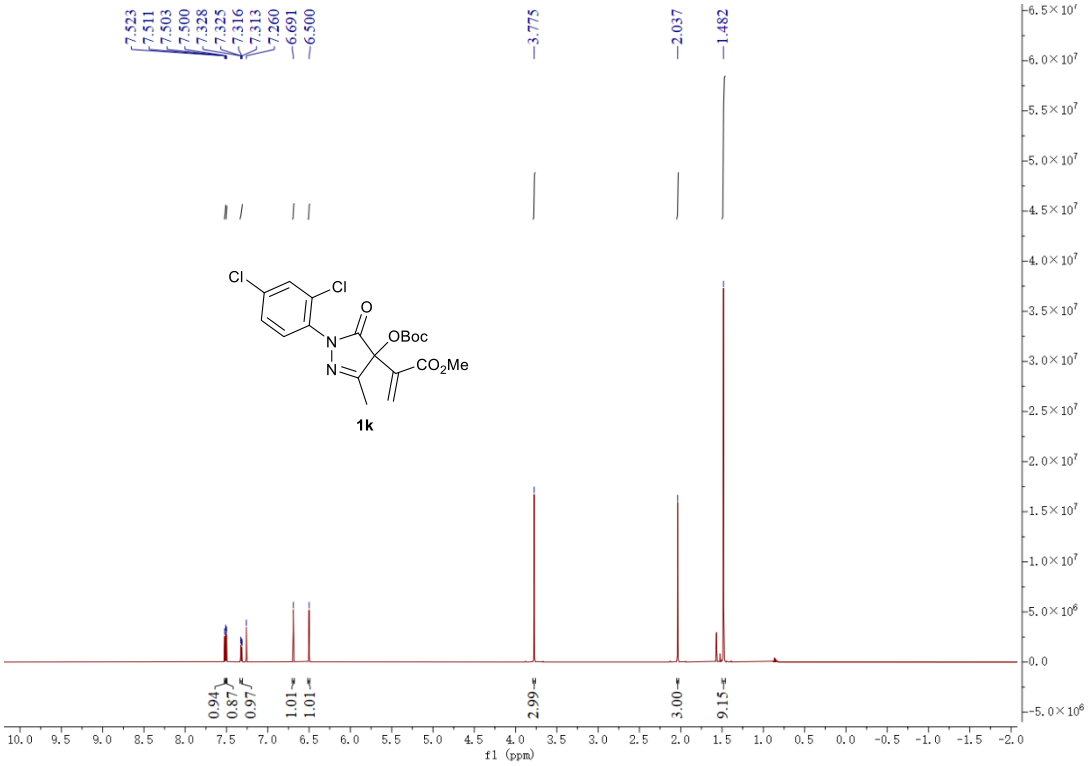
O
N
N
OBoc
CO2Me
1j
f1 (ppm)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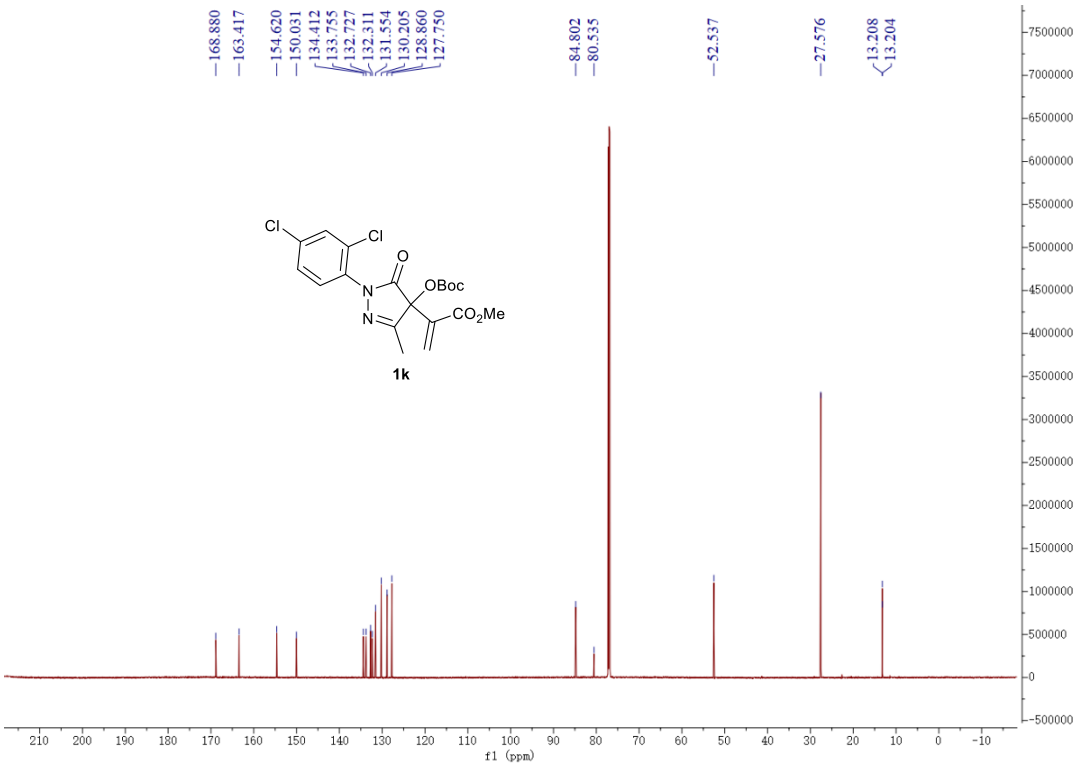
7.500
7.328
7.325
7.316
7.313
7.260
6.691
6.500
3.775
2.037
1.482
Cl
Cl
O
N
N
OBoc
CO2Me
1k
0.94
0.87
0.97
1.01
1.01
2.99
3.00
9.15
f1 (ppm)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128.860
127.750
84.802
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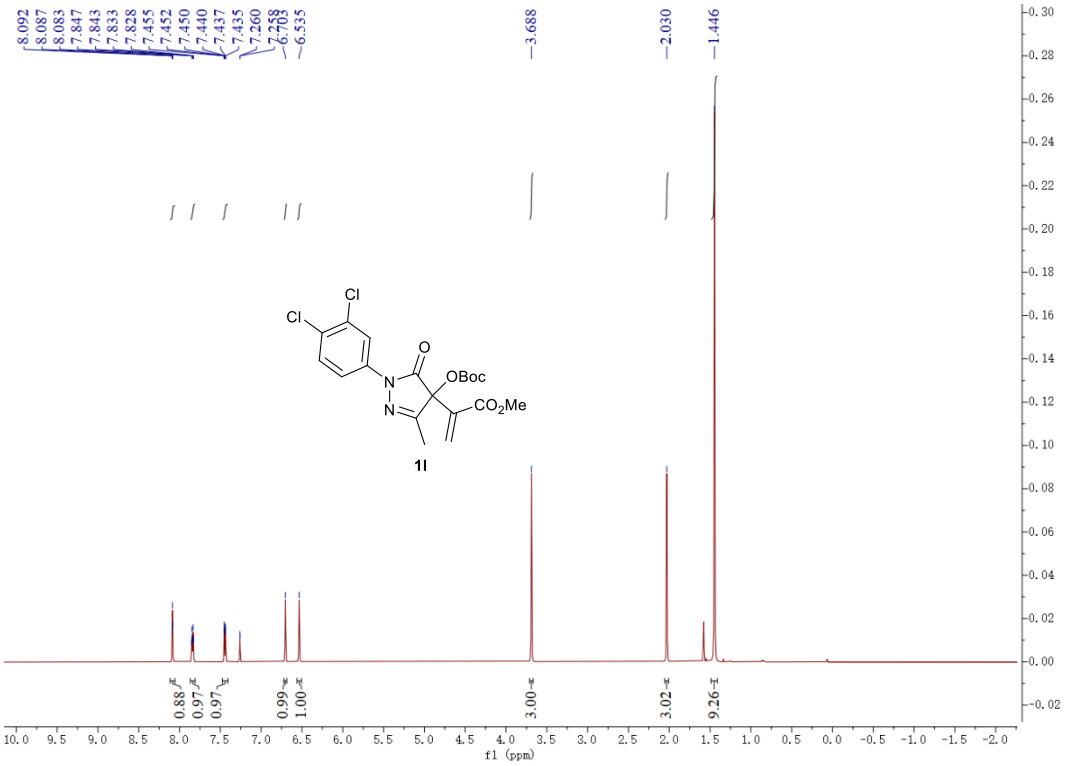
13.208
13.204
Cl
Cl
O
N
N
OBoc
CO2Me
1k
f1 (ppm)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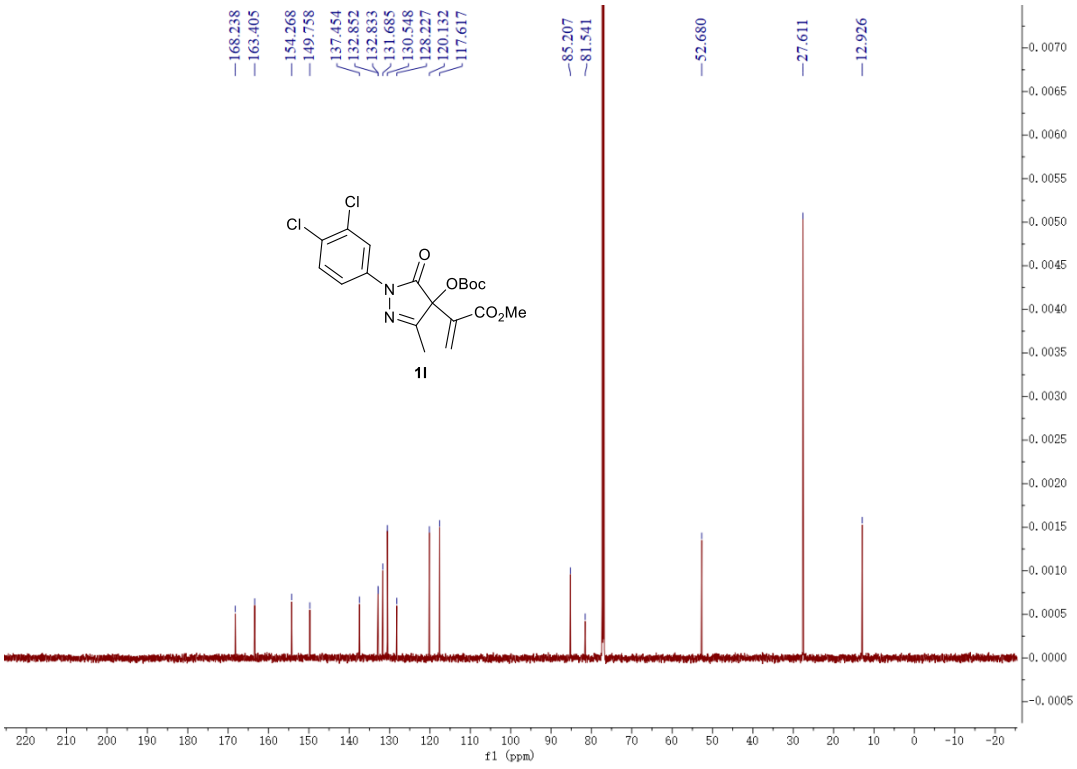
7.833
7.828
7.455
7.452
7.450
7.440
7.437
7.435
7.260
6.703
6.535
3.688
2.030
1.446
Cl
Cl
O
N
N
OBoc
CO2Me
1l
0.88
0.97
0.97
0.99
1.00
3.00
3.02
9.26
f1 (ppm)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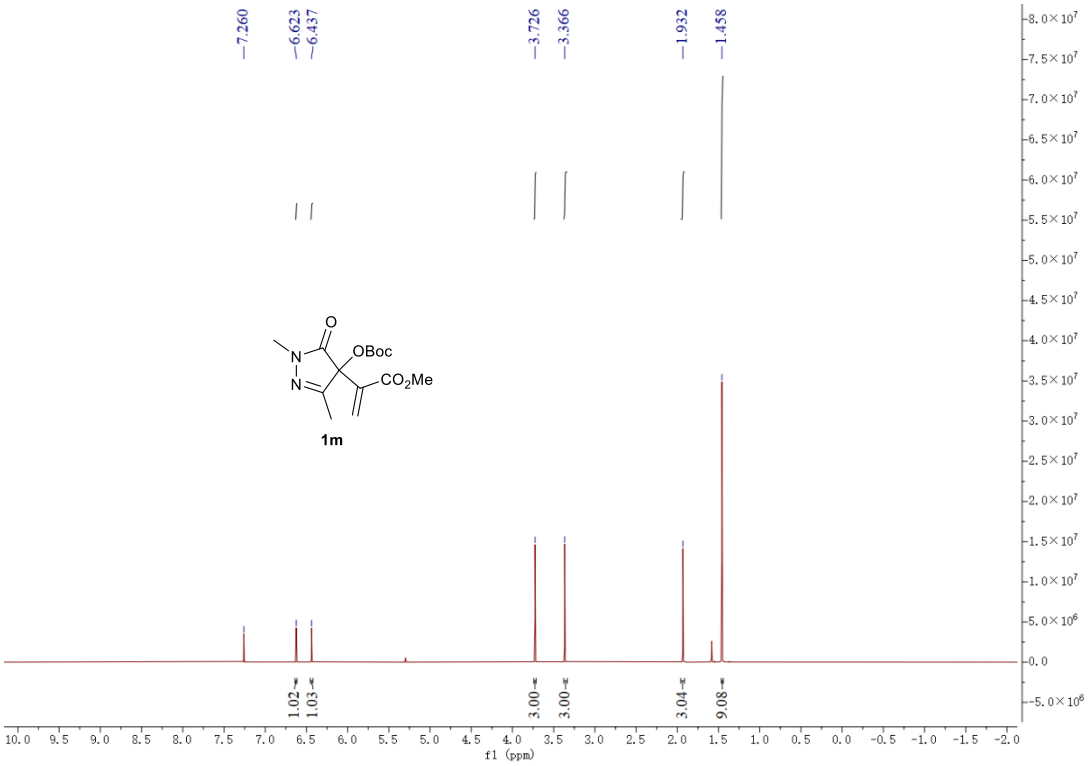
132.852
132.833
131.685
130.548
128.227
120.132
117.617
85.207
81.541
52.680
27.611
12.926
Cl
Cl
O
N
N
OBoc
CO2Me
1l
f1 (ppm)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6.437
3.726
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1.02
1.03
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3.04
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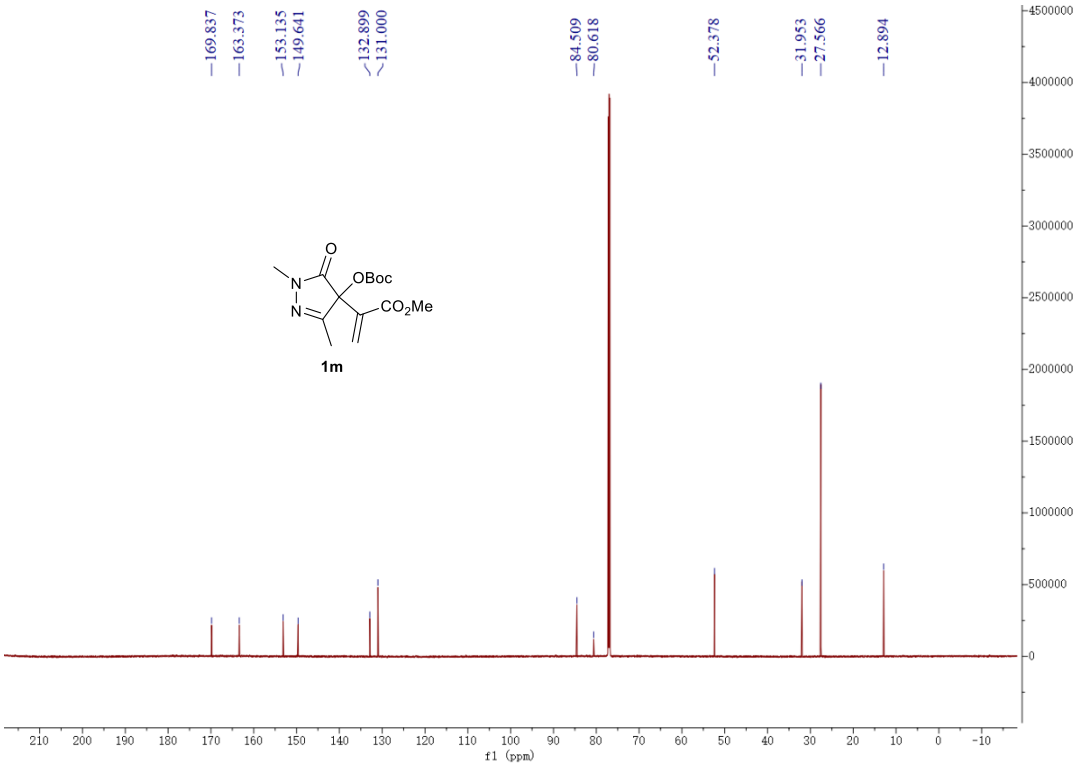
f1 (ppm)
1m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80.618
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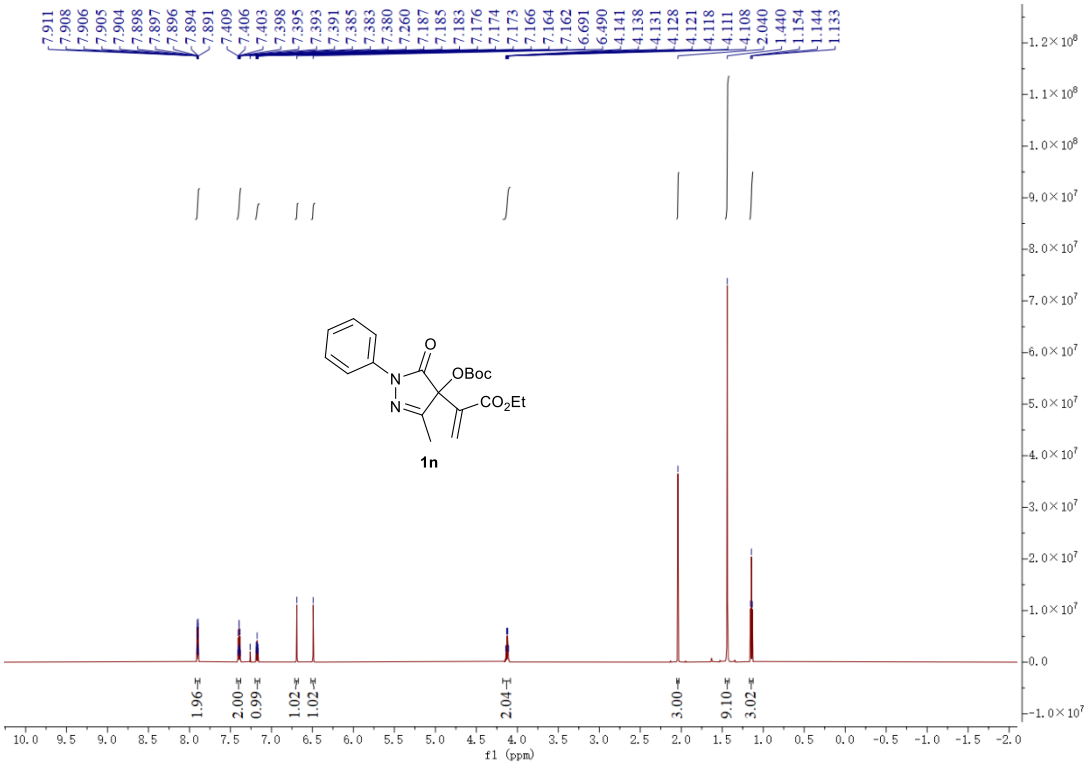
f1 (ppm)
1m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7.904
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7.896
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7.891
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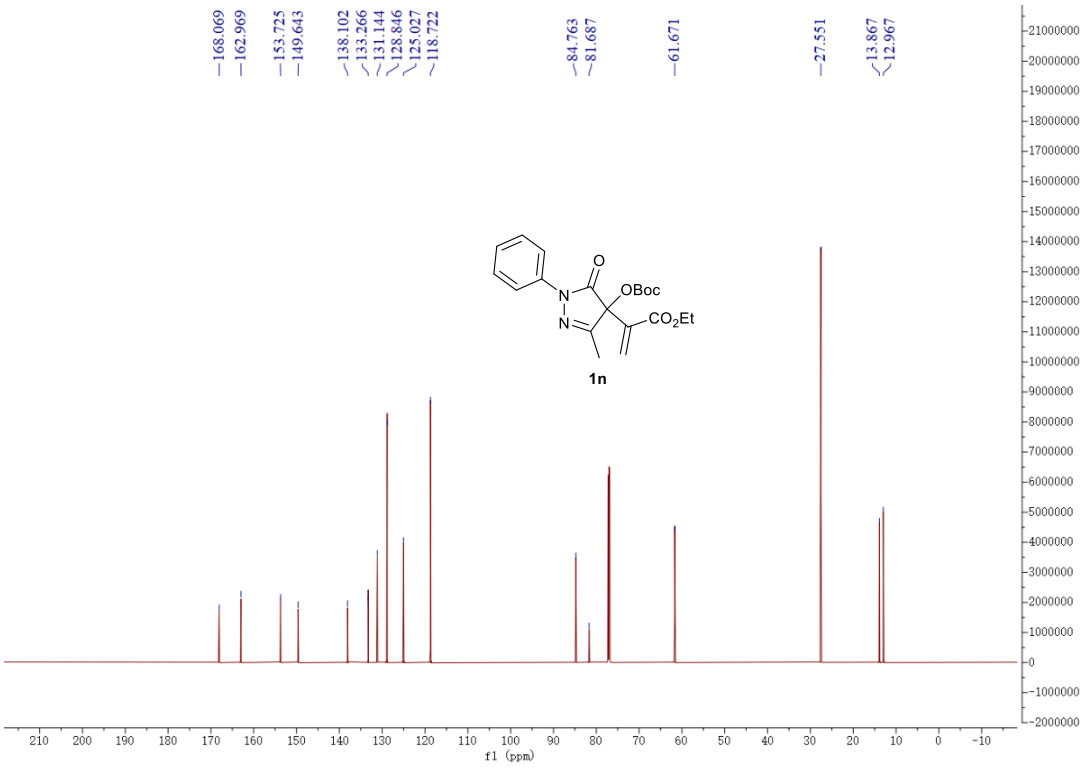
7.406
7.403
7.398
7.395
7.393
7.391
7.385
7.383
7.380
7.260
7.187
7.185
7.183
7.176
7.174
7.173
7.166
7.164
7.162
6.691
6.490
4.141
4.138
4.131
4.128
4.121
4.118
4.111
4.108
2.040
1.440
1.154
1.144
1.133
O
N
N
OBoc
CO2Et
1n
1.96
2.00
0.99
1.02
1.02
2.04
3.00
9.10
3.02
f1 (ppm)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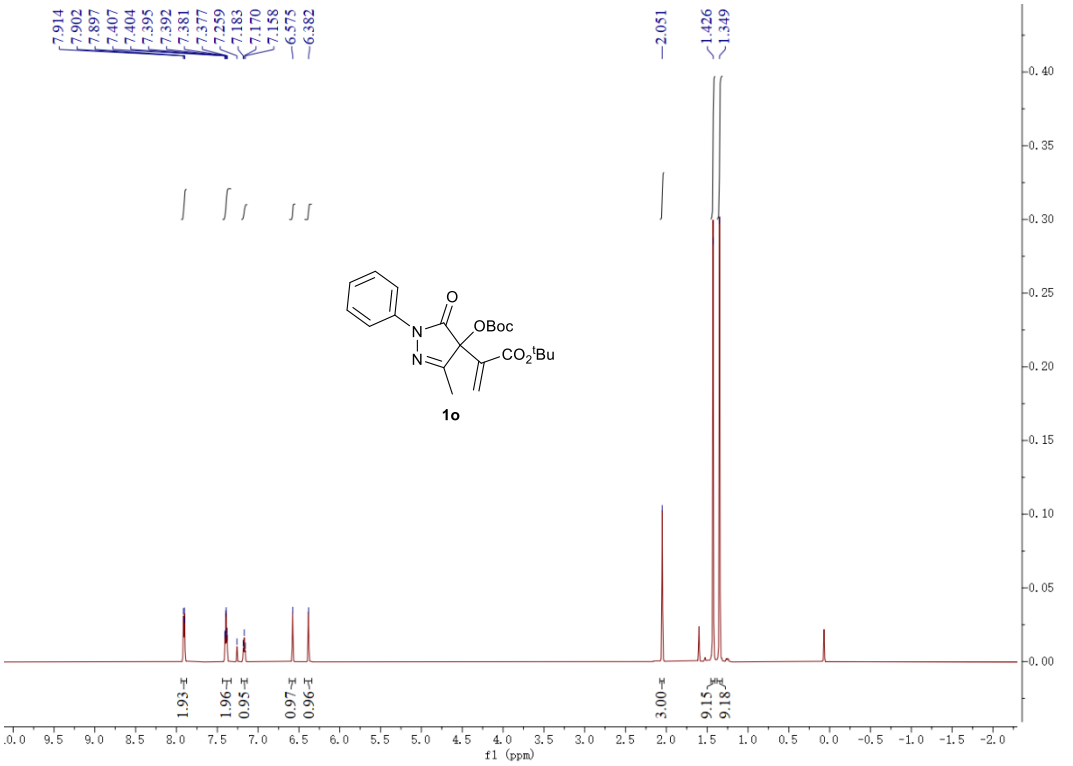
27.551
13.867
12.967
O
N
N
OBoc
CO2Et
1n
f1 (ppm)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7.381
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7.259
7.183
7.170
7.158
6.575
6.382
2.051
1.426
1.349
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1.96
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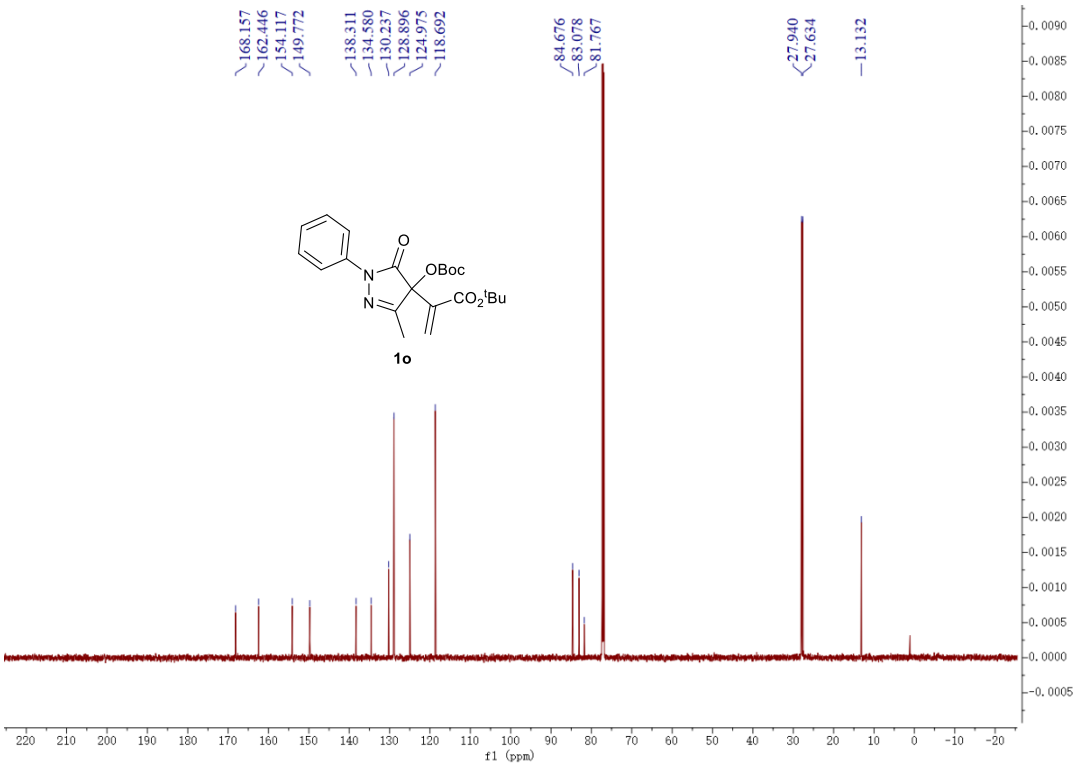
0.97
0.96
3.00
9.15
9.18
f1 (ppm)
OBoc
CO2tBu
1o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134.580
130.237
128.896
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83.078
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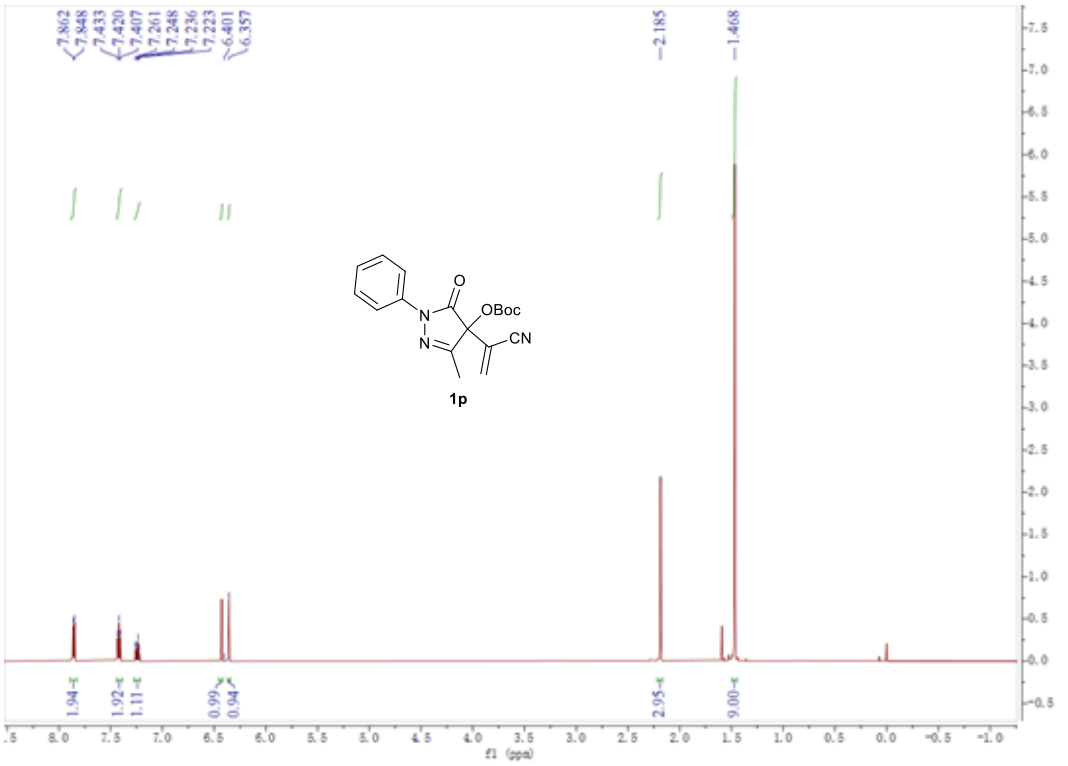
27.940
27.634
13.132
f1 (ppm)
OBoc
CO2tBu
1o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7.248
7.236
7.223
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6.357
2.185
1.468
1.94
1.92
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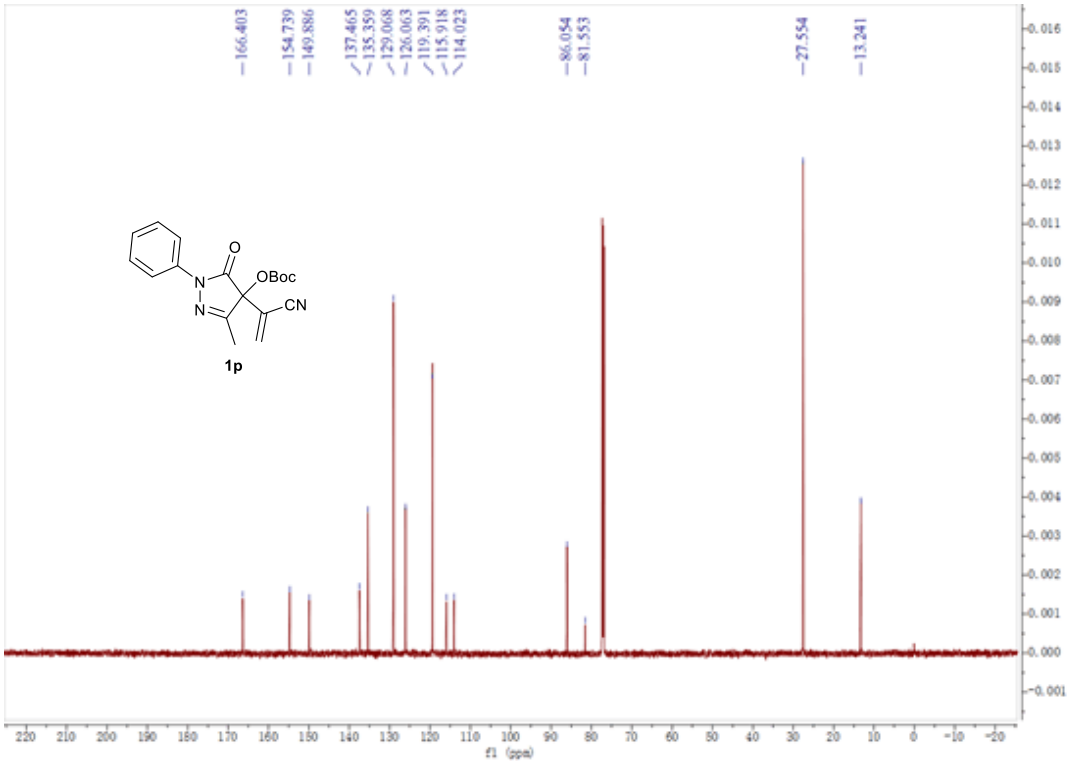
0.94
2.95
9.00
O
OBoc
N
N
CN
1p
f1 (ppm)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129.068
126.063
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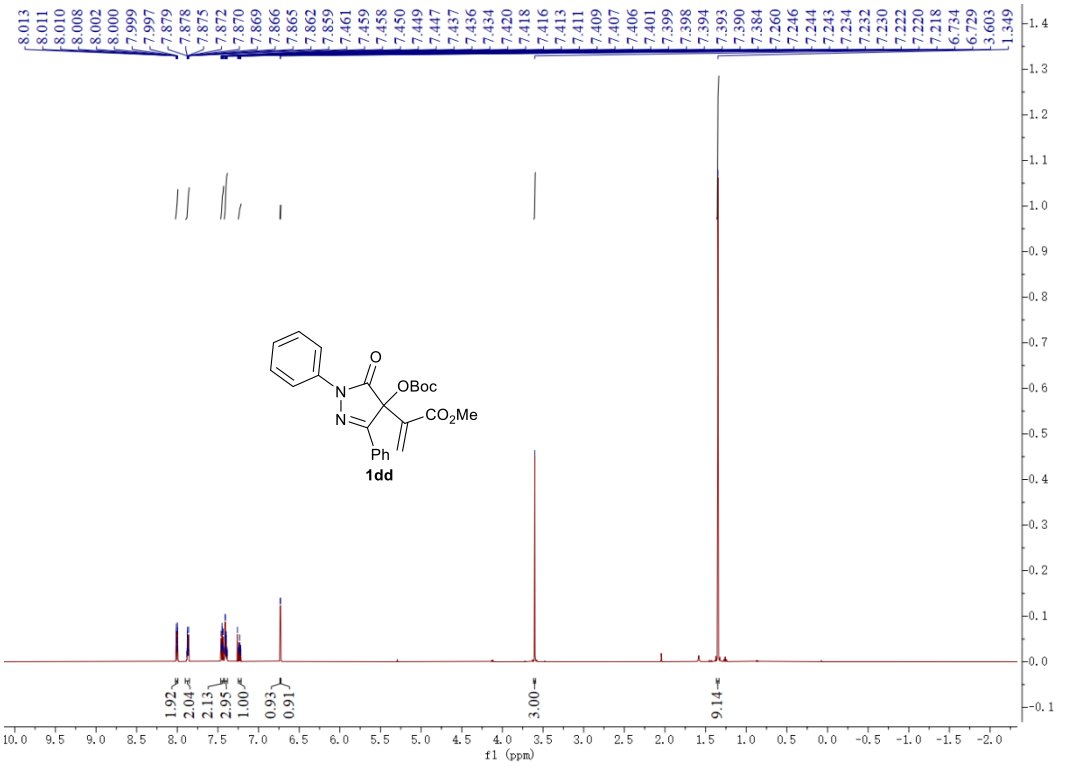
O
OBoc
N
N
CN
1p
f1 (ppm)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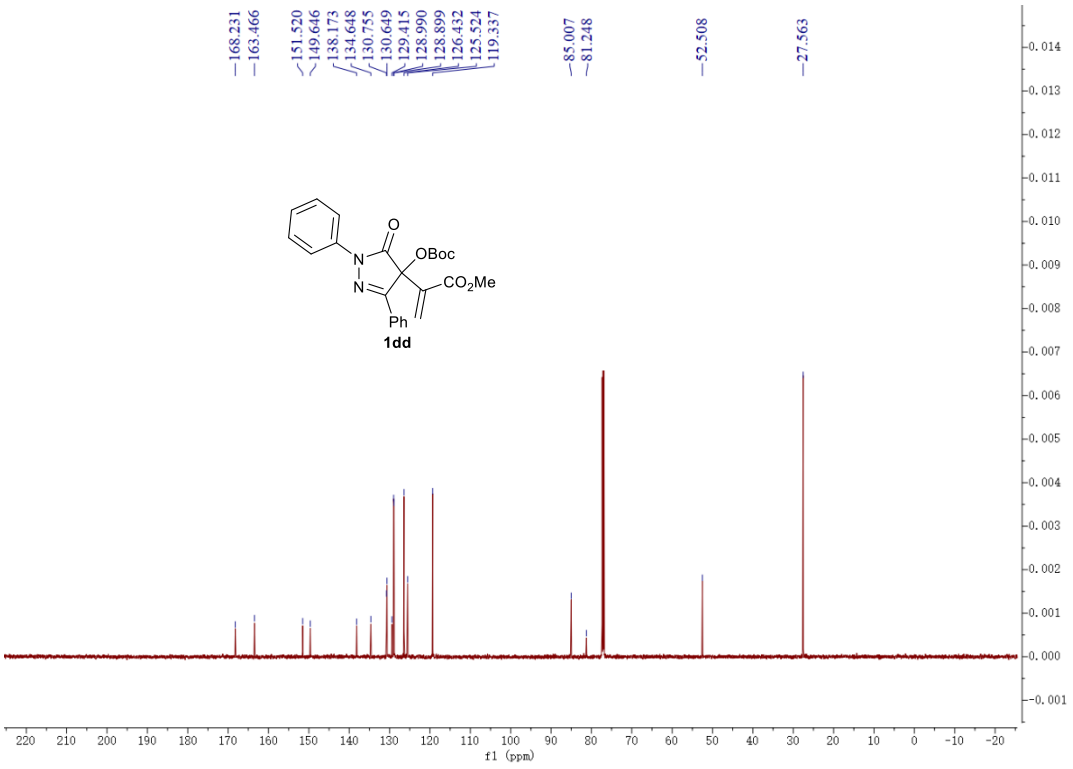
8.000
7.999
7.997
7.879
7.878
7.875
7.872
7.870
7.869
7.866
7.865
7.862
7.859
7.461
7.459
7.458
7.450
7.449
7.447
7.437
7.436
7.434
7.420
7.418
7.416
7.413
7.411
7.409
7.407
7.406
7.401
7.399
7.398
7.394
7.393
7.390
7.384
7.260
7.246
7.244
7.243
7.234
7.232
7.230
7.222
7.220
7.218
6.734
6.729
3.603
1.349
1.92
2.04
2.13
2.95
1.00
0.93
0.91
3.00
9.14
f1 (ppm)
O
OBoc
N
N
CO2Me
Ph
1dd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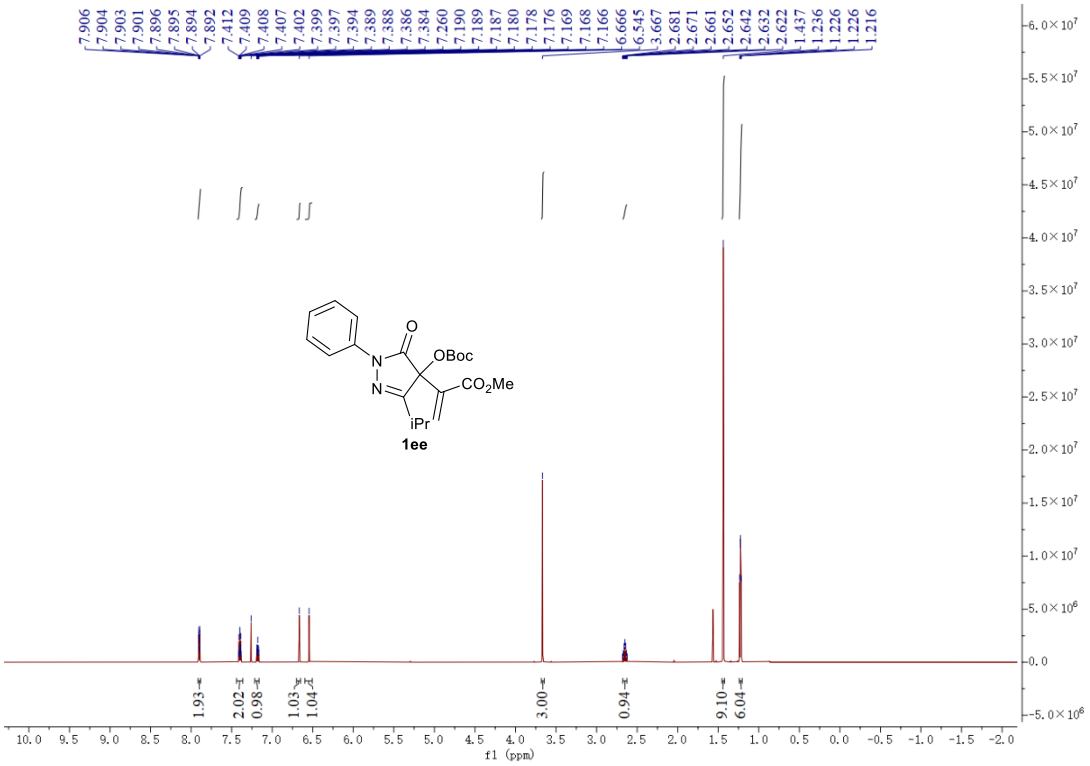
134.648
130.755
130.649
129.415
128.990
128.899
126.432
125.524
119.337
85.007
81.248
52.508
27.563
f1 (ppm)
O
OBoc
N
N
CO2Me
Ph
1dd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7.903
7.901
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7.895
7.894
7.892
7.412
7.409
7.408
7.407
7.402
7.399
7.397
7.394
7.389
7.388
7.386
7.384
7.260
7.190
7.189
7.187
7.180
7.178
7.176
7.169
7.168
7.166
6.666
6.545
3.667
2.681
2.671
2.661
2.652
2.642
2.632
2.622
1.437
1.236
1.226
1.226
1.216
O
OBoc
N
N
CO2Me
iPr
1ee
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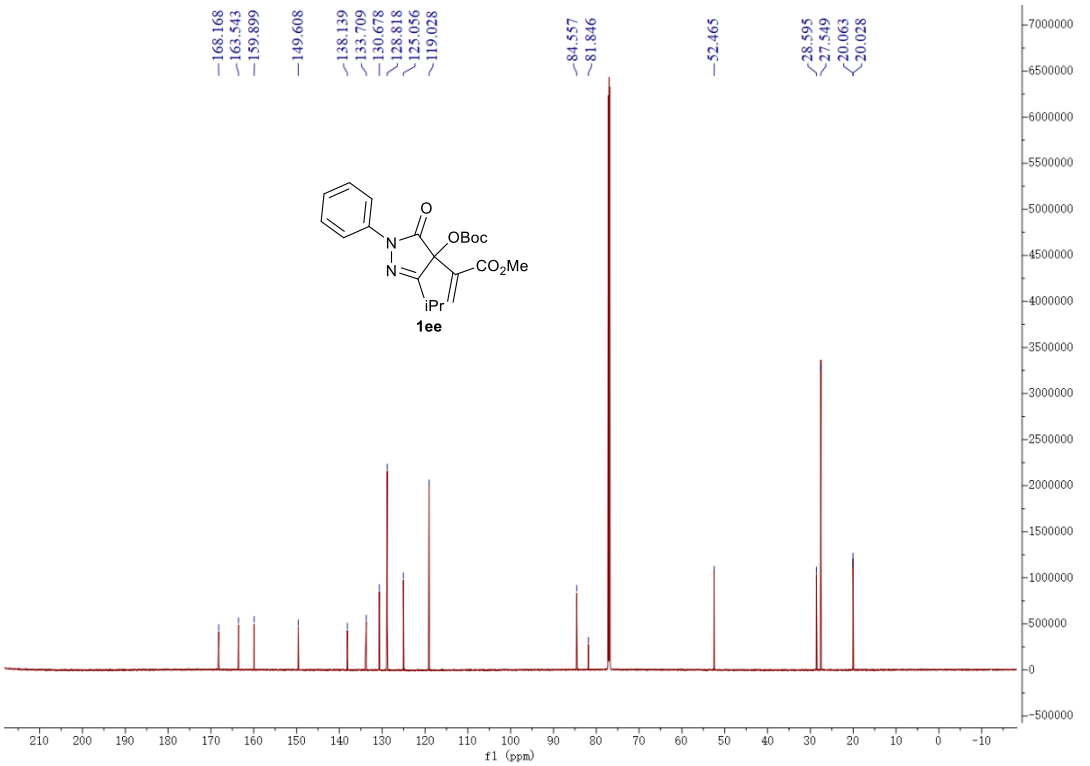
2.02
0.98
1.03
1.04
3.00
0.94
9.10
6.04
f1 (ppm)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159.899
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138.139
133.709
130.678
128.818
125.056
119.028
84.557
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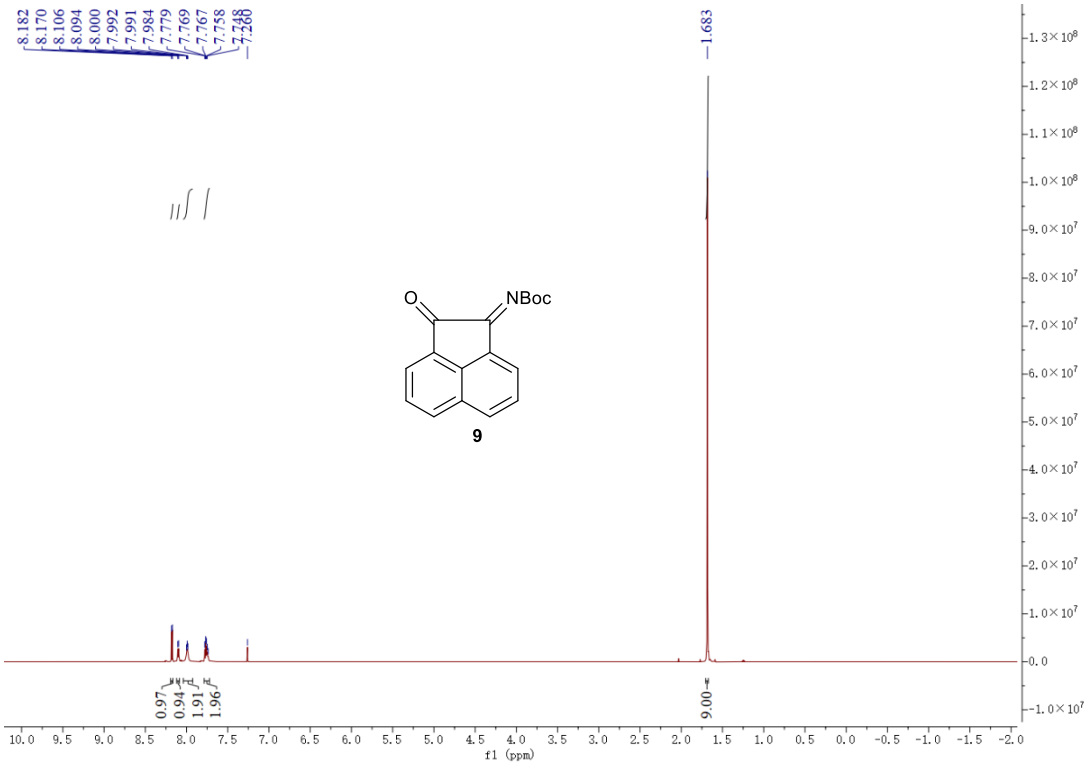
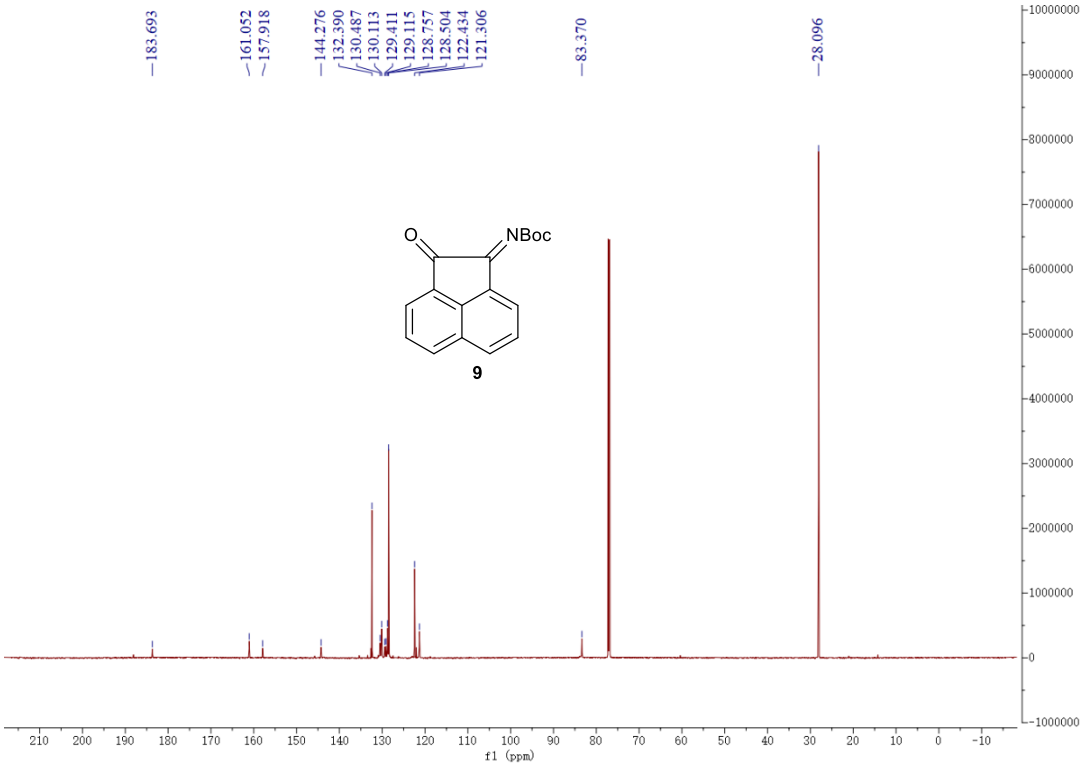
52.465
28.595
27.549
20.063
20.028
O
OBoc
N
N
CO2Me
iPr
1ee
f1 (ppm)


8.182
8.170
8.106
8.094
8.000
7.992
7.991
7.984
7.779
7.769
7.767
7.758
7.748
7.260
1.683
0.97
0.94
1.91
1.96
9.00
O
NBoc
9
f1 (ppm)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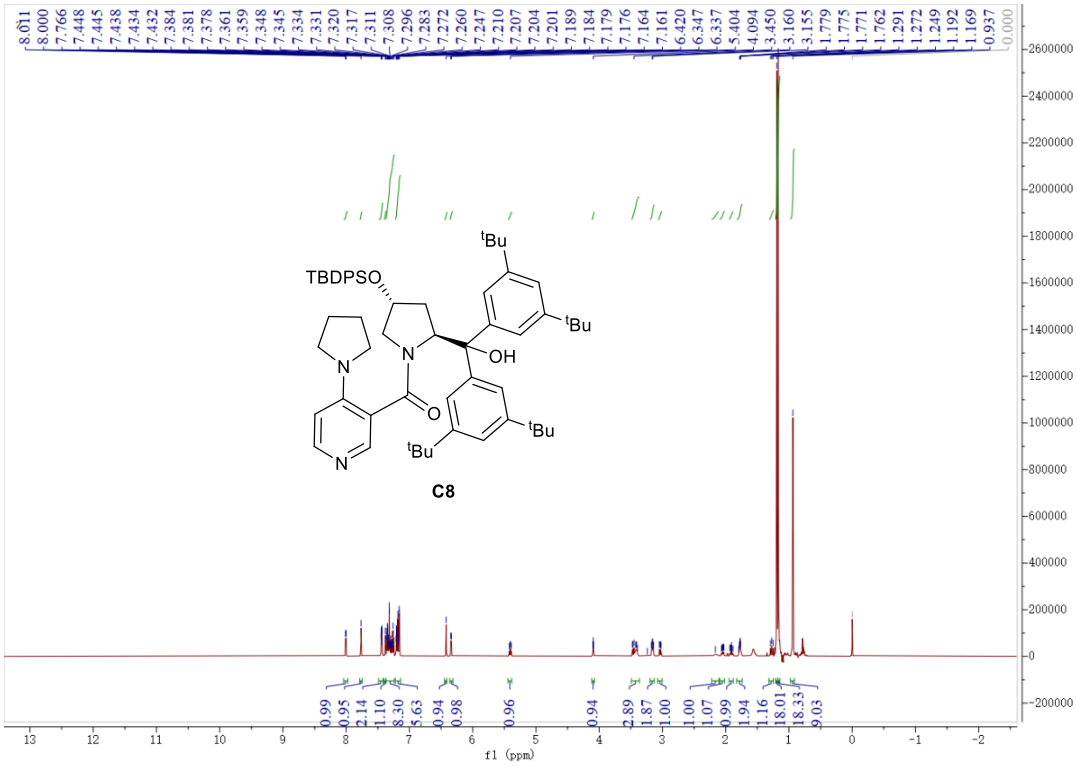
132.390
130.487
130.113
129.411
129.115
128.757
128.504
122.434
121.306
83.370
28.096
O
NBoc
9
f1 (ppm)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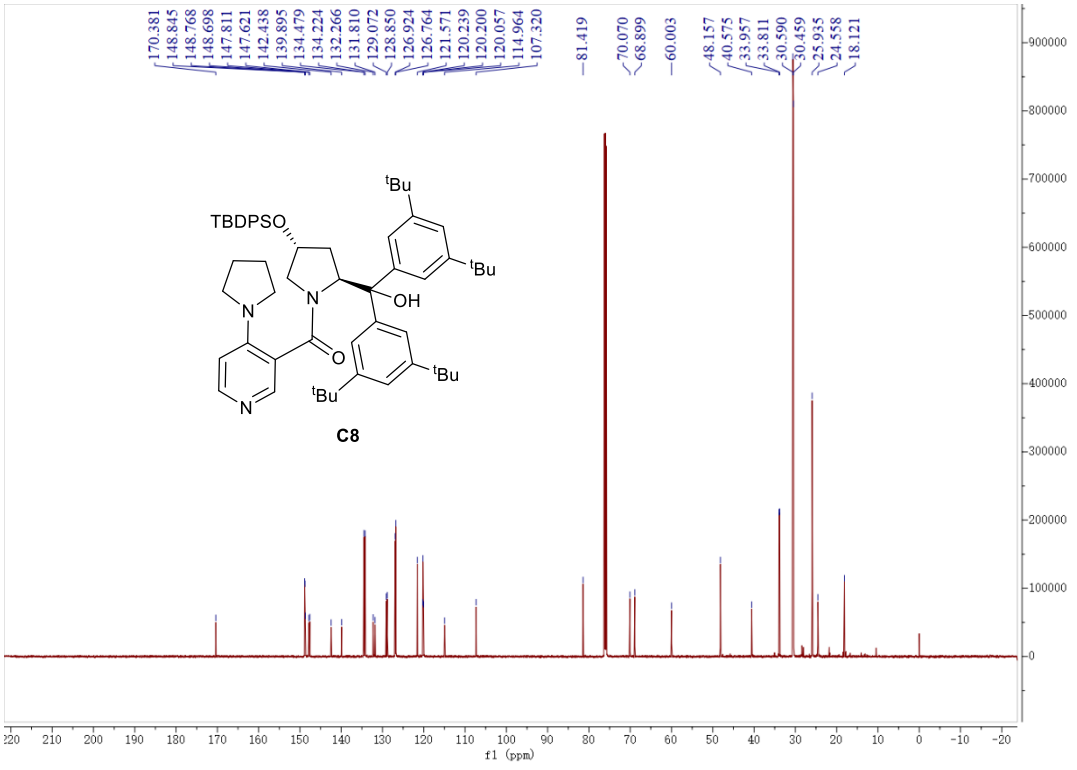
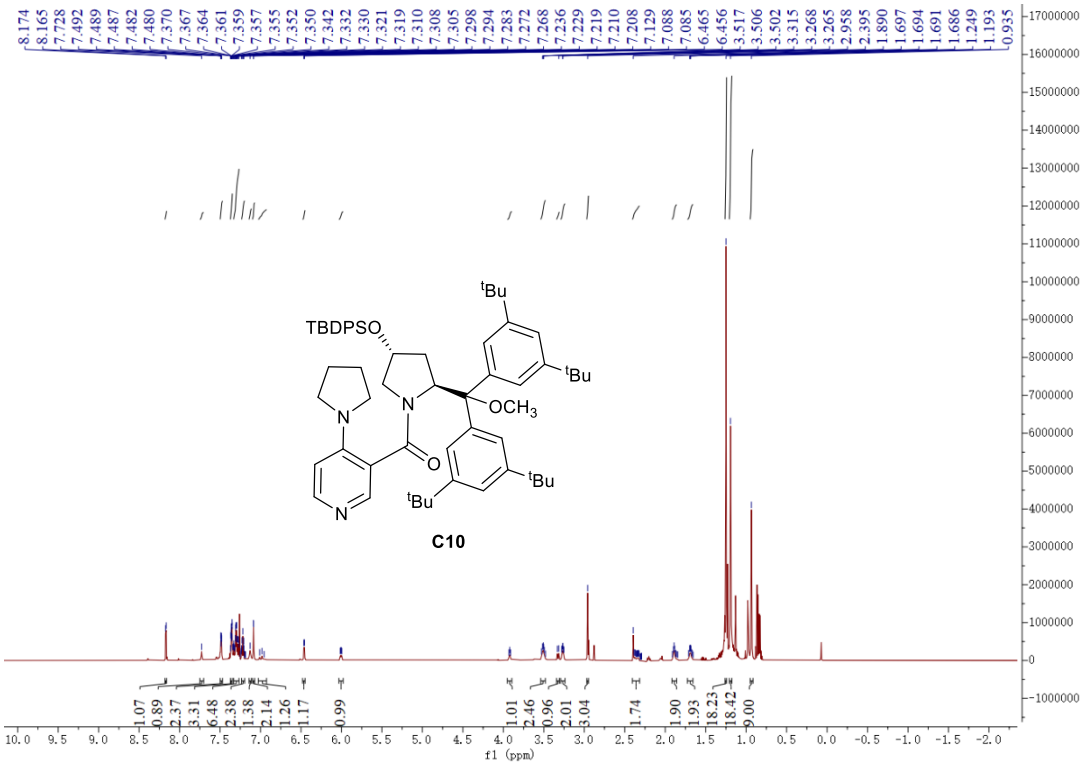
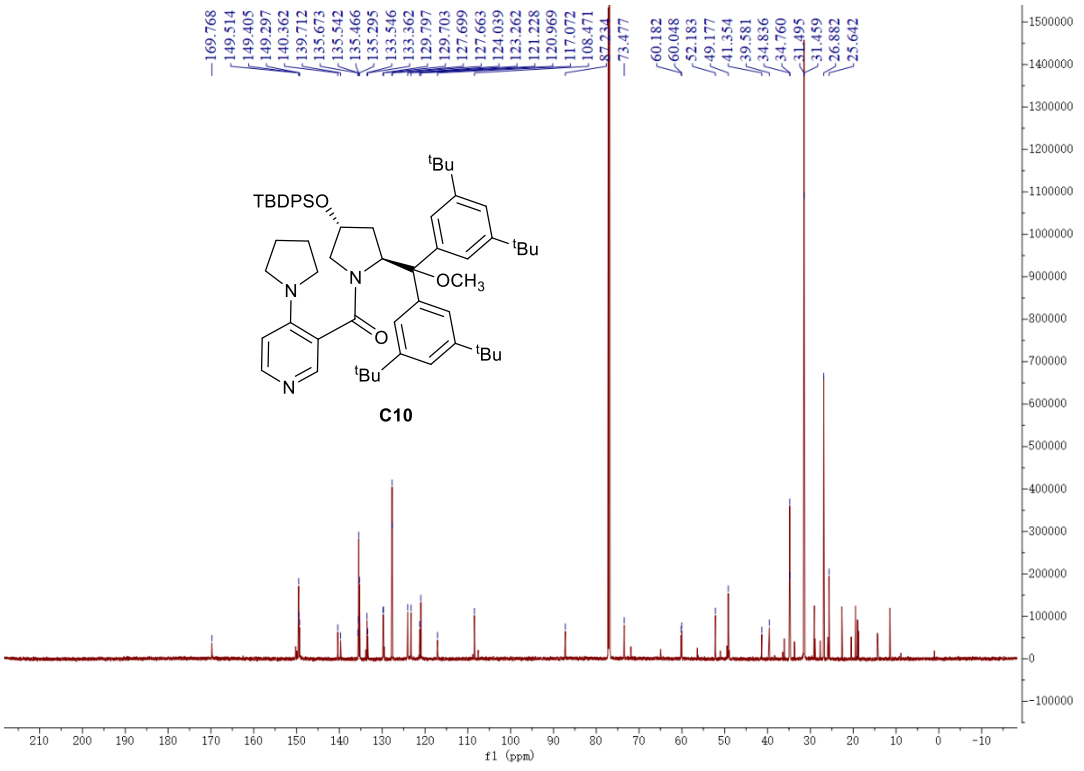
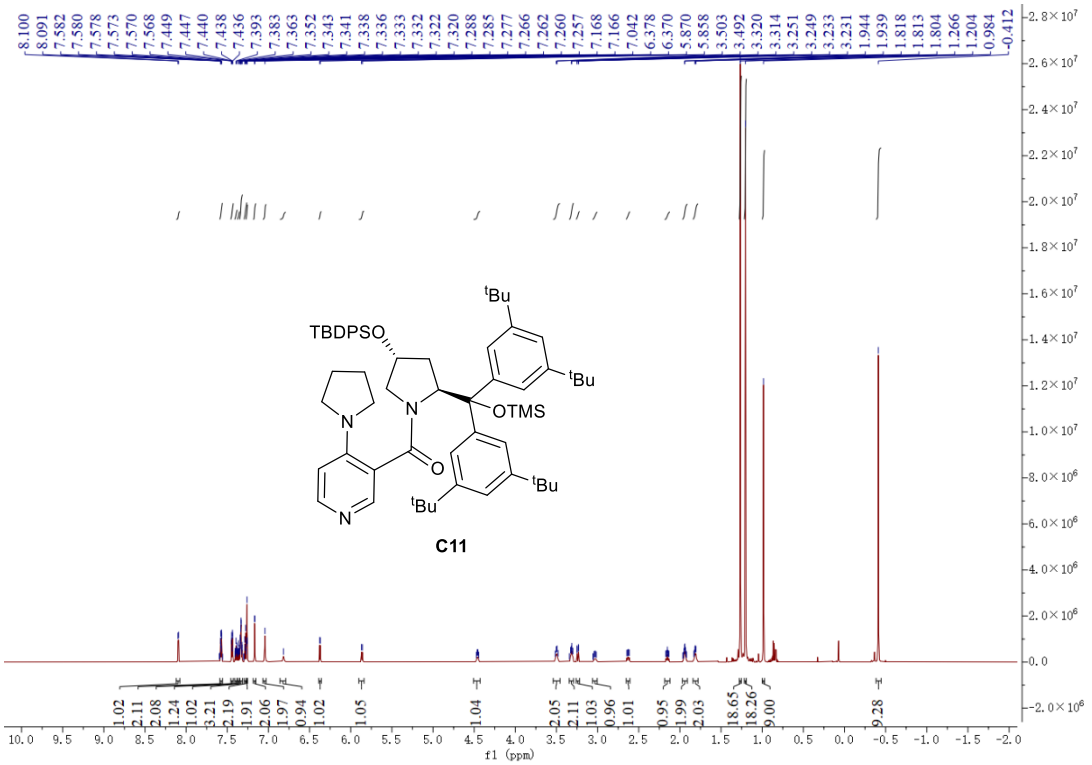
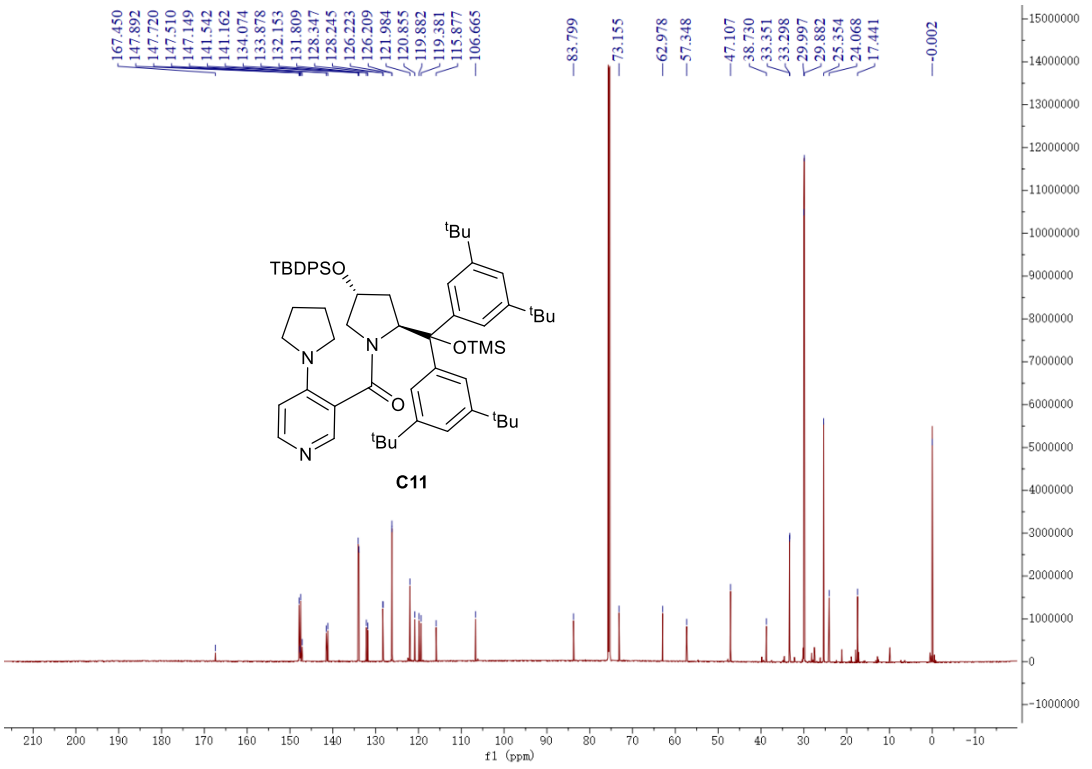
tBu
tBu
OH
N
O
N
tBu
tBu
C8
f1 (ppm)


TBDPSO
tBu
tBu
OH
N
O
N
tBu
tBu
C8
f1 (ppm)

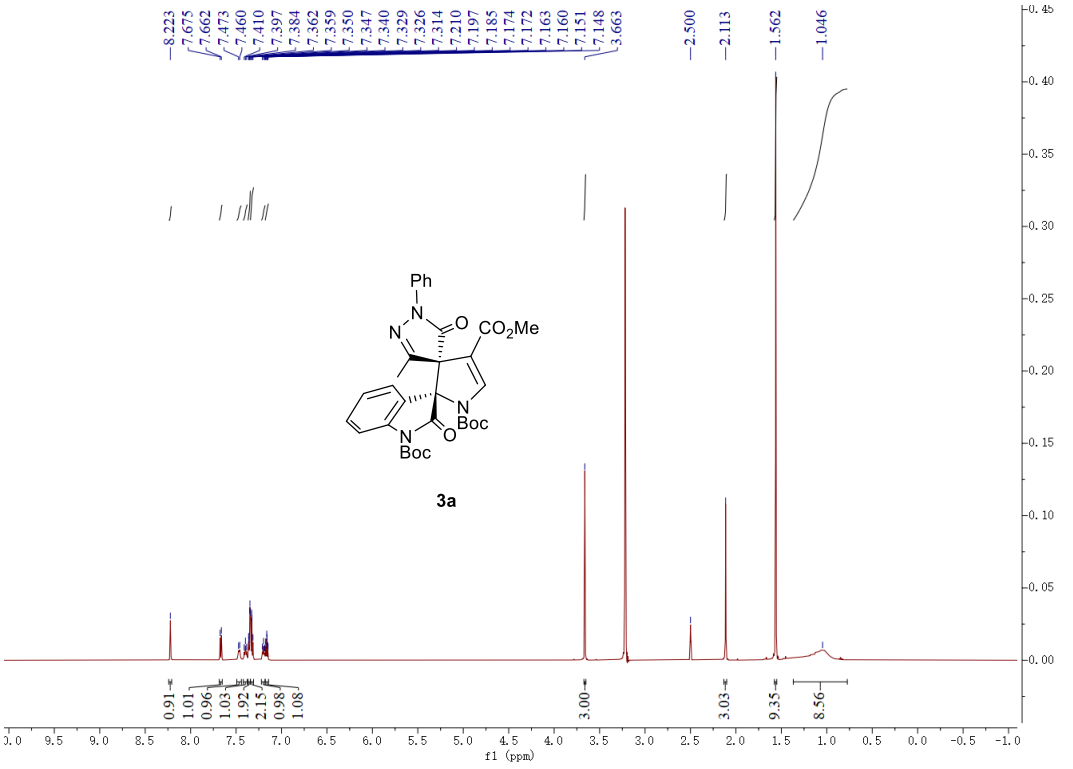

TBDPSO
tBu
tBu
OCH3
tBu
tBu
tBu
N
N
N
O
C10
f1 (ppm)

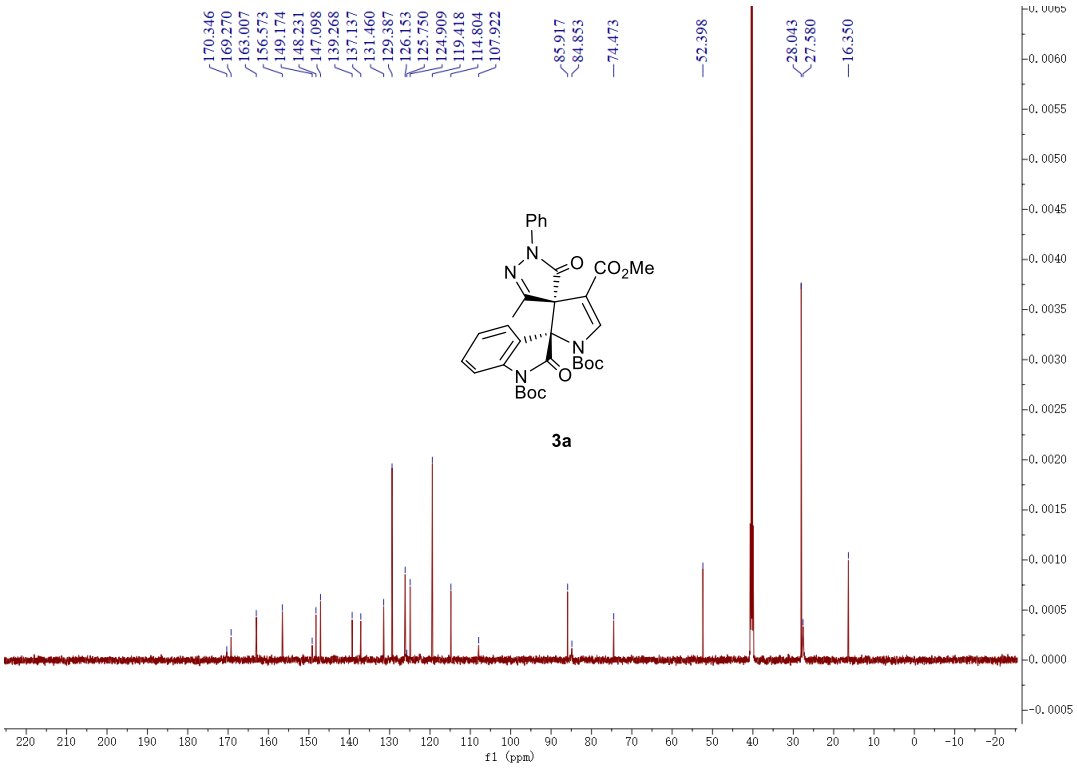

TBDPSO
tBu
tBu
OCH3
tBu
tBu
tBu
N
N
N
O
C10
f1 (ppm)

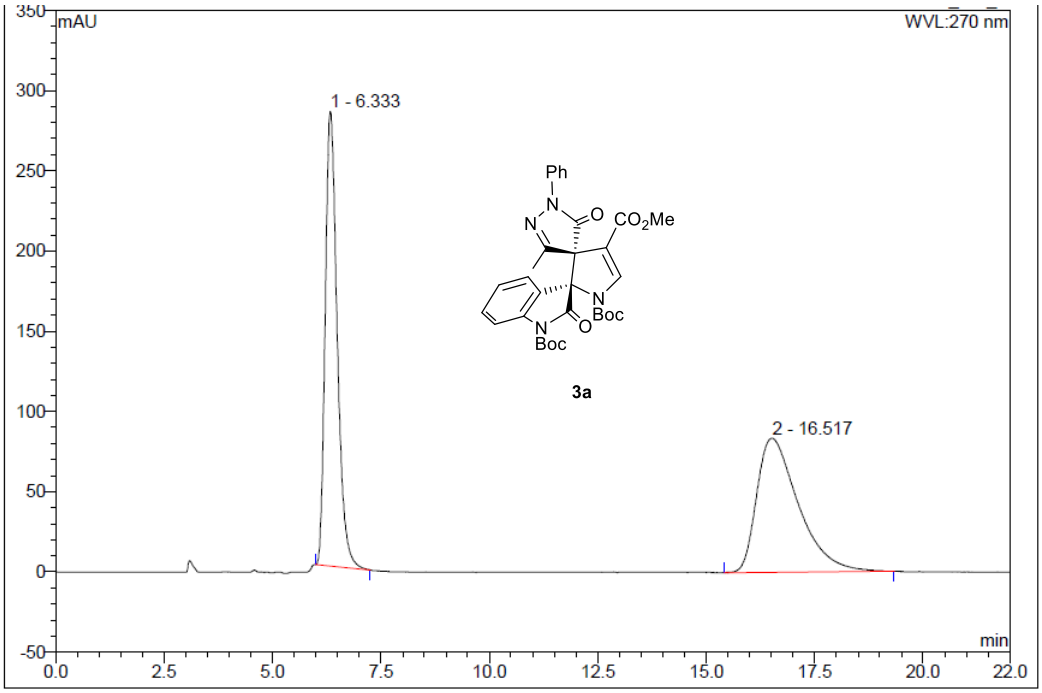

TBDPSO
OTMS
tBu
tBu
tBu
tBu
N
N
O
N
C11
f1 (ppm)


TBDPSO
OTMS
tBu
tBu
tBu
tBu
N
N
O
N
C11
f1 (ppm)

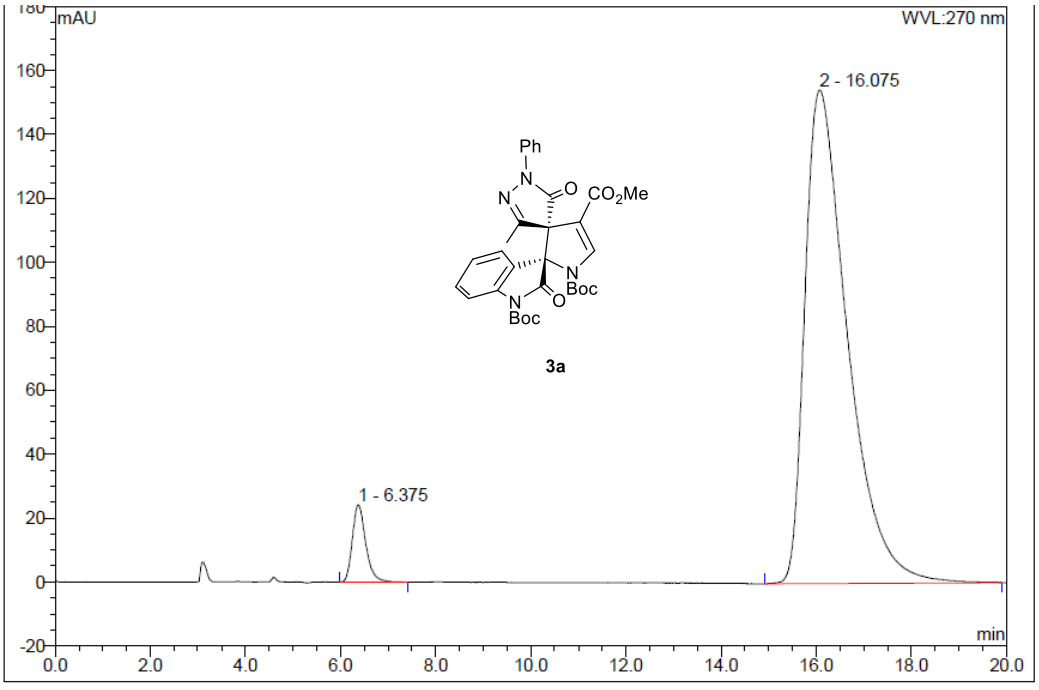
9.2 NMR spectra and HPLC chromatograms of 3



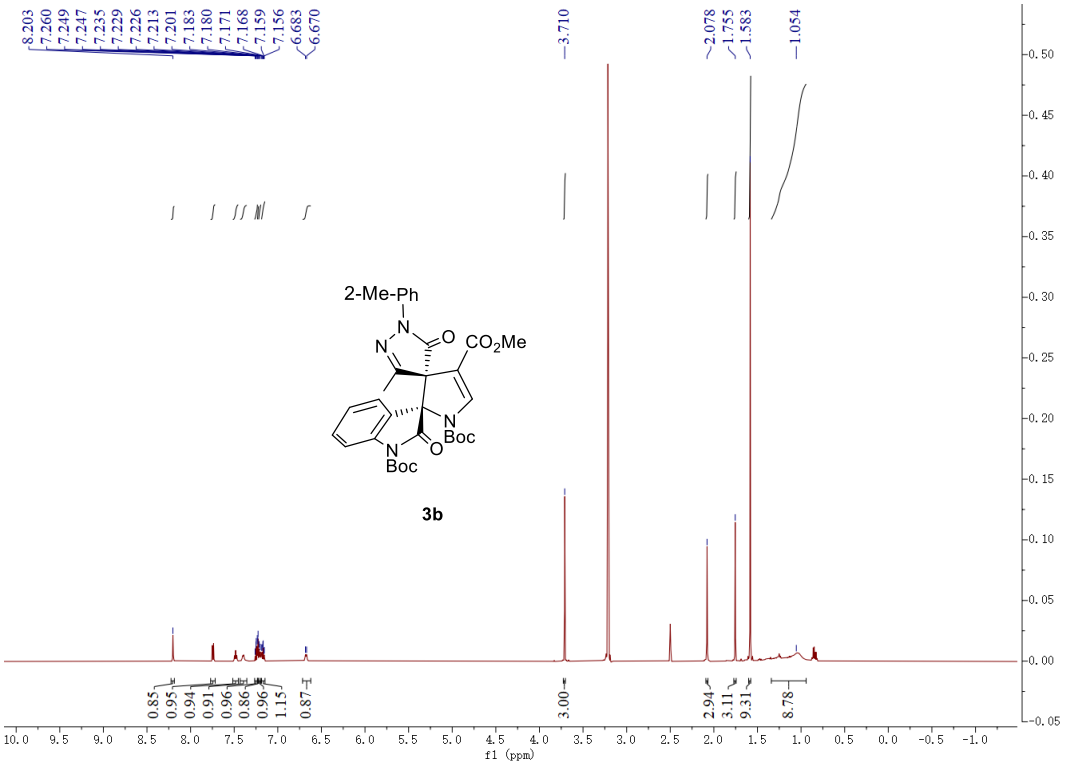




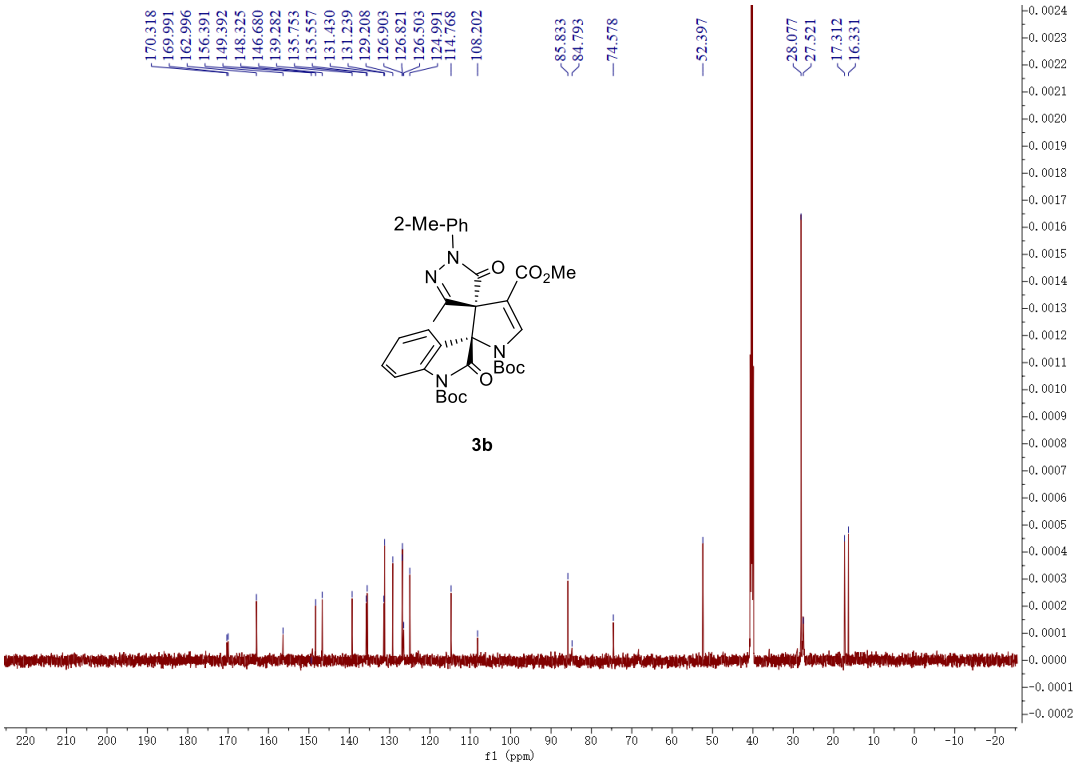
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.33	n.a.	283.297	90.137	49.24	n.a.	BMB
2	16.52	n.a.	83.525	92.927	50.76	n.a.	BMB
Total:			366.822	183.065	100.00	0.000	



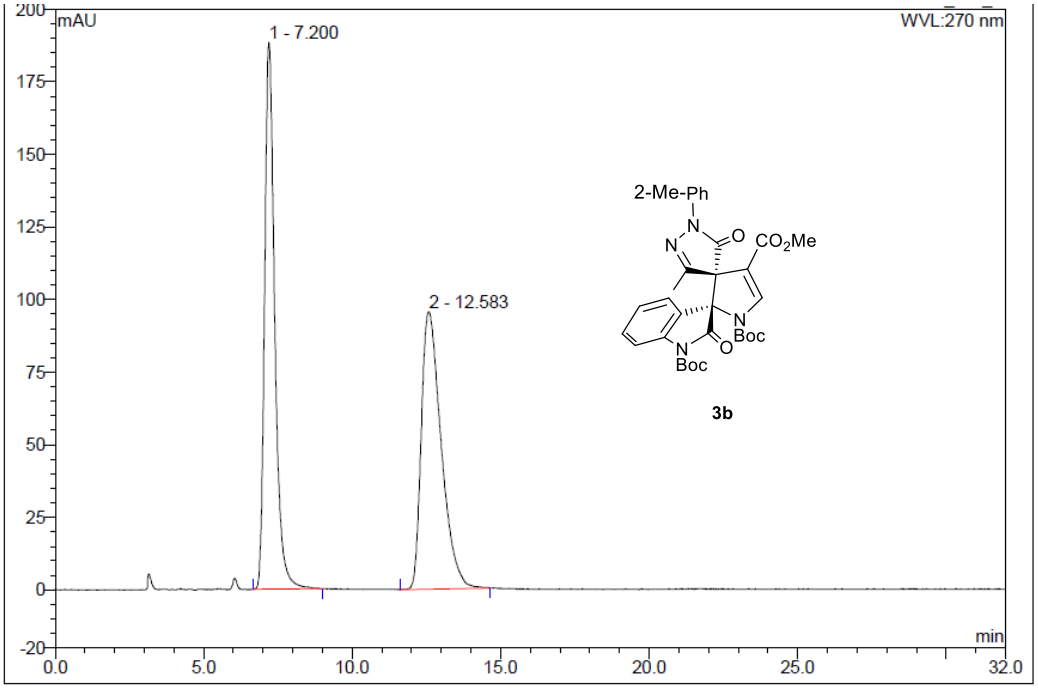
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.38	n.a.	24.206	7.966	4.74	n.a.	BMB
2	16.08	n.a.	154.363	160.089	95.26	n.a.	BMB
Total:			178.569	168.055	100.00	0.000	


8.203
7.260
7.249
7.247
7.235
7.229
7.226
7.213
7.201
7.183
7.180
7.171
7.168
7.159
7.156
6.683
6.670
3.710
2.078
1.755
1.583
1.054
2-Me-Ph
CO2Me
Boc
Boc
0.85
0.95
0.94
0.91
0.96
0.86
0.96
1.15
0.87
3.00
2.94
3.11
9.31
8.78
f1 (ppm)

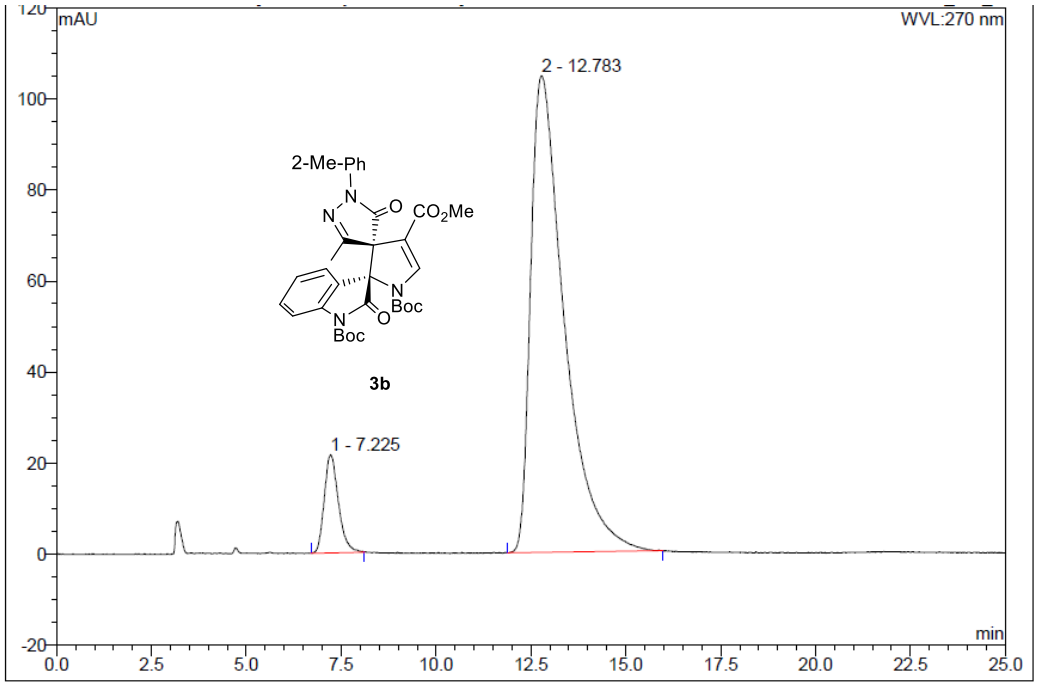
3b


170.318
169.991
162.996
156.391
149.392
148.325
146.680
139.282
135.753
135.557
131.430
131.239
129.208
126.903
126.821
126.503
124.991
114.768
108.202
85.833
84.793
74.578
52.397
28.077
27.521
17.312
16.331
2-Me-Ph
CO2Me
Boc
Boc
f1 (ppm)

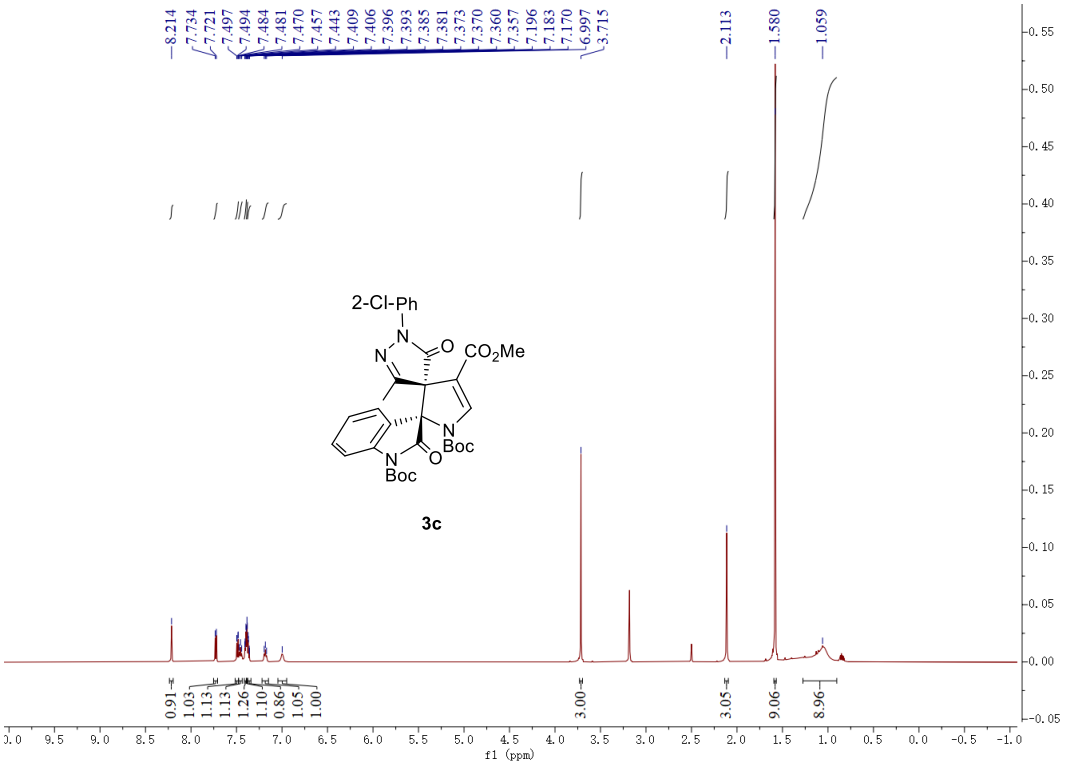
3b



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.20	n.a.	188.368	74.722	50.24	n.a.	BMB
2	12.58	n.a.	95.617	73.999	49.76	n.a.	BMB
Total:			283.985	148.720	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.23	n.a.	21.501	9.317	7.97	n.a.	BMB
2	12.78	n.a.	104.733	107.602	92.03	n.a.	BMB*
Total:			126.234	116.918	100.00	0.000	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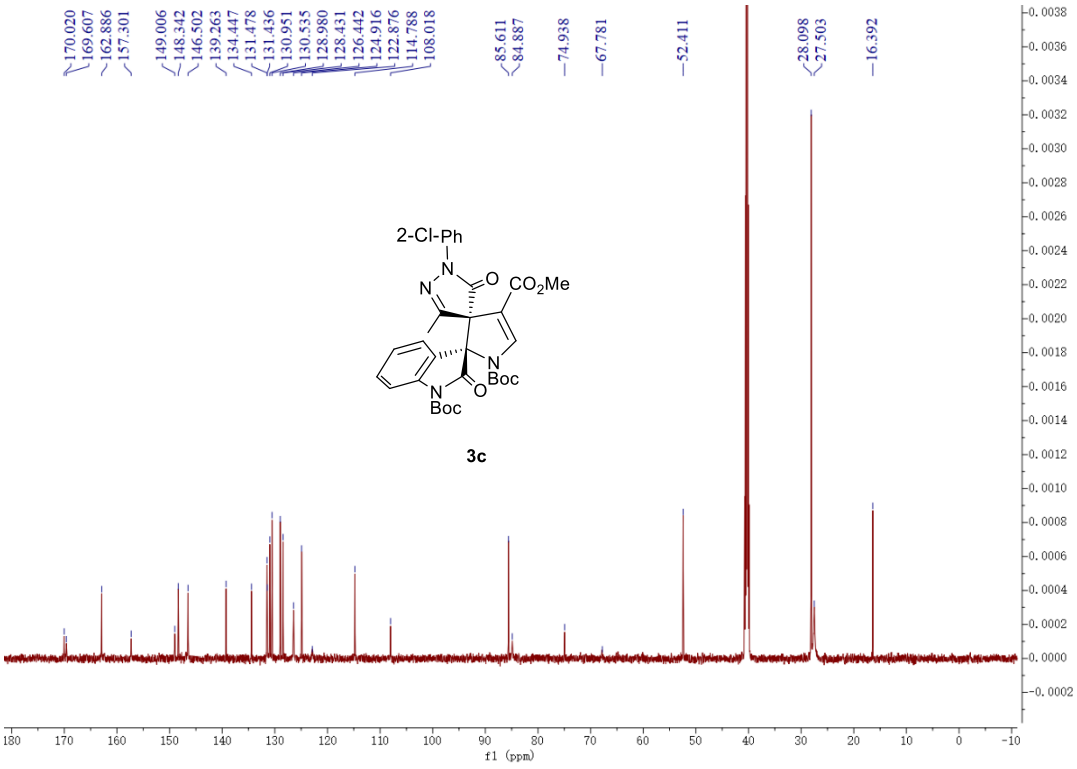
7.721
7.497
7.494
7.484
7.481
7.470
7.457
7.443
7.409
7.406
7.396
7.393
7.385
7.381
7.373
7.370
7.360
7.357
7.196
7.183
7.170
6.997
3.715
2.113
1.580
1.059
0.91
1.03
1.13
1.13
1.26
1.10
0.86
1.05
1.00
3.00
3.05
9.06
8.96
f1 (ppm)

2-Cl-Ph
N
N
O
CO2Me
N
Boc
O
N
Boc

3c


170.020
169.607
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146.502
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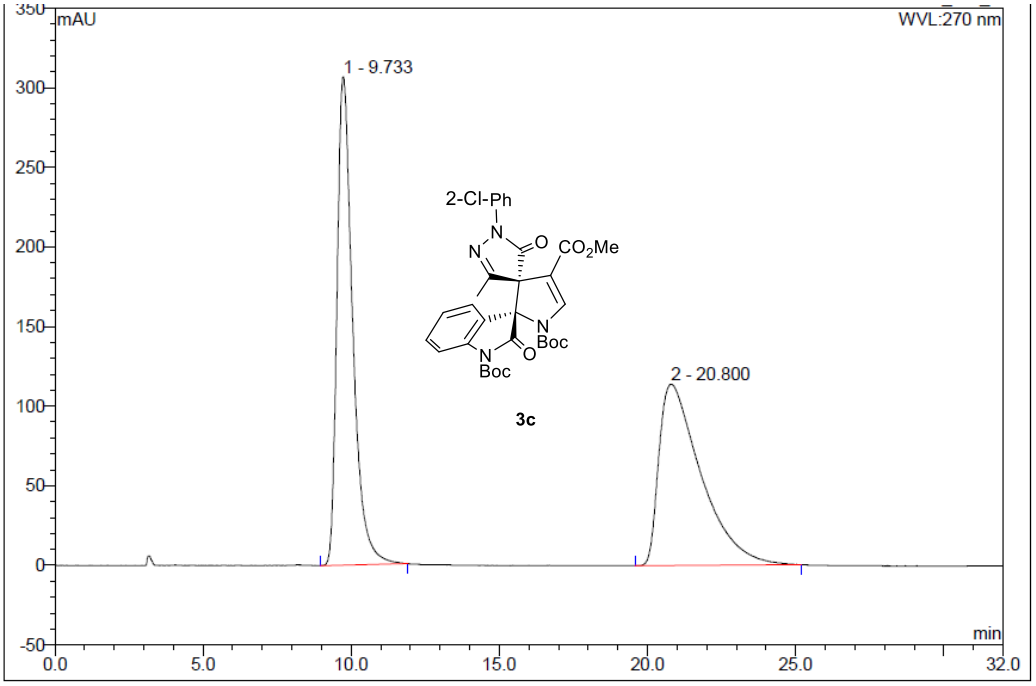
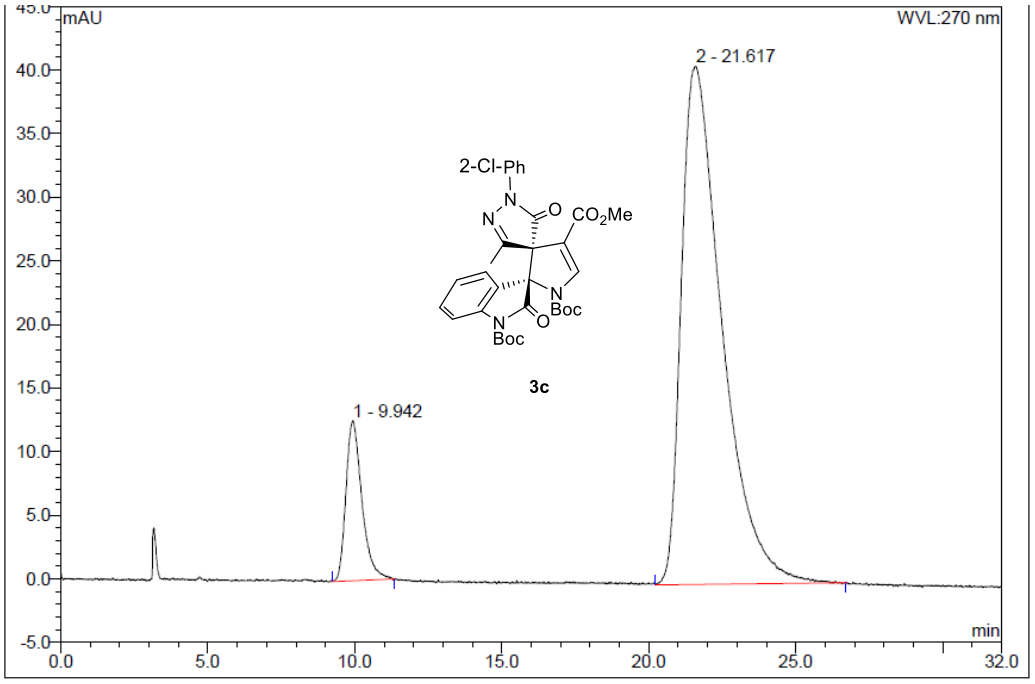
131.478
131.436
130.951
130.535
128.980
128.431
126.442
124.916
122.876
114.788
108.018
85.611
84.887
74.938
67.781
52.411
28.098
27.503
16.392
f1 (ppm)

2-Cl-Ph
N
N
O
CO2Me
N
Boc
O
N
Boc

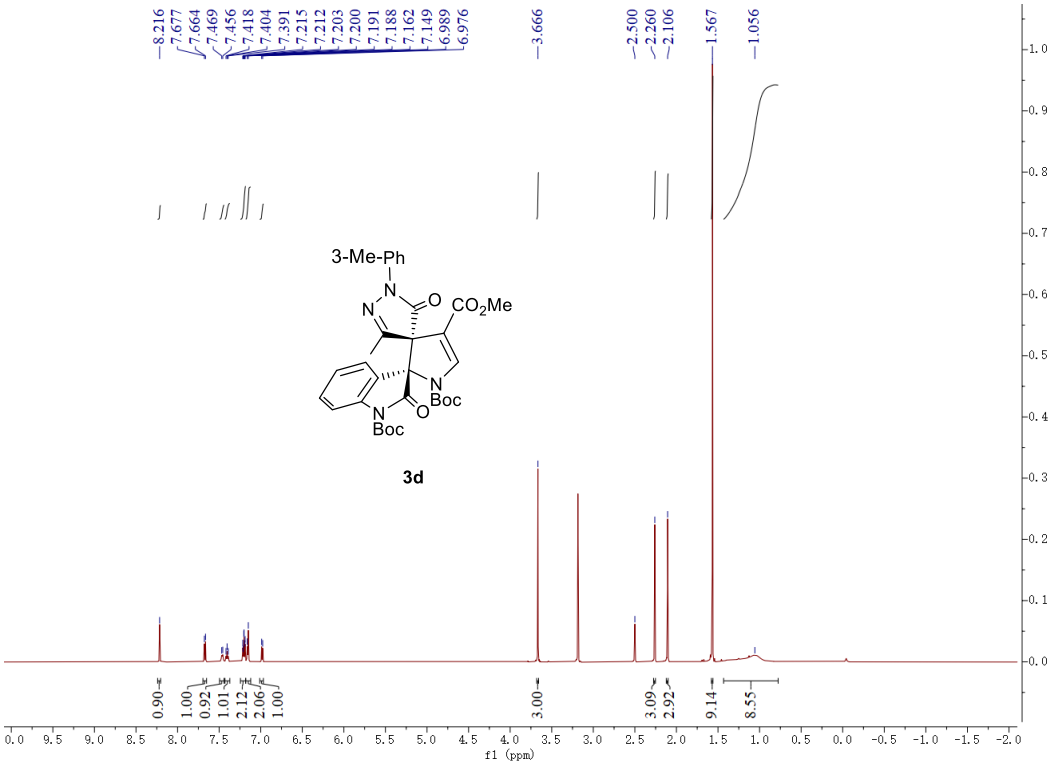
3c



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.73	n.a.	306.647	188.093	50.03	n.a.	BMB
2	20.80	n.a.	114.006	187.905	49.97	n.a.	BMB
Total:			420.653	375.999	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.94	n.a.	12.609	7.922	10.82	n.a.	BMB*
2	21.62	n.a.	40.742	65.289	89.18	n.a.	BMB*
Total:			53.351	73.211	100.00	0.000	


8.216
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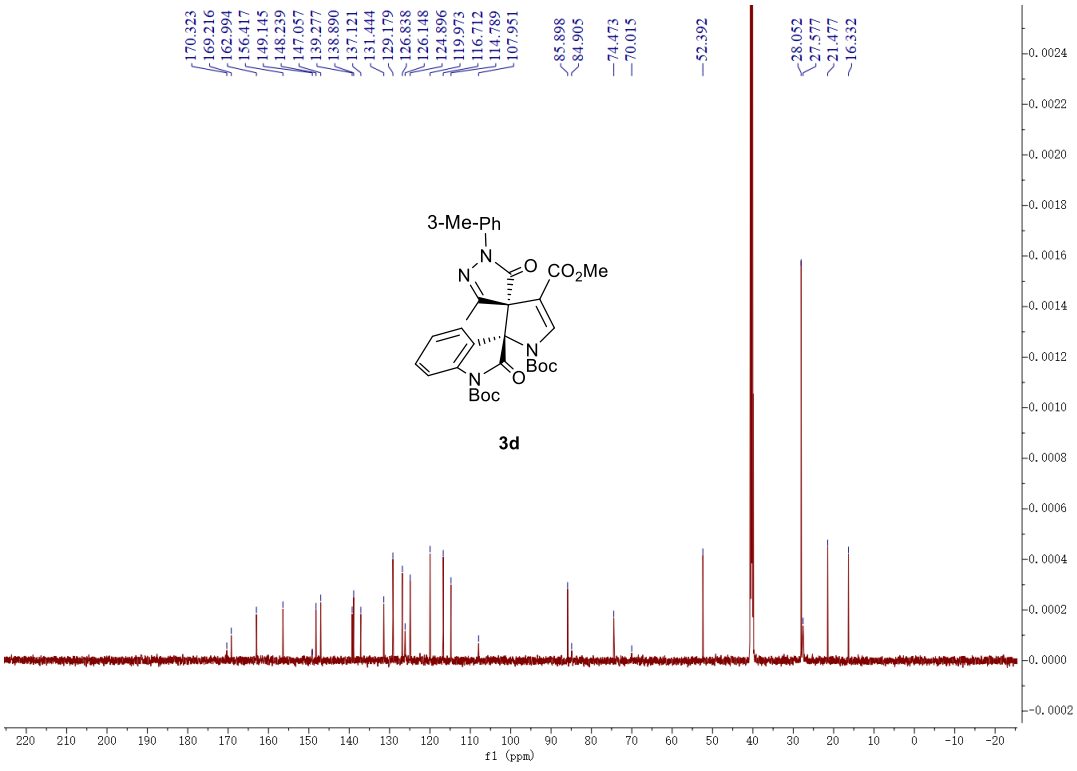
7.469
7.456
7.418
7.404
7.391
7.215
7.212
7.203
7.200
7.191
7.188
7.162
7.149
6.989
6.976
3.666
2.500
2.260
2.106
1.567
1.056
3-Me-Ph
CO2Me
Boc
Boc
0.90
1.00
0.92
1.01
2.12
2.06
1.00
3.00
3.09
2.92
9.14
8.55
f1 (ppm)

3d


170.323
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147.057
139.277
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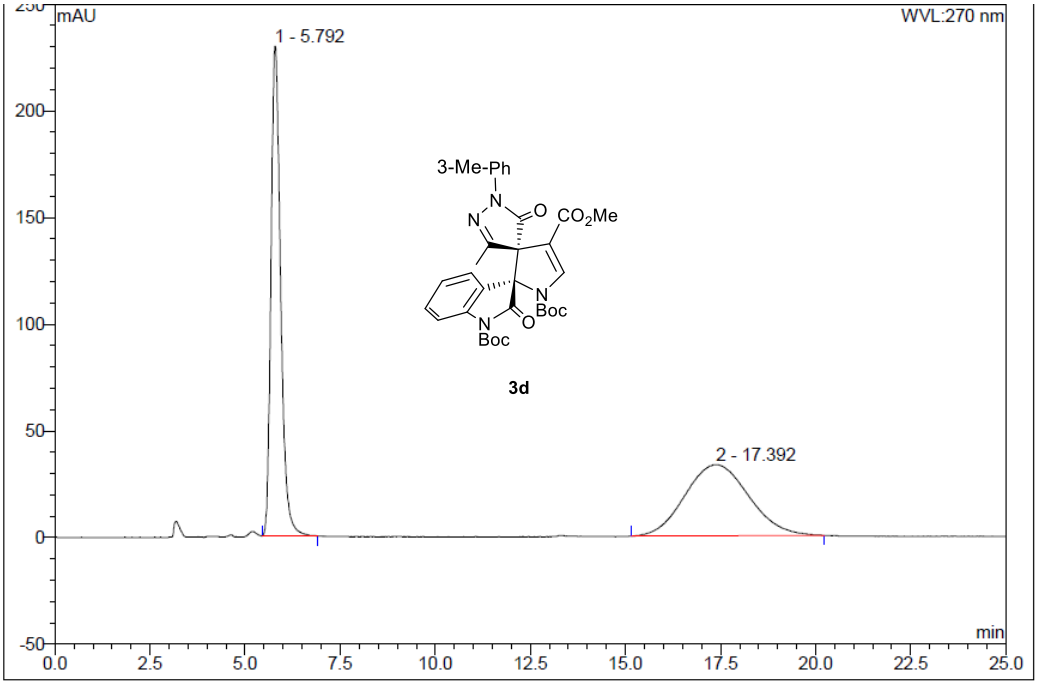
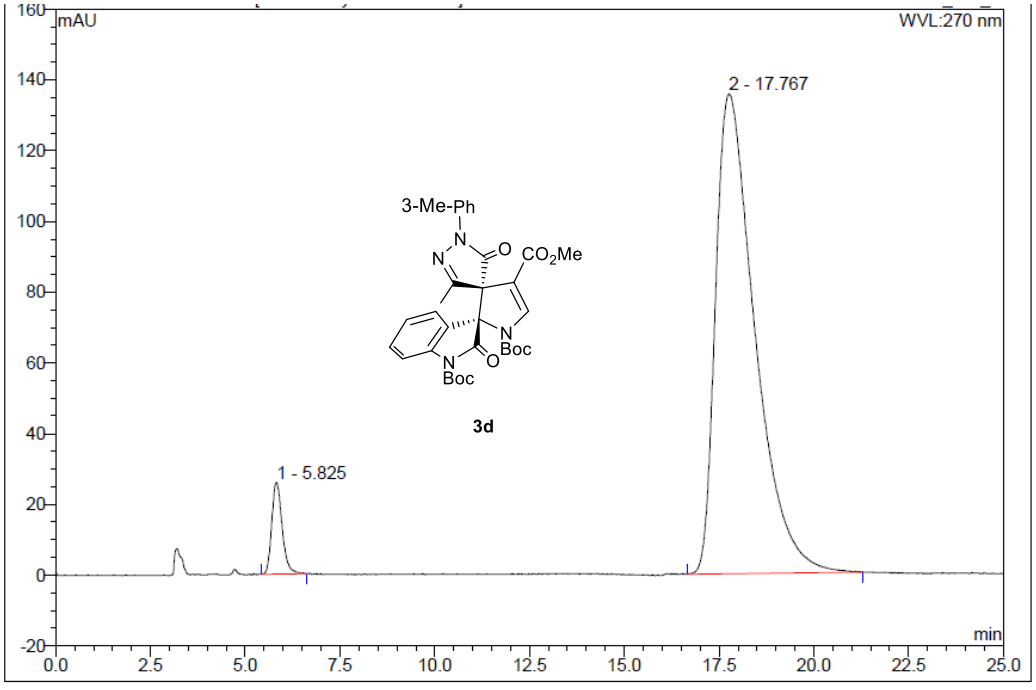
131.444
129.179
126.838
126.148
124.896
119.973
116.712
114.789
107.951
85.898
84.905
74.473
70.015
52.392
28.052
27.577
21.477
16.332
3-Me-Ph
CO2Me
Boc
Boc
f1 (ppm)

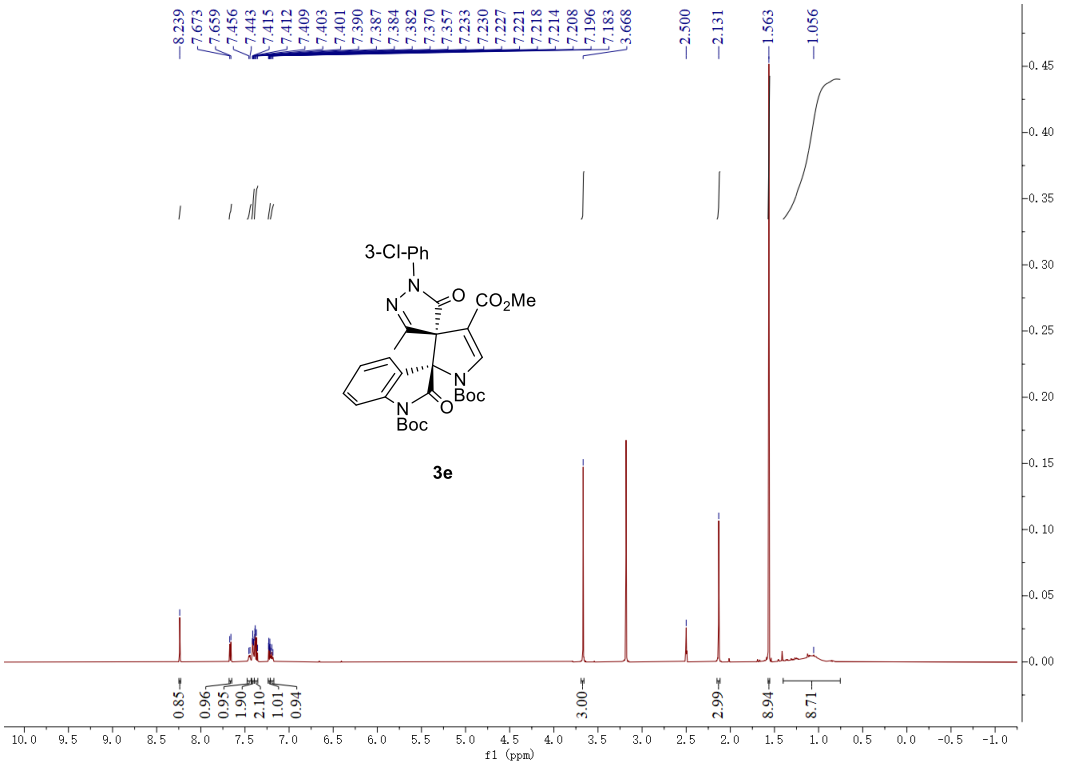
3d



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.79	n.a.	229.713	67.473	50.98	n.a.	BMB
2	17.39	n.a.	33.336	64.870	49.02	n.a.	BMB*
Total:			263.050	132.343	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.83	n.a.	25.967	8.243	4.83	n.a.	BMB
2	17.77	n.a.	135.559	162.461	95.17	n.a.	BMB*
Total:			161.526	170.704	100.00	0.000	


8.239
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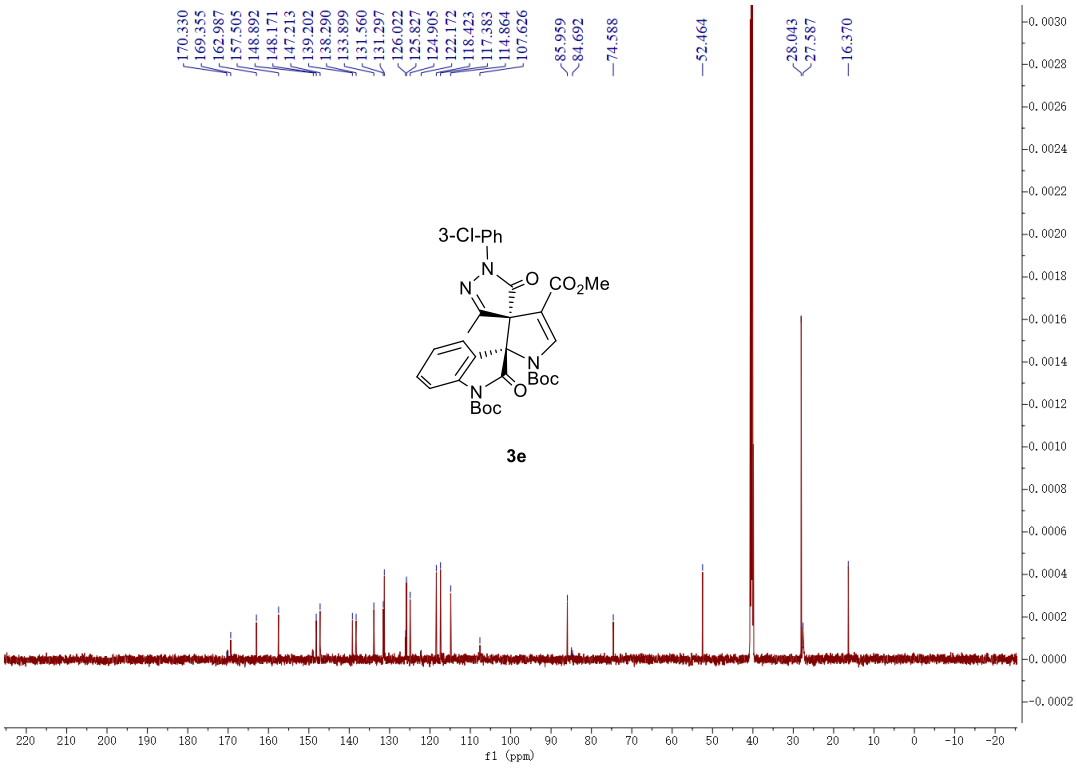
7.659
7.456
7.443
7.415
7.412
7.409
7.403
7.401
7.390
7.387
7.384
7.382
7.370
7.357
7.233
7.230
7.227
7.221
7.218
7.214
7.208
7.196
7.183
3.668
2.500
2.131
1.563
1.056
3-Cl-Ph
CO2Me
Boc
Boc
3e
0.85
0.96
0.95
1.90
2.10
1.01
0.94
3.00
2.99
8.94
8.71
f1 (ppm)


170.330
169.355
162.987
157.505
148.892
148.171
147.213
139.202
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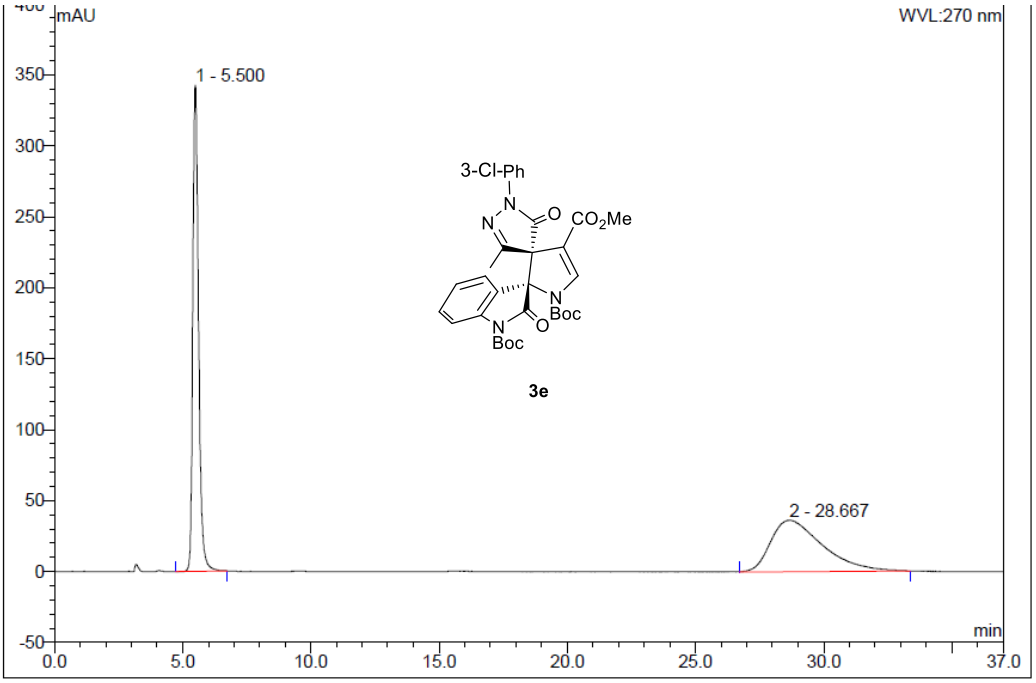
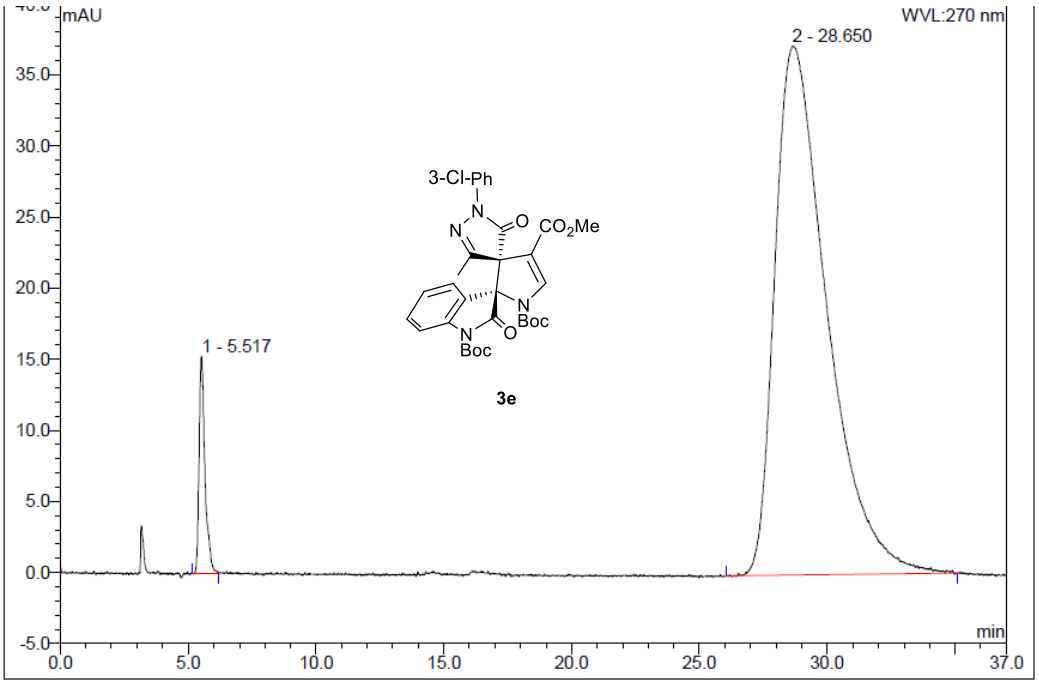
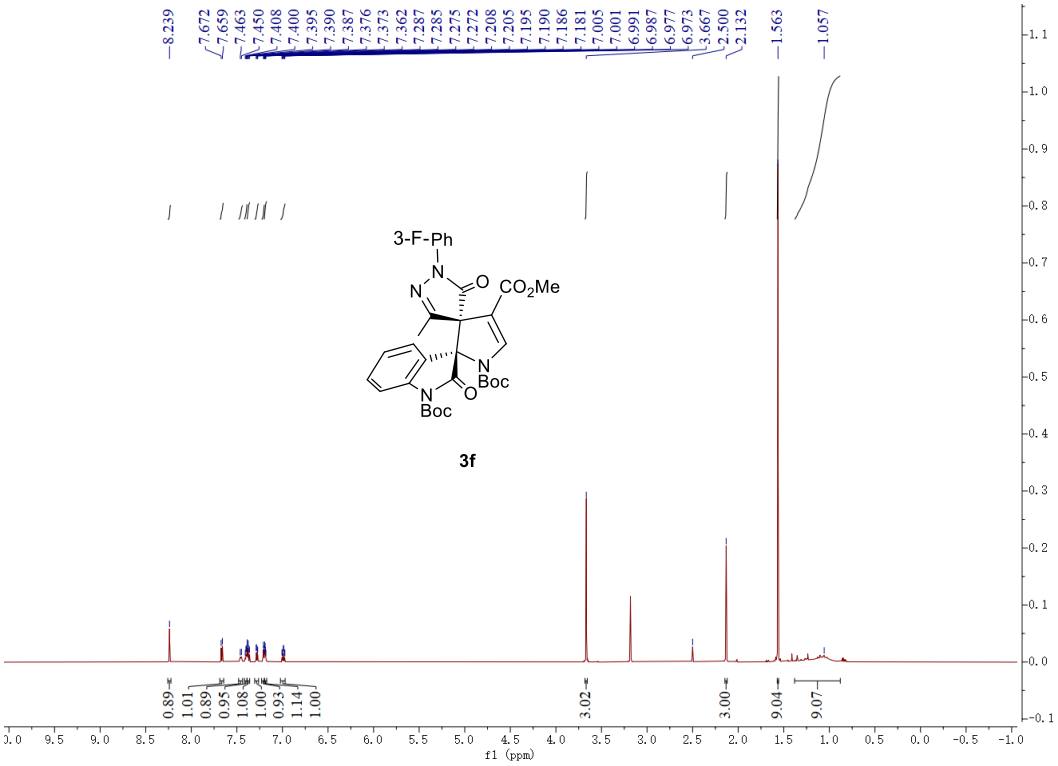
133.899
131.560
131.297
126.022
125.827
124.905
122.172
118.423
117.383
114.864
107.626
85.959
84.692
74.588
52.464
28.043
27.587
16.370
3-Cl-Ph
CO2Me
Boc
Boc
3e
f1 (ppm)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.50	n.a.	343.100	89.230	51.32	n.a.	BMB
2	28.67	n.a.	36.167	84.644	48.68	n.a.	BMB*
Total:			379.267	173.875	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.52	n.a.	15.326	4.124	4.49	n.a.	BMB*
2	28.65	n.a.	37.218	87.795	95.51	n.a.	BMB*
Total:			52.544	91.919	100.00	0.000	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7.463
7.450
7.408
7.400
7.395
7.390
7.387
7.376
7.373
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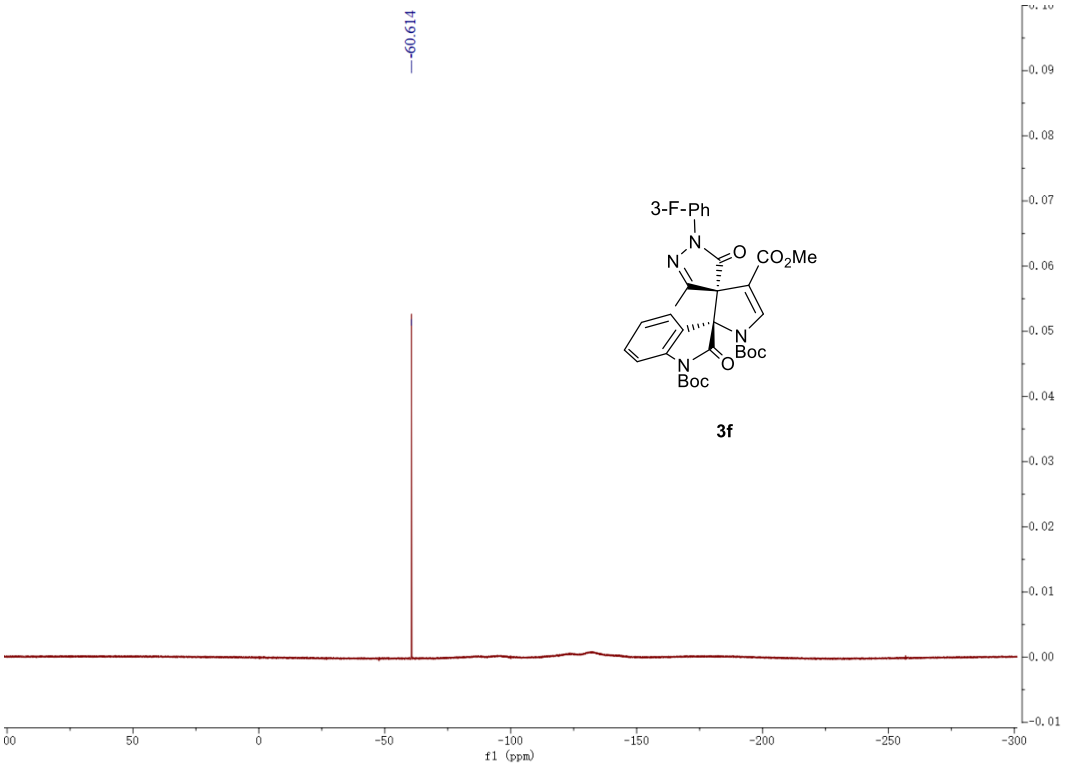
7.287
7.285
7.275
7.272
7.208
7.205
7.195
7.190
7.186
7.181
7.005
7.001
6.991
6.987
6.977
6.973
3.667
2.500
2.132
1.563
1.057
3-F-Ph
CO2Me
Boc
Boc
0.89
1.01
0.89
0.95
1.08
1.00
0.93
1.14
1.00
3.02
3.00
9.04
9.07
f1 (ppm)

3f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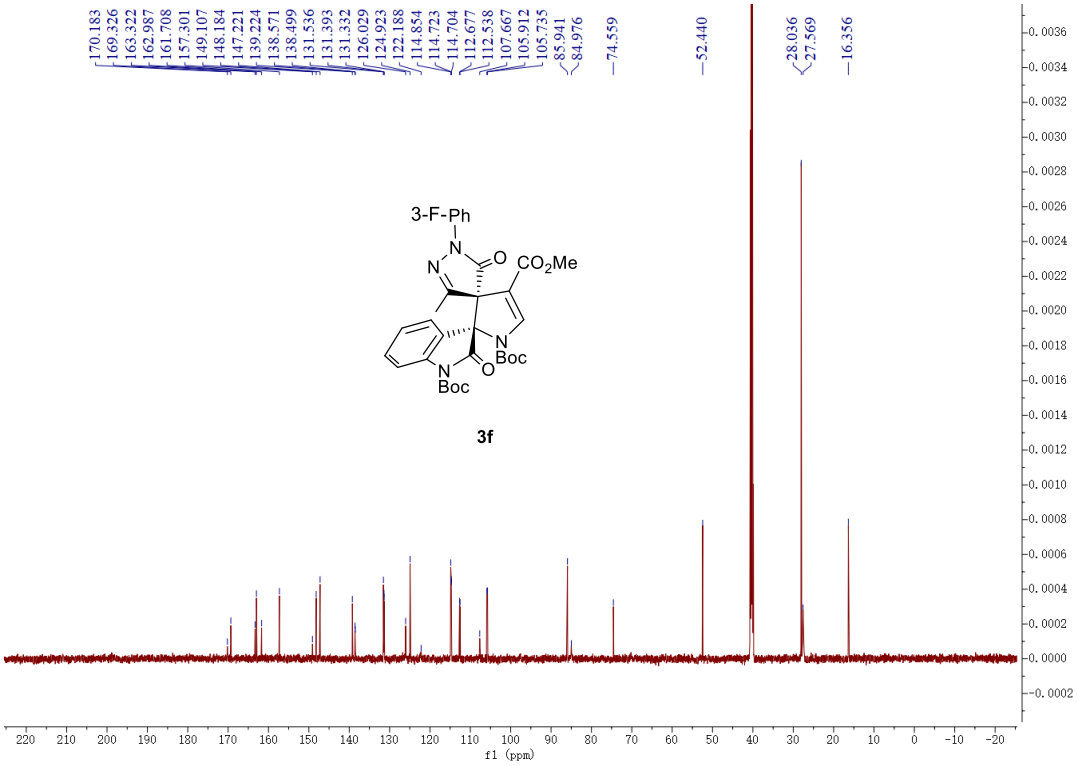
CO2Me
Boc
Boc
f1 (ppm)

3f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148.184
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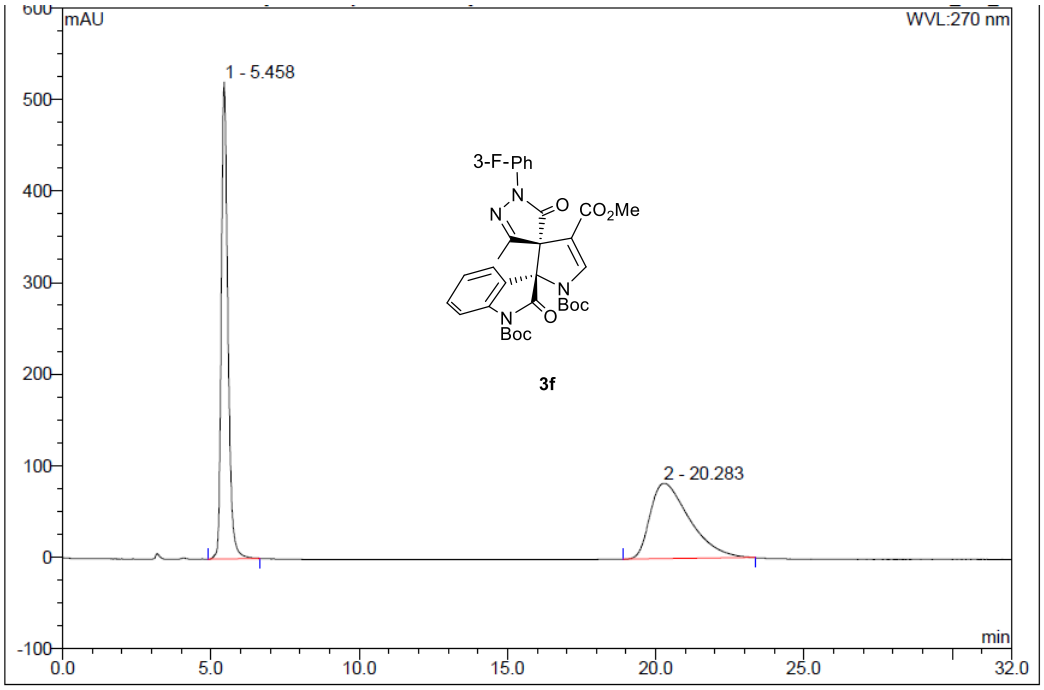
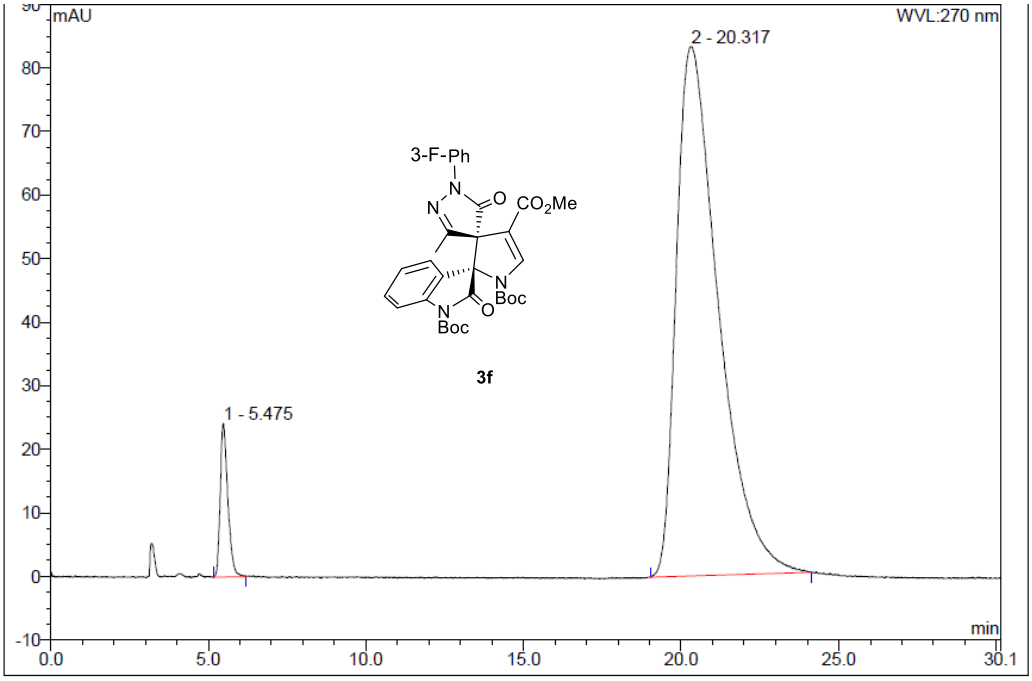
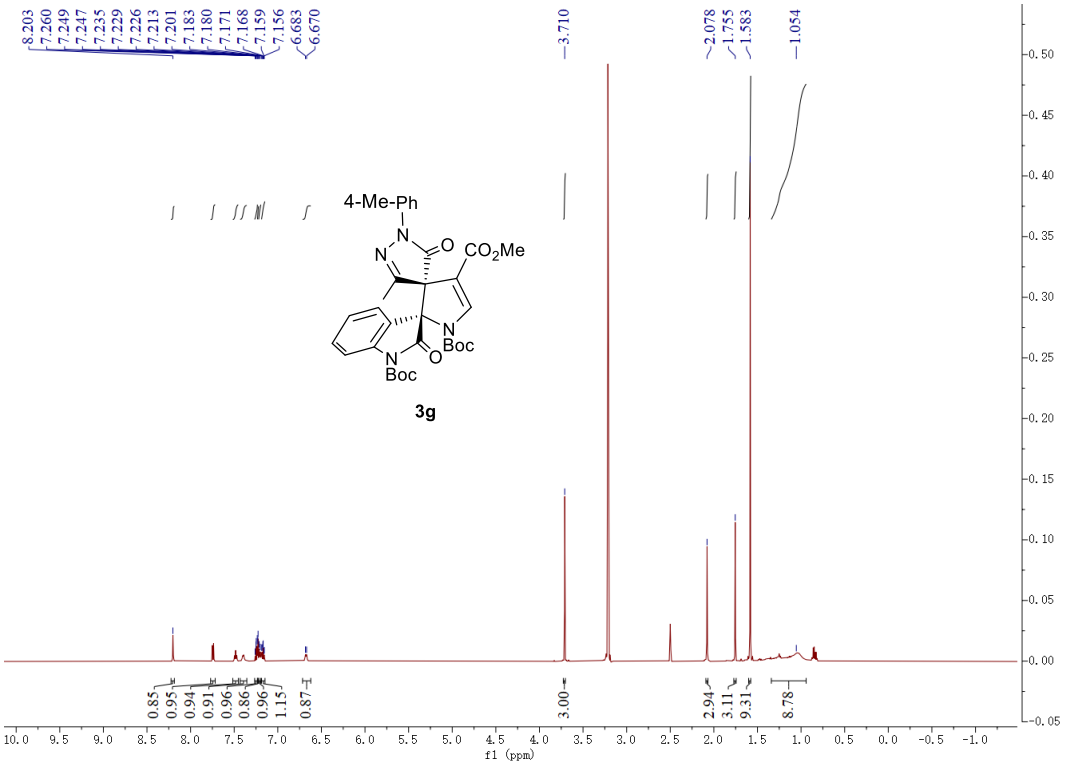
139.224
138.571
138.499
131.536
131.393
131.332
126.029
124.923
122.188
114.854
114.723
114.704
112.677
112.538
107.667
105.912
105.735
85.941
84.976
74.559
52.440
28.036
27.569
16.356
3-F-Ph
N
N
O
CO2Me
N
Boc
N
Boc
O
3f
f1 (ppm)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.46	n.a.	520.770	134.660	51.37	n.a.	BMB
2	20.28	n.a.	82.430	127.501	48.63	n.a.	BMB*
Total:			603.200	262.160	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.48	n.a.	24.148	6.758	4.97	n.a.	BMB
2	20.32	n.a.	83.354	129.158	95.03	n.a.	BMB*
Total:			107.502	135.916	100.00	0.000	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7.213
7.201
7.183
7.180
7.171
7.168
7.159
7.156
6.683
6.670
3.710
2.078
1.755
1.583
1.054
4-Me-Ph
CO2Me
Boc
Boc
3g
0.85
0.95
0.94
0.91
0.96
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0.96
1.15
0.87
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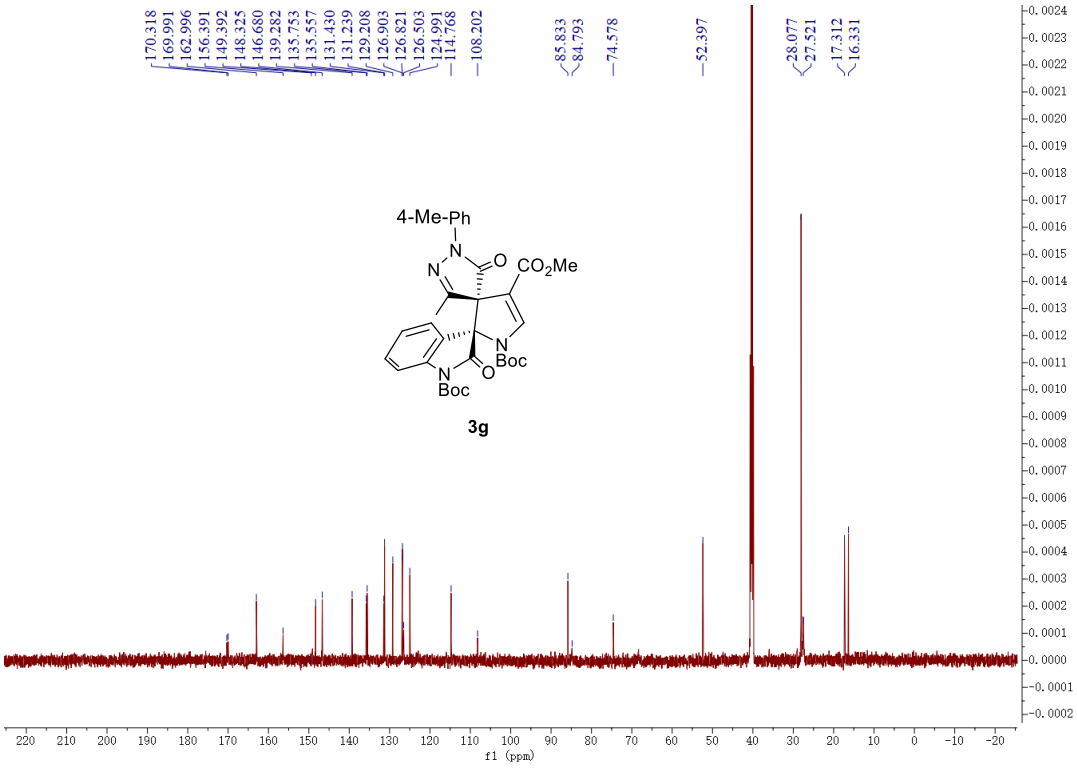
2.94
3.11
9.31
8.78
f1 (ppm)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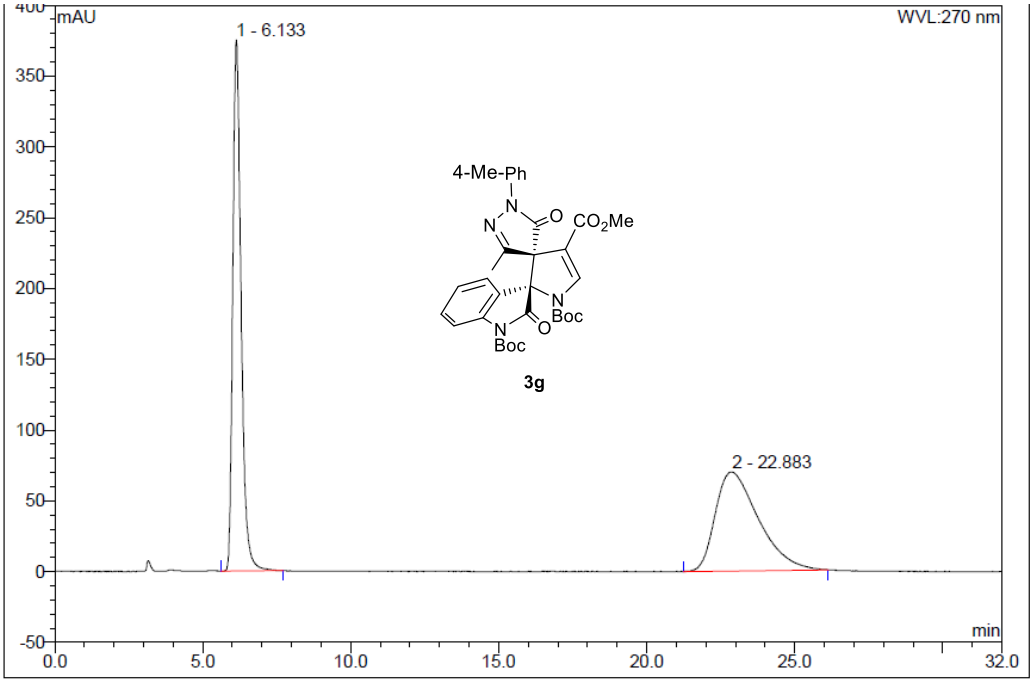
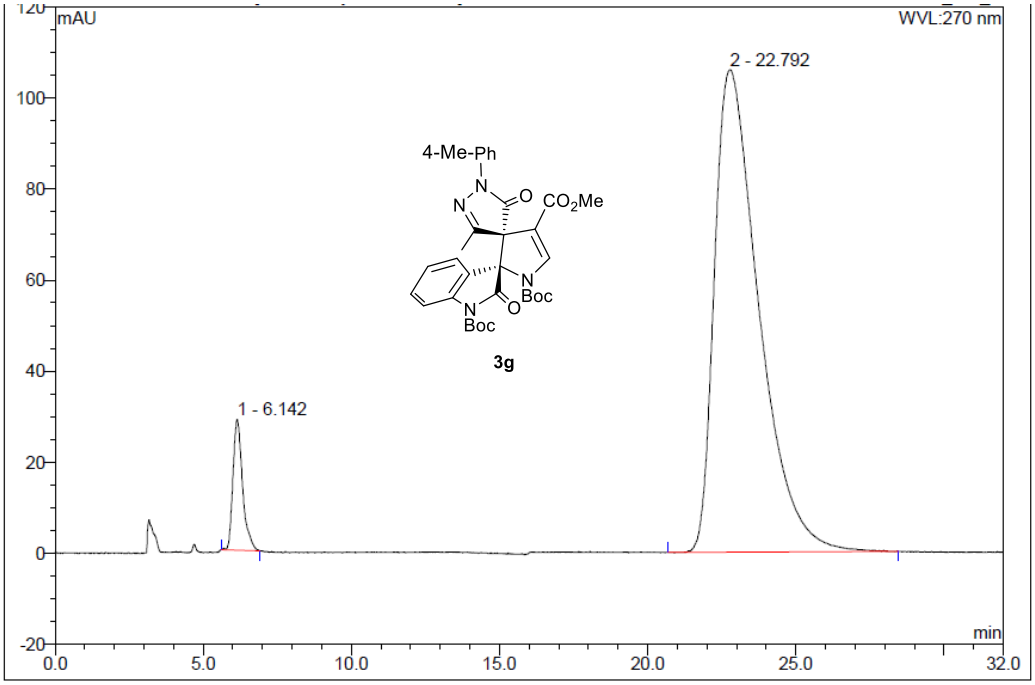
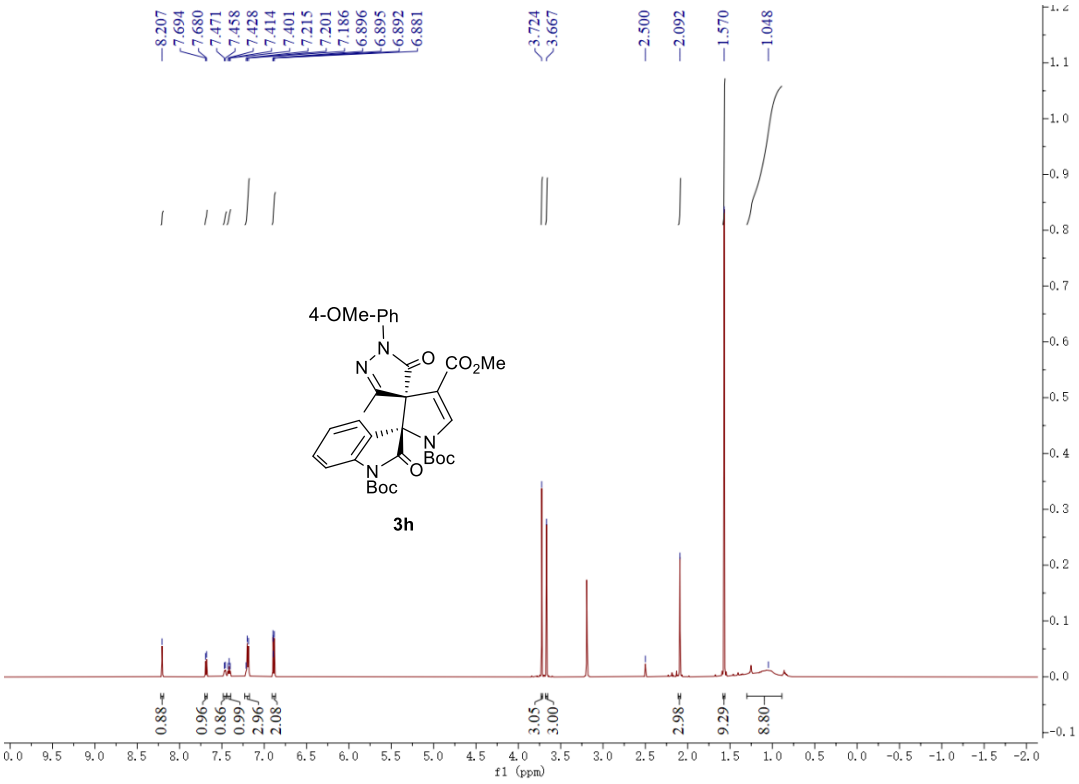
135.557
131.430
131.239
129.208
126.903
126.821
126.503
124.991
114.768
108.202
85.833
84.793
74.578
52.397
28.077
27.521
17.312
16.331
4-Me-Ph
CO2Me
Boc
Boc
3g
f1 (ppm)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.13	n.a.	375.447	122.281	50.81	n.a.	BMB
2	22.88	n.a.	69.952	118.379	49.19	n.a.	BMB*
Total:			445.399	240.660	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.14	n.a.	28.721	10.877	5.60	n.a.	BMB*
2	22.79	n.a.	105.883	183.238	94.40	n.a.	BMB*
Total:			134.604	194.114	100.00	0.000	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7.201
7.186
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6.881
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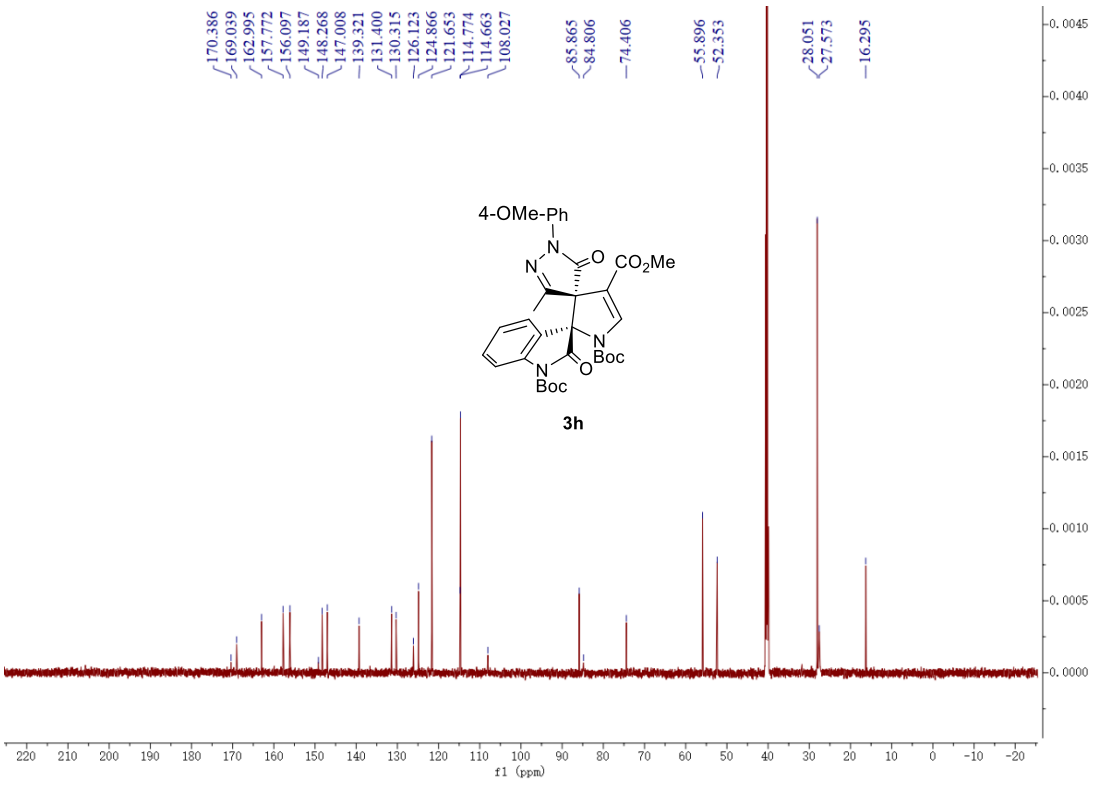
3.667
2.500
2.092
1.570
1.048
4-OMe-Ph
CO2Me
Boc
Boc
3h
0.88
0.96
0.86
0.99
2.96
2.08
3.05
3.00
2.98
9.29
8.80
f1 (ppm)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131.400
130.315
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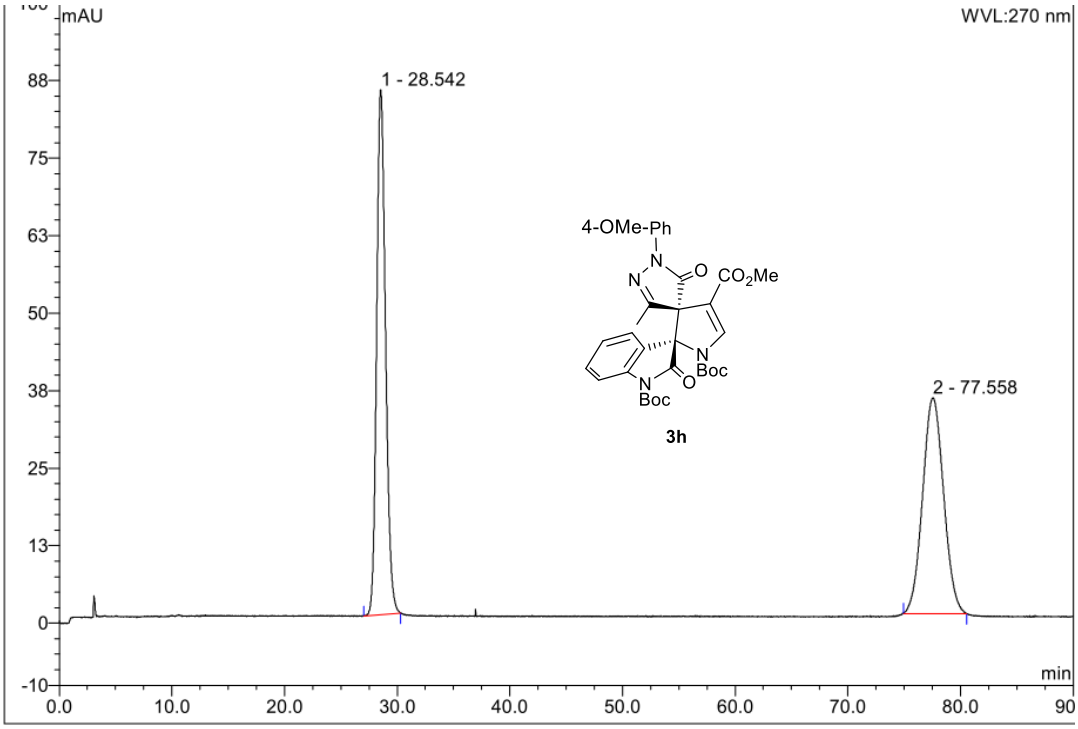
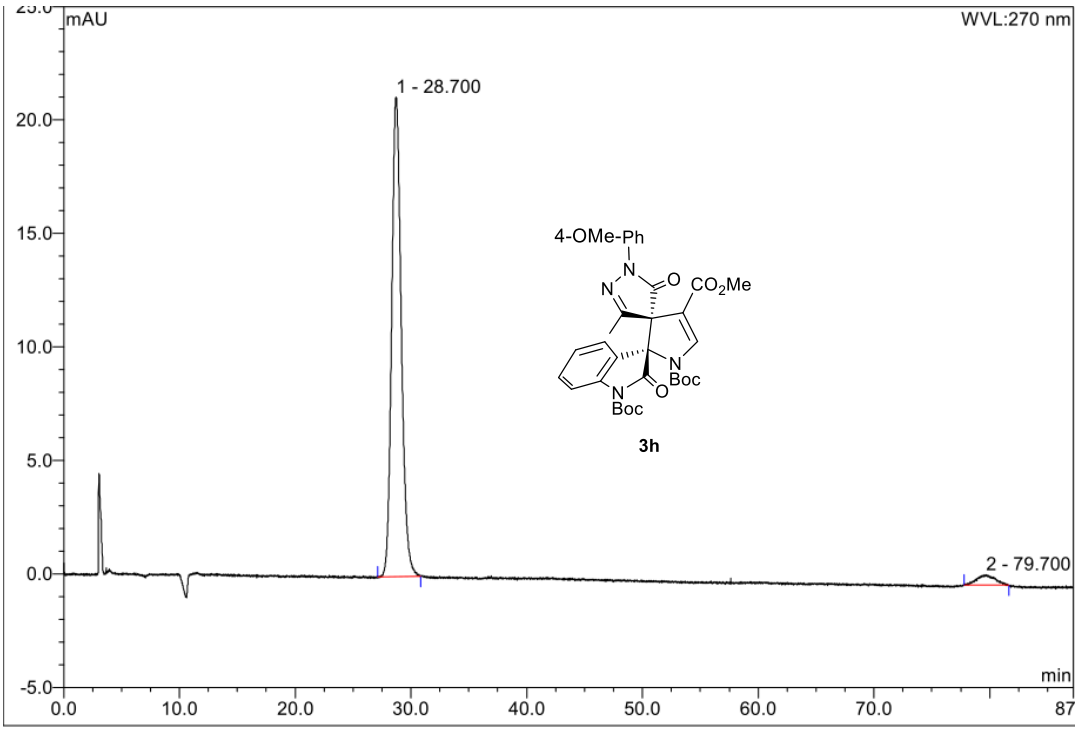
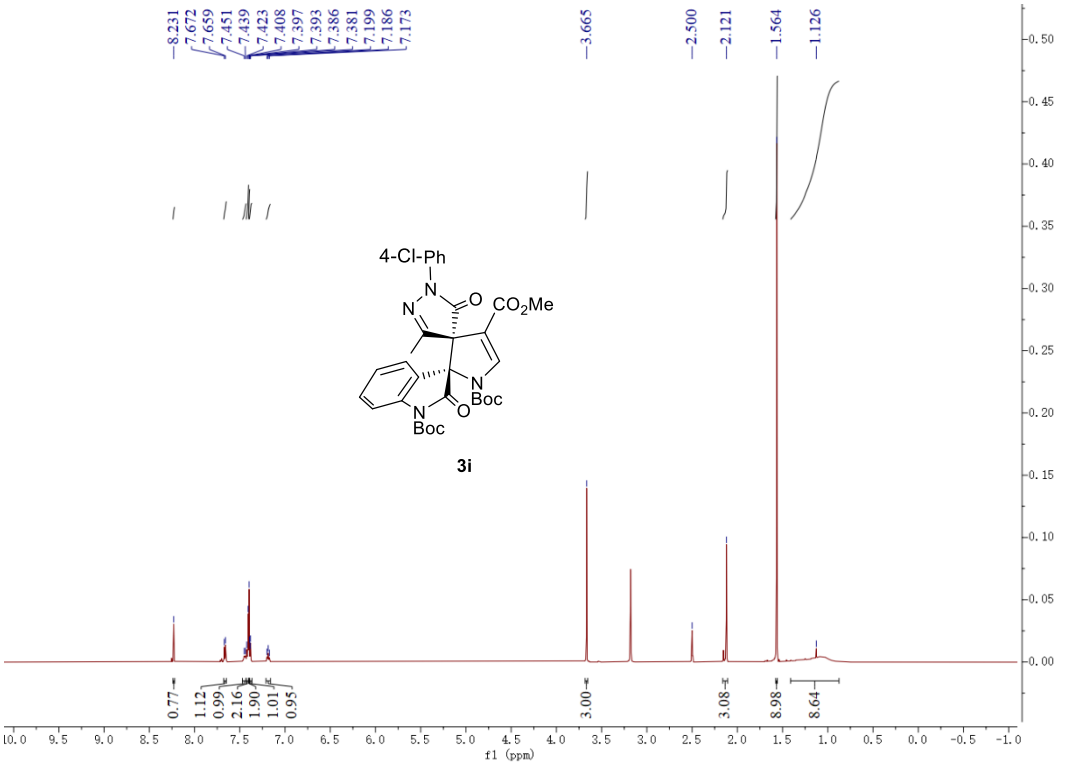
124.866
121.653
114.774
114.663
108.027
85.865
84.806
74.406
55.896
52.353
28.051
27.573
16.295
4-OMe-Ph
CO2Me
Boc
Boc
3h
f1 (ppm)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	28.54	n.a.	84.680	77.502	50.69	n.a.	BMB
2	77.56	n.a.	34.843	75.392	49.31	n.a.	BMB
Total:			119.523	152.894	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	28.70	n.a.	21.154	20.329	96.16	n.a.	BMB*
2	79.70	n.a.	0.465	0.812	3.84	n.a.	BMB*
Total:			21.619	21.141	100.00	0.000	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7.397
7.393
7.386
7.381
7.199
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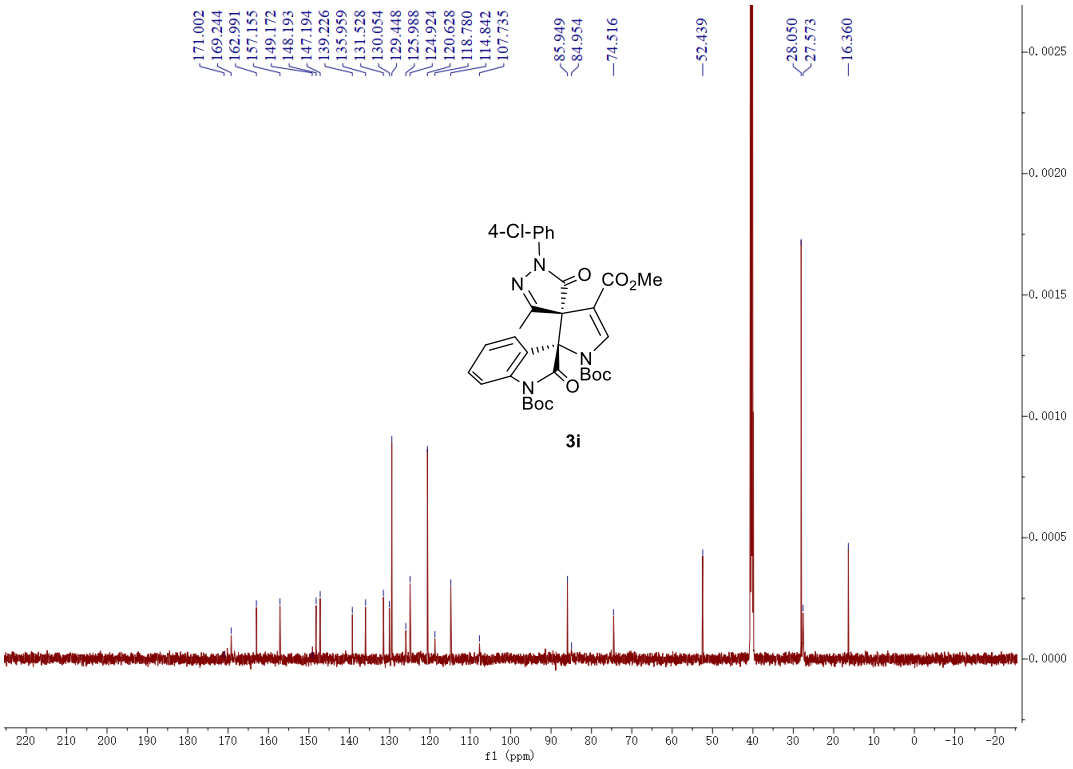
3.665
2.500
2.121
1.564
1.126
4-Cl-Ph
CO2Me
Boc
Boc
3i
0.77
1.12
0.99
2.16
1.90
1.01
0.95
3.00
3.08
8.98
8.64
f1 (ppm)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130.054
129.448
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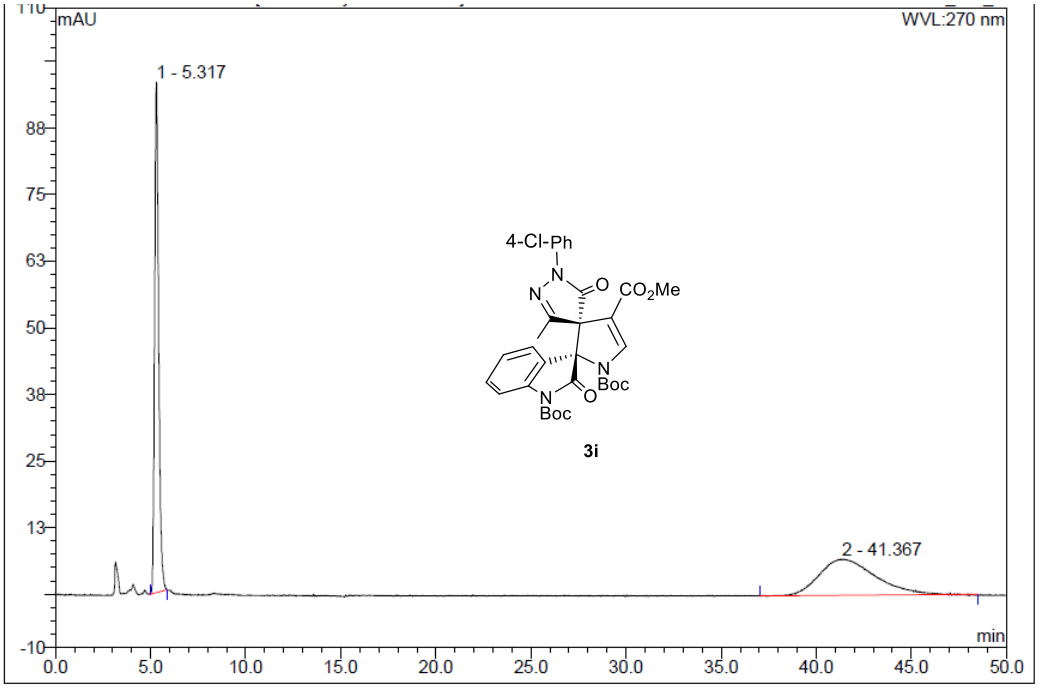
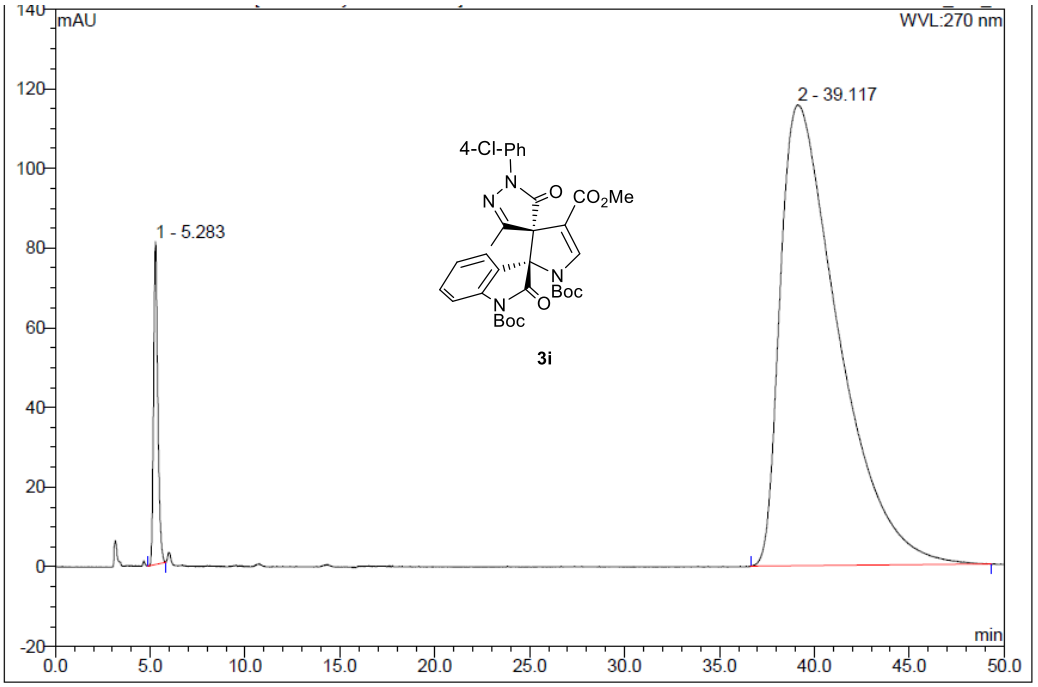
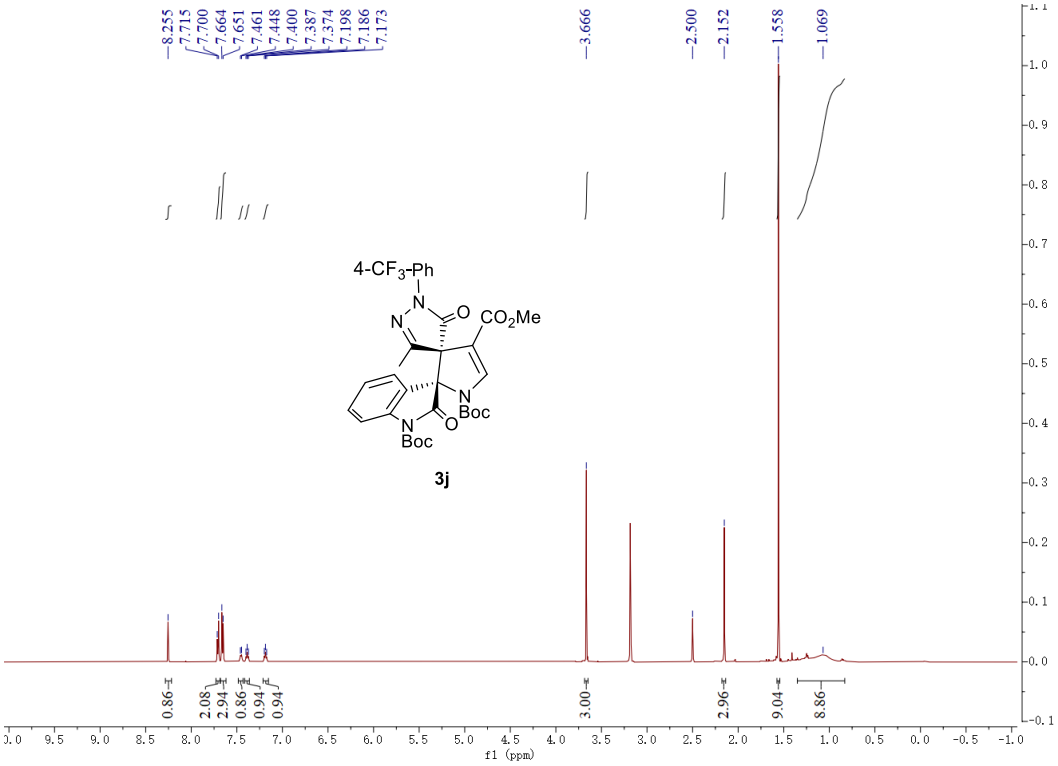
118.780
114.842
107.735
85.949
84.954
74.516
52.439
28.050
27.573
16.360
4-Cl-Ph
CO2Me
Boc
Boc
3i
f1 (ppm)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.32	n.a.	95.752	23.839	50.72	n.a.	BMB*
2	41.37	n.a.	6.768	23.163	49.28	n.a.	BMB*
Total:			102.520	47.002	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.28	n.a.	81.039	21.202	4.90	n.a.	BMB
2	39.12	n.a.	115.682	411.930	95.10	n.a.	BMB*
Total:			196.721	433.132	100.00	0.000	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7.374
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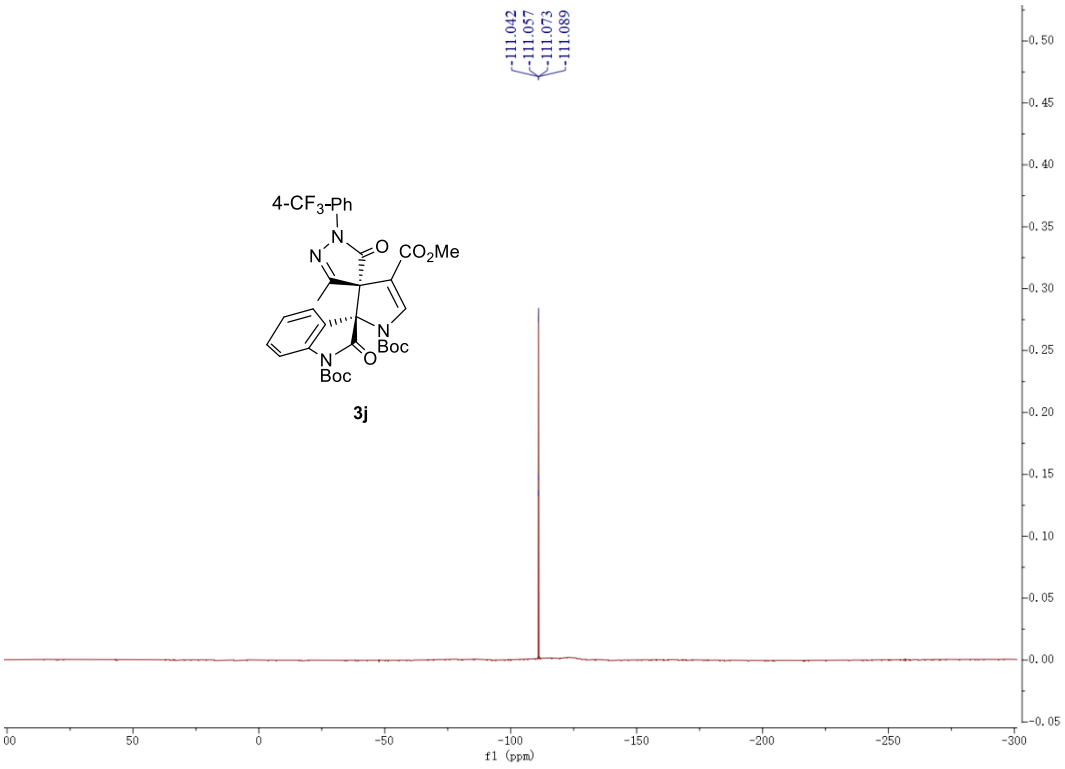
7.186
7.173
3.666
2.500
2.152
1.558
1.069
4-CF3-Ph
CO2Me
Boc
Boc
3j
0.86
2.08
2.94
0.86
0.94
0.94
3.00
2.96
9.04
8.86
f1 (ppm)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111.089
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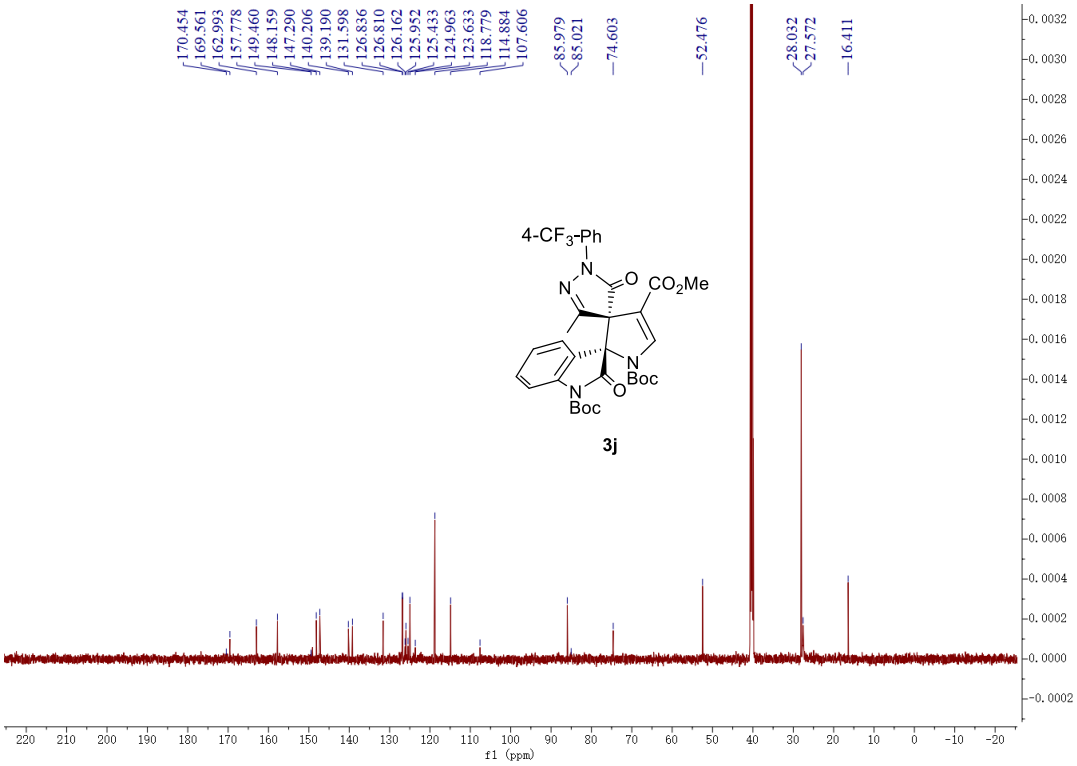
CO2Me
Boc
Boc
3j
f1 (ppm)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131.598
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126.162
125.952
125.433
124.963
123.633
118.779
114.884
107.606
85.979
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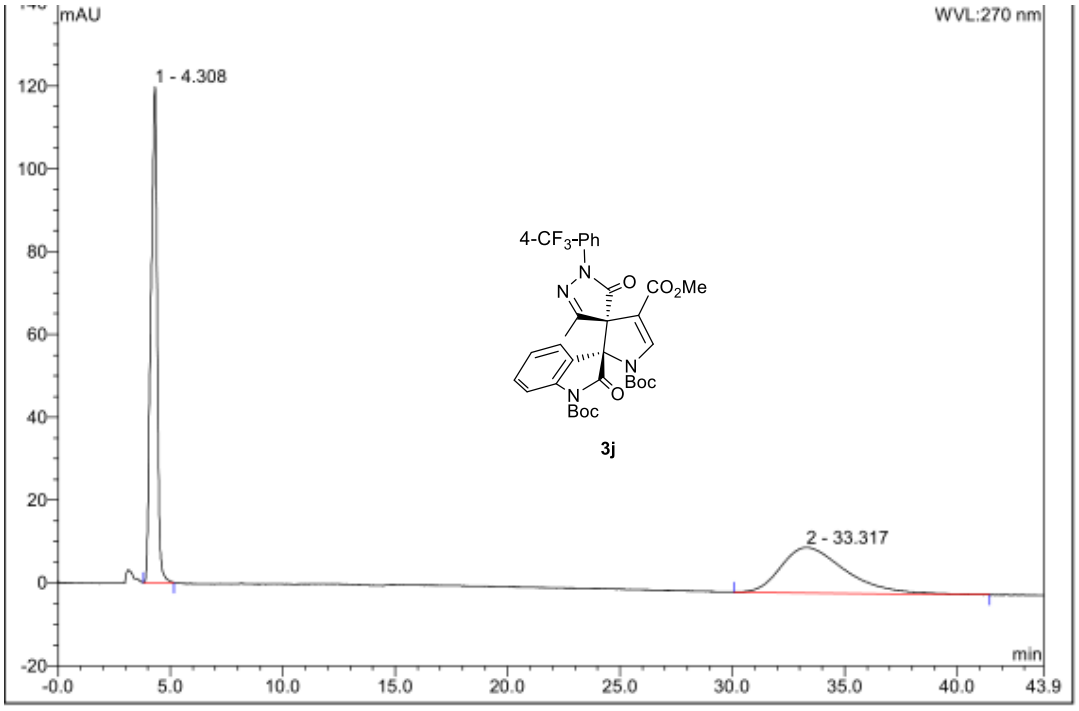
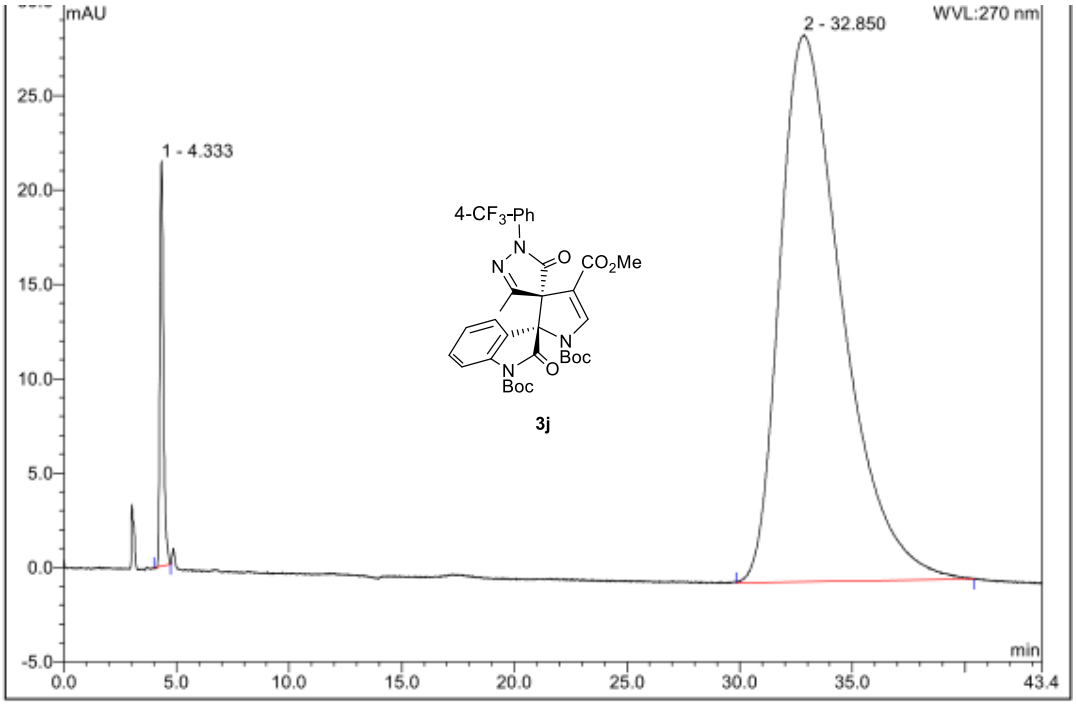
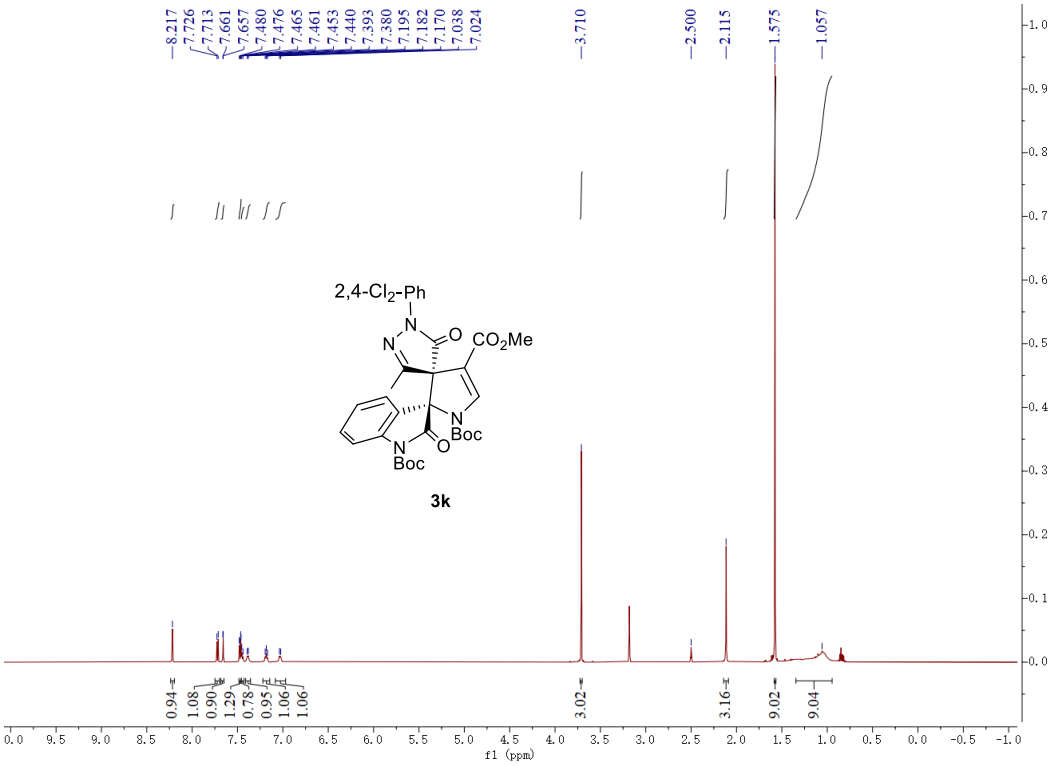
28.032
27.572
16.411
4-CF3-Ph
CO2Me
Boc
Boc
3j
f1 (ppm)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	4.31	n.a.	119.746	38.747	51.56	n.a.	BMB
2	33.32	n.a.	10.991	36.405	48.44	n.a.	BMB*
Total:			130.738	75.152	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	4.33	n.a.	21.474	3.953	4.08	n.a.	BMB*
2	32.85	n.a.	28.995	92.923	95.92	n.a.	BMB*
Total:			50.469	96.875	100.00	0.000	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7.661
7.657
7.480
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7.465
7.461
7.453
7.440
7.393
7.380
7.195
7.182
7.170
7.038
7.024
3.710
2.500
2.115
1.575
1.057
2,4-Cl2-Ph
CO2Me
Boc
Boc
3k
0.94
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0.90
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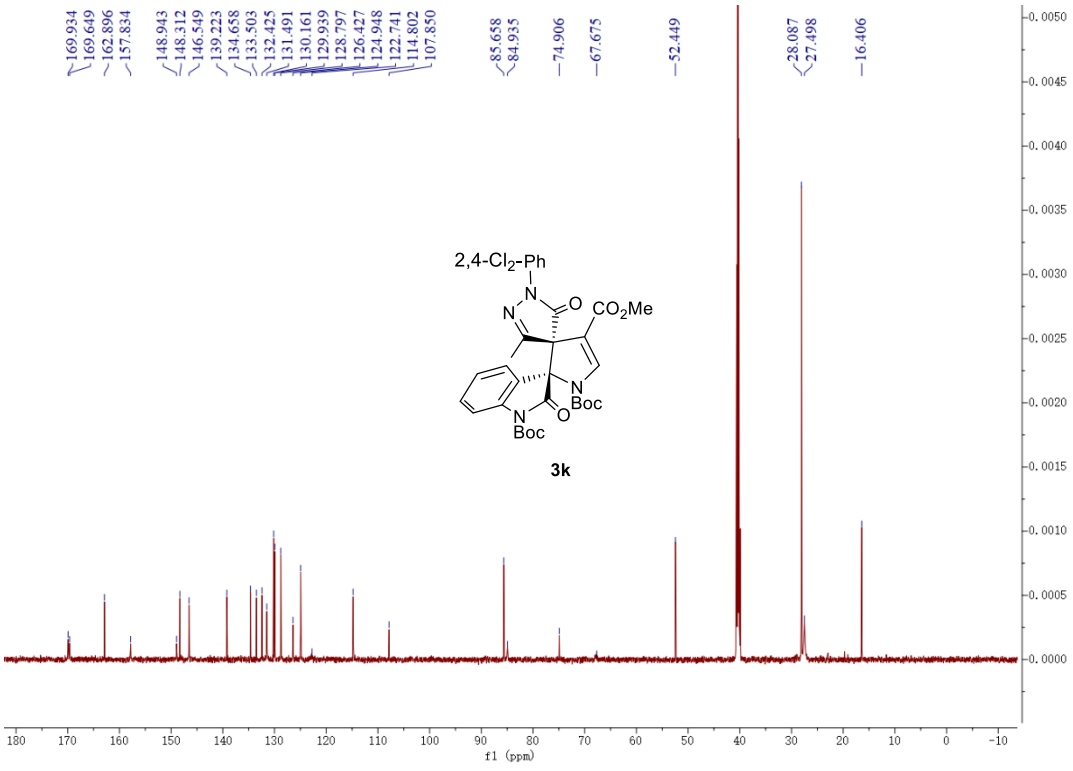
0.78
0.95
1.06
1.06
3.02
3.16
9.02
9.04
f1 (ppm)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129.939
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124.948
122.741
114.802
107.850
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84.935
74.906
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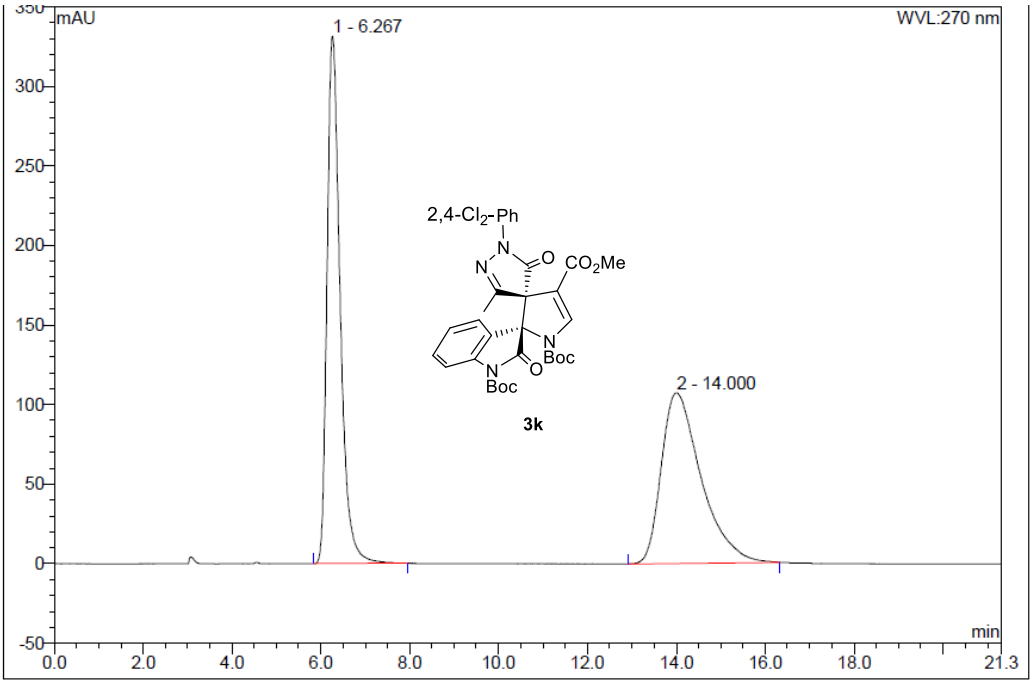
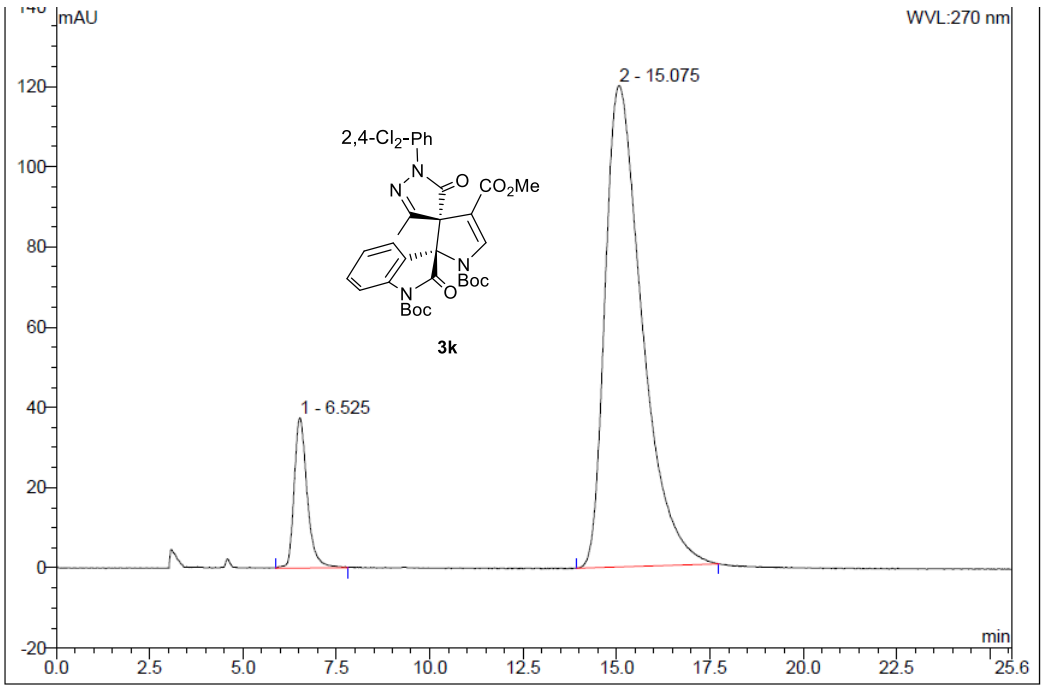
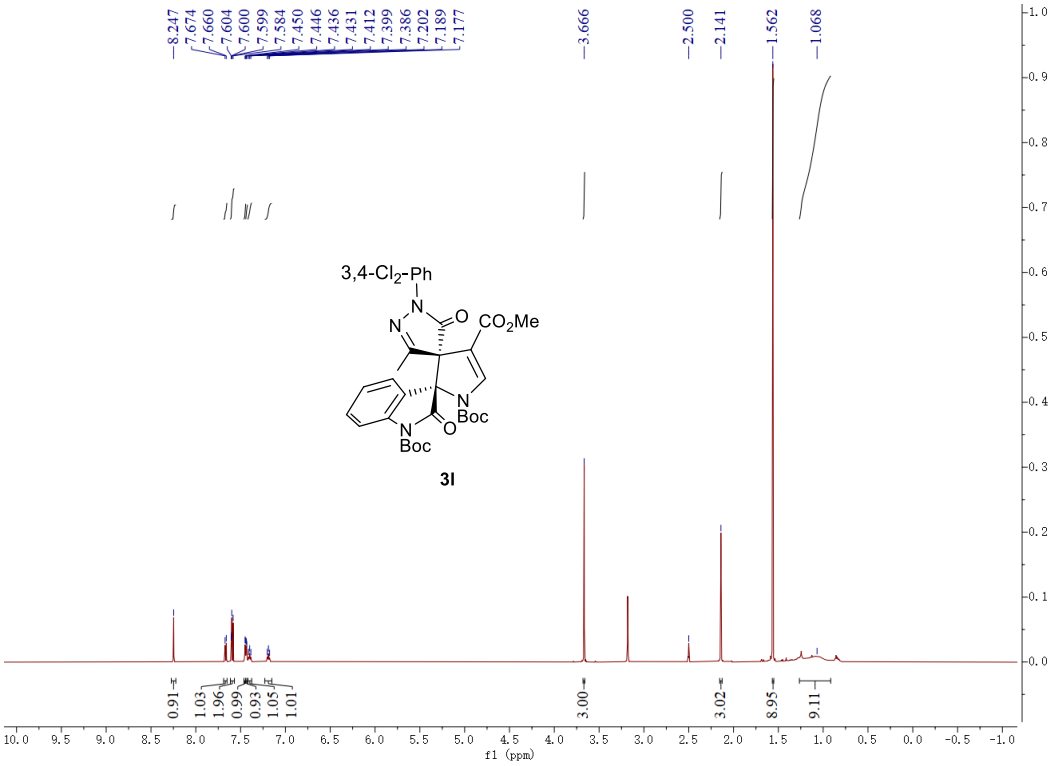
28.087
27.498
16.406
2,4-Cl2-Ph
CO2Me
Boc
Boc
3k
f1 (ppm)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.27	n.a.	331.260	113.142	50.47	n.a.	BMB
2	14.00	n.a.	107.190	111.016	49.53	n.a.	BMB
Total:			438.450	224.158	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.53	n.a.	37.441	15.135	9.87	n.a.	BMB
2	15.08	n.a.	119.958	138.219	90.13	n.a.	BMB
Total:			157.399	153.354	100.00	0.000	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7.446
7.436
7.431
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7.386
7.202
7.189
7.177
3.666
2.500
2.141
1.562
1.068
3,4-Cl2-Ph
CO2Me
Boc
Boc
3l
0.91
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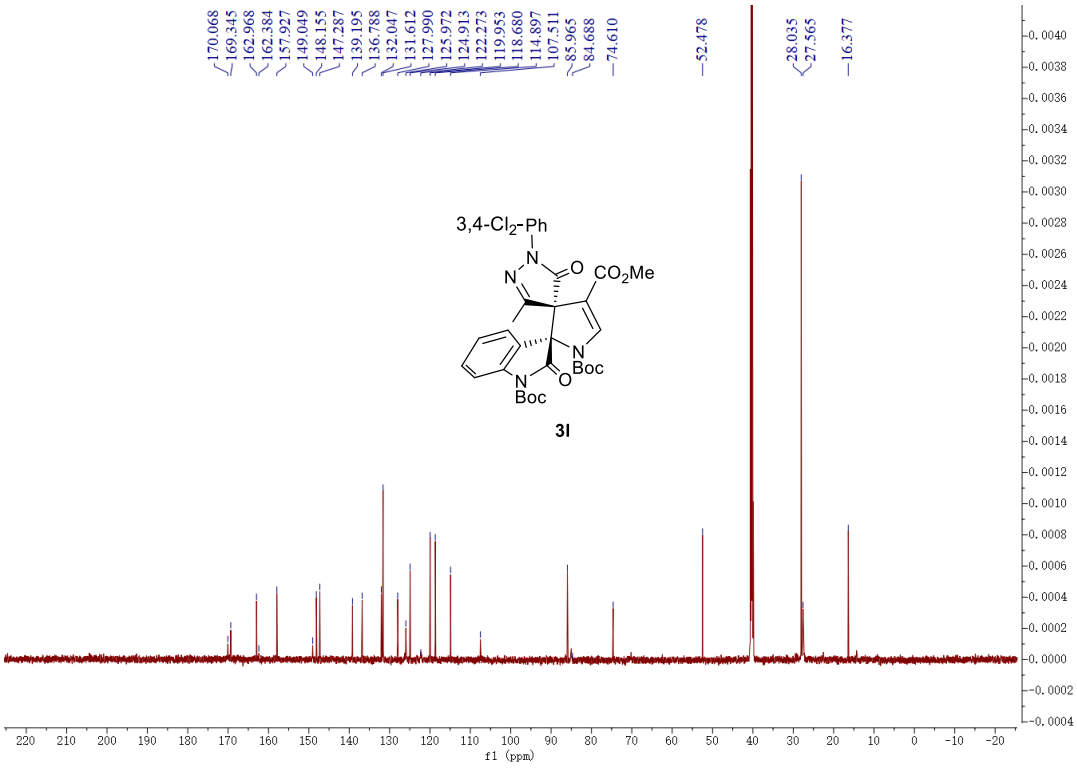
0.99
0.93
1.05
1.01
3.00
3.02
8.95
9.11
f1 (ppm)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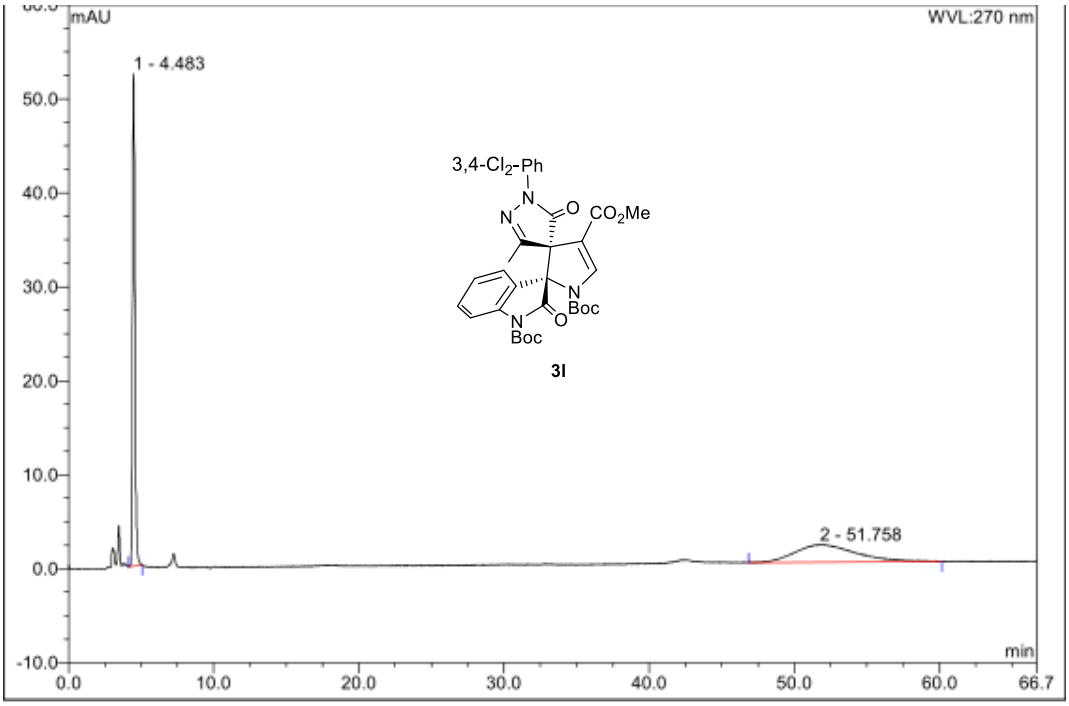
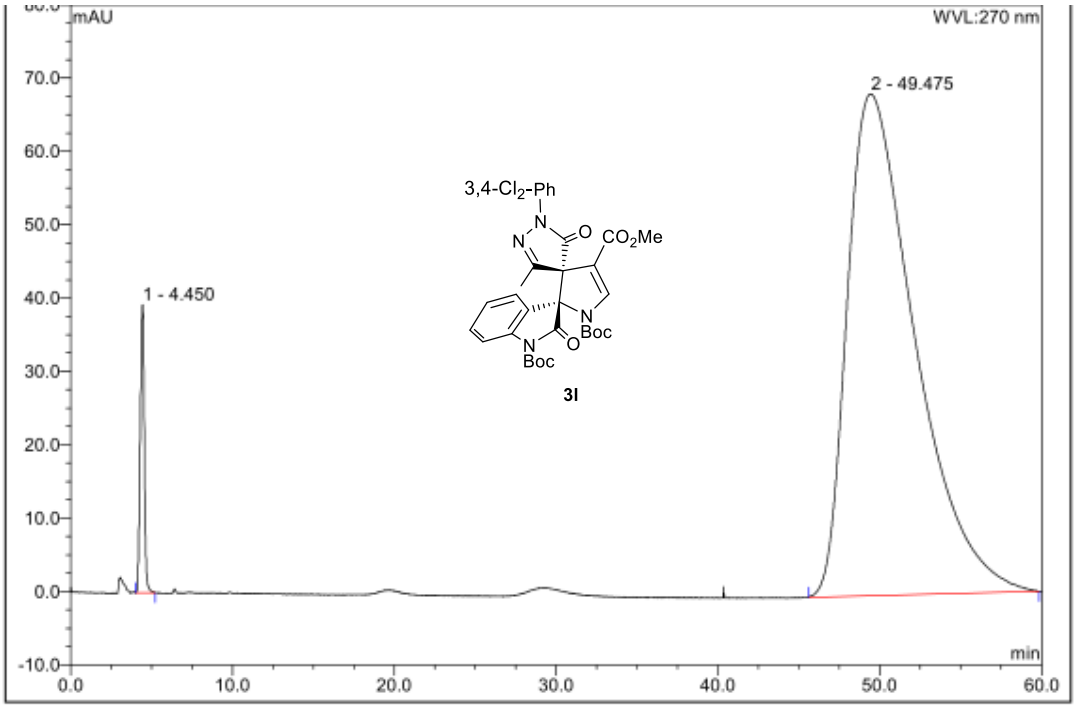
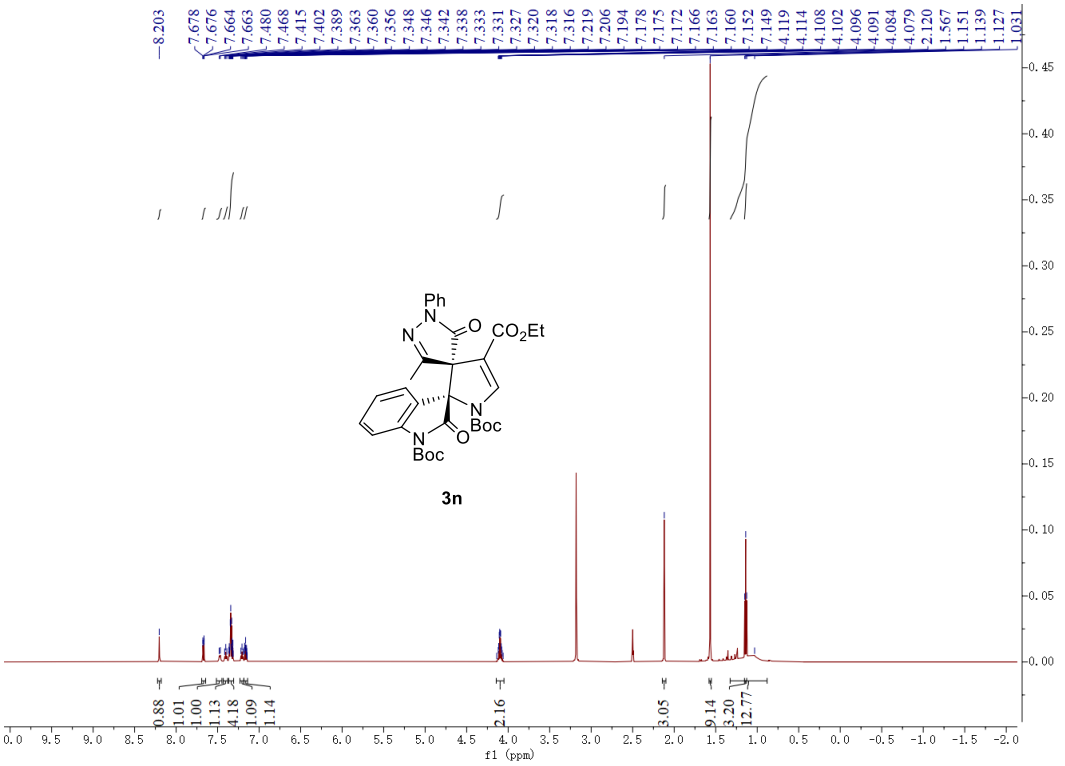
127.990
125.972
124.913
122.273
119.953
118.680
114.897
107.511
85.965
84.688
74.610
52.478
28.035
27.565
16.377
3,4-Cl2-Ph
CO2Me
Boc
Boc
3l
f1 (ppm)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	4.48	n.a.	52.366	9.740	50.91	n.a.	BMB*
2	51.76	n.a.	1.896	9.390	49.09	n.a.	BMB*
Total:			54.262	19.130	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	4.45	n.a.	39.353	11.505	3.37	n.a.	BMB*
2	49.48	n.a.	68.401	330.331	96.63	n.a.	BMB*
Total:			107.754	341.836	100.00	0.000	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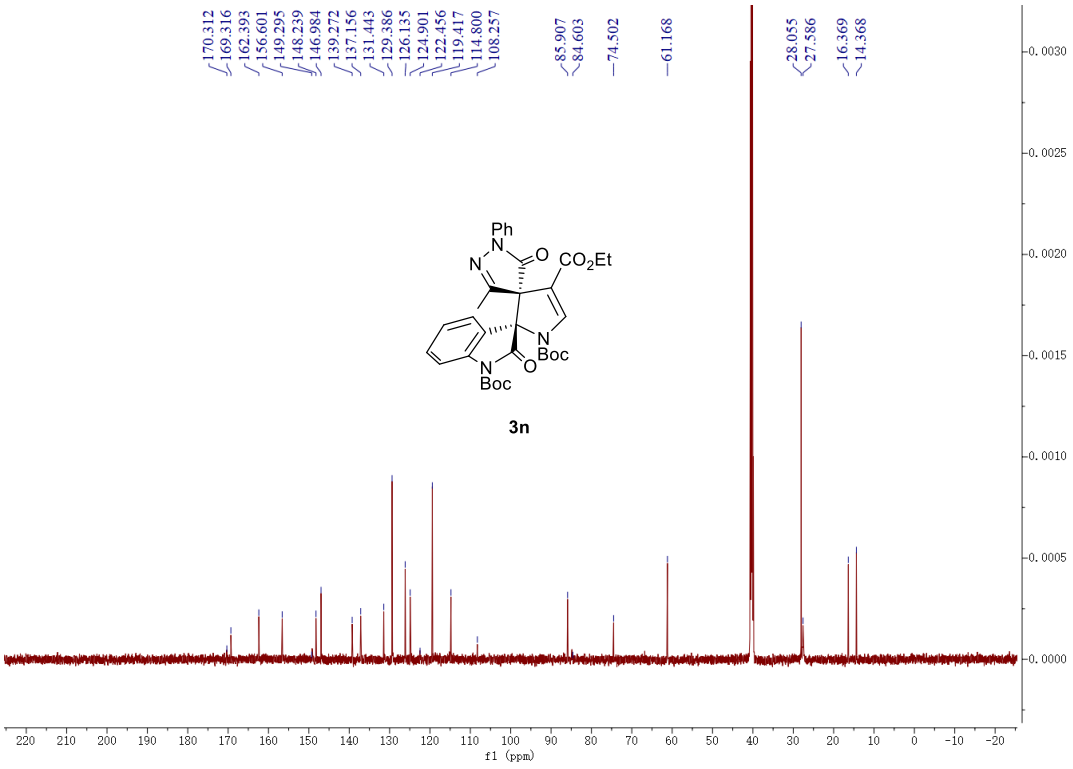
7.676
7.664
7.663
7.480
7.468
7.415
7.402
7.389
7.363
7.360
7.356
7.348
7.346
7.342
7.338
7.333
7.331
7.327
7.320
7.318
7.316
7.219
7.206
7.194
7.178
7.175
7.172
7.166
7.163
7.160
7.152
7.149
4.119
4.114
4.108
4.102
4.096
4.091
4.084
4.079
2.120
1.567
1.151
1.139
1.127
1.031
0.88
1.01
1.00
1.13
4.18
1.09
1.14
2.16
3.05
9.14
3.20
12.77
f1 (ppm)

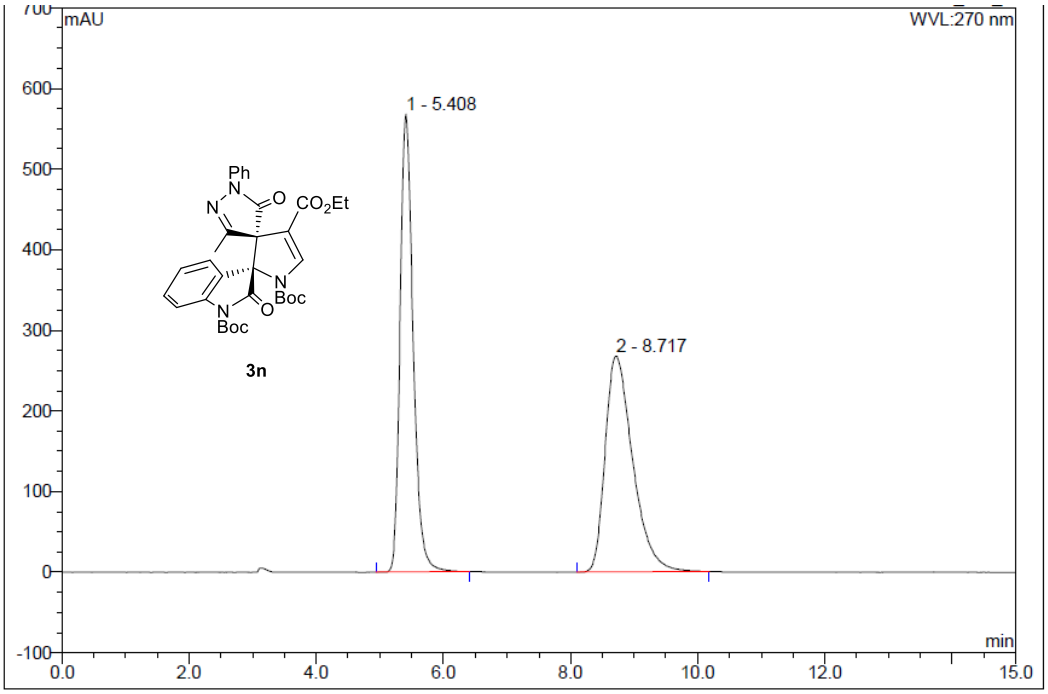
Ph
N
N
O
CO2Et
N
Boc
O
N
Boc

3n

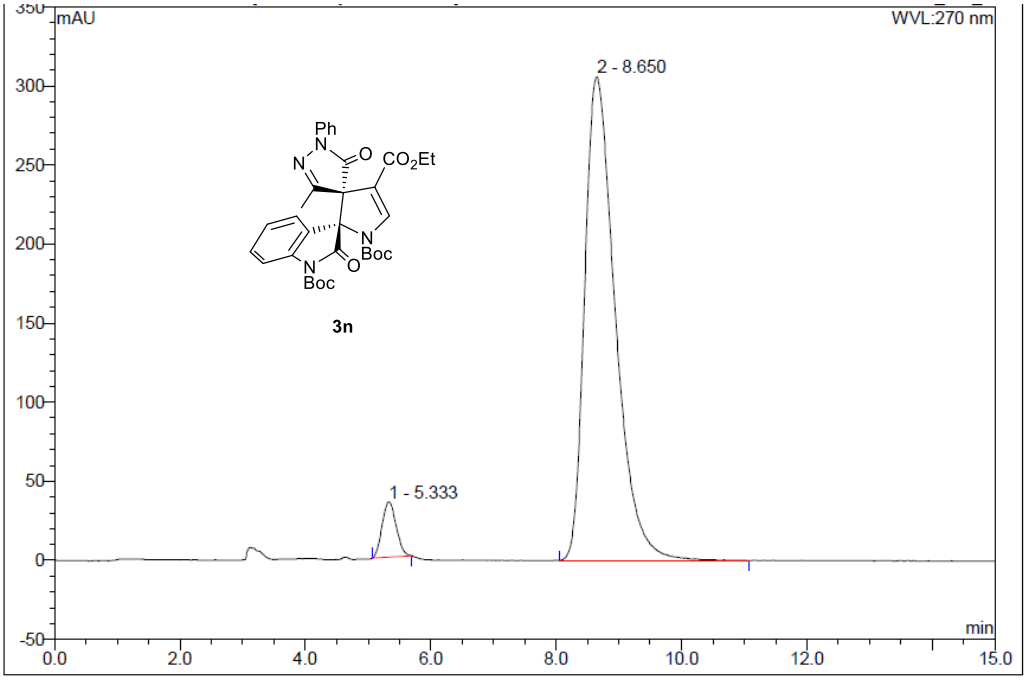

170.312
169.316
162.393
156.601
149.295
148.239
146.984
139.272
137.156
131.443
129.386
126.135
124.901
122.456
119.417
114.800
108.257
85.907
84.603
74.502
61.168
28.055
27.586
16.369
14.368
f1 (ppm)

Ph
N
N
O
CO2Et
N
Boc
O
N
Boc

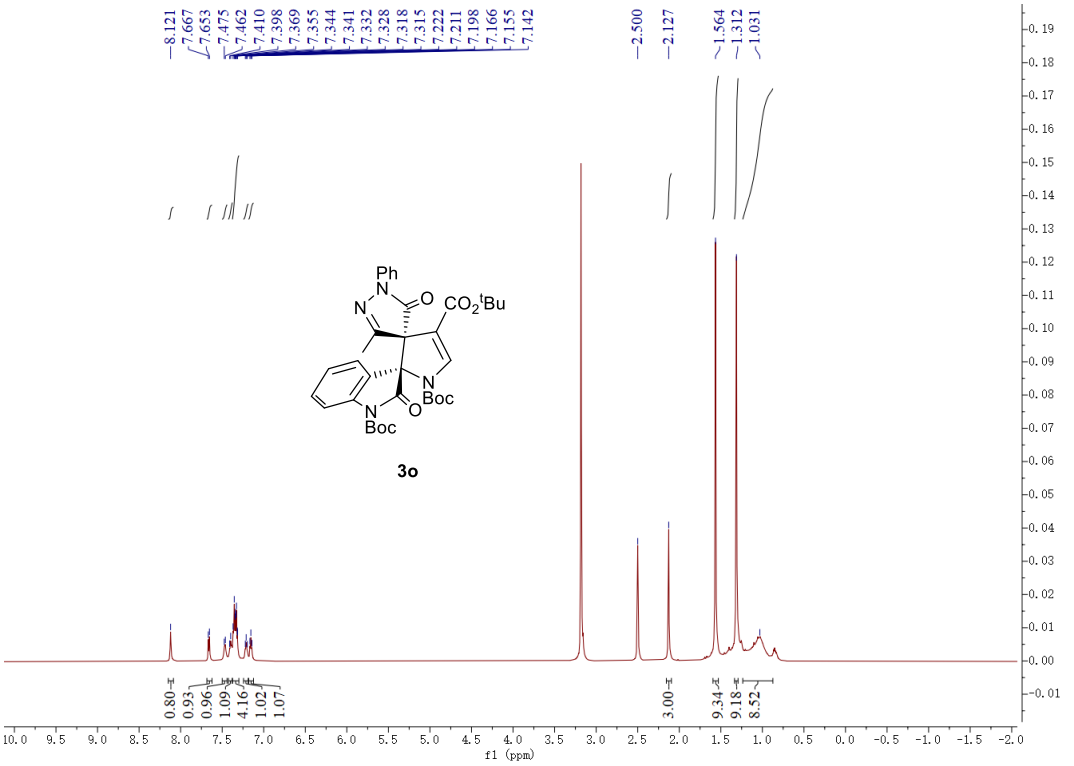
3n



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.41	n.a.	567.900	134.997	50.03	n.a.	BMB
2	8.72	n.a.	267.937	134.824	49.97	n.a.	BMB
Total:			835.837	269.820	100.00	0.000	

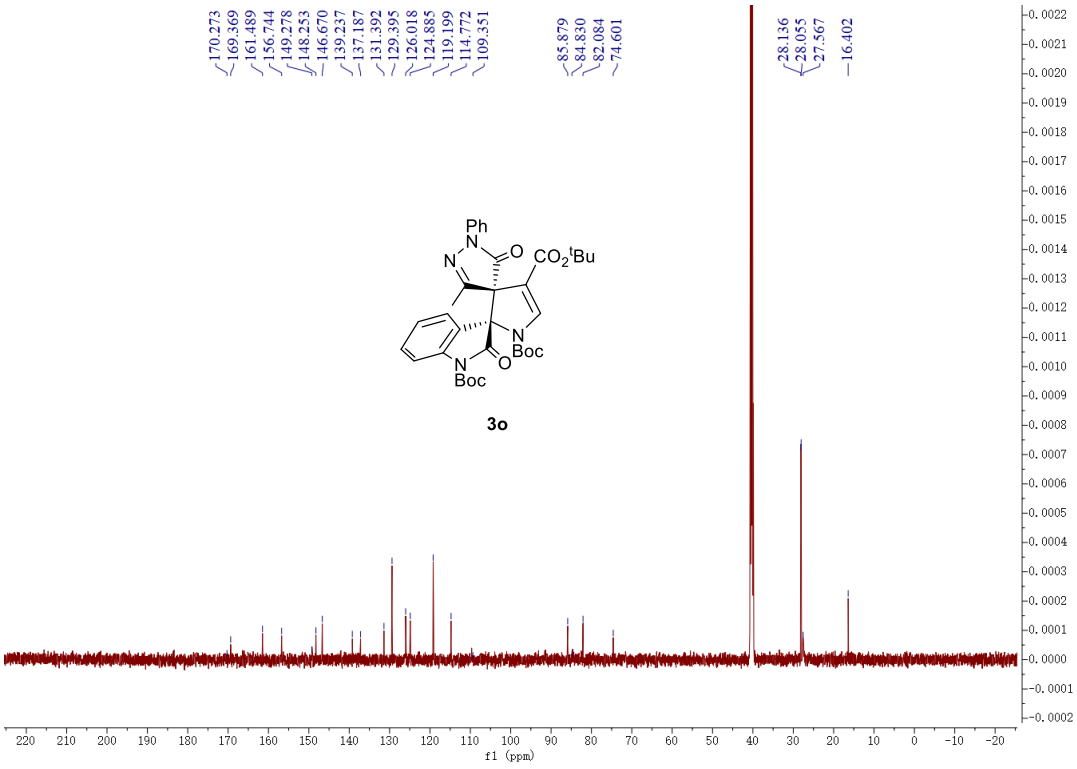


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.33	n.a.	34.902	9.082	5.00	n.a.	BMB*
2	8.65	n.a.	305.654	172.625	95.00	n.a.	BMB*
Total:			340.556	181.707	100.00	0.000	


8.121
7.667
7.653
7.475
7.462
7.410
7.398
7.369
7.355
7.344
7.341
7.332
7.328
7.318
7.315
7.222
7.211
7.198
7.166
7.155
7.142
2.500
2.127
1.564
1.312
1.031
0.80
0.93
0.96
1.09
4.16
1.02
1.07
3.00
9.34
9.18
8.52
f1 (ppm)

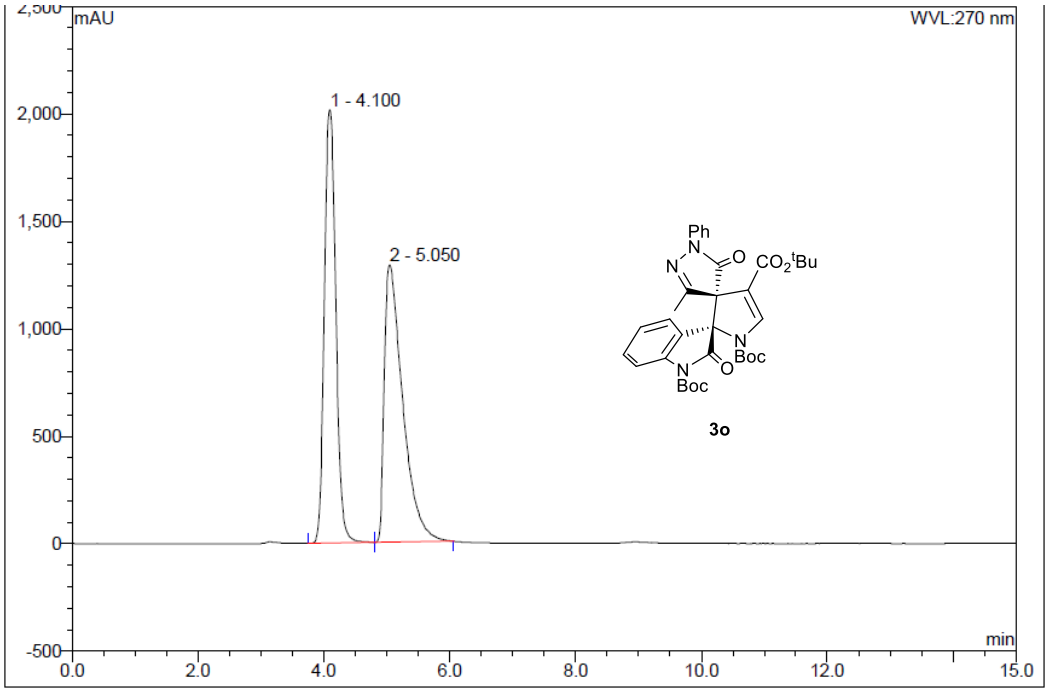
Ph
N
N
O
CO2tBu
N
Boc
O
N
Boc

3o

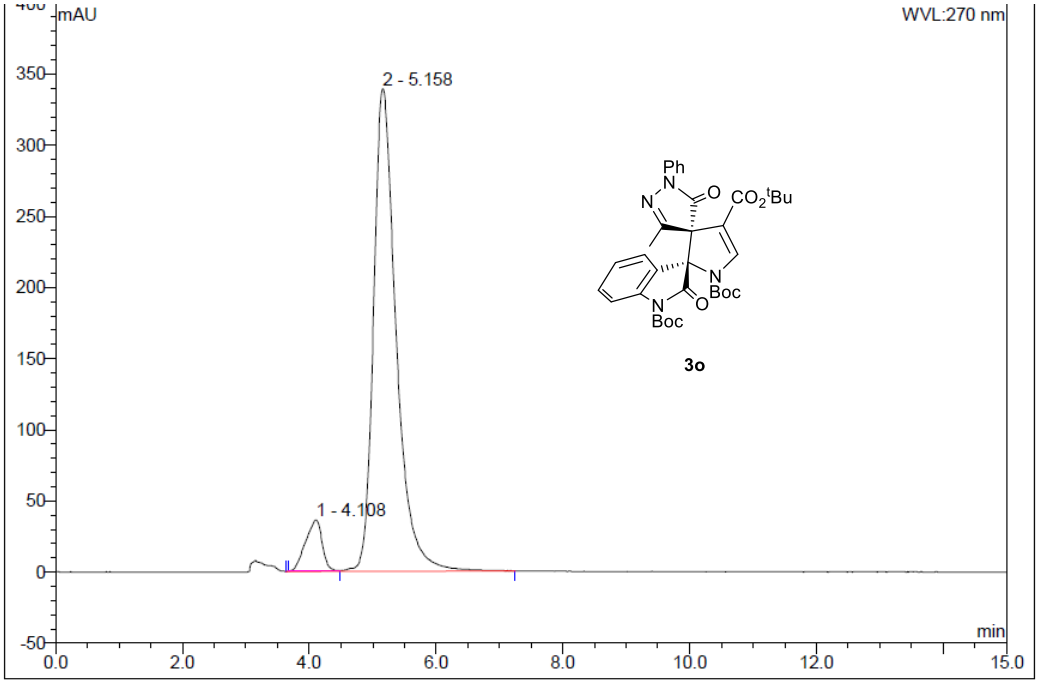

170.273
169.369
161.489
156.744
149.278
148.253
146.670
139.237
137.187
131.392
129.395
126.018
124.885
119.199
114.772
109.351
85.879
84.830
82.084
74.601
28.136
28.055
27.567
16.402
f1 (ppm)

Ph
N
N
O
CO2tBu
N
Boc
O
N
Boc

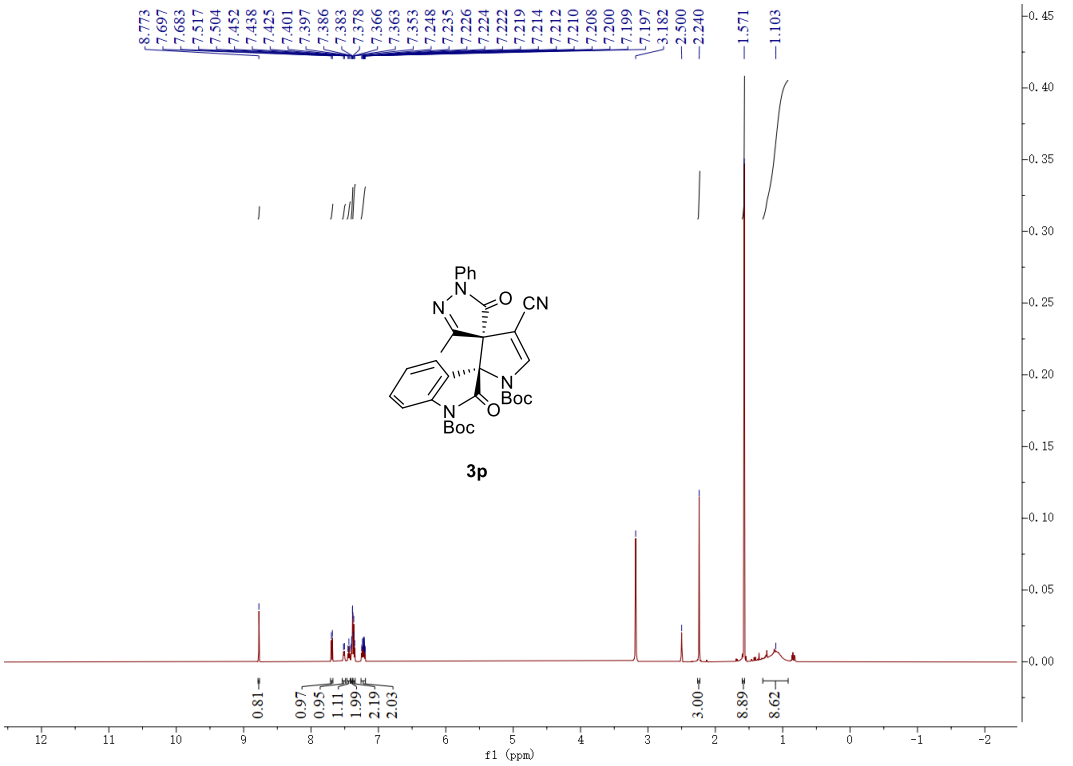
3o

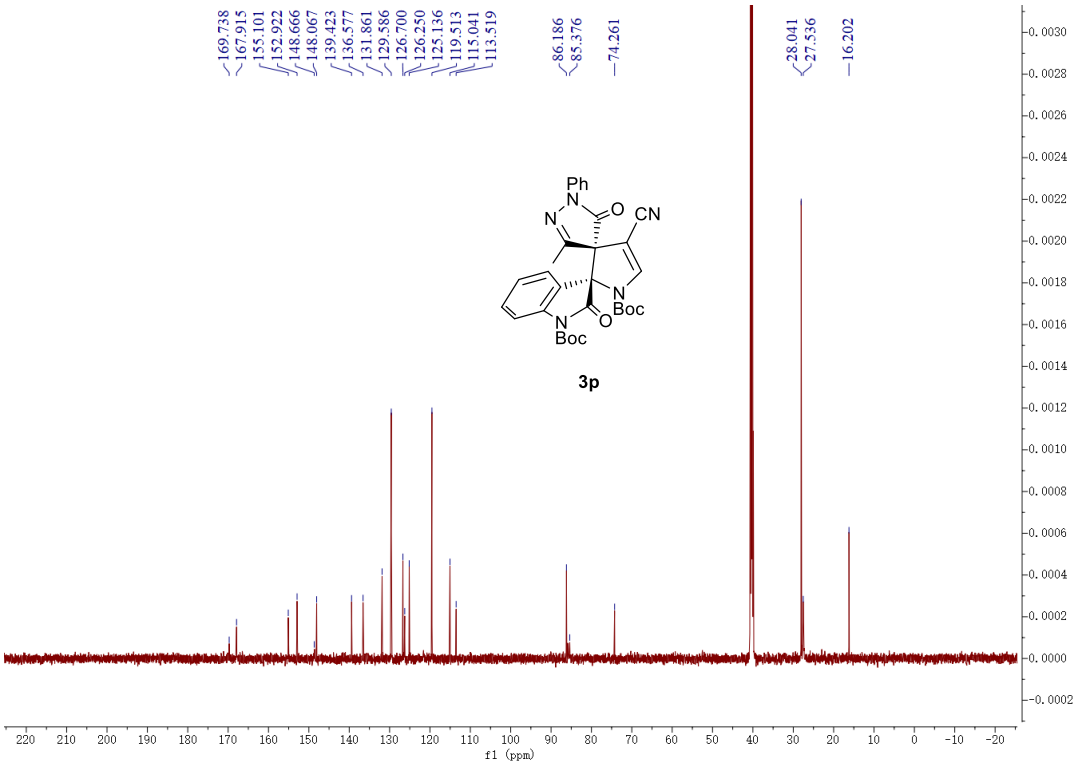


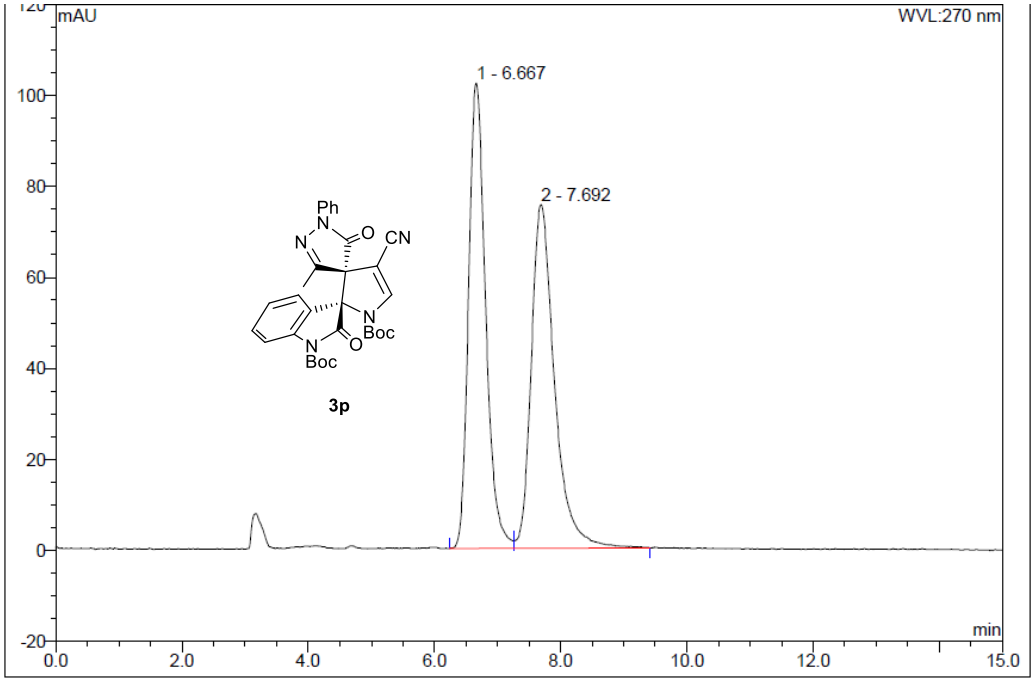
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	4.10	n.a.	2017.846	428.348	49.43	n.a.	BM *
2	5.05	n.a.	1290.814	438.288	50.57	n.a.	MB*
Total:			3308.660	866.636	100.00	0.000	



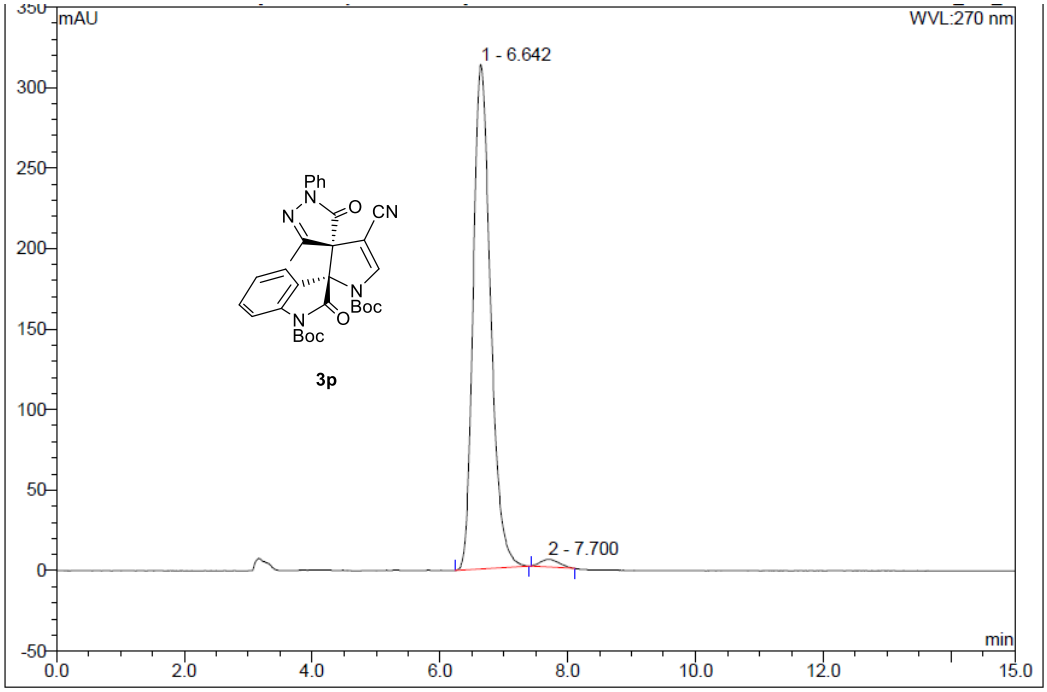
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	4.11	n.a.	35.734	10.849	7.18	n.a.	Ru
2	5.16	n.a.	339.395	140.308	92.82	n.a.	BMB
Total:			375.128	151.157	100.00	0.000	


8.773
7.697
7.683
7.517
7.504
7.452
7.438
7.425
7.401
7.397
7.386
7.383
7.378
7.366
7.363
7.353
7.248
7.235
7.226
7.224
7.222
7.219
7.214
7.212
7.210
7.208
7.200
7.199
7.197
3.182
2.500
2.240
1.571
1.103
Ph
N
N
O
CN
N
Boc
O
N
Boc
3p
0.81
0.97
0.95
1.11
1.99
2.19
2.03
3.00
8.89
8.62
f1 (ppm)

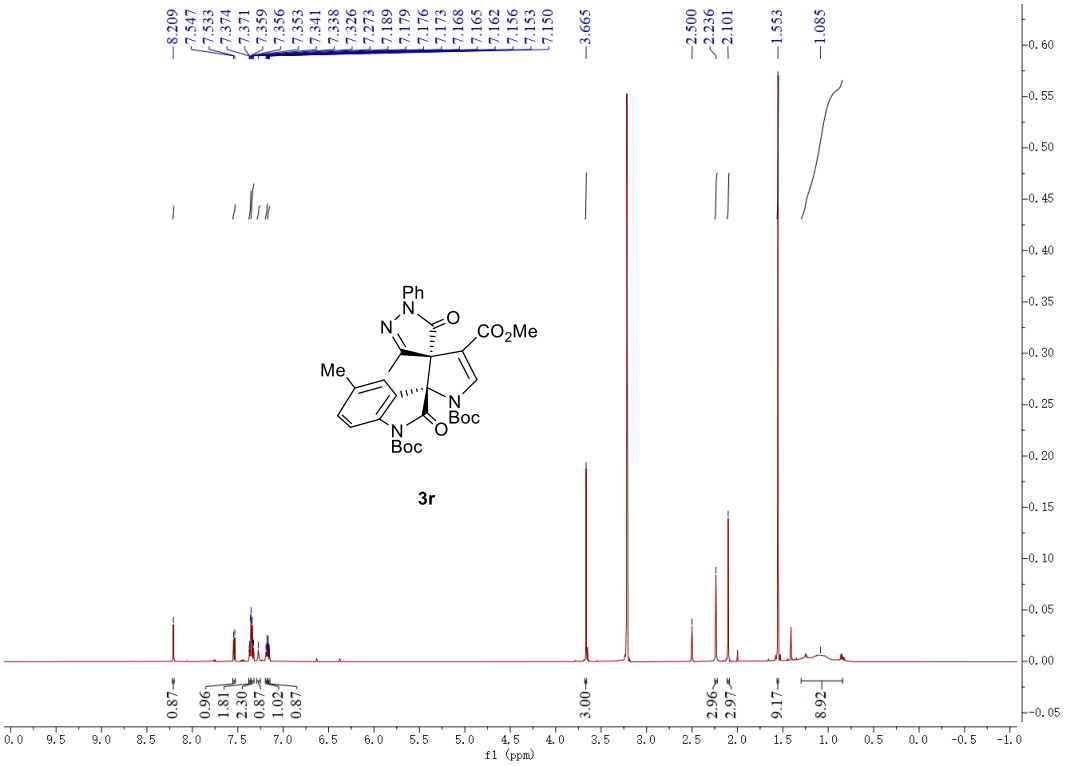

169.738
167.915
155.101
152.922
148.666
148.067
139.423
136.577
131.861
129.586
126.700
126.250
125.136
119.513
115.041
113.519
86.186
85.376
74.261
28.041
27.536
16.202
Ph
N
N
O
CN
N
Boc
O
N
Boc
3p
f1 (ppm)



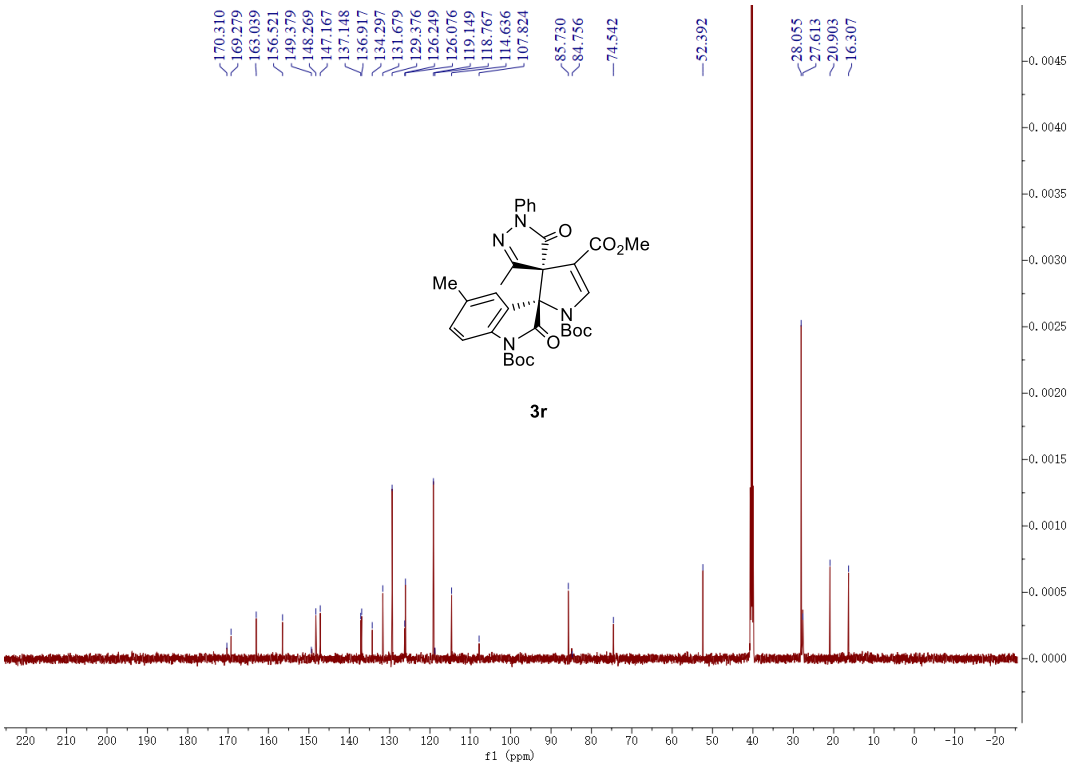
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.67	n.a.	102.246	31.971	49.75	n.a.	BM
2	7.69	n.a.	75.549	32.287	50.25	n.a.	MB
Total:			177.795	64.258	100.00	0.000	



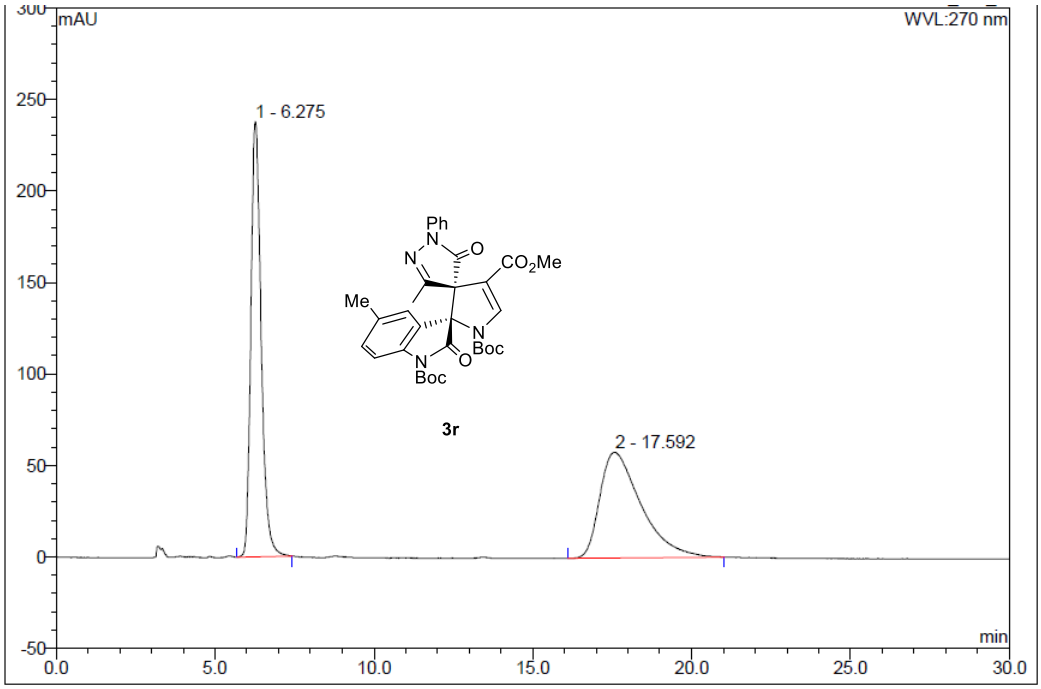
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.64	n.a.	313.052	98.808	98.38	n.a.	BMB
2	7.70	n.a.	4.772	1.630	1.62	n.a.	BMB*
Total:			317.823	100.438	100.00	0.000	


8.209
7.547
7.533
7.374
7.371
7.359
7.356
7.353
7.341
7.338
7.326
7.273
7.189
7.179
7.176
7.173
7.168
7.165
7.162
7.156
7.153
7.150
3.665
2.500
2.236
2.101
1.553
1.085
Ph
N
N
O
CO2Me
Me
N
Boc
O
N
Boc
0.87
0.96
1.81
2.30
0.87
1.02
0.87
3.00
2.96
2.97
9.17
8.92
f1 (ppm)

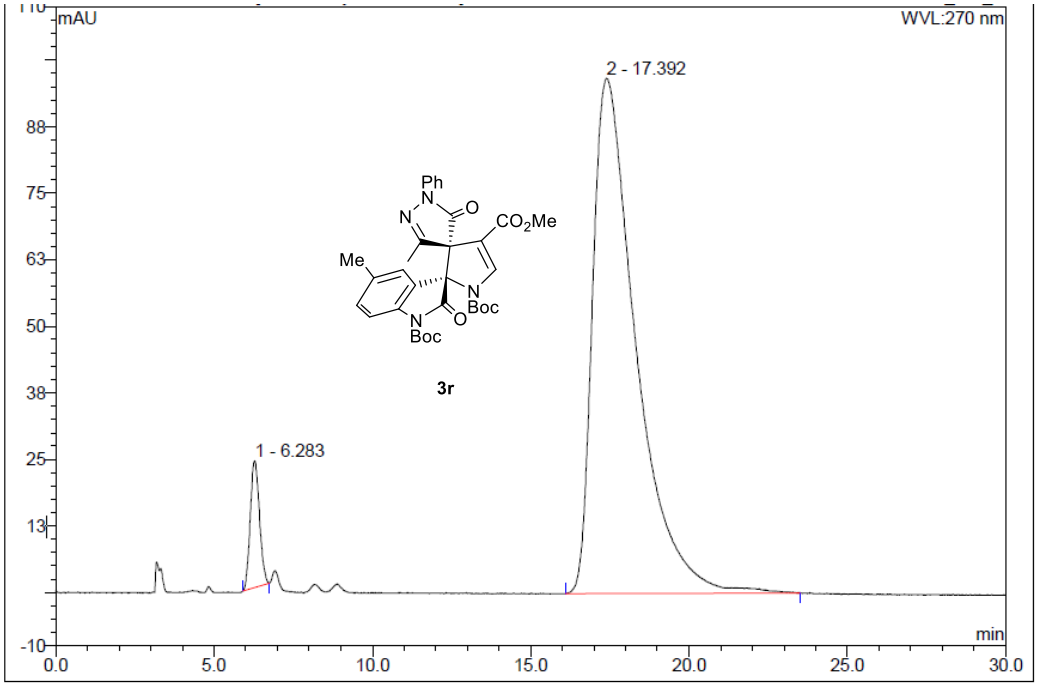
3r


170.310
169.279
163.039
156.521
149.379
148.269
147.167
137.148
136.917
134.297
131.679
129.376
126.249
126.076
119.149
118.767
114.636
107.824
85.730
84.756
74.542
52.392
28.055
27.613
20.903
16.307
Ph
N
N
O
CO2Me
Me
N
Boc
O
N
Boc
f1 (ppm)

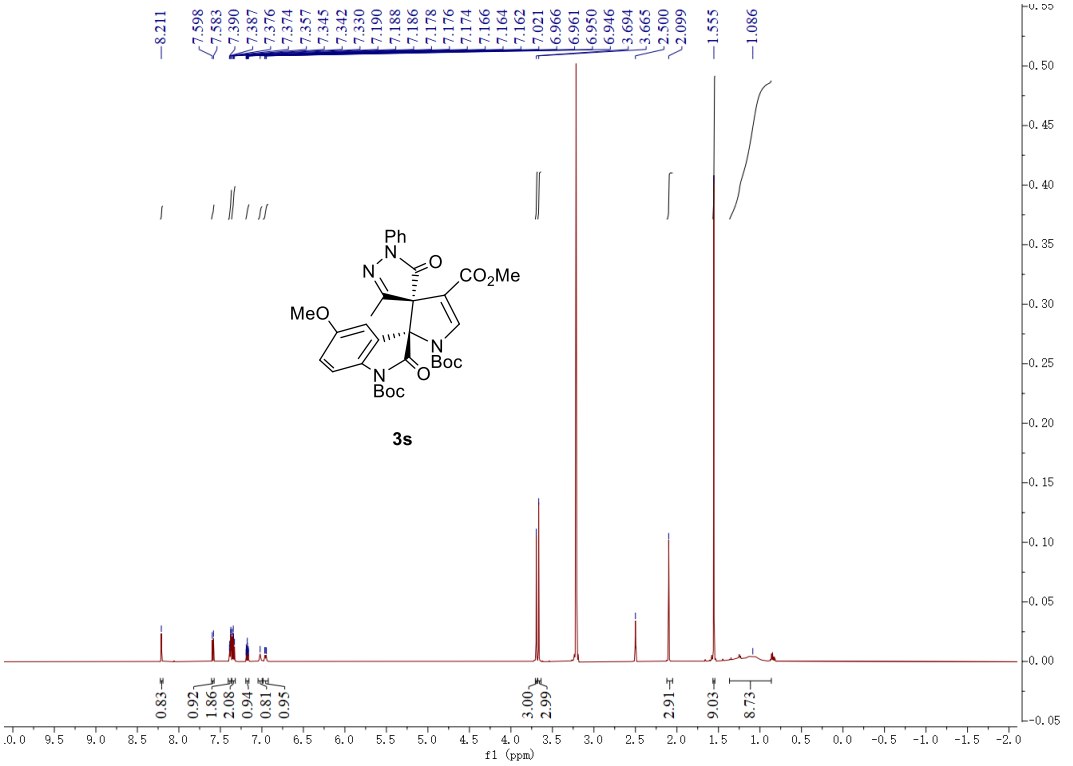
3r



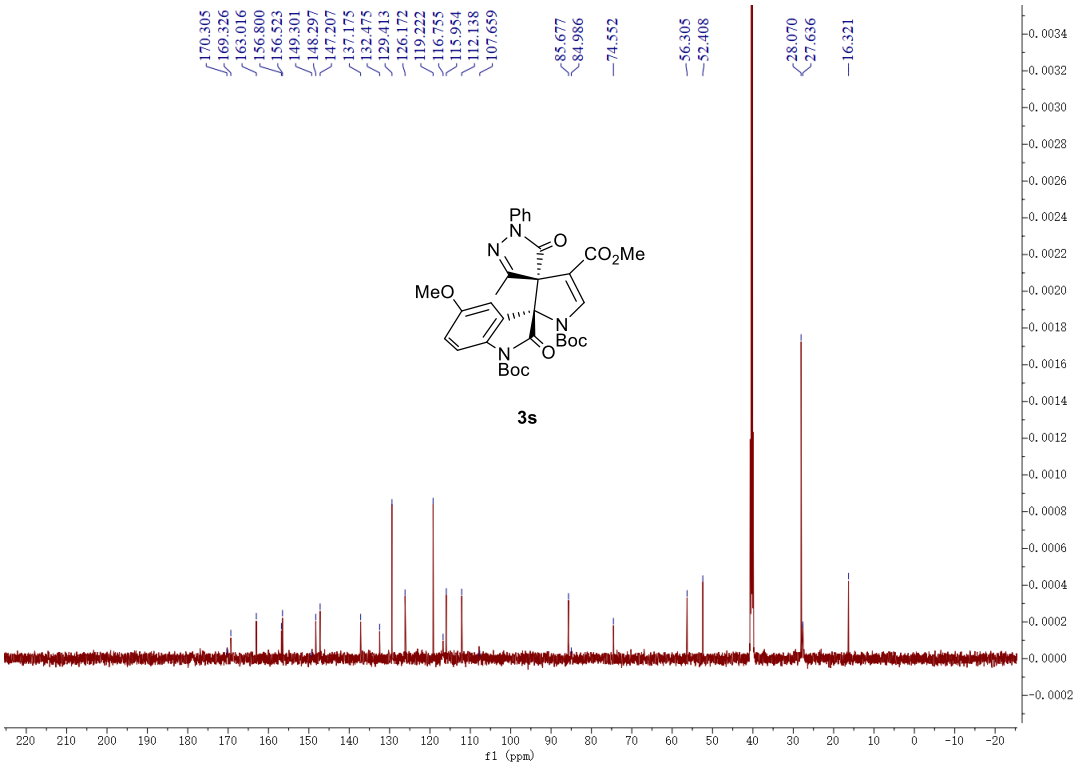
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.28	n.a.	237.891	88.944	50.57	n.a.	BMB
2	17.59	n.a.	57.778	86.946	49.43	n.a.	BMB
Total:			295.669	175.890	100.00	0.000	



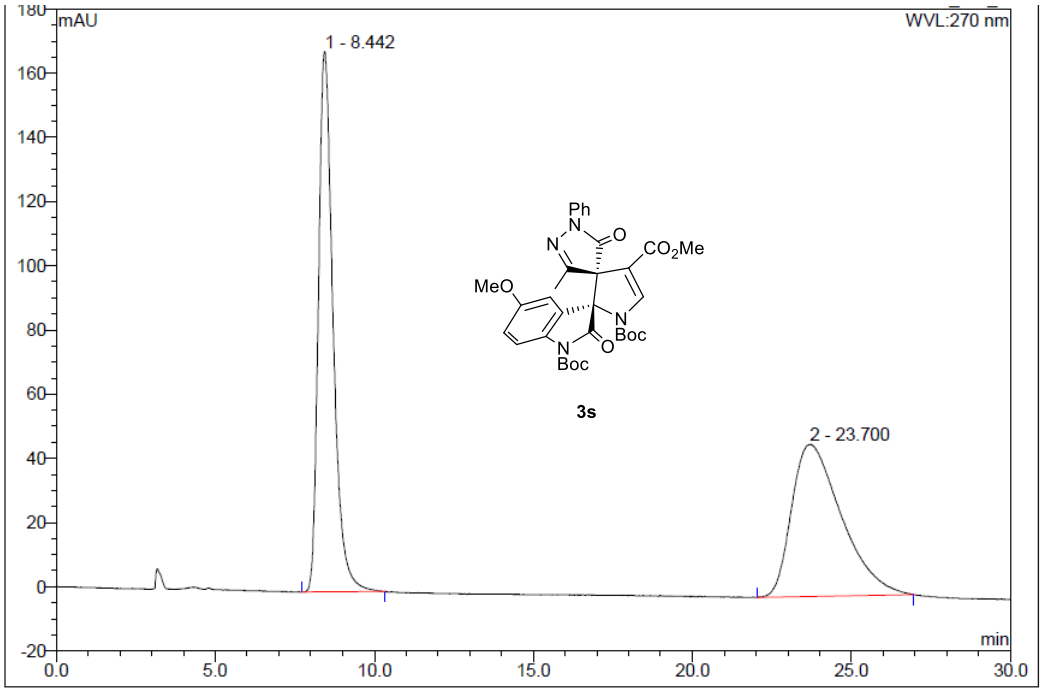
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.28	n.a.	23.788	8.029	5.00	n.a.	BMB
2	17.39	n.a.	96.726	152.666	95.00	n.a.	BMB*
Total:			120.514	160.695	100.00	0.000	


8.211
7.598
7.583
7.390
7.387
7.376
7.374
7.357
7.345
7.342
7.330
7.190
7.188
7.186
7.178
7.176
7.174
7.166
7.164
7.162
7.021
6.966
6.961
6.950
6.946
3.694
3.665
2.500
2.099
1.555
1.086
Ph
N
N
O
CO2Me
MeO
N
Boc
O
N
Boc
0.83
0.92
1.86
2.08
0.94
0.81
0.95
3.00
2.99
2.91
9.03
8.73
f1 (ppm)

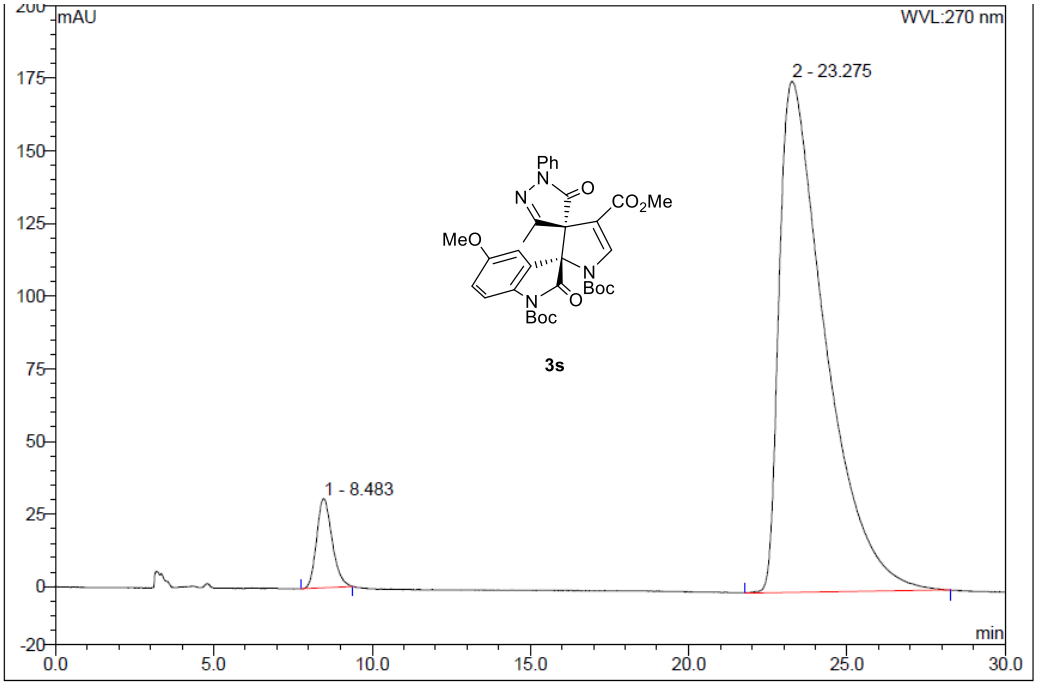
3s


170.305
169.326
163.016
156.800
156.523
149.301
148.297
147.207
137.175
132.475
129.413
126.172
119.222
116.755
115.954
112.138
107.659
85.677
84.986
74.552
56.305
52.408
28.070
27.636
16.321
Ph
N
N
O
CO2Me
MeO
N
Boc
O
N
Boc
f1 (ppm)

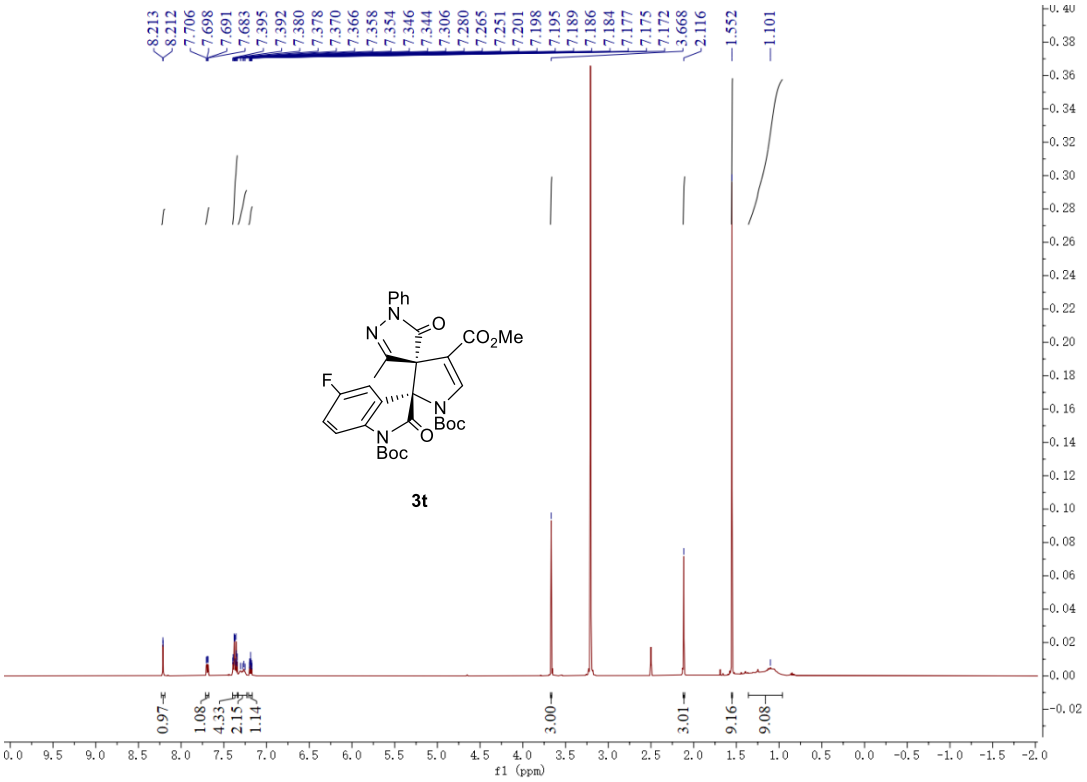
3s



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.44	n.a.	168.399	89.876	51.10	n.a.	BMB
2	23.70	n.a.	47.380	86.005	48.90	n.a.	BMB
Total:			215.779	175.881	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.48	n.a.	30.663	17.413	5.54	n.a.	BMB*
2	23.28	n.a.	175.808	296.723	94.46	n.a.	BMB*
Total:			206.471	314.136	100.00	0.000	


8.213
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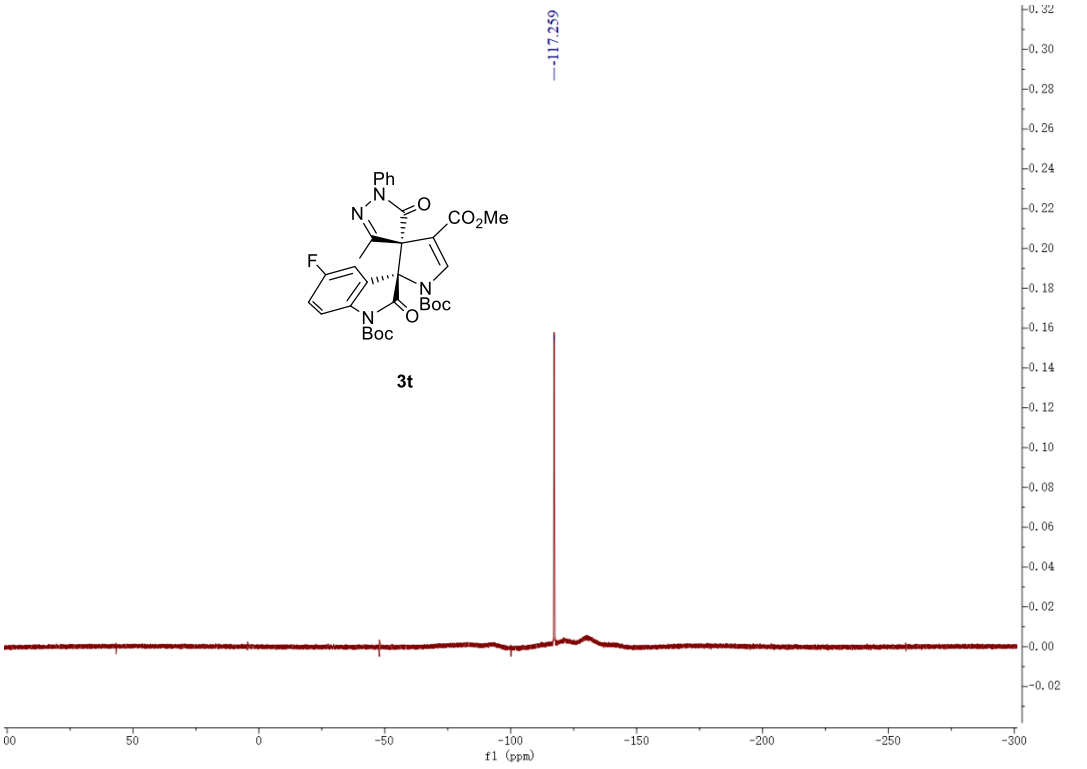
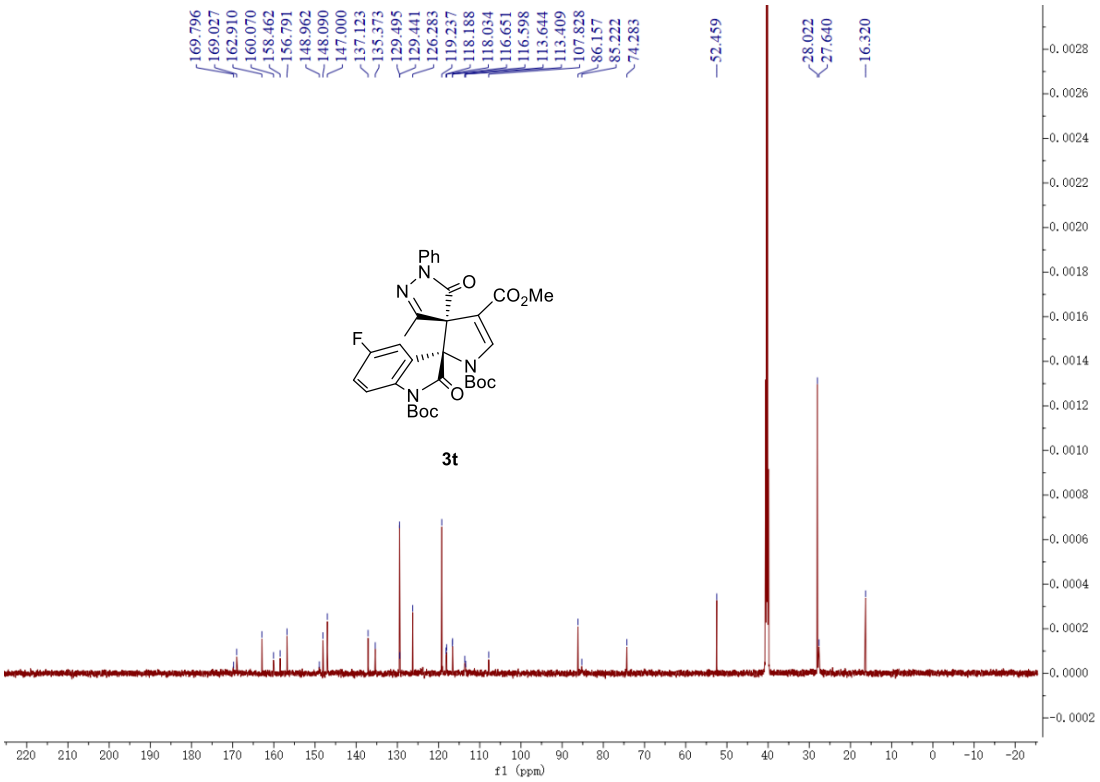
7.706
7.698
7.691
7.683
7.395
7.392
7.380
7.378
7.370
7.366
7.358
7.354
7.346
7.344
7.306
7.280
7.265
7.251
7.201
7.198
7.195
7.189
7.186
7.184
7.177
7.175
7.172
3.668
2.116
1.552
1.101
Ph
N
N
O
CO2Me
F
N
Boc
O
N
Boc
0.97
1.08
4.33
2.15
1.14
3.00
3.01
9.16
9.08
f1 (ppm)

3t


-117.259
Ph
N
N
O
CO2Me
F
N
Boc
O
N
Boc
f1 (ppm)

3t


169.796
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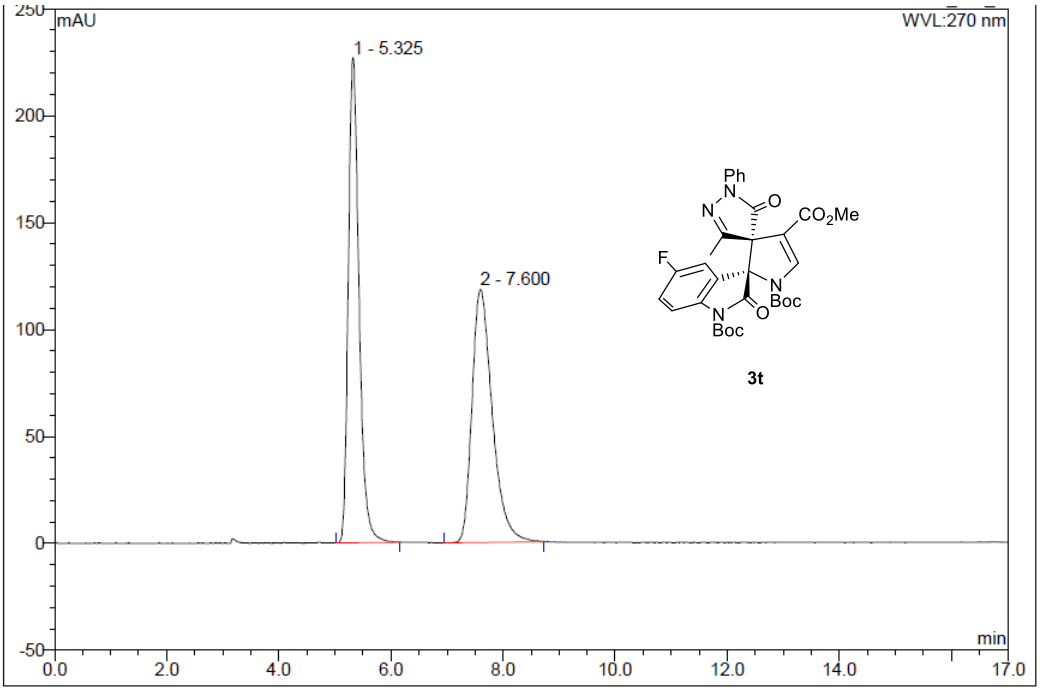
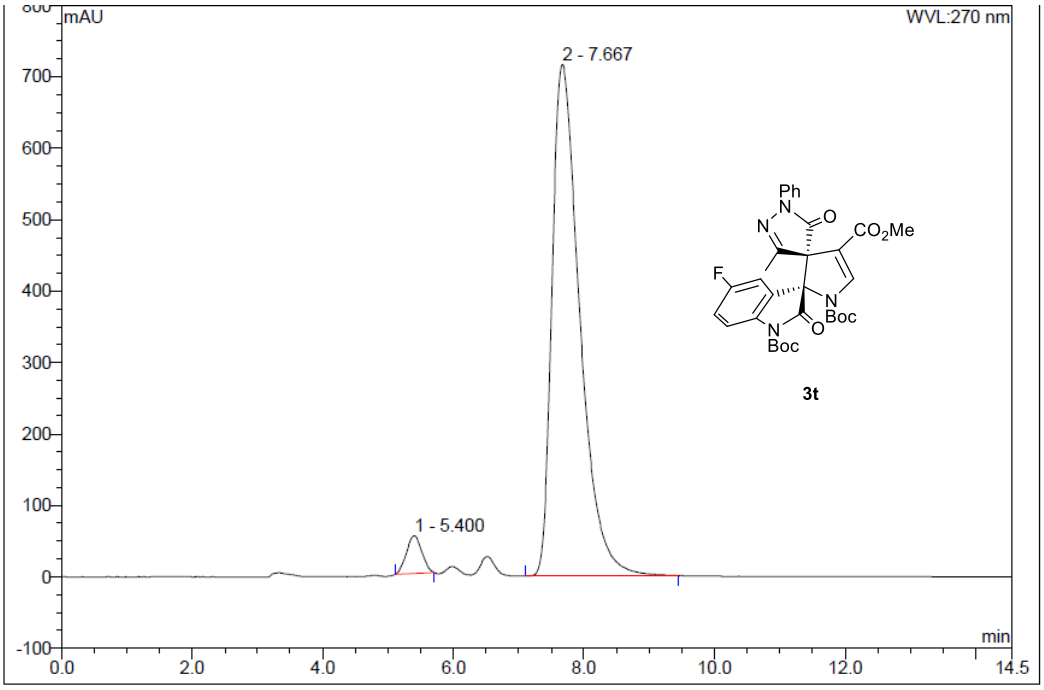
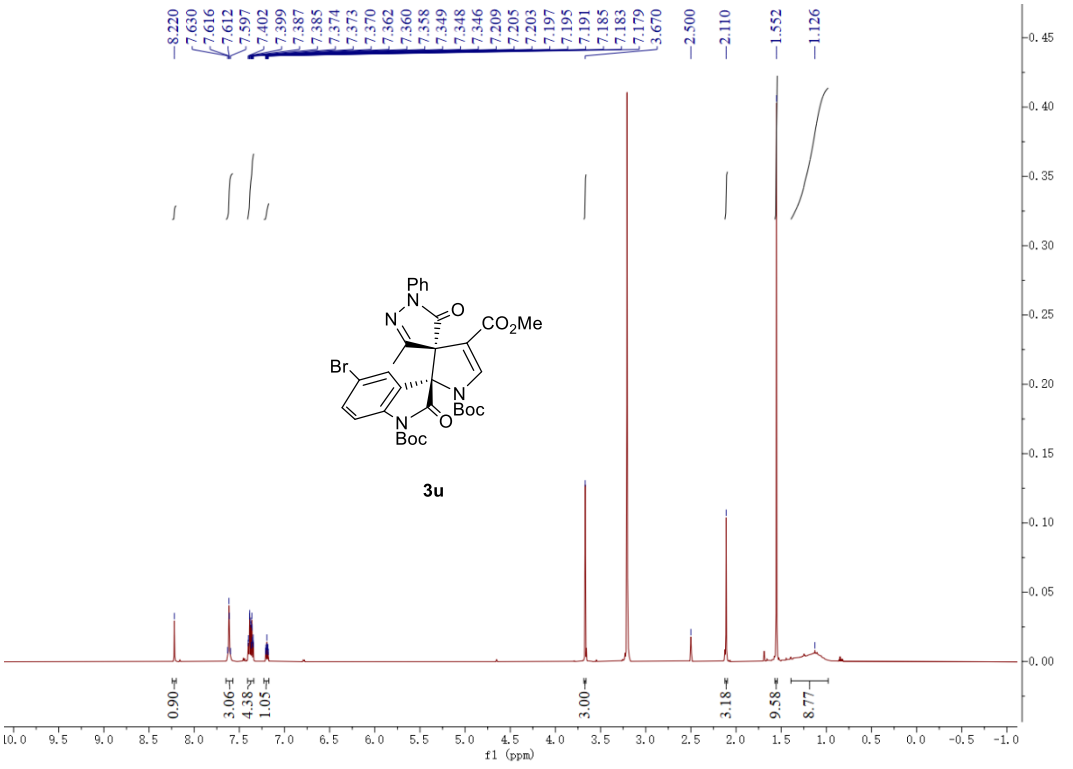
158.462
156.791
148.962
148.090
147.000
137.123
135.373
129.495
129.441
126.283
119.237
118.188
118.034
116.651
116.598
113.644
113.409
107.828
86.157
85.222
74.283
52.459
28.022
27.640
16.320
Ph
N
N
O
CO2Me
F
N
Boc
N
Boc
O
3t
f1 (ppm)



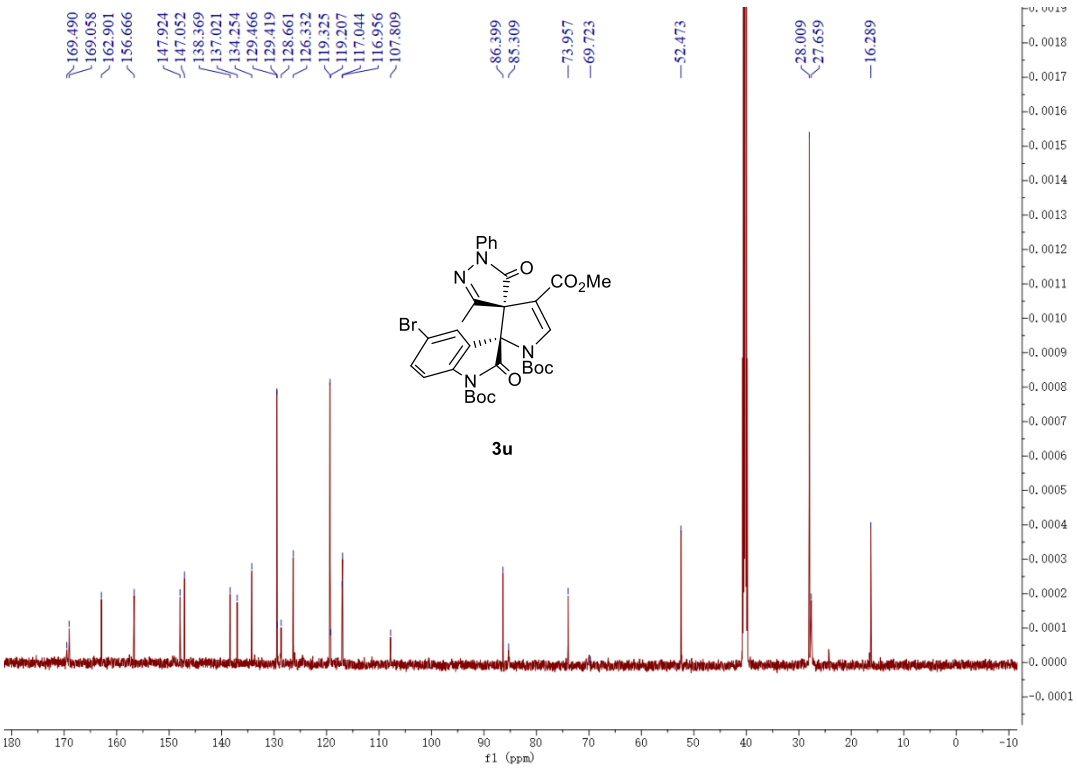
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.33	n.a.	227.058	50.228	50.34	n.a.	BMB
2	7.60	n.a.	118.445	49.545	49.66	n.a.	BMB
Total:			345.503	99.773	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.40	n.a.	52.297	14.260	3.89	n.a.	BMB*
2	7.67	n.a.	716.217	352.748	96.11	n.a.	BMB*
Total:			768.514	367.008	100.00	0.000	


8.220
7.630
7.616
7.612
7.597
7.402
7.399
7.387
7.385
7.374
7.373
7.370
7.362
7.360
7.358
7.349
7.348
7.346
7.209
7.205
7.203
7.197
7.195
7.191
7.185
7.183
7.179
3.670
2.500
2.110
1.552
1.126
0.90
3.06
4.38
1.05
3.00
3.18
9.58
8.77
f1 (ppm)
Ph
N
N
O
CO2Me
Br
N
Boc
O
N
Boc

3u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147.052
138.369
137.021
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129.466
129.419
128.661
126.332
119.325
119.207
117.044
116.956
107.809
86.399
85.309
73.957
69.723
52.473
28.009
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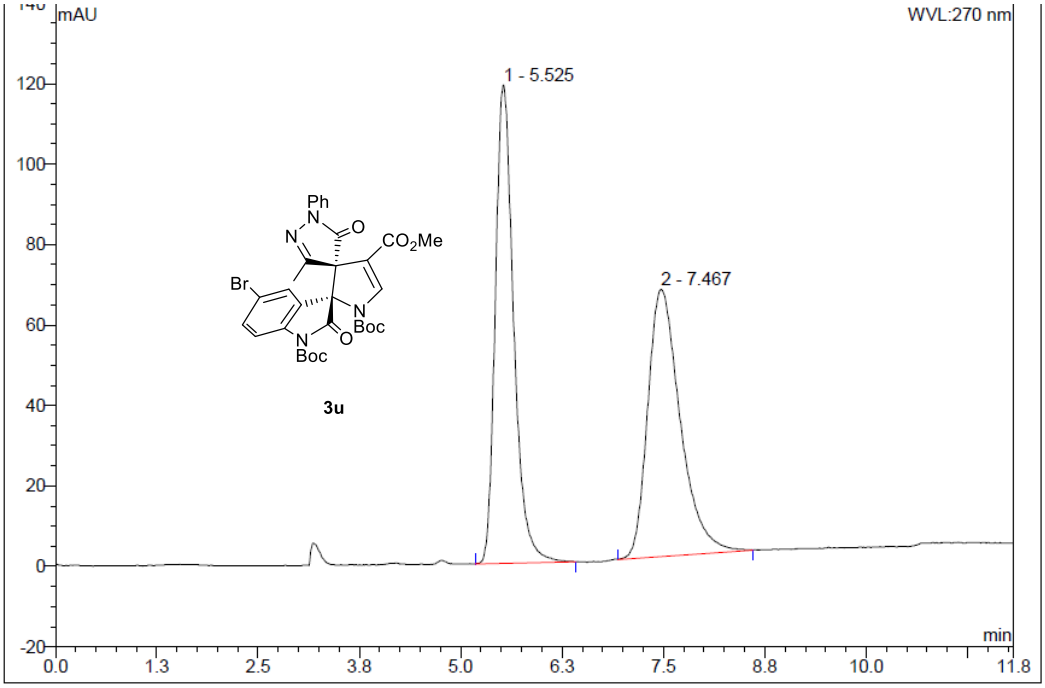
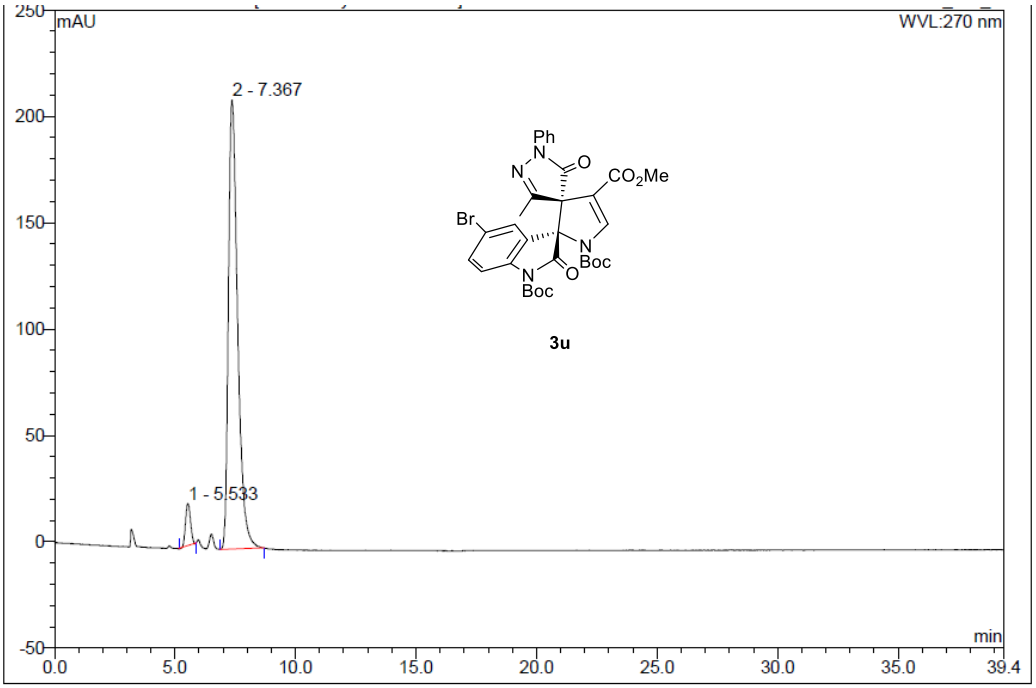
16.289
f1 (ppm)
Ph
N
N
O
CO2Me
Br
N
Boc
O
N
Boc

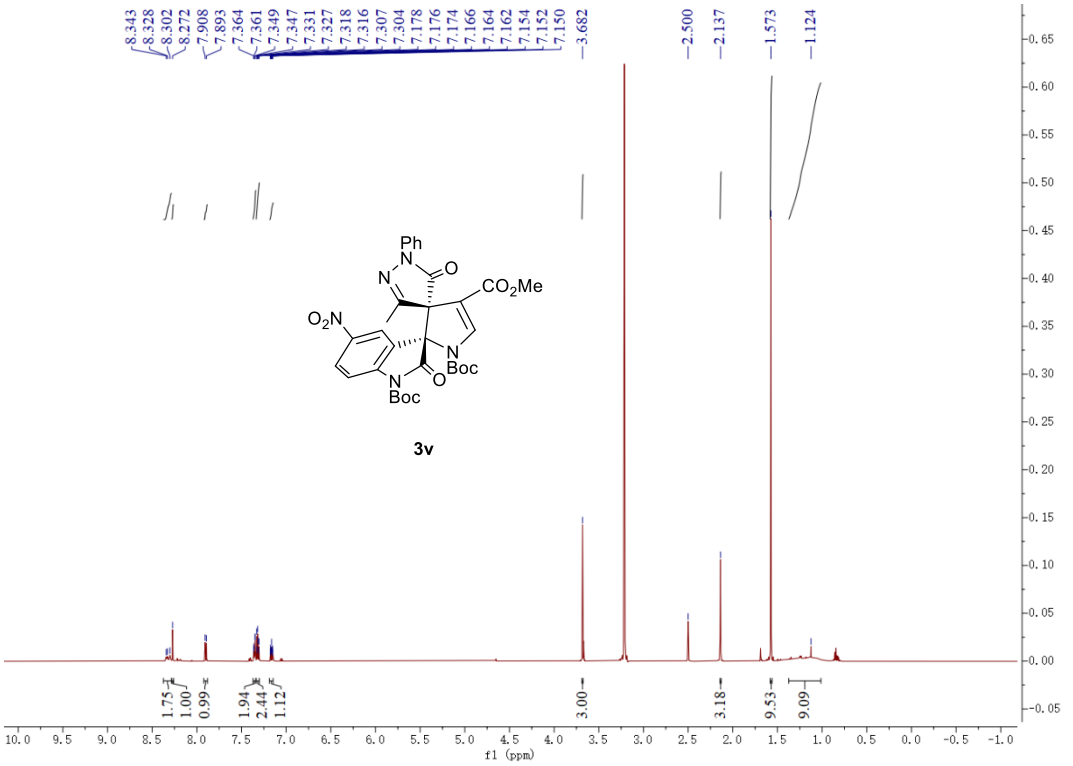
3u



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.53	n.a.	118.966	31.196	50.32	n.a.	BMB
2	7.47	n.a.	66.363	30.799	49.68	n.a.	BMB
Total:			185.329	61.996	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.53	n.a.	19.900	4.681	4.76	n.a.	BMB*
2	7.37	n.a.	211.145	93.688	95.24	n.a.	BMB
Total:			231.045	98.369	100.00	0.000	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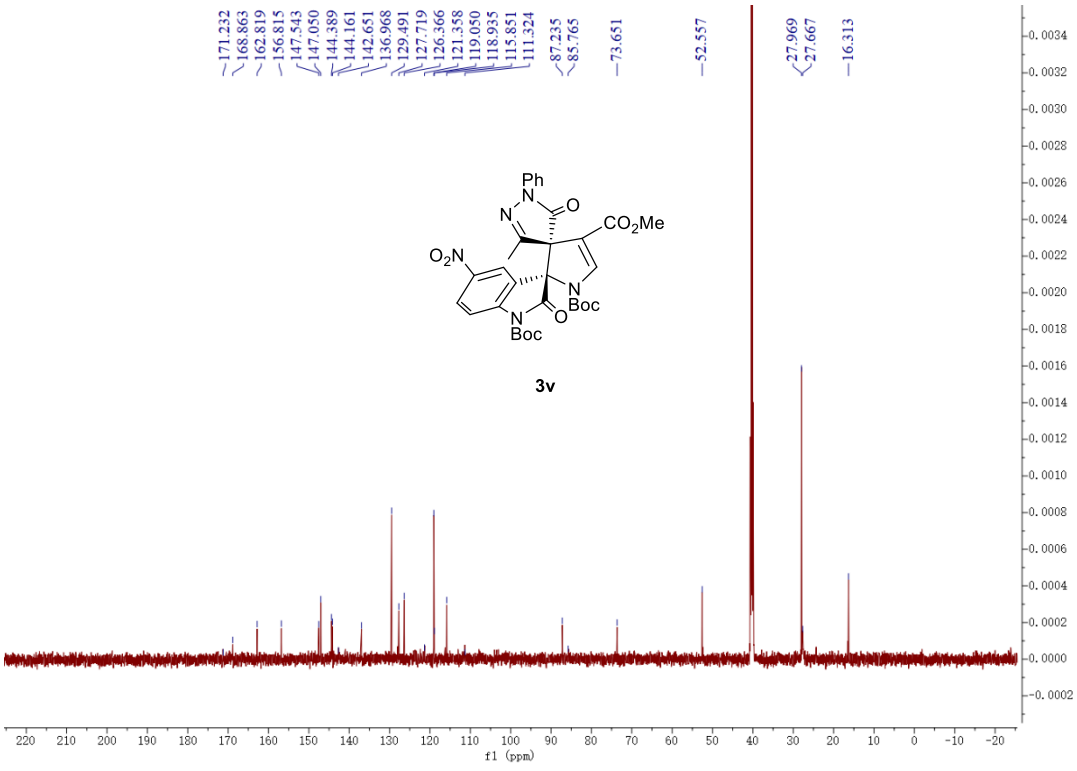
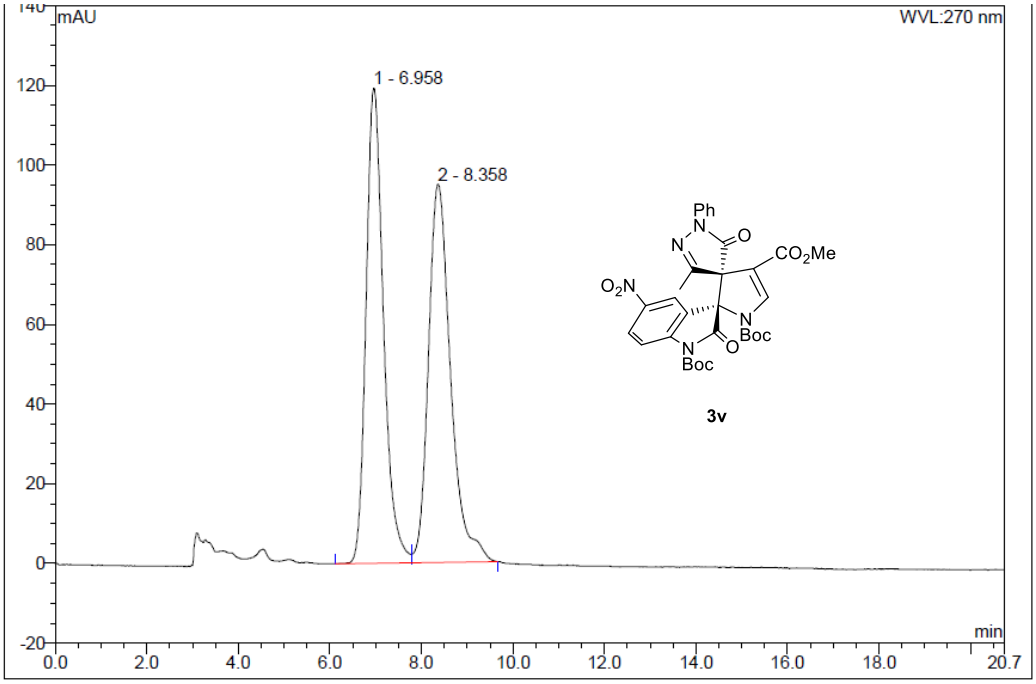
7.893
7.364
7.361
7.349
7.347
7.331
7.327
7.318
7.316
7.307
7.304
7.178
7.176
7.174
7.166
7.164
7.162
7.154
7.152
7.150
3.682
2.500
2.137
1.573
1.124
Ph
N
N
O
CO2Me
O2N
N
Boc
O
N
Boc
1.75
1.00
0.99
1.94
2.44
1.12
3.00
3.18
9.53
9.09
f1 (ppm)

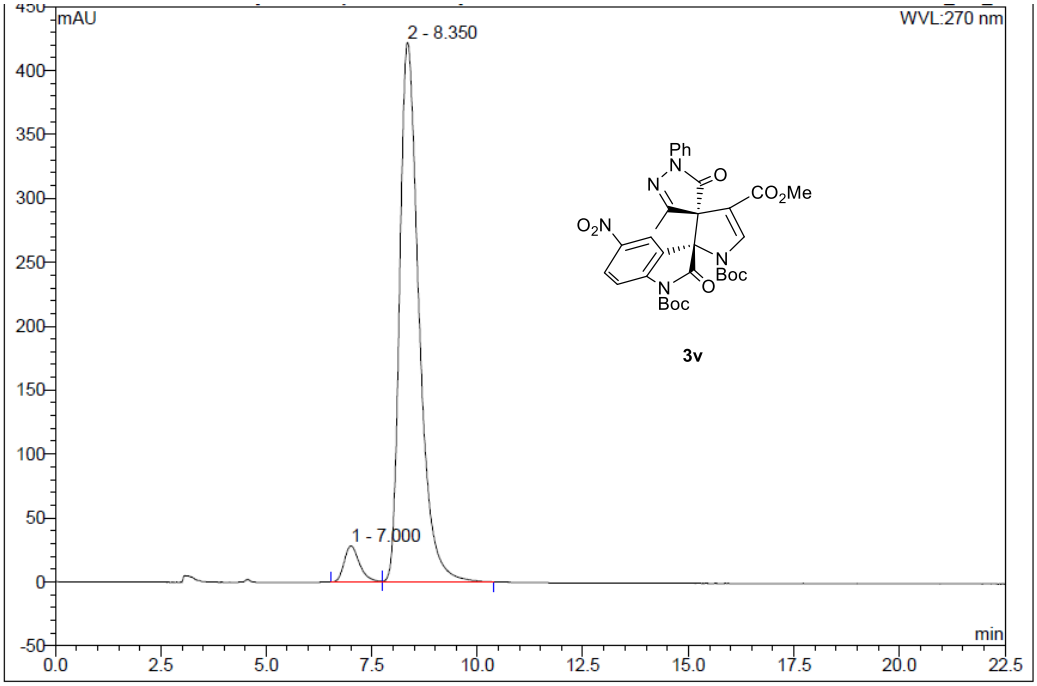
3v


171.232
168.863
162.819
156.815
147.543
147.050
144.389
144.161
142.651
136.968
129.491
127.719
126.366
121.358
119.050
118.935
115.851
111.324
87.235
85.765
73.651
52.557
27.969
27.667
16.313
Ph
N
N
O
CO2Me
O2N
N
Boc
O
N
Boc
f1 (ppm)

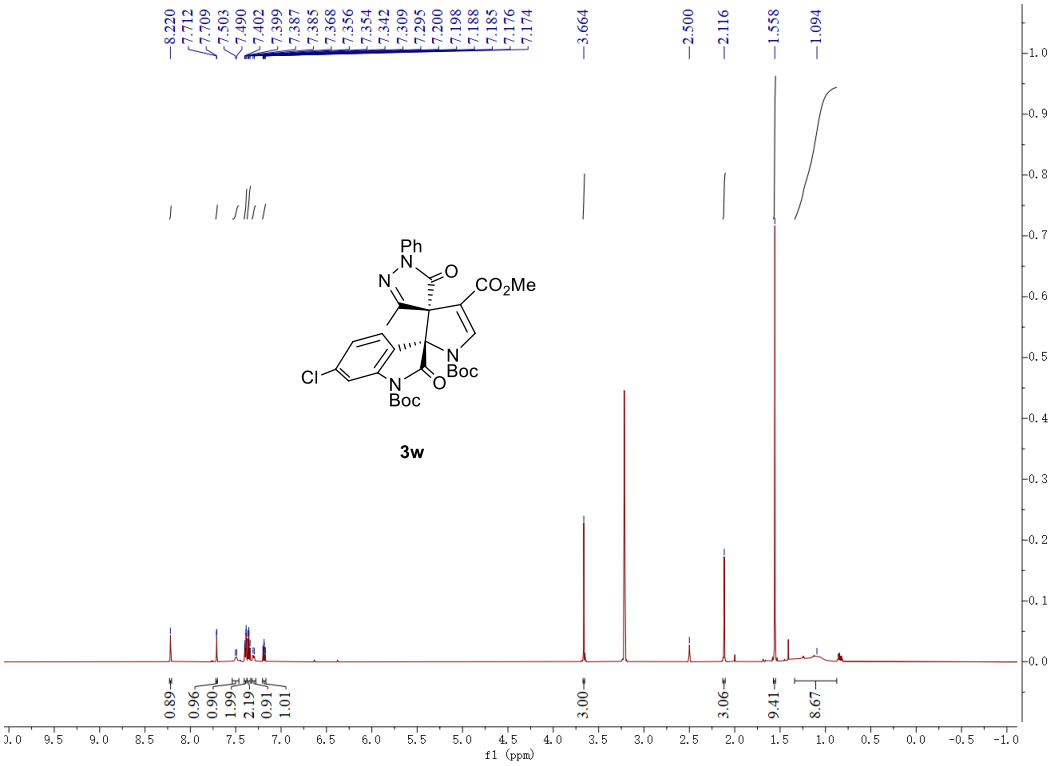
3v



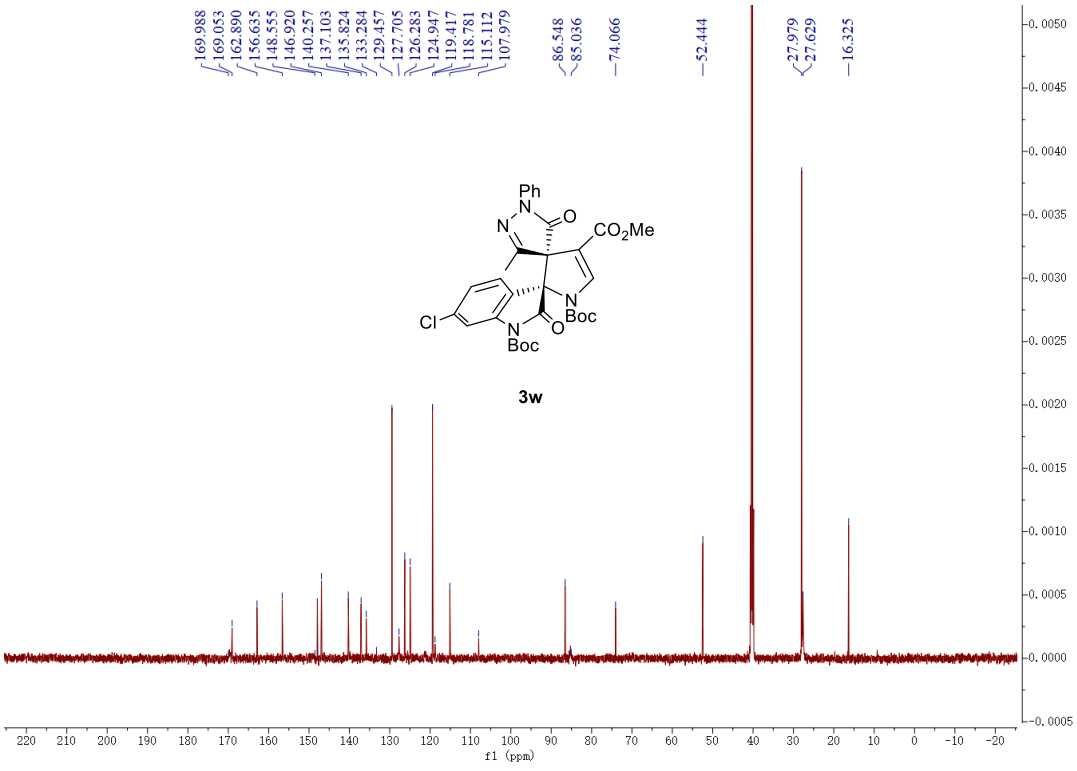
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.96	n.a.	119.267	52.589	49.62	n.a.	BM
2	8.36	n.a.	94.856	53.387	50.38	n.a.	MB
Total:			214.123	105.976	100.00	0.000	



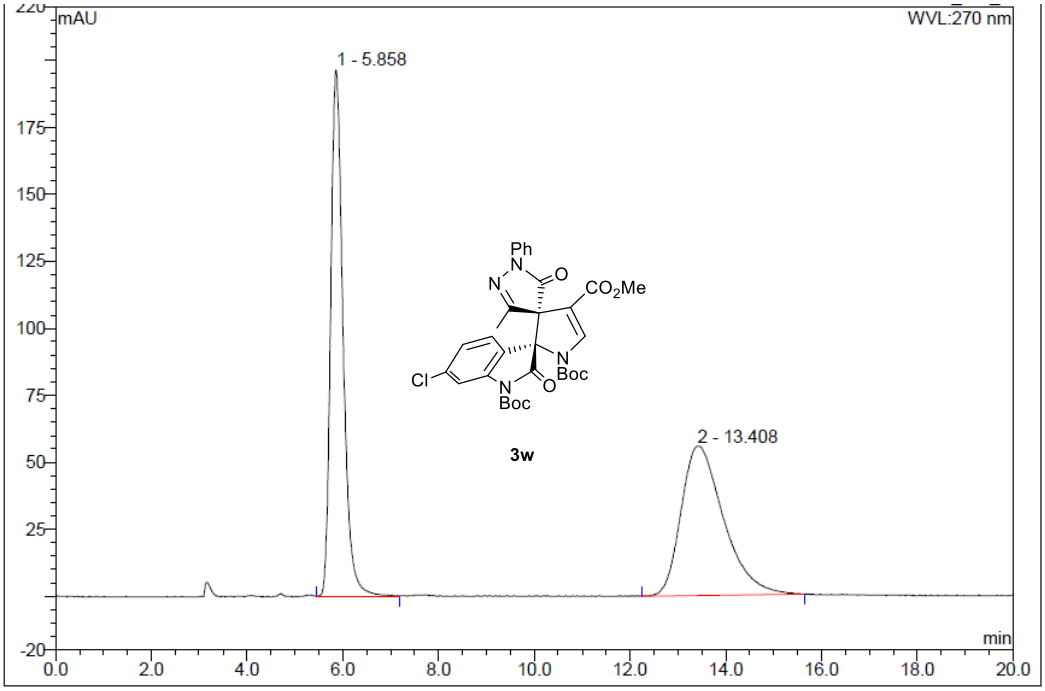
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.00	n.a.	28.297	12.028	5.10	n.a.	BM *
2	8.35	n.a.	422.221	223.604	94.90	n.a.	MB*
Total:			450.518	235.632	100.00	0.000	


8.220
7.712
7.709
7.503
7.490
7.402
7.399
7.387
7.385
7.368
7.356
7.354
7.342
7.309
7.295
7.200
7.198
7.188
7.185
7.176
7.174
3.664
2.500
2.116
1.558
1.094
Ph
N
N
O
CO2Me
Cl
N
Boc
O
N
Boc
0.89
0.96
0.90
1.99
2.19
0.91
1.01
3.00
3.06
9.41
8.67
f1 (ppm)

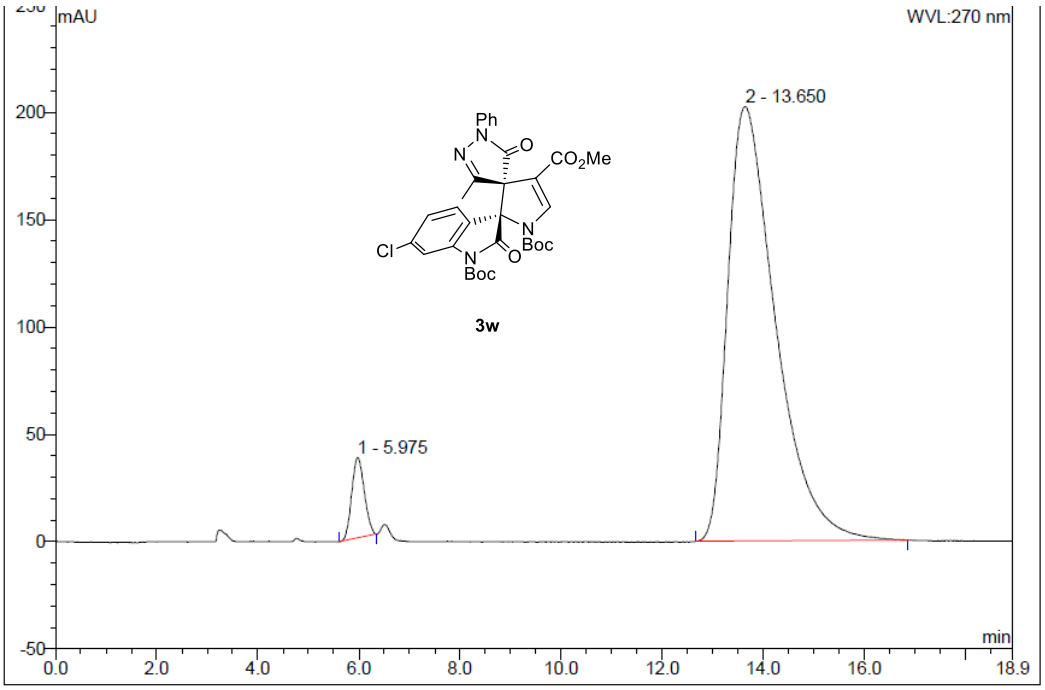
3w


169.988
169.053
162.890
156.635
148.555
146.920
140.257
137.103
135.824
133.284
129.457
127.705
126.283
124.947
119.417
118.781
115.112
107.979
86.548
85.036
74.066
52.444
27.979
27.629
16.325
Ph
N
N
O
CO2Me
Cl
N
Boc
O
N
Boc
f1 (ppm)

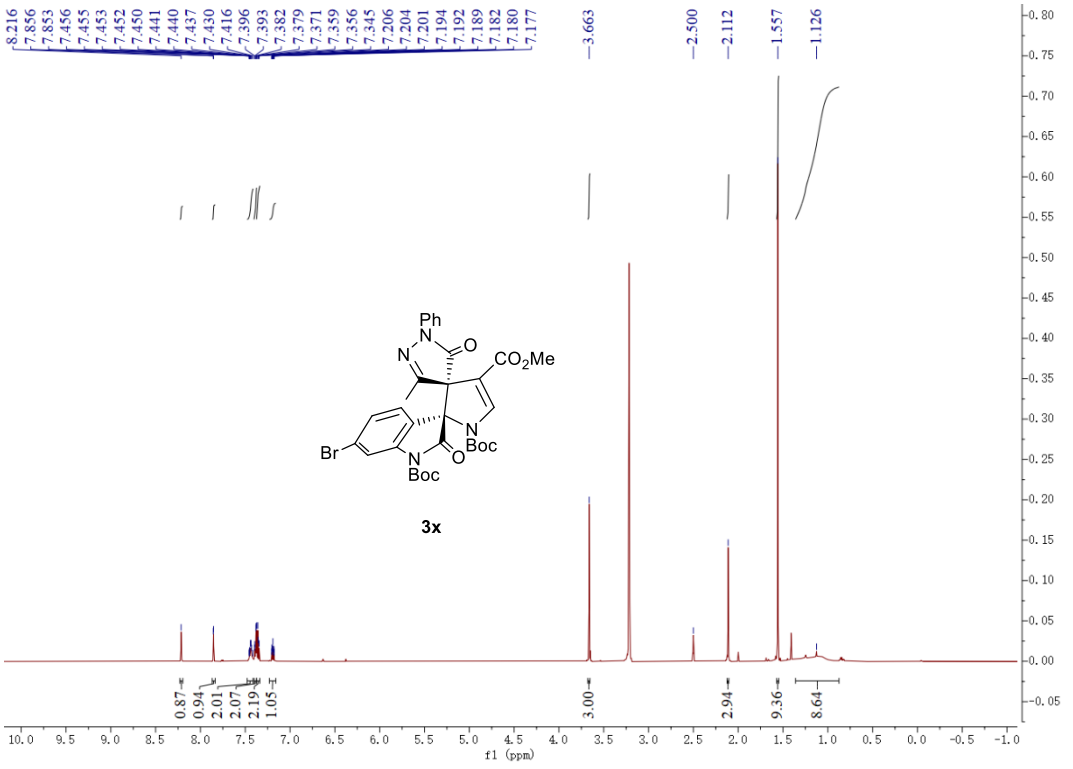
3w



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.86	n.a.	196.461	58.636	50.60	n.a.	BMB
2	13.41	n.a.	55.732	57.243	49.40	n.a.	BMB
Total:			252.194	115.879	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.98	n.a.	37.480	10.830	4.66	n.a.	BMB*
2	13.65	n.a.	202.490	221.774	95.34	n.a.	BMB*
Total:			239.970	232.605	100.00	0.000	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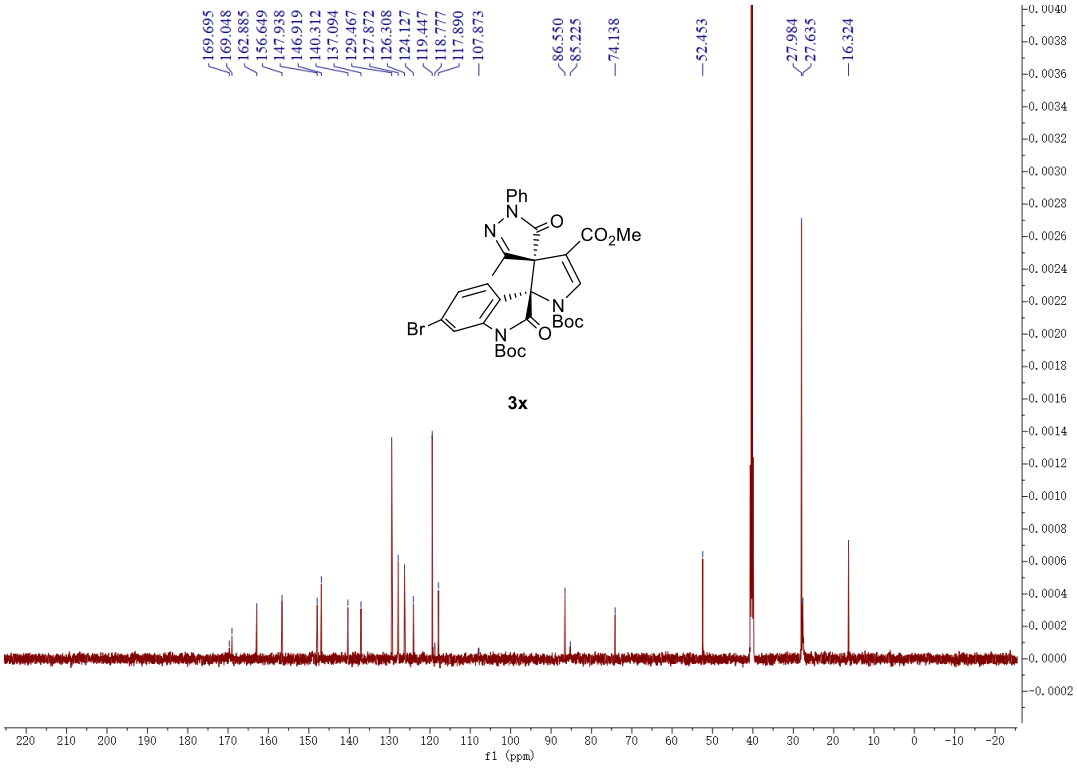
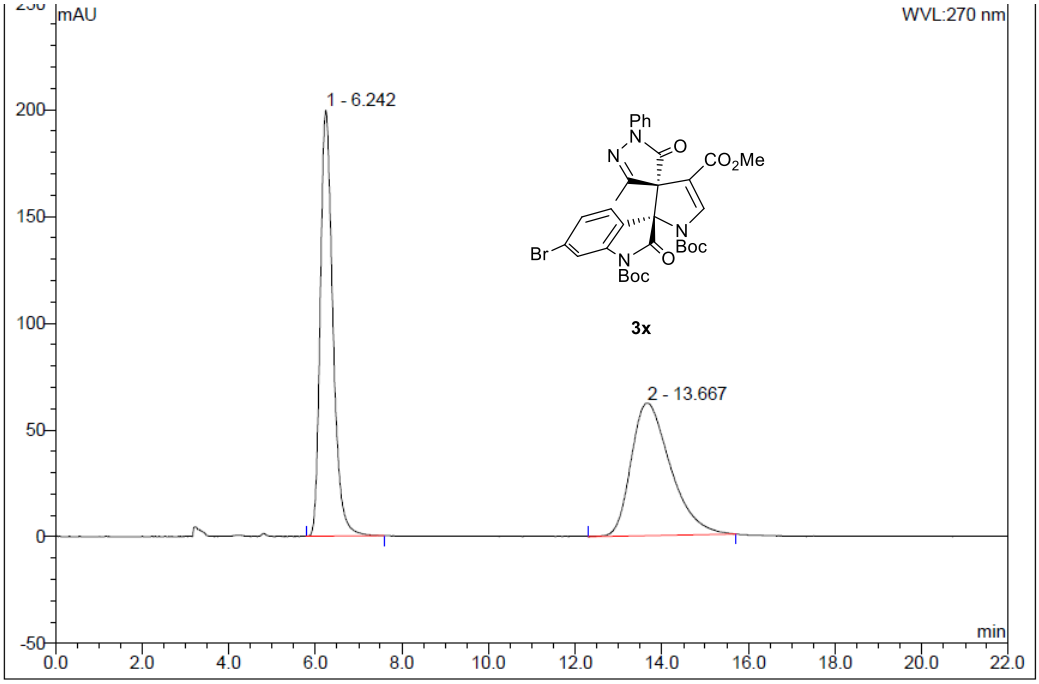
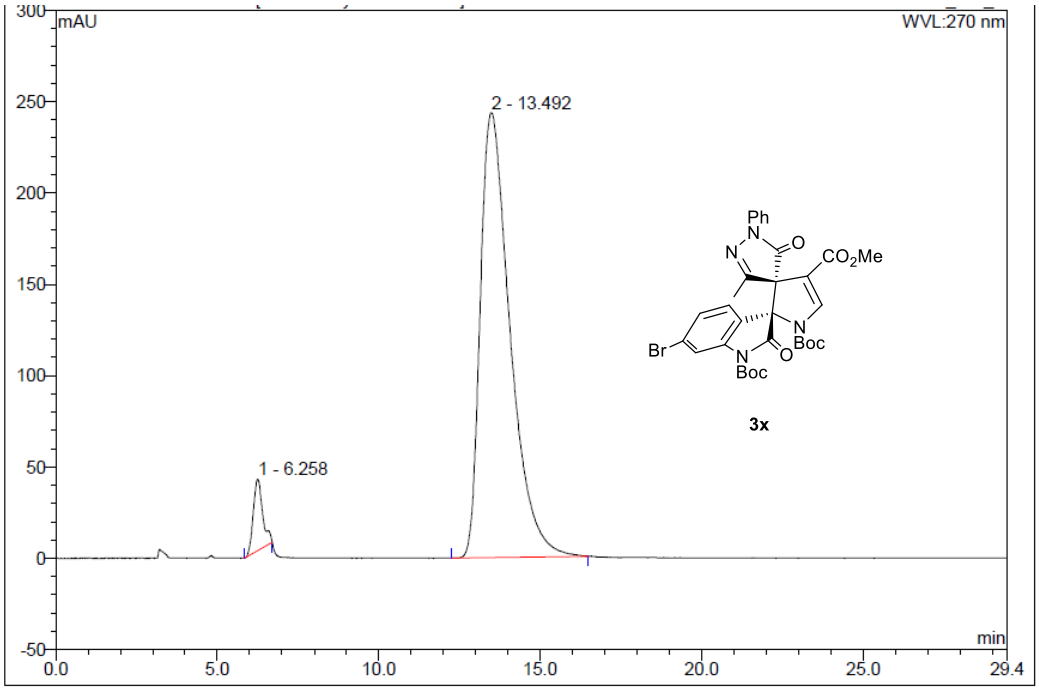
7.853
7.456
7.455
7.453
7.452
7.450
7.441
7.440
7.437
7.430
7.416
7.396
7.393
7.382
7.379
7.371
7.359
7.356
7.345
7.206
7.204
7.201
7.194
7.192
7.189
7.182
7.180
7.177
3.663
2.500
2.112
1.557
1.126
Ph
N
N
O
CO2Me
Br
N
Boc
O
N
Boc
3x
0.87
0.94
2.01
2.07
2.19
1.05
3.00
2.94
9.36
8.64
f1 (ppm)

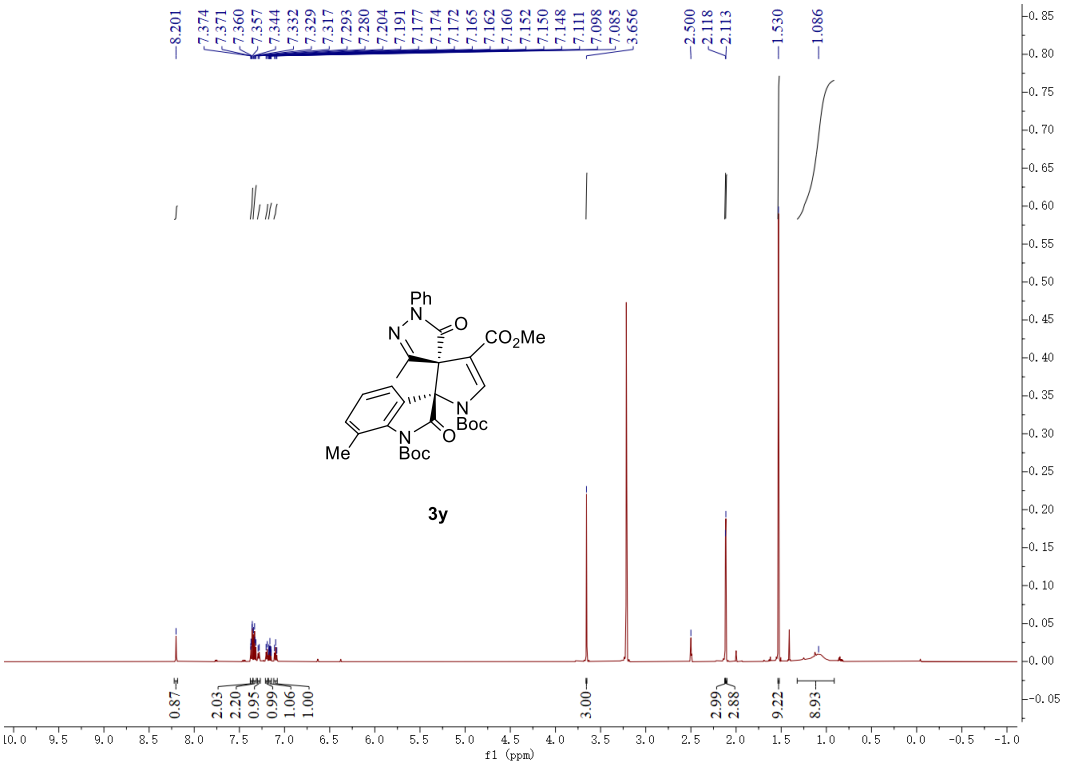

169.695
169.048
162.885
156.649
147.938
146.919
140.312
137.094
129.467
127.872
126.308
124.127
119.447
118.777
117.890
107.873
86.550
85.225
74.138
52.453
27.984
27.635
16.324
Ph
N
N
O
CO2Me
Br
N
Boc
O
N
Boc
3x
f1 (ppm)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.24	n.a.	199.813	67.437	50.75	n.a.	BMB
2	13.67	n.a.	62.171	65.433	49.25	n.a.	BMB
Total:			261.984	132.871	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.26	n.a.	38.832	13.135	4.81	n.a.	BMB*
2	13.49	n.a.	243.556	260.149	95.19	n.a.	BMB*
Total:			282.388	273.284	100.00	0.000	


8.201
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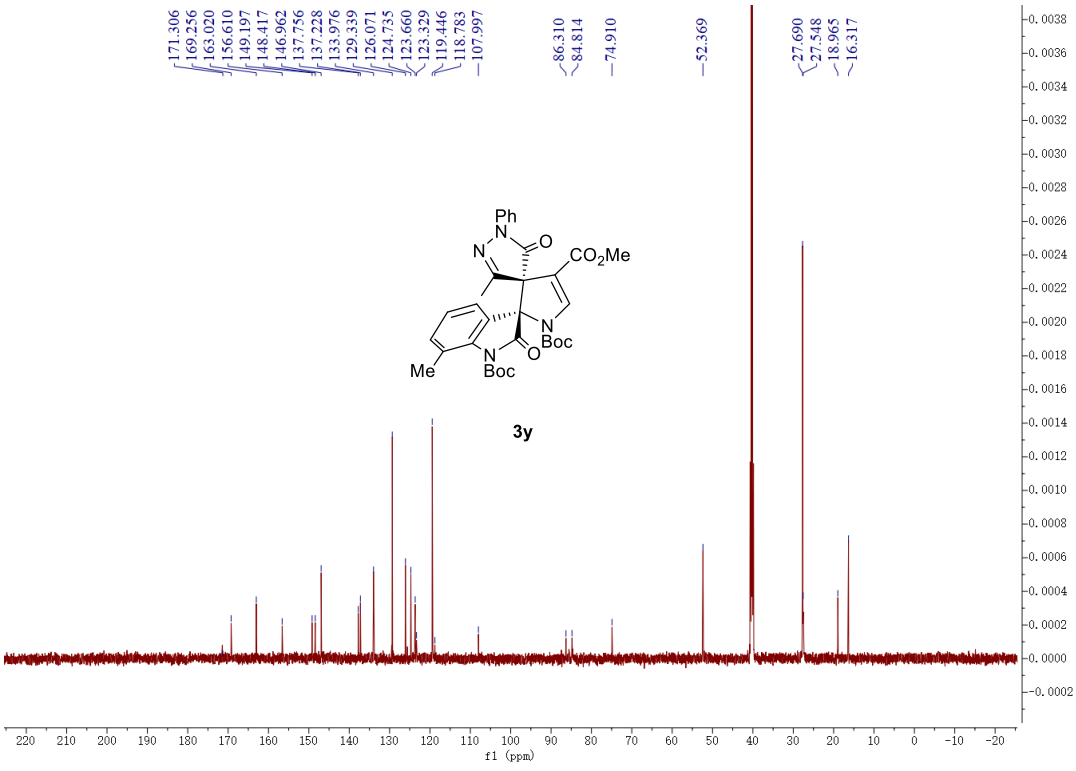
7.360
7.357
7.344
7.332
7.329
7.317
7.293
7.280
7.204
7.191
7.177
7.174
7.172
7.165
7.162
7.160
7.152
7.150
7.148
7.111
7.098
7.085
3.656
2.500
2.118
2.113
1.530
1.086
0.87
2.03
2.20
0.95
0.99
1.06
1.00
3.00
2.99
2.88
9.22
8.93
f1 (ppm)

Ph
N
N
O
CO2Me
N
Boc
O
N
Boc
Me

3y


171.306
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156.610
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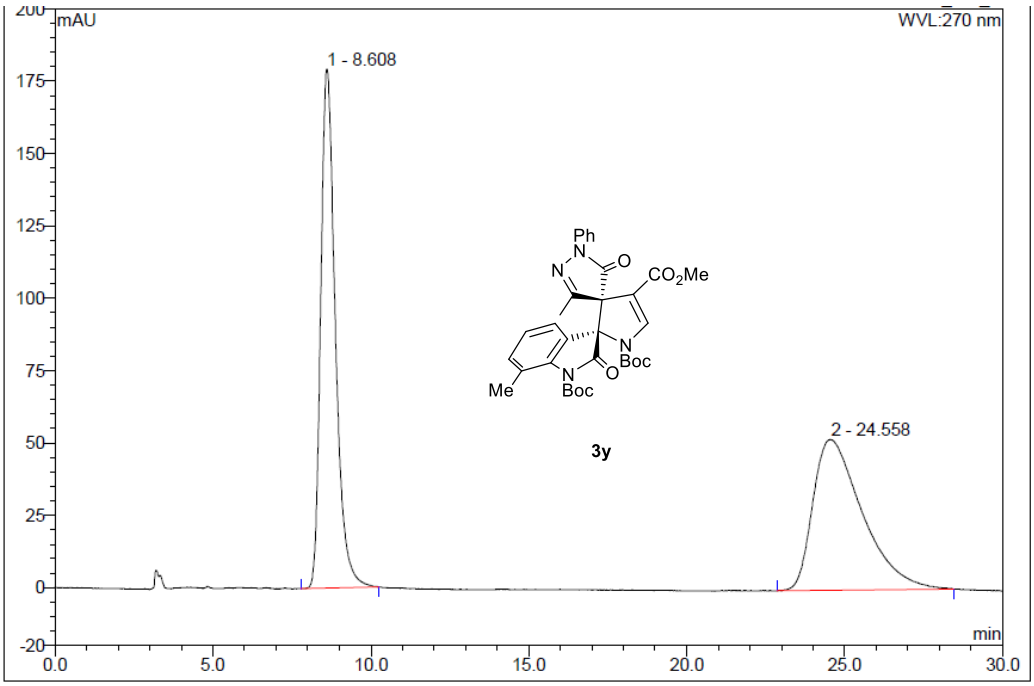
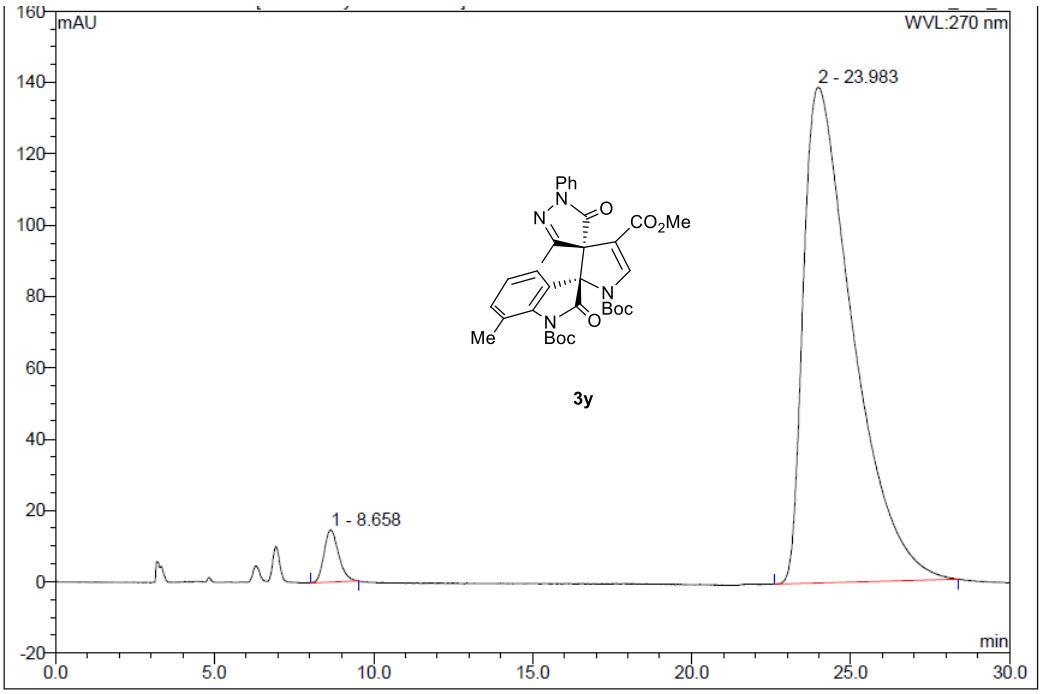
148.417
146.962
137.756
137.228
133.976
129.339
126.071
124.735
123.660
123.329
119.446
118.783
107.997
86.310
84.814
74.910
52.369
27.690
27.548
18.965
16.317
f1 (ppm)

Ph
N
N
O
CO2Me
N
Boc
O
N
Boc
Me

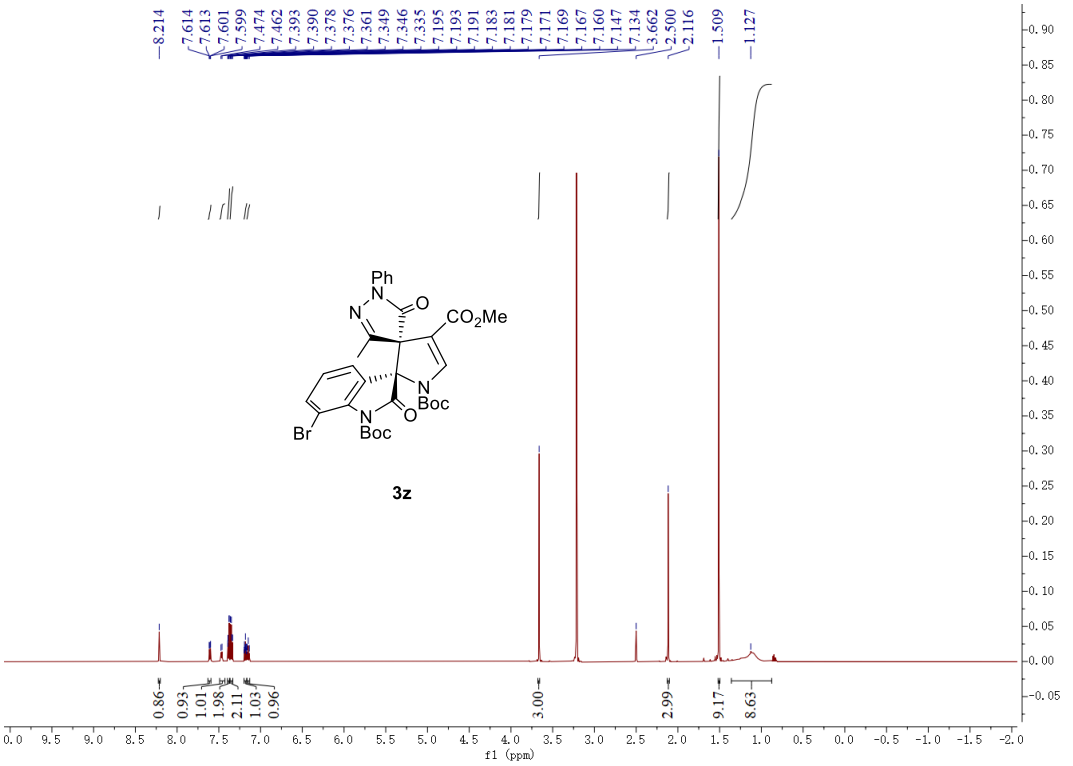
3y



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.61	n.a.	179.410	96.134	50.38	n.a.	BMB
2	24.56	n.a.	52.094	94.691	49.62	n.a.	BMB
Total:			231.505	190.825	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.66	n.a.	14.636	7.753	3.00	n.a.	BMB*
2	23.98	n.a.	139.081	251.077	97.00	n.a.	BMB*
Total:			153.717	258.830	100.00	0.000	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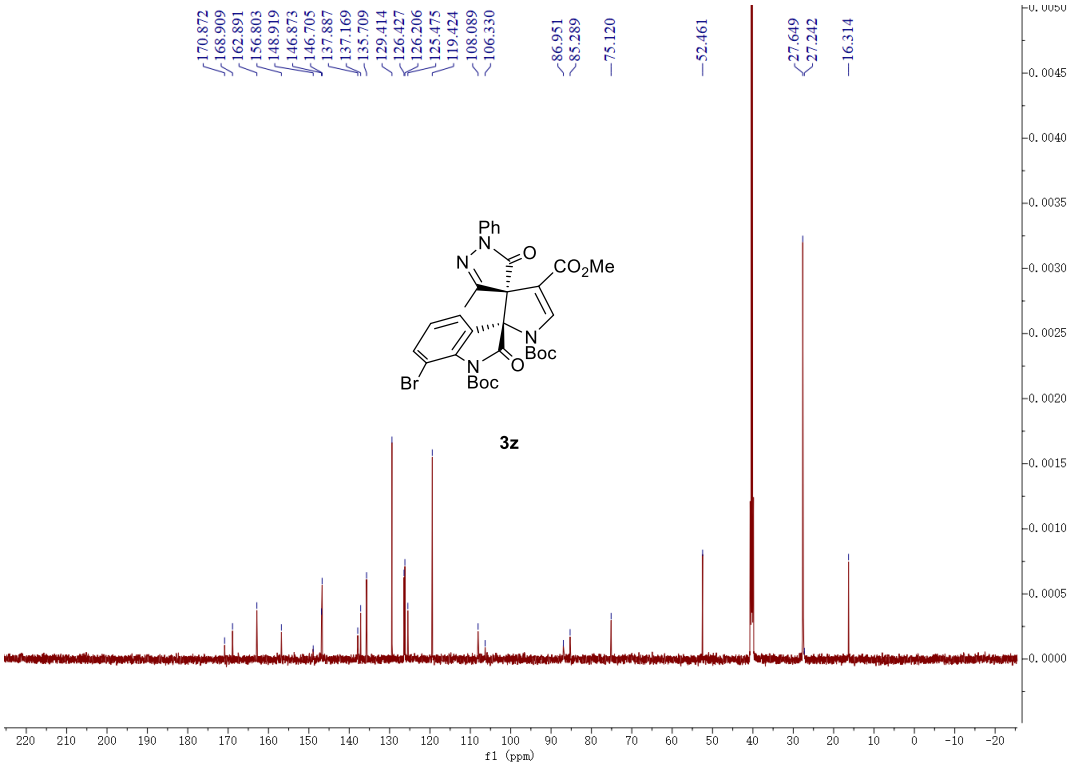
7.613
7.601
7.599
7.474
7.462
7.393
7.390
7.378
7.376
7.361
7.349
7.346
7.335
7.195
7.193
7.191
7.183
7.181
7.179
7.171
7.169
7.167
7.160
7.147
7.134
3.662
2.500
2.116
1.509
1.127
Ph
N
N
O
CO2Me
N
Boc
O
N
Boc
Br
0.86
0.93
1.01
1.98
2.11
1.03
0.96
3.00
2.99
9.17
8.63
f1 (ppm)

3z


170.872
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146.705
137.887
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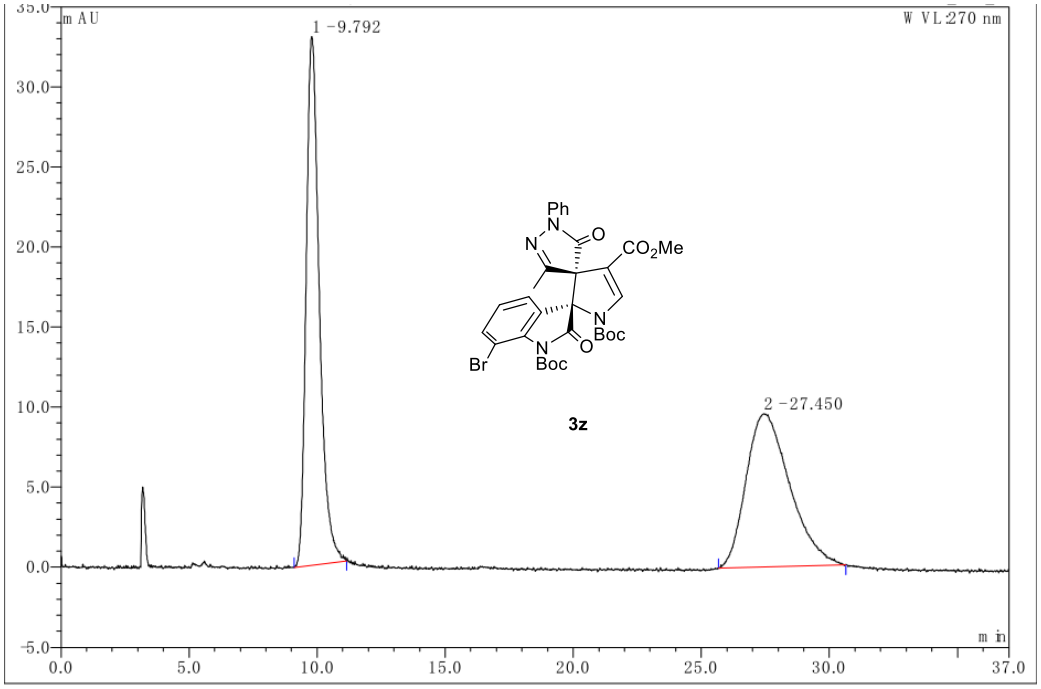
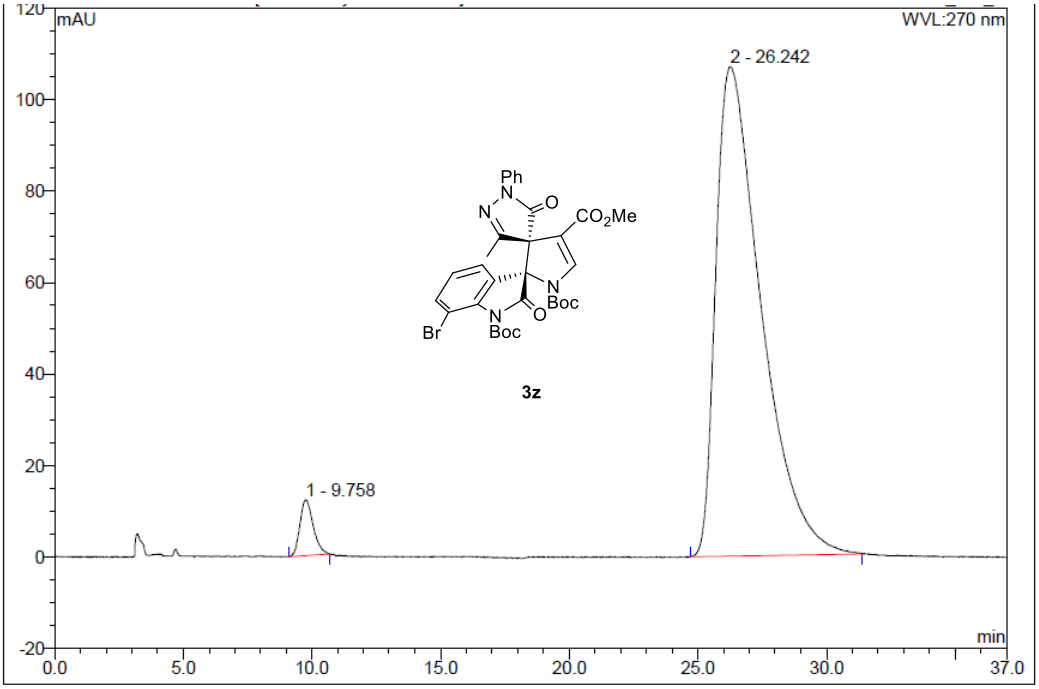
135.709
129.414
126.427
126.206
125.475
119.424
108.089
106.330
86.951
85.289
75.120
52.461
27.649
27.242
16.314
Ph
N
N
O
CO2Me
N
Boc
O
N
Boc
Br
f1 (ppm)

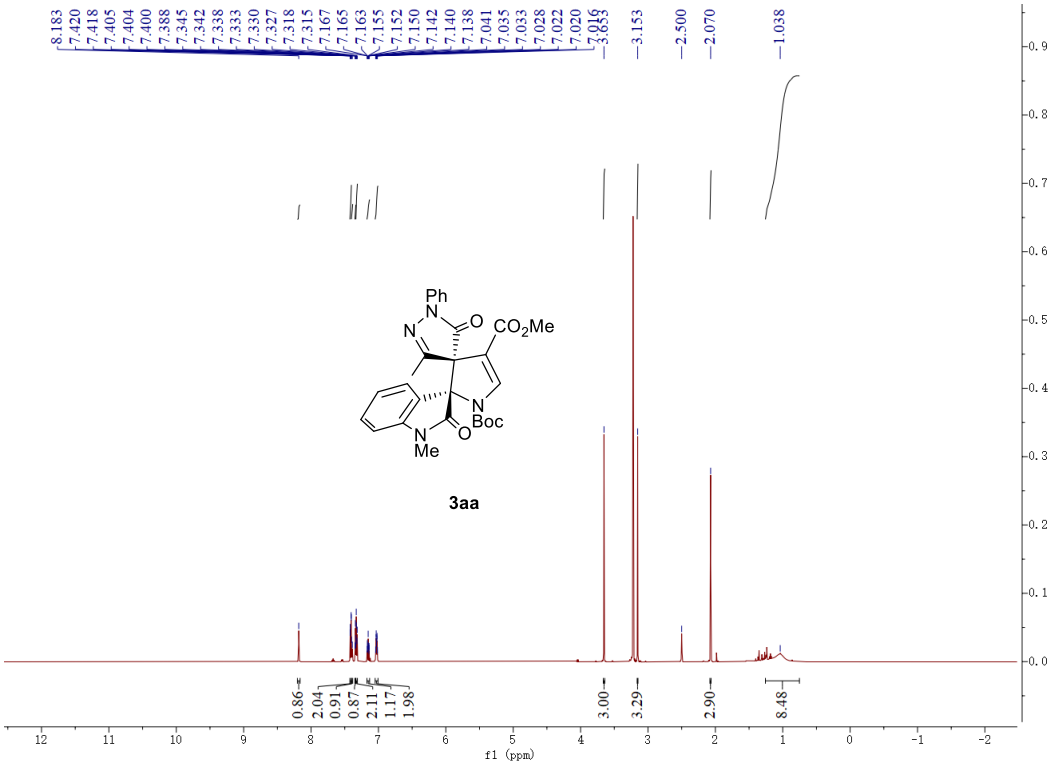
3z



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.79	n.a.	33.026	19.672	50.94	n.a.	BMB
2	27.45	n.a.	9.573	18.949	49.06	n.a.	BMB*
Total:			42.599	38.621	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.76	n.a.	12.198	7.316	3.25	n.a.	BMB
2	26.24	n.a.	106.962	217.759	96.75	n.a.	BMB*
Total:			119.160	225.075	100.00	0.000	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7.388
7.345
7.342
7.338
7.333
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7.165
7.163
7.155
7.152
7.150
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7.035
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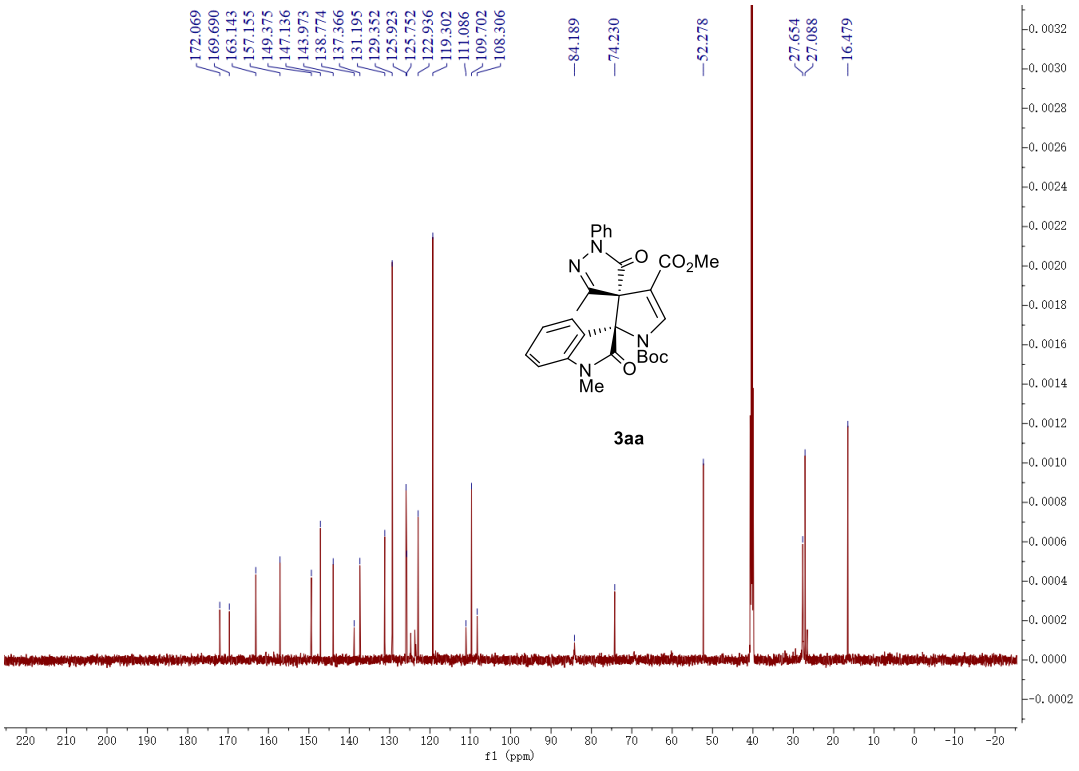
2.500
2.070
1.038
Ph
N
N
O
CO2Me
N
Boc
O
N
Me
3aa
0.86
2.04
0.91
0.87
2.11
1.17
1.98
3.00
3.29
2.90
8.48
f1 (ppm)


172.069
169.690
163.143
157.155
149.375
147.136
143.973
138.774
137.366
131.195
129.352
125.923
125.752
122.936
119.302
111.086
109.702
108.306
84.189
74.230
52.278
27.654
27.088
16.479
Ph
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Boc
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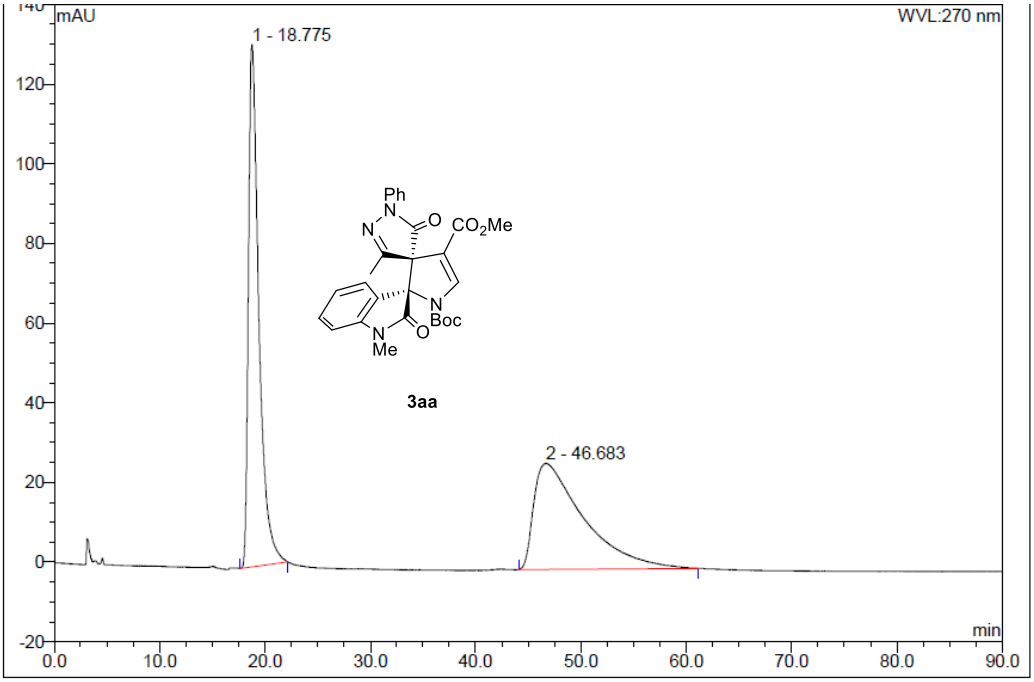
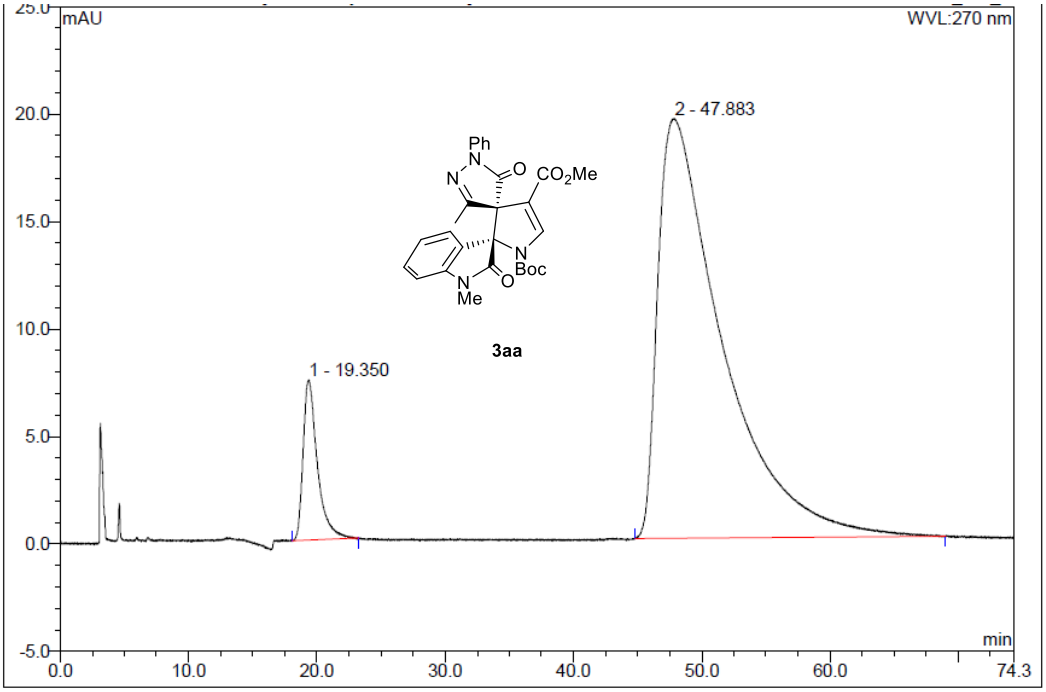
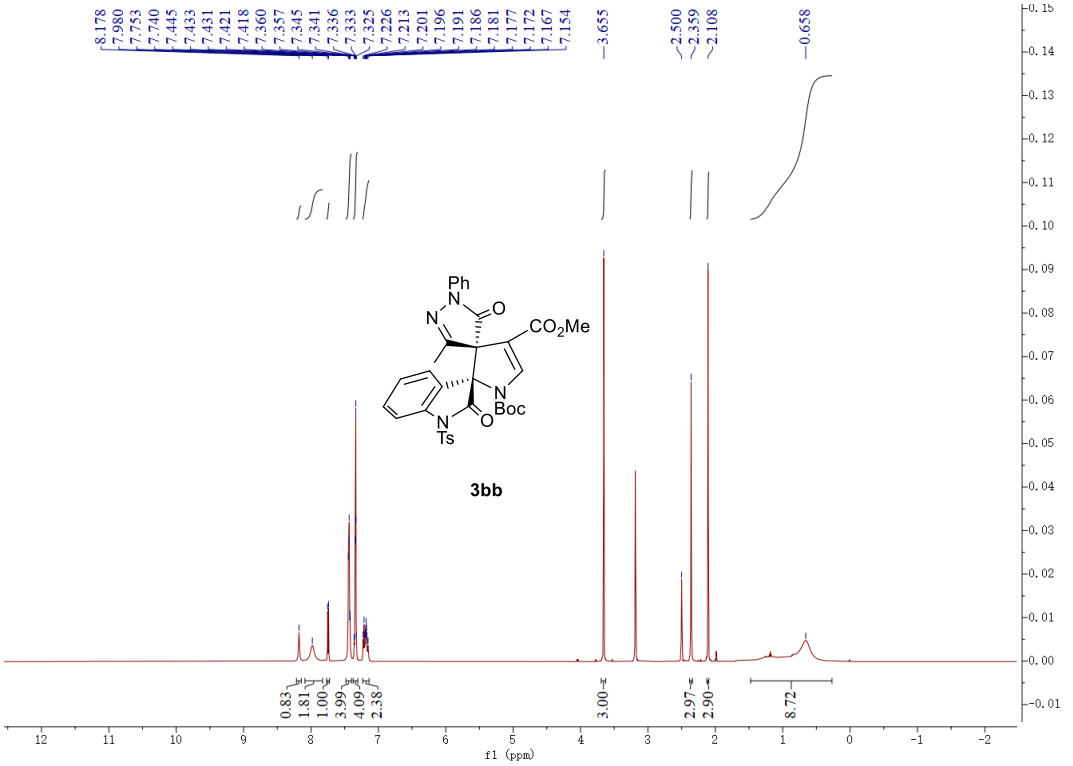
N
Me
3aa
f1 (ppm)



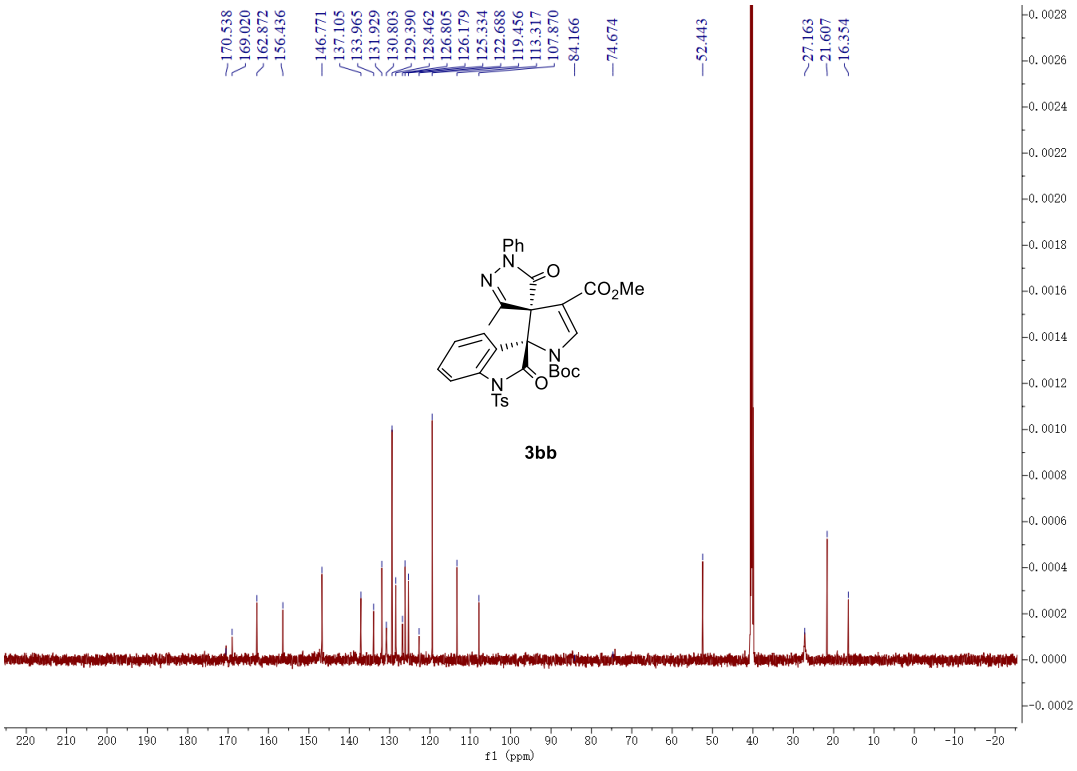
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	18.78	n.a.	131.138	150.921	50.82	n.a.	BMB
2	46.68	n.a.	26.615	146.037	49.18	n.a.	BMB*
Total:			157.754	296.958	100.00	0.000	



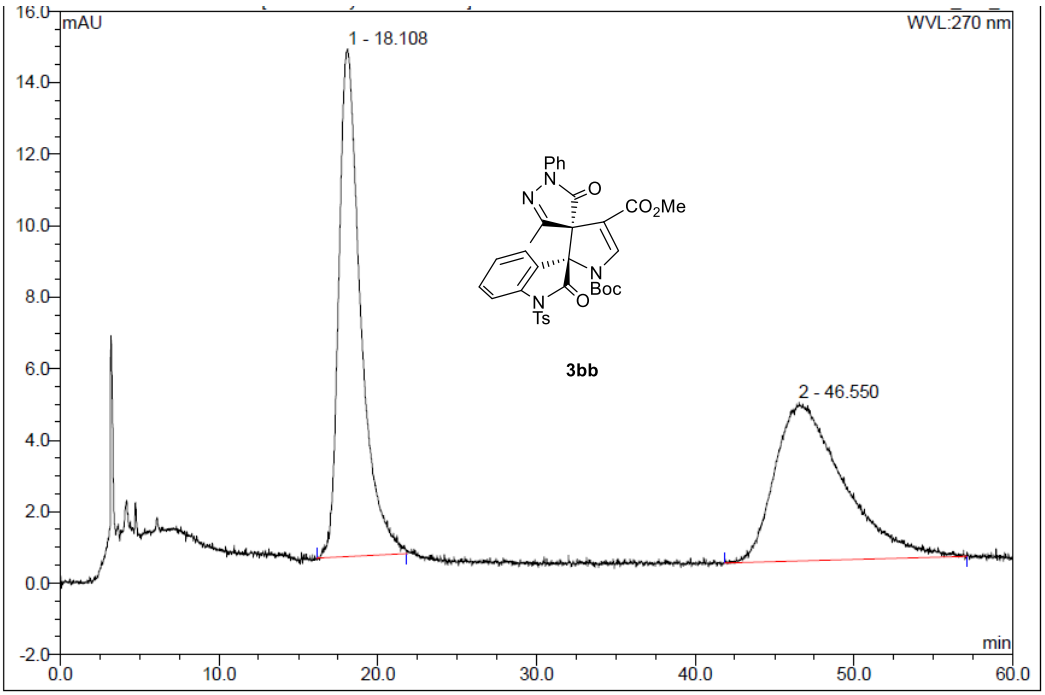
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	19.35	n.a.	7.453	9.587	7.78	n.a.	BMB*
2	47.88	n.a.	19.540	113.593	92.22	n.a.	BMB*
Total:			26.993	123.181	100.00	0.000	


8.178
7.980
7.753
7.740
7.445
7.433
7.431
7.421
7.418
7.360
7.357
7.345
7.341
7.336
7.333
7.325
7.226
7.213
7.201
7.196
7.191
7.186
7.181
7.177
7.172
7.167
7.154
3.655
2.500
2.359
2.108
0.658
Ph
N
N
O
CO2Me
N
Boc
O
N
Ts
0.83
1.81
1.00
3.99
4.09
2.38
3.00
2.97
2.90
8.72
f1 (ppm)

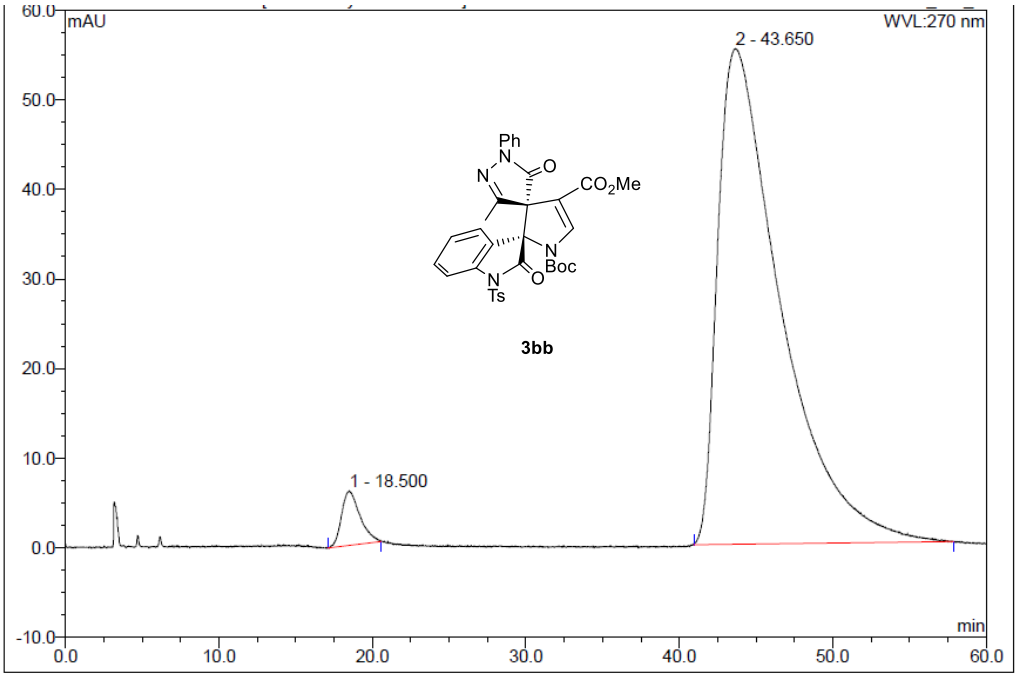
3bb


170.538
169.020
162.872
156.436
146.771
137.105
133.965
131.929
130.803
129.390
128.462
126.805
126.179
125.334
122.688
119.456
113.317
107.870
84.166
74.674
52.443
27.163
21.607
16.354
Ph
N
N
O
CO2Me
N
Boc
O
N
Ts
f1 (ppm)

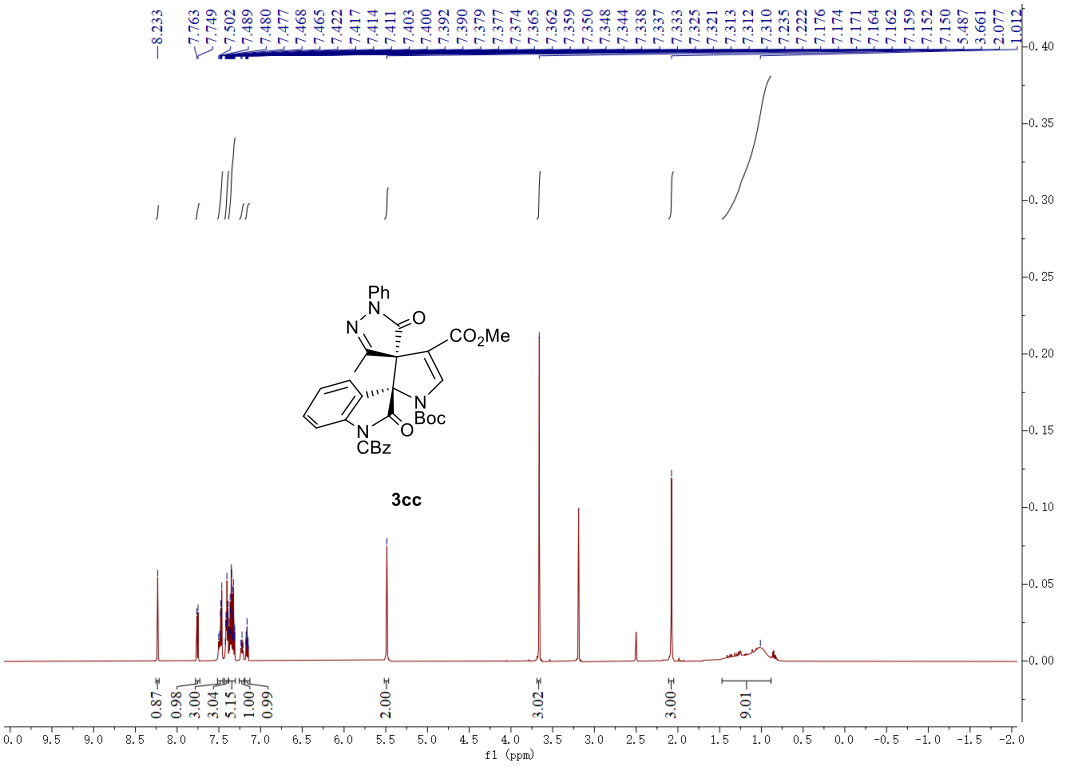
3bb

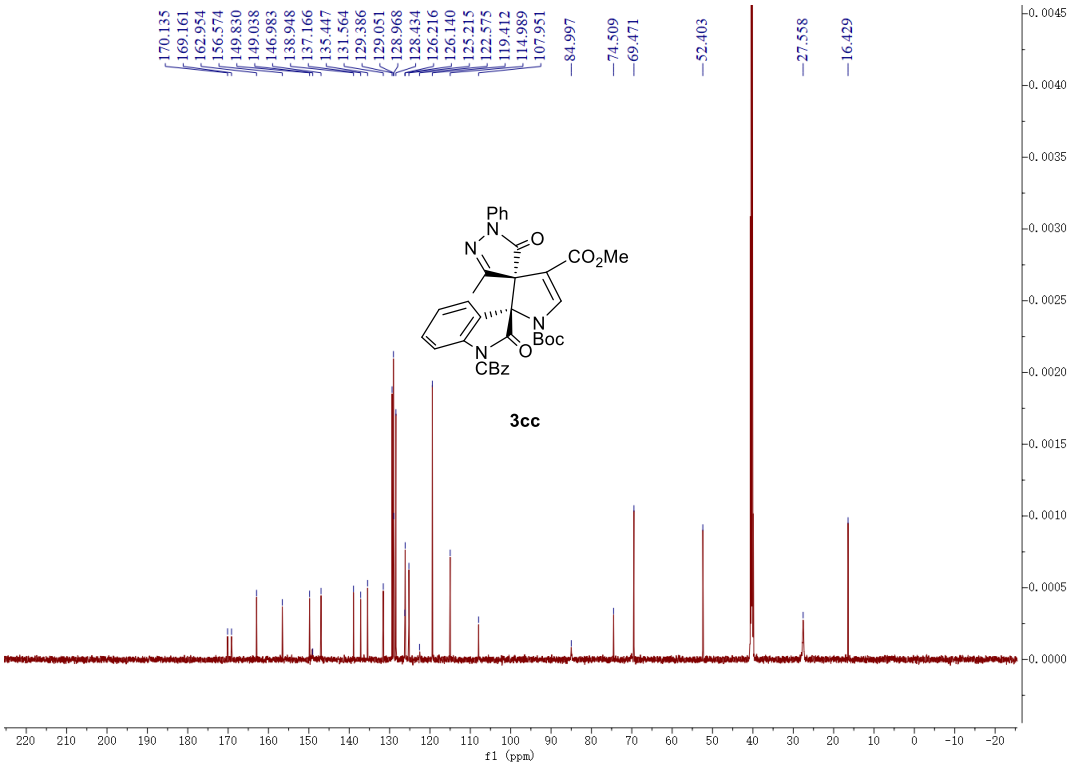


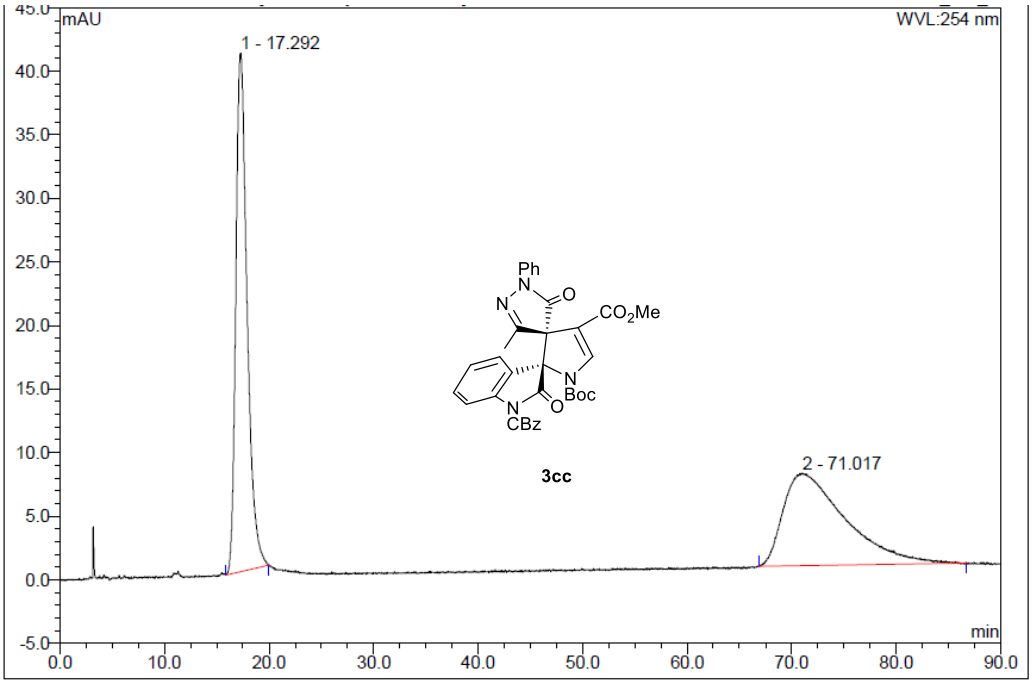
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	18.11	n.a.	14.202	22.781	50.75	n.a.	BMB*
2	46.55	n.a.	4.434	22.106	49.25	n.a.	BMB*
Total:			18.635	44.887	100.00	0.000	



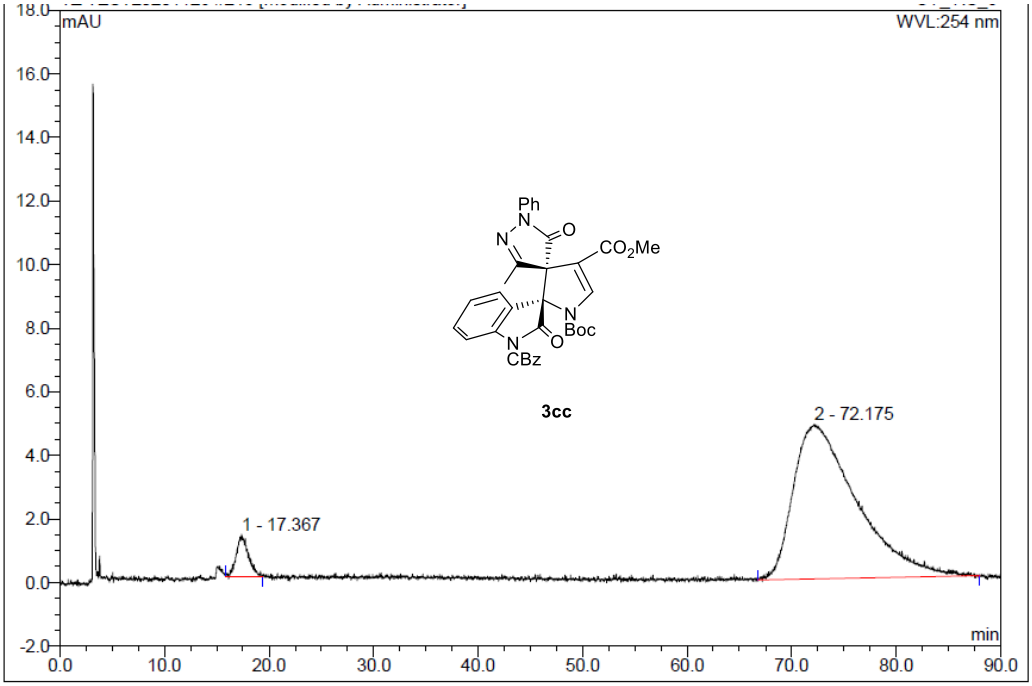
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	18.50	n.a.	6.106	8.424	3.11	n.a.	BMB*
2	43.65	n.a.	55.326	262.205	96.89	n.a.	BMB*
Total:			61.432	270.629	100.00	0.000	


8.233
7.763
7.749
7.502
7.489
7.480
7.477
7.468
7.465
7.422
7.417
7.414
7.411
7.403
7.400
7.392
7.390
7.379
7.377
7.374
7.365
7.362
7.359
7.350
7.348
7.344
7.338
7.337
7.333
7.325
7.321
7.313
7.312
7.310
7.235
7.222
7.176
7.174
7.171
7.164
7.162
7.159
7.152
7.150
5.487
3.661
2.077
1.012
Ph
N
N
O
CO2Me
N
Boc
O
N
CBz
3cc
0.87
0.98
3.00
3.04
5.15
1.00
0.99
2.00
3.02
3.00
9.01
f1 (ppm)


170.135
169.161
162.954
156.574
149.830
149.038
146.983
138.948
137.166
135.447
131.564
129.386
129.051
128.968
128.434
126.216
126.140
125.215
122.575
119.412
114.989
107.951
84.997
74.509
69.471
52.403
27.558
16.429
Ph
N
N
O
CO2Me
N
Boc
O
N
CBz
3cc
f1 (ppm)

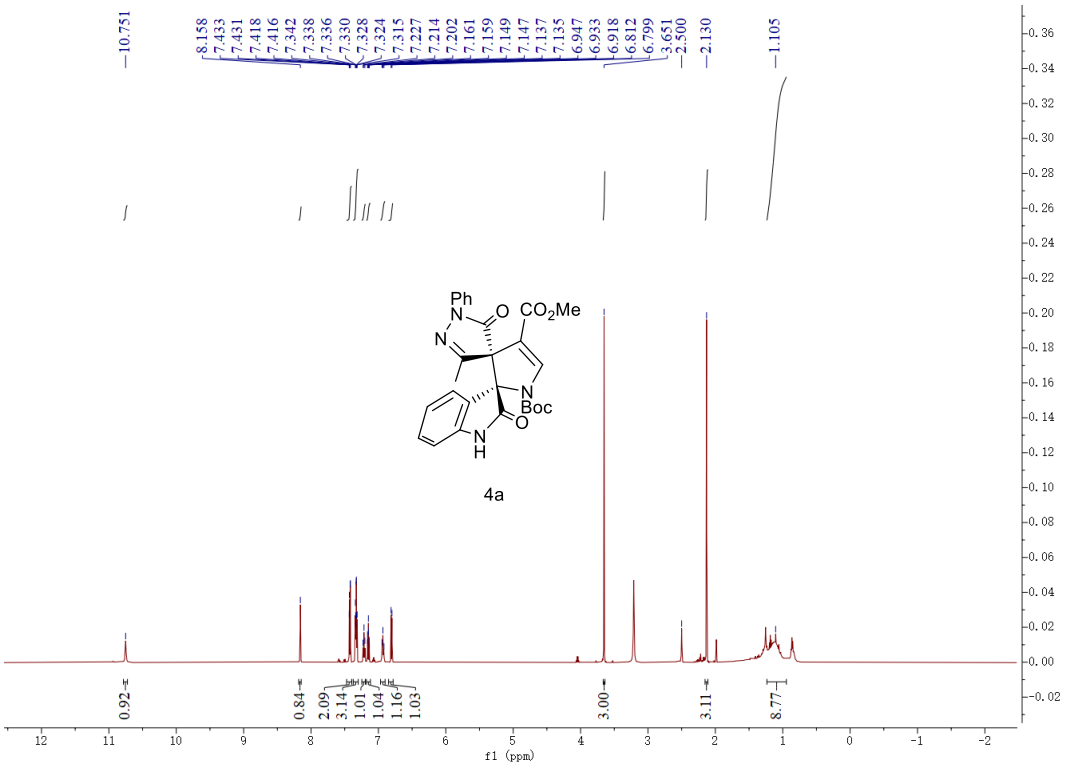


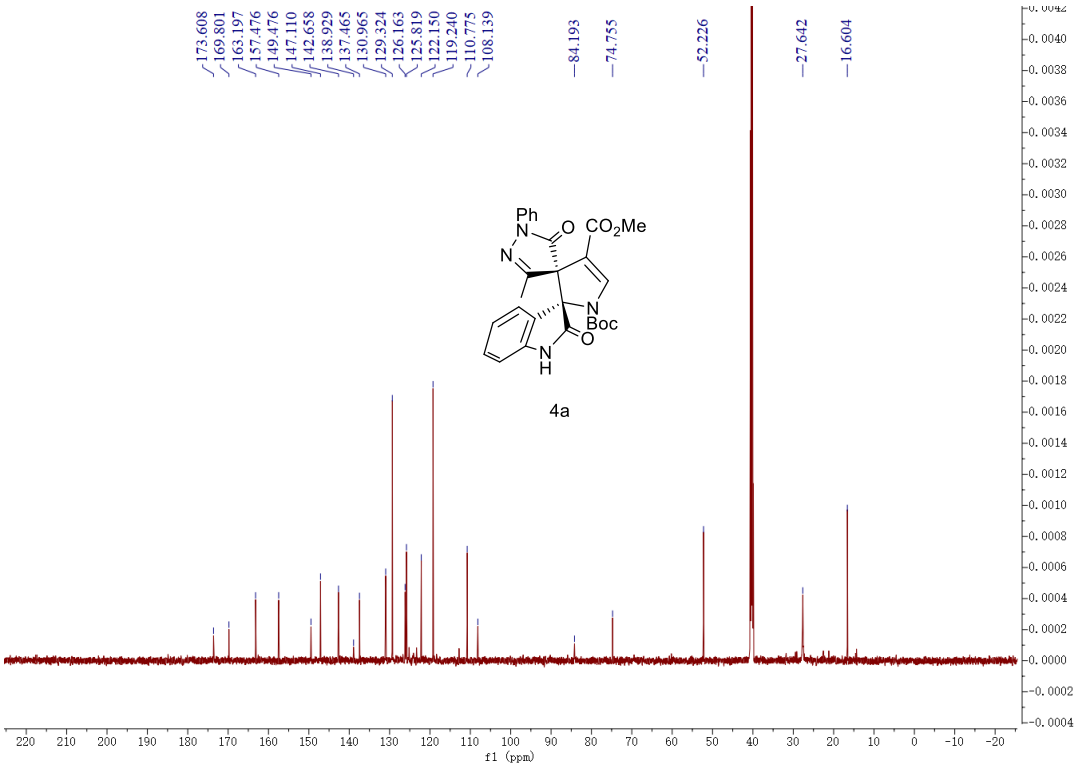
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	17.29	n.a.	40.801	51.034	50.61	n.a.	BMB
2	71.02	n.a.	7.318	49.805	49.39	n.a.	BMB*
Total:			48.118	100.839	100.00	0.000	

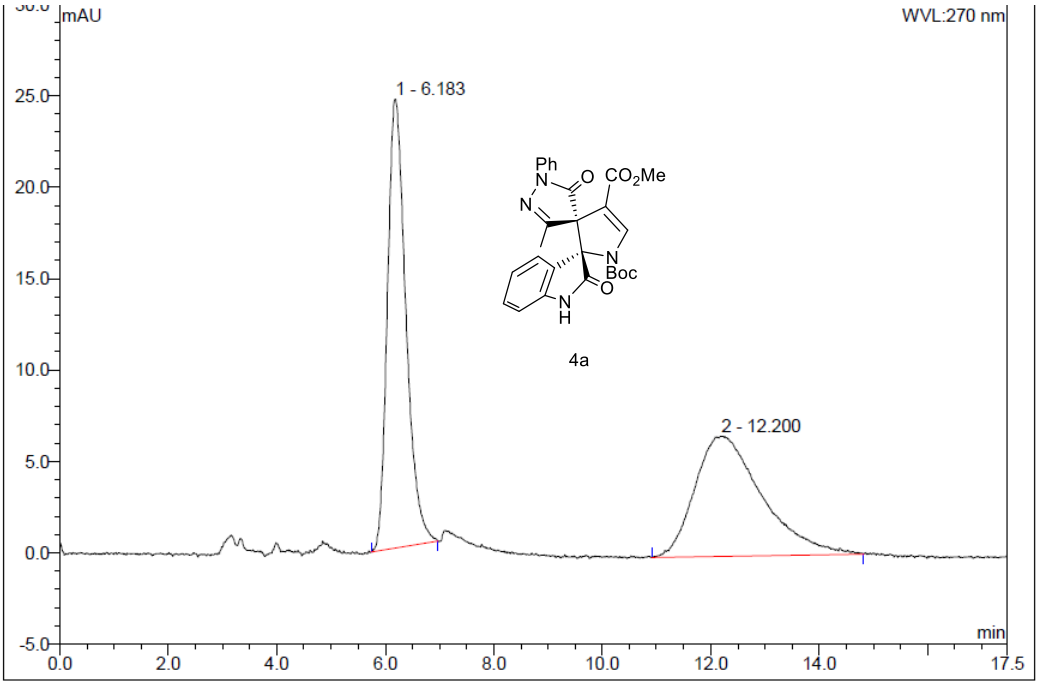


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	17.37	n.a.	1.311	1.671	4.67	n.a.	BMB*
2	72.18	n.a.	4.870	34.122	95.33	n.a.	BMB*
Total:			6.182	35.793	100.00	0.000	

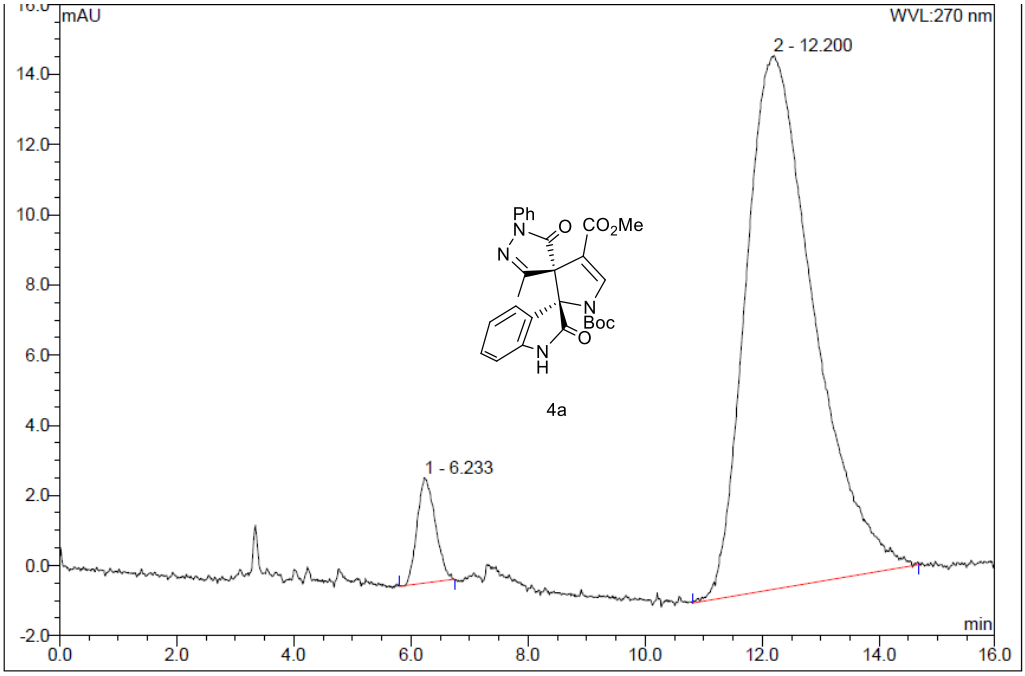
9.3 NMR spectra and HPLC chromatograms of derivatives



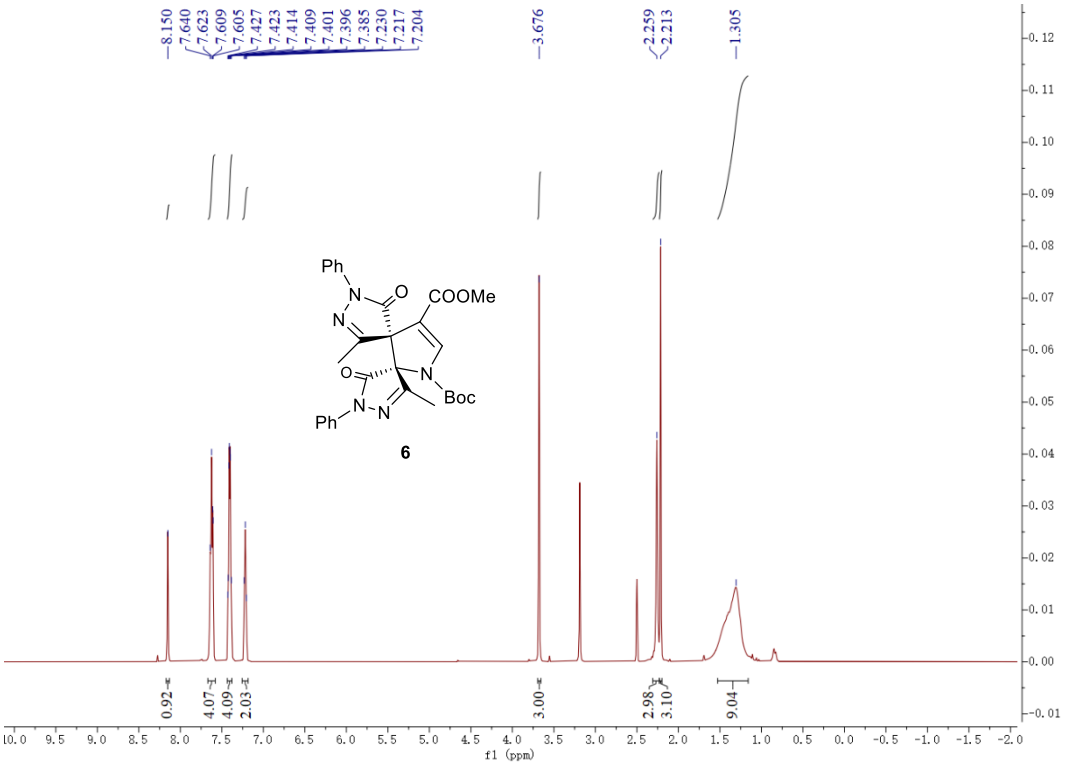


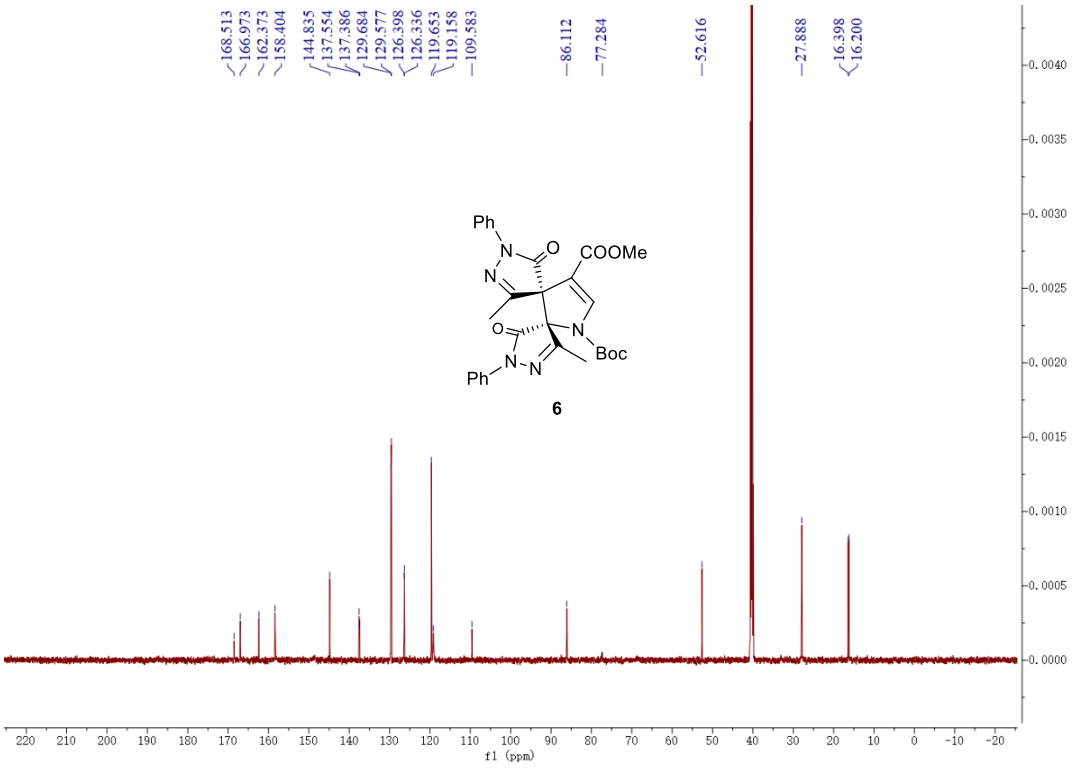


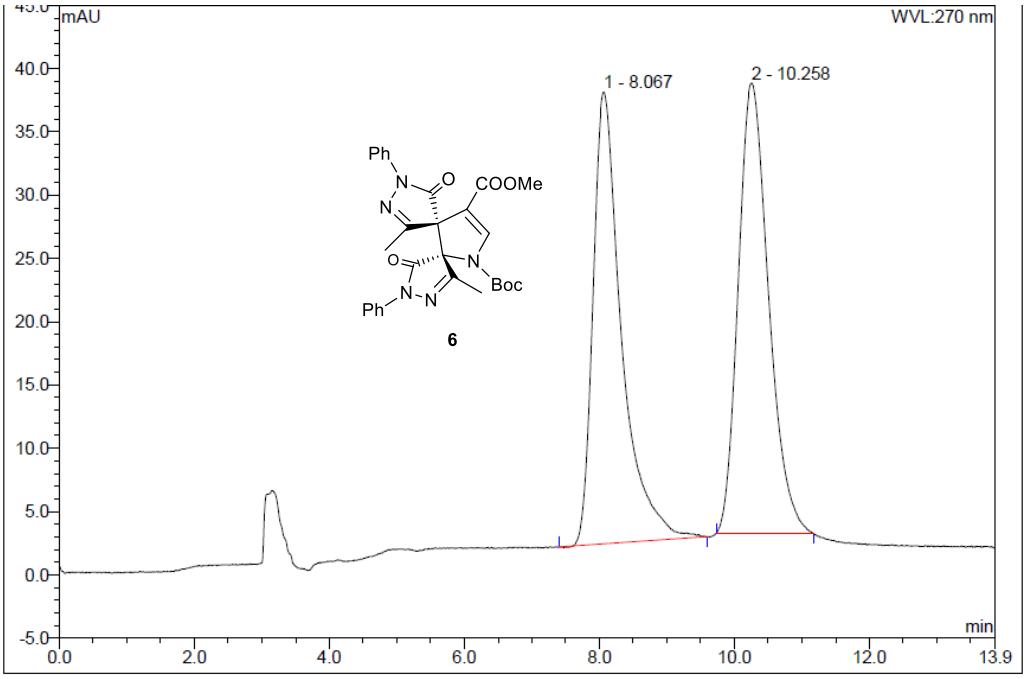
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.18	n.a.	24.540	9.700	50.85	n.a.	BMB
2	12.20	n.a.	6.561	9.375	49.15	n.a.	BMB*
Total:			31.101	19.075	100.00	0.000	



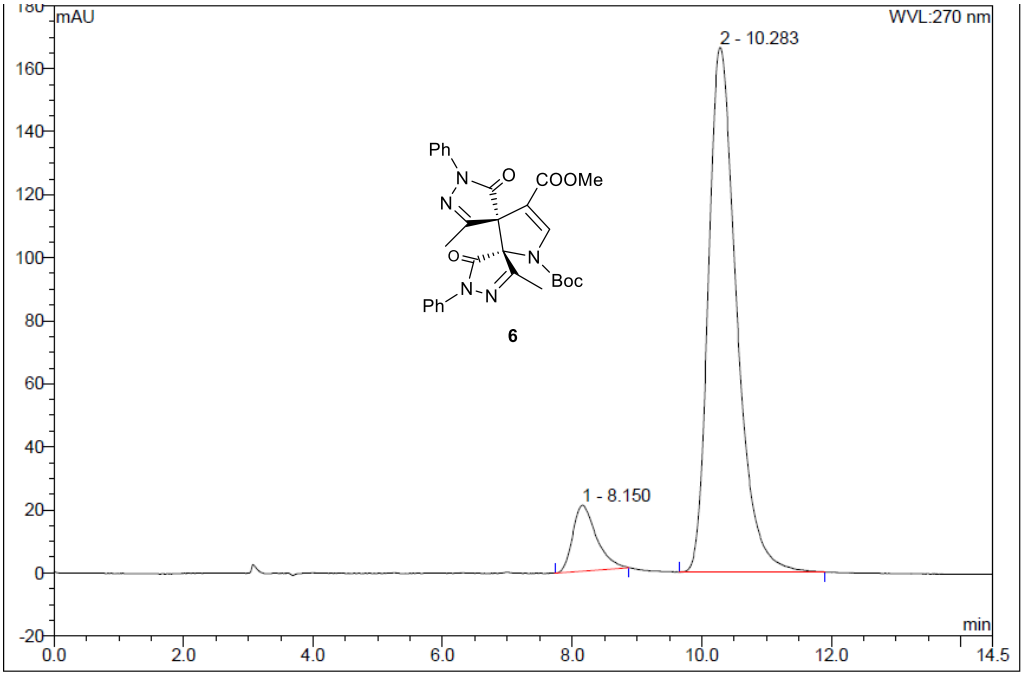
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.23	n.a.	3.003	1.080	5.00	n.a.	BMB*
2	12.20	n.a.	15.222	20.530	95.00	n.a.	BMB*
Total:			18.224	21.610	100.00	0.000	


8.150
7.640
7.623
7.609
7.605
7.427
7.423
7.414
7.409
7.401
7.396
7.385
7.230
7.217
7.204
3.676
2.259
2.213
1.305
Ph
N
O
COOMe
N
O
N
Boc
N
N
Ph
6
0.92
4.07
4.09
2.03
3.00
2.98
3.10
9.04
f1 (ppm)

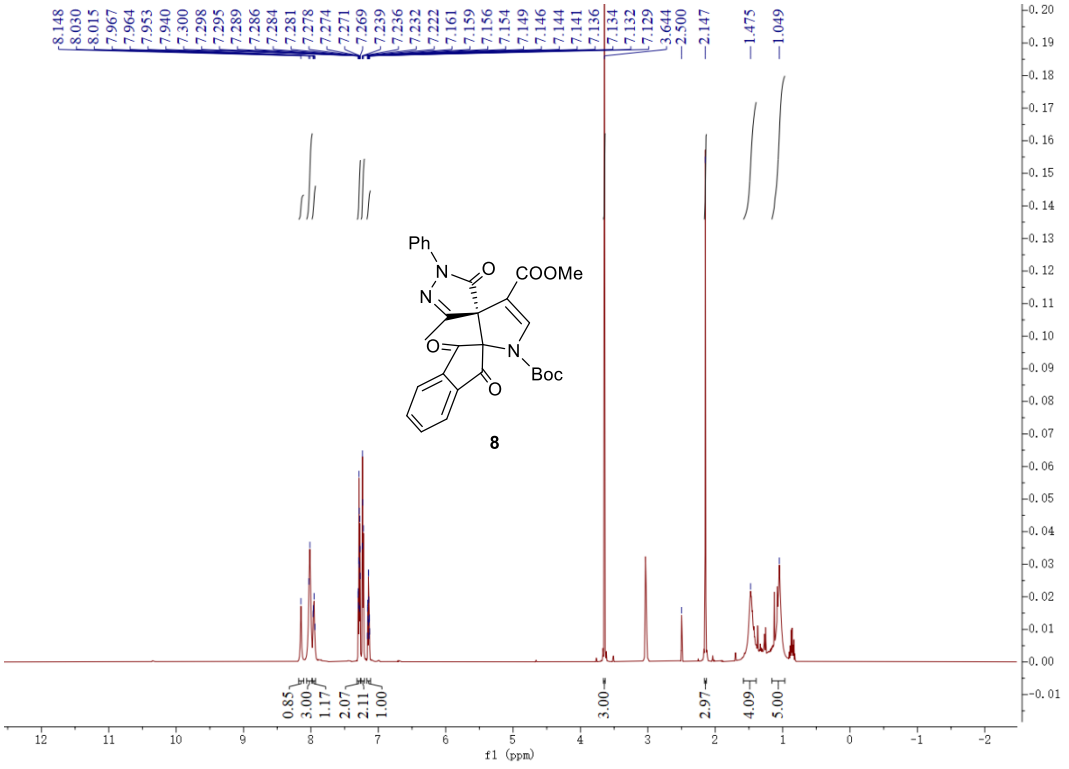

168.513
166.973
162.373
158.404
144.835
137.554
137.386
129.684
129.577
126.398
126.336
119.653
119.158
109.583
86.112
77.284
52.616
27.888
16.398
16.200
Ph
N
O
COOMe
N
O
N
Boc
N
N
Ph
6
f1 (ppm)

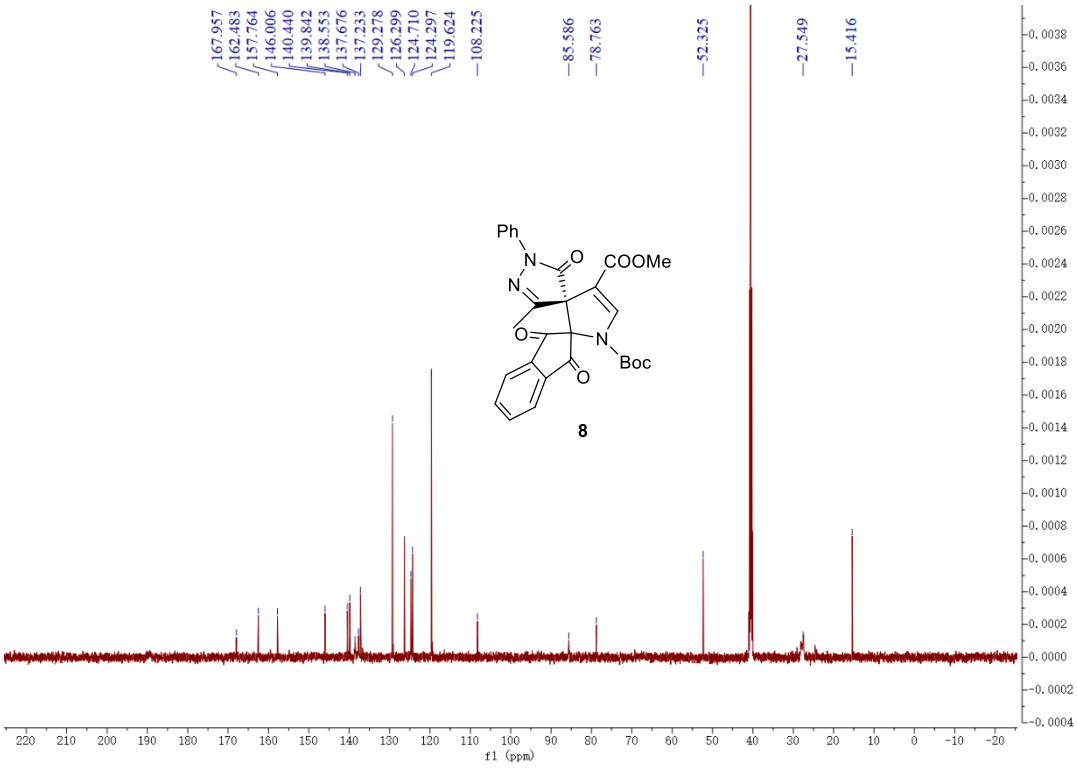


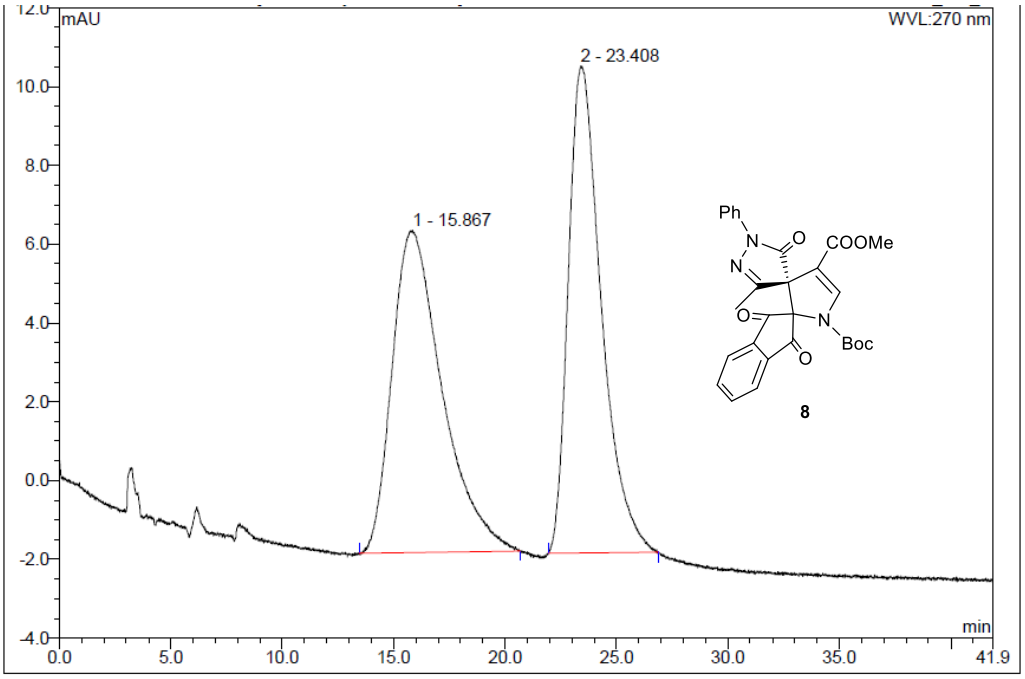
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.07	n.a.	35.700	17.528	48.52	n.a.	BMB*
2	10.26	n.a.	35.601	18.601	51.48	n.a.	BMB*
Total:			71.301	36.129	100.00	0.000	



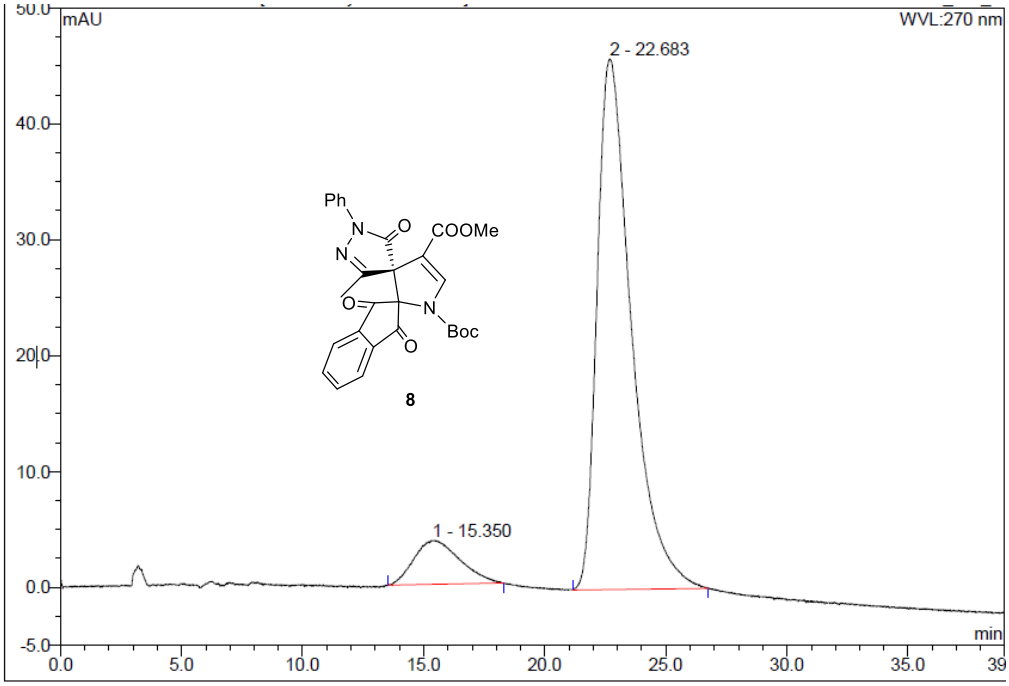
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.15	n.a.	20.887	8.813	9.52	n.a.	BMB*
2	10.28	n.a.	166.478	83.765	90.48	n.a.	BMB
Total:			187.365	92.577	100.00	0.000	


8.148
8.030
8.015
7.967
7.964
7.953
7.940
7.300
7.298
7.295
7.289
7.286
7.284
7.281
7.278
7.274
7.271
7.269
7.239
7.236
7.232
7.222
7.161
7.159
7.156
7.154
7.149
7.146
7.144
7.141
7.136
7.134
7.132
7.129
3.644
2.500
2.147
1.475
1.049
Ph
N
N
O
COOMe
O
N
Boc
O
8
0.85
3.00
1.17
2.07
2.11
1.00
3.00
2.97
4.09
5.00
f1 (ppm)

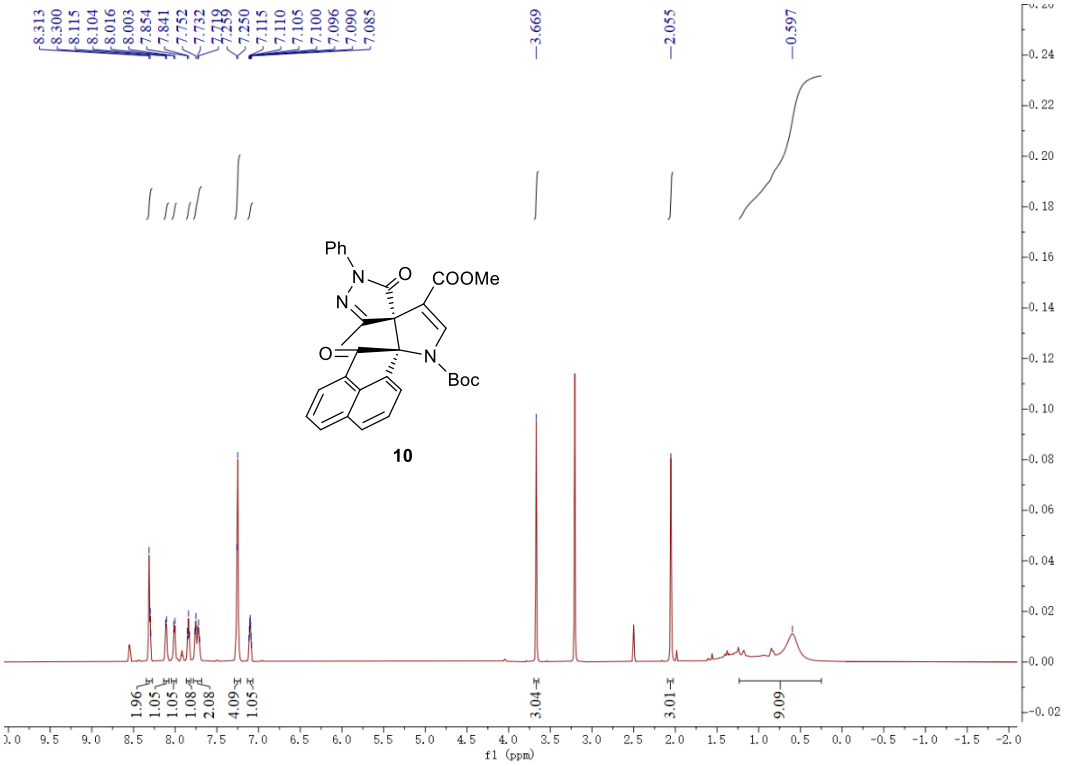

167.957
162.483
157.764
146.006
140.440
139.842
138.553
137.676
137.233
129.278
126.299
124.710
124.297
119.624
108.225
85.586
78.763
52.325
27.549
15.416
Ph
N
N
O
COOMe
O
N
Boc
O
8
f1 (ppm)

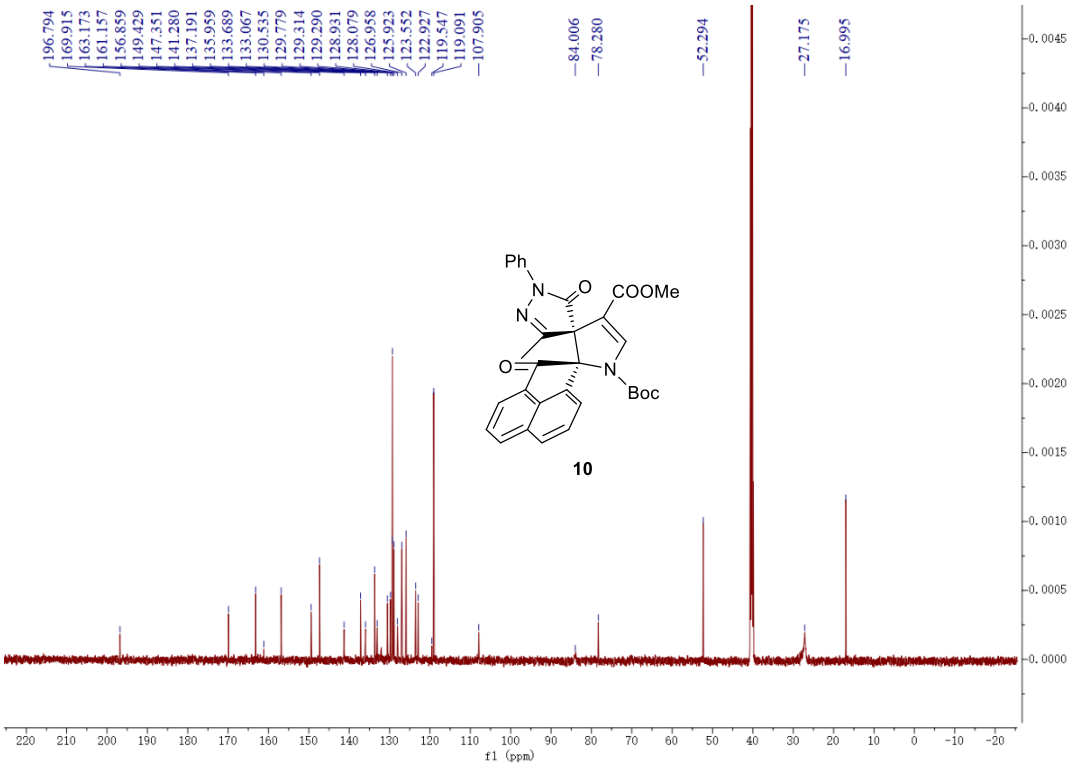


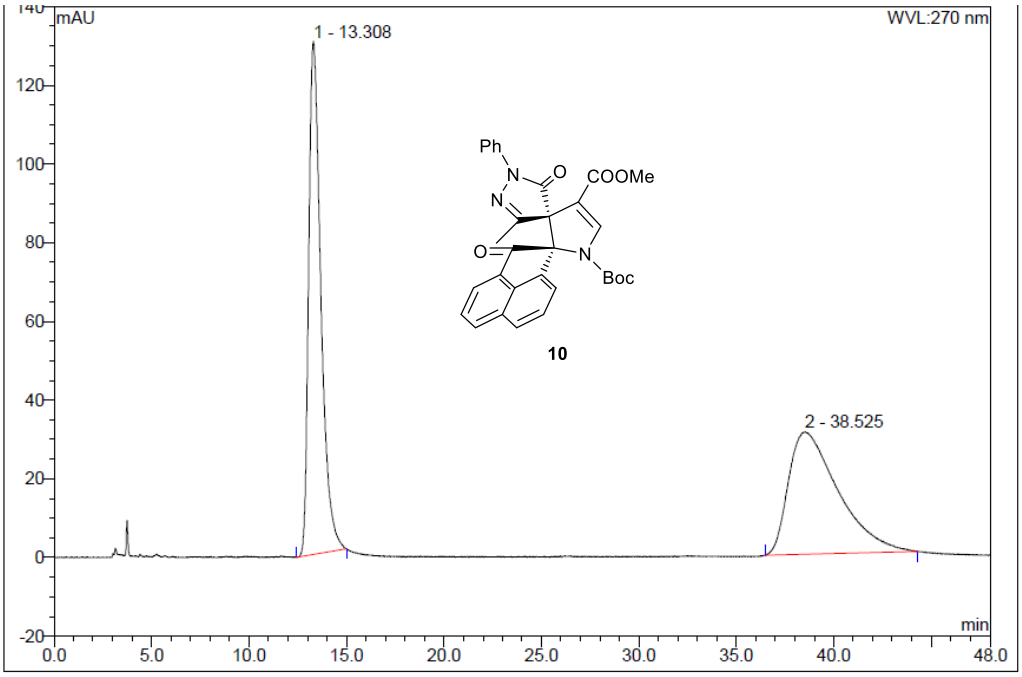
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	15.87	n.a.	8.170	21.251	49.99	n.a.	BMB*
2	23.41	n.a.	12.370	21.257	50.01	n.a.	BMB*
Total:			20.540	42.508	100.00	0.000	



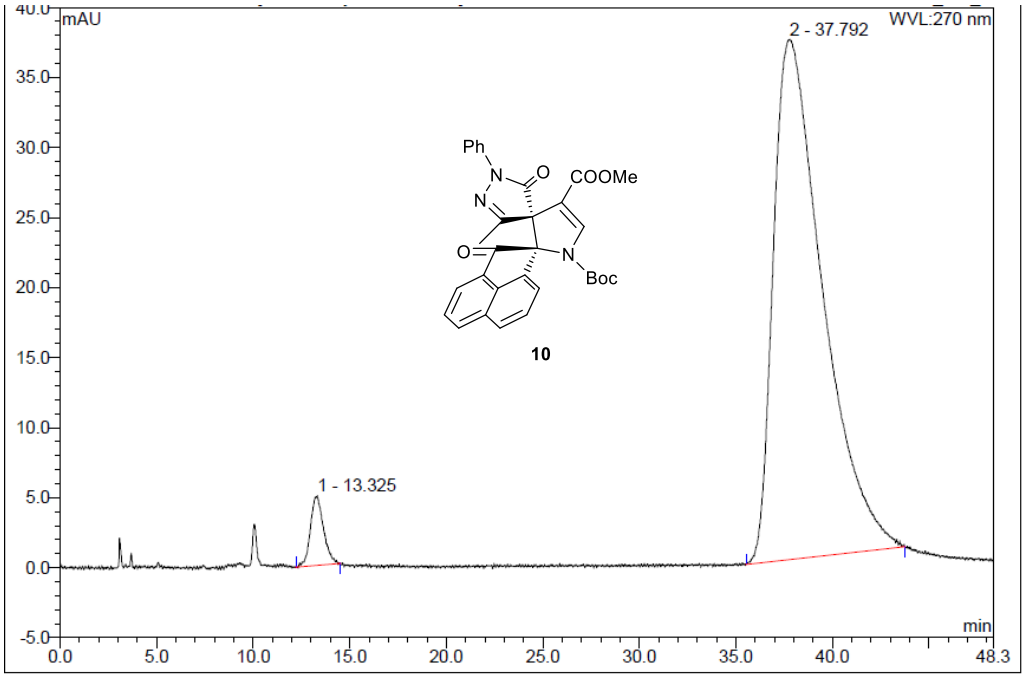
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	15.35	n.a.	3.802	8.309	9.94	n.a.	BMB*
2	22.68	n.a.	45.771	75.263	90.06	n.a.	BMB*
Total:			49.573	83.572	100.00	0.000	


8.313
8.300
8.115
8.104
8.016
8.003
7.854
7.841
7.752
7.732
7.719
7.259
7.250
7.115
7.110
7.105
7.100
7.096
7.090
7.085
3.669
2.055
0.597
Ph
N
N
O
COOMe
O
N
Boc
10
1.96
1.05
1.05
1.08
2.08
4.09
1.05
3.04
3.01
9.09
f1 (ppm)

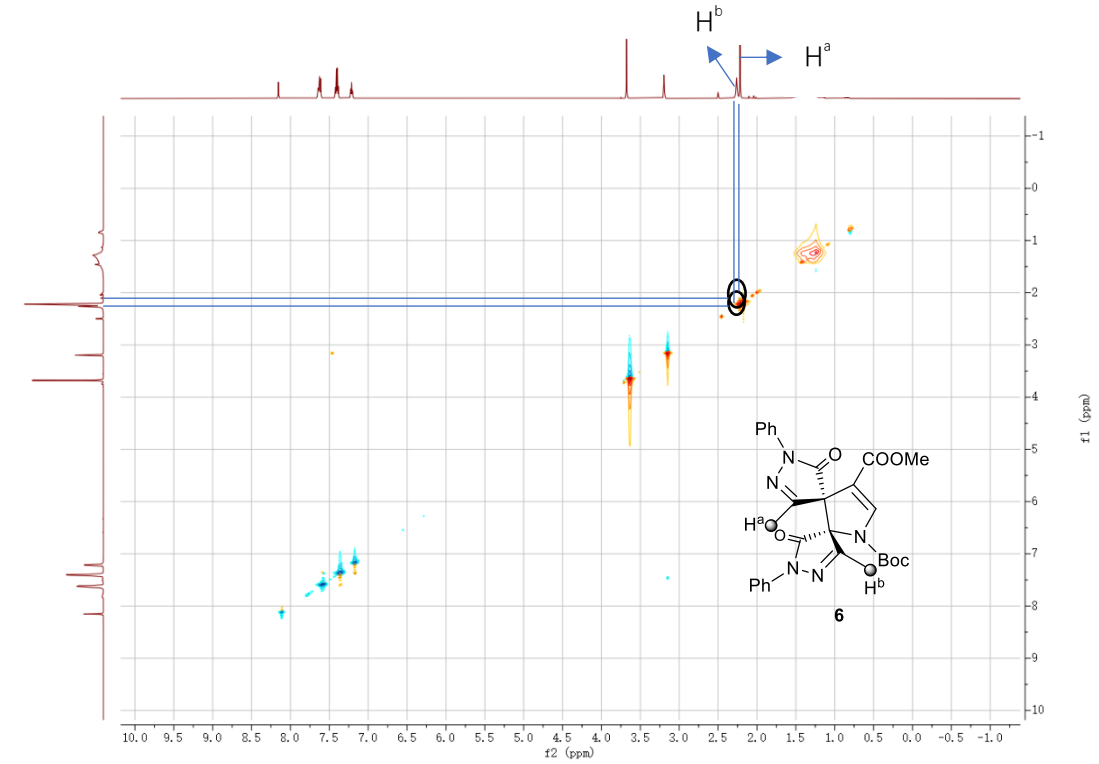

196.794
169.915
163.173
161.157
156.859
149.429
147.351
141.280
137.191
135.959
133.689
133.067
130.535
129.779
129.314
129.290
128.931
128.079
126.958
125.923
123.552
122.927
119.547
119.091
107.905
84.006
78.280
52.294
27.175
16.995
Ph
N
N
O
COOMe
O
N
Boc
10
f1 (ppm)

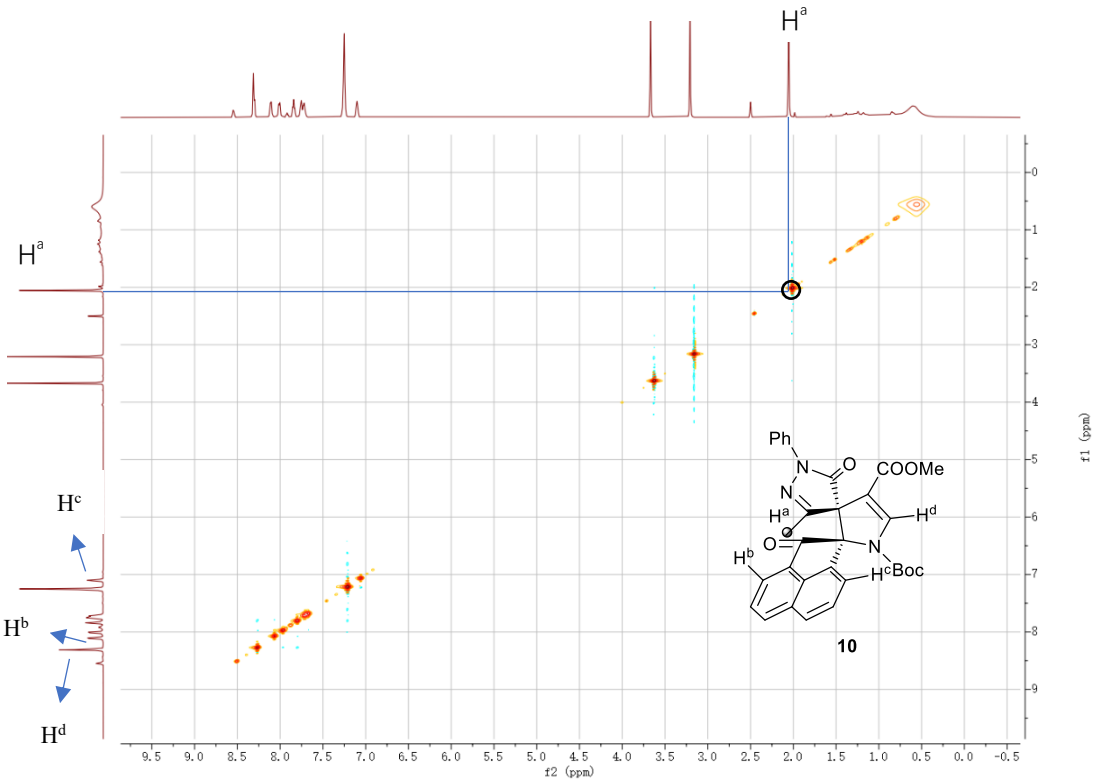


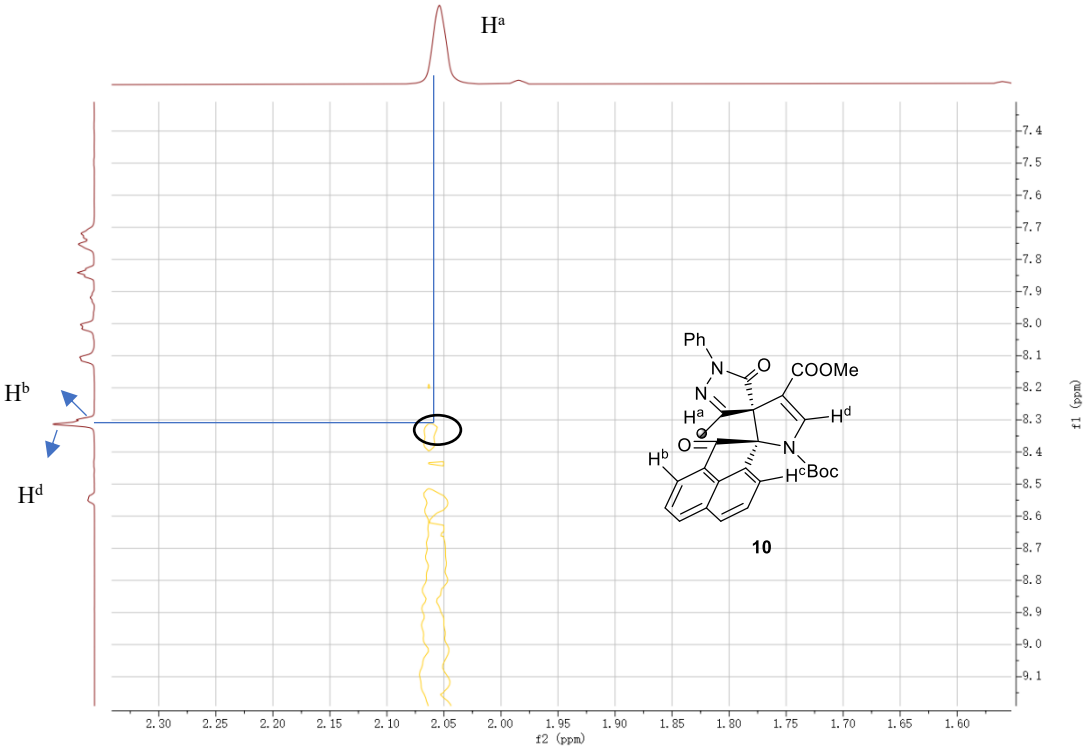
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	13.31	n.a.	130.405	94.347	50.66	n.a.	BMB*
2	38.53	n.a.	31.145	91.887	49.34	n.a.	BMB*
Total:			161.550	186.234	100.00	0.000	

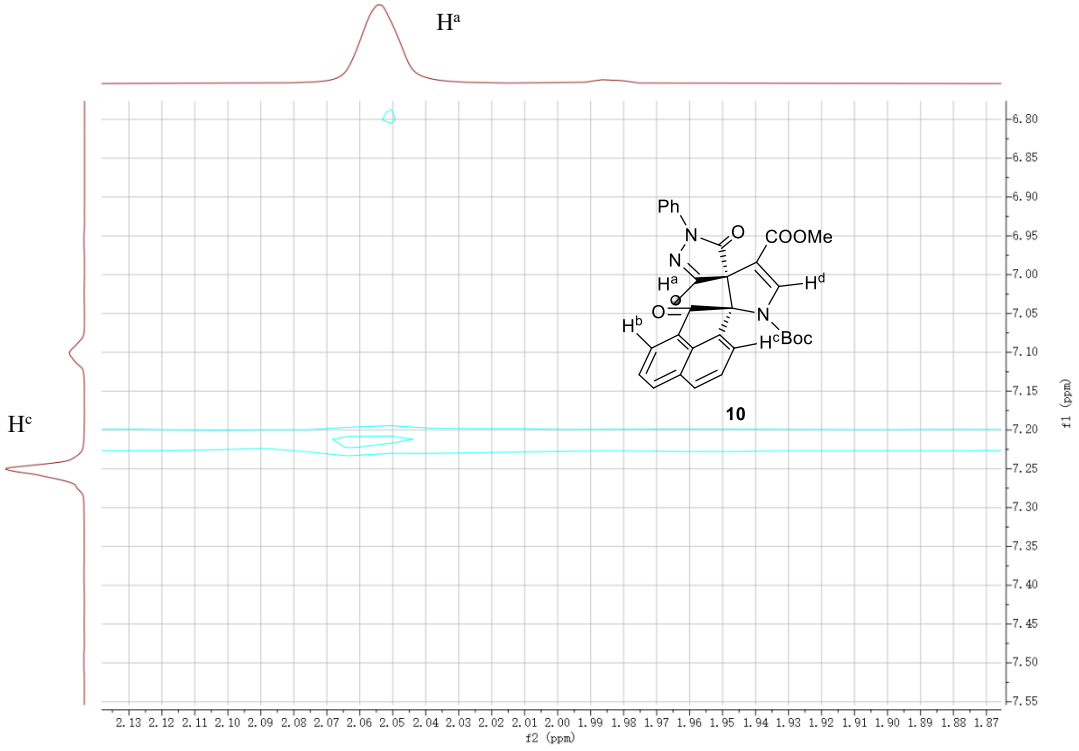


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	13.33	n.a.	4.973	3.885	3.42	n.a.	BMB*
2	37.79	n.a.	37.179	109.864	96.58	n.a.	BMB*
Total:			42.151	113.750	100.00	0.000	

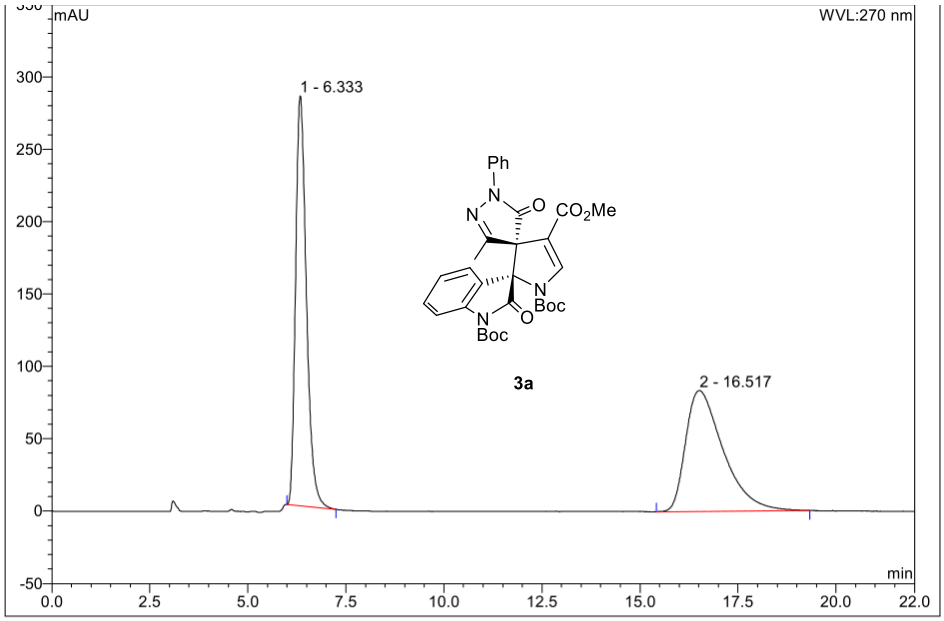

H^b
H^a
Ph
N
O
COOMe
N
H^a
O
N
Boc
Ph
N
N
H^b
6
f2 (ppm)
f1 (ppm)


H^a
H^a
H^c
H^b
H^d
Ph
N
O
COOMe
N
H^a
H^d
O
H^b
N
H^cBoc
10
f2 (ppm)
f1 (ppm)

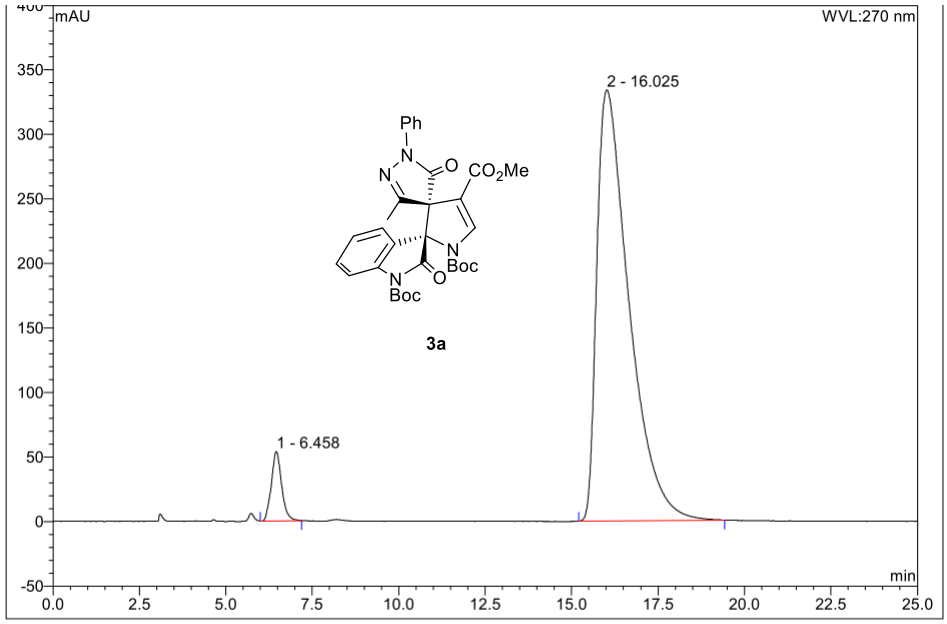

Ha
Hb
Hd
Ph
N
O
COOMe
N
Ha
Hd
O
N
Hb
HcBoc
10
7.4
7.5
7.6
7.7
7.8
7.9
8.0
8.1
8.2
8.3
8.4
8.5
8.6
8.7
8.8
8.9
9.0
9.1
f1 (ppm)
2.30 2.25 2.20 2.15 2.10 2.05 2.00 1.95 1.90 1.85 1.80 1.75 1.70 1.65 1.60
f2 (ppm)


Ha
Hc
Ph
N
O
COOMe
N
Ha
Hd
O
N
Hb
HcBoc
10
6.80
6.85
6.90
6.95
7.00
7.05
7.10
7.15
7.20
7.25
7.30
7.35
7.40
7.45
7.50
7.55
f1 (ppm)
2.13 2.12 2.11 2.10 2.09 2.08 2.07 2.06 2.05 2.04 2.03 2.02 2.01 2.00 1.99 1.98 1.97 1.96 1.95 1.94 1.93 1.92 1.91 1.90 1.89 1.88 1.87
f2 (ppm)

9.4 HPLC chromatograms of gram-scale reaction

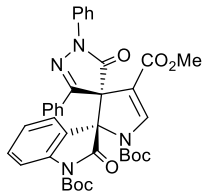


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.33	n.a.	283.297	90.137	49.24	n.a.	BMB
2	16.52	n.a.	83.525	92.927	50.76	n.a.	BMB
Total:			366.822	183.065	100.00	0.000	



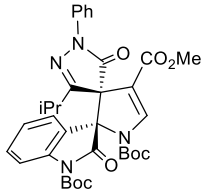
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.46	n.a.	53.882	18.659	4.92	n.a.	BMB
2	16.03	n.a.	334.086	360.235	95.08	n.a.	BMB
Total:			387.968	378.894	100.00	0.000	

1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-2,5''-dioxo-1'',3''-diphenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3dd).

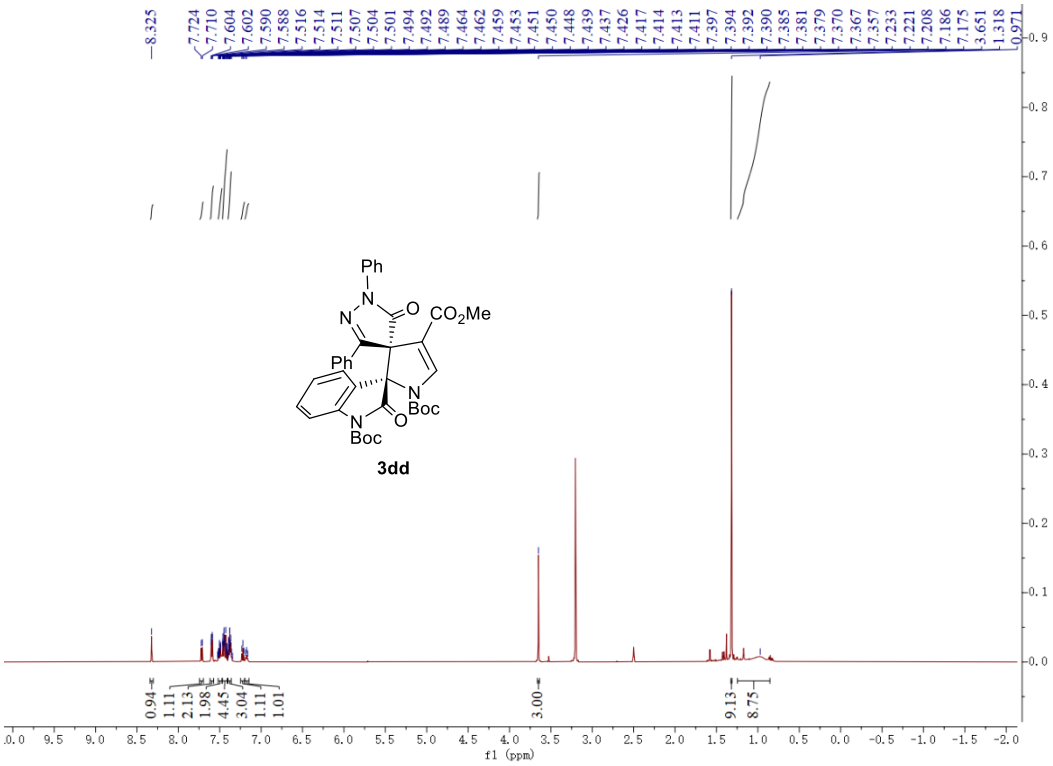


31.9 mg, 48% yield, white solid, mp 97.5 – 99.1 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 7.36 min (minor), t_R = 24.03 min (major); 89% *ee*, $[\alpha]D^{20}$ = −250.3 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.32 (s, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.53 – 7.47 (m, 2H), 7.47 – 7.41 (m, 4H), 7.40 – 7.34 (m, 3H), 7.22 (t, *J* = 7.2, 1H), 7.20 – 7.15 (m, 1H), 3.65 (s, 3H), 1.32 (s, 9H), 0.97 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 169.6, 169.2, 163.4, 154.5, 149.3, 148.1, 146.7, 139.7, 136.9, 131.5, 131.3, 130.8, 129.5, 128.8, 127.8, 126.6, 125.8, 124.8, 119.8, 114.9, 109.1, 84.8, 74.6, 52.5, 27.9, 27.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{37}H_{36}N_4O_8$ 687.2425; Found 687.2419.

1,1'-di-tert-butyl 4'-methyl (3*R*,3'*R*)-3''-isopropyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydro-1'H-dispiro[indoline-3,2'-pyrrole-3',4''-pyrazole]-1,1',4'-tricarboxylate (3ee).



15.0 mg, 24% yield, white solid, mp 78.5 – 80.2 °C; HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 94:6, 1.0 mL/min, at 270 nm): t_R = 5.16 min (minor), t_R = 14.51 min (major); 76% *ee*, $[\alpha]D^{20}$ = −220.1 (c = 0.45, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6, 60 ℃) δ 8.19 (s, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.43 – 7.28 (m, 5H), 7.20 – 7.16 (m, 2H), 3.63 (s, 3H), 2.95 (q, *J* = 7.2 Hz, 1H), 1.54 (s, 9H), 1.24 (d, *J* = 6.6 Hz, 3H), 1.11 (s, 9H), 1.03 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6, 60 ℃) δ 170.8, 169.2, 163.3, 151.6, 149.1, 148.2, 146.2, 139.1, 137.4, 131.5, 129.4, 126.3, 126.2, 124.8, 119.5, 114.7, 108.9, 85.8, 74.6, 52.3, 30.3, 28.0, 27.5, 22.6, 20.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{34}H_{38}N_4O_8$ 653.2582; Found 653.2580.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7.511
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7.492
7.489
7.464
7.462
7.459
7.453
7.451
7.450
7.448
7.439
7.437
7.426
7.417
7.414
7.413
7.411
7.397
7.394
7.392
7.390
7.385
7.381
7.379
7.370
7.367
7.357
7.233
7.221
7.208
7.186
7.175
3.651
1.318
0.971
0.94
1.11
2.13
1.98
4.45
3.04
1.11
1.01
3.00
9.13
8.75
f1 (ppm)

Ph
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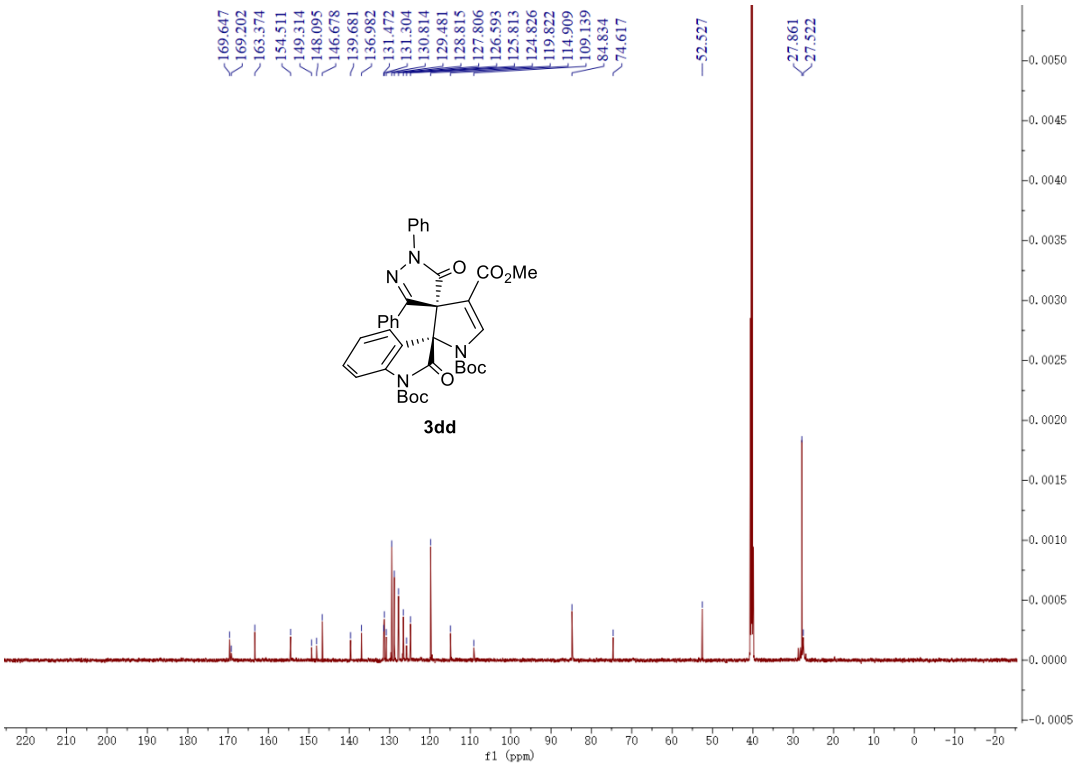
N
O
CO2Me
Ph
N
Boc
O
N
Boc

3dd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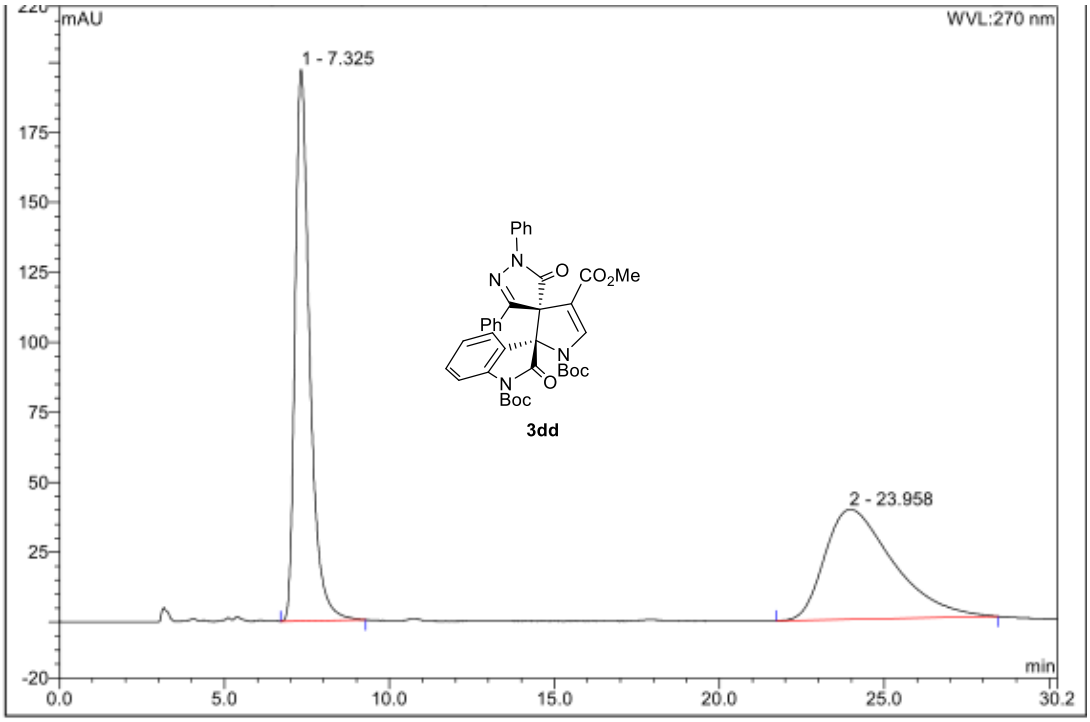
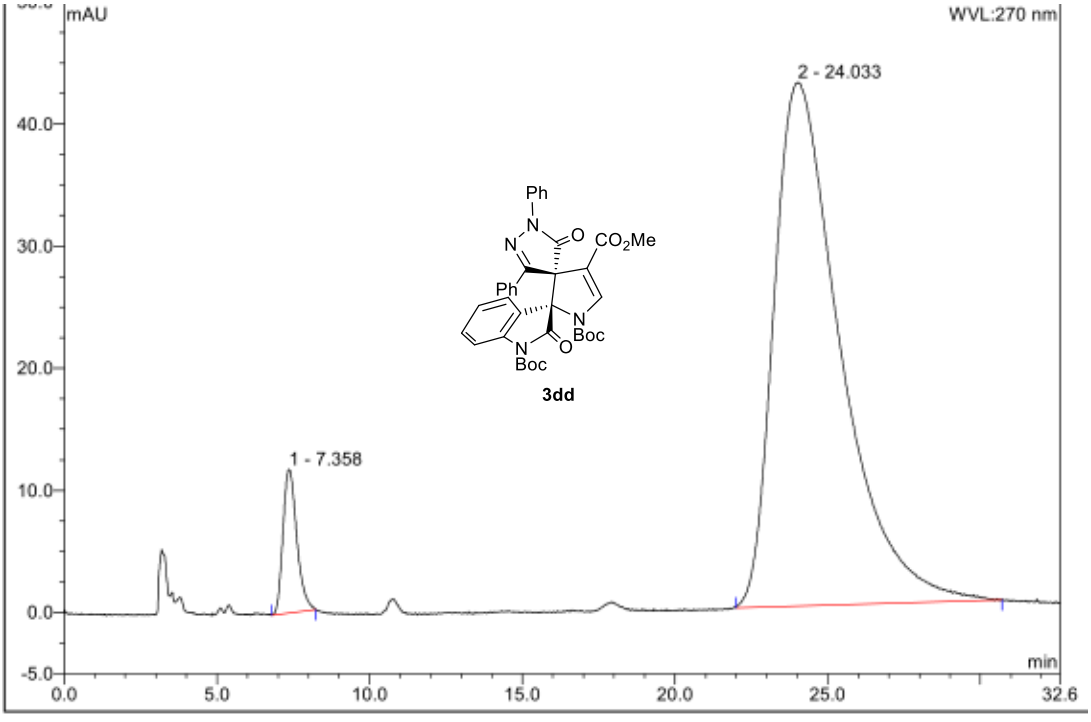
154.511
149.314
148.095
146.678
139.681
136.982
131.472
131.304
130.814
129.481
128.815
127.806
126.593
125.813
124.826
119.822
114.909
109.139
84.834
74.617
52.527
27.861
27.522
f1 (ppm)

Ph
N
N
O
CO2Me
Ph
N
Boc
O
N
Boc

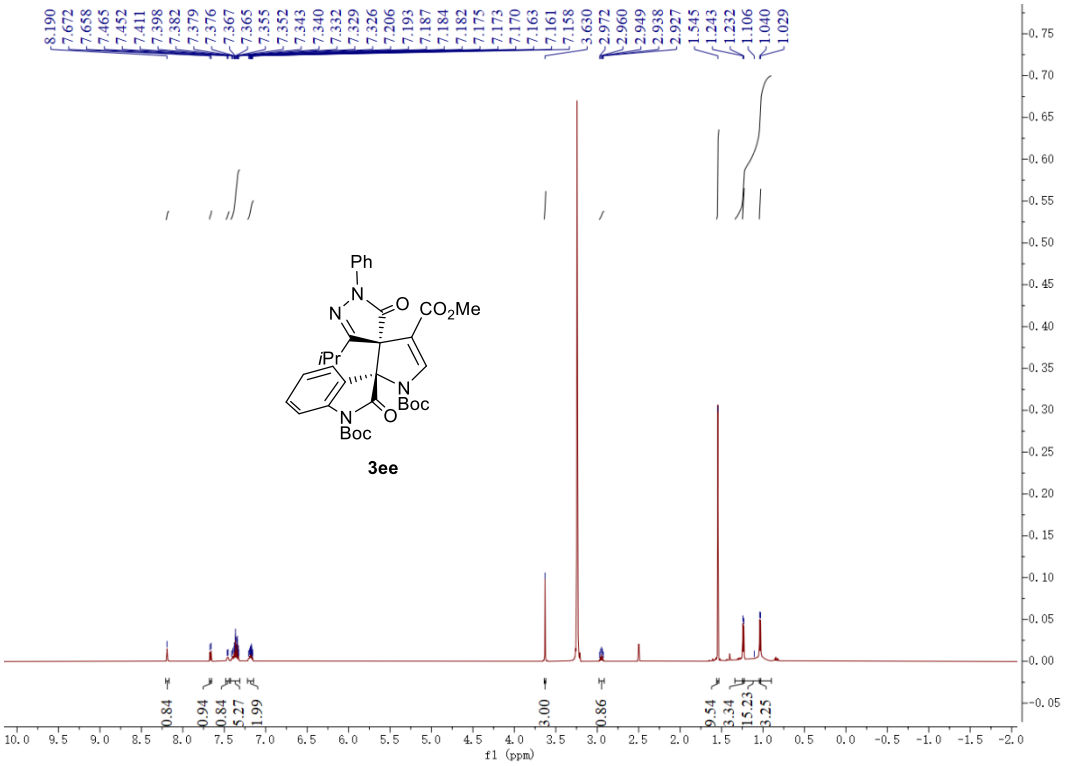
3dd



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.33	n.a.	197.280	102.081	51.86	n.a.	BMB
2	23.96	n.a.	39.377	94.753	48.14	n.a.	BMB*
Total:			236.656	196.833	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.36	n.a.	11.763	6.181	5.42	n.a.	BMB
2	24.03	n.a.	42.870	107.932	94.58	n.a.	BMB*
Total:			54.634	114.112	100.00	0.000	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7.332
7.329
7.326
7.206
7.193
7.187
7.184
7.182
7.175
7.173
7.170
7.163
7.161
7.158
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1.232
1.106
1.040
1.029
Ph
N
N
O
CO2Me
iPr
N
Boc
N
Boc
O
3ee
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0.94
0.84
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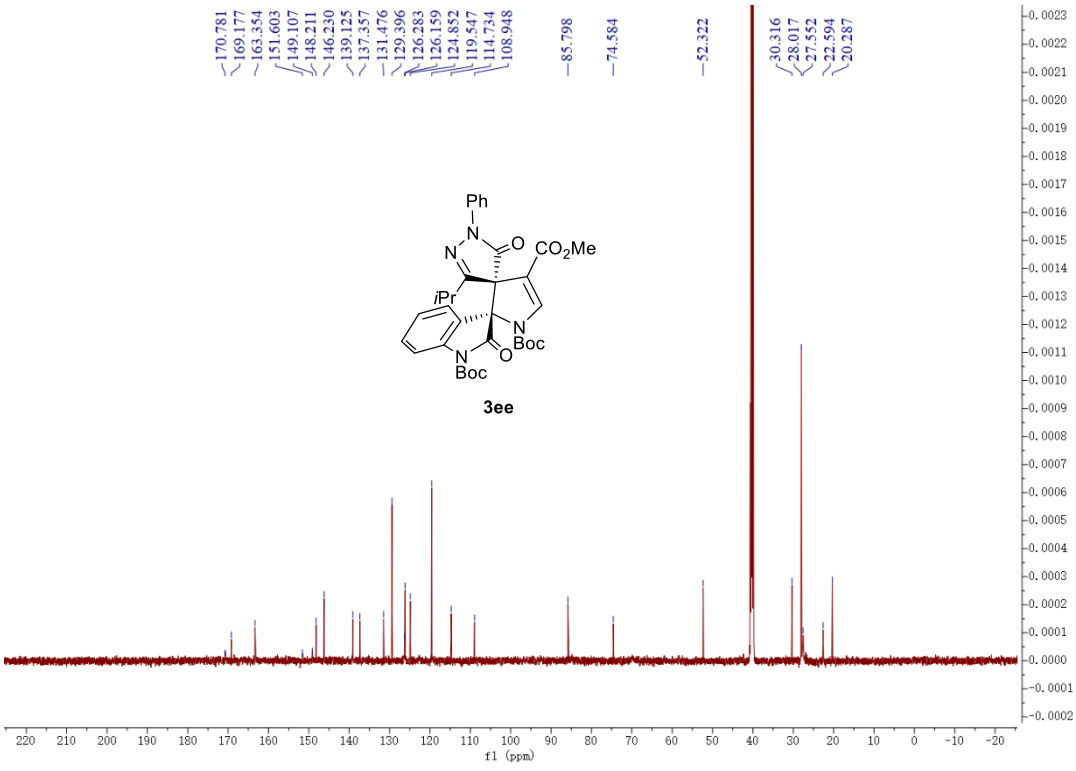
1.99
3.00
0.86
9.54
3.34
15.23
3.25
f1 (ppm)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151.603
149.107
148.211
146.230
139.125
137.357
131.476
129.396
126.283
126.159
124.852
119.547
114.734
108.948
85.798
74.584
52.322
30.316
28.017
27.552
22.594
20.287
Ph
N
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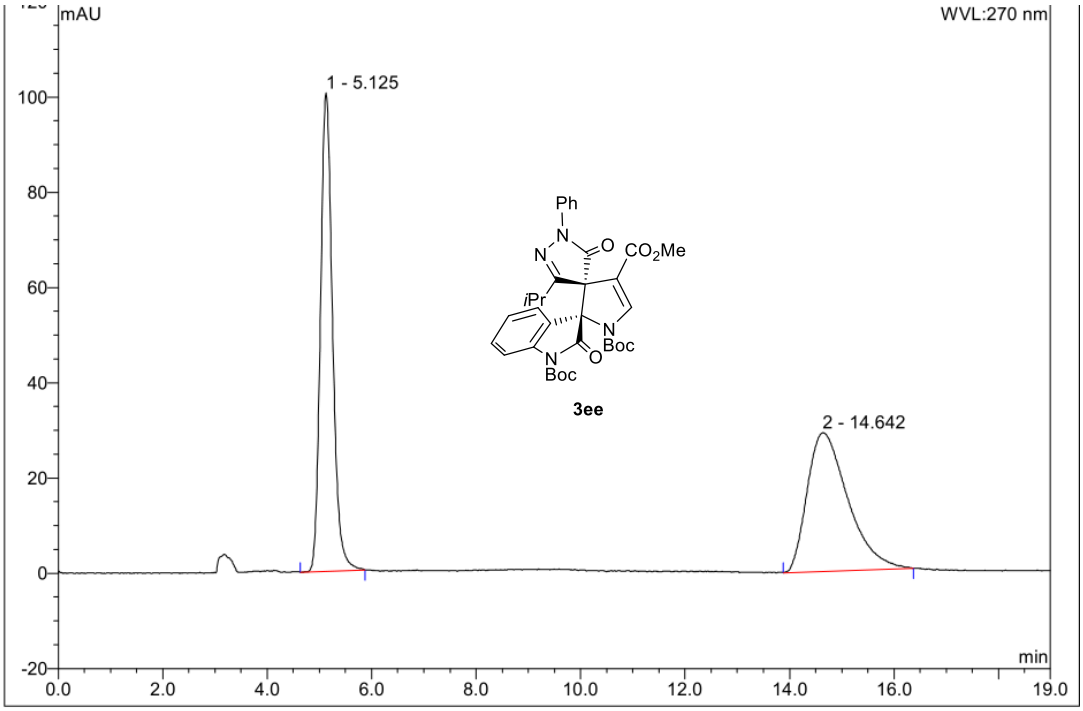
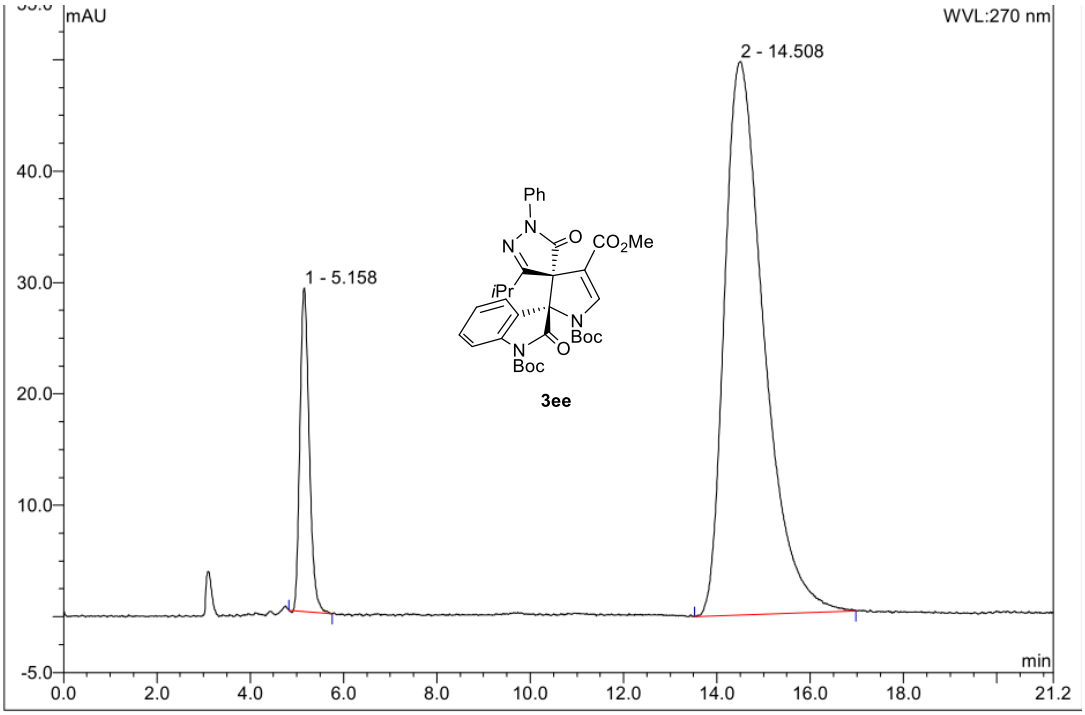
O
CO2Me
iPr
N
Boc
N
Boc
O
3ee
f1 (ppm)



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.13	n.a.	100.505	26.946	50.61	n.a.	BMB
2	14.64	n.a.	29.162	26.295	49.39	n.a.	BMB
Total:			129.667	53.241	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.16	n.a.	29.018	6.677	12.05	n.a.	BMB*
2	14.51	n.a.	49.707	48.733	87.95	n.a.	BMB
Total:			78.725	55.410	100.00	0.000	