Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.


# Catalytic stereodivergent and simultaneous construction of axial and point chirality

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# Supplementary Information

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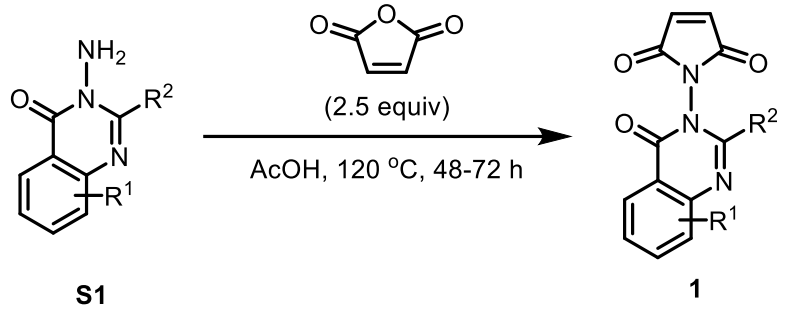
## 1. General information

**$^{1}$H**, **$^{13}$C**, and **$^{19}$F NMR** spectra were recorded on a JNM-ECZ 400S (400 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: $^{1}$H (chloroform δ 7.26; acetone δ 2.05), $^{13}$C (chloroform δ 77.16; acetone δ 29.84). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, br = broad), coupling constants (Hz) and integration. Melting point (**MP**) was obtained on Buchi M-560. For thin layer chromatography (**TLC**), Huanghai TLC plates (HSGF 254) were used, and compounds were visualized with a UV light at 254 nm. High-resolution mass spectra (**HRMS**) were obtained on an Agilent G6545 or a Waters XEVO G2-S TOF Premier spectrometer using ESI ionization. X-ray diffraction analysis was performed on a Bruker D8 Venture diffractometer. **Optical rotations** were recorded on an InsMark IP-digi 300 automatic polarimeter. Enantiomeric excesses (**ee**) were determined by HPLC analysis on an Agilent HPLC 1260 Infinity II; column, Chiralpak IA, IB N-5, and IH.

Unless otherwise noted, all reactions were carried out under an ambient atmosphere; exclusion of air or moisture was not required. Anhydrous and deuterated solvents were purchased from commercial suppliers and used as received without further purification. Ligands **L1**, **L2**, **L3**, ***ent*-L3**, **L4**, **L5**, **L6**, and **L7** were prepared according to literature procedures.[1-5] Ligands **L8**, **L9**, and ***ent*-L9** were purchased from commercial suppliers and used as received without further purification. The structure of **1a** was unambiguously determined by X-ray diffraction analysis (CCDC 2261237). The relative and absolute configurations of **3pa**, **6a**, and **7** were unambiguously determined by X-ray diffraction analysis (CCDC 2261239, CCDC 2261241, and CCDC 2261240, respectively), and those of other products were assigned by analogy.

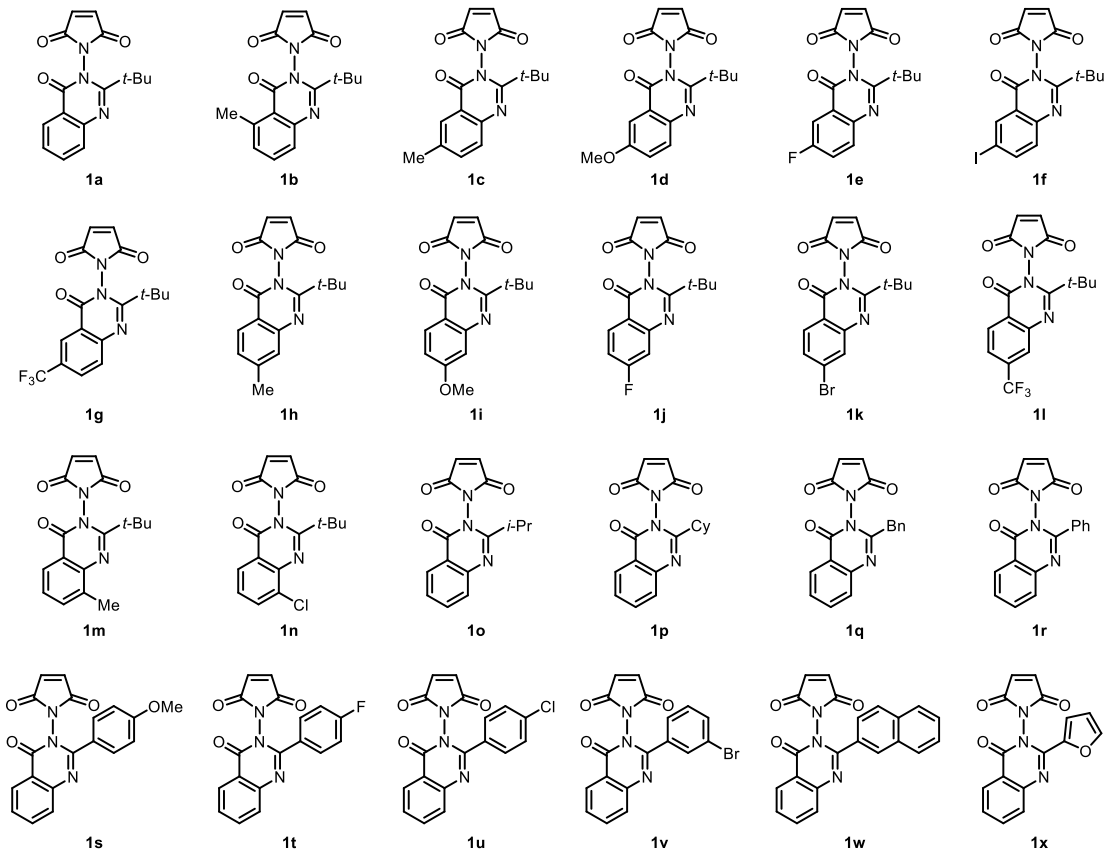
## 2. Preparation of substrates

N-quinazolinone maleimides **1** were prepared from the corresponding **S1**[6,7] with the use of maleic anhydride according to the following procedure.



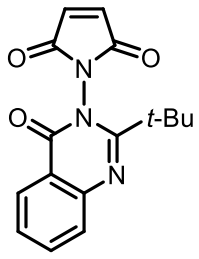

**S1** **1**

**General procedure.** To a solution of **S1** (1.0 equiv) in AcOH (1.0 M) was added maleic anhydride (2.5 equiv), and the resulting mixture was allowed to stir at 120 ℃ for 48-72 h. After completion of the reaction, the reaction mixture was allowed to cool to room temperature and EtOAc was added. Then saturated aqueous $Na_2CO_3$ solution was added to the mixture until effervescence stopped. The organic layer was further washed with saturated aqueous $Na_2CO_3$ solution and finally with brine, and then dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (PE/EtOAc/$CH_2Cl_2$) to give the pure compound.




Scheme S1. N-quinazolinone maleimides **1** involved in this study

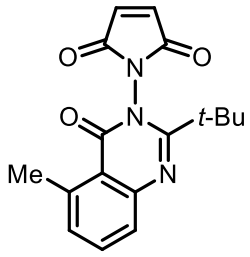
**1-(2-(*tert*-Butyl)-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1a)**



**1a**

White solid, 1.88 g, 32% yield. **MP**: 215-217 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.81-7.76 (m, 1H), 7.74-7.70 (m, 1H), 7.49-7.44 (m, 1H), 7.02 (s, 2H), 1.40 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 168.1, 161.7, 159.9, 146.6, 135.4, 134.6, 128.4, 127.4, 127.1, 120.1, 39.0, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{16}N_3O_3$ 298.1186; Found 298.1191.

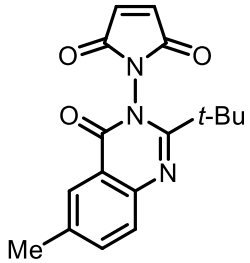
**1-(2-(*tert*-Butyl)-5-methyl-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1b)**




**1b**

White solid, 150 mg, 15% yield. **MP**: 218-219 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.61 (dd, *J* = 8.2, 7.3 Hz, 1H), 7.57-7.53 (m, 1H), 7.23-7.19 (m, 1H), 7.01 (s, 2H), 2.74 (d, *J* = 0.7 Hz, 3H), 1.38 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 168.4, 161.3, 160.0, 148.1, 141.6, 134.6, 134.5, 129.8, 126.6, 118.7, 38.8, 29.4, 22.7; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_3O_3$ 312.1343; Found 312.1342.

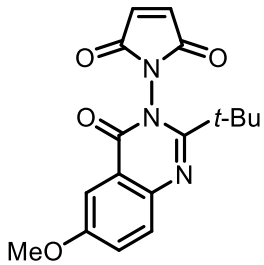
**1-(2-(*tert*-Butyl)-6-methyl-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1c)**




**1c**

White solid, 684 mg, 25% yield. **MP**: 257-258 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.93-7.90 (m, 1H), 7.64-7.57 (m, 2H), 7.01 (s, 2H), 2.45 (d, *J* = 0.9 Hz, 3H), 1.39 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 168.1, 160.7, 159.9, 144.6, 137.7, 136.9, 134.6, 128.2, 126.5, 119.9, 38.9, 29.4, 21.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_3O_3$ 312.1343; Found 312.1349.

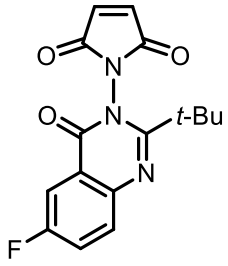
**1-(2-(*tert*-Butyl)-6-methoxy-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1d)**




**1d**

White solid, 410 mg, 30% yield. **MP**: 217-218 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.9 Hz, 1H), 7.49 (d, *J* = 2.9 Hz, 1H), 7.37 (dd, *J* = 8.9, 2.9 Hz, 1H), 7.02 (s, 2H), 3.87 (s, 3H), 1.39 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 168.1, 159.8, 159.3, 158.7, 141.3, 134.6, 130.0, 125.6, 120.9, 106.3, 55.9, 38.8, 29.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_3O_4$ 328.1292; Found 328.1296.

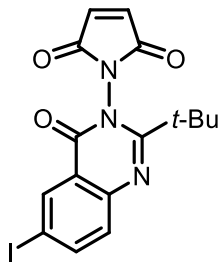
**1-(2-(*tert*-Butyl)-6-fluoro-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1e)**




**1e**

White solid, 400 mg, 28% yield. **MP**: 235-237 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.79-7.70 (m, 2H), 7.54-7.46 (m, 1H), 7.03 (s, 2H), 1.39 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.9, 161.1 (d, *J* = 249.4 Hz), 161.0, 159.2, 143.3, 134.7, 130.9 (d, *J* = 8.3 Hz), 124.0 (d, *J* = 24.0 Hz), 121.4 (d, *J* = 9.0 Hz), 112.0 (d, *J* = 23.9 Hz), 39.0, 29.4; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -111.7; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}FN_3O_3$ 316.1092; Found 316.1098.

**1-(2-(*tert*-Butyl)-6-iodo-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1f)**

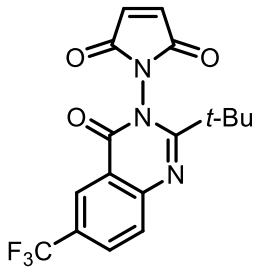



**1f**

White solid, 700 mg, 22% yield. **MP**: 206-207 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.46 (d, *J* = 2.1 Hz, 1H), 8.03 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.45 (dd, *J* = 8.6, 0.4 Hz, 1H), 7.02 (s, 2H), 1.38 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.8, 162.6, 158.5, 145.8, 144.2, 135.9, 134.7, 130.2, 121.8, 91.7, 39.2, 29.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for

$C_{16}H_{15}IN_3O_3$ 424.0153; Found 424.0155.

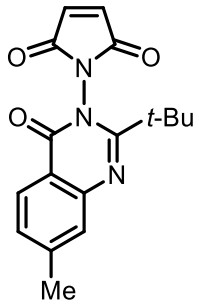
**1-(2-(*tert*-Butyl)-4-oxo-6-(trifluoromethyl)quinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1g)**




**1g**

White solid, 742 mg, 21% yield. **MP**: 139-140 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.44-8.41 (m, 1H), 8.00-7.96 (m, 1H), 7.86-7.82 (m, 1H), 7.05 (s, 2H), 1.41 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.7, 164.2, 159.1, 148.7, 134.8, 131.6 (d, $J$ = 3.5 Hz), 129.5, 129.4 (d, $J$ = 33.6 Hz), 125.1 (d, $J$ = 4.3 Hz), 123.6 (d, $J$ = 272.3 Hz), 120.1, 39.3, 29.3; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -62.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}F_3N_3O_3$ 366.1060; Found 366.1063.

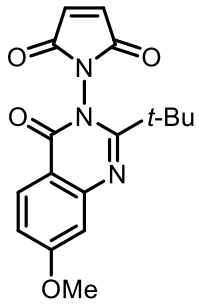
**1-(2-(*tert*-Butyl)-7-methyl-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1h)**




**1h**

White solid, 400 mg, 12% yield. **MP**: 188-189 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.02 (d, $J$ = 8.1 Hz, 1H), 7.54-7.52 (m, 1H), 7.30-7.26 (m, 1H), 7.01 (s, 2H), 2.50 (s, 3H), 1.39 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 168.2, 161.7, 159.7, 146.7, 146.6, 134.6, 129.0, 128.2, 127.0, 117.7, 38.9, 29.4, 22.1; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_3O_3$ 312.1343; Found 312.1348.

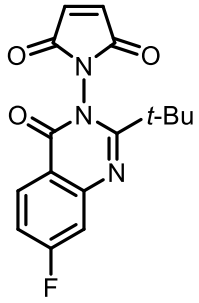
**1-(2-(*tert*-Butyl)-7-methoxy-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1i)**




**1i**

White solid, 250 mg, 22% yield. **MP**: 127-128 ℃; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 8.8 Hz, 1H), 7.09 (d, *J* = 2.4 Hz, 1H), 7.04-7.00 (m, 3H), 3.94 (s, 3H), 1.39 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 168.2, 165.5, 162.4, 159.3, 148.9, 134.6, 128.7, 117.6, 113.5, 109.1, 55.9, 39.0, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_3O_4$ 328.1292; Found 328.1295.

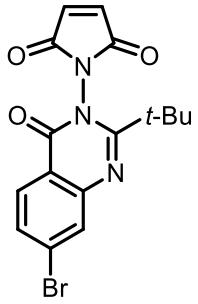
**1-(2-(*tert*-Butyl)-7-fluoro-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1j)**




**1j**

White solid, 486 mg, 18% yield. **MP**: 228-230 ℃; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.15 (dd, *J* = 8.9, 6.0 Hz, 1H), 7.37 (dd, *J* = 9.6, 2.5 Hz, 1H), 7.22-7.15 (m, 1H), 7.03 (s, 2H), 1.39 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 168.0, 167.3 (d, *J* = 255.8 Hz), 163.2, 159.1, 148.8 (d, *J* = 13.4 Hz), 134.7, 129.9 (d, *J* = 10.8 Hz), 116.9 (d, *J* = 2.0 Hz), 116.3 (d, *J* = 23.7 Hz), 113.9 (d, *J* = 21.8 Hz), 39.2, 29.4; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -101.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}FN_3O_3$ 316.1092; Found 316.1099.

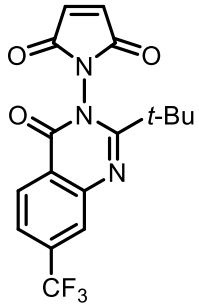
**1-(7-Bromo-2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1k)**



**1k**

White solid, 551 mg, 25% yield. **MP**: 175-177 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 1.9 Hz, 1H), 7.57 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.03 (s, 2H), 1.38 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.9, 163.2, 159.4, 147.4, 134.7, 131.2, 130.8, 130.3, 128.5, 119.0, 39.2, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}BrN_3O_3$ 376.0291; Found 376.0299.

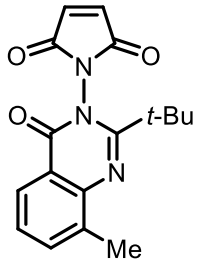
**1-(2-(*tert*-Butyl)-4-oxo-7-(trifluoromethyl)quinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1l)**



**1l**

White solid, 1.07 g, 24% yield. **MP**: 139-140 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.26 (d, *J* = 8.3 Hz, 1H), 8.04-8.01 (m, 1H), 7.67 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.04 (s, 2H), 1.41 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.7, 163.5, 159.1, 146.6, 136.9 (d, *J* = 32.9 Hz), 134.8, 128.3, 126.0 (d, *J* = 4.2 Hz), 123.44 (d, *J* = 3.6 Hz), 123.40 (d, *J* = 273.3 Hz), 122.5, 39.3, 29.4; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -63.2; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}F_3N_3O_3$ 366.1060; Found 366.1061.

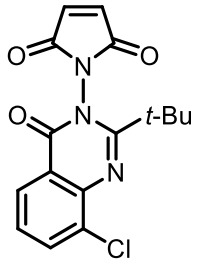
**1-(2-(*tert*-Butyl)-8-methyl-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1m)**




**1m**

White solid, 260 mg, 31% yield. **MP**: 233-234 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.00-7.96 (m, 1H), 7.65-7.61 (m, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.02 (s, 2H), 2.62 (s, 3H), 1.41 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 168.1, 160.2, 144.9, 137.2, 136.0, 134.6, 127.1, 124.8, 120.1, 39.3, 29.4, 17.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_3O_3$ 312.1343; Found 312.1346.

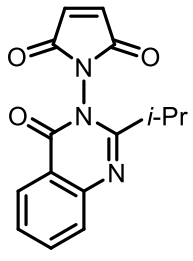
**1-(2-(*tert*-Butyl)-8-chloro-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1n)**




**1n**

White solid, 282 mg, 24% yield. **MP**: 246-248 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.05 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.86 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.03 (s, 2H), 1.43 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.8, 162.5, 159.3, 143.1, 135.7, 134.7, 133.3, 127.6, 125.9, 121.7, 39.7, 29.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}ClN_3O_3$ 332.0796; Found 332.0799.

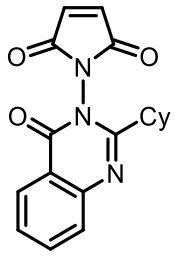
**1-(2-Isopropyl-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1o)**




**1o**

White solid, 608 mg, 49% yield. **MP**: 185-186 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.17 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.82-7.71 (m, 2H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.01 (s, 2H), 3.01-2.89 (m, 1H), 1.32 (d, *J* = 6.7 Hz, 6H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.1, 161.2, 158.8, 147.1, 135.4, 134.3, 128.0, 127.3, 127.2, 120.5, 31.4, 20.9; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{14}N_3O_3$ 284.1030; Found 284.1035.

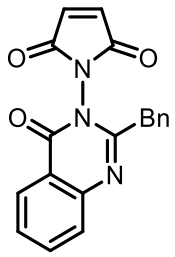
**1-(2-Cyclohexyl-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1p)**




**1p**

White solid, 1.08 g, 45% yield. **MP**: 192-193 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.16 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.81-7.75 (m, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.49-7.42 (m, 1H), 7.02 (s, 2H), 2.61-2.51 (m, 1H), 1.95-1.80 (m, 4H), 1.76-1.65 (m, 3H), 1.35-1.20 (m, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.2, 160.4, 158.8, 147.2, 135.4, 134.3, 128.0, 127.3, 127.1, 120.4, 41.2, 31.0, 26.1, 25.7; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{18}N_3O_3$ 324.1343; Found 324.1348.

**1-(2-Benzyl-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1q)**

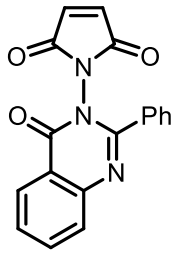



**1q**

White solid, 673 mg, 24% yield. **MP**: 163-165 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.20 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.86-7.76 (m, 2H), 7.54-7.49 (m, 1H), 7.31-7.16 (m, 5H), 6.84 (s, 2H), 4.07 (s, 2H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 165.5, 158.7, 155.2, 146.8, 135.6, 134.3, 133.9, 128.9, 128.8, 128.1, 127.7, 127.6, 127.4, 120.7, 41.6; **HRMS** (ESI)

m/z: $[M+H]^+$ Calcd for $C_{19}H_{14}N_3O_3$ 332.1030; Found 332.1035.

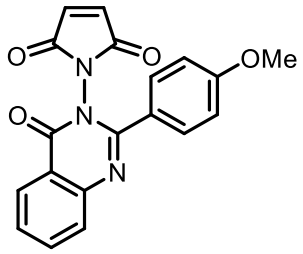
**1-(4-Oxo-2-phenylquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1r)**



**1r**

White solid, 710 mg, 48% yield. **MP**: 165-166 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.30-8.25 (m, 1H), 7.88-7.81 (m, 2H), 7.59-7.53 (m, 3H), 7.50-7.39 (m, 3H), 6.81 (s, 2H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 166.3, 158.9, 155.4, 147.0, 135.8, 133.8, 132.8, 130.8, 128.7, 128.5, 127.99, 127.96, 127.5, 120.8; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{12}N_3O_3$ 318.0873; Found 318.0885.

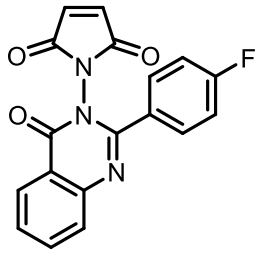
**1-(2-(4-Methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1s)**



**1s**

White solid, 698 mg, 34% yield. **MP**: 144-145 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.27-8.22 (m, 1H), 7.86-7.78 (m, 2H), 7.56-7.50 (m, 3H), 6.94-6.89 (m, 2H), 6.83 (s, 2H), 3.82 (s, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 166.4, 161.5, 159.1, 155.2, 147.1, 135.7, 133.8, 129.8, 128.4, 127.7, 127.5, 125.0, 120.6, 114.1, 55.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{14}N_3O_4$ 348.0979; Found 348.0984.

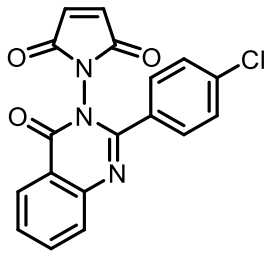
**1-(2-(4-Fluorophenyl)-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1t)**



**1t**

White solid, 815 mg, 49% yield. **MP**: 169-171 ℃; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.28-8.24 (m, 1H), 7.88-7.79 (m, 2H), 7.61-7.53 (m, 3H), 7.14-7.08 (m, 2H), 6.84 (s, 2H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 166.4, 164.1 (d, *J* = 251.8 Hz), 158.8, 154.4, 146.8, 135.9, 133.9, 130.3 (d, *J* = 8.7 Hz), 128.9 (d, *J* = 3.4 Hz), 128.4, 128.1, 127.6, 120.7, 116.0 (d, *J* = 22.1 Hz); **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -108.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{11}FN_3O_3$ 336.0779; Found 336.0784.

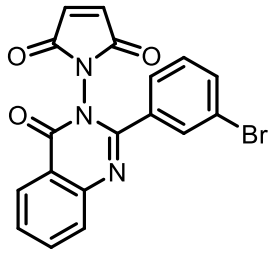
**1-(2-(4-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1u)**



**1u**

White solid, 975 mg, 46% yield. **MP**: 175-176 ℃; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.26 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.89-7.79 (m, 2H), 7.60-7.49 (m, 3H), 7.44-7.36 (m, 2H), 6.84 (s, 2H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 166.4, 158.7, 154.3, 146.8, 137.1, 135.9, 134.0, 131.2, 129.5, 129.0, 128.5, 128.2, 127.6, 120.7; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{11}ClN_3O_3$ 352.0483; Found 352.0489.

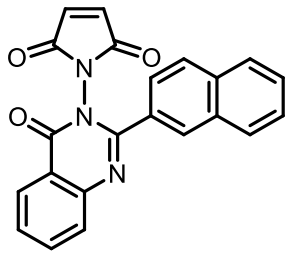
**1-(2-(3-Bromophenyl)-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1v)**



**1v**

White solid, 375 mg, 40% yield. **MP**: 130-132 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.27 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.90-7.80 (m, 2H), 7.76 (t, *J* = 1.9 Hz, 1H), 7.63-7.55 (m, 2H), 7.51-7.47 (m, 1H), 7.29 (t, *J* = 7.9 Hz, 1H), 6.86 (s, 2H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 166.4, 158.6, 153.8, 146.7, 136.0, 134.5, 134.00, 133.95, 131.2, 130.2, 128.5, 128.3, 127.6, 126.5, 122.8, 120.8; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{11}BrN_3O_3$ 395.9978; Found 395.9977.

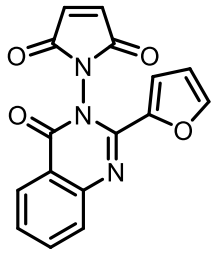
**1-(2-(Naphthalen-2-yl)-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1w)**



**1w**

White solid, 460 mg, 33% yield. **MP**: 195-196 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.32-8.28 (m, 1H), 8.17-8.13 (m, 1H), 7.91-7.84 (m, 5H), 7.64-7.51 (m, 4H), 6.77 (s, 2H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 166.4, 158.9, 155.4, 147.0, 135.8, 134.0, 133.8, 132.7, 130.1, 128.9, 128.6, 128.5, 128.0, 127.9, 127.8, 127.5, 127.0, 124.3, 120.8; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{14}N_3O_3$ 368.1030; Found 368.1039.

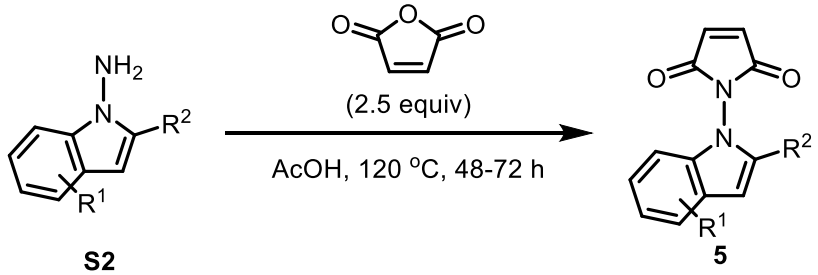
**1-(2-(Furan-2-yl)-4-oxoquinazolin-3(4*H*)-yl)-1*H*-pyrrole-2,5-dione (1x)**



**1x**

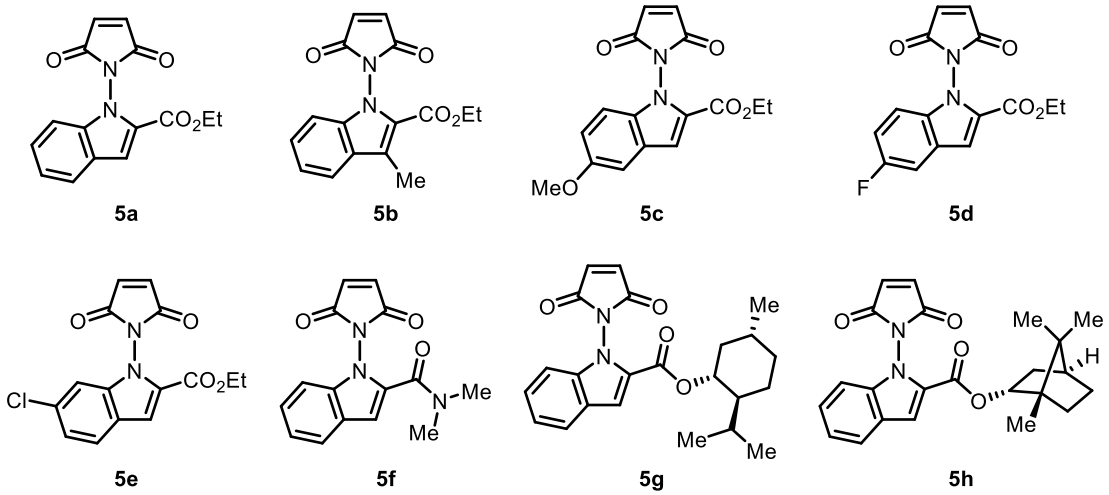
Pale yellow solid, 863 mg, 43% yield. **MP**: 207-209 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.25-8.20 (m, 1H), 7.85-7.78 (m, 2H), 7.56-7.47 (m, 2H), 7.17 (dd, *J* = 3.6, 0.8 Hz, 1H), 7.00 (s, 2H), 6.53 (dd, *J* = 3.6, 1.8 Hz, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 166.1, 158.7, 147.2, 146.1, 145.2, 144.5, 135.8, 134.1, 128.3, 127.8, 127.5, 120.4, 117.1, 112.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{10}N_3O_4$ 308.0666; Found 308.0672.

N-indole maleimides **5** were prepared from the corresponding **S2**[8] with the use of maleic anhydride according to the following procedure.



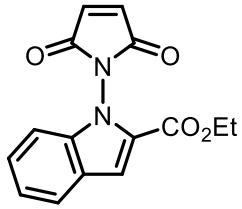

**S2** **5**

**General procedure.** To a solution of **S2** (1.0 equiv) in AcOH (1.0 M) was added maleic anhydride (2.5 equiv), and the resulting mixture was allowed to stir at 120 °C for 48-72 h. After completion of the reaction, the reaction mixture was allowed to cool to room temperature and EtOAc was added. Then saturated aqueous $Na_2CO_3$ solution was added to the mixture until effervescence stopped. The organic layer was further washed with saturated aqueous $Na_2CO_3$ solution and finally with brine, and then dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (PE/EtOAc/$CH_2Cl_2$) to give the pure compound.



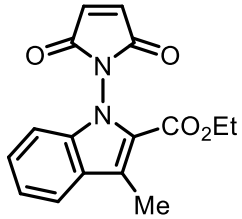

Scheme S2. N-indole maleimides **5** involved in this study

**Ethyl 1-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-1*H*-indole-2-carboxylate (5a)**




Pale yellow solid, 1.35 g, 55% yield. **MP**: 142-143 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.76-7.73 (m, 1H), 7.47 (d, $J$ = 0.9 Hz, 1H), 7.46-7.40 (m, 1H), 7.31-7.25 (m, 2H), 6.99 (s, 2H), 4.31 (q, $J$ = 7.2 Hz, 2H), 1.35 (t, $J$ = 7.1 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.2, 160.5, 139.4, 133.9, 127.1, 125.9, 124.5, 123.3, 122.7, 112.0, 109.2, 61.2, 14.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{13}N_2O_4$ 285.0870; Found 285.0864.

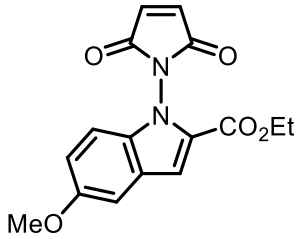
**Ethyl 1-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-3-methyl-1*H*-indole-2-carboxylate (5b)**




Yellow solid, 1.42 g, 63% yield. **MP**: 163-164 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.75-

7.70 (m, 1H), 7.43-7.38 (m, 1H), 7.28-7.23 (m, 1H), 7.22-7.17 (m, 1H), 6.96 (s, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.64 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.5, 161.4, 138.7, 133.8, 127.4, 126.1, 123.7, 122.4, 122.1, 121.3, 109.0, 60.9, 14.4, 11.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}N_2O_4$ 299.1026; Found 299.1029.

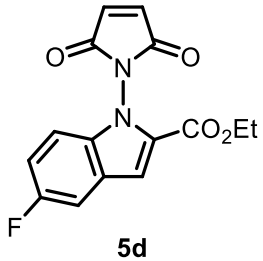
**Ethyl 1-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-5-methoxy-1*H*-indole-2-carboxylate (5c)**




**5c**

Yellow solid, 1.33 g, 63% yield. **MP**: 121-123 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 0.9 Hz, 1H), 7.16-7.04 (m, 3H), 6.96 (s, 2H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.3, 160.4, 156.1, 134.7, 133.9, 126.3, 125.0, 118.3, 111.5, 110.2, 103.6, 61.1, 55.9, 14.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}N_2O_5$ 315.0975; Found 315.0982.

**Ethyl 1-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-5-fluoro-1*H*-indole-2-carboxylate (5d)**

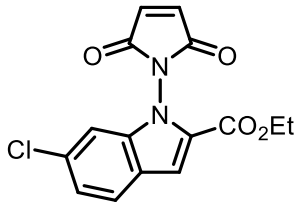



**5d**

Pale yellow solid, 235 mg, 10% yield. **MP**: 187-189 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 0.8 Hz, 1H), 7.38-7.34 (m, 1H), 7.22-7.13 (m, 2H), 6.99 (s, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.1, 160.2, 159.3 (d, *J* = 239.0 Hz), 135.9, 134.0, 127.3, 124.8 (d, *J* = 10.6 Hz), 116.0 (d, *J* = 27.1

Hz), 111.6 (d, $J$ = 5.2 Hz), 110.4 (d, $J$ = 9.5 Hz), 107.9 (d, $J$ = 24.1 Hz), 61.4, 14.3; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -120.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{12}FN_2O_4$ 303.0776; Found 303.0780.

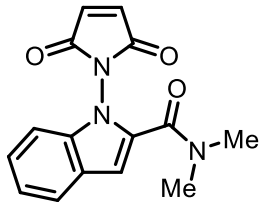
**Ethyl 6-chloro-1-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-1*H*-indole-2-carboxylate (5e)**




**5e**

Pale yellow solid, 1.34 g, 59% yield. **MP**: 185-187 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.63 (dd, $J$ = 8.5, 0.6 Hz, 1H), 7.40 (d, $J$ = 1.0 Hz, 1H), 7.28-7.25 (m, 1H), 7.22 (dd, $J$ = 8.5, 1.8 Hz, 1H), 6.99 (s, 2H), 4.28 (q, $J$ = 7.1 Hz, 2H), 1.32 (t, $J$ = 7.2 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.0, 160.2, 139.7, 134.0, 133.3, 126.6, 124.2, 123.8, 123.0, 111.8, 109.5, 61.4, 14.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{12}ClN_2O_4$ 319.0480; Found 319.0486.

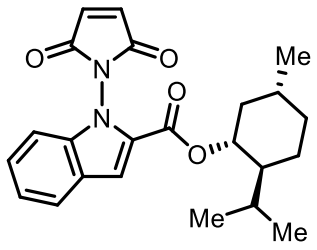
**1-(2,5-Dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-*N*,*N*-dimethyl-1*H*-indole-2-carboxamide (5f)**




**5f**

Yellow solid, 245 mg, 20% yield. **MP**: 224-226 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.70-7.64 (m, 1H), 7.38-7.32 (m, 1H), 7.26-7.20 (m, 2H), 6.92 (s, 2H), 6.89 (d, $J$ = 0.8 Hz, 1H), 3.30 (br s, 3H), 3.04 (br s, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.2, 162.1, 137.6, 133.8, 128.6, 125.8, 124.5, 122.39, 122.36, 109.0, 107.3, 39.9, 36.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{14}N_3O_3$ 284.1030; Found 284.1035.

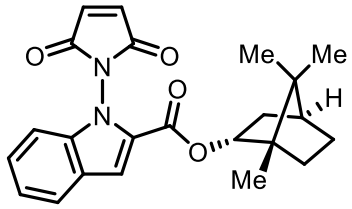
**(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 1-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-1*H*-indole-2-carboxylate (5g)**



**5g**

Yellow foam, 2.54 g, 57% yield. **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.73-7.70 (m, 1H), 7.44 (d, *J* = 0.9 Hz, 1H), 7.42-7.37 (m, 1H), 7.27-7.22 (m, 2H), 6.98 (s, 2H), 4.87-4.79 (m, 1H), 2.07-2.00 (m, 1H), 1.94-1.85 (m, 1H), 1.74-1.66 (m, 2H), 1.53-1.41 (m, 2H), 1.10-0.99 (m, 2H), 0.93-0.86 (m, 7H), 0.75 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.17, 167.15, 160.1, 139.4, 133.9, 127.0, 126.3, 124.6, 123.2, 122.7, 111.9, 109.2, 75.3, 47.3, 40.9, 34.3, 31.6, 26.5, 23.7, 22.1, 20.8, 16.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{27}N_2O_4$ 395.1965; Found 395.1968.

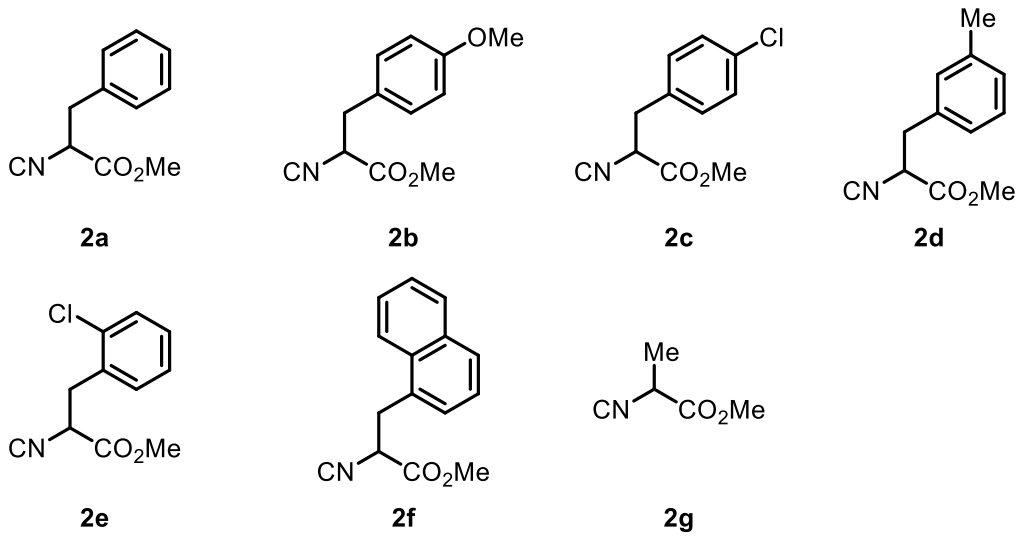
**(1*S*,2*R*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl 1-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-1*H*-indole-2-carboxylate (5h)**



**5h**

White solid, 2.14 g, 71% yield. **MP**: 153-154 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.75-7.71 (m, 1H), 7.45 (d, *J* = 0.9 Hz, 1H), 7.43-7.38 (m, 1H), 7.29-7.22 (m, 2H), 6.98 (s, 2H), 5.05-4.99 (m, 1H), 2.43-2.33 (m, 1H), 2.13-2.04 (m, 1H), 1.85-1.75 (m, 1H), 1.72 (t, *J* = 4.5 Hz, 1H), 1.44-1.35 (m, 1H), 1.34-1.26 (m, 1H), 1.09 (dd, *J* = 13.9, 3.5 Hz, 1H), 0.91 (s, 3H), 0.90 (s, 3H), 0.88 (s, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 167.2, 160.8, 139.3, 133.92, 133.89, 127.0, 126.1, 124.5, 123.2, 122.7, 111.7, 109.2, 81.0, 49.3, 48.0, 45.0, 36.8, 28.1, 27.4, 19.8, 18.9, 13.7; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{25}N_2O_4$ 393.1809; Found 393.1814.

Isocyanoacetates **2** were prepared according to literature procedures, among which **2a** and **2c**-**2g** are known compounds.[9,10]

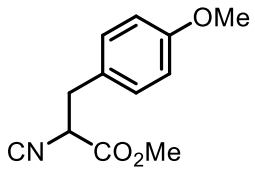



**2a** **2b** **2c** **2d**

**2e** **2f** **2g**

Scheme S3. Isocyanoacetates **2** involved in this study

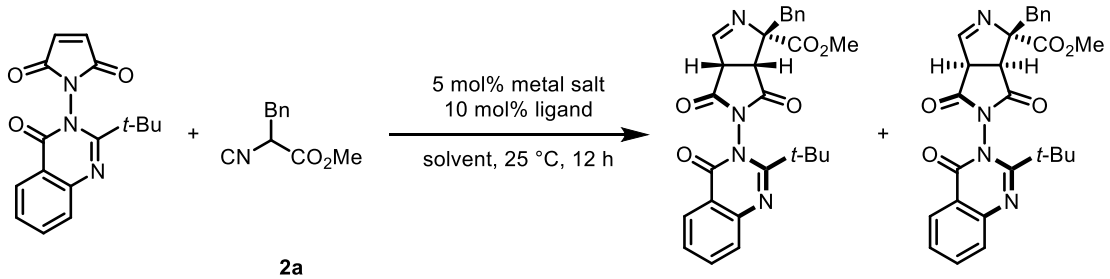
**Methyl 2-isocyano-3-(4-methoxyphenyl)propanoate (2b)**




**2b**

Yellow oil, 1.41 g, 66% yield. **$^1$H NMR** (400 MHz, acetone-$d_6$): δ 7.26-7.20 (m, 2H), 6.93-6.88 (m, 2H), 4.83 (dd, $J$ = 7.9, 4.9 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.22 (dd, $J$ = 14.1, 4.9 Hz, 1H), 3.11 (dd, $J$ = 14.1, 7.9 Hz, 1H); **$^{13}$C NMR** (101 MHz, acetone-$d_6$): δ 167.6, 161.7, 160.1, 131.3, 127.8, 114.7, 58.7, 55.5, 53.4, 38.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{14}NO_3$ 220.0968; Found 220.0972.

## 3. Metal salt and solvent screening

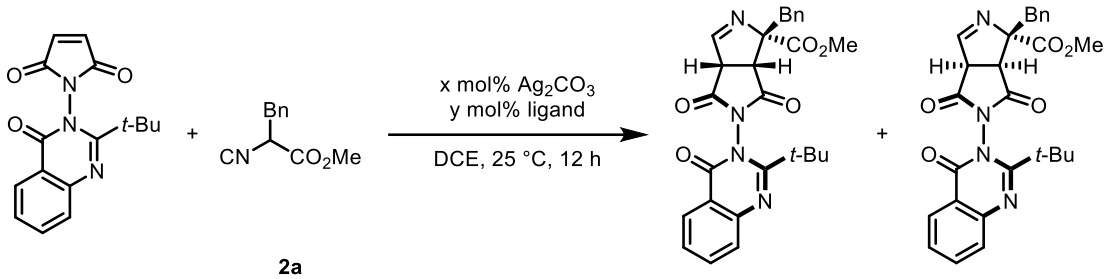



**1a** | **2a** (1.0 equiv) | **3aa** | **4aa**

| entry | metal salt | ligand | solvent | dr (**3aa**:**4aa**)[a] | yield (%)[b] | ee of **3aa** (%)[d] | ee of **4aa** (%)[d] |
|---|---|---|---|---|---|---|---|
| 1 | $Ag_2O$ | **L3** | DCE | >20:1 | 92 | 95 | / |
| 2 | AgOAc | **L3** | DCE | >20:1 | 88 | 97 | / |
| 3 | $Ag_2CO_3$ | **L3** | $CH_2Cl_2$ | 17:1 | 88 | 97 | / |
| 4 | $Ag_2CO_3$ | **L3** | THF | 6:1 | 84[c] | 82 | / |
| 5 | $Ag_2CO_3$ | **L3** | EtOAc | >20:1 | 91 | 73 | / |
| 6 | $Ag_2CO_3$ | **L3** | PhCl | 14:1 | 45 | 82 | / |
| 7 | $Ag_2O$ | **L9** | DCE | 1:>20 | 78 | / | 95 |
| 8 | AgOAc | **L9** | DCE | 1:>20 | 62 | / | 95 |
| 9 | $Ag_2CO_3$ | **L9** | $CH_2Cl_2$ | 1:>20 | 55 | / | 91 |
| 10 | $Ag_2CO_3$ | **L9** | THF | 1:20 | 19 | / | 81 |
| 11 | $Ag_2CO_3$ | **L9** | EtOAc | 1:6 | 46[c] | / | 88 |
| 12 | $Ag_2CO_3$ | **L9** | PhCl | 1:>20 | 55 | / | 95 |

Reaction conditions: **1a** (0.1 mmol), **2a** (0.1 mmol), metal salt (5 mol%), and ligand (10 mol%) in 1.0 mL of solvent at 25 °C for 12 h. [a]Determined by crude $^1$H NMR. [b]Isolated yield in pure form. [c]Combined yield. [d]Determined by chiral HPLC.

## 4. Effect of the ligand/metal salt ratio

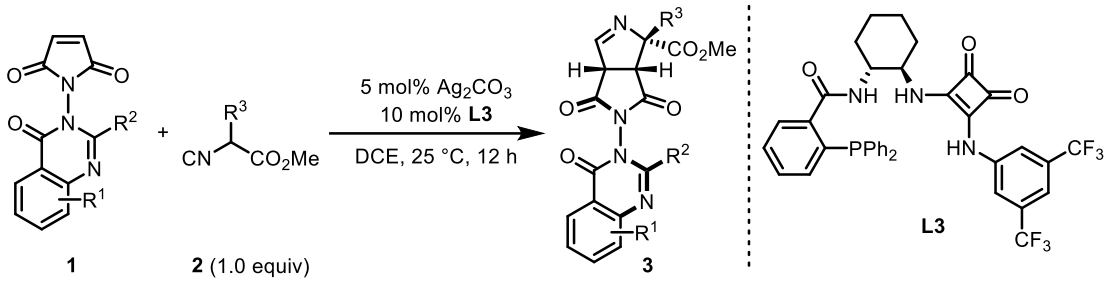



**1a** **2a** (1.0 equiv) **3aa** **4aa**

| entry | x | y | ligand | dr (**3aa**:**4aa**)[a] | yield (%)[b] | ee of **3aa** (%)[c] | ee of **4aa** (%)[c] |
|---|---|---|---|---|---|---|---|
| 1 | 5 | 10 | **L3** | >20:1 | 91 | 98 | / |
| 2 | 10 | 10 | **L3** | >20:1 | 88 | 98 | / |
| 3 | 20 | 10 | **L3** | >20:1 | 87 | 98 | / |
| 4 | 5 | 10 | **L9** | 1:>20 | 80 | / | 95 |
| 5 | 10 | 10 | **L9** | 1:>20 | 80 | / | 95 |
| 6 | 20 | 10 | **L9** | 1:>20 | 77 | / | 94 |

Reaction conditions: **1a** (0.1 mmol), **2a** (0.1 mmol), $Ag_2CO_3$ (x mol%), and ligand (y mol%) in 1.0 mL of DCE at 25 °C for 12 h. [a]Determined by crude $^1H$ NMR. [b]Isolated yield in pure form. [c]Determined by chiral HPLC.

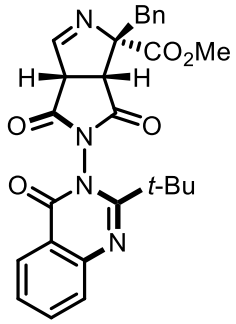
## 5. Diastereo- and enantioselective synthesis of 3




**General procedure.** To a 10 mL vial charged with **L3** (7.1 mg, 0.010 mmol, 10 mol%) and $Ag_2CO_3$ (1.4 mg, 0.005 mmol, 5 mol%) was added anhydrous DCE (1.0 mL, 0.1 M). The mixture was stirred for 10 min, and then N-quinazolinone maleimide **1** (0.10 mmol, 1.0 equiv) and isocyanoacetate **2** (0.10 mmol, 1.0 equiv) were added successively in one portion. The reaction mixture was stirred at 25 ℃ for 12 h, then concentrated and purified by flash column chromatography to afford the product **3**.

The racemic sample for the standard of chiral HPLC spectra was prepared by using a mixture of approximately 1:1 **L3** and ***ent*-L3**.

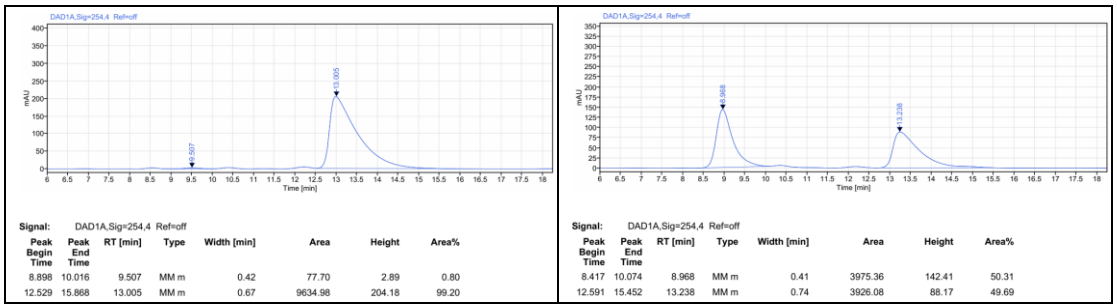
**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3aa)**



**3aa**

>20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 44.2 mg, 91% yield. **MP**: 129-130 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.16-8.12 (m, 1H), 7.78-7.72 (m, 1H), 7.69-7.65 (m, 2H), 7.46-7.41 (m, 1H), 7.36-7.30 (m, 3H), 7.21-7.16 (m, 2H), 3.71 (s, 3H), 3.61 (d, *J* = 8.3 Hz, 1H), 3.56 (d, *J* = 14.1 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H), 3.04 (dd, *J* = 8.3, 1.2 Hz, 1H), 1.30 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.4, 169.9,

168.0, 160.2, 160.1, 157.9, 146.2, 135.3, 134.2, 131.2, 128.7, 128.4, 127.7, 127.5, 127.2, 120.1, 86.4, 57.0, 53.0, 47.2, 42.9, 39.0, 29.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{27}N_4O_5$ 487.1976; Found 487.1987. **Optical Rotation**: $[\alpha]^{20}_D$ = -369.7 (c = 0.1, $CH_2Cl_2$). 98% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 9.5 min for minor isomer, $t_R$ = 13.0 min for major isomer).



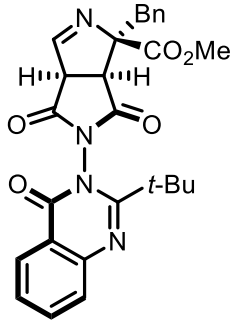

Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.898 | 10.016 | 9.507 | MM m | 0.42 | 77.70 | 2.89 | 0.80 |
| 12.529 | 15.868 | 13.005 | MM m | 0.67 | 9634.98 | 204.18 | 99.20 |

Signal: DAD1A,Sig=254,4 Ref=off

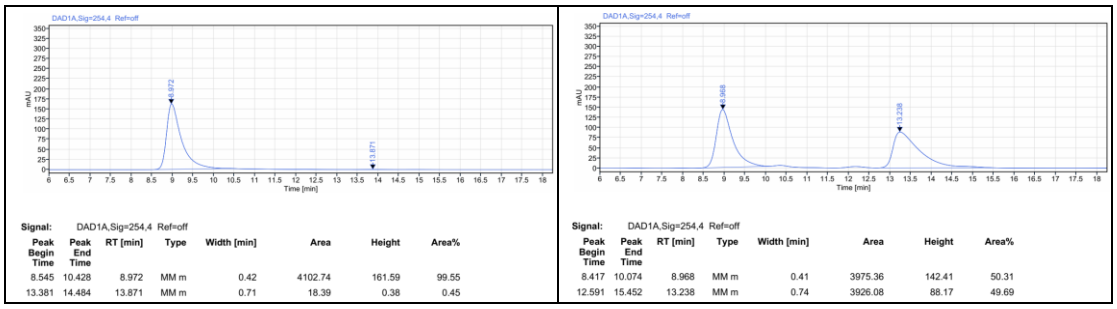
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.417 | 10.074 | 8.968 | MM m | 0.41 | 3975.36 | 142.41 | 50.31 |
| 12.591 | 15.452 | 13.238 | MM m | 0.74 | 3926.08 | 88.17 | 49.69 |

**Methyl (*R*a,1*R*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (*ent*-3aa)**




***ent*-3aa**

With ***ent*-L3**. >20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 45.7 mg, 94% yield. **Optical Rotation**: $[\alpha]^{20}_D$ = +366.6 (c = 0.1, $CH_2Cl_2$). 99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 9.0 min for major isomer, $t_R$ = 13.9 min for minor isomer).



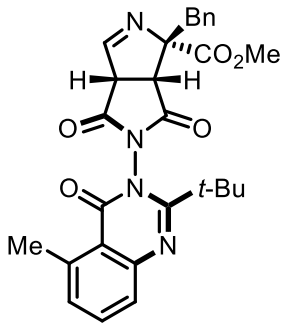

Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.545 | 10.428 | 8.972 | MM m | 0.42 | 4102.74 | 161.59 | 99.55 |
| 13.381 | 14.484 | 13.871 | MM m | 0.71 | 18.39 | 0.38 | 0.45 |

Signal: DAD1A,Sig=254,4 Ref=off

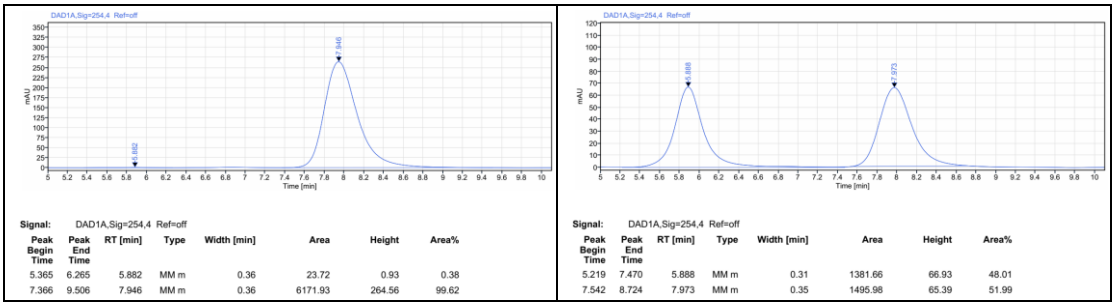
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.417 | 10.074 | 8.968 | MM m | 0.41 | 3975.36 | 142.41 | 50.31 |
| 12.591 | 15.452 | 13.238 | MM m | 0.74 | 3926.08 | 88.17 | 49.69 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-5-methyl-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ba)**



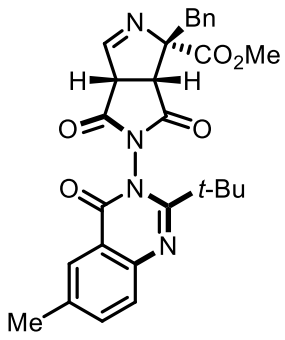

**3ba**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 32.1 mg, 64% yield. **MP**: 137-139 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 1.1 Hz, 1H), 7.57 (dd, *J* = 8.1, 7.3 Hz, 1H), 7.50-7.47 (m, 1H), 7.36-7.30 (m, 3H), 7.20-7.16 (m, 3H), 3.70 (s, 3H), 3.58 (d, *J* = 8.5 Hz, 1H), 3.55 (d, *J* = 14.0 Hz, 1H), 3.43 (d, *J* = 14.0 Hz, 1H), 3.09 (dd, *J* = 8.4, 1.2 Hz, 1H), 2.72 (s, 3H), 1.28 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.4, 169.9, 168.2, 160.3, 159.8, 157.7, 147.7, 141.7, 134.4, 134.2, 131.2, 129.8, 128.6, 127.7, 126.5, 118.6, 86.3, 57.0, 53.0, 47.1, 42.9, 38.8, 29.5, 22.8; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_5$ 501.2132; Found 501.2131. **Optical Rotation**: $[\alpha]^{20}_D$ = -359.4 (c = 0.1, $CH_2Cl_2$). 99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 5.9 min for minor isomer, $t_R$ = 7.9 min for major isomer).



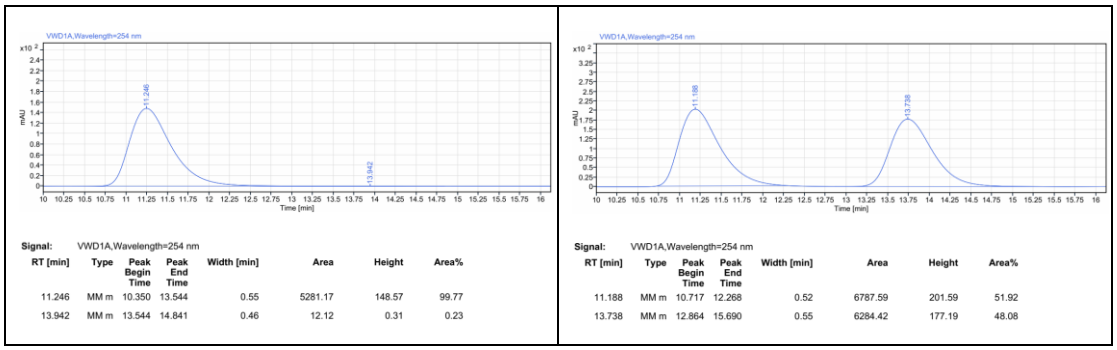

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-6-methyl-4-oxoquinazolin-**

**3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ca)**

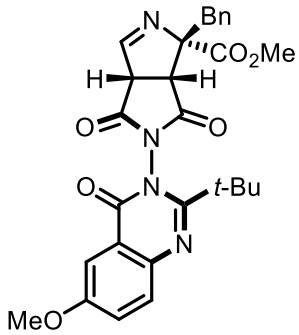



**3ca**

>20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 35.0 mg, 70% yield. **MP**: 120-121 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.94-7.91 (m, 1H), 7.67 (d, *J* = 1.1 Hz, 1H), 7.56 (d, *J* = 1.3 Hz, 2H), 7.35-7.30 (m, 3H), 7.21-7.16 (m, 2H), 3.72 (s, 3H), 3.60 (d, *J* = 8.3 Hz, 1H), 3.56 (d, *J* = 14.1 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H), 3.02 (dd, *J* = 8.3, 1.1 Hz, 1H), 2.43 (d, *J* = 0.8 Hz, 3H), 1.29 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.4, 170.0, 168.1, 160.3, 159.2, 158.0, 144.2, 137.7, 136.7, 134.2, 131.2, 128.7, 128.2, 127.7, 126.7, 119.8, 86.3, 57.0, 53.1, 47.2, 42.9, 38.9, 29.5, 21.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_5$ 501.2132; Found 501.2140. **Optical Rotation**: $[\alpha]^{20}_D$ = -269.3 (c = 0.2, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 11.2 min for major isomer, $t_R$ = 13.9 min for minor isomer).

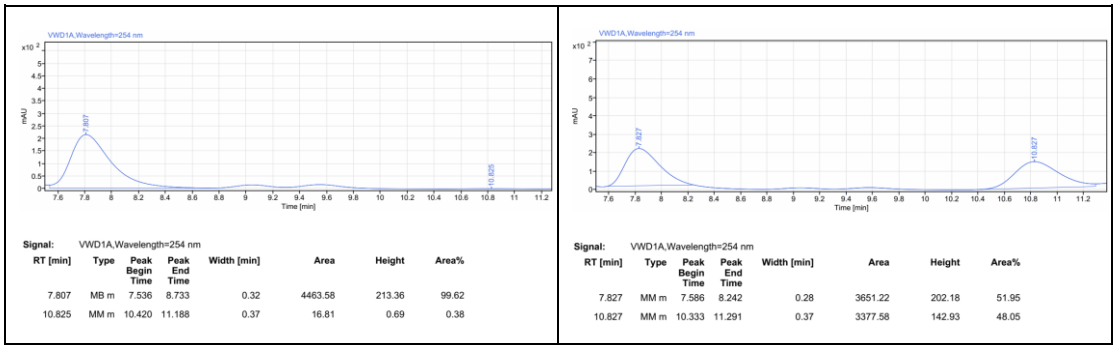



**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-6-methoxy-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3da)**



**3da**

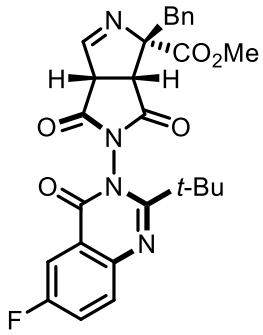
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 43.4 mg, 84% yield. **MP**: 151-152 ℃; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 1.2 Hz, 1H), 7.59 (d, *J* = 8.9 Hz, 1H), 7.50 (d, *J* = 2.9 Hz, 1H), 7.35-7.30 (m, 4H), 7.20-7.16 (m, 2H), 3.84 (s, 3H), 3.73 (s, 3H), 3.61 (d, *J* = 8.3 Hz, 1H), 3.56 (d, *J* = 14.0 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H), 3.01 (dd, *J* = 8.2, 1.1 Hz, 1H), 1.28 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.4, 170.0, 168.0, 160.3, 158.8, 157.9, 157.7, 140.9, 134.2, 131.2, 129.9, 128.7, 127.7, 125.5, 120.8, 106.6, 86.3, 57.0, 56.0, 53.0, 47.2, 42.9, 38.8, 29.6; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_6$ 517.2082; Found 517.2084. **Optical Rotation**: $[\alpha]^{20}_D$ = -297.3 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 7.8 min for major isomer, $t_R$ = 10.8 min for minor isomer).



| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 7.807 | MB m | 7.536 | 8.733 | 0.32 | 4463.58 | 213.36 | 99.62 |
| 10.825 | MM m | 10.420 | 11.188 | 0.37 | 16.81 | 0.69 | 0.38 |

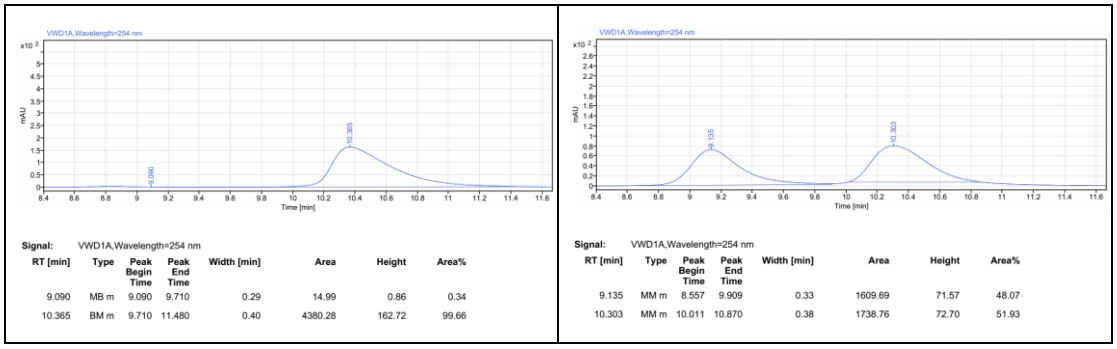
| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 7.827 | MM m | 7.586 | 8.242 | 0.28 | 3651.22 | 202.18 | 51.95 |
| 10.827 | MM m | 10.333 | 11.291 | 0.37 | 3377.58 | 142.93 | 48.05 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-6-fluoro-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ea)**



**3ea**

16:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 36.8 mg, 73% yield. **MP**: 124-125 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.77 (dd, *J* = 8.1, 3.0 Hz, 1H), 7.70-7.65 (m, 2H), 7.50-7.44 (m, 1H), 7.36-7.30 (m, 3H), 7.21-7.16 (m, 2H), 3.71 (s, 3H), 3.61 (d, *J* = 8.3 Hz, 1H), 3.56 (d, *J* = 14.1 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H), 3.03 (dd, *J* = 8.3, 1.1 Hz, 1H), 1.29 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.2, 169.9, 167.9, 161.1 (d, *J* = 249.7 Hz), 160.1, 159.5, 157.3 (d, *J* = 3.4 Hz), 143.0, 134.2, 131.2, 130.9 (d, *J* = 8.2 Hz), 128.7, 127.7, 123.9 (d, *J* = 24.0 Hz), 121.4 (d, *J* = 8.9 Hz), 112.2 (d, *J* = 24.0 Hz), 86.4, 57.0, 53.1, 47.2, 42.9, 39.0, 29.5; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -111.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}FN_4O_5$ 505.1882; Found 505.1886. **Optical Rotation**: $[\alpha]^{20}_D$ = -290.7 (c = 0.09, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 9.1 min for minor isomer, $t_R$ = 10.4 min for major isomer).



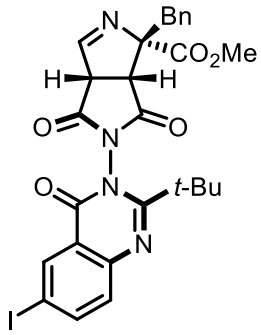

Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.090 | MB m | 9.090 | 9.710 | 0.29 | 14.99 | 0.86 | 0.34 |
| 10.365 | BM m | 9.710 | 11.480 | 0.40 | 4380.28 | 162.72 | 99.66 |

Signal: VWD1A,Wavelength=254 nm

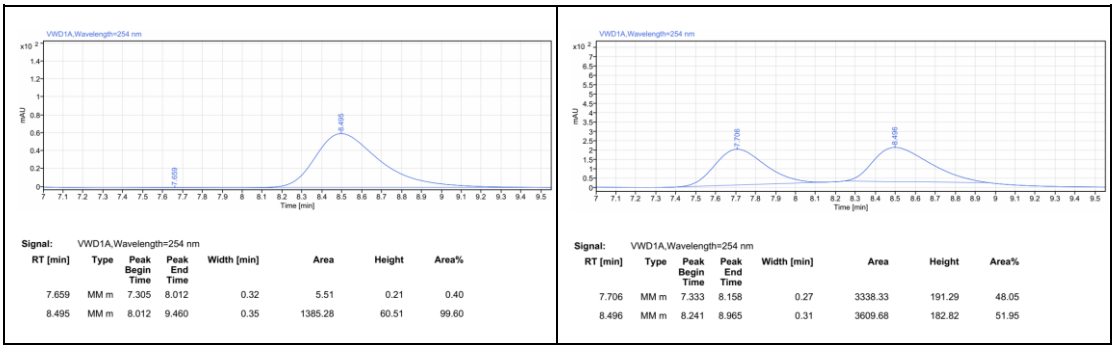
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.135 | MM m | 8.557 | 9.909 | 0.33 | 1609.69 | 71.57 | 48.07 |
| 10.303 | MM m | 10.011 | 10.870 | 0.38 | 1738.76 | 72.70 | 51.93 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-6-iodo-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3fa)**



**3fa**

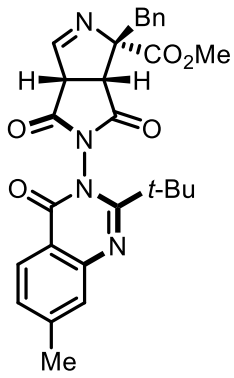
17:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 44.1 mg, 72% yield. **MP**: 143-144 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.48 (d, *J* = 2.0 Hz, 1H), 8.01 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.67-7.64 (m, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.36-7.30 (m, 3H), 7.21-7.16 (m, 2H), 3.73 (s, 3H), 3.60 (d, *J* = 8.3 Hz, 1H), 3.56 (d, *J* = 14.0 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H), 3.01 (dd, *J* = 8.4, 1.1 Hz, 1H), 1.28 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.1, 169.8, 167.8, 161.0, 160.1, 156.6, 145.5, 144.1, 136.0, 134.1, 131.2, 130.2, 128.7, 127.7, 121.7, 91.8, 86.4, 57.0, 53.1, 47.2, 42.9, 39.2, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}IN_4O_5$ 613.0942; Found 613.0951. **Optical Rotation**: $[\alpha]^{20}_D$ = -307.3 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 7.7 min for minor isomer, $t_R$ = 8.5 min for major isomer).



| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 7.659 | MM m | 7.305 | 8.012 | 0.32 | 5.51 | 0.21 | 0.40 |
| 8.495 | MM m | 8.012 | 9.460 | 0.35 | 1385.28 | 60.51 | 99.60 |

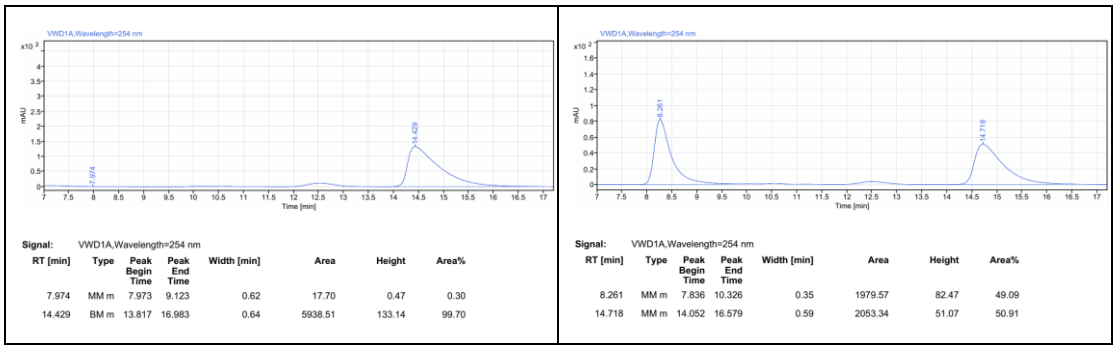
| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 7.706 | MM m | 7.333 | 8.158 | 0.27 | 3338.33 | 191.29 | 48.05 |
| 8.496 | MM m | 8.241 | 8.965 | 0.31 | 3609.68 | 182.82 | 51.95 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-7-methyl-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ga)**



**3ga**

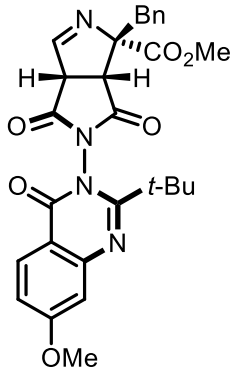
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 35.1 mg, 70% yield. **MP**: 122-124 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 8.1 Hz, 1H), 7.67 (d, *J* = 1.1 Hz, 1H), 7.47 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.35-7.29 (m, 3H), 7.27-7.23 (m, 1H), 7.20-7.16 (m, 2H), 3.70 (s, 3H), 3.60 (d, *J* = 8.3 Hz, 1H), 3.56 (d, *J* = 14.0 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H), 3.03 (dd, *J* = 8.3, 1.1 Hz, 1H), 2.47 (s, 3H), 1.29 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.4, 170.0, 168.1, 160.3, 160.2, 157.8, 146.6, 146.3, 134.2, 131.2, 129.0, 128.7, 128.2, 127.7, 127.1, 117.6, 86.4, 57.0, 53.0, 47.2, 42.9, 39.0, 29.5, 22.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_5$ 501.2132; Found 501.2140. **Optical Rotation**: $[\alpha]^{20}_D$ = -304.3 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 8.0 min for minor isomer, $t_R$ = 14.4 min for major isomer).



| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 7.974 | MM m | 7.973 | 9.123 | 0.62 | 17.70 | 0.47 | 0.30 |
| 14.429 | BM m | 13.817 | 16.983 | 0.64 | 5938.51 | 133.14 | 99.70 |

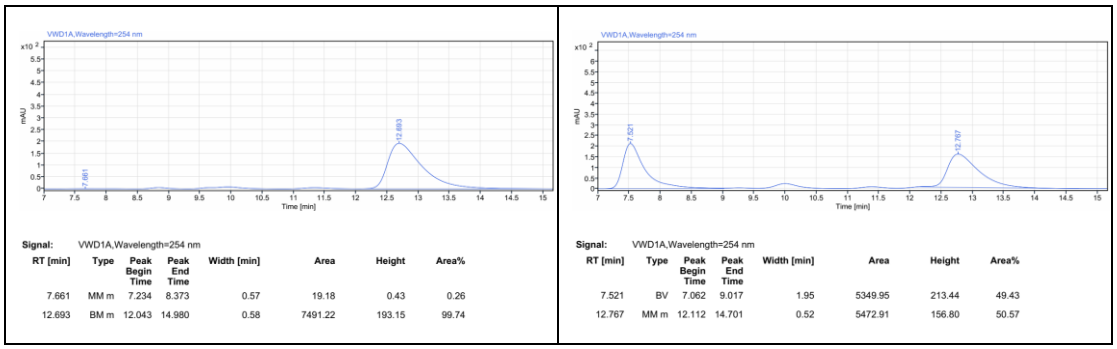
| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 8.261 | MM m | 7.836 | 10.326 | 0.35 | 1979.57 | 82.47 | 49.09 |
| 14.718 | MM m | 14.052 | 16.579 | 0.59 | 2053.34 | 51.07 | 50.91 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-7-methoxy-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ha)**



**3ha**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 49.2 mg, 95% yield. **MP**: 109-111 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 8.8 Hz, 1H), 7.66 (d, *J* = 1.1 Hz, 1H), 7.34-7.29 (m, 3H), 7.20-7.15 (m, 2H), 7.03 (d, *J* = 2.5 Hz, 1H), 6.99 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.90 (s, 3H), 3.70 (s, 3H), 3.60 (d, *J* = 8.3 Hz, 1H), 3.55 (d, *J* = 13.9 Hz, 1H), 3.41 (d, *J* = 14.0 Hz, 1H), 3.03 (dd, *J* = 8.3, 1.1 Hz, 1H), 1.29 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.5, 170.0, 168.1, 165.4, 160.9, 160.3, 157.3, 148.5, 134.2, 131.1, 128.8, 128.6, 127.7, 117.5, 113.3, 109.1, 86.3, 57.0, 55.9, 53.0, 47.2, 42.9, 39.0, 29.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_6$ 517.2082; Found 517.2084. **Optical Rotation**: $[\alpha]^{20}_D$ = -282.6 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 7.7 min for minor isomer, $t_R$ = 12.7 min for major isomer).



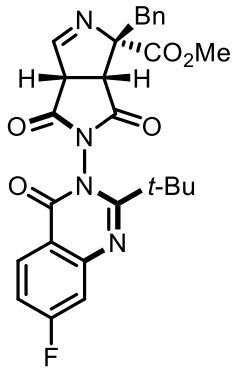
Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 7.661 | MM m | 7.234 | 8.373 | 0.57 | 19.18 | 0.43 | 0.26 |
| 12.693 | BM m | 12.043 | 14.980 | 0.58 | 7491.22 | 193.15 | 99.74 |

Signal: VWD1A,Wavelength=254 nm

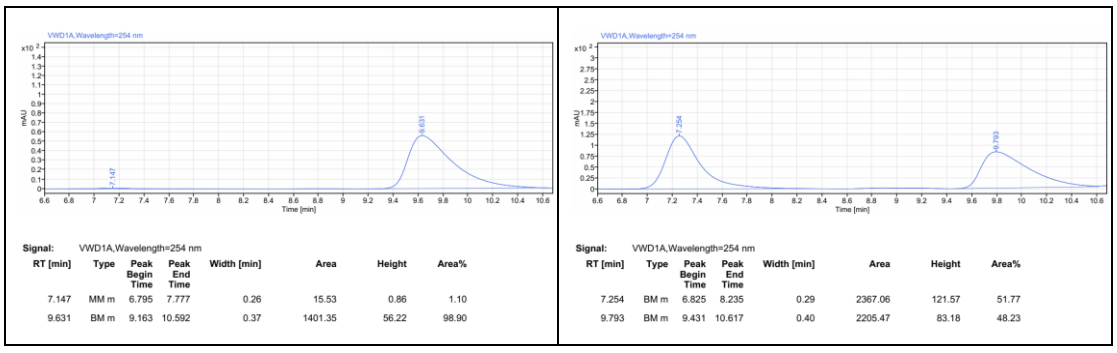
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 7.521 | BV | 7.062 | 9.017 | 1.95 | 5349.95 | 213.44 | 49.43 |
| 12.767 | MM m | 12.112 | 14.701 | 0.52 | 5472.91 | 156.80 | 50.57 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-7-fluoro-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ia)**



**3ia**

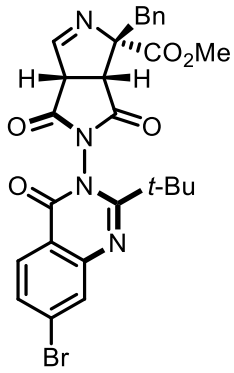
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 41.9 mg, 83% yield. **MP**: 137-138 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 8.9, 6.0 Hz, 1H), 7.66 (d, *J* = 1.1 Hz, 1H), 7.36-7.29 (m, 4H), 7.20-7.12 (m, 3H), 3.71 (s, 3H), 3.61 (d, *J* = 8.3 Hz, 1H), 3.55 (d, *J* = 14.0 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H), 3.03 (dd, *J* = 8.3, 1.1 Hz, 1H), 1.29 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.3, 169.9, 167.9, 167.2 (d, *J* = 255.8 Hz), 161.6, 160.1, 157.1, 148.5 (d, *J* = 13.6 Hz), 134.1, 131.2, 130.0 (d, *J* = 10.7 Hz), 128.7, 127.7, 116.8, 116.3 (d, *J* = 23.6 Hz), 113.9 (d, *J* = 21.9 Hz), 86.4, 57.0, 53.0, 47.2, 42.9, 39.2, 29.4; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -101.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}FN_4O_5$ 505.1882; Found 505.1884. **Optical Rotation**: $[\alpha]^{20}_D$ = -313.3 (c = 0.1, $CH_2Cl_2$). 98% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 7.1 min for minor isomer, $t_R$ = 9.6 min for major isomer).



| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 7.147 | MM m | 6.795 | 7.777 | 0.26 | 15.53 | 0.86 | 1.10 |
| 9.631 | BM m | 9.163 | 10.592 | 0.37 | 1401.35 | 56.22 | 98.90 |

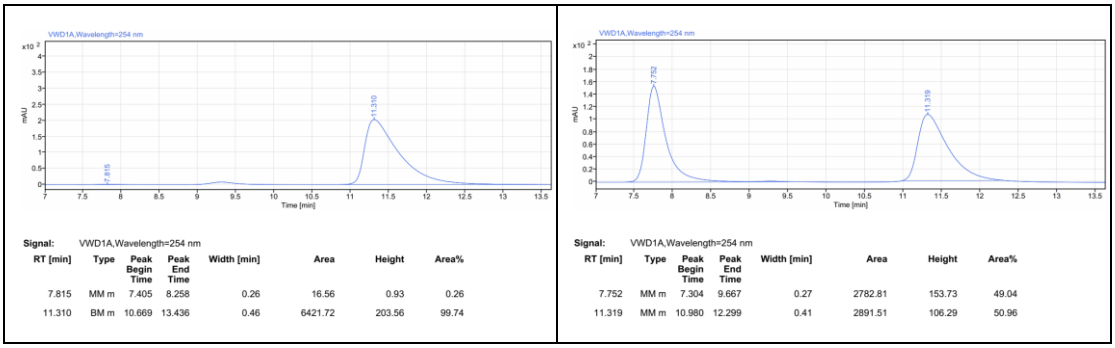
| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 7.254 | BM m | 6.825 | 8.235 | 0.29 | 2367.06 | 121.57 | 51.77 |
| 9.793 | BM m | 9.431 | 10.617 | 0.40 | 2205.47 | 83.18 | 48.23 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(7-bromo-2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ja)**



**3ja**

20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 49.3 mg, 87% yield. **MP**: 165-166 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 1.8 Hz, 1H), 7.66 (d, *J* = 1.1 Hz, 1H), 7.54 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.36-7.29 (m, 3H), 7.20-7.15 (m, 2H), 3.71 (s, 3H), 3.61 (d, *J* = 8.4 Hz, 1H), 3.55 (d, *J* = 14.0 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H), 3.04 (dd, *J* = 8.3, 1.1 Hz, 1H), 1.28 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.2, 169.8, 167.9, 161.7, 160.1, 157.4, 147.1, 134.1, 131.2, 131.1, 130.9, 130.2, 128.7, 128.6, 127.7, 118.9, 86.4, 57.0, 53.0, 47.2, 42.9, 39.2, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}BrN_4O_5$ 565.1081; Found 565.1089. **Optical Rotation**: $[\alpha]^{20}_D$ = -316.3 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 7.8 min for minor isomer, $t_R$ = 11.3 min for major isomer).



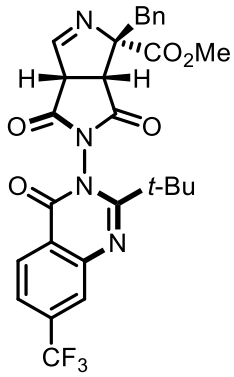

Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 7.815 | MM m | 7.405 | 8.258 | 0.26 | 16.56 | 0.93 | 0.26 |
| 11.310 | BM m | 10.669 | 13.436 | 0.46 | 6421.72 | 203.56 | 99.74 |

Signal: VWD1A,Wavelength=254 nm

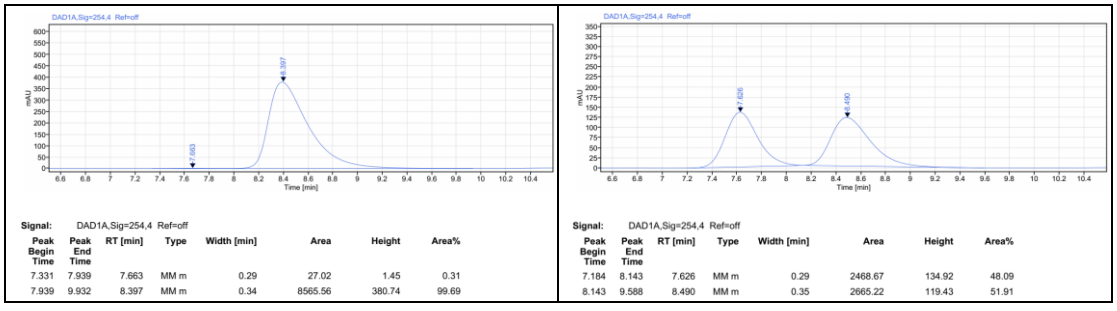
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 7.752 | MM m | 7.304 | 9.667 | 0.27 | 2782.81 | 153.73 | 49.04 |
| 11.319 | MM m | 10.980 | 12.299 | 0.41 | 2891.51 | 106.29 | 50.96 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-4-oxo-7-(trifluoromethyl)quinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ka)**



**3ka**

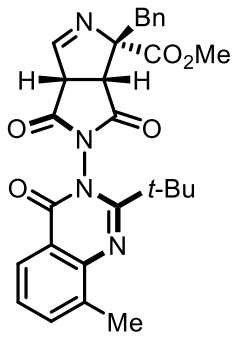
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 44.4 mg, 80% yield. **MP**: 127-129 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.28-8.23 (m, 1H), 7.97 (dd, *J* = 1.6, 0.9 Hz, 1H), 7.68-7.62 (m, 2H), 7.36-7.30 (m, 3H), 7.21-7.15 (m, 2H), 3.71 (s, 3H), 3.63 (d, *J* = 8.3 Hz, 1H), 3.56 (d, *J* = 14.0 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H), 3.05 (dd, *J* = 8.3, 1.1 Hz, 1H), 1.31 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.1, 169.8, 167.8, 162.0, 160.0, 157.2, 146.2, 136.9 (d, *J* = 33.0 Hz), 134.1, 131.2, 128.7, 128.4, 127.8, 126.0 (d, *J* = 4.3 Hz), 123.5, 123.3 (d, *J* = 273.6 Hz), 122.5, 86.4, 57.0, 53.0, 47.2, 42.9, 39.3, 29.4; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -63.2; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{26}F_3N_4O_5$ 555.1850; Found 555.1854. **Optical Rotation**: $[\alpha]^{20}_D$ = -282.6 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 7.7 min for minor isomer, $t_R$ = 8.4 min for major isomer).



| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 7.331 | 7.939 | 7.663 | MM m | 0.29 | 27.02 | 1.45 | 0.31 |
| 7.939 | 9.932 | 8.397 | MM m | 0.34 | 8565.56 | 380.74 | 99.69 |

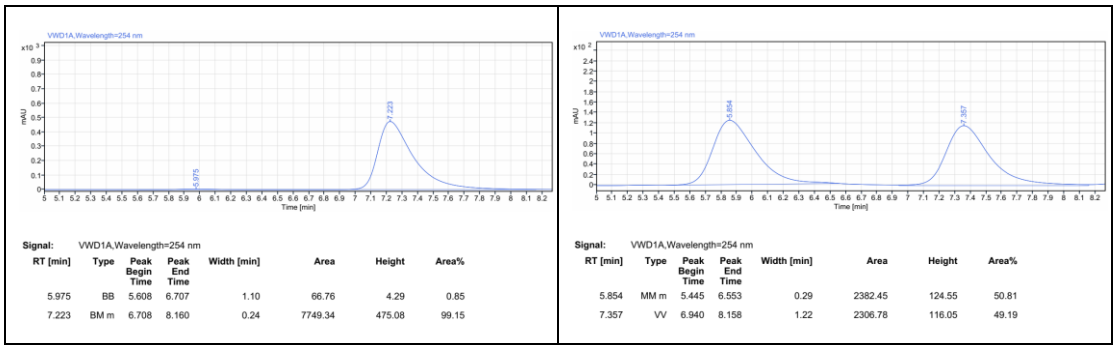
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 7.184 | 8.143 | 7.626 | MM m | 0.29 | 2468.67 | 134.92 | 48.09 |
| 8.143 | 9.588 | 8.490 | MM m | 0.35 | 2665.22 | 119.43 | 51.91 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-8-methyl-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3la)**

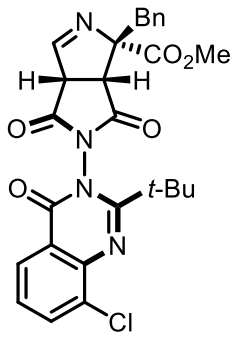



**3la**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 31.6 mg, 63% yield. **MP**: 118-120 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.01-7.96 (m, 1H), 7.67 (d, *J* = 1.1 Hz, 1H), 7.62-7.58 (m, 1H), 7.36-7.29 (m, 4H), 7.21-7.16 (m, 2H), 3.70 (s, 3H), 3.60 (d, *J* = 8.3 Hz, 1H), 3.56 (d, *J* = 14.0 Hz, 1H), 3.43 (d, *J* = 14.0 Hz, 1H), 3.04 (dd, *J* = 8.3, 1.2 Hz, 1H), 2.57 (s, 3H), 1.31 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.4, 170.0, 168.0, 160.3, 158.7, 158.3, 144.5, 137.2, 136.0, 134.2, 131.2, 128.7, 127.7, 127.2, 124.9, 120.1, 86.4, 57.1, 53.0, 47.2, 42.9, 39.4, 29.5, 17.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_5$ 501.2132; Found 501.2141. **Optical Rotation**: $[\alpha]^{20}_D$ = -263.3 (c = 0.11, $CH_2Cl_2$). 98% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 6.0 min for minor isomer, $t_R$ = 7.2 min for major isomer).

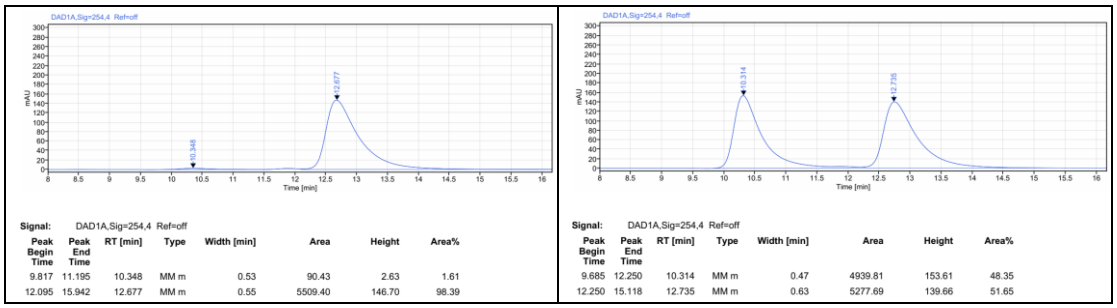



**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-8-chloro-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ma)**



**3ma**

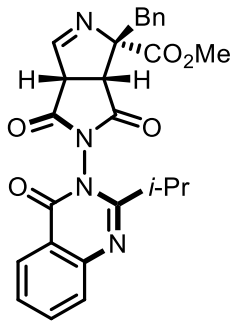
>20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 47.9 mg, 92% yield. **MP**: 135-137 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.05 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.83 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.66 (d, *J* = 1.1 Hz, 1H), 7.37-7.30 (m, 4H), 7.20-7.15 (m, 2H), 3.70 (s, 3H), 3.62 (d, *J* = 8.4 Hz, 1H), 3.55 (d, *J* = 14.1 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H), 3.05 (dd, *J* = 8.3, 1.1 Hz, 1H), 1.33 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.1, 169.8, 167.8, 161.0, 160.1, 157.4, 142.7, 135.7, 134.1, 133.2, 131.1, 128.7, 127.7, 127.6, 126.0, 121.7, 86.4, 57.0, 53.0, 47.2, 42.9, 39.7, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}ClN_4O_5$ 521.1586; Found 521.1582. **Optical Rotation**: $[\alpha]^{20}_D$ = -329.3 (c = 0.1, $CH_2Cl_2$). 97% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.3 min for minor isomer, $t_R$ = 12.7 min for major isomer).



| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.817 | 11.195 | 10.348 | MM m | 0.53 | 90.43 | 2.63 | 1.61 |
| 12.095 | 15.942 | 12.677 | MM m | 0.55 | 5509.40 | 146.70 | 98.39 |

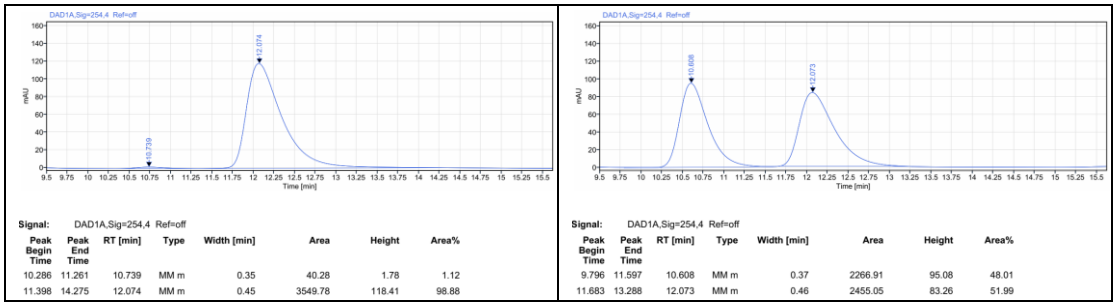
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.685 | 12.250 | 10.314 | MM m | 0.47 | 4939.81 | 153.61 | 48.35 |
| 12.250 | 15.118 | 12.735 | MM m | 0.63 | 5277.69 | 139.66 | 51.65 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-isopropyl-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3na)**

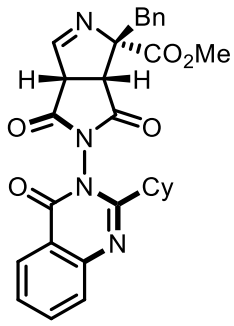


**3na**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 24.6 mg, 52% yield. **MP**: 131-132 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.17 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.80-7.74 (m, 1H), 7.70-7.66 (m, 2H), 7.47-7.42 (m, 1H), 7.36-7.30 (m, 3H), 7.21-7.16 (m, 2H), 3.69 (s, 3H), 3.64 (d, *J* = 8.3 Hz, 1H), 3.57 (d, *J* = 14.1 Hz, 1H), 3.45 (d, *J* = 14.1 Hz, 1H), 3.09 (dd, *J* = 8.3, 1.2 Hz, 1H), 2.59 (p, *J* = 6.7 Hz, 1H), 1.28 (d, *J* = 6.7 Hz, 3H), 1.22 (d, *J* = 6.7 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.5, 169.7, 167.1, 160.1, 159.7, 157.3, 146.8, 135.4, 134.2, 131.2, 128.7, 128.0, 127.7, 127.4, 127.3, 120.6, 86.7, 57.4, 53.1, 47.3, 42.6, 31.3, 21.3, 20.9; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{25}N_4O_5$ 473.1819; Found 473.1822. **Optical Rotation**: $[\alpha]^{20}_D$ = -262.9 (c = 0.05, $CH_2Cl_2$). 98% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.7 min for minor isomer, $t_R$ = 12.1 min for major isomer).

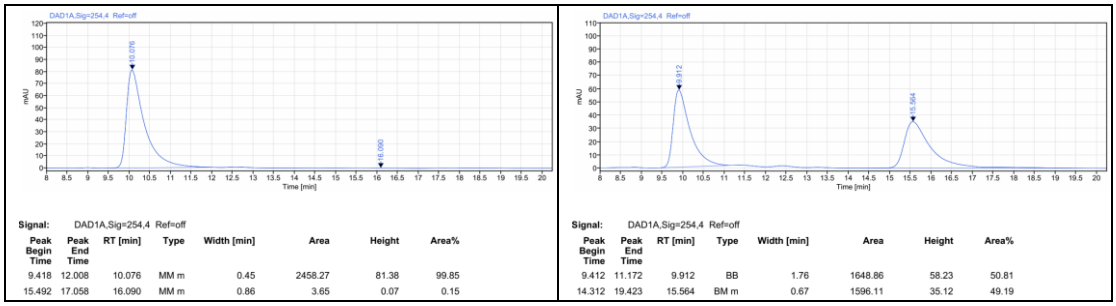



**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-cyclohexyl-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3oa)**



**3oa**

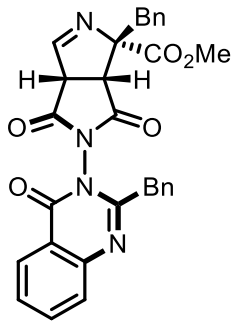
>20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 42.0 mg, 82% yield. **MP**: 237-239 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.16 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.78-7.72 (m, 1H), 7.70-7.64 (m, 2H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.37-7.30 (m, 3H), 7.23-7.16 (m, 2H), 3.69 (s, 3H), 3.65 (d, *J* = 8.2 Hz, 1H), 3.56 (d, *J* = 14.2 Hz, 1H), 3.45 (d, *J* = 14.1 Hz, 1H), 3.13 (d, *J* = 8.2 Hz, 1H), 2.25-2.15 (m, 1H), 1.92-1.75 (m, 4H), 1.70-1.56 (m, 2H), 1.36-1.13 (m, 4H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.6, 169.7, 167.1, 160.1, 158.8, 157.2, 146.9, 135.4, 134.2, 131.2, 128.7, 127.9, 127.7, 127.3, 127.2, 120.5, 86.7, 57.3, 53.1, 47.2, 42.7, 41.1, 31.2, 30.9, 26.0, 25.9, 25.6; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{29}N_4O_5$ 513.2132; Found 513.2137. **Optical Rotation**: $[\alpha]^{20}_D$ = -265.9 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.1 min for major isomer, $t_R$ = 16.1 min for minor isomer).



| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 9.418 | 12.008 | 10.076 | MM m | 0.45 | 2458.27 | 81.38 | 99.85 |
| 15.492 | 17.058 | 16.090 | MM m | 0.86 | 3.65 | 0.07 | 0.15 |

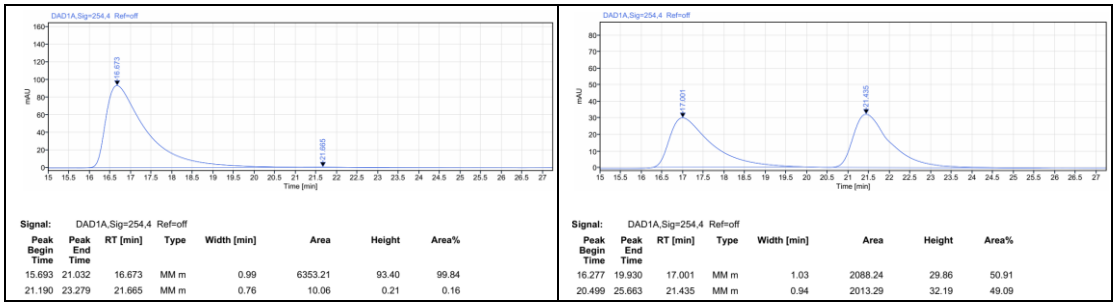
| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 9.412 | 11.172 | 9.912 | BB | 1.76 | 1648.86 | 58.23 | 50.81 |
| 14.312 | 19.423 | 15.564 | BM m | 0.67 | 1596.11 | 35.12 | 49.19 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-benzyl-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3pa)**



**3pa**

>20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 32.3 mg, 62% yield. **MP**: 114-115 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.18 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.84-7.78 (m, 1H), 7.73 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.53-7.47 (m, 2H), 7.38-7.33 (m, 3H), 7.26-7.19 (m, 3H), 7.14-7.10 (m, 2H), 7.08-7.04 (m, 2H), 4.03 (d, *J* = 15.8 Hz, 1H), 3.95 (d, *J* = 15.7 Hz, 1H), 3.66 (s, 3H), 3.47 (d, *J* = 14.1 Hz, 1H), 3.38 (d, *J* = 14.0 Hz, 1H), 3.14 (d, *J* = 8.6 Hz, 1H), 2.59 (dd, *J* = 8.6, 1.2 Hz, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.1, 169.4, 165.6, 159.9, 157.4, 153.0, 146.5, 135.6, 134.33, 134.26, 131.1, 129.2, 128.5, 128.2, 128.0, 127.9, 127.8, 127.7, 127.4, 120.9, 86.0, 57.0, 53.1, 46.9, 42.2, 42.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{30}H_{25}N_4O_5$ 521.1819; Found 521.1829. **Optical Rotation**: $[\alpha]^{20}_D$ = -258.2 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 16.7 min for major isomer, $t_R$ = 21.7 min for minor isomer).



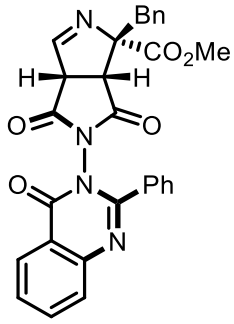
Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 15.693 | 21.032 | 16.673 | MM m | 0.99 | 6353.21 | 93.40 | 99.84 |
| 21.190 | 23.279 | 21.665 | MM m | 0.76 | 10.06 | 0.21 | 0.16 |

Signal: DAD1A,Sig=254,4 Ref=off

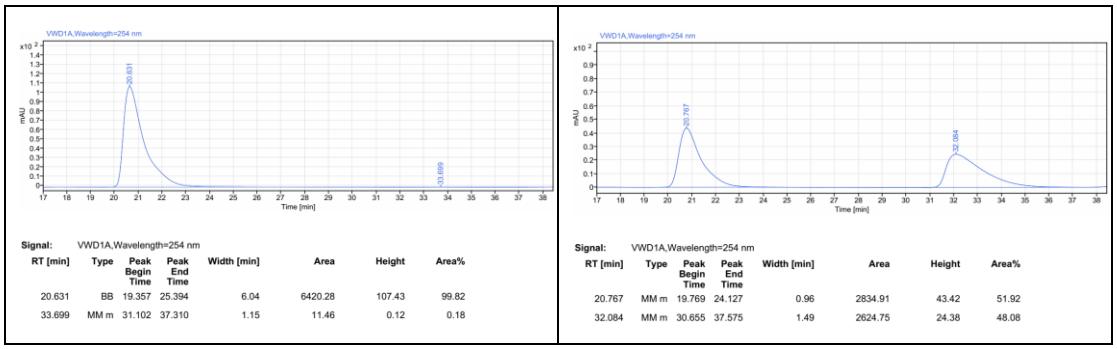
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 16.277 | 19.930 | 17.001 | MM m | 1.03 | 2088.24 | 29.86 | 50.91 |
| 20.499 | 25.663 | 21.435 | MM m | 0.94 | 2013.29 | 32.19 | 49.09 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-4,6-dioxo-5-(4-oxo-2-phenylquinazolin-3(4*H*)-yl)-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3qa)**



**3qa**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 35.5 mg, 70% yield. **MP**: 108-110 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.27-8.24 (m, 1H), 7.86-7.76 (m, 2H), 7.59 (d, *J* = 1.1 Hz, 1H), 7.56-7.38 (m, 6H), 7.26-7.22 (m, 3H), 7.07-7.03 (m, 2H), 3.70 (s, 3H), 3.39 (s, 2H), 3.13 (d, *J* = 8.3 Hz, 1H), 2.84 (dd, *J* = 8.4, 1.2 Hz, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.7, 169.5, 166.7, 159.9, 157.3, 154.1, 146.7, 135.7, 134.0, 132.4, 131.03, 130.98, 128.7, 128.50, 128.45, 128.1, 127.6, 127.5, 120.9, 86.4, 57.0, 53.1, 47.0, 42.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{23}N_4O_5$ 507.1663; Found 507.1670. **Optical Rotation**: $[\alpha]^{20}_D$ = -290.9 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 20.6 min for major isomer, $t_R$ = 33.7 min for minor isomer).



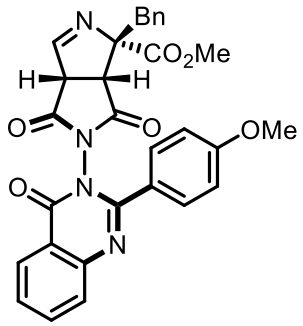
Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 20.631 | BB | 19.357 | 25.394 | 6.04 | 6420.28 | 107.43 | 99.82 |
| 33.699 | MM m | 31.102 | 37.310 | 1.15 | 11.46 | 0.12 | 0.18 |

Signal: VWD1A,Wavelength=254 nm

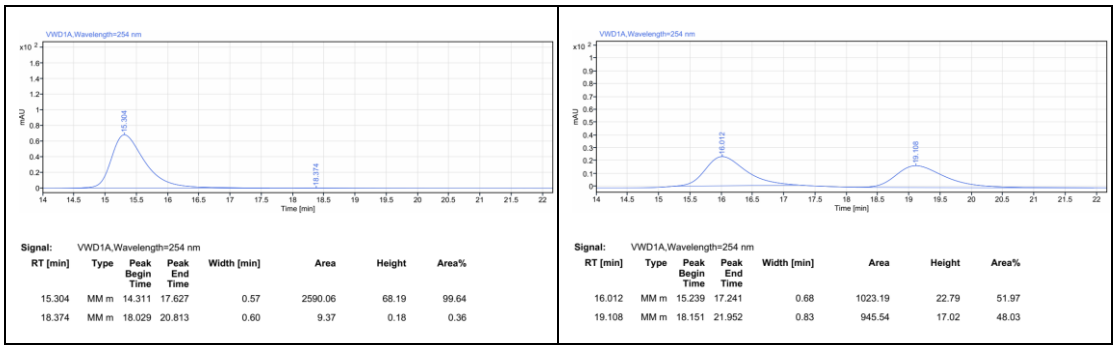
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 20.767 | MM m | 19.769 | 24.127 | 0.96 | 2834.91 | 43.42 | 51.92 |
| 32.084 | MM m | 30.655 | 37.575 | 1.49 | 2624.75 | 24.38 | 48.08 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(4-methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ra)**

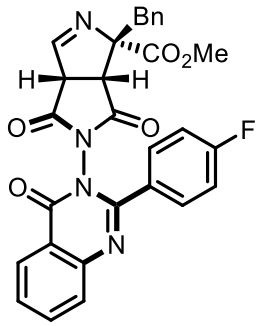


**3ra**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 29.9 mg, 56% yield. **MP**: 110-112 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.25-8.21 (m, 1H), 7.84-7.78 (m, 1H), 7.77-7.74 (m, 1H), 7.61 (d, *J* = 1.2 Hz, 1H), 7.54-7.48 (m, 1H), 7.43-7.39 (m, 2H), 7.29-7.23 (m, 3H), 7.10-7.05 (m, 2H), 6.92-6.88 (m, 2H), 3.85 (s, 3H), 3.69 (s, 3H), 3.41 (d, *J* = 1.4 Hz, 2H), 3.21 (d, *J* = 8.4 Hz, 1H), 2.90 (dd, *J* = 8.3, 1.2 Hz, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.9, 169.6, 166.8, 161.6, 159.9, 157.5, 154.0, 146.8, 135.7, 134.1, 131.1, 129.3, 128.5, 128.4, 127.8, 127.6, 127.5, 124.7, 120.7, 114.2, 86.4, 57.0, 55.6, 53.1, 47.0, 42.6; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{30}H_{25}N_4O_6$ 537.1769; Found 537.1777. **Optical Rotation**: $[\alpha]^{20}_D$ = -267.0 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 15.3 min for major isomer, $t_R$ = 18.4 min for minor isomer).

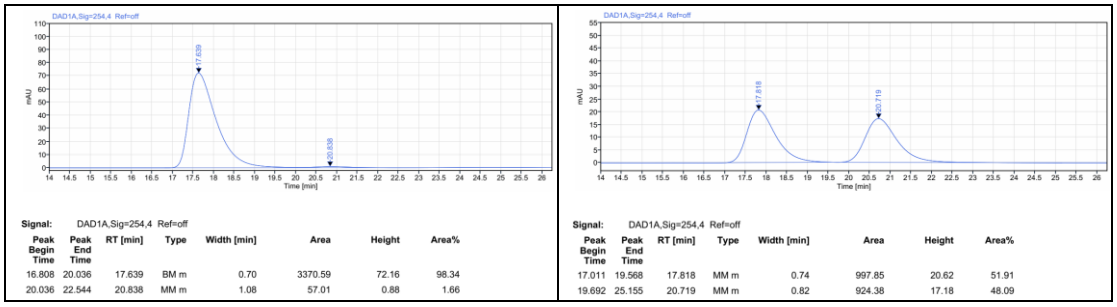



**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(4-fluorophenyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3sa)**



**3sa**

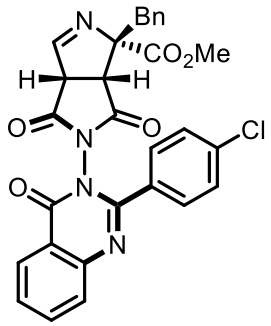
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 30.4 mg, 58% yield. **MP**: 131-133 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.25 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.86-7.81 (m, 1H), 7.76 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.60 (d, *J* = 1.1 Hz, 1H), 7.57-7.52 (m, 1H), 7.50-7.44 (m, 2H), 7.30-7.24 (m, 3H), 7.14-7.05 (m, 4H), 3.69 (s, 3H), 3.41 (d, *J* = 2.6 Hz, 2H), 3.19 (d, *J* = 8.3 Hz, 1H), 2.87 (dd, *J* = 8.3, 1.2 Hz, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.9, 169.5, 166.8, 164.2 (d, *J* = 252.0 Hz), 159.8, 157.3, 153.2, 146.5, 135.9, 134.0, 131.1, 129.9 (d, *J* = 8.6 Hz), 128.59, 128.55, 128.5, 128.2, 127.6 (d, *J* = 6.2 Hz), 120.8, 116.1 (d, *J* = 22.2 Hz), 86.6, 57.0, 53.1, 47.0, 42.6; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -107.8; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{22}FN_4O_5$ 525.1569; Found 525.1569. **Optical Rotation**: $[\alpha]^{20}_D$ = -235.0 (c = 0.21, $CH_2Cl_2$). 97% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 17.6 min for major isomer, $t_R$ = 20.8 min for minor isomer).



| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 16.808 | 20.036 | 17.639 | BM m | 0.70 | 3370.59 | 72.16 | 98.34 |
| 20.036 | 22.544 | 20.838 | MM m | 1.08 | 57.01 | 0.88 | 1.66 |

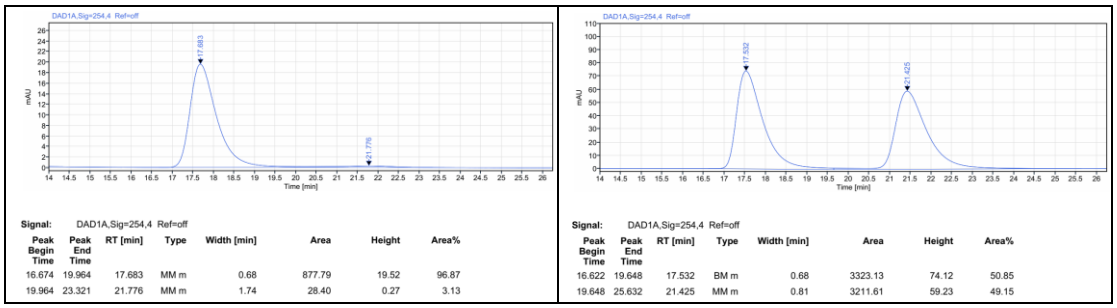
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 17.011 | 19.568 | 17.818 | MM m | 0.74 | 997.85 | 20.62 | 51.91 |
| 19.692 | 25.155 | 20.719 | MM m | 0.82 | 924.38 | 17.18 | 48.09 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(4-chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ta)**



**3ta**

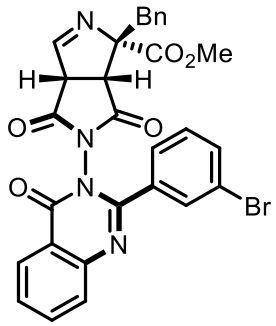
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 32.4 mg, 60% yield. **MP**: 126-127 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.25 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.86-7.81 (m, 1H), 7.76 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.57-7.52 (m, 1H), 7.44-7.37 (m, 4H), 7.31-7.25 (m, 3H), 7.12-7.06 (m, 2H), 3.69 (s, 3H), 3.42 (d, *J* = 2.9 Hz, 2H), 3.22 (d, *J* = 8.3 Hz, 1H), 2.89 (dd, *J* = 8.2, 1.2 Hz, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.9, 169.5, 166.8, 159.8, 157.2, 153.0, 146.5, 137.4, 135.9, 134.0, 131.1, 130.9, 129.2, 129.1, 128.6, 128.5, 128.3, 127.7, 127.6, 120.8, 86.6, 57.0, 53.1, 47.1, 42.6; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{22}ClN_4O_5$ 541.1273; Found 541.1279. **Optical Rotation**: $[\alpha]^{20}_D$ = -215.4 (c = 0.15, $CH_2Cl_2$). 94% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 17.7 min for major isomer, $t_R$ = 21.8 min for minor isomer).



| Signal: | DAD1A,Sig=254,4 Ref=off | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 16.674 | 19.964 | 17.683 | MM m | 0.68 | 877.79 | 19.52 | 96.87 |
| 19.964 | 23.321 | 21.776 | MM m | 1.74 | 28.40 | 0.27 | 3.13 |

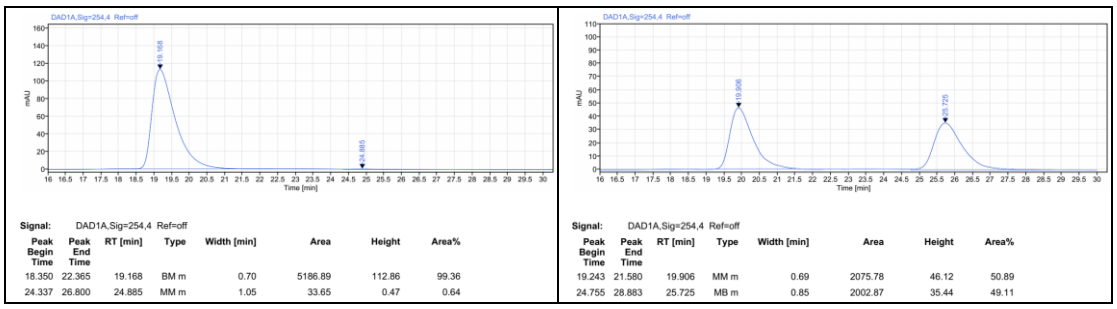
| Signal: | DAD1A,Sig=254,4 Ref=off | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 16.622 | 19.648 | 17.532 | BM m | 0.68 | 3323.13 | 74.12 | 50.85 |
| 19.648 | 25.632 | 21.425 | MM m | 0.81 | 3211.61 | 59.23 | 49.15 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(3-bromophenyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ua)**



**3ua**

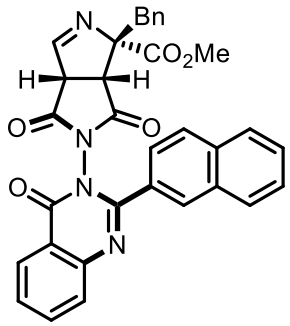
>20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 37.5 mg, 64% yield. **MP**: 126-128 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.25 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.87-7.81 (m, 1H), 7.77 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.65-7.61 (m, 2H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.58-7.53 (m, 1H), 7.41-7.37 (m, 1H), 7.31-7.24 (m, 4H), 7.11-7.06 (m, 2H), 3.70 (s, 3H), 3.45 (d, *J* = 14.1 Hz, 1H), 3.40 (d, *J* = 14.1 Hz, 1H), 3.23 (d, *J* = 8.4 Hz, 1H), 2.88 (dd, *J* = 8.4, 1.2 Hz, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.8, 169.5, 166.7, 159.7, 157.1, 152.4, 146.4, 135.9, 134.2, 134.1, 134.0, 131.1, 130.8, 130.3, 128.6, 128.5, 128.4, 127.7, 127.6, 126.2, 122.8, 120.9, 86.5, 57.0, 53.1, 47.0, 42.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{22}BrN_4O_5$ 585.0768; Found 585.0772. **Optical Rotation**: $[\alpha]^{20}_D$ = -212.2 (c = 0.1, $CH_2Cl_2$). 99% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 19.2 min for major isomer, $t_R$ = 24.9 min for minor isomer).



| Signal: | DAD1A,Sig=254,4 | Ref=off | | | | |
|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 18.350 | 22.365 | 19.168 | BM m | 0.70 | 5186.89 | 112.86 | 99.36 |
| 24.337 | 26.800 | 24.885 | MM m | 1.05 | 33.65 | 0.47 | 0.64 |

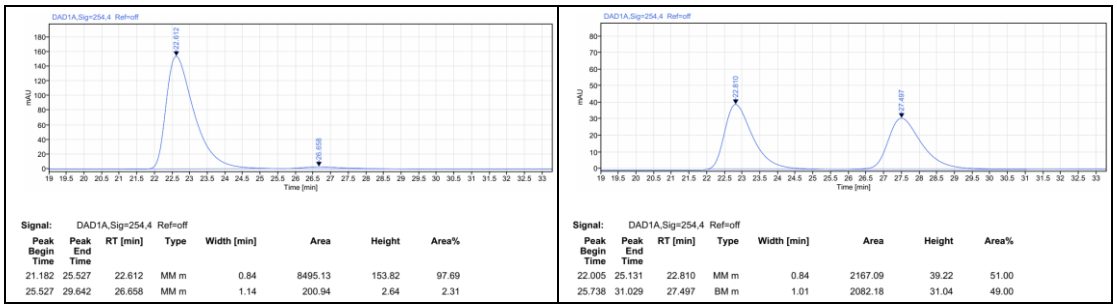
| Signal: | DAD1A,Sig=254,4 | Ref=off | | | | |
|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 19.243 | 21.580 | 19.906 | MM m | 0.69 | 2075.78 | 46.12 | 50.89 |
| 24.755 | 28.883 | 25.725 | MB m | 0.85 | 2002.87 | 35.44 | 49.11 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(naphthalen-2-yl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3va)**



**3va**

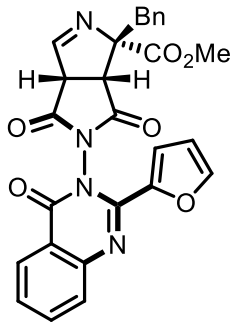
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 32.4 mg, 58% yield. **MP**: 130-132 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.28 (dd, *J* = 8.1, 1.5 Hz, 1H), 8.04 (d, *J* = 1.8 Hz, 1H), 7.92-7.79 (m, 5H), 7.65-7.53 (m, 4H), 7.49 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.21-7.15 (m, 3H), 7.02-6.97 (m, 2H), 3.71 (s, 3H), 3.36 (s, 2H), 3.10 (d, *J* = 8.3 Hz, 1H), 2.80 (dd, *J* = 8.3, 1.1 Hz, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.9, 169.6, 166.8, 159.8, 157.4, 154.2, 146.8, 135.8, 134.1, 133.9, 132.7, 131.0, 129.7, 128.9, 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.6, 127.5, 127.2, 123.7, 120.9, 86.4, 57.0, 53.1, 47.0, 42.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{33}H_{25}N_4O_5$ 557.1819; Found 557.1823. **Optical Rotation**: $[\alpha]^{20}_D$ = -224.9 (c = 0.1, $CH_2Cl_2$). 95% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 22.6 min for major isomer, $t_R$ = 26.7 min for minor isomer).



| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 21.182 | 25.527 | 22.612 | MM m | 0.84 | 8495.13 | 153.82 | 97.69 |
| 25.527 | 29.642 | 26.658 | MM m | 1.14 | 200.94 | 2.64 | 2.31 |

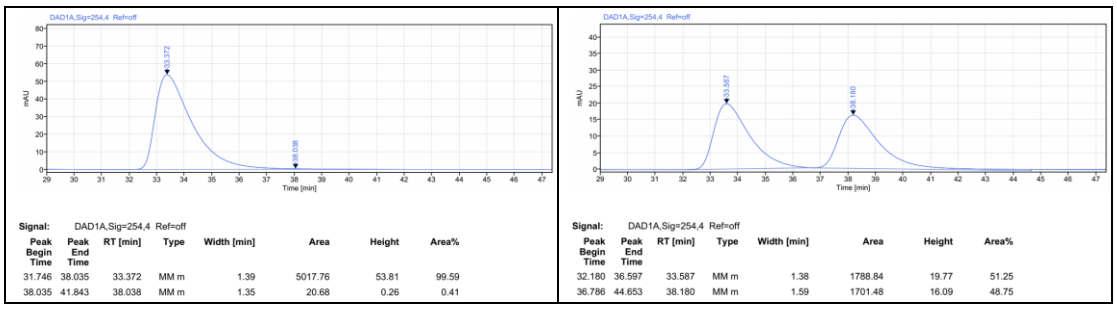
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 22.005 | 25.131 | 22.810 | MM m | 0.84 | 2167.09 | 39.22 | 51.00 |
| 25.738 | 31.029 | 27.497 | BM m | 1.01 | 2082.18 | 31.04 | 49.00 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(furan-2-yl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3wa)**



**3wa**

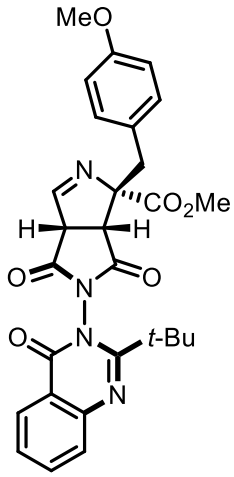
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 25.8 mg, 52% yield. **MP**: 110-112 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.21 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.82-7.76 (m, 1H), 7.72 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.68 (d, *J* = 1.2 Hz, 1H), 7.51-7.45 (m, 1H), 7.41 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.34-7.27 (m, 4H), 7.19-7.15 (m, 2H), 6.56 (dd, *J* = 3.6, 1.8 Hz, 1H), 3.72 (s, 3H), 3.59 (d, *J* = 8.6 Hz, 1H), 3.52 (d, *J* = 14.1 Hz, 1H), 3.47 (d, *J* = 14.1 Hz, 1H), 3.19 (dd, *J* = 8.5, 1.2 Hz, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.7, 169.6, 166.6, 160.2, 157.3, 147.0, 145.7, 145.5, 143.0, 135.7, 134.3, 131.1, 128.6, 128.3, 127.8, 127.7, 127.5, 120.6, 117.5, 112.8, 86.3, 57.4, 53.1, 47.3, 42.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{21}N_4O_6$ 497.1456; Found 497.1458. **Optical Rotation**: $[\alpha]^{20}_D$ = -272.6 (c = 0.1, $CH_2Cl_2$). 99% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 33.4 min for major isomer, $t_R$ = 38.0 min for minor isomer).



| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 31.746 | 38.035 | 33.372 | MM m | 1.39 | 5017.76 | 53.81 | 99.59 |
| 38.035 | 41.843 | 38.038 | MM m | 1.35 | 20.68 | 0.26 | 0.41 |

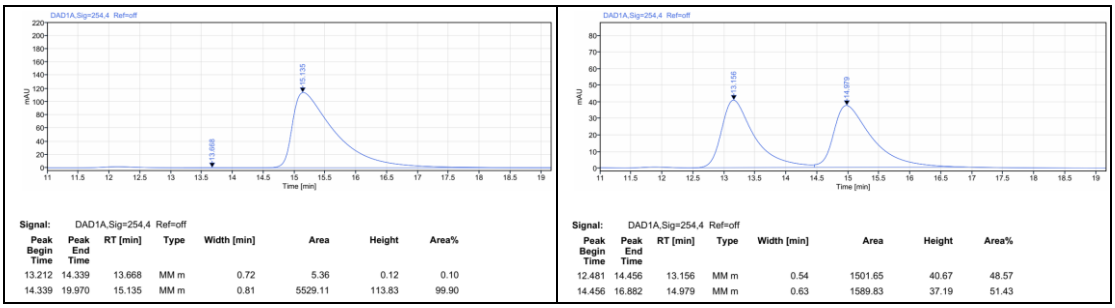
| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 32.180 | 36.597 | 33.587 | MM m | 1.38 | 1788.84 | 19.77 | 51.25 |
| 36.786 | 44.653 | 38.180 | MM m | 1.59 | 1701.48 | 16.09 | 48.75 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1-(4-methoxybenzyl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ab)**

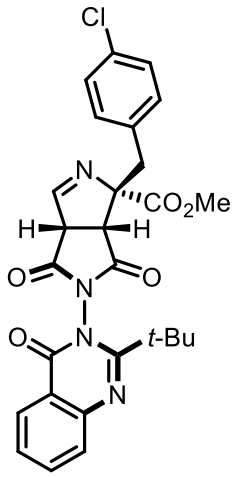



**3ab**

10:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 46.5 mg, 90% yield. **MP**: 127-129 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.15-8.12 (m, 1H), 7.77-7.72 (m, 1H), 7.69-7.64 (m, 2H), 7.45-7.40 (m, 1H), 7.12-7.07 (m, 2H), 6.88-6.83 (m, 2H), 3.80 (s, 3H), 3.70 (s, 3H), 3.58 (d, *J* = 8.3 Hz, 1H), 3.50 (d, *J* = 14.2 Hz, 1H), 3.35 (d, *J* = 14.2 Hz, 1H), 3.10 (dd, *J* = 8.3, 1.1 Hz, 1H), 1.30 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.4, 170.0, 168.1, 160.1, 159.1, 157.9, 146.2, 135.3, 132.2, 128.4, 127.4, 127.2, 125.9, 120.1, 114.0, 86.5, 57.0, 55.3, 53.0, 47.2, 42.0, 39.0, 29.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_6$ 517.2082; Found 517.2084. **Optical Rotation**: $[\alpha]^{20}_D$ = -309.0 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 13.7 min for minor isomer, $t_R$ = 15.1 min for major isomer).

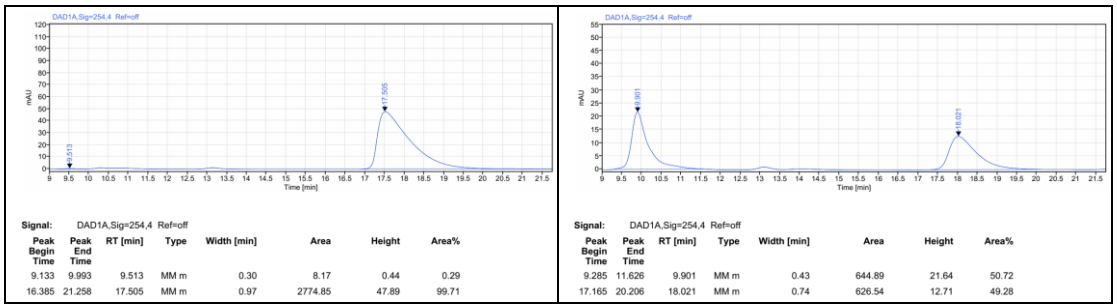



**Methyl (*S*a,1*S*,3a*S*,6a*R*)-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1-(4-chlorobenzyl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ac)**

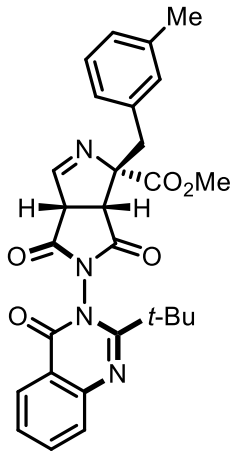



**3ac**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 44.8 mg, 86% yield. **MP**: 150-151 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.13 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.78-7.73 (m, 1H), 7.72 (d, *J* = 1.1 Hz, 1H), 7.67 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.46-7.40 (m, 1H), 7.33-7.28 (m, 2H), 7.16-7.11 (m, 2H), 3.69 (s, 3H), 3.55 (d, *J* = 8.4 Hz, 1H), 3.48 (d, *J* = 14.2 Hz, 1H), 3.42 (d, *J* = 14.1 Hz, 1H), 3.27 (dd, *J* = 8.5, 1.2 Hz, 1H), 1.30 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.1, 169.6, 167.8, 160.3, 160.1, 157.9, 146.2, 135.4, 133.8, 132.7, 132.4, 128.8, 128.4, 127.5, 127.2, 120.1, 86.3, 57.0, 53.1, 47.2, 42.4, 39.0, 29.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}ClN_4O_5$ 521.1586; Found 521.1590. **Optical Rotation**: $[\alpha]^{20}_D$ = -300.0 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 9.5 min for minor isomer, $t_R$ = 17.5 min for major isomer).

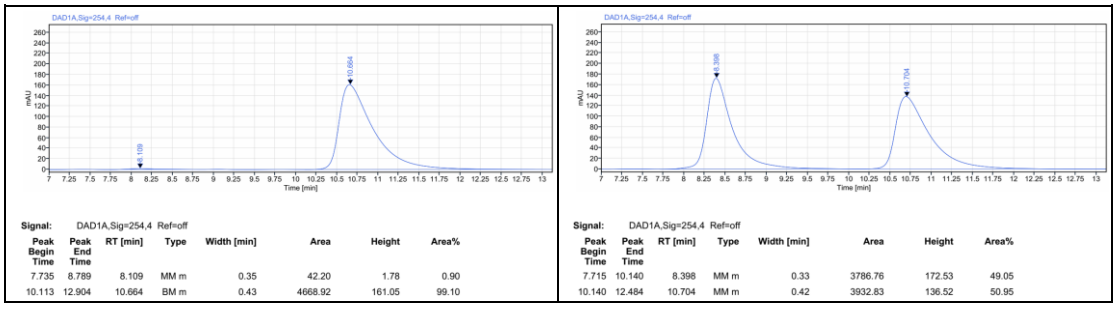



**Methyl (*S*a,1*S*,3a*S*,6a*R*)-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1-(3-methylbenzyl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3ad)**



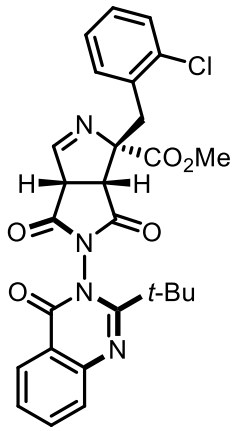

**3ad**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 40.0 mg, 80% yield. **MP**: 113-114 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.78-7.72 (m, 1H), 7.69-7.65 (m, 2H), 7.46-7.40 (m, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.13-7.09 (m, 1H), 7.01-6.96 (m, 2H), 3.71 (s, 3H), 3.61 (d, *J* = 8.3 Hz, 1H), 3.52 (d, *J* = 14.0 Hz, 1H), 3.38 (d, *J* = 14.0 Hz, 1H), 3.09 (dd, *J* = 8.3, 1.0 Hz, 1H), 2.34 (s, 3H), 1.30 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.4, 170.0, 168.1, 160.12, 160.07, 157.9, 146.2, 138.2, 135.3, 134.1, 132.0, 128.6, 128.43, 128.36, 128.0, 127.5, 127.2, 120.1, 86.4, 57.1, 53.0, 47.2, 42.8, 39.0, 29.5, 21.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_5$ 501.2132; Found 501.2135. **Optical Rotation**: $[\alpha]^{20}_D$ = -356.0 (c = 0.1, $CH_2Cl_2$). 98% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 8.1 min for minor isomer, $t_R$ = 10.7 min for major isomer).



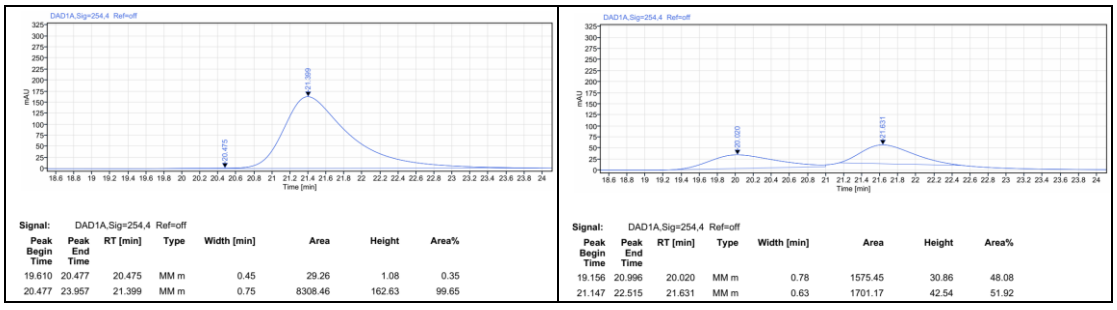

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1-(2-chlorobenzyl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-**

**carboxylate (3ae)**



**3ae**

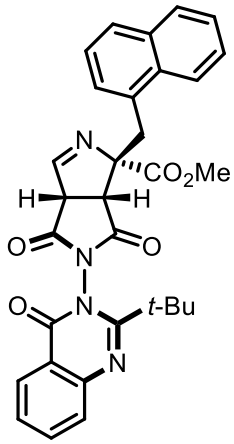
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 25.0 mg, 48% yield. **MP**: 159-161 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.78-7.73 (m, 1H), 7.72 (d, *J* = 1.1 Hz, 1H), 7.67 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.46-7.40 (m, 2H), 7.28-7.16 (m, 3H), 4.08 (d, *J* = 14.4 Hz, 1H), 3.92 (d, *J* = 8.3 Hz, 1H), 3.72 (s, 3H), 3.34 (d, *J* = 14.4 Hz, 1H), 3.30 (dd, *J* = 8.2, 1.1 Hz, 1H), 1.31 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.1, 169.6, 167.9, 160.4, 160.2, 158.0, 146.3, 135.4, 134.7, 133.8, 132.3, 130.2, 129.3, 128.4, 127.5, 127.3, 126.9, 120.1, 86.4, 57.1, 53.1, 46.8, 39.2, 39.0, 29.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}ClN_4O_5$ 521.1586; Found 521.1591. **Optical Rotation**: $[\alpha]^{20}_D$ = -338.4 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 20.5 min for minor isomer, $t_R$ = 21.4 min for major isomer).



| Signal: | DAD1A,Sig=254,4 | Ref=off | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 19.610 | 20.477 | 20.475 | MM m | 0.45 | 29.26 | 1.08 | 0.35 |
| 20.477 | 23.957 | 21.399 | MM m | 0.75 | 8308.46 | 162.63 | 99.65 |

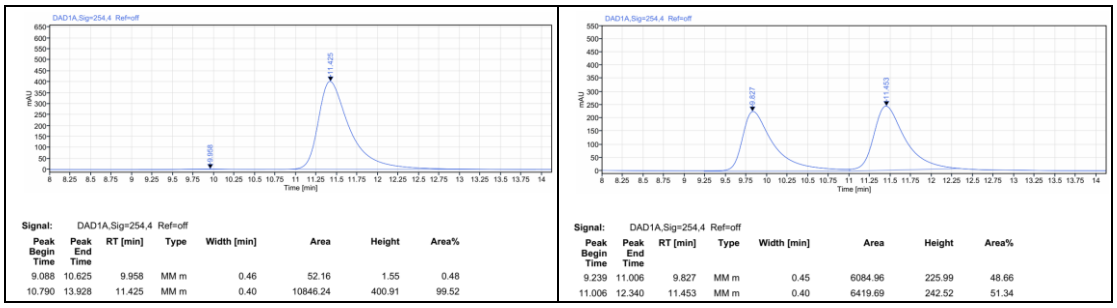
| Signal: | DAD1A,Sig=254,4 | Ref=off | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 19.156 | 20.996 | 20.020 | MM m | 0.78 | 1575.45 | 30.86 | 48.08 |
| 21.147 | 22.515 | 21.631 | MM m | 0.63 | 1701.17 | 42.54 | 51.92 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1-(naphthalen-1-ylmethyl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (3af)**

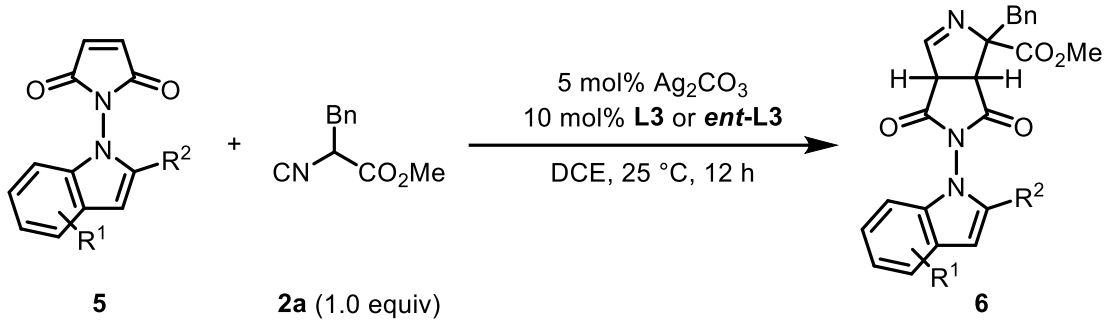


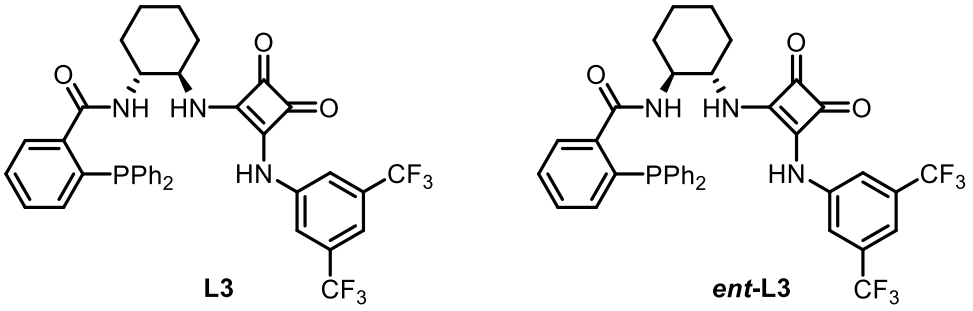
**3af**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 45.2 mg, 84% yield. **MP**: 198-200 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.22 (dd, *J* = 8.5, 1.3 Hz, 1H), 8.15-8.10 (m, 1H), 7.87 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.84-7.81 (m, 1H), 7.76-7.71 (m, 1H), 7.67-7.63 (m, 1H), 7.59-7.49 (m, 2H), 7.48 (d, *J* = 1.1 Hz, 1H), 7.46-7.40 (m, 2H), 7.35 (dd, *J* = 7.2, 1.3 Hz, 1H), 4.26 (d, *J* = 14.7 Hz, 1H), 3.83 (d, *J* = 14.6 Hz, 1H), 3.78-3.74 (m, 4H), 2.85 (dd, *J* = 8.2, 1.1 Hz, 1H), 1.24 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.4, 170.2, 167.9, 160.1, 160.0, 157.9, 146.2, 135.3, 134.1, 132.7, 130.5, 130.0, 129.0, 128.7, 128.3, 127.4, 127.2, 126.6, 126.2, 125.2, 124.8, 120.1, 86.9, 57.0, 53.1, 46.9, 38.9, 38.6, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{31}H_{29}N_4O_5$ 537.2132; Found 537.2137. **Optical Rotation**: $[\alpha]^{20}_D$ = -348.7 (c = 0.1, $CH_2Cl_2$). 99% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.0 min for minor isomer, $t_R$ = 11.4 min for major isomer).




## 6. Diastereo- and enantioselective synthesis of 6

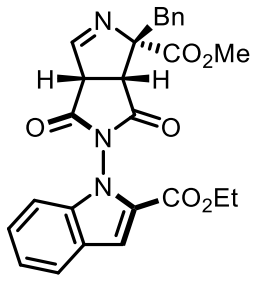



**General procedure.** To a 10 mL vial charged with **L3** or ***ent*-L3** (7.1 mg, 0.010 mmol, 10 mol%) and $Ag_2CO_3$ (1.4 mg, 0.005 mmol, 5 mol%) was added anhydrous DCE (1.0 mL, 0.1 M). The mixture was stirred for 10 min, and then N-indole maleimide **5** (0.10 mmol, 1.0 equiv) and isocyanoacetate **2a** (0.10 mmol, 1.0 equiv) were added successively in one portion. The reaction mixture was stirred at 25 ℃ for 12 h, then concentrated and purified by flash column chromatography to afford the product **6**.

The racemic sample for the standard of chiral HPLC spectra was prepared by using a mixture of approximately 1:1 **L3** and ***ent*-L3**.

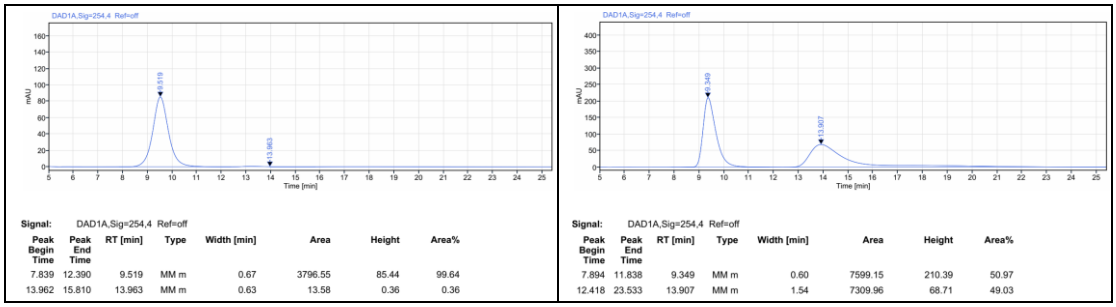
**Ethyl 1-((*S*a,3a*R*,4*S*,6a*S*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-1*H*-indole-2-carboxylate (6a)**



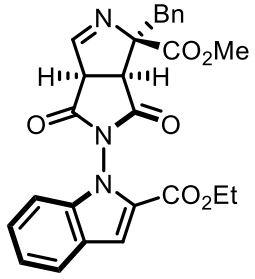
**6a**

With **L3**. >20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:1). White solid, 44.2 mg, 93%

yield. **MP**: 189-190 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 1.2 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 0.9 Hz, 1H), 7.40-7.36 (m, 1H), 7.35-7.28 (m, 3H), 7.26-7.21 (m, 1H), 7.20-7.13 (m, 3H), 4.31-4.22 (m, 2H), 3.70 (s, 3H), 3.68 (d, *J* = 8.6 Hz, 1H), 3.53 (s, 2H), 3.36 (dd, *J* = 8.7, 1.2 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.7, 169.9, 167.9, 161.2, 160.4, 137.9, 134.0, 131.2, 128.6, 127.6, 127.2, 125.5, 124.5, 123.3, 122.9, 112.2, 109.0, 87.1, 61.2, 57.9, 53.3, 47.4, 42.4, 14.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{24}N_3O_6$ 474.1660; Found 474.1659. **Optical Rotation**: $[\alpha]^{20}_D$ = -333.3 (c = 0.1, $CH_2Cl_2$). 99% ee (HPLC condition: Chiralpak IH column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 9.5 min for major isomer, $t_R$ = 14.0 min for minor isomer).

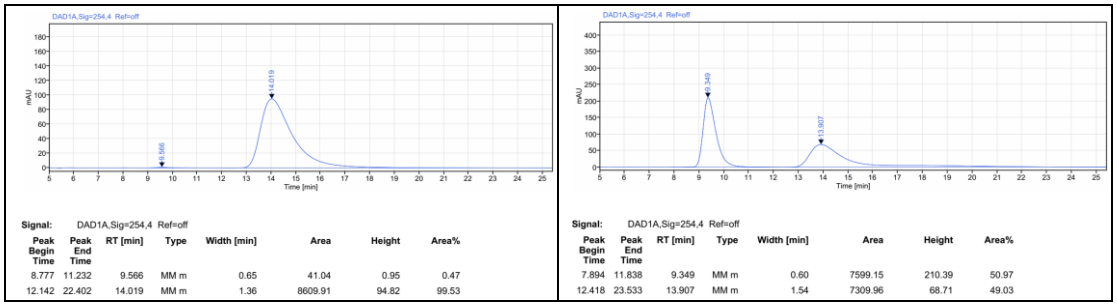



**Ethyl 1-((*R*a,3a*S*,4*R*,6a*R*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-1*H*-indole-2-carboxylate (*ent*-6a)**




***ent*-6a**

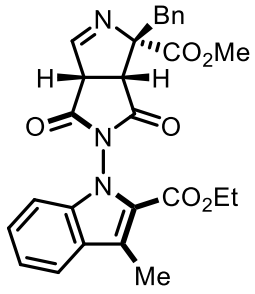
With ***ent*-L3**. >20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:1). White solid, 44.2 mg, 93% yield. **Optical Rotation**: $[\alpha]^{20}_D$ = +332.6 (c = 0.1, $CH_2Cl_2$). 99% ee (HPLC condition: Chiralpak IH column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 9.6 min for minor isomer, $t_R$ = 14.0 min for major isomer).




| Signal: | DAD1A,Sig=254,4 Ref=off | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 8.777 | 11.232 | 9.566 | MM m | 0.65 | 41.04 | 0.95 | 0.47 |
| 12.142 | 22.402 | 14.019 | MM m | 1.36 | 8609.91 | 94.82 | 99.53 |

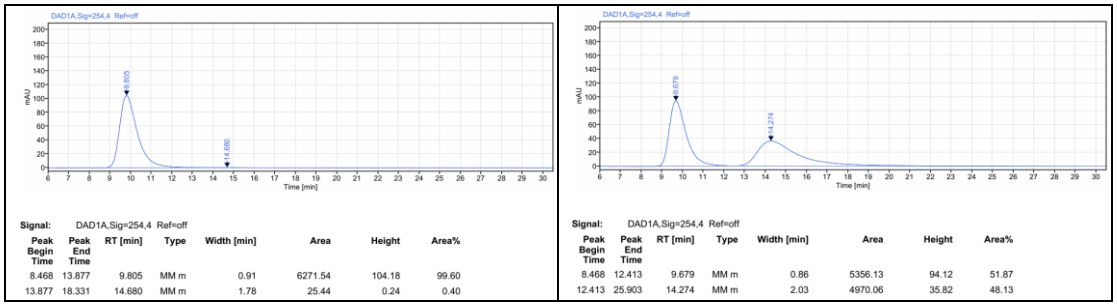
| Signal: | DAD1A,Sig=254,4 Ref=off | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 7.894 | 11.838 | 9.349 | MM m | 0.60 | 7599.15 | 210.39 | 50.97 |
| 12.418 | 23.533 | 13.907 | MM m | 1.54 | 7309.96 | 68.71 | 49.03 |

**Ethyl 1-((*S*a,3a*R*,4*S*,6a*S*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-3-methyl-1*H*-indole-2-carboxylate (6b)**




**6b**

With **L3**. >20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:1). White solid, 41.4 mg, 85% yield. **MP**: 151-153 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 1.3 Hz, 1H), 7.70-7.66 (m, 1H), 7.41-7.36 (m, 1H), 7.34-7.28 (m, 3H), 7.25-7.21 (m, 1H), 7.19-7.15 (m, 2H), 7.12-7.07 (m, 1H), 4.32-4.23 (m, 2H), 3.68 (s, 3H), 3.66 (d, *J* = 8.7 Hz, 1H), 3.55 (d, *J* = 14.1 Hz, 1H), 3.50 (d, *J* = 14.0 Hz, 1H), 3.33 (dd, *J* = 8.7, 1.2 Hz, 1H), 2.59 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 172.0, 169.9, 168.2, 161.4, 161.3, 137.2, 134.1, 131.2, 128.6, 127.6, 127.5, 126.2, 123.8, 122.2, 122.0, 121.4, 108.8, 86.9, 60.9, 57.8, 53.2, 47.4, 42.4, 14.3, 11.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}N_3O_6$ 488.1816; Found 488.1819. **Optical Rotation**: $[\alpha]^{20}_D$ = -339.0 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IH column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 9.8 min for major isomer, $t_R$ = 14.7 min for minor isomer).



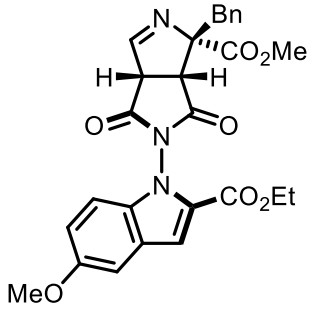

Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.468 | 13.877 | 9.805 | MM m | 0.91 | 6271.54 | 104.18 | 99.60 |
| 13.877 | 18.331 | 14.680 | MM m | 1.78 | 25.44 | 0.24 | 0.40 |

Signal: DAD1A,Sig=254,4 Ref=off

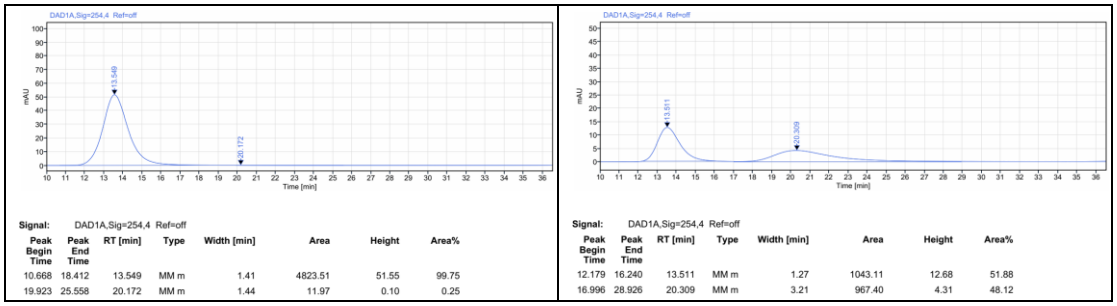
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.468 | 12.413 | 9.679 | MM m | 0.86 | 5356.13 | 94.12 | 51.87 |
| 12.413 | 25.903 | 14.274 | MM m | 2.03 | 4970.06 | 35.82 | 48.13 |

**Ethyl 1-((*S*a,3a*R*,4*S*,6a*S*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-5-methoxy-1*H*-indole-2-carboxylate (6c)**

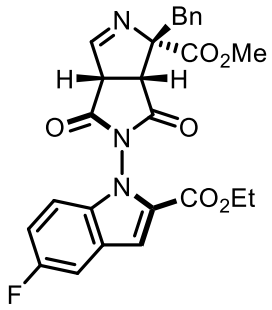



**6c**

With **L3**. >20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 45.5 mg, 90% yield. **MP**: 106-108 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 1.2 Hz, 1H), 7.34-7.28 (m, 4H), 7.19-7.15 (m, 2H), 7.08-7.02 (m, 3H), 4.28-4.22 (m, 2H), 3.83 (s, 3H), 3.69 (s, 3H), 3.66 (d, *J* = 8.7 Hz, 1H), 3.52 (s, 2H), 3.35 (dd, *J* = 8.7, 1.2 Hz, 1H), 1.32 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.7, 170.0, 167.9, 161.2, 160.3, 156.2, 134.1, 133.1, 131.2, 128.6, 127.6, 125.8, 125.1, 118.3, 111.7, 110.1, 103.6, 87.1, 61.1, 57.9, 55.9, 53.3, 47.3, 42.4, 14.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}N_3O_7$ 504.1765; Found 504.1769. **Optical Rotation**: $[\alpha]^{20}_D$ = -250.7 (c = 0.14, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IH column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 13.5 min for major isomer, $t_R$ = 20.2 min for minor isomer).

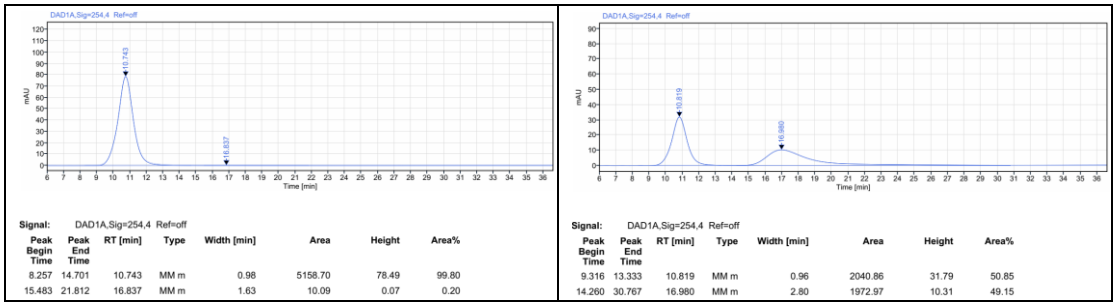



**Ethyl 1-((*S*a,3a*R*,4*S*,6a*S*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-5-fluoro-1*H*-indole-2-carboxylate (6d)**




**6d**

With **L3**. >20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:1). White solid, 41.1 mg, 84% yield. **MP**: 142-144 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 1.2 Hz, 1H), 7.36-7.28 (m, 5H), 7.19-7.13 (m, 4H), 4.30-4.22 (m, 2H), 3.72 (s, 3H), 3.67 (d, *J* = 8.8 Hz, 1H), 3.53 (s, 2H), 3.39 (dd, *J* = 8.8, 1.3 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.6, 170.1, 167.8, 161.1, 160.1, 159.3 (d, *J* = 239.4 Hz), 134.4, 134.0, 131.2, 128.7, 127.6, 126.8, 124.9 (d, *J* = 10.6 Hz), 116.1 (d, *J* = 27.0 Hz), 111.7 (d, *J* = 5.1 Hz), 110.4 (d, *J* = 9.5 Hz), 107.9 (d, *J* = 24.1 Hz), 87.3, 61.3, 57.9, 53.3, 47.4, 42.3, 14.2; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -120.1; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{23}FN_3O_6$ 492.1565; Found 492.1576. **Optical Rotation**: $[\alpha]^{20}_D$ = -320.6 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IH column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.7 min for major isomer, $t_R$ = 16.8 min for minor isomer).



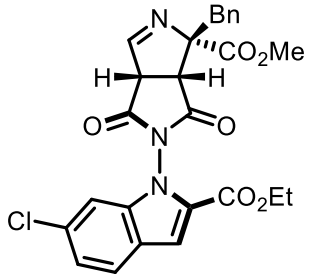

Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.257 | 14.701 | 10.743 | MM m | 0.98 | 5158.70 | 78.49 | 99.80 |
| 15.483 | 21.812 | 16.837 | MM m | 1.63 | 10.09 | 0.07 | 0.20 |

Signal: DAD1A,Sig=254,4 Ref=off

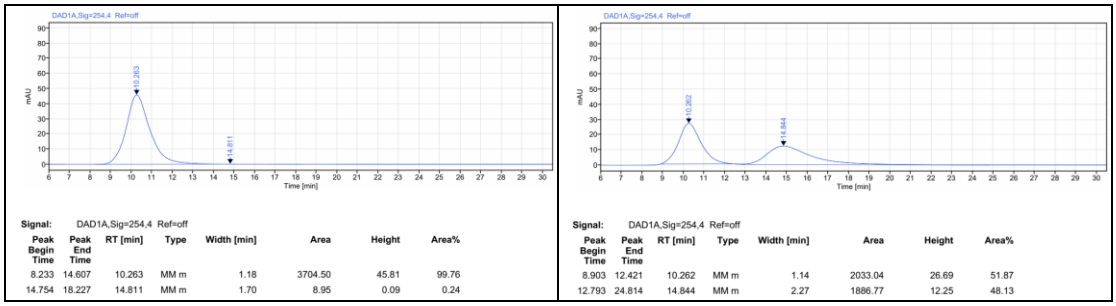
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.316 | 13.333 | 10.819 | MM m | 0.96 | 2040.86 | 31.79 | 50.85 |
| 14.260 | 30.767 | 16.980 | MM m | 2.80 | 1972.97 | 10.31 | 49.15 |

**Ethyl 1-((*S*a,3a*R*,4*S*,6a*S*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-6-chloro-1*H*-indole-2-carboxylate (6e)**




**6e**

With **L3**. >20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:1). White solid, 38.0 mg, 75% yield. **MP**: 105-106 ℃; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 1.2 Hz, 1H), 7.60 (dd, *J* = 8.5, 0.6 Hz, 1H), 7.36 (d, *J* = 1.0 Hz, 1H), 7.34-7.28 (m, 3H), 7.20 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.19-7.14 (m, 3H), 4.29-4.22 (m, 2H), 3.75 (s, 3H), 3.67 (d, *J* = 8.8 Hz, 1H), 3.53 (s, 2H), 3.40 (dd, *J* = 8.7, 1.2 Hz, 1H), 1.32 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.5, 169.8, 167.7, 161.0, 160.1, 138.2, 134.0, 133.4, 131.3, 128.7, 127.6, 126.1, 124.3, 124.0, 123.0, 111.9, 109.2, 87.1, 61.4, 57.9, 53.3, 47.3, 42.4, 14.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{23}ClN_3O_6$ 508.1270; Found 508.1272. **Optical Rotation**: $[\alpha]^{20}_D$ = -300.0 (c = 0.1, $CH_2Cl_2$). >99% ee (HPLC condition: Chiralpak IH column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.3 min for major isomer, $t_R$ = 14.8 min for minor isomer).



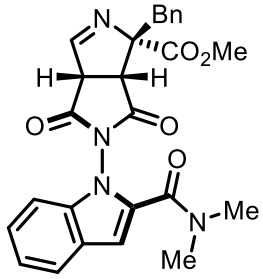

Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.233 | 14.607 | 10.263 | MM m | 1.18 | 3704.50 | 45.81 | 99.76 |
| 14.754 | 18.227 | 14.811 | MM m | 1.70 | 8.95 | 0.09 | 0.24 |

Signal: DAD1A,Sig=254,4 Ref=off

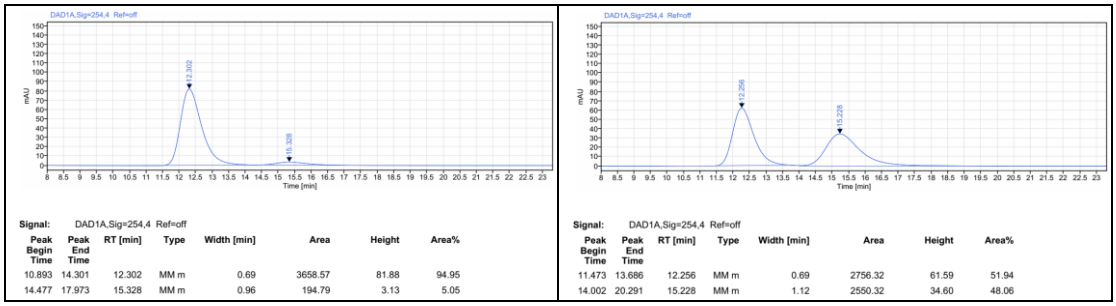
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.903 | 12.421 | 10.262 | MM m | 1.14 | 2033.04 | 26.69 | 51.87 |
| 12.793 | 24.814 | 14.844 | MM m | 2.27 | 1886.77 | 12.25 | 48.13 |

**Methyl (*S*a,1*S*,3a*S*,6a*R*)-1-benzyl-5-(2-(dimethylcarbamoyl)-1*H*-indol-1-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (6f)**




**6f**

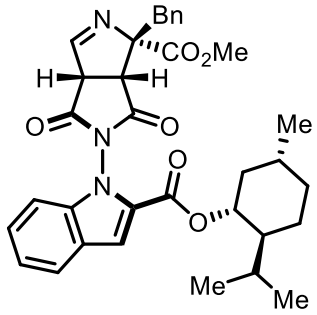
With **L3**. >20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:2). White solid, 33.8 mg, 72% yield. **MP**: 140-142 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 1.2 Hz, 1H), 7.67-7.60 (m, 1H), 7.36-7.28 (m, 4H), 7.24-7.18 (m, 1H), 7.17-7.13 (m, 2H), 7.12-7.09 (m, 1H), 6.86 (d, *J* = 0.9 Hz, 1H), 3.66 (s, 3H), 3.63 (d, *J* = 8.6 Hz, 1H), 3.50 (s, 2H), 3.36 (dd, *J* = 8.6, 1.2 Hz, 1H), 3.28 (br s, 3H), 3.04 (br s, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.8, 170.0, 167.7, 161.9, 161.4, 136.2, 134.0, 131.3, 128.6, 128.4, 127.6, 125.9, 124.5, 122.6, 122.4, 108.9, 107.7, 87.0, 57.9, 53.2, 47.3, 42.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{25}N_4O_5$ 473.1819; Found 473.1827. **Optical Rotation**: $[\alpha]^{20}_D$ = -202.5 (c = 0.1, $CH_2Cl_2$). 90% ee (HPLC condition: Chiralpak IH column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 12.3 min for major isomer, $t_R$ = 15.3 min for minor isomer).



| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 10.893 | 14.301 | 12.302 | MM m | 0.69 | 3658.57 | 81.88 | 94.95 |
| 14.477 | 17.973 | 15.328 | MM m | 0.96 | 194.79 | 3.13 | 5.05 |

| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 11.473 | 13.686 | 12.256 | MM m | 0.69 | 2756.32 | 61.59 | 51.94 |
| 14.002 | 20.291 | 15.228 | MM m | 1.12 | 2550.32 | 34.60 | 48.06 |

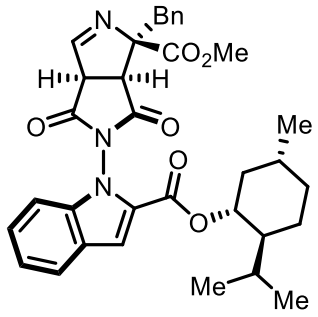
**(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 1-((*S*a,3a*R*,4*S*,6a*S*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-1*H*-indole-2-carboxylate (6g)**




**6g**

With **L3**. >20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 53.2 mg, 91% yield. **MP**: 106-108 °C; **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 1.2 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.41-7.36 (m, 2H), 7.35-7.29 (m, 3H), 7.25-7.13 (m, 4H), 4.81-4.72 (m, 1H), 3.71-3.66 (m, 4H), 3.54 (s, 2H), 3.37 (dd, *J* = 8.7, 1.3 Hz, 1H), 2.07-2.00 (m, 1H), 1.96-1.84 (m, 1H), 1.75-1.67 (m, 2H), 1.54-1.42 (m, 2H), 1.12-1.00 (m, 2H), 0.96-0.86 (m, 7H), 0.73 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.6, 170.0, 167.8, 161.2, 160.0, 137.8, 134.1, 131.3, 128.7, 127.6, 127.1, 125.9, 124.6, 123.2, 122.8, 112.0, 109.0, 87.1, 75.4, 57.8, 53.3, 47.3, 42.4, 40.9, 34.3, 31.6, 26.5, 23.8, 22.1, 20.8, 16.6; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{34}H_{38}N_3O_6$ 584.2755; Found 584.2763. **Optical Rotation**: $[\alpha]^{20}_D$ = -292.6 (c = 0.1, $CH_2Cl_2$).

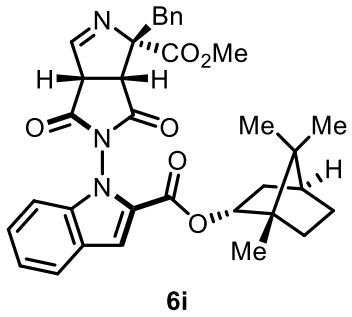
**(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 1-((*R*a,3a*S*,4*R*,6a*R*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-1*H*-indole-2-carboxylate (6h)**



**6h**

With ***ent*-L3**. >20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 54.0 mg, 93% yield. **MP**: 104-105 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 1.2 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.42-7.29 (m, 5H), 7.25-7.12 (m, 4H), 4.84-4.74 (m, 1H), 3.68 (s, 3H), 3.66 (d, *J* = 8.6 Hz, 1H), 3.56 (d, *J* = 14.2 Hz, 1H), 3.52 (d, *J* = 14.2 Hz, 1H), 3.36 (dd, *J* = 8.7, 1.2 Hz, 1H), 2.06-1.96 (m, 1H), 1.93-1.81 (m, 1H), 1.77-1.67 (m, 2H), 1.56-1.38 (m, 2H), 1.14-1.00 (m, 2H), 0.96-0.84 (m, 7H), 0.76 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.6, 169.9, 167.8, 161.2, 159.9, 137.8, 134.1, 131.2, 128.6, 127.6, 127.1, 125.9, 124.6, 123.2, 122.8, 112.1, 109.0, 87.1, 75.3, 57.9, 53.2, 47.4, 47.3, 42.3, 40.9, 34.3, 31.5, 26.5, 23.7, 22.1, 20.8, 16.6; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{34}H_{38}N_3O_6$ 584.2755; Found 584.2755. **Optical Rotation**: $[\alpha]^{20}_D$ = +233.4 (c = 0.1, $CH_2Cl_2$).

**(1*S*,2*R*,4*S*)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl 1-((*S*a,3a*R*,4*S*,6a*S*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-1*H*-indole-2-carboxylate (6i)**

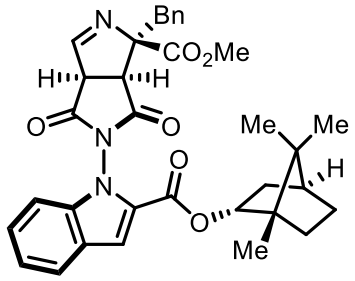


**6i**

With **L3**. >20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 55.4 mg, 95%

yield. **MP**: 120-122 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 1.3 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 0.9 Hz, 1H), 7.41-7.36 (m, 1H), 7.35-7.29 (m, 3H), 7.26-7.21 (m, 1H), 7.20-7.13 (m, 3H), 5.00-4.90 (m, 1H), 3.71-3.66 (m, 4H), 3.55 (d, *J* = 16.0 Hz, 1H), 3.51 (d, *J* = 16.0 Hz, 1H), 3.38 (dd, *J* = 8.6, 1.3 Hz, 1H), 2.45-2.33 (m, 1H), 2.10-2.00 (m, 1H), 1.84-1.71 (m, 2H), 1.44-1.34 (m, 1H), 1.32-1.24 (m, 1H), 1.08 (dd, *J* = 13.9, 3.5 Hz, 1H), 0.92 (s, 3H), 0.90 (s, 3H), 0.87 (s, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.7, 169.9, 167.8, 161.2, 160.7, 137.8, 134.0, 131.3, 128.6, 127.6, 127.1, 125.8, 124.6, 123.2, 122.9, 112.0, 109.0, 87.1, 81.1, 57.9, 53.2, 49.2, 48.0, 47.4, 45.0, 42.4, 36.8, 28.1, 27.4, 19.8, 18.9, 13.7; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{34}H_{36}N_3O_6$ 582.2599; Found 582.2601. **Optical Rotation**: $[\alpha]^{20}_D$ = -309.3 (c = 0.1, $CH_2Cl_2$).

**(1*S*,2*R*,4*S*)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl 1-((*R*a,3a*S*,4*R*,6a*R*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-1*H*-indole-2-carboxylate (6j)**

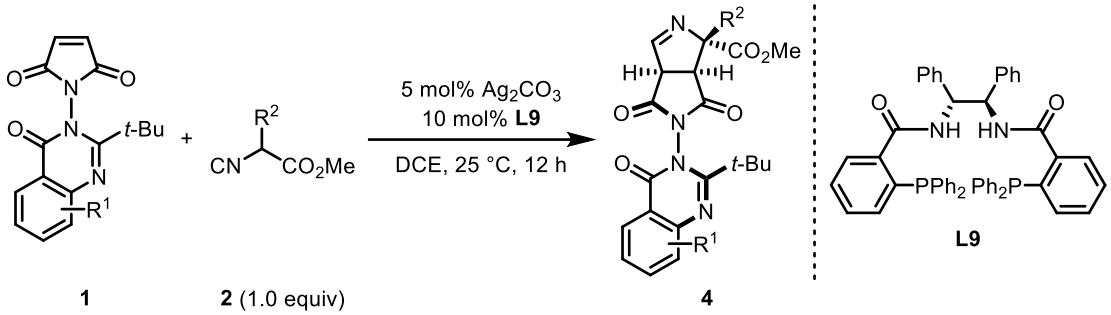



**6j**

With ***ent*-L3**. >20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 51.9 mg, 89% yield. **MP**: 123-125 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 1.2 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 0.9 Hz, 1H), 7.41-7.36 (m, 1H), 7.34-7.29 (m, 3H), 7.26-7.21 (m, 1H), 7.19-7.13 (m, 3H), 5.04-4.95 (m, 1H), 3.73-3.65 (m, 4H), 3.53 (s, 2H), 3.38 (dd, *J* = 8.7, 1.2 Hz, 1H), 2.41-2.31 (m, 1H), 2.09-1.99 (m, 1H), 1.85-1.75 (m, 1H), 1.74-1.70 (m, 1H), 1.43-1.34 (m, 1H), 1.32-1.24 (m, 1H), 1.07 (dd, *J* = 13.8, 3.4 Hz, 1H), 0.92 (s, 3H), 0.90 (s, 3H), 0.87 (s, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.7, 170.0, 167.8, 161.2, 160.7, 137.8, 134.0, 131.3, 128.7, 127.6, 127.1, 125.9, 124.6,

123.2, 122.9, 112.0, 109.0, 87.1, 81.0, 57.9, 53.2, 49.3, 48.0, 47.3, 45.0, 42.4, 36.7, 28.1, 27.4, 19.8, 18.9, 13.7; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{34}H_{36}N_3O_6$ 582.2599; Found 582.2604. **Optical Rotation**: $[\alpha]^{20}_D$ = +242.4 (c = 0.1, $CH_2Cl_2$).

## 7. Diastereo- and enantioselective synthesis of 4

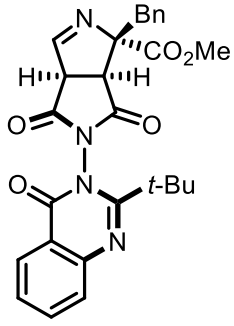



1 2 (1.0 equiv) 4

**General procedure.** To a 10 mL vial charged with **L9** (7.9 mg, 0.010 mmol, 10 mol%) and $Ag_2CO_3$ (1.4 mg, 0.005 mmol, 5 mol%) was added anhydrous DCE (1.0 mL, 0.1 M). The mixture was stirred for 10 min, and then N-quinazolinone maleimide **1** (0.10 mmol, 1.0 equiv) and isocyanoacetate **2** (0.10 mmol, 1.0 equiv) were added successively in one portion. The reaction mixture was stirred at 25 ℃ for 12 h, then concentrated and purified by flash column chromatography to afford the product **4**.

The racemic sample for the standard of chiral HPLC spectra was prepared by using a mixture of approximately 1:1 **L9** and ***ent*-L9**.

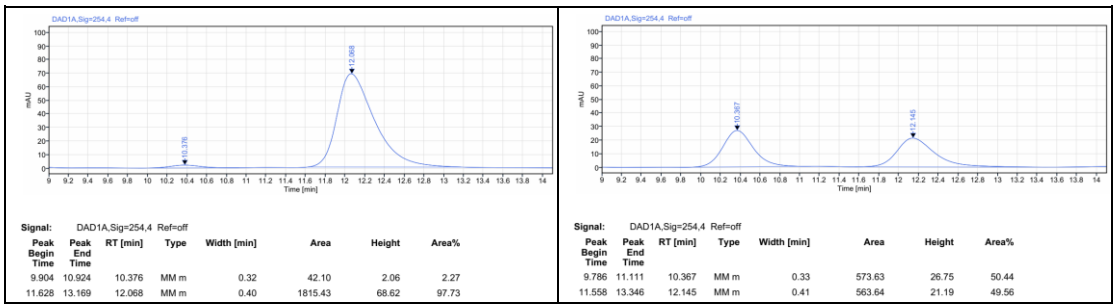
**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4aa)**



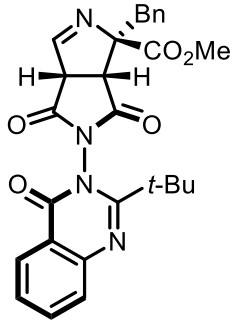

**4aa**

>20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by

flash column chromatography (PE/EtOAc 2:1). White solid, 38.9 mg, 80% yield. **MP**: 182-184 °C. **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.17 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.87 (d, *J* = 1.1 Hz, 1H), 7.83-7.78 (m, 1H), 7.75-7.71 (m, 1H), 7.52-7.47 (m, 1H), 7.37-7.24 (m, 5H), 4.49 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.28 (d, *J* = 8.8 Hz, 1H), 3.84 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.89 (d, *J* = 13.9 Hz, 1H), 1.36 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.0, 170.8, 169.0, 160.1, 159.8, 158.5, 146.4, 135.6, 135.5, 130.3, 128.50, 128.45, 127.6, 127.5, 127.3, 120.0, 87.5, 58.0, 53.1, 49.3, 42.1, 39.1, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{27}N_4O_5$ 487.1976; Found 487.1980. **Optical Rotation**: $[\alpha]^{20}_D$ = +77.5 (c = 0.1, $CH_2Cl_2$). 95% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.4 min for minor isomer, $t_R$ = 12.1 min for major isomer).

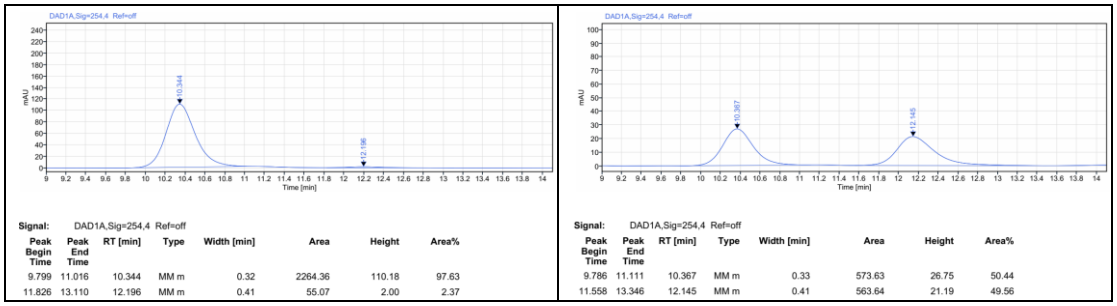



**Methyl (*R*a,1*R*,3a*S*,6a*R*)-1-benzyl-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (*ent*-4aa)**

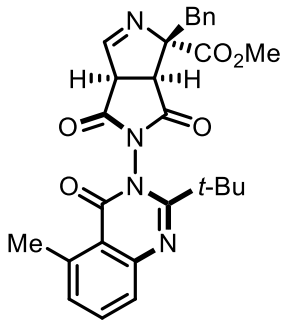



***ent*-4aa**

With ***ent*-L9**. >20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 37.0 mg, 76% yield. **Optical Rotation**: $[\alpha]^{20}_D$ = -75.4 (c = 0.1, $CH_2Cl_2$). 95% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.3 min for major isomer, $t_R$ = 12.2 min for major isomer).

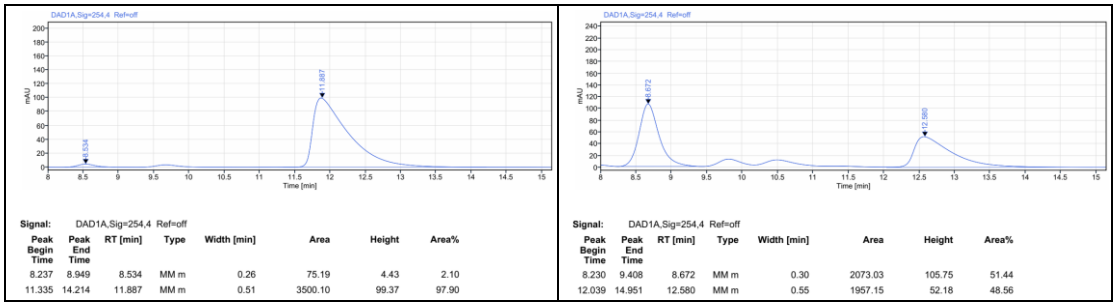



**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-5-methyl-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ba)**




**4ba**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 33.6 mg, 67% yield. **MP**: 125-126 ℃. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 1.1 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 1H), 7.55 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.37-7.27 (m, 5H), 7.26-7.22 (m, 1H), 4.49 (dd, *J* = 8.7, 1.0 Hz, 1H), 4.29 (d, *J* = 8.8 Hz, 1H), 3.84 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.90 (d, *J* = 14.0 Hz, 1H), 2.77 (s, 3H), 1.35 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.02, 170.99, 169.2, 159.8, 159.7, 158.5, 147.8, 141.7, 135.6, 134.7, 130.3, 130.0, 128.4, 127.4, 126.7, 118.5, 87.4, 58.0, 53.0, 49.2, 42.1, 38.8, 29.3, 22.7; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_5$ 501.2132; Found 501.2136. **Optical Rotation**: $[\alpha]^{20}_D$ = +82.9 (c = 0.2, $CH_2Cl_2$). 96% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 8.5 min for minor isomer, $t_R$ = 11.9 min for major isomer).



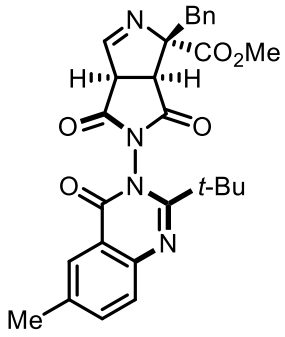

Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.237 | 8.949 | 8.534 | MM m | 0.26 | 75.19 | 4.43 | 2.10 |
| 11.335 | 14.214 | 11.887 | MM m | 0.51 | 3500.10 | 99.37 | 97.90 |

Signal: DAD1A,Sig=254,4 Ref=off

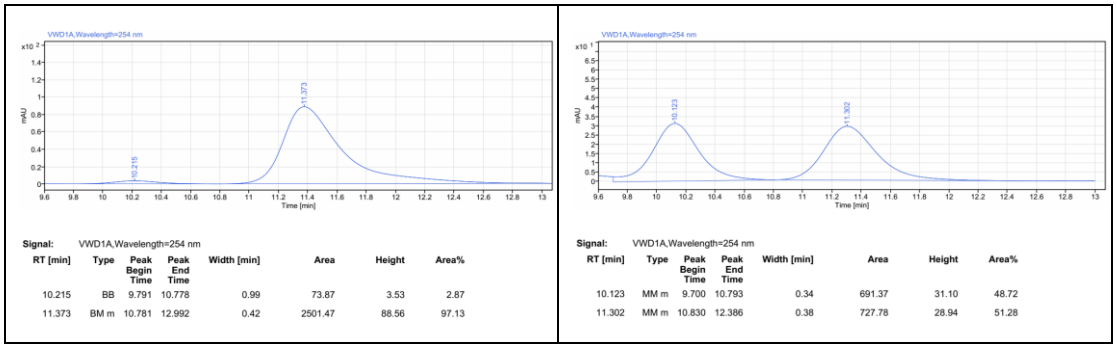
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.230 | 9.408 | 8.672 | MM m | 0.30 | 2073.03 | 105.75 | 51.44 |
| 12.039 | 14.951 | 12.580 | MM m | 0.55 | 1957.15 | 52.18 | 48.56 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-6-methyl-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ca)**

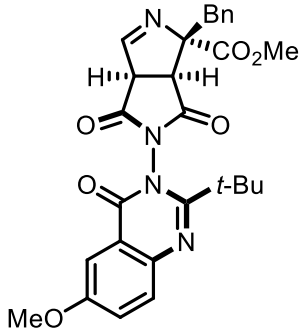



**4ca**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 39.0 mg, 78% yield. **MP**: 177-179 °C. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.96-7.93 (m, 1H), 7.87 (t, *J* = 0.9 Hz, 1H), 7.63-7.60 (m, 2H), 7.37-7.24 (m, 5H), 4.48 (dt, *J* = 8.8, 1.0 Hz, 1H), 4.26 (dd, *J* = 8.8, 0.8 Hz, 1H), 3.84 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.89 (d, *J* = 13.9 Hz, 1H), 2.48 (s, 3H), 1.35 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.0, 170.8, 169.0, 159.8, 159.2, 158.5, 144.4, 137.9, 137.1, 135.6, 130.4, 128.5, 128.3, 127.5, 126.7, 119.7, 87.5, 58.0, 53.1, 49.3, 42.1, 39.0, 29.4, 21.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_5$ 501.2132; Found 501.2135. **Optical Rotation**: $[\alpha]^{20}_D$ = +80.0 (c = 0.05, $CH_2Cl_2$). 94% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.2 min for minor isomer, $t_R$ = 11.4 min for major isomer).

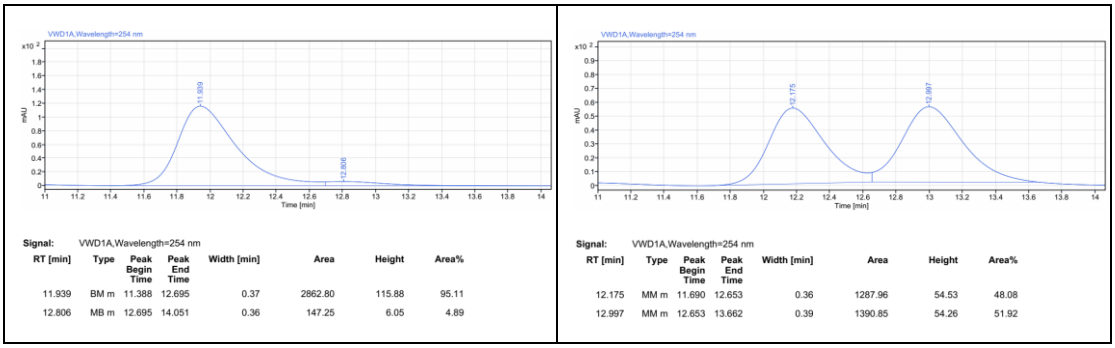



**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-6-methoxy-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4da)**




**4da**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 40.3 mg, 78% yield. **MP**: 108-109 ℃. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 1.1 Hz, 1H), 7.65 (d, *J* = 8.9 Hz, 1H), 7.51 (d, *J* = 3.0 Hz, 1H), 7.41-7.24 (m, 6H), 4.48 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.26 (d, *J* = 8.8 Hz, 1H), 3.89 (s, 3H), 3.84 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.89 (d, *J* = 13.9 Hz, 1H), 1.35 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.0, 170.8, 169.0, 159.8, 158.9, 158.5, 157.7, 141.0, 135.5, 130.4, 130.1, 128.5, 127.5, 125.8, 120.7, 106.5, 87.5, 58.0, 56.0, 53.1, 49.3, 42.1, 38.8, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_6$ 517.2082; Found 517.2079. **Optical Rotation**: $[\alpha]^{20}_D$ = +47.5 (c = 0.2, $CH_2Cl_2$). 90% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 11.9 min for major isomer, $t_R$ = 12.8 min for minor isomer).



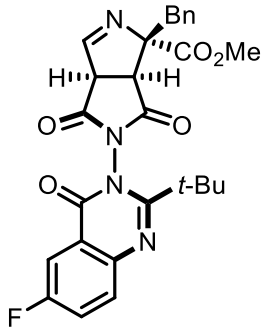

Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 11.939 | BM m | 11.388 | 12.695 | 0.37 | 2862.80 | 115.88 | 95.11 |
| 12.806 | MB m | 12.695 | 14.051 | 0.36 | 147.25 | 6.05 | 4.89 |

Signal: VWD1A,Wavelength=254 nm

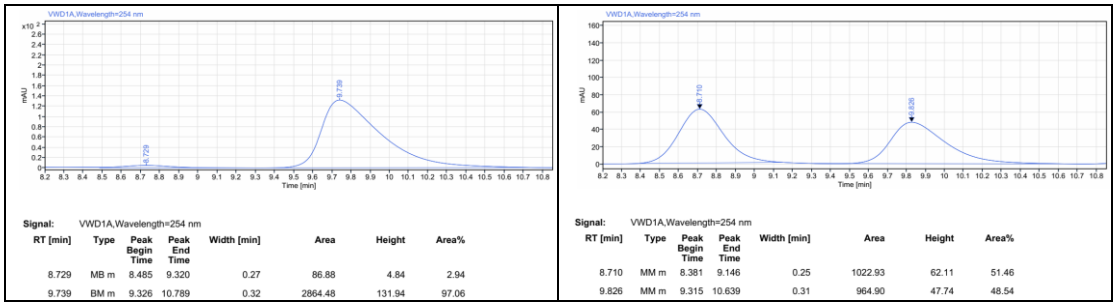
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 12.175 | MM m | 11.690 | 12.653 | 0.36 | 1287.96 | 54.53 | 48.08 |
| 12.997 | MM m | 12.653 | 13.662 | 0.39 | 1390.85 | 54.26 | 51.92 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-6-fluoro-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ea)**




**4ea**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 37.8 mg, 75% yield. **MP**: 140-141 °C. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 1.1 Hz, 1H), 7.79 (dd, *J* = 8.1, 2.9 Hz, 1H), 7.74 (dd, *J* = 8.9, 4.8 Hz, 1H), 7.55-7.49 (m, 1H), 7.37-7.24 (m, 5H), 4.48 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.27 (d, *J* = 8.8 Hz, 1H), 3.83 (d, *J* = 13.9 Hz, 1H), 3.58 (s, 3H), 2.89 (d, *J* = 13.9 Hz, 1H), 1.35 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.9, 170.6, 168.8, 161.2 (d, *J* = 249.9 Hz), 159.7, 159.4, 157.9 (d, *J* = 3.4 Hz), 143.1 (d, *J* = 2.0 Hz), 135.5, 131.0 (d, *J* = 8.4 Hz), 130.3, 128.5, 127.5, 124.2 (d, *J* = 24.0 Hz), 121.2 (d, *J* = 9.0 Hz), 112.2 (d, *J* = 23.9 Hz), 87.5, 58.0, 53.1, 49.3, 42.1, 39.1, 29.4; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -111.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}FN_4O_5$ 505.1882; Found 505.1889. **Optical Rotation**: $[\alpha]^{20}_D$ = +78.4 (c = 0.2, $CH_2Cl_2$). 94% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 8.7 min for minor isomer, $t_R$ = 9.7 min for major isomer).



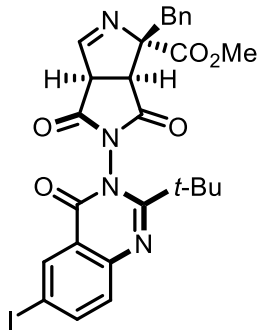
Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.729 | MB m | 8.485 | 9.320 | 0.27 | 86.88 | 4.84 | 2.94 |
| 9.739 | BM m | 9.326 | 10.789 | 0.32 | 2864.48 | 131.94 | 97.06 |

Signal: VWD1A,Wavelength=254 nm

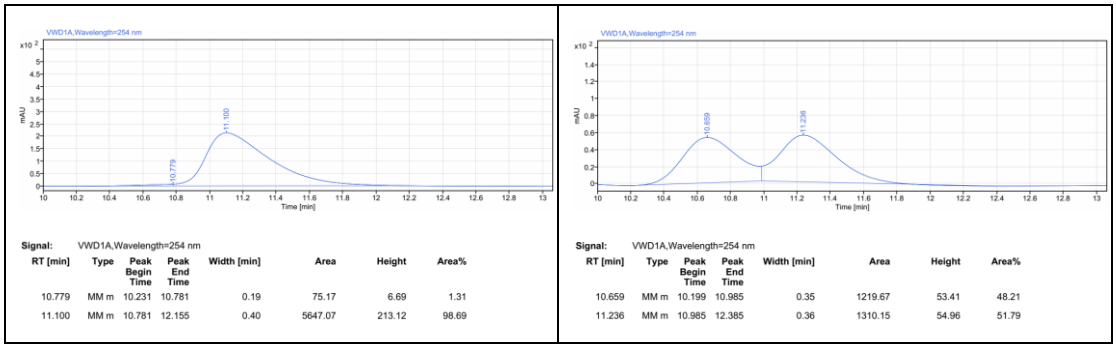
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.710 | MM m | 8.381 | 9.146 | 0.25 | 1022.93 | 62.11 | 51.46 |
| 9.826 | MM m | 9.315 | 10.639 | 0.31 | 964.90 | 47.74 | 48.54 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-6-iodo-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4fa)**



**4fa**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 38.0 mg, 62% yield. **MP**: 169-171 ℃. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 2.0 Hz, 1H), 8.06 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.86 (d, *J* = 1.1 Hz, 1H), 7.47-7.44 (m, 1H), 7.36-7.24 (m, 5H), 4.48 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.27 (d, *J* = 8.8 Hz, 1H), 3.83 (d, *J* = 13.9 Hz, 1H), 3.58 (s, 3H), 2.87 (d, *J* = 13.9 Hz, 1H), 1.34 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.9, 170.6, 168.8, 161.0, 159.7, 157.1, 145.7, 144.4, 136.1, 135.5, 130.4, 130.3, 128.5, 127.5, 121.6, 92.0, 87.5, 58.0, 53.1, 49.3, 42.1, 39.3, 29.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}IN_4O_5$ 613.0942; Found 613.0940. **Optical Rotation**: $[\alpha]^{20}_D$ = +28.3 (c = 0.1, $CH_2Cl_2$). 97% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.8 min for minor isomer, $t_R$ = 11.1 min for major isomer).



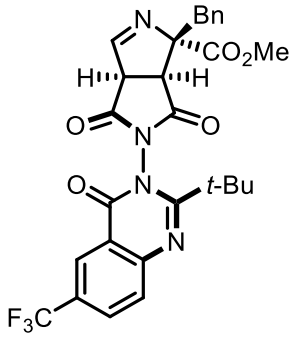

Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 10.779 | MM m | 10.231 | 10.781 | 0.19 | 75.17 | 6.69 | 1.31 |
| 11.100 | MM m | 10.781 | 12.155 | 0.40 | 5647.07 | 213.12 | 98.69 |

Signal: VWD1A,Wavelength=254 nm

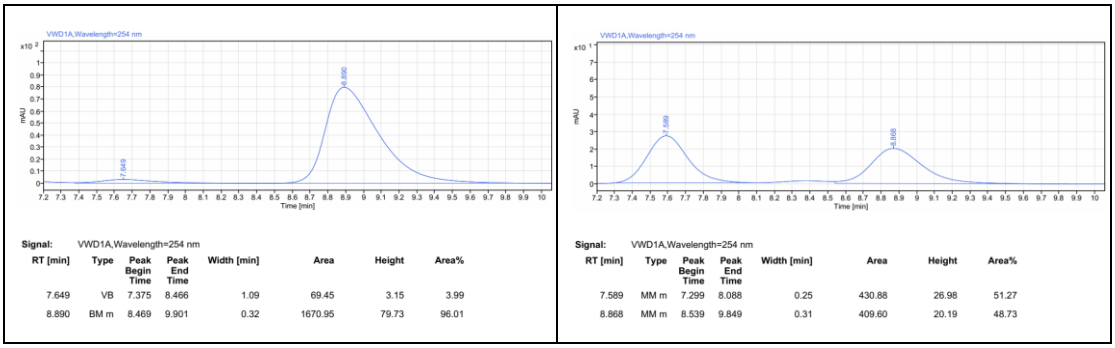
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 10.659 | MM m | 10.199 | 10.985 | 0.35 | 1219.67 | 53.41 | 48.21 |
| 11.236 | MM m | 10.985 | 12.385 | 0.36 | 1310.15 | 54.96 | 51.79 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-4-oxo-6-(trifluoromethyl)quinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ga)**




**4ga**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 31.0 mg, 56% yield. **MP**: 196-198 ℃. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.47-8.44 (m, 1H), 8.00 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.88-7.83 (m, 2H), 7.36-7.25 (m, 5H), 4.50 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.29 (d, *J* = 8.8 Hz, 1H), 3.83 (d, *J* = 14.0 Hz, 1H), 3.58 (s, 3H), 2.88 (d, *J* = 13.9 Hz, 1H), 1.37 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.9, 170.5, 168.7, 162.6, 159.6, 157.8, 148.4, 135.4, 131.7, 130.3, 129.6 (d, *J* = 33.5 Hz), 129.5, 128.5, 127.5, 125.2 (d, *J* = 4.2 Hz), 123.5 (d, *J* = 272.5 Hz), 120.0, 87.5, 58.0, 53.1, 49.3, 42.1, 39.4, 29.3; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -62.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{26}F_3N_4O_5$ 555.1850; Found 555.1855. **Optical Rotation**: $[\alpha]^{20}_D$ = +83.4 (c = 0.05, $CH_2Cl_2$). 92% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 7.6 min for minor isomer, $t_R$ = 8.9 min for major isomer).



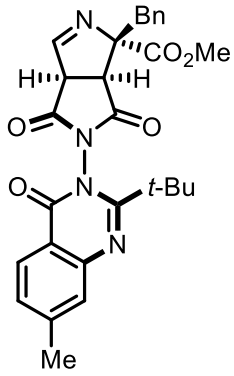

Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 7.649 | VB | 7.375 | 8.466 | 1.09 | 69.45 | 3.15 | 3.99 |
| 8.890 | BM m | 8.469 | 9.901 | 0.32 | 1670.95 | 79.73 | 96.01 |

Signal: VWD1A,Wavelength=254 nm

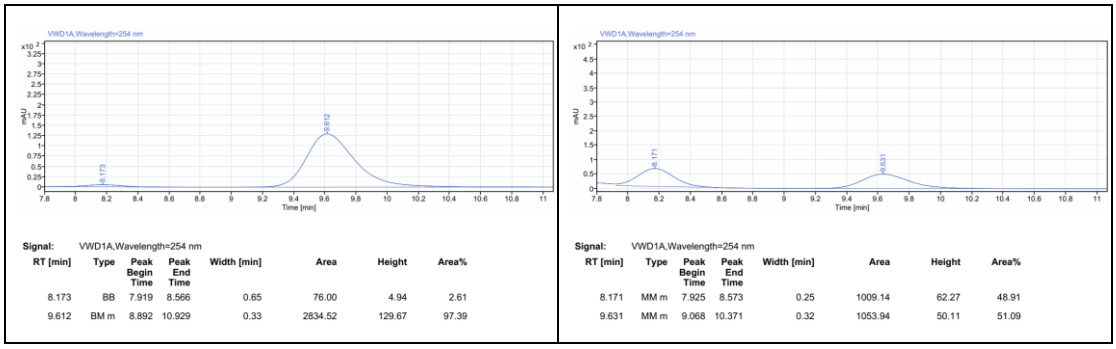
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 7.589 | MM m | 7.299 | 8.088 | 0.25 | 430.88 | 26.98 | 51.27 |
| 8.868 | MM m | 8.539 | 9.849 | 0.31 | 409.60 | 20.19 | 48.73 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-7-methyl-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ha)**




**4ha**

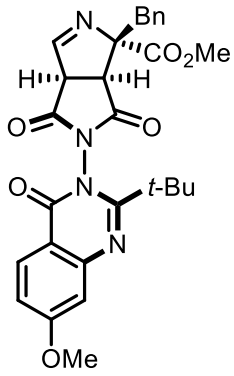
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 36.1mg, 72% yield. **MP**: 112-113 ℃. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 1.0 Hz, 1H), 7.55-7.52 (m, 1H), 7.37-7.24 (m, 6H), 4.48 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.27 (d, *J* = 8.8 Hz, 1H), 3.84 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.89 (d, *J* = 13.9 Hz, 1H), 2.51 (s, 3H), 1.35 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.0, 170.8, 169.0, 160.1, 159.8, 158.4, 146.9, 146.4, 135.6, 130.4, 129.2, 128.5, 128.3, 127.5, 127.1, 117.5, 87.5, 58.0, 53.1, 49.2, 42.1, 39.0, 29.4, 22.1; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_5$ 501.2132; Found 501.2137. **Optical Rotation**: $[\alpha]^{20}_D$ = +105.6 (c = 0.15, $CH_2Cl_2$). 95% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 8.2 min for minor isomer, $t_R$ = 9.6 min for major isomer).



| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 8.173 | BB | 7.919 | 8.566 | 0.65 | 76.00 | 4.94 | 2.61 |
| 9.612 | BM m | 8.892 | 10.929 | 0.33 | 2834.52 | 129.67 | 97.39 |

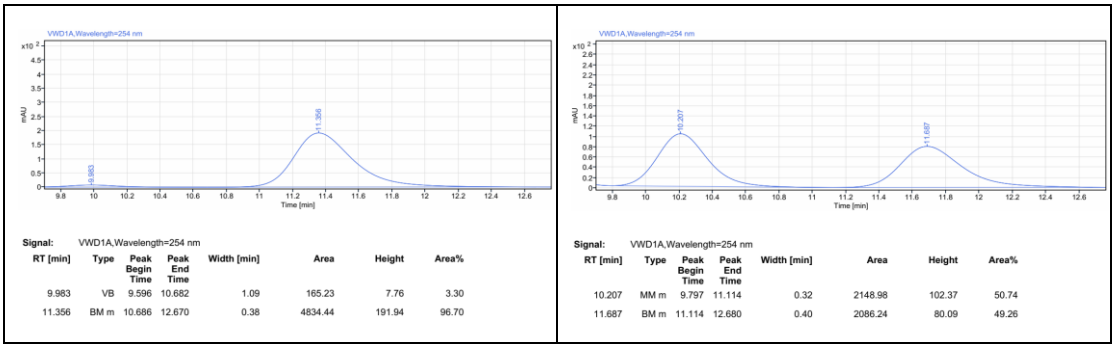
| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 8.171 | MM m | 7.925 | 8.573 | 0.25 | 1009.14 | 62.27 | 48.91 |
| 9.631 | MM m | 9.068 | 10.371 | 0.32 | 1053.94 | 50.11 | 51.09 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-7-methoxy-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ia)**



**4ia**

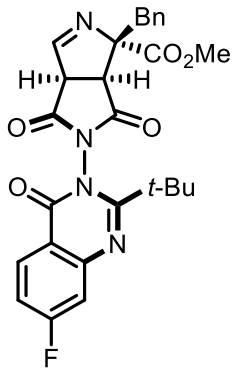
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 34.0 mg, 66% yield. **MP**: 109-111 ℃. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.9 Hz, 1H), 7.87 (d, *J* = 1.1 Hz, 1H), 7.37-7.24 (m, 5H), 7.10 (d, *J* = 2.4 Hz, 1H), 7.05 (dd, *J* = 8.8, 2.5 Hz, 1H), 4.48 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.26 (d, *J* = 8.8 Hz, 1H), 3.94 (s, 3H), 3.83 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.88 (d, *J* = 13.9 Hz, 1H), 1.35 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.0, 170.9, 169.1, 165.7, 160.8, 159.8, 157.9, 148.8, 135.5, 130.3, 128.9, 128.4, 127.4, 117.8, 113.2, 109.2, 87.4, 58.0, 55.9, 53.1, 49.2, 42.1, 39.0, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_6$ 517.2082; Found 517.2084. **Optical Rotation**: $[\alpha]^{20}_D$ = +89.4 (c = 0.1, $CH_2Cl_2$). 93% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.0 min for minor isomer, $t_R$ = 11.4 min for major isomer).



| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.983 | VB | 9.596 | 10.682 | 1.09 | 165.23 | 7.76 | 3.30 |
| 11.356 | BM m | 10.686 | 12.670 | 0.38 | 4834.44 | 191.94 | 96.70 |

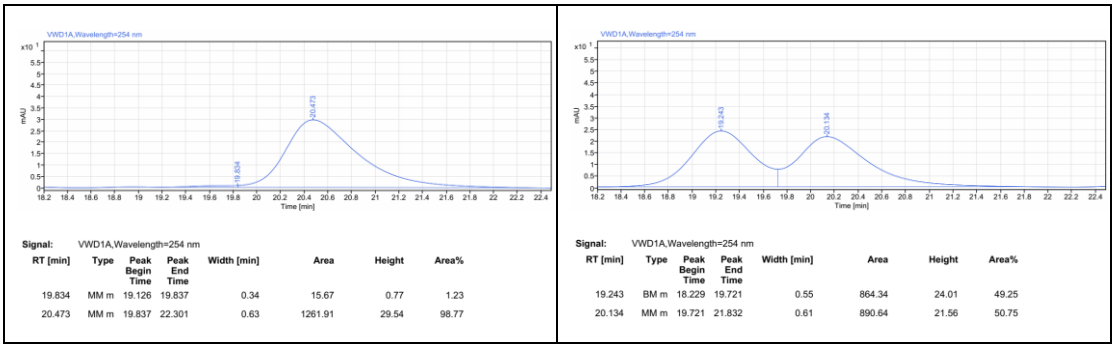
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 10.207 | MM m | 9.797 | 11.114 | 0.32 | 2148.98 | 102.37 | 50.74 |
| 11.687 | BM m | 11.114 | 12.680 | 0.40 | 2086.24 | 80.09 | 49.26 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-7-fluoro-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ja)**



**4ja**

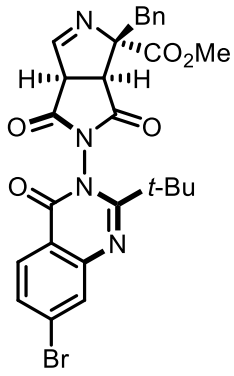
>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 28.8 mg, 57% yield. **MP**: 152-153 ℃. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.18 (dd, *J* = 8.9, 6.0 Hz, 1H), 7.87 (d, *J* = 1.0 Hz, 1H), 7.40-7.26 (m, 6H), 7.24-7.19 (m, 1H), 4.48 (dd, *J* = 8.8, 1.0 Hz, 1H), 4.27 (d, *J* = 8.8 Hz, 1H), 3.83 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.88 (d, *J* = 13.9 Hz, 1H), 1.35 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.0, 170.7, 168.9, 167.3 (d, *J* = 256.4 Hz), 161.6, 159.6, 157.7, 148.6 (d, *J* = 13.5 Hz), 135.5, 130.3, 130.1 (d, *J* = 10.6 Hz), 128.5, 127.5, 116.7, 116.5 (d, *J* = 23.7 Hz), 114.0 (d, *J* = 21.9 Hz), 87.5, 58.0, 53.1, 49.3, 42.1, 39.2, 29.3; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -101.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}FN_4O_5$ 505.1882; Found 505.1881. **Optical Rotation**: $[\alpha]^{20}_D$ = +115.4 (c = 0.1, $CH_2Cl_2$). 98% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 19.8 min for minor isomer, $t_R$ = 20.5 min for major isomer).



| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 19.834 | MM m | 19.126 | 19.837 | 0.34 | 15.67 | 0.77 | 1.23 |
| 20.473 | MM m | 19.837 | 22.301 | 0.63 | 1261.91 | 29.54 | 98.77 |

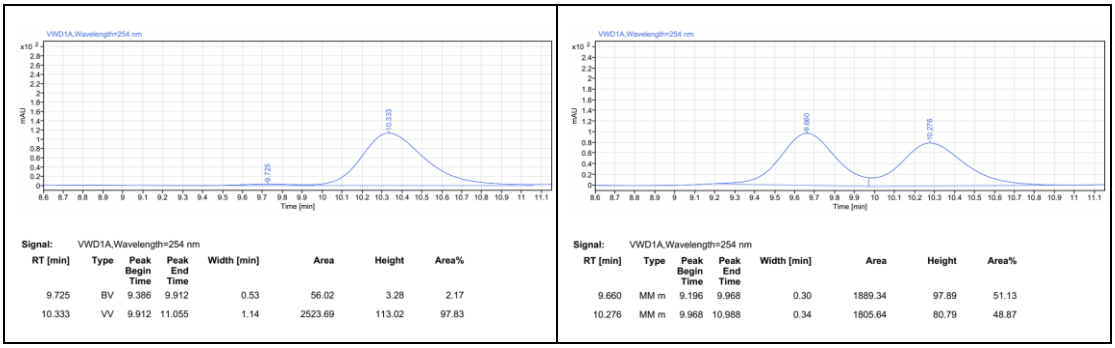
| Signal: VWD1A,Wavelength=254 nm | | | | | | | |
|---|---|---|---|---|---|---|---|
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
| 19.243 | BM m | 18.229 | 19.721 | 0.55 | 864.34 | 24.01 | 49.25 |
| 20.134 | MM m | 19.721 | 21.832 | 0.61 | 890.64 | 21.56 | 50.75 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(7-bromo-2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ka)**



**4ka**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 42.4 mg, 75% yield. **MP**: 110-111 ℃. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.6 Hz, 1H), 7.93 (d, *J* = 1.9 Hz, 1H), 7.86 (d, *J* = 1.1 Hz, 1H), 7.60 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.36-7.24 (m, 5H), 4.48 (dd, *J* = 8.7, 1.1 Hz, 1H), 4.27 (d, *J* = 8.8 Hz, 1H), 3.82 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.88 (d, *J* = 13.9 Hz, 1H), 1.34 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.0, 170.6, 168.8, 161.7, 159.6, 158.0, 147.2, 135.5, 131.3, 131.1, 130.5, 130.3, 128.7, 128.5, 127.5, 118.8, 87.5, 58.0, 53.1, 49.3, 42.1, 39.3, 29.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}BrN_4O_5$ 565.1081; Found 565.1082. **Optical Rotation**: $[\alpha]^{20}_D$ = +64.2 (c = 0.15, $CH_2Cl_2$). 96% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 9.7 min for minor isomer, $t_R$ = 10.3 min for major isomer).



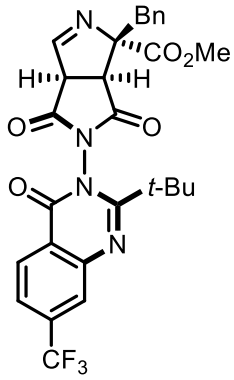

Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.725 | BV | 9.386 | 9.912 | 0.53 | 56.02 | 3.28 | 2.17 |
| 10.333 | VV | 9.912 | 11.055 | 1.14 | 2523.69 | 113.02 | 97.83 |

Signal: VWD1A,Wavelength=254 nm

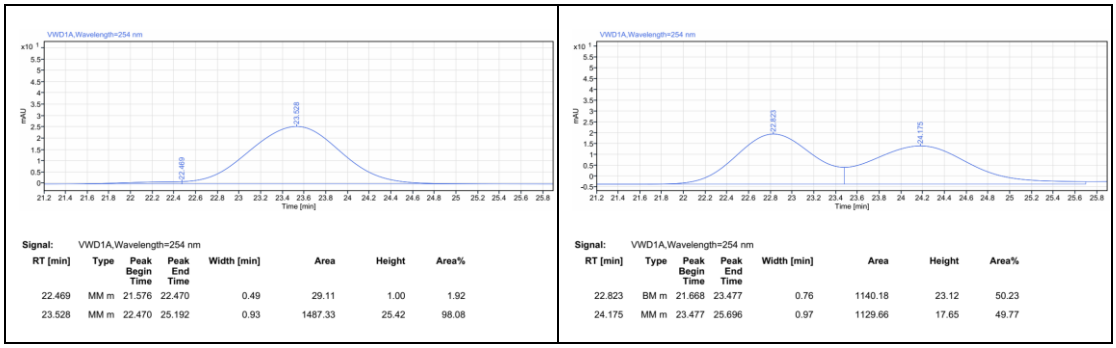
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.660 | MM m | 9.196 | 9.968 | 0.30 | 1889.34 | 97.89 | 51.13 |
| 10.276 | MM m | 9.968 | 10.988 | 0.34 | 1805.64 | 80.79 | 48.87 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-4-oxo-7-(trifluoromethyl)quinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4la)**

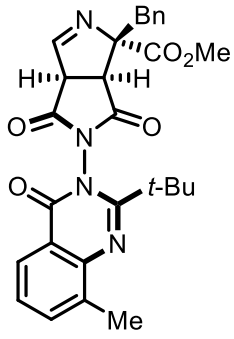



**4la**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 33.3 mg, 60% yield. **MP**: 134-136 ℃. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.31-8.27 (m, 1H), 8.05-8.01 (m, 1H), 7.87 (d, *J* = 1.1 Hz, 1H), 7.70 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.37-7.25 (m, 5H), 4.50 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.29 (d, *J* = 8.8 Hz, 1H), 3.83 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.89 (d, *J* = 13.9 Hz, 1H), 1.37 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.9, 170.5, 168.7, 161.9, 159.6, 157.8, 146.4, 137.1 (d, *J* = 33.1 Hz), 135.4, 130.3, 128.51, 128.49, 127.5, 126.1 (d, *J* = 4.2 Hz), 123.7 (d, *J* = 3.5 Hz), 123.3 (d, *J* = 273.2 Hz), 122.4, 87.6, 58.0, 53.1, 49.3, 42.1, 39.3, 29.3; **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -63.2; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{26}F_3N_4O_5$ 555.1850; Found 555.1856. **Optical Rotation**: $[\alpha]^{20}_D$ = +164.7 (c = 0.05, $CH_2Cl_2$). 96% ee (HPLC condition: Chiralpak IB N-5 column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 22.5 min for minor isomer, $t_R$ = 23.5 min for major isomer).

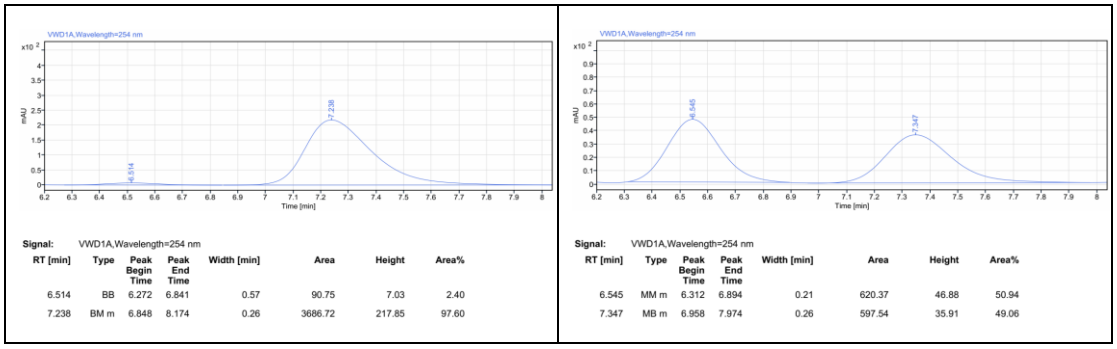



**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-8-methyl-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ma)**




**4ma**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 30.9 mg, 62% yield. **MP**: 104-106 °C. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.03-7.99 (m, 1H), 7.88 (d, *J* = 1.1 Hz, 1H), 7.67-7.63 (m, 1H), 7.40-7.24 (m, 6H), 4.49 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.27 (d, *J* = 8.8 Hz, 1H), 3.84 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.89 (d, *J* = 13.9 Hz, 1H), 2.62 (s, 3H), 1.37 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.0, 170.8, 169.0, 159.8, 158.8, 158.7, 144.7, 137.3, 136.2, 135.6, 130.4, 128.5, 127.5, 127.3, 125.0, 120.0, 87.5, 58.1, 53.1, 49.3, 42.1, 39.4, 29.4, 17.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_5$ 501.2132; Found 501.2140. **Optical Rotation**: $[\alpha]^{20}_D$ = +91.4 (c = 0.1, $CH_2Cl_2$). 95% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 6.5 min for minor isomer, $t_R$ = 7.2 min for major isomer).



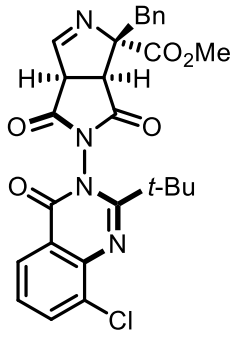

Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 6.514 | BB | 6.272 | 6.841 | 0.57 | 90.75 | 7.03 | 2.40 |
| 7.238 | BM m | 6.848 | 8.174 | 0.26 | 3686.72 | 217.85 | 97.60 |

Signal: VWD1A,Wavelength=254 nm

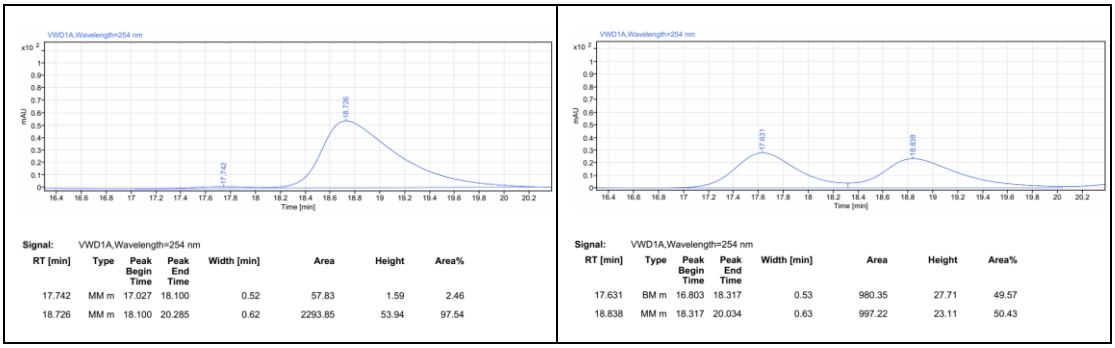
| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 6.545 | MM m | 6.312 | 6.894 | 0.21 | 620.37 | 46.88 | 50.94 |
| 7.347 | MB m | 6.958 | 7.974 | 0.26 | 597.54 | 35.91 | 49.06 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-8-chloro-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4na)**




**4na**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 30.3 mg, 58% yield. **MP**: 204-206 °C. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.08 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.90-7.86 (m, 2H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.37-7.24 (m, 5H), 4.49 (dd, *J* = 8.7, 1.1 Hz, 1H), 4.28 (d, *J* = 8.8 Hz, 1H), 3.83 (d, *J* = 13.9 Hz, 1H), 3.57 (s, 3H), 2.89 (d, *J* = 13.9 Hz, 1H), 1.39 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.0, 170.5, 168.7, 161.0, 159.6, 158.0, 142.9, 135.9, 135.5, 133.4, 130.3, 128.5, 127.8, 127.5, 126.1, 121.6, 87.5, 58.0, 53.1, 49.3, 42.1, 39.8, 29.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}ClN_4O_5$ 521.1586; Found 521.1586. **Optical Rotation**: $[\alpha]^{20}_D$ = +128.2 (c = 0.1, $CH_2Cl_2$). 95% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 17.7 min for minor isomer, $t_R$ = 18.7 min for major isomer).



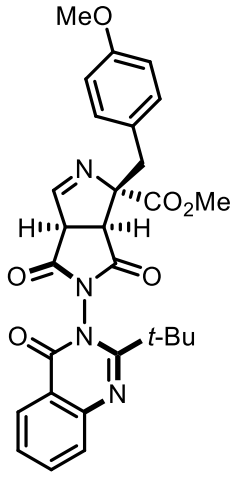

Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 17.742 | MM m | 17.027 | 18.100 | 0.52 | 57.83 | 1.59 | 2.46 |
| 18.726 | MM m | 18.100 | 20.285 | 0.62 | 2293.85 | 53.94 | 97.54 |

Signal: VWD1A,Wavelength=254 nm

| RT [min] | Type | Peak Begin Time | Peak End Time | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 17.631 | BM m | 16.803 | 18.317 | 0.53 | 980.35 | 27.71 | 49.57 |
| 18.838 | MM m | 18.317 | 20.034 | 0.63 | 997.22 | 23.11 | 50.43 |

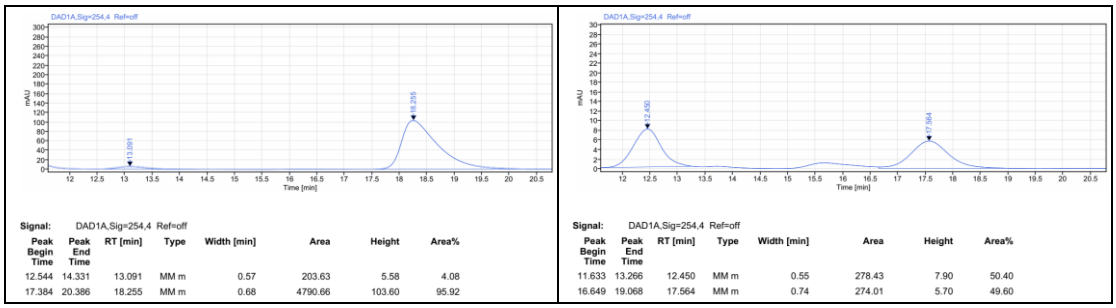
**Methyl (*S*a,1*S*,3a*R*,6a*S*)-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1-(4-methoxybenzyl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ab)**




**4ab**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 33.5 mg, 65% yield. **MP**: 193-195 °C. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.18-8.15 (m, 1H), 7.86 (d, *J* = 1.1 Hz, 1H), 7.83-7.78 (m, 1H), 7.74-7.71 (m, 1H), 7.52-7.47 (m, 1H), 7.29-7.25 (m, 2H), 6.87-6.83 (m, 2H), 4.48 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.25 (d, *J* = 8.8 Hz, 1H), 3.79 (s, 3H), 3.78 (d, *J* = 14.0 Hz, 1H), 3.59 (s, 3H), 2.83 (d, *J* = 14.0 Hz, 1H), 1.36 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.1, 170.8, 169.0, 160.1, 159.6, 158.9, 158.5, 146.4, 135.6, 131.4, 128.5, 127.6, 127.5, 127.3, 120.0, 113.8, 87.7, 58.1, 55.3, 53.1, 49.2, 41.3, 39.1, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_6$ 517.2082; Found 517.2084. **Optical Rotation**: $[\alpha]^{20}_D$ = +94.4 (c = 0.17, $CH_2Cl_2$). 92% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength =

254 nm, $t_R$ = 13.1 min for minor isomer, $t_R$ = 18.3 min for major isomer).



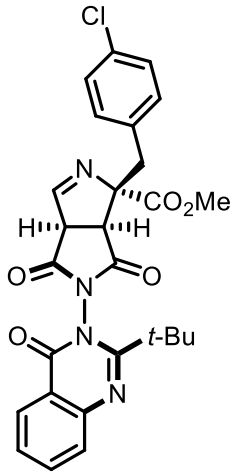

Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 12.544 | 14.331 | 13.091 | MM m | 0.57 | 203.63 | 5.58 | 4.08 |
| 17.384 | 20.386 | 18.255 | MM m | 0.68 | 4790.66 | 103.60 | 95.92 |

Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 11.633 | 13.266 | 12.450 | MM m | 0.55 | 278.43 | 7.90 | 50.40 |
| 16.649 | 19.068 | 17.564 | MM m | 0.74 | 274.01 | 5.70 | 49.60 |

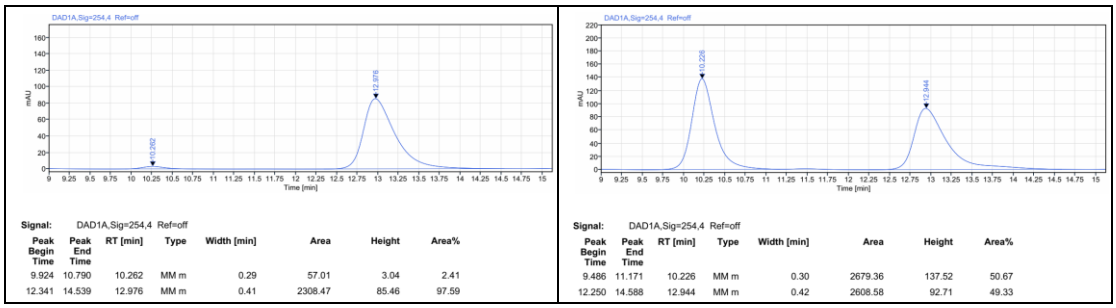
**Methyl (*S*a,1*S*,3a*R*,6a*S*)-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1-(4-chlorobenzyl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ac)**




**4ac**

>20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 38.5 mg, 74% yield. **MP**: 187-189 °C. **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.18-8.14 (m, 1H), 7.88 (d, *J* = 1.0 Hz, 1H), 7.83-7.78 (m, 1H), 7.75-7.71 (m, 1H), 7.52-7.47 (m, 1H), 7.32-7.27 (m, 4H), 4.50 (dd, *J* = 8.8, 1.0 Hz, 1H), 4.24 (d, *J* = 8.8 Hz, 1H), 3.81 (d, *J* = 14.1 Hz, 1H), 3.59 (s, 3H), 2.84 (d, *J* = 14.0 Hz, 1H), 1.35 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 170.73, 170.68, 168.8, 160.1, 160.0, 158.5, 146.4, 135.6, 134.0, 133.4, 131.8, 128.6, 128.5, 127.7, 127.3, 119.9, 87.1, 58.0, 53.2, 49.2, 41.2, 39.1, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}ClN_4O_5$ 521.1586; Found 521.1588. **Optical Rotation**: $[\alpha]^{20}_D$ = +112.4 (c = 0.1, $CH_2Cl_2$). 95% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.3 min for minor isomer, $t_R$

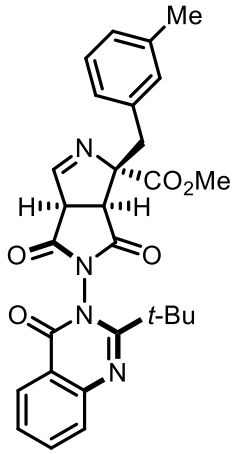
= 13.0 min for major isomer).



| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.924 | 10.790 | 10.262 | MM m | 0.29 | 57.01 | 3.04 | 2.41 |
| 12.341 | 14.539 | 12.976 | MM m | 0.41 | 2308.47 | 85.46 | 97.59 |

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.486 | 11.171 | 10.226 | MM m | 0.30 | 2679.36 | 137.52 | 50.67 |
| 12.250 | 14.588 | 12.944 | MM m | 0.42 | 2608.58 | 92.71 | 49.33 |

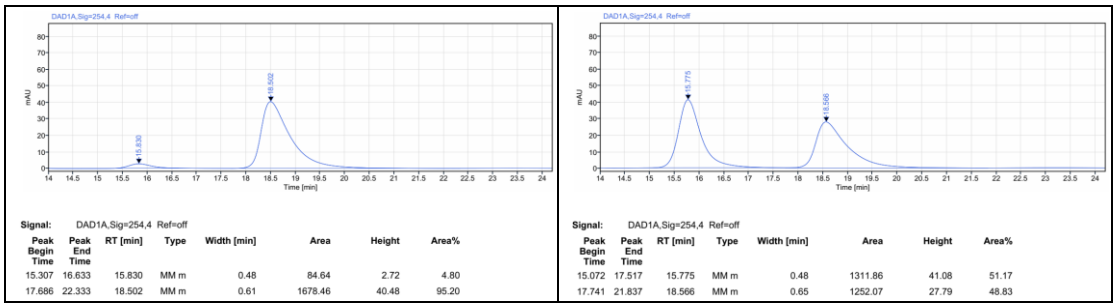
**Methyl (*S*a,1*S*,3a*R*,6a*S*)-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1-(3-methylbenzyl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ad)**




**4ad**

>20:1 dr (determined by crude $^{1}$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 27.0 mg, 54% yield. **MP**: 212-214 ℃. **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 8.17 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.87 (d, *J* = 1.1 Hz, 1H), 7.83-7.78 (m, 1H), 7.73 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.52-7.47 (m, 1H), 7.23-7.18 (m, 1H), 7.16-7.06 (m, 3H), 4.49 (dd, *J* = 8.8, 1.1 Hz, 1H), 4.27 (d, *J* = 8.8 Hz, 1H), 3.80 (d, *J* = 13.9 Hz, 1H), 3.59 (s, 3H), 2.84 (d, *J* = 13.9 Hz, 1H), 2.34 (s, 3H), 1.36 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.1, 170.8, 169.0, 160.1, 159.6, 158.5, 146.4, 138.0, 135.6, 135.4, 131.1, 128.5, 128.3, 128.2, 127.6, 127.3, 120.0, 87.5, 58.0, 53.0, 49.3, 42.1, 39.1, 29.4, 21.6; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_5$ 501.2132; Found 501.2133. **Optical Rotation**: $[\alpha]^{20}_D$ = +136.0 (c = 0.09, $CH_2Cl_2$). 90% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1

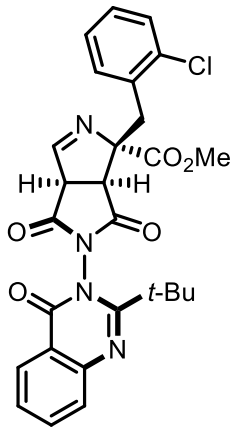
mL/min, wavelength = 254 nm, $t_R$ = 15.8 min for minor isomer, $t_R$ = 18.5 min for major isomer).



| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 15.307 | 16.633 | 15.830 | MM m | 0.48 | 84.64 | 2.72 | 4.80 |
| 17.686 | 22.333 | 18.502 | MM m | 0.61 | 1678.46 | 40.48 | 95.20 |

| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 15.072 | 17.517 | 15.775 | MM m | 0.48 | 1311.86 | 41.08 | 51.17 |
| 17.741 | 21.837 | 18.566 | MM m | 0.65 | 1252.07 | 27.79 | 48.83 |

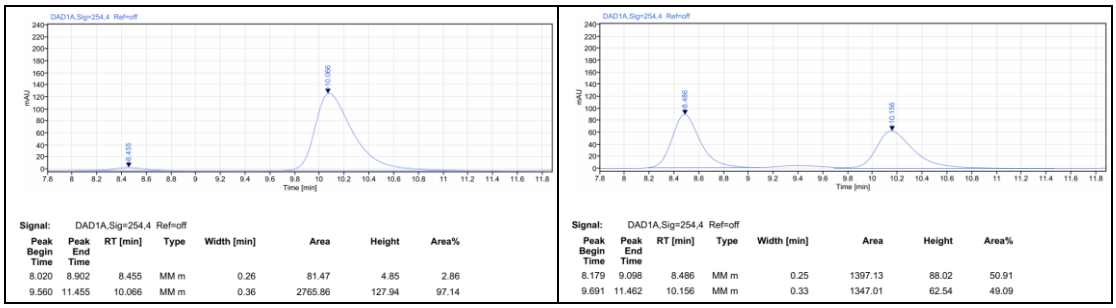
**Methyl (*S*a,1*S*,3a*R*,6a*S*)-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1-(2-chlorobenzyl)-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4ae)**



**4ae**

>20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 26.6 mg, 51% yield. **MP**: 208-209 °C. **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.16 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.84 (d, *J* = 1.1 Hz, 1H), 7.83-7.78 (m, 1H), 7.73 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.52-7.46 (m, 1H), 7.42-7.36 (m, 2H), 7.25-7.18 (m, 2H), 4.52 (dd, *J* = 8.9, 1.1 Hz, 1H), 4.38 (d, *J* = 9.0 Hz, 1H), 3.95 (d, *J* = 14.5 Hz, 1H), 3.67 (s, 3H), 3.21 (d, *J* = 14.5 Hz, 1H), 1.38 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.1, 170.8, 169.0, 160.2, 159.7, 158.5, 146.4, 135.6, 135.3, 133.8, 131.3, 130.0, 128.8, 128.5, 127.6, 127.3, 126.8, 120.0, 87.4, 58.2, 53.4, 49.4, 39.1, 38.7, 29.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}ClN_4O_5$ 521.1586; Found 521.1597. **Optical Rotation**: $[\alpha]^{20}_D$ = +77.5 (c = 0.13, $CH_2Cl_2$). 94% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min,

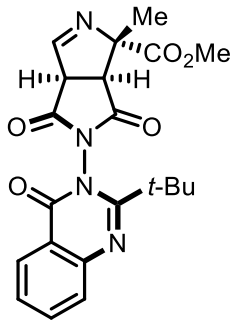
wavelength = 254 nm, $t_R$ = 8.5 min for minor isomer, $t_R$ = 10.1 min for major isomer).



| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.020 | 8.902 | 8.455 | MM m | 0.26 | 81.47 | 4.85 | 2.86 |
| 9.560 | 11.455 | 10.066 | MM m | 0.36 | 2765.86 | 127.94 | 97.14 |

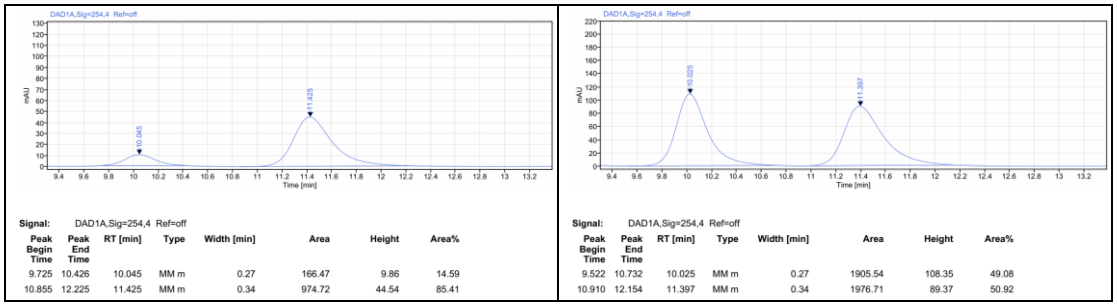
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.179 | 9.098 | 8.486 | MM m | 0.25 | 1397.13 | 88.02 | 50.91 |
| 9.691 | 11.462 | 10.156 | MM m | 0.33 | 1347.01 | 62.54 | 49.09 |

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-1-methyl-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4af)**



**4af**

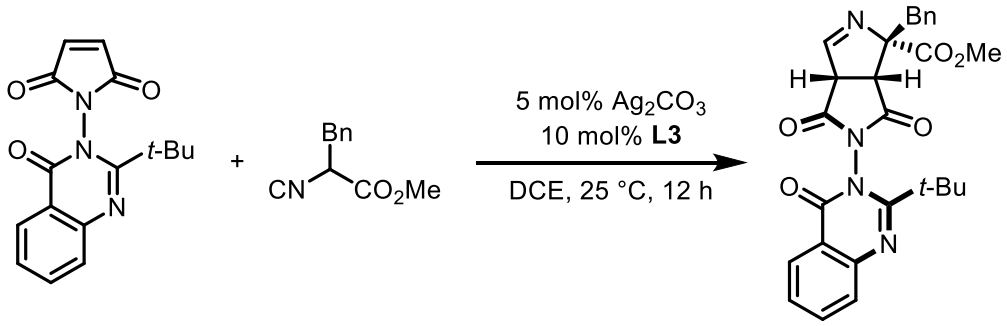
>20:1 dr (determined by crude $^1$H NMR). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1). White solid, 20.9 mg, 51% yield. **MP**: 108-109 °C. **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.15 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.82-7.76 (m, 1H), 7.73 (d, *J* = 1.2 Hz, 1H), 7.71 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.51-7.45 (m, 1H), 4.59 (dd, *J* = 8.9, 1.1 Hz, 1H), 4.25 (d, *J* = 9.0 Hz, 1H), 3.82 (s, 3H), 1.82 (s, 3H), 1.31 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.5, 171.1, 169.3, 160.2, 160.0, 158.5, 146.4, 135.6, 128.5, 127.6, 127.3, 120.0, 83.8, 59.4, 53.7, 48.3, 39.0, 29.3, 21.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{23}N_4O_5$ 411.1663; Found 411.1658. **Optical Rotation**: $[\alpha]^{20}_D$ = +206.1 (c = 0.05, $CH_2Cl_2$). 71% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 10.0 min for minor isomer, $t_R$ = 11.4 min for major isomer).



| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 9.725 | 10.426 | 10.045 | MM m | 0.27 | 166.47 | 9.86 | 14.59 |
| 10.855 | 12.225 | 11.425 | MM m | 0.34 | 974.72 | 44.54 | 85.41 |

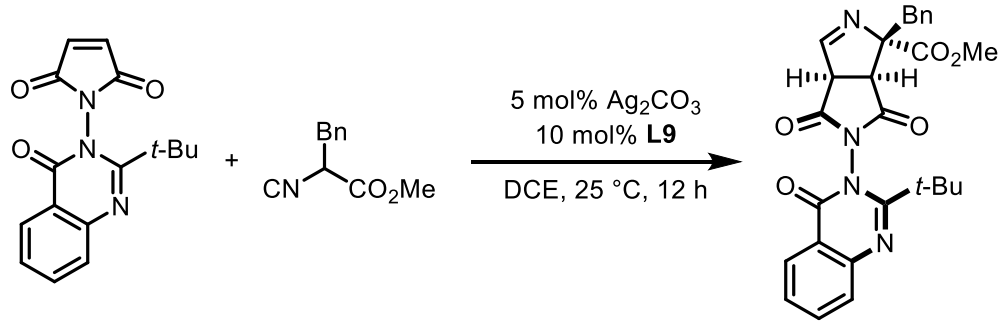
| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 9.522 | 10.732 | 10.025 | MM m | 0.27 | 1905.54 | 108.35 | 49.08 |
| 10.910 | 12.154 | 11.397 | MM m | 0.34 | 1976.71 | 89.37 | 50.92 |

## 8. Gram-scale synthesis and follow-up transformations




**1a**: 1.0 g **2a** (1.0 equiv) **3aa**: dr >20:1
1.51 g, 92%, 98% ee

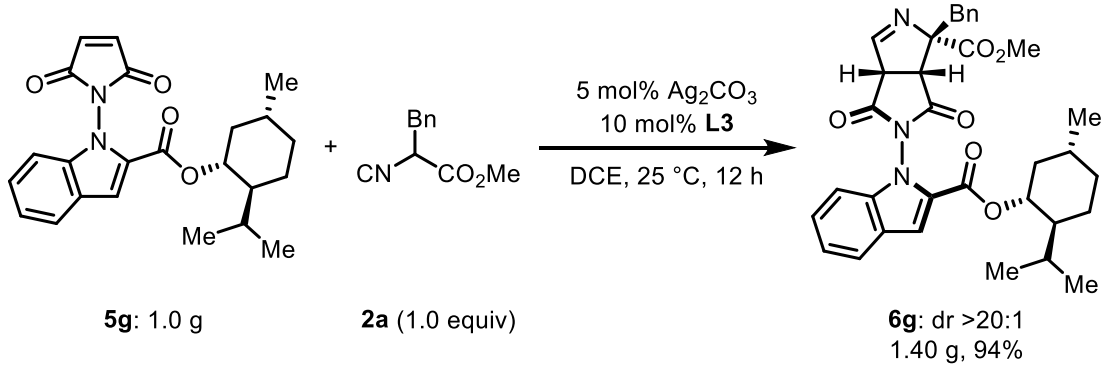
To a 100 mL round-bottom flask charged with **L3** (238.7 mg, 0.34 mmol) and $Ag_2CO_3$ (46.3 mg, 0.17 mmol) was added anhydrous DCE (33.6 mL). The mixture was stirred for 10 min, then **1a** (1.0 g, 3.36 mmol) and **2a** (636.4 mg, 3.36 mmol) were added successively in one portion. The reaction mixture was stirred at 25 ℃ for 12 h, then concentrated and purified by flash column chromatography (PE/EtOAc 2:1) to afford the product **3aa**.




**1a**: 1.0 g **2a** (1.0 equiv) **4aa**: dr >20:1
1.16 g, 71%, 94% ee

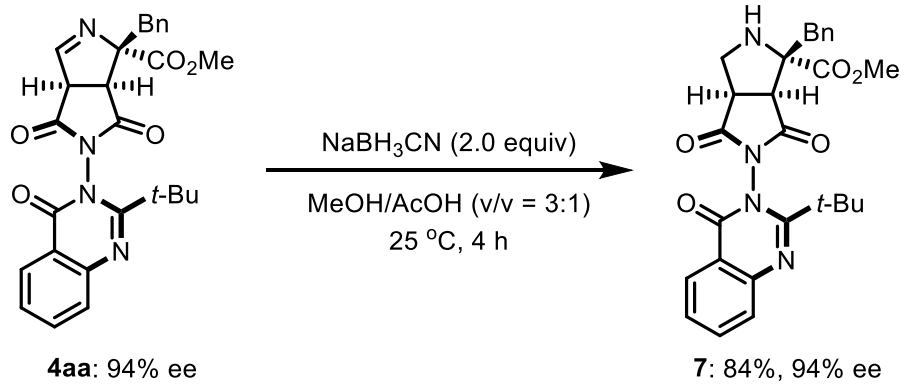
To a 100 mL round-bottom flask charged with **L9** (265.3 mg, 0.34 mmol) and $Ag_2CO_3$ (46.2 mg, 0.17 mmol) was added anhydrous DCE (33.6 mL). The mixture was stirred

for 10 min, then **1a** (1.0 g, 3.36 mmol) and **2a** (636.6 mg, 3.36 mmol) were added successively in one portion. The reaction mixture was stirred at 25 ℃ for 12 h, then concentrated and purified by flash column chromatography (PE/EtOAc 2:1) to afford the product **4aa**.




**5g**: 1.0 g　　**2a** (1.0 equiv)　　**6g**: dr >20:1
1.40 g, 94%

To a 100 mL round-bottom flask charged with **L3** (180.2 mg, 0.254 mmol) and $Ag_2CO_3$ (35.0 mg, 0.127 mmol) was added anhydrous DCE (25.4 mL). The mixture was stirred for 10 min, then **5g** (1.0 g, 2.54 mmol) and **2a** (480.6 mg, 2.54 mmol) were added successively in one portion. The reaction mixture was stirred at 25 ℃ for 12 h, then concentrated and purified by flash column chromatography (PE/EtOAc 2:1) to afford the product **6g**.

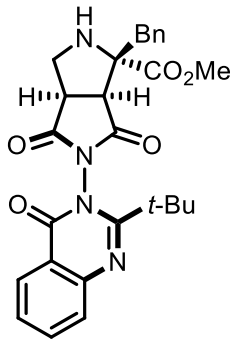



**4aa**: 94% ee　　**7**: 84%, 94% ee

To a 10 mL vial charged with **4aa** (48.6 mg, 0.10 mmol) was added MeOH/AcOH (v/v = 3:1, 2.0 mL). Then $NaBH_3CN$ (12.8 mg, 0.20 mmol) was added in one portion and the reaction mixture was stirred at 25 ℃ for 4 h. After that the reaction mixture was quenched with 10% $NaHCO_3$ solution. The organic phase was extracted with EtOAc and washed repeatedly with brine, and then dried over $Na_2SO_4$. The solvent was

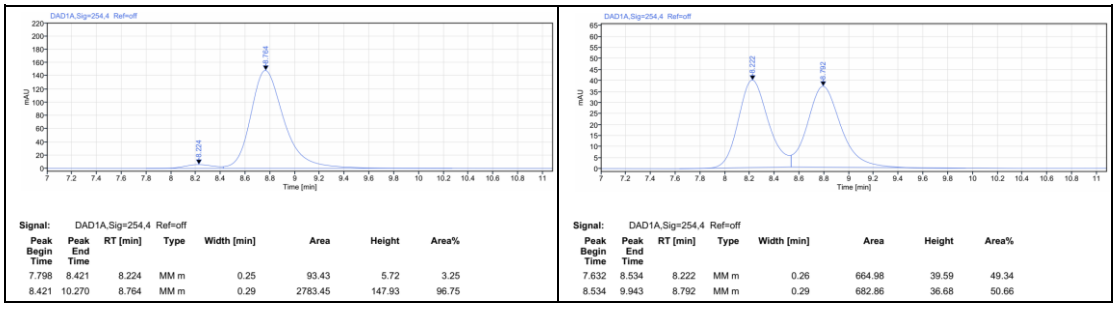
removed under reduced pressure and the residue was purified by flash column chromatography (PE/EtOAc 3:1) to afford the product **7**.

**Methyl (*S*a,1*S*,3a*R*,6a*S*)-1-benzyl-5-(2-(tert-butyl)-4-oxoquinazolin-3(4*H*)-yl)-4,6-dioxooctahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (7)**



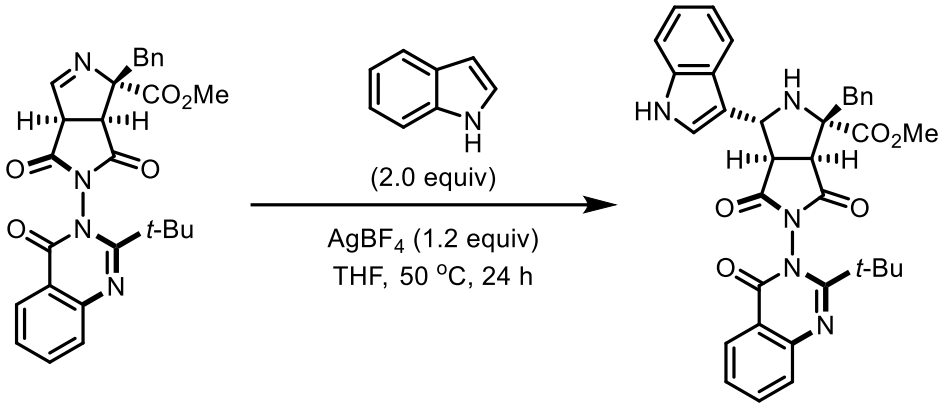
**7**

White solid, 41.0 mg, 84% yield. **MP**: 192-194 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.20-8.16 (m, 1H), 7.82-7.76 (m, 1H), 7.75-7.71 (m, 1H), 7.50-7.45 (m, 1H), 7.32-7.24 (m, 3H), 7.16-7.11 (m, 2H), 4.05 (d, *J* = 8.5 Hz, 1H), 3.65 (s, 3H), 3.57-3.44 (m, 3H), 3.20 (dd, *J* = 10.3, 8.8 Hz, 1H), 2.98 (d, *J* = 13.5 Hz, 1H), 1.50 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 175.8, 173.2, 172.8, 160.9, 158.5, 146.5, 135.9, 135.4, 129.5, 128.7, 128.4, 127.5, 127.4, 127.3, 120.2, 73.7, 52.7, 49.5, 47.8, 43.8, 41.5, 39.1, 29.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{29}N_4O_5$ 489.2132; Found 489.2136. **Optical Rotation**: $[\alpha]^{20}_D$ = -31.4 (c = 0.1, $CH_2Cl_2$). 94% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 8.2 min for minor isomer, $t_R$ = 8.8 min for major isomer).



| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 7.798 | 8.421 | 8.224 | MM m | 0.25 | 93.43 | 5.72 | 3.25 |
| 8.421 | 10.270 | 8.764 | MM m | 0.29 | 2783.45 | 147.93 | 96.75 |

| Signal: DAD1A,Sig=254,4 Ref=off | | | | | | | |
|---|---|---|---|---|---|---|---|
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
| 7.632 | 8.534 | 8.222 | MM m | 0.26 | 664.98 | 39.59 | 49.34 |
| 8.534 | 9.943 | 8.792 | MM m | 0.29 | 682.86 | 36.68 | 50.66 |

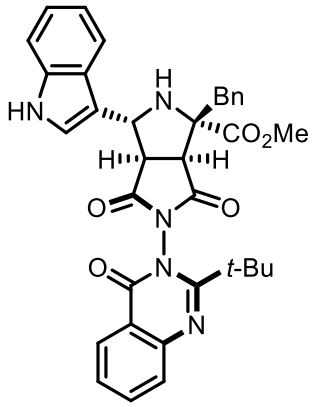



**4aa**: 94% ee

**8**: dr >20:1, 98%, 94% ee

To a mixture of **4aa** (48.6 mg, 0.10 mmol) and $AgBF_4$ (24.0 mg, 0.12 mmol) in anhydrous THF (0.5 mL) was added a solution of indole (23.4 mg, 0.20 mmol) in anhydrous THF (0.5 mL). The reaction mixture was stirred at 50 ℃ for 24 h, then filtered through a plug of Celite with the aid of $CH_2Cl_2$, and washed with saturated aqueous $NH_4Cl$ solution. The organic layer was dried over anhydrous $Na_2SO_4$, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography (PE/EtOAc 1:1) to afford the product **8**.

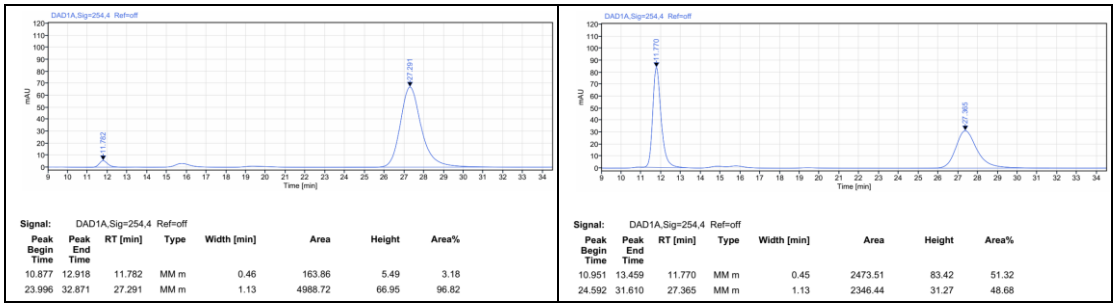
**Methyl (*S*a,1*S*,3*R*,3a*R*,6a*S*)-1-benzyl-5-(2-(*tert*-butyl)-4-oxoquinazolin-3(4*H*)-yl)-3-(1*H*-indol-3-yl)-4,6-dioxooctahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (8)**




**8**

>20:1 dr (determined by crude $^1$H NMR). Pale brown solid, 59.2 mg, 98% yield. **MP**: 140-142 ℃; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 2.7 Hz, 1H), 8.26 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.88-7.83 (m, 1H), 7.80 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.56-7.51 (m, 1H), 7.37-7.33 (m, 1H), 7.29 (s, 1H), 7.28-7.21 (m, 5H), 7.20-7.14 (m, 1H), 6.89 (d, *J* = 2.5 Hz, 1H), 5.26-5.22 (m, 1H), 4.54 (d, *J* = 9.0 Hz, 1H), 3.98 (dd, *J*

= 9.0, 2.9 Hz, 1H), 3.51 (d, *J* = 13.6 Hz, 1H), 3.04 (d, *J* = 13.6 Hz, 1H), 2.82 (s, 3H), 1.61 (s, 9H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 175.1, 173.6, 173.5, 160.8, 158.8, 146.5, 136.7, 135.8, 135.5, 129.9, 128.43, 128.35, 127.4, 127.3, 127.2, 126.1, 122.9, 121.7, 120.2, 120.1, 118.6, 115.7, 111.6, 72.5, 56.6, 51.5, 50.3, 49.5, 42.0, 39.2, 29.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{35}H_{34}N_5O_5$ 604.2554; Found 604.2559. **Optical Rotation**: $[\alpha]^{20}_D$ = -52.1 (c = 0.1, $CH_2Cl_2$). 94% ee (HPLC condition: Chiralpak IA column, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 11.8 min for minor isomer, $t_R$ = 27.3 min for major isomer).



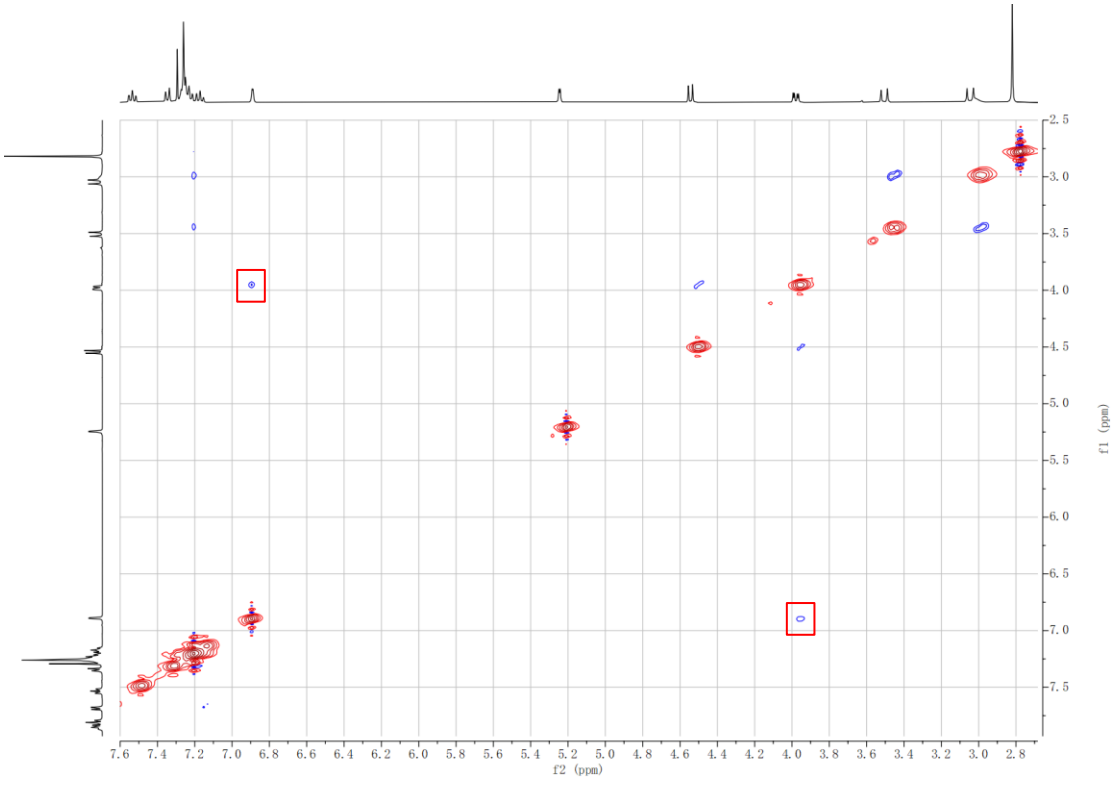
Signal: DAD1A,Sig=254,4 Ref=off

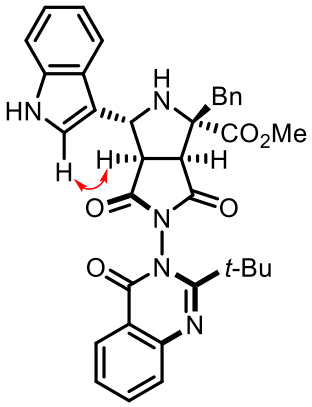
| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 10.877 | 12.918 | 11.782 | MM m | 0.46 | 163.86 | 5.49 | 3.18 |
| 23.996 | 32.871 | 27.291 | MM m | 1.13 | 4988.72 | 66.95 | 96.82 |

Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 10.951 | 13.459 | 11.770 | MM m | 0.45 | 2473.51 | 83.42 | 51.32 |
| 24.592 | 31.610 | 27.365 | MM m | 1.13 | 2346.44 | 31.27 | 48.68 |

The absolute configuration of the newly generated stereogenic center in **8** was determined by NOE analysis (Figure S1).






**8**

Figure S1. NOESY spectra of **8**

## 9. Crystal structure data of 1a, 3pa, 6a, and 7

The structure of **1a** was unambiguously determined by X-ray crystallographic analysis of a single crystal of **1a** (Figure S2). The crystal was prepared from the solution of **1a** in hexane/EtOAc/$CH_2Cl_2$ 5:1:1 at ambient temperature.

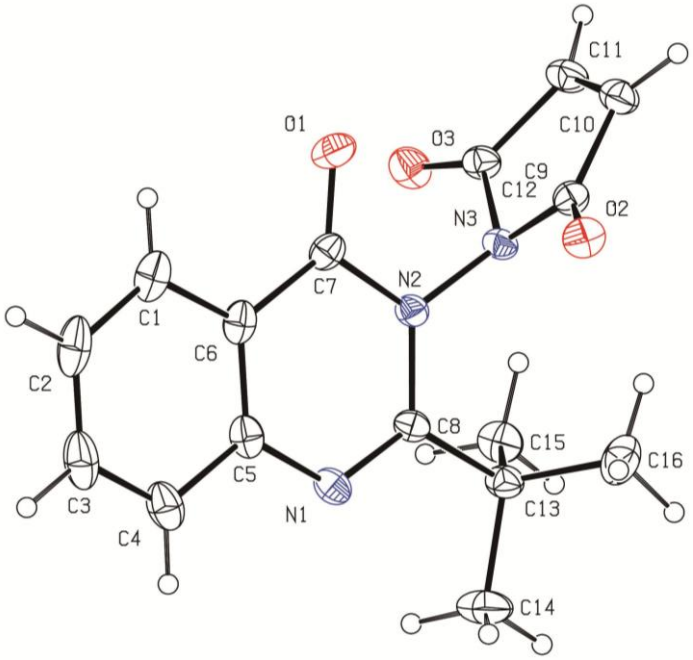



Figure S2. X-ray structure of **1a** (ellipsoid contour at 30% probability)

Table S1. Crystal data and structure refinement for 221108_WT_S1

| | |
|---|---|
| Identification code | 221108_WT_S1 |
| Empirical formula | $C_{16}H_{15}N_3O_3$ |
| Formula weight | 297.31 |

| | |
|---|---|
| Temperature/K | 170.0 |
| Crystal system | monoclinic |
| Space group | $P2_1/c$ |
| a/Å | 15.2814(6) |
| b/Å | 9.8263(5) |
| c/Å | 9.7772(4) |
| α/° | 90 |
| β/° | 93.082(2) |
| γ/° | 90 |
| Volume/$Å^3$ | 1466.02(11) |
| Z | 4 |
| $\rho_{calc}g/cm^3$ | 1.347 |
| $\mu/mm^{-1}$ | 0.095 |
| F(000) | 624.0 |
| Crystal size/$mm^3$ | 0.48 × 0.23 × 0.15 |
| Radiation | MoKα (λ = 0.71073) |
| 2θ range for data collection/° | 4.93 to 54.218 |
| Index ranges | $-19 \leq h \leq 18$, $-12 \leq k \leq 11$, $-12 \leq l \leq 12$ |
| Reflections collected | 16830 |
| Independent reflections | 3239 [$R_{int} = 0.0389$, $R_{sigma} = 0.0274$] |
| Data/restraints/parameters | 3239/1/202 |
| Goodness-of-fit on $F^2$ | 1.040 |
| Final R indexes [I>=2σ (I)] | $R_1 = 0.0397$, $wR_2 = 0.0933$ |
| Final R indexes [all data] | $R_1 = 0.0560$, $wR_2 = 0.1050$ |
| Largest diff. peak/hole / e $Å^{-3}$ | 0.17/-0.19 |

The relative and absolute configurations of **3pa** (*S*a,1*S*,3a*S*,6a*R*) were assigned by X-ray crystallographic analysis of a single crystal of **3pa** (Figure S3). The crystal was prepared from the solution of **3pa** in $CH_2Cl_2$ at ambient temperature.

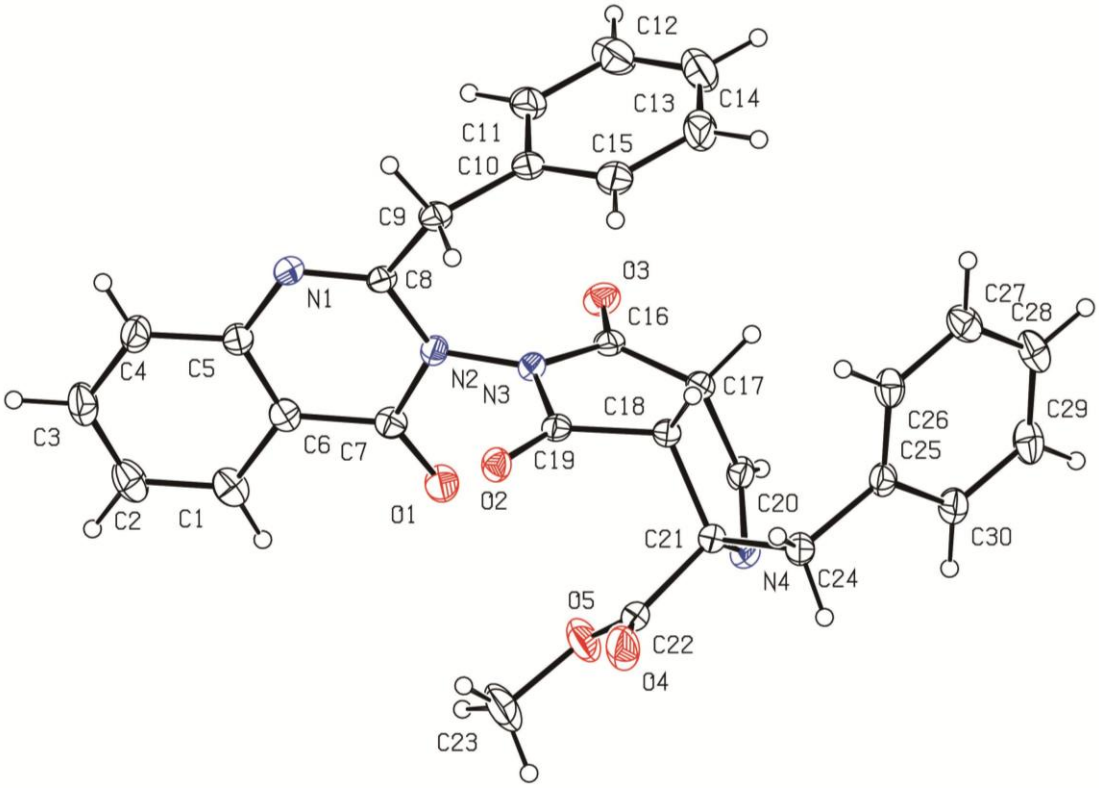



Figure S3. X-ray structure of **3pa** (ellipsoid contour at 30% probability)

Table S2. Crystal data and structure refinement for cu_221109_WT_FP_Bn_0m

| | |
|---|---|
| Identification code | cu_221109_WT_FP_Bn_0m |
| Empirical formula | $C_{30}H_{24}N_4O_5$ |
| Formula weight | 520.53 |
| Temperature/K | 170.00 |
| Crystal system | triclinic |
| Space group | P1 |
| a/Å | 7.6482(5) |
| b/Å | 9.5877(7) |
| c/Å | 10.0552(7) |
| α/° | 115.079(2) |
| β/° | 99.469(2) |
| γ/° | 97.668(2) |
| Volume/Å$^3$ | 641.46(8) |
| Z | 1 |
| $\rho_{calc}$g/cm$^3$ | 1.347 |

| | |
|---|---|
| $\mu/mm^{-1}$ | 0.768 |
| F(000) | 272.0 |
| Crystal size/$mm^3$ | 0.48 × 0.29 × 0.19 |
| Radiation | CuKα (λ = 1.54178) |
| 2θ range for data collection/° | 10.46 to 136.782 |
| Index ranges | $-9 \leq h \leq 9$, $-11 \leq k \leq 11$, $-12 \leq l \leq 12$ |
| Reflections collected | 21343 |
| Independent reflections | 4563 [$R_{int}$ = 0.0470, $R_{sigma}$ = 0.0393] |
| Data/restraints/parameters | 4563/3/353 |
| Goodness-of-fit on $F^2$ | 1.070 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0318, $wR_2$ = 0.0780 |
| Final R indexes [all data] | $R_1$ = 0.0320, $wR_2$ = 0.0782 |
| Largest diff. peak/hole / e $Å^{-3}$ | 0.15/-0.21 |
| Flack parameter | 0.08(6) |

The relative and absolute configurations of **6a** (*S*a,3a*R*,4*S*,6a*S*) were assigned by X-ray crystallographic analysis of a single crystal of **6a** (Figure S4). The crystal was prepared from the solution of **6a** in hexane/EtOAc 3:1 at ambient temperature.

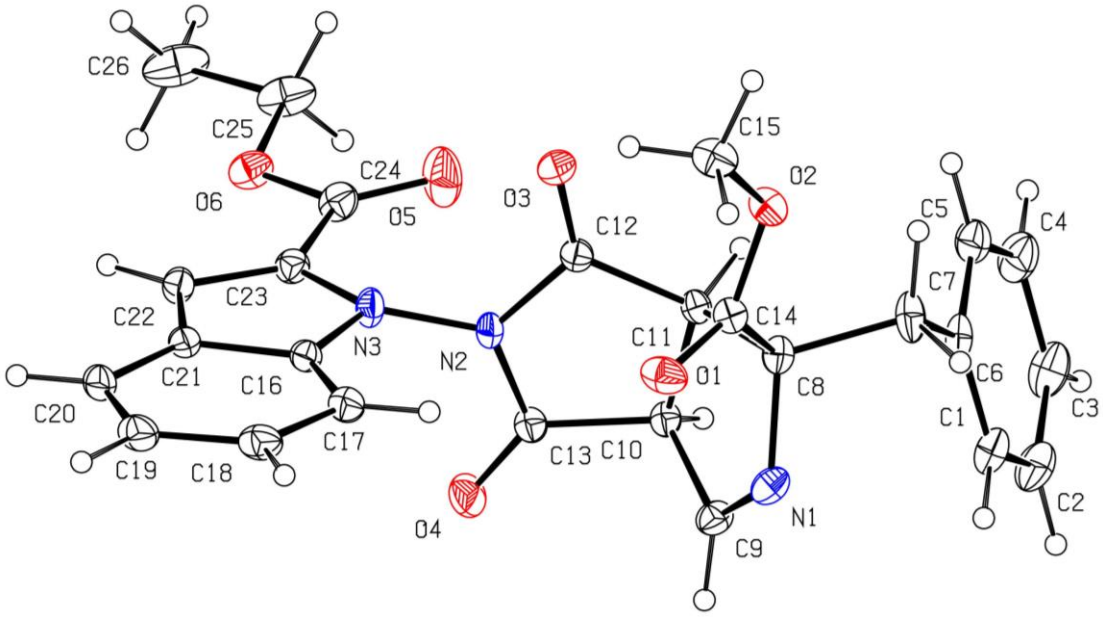



Figure S4. X-ray structure of **6a** (ellipsoid contour at 30% probability)

Table S3. Crystal data and structure refinement for 230301_WF_FP_Ind_0m

| | |
|---|---|
| Identification code | 230301_WF_FP_Ind_0m |
| Empirical formula | $C_{26}H_{23}N_3O_6$ |
| Formula weight | 473.47 |
| Temperature/K | 170.0 |
| Crystal system | monoclinic |
| Space group | $P2_1$ |
| a/Å | 11.7753(6) |
| b/Å | 7.5349(4) |
| c/Å | 13.0392(7) |
| α/° | 90 |
| β/° | 95.653(2) |
| γ/° | 90 |
| Volume/Å$^3$ | 1151.29(10) |
| Z | 2 |
| $\rho_{calc}$g/cm$^3$ | 1.366 |
| μ/mm$^{-1}$ | 0.519 |
| F(000) | 496.0 |
| Crystal size/mm$^3$ | 0.16 × 0.08 × 0.04 |
| Radiation | GaKα (λ = 1.34139) |
| 2θ range for data collection/° | 5.926 to 113.932 |
| Index ranges | -14 ≤ h ≤ 14, -9 ≤ k ≤ 9, -16 ≤ l ≤ 16 |
| Reflections collected | 22355 |
| Independent reflections | 4618 [$R_{int}$ = 0.0495, $R_{sigma}$ = 0.0424] |
| Data/restraints/parameters | 4618/1/318 |
| Goodness-of-fit on F$^2$ | 1.071 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0372, $wR_2$ = 0.0896 |
| Final R indexes [all data] | $R_1$ = 0.0383, $wR_2$ = 0.0904 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.20/-0.26 |

| | |
|---|---|
| Flack parameter | 0.05(8) |

The relative and absolute configurations of **7** (*S*a,1*S*,3a*R*,6a*S*) were assigned by X-ray crystallographic analysis of a single crystal of **7** (Figure S5). The crystal was prepared from the solution of **7** in hexane/$CHCl_3$ 2:1 at 0 °C.

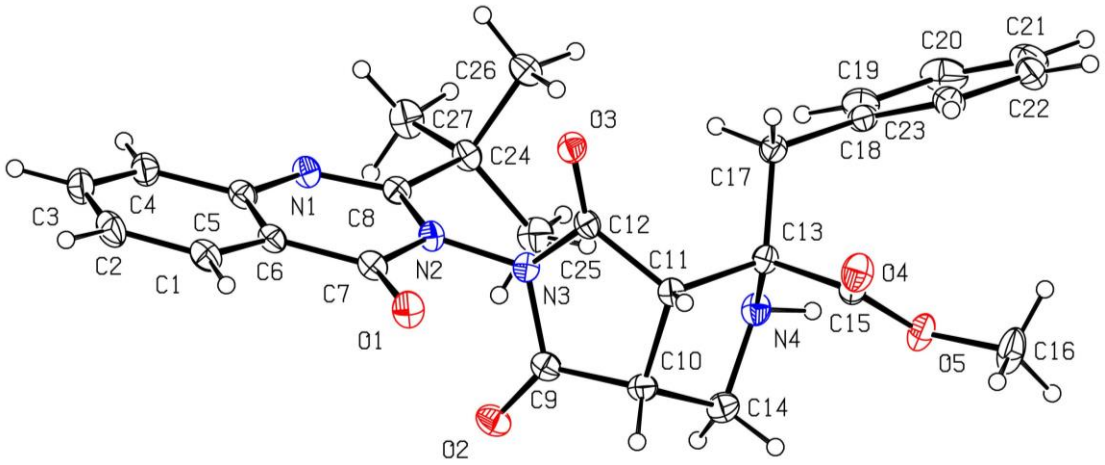



Figure S5. X-ray structure of **7** (ellipsoid contour at 30% probability)

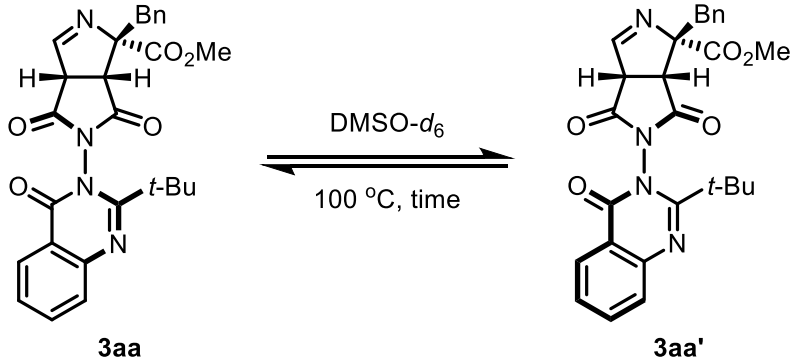
Table S4. Crystal data and structure refinement for cu_230104_TP_RED_0m

| | |
|---|---|
| Identification code | cu_230104_TP_RED_0m |
| Empirical formula | $C_{27}H_{28}N_4O_5$ |
| Formula weight | 488.53 |
| Temperature/K | 170.00 |
| Crystal system | monoclinic |
| Space group | $P2_1$ |
| a/Å | 9.5810(2) |
| b/Å | 13.3130(3) |
| c/Å | 10.2528(2) |
| α/° | 90 |
| β/° | 111.0290(10) |
| γ/° | 90 |
| Volume/Å$^3$ | 1220.66(5) |
| Z | 2 |

| | |
|---|---|
| $\rho_{calc}$g/cm$^3$ | 1.329 |
| $\mu$/mm$^{-1}$ | 0.763 |
| F(000) | 516.0 |
| Crystal size/mm$^3$ | 0.48 × 0.36 × 0.35 |
| Radiation | CuKα (λ = 1.54178) |
| 2θ range for data collection/° | 9.24 to 136.41 |
| Index ranges | -11 ≤ h ≤ 11, -15 ≤ k ≤ 15, -11 ≤ l ≤ 12 |
| Reflections collected | 18538 |
| Independent reflections | 4443 [$R_{int}$ = 0.0277, $R_{sigma}$ = 0.0254] |
| Data/restraints/parameters | 4443/2/332 |
| Goodness-of-fit on F$^2$ | 1.080 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0295, w$R_2$ = 0.0748 |
| Final R indexes [all data] | $R_1$ = 0.0297, w$R_2$ = 0.0751 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.19/-0.30 |
| Flack parameter | 0.04(4) |

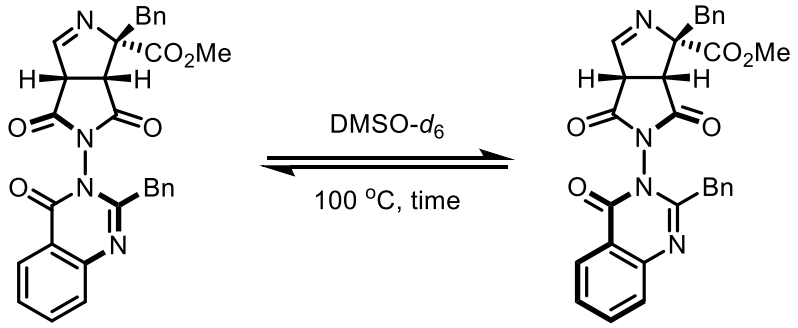
## 10. Evaluation of the thermal stability of the chiral axis

Approximately 100 mg of a pure sample was dissolved in DMSO-$d_6$ and heated at the given temperature in a sealed vial for 12 h. At various time intervals, a small portion of the solution was taken out from the vial, cooled to room temperature, and transferred to an NMR tube to measure the diastereomeric ratio. This ratio was plotted against time, and the barrier to rotation was calculated from the plot as described in the literature report.[11,12]



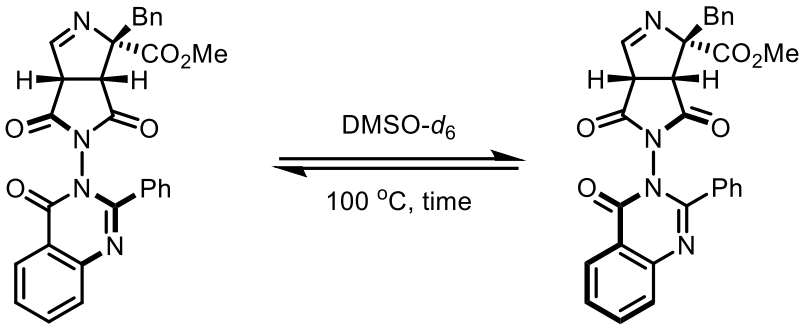

**3aa** **3aa'**

| time (h) | dr (**3aa**:**3aa'**) |
|---|---|
| 0 | >20:1 |
| 1 | >20:1 |
| 2 | >20:1 |
| 4 | >20:1 |
| 6 | >20:1 |
| 9 | >20:1 |
| 12 | >20:1 |



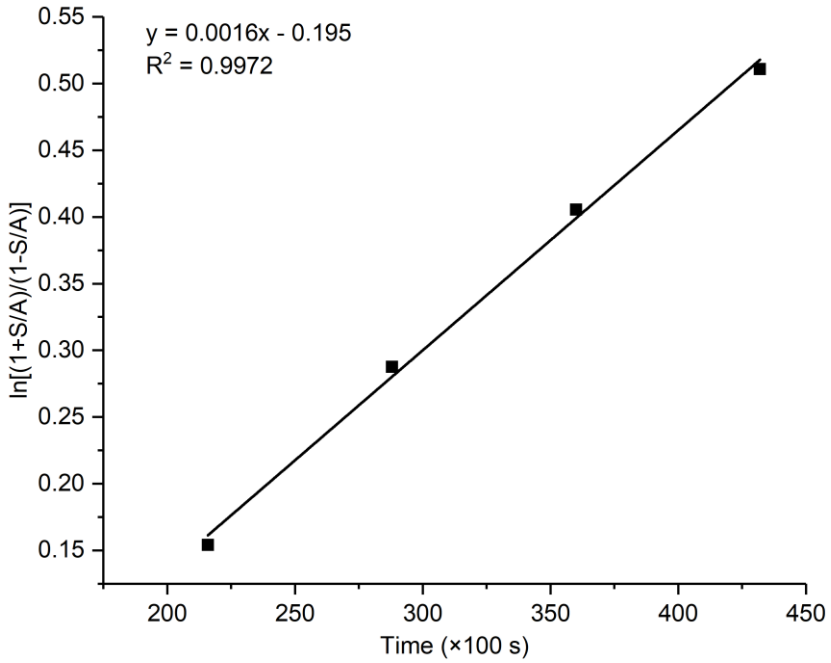

**3pa** **3pa'**

| time (h) | dr (**3pa**:**3pa'**) |
|---|---|
| 0 | >20:1 |
| 1 | >20:1 |
| 2 | >20:1 |
| 4 | >20:1 |
| 6 | >20:1 |
| 9 | >20:1 |
| 12 | >20:1 |




**3qa** **3qa'**

| time (h) | dr (**3qa**:**3qa'**) |
|---|---|
| 0 | >20:1 |
| 1 | >20:1 |
| 2 | >20:1 |
| 4 | >20:1 |
| 6 | 13:1 |
| 8 | 7:1 |
| 10 | 5:1 |
| 12 | 4:1 |

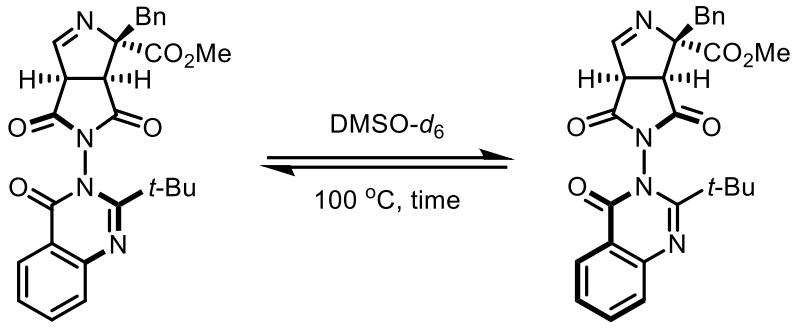



$k_{rot} = 8.00 \times 10^{-6}\ s^{-1}$

$K^{‡}_{rot} = 1.029 \times 10^{-18}\ s^{-1}$

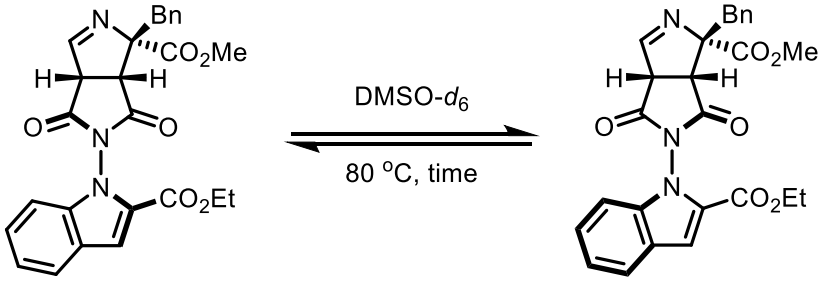
$\Delta G^{‡}_{rot} = 30.7$ kcal/mol

$t_{1/2}$ at 25 °C = 57.5 years




**4aa** **4aa'**

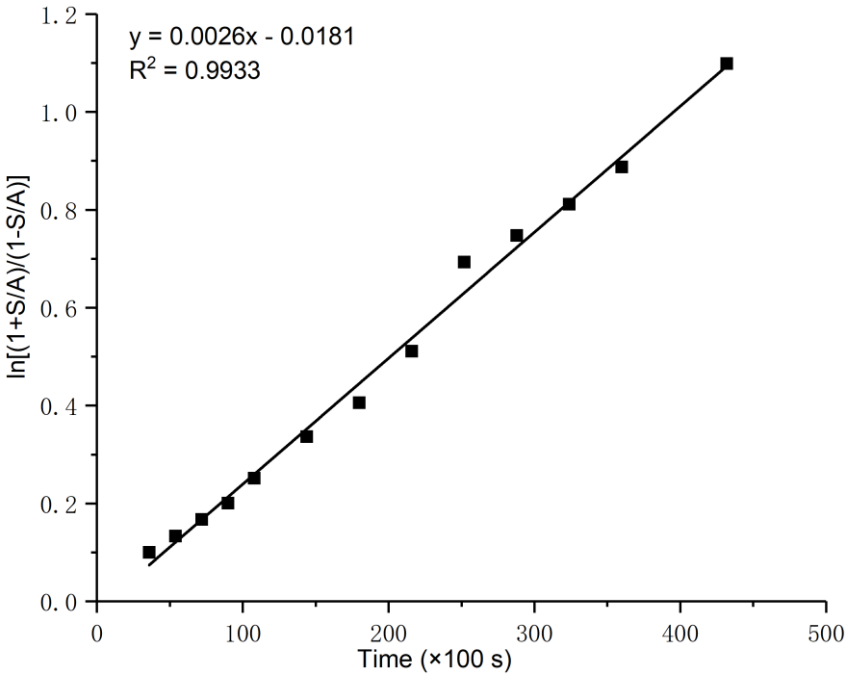
| time (h) | dr (**4aa**:**4aa'**) |
|---|---|
| 0 | >20:1 |
| 1 | >20:1 |
| 2 | >20:1 |
| 4 | >20:1 |
| 6 | >20:1 |
| 9 | >20:1 |
| 12 | >20:1 |




**6a** **6a'**

| time (h) | dr (**6a**:**6a'**) |
|---|---|
| 0 | >20:1 |
| 0.5 | >20:1 |
| 1 | 20:1 |
| 1.5 | 15:1 |
| 2 | 12:1 |

| | |
|---|---|
| 2.5 | 10:1 |
| 3 | 8:1 |
| 4 | 6:1 |
| 5 | 5:1 |
| 6 | 4:1 |
| 7 | 3:1 |
| 8 | 2.8:1 |
| 9 | 2.6:1 |
| 10 | 2.4:1 |
| 12 | 2:1 |



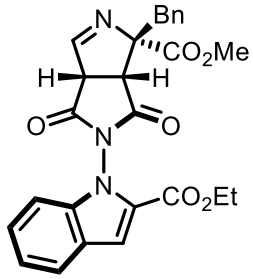

$k_{rot} = 1.30 \times 10^{-5}\ s^{-1}$

$K^{\ddagger}_{rot} = 1.767 \times 10^{-18}\ s^{-1}$

$\Delta G^{\ddagger}_{rot} = 28.7$ kcal/mol

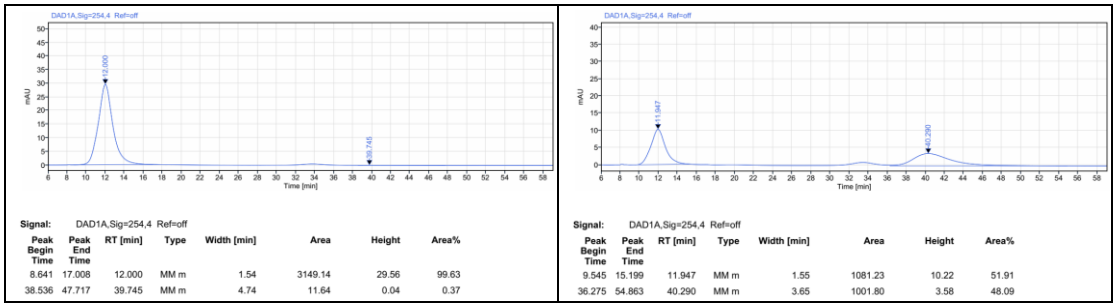
$t_{1/2}$ at 25 °C = 1.9 years

**Ethyl 1-((*R*a,3a*R*,4*S*,6a*S*)-4-benzyl-4-(methoxycarbonyl)-1,3-dioxo-3,3a,4,6a-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)-1*H*-indole-2-carboxylate (6a')**



**6a'**

White solid. **MP**: 163-164 °C; **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.70-7.66 (m, 2H), 7.38 (d, *J* = 1.0 Hz, 1H), 7.36-7.30 (m, 4H), 7.25-7.21 (m, 1H), 7.20-7.15 (m, 2H), 7.03 (dd, *J* = 8.3, 0.9 Hz, 1H), 4.39-4.22 (m, 2H), 3.70 (d, *J* = 8.0 Hz, 1H), 3.68 (s, 3H), 3.53 (d, *J* = 14.0 Hz, 1H), 3.37 (d, *J* = 13.9 Hz, 1H), 3.02 (dd, *J* = 8.0, 1.1 Hz, 1H), 1.32 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 171.1, 169.9, 167.6, 160.7, 159.5, 137.9, 134.2, 131.2, 128.6, 127.7, 127.0, 126.3, 124.8, 123.4, 122.9, 112.2, 108.9, 85.9, 61.2, 57.2, 52.8, 47.6, 43.1, 14.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{24}N_3O_6$ 474.1660; Found 474.1671. **Optical Rotation**: $[\alpha]^{20}_D$ = -282.2 (c = 0.1, $CH_2Cl_2$). 99% ee (HPLC condition: Chiralpak IH column, *n*-hexane/*i*-PrOH = 70:30, flow rate = 1 mL/min, wavelength = 254 nm, $t_R$ = 12.0 min for major isomer, $t_R$ = 39.7 min for minor isomer).



Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 8.641 | 17.008 | 12.000 | MM m | 1.54 | 3149.14 | 29.56 | 99.63 |
| 38.536 | 47.717 | 39.745 | MM m | 4.74 | 11.64 | 0.04 | 0.37 |

Signal: DAD1A,Sig=254,4 Ref=off

| Peak Begin Time | Peak End Time | RT [min] | Type | Width [min] | Area | Height | Area% |
|---|---|---|---|---|---|---|---|
| 9.545 | 15.199 | 11.947 | MM m | 1.55 | 1081.23 | 10.22 | 51.91 |
| 36.275 | 54.863 | 40.290 | MM m | 3.65 | 1001.80 | 3.58 | 48.09 |

## 11. DFT calculations

### I. Complete reference for Gaussian 09

M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, Jr. J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand,

K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, Gaussian 09, revision D.01, Gaussian Inc., Wallingford CT, **2013**.

## II. Computational methods

All the DFT calculations were carried out with the Gaussian 09 series of programs. The B3LYP-D3 functional[13-16] with basis set 6-31G(d)[17] (Lanl2DZ[18] basis set for Ag) was used for geometry optimization of all structures. Harmonic frequency calculations were performed in the same theoretical level for all stationary points to confirm them as a local minima or transition structures and to derive the thermochemical corrections for free energies. M06-L[19] functional with basis set 6-311+G(d,p) (SDD[20] basis set for Ag) was employed to calculate the single point energies to give more accurate energy information. The solvent effects of dichloroethane were considered in both single point calculations and geometry optimizations with a SMD[21-23] continuum solvation model. The geometries of the key intermediates and transition states were drawn using CYLView v1.0[24]. The visualization of molecular orbitals was performed using Multiwfn v3.8.0[25] and VMD v1.9.3[26].

## III. Calculated absolute energies, enthalpies, and free energies of all structures

| Geometry | $E_{elec}$(M06-L)[a] | $H_{corr}$(B3LYP-D3)[b] | $G_{corr}$(B3LYP-D3)[c] | IF[d] |
|---|---|---|---|---|
| **L3-Int1** | -3536.3757 | 0.861276 | 0.696894 | |
| **1a** | -1008.8386 | 0.310028 | 0.242869 | |
| **L3-TS2-A** | -4545.2338 | 1.172548 | 0.972908 | -137.32 |
| **L3-TS2-B** | -4545.2236 | 1.172621 | 0.969411 | -75.38 |

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|---|---|---|---|---|
| **L3-Int3-A** | -4545.2768 | 1.175562 | 0.981358 | |
| **L3-Int3-B** | -4545.2594 | 1.175567 | 0.979096 | |
| **L9-Int1** | -3727.4589 | 1.061037 | 0.886159 | |
| **L9-TS2-A** | -4736.3096 | 1.372929 | 1.161492 | -26.23 |
| **L9-TS2-B** | -4736.311 | 1.374514 | 1.158861 | -354.13 |
| **L9-Int3-A** | -4736.3442 | 1.376318 | 1.168006 | |
| **L9-Int3-B** | -4736.3495 | 1.378273 | 1.164911 | |

[a]The electronic energy calculated by M06-L in dichloroethane solvent. [b]The thermal correction to enthalpy calculated by B3LYP-D3 in dichloroethane solvent. [c]The thermal correction to Gibbs free energy calculated by B3LYP-D3 in dichloroethane solvent. [d]The B3LYP-D3 calculated imaginary frequencies for the transition states.

## IV. Geometries for all the optimized compounds and transition states

### L3-Int1

| | | | |
|---|---|---|---|
| C | -3.70005400 | 0.20598700 | 1.84796100 |
| C | -3.49694800 | -1.29630500 | 2.15751100 |
| C | -4.68595900 | -2.12544900 | 1.66432000 |
| C | -6.00474000 | -1.62432700 | 2.26149000 |
| C | -6.21970400 | -0.13689500 | 1.96053700 |
| C | -5.03028700 | 0.70338000 | 2.43685300 |
| N | -2.58345300 | 0.96466300 | 2.39707500 |
| N | -2.26959300 | -1.80927800 | 1.54624900 |
| C | -1.82840700 | 1.84604800 | 1.70618600 |
| C | -0.69562100 | 2.45470600 | 2.48156300 |
| O | -2.02386800 | 2.13461300 | 0.51332900 |
| C | -0.87625200 | 2.77086500 | 3.83476000 |
| C | 0.15107000 | 3.34242100 | 4.58188300 |
| C | 1.38423100 | 3.59268500 | 3.98184700 |

| | | | |
|---|---|---|---|
| C | 1.57987600 | 3.27761100 | 2.63779400 |
| C | 0.54963900 | 2.71859900 | 1.86735000 |
| C | -1.05057100 | -1.65143700 | 2.05171000 |
| C | 0.24416300 | -1.93182500 | 1.56151700 |
| C | 0.89866600 | -1.34734600 | 2.75312900 |
| C | -0.49652600 | -1.07921400 | 3.30593800 |
| O | -0.97149700 | -0.54841200 | 4.30392600 |
| O | 2.04682800 | -1.11891800 | 3.11070400 |
| N | 0.66437500 | -2.45110000 | 0.38740400 |
| C | 2.00159100 | -2.36004300 | -0.06677400 |
| C | 2.24450000 | -1.85428100 | -1.34876200 |
| C | 3.55458600 | -1.67758900 | -1.78190700 |
| C | 4.63291900 | -2.03754400 | -0.97235800 |
| C | 4.37387200 | -2.57678500 | 0.28560900 |
| C | 3.06809300 | -2.73380000 | 0.75232700 |
| P | 0.86623700 | 2.34377200 | 0.09826900 |
| C | 2.68575100 | 2.15796900 | -0.00777100 |
| C | 3.45554700 | 2.92351200 | -0.89282700 |
| C | 4.82492600 | 2.67805800 | -1.02426000 |
| C | 5.43598900 | 1.68296000 | -0.26121500 |
| C | 4.67284300 | 0.92328300 | 0.63083300 |
| C | 3.30184900 | 1.14392400 | 0.74574100 |
| C | 0.49286000 | 3.89069100 | -0.79956000 |
| C | 0.62667300 | 5.14914400 | -0.19727800 |
| C | 0.35513300 | 6.30606700 | -0.92826300 |
| C | -0.04467600 | 6.21550800 | -2.26397300 |
| C | -0.17530500 | 4.96375600 | -2.86987600 |
| C | 0.08817900 | 3.80442200 | -2.13959300 |
| C | 5.51075900 | -2.94254500 | 1.19678100 |
| F | 5.71901000 | -1.99607400 | 2.14892000 |

| | | | |
|---|---|---|---|
| F | 6.67528600 | -3.08776100 | 0.53107100 |
| F | 5.27419600 | -4.09764500 | 1.85782700 |
| C | 3.81677100 | -1.06305300 | -3.12756200 |
| F | 2.74410300 | -0.37883800 | -3.58949900 |
| F | 4.12354000 | -1.98918200 | -4.06585200 |
| F | 4.85478300 | -0.19712600 | -3.08383000 |
| H | -3.69045300 | 0.34839700 | 0.76378200 |
| H | -3.39951900 | -1.40924400 | 3.24353300 |
| H | -4.72451400 | -2.06003700 | 0.56862800 |
| H | -4.51831200 | -3.17788800 | 1.91913800 |
| H | -6.83546000 | -2.21923300 | 1.86463500 |
| H | -5.99194300 | -1.77970200 | 3.34933500 |
| H | -6.34709900 | -0.00199000 | 0.88009700 |
| H | -7.14002000 | 0.22020100 | 2.43756100 |
| H | -5.15956800 | 1.75692400 | 2.16447200 |
| H | -4.96144400 | 0.65988600 | 3.53300700 |
| H | -2.26981100 | 0.69720100 | 3.32721900 |
| H | -2.34922600 | -2.28116600 | 0.64769300 |
| H | -1.83875900 | 2.58804500 | 4.30103800 |
| H | -0.01301000 | 3.58935400 | 5.62623100 |
| H | 2.19465200 | 4.03437000 | 4.55374000 |
| H | 2.54540300 | 3.46798800 | 2.18324400 |
| H | -0.04722400 | -2.65511900 | -0.31109800 |
| H | 1.41107000 | -1.56562300 | -1.97720000 |
| H | 5.65096100 | -1.88862400 | -1.31012800 |
| H | 2.88193900 | -3.13123300 | 1.74132900 |
| H | 2.99164200 | 3.70823200 | -1.48105500 |
| H | 5.41179100 | 3.27244400 | -1.71886700 |
| H | 6.50158200 | 1.49648600 | -0.36022900 |
| H | 5.13943200 | 0.14749500 | 1.22685000 |

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|---|---|---|---|
| H | 2.72195400 | 0.53194400 | 1.43148400 |
| H | 0.93668800 | 5.22724800 | 0.83968900 |
| H | 0.45517300 | 7.27792800 | -0.45341400 |
| H | -0.25730400 | 7.11805600 | -2.82981500 |
| H | -0.48840400 | 4.88806300 | -3.90721400 |
| H | -0.02274700 | 2.82981300 | -2.60933200 |
| Ag | -0.29895100 | 0.50397500 | -0.94791700 |
| C | -1.23931700 | -1.07163700 | -1.96658600 |
| N | -2.10701000 | -1.86541100 | -2.03112700 |
| C | -3.13566500 | -2.72572700 | -2.11824300 |
| C | -4.28961600 | -2.35336500 | -3.02576200 |
| H | -5.13887600 | -2.97867100 | -2.73447400 |
| H | -4.06219300 | -2.58533900 | -4.07704300 |
| C | -4.63135700 | -0.88185700 | -2.90775200 |
| C | -5.50053300 | -0.41683000 | -1.91181300 |
| C | -3.99989000 | 0.05675100 | -3.73418400 |
| C | -5.72750800 | 0.95048400 | -1.74300400 |
| H | -5.99957700 | -1.13213800 | -1.26268800 |
| C | -4.21913500 | 1.42644700 | -3.56604700 |
| H | -3.32476100 | -0.29112800 | -4.51242000 |
| C | -5.08262900 | 1.87828500 | -2.56611600 |
| H | -6.40882700 | 1.29351000 | -0.96944900 |
| H | -3.71788100 | 2.13831500 | -4.21676500 |
| H | -5.25739600 | 2.94213200 | -2.43197500 |
| C | -3.13111200 | -3.87136100 | -1.28783000 |
| O | -3.99582800 | -4.74379800 | -1.20531000 |
| O | -1.97675400 | -3.92785800 | -0.48722100 |
| C | -1.90452400 | -5.04810000 | 0.40194200 |
| H | -0.93618900 | -4.96736000 | 0.89923800 |
| H | -2.70727800 | -5.01879000 | 1.14487000 |

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|---|---|---|---|
| H | -1.96177100 | -5.98911000 | -0.15155900 |

**1a**

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|---|---|---|---|
| C | -4.70448200 | -0.10563700 | -0.01626900 |
| C | -3.71788300 | 0.86869900 | -0.02736700 |
| C | -2.35972500 | 0.49727600 | -0.01295900 |
| C | -2.03018300 | -0.87409200 | 0.01080800 |
| C | -3.03573100 | -1.85530300 | 0.02169000 |
| C | -4.36728500 | -1.47225000 | 0.00877100 |
| H | -5.75000600 | 0.18847800 | -0.02713900 |
| H | -3.96371500 | 1.92560600 | -0.04642100 |
| C | -0.62777600 | -1.25143100 | 0.01835600 |
| H | -2.74840100 | -2.90126700 | 0.03995600 |
| H | -5.15076000 | -2.22366600 | 0.01745800 |
| C | -0.14015700 | 1.19603000 | -0.00801400 |
| N | -1.39890900 | 1.49301900 | -0.02133300 |
| N | 0.26574900 | -0.14366000 | 0.01266200 |
| C | 0.89002300 | 2.33417200 | 0.01017200 |
| C | 1.66576000 | 2.33375700 | 1.34585300 |
| C | 1.87295700 | 2.25266700 | -1.18001000 |
| C | 0.13569400 | 3.67352300 | -0.09581900 |
| H | 0.97975800 | 2.38375100 | 2.19829500 |
| H | 2.29954400 | 1.45516700 | 1.46725500 |
| H | 2.31183100 | 3.21805400 | 1.37861800 |
| H | 2.62960200 | 1.47804100 | -1.05132200 |
| H | 1.34738600 | 2.07436200 | -2.12369900 |
| H | 2.39788400 | 3.21042000 | -1.26372700 |
| H | -0.57052900 | 3.80690000 | 0.72731900 |
| H | 0.86849700 | 4.48668400 | -0.06108300 |

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|---|---|---|---|
| H | -0.42145800 | 3.75060600 | -1.03404700 |
| N | 1.59580500 | -0.50605000 | -0.00056600 |
| C | 2.18629000 | -1.10250100 | 1.14584900 |
| C | 2.15675000 | -1.08111500 | -1.17461100 |
| C | 3.36395900 | -1.85914000 | 0.63210300 |
| C | 3.34812100 | -1.84525500 | -0.70701700 |
| O | 1.71716600 | -0.93488900 | -2.29102100 |
| O | 1.78285400 | -0.97362800 | 2.27850700 |
| O | -0.17609300 | -2.38967900 | 0.02691200 |
| H | 4.04511200 | -2.29974000 | -1.39931500 |
| H | 4.07732400 | -2.32740000 | 1.29810700 |

**L3-TS2-A**

| | | | |
|---|---|---|---|
| C | 3.27477100 | 1.30007200 | -3.01948500 |
| C | 2.15773800 | 0.42411500 | -3.63135700 |
| C | 2.69734200 | -0.95285100 | -4.03355900 |
| C | 3.90155800 | -0.83487300 | -4.97413700 |
| C | 5.00224600 | 0.04164600 | -4.36566300 |
| C | 4.45712000 | 1.42410400 | -3.98920500 |
| N | 2.72154300 | 2.60060800 | -2.66129400 |
| N | 1.03676400 | 0.24478000 | -2.69912700 |
| C | 2.83402700 | 3.14268000 | -1.43059500 |
| C | 1.98587100 | 4.35755300 | -1.19172200 |
| O | 3.54602800 | 2.67227400 | -0.52780100 |
| C | 2.08235200 | 5.44380400 | -2.06857300 |
| C | 1.33966700 | 6.60260300 | -1.84787700 |
| C | 0.48064300 | 6.67461700 | -0.75170100 |
| C | 0.36088200 | 5.58725500 | 0.11341800 |
| C | 1.10587700 | 4.41526800 | -0.08866000 |

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|---|---|---|---|
| C | 0.00765900 | 1.08252400 | -2.61085900 |
| C | -1.17264600 | 1.12237500 | -1.82673000 |
| C | -1.67720500 | 2.32672000 | -2.53759700 |
| C | -0.36196000 | 2.33750400 | -3.30842300 |
| O | 0.20724600 | 3.10167100 | -4.08276500 |
| O | -2.68294500 | 3.02039100 | -2.51355500 |
| N | -1.58034400 | 0.38614000 | -0.77073000 |
| C | -2.88035700 | 0.35424200 | -0.24715500 |
| C | -3.05300100 | -0.06344400 | 1.07999600 |
| C | -4.32904100 | -0.10785200 | 1.62271400 |
| C | -5.45231600 | 0.25007000 | 0.87182500 |
| C | -5.26310400 | 0.64912900 | -0.44705200 |
| C | -3.99131100 | 0.69709100 | -1.01904500 |
| P | 0.88632900 | 2.98451800 | 1.04545100 |
| C | -0.86587200 | 3.08770100 | 1.58651100 |
| C | -1.22072700 | 2.68943100 | 2.88459200 |
| C | -2.56184500 | 2.66513300 | 3.26998400 |
| C | -3.56136400 | 3.03813900 | 2.36844600 |
| C | -3.21517500 | 3.42411500 | 1.07305400 |
| C | -1.87651500 | 3.44334400 | 0.68186600 |
| C | 1.85125000 | 3.39314000 | 2.55170600 |
| C | 2.11102700 | 4.71308200 | 2.94565200 |
| C | 2.82957600 | 4.96739500 | 4.11429700 |
| C | 3.28667500 | 3.90942300 | 4.90404600 |
| C | 3.03218300 | 2.59226400 | 4.51709200 |
| C | 2.32626800 | 2.33410900 | 3.34138900 |
| C | -6.42455400 | 1.07998400 | -1.29378200 |
| F | -6.37092300 | 2.40716400 | -1.56586300 |
| F | -7.61503200 | 0.84408800 | -0.70375500 |
| F | -6.43820800 | 0.44623700 | -2.49184600 |

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|---|---|---|---|
| C | -4.52387600 | -0.46975000 | 3.06530000 |
| F | -3.36565100 | -0.76979300 | 3.69201600 |
| F | -5.34745100 | -1.53754800 | 3.21522600 |
| F | -5.09642200 | 0.54511200 | 3.76067200 |
| H | 3.61646400 | 0.83388200 | -2.09226500 |
| H | 1.77663600 | 0.93838900 | -4.52103200 |
| H | 2.98467000 | -1.50037100 | -3.12803300 |
| H | 1.89188900 | -1.52456600 | -4.50885300 |
| H | 4.28765600 | -1.83643100 | -5.19673600 |
| H | 3.57700100 | -0.39890600 | -5.92938100 |
| H | 5.40145100 | -0.44637300 | -3.46513300 |
| H | 5.83737400 | 0.14761500 | -5.06780500 |
| H | 5.23300600 | 2.03968500 | -3.52041000 |
| H | 4.12427100 | 1.95467900 | -4.89230200 |
| H | 2.04486000 | 3.00924100 | -3.30675900 |
| H | 0.93733000 | -0.66928100 | -2.25142700 |
| H | 2.75758300 | 5.38165800 | -2.91662300 |
| H | 1.43145200 | 7.44236700 | -2.52990900 |
| H | -0.10155500 | 7.57261400 | -0.56831900 |
| H | -0.33009300 | 5.64667600 | 0.94661800 |
| H | -0.88872700 | -0.15357900 | -0.24872000 |
| H | -2.18702600 | -0.32916400 | 1.66959700 |
| H | -6.44288700 | 0.22168800 | 1.30897500 |
| H | -3.87326500 | 1.00701500 | -2.04743300 |
| H | -0.45415200 | 2.40112200 | 3.59710900 |
| H | -2.82666000 | 2.34376500 | 4.27291500 |
| H | -4.60363000 | 3.00324600 | 2.66799600 |
| H | -3.98391000 | 3.68726300 | 0.35308900 |
| H | -1.62949500 | 3.74250000 | -0.32849200 |
| H | 1.76225500 | 5.54326500 | 2.34092100 |

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|---|---|---|---|
| H | 3.03136200 | 5.99367800 | 4.40758700 |
| H | 3.84473300 | 4.11123800 | 5.81389300 |
| H | 3.38897400 | 1.76348100 | 5.12082100 |
| H | 2.14632000 | 1.30576700 | 3.03781500 |
| Ag | 1.73056500 | 0.79458100 | 0.32233500 |
| C | -4.47980700 | -1.95111200 | -3.41759300 |
| C | -4.52009200 | -2.58703300 | -2.18742900 |
| C | -3.32399200 | -2.85630400 | -1.49459800 |
| C | -2.09716600 | -2.47181600 | -2.07330700 |
| C | -2.06429300 | -1.83271300 | -3.32539200 |
| C | -3.25001900 | -1.57517200 | -3.99333500 |
| H | -5.40566300 | -1.73158800 | -3.93980300 |
| H | -5.45928800 | -2.87493300 | -1.72682200 |
| C | -0.88401000 | -2.66422500 | -1.30252900 |
| H | -1.10821800 | -1.54139300 | -3.74599900 |
| H | -3.23410400 | -1.07863000 | -4.95844900 |
| C | -2.32551300 | -3.70253500 | 0.43008400 |
| N | -3.39439800 | -3.47594000 | -0.26218600 |
| N | -1.06666400 | -3.31095400 | -0.06207900 |
| C | -2.46072400 | -4.47353400 | 1.75338500 |
| C | -1.88144500 | -5.89295400 | 1.56058900 |
| C | -1.78579000 | -3.78056700 | 2.95985700 |
| C | -3.95979300 | -4.61353700 | 2.08340000 |
| H | -2.41997700 | -6.42713000 | 0.76957000 |
| H | -0.82260700 | -5.88460900 | 1.30049000 |
| H | -2.00245200 | -6.45518500 | 2.49338800 |
| H | -0.70254800 | -3.90261600 | 2.97217100 |
| H | -2.01897400 | -2.71373700 | 2.99522500 |
| H | -2.17606500 | -4.23521800 | 3.87688000 |
| H | -4.50725700 | -5.11683900 | 1.28373700 |

| | | | |
|---|---|---|---|
| H | -4.05566800 | -5.20792300 | 2.99839200 |
| H | -4.42842300 | -3.64111200 | 2.25586400 |
| N | 0.05067000 | -3.34489500 | 0.73778600 |
| C | 1.08890900 | -4.28970900 | 0.62940100 |
| C | 0.50761000 | -2.16437600 | 1.41656600 |
| C | 2.20069300 | -3.73692100 | 1.46929300 |
| C | 1.77741400 | -2.50684100 | 1.97479600 |
| O | -0.18319200 | -1.13743000 | 1.45568200 |
| O | 1.01832900 | -5.32886400 | 0.00035700 |
| O | 0.24198100 | -2.28136600 | -1.62016900 |
| H | 2.29972200 | -1.87025900 | 2.67319600 |
| H | 2.89231000 | -4.42456200 | 1.93533100 |
| C | 2.69706600 | -1.04218600 | -0.10913900 |
| N | 3.27248700 | -2.04089700 | -0.35268800 |
| C | 3.77294200 | -3.27337600 | -0.08838000 |
| C | 5.08778600 | -3.29682300 | 0.69367900 |
| H | 5.90529300 | -3.03567400 | 0.00664700 |
| H | 5.25171400 | -4.33346100 | 0.99815500 |
| C | 5.11255300 | -2.37590200 | 1.89151000 |
| C | 5.26837000 | -0.99109900 | 1.72857300 |
| C | 4.93586700 | -2.87969000 | 3.18646100 |
| C | 5.21398300 | -0.12969700 | 2.82577700 |
| H | 5.42775600 | -0.58257700 | 0.73492900 |
| C | 4.89040400 | -2.02395400 | 4.28883500 |
| H | 4.82760300 | -3.95149700 | 3.33023500 |
| C | 5.01974200 | -0.64436100 | 4.11044500 |
| H | 5.32248900 | 0.94117900 | 2.67782900 |
| H | 4.75347900 | -2.43489100 | 5.28535200 |
| H | 4.98527500 | 0.02383800 | 4.96609600 |
| C | 3.59834300 | -4.31939700 | -1.10338600 |

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|---|---|---|---|
| O | 4.14781400 | -5.41060400 | -1.05325700 |
| O | 2.73710200 | -3.95363600 | -2.07384900 |
| C | 2.35304600 | -4.98088700 | -2.99637800 |
| H | 1.60139000 | -4.52399400 | -3.64101200 |
| H | 3.21023600 | -5.31003800 | -3.59135300 |
| H | 1.92679600 | -5.83197100 | -2.46162400 |

**L3-TS2-B**

| | | | |
|---|---|---|---|
| C | -0.56787700 | 3.77538900 | 2.62706700 |
| C | -0.30833900 | 2.83041900 | 3.82989100 |
| C | -1.59643600 | 2.61261800 | 4.62655400 |
| C | -2.17227900 | 3.95349900 | 5.10194200 |
| C | -2.38338100 | 4.92818100 | 3.93550700 |
| C | -1.09461600 | 5.12581900 | 3.12494700 |
| N | 0.64113200 | 3.88501800 | 1.81675700 |
| N | 0.27109800 | 1.56348400 | 3.37933900 |
| C | 0.69043600 | 3.42357900 | 0.53946100 |
| C | 2.02152600 | 3.02585400 | -0.02559600 |
| O | -0.34547800 | 3.27125300 | -0.12814800 |
| C | 3.20767800 | 3.19943500 | 0.70264300 |
| C | 4.41682800 | 2.66434800 | 0.26561200 |
| C | 4.45607000 | 1.93451600 | -0.91887900 |
| C | 3.29888200 | 1.79684400 | -1.68480000 |
| C | 2.07751800 | 2.34721300 | -1.27150000 |
| C | 1.59220700 | 1.38848000 | 3.31946300 |
| C | 2.46787200 | 0.58177400 | 2.55755600 |
| C | 3.66700900 | 1.13125800 | 3.24066500 |
| C | 2.72319600 | 2.05038100 | 4.01131300 |
| O | 2.84140600 | 2.99150300 | 4.78363900 |

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|---|---|---|---|
| O | 4.87931400 | 0.97044500 | 3.19784300 |
| N | 2.17741700 | -0.22798300 | 1.51990600 |
| C | 3.03525200 | -0.94662200 | 0.68988900 |
| C | 2.44469500 | -1.67807400 | -0.35366500 |
| C | 3.24549000 | -2.40125500 | -1.22858000 |
| C | 4.63640500 | -2.40708100 | -1.09974700 |
| C | 5.20386800 | -1.67772700 | -0.05744600 |
| C | 4.42453100 | -0.95937700 | 0.84788500 |
| P | 0.61767400 | 2.18851800 | -2.39453600 |
| C | 1.31046200 | 1.35009900 | -3.87357900 |
| C | 1.92897700 | 2.02612400 | -4.93484200 |
| C | 2.43743400 | 1.30979000 | -6.01962400 |
| C | 2.34196900 | -0.08392100 | -6.04965900 |
| C | 1.72844200 | -0.76449300 | -4.99522400 |
| C | 1.20636500 | -0.04850400 | -3.91818200 |
| C | 0.30181000 | 3.89740800 | -2.95837300 |
| C | 1.31364600 | 4.86698600 | -2.99449500 |
| C | 1.03363900 | 6.15291900 | -3.45990900 |
| C | -0.25400400 | 6.47820600 | -3.89274000 |
| C | -1.26528200 | 5.51473300 | -3.85822600 |
| C | -0.98910000 | 4.22972900 | -3.39074900 |
| C | 6.69710600 | -1.57501600 | 0.05852700 |
| F | 7.15859500 | -0.42882400 | -0.51014000 |
| F | 7.33542300 | -2.59504900 | -0.55475500 |
| F | 7.10951800 | -1.55621000 | 1.34486400 |
| C | 2.62023300 | -3.26557900 | -2.28349600 |
| F | 1.33090100 | -2.92915200 | -2.53939300 |
| F | 2.61407800 | -4.57272200 | -1.92494400 |
| F | 3.28735700 | -3.19527900 | -3.45893400 |
| H | -1.32095600 | 3.32262800 | 1.97816100 |

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|---|---|---|---|
| H | 0.44070700 | 3.29872000 | 4.47668200 |
| H | -2.32546700 | 2.09091100 | 3.99213600 |
| H | -1.38370500 | 1.95675100 | 5.47792700 |
| H | -3.11696700 | 3.78303400 | 5.63129500 |
| H | -1.47847400 | 4.40208100 | 5.82653300 |
| H | -3.16586500 | 4.53545800 | 3.27024400 |
| H | -2.74094100 | 5.89476300 | 4.30916500 |
| H | -1.27116700 | 5.78023200 | 2.26414600 |
| H | -0.32667100 | 5.60548300 | 3.74753100 |
| H | 1.50456300 | 4.01525400 | 2.32542100 |
| H | -0.33609500 | 0.92774400 | 2.87128300 |
| H | 3.21292100 | 3.75193700 | 1.63519500 |
| H | 5.30995300 | 2.79343100 | 0.86719700 |
| H | 5.37857600 | 1.46562700 | -1.24541900 |
| H | 3.35366600 | 1.24912100 | -2.61678100 |
| H | 1.19600100 | -0.24195300 | 1.22482000 |
| H | 1.36731300 | -1.67361500 | -0.46102200 |
| H | 5.25668900 | -2.96468500 | -1.79055100 |
| H | 4.89096900 | -0.39975200 | 1.65194200 |
| H | 2.01401200 | 3.10758100 | -4.91559600 |
| H | 2.91099100 | 1.84051200 | -6.84070900 |
| H | 2.74208900 | -0.63778500 | -6.89415300 |
| H | 1.65552500 | -1.84641100 | -5.00950000 |
| H | 0.72399600 | -0.57515400 | -3.10001300 |
| H | 2.31629100 | 4.62092600 | -2.65964900 |
| H | 1.82187800 | 6.90016500 | -3.48355100 |
| H | -0.46998900 | 7.48063100 | -4.25119900 |
| H | -2.26978300 | 5.76519100 | -4.18735600 |
| H | -1.77822100 | 3.48223100 | -3.35042300 |
| Ag | -1.43090900 | 1.10709400 | -1.64097900 |

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|---|---|---|---|
| C | 3.78715500 | -4.25876300 | 2.53072900 |
| C | 2.82182300 | -4.59640600 | 1.59634700 |
| C | 1.54004400 | -4.01714000 | 1.67150400 |
| C | 1.26389100 | -3.09931500 | 2.70377900 |
| C | 2.24413500 | -2.77390900 | 3.65723500 |
| C | 3.49992200 | -3.35077800 | 3.56989900 |
| H | 4.78059800 | -4.69127800 | 2.45756700 |
| H | 3.03274400 | -5.27681700 | 0.77849600 |
| C | -0.00098000 | -2.38819600 | 2.67415200 |
| H | 2.00627500 | -2.05153100 | 4.43022300 |
| H | 4.26865500 | -3.09469400 | 4.29206100 |
| C | -0.53830300 | -3.74138300 | 0.66001400 |
| N | 0.60374200 | -4.34618600 | 0.70967500 |
| N | -0.85895400 | -2.74732600 | 1.60029000 |
| C | -1.55547500 | -4.18485800 | -0.39722100 |
| C | -2.78481400 | -4.79159000 | 0.31418500 |
| C | -1.96739800 | -3.02657700 | -1.33240600 |
| C | -0.92486100 | -5.28449500 | -1.27143100 |
| H | -2.50320100 | -5.71193500 | 0.83860600 |
| H | -3.22846500 | -4.11962800 | 1.04842400 |
| H | -3.54712900 | -5.04614300 | -0.43053700 |
| H | -2.59714300 | -2.29377600 | -0.83663000 |
| H | -1.08679600 | -2.51474500 | -1.73418100 |
| H | -2.52787500 | -3.44092800 | -2.17777800 |
| H | -0.60639500 | -6.14277700 | -0.67493500 |
| H | -1.67635600 | -5.62360100 | -1.99303800 |
| H | -0.05716300 | -4.91616200 | -1.82186100 |
| N | -1.89375300 | -1.84215900 | 1.39766000 |
| C | -3.02195700 | -1.79196300 | 2.26384400 |
| C | -1.49222500 | -0.48749200 | 1.10067400 |

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|---|---|---|---|
| C | -3.51827100 | -0.38745100 | 2.17165000 |
| C | -2.50103100 | 0.37862600 | 1.60516400 |
| O | -0.41547000 | -0.26099400 | 0.52109400 |
| O | -3.45169600 | -2.72928000 | 2.90300100 |
| O | -0.33168700 | -1.48111900 | 3.43422500 |
| H | -2.48608000 | 1.44876900 | 1.46627000 |
| H | -4.26447000 | -0.04965600 | 2.87797600 |
| C | -3.31463400 | 0.27829300 | -1.03546400 |
| N | -4.23797700 | -0.19555500 | -0.48126700 |
| C | -5.05560300 | -0.65868400 | 0.50265200 |
| C | -5.50904500 | -2.10041900 | 0.39544800 |
| H | -5.96214100 | -2.37370800 | 1.35094200 |
| H | -4.63466300 | -2.73480600 | 0.24661800 |
| C | -6.48156500 | -2.30821200 | -0.74868000 |
| C | -7.86162800 | -2.14823600 | -0.56667400 |
| C | -5.99847200 | -2.61812600 | -2.02750400 |
| C | -8.74050900 | -2.29989800 | -1.64069400 |
| H | -8.24081000 | -1.89724100 | 0.41917200 |
| C | -6.87588600 | -2.76842600 | -3.10300400 |
| H | -4.92923200 | -2.74519000 | -2.17723300 |
| C | -8.25078800 | -2.60946700 | -2.91226000 |
| H | -9.80898100 | -2.17793600 | -1.48388200 |
| H | -6.48679000 | -3.01421100 | -4.08753500 |
| H | -8.93570700 | -2.72924700 | -3.74713200 |
| C | -6.00708600 | 0.31581400 | 1.06169800 |
| O | -6.93673200 | 0.00957500 | 1.79417800 |
| O | -5.69051300 | 1.59145000 | 0.75219800 |
| C | -6.53330300 | 2.59772000 | 1.33967200 |
| H | -6.13799100 | 3.55104100 | 0.98754600 |
| H | -7.56852000 | 2.47259100 | 1.01129500 |

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|---|---|---|---|
| H | -6.48974600 | 2.54904700 | 2.43128300 |

**L3-Int3-A**

| | | | |
|---|---|---|---|
| C | 3.59131300 | 1.22300500 | -2.71364200 |
| C | 2.49257300 | 0.47345300 | -3.50165900 |
| C | 2.98114000 | -0.90013900 | -3.96725500 |
| C | 4.28085500 | -0.79656600 | -4.77202400 |
| C | 5.36673300 | -0.06975300 | -3.97058600 |
| C | 4.88335700 | 1.31831200 | -3.53680200 |
| N | 3.08840600 | 2.54141600 | -2.34525400 |
| N | 1.27140000 | 0.30638000 | -2.70002200 |
| C | 3.12553800 | 3.03380000 | -1.08933200 |
| C | 2.32397200 | 4.28550100 | -0.87510400 |
| O | 3.73640400 | 2.49570000 | -0.15244200 |
| C | 2.52462900 | 5.38499500 | -1.71696100 |
| C | 1.82293900 | 6.57245800 | -1.51420500 |
| C | 0.90082800 | 6.66105300 | -0.47184400 |
| C | 0.67711500 | 5.56138700 | 0.35668100 |
| C | 1.38083600 | 4.36176600 | 0.17341900 |
| C | 0.30187900 | 1.21314600 | -2.65404400 |
| C | -0.93050700 | 1.33511600 | -1.96480100 |
| C | -1.25593700 | 2.61817400 | -2.63276200 |
| C | 0.09654200 | 2.52217600 | -3.32476400 |
| O | 0.78387300 | 3.25305300 | -4.03164200 |
| O | -2.17691100 | 3.42311900 | -2.61922200 |
| N | -1.47280200 | 0.58071700 | -0.98518400 |
| C | -2.78383400 | 0.62846200 | -0.49711600 |
| C | -3.04872800 | 0.01406200 | 0.73450100 |
| C | -4.33641400 | 0.03438300 | 1.24871000 |

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|---|---|---|---|
| C | -5.38765100 | 0.64044200 | 0.55562600 |
| C | -5.10843600 | 1.23271600 | -0.67066000 |
| C | -3.82183100 | 1.22980500 | -1.21072700 |
| P | 1.03938800 | 2.90217800 | 1.24044300 |
| C | -0.73000900 | 3.06063000 | 1.70749900 |
| C | -1.15035800 | 2.58637200 | 2.96052100 |
| C | -2.50562600 | 2.57525500 | 3.29146400 |
| C | -3.45642700 | 3.04539100 | 2.38233200 |
| C | -3.04575500 | 3.51317900 | 1.13328100 |
| C | -1.69262000 | 3.50942200 | 0.79138000 |
| C | 1.94122000 | 3.21985700 | 2.80843400 |
| C | 2.00877700 | 4.49572800 | 3.38703000 |
| C | 2.68514900 | 4.68523600 | 4.59189600 |
| C | 3.29748900 | 3.60422900 | 5.23262200 |
| C | 3.23418200 | 2.33149200 | 4.66301000 |
| C | 2.56171400 | 2.14031000 | 3.45472600 |
| C | -6.18618300 | 1.91776400 | -1.45673200 |
| F | -5.93586800 | 3.24432900 | -1.58927100 |
| F | -7.40377500 | 1.79861400 | -0.88829600 |
| F | -6.28212200 | 1.42070100 | -2.71502100 |
| C | -4.62108600 | -0.58236600 | 2.58537900 |
| F | -3.49846500 | -0.94964000 | 3.24119700 |
| F | -5.39873700 | -1.68950400 | 2.47834400 |
| F | -5.28939200 | 0.27467000 | 3.39531500 |
| H | 3.78843300 | 0.67915500 | -1.78621600 |
| H | 2.22604200 | 1.08321600 | -4.37154900 |
| H | 3.13998000 | -1.52295500 | -3.08160900 |
| H | 2.19085200 | -1.37323700 | -4.56195600 |
| H | 4.61708300 | -1.80284200 | -5.04939500 |
| H | 4.09479000 | -0.25269700 | -5.70907100 |

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|---|---|---|---|
| H | 5.61496900 | -0.66052600 | -3.07776900 |
| H | 6.28562200 | 0.02171500 | -4.56173600 |
| H | 5.64287400 | 1.83215800 | -2.93683400 |
| H | 4.69317000 | 1.94144100 | -4.42214500 |
| H | 2.50744500 | 3.01983600 | -3.03296300 |
| H | 1.17223600 | -0.55300800 | -2.16281600 |
| H | 3.24788300 | 5.31060100 | -2.52347200 |
| H | 1.99653200 | 7.42189700 | -2.16778300 |
| H | 0.34848600 | 7.58080500 | -0.30423500 |
| H | -0.06489400 | 5.63339900 | 1.14379300 |
| H | -0.85304100 | -0.09114000 | -0.54105900 |
| H | -2.24469300 | -0.46102700 | 1.28017800 |
| H | -6.38943300 | 0.65491600 | 0.96672800 |
| H | -3.63262200 | 1.71944700 | -2.15598500 |
| H | -0.42058100 | 2.22648900 | 3.67973300 |
| H | -2.81897100 | 2.19528200 | 4.25972700 |
| H | -4.51075000 | 3.02632600 | 2.63986000 |
| H | -3.77759100 | 3.85548600 | 0.40832200 |
| H | -1.39779700 | 3.85669100 | -0.19168400 |
| H | 1.54029000 | 5.34328200 | 2.89800100 |
| H | 2.73455500 | 5.67788600 | 5.03036300 |
| H | 3.82488700 | 3.75590400 | 6.17016000 |
| H | 3.71008800 | 1.48659800 | 5.15243000 |
| H | 2.52413300 | 1.14899700 | 3.01112900 |
| Ag | 1.72741900 | 0.65600800 | 0.48430400 |
| C | -5.14072000 | -1.67534600 | -2.80703400 |
| C | -5.05268500 | -2.40284100 | -1.63088700 |
| C | -3.79146900 | -2.77864900 | -1.12946200 |
| C | -2.63499900 | -2.38830500 | -1.83660200 |
| C | -2.73314700 | -1.66581500 | -3.03824400 |

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|---|---|---|---|
| C | -3.98152100 | -1.31474300 | -3.52228200 |
| H | -6.11381100 | -1.36832900 | -3.17694600 |
| H | -5.93655800 | -2.68521500 | -1.06860100 |
| C | -1.34672200 | -2.62564300 | -1.22138900 |
| H | -1.82423500 | -1.37902600 | -3.55532800 |
| H | -4.07036700 | -0.74885100 | -4.44414400 |
| C | -2.59346500 | -3.82140800 | 0.57322800 |
| N | -3.73059100 | -3.50601700 | 0.04464900 |
| N | -1.39990900 | -3.39258700 | -0.02810600 |
| C | -2.56849000 | -4.71642500 | 1.81989500 |
| C | -1.90179800 | -6.06413900 | 1.46694600 |
| C | -1.84685400 | -4.06593900 | 3.02336800 |
| C | -4.02240000 | -4.99321700 | 2.24806400 |
| H | -2.44806100 | -6.57302300 | 0.66513500 |
| H | -0.86348600 | -5.95444800 | 1.15004500 |
| H | -1.91868800 | -6.71043300 | 2.35147700 |
| H | -0.76049300 | -4.08422100 | 2.92585100 |
| H | -2.17119700 | -3.03356600 | 3.17474200 |
| H | -2.10084200 | -4.63555700 | 3.92375000 |
| H | -4.59871500 | -5.46434200 | 1.44824800 |
| H | -4.00654400 | -5.66906400 | 3.10962400 |
| H | -4.53592200 | -4.07311900 | 2.53858600 |
| N | -0.17656400 | -3.46632500 | 0.61321500 |
| C | 0.87011800 | -4.27862000 | 0.11418900 |
| C | 0.29124900 | -2.32683500 | 1.29599500 |
| C | 2.16437100 | -3.75948600 | 0.73019600 |
| C | 1.77707300 | -2.40434200 | 1.33161300 |
| O | -0.43439600 | -1.42989500 | 1.67978700 |
| O | 0.69017000 | -5.22204300 | -0.62007800 |
| O | -0.26643800 | -2.18010900 | -1.60529100 |

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|---|---|---|---|
| H | 2.17842700 | -2.17541200 | 2.31993000 |
| H | 2.51571500 | -4.49683800 | 1.45512100 |
| C | 2.31192500 | -1.37490000 | 0.27861500 |
| N | 3.07084200 | -1.94319000 | -0.58401300 |
| C | 3.29150600 | -3.37006200 | -0.29060100 |
| C | 4.70656600 | -3.53437500 | 0.33948400 |
| H | 5.42470400 | -3.16419500 | -0.39968000 |
| H | 4.89168200 | -4.60314200 | 0.47305600 |
| C | 4.86708300 | -2.79560400 | 1.64550800 |
| C | 5.12328000 | -1.41572200 | 1.66560300 |
| C | 4.68511200 | -3.45785700 | 2.86789000 |
| C | 5.15956000 | -0.71147300 | 2.87026100 |
| H | 5.27552200 | -0.88871200 | 0.72936900 |
| C | 4.72071300 | -2.75840900 | 4.07597200 |
| H | 4.50476700 | -4.53019400 | 2.87002600 |
| C | 4.94745200 | -1.37944600 | 4.07955300 |
| H | 5.34651000 | 0.35880600 | 2.86316800 |
| H | 4.57289700 | -3.28965700 | 5.01238000 |
| H | 4.97459300 | -0.83269700 | 5.01829400 |
| C | 3.22484800 | -4.22305100 | -1.56013200 |
| O | 3.86161400 | -5.24332800 | -1.73649600 |
| O | 2.35936200 | -3.71728900 | -2.44320000 |
| C | 2.10509500 | -4.51115300 | -3.61193700 |
| H | 1.30484300 | -3.99680000 | -4.14383000 |
| H | 3.00008900 | -4.57316900 | -4.23719800 |
| H | 1.78563900 | -5.51556500 | -3.32471000 |

**L3-Int3-B**

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|---|---|---|---|
| C | 0.66548700 | 2.16787600 | 4.22128900 |

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|---|---|---|---|
| C | 1.19967700 | 0.79109300 | 4.68778600 |
| C | 0.22542000 | 0.16151600 | 5.68553200 |
| C | 0.00997500 | 1.09158700 | 6.88771300 |
| C | -0.45412000 | 2.48795500 | 6.45108400 |
| C | 0.50018800 | 3.10729000 | 5.42018100 |
| N | 1.52377900 | 2.70348600 | 3.16929400 |
| N | 1.42678800 | -0.07386500 | 3.52784900 |
| C | 1.06015600 | 2.87546200 | 1.90284100 |
| C | 2.03498400 | 2.86621000 | 0.76419300 |
| O | -0.15474900 | 2.98536800 | 1.67685600 |
| C | 3.39652200 | 2.60171400 | 0.97006300 |
| C | 4.27881600 | 2.44524900 | -0.09629200 |
| C | 3.80254300 | 2.55406300 | -1.39930400 |
| C | 2.45688900 | 2.84267500 | -1.62559300 |
| C | 1.55539700 | 3.01191900 | -0.56531900 |
| C | 2.64155800 | -0.21500000 | 2.99408700 |
| C | 3.13721300 | -0.53877100 | 1.71297500 |
| C | 4.54861000 | -0.44869400 | 2.16286100 |
| C | 4.01158600 | -0.05146600 | 3.53981300 |
| O | 4.48459900 | 0.32326700 | 4.60229100 |
| O | 5.65568200 | -0.59159000 | 1.66425100 |
| N | 2.47597600 | -0.69238700 | 0.54554900 |
| C | 3.01767500 | -0.88651500 | -0.72702900 |
| C | 2.23703800 | -0.51476000 | -1.82894600 |
| C | 2.71274600 | -0.72259600 | -3.11947400 |
| C | 3.96394000 | -1.30018900 | -3.34152800 |
| C | 4.73444600 | -1.65057900 | -2.23418500 |
| C | 4.28173000 | -1.44811200 | -0.93185000 |
| P | -0.21688800 | 3.35533100 | -0.96788300 |
| C | -0.20418500 | 3.59417500 | -2.78910500 |

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|---|---|---|---|
| C | 0.22957000 | 4.77529900 | -3.41126900 |
| C | 0.21710300 | 4.88054500 | -4.80164900 |
| C | -0.22166900 | 3.80759900 | -5.58431300 |
| C | -0.65551900 | 2.63031500 | -4.97317400 |
| C | -0.65605900 | 2.52916400 | -3.58104800 |
| C | -0.54605200 | 5.03686200 | -0.33125800 |
| C | 0.47625800 | 5.96532800 | -0.09513800 |
| C | 0.16525500 | 7.24875300 | 0.35812300 |
| C | -1.16535100 | 7.61397500 | 0.57481400 |
| C | -2.18766000 | 6.69105300 | 0.33943500 |
| C | -1.87975500 | 5.40670500 | -0.10971800 |
| C | 6.05066600 | -2.34939100 | -2.41862900 |
| F | 6.98505400 | -1.90697600 | -1.54856300 |
| F | 6.55050900 | -2.19350100 | -3.66270600 |
| F | 5.93529800 | -3.68782700 | -2.20908900 |
| C | 1.89021600 | -0.25387800 | -4.28461600 |
| F | 0.56116400 | -0.38476300 | -4.05392500 |
| F | 2.16642600 | -0.93334000 | -5.41704500 |
| F | 2.10899300 | 1.05842900 | -4.55486500 |
| H | -0.31225200 | 2.01611700 | 3.75546600 |
| H | 2.17248500 | 0.93302000 | 5.16865200 |
| H | -0.73084800 | -0.02582800 | 5.17631900 |
| H | 0.61610700 | -0.81049500 | 6.00604600 |
| H | -0.71951700 | 0.64700200 | 7.57472600 |
| H | 0.95471300 | 1.18059400 | 7.44220100 |
| H | -1.45724400 | 2.41414500 | 6.00783400 |
| H | -0.54105700 | 3.14753800 | 7.32233200 |
| H | 0.12149200 | 4.07374000 | 5.06922200 |
| H | 1.48363800 | 3.28747900 | 5.87616900 |
| H | 2.51978800 | 2.64006900 | 3.33112200 |

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|---|---|---|---|
| H | 0.62858700 | -0.21976600 | 2.91464400 |
| H | 3.79366600 | 2.48391400 | 1.97080000 |
| H | 5.32092700 | 2.21358200 | 0.09757700 |
| H | 4.46795300 | 2.40623100 | -2.24436000 |
| H | 2.10695300 | 2.91805600 | -2.64660700 |
| H | 1.46502500 | -0.56273300 | 0.58324100 |
| H | 1.27329200 | -0.04681400 | -1.66612600 |
| H | 4.32543700 | -1.47167800 | -4.34716300 |
| H | 4.90964900 | -1.70301400 | -0.08915100 |
| H | 0.57615000 | 5.60950200 | -2.80945800 |
| H | 0.55160600 | 5.79889200 | -5.27600500 |
| H | -0.22586500 | 3.89189800 | -6.66735900 |
| H | -0.99099800 | 1.79088300 | -5.57493200 |
| H | -0.99957400 | 1.61443900 | -3.10485700 |
| H | 1.51255200 | 5.68877700 | -0.26093000 |
| H | 0.96351200 | 7.96276800 | 0.54052900 |
| H | -1.40496100 | 8.61279500 | 0.92835900 |
| H | -3.22392000 | 6.96825500 | 0.51128900 |
| H | -2.67455800 | 4.68479400 | -0.28175100 |
| Ag | -1.89569600 | 1.69838600 | -0.30746800 |
| C | 4.51238500 | -4.43505500 | 1.49732000 |
| C | 3.66495500 | -4.35516300 | 0.40158200 |
| C | 2.31325000 | -4.00841200 | 0.58348400 |
| C | 1.84266700 | -3.75617800 | 1.88903800 |
| C | 2.70702900 | -3.84205300 | 2.99335400 |
| C | 4.03681200 | -4.18069500 | 2.79693000 |
| H | 5.55800400 | -4.68747300 | 1.34795200 |
| H | 4.02717800 | -4.52725300 | -0.60560200 |
| C | 0.47604500 | -3.29692100 | 2.06035900 |
| H | 2.31925400 | -3.62334600 | 3.98237500 |

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|---|---|---|---|
| H | 4.71433600 | -4.24020300 | 3.64275500 |
| C | 0.28291700 | -3.48564000 | -0.43081200 |
| N | 1.50372400 | -3.89347700 | -0.53313400 |
| N | -0.25015200 | -3.17825000 | 0.83645100 |
| C | -0.58706900 | -3.41816900 | -1.69506900 |
| C | -1.63642300 | -4.55191000 | -1.64027700 |
| C | -1.29075600 | -2.05184200 | -1.88563900 |
| C | 0.31257800 | -3.66802000 | -2.91985400 |
| H | -1.14619000 | -5.53130600 | -1.66595000 |
| H | -2.25824100 | -4.51306900 | -0.74525600 |
| H | -2.29084600 | -4.47644300 | -2.51583600 |
| H | -2.21067100 | -1.96559900 | -1.30970400 |
| H | -0.64052900 | -1.21394200 | -1.62142200 |
| H | -1.55853000 | -1.94049100 | -2.94097000 |
| H | 0.82220700 | -4.63150100 | -2.85364800 |
| H | -0.31540600 | -3.66569200 | -3.81720100 |
| H | 1.07271500 | -2.89223900 | -3.03040800 |
| N | -1.42128000 | -2.46141100 | 0.98438200 |
| C | -2.65170100 | -3.02782500 | 1.41364600 |
| C | -1.33187700 | -1.10692700 | 1.29561500 |
| C | -3.58249500 | -1.86389100 | 1.71838000 |
| C | -2.69603800 | -0.61741300 | 1.63103500 |
| O | -0.29934100 | -0.45527000 | 1.20076300 |
| O | -2.84741600 | -4.21544100 | 1.50521900 |
| O | -0.05639500 | -2.96244000 | 3.11071100 |
| H | -2.67298200 | 0.03332200 | 2.50829300 |
| H | -4.02874700 | -2.05018300 | 2.69508800 |
| C | -3.21019400 | 0.15754200 | 0.37059000 |
| N | -4.25864200 | -0.39624300 | -0.11651200 |
| C | -4.70444500 | -1.57545800 | 0.64911500 |

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|---|---|---|---|
| C | -4.97180300 | -2.77255300 | -0.30614300 |
| H | -5.13996100 | -3.66017200 | 0.30961500 |
| H | -4.05541000 | -2.93763500 | -0.88016500 |
| C | -6.13653900 | -2.56173500 | -1.24303800 |
| C | -7.41727200 | -3.01138200 | -0.89403800 |
| C | -5.96700800 | -1.89506100 | -2.46355800 |
| C | -8.50680600 | -2.79107100 | -1.73935600 |
| H | -7.56008800 | -3.53386500 | 0.04839500 |
| C | -7.05234600 | -1.67739900 | -3.31304500 |
| H | -4.97823200 | -1.54335500 | -2.74322600 |
| C | -8.32725200 | -2.12194300 | -2.95196200 |
| H | -9.49280300 | -3.14691700 | -1.45268500 |
| H | -6.90308100 | -1.15982500 | -4.25688500 |
| H | -9.17261700 | -1.95212800 | -3.61311300 |
| C | -6.01835000 | -1.30269000 | 1.39484500 |
| O | -6.41518900 | -2.00431800 | 2.30695400 |
| O | -6.69226200 | -0.25951600 | 0.90812700 |
| C | -7.99765100 | -0.03781700 | 1.47785900 |
| H | -8.38509600 | 0.84734700 | 0.97348400 |
| H | -8.64366800 | -0.89823800 | 1.28632200 |
| H | -7.92354900 | 0.13576800 | 2.55412800 |

**L9-Int1**

| | | | |
|---|---|---|---|
| Ag | -0.52203300 | -0.54952400 | -0.80620400 |
| O | 0.31726600 | -0.11947600 | 2.13917200 |
| N | 1.63214300 | 1.32545700 | 0.95882200 |
| H | 1.70136200 | 2.23962800 | 0.49122400 |
| P | -2.35396200 | 0.16206300 | 0.84922200 |
| N | 2.68044800 | -0.69256400 | -1.51265200 |

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|---|---|---|---|
| H | 2.24093800 | -0.46352700 | -2.39537500 |
| O | 3.22439000 | -2.43579600 | -0.12946800 |
| P | -0.16929500 | -3.01005400 | -0.75604900 |
| C | -1.88051900 | 1.79239000 | 1.56140400 |
| C | -2.82011200 | 2.81226800 | 1.74645700 |
| H | -3.86980000 | 2.61739200 | 1.56109700 |
| C | -2.42234500 | 4.09018700 | 2.14359300 |
| H | -3.16955400 | 4.86433000 | 2.28029400 |
| C | -1.07183800 | 4.37501600 | 2.33459300 |
| H | -0.75716900 | 5.37213300 | 2.62782900 |
| C | -0.12031400 | 3.37288600 | 2.14423400 |
| H | 0.93277700 | 3.58502100 | 2.29506800 |
| C | -0.51204900 | 2.08470000 | 1.76854100 |
| C | 0.51915000 | 1.00161300 | 1.64227100 |
| C | 2.72865400 | 0.38147700 | 0.77297800 |
| H | 2.32431000 | -0.60907100 | 0.96316000 |
| C | 3.18852500 | 0.44803000 | -0.73587400 |
| H | 2.67487200 | 1.30893000 | -1.16275400 |
| C | 2.74536000 | -2.00215700 | -1.18191600 |
| C | 2.20840700 | -2.95707100 | -2.22657200 |
| C | 3.03408300 | -3.28363100 | -3.30503000 |
| H | 3.99707900 | -2.79042200 | -3.40522900 |
| C | 2.62906600 | -4.23667600 | -4.24274300 |
| H | 3.27691700 | -4.48097000 | -5.07936700 |
| C | 1.39401900 | -4.86901300 | -4.10096900 |
| H | 1.07432200 | -5.61410900 | -4.82364800 |
| C | 0.55958400 | -4.54175300 | -3.02956300 |
| H | -0.40624700 | -5.02658500 | -2.93065200 |
| C | 0.95320800 | -3.58678700 | -2.08462100 |
| C | -3.95976300 | 0.43091400 | 0.00739600 |

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|---|---|---|---|
| C | -3.95133300 | 0.50952000 | -1.39355700 |
| H | -3.00646500 | 0.44533500 | -1.92630700 |
| C | -5.14312800 | 0.66333900 | -2.10354800 |
| H | -5.12233500 | 0.72338700 | -3.18804500 |
| C | -6.35830800 | 0.73451700 | -1.41796100 |
| H | -7.28804700 | 0.84867800 | -1.96810100 |
| C | -6.37723900 | 0.65109700 | -0.02235900 |
| H | -7.32116700 | 0.70087500 | 0.51312200 |
| C | -5.18586400 | 0.49570900 | 0.68717400 |
| H | -5.20882500 | 0.41322100 | 1.76950200 |
| C | -2.79392900 | -0.94825000 | 2.23195800 |
| C | -3.38095200 | -2.18435000 | 1.91120600 |
| H | -3.64025000 | -2.41373400 | 0.88172100 |
| C | -3.62333400 | -3.12759200 | 2.90788600 |
| H | -4.06978300 | -4.08256000 | 2.64546200 |
| C | -3.28089600 | -2.84957900 | 4.23468500 |
| H | -3.46193600 | -3.58783400 | 5.01080200 |
| C | -2.70094900 | -1.62081000 | 4.55804500 |
| H | -2.43412100 | -1.39819100 | 5.58754400 |
| C | -2.45610200 | -0.67264900 | 3.56176100 |
| H | -1.98628800 | 0.27092700 | 3.81553100 |
| C | -1.81318000 | -3.73119200 | -1.12705600 |
| C | -2.27659000 | -4.91116200 | -0.52958100 |
| H | -1.62698800 | -5.48000200 | 0.12714500 |
| C | -3.58388900 | -5.34684800 | -0.75739300 |
| H | -3.93629700 | -6.25857000 | -0.28334900 |
| C | -4.43769800 | -4.61091800 | -1.58206700 |
| H | -5.45773400 | -4.94579200 | -1.74723100 |
| C | -3.97987600 | -3.43746400 | -2.18829700 |
| H | -4.64106800 | -2.85477600 | -2.82313100 |

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|---|---|---|---|
| C | -2.67701300 | -2.99847800 | -1.95829700 |
| H | -2.33274200 | -2.07136600 | -2.41007500 |
| C | 0.36857000 | -3.86474900 | 0.76175500 |
| C | 1.04174400 | -5.09417400 | 0.72399100 |
| H | 1.30069100 | -5.54286200 | -0.23028500 |
| C | 1.38037000 | -5.73894100 | 1.91361200 |
| H | 1.90361500 | -6.69053100 | 1.88116000 |
| C | 1.05043000 | -5.16074700 | 3.14320800 |
| H | 1.31616800 | -5.66528200 | 4.06806500 |
| C | 0.38792600 | -3.93194800 | 3.18175400 |
| H | 0.13678100 | -3.47242900 | 4.13315500 |
| C | 0.05087700 | -3.27926600 | 1.99522100 |
| H | -0.43328900 | -2.31143200 | 2.02904400 |
| C | 3.84260100 | 0.62933300 | 1.77432000 |
| C | 4.25854300 | 1.92841200 | 2.09094600 |
| C | 4.47976400 | -0.45843500 | 2.37918400 |
| C | 5.29726000 | 2.13398400 | 2.99912500 |
| H | 3.77350700 | 2.77872100 | 1.61983200 |
| C | 5.51856100 | -0.25390800 | 3.29004800 |
| H | 4.16310800 | -1.46415800 | 2.12014700 |
| C | 5.93060000 | 1.04326300 | 3.60218500 |
| H | 5.61398400 | 3.14640000 | 3.23566700 |
| H | 6.00315800 | -1.10761600 | 3.75644700 |
| H | 6.73812700 | 1.20473200 | 4.31119400 |
| C | 4.67251000 | 0.68432200 | -0.95478200 |
| C | 5.61919600 | -0.34554900 | -0.88473800 |
| C | 5.10521000 | 1.99109600 | -1.21034700 |
| C | 6.97405200 | -0.06951800 | -1.07111000 |
| H | 5.29741300 | -1.35779600 | -0.66724000 |
| C | 6.46184900 | 2.26808200 | -1.39154900 |

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|---|---|---|---|
| H | 4.37197600 | 2.79309700 | -1.24831800 |
| C | 7.40085300 | 1.23731700 | -1.32353400 |
| H | 7.69971200 | -0.87641300 | -1.01176300 |
| H | 6.78276500 | 3.28762800 | -1.58826700 |
| H | 8.45720000 | 1.44927100 | -1.46493200 |
| C | -0.01034300 | 1.29895400 | -1.90757600 |
| N | 0.09937600 | 2.47086500 | -1.85707800 |
| C | 0.22417400 | 3.82070800 | -1.82656500 |
| C | -0.80870100 | 4.63617700 | -2.57166100 |
| C | 1.26003100 | 4.34702400 | -1.03618500 |
| H | -1.04145300 | 4.12954600 | -3.51774000 |
| H | -0.36176200 | 5.60089900 | -2.82597500 |
| C | -2.10203500 | 4.86787600 | -1.80956100 |
| O | 2.12860200 | 3.70159500 | -0.39558500 |
| O | 1.27881600 | 5.71848700 | -1.02163900 |
| C | -3.12874400 | 3.91505100 | -1.83911200 |
| C | -2.29629800 | 6.03739800 | -1.06215700 |
| C | 2.31110300 | 6.31506100 | -0.23611600 |
| C | -4.32377000 | 4.12524100 | -1.14810500 |
| H | -2.99210600 | 3.00431100 | -2.41553000 |
| C | -3.49325800 | 6.25766500 | -0.37805800 |
| H | -1.50211800 | 6.77852400 | -1.02332300 |
| H | 2.21302200 | 6.04790900 | 0.82114800 |
| H | 3.30471000 | 6.01713700 | -0.58542100 |
| H | 2.18436400 | 7.39305200 | -0.35655500 |
| C | -4.51345400 | 5.30381100 | -0.42255400 |
| H | -5.10490500 | 3.37162800 | -1.18232500 |
| H | -3.63079000 | 7.17578300 | 0.18762200 |
| H | -5.44637200 | 5.47534100 | 0.10795600 |

**L9-TS2-A**

| | | | |
|---|---|---|---|
| Ag | 1.83526400 | -0.39571300 | 0.13455700 |
| O | 1.24217500 | -2.61006100 | -2.47093600 |
| N | -0.55817900 | -1.41741100 | -1.73572800 |
| H | -1.09499200 | -0.55444200 | -1.83650200 |
| P | 3.39059000 | -0.56809500 | -1.83837500 |
| N | -1.53257200 | -1.44994600 | 1.11978100 |
| H | -2.02584400 | -0.62994200 | 1.47290400 |
| O | 0.30321500 | -2.79026400 | 1.47906600 |
| P | 2.38672900 | -0.83154700 | 2.52076400 |
| C | 2.33207800 | 0.09846800 | -3.18931900 |
| C | 2.71611100 | 1.17397800 | -3.99563000 |
| H | 3.72285000 | 1.56772300 | -3.92777000 |
| C | 1.80653900 | 1.76952300 | -4.87414600 |
| H | 2.12446700 | 2.60549900 | -5.48983000 |
| C | 0.49625700 | 1.30159100 | -4.94902600 |
| H | -0.21534300 | 1.76669900 | -5.62469900 |
| C | 0.09517800 | 0.23141000 | -4.14553100 |
| H | -0.92410600 | -0.13616100 | -4.19830000 |
| C | 1.00102000 | -0.37421000 | -3.27202500 |
| C | 0.57333700 | -1.56964000 | -2.46240000 |
| C | -1.22913400 | -2.57188400 | -1.14135400 |
| H | -0.46459400 | -3.20908500 | -0.70203200 |
| C | -2.19264300 | -2.09224000 | -0.02334000 |
| H | -2.80574500 | -1.30265100 | -0.46499700 |
| C | -0.47818000 | -1.89396700 | 1.83764100 |
| C | -0.31780800 | -1.22881100 | 3.18043200 |
| C | -1.43697500 | -1.13096100 | 4.01485700 |
| H | -2.38847000 | -1.51728800 | 3.66706200 |

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|---|---|---|---|
| C | -1.33364600 | -0.56740000 | 5.28596300 |
| H | -2.21241100 | -0.49898700 | 5.92009100 |
| C | -0.10156200 | -0.09001300 | 5.73164600 |
| H | -0.01132200 | 0.35965100 | 6.71615500 |
| C | 1.02269300 | -0.19208600 | 4.91146300 |
| H | 1.97388200 | 0.19755100 | 5.25793400 |
| C | 0.93497600 | -0.77103500 | 3.63866600 |
| C | 4.75516800 | 0.63307000 | -1.59551300 |
| C | 4.81931000 | 1.33229500 | -0.38158500 |
| H | 4.06109000 | 1.16858400 | 0.37817000 |
| C | 5.85116900 | 2.24218300 | -0.14133100 |
| H | 5.88339000 | 2.77788500 | 0.80199000 |
| C | 6.83026000 | 2.45705200 | -1.11229400 |
| H | 7.63242700 | 3.16626600 | -0.92891500 |
| C | 6.78467500 | 1.75124900 | -2.31928100 |
| H | 7.55260300 | 1.90789500 | -3.07150100 |
| C | 5.75969900 | 0.83601400 | -2.55624400 |
| H | 5.74014900 | 0.27475100 | -3.48568800 |
| C | 4.29160400 | -2.00738900 | -2.51825400 |
| C | 5.18311500 | -2.67682700 | -1.66614800 |
| H | 5.31462400 | -2.33689600 | -0.64238500 |
| C | 5.90569600 | -3.77627400 | -2.12854000 |
| H | 6.59323500 | -4.28862700 | -1.46120400 |
| C | 5.74303200 | -4.21616400 | -3.44528900 |
| H | 6.30392700 | -5.07372300 | -3.80602200 |
| C | 4.85640400 | -3.55132000 | -4.29544900 |
| H | 4.72683100 | -3.88964400 | -5.31978100 |
| C | 4.13016600 | -2.45119700 | -3.83514300 |
| H | 3.43525800 | -1.94401600 | -4.49572300 |
| C | 3.41686800 | 0.57741500 | 3.07950100 |

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|---|---|---|---|
| C | 4.77524000 | 0.44480000 | 3.39340500 |
| H | 5.23125300 | -0.53907600 | 3.43266700 |
| C | 5.55055600 | 1.57777900 | 3.65827400 |
| H | 6.60252700 | 1.46161100 | 3.90369000 |
| C | 4.97947000 | 2.85019000 | 3.60986400 |
| H | 5.58419000 | 3.72857300 | 3.81658300 |
| C | 3.62293300 | 2.98959000 | 3.29476200 |
| H | 3.16858800 | 3.97603200 | 3.25594700 |
| C | 2.84728200 | 1.86367100 | 3.02765200 |
| H | 1.79640500 | 1.98016700 | 2.78421300 |
| C | 3.32880200 | -2.33391700 | 2.94891700 |
| C | 3.59443300 | -2.71629900 | 4.27163200 |
| H | 3.21826800 | -2.11925900 | 5.09697500 |
| C | 4.34067700 | -3.86674500 | 4.52827100 |
| H | 4.54321400 | -4.16076300 | 5.55432500 |
| C | 4.82439000 | -4.64095500 | 3.46887000 |
| H | 5.40362000 | -5.53707900 | 3.67326100 |
| C | 4.55804800 | -4.26664100 | 2.14991800 |
| H | 4.92460800 | -4.86885900 | 1.32333900 |
| C | 3.80858600 | -3.11808100 | 1.89076900 |
| H | 3.58198700 | -2.83073900 | 0.86807700 |
| C | -1.99721800 | -3.35183600 | -2.19782400 |
| C | -2.87386800 | -2.69497900 | -3.07162500 |
| C | -1.86546900 | -4.74022500 | -2.28120700 |
| C | -3.61213700 | -3.42003300 | -4.00725500 |
| H | -2.98755500 | -1.61605100 | -3.01136200 |
| C | -2.60361300 | -5.46815700 | -3.21694700 |
| H | -1.18772800 | -5.25156700 | -1.60302100 |
| C | -3.48034600 | -4.80972500 | -4.08147400 |
| H | -4.29272700 | -2.90089900 | -4.67691200 |

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|---|---|---|---|
| H | -2.49156400 | -6.54763600 | -3.27120100 |
| H | -4.05530900 | -5.37419500 | -4.81045700 |
| C | -3.13263700 | -3.19947100 | 0.43221700 |
| C | -4.46408500 | -3.19129900 | 0.00448200 |
| C | -2.69089600 | -4.24003400 | 1.26005000 |
| C | -5.34450300 | -4.20135400 | 0.39435800 |
| H | -4.81258200 | -2.38999400 | -0.63951600 |
| C | -3.57154600 | -5.24759200 | 1.65608000 |
| H | -1.65740200 | -4.26626000 | 1.58839800 |
| C | -4.90085400 | -5.23211500 | 1.22476300 |
| H | -6.37642200 | -4.17529200 | 0.05674100 |
| H | -3.21676900 | -6.04837500 | 2.29933600 |
| H | -5.58444200 | -6.01808100 | 1.53389200 |
| C | 0.48161000 | 1.40044800 | 0.16270900 |
| C | -1.37961800 | 2.77242600 | -1.56463100 |
| N | 0.25586600 | 2.40275300 | 0.74498600 |
| C | -2.41371100 | 1.76871700 | -1.49858400 |
| C | -1.69867200 | 3.80968300 | -0.71140000 |
| H | -0.53330200 | 2.69529200 | -2.23124500 |
| C | -0.15757200 | 3.61800900 | 1.15211200 |
| N | -3.47719200 | 2.35548300 | -0.74120700 |
| O | -2.52482300 | 0.64856400 | -1.99927300 |
| C | -3.02853000 | 3.53680200 | -0.10277200 |
| H | -1.32341200 | 4.81871500 | -0.73381700 |
| C | 0.76449200 | 4.80780300 | 0.88366100 |
| C | -0.98499600 | 3.61195000 | 2.35641400 |
| N | -4.51699200 | 1.59350100 | -0.26310800 |
| O | -3.67688200 | 4.16542500 | 0.71192800 |
| H | 1.52742300 | 4.84730600 | 1.67617200 |
| H | 0.16200700 | 5.71284700 | 0.99043400 |

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|---|---|---|---|
| C | 1.45706900 | 4.80606600 | -0.46062300 |
| O | -1.33305400 | 2.62615500 | 2.99098300 |
| O | -1.35112300 | 4.87581700 | 2.70083800 |
| C | -4.20812000 | 0.82298500 | 0.87906800 |
| C | -5.73594300 | 1.50689600 | -0.95050100 |
| C | 2.55277600 | 3.96492300 | -0.70174500 |
| C | 1.02985400 | 5.65579700 | -1.49000500 |
| C | -2.27949500 | 4.96201300 | 3.78742400 |
| C | -5.29098700 | -0.02040000 | 1.34835600 |
| O | -3.08375800 | 0.89685200 | 1.36960400 |
| N | -6.65582200 | 0.68703700 | -0.55270300 |
| C | -6.03876700 | 2.42662500 | -2.14365100 |
| C | 3.19160600 | 3.96142100 | -1.94220900 |
| H | 2.91379800 | 3.31757900 | 0.09124600 |
| C | 1.66105300 | 5.65048500 | -2.73584400 |
| H | 0.20096100 | 6.33591300 | -1.31123400 |
| H | -3.19971000 | 4.42229900 | 3.55077800 |
| H | -1.84768700 | 4.55470500 | 4.70677000 |
| H | -2.48893500 | 6.02590000 | 3.91226500 |
| C | -6.46957000 | -0.08698500 | 0.57766700 |
| C | -5.14857400 | -0.79152600 | 2.51368600 |
| C | -7.38664300 | 1.99997500 | -2.75643400 |
| C | -6.18413400 | 3.87706200 | -1.63072100 |
| C | -4.97683200 | 2.36411700 | -3.26605800 |
| C | 2.74298800 | 4.79943200 | -2.96604400 |
| H | 4.04149900 | 3.30936300 | -2.10697500 |
| H | 1.31162700 | 6.31627600 | -3.52042700 |
| C | -7.49470300 | -0.96503200 | 0.98079900 |
| C | -6.16958800 | -1.64163600 | 2.90278700 |
| H | -4.23806100 | -0.69866400 | 3.09318300 |

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|---|---|---|---|
| H | -7.34094100 | 0.98142700 | -3.15487500 |
| H | -8.19664800 | 2.04027200 | -2.02513200 |
| H | -7.62559900 | 2.68173700 | -3.57958100 |
| H | -5.27333100 | 4.25058200 | -1.16099900 |
| H | -6.42579400 | 4.53155100 | -2.47583100 |
| H | -6.99732900 | 3.94984500 | -0.89988700 |
| H | -5.41738200 | 2.77417500 | -4.18121900 |
| H | -4.08904500 | 2.95560600 | -3.03933500 |
| H | -4.66577200 | 1.33612400 | -3.47270500 |
| H | 3.24101800 | 4.79544800 | -3.93161100 |
| C | -7.34044800 | -1.73178800 | 2.12597200 |
| H | -8.39717600 | -1.01701300 | 0.38018000 |
| H | -6.06570300 | -2.24407900 | 3.79949100 |
| H | -8.13466900 | -2.40717100 | 2.43027000 |

**L9-TS2-B**

| | | | |
|---|---|---|---|
| Ag | -0.02921200 | 1.33356700 | 0.09508100 |
| O | 2.99014500 | 2.30092900 | -0.93804500 |
| N | 2.97238200 | 0.04211600 | -1.26612000 |
| H | 2.62738600 | -0.71801600 | -1.85139600 |
| P | 0.23608500 | 3.24493800 | -1.55817000 |
| N | 2.39077200 | -1.47882600 | 1.31986800 |
| H | 1.91866000 | -2.37211900 | 1.38415900 |
| O | 2.37280500 | 0.66881000 | 2.13142000 |
| P | -0.42329800 | 1.54611800 | 2.55040600 |
| C | 0.93999200 | 2.44884700 | -3.06576600 |
| C | 0.35180400 | 2.63777700 | -4.32203500 |
| H | -0.45951700 | 3.34765200 | -4.43548800 |
| C | 0.78571300 | 1.91165100 | -5.43406700 |

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|---|---|---|---|
| H | 0.31528000 | 2.07678100 | -6.39908400 |
| C | 1.81479200 | 0.98130900 | -5.30201800 |
| H | 2.15878800 | 0.41549500 | -6.16282500 |
| C | 2.40606000 | 0.77684600 | -4.05465100 |
| H | 3.21386500 | 0.06162100 | -3.95111600 |
| C | 1.97598800 | 1.49596700 | -2.93499200 |
| C | 2.68444600 | 1.31541900 | -1.62176000 |
| C | 3.97762900 | -0.24847500 | -0.25098400 |
| H | 3.98765400 | 0.59520500 | 0.43478300 |
| C | 3.63512400 | -1.53703100 | 0.54171000 |
| H | 3.46490600 | -2.33200400 | -0.19093300 |
| C | 1.94661300 | -0.49419100 | 2.13599500 |
| C | 0.87908900 | -0.90855300 | 3.11407100 |
| C | 1.00761000 | -2.13777300 | 3.77258800 |
| H | 1.85225700 | -2.77694000 | 3.54156700 |
| C | 0.09113500 | -2.53087500 | 4.74786100 |
| H | 0.21362100 | -3.48433100 | 5.25295600 |
| C | -0.97207400 | -1.68926600 | 5.07022600 |
| H | -1.69680900 | -1.98316700 | 5.82362100 |
| C | -1.10753200 | -0.45928200 | 4.42322700 |
| H | -1.94975800 | 0.17710900 | 4.67001700 |
| C | -0.18645600 | -0.04373500 | 3.45355900 |
| C | -1.36820500 | 3.91694800 | -2.13817400 |
| C | -1.49447300 | 5.17981200 | -2.73844500 |
| H | -0.62275000 | 5.81472000 | -2.85975500 |
| C | -2.74059300 | 5.62168500 | -3.18486800 |
| H | -2.83022500 | 6.60071900 | -3.64756200 |
| C | -3.86855200 | 4.80811300 | -3.04086000 |
| H | -4.83705100 | 5.15593200 | -3.38957700 |
| C | -3.74666100 | 3.55093800 | -2.44530500 |

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|---|---|---|---|
| H | -4.61549200 | 2.90925400 | -2.32800200 |
| C | -2.50333800 | 3.10894700 | -1.99010400 |
| H | -2.42984200 | 2.12623700 | -1.53392900 |
| C | 1.19686900 | 4.77216400 | -1.25071800 |
| C | 0.75866900 | 5.62286400 | -0.22436200 |
| H | -0.12917300 | 5.36979100 | 0.34909400 |
| C | 1.45339900 | 6.79871700 | 0.06141300 |
| H | 1.10535800 | 7.44926100 | 0.85883300 |
| C | 2.59107600 | 7.13530100 | -0.67724200 |
| H | 3.13491000 | 8.04906100 | -0.45459700 |
| C | 3.02532300 | 6.29440200 | -1.70457200 |
| H | 3.90704800 | 6.55295100 | -2.28448500 |
| C | 2.33254000 | 5.11687100 | -1.99128100 |
| H | 2.68024900 | 4.46282700 | -2.78288500 |
| C | -2.18946200 | 1.94409800 | 2.85283000 |
| C | -2.65917600 | 2.64744000 | 3.97145000 |
| H | -1.96035800 | 3.01777600 | 4.71439200 |
| C | -4.02794900 | 2.87227600 | 4.13490300 |
| H | -4.38269300 | 3.41949200 | 5.00397400 |
| C | -4.93883100 | 2.39468800 | 3.18861200 |
| H | -6.00292800 | 2.56775400 | 3.32307500 |
| C | -4.47678600 | 1.70641600 | 2.06400900 |
| H | -5.17316500 | 1.34024900 | 1.31525100 |
| C | -3.10906300 | 1.49425500 | 1.89002600 |
| H | -2.76692300 | 0.98216100 | 0.99553100 |
| C | 0.52401700 | 2.78181200 | 3.50444600 |
| C | 0.66929800 | 2.72285600 | 4.89748300 |
| H | 0.22771600 | 1.90410600 | 5.45764200 |
| C | 1.39098500 | 3.71299000 | 5.56696300 |
| H | 1.50147300 | 3.66183700 | 6.64660800 |

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|---|---|---|---|
| C | 1.97378900 | 4.76324000 | 4.85219300 |
| H | 2.53673000 | 5.53024300 | 5.37673300 |
| C | 1.84133100 | 4.81861200 | 3.46248500 |
| H | 2.30231700 | 5.62295300 | 2.89611900 |
| C | 1.12436100 | 3.82811500 | 2.79170900 |
| H | 1.04629900 | 3.85443600 | 1.70997600 |
| C | 5.34349900 | -0.39658000 | -0.90841400 |
| C | 5.51779000 | -1.26100500 | -1.99794900 |
| C | 6.44354200 | 0.31358800 | -0.42130600 |
| C | 6.77454700 | -1.41746100 | -2.58245200 |
| H | 4.66935600 | -1.81473500 | -2.39221100 |
| C | 7.70302100 | 0.15963200 | -1.00550300 |
| H | 6.31235100 | 0.98325900 | 0.42402400 |
| C | 7.87221900 | -0.70814500 | -2.08594200 |
| H | 6.89794000 | -2.09251200 | -3.42507300 |
| H | 8.54991400 | 0.71841300 | -0.61667600 |
| H | 8.85112300 | -0.82920400 | -2.54158700 |
| C | 4.80083300 | -1.95791000 | 1.42682700 |
| C | 5.11965700 | -1.23886900 | 2.58656200 |
| C | 5.58645900 | -3.05849200 | 1.07189500 |
| C | 6.20554000 | -1.61938600 | 3.37548500 |
| H | 4.52434600 | -0.37610100 | 2.86724000 |
| C | 6.67461800 | -3.43986800 | 1.85947500 |
| H | 5.34588600 | -3.61458000 | 0.17125500 |
| C | 6.98681700 | -2.72081100 | 3.01473700 |
| H | 6.44370500 | -1.05228000 | 4.27126200 |
| H | 7.27587000 | -4.29760000 | 1.57035900 |
| H | 7.83311700 | -3.01457900 | 3.62952800 |
| C | -0.03463800 | -0.73217700 | -0.71069500 |
| C | -1.78509200 | -0.90178200 | -2.63164700 |

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|---|---|---|---|
| N | 0.22433200 | -1.85035000 | -1.00637400 |
| C | -2.77064200 | -0.73264800 | -1.62773100 |
| C | -1.58295900 | -2.28621300 | -2.88236200 |
| H | -1.30325700 | -0.07449900 | -3.13369600 |
| C | 0.05355100 | -2.92278100 | -1.85968300 |
| N | -3.19221300 | -2.08972700 | -1.23502300 |
| O | -3.30155500 | 0.23920400 | -1.08842100 |
| C | -2.69868600 | -3.00891600 | -2.17068500 |
| H | -1.30707100 | -2.68730100 | -3.85204600 |
| C | -0.19746100 | -4.26683900 | -1.17351600 |
| C | 1.11067900 | -2.92848700 | -2.91133300 |
| N | -4.46990000 | -2.19905300 | -0.71316600 |
| O | -3.08798700 | -4.15308200 | -2.31579100 |
| H | -0.46113800 | -4.99136300 | -1.94705000 |
| H | -1.06035700 | -4.16826300 | -0.51576200 |
| C | 0.98756800 | -4.74522700 | -0.35954200 |
| O | 1.99857000 | -2.09343200 | -3.03528400 |
| O | 0.95105000 | -3.94760500 | -3.76777200 |
| C | -5.49550000 | -1.85787700 | -1.63644900 |
| C | -4.69152000 | -2.36200500 | 0.65873200 |
| C | 2.11422700 | -5.31392000 | -0.97216400 |
| C | 0.97931000 | -4.60847400 | 1.03571100 |
| C | 1.90398200 | -4.01283700 | -4.84845300 |
| C | -6.80209400 | -1.65058600 | -1.02908400 |
| O | -5.23120200 | -1.73575800 | -2.82574800 |
| N | -5.86421800 | -2.15884400 | 1.17084400 |
| C | -3.59657500 | -2.93503600 | 1.57104300 |
| C | 3.20688400 | -5.72951000 | -0.20960100 |
| H | 2.12833400 | -5.44593500 | -2.04992100 |
| C | 2.06856000 | -5.03479100 | 1.80133100 |

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|---|---|---|---|
| H | 0.11074300 | -4.17296100 | 1.52285900 |
| H | 1.62287100 | -4.89121800 | -5.42875500 |
| H | 1.84085100 | -3.11150300 | -5.46268400 |
| H | 2.91832500 | -4.12162900 | -4.45671000 |
| C | -6.92332200 | -1.77507200 | 0.36950500 |
| C | -7.90700900 | -1.28283900 | -1.81480100 |
| C | -3.38470600 | -4.41036500 | 1.15819400 |
| C | -2.26050500 | -2.17049900 | 1.52394000 |
| C | -4.08740000 | -2.90071000 | 3.02998000 |
| C | 3.18859800 | -5.59039700 | 1.18074100 |
| H | 4.07019900 | -6.17001000 | -0.70085100 |
| H | 2.03996500 | -4.93799800 | 2.88253200 |
| C | -8.17113200 | -1.51673600 | 0.97031000 |
| C | -9.12916100 | -1.03578500 | -1.20935800 |
| H | -7.77900800 | -1.19330600 | -2.88846800 |
| H | -2.56823600 | -4.84192900 | 1.74846500 |
| H | -4.29033300 | -4.99702000 | 1.35151400 |
| H | -3.14191600 | -4.51507800 | 0.09844600 |
| H | -1.73889000 | -2.29554600 | 0.58252700 |
| H | -2.41070300 | -1.10261900 | 1.69307300 |
| H | -1.61738000 | -2.54674200 | 2.32479800 |
| H | -4.25718100 | -1.87367400 | 3.36913900 |
| H | -5.01659200 | -3.45909900 | 3.16212400 |
| H | -3.31652100 | -3.34792700 | 3.66700100 |
| H | 4.03839200 | -5.91274100 | 1.77450900 |
| C | -9.25613200 | -1.15141600 | 0.18800200 |
| H | -8.25584800 | -1.61509200 | 2.04803700 |
| H | -9.98808600 | -0.75222300 | -1.80980200 |
| H | -10.21532900 | -0.95443900 | 0.65831900 |

**L9-Int3-A**

| | | | |
|---|---|---|---|
| Ag | 1.94844800 | -0.33951200 | 0.17524300 |
| O | 1.31302600 | -1.67162100 | -2.67871400 |
| N | -0.66167200 | -0.77848900 | -1.96489600 |
| H | -1.28644500 | 0.04316400 | -1.94047300 |
| P | 3.38368400 | 0.14161600 | -1.81536600 |
| N | -1.52690200 | -1.67675400 | 0.78434600 |
| H | -2.01295900 | -0.99828300 | 1.36995000 |
| O | 0.29536500 | -3.07740100 | 0.69857200 |
| P | 2.47517200 | -1.68099400 | 2.18570200 |
| C | 2.29513400 | 1.06193900 | -2.97980200 |
| C | 2.68904500 | 2.24838700 | -3.60350800 |
| H | 3.70532800 | 2.60636200 | -3.49291100 |
| C | 1.77828300 | 2.99745700 | -4.35404800 |
| H | 2.10610800 | 3.91352900 | -4.83545200 |
| C | 0.45358700 | 2.58213200 | -4.46505900 |
| H | -0.26073800 | 3.17016600 | -5.03348800 |
| C | 0.04153300 | 1.40253300 | -3.84129300 |
| H | -0.99002600 | 1.07809800 | -3.92134800 |
| C | 0.95262700 | 0.63355800 | -3.11285800 |
| C | 0.54361400 | -0.70309000 | -2.56397800 |
| C | -1.27195900 | -2.07916100 | -1.70244000 |
| H | -0.47254600 | -2.77691000 | -1.46515800 |
| C | -2.21894700 | -1.96527200 | -0.47835100 |
| H | -2.84083500 | -1.08556900 | -0.66178100 |
| C | -0.46205600 | -2.31336100 | 1.31787300 |
| C | -0.24593400 | -2.07354300 | 2.78969600 |
| C | -1.34166400 | -2.15438700 | 3.65571400 |
| H | -2.32585300 | -2.34703500 | 3.24406800 |

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|---|---|---|---|
| C | -1.17429200 | -2.03014400 | 5.03475200 |
| H | -2.03550000 | -2.10058300 | 5.69227600 |
| C | 0.09949200 | -1.81621000 | 5.55974200 |
| H | 0.24106100 | -1.71342800 | 6.63162000 |
| C | 1.20061200 | -1.73710300 | 4.70513000 |
| H | 2.18645500 | -1.55541300 | 5.12028900 |
| C | 1.04783000 | -1.87709200 | 3.31979600 |
| C | 4.72105000 | 1.29113800 | -1.30553400 |
| C | 4.77322400 | 1.68561000 | 0.03966300 |
| H | 4.01174300 | 1.34384000 | 0.73457500 |
| C | 5.79848000 | 2.51437100 | 0.49893800 |
| H | 5.82530400 | 2.80494900 | 1.54486300 |
| C | 6.78249700 | 2.95979600 | -0.38550300 |
| H | 7.58072300 | 3.60615000 | -0.03170000 |
| C | 6.74750300 | 2.56183300 | -1.72611700 |
| H | 7.51898800 | 2.89660600 | -2.41378400 |
| C | 5.73062800 | 1.72272400 | -2.18142100 |
| H | 5.72648000 | 1.39426700 | -3.21638900 |
| C | 4.31959800 | -1.08263800 | -2.80036900 |
| C | 5.27848200 | -1.86171100 | -2.13527300 |
| H | 5.44879100 | -1.72213700 | -1.07101000 |
| C | 6.01701700 | -2.81575400 | -2.83506500 |
| H | 6.75606000 | -3.41560700 | -2.31110900 |
| C | 5.80447900 | -2.99862300 | -4.20441400 |
| H | 6.37751600 | -3.74332300 | -4.74959900 |
| C | 4.85185900 | -2.22312400 | -4.86912200 |
| H | 4.68257300 | -2.36167700 | -5.93339400 |
| C | 4.10957300 | -1.26846400 | -4.17087500 |
| H | 3.36391200 | -0.67481400 | -4.68883800 |
| C | 3.63171100 | -0.60046100 | 3.11352900 |

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|---|---|---|---|
| C | 4.96786000 | -0.94675700 | 3.34915900 |
| H | 5.32336500 | -1.94177400 | 3.10166100 |
| C | 5.85153200 | -0.01277100 | 3.89842800 |
| H | 6.88615300 | -0.29343700 | 4.07517700 |
| C | 5.40958100 | 1.27042700 | 4.22182100 |
| H | 6.09855800 | 1.99385200 | 4.64825600 |
| C | 4.07388500 | 1.62192200 | 3.99414000 |
| H | 3.72112400 | 2.61848900 | 4.24548400 |
| C | 3.19253200 | 0.69701700 | 3.43881200 |
| H | 2.15969600 | 0.98072900 | 3.25645500 |
| C | 3.30849700 | -3.29731300 | 2.06240000 |
| C | 3.47388700 | -4.15273700 | 3.16065900 |
| H | 3.07750600 | -3.87457000 | 4.13250200 |
| C | 4.14664000 | -5.36512700 | 3.00423600 |
| H | 4.27016300 | -6.02734700 | 3.85655500 |
| C | 4.65795000 | -5.72852800 | 1.75459100 |
| H | 5.17976100 | -6.67406100 | 1.63657100 |
| C | 4.49332300 | -4.87972500 | 0.65762200 |
| H | 4.88119500 | -5.16060800 | -0.31741700 |
| C | 3.81538700 | -3.66962700 | 0.80939100 |
| H | 3.66742600 | -3.01549200 | -0.04473300 |
| C | -2.02842000 | -2.56843700 | -2.92828700 |
| C | -2.92111800 | -1.72408200 | -3.60322700 |
| C | -1.86502600 | -3.88281600 | -3.37401000 |
| C | -3.64285900 | -2.19525100 | -4.70025200 |
| H | -3.06133300 | -0.70328600 | -3.25895200 |
| C | -2.58795900 | -4.35612300 | -4.47125700 |
| H | -1.17597800 | -4.54027400 | -2.85069000 |
| C | -3.48035200 | -3.51339100 | -5.13687200 |
| H | -4.33598300 | -1.53347700 | -5.21315400 |

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|---|---|---|---|
| H | -2.45208300 | -5.38113300 | -4.80569300 |
| H | -4.04403600 | -3.87935500 | -5.99077600 |
| C | -3.14408100 | -3.16726700 | -0.35616300 |
| C | -4.45394300 | -3.07054100 | -0.83848400 |
| C | -2.71214900 | -4.38133400 | 0.19292000 |
| C | -5.31876500 | -4.16312300 | -0.78014700 |
| H | -4.79589400 | -2.13346300 | -1.26545700 |
| C | -3.57928400 | -5.47331000 | 0.26078800 |
| H | -1.69489500 | -4.47963200 | 0.55541100 |
| C | -4.88441800 | -5.36918000 | -0.22639400 |
| H | -6.33291300 | -4.06709800 | -1.15658400 |
| H | -3.23084600 | -6.40920100 | 0.68940400 |
| H | -5.55704900 | -6.22096300 | -0.17475100 |
| C | 0.58841800 | 1.32091400 | 0.86373700 |
| C | -1.50561700 | 3.00147400 | -0.79371800 |
| N | 0.08129500 | 2.26831000 | 1.31422800 |
| C | -2.48232700 | 2.06639200 | -1.01384400 |
| C | -1.73147900 | 3.71635500 | 0.50516800 |
| H | -0.59966200 | 3.07621800 | -1.37642300 |
| C | -0.57468000 | 3.50034100 | 1.58991100 |
| N | -3.55005500 | 2.35688800 | -0.01649200 |
| O | -2.68403900 | 1.12567100 | -1.82893600 |
| C | -3.09853700 | 3.18635600 | 0.98079100 |
| H | -1.82869700 | 4.80674200 | 0.43644700 |
| C | 0.47276200 | 4.65694100 | 1.54897200 |
| C | -1.12047600 | 3.41448000 | 3.02794400 |
| N | -4.56100400 | 1.45799500 | 0.23390200 |
| O | -3.70648000 | 3.46516100 | 2.00240100 |
| H | 1.19141700 | 4.46611300 | 2.35325800 |
| H | -0.08047800 | 5.56034400 | 1.81233800 |

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|---|---|---|---|
| C | 1.21422000 | 4.86675400 | 0.25278300 |
| O | -1.13685500 | 2.40450300 | 3.69561900 |
| O | -1.52547600 | 4.61726900 | 3.44231600 |
| C | -4.23732200 | 0.44203900 | 1.15581300 |
| C | -5.77923500 | 1.52459300 | -0.44813100 |
| C | 2.48050300 | 4.29778500 | 0.06274900 |
| C | 0.69044700 | 5.69365300 | -0.75131600 |
| C | -2.19029700 | 4.64031800 | 4.71915400 |
| C | -5.28216600 | -0.54336600 | 1.35670900 |
| O | -3.13310600 | 0.44102500 | 1.70365200 |
| N | -6.66955500 | 0.59324000 | -0.30284100 |
| C | -6.13577600 | 2.75523700 | -1.29817600 |
| C | 3.21443800 | 4.56138200 | -1.09454600 |
| H | 2.90430400 | 3.66679400 | 0.83869100 |
| C | 1.41600500 | 5.94884000 | -1.91519100 |
| H | -0.28292700 | 6.15541100 | -0.61182200 |
| H | -3.10096800 | 4.03986700 | 4.66941300 |
| H | -1.53052600 | 4.25762800 | 5.50155600 |
| H | -2.43161900 | 5.68737600 | 4.90277400 |
| C | -6.45212700 | -0.45021500 | 0.57544600 |
| C | -5.11557600 | -1.59132600 | 2.27781400 |
| C | -7.49145300 | 2.49971600 | -1.98387100 |
| C | -6.29350700 | 3.97002700 | -0.35386900 |
| C | -5.10974700 | 3.08388900 | -2.40635900 |
| C | 2.68477700 | 5.39089500 | -2.08419900 |
| H | 4.20044000 | 4.12803500 | -1.21723300 |
| H | 0.99637500 | 6.59503400 | -2.68121300 |
| C | -7.44299000 | -1.44245800 | 0.71617200 |
| C | -6.10209700 | -2.55285300 | 2.41143800 |
| H | -4.21372100 | -1.62059300 | 2.87724200 |

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|---|---|---|---|
| H | -7.43103700 | 1.66605000 | -2.69102500 |
| H | -8.27882700 | 2.27305600 | -1.26178100 |
| H | -7.77595900 | 3.40022400 | -2.53884700 |
| H | -5.38161000 | 4.18657400 | 0.20547400 |
| H | -6.54610200 | 4.85419100 | -0.95013000 |
| H | -7.10256700 | 3.80571600 | 0.36666700 |
| H | -5.58148600 | 3.77371000 | -3.11515800 |
| H | -4.21293500 | 3.56925300 | -2.02050000 |
| H | -4.80175800 | 2.18788000 | -2.95065000 |
| H | 3.25878200 | 5.60203300 | -2.98184500 |
| C | -7.26437900 | -2.47819300 | 1.61975500 |
| H | -8.33981200 | -1.36705700 | 0.10965400 |
| H | -5.97803600 | -3.36759400 | 3.11764000 |
| H | -8.03172600 | -3.24010600 | 1.72162300 |

**L9-Int3-B**

| | | | |
|---|---|---|---|
| Ag | 0.10550600 | 1.17334700 | 0.08445900 |
| O | 2.95988000 | 2.02564400 | -1.44002400 |
| N | 2.87400800 | -0.25152500 | -1.46814800 |
| H | 2.38913000 | -1.07667100 | -1.81557700 |
| P | 0.30180400 | 3.10965100 | -1.72311300 |
| N | 2.35794700 | -1.39700000 | 1.24232400 |
| H | 1.51538400 | -1.83973800 | 0.85633600 |
| O | 2.95125600 | 0.54308200 | 2.32784400 |
| P | 0.12431600 | 1.94764400 | 2.45395900 |
| C | 0.61371900 | 2.02481600 | -3.18561800 |
| C | -0.23096800 | 2.04788200 | -4.30234100 |
| H | -0.99459900 | 2.81327300 | -4.38334700 |
| C | -0.11813000 | 1.08742300 | -5.31164100 |

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|---|---|---|---|
| H | -0.78457300 | 1.12853200 | -6.16854200 |
| C | 0.84506200 | 0.08420000 | -5.21697800 |
| H | 0.94162800 | -0.66235000 | -5.99999000 |
| C | 1.69571000 | 0.04688600 | -4.11092600 |
| H | 2.45646500 | -0.72242300 | -4.04203500 |
| C | 1.58498500 | 0.99966300 | -3.09293400 |
| C | 2.52985200 | 0.96887300 | -1.92589500 |
| C | 3.94330600 | -0.44682600 | -0.49735500 |
| H | 4.02805200 | 0.46593100 | 0.09006200 |
| C | 3.56538200 | -1.62371600 | 0.44064200 |
| H | 3.29040000 | -2.46088000 | -0.20628800 |
| C | 2.18633600 | -0.41601200 | 2.16083300 |
| C | 1.03813200 | -0.62464800 | 3.11952100 |
| C | 0.96442400 | -1.85149900 | 3.78692400 |
| H | 1.66189500 | -2.63635300 | 3.51573400 |
| C | 0.03353500 | -2.05603100 | 4.80862900 |
| H | -0.00645000 | -3.01292000 | 5.32077900 |
| C | -0.83435000 | -1.02611500 | 5.16697800 |
| H | -1.56265100 | -1.17205400 | 5.95950900 |
| C | -0.77809200 | 0.19902700 | 4.49622000 |
| H | -1.47650300 | 0.98488200 | 4.76294400 |
| C | 0.15534700 | 0.41931900 | 3.47705000 |
| C | -1.32848900 | 3.86942400 | -2.10708000 |
| C | -1.47633400 | 5.03201000 | -2.88037700 |
| H | -0.60110900 | 5.52462600 | -3.29164200 |
| C | -2.74575100 | 5.55805700 | -3.12397900 |
| H | -2.84971300 | 6.45920000 | -3.72223900 |
| C | -3.88018700 | 4.93049000 | -2.60016300 |
| H | -4.86659800 | 5.34542000 | -2.78846300 |
| C | -3.74057200 | 3.77132100 | -1.83415200 |

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|---|---|---|---|
| H | -4.61577100 | 3.27560100 | -1.42322700 |
| C | -2.47094100 | 3.24776700 | -1.58482700 |
| H | -2.37446700 | 2.34195900 | -0.99754600 |
| C | 1.40731700 | 4.56344500 | -1.86946500 |
| C | 1.27148100 | 5.57328800 | -0.90375300 |
| H | 0.52118400 | 5.47857800 | -0.12270300 |
| C | 2.09077500 | 6.70201200 | -0.94043900 |
| H | 1.97658700 | 7.47502500 | -0.18541000 |
| C | 3.05353700 | 6.83442600 | -1.94460000 |
| H | 3.69483200 | 7.71093000 | -1.97307300 |
| C | 3.18875000 | 5.83448400 | -2.91084900 |
| H | 3.93416600 | 5.93306000 | -3.69538100 |
| C | 2.37030100 | 4.70384400 | -2.87498600 |
| H | 2.48779400 | 3.92775700 | -3.62356500 |
| C | -1.51492600 | 2.68283700 | 2.82925900 |
| C | -1.72327100 | 3.66404200 | 3.80792700 |
| H | -0.88958700 | 4.02772700 | 4.39978400 |
| C | -3.00391600 | 4.17924300 | 4.02451000 |
| H | -3.15441700 | 4.94129800 | 4.78418700 |
| C | -4.08545800 | 3.72009200 | 3.26926000 |
| H | -5.07915700 | 4.12472100 | 3.43988500 |
| C | -3.88417100 | 2.74465000 | 2.28842400 |
| H | -4.71699000 | 2.38566900 | 1.69014200 |
| C | -2.60597300 | 2.23553500 | 2.06478100 |
| H | -2.45493600 | 1.49119400 | 1.28937400 |
| C | 1.33208300 | 3.09987600 | 3.18970800 |
| C | 1.65692500 | 3.09641000 | 4.55299200 |
| H | 1.20316200 | 2.36697400 | 5.21753400 |
| C | 2.57055200 | 4.02494000 | 5.05426600 |
| H | 2.82207600 | 4.01722900 | 6.11124200 |

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|---|---|---|---|
| C | 3.16363600 | 4.95925700 | 4.19994100 |
| H | 3.87573200 | 5.67909500 | 4.59380800 |
| C | 2.84835000 | 4.95946700 | 2.83892200 |
| H | 3.31449300 | 5.67426500 | 2.16644100 |
| C | 1.94037500 | 4.02842000 | 2.33406600 |
| H | 1.71410900 | 4.01190500 | 1.27265000 |
| C | 5.25778600 | -0.72305800 | -1.21041300 |
| C | 5.34693300 | -1.75119500 | -2.15950300 |
| C | 6.39755500 | 0.02981800 | -0.91575500 |
| C | 6.55761000 | -2.02164500 | -2.79692800 |
| H | 4.46558600 | -2.33940800 | -2.40168800 |
| C | 7.61095300 | -0.23781300 | -1.55436600 |
| H | 6.33286600 | 0.82829800 | -0.18155800 |
| C | 7.69497000 | -1.26639600 | -2.49444600 |
| H | 6.61502800 | -2.82232800 | -3.52964600 |
| H | 8.48844200 | 0.35768200 | -1.31704800 |
| H | 8.63780000 | -1.47630100 | -2.99211300 |
| C | 4.73659700 | -2.09481400 | 1.29027500 |
| C | 5.40615600 | -1.25178900 | 2.18928500 |
| C | 5.18194800 | -3.41400700 | 1.14710300 |
| C | 6.48283100 | -1.73002300 | 2.93758900 |
| H | 5.07694500 | -0.22680000 | 2.30496200 |
| C | 6.25938800 | -3.89379200 | 1.89418600 |
| H | 4.68055700 | -4.06930500 | 0.44202300 |
| C | 6.91300800 | -3.05192000 | 2.79557100 |
| H | 6.99028500 | -1.06438200 | 3.63090400 |
| H | 6.58751400 | -4.92222000 | 1.76819700 |
| H | 7.75304600 | -3.41963000 | 3.37866800 |
| C | -0.38607500 | -0.77104200 | -0.78046600 |
| C | -1.55553700 | -0.90395200 | -1.78939000 |

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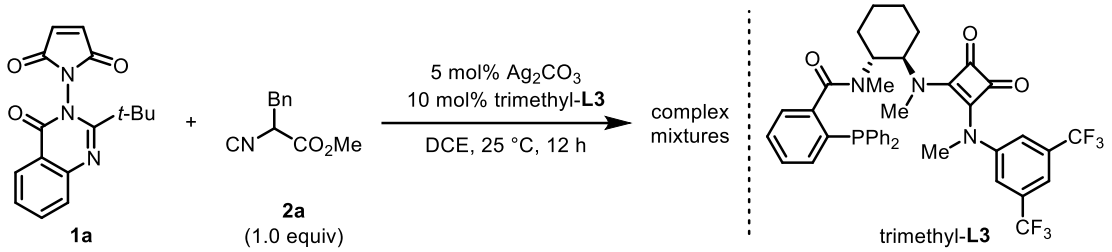
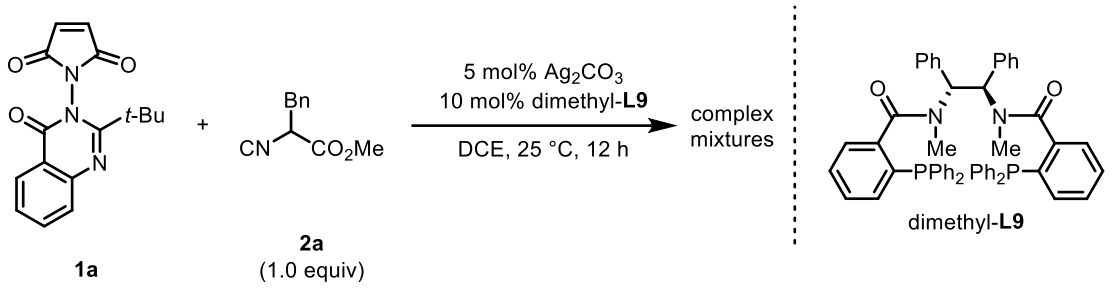
|---|---|---|---|
| N | 0.20740400 | -1.90263900 | -0.61599700 |
| C | -2.84754700 | -0.65356200 | -1.05773500 |
| C | -1.58512300 | -2.38994500 | -2.18964300 |
| H | -1.44390500 | -0.19219900 | -2.61133800 |
| C | -0.30362800 | -2.97757700 | -1.47909900 |
| N | -3.45648800 | -1.90912300 | -0.85644900 |
| O | -3.31964100 | 0.37533100 | -0.62499200 |
| C | -2.90352300 | -2.92746600 | -1.65248900 |
| H | -1.56594500 | -2.56866500 | -3.26466200 |
| C | -0.58714200 | -4.26085400 | -0.65452800 |
| C | 0.76678400 | -3.28892400 | -2.53028000 |
| N | -4.75532400 | -1.94491400 | -0.39532600 |
| O | -3.41861500 | -4.00826800 | -1.83059200 |
| H | -1.07784100 | -4.98674600 | -1.30700100 |
| H | -1.30274900 | -3.97984700 | 0.12078000 |
| C | 0.62683800 | -4.87743600 | -0.00378600 |
| O | 1.87762300 | -2.78841800 | -2.57748400 |
| O | 0.34318600 | -4.20166800 | -3.40812200 |
| C | -5.70523800 | -1.58177300 | -1.39361700 |
| C | -5.05975500 | -2.09940400 | 0.96624000 |
| C | 1.43296500 | -5.79332500 | -0.69426700 |
| C | 0.95783200 | -4.55723000 | 1.31932000 |
| C | 1.28061700 | -4.57486100 | -4.44185100 |
| C | -7.05879900 | -1.43437400 | -0.88628400 |
| O | -5.33730500 | -1.40911600 | -2.54764000 |
| N | -6.27349000 | -1.93402700 | 1.37975300 |
| C | -3.99867300 | -2.57836100 | 1.97097000 |
| C | 2.54562500 | -6.37070500 | -0.07852900 |
| H | 1.17710400 | -6.07020000 | -1.71331500 |
| C | 2.06732600 | -5.13275300 | 1.93861100 |

| | | | |
|---|---|---|---|
| H | 0.33580600 | -3.85532500 | 1.86650800 |
| H | 0.77453800 | -5.34207900 | -5.02694000 |
| H | 1.51498300 | -3.70883700 | -5.06565500 |
| H | 2.19698800 | -4.97039700 | -3.99843800 |
| C | -7.28425800 | -1.59752200 | 0.49649100 |
| C | -8.11205100 | -1.09397800 | -1.75111400 |
| C | -3.72939700 | -4.07469700 | 1.68682100 |
| C | -2.67562500 | -1.77987400 | 1.95058500 |
| C | -4.57699400 | -2.45275000 | 3.39332000 |
| C | 2.86512600 | -6.04332800 | 1.24117900 |
| H | 3.15585700 | -7.08321900 | -0.62697000 |
| H | 2.31118200 | -4.87034200 | 2.96435200 |
| C | -8.58740900 | -1.41530500 | 0.99780700 |
| C | -9.38915400 | -0.92098400 | -1.24180800 |
| H | -7.90250700 | -0.97114700 | -2.80840000 |
| H | -2.92261900 | -4.42979100 | 2.33773800 |
| H | -4.62442500 | -4.67162700 | 1.89479100 |
| H | -3.44239000 | -4.26089000 | 0.65012500 |
| H | -2.03163600 | -2.02411500 | 1.10882500 |
| H | -2.85243100 | -0.70131900 | 1.95530800 |
| H | -2.11687700 | -2.02414900 | 2.85789400 |
| H | -4.77364400 | -1.40695200 | 3.65169000 |
| H | -5.50761600 | -3.01206600 | 3.50627800 |
| H | -3.84206500 | -2.84842800 | 4.10242800 |
| H | 3.72871000 | -6.49282400 | 1.72274200 |
| C | -9.62244600 | -1.08204500 | 0.13703500 |
| H | -8.75431100 | -1.54327100 | 2.06255300 |
| H | -10.20955700 | -0.66048400 | -1.90319900 |
| H | -10.62521400 | -0.94450400 | 0.53101600 |

## V. Control experiments




To a 10 mL vial charged with trimethyl-**L3**[1] (7.5 mg, 0.010 mmol) and $Ag_2CO_3$ (1.4 mg, 0.005 mmol) was added anhydrous DCE (1.0 mL). The mixture was stirred for 10 min, and then N-quinazolinone maleimide **1a** (29.7 mg, 0.10 mmol) and isocyanoacetate **2a** (18.9 mg, 0.10 mmol) were added successively in one portion. The reaction mixture was stirred at 25 ℃ for 12 h. It was found that complex mixtures were obtained. Such a result further demonstrates the importance of the free NH in **L3** for this reaction and is consistent with the DFT calculations.




To a 10 mL vial charged with dimethyl-**L9**[27] (8.2 mg, 0.010 mmol) and $Ag_2CO_3$ (1.4 mg, 0.005 mmol) was added anhydrous DCE (1.0 mL). The mixture was stirred for 10 min, and then N-quinazolinone maleimide **1a** (29.7 mg, 0.10 mmol) and isocyanoacetate **2a** (18.9 mg, 0.10 mmol) were added successively in one portion. The reaction mixture was stirred at 25 ℃ for 12 h. It was found that complex mixtures were obtained. Such a result further demonstrates the importance of the free NH in **L9** for this reaction and is consistent with the DFT calculations.

## 12. References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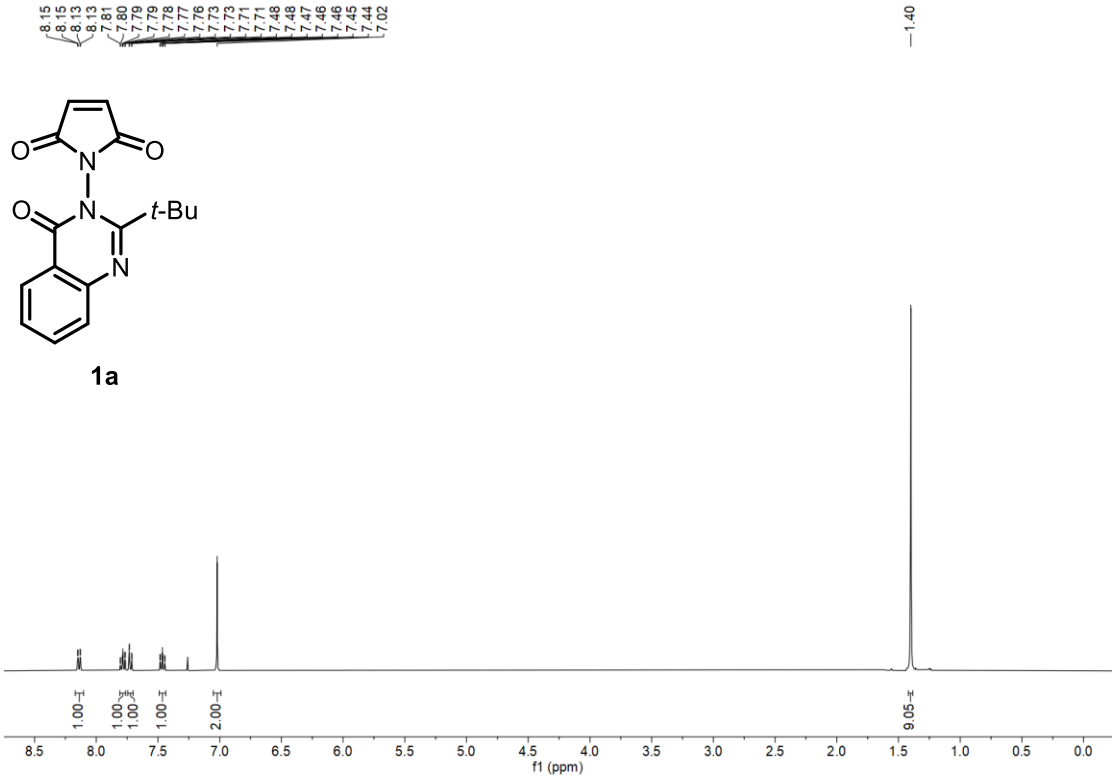
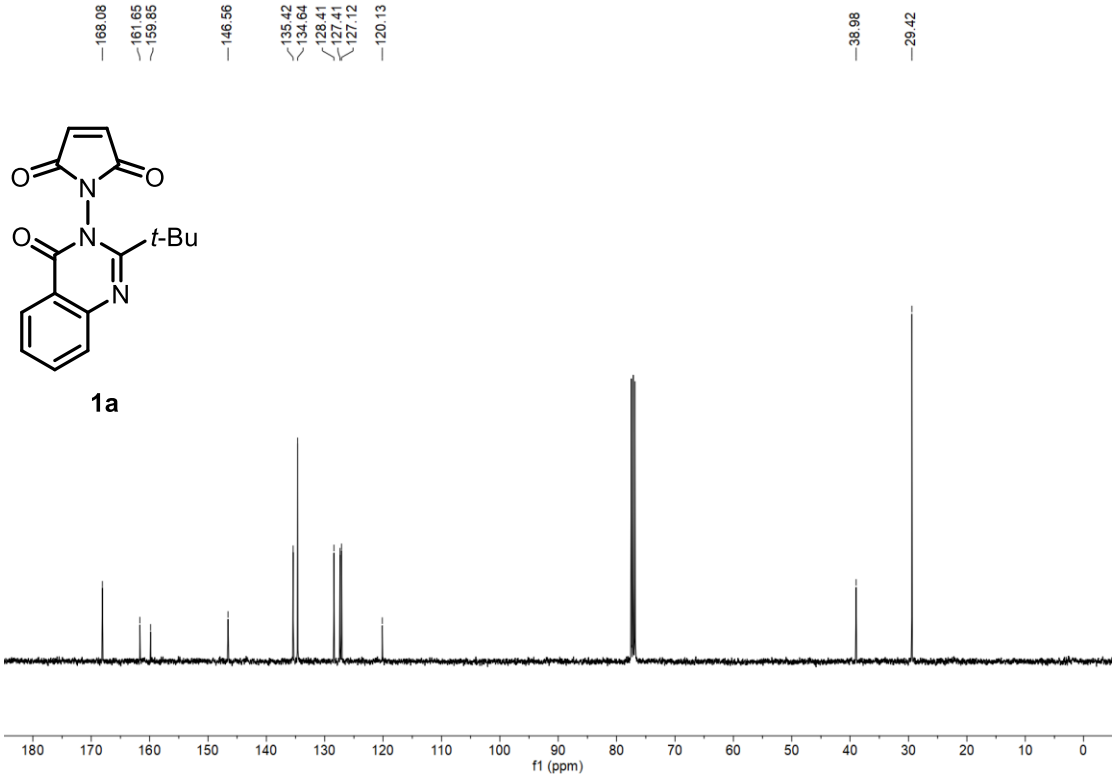
## 13. NMR spectra

**$^{1}$H NMR** (400 MHz, $CDCl_3$)




**$^{13}$C NMR** (101 MHz, $CDCl_3$)



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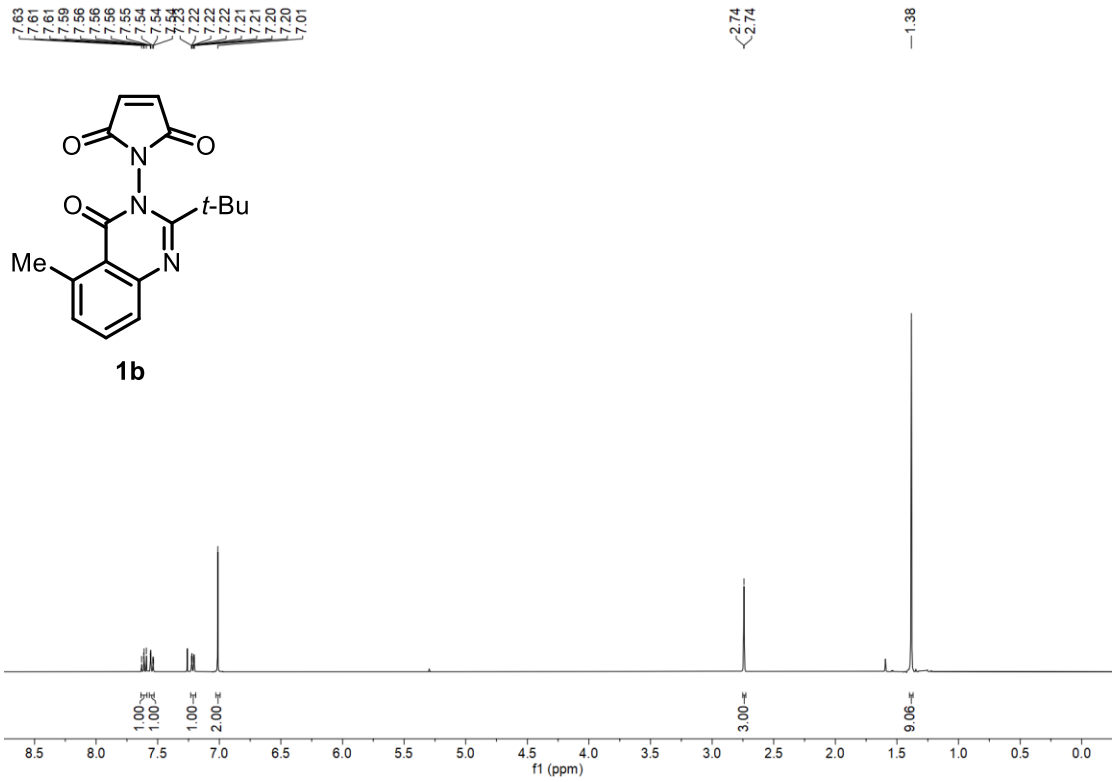


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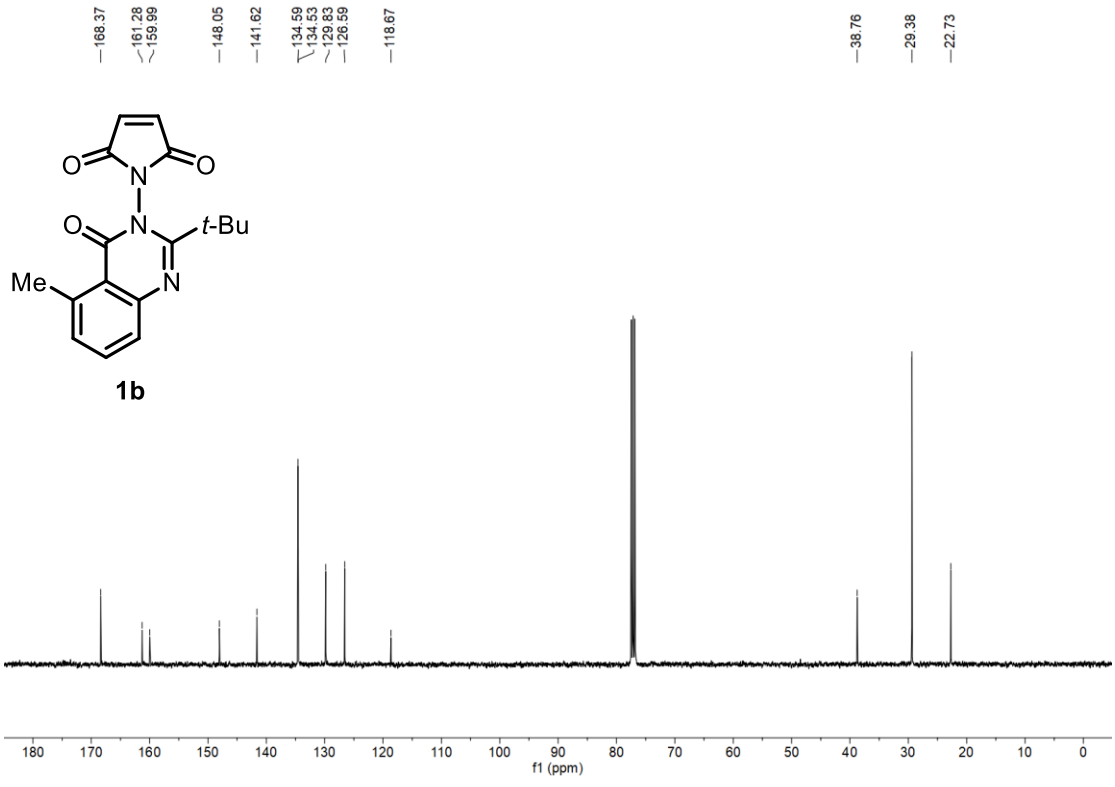

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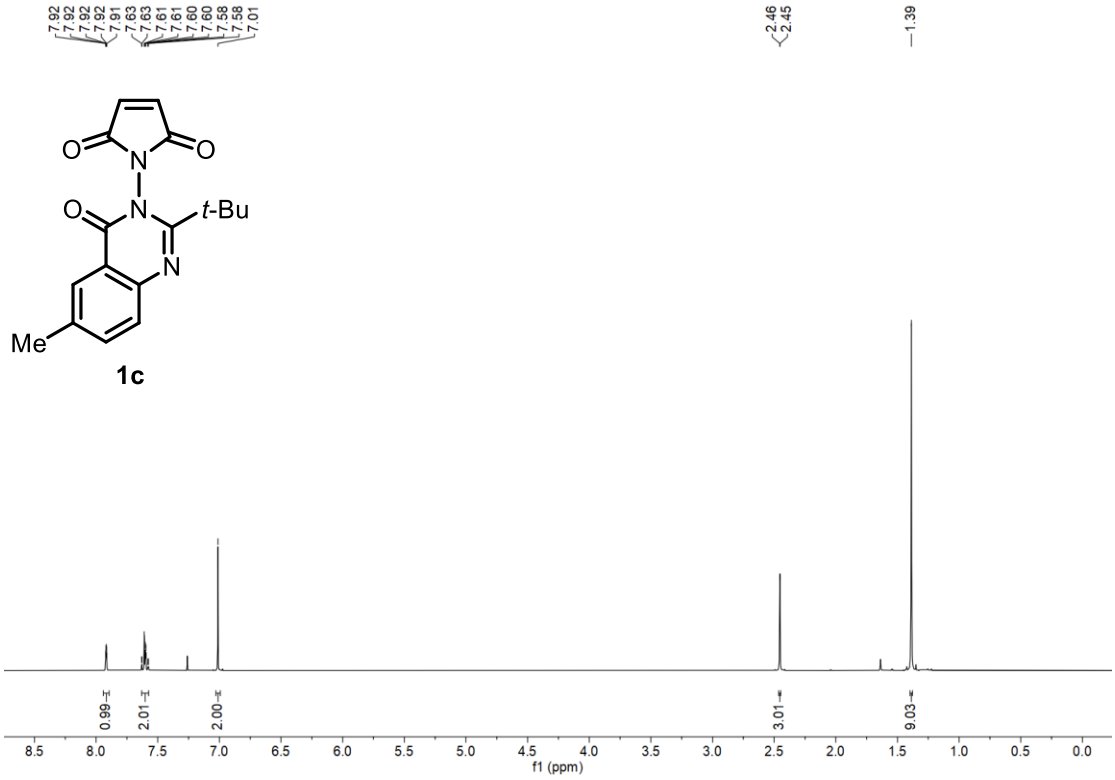


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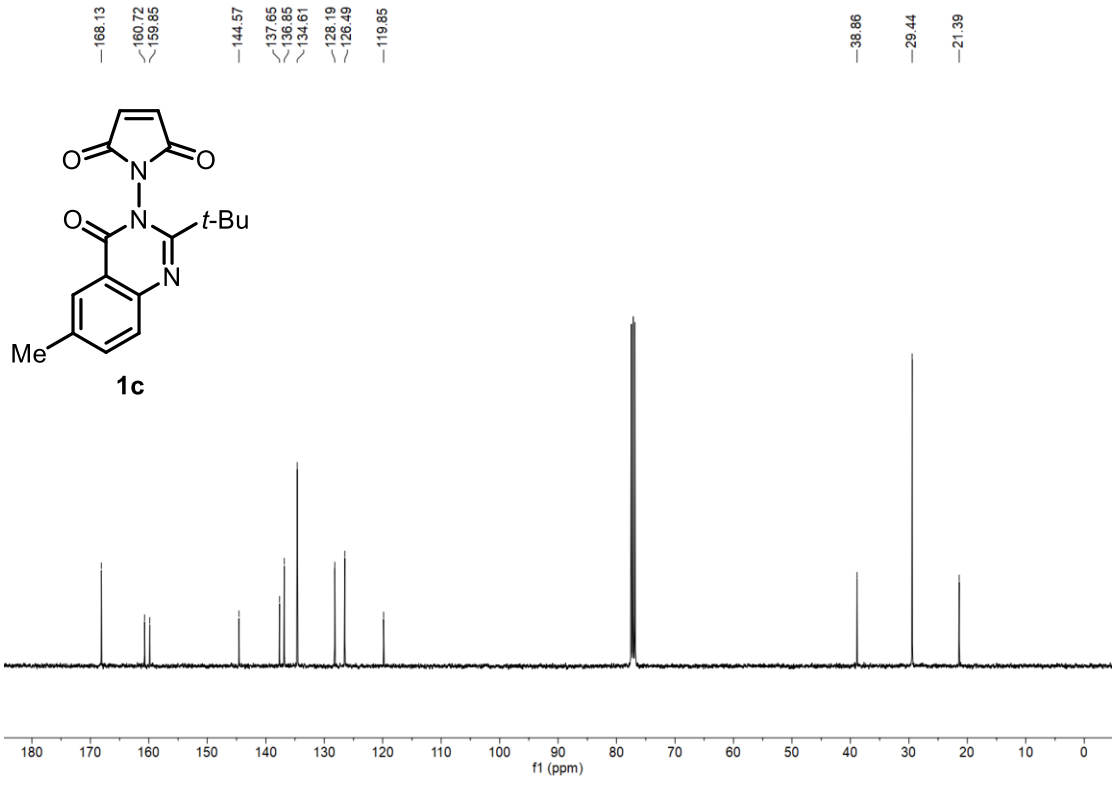

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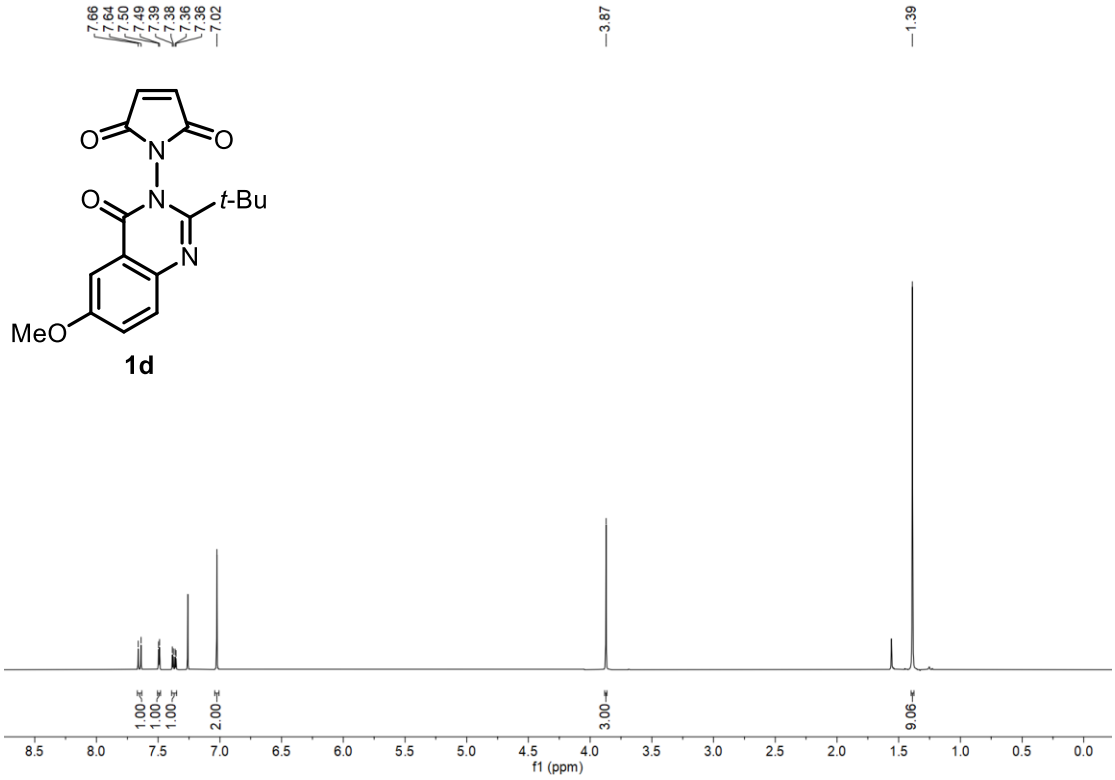


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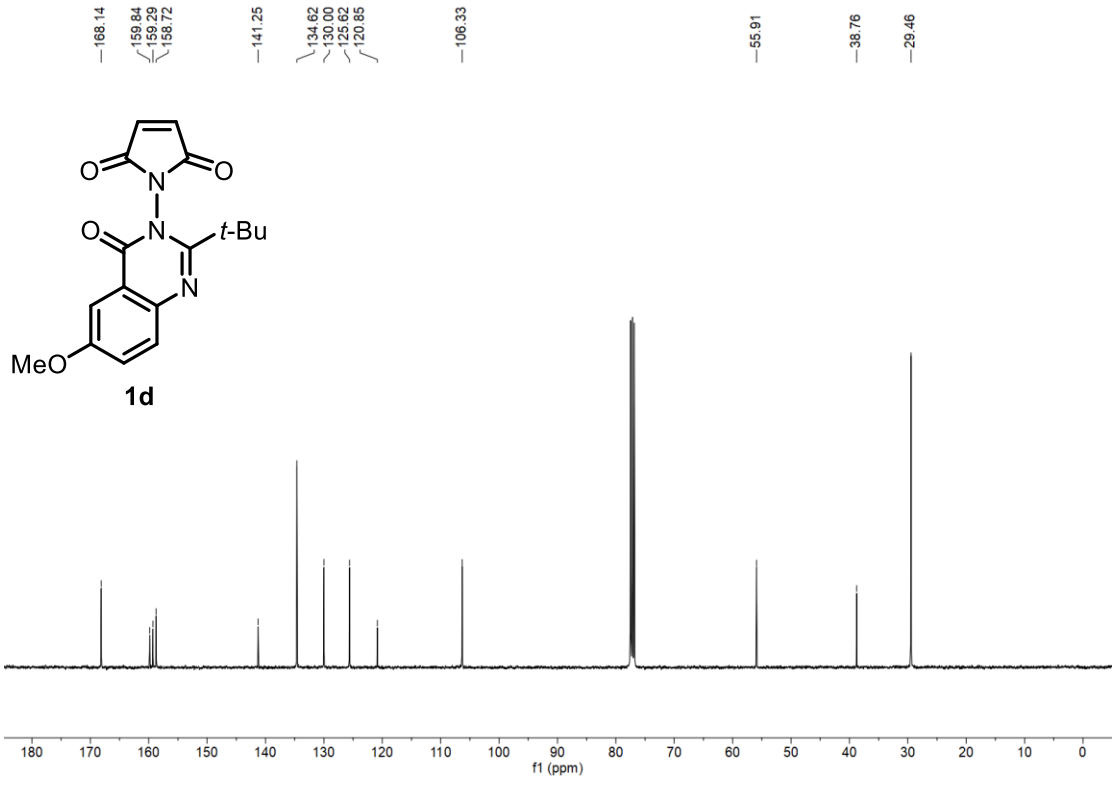

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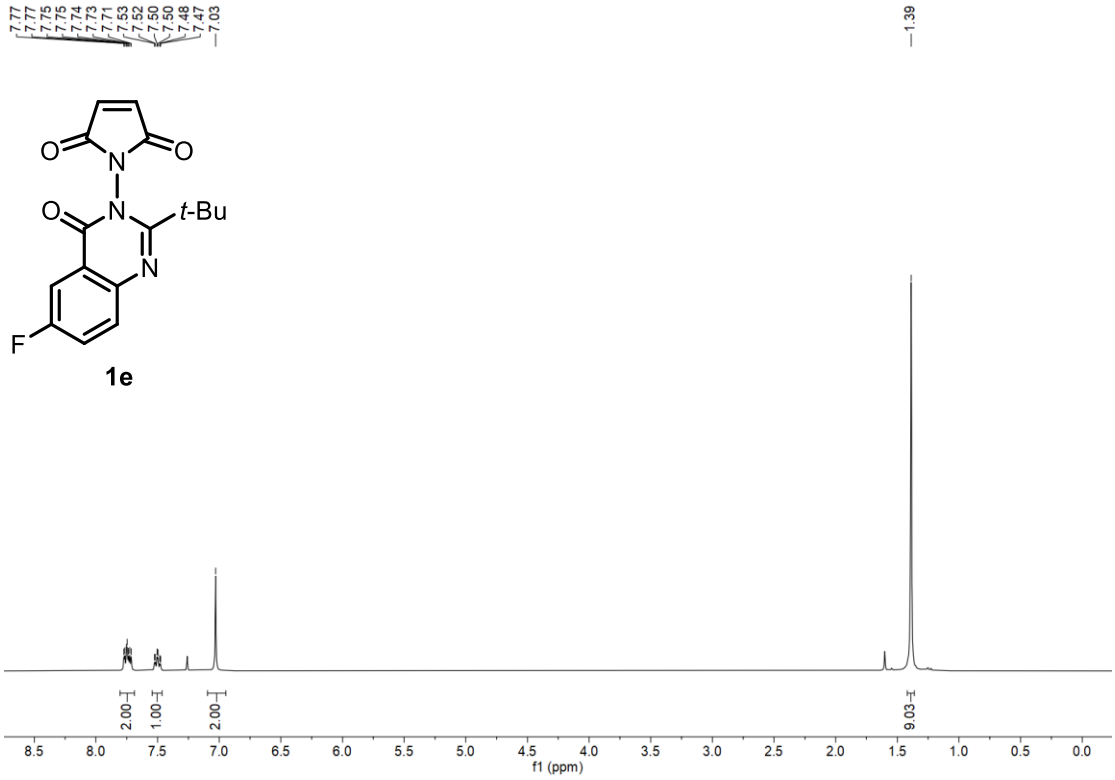


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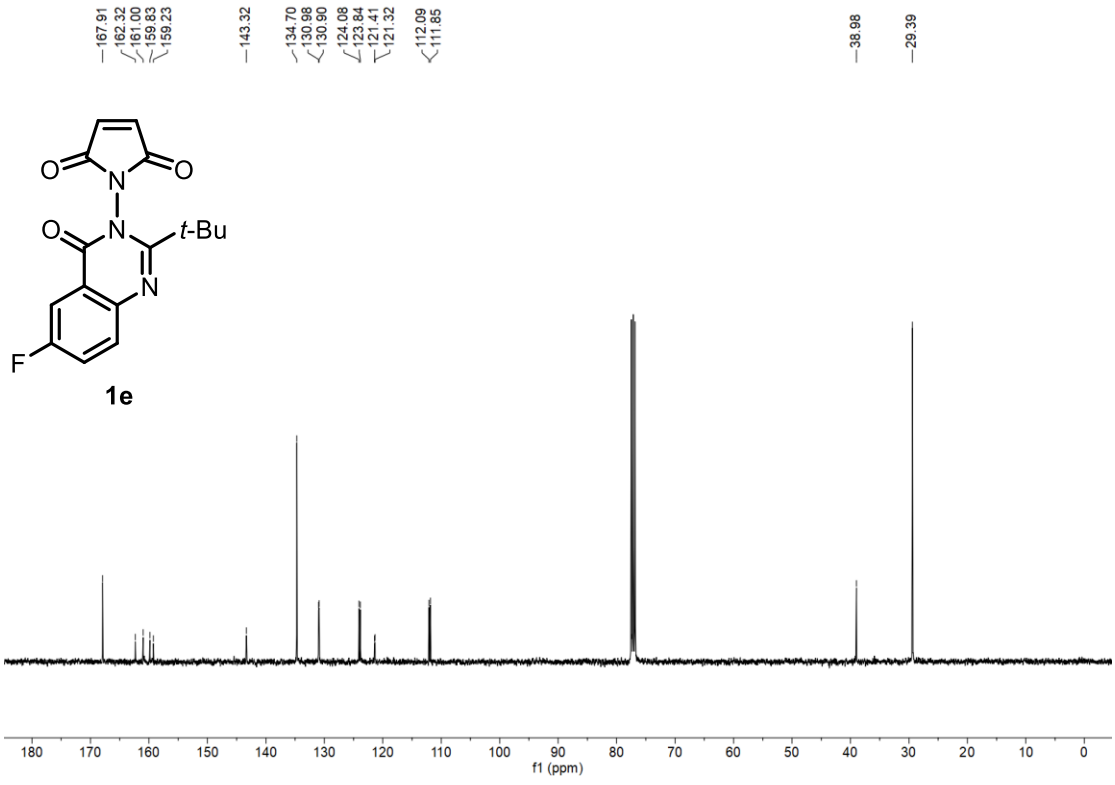
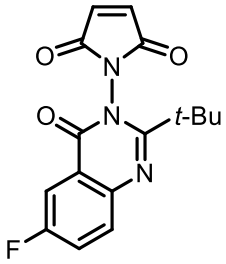


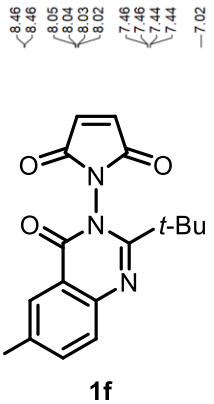
**$^{19}$F NMR** (376 MHz, $CDCl_3$)



**1e**




**$^{1}$H NMR** (400 MHz, $CDCl_3$)



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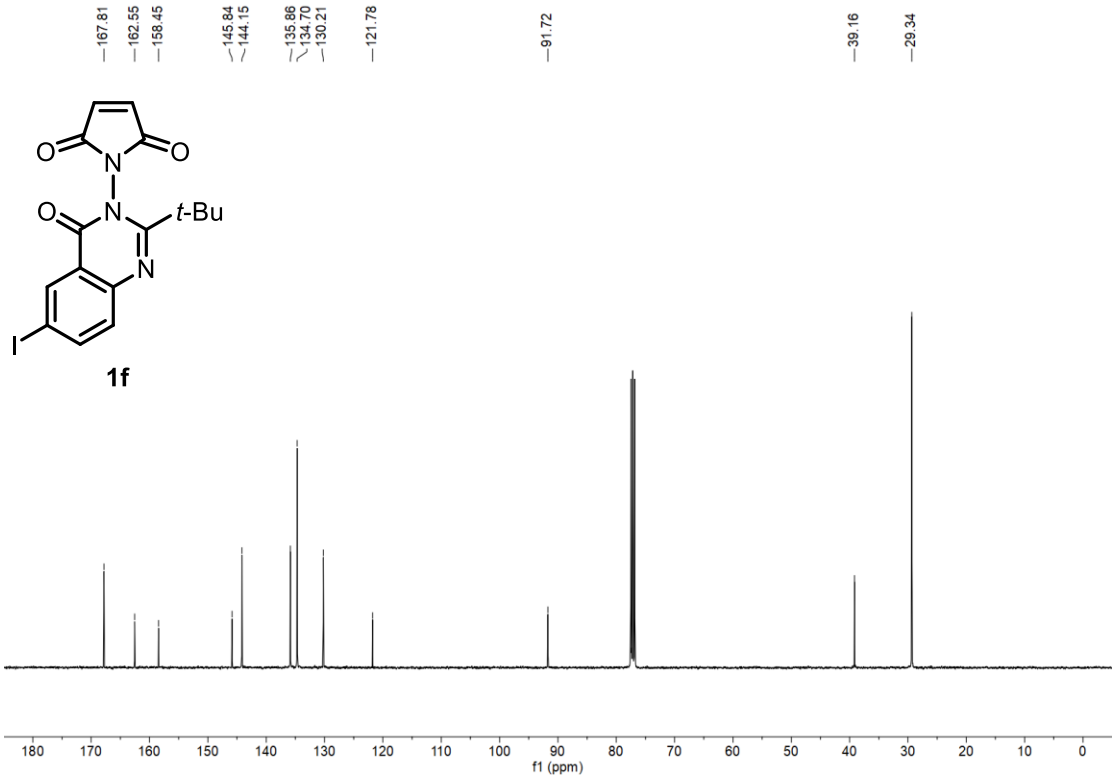


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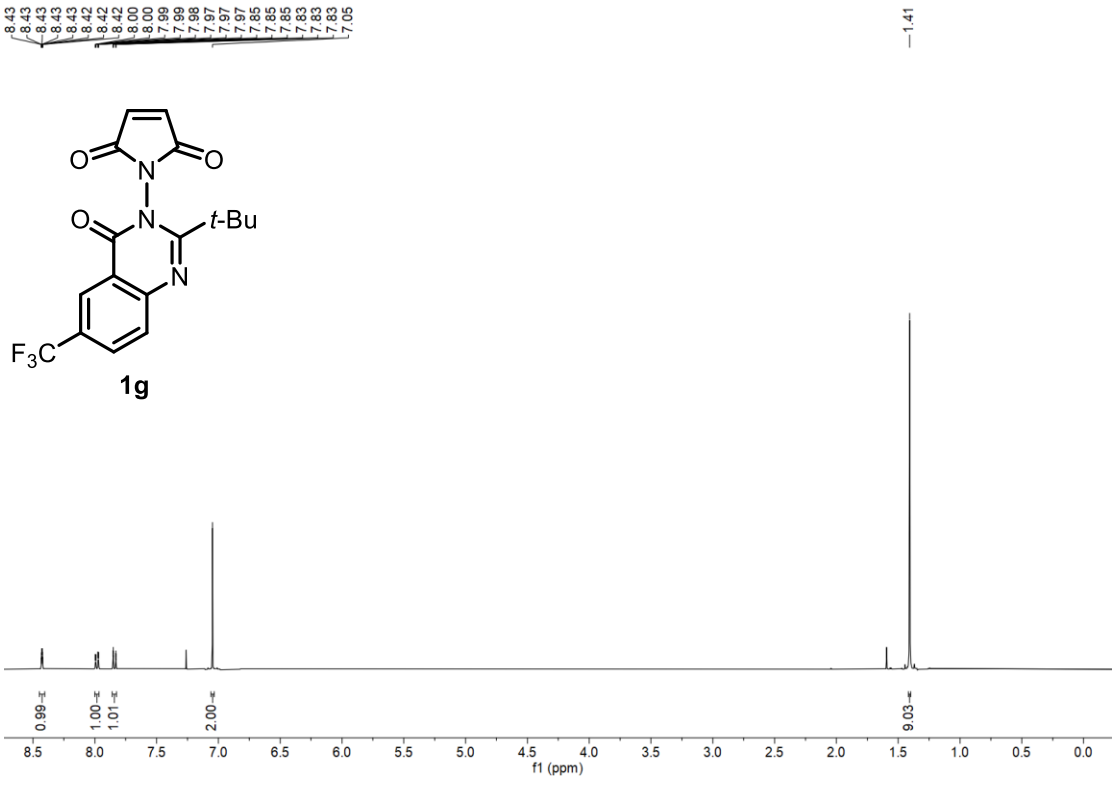

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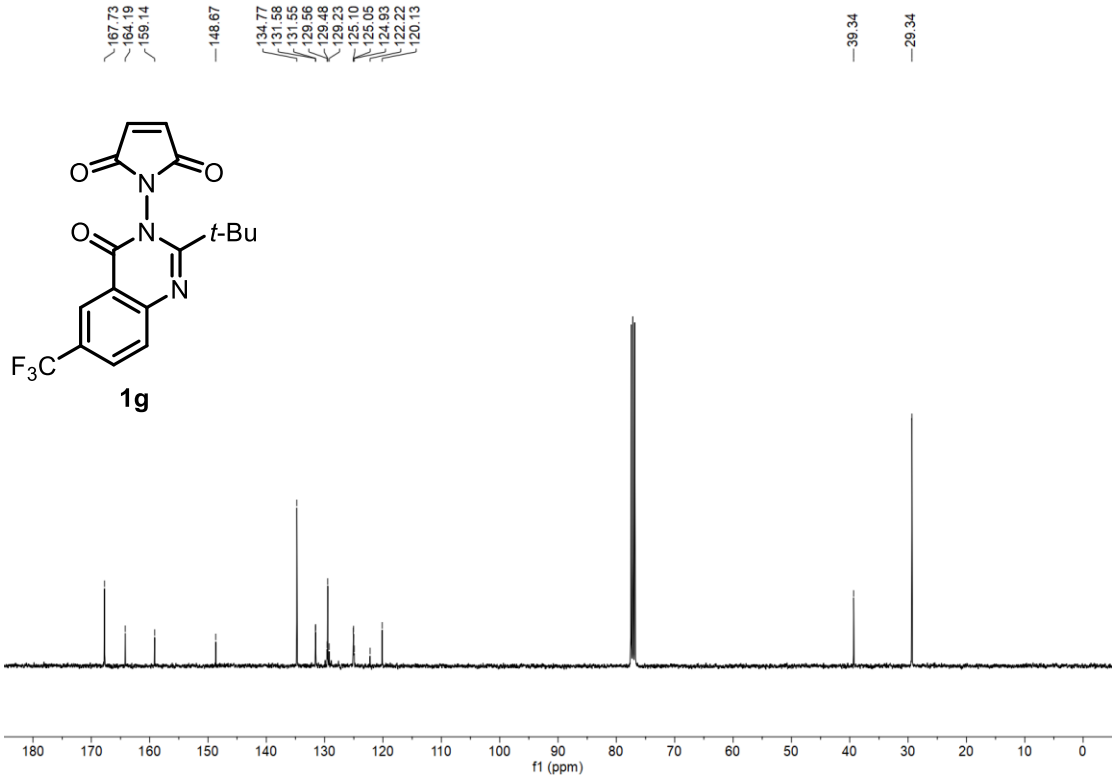


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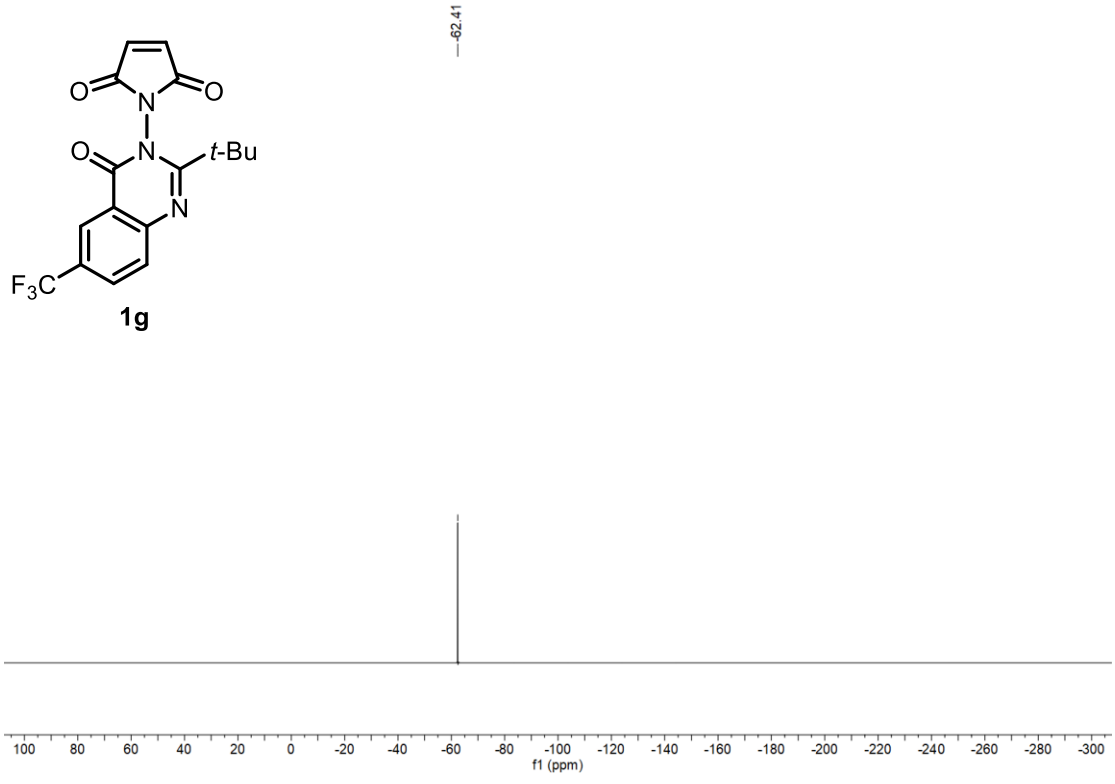

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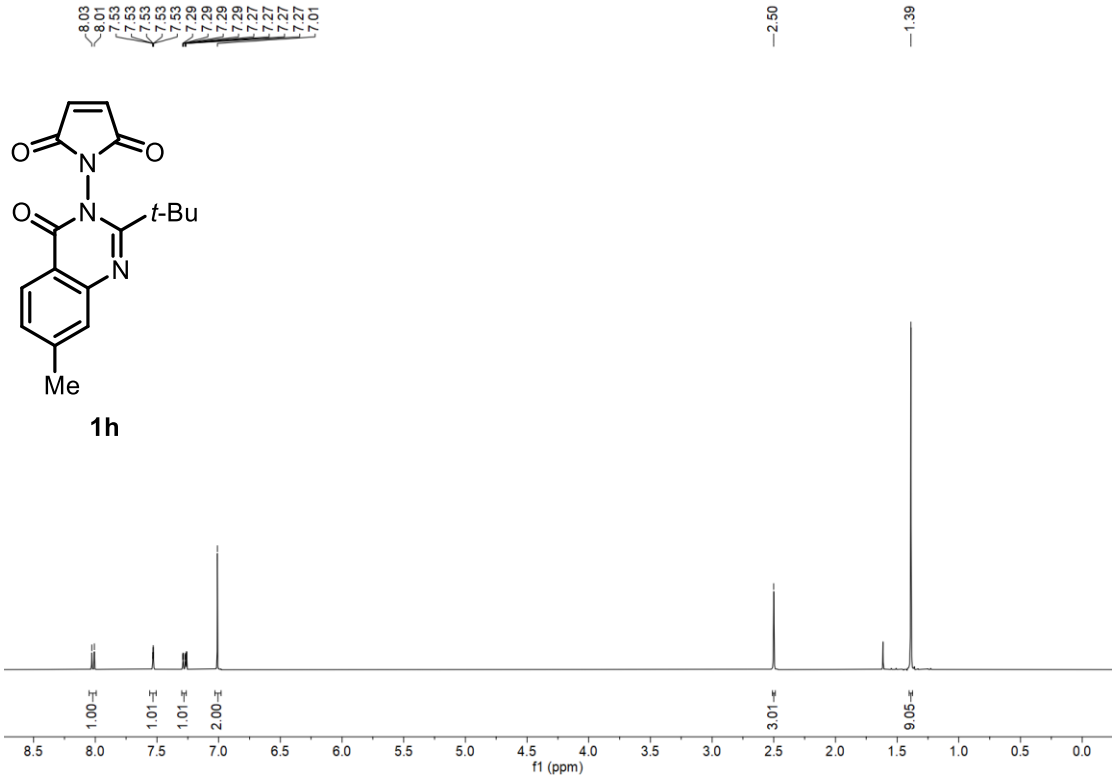


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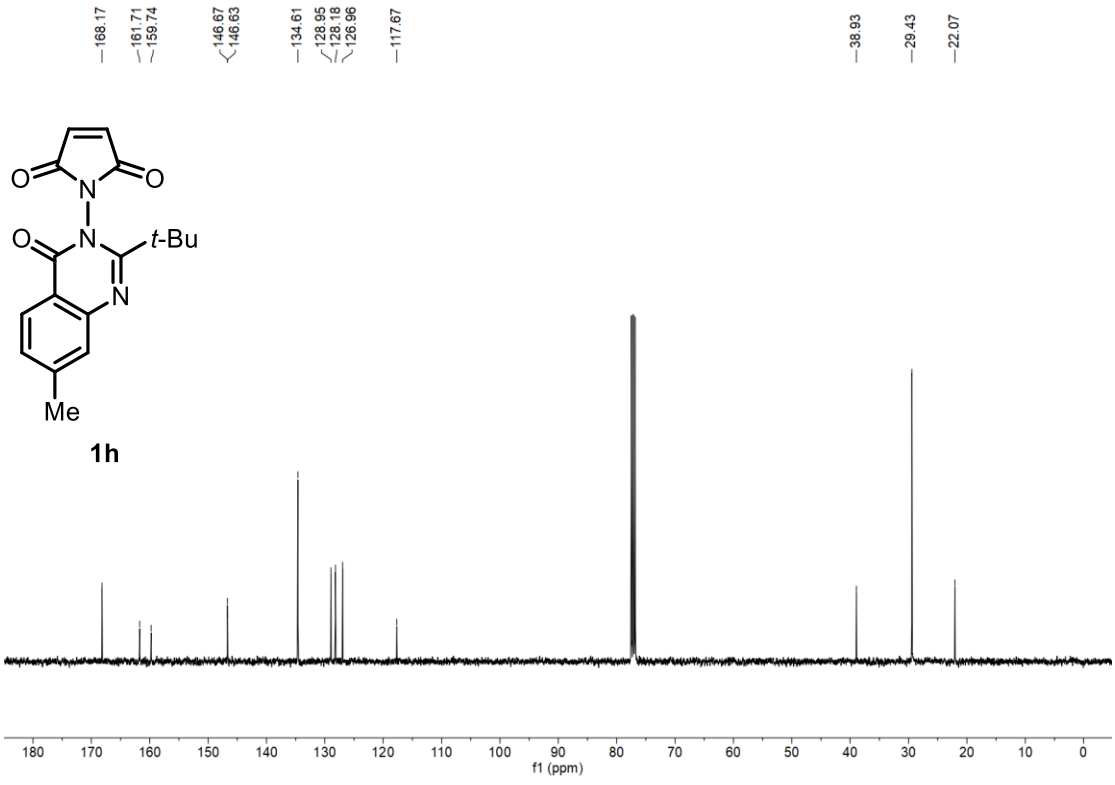

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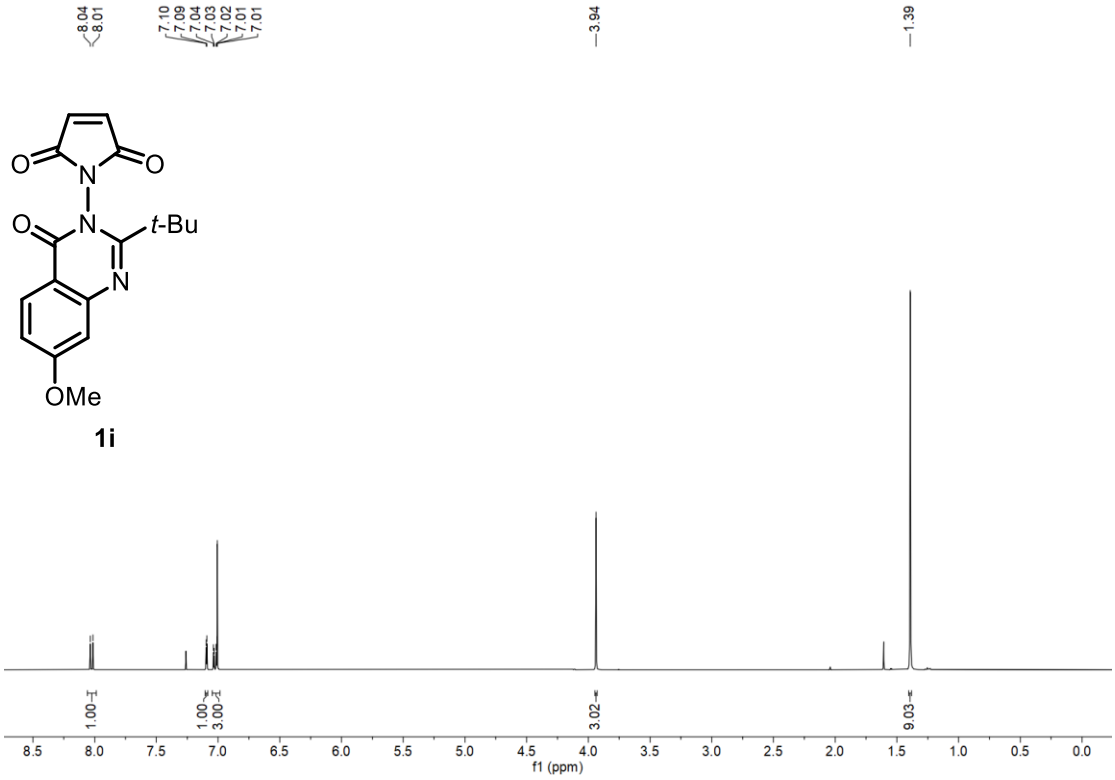


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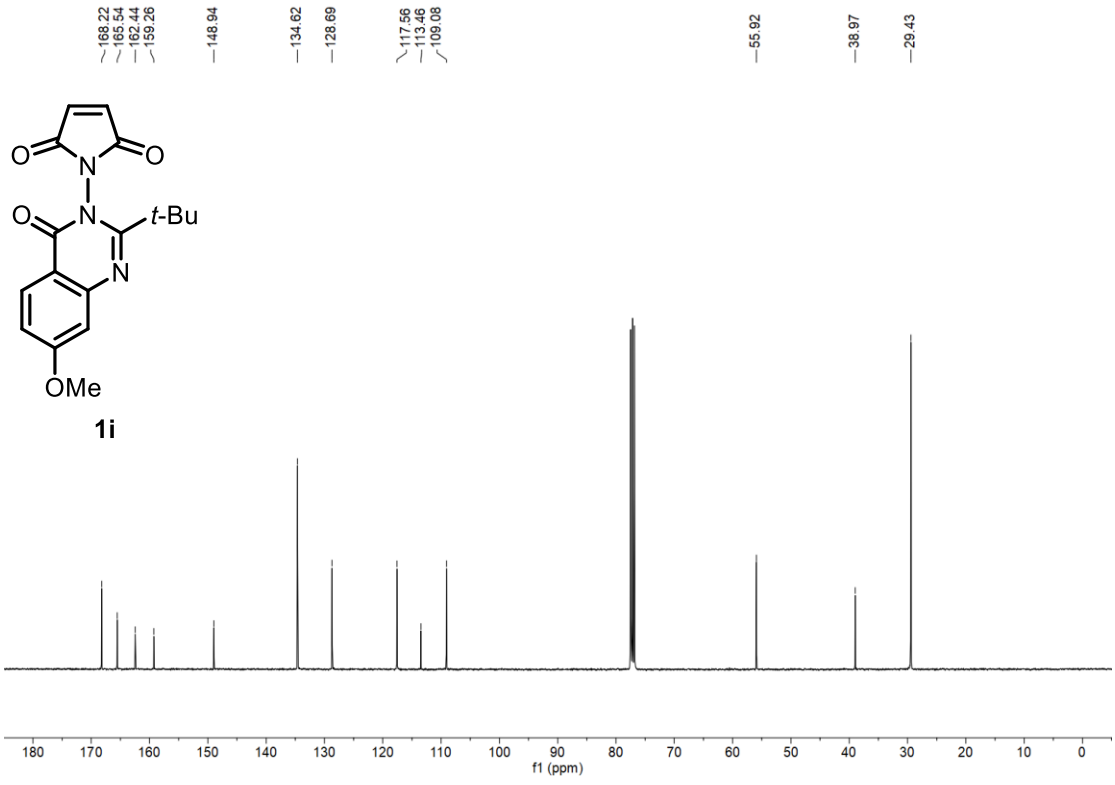

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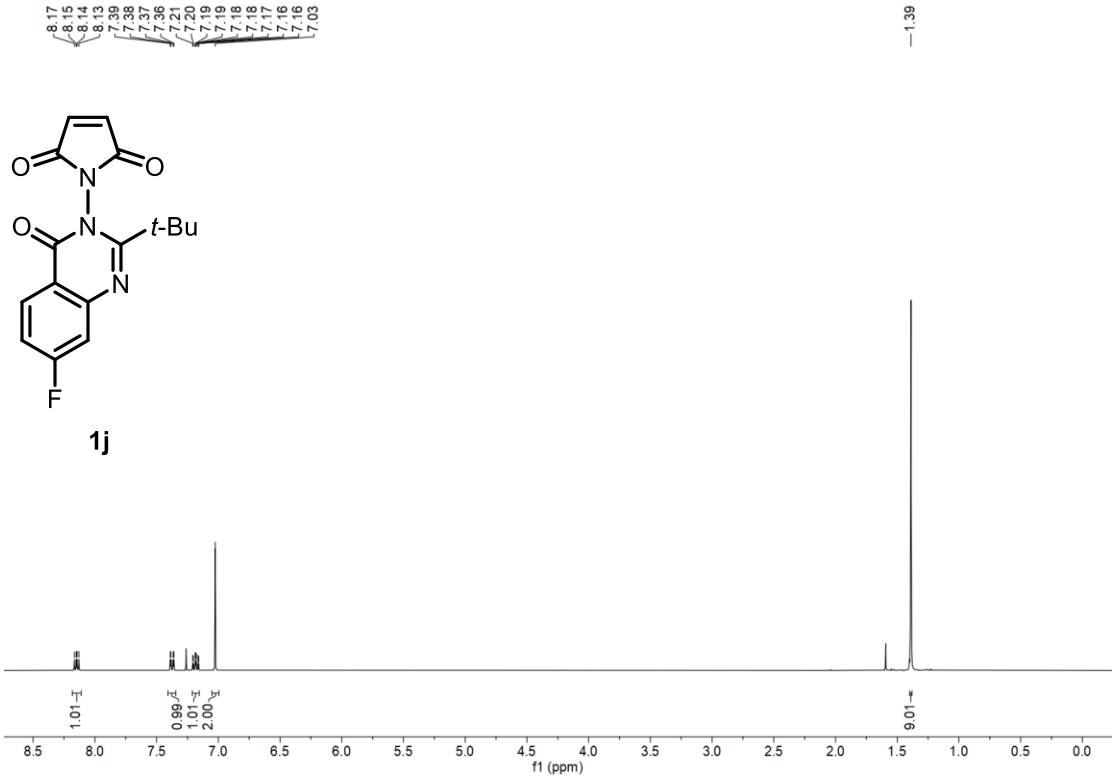


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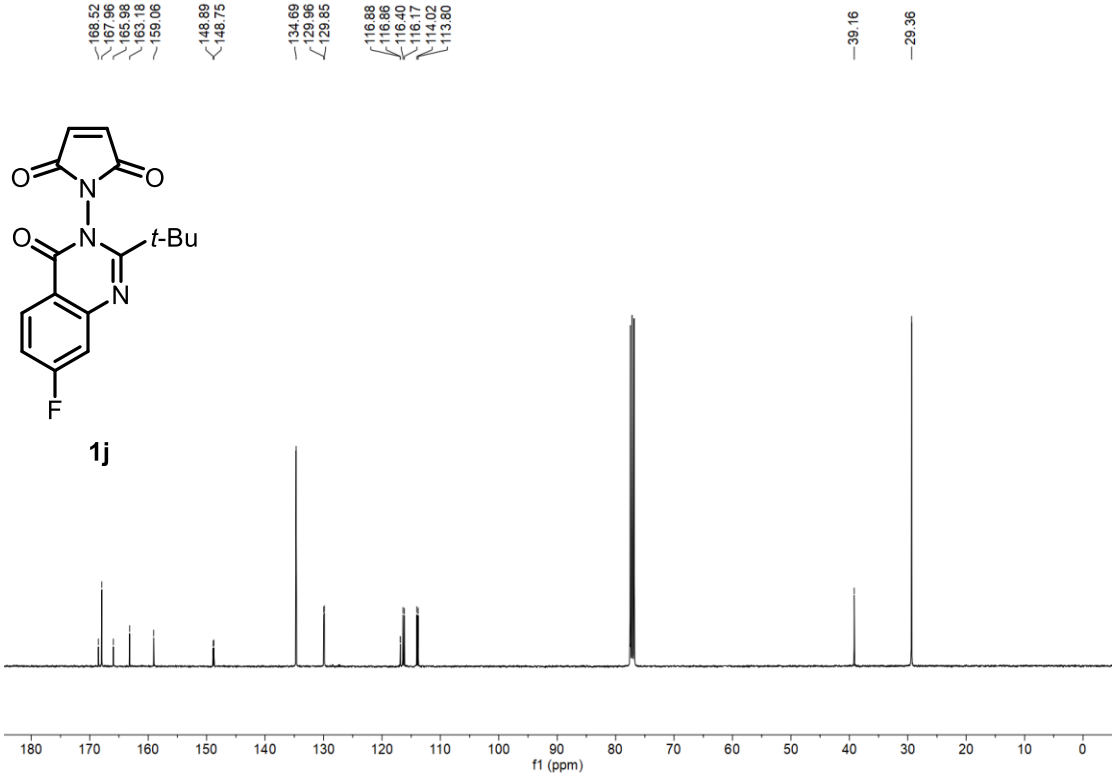
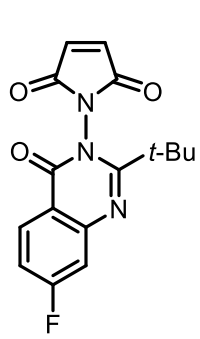


**$^{19}$F NMR** (376 MHz, $CDCl_3$)




**1j**

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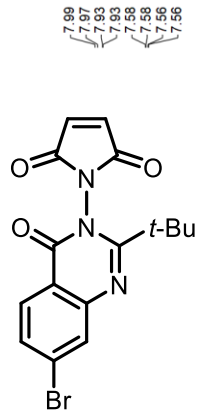


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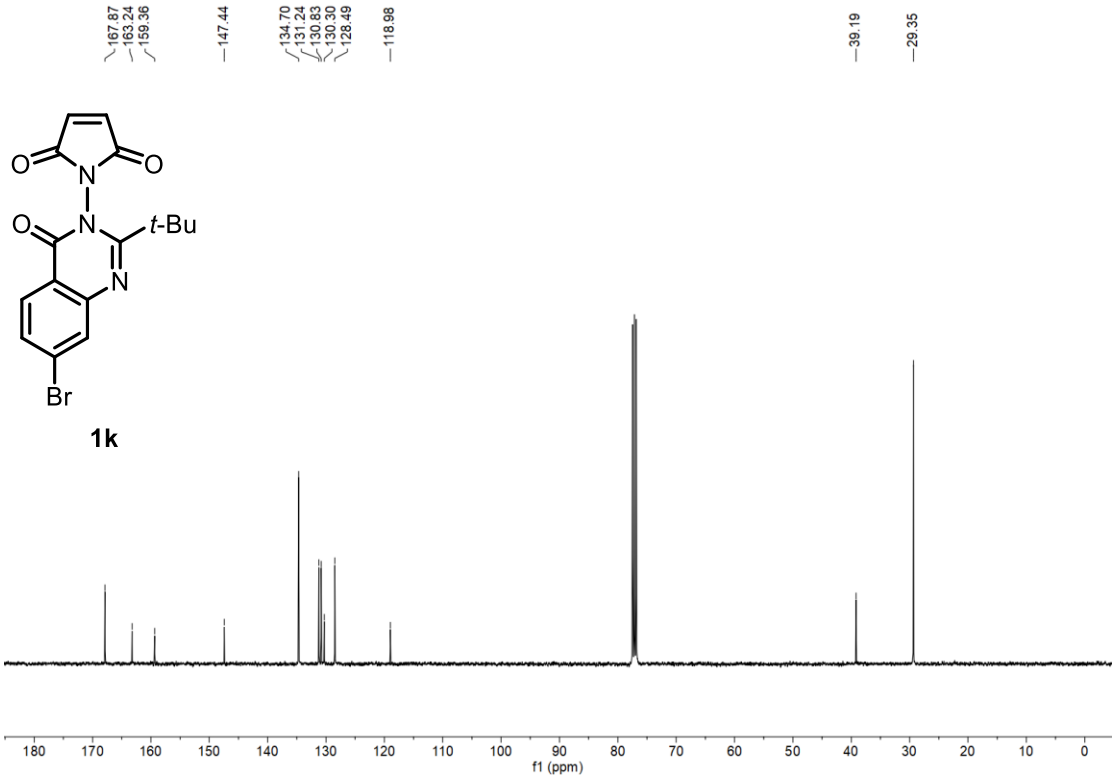


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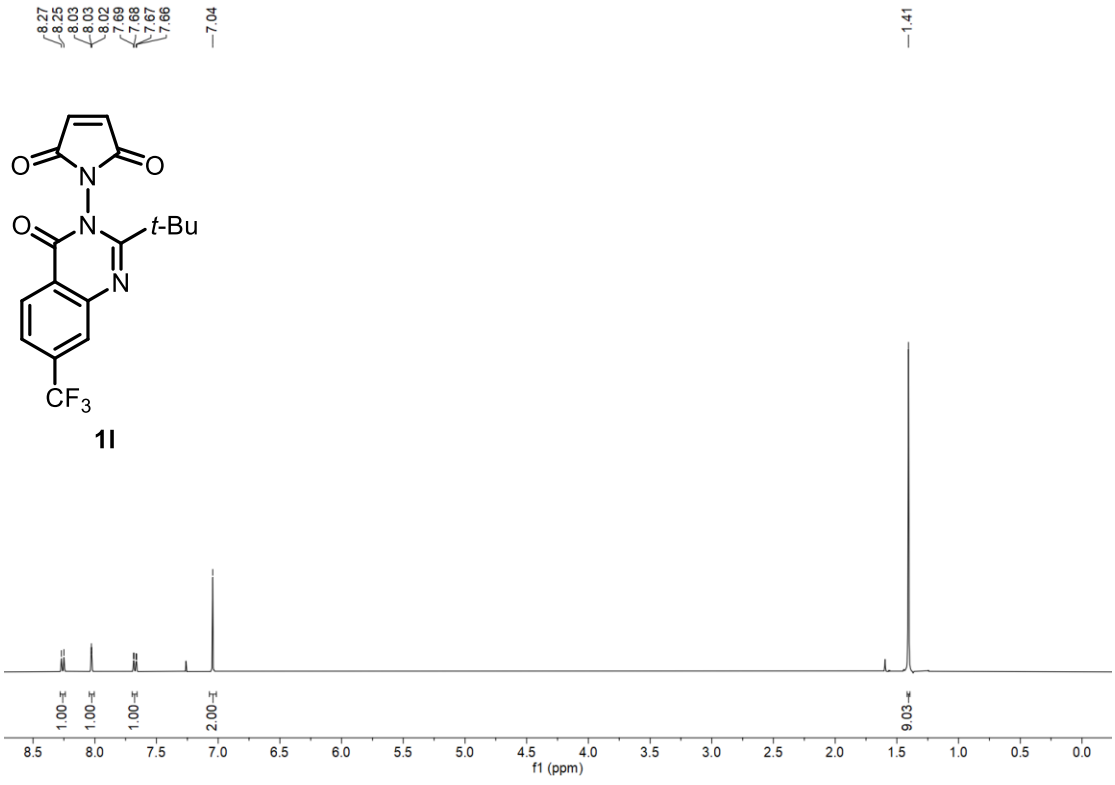

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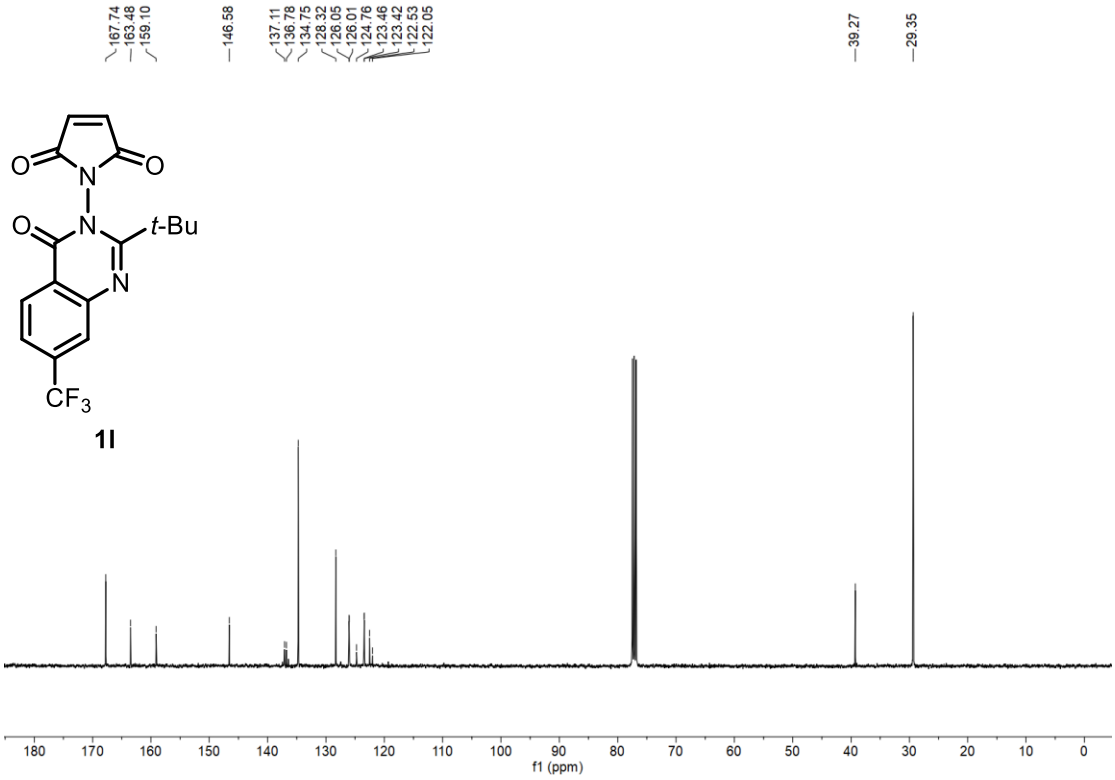


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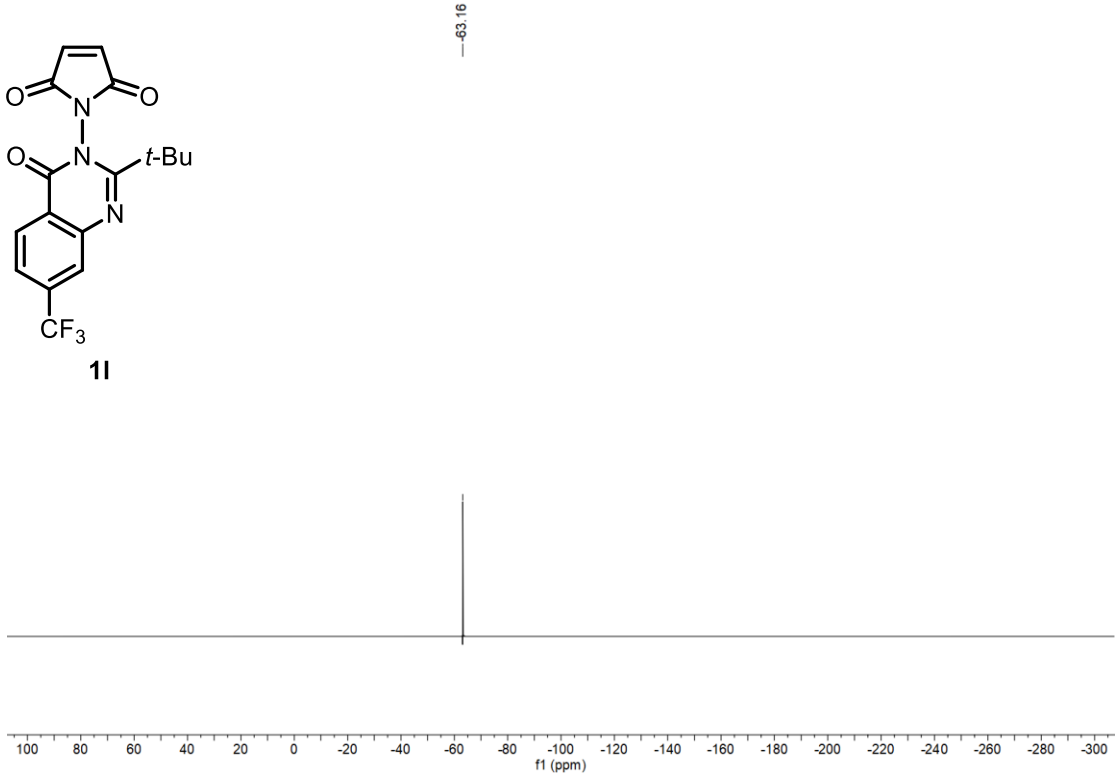

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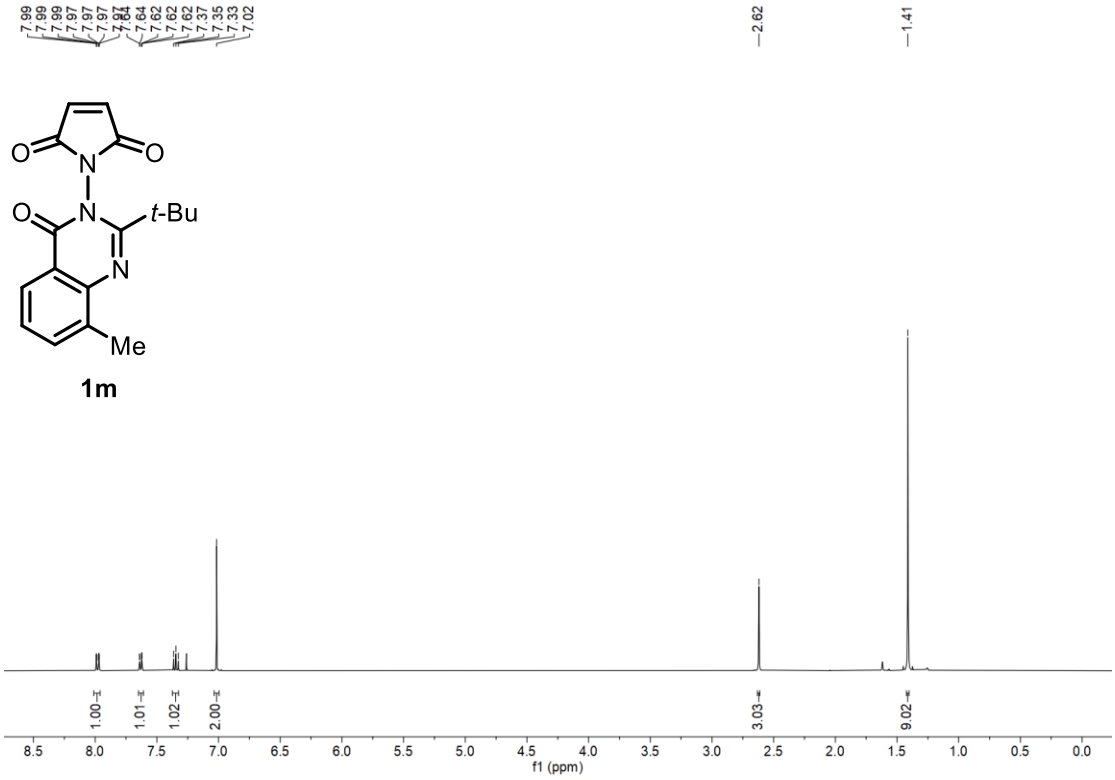


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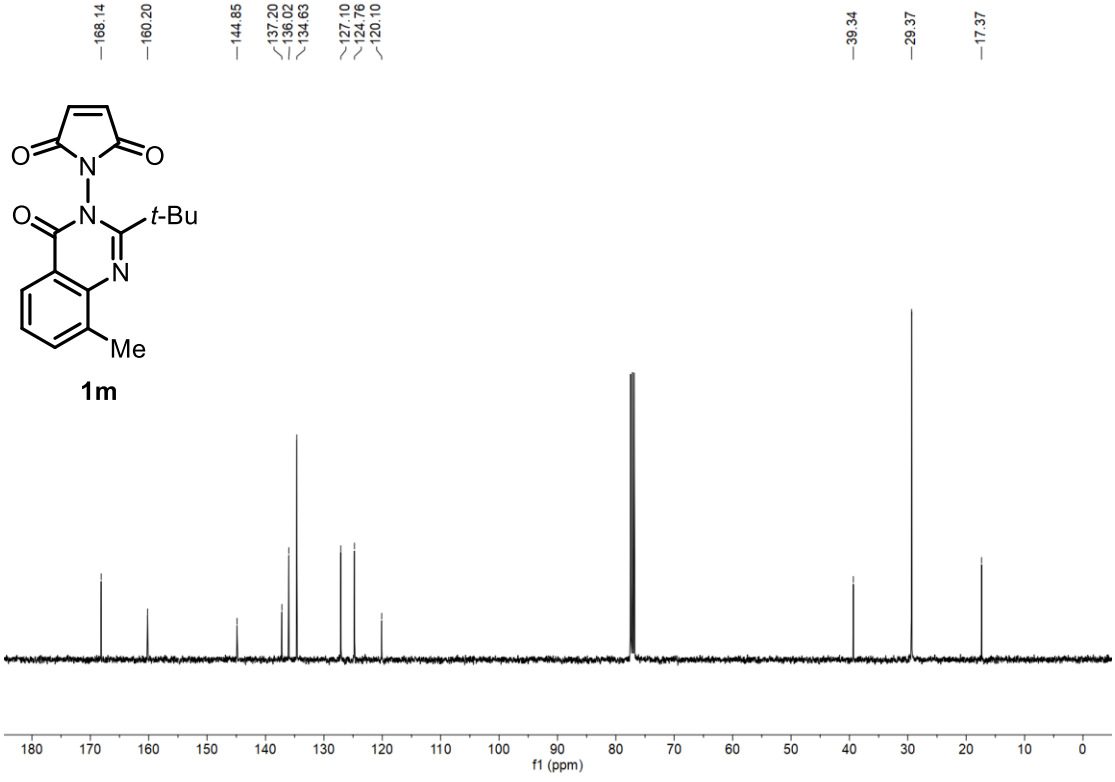

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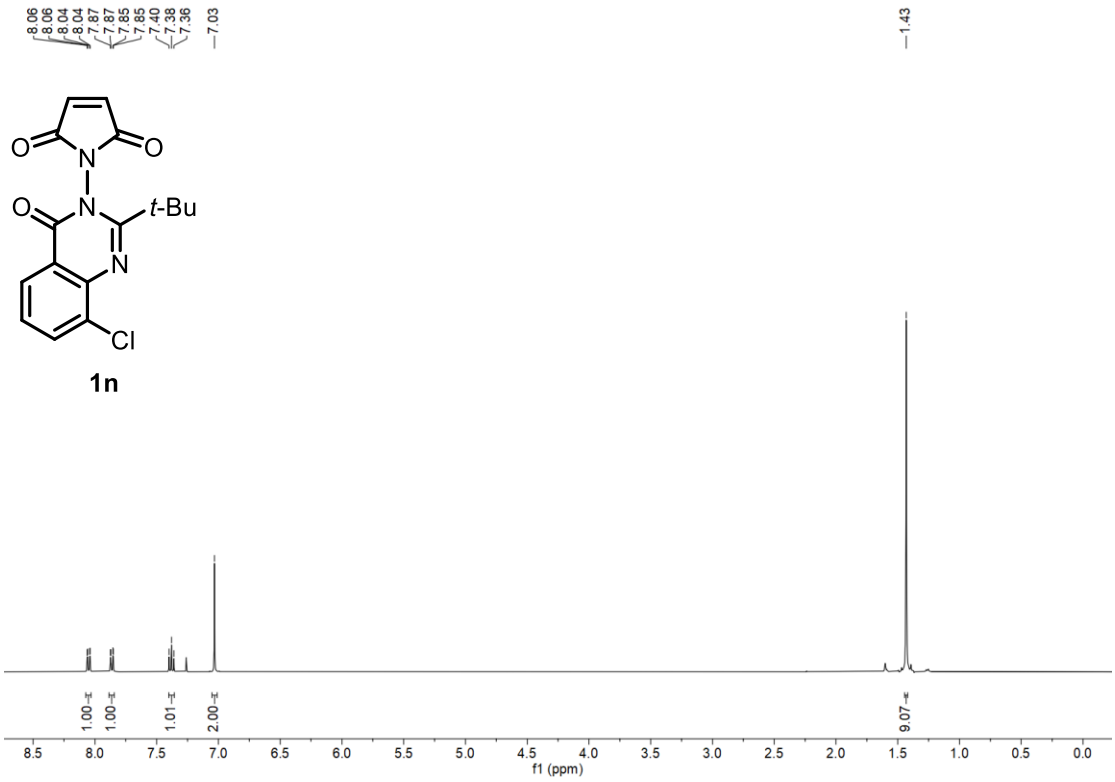


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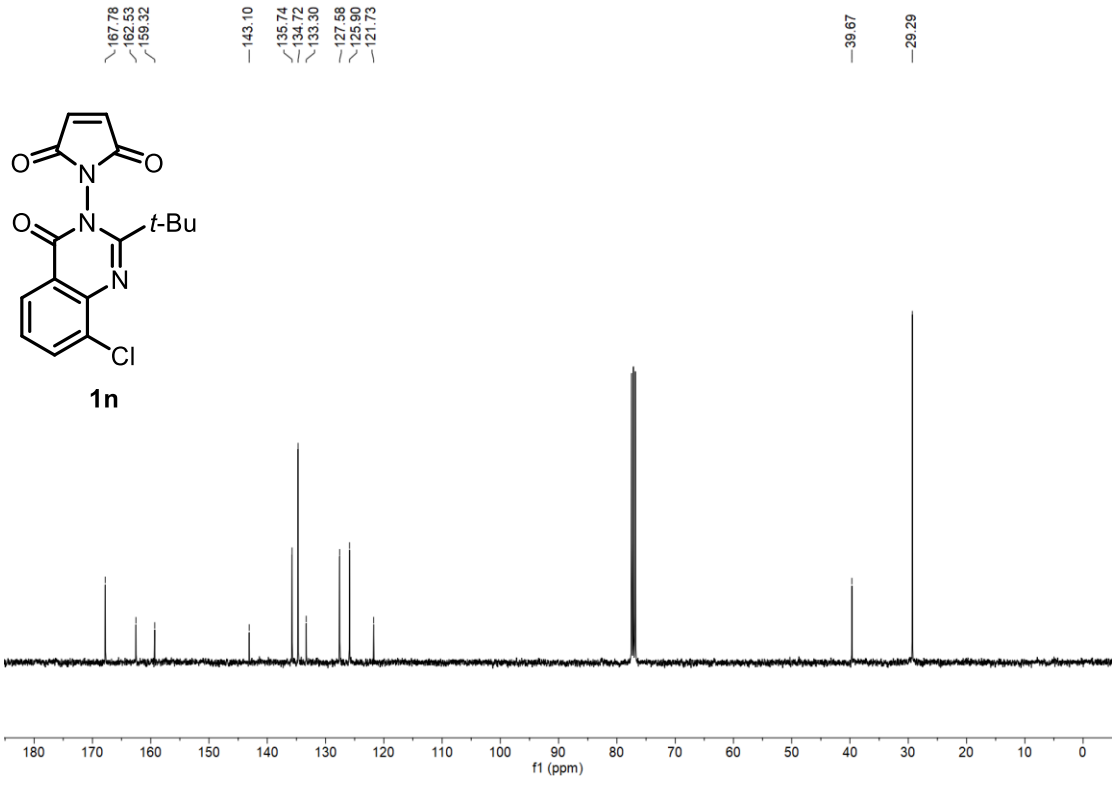

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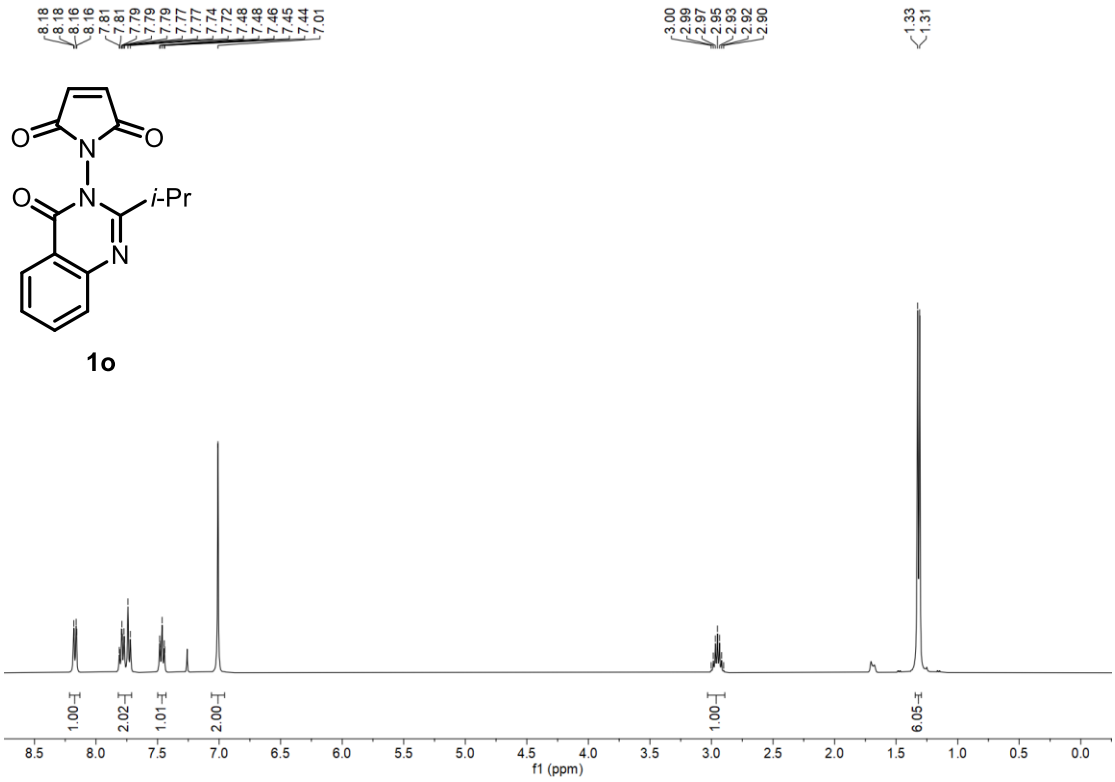


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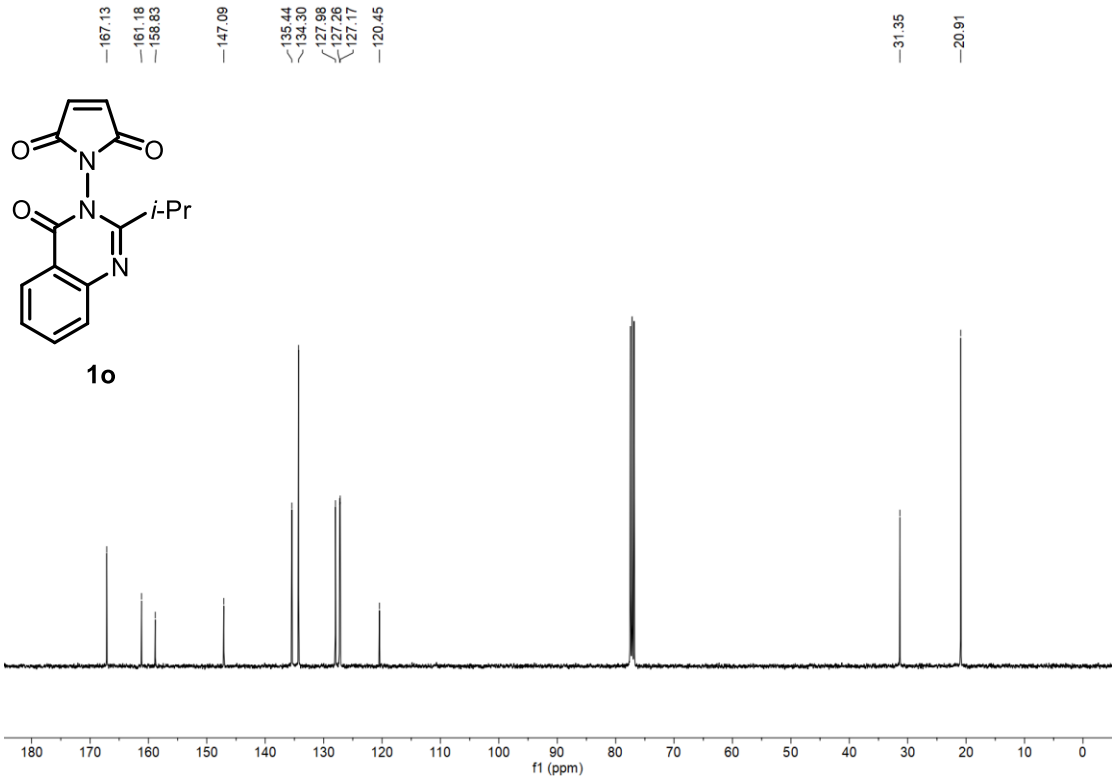

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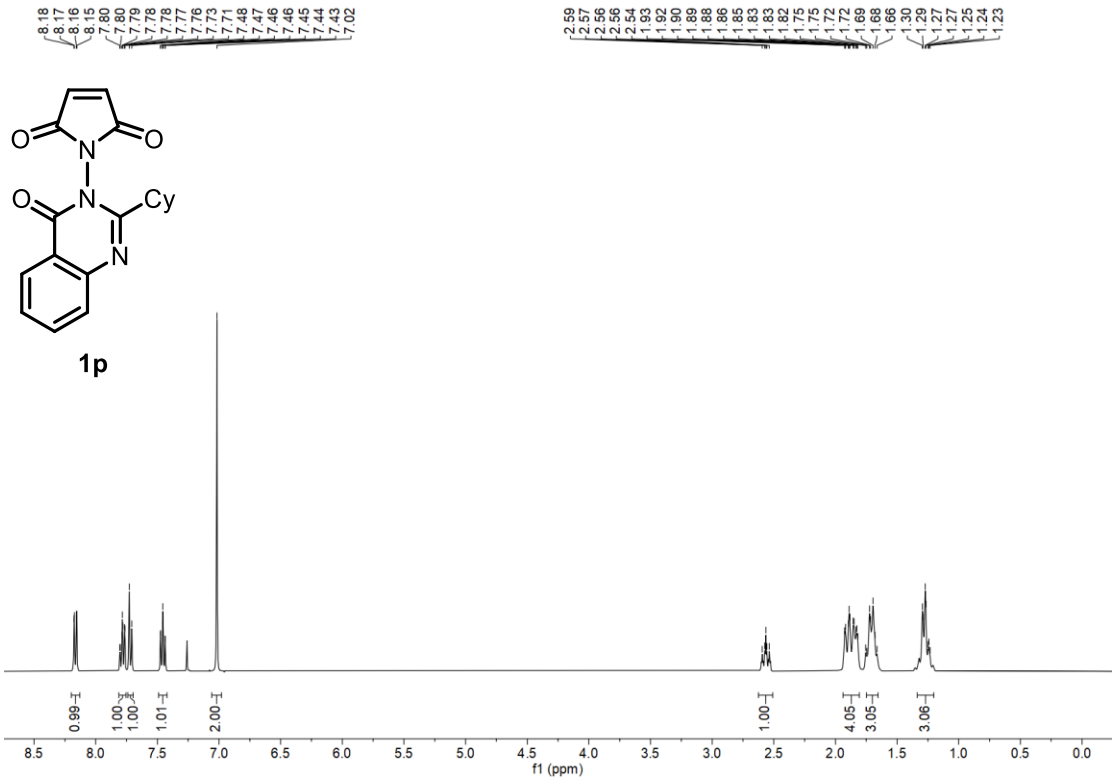


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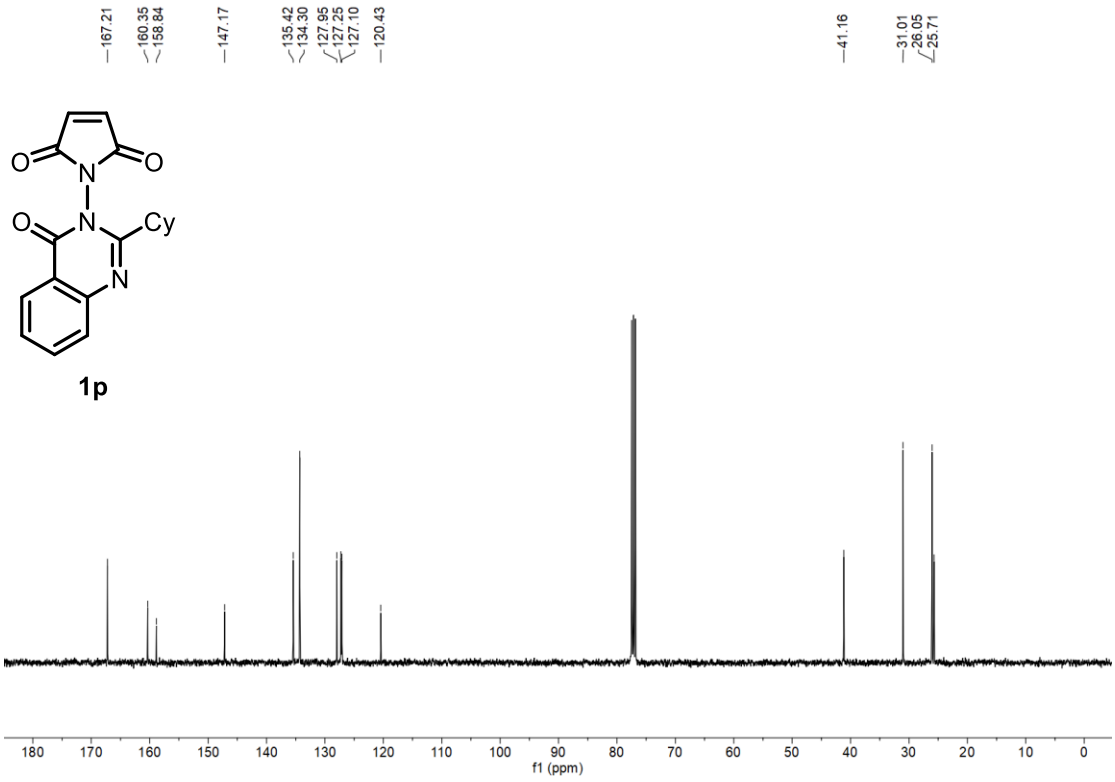

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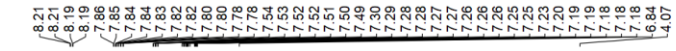


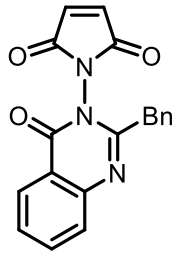


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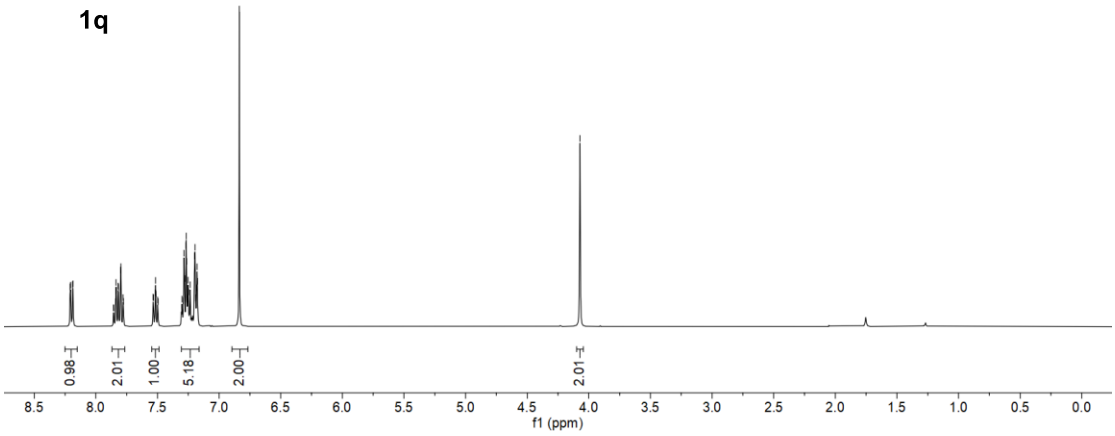


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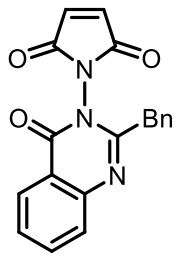


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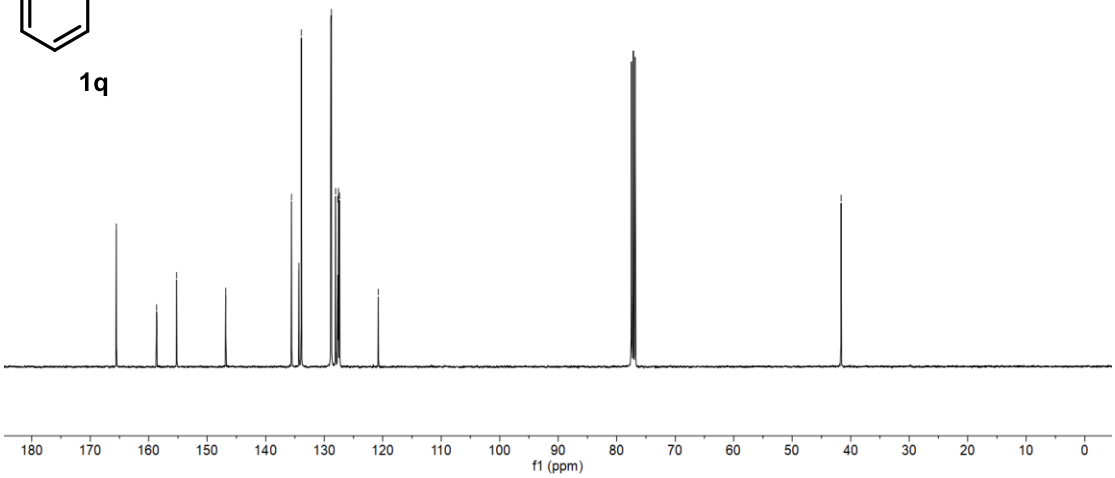

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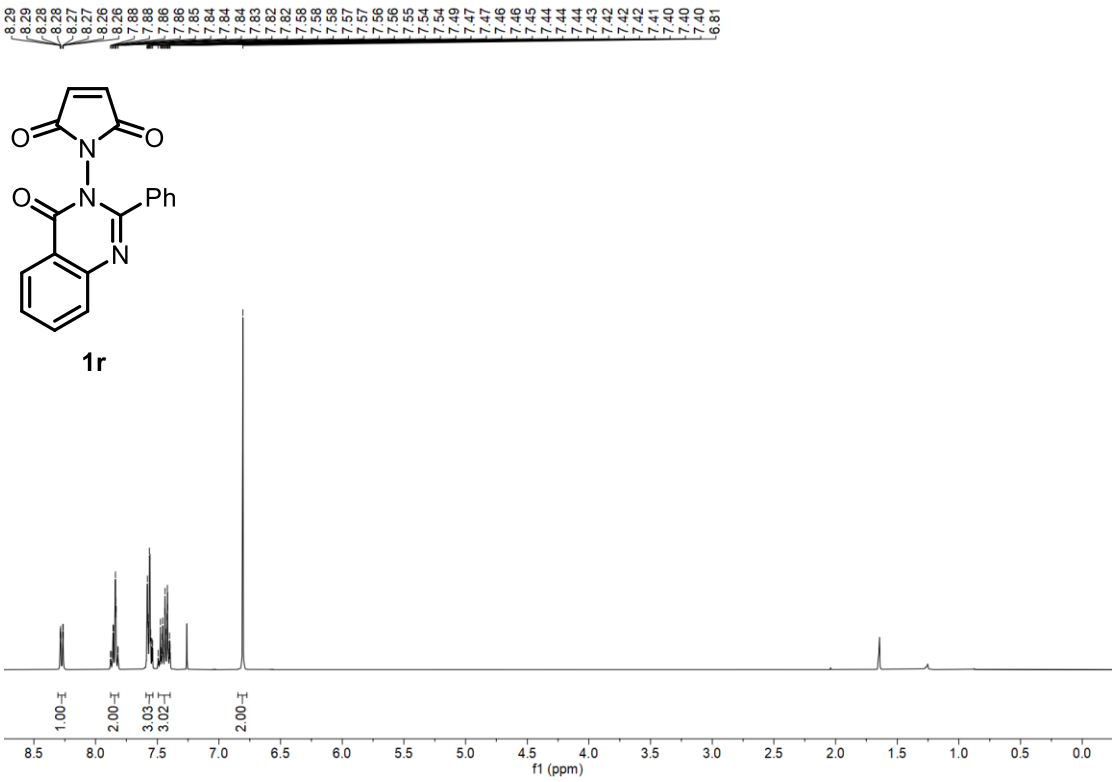
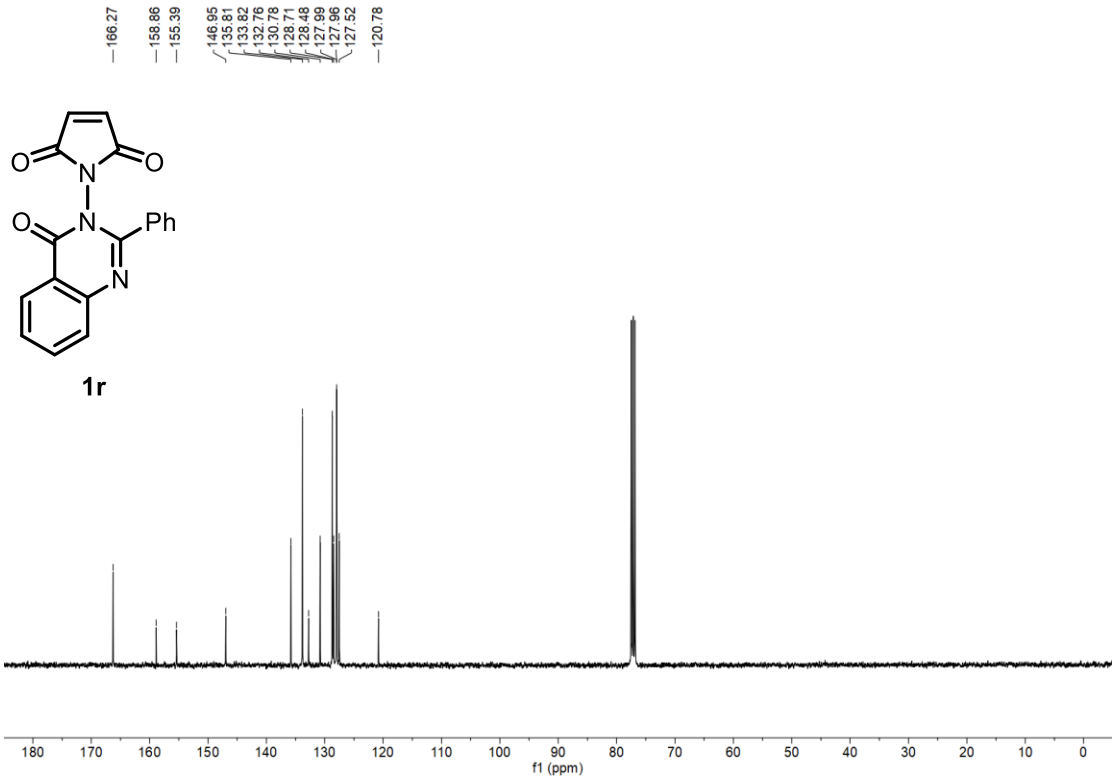
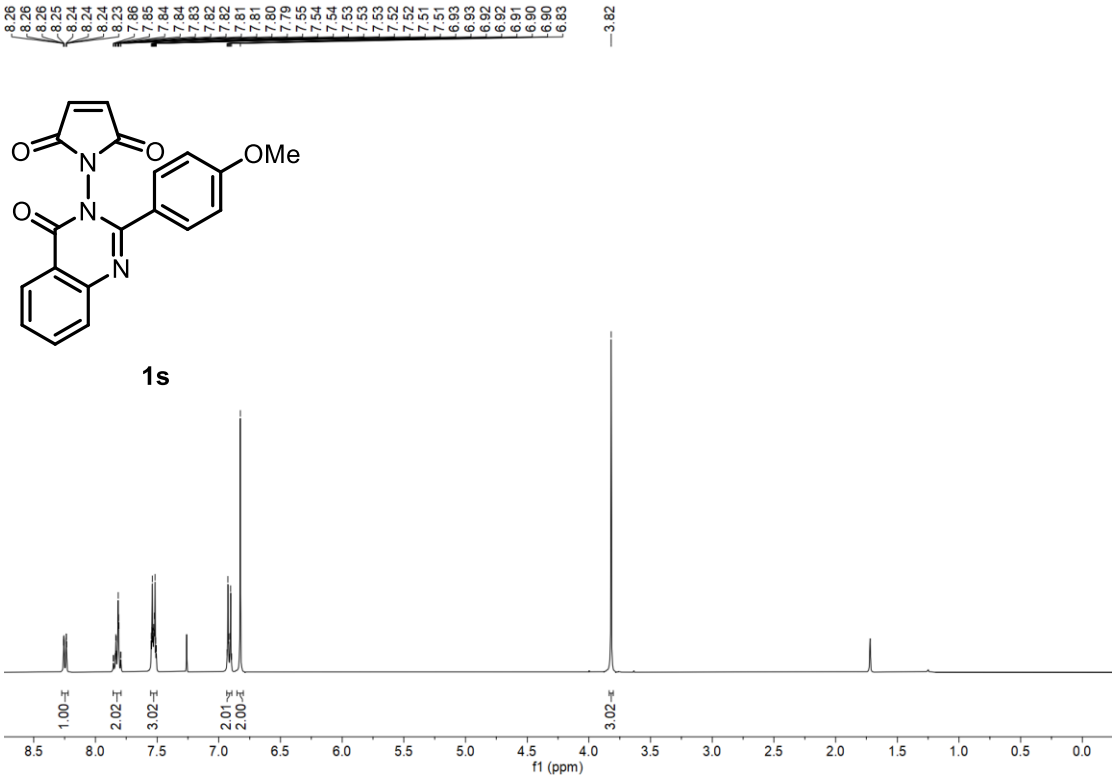


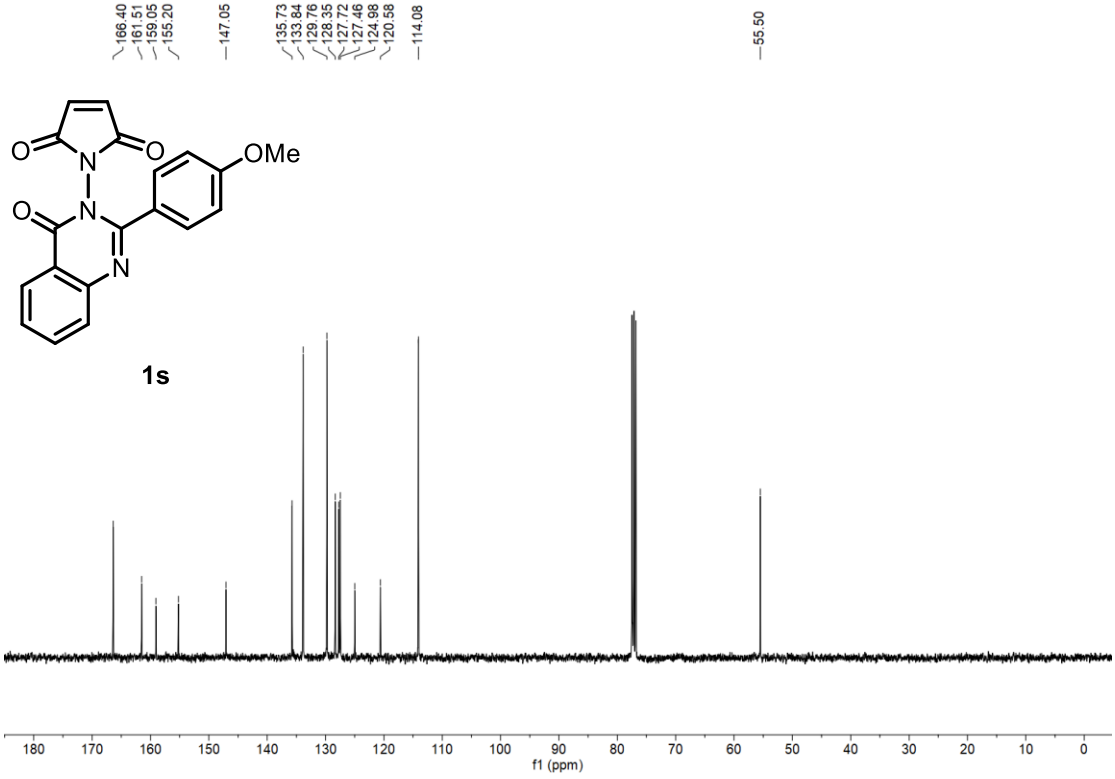

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



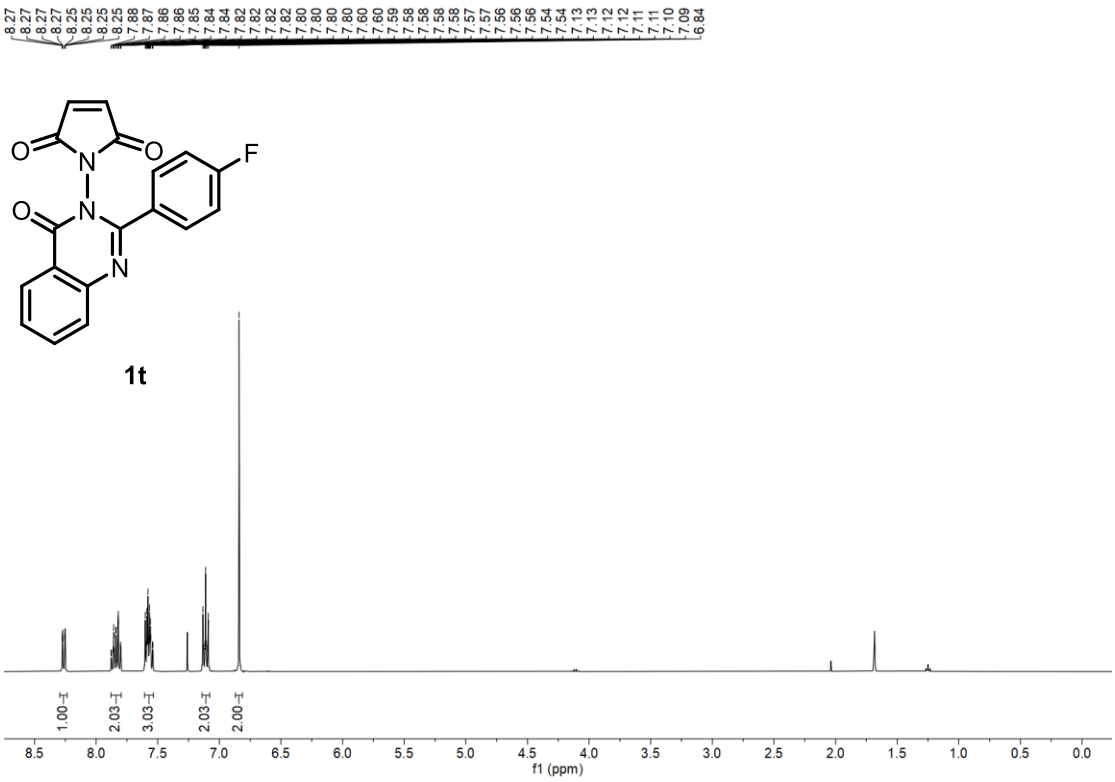
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



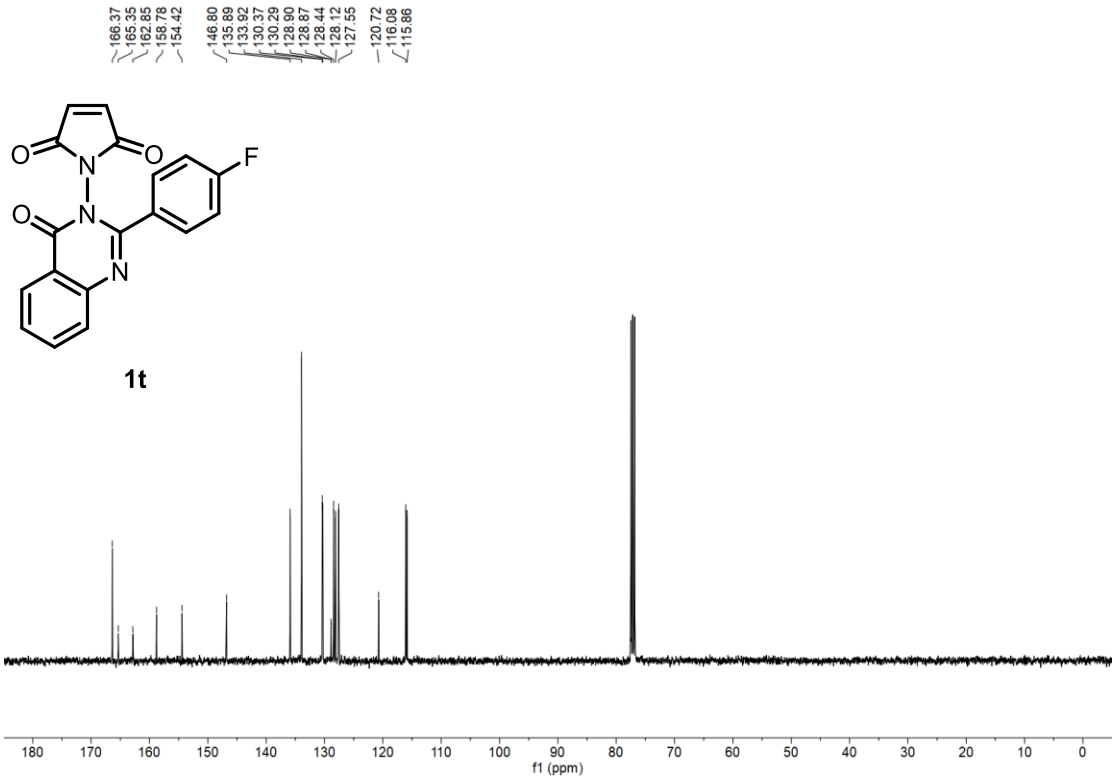

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



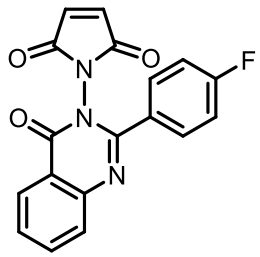
**$^{1}$H NMR** (400 MHz, $CDCl_3$)




**$^{13}$C NMR** (101 MHz, $CDCl_3$)



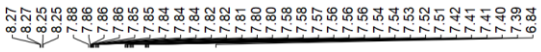
**$^{19}$F NMR** (376 MHz, $CDCl_3$)

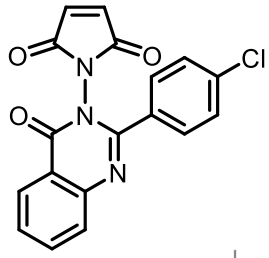


**1t**

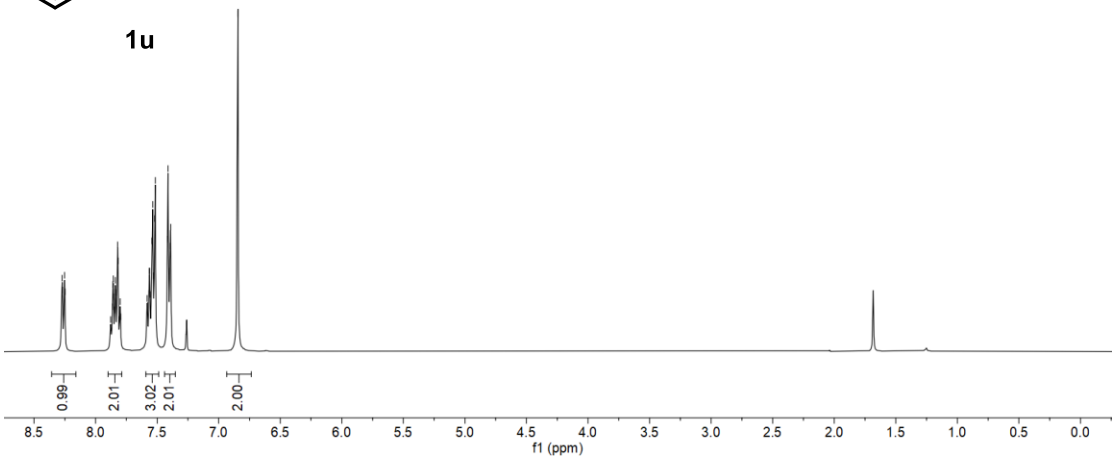



**$^{1}$H NMR** (400 MHz, $CDCl_3$)

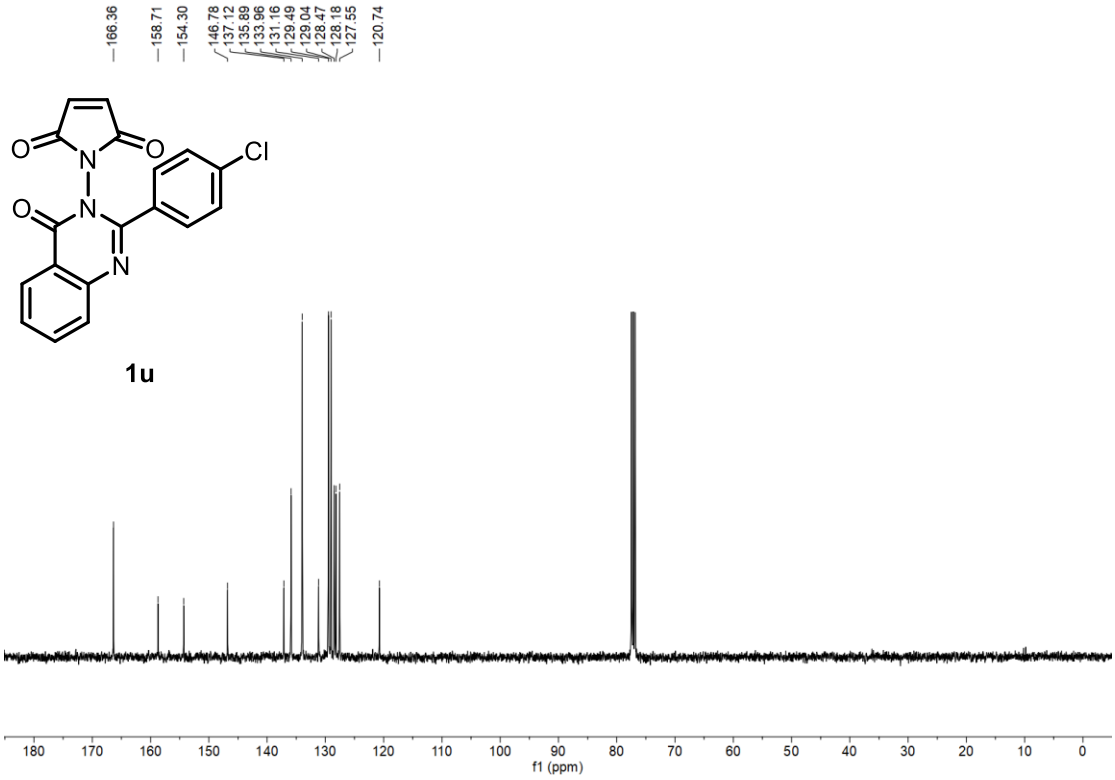


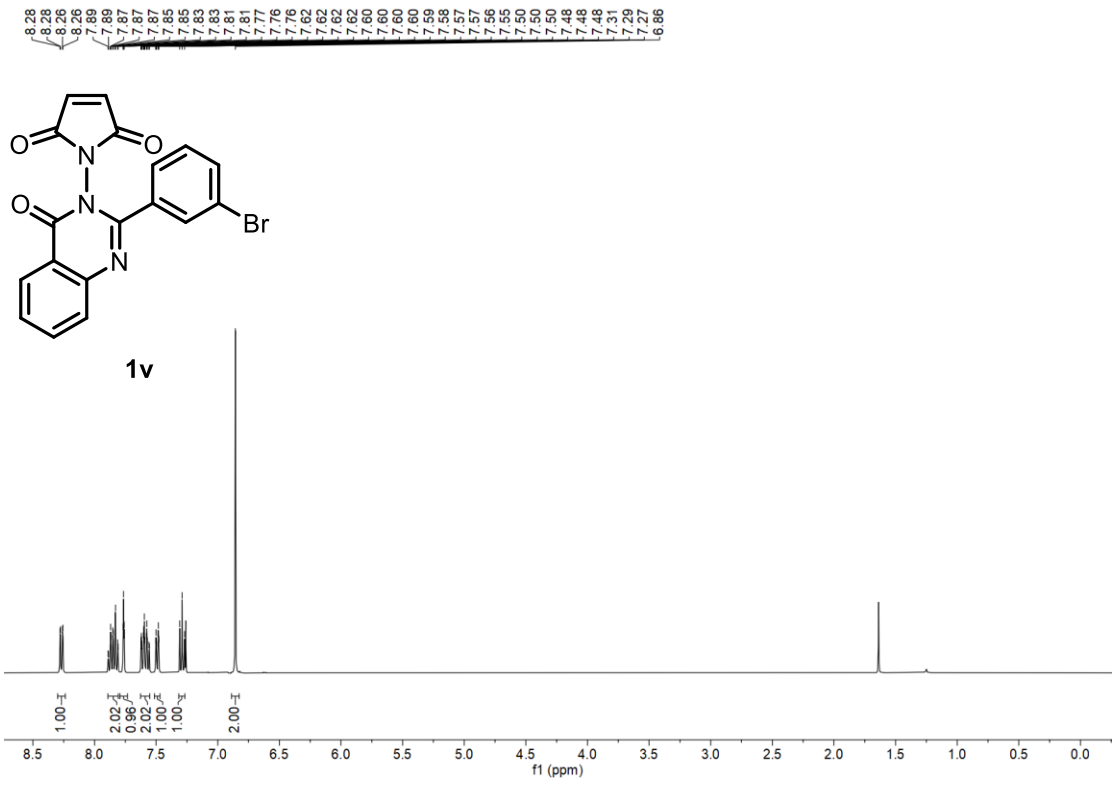
**1u**



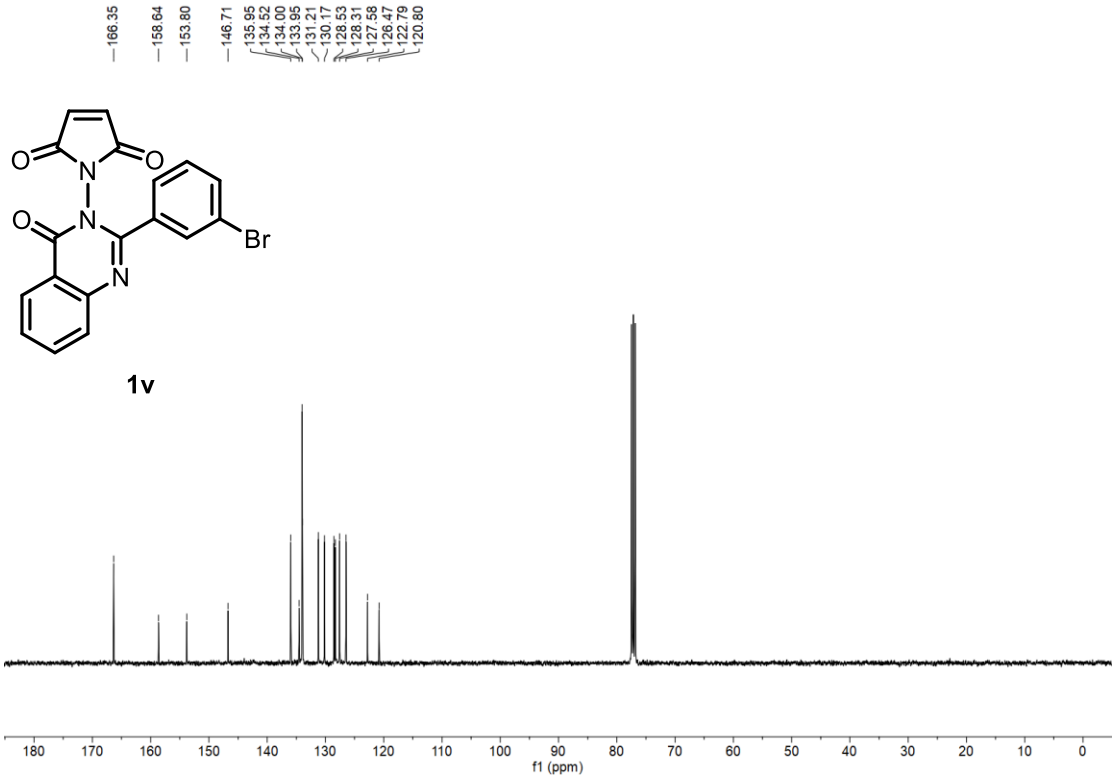
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



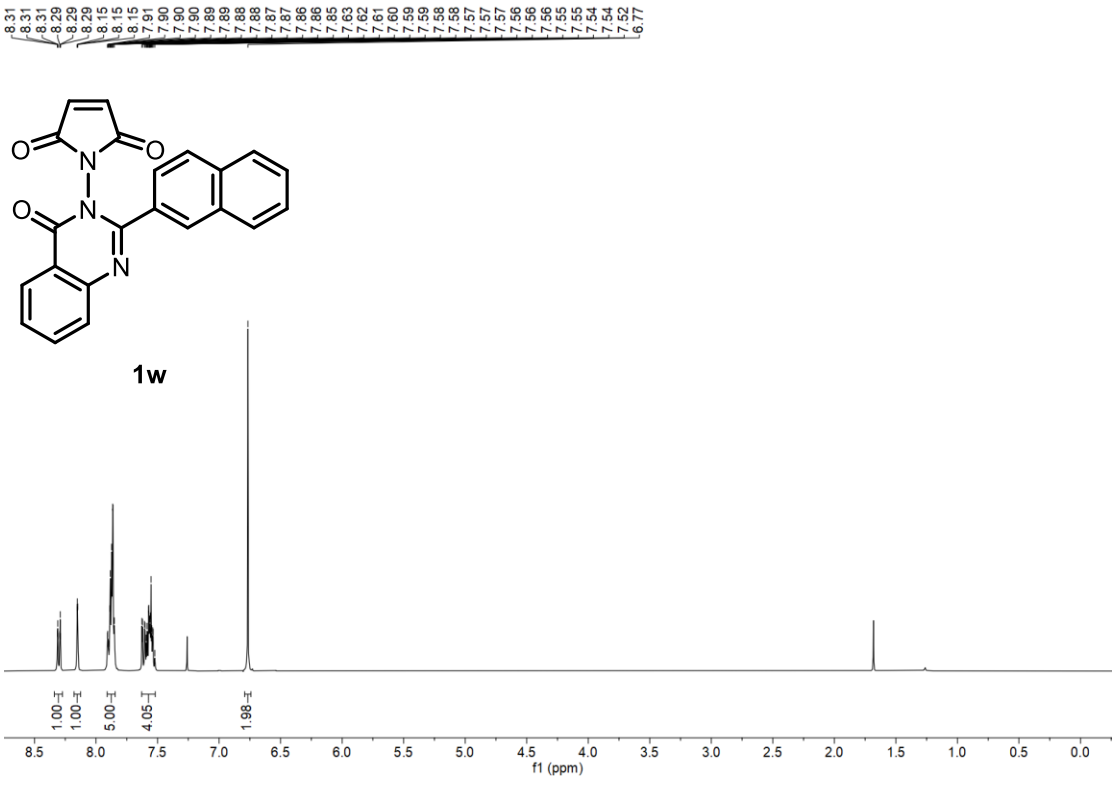

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



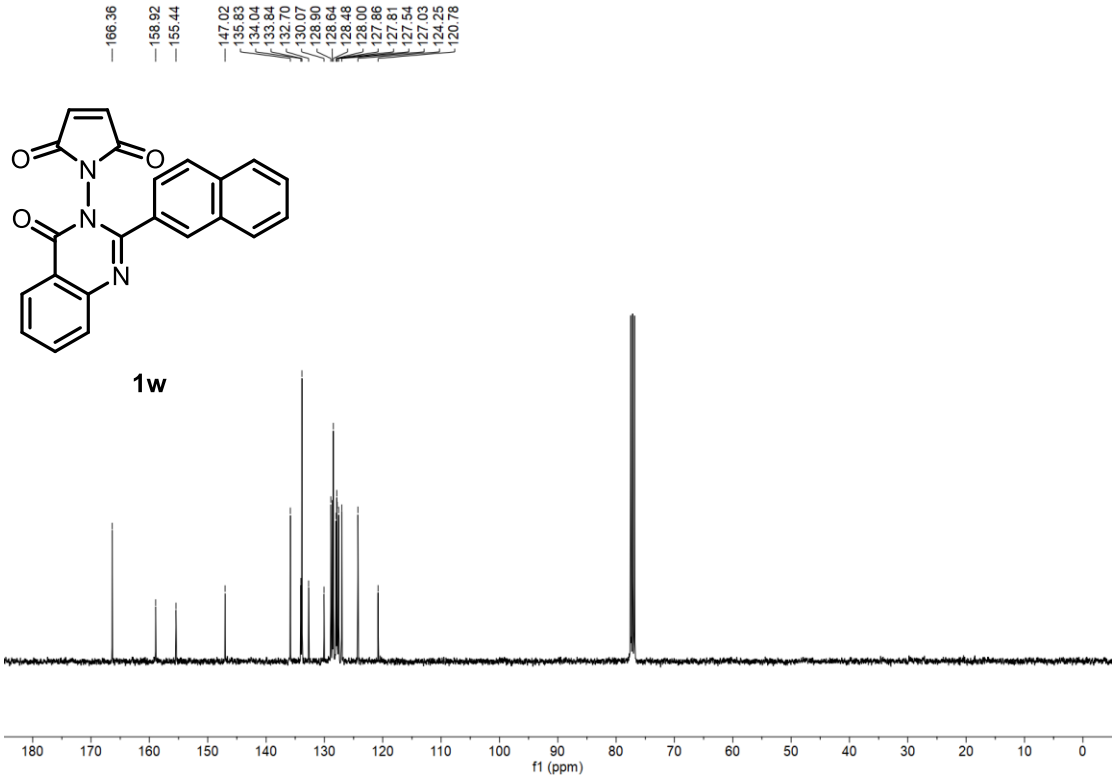
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



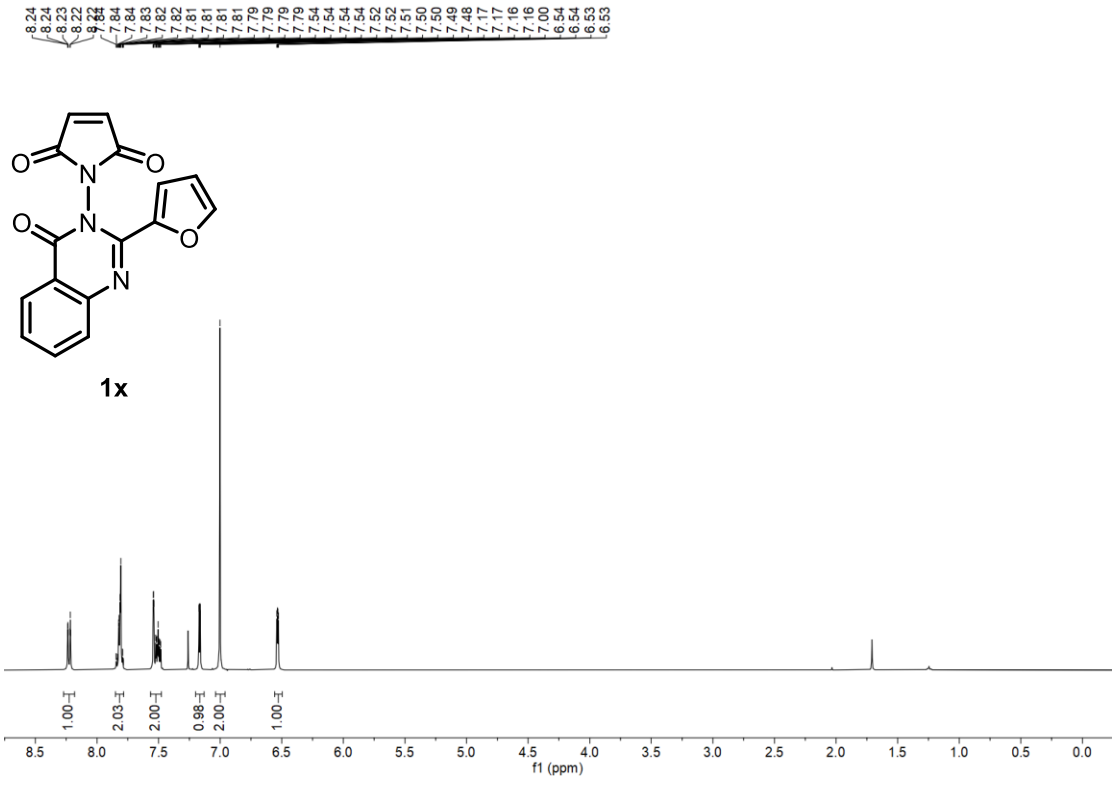

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



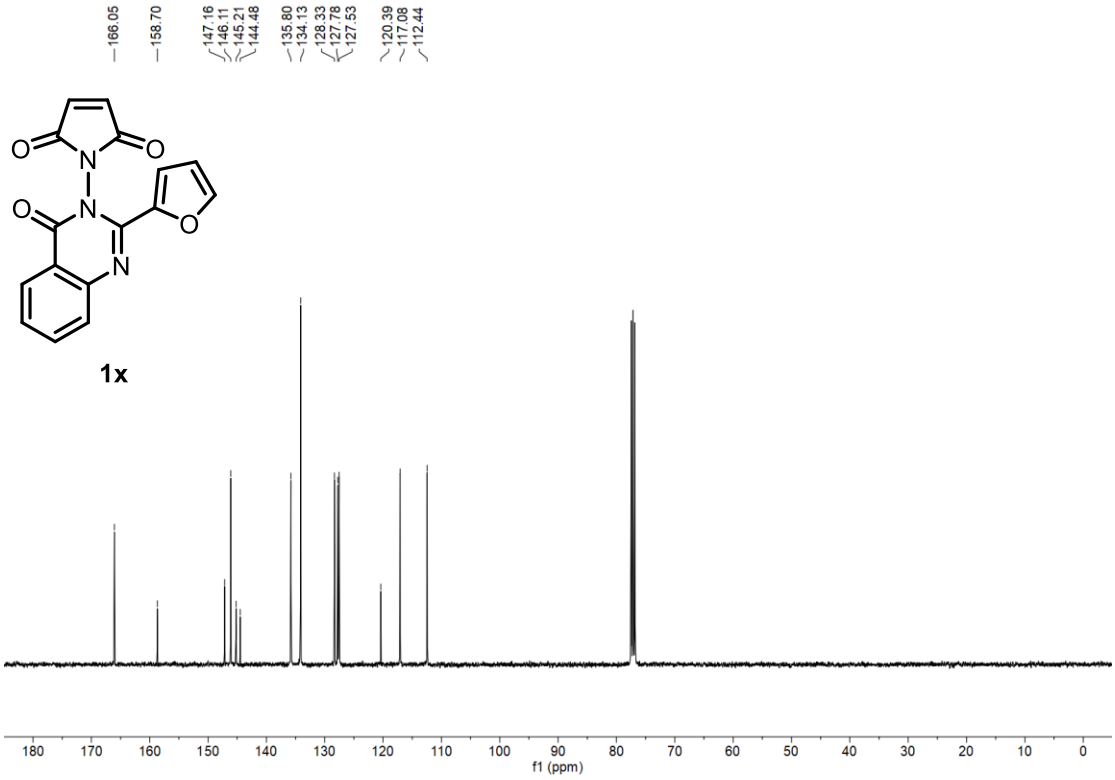
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



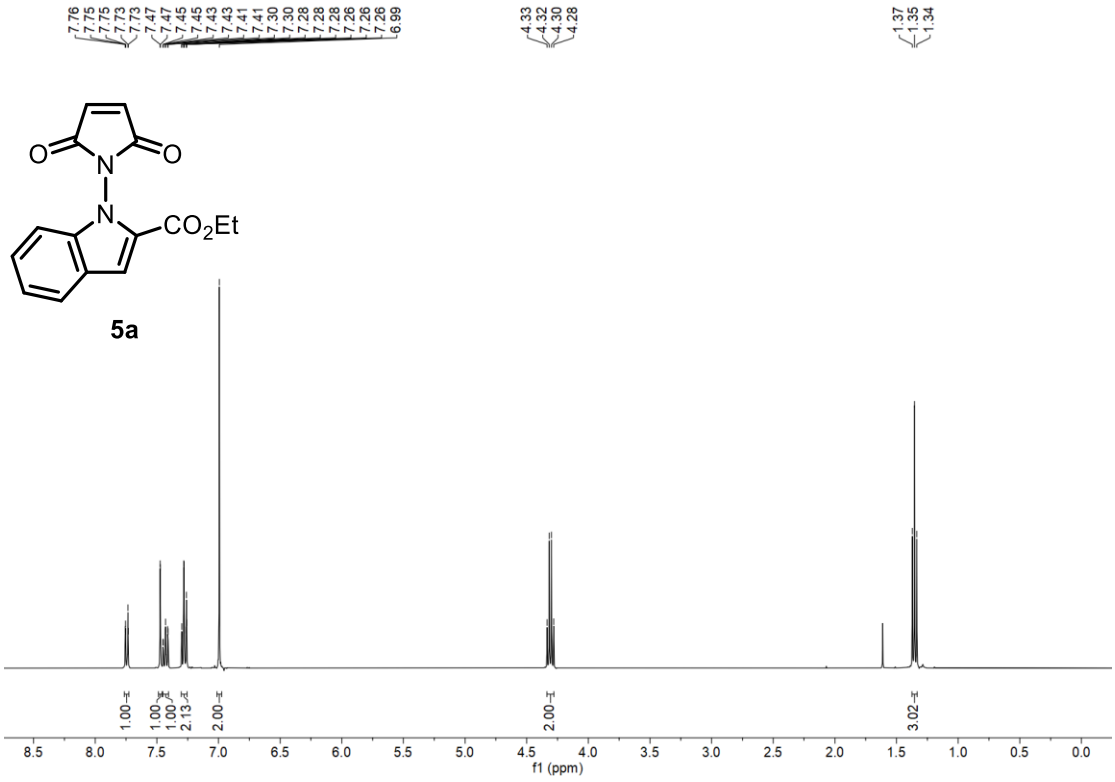

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



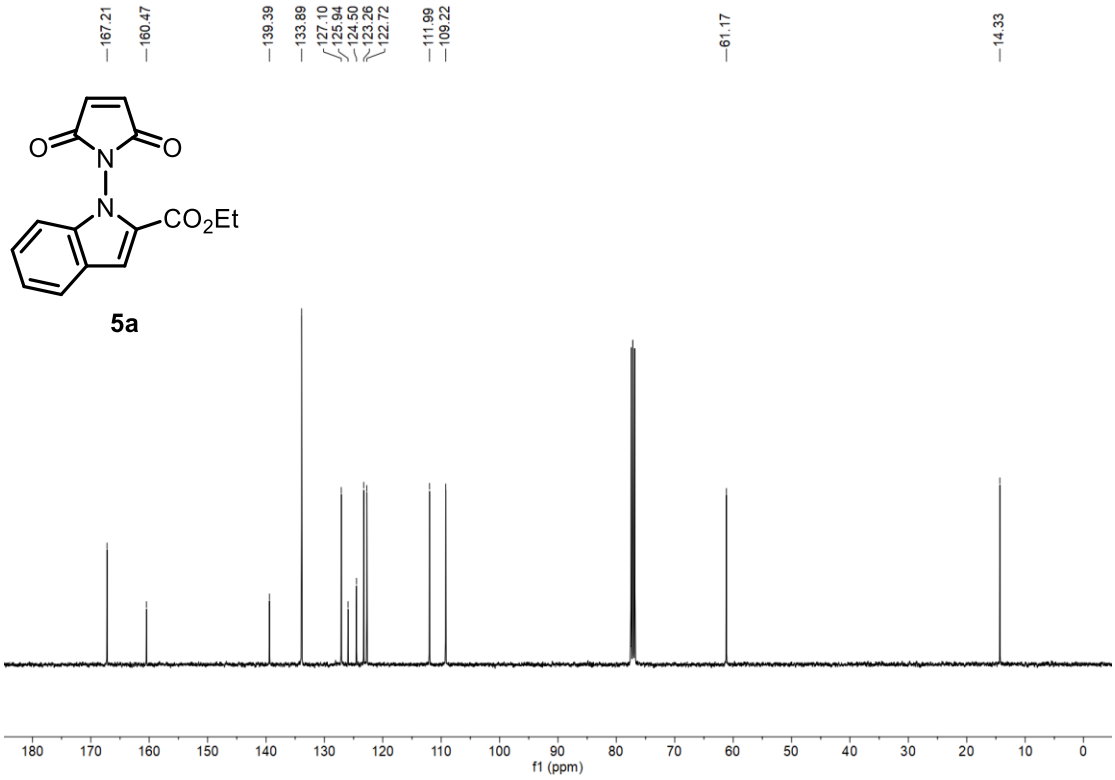
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



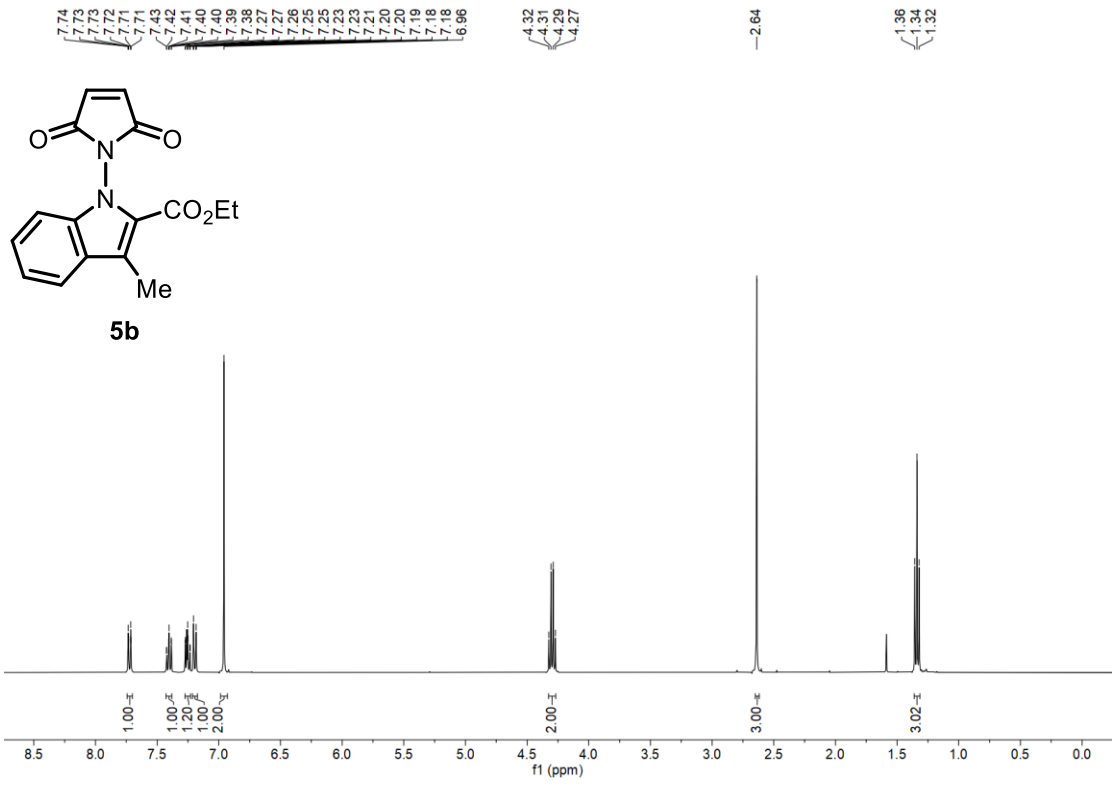

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



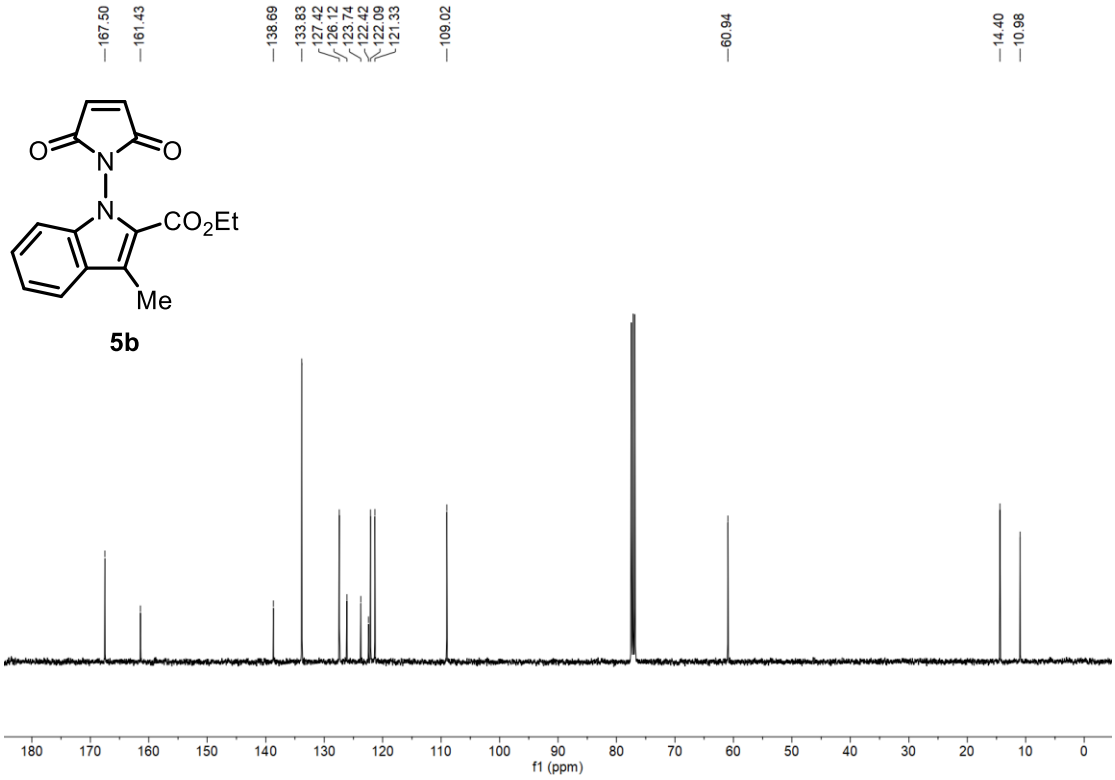
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



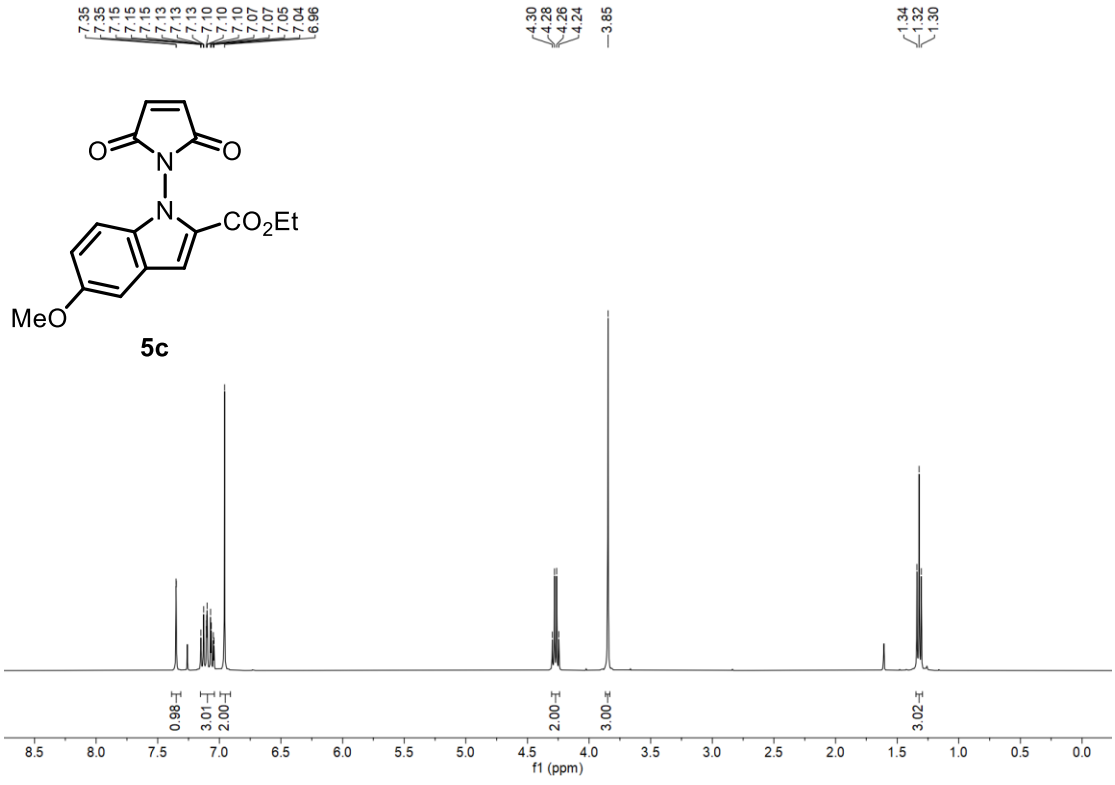

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



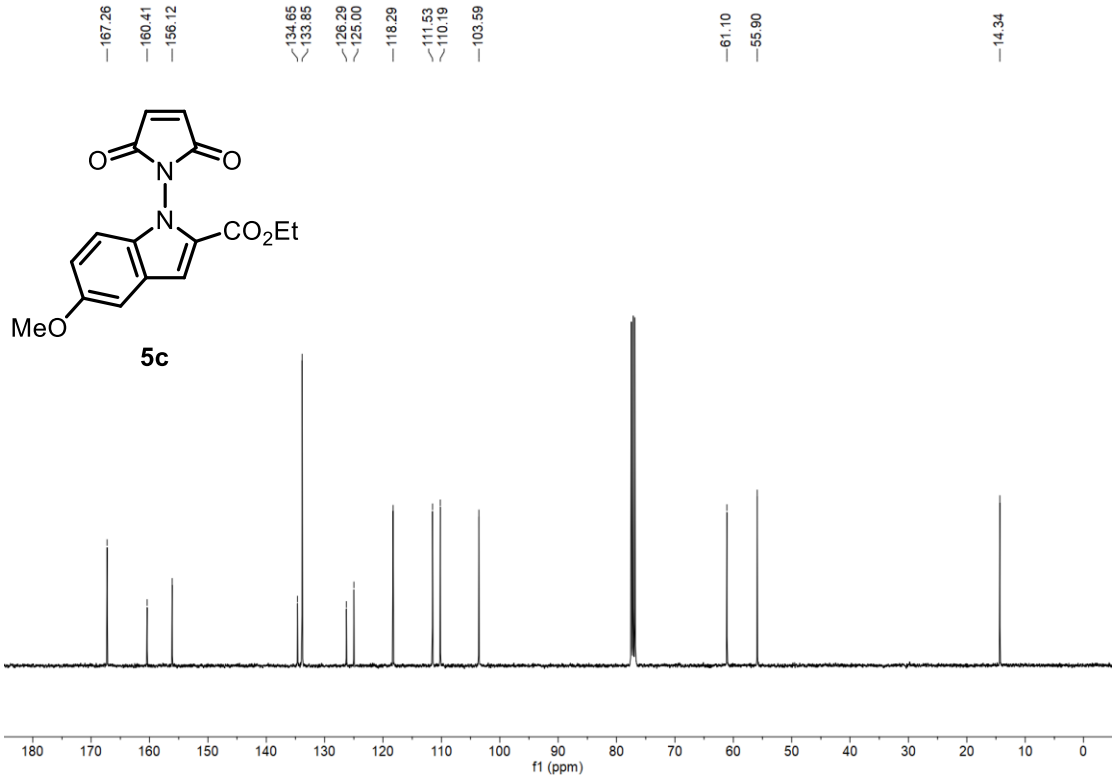
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



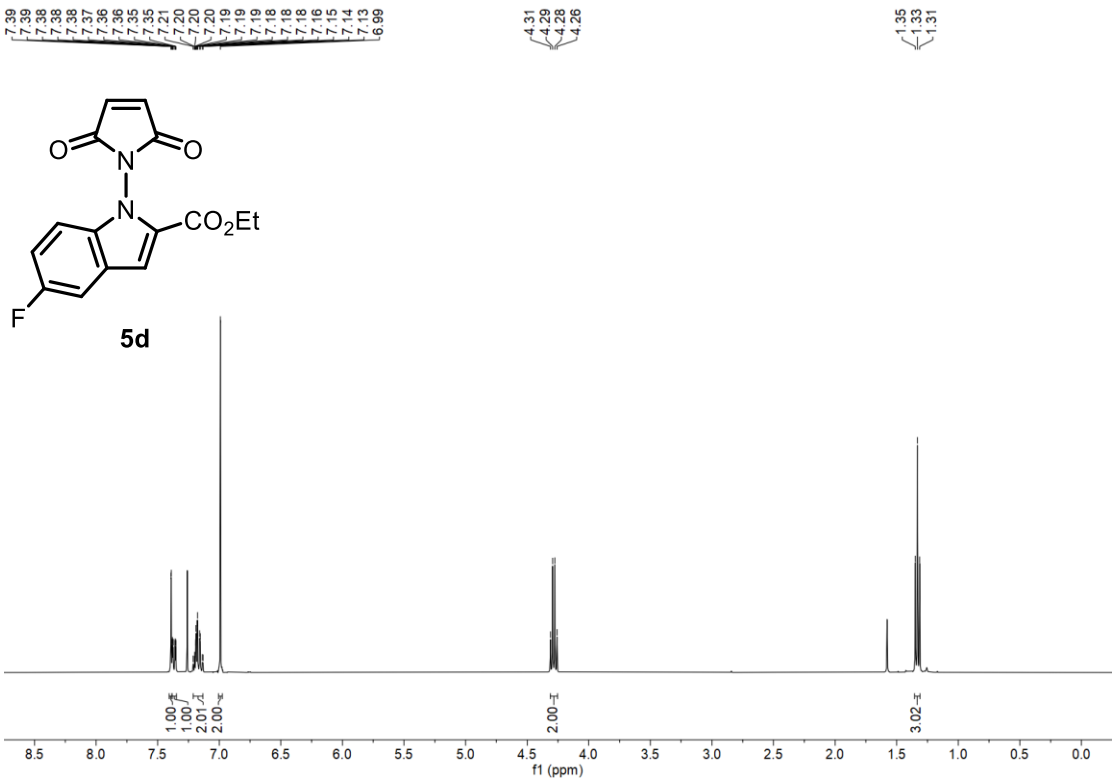

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



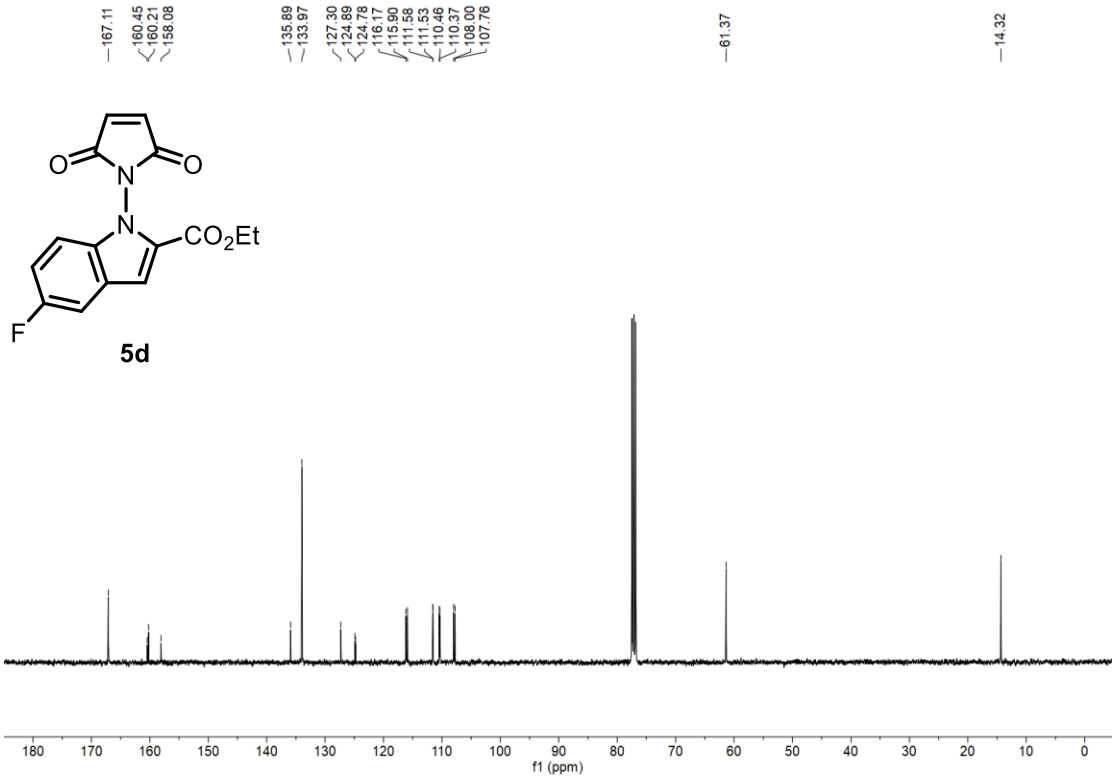
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



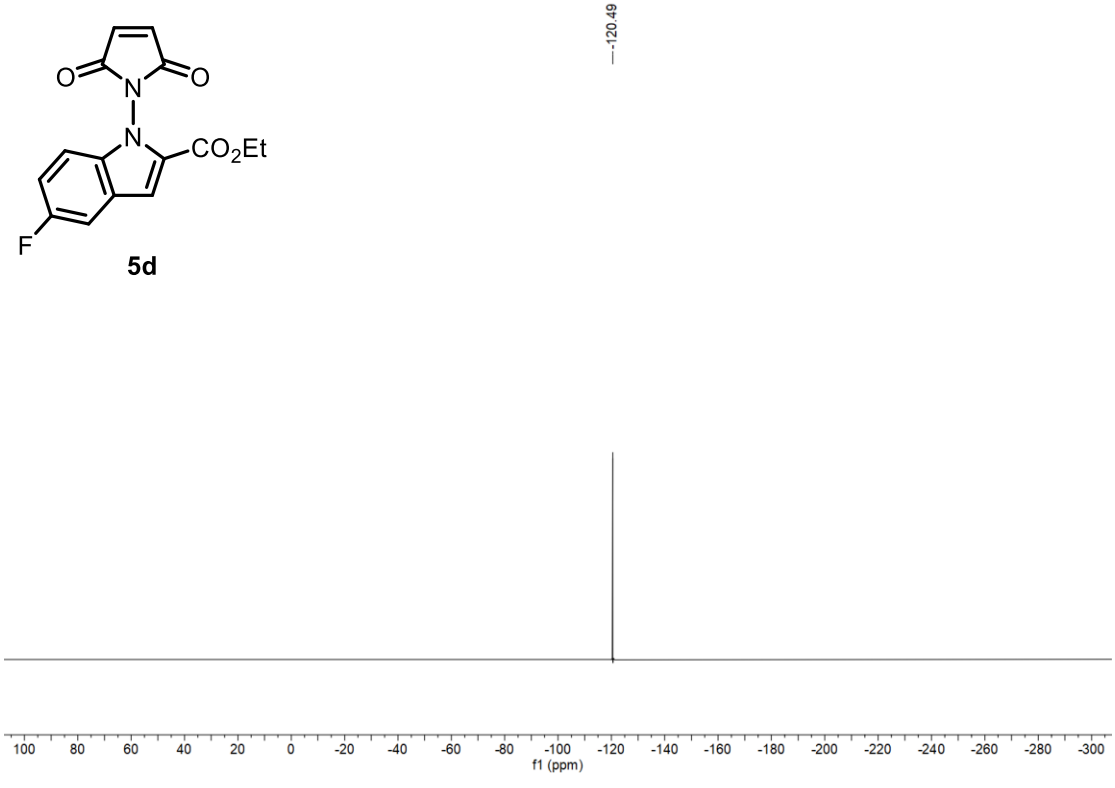

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



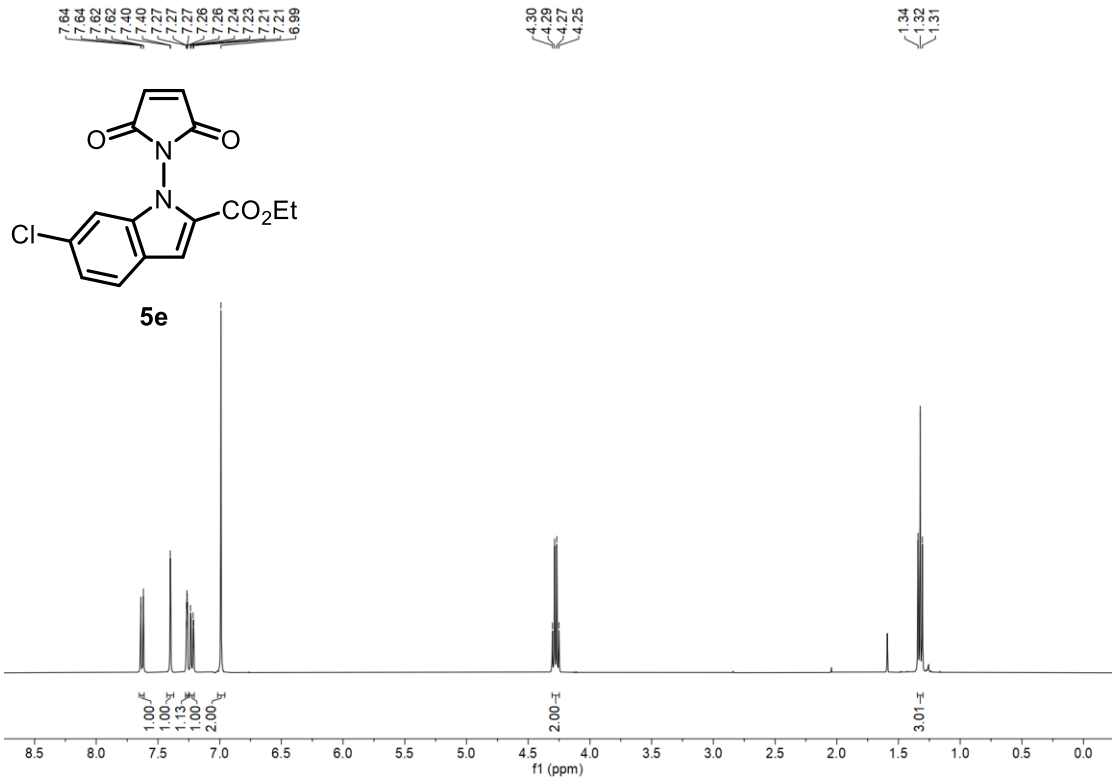
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



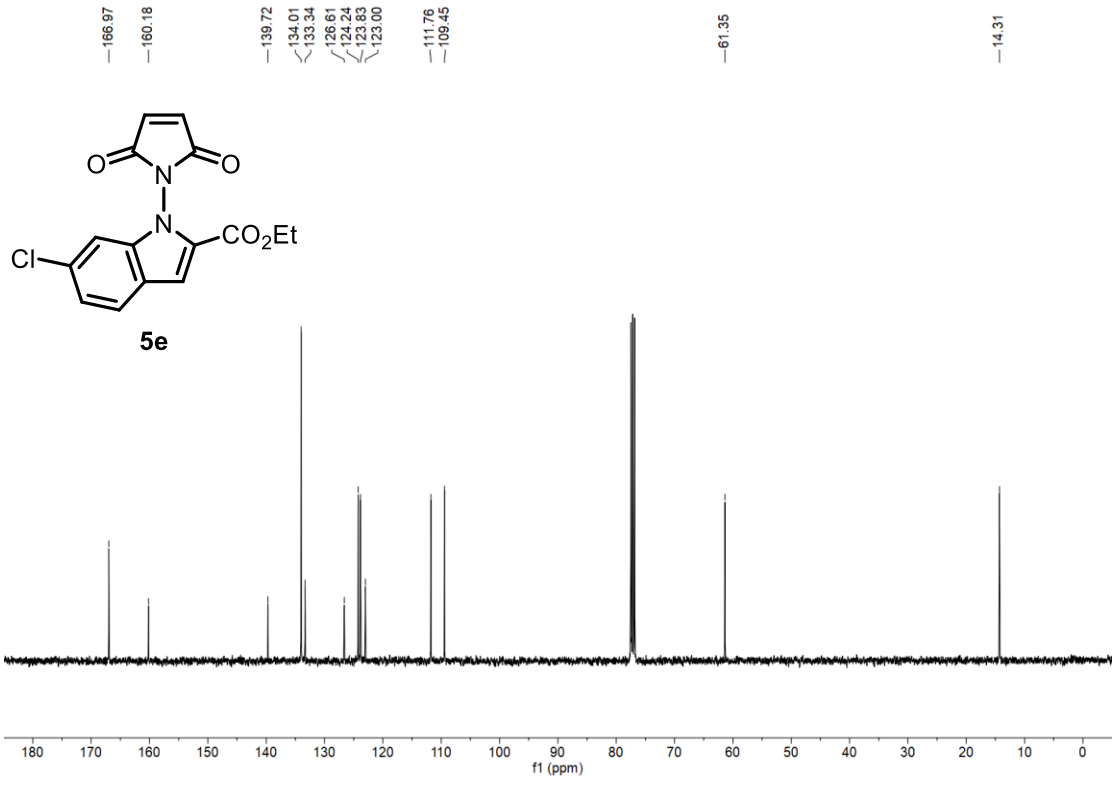

**$^{19}$F NMR** (376 MHz, $CDCl_3$)



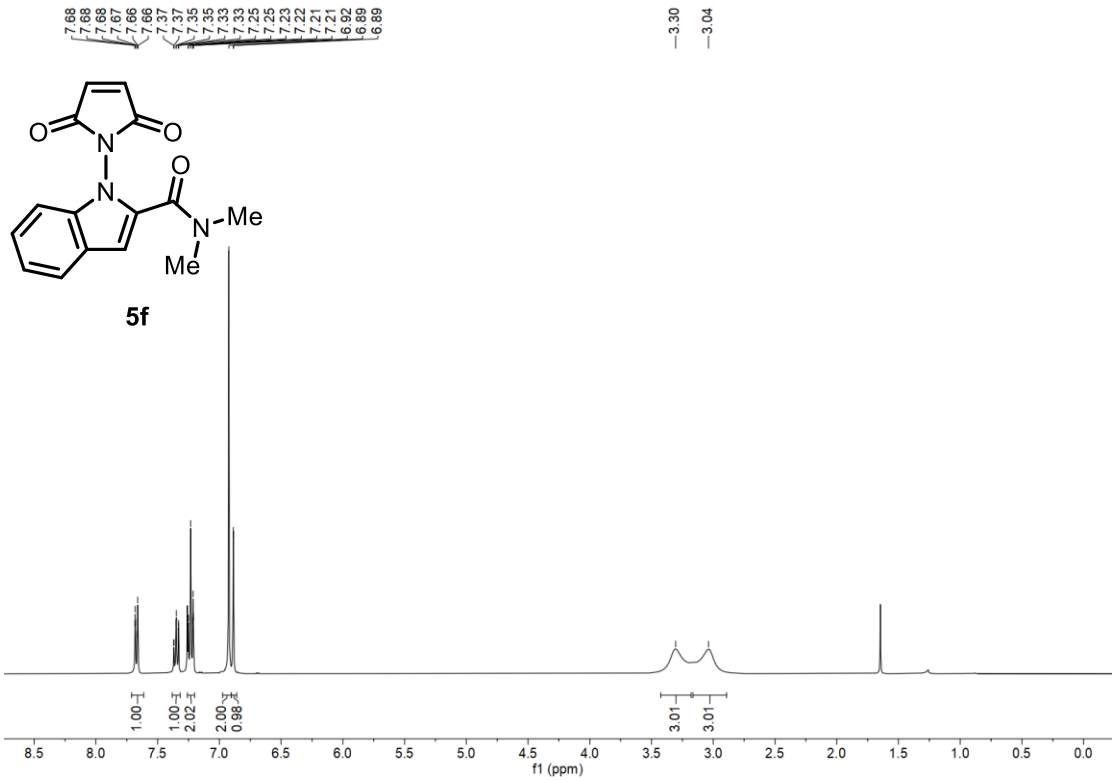
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



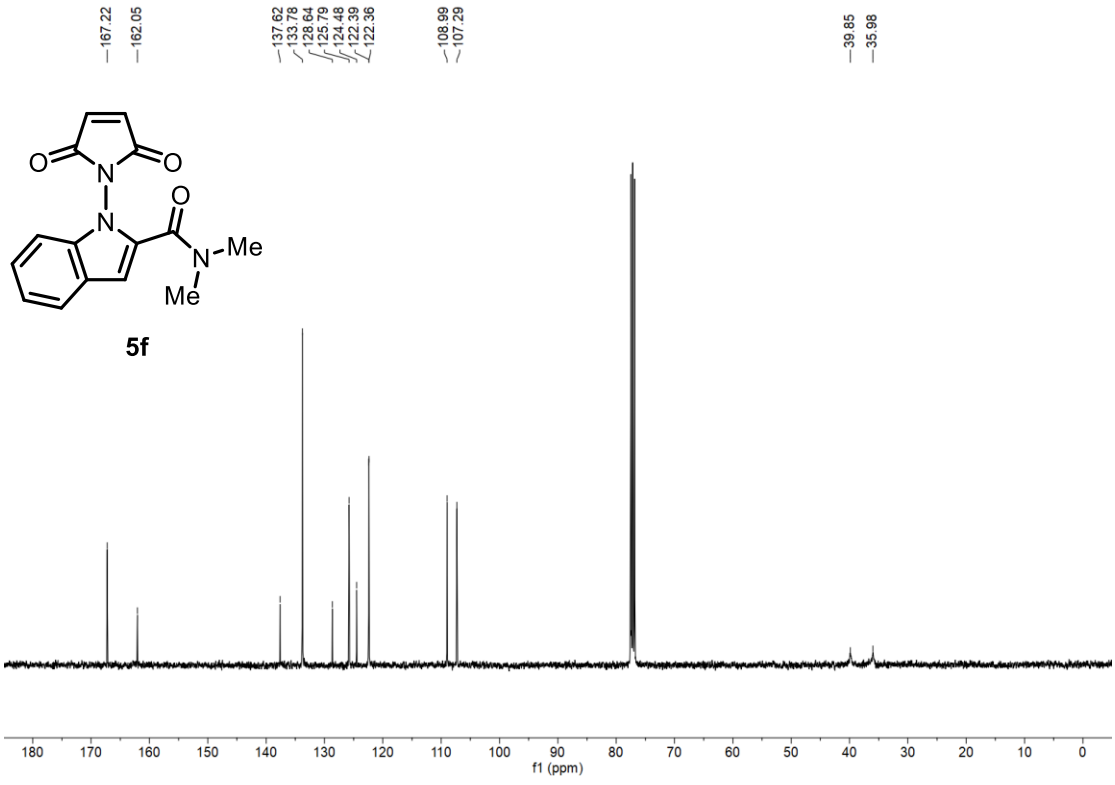

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



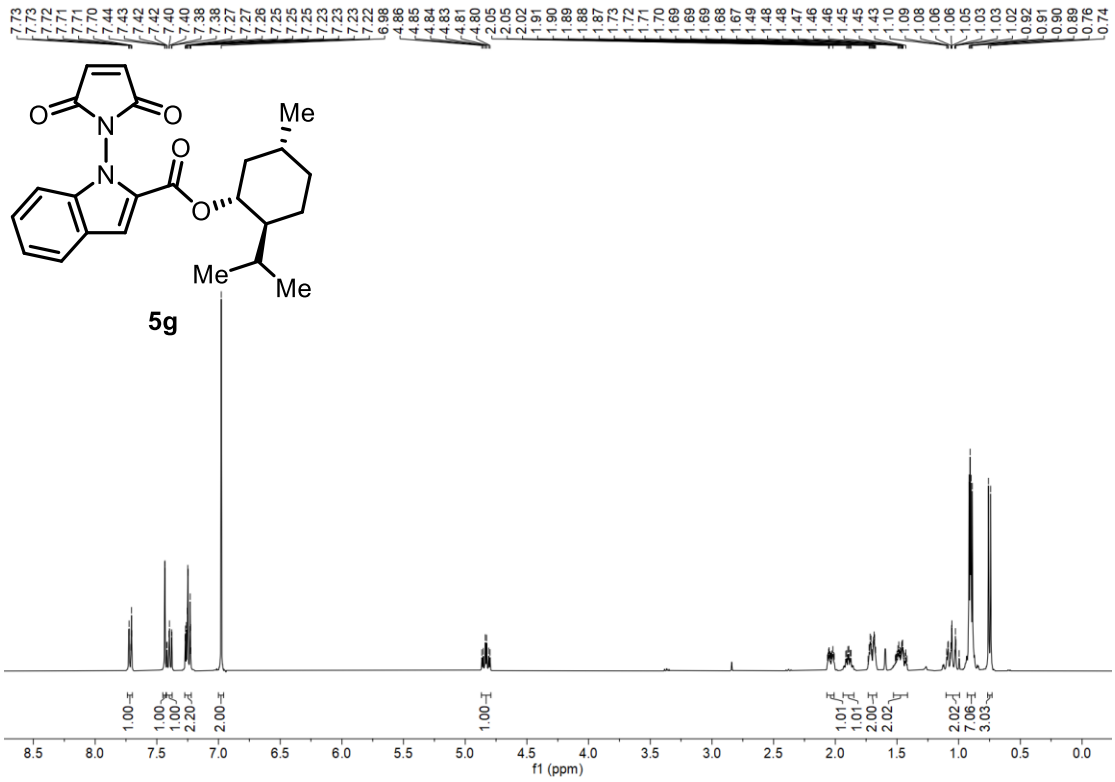
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



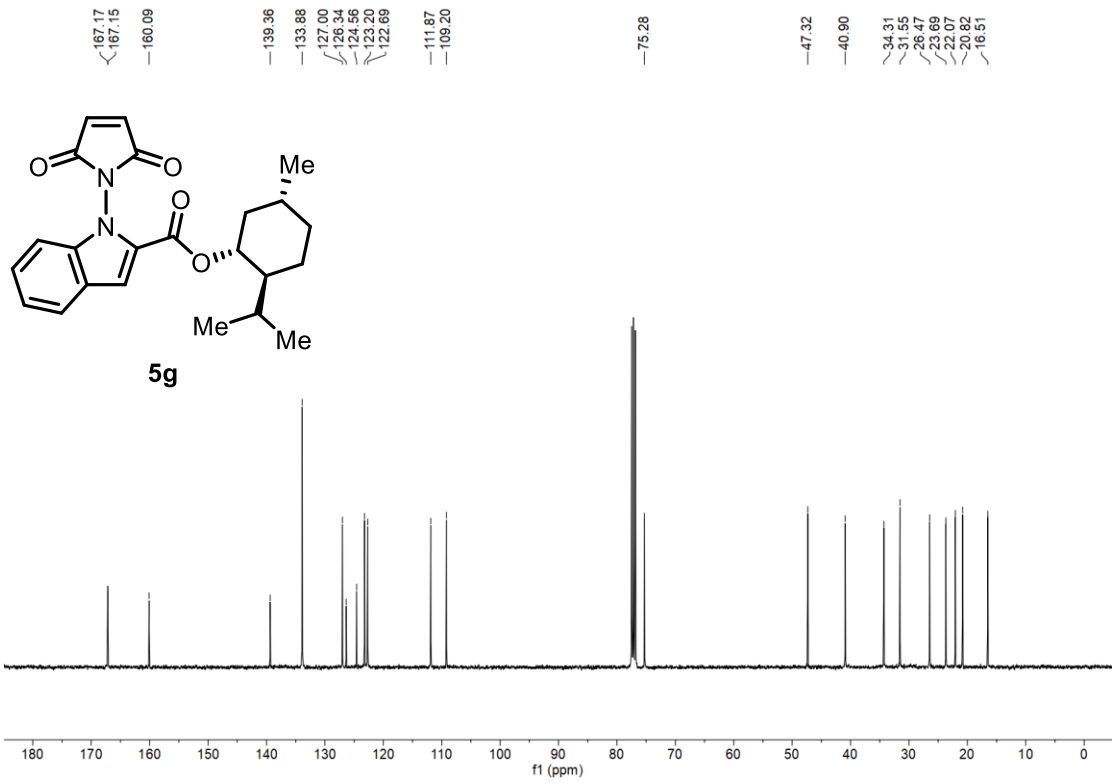

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



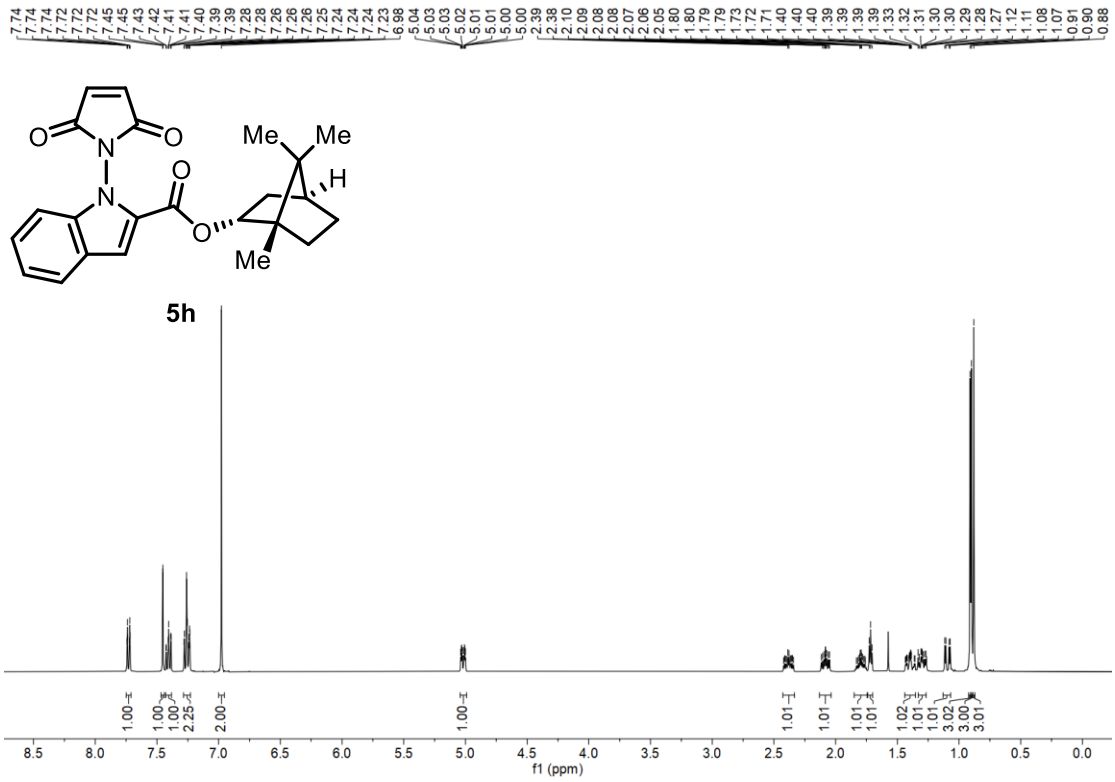
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



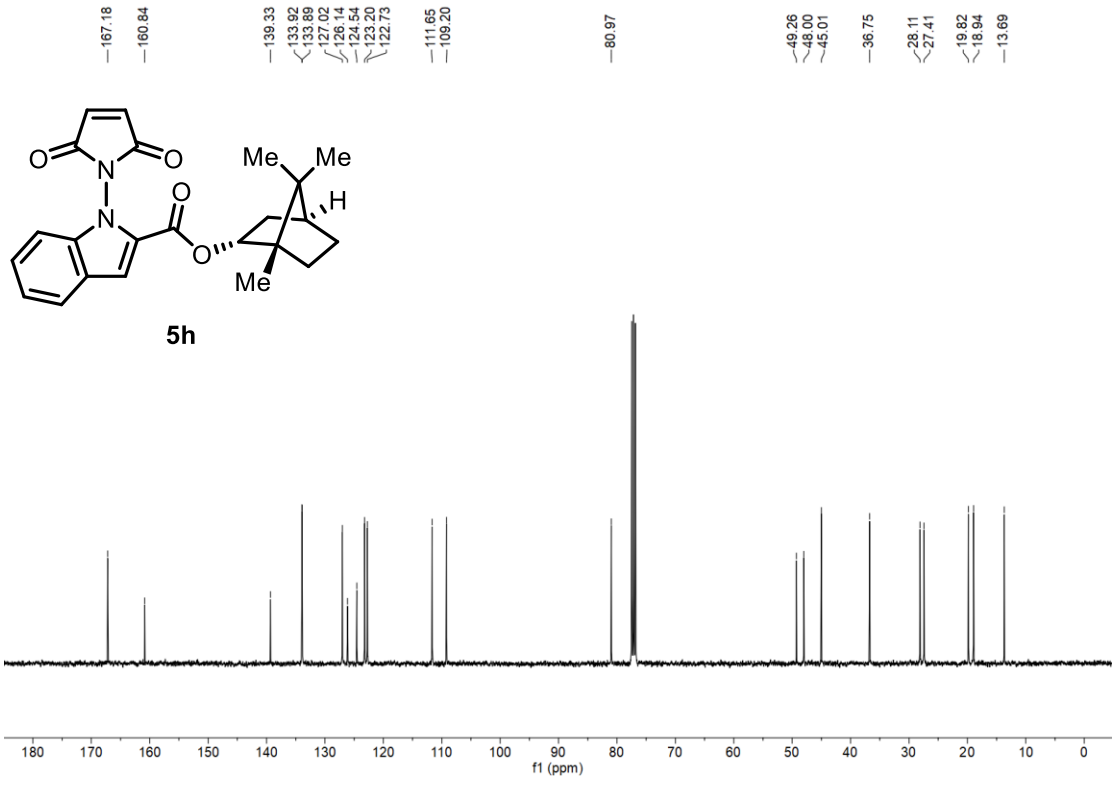

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



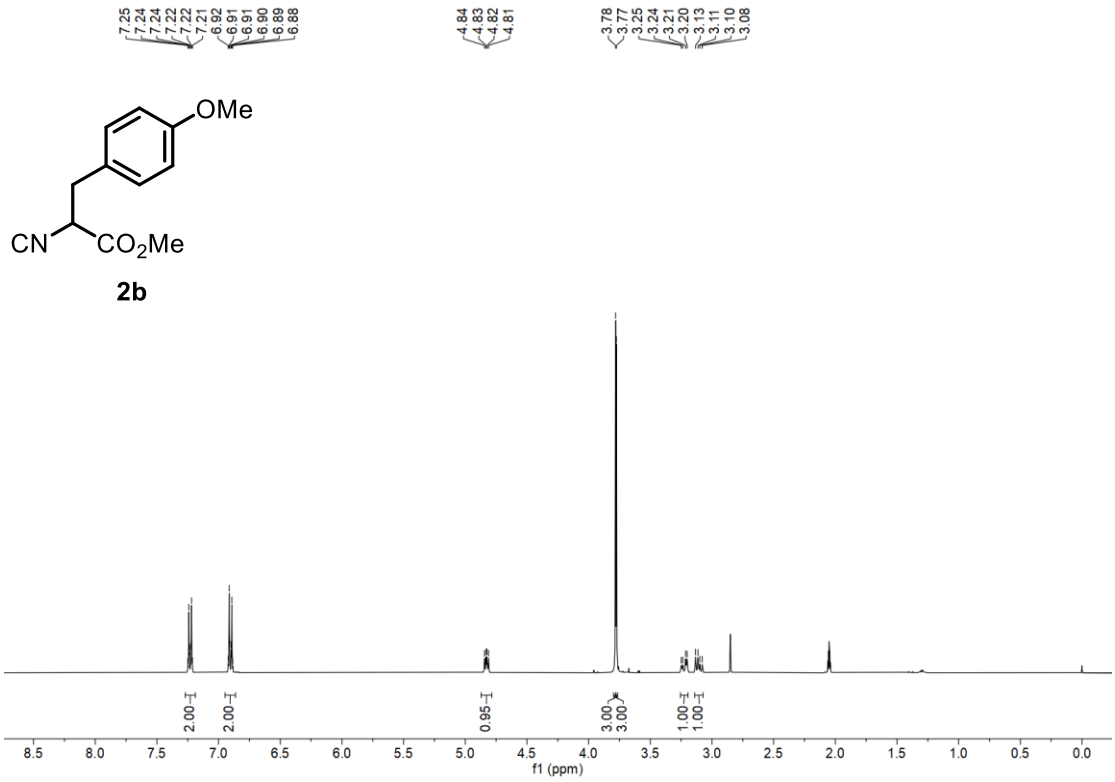
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



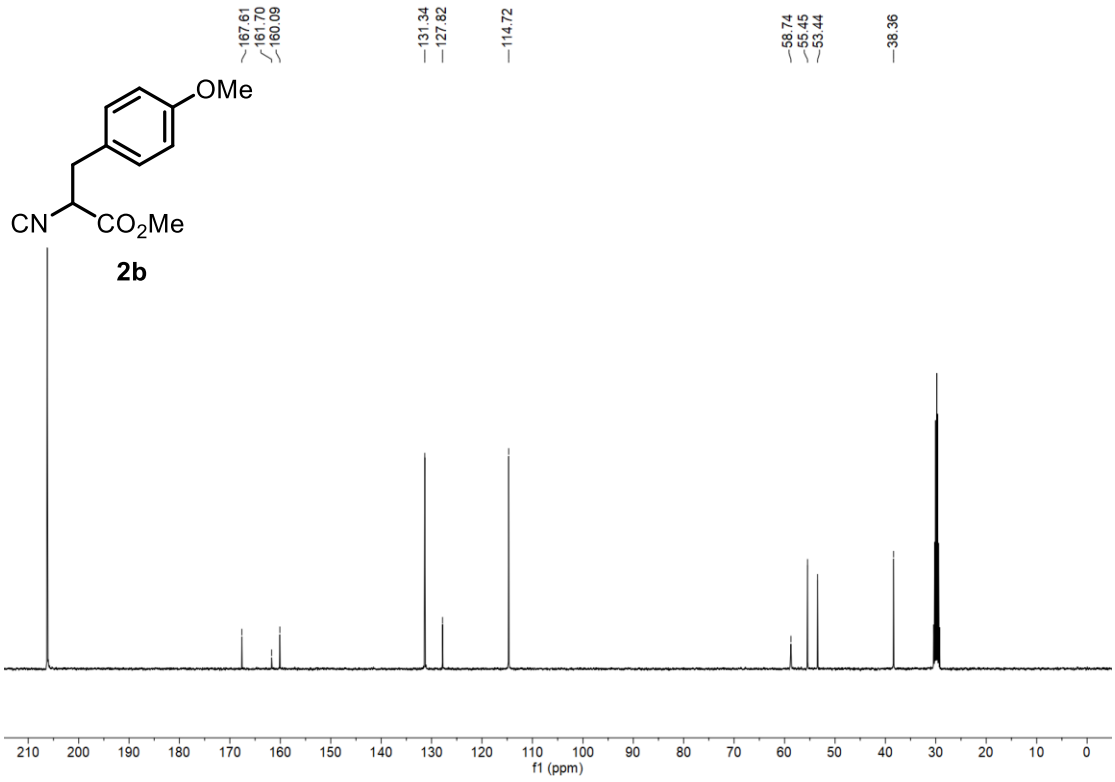

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



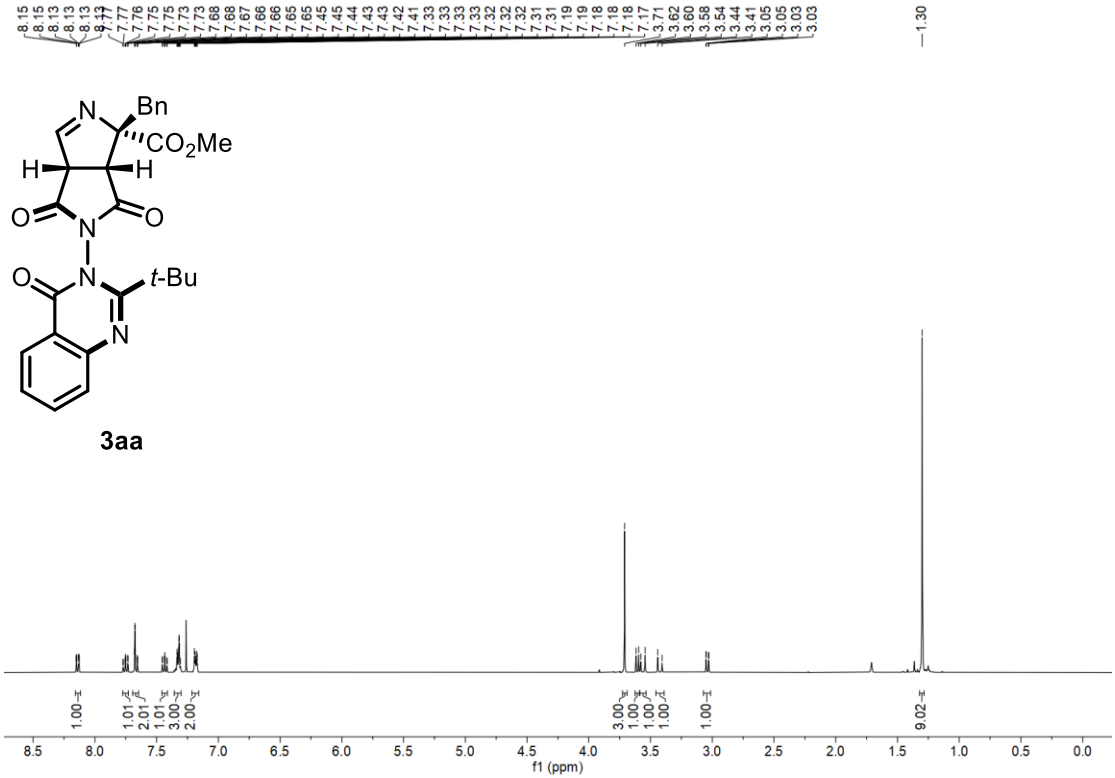
**$^{1}$H NMR** (400 MHz, acetone-$d_6$)



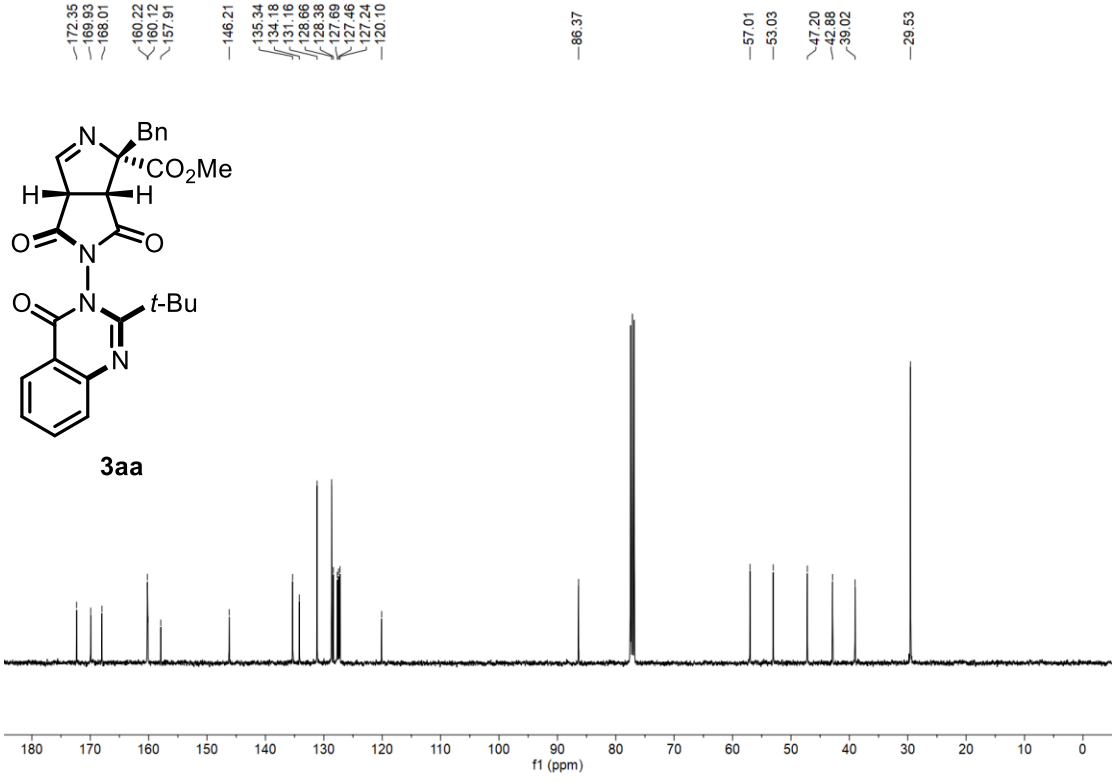

**$^{13}$C NMR** (101 MHz, acetone-$d_6$)



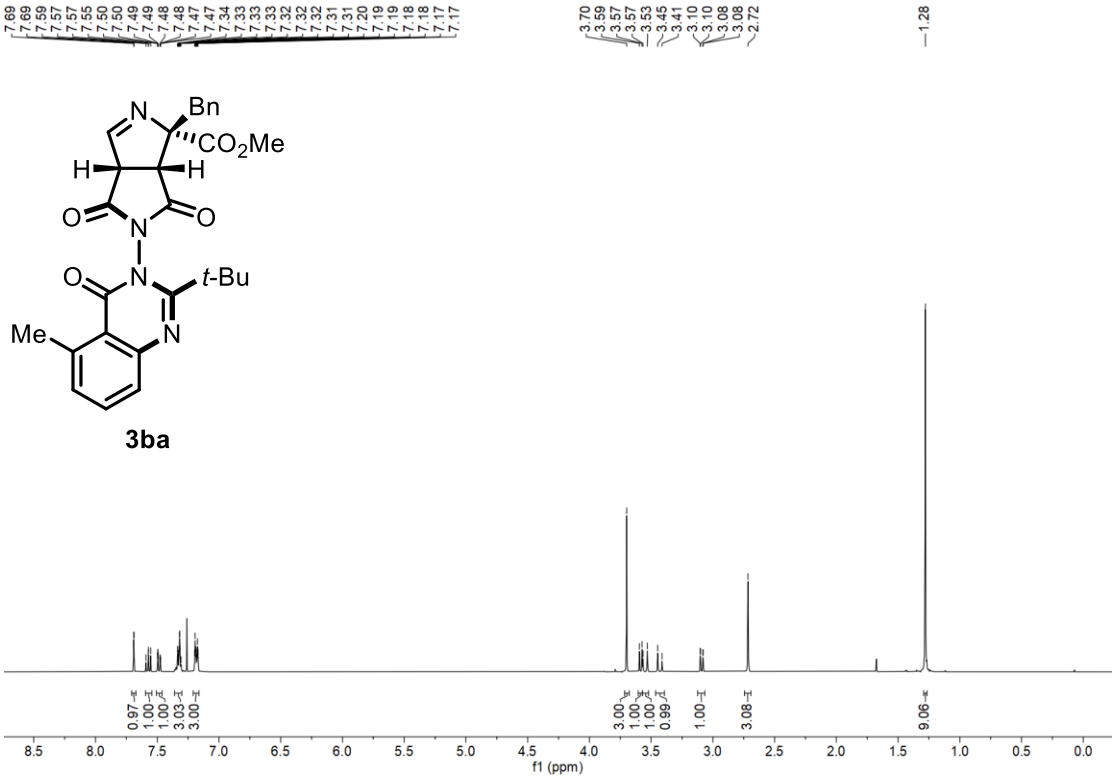
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



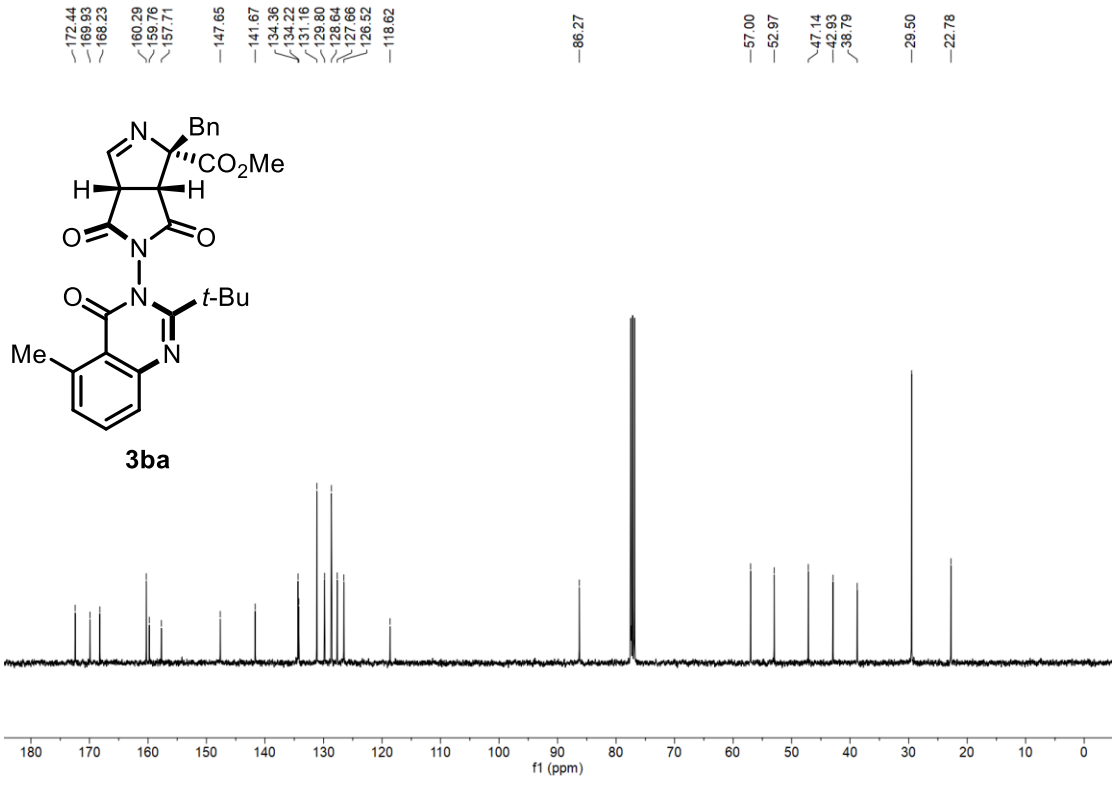

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



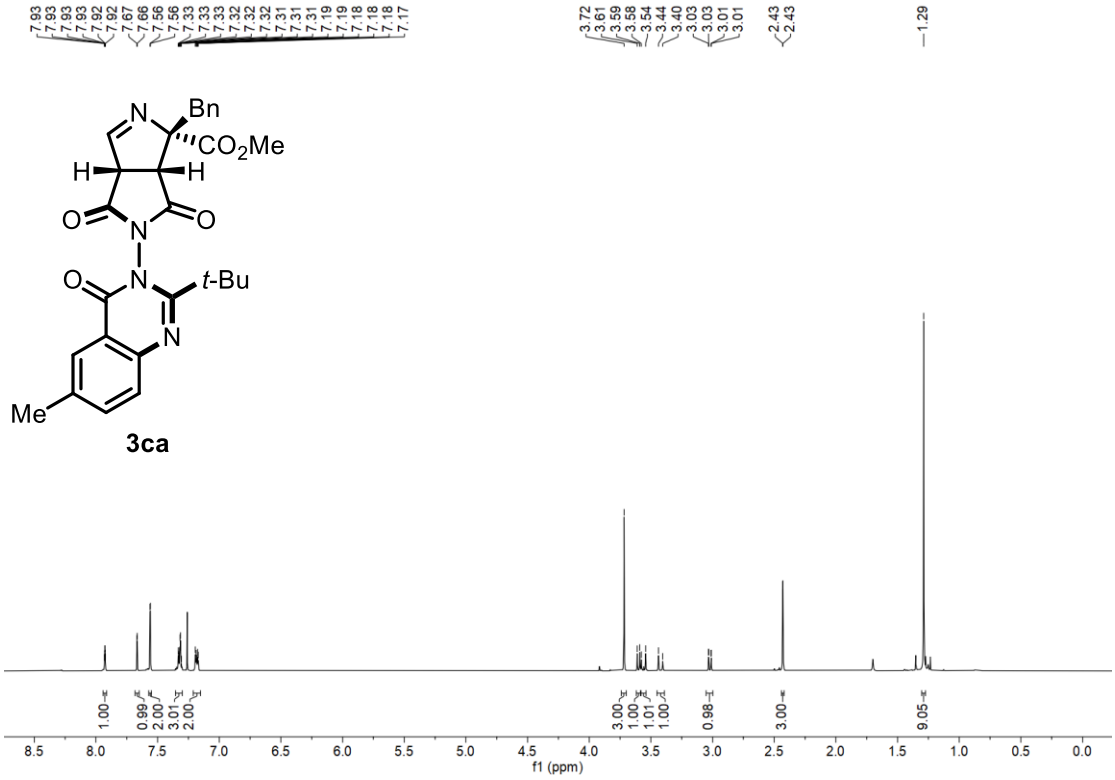
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



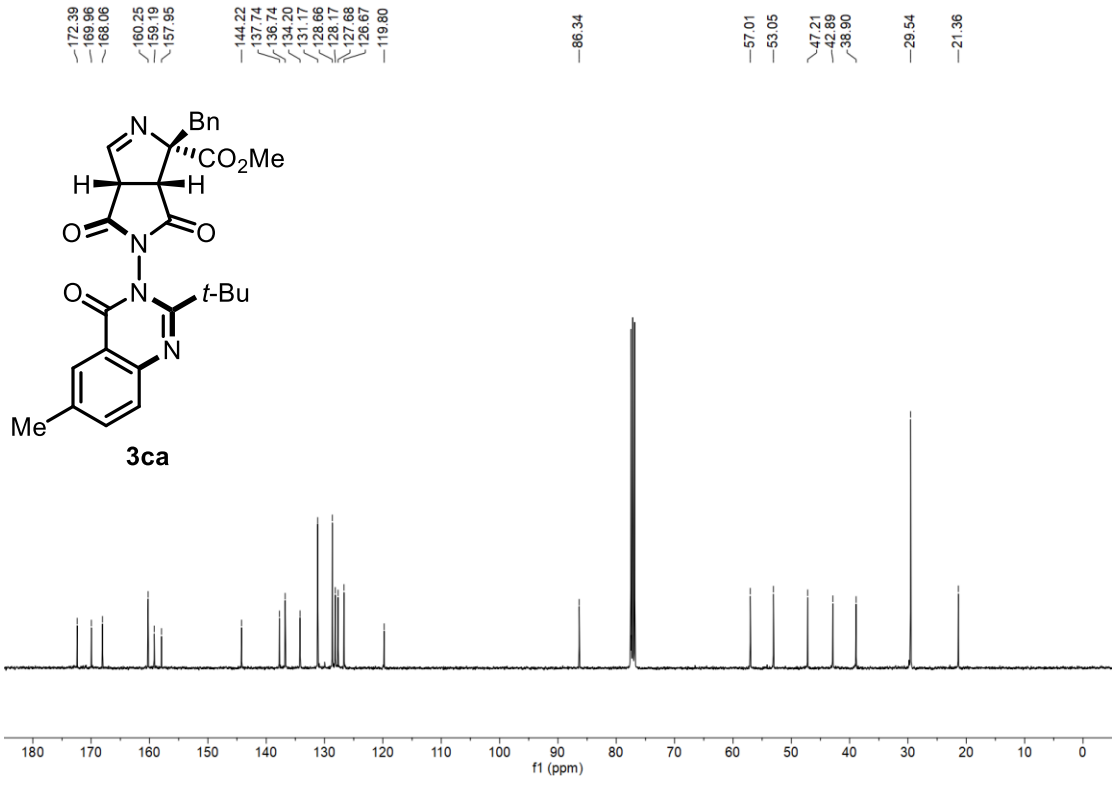

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



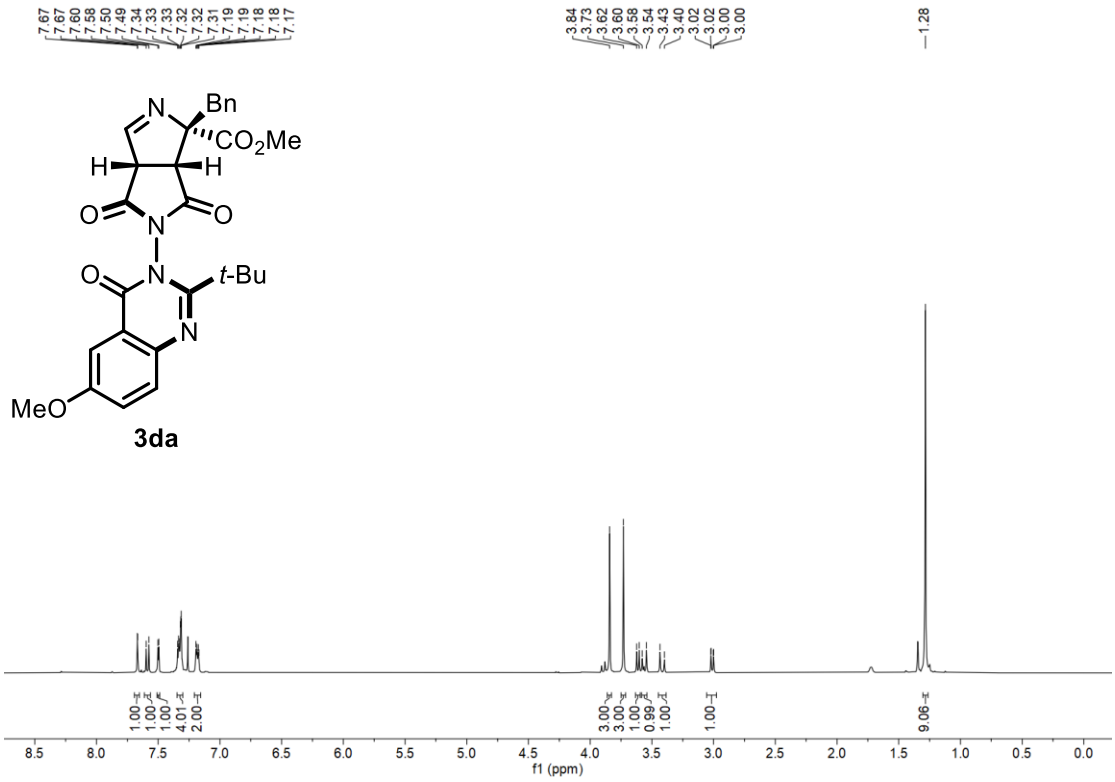
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



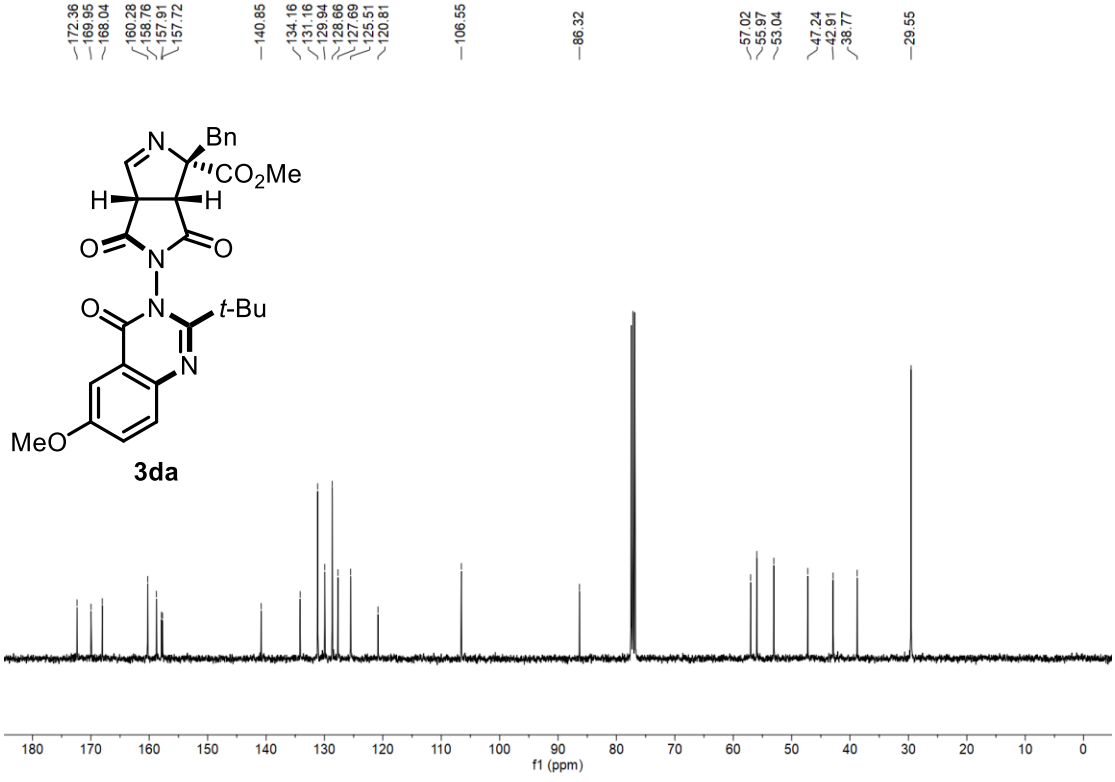

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



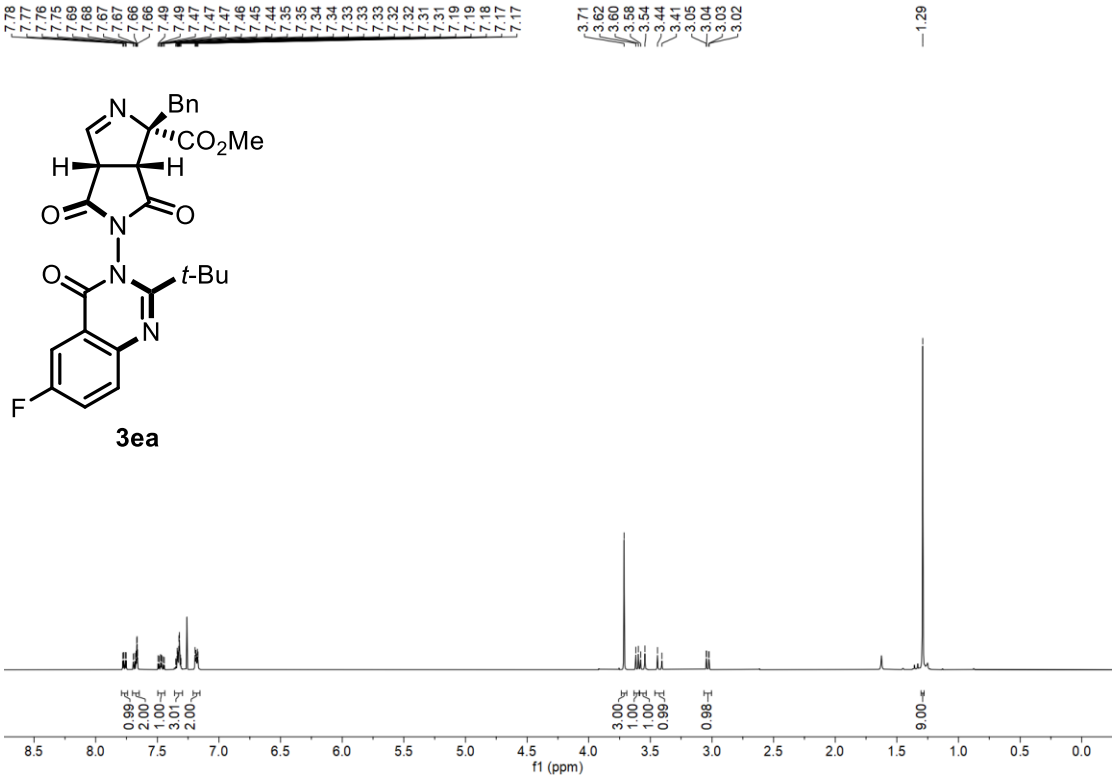
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



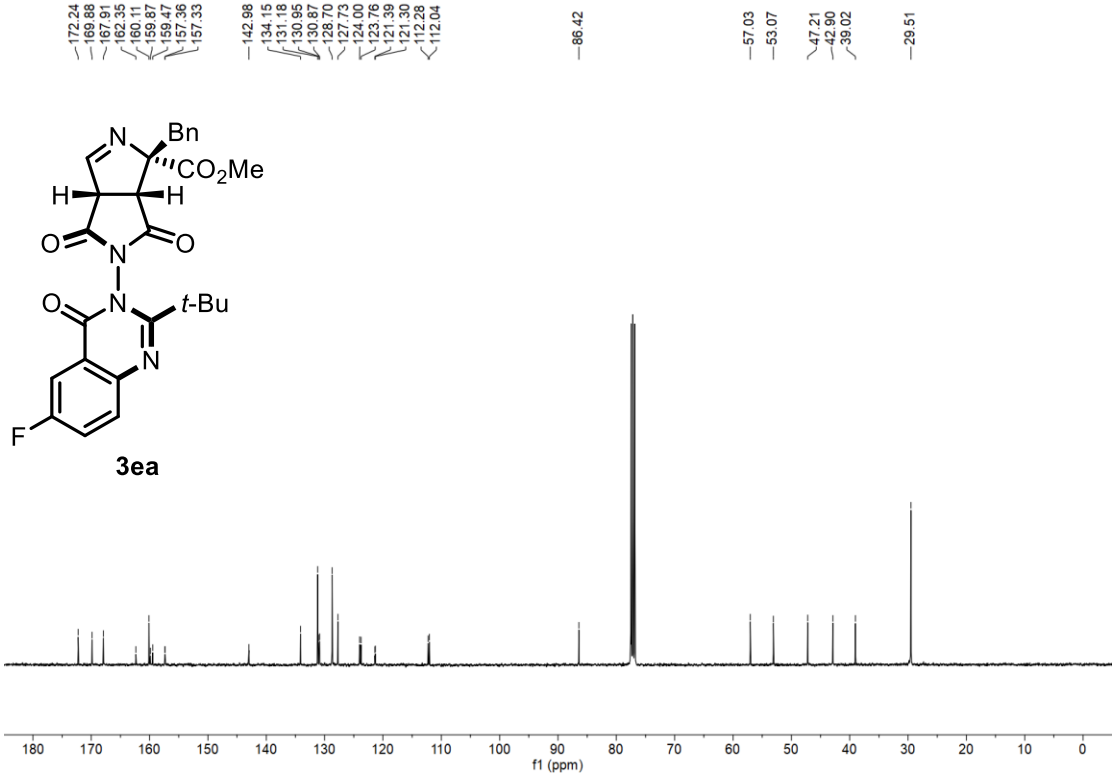

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



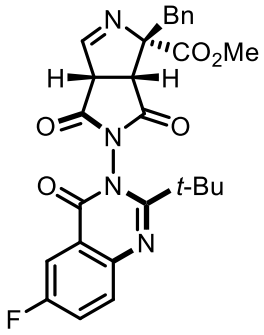
**$^{1}$H NMR** (400 MHz, $CDCl_3$)




**$^{13}$C NMR** (101 MHz, $CDCl_3$)



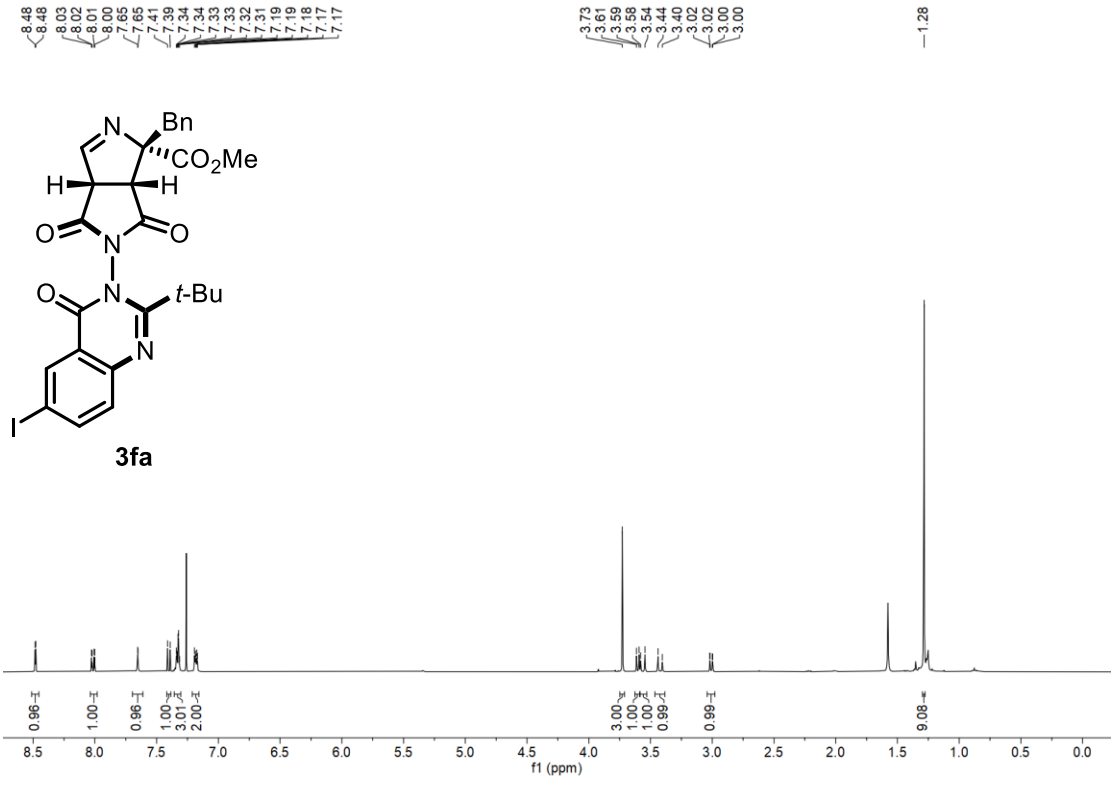
**$^{19}$F NMR** (376 MHz, $CDCl_3$)




**3ea**

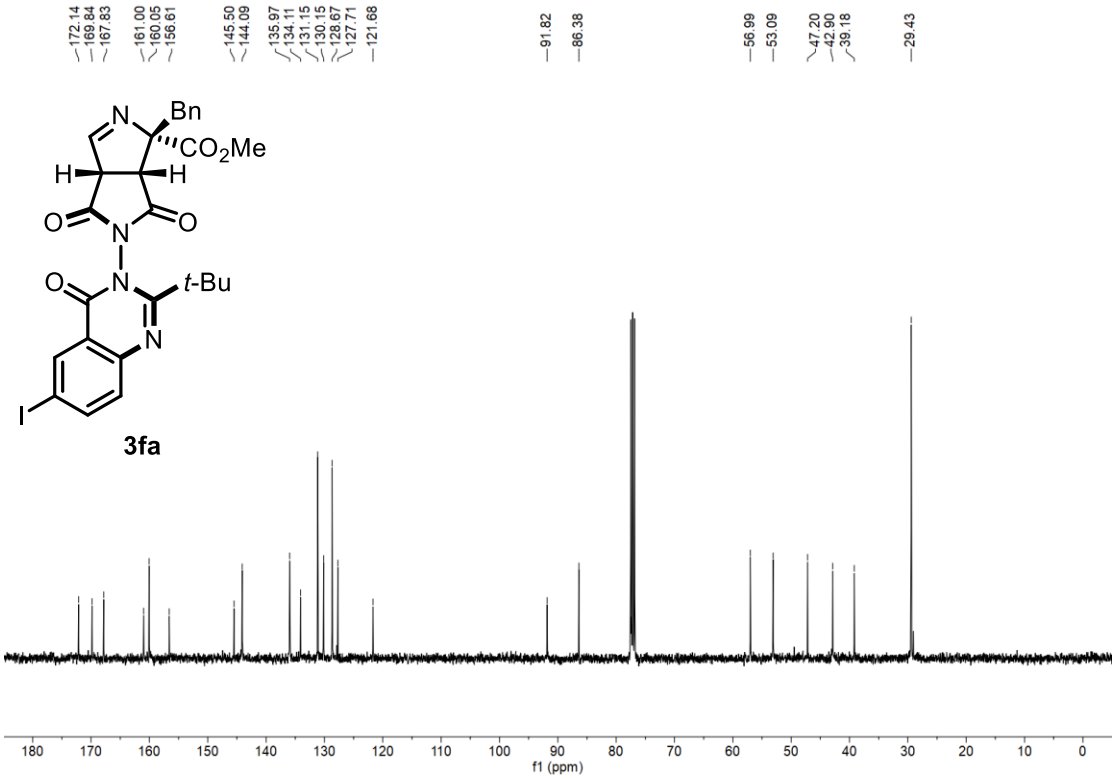



**$^{1}$H NMR** (400 MHz, $CDCl_3$)

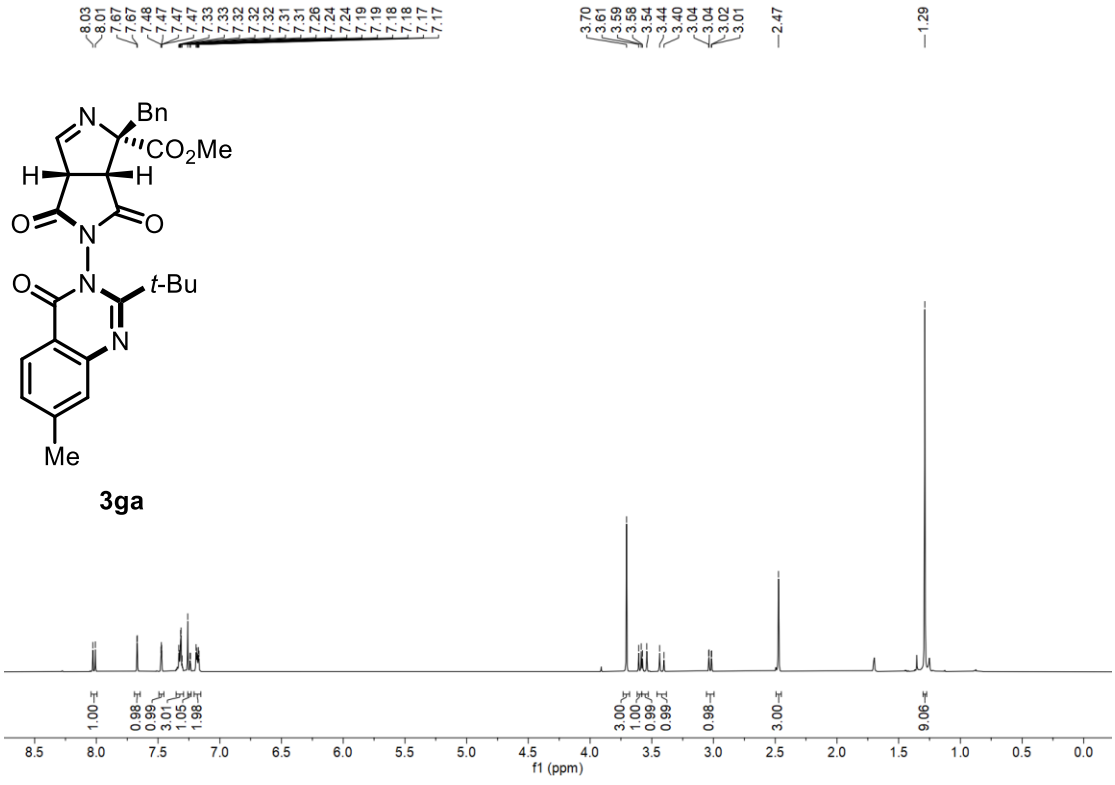



**3fa**

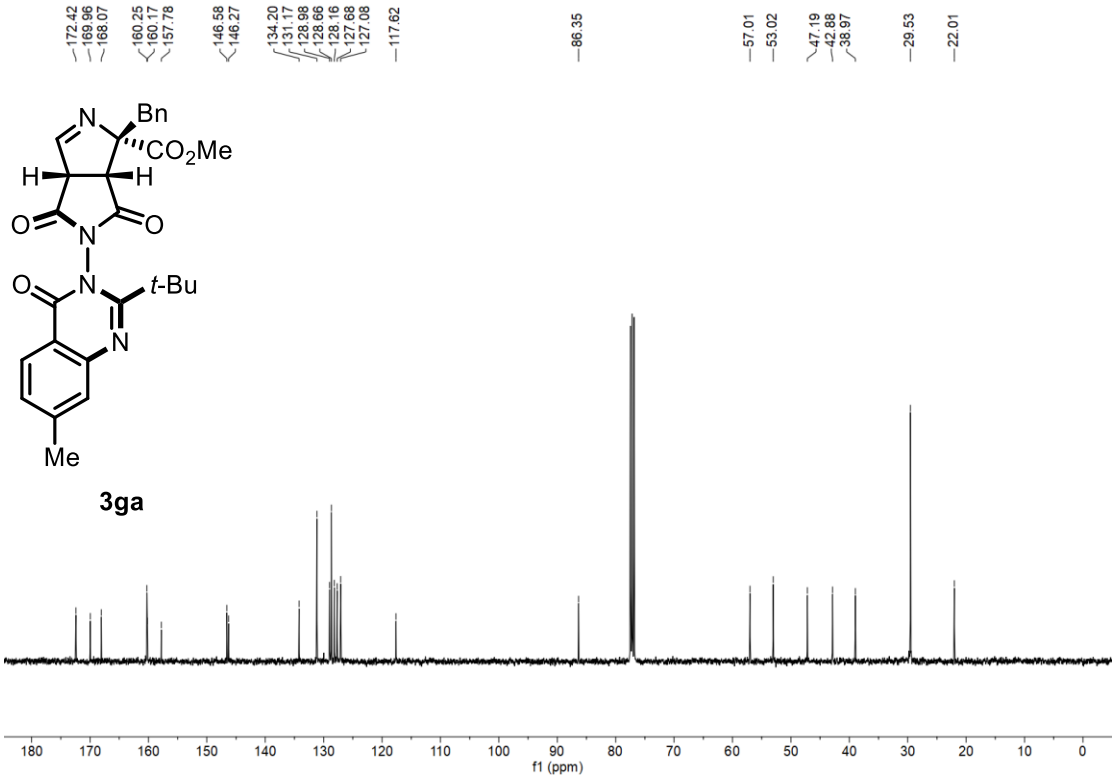
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



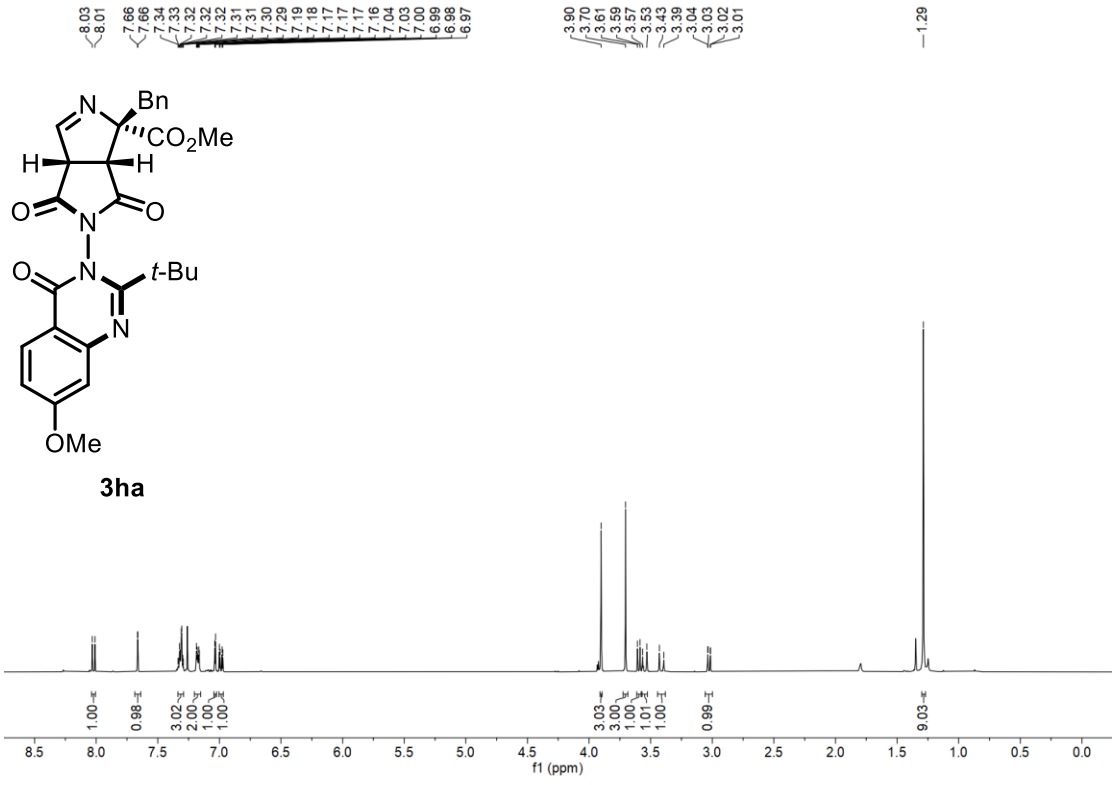

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



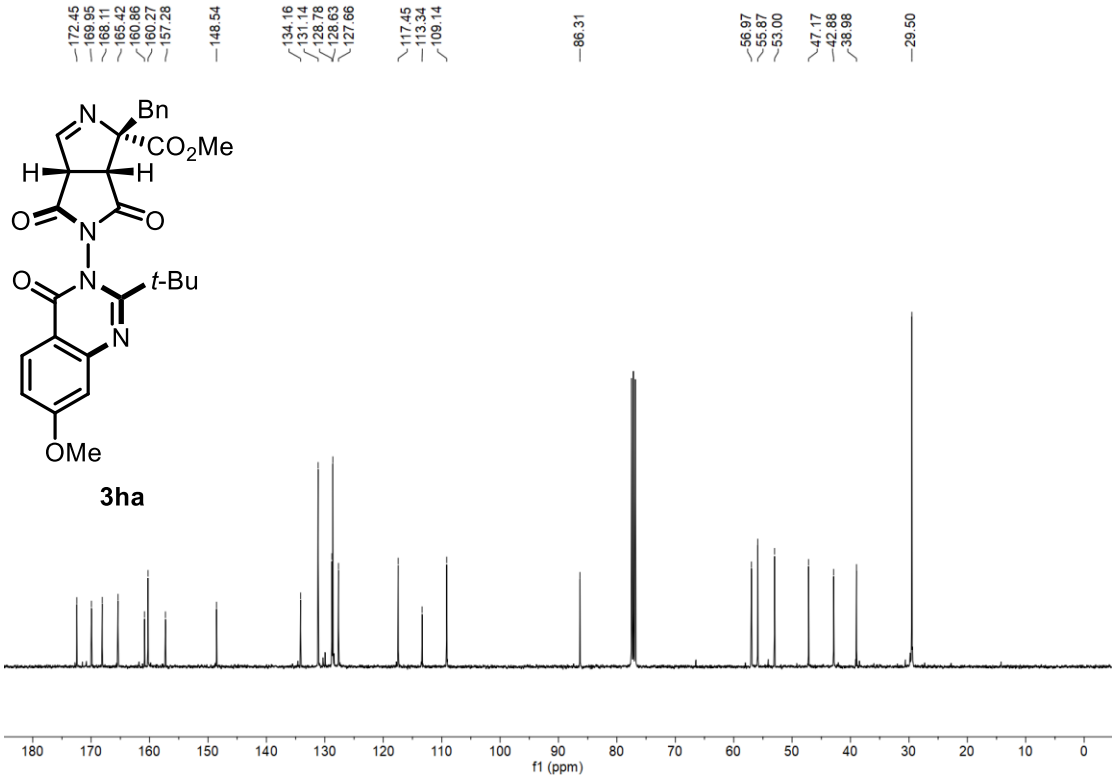
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



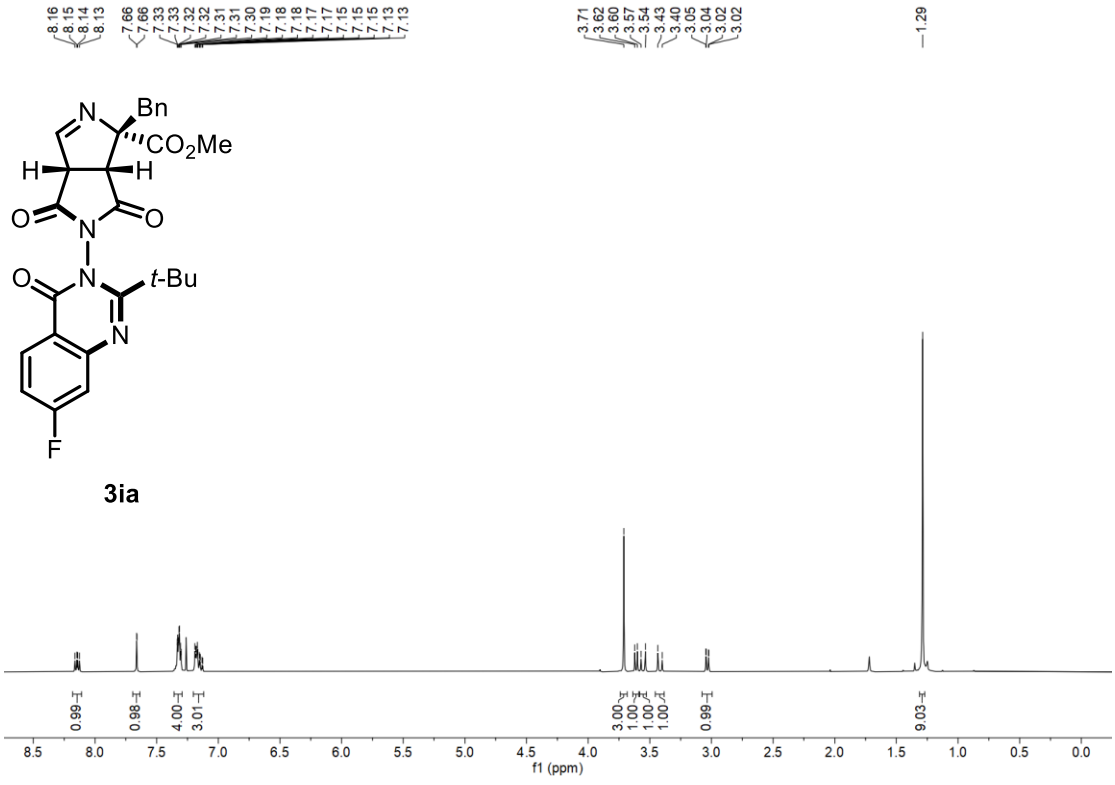

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



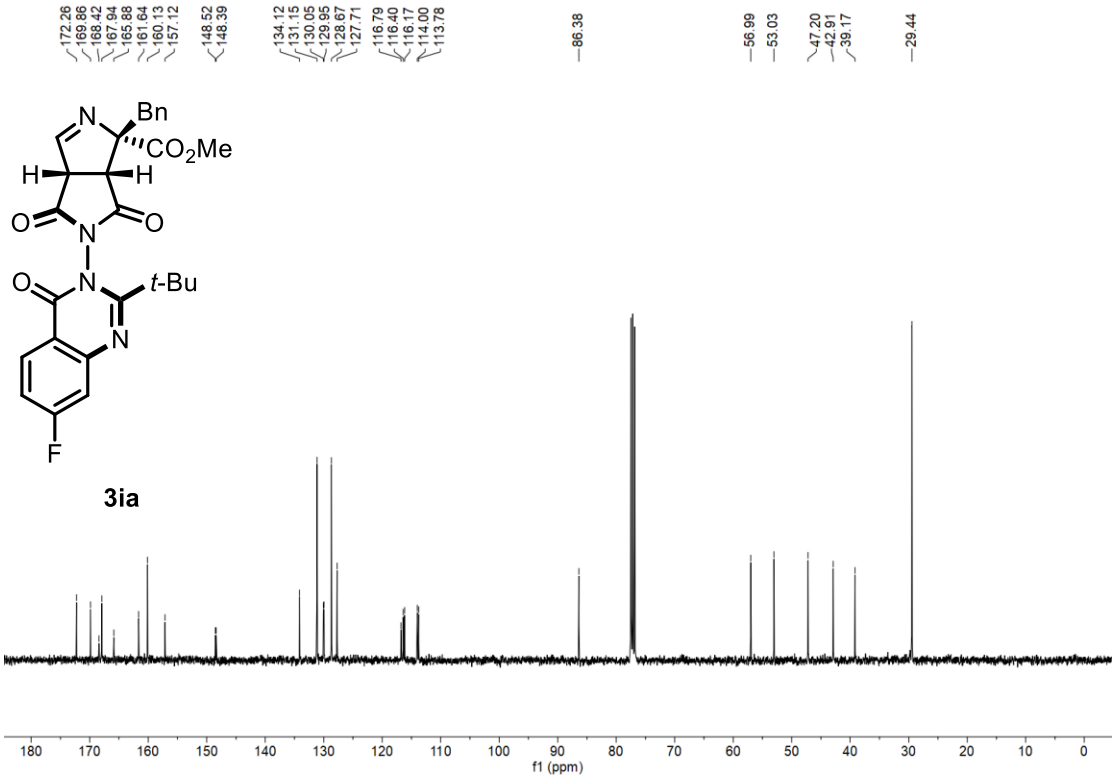
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



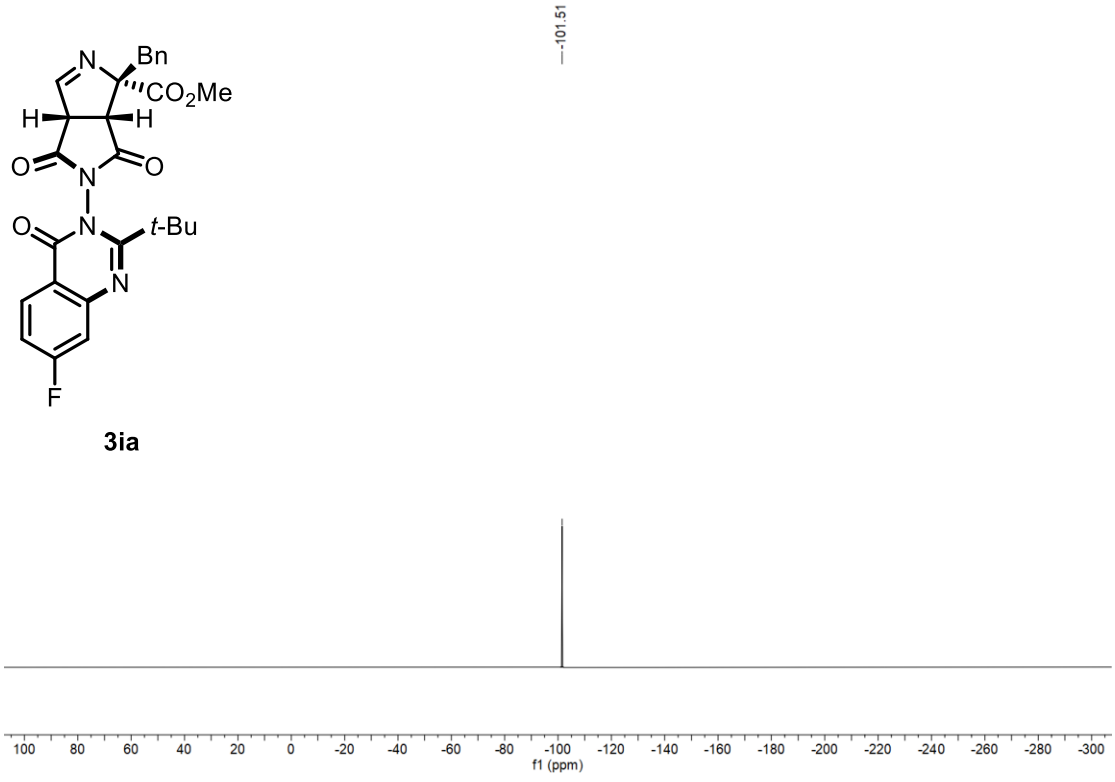

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



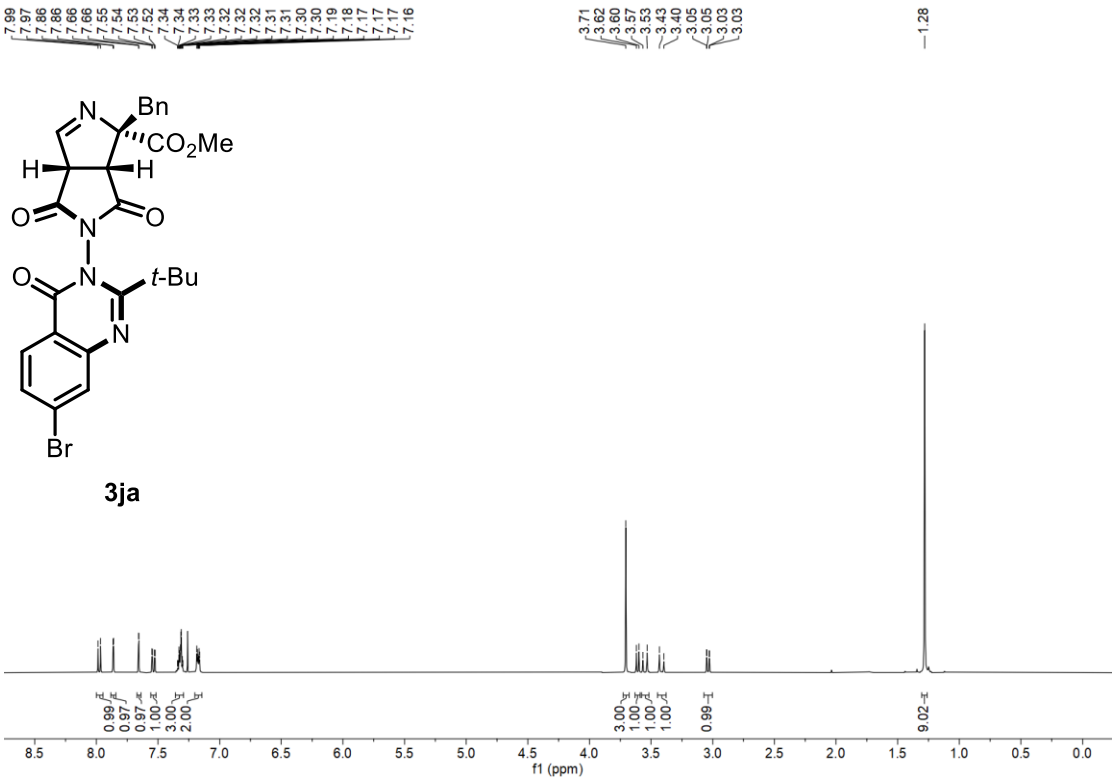
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



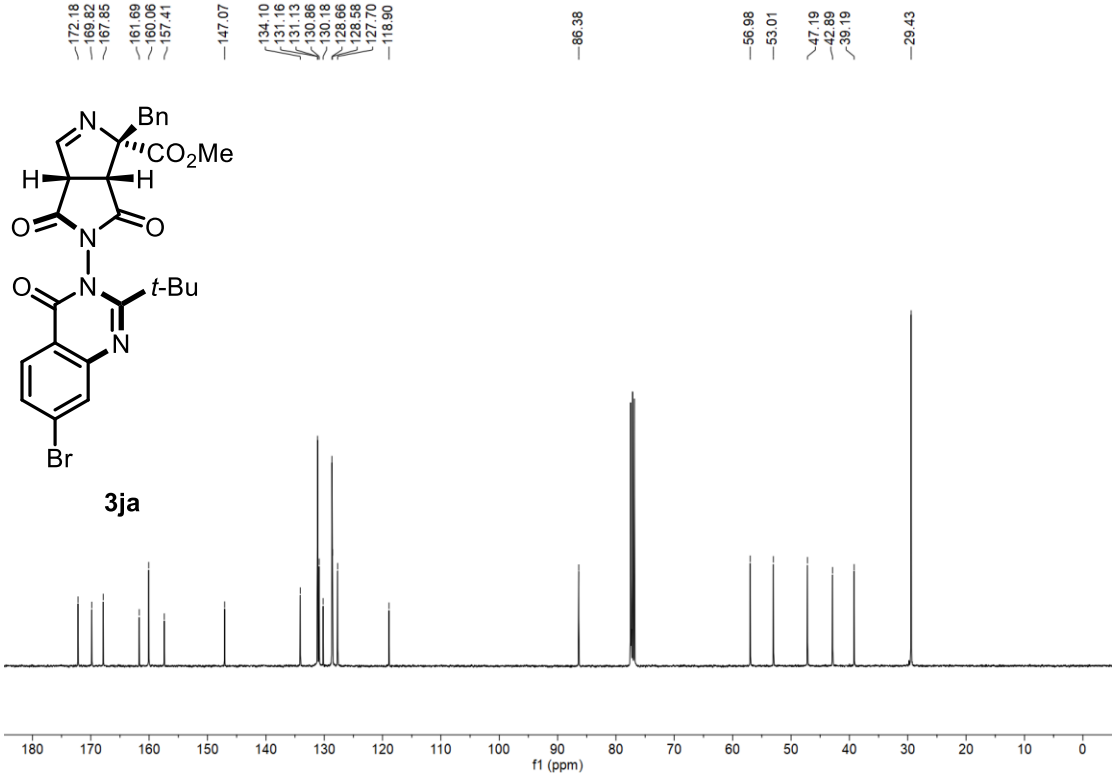

**$^{19}$F NMR** (376 MHz, $CDCl_3$)



**$^{1}$H NMR** (400 MHz, $CDCl_3$)




**$^{13}$C NMR** (101 MHz, $CDCl_3$)



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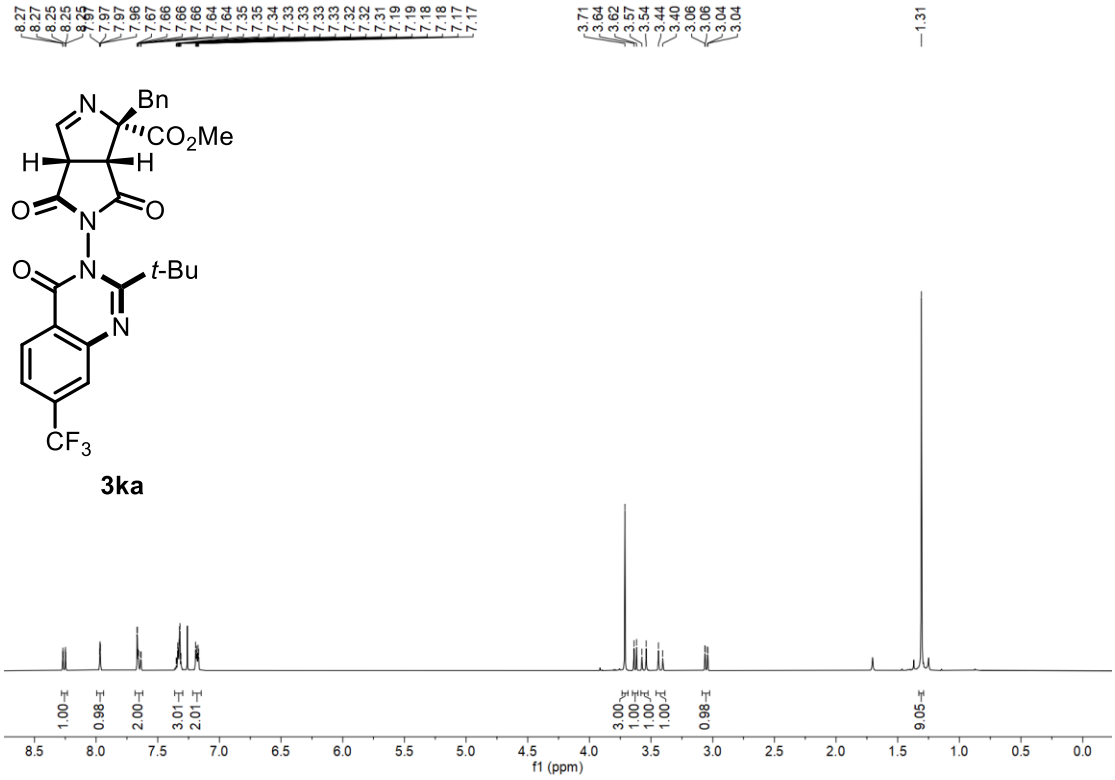
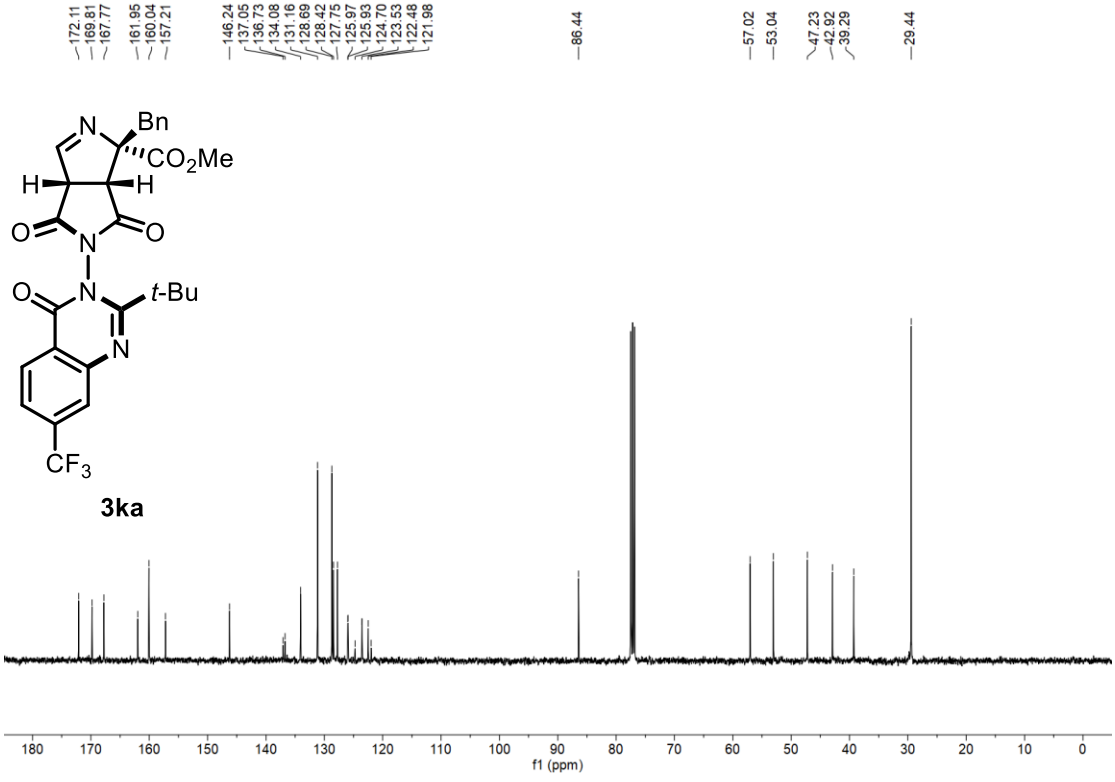
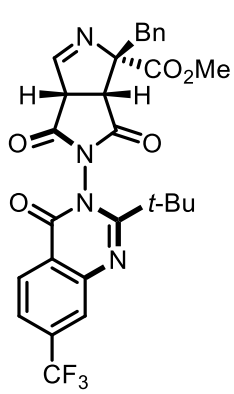



**$^{13}$C NMR** (101 MHz, $CDCl_3$)



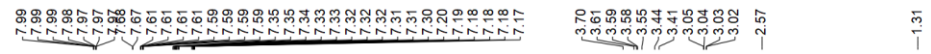
**$^{19}$F NMR** (376 MHz, $CDCl_3$)

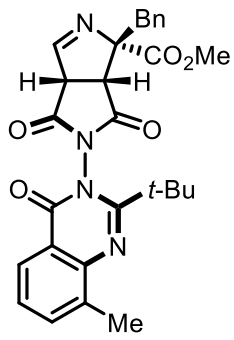


**3ka**

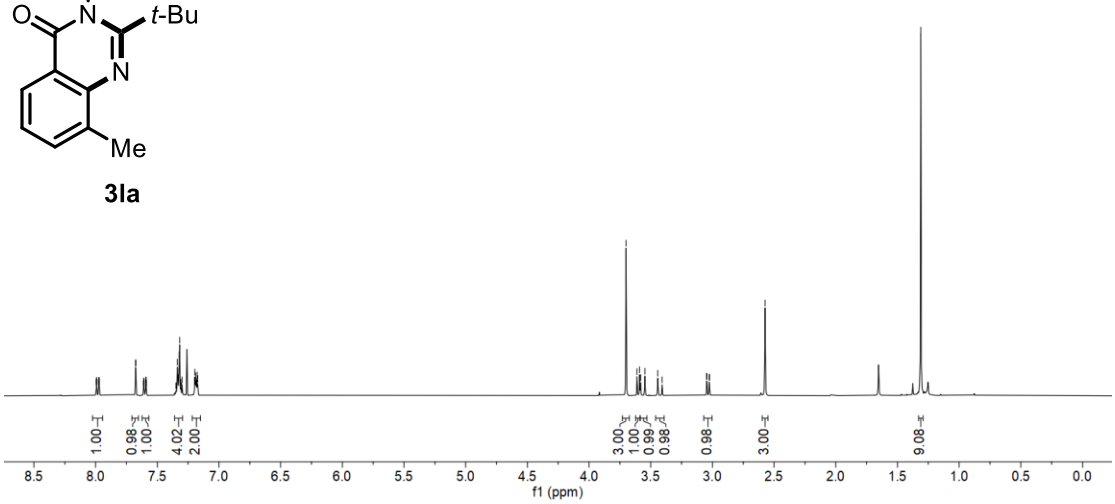



**$^{1}$H NMR** (400 MHz, $CDCl_3$)

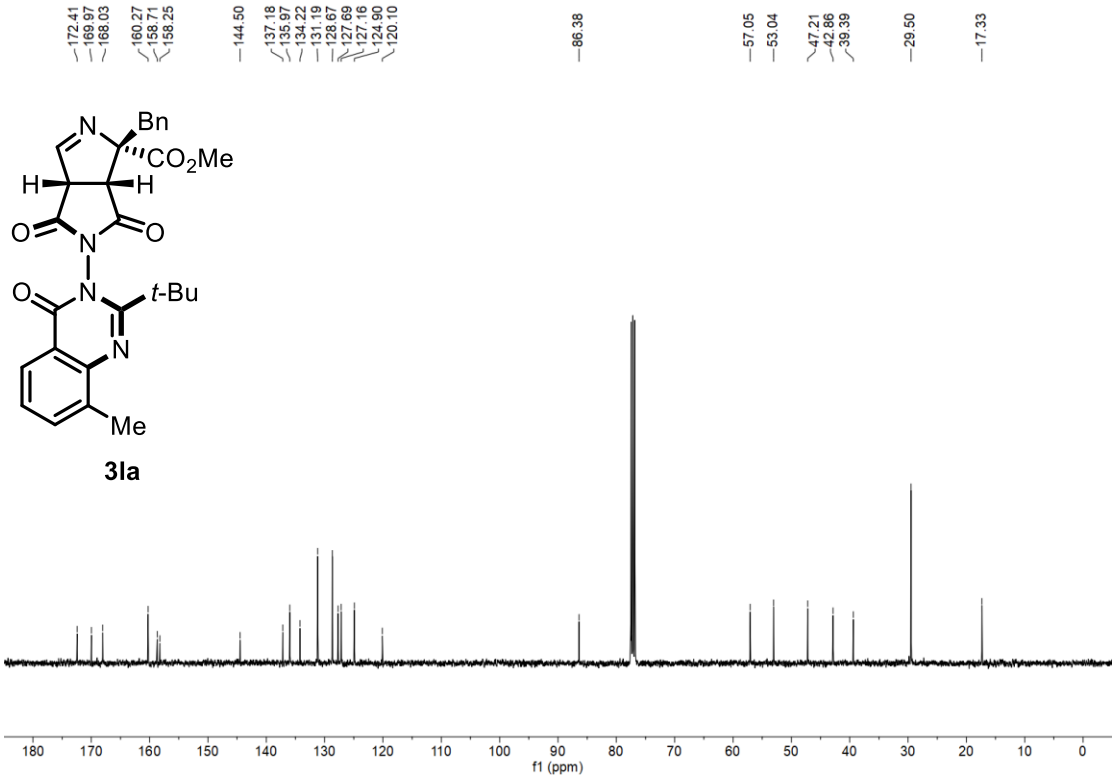


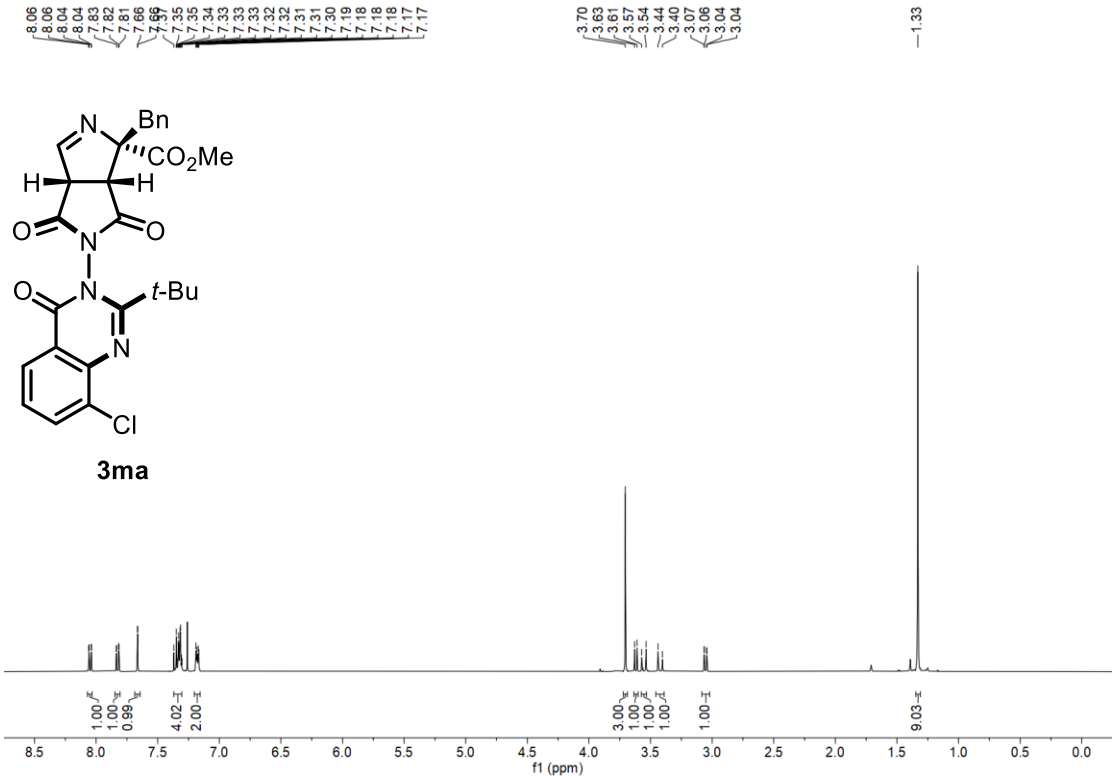
**3la**



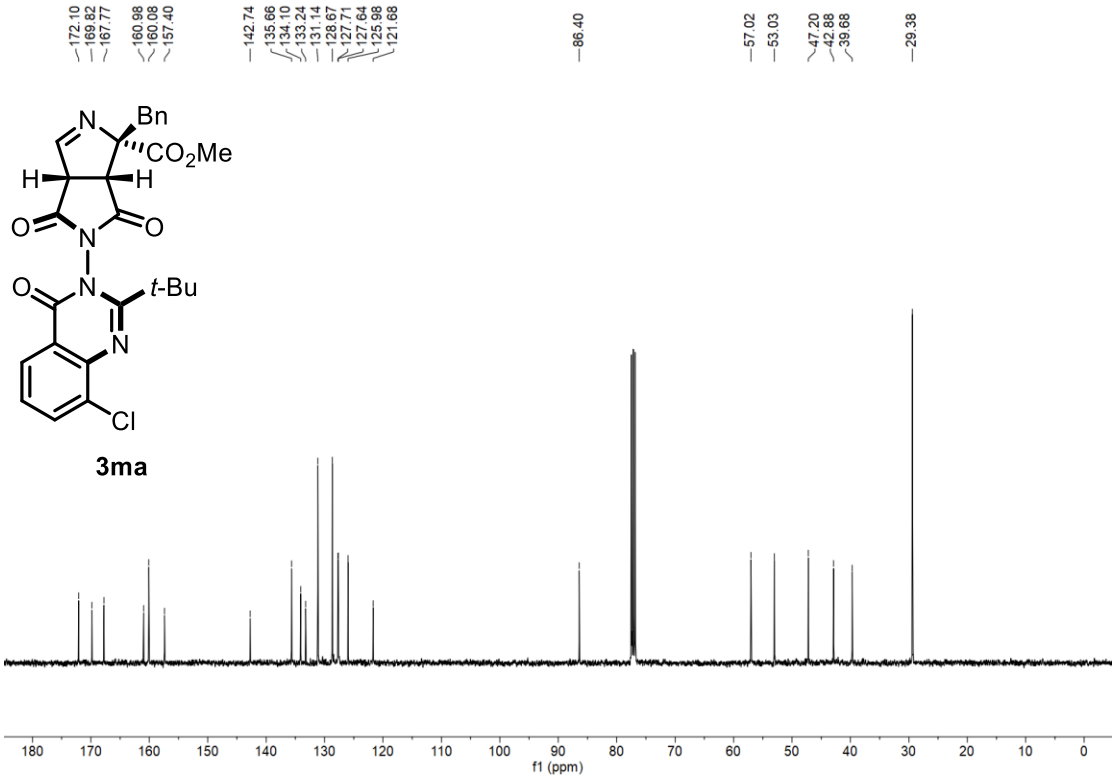
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



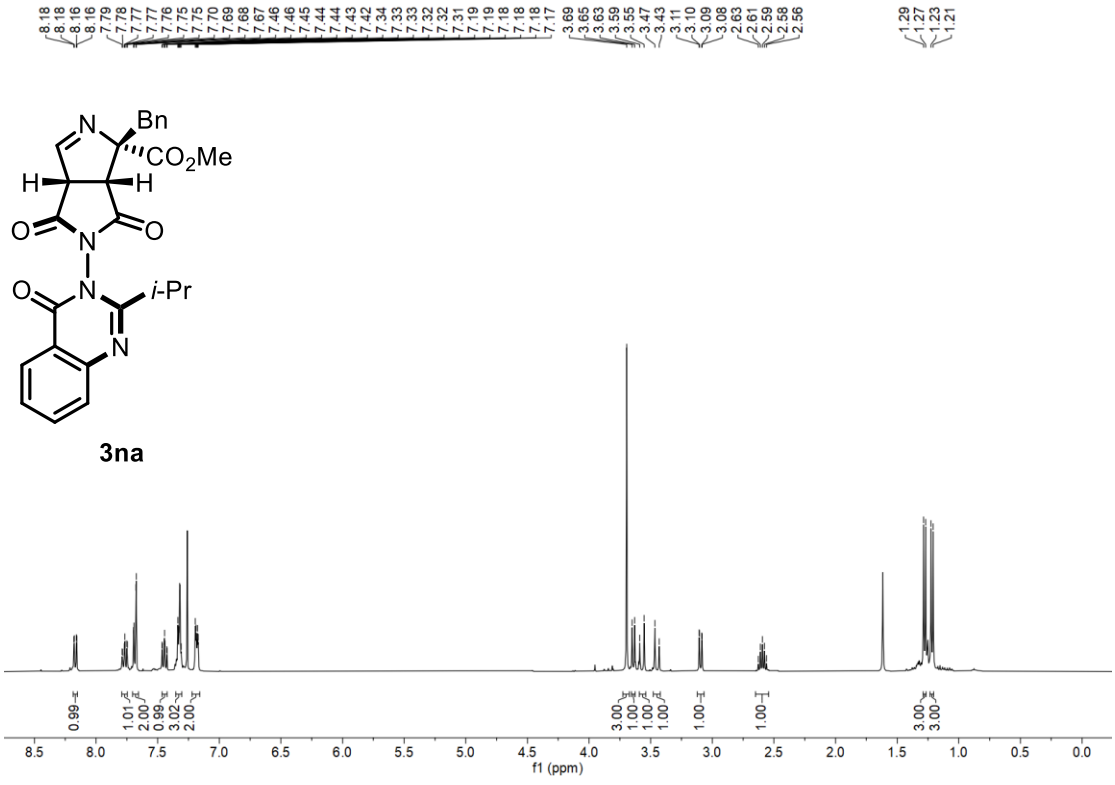

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



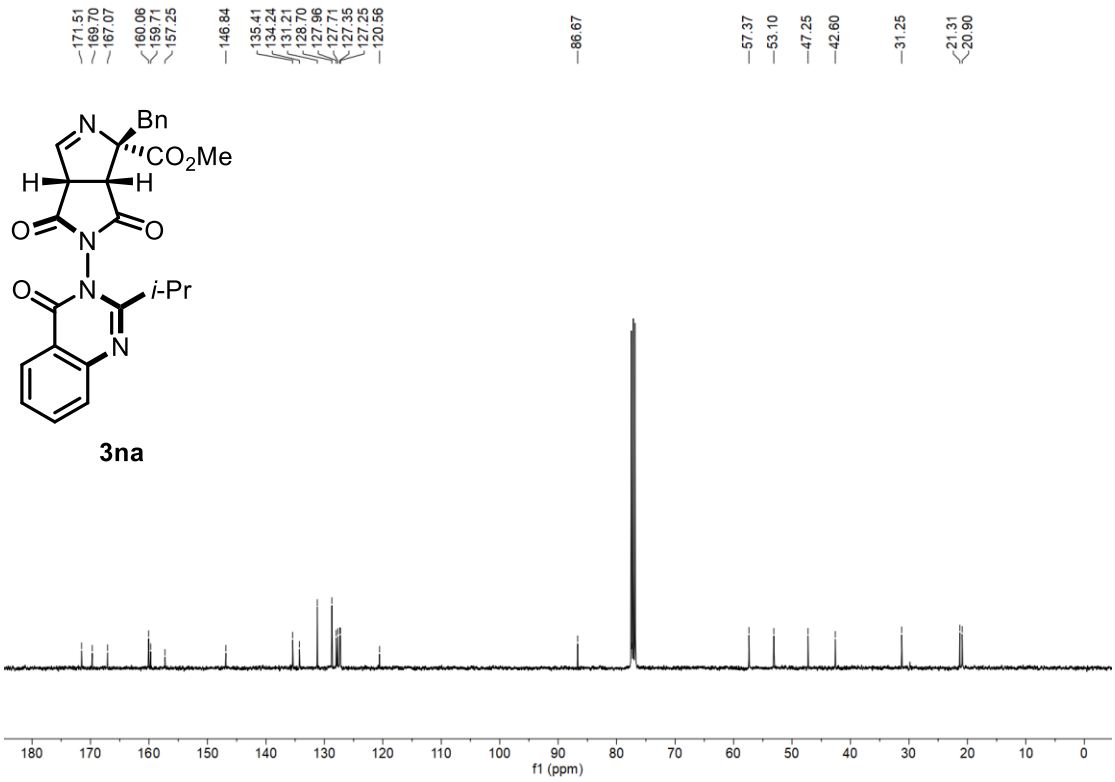
**$^{13}$C NMR** (101 MHz, $CDCl_3$)




**$^{1}$H NMR** (400 MHz, $CDCl_3$)



**$^{13}$C NMR** (101 MHz, $CDCl_3$)

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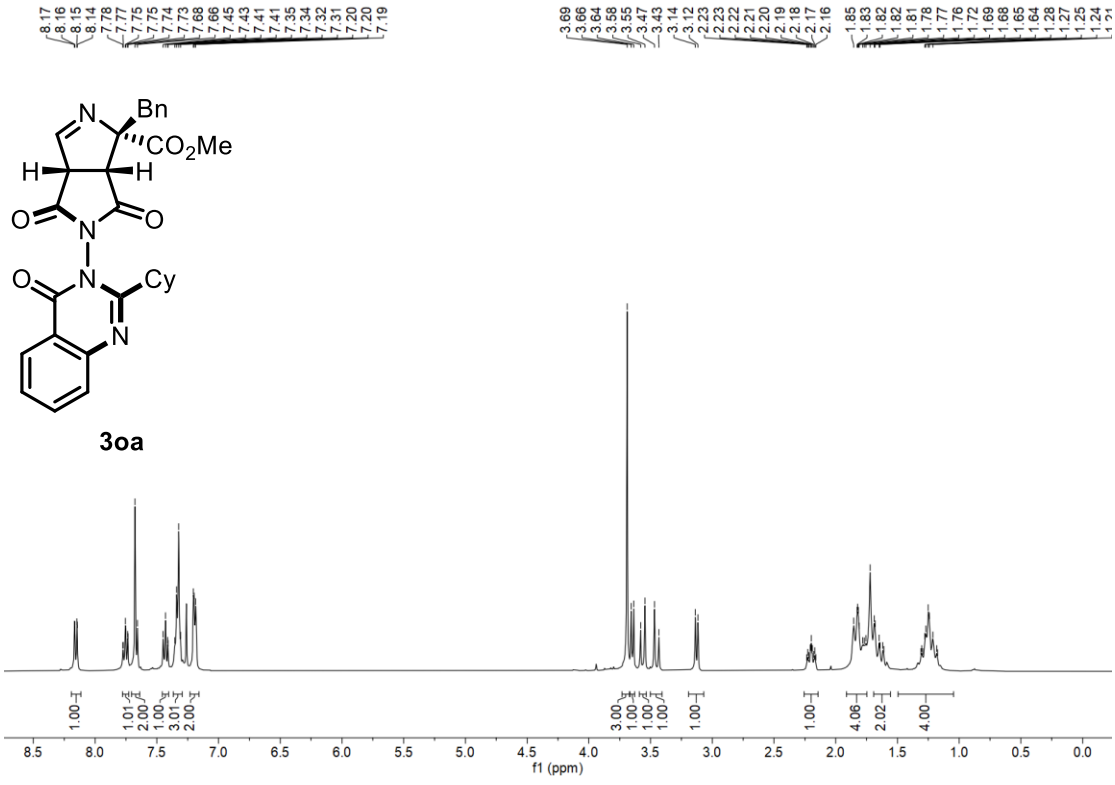

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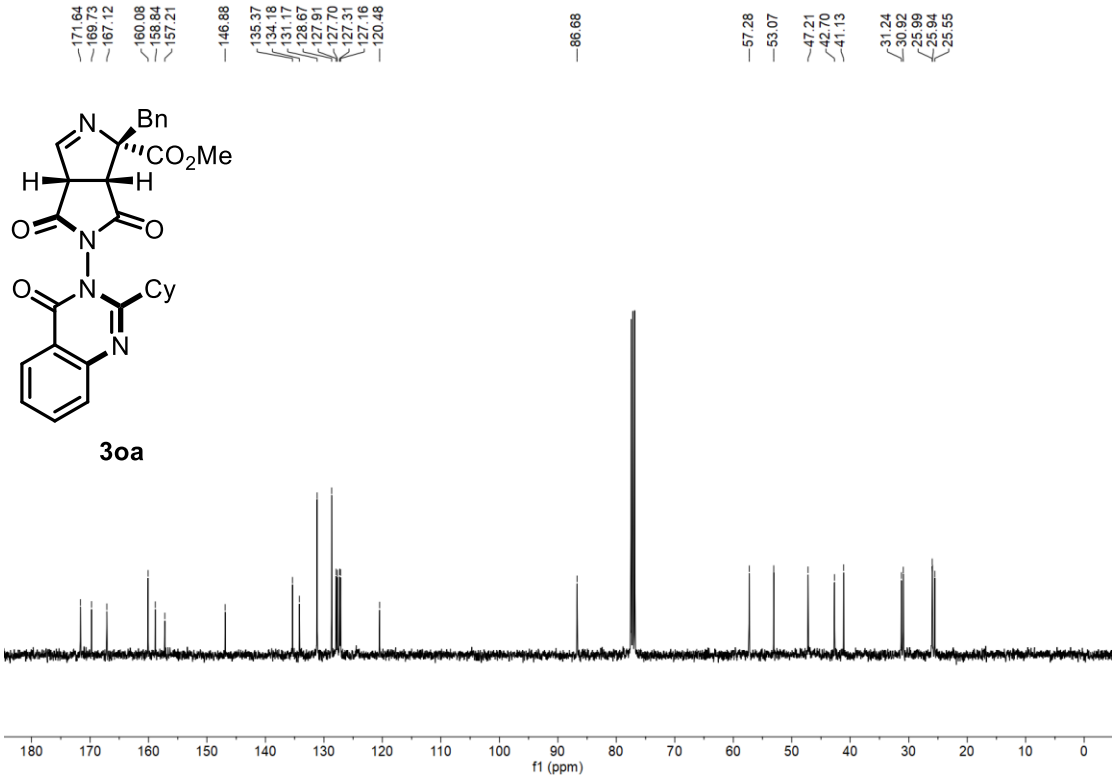


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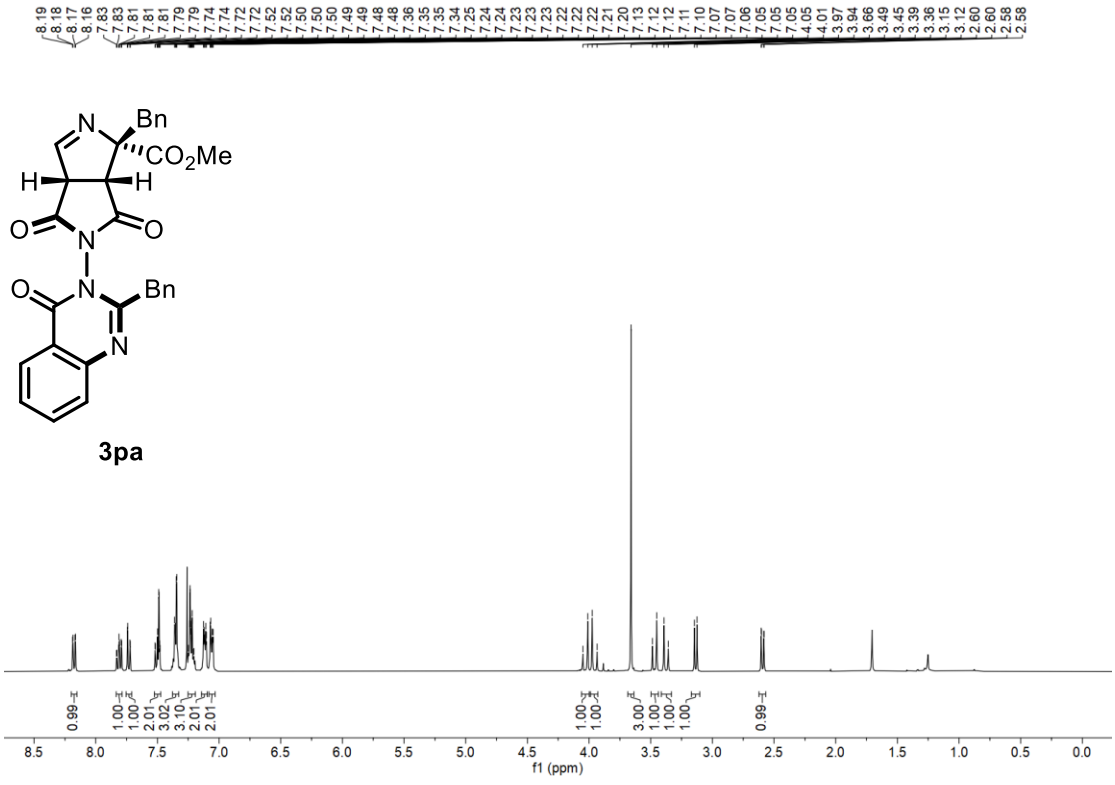
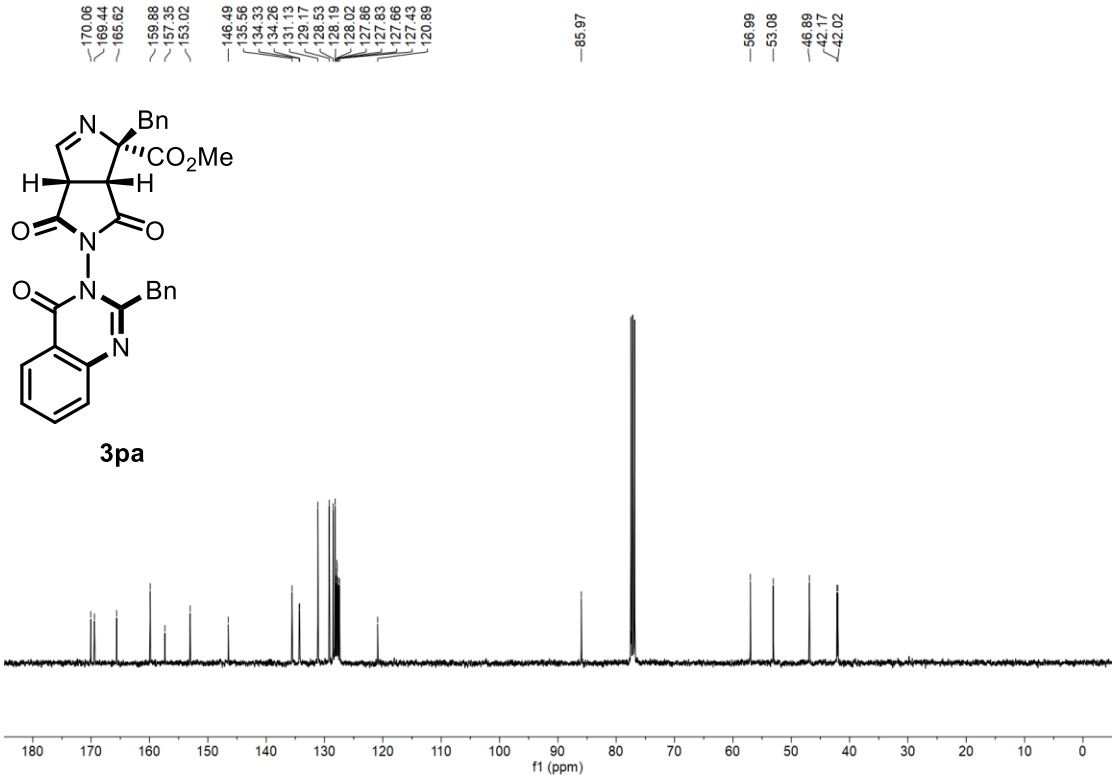


**$^{13}$C NMR** (101 MHz, $CDCl_3$)

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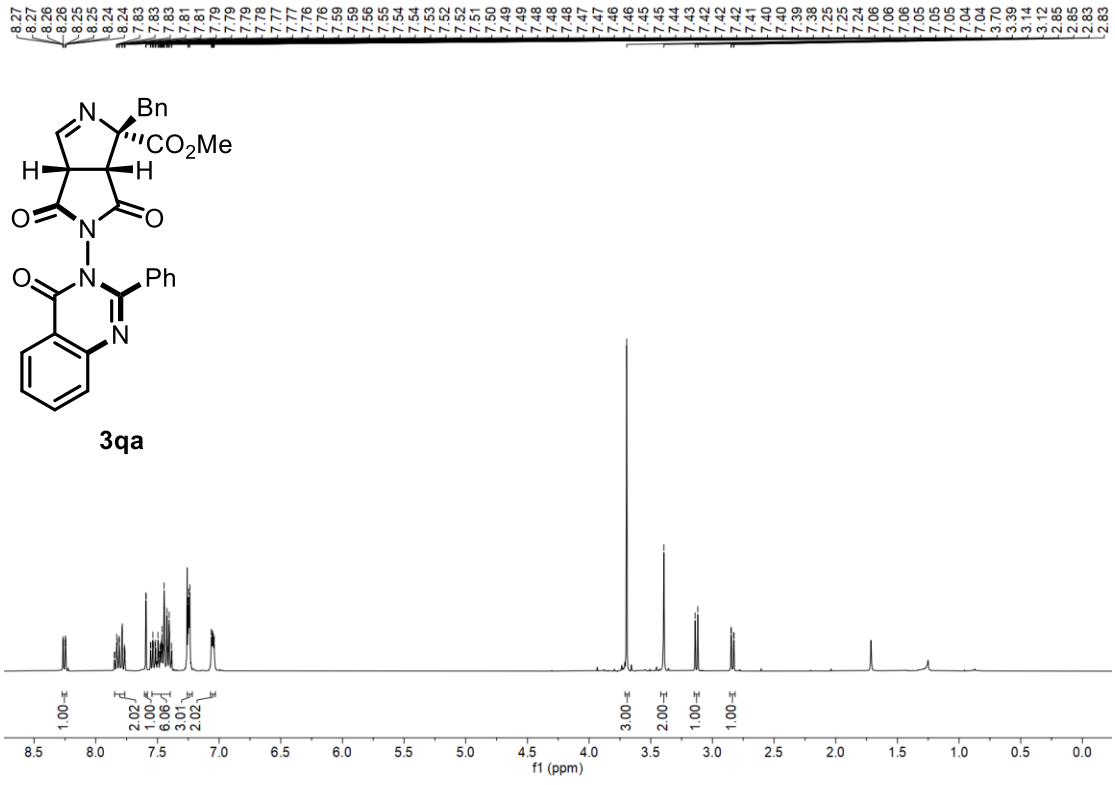

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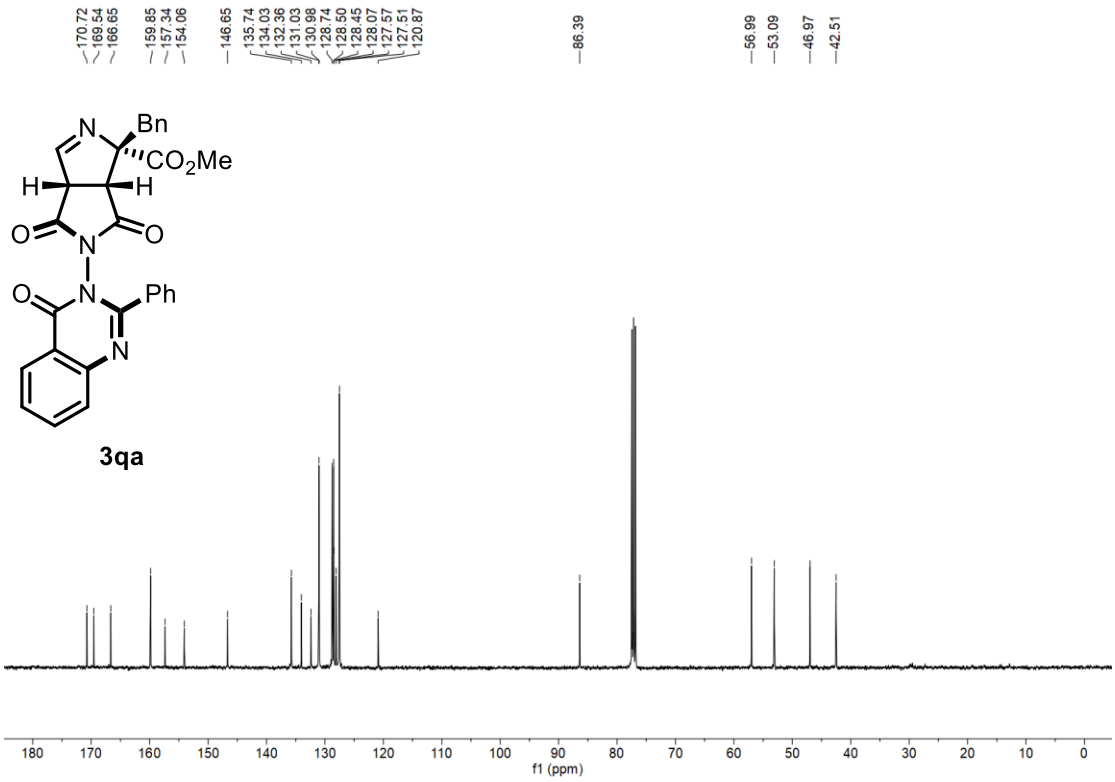
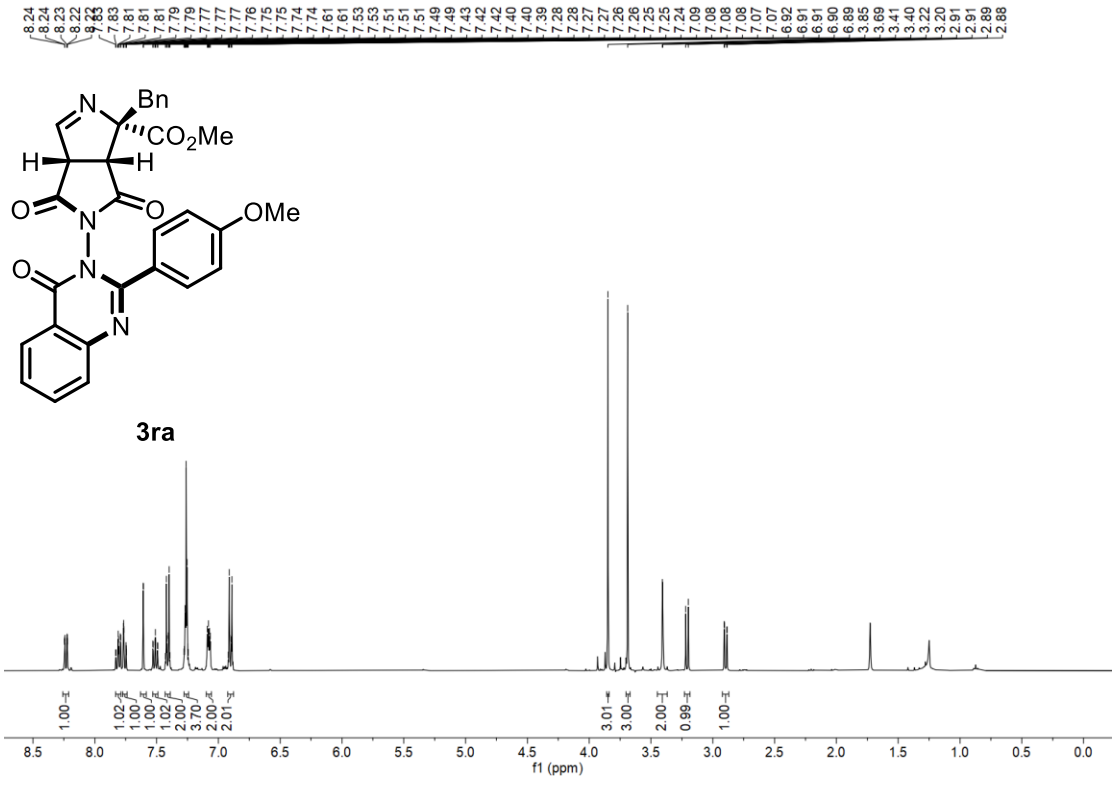
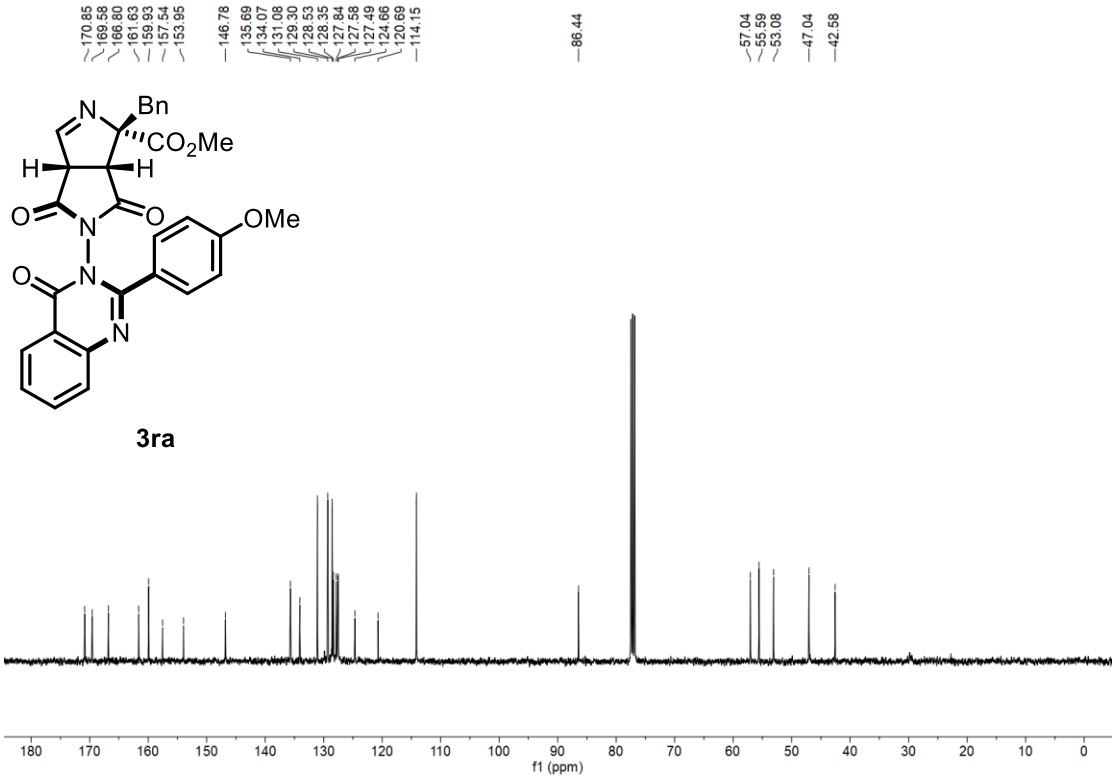



**$^{1}$H NMR** (400 MHz, $CDCl_3$)



**$^{13}$C NMR** (101 MHz, $CDCl_3$)

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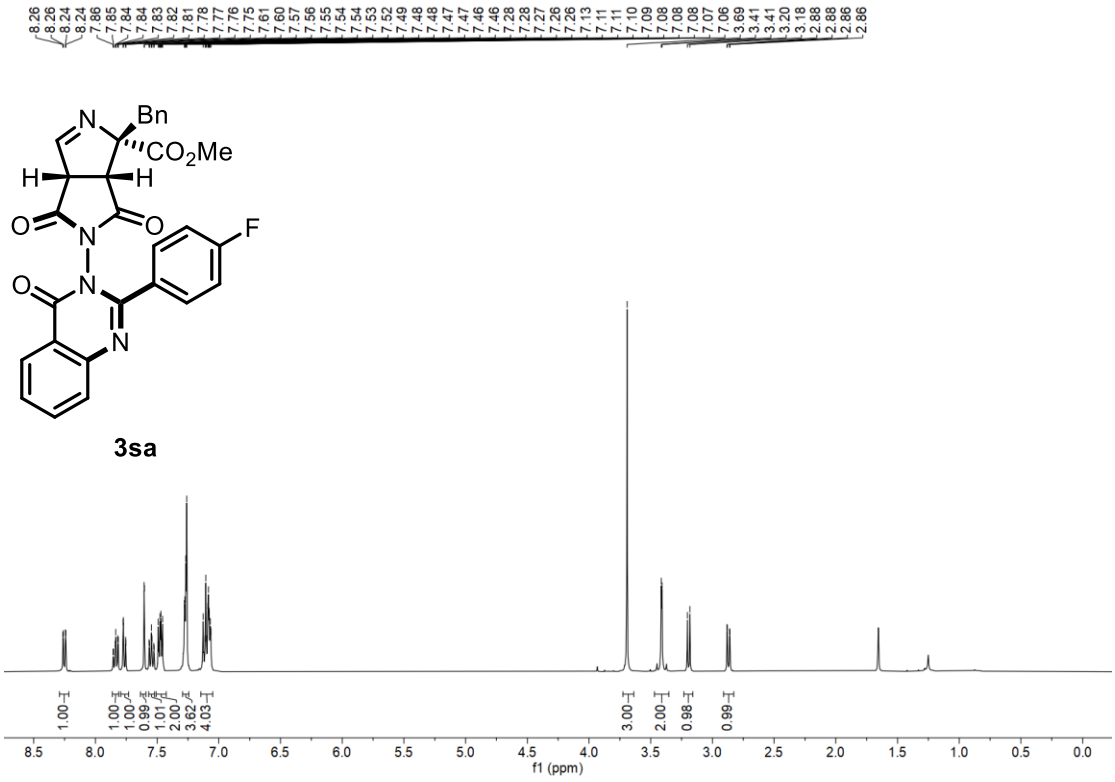

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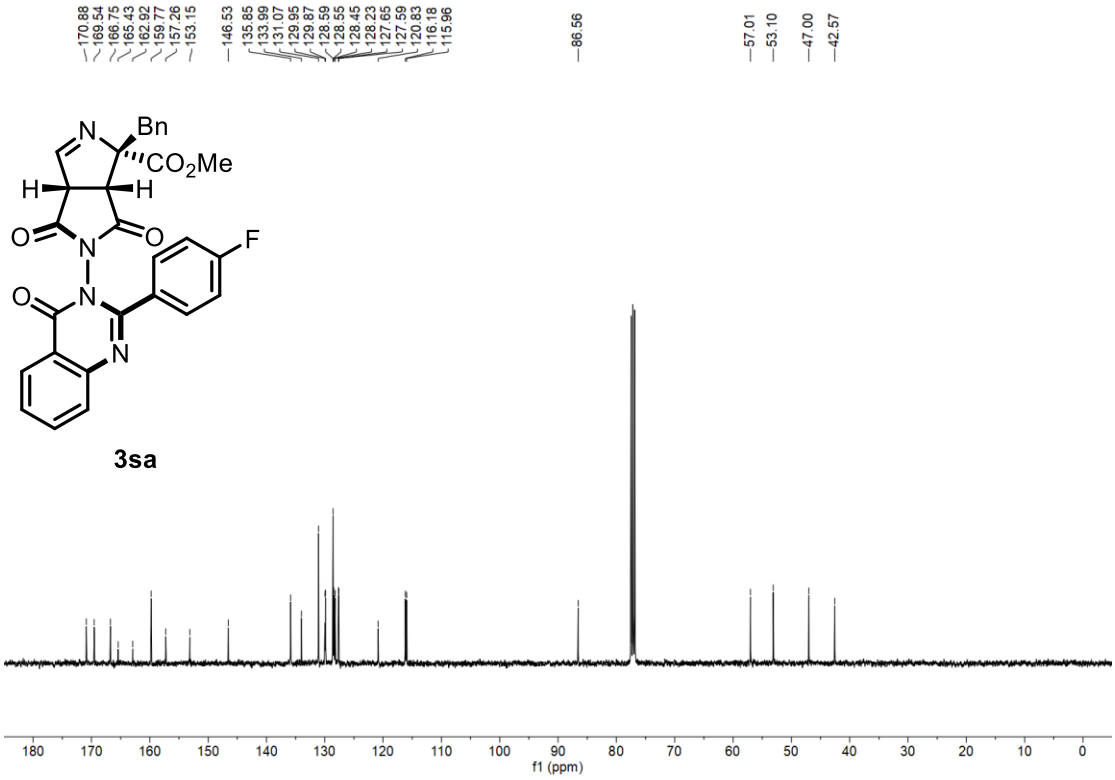
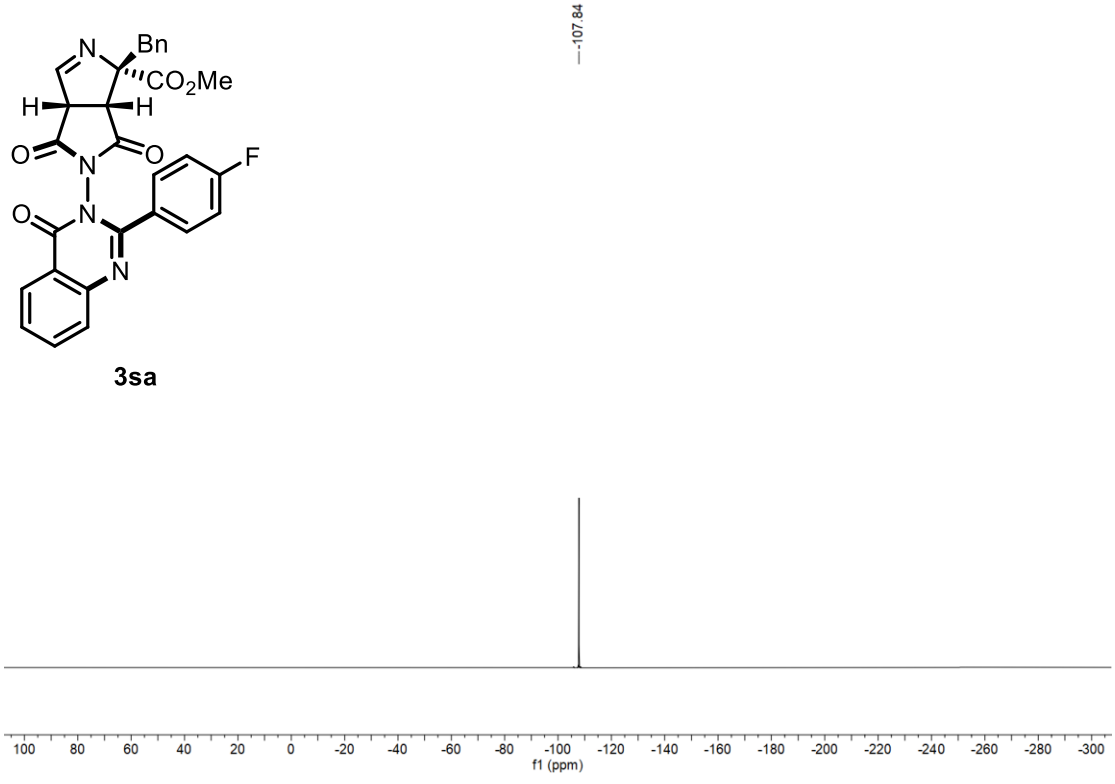
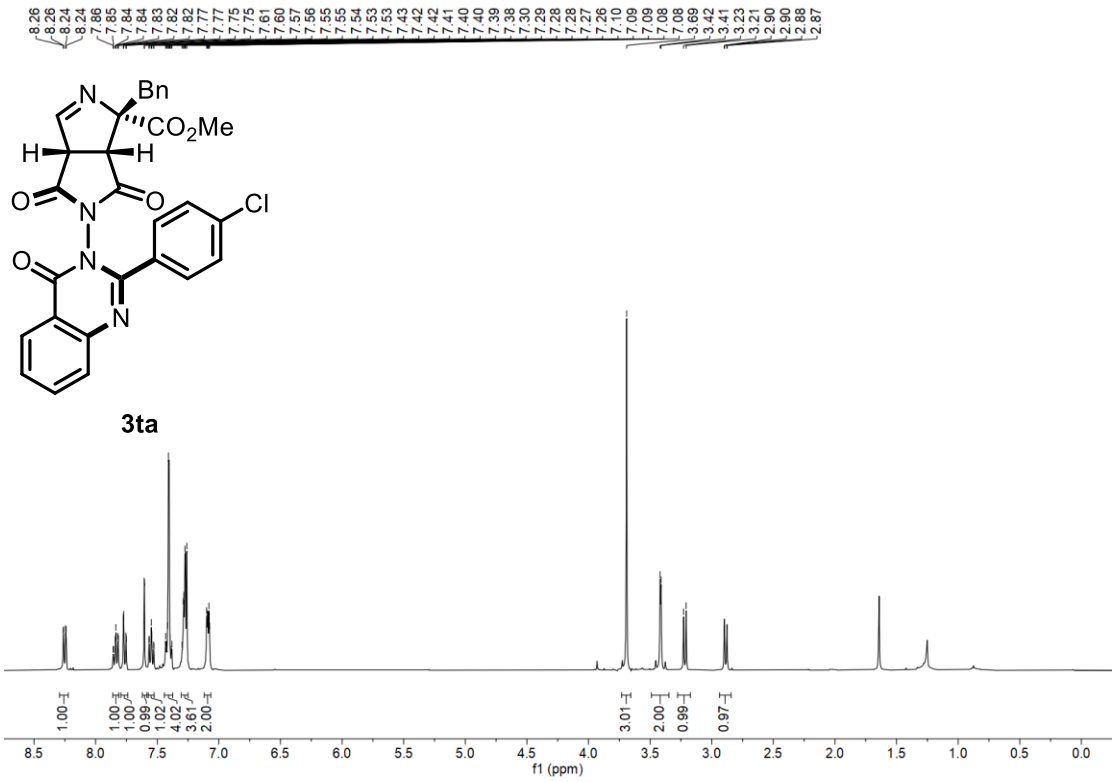


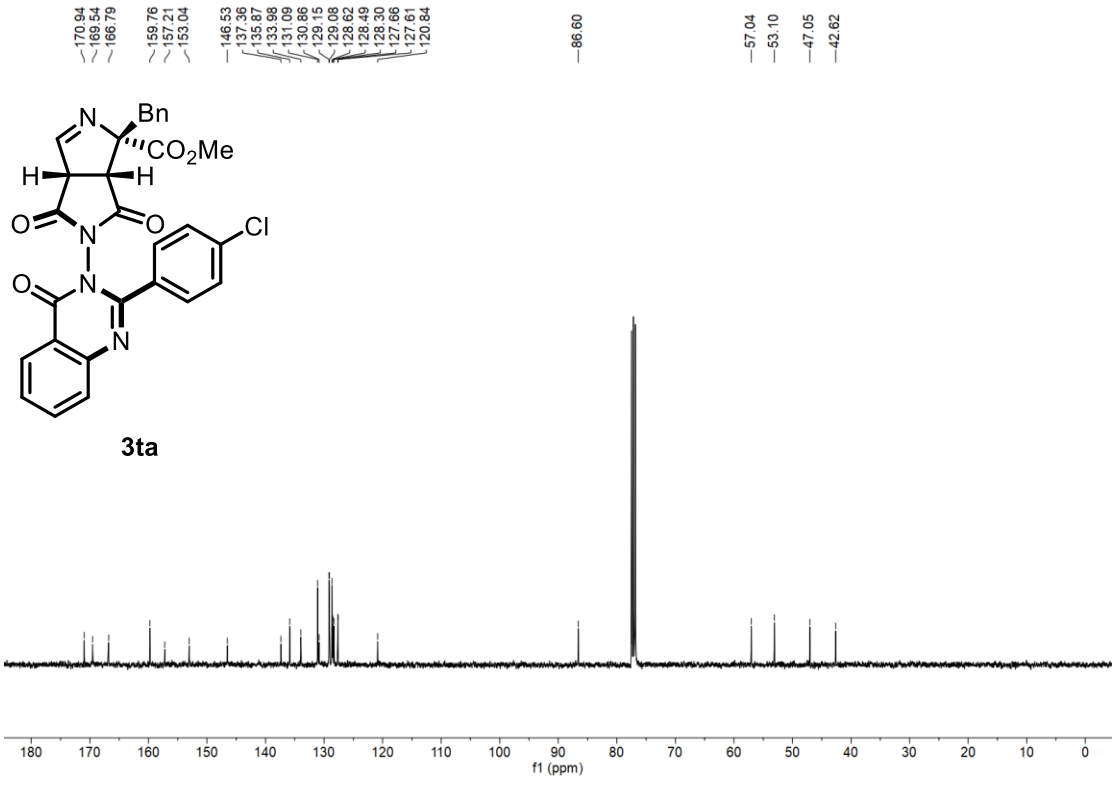

**$^{19}$F NMR** (376 MHz, $CDCl_3$)



**$^{1}$H NMR** (400 MHz, $CDCl_3$)




**$^{13}$C NMR** (101 MHz, $CDCl_3$)



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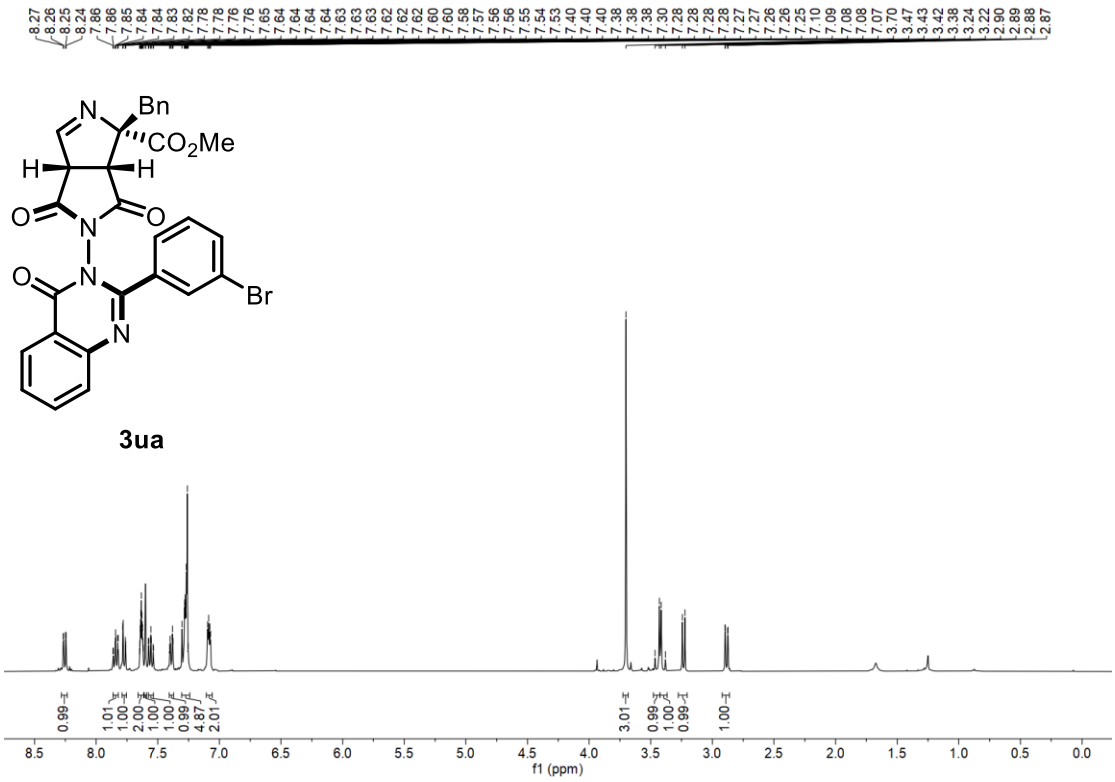


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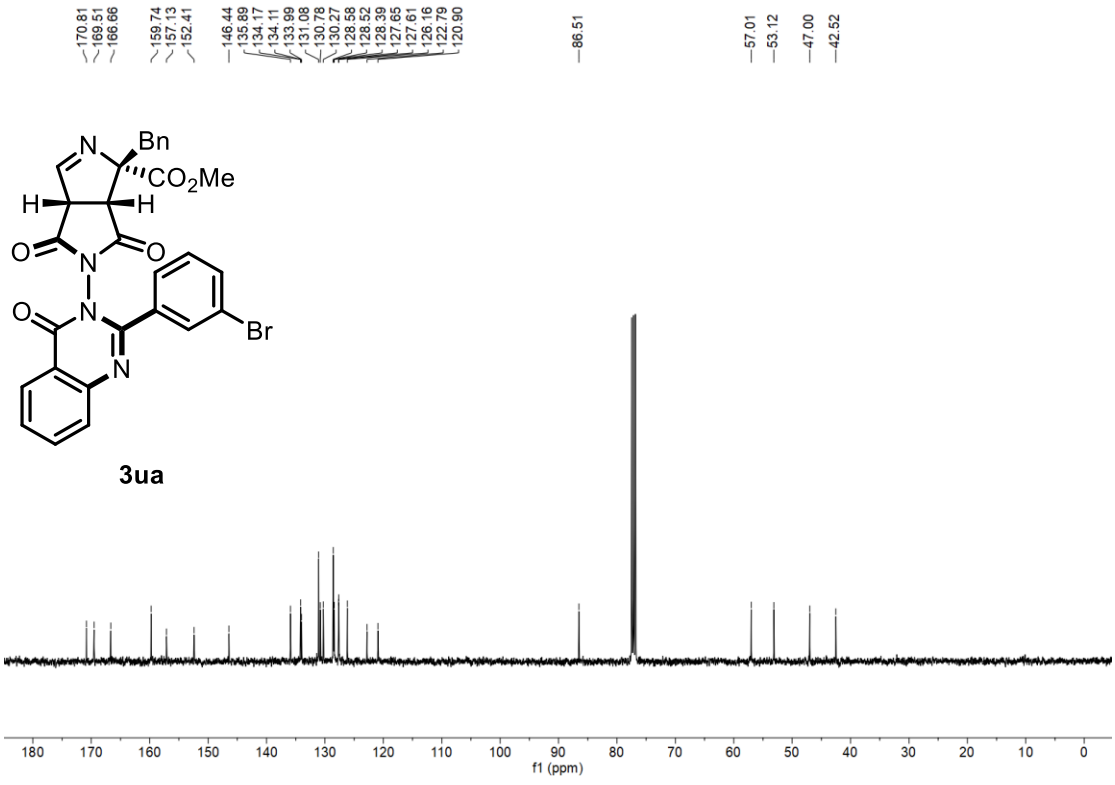

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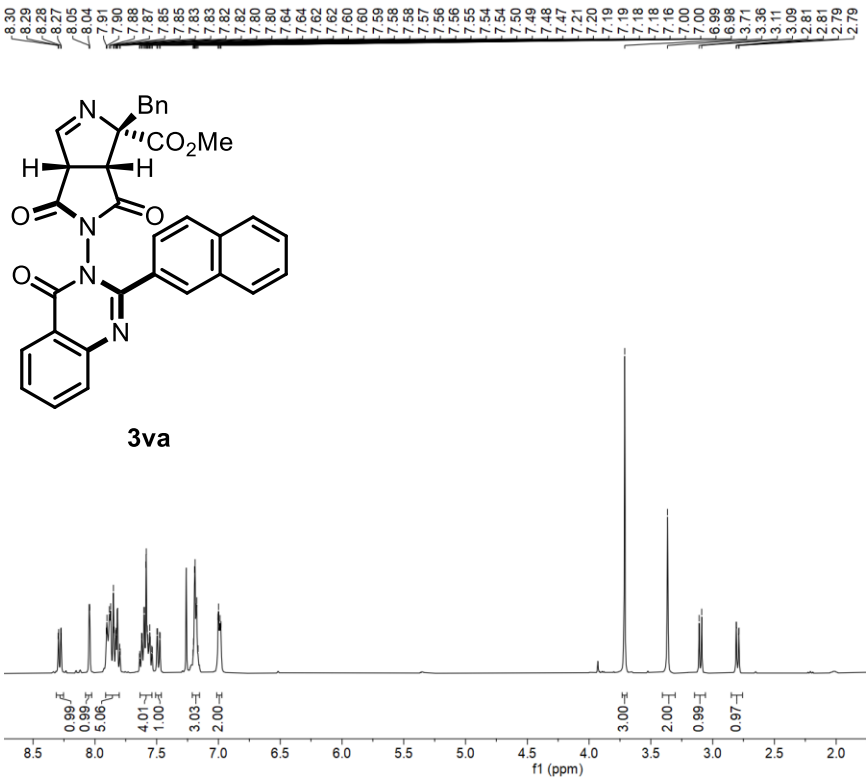
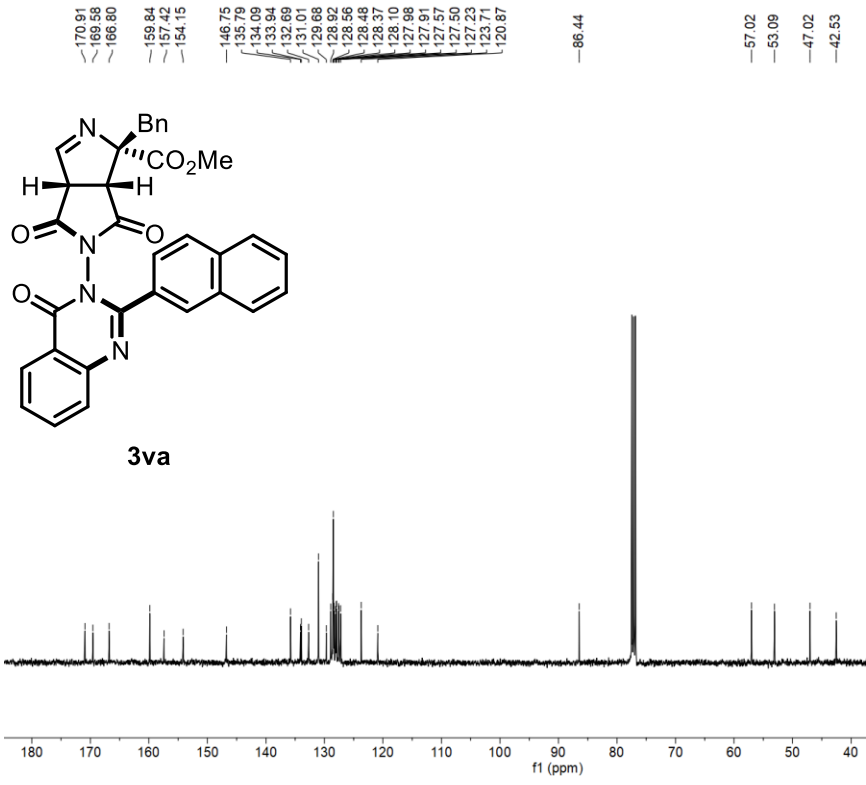



**$^{13}$C NMR** (101 MHz, $CDCl_3$)



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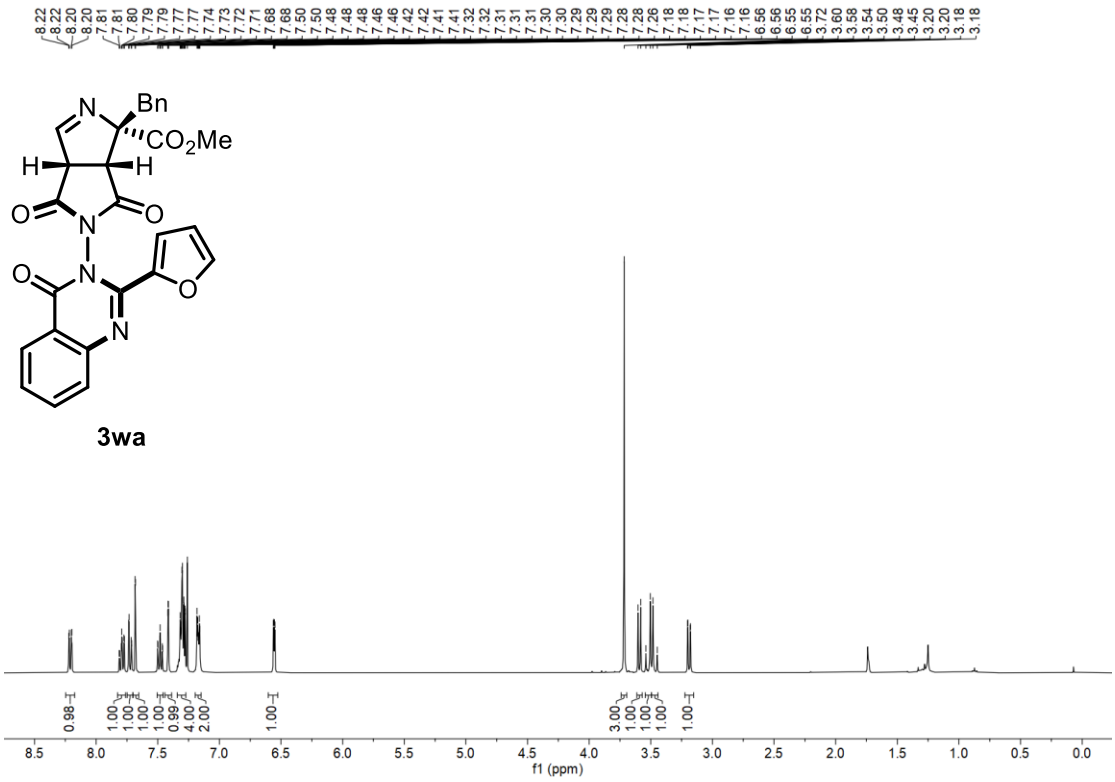
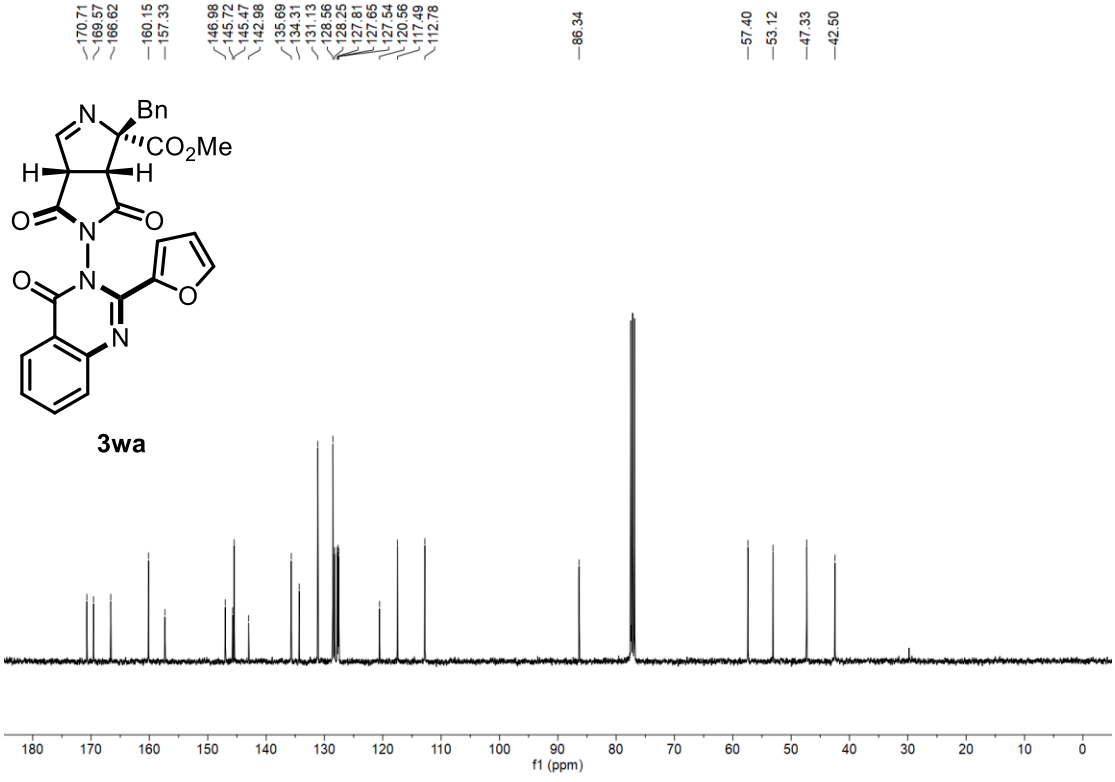



**$^{13}$C NMR** (101 MHz, $CDCl_3$)



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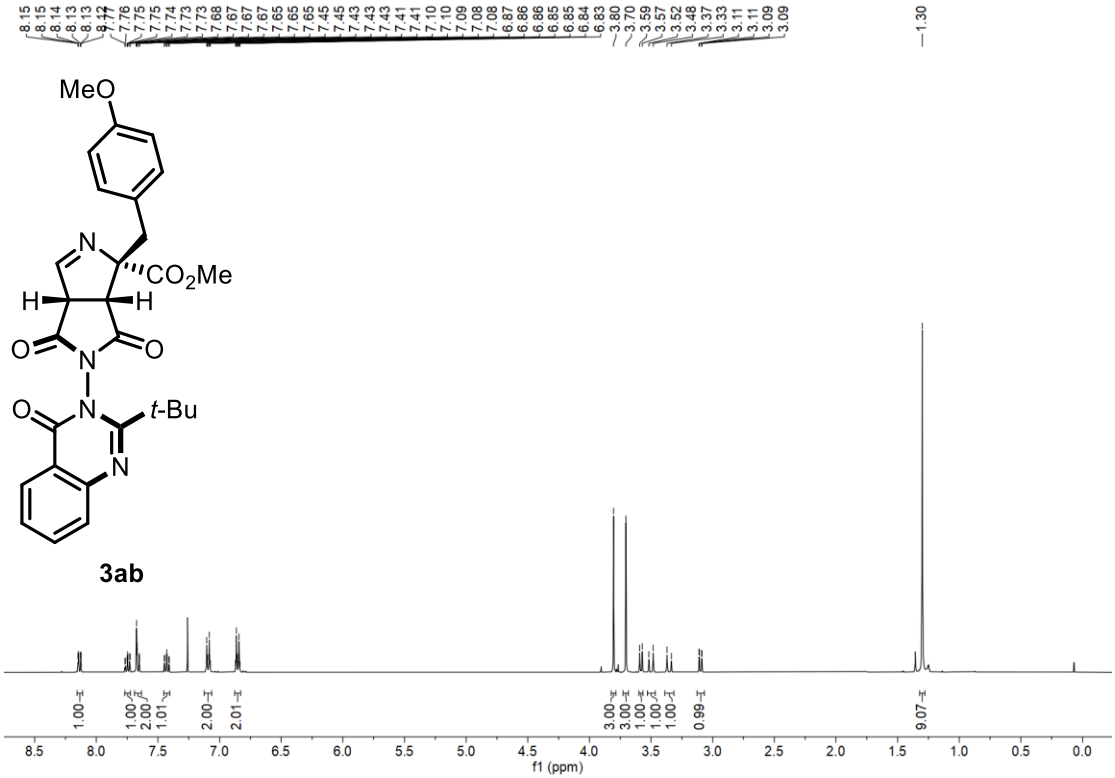
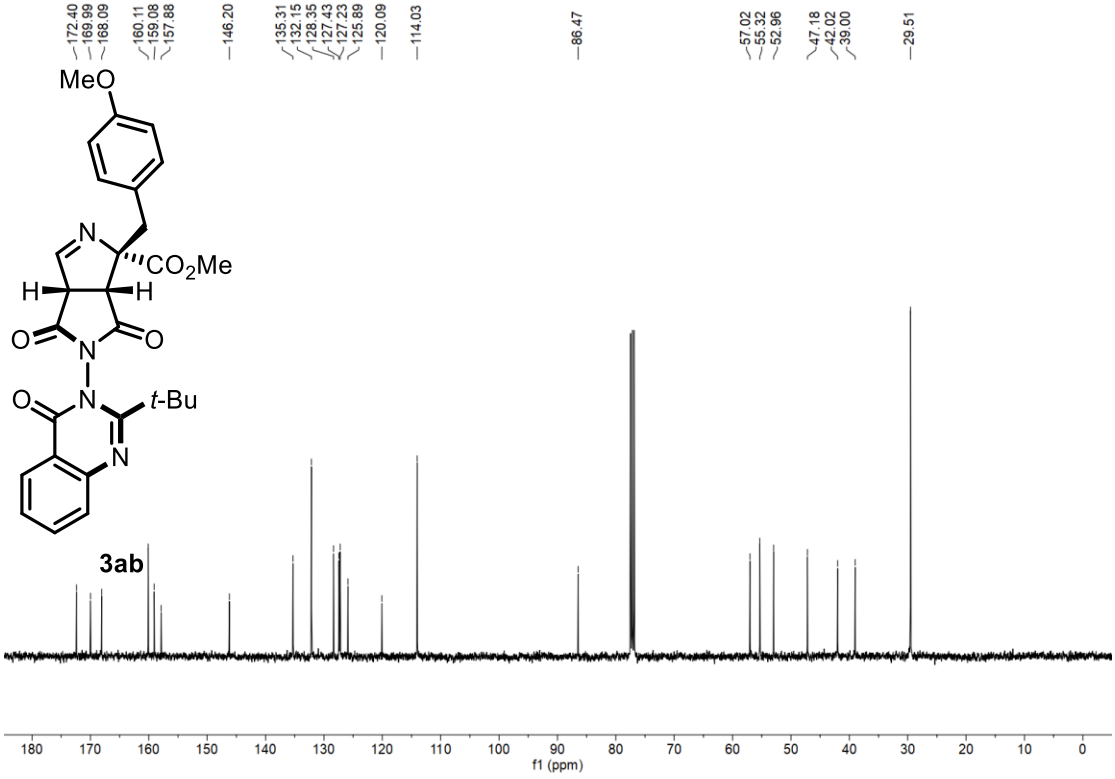



**$^{13}$C NMR** (101 MHz, $CDCl_3$)



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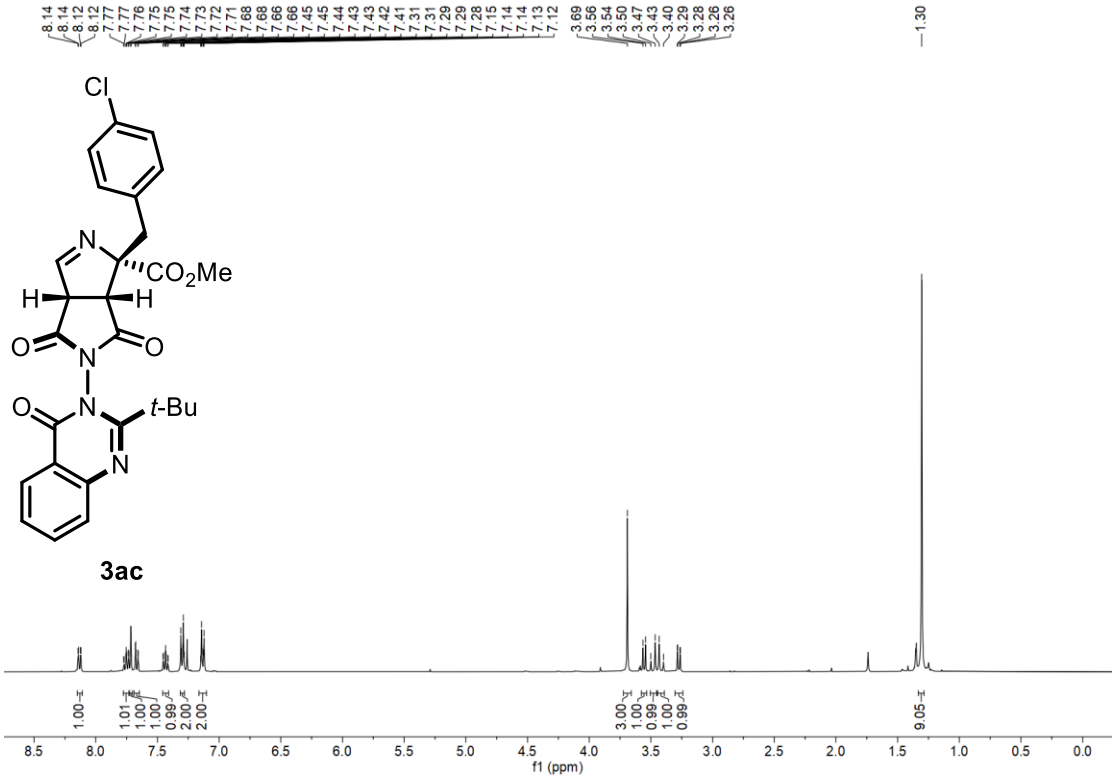
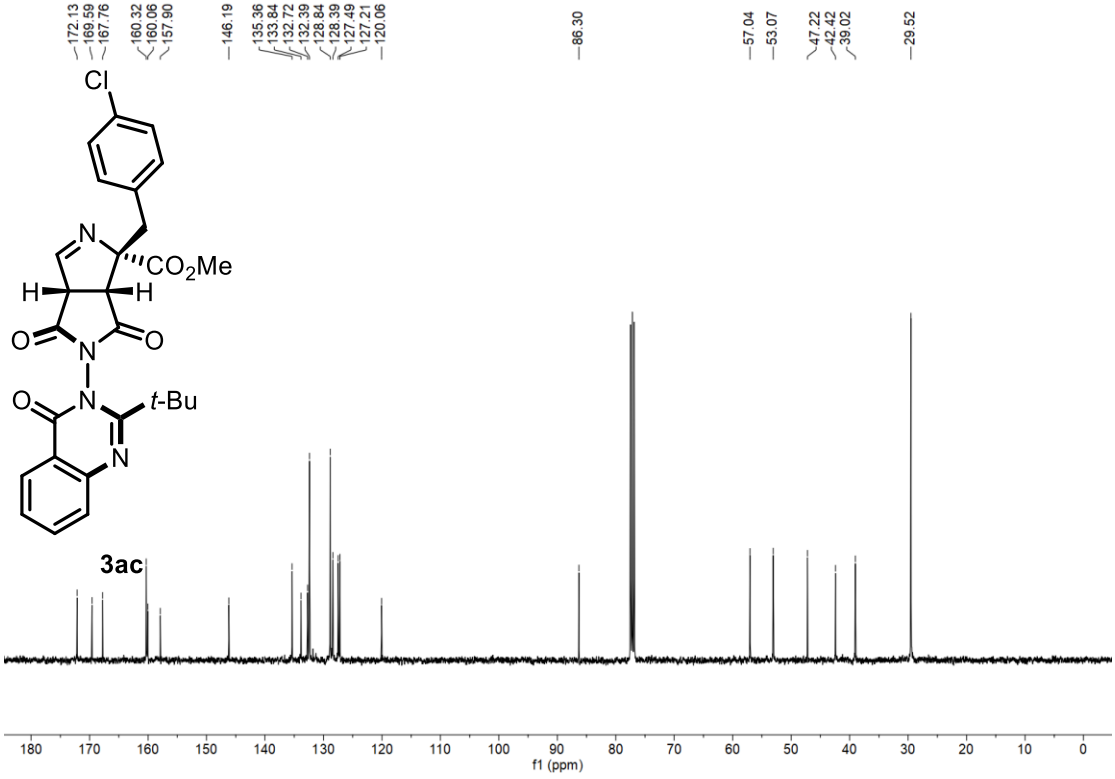



**$^{13}$C NMR** (101 MHz, $CDCl_3$)



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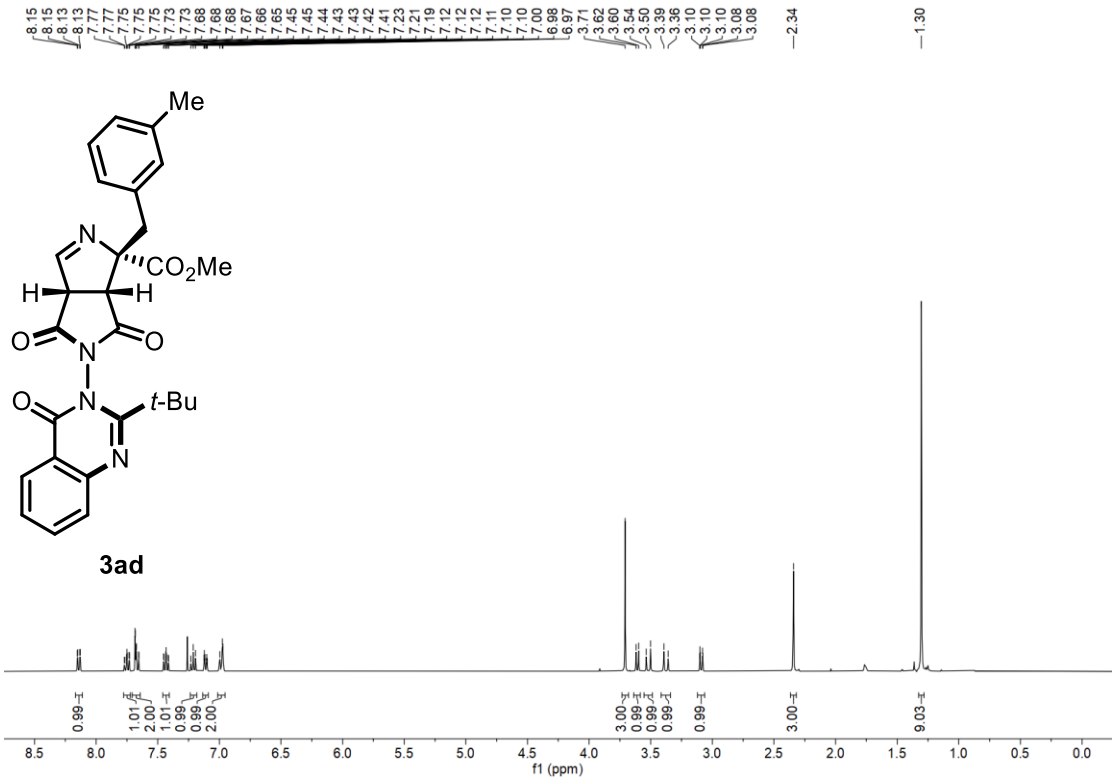


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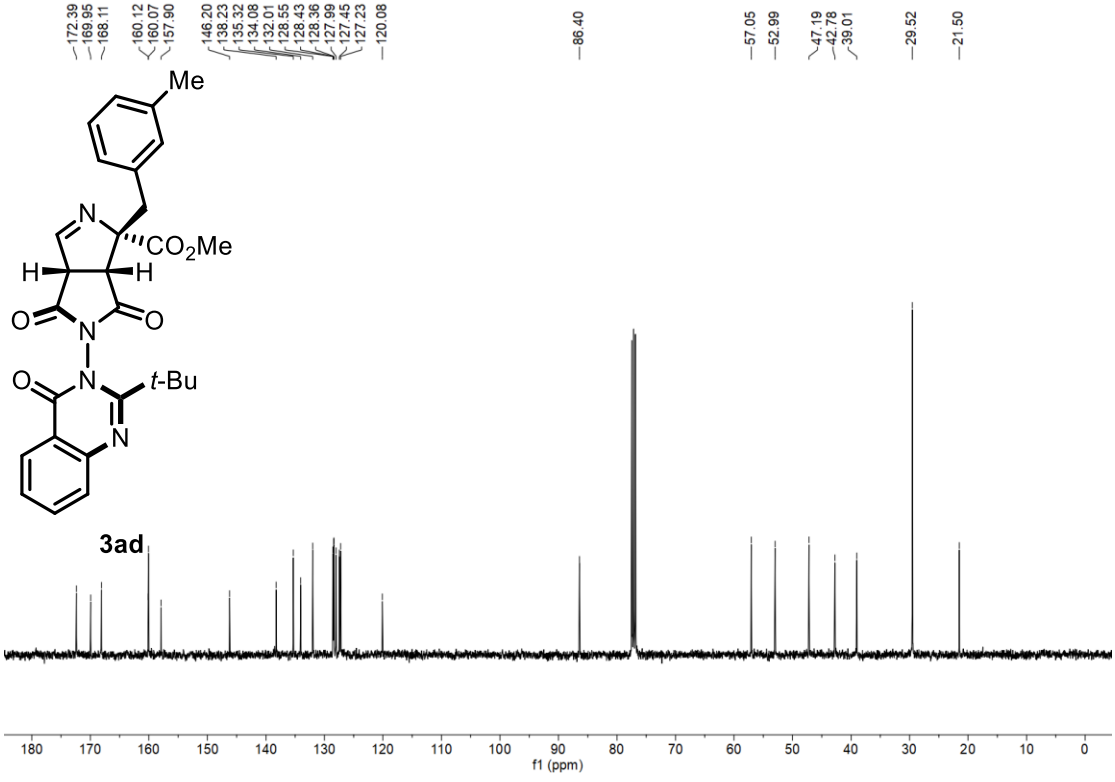

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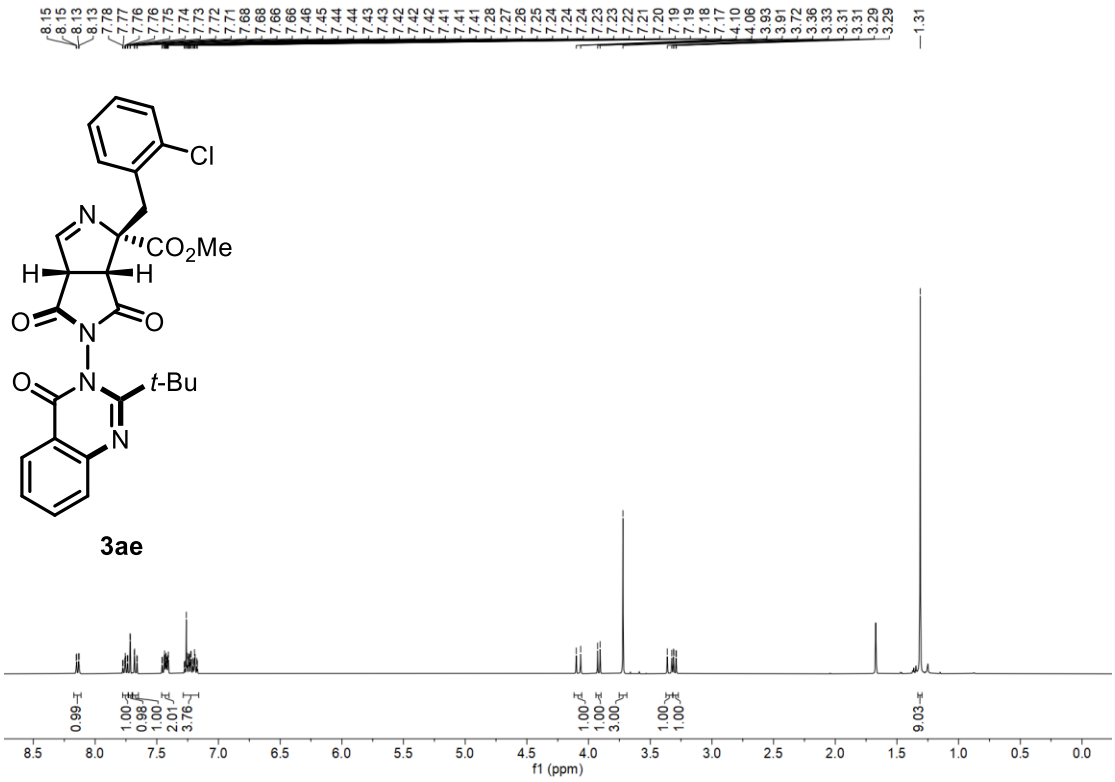
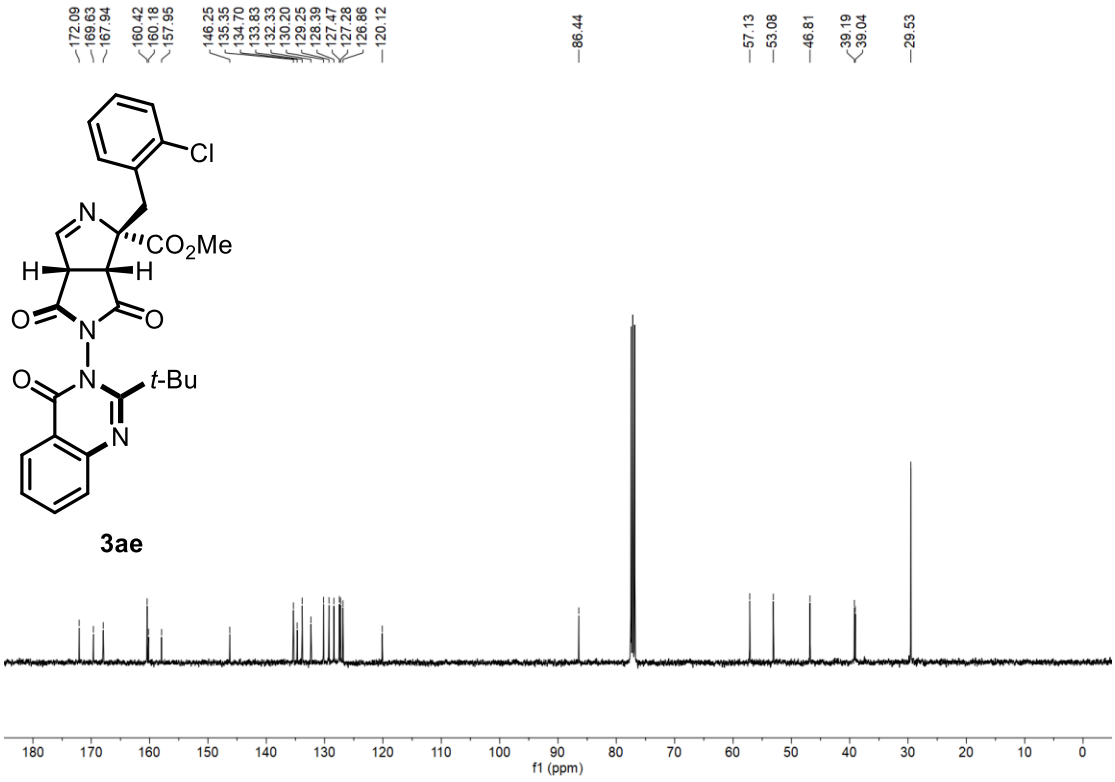
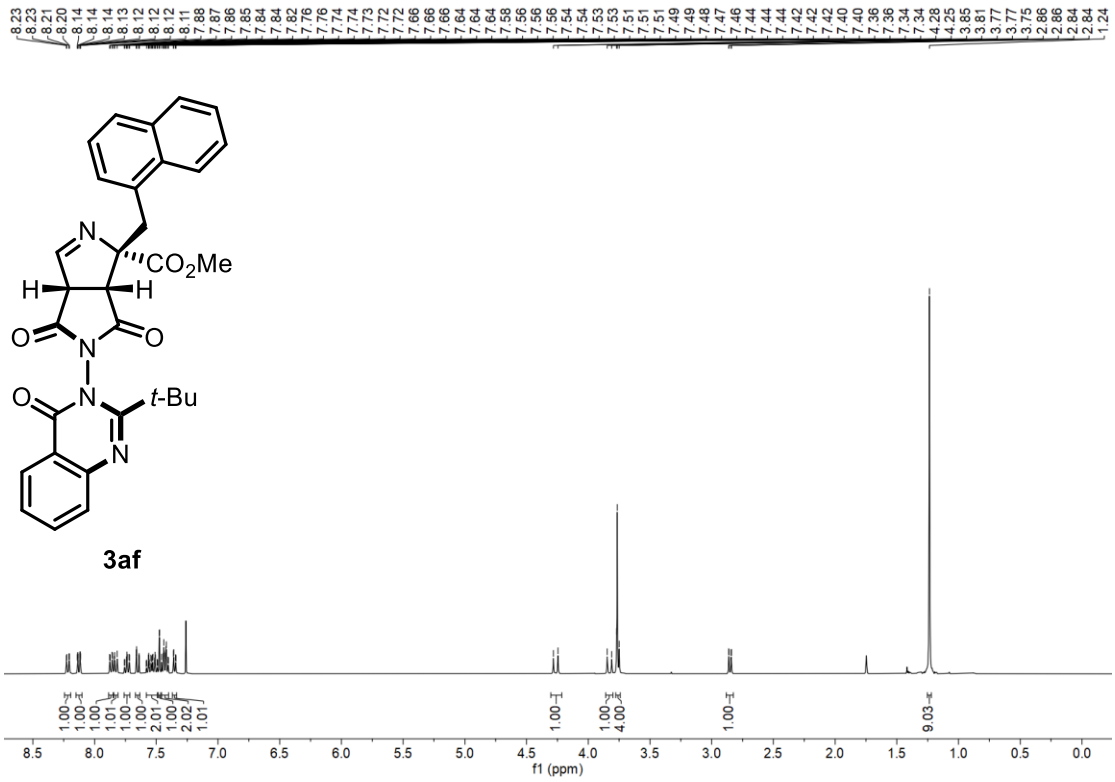


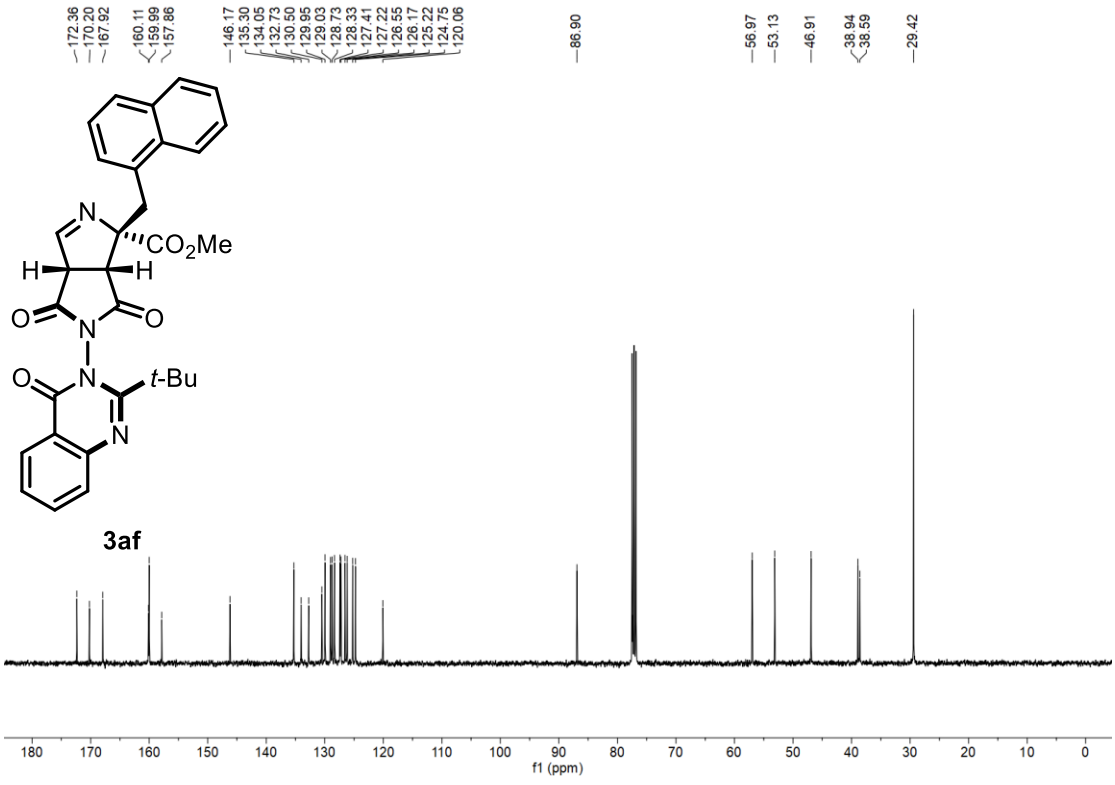

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



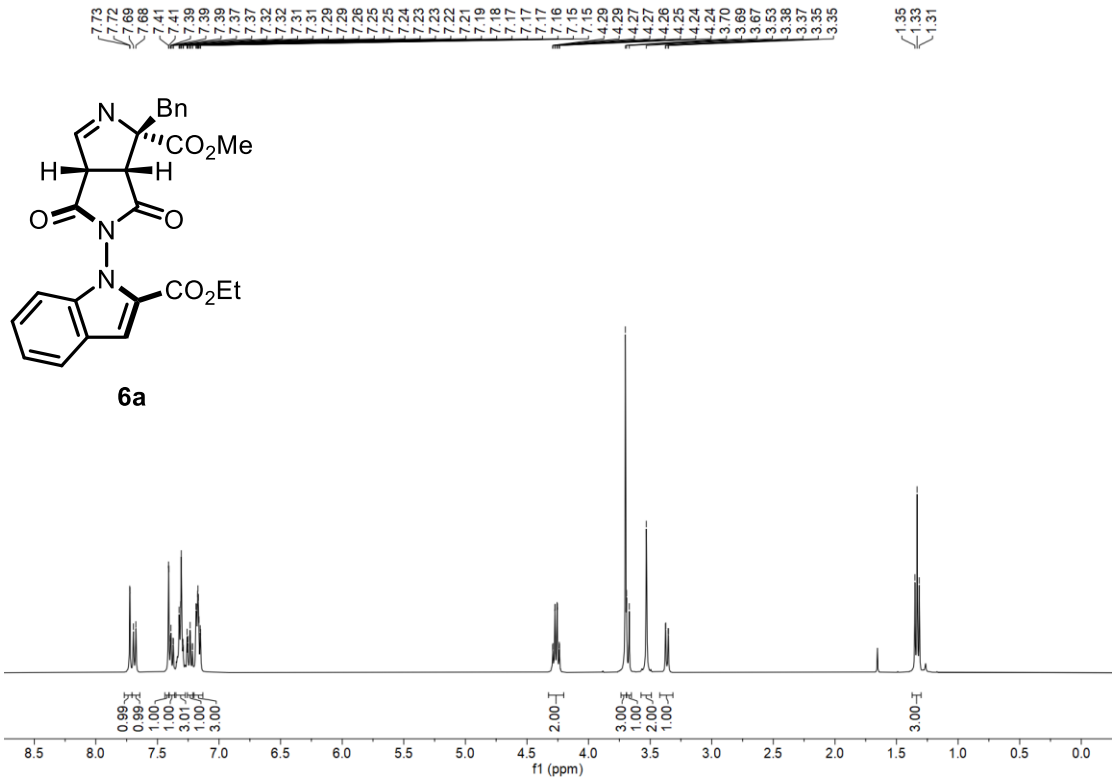
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



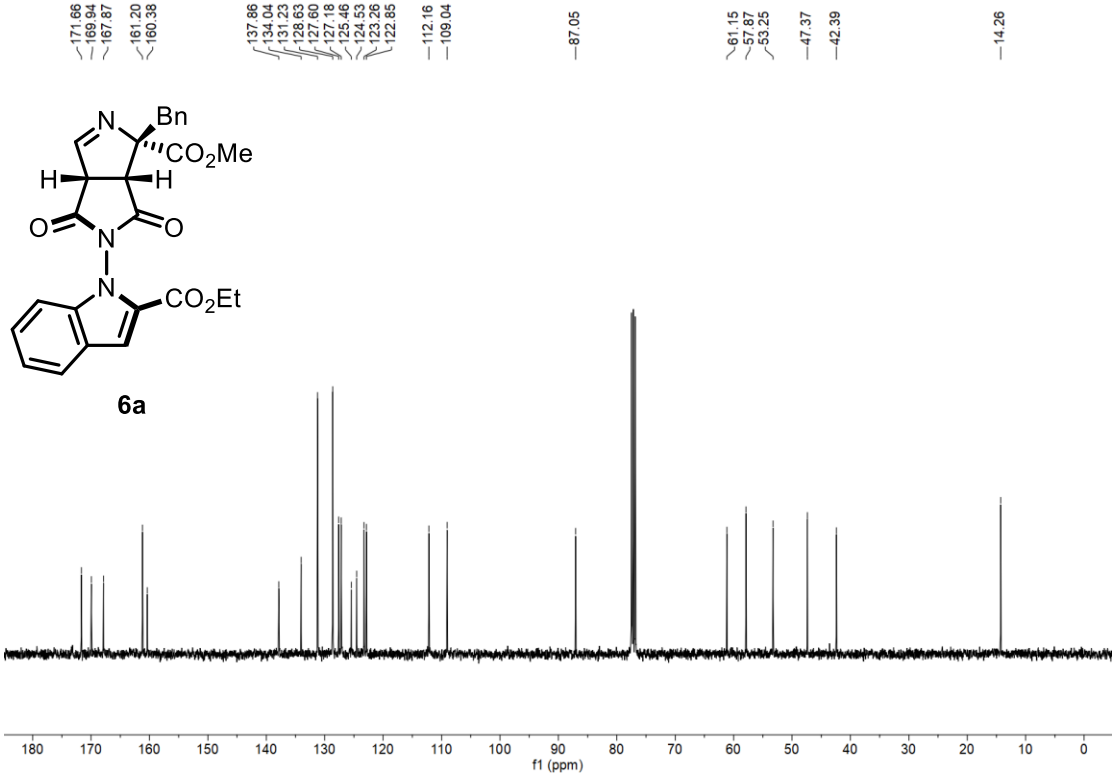

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



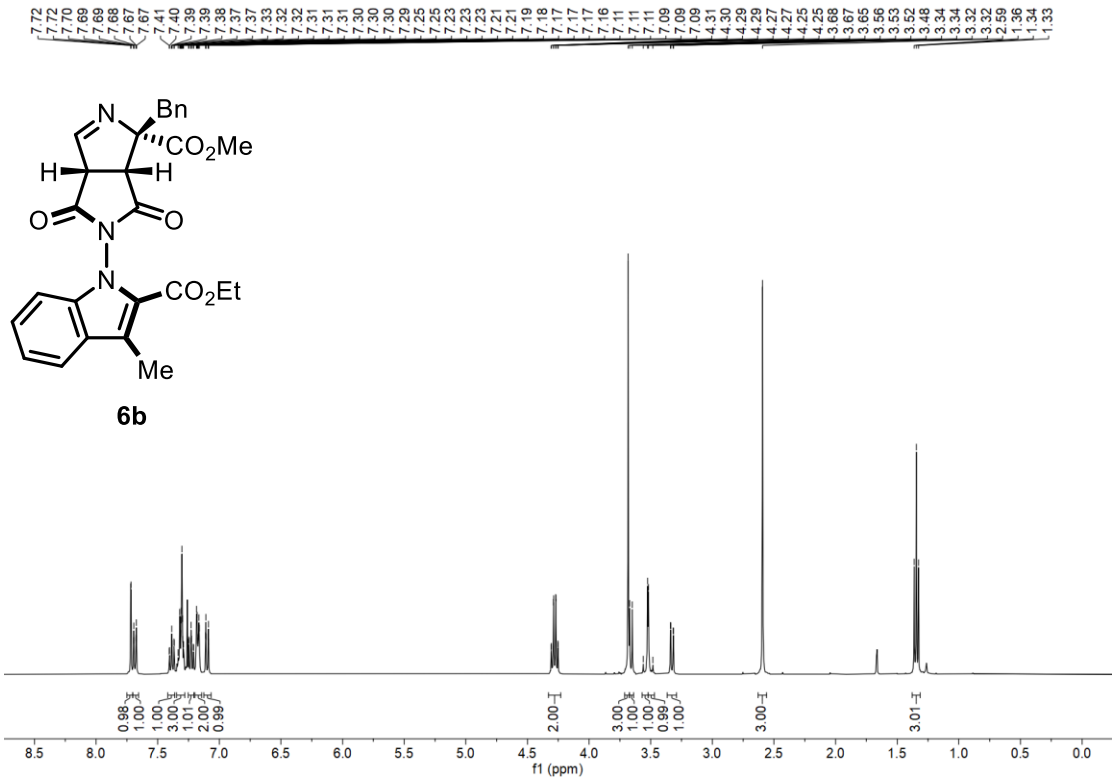
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



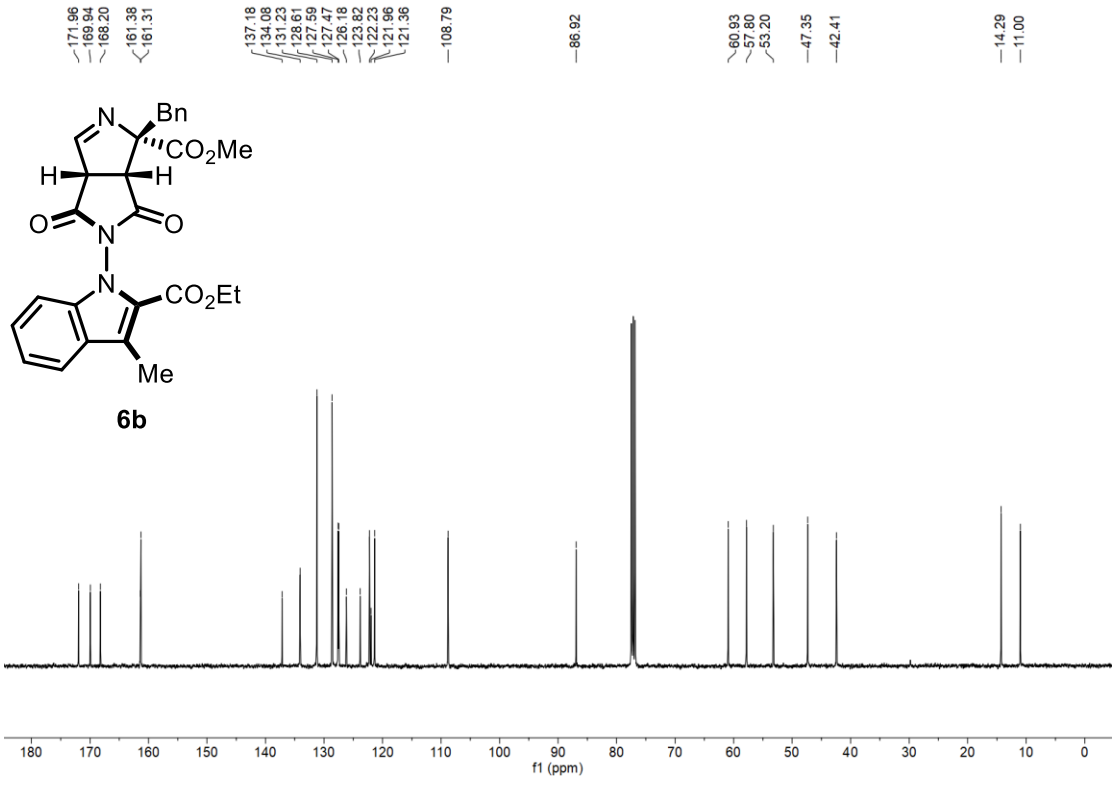

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



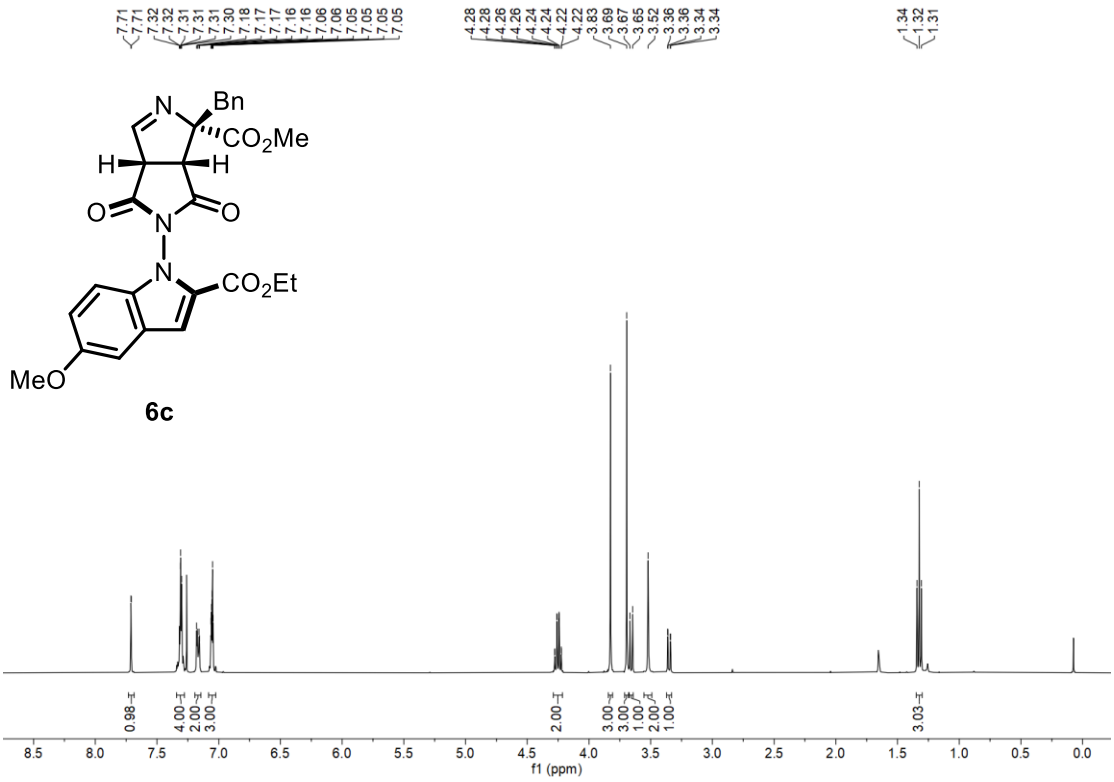
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



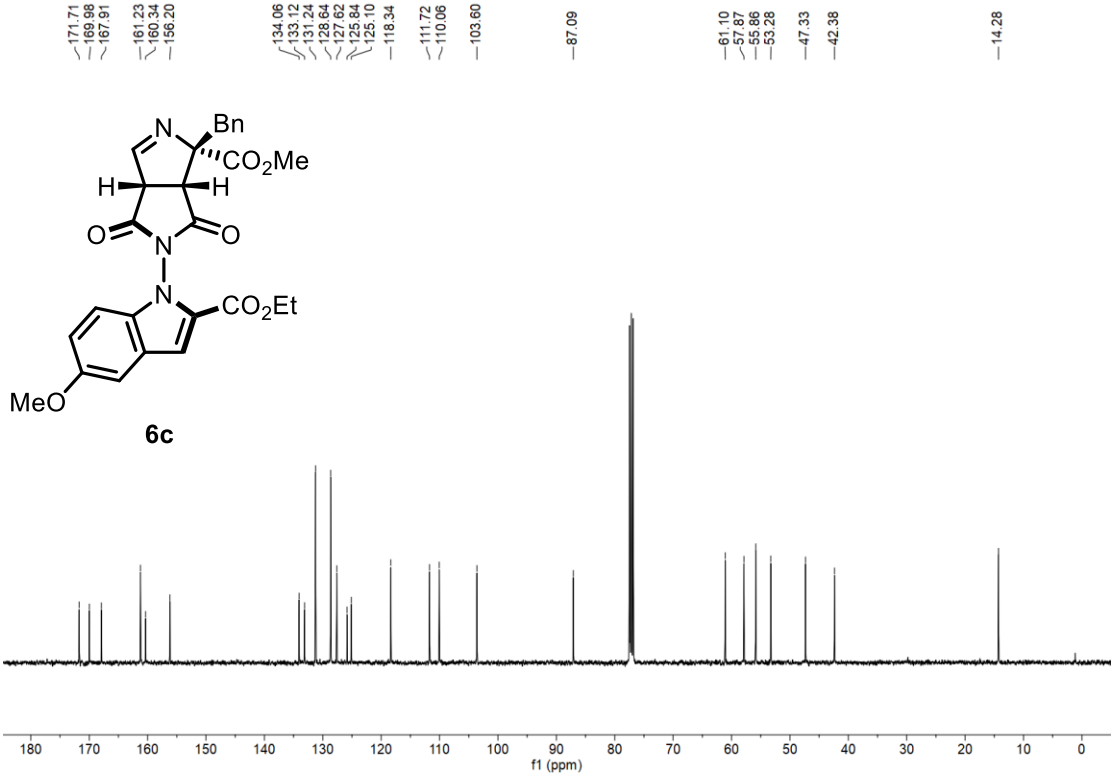

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



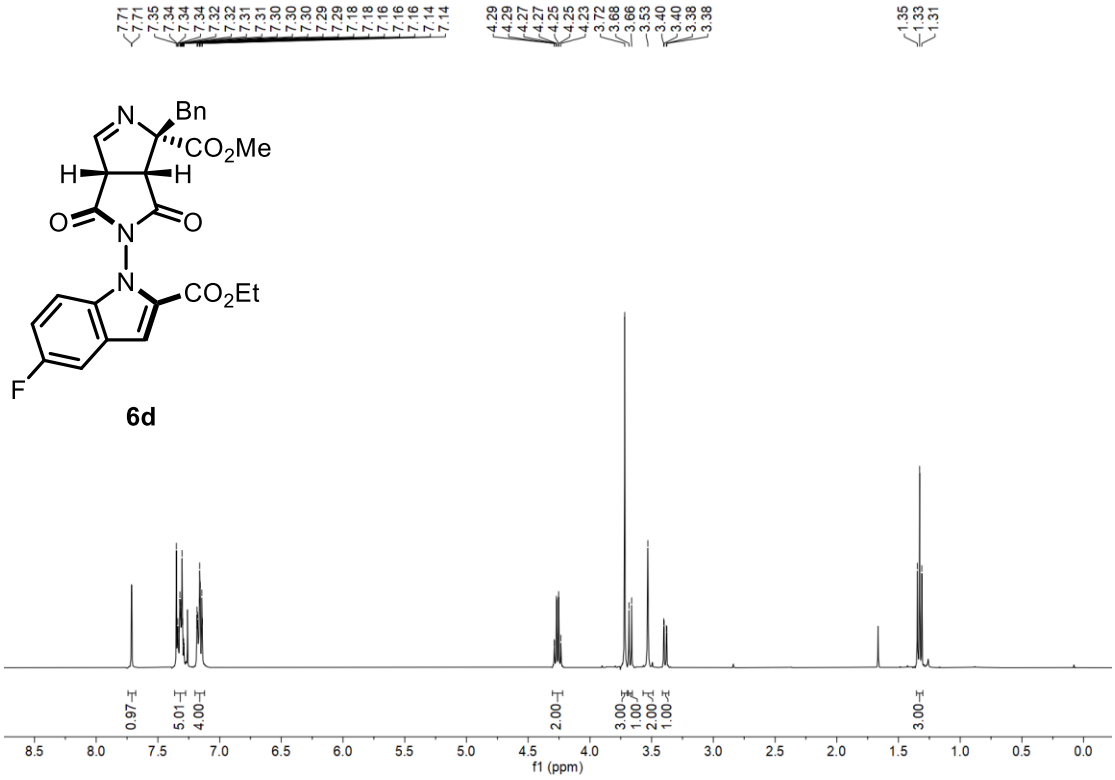
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



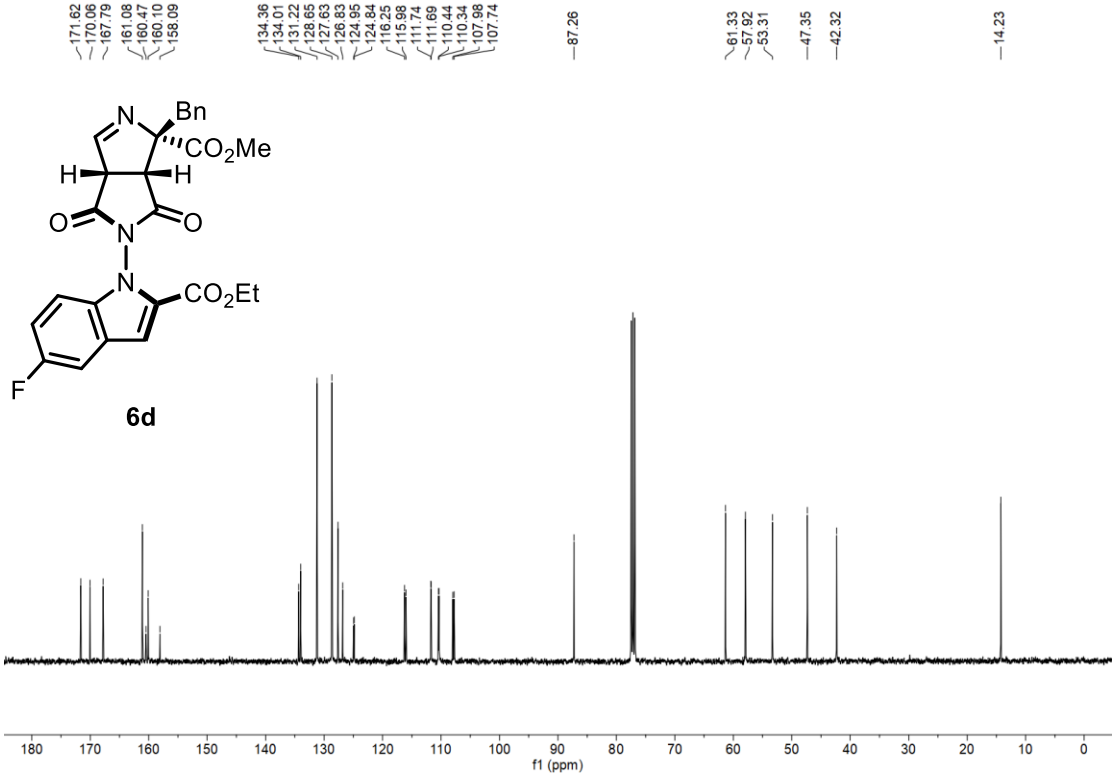

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



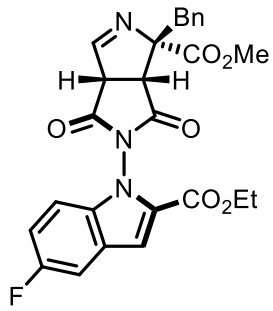
**$^{1}$H NMR** (400 MHz, $CDCl_3$)




**$^{13}$C NMR** (101 MHz, $CDCl_3$)



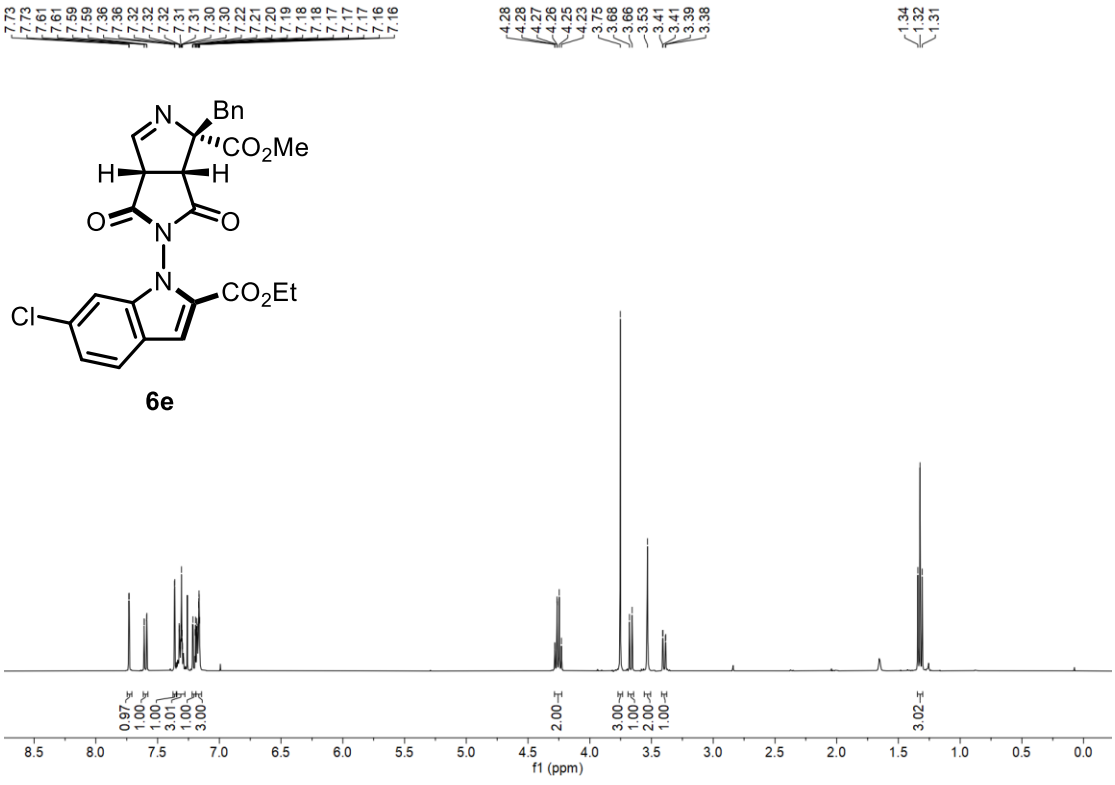
**$^{19}$F NMR** (376 MHz, $CDCl_3$)




**6d**




**$^{1}$H NMR** (400 MHz, $CDCl_3$)

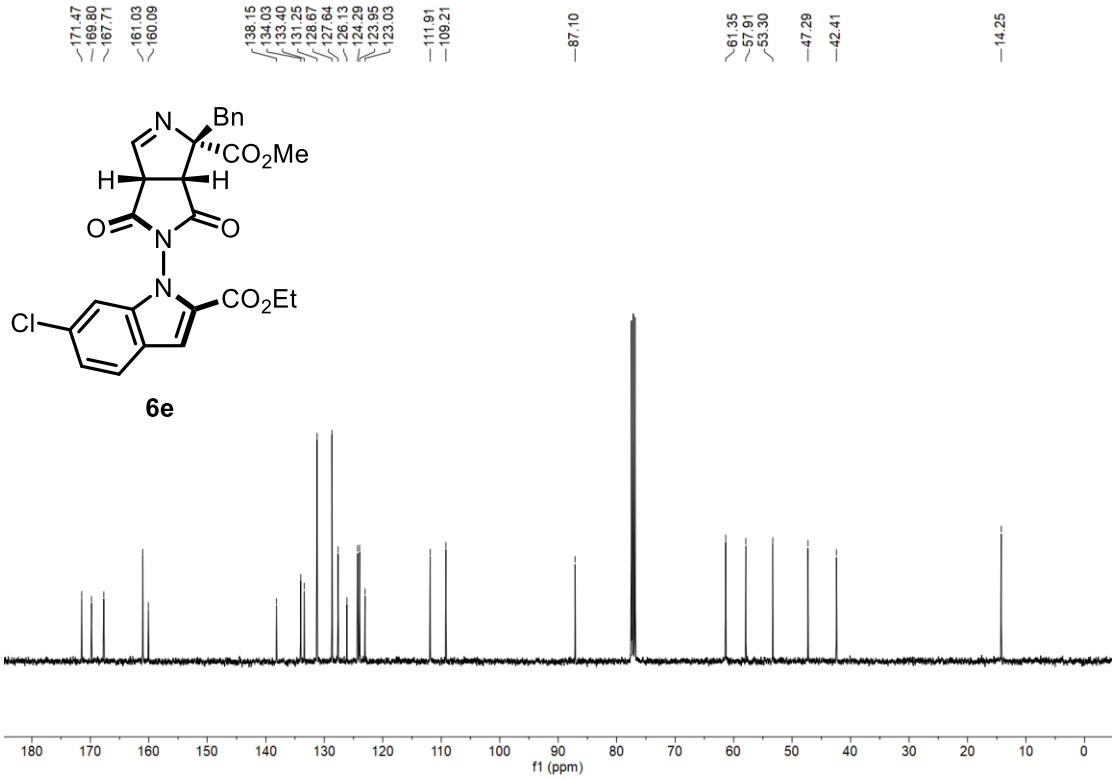




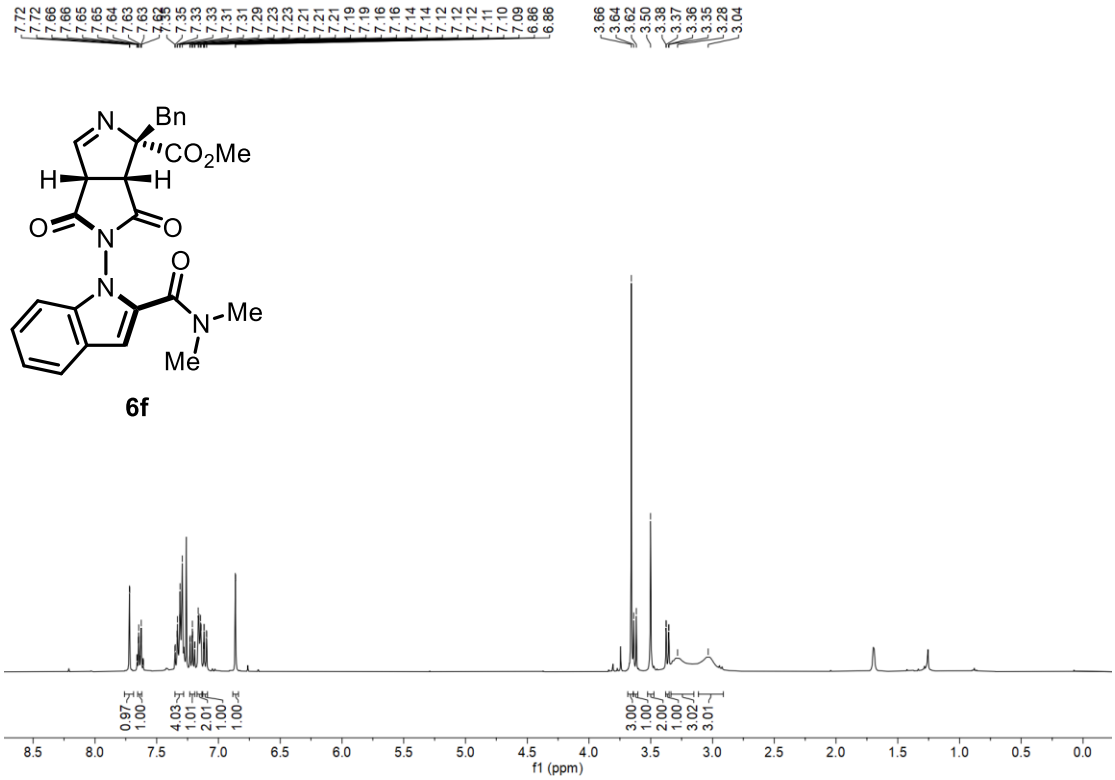


**6e**

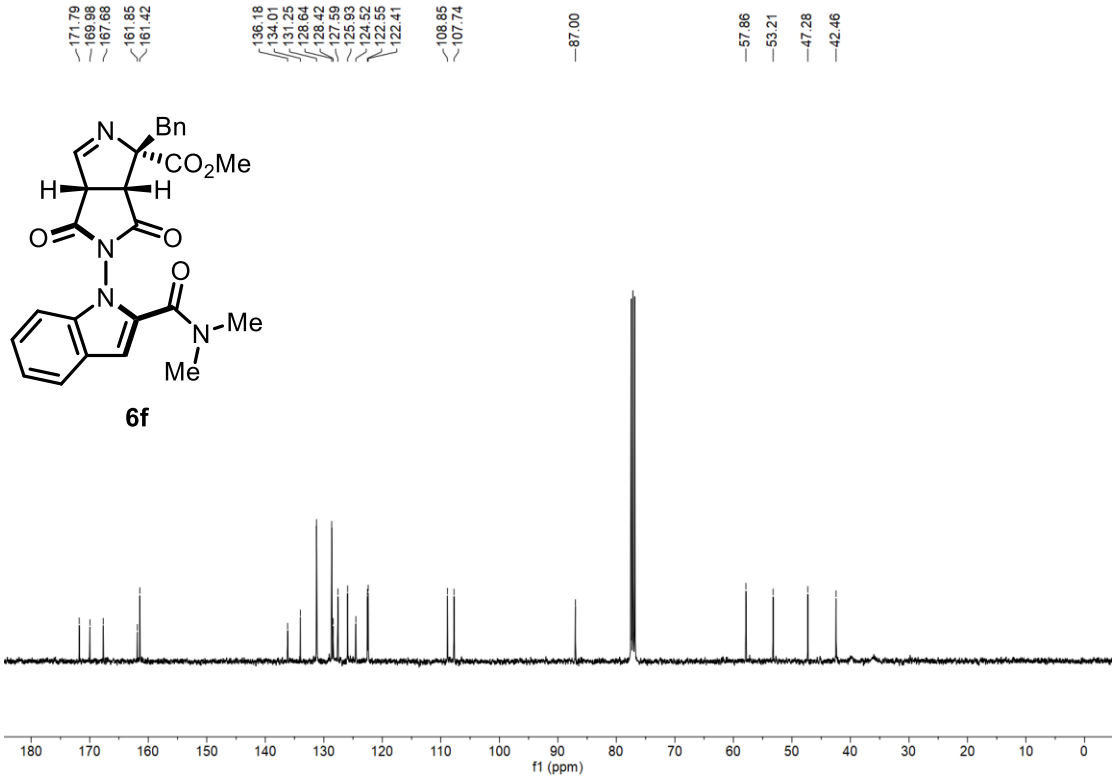
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



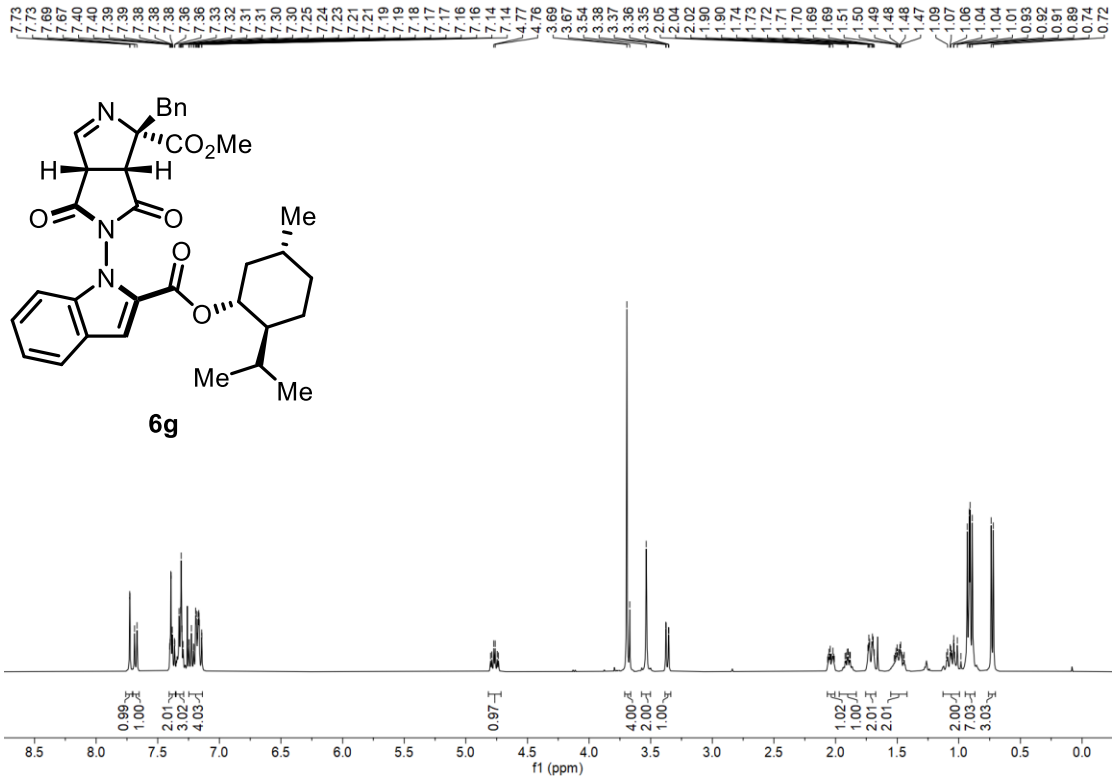

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



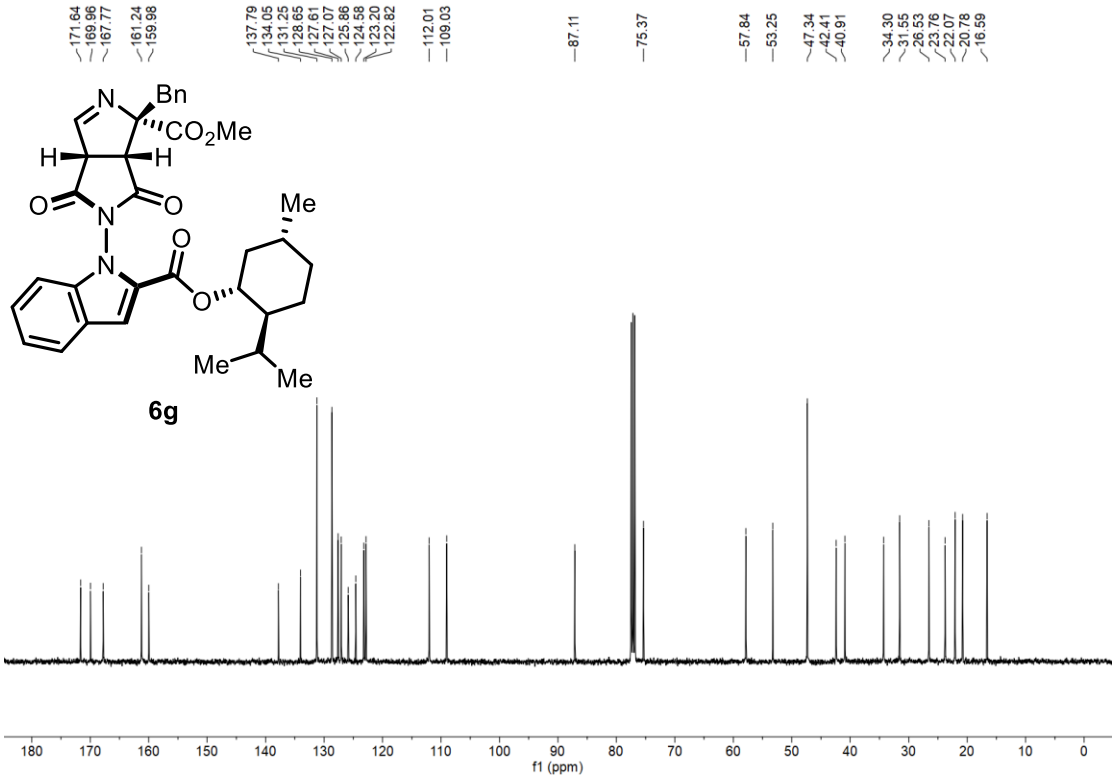
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



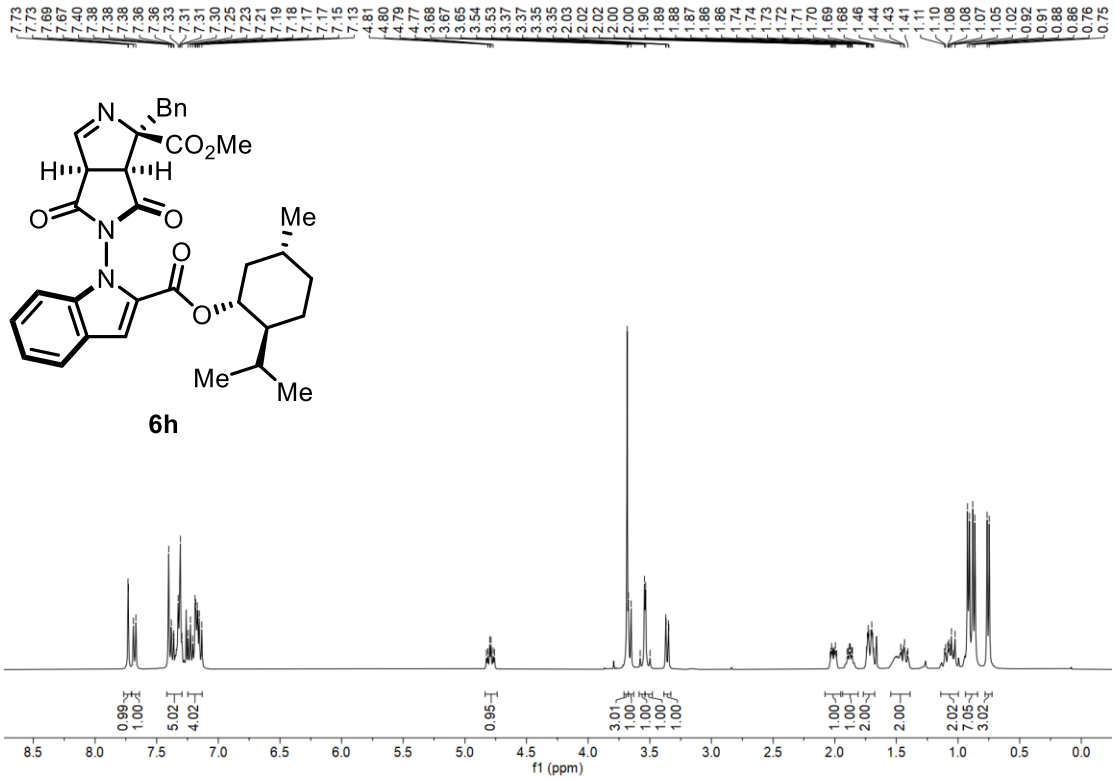

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



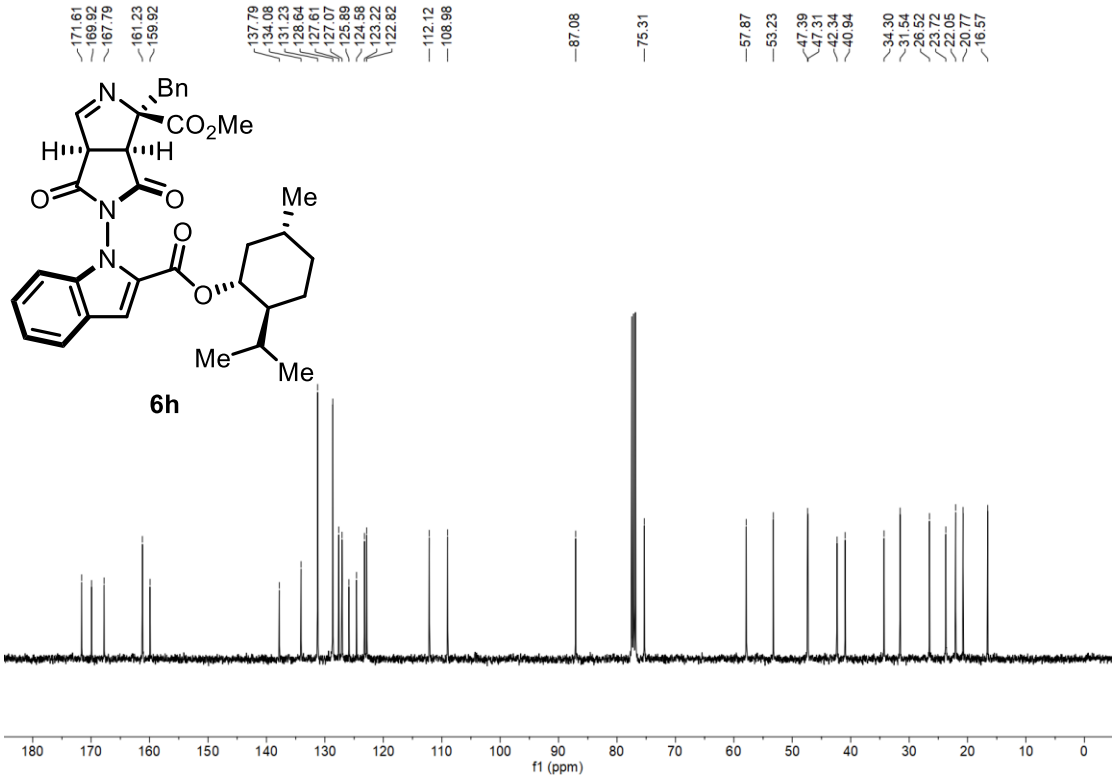
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



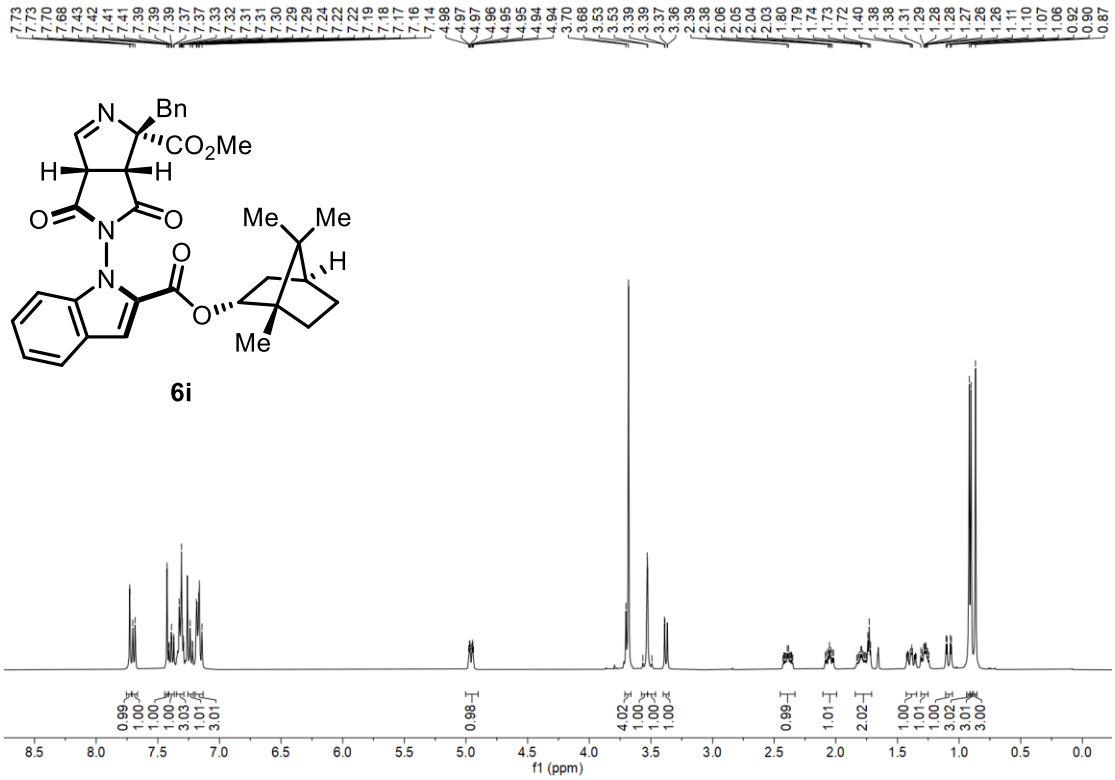

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



**$^{13}$C NMR** (101 MHz, $CDCl_3$)




**$^{1}$H NMR** (400 MHz, $CDCl_3$)



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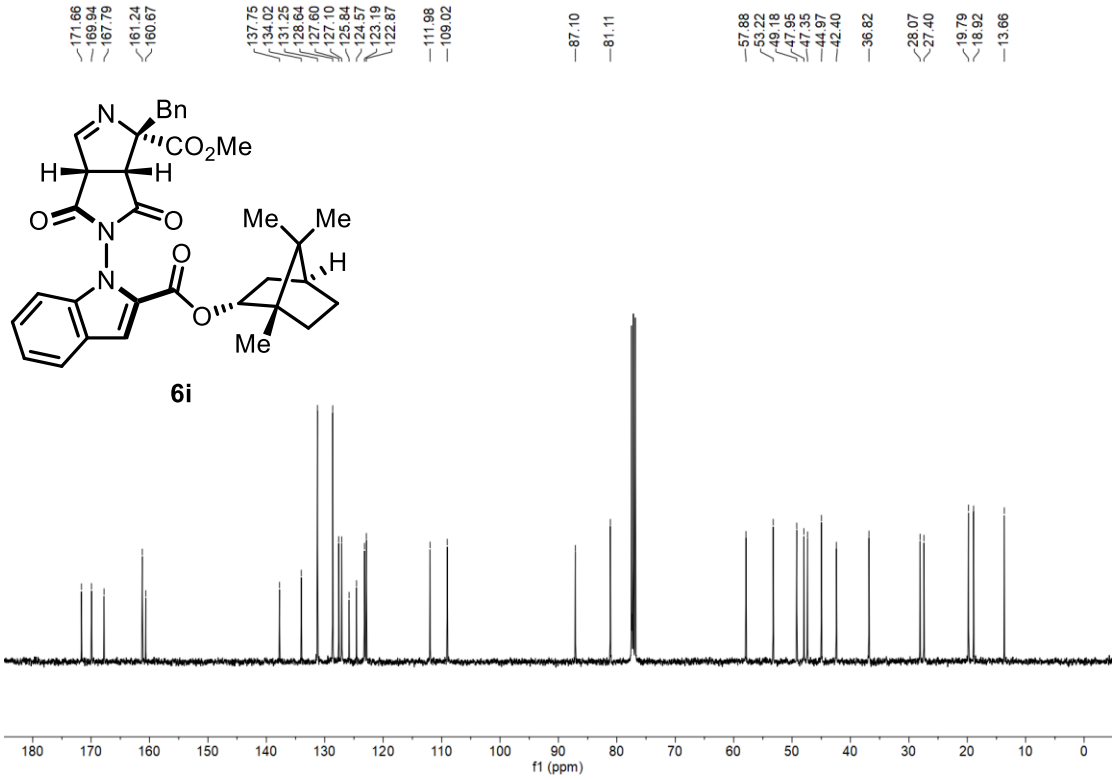
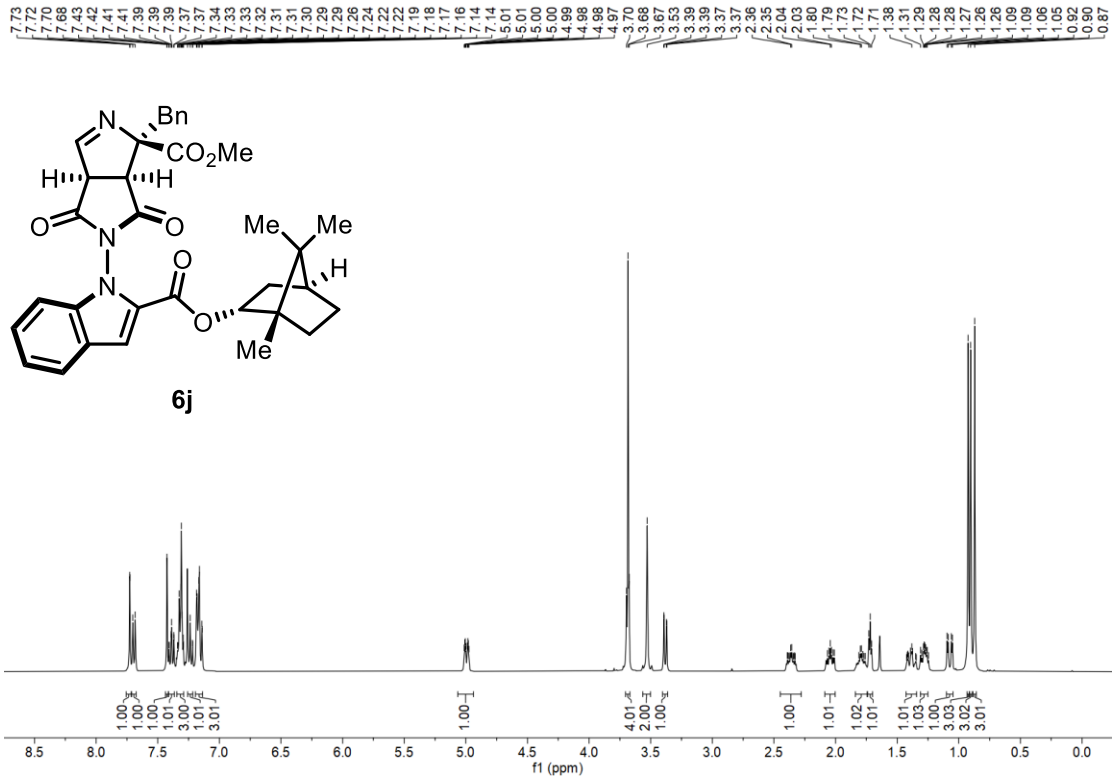



**$^{1}$H NMR** (400 MHz, $CDCl_3$)



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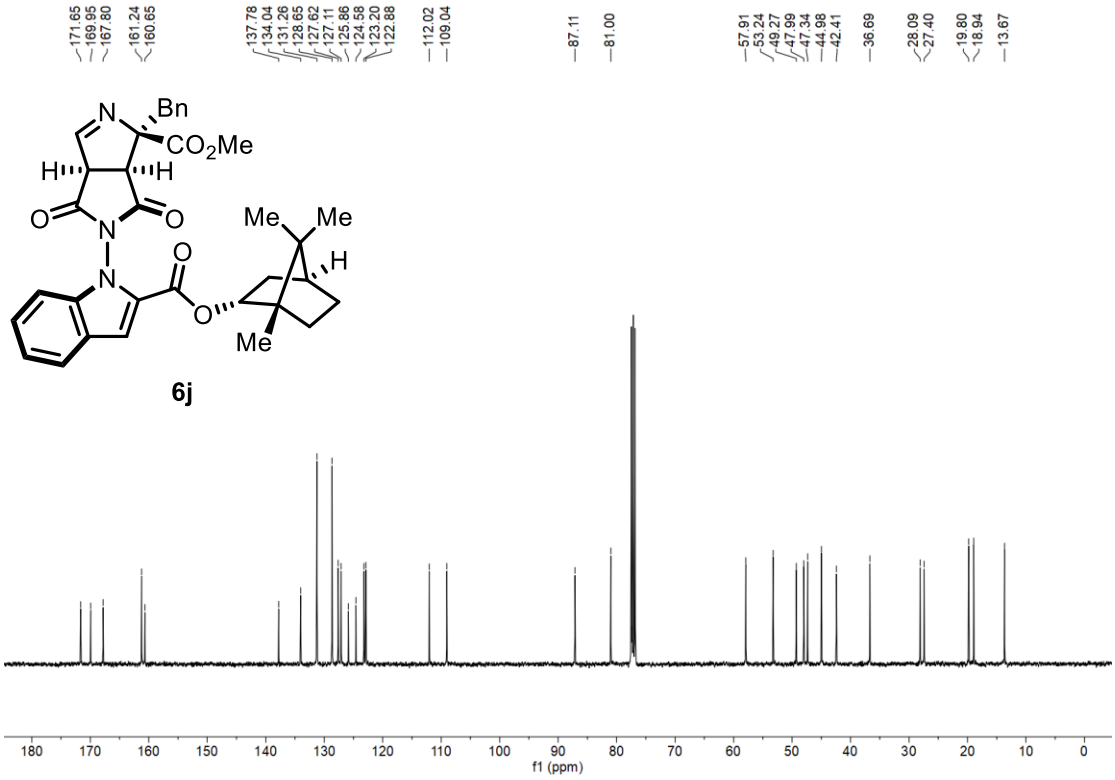
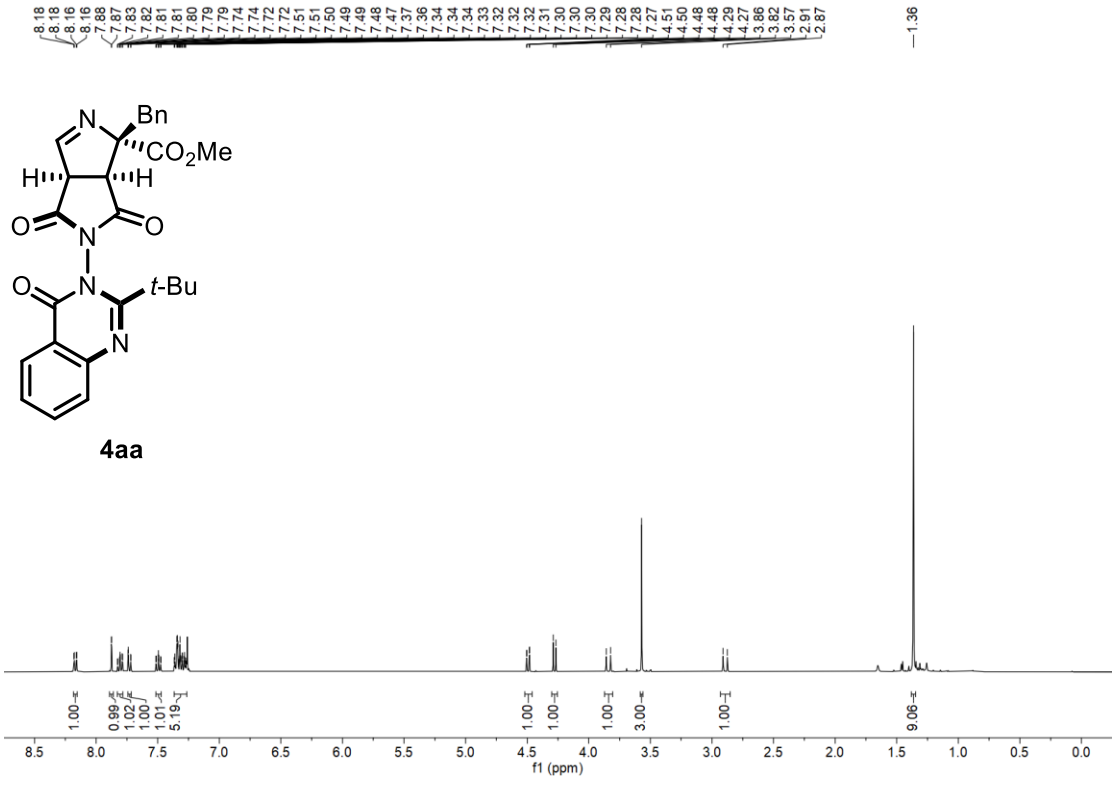
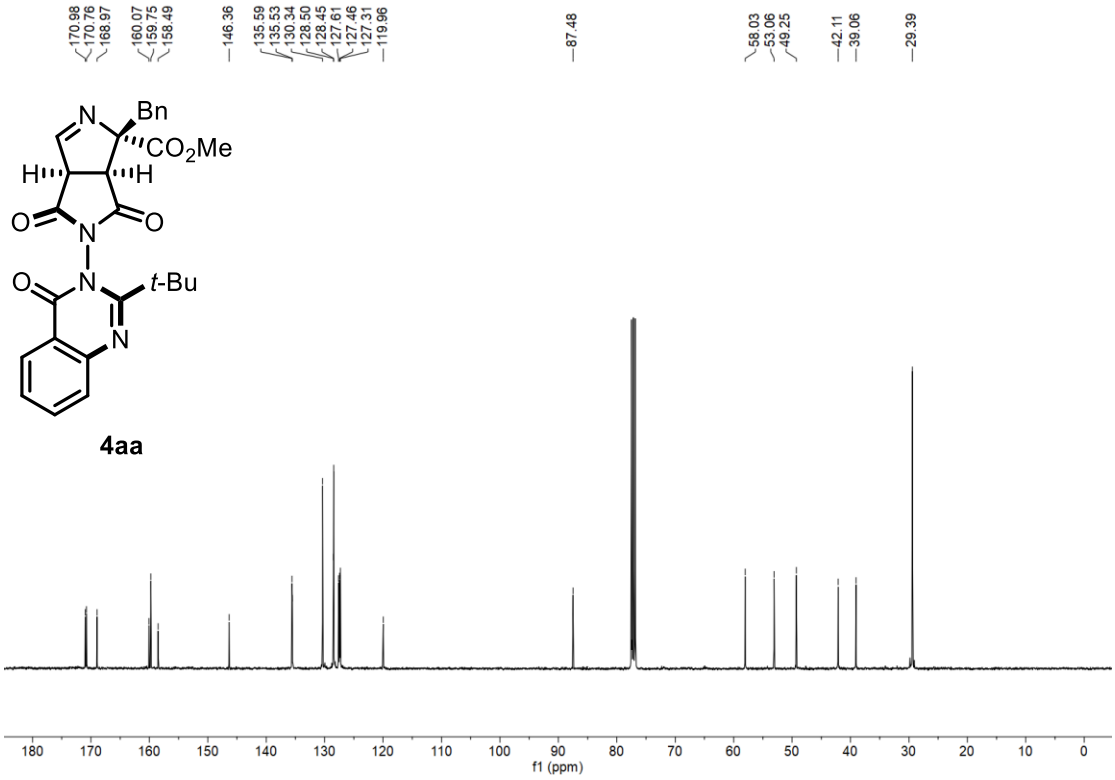


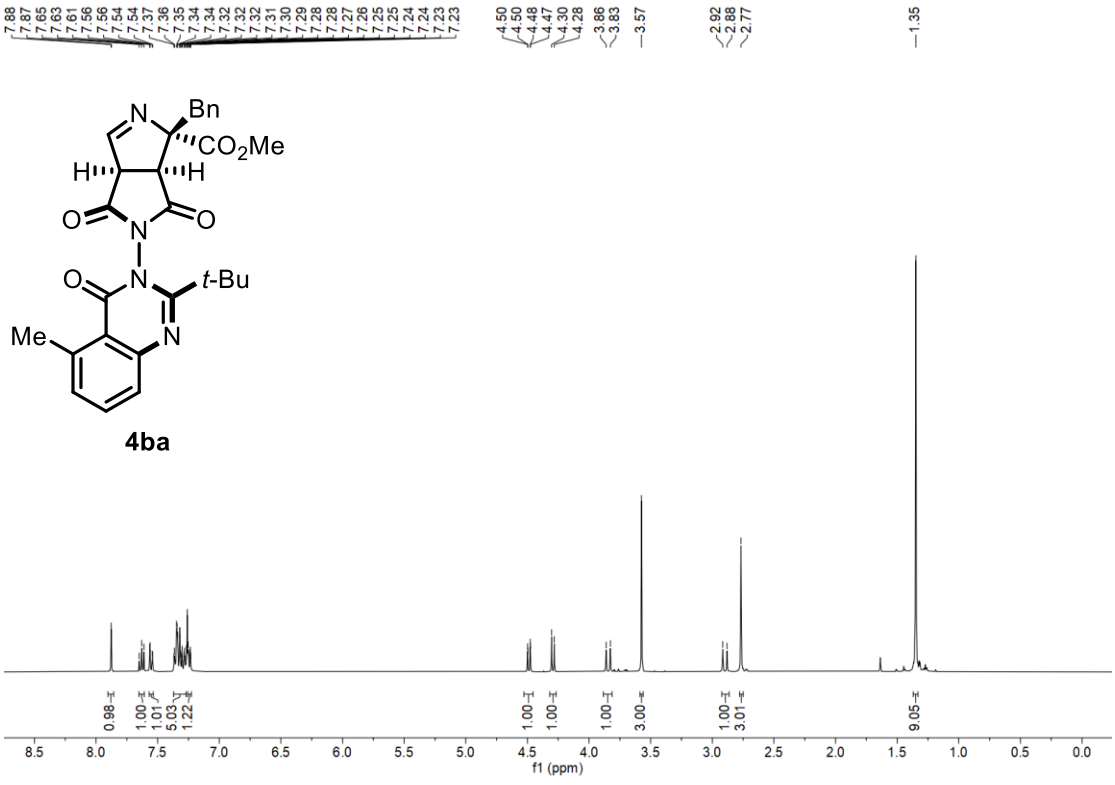

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



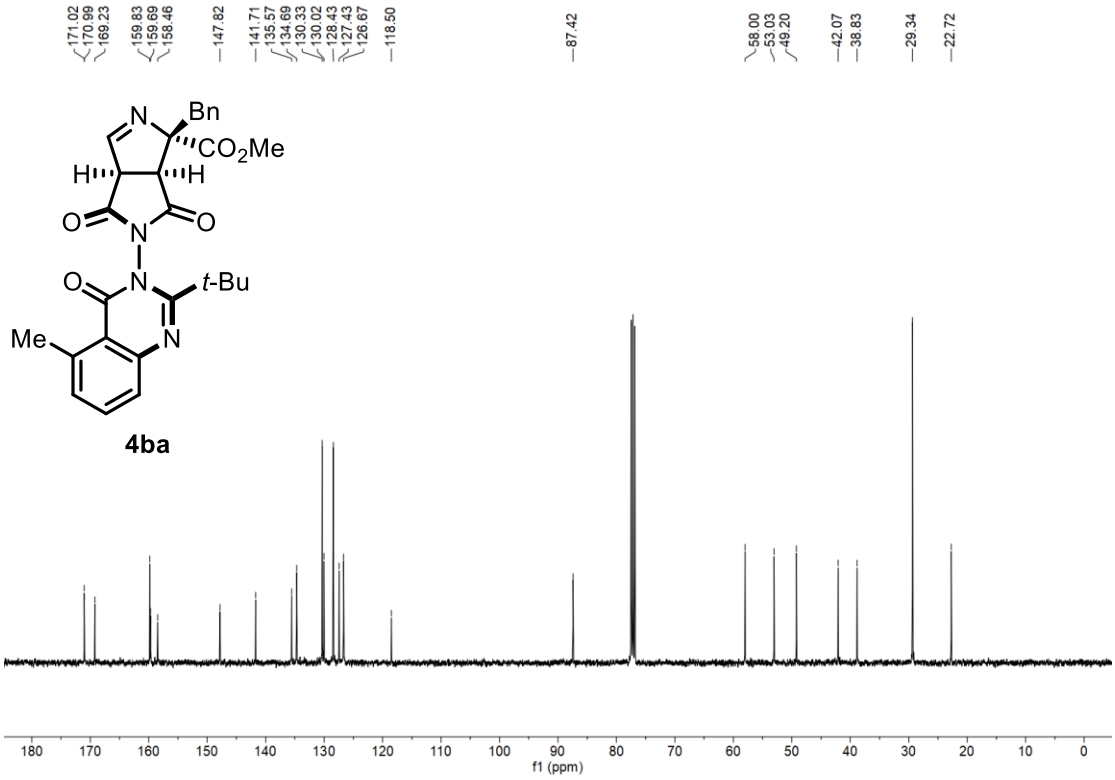
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



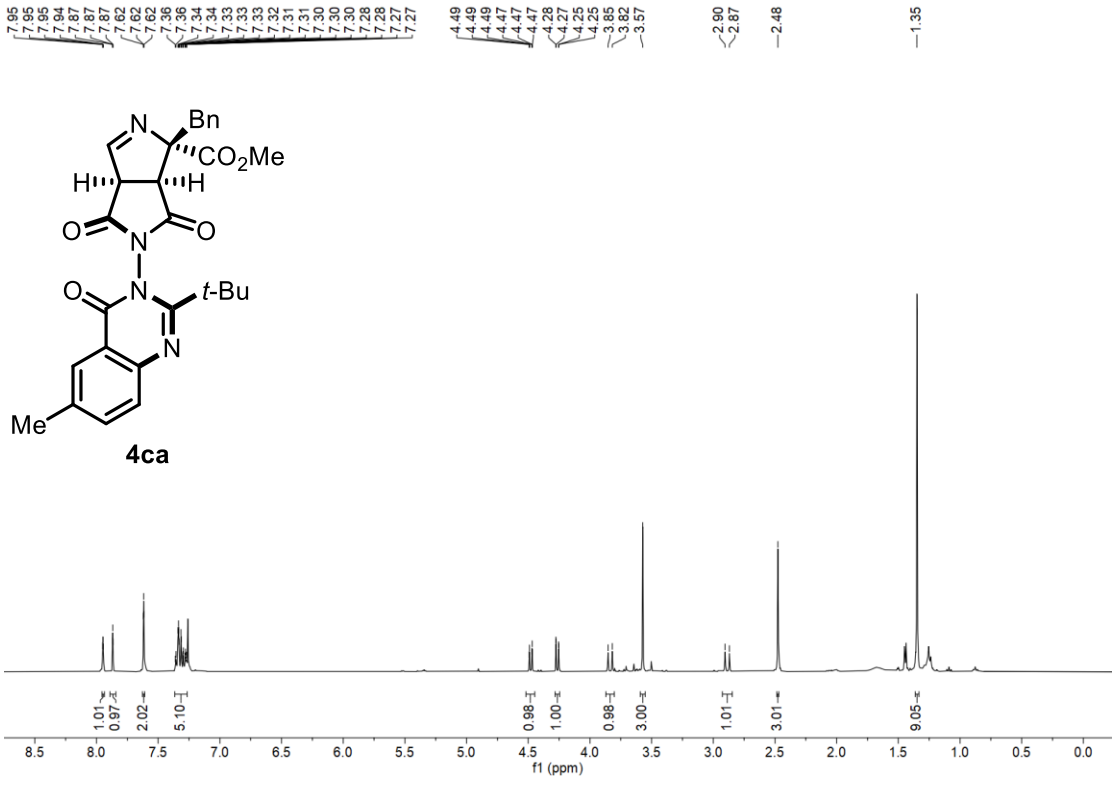

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



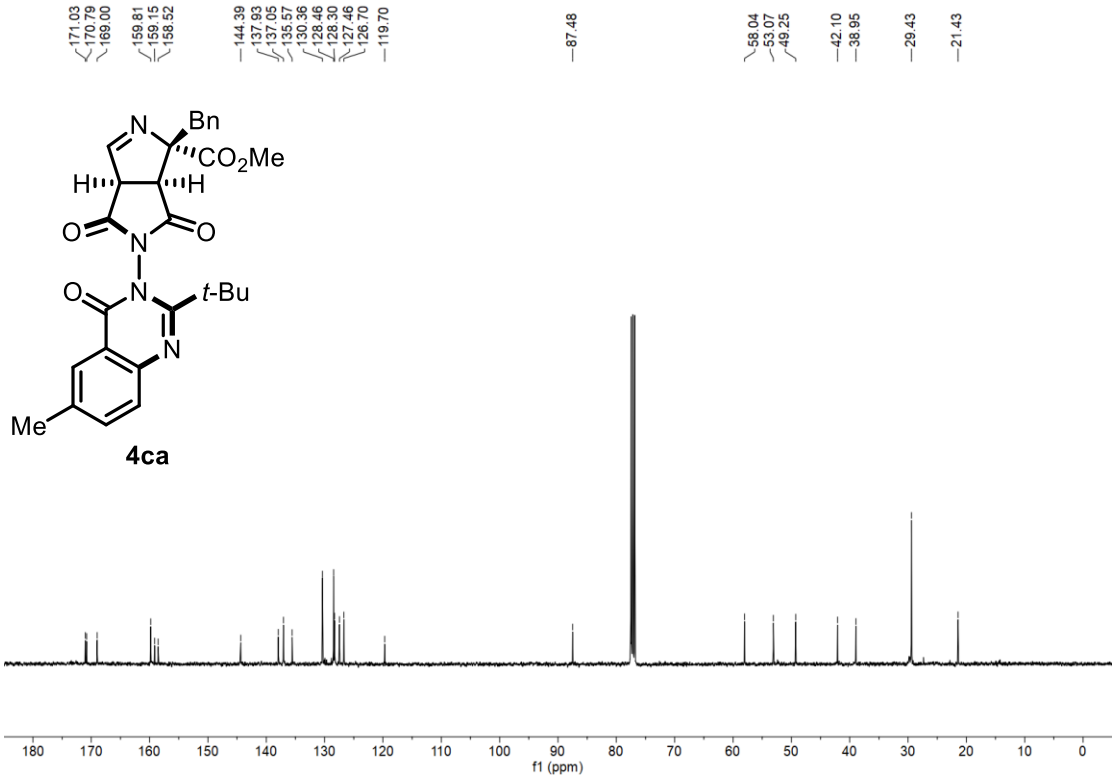
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



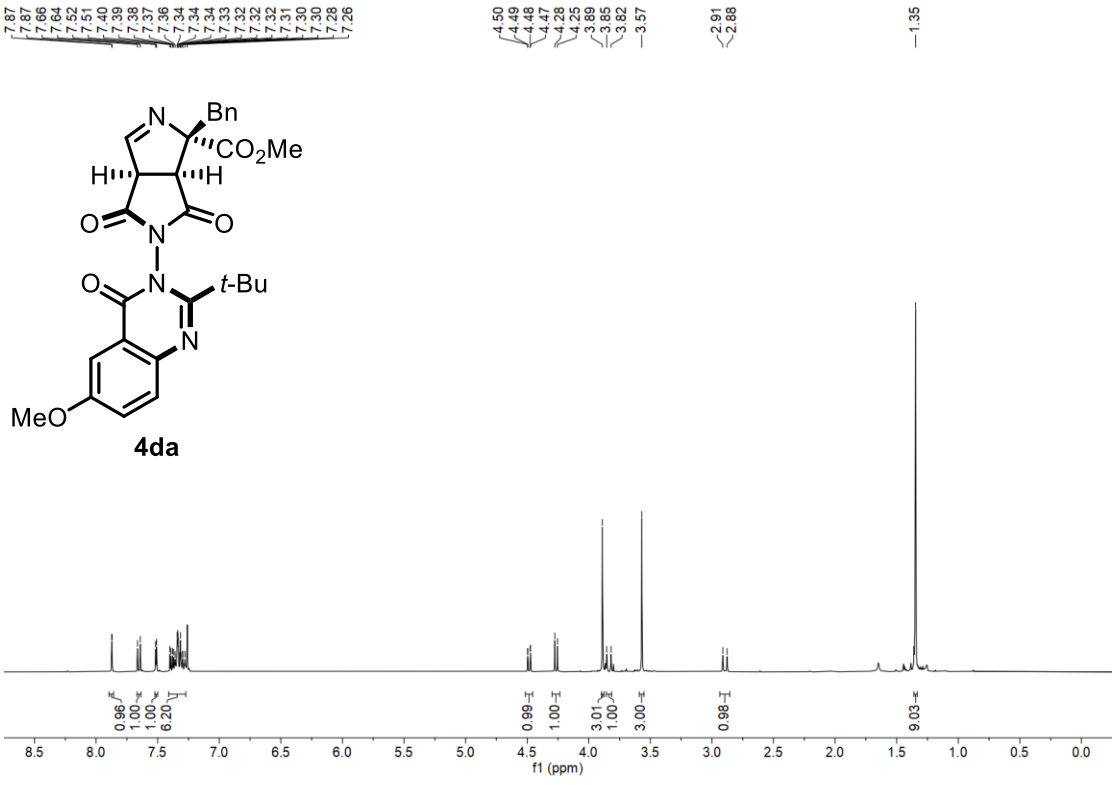

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



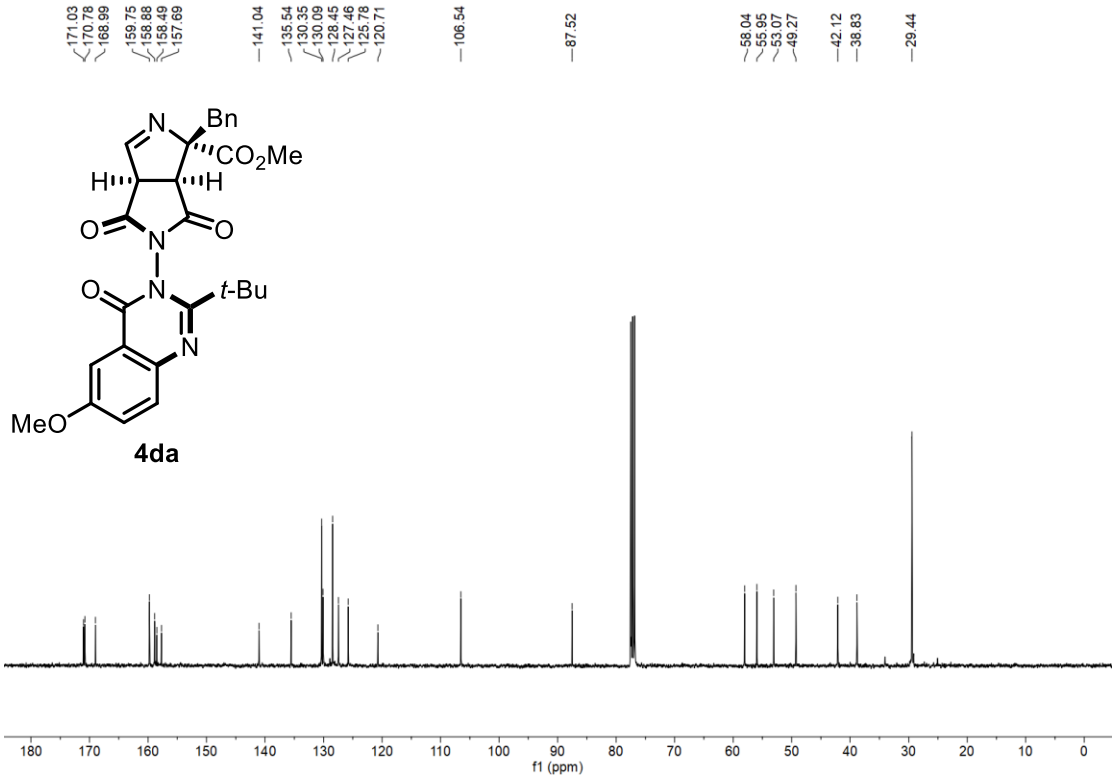
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



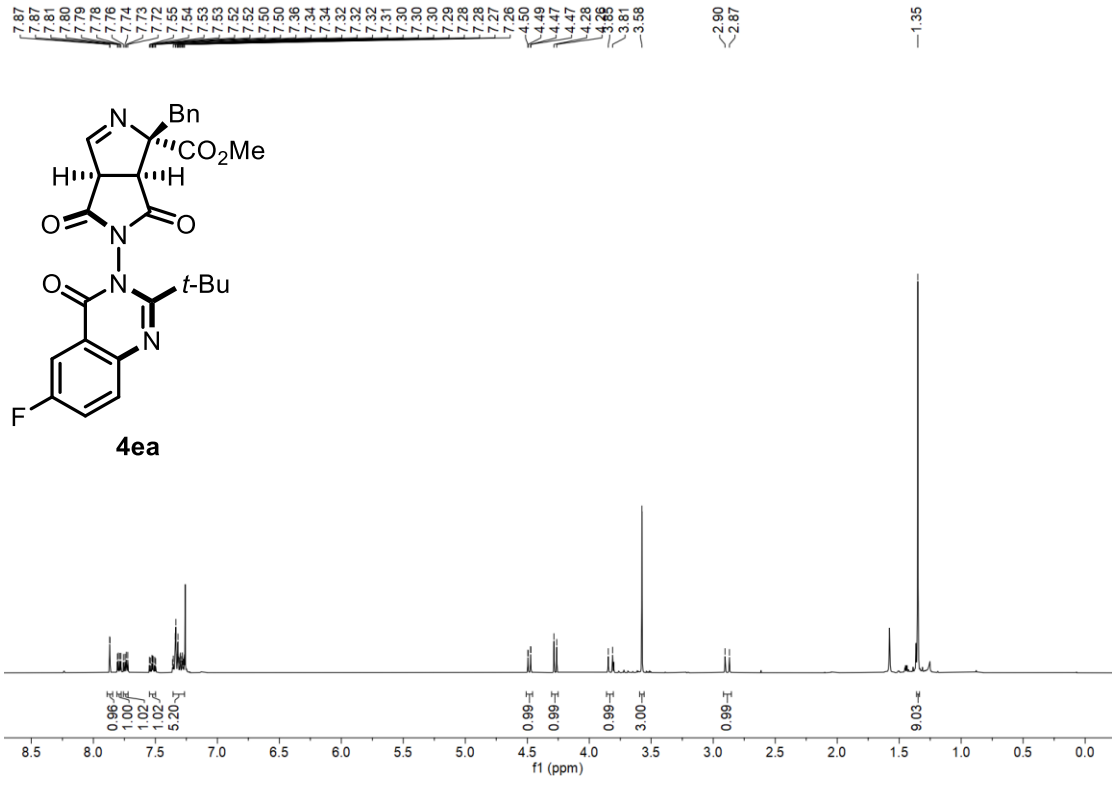

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



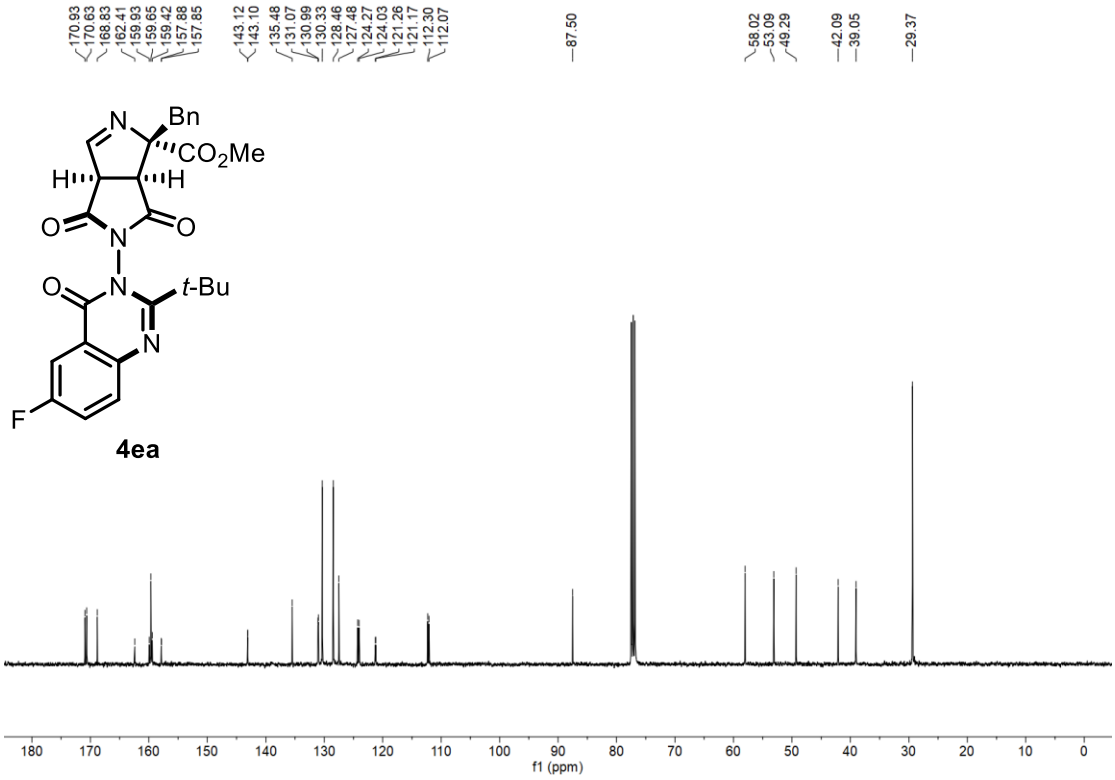
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



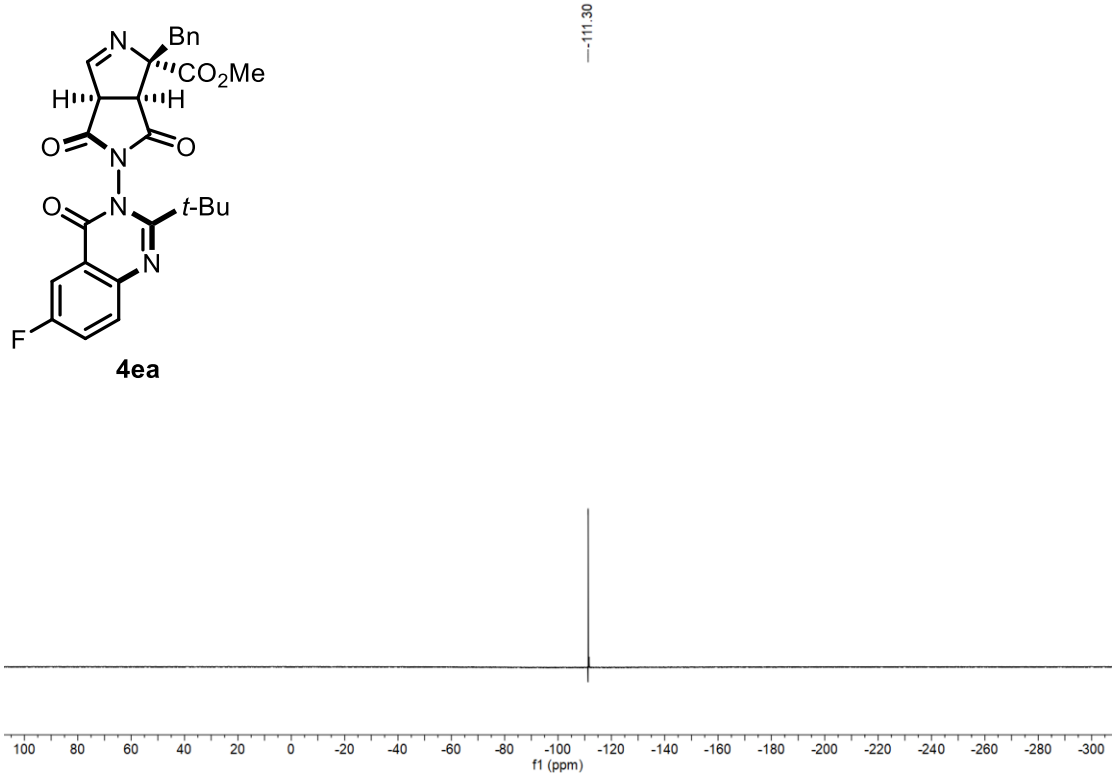

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



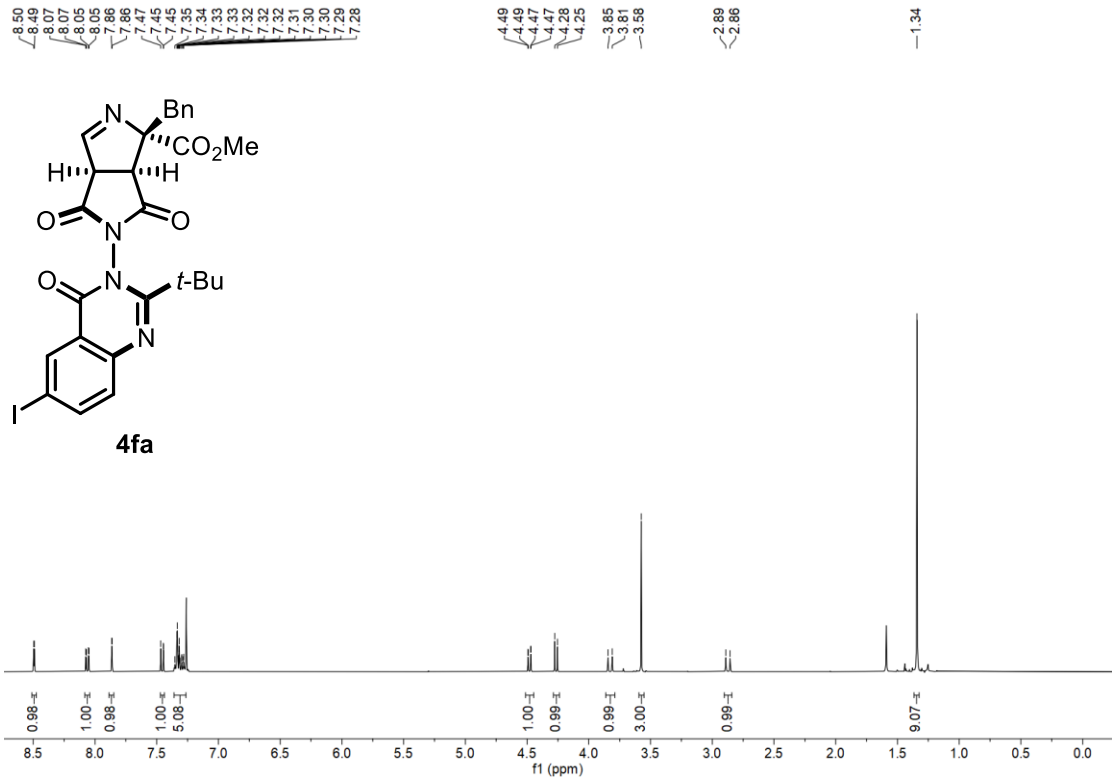
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



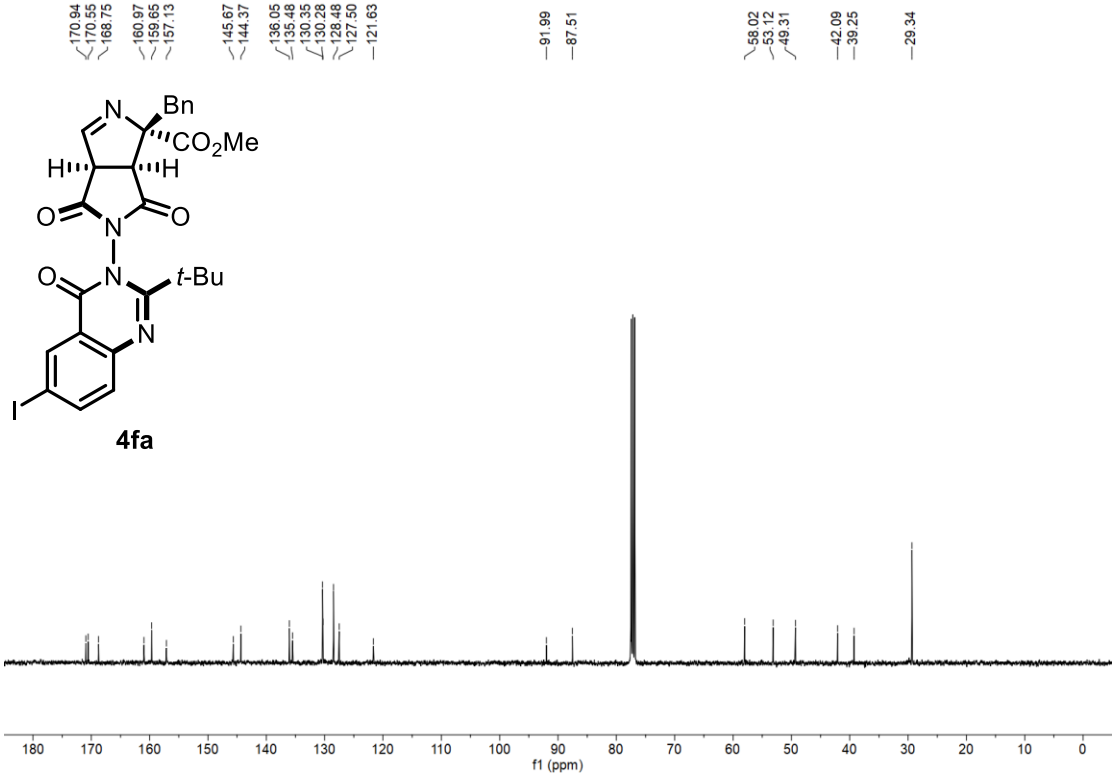

**$^{19}$F NMR** (376 MHz, $CDCl_3$)



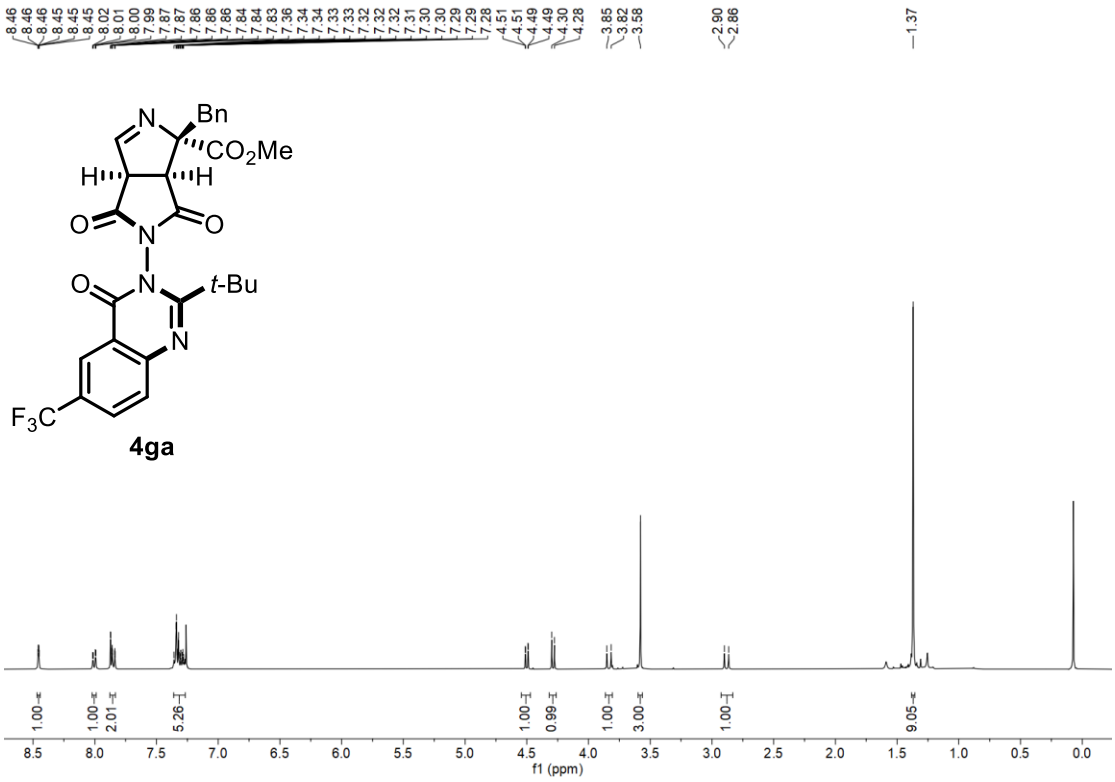
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



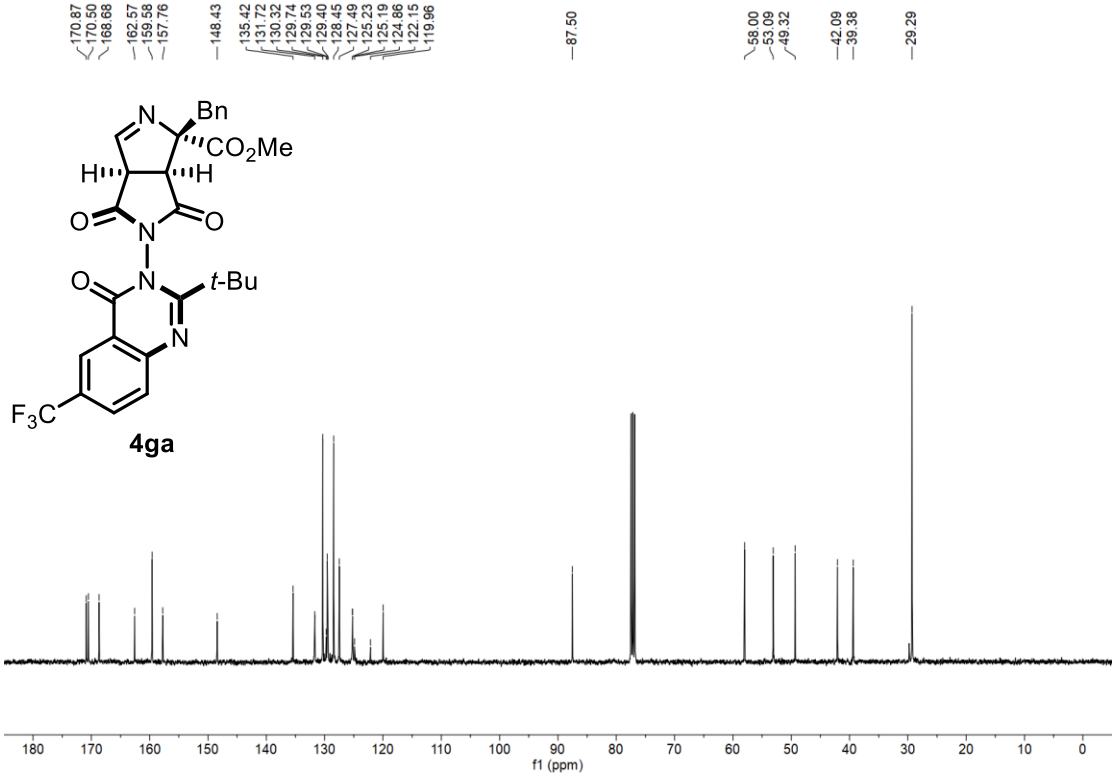

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



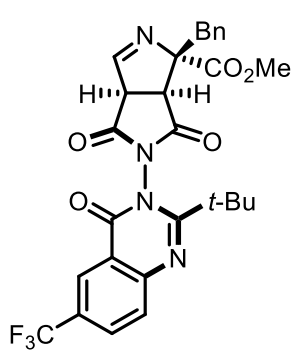
**$^{1}$H NMR** (400 MHz, $CDCl_3$)




**$^{13}$C NMR** (101 MHz, $CDCl_3$)



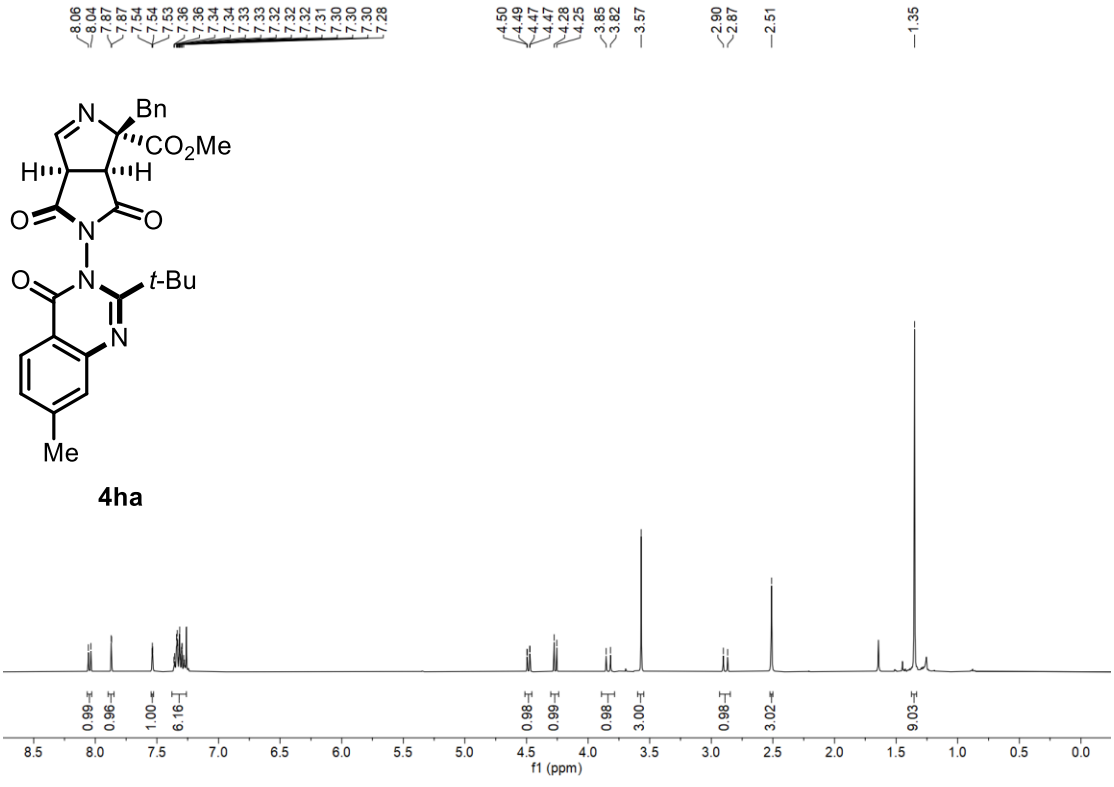
**$^{19}$F NMR** (376 MHz, $CDCl_3$)




**4ga**




**$^{1}$H NMR** (400 MHz, $CDCl_3$)

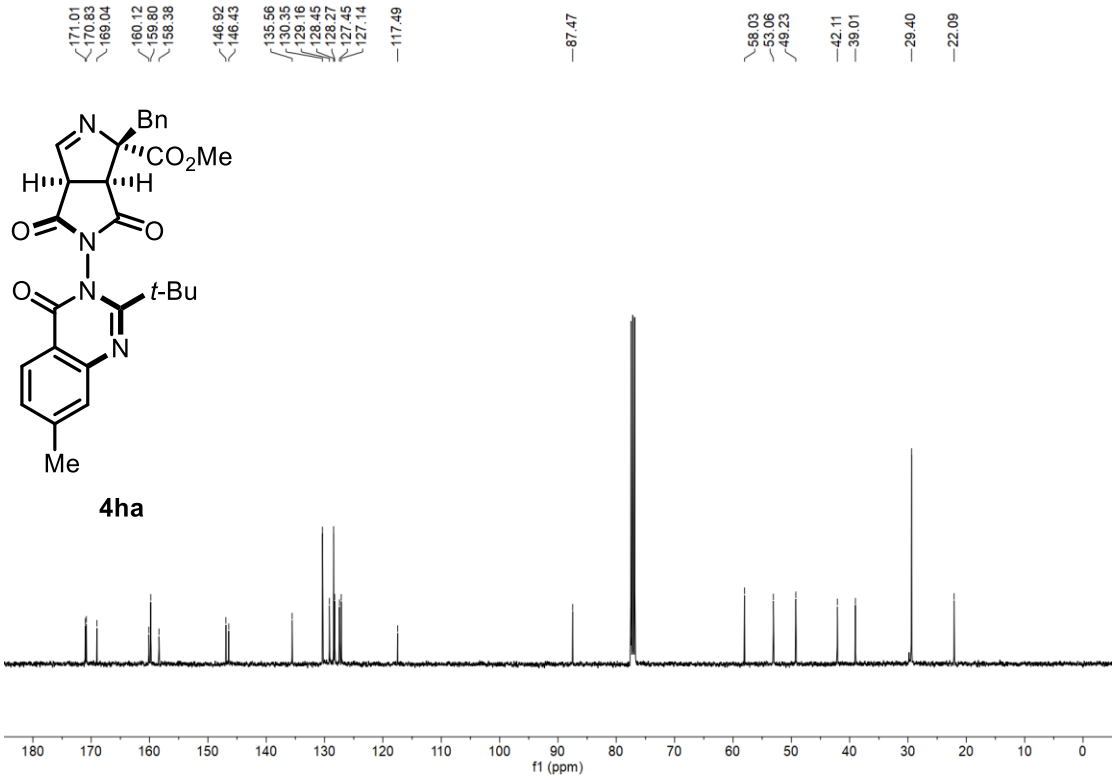




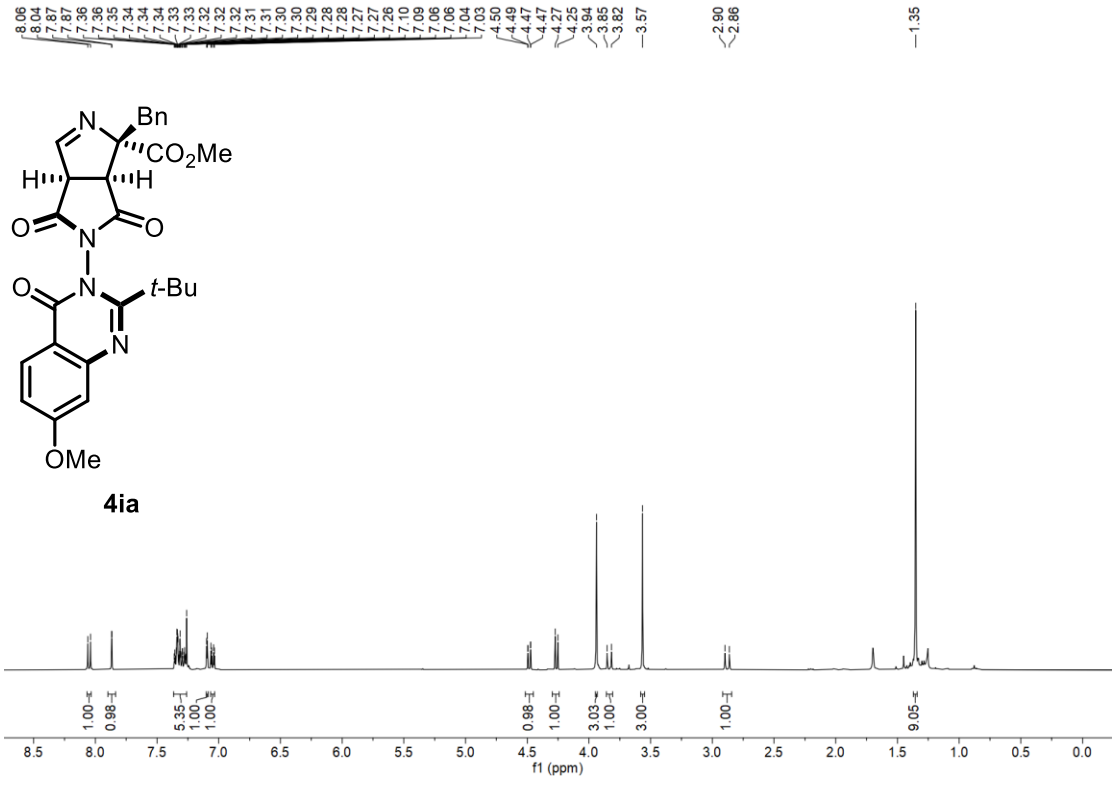


**4ha**

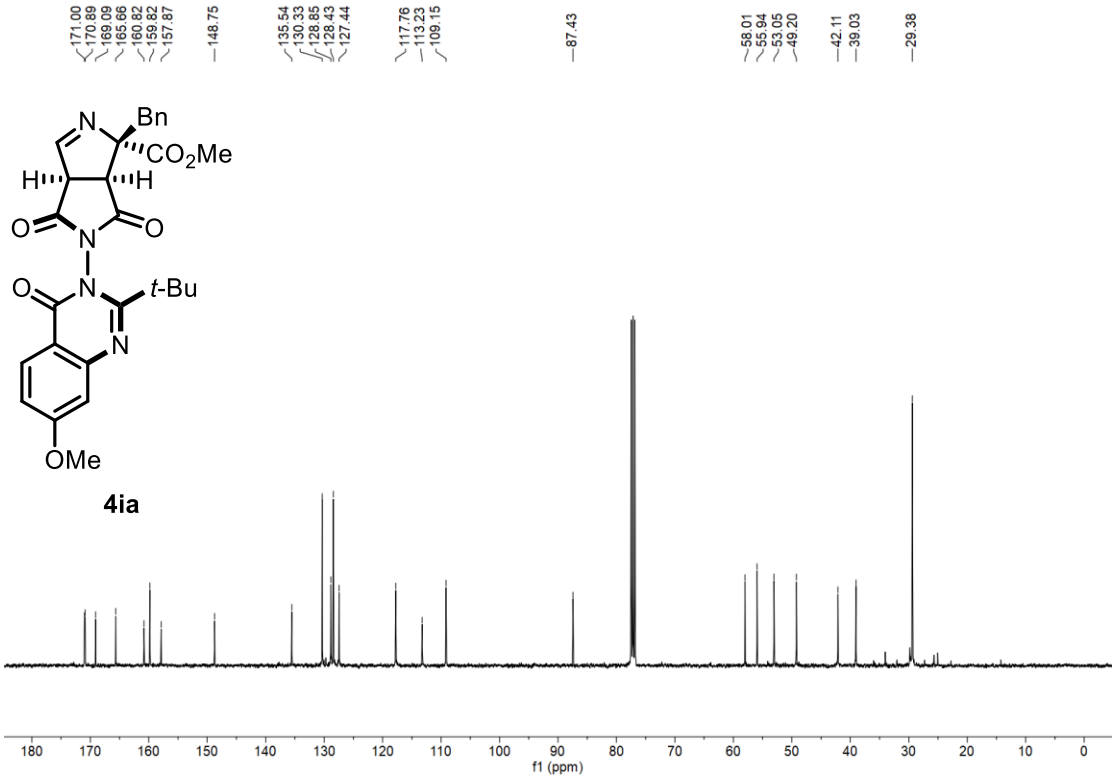
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



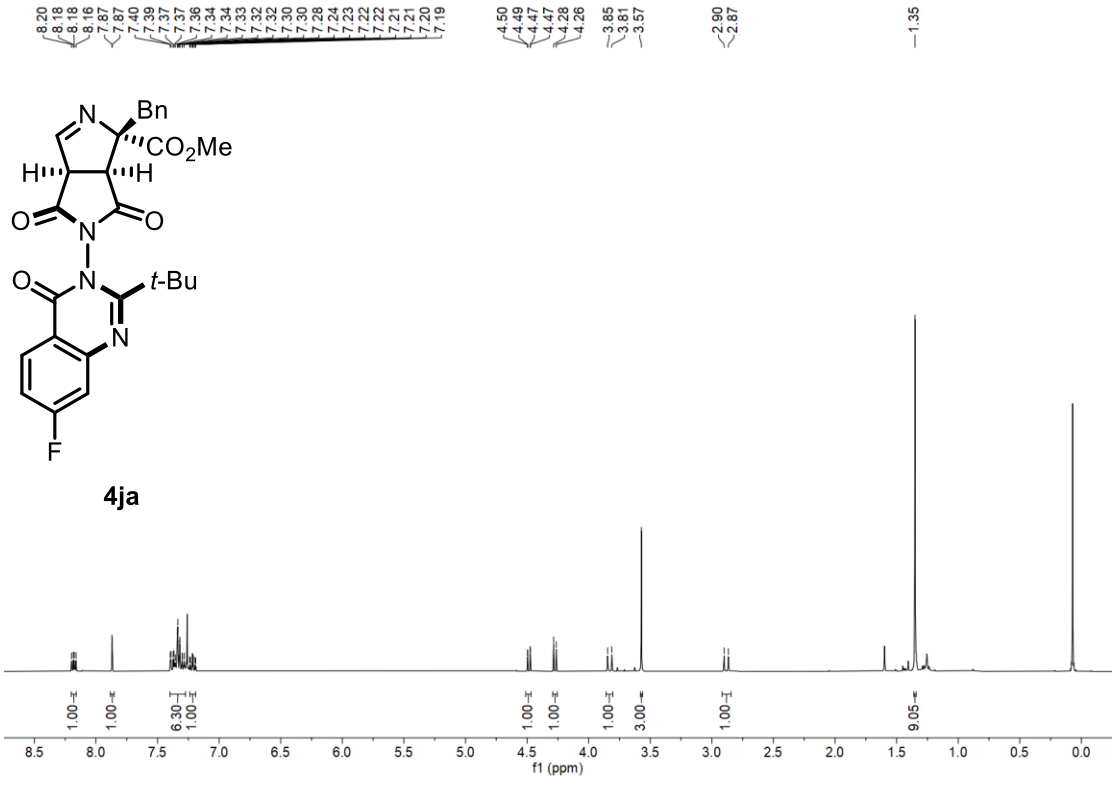

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



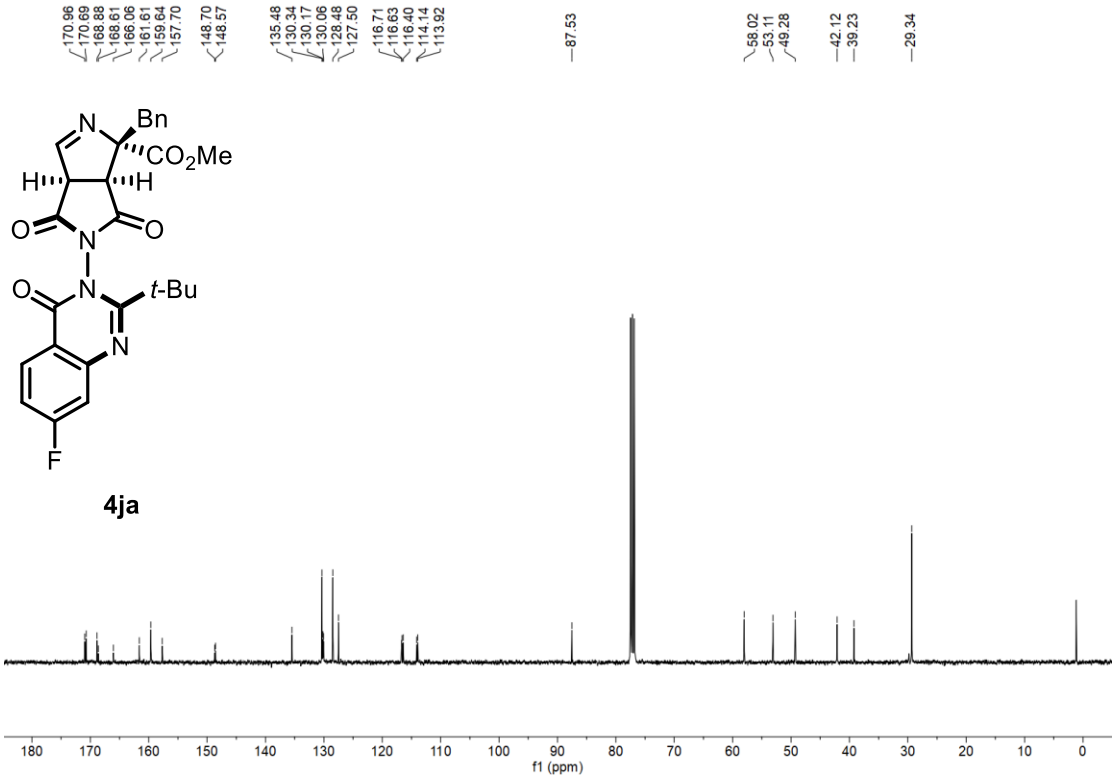
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



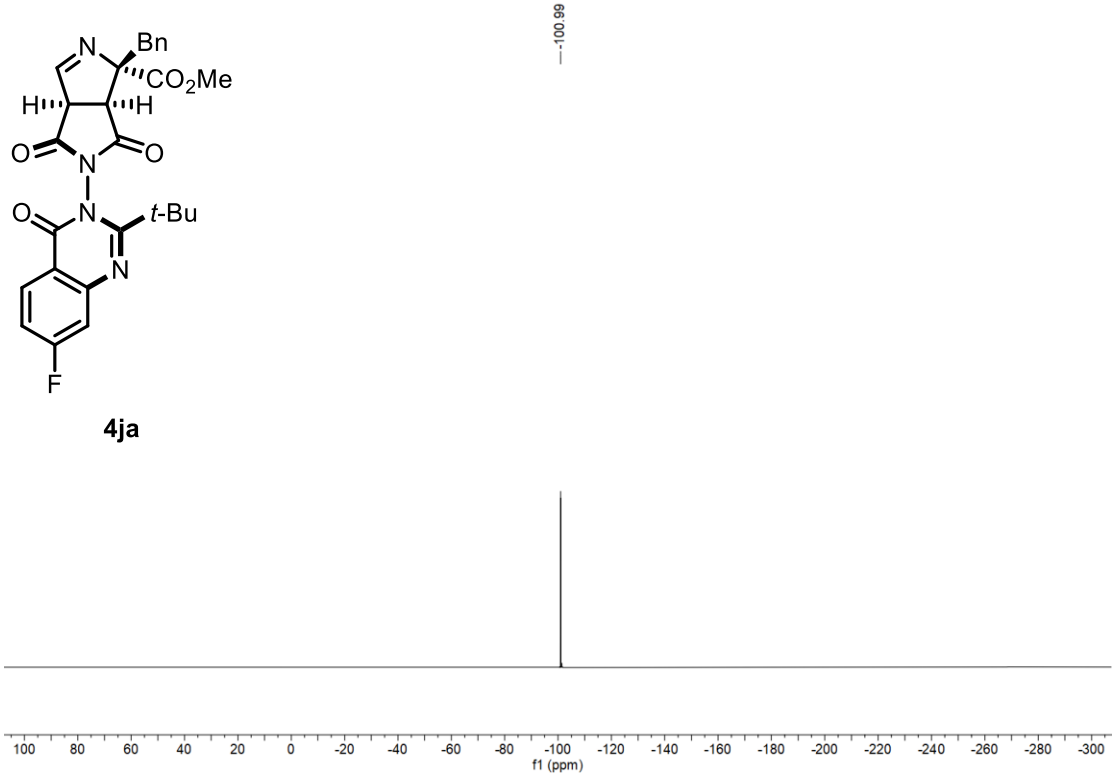

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



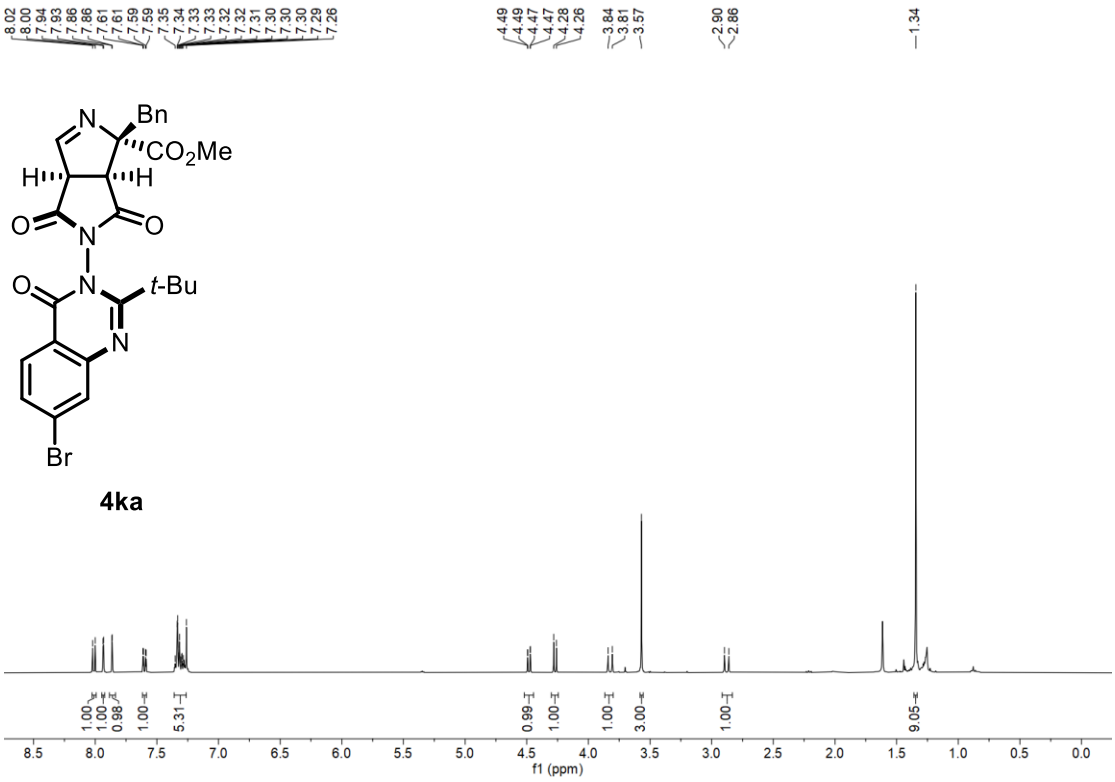
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



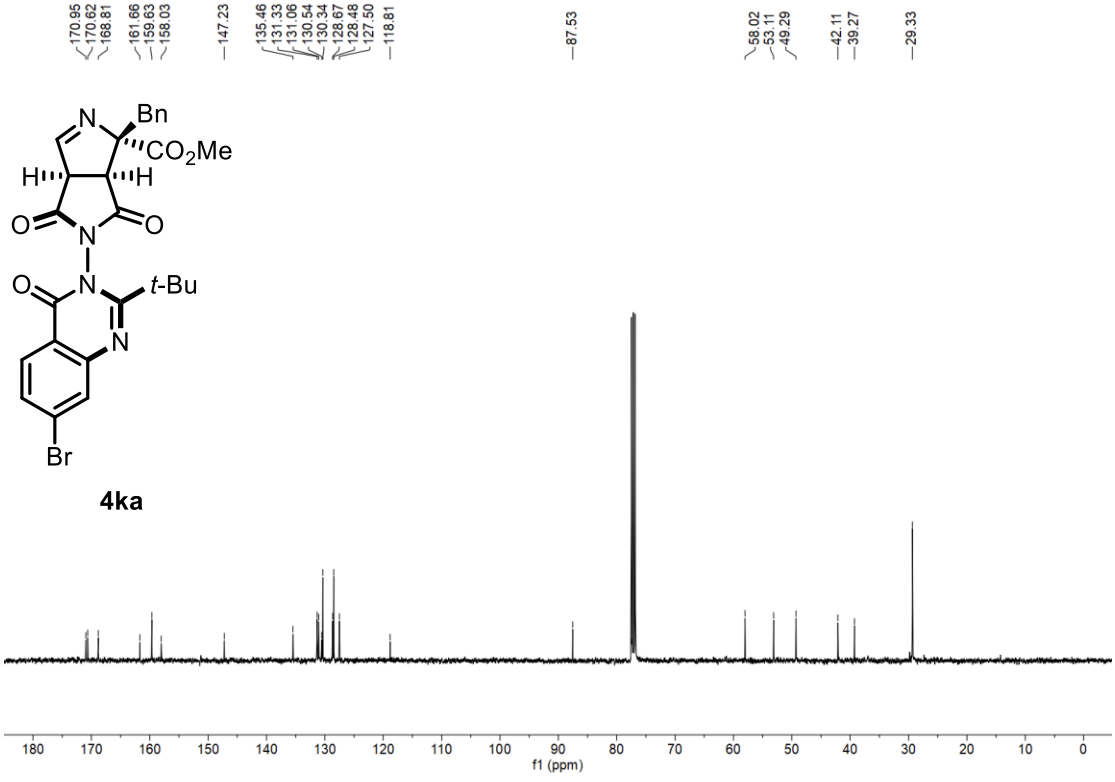

**$^{19}$F NMR** (376 MHz, $CDCl_3$)



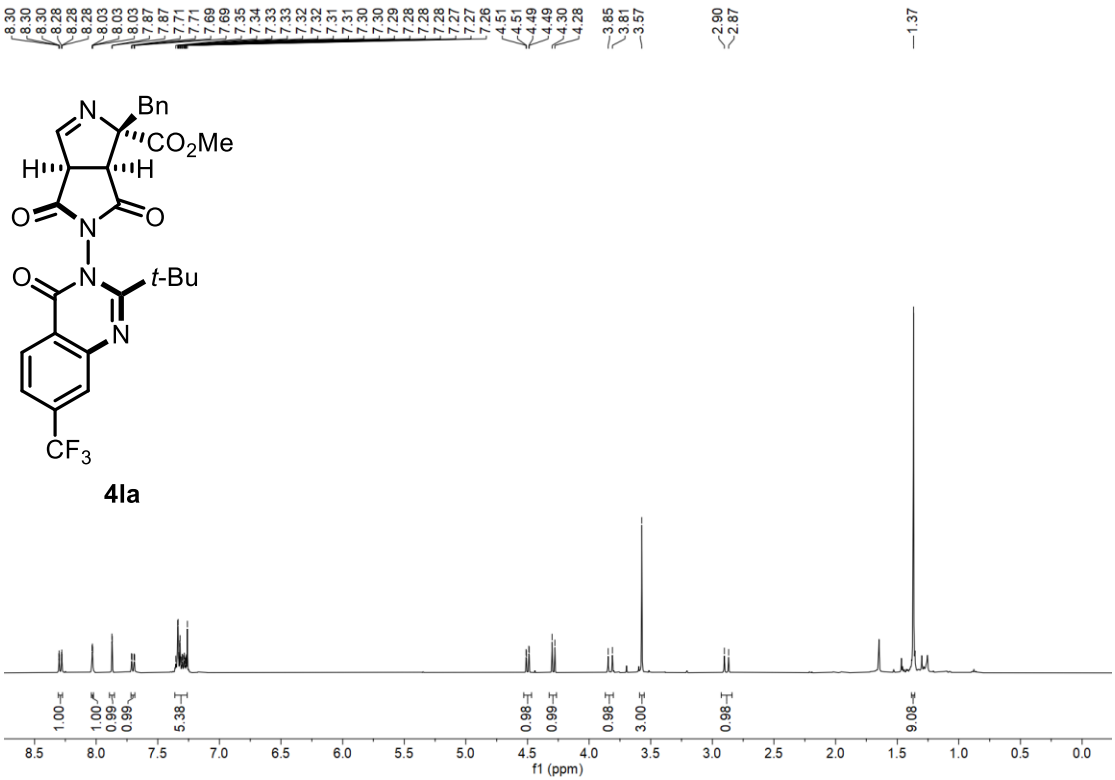
**$^{1}$H NMR** (400 MHz, $CDCl_3$)



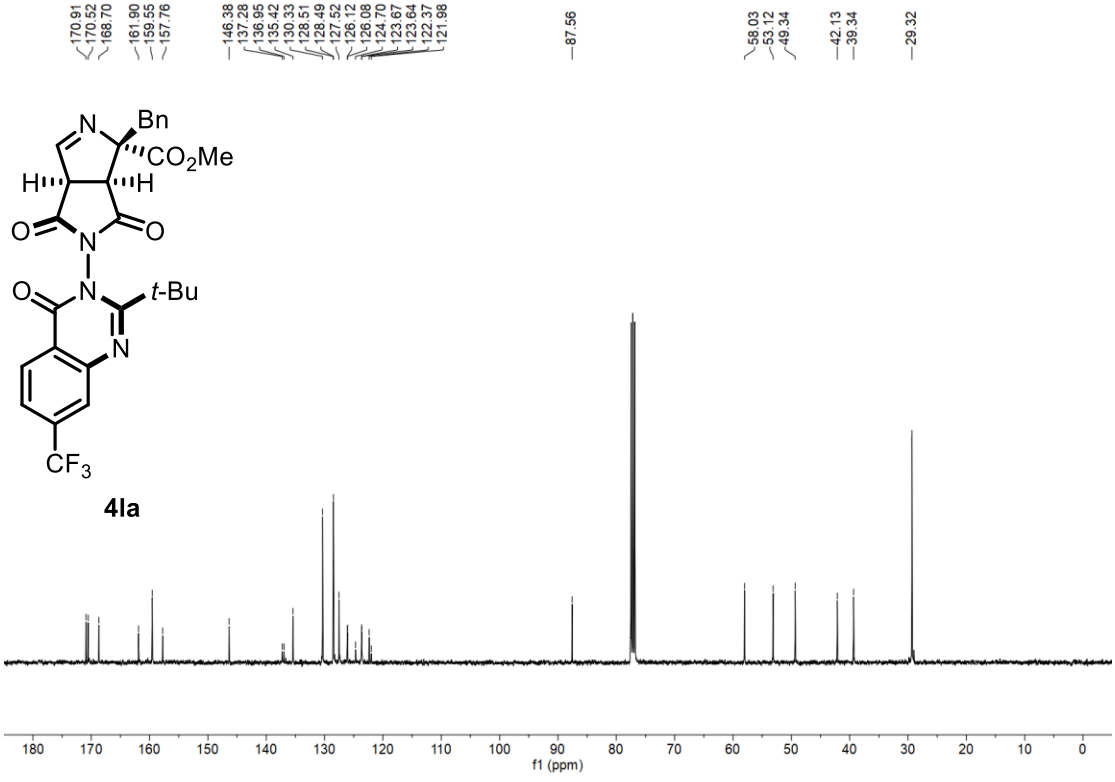

**$^{13}$C NMR** (101 MHz, $CDCl_3$)



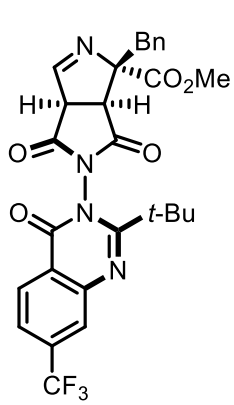
**$^{1}$H NMR** (400 MHz, $CDCl_3$)




**$^{13}$C NMR** (101 MHz, $CDCl_3$)



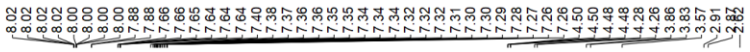
**$^{19}$F NMR** (376 MHz, $CDCl_3$)

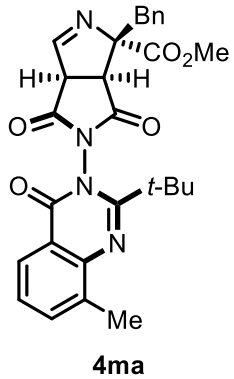


**4la**

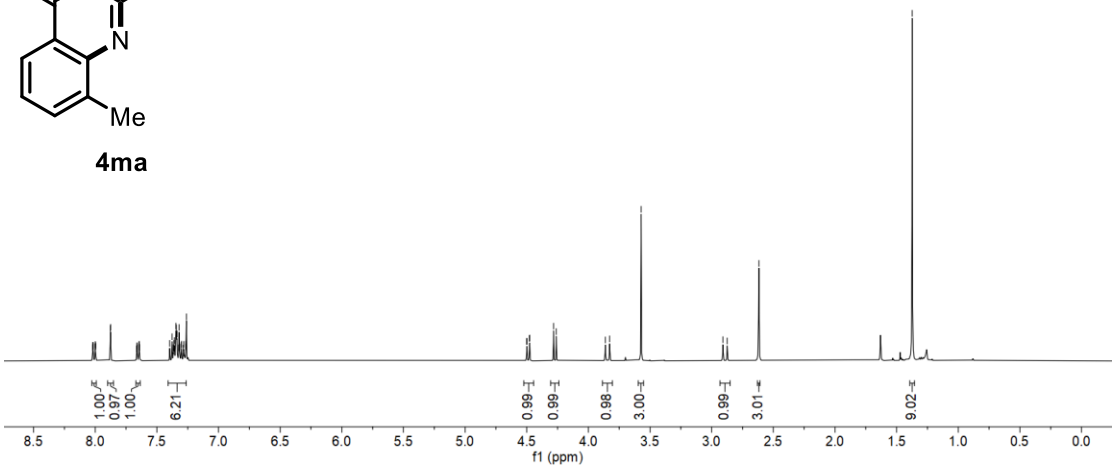



**$^{1}$H NMR** (400 MHz, $CDCl_3$)

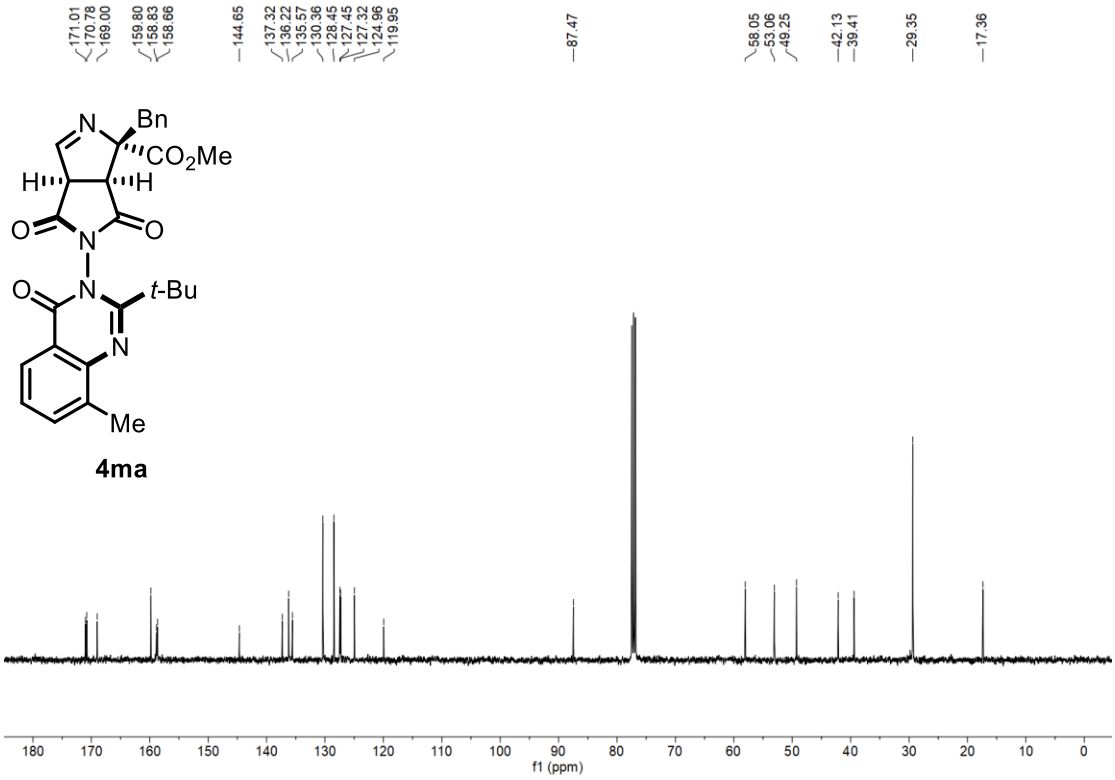


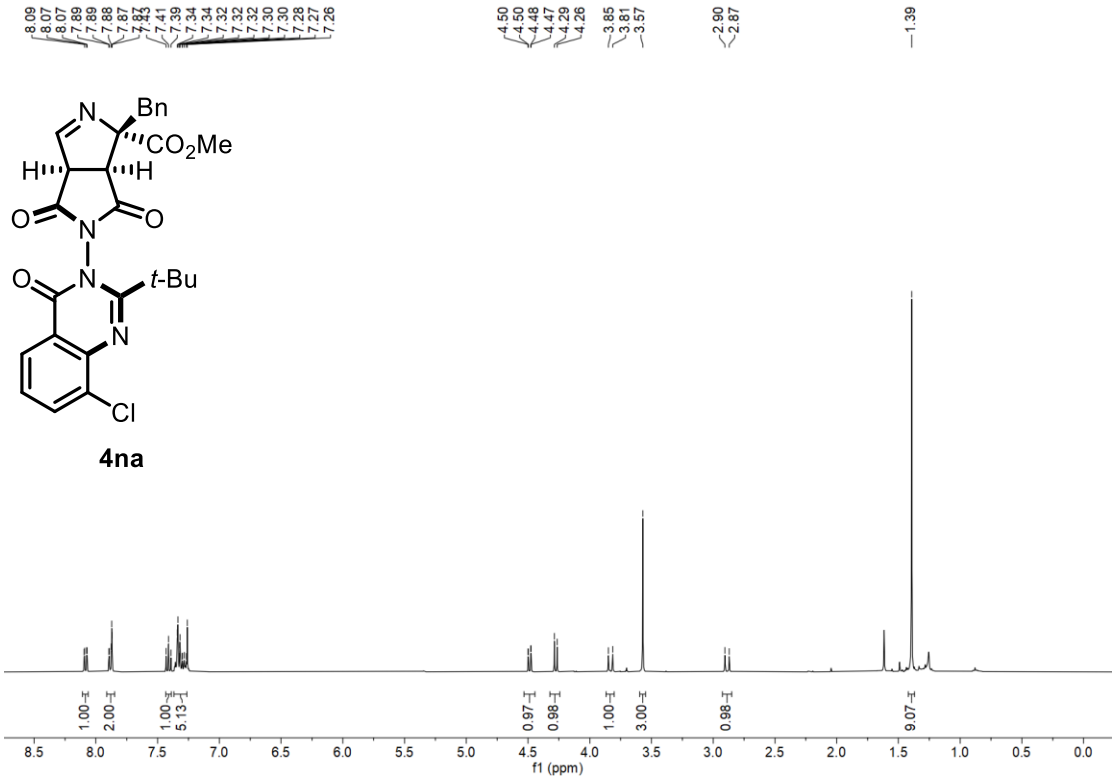
**4ma**



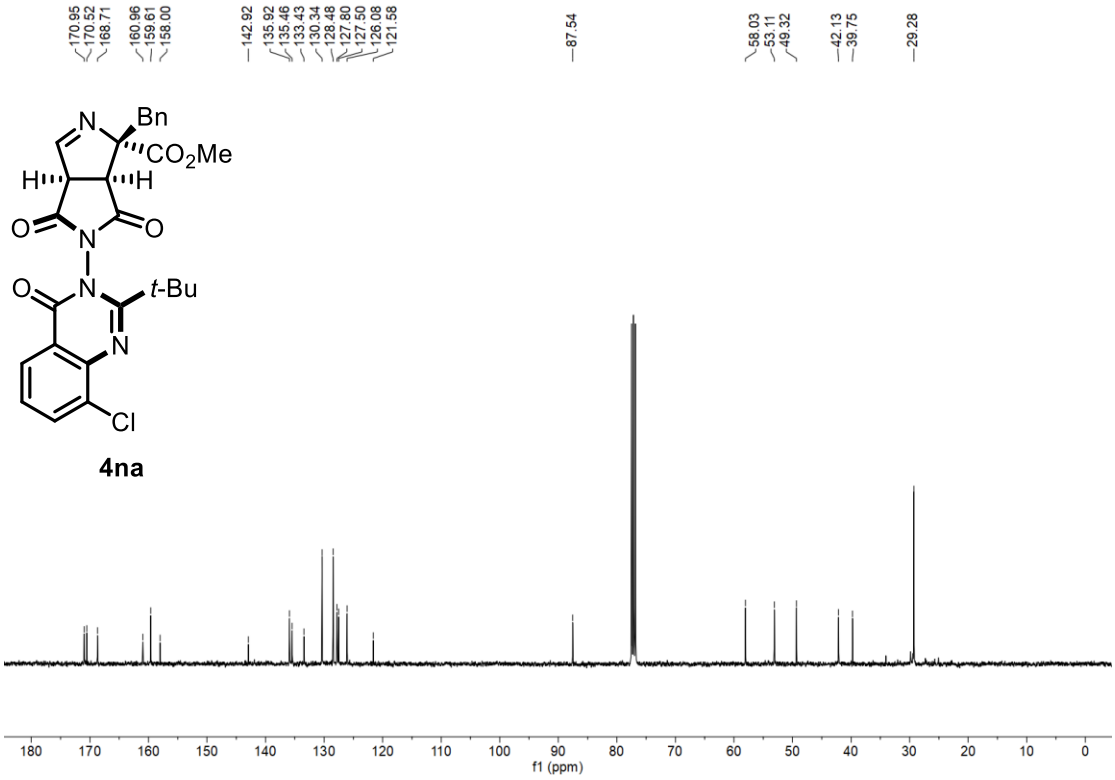
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



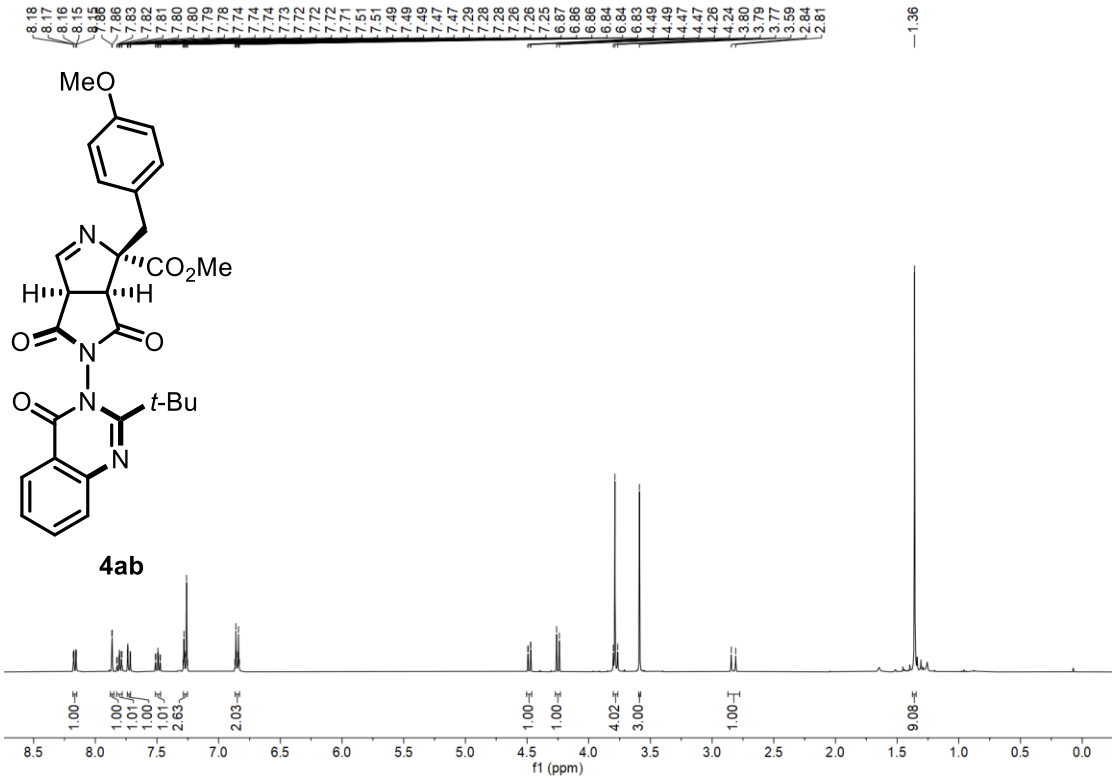

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



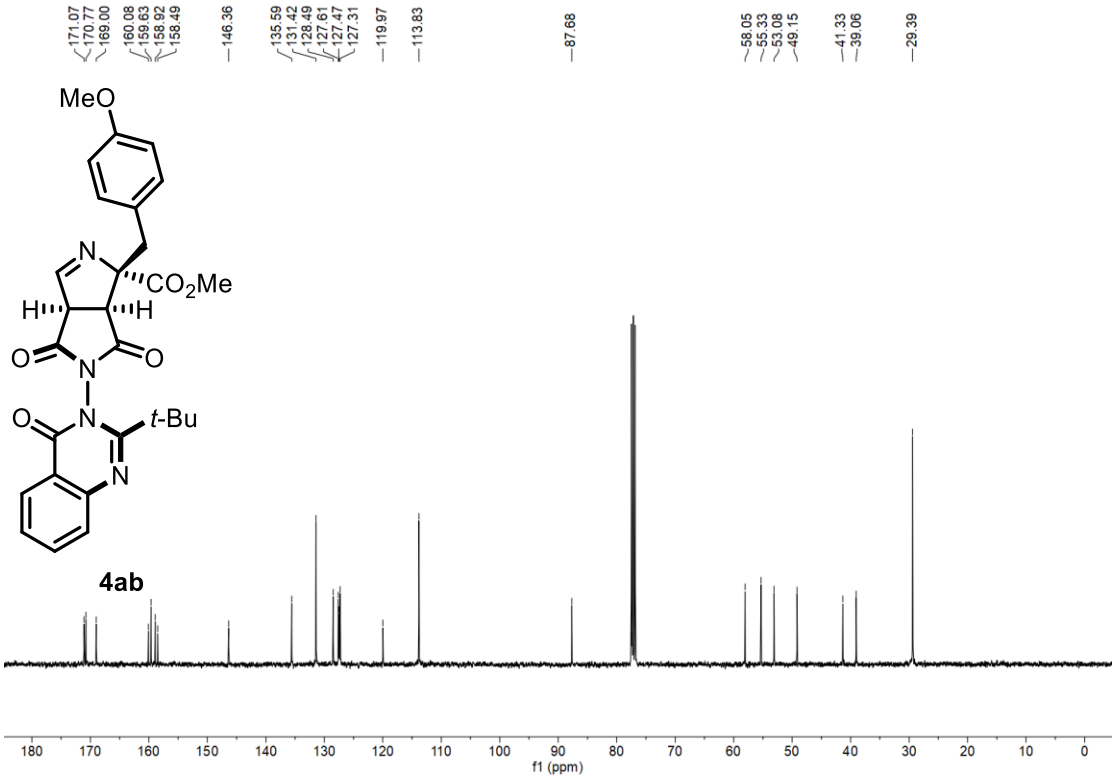
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



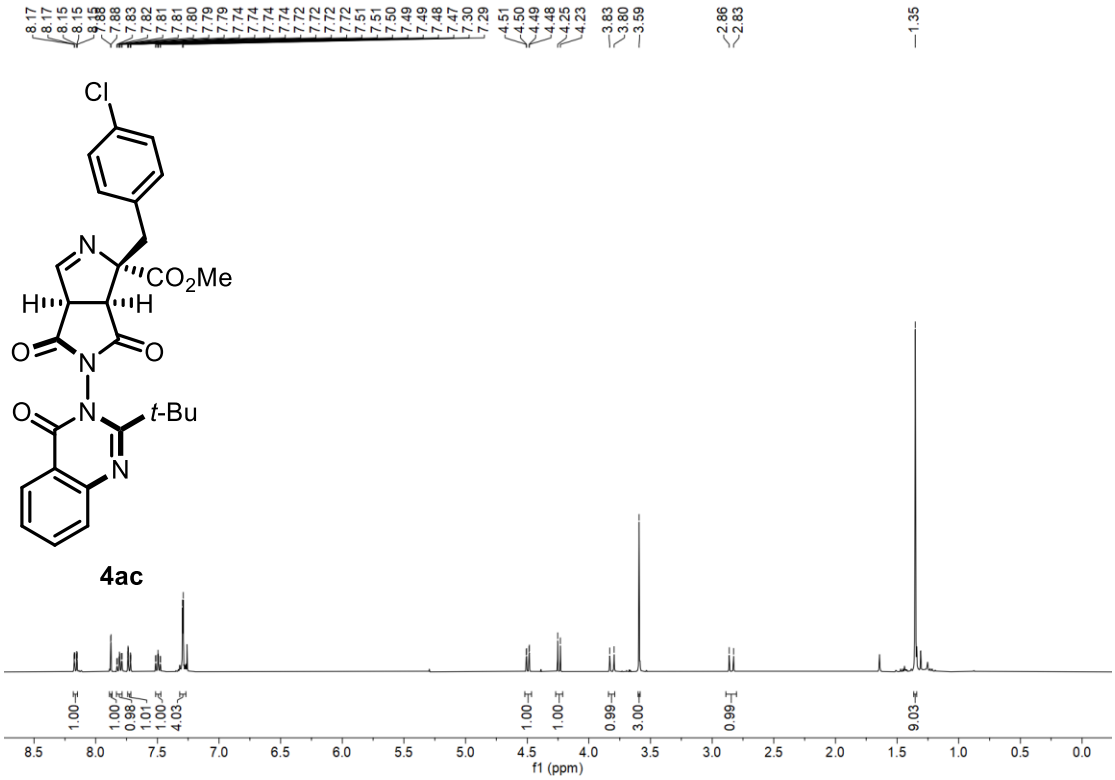

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



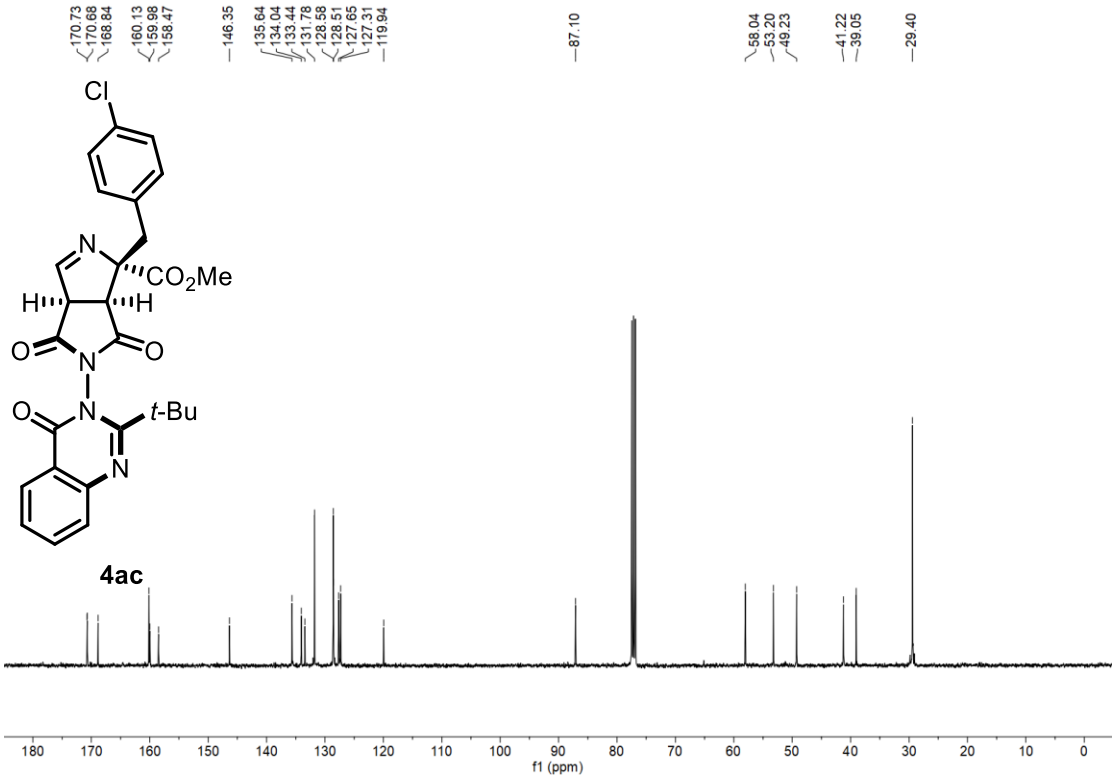
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



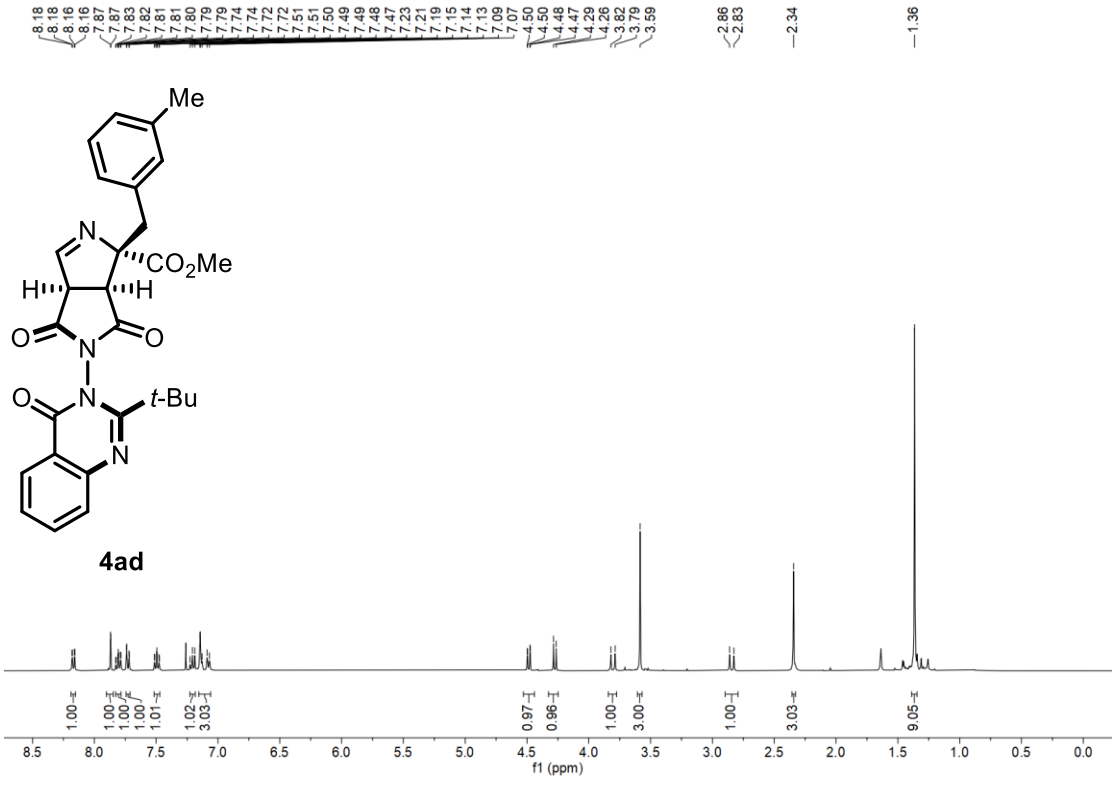

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



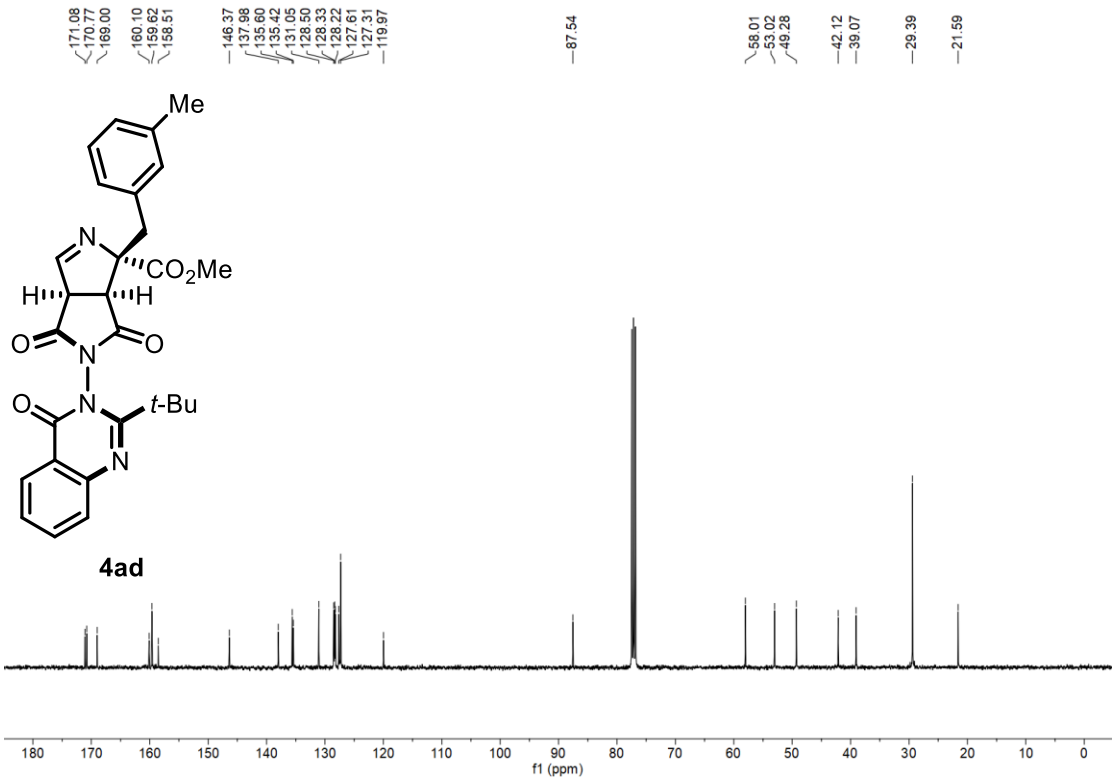
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



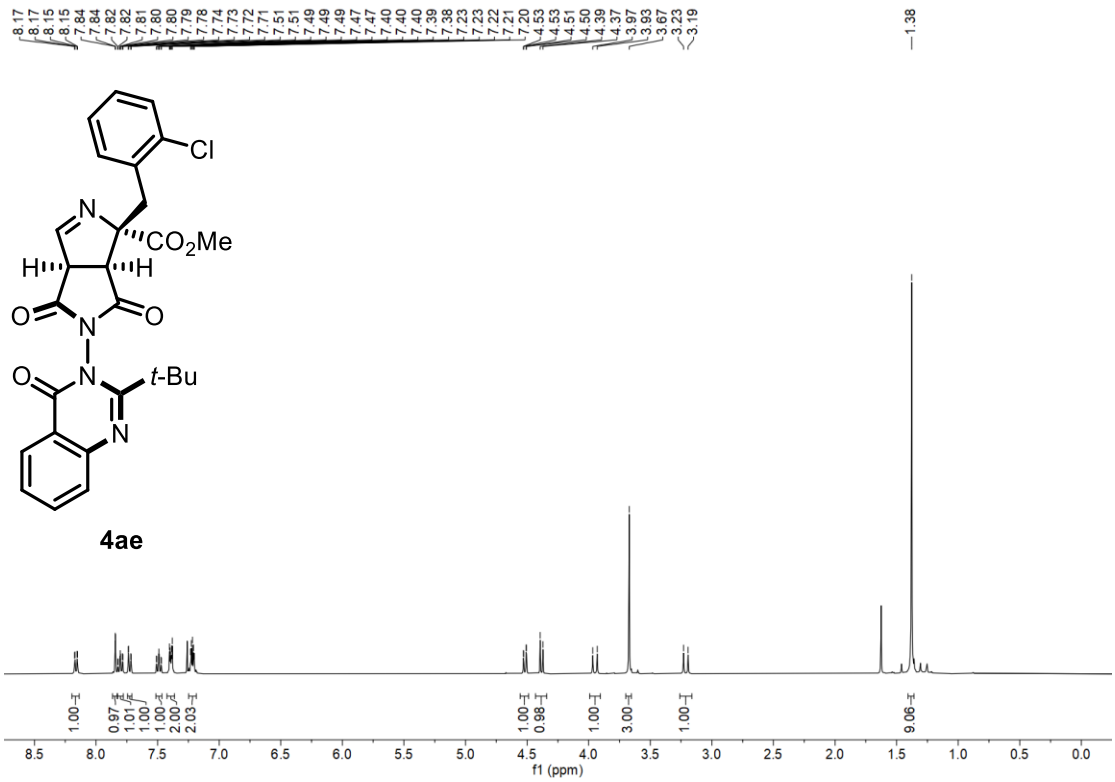

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



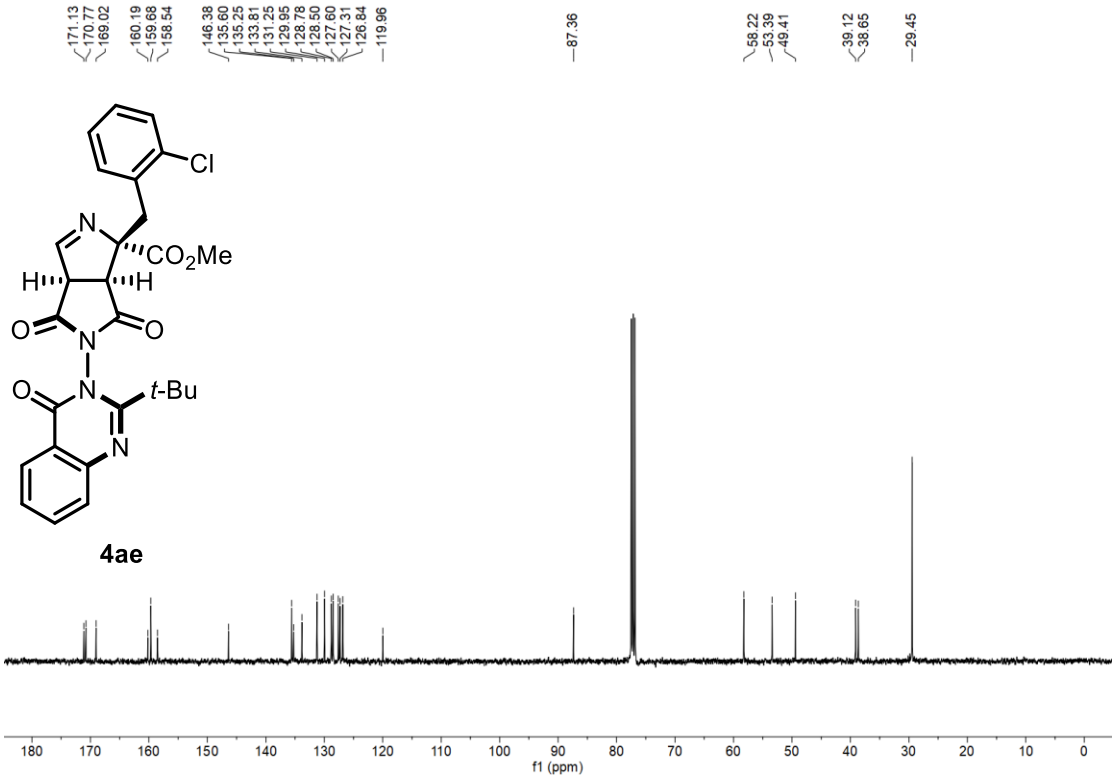
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



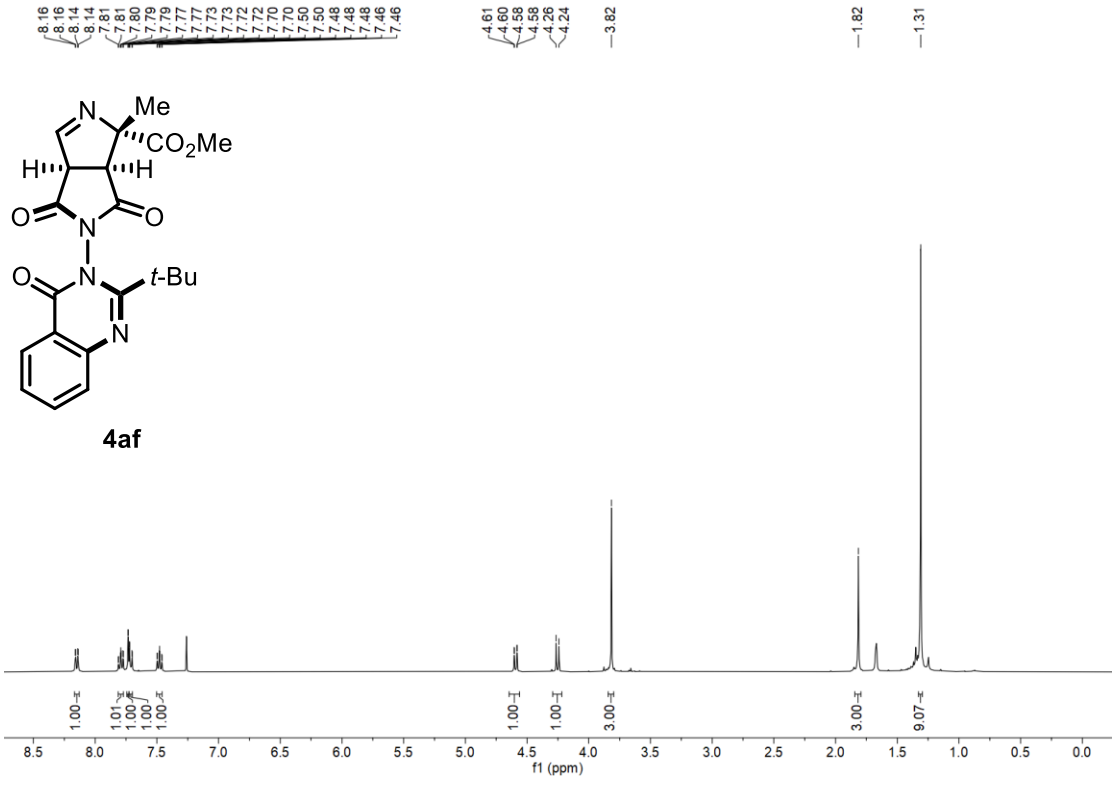

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



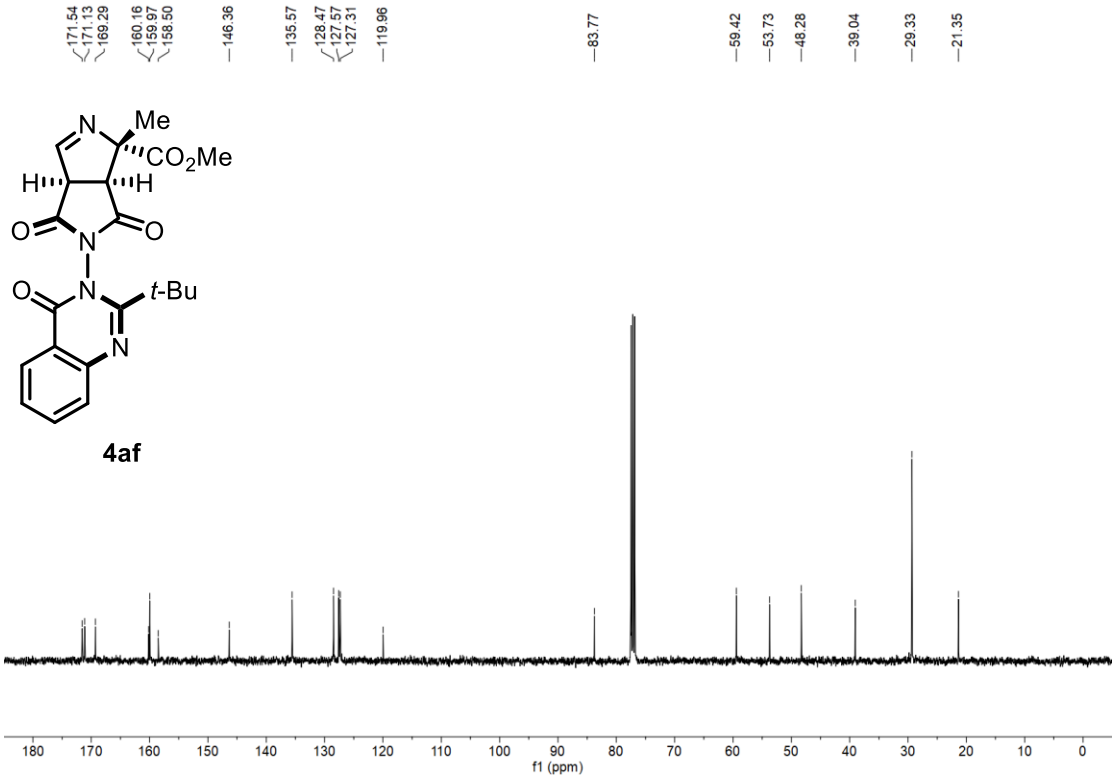
**$^{13}$C NMR** (101 MHz, $CDCl_3$)



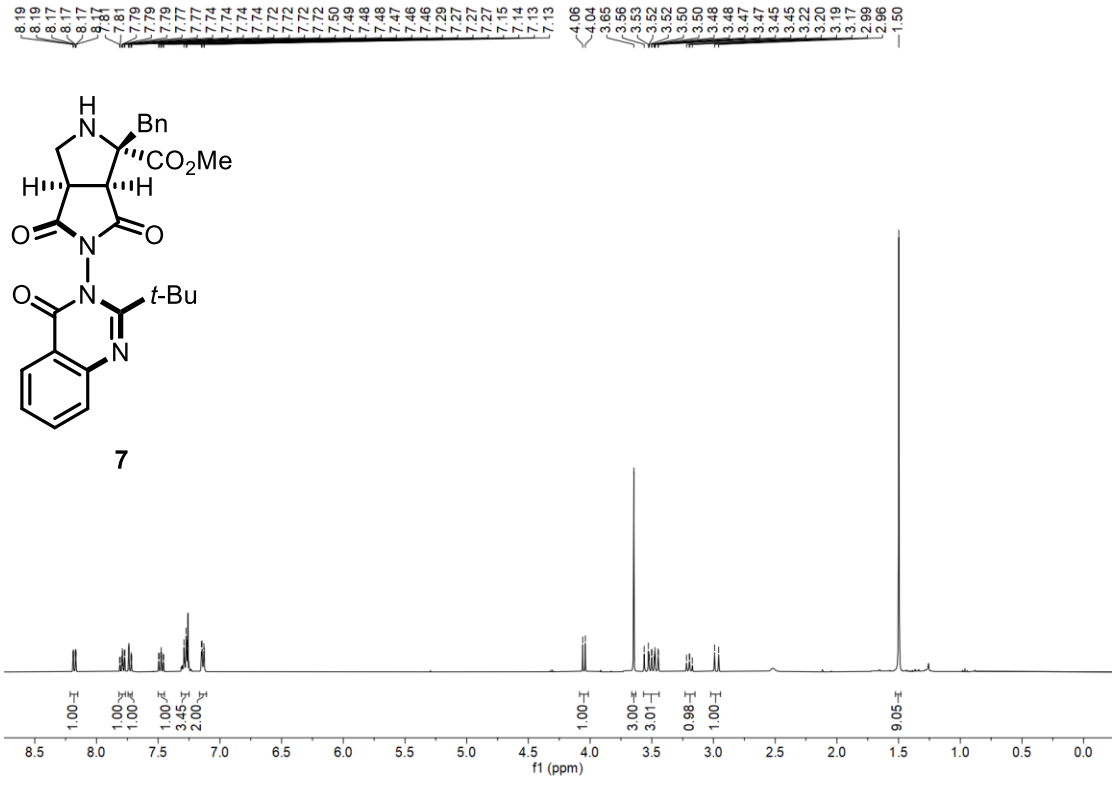

**$^{1}$H NMR** (400 MHz, $CDCl_3$)



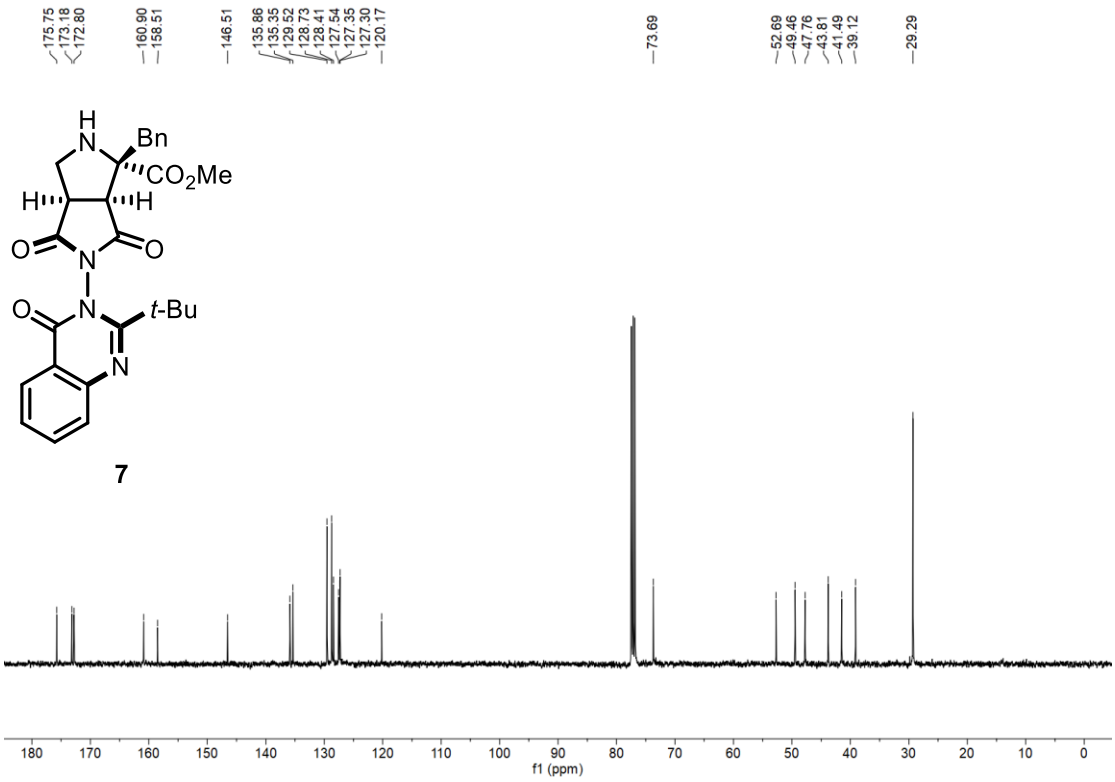
**$^{13}$C NMR** (101 MHz, $CDCl_3$)




**$^{1}$H NMR** (400 MHz, $CDCl_3$)

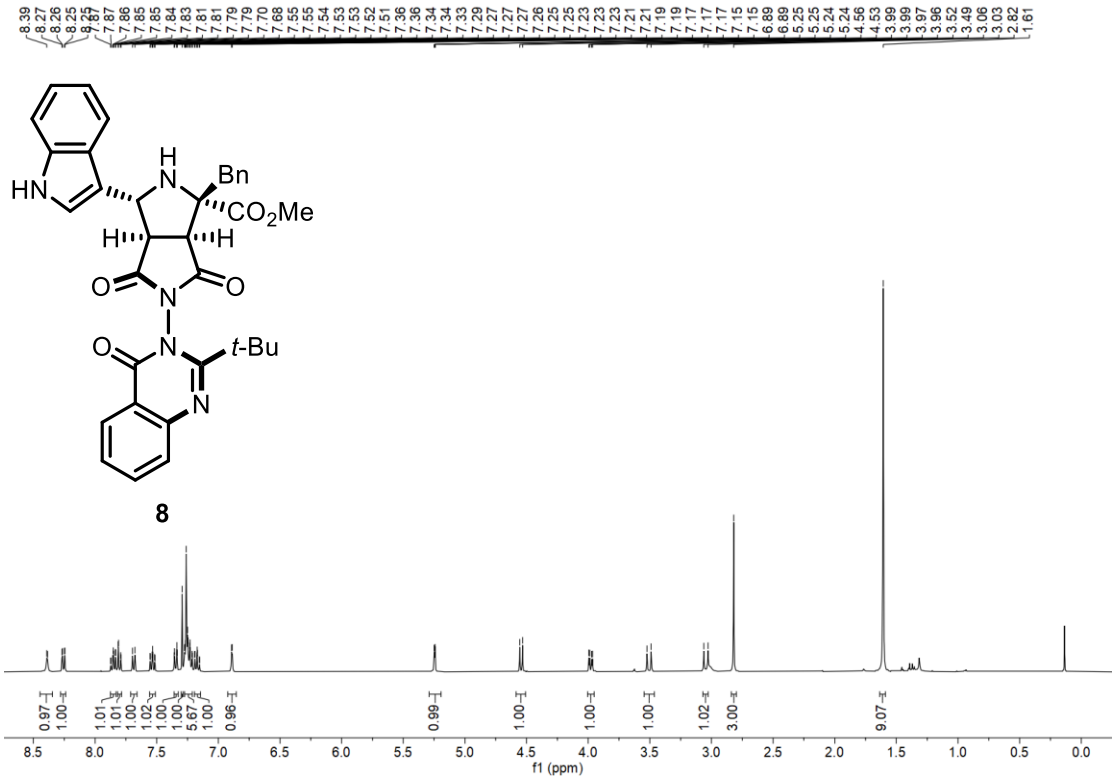


**$^{13}$C NMR** (101 MHz, $CDCl_3$)



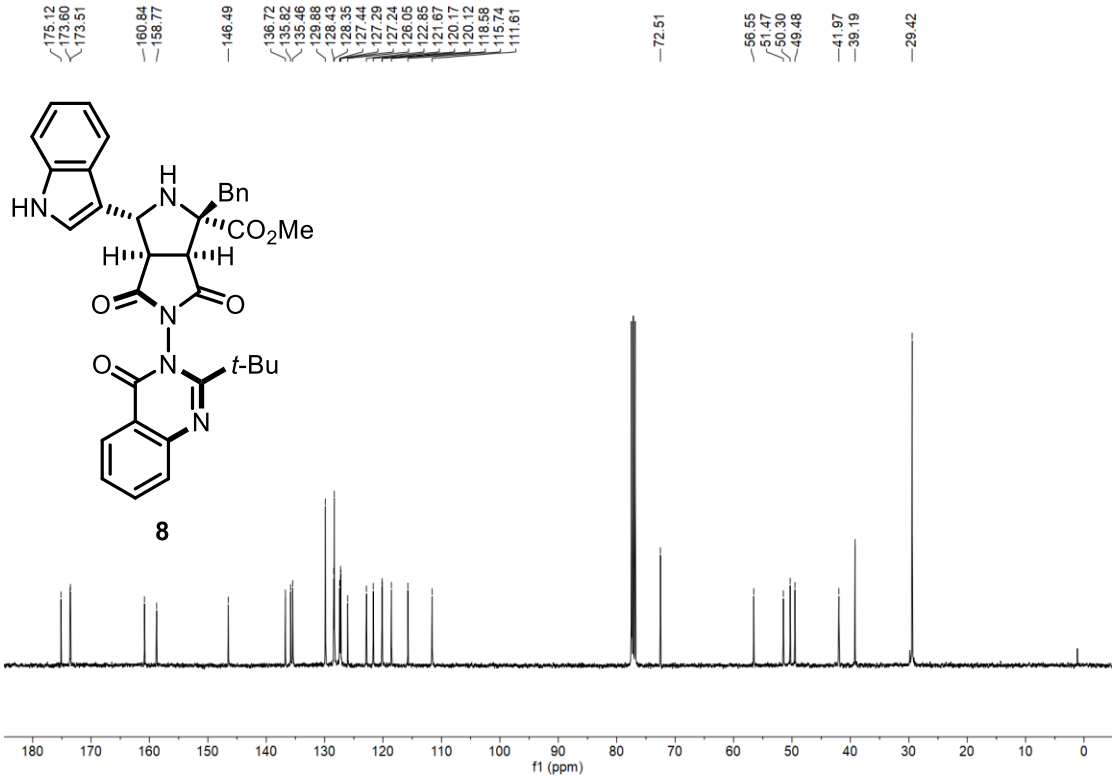

**7**

**$^{1}$H NMR** (400 MHz, $CDCl_3$)

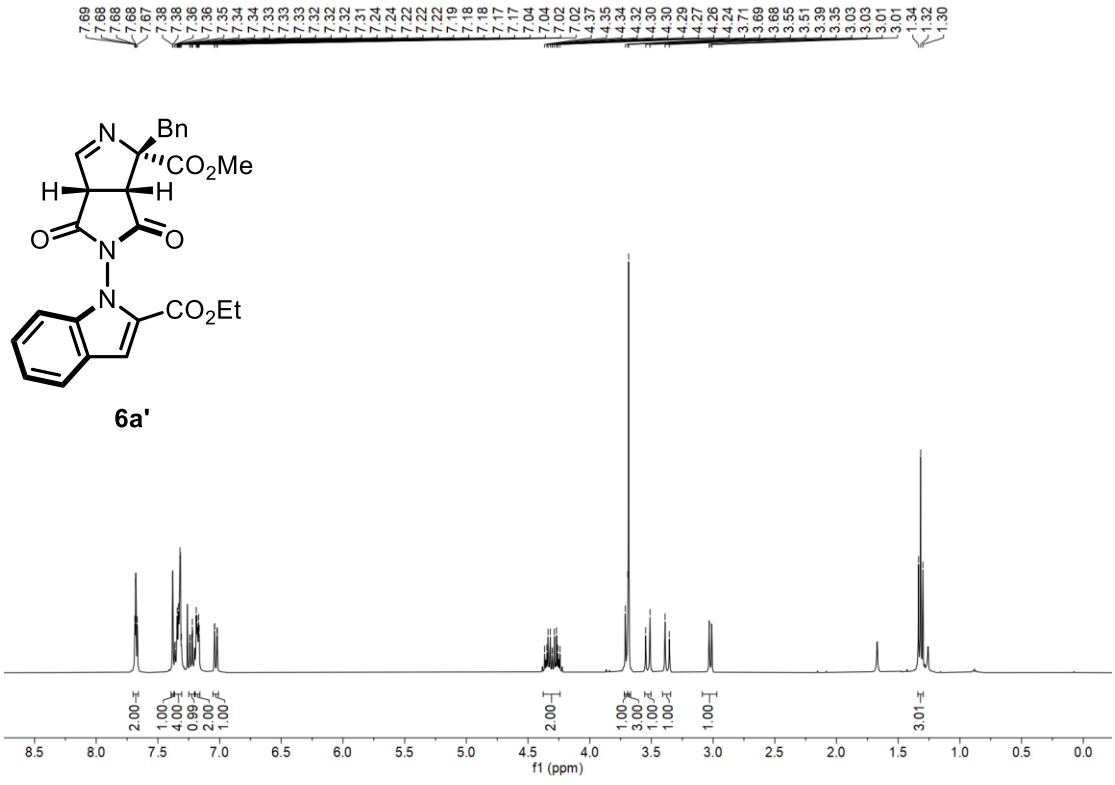



**8**

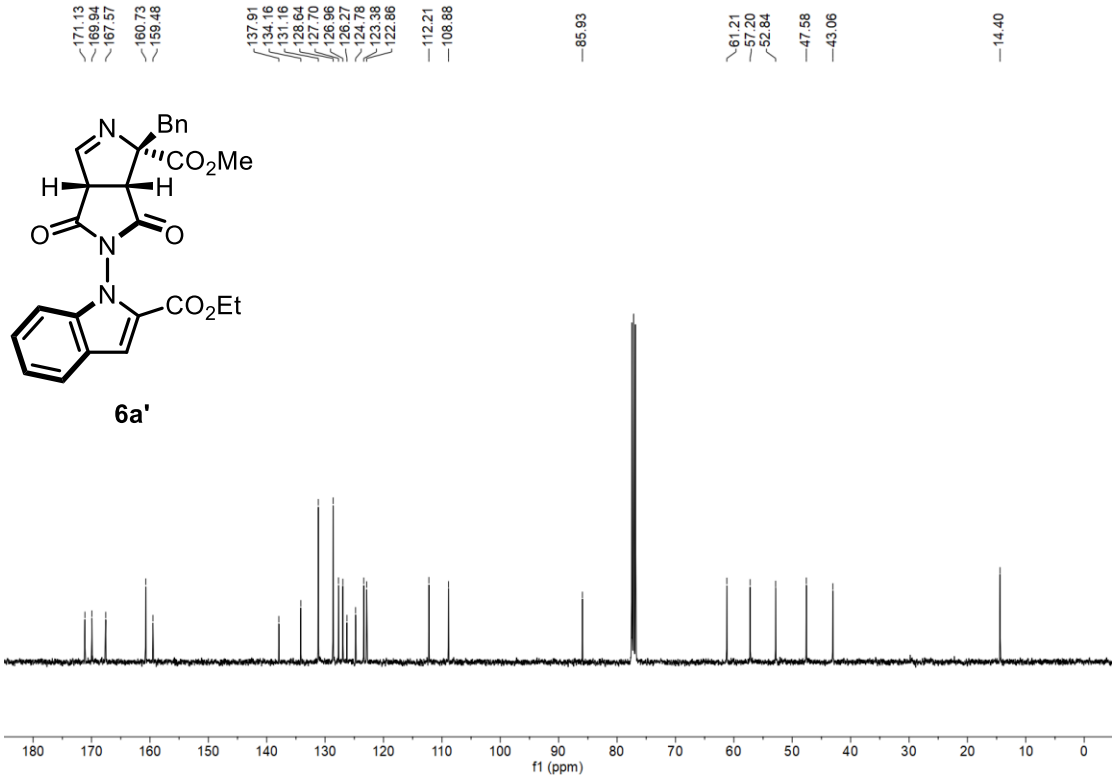
**$^{13}$C NMR** (101 MHz, $CDCl_3$)




**$^{1}$H NMR** (400 MHz, $CDCl_3$)



**$^{13}$C NMR** (101 MHz, $CDCl_3$)




**6a'**