SUPPORTING INFORMATION

Diastereoselective aldol-type interception of phenolic oxonium ylide for the direct assembly of 2,2-disubstituted dihydrobenzofurans

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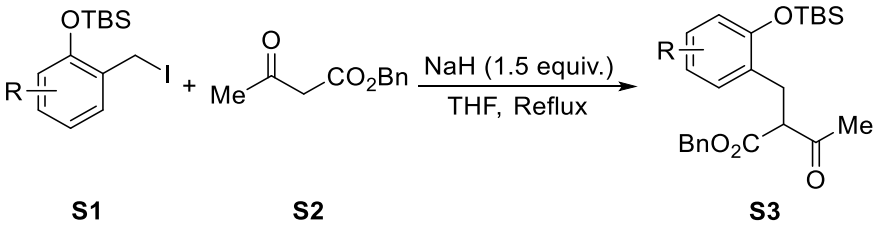
General Information

All reactions were carried out in oven-dried glassware. Solvents were purified by following the standard methods. Flash column chromatography was performed using silica gel (300-400 mesh). Analytical thin-layer chromatography was performed using glass plates pre-coated with 200-300 mesh silica gel impregnated with a fluorescent indicator (254 nm). ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded in $CDCl_3$ on 400 MHz and 500 MHz spectrometer; chemical shifts were reported in ppm with the solvent signal as reference, and coupling constants (*J*) were given in Hertz. The peak information was described as: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite. High-resolution mass spectra (HRMS) were recorded on a commercial apparatus (ESI Source).

General Procedure for the Synthesis of Diazo Compounds 1.[1]

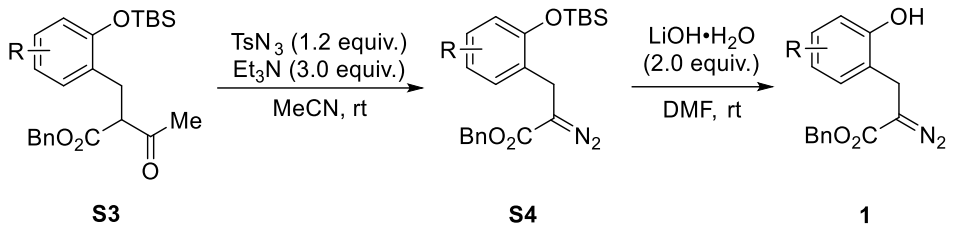
Diazo compounds **1a**, **1b**, **1c**, **1d**, **1g** and **1h** were synthesized according to previously published procedure and had physical and spectral properties identical to those earlier reported.[1] Isatines **2a-2u** and Methyl (*E*)-2-oxo-4-phenylbut-3-enoate **2v** were synthesized according to previously published procedure and had physical and spectral properties identical to those earlier reported.[2]



S1 **S2** **S3**

Synthesis of S3: To a 100-mL oven-dried vial containing a magnetic stirring bar and sodium hydride (60% dispersion in mineral oil, 1.2 g, 30 mmol, 1.5 equiv.) in anhydrous THF (30 mL), was added **S2** (7.7 g, 40 mmol, 2.0 equiv.) dropwise at 0 °C. When the mixture turned clear, a solution of the compound **S1** (20 mmol, 1.0 equiv.) in anhydrous THF (10 mL) was added dropwise at room temperature, and the reaction mixture was refluxed for 4 h. When the reaction mixture was completed (monitored by TLC), saturated NH_4Cl aqueous solution (50 mL) was added to quench the reaction, and the aqueous layer was extracted with EtOAc (50 mL × 3). The combined organic layer was

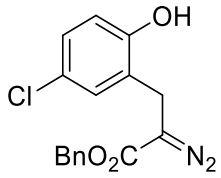
washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated in *vacuo* after filtration. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20 : 1) to give pure product in good to high yield. Pale yellow oil.



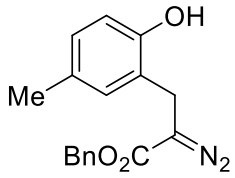
S3 **S4** **1**

Synthesis of 1: To a 50-mL oven-dried vial containing a magnetic stirring bar, compound **S3** (15 mmol, 1.0 equiv.) and p-Toluenesulfonyl azide (75% in EtOAc, 4.6 g, 18 mmol, 1.2 equiv.) in MeCN (20 mL), was added Et_3N (4.5 g, 45 mmol, 3.0 equiv.) dropwise at room temperature, and the reaction was stirred overnight under these conditions after addtion. When the reaction mixture was completed (monitored by TLC), saturated NH_4Cl aqueous solution (50 mL) was added to the reaction, and the aqueous layer was extracted with EtOAc (50 mL × 3). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated in *vacuo* after filtration. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20 : 1) to give the pure product **S4** as a yellow oil. To a solution of compound **S4** (9.0 mmol, 1.0 equiv.) in DMF (20 mL), lithium hydroxide hydrate (0.76 g, 18 mmol, 2.0 equiv.) was added in one portion at room temperature, and the reaction mixture was stirred for 0.5 h under these conditions after addition. When the reaction was completed (monitored by TLC), EtOAc (40 mL) was added, and the organic layer was washed with saturated NH_4Cl aqueous solution (40 mL × 3). The combined aqueous layer was extracted with EtOAc (50 mL × 3), the combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated in *vacuo* after filtration. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5 : 1) to give the pure products **1** in good to high yields. Diazo compounds **1a**, **1b**, **1c**, **1d**, **1g**, and **1h** had physical and spectral properties

identical to those earlier reported.[1]



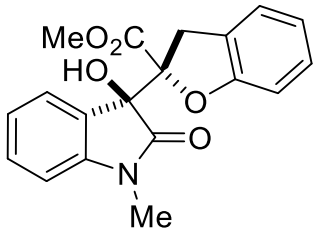
1e: Yellow solid, mp = 107 - 108 ℃. ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.74 (d, J = 7.8 Hz, 1H), 7.38 – 7.31 (m, 5H), 7.11 (dd, J = 8.5, 2.2 Hz, 1H), 7.05 (d, J = 2.5 Hz, 1H), 6.83 (d, J = 7.3 Hz, 1H), 5.23 (s, 2H), 3.53 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 153.6, 135.4, 130.0, 129.0, 128.8, 128.7, 128.4, 126.0, 125.2, 119.0, 67.6, 25.8; HRMS (TOF MS ESI$^+$) calculated for $C_{16}H_{13}ClN_2O_3Na$ $[M+Na]^+$: 339.0507, found 339.0500.



1f: Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.25 (d, J = 1.6 Hz, 1H), 7.23 (d, J = 4.0 Hz, 3H), 7.22 (d, J = 3.1 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 6.78 (d, J = 1.7 Hz, 1H), 6.71 – 6.70 (m, 1H), 5.12 (s, 2H), 3.44 (s, 2H), 2.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 152.4, 135.6, 131.0, 130.0, 129.7, 128.7, 128.6, 128.4, 124.0, 117.4, 67.3, 25.8, 20.5; HRMS (TOF MS ESI$^+$) calculated for $C_{17}H_{16}N_2O_3Na$ $[M+Na]^+$: 319.1053, found 319.1050.

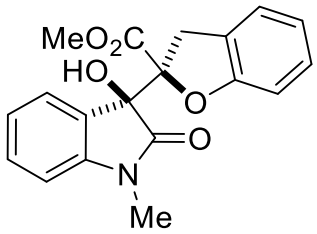
General Procedure for the Cascade Reaction

To a 10-mL oven-dried vial containing a magnetic stirring bar, isatine **2** (0.1 mmol, 1.0 equiv.), $Rh_2(OAc)_4$ (0.4 mg, 1.0 mol %) and 4Å MS (50 mg) in anhydrous toluene (1.0 mL), was added a solution of diazo compound **1** (0.15 mmol, 1.5 equiv.) in 1.0 mL anhydrous toluene *via* a syringe pump under stirring over 10 min at 40 ℃, and the reaction mixture was stirred for additional 0.5 h under these conditions after addition. When the reaction was completed (monitored by TLC), the reaction mixture was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 8 : 1 to 3 : 1) to give the pure products **3** or **4** in good to high yields and excellent diastereoselectivity.



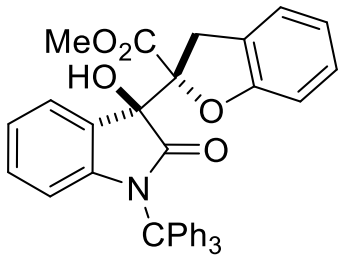
***anti*-3a**

Methyl (*R)-2-((*S**)-3-hydroxy-1-methyl-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (*anti*-3a).** Yellow solid, mp = 144 - 145 ℃. 26.7 mg, 79% yield. ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.35 – 7.32 (t, *J* = 7.9 Hz, 2H), 7.12 – 7.06 (m, 2H), 7.01 – 6.98 (t, *J* = 7.5 Hz, 1H), 6.87 – 6.83 (comp, 3H), 4.65 (s, 1H), 3.81 (s, 3H), 3.79 – 3.76 (d, *J* = 16.2 Hz, 1H), 3.63 (d, *J* = 16.2 Hz, 1H), 3.16 (s, 3H), 1.58 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 174.0, 171.5, 158.3, 144.5, 130.8, 128.4, 126.6, 125.3, 125.1, 124.7, 123.4, 121.9, 109.8, 108.7, 90.7, 77.4, 53.5, 34.7, 26.5; HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{18}NO_5$ $[M+H]^+$: 340.1179, found 340.1180.

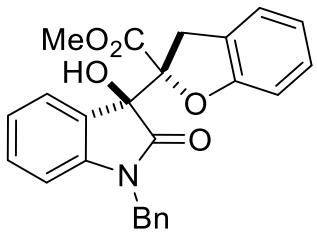


***syn*-3a**

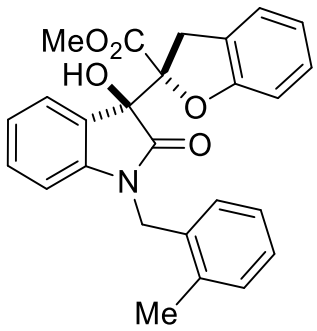
Methyl (*S)-2-((*S**)-3-hydroxy-1-methyl-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (*syn*-3a).** Yellow solid, mp = 144 - 145 ℃. 5.5 mg, 6.0% yield.^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.51 (d, *J* = 7.4 Hz, 1H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.17 (d, *J* = 7.3 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.77 (dd, *J* = 12.4, 8.0 Hz, 2H), 4.47 (d, *J* = 17.2 Hz, 1H), 3.87 (s, 1H), 3.65 (s, 3H), 3.43 (d, *J* = 17.2 Hz, 1H), 3.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 174.5, 172.2, 158.8, 144.4, 130.7, 128.4, 126.5, 125.5, 125.2 124.6 123.0, 121.8, 109.6, 108.4, 91.0, 76.7, 53.1, 35.5, 26.5; HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{18}NO_5$ $[M+H]^+$: 340.1179, found 340.1180.



Methyl (*R)-2-((*S**)-3-hydroxy-2-oxo-1-tritylindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3b).** Yellow solid, mp = 224 - 225 ℃. 32.9 mg, 58% yield, 81:19 *dr*. ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.30 (dd, *J* = 7.7, 1.8 Hz, 6H), 7.20 (dd, *J* = 7.2, 1.5 Hz, 1H), 7.15 (t, *J* = 7.2 Hz, 2H), 7.12 – 7.08 (comp, 9H), 6.96 – 6.88 (comp, 4H), 6.37 – 6.35 (m, 1H), 4.39 (d, *J* = 16.8 Hz, 1H), 4.29 (s, 1H), 3.84 (s, 3H), 3.45 (d, *J* = 16.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 175.8, 172.8, 158.3, 144.3, 141.8, 129.2, 128.9, 128.5, 128.0, 127.8, 126.9, 125.4, 125.3, 123.7, 122.6, 122.0, 116.3, 109.9, 90.9, 76.1, 74.8, 53.4, 34.7; HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{29}NO_5Na$ $[M+Na]^+$: 590.1938, found 590.1936.

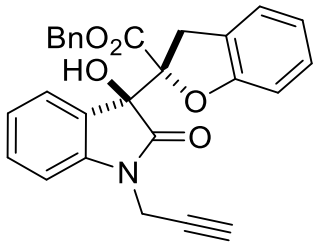


Methyl (*R)-2-((*S**)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3c).** Yellow solid, mp = 169 - 170 ℃. 40.6 mg, 98% yield, 90:10 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.31 – 7.20 (comp, 7H), 7.11 (t, *J* = 7.1 Hz, 2H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 7.9 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 5.09 (d, *J* = 15.7 Hz, 1H), 4.70 (s, 1H), 4.56 (d, *J* = 15.7 Hz, 1H), 4.22 (d, *J* = 16.3 Hz, 1H), 3.78 (s, 3H), 3.57 (d, *J* = 16.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.9, 172.3, 158.1, 143.7, 135.3, 130.6, 128.9, 128.3, 127.8, 127.4, 127.2, 125.4, 124.8, 124.7, 123.4, 121.9, 109.9, 109.8, 90.7, 76.9, 53.4, 44.0, 35.1; HRMS (TOF MS ESI$^+$) calculated for $C_{25}H_{21}NO_5Na$ $[M+Na]^+$: 438.1312, found 438.1319.

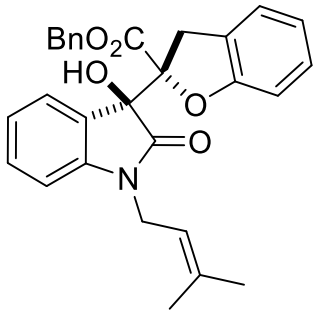


Methyl (*R)-2-((*S**)-3-hydroxy-1-(2-methylbenzyl)-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3d).** Yellow solid, mp = 145 - 146 ℃. 25.8 mg, 60% yield, 84:16 *dr*. ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.31 (d, *J* = 7.4 Hz, 1H), 7.20 (td, *J* = 7.8, 1.0 Hz, 1H), 7.16 – 7.15 (m, 2H), 7.12 – 7.07 (comp, 4H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.85 (dd, *J* = 15.1, 7.8 Hz, 2H), 6.60 (d, *J* = 7.9 Hz, 1H), 5.02 (d, *J* = 16.5 Hz, 1H), 4.73 (s, 1H), 4.60 (d, *J* = 16.5 Hz, 1H), 4.30 (d, *J* = 16.3 Hz, 1H), 3.82 (s, 3H), 3.57 (d, *J* = 16.3 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.9, 172.6, 158.1, 144.0, 135.5, 132.7, 130.7, 130.6, 128.3, 127.5, 127.3, 126.4, 126.3, 125.4,

124.8, 124.6, 123.4, 121.9, 109.93, 109.87, 90.6, 76.8, 53.4, 42.1, 35.2, 19.3; HRMS (TOF MS ESI$^+$) calculated for $C_{26}H_{24}NO_5$ $[M+H]^+$: 430.1649, found 430.1652.

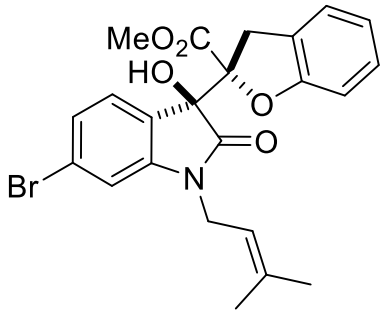


Benzyl (*R)-2-((*S**)-3-hydroxy-2-oxo-1-(prop-2-yn-1-yl)indolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3e).** Yellow oil. 35.2 mg, 80% yield, 89:11 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.26 (ddd, *J* = 14.2, 5.8, 3.1 Hz, 7H), 7.09 (dd, *J* = 15.3, 7.5 Hz, 2H), 6.99 – 6.92 (m, 2H), 6.86 (t, *J* = 6.9 Hz, 2H), 5.25 (d, *J* = 12.2 Hz, 1H), 5.15 (d, *J* = 12.2 Hz, 1H), 4.60 (s, 1H), 4.35 (dd, *J* = 17.7, 2.2 Hz, 1H), 4.27 (dd, *J* = 17.7, 2.2 Hz, 1H), 3.89 (d, *J* = 16.2 Hz, 1H), 3.61 (d, *J* = 16.2 Hz, 1H), 2.19 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.1, 170.7, 158.3, 142.5, 134.7, 130.6, 128.74, 128.70, 128.6, 128.4, 126.4, 125.3, 125.2, 124.7, 123.6, 121.9, 109.9, 109.7, 90.9, 76.5, 72.7, 68.3, 34.7, 29.8, 29.4; HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{21}NO_5Na$ $[M+Na]^+$: 462.1312, found 462.1310.

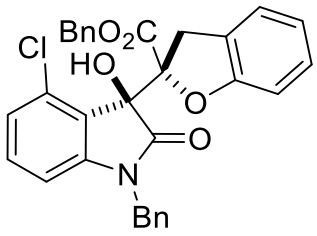


Benzyl (*R)-2-((*S**)-3-hydroxy-1-(3-methylbut-2-en-1-yl)-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3f).** Yellow oil. 33.9 mg, 85% yield, 91:9 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.23 – 7.11 (comp, 7H), 7.01 (dd, *J* = 14.3, 7.2 Hz, 2H), 6.78 (dd, *J* = 17.6, 8.4 Hz, 3H), 6.65 (d, *J* = 7.8 Hz, 1H), 5.17 (d, *J* = 12.2 Hz, 1H), 5.09 (d, *J* = 12.2 Hz, 1H), 5.00 (t, *J* = 6.0 Hz, 1H), 4.50 (s, 1H), 4.12 (dd, *J* = 15.5, 6.3 Hz, 1H), 4.01 (dd, *J* = 15.4, 6.9 Hz, 1H), 3.85 (d, *J* = 16.1 Hz, 1H), 3.50 (d, *J* = 16.2

Hz, 1H), 1.65 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.4, 171.0, 158.3, 143.8, 137.1, 134.8, 130.5, 128.7, 128.6, 128.5, 128.2, 126.8, 125.4, 125.0, 124.7, 123.0, 121.7, 118.0, 109.8, 109.3, 90.8, 77.1, 68.2, 38.1, 34.7, 25.7, 18.2; HRMS (TOF MS ESI$^+$) calculated for $C_{29}H_{28}NO_5$ $[M+H]^+$: 470.1962, found 470.1965.

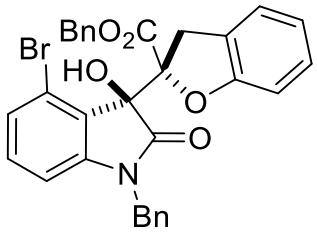


Methyl (*R)-2-((*S**)-6-bromo-3-hydroxy-1-(3-methylbut-2-en-1-yl)-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3g).** Yellow solid, mp = 145 - 146 °C; 41.0 mg, 87% yield, 89:11 *dr*; ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.16 (d, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 1.5 Hz, 1H), 7.10 (t, *J* = 5.7 Hz, 2H), 6.93 (d, *J* = 1.4 Hz, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 7.9 Hz, 1H), 5.07 (t, *J* = 6.7 Hz, 1H), 4.69 (s, 1H), 4.31 (dd, *J* = 15.5, 6.4 Hz, 1H), 4.07 (dd, *J* = 15.5, 7.0 Hz, 1H), 3.91 (d, *J* = 16.2 Hz, 1H), 3.80 (s, 3H), 3.57 (d, *J* = 16.3 Hz, 1H), 1.75 (s, 3H), 1.72 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.2, 171.8, 158.1, 145.2, 137.9, 128.4, 126.2, 125.9, 125.9, 125.6, 124.8, 124.5, 122.0, 117.3, 112.8, 109.7, 90.4, 76.9, 53.5, 38.3, 34.7, 25.8, 18.3; HRMS (TOF MS ESI$^+$) calculated for $C_{23}H_{23}BrNO_5$ $[M+H]^+$: 472.0754, found 472.0760.

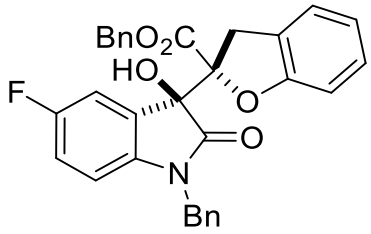


Benzyl (*R)-2-((*S**)-1-benzyl-4-chloro-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3h).** Yellow oil. 47.3 mg, 90% yield, 90:10 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.30 – 7.19 (comp, 10H), 7.10 (dd, *J* = 13.2, 7.8 Hz,

3H), 6.91 (d, J = 8.2 Hz, 1H), 6.86 (t, J = 7.4 Hz, 1H), 6.80 (d, J = 7.9 Hz, 1H), 6.57 (d, J = 7.8 Hz, 1H), 5.22 (q, J = 12.3 Hz, 2H), 4.97 (d, J = 15.8 Hz, 1H), 4.57 (s, 1H), 4.48 (d, J = 15.7 Hz, 1H), 4.25 (d, J = 16.5 Hz, 1H), 3.65 (d, J = 16.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.8, 170.9, 157.6, 145.6, 134.9, 134.8, 131.7, 131.5, 129.0, 128.7, 128.6, 128.4, 128.2, 128.0, 127.5, 125.3, 124.9, 124.8, 124.0, 122.0, 110.3, 108.3, 91.2, 79.4, 68.6, 44.4, 35.2; HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{25}ClNO_5$ $[M+H]^+$: 526.1416, found 526.1418.

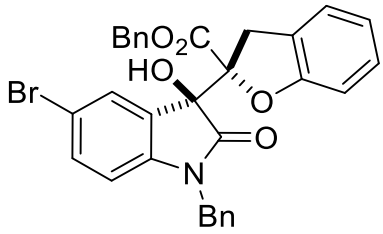


Benzyl (*R)-2-((*S**)-1-benzyl-4-bromo-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3i).** Yellow oil. 52.5 mg, 92% yield, 90:10 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.30 – 7.28 (comp, 3H), 7.25 (t, J = 5.4 Hz, 5H), 7.20 (d, J = 7.6 Hz, 2H),, 7.11 – 6.98 (comp, 4H), 6.83 (dd, J = 15.4, 7.8 Hz, 2H), 6.61 (d, J = 7.7 Hz, 1H), 5.26 (d, J = 12.4 Hz, 1H), 5.21 (d, J = 12.4 Hz, 1H), 4.94 (d, J = 15.7 Hz, 1H), 4.67 (s, 1H), 4.48 (d, J = 15.7 Hz, 1H), 4.01 (d, J = 16.5 Hz, 1H), 3.68 (d, J = 16.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 174.0, 170.5, 157.4, 145.7, 134.9, 134.8, 131.6, 129.0, 128.7, 128.6, 128.34, 128.26, 128.2, 128.0, 127.5, 125.7, 125.2, 124.7, 121.9, 119.7, 110.4, 108.7, 91.4, 80.0, 68.6, 44.4, 35.2; HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{25}BrNO_5$ $[M+H]^+$: 570.0911, found 570.0914.

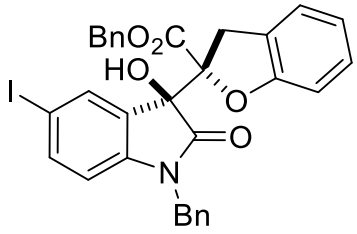


Benzyl (*R)-2-((*S**)-1-benzyl-5-fluoro-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3j).** Yellow oil. 48.4 mg, 95% yield, 95:5 *dr*. ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.32 – 7.20 (comp, 10H), 7.12 (t, J = 7.9 Hz, 2H),

6.95 (dd, J = 7.9, 2.6 Hz, 1H), 6.92 – 6.84 (m, 2H), 6.82 (d, J = 7.9 Hz, 1H), 6.56 (dd, J = 8.6, 4.1 Hz, 1H), 5.26 (d, J = 12.2 Hz, 1H), 5.22 (d, J = 12.2 Hz, 1H), 4.99 (d, J = 15.8 Hz, 1H), 4.73 (s, 1H), 4.51 (d, J = 15.8 Hz, 1H), 4.24 (d, J = 16.3 Hz, 1H), 3.52 (d, J = 16.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 173.6, 171.6, 160.5, 158.2, 158.1, 139.6 (d, J = 2.2 Hz), 135.0, 134.5, 129.0, 128.8, 128.4, 127.9, 127.4, 125.2, 124.8, 122.1, 116.8 (d, J = 23.6 Hz), 113.3 (d, J = 25.4 Hz), 110.4 (d, J = 8.0 Hz), 109.9, 90.4, 68.4, 44.1, 35.1. ^{19}F NMR (471 MHz, $CDCl_3$) (δ, ppm) -118.96; HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{25}FNO_5$ $[M+H]^+$: 510.1711, found 510.1712.

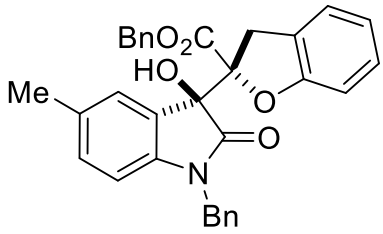


Benzyl (*R)-2-((*S**)-1-benzyl-5-bromo-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3k).** Yellow oil. 45.6 mg, 80% yield, 95:5 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.39 (d, J = 1.8 Hz, 1H), 7.31 – 7.25 (comp, 7H), 7.20 – 7.11 (comp, 6H), 6.89 (t, J = 7.4 Hz, 1H), 6.81 (d, J = 8.3 Hz, 1H), 6.52 (d, J = 8.3 Hz, 1H), 5.27 – 5.13 (m, 2H), 4.96 (d, J = 15.8 Hz, 1H), 4.66 (s, 1H), 4.50 (d, J = 15.8 Hz, 1H), 4.31 (d, J = 16.3 Hz, 1H), 3.52 (d, J = 16.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.3, 171.6, 158.2, 142.7, 134.9, 134.5, 133.4, 129.3, 129.0, 128.9, 128.8, 128.43, 128.37, 128.2, 128.0, 127.4, 125.2, 124.8, 122.1, 116.0, 111.2, 109.9, 90.5, 76.6, 68.3, 44.1, 35.1; HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{24}BrNO_5Na$ $[M+Na]^+$: 592.0730, found 592.0729.

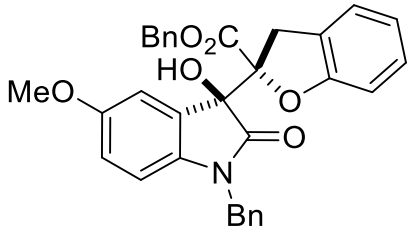


Benzyl (*R)-2-((*S**)-1-benzyl-3-hydroxy-5-iodo-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3l).** Yellow oil. 54.3 mg, 88% yield, 95:5 *dr*. ^{1}H

NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.58 (d, *J* = 1.4 Hz, 1H), 7.49 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.31 – 7.24 (comp, 6H), 7.20 – 7.17 (comp, 4H), 7.14 – 7.11 (m, 2H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.42 (d, *J* = 8.3 Hz, 1H), 5.22 (s, 2H), 4.95 (d, *J* = 15.8 Hz, 1H), 4.64 (s, 1H), 4.49 (d, *J* = 15.8 Hz, 1H), 4.29 (d, *J* = 16.3 Hz, 1H), 3.52 (d, *J* = 16.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.1, 171.6, 158.2, 143.4, 139.3, 134.8, 134.4, 133.7, 129.5, 129.0, 128.9, 128.8, 128.44, 128.35, 128.0, 127.4, 125.2, 124.8, 122.1, 111.8, 109.9, 90.6, 85.9, 76.5, 68.3, 44.0, 35.1; HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{25}INO_5$ $[M+H]^+$: 618.0772, found 618.0768.

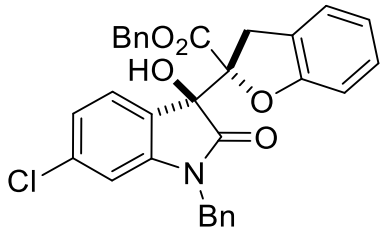


Benzyl (*R)-2-((*S**)-1-benzyl-3-hydroxy-5-methyl-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3m).** Yellow oil. 48.0 mg, 95% yield, 92:8 *dr*. ^1H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.31 – 7.20 (comp, 10H), 7.11 (t, *J* = 7.7 Hz, 2H), 7.03 (s, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.90 – 6.81 (m, 2H), 6.54 (d, *J* = 8.0 Hz, 1H), 5.24 (d, *J* = 12.2 Hz, 1H), 5.19 (d, *J* = 12.3 Hz, 1H), 4.95 (d, *J* = 15.7 Hz, 1H), 4.58 (s, 1H), 4.53 (d, *J* = 15.7 Hz, 1H), 4.23 (d, *J* = 16.2 Hz, 1H), 3.55 (d, *J* = 16.2 Hz, 1H), 2.12 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.8, 171.5, 158.3, 141.2, 135.5, 134.7, 132.9, 130.8, 128.83, 128.76, 128.7, 128.5, 128.3, 127.7, 127.5, 127.0, 125.7, 125.5, 124.8, 121.9, 109.9, 109.5, 90.8, 68.1, 44.0, 35.1, 21.2; HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{28}NO_5$ $[M+H]^+$: 506.1962, found 506.1967.

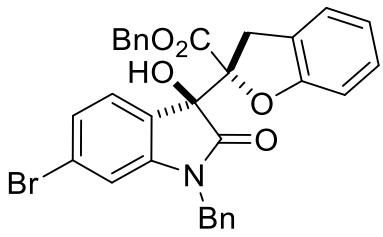


Benzyl (*R)-2-((*S**)-1-benzyl-3-hydroxy-5-methoxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3n).** Yellow oil. 36.5 mg, 70% yield, 93:7 *dr*. ^1H

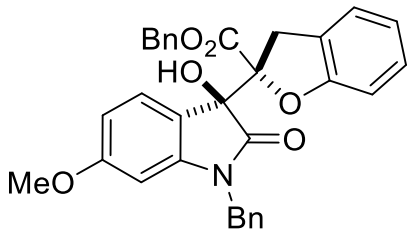
NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.30 – 7.20 (comp, 10H), 7.13 – 7.05 (m, 2H), 6.91 (d, *J* = 2.5 Hz, 1H), 6.86 (t, *J* = 7.1 Hz, 2H), 6.69 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.56 (d, *J* = 8.6 Hz, 1H), 5.28 – 5.21 (m, 2H), 4.95 (d, *J* = 15.7 Hz, 1H), 4.76 (s, 1H), 4.55 (d, *J* = 15.7 Hz, 1H), 3.95 (d, *J* = 16.3 Hz, 1H), 3.59 (d, *J* = 16.8 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 173.7, 171.1, 158.3, 156.3, 136.8, 135.4, 134.7, 128.9, 128.7, 128.6, 128.3, 127.9, 127.8, 127.5, 125.4, 124.8, 121.9, 115.3, 112.2, 110.2, 109.8, 90.7, 77.4, 68.2, 55.7, 44.1, 34.9; HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{28}NO_6$ $[M+H]^+$: 522.1911, found 522.1916.



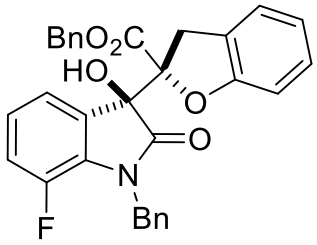
Benzyl (*R)-2-((*S**)-1-benzyl-6-chloro-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3o).** Yellow solid, mp = 109 - 110 ℃. 48.4mg, 92% yield, 94:6 *dr*. ^1H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.33 – 7.24 (comp, 6H), 7.21 (dd, *J* = 10.0, 4.7 Hz, 4H), 7.11 (t, *J* = 6.5 Hz, 2H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.88 (t, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 8.2 Hz, 1H), 6.77 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.62 (d, *J* = 1.8 Hz, 1H), 5.24 (d, *J* = 12.1 Hz, 1H), 5.16 (d, *J* = 12.1 Hz, 1H), 4.94 (d, *J* = 15.8 Hz, 1H), 4.69 (s, 1H), 4.47 (d, *J* = 15.8 Hz, 1H), 4.26 (d, *J* = 16.3 Hz, 1H), 3.52 (d, *J* = 16.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.8, 171.6, 158.2, 144.9, 136.3, 134.8, 134.6, 129.0, 128.80, 128.75, 128.7, 128.4, 128.0, 127.4, 125.8, 125.6, 125.3, 124.8, 123.1, 122.0, 110.3, 109.9, 90.5, 76.4, 68.3, 44.0, 35.0; HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{25}ClNO_5$ $[M+H]^+$: 526.1416, found 526.1421.



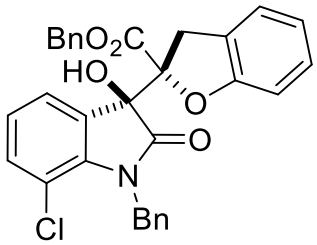
Benzyl (*R)-2-((*S**)-1-benzyl-6-bromo-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3p).** Yellow solid, mp = 126 - 127 ℃. 50.1 mg, 88% yield, 95:5 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.32 – 7.24 (comp, 6H), 7.20 (t, *J* = 6.3 Hz, 4H), 7.11 (t, *J* = 6.5 Hz, 2H), 6.94 (s, 2H), 6.88 (t, *J* = 7.4 Hz, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.77 (s, 1H), 5.24 (d, *J* = 12.1 Hz, 1H), 5.15 (d, *J* = 12.1 Hz, 1H), 4.93 (d, *J* = 15.8 Hz, 1H), 4.68 (s, 1H), 4.47 (d, *J* = 15.8 Hz, 1H), 4.26 (d, *J* = 16.3 Hz, 1H), 3.52 (d, *J* = 16.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.6, 171.5, 158.1, 144.9, 134.7, 134.5, 128.9, 128.72, 128.68, 128.6, 128.3, 127.9, 127.3, 126.1, 126.0, 125.2, 124.8, 124.2, 121.9, 113.0, 109.8, 90.3, 76.4, 68.2, 43.9, 35.0; HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{25}BrNO_5$ $[M+H]^+$: 570.0911, found 570.0917.



Benzyl (*R)-2-((*S**)-1-benzyl-3-hydroxy-6-methoxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3q).** Yellow solid, mp = 140 - 141 ℃. 44.3 mg, 85% yield, 91:9 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.31 – 7.20 (comp, 10H), 7.11 (t, *J* = 7.4 Hz, 2H), 7.05 (d, *J* = 8.3 Hz, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 8.1 Hz, 1H), 6.30 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.22 (d, *J* = 2.2 Hz, 1H), 5.24 (d, *J* = 12.2 Hz, 1H), 5.16 (d, *J* = 12.2 Hz, 1H), 4.92 (d, *J* = 15.7 Hz, 1H), 4.53 – 4.50 (m, 2H), 4.19 (d, *J* = 16.2 Hz, 1H), 3.67 (s, 3H), 3.55 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 174.4, 171.5, 161.7, 158.3, 145.1, 135.4, 134.8, 128.9, 128.7, 128.64, 128.59, 128.3, 127.8, 127.5, 125.8, 125.5, 124.8, 121.8, 118.9, 109.9, 106.7, 97.9, 91.0, 76.6, 68.1, 55.5, 44.0, 35.0; HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{28}NO_6$ $[M+H]^+$: 522.1911, found 522.1913.

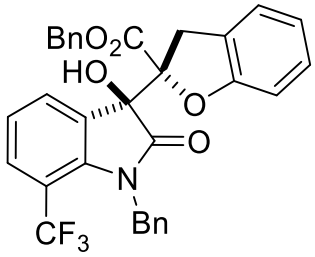


Benzyl (*R)-2-((*S**)-1-benzyl-7-fluoro-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3r).** Yellow solid, mp = 151- 152 ℃. 44.3 mg, 87% yield, 89:11 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.31 – 7.28 (comp, 3H), 7.24 (s, 7H), 7.09 (dd, *J* = 12.9, 7.2 Hz, 2H), 6.94 (dd, *J* = 13.4, 6.3 Hz, 2H), 6.86 (t, *J* = 7.4 Hz, 1H), 6.77 (dd, *J* = 11.5, 6.4 Hz, 2H), 5.25 (d, *J* = 12.1 Hz, 1H), 5.17 (d, *J* = 12.2 Hz, 1H), 5.00 (d, *J* = 15.3 Hz, 1H), 4.78 (d, *J* = 15.3 Hz, 1H), 4.73 (s, 1H), 4.15 (d, *J* = 16.3 Hz, 1H), 3.52 (d, *J* = 16.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 173.6, 171.5, 158.2, 147.5 (d, *J* = 245.1 Hz), 136.6, 134.6, 130.3 (d, *J* = 8.7 Hz), 130.0 (d, *J* = 2.8 Hz), 128.7, 128.6 (d, *J* = 3.3 Hz), 128.3, 127.7, 127.6, 125.2, 124.8, 124.0 (d, *J* = 6.4 Hz), 121.9, 120.9 (d, *J* = 2.9 Hz), 118.8, 118.7, 110.0, 90.5, 68.3, 45.5, 35.0, 29.8; ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -132.74; HRMS (TOF MS ESI^{+}) calculated for $C_{31}H_{25}FNO_5$ $[M+H]^{+}$: 510.1711, found 510.1711.

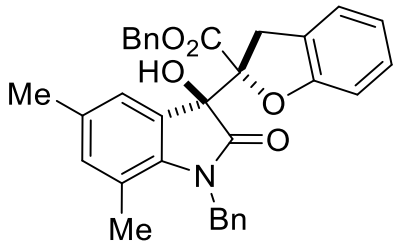


Benzyl (*R)-2-((*S**)-1-benzyl-7-chloro-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3s).** Yellow solid, mp = 150 - 151 ℃. 45.8 mg, 87% yield, 89:11 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.32 – 7.31 (comp, 3H), 7.24 (dd, *J* = 4.5, 2.8 Hz, 4H), 7.20 – 7.12 (comp, 4H), 7.10 – 7.06 (comp, 3H), 6.85 (dd, *J* = 12.7, 7.6 Hz, 2H), 6.74 (t, *J* = 7.8 Hz, 1H), 5.27 (d, *J* = 12.3 Hz, 1H), 5.18 (dd, *J* = 20.2, 9.3 Hz, 3H), 4.79 (s, 1H), 4.13 (d, *J* = 16.3 Hz, 1H), 3.53 (d, *J* = 16.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 174.6, 171.5, 158.1, 139.8, 137.0, 134.6, 133.1, 130.1, 128.8, 128.64, 128.62, 128.4, 127.2, 126.6, 125.2, 124.8, 124.2, 123.6, 122.0,

115.9, 110.0, 90.5, 76.2, 68.4, 45.1, 35.1; HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{24}ClNO_5Na$ [M+Na]$^+$: 548.1235, found 548.1235.

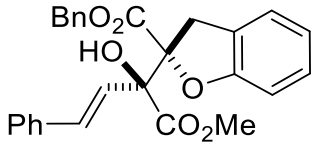


Benzyl (*R)-2-((*S**)-1-benzyl-3-hydroxy-2-oxo-7-(trifluoromethyl)indolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3t).** Yellow oil. 49.2 mg, 88% yield, 95:5 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.54 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 6.9 Hz, 1H), 7.34 – 7.30 (comp, 3H), 7.25 (dd, *J* = 6.5, 2.6 Hz, 2H), 7.21 – 7.11 (comp, 4H), 7.07 (d, *J* = 7.0 Hz, 3H), 6.93 – 6.86 (comp, 3H), 5.28 (d, *J* = 12.1 Hz, 1H), 5.23 (d, *J* = 12.1 Hz, 1H), 5.14 (d, *J* = 17.1 Hz, 1H), 5.00 (d, *J* = 17.0 Hz, 1H), 4.86 (s, 1H), 4.06 (d, *J* = 16.3 Hz, 1H), 3.54 (d, *J* = 16.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 175.5, 171.5, 158.1, 142.1, 135.8, 134.5, 130.1, 128.83, 128.80, 128.7, 128.6, 128.5, 127.0, 125.8, 125.1, 124.9, 123.2 (q, *J* = 271.8 Hz), 122.9, 122.1, 113.4 (q, *J* = 33.1 Hz), 110.0, 90.3, 75.0, 68.6, 46.2 (q, *J* = 4.9 Hz), 35.0, 29.8; ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -54.74; HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{24}F_3NO_5Na$ [M+Na]$^+$: 582.1499, found 582.1496.

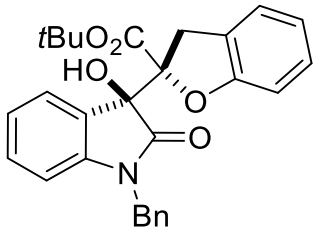


Benzyl (*R)-2-((*S**)-1-benzyl-3-hydroxy-5,7-dimethyl-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (3u).** Yellow solid, mp = 158 - 159 ℃. 44.2 mg, 85% yield, 91:9 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.29 – 7.27 (comp, 3H), 7.25 – 7.18 (comp, 5H), 7.11 (dd, *J* = 16.2, 7.6 Hz, 4H), 6.94 (s, 1H), 6.86 (dd, *J* = 14.7, 7.6 Hz, 2H), 6.75 (s, 1H), 5.27 – 5.21 (m, 2H), 5.09 (d, *J* = 16.9 Hz, 1H), 4.90 (d, *J* = 16.8

Hz, 1H), 4.61 (s, 1H), 4.23 (d, *J* = 16.2 Hz, 1H), 3.57 (d, *J* = 16.2 Hz, 1H), 2.14 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 175.1, 171.5, 158.3, 139.2, 137.2, 135.0, 134.8, 132.8, 128.9, 128.7, 128.6, 128.4, 128.2, 127.9, 127.2, 125.9, 125.5, 124.8, 123.5, 121.8, 120.0, 109.9, 91.0, 76.2, 68.1, 45.3, 35.1, 20.8, 18.8; HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{30}NO_5$ $[M+H]^+$: 520.2118, found 520.2119.

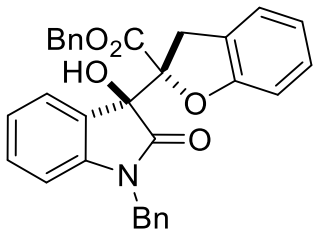


Benzyl (*R)-2-((*S**, *E*)-2-(2-hydroxy-1-methoxy-1-oxo-4-phenylbut-3-en-2-yl)-2,3-dihydrobenzofuran-2-carboxylate (3v).** Yellow oil. 32.8 mg, 74% yield, 87:13 *dr* . ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.36 (s, 5H), 7.26 (dd, *J* = 8.1, 2.7 Hz, 5H), 7.12 (dd, *J* = 16.0, 7.7 Hz, 2H), 6.97 (d, *J* = 15.8 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.88 (t, *J* = 7.4 Hz, 1H), 6.58 (d, *J* = 15.8 Hz, 1H), 5.30 (d, *J* = 12.2 Hz, 1H), 5.17 (d, *J* = 12.1 Hz, 1H), 3.77 (s, 1H), 3.75 – 3.72 (m, 1H), 3.67 (s, 3H), 3.35 (d, *J* = 16.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 171.9, 171.1, 159.0, 136.3, 135.2, 132.8, 128.80, 128.77, 128.70, 128.68, 128.4, 128.2, 127.1, 125.2, 124.5, 123.7, 121.6, 109.9, 93.3, 80.0, 68.0, 53.5, 36.4. HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{24}O_6Na$ $[M+Na]^+$: 467.1645, found 467.1645.

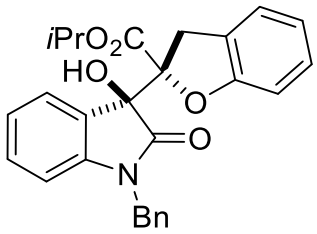


***Tert*-butyl (*R**)-2-((*S**)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (4a).** Yellow solid, mp = 170 - 171 ℃. 41.2 mg, 90% yield, 87:13 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.40 (d, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 7.1 Hz, 1H), 7.27 (s, 1H), 7.26 – 7.22 (comp, 3H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.10 – 7.07 (m, 2H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.69 (d, *J* = 7.9 Hz, 1H), 5.11 – 4.99 (m, 2H), 4.61 (d, *J* = 15.7 Hz, 1H), 4.13

(d, J = 16.0 Hz, 1H), 3.50 (d, J = 16.3 Hz, 1H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 174.0, 170.9, 158.5, 143.8, 135.4, 130.4, 128.9, 128.1, 127.8, 127.6, 127.4, 125.6, 125.2, 124.7, 123.2, 121.6, 109.7, 109.7, 90.4, 84.8, 77.1, 44.0, 35.1, 27.9; HRMS (TOF MS ESI$^+$) calculated for $C_{28}H_{27}NO_5Na$ $[M+Na]^+$: 480.1781, found 480.1777.

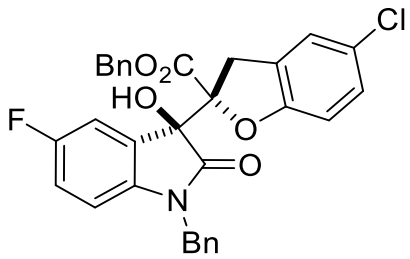


Benzyl (*R)-2-((*S**)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (4b).** Yellow oil. 45.2 mg, 92% yield, 95:5 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.32 – 7.22 (comp, 10H), 7.15 (dd, J = 7.6, 3.9 Hz, 2H), 7.10 (d, J = 7.7 Hz, 2H), 6.89 – 6.81 (comp, 3H), 6.65 (d, J = 7.8 Hz, 1H), 5.26 (d, J = 12.2 Hz, 1H), 5.18 (d, J = 12.2 Hz, 1H), 4.98 (d, J = 15.7 Hz, 1H), 4.61 (s, 1H), 4.55 (d, J = 15.7 Hz, 1H), 4.21 (d, J = 16.2 Hz, 1H), 3.55 (d, J = 16.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.9, 171.6, 158.3, 143.6, 135.4, 134.7, 130.5, 128.9, 128.8, 128.7, 128.6, 128.3, 127.8, 127.5, 127.1, 125.4, 124.9, 124.8, 123.3, 121.9, 109.9, 109.7, 90.7, 76.8, 68.3, 44.0, 35.1; HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{25}NO_5Na$ $[M+Na]^+$: 514.1625, found 514.1618.

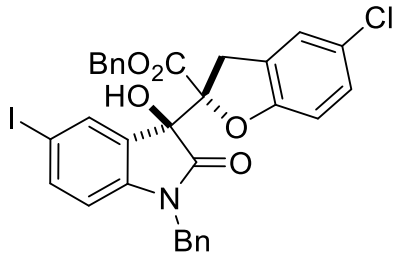


Isopropyl (*R)-2-((*S**)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,3-dihydrobenzofuran-2-carboxylate (4c).** Yellow solid, mp = 135 – 136 ℃. 40.4 mg, 91% yield, 90:10 *dr*. ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 7.35 (d, J = 7.4 Hz, 1H), 7.29 (dd, J = 10.6, 3.9 Hz, 2H), 7.25 – 7.24 (comp, 3H), 7.20 (t, J = 7.8 Hz, 1H), 7.10 (t, J = 8.1 Hz, 2H), 6.96 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 7.4 Hz, 1H), 6.84 – 6.81 (m,

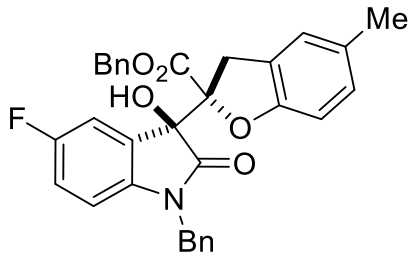
1H), 6.70 (d, *J* = 7.9 Hz, 1H), 5.15 (dt, *J* = 12.5, 6.3 Hz, 1H), 5.05 (d, *J* = 15.7 Hz, 1H), 4.87 (s, 1H), 4.60 (d, *J* = 15.7 Hz, 1H), 4.08 (d, *J* = 16.2 Hz, 1H), 3.55 (d, *J* = 16.2 Hz, 1H), 1.26 (d, *J* = 6.3 Hz, 3H), 1.19 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 174.0, 171.1, 158.4, 143.7, 135.4, 130.5, 128.9, 128.2, 127.8, 127.5, 127.3, 125.5, 125.0, 124.7, 123.3, 121.7, 109.8, 109.7, 90.4, 77.0, 71.2, 44.0, 35.0, 21.7, 21.6; HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{26}NO_5$ $[M+H]^+$: 444.1805, found 444.1801.



Benzyl (*R*)-2-((*S*)-1-benzyl-5-fluoro-3-hydroxy-2-oxoindolin-3-yl)-5-chloro-2,3-dihydrobenzofuran-2-carboxylate (4d). Yellow oil. 51.7 mg, 95% yield, 87:13 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.33 – 7.31 (comp, 3H), 7.28 – 7.25 (comp, 3H), 7.22 – 7.18 (comp, 4H), 7.07 (d, *J* = 8.1 Hz, 2H), 6.94 – 6.85 (m, 2H), 6.70 (d, *J* = 8.2 Hz, 1H), 6.57 (dd, *J* = 8.6, 4.1 Hz, 1H), 5.27 – 5.20 (m, 2H), 4.97 (d, *J* = 15.8 Hz, 1H), 4.69 (s, 1H), 4.49 (d, *J* = 15.8 Hz, 1H), 4.30 (d, *J* = 16.6 Hz, 1H), 3.47 (d, *J* = 16.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.4, 171.3, 160.3, 158.3, 156.9, 139.50 (d, *J* = 2.1 Hz), 135.0, 134.3, 129.0, 128.9, 128.6, 128.53 (d, *J* = 7.5 Hz), 128.52, 128.2 (d, *J* = 50.6 Hz), 127.4, 127.3, 126.9, 125.0, 116.9 (d, *J* = 23.4 Hz), 113.2 (d, *J* = 25.6 Hz), 110.8, 110.4 (d, *J* = 8.0 Hz), 91.0, 76.7, 68.5, 44.1, 35.0; ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -118.73; HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{24}ClFNO_5$ $[M+H]^+$: 544.1322, found 544.1321.

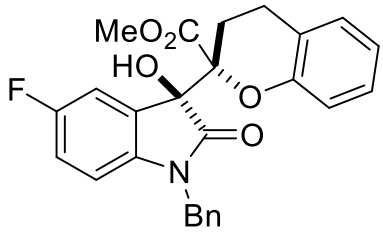


Benzyl (*R)-2-((*S**)-1-benzyl-3-hydroxy-5-iodo-2-oxoindolin-3-yl)-5-chloro-2,3-dihydrobenzofuran-2-carboxylate (4e)**. Pale yellow oil. 57.5 mg, 88% yield, 81:19 *dr* . ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.56 (d, *J* = 1.6 Hz, 1H), 7.51 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.33 – 7.32 (comp, 3H), 7.28 – 7.25 (comp, 3H), 7.20 – 7.17 (comp, 4H), 7.09 – 7.06 (m, 2H), 6.69 (d, *J* = 8.3 Hz, 1H), 6.44 (d, *J* = 8.2 Hz, 1H), 5.22 (s, 2H), 4.95 (d, *J* = 15.7 Hz, 1H), 4.50 (d, *J* = 15.7 Hz, 1H), 4.33 (d, *J* = 16.6 Hz, 1H), 3.47 (d, *J* = 16.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 172.9, 171.2, 156.9, 143.4, 139.5, 134.8, 134.3, 133.7, 129.4, 129.0, 128.9, 128.5, 128.4, 128.0, 127.4, 127.3, 127.0, 125.0, 111.8, 110.8, 91.2, 85.9, 76.3, 68.5, 44.0, 35.0. HRMS (TOF MS ESI^{+}) calculated for $C_{24}H_{19}ClINO_3Na$ $[M+Na]^{+}$: 674.0202, found 674.0200.

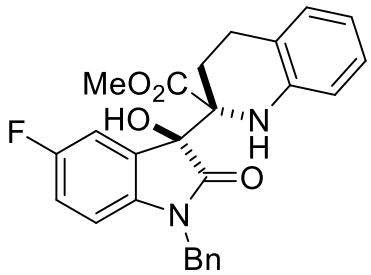


Benzyl (*R)-2-((*S**)-1-benzyl-5-fluoro-3-hydroxy-2-oxoindolin-3-yl)-5-methyl-2,3-dihydrobenzofuran-2-carboxylate (4f).** Yellow oil. 49.2 mg, 94% yield, 90:10 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.31 – 7.19 (comp, 10H), 6.93 (dt, *J* = 11.7, 5.3 Hz, 3H), 6.85 (td, *J* = 8.8, 2.5 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.54 (dd, *J* = 8.6, 4.1 Hz, 1H), 5.25 (d, *J* = 13.0 Hz, 1H), 5.20 (d, *J* = 12.2 Hz, 1H), 4.99 (d, *J* = 15.8 Hz, 1H), 4.73 (s, 1H), 4.49 (d, *J* = 15.8 Hz, 1H), 4.23 (d, *J* = 16.3 Hz, 1H), 3.47 (d, *J* = 16.3 Hz, 1H), 2.25 (d, *J* = 8.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 173.6, 171.8, 160.5, 158.1, 156.2, 139.6 (d, *J* = 2.0 Hz), 135.0, 134.6, 131.4, 128.9, 128.8, 128.5, 127.9, 127.4, 125.4, 125.2, 116.7 (d, *J* = 23.4 Hz), 113.3 (d, *J* = 25.6 Hz), 110.3 (d, *J* =

7.9 Hz), 109.4, 90.4, 76.9, 68.3, 44.1, 35.2, 20.9; ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -119.03; HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{27}FNO_5$ $[M+H]^+$: 524.1868, found 524.1863.



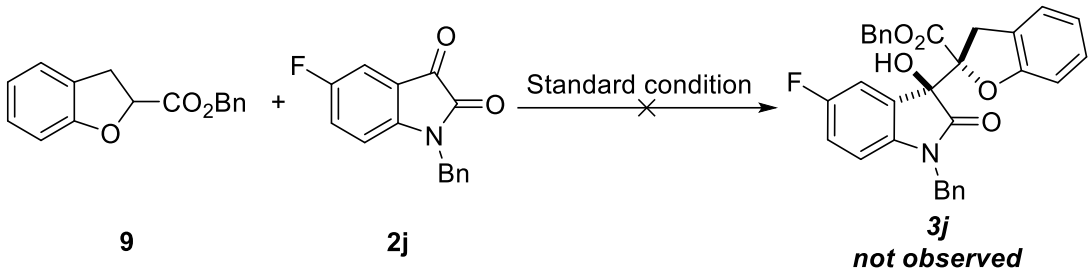
Methyl (*R)-2-((*S**)-1-benzyl-5-fluoro-3-hydroxy-2-oxoindolin-3-yl)chromane-2-carboxylate (4g).** Yellow oil. 33.6 mg, 75% yield, 83:17 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.33 (dd, *J* = 7.9, 2.9 Hz, 5H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.03 (dd, *J* = 7.8, 2.7 Hz, 2H), 6.95 (dt, *J* = 8.8, 4.3 Hz, 1H), 6.89 (t, *J* = 7.3 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.67 (dd, *J* = 8.6, 4.1 Hz, 1H), 5.20 (d, *J* = 15.8 Hz, 1H), 4.56 (d, *J* = 15.8 Hz, 1H), 4.45 (s, 1H), 3.80 (s, 3H), 2.78 (dd, *J* = 15.7, 6.0 Hz, 1H), 2.74 – 2.71 (m, 1H), 2.68 – 2.63 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 173.9, 172.3, 160.3, 158.4, 152.7, 139.9, 135.1, 129.6 (d, *J* = 7.8 Hz), 129.4, 129.0, 127.8 (d, *J* = 36.2 Hz), 127.4, 121.4, 121.1, 116.9, 116.6 (d, *J* = 23.5 Hz), 112.76 (d, *J* = 25.5 Hz), 110.2 (d, *J* = 7.9 Hz), 83.2, 78.3, 53.1, 44.2, 22.7, 22.0; ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -119.39; HRMS (TOF MS ESI$^+$) calculated for $C_{26}H_{22}FNO_5Na$ $[M+Na]^+$: 470.1374, found 470.1369.



Methyl (*R)-2-((*S**)-1-benzyl-5-fluoro-3-hydroxy-2-oxoindolin-3-yl)-1,2,3,4-tetrahydroquinoline-2-carboxylate (4h).** Yellow oil. 31.2 mg, 70% yield, 60:40 *dr*. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.35 – 7.26 (comp, 7H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.95 (td, *J* = 8.7, 3.5 Hz, 2H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.66 (dd, *J* = 8.6, 4.1 Hz, 1H), 5.59 (s, 1H), 5.00 (d, *J* = 15.6 Hz, 1H), 4.64 (d, *J* = 15.6 Hz,

1H), 4.58 (s, 1H), 3.44 (s, 3H), 2.71 (dd, J = 9.0, 5.1 Hz, 2H), 2.50 – 2.47 (m, 1H), 2.21 (td, J = 12.1, 7.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 176.4, 172.9, 160.3, 158.4, 142.1, 139.5, 135.1, 129.08, 129.05, 128.4 (d, J = 8.0 Hz), 128.1, 127.7, 127.3, 121.0, 119.3, 116.6 (d, J = 23.5 Hz), 116.2, 114.3 (d, J = 25.4 Hz), 110.1 (d, J = 8.0 Hz), 65.7, 52.8, 44.3, 23.8, 23.7; ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -119.20; HRMS (TOF MS ESI$^+$) calculated for $C_{26}H_{24}FN_2O_4$ $[M+H]^+$: 447.1715, found 447.1722.

Control Experiments



9 **2j** ***3j*** ***not observed***

To a 10-mL oven-dried vial containing a magnetic stirring bar, isatine **2j** (20.4 mg, 0.08 mmol, 1.0 equiv.), $Rh_2(OAc)_4$ (0.35 mg, 1.0 mol %) and 4Å MS (50 mg) in anhydrous toluene (1.0 mL), was added a solution of **9** (30.5 mg, 0.12 mmol, 1.5 equiv.) in 1.0 mL anhydrous toluene *via* a syringe pump under stirring over 10 min at 40 °C, and the reaction mixture was stirred for additional 0.5 h under these conditions after addition. Then, the crude reaction mixture was subjected to proton NMR analysis after evaporation (see third spectra in Figure S1), and no reaction occurred according to these results.

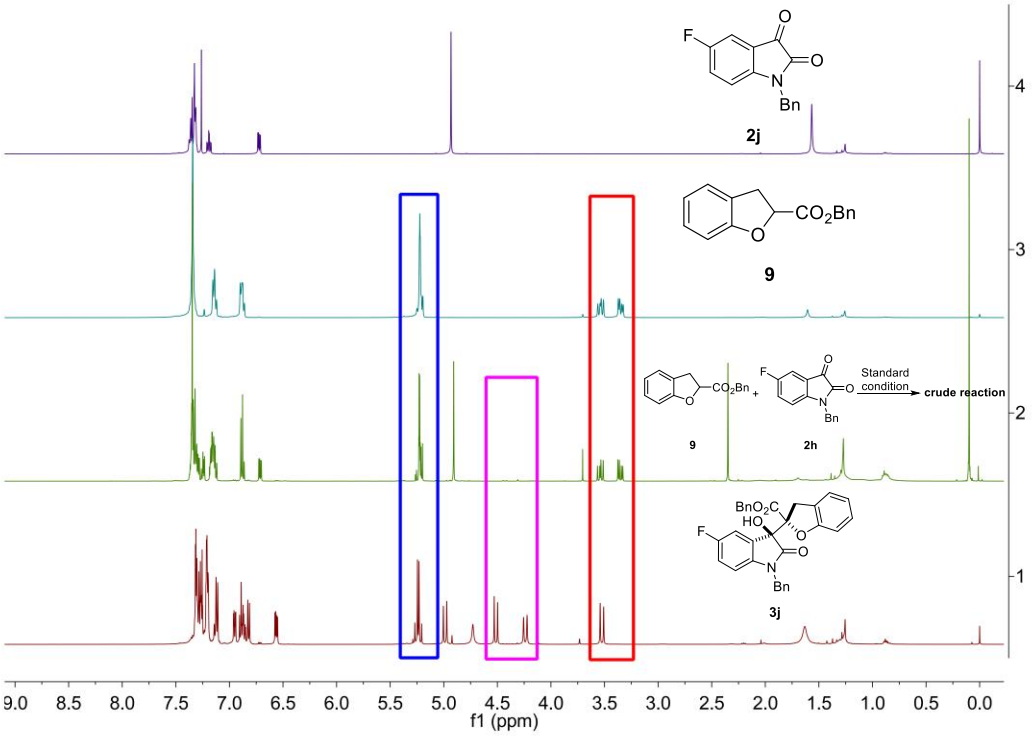
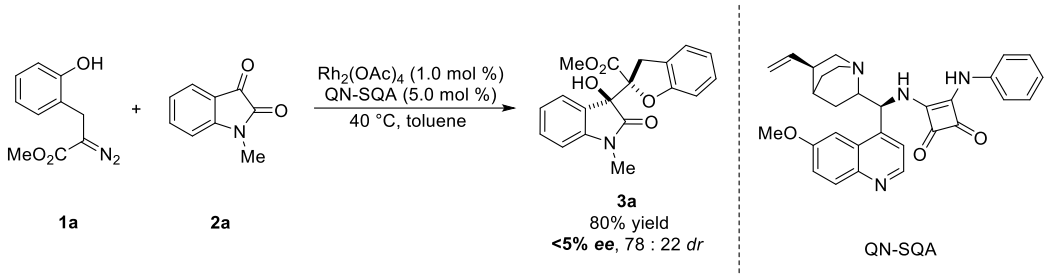
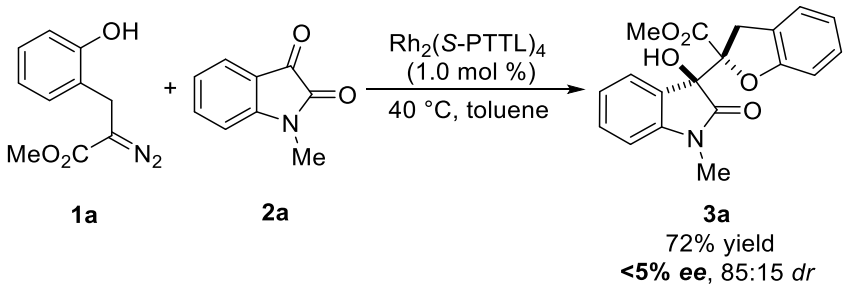


Figure S1. Proton NMR analysis of the crude reaction mixture of **9** with **2j**.

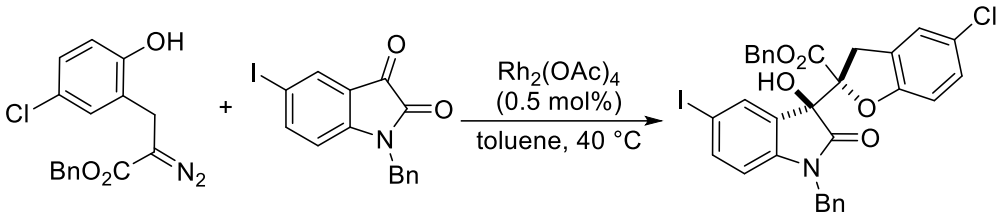


To a 10-mL oven-dried vial containing a magnetic stirring bar, N-Me-isatine **2a** (16.1 mg, 0.1 mmol, 1.0 equiv.), $Rh_2(OAc)_4$ (0.4 mg, 1.0 mol %), QN-SQA (2.5 mg, 5.0 mol %), and 4Å MS (50 mg) in anhydrous toluene (1.0 mL), was added a solution of diazo compound **1a** (30.9 mg, 0.15 mmol, 1.5 equiv.) in 1.0 mL anhydrous toluene *via* a syringe pump under stirring over 10 min at 40 °C, and the reaction mixture was stirred for additional 0.5 h under these conditions after addition. When the reaction mixture was completed (monitored by TLC), the reaction mixture was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 8 : 1 to 3 : 1) to give the racemic products **3a** in 80% yield with <5% *ee*, 78 : 22 *dr*.



To a 10-mL oven-dried vial containing a magnetic stirring bar, isatine **2a** (16.1 mg, 0.1 mmol, 1.0 equiv.), Rh_2(*S*-PTTL)$_4$ (1.2 mg, 1.0 mol %) and 4Å MS (50 mg) in anhydrous toluene (1.0 mL), was added a solution of diazo compound **1a** (30.9 mg, 0.15 mmol, 1.5 equiv.) in 1.0 mL anhydrous toluene *via* a syringe pump over 10 min at 40 °C, and the reaction mixture was stirred for additional 0.5 h under these conditions after addition. When the reaction was completed (monitored by TLC), the reaction mixture was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 8 : 1 to 3 : 1) to give the racemic products **3a** in 72% yield with <5% *ee*, 85 : 15 *dr*.

General Procedure for Scale up and Derivatizations

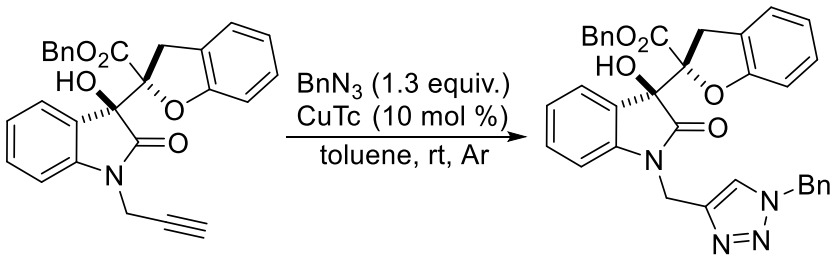


1e, 1.0 g
3.3 mmol

2l, 0.8 g
2.2 mmol

4e, 1.23 g
85% yield
81 : 19 *dr*

Scale up: To a 50-mL oven-dried vial containing a magnetic stirring bar, isatine **2l** (0.8 g, 2.2 mmol, 1.0 equiv.), $Rh_2(OAc)_4$ (4.9 mg, 0.5 mol %), and 4Å MS (1.5 g) in anhydrous toluene (15 mL), was added a solution of diazo compound **1e** (1.0 g, 3.3 mmol, 1.5 equiv.) in anhydrous toluene (10 mL) *via* a syringe pump over 1.0 h at 40 ℃, and the reaction mixture was stirred for additional 0.5 h under these conditions after addition. When the reaction was completed (monitored by TLC), the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (Hexanes : EtOAc = 8 : 1 to 3 : 1) to give 1.23 g pure product **4e** in 85% yield with 81 : 19 *dr*.

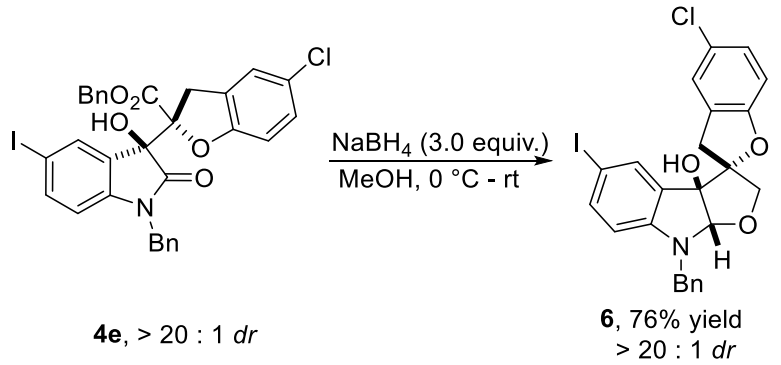


3e, > 20 : 1 *dr*

5, 84% yield
> 20 : 1 *dr*

Synthesis of 5: To a 10-mL oven-dried vial containing a magnetic stirring bar, CuTc (1.2 mg, 10 mol %), and **3e** (28.1 mg, 0.064 mmol, 1.0 equiv.) in toluene (0.5 mL), was added a solution of benzyl azide (11.1 mg, 0.083 mmol, 1.3 equiv.) in toluene (0.5 mL) dropwise under stirring at room temperature under argon atmosphere, and the reaction mixture was stirred for additional 2.0 h under these conditions after addition. When the reaction was completed (monitored by TLC), the solvent was removed and the crude residue was purified by flash chromatography on silica gel without any treatment

(Hexanes : EtOAc = 5 : 1 to 3 : 1) to give 37.2 mg pure product **5** in 84% yield, > 20 : 1 *dr*. White solid, mp = 170 - 174 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.32 – 7.25 (comp, 7H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.18 – 7.13 (comp, 5H), 7.08 – 7.01 (comp, 3H), 6.88 – 6.84 (m, 2H), 6.65 (d, *J* = 8.0 Hz, 1H), 5.38 (s, 2H), 5.12 (d, *J* = 12.2 Hz, 1H), 5.01 (d, *J* = 12.2 Hz, 1H), 4.92 (d, *J* = 15.7 Hz, 1H), 4.73 (d, *J* = 15.7 Hz, 1H), 4.58 (s, 1H), 4.11 (d, *J* = 16.3 Hz, 1H), 3.50 (d, *J* = 16.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 173.6, 171.0, 158.2, 143.0, 142.9, 134.6, 134.4, 130.7, 129.2, 128.9, 128.7, 128.5, 128.2, 128.1, 126.5, 125.5, 124.8, 123.4, 122.7, 121.8, 110.0, 109.6, 91.0, 76.7, 68.1, 54.3, 35.6, 34.7. HRMS (TOF MS ESI$^+$) calculated for $C_{34}H_{29}N_4O_5$ $[M+H]^+$: 573.2132, found 573.2134.

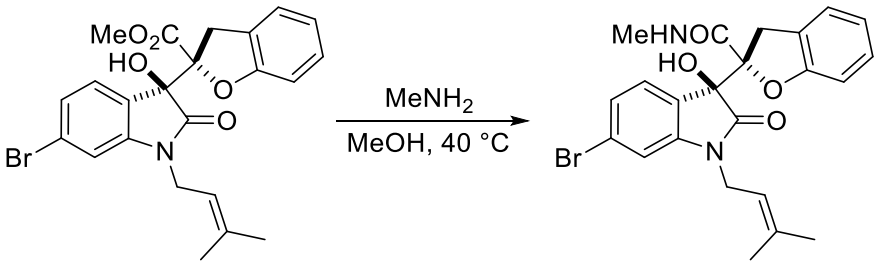


4e, > 20 : 1 *dr*

6, 76% yield
> 20 : 1 *dr*

Synthesis of 6: To an oven-dried tube containing a magnetic stirring bar and compound **4e** (32.5 mg, 0.05 mmol, 1.0 equiv.) in THF (2.0 mL), $NaBH_4$ (5.7 mg, 0.15 mmol, 3.0 equiv.) was added in one portion under stirring at 0 ℃, and the reaction mixture was stirred for 2.0 h at room temperature after addtion. When the reaction was completed (monitored by TLC), cold water (5.0 mL) was added to quench the reaction, and the aqueous layer was extracted with EtOAc (5.0 mL × 3). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated in *vacuo* after filtration. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10 : 1) to give 20.3 mg pure product in 76% yield, > 20 : 1 *dr*. Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.53 (d, *J* = 1.7 Hz, 1H), 7.43 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.33 (dd, *J* = 7.0, 1.4 Hz, 1H), 7.29 (dt, *J* = 7.1, 2.8 Hz, 4H), 7.19 (s, 1H), 7.15 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.83 (d, *J* = 8.5 Hz, 1H), 6.22 (d, *J* = 8.4 Hz, 1H), 5.50 (s, 1H), 4.54 (d, *J* = 16.0 Hz, 1H), 4.44 (d, *J* = 16.0 Hz, 1H), 4.15

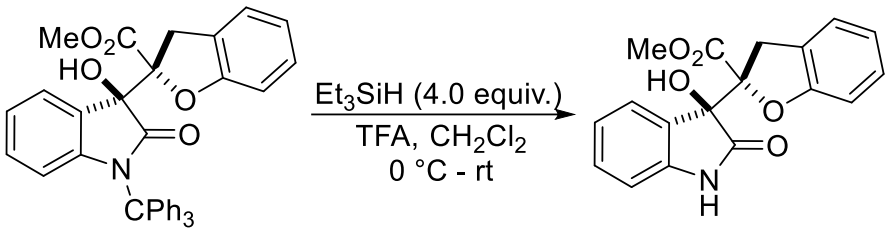
(d, J = 10.5 Hz, 1H), 3.65 (d, J = 16.7 Hz, 1H), 3.60 (d, J = 10.6 Hz, 1H), 3.59 – 3.52 (m, 1H), 2.80 (d, J = 16.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 156.3, 151.3, 139.7, 137.2, 134.2, 128.9, 128.7, 127.8, 127.7, 127.6, 127.4, 126.8, 125.3, 111.3, 108.9, 103.9, 96.6, 87.9, 78.1, 75.0, 49.4, 31.4. HRMS (TOF MS ESI$^+$) calculated for $C_{24}H_{19}ClINO_3Na$ [M+Na]$^+$: 553.9995, found 553.9995.



3g, > 20 : 1 *dr*

7, 55% yield
> 20 : 1 *dr*

Synthesis of 7: To an oven-dried tube containing a magnetic stirring bar, compound **3g** (47.2 mg, 0.1 mmol, 1.0 equiv.) in MeOH (2.0 mL), was added 33% NH_2Me aqueous solution (1.0 mL) dropwise under stirring at 0 ℃, and the reaction mixture was stirred overnight at 40 ℃ after addition. When the reaction was completed (monitored by TLC), saturated NH_4Cl aqueous solution (5.0 mL) was added to quench the reaction, and the aqueous layer was extracted with EtOAc (5.0 mL × 3). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated in *vacuo* after filtration. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2 : 1) to give 26.1 mg pure product in 55% yield, > 20 : 1 *dr*. Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.18 (dd, J = 12.3, 4.3 Hz, 2H), 7.11 (d, J = 8.0 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.95 – 6.92 (m, 2H), 6.64 (d, J = 8.0 Hz, 1H), 6.62 (d, J = 4.8 Hz, 1H), 5.71 (s, 1H), 4.98 (t, J = 6.7 Hz, 1H), 4.88 (d, J = 16.8 Hz, 1H), 4.28 (dd, J = 15.4, 6.4 Hz, 1H), 3.90 (dd, J = 15.4, 7.1 Hz, 1H), 3.38 (d, J = 16.8 Hz, 1H), 2.82 (d, J = 5.0 Hz, 3H), 1.69 (s, 3H), 1.66 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 174.0, 172.2, 157.1, 145.4, 137.5, 128.0, 127.7, 126.2, 125.4, 125.3, 123.9, 122.7, 117.6, 112.5, 109.5, 100.1, 89.4, 76.2, 38.1, 34.8, 25.9, 25.8, 18.2. HRMS (TOF MS ESI$^+$) calculated for $C_{23}H_{23}BrN_2O_4Na$ [M+Na]$^+$: 493.0733, found 493.0730.

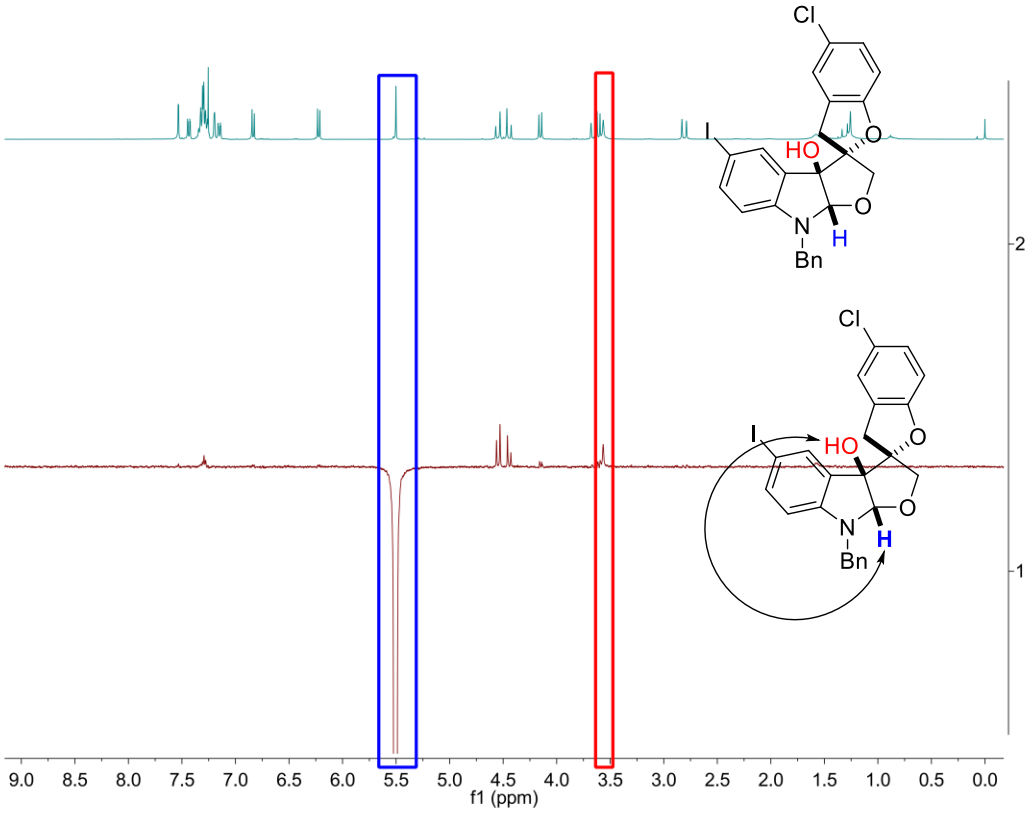


3b, > 20 : 1 *dr*

8, 84% yield
> 20 : 1 *dr*

Synthesis of 8: To an oven-dried tube containing a magnetic stirring bar and compound **3b** (56.7 mg, 0.1 mmol, 1.0 equiv.) in DCM (2.0 mL), was added triethylsilane (64 μl, 0.4 mmol, 4.0 equiv.) and trifluoroacetic acid (1.0 ml) in sequence under stirring at 0 ℃, and the reaction mixture was stirred for 2.0 h at room temperature after addition. When the reaction was completed (monitored by TLC), saturated $NaHCO_3$ aqueous solution (5.0 mL) was added to quench the reaction, and the aqueous layer was extracted with EtOAc (5.0 mL × 3). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuo after filtration. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 1 : 1) to give 27 mg pure product in 84% yield, > 20 : 1 dr. White solid, mp = 193 - 194 ℃. ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 8.66 (s, 1H), 7.29 – 7.28 (m, 1H), 7.23 (dd, *J* = 7.2, 4.6 Hz, 1H), 7.07 (d, *J* = 4.5 Hz, 2H), 6.95 (dd, *J* = 7.0, 4.1 Hz, 1H), 6.84 (d, *J* = 4.0 Hz, 3H), 4.85 (s, 1H), 3.89 (d, *J* = 16.6 Hz, 1H), 3.77 (d, *J* = 3.1 Hz, 3H), 3.61 (d, *J* = 16.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 176.3, 171.5, 158.2, 141.6, 130.7, 128.4, 127.1, 125.31, 125.28, 124.7, 123.3, 121.8, 110.8, 109.9, 90.8, 77.6, 53.4, 34.7. HRMS (TOF MS ESI+) calculated for $C_{18}H_{15}NO_5Na$ [M+Na]+: 348.0842, found 348.0841.

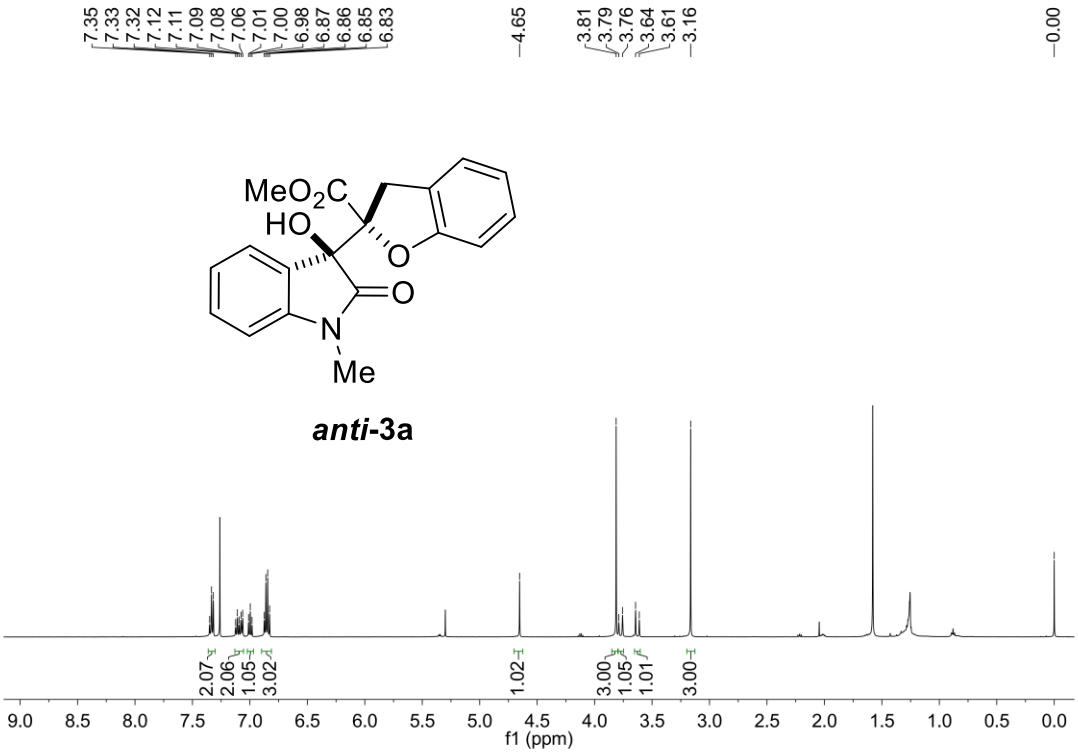
1D-noe NMR Analysis of 6



References

1 (a) X.-G. Song, S.-F. Zhu, X.-L. Xie and Q.-L. Zhou, *Angew. Chem., Int. Ed.,* 2013, **52**, 2555-2558; (b) X.-G. Song, Y.-Y. Ren, S.-F. Zhu and Zhou, Q.-L, *Adv. Synth. Catal.*, 2016, **358**, 2366-2370; (c) K. Hong, S. Dong, X. Xu, Z. Zhang, T. Shi, H. Yuan, X. Xu and W. Hu, *ACS Catal.*, 2021, **11**, 6750-6756.

2 (a) M. Li, L. Zan, D. Prajapati and W. Hu, *Org. Biomol. Chem.*, 2012, **10**, 8808-8813; (b) H. He, Z. Yang, Y. Chai, R. Wu, P. Chen, J. Zhou and H. Zhou, *Org. Lett.*, 2021, **23**, 5739-5743; (c) L. Jiang, W. Jin and W. Hu, *ACS Catal.*, 2016, **6**, 6146-6150.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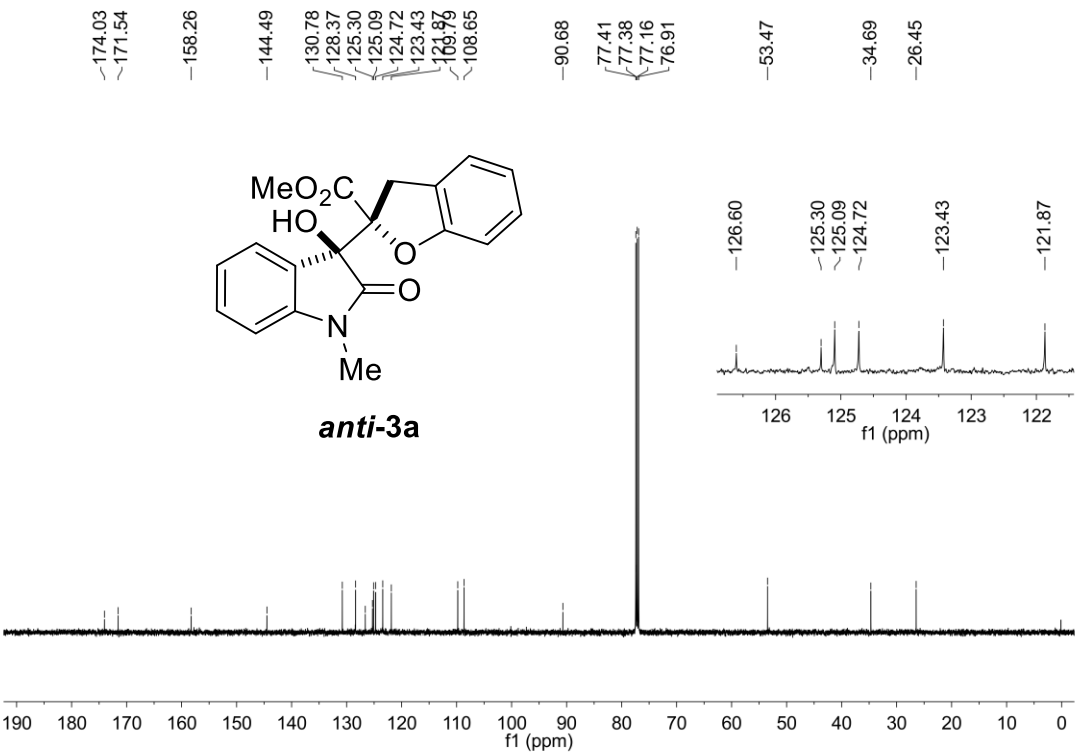
6.85
6.83
4.65
3.81
3.79
3.76
3.64
3.61
3.16
0.00
MeO2C
HO
O
O
N
Me
anti-3a
2.07
2.06
1.05
3.02
1.02
3.00
1.05
1.01
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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90.68
77.41
77.38
77.16
76.91
53.47
34.69
26.45
MeO2C
HO
O
O
N
Me
anti-3a
126.60
125.30
125.09
124.72
123.43
121.87
126 125 124 123 122
f1 (ppm)
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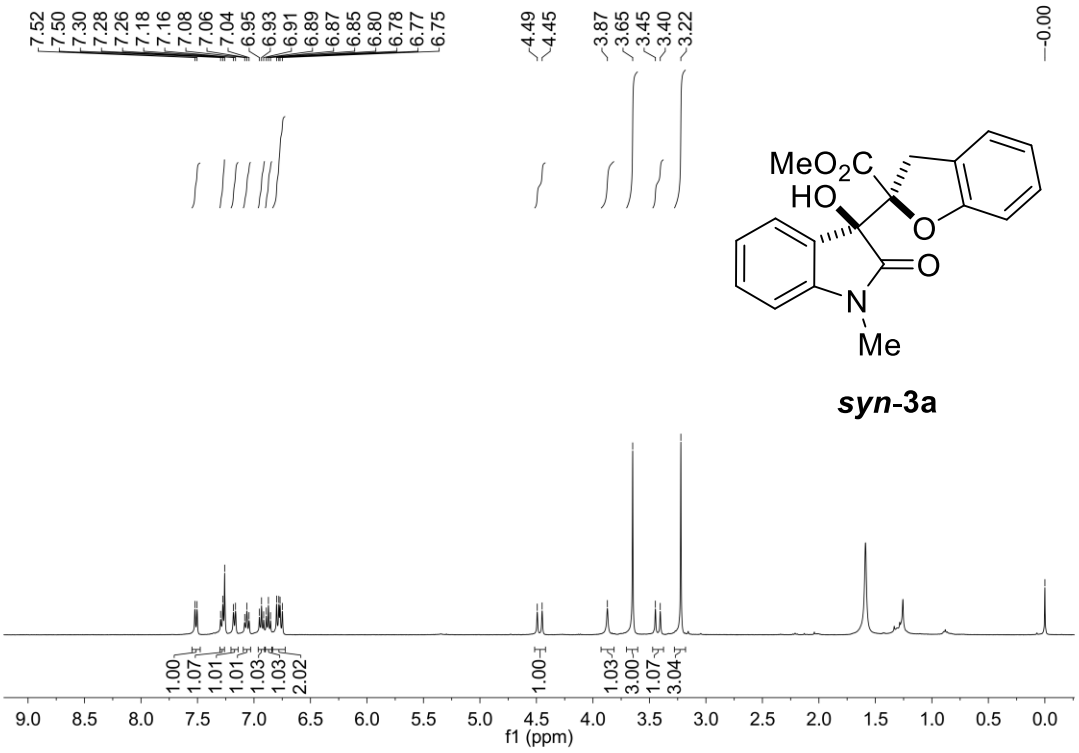
f1 (ppm)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3.45
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1.07
1.01
1.01
1.03
1.03
2.02
1.00
1.03
3.00
1.07
3.04
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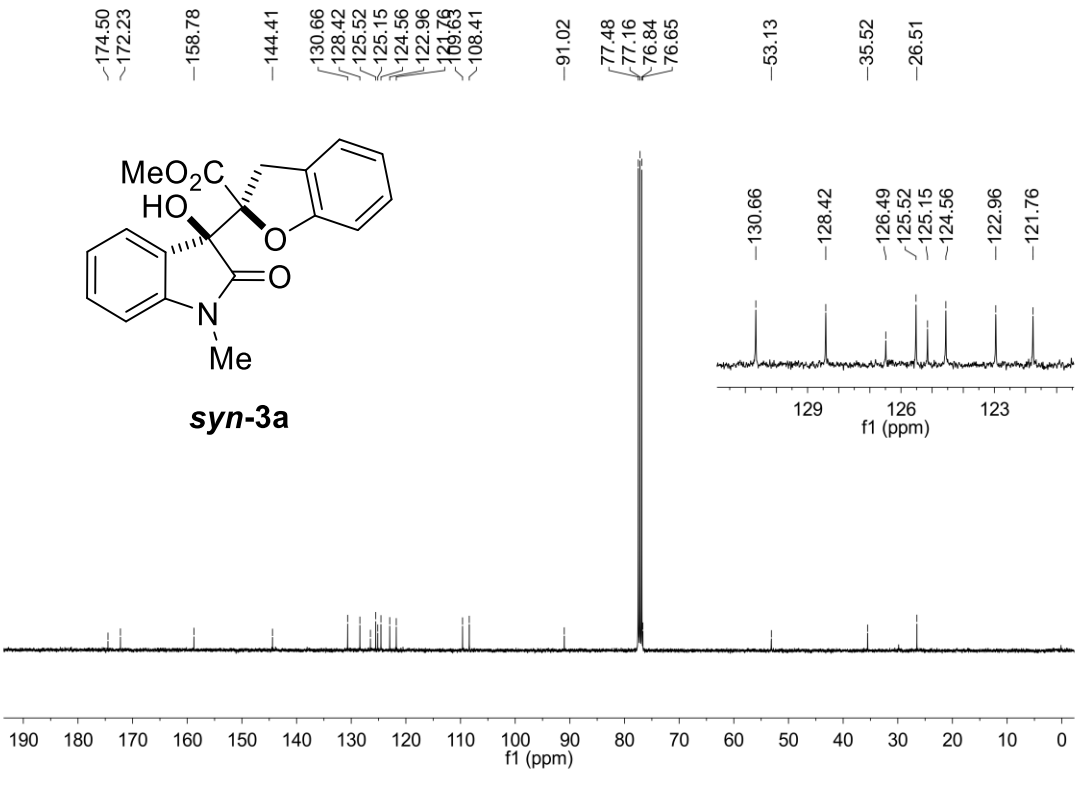
f1 (ppm)

***syn*-3a**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91.02
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76.65
53.13
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128.42
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125.52
125.15
124.56
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123
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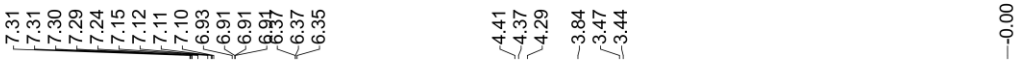
f1 (ppm)

***syn*-3a**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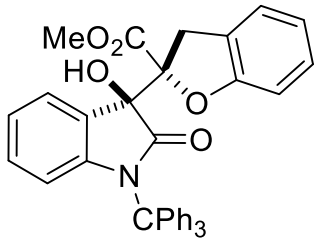
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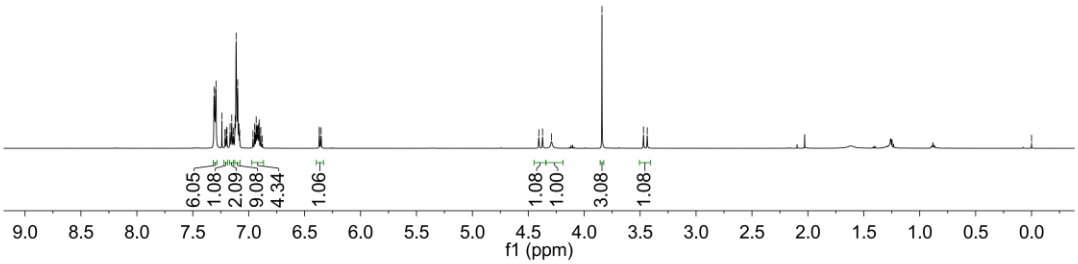
O
N
CPh3

3b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1.08
1.00
3.08
1.08
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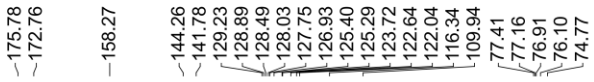
f1 (ppm)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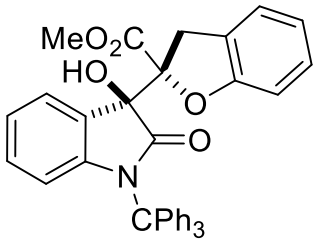
74.77
34.73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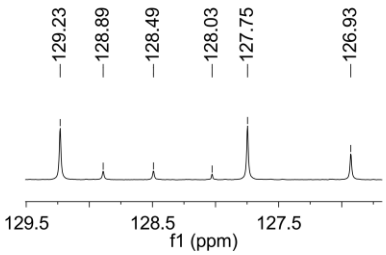
CPh3

3b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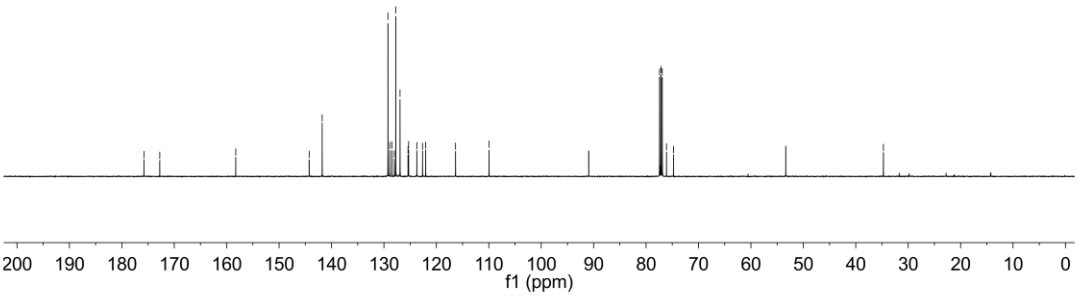
f1 (ppm)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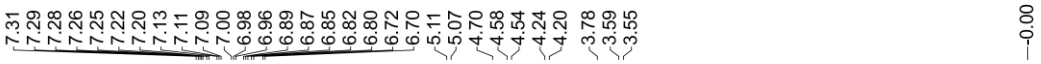
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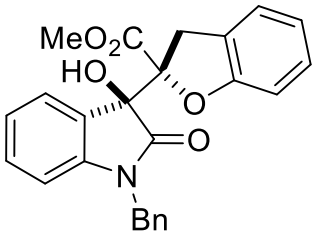
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Bn

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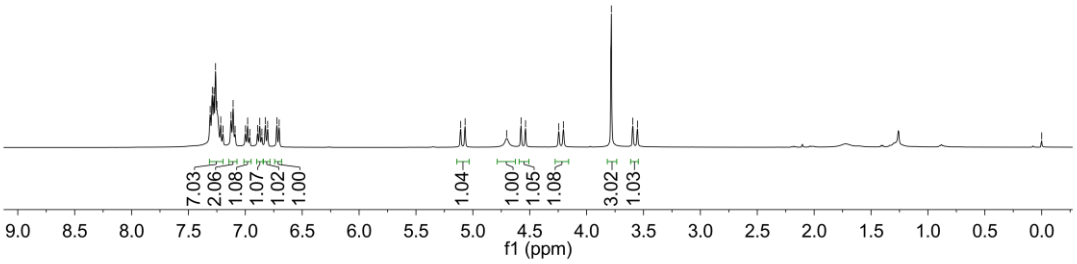
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3.02
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f1 (ppm)


173.87
172.34
158.13
143.69
128.88
128.29
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77.41
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76.91
76.86
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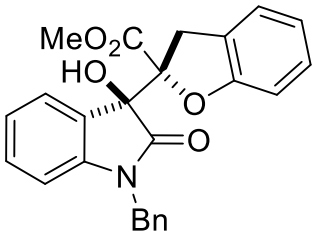
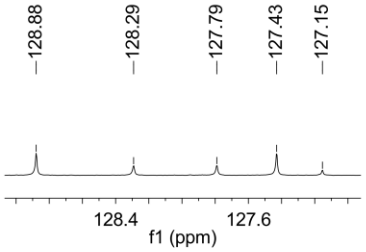
44.03
35.05


MeO2C
HO
O
O
N
Bn

3c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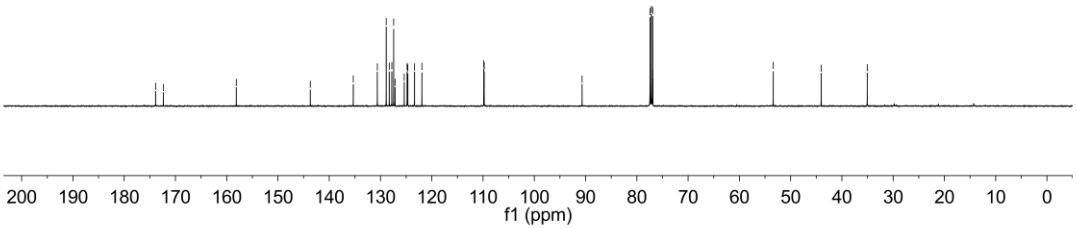
128.29
127.79
127.43
127.15
128.4
127.6
f1 (ppm)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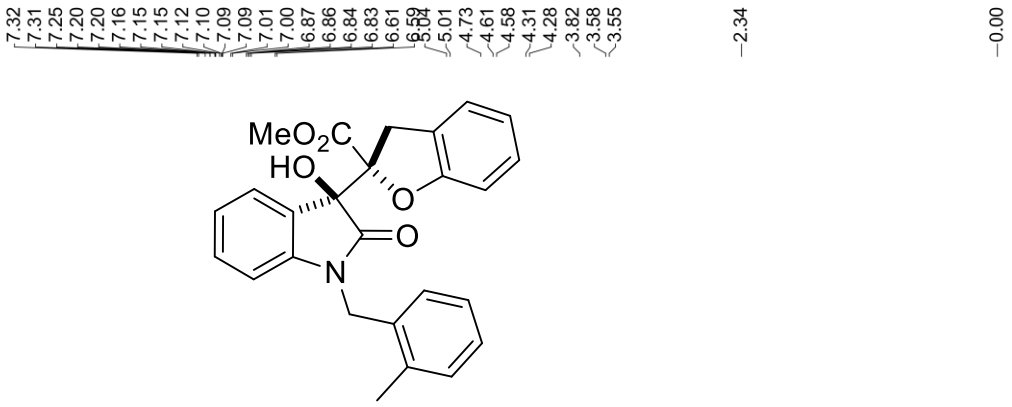
f1 (ppm)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7.15
7.15
7.12
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7.09
7.09
7.01
7.00
6.87
6.86
6.84
6.83
6.61
6.59
5.04
5.01
4.73
4.61
4.58
4.31
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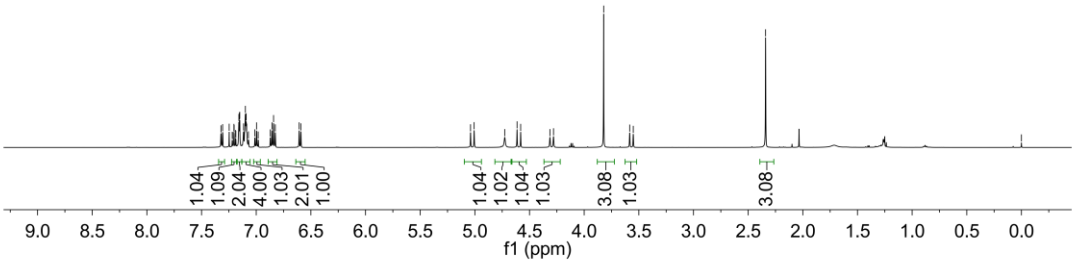
3.82
3.58
3.55
2.34
0.00
MeO2C
HO
O
O
N

3d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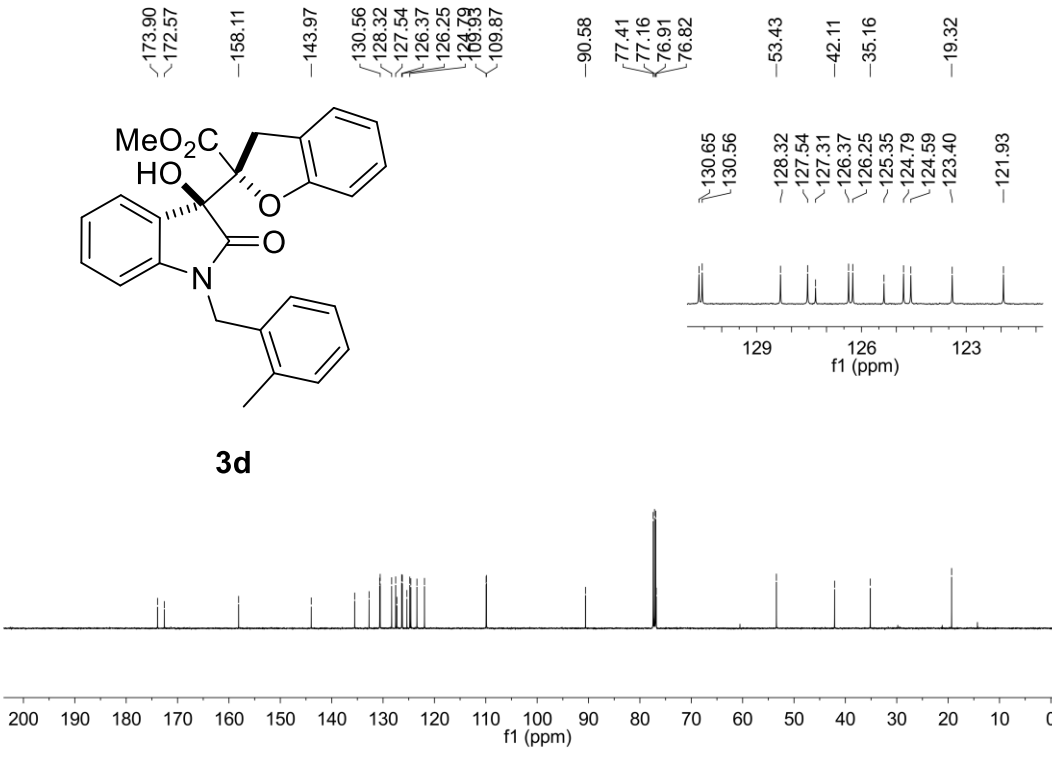
1.09
2.04
4.00
1.03
2.01
1.00
1.04
1.02
1.04
1.03
3.08
1.03
3.08
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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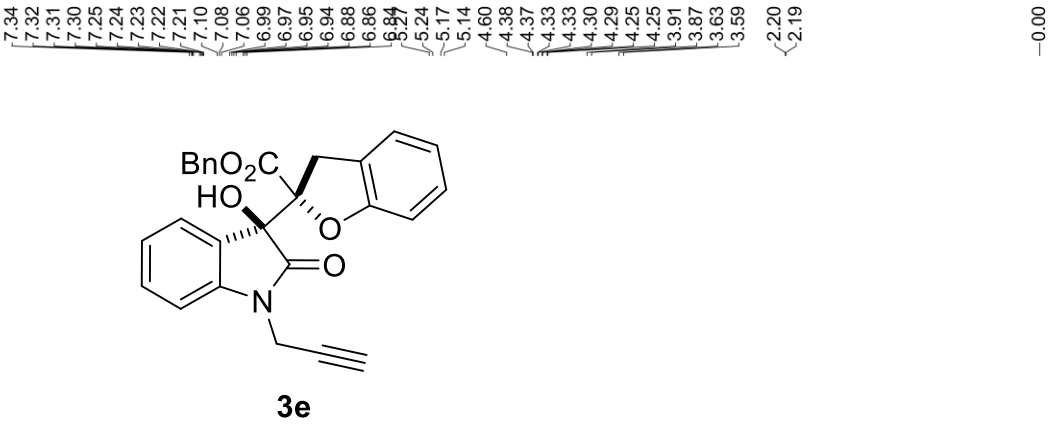
126.25
124.79
109.93
109.87
90.58
77.41
77.16
76.91
76.82
53.43
42.11
35.16
19.32
MeO2C
HO
O
O
N
130.65
130.56
128.32
127.54
127.31
126.37
126.25
125.35
124.79
124.59
123.40
121.93
129
126
123
f1 (ppm)

3d

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.32
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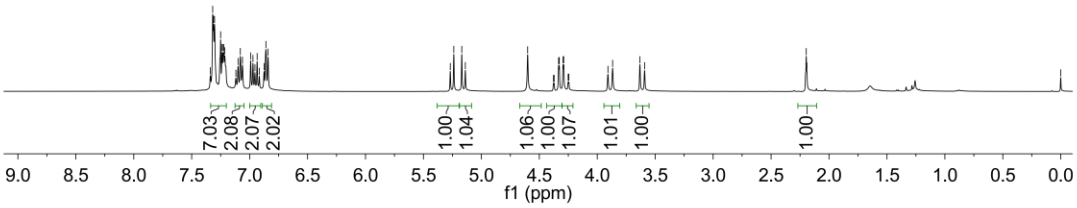
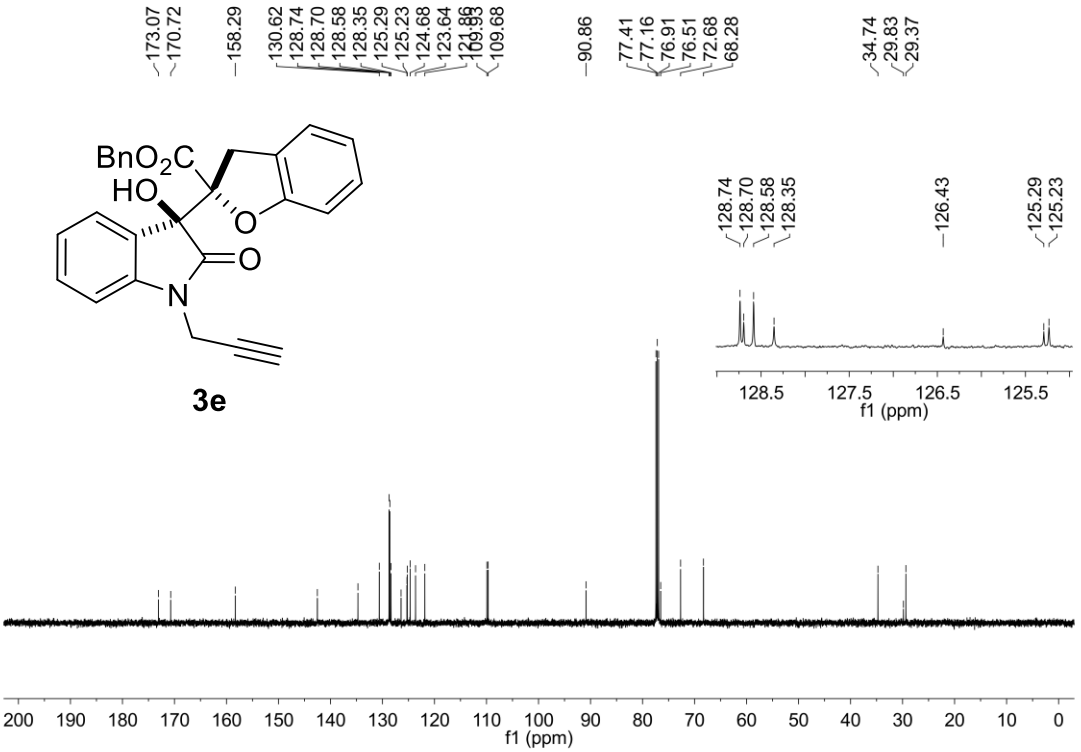
7.24
7.23
7.22
7.21
7.10
7.08
7.06
6.99
6.97
6.95
6.94
6.88
6.86
5.24
5.17
5.14
4.60
4.38
4.37
4.33
4.33
4.30
4.29
4.25
4.25
3.91
3.87
3.63
3.59
2.20
2.19
0.00
BnO2C
HO
O
O
N

3e


7.03
2.08
2.07
2.02
1.00
1.04
1.06
1.00
1.07
1.01
1.00
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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170.72
158.29
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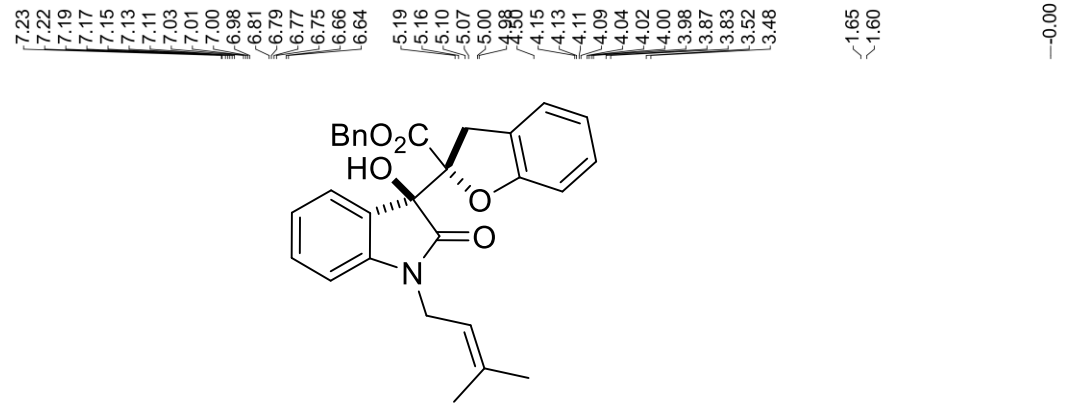
128.70
128.58
128.35
125.29
125.23
124.68
123.64
109.68
90.86
77.41
77.16
76.91
76.51
72.68
68.28
34.74
29.83
29.37
BnO2C
HO
O
O
N
128.74
128.70
128.58
128.35
126.43
125.29
125.23
128.5 127.5 126.5 125.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3e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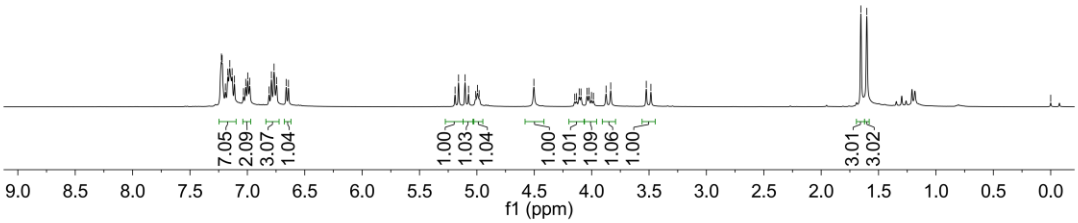
7.22
7.19
7.17
7.15
7.13
7.11
7.03
7.01
7.00
6.98
6.81
6.79
6.77
6.75
6.66
6.64
5.19
5.16
5.10
5.07
5.00
4.98
4.90
4.15
4.13
4.11
4.09
4.04
4.02
4.00
3.98
3.87
3.83
3.52
3.48
1.65
1.60
0.00
BnO2C
HO
O
O
N

3f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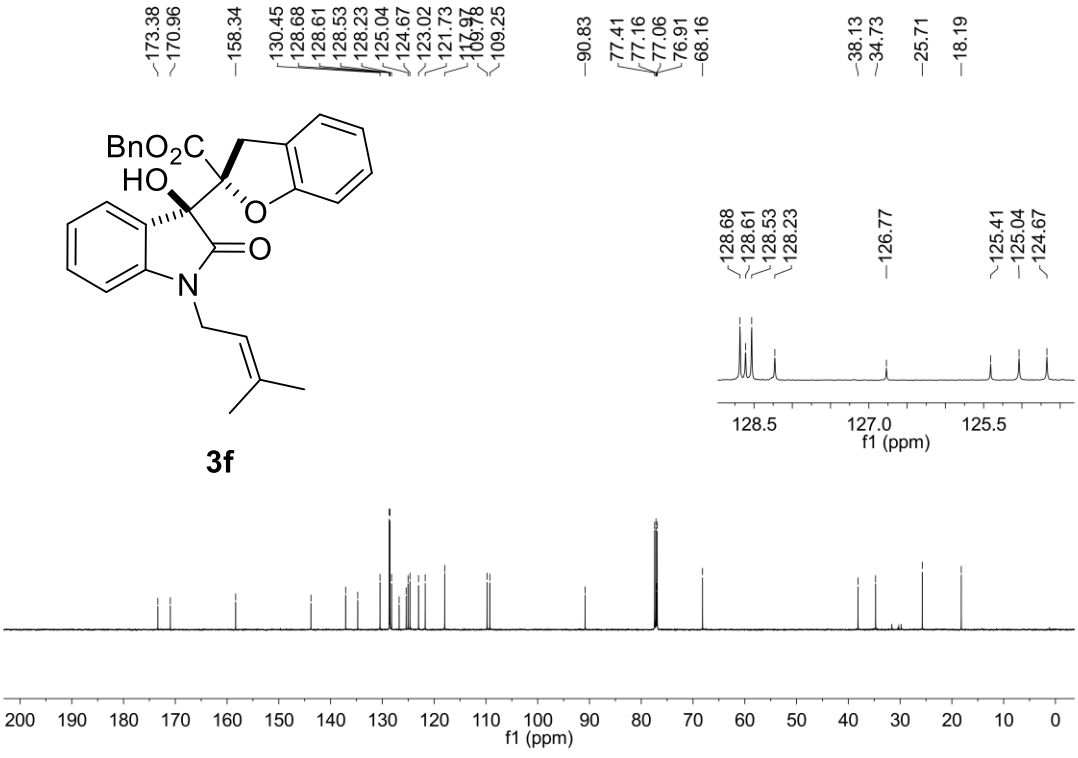
2.09
3.07
1.04
1.00
1.03
1.04
1.00
1.01
1.09
1.06
1.00
3.01
3.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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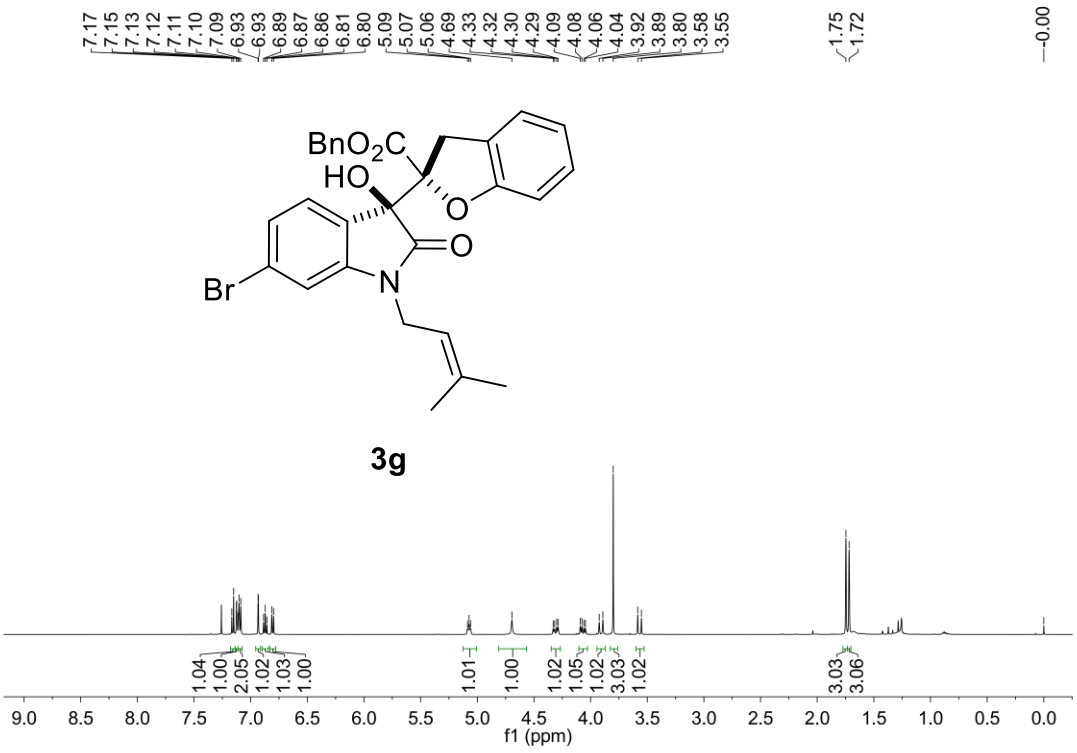
170.96
158.34
130.45
128.68
128.61
128.53
128.23
125.04
124.67
123.02
121.73
117.97
109.78
109.25
90.83
77.41
77.16
77.06
76.91
68.16
38.13
34.73
25.71
18.19
BnO2C
HO
O
O
N
128.68
128.61
128.53
128.23
126.77
125.41
125.04
124.67
128.5
127.0
125.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3f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7.15
7.13
7.12
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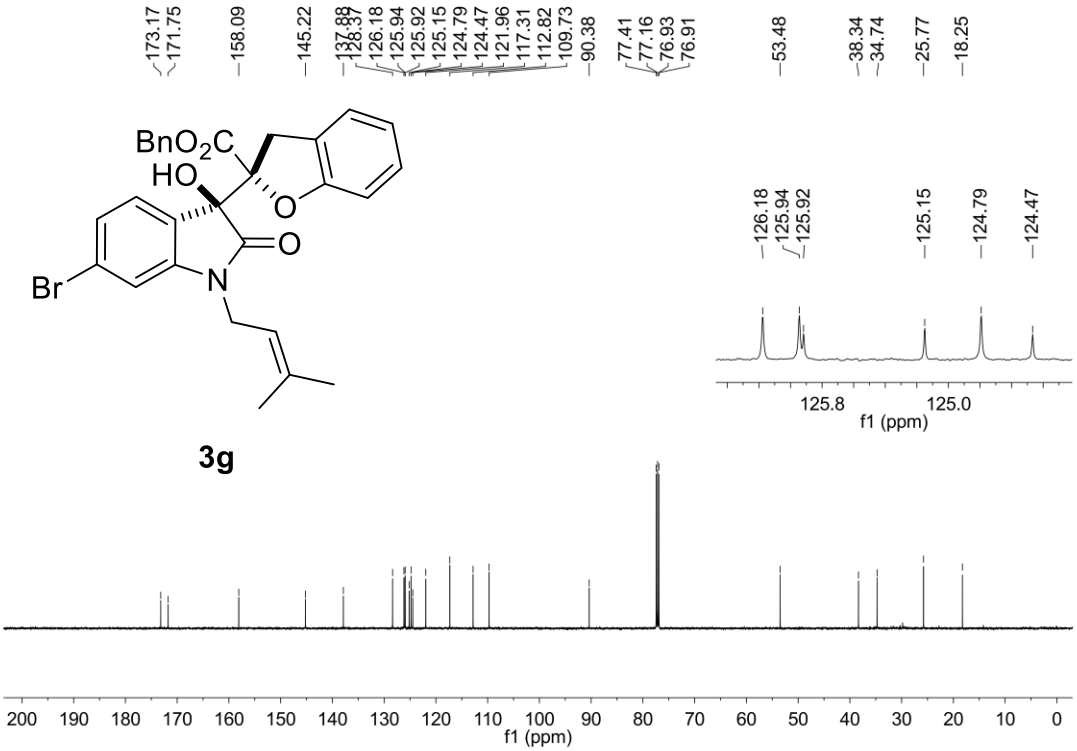
7.10
7.09
6.93
6.93
6.89
6.87
6.86
6.81
6.80
5.09
5.07
5.06
4.69
4.33
4.32
4.30
4.29
4.09
4.08
4.06
4.04
3.92
3.89
3.80
3.58
3.55
1.75
1.72
0.00
BnO2C
HO
O
O
N
Br
3g
1.04
1.00
2.05
1.02
1.03
1.00
1.01
1.00
1.02
1.05
1.02
3.03
1.02
3.03
3.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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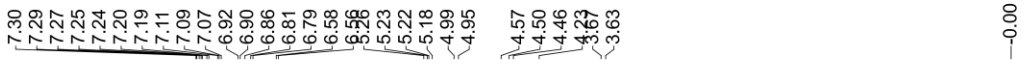
125.94
125.92
125.15
124.79
124.47
121.96
117.31
112.82
109.73
90.38
77.41
77.16
76.93
76.91
53.48
38.34
34.74
25.77
18.25
BnO2C
HO
O
O
N
Br
126.18
125.94
125.92
125.15
124.79
124.47
125.8
125.0
f1 (ppm)
3g
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.29
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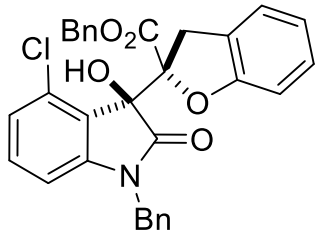
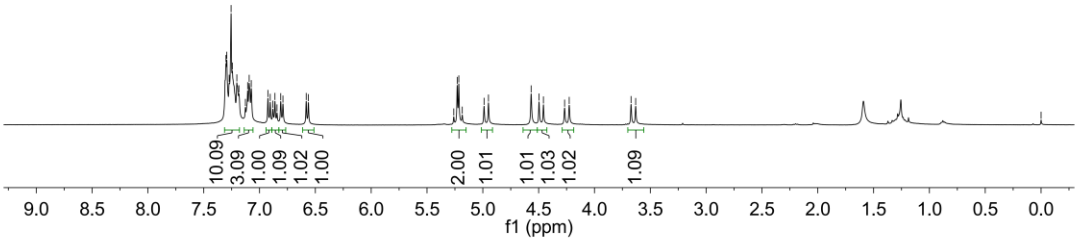
7.25
7.24
7.20
7.19
7.11
7.09
7.07
6.92
6.90
6.86
6.81
6.79
6.58
5.23
5.22
5.18
4.99
4.95
4.57
4.50
4.46
4.23
3.67
3.63
0.00


BnO2C
Cl
HO
O
O
N
Bn

3h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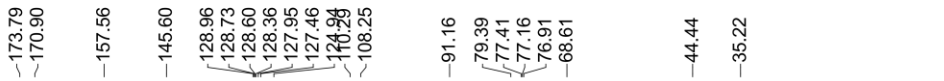
3.09
1.00
1.09
1.02
1.00
2.00
1.01
1.01
1.03
1.02
1.09
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.73
128.60
128.36
127.95
127.46
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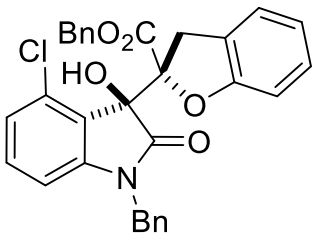
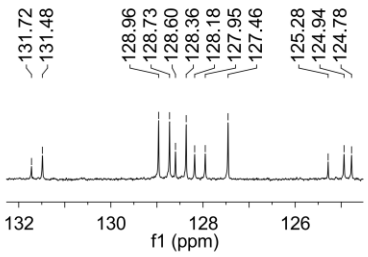
110.29
108.25
91.16
79.39
77.41
77.16
76.91
68.61
44.44
35.22


BnO2C
Cl
HO
O
O
N
Bn

3h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131.48
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128.73
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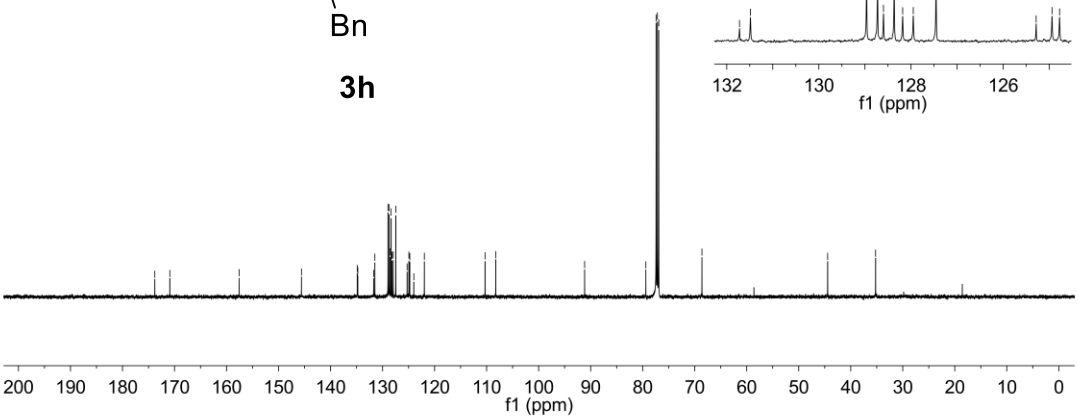
128.36
128.18
127.95
127.46
125.28
124.94
124.78
132 130 128 126
f1 (ppm)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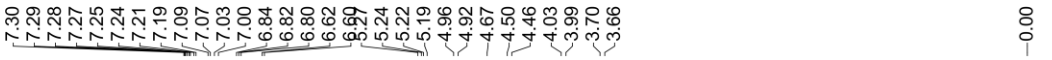
f1 (ppm)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7.21
7.19
7.09
7.07
7.03
7.00
6.84
6.82
6.80
6.62
5.27
5.24
5.22
5.19
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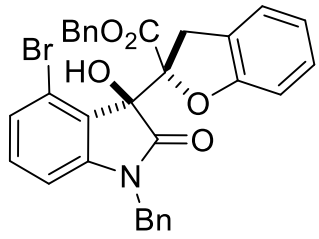
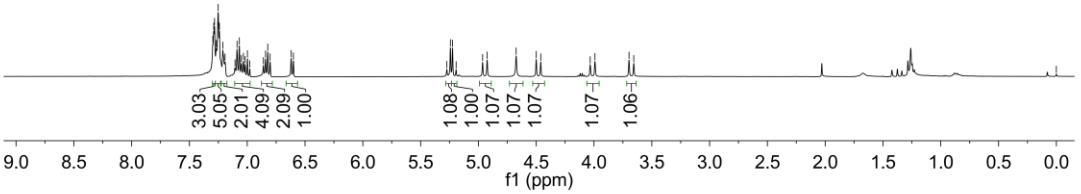
4.92
4.67
4.50
4.46
4.03
3.99
3.70
3.66
0.00


Br
BnO2C
HO
O
O
N
Bn

3i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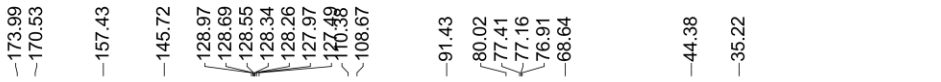
5.05
2.01
4.09
2.09
1.00
1.08
1.00
1.07
1.07
1.07
1.07
1.06
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.34
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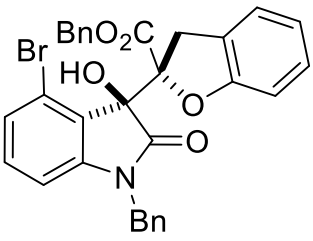
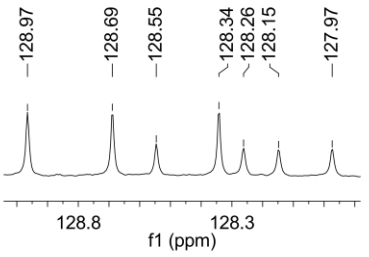
80.02
77.41
77.16
76.91
68.64
44.38
35.22


Br
BnO2C
HO
O
O
N
Bn

3i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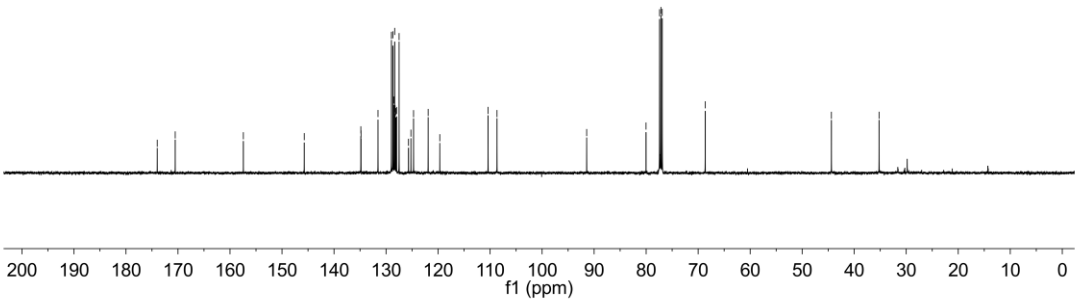
128.26
128.15
127.97
128.8
128.3
f1 (ppm)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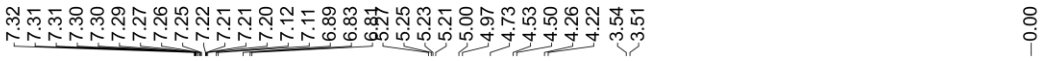
f1 (ppm)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7.26
7.25
7.22
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7.21
7.20
7.12
7.11
6.89
6.83
5.27
5.25
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5.21
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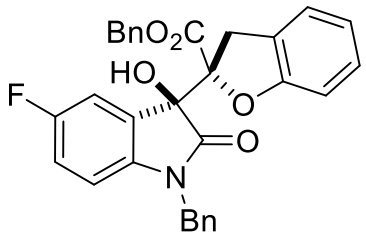
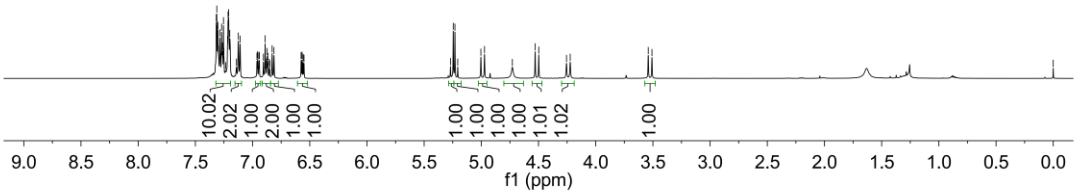
4.97
4.73
4.53
4.50
4.26
4.22
3.54
3.51
0.00


BnO2C
HO
F
O
O
N
Bn

3j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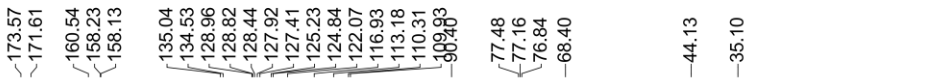
2.00
1.00
1.00
1.00
1.00
1.00
1.01
1.02
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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158.23
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135.04
134.53
128.96
128.82
128.44
127.92
127.41
125.23
124.84
122.07
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113.18
110.31
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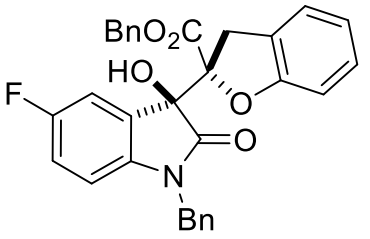
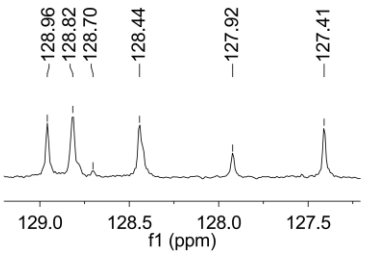
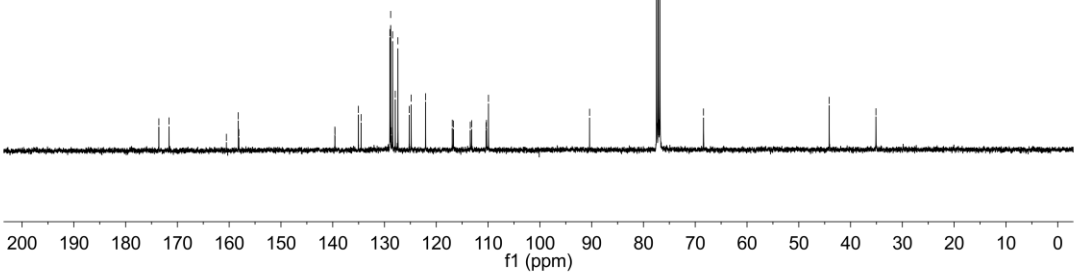
90.40
77.48
77.16
76.84
68.40
44.13
35.10


BnO2C
HO
F
O
O
N
Bn

3j


128.96
128.82
128.70
128.44
127.92
127.41
129.0 128.5 128.0 127.5
f1 (ppm)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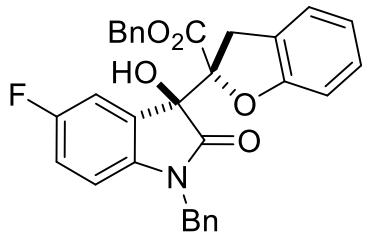
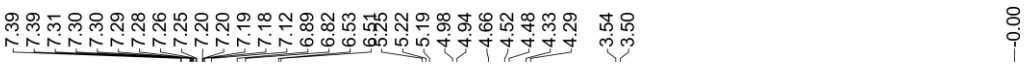
f1 (ppm)


BnO2C
HO
F
O
O
N
Bn

3j

-118.96
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)


7.39
7.39
7.31
7.30
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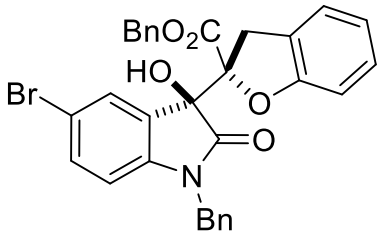
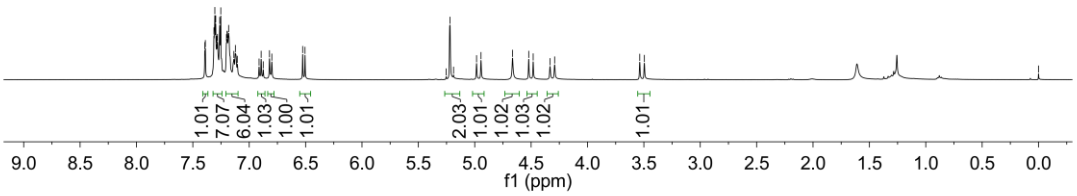
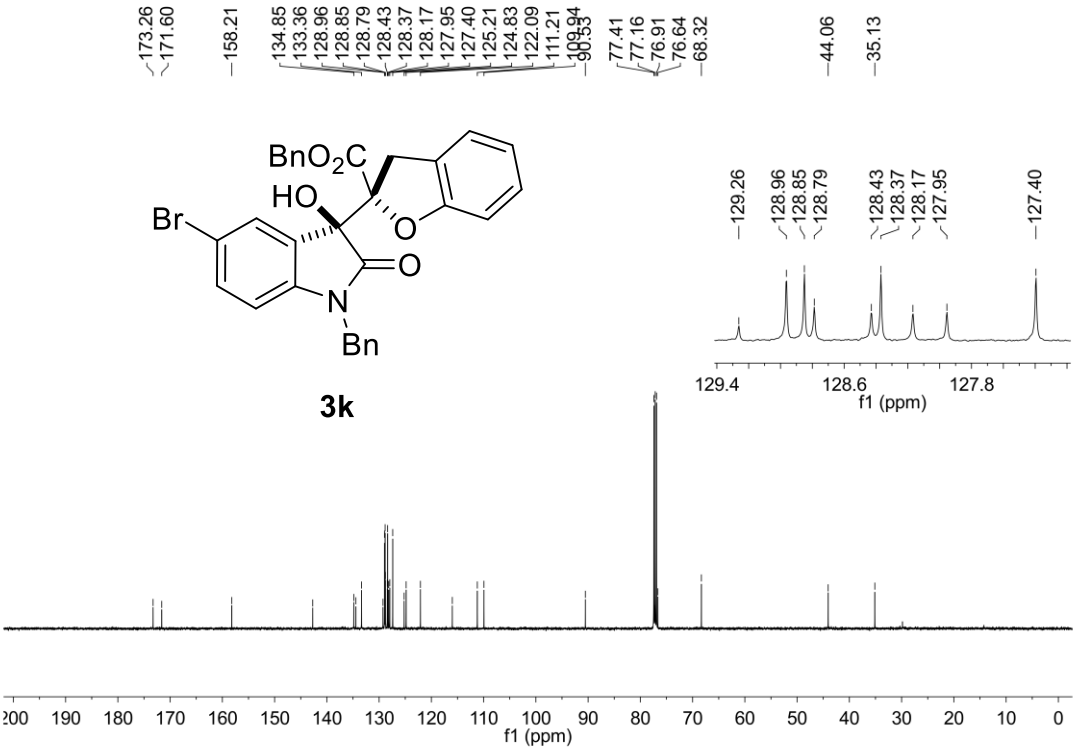
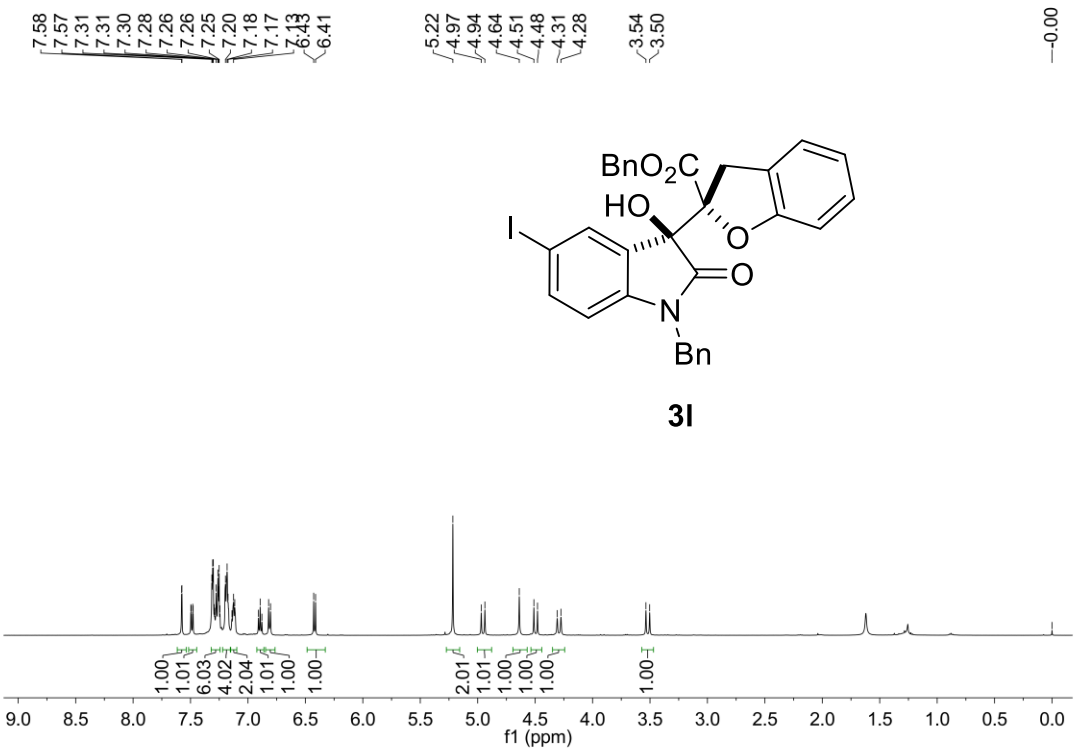
7.29
7.28
7.26
7.25
7.20
7.20
7.19
7.18
7.12
6.89
6.82
6.53
6.51
5.25
5.22
5.19
4.98
4.94
4.66
4.52
4.48
4.33
4.29
3.54
3.50
-0.00


BnO2C
HO
Br
O
O
N
Bn

3k


1.01
7.07
6.04
1.03
1.00
1.01
2.03
1.01
1.02
1.03
1.02
1.01
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


173.26
171.60
158.21
134.85
133.36
128.96
128.85
128.79
128.43
128.37
128.17
127.95
127.40
125.21
124.83
122.09
111.21
77.41
77.16
76.91
76.64
68.32
44.06
35.13
BnO2C
HO
Br
O
O
N
Bn
129.26
128.96
128.85
128.79
128.43
128.37
128.17
127.95
127.40
129.4
128.6
127.8
f1 (ppm)
3k
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.58
7.57
7.31
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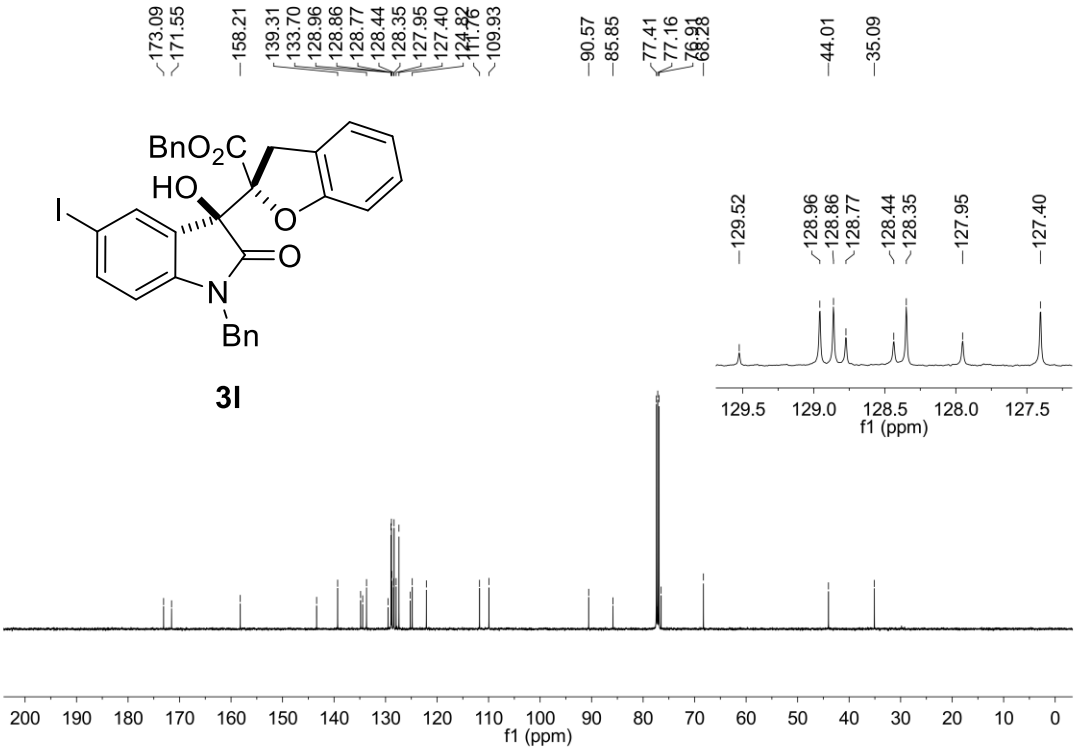
7.28
7.26
7.26
7.25
7.20
7.18
7.17
7.13
6.43
6.41
5.22
4.97
4.94
4.64
4.51
4.48
4.31
4.28
3.54
3.50
0.00
BnO2C
HO
I
O
O
N
Bn
3l
1.00
1.01
6.03
4.02
2.04
1.01
1.00
1.00
2.01
1.01
1.00
1.00
1.00
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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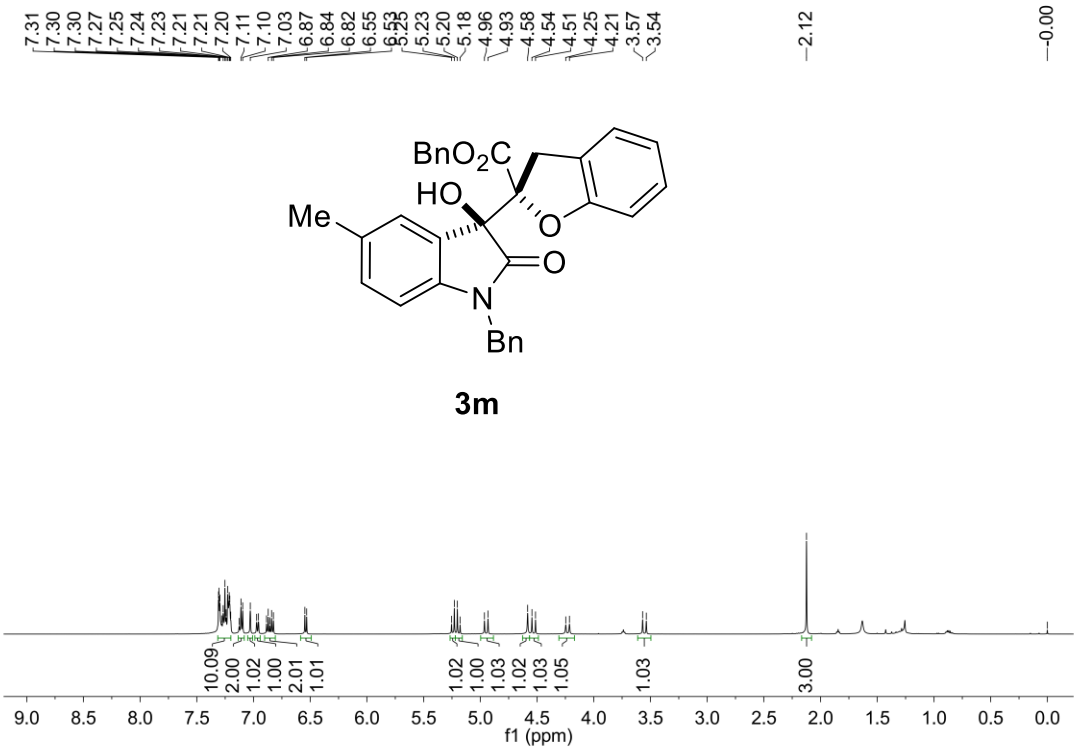
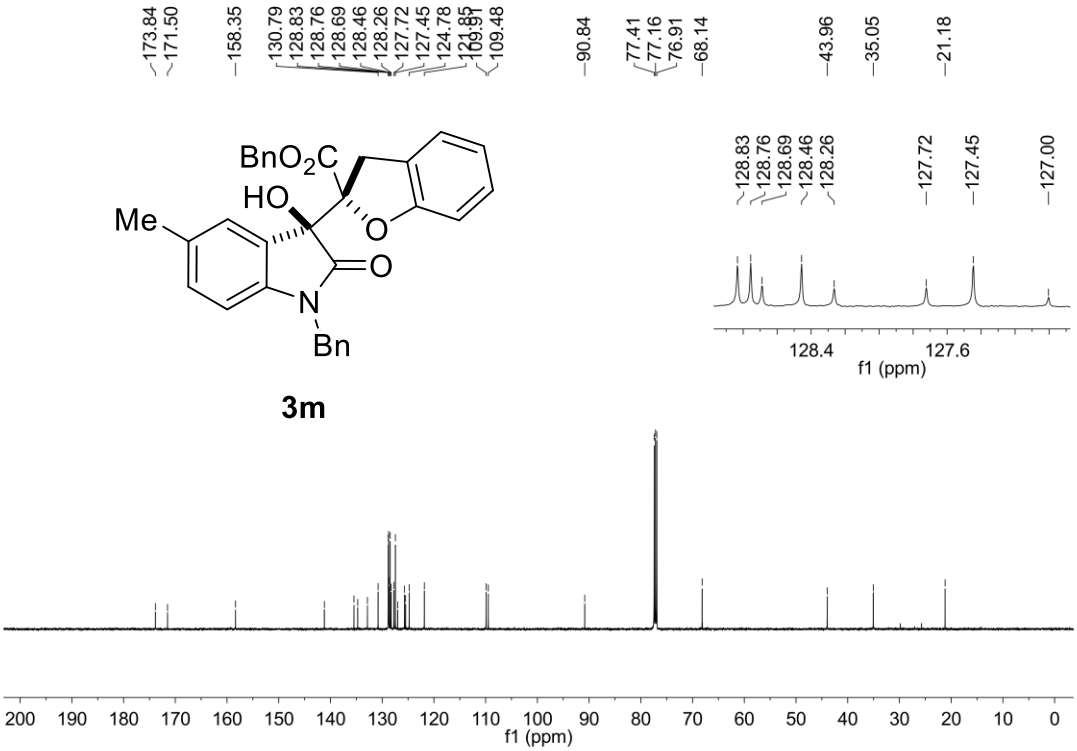
171.55
158.21
139.31
133.70
128.96
128.86
128.77
128.44
128.35
127.95
127.40
111.76
109.93
90.57
85.85
77.41
77.16
76.91
68.28
44.01
35.09
BnO2C
HO
I
O
O
N
Bn
129.52
128.96
128.86
128.77
128.44
128.35
127.95
127.40
129.5
129.0
128.5
128.0
127.5
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3l


7.31
7.30
7.30
7.27
7.25
7.24
7.23
7.21
7.21
7.20
7.11
7.10
7.03
6.87
6.84
6.82
6.55
5.23
5.20
5.18
4.96
4.93
4.58
4.54
4.51
4.25
4.21
3.57
3.54
2.12
0.00
BnO2C
HO
Me
O
O
N
Bn
10.09
2.00
1.02
1.00
2.01
1.01
1.02
1.00
1.03
1.02
1.03
1.05
1.03
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

3m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171.50
158.35
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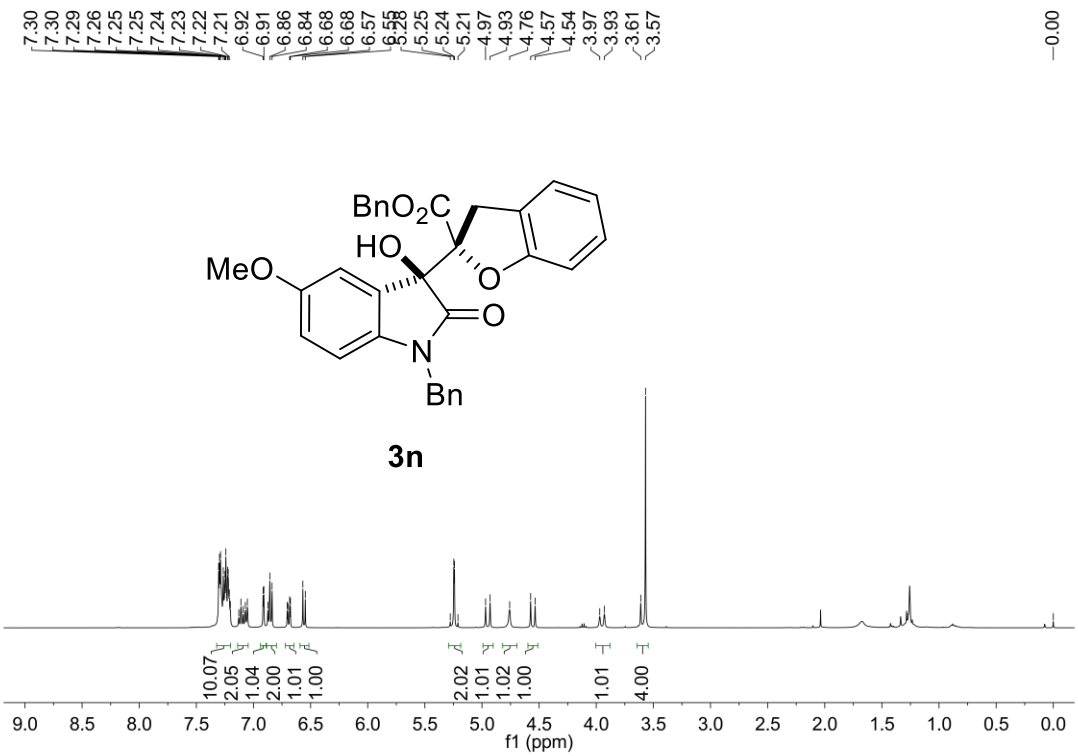
128.76
128.69
128.46
128.26
127.72
127.45
124.78
109.91
109.48
90.84
77.41
77.16
76.91
68.14
43.96
35.05
21.18
BnO2C
HO
Me
O
O
N
Bn
128.83
128.76
128.69
128.46
128.26
127.72
127.45
127.00
128.4
127.6
f1 (ppm)
3m
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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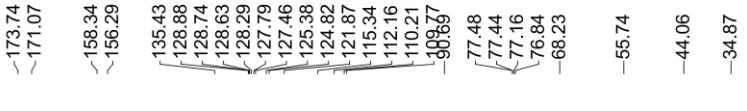
7.30
7.29
7.26
7.25
7.25
7.24
7.23
7.22
7.21
6.92
6.91
6.86
6.84
6.68
6.68
6.57
5.25
5.24
5.21
4.97
4.93
4.76
4.57
4.54
3.97
3.93
3.61
3.57
0.00
BnO2C
HO
MeO
O
O
N
Bn
3n
10.07
2.05
1.04
2.00
1.01
1.00
2.02
1.01
1.02
1.00
1.01
4.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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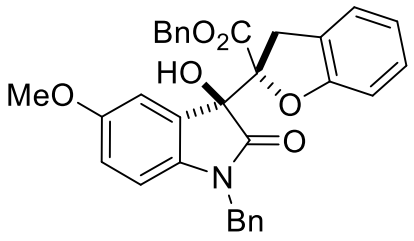
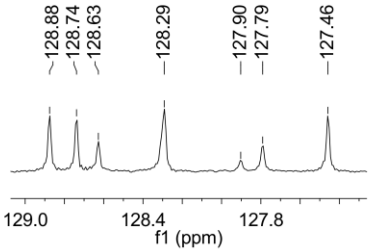
128.88
128.74
128.63
128.29
127.79
127.46
125.38
124.82
121.87
115.34
112.16
110.21
77.48
77.44
77.16
76.84
68.23
55.74
44.06
34.87


BnO2C
HO
MeO
O
O
N
Bn

3n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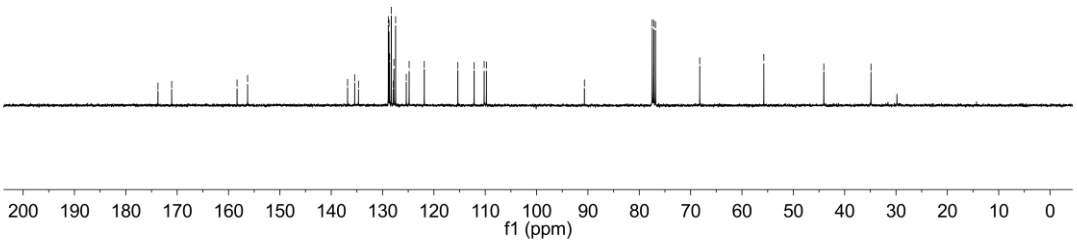
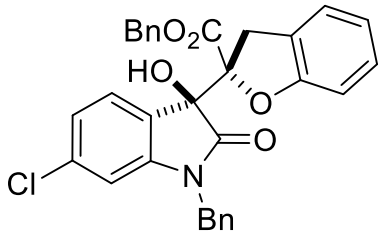
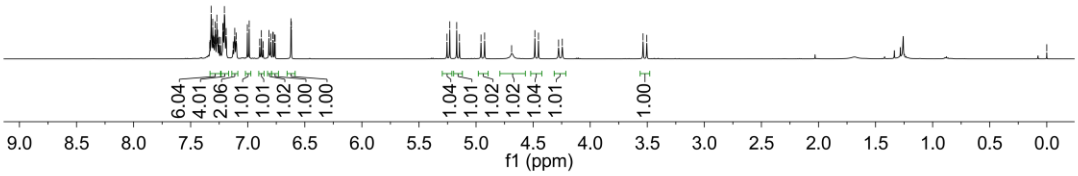
128.74
128.63
128.29
127.90
127.79
127.46
129.0
128.4
127.8
f1 (ppm)

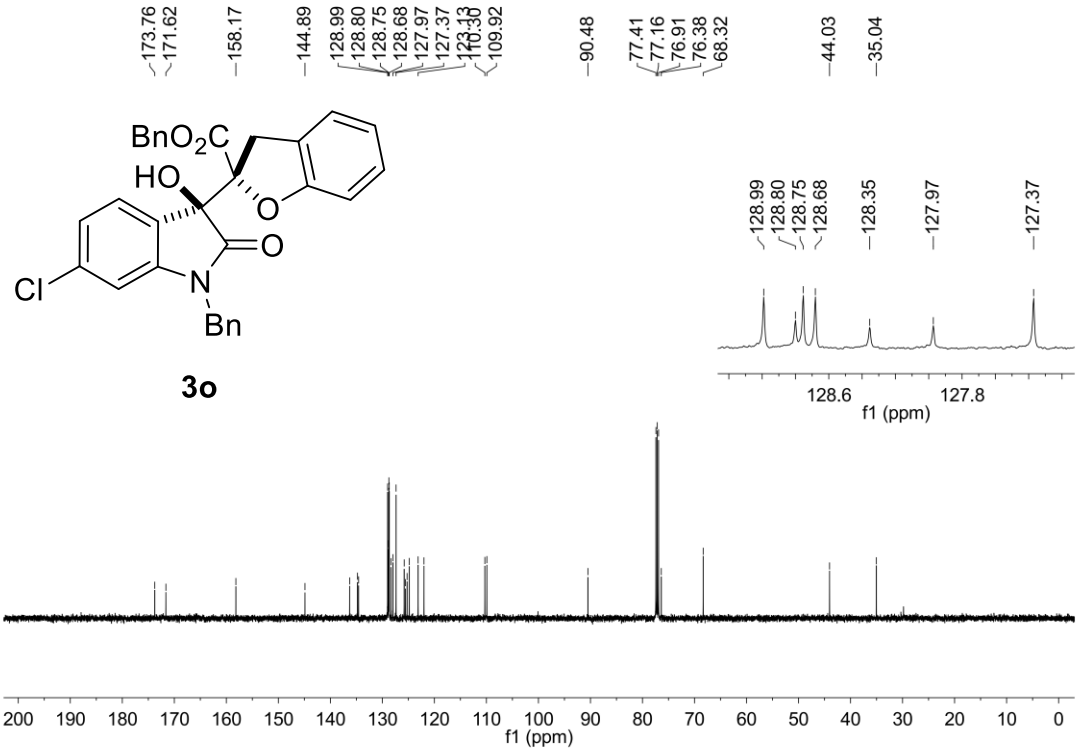

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.32
7.31
7.29
7.27
7.26
7.22
7.22
7.20
7.19
7.11
7.00
6.99
6.88
6.81
6.78
6.78
6.62
5.23
5.17
5.15
4.96
4.92
4.69
4.48
4.45
4.28
4.24
3.54
3.50
0.00


BnO2C
HO
O
O
Cl
N
Bn

3o


6.04
4.01
2.06
1.01
1.01
1.02
1.00
1.00
1.04
1.01
1.02
1.02
1.04
1.01
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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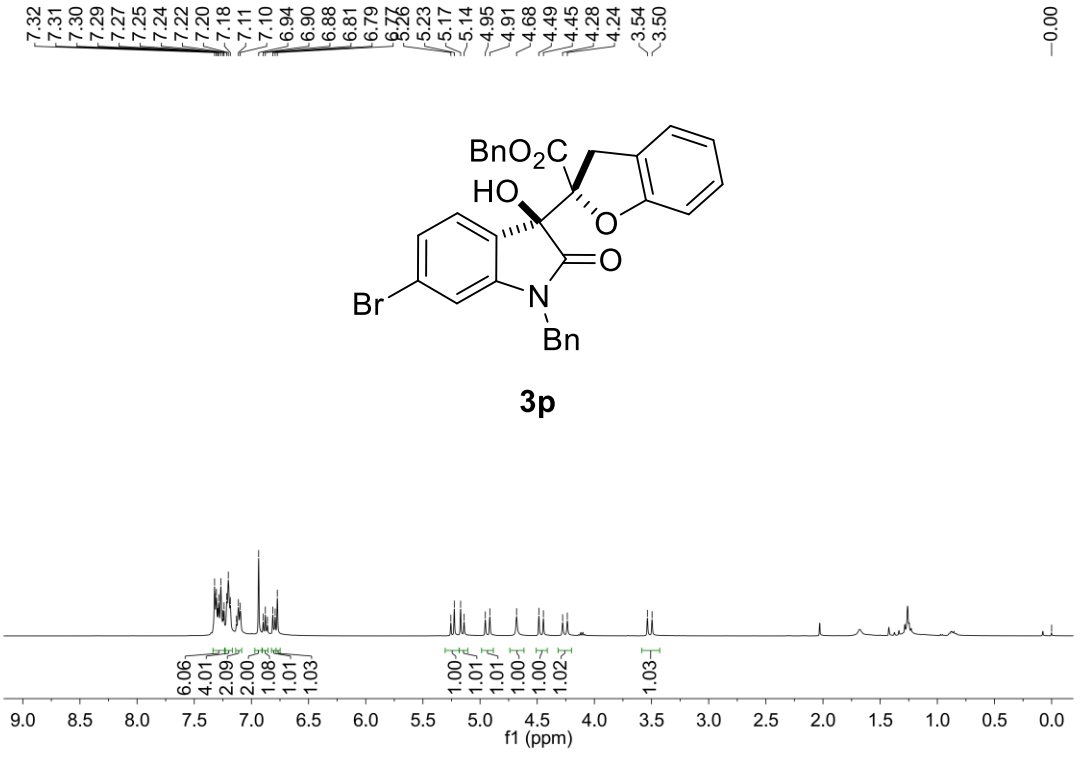
128.80
128.75
128.68
127.97
127.37
110.30
109.92
90.48
77.41
77.16
76.91
76.38
68.32
44.03
35.04
BnO2C
HO
O
O
Cl
N
Bn
128.99
128.80
128.75
128.68
128.35
127.97
127.37
128.6
127.8
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3o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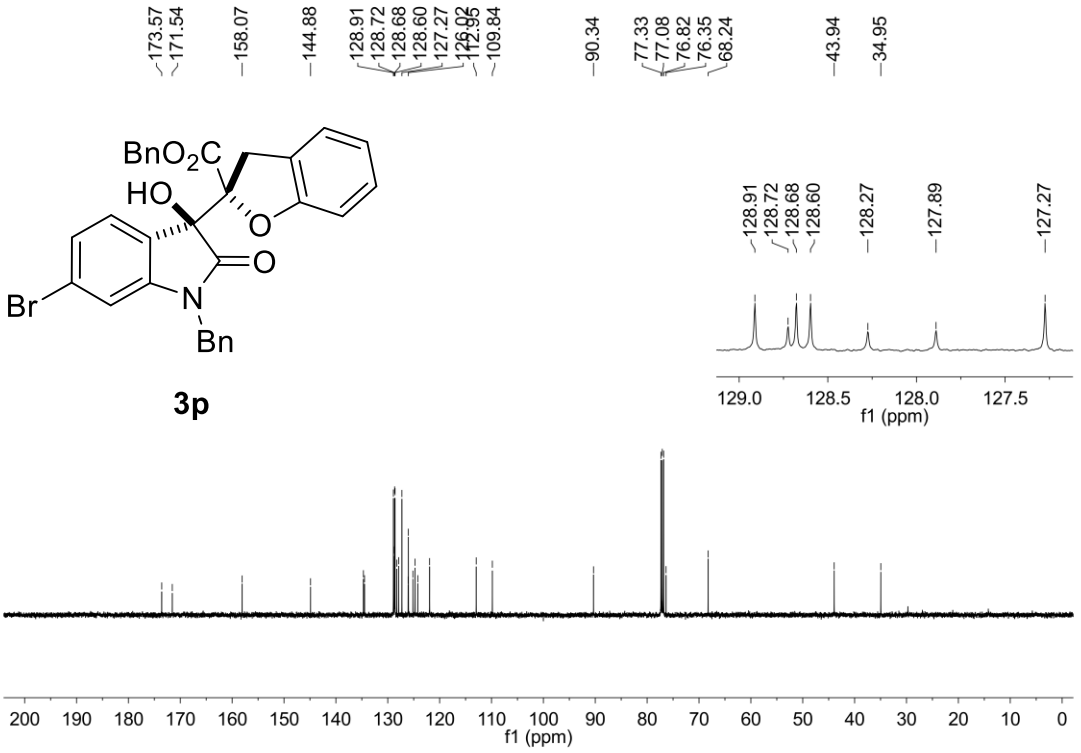
7.31
7.30
7.29
7.27
7.25
7.24
7.22
7.20
7.18
7.11
7.10
6.94
6.90
6.88
6.81
6.79
5.26
5.23
5.17
5.14
4.95
4.91
4.68
4.49
4.45
4.28
4.24
3.54
3.50
0.00
BnO2C
HO
O
O
Br
N
Bn
6.06
4.01
2.09
2.00
1.08
1.01
1.03
1.00
1.01
1.01
1.00
1.00
1.02
1.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

3p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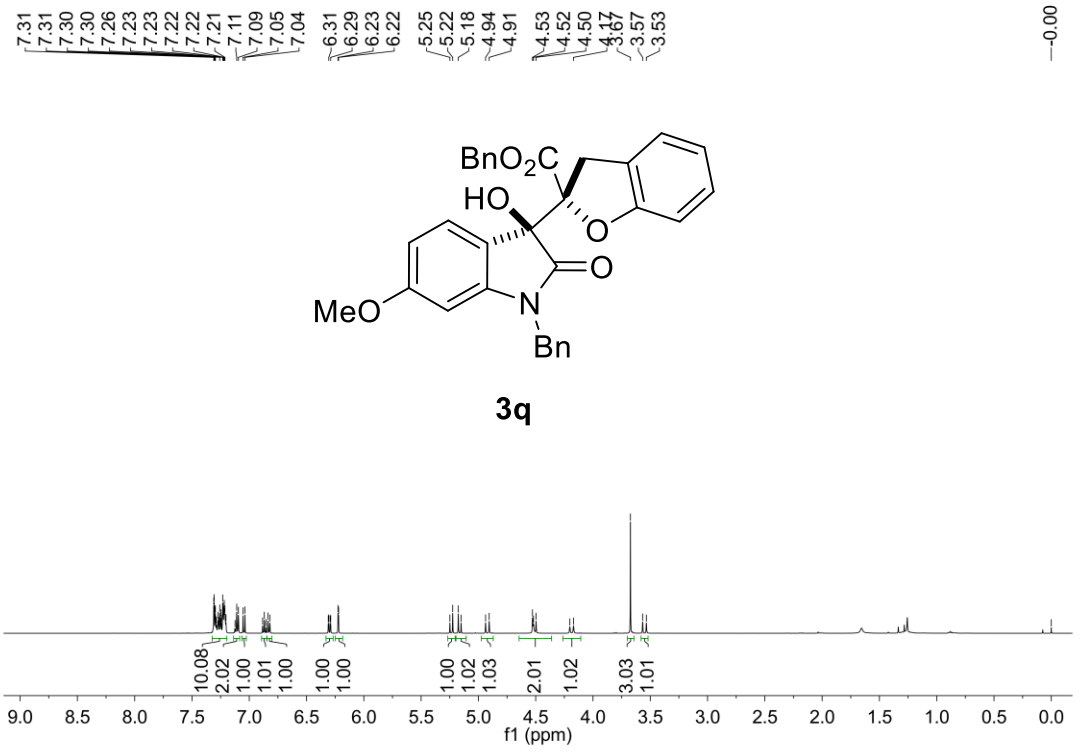
128.60
127.27
109.84
90.34
77.33
77.08
76.82
76.35
68.24
43.94
34.95
BnO2C
HO
O
O
Br
N
Bn
3p
128.91
128.72
128.68
128.60
128.27
127.89
127.27
129.0
128.5
128.0
127.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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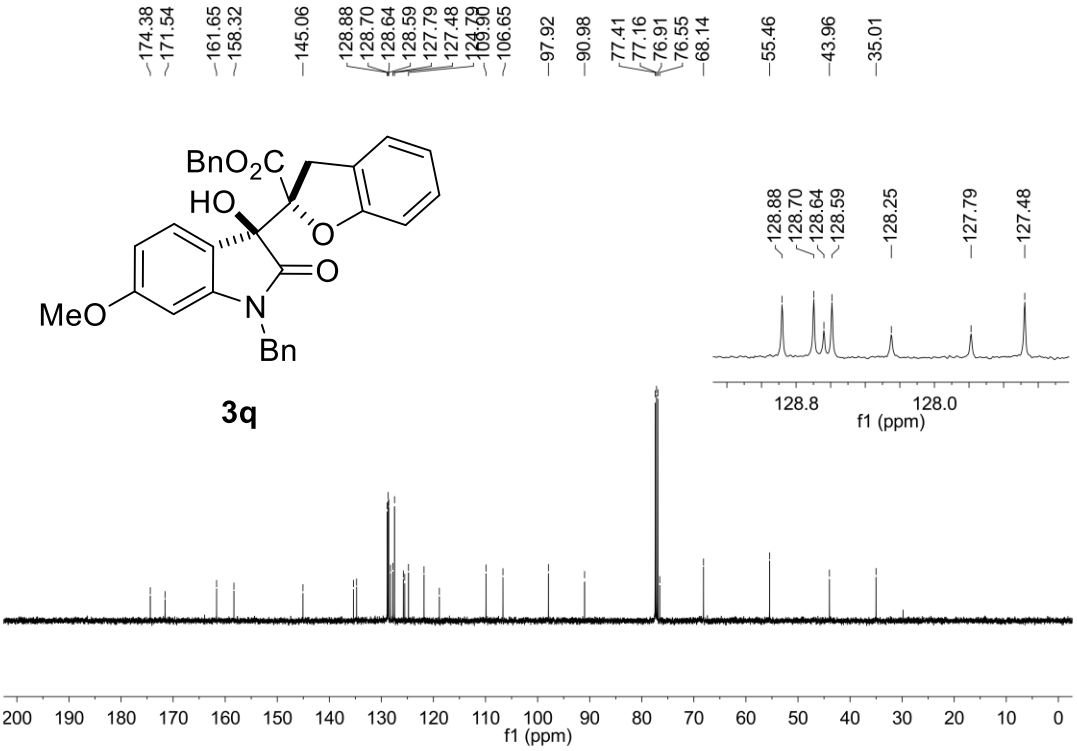
7.31
7.30
7.30
7.26
7.23
7.23
7.22
7.22
7.21
7.11
7.09
7.05
7.04
6.31
6.29
6.23
6.22
5.25
5.22
5.18
4.94
4.91
4.53
4.52
4.50
4.17
3.67
3.57
3.53
0.00
BnO2C
HO
O
O
MeO
N
Bn
3q
10.08
2.02
1.00
1.01
1.00
1.00
1.00
1.00
1.02
1.03
2.01
1.02
3.03
1.01
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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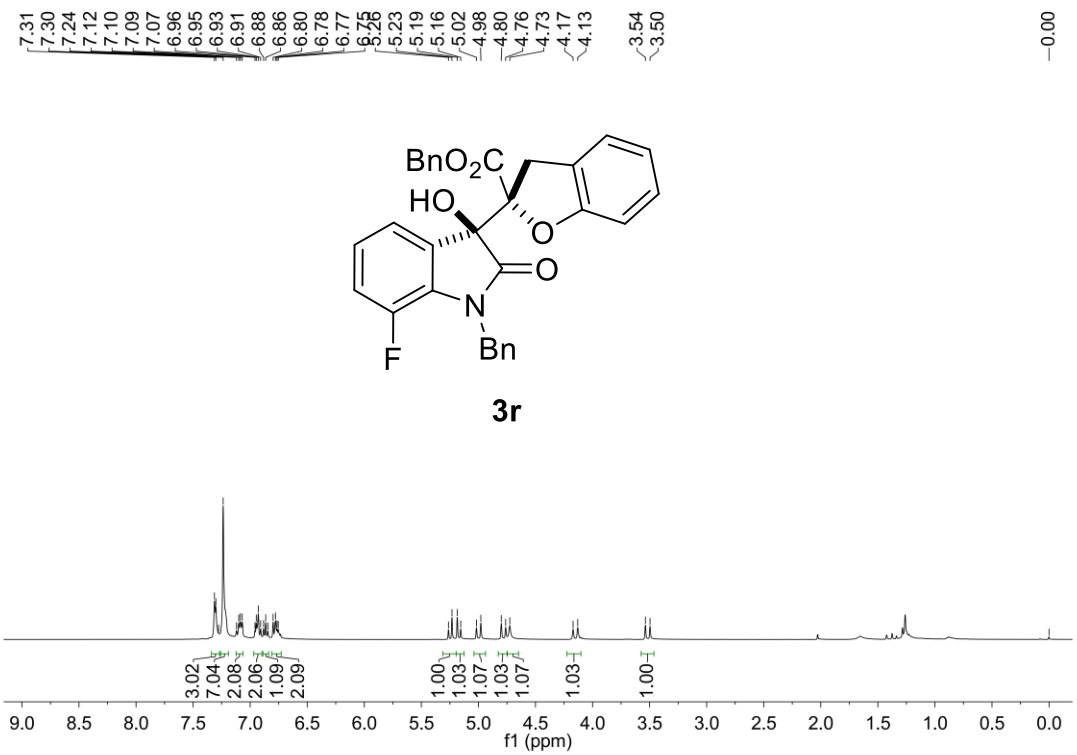
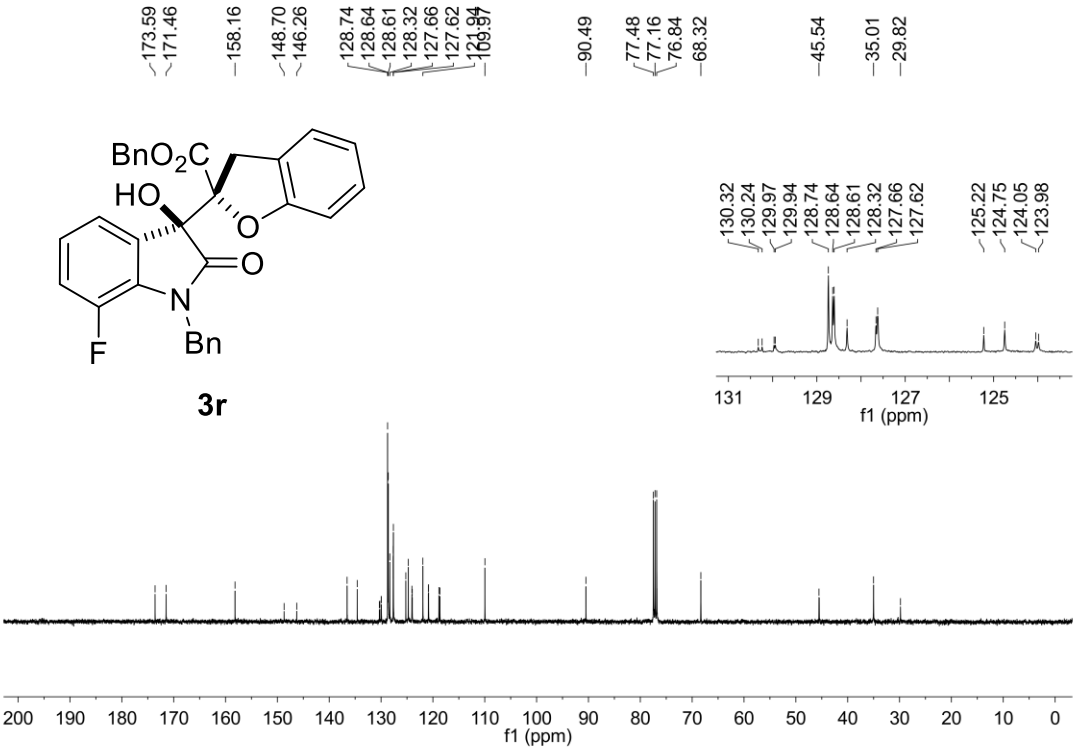
158.32
145.06
128.88
128.70
128.64
128.59
127.79
127.48
106.65
97.92
90.98
77.41
77.16
76.91
76.55
68.14
55.46
43.96
35.01
BnO2C
HO
O
O
MeO
N
Bn
3q
128.88
128.70
128.64
128.59
128.25
127.79
127.48
128.8
128.0
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.31
7.30
7.24
7.12
7.10
7.09
7.07
6.96
6.95
6.93
6.91
6.88
6.86
6.80
6.78
6.77
5.23
5.19
5.16
5.02
4.98
4.80
4.76
4.73
4.17
4.13
3.54
3.50
0.00
BnO2C
HO
O
O
N
F
Bn
3r
3.02
7.04
2.08
2.06
1.09
2.09
1.00
1.03
1.07
1.03
1.07
1.03
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


173.59
171.46
158.16
148.70
146.26
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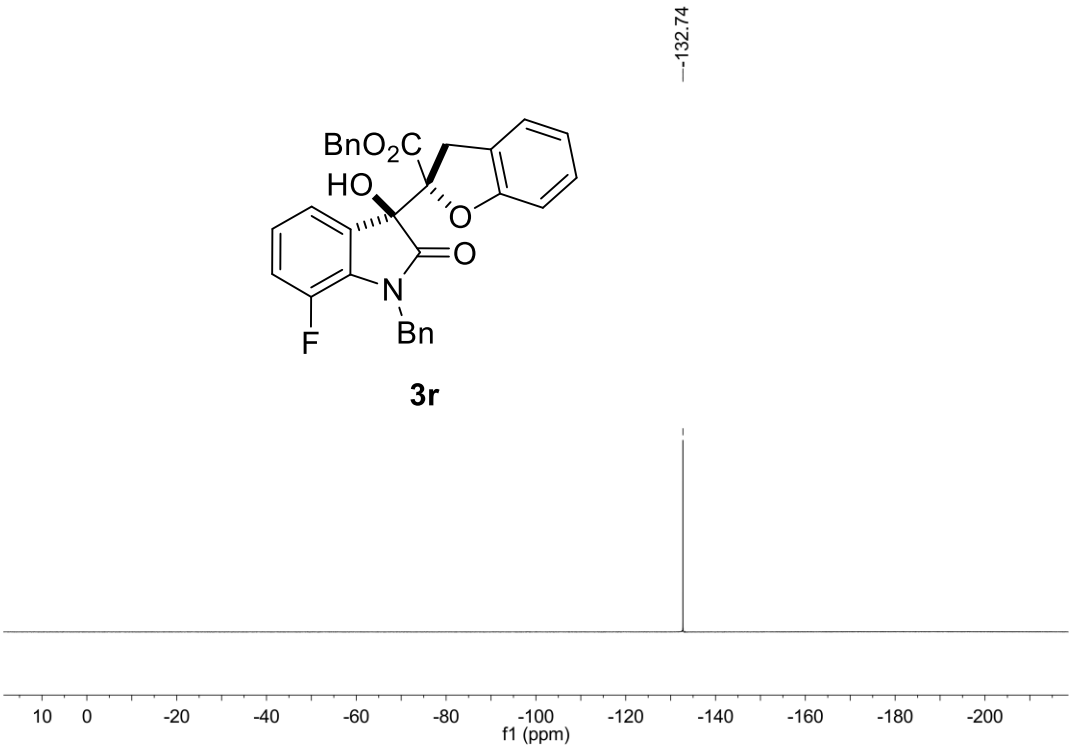
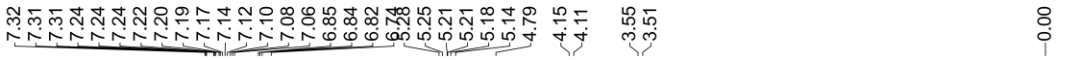
128.64
128.61
128.32
127.66
127.62
121.94
90.49
77.48
77.16
76.84
68.32
45.54
35.01
29.82
BnO2C
HO
O
O
N
Bn
F
3r
130.32
130.24
129.97
129.94
128.74
128.64
128.61
128.32
127.66
127.62
125.22
124.75
124.05
123.98
131
129
127
125
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-132.74
BnO2C
HO
O
O
N
Bn
F
3r
10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200
f1 (ppm)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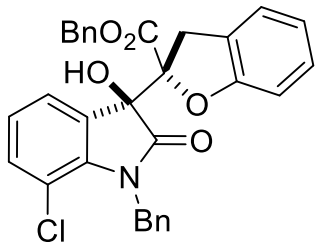
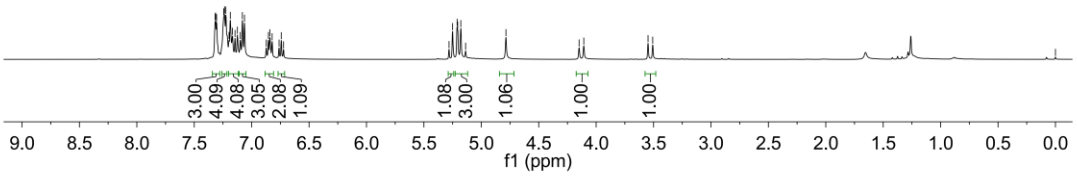
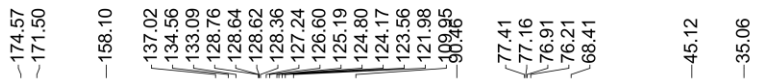
7.31
7.31
7.24
7.24
7.24
7.22
7.20
7.19
7.17
7.14
7.12
7.10
7.08
7.06
6.85
6.84
6.82
6.74
5.25
5.21
5.21
5.18
5.14
4.79
4.15
4.11
3.55
3.51
0.00


BnO2C
HO
O
O
N
Bn
Cl

3s


3.00
4.09
4.08
3.05
2.08
1.09
1.08
3.00
1.06
1.00
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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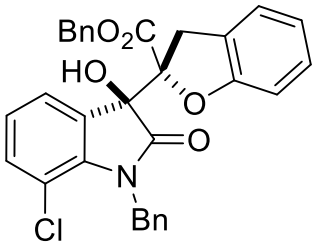
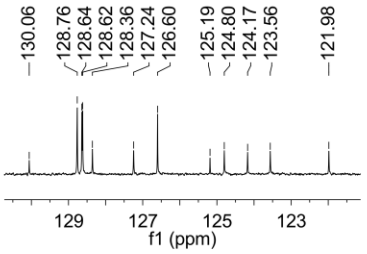
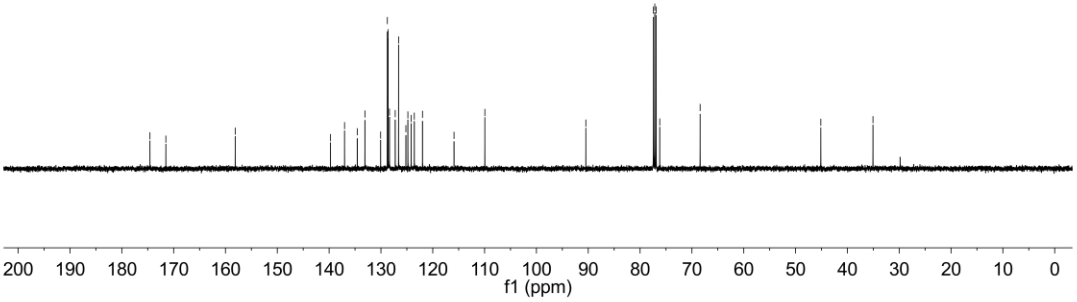
171.50
158.10
137.02
134.56
133.09
128.76
128.64
128.62
128.36
127.24
126.60
125.19
124.80
124.17
123.56
121.98
109.95
90.46
77.41
77.16
76.91
76.21
68.41
45.12
35.06


BnO2C
HO
O
O
N
Bn
Cl

3s


130.06
128.76
128.64
128.62
128.36
127.24
126.60
125.19
124.80
124.17
123.56
121.98
129
127
125
123
f1 (ppm)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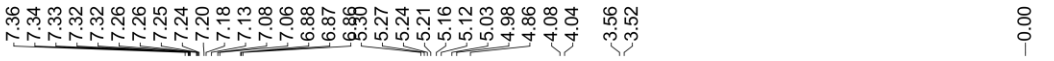
f1 (ppm)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7.34
7.33
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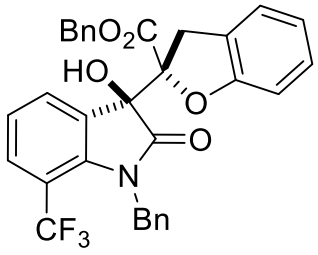
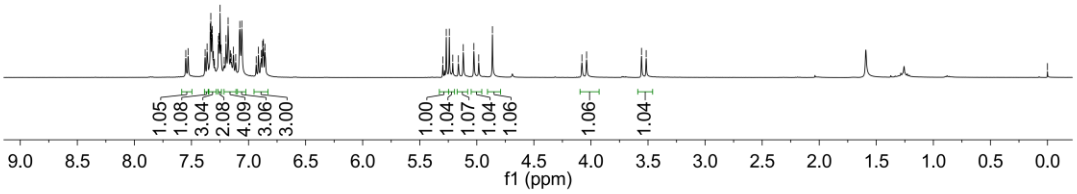
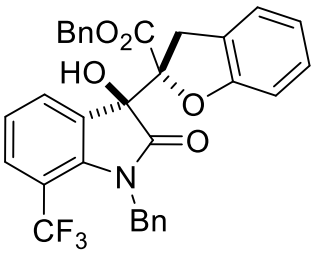
7.32
7.26
7.26
7.25
7.24
7.20
7.18
7.13
7.08
7.06
6.88
6.87
5.27
5.24
5.21
5.16
5.12
5.03
4.98
4.86
4.08
4.04
3.56
3.52
0.00


BnO2C
HO
O
O
N
Bn
CF3

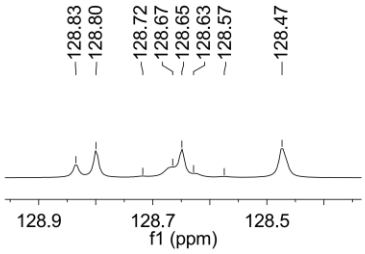
3t

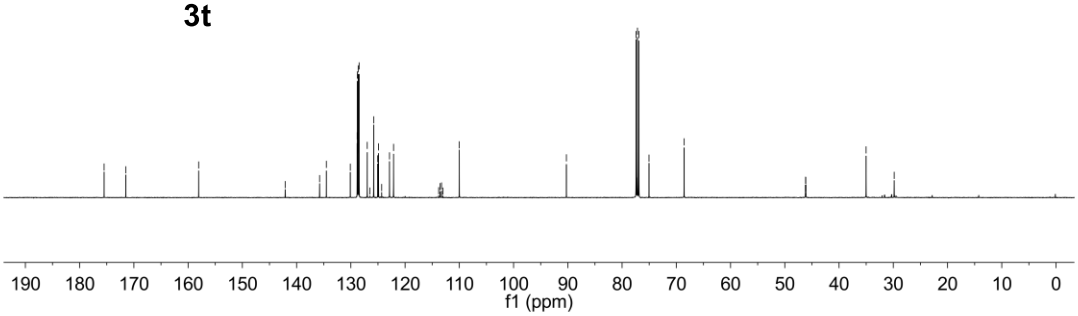

1.05
1.08
3.04
2.08
4.09
3.06
3.00
1.00
1.04
1.07
1.04
1.06
1.06
1.04
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

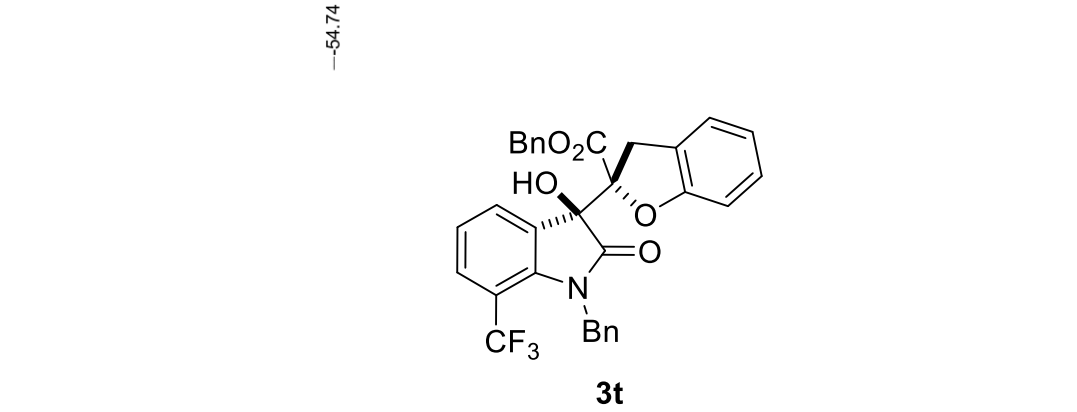

175.49
171.49
158.06
128.83
128.80
128.67
128.65
128.47
126.98
125.79
124.89
122.13
113.81
113.54
113.28
113.02
110.00
90.26
77.41
77.16
76.91
75.03
68.56
46.21
46.17
46.13
46.09
35.02
29.83


BnO2C
HO
O
O
N
Bn
CF3

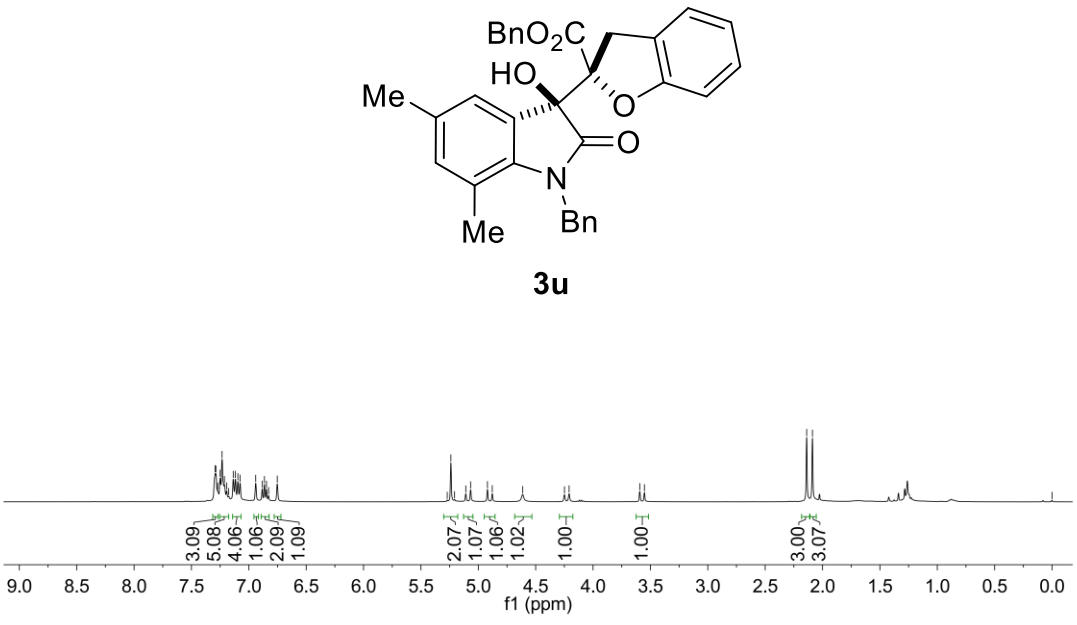
3t


128.83
128.80
128.72
128.67
128.65
128.63
128.57
128.47
128.9
128.7
128.5
f1 (ppm)

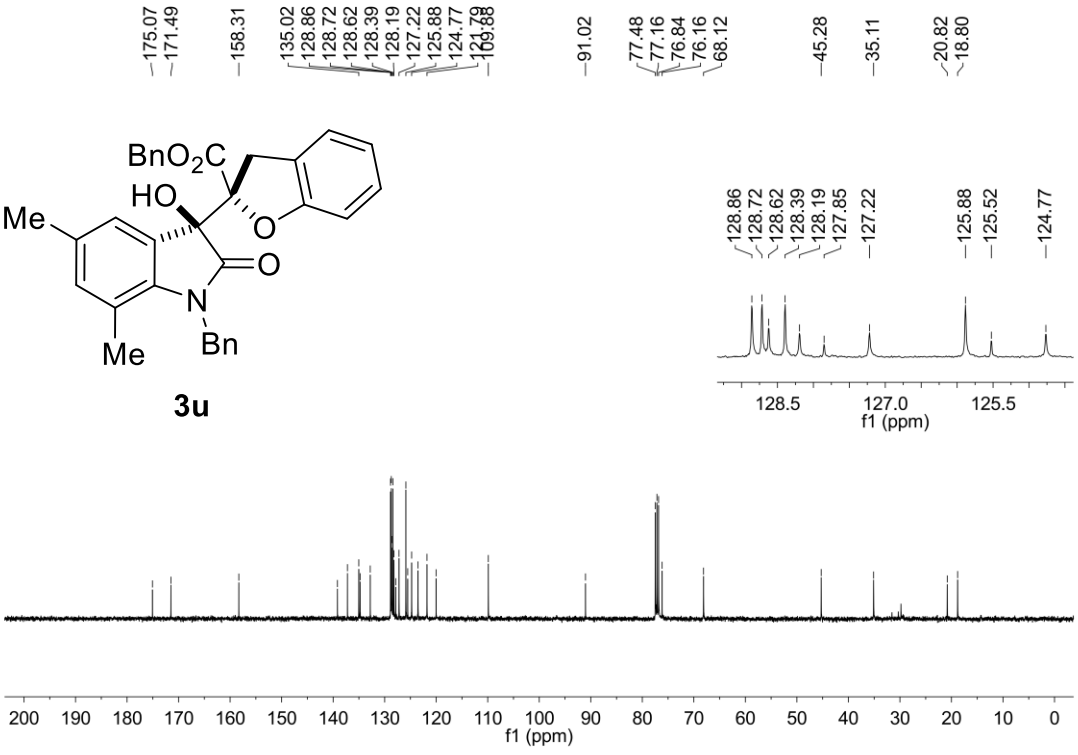

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-54.74
BnO2C
HO
O
O
N
Bn
CF3
10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200
f1 (ppm)
7.29 7.29 7.27 7.25 7.23 7.21 7.19 7.18 7.14 7.12 7.10 7.08 6.94 6.88 6.86 6.85 6.83 6.75 5.27 5.24 5.21 5.11 5.07 4.92 4.88 4.61 4.25 4.21 3.59 3.55 2.14 2.09 0.00

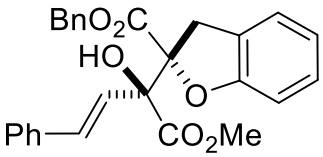
3t


BnO2C
HO
Me
O
O
N
Bn
Me
3.09 5.08 4.06 1.06 2.09 1.09 2.07 1.07 1.06 1.02 1.00 1.00 3.00 3.07
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

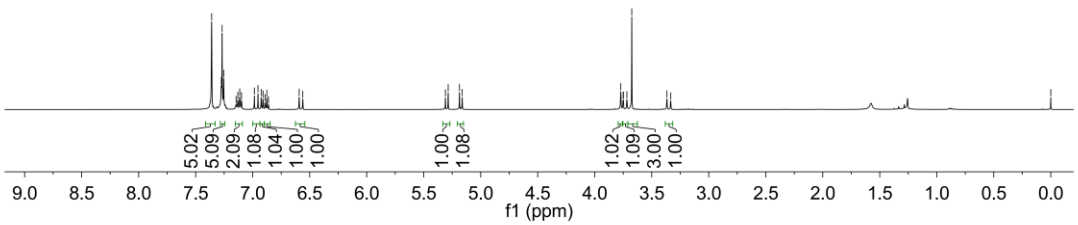
3u

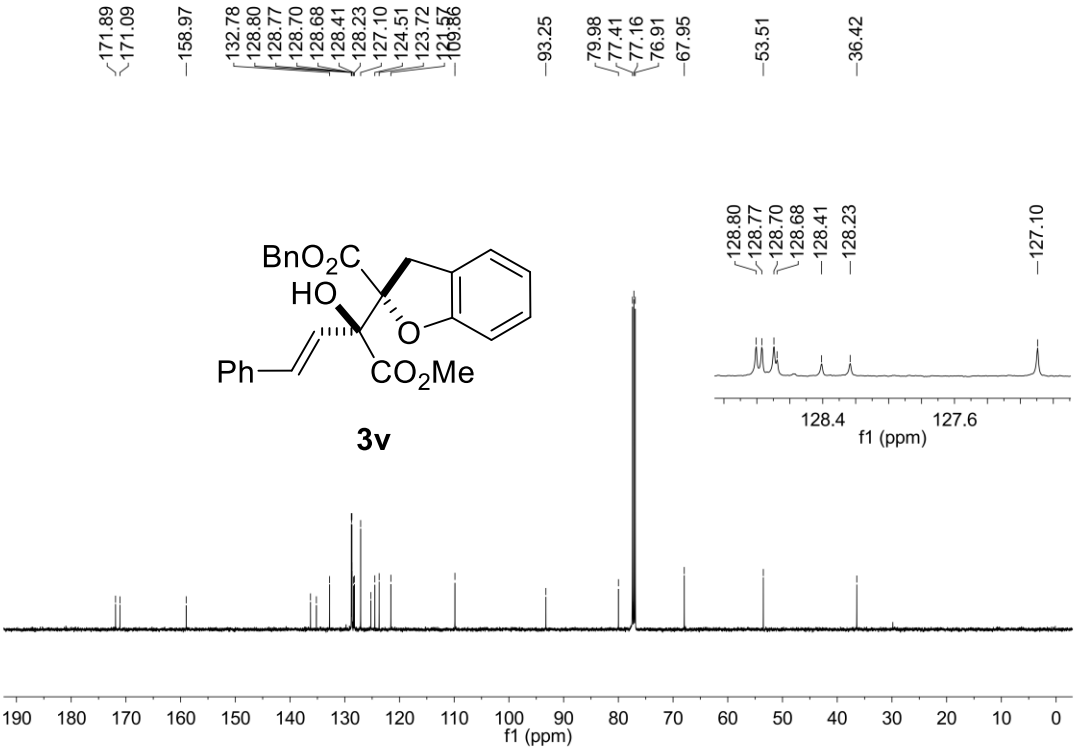

175.07
171.49
158.31
135.02
128.86
128.72
128.62
128.39
128.19
127.22
125.88
124.77
91.02
77.48
77.16
76.84
76.16
68.12
45.28
35.11
20.82
18.80
BnO2C
HO
Me
O
O
N
Bn
Me
3u
128.86
128.72
128.62
128.39
128.19
127.85
127.22
125.88
125.52
124.77
128.5
127.0
125.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.36
7.27
7.27
7.26
7.25
7.15
7.13
7.11
7.10
6.99
6.95
6.92
6.91
6.89
6.88
6.86
6.59
6.56
5.31
5.29
5.19
5.16
3.77
3.75
3.75
3.72
3.67
3.37
3.33
0.00


BnO2C
HO
O
Ph
CO2Me

3v


5.02
5.09
2.09
1.08
1.04
1.00
1.00
1.00
1.08
1.02
1.09
3.00
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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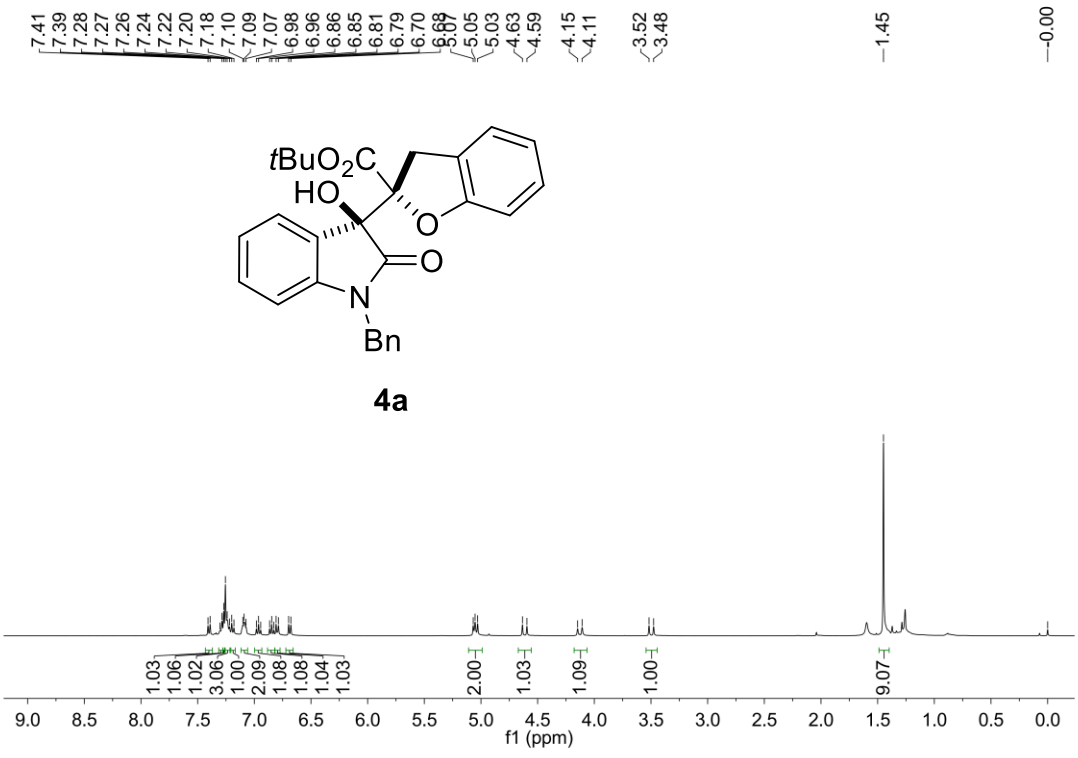
171.09
158.97
132.78
128.80
128.77
128.70
128.68
128.41
128.23
127.10
124.51
123.72
93.25
79.98
77.41
77.16
76.91
67.95
53.51
36.42
BnO2C
HO
O
Ph
CO2Me
3v
128.80
128.77
128.70
128.68
128.41
128.23
127.10
128.4
127.6
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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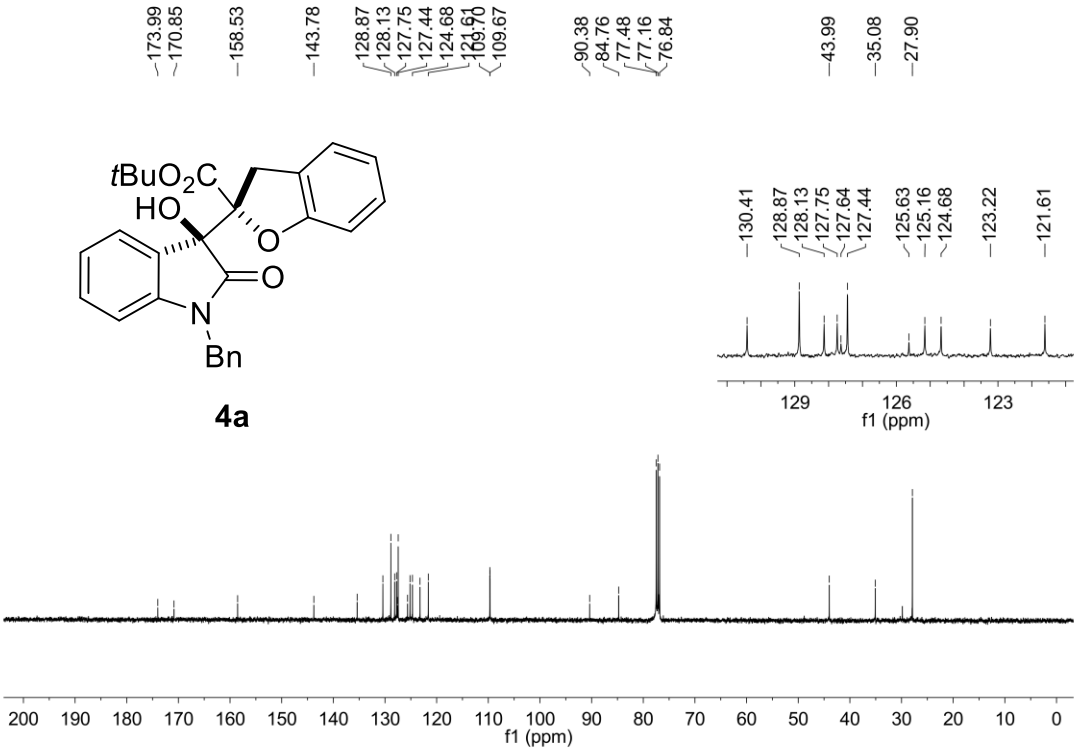
7.24
7.22
7.20
7.18
7.10
7.09
7.07
6.98
6.96
6.86
6.85
6.81
6.79
6.70
5.05
5.03
4.63
4.59
4.15
4.11
3.52
3.48
1.45
0.00
tBuO2C
HO
O
O
N
Bn
4a
1.03
1.06
1.02
3.06
1.00
2.09
1.08
1.08
1.04
1.03
2.00
1.03
1.09
1.00
9.07
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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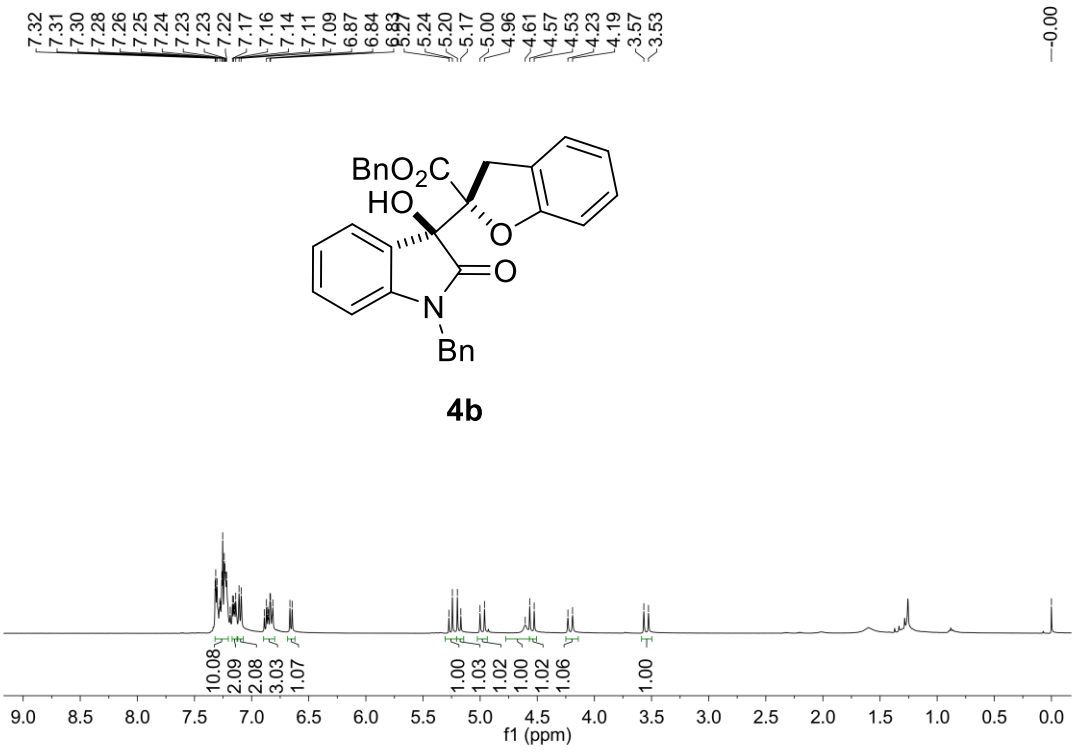
127.75
127.44
124.68
121.61
109.67
90.38
84.76
77.48
77.16
76.84
43.99
35.08
27.90
tBuO2C
HO
O
O
N
Bn
4a
130.41
128.87
128.13
127.75
127.64
127.44
125.63
125.16
124.68
123.22
121.61
129
126
123
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.31
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7.24
7.23
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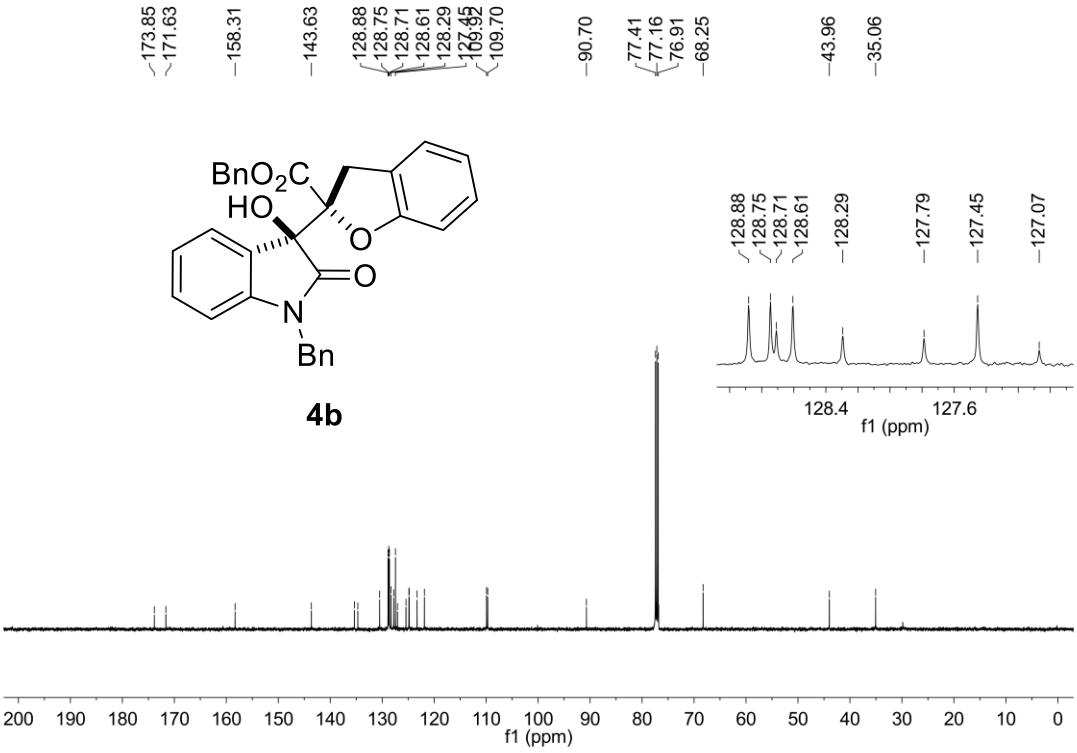
7.22
7.17
7.16
7.14
7.11
7.09
6.87
6.84
5.24
5.20
5.17
5.00
4.96
4.61
4.57
4.53
4.23
4.19
3.57
3.53
0.00
BnO2C
HO
O
O
N
Bn
4b
10.08
2.09
2.08
3.03
1.07
1.00
1.03
1.02
1.00
1.02
1.06
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.75
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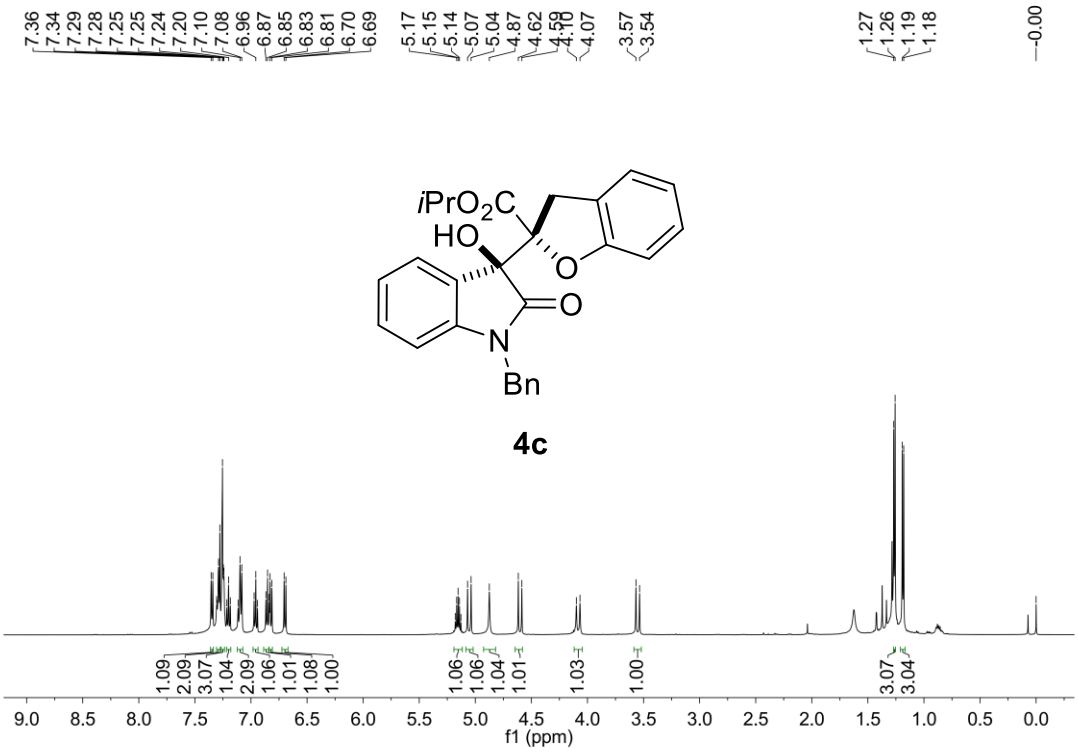
128.61
128.29
109.70
90.70
77.41
77.16
76.91
68.25
43.96
35.06
BnO2C
HO
O
O
N
Bn
4b
128.88
128.75
128.71
128.61
128.29
127.79
127.45
127.07
128.4
127.6
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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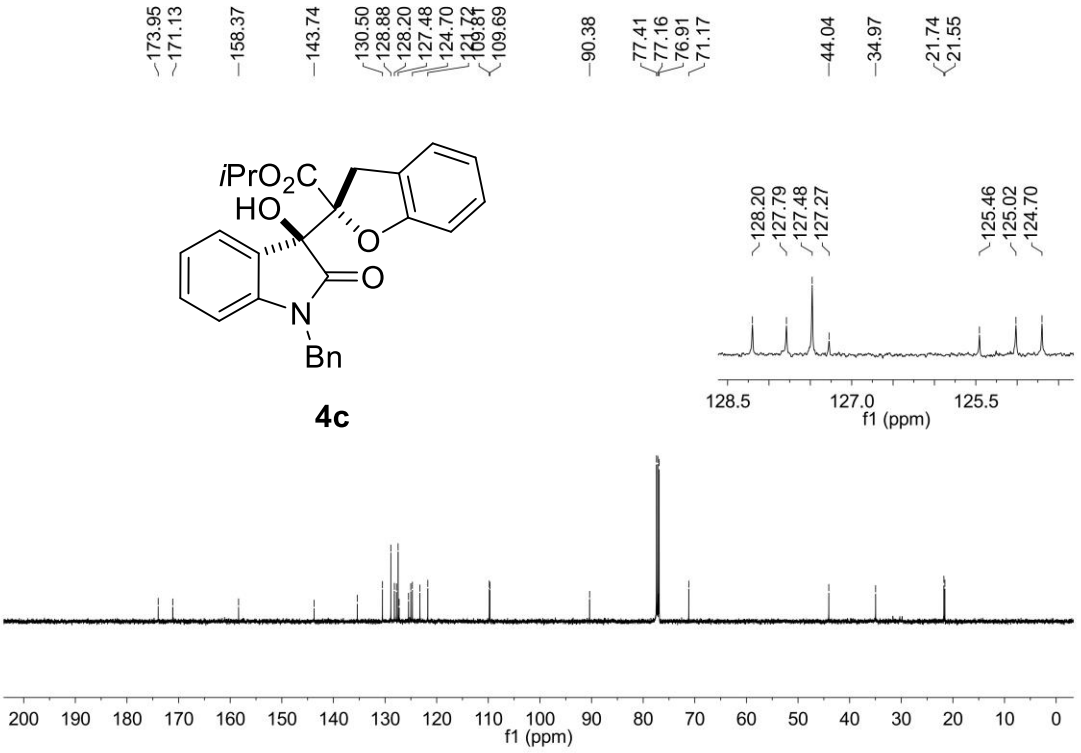
7.10
7.08
6.96
6.87
6.85
6.83
6.81
6.70
6.69
5.17
5.15
5.14
5.07
5.04
4.87
4.62
4.59
4.10
4.07
3.57
3.54
1.27
1.26
1.19
1.18
0.00
iPrO2C
HO
O
O
N
Bn
4c
1.09
2.09
3.07
1.04
2.09
1.06
1.01
1.08
1.00
1.06
1.06
1.04
1.01
1.03
1.00
3.07
3.04
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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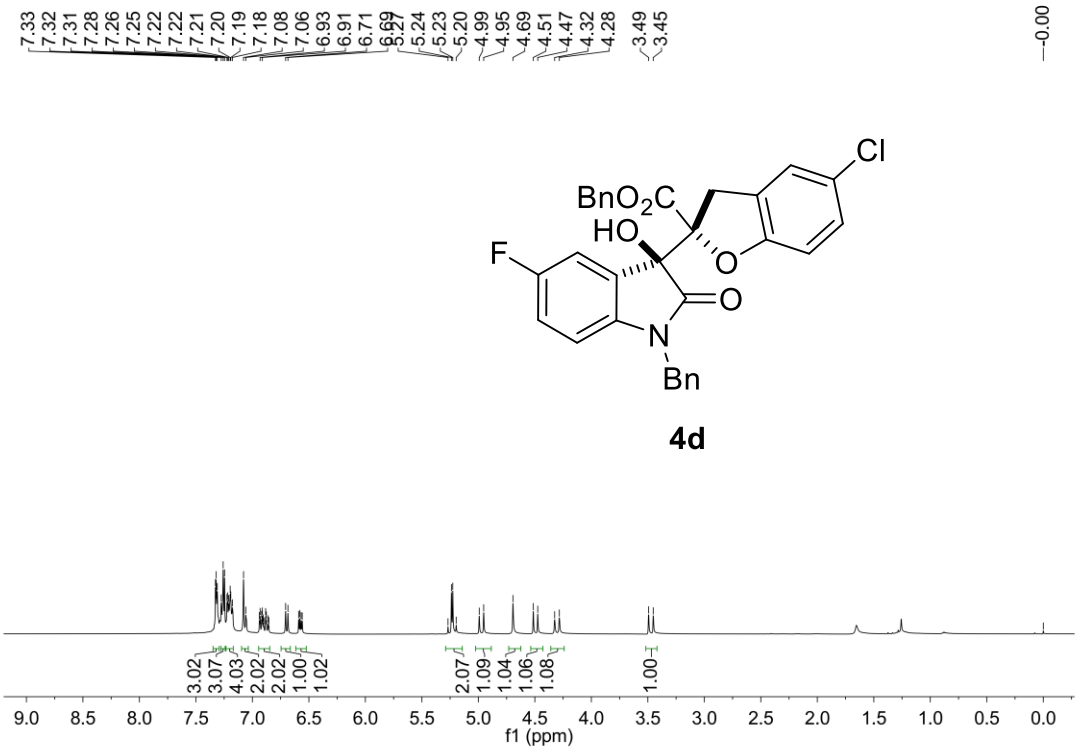
128.20
127.48
124.70
109.69
90.38
77.41
77.16
76.91
71.17
44.04
34.97
21.74
21.55
iPrO2C
HO
O
O
N
Bn
4c
128.20
127.79
127.48
127.27
125.46
125.02
124.70
128.5
127.0
125.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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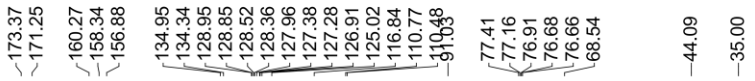
7.19
7.18
7.08
7.06
6.93
6.91
6.71
5.24
5.23
5.20
4.99
4.95
4.69
4.51
4.47
4.32
4.28
3.49
3.45
0.00
Cl
BnO2C
HO
F
O
O
N
Bn
4d
3.02
3.07
4.03
2.02
2.02
1.00
1.02
2.07
1.09
1.04
1.06
1.08
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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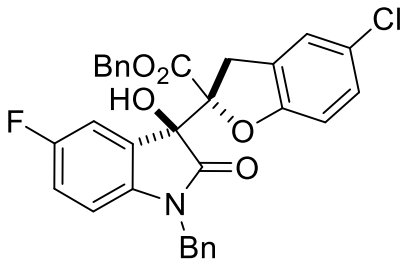
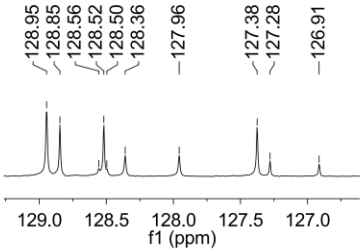
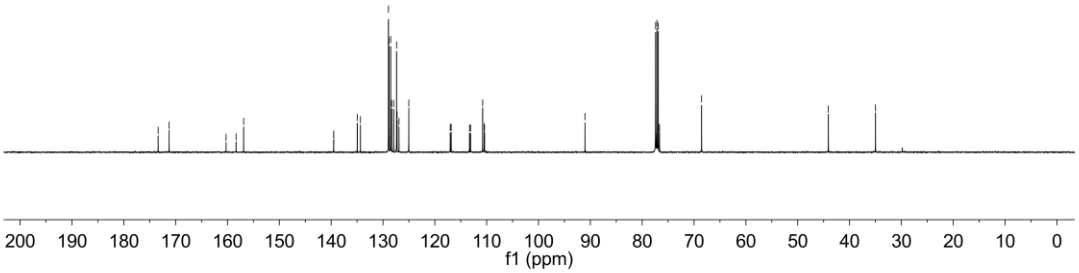
156.88
134.95
134.34
128.95
128.85
128.52
128.36
127.96
127.38
127.28
126.91
125.02
116.84
110.77
110.48
91.03
77.41
77.16
76.91
76.68
76.66
68.54
44.09
35.00

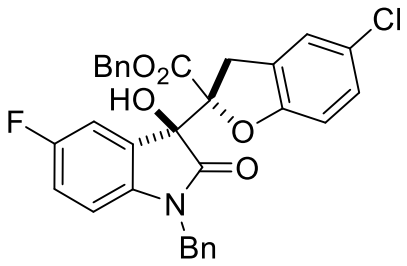

Cl
BnO2C
HO
F
O
O
N
Bn

4d

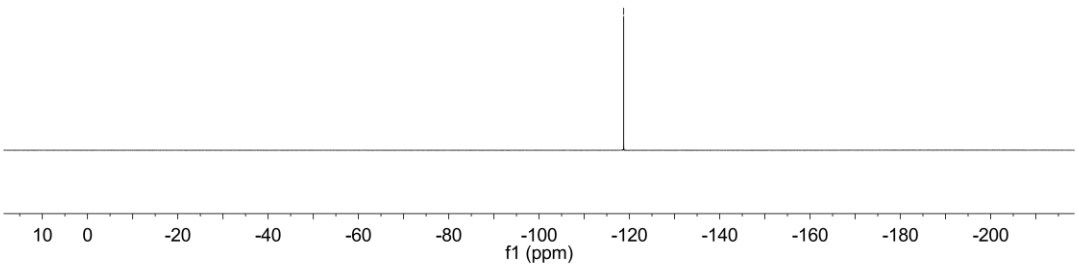

128.95
128.85
128.56
128.52
128.50
128.36
127.96
127.38
127.28
126.91
129.0
128.5
128.0
127.5
127.0
f1 (ppm)

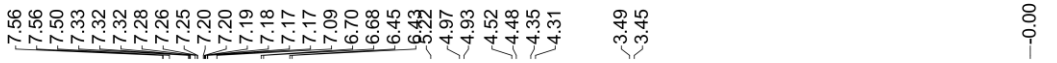

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

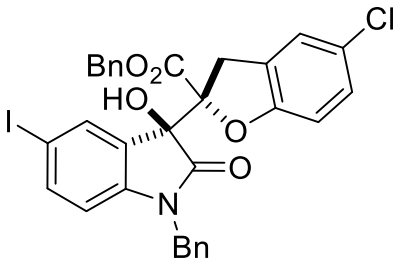

-118.73


Cl
BnO2C
HO
F
O
O
N
Bn

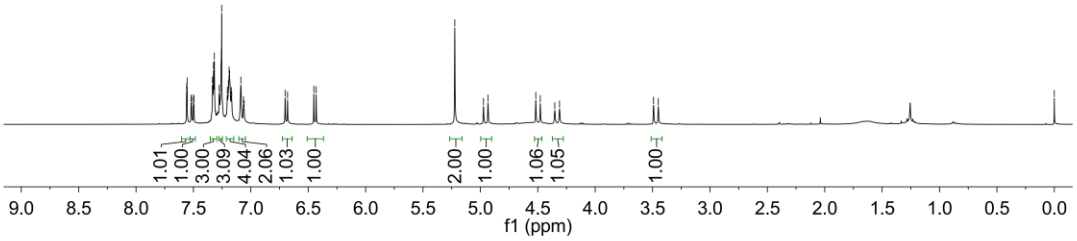
4d

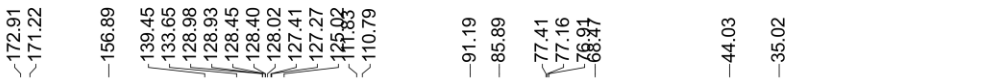

10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

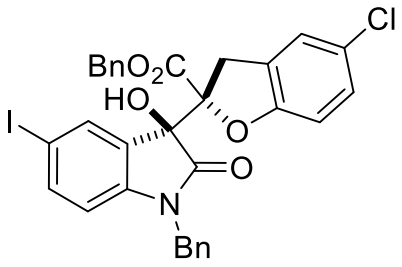

7.56
7.56
7.50
7.33
7.32
7.32
7.28
7.26
7.25
7.20
7.20
7.19
7.18
7.17
7.17
7.09
6.70
6.68
6.45
5.22
4.97
4.93
4.52
4.48
4.35
4.31
3.49
3.45
0.00


Cl
BnO2C
HO
I
O
O
N
Bn

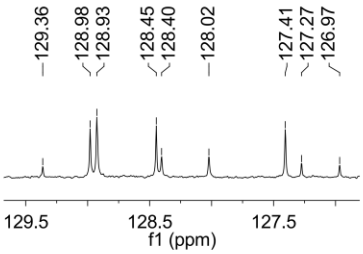
4e

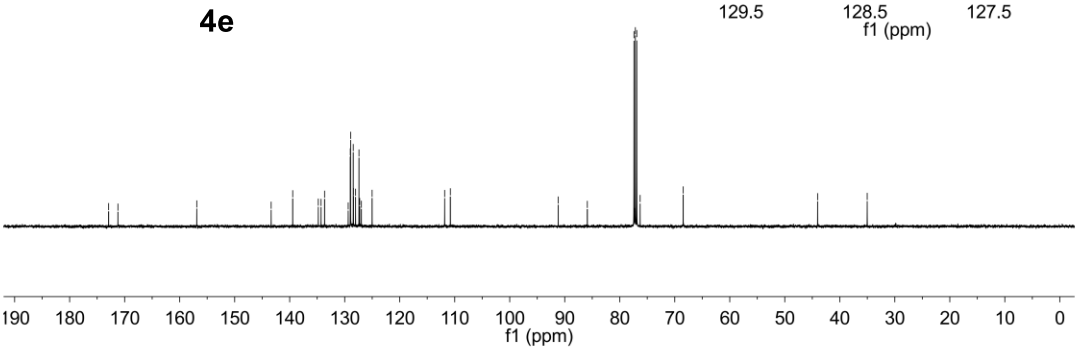

1.01
1.00
3.00
3.09
4.04
2.06
1.03
1.00
2.00
1.00
1.06
1.05
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


172.91
171.22
156.89
139.45
133.65
128.98
128.93
128.45
128.40
128.02
127.41
127.27
125.02
111.83
110.79
91.19
85.89
77.41
77.16
76.91
68.47
44.03
35.02

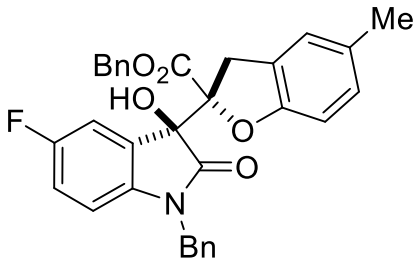

Cl
BnO2C
HO
I
O
O
N
Bn

4e

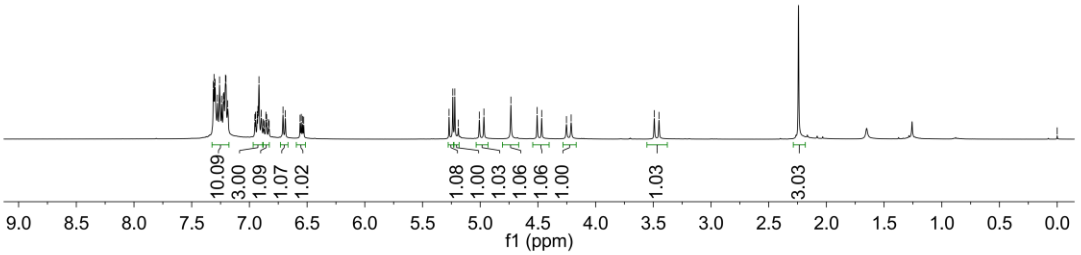

129.36
128.98
128.93
128.45
128.40
128.02
127.41
127.27
126.97
129.5
128.5
127.5
f1 (ppm)

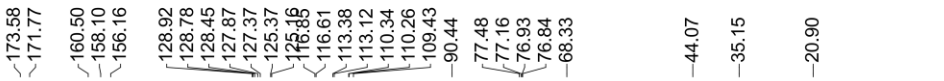

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

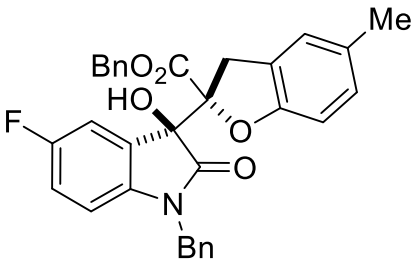

7.31
7.31
7.30
7.28
7.26
7.24
7.23
7.22
7.21
7.20
7.19
6.93
6.93
6.92
6.90
6.86
6.71
6.69
5.27
5.24
5.22
5.19
5.01
4.97
4.73
4.51
4.47
4.25
4.21
3.49
3.45
0.00


Me
BnO2C
HO
F
O
O
N
Bn

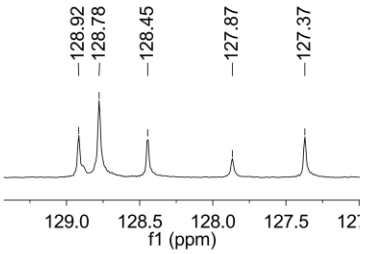
4f

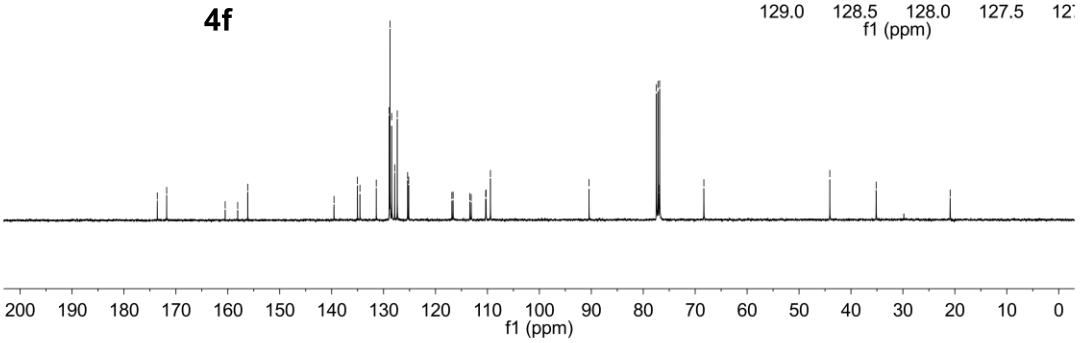

10.09
3.00
1.09
1.07
1.02
1.08
1.00
1.03
1.06
1.06
1.00
1.03
3.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

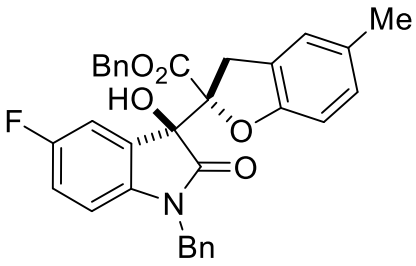

173.58
171.77
160.50
158.10
156.16
128.92
128.78
128.45
127.87
127.37
125.37
125.16
116.85
116.61
113.38
113.12
110.34
110.26
109.43
90.44
77.48
77.16
76.93
76.84
68.33
44.07
35.15
20.90


Me
BnO2C
HO
F
O
O
N
Bn

4f

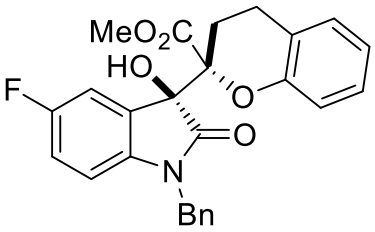

128.92
128.78
128.45
127.87
127.37
129.0 128.5 128.0 127.5
f1 (ppm)


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

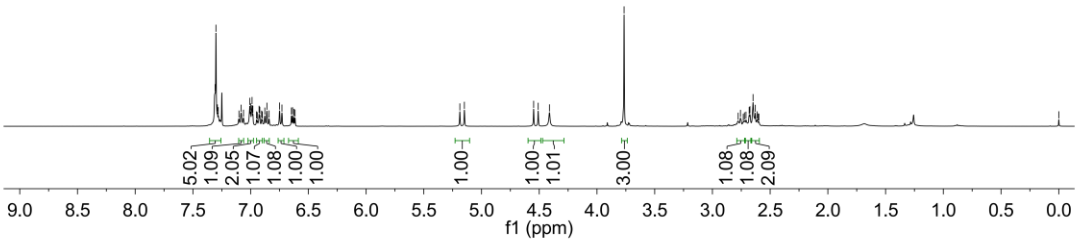

Me
BnO2C
HO
F
O
O
N
Bn

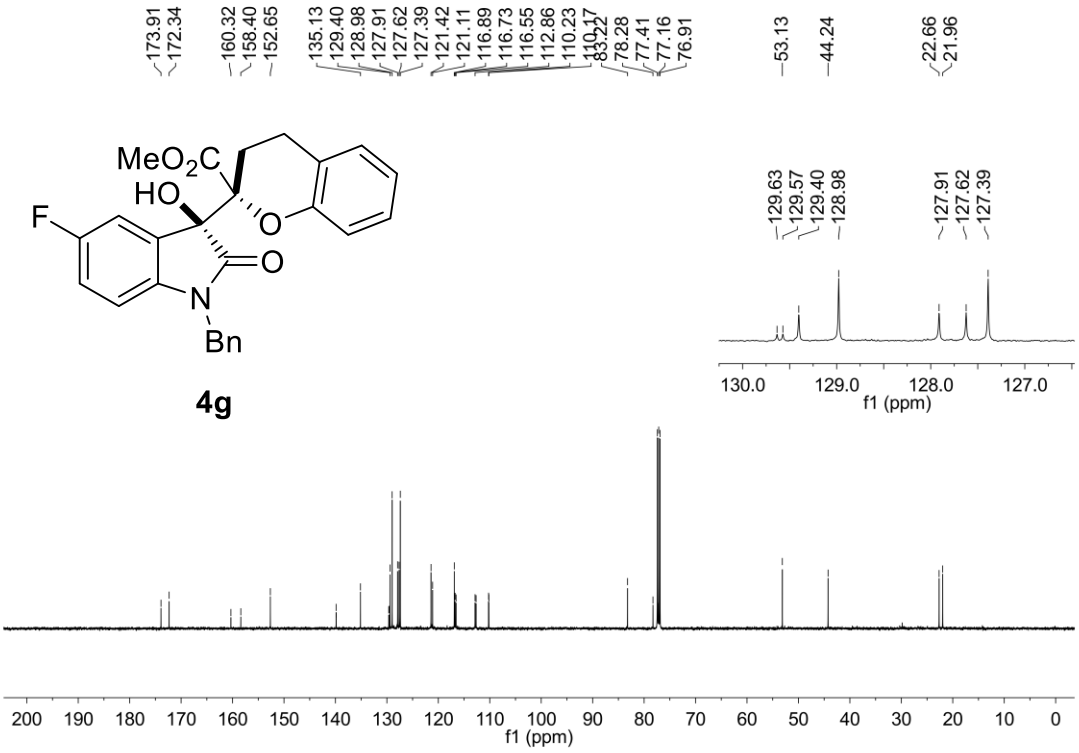
4f

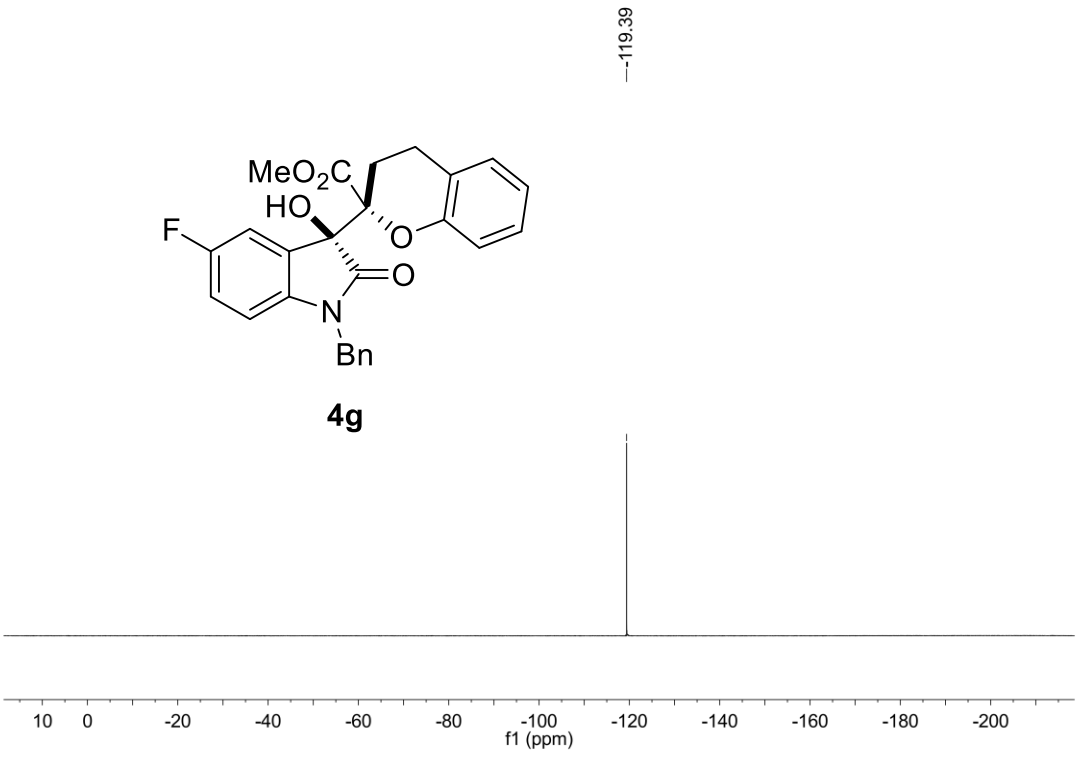
-119.03
10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200
f1 (ppm)
7.31 7.30 7.29 7.28 7.08 7.06 7.01 7.00 6.99 6.98 6.93 6.92 6.88 6.86 6.75 6.73 6.65 6.64 6.63 6.62 5.19 5.15
4.55 4.51 4.41
3.77
2.78 2.76 2.73 2.72 2.71 2.68 2.67 2.65 2.63 2.61 2.60 2.60
-0.00

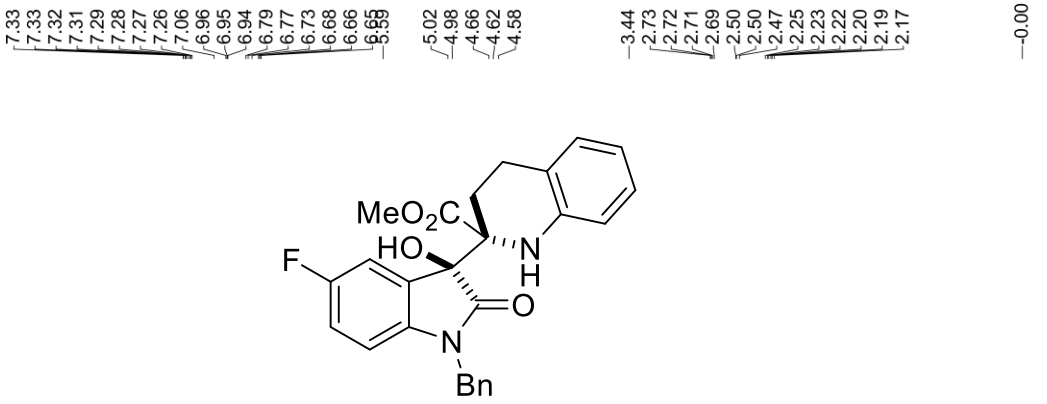

MeO2C
HO
F
O
O
N
Bn

4g


5.02 1.09 2.05 1.07 1.08 1.00 1.00
1.00
1.00 1.01
3.00
1.08 1.08 2.09
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

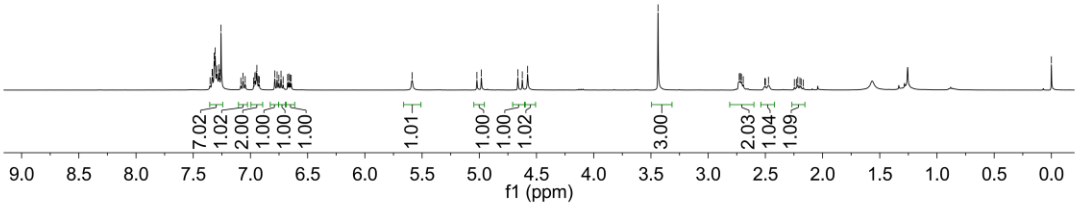

173.91
172.34
160.32
158.40
152.65
135.13
129.40
128.98
127.91
127.62
127.39
121.42
121.11
116.89
116.73
116.55
112.86
110.23
110.17
83.22
78.28
77.41
77.16
76.91
53.13
44.24
22.66
21.96
MeO2C
HO
F
O
O
N
Bn
4g
129.63
129.57
129.40
128.98
127.91
127.62
127.39
130.0
129.0
128.0
127.0
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

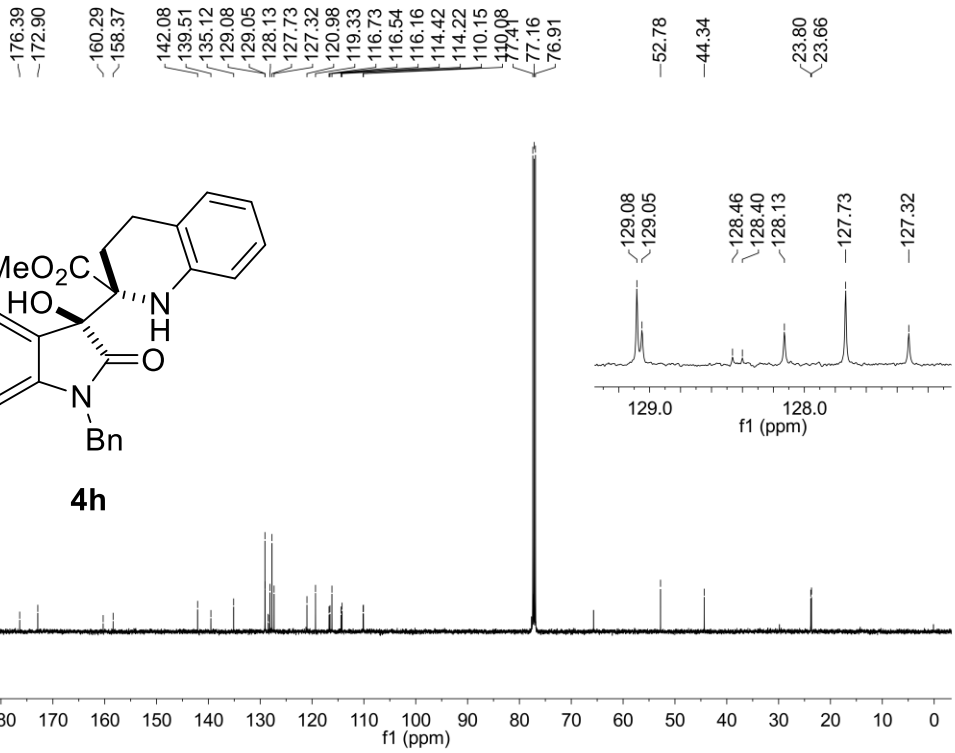

-119.39
MeO2C
HO
F
O
O
N
Bn
4g
10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200
f1 (ppm)


7.33
7.33
7.32
7.31
7.29
7.28
7.27
7.26
7.06
6.96
6.95
6.94
6.79
6.77
6.73
6.68
6.66
6.65
6.59
5.02
4.98
4.66
4.62
4.58
3.44
2.73
2.72
2.71
2.69
2.50
2.50
2.47
2.25
2.23
2.22
2.20
2.19
2.17
0.00

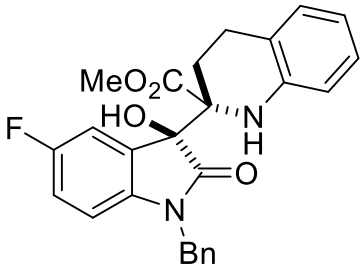
MeO2C
HO
F
N
H
O
N
Bn

4h


7.02
1.02
2.00
1.00
1.00
1.00
1.01
1.00
1.00
1.02
3.00
2.03
1.04
1.09
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

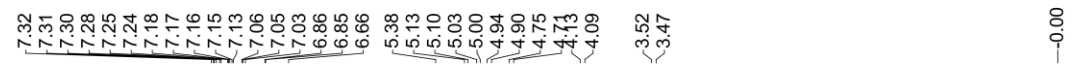

176.39
172.90
160.29
158.37
142.08
139.51
135.12
129.08
129.05
128.13
127.73
127.32
120.98
119.33
116.73
116.54
116.16
114.42
114.22
110.15
110.08
77.41
77.16
76.91
52.78
44.34
23.80
23.66
MeO2C
HO
F
N
H
O
N
Bn
129.08
129.05
128.46
128.40
128.13
127.73
127.32
129.0
128.0
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

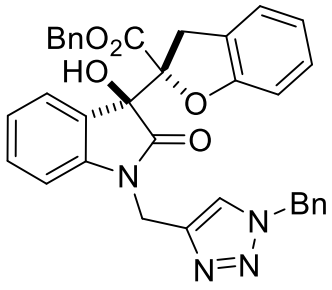
4h


MeO2C
HO
F
N
H
O
N
Bn

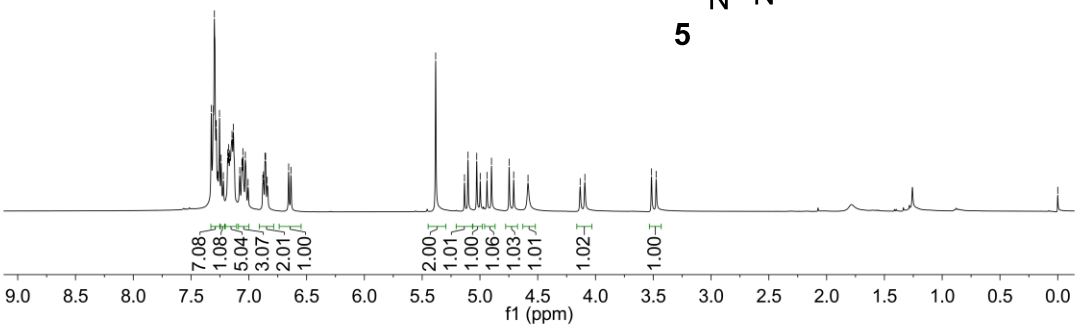
4h

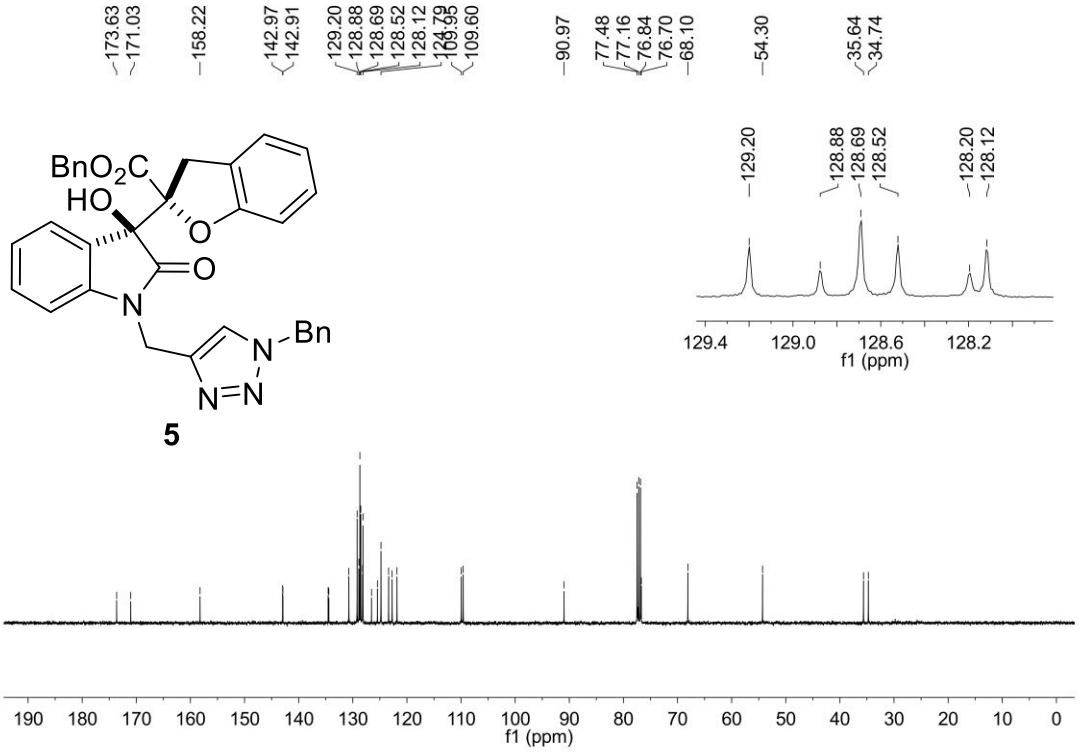
-119.20
10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200
f1 (ppm)

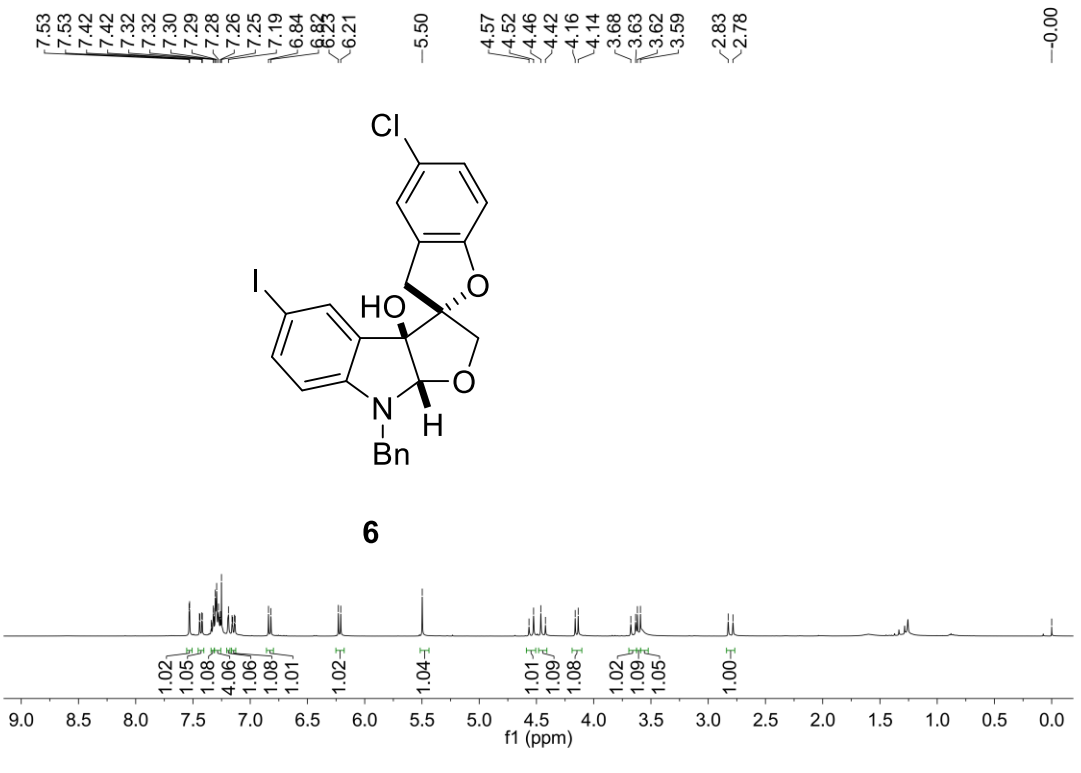

7.32 7.31 7.30 7.28 7.25 7.24 7.18 7.17 7.16 7.15 7.13 7.06 7.05 7.03 6.86 6.85 6.66
5.38 5.13 5.10 5.03 5.00 4.94 4.90 4.75 4.71 4.13 4.09
3.52 3.47
-0.00

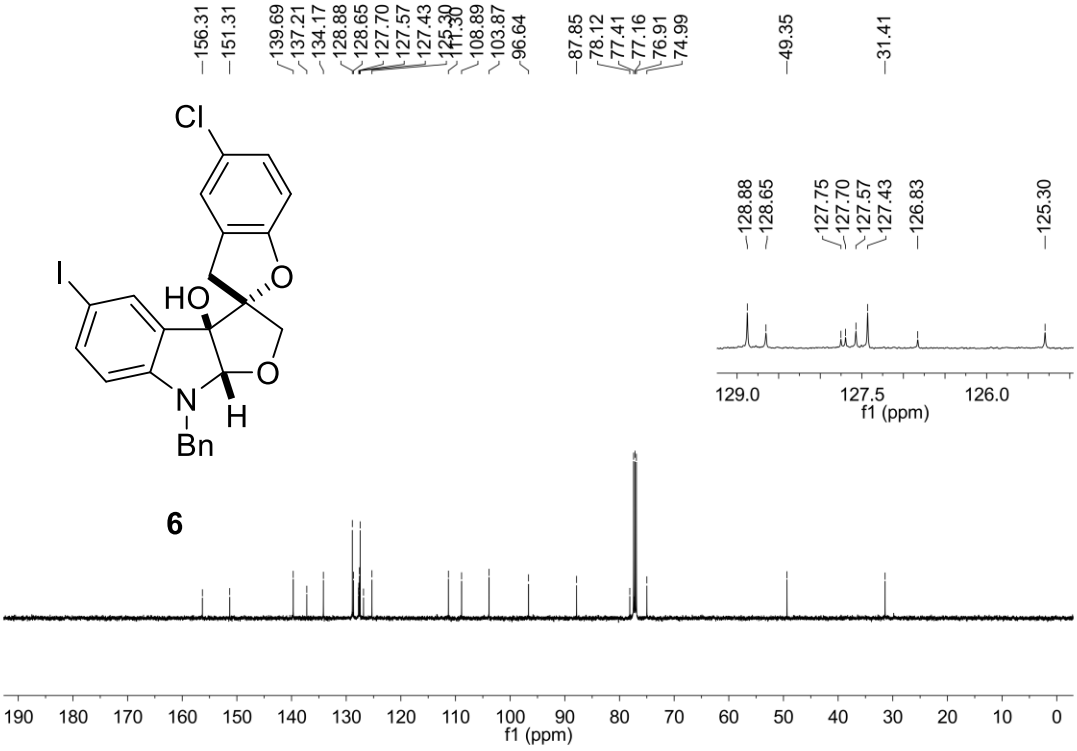

BnO2C
HO
O
O
N
N
Bn
N=N

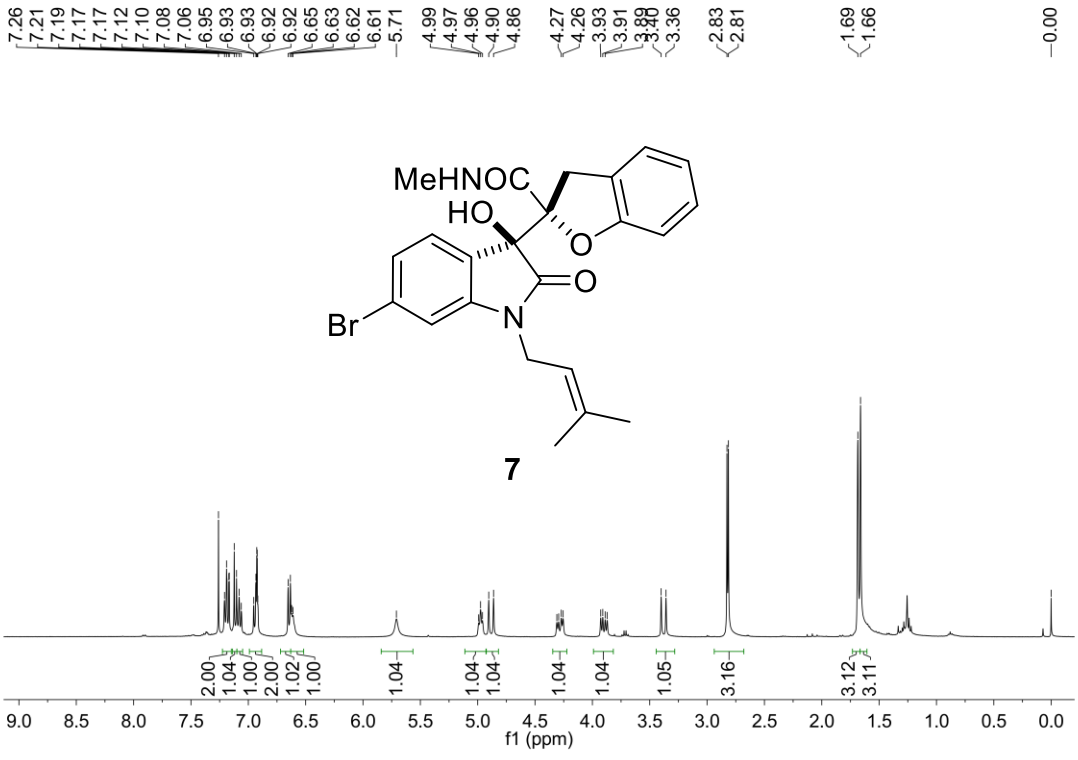
5


7.08 1.08 5.04 3.07 2.01 1.00
2.00 1.01 1.00 1.06 1.03 1.01 1.02 1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


173.63
171.03
158.22
142.97
142.91
129.20
128.88
128.69
128.52
128.12
109.60
90.97
77.48
77.16
76.84
76.70
68.10
54.30
35.64
34.74
BnO2C
HO
O
O
N
N
Bn
N=N
129.20
128.88
128.69
128.52
128.20
128.12
129.4
129.0
128.6
128.2
f1 (ppm)
5
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.53
7.53
7.42
7.42
7.32
7.32
7.30
7.29
7.28
7.26
7.25
7.19
6.84
6.21
5.50
4.57
4.52
4.46
4.42
4.16
4.14
3.68
3.63
3.62
3.59
2.83
2.78
0.00
Cl
I
HO
O
O
N
H
Bn
6
1.02
1.05
1.08
4.06
1.06
1.08
1.01
1.02
1.04
1.01
1.09
1.08
1.02
1.09
1.05
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


156.31
151.31
139.69
137.21
134.17
128.88
128.65
127.70
127.57
127.43
125.30
111.30
108.89
103.87
96.64
87.85
78.12
77.41
77.16
76.91
74.99
49.35
31.41
Cl
I
HO
O
O
N
H
Bn
6
128.88
128.65
127.75
127.70
127.57
127.43
126.83
125.30
129.0
127.5
126.0
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.08
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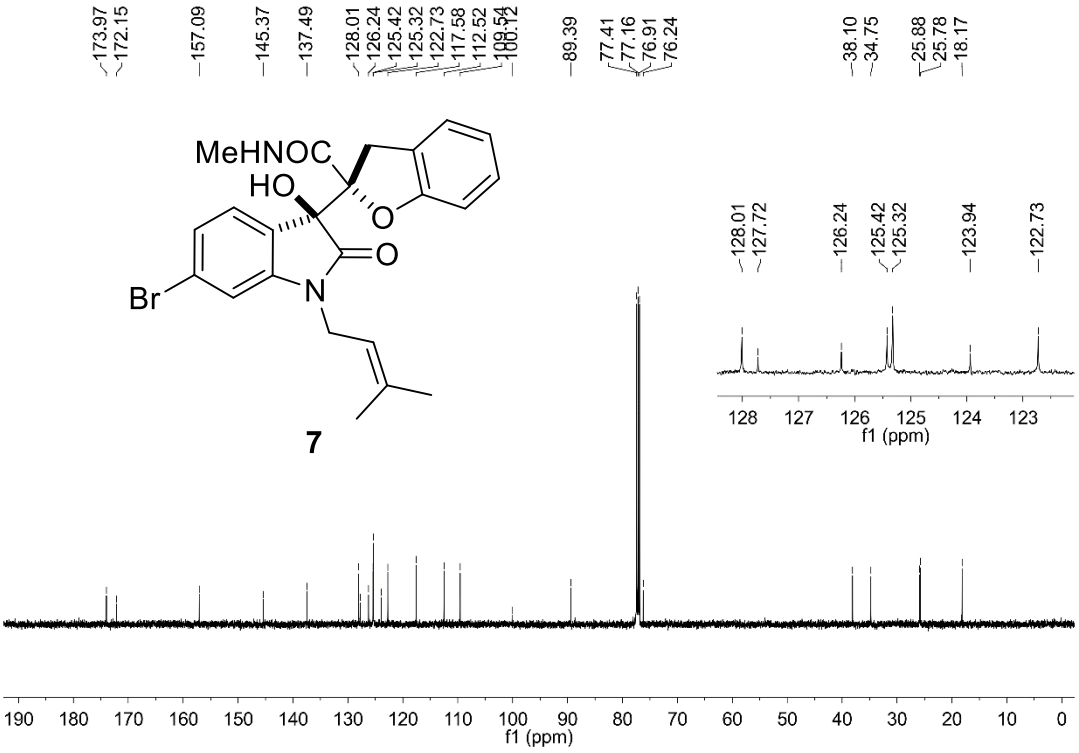
6.93
6.93
6.92
6.92
6.65
6.63
6.62
6.61
5.71
4.99
4.97
4.96
4.90
4.86
4.27
4.26
3.93
3.91
3.40
3.36
2.83
2.81
1.69
1.66
0.00
MeHNOC
HO
O
O
N
Br
7
2.00
1.04
1.00
2.00
1.02
1.00
1.04
1.04
1.04
1.04
1.04
1.05
3.16
3.12
3.11
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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77.41
77.16
76.91
76.24
38.10
34.75
25.88
25.78
18.17
MeHNOC
HO
O
O
N
Br
128.01
127.72
126.24
125.42
125.32
123.94
122.73
128 127 126 125 124 123
f1 (ppm)
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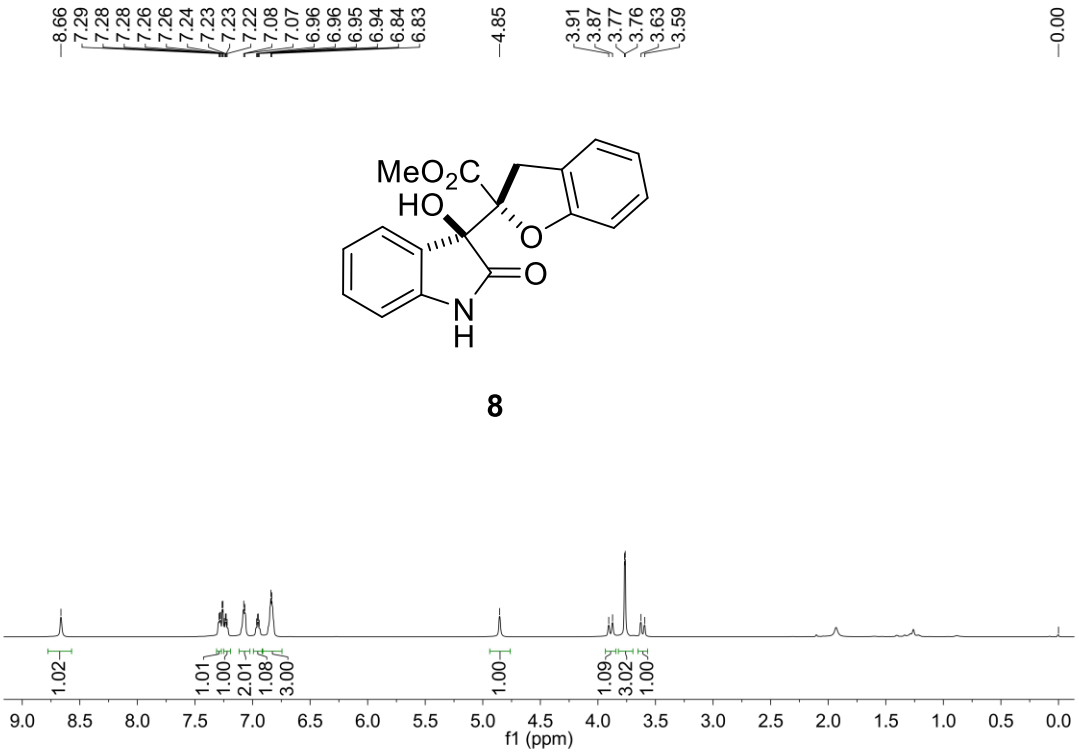
f1 (ppm)

7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7.26
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7.23
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7.22
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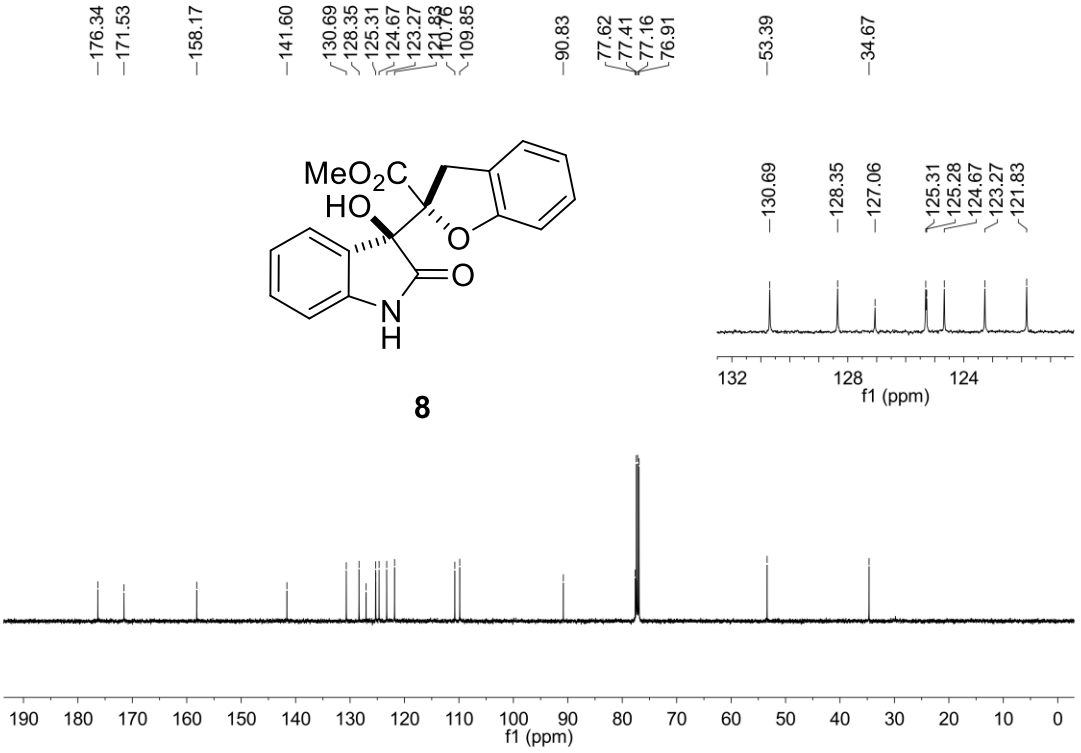
6.96
6.95
6.94
6.84
6.83
4.85
3.91
3.87
3.77
3.76
3.63
3.59
0.00
MeO2C
HO
O
O
N
H
1.02
1.01
1.00
2.01
1.08
3.00
1.00
1.09
3.02
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

8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158.17
141.60
130.69
128.35
125.31
124.67
123.27
121.83
110.76
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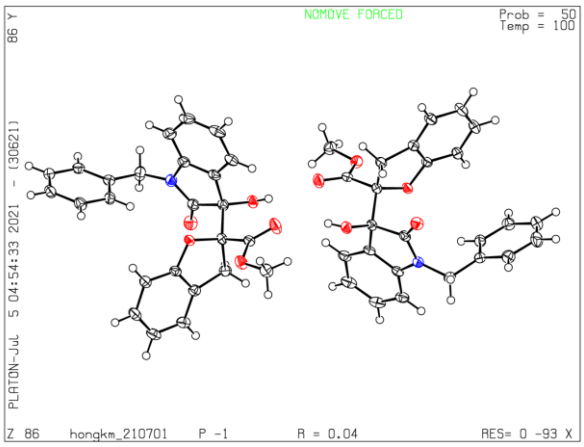
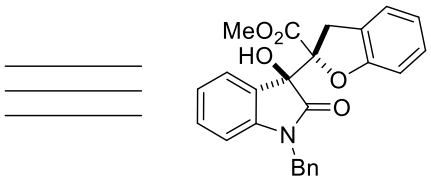
90.83
77.62
77.41
77.16
76.91
53.39
34.67
MeO2C
HO
O
O
N
H
8
130.69
128.35
127.06
125.31
125.28
124.67
123.27
121.83
132
128
124
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Crystallographic Data for 3c





3c CCDC: 2124796

Bond precision: C-C = 0.0020 A Wavelength=1.54184

Cell: a=11.8311(3) b=12.9022(3) c=14.4374(3)
alpha=75.339(2) beta=70.665(2) gamma=78.677(2)
Temperature: 100 K

	Calculated	Reported
Volume	1996.48(9)	1996.48(9)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C25 H21 N O5	C25 H21 N O5
Sum formula	C25 H21 N O5	C25 H21 N O5
Mr	415.43	415.43
Dx,g cm-3	1.382	1.382
Z	4	4
Mu (mm-1)	0.792	0.792
F000	872.0	872.0
F000'	874.80	
h,k,lmax	14,16,18	14,16,18
Nref	8364	8018
Tmin,Tmax	0.827,0.854	0.778,1.000
Tmin'	0.789	

Correction method= # Reported T Limits: Tmin=0.778 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.959 Theta(max)= 76.296

R(reflections)= 0.0410(7044) wR2(reflections)= 0.1059(8018)

S = 1.039 Npar= 564

General Procedure for the in vitro Anti-tumor Activity Study Cell viability was measured by CCK-8 assay

Human cancer cell lines HCT116, A549 and SAOS-2 were obtained from Cell Cook. Cells were cultured in RPMI1640 medium containing 10% fetal bovine serum and 1% penicillin/streptomycin (Gibco) in a humidified incubator containing 5% CO2 at 37 °C. Human cancer cell lines MCF-7 was obtained from Procell and cells were cultured in MEM medium containing 10% fetal bovine serum, 1% penicillin/streptomycin (Gibco) and 0.01 mg/mL insulin (Procell) in a humidified incubator containing 5% CO2 at 37 °C. For cell viability, cells were seeded in 96-well plates at 5000 cells per well. After 24 hours, serially diluted compounds were added and cells were cultured for another 48 hours. Cell viability was measured using a Cell Counting Kit-8 (CCK-8) assay according to the manufacturer's instructions (Yeasen Biotechnology, China). These representative products **3a - 3d, 3g – 3j, 3m, 3p, 3q, 3s – 3v, 4a – 4c, 4e, 5, 6, 7** and **8** on cell viability was evaluated *via* CCK8 assay in HCT116 (colon cancer), A549 (lung adenocarcinoma), MCF-7 (breast cancer), and SAOS-2 (osteosarcoma cancer) human cancer cell lines, and the *in vitro* anti-tumor activity results are listed in Table S1. The results show that compound **3s** and **3t** exhibits high anticancer potency against human colon cancer cells (HCT116 cells, **3s**: IC_{50}=15.99 μM, R^2=0.9312; **3t**: IC_{50}= 14.48μM, R^2=0.981). The results were presented as percentages and vehicle-treated cells set at 100 (Figure S2).

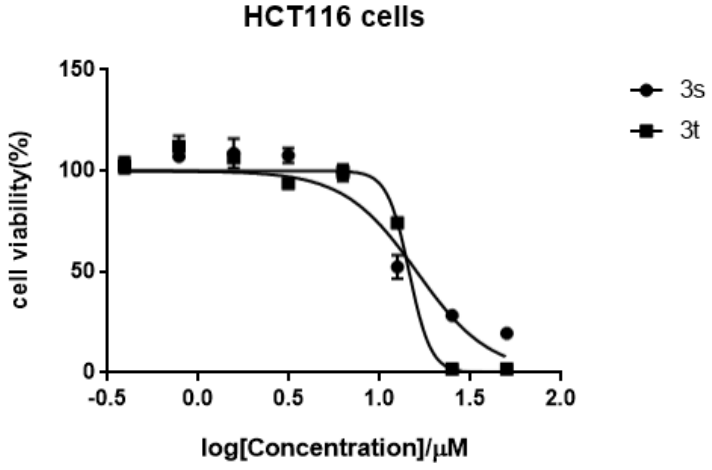


Figure S2. Compounds **3s** and **3t** on the viabilities of HCT116 cells.

Table S1. Anti-tumor activities of compounds **3a - 3d, 3g-3j, 3m, 3p, 3q, 3s-3v, 4a-4c, 4e, 5, 6, 7** and **8** (Inhibition rate at 20 μM)

Compound.	HCT-116 (%)	A549 (%)	MCF-7 (%)	SAOS-2 (%)
3a	< 0	< 0	< 0	11.61±3.85
3b	< 0	32.97±2.38	2.86±2.57	33.60±3.06
3c	< 0	< 0	< 0	6.40±4.61
3d	< 0	9.51±4.13	< 0	10.57±3.24
3g	< 0	10.99±2.71	< 0	3.34±0.45
3h	22.67	36.81±2.80	< 0	22.37±2.75
3i	22.83±9.31	42.79±5.52	19.44±2.59	38.93±2.59
3j	< 0	37.7±19.13	20.33±4.83	34.50±2.12
3m	26.47±13.18	49.29±2.63	< 0	14.29±5.45
3p	22.70±7.56	51.15±3.69	4.94±2.81	28.19±3.37
3q	37.72±6.72	41.39±3.48	14.99±3.78	26.85±1.73
3s	72.09±4.59	55.23±2.13	26.17±6.13	43.67±2.42
3t	89.44±3.03	55.40±1.65	14.46±2.56	40.77±3.68
3u	21.54±7.09	34.67±1.13	< 0	20.28±6.29
3v	35.09±5.32	25.30±7.82	9.02±2.66	41.96±2.08
4a	< 0	8.51±5.35	< 0	8.04±0.38
4b	22.24±4.76	32.71±1.25	7.85±0.59	22.09±1.45
4c	< 0	6.95±0.07	4.98±0.12	10.66±2.32
4e	54.77±3.43	54.76±5.08	9.13±5.99	38.08±2.24
5	31.12±4.38	35.61±9.29	< 0	23.13±7.60
6	18.47±12.16	7.53±4.15	1.48±0.67	3.23±1.39
7	< 0	7.54±5.68	< 0	< 0
8	< 0	< 0	< 0	7.34±4.40