

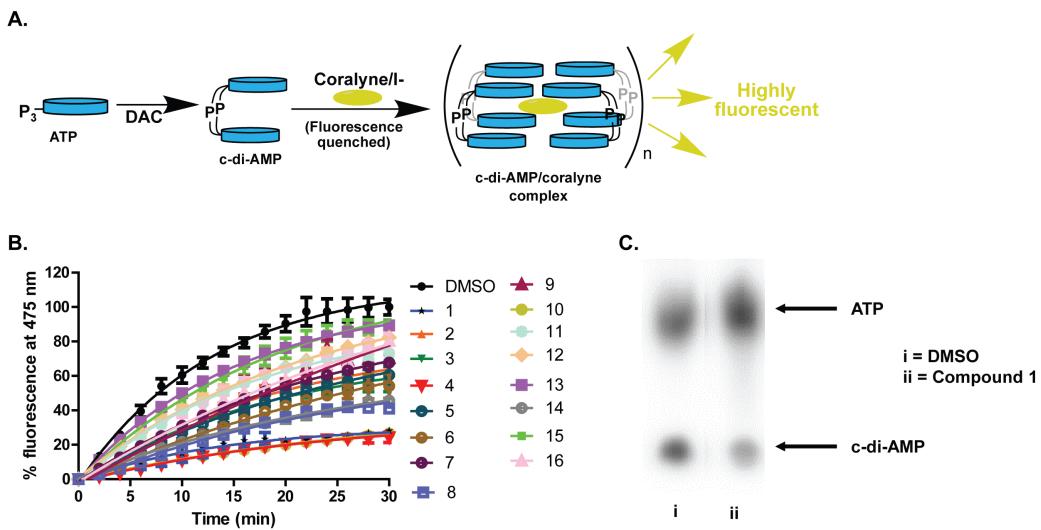
## Supporting Information

**Hydroxybenzylidene-indolinones, c-di-AMP synthase inhibitors, have antibacterial and anti-biofilm activities and also re-sensitize resistant bacteria to methicillin and vancomycin**

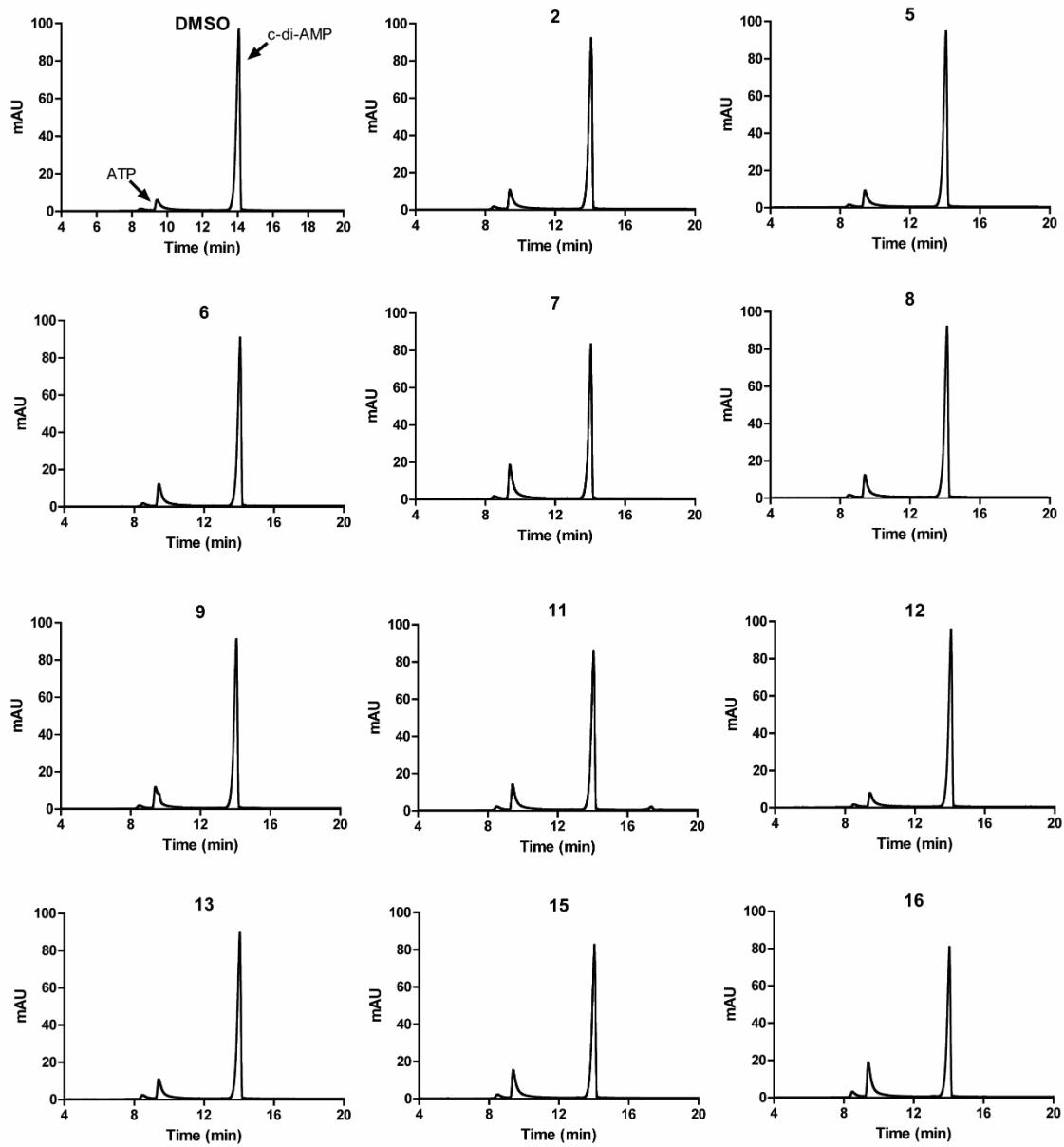
Clement Opoku-Temeng<sup>ac</sup>, Neetu Dayal<sup>ab</sup>, Jacob Miller<sup>b</sup> and Herman O. Sintim<sup>abd\*</sup>

\* Corresponding author email: [hsintim@purdue.edu](mailto:hsintim@purdue.edu)

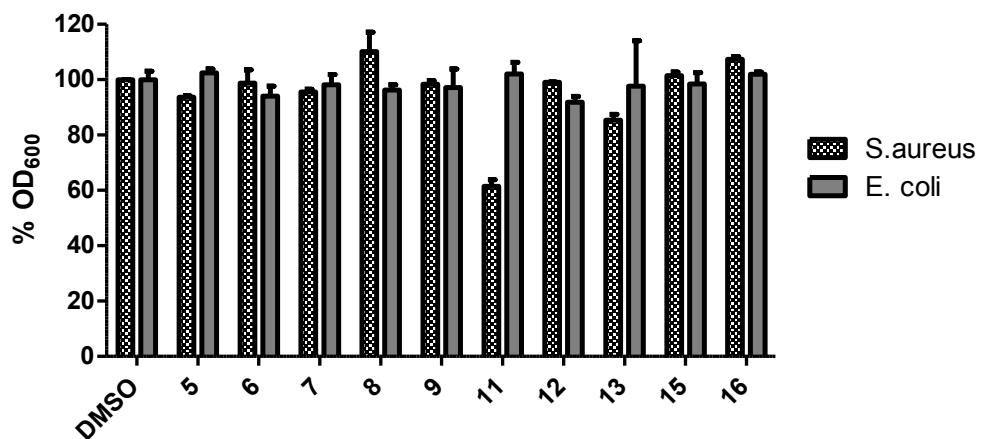
## A. Supplementary Figures



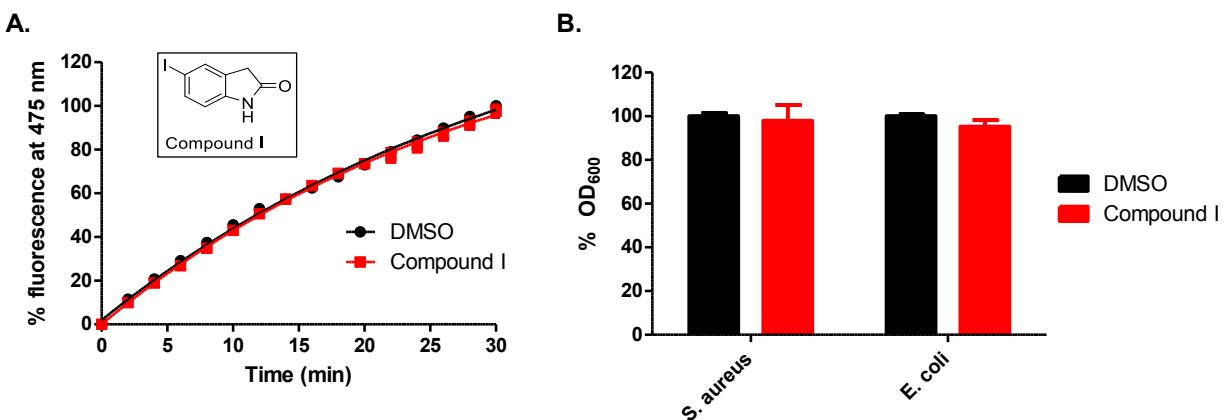
**Figure S1. A.** Principle of the coraline assay detection of c-di-AMP. In the presence of c-di-AMP, coraline fluorescence, which is otherwise quenched by iodide ions, is increased due to the formation of c-di-AMP/coraline complex. **B.** Plot of percent fluorescence (emission 475 nm) of coraline against time for the screening of benzylidene-indolinones (20  $\mu$ M) against DisA (0.5  $\mu$ M). **C.** Radioactive TLC confirmation of the inhibition of DisA (0.25  $\mu$ M) by compound **1** (20  $\mu$ M).



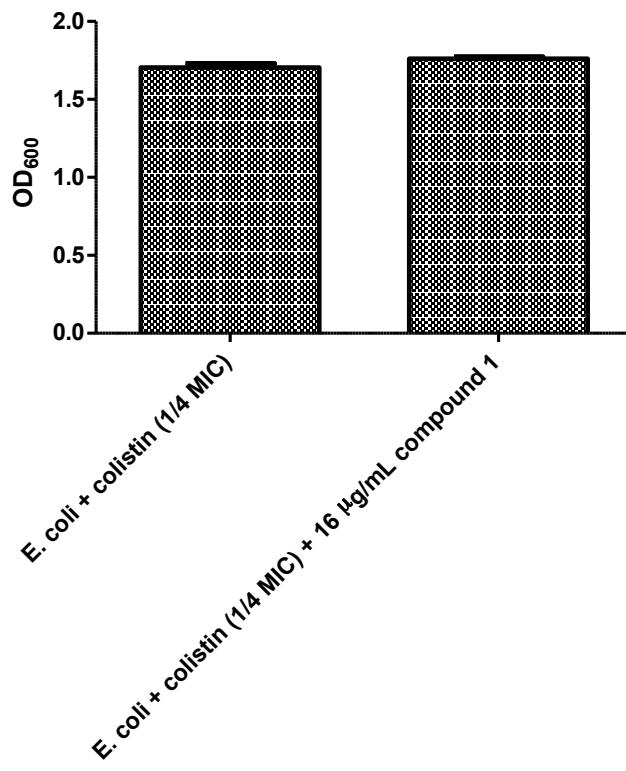
**Figure S2.** HPLC analysis of benzylidene-indolinones that did not inhibit DAC activity of DisA. Compounds were tested at 20  $\mu$ M in a 40 mM Tris-HCl pH 7.5, 100 mM NaCl and 10 mM MgCl<sub>2</sub> reaction buffer with 100  $\mu$ M ATP and 0.25  $\mu$ M DisA for 2 h. ATP and c-di-AMP peaks are as indicated on compound **2**.



**Figure S3.** Plot of the effect of other benzylidene-indolinones on *S. aureus* and *E. coli* at 16 µg/mL. We screened these compounds against *S. aureus* and *E. coli* as representative Gram-positive and Gram-negative bacteria respectively. These compounds were inactive.



**Figure S4.** **A.** Coralyne assay of DisA activity in the presence of compound I (indolinone). The structure of compound I is as shown in the insert. **B.** The effect of compound I on the growth of *S. aureus* and *E. coli* at 16 µg/mL. Compound I did not have any effect on DAC activity and growth of the bacteria tested.



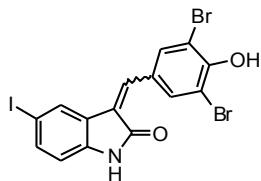
**Figure S5.** Compound **1** does not affect the growth of *E. coli* in the presence of sub-inhibitory concentrations of colistin. *E. coli* was cultured in the presence of  $\frac{1}{4}$  MIC of colistin (0.03125 µg/mL) with and without 16 µg/mL of compound **1**.

## Methods

### General procedure for the synthesis of 3-(Benzylidene)indolin-2-ones:

Following a literature procedure<sup>1</sup> a solution of indolinone (1 mmol) in acetic acid (10 mL) was treated with aldehyde (1 mmol) and sodium acetate (2 mmol). Reaction mixture was refluxed for 5 h. After the completion of reaction cold water (15 mL) was added to the reaction mixture and the resulted precipitate was filtered, washed with cold water and recrystallized from ethanol or purified by silica column chromatography (methanol : dichloromethane = 1 : 40, v/v) to give the corresponding desired product. *E* and *Z* isomers of the product were characterized from the precedent literature<sup>1</sup>.

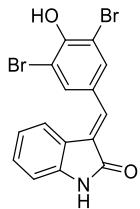
### 3-(3,5-Dibromo-4-hydroxybenzylidene)-5-iodoindolin-2-one (1)



*Z / E* ≈ (1/1)

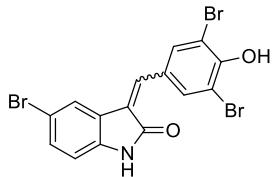
Yellow solid (40%); <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.75 (s, 1H), 10.71 (s, 1H), 8.78 (s, 2H), 8.01 (s, 1H), 7.91 (s, 1H), 7.79 (d, *J* = 2.4 Hz, 2H), 7.55 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.52 (s, 1H), 7.50 (dd, *J* = 8.1, 1.7 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 6.66 (d, *J* = 8.1 Hz, 1H); <sup>13</sup>C NMR (126 MHz, DMSO) δ 167.20, 155.08, 140.51, 137.24, 136.88, 136.16, 135.16, 133.88, 128.40, 128.05, 126.92, 117.25, 113.06, 112.31, 111.63, 84.55, 62.88; LR-MS(ESI) m/z calcd for C<sub>15</sub>H<sub>9</sub>Br<sub>2</sub>INO<sub>2</sub> ([M+H]<sup>+</sup>) 519.8, found 519.7.

### (*E*)-3-(3,5-Dibromo-4-hydroxybenzylidene)indolin-2-one (2)



Yellow solid (58%); <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.58 (s, 1H), 7.89 (s, 2H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.22 (td, *J* = 7.7, 1.1 Hz, 1H), 6.85 (t, *J* = 6.25 Hz, 1H). <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 168.90, 152.44, 143.53, 133.67, 130.77, 129.11, 128.02, 122.42, 121.65, 121.20, 112.26, 110.78; HRMS (ESI) m/z calcd for C<sub>15</sub>H<sub>10</sub>Br<sub>2</sub>NO<sub>2</sub> [M + H]<sup>+</sup> 393.9078, found 393.9078.

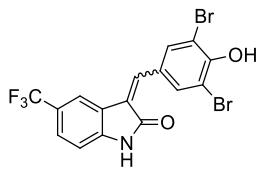
### 5-Bromo-3-(3,5-dibromo-4-hydroxybenzylidene)indolin-2-one (3)



*Z* major/ *E* minor ≈ (2/1)

Yellow solid (70%);  $^1\text{H}$  NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.78 (s, 1H), 10.73 (s, 0.5 H), 8.77 (s, 2H), 7.92 (s, 1H), 7.87 (s, 1H), 7.81 (s, 1H), 7.58 (d, *J* = 1.9 Hz, 0.3H), 7.54 (s, 0.3H), 7.40 (dd, *J* = 8.4, 1.9 Hz, 0.3H), 7.34 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.83 (d, *J* = 8.3 Hz, 0.3H), 6.77 (d, *J* = 8.2 Hz, 1H);  $^{13}\text{C}$  NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 168.46, 167.37, 153.53, 152.74, 143.46, 142.57, 140.05, 136.88, 136.37, 135.43, 133.84, 132.89, 131.45, 130.53, 128.99, 128.78, 127.69, 125.12, 124.96, 123.38, 122.84, 113.57, 113.26, 113.06, 112.57, 112.31, 111.78, 111.60, 111.34; HRMS (ESI) m/z calcd for C<sub>15</sub>H<sub>9</sub>Br<sub>3</sub>NO<sub>2</sub> [M + H]<sup>+</sup> 471.8183, found 471.8192.

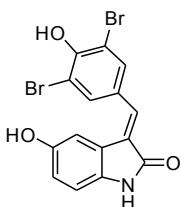
### 3-(3,5-Dibromo-4-hydroxybenzylidene)-5-(trifluoromethyl)indolin-2-one (4)



*Z/E* ≈ (1/1)

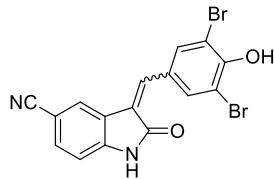
Yellow solid (55%);  $^1\text{H}$  NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.75 (s, 1H), 10.70 (s, 1H) 8.77 (s, 1H), 8.04 (s, 1H), 8.00 (s, 1H), 7.90 (s, 1.7H), 7.78 (s, 1H), 7.54 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.51 (s, 1H), 7.49 (dd, *J* = 8.1, 1.7 Hz, 1H), 6.71 (d, *J* = 8.2 Hz, 1H), 6.66 (d, *J* = 8.1 Hz, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 168.25, 167.17, 153.35, 152.65, 142.96, 140.51, 138.61, 137.78, 137.26, 136.84, 136.08, 135.09, 134.12, 133.85, 130.78, 128.95, 128.69, 128.42, 128.00, 126.89, 125.04, 123.82, 113.05, 112.50, 112.27, 111.55, 84.54, 84.24; HRMS (ESI) m/z calcd for C<sub>16</sub>H<sub>9</sub>Br<sub>2</sub>F<sub>3</sub>NO<sub>2</sub> [M + H]<sup>+</sup> 461.8952, found 461.8955.

### (E)3-(3,5-Dibromo-4-hydroxybenzylidene)-5-hydroxyindolin-2-one (5)



Orange solid (88%);  $^1\text{H}$  NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.50 (s, 1H), 10.25 (s, 1H), 9.03 (s, 1H), 7.84 (s, 2H), 7.40 (s, 1H), 6.93 (d, *J* = 1.9 Hz, 1H), 6.67-6.63 (m, 2H).  $^{13}\text{C}$  NMR (126 MHz, DMSO) δ 168.90, 152.35, 152.19, 135.87, 133.46, 133.16, 129.24, 128.97, 121.85, 117.34, 112.29, 111.09, 110.13; HRMS (ESI) m/z calcd for C<sub>15</sub>H<sub>10</sub>Br<sub>2</sub>NO<sub>3</sub> [M + H]<sup>+</sup> 409.9027, found 409.9030

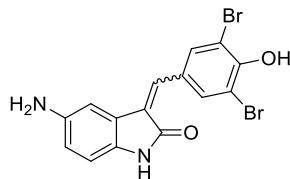
### 3-(3,5-Dibromo-4-hydroxybenzylidene)-2-oxoindoline-5-carbonitrile (6)



*Z* major/*E* minor ≈ (2/1)

Orange solid (72%);  $^1\text{H}$  NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 11.16 (s, 1H), 11.12 (s, 0.4H), 8.75 (s, 2H), 8.10 (s, 1H), 7.95 (s, 1H), 7.90 (s, 1H), 7.76 (s, 0.4H), 7.69 (dd, *J* = 8.1, 1.6 Hz, 0.4 H), 7.67 – 7.61 (m, 1.4H), 7.01 (d, *J* = 8.2 Hz, 0.4H), 6.96 (d, *J* = 8.1 Hz, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO) δ 167.55, 153.87, 147.09, 144.49, 137.49, 136.97, 136.68, 135.00, 133.96, 133.54, 128.54, 126.35, 125.72, 124.08, 123.72, 122.04, 120.05, 112.36, 111.66, 110.67, 103.60. HRMS (ESI) m/z calcd for C<sub>16</sub>H<sub>9</sub>Br<sub>2</sub>N<sub>2</sub>O<sub>2</sub> [M + H]<sup>+</sup> 418.9030, found 418.9030.

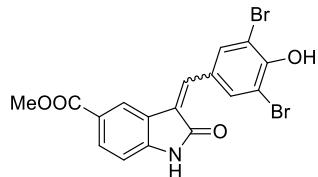
### 5-Amino-3-(3,5-dibromo-4-hydroxybenzylidene)indolin-2-one (7)



*Z* major/*E* minor ≈ (1/1)

Brown solid (52%);  $^1\text{H}$  NMR (500 MHz, MeOD-*d*<sub>4</sub>) δ 8.62 (s, 2H), 7.80 (s, 2H), 7.47 (s, 1H), 7.40 (s, 1H), 7.09 (s, 1H), 7.04 (s, 1H), 6.71 – 6.67 (m, 2H), 6.65 (d, *J* = 8.2 Hz, 1H);  $^{13}\text{C}$  NMR (126 MHz, MeOD) δ 170.06, 168.34, 153.18, 152.71, 141.23, 140.88, 135.99, 135.16, 133.98, 133.58, 133.40, 132.96, 128.37, 128.21, 126.34, 125.96, 121.73, 117.76, 116.73, 111.03, 110.84, 110.52, 110.21, 109.73, 107.58; HRMS (ESI) m/z calcd for C<sub>15</sub>H<sub>11</sub>Br<sub>2</sub>N<sub>2</sub>O<sub>2</sub> [M + H]<sup>+</sup> 408.9187, found 408.9170.

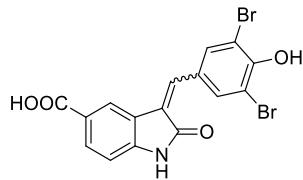
### Methyl 3-(3,5-dibromo-4-hydroxybenzylidene)-2-oxoindoline-5-carboxylate (8)



*E* major /*Z* minor ≈ (20/1)

Yellow solid (89%);  $^1\text{H}$  NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 11.04 (s, 0.1H), 11.00 (s, 1H), 10.66 (s, 1H), 8.83 (s, 0.1H), 8.26 (s, 0.1H), 8.22 (s, 1H), 7.95 (s, 2H), 7.91 (s, 0.1H), 7.85 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.56 (s, 1H), 6.95 (d, *J* = 8.2 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, OH), 3.83 (s, 0.2H), 3.76 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO) δ 169.14, 166.21, 152.74, 147.45, 136.94, 135.17, 134.02, 132.31, 131.07, 128.95, 128.62, 126.83, 123.48, 122.78, 121.22, 112.29, 111.51, 110.53, 52.37; HRMS (ESI) m/z calcd for C<sub>17</sub>H<sub>12</sub>Br<sub>2</sub>NO<sub>4</sub> [M + H]<sup>+</sup> 451.9133, found 451.9118.

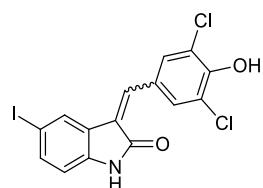
**3-(3,5-Dibromo-4-hydroxybenzylidene)-2-oxoindoline-5-carboxylic acid (9)**



*Z* major /*E* minor ≈ (1.5/1)

Yellow solid (63%);  $^1\text{H}$  NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.99 (s, 1H), 10.96 (s, 0.6H), 10.69 (s, 1H), 8.84 (s, 2H), 8.27 (d, *J* = 1.6 Hz, 1H), 8.19 (d, *J* = 1.6 Hz, 0.6H), 7.94 (s, 1.3H), 7.89 (s, 0.8H), 7.85 (dd, *J* = 8.2, 1.6 Hz, 0.7H), 7.82 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.55 (s, 0.6H), 6.95 (d, *J* = 8.2 Hz, 0.7H), 6.90 (d, *J* = 8.2 Hz, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO) δ 169.20, 168.05, 167.81, 167.31, 148.42, 147.11, 144.54, 136.96, 133.94, 132.45, 131.04, 130.44, 126.40, 125.88, 125.50, 124.00, 123.60, 121.33, 112.42, 111.72, 110.37, 109.53, 109.19. HRMS (ESI) m/z calcd for C<sub>16</sub>H<sub>10</sub>Br<sub>2</sub>NO<sub>4</sub> [M + H]<sup>+</sup> 437.8976, found 437.8971.

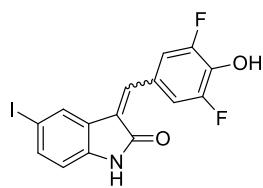
**3-(3,5-Dichloro-4-hydroxybenzylidene)-5-iodoindolin-2-one (10)**



*Z* major/*E* minor ≈ (2/1)

Yellow solid (66%);  $^1\text{H}$  NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.74 (s, 1H), 10.70 (s, 0.5H), 8.78 (s, 2H), 8.00 (s, 1H), 7.91 (s, 1H), 7.78 (s, 1H), 7.58 – 7.53 (m, 0.5 H), 7.52 – 7.49 (m, 1H), 6.72 (d, *J* = 8.1 Hz, 0.5H), 6.66 (d, *J* = 8.2 Hz, 1H);  $^{13}\text{C}$  NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 168.30, 167.20, 142.91, 140.38, 138.54, 136.91, 136.26, 135.22, 133.89, 133.17, 130.73, 128.29, 128.14, 123.88, 122.14, 113.04, 112.36, 112.22, 111.77, 84.51, 84.25; HRMS (ESI) m/z calcd for C<sub>15</sub>H<sub>8</sub>Cl<sub>2</sub>INO<sub>2</sub> [M + H]<sup>+</sup> 430.8976, found 430.8985.

**(Z)-3-(3,5-Difluoro-4-hydroxybenzylidene)-5-iodoindolin-2-one (11)**

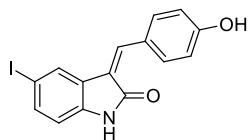


*E* major/*Z* minor ≈ (2/1)

Yellow solid (48%);  $^1\text{H}$  NMR (500 MHz, MeOD + DMSO-*d*<sub>6</sub>) δ 9.56 (s, 1H), 8.16 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.98 (s, 0.5H), 7.90 (s, 0.5H), 7.61 – 7.44 (m, 2H), 7.36 (s, 2H), 7.34 (s, 1H), 6.73 – 6.66 (m, 1.5H);  $^{13}\text{C}$  NMR (126 MHz, MeOD+ DMSO-*d*<sub>6</sub>) δ 189.52, 139.49, 137.96, 136.99, 136.49, 136.38, 130.71, 127.97, 127.56,

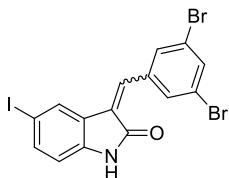
123.71, 122.99, 116.04, 112.41, 112.03, 111.35, 111.17, 83.20; LR-MS(ESI) m/z calcd for  $C_{15}H_9F_2INO_2$  ( $[M+H]^+$ ) 339.9, found 339.9.

**(Z)-3-(4-Hydroxybenzylidene)-5-iodoindolin-2-one (12)**



Yellow solid (53%);  $^1H$  NMR (500 MHz, MeOD)  $\delta$  8.50 (d,  $J = 8.7$  Hz, 2H), 8.06 (d,  $J = 1.3$  Hz, 1H), 7.80 (s, 1H), 7.58 (dd,  $J = 8.1, 1.4$  Hz, 1H), 6.95 (d,  $J = 8.7$  Hz, 2H), 6.79 (d,  $J = 8.1$  Hz, 1H);  $^{13}C$  NMR (126 MHz, MeOD)  $\delta$  167.02, 160.54, 139.33, 136.15, 135.19, 128.39, 127.18, 125.71, 121.71, 119.41, 115.21, 111.45, 83.35; LR-MS(ESI) m/z calcd for  $C_{15}H_{11}INO_2$  ( $[M+H]^+$ ) 363.9, found 363.2.

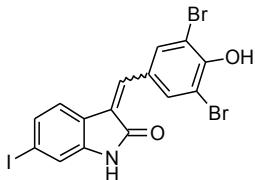
**3-(3,5-Dibromobenzylidene)-5-iodoindolin-2-one (13)**



*E* major/*Z* minor  $\approx$  (5/1)

Yellow solid (83%);  $^1H$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  10.82 (s, 0.2 H), 10.77 (s, 1H), 8.62 (s, 0.4H), 8.04 (s, 0.2H), 7.96 (s, 1H), 7.90 (s, 2H), 7.85 (s, 0.2H), 7.60 (s, 1H), 7.63-7.55 (m, 2H), 6.72 (d,  $J = 8.2$  Hz, 1H), 6.67 (d,  $J = 8.1$  Hz, 0.3H);  $^{13}C$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  167.92, 143.32, 141.19, 139.21, 138.68, 138.28, 135.14, 134.72, 134.25, 133.66, 131.27, 131.17, 129.13, 123.44, 123.23, 122.64, 113.20, 112.49, 84.36; HRMS (ESI) m/z calcd for  $C_{15}H_9Br_2INO$  [ $M + H]^+$  503.8095, found 503.8103.

**3-(3,5-Dibromo-4-hydroxybenzylidene)-6-iodoindolin-2-one (14)**

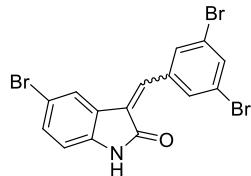


*E* major /*Z* minor  $\approx$  (3/1)

Yellow solid (85%);  $^1H$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  10.73 (s, 0.3H), 10.67 (s, 1H), 10.61 (s, 1H), 8.76 (s, 0.6H), 7.87 (s, 2H), 7.74 (s, 0.3), 7.52 (s, 1H), 7.43 (d,  $J = 8.0$  Hz, 1H), 7.35 (dd,  $J = 8.0, 1.5$  Hz, 1H), 7.26 (dd,  $J = 8.1, 1.5$  Hz, 1H), 7.23 (d,  $J = 8.1$  Hz, 1H), 7.18 (s, 1H), 7.13 (s, 0.3H);  $^{13}C$  NMR (126 MHz, DMSO)  $\delta$  168.54, 167.34, 152.56, 144.67, 142.25, 136.69, 135.46, 134.61, 133.70, 130.28, 130.18, 128.96, 127.18,

125.50, 125.09, 123.89, 121.90, 120.85, 119.09, 118.21, 112.30, 111.58, 96.44. HRMS (ESI) m/z calcd for  $C_{15}H_9Br_2INO_2$  [M + H]<sup>+</sup> 519.8044, found 519.8037.

**(Z)-5-Bromo-3-(3,5-dibromobenzylidene)indolin-2-one (15)**



E major/ Z minor ≈ (3/1)

Yellow solid (81%); <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.84 (s, 0.3 H), 10.80 (s, 1H), 8.61 (s, 0.7H), 7.96 (s, 1H), 7.90 (s, 2H), 7.86 (s, 0.3 H), 7.59 (s, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.39 (m, 1.3 H), 6.83 (d, *J* = 8.3 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 0.3 H). <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 168.10, 166.98, 142.94, 140.76, 138.65, 137.89, 135.38, 135.24, 134.76, 134.55, 133.67, 133.49, 132.50, 131.22, 129.29, 128.67, 127.04, 125.35, 123.58, 123.27, 122.98, 122.64, 113.72, 113.15, 112.74, 112.03; HRMS (ESI) m/z calcd for  $C_{15}H_9Br_3NO$  [M + H]<sup>+</sup> 455.8234, found 455.8242.

**(E) 3-(3,5-dibromo-2-hydroxybenzylidene)-5-iodoindolin-2-one (16)**

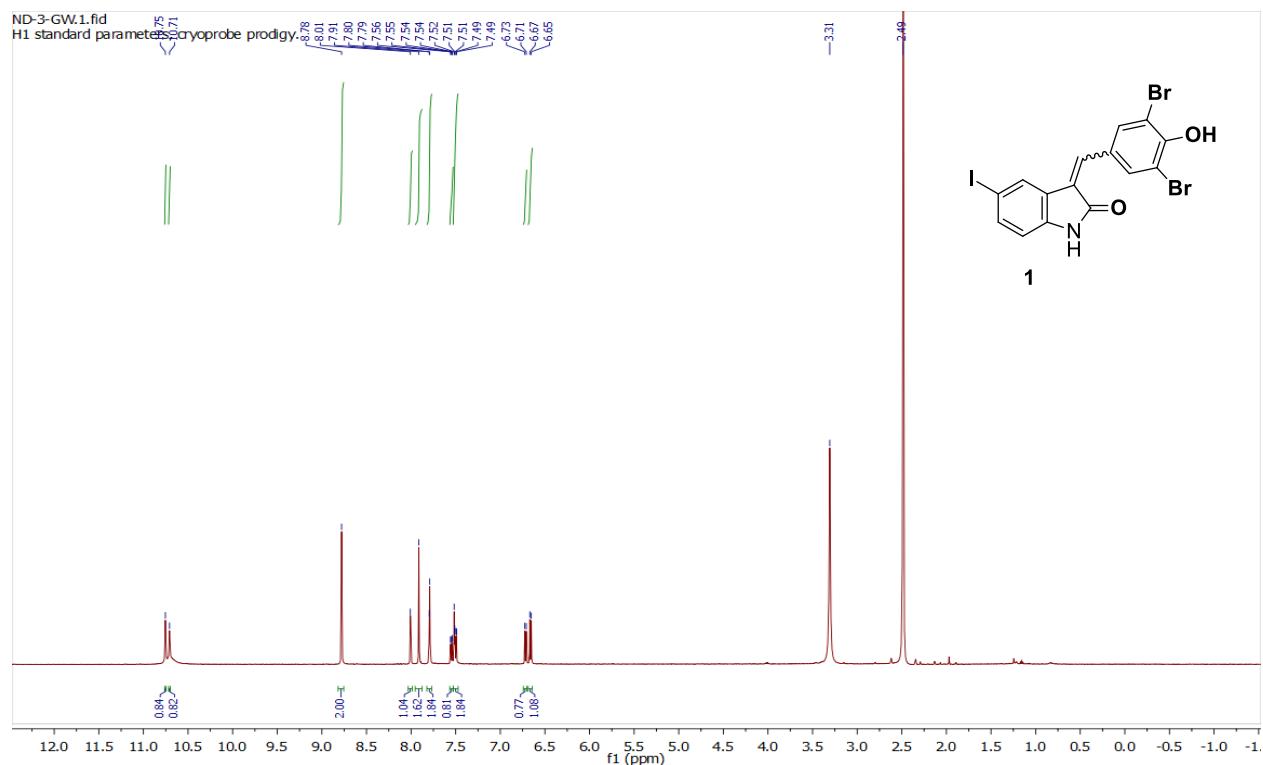


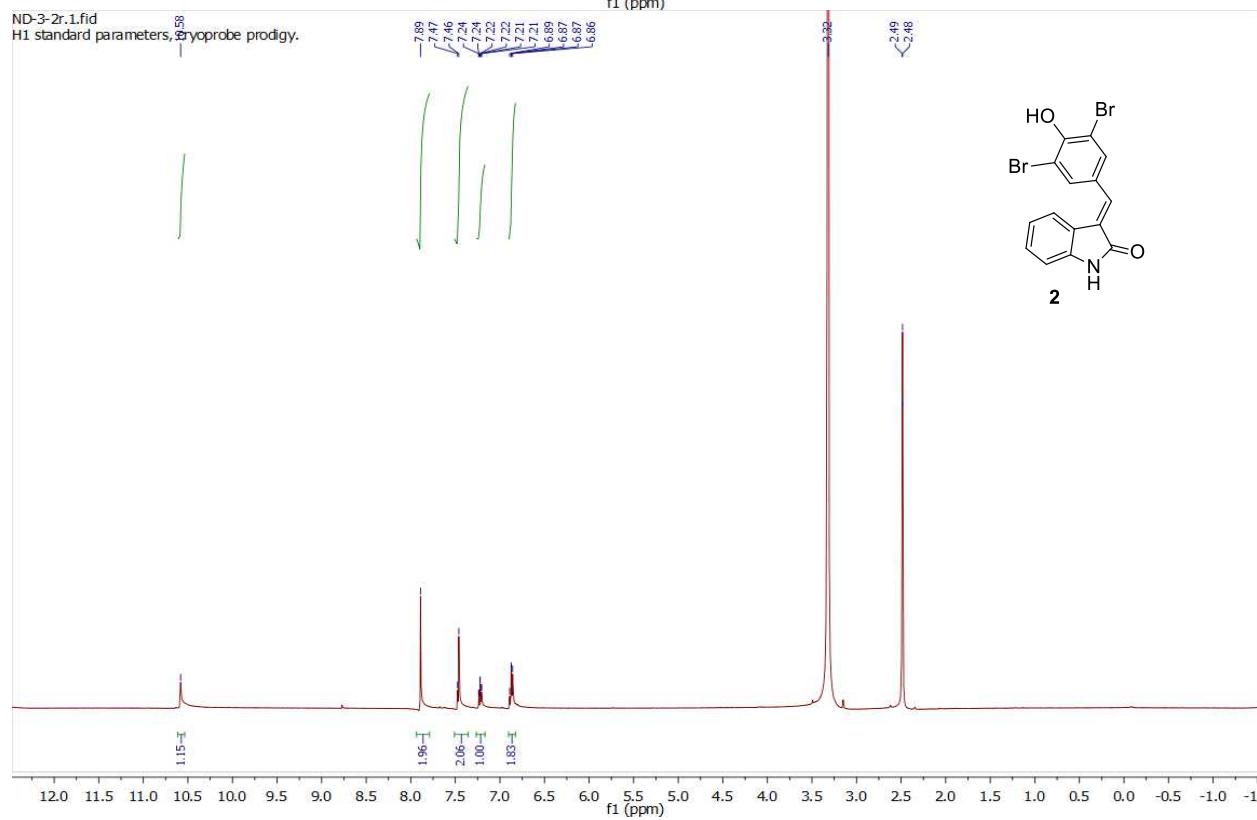
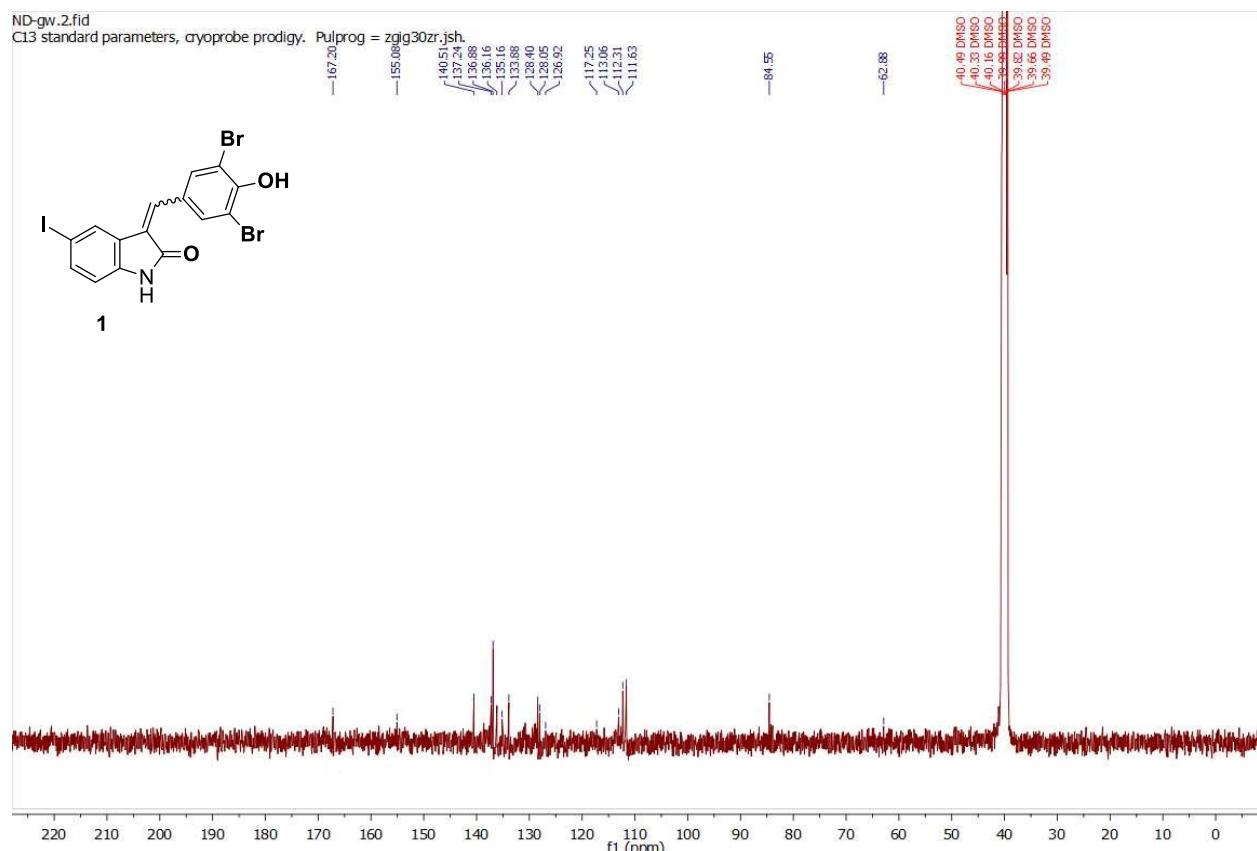
Brown solid (65%); <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.74 (s, 1H), 10.26 (s, 1H), 7.88 (d, *J* = 2.4 Hz, 1H), 7.71 (d, *J* = 2.4 Hz, 1H), 7.56 (s, 1H), 7.55 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.50 (s, 1H), 6.71 (d, *J* = 8.2 Hz, 1H); <sup>13</sup>C NMR (126 MHz, DMSO) δ 168.07, 152.59, 143.02, 138.81, 136.37, 131.91, 131.67, 131.37, 128.50, 126.07, 123.80, 113.93, 113.00, 84.35; HRMS (ESI) m/z calcd for  $C_{15}H_9Br_2INO_2$  [M + H]<sup>+</sup> 519.8044, found 519.8053.

**Reference**

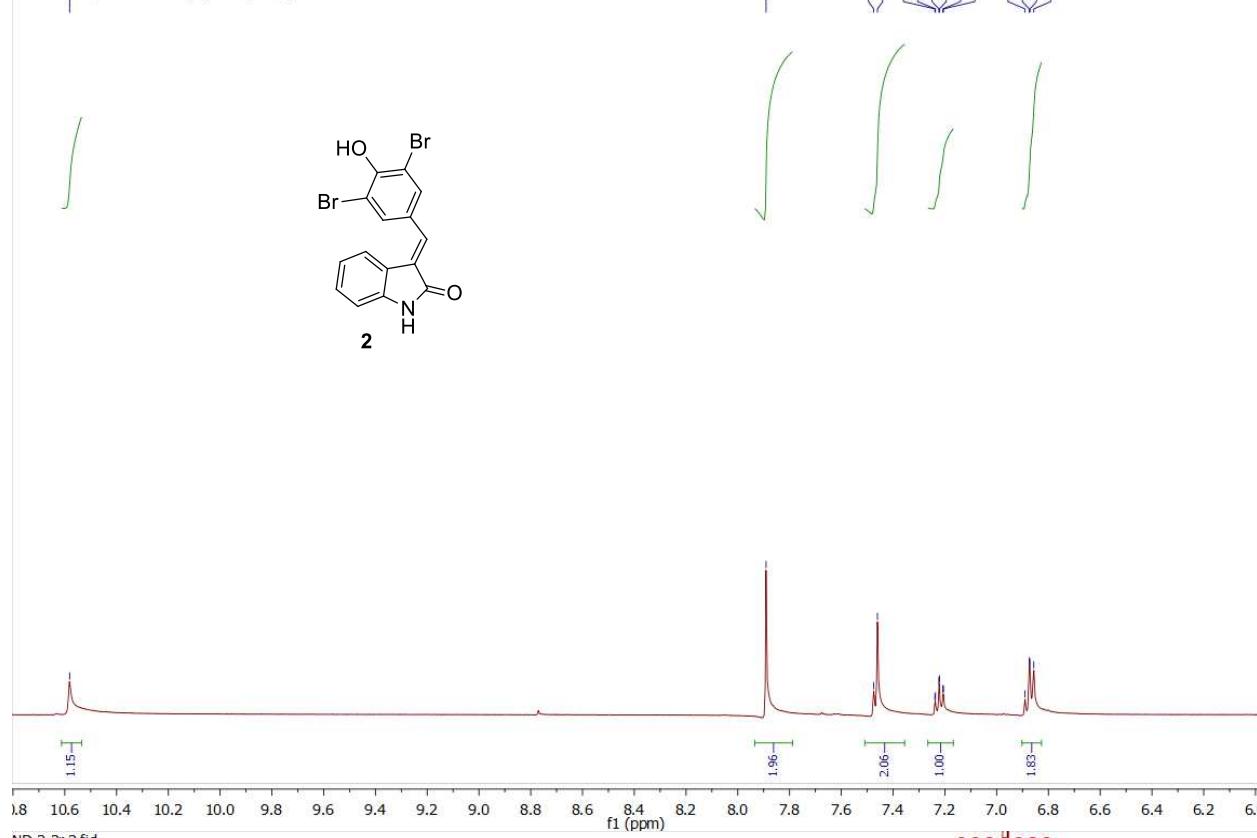
1. S. R. D'Mello and E. Biehl, U.S. Pat. Appl., Publ., US2009/0264494.

**Characterization of synthesized compounds**

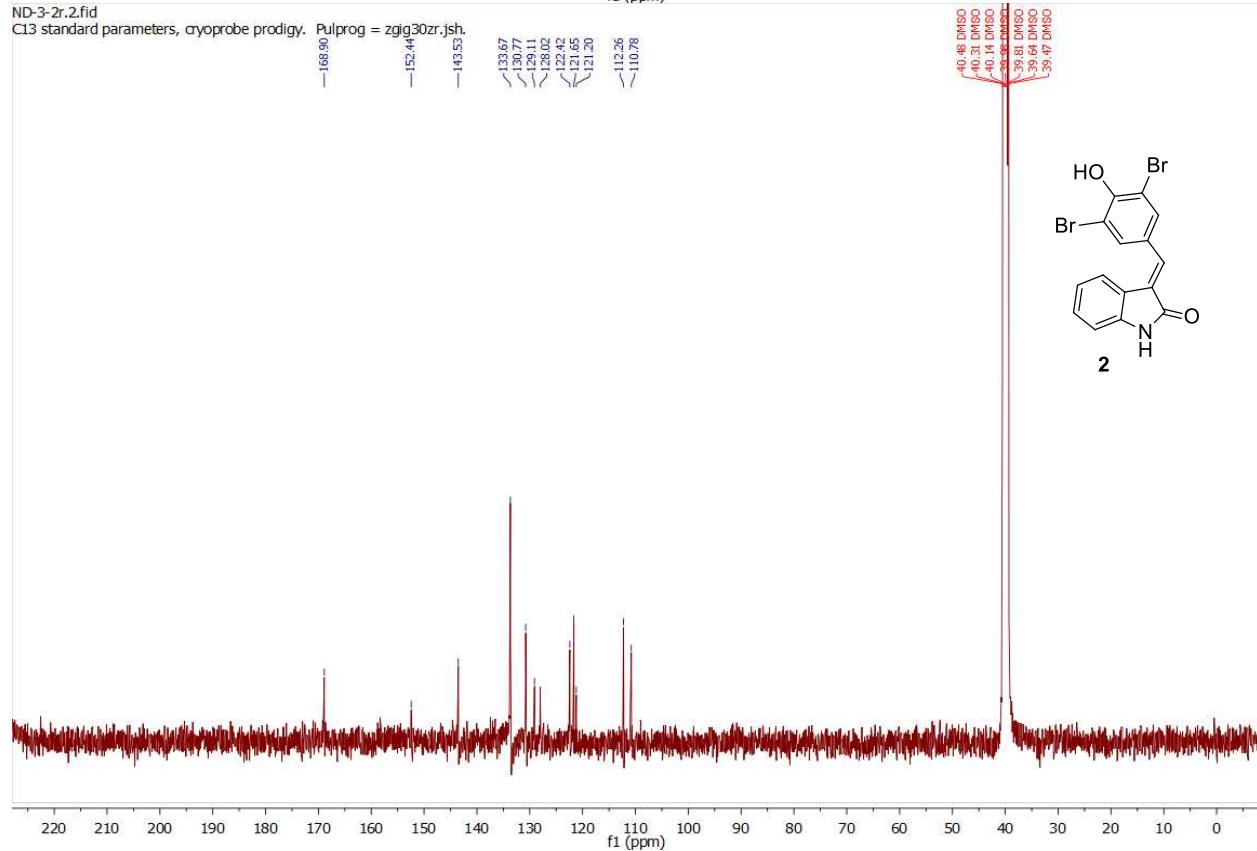


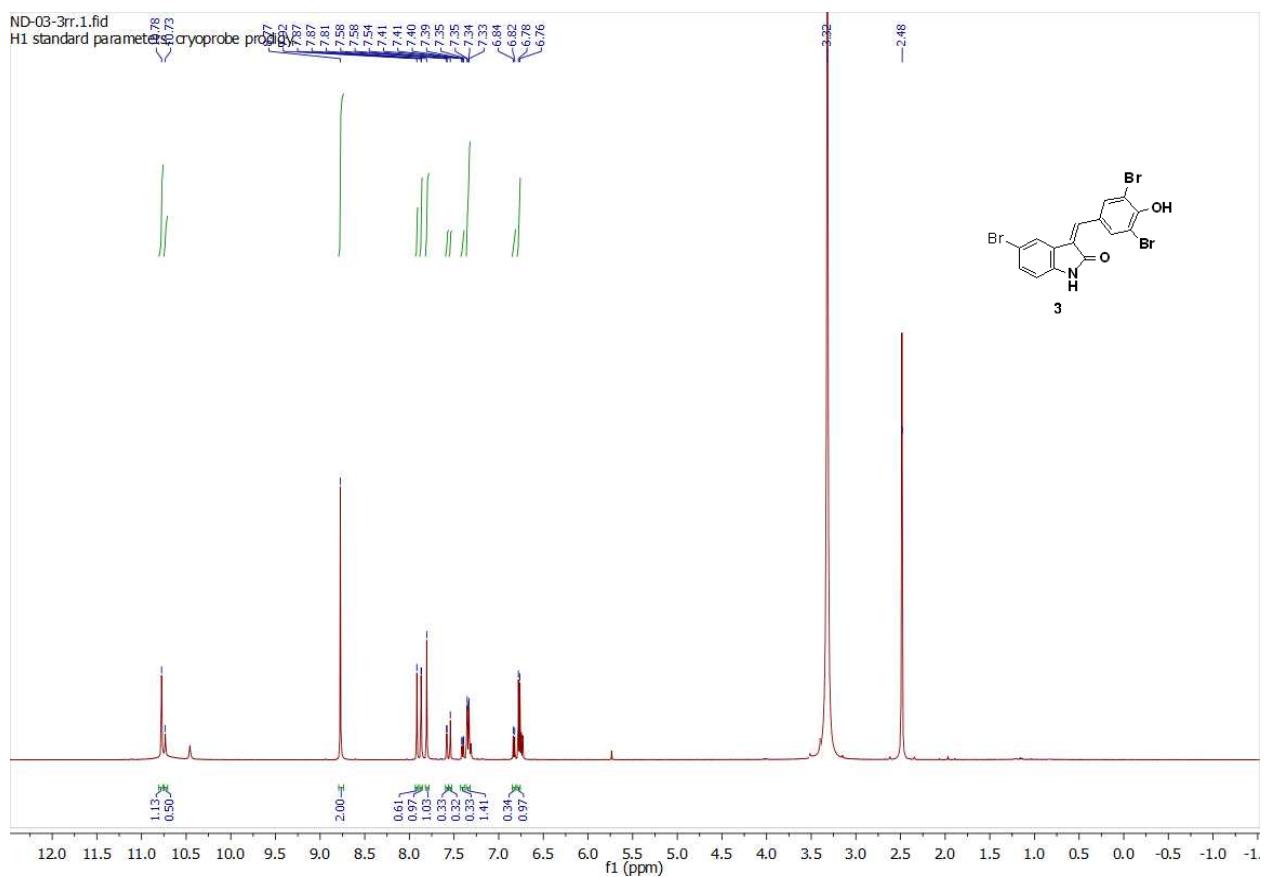


ND-3-2nd.fid  
H1 standard parameters, cryoprobe prodigy.



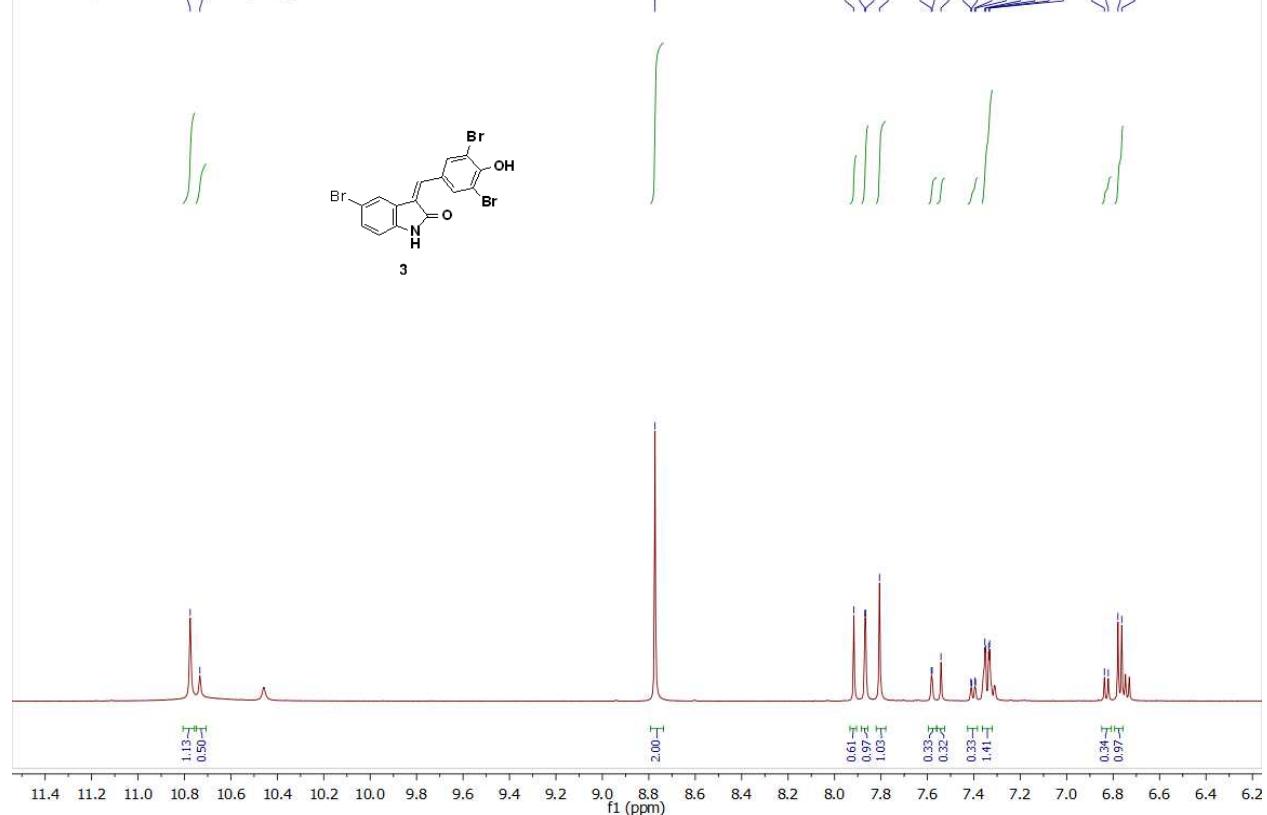
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C13 standard parameters, cryoprobe prodigy. Pulprog = zgig30zr.jsh.





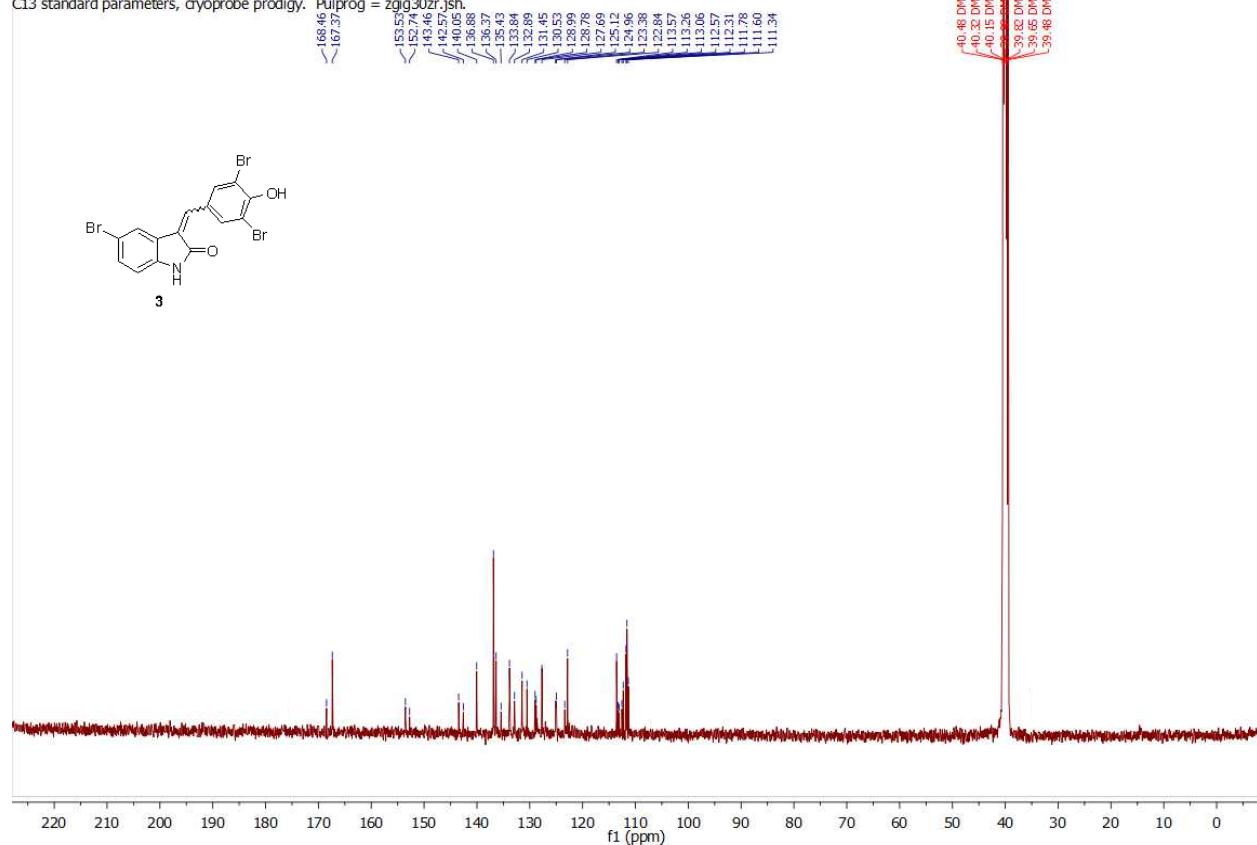
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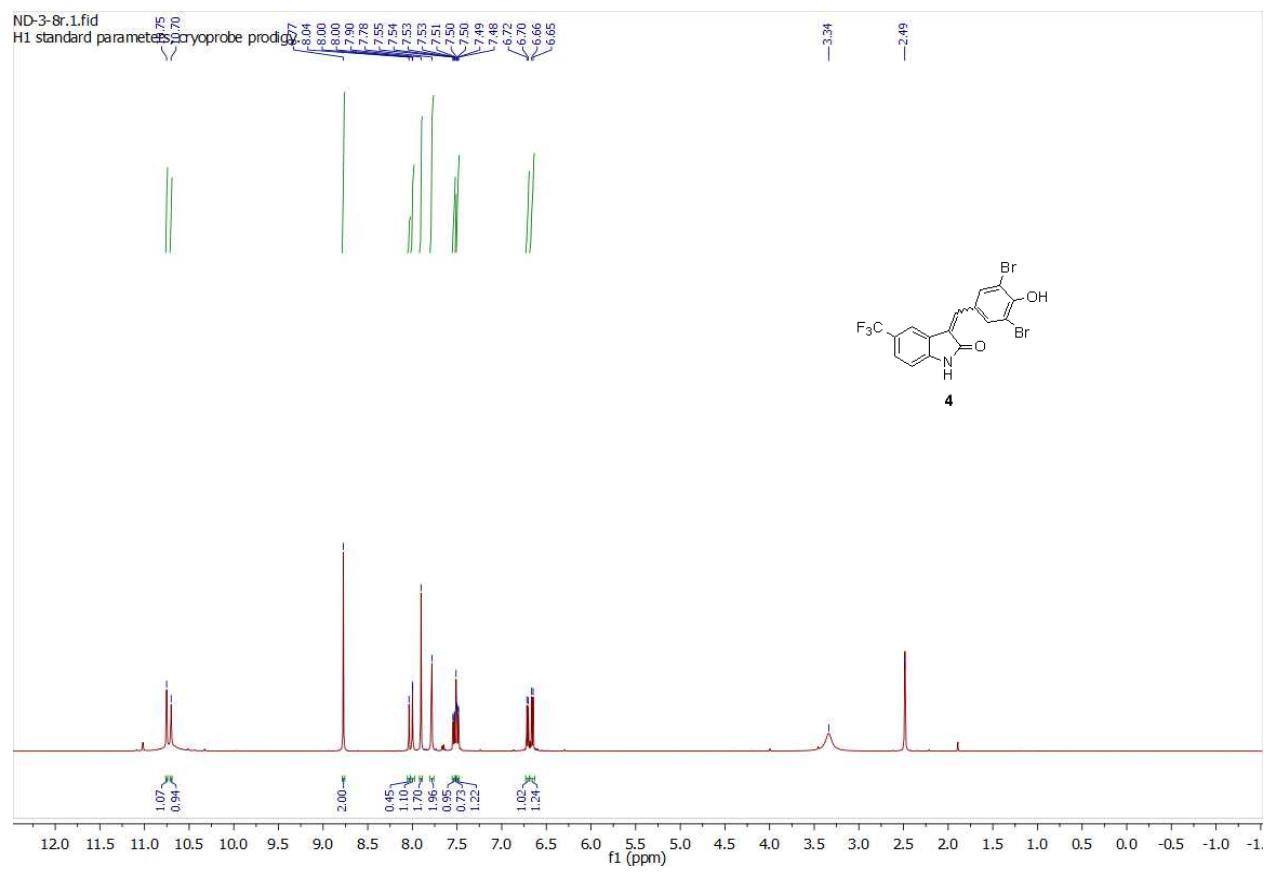
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H1 standard parameters,  $\delta_{ppm}$  7.26

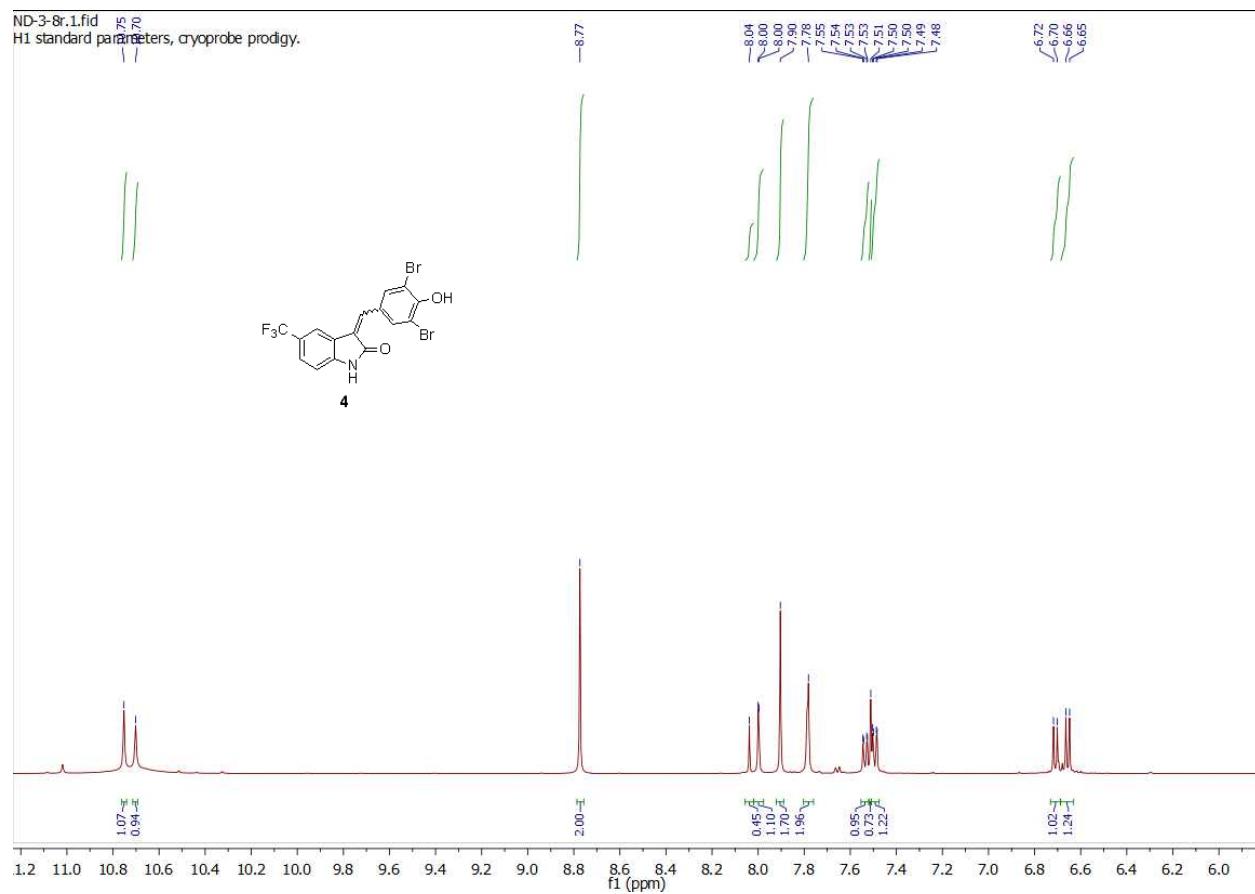


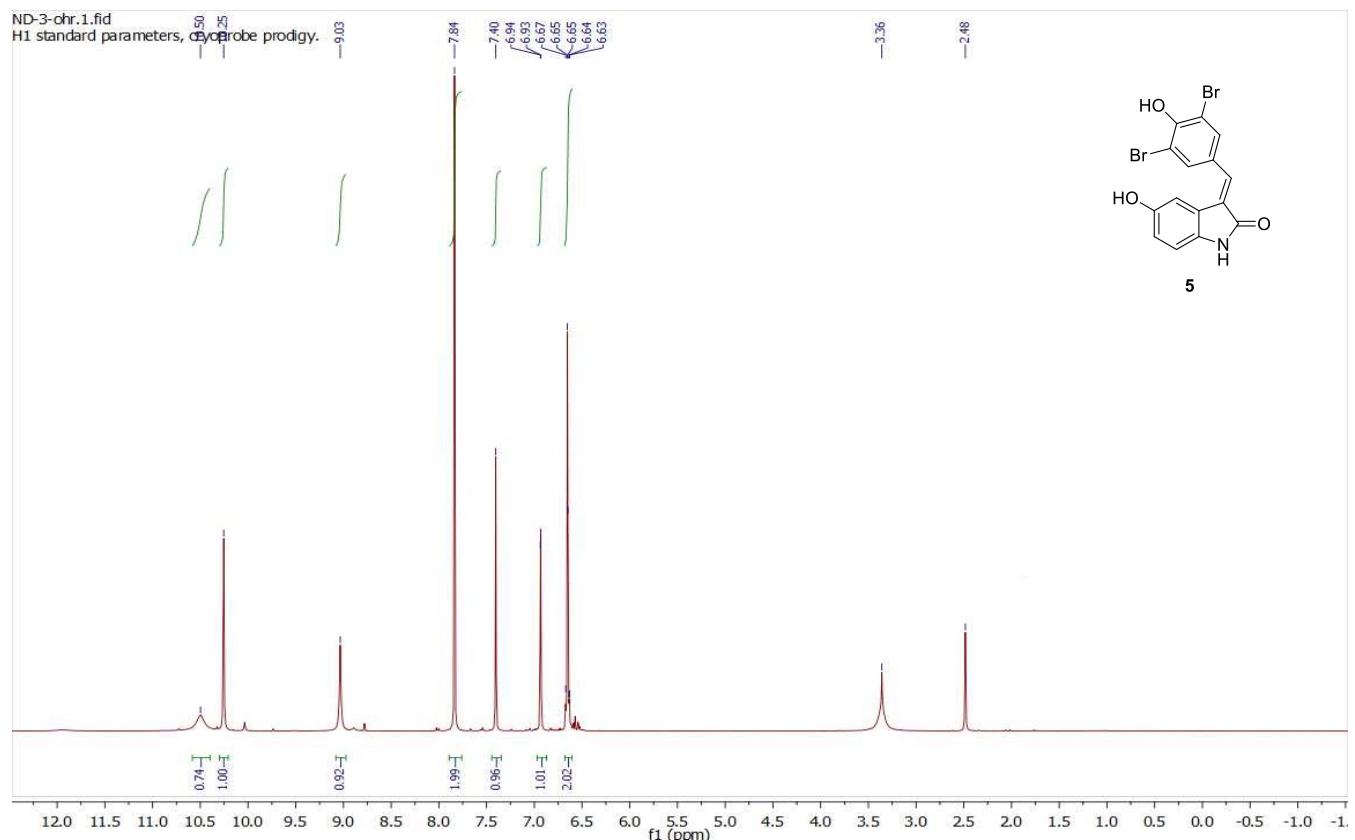
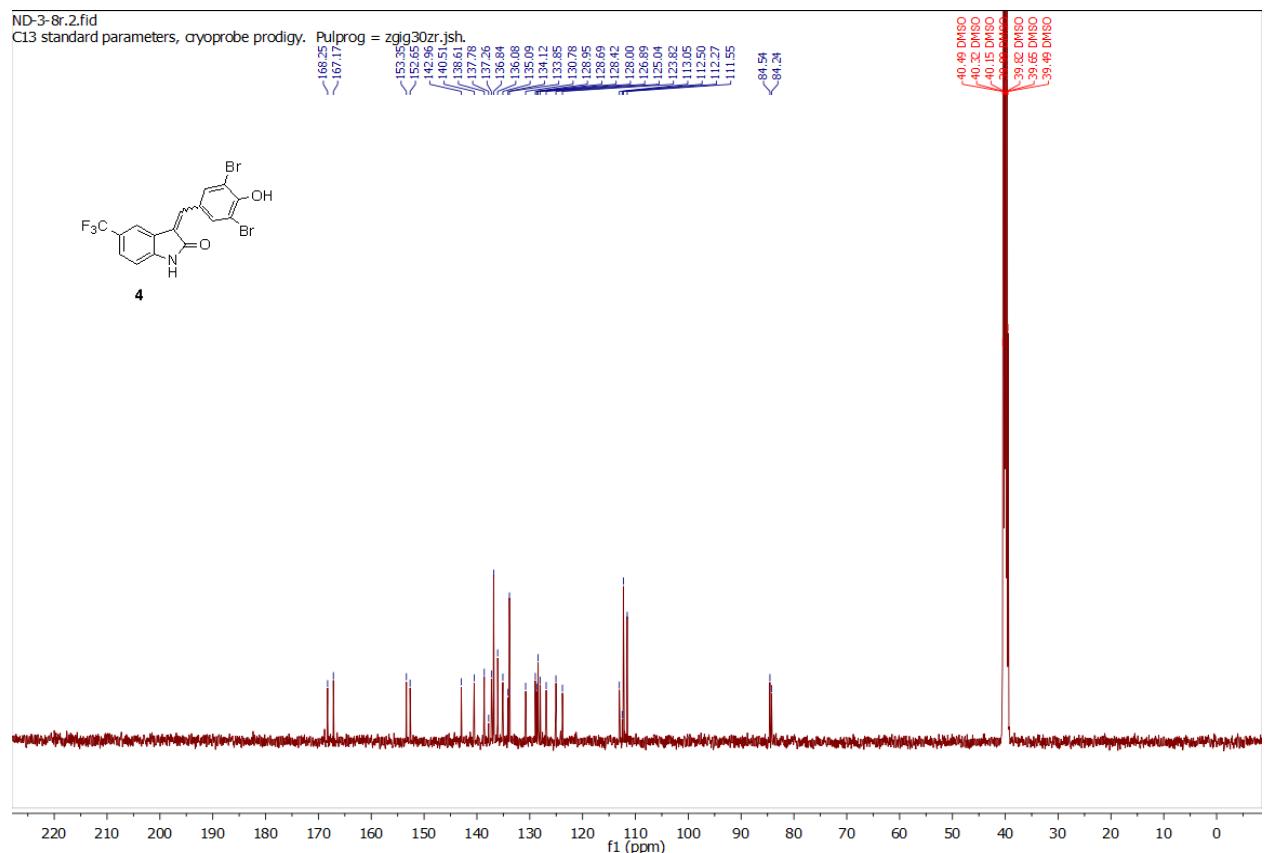
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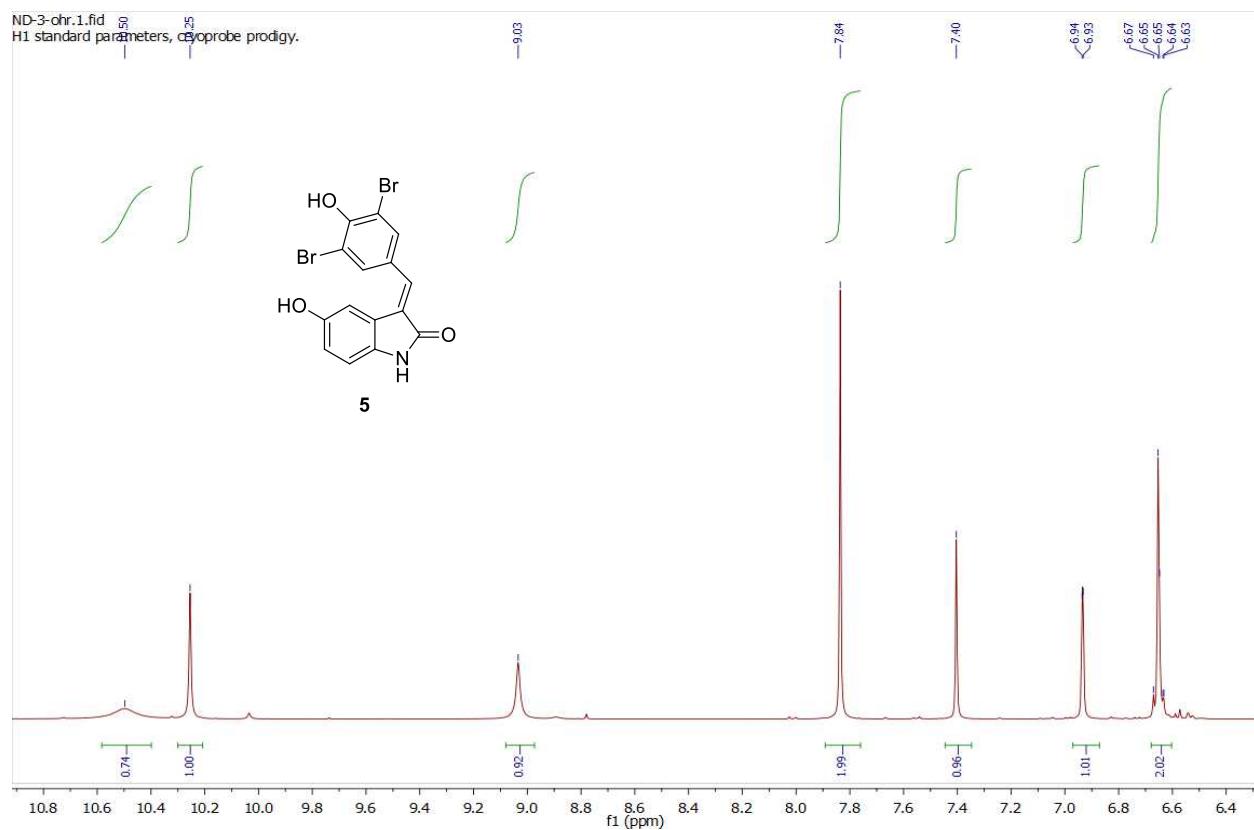
C13 standard parameters, cryoprobe prodigy. Pulprog = zgig30zr.jsh.

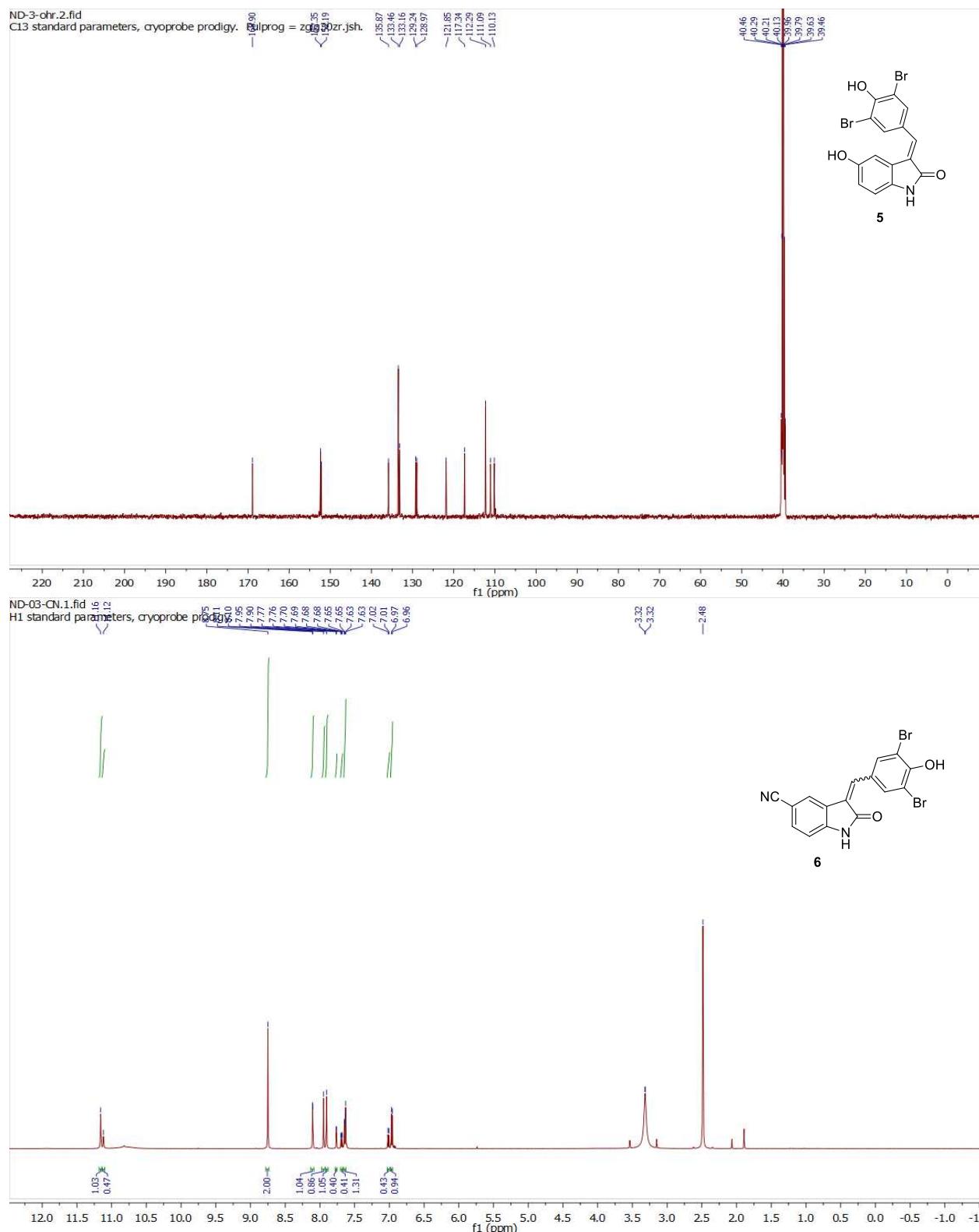






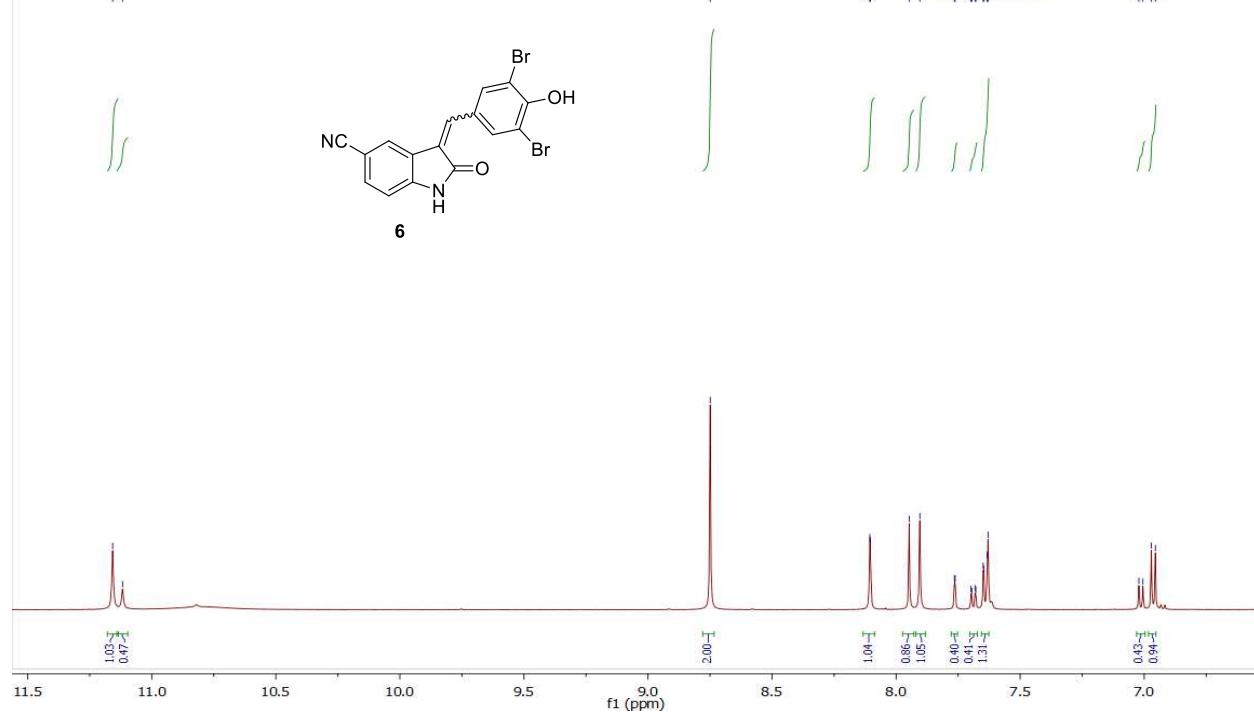




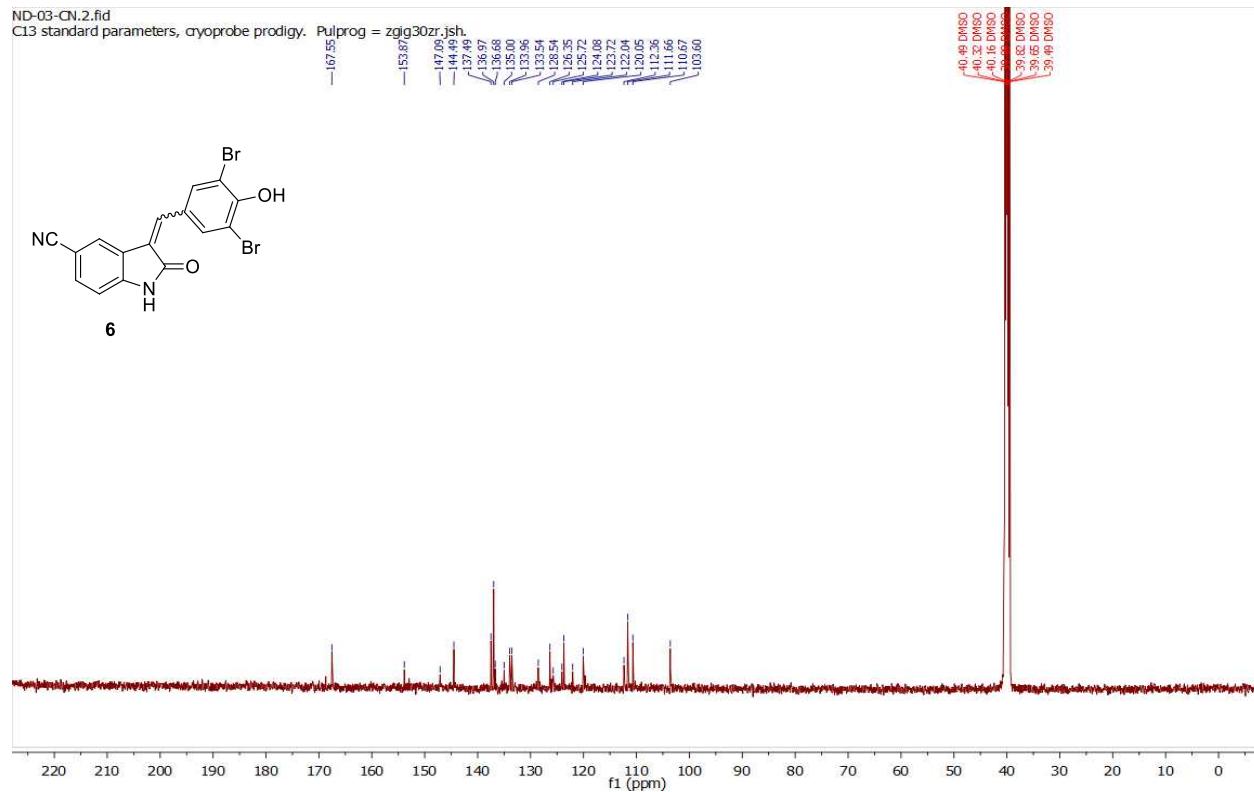


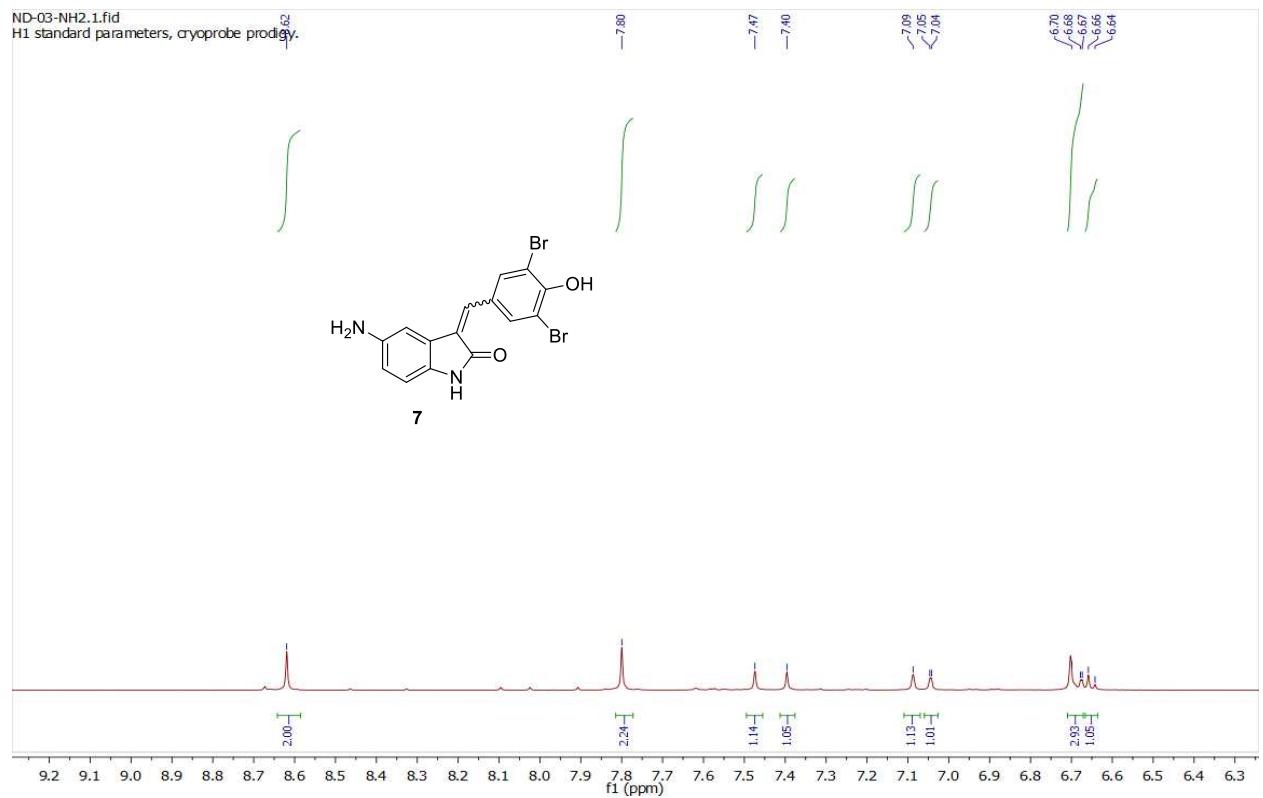
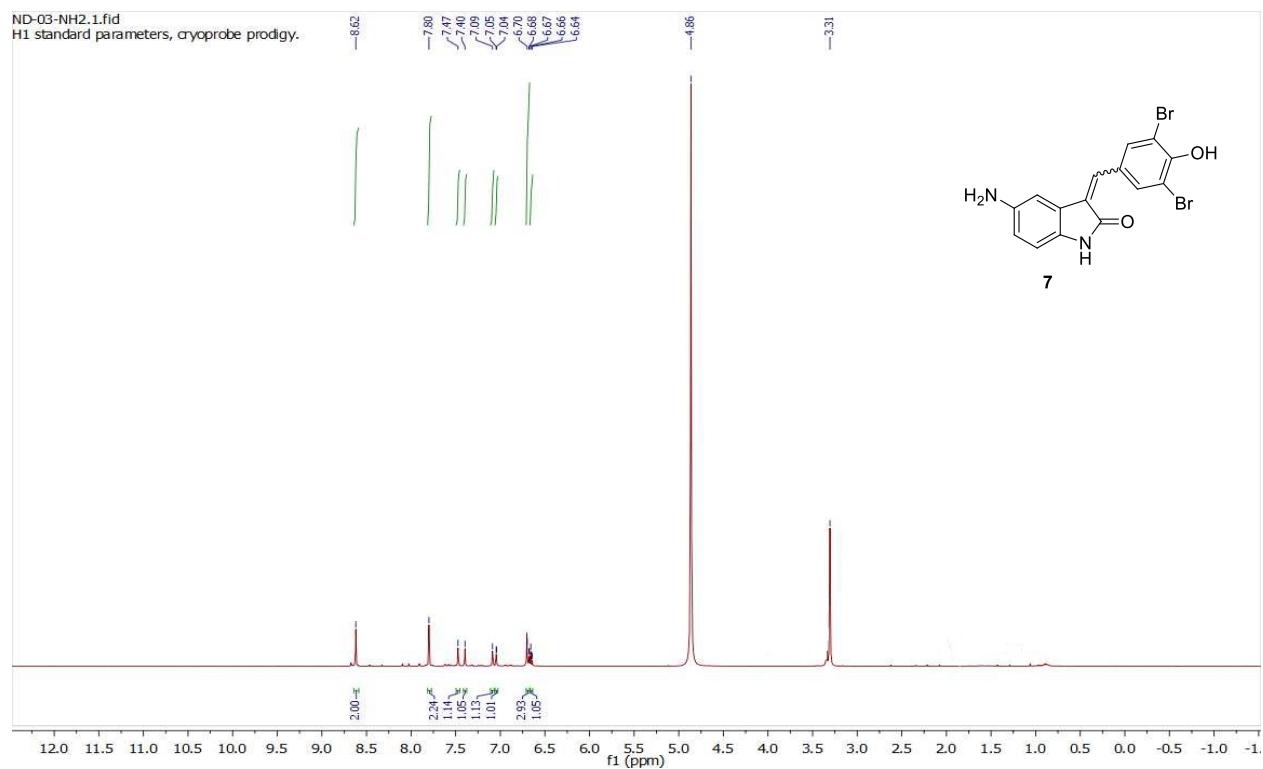
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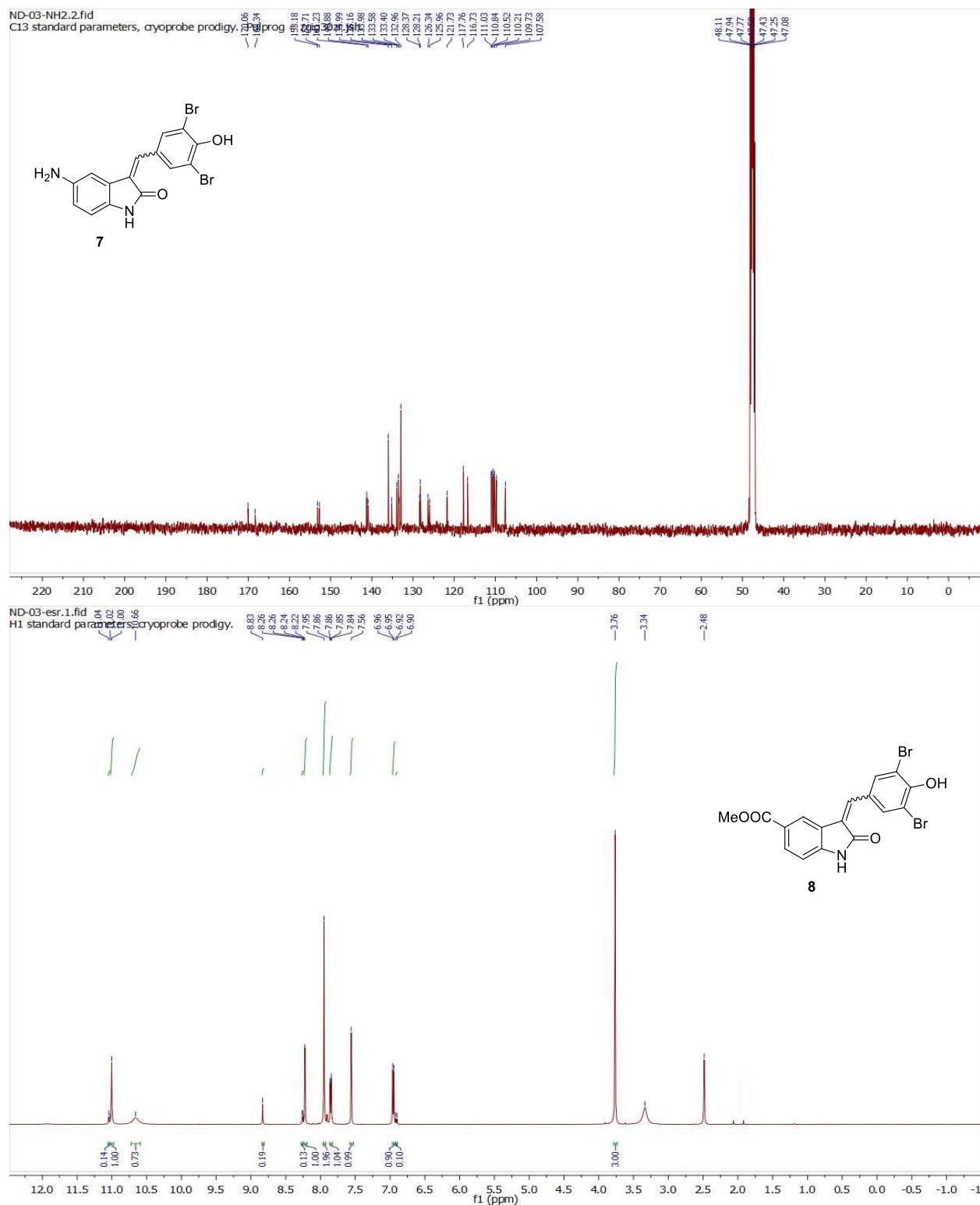
ND-03-CN.1.fid  
H1 standard parameters, cryoprobe prodigy.

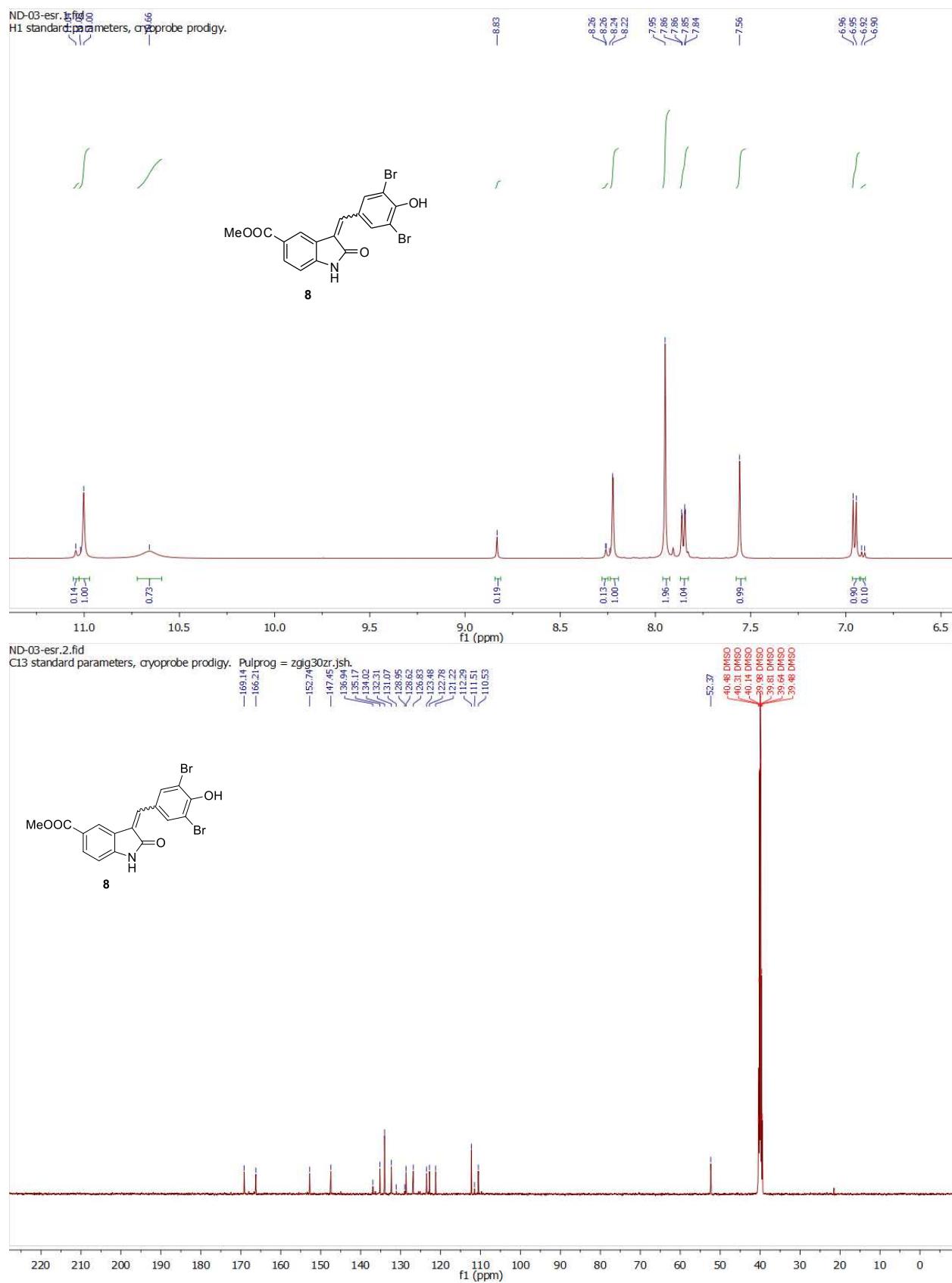


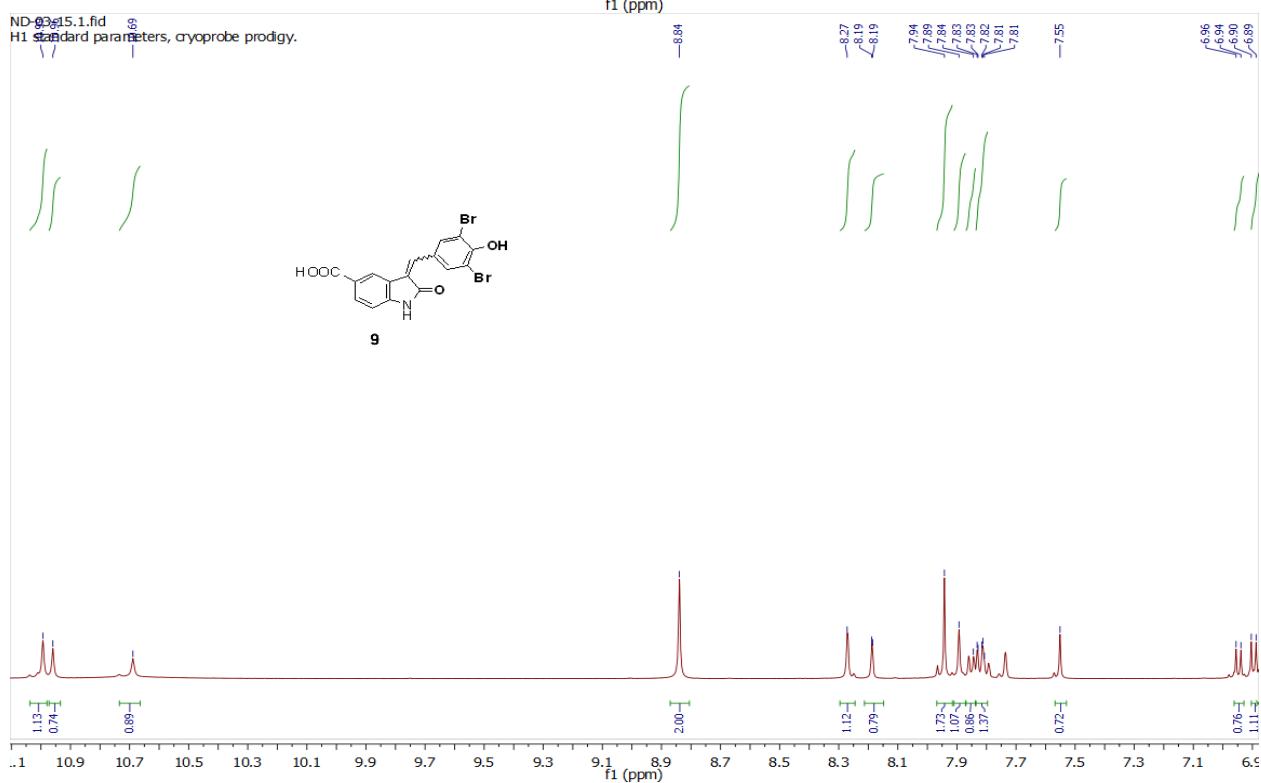
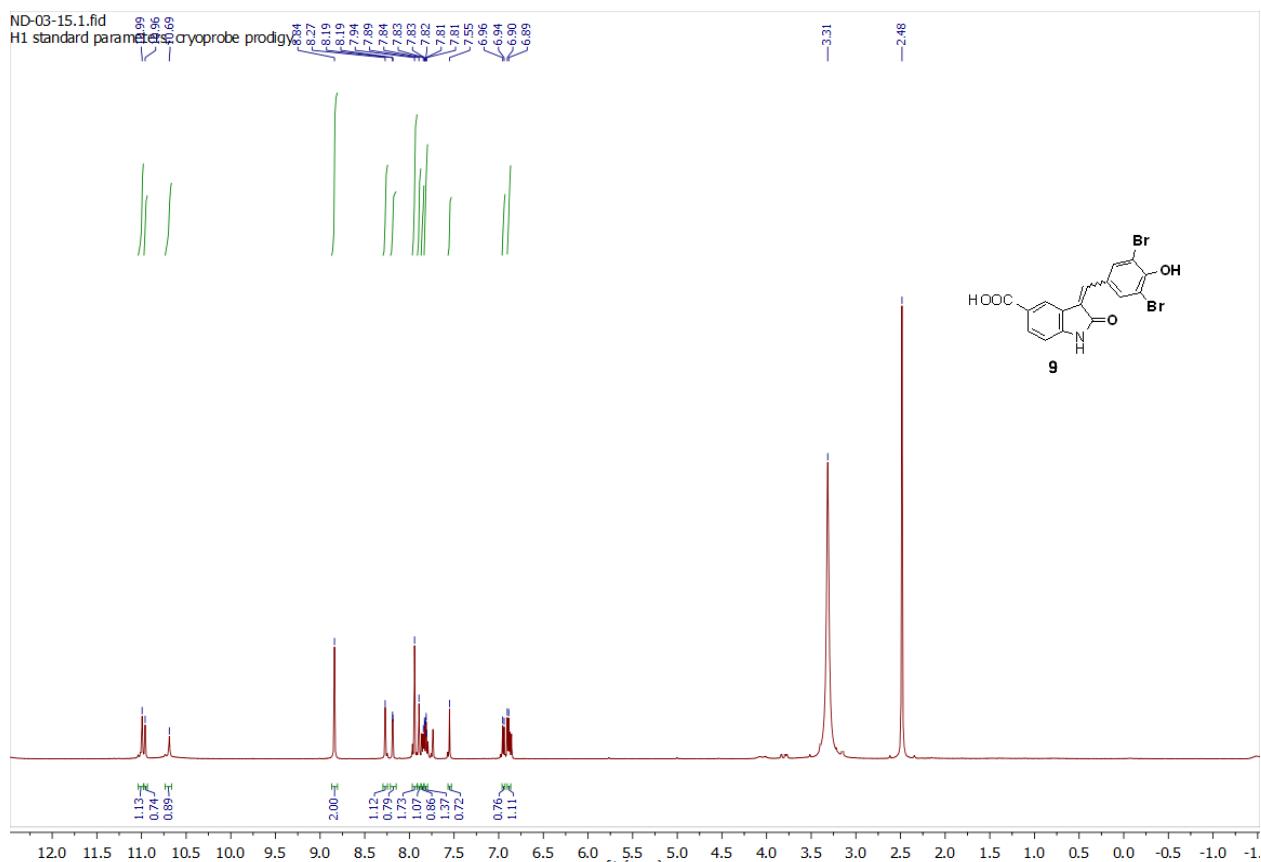
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C13 standard parameters, cryoprobe prodigy. Pulporg = zgjg30zr.jsh.



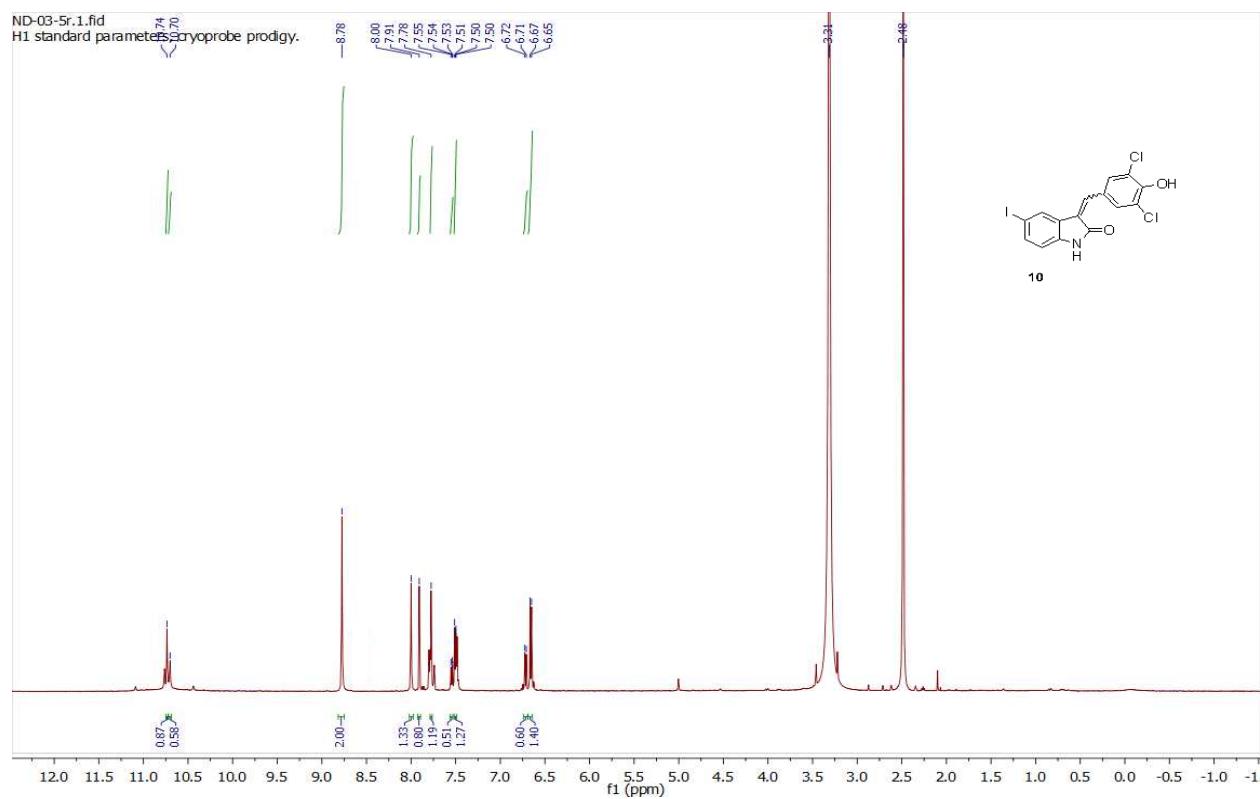
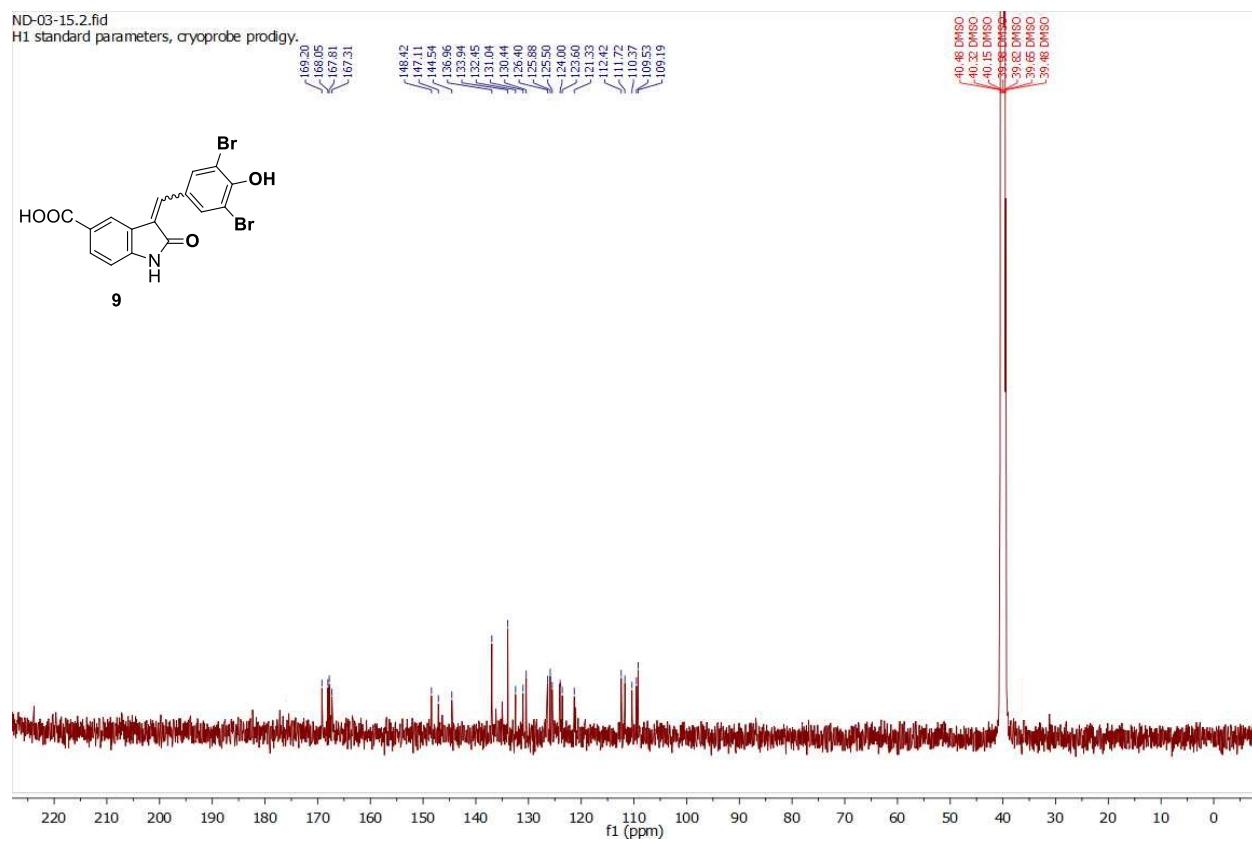




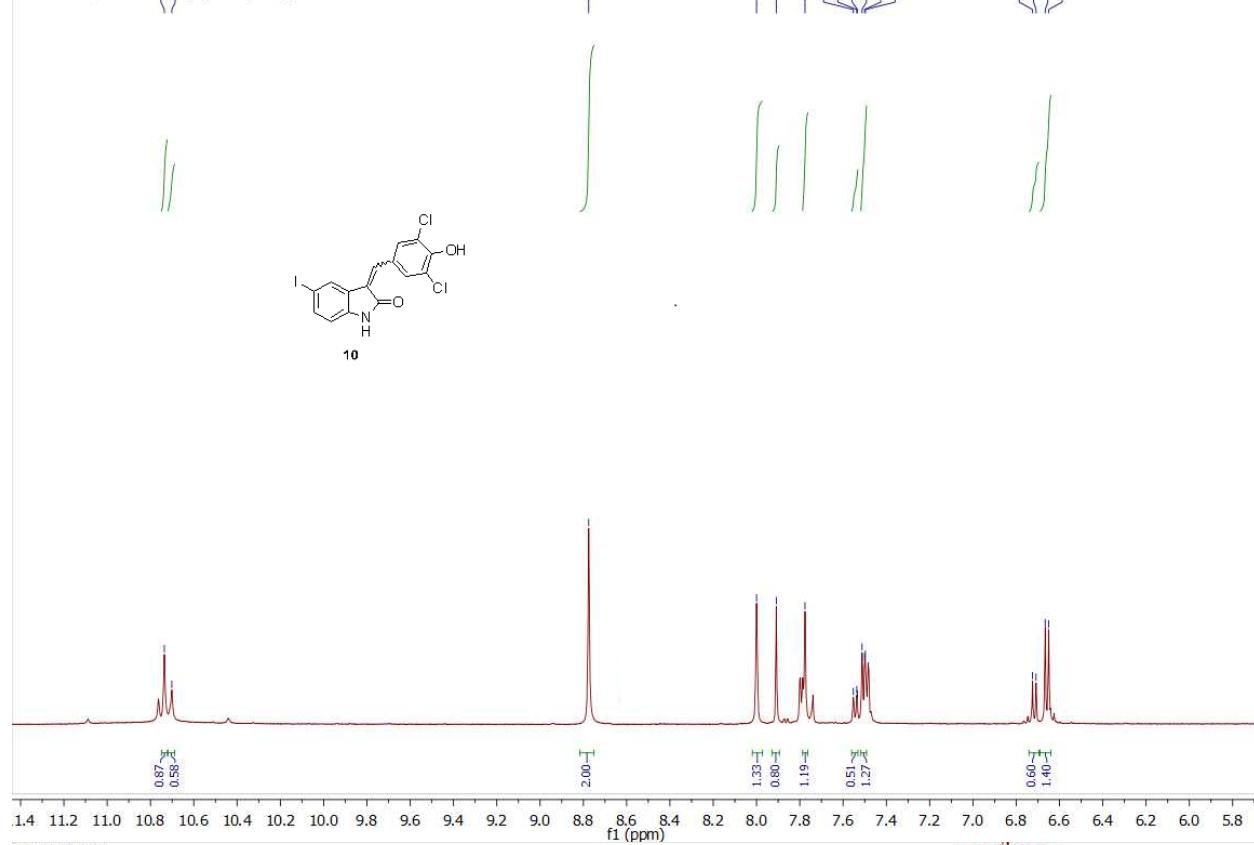




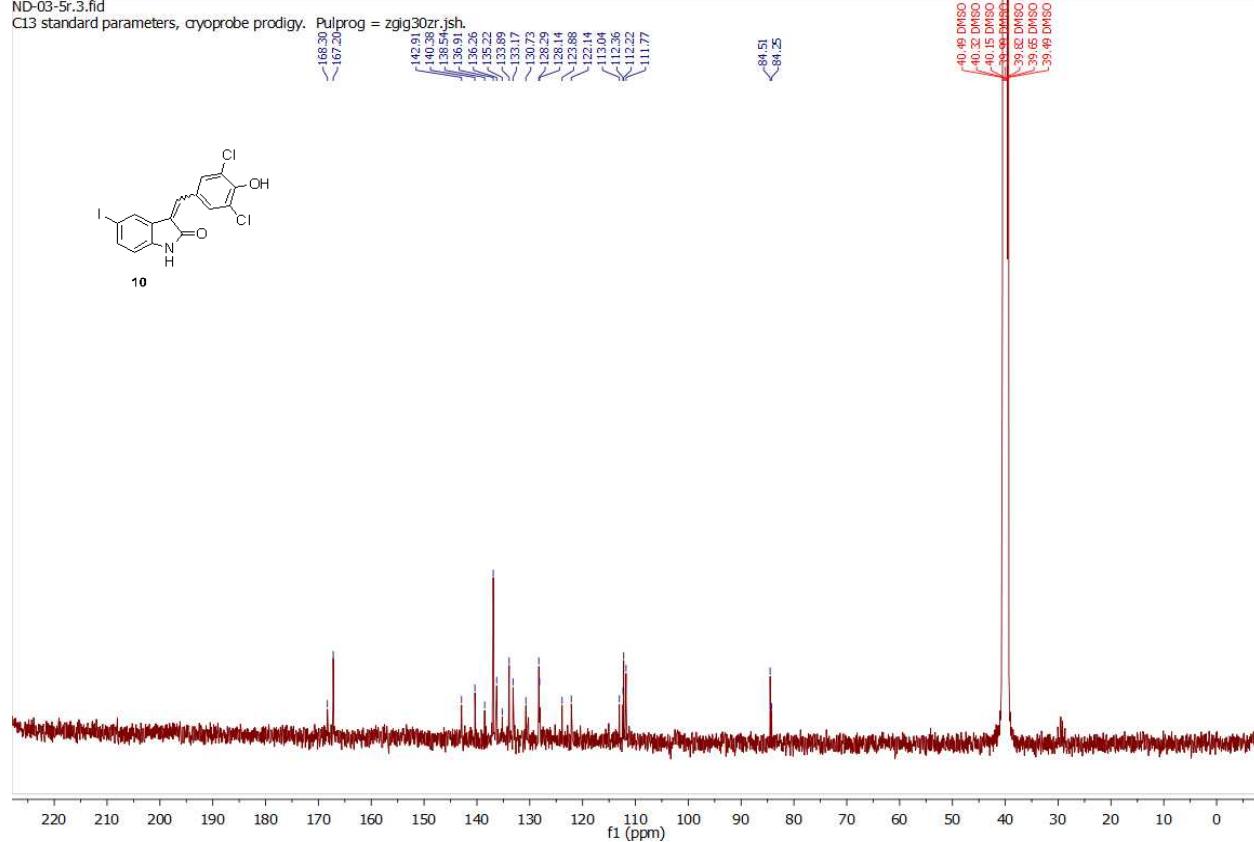
[S-28]



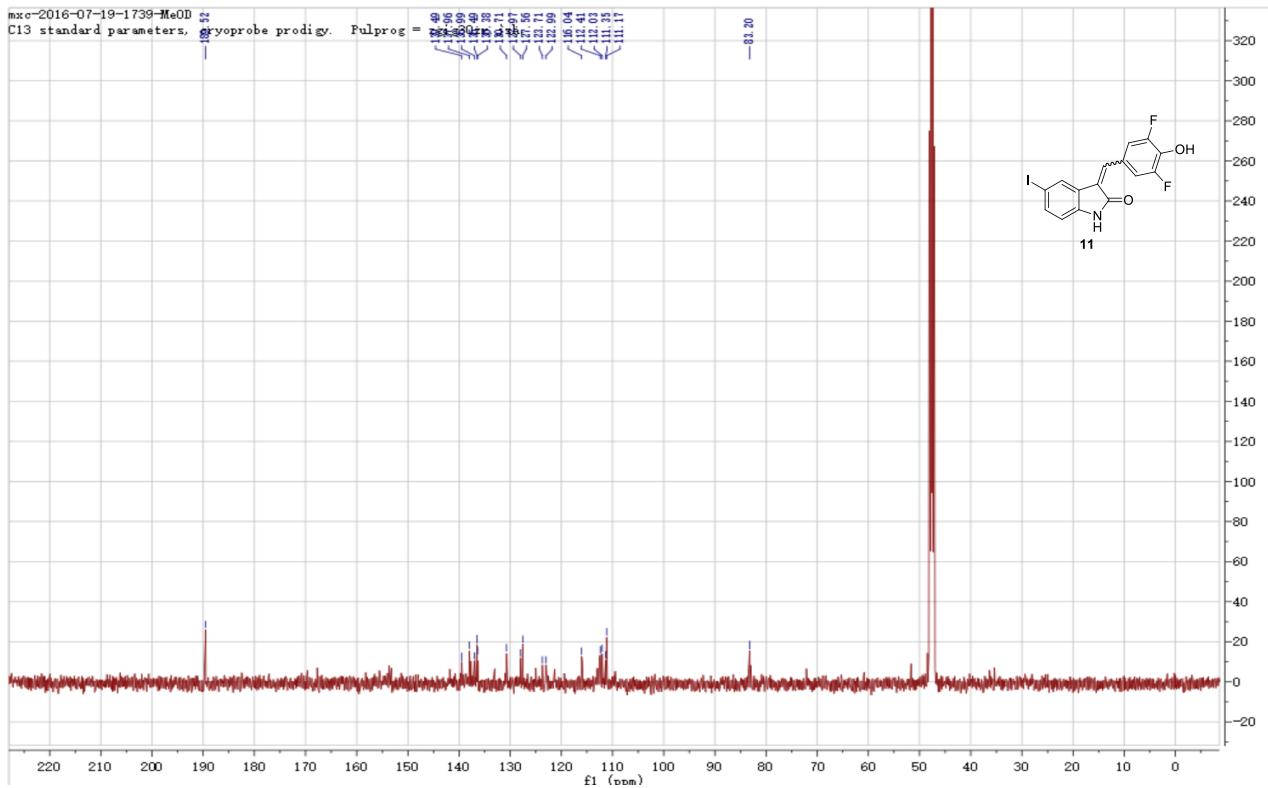
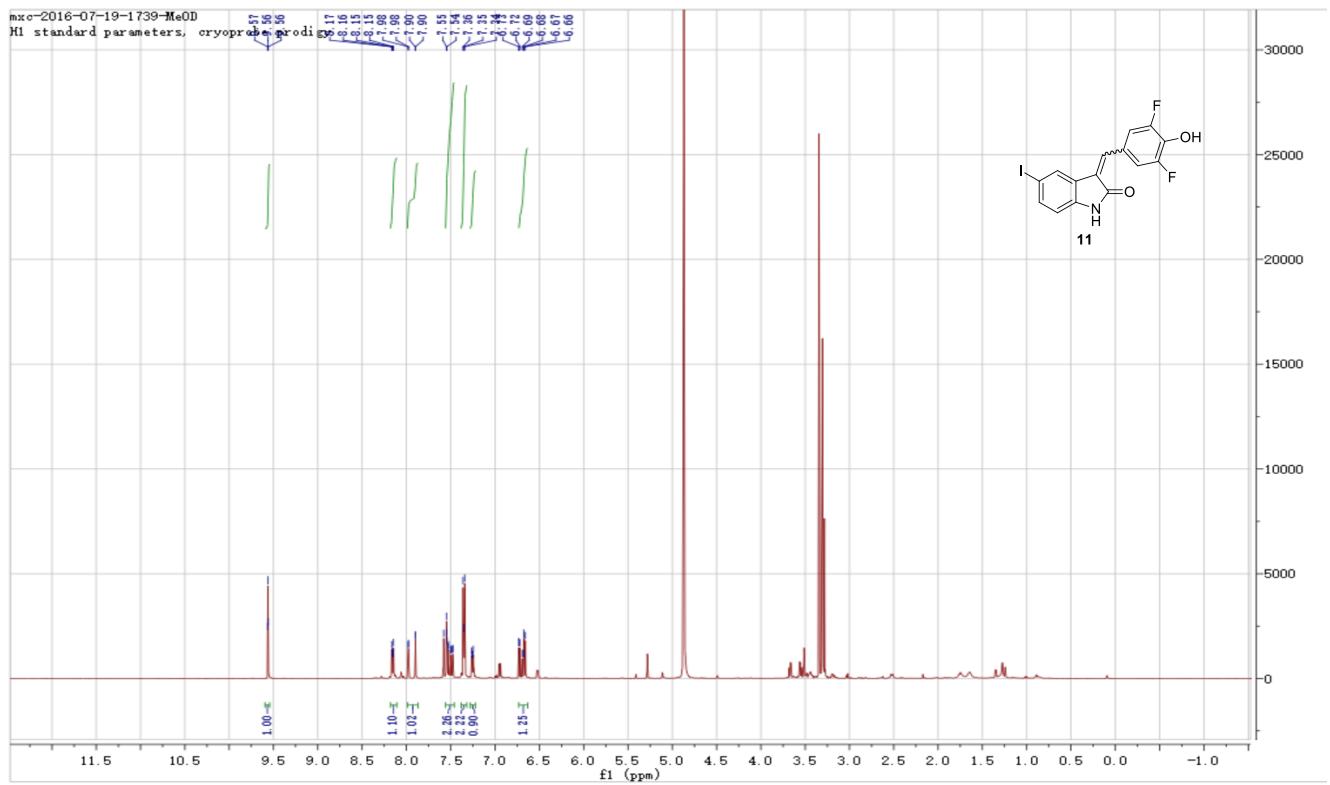
ND-03-5r.1.fid  
H1 standard parameters, cryoprobe prodigy.

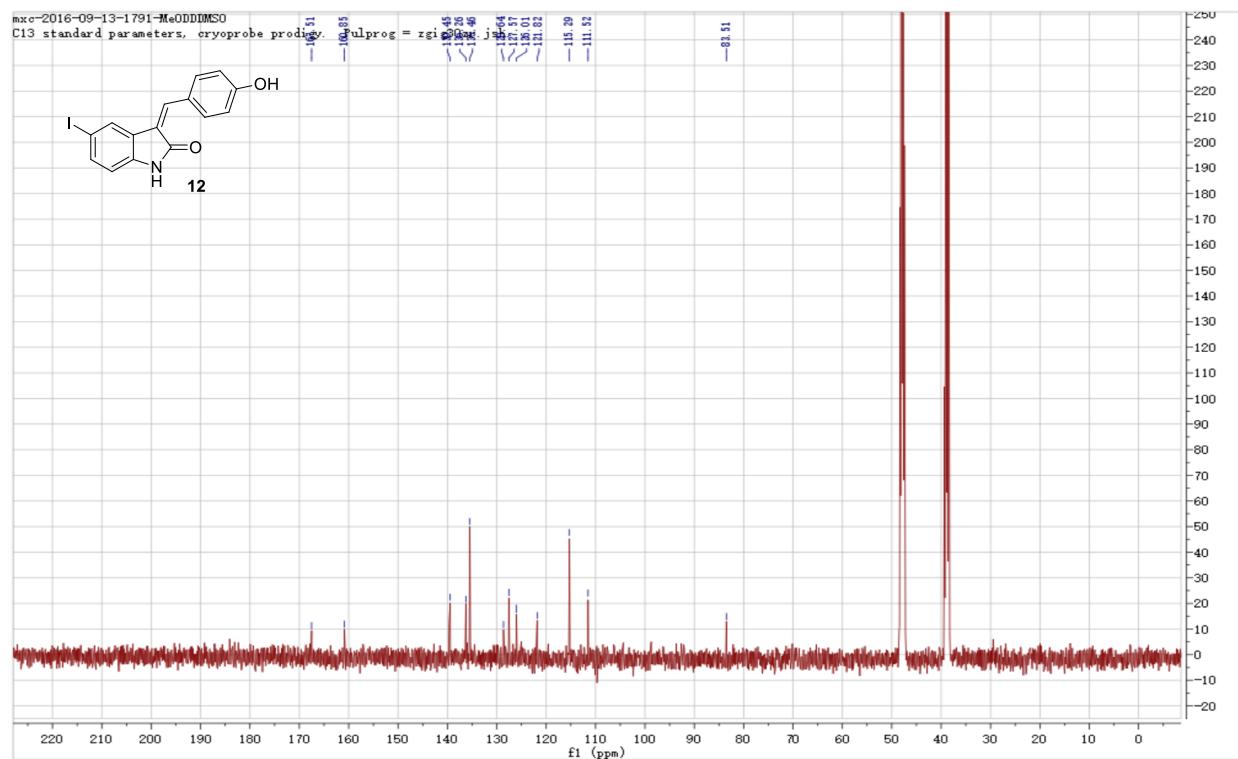
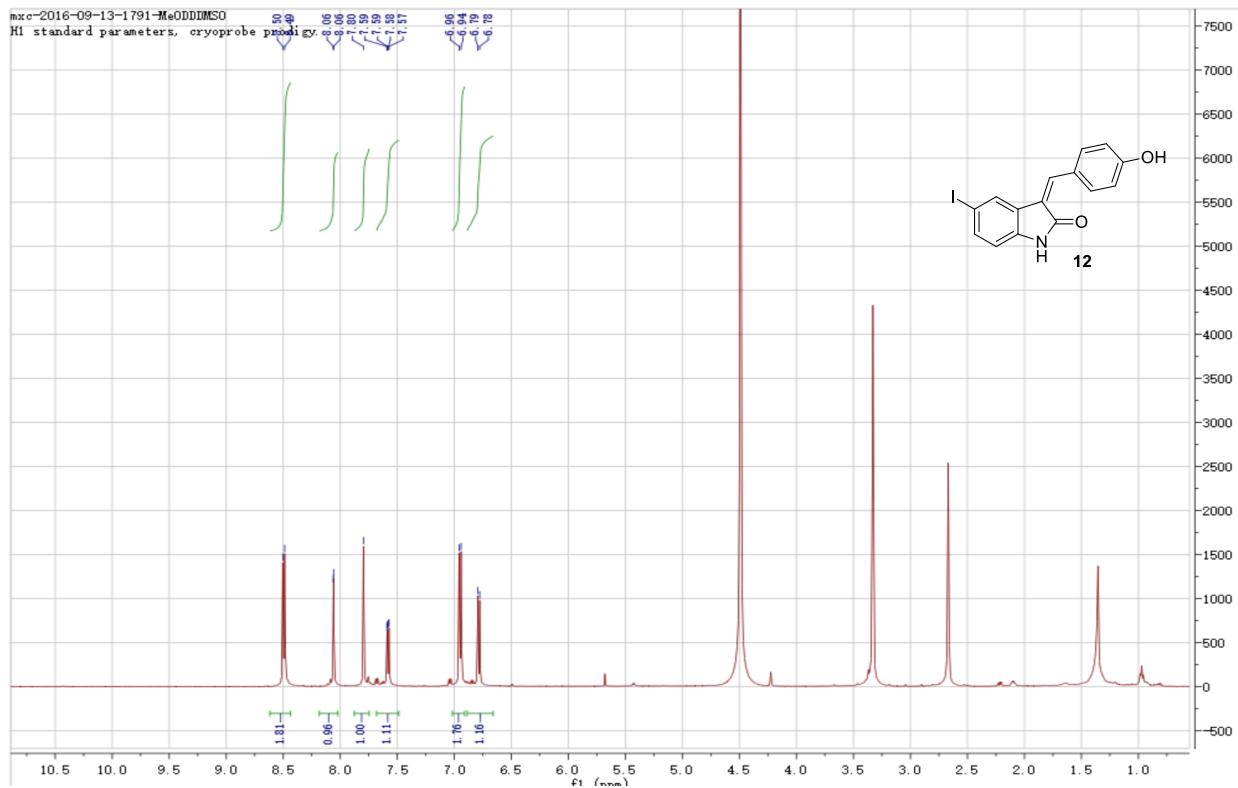


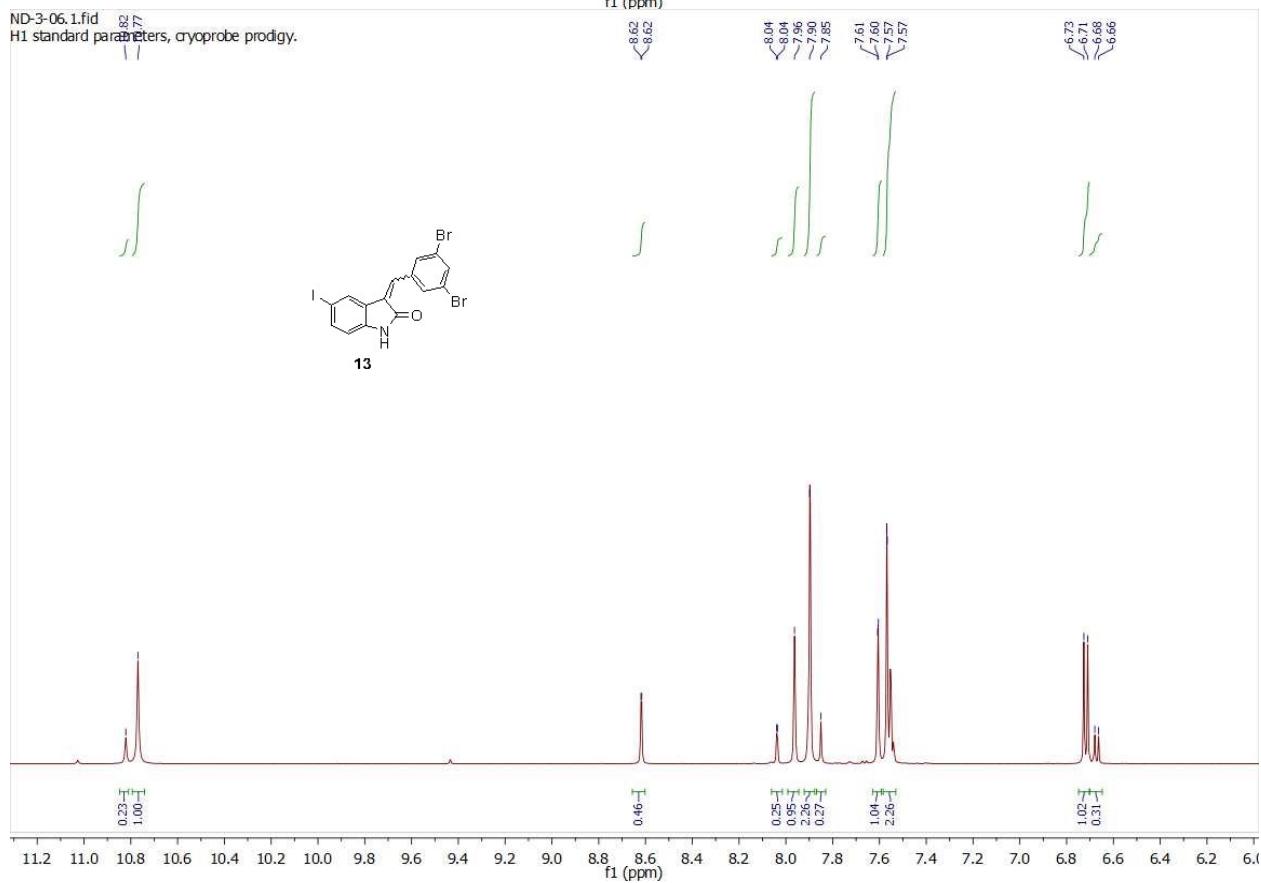
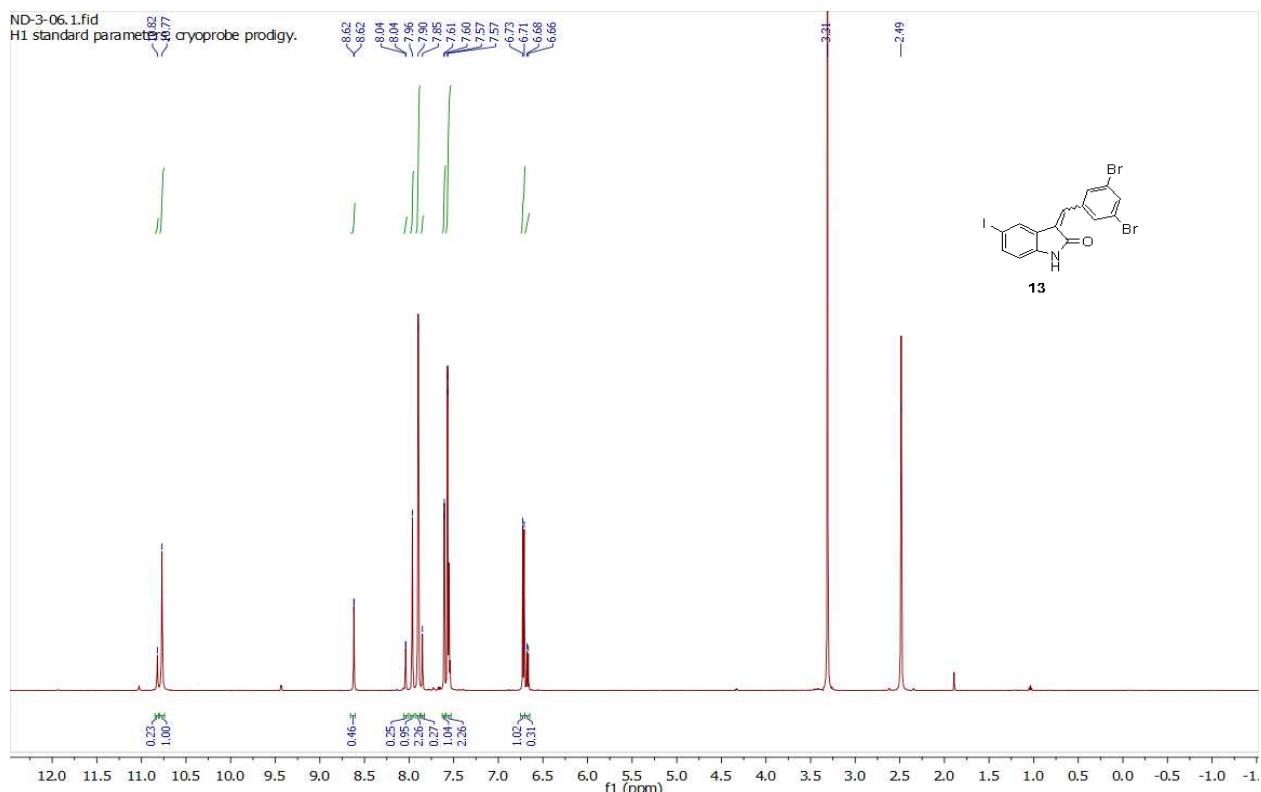
ND-03-5r.3.fid  
C13 standard parameters, cryoprobe prodigy. Pulprog = zgig30zr.jsh.



[S-30]

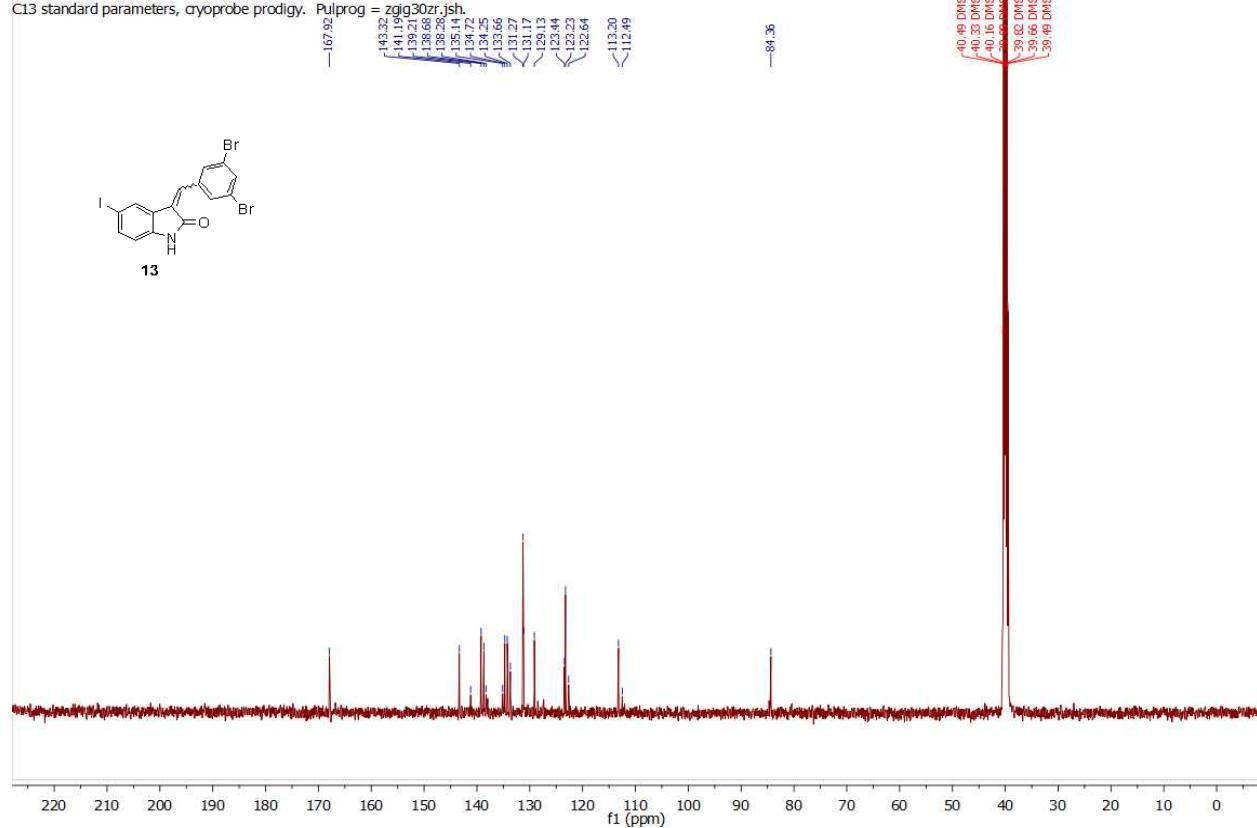






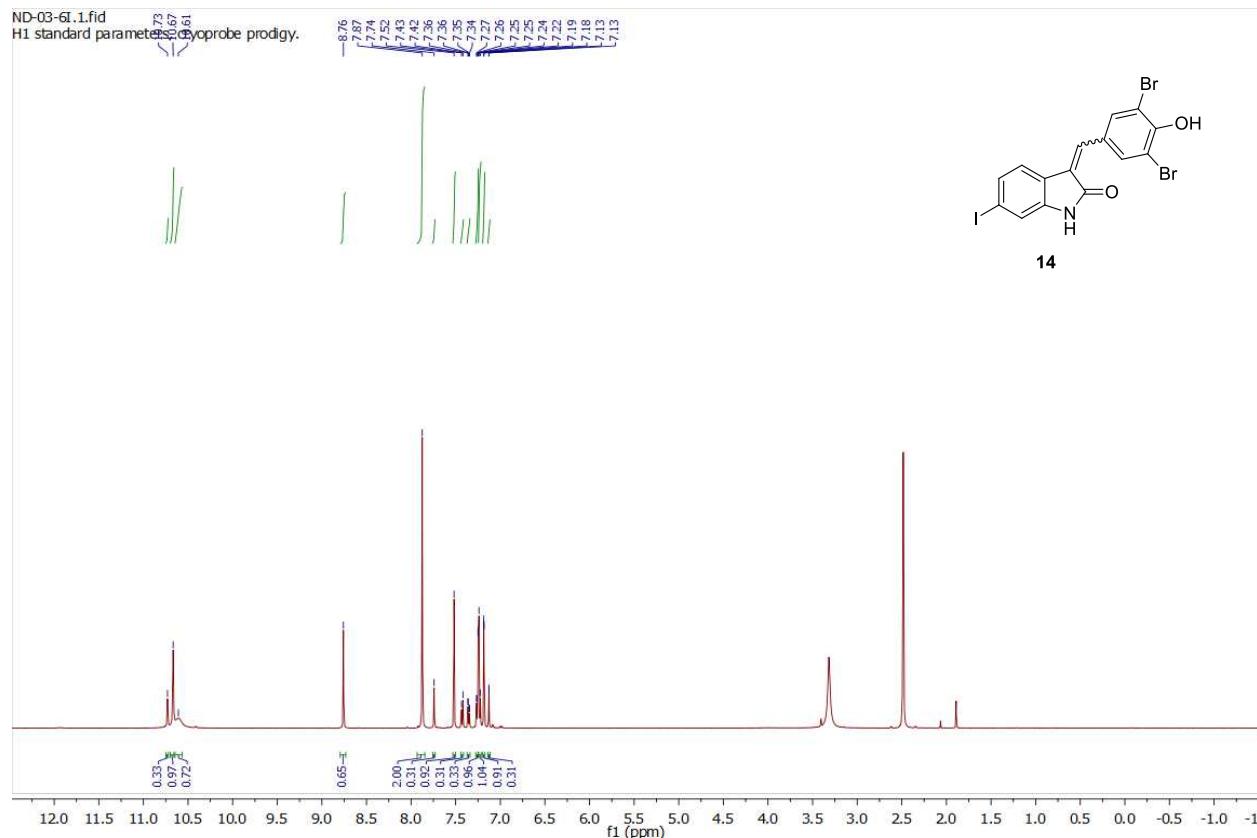
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C13 standard parameters, cryoprobe prodigy, Pulprog = zgig30zr.jsh.

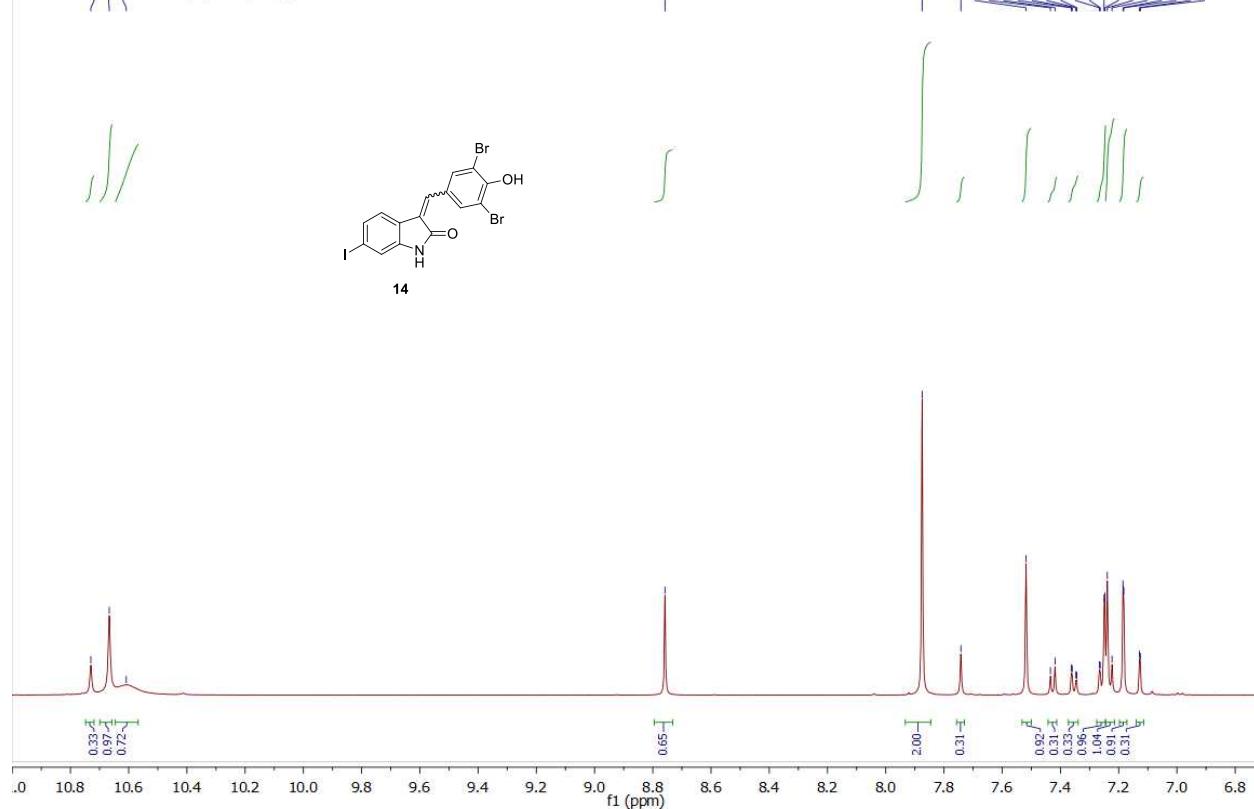


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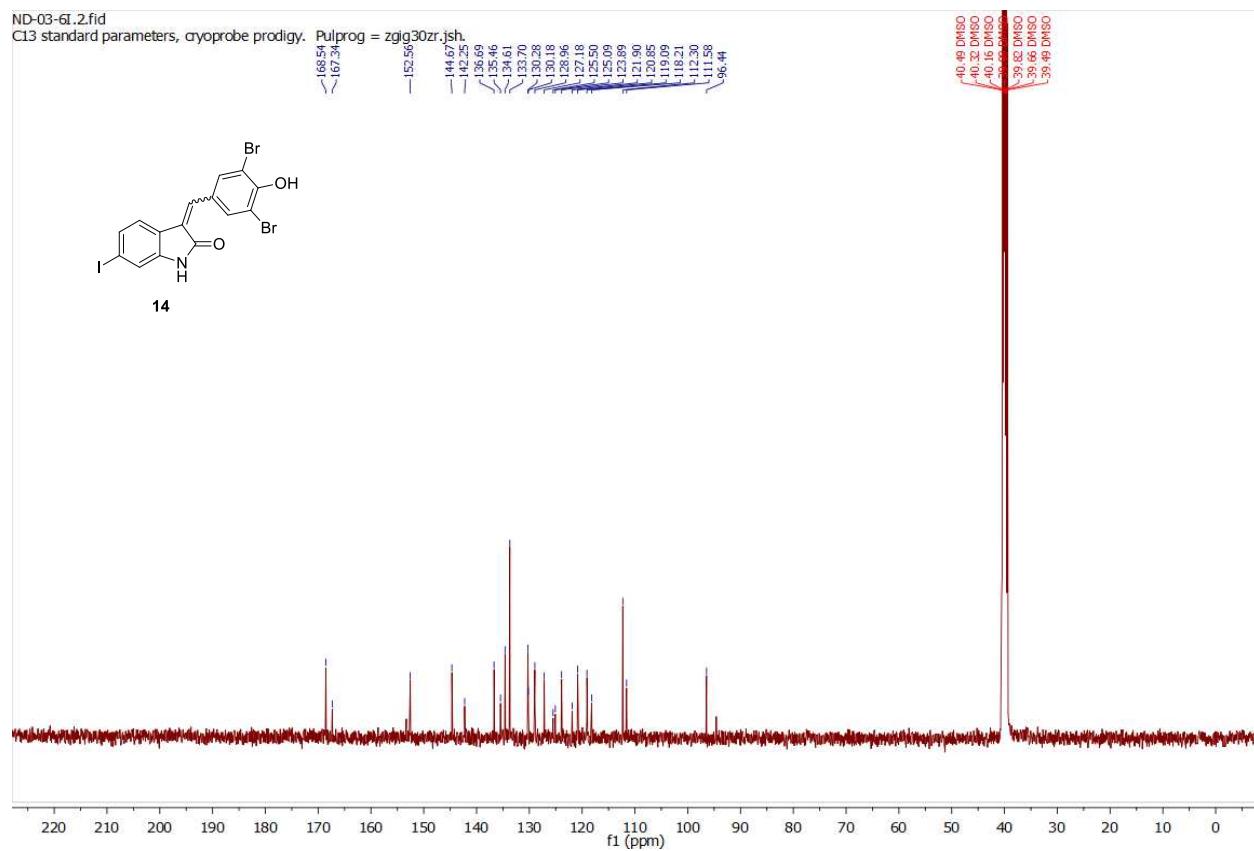
H1 standard parameters, cryoprobe prodigy.

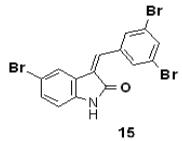
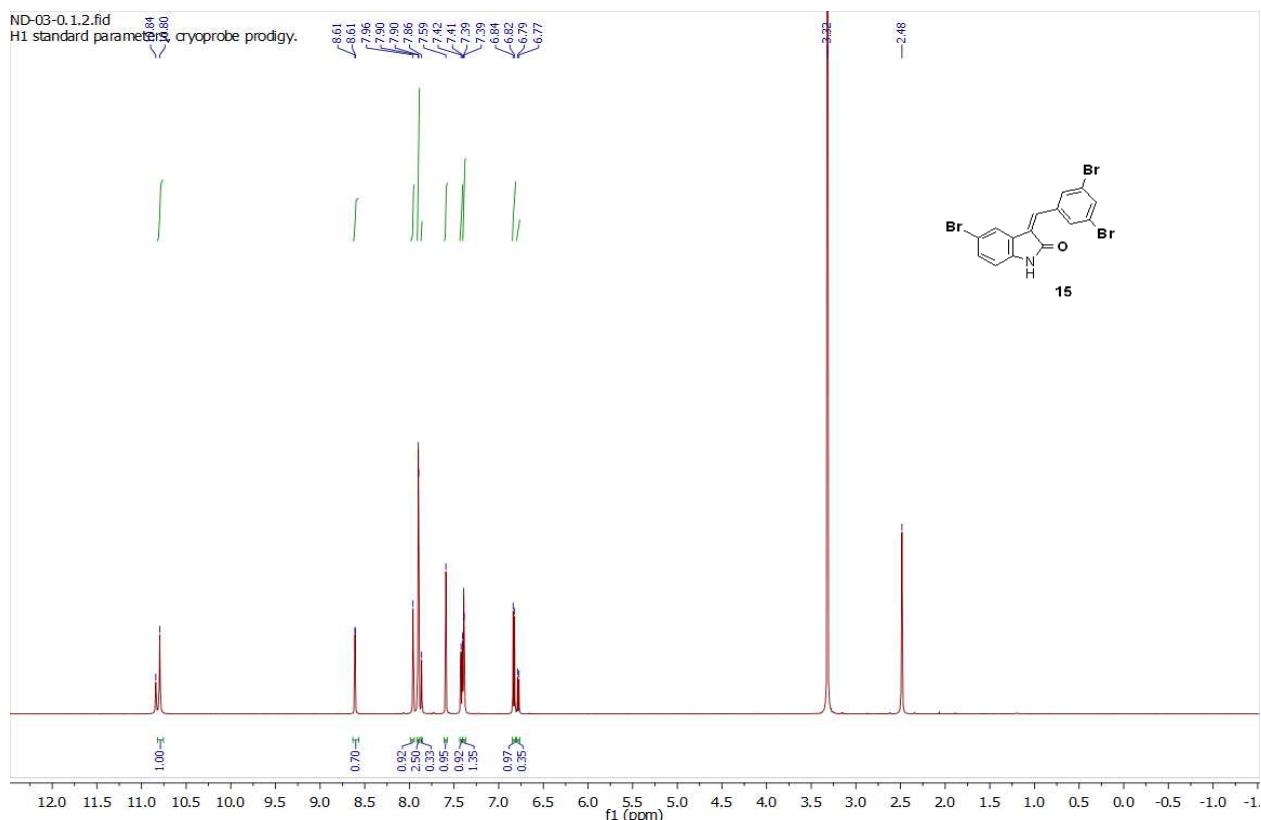


ND-03-6I.1.fid  
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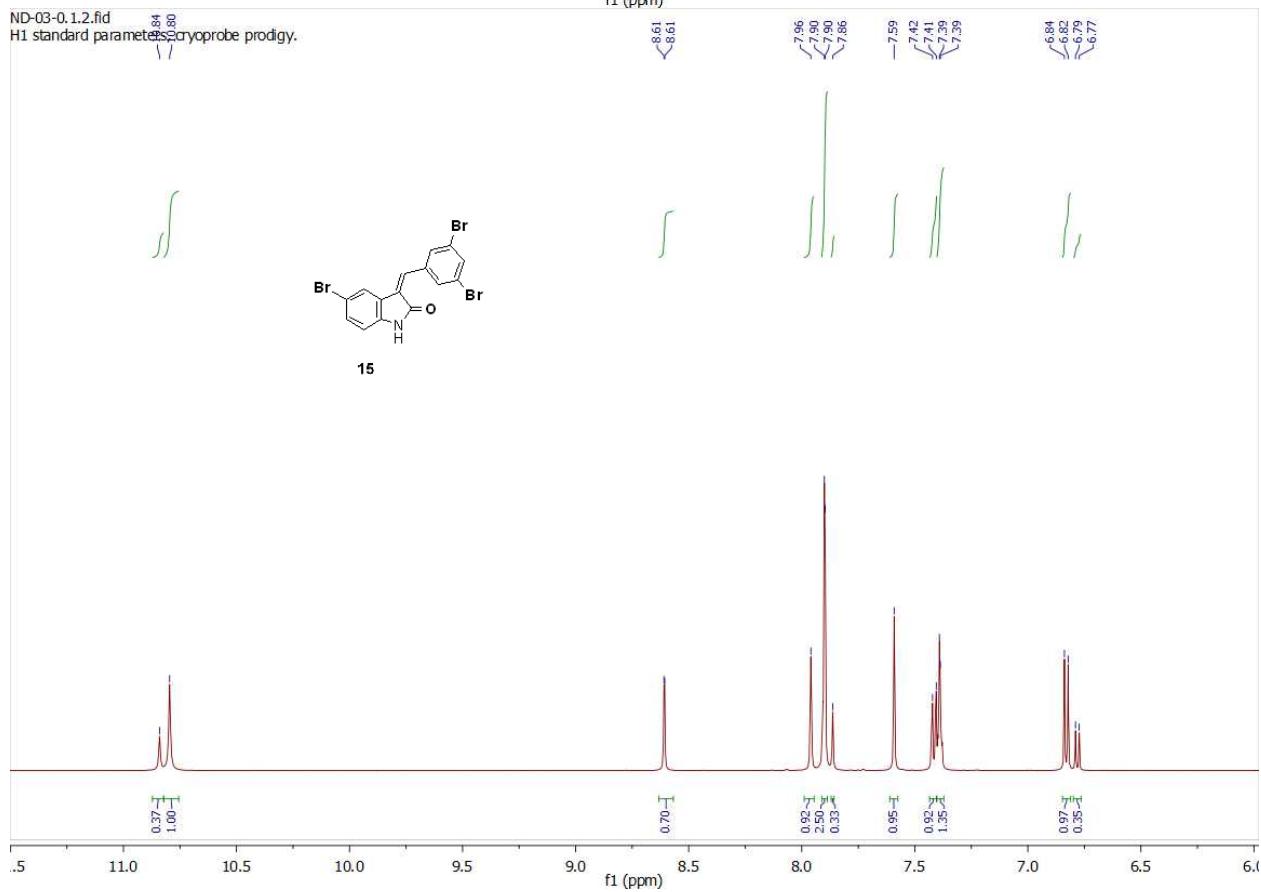


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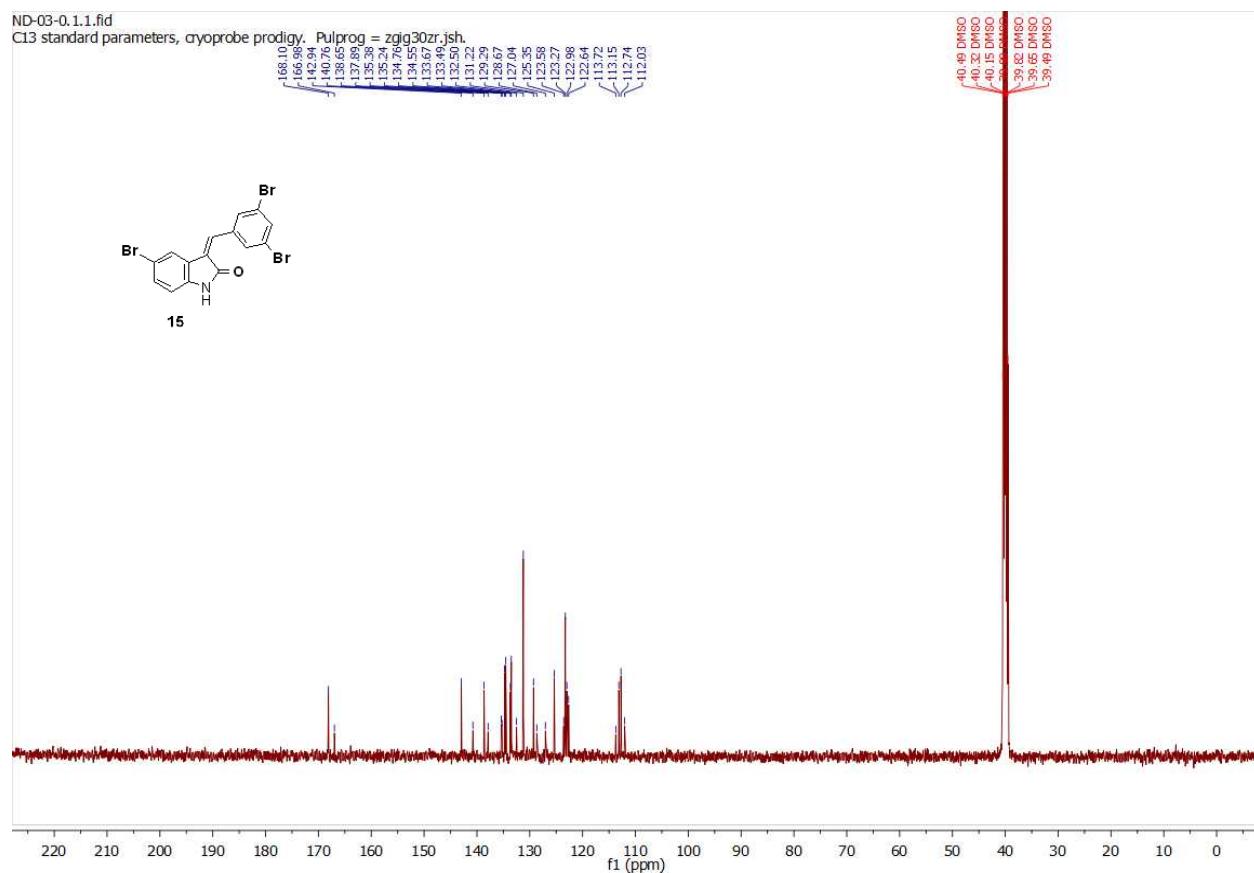
15



[S-36]

ND-03-0.1.1.fid

C13 standard parameters, cryoprobe prodigy. Pulprog = zgig30zr.jsh.



ND-3-16r.1.fid  
H1 standard parameters, cryoprobe prodigy.

