

# Supporting Information

## Stereoselective Desymmetrization of Cyclohexadienone-Tethered Enones: Efficient Access to Highly Strained Polycyclic Indoles

Satish B. Thopate<sup>a, ‡</sup>, Sandip B. Jadhav <sup>a,‡</sup>, Jagadeesh Babu Nanubolu<sup>b</sup> and Rambabu Chegondi<sup>a,\*</sup>

<sup>a</sup>Department of Organic Synthesis and Process Chemistry, <sup>b</sup>Department of Analytical Chemistry, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad 500007, India.

<sup>a,b</sup>Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201 002, India.

\* E-mail: [rchegondi@iict.res.in](mailto:rchegondi@iict.res.in)/[cramhcu@gmail.com](mailto:cramhcu@gmail.com)

### ‡Author Contributions

First two authors contributed equally to this work

## Table of Contents

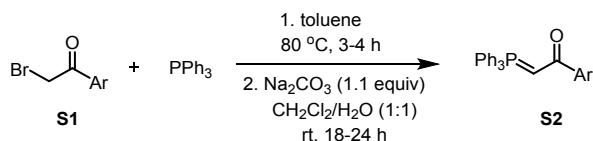
	Pages
1. General details	S-3
2. Experimental procedures and analytical data	S-3 to S-45
2a. General procedure for the preparation of phosphoranes	S-3
2b. General procedure for the synthesis of enone tethered-cyclohexadienones	S-4
2c. General procedure for the C-2/C-3 annulation reaction	S-8
2d. Mechanism for C-2/N annulation with 3-methylindole	S-21
2e. General procedure for the C-2/N annulation reaction	S-22
2f. Control experiments	S-33
2g. Gram-scale synthesis of <b>3a</b> & <b>10a</b>	S-35
2h. Subsequent trasformations on product <b>3a</b>	S-36
2i. Subsequent trasformation on product <b>10a</b>	S-38
2j. Asymmetric Friedel–Crafts alkylation	S-42
3. X-ray crystallographic data	S-46 to S-50
4. References	S-51
5. $^1\text{H}$ & $^{13}\text{C}$ NMR spectra	S-52 to S-126

## 1. General details

**General information:** Unless otherwise noted, all were purchased from commercial suppliers and used without further purification. All reactions were performed under nitrogen atmosphere and in a flame-dried or oven-dried glassware with magnetic stirring. All solvents were dried before use following the standard procedures. Reactions were monitored using thin-layer chromatography ( $\text{SiO}_2$ ). TLC plates were visualized with UV light (254 nm), iodine treatment or using *p*-anisaldehyde stain or  $\beta$ -naphthol stain. Column chromatography was carried out using 100-200 mesh silica gel packed in glass columns. NMR spectra were recorded at 300, 400, 500 MHz (H) and at 75, 100, 125 MHz (C), respectively. Chemical shifts ( $\delta$ ) are reported in ppm, using the residual solvent peak in  $\text{CDCl}_3$  (H:  $\delta = 7.26$  and C:  $\delta = 77.16$  ppm) as internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet), coupling constants (Hz) and integration. HRMS were recorded using ESI-TOF techniques. Enantiomeric excess (ee) values were determined by chiral HPLC of the purified product and diastereomer ratio (dr) values were determined by  $^1\text{H}$  NMR of the crude reaction mixture.

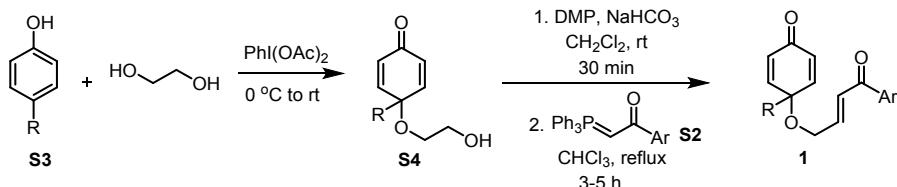
## 2. Experimental procedures and analytical data

### 2a. General Procedure for the Preparation of Phosphoranes<sup>1</sup>



To a solution of 2-bromoacetophenone **S1** (10 mmol) in toluene (0.3 M) was added  $\text{PPh}_3$  (11 mmol) at room temperature. The reaction mixture was stirred at  $80^\circ\text{C}$  for 3-4 h. Then the resulting precipitate was filtered, washed with more  $\text{Et}_2\text{O}$ , dried and concentrated in *vacuo* to give the phosphonium salt. To a solution of phosphonium salt in  $\text{CH}_2\text{Cl}_2$  and was added  $\text{Na}_2\text{CO}_3$  (11 mmol) in  $\text{H}_2\text{O}$  (1 M) and the resulting biphasic solution was stirred vigorously at room temperature for 18-24 h. The layers were separated and the aqueous layers was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were dried ( $\text{Na}_2\text{SO}_4$ ), filtered, and concentrated in *vacuo* to give the phosphorene **S2**. The crude Wittig reagent **S2** was used for next reaction without further purification.

**2b. General Procedure for the Synthesis of Enone Tethered-Cyclohexadienones 1:<sup>1</sup>**



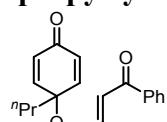
To a stirred solution of phenol **S3** (10 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) and ethylene glycol (300 mmol) was added PhI(OAc)<sub>2</sub> (15 mmol, dissolved in 40 ml CH<sub>2</sub>Cl<sub>2</sub>) dropwise over 2 hours at room temperature under inert atmosphere. After completion of addition, the reaction mixture was stirred for another 30 minutes and then concentrated in *vacuo*. The crude residue was purified by column chromatography (EtOAc/hexane) to give the desired alcohol **S4**.<sup>2</sup>

To a stirred solution of pure alcohol **S4** (10 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.1 M) was added Dess Martin periodinane (12 mmol) in one portion at room-temperature and stirred the reaction mixture for 30 minutes to 1 hour under nitrogen atmosphere. The reaction mixture was diluted with hexanes and filtered through Celite and then concentrated in *vacuo*. The crude product was purified by column chromatography (EtOAc/hexane) to give aldehyde in excellent yields.<sup>3</sup>

The solution of aldehyde in CHCl<sub>3</sub> (0.3 M) was added desired phosphorene **S2** (12 mmol) in one portion at room temperature under nitrogen atmosphere. The reaction mixture stirred at 65 °C for 3 to 5 h and then concentrated in *vacuo*. The crude reaction mixture was purified by column chromatography (EtOAc/petroleum ether) to give enone tethered-cyclohexadienones **1** in good yields.<sup>4</sup>

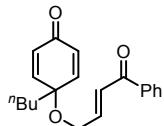
All enone tethered-cyclohexadienones **1** were prepared according to a previously reported procedure unless otherwise mentioned below.<sup>4a,b</sup>

**(E)-4-((4-Oxo-4-phenylbut-2-en-1-yl)oxy)-4-propylcyclohexa-2,5-dien-1-one (1c):**



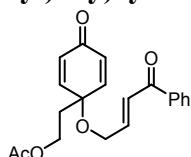
Prepared according to the general procedure as described above in 62% yield (850 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R<sub>f</sub> = 0.5) to afford an orange oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.99 – 7.93 (m, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.49 (tt, J = 6.7, 1.3 Hz, 2H), 7.16 (dt, J = 15.5, 2.0 Hz, 1H), 6.99 (dt, J = 15.5, 4.1 Hz, 1H), 6.79 (d, J = 10.3 Hz, 2H), 6.37 (d, J = 10.2 Hz, 2H), 4.14 (dd, J = 4.1, 2.0 Hz, 2H), 1.82 (d, J = 17.0 Hz, 1H), 1.82 (dd, J = 4.2, 3.3 Hz, 1H), 1.40 – 1.29 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 190.4, 185.3, 150.6, 144.5, 137.7, 133.0, 131.6, 128.7, 128.7, 125.0, 76.1, 64.6, 41.7, 17.0, 14.4; IR (neat): ν<sub>max</sub> 2920, 1669, 1446, 1364, 1266, 1227, 1158, 1122, 1055, 753, 695, 652 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>19</sub>H<sub>21</sub>O<sub>3</sub> [M+H]<sup>+</sup>: 297.1492; found: 297.1501.

**(E)-4-Butyl-4-((4-oxo-4-phenylbut-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-one (1d):**



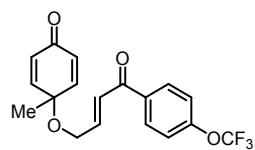
Prepared according to the general procedure as described above in 55% yield (800 mg). It was purified by flash chromatography (20% EtOAc/hexanes;  $R_f = 0.5$ ) to afford an orange oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 – 7.91 (m, 2H), 7.60 – 7.56 (m, 1H), 7.51 – 7.46 (m, 2H), 7.16 (dt,  $J = 15.4, 2.0$  Hz, 1H), 6.99 (dt,  $J = 15.5, 4.1$  Hz, 1H), 6.79 (d,  $J = 10.2$  Hz, 2H), 6.37 (d,  $J = 10.2$  Hz, 2H), 4.14 (dd,  $J = 4.1, 2.0$  Hz, 2H), 1.84 (d,  $J = 16.6$  Hz, 1H), 1.86 – 1.81 (m, 1H), 1.40 – 1.24 (m, 4H), 0.90 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  190.3, 185.3, 150.6, 144.5, 137.7, 133.0, 131.5, 128.7, 128.7, 124.9, 76.1, 64.6, 39.2, 25.7, 23.0, 14.0; IR (neat):  $\nu_{\text{max}}$  3045, 2972, 2931, 1672, 1437, 1044, 971, 759, 653  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{23}\text{O}_3$  [ $\text{M}+\text{H}]^+$ : 311.1647; found: 311.1656.

**(E)-2-(4-Oxo-1-((4-oxo-4-phenylbut-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-yl)ethyl acetate (1e):**



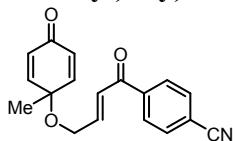
Prepared according to the general procedure as described above in 53% yield (740 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.4$ ) to afford as an orange oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 – 7.92 (m, 2H), 7.61 – 7.54 (m, 1H), 7.52 – 7.45 (m, 2H), 7.14 (dt,  $J = 15.5, 2.0$  Hz, 1H), 6.97 (dt,  $J = 15.5, 4.1$  Hz, 1H), 6.82 (d,  $J = 10.2$  Hz, 2H), 6.38 (d,  $J = 10.2$  Hz, 2H), 4.22 (t,  $J = 6.6$  Hz, 2H), 4.13 (dd,  $J = 4.1, 2.0$  Hz, 2H), 2.18 (t,  $J = 6.6$  Hz, 2H), 2.02 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  190.3, 184.8, 170.8, 149.4, 143.9, 137.6, 133.2, 131.7, 128.8, 128.7, 125.1, 74.2, 64.6, 59.5, 38.8, 21.0; IR (neat):  $\nu_{\text{max}}$  3100, 2900, 1779, 1422, 1346, 1344, 1276, 1244, 1188, 1144, 1055, 773, 655, 662  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{21}\text{O}_5$  [ $\text{M}+\text{H}]^+$ : 341.1389; found: 341.1413.

**(E)-4-Methyl-4-((4-oxo-4-(4-(trifluoromethoxy)phenyl)but-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-one (1h):**



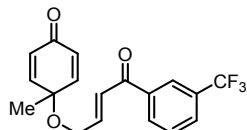
Prepared according to the general procedure as described above in 57% yield (1.20 g). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.4$ ) to afford an orange oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 (d,  $J = 8.9$  Hz, 2H), 7.30 (dd,  $J = 8.8, 0.8$  Hz, 2H), 7.12 (dt,  $J = 15.4, 2.0$  Hz, 1H), 7.00 (dt,  $J = 15.4, 0$  Hz, 1H), 6.80 (d,  $J = 10.2$  Hz, 2H), 6.32 (d,  $J = 10.2$  Hz, 2H), 4.12 (dd,  $J = 4.0, 2.0$  Hz, 2H), 1.52 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  188.7, 184.9, 152.6, 151.0, 145.0, 135.9, 130.7, 130.7, 124.5, 120.5, 120.4 (q,  $J_{\text{CF}} = 258.9$  Hz), 73.0, 64.8, 26.4;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.62 (s, 3F); IR (neat):  $\nu_{\text{max}}$  2936, 1868, 1706, 1670, 1628, 1509, 1393, 1258, 1216, 1171, 1086, 964, 865, 817, 672  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{16}\text{O}_3\text{F}_3$  [ $\text{M}+\text{H}]^+$ : 353.1001; found: 353.1006.

**(E)-4-((1-Methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)but-2-enoylbenzonitrile (1j):**



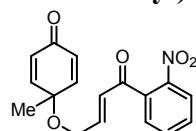
Prepared according to the general procedure as described above in 62% yield (1.0 g). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.2$ ) to afford an orange solid; mp = 160–162°C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.01 (d,  $J = 8.5$  Hz, 2H), 7.78 (d,  $J = 8.5$  Hz, 2H), 7.11 (dt,  $J = 15.4, 1.8$  Hz, 1H), 7.02 (dt,  $J = 15.4, 3.7$  Hz, 1H), 6.79 (d,  $J = 10.2$  Hz, 2H), 6.32 (d,  $J = 10.2$  Hz, 2H), 4.13 (dt,  $J = 6.1, 3.0$  Hz, 2H), 1.53 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 188.9, 184.9, 150.8, 146.2, 140.9, 132.6, 130.8, 129.1, 124.1, 118.1, 116.2, 73.0, 64.7, 26.34; IR (neat):  $\nu_{\text{max}}$  3045, 2972, 2255, 1702, 1660, 1638, 1512, 1393, 1252, 1211, 1161, 1086, 946, 865, 822, 652 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>18</sub>H<sub>16</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 294.1130; found: 294.1144.

**(E)-4-Methyl-4-((4-oxo-4-(3-(trifluoromethyl)phenyl)but-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-one (1l):**



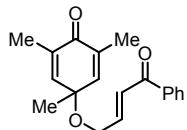
Prepared according to the general procedure as described above in 55% yield (1.1 g). It was purified by flash chromatography (20% EtOAc/hexanes;  $R_f = 0.4$ ) to afford an orange oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.18 (s, 1H), 8.12 (d,  $J = 7.8$  Hz, 1H), 7.82 (d,  $J = 7.8$  Hz, 1H), 7.62 (t,  $J = 7.8$  Hz, 1H), 7.14 (dt,  $J = 15.4, 1.9$  Hz, 1H), 7.05 (dd,  $J = 15.4, 3.9$  Hz, 1H), 6.81 (d,  $J = 10.2$  Hz, 2H), 6.33 (d,  $J = 10.2$  Hz, 2H), 4.14 (dd,  $J = 3.9, 1.9$  Hz, 2H), 1.54 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 188.9, 184.9, 150.9, 145.6, 138.2, 131.8, 131.4 (q,  $J_{\text{CF}} = 32.9$  Hz), 130.8, 129.5 (q,  $J_{\text{CF}} = 3.9$  Hz), 129.4, 125.5 (q,  $J_{\text{CF}} = 3.5$  Hz), 124.3, 123.8 (q,  $J_{\text{CF}} = 272.3$  Hz), 73.0, 64.8, 26.4; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -62.78 (s, 3F); IR (neat):  $\nu_{\text{max}}$  2930, 1868, 1706, 1509, 1447, 1054, 971, 759, 693 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>18</sub>H<sub>16</sub>O<sub>3</sub>F<sub>3</sub> [M+H]<sup>+</sup>: 337.1052; found: 337.1077.

**(E)-4-Methyl-4-((4-(2-nitrophenyl)-4-oxobut-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-one (1m):**



Prepared according to the general procedure as described above in 60% yield (1.1 g). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.2$ ) to afford an orange oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.13 (dd,  $J = 8.2, 0.9$  Hz, 1H), 7.73 (dt,  $J = 7.5, 1.1$  Hz, 1H), 7.62 (ddd,  $J = 8.2, 6.2, 1.4$  Hz, 1H), 7.42 (dd,  $J = 7.5, 1.3$  Hz, 1H), 6.75 (d,  $J = 10.2$  Hz, 2H), 6.64 (dt,  $J = 16.0, 2.0$  Hz, 1H), 6.44 (dt,  $J = 15.9, 4.0$  Hz, 1H), 6.29 (d,  $J = 10.2$  Hz, 2H), 4.01 (dd,  $J = 3.9, 2.0$  Hz, 2H), 1.47 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 192.6, 184.9, 150.8, 146.7, 145.9, 136.0, 134.2, 130.8, 130.7, 129.4, 128.8, 124.6, 73.0, 64.2, 26.3; IR (neat):  $\nu_{\text{max}}$  3045, 2972, 2931, 2236, 1770, 1671, 1573, 1447, 1380, 1054, 971, 759, 693 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>17</sub>H<sub>15</sub>NO<sub>5</sub>Na [M+Na]<sup>+</sup>: 336.0848; found: 336.0847.

**(E)-2,4,6-Trimethyl-4-((4-oxo-4-phenylbut-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-one (1y):**

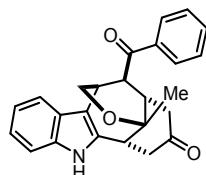


Prepared according to the general procedure as described above in 40% yield (600 mg). It was purified by flash chromatography (20% EtOAc/hexanes;  $R_f = 0.5$ ) to afford as an orange oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 – 7.89 (m, 2H), 7.56 – 7.50 (m, 1H), 7.48 – 7.40 (m, 2H), 7.11 (dt,  $J = 15.4, 1.9$  Hz, 1H), 6.96 (dt,  $J = 15.4, 4.1$  Hz, 1H), 6.52 (s, 2H), 4.05 (dd,  $J = 4.1, 2.0$  Hz, 2H), 1.88 (s, 6H), 1.44 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  190.4, 186.4, 146.2, 145.0, 137.7, 136.9, 132.9, 128.6, 124.7, 72.8, 64.4, 26.6, 16.0; IR (neat):  $\nu_{\text{max}}$  2900, 1679, 1446, 1344, 1256, 1207, 1138, 1102, 1035, 753, 695, 662  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{21}\text{O}_3$  [ $\text{M}+\text{H}]^+$ : 297.1491; found: 297.1491.

## 2c. General Procedure for the C-2/C-3 annulation reaction

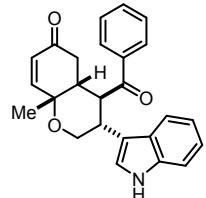
A dried screw-cap vial was charged with enone tethered-cyclohexadienones **1** (1 equiv), indole **2** (1.2 equiv) and Al(OTf)<sub>3</sub> (10.0 mol%) in acetonitrile (0.1 M) under nitrogen atmosphere. The reaction mixture was stirred at 60 °C for 1 hour till consumption of starting material **1** monitored by thin layer chromatography (TLC). Then, the reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (hexanes/ethyl acetate) to afford the desired product **3**.

### **13-Benzoyl-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3a):**



Prepared according to the general procedure as described above in 88% yield (75 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a yellow solid; mp = 202–204°C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.19 (br.s, 1H), 7.96 (dd, *J* = 7.3, 1.2 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.34 (d, *J* = 7.7 Hz, 1H), 7.32 – 7.26 (m, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.11 (dt, *J* = 7.0, 0.9 Hz, 1H), 4.11 (d, *J* = 9.9 Hz, 1H), 3.70 (dd, *J* = 9.5, 2.2 Hz, 2H), 3.67 – 3.60 (m, 1H), 3.57 (d, *J* = 8.3 Hz, 1H), 3.42 (d, *J* = 2.0 Hz, 1H), 2.87 (dd, *J* = 14.8, 5.4 Hz, 2H), 2.70 (d, *J* = 15.2 Hz, 1H), 2.05 (d, *J* = 15.0 Hz, 1H), 1.85 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 207.9, 198.0, 136.1, 135.1, 135.0, 133.8, 129.1, 128.9, 125.8, 121.9, 120.0, 117.2, 116.1, 111.1, 72.7, 65.0, 52.8, 48.1, 46.1, 45.0, 38.0, 33.4, 29.2; IR (neat):  $\nu_{\text{max}}$  3363, 2930, 2870, 1710, 1679, 1105, 1001, 752, 697 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>25</sub>H<sub>24</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 386.1756; found: 386.1768.

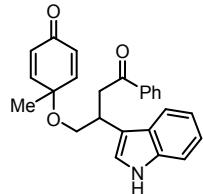
### **4-Benzoyl-3-(1*H*-indol-3-yl)-8a-methyl-3,4,4a,8a-tetrahydro-2*H*-chromen-6(5*H*)-one (4a):**



Prepared according to the general procedure as described above at room temperature in 73% yield (62 mg). It was purified by flash chromatography (20% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a white solid; mp = 220–222°C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.75 (br.s, 1H), 7.61 – 7.56 (m, 1H), 7.49 – 7.45 (m, 2H), 7.34 – 7.29 (m, 1H), 7.17 – 7.10 (m, 3H), 7.10 – 7.06 (m, 2H), 6.99 (dd, *J* = 10.3, 2.2 Hz, 1H), 6.77 (d, *J* = 2.5 Hz, 1H), 6.27 (dd, *J* = 10.3, 1.2 Hz, 1H), 4.12 (t, *J* = 11.3 Hz, 1H), 3.99 (dd, *J* = 11.9, 5.0 Hz, 1H), 3.96 – 3.90 (m, 1H), 3.56 (td, *J* = 11.2, 4.9 Hz, 1H), 2.82 (ddt, *J* = 7.2, 4.4, 2.1 Hz, 1H), 2.70 (dd, *J* = 17.5, 5.1 Hz, 1H), 2.21 – 2.18 (ddd, *J* = 17.5, 1.9, 1.4 Hz, 1H), 1.64 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 203.7, 197.5, 156.0, 138.3, 136.2, 133.1, 130.6, 128.3, 127.8, 126.3, 122.4, 121.9, 119.8, 119.4, 113.2,

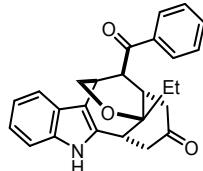
111.3, 74.1, 67.7, 48.5, 44.2, 40.6, 38.6, 26.6; IR (neat):  $\nu_{\text{max}}$  3359, 2928, 1712, 1661, 1107, 1009, 759, 695  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{24}\text{NO}_3$  [M+H]<sup>+</sup>: 386.1756; found: 386.1759.

**4-(2-(1*H*-Indol-3-yl)-4-oxo-4-phenylbutoxy)-4-methylcyclohexa-2,5-dien-1-one (4a'):**



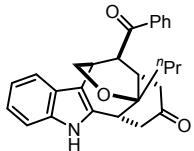
Prepared according to the general procedure as described above in 8% yield (7 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.4$ ) to afford an orange semi-solid; <sup>1</sup>H NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (br.s, 1H), 7.97 (d,  $J = 8.0$  Hz, 2H), 7.64 (d,  $J = 7.9$  Hz, 1H), 7.55 (t,  $J = 6.8$  Hz, 1H), 7.45 (t,  $J = 7.1$  Hz, 2H), 7.34 (d,  $J = 8.1$  Hz, 1H), 7.18 (t,  $J = 7.6$  Hz, 1H), 7.11 (t,  $J = 7.5$  Hz, 1H), 7.07 (s, 1H), 6.67 – 6.62 (m, 2H), 6.18 (t,  $J = 8.4$  Hz, 2H), 3.99 – 3.92 (m, 1H), 3.70 – 3.64 (m, 1H), 3.64 – 3.53 (m, 2H), 3.33 (dd,  $J = 16.1, 6.3$  Hz, 1H), 1.33 (s, 3H); <sup>13</sup>C NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  199.5, 185.3, 152.1, 137.4, 136.3, 133.1, 130.1, 130.1, 128.7, 128.3, 122.3, 121.7, 119.6, 119.3, 116.7, 111.4, 72.6, 69.1, 41.5, 34.0, 26.4; IR (neat):  $\nu_{\text{max}}$  3361, 2931, 2871, 1715, 1671, 1110, 1006, 758, 681  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{24}\text{NO}_3$  [M+H]<sup>+</sup>: 386.1756; found: 386.1760.

**13-Benzoyl-4a-ethyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3b):**



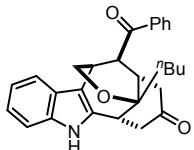
Prepared according to the general procedure as described above in 74% yield (62 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a white solid; mp = 230–232°C; <sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.12 (br. s, 1H), 7.96 (dd,  $J = 8.4, 1.2$  Hz, 2H), 7.60 (t,  $J = 7.4$  Hz, 1H), 7.47 (t,  $J = 7.7$  Hz, 2H), 7.34 (d,  $J = 7.7$  Hz, 1H), 7.28 (d,  $J = 8.0$  Hz, 1H), 7.19 – 7.14 (m, 1H), 7.13 – 7.08 (m, 1H), 4.05 (dd,  $J = 10.0, 0.9$  Hz, 1H), 3.80 – 3.69 (m, 3H), 3.57 (d,  $J = 8.3$  Hz, 1H), 3.40 (d,  $J = 2.4$  Hz, 1H), 2.86 (dd,  $J = 15.4, 7.4$  Hz, 1H), 2.75 (dd,  $J = 15.0, 5.7$  Hz, 1H), 2.69 (d,  $J = 15.5$  Hz, 1H), 2.28 (dq,  $J = 14.4, 7.2$  Hz, 1H), 2.06 – 1.94 (m, 2H), 1.24 (t,  $J = 7.3$  Hz, 3H); <sup>13</sup>C NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  208.1, 198.1, 136.1, 135.4, 135.0, 133.8, 129.1, 128.9, 125.9, 121.9, 120.0, 117.2, 116.1, 111.0, 74.0, 65.3, 52.6, 47.0, 45.8, 44.5, 33.8, 33.4, 32.6, 7.8; IR (neat):  $\nu_{\text{max}}$  3363, 2931, 2872, 1710, 1679, 1595, 1326, 1217, 1105, 1002, 752, 698  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{26}\text{NO}_3$  [M+H]<sup>+</sup>: 400.1913; found: 400.1931.

**13-Benzoyl-4a-propyl-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2(3H)-one (3c):**



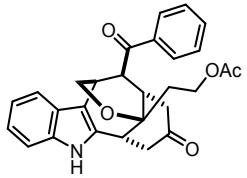
Prepared according to the general procedure as described above in 75% yield (62 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a white solid; mp = 250–252°C;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (d,  $J = 7.5$  Hz, 2H), 7.94 (s, 1H), 7.60 (t,  $J = 7.3$  Hz, 1H), 7.46 (t,  $J = 7.6$  Hz, 2H), 7.34 (d,  $J = 8.1$  Hz, 2H), 7.19 (t,  $J = 7.7$  Hz, 1H), 7.11 (t,  $J = 7.4$  Hz, 1H), 4.03 (d,  $J = 9.9$  Hz, 1H), 3.82 – 3.64 (m, 3H), 3.56 (d,  $J = 8.3$  Hz, 1H), 3.39 (d,  $J = 1.7$  Hz, 1H), 2.96 (dd,  $J = 15.3, 7.5$  Hz, 1H), 2.78 (dd,  $J = 14.9, 5.2$  Hz, 1H), 2.73 (d,  $J = 14.2$  Hz, 1H), 2.31 – 2.19 (m, 1H), 2.01 (d,  $J = 15.0$  Hz, 1H), 1.97 – 1.86 (m, 1H), 1.85 – 1.64 (m, 2H), 1.08 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  208.1, 198.1, 136.1, 135.4, 135.0, 133.8, 129.1, 128.9, 125.9, 121.9, 120.0, 117.2, 116.1, 111.0, 74.2, 65.2, 52.7, 47.3, 45.9, 44.6, 42.3, 34.2, 33.4, 16.7, 14.7; IR (neat):  $\nu_{\text{max}}$  3364, 2930, 2921, 2878, 1712, 1680, 1216, 1107, 751, 742, 699  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{27}\text{H}_{27}\text{NO}_3$  [M+H] $^+$ : 414.2069; found: 414.2070.

**13-Benzoyl-4a-butyl-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2(3H)-one (3d):**



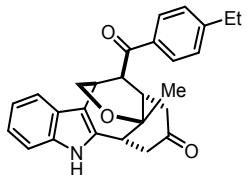
Prepared according to the general procedure as described above in 72% yield (59 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a yellow semi-solid;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (br.s, 1H), 7.95 (dd,  $J = 8.4, 1.2$  Hz, 2H), 7.59 (t,  $J = 7.4$  Hz, 1H), 7.46 (t,  $J = 7.8$  Hz, 2H), 7.33 (d,  $J = 7.8$  Hz, 1H), 7.27 (d,  $J = 8.0$  Hz, 1H), 7.15 (ddd,  $J = 8.1, 7.0, 1.1$  Hz, 1H); 7.10 (ddd,  $J = 8.0, 7.1, 0.9$  Hz, 1H); 4.03 (dd,  $J = 10.0, 0.9$  Hz, 1H), 3.74 (ddd,  $J = 8.1, 5.1, 2.3$  Hz, 1H), 3.72 – 3.68 (m, 2H), 3.55 (d,  $J = 8.3$  Hz, 1H), 3.39 (d,  $J = 2.4$  Hz, 1H), 2.88 (dd,  $J = 15.5, 7.6$  Hz, 1H), 2.76 (dd,  $J = 15.0, 5.7$  Hz, 1H), 2.68 (d,  $J = 15.6$  Hz, 1H), 2.25 (ddd,  $J = 13.9, 11.9, 4.9$  Hz, 1H), 2.01 (dt,  $J = 15.0, 2.5$  Hz, 1H), 1.94 – 1.86 (m, 1H), 1.80 – 1.60 (m, 2H), 1.53 – 1.42 (m, 2H), 1.03 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  208.1, 198.2, 136.1, 135.4, 135.0, 133.8, 129.1, 128.9, 125.9, 121.9, 120.0, 117.1, 116.1, 111.0, 74.14, 65.2, 52.7, 47.4, 45.9, 44.5, 39.9, 34.2, 33.4, 25.6, 23.4, 14.4; IR (neat):  $\nu_{\text{max}}$  3363, 2927, 2916, 1710, 1677, 1596, 1213, 1221, 1109, 1005, 749, 701  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{28}\text{H}_{30}\text{NO}_3$  [M+H] $^+$ : 428.2226; found: 428.2229.

**13-Benzoyl-2-oxo-1,2,3,4,6,7,12,12b-octahydro-4aH-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-4a-yl)ethyl acetate (3e):**



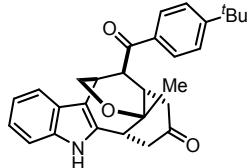
Prepared according to the general procedure as described above in 65% yield (52 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a yellow semi-solid;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 (br.s, 1H), 7.95 (dd,  $J = 8.4, 1.1$  Hz, 2H), 7.60 (t,  $J = 7.4$  Hz, 1H), 7.47 (t,  $J = 7.8$  Hz, 2H), 7.34 (dd,  $J = 7.8, 4.2$  Hz, 2H), 7.19 (t,  $J = 8.1$  Hz, 1H), 7.11 (td,  $J = 7.5, 0.9$  Hz, 1H), 4.60 – 4.50 (m, 2H), 4.03 (dd,  $J = 10.0, 1.0$  Hz, 1H), 3.86 (d,  $J = 7.5$  Hz, 1H), 3.74 (qd,  $J = 5.2, 2.3$  Hz, 1H), 3.70 (ddd,  $J = 10.0, 2.8, 1.1$  Hz, 1H), 3.58 (d,  $J = 8.3$  Hz, 1H), 3.40 (d,  $J = 2.3$  Hz, 1H), 2.96 (dd,  $J = 15.4, 7.5$  Hz, 1H), 2.87 (dd,  $J = 15.1, 5.8$  Hz, 1H), 2.75 (d,  $J = 15.5$  Hz, 1H), 2.62 (dt,  $J = 14.2, 7.1$  Hz, 1H), 2.39 – 2.33 (m, 1H), 2.13 (s, 3H), 2.04 (dt,  $J = 15.1, 2.5$  Hz, 1H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.3, 197.7, 171.4, 136.1, 134.9, 134.8, 133.8, 129.1, 128.9, 125.8, 122.1, 120.1, 117.2, 116.2, 111.0, 73.5, 65.2, 60.8, 52.8, 47.1, 45.7, 44.6, 38.5, 35.5, 33.3, 21.3; IR (neat):  $\nu_{\text{max}}$  2930, 1726, 1682, 1590, 1460, 1371, 1330, 1235, 1114, 1041, 753, 702  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{28}\text{H}_{28}\text{NO}_5$  [ $\text{M}+\text{H}]^+$ : 458.1967; found: 458.1966.

**13-(4-Ethylbenzoyl)-4a-methyl-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3f):**



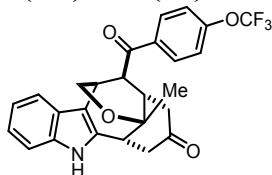
Prepared according to the general procedure as described above in 71% yield (59 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a brown solid; mp = 214–216°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.14 (br. s, 1H), 7.89 (d,  $J = 8.4$  Hz, 2H), 7.37 (d,  $J = 7.7$  Hz, 1H), 7.30 (d,  $J = 6.9$  Hz, 1H), 7.28 (d,  $J = 8.4$  Hz, 2H), 7.17 (dd,  $J = 8.2, 7.0, 1.2$  Hz, 1H), 7.12 (dd,  $J = 8.1, 7.1, 1.0$  Hz, 1H), 4.12 (dd,  $J = 10.0, 1.0$  Hz, 1H), 3.76 – 3.67 (m, 2H), 3.67 – 3.59 (m, 1H), 3.56 (d,  $J = 8.3$  Hz, 1H), 3.42 (d,  $J = 2.1$  Hz, 1H), 2.94 – 2.81 (m, 2H), 2.77 – 2.67 (m, 1H), 2.74 (q,  $J = 7.6$  Hz, 2H), 2.04 (dt,  $J = 4.8, 2.6$  Hz, 1H), 1.85 (s, 3H), 1.27 (t,  $J = 7.6$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.9, 197.6, 150.9, 136.1, 135.1, 132.7, 129.1, 128.5, 125.9, 121.9, 120.0, 117.2, 116.2, 111.0, 72.7, 65.1, 52.7, 48.1, 46.1, 45.0, 38.1, 33.5, 29.2, 29.1, 15.3; IR (neat):  $\nu_{\text{max}}$  3343, 2968, 2929, 1714, 1679, 1605, 1461, 1330, 1113, 1050, 1005, 845, 750  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{27}\text{H}_{28}\text{NO}_3$  [ $\text{M}+\text{H}]^+$ : 414.2069; found: 414.2078.

**13-(4-(*tert*-Butyl)benzoyl)-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3g):**



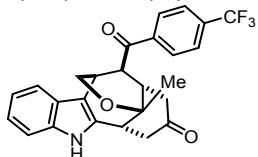
Prepared according to the general procedure as described above in 74% yield (60 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a white solid; mp = 229–231°C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 (br.s, 1H), 7.93 – 7.87 (m, 2H), 7.50 – 7.45 (m, 2H), 7.39 (d,  $J = 7.8$  Hz, 1H), 7.33 (d,  $J = 8.0$  Hz, 1H), 7.19 (ddd,  $J = 8.2, 7.1, 1.1$  Hz, 1H), 7.14 (ddd,  $J = 8.0, 7.1, 1.0$  Hz, 1H), 4.13 (dd,  $J = 10.0, 1.0$  Hz, 1H), 3.75 (dt,  $J = 5.7, 1.8$  Hz, 1H), 3.70 (dd,  $J = 9.9, 2.8, 1.0$  Hz, 1H), 3.64 – 3.59 (m, 1H), 3.57 (d,  $J = 8.4$  Hz, 1H), 3.43 (d,  $J = 2.2$  Hz, 1H), 2.93 (dd,  $J = 15.3, 7.5$  Hz, 1H), 2.86 (dd,  $J = 14.9, 5.7$  Hz, 1H), 2.73 (ddd,  $J = 15.3, 2.3, 1.8$  Hz, 1H), 2.03 (dt,  $J = 14.9, 2.5$  Hz, 1H), 1.86 (s, 3H), 1.34 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.8, 197.6, 157.7, 136.2, 135.1, 132.5, 128.9, 126.0, 125.9, 121.9, 120.0, 117.2, 116.3, 111.0, 72.7, 65.1, 52.6, 48.2, 46.1, 45.1, 38.2, 35.3, 33.5, 31.2, 29.2; IR (neat):  $\nu_{\text{max}}$  3368, 2962, 1712, 1675, 1605, 1461, 1263, 1226, 1107, 1003, 845, 754  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{29}\text{H}_{32}\text{NO}_3$  [M+H] $^+$ : 442.2382; found: 442.2391.

**4a-Methyl-13-(4-(trifluoromethoxy)benzoyl)-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3h):**



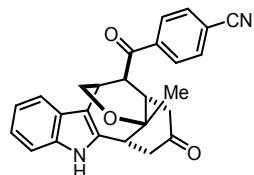
Prepared according to the general procedure as described above in 72% yield (57 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford an orange solid; mp = 192–194°C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 (br.s, 1H), 8.03 – 7.98 (m, 2H), 7.33 (d,  $J = 8.3$  Hz, 2H), 7.29 (d,  $J = 8.8$  Hz, 2H), 7.19 (dt,  $J = 8.1, 1.1$  Hz, 1H), 7.13 (dt,  $J = 7.1, 0.9$  Hz, 1H), 4.10 (dd,  $J = 10.0, 1.0$  Hz, 1H), 3.79 – 3.74 (m, 1H), 3.71 (ddd,  $J = 10.0, 2.8, 1.1$  Hz, 1H), 3.61 – 3.57 (m, 1H), 3.53 (d,  $J = 8.4$  Hz, 1H), 3.37 (d,  $J = 2.3$  Hz, 1H), 2.98 – 2.84 (m, 2H), 2.73 (d,  $J = 15.3, 1.8$  Hz, 1H), 2.03 (dt,  $J = 14.9, 2.5$  Hz, 1H), 1.86 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.4, 196.3, 153.0, 136.0, 134.9, 133.1, 130.9, 125.7, 122.0, 120.6, 120.3 (q,  $J_{\text{CF}} = 259.4$  Hz), 120.1, 116.9, 115.9, 111.0, 72.5, 64.8, 52.7, 48.0, 46.0, 44.9, 38.0, 33.2, 29.1;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.57 (s, 3F); IR (neat):  $\nu_{\text{max}}$  3384, 2936, 1687, 1600, 1459, 1257, 1212, 1171, 1106, 1003, 860, 753  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{23}\text{NO}_4\text{F}_3$  [M+H] $^+$ : 470.1579; found: 470.1584.

**4a-Methyl-13-(4-(trifluoromethyl)benzoyl)-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3i):**



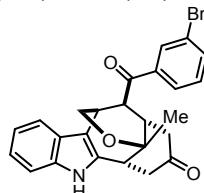
Prepared according to the general procedure as described above in 66% yield (53 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a white solid; mp = 178–180°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 (d,  $J = 8.1$  Hz, 2H), 7.99 (br.s, 1H), 7.73 (d,  $J = 8.2$  Hz, 2H), 7.33 (dd,  $J = 9.4$ , 8.4 Hz, 2H), 7.20 (ddd,  $J = 8.2$ , 7.1, 1.2 Hz, 1H), 7.14 (ddd,  $J = 8.0$ , 7.1, 1.0 Hz, 1H), 4.08 (dd,  $J = 10.0$ , 1.1 Hz, 1H), 3.78 (dt,  $J = 7.4$ , 1.7 Hz, 1H), 3.71 (ddd,  $J = 10.1$ , 2.8, 1.0 Hz, 1H), 3.64 – 3.54 (m, 2H), 3.37 (d,  $J = 2.1$  Hz, 1H), 2.97 (dd,  $J = 15.2$ , 7.4 Hz, 1H), 2.91 (dd,  $J = 14.9$ , 5.4 Hz, 1H), 2.75 (ddd,  $J = 15.2$ , 2.3, 1.9 Hz, 1H), 2.03 (dt,  $J = 15.0$ , 2.3 Hz, 1H), 1.88 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  207.5, 196.9, 137.7, 136.1, 135.1 ( $q, J_{\text{CF}} = 32.6$  Hz), 135.0, 129.3, 126.1 ( $q, J_{\text{CF}} = 3.3$  Hz), 125.7, 123.6 ( $q, J_{\text{CF}} = 272.6$  Hz), 122.2, 120.3, 117.0, 115.9, 111.1, 72.6, 64.9, 53.1, 48.2, 46.1, 45.1, 38.1, 33.2, 29.2;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -63.15 (s, 3F); IR (neat):  $\nu_{\text{max}}$  3291, 2987, 1685, 1318, 1233, 1169, 1125, 1003, 856, 742  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{23}\text{NO}_3\text{F}_3$  [ $\text{M}+\text{H}]^+$ : 454.1630; found: 454.1634.

**4a-Methyl-2-oxo-2,3,4,4a,6,7,12,12b-octahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indole-13-carbonyl)benzonitrile (3j):**



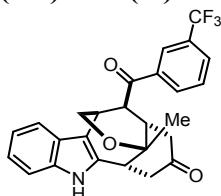
Prepared according to the general procedure as described above in 80% yield (67 mg). It was purified by flash chromatography (50% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a yellow solid; mp = 222–224°C;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.09 (br. s, 1H), 8.03 (d,  $J = 8.5$  Hz, 2H), 7.76 (d,  $J = 8.5$  Hz, 2H), 7.34 (d,  $J = 7.8$  Hz, 1H), 7.28 (d,  $J = 9.1$  Hz, 1H), 7.20 (d,  $J = 7.1$ , 1.4 Hz, 1H), 7.13 (d,  $J = 7.1$ , 1.2 Hz, 1H), 4.05 (d,  $J = 10.0$  Hz, 1H), 3.77 (d,  $J = 7.3$  Hz, 1H), 3.70 (dd,  $J = 10.1$ , 1.9 Hz, 1H), 3.64 – 3.52 (m, 1H), 3.52 (d,  $J = 8.3$  Hz, 1H), 3.32 (d,  $J = 1.6$  Hz, 1H), 3.03 – 2.84 (m, 2H), 2.74 (d,  $J = 15.2$  Hz, 1H), 2.03 (dt,  $J = 14.8$ , 2.2 Hz, 1H), 1.87 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  207.5, 196.6, 138.0, 136.1, 135.1, 132.9, 129.3, 125.6, 122.2, 120.3, 117.9, 117.0, 116.8, 115.7, 111.1, 72.6, 64.8, 53.1, 48.1, 46.1, 45.0, 38.1, 33.1, 29.2; IR (neat):  $\nu_{\text{max}}$  3383, 2930, 2396, 1692, 1458, 1296, 1215, 1105, 1002, 855, 750, 674  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{23}\text{N}_2\text{O}_3$  [ $\text{M}+\text{H}]^+$ : 411.1709; found: 411.1713.

**13-(3-Bromobenzoyl)-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3k):**



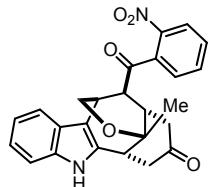
Prepared according to the general procedure as described above in 65% yield (52 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a white solid; mp = 204–206°C;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.13 (s, 1H), 8.10 (s, 1H), 7.82 (d,  $J = 7.8$  Hz, 1H), 7.73 (d,  $J = 7.9$  Hz, 1H), 7.40 – 7.27 (m, 3H), 7.22 – 7.08 (m, 2H), 4.05 (d,  $J = 9.9$  Hz, 1H), 3.78 – 3.66 (m, 2H), 3.65 – 3.54 (m, 1H), 3.48 (d,  $J = 8.3$  Hz, 1H), 3.39 (d,  $J = 1.1$  Hz, 1H), 2.96 – 2.82 (m, 2H), 2.71 (d,  $J = 15.3$  Hz, 1H), 2.03 (d,  $J = 15.1$  Hz, 1H), 1.85 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  207.5, 196.6, 136.7, 136.7, 136.1, 134.9, 132.0, 130.6, 127.3, 125.7, 123.6, 122.1, 120.2, 117.2, 116.0, 111.0, 72.6, 64.9, 53.1, 48.1, 46.2, 45.1, 38.0, 33.3, 29.2; IR (neat):  $\nu_{\text{max}}$  3388, 3304, 2929, 1709, 1461, 1296, 1214, 1106, 1011, 755, 678  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{Br} [\text{M}+\text{H}]^+$ : 464.0861; found: 464.0871.

**4a-Methyl-13-(3-(trifluoromethyl)benzoyl)-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3l):**



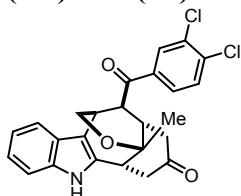
Prepared according to the general procedure as described above in 57% yield (46 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a brown solid; mp = 186–188°C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.28 (br.s, 1H), 8.06 (d,  $J = 7.9$  Hz, 1H), 8.05 (s, 1H), 7.86 (d,  $J = 7.8$  Hz, 1H), 7.59 (t,  $J = 7.8$  Hz, 1H), 7.31 (t,  $J = 7.3$  Hz, 2H), 7.18 (dt,  $J = 8.0, 1.0$  Hz, 1H), 7.11 (dr,  $J = 7.7, 0.8$  Hz, 1H), 4.07 (dd,  $J = 10.0, 0.8$  Hz, 1H), 3.75 (dt,  $J = 7.5, 1.7$  Hz, 1H), 3.71 (ddd,  $J = 10.0, 1.8, 0.9$  Hz, 1H), 3.66 – 3.59 (m, 1H), 3.55 (d,  $J = 8.3$  Hz, 1H), 3.38 (d,  $J = 2.3$  Hz, 1H), 2.97 – 2.88 (m, 2H), 2.74 (ddd,  $J = 15.4, 2.0, 1.9$  Hz, 1H), 2.04 (dt,  $J = 4.9, 2.7$  Hz, 1H), 1.87 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.6, 196.6, 136.1, 135.6, 135.0, 132.0 ( $q, J_{\text{CF}} = 33.3$  Hz), 131.9, 130.2 ( $q, J_{\text{CF}} = 2.9$  Hz), 129.7, 125.9 ( $q, J_{\text{CF}} = 3.7$  Hz), 125.7, 123.7 ( $q, J_{\text{CF}} = 272.7$  Hz), 122.2, 120.1, 117.0, 115.8, 111.1, 72.6, 64.9, 53.1, 48.1, 46.1, 45.0, 38.0, 33.2, 29.2;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.76 (s, 3F); IR (neat):  $\nu_{\text{max}}$  3323, 2987, 1689, 1203, 1165, 1119, 1010, 856, 742  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{23}\text{NO}_3\text{F}_3 [\text{M}+\text{H}]^+$ : 454.1630; found: 454.1642.

**4a-Methyl-13-(2-nitrobenzoyl)-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3m):**



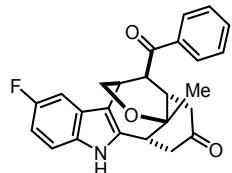
Prepared according to the general procedure as described above in 73% yield (60 mg). It was purified by flash chromatography (50% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a brown solid; mp = 238–240°C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 (d,  $J = 7.9$  Hz, 1H), 7.97 (br.s, 1H), 7.72 – 7.62 (m, 2H), 7.44 (d,  $J = 7.2$  Hz, 1H), 7.25 (d,  $J = 7.1$  Hz, 1H), 7.14 – 7.07 (m, 2H), 7.00 (t,  $J = 7.5$  Hz, 1H), 4.32 (d,  $J = 10.0$  Hz, 1H), 3.81 (d,  $J = 10.1$  Hz, 1H), 3.72 (d,  $J = 6.8$  Hz, 1H), 3.54 (s, 1H), 3.47 (t,  $J = 4.6$  Hz, 1H), 3.22 (d,  $J = 8.2$  Hz, 1H), 2.96 – 2.86 (m, 2H), 2.67 (d,  $J = 15.1$  Hz, 1H), 2.25 (d,  $J = 14.7$  Hz, 1H), 1.85 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.6, 199.8, 147.7, 136.1, 135.8, 134.8, 133.6, 131.6, 128.2, 125.6, 125.1, 120.0, 119.8, 117.0, 115.8, 110.9, 72.6, 65.3, 55.9, 48.2, 46.0, 44.6, 38.6, 31.5, 29.3; IR (neat):  $\nu_{\text{max}}$  3354, 3297, 2932, 1703, 1526, 1449, 1341, 1212, 1089, 1003, 735  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{23}\text{N}_2\text{O}_5$  [M+H] $^+$ : 431.1607; found: 431.1618.

**13-(3,4-Dichlorobenzoyl)-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3n):**



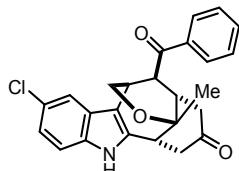
Prepared according to the general procedure as described above in 63% yield (51 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a brown semi-solid;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 (d,  $J = 2.1$  Hz, 1H), 7.96 (br.s, 1H), 7.72 (dd,  $J = 8.4, 2.1$  Hz, 1H), 7.53 (d,  $J = 4.1$  Hz, 1H), 7.34 (dd,  $J = 7.6, 3.4$  Hz, 2H), 7.22 – 7.18 (m, 1H), 7.15 – 7.12 (m, 1H), 4.05 (dd,  $J = 10.1, 1.1$  Hz, 1H), 3.77 (d,  $J = 7.5$  Hz, 1H), 3.70 (ddd,  $J = 10.0, 2.9, 1.2$  Hz, 1H), 3.60 – 3.54 (m, 1H), 3.45 (d,  $J = 8.3$  Hz, 1H), 3.35 (d,  $J = 2.3$  Hz, 1H), 2.97 (dd,  $J = 15.3, 7.4$  Hz, 1H), 2.89 (dd,  $J = 15.0, 5.8$  Hz, 1H), 2.74 (d,  $J = 15.3$  Hz, 1H), 2.02 (dt,  $J = 5.0, 2.3$  Hz, 1H), 1.87 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  207.5, 195.8, 138.5, 136.1, 134.9, 134.5, 134.1, 131.1, 131.0, 127.7, 125.7, 122.2, 120.3, 117.0, 115.8, 111.1, 72.6, 64.9, 53.0, 48.1, 46.1, 45.0, 38.0, 33.3, 29.2; IR (neat):  $\nu_{\text{max}}$  3392, 2927, 2864, 1691, 1584, 1462, 1381, 1249, 1213, 1110, 1026, 754  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{22}\text{NO}_3\text{Cl}_2$  [M+H] $^+$ : 454.0977; found: 454.0985.

**13-Benzoyl-9-fluoro-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3o):**



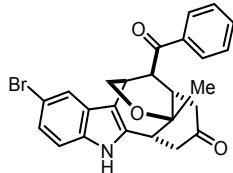
Prepared according to the general procedure as described above in 75% yield (67 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a brown solid; mp = 186–188°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) δ 8.13 (s, 1H), 7.96 – 7.91 (m, 2H), 7.61 (tt,  $J = 7.4, 1.2$  Hz, 1H), 7.48 (t,  $J = 8.0$  Hz, 2H), 7.18 (dd,  $J = 8.7, 4.3$  Hz, 1H), 6.96 (dd,  $J = 9.5, 2.4$  Hz, 1H), 6.90 (td,  $J = 9.1, 2.4$  Hz, 1H), 4.09 (dd,  $J = 10.0, 1.0$  Hz, 1H), 3.71 (d,  $J = 7.4$  Hz, 1H), 3.67 (ddd,  $J = 10.0, 2.9, 1.1$  Hz, 1H), 3.62 (ddd,  $J = 7.9, 5.1, 2.2$  Hz, 1H), 3.55 (d,  $J = 8.4$  Hz, 1H), 3.31 (d,  $J = 2.2$  Hz, 1H), 2.95 – 2.84 (m, 2H), 2.71 (d,  $J = 15.3$  Hz, 1H), 2.05 (dt,  $J = 14.9, 2.4$  Hz, 1H), 1.85 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ) δ 207.8, 197.8, 158.3 (d,  $J_{\text{CF}} = 235.1$  Hz), 137.0, 134.9, 134.0, 132.6, 129.1, 128.8, 126.1 (d,  $J_{\text{CF}} = 9.7$  Hz), 116.3 (d,  $J_{\text{CF}} = 4.4$  Hz), 111.6 (d,  $J_{\text{CF}} = 9.6$  Hz), 110.2 (d,  $J_{\text{CF}} = 26.2$  Hz), 102.3 (d,  $J_{\text{CF}} = 23.8$  Hz), 72.7, 64.9, 52.6, 48.2, 46.0, 45.0, 38.0, 33.5, 29.2;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ) δ -124.01 (s, 1F); IR (neat):  $\nu_{\text{max}}$  3357, 2933, 1679, 1588, 1455, 1227, 1099, 1002, 851, 757, 699 cm<sup>-1</sup>; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{F}$  [M+H]<sup>+</sup>: 404.1662; found: 404.1678

**13-Benzoyl-9-chloro-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3p):**



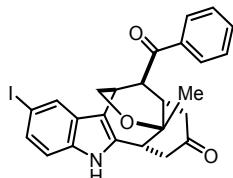
Prepared according to the general procedure as described above in 78% yield (73 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a white solid; mp = 274–276°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) δ 7.97 – 7.91 (m, 3H), 7.63 (t,  $J = 7.4$  Hz, 1H), 7.50 (t,  $J = 7.7$  Hz, 2H), 7.29 (d,  $J = 1.9$  Hz, 1H), 7.25 (d,  $J = 8.1$  Hz, 1H), 7.14 (dd,  $J = 8.6, 2.0$  Hz, 1H), 4.09 (dd,  $J = 10.0, 1.1$  Hz, 1H), 3.77 (dt,  $J = 7.4, 1.7$  Hz, 1H), 3.66 (ddd,  $J = 10.0, 2.9, 1.2$  Hz, 1H), 3.61 (ddt,  $J = 8.0, 5.5, 2.3$  Hz, 1H), 3.54 (d,  $J = 8.4$  Hz, 1H), 3.32 (d,  $J = 2.3$  Hz, 1H), 3.00 (dd,  $J = 15.2, 7.5$  Hz, 1H), 2.89 (dd,  $J = 14.9, 5.7$  Hz, 1H), 2.73 (ddd,  $J = 15.2, 2.3, 1.9$  Hz, 1H), 2.06 (dt,  $J = 14.9, 2.5$  Hz, 1H), 1.87 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ ) δ 207.5, 197.8, 136.6, 134.9, 134.4, 134.0, 129.2, 128.9, 126.9, 125.9, 122.3, 116.8, 116.1, 112.0, 72.6, 64.9, 52.5, 48.2, 46.1, 45.0, 38.1, 33.4, 29.2; IR (neat):  $\nu_{\text{max}}$  3347, 2921, 1701, 1603, 1399, 1221, 1045, 1011, 856, 757, 688 cm<sup>-1</sup>; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{Cl}$  [M+H]<sup>+</sup>: 420.1366; found: 420.1382.

**13-Benzoyl-9-bromo-4a-methyl-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2(3H)-one (3q):**



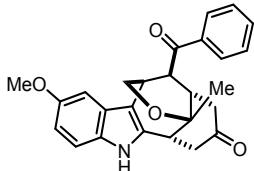
Prepared according to the general procedure as described above in 80% yield (82 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a white solid; mp = 290–292°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (s, 1H), 7.94 (d,  $J = 7.2$  Hz, 2H), 7.63 (t,  $J = 7.4$  Hz, 1H), 7.50 (t,  $J = 7.7$  Hz, 2H), 7.45 (d,  $J = 1.5$  Hz, 1H), 7.26 (dd,  $J = 8.5, 1.8$  Hz, 1H), 7.20 (d,  $J = 8.6$  Hz, 1H), 4.09 (dd,  $J = 10.0, 0.8$  Hz, 1H), 3.76 (d,  $J = 7.5$  Hz, 1H), 3.66 (dd,  $J = 10.0, 1.7$  Hz, 1H), 3.61 (ddd,  $J = 7.9, 5.0, 2.2$  Hz, 1H), 3.53 (d,  $J = 8.4$  Hz, 1H), 3.33 (d,  $J = 2.0$  Hz, 1H), 2.98 (dd,  $J = 15.3, 7.5$  Hz, 1H), 2.89 (dd,  $J = 14.9, 5.7$  Hz, 1H), 2.72 (ddd,  $J = 15.3, 2.0, 1.9$  Hz, 1H), 2.06 (dt,  $J = 14.9, 2.4$  Hz, 1H), 1.86 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.5, 197.8, 136.5, 134.9, 134.7, 134.0, 129.2, 128.9, 127.6, 124.9, 120.0, 116.0, 113.3, 112.4, 72.6, 64.9, 52.5, 48.2, 46.0, 45.0, 38.1, 33.4, 29.2; IR (neat):  $v_{\text{max}}$  3334, 2929, 2841, 1710, 1679, 1583, 1225, 1087, 1001, 837, 756, 679  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{Br}$  [M+H] $^+$ : 464.0861; found: 464.0873.

**13-Benzoyl-9-iodo-4a-methyl-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2(3H)-one (3r):**



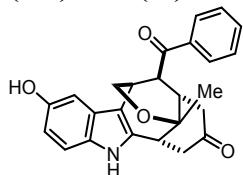
Prepared according to the general procedure as described above in 85% yield (97 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a white solid; mp = 240–242°C;  $^1\text{H}$  NMR (300 MHz, DMSO)  $\delta$  11.25 (s, 1H), 7.82 (d,  $J = 7.4$  Hz, 2H), 7.75 – 7.67 (m, 2H), 7.55 (t,  $J = 7.6$  Hz, 2H), 7.31 (dd,  $J = 8.5, 1.3$  Hz, 1H), 7.19 (d,  $J = 8.4$  Hz, 1H), 3.90 (d,  $J = 9.9$  Hz, 1H), 3.68 (d,  $J = 7.0$  Hz, 1H), 3.51 (d,  $J = 9.7$  Hz, 1H), 3.44 – 3.25 (m, 3H), 3.18 (dd,  $J = 15.1, 7.4$  Hz, 1H), 3.00 (dd,  $J = 14.4, 5.6$  Hz, 1H), 2.61 (d,  $J = 14.8$  Hz, 1H), 1.80 (d,  $J = 14.2$  Hz, 1H); 1.79 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz, DMSO)  $\delta$  208.2, 197.7, 137.6, 135.1, 134.7, 133.8, 129.0, 128.5, 128.2, 127.9, 125.5, 114.0, 113.3, 82.3, 72.2, 64.1, 52.0, 47.4, 45.5, 44.4, 38.3, 32.2; IR (neat):  $v_{\text{max}}$  3424, 2972, 2254, 2189, 1660, 1012, 822, 752  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{I}$  [M+H] $^+$ : 512.0723; found: 512.0730.

**13-Benzoyl-9-methoxy-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3s):**



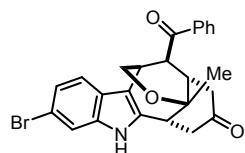
Prepared according to the general procedure as described above in 72% yield (66 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a brown solid; mp = 270–272°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.98 (dd,  $J = 8.3, 1.1$  Hz, 2H), 7.86 (br.s, 1H), 7.60 (t,  $J = 7.4$  Hz, 1H), 7.47 (t,  $J = 7.7$  Hz, 2H), 7.21 (d,  $J = 8.7$  Hz, 1H), 6.84 (dd,  $J = 8.7, 2.4$  Hz, 1H), 6.78 (d,  $J = 2.3$  Hz, 1H), 4.09 (dd,  $J = 10.0, 1.0$  Hz, 1H), 3.78 (s, 3H), 3.74 (dt,  $J = 5.7, 1.7$  Hz, 1H), 3.70 (ddd,  $J = 10.0, 2.8, 1.0$  Hz, 1H), 3.64 – 3.59 (m, 1H), 3.56 (d,  $J = 8.4$  Hz, 1H), 3.37 (d,  $J = 2.1$  Hz, 1H), 2.95 (dd,  $J = 15.3, 7.4$  Hz, 1H), 2.88 (dd,  $J = 15.0, 5.6$  Hz, 1H), 2.73 (dt,  $J = 15.2, 2.1$  Hz, 1H), 2.05 (dt,  $J = 15.0, 2.4$  Hz, 1H), 1.86 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.7, 197.9, 154.6, 135.8, 135.0, 133.8, 131.2, 129.0, 126.2, 116.2, 111.9, 111.8, 99.3, 72.6, 65.0, 56.0, 52.8, 48.2, 46.2, 45.0, 38.0, 33.5, 29.3; IR (neat):  $\nu_{\text{max}}$  3372, 2927, 2863, 1710, 1681, 1592, 1456, 1218, 1103, 1035, 761, 699  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{26}\text{NO}_4$  [M+H] $^+$ : 416.1862; found: 416.1866.

**13-Benzoyl-9-hydroxy-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3t):**



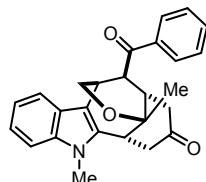
Prepared according to the general procedure as described above in 71% yield (63 mg). It was purified by flash chromatography (50% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a white semi-solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  7.94 (d,  $J = 8.1$  Hz, 2H), 7.64 (t,  $J = 6.9$  Hz, 1H), 7.52 (t,  $J = 7.6$  Hz, 2H), 7.15 (d,  $J = 8.2$  Hz, 1H), 6.71 – 6.64 (m, 2H), 4.05 (d,  $J = 9.8$  Hz, 1H), 3.74 (d,  $J = 6.5$  Hz, 1H), 3.62 (d,  $J = 8.8$  Hz, 1H), 3.59 – 3.50 (m, 2H), 3.28 (s, 1H), 3.14 (dd,  $J = 15.1, 7.3$  Hz, 1H), 3.04 (dd,  $J = 14.6, 4.9$  Hz, 1H), 2.76 (d,  $J = 15.1$  Hz, 1H), 1.89 (d,  $J = 17.1$  Hz, 1H), 1.87 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  211.0, 199.5, 151.7, 137.4, 136.6, 134.7, 132.6, 130.1, 129.6, 127.3, 115.5, 112.3, 112.1, 102.0, 79.5, 74.1, 65.9, 54.2, 46.9, 45.8, 39.7, 34.8, 29.5; IR (neat):  $\nu_{\text{max}}$  3367, 2929, 2857, 1712, 1679, 1460, 1260, 1212, 1112, 1035, 762, 691  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{24}\text{NO}_4$  [M+H] $^+$ : 402.1705; found: 402.1705.

**13-Benzoyl-10-bromo-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3u):**



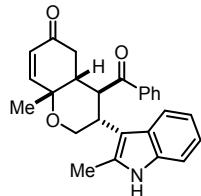
Prepared according to the general procedure as described above in 73% yield (75 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a white solid; mp = 288–290°C;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (s, 1H), 7.96 – 7.89 (m, 2H), 7.61 (t,  $J = 7.4$  Hz, 1H), 7.51 – 7.42 (m, 3H), 7.23 – 7.14 (m, 2H), 4.09 (dd,  $J = 10.0, 0.6$  Hz, 1H), 3.76 – 3.57 (m, 3H), 3.53 (d,  $J = 8.3$  Hz, 1H), 3.35 (d,  $J = 1.7$  Hz, 1H), 2.98 – 2.83 (m, 2H), 2.70 (d,  $J = 15.2$  Hz, 1H), 2.05 (dt,  $J = 15.0, 2.2$  Hz, 1H), 1.86 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  207.5, 197.8, 136.8, 135.7, 134.9, 133.9, 129.1, 128.8, 124.8, 123.4, 118.4, 116.4, 115.5, 114.0, 72.6, 64.9, 52.5, 48.2, 46.0, 45.0, 38.03, 33.3, 29.2; IR (neat):  $\nu_{\text{max}}$  3341, 2929, 2841, 1710, 1671, 1447, 1225, 1054, 971, 759, 693  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{Br} [\text{M}+\text{H}]^+$ : 464.0861; found: 464.0866.

**13-Benzoyl-4a,12-dimethyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3v):**



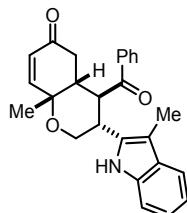
Prepared according to the general procedure as described above in 85% yield (76 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a yellow solid; mp = 206–208°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 – 7.93 (m, 2H), 7.63 – 7.58 (m, 1H), 7.50 – 7.44 (m, 2H), 7.36 – 7.31 (m, 2H), 7.26 – 7.21 (m, 1H), 7.13 (ddd,  $J = 8.0, 7.0, 0.9$  Hz, 1H), 4.10 (dd,  $J = 9.9, 1.1$  Hz, 1H), 3.81 (dt,  $J = 8.1, 1.5$  Hz, 1H), 3.69 (s, 3H), 3.66 – 3.59 (m, 2H), 3.57 (d,  $J = 8.7$  Hz, 1H), 3.43 (d,  $J = 2.4$  Hz, 1H), 3.00 (dd,  $J = 15.5, 8.1$  Hz, 1H), 2.91 (dd,  $J = 15.0, 5.4$  Hz, 1H), 2.72 (ddd,  $J = 15.6, 2.4, 1.4$  Hz, 1H), 2.09 (dt,  $J = 15.0, 2.5$  Hz, 1H), 1.90 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  207.6, 197.9, 137.2, 136.2, 135.0, 133.8, 129.1, 128.9, 125.1, 121.5, 119.7, 117.1, 115.1, 109.3, 72.6, 64.9, 52.3, 46.6, 45.0, 44.9, 38.1, 33.4, 30.1, 29.5; IR (neat):  $\nu_{\text{max}}$  2930, 2871, 1710, 1679, 1464, 1321, 1218, 1000, 920, 752, 701  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{26}\text{NO}_3 [\text{M}+\text{H}]^+$ : 400.1913; found: 400.1929.

**4-Benzoyl-8a-methyl-3-(2-methyl-1*H*-indol-3-yl)-3,4,4a,8a-tetrahydro-2*H*-chromen-6(5*H*)-one (6):**



A dried screw-cap vial was charged with enone tethered-cyclohexadienones **1a** (60 mg, 0.224 mmol, 1 equiv), 2-methyl indole **5** (35.2 mg, 0.269 mmol, 1.2 equiv) and Al(OTf)<sub>3</sub> (10.6 mg, 0.022 mmol, 10 mol%) in acetonitrile (2.2 mL, 0.1 M) under nitrogen atmosphere. The reaction mixture was stirred at 60 °C for 1 hour till consumption of starting material **1a** monitored by thin layer chromatography (TLC). Then, it was cooled to room temperature and the solvent was removed under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (20% EtOAc/hexanes; R<sub>f</sub> = 0.5) to afford the desired product **6** in 67% yield (60 mg) as a yellow semi-solid. The same reaction at room temperature gave product **6** in 50% yield (45 mg); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.67 (br.s, 1H), 7.52 (d, J = 7.7 Hz, 1H), 7.37 (d, J = 7.7 Hz, 2H), 7.18 (t, J = 7.0 Hz, 1H), 7.10 – 7.00 (m, 2H), 7.02 – 6.91 (m, 4H), 6.32 (d, J = 10.3 Hz, 1H), 4.36 (t, J = 11.6 Hz, 2H), 3.83 (dd, J = 12.0, 4.6 Hz, 1H), 3.43 (td, J = 11.6, 4.4 Hz, 1H), 2.81 (d, J = 6.9 Hz, 1H), 2.67 (dd, J = 17.5, 4.8 Hz, 1H), 2.11 (d, J = 17.4 Hz, 1H), 2.10 (s, 3H), 1.63 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 204.1, 197.4, 156.0, 137.7, 135.5, 133.0, 132.3, 130.5, 128.1, 127.4, 126.6, 120.9, 119.5, 118.7, 110.8, 107.8, 73.9, 66.2, 46.8, 43.8, 40.6, 38.6, 26.6, 11.4; IR (neat): ν<sub>max</sub> 3359, 2928, 1712, 1661, 1107, 1009, 759, 695 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>26</sub>H<sub>26</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 400.1913; found: 400.1922.

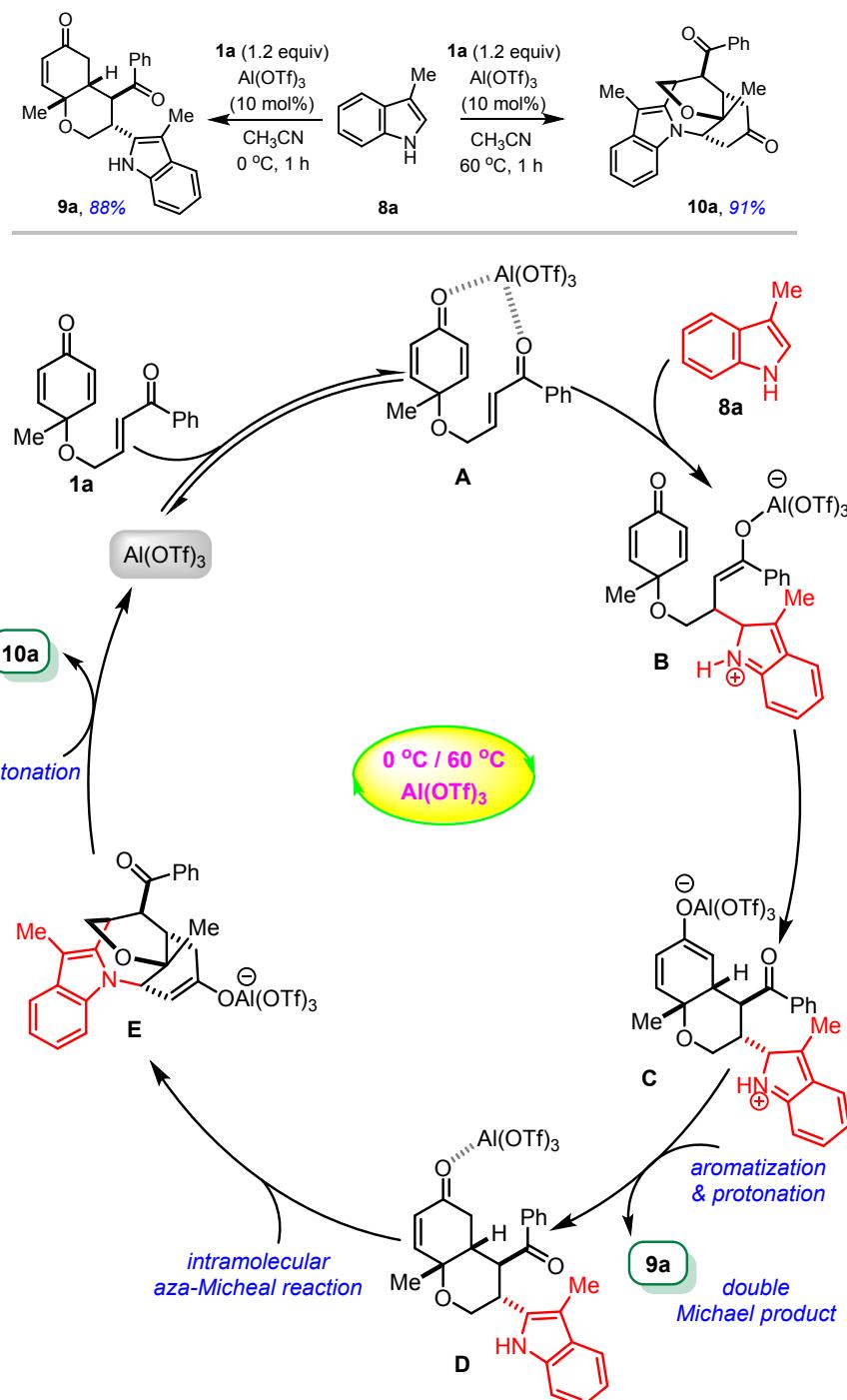
**4-Benzoyl-8a-methyl-3-(3-methyl-1*H*-indol-2-yl)-3,4,4a,8a-tetrahydro-2*H*-chromen-6(5*H*)-one (9):**



A 10 mL round-bottom flask was charged with enone tethered-cyclohexadienones **1a** (60 mg, 0.224 mmol, 1 equiv), 3-methyl indole **8** (35.2 mg, 0.269 mmol, 1.2 equiv) and Al(OTf)<sub>3</sub> (10.6 mg, 0.022 mmol, 10 mol%) in acetonitrile (2.2 mL, 0.1 M) at 0 °C under nitrogen atmosphere. The reaction mixture was stirred same temperature for 1 hour till consumption of starting material **1a** monitored by thin layer chromatography (TLC). The solvent was removed under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (20% EtOAc/hexanes; R<sub>f</sub> = 0.5) to afford the desired product **6** in 88% yield (79 mg) as a yellow semi-solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.84 (s, 1H), 7.55 – 7.47 (m, 2H), 7.32 – 7.24 (m, 2H), 7.17 – 7.10 (m, 2H), 7.08 – 6.98 (m, 2H), 6.98 – 6.92 (m, 2H), 6.25 (dd, J = 10.3, 1.2 Hz, 1H), 4.02 (t, J = 11.3 Hz, 1H), 3.99 – 3.88 (m, 2H), 3.57 (td, J = 11.1, 5.0 Hz, 1H), 2.83 (ddt, J = 7.2, 4.3, 2.1 Hz, 1H), 2.72 (dd, J = 17.4, 5.1 Hz, 1H), 2.24 – 2.17 (m, 1H), 2.12 (s, 3H), 1.64 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 202.8, 197.3, 155.4, 137.6, 135.4, 133.5, 130.7,

130.2, 128.9, 128.5, 127.5, 121.8, 119.2, 118.4, 110.3, 109.2, 74.1, 66.1, 47.8, 43.8, 40.4, 39.1, 26.5, 8.8; IR (neat):  $\nu_{\text{max}}$  3361, 2920, 1710, 1689, 1107, 1010, 756, 699  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{26}\text{NO}_3$  [ $\text{M}+\text{H}]^+$ : 400.1913; found: 400.1912.

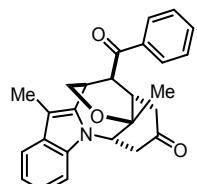
## 2d. Mechanism for C-2/N annulation with 3-methylindole



## 2e. General Procedure for the C-2/N annulation reaction:

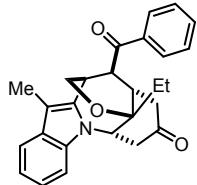
A dried screw-cap vial was charged with enone tethered-cyclohexadienones **1** (1 equiv), 3-substituted indole **8** (1.2 equiv) and Al(OTf)<sub>3</sub> (10 mol%) in acetonitrile (0.1 M) under nitrogen atmosphere. The reaction mixture was stirred at 60 °C for 1 hour till consumption of starting material **1** monitored by thin layer chromatography (TLC). Then, it was cooled to room temperature and the solvent was removed under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (hexanes/ethyl acetate) to afford the desired product **9**.

### **14-Benzoyl-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10a):**



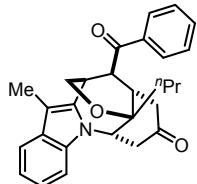
Prepared according to the general procedure as described above in 91% yield (81 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a white solid; mp = 210–212°C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.94 (d, *J* = 7.4 Hz, 2H), 7.61 (dd, *J* = 16.3, 7.7 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.30 – 7.17 (m, 2H), 7.14 (d, *J* = 8.3 Hz, 1H), 4.93 (d, *J* = 6.1 Hz, 1H), 4.10 (d, *J* = 10.2 Hz, 1H), 3.71 (dd, *J* = 10.1, 2.5 Hz, 1H), 3.60 (br.s, 2H), 3.50 (br.s, 1H), 3.26 (d, *J* = 16.8 Hz, 1H), 3.05 – 2.86 (m, 2H), 2.19 (s, 3H), 2.19 (d, *J* = 15.2 Hz, 1H), 1.89 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 206.9, 197.4, 137.9, 136.2, 134.6, 134.1, 129.2, 129.0, 128.8, 122.1, 119.7, 119.2, 109.4, 104.9, 72.2, 64.5, 63.4, 49.2, 45.2, 44.3, 37.0, 35.3, 28.3, 8.4; IR (neat):  $\nu_{\text{max}}$  3018, 2953, 1713, 1680, 1459, 1330, 1211, 1105, 1006, 912, 745, 680 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>26</sub>H<sub>26</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 400.1913; found: 400.1915.

**14-Benzoyl-4a-ethyl-8-methyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10b):**



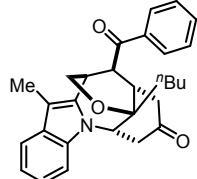
Prepared according to the general procedure as described above in 89% yield (78 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.5$ ) to afford a white solid; mp = 200–202°C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 – 7.90 (m, 2H), 7.60 (tt,  $J = 7.4, 1.2$  Hz, 1H), 7.57 (d,  $J = 7.7$  Hz, 1H), 7.50 – 7.45 (m, 2H), 7.25 – 7.21 (m, 1H), 7.19 – 7.15 (m, 1H), 7.13 (d,  $J = 8.1$  Hz, 1H), 4.89 (d,  $J = 6.7$  Hz, 1H), 4.03 (dd,  $J = 10.2, 1.1$  Hz, 1H), 3.71 (ddd,  $J = 10.3, 2.8, 1.1$  Hz, 1H), 3.72 – 3.66 (m, 1H), 3.59 (d,  $J = 9.4$  Hz, 1H), 3.47 (d,  $J = 2.2$  Hz, 1H), 3.22 (ddd,  $J = 16.9, 2.3, 1.4$  Hz, 1H), 2.96 (dd,  $J = 16.9, 6.7$  Hz, 1H), 2.77 (dd,  $J = 15.7, 5.1$  Hz, 1H), 2.27 (dq,  $J = 14.3, 7.2$  Hz, 1H), 2.17 (s, 3H), 2.14 (dt,  $J = 15.8, 2.6$  Hz, 1H), 2.02 (dq,  $J = 14.6, 7.4$  Hz, 1H), 1.24 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.2, 197.5, 138.0, 136.3, 134.6, 134.0, 129.1, 129.0, 128.8, 122.0, 119.6, 119.2, 109.4, 104.7, 73.7, 64.8, 62.7, 49.0, 45.1, 43.6, 35.3, 32.8, 31.9, 8.4, 7.5; IR (neat):  $\nu_{\text{max}}$  2956, 1709, 1679, 1459, 1326, 1209, 1109, 1003, 756, 689  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{27}\text{H}_{28}\text{NO}_3$  [M+H] $^+$ : 414.2069; found: 414.2072.

**14-Benzoyl-8-methyl-4a-propyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10c):**



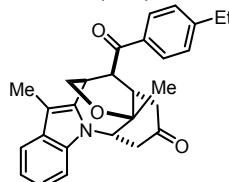
Prepared according to the general procedure as described above in 88% yield (76 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a brown solid; mp = 185–187°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 – 7.91 (m, 2H), 7.64 – 7.59 (m, 1H), 7.59 – 7.56 (m, 1H), 7.52 – 7.46 (m, 2H), 7.27 – 7.22 (m, 1H), 7.18 (td,  $J = 7.5, 1.0$  Hz, 1H), 7.13 (d,  $J = 8.1$  Hz, 1H), 4.92 (dd,  $J = 5.1, 1.5$  Hz, 1H), 4.03 (dd,  $J = 10.2, 1.1$  Hz, 1H), 3.75 – 3.67 (m, 2H), 3.59 (d,  $J = 9.4$  Hz, 1H), 3.47 (d,  $J = 2.2$  Hz, 1H), 3.24 (ddd,  $J = 16.9, 2.4, 1.4$  Hz, 1H), 3.00 (dd,  $J = 16.9, 6.7$  Hz, 1H), 2.81 (dd,  $J = 15.7, 5.1$  Hz, 1H), 2.30 – 2.20 (m, 1H), 2.18 (s, 3H), 2.20 – 2.12 (m, 1H), 2.01 – 1.90 (m, 1H), 1.88 – 1.66 (m, 2H), 1.09 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.1, 197.5, 138.0, 136.3, 134.6, 134.0, 129.1, 129.0, 128.8, 122.0, 119.7, 119.2, 109.4, 104.8, 73.8, 64.7, 62.9, 49.0, 45.1, 43.8, 41.6, 35.3, 33.4, 16.4, 14.6, 8.4; IR (neat):  $\nu_{\text{max}}$  3020, 2946, 1710, 1681, 1456, 1307, 1228, 1102, 1011, 916, 756, 681  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{28}\text{H}_{30}\text{NO}_3$  [M+H] $^+$ : 428.2226; found: 428.2227.

**14-Benzoyl-4a-butyl-8-methyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10d):**



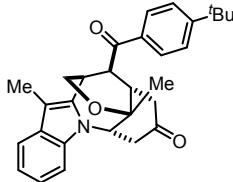
Prepared according to the general procedure as described above in 85% yield (72 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a white solid; mp = 110–112°C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.94 (dd,  $J = 8.3, 1.1$  Hz, 2H), 7.62 (t,  $J = 7.4$  Hz, 1H), 7.59 (d,  $J = 7.8$  Hz, 1H), 7.50 (t,  $J = 7.8$  Hz, 2H), 7.25 (ddd,  $J = 8.2, 7.2, 1.2$  Hz, 1H), 7.18 (dt,  $J = 7.4, 0.9$  Hz, 1H), 7.14 (d,  $J = 8.1$  Hz, 1H), 4.92 (d,  $J = 6.7$  Hz, 1H), 4.05 (dd,  $J = 10.2, 1.0$  Hz, 1H), 3.75 – 3.68 (m, 2H), 3.60 (d,  $J = 9.4$  Hz, 1H), 3.48 (d,  $J = 2.2$  Hz, 1H), 3.24 (ddd,  $J = 17.0, 2.0, 1.3$  Hz, 1H), 3.01 (dd,  $J = 16.9, 6.7$  Hz, 1H), 2.82 (dd,  $J = 15.7, 5.1$  Hz, 1H), 2.27 (ddd,  $J = 13.8, 11.8, 4.9$  Hz, 1H), 2.19 (s, 3H), 2.17 (dt,  $J = 16.0, 2.6$  Hz, 1H), 1.96 (ddd,  $J = 16.1, 11.0, 2.8$  Hz, 1H), 1.83 – 1.72 (m, 1H), 1.72 – 1.60 (m, 1H), 1.54 – 1.43 (m, 2H), 1.04 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.2, 197.5, 138.0, 136.3, 134.6, 134.0, 129.1, 129.0, 128.8, 122.0, 119.6, 119.2, 109.4, 104.7, 73.7, 64.7, 62.9, 49.0, 45.1, 43.7, 39.1, 35.3, 33.2, 25.2, 23.3, 14.3, 8.4; IR (neat):  $\nu_{\text{max}}$  3045, 2972, 2931, 1713, 1671, 1459, 1211, 1105, 1054, 971, 759, 693  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{29}\text{H}_{32}\text{NO}_3$  [M+H] $^+$ : 442.2382; found: 442.2384.

**14-(4-Ethylbenzoyl)-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10e):**



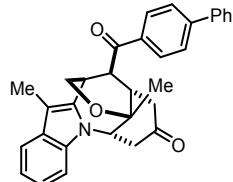
Prepared according to the general procedure as described above in 90% yield (78 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.5$ ) to afford a white solid; mp = 248–250°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.87 (d,  $J = 8.3$  Hz, 2H), 7.58 (d,  $J = 7.5$  Hz, 1H), 7.31 (d,  $J = 8.3$  Hz, 2H), 7.25 (ddd,  $J = 8.2, 5.0, 1.3$  Hz, 1H), 7.18 (td,  $J = 7.6, 1.0$  Hz, 1H), 7.14 (d,  $J = 8.1$  Hz, 1H), 4.93 (d,  $J = 6.4$  Hz, 1H), 4.11 (dd,  $J = 10.1, 1.1$  Hz, 1H), 3.70 (dd,  $J = 10.1, 2.5$  Hz, 1H), 3.63 – 3.55 (m, 2H), 3.50 (d,  $J = 1.7$  Hz, 1H), 3.26 (ddd,  $J = 16.8, 2.2, 1.5$  Hz, 1H), 2.99 (dd,  $J = 16.7, 6.4$  Hz, 1H), 2.91 (dd,  $J = 15.7, 4.7$  Hz, 1H), 2.73 (q,  $J = 7.6$  Hz, 2H), 2.20 (s, 3H), 2.18 (dt,  $J = 15.8, 2.3$  Hz, 1H), 1.89 (s, 3H), 1.27 (t,  $J = 7.6$  Hz, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  206.9, 197.0, 151.3, 138.0, 136.2, 132.3, 129.1, 129.0, 128.6, 122.0, 119.7, 119.2, 109.4, 104.8, 72.2, 64.5, 63.4, 49.1, 45.2, 44.2, 37.0, 35.4, 29.1, 28.3, 15.3, 8.5; IR (neat):  $\nu_{\text{max}}$  2968, 2929, 1714, 1676, 1605, 1461, 1330, 1216, 1113, 1005, 845, 750  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{28}\text{H}_{30}\text{NO}_3$  [M+H] $^+$ : 428.2226; found: 428.2234.

**14-(4-(*tert*-Butyl)benzoyl)-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-*a*]indol-2(1*H*)-one (10f):**



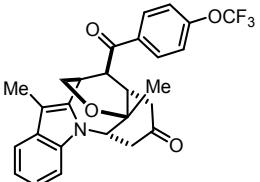
Prepared according to the general procedure as described above in 78% yield (66 mg). It was purified by flash chromatography (20% EtOAc/hexanes;  $R_f = 0.5$ ) to afford a white solid; mp = 227–229°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.88 (d,  $J = 8.6$  Hz, 2H), 7.58 (d,  $J = 7.3$  Hz, 1H), 7.50 (d,  $J = 8.6$  Hz, 2H), 7.27 – 7.22 (m, 1H), 7.18 (td,  $J = 7.6, 1.0$  Hz, 1H), 7.13 (d,  $J = 8.1$  Hz, 1H), 4.93 (d,  $J = 6.3$  Hz, 1H), 4.12 (dd,  $J = 10.1, 1.2$  Hz, 1H), 3.70 (dd,  $J = 10.1, 2.8$  Hz, 1H), 3.64 – 3.55 (m, 2H), 3.51 (d,  $J = 1.7$  Hz, 1H), 3.26 (ddd,  $J = 16.7, 2.3, 1.5$  Hz, 1H), 2.99 (dd,  $J = 16.7, 6.4$  Hz, 1H), 2.91 (dt,  $J = 15.5, 2.8$  Hz, 1H), 2.21 (s, 3H), 2.17 (d,  $J = 15.8$  Hz, 1H), 1.89 (s, 3H), 1.35 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  206.9, 197.1, 158.1, 138.0, 136.3, 132.1, 129.1, 128.9, 126.1, 122.0, 119.7, 119.2, 109.4, 104.8, 72.2, 64.5, 63.4, 49.1, 45.2, 44.3, 37.1, 35.4, 35.4, 31.2, 28.4, 8.5; IR (neat):  $v_{\text{max}}$  3043, 2968, 2929, 1714, 1679, 1461, 1330, 1113, 1050, 1005, 845, 750, 691  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{30}\text{H}_{34}\text{NO}_3$  [M+H] $^+$ : 456.2539; found: 456.2560.

**14-([1,1'-Biphenyl]-4-carbonyl)-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-*a*]indol-2(1*H*)-one (10g):**



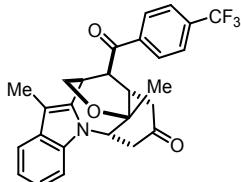
Prepared according to the general procedure as described above in 83% yield (67 mg). It was purified by flash chromatography (20% EtOAc/hexanes;  $R_f = 0.5$ ) to afford a white solid; mp = 240–242°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 – 7.99 (m, 2H), 7.74 – 7.68 (m, 2H), 7.67 – 7.61 (m, 2H), 7.58 (d,  $J = 7.7$  Hz, 1H), 7.53 – 7.46 (m, 2H), 7.45 – 7.40 (m, 1H), 7.28 – 7.22 (m, 1H), 7.18 (td,  $J = 7.6, 1.0$  Hz, 1H), 7.14 (d,  $J = 8.1$  Hz, 1H), 4.94 (d,  $J = 6.3$  Hz, 1H), 4.13 (dd,  $J = 10.1, 1.2$  Hz, 1H), 3.72 (dd,  $J = 10.1, 2.8$  Hz, 1H), 3.67 – 3.58 (m, 2H), 3.54 (d,  $J = 1.7$  Hz, 1H), 3.28 (ddd,  $J = 16.7, 2.2, 1.5$  Hz, 1H), 3.00 (dd,  $J = 16.7, 6.5$  Hz, 1H), 2.97 – 2.90 (m, 1H), 2.25 – 2.18 (m, 1H), 2.21 (s, 3H), 1.90 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  206.9, 197.0, 146.8, 139.7, 137.9, 136.3, 133.3, 129.5, 129.2, 129.0, 128.6, 127.7, 127.5, 122.1, 119.7, 119.2, 109.4, 104.9, 72.3, 64.5, 63.5, 49.3, 45.2, 44.3, 37.0, 35.4, 28.4, 8.5; IR (neat):  $v_{\text{max}}$  2926, 2863, 1715, 1677, 1602, 1461, 1330, 1210, 1116, 1006, 851, 752, 698  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{32}\text{H}_{30}\text{NO}_3$  [M+H] $^+$ : 476.2226; found: 476.2228.

**4a,8-Dimethyl-14-(4-(trifluoromethoxy)benzoyl)-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10h):**



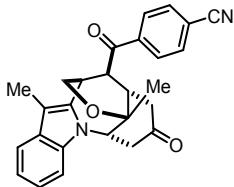
Prepared according to the general procedure as described above in 80% yield (65 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a brown semi-solid;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 (d,  $J = 8.9$  Hz, 2H), 7.58 (d,  $J = 7.7$  Hz, 1H), 7.31 (d,  $J = 8.0$  Hz, 2H), 7.27 – 7.23 (m, 1H), 7.20 – 7.16 (m, 1H), 7.13 (d,  $J = 8.1$  Hz, 1H), 4.93 (d,  $J = 6.4$  Hz, 1H), 4.08 (dd,  $J = 10.2, 1.2$  Hz, 1H), 3.71 (dd,  $J = 10.2, 2.0$  Hz, 1H), 3.61 – 3.52 (m, 2H), 3.45 (d,  $J = 1.8$  Hz, 1H), 3.26 (ddd,  $J = 16.7, 2.3, 1.5$  Hz, 1H), 3.00 (dd,  $J = 16.7, 6.5$  Hz, 1H), 2.93 (dd,  $J = 15.6, 4.7$  Hz, 1H), 2.18 (s, 3H), 2.17 (dt,  $J = 15.6, 2.5$  Hz, 1H), 1.89 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  206.8, 195.9, 153.4, 137.6, 136.3, 132.8, 131.0, 129.0, 122.2, 120.1, 120.4 (d,  $J_{\text{CF}} = 259.3$  Hz), 119.8, 119.3, 109.4, 104.9, 72.2, 64.4, 63.5, 49.3, 45.2, 44.3, 37.1, 35.2, 28.3, 8.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.58 (s, 3F); IR (neat):  $\nu_{\text{max}}$  2926, 1711, 1687, 1459, 1256, 1212, 1169, 1106, 1003, 860, 753, 694  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{27}\text{H}_{25}\text{NO}_4\text{F}_3$  [M+H] $^+$ : 484.1736; found: 484.1754.

**4a,8-Dimethyl-14-(4-(trifluoromethyl)benzoyl)-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10i):**



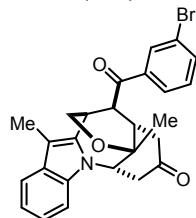
Prepared according to the general procedure as described above in 82% yield (68 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.5$ ) to afford a brown semi-solid;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 (d,  $J = 8.1$  Hz, 2H), 7.76 (d,  $J = 8.2$  Hz, 2H), 7.58 (d,  $J = 7.7$  Hz, 1H), 7.28 – 7.23 (m, 1H), 7.21 – 7.16 (m, 1H), 7.13 (d,  $J = 8.1$  Hz, 1H), 4.93 (d,  $J = 6.4$  Hz, 1H), 4.07 (dd,  $J = 10.2, 1.2$  Hz, 1H), 3.72 (dd,  $J = 10.2, 2.8$  Hz, 1H), 3.62 – 3.54 (m, 2H), 3.45 (d,  $J = 1.8$  Hz, 1H), 3.27 (ddd,  $J = 16.7, 2.4, 1.5$  Hz, 1H), 3.00 (dd,  $J = 16.7, 6.5$  Hz, 1H), 2.97 – 2.91 (m, 1H), 2.18 (s, 3H), 2.17 (d,  $J = 12.8$  Hz, 1H), 1.90 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  206.7, 196.4, 137.5, 137.3, 136.3, 135.4 (q,  $J_{\text{CF}} = 32.8$  Hz), 129.3, 129.0, 126.2 (q,  $J_{\text{CF}} = 3.3$  Hz), 123.5 (q,  $J_{\text{CF}} = 272.8$  Hz), 122.3, 119.9, 119.3, 109.4, 105.0, 72.2, 64.4, 63.5, 49.6, 45.2, 44.3, 37.1, 35.0, 28.4, 8.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -63.20 (s, 3F); IR (neat):  $\nu_{\text{max}}$  2918, 1710, 1689, 1203, 1165, 1119, 1010, 856, 742, 684  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{27}\text{H}_{25}\text{NO}_3\text{F}_3$  [M+H] $^+$ : 468.1787; found: 468.1798.

**4-(4a,8-Dimethyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indole-14-carbonyl)benzonitrile (10j):**



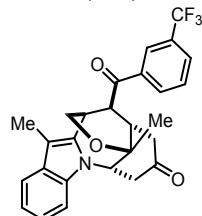
Prepared according to the general procedure as described above in 75% yield (65 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.2$ ) to afford a white solid; mp = 252–254°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02 (d,  $J = 8.6$  Hz, 2H), 7.80 (d,  $J = 8.6$  Hz, 2H), 7.58 (d,  $J = 7.5$  Hz, 1H), 7.29 – 7.23 (m, 1H), 7.19 (td,  $J = 7.6, 0.9$  Hz, 1H), 7.13 (d,  $J = 8.1$  Hz, 1H), 4.93 (d,  $J = 6.2$  Hz, 1H), 4.06 (dd,  $J = 10.3, 1.2$  Hz, 1H), 3.71 (dd,  $J = 10.3, 2.8$  Hz, 1H), 3.62 – 3.51 (m, 2H), 3.41 (d,  $J = 1.7$  Hz, 1H), 3.27 (ddd,  $J = 16.7, 2.3, 1.5$  Hz, 1H), 3.00 (dd,  $J = 16.6, 6.4$  Hz, 1H), 2.98 – 2.92 (m, 1H), 2.16 (s, 3H), 2.16 (d,  $J = 15.5$  Hz, 1H), 1.90 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  206.7, 196.1, 137.6, 137.3, 136.3, 133.0, 129.3, 128.9, 122.4, 119.9, 119.4, 117.8, 117.4, 109.4, 105.0, 72.2, 64.3, 63.5, 49.6, 45.2, 44.3, 37.1, 34.9, 28.3, 8.5; IR (neat):  $\nu_{\text{max}}$  2933, 2372, 1698, 1467, 1205, 1203, 1122, 1010, 842, 751  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_3$  [ $\text{M}+\text{H}]^+$ : 425.1866; found: 425.1871.

**14-(3-Bromobenzoyl)-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10k):**



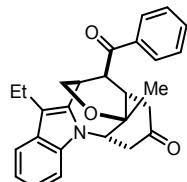
Prepared according to the general procedure as described above in 77% yield (64 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.5$ ) to afford a white solid; mp = 226–228°C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 (t,  $J = 1.8$  Hz, 1H), 7.83 (ddd,  $J = 7.9, 1.5, 1.1$  Hz, 1H), 7.75 (ddd,  $J = 7.9, 1.9, 1.0$  Hz, 1H), 7.58 (d,  $J = 7.7$  Hz, 1H), 7.37 (t,  $J = 7.9$  Hz, 1H), 7.25 (ddd,  $J = 8.2, 4.7, 1.3$  Hz, 1H), 7.18 (td,  $J = 7.5, 0.9$  Hz, 1H), 7.13 (d,  $J = 8.1$  Hz, 1H), 4.93 (dt,  $J = 6.3, 1.4$  Hz, 1H), 4.04 (dd,  $J = 10.2, 1.2$  Hz, 1H), 3.70 (ddd,  $J = 10.2, 2.9, 1.1$  Hz, 1H), 3.58 (ddt,  $J = 9.5, 4.8, 2.4$  Hz, 1H), 3.51 (d,  $J = 9.3$  Hz, 1H), 3.47 (d,  $J = 2.1$  Hz, 1H), 3.26 (ddd,  $J = 16.8, 2.4, 1.5$  Hz, 1H), 2.99 (dd,  $J = 16.8, 6.5$  Hz, 1H), 2.93 (dd,  $J = 15.7, 5.2$  Hz, 1H), 2.21 (s, 3H), 2.17 (dt,  $J = 15.7, 2.6$  Hz, 1H), 1.89 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  206.7, 196.0, 137.5, 137.0, 136.3, 136.3, 131.9, 130.7, 129.0, 127.3, 123.6, 122.2, 119.8, 119.4, 109.4, 105.0, 72.2, 64.4, 63.4, 49.6, 45.2, 44.3, 36.9, 35.2, 28.4, 8.4; IR (neat):  $\nu_{\text{max}}$  2938, 1733, 1431, 1285, 1222, 1112, 1001, 751, 693  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{25}\text{NO}_3\text{Br}$  [ $\text{M}+\text{H}]^+$ : 478.1018; found: 478.1025.

**4a,8-Dimethyl-14-(3-(trifluoromethyl)benzoyl)-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10l):**



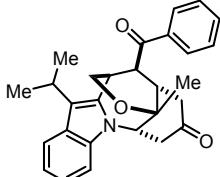
Prepared according to the general procedure as described above in 80% yield (67 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.5$ ) to afford a brown semi-solid;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H), 8.07 (d,  $J = 7.9$  Hz, 1H), 7.89 (d,  $J = 7.8$  Hz, 1H), 7.64 (t,  $J = 7.8$  Hz, 1H), 7.61 – 7.57 (m, 1H), 7.26 (td,  $J = 7.4$ , 1.2 Hz, 1H), 7.21 – 7.17 (m, 1H), 7.14 (d,  $J = 8.1$  Hz, 1H), 4.94 (d,  $J = 6.4$  Hz, 1H), 4.07 (dd,  $J = 10.2$ , 1.1 Hz, 1H), 3.71 (ddd,  $J = 10.2$ , 2.8, 0.7 Hz, 1H), 3.65 – 3.57 (m, 2H), 3.47 (d,  $J = 1.9$  Hz, 1H), 3.27 (ddd,  $J = 16.7$ , 2.3, 1.5 Hz, 1H), 3.00 (dd,  $J = 16.7$ , 6.5 Hz, 1H), 2.94 (dd,  $J = 15.7$ , 4.8 Hz, 1H), 2.18 (s, 3H), 2.17 (dt,  $J = 15.7$ , 2.4 Hz, 1H), 1.90 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  206.7, 196.0, 137.3, 136.3, 135.2, 132.0 ( $q, J_{\text{CF}} = 33.3$  Hz), 131.9, 130.5 ( $q, J_{\text{CF}} = 3.2$  Hz), 129.8, 129.0, 125.7 ( $q, J_{\text{CF}} = 3.5$  Hz), 123.6 ( $q, J_{\text{CF}} = 272.8$  Hz), 122.3, 119.8, 119.4, 109.4, 105.1, 72.2, 64.4, 63.4, 49.5, 45.2, 44.3, 37.0, 35.0, 28.3, 8.4;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.74 (s, 3F); IR (neat):  $\nu_{\text{max}}$  2977, 1665, 1316, 1233, 1169, 1011, 851, 755 cm $^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{27}\text{H}_{25}\text{NO}_3\text{F}_3$  [M+H] $^+$ : 468.1787; found: 468.1807.

**4-Benzoyl-8-ethyl-4a-methyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10m):**



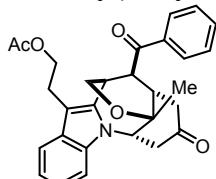
Prepared according to the general procedure as described above in 82% yield (76 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.5$ ) to afford a white solid; mp = 240–242°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 – 7.92 (m, 2H), 7.66 – 7.59 (m, 2H), 7.54 – 7.46 (m, 2H), 7.27 – 7.22 (m, 1H), 7.19 – 7.12 (m, 2H), 4.92 (dt,  $J = 6.5$ , 1.4 Hz, 1H), 4.13 (dd,  $J = 10.1$ , 1.2 Hz, 1H), 3.69 (ddd,  $J = 10.1$ , 2.8, 0.7 Hz, 1H), 3.66 – 3.57 (m, 2H), 3.45 (d,  $J = 1.7$  Hz, 1H), 3.27 (ddd,  $J = 16.8$ , 2.5, 1.5 Hz, 1H), 3.00 (dd,  $J = 16.7$ , 6.5 Hz, 1H), 2.92 (dd,  $J = 15.6$ , 4.6 Hz, 1H), 2.68 (dq,  $J = 15.1$ , 7.5 Hz, 1H), 2.56 (dq,  $J = 15.0$ , 7.5 Hz, 1H), 2.19 (dt,  $J = 15.5$ , 2.4 Hz, 1H), 1.89 (s, 3H), 1.17 (t,  $J = 7.5$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  206.9, 197.4, 137.3, 136.5, 134.7, 134.1, 129.2, 128.9, 128.1, 122.0, 119.7, 119.4, 112.0, 109.5, 72.2, 64.8, 63.4, 49.1, 45.2, 44.2, 37.1, 35.2, 28.3, 17.4, 16.5; IR (neat):  $\nu_{\text{max}}$  3010, 2955, 2877, 1713, 1681, 1460, 1335, 1212, 1155, 1006, 915, 747, 685 cm $^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{27}\text{H}_{28}\text{NO}_3$  [M+H] $^+$ : 414.2069; found: 414.2070.

**14-Benzoyl-8-isopropyl-4a-methyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10n):**



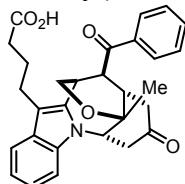
Prepared according to the general procedure as described above in 80% yield (76 mg). It was purified by flash chromatography (20% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a white solid; mp = 268–270°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.94 – 7.90 (m, 2H), 7.81 – 7.76 (m, 1H), 7.65 – 7.59 (m, 1H), 7.52 – 7.46 (m, 2H), 7.24 – 7.19 (m, 1H), 7.17 – 7.09 (m, 2H), 4.91 (d,  $J = 6.5$  Hz, 1H), 4.09 (dd,  $J = 10.2, 1.3$  Hz, 1H), 3.66 (dd,  $J = 10.2, 2.8$  Hz, 1H), 3.61 – 3.57 (m, 2H), 3.51 (d,  $J = 1.5$  Hz, 1H), 3.26 (ddd,  $J = 16.9, 2.5, 1.4$  Hz, 1H), 3.00 (dd,  $J = 16.9, 6.6$  Hz, 1H), 2.96 – 2.85 (m, 2H), 2.20 (d,  $J = 15.8$  Hz, 1H), 1.88 (s, 3H), 1.52 (d,  $J = 7.0$  Hz, 3H), 1.30 (d,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  206.9, 197.3, 136.8, 136.3, 134.6, 134.2, 129.1, 128.9, 126.7, 121.8, 121.0, 119.4, 116.0, 109.6, 72.2, 64.9, 63.2, 49.3, 45.2, 44.2, 36.8, 35.1, 28.3, 26.2, 23.9, 23.4; IR (neat):  $\nu_{\text{max}}$  3033, 2942, 1724, 1670, 1445, 1320, 1142, 1011, 915, 751, 655  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{28}\text{H}_{30}\text{NO}_3$  [M+H] $^+$ : 428.2226; found: 428.2228.

**2-(14-Benzoyl-4a-methyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-8-yl)ethyl acetate (10o):**



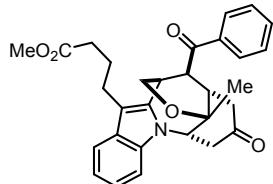
Prepared according to the general procedure as described above in 35% yield (35 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.3$ ) to afford a yellow semi-solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 – 7.88 (m, 2H), 7.66 – 7.60 (m, 2H), 7.50 (t,  $J = 7.7$  Hz, 2H), 7.29 – 7.23 (m, 1H), 7.21 – 7.13 (m, 2H), 4.94 (d,  $J = 6.4$  Hz, 1H), 4.22 – 4.12 (m, 2H), 4.12 – 4.02 (m, 1H), 3.72 (dd,  $J = 10.1, 2.5$  Hz, 1H), 3.64 – 3.55 (m, 2H), 3.43 (d,  $J = 1.7$  Hz, 1H), 3.26 (d,  $J = 17.3$  Hz, 1H), 3.10 – 2.97 (m, 2H), 2.93 (dd,  $J = 15.3, 4.2$  Hz, 1H), 2.85 – 2.75 (m, 1H), 2.19 (dt,  $J = 15.8, 2.3$  Hz, 1H), 1.92 (s, 3H), 1.90 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  206.7, 197.3, 171.0, 139.0, 136.4, 134.7, 134.3, 129.3, 128.8, 128.2, 122.4, 120.1, 119.2, 109.6, 105.6, 72.2, 64.8, 63.5, 48.9, 45.1, 44.2, 37.2, 35.2, 28.3, 23.7, 21.1; IR (neat):  $\nu_{\text{max}}$  2926, 2863, 1715, 1677, 1602, 1461, 1330, 1210, 1116, 1006, 851, 752, 698  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{29}\text{H}_{30}\text{NO}_5$  [M+H] $^+$ : 472.2124; found: 472.2121.

**4-(14-Benzoyl-4a-methyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-8-yl)butanoic acid (10p):**



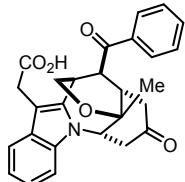
Prepared according to the general procedure as described above in 40 % yield (42 mg). It was purified by flash chromatography (40% EtOAc/hexanes;  $R_f = 0.1$ ) to afford a white solid; mp = 258–260°C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.89 (dd,  $J = 8.3, 1.1$  Hz, 2H), 7.63 – 7.55 (m, 2H), 7.46 (t,  $J = 7.7$  Hz, 2H), 7.27 – 7.21 (m, 1H), 7.19 – 7.11 (m, 2H), 4.93 (d,  $J = 6.4$  Hz, 1H), 4.14 (dd,  $J = 10.2, 1.0$  Hz, 1H), 3.69 (dd,  $J = 10.2, 2.4$  Hz, 1H), 3.65 – 3.54 (m, 2H), 3.40 (d,  $J = 1.6$  Hz, 1H), 3.26 (d,  $J = 16.8$  Hz, 1H), 3.00 (dd,  $J = 16.8, 6.5$  Hz, 1H), 2.92 (dd,  $J = 15.7, 4.5$  Hz, 1H), 2.74 (ddd,  $J = 14.7, 8.4, 6.6$  Hz, 1H), 2.59 – 2.48 (m, 1H), 2.32 – 2.13 (m, 3H), 1.89 (s, 3H), 1.90 – 1.78 (m, 2H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 206.9, 197.5, 178.6, 138.1, 136.4, 134.7, 134.2, 129.2, 128.8, 128.2, 122.2, 119.9, 119.3, 109.5, 109.0, 72.2, 64.8, 63.4, 49.0, 45.1, 44.2, 37.2, 35.1, 33.5, 28.3, 26.4, 23.4; IR (neat):  $\nu_{\text{max}}$  3019, 2931, 1708, 1457, 1416, 1329, 1212, 1111, 1003, 913, 748, 700 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>29</sub>H<sub>30</sub>NO<sub>5</sub> [M+H]<sup>+</sup>: 472.2124; found: 472.2125.

**Methyl 4-(14-benzoyl-4a-methyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-8-yl)butanoate (10q):**



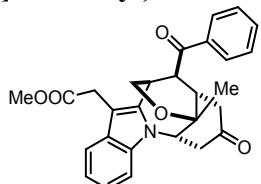
Prepared according to the general procedure as described above in 71% yield (77 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a yellow semi-solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.96 – 7.87 (m, 2H), 7.65 – 7.57 (m, 2H), 7.53 – 7.46 (m, 2H), 7.26 – 7.21 (m, 1H), 7.20 – 7.10 (m, 2H), 4.93 (d,  $J = 6.5$  Hz, 1H), 4.15 (dd,  $J = 10.2, 1.2$  Hz, 1H), 3.70 (ddd,  $J = 10.3, 2.8, 0.7$  Hz, 1H), 3.64 – 3.55 (m, 2H), 3.52 (s, 3H), 3.41 (d,  $J = 1.7$  Hz, 1H), 3.26 (ddd,  $J = 16.8, 2.3, 1.5$  Hz, 1H), 3.00 (dd,  $J = 16.8, 6.5$  Hz, 1H), 2.92 (dd,  $J = 15.8, 4.7$  Hz, 1H), 2.74 (ddd,  $J = 14.7, 8.0, 7.0$  Hz, 1H), 2.51 (dt,  $J = 8.4, 7.7$  Hz, 1H), 2.27 – 2.15 (m, 3H), 1.89 (s, 3H), 1.88 – 1.80 (m, 2H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 206.8, 197.5, 173.8, 138.1, 136.4, 134.8, 134.2, 129.2, 128.9, 128.3, 122.2, 119.9, 119.4, 109.5, 109.2, 72.2, 64.8, 63.5, 51.5, 49.0, 45.2, 44.2, 37.2, 35.2, 33.7, 28.3, 26.7, 23.5; IR (neat):  $\nu_{\text{max}}$  2940, 1720, 1685, 1450, 1333, 1208, 1165, 1118, 1000, 800, 742, 680 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>30</sub>H<sub>32</sub>NO<sub>5</sub> [M+H]<sup>+</sup>: 486.2280; found: 486.2278.

**2-(14-Benzoyl-4a-methyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-8-yl)acetic acid (10r):**



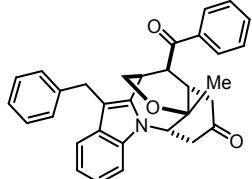
Prepared according to the general procedure as described above in 53% yield (52 mg). It was purified by flash chromatography (50% EtOAc/hexanes;  $R_f = 0.1$ ) to afford a white solid; mp = 238–240°C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.89 (dd,  $J = 8.3, 1.1$  Hz, 2H), 7.59 (d,  $J = 7.8$  Hz, 1H), 7.53 (t,  $J = 7.4$  Hz, 1H), 7.42 (t,  $J = 7.7$  Hz, 2H), 7.28 – 7.23 (m, 1H), 7.20 – 7.16 (m, 1H), 7.14 (d,  $J = 8.2$  Hz, 1H), 4.93 (d,  $J = 6.6$  Hz, 1H), 4.10 (dd,  $J = 10.2, 0.9$  Hz, 1H), 3.74 (dd,  $J = 10.2, 2.4$  Hz, 1H), 3.66 (d,  $J = 15.8$  Hz, 1H), 3.63 – 3.55 (m, 2H), 3.47 (d,  $J = 15.8$  Hz, 1H), 3.41 (d,  $J = 1.6$  Hz, 1H), 3.25 (d,  $J = 17.4$  Hz, 1H), 3.00 (dd,  $J = 16.9, 6.6$  Hz, 1H), 2.91 (dd,  $J = 15.7, 4.7$  Hz, 1H), 2.19 (dt,  $J = 15.5, 2.3$  Hz, 1H), 1.88 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 206.7, 197.2, 176.7, 139.7, 136.3, 134.6, 134.2, 129.2, 128.8, 127.9, 122.6, 120.5, 119.2, 109.7, 101.9, 72.2, 64.3, 63.6, 48.7, 45.1, 44.1, 37.1, 35.3, 29.9, 28.3; IR (neat):  $\nu_{\text{max}}$  3001, 2940, 1710, 1455, 1416, 1335, 1217, 1117, 1008, 900, 745, 709 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>27</sub>H<sub>26</sub>NO<sub>5</sub> [M+H]<sup>+</sup>: 444.1811; found: 444.1815.

**Methyl 2-(14-benzoyl-4a-methyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-8-yl)acetate (10s):**



Prepared according to the general procedure as described above in 88% yield (90 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.4$ ) to afford a brown semi-solid; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.93 (d,  $J = 7.3$  Hz, 2H), 7.62 (t,  $J = 7.3$  Hz, 2H), 7.49 (t,  $J = 7.8$  Hz, 2H), 7.29 – 7.24 (m, 1H), 7.20 (t,  $J = 7.1$  Hz, 1H), 7.15 (d,  $J = 8.1$  Hz, 1H), 4.94 (d,  $J = 6.6$  Hz, 1H), 4.14 (dd,  $J = 10.1, 0.8$  Hz, 1H), 3.78 (dd,  $J = 10.1, 2.0$  Hz, 1H), 3.71 (d,  $J = 15.5$  Hz, 1H), 3.67 – 3.54 (m, 2H), 3.57 (s, 3H), 3.55 – 3.40 (m, 2H), 3.26 (d,  $J = 16.9$  Hz, 1H), 3.01 (dd,  $J = 16.9, 6.6$  Hz, 1H), 2.92 (dd,  $J = 15.7, 4.8$  Hz, 1H), 2.20 (dt,  $J = 15.6, 2.4$  Hz, 1H), 1.89 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 206.6, 197.3, 171.9, 139.5, 136.3, 134.7, 134.2, 129.2, 128.8, 128.0, 122.5, 120.4, 119.2, 109.6, 102.5, 72.2, 64.4, 63.6, 52.1, 48.8, 45.1, 44.2, 37.1, 35.4, 30.1, 28.3; IR (neat):  $\nu_{\text{max}}$  2936, 1724, 1680, 1594, 1454, 1329, 1208, 1160, 1116, 1006, 814, 748, 683 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>28</sub>H<sub>28</sub>NO<sub>5</sub> [M+H]<sup>+</sup>: 458.1967; found: 458.1970.

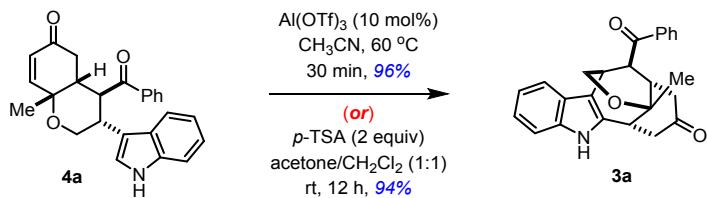
**14-Benzoyl-8-benzyl-4a-methyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10t):**



Prepared according to the general procedure as described above in 86% yield (91 mg). It was purified by flash chromatography (30% EtOAc/hexanes;  $R_f = 0.5$ ) to afford a yellow solid; mp = 212–214°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.85 (dd,  $J = 8.4, 1.1$  Hz, 2H), 7.55 (t,  $J = 7.4$  Hz, 1H), 7.45 (d,  $J = 7.8$  Hz, 1H), 7.29 (dd,  $J = 8.2, 7.6$  Hz, 2H), 7.27 – 7.22 (m, 1H), 7.21 – 7.09 (m, 5H), 7.03 (d,  $J = 6.8$  Hz, 2H), 4.98 (d,  $J = 6.4$  Hz, 1H), 4.10 (d,  $J = 16.8$  Hz, 1H), 4.03 (dd,  $J = 10.2, 1.1$  Hz, 1H), 3.93 (d,  $J = 16.8$  Hz, 1H), 3.67 – 3.58 (m, 2H), 3.56 (dd,  $J = 10.2, 1.9$  Hz, 1H), 3.45 (d,  $J = 1.6$  Hz, 1H), 3.31 (ddd,  $J = 16.6, 2.2, 1.4$  Hz, 1H), 3.03 (dd,  $J = 16.7, 6.5$  Hz, 1H), 2.94 (dd,  $J = 15.6, 4.8$  Hz, 1H), 2.19 (dt,  $J = 15.5, 2.4$  Hz, 1H), 1.90 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  206.9, 197.4, 141.0, 138.9, 136.5, 134.5, 134.0, 129.1, 128.8, 128.6, 128.5, 128.0, 126.0, 122.2, 120.0, 119.7, 109.5, 108.0, 72.2, 64.5, 63.6, 49.1, 45.1, 44.3, 37.1, 35.3, 29.8, 28.4; IR (neat):  $v_{\text{max}}$  3000, 2960, 2250, 1711, 1677, 1596, 1457, 1330, 1280, 1209, 1114, 1015, 824, 748, 703  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{32}\text{H}_{30}\text{NO}_3\text{Z}$  [M+H] $^+$ : 476.2226; found: 476.2231.

## 2f. Control experiments

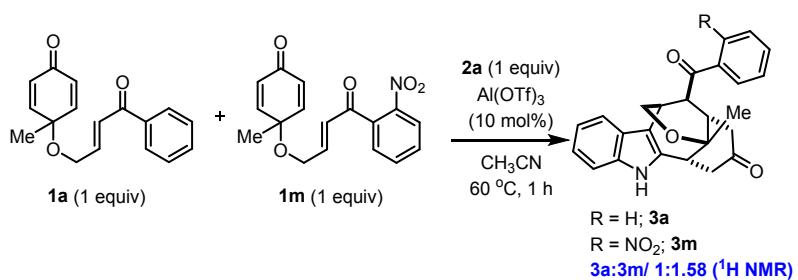
### Cyclization of compound 4a



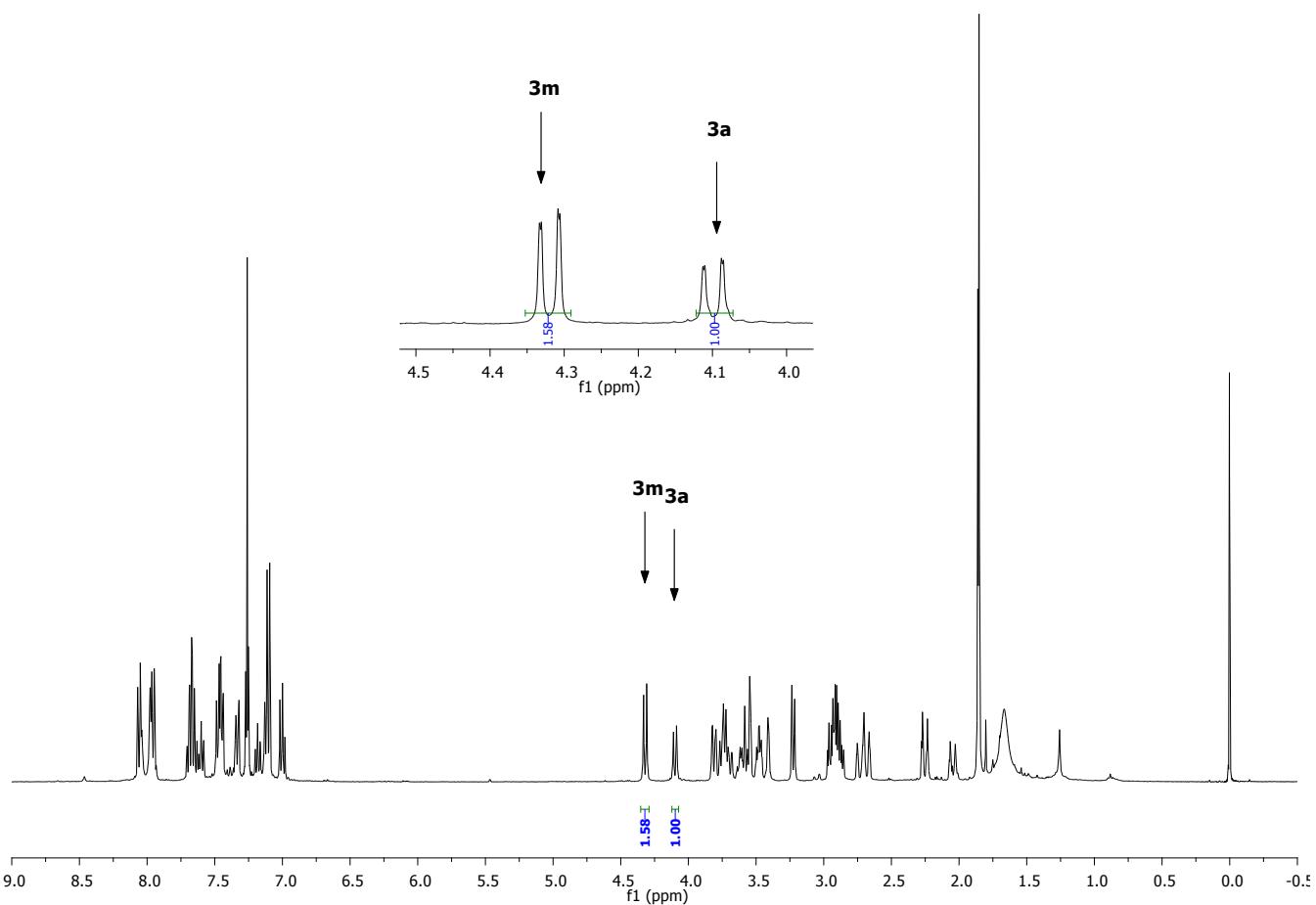
A dried screw-cap vial with a spinvane triangular-shaped Teflon stirbar was charged bicycle **4a** (30 mg, 0.078 mmol) and  $\text{Al(OTf)}_3$  (3.7 mg, 0.008. 10 mol%) in acetonitrile (~1 mL, 0.1 M) under nitrogen atmosphere. The reaction mixture was stirred at 60 °C for 30 minutes (monitored by TLC). Then, it was cooled to room temperature and the solvent was removed under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (40% EtOAc in hexanes) to afford C-2/C-3 annulated product **3a** in 96% yield (29 mg).

The same reaction with *p*-TSA catalyst (30 mg, 0.156 mmol, 2 equiv) in acetone/ $\text{CH}_2\text{Cl}_2$  (1:1 ratio, 1.5 mL, 0.05 M) was performed at room temperature under nitrogen atmosphere. The reaction was completed in 12 hours and then solvent was removed under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (40% EtOAc in hexanes) to afford C-2/C-3 annulated product **3a** in 94% yield (28 mg).

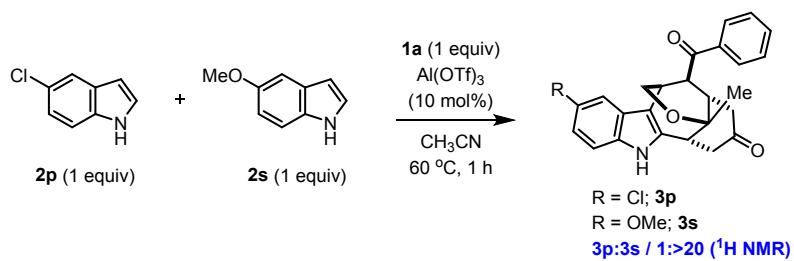
### Intermolecular competition between cyclohexadienone-tethered enones



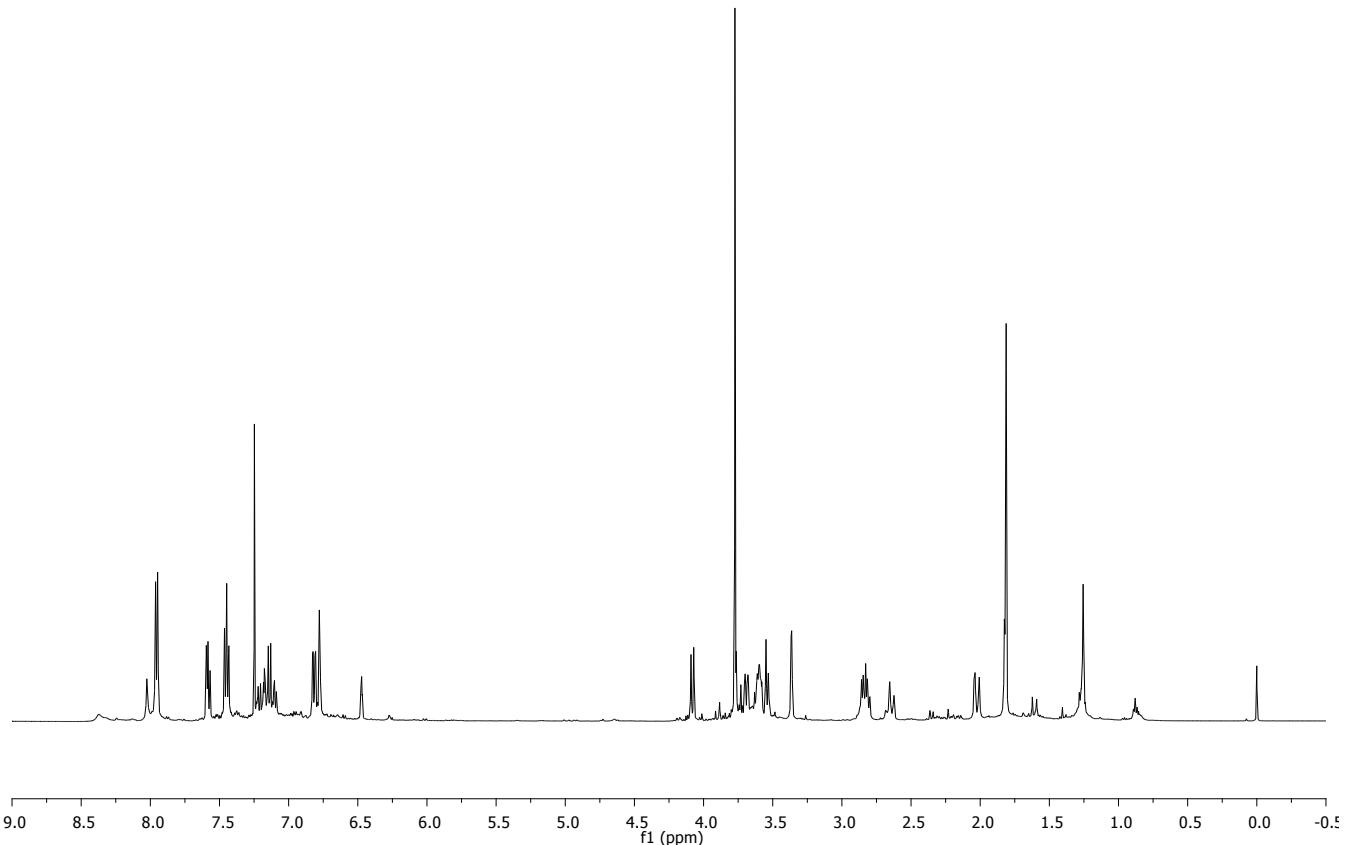
A dried screw-cap vial was charged with cyclohexadienones **1a** (40 mg, 0.15 mmol, 1 equiv), **1m** (47 mg, 0.15 mmol, 1 equiv), indole **2a** (18 mg, 0.15, 1 equiv) and  $\text{Al(OTf)}_3$  (7 mg, 0.015 mmol, 10 mol%) in acetonitrile (1.5 mL, 0.1 M) under nitrogen atmosphere. The reaction mixture was stirred at 60 °C for 1 hour. Then, it was cooled to room temperature and the solvent was removed under reduced pressure. The crude  $^1\text{H}$  NMR was recorded to determine the ratio of the products **3a** and **3m**.



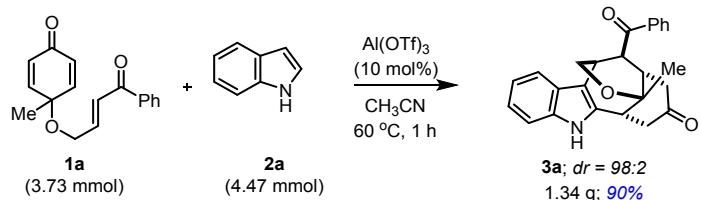
### Intermolecular competition between indoles



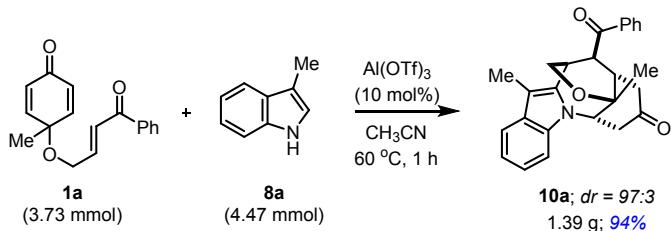
A dried screw-cap vial was charged with indole **2p** (23 mg, 0.15 mmol, 1 equiv), indole **2s** (22 mg, 0.15 mmol, 1 equiv), cyclohexadienones **1a** (40 mg, 0.15 mmol, 1 equiv) and Al(OTf)<sub>3</sub> (7 mg, 0.015 mmol, 10 mol%) in acetonitrile (1.5 mL, 0.1 M) under nitrogen atmosphere. The reaction mixture was stirred at 60 °C for 1 hour. Then, it was cooled to room temperature and the solvent was removed under reduced pressure. The crude <sup>1</sup>H NMR was recorded to determine the ratio of the products **3p** and **3s**.



## 2g. Gram-scale synthesis of 3a & 10a



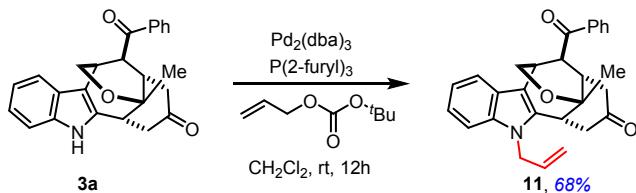
To a solution of compound **1a** (1.0 g, 3.73 mmol) in acetonitrile (12.5 mL, 0.3M) with stirring under argon, was added indole **2a** (0.52 g, 4.47 mmol) and  $\text{Al}(\text{OTf})_3$  (1.8 g, 10 mol%). The resulting suspension was stirred at 60 °C and monitored by TLC until the complete consumption of **1a**. After 1 h, the reaction was cooled down to room temperature prior to be quenched by a saturated aqueous  $\text{NaHCO}_3$  solution (10 mL) and extracted with EtOAc (3 x 20 mL). The combined organic solution was dried over  $\text{Na}_2\text{SO}_4$  and then concentrated under vacuum. The residue was purified by flash column chromatography over silica gel (hexane/EtOAc 60:40) to afford the desired product **3a** in 90% yield (1.34 g) with >98:2 diastereoselectivity.



To a solution of compound **1a** (1.0 g, 3.73 mmol) in acetonitrile (12.5 mL, 0.3M) with stirring under argon, was added indole **8a** (0.59 g, 4.47 mmol) and  $\text{Al}(\text{OTf})_3$  (1.8 g, 10 mol%). The resulting suspension was stirred at 60 °C and monitored by TLC until the complete consumption of **1a**. After 1 h, the reaction was cooled down to room temperature prior to be quenched by a saturated aqueous  $\text{NaHCO}_3$  solution (10 mL) and extracted with  $\text{EtOAc}$  (3 x 20 mL). The combined organic solution was dried over  $\text{Na}_2\text{SO}_4$  and then concentrated under vacuum. The residue was purified by flash column chromatography over silica gel (hexane/ $\text{EtOAc}$  80:20) to afford the desired product **10a** in 94% yield (1.39 g) with >97:3 diastereoselectivity.

## 2h. Subsequent transformations of product 3a

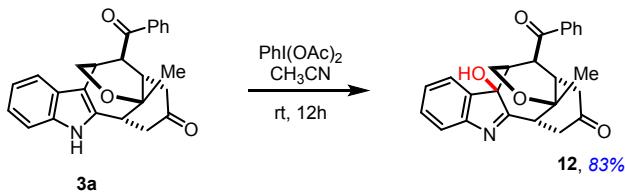
**12-Allyl-13-benzoyl-4a-methyl-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2(3H)-one (11):**



To a stirred solution of  $\text{Pd}_2(\text{dba})_3$  (2.8 mg, 0.0031 mmol, 2 mol%) and  $\text{PPh}_3$  (6.12 mg, 0.023 mmol, 15 mol%) in  $\text{CH}_2\text{Cl}_2$  (2 mL) at room temperature was added allyl *tert*-butyl carbonate (52  $\mu\text{L}$ , 0.311 mmol, 2 equiv). After 10 min, a solution of indole **3a** (60 mg 0.156 mmol, 1 equiv) in  $\text{CH}_2\text{Cl}_2$  (1.5 mL) was added. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (30%  $\text{EtOAc}/\text{hexanes}$ ;  $R_f = 0.4$ ) to afford the *N*-allyl product **11** (45 mg, 68% yield) as a white solid; mp = 216–218°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (dd,  $J = 8.3, 1.2$  Hz, 2H), 7.60 (t,  $J = 7.4$  Hz, 1H), 7.47 (t,  $J = 7.7$  Hz, 2H), 7.34 (d,  $J = 7.8$  Hz, 1H), 7.29 (d,  $J = 8.2$  Hz, 1H), 7.20 (t,  $J = 8.1$  Hz, 1H), 7.11 (t,  $J = 7.9$  Hz, 1H), 5.98 (ddt,  $J = 17.1, 10.4, 4.5$  Hz, 1H), 5.24 (dd,  $J = 10.4, 0.8$  Hz, 1H), 4.96 (dd,  $J = 17.2, 0.8$  Hz, 1H), 4.72 (ddt,  $J = 17.6, 4.0, 1.8$  Hz, 1H), 4.64 – 4.56 (m, 1H), 4.09 (dd,  $J = 9.9, 1.0$  Hz, 1H), 3.76 (d,  $J = 7.9$  Hz, 1H), 3.66 – 3.56 (m, 3H), 3.43 (d,  $J = 2.0$  Hz, 1H), 2.98 – 2.86 (m, 2H), 2.77 (ddd,  $J = 15.5, 2.3, 1.6$  Hz, 1H), 2.07 (dt,  $J = 15.3, 2.1$  Hz, 1H), 1.88 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.7, 198.0, 136.8, 136.2, 135.0, 133.8, 132.9, 129.1, 128.9, 125.4, 121.6, 119.9, 117.4, 117.1, 115.5, 110.2, 72.6, 65.0, 52.2, 46.8, 45.9,

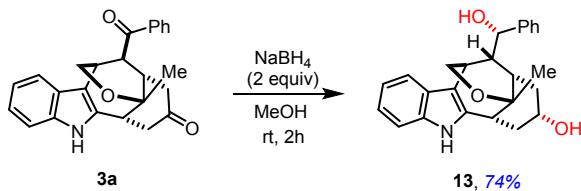
45.1, 44.9, 38.2, 33.4, 29.6; IR (neat):  $\nu_{\text{max}}$  3017, 2883, 1713, 1605, 1516, 1469, 1383, 1217, 1088, 990, 922, 816, 752, 678  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{28}\text{H}_{28}\text{NO}_3$  [ $\text{M}+\text{H}]^+$ : 426.2069; found: 426.2069.

**13-Benzoyl-7a-hydroxy-4a-methyl-4,4a,6,7,7a,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (12):**



To a stirred solution of compound **3a** (60 mg, 0.1 mmol, 1 equiv) in MeCN (2 mL) and  $\text{H}_2\text{O}$  (1.5 mL) was added  $\text{PhI(OAc)}_2$  (52.2 mg, 0.1 mmol, 1 equiv) dissolved in MeCN (1 mL) dropwise at 0 °C under nitrogen atmosphere. After 30 min, TLC analysis indicated the consumption of starting material. The reaction mixture was quenched with saturated aqueous  $\text{NaHCO}_3$  (5 mL) and extracted with  $\text{CH}_2\text{Cl}_2$  (4 x 5 mL). The combined organic layers were washed with brine (5 mL), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated under reduced pressure. Purification by column chromatography on silica gel (40% EtOAc/hexanes;  $R_f = 0.2$ ) to afford imine **12** (52 mg, 83%) as a yellow solid; mp = 208–210°C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.67 (d,  $J = 7.7$  Hz, 1H), 7.52 (td,  $J = 7.6, 1.3$  Hz, 1H), 7.40 (t,  $J = 7.3$  Hz, 1H), 7.30 (t,  $J = 7.4$  Hz, 1H), 7.27 (d,  $J = 5.1$  Hz, 1H), 7.07 (t,  $J = 7.8$  Hz, 2H), 7.01 (dd,  $J = 8.3, 1.1$  Hz, 2H), 4.23 (ddd,  $J = 11.1, 3.3, 1.3$  Hz, 1H), 3.98 (d,  $J = 11.1$  Hz, 1H), 3.58 (dt,  $J = 16.4, 2.1$  Hz, 1H), 3.45 – 3.35 (m, 3H), 2.74 (dd,  $J = 16.4, 5.4$  Hz, 1H), 2.65 (dd,  $J = 17.8, 7.0$  Hz, 1H), 2.52 (d,  $J = 8.8$  Hz, 1H), 2.44 (d,  $J = 3.2$  Hz, 1H), 1.95 (d,  $J = 17.7$  Hz, 1H), 1.81 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  206.7, 197.5, 184.5, 153.3, 139.1, 134.4, 133.6, 130.7, 128.8, 128.4, 127.5, 123.4, 121.8, 87.7, 75.0, 59.7, 48.3, 44.4, 44.3, 42.3, 40.5, 35.2, 27.6; IR (neat):  $\nu_{\text{max}}$  3015, 2863, 1714, 1675, 1550, 1475, 1380, 1227, 1080, 970, 942, 742, 652  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{24}\text{NO}_4$  [ $\text{M}+\text{H}]^+$ : 402.1705; found: 402.1725.

**13-(Hydroxy(phenyl)methyl)-4a-methyl-2,3,4,4a,6,7,12,12b-octahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2-ol (13):**

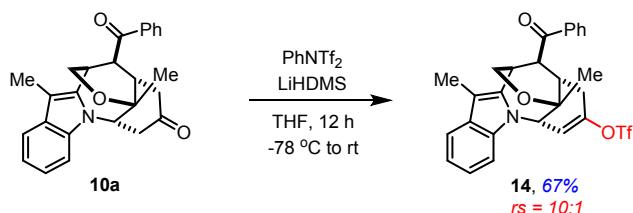


To a stirred solution of compound **3a** (60.0 mg, 0.155 mmol, 1 equiv) in MeOH (3 mL) was added  $\text{NaBH}_4$  (17.76 mg, 0.467 mmol, 3 equiv) in small portions at 0°C. After completion of the reaction (monitored by TLC), acetone (1 mL) was added to the reaction mixture. Half of the solvent was evaporated and then the mixture is diluted in water (4 mL) and EtOAc (10 mL), extracted with EtOAc (3 x 10 mL). The solvent was removed under reduced pressure and purified by silica gel column chromatography using hexanes/EtOAc (50:50) to afford diol **13** with exclusive diastereoselectivity in 74% yield (45 mg) as a

white solid; mp = 254–256°C;  $^1\text{H}$  NMR (400 MHz, DMSO)  $\delta$  10.54 (s, 1H), 7.39 (d,  $J$  = 7.2 Hz, 2H), 7.29 (t,  $J$  = 7.4 Hz, 2H), 7.21 (t,  $J$  = 7.2 Hz, 1H), 7.17 (d,  $J$  = 7.9 Hz, 1H), 7.05 (d,  $J$  = 7.7 Hz, 1H), 6.92 – 6.86 (m, 1H), 6.84 – 6.79 (m, 1H), 5.30 (d,  $J$  = 4.5 Hz, 1H), 4.51 (dd,  $J$  = 6.9, 4.7 Hz, 1H), 4.41 (d,  $J$  = 8.7 Hz, 1H), 3.66 (br.s, 1H), 3.54 (d,  $J$  = 3.5 Hz, 1H), 3.51 (d,  $J$  = 8.5 Hz, 1H), 3.37 (br.s, 1H), 3.01 (d,  $J$  = 5.3 Hz, 1H), 2.93 (t,  $J$  = 7.4 Hz, 1H), 2.26 (d,  $J$  = 14.1 Hz, 1H), 1.98 – 1.86 (m, 2H), 1.41 (dt,  $J$  = 14.4, 4.3 Hz, 1H), 1.31 (s, 3H), 1.08 (d,  $J$  = 14.5 Hz, 1H);  $^{13}\text{C}$  NMR (101 MHz, DMSO)  $\delta$  145.1, 138.8, 135.3, 127.6, 127.1, 126.5, 126.2, 119.0, 117.4, 116.4, 114.2, 110.2, 74.5, 73.6, 65.7, 63.7, 47.3, 43.5, 38.2, 36.7, 33.0, 29.2, 28.5; IR (neat):  $\nu_{\text{max}}$  3640, 3570, 3360, 2935, 2877, 1715, 1673, 1590, 1460, 1328, 1213, 1103, 1001, 750, 691 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>25</sub>H<sub>28</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 390.2069; found: 390.2069.

## 2i. Subsequent transformations of product **10a**

### **14-Benzoyl-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2-yl trifluoromethanesulfonate (14):**



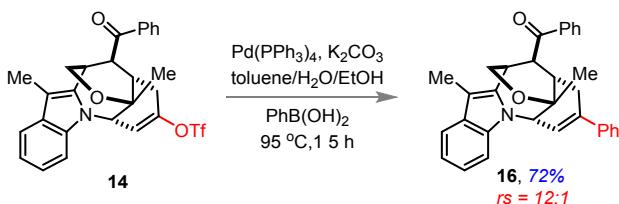
To a cold solution (-78 °C) of compound **10a** (400 mg, 1 mmol, 1 equiv) and *N*-phenyl-bis(trifluoromethanesulfonamide) (394 mg, 1.1 mmol, 1.1 equiv) in THF (5.0 mL, 0.2M) was slowly added lithium bis(trimethylsilyl)amide (0.9 mL, 1.3 M solution in THF) over 10 minutes under argon. Then slowly warming up the solution to room temperature and stirring overnight, the reaction was quenched with an aqueous saturated NaHCO<sub>3</sub> solution (10 mL). The mixture was then extracted with EtOAc. The combined organic solvent was washed by brine (10 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and filtered. The solvent was removed under reduced pressure and purified by silica gel column chromatography using hexanes/EtOAc (95:5) to afford compound **15** in 67% yield (355 mg) with 10:1 ratio of regioselectivity as a colorless liquid;  $^1\text{H}$  NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.98 (d,  $J$  = 8.3 Hz, 2H), 7.69 – 7.60 (m, 2H), 7.52 (t,  $J$  = 7.8 Hz, 2H), 7.40 – 7.21 (m, 3H), 6.27 (dd,  $J$  = 5.2, 2.3 Hz, 1H), 5.02 (d,  $J$  = 5.1 Hz, 1H), 4.10 (d,  $J$  = 10.2 Hz, 1H), 3.80 (d,  $J$  = 9.5 Hz, 1H), 3.69 (d,  $J$  = 9.8 Hz, 1H), 3.52 – 3.43 (m, 2H), 3.01 – 2.91 (m, 1H), 2.21 (s, 3H), 2.09 (d,  $J$  = 18.2 Hz, 1H), 1.67 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  197.8, 149.2, 137.3, 135.8, 134.6, 134.1, 129.7, 129.2, 128.9, 127.5, 123.7, 122.3, 119.7, 119.4, 118.5, 118.4 (q,  $J$  = 320.2 Hz, CF<sub>3</sub>), 108.6, 105.3, 71.6, 64.3, 59.0, 48.6, 35.1, 34.7, 32.8, 27.2, 8.4; IR (neat):  $\nu_{\text{max}}$  3060, 2929, 2864, 1680, 1596, 1421, 1377, 1212, 1142, 1086, 1030, 860, 754, 694 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>27</sub>H<sub>25</sub>NO<sub>5</sub>SF<sub>3</sub> [M+H]<sup>+</sup>: 432.1406; found: 432.1402.

### **4a,8-Dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-14-yl(phenyl)methanone (15):**



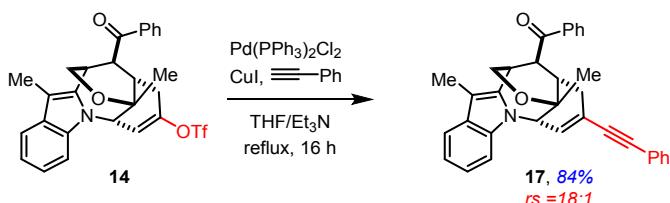
A dry vial was charged with  $\text{Pd}(\text{OAc})_2$  (1.3 mg, 0.005 mmol, 0.05 equiv), and  $\text{PPh}_3$  (3 mg, 4.47 mmol, 0.1 equiv) under nitrogen atmosphere. A solution of enol triflate (60 mg, 0.11 mmol, 1 equiv), dissolved in anhydrous DMF (2 mL) was added through a syringe to the vial. The resulting reaction mixture was added with  $\text{Et}_3\text{N}$  (47.0  $\mu\text{L}$ , 0.34 mmol, 3 equiv), followed by formic acid (8.6  $\mu\text{L}$ , 0.22 mmol, 2 equiv) and was heated at  $60^\circ\text{C}$  for 30 min. The mixture was turned to black and then cool to room temperature, diluted with water, followed by washing with cold ether (3 x 5 mL). The combined organic layer were dried over  $\text{Na}_2\text{SO}_4$ . The solvent was removed under reduced pressure and purified by silica gel column chromatography using hexanes/EtOAc (95:5) to afford compound **15** in 94% yield (41 mg) with 10:1 ratio of regioselectivity as a colorless liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (d,  $J = 7.5$  Hz, 2H), 7.63 – 7.57 (m, 2H), 7.48 (t,  $J = 7.7$  Hz, 2H), 7.39 (d,  $J = 8.1$  Hz, 1H), 7.25 (t,  $J = 7.6$  Hz, 1H), 7.16 (t,  $J = 7.4$  Hz, 1H), 6.26 – 6.18 (m, 1H), 5.68 (dd,  $J = 9.9, 5.0$  Hz, 1H), 4.77 (d,  $J = 4.2$  Hz, 1H), 4.15 (d,  $J = 10.1$  Hz, 1H), 3.75 (d,  $J = 9.5$  Hz, 1H), 3.68 (dd,  $J = 10.1, 2.5$  Hz, 1H), 3.44 (s, 1H), 3.27 (dd,  $J = 9.3, 5.4$  Hz, 1H), 2.56 (ddd,  $J = 18.7, 5.1, 2.5$  Hz, 1H), 2.20 (s, 3H), 1.87 (dd,  $J = 18.7, 5.3$  Hz, 1H), 1.59 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.8, 137.9, 136.1, 135.1, 133.7, 129.0, 128.9, 128.5, 127.4, 126.3, 121.6, 119.1, 119.0, 109.1, 104.2, 72.5, 64.3, 59.3, 48.6, 35.4, 33.7, 30.4, 27.5, 8.5; IR (neat):  $\nu_{\text{max}}$  3034, 2927, 2864, 1681, 1589, 1059, 1332, 1277, 1218, 1130, 1001, 908, 727, 655  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{26}\text{NO}_2$  [ $\text{M}+\text{H}]^+$ : 384.1964; found: 384.1967.

**4a,8-Dimethyl-2-phenyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-14-yl)(phenyl)methanone (16):**



To a stirred solution of triflate **14** (60.0 mg, 0.11 mmol, 1.0 equiv), phenyl boronic acid (21 mg, 0.16 mmol, 1.5 equiv),  $\text{K}_2\text{CO}_3$  (62 mg, 0.45 mmol, 4 equiv), in toluene / water / ethanol ( $\sim$ 2 mL, 5:2:1, 0.06 M) was added  $\text{Pd}(\text{PPh}_3)_4$  (10 mol%) at room temperature under inert atmosphere. The reaction mixture was heated to 95°C for 15 h. Then reaction was cooled to room temperature, diluted with saturated aqueous  $\text{NH}_4\text{Cl}$  (5 mL) and extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 5 mL). The combined organic solvent was dried over  $\text{Na}_2\text{SO}_4$ . The solution was concentrated under reduced pressure. Purification by column chromatography (hexanes/EtOAc 95:5), afforded the corresponding product **16** in 72% yield (37 mg) with 12:1 ratio of regioselectivity as a colorless liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (d,  $J$  = 8.3 Hz, 2H), 7.64 – 7.56 (m, 2H), 7.51 – 7.43 (m, 3H), 7.33 – 7.15 (m, 7H), 6.60 (dd,  $J$  = 4.1, 2.1 Hz, 1H), 4.98 (d,  $J$  = 4.1 Hz, 1H), 4.19 (d,  $J$  = 10.2 Hz, 1H), 3.80 (d,  $J$  = 9.4 Hz, 1H), 3.71 (d,  $J$  = 10.1 Hz, 1H), 3.52 – 3.43 (m, 2H), 3.04 – 2.92 (m, 1H), 2.30 (d,  $J$  = 18.1 Hz, 1H), 2.22 (s, 3H), 1.66 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.7, 140.2, 137.8, 136.2, 135.9, 135.0, 135.0, 133.8, 129.0, 128.9, 128.6, 128.5, 128.1, 125.5, 123.3, 121.8, 119.2, 119.1, 109.1, 104.3, 72.2, 64.4, 59.7, 48.6, 35.4, 34.1, 32.5, 27.6, 8.5; IR (neat):  $\nu_{\text{max}}$  3051, 2927, 2867, 1680, 1551, 1458, 1368, 1319, 1268, 1214, 1109, 1002, 910, 872, 729, 648  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{32}\text{H}_{30}\text{NO}_2$  [ $\text{M}+\text{H}]^+$ : 460.2277; found: 460.2273.

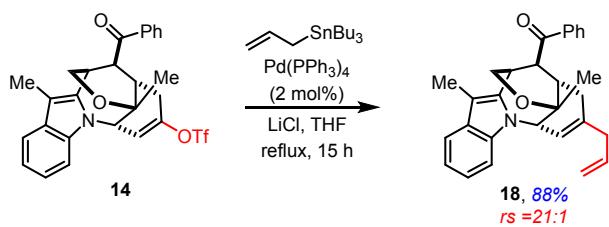
**4a,8-Dimethyl-2-(phenylethyynyl)-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-14-yl)(phenyl)methanone (17):**



$\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$  (4 mg, 0.006 mmol, 0.05 equiv) and copper (I) iodide (2.1 mg, 0.013 mmol, 0.1 equiv) were dissolved in a 1:1 ratio of THF:TEA (2 mL) at room temperature and the solution was degassed with  $\text{N}_2$  for 10 minutes. Later, degassed solution of vinyl triflate (60.0 mg, 0.113 mmol, 1.0 eq) in THF (1 mL) followed by phenylacetylene (14 $\mu$ L, 0.124 mmol 1.1 equiv) were added to the reaction mixture via syringe. The initial green solution changed from yellow to orange to red. The solution was refluxed for 16 hours under inert atmosphere. After completion of the reaction, solvent was removed under reduced pressure. The crude reaction was purification by column chromatography (hexanes/EtOAc, 95:5),

afforded the corresponding product **17** in 84% yield (46 mg) with 18:1 ratio of regioselectivity as a colorless liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.02 – 7.95 (m, 2H), 7.64 – 7.56 (m, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.28 – 7.21 (m, 4H), 7.19 – 7.15 (m, 1H), 6.59 (dd, *J* = 5.0, 2.3 Hz, 1H), 4.88 (d, *J* = 4.9 Hz, 1H), 4.13 (dd, *J* = 10.2, 1.3 Hz, 1H), 3.75 (d, *J* = 9.5 Hz, 1H), 3.68 (ddd, *J* = 10.1, 2.6, 0.9 Hz, 1H), 3.45 (s, 1H), 3.33 (dd, *J* = 9.4, 5.1 Hz, 1H), 2.83 – 2.74 (m, 1H), 2.19 (s, 3H), 2.07 (dd, *J* = 18.3, 1.1 Hz, 1H), 1.62 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 198.4, 137.6, 136.0, 134.9, 133.9, 132.5, 131.6, 129.1, 129.0, 128.6, 128.6, 128.4, 122.7, 121.9, 120.5, 119.4, 119.1, 109.1, 104.6, 90.2, 89.2, 71.8, 64.3, 59.3, 48.4, 35.3, 34.6, 33.9, 27.6, 8.5; IR (neat):  $\nu_{\text{max}}$  3051, 2926, 2864, 1680, 1591, 1456, 1281, 1212, 1096, 1023, 911, 875, 728, 696 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>34</sub>H<sub>30</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 484.2277; found: 484.2256.

**2-Allyl-4a,8-dimethyl-3,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-14-yl)(phenyl)methanone (18):**



The vinyl triflate **14** (60.0 mg, 0.113 mmol, 1.0 equiv) was dissolved in THF (2 mL) and the solution degassed with N<sub>2</sub> for 10 minutes. Later, Pd(PPh<sub>3</sub>)<sub>4</sub> (3 mg, 0.002 mmol, 0.02 equiv), LiCl (31 mg, 0.677 mmol, 6 equiv) and allyltributylstannane (38 μL, 0.124 mmol, 1.1 equiv) were added successively and the reaction mixture was refluxed for 15 hours under inert atmosphere. After completion of the reaction, solvent was removed under reduced pressure. The crude reaction was purification by column chromatography (hexanes/EtOAc, 95:5), afforded the corresponding product **18** in 88% yield (43 mg) with 21:1 ratio of regioselectivity (structure confirmed with <sup>1</sup>H NMR coupling constants) as a colorless liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.64 – 7.57 (m, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.26 (d, *J* = 15.2 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 5.98 (d, *J* = 3.2 Hz, 1H), 5.61 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 4.95 (dd, *J* = 13.8, 5.3 Hz, 2H), 4.78 (d, *J* = 4.5 Hz, 1H), 4.13 (d, *J* = 10.2 Hz, 1H), 3.67 (dd, *J* = 9.4, 3.7 Hz, 2H), 3.42 (s, 1H), 3.26 (dd, *J* = 9.1, 5.2 Hz, 1H), 2.68 – 2.56 (m, 2H), 2.51 (dd, *J* = 18.3, 4.9 Hz, 1H), 2.19 (s, 3H), 1.74 (d, *J* = 18.3 Hz, 1H), 1.57 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 198.9, 137.8, 136.3, 136.0, 135.1, 135.0, 133.8, 129.0, 128.8, 128.5, 122.1, 121.6, 119.1, 119.0, 117.3, 109.2, 104.1, 72.3, 64.3, 59.6, 48.6, 41.9, 35.3, 34.0, 33.3, 27.5, 8.5; IR (neat):  $\nu_{\text{max}}$  3062, 2929, 1681, 1594, 1461, 1375, 1329, 1283, 1214, 1145, 1097, 1006, 914, 866, 651 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>29</sub>H<sub>30</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 424.2277; found: 424.2281.

## 2j. Asymmetric Friedel–Crafts alkylation

### I. Asymmetric Friedel–Crafts alkylation on Cyclohexadienone **1a** at room temperature

A 25 mL round-bottom flask was charged with Lewis acid (10 mol%), and Ligand (15 mol%) in acetonitrile (1.5 mL, 0.05 M) and stirred at room temperature for 15 minutes under nitrogen atmosphere. Later, cyclohexadienones **1a** (20 mg, 0.075 mmol, 1 equiv), indole **2a** (11 mg, 0.09, 1.2 equiv) were added to the reaction mixture and stirred for another 1 hour. Then, it was cooled to room temperature and the solvent was removed under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (30% EtOAc in hexanes) to afford the bicyclic product **4a**.

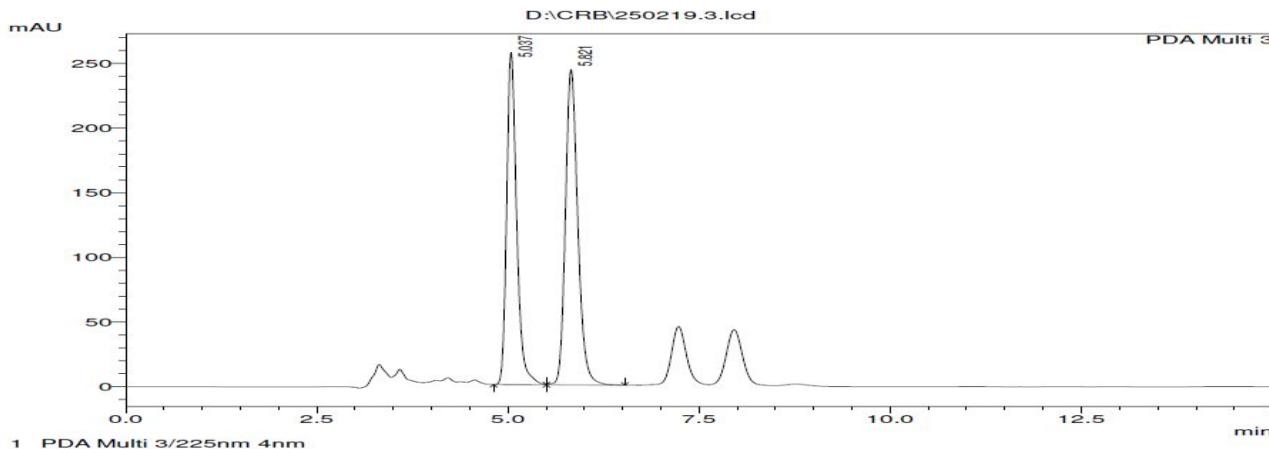
**Table S1:** Asymmetric Friedel–Crafts alkylation at room temperature<sup>a</sup>

entry	Lewis acid	ligand	<b>4a</b> , yield [%] <sup>b</sup>	er
1	Sc(OTf) <sub>3</sub>	<b>L1</b>	62	51:49
2	Zn(OTf) <sub>2</sub>	<b>L1</b>	15	41:59
3	Ti(O <i>i</i> Pr) <sub>4</sub>	<b>L1</b>	21	45:55
4	Cu(OTf) <sub>2</sub>	<b>L1</b>	23	47:53
5	In(OTf) <sub>3</sub>	<b>L1</b>	59	49:51
6	Al(OTf) <sub>3</sub>	<b>L1</b>	78	47:53
7	Ti(O <i>i</i> Pr) <sub>4</sub>	<b>L2</b>	62	47:53
8	Zr(O <i>i</i> Pr) <sub>4</sub>	<b>L2</b>	<5	-
9	Sc(OTf) <sub>3</sub>	<b>L3</b>	67	47:53
10	Sc(OTf) <sub>3</sub>	<b>L3</b>	52	47:53
11	Cu(OTf) <sub>2</sub>	<b>L4</b>	68	49:51
12	Cu(OTf) <sub>2</sub>	<b>L3</b>	72	47:53
13	(S,S)- <b>L5</b>	-	48	55:45

<sup>a</sup>Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol), Lewis acid (10 mol %) and Ligand (15 mol%) in CH<sub>3</sub>CN (0.8 mL) for 1 h. <sup>b</sup>Isolated yields

**HPLC analysis details of compound *rac*-4a:**

Daicel Chiralpak IC 250X4.6 mm 5u column; hexane/2-propanol = 60/40, detected at 225 nm, Flow rate = 1 mL/min, Retention times: 5.03 min and 5.82 min.



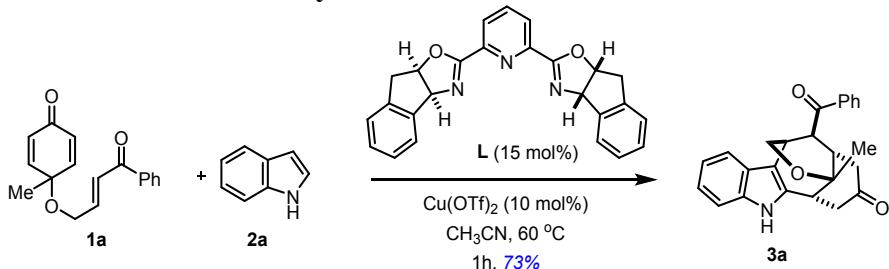
PDA Ch3 225nm 4nm

PeakTable

PDA Ch3 225nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.037	2357301	256996	46.216	51.290
2	5.821	2743321	244070	53.784	48.710
Total		5100622	501065	100.000	100.000

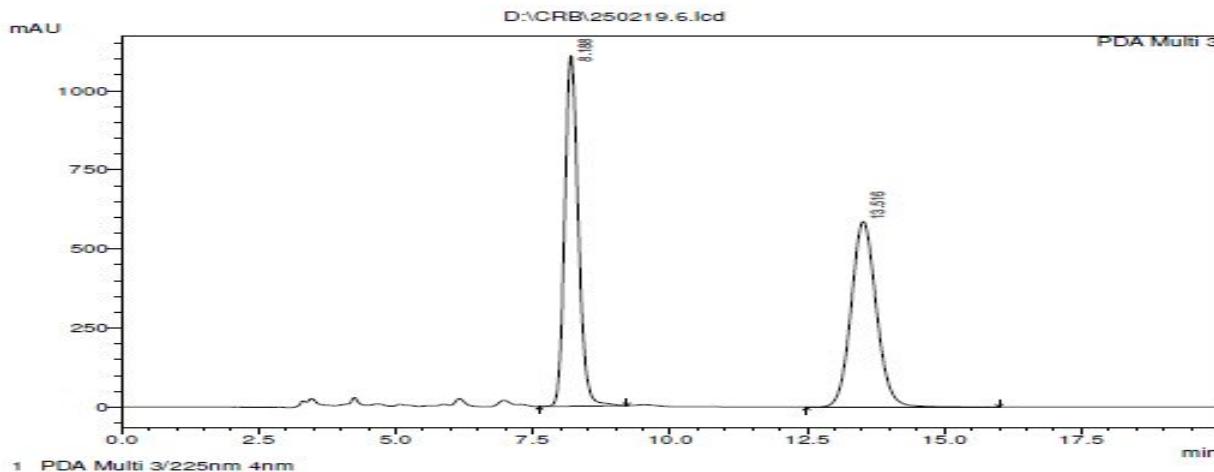
## II. Asymmetric C-2/C-3 annulation of cyclohexadienone **1a** with indole **2a**



A dried screw-cap vial was charged with Cu(OTf)<sub>2</sub> (2.7 mg, 10 mol%), and Ligand **L** (4.4 mg, 15 mol%) in acetonitrile (1.5 mL, 0.05 M) and stirred at room temperature for 15 minutes under nitrogen atmosphere. Later, cyclohexadienones **1a** (20 mg, 0.075 mmol, 1 equiv), indole **2a** (11 mg, 0.09, 1.2 equiv) were added to the reaction mixture and stirred for another 1 hour at 60 °C. Then, it was cooled to room temperature and the solvent was removed under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (40% EtOAc in hexanes) to afford the polycyclic indole **3a** in 73% yield (21 mg) as white solid with ~1:1 ratio of enantiomeric excess.

### HPLC analysis details of compound *rac*-3a:

Daicel Chiralpak IC 250X4.6 mm 5 $\mu$  column; hexane/2-propanol = 60/40, detected at 225 nm, Flow rate = 1 mL/min, Retention times: 3.18 min and 13.51min.



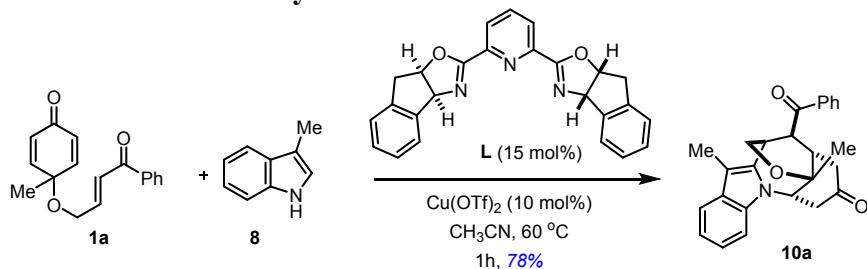
PDA Ch3 225nm 4nm

PeakTable

PDA Ch3 225nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.188	19150177	1108232	50.486	65.393
2	13.516	18781563	586489	49.514	34.607
Total		37931740	1694721	100.000	100.000

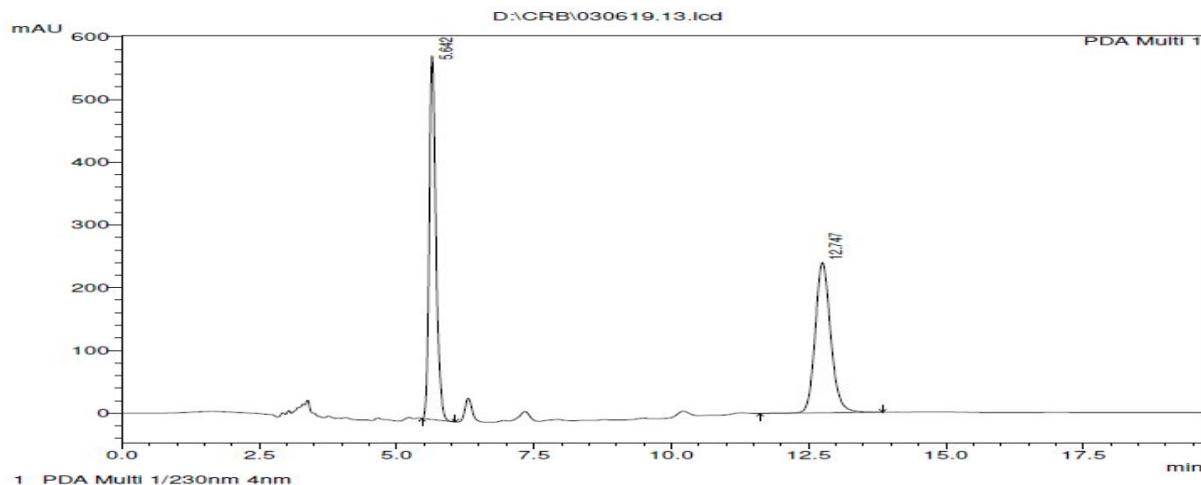
### III. Asymmetric C-2/N annulation of cyclohexadienone **1a** with indole **8**



A dried screw-cap vial was charged with Cu(OTf)<sub>2</sub> (2.7 mg, 10 mol%), and Ligand **L** (4.4 mg, 15 mol%) in acetonitrile (1.5 mL, 0.05 M) and stirred at room temperature for 15 minutes under nitrogen atmosphere. Later, cyclohexadienones **1a** (20 mg, 0.075 mmol, 1 equiv), indole **8** (12 mg, 0.09 mmol, 1.2 equiv) were added to the reaction mixture and stirred for another 1 hour at 60 °C. Then, it was cooled to room temperature and the solvent was removed under reduced pressure. The residue was directly subjected to flash column chromatography on silica gel (EtOAc in hexanes) to afford the polycyclic indole **10a** in 78% yield (23 mg) as white solid with ~1:1 ratio of enantiomeric excess.

**HPLC analysis details of compound *rac*-9a:**

Daicel Chiralpak IA 250X4.6 mm 5 $\mu$  column; hexane/2-propanol = 70/30, detected at 230 nm, Flow rate = 1 mL/min, Retention times: 5.64 min and 12.74 min.



PeakTable

PDA Ch1 230nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.642	4895012	579902	50.994	70.764
2	12.747	4704241	239588	49.006	29.236
Total		9599253	819490	100.000	100.000

### 3. X-ray crystallographic data

#### 3a. Crystallographic data for compound 3m:

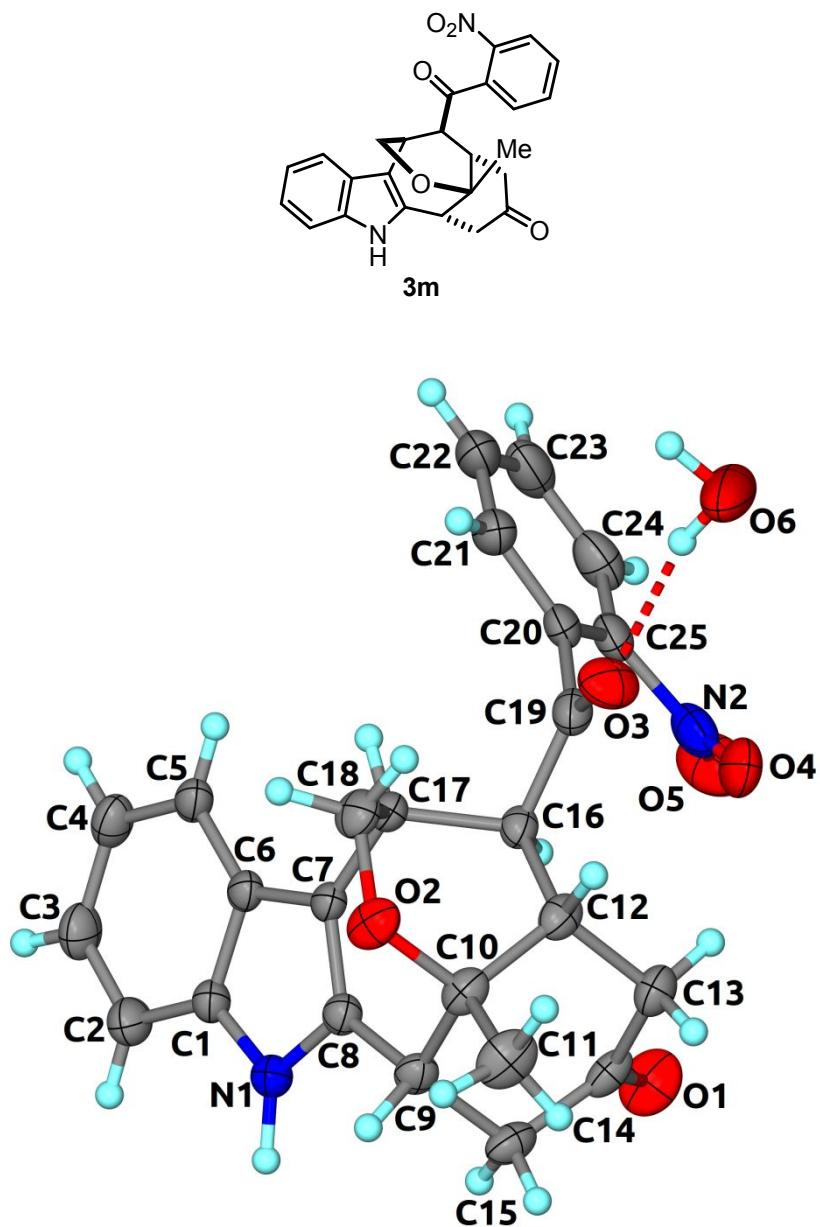


Figure caption: ORTEP diagram of compound **3m** with the atom-numbering. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius. The molecule crystallizes with half a molecule of water (hemihydrate). The asymmetric unit contains water occupying the special position (on two fold axis) with 0.5 site occupancy factor, and the other half is generated by symmetry operation for clarity purpose. CCDC 1921715 contains the supplementary crystallographic data for this paper which can be obtained free of charge at <https://summary.ccdc.cam.ac.uk/structure-summary-form>

**Table S2. Crystal Data Collection and Refinement Parameters for Compound 3m.**

	<b>Compound 3m</b>
<b>chemical formula</b>	2(C <sub>25</sub> H <sub>22</sub> N <sub>2</sub> O <sub>5</sub> ),H <sub>2</sub> O
<b>Fw; F(000)</b>	878.91; 1848
<b>T (K)</b>	293(2)
<b>wavelength (Å)</b>	0.71073
<b>Crystal system</b>	Tetragonal
<b>space group</b>	P42/n
<b>a (Å)</b>	20.036(8)
<b>b (Å)</b>	20.036(8)
<b>c (Å)</b>	10.846(5)
<b>α (deg)</b>	90
<b>β (deg)</b>	90
<b>γ (deg)</b>	90
<b>Z</b>	4
<b>V (Å<sup>3</sup>)</b>	4354(4)
<b>ρ<sub>calcd</sub> (g·cm<sup>-3</sup>)</b>	1.341
<b>μ (mm<sup>-1</sup>)</b>	0.096
<b>θ range (deg); completeness</b>	2.135 – 24.998; 0.999
<b>collected reflections; R<sub>σ</sub></b>	42317; 0.0426
<b>unique reflections; R<sub>int</sub></b>	42317; 0.0946
<b>R1<sup>a</sup>; wR2<sup>b</sup> [I &gt; 2σ(I)]</b>	0.0533; 0.1511
<b>R1; wR2 [all data]</b>	0.0983; 0.1822
<b>GOF</b>	1.141
<b>largest diff peak and hole</b>	0.242 and -0.370

<sup>a</sup> R<sub>1</sub>=Σ(||F<sub>o</sub>|-|F<sub>c</sub>||)/Σ|F<sub>o</sub>|<sup>b</sup> wR<sub>2</sub>={Σ[w(F<sub>o</sub><sup>2</sup>-F<sub>c</sub><sup>2</sup>)<sup>2</sup>]/Σ[w(F<sub>o</sub><sup>2</sup>)<sup>2</sup>]}<sup>1/2</sup>

**3b. Crystallographic data for compound **10e**:**

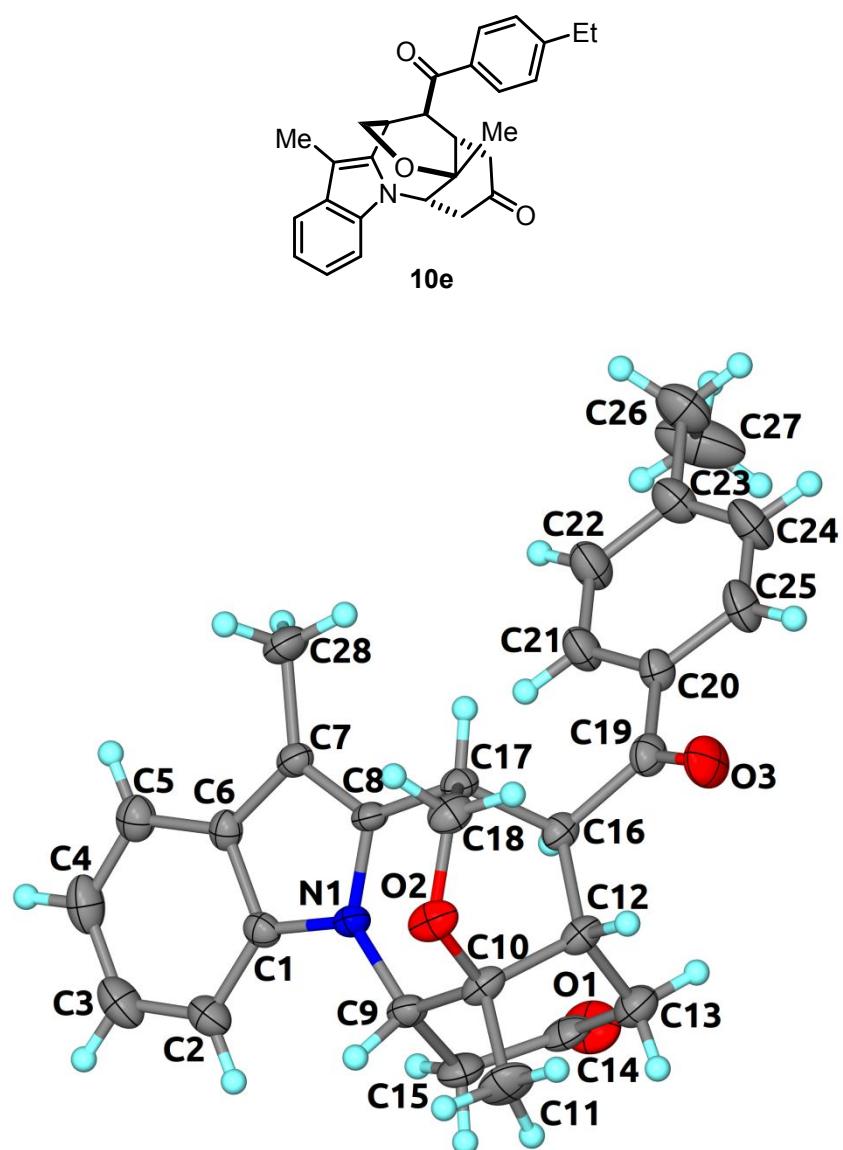


Figure caption: ORTEP diagram of compound **10e** with the atom-numbering. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius. CCDC 1921716 contains the supplementary crystallographic data for this paper which can be obtained free of charge at <https://summary.ccdc.cam.ac.uk/structure-summary-form>.

**Table S3. Crystal Data Collection and Refinement Parameters for Compound 10e.**

	<b>Compound 10e</b>
<b>chemical formula</b>	C <sub>28</sub> H <sub>29</sub> NO <sub>3</sub>
<b>Fw; F(000)</b>	427.52; 1824
<b>T (K)</b>	293(2)
<b>wavelength (Å)</b>	0.71073
<b>Crystal system</b>	Orthorhombic
<b>space group</b>	Pbca
<b>a (Å)</b>	19.6581(13)
<b>b (Å)</b>	8.4966(4)
<b>c (Å)</b>	27.1209(15)
<b>α (deg)</b>	90
<b>β (deg)</b>	90
<b>γ (deg)</b>	90
<b>Z</b>	8
<b>V (Å<sup>3</sup>)</b>	4529.9(4)
<b>ρ<sub>calcd</sub> (g·cm<sup>-3</sup>)</b>	1.254
<b>μ (mm<sup>-1</sup>)</b>	0.081
<b>θ range (deg); completeness</b>	2.559 – 25.000; 0.999
<b>collected reflections; R<sub>σ</sub></b>	38580; 0.0923
<b>unique reflections; R<sub>int</sub></b>	38580; 0.1632
<b>R1<sup>a</sup>; wR2<sup>b</sup> [I &gt; 2σ(I)]</b>	0.0660; 0.1493
<b>R1; wR2 [all data]</b>	0.1703; 0.1989
<b>GOF</b>	1.001
<b>largest diff peak and hole</b>	0.222 and -0.166

<sup>a</sup> R<sub>1</sub>=Σ(||F<sub>o</sub>|-|F<sub>c</sub>||)/Σ|F<sub>o</sub>|<sup>b</sup> wR<sub>2</sub>={Σ[w(F<sub>o</sub><sup>2</sup>-F<sub>c</sub><sup>2</sup>)<sup>2</sup>]/Σ[w(F<sub>o</sub><sup>2</sup>)<sup>2</sup>]}\<sup>1/2</sup>

**Data collection and Structure solution details:** Single crystal X-ray data for compounds **3m** and **10e** were collected at room temperature on a Bruker D8 QUEST equipped with a four-circle kappa diffractometer and Photon 100 detector. An I $\mu$ s microfocus Mo source ( $\lambda=0.71073\text{\AA}$ ) supplied the multi-mirror monochromated incident beam. A combination of Phi and Omega scans were used to collect the necessary data and unit cell dimensions were determined using 9515 reflections for compound **3m** and 4519 reflections for compound **10e** data. Integration and scaling of intensity data were accomplished using SAINT program.<sup>1</sup> The structures were solved by Direct Methods using SHELXS97<sup>2</sup> and refinement was carried out by full-matrix least-squares technique using SHELXL-2014/7.<sup>2-3</sup> Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97  $\text{\AA}$ , and with  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$  or  $1.5U_{\text{eq}}$  for methyl atoms. The N bound H atoms were located from the difference Fourier map. Structures with CCDC Deposition Numbers 1921714-1921716 contain the supplementary crystallographic data for this paper which can be obtained free of charge at <https://summary.ccdc.cam.ac.uk/structure-summary-form>.

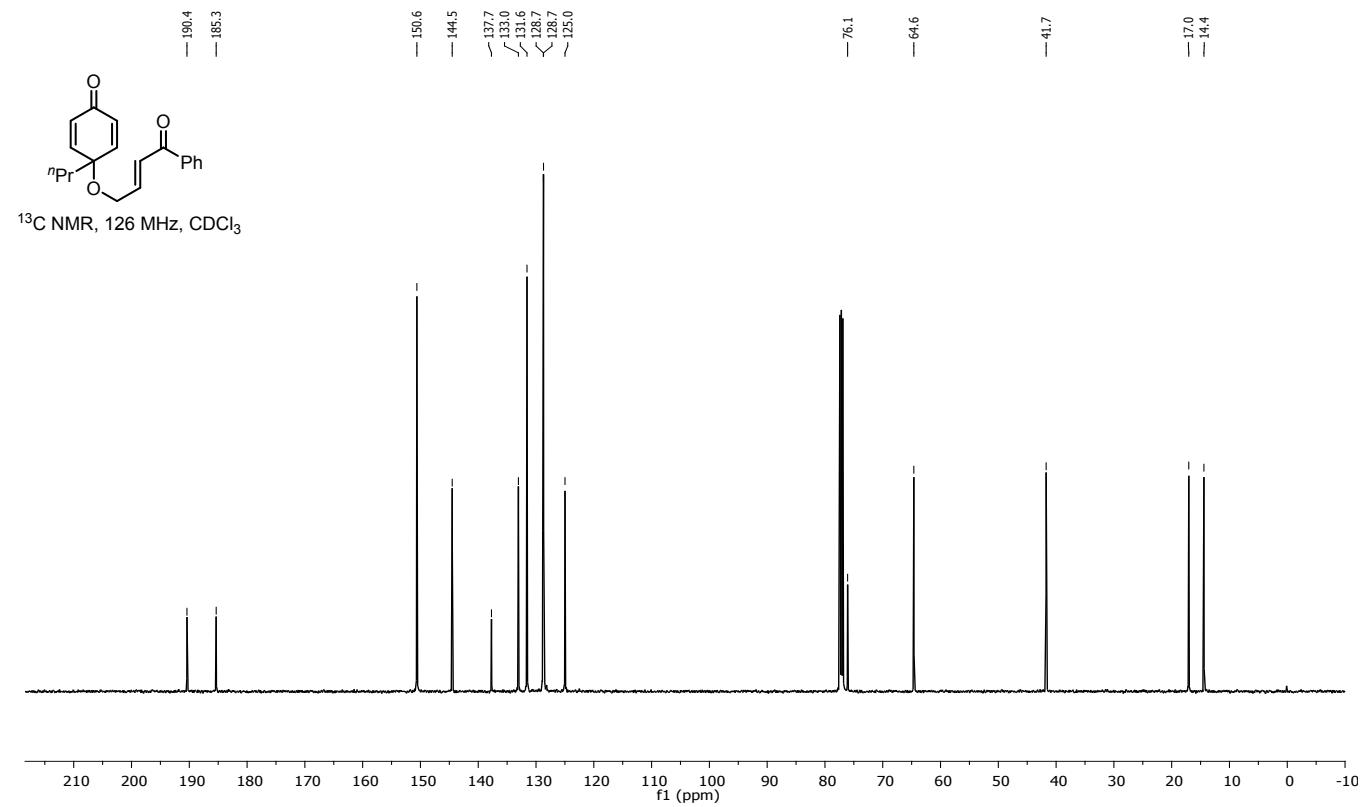
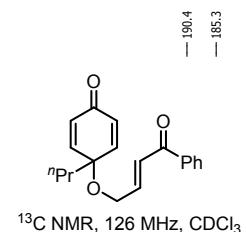
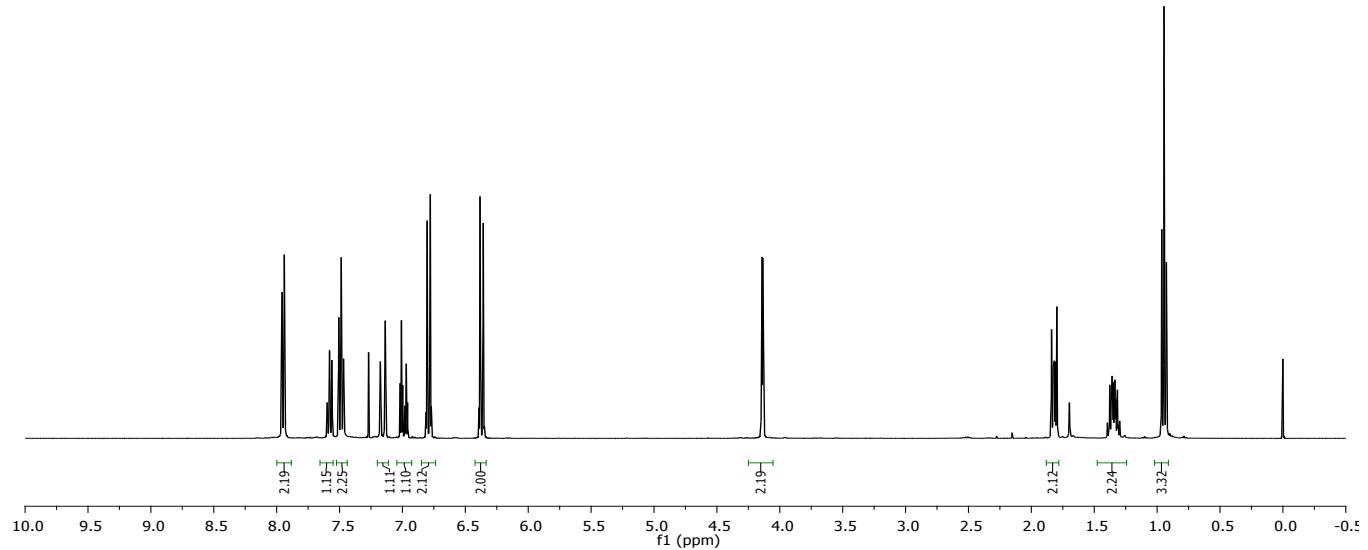
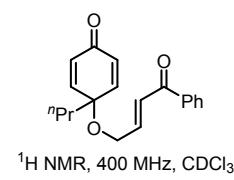
1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. SHELXS97 and SHELXL Version 2014/7, <http://shelx.uni-ac.gwdg.de/SHELX/index.php>
3. Muller, P.; Herbst-Imer, R.; Spek, A. L.; Schneider, T. R.; Sawaya, M. R. Crystal Structure Refinement: A Crystallographer's Guide to SHELXL. Muller, P. Ed. 2006 Oxford University Press: Oxford, New York, pp. 57–91.

## 4. References

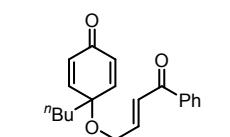
- [1] Wei, H.; Li, Y.; Xiao, K.; Cheng, B.; Wang, H.; Hu, L.; Zhai, H. Synthesis of Polysubstituted Pyridines via a One-Pot Metal-Free Strategy. *Org. Lett.* **2015**, *17*, 5974–5977.
- [2] Wu, W.; Li, X.; Huang, H.; Yuan, X.; Lu, J.; Zhu, K.; Ye, J. Asymmetric Intramolecular Oxa-Michael Reactions of Cyclohexadienones Catalyzed by a Primary Amine Salt. *Angew. Chem. Int. Ed.* **2013**, *52*, 1743–1747.
- [3] Liu, Q.; Rovis, T. Asymmetric Synthesis of Hydrobenzofuranones via Desymmetrization of Cyclohexadienones Using the Intramolecular Stetter Reaction. *J. Am. Chem. Soc.* **2006**, *128*, 2552–2553.
- [4] a) Li, K.; Jin, Z.; Chan, W.-L.; Lu, Y. Enantioselective Construction of Bicyclic Pyran and Hydrindane Scaffolds via Intramolecular Rauhut–Currier Reactions Catalyzed by Thiourea-Phosphines. *ACS Catal.* **2018**, *8*, 8810–8815; b) Jadhav, S.B.; Thopate, S.B.; Nanubolu, J. B.; Chegondi, R. Rh-Catalyzed diastereoselective desymmetrization of enone tethered-cyclohexadienones via tandem arylative cyclization. *Org. Biomol. Chem.* **2019**, *17*, 1937–1946; c) Huddleston, R. R.; Krische, M. J. Enolate Generation under Hydrogenation Conditions: Catalytic Aldol Cycloreduction of Keto-Enones. *Org. Lett.* **2003**, *5*, 1143–1146; d) Burns, A. R.; Solana González, J.; Lam, H. W. Enantioselective Copper(I) - Catalyzed Borylative Aldol Cyclizations of Enone Diones. *Angew. Chem. Int. Ed.* **2012**, *51*, 10827-10831.

## V. $^1\text{H}$ & $^{13}\text{C}$ NMR Spectra

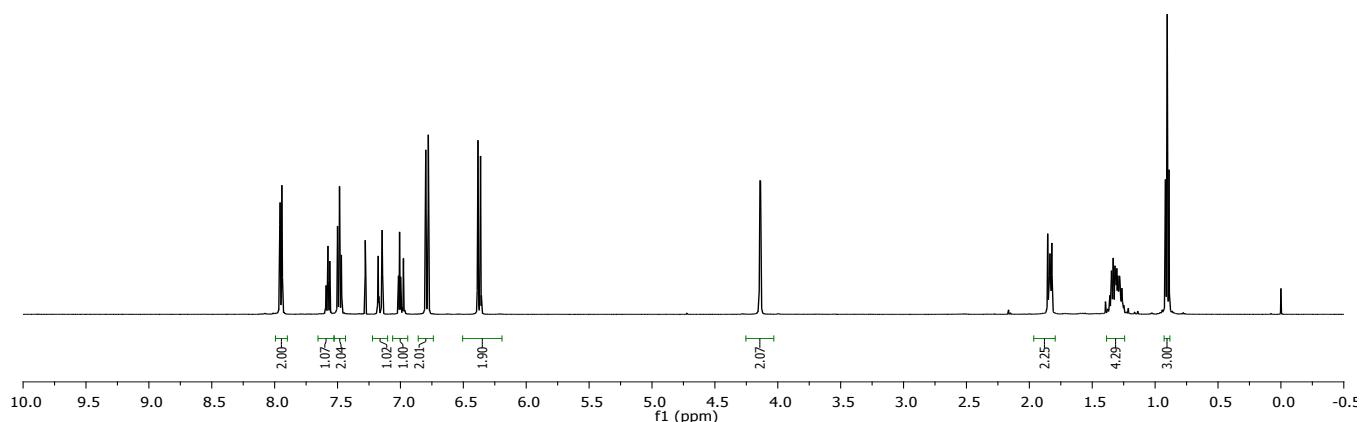
(E)-4-((4-Oxo-4-phenylbut-2-en-1-yl)oxy)-4-propylcyclohexa-2,5-dien-1-one (1c):



**(E)-4-Butyl-4-((4-oxo-4-phenylbut-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-one (1d):**



$^1\text{H}$  NMR, 500 MHz,  $\text{CDCl}_3$

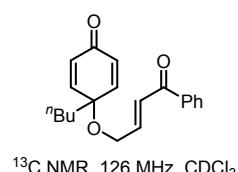


—190.3  
—185.3

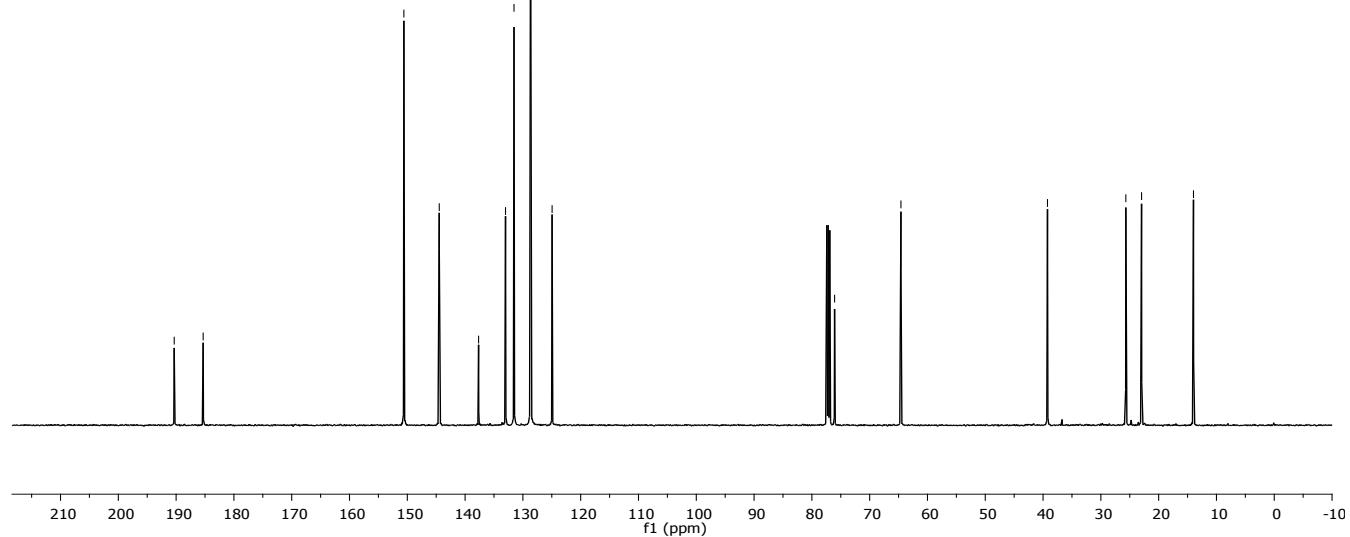
—150.6  
—144.5  
—137.7  
—133.0  
—131.5  
—128.7  
—128.7  
—124.9

—76.1  
—64.6

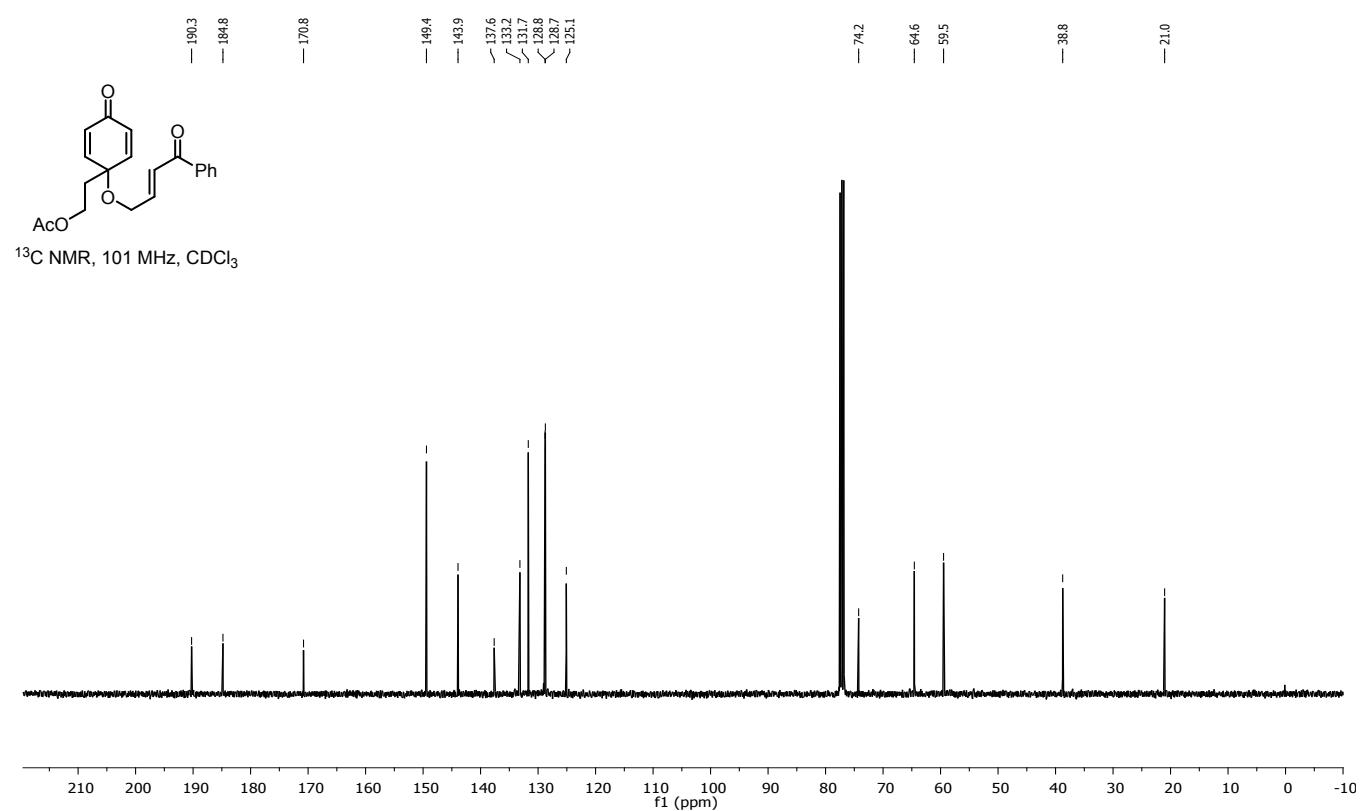
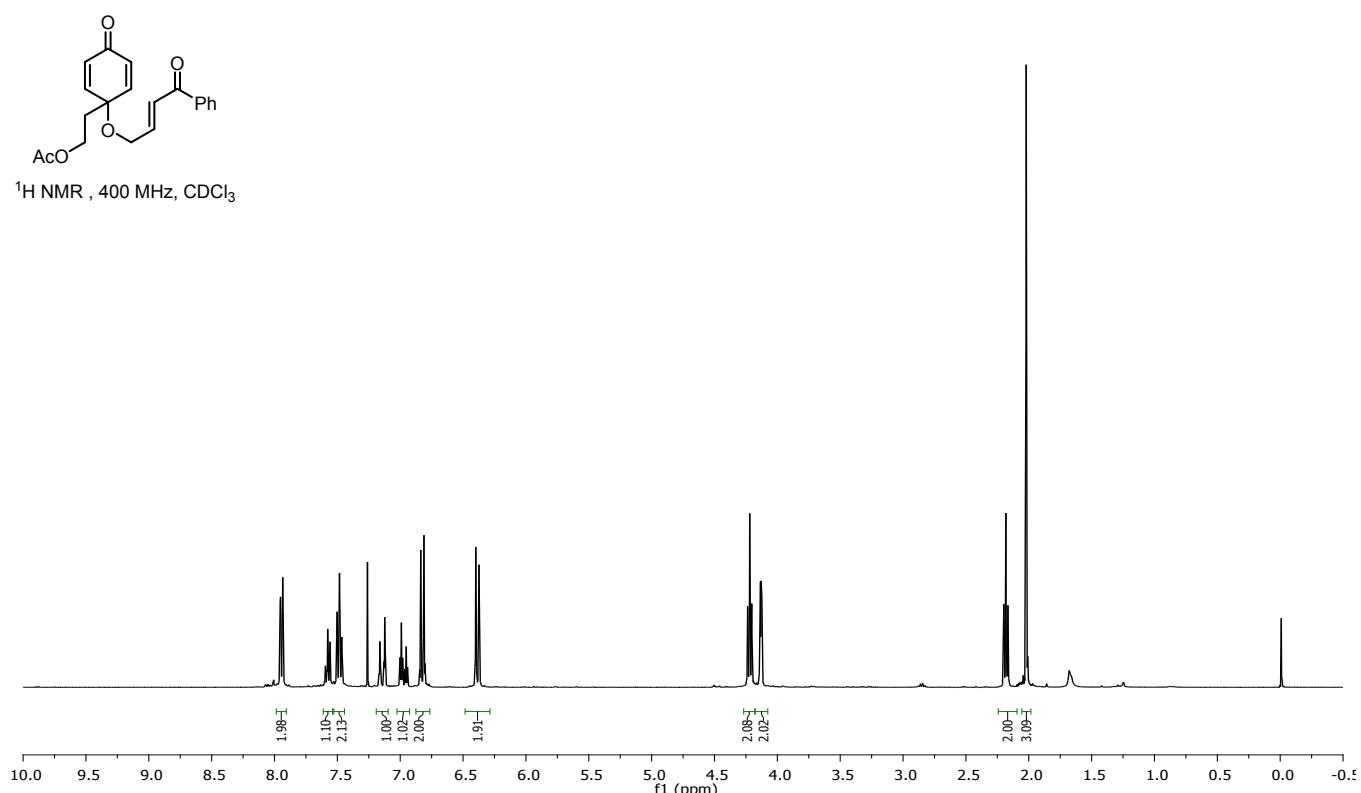
—39.2  
—25.7  
—23.0  
—14.0



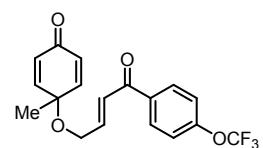
$^{13}\text{C}$  NMR, 126 MHz,  $\text{CDCl}_3$



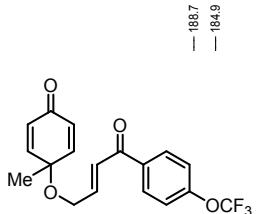
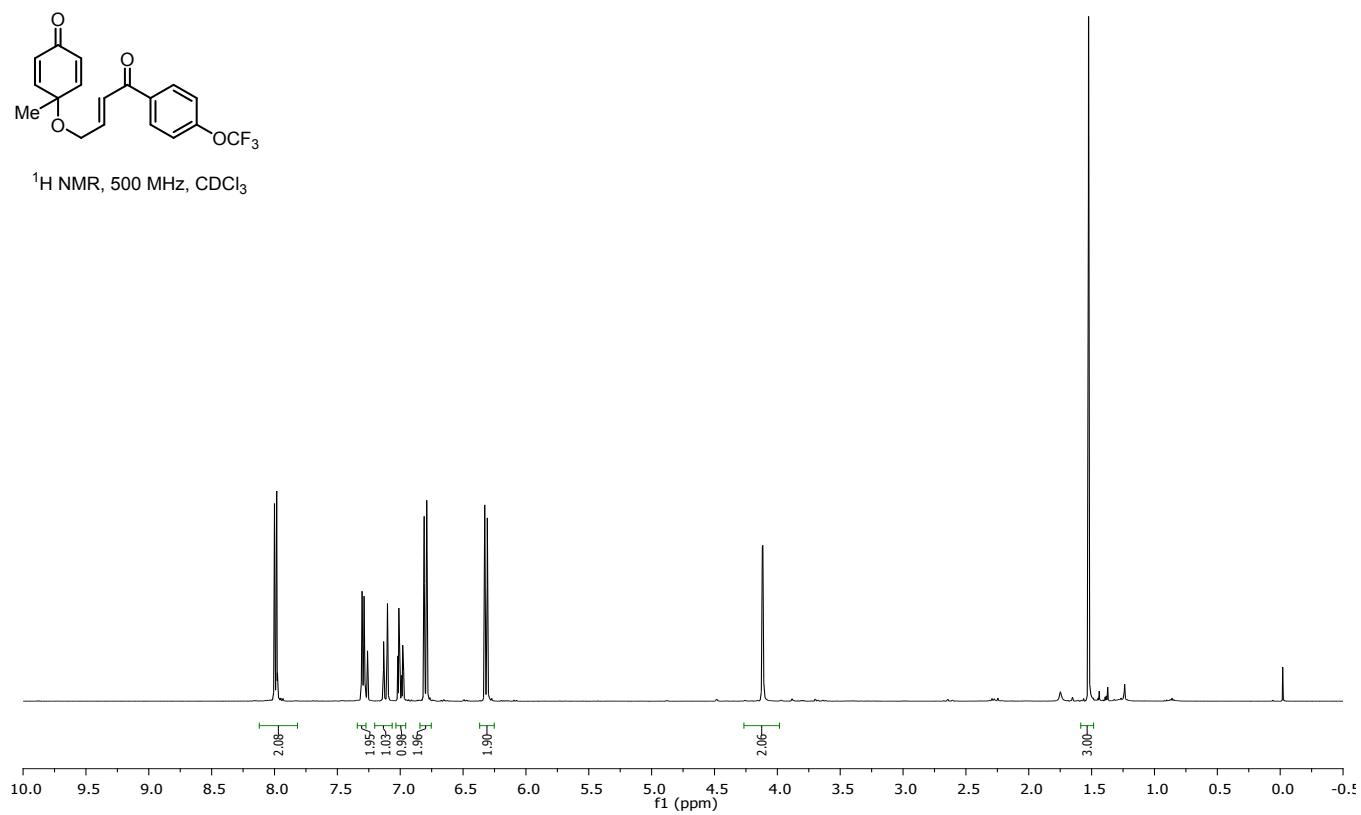
**(E)-2-(4-Oxo-1-((4-oxo-4-phenylbut-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-yl)ethyl acetate (1e):**



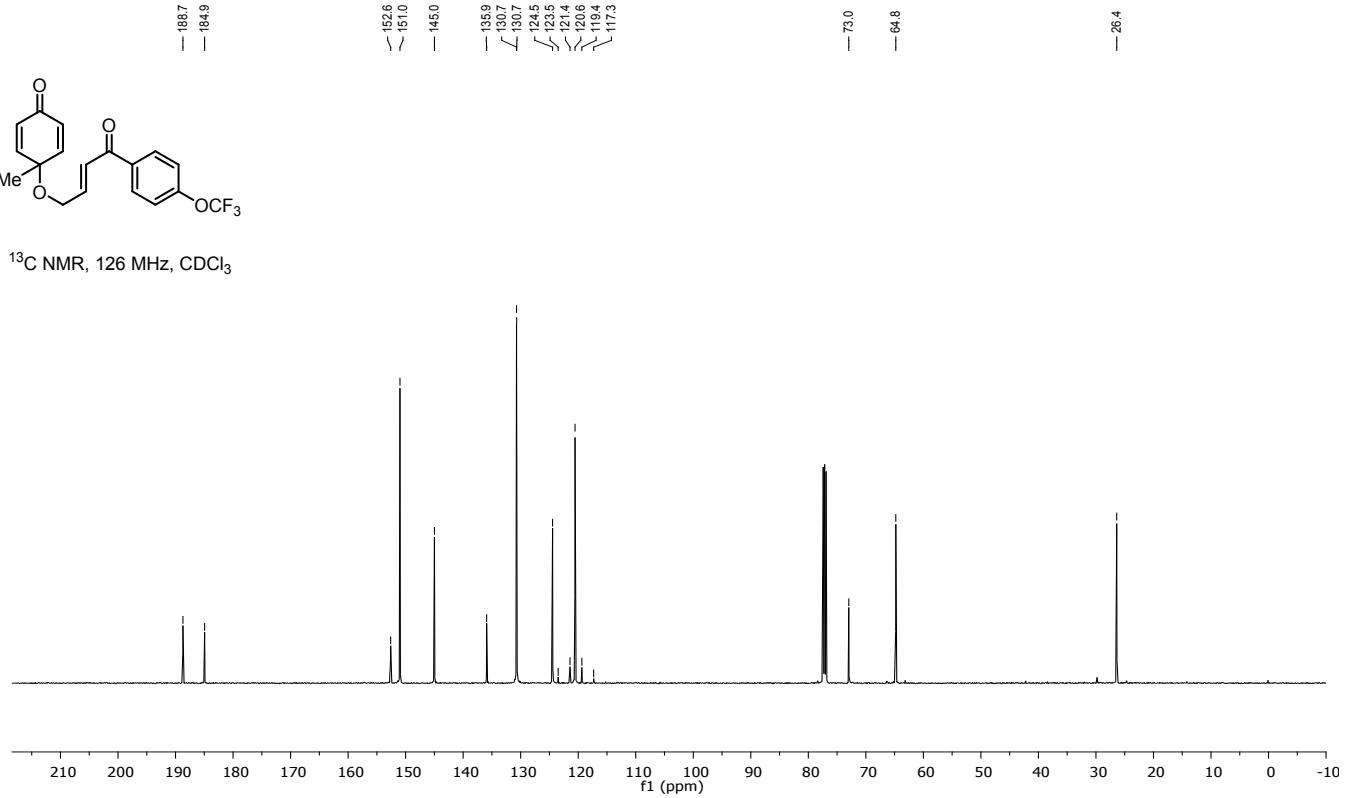
**(E)-4-Methyl-4-((4-oxo-4-(4-(trifluoromethoxy)phenyl)but-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-one  
(1h):**

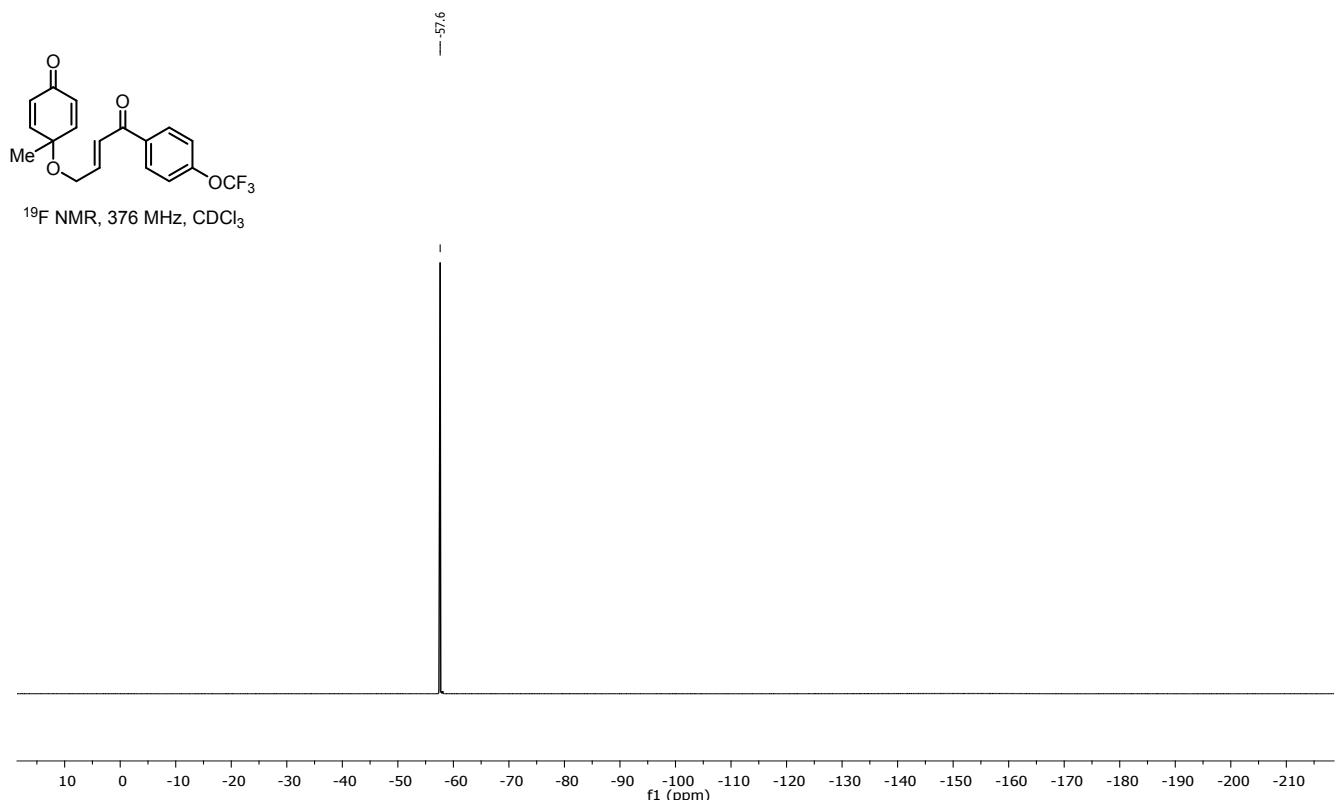


$^1\text{H}$  NMR, 500 MHz,  $\text{CDCl}_3$

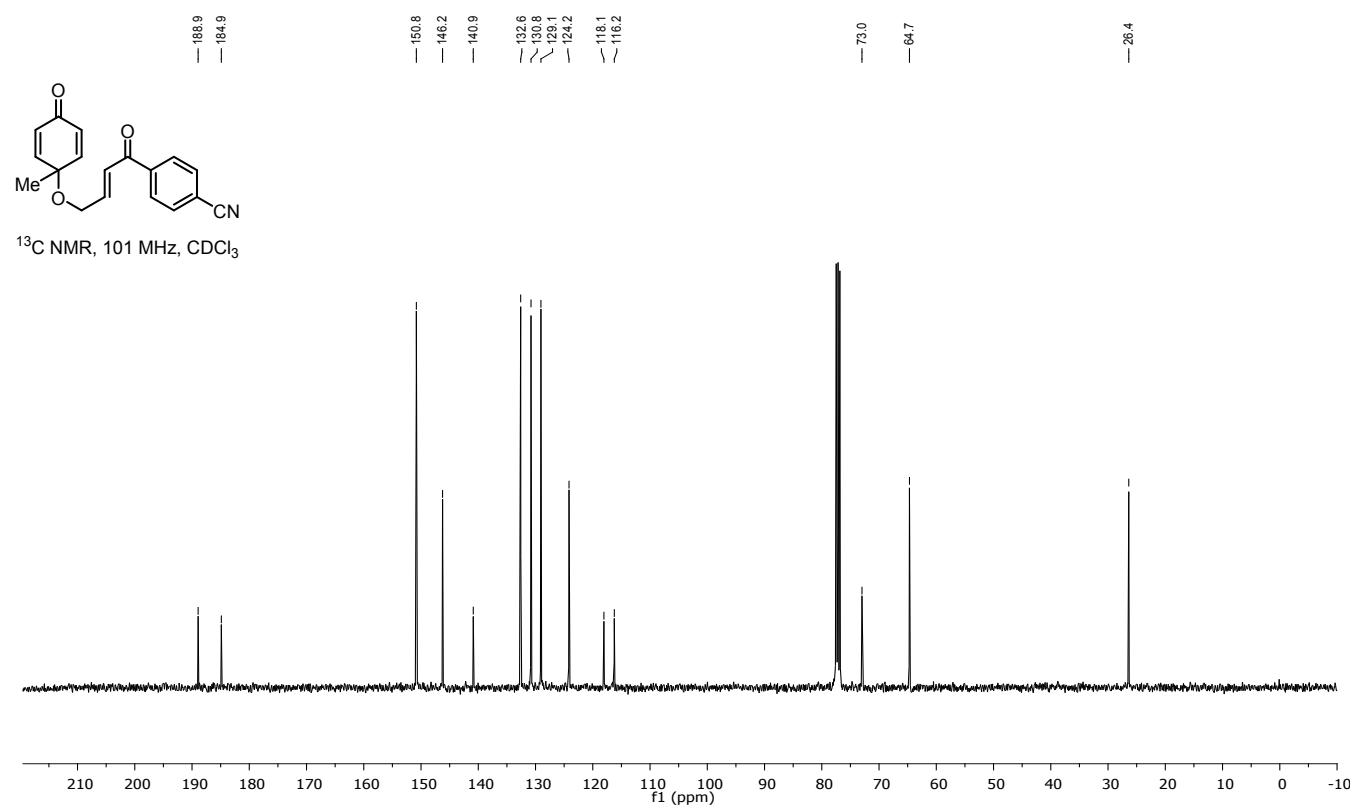
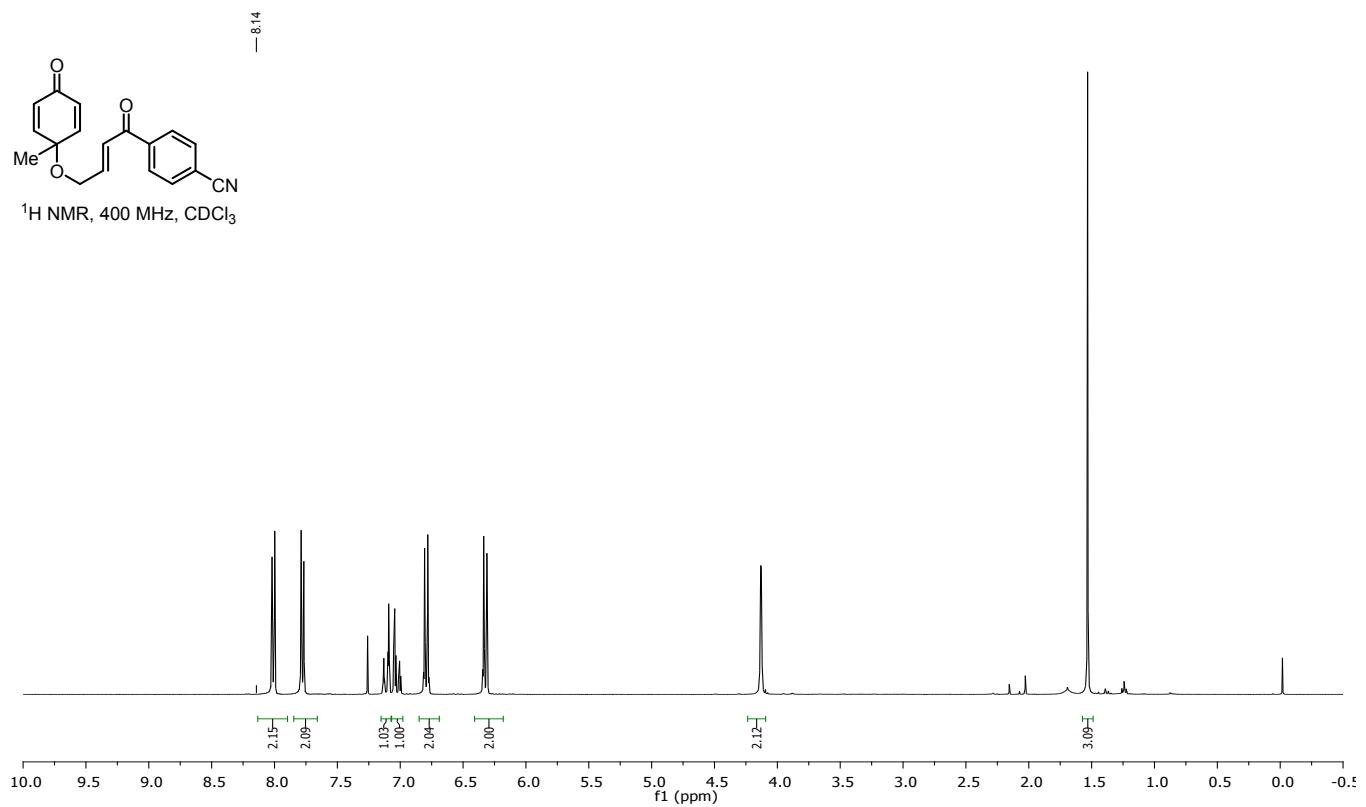


$^{13}\text{C}$  NMR, 126 MHz,  $\text{CDCl}_3$

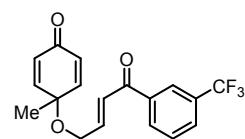




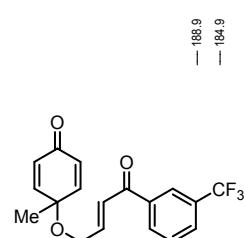
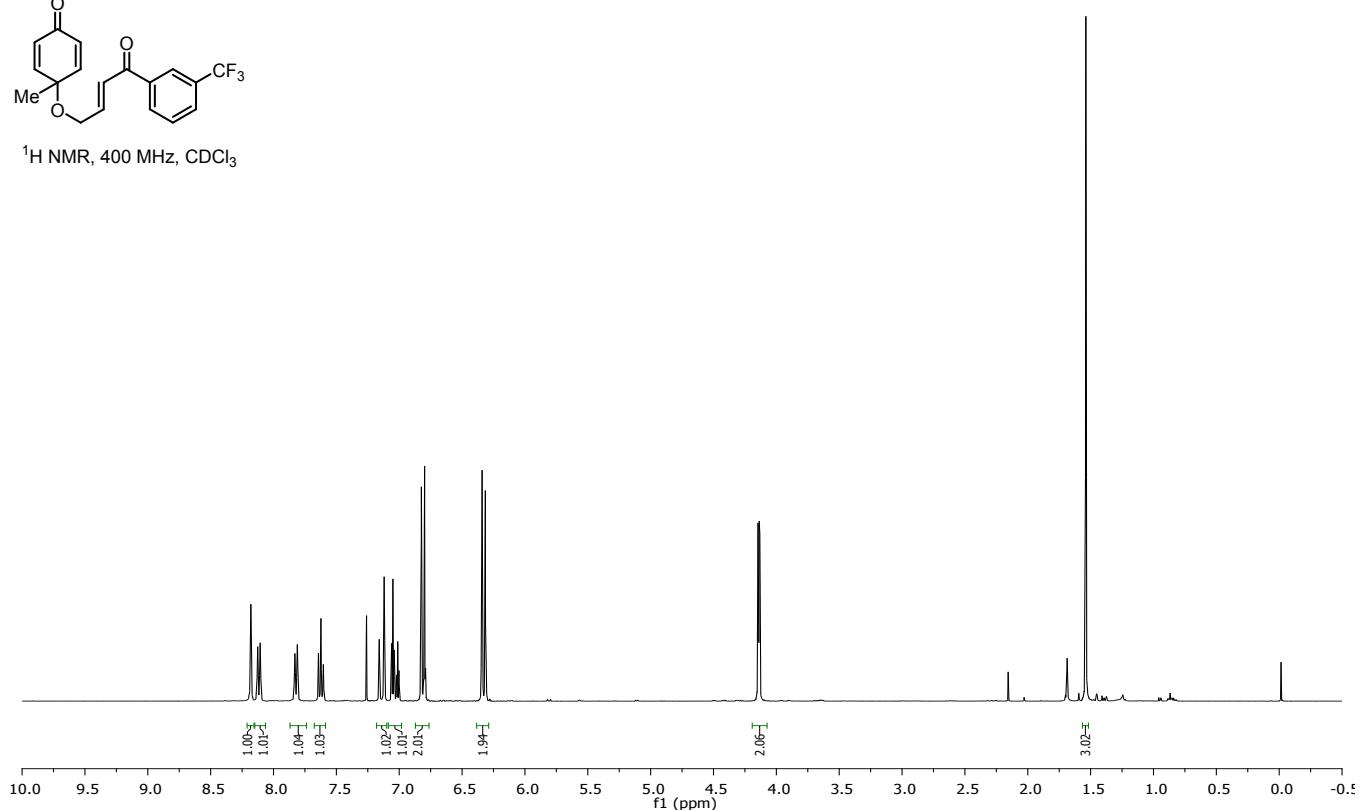
**(E)-4-((1-Methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)but-2-enoylbenzonitrile (1j):**



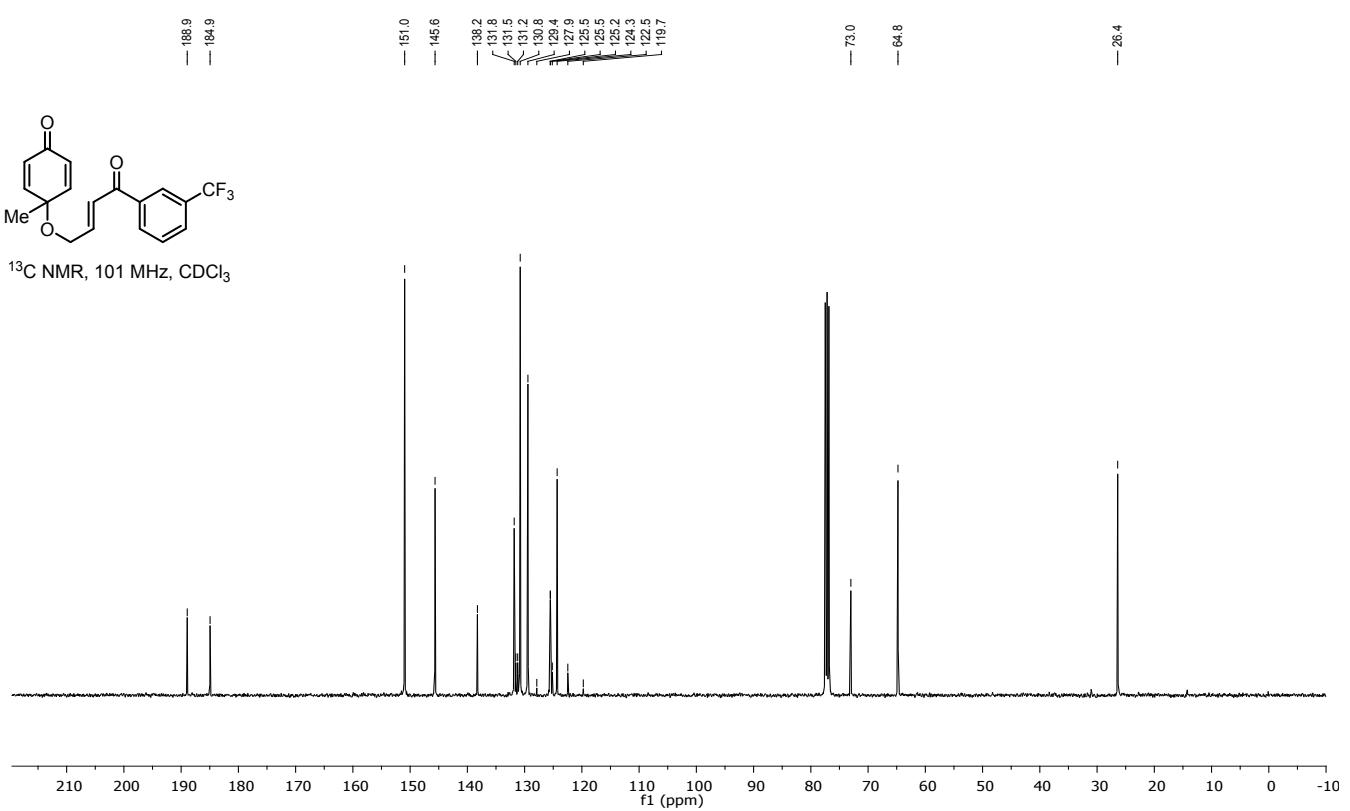
**(E)-4-Methyl-4-((4-oxo-4-(3-(trifluoromethyl)phenyl)but-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-one (1l):**

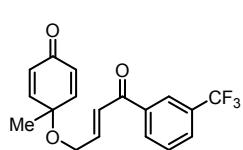


$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$

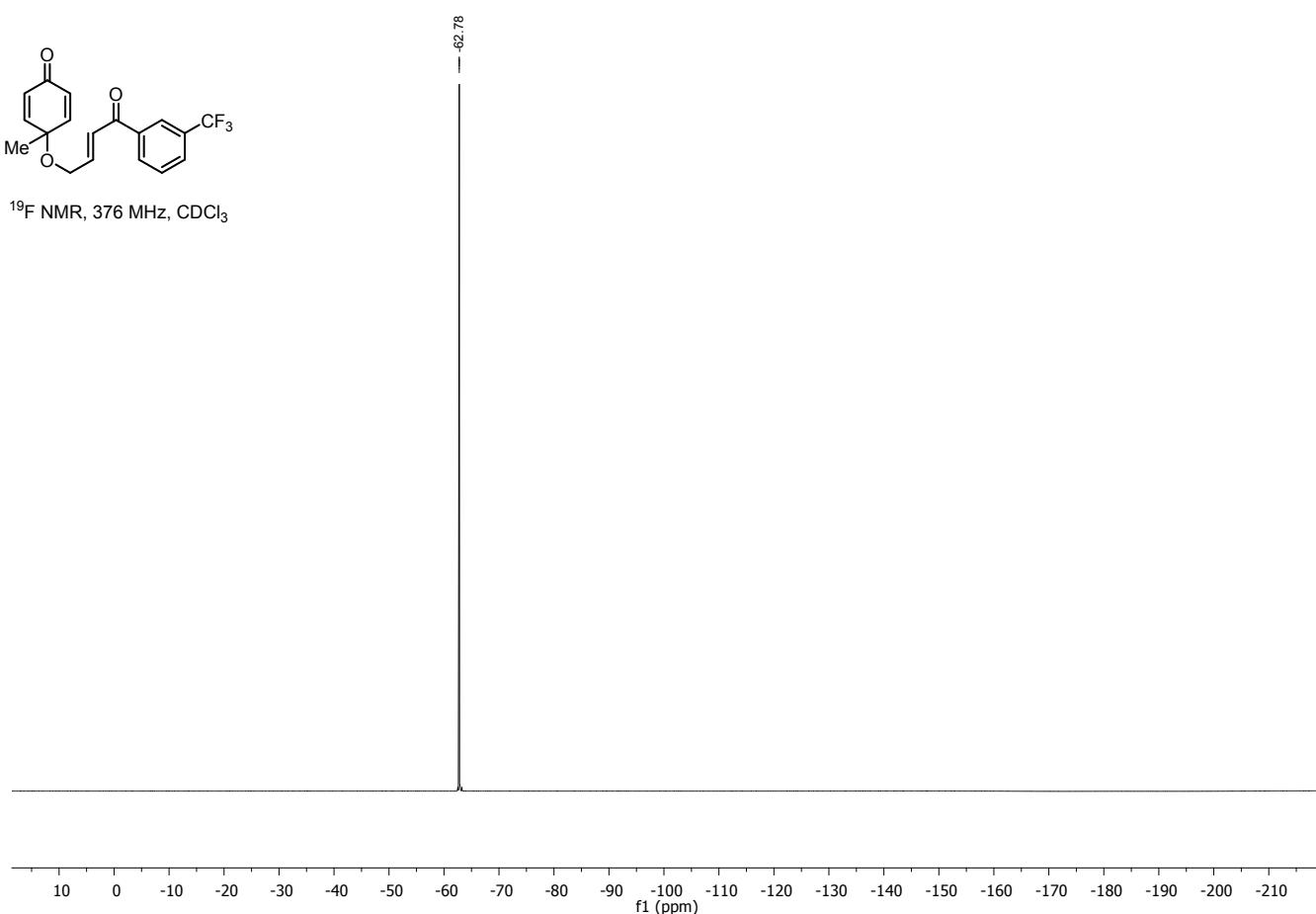


$^{13}\text{C}$  NMR, 101 MHz,  $\text{CDCl}_3$

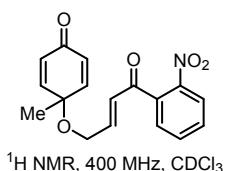




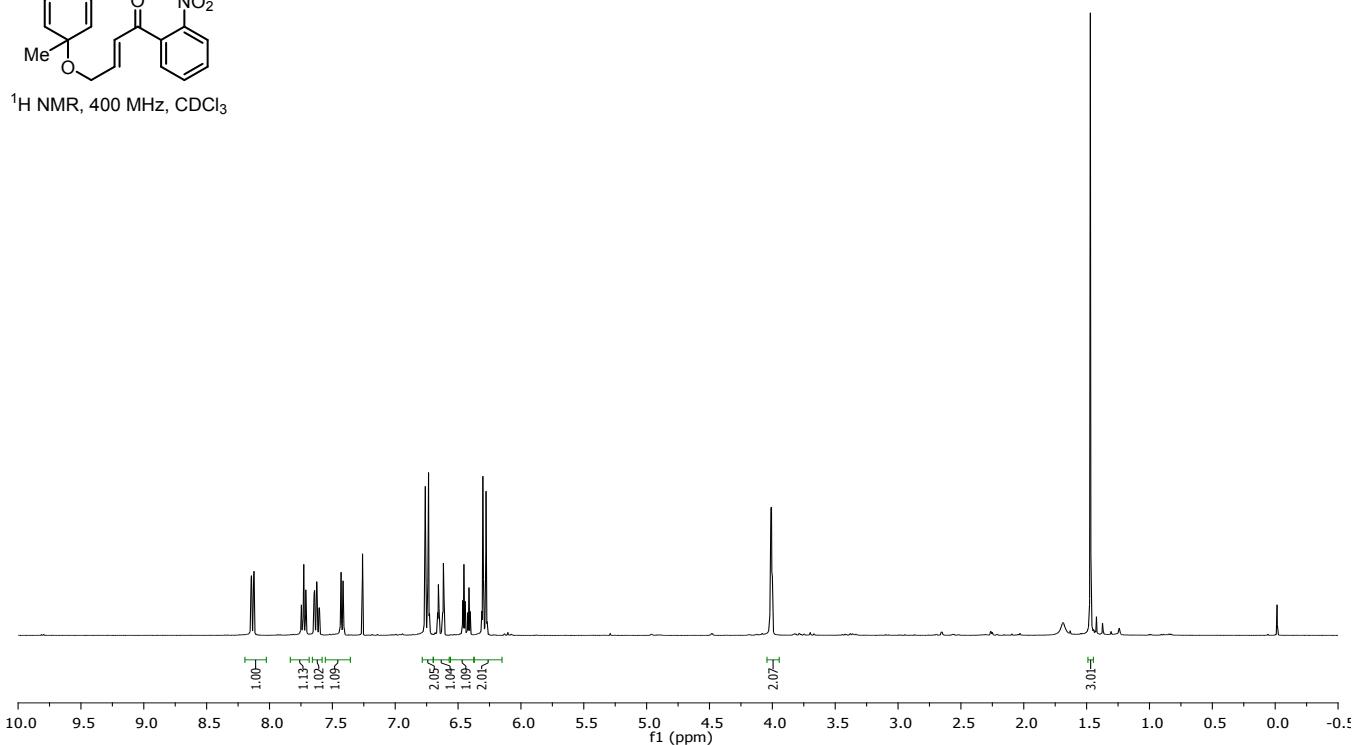
<sup>19</sup>F NMR, 376 MHz, CDCl<sub>3</sub>



**(E)-4-Methyl-4-((4-(2-nitrophenyl)-4-oxobut-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-one (1m):**



$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$

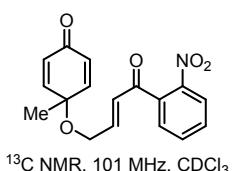


— 192.6  
— 185.0

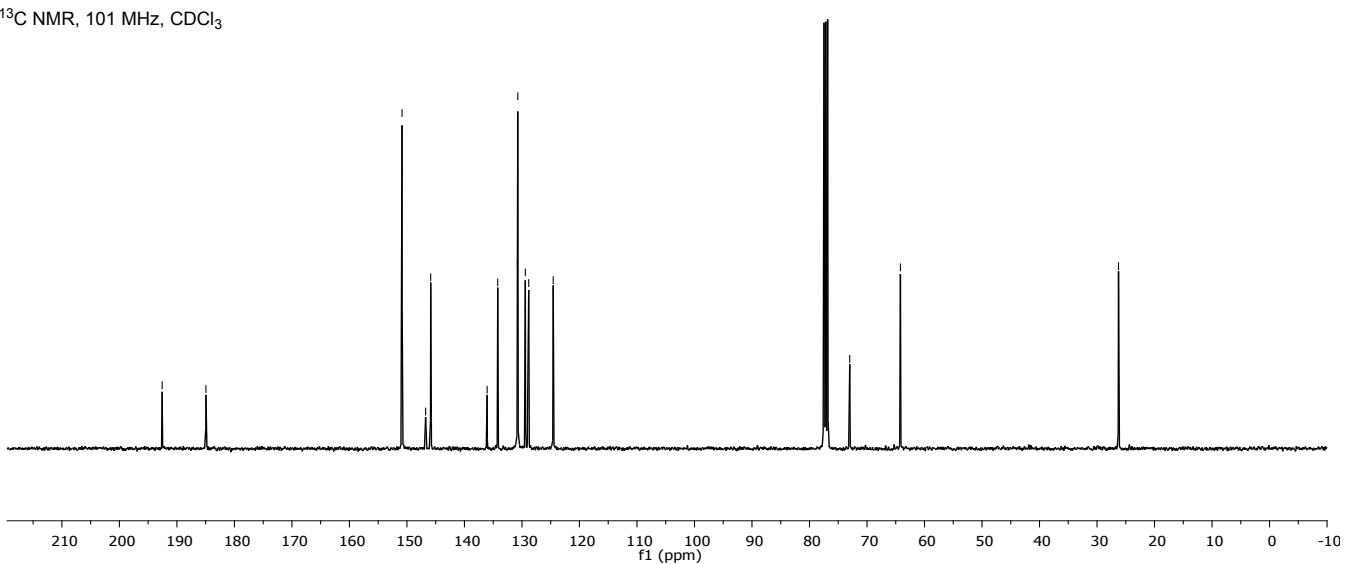
— 150.8  
— 146.8  
— 145.9

— 136.1  
— 134.2  
— 130.8  
— 130.7  
— 129.4  
— 128.8  
— 124.6

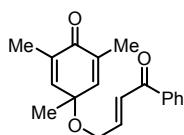
— 73.0  
— 64.2



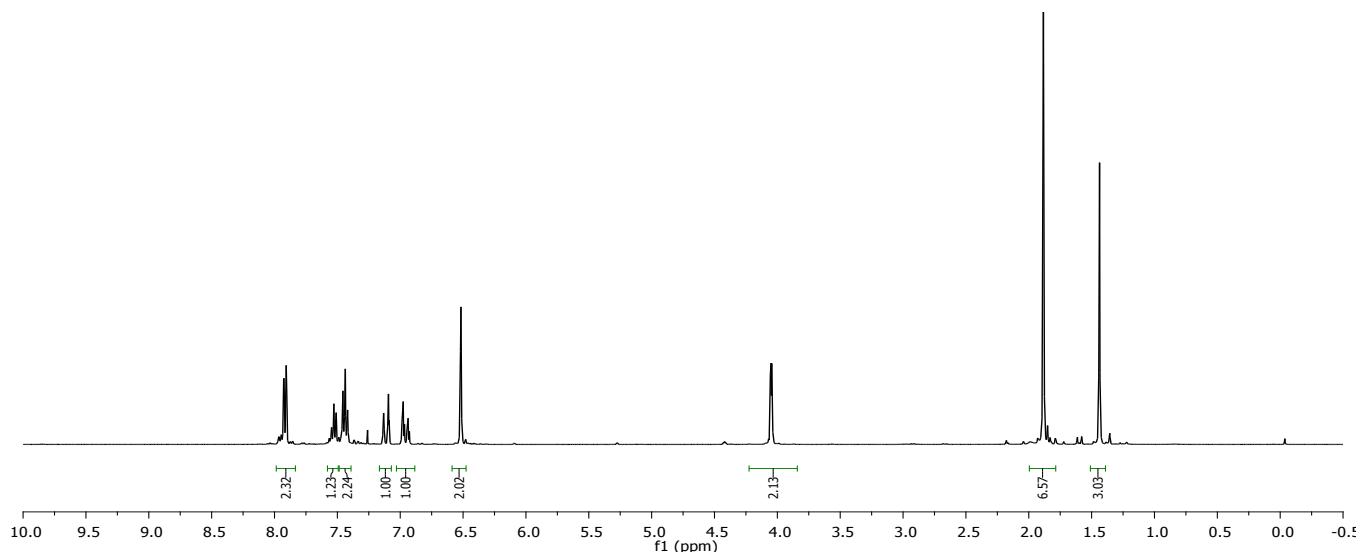
$^{13}\text{C}$  NMR, 101 MHz,  $\text{CDCl}_3$



**(E)-2,4,6-Trimethyl-4-((4-oxo-4-phenylbut-2-en-1-yl)oxy)cyclohexa-2,5-dien-1-one (1y):**



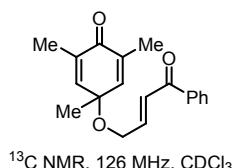
$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$



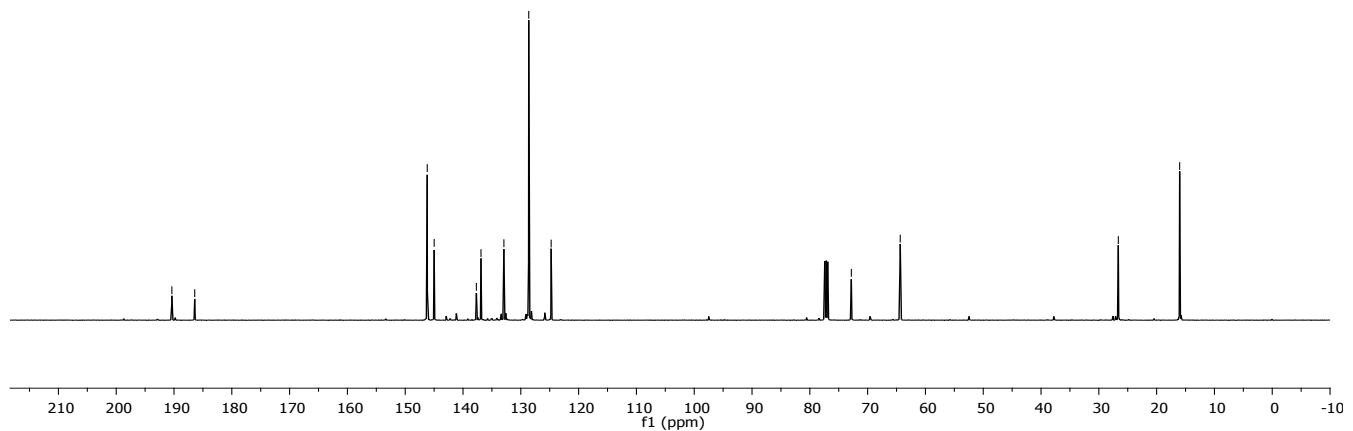
— 190.4  
— 186.4

— 146.2  
— 145.0  
— 137.7  
— 136.9  
— 132.9  
— 128.6  
— 124.8

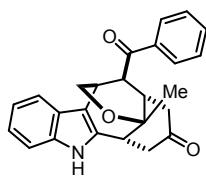
— 72.8  
— 64.4  
— 26.6  
— 16.0



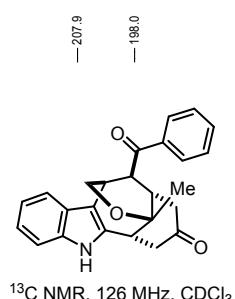
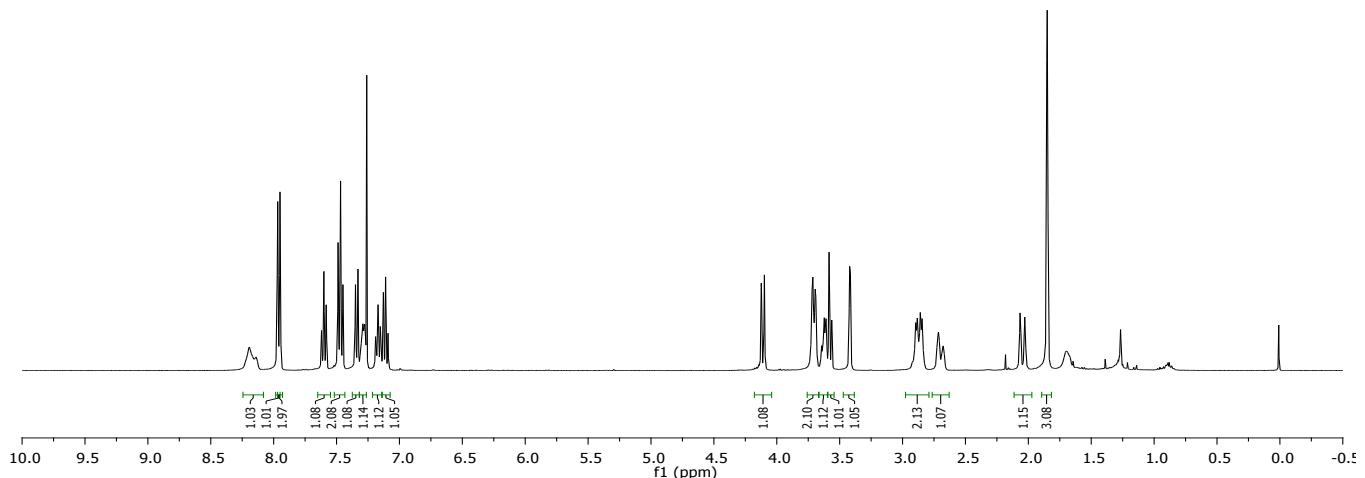
$^{13}\text{C}$  NMR, 126 MHz,  $\text{CDCl}_3$



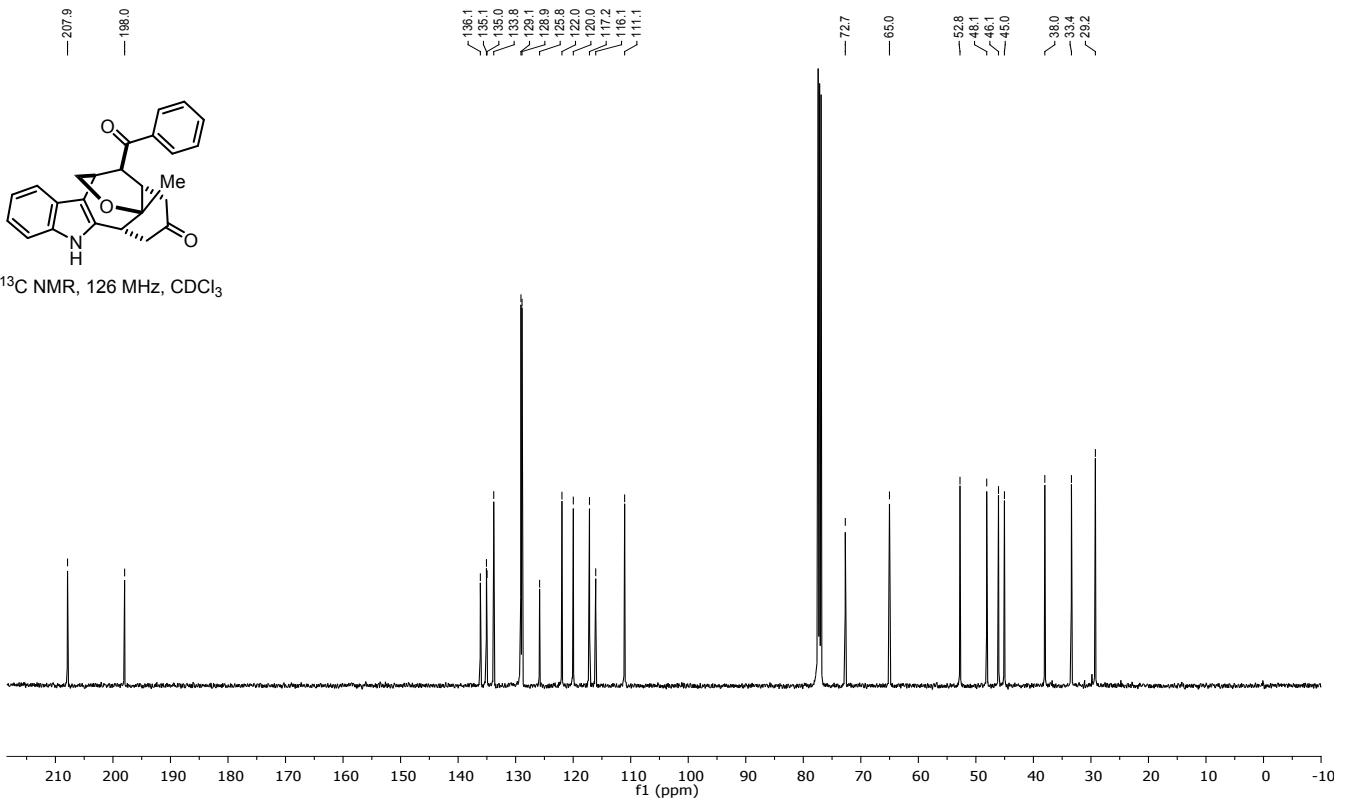
**13-Benzoyl-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3a):**



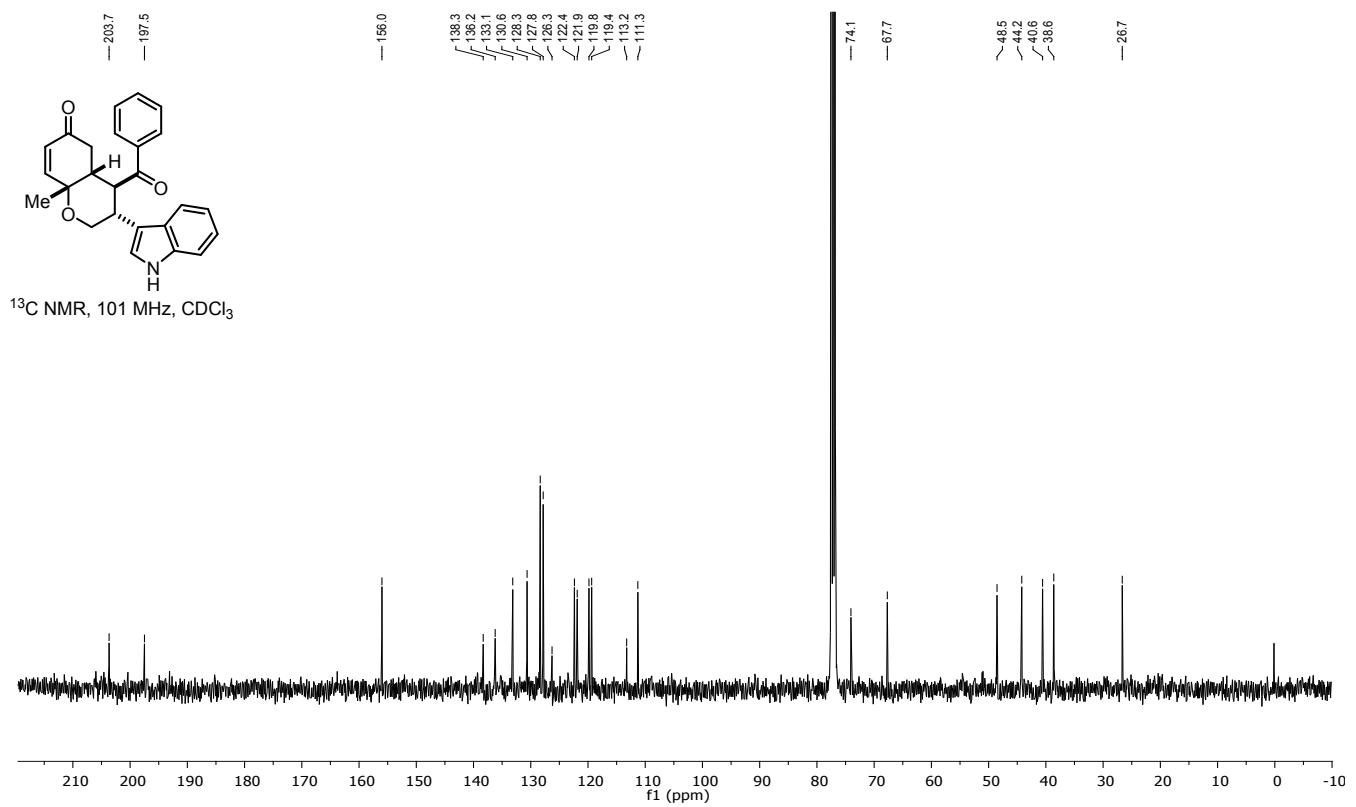
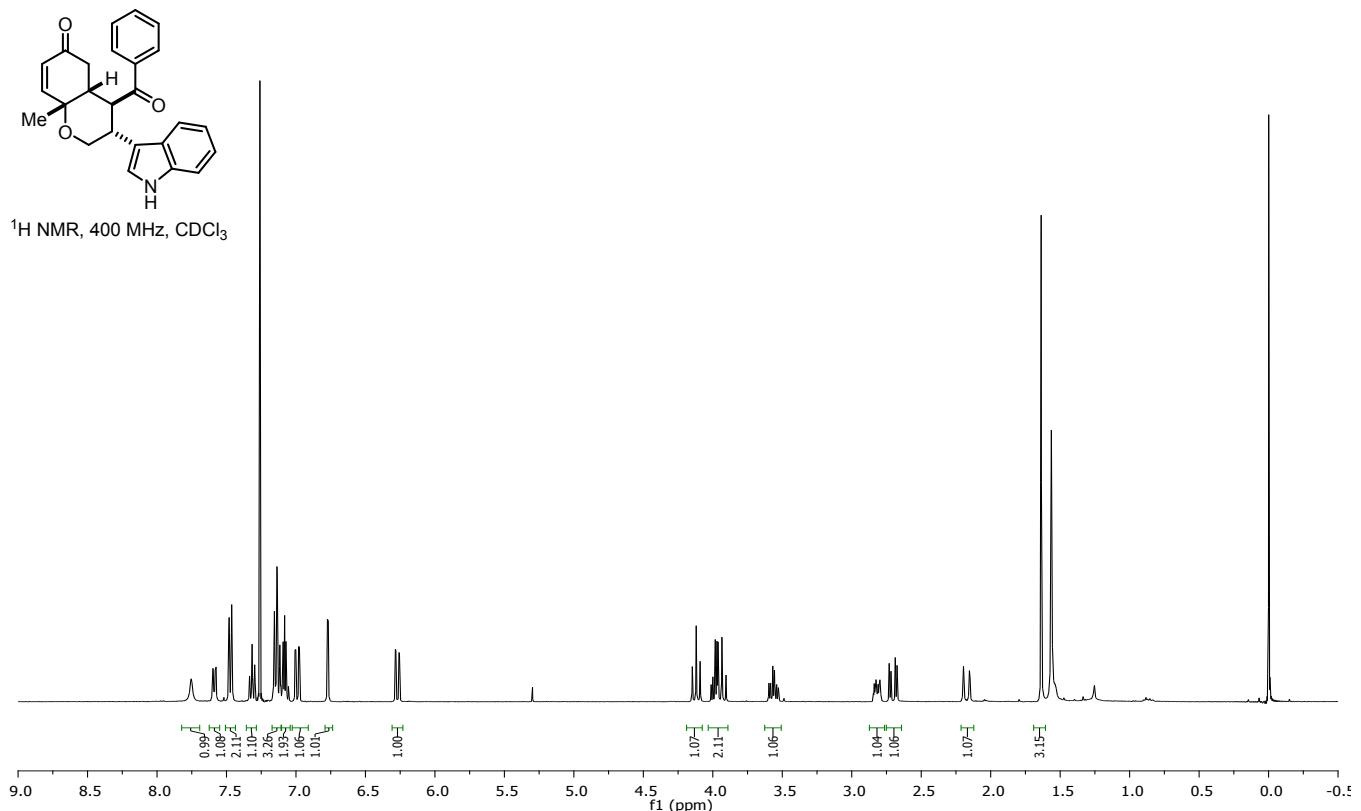
<sup>1</sup>H NMR, 400 MHz, CDCl<sub>3</sub>



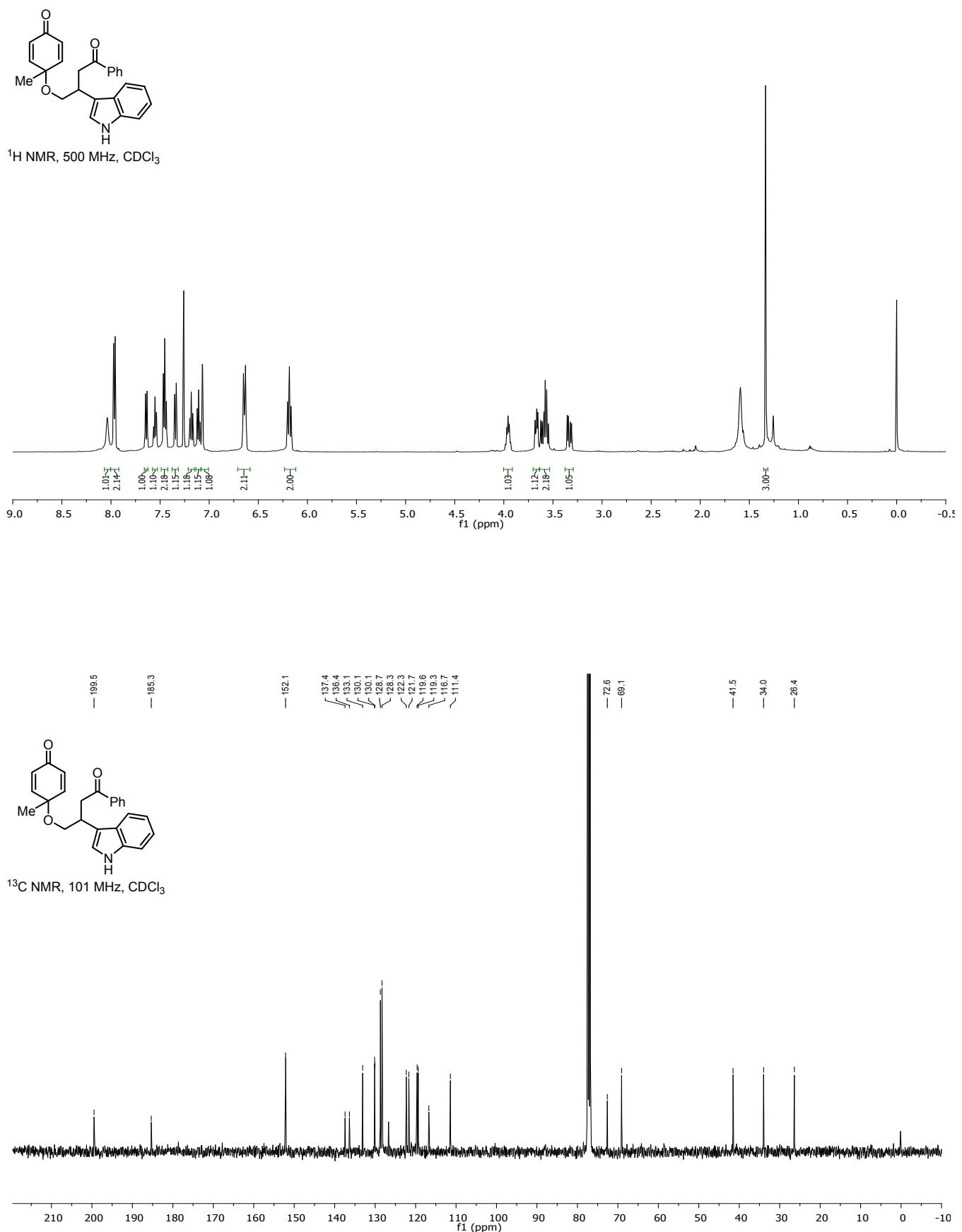
<sup>13</sup>C NMR, 126 MHz, CDCl<sub>3</sub>



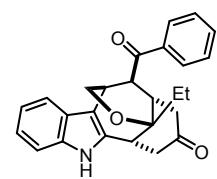
**4-Benzoyl-3-(1*H*-indol-3-yl)-8*a*-methyl-3,4,4*a*,8*a*-tetrahydro-2*H*-chromen-6(5*H*)-one (4a):**



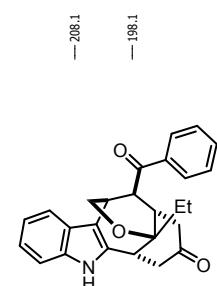
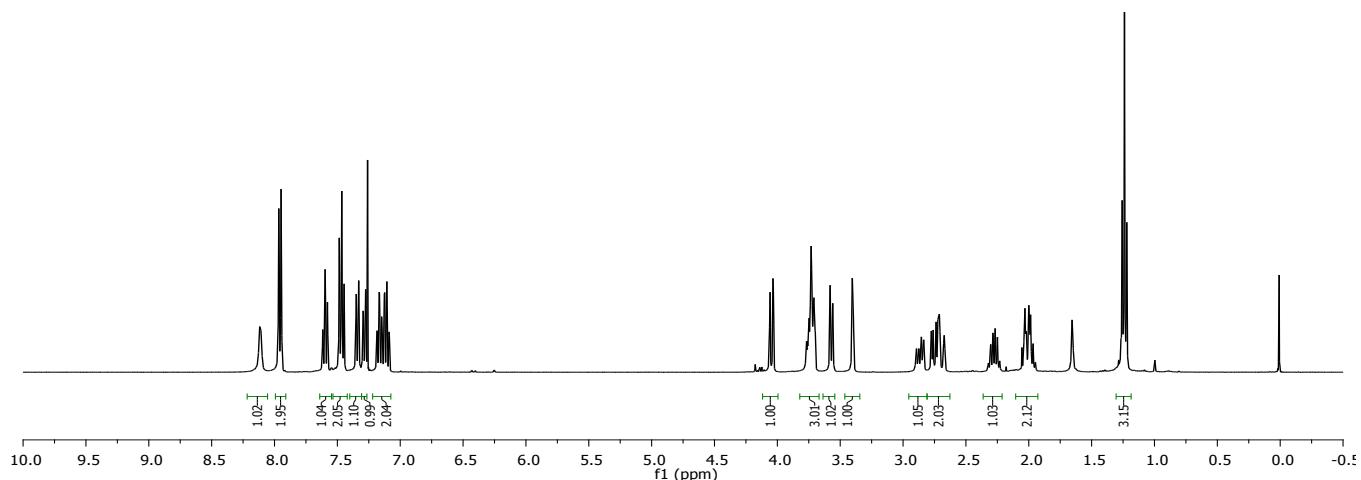
**4-(2-(1*H*-Indol-3-yl)-4-oxo-4-phenylbutoxy)-4-methylcyclohexa-2,5-dien-1-one (4a'):**



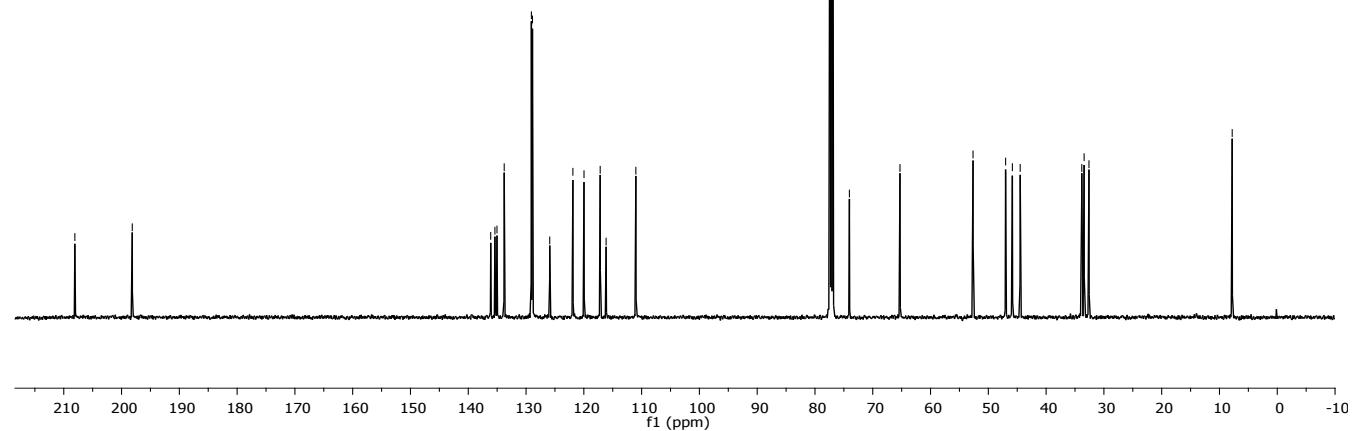
**13-Benzoyl-4a-ethyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3b):**



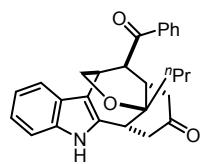
$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$



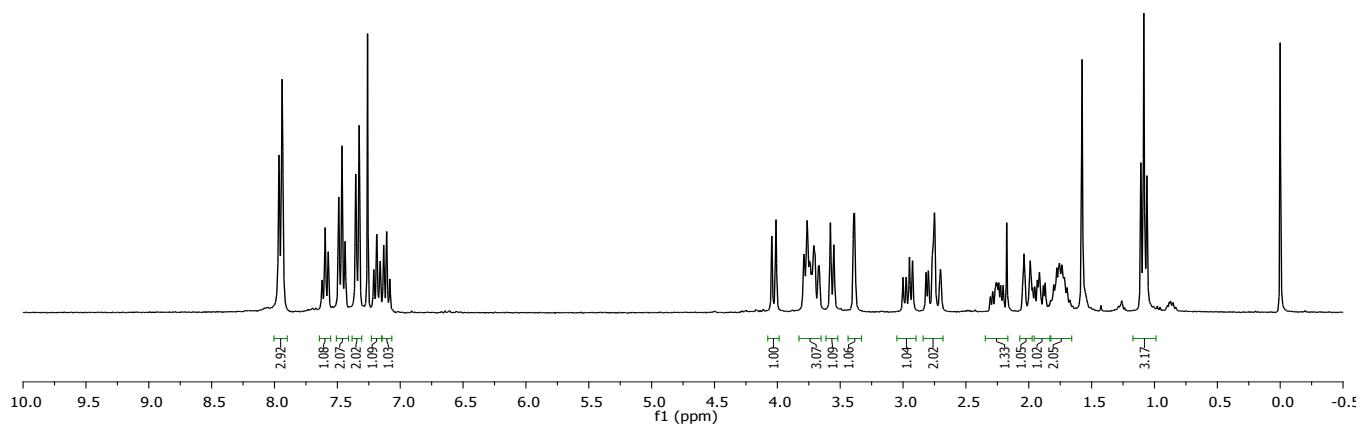
$^{13}\text{C}$  NMR, 126 MHz,  $\text{CDCl}_3$



**13-Benzoyl-4a-propyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3c):**



$^1\text{H}$  NMR, 300 MHz,  $\text{CDCl}_3$



—208.1

—198.1

—136.1  
—135.4  
—135.0  
—133.8  
—129.1  
—128.9  
—125.9  
—121.9  
—120.0  
—117.2  
—116.1  
—111.0

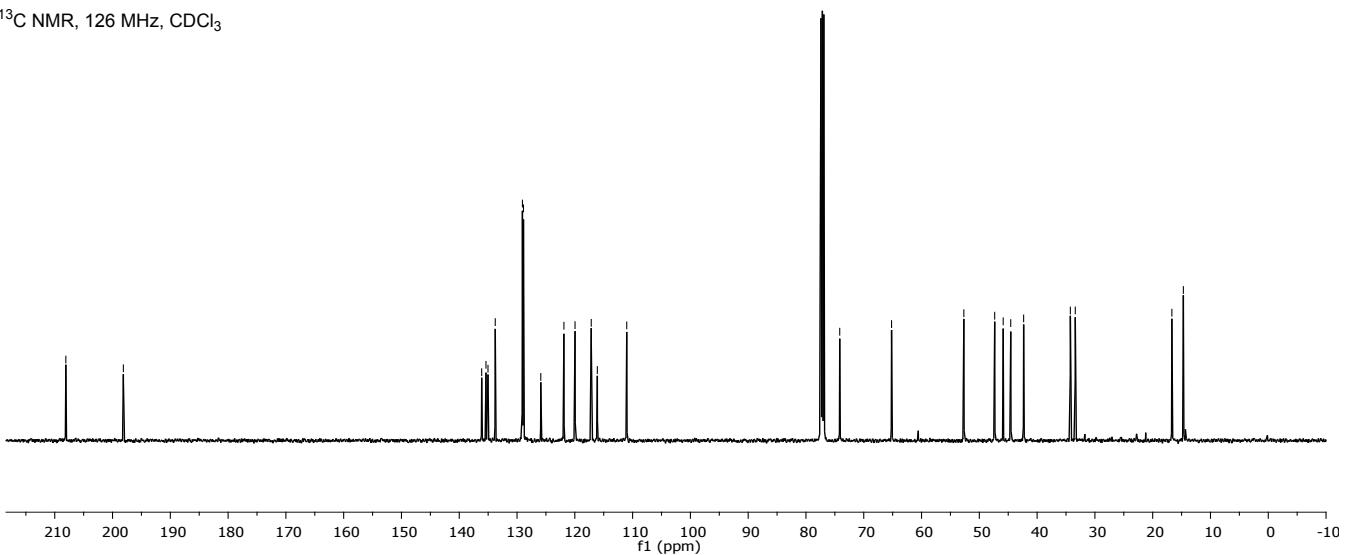
—74.2

—52.7  
—47.3  
—45.9  
—44.6  
—42.3  
—34.2  
—33.4

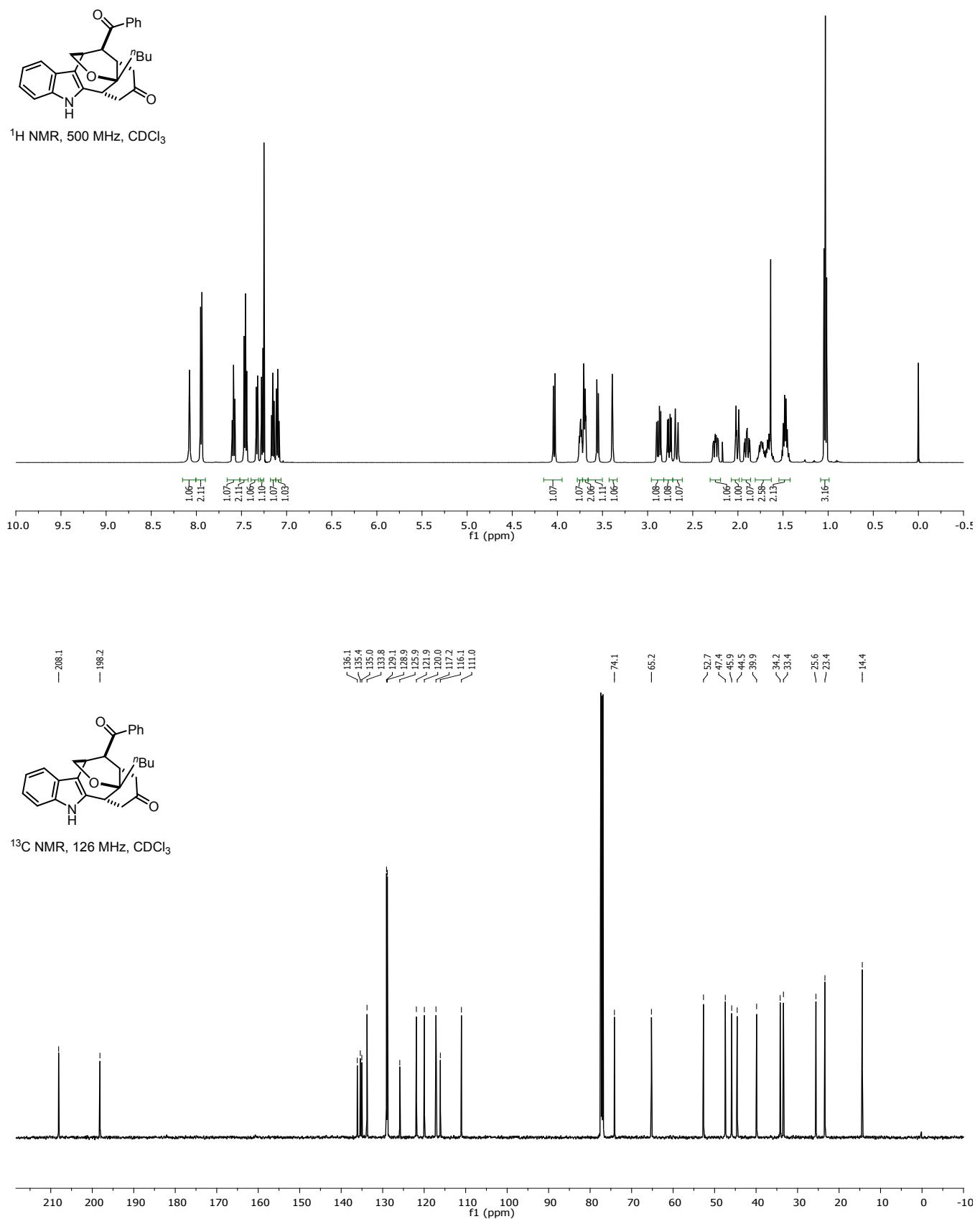
—16.7

—14.7

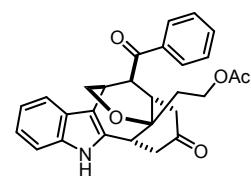
$^{13}\text{C}$  NMR, 126 MHz,  $\text{CDCl}_3$



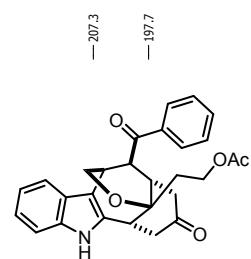
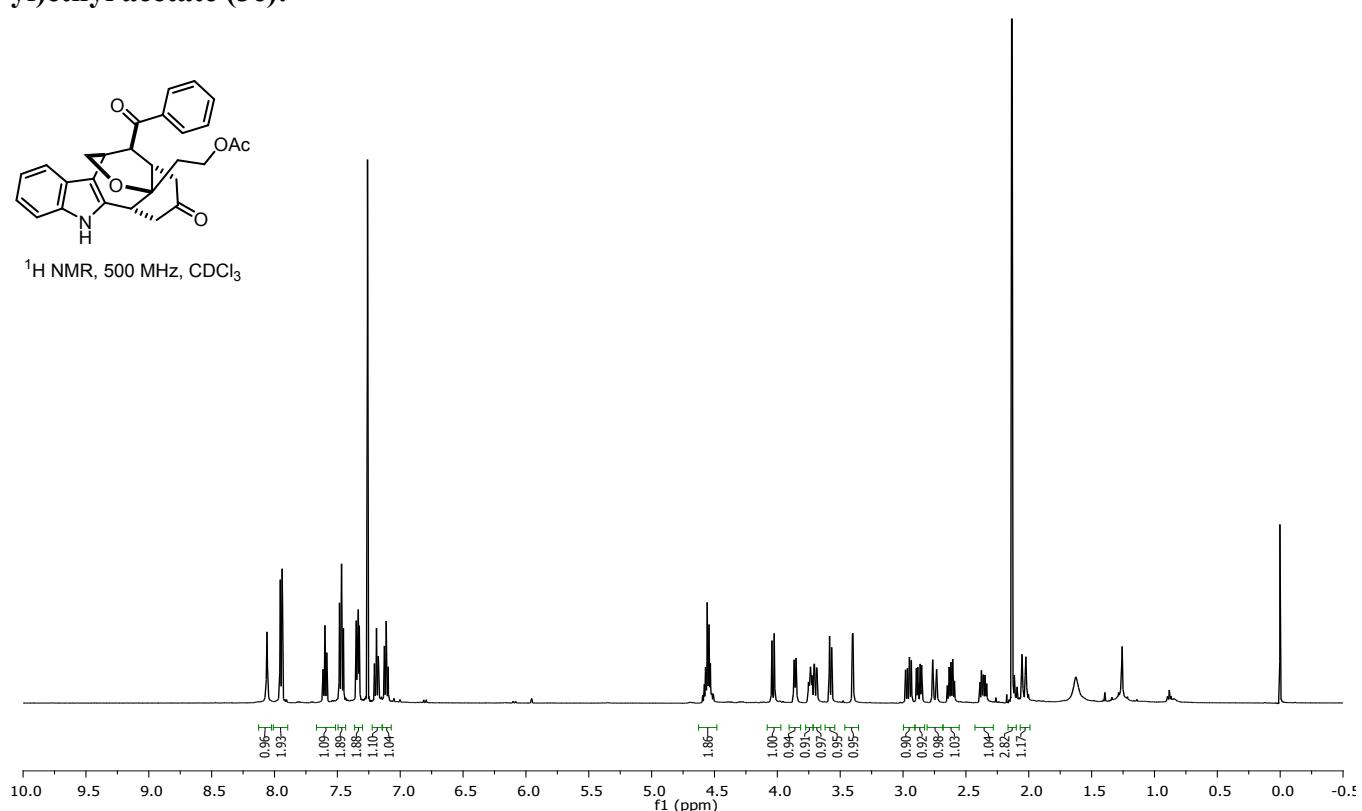
**13-Benzoyl-4a-butyl-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2(3H)-one (3d):**



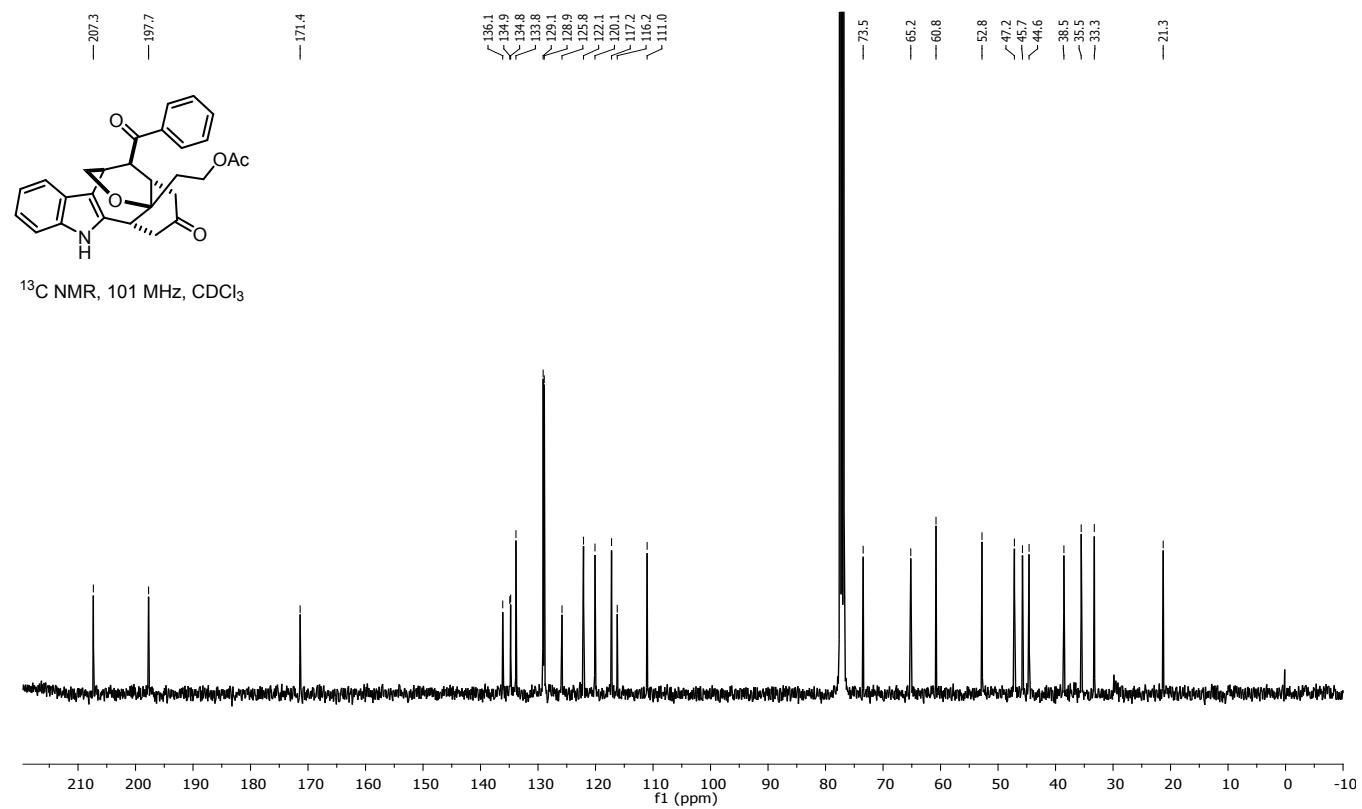
**13-Benzoyl-2-oxo-1,2,3,4,6,7,12,12b-octahydro-4aH-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-4a-yl)ethyl acetate (**3e**):**



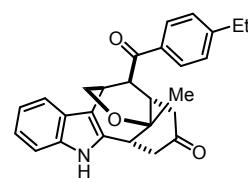
<sup>1</sup>H NMR, 500 MHz, CDCl<sub>3</sub>



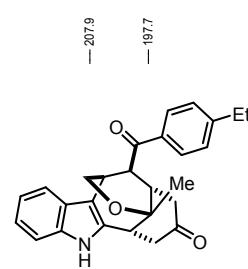
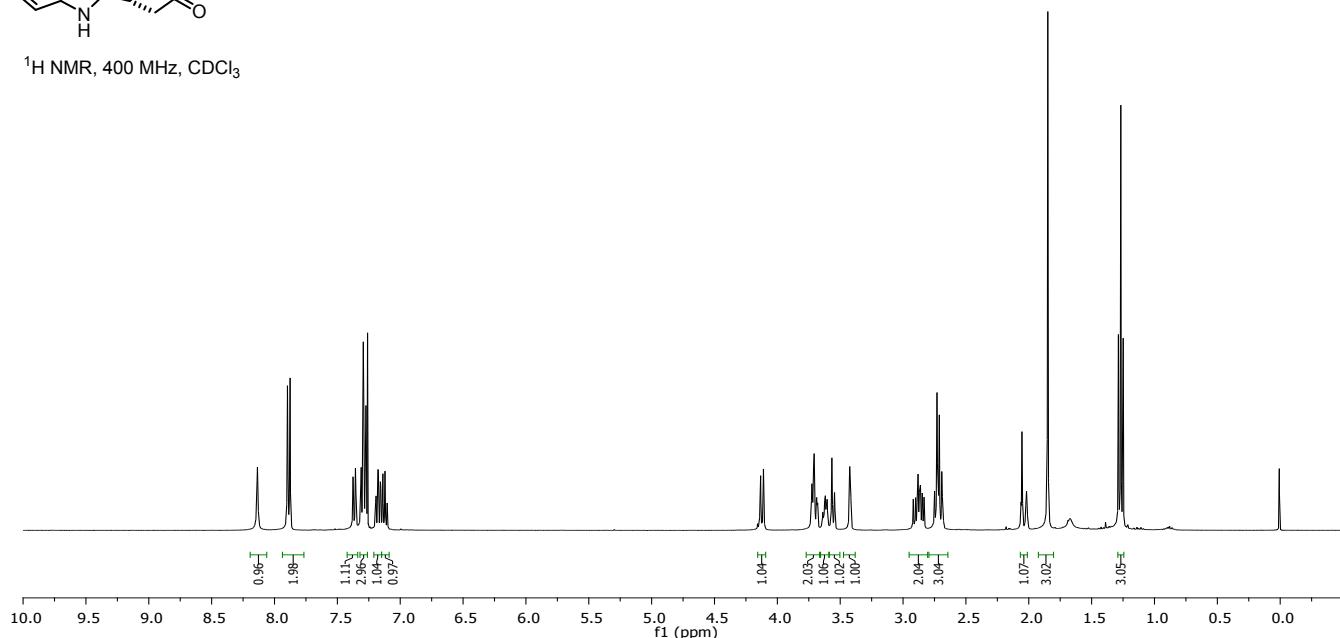
<sup>13</sup>C NMR, 101 MHz, CDCl<sub>3</sub>



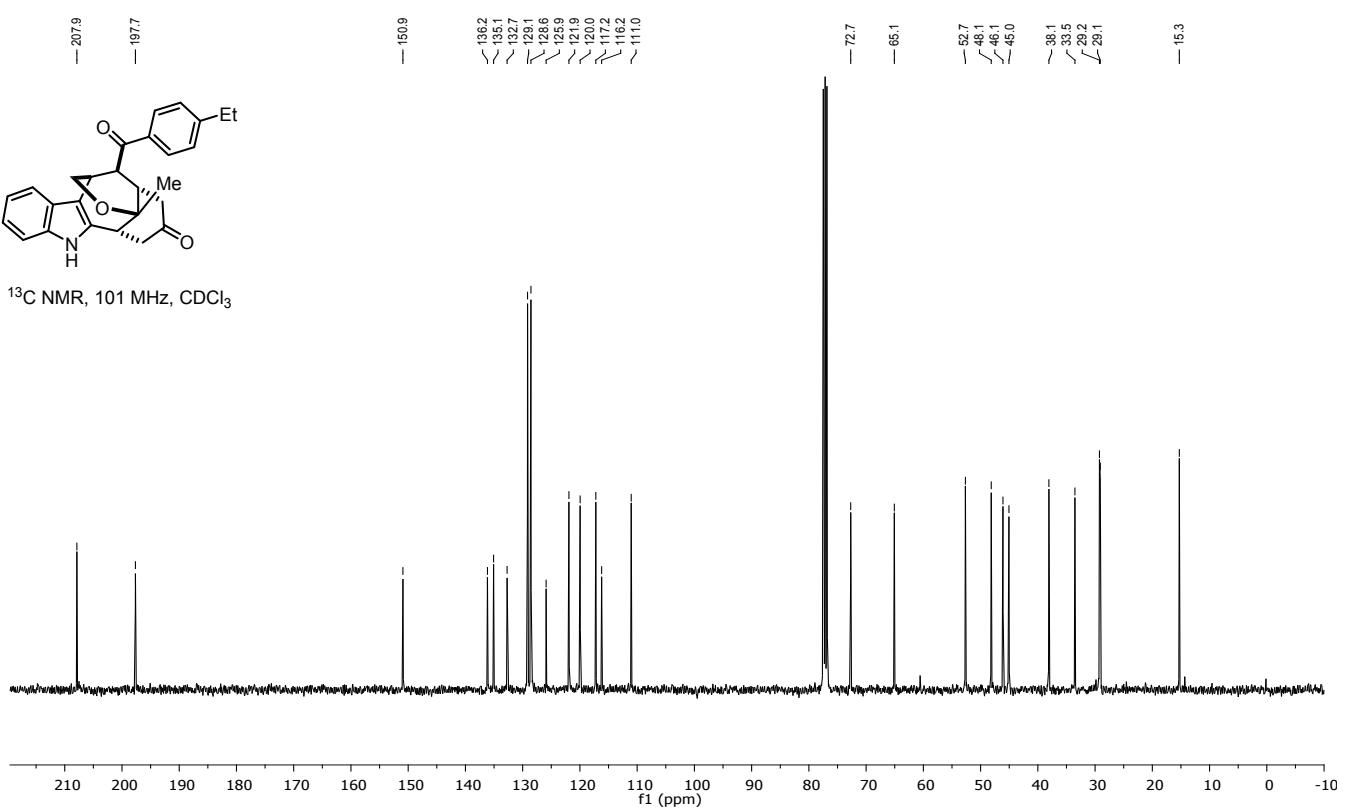
**13-(4-Ethylbenzoyl)-4a-methyl-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2(3H)-one (3f):**



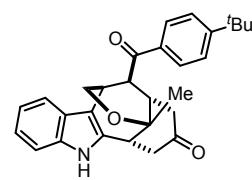
<sup>1</sup>H NMR, 400 MHz, CDCl<sub>3</sub>



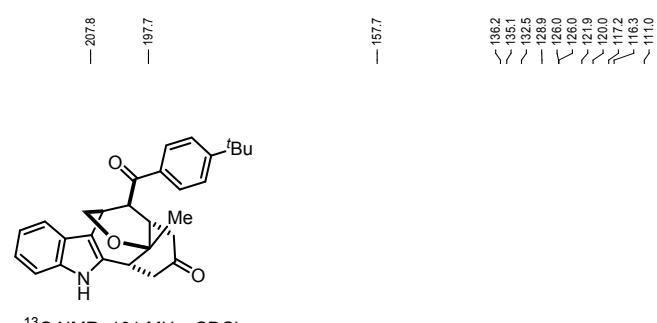
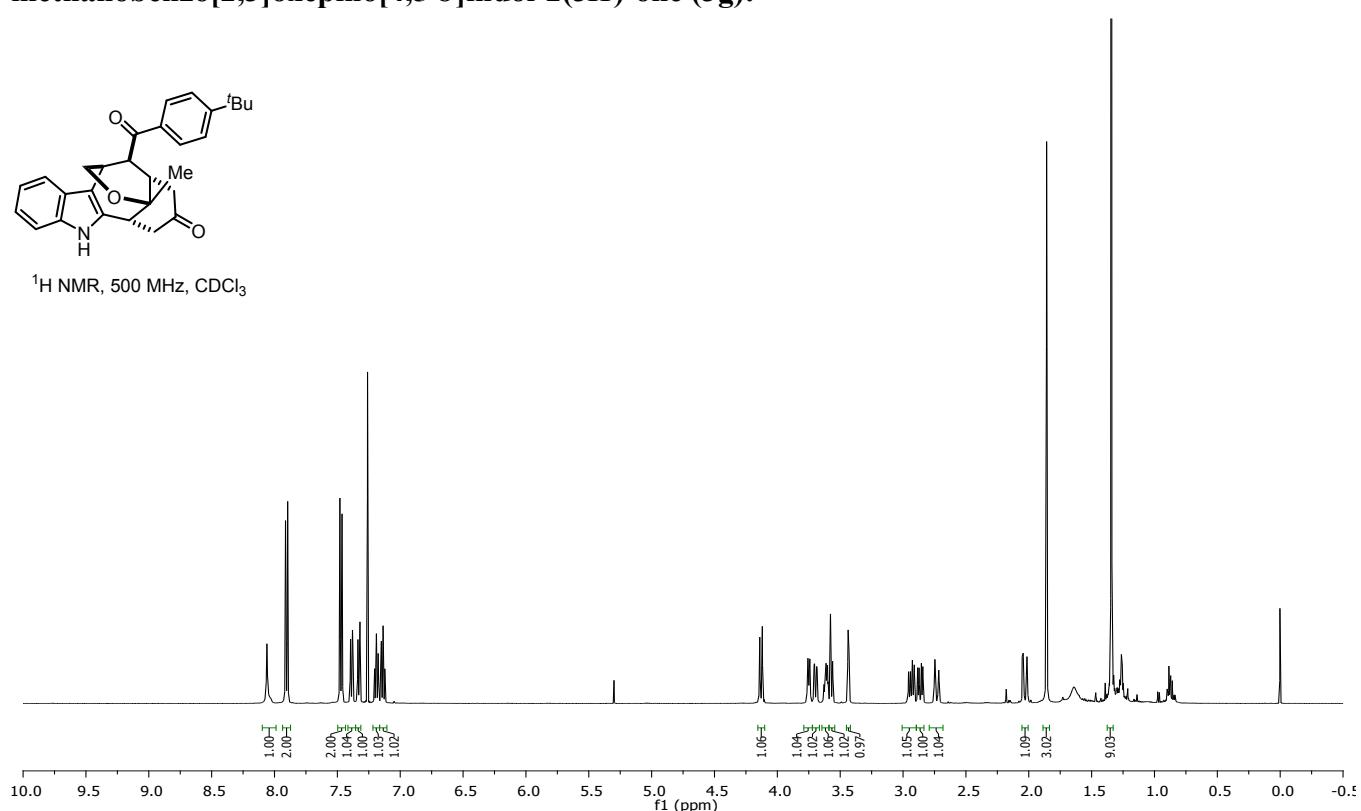
<sup>13</sup>C NMR, 101 MHz, CDCl<sub>3</sub>



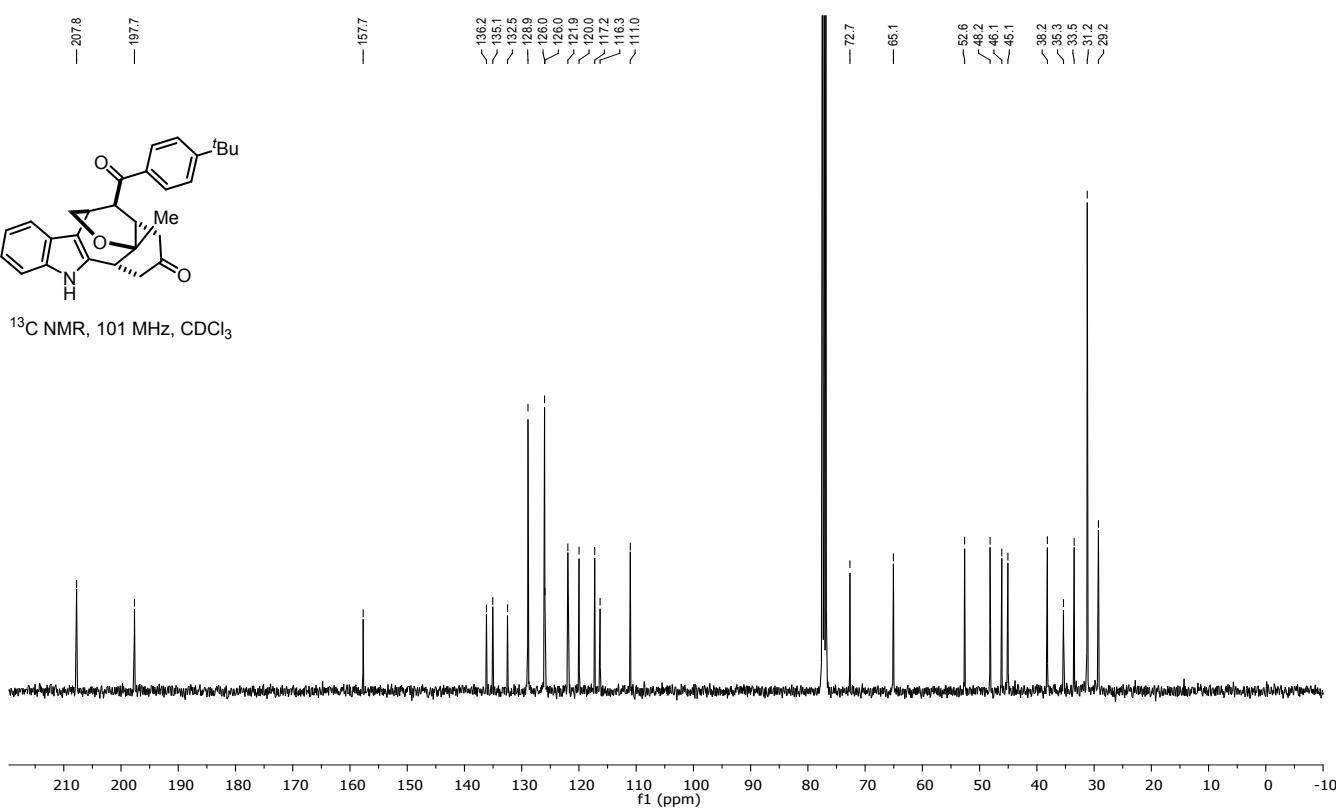
**13-(4-(*tert*-Butyl)benzoyl)-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3g):**



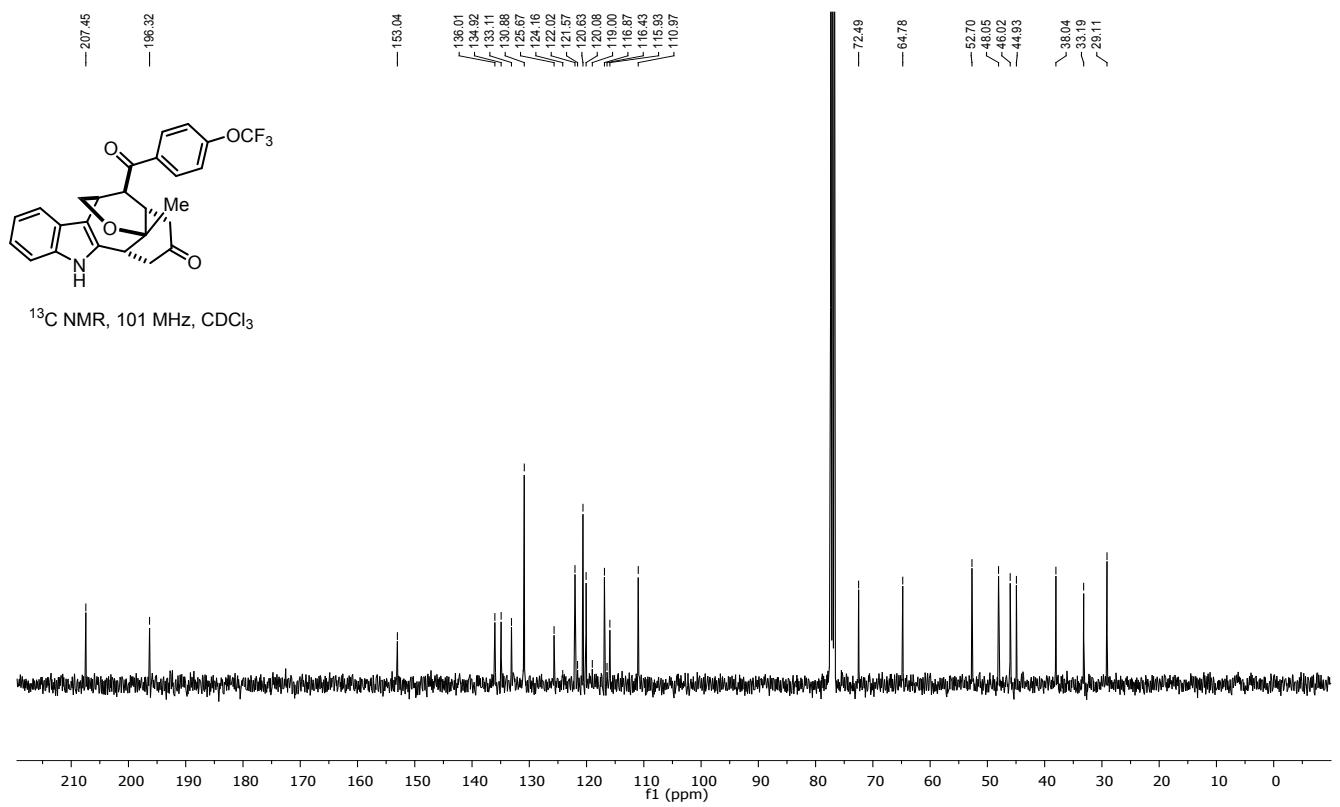
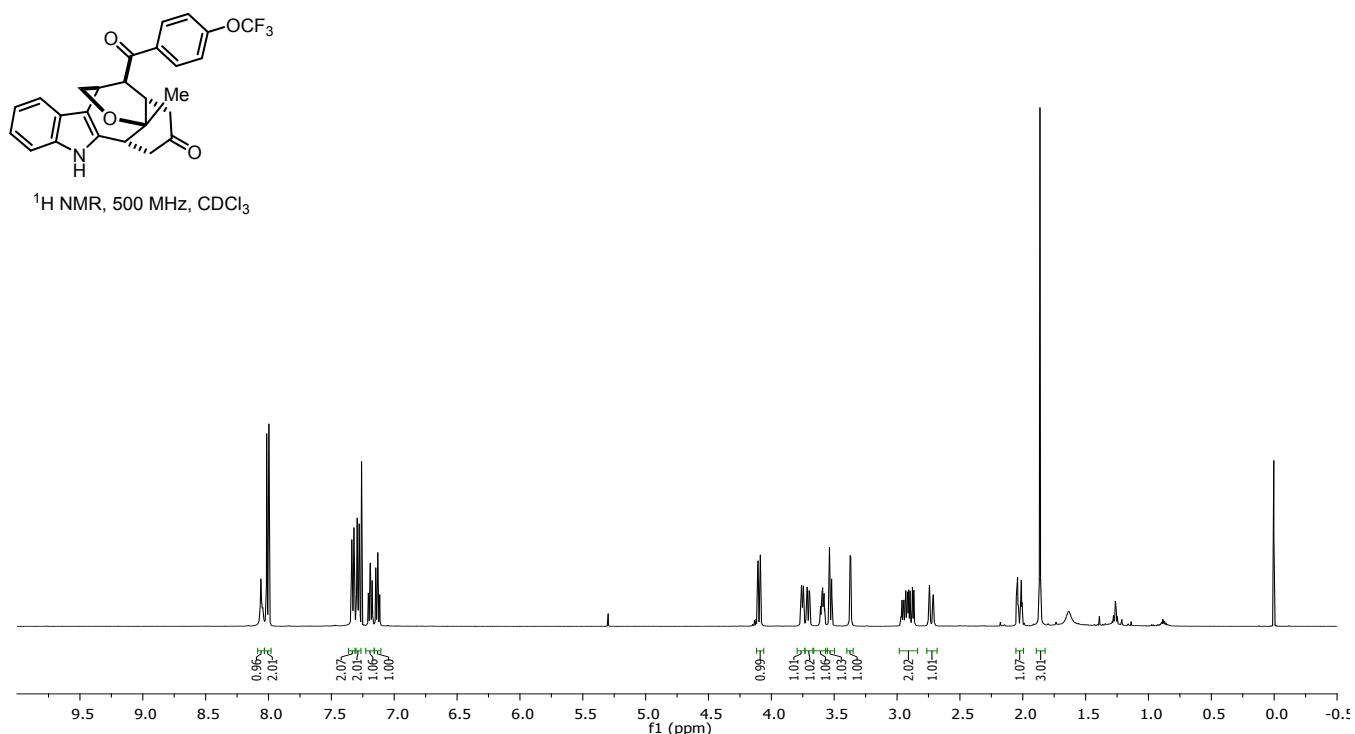
$^1\text{H}$  NMR, 500 MHz,  $\text{CDCl}_3$

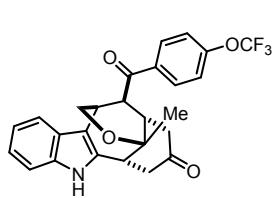


$^{13}\text{C}$  NMR, 101 MHz,  $\text{CDCl}_3$

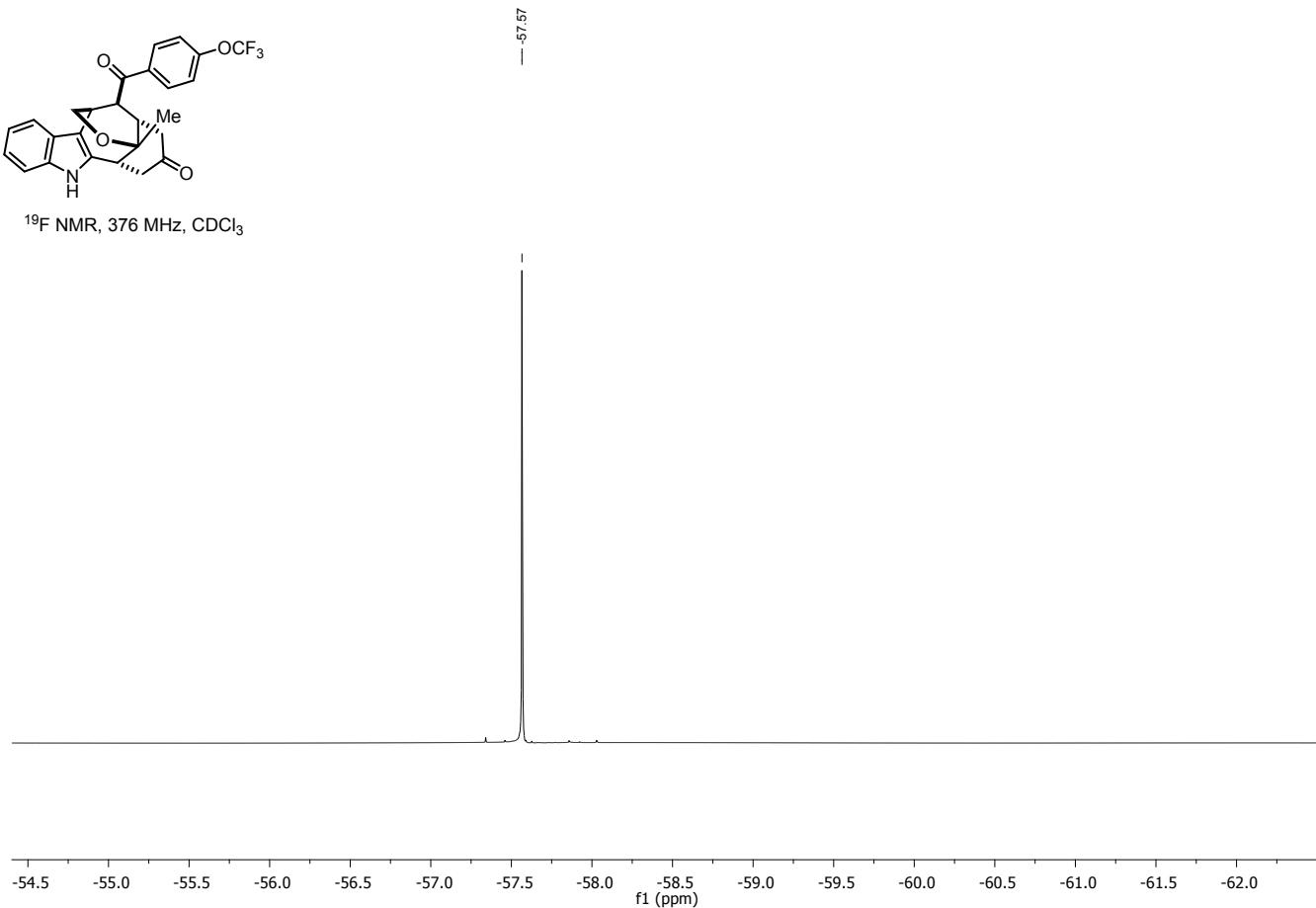


**4a-Methyl-13-(4-(trifluoromethoxy)benzoyl)-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3h):**

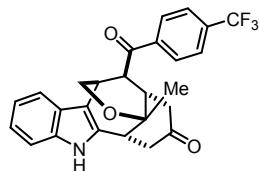




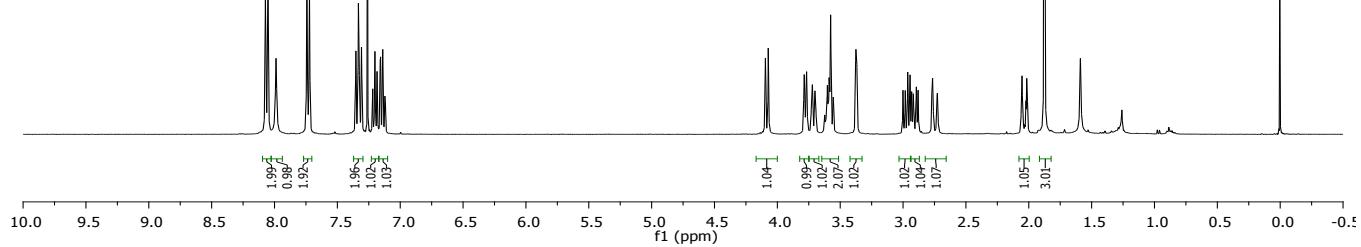
<sup>19</sup>F NMR, 376 MHz, CDCl<sub>3</sub>



**4a-Methyl-13-(4-(trifluoromethyl)benzoyl)-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3i):**

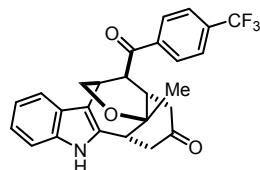


$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$

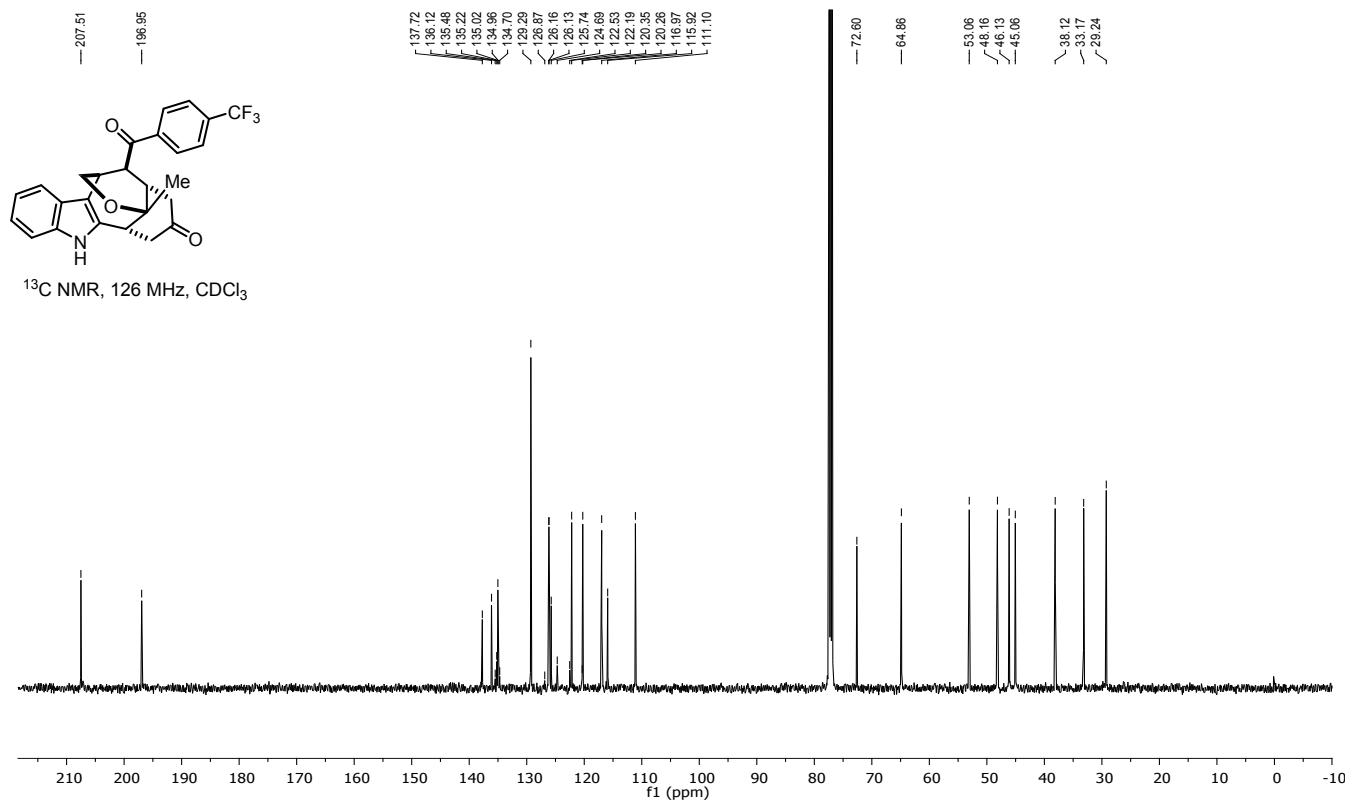


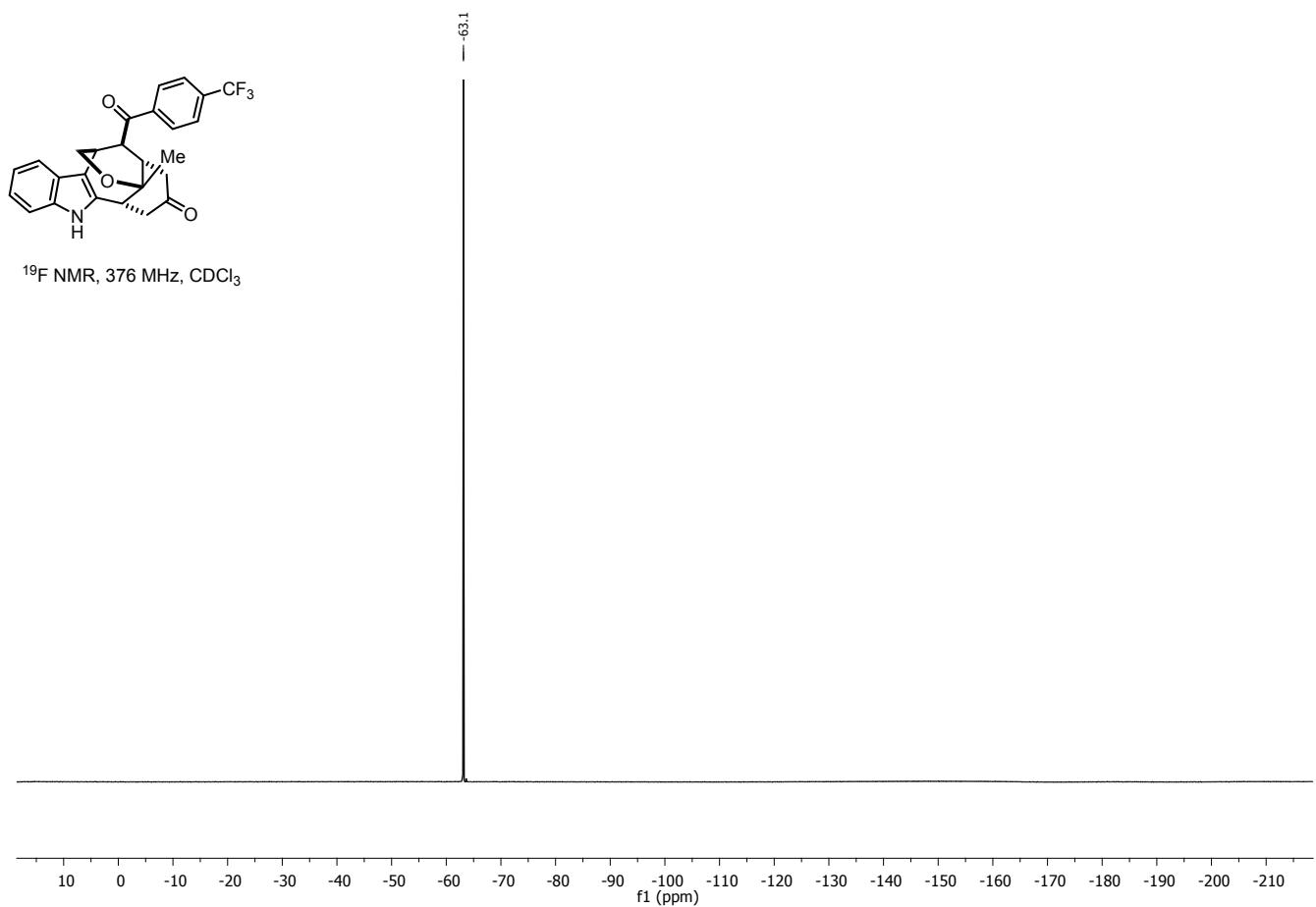
— 207.51

— 196.95

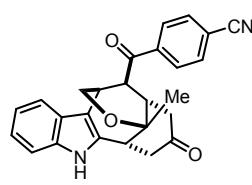


$^{13}\text{C}$  NMR, 126 MHz,  $\text{CDCl}_3$

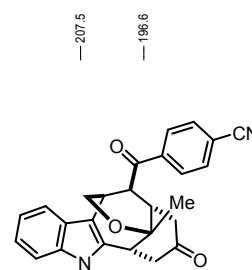
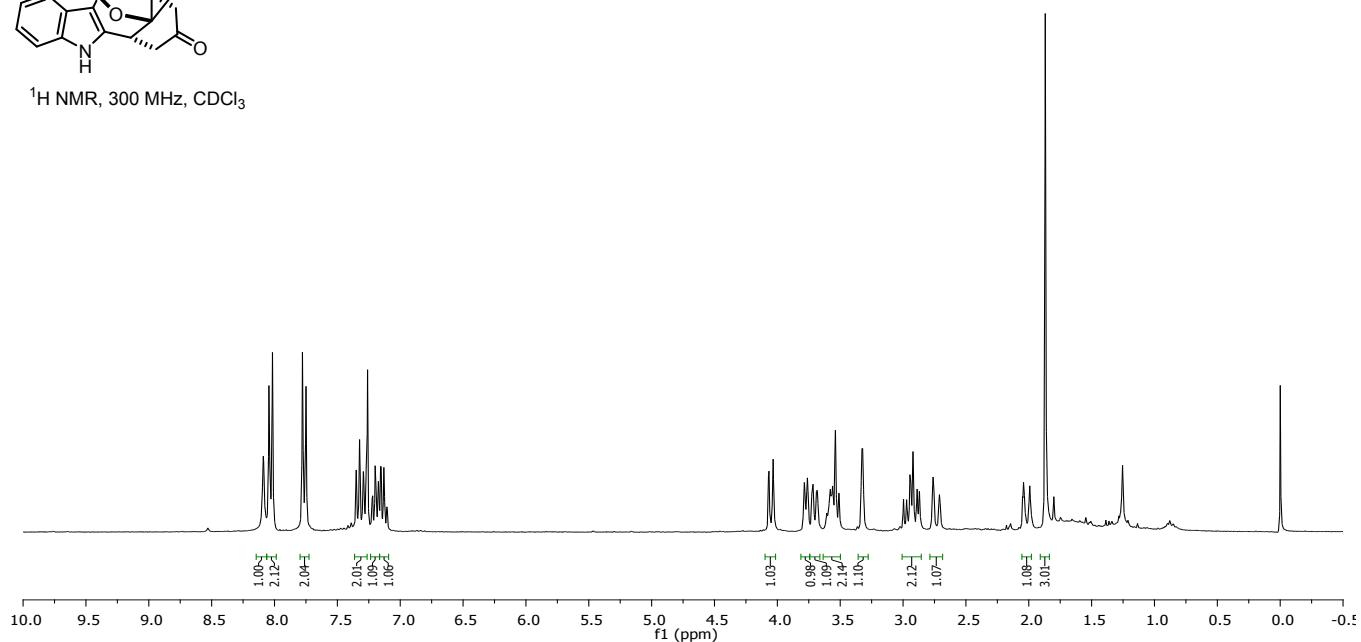




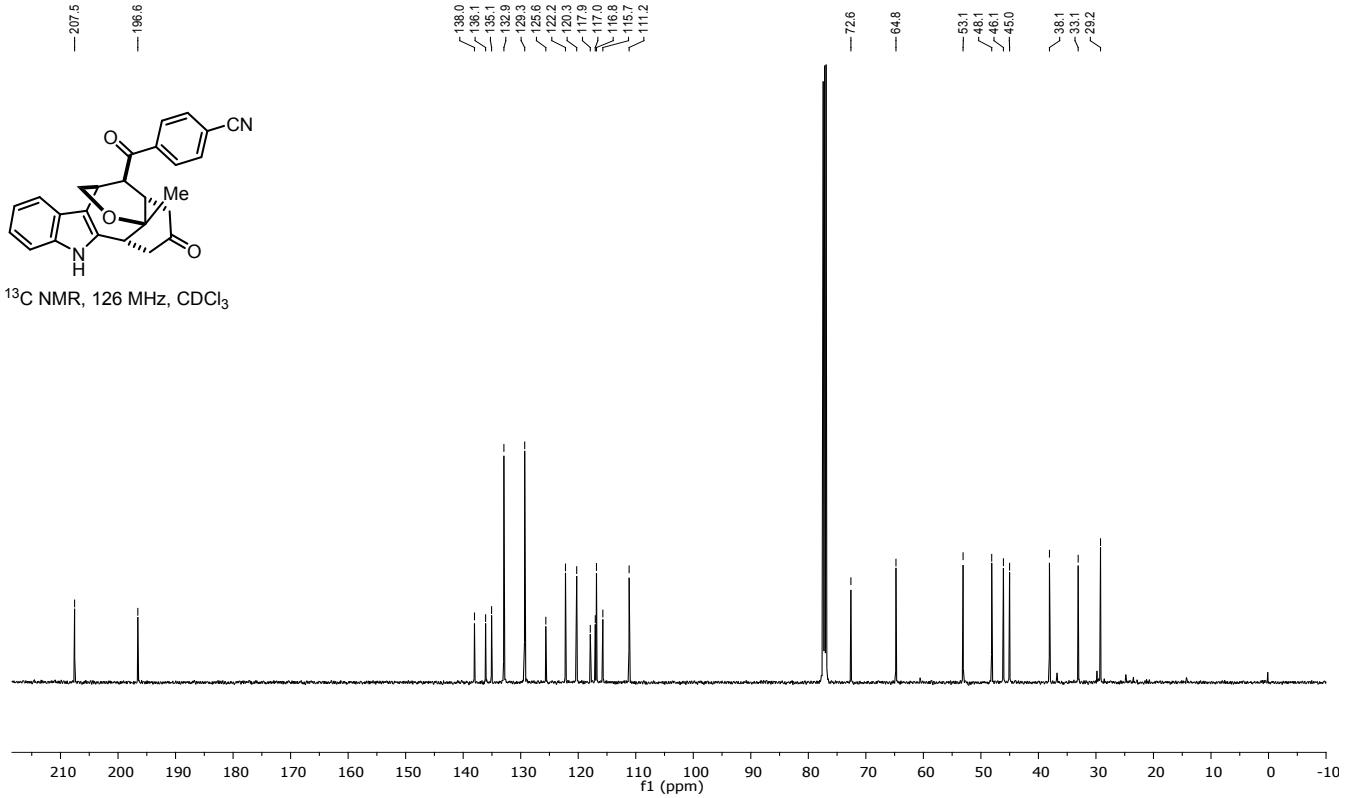
**4a-Methyl-2-oxo-2,3,4,4a,6,7,12,12b-octahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indole-13-carbonyl)benzonitrile (3j):**



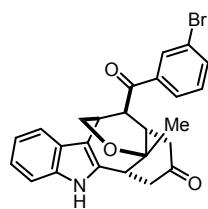
<sup>1</sup>H NMR, 300 MHz, CDCl<sub>3</sub>



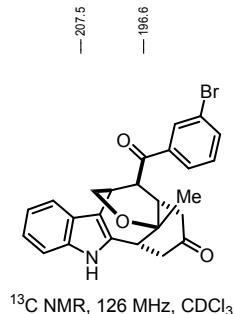
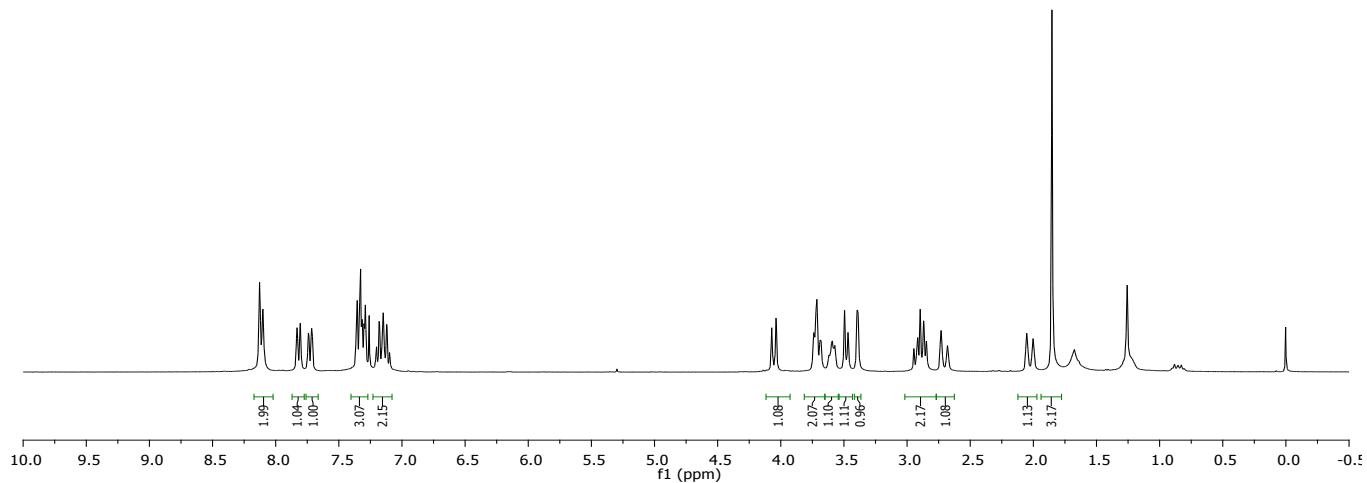
<sup>13</sup>C NMR, 126 MHz, CDCl<sub>3</sub>



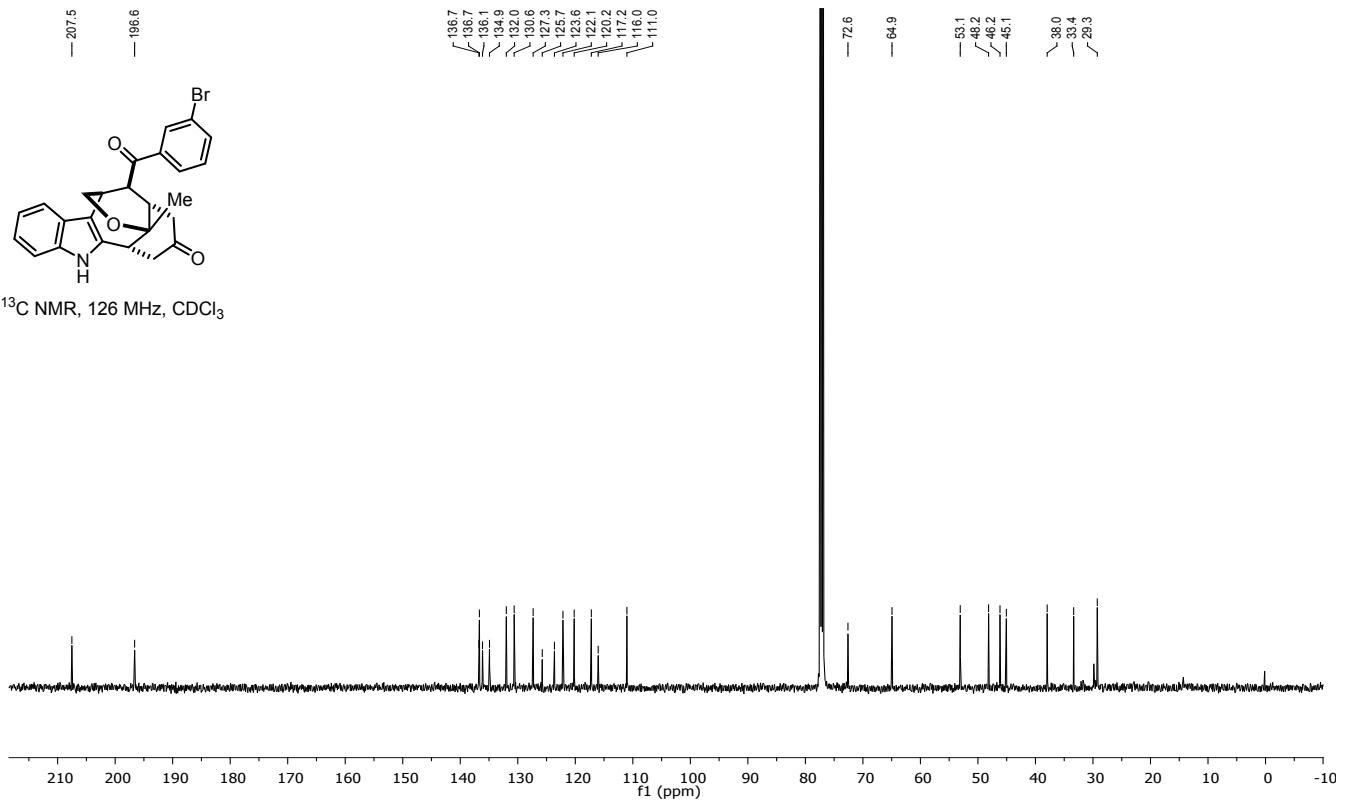
**13-(3-Bromobenzoyl)-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3k):**



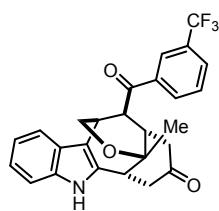
<sup>1</sup>H NMR, 400 MHz, CDCl<sub>3</sub>



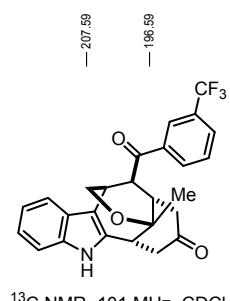
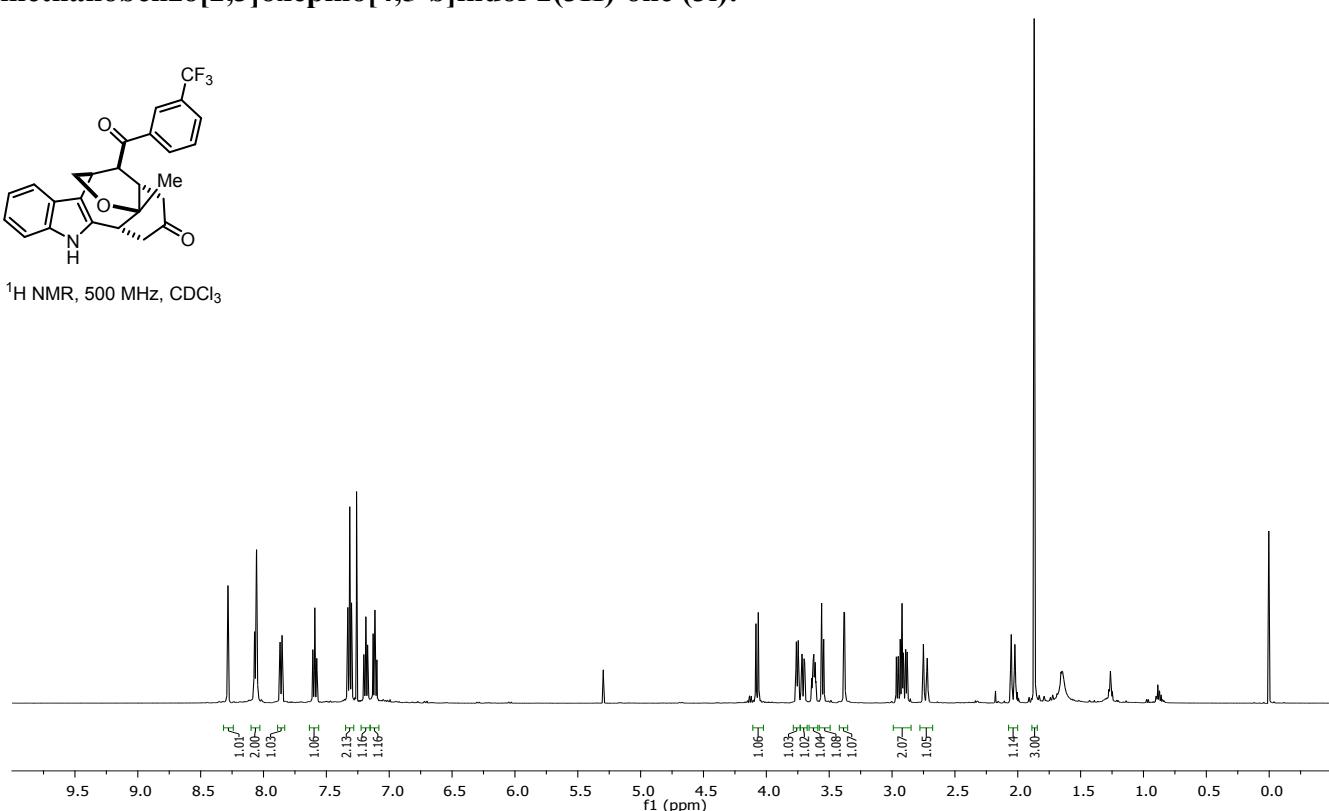
<sup>13</sup>C NMR, 126 MHz, CDCl<sub>3</sub>



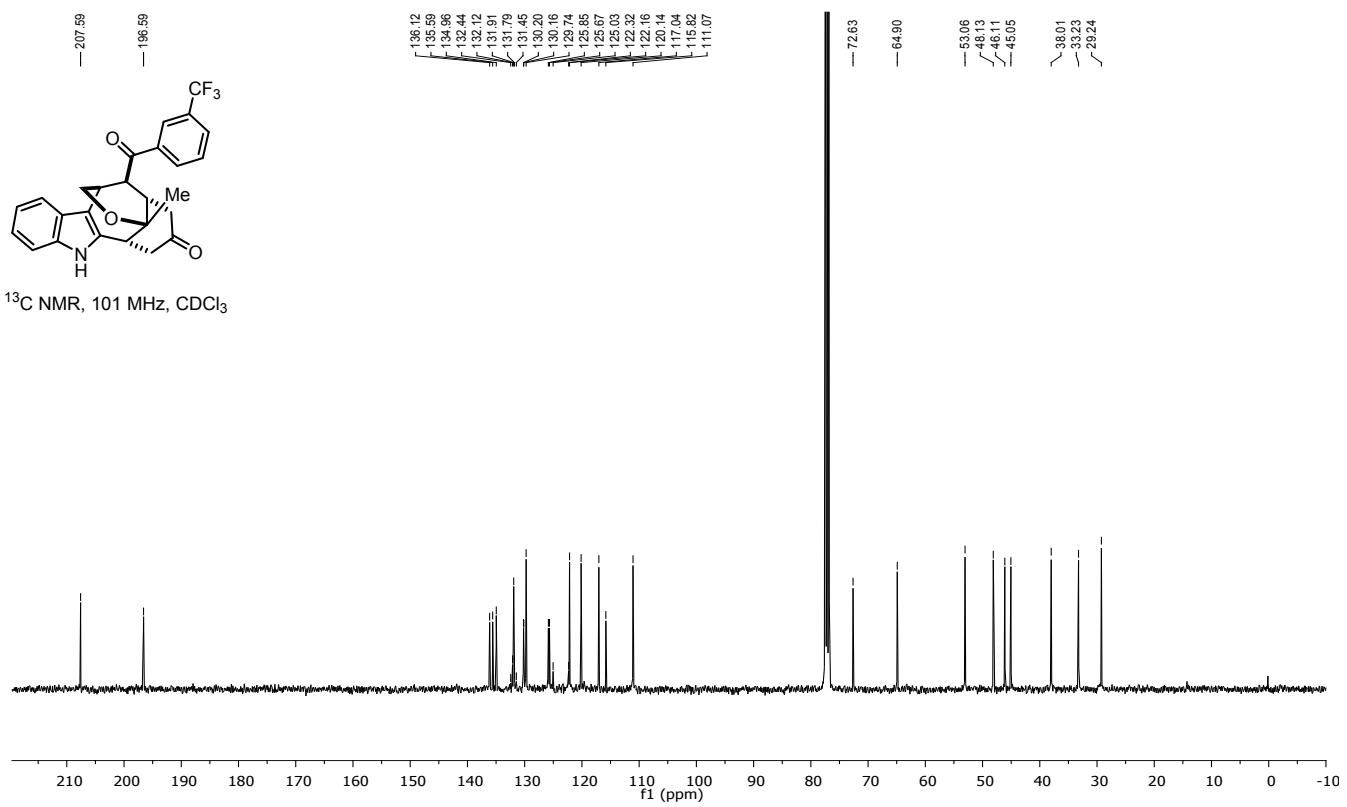
**4a-Methyl-13-(3-(trifluoromethyl)benzoyl)-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2(3H)-one (3l):**

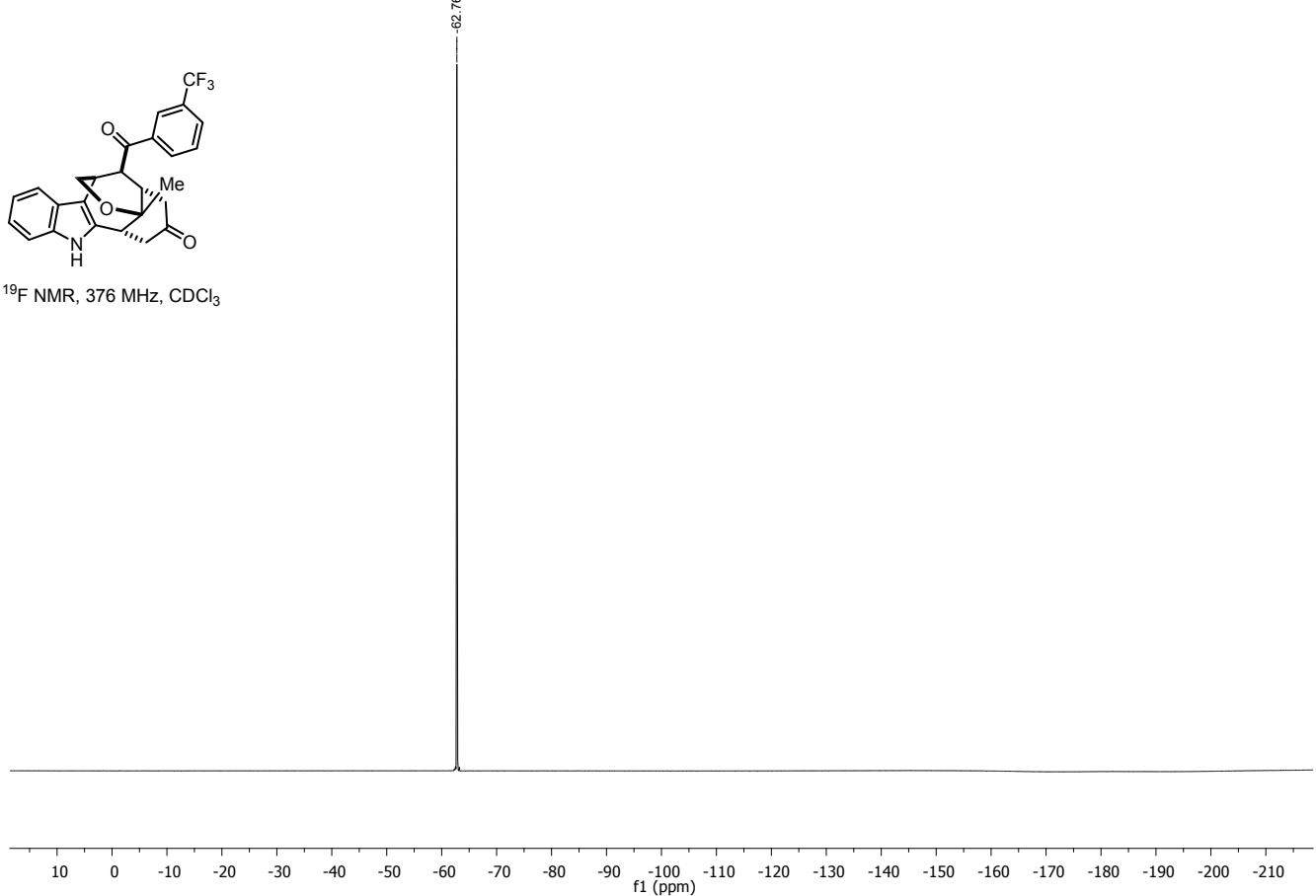


<sup>1</sup>H NMR, 500 MHz, CDCl<sub>3</sub>

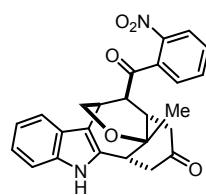


<sup>13</sup>C NMR, 101 MHz, CDCl<sub>3</sub>

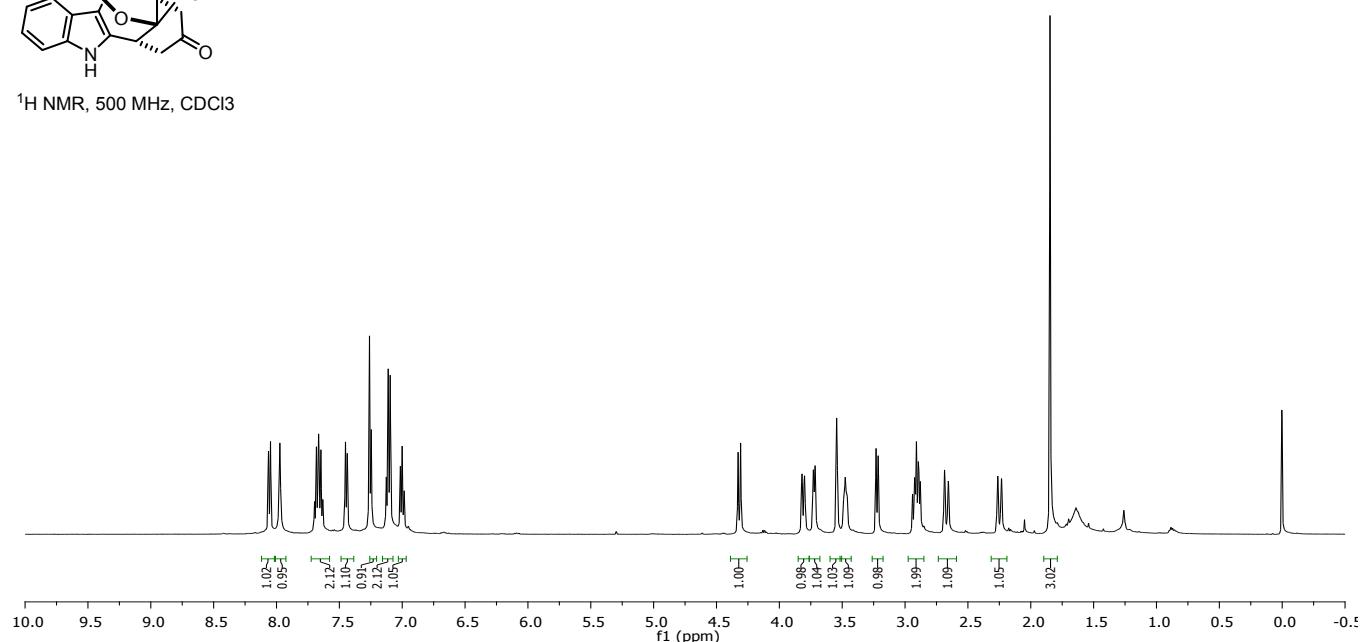




**4a-Methyl-13-(2-nitrobenzoyl)-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3m):**



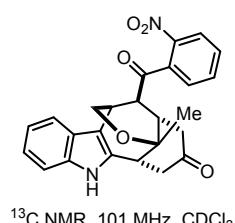
<sup>1</sup>H NMR, 500 MHz, CDCl<sub>3</sub>



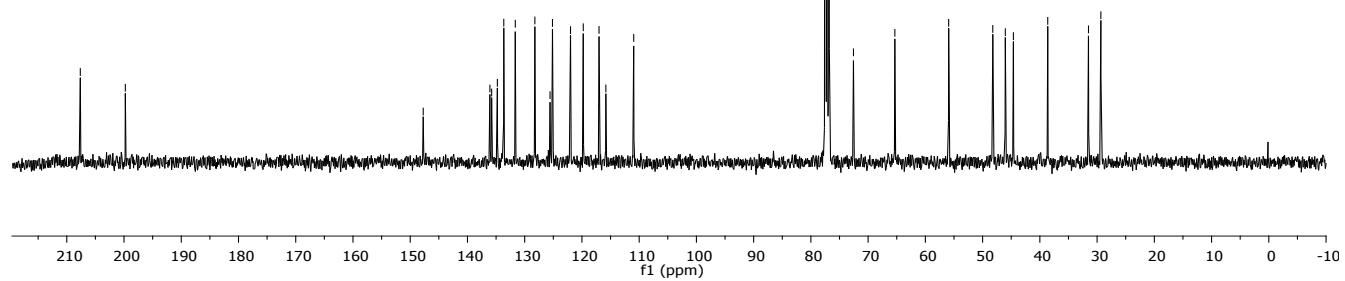
— 207.6  
— 199.8

— 136.1  
— 135.8  
— 134.8  
— 133.7  
— 131.6  
— 125.6  
— 125.1  
— 122.0  
— 119.8  
— 117.0  
— 115.8  
— 111.0

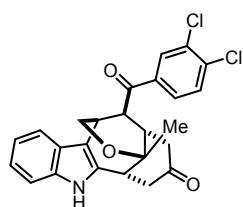
— 72.6  
— 65.3  
— 55.9  
— 48.2  
— 46.0  
— 44.6  
— 38.6  
— 31.5  
— 29.3



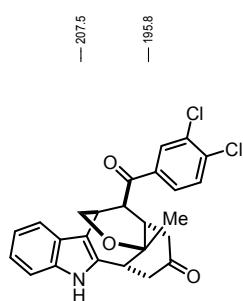
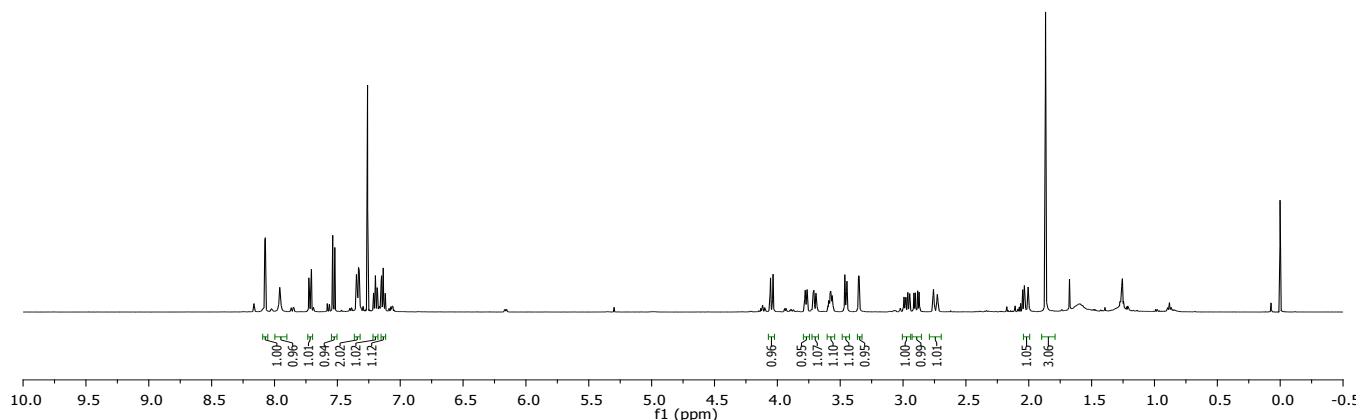
<sup>13</sup>C NMR, 101 MHz, CDCl<sub>3</sub>



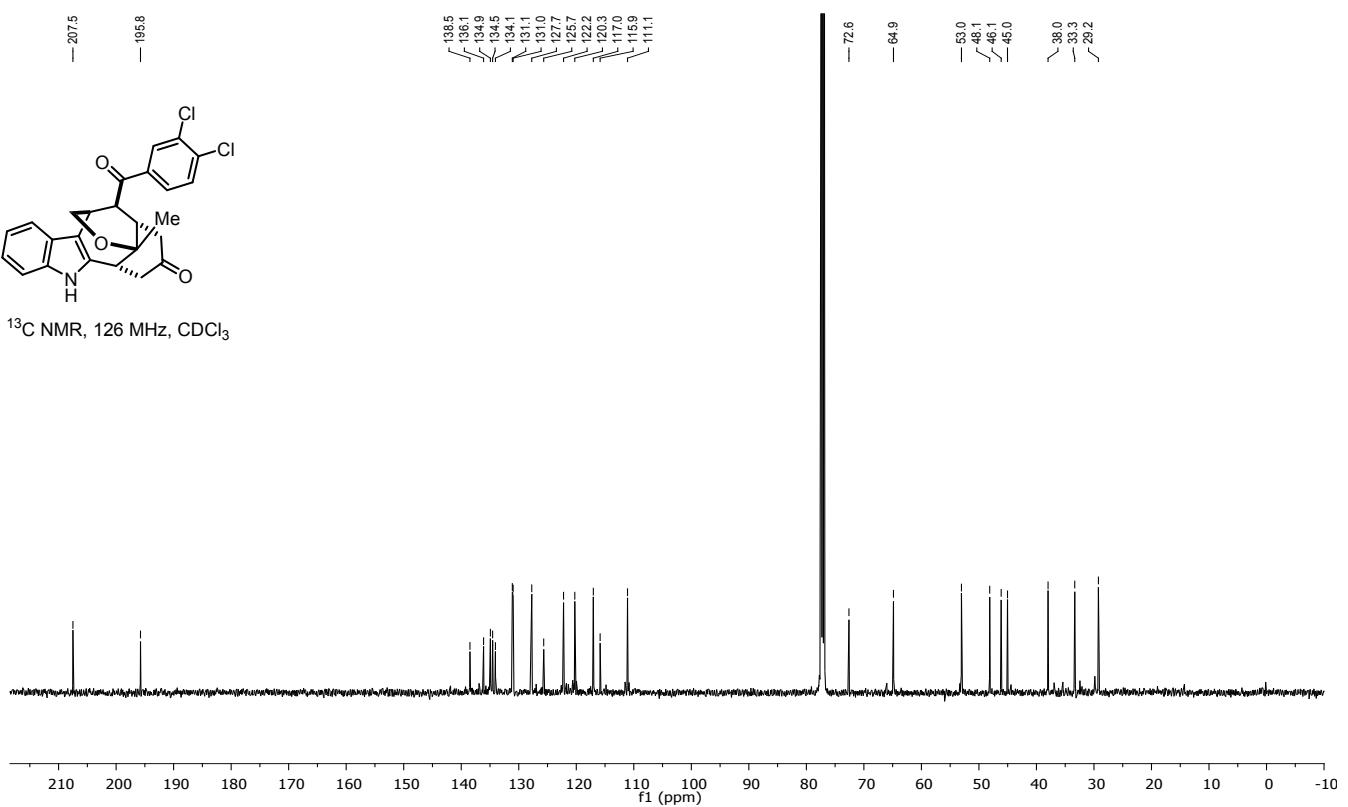
**13-(3,4-Dichlorobenzoyl)-4a-methyl-4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3n):**



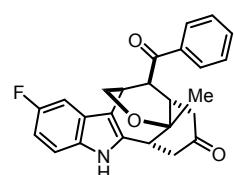
$^1\text{H}$  NMR, 500 MHz,  $\text{CDCl}_3$



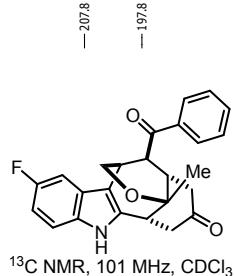
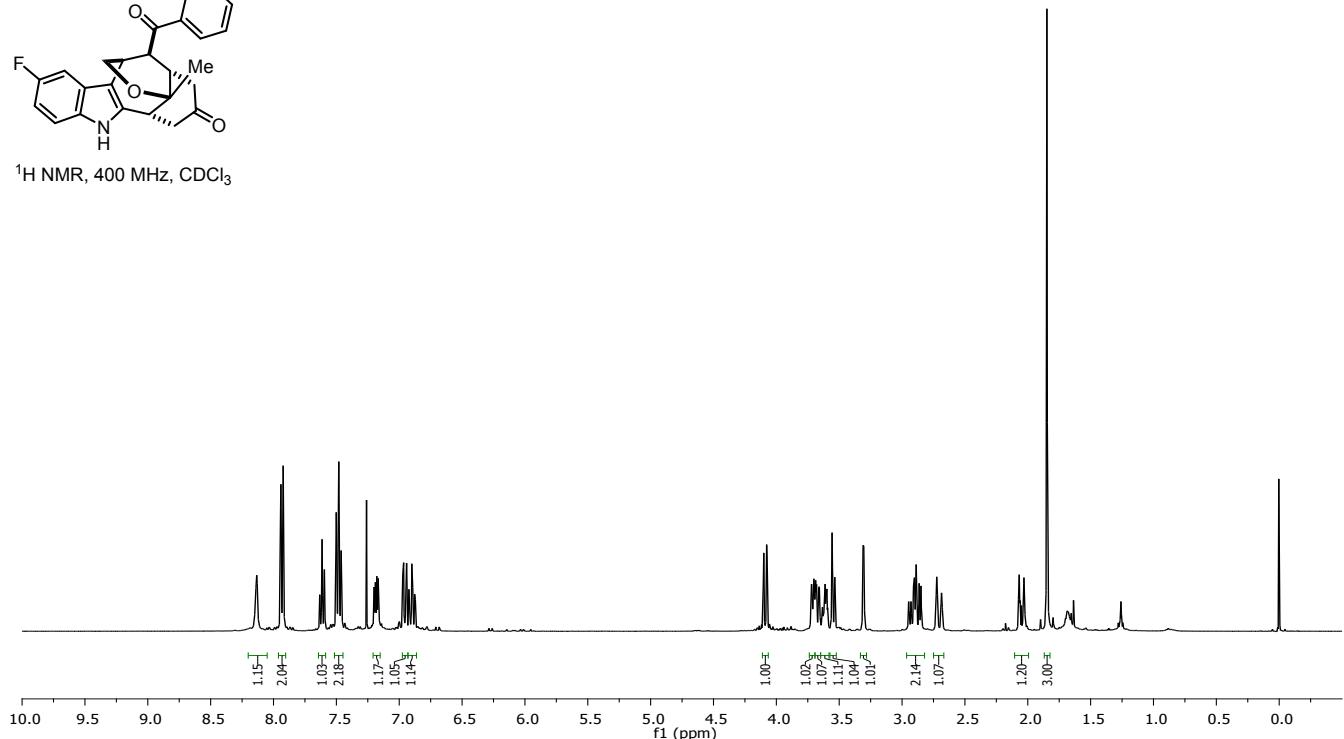
$^{13}\text{C}$  NMR, 126 MHz,  $\text{CDCl}_3$



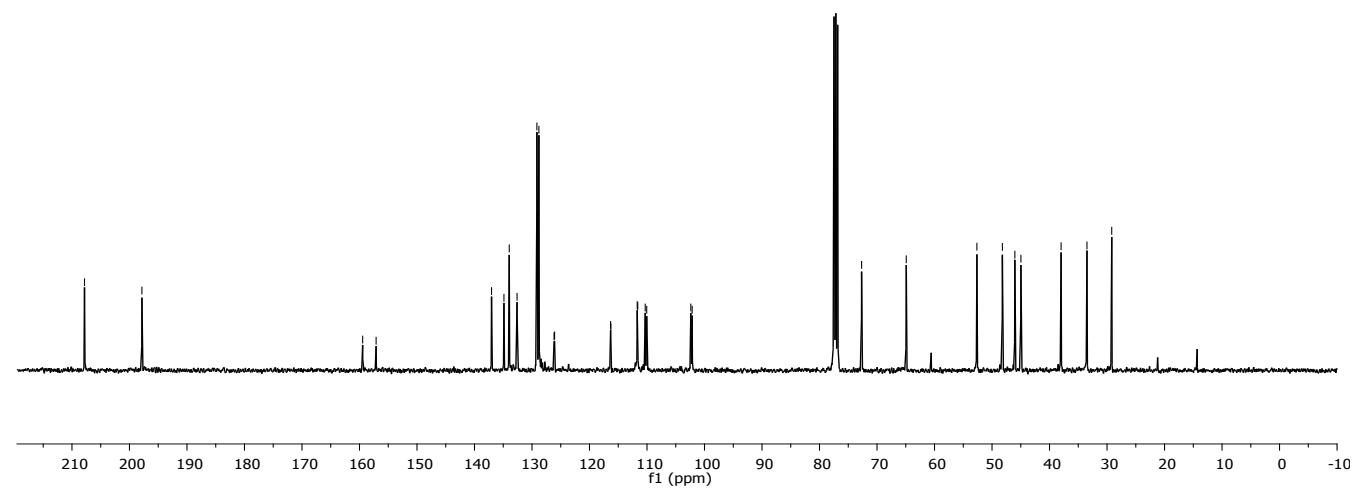
**13-Benzoyl-9-fluoro-4a-methyl-4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3o):**

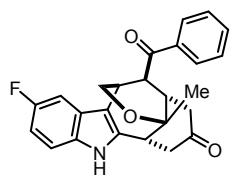


<sup>1</sup>H NMR, 400 MHz, CDCl<sub>3</sub>

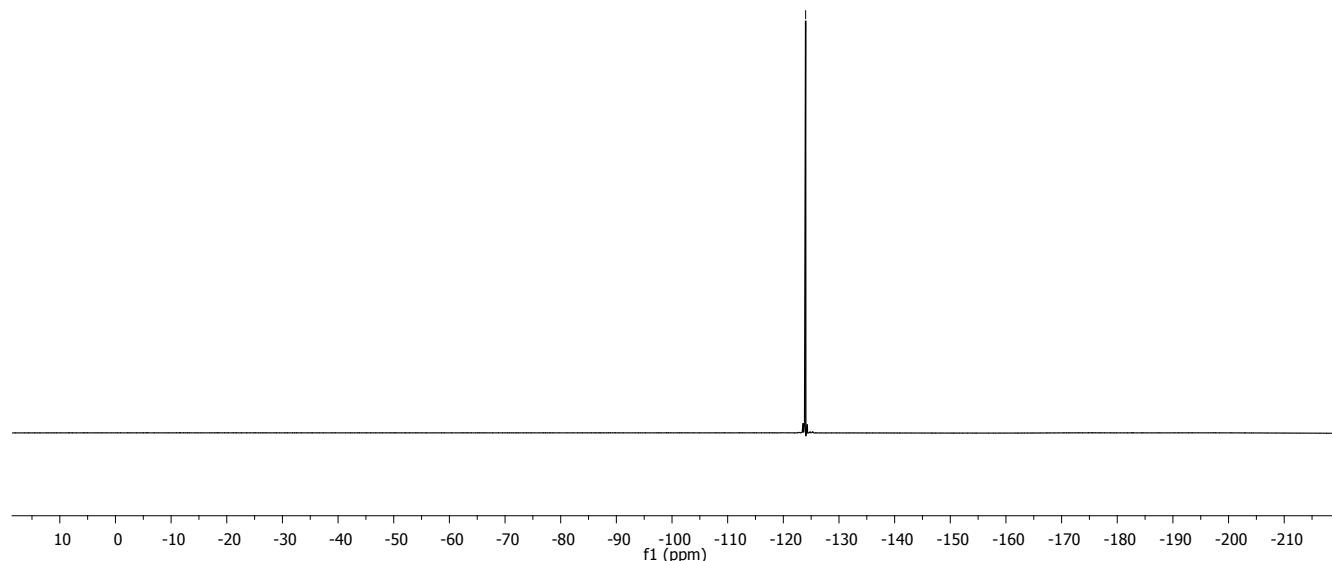


<sup>13</sup>C NMR, 101 MHz, CDCl<sub>3</sub>

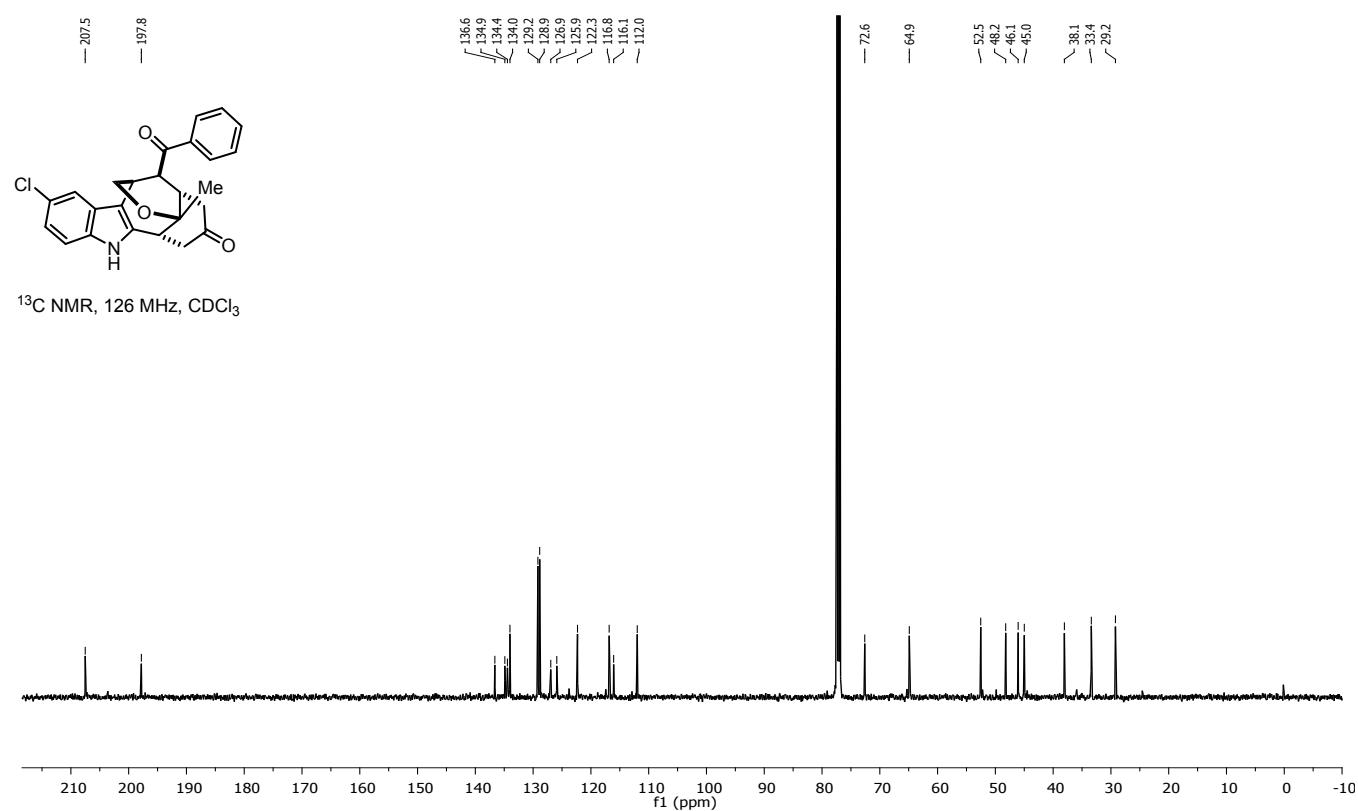
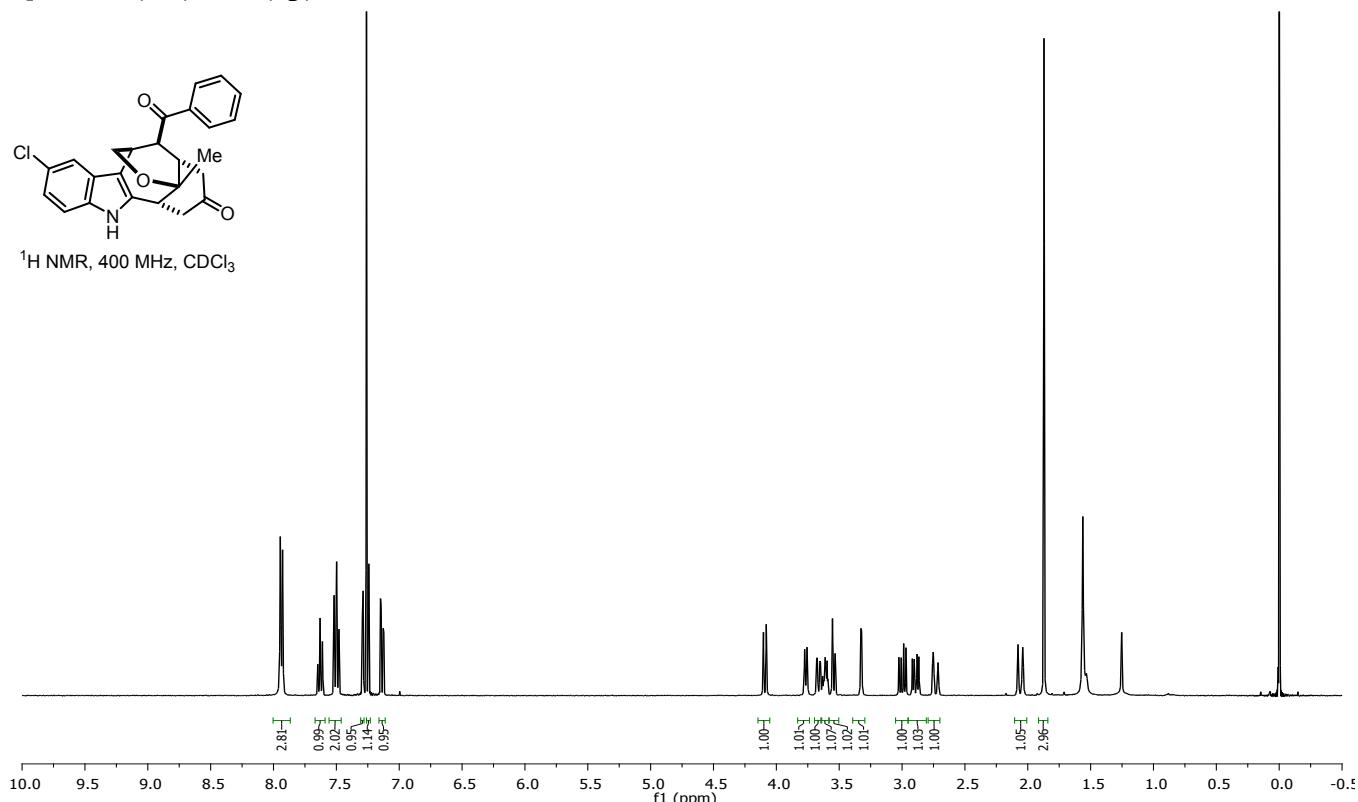




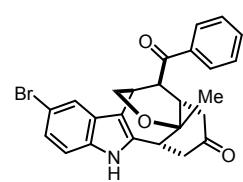
<sup>19</sup>F NMR, 376 MHz, CDCl<sub>3</sub>



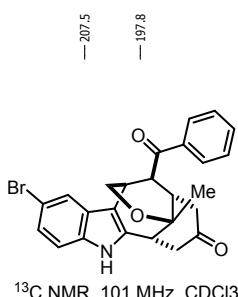
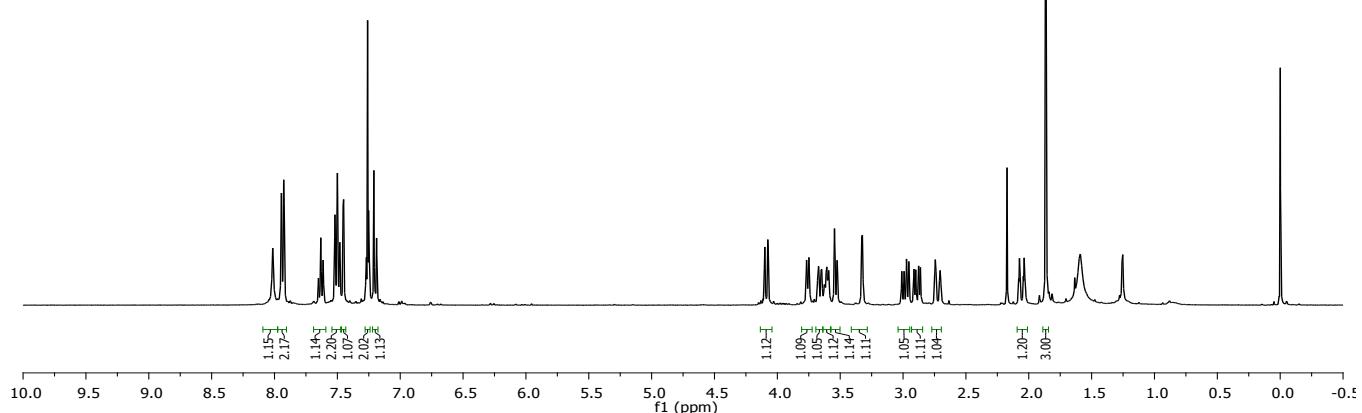
**13-Benzoyl-9-chloro-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3p):**



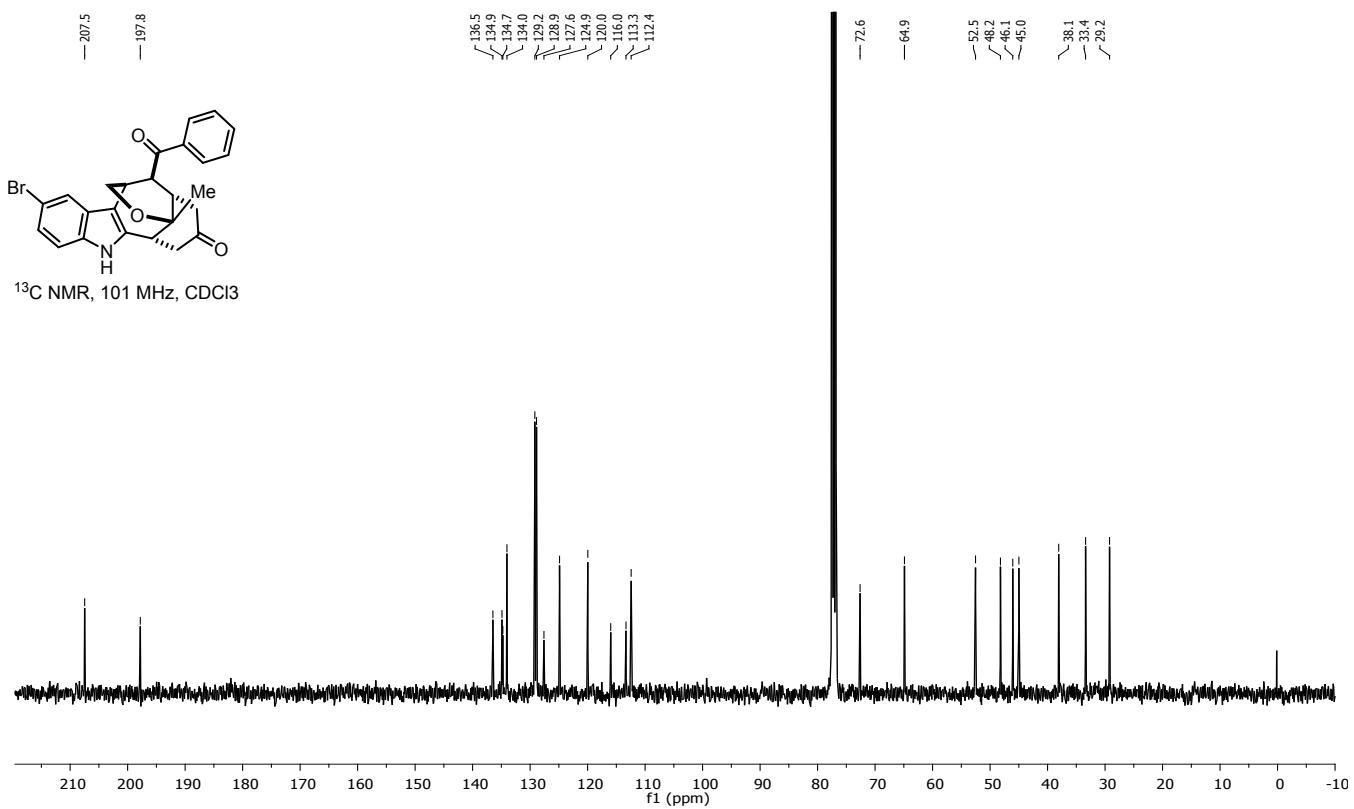
**13-Benzoyl-9-bromo-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3q):**



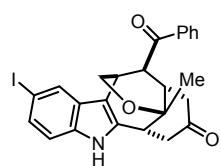
$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$



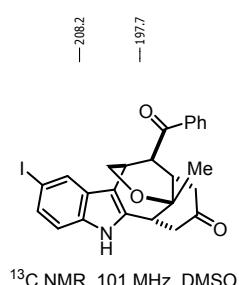
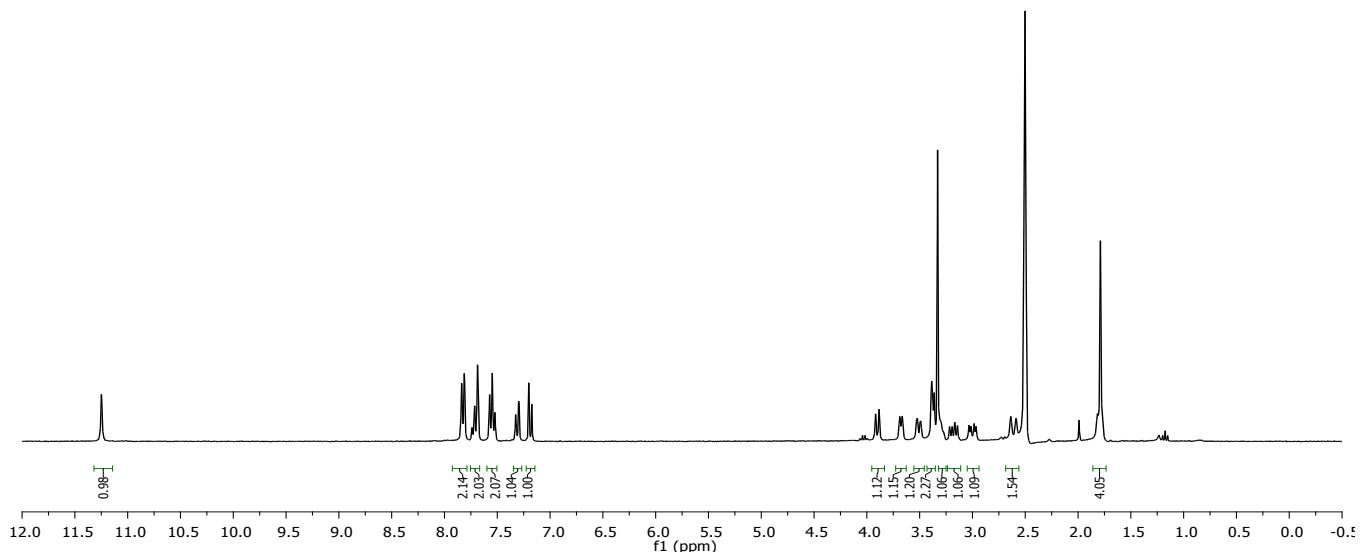
$^{13}\text{C}$  NMR, 101 MHz,  $\text{CDCl}_3$



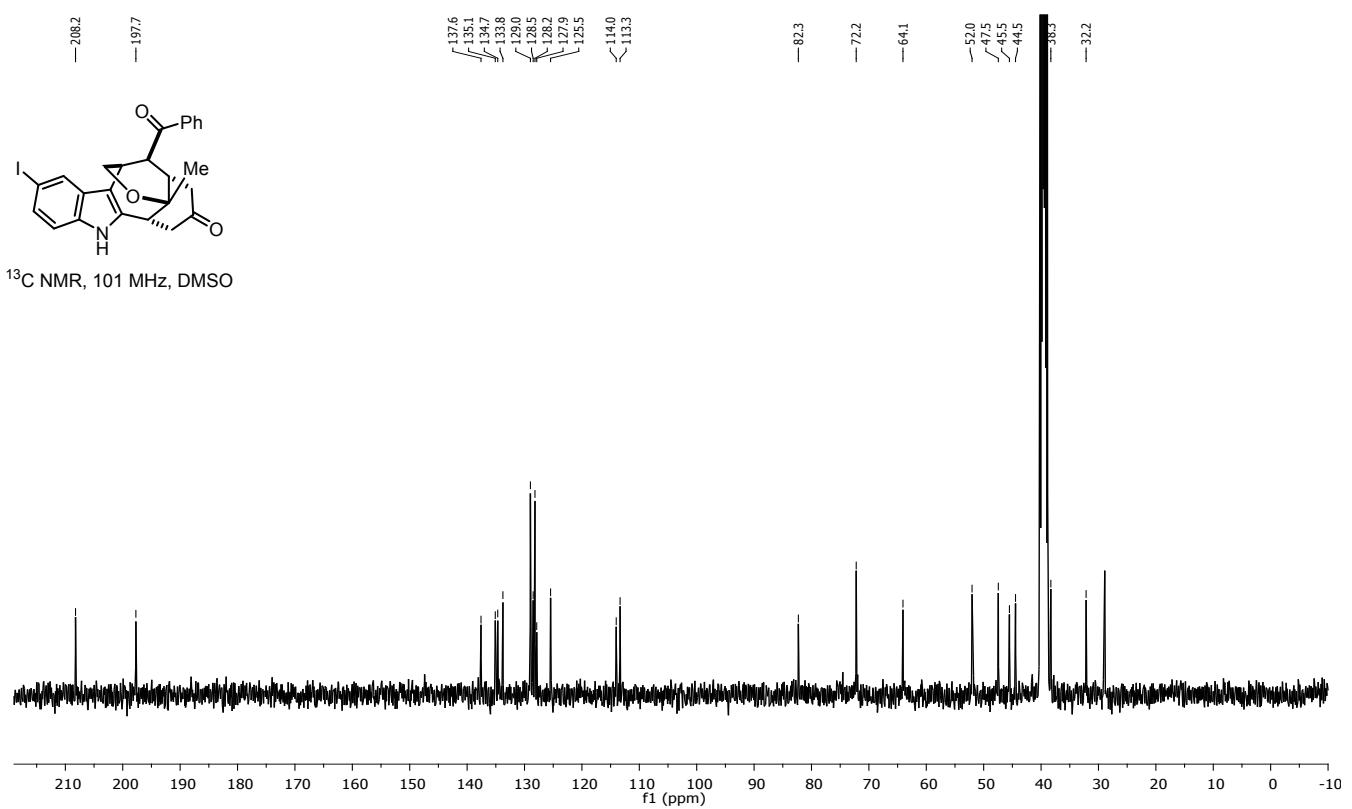
**13-Benzoyl-9-iodo-4a-methyl-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2(3H)-one (3r):**



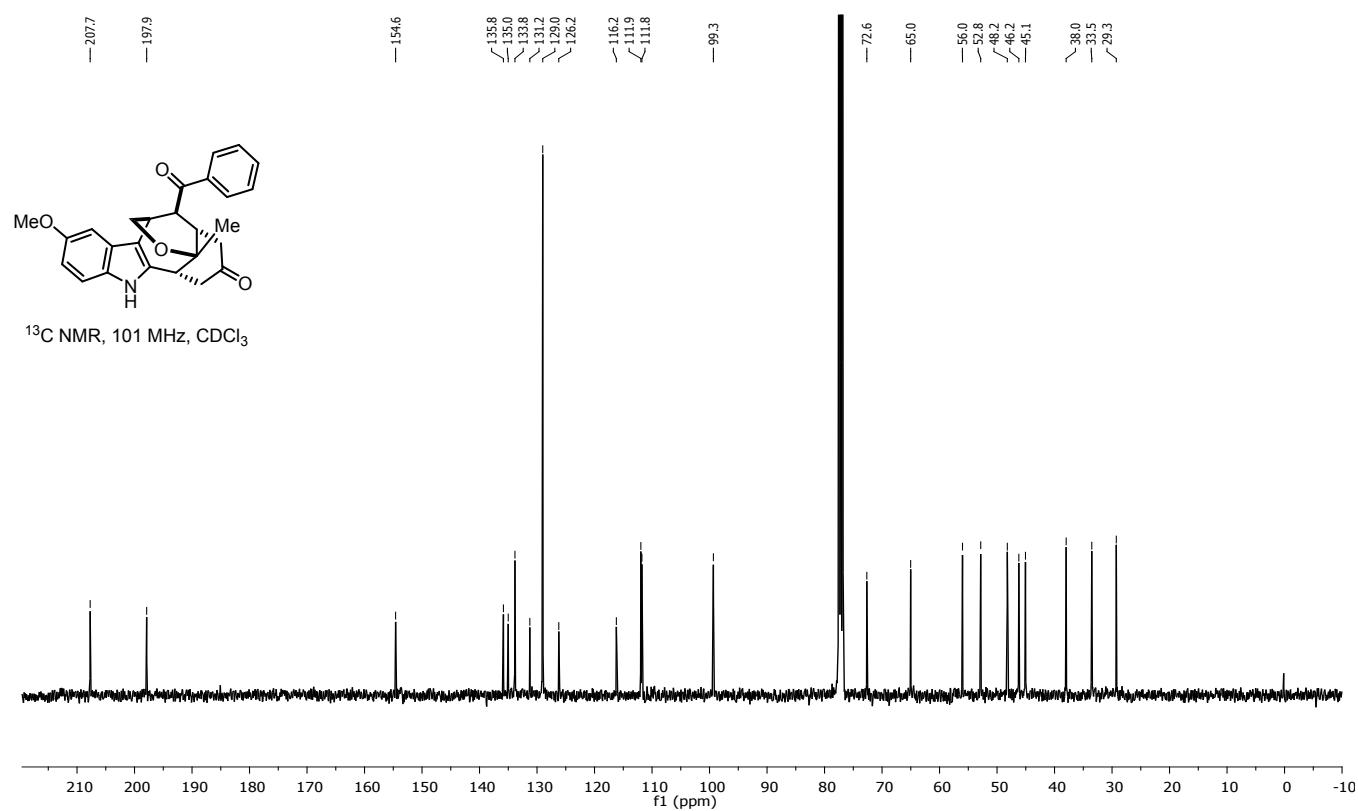
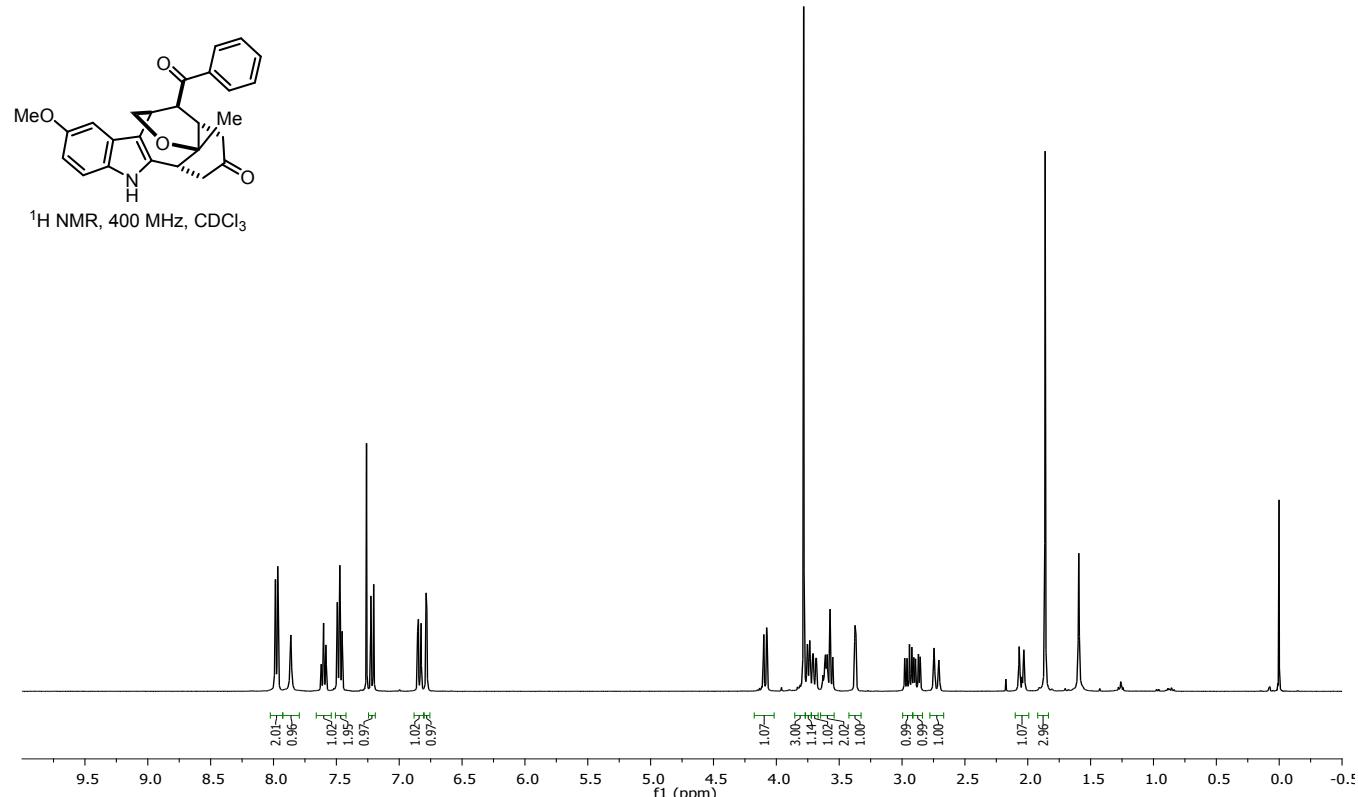
<sup>1</sup>H NMR, 300 MHz, DMSO



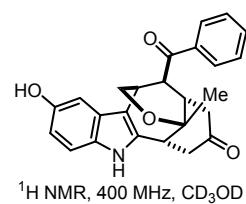
<sup>13</sup>C NMR, 101 MHz, DMSO



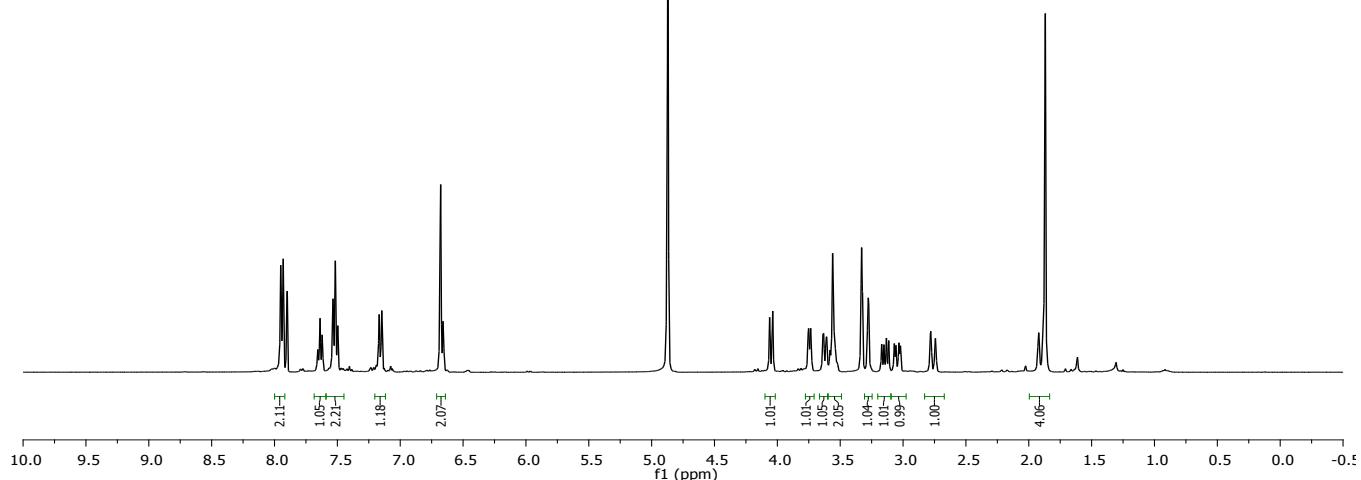
**13-Benzoyl-9-methoxy-4a-methyl-4,4a,6,7,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3s):**



**13-Benzoyl-9-hydroxy-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3t):**



$^1\text{H}$  NMR, 400 MHz, CD<sub>3</sub>OD



—211.0

—199.5

—151.7

—137.4  
—136.7  
—134.7  
—132.6  
—130.1  
—129.6  
—127.3

—115.5  
—112.3  
—112.1

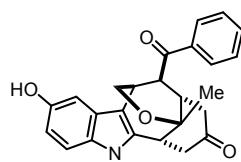
—102.1

—79.5  
—74.1

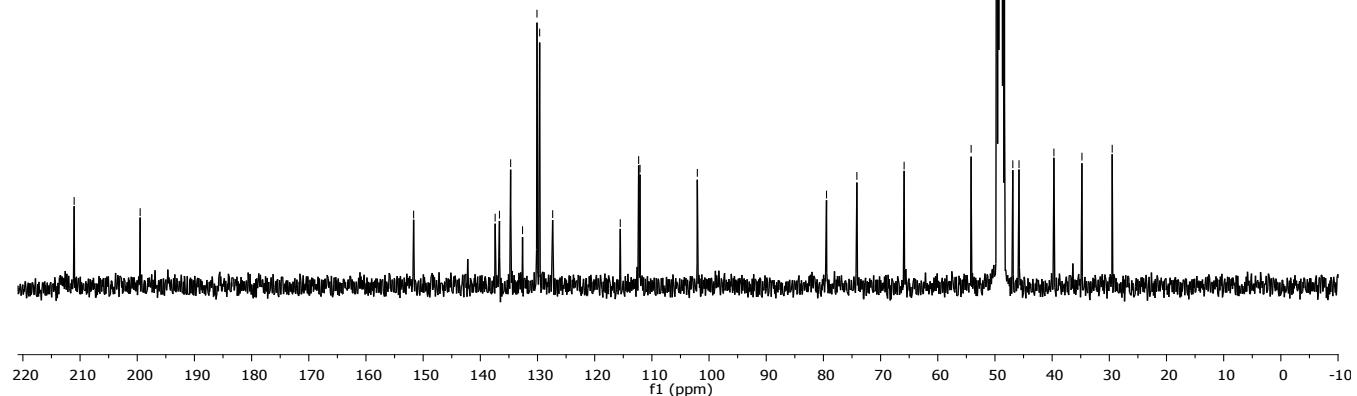
—65.9

—54.2

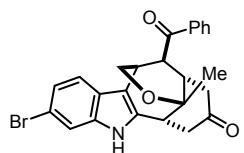
—46.9  
—45.8  
—39.7  
—34.8  
—29.5



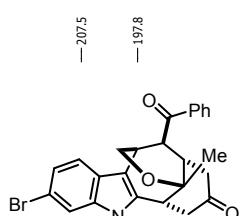
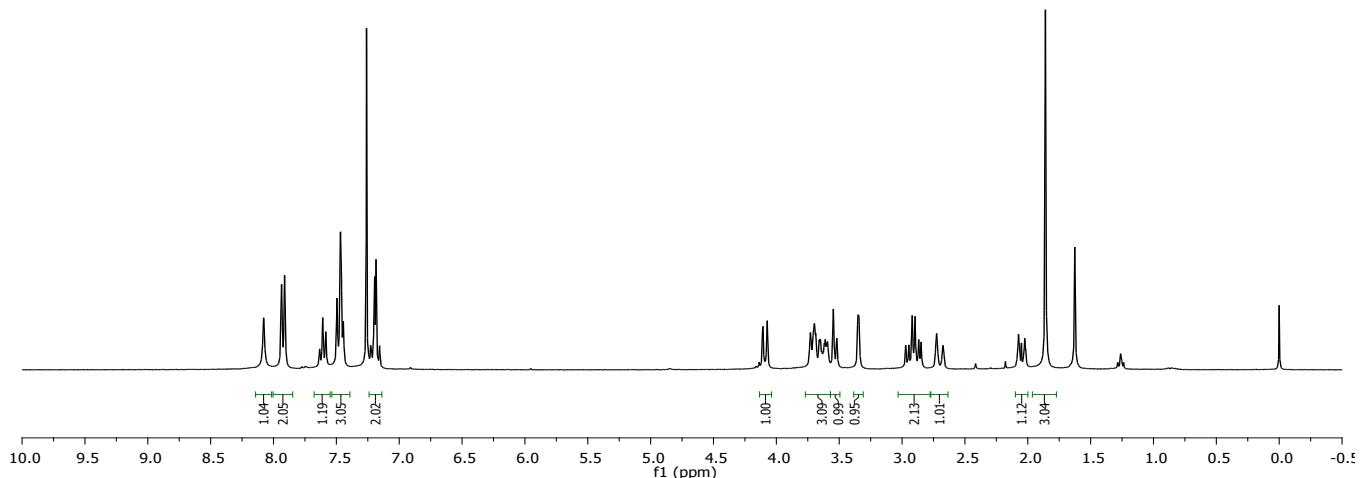
$^{13}\text{C}$  NMR, 101 MHz, CD<sub>3</sub>OD



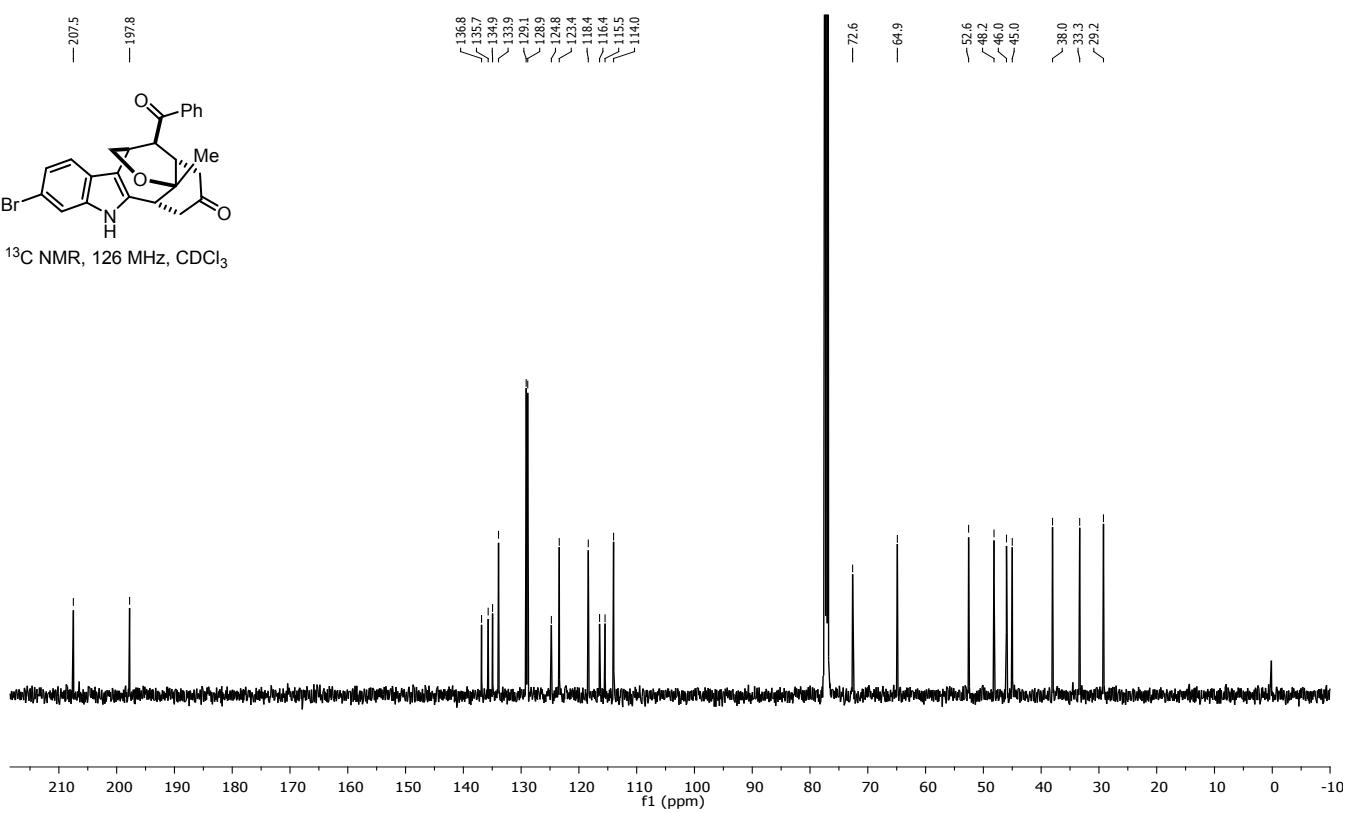
**13-Benzoyl-10-bromo-4a-methyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3u):**



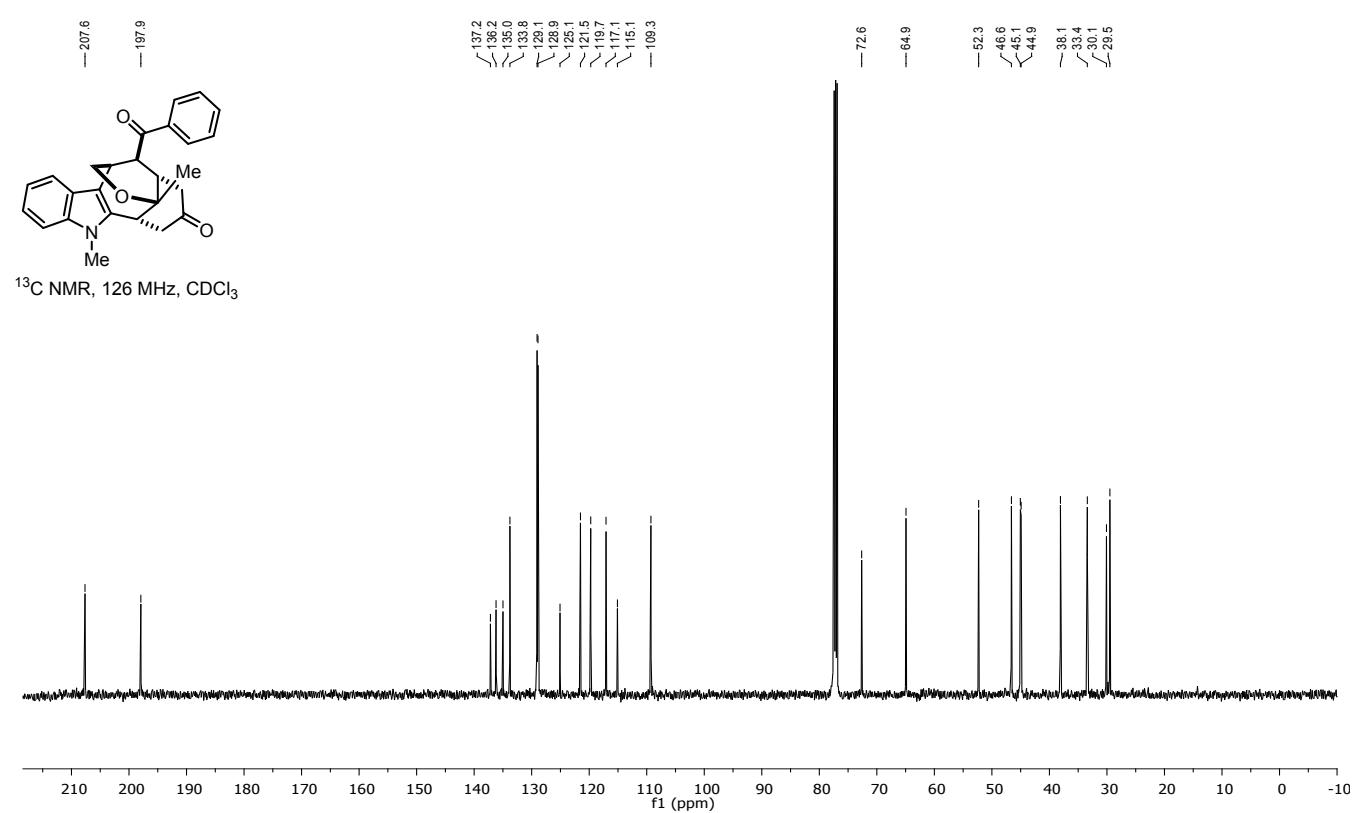
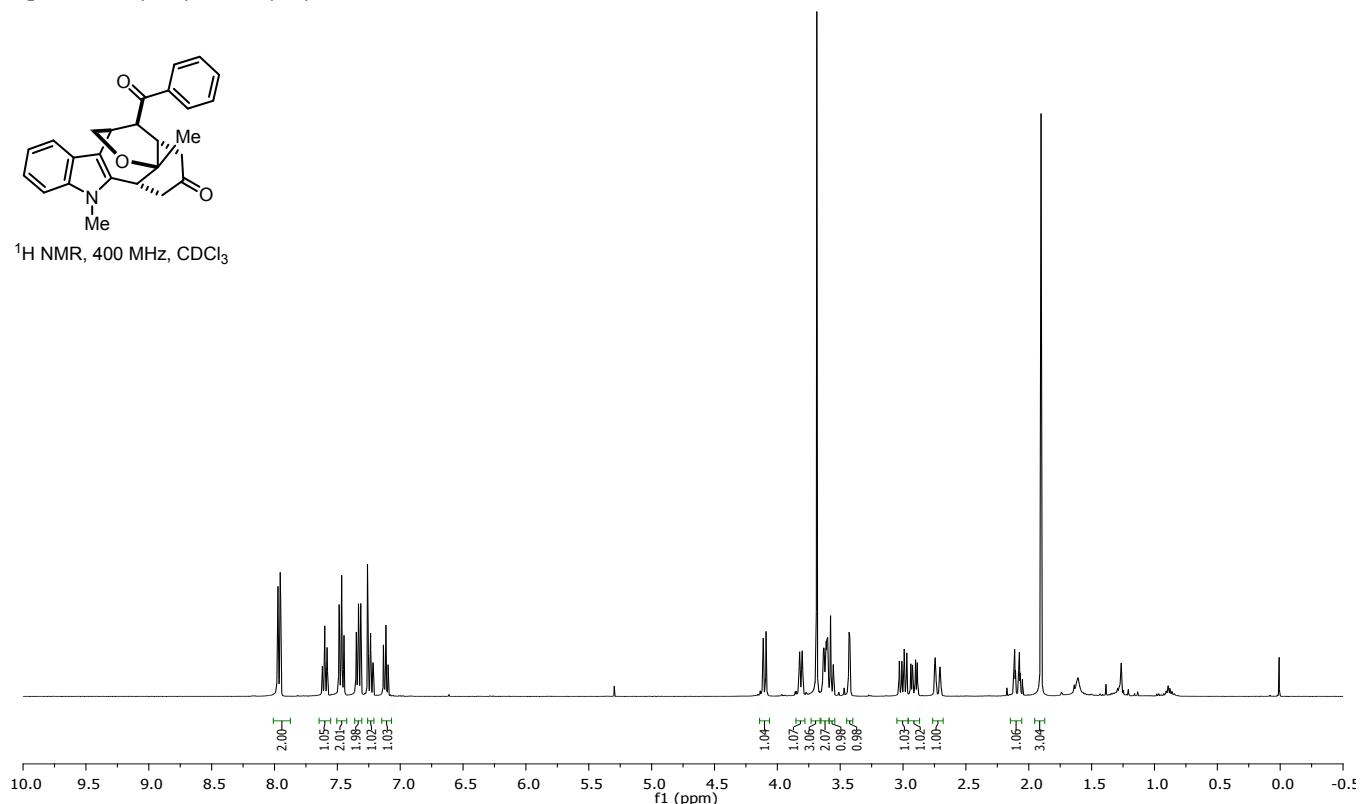
<sup>1</sup>H NMR, 300 MHz, CDCl<sub>3</sub>



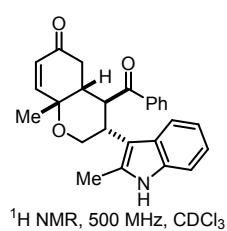
<sup>13</sup>C NMR, 126 MHz, CDCl<sub>3</sub>



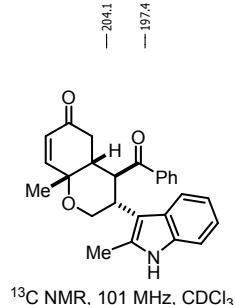
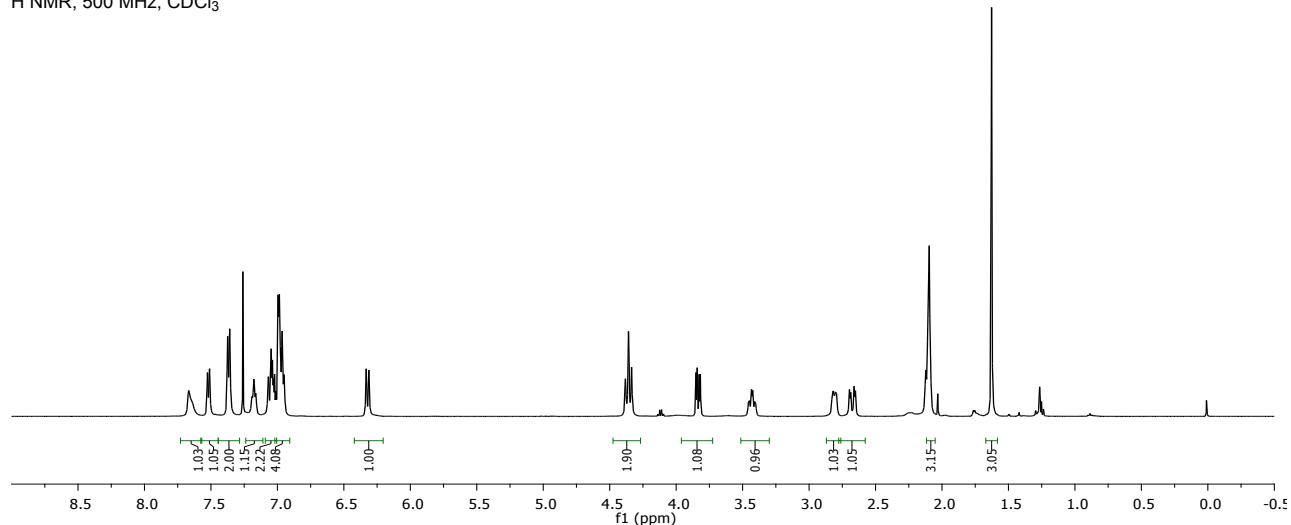
**13-Benzoyl-4a,12-dimethyl-4,4a,6,7,12,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (3v):**



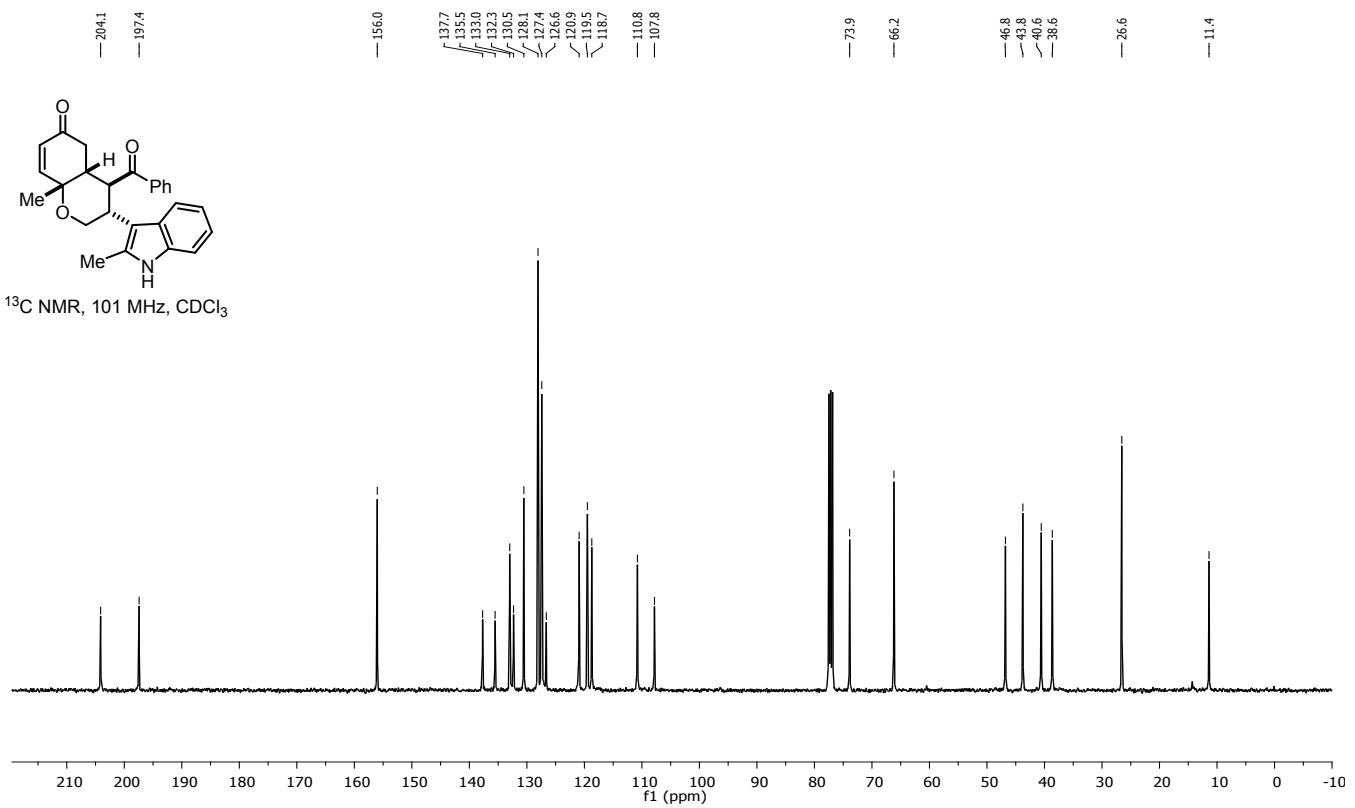
**4-Benzoyl-8a-methyl-3-(2-methyl-1*H*-indol-3-yl)-3,4,4a,8a-tetrahydro-2*H*-chromen-6(5*H*)-one (6):**



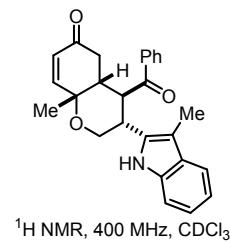
<sup>1</sup>H NMR, 500 MHz, CDCl<sub>3</sub>



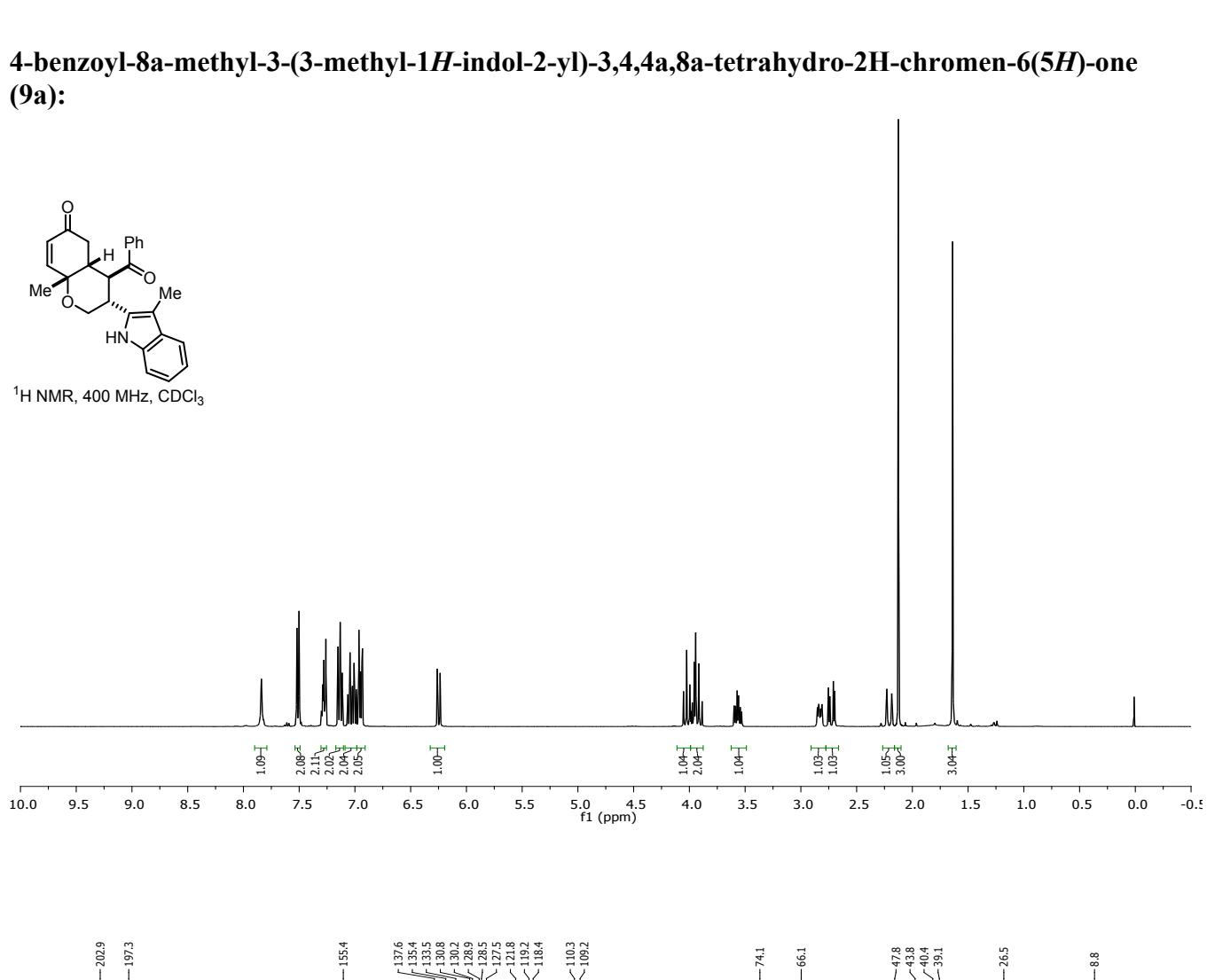
<sup>13</sup>C NMR, 101 MHz, CDCl<sub>3</sub>



**4-benzoyl-8a-methyl-3-(3-methyl-1*H*-indol-2-yl)-3,4,4a,8a-tetrahydro-2*H*-chromen-6(*5H*)-one  
(9a):**



$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$



—202.9  
—197.3

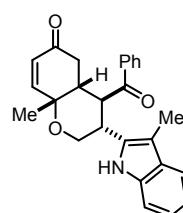
—155.4

—137.6  
—135.4  
—133.5  
—130.8  
—130.2  
—128.9  
—128.5  
—127.5  
—121.8  
—119.2  
—118.4

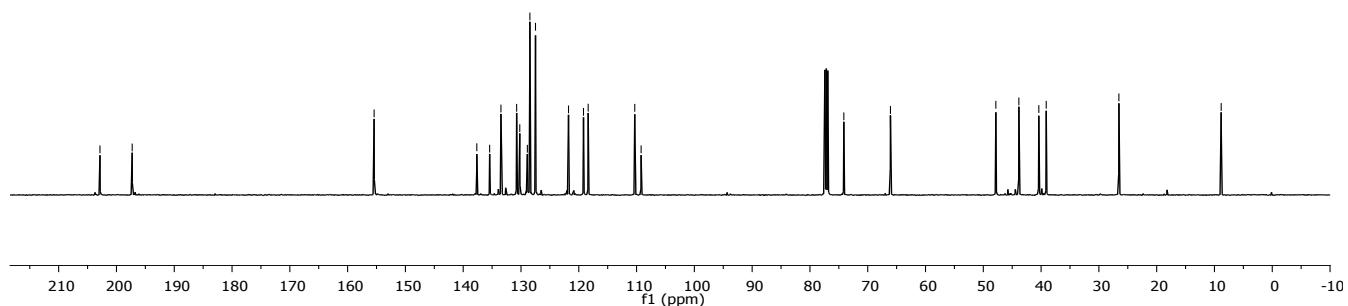
—74.1

—66.1  
—47.8  
—43.8  
—40.4  
—39.1

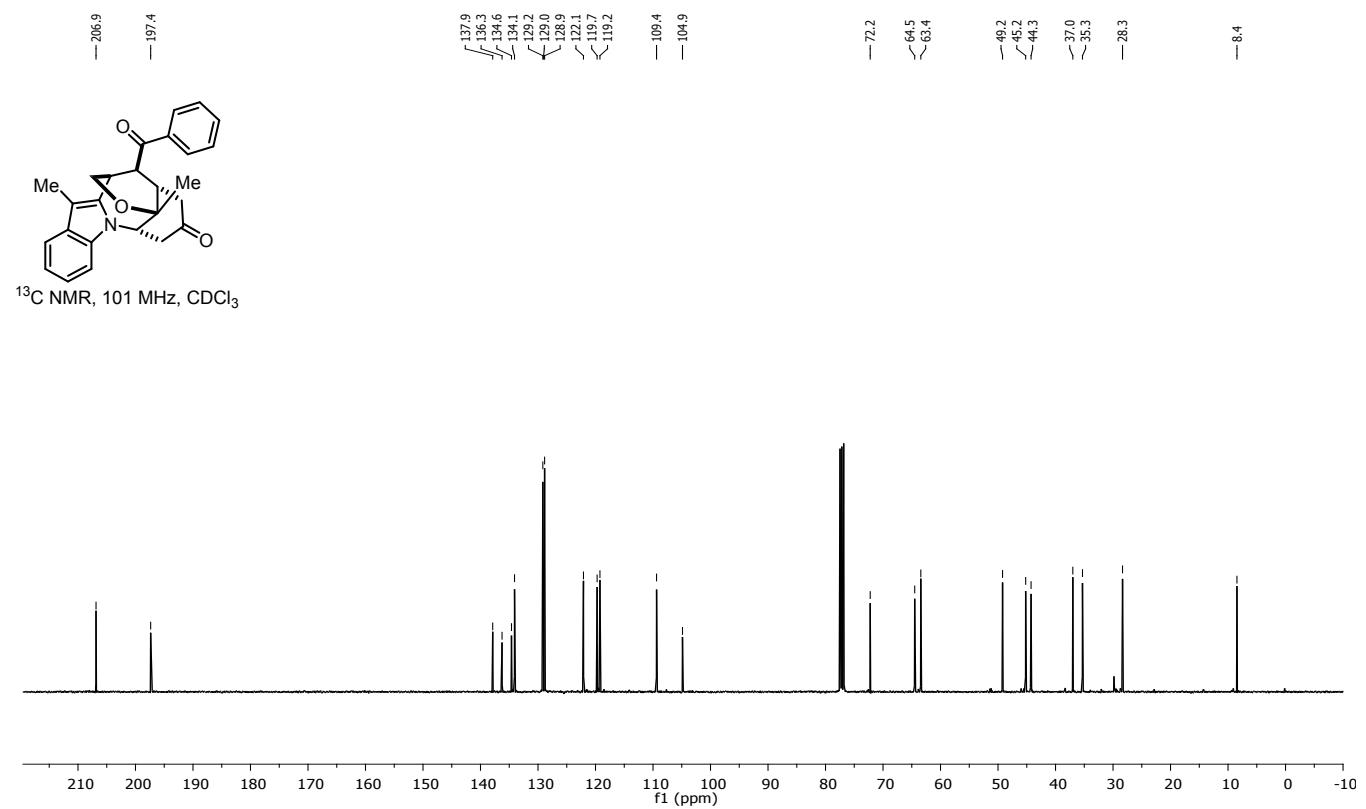
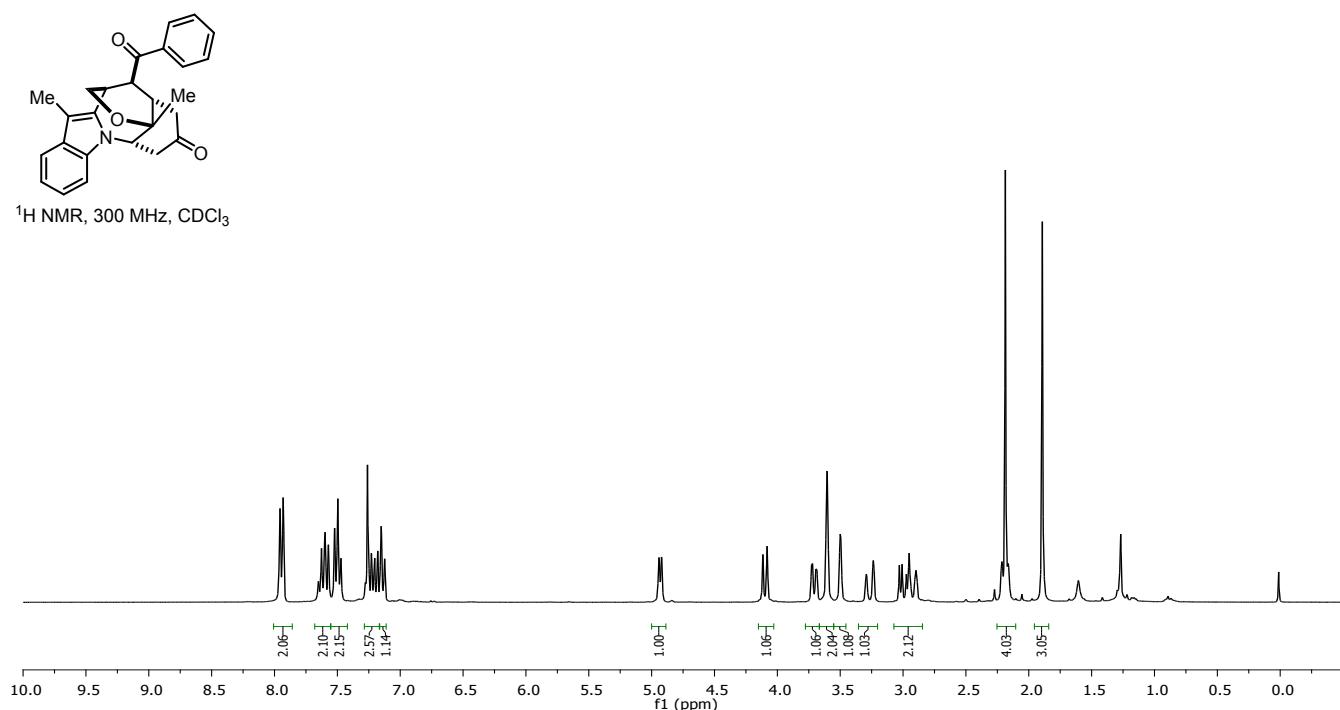
—26.5  
—8.8



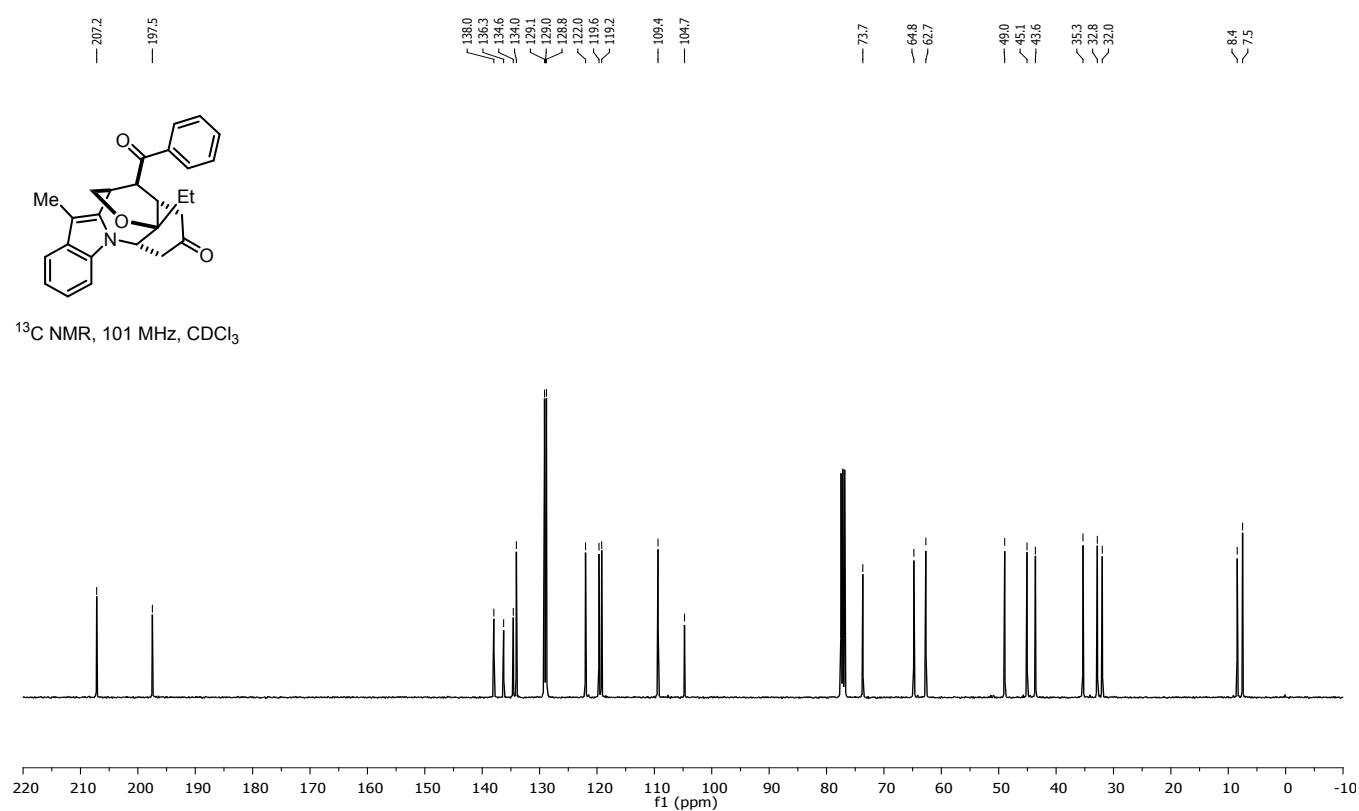
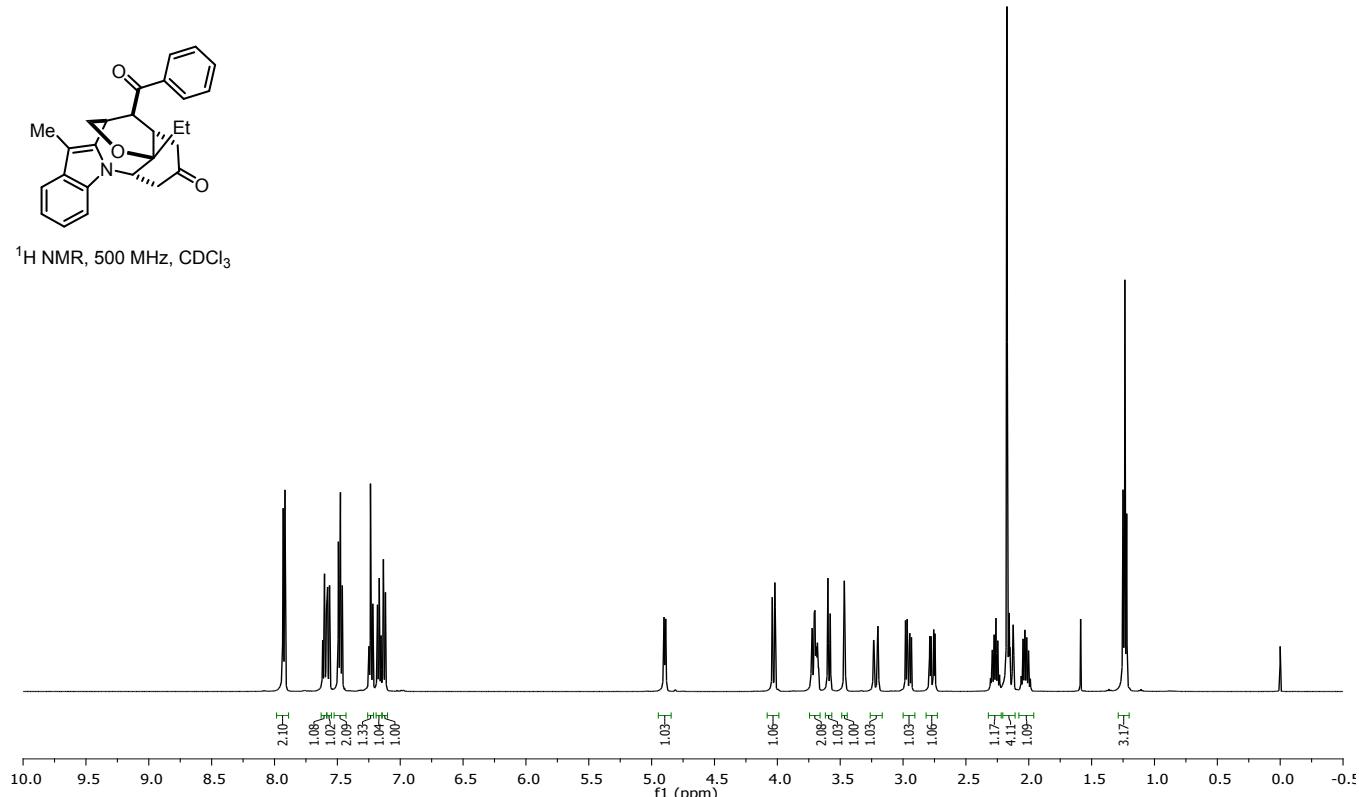
$^{13}\text{C}$  NMR, 126 MHz,  $\text{CDCl}_3$



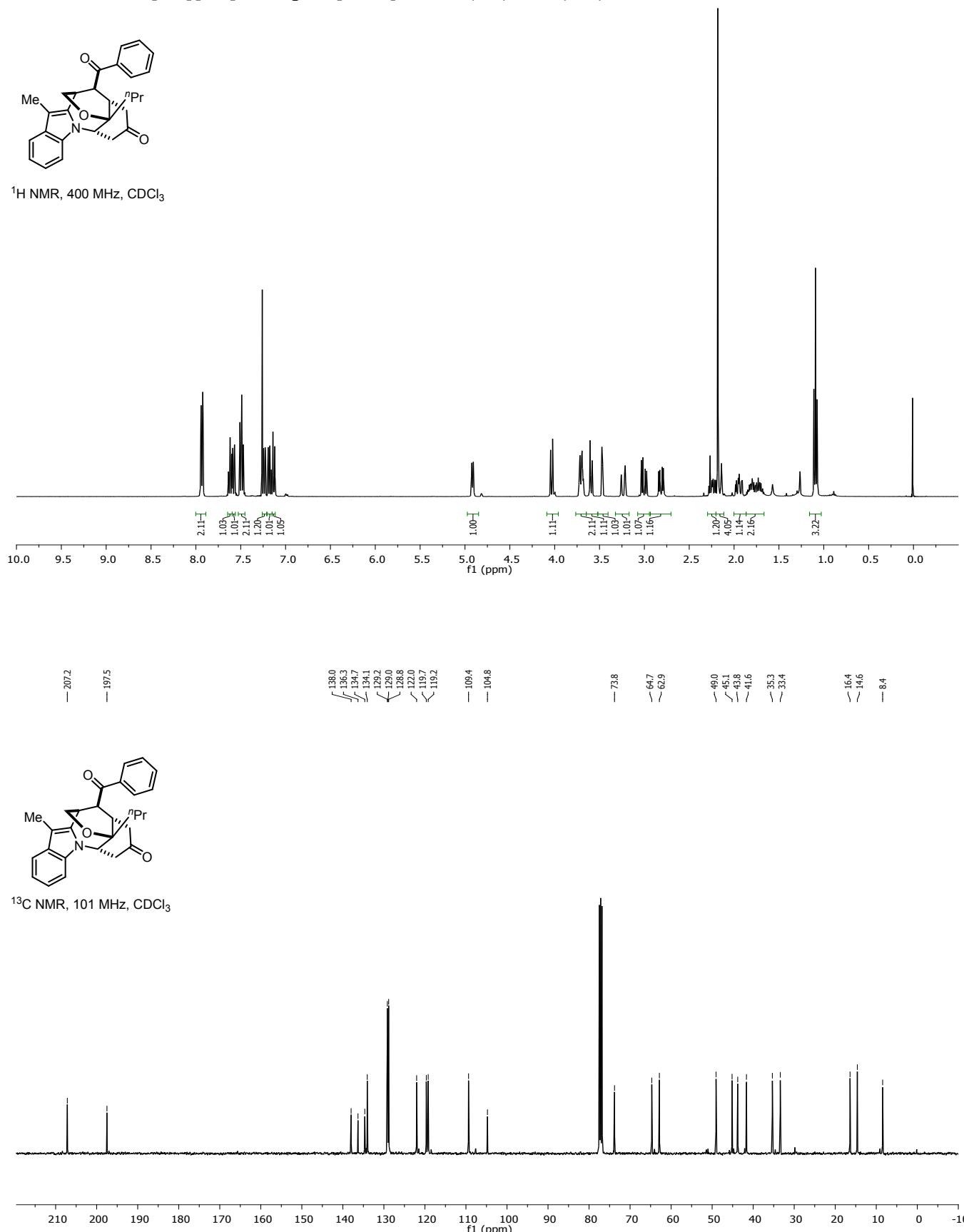
**14-Benzoyl-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10a):**



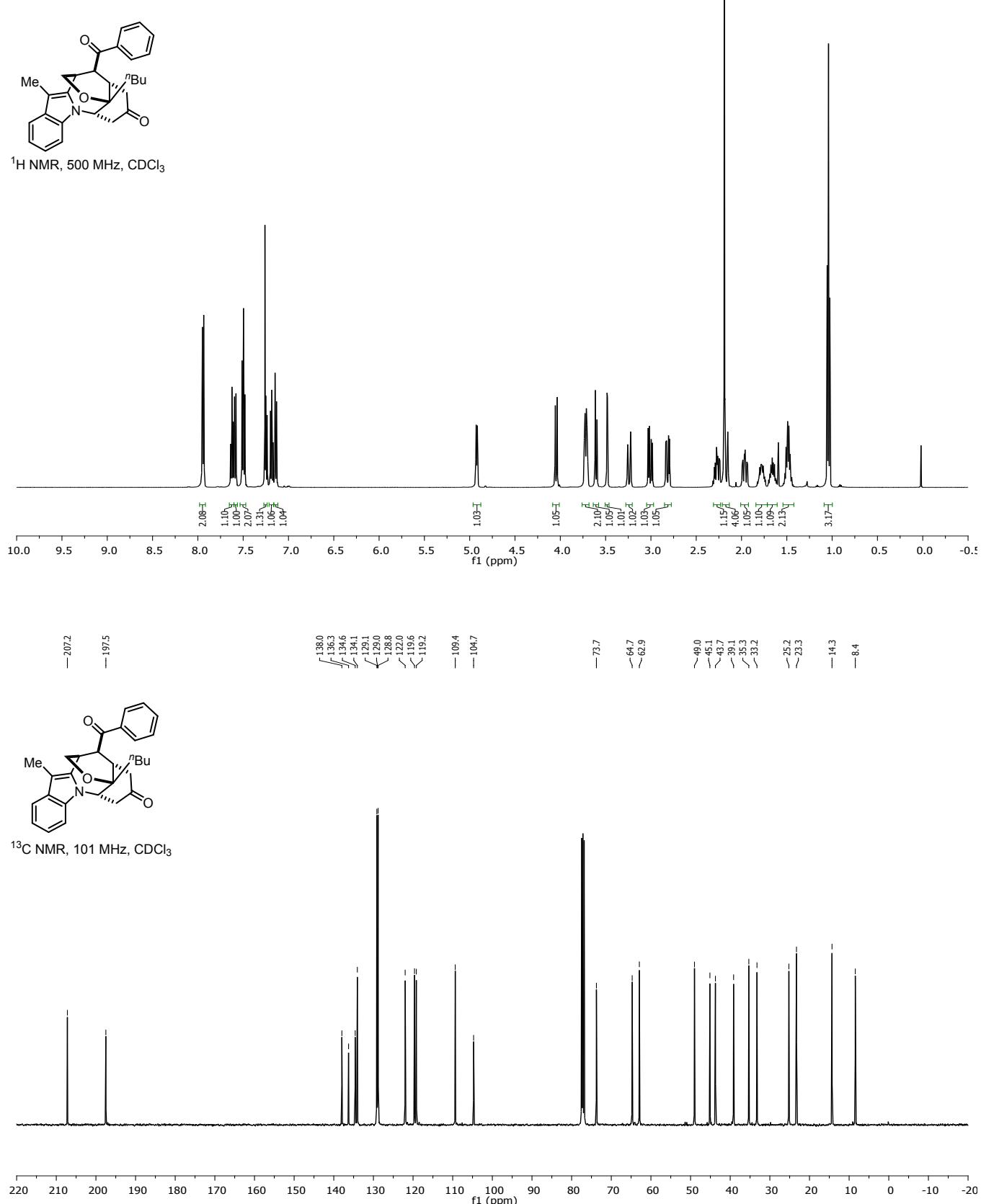
**14-Benzoyl-4a-ethyl-8-methyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10b):**



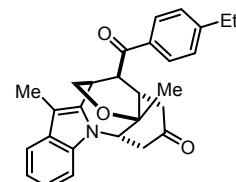
**14-Benzoyl-8-methyl-4a-propyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10c):**



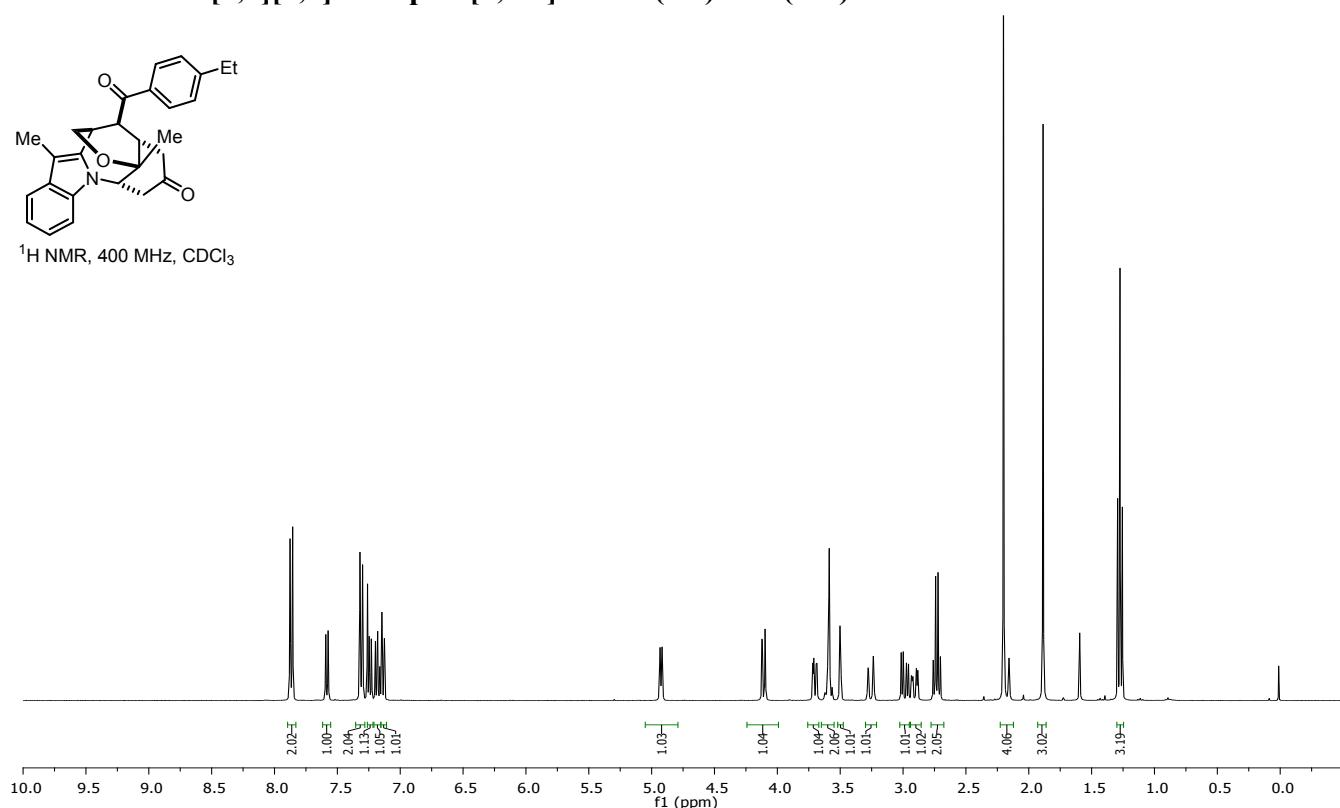
**14-Benzoyl-4a-butyl-8-methyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10d):**



**14-(4-Ethylbenzoyl)-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10e):**



$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$



—206.9

—197.0

—151.3

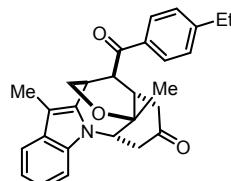
—138.0  
—136.2  
—132.3  
—129.1  
—128.0  
—128.6  
—122.0  
—119.7  
—119.2

—109.4  
—104.8

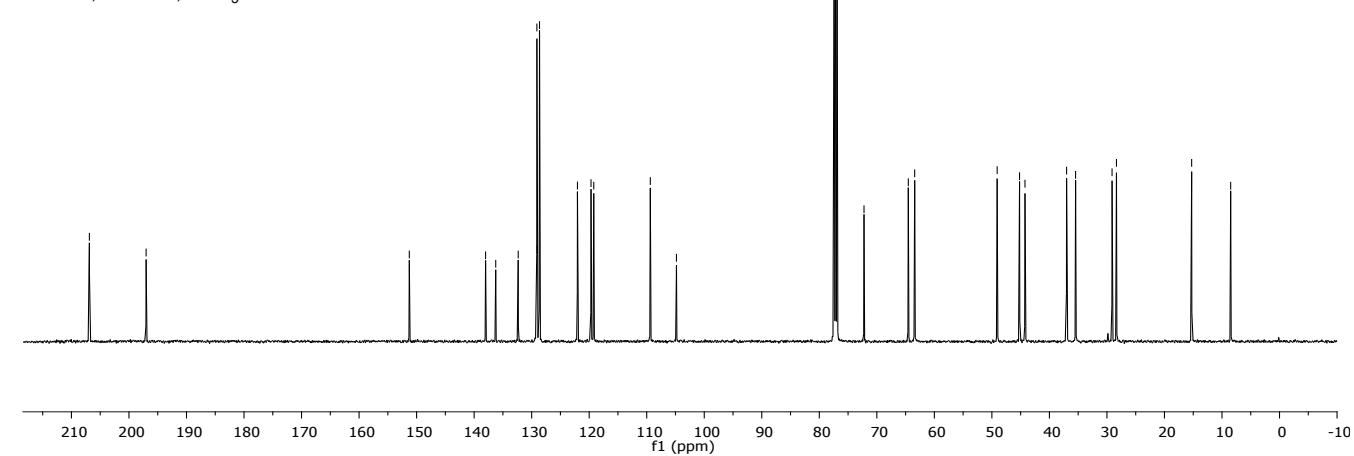
—72.2  
—64.5  
—63.4

—49.1  
—45.2  
—44.2  
—37.0  
—35.4  
—29.1  
—28.3

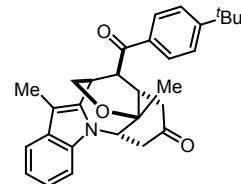
—15.3  
—8.5



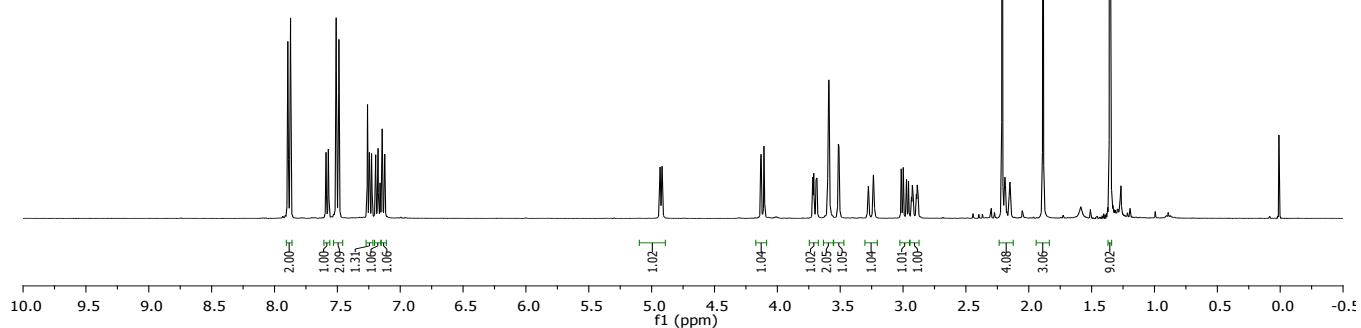
$^{13}\text{C}$  NMR, 126 MHz,  $\text{CDCl}_3$



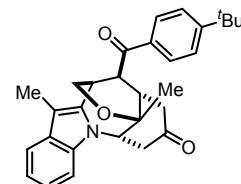
**14-(4-(*tert*-Butyl)benzoyl)-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-*a*]indol-2(1*H*)-one (10f):**



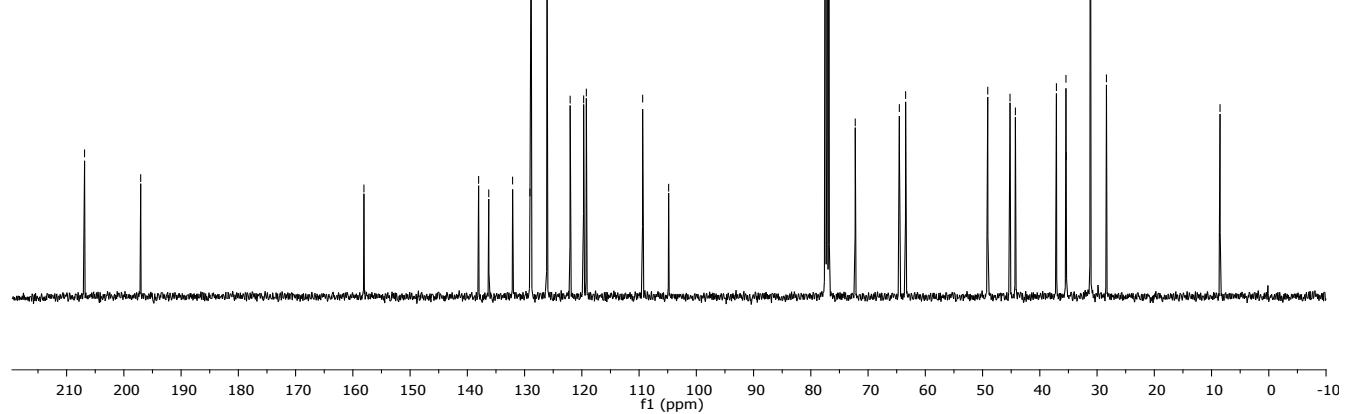
$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$



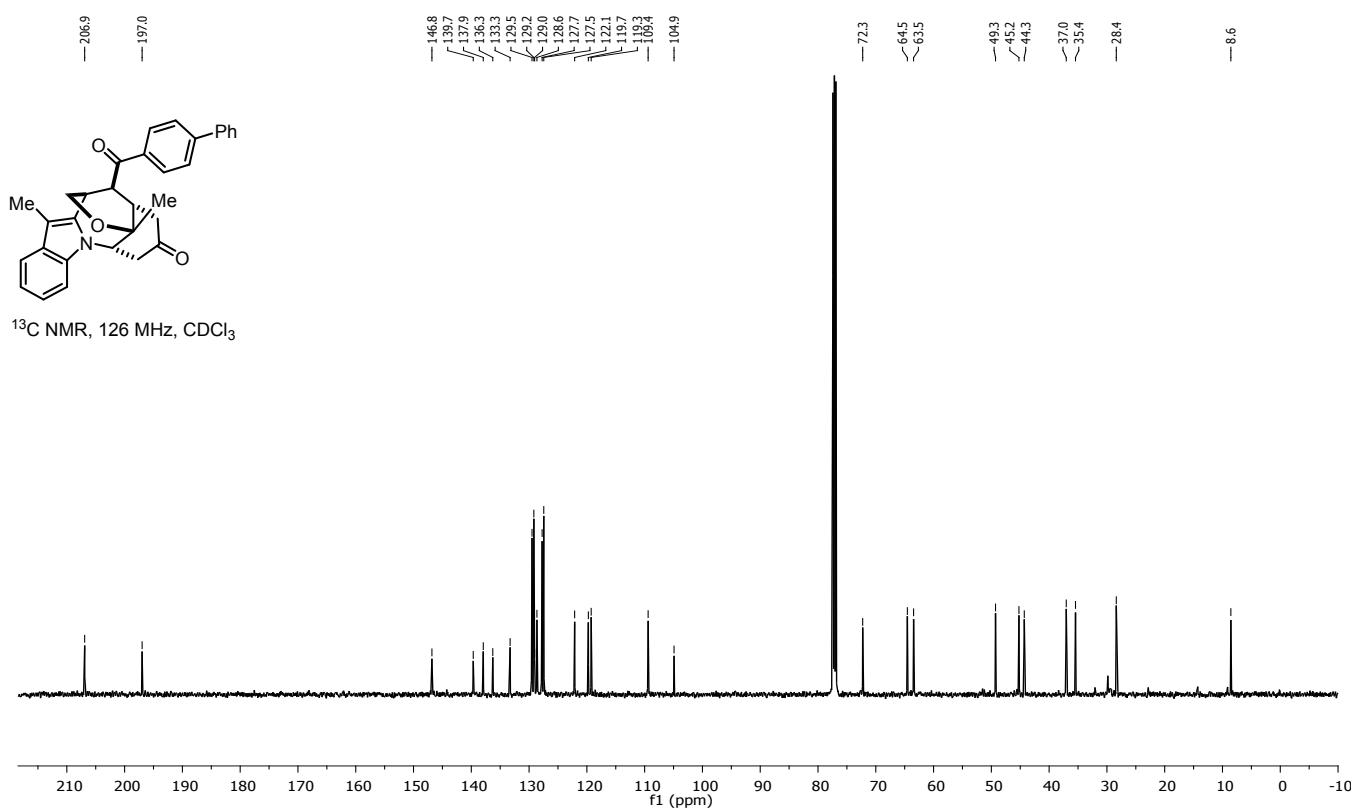
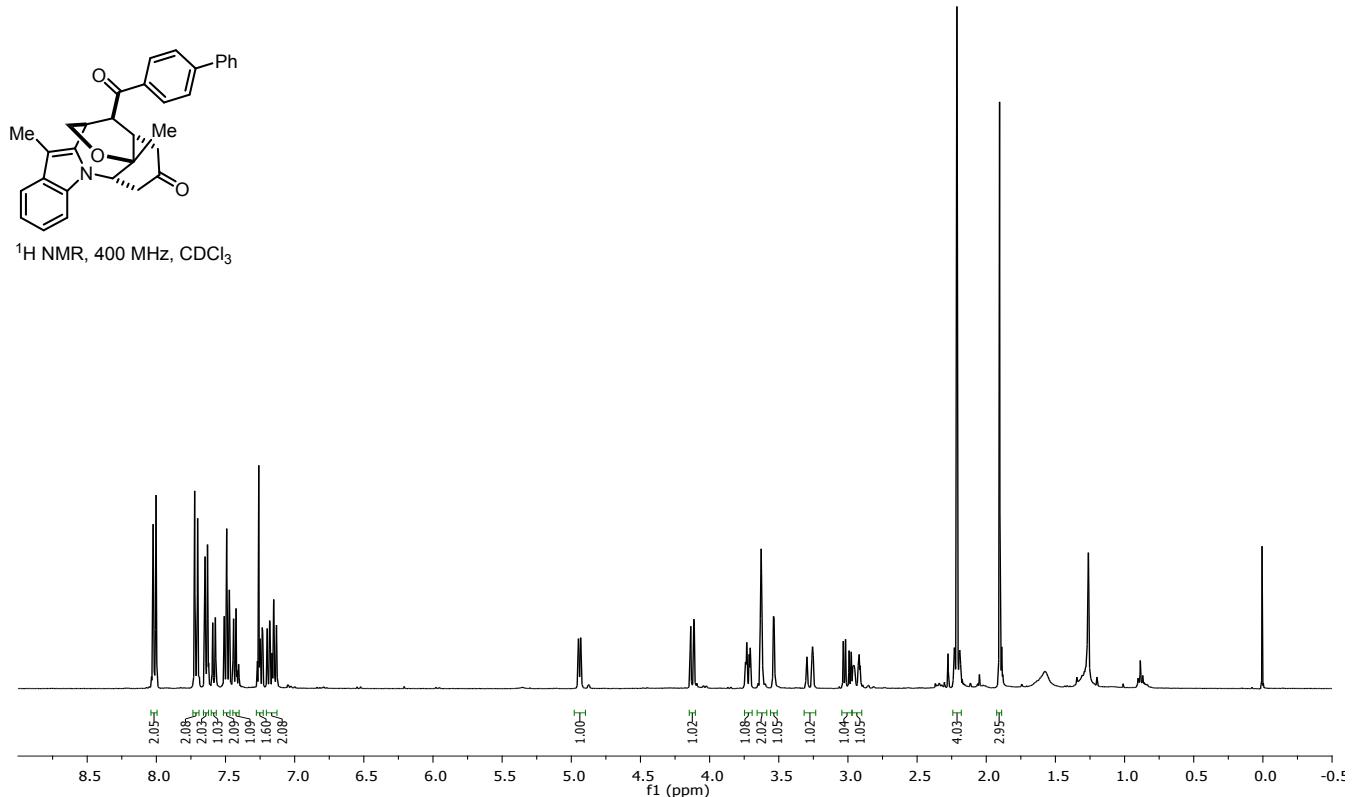
— 206.9      — 197.1      — 158.1      — 138.0  
— 136.3      — 132.1      — 129.1      — 128.9  
— 126.1      — 122.0      — 119.7      — 119.2  
— 109.4      — 104.8      — 72.2      — 64.5  
— 63.4      — 49.1      — 45.2  
— 44.3      — 37.1      — 35.4  
— 31.2      — 28.4      — 8.5



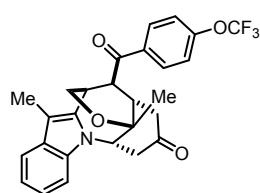
$^{13}\text{C}$  NMR, 101 MHz,  $\text{CDCl}_3$



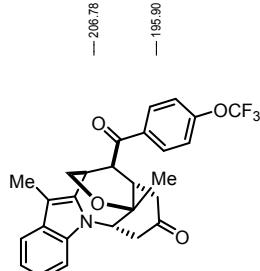
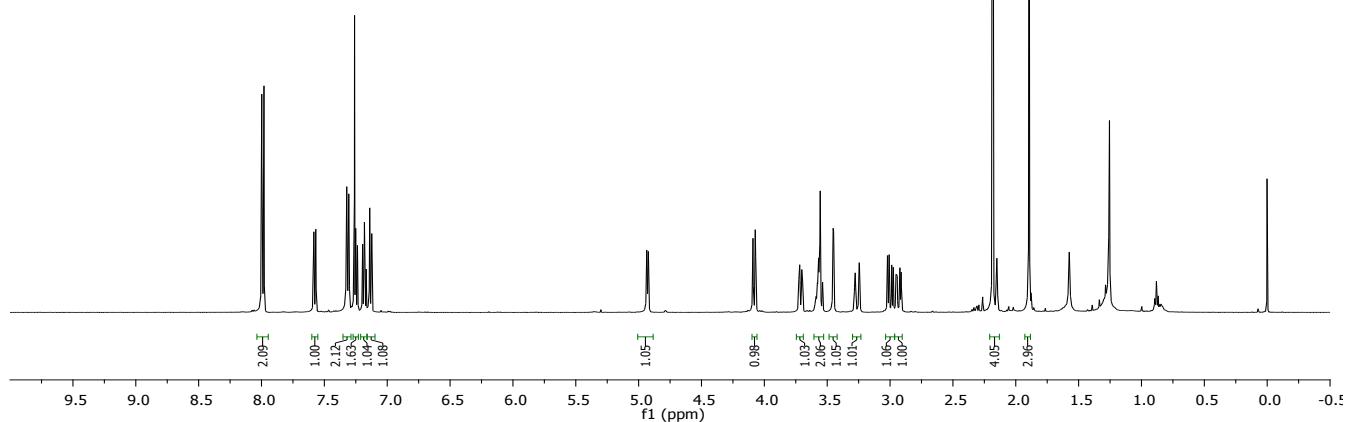
**14-([1,1'-Biphenyl]-4-carbonyl)-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10g):**



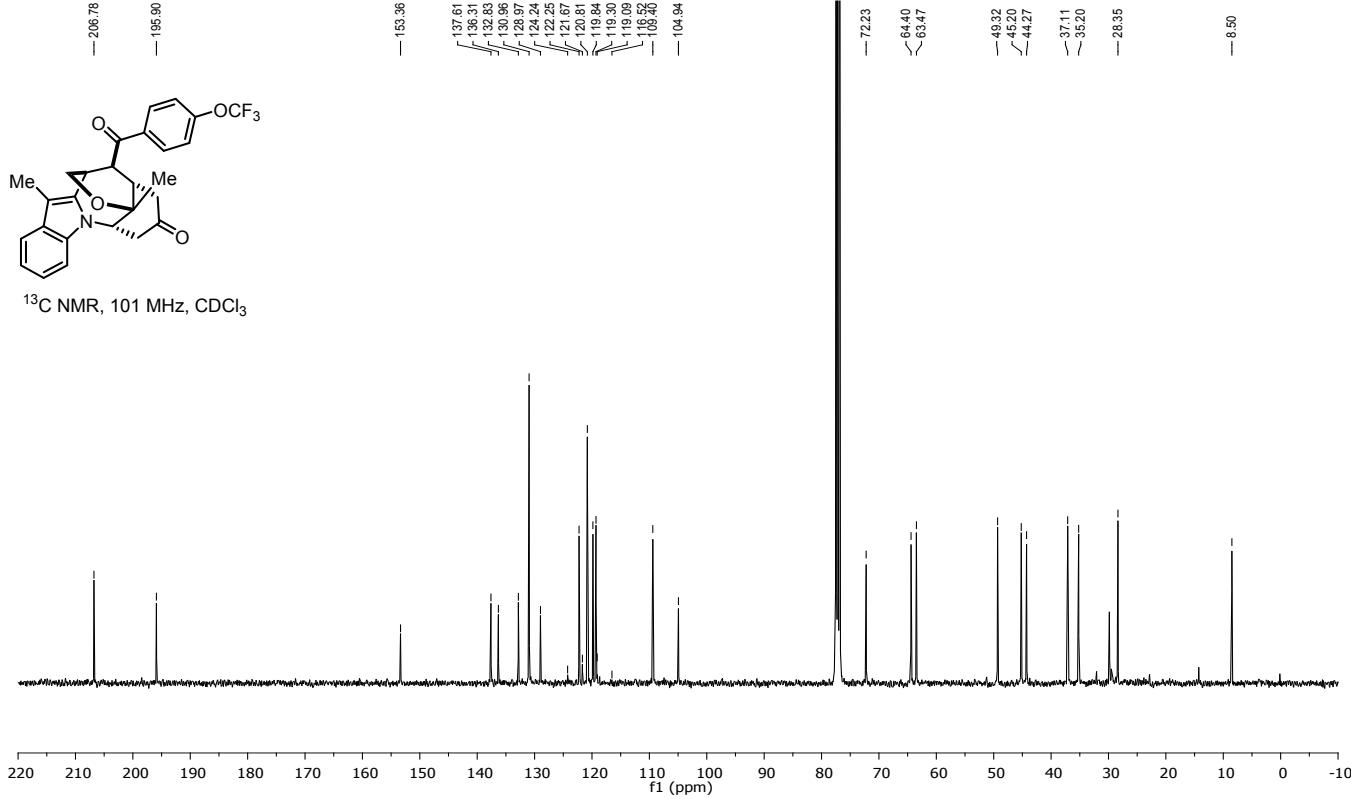
**4a,8-Dimethyl-14-(4-(trifluoromethoxy)benzoyl)-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10h):**

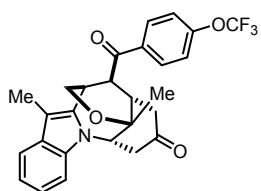


$^1\text{H}$  NMR, 500 MHz,  $\text{CDCl}_3$

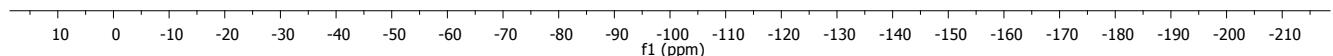


$^{13}\text{C}$  NMR, 101 MHz,  $\text{CDCl}_3$

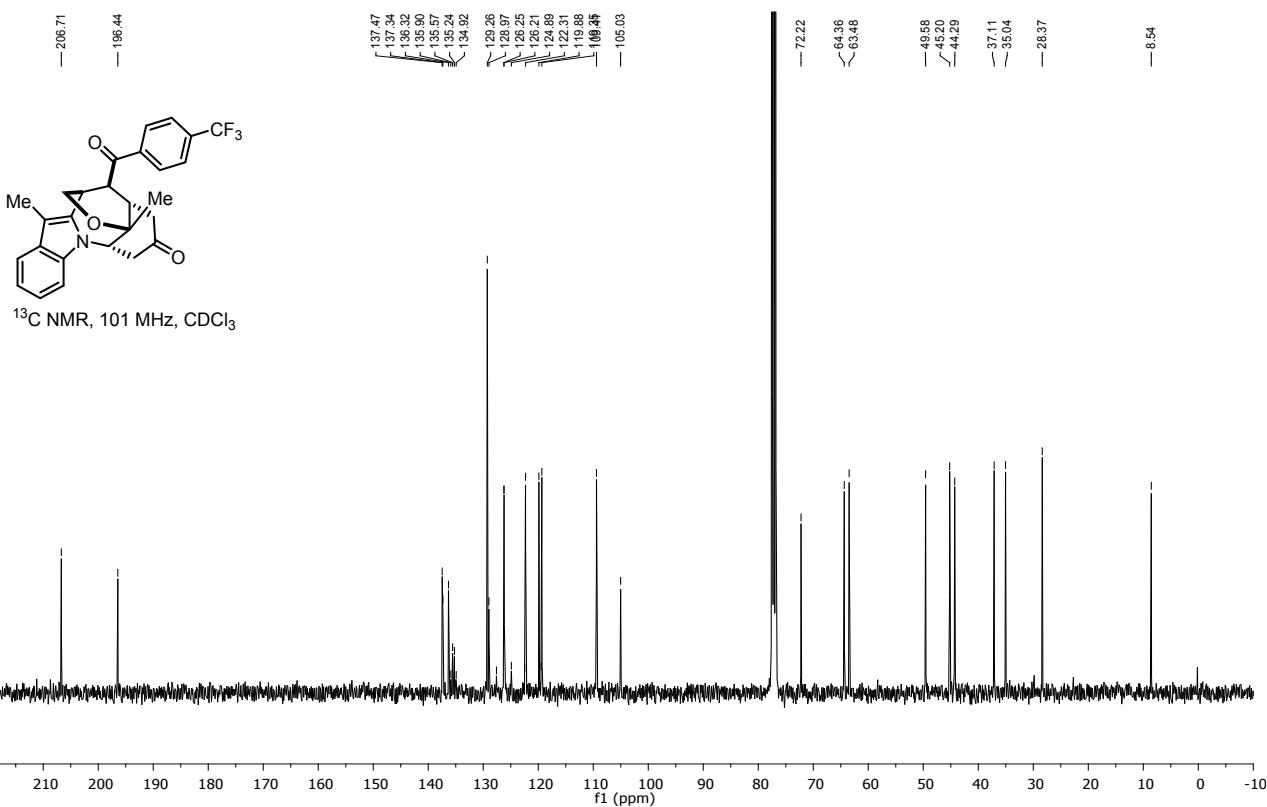
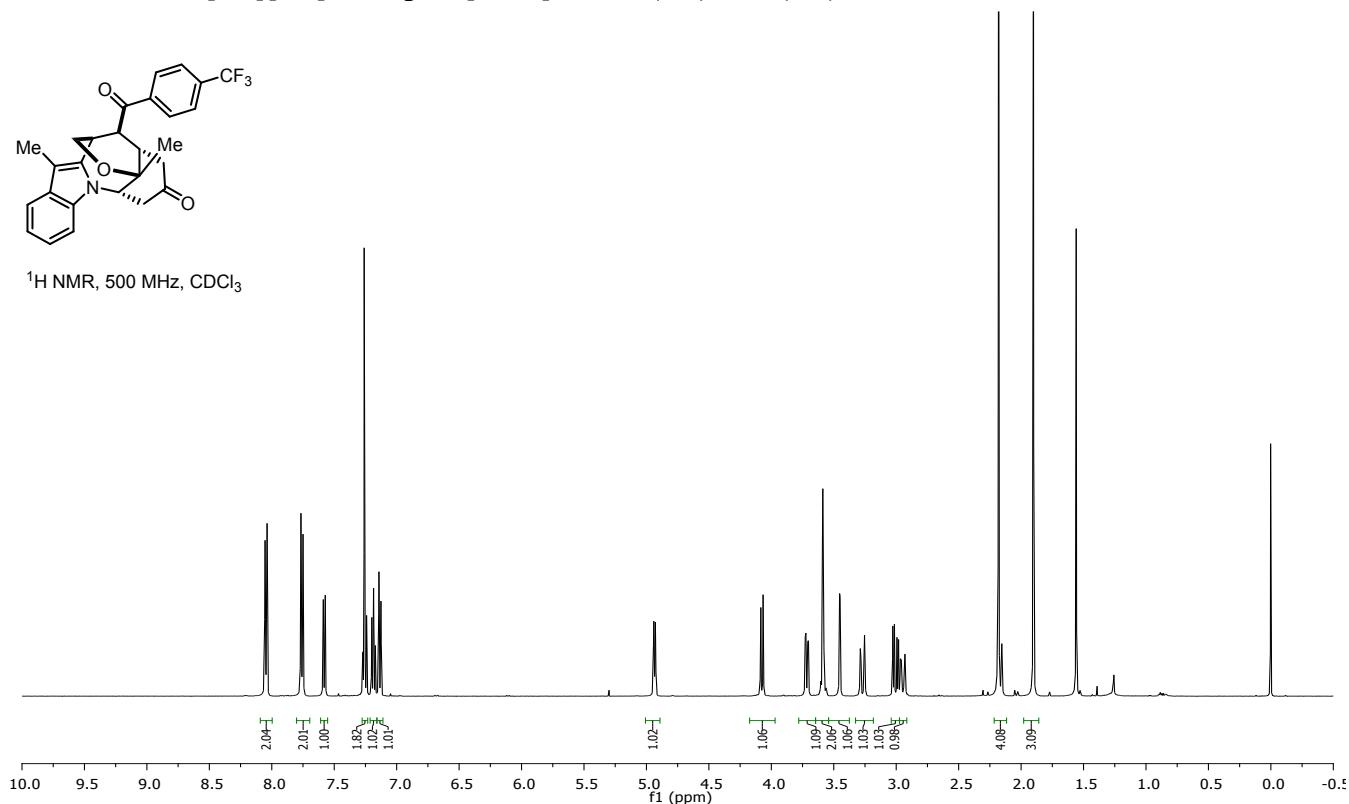


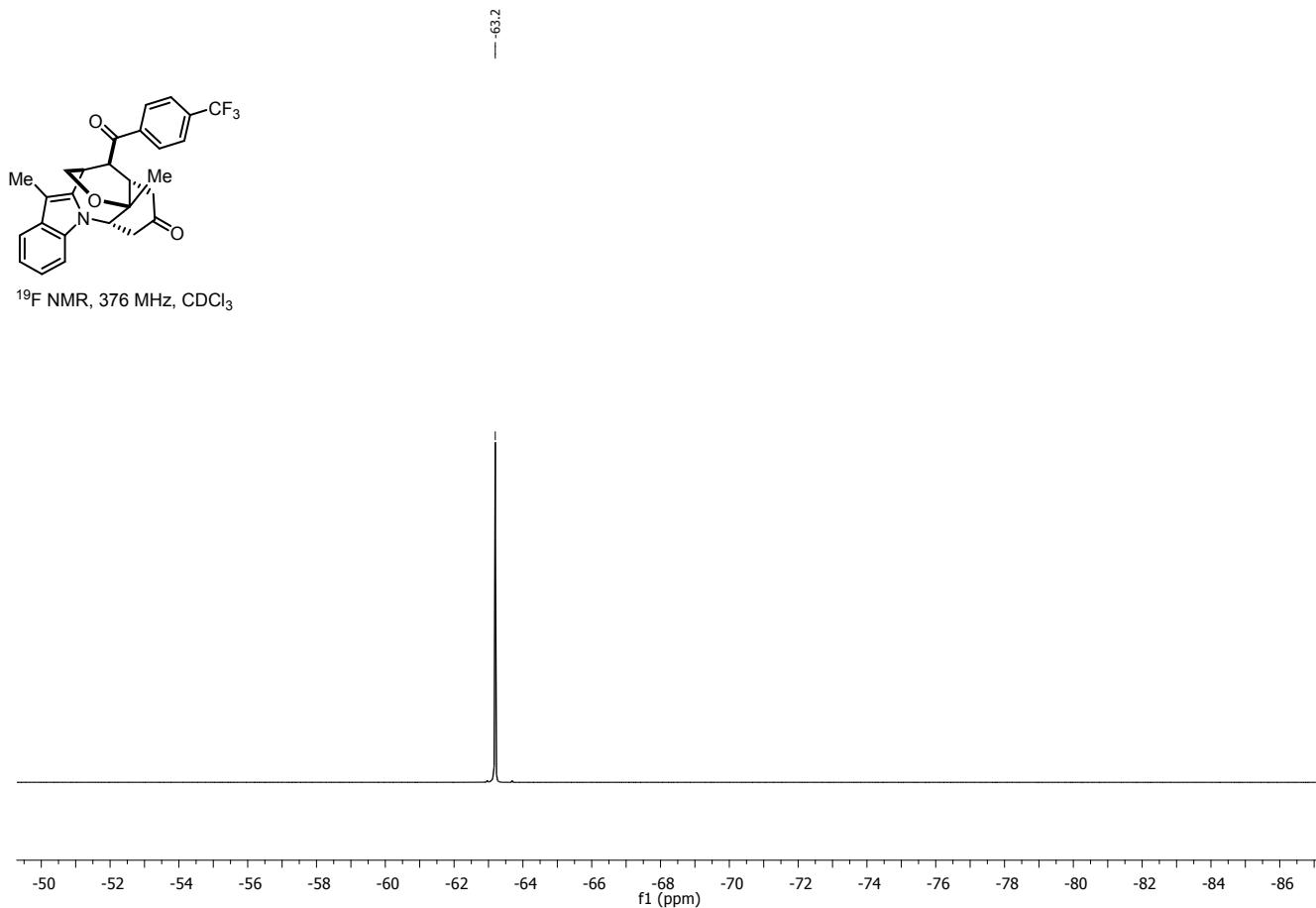


<sup>19</sup>F NMR, 376 MHz, CDCl<sub>3</sub>

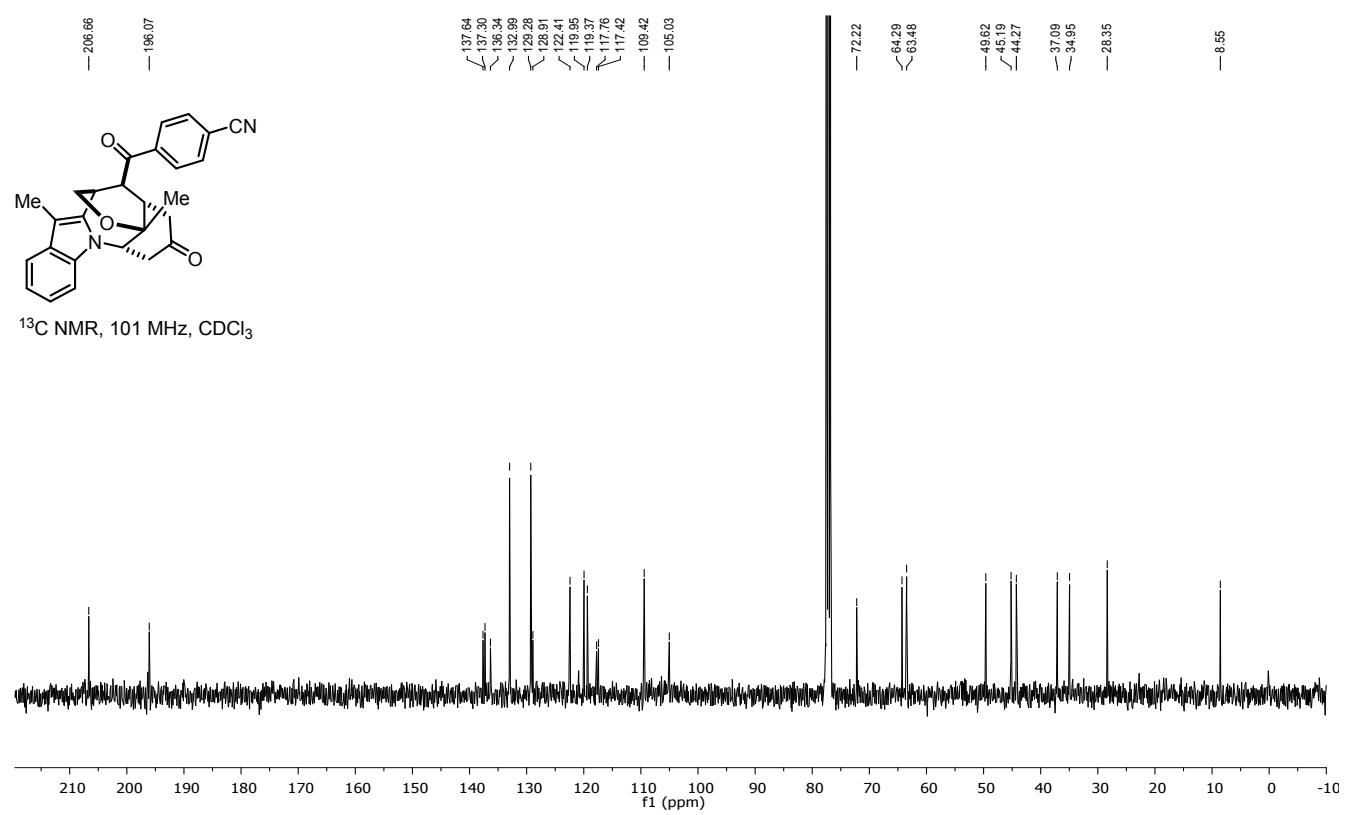
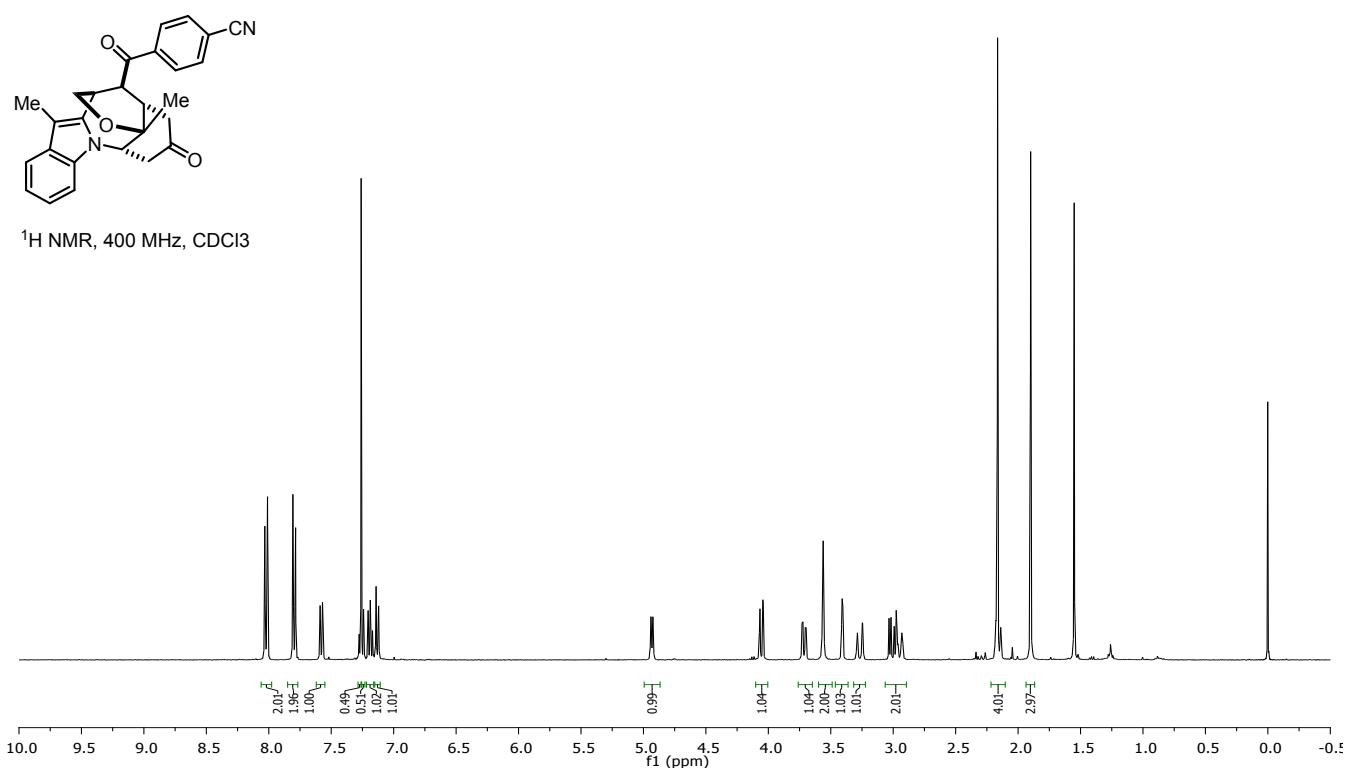


**4a,8-Dimethyl-14-(4-(trifluoromethyl)benzoyl)-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-*a*]indol-2(1*H*)-one (10i):**

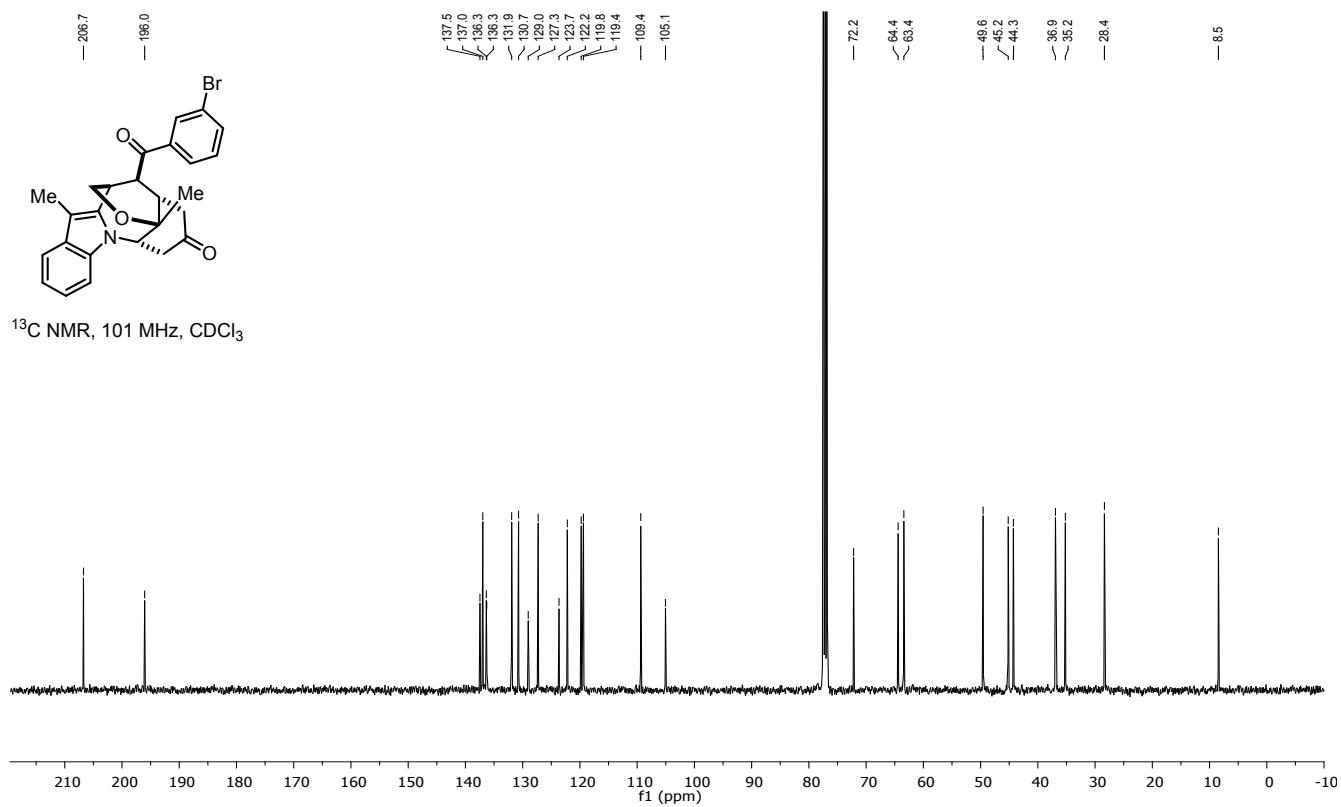
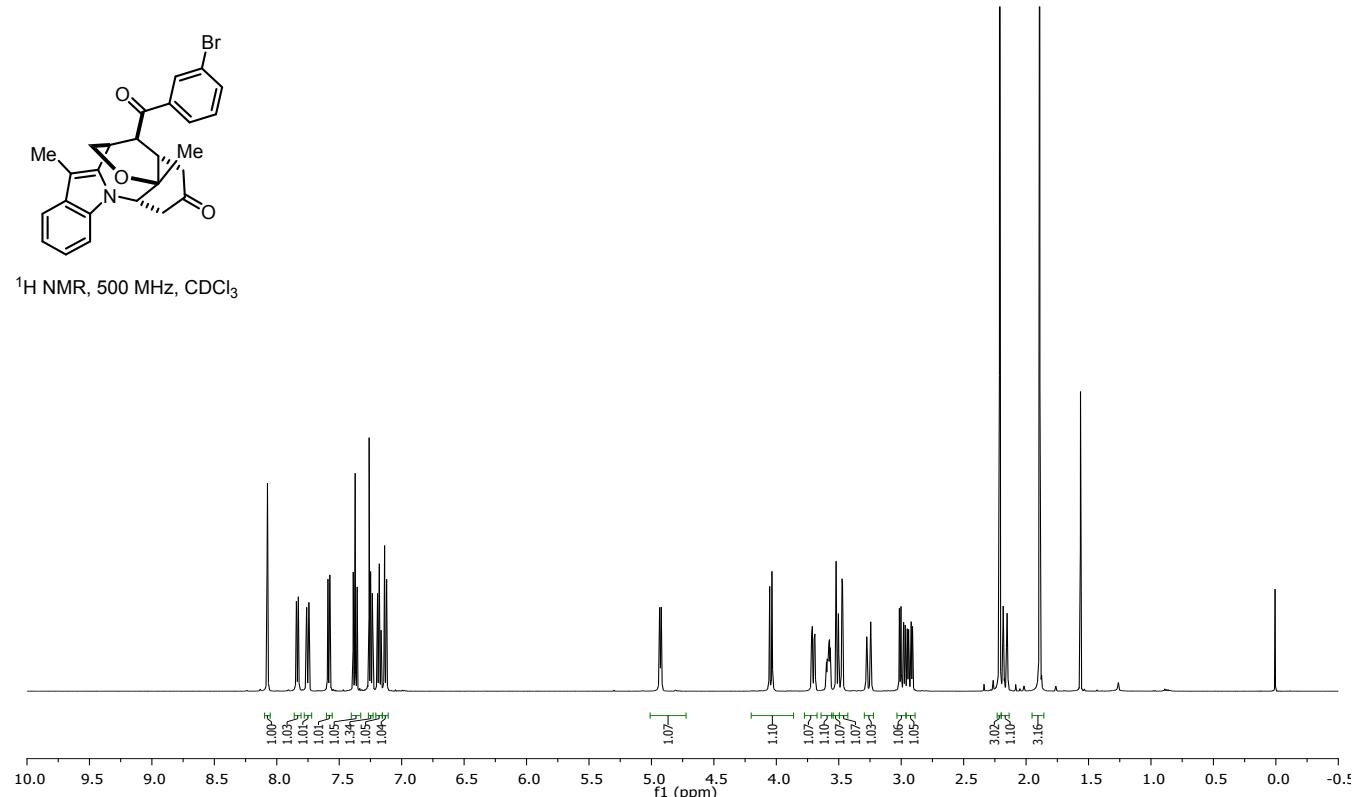




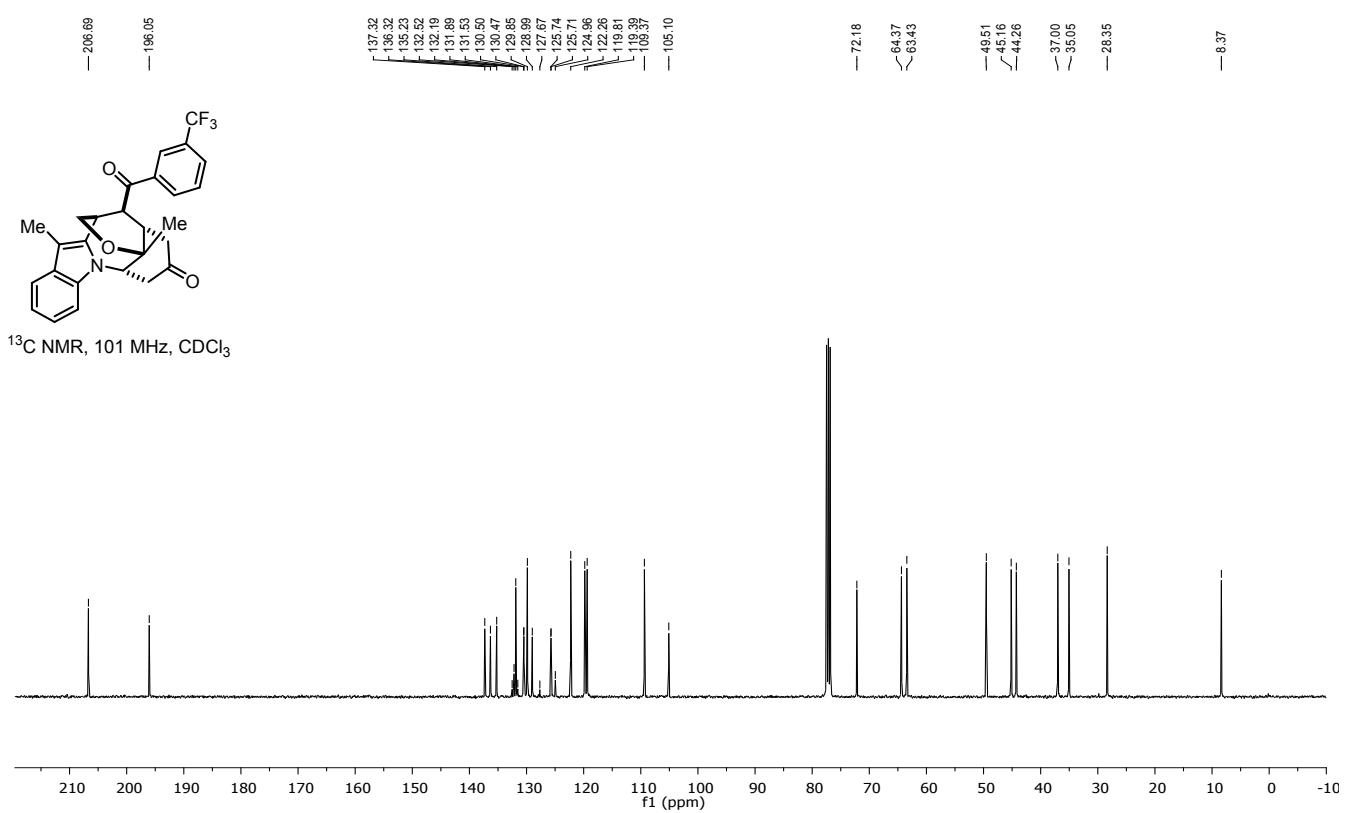
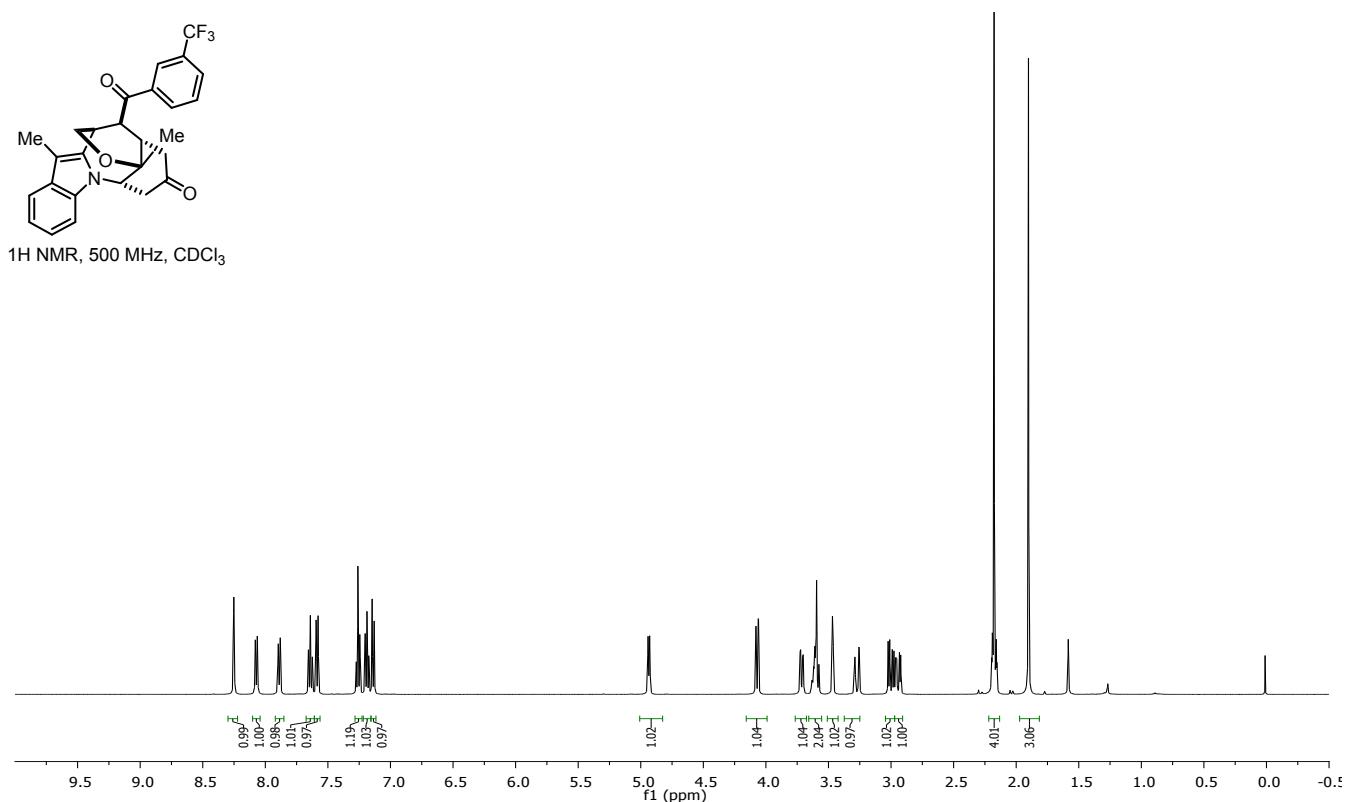
**4-(4a,8-Dimethyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indole-14-carbonyl)benzonitrile (10j):**

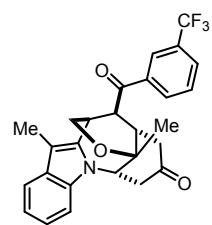


**14-(3-Bromobenzoyl)-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-*a*]indol-2(1*H*)-one (10k):**



**4a,8-Dimethyl-14-(3-(trifluoromethyl)benzoyl)-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10l):**





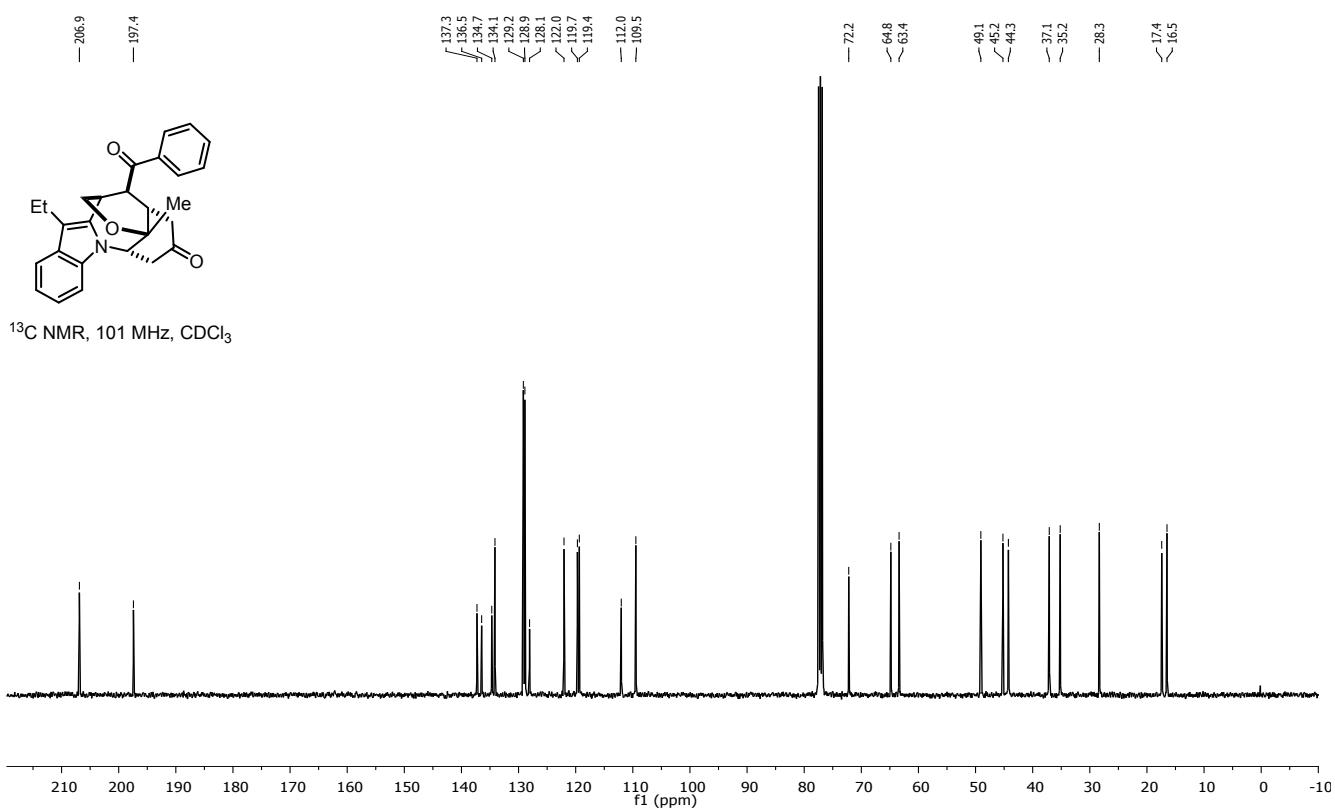
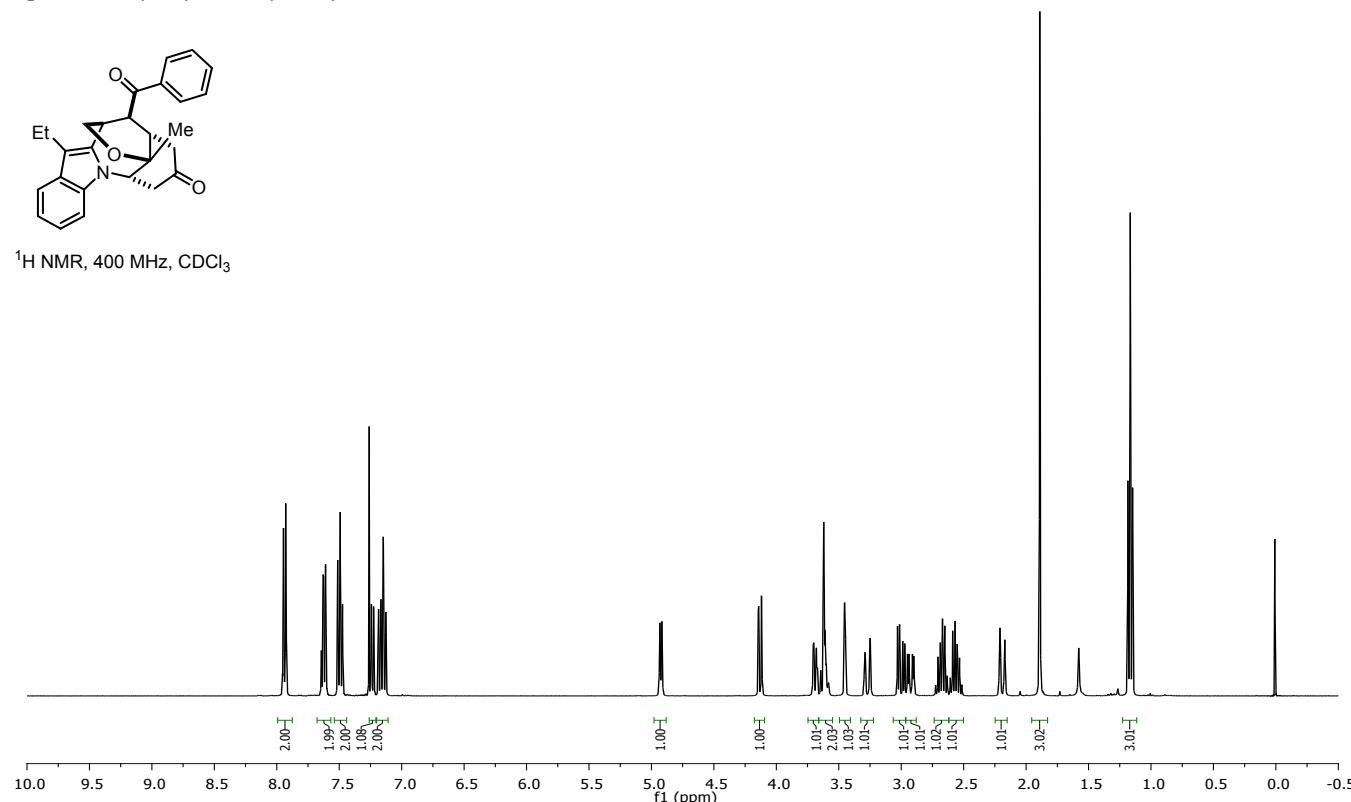
$^{19}\text{F}$  NMR, 376 MHz,  $\text{CDCl}_3$

-62.7

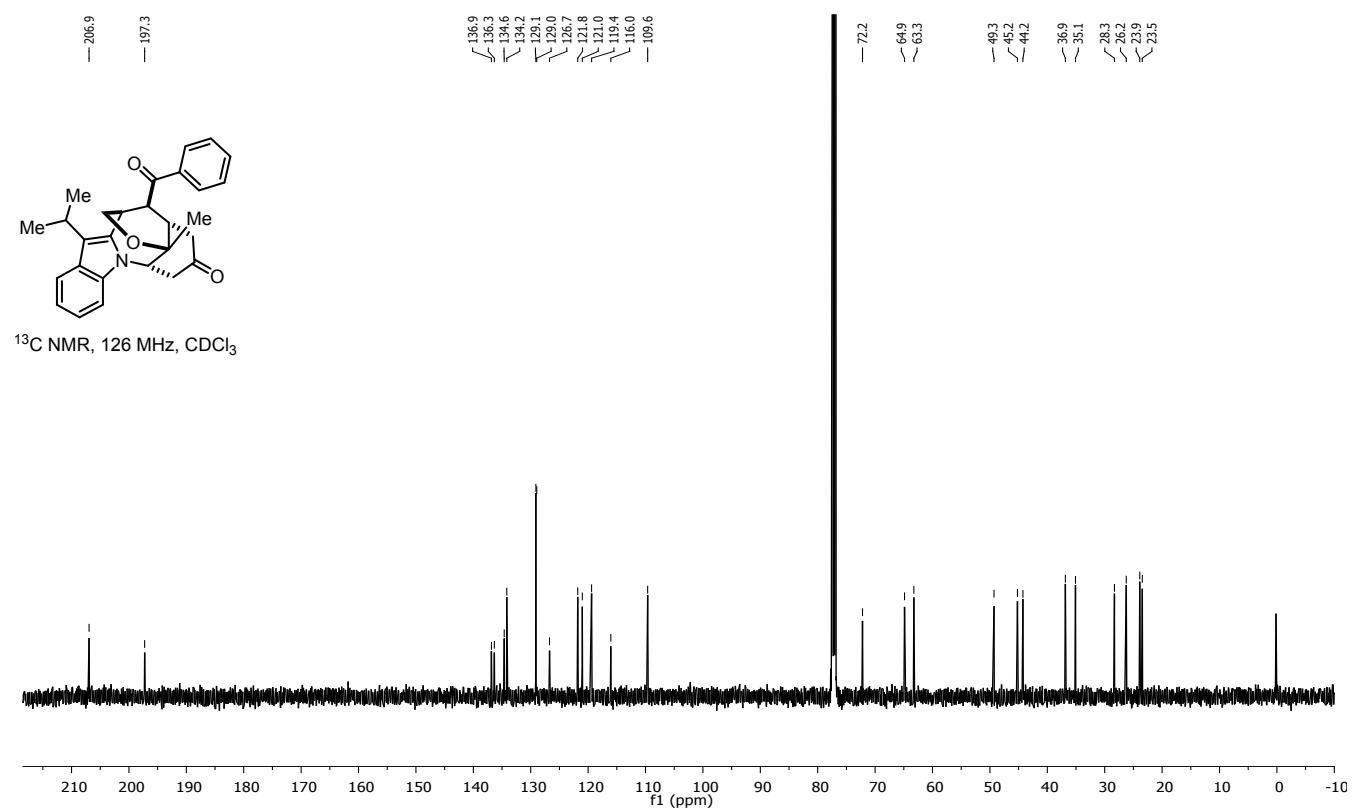
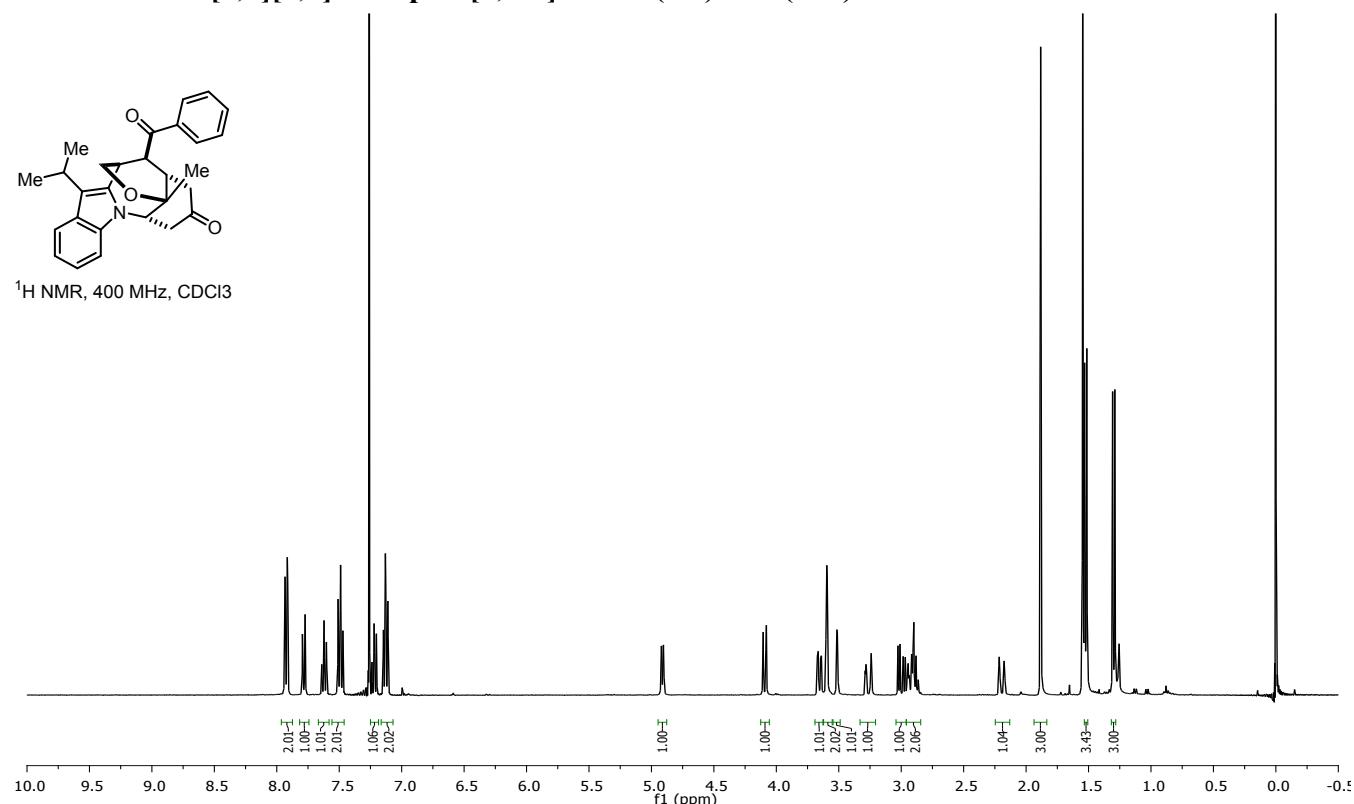
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

f1 (ppm)

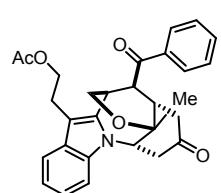
**4-Benzoyl-8-ethyl-4a-methyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10m):**



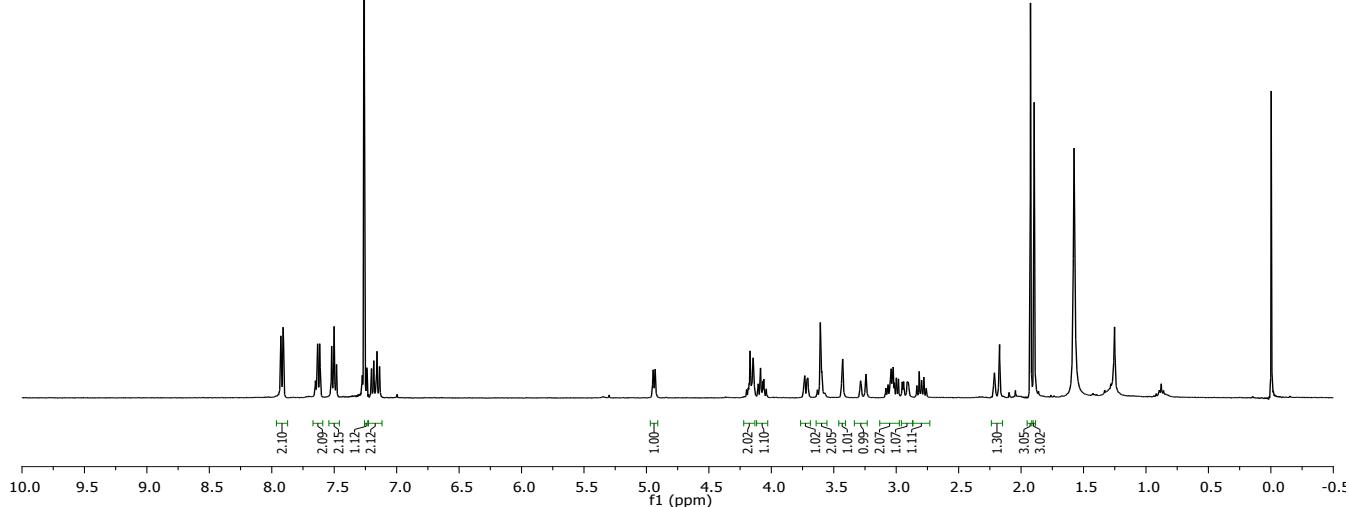
**14-Benzoyl-8-isopropyl-4a-methyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-*a*]indol-2(1*H*)-one (10n):**



**2-(14-Benzoyl-4a-methyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-8-yl)ethyl acetate (10o):**



$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$



— 197.3

— 171.0

— 139.0

— 134.4

— 134.7

— 134.3

— 129.3

— 128.8

— 128.2

— 122.4

— 120.1

— 119.2

— 109.6

— 105.6

— 72.2

— 64.8

— 63.5

— 48.9

— 45.1

— 44.2

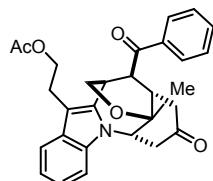
— 37.2

— 35.2

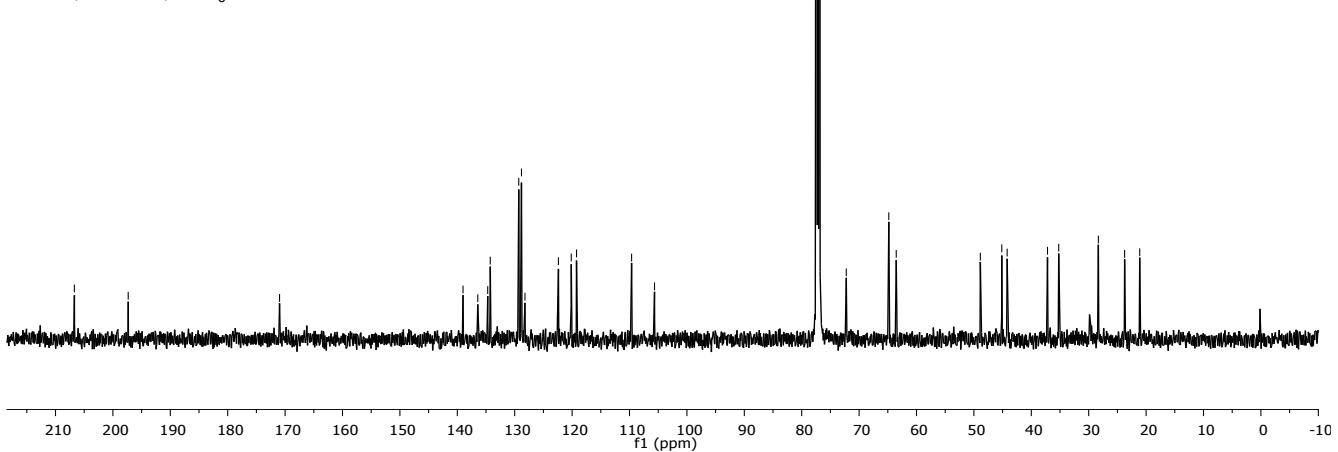
— 28.3

— 23.7

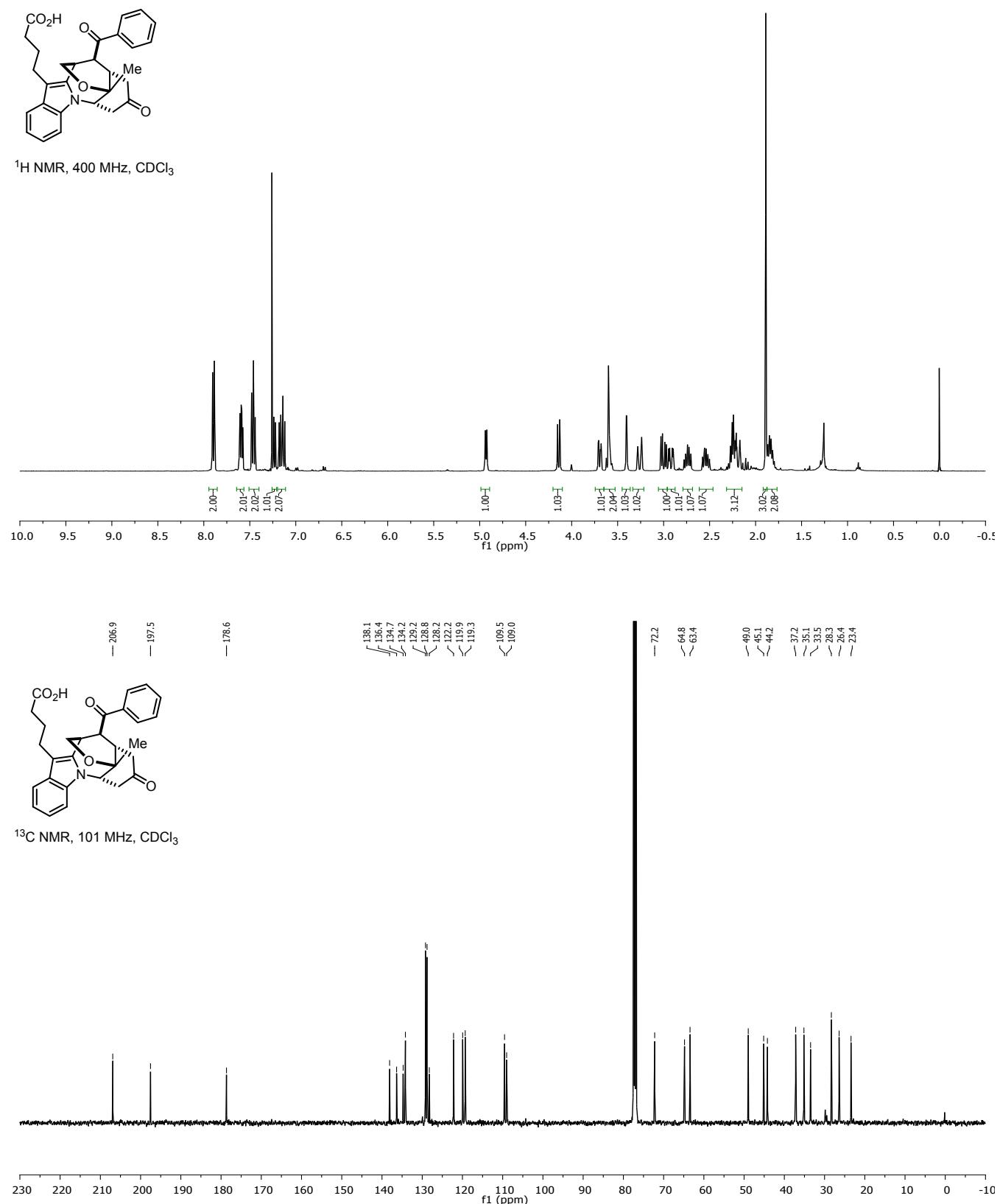
— 21.1



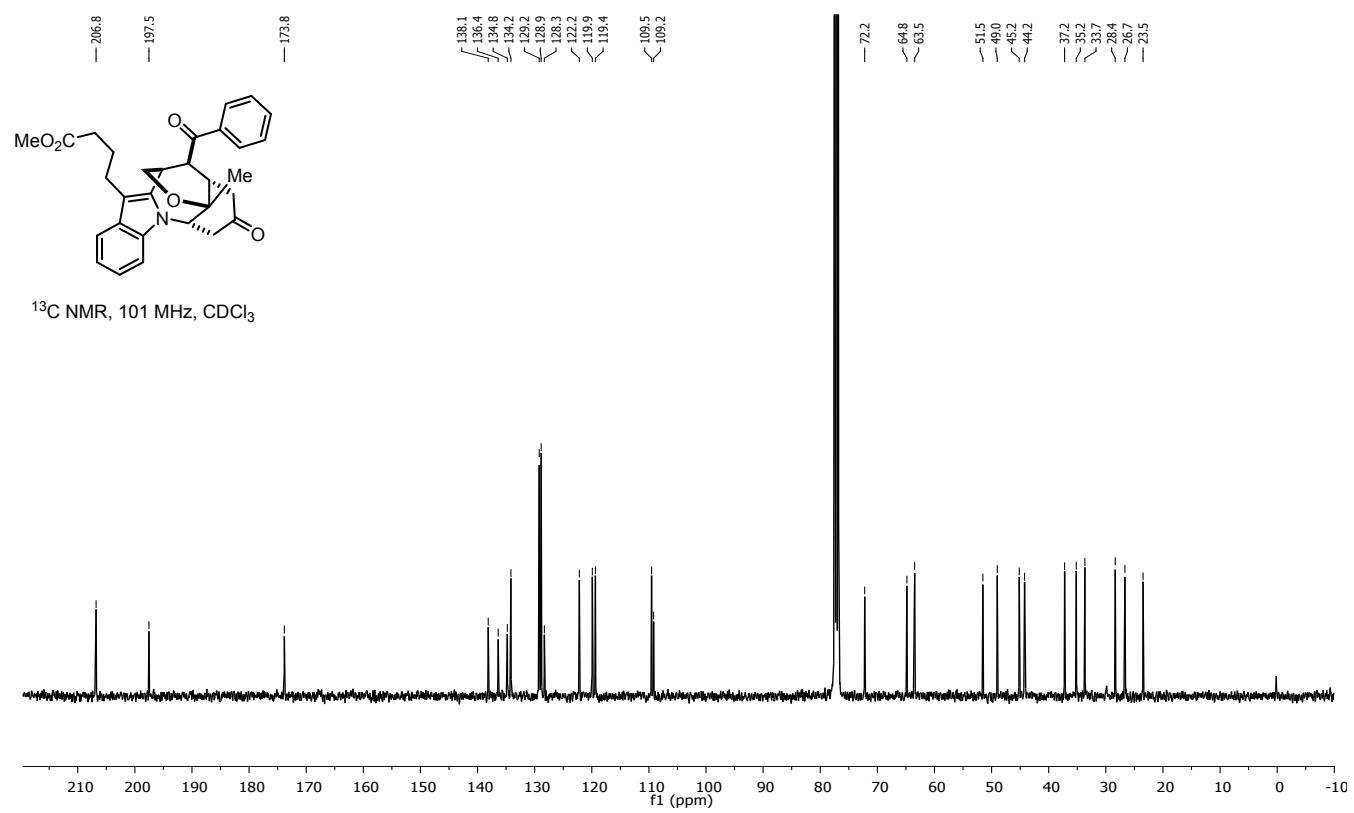
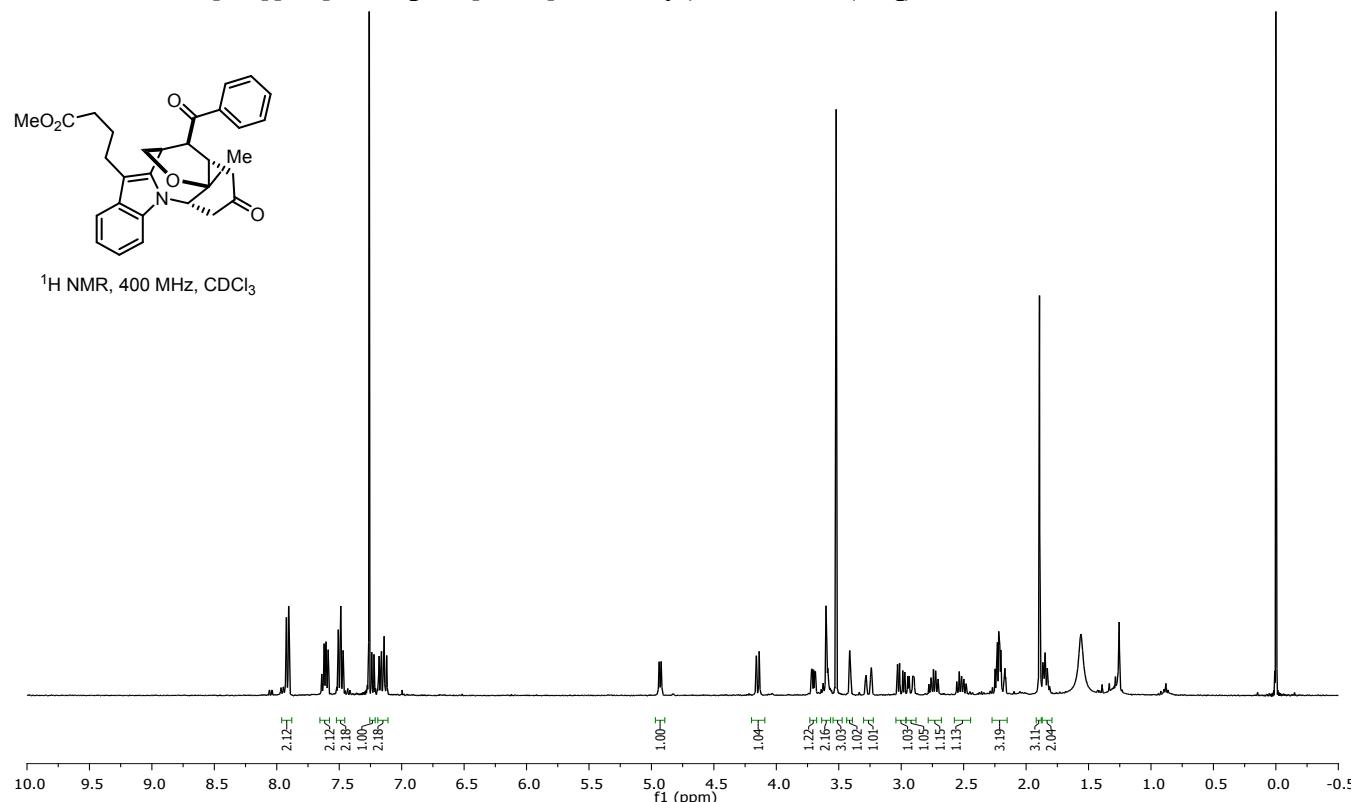
$^{13}\text{C}$  NMR, 126 MHz,  $\text{CDCl}_3$



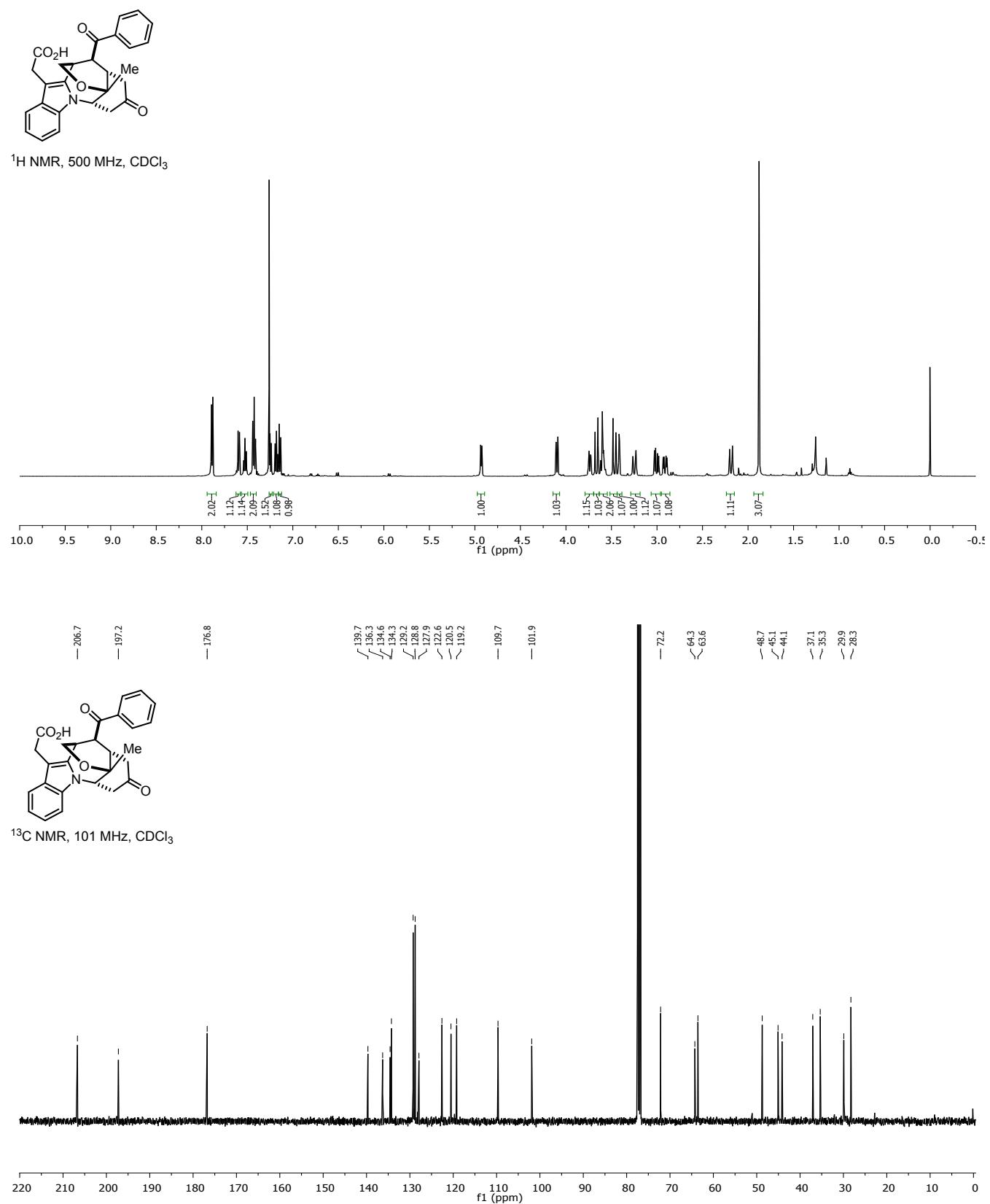
**4-(14-benzoyl-4a-methyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-8-yl)butanoic acid (10p):**



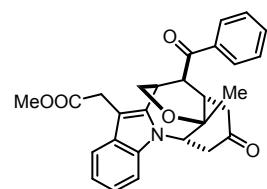
**Methyl 4-(14-benzoyl-4a-methyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-8-yl)butanoate (10q):**



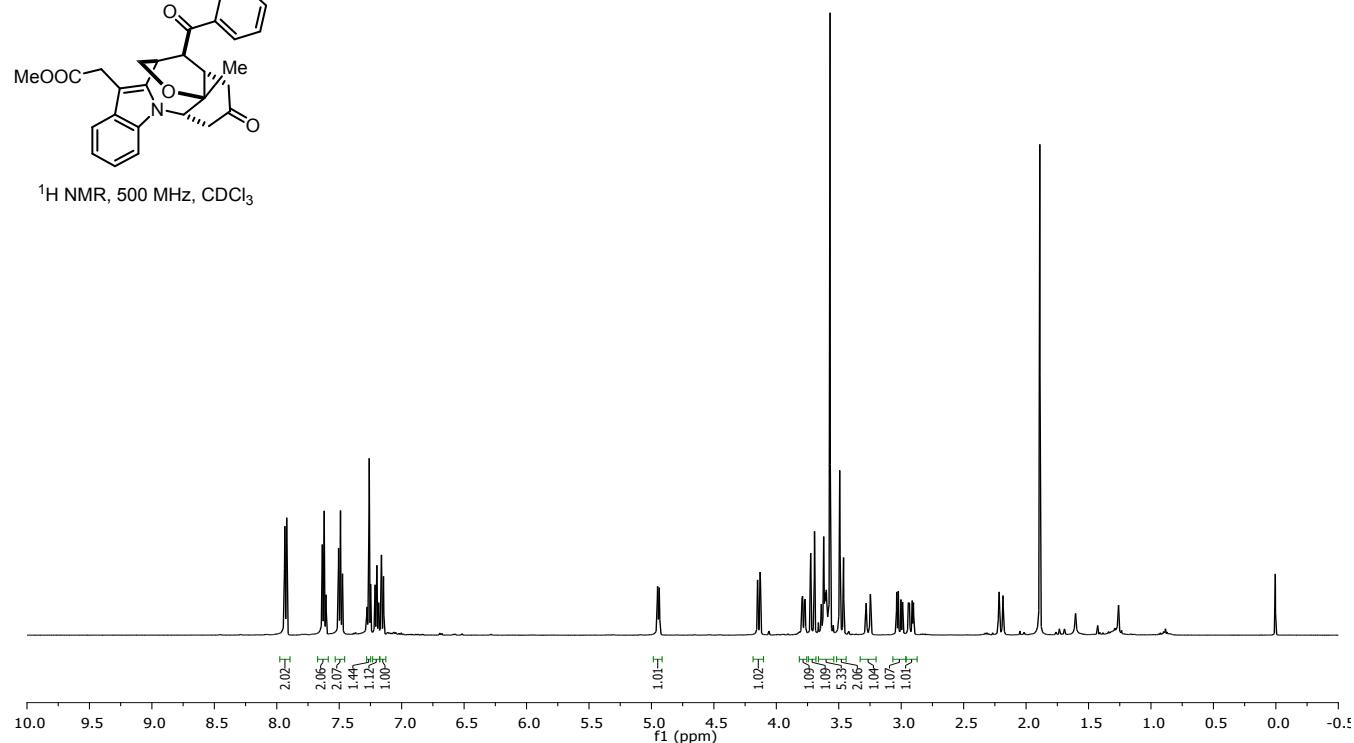
**2-(14-Benzoyl-4a-methyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-8-yl)acetic acid (10r):**



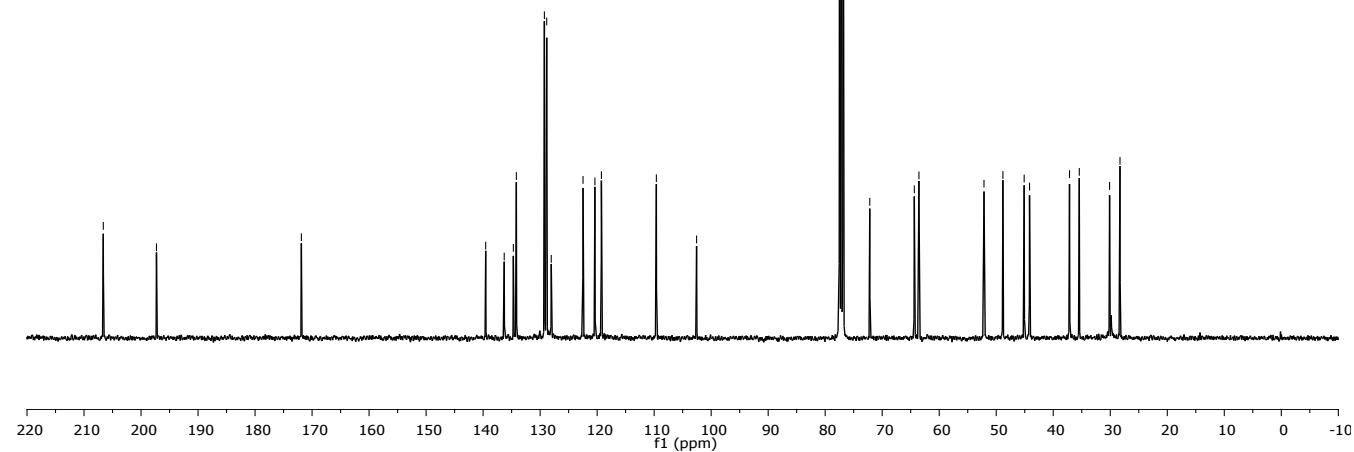
**Methyl 2-(14-benzoyl-4a-methyl-2-oxo-1,2,3,4,4a,6,7,13a-octahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-8-yl)acetate (10s):**



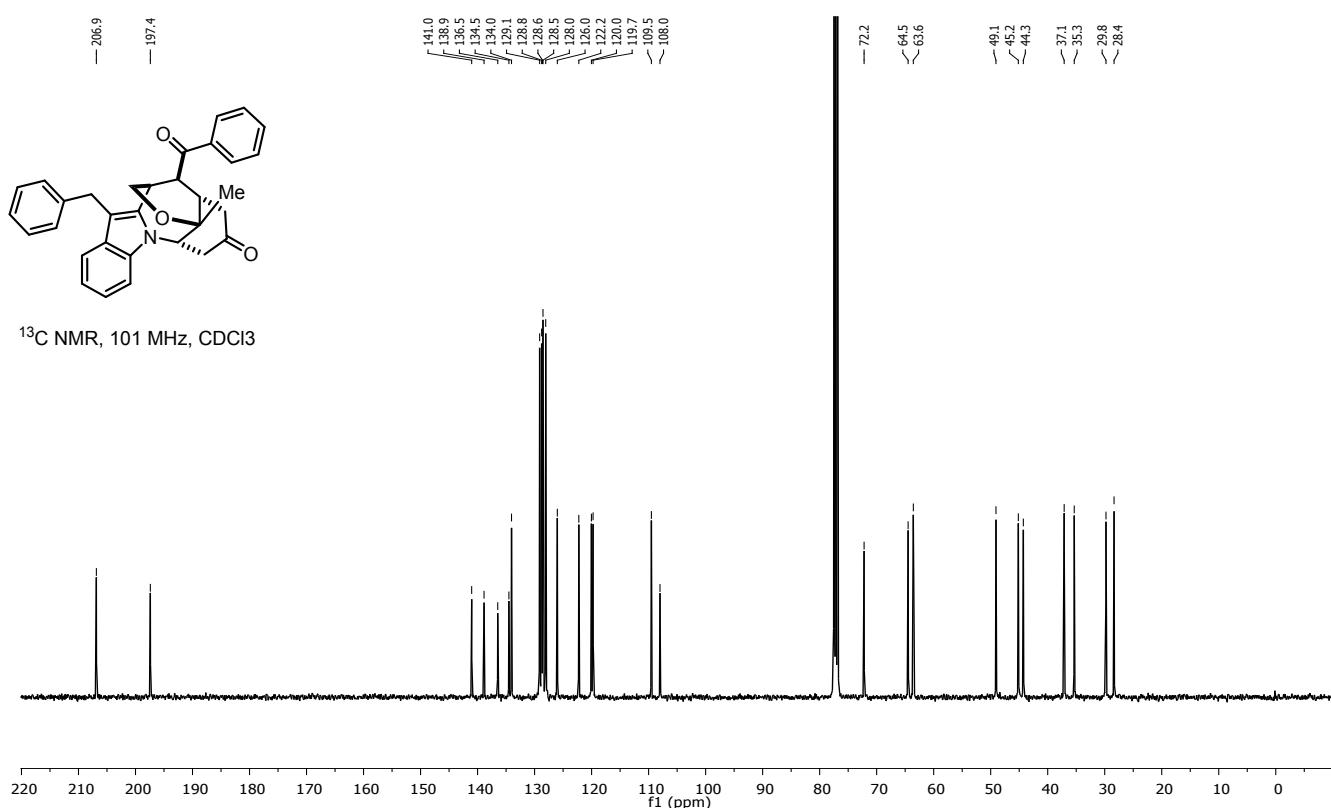
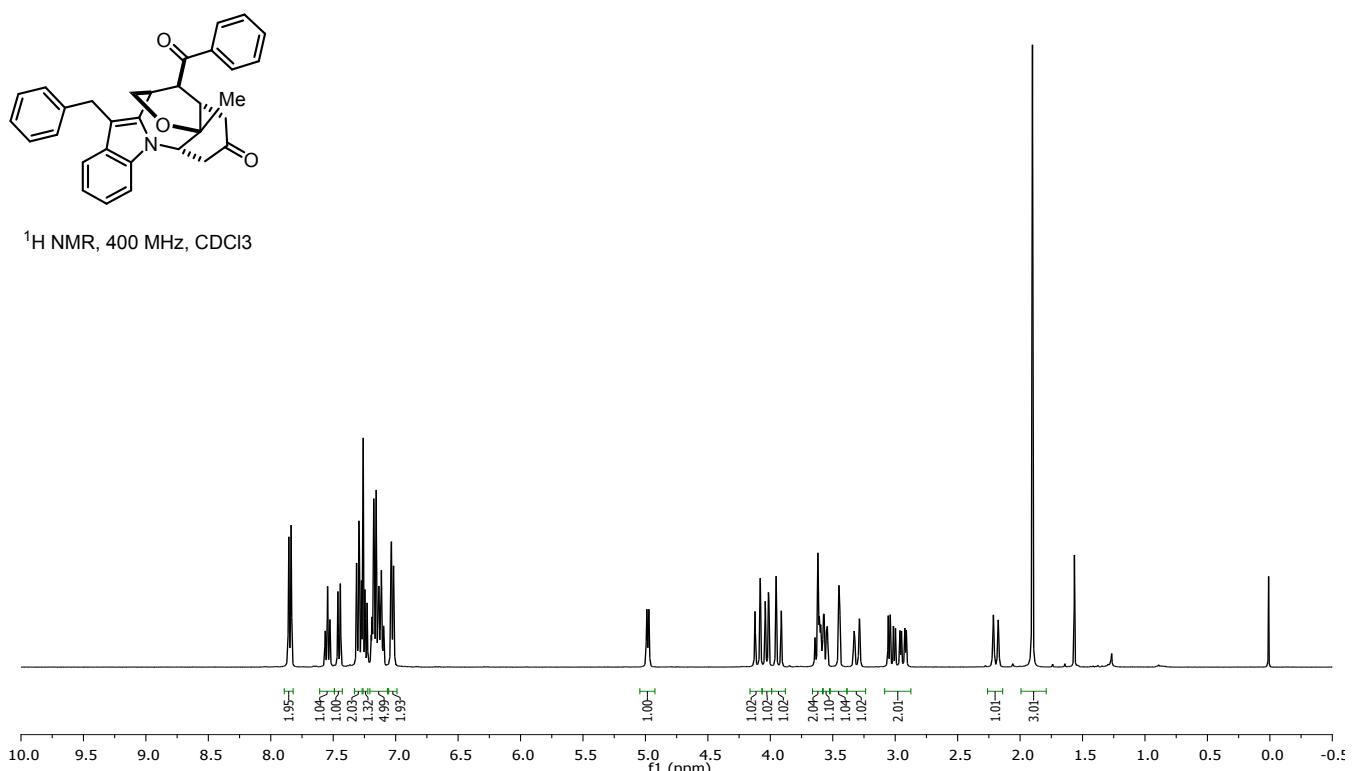
<sup>1</sup>H NMR, 500 MHz, CDCl<sub>3</sub>



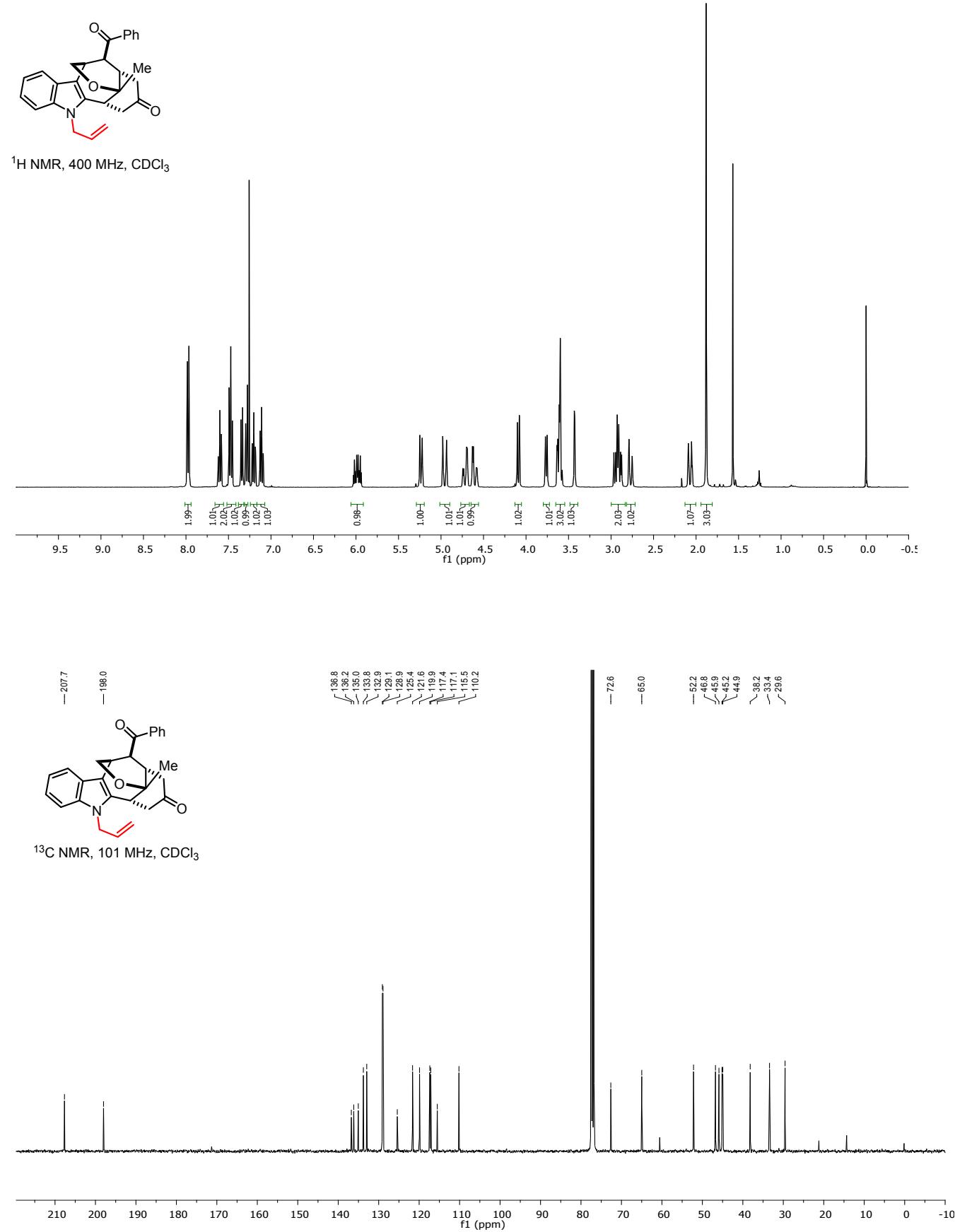
<sup>13</sup>C NMR, 101 MHz, CDCl<sub>3</sub>



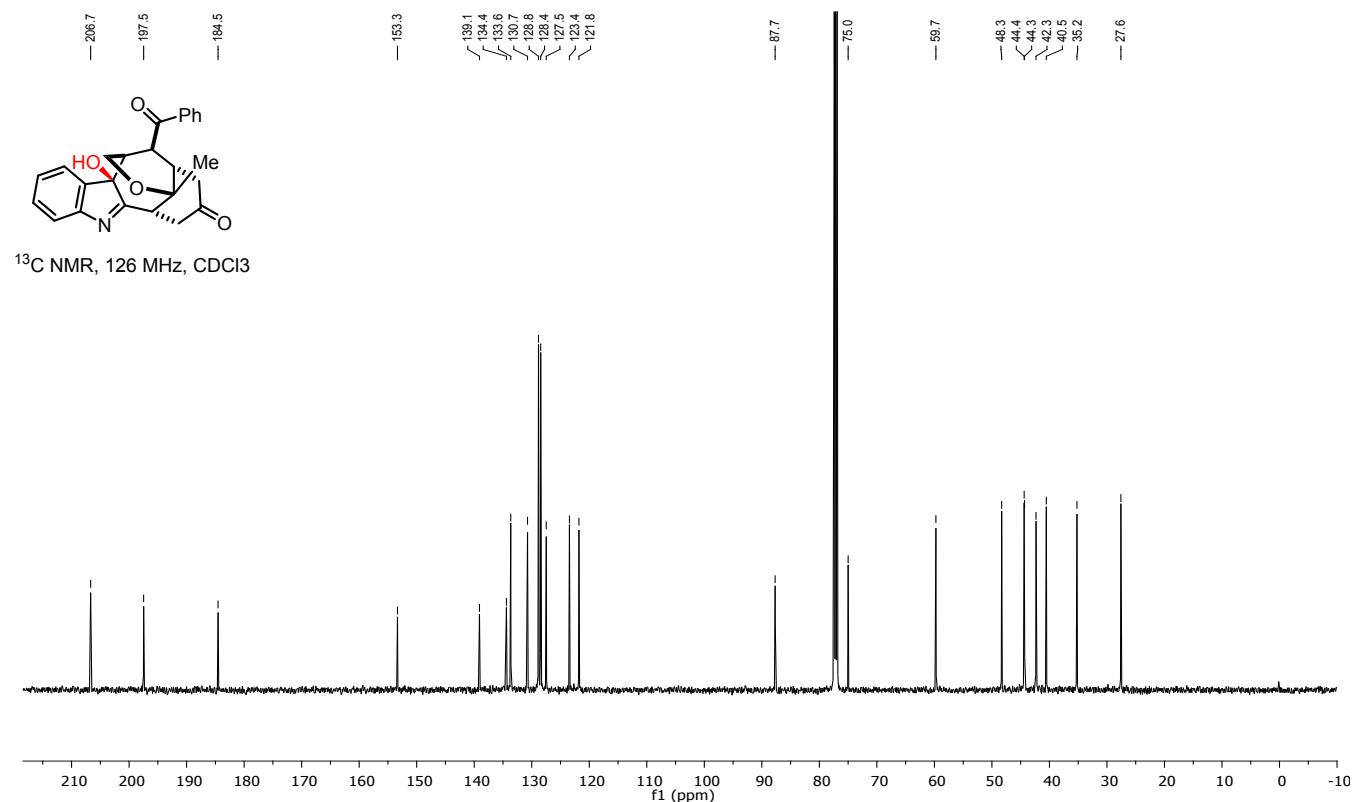
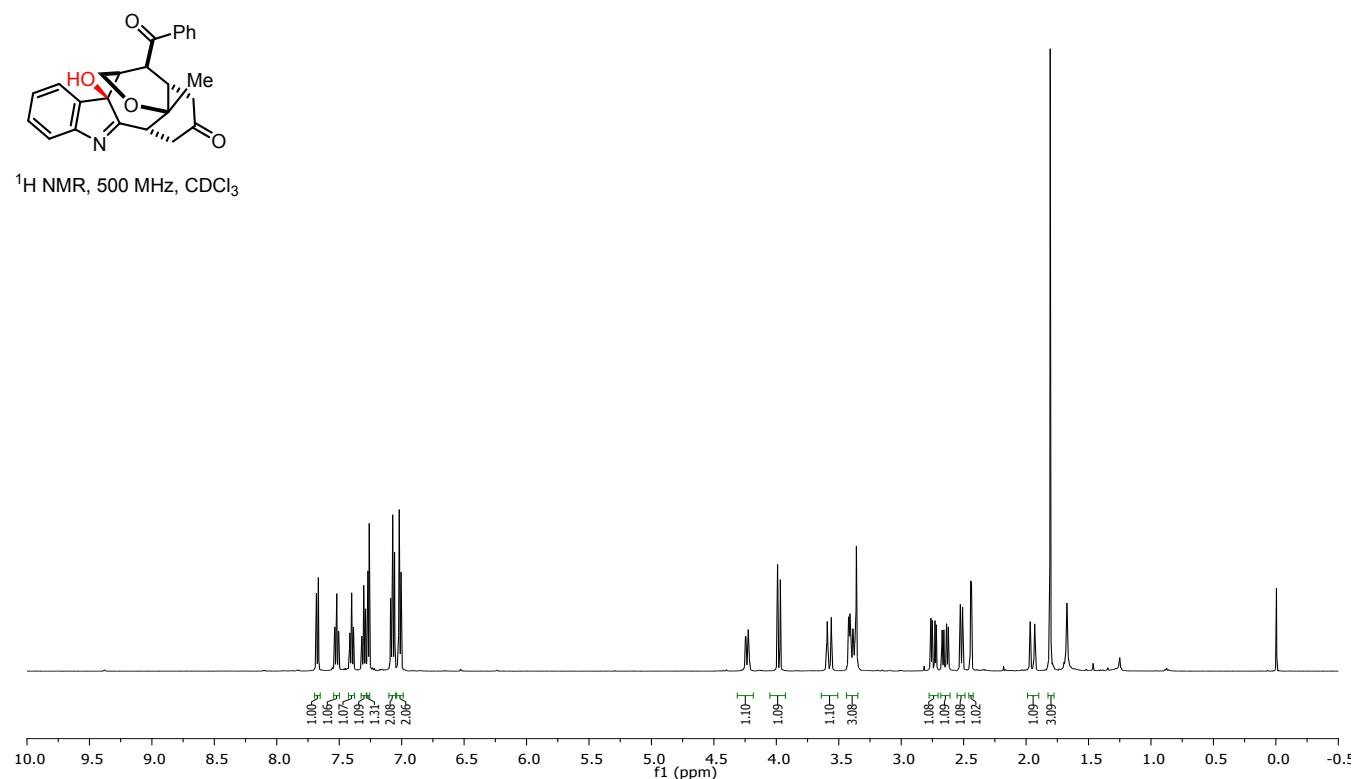
**14-Benzoyl-8-benzyl-4a-methyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2(1H)-one (10t):**



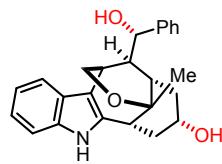
**12-Allyl-13-benzoyl-4a-methyl-4,4a,6,7,12,12b-hexahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2(3H)-one (11):**



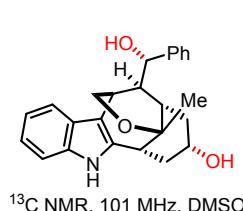
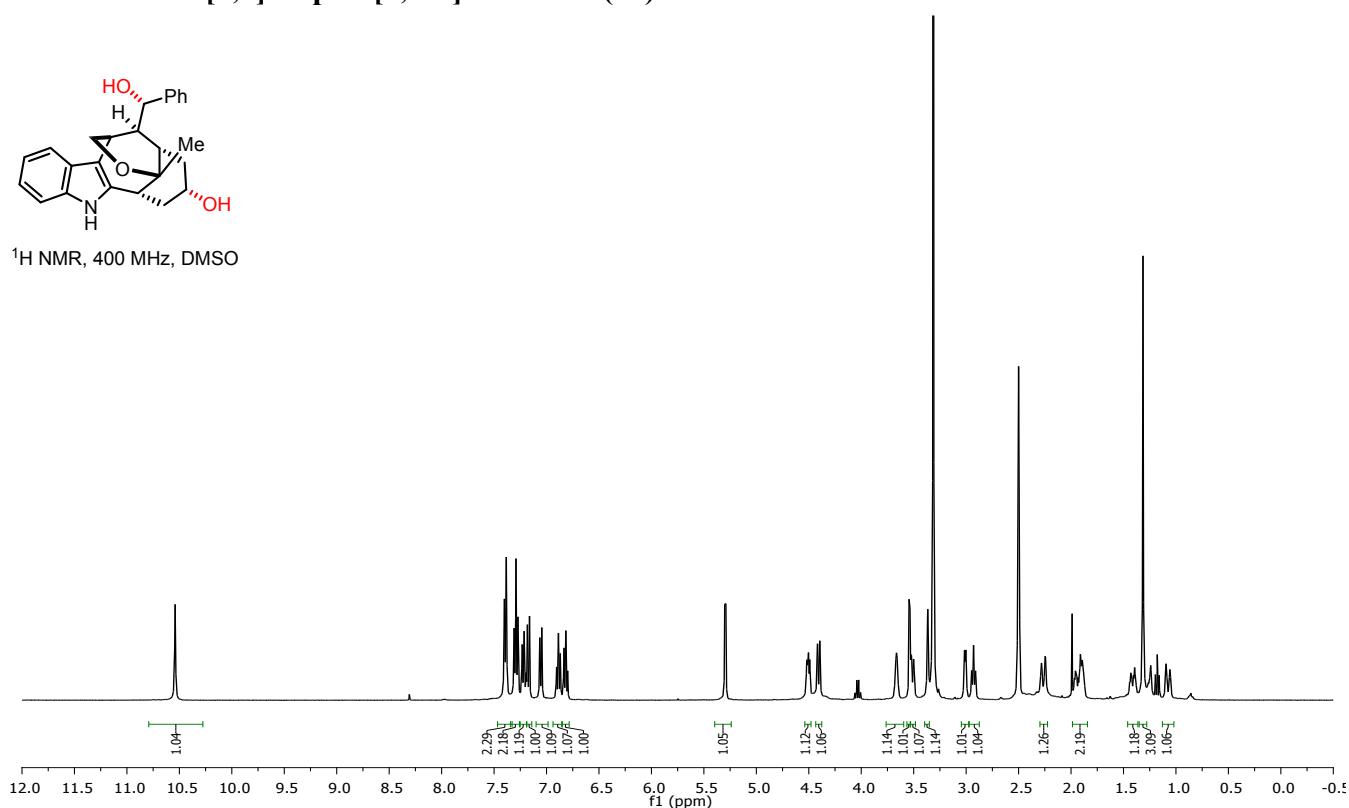
**13-Benzoyl-7a-hydroxy-4a-methyl-4,4a,6,7,7a,12b-hexahydro-1*H*-4,7-methanobenzo[2,3]oxepino[4,5-*b*]indol-2(3*H*)-one (12):**



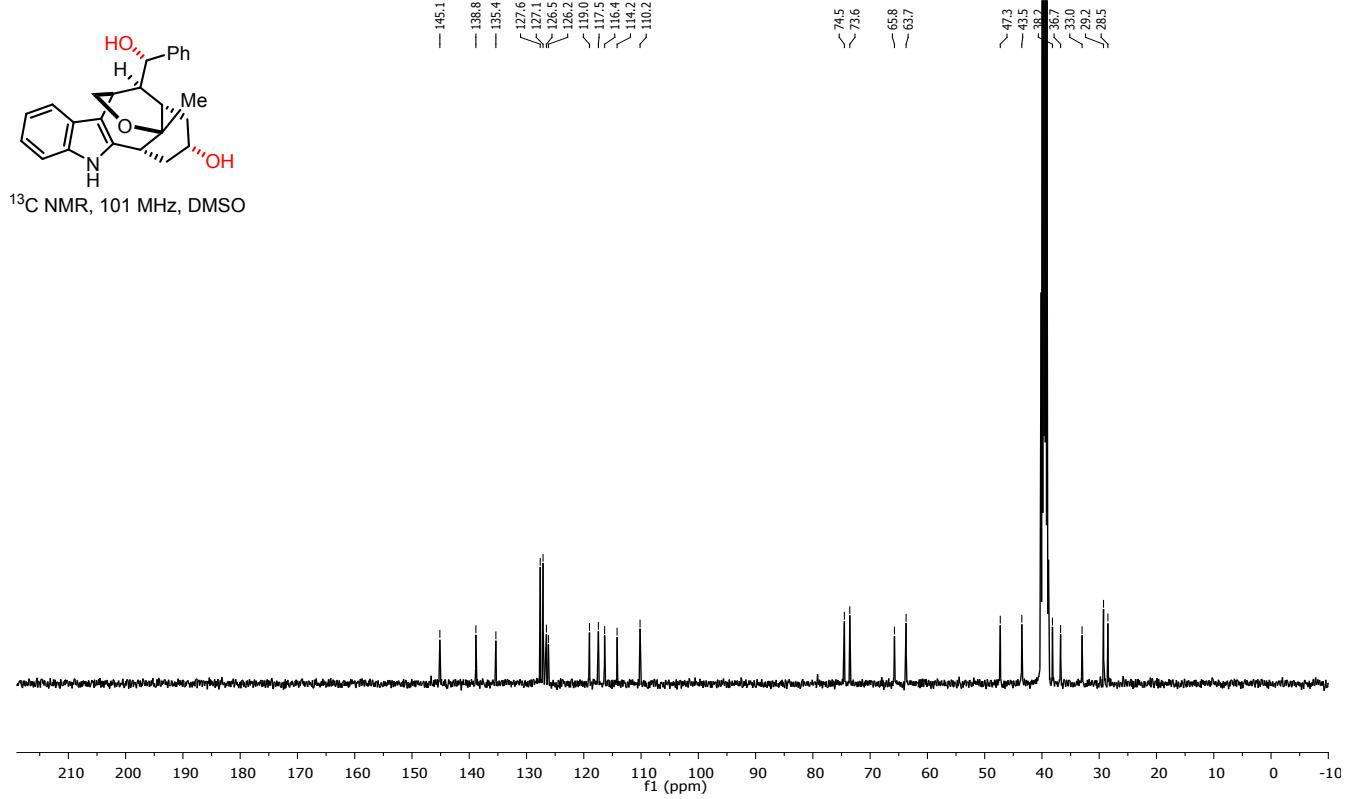
**13-(Hydroxy(phenyl)methyl)-4a-methyl-2,3,4,4a,6,7,12,12b-octahydro-1H-4,7-methanobenzo[2,3]oxepino[4,5-b]indol-2-ol (13):**

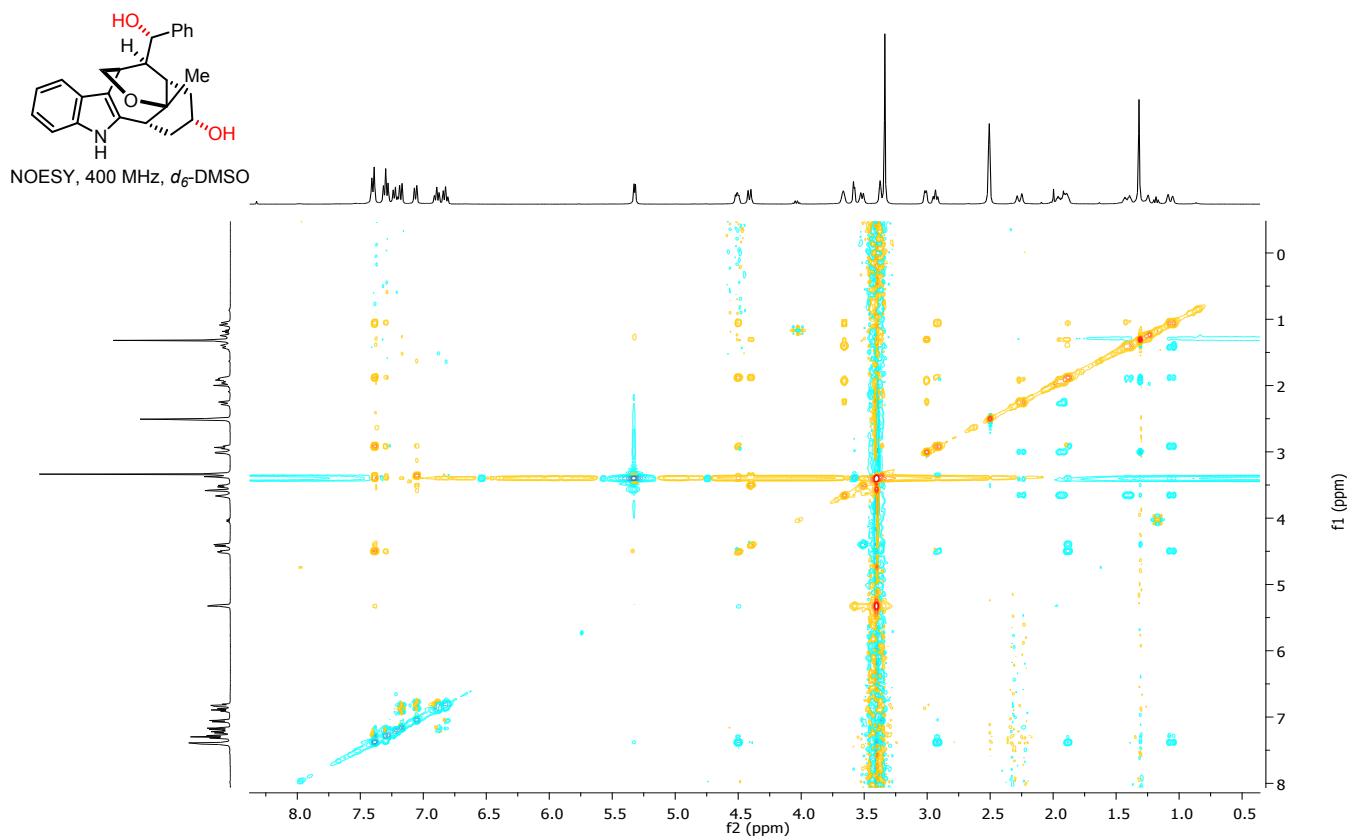
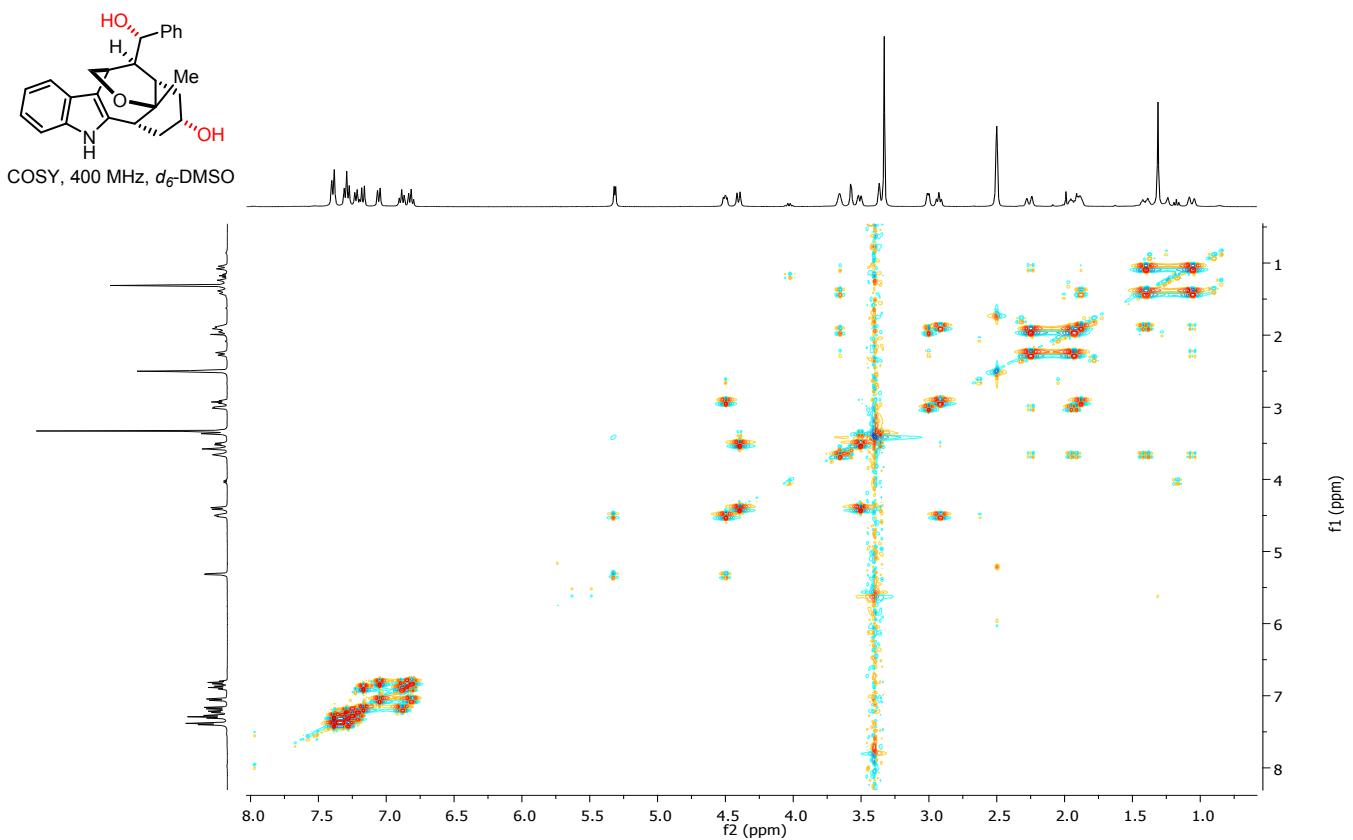


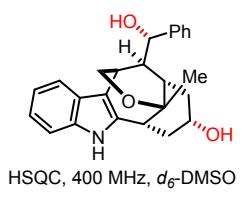
<sup>1</sup>H NMR, 400 MHz, DMSO



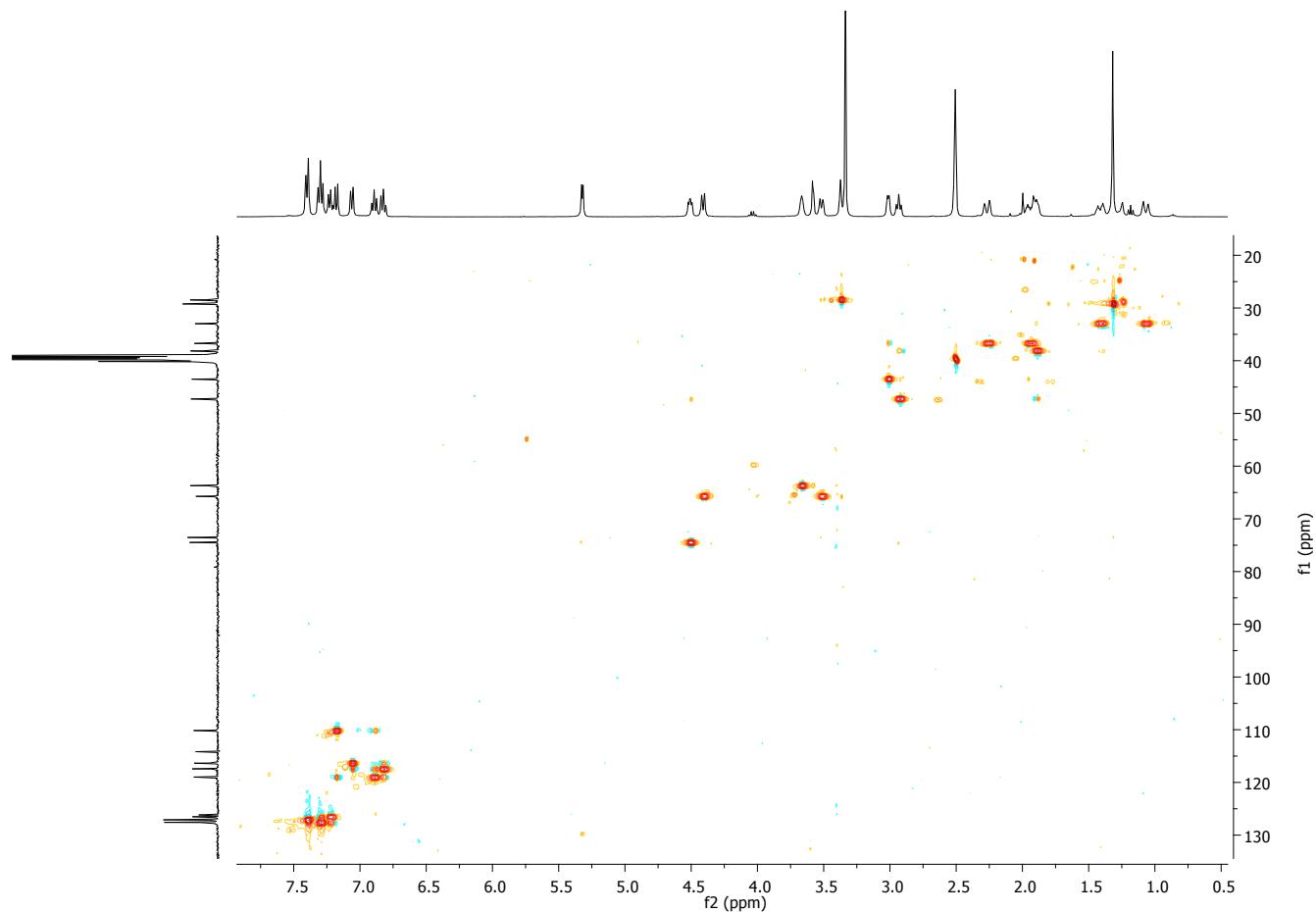
<sup>13</sup>C NMR, 101 MHz, DMSO



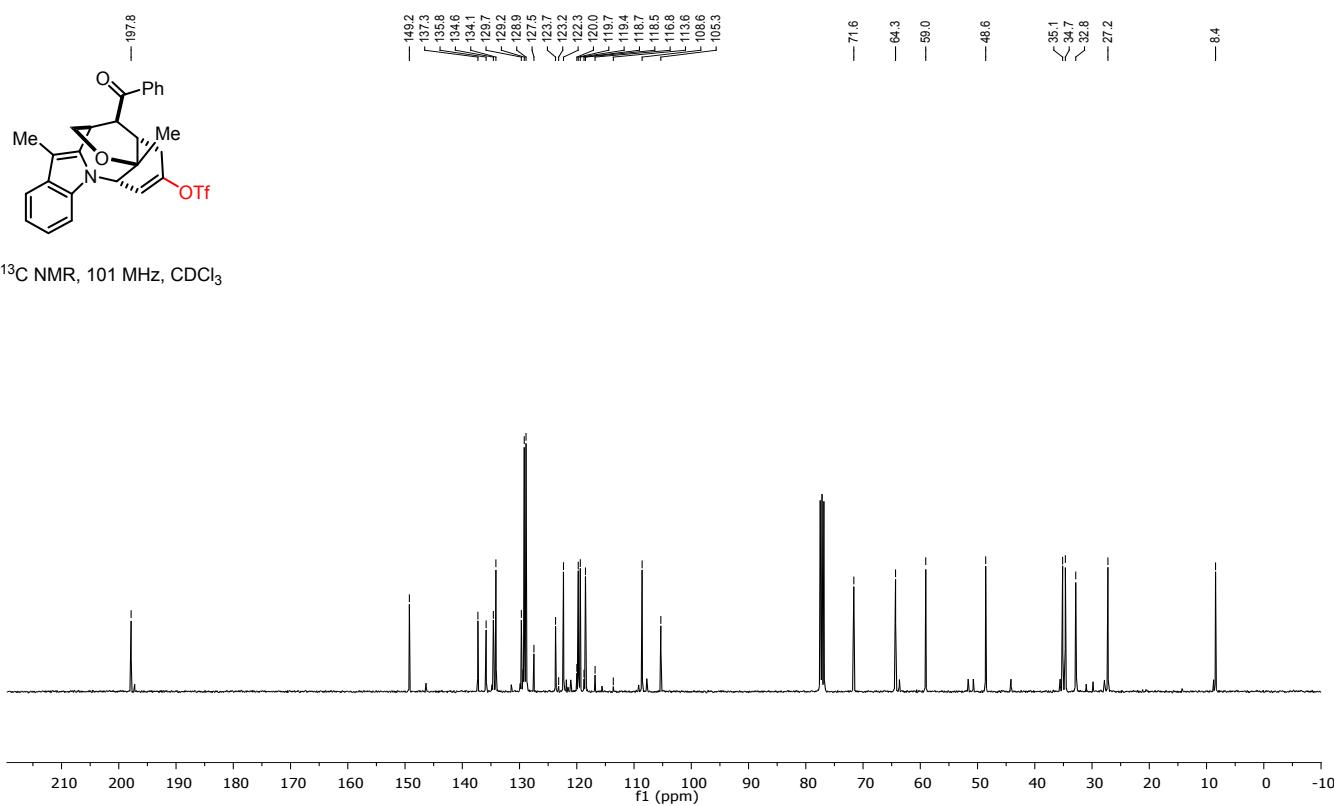
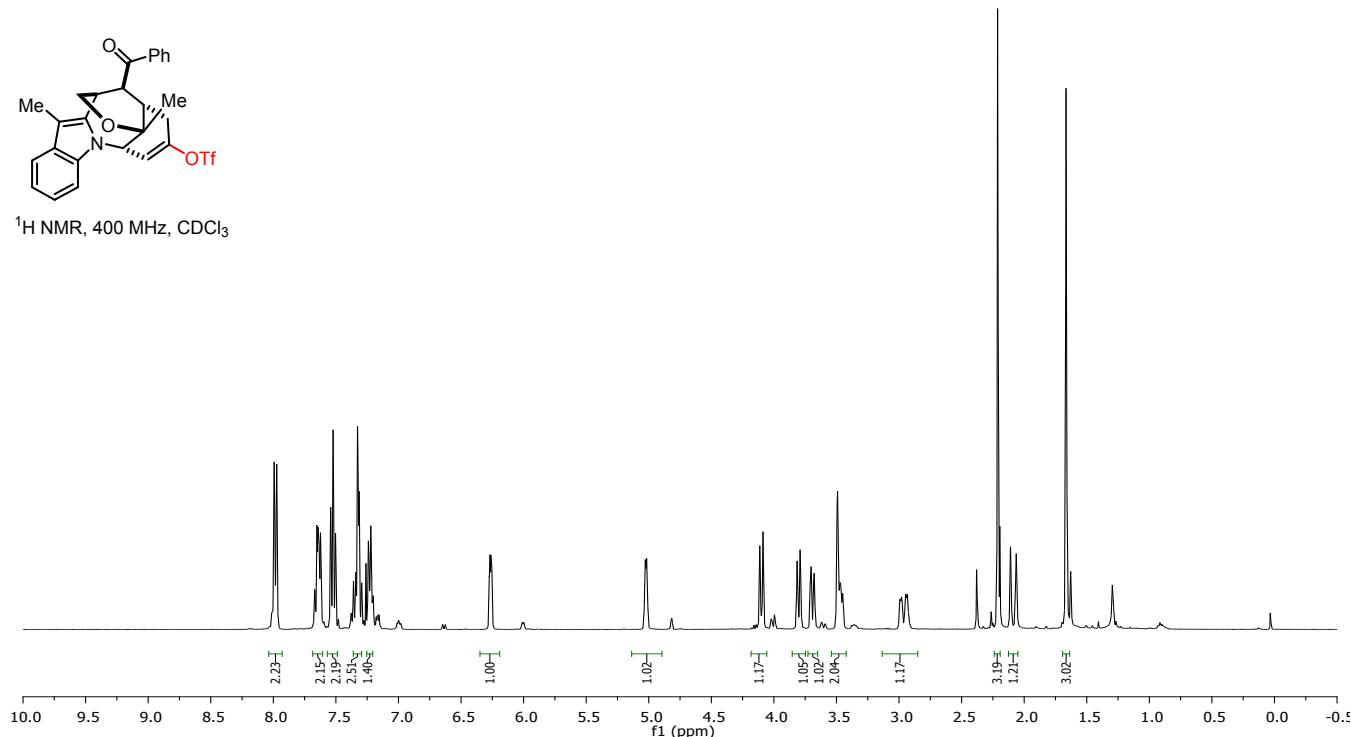




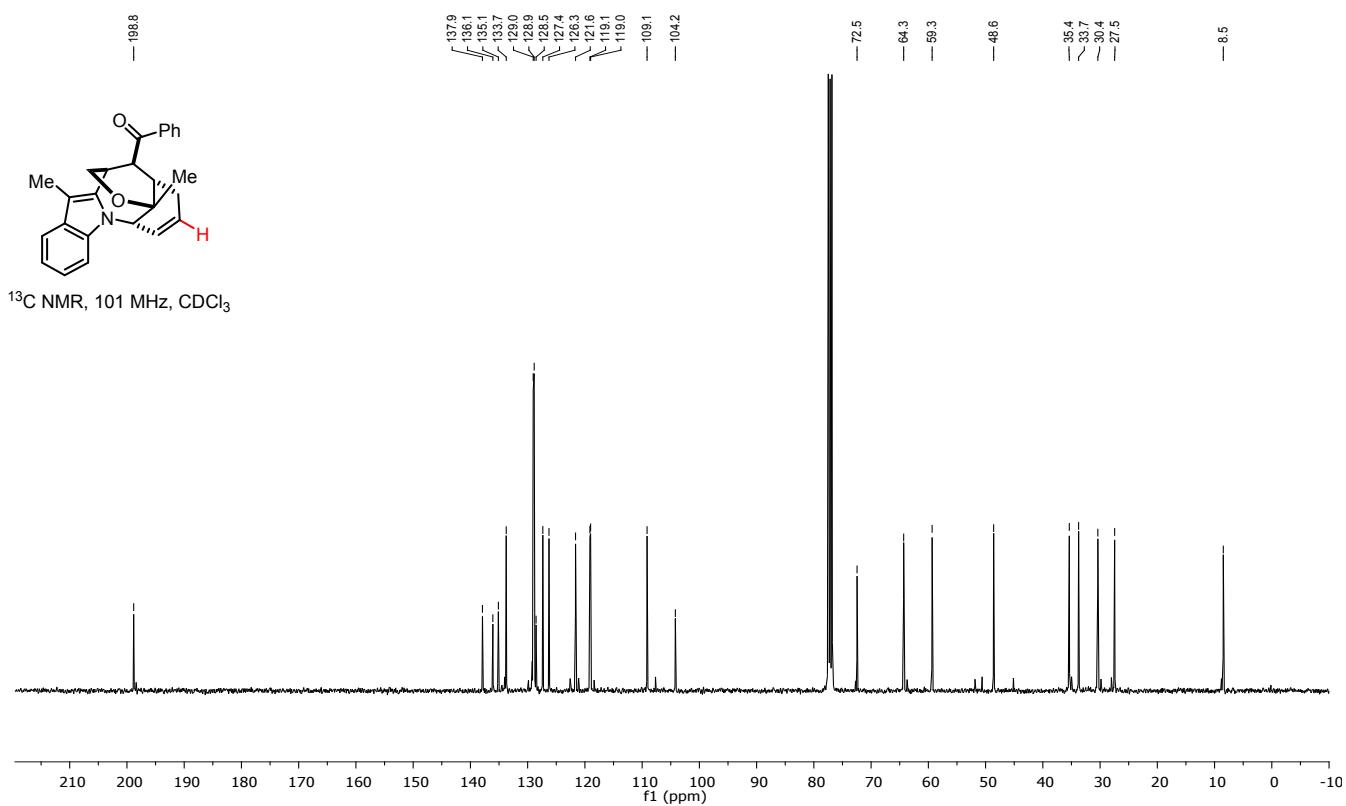
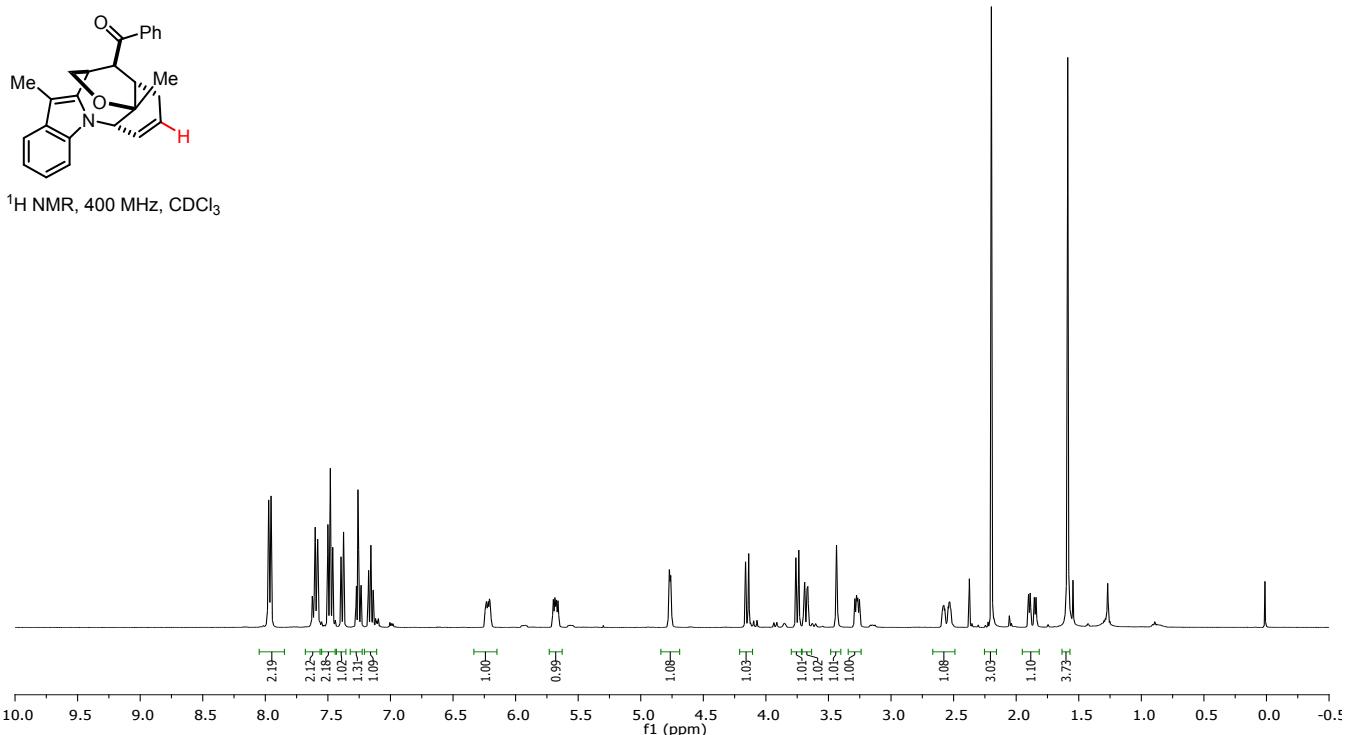
HSQC, 400 MHz,  $d_6$ -DMSO



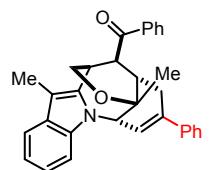
**14-Benzoyl-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-2-yl trifluoromethanesulfonate (14):**



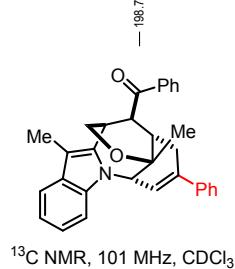
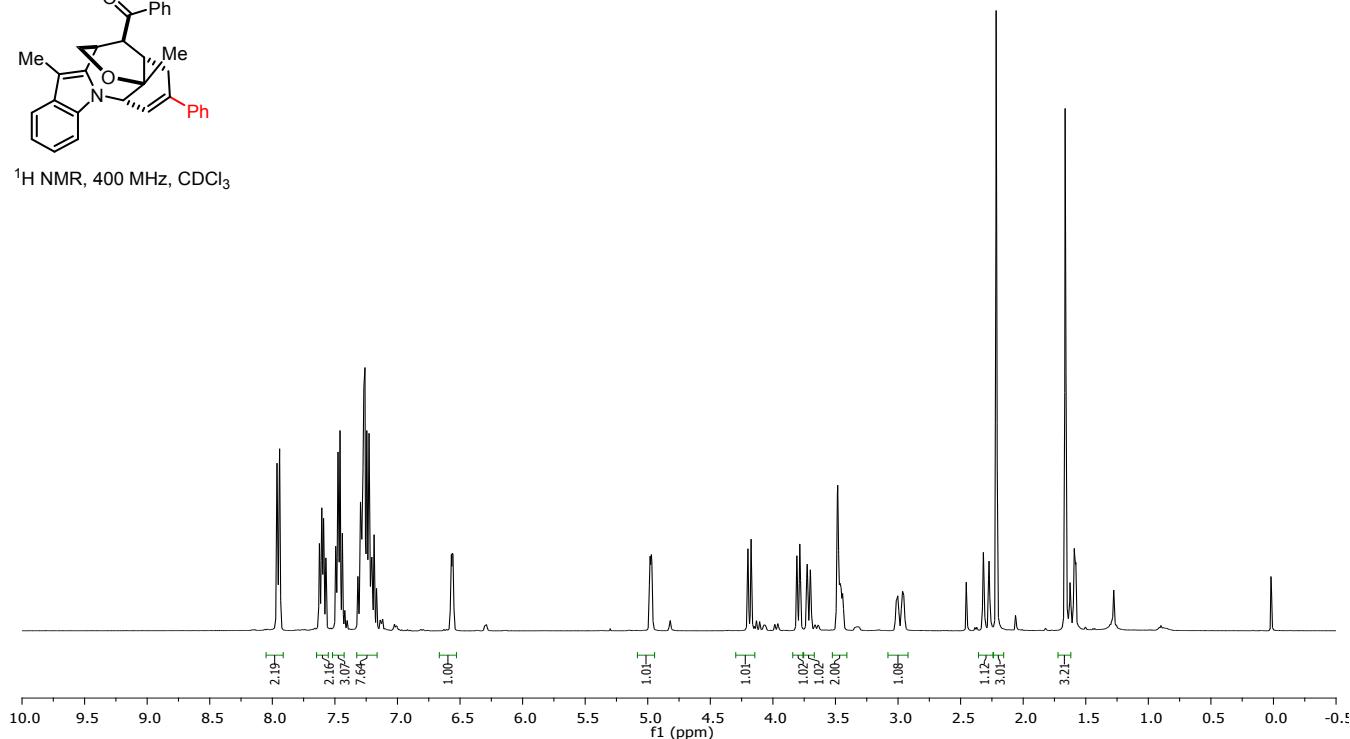
**4a,8-Dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-14-yl)(phenyl)methanone (15):**



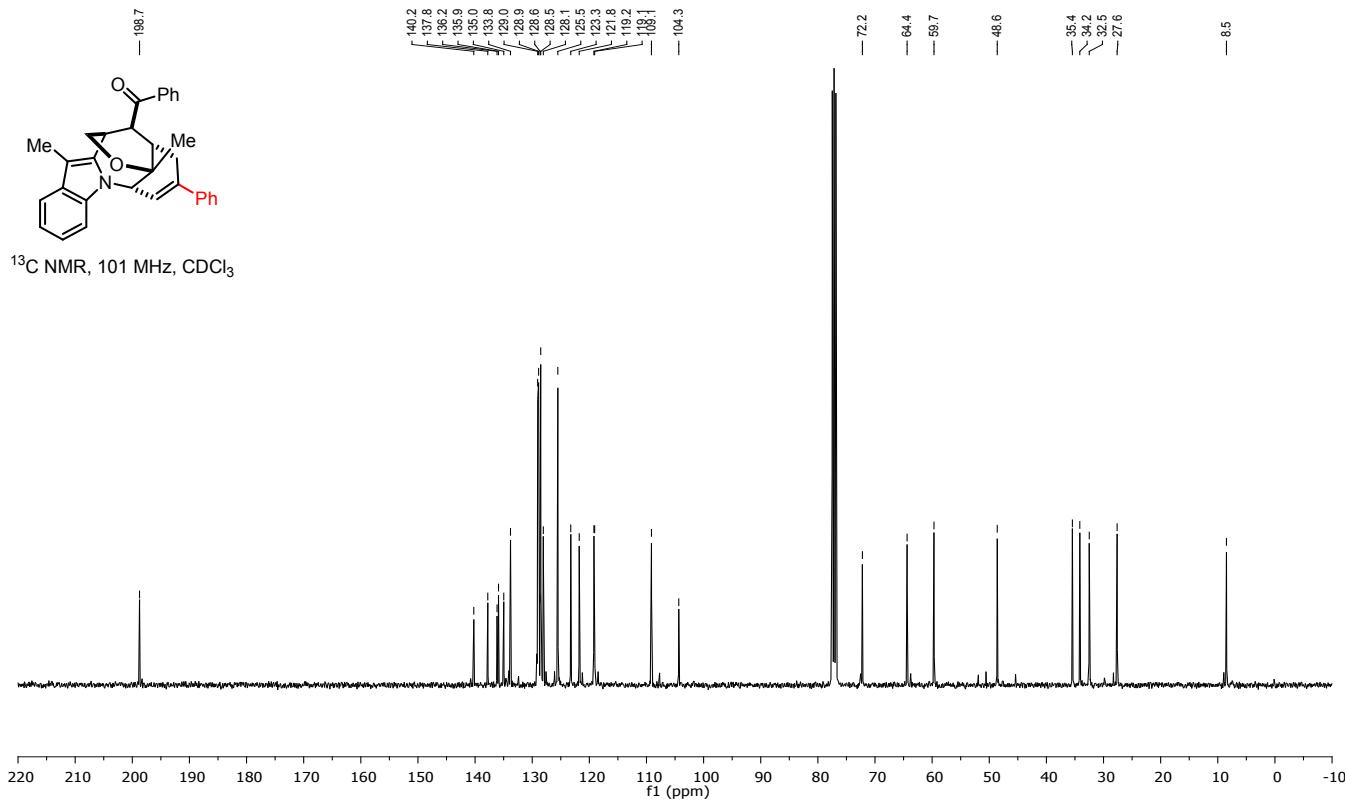
**4a,8-Dimethyl-2-phenyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-14-yl)(phenyl)methanone (16):**



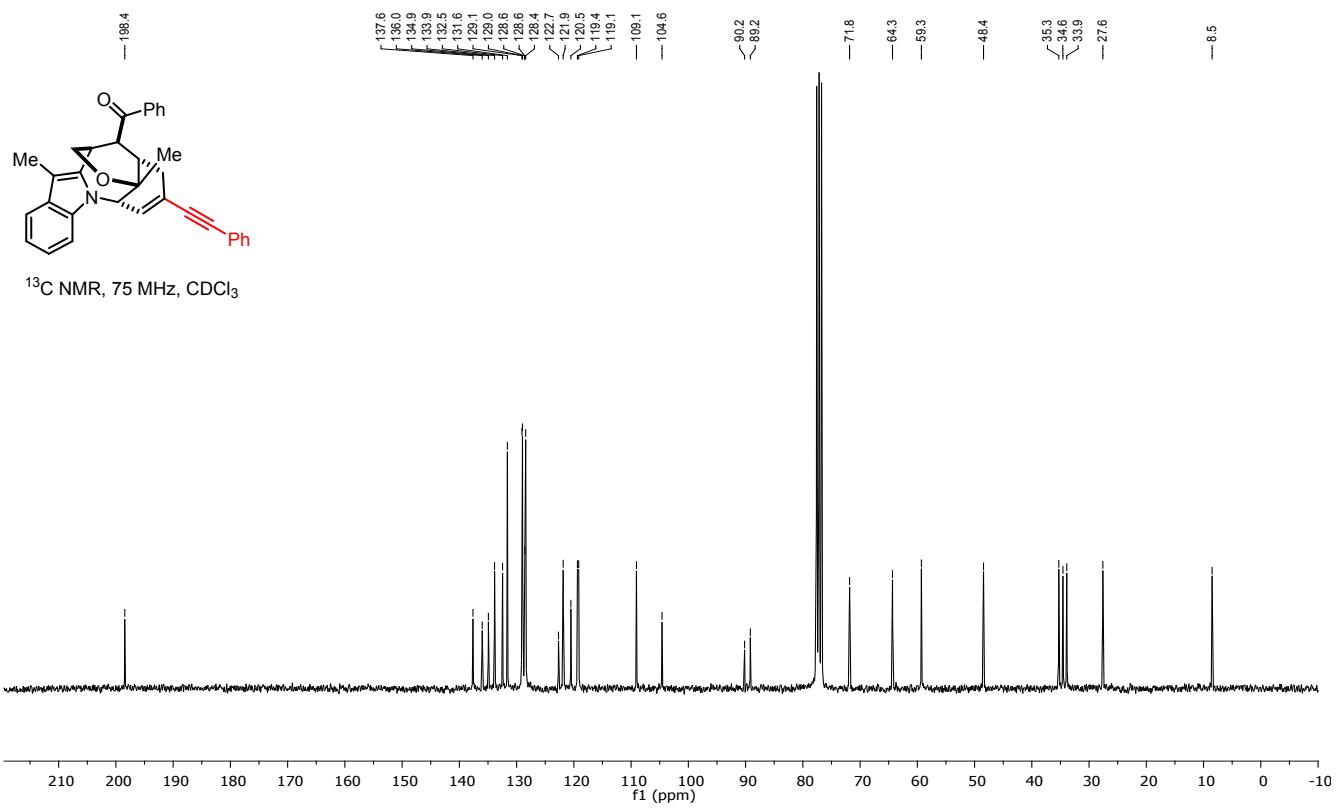
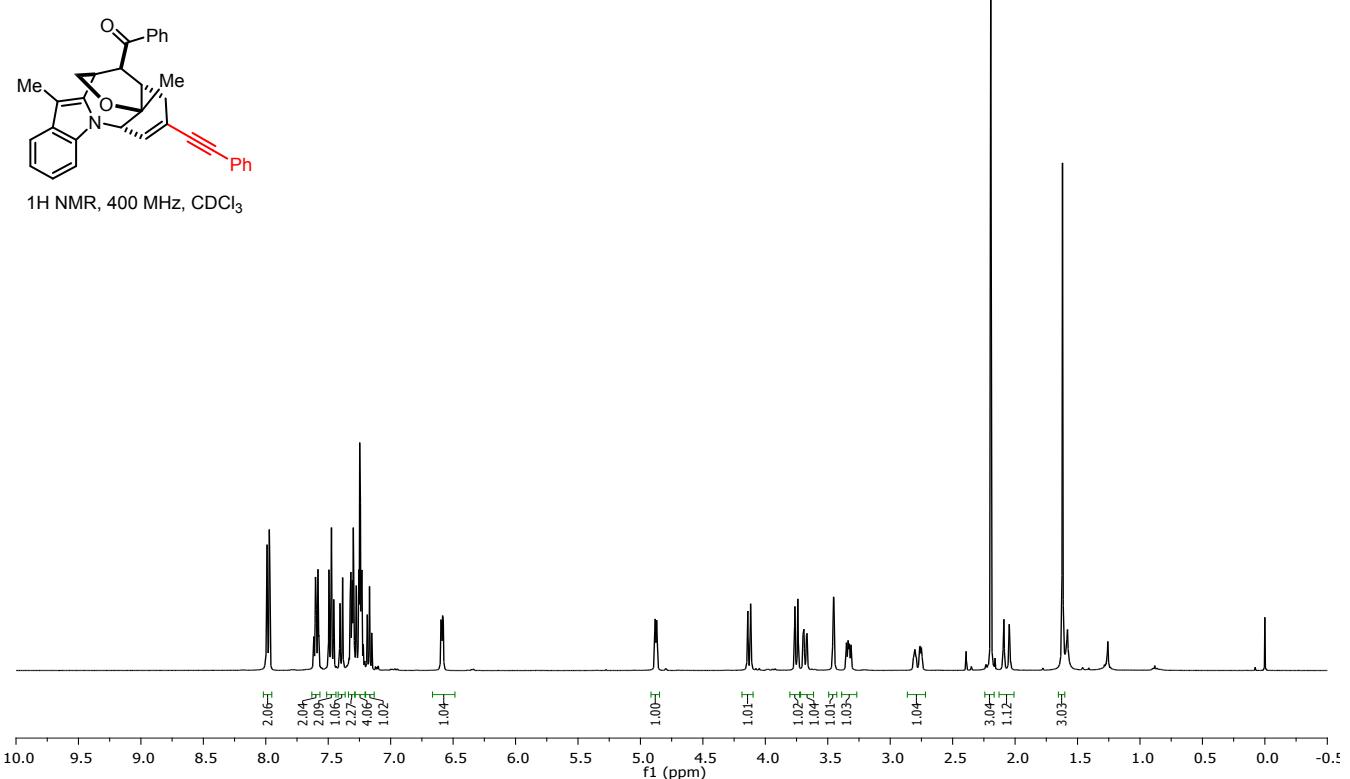
$^1\text{H}$  NMR, 400 MHz,  $\text{CDCl}_3$



$^{13}\text{C}$  NMR, 101 MHz,  $\text{CDCl}_3$



**4a,8-Dimethyl-2-(phenylethyynyl)-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-14-yl)(phenyl)methanone (17):**



**2-Allyl-4a,8-dimethyl-3,4,4a,6,7,13a-hexahydro-4,7-methanobenzo[2,3][1,4]oxazepino[4,5-a]indol-14-yl)(phenyl)methanone (18):**

