

## Electronic Supplementary Information

### FeCl<sub>3</sub> catalysed 7-membered ring formation in a single pot: a new route to indole-fused oxepines/azepines and their cytotoxic activity

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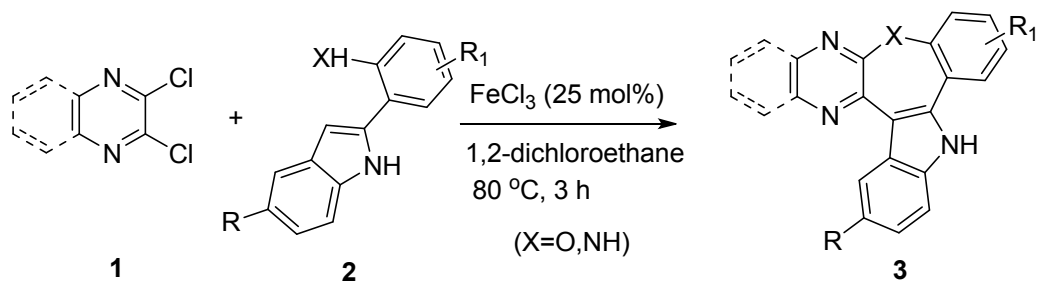
<sup>a</sup>Department of Chemistry, Osmania University, Hyderabad 500 007, India.

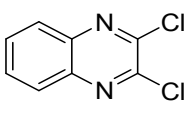
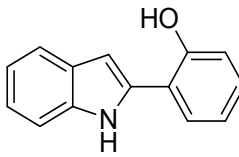
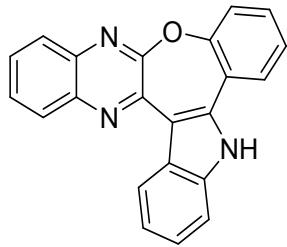
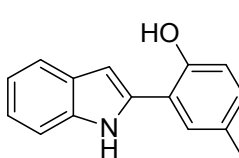
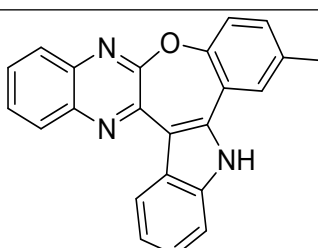
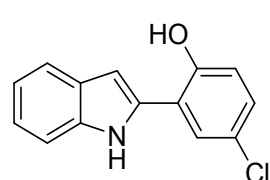
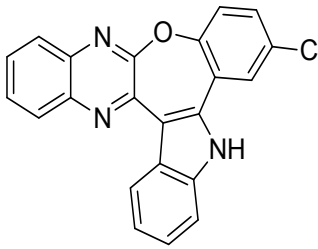
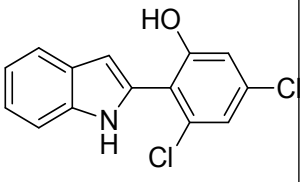
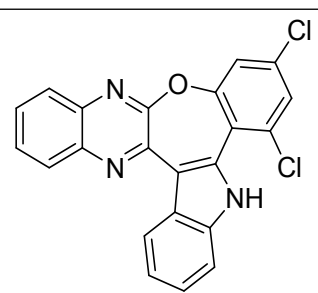
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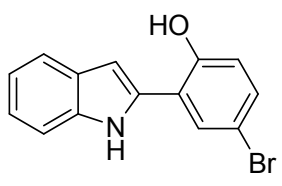
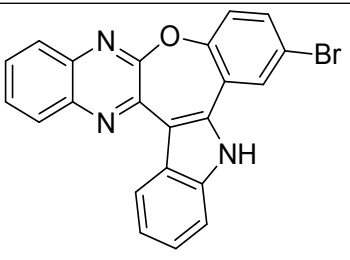
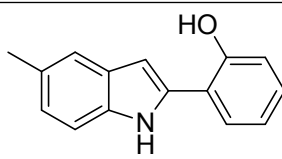
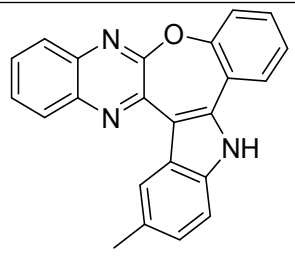
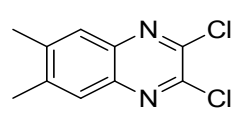
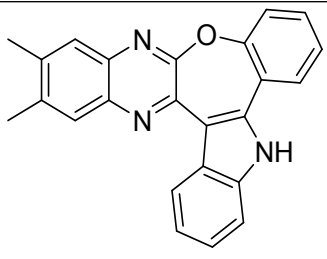
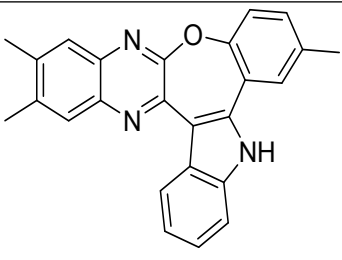
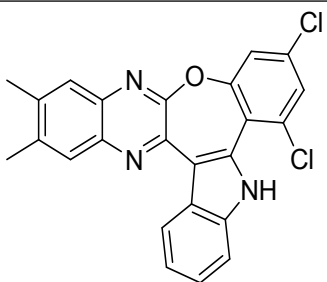
<sup>b</sup>Molecular Medicine and Therapeutics Laboratory, CPMB, Osmania University, Hyderabad-500007.

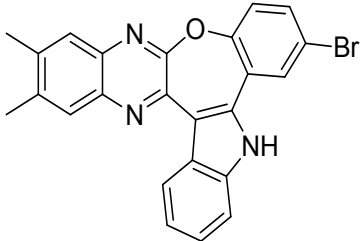
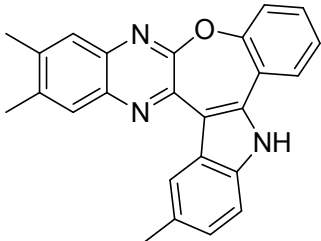
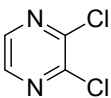
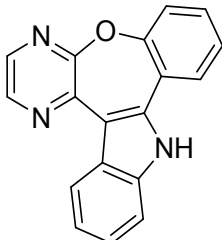
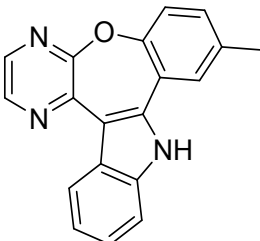
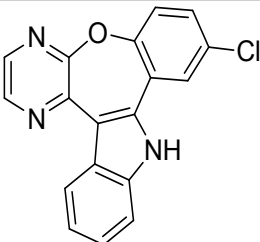
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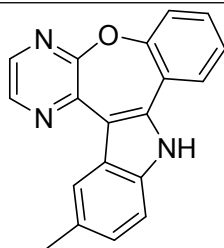
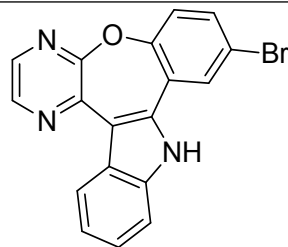
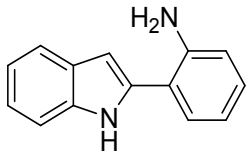
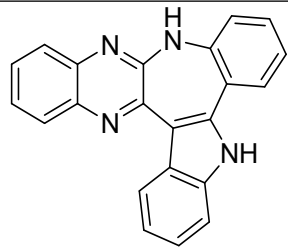
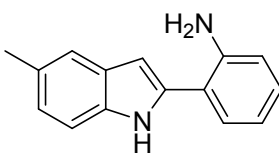
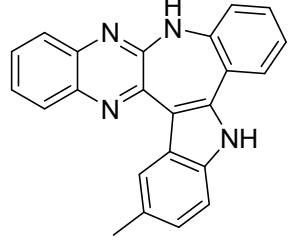
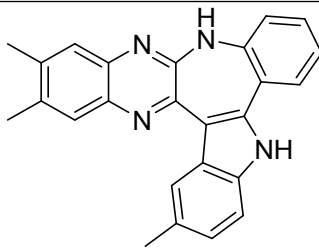
**Table S-1.** Synthesis of oxepine/azepine fused *N*-heterocycles via FeCl<sub>3</sub>-catalysed C–C and C–O/N bond forming reaction between **1** and **2**.



Entry	Dichloro <i>N</i> -heterocycles ( <b>1</b> )	Indole <b>2</b> ; R, R <sub>1</sub> =	Oxepine/azepine <b>3</b> ; R, R <sub>1</sub> =	% Yield <sup>b</sup>
1	 <b>1a</b>	 <b>2a</b>	 <b>3a</b>	87
2	<b>1a</b>	 <b>2b</b>	 <b>3b</b>	85
3	<b>1a</b>	 <b>2c</b>	 <b>3c</b>	85
4	<b>1a</b>	 <b>2d</b>	 <b>3d</b>	81

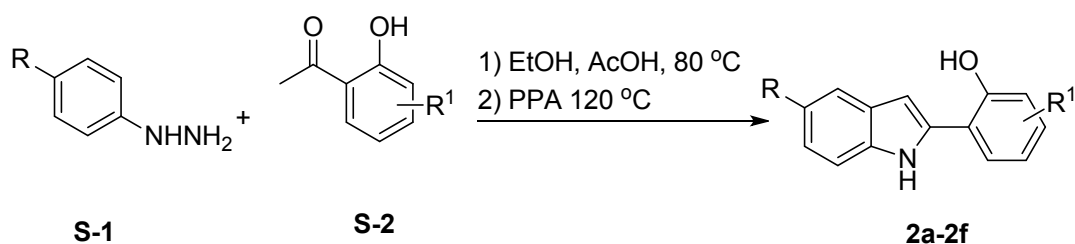
5	<b>1a</b>	 <p><b>2e</b></p>	<p><b>3d</b></p>  <p><b>3e</b></p>	81
6	<b>1a</b>	 <p><b>2f</b></p>	 <p><b>3f</b></p>	85
7	 <p><b>1b</b></p>	<b>2a</b>	 <p><b>3g</b></p>	78
8	<b>1b</b>	<b>2b</b>	 <p><b>3h</b></p>	78
9	<b>1b</b>	<b>2d</b>	 <p><b>3i</b></p>	78

10	<b>1b</b>	<b>2e</b>	 <p><b>3j</b></p>	81
11	<b>1b</b>	<b>2f</b>	 <p><b>3k</b></p>	83
12	 <p><b>1c</b></p>	<b>2a</b>	 <p><b>3l</b></p>	81
13	<b>1c</b>	<b>2b</b>	 <p><b>3m</b></p>	80
14	<b>1c</b>	<b>2c</b>	 <p><b>3n</b></p>	82

15	<b>1c</b>	<b>2f</b>	 <p><b>3o</b></p>	81
16	<b>1c</b>	<b>2e</b>	 <p><b>3p</b></p>	83
17	<b>1a</b>	 <p><b>2g</b></p>	 <p><b>3q</b></p>	75
18	<b>1a</b>	 <p><b>2h</b></p>	 <p><b>3r</b></p>	74
19	<b>1b</b>	<b>2h</b>	 <p><b>3s</b></p>	75

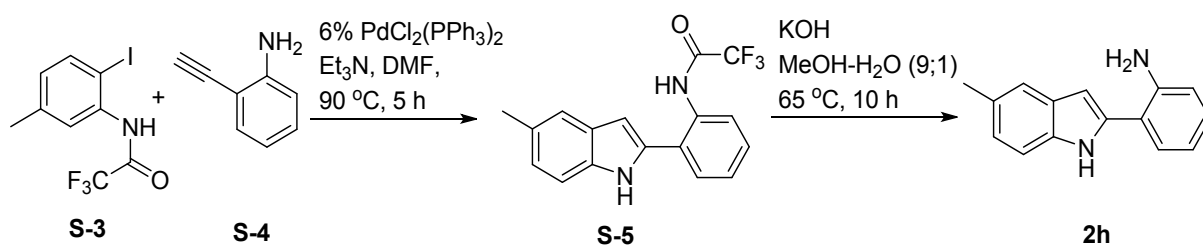
<sup>a</sup>All the reactions were carried out using compound **1** (1.0 equiv), **2** (1.0 equiv) and FeCl<sub>3</sub> (25 mol%) in a DCE (5 mL) at 80 °C for 3 h. <sup>b</sup>Isolated yield

### General procedure for the synthesis of 2-(2-phenylaryl)indoles (2a-f)<sup>1</sup>



To a mixture of acetophenone (**S-2**) (15.00 mmol) in EtOH, phenylhydrazine (**S-1**) (1.47 mL, 15.00 mmol) was added, followed by 5 drops of AcOH. Then, the reaction mixture stirred at 80 °C for 1 h. After cooled to room temperature, solvent was removed under reduced pressure. Polyphosphonic acid (PPA, 10.00 mL) was added then heated at 120 °C for 1 h. The reaction mixture then was poured on ice and neutralised with 2 M NaOH and extracted with EtOAc. The combined organic layer was washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give indolyl phenol (**2**).

### Synthesis of 2-(5-methyl-1H-indol-2-yl)aniline (**2h**)<sup>2,3</sup>



To a solution of aromatic 2-ethynylaniline (**S-4**) (1.0 equiv.), 2,2,2-trifluoro-N-(2-iodo-5-methylphenyl)acetamide (1.1 equiv.) (**S-3**) and 4 equiv. Et<sub>3</sub>N in DMF (5 ml) was added PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (6 mol%) at room temperature with stirring. The mixture was warmed to 90 °C under stirring. After completion of the starting material, (the reaction was monitored by TLC) the reaction mixture was cooled to room temperature and then filtered through a short pad of silica gel. The filtrate was concentrated under reduced pressure. The residue was purified by chromatography (EtOAc/n-Hexane) to give the desired products (**S-5**) which were directly used for next step.

To a solution of **S-5** in methanol-H<sub>2</sub>O (9:1) was added 3 equiv. KOH. The mixture was stirred at 65 °C for 10 h. After completion of the reaction (monitored by TLC), the

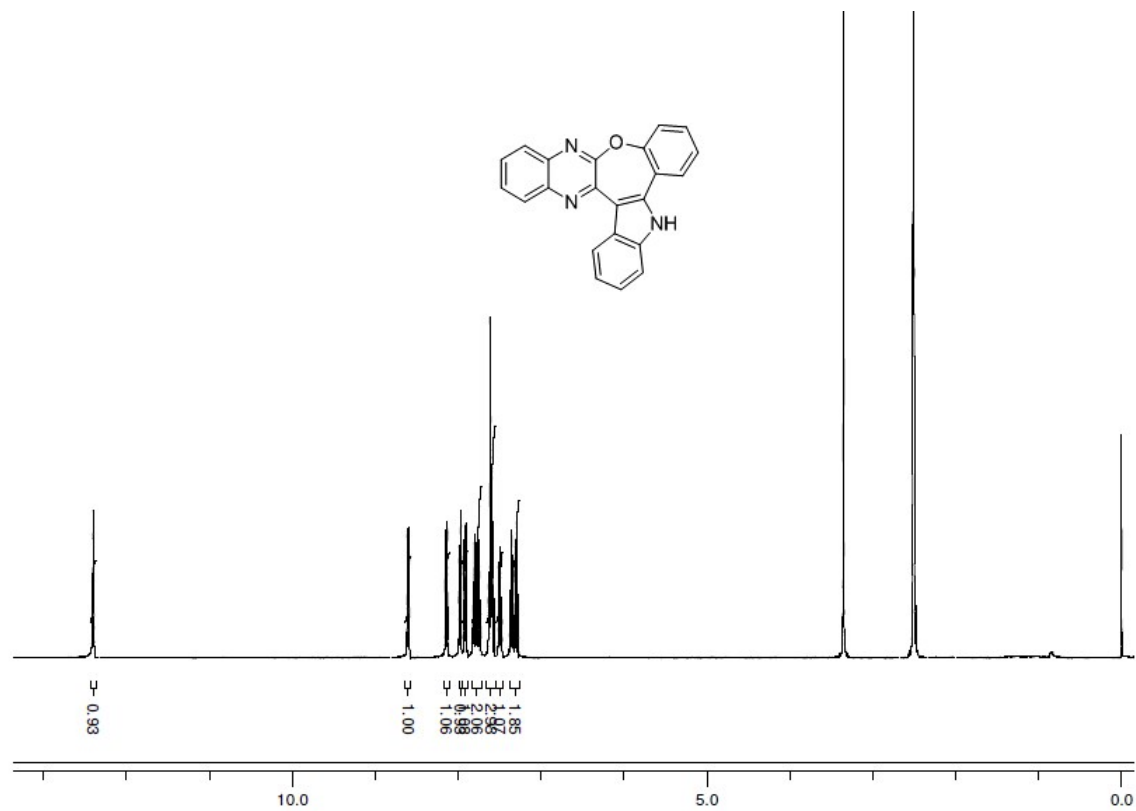
mixture was poured into cold water (10 mL) and extracted with EtOAc (3 × 20 mL). The organic layers were collected, combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by column chromatography using EtOAc/n-hexane to give the desired product (**2h**). Brown solid; Yield: 75%; mp: 163-165 °C (lit<sup>2a</sup> 166-168 °C); R<sub>f</sub> = 0.3 (20% EtOAc/n-hexane); <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ 11.03 (s, 1H), 7.32-7.23 (m, 3H), 7.03 (t, *J* = 8.4 Hz, 1H), 6.88 (d, *J* = 6.8 Hz, 1H), 6.79 (d, *J* = 8 Hz, 1H), 6.65 (t, *J* = 7.6 Hz, 1H), 6.54 (s, 1H), 5.12 (s, 2H), 2.35 (s, 3H); Mass: m/z (CI) 223 (M + 1, 100%).

## References

1. X.-H. Xu, M. Taniguchi, A. Azuma, G.-K. Liu, E. Tokunaga, N. Shibata, *Org. Lett.* 2013, **15**, 686-689.
2. (a) N. T. Patil, R. D. Kavthe, V. S. Shinde, B. Sridhar, *J. Org. Chem.* 2010, **75**, 3371-3380;  
(b) A. Arcadi, S. Cacchi, G. Fabrizi, F. Marinelli, L. Parisi, M. *Heterocycles*, 2004, **64**, 475-482.
3. T. J. Snape, *Synlett* 2008, 2689-2691.

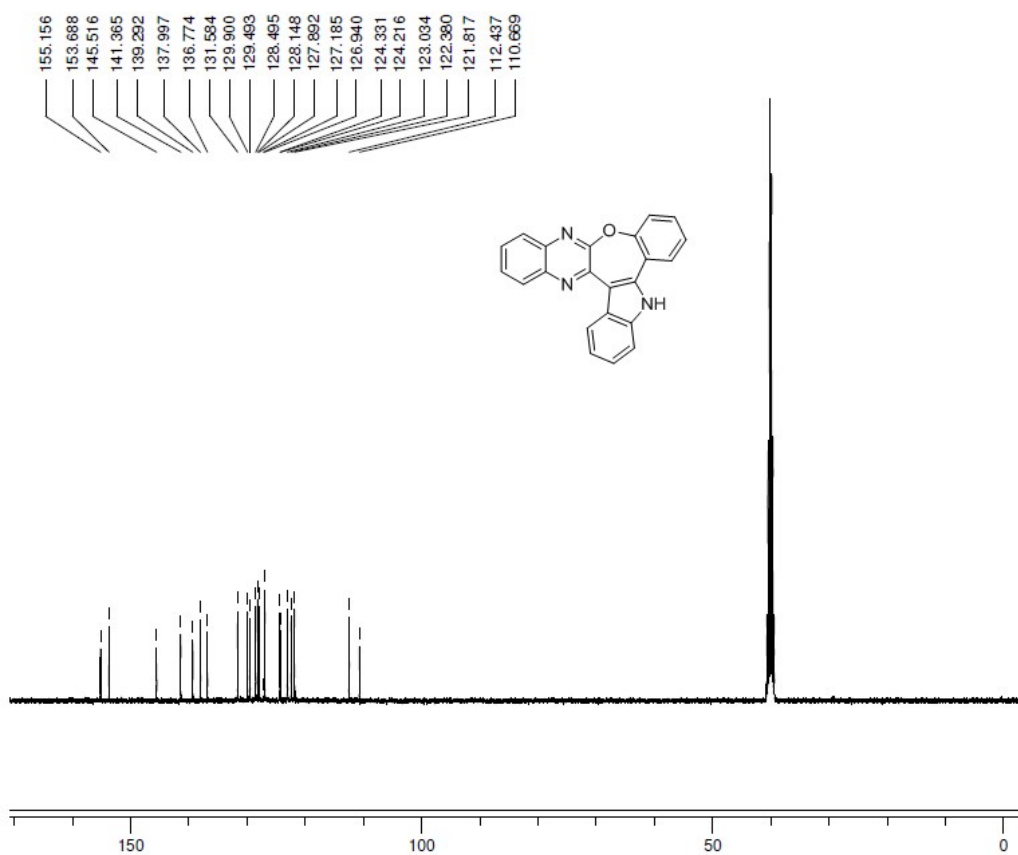
## Copies of $^1\text{H}$ and $^{13}\text{C}$ NMR spectra

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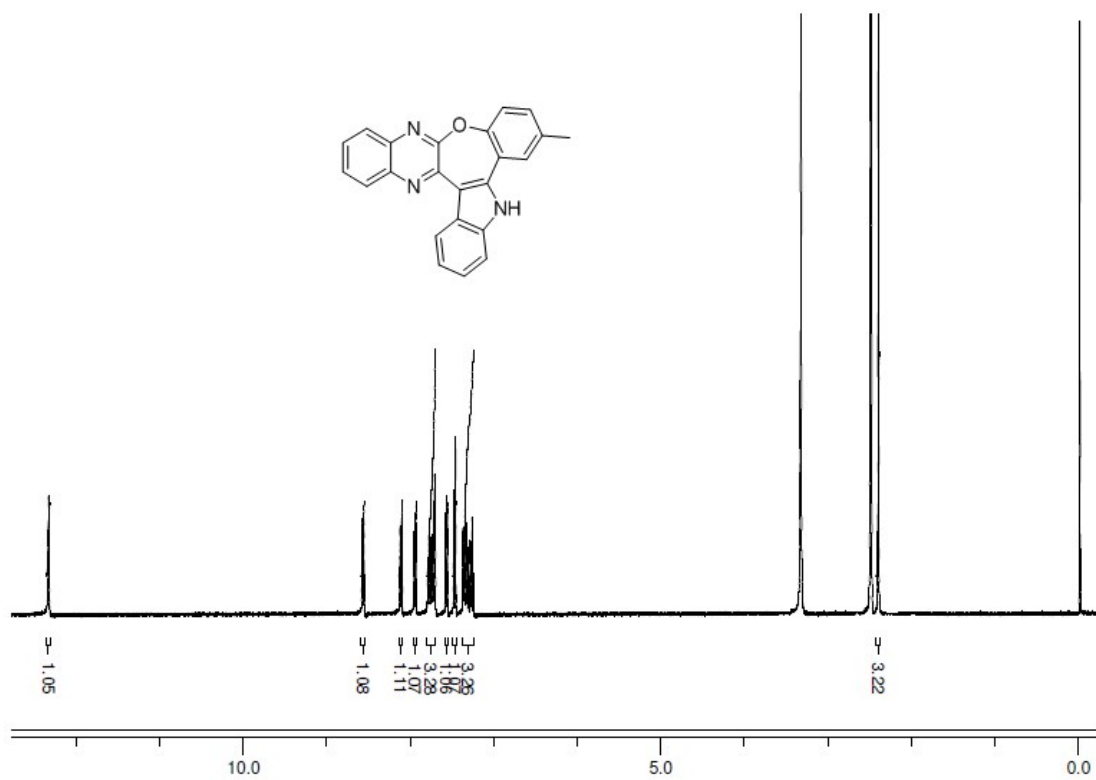




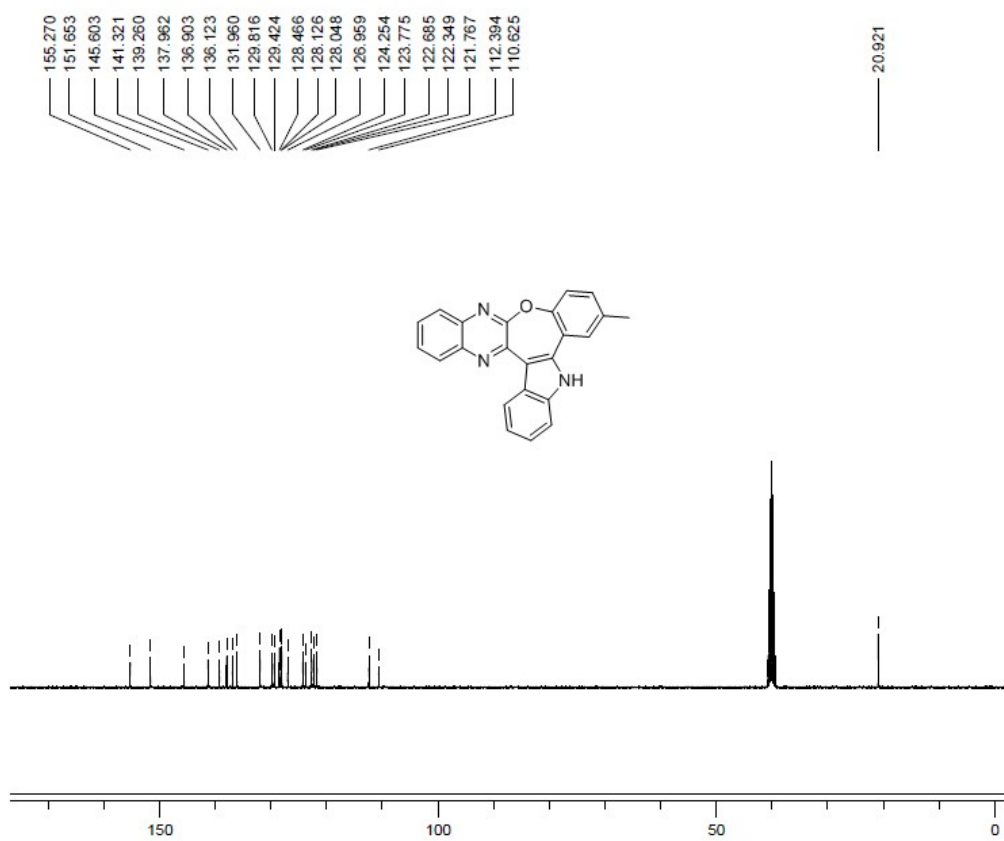
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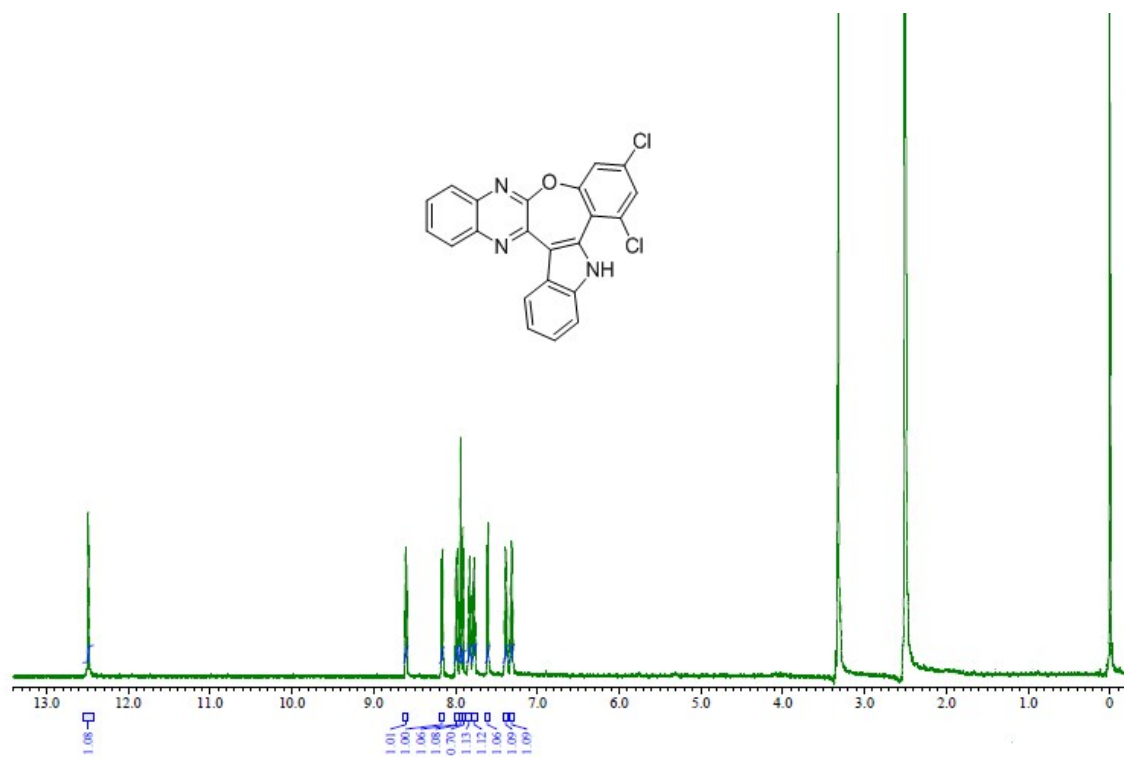


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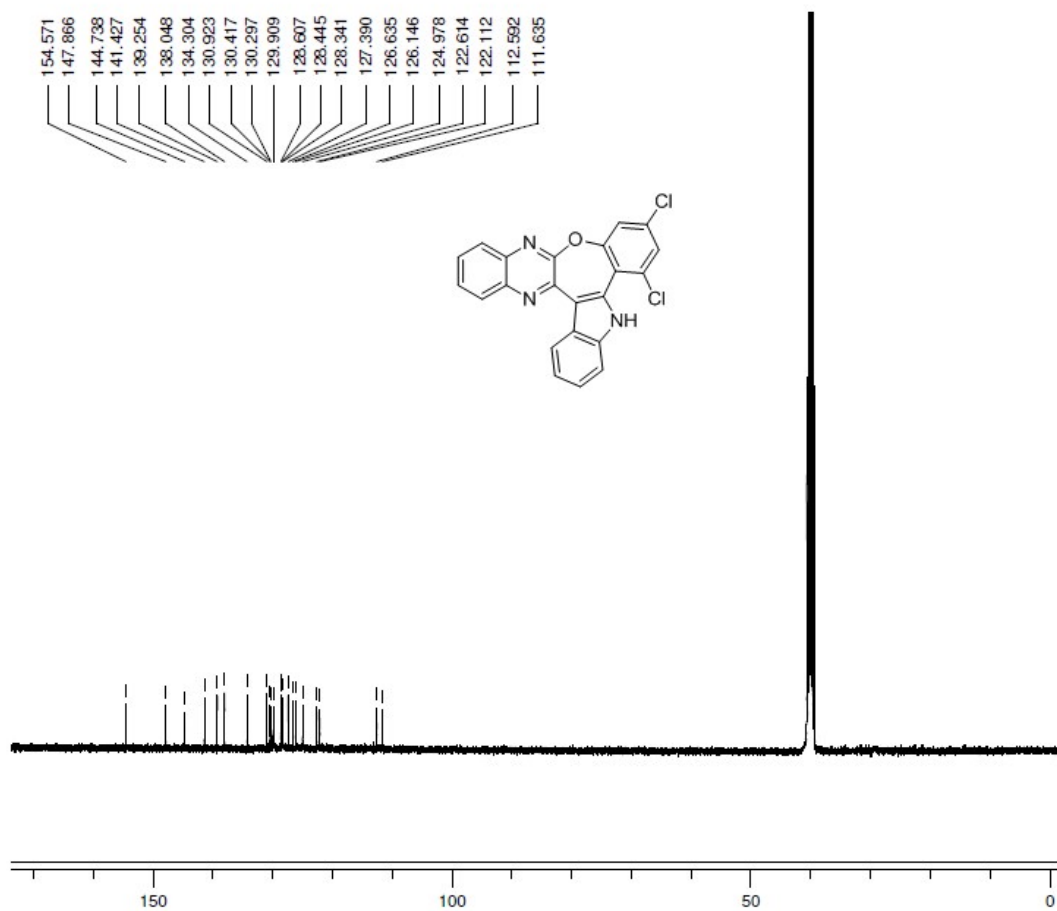




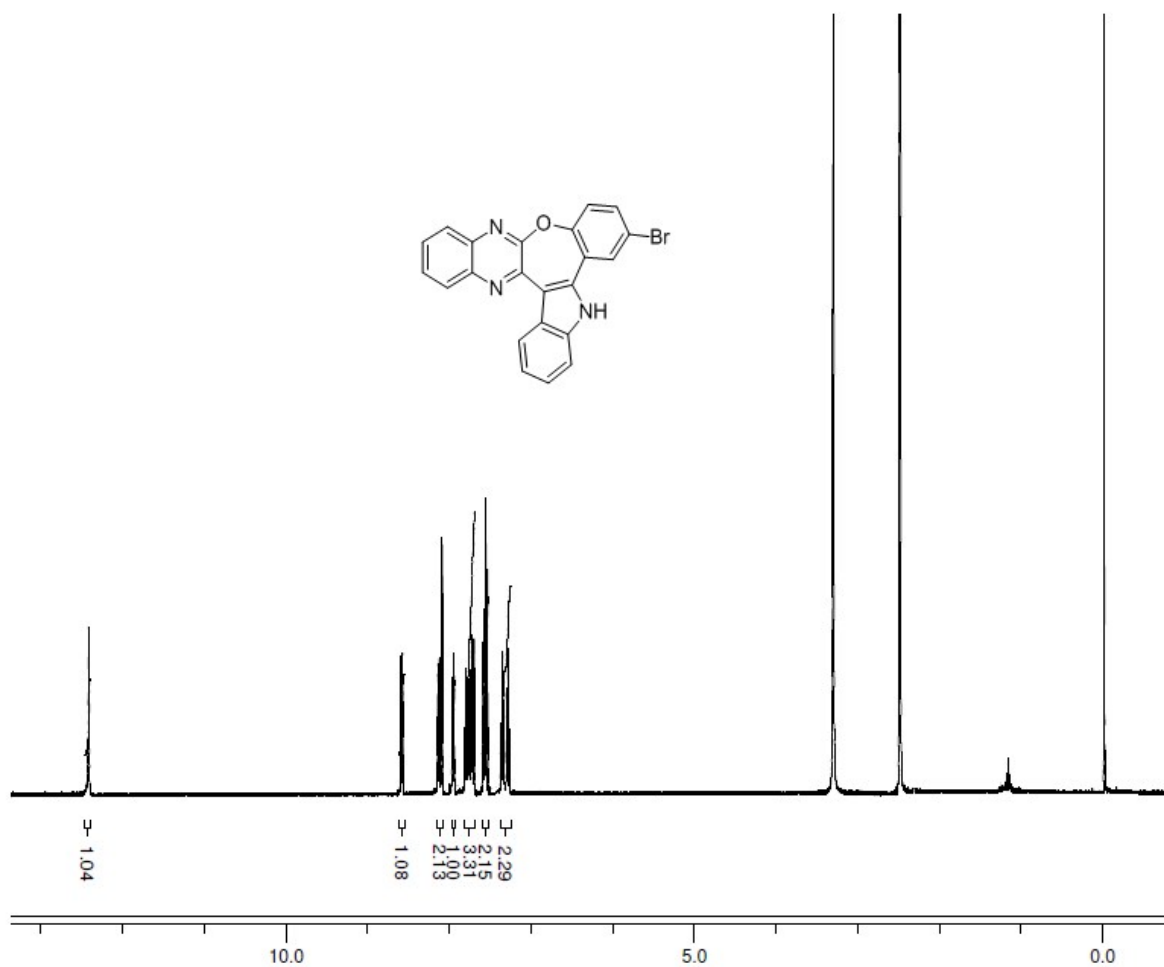
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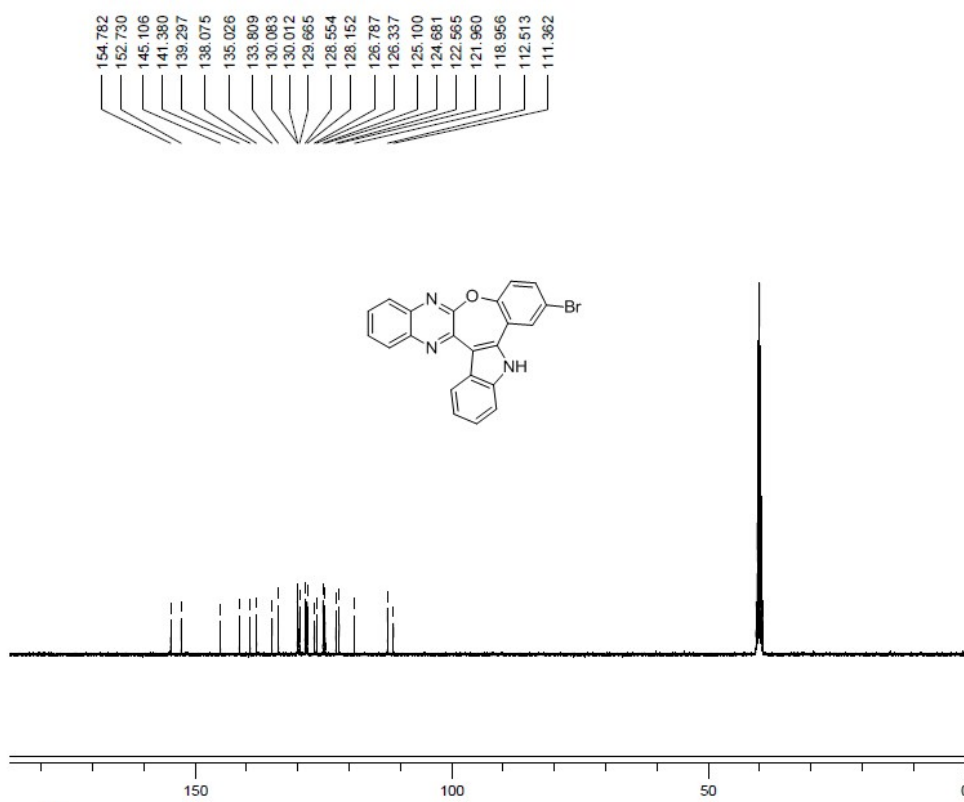
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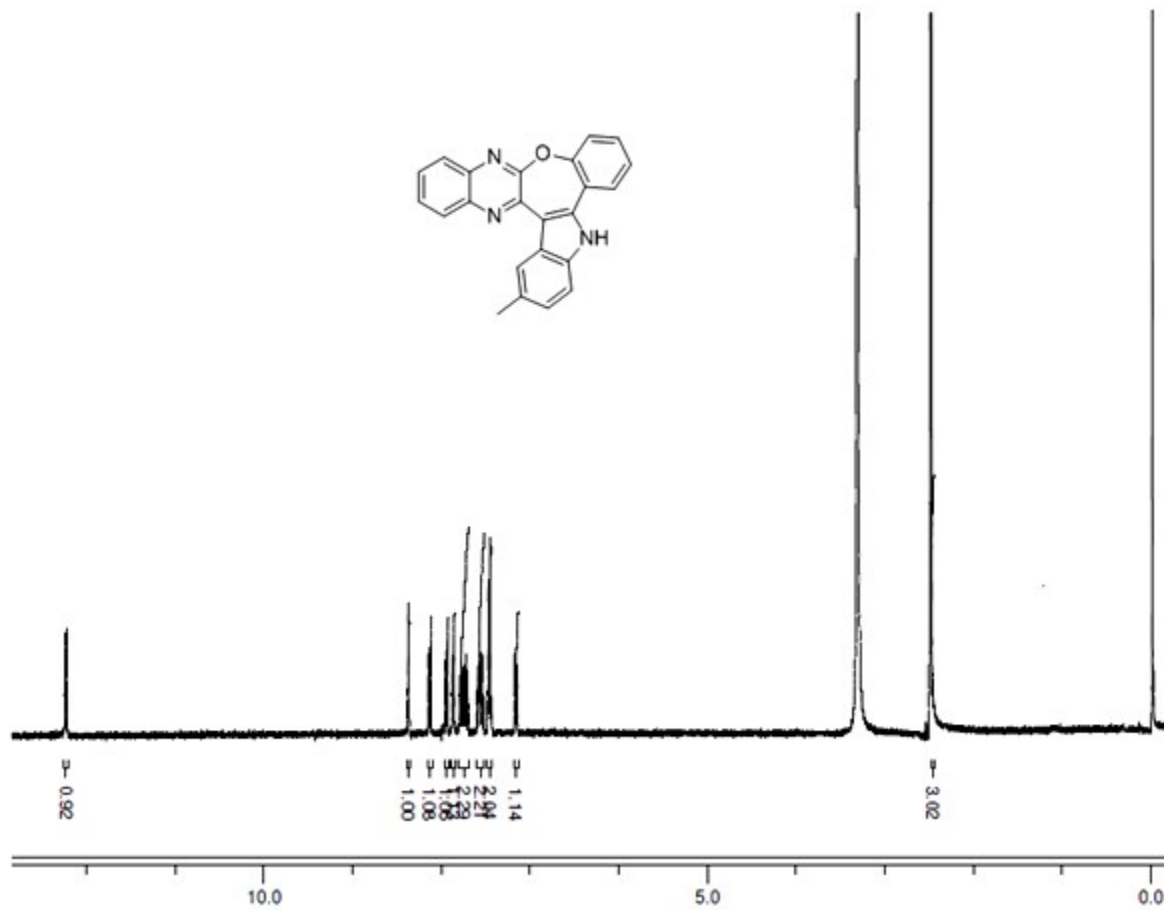


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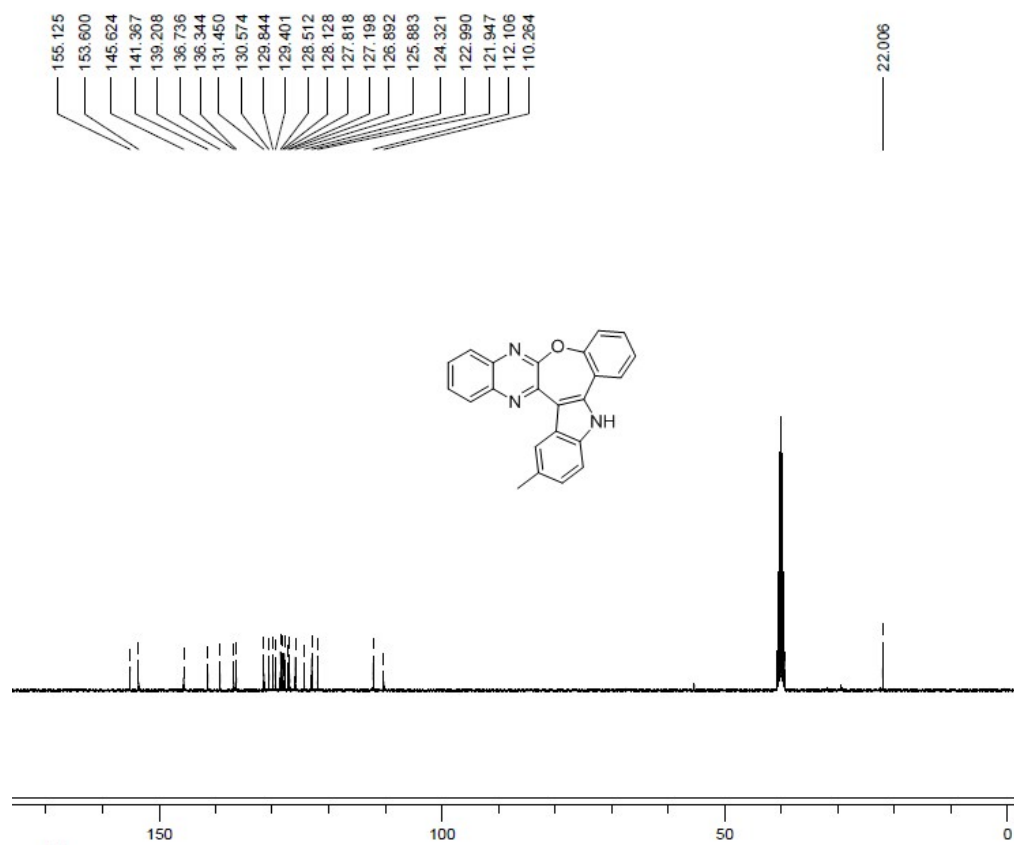




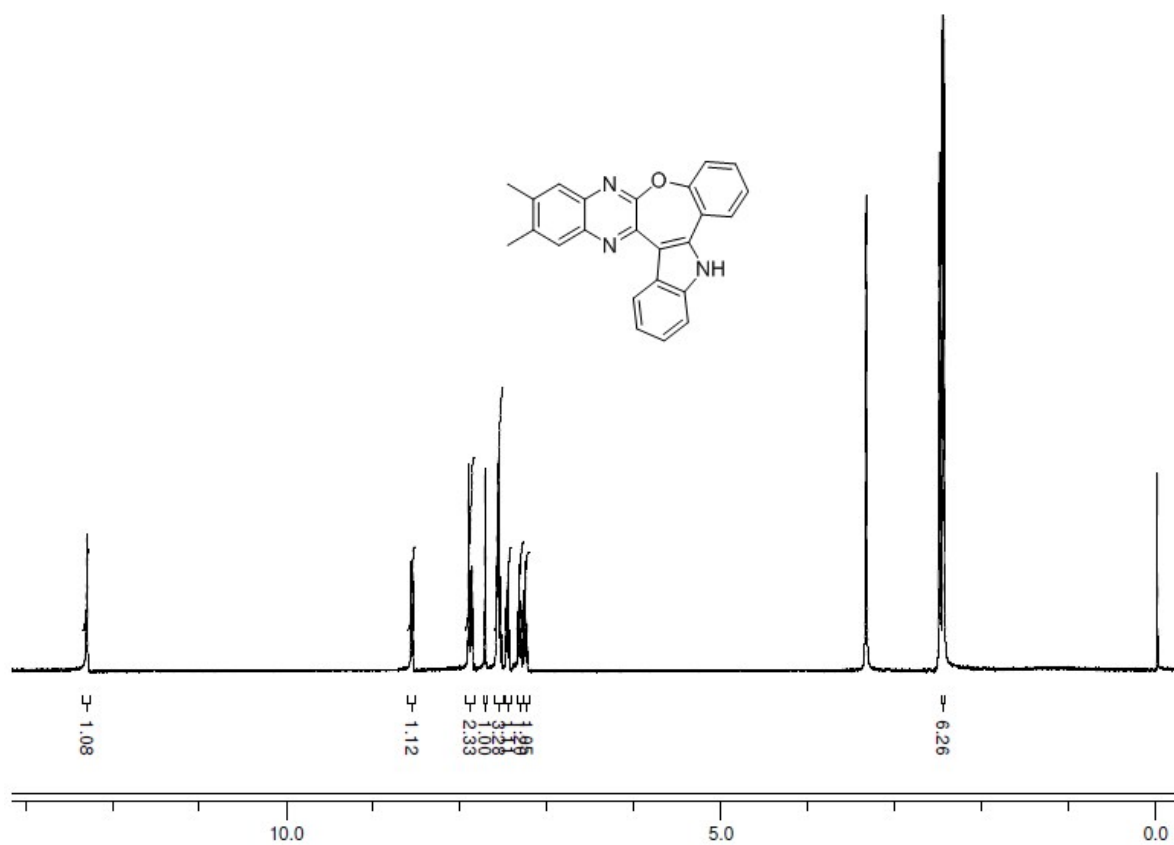
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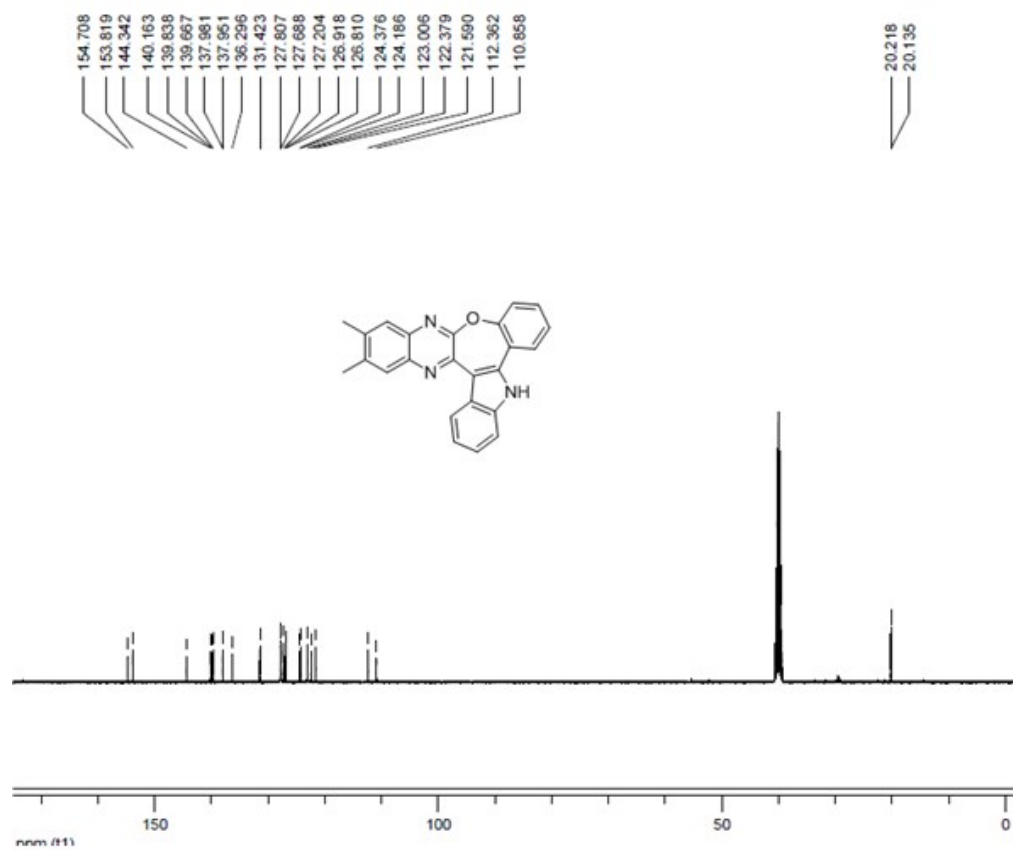
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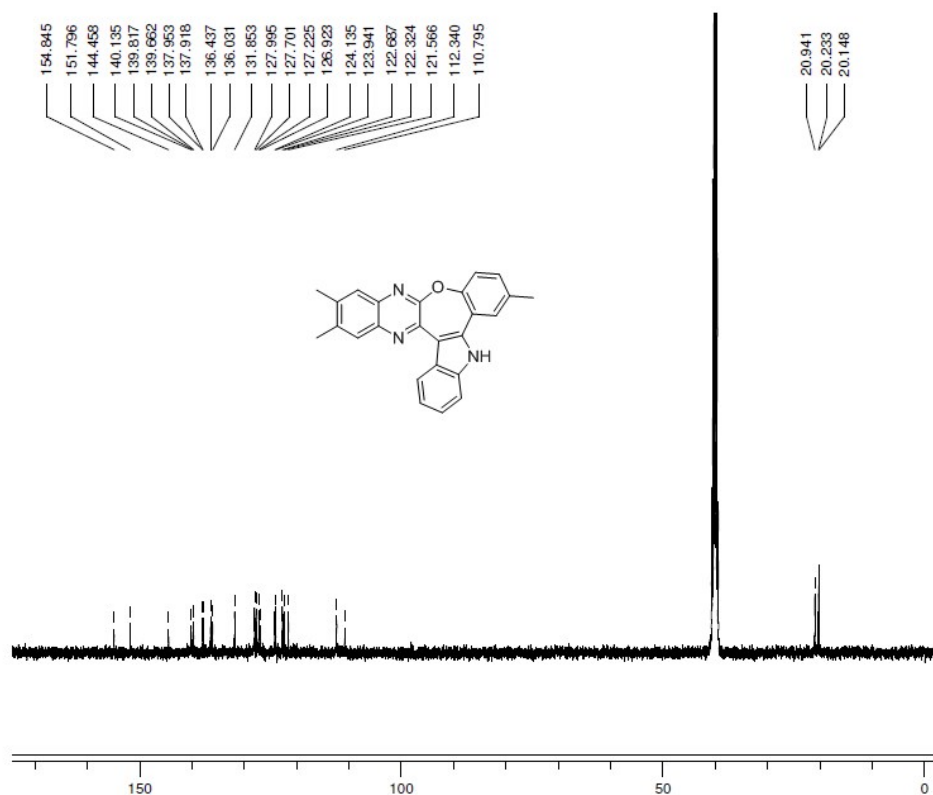


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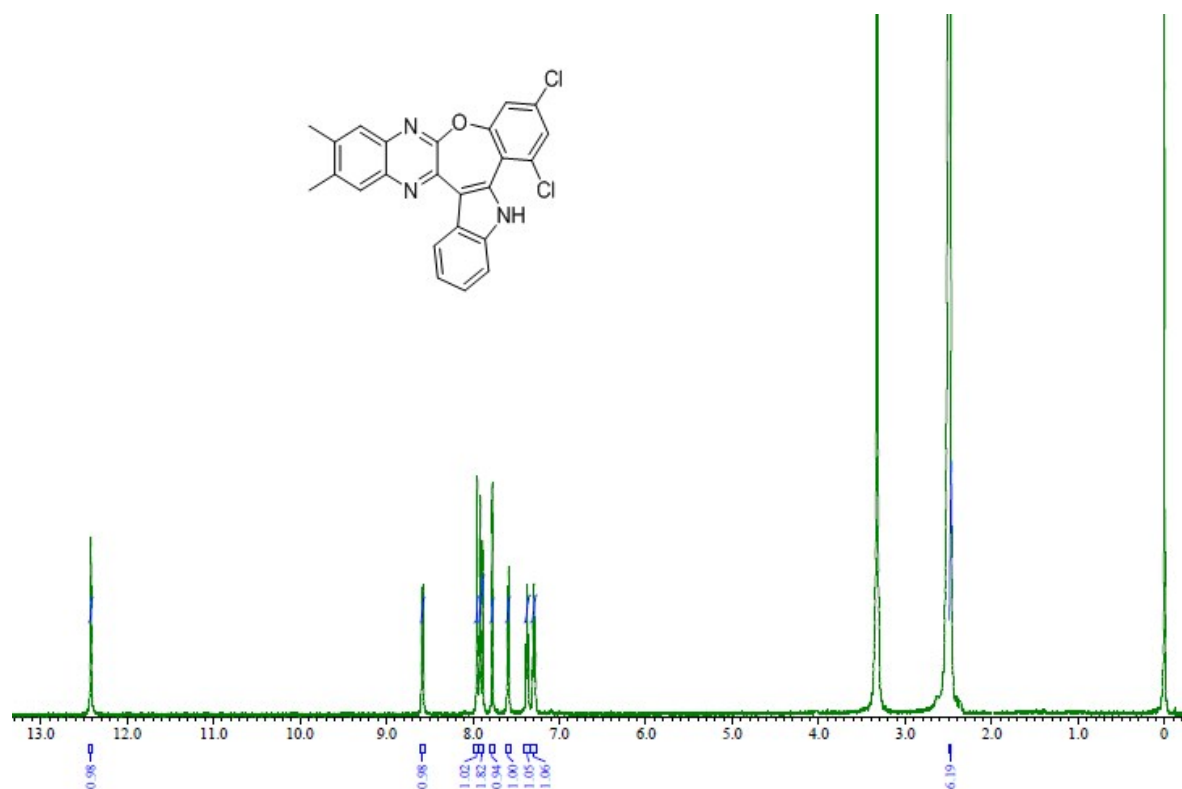




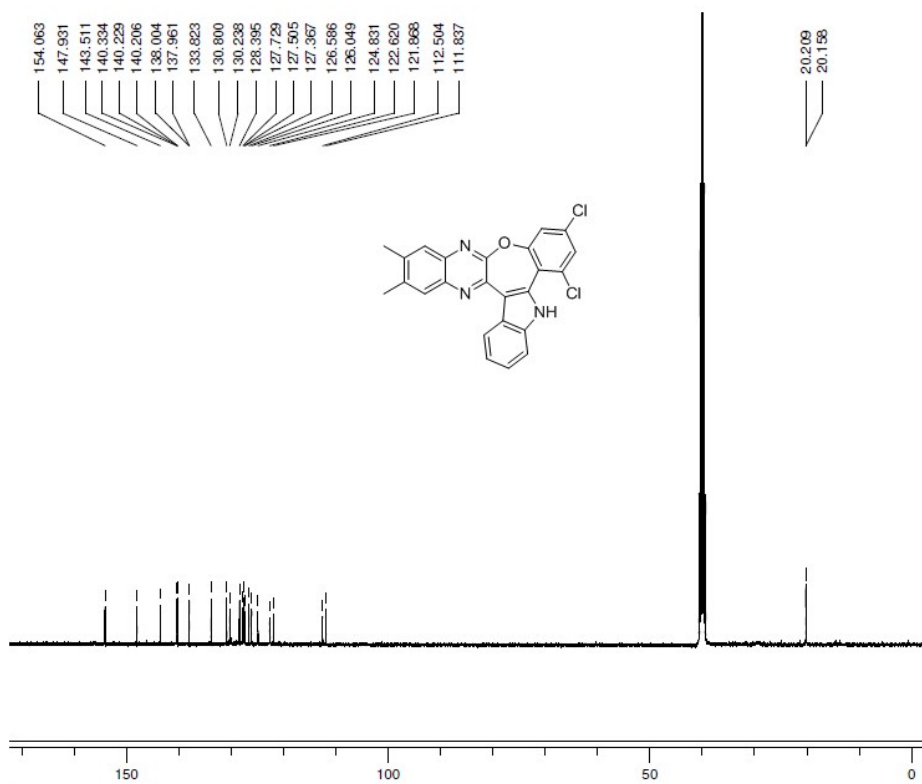
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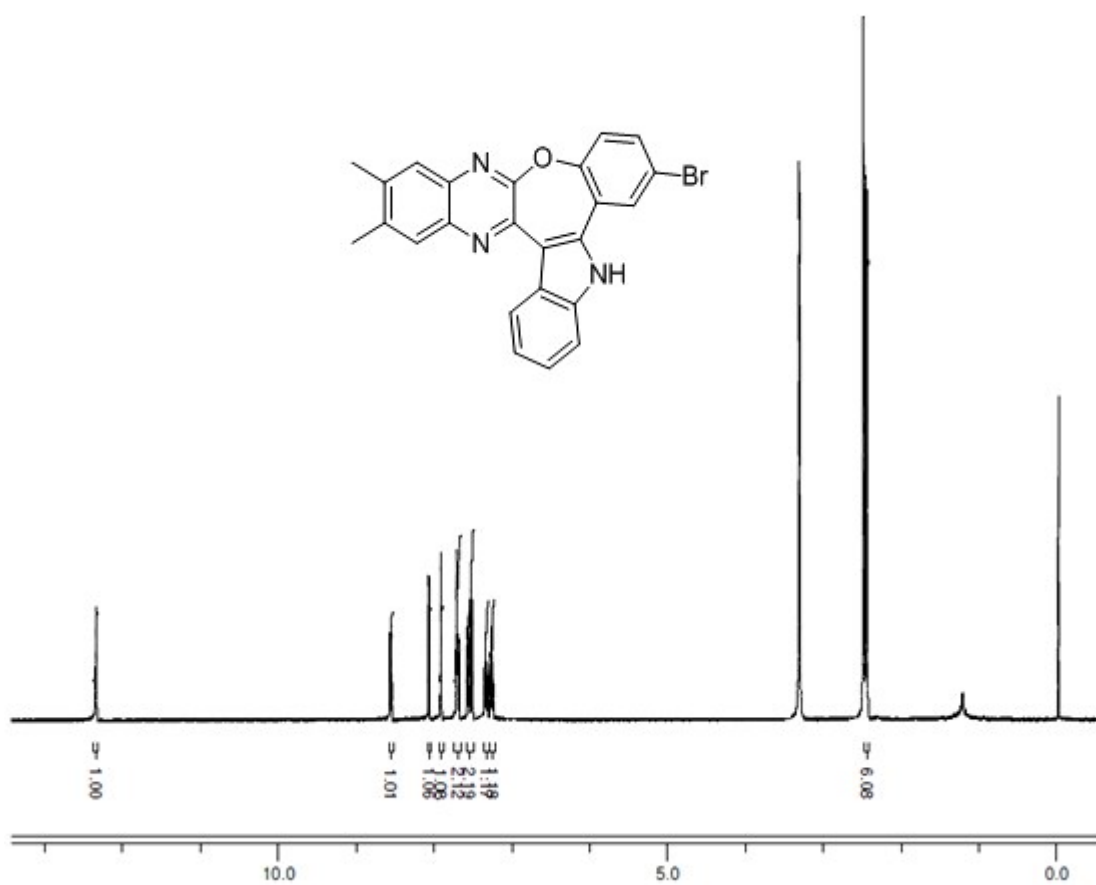


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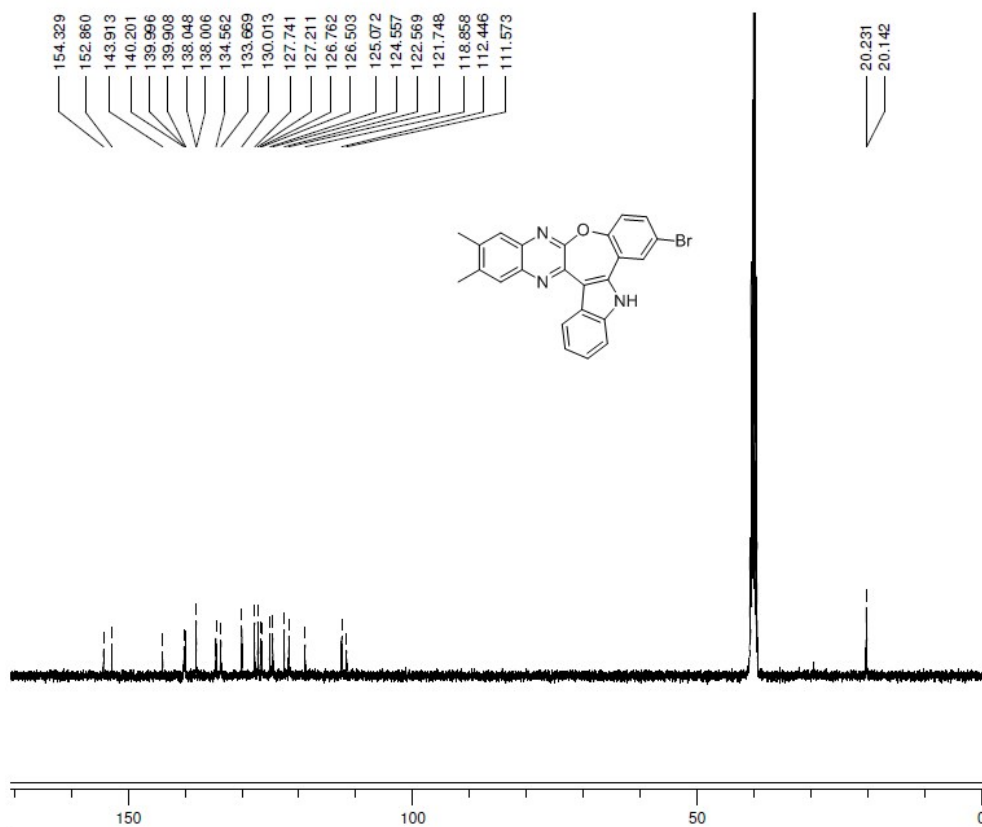




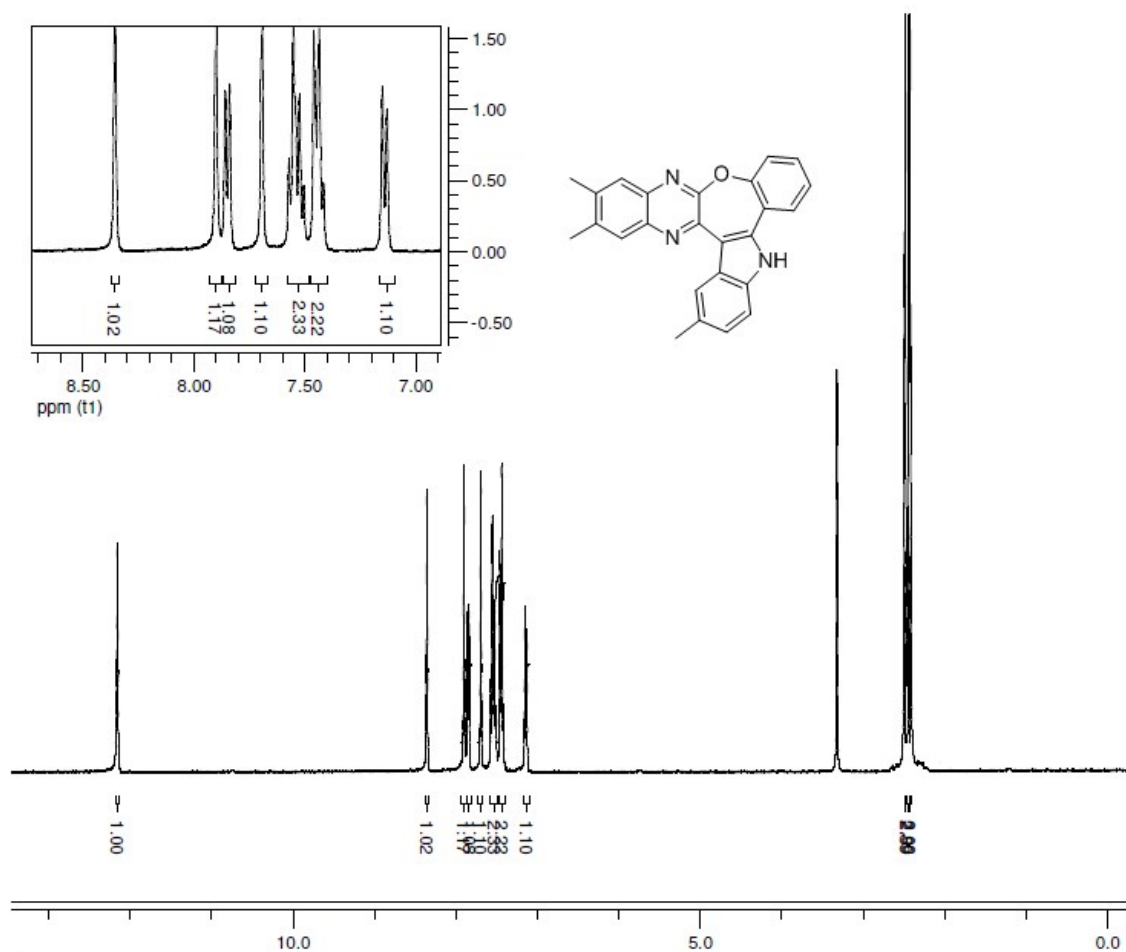
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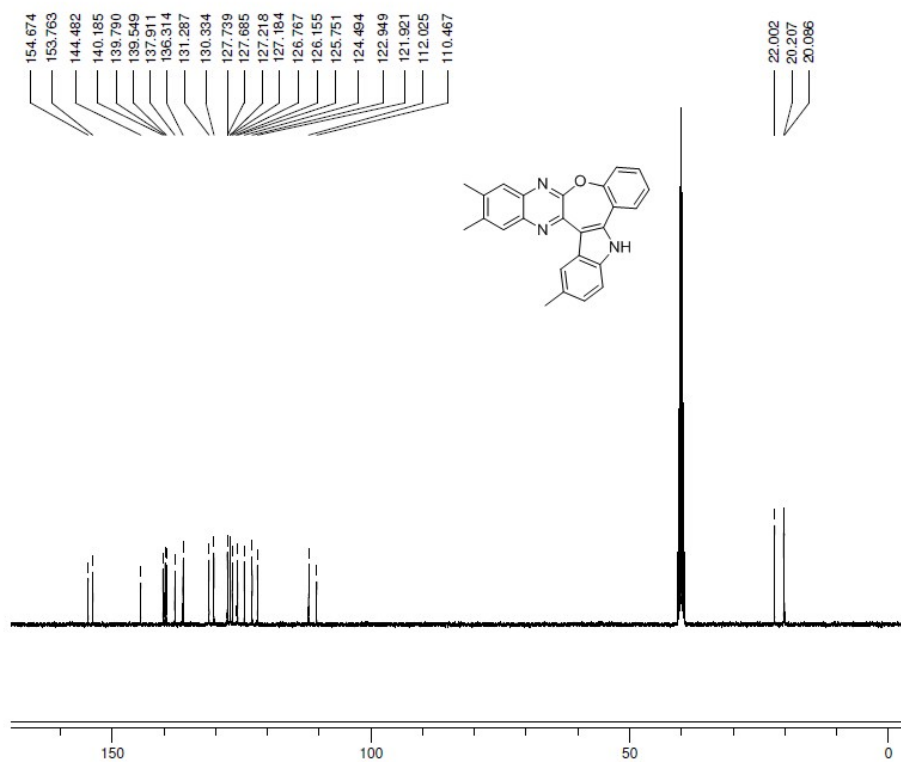
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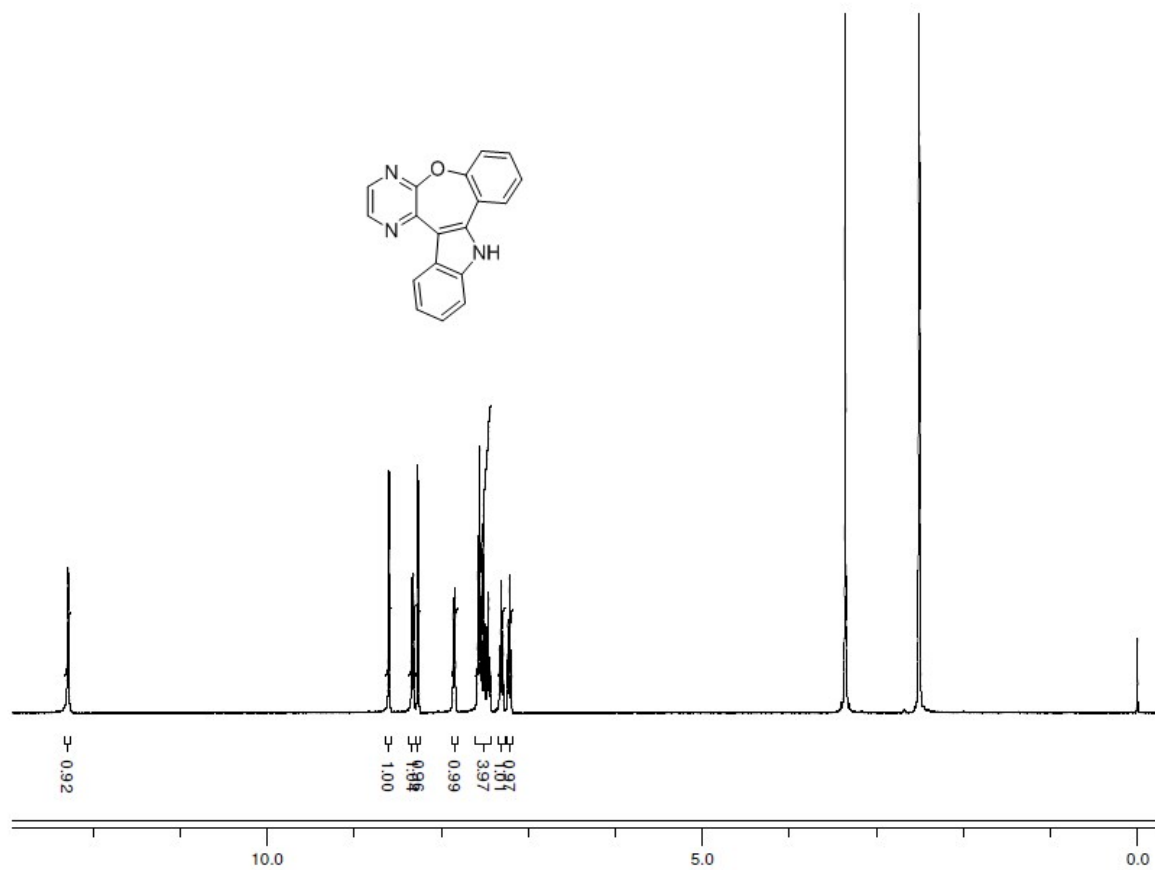
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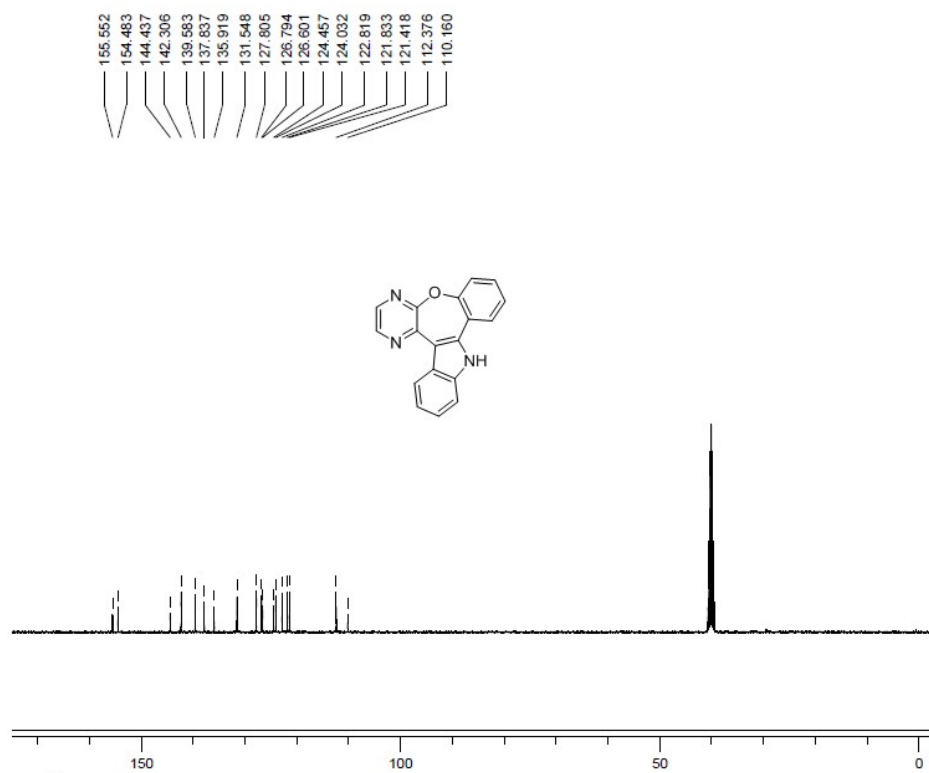
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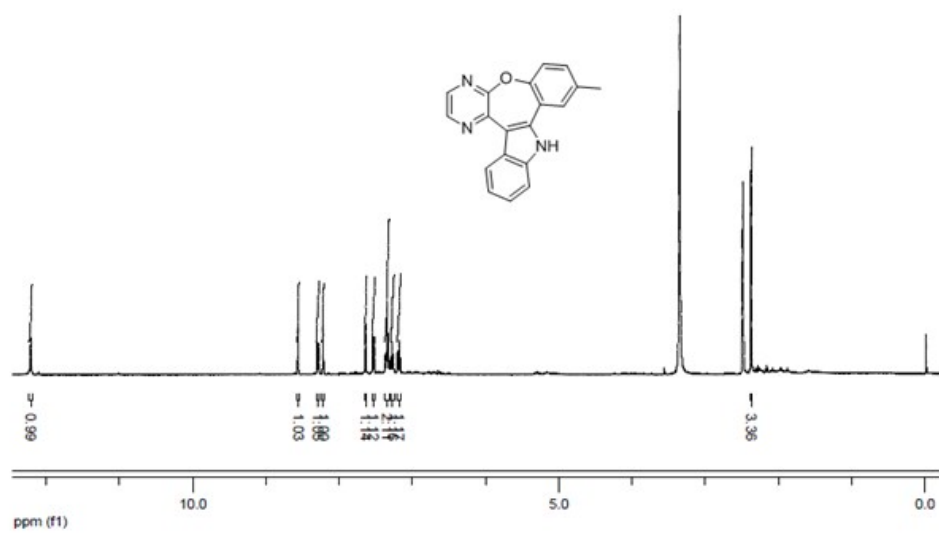
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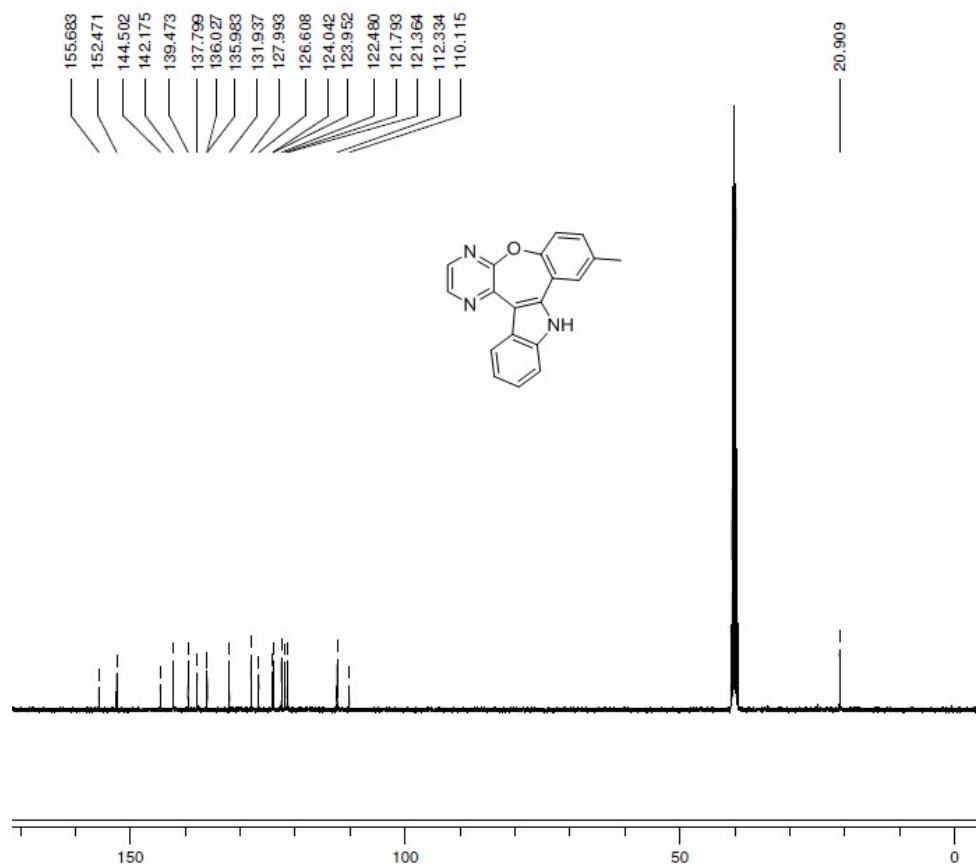
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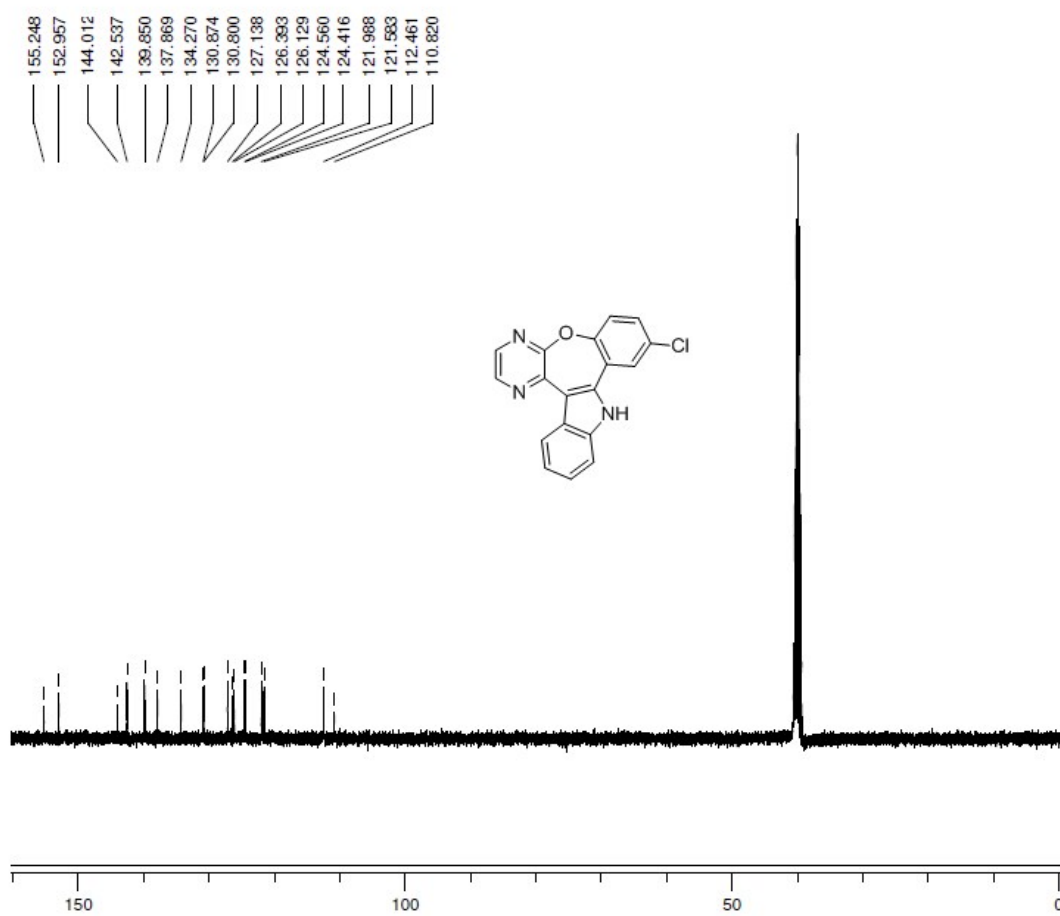
**3m**  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )



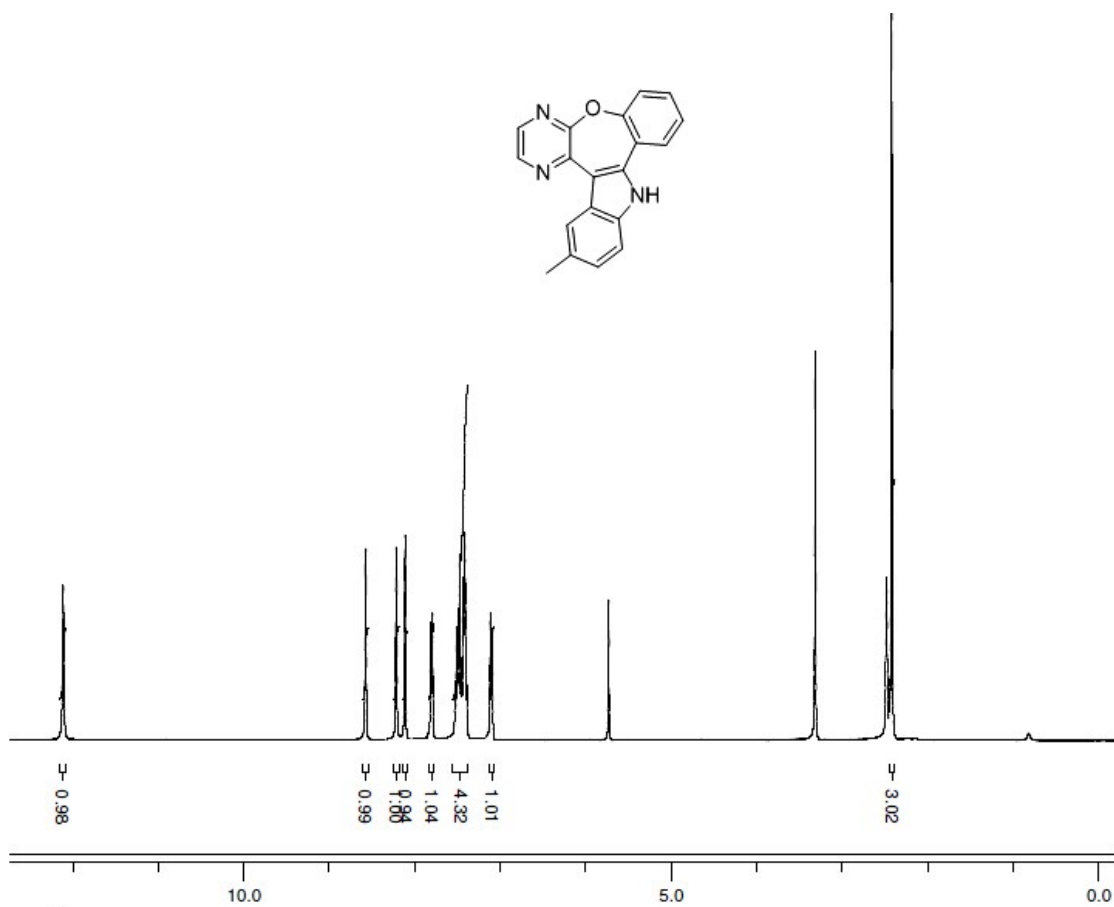




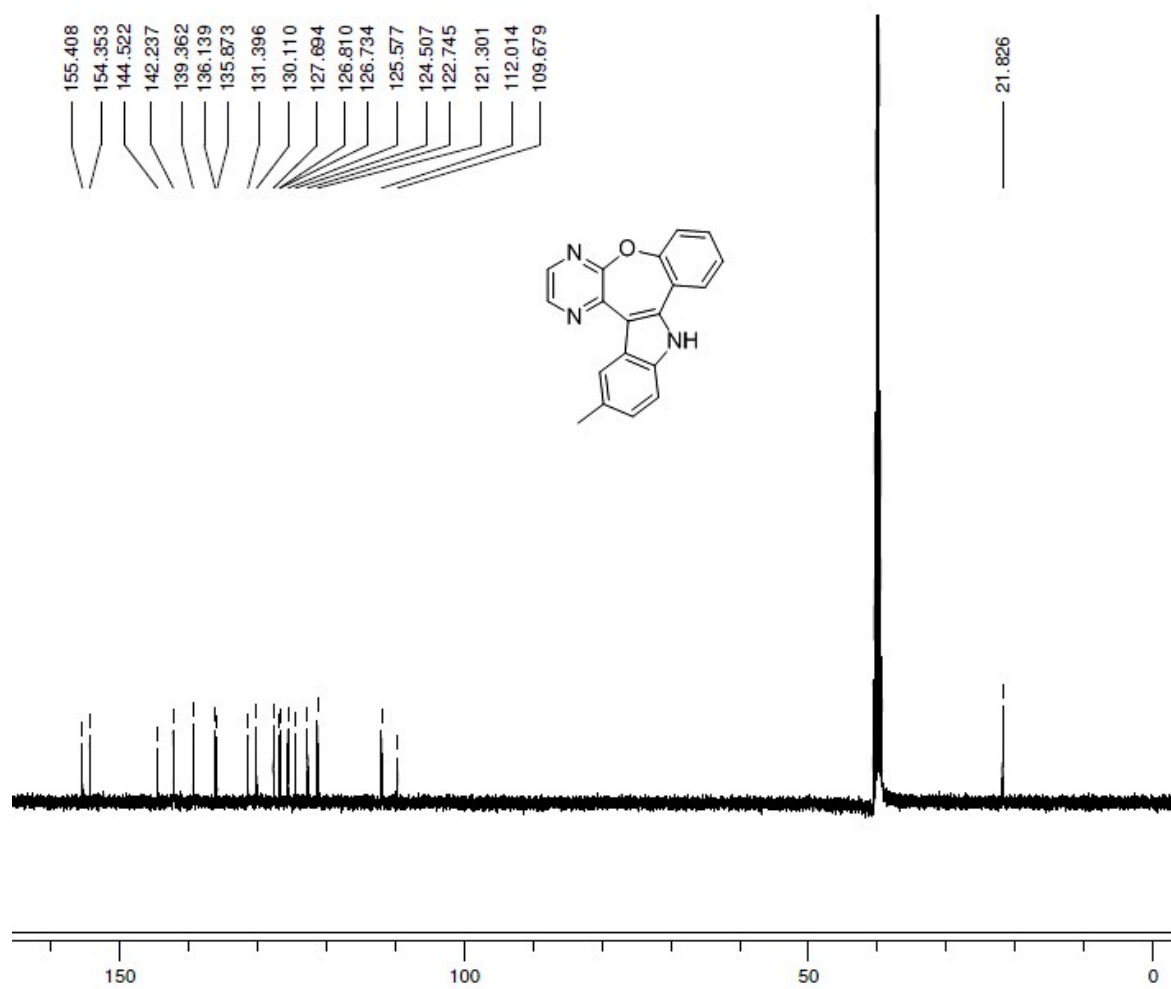
**3n**  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )



**3o**  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )

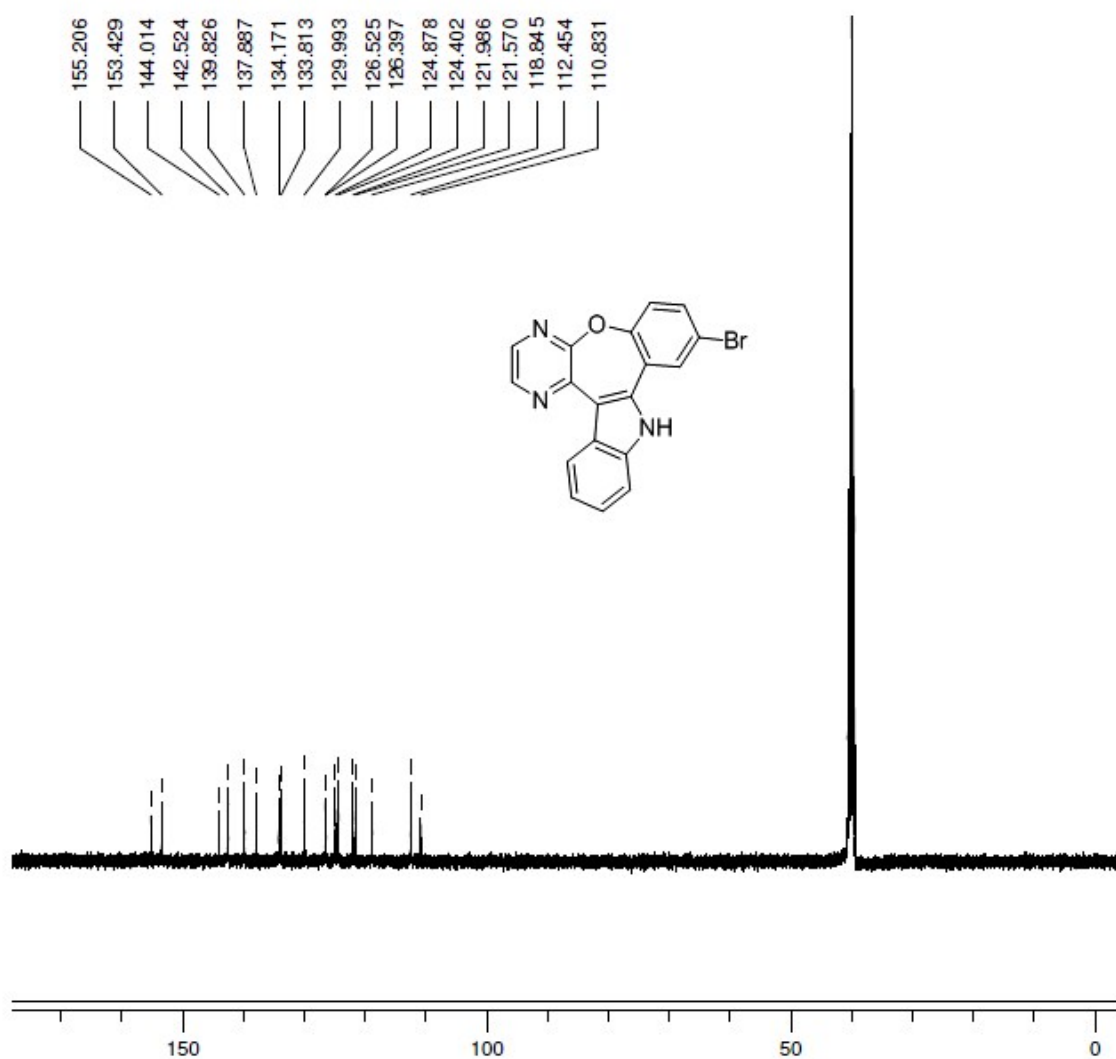


**3o**  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )



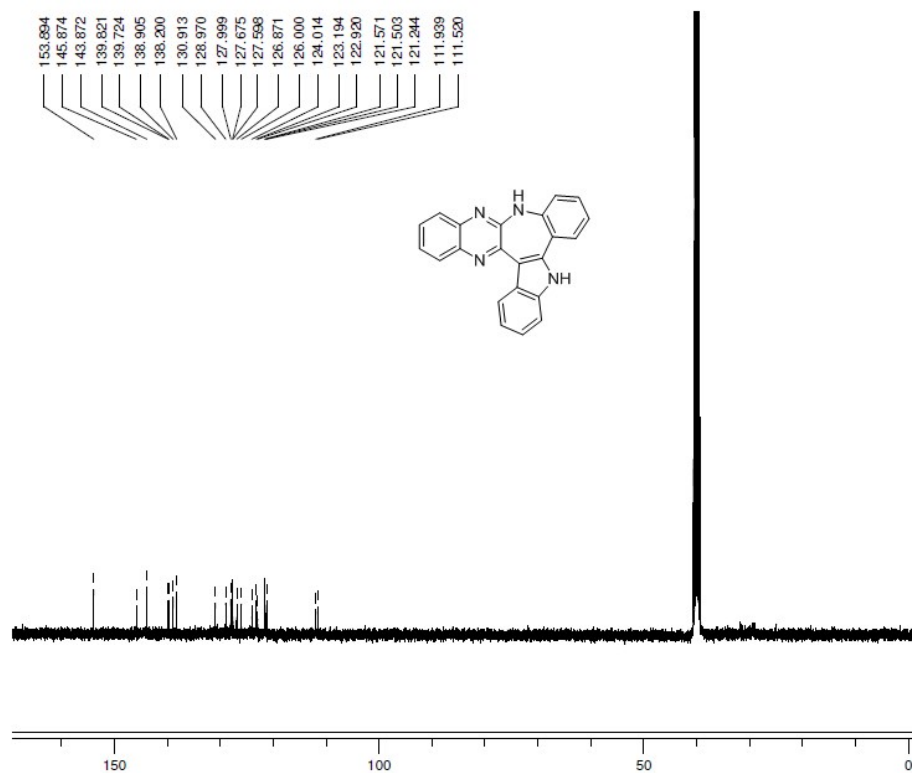


**3p**  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )



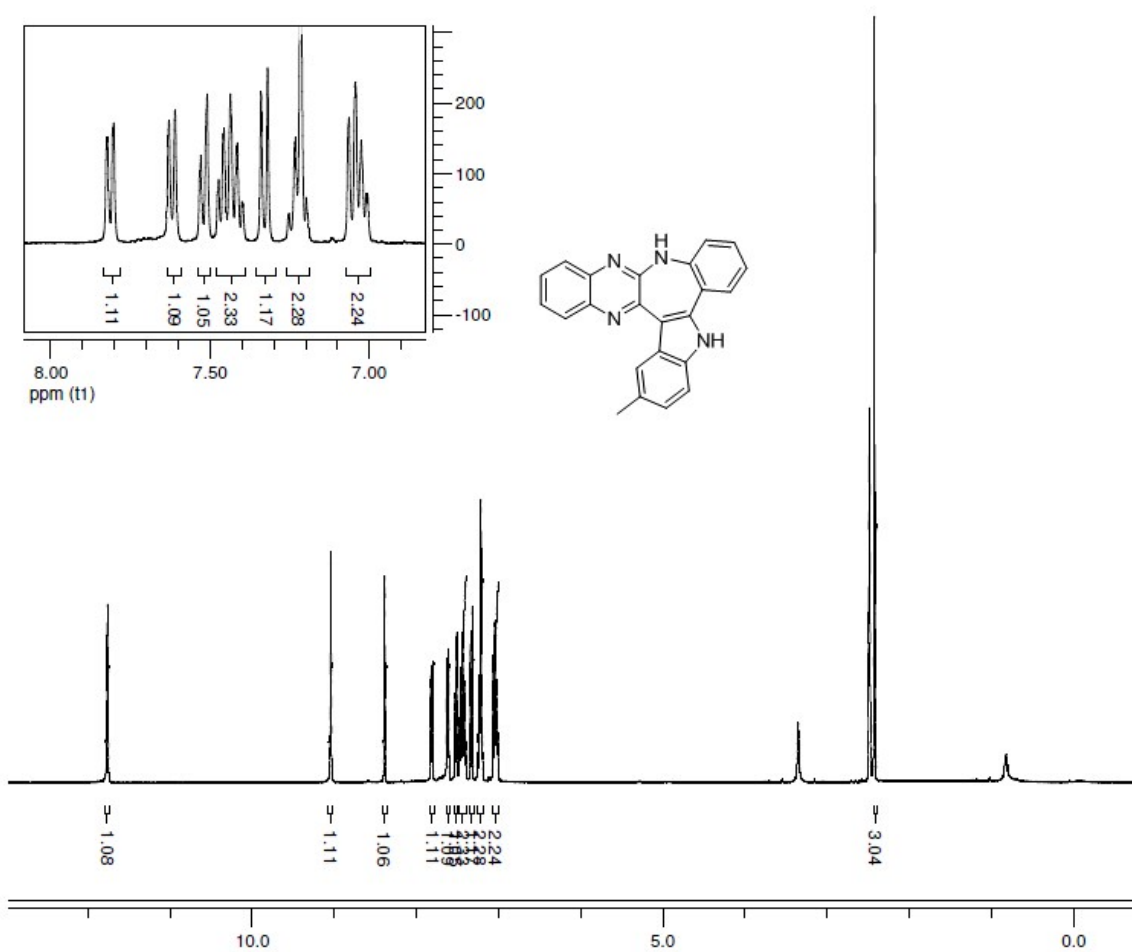


**3q**  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )

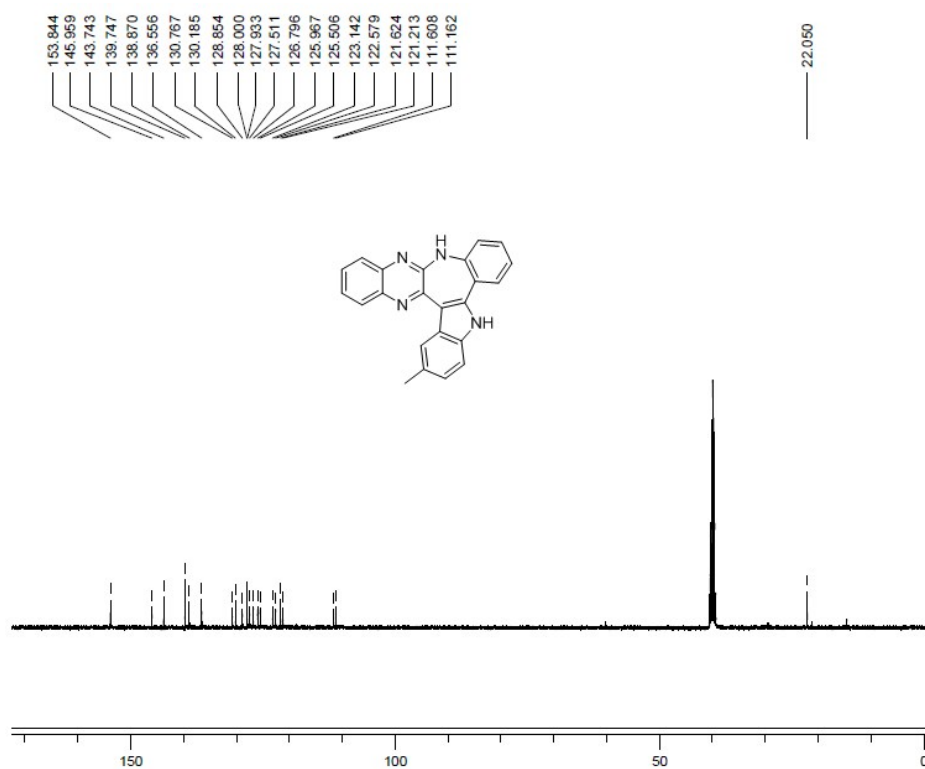




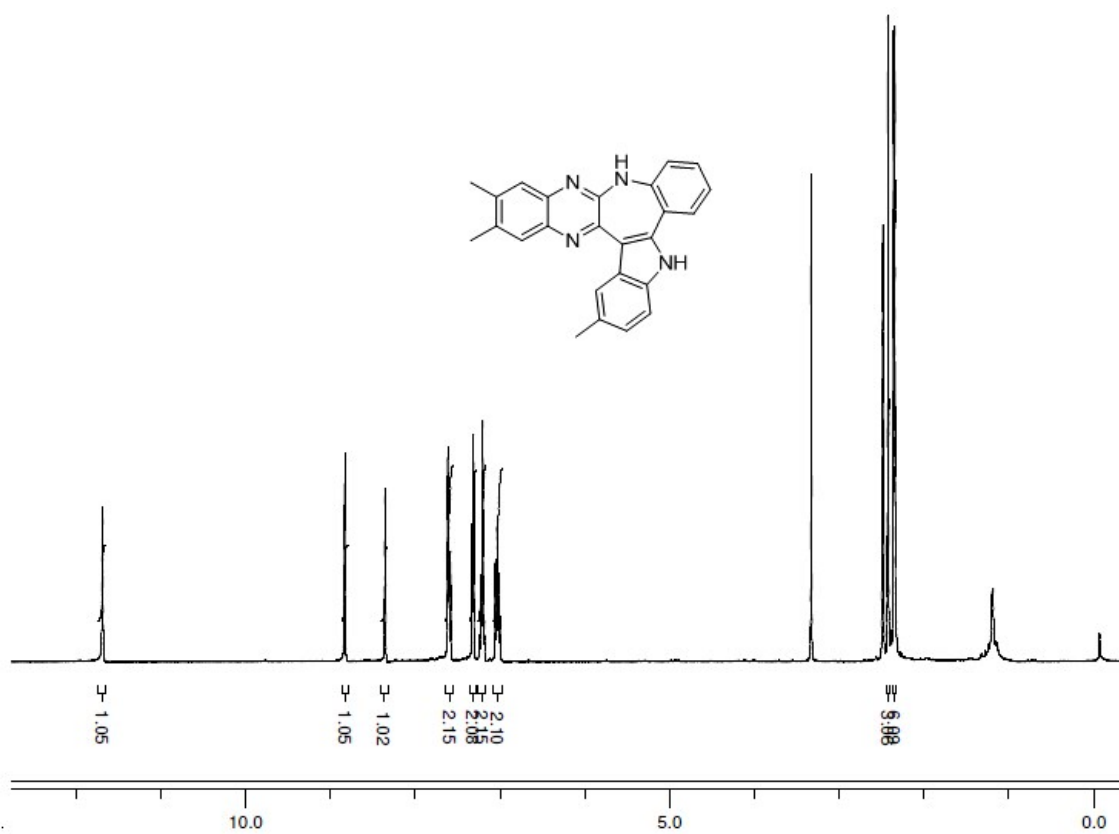
**3r**  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )



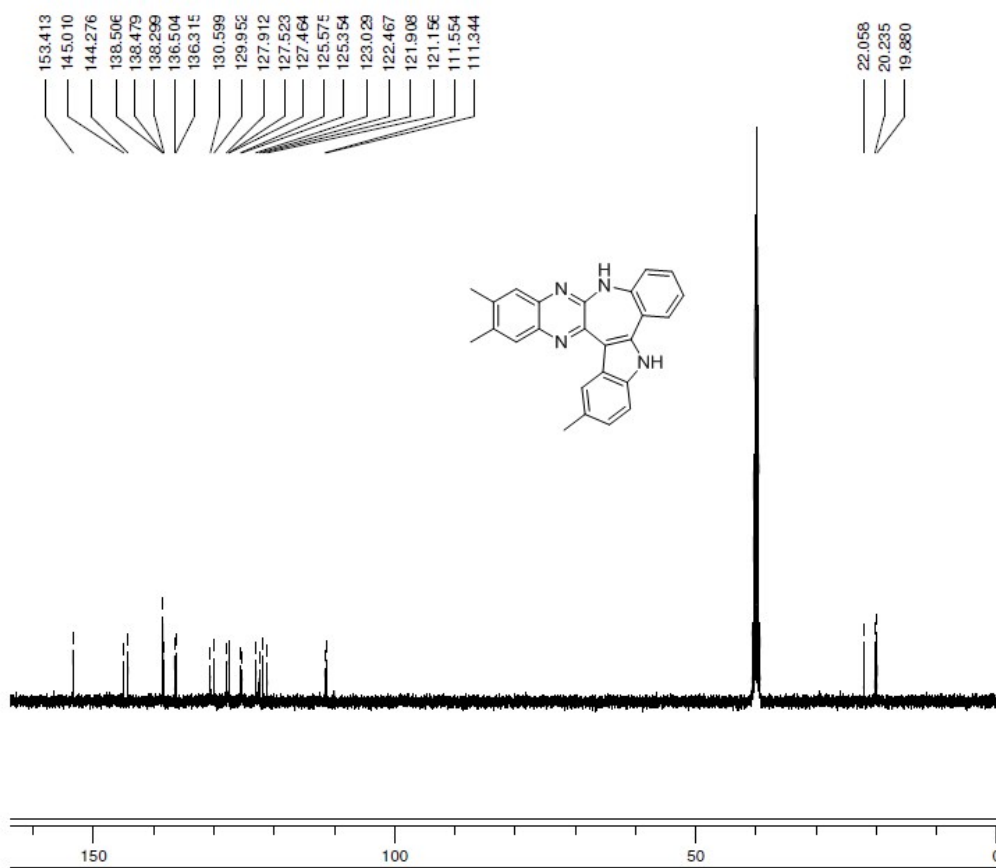
**3r**  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ )



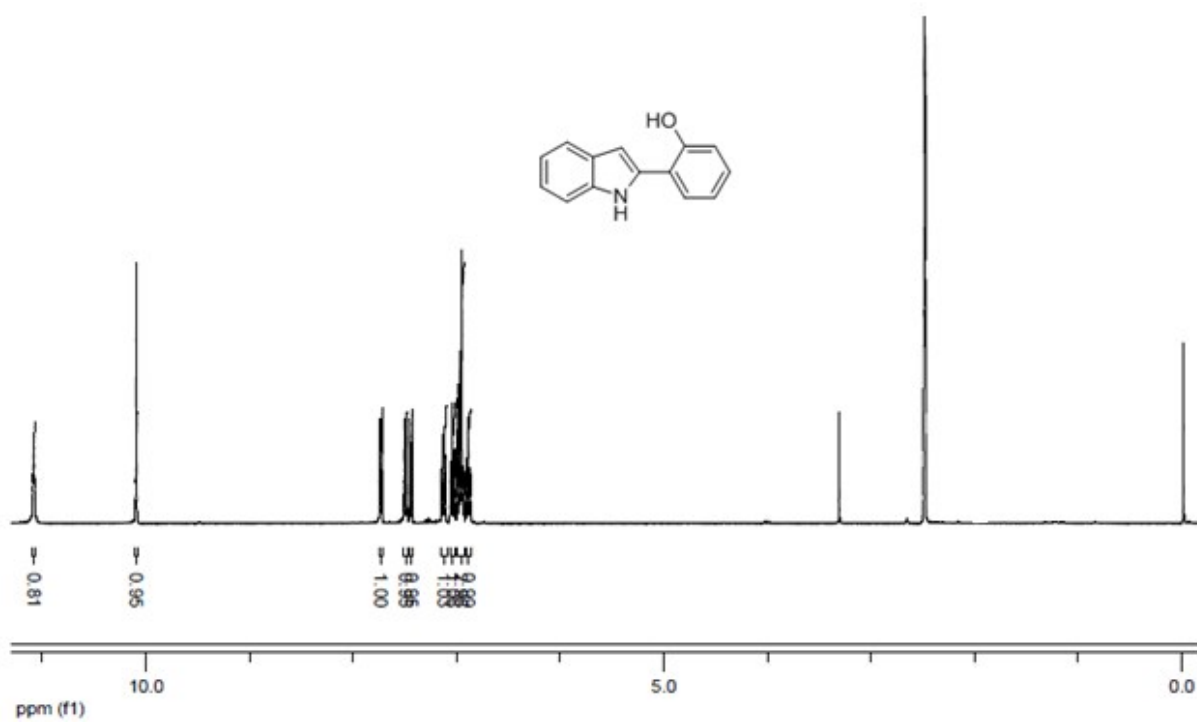
**3s**  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )



**3s**  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ )

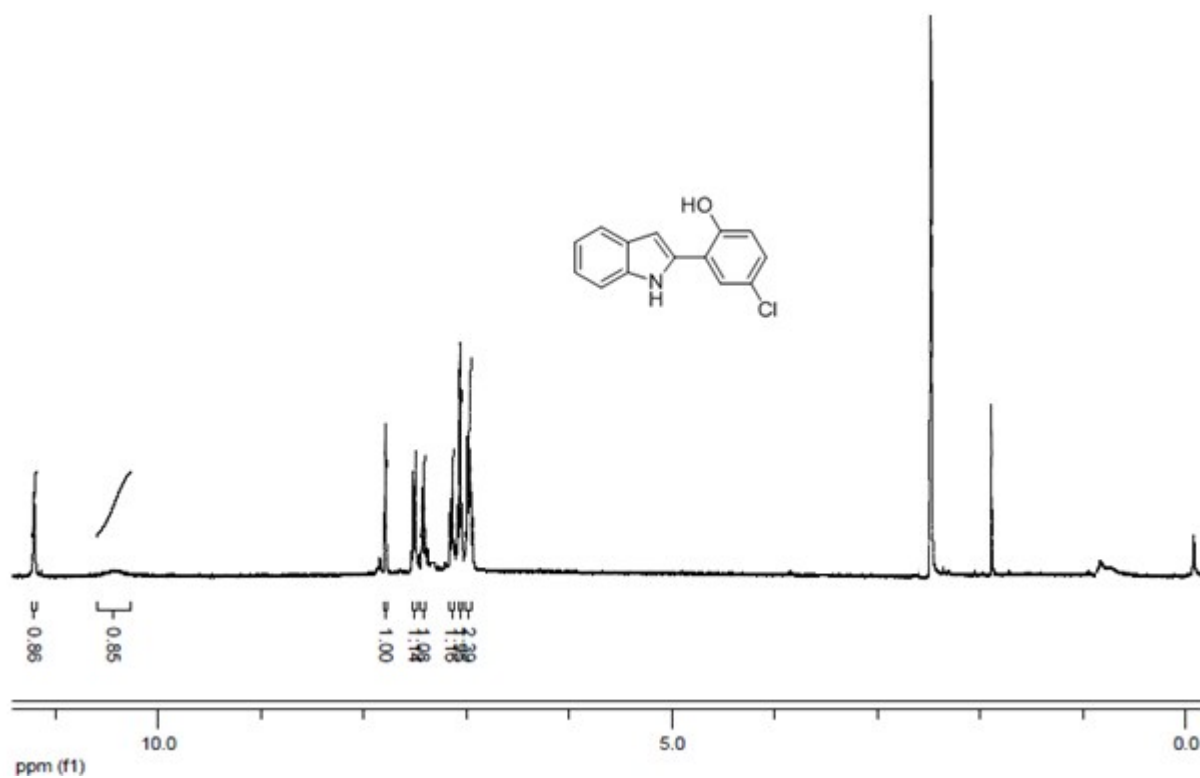


**2a**  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )

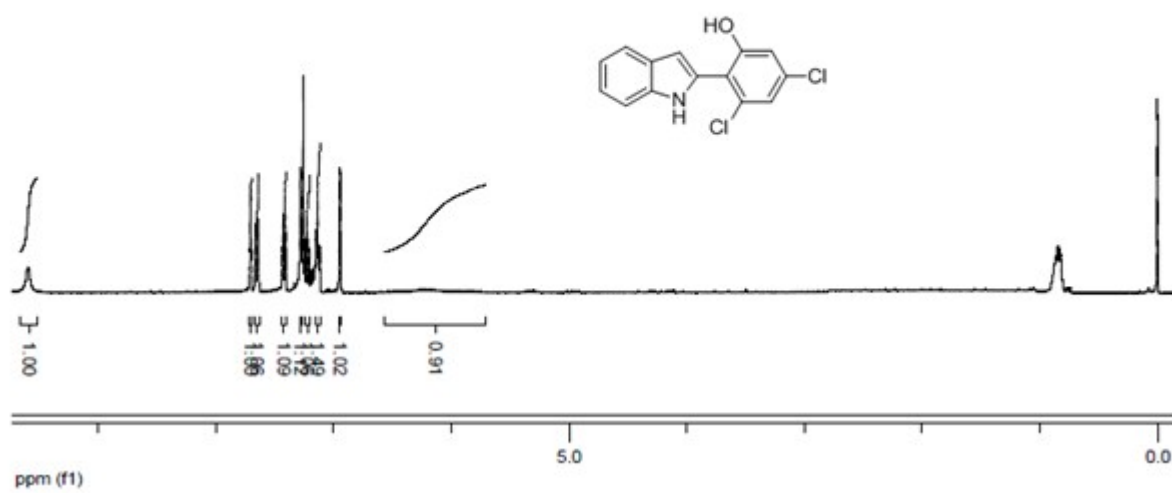




**2c**  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )

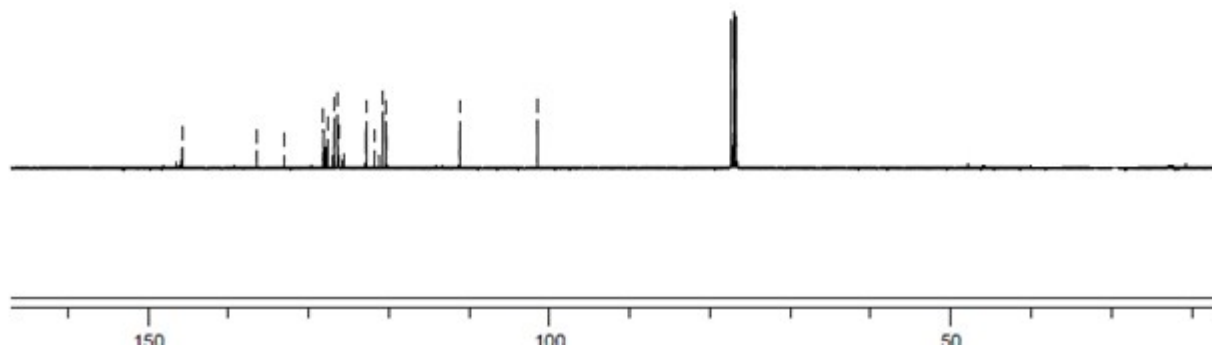
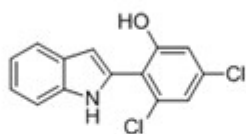


**2d**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

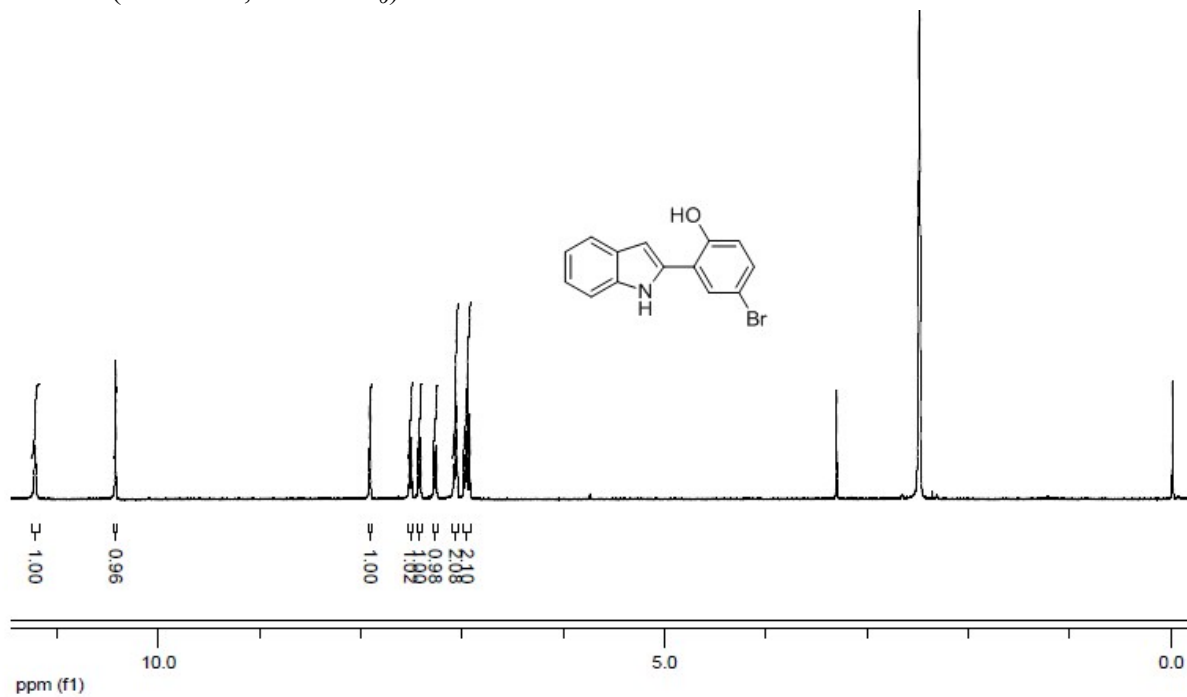




**2d**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )

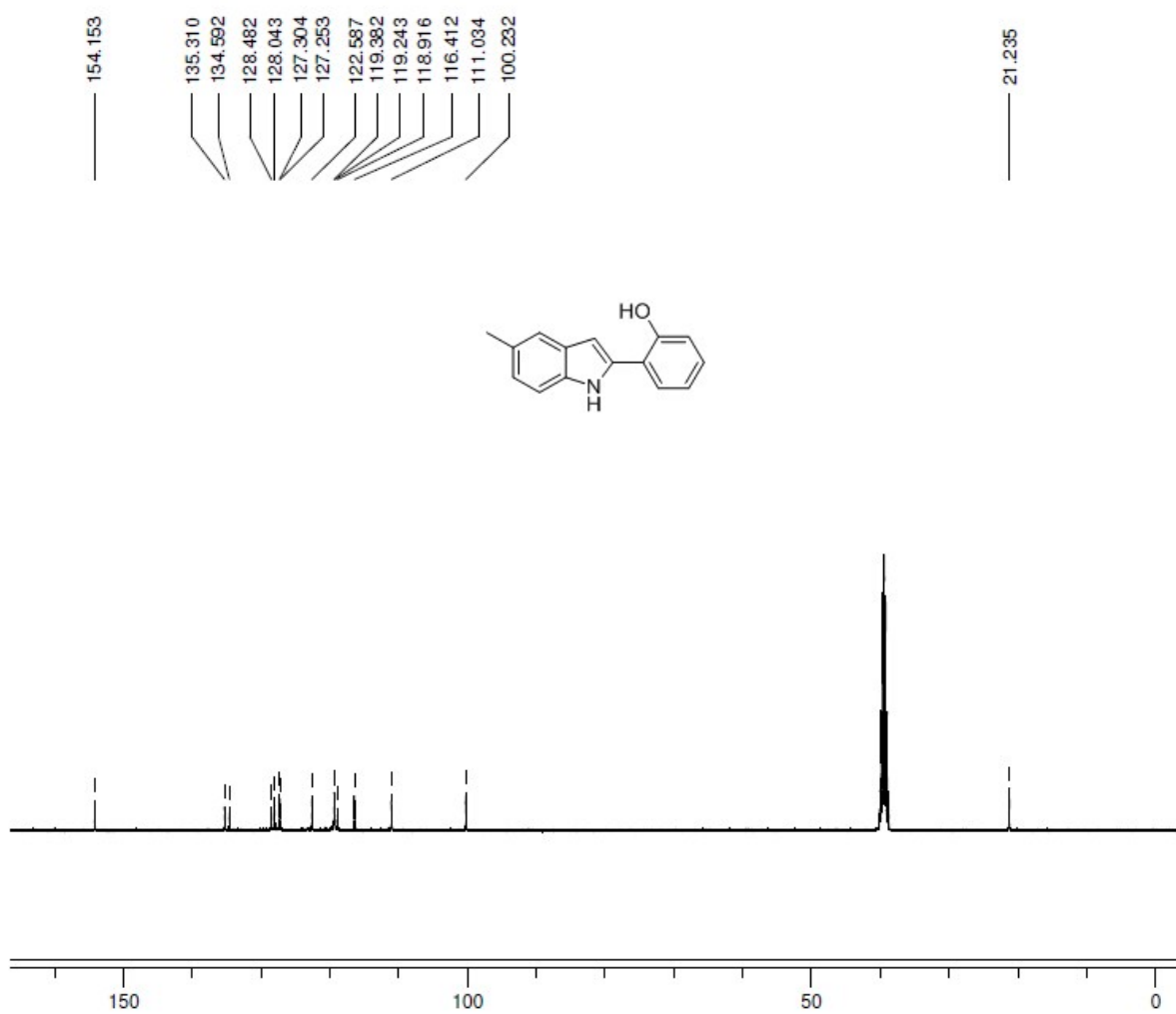


**2e**  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )





**2f**  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )



**2h**  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )

