

Graphene oxide catalysed carbene transfer reaction in water: A highly green and selective approach to access 3,3',3''-trisindoles

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Procedure for reusability of graphene oxide:

To achieve the reusability of the catalyst, we set up the reaction with (1a) 3-diazo oxindole (1 equivalent, 6.2 mmol), and indole (2a) (2 equivalents, 12 mmol) using graphene oxide (200 mg), in a closed round bottom flask in the presence of 20% DMSO in water (50 mL) as solvent at 60°C for a duration of 20 hours. The thin-layer chromatography (TLC) technique was employed to observe the completion of the reaction. After the reaction was finished, the resultant mixture underwent multiple washings with a mixture of ethyl acetate and water. This was done to ensure the thorough extraction of the graphene oxide from the reaction mixture, enabling its reuse in the following cycles. The graphene oxide was extracted along the aqueous phase and the resulting water layer was subsequently subjected to filtration using filter paper, resulting in the isolation of graphene oxide in powder form. Additionally, the ethyl acetate layer was subjected to filtration using filter paper to ensure the full retrieval of the catalyst. Following the filtration process of the catalyst, it was subjected to drying in an oven at 60°C. The dried catalyst was then utilized for the subsequent catalytic cycles. The process was repeated for a total of six cycles. After six cycles, the amount of catalyst recovered (GO) was found to be up to 188 mg. During each cycle of the reaction, the recovered ethyl acetate layer after separation was subjected to rotary evaporation, and the resulting product was isolated by column chromatography employing silica with a mesh size of 60-120. The obtained yields for the consecutive 6 catalytic cycles were 87%, 84%, 83%, 82%, 82%, and 80%, respectively.

Preparation of graphene oxide by a modified hummer's method

The synthesis of graphene oxide (GO) was carried out using a modified Hummers method (MHM), following the standard procedure as reported in the literature and starting with pure graphite powder (Figure S1).¹ In the experimental procedure, a mixture was prepared by mixing 23 ml of sulfuric acid (H₂SO₄) and 0.50 g of sodium nitrate (NaNO₃). The resulting mixture was then subjected to stirring for a duration of 10 minutes. Next, 1 gram of graphite powder was introduced into the mixed solution while maintaining continuous stirring at 0 °C. Subsequently, 3 grams of potassium permanganate (KMnO₄) was gradually introduced into the solution. The mixture was stirred for a duration of 1 h, resulting in a dark green solution and this solution was kept at 35°C

for 30 min and then 46ml of distilled water added dropwise. In order to remove the excess of KMnO_4 , 140 ml water and 10 ml of hydrogen peroxide (H_2O_2) were gradually added and stirred for 10 minutes. The exothermic reaction occurred and subsequently allowed for the cooling. Further, a mixture consisting of 10 mL of hydrochloric acid (HCl) and 30 mL of deionized water (DIW) was centrifuged at a speed of 5000 revolutions per minute (rpm) for a duration of 7 minutes. Next, the liquid portion was carefully poured off and the remaining substances were subsequently subjected to three more washes using hydrochloric acid (HCl) and deionized water (DIW). The GO solution was subjected to a drying process in an oven set at a temperature of 60 °C for a duration of 24 hours, resulting in the formation of GO powder.

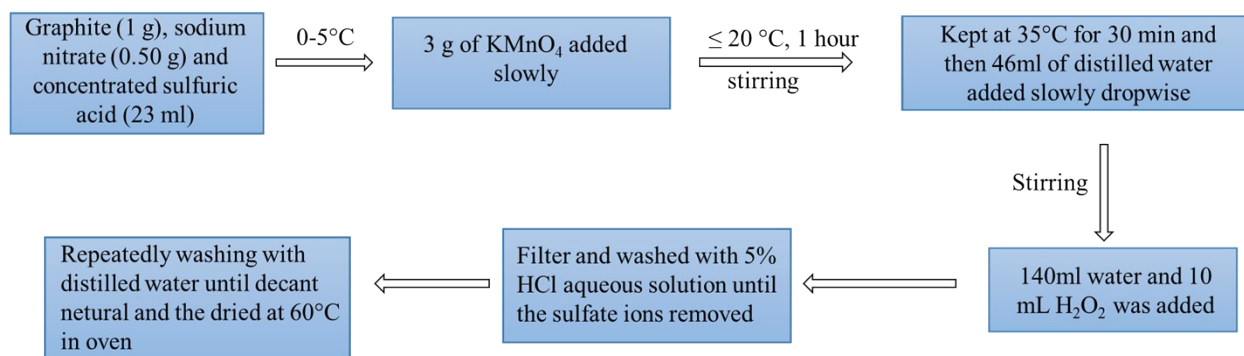


Figure S1. Procedure for synthesis of graphene Oxide

FTIR spectra

The Fourier Transform Infrared (FTIR) spectrum of the graphene oxide (GO) layer is depicted in Figure S2(a). The spectrum encompasses many vibrational groups present in the GO layer, such as carbonyl ($\text{C}=\text{O}$), aromatic ($\text{C}=\text{C}$), carboxyl ($-\text{COOH}$), epoxy ($\text{C}-\text{O}-\text{C}$), and hydroxyl ($\text{O}-\text{H}$) groups. The presence of oxygen-containing compounds is evident, as indicated by the primary absorption band observed at 3148 cm^{-1} , which is attributed to the stretching vibrations of the $\text{O}-\text{H}$ group.¹ The observed absorption peaks at 1716 cm^{-1} and 1613 cm^{-1} can be attributed to the stretching of the $\text{C}=\text{O}$ bonds in carboxylic and/or carbonyl functional groups.² The spectral peak observed at a wavenumber of 1218 cm^{-1} corresponds to the stretching vibration of $\text{C}-\text{OH}$ of alcohol.³ The 1042 cm^{-1} mode provides insights into the bending of $\text{C}-\text{O}-\text{C}$ bonds in alkoxy groups. The absorption peak seen at a wavenumber of 970 cm^{-1} is attributed to the stretching vibration of $\text{C}=\text{C}$ of carboxylic acid and carbonyl groups present at the edges of graphene oxide.⁴ The reused

graphene oxide generated after the sixth cycle likewise exhibited similar functional groups, indicating minimal alteration in the sample's morphology (Figure S2(b)).

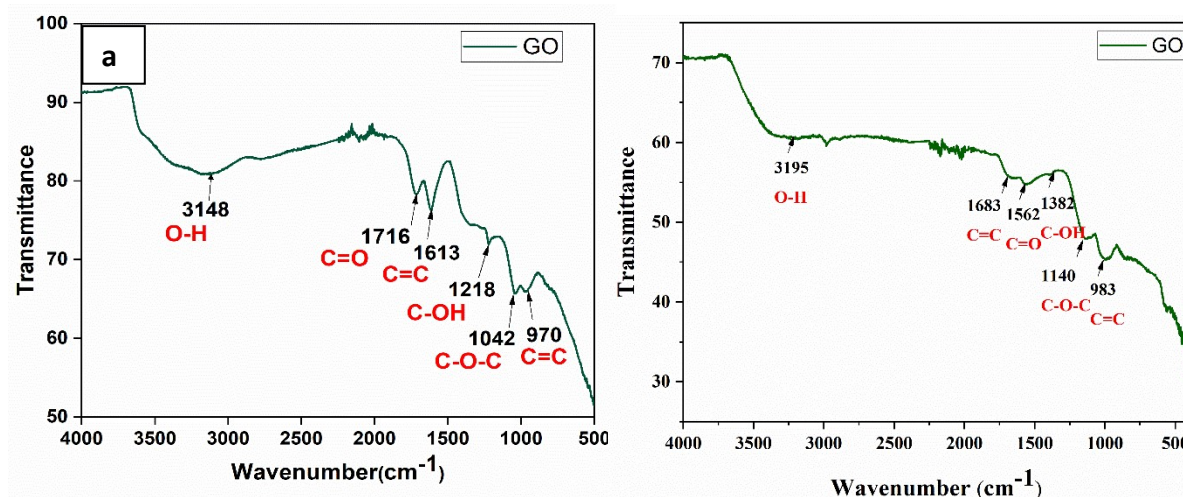


Figure S2. FTIR spectrum of (a) GO films prepared by MHM (b) Reused GO after 6th cycle

XRD analysis of GO

The crystalline characteristics of the GO sheet were determined using X-ray diffraction (XRD) analysis. The results are depicted in Figure S3(a). The generated GO sheet exhibited a prominent peak at $2\theta = 11.2^\circ$, aligning well with the results reported in the literature.⁵ The X-ray diffraction (XRD) analysis provided initial evidence of the effective fabrication of graphene oxide (GO) sheets. An additional diffraction peak of significant breadth was detected at an angle of 42.1 degrees, this diffraction peak can be attributed to the (002) crystallographic plane with Miller indices of (002).⁶ The observed peak had a wider breadth and significantly lower intensity compared to that of normal graphite, indicating the presence of graphene with a reduced number of layers.

Raman's analysis of GO

Figure S3(b) displays the Raman spectrum of graphene oxide (GO). The Raman spectra of graphene oxide (GO) nanosheets exhibit a prominent peak at approximately 1602 cm^{-1} (G-band). Additionally, a less intense peak is observed at around 1351 cm^{-1} (D-band). The G peak is

associated with the optical E_{2g} phonons located near the center of the Brillouin zone which arise from the stretching of bonds between sp^2 carbon pairs in both rings and chains. The D peak corresponds to the breathing mode of aromatic rings, which is observed as a result of a defect present in the sample.⁷ The intensity of the D-peak is frequently employed as an indicator of the level of disorder.⁸ The correlation between the number of graphene layers (N) and the shift and form of the overtone of the D peak, commonly referred to as the 2D peak at approximately 2644 cm^{-1} , has been established.⁹ The occurrence of a two-dimensional peak can be ascribed to the phenomenon of double resonance transitions, which lead to the generation of two phonons possessing opposing momentum. Moreover, in contrast to the D peak, which exhibits Raman activity solely in the presence of defects, the 2D peak has Raman activity even in the absence of any defects. Figure 2b illustrates the conventional Raman spectra of graphene oxide (GO) acquired with an excitation wavelength of 532 nm . The presence of a conspicuous D peak at approximately 1348 cm^{-1} , with a comparable intensity to the G peak at around 1592 cm^{-1} , coupled with their substantial band width, suggests the existence of considerable structural disorder in graphene oxide (GO). The presence of weak and broad two-dimensional peaks can serve as an additional indication of dysfunction. In accordance with previous research,¹⁰ it is observed that a distinct peak known as D+G emerges prominently at approximately 2928 cm^{-1} .¹¹

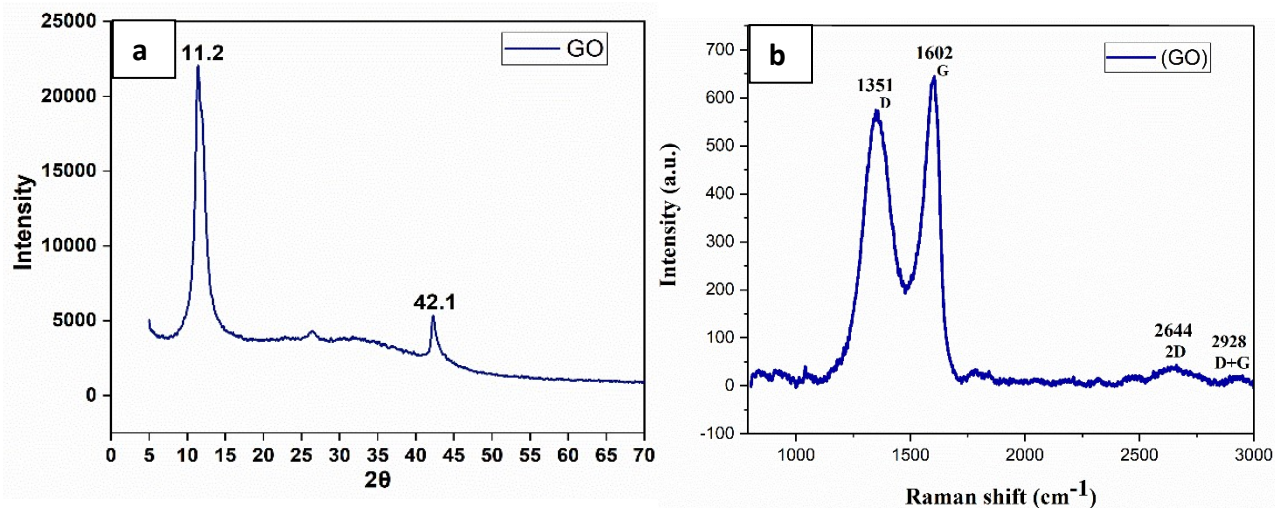


Figure 3. XRD and Raman spectra of GO film

FESEM

The scanning electron microscopy (SEM) characterization of the synthesized graphene oxide (GO) was done to check the morphology of the catalyst (Figure S4). The figure illustrates the layered structure of graphene oxide, which depicts the aggregated and crumpled thin sheets bearing a folded or continuous structure, allowing for the discrimination of distinct boundaries between separate sheets, which may also exhibit areas of kinks and wrinkles (Figure S4(a)). Additionally, an examination was conducted on the morphology of the graphene oxide that was reused after the sixth reaction cycle. The results indicated a modest alteration in its morphological properties, with the material still retaining folded and aggregated sheets (Figure S4(b)).

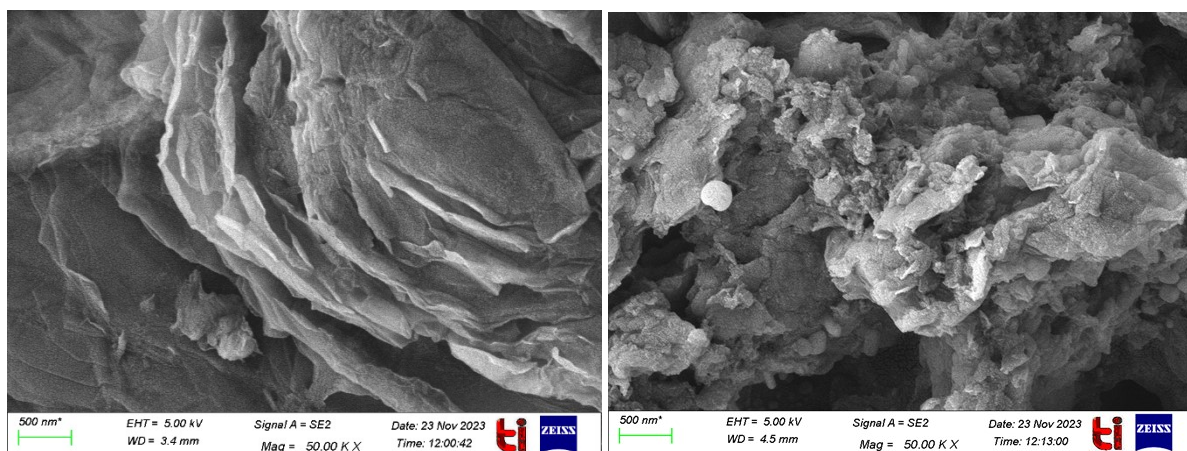


Figure S4: FESEM images of (a) Graphene Oxide (b) Reused GO after 6th cycle.

Calculation of green chemistry metrics for the scale-up reaction of the product (3a):

Green chemistry matrix has been calculated based on the following parameters.

- 1) E-factor or environmental factor
- 2) Atom economy (AE)
- 3) Product mass intensity (PMI)
- 4) Reaction mass efficiency (RME)

E-factor: E-factor is defined as the ratio of the mass of waste per mass of the product.

E-Factor = Amount of waste / Amount of product

Amount of reactants: Diazoisatin (1a) = 3.1 mmol and Indole (2a) = 6.3 mmol

Total amount of reactants (1a+2a) = (159.15 mg x 3.1) + (117.15 mg x 6.3) = 493.36 + 491.4 = 1231.4 mg = 1.231 g

Amount of product (3k) = 0.987 g

Amount of waste = 1.231 – 0.987 = 0.244g

E-factor = 0.244/ 0.987 = 0.25 (Ideal value of E-factor is considered zero)

Process mass index (PMI): PMI is defined as the total mass used in a chemical process divided by the mass of product

$PMI = \Sigma(\text{mass of stoichiometric reactants} + \text{solvent})/\text{mass of product}$

$PMI = (159.15 \text{ mg} \times 3.1) + (117.15 \text{ mg} \times 6.3)/987 = 1.25$

OR

$PMI = E\text{-factor} + 1 = 0.25 + 1 = 1.25$

Atomic economy (AE): AE of a chemical reaction is a measure of the efficiency of that reaction with regard to how many atoms from the starting materials reside within the product. The ideal value of AE factor is 100% (i.e., all atoms from the starting materials reside in the product).

$\text{Atom economy (AE)} = \text{MW of product} \div \Sigma (\text{MW of stoichiometric reactants}) \times 100$

Molecular weight of product (3a) = 363.42 g/mol

Molecular weight of stoichiometric reactants (1a+2a) = 159.15 + 117.15 x 2 = 393.45g/mol

$\text{Atom economy (AE)} = 363.42 \times 100 / 393.45 = 92.36\%$

Reaction mass efficiency (RME): Reaction mass efficiency is defined as the mass of product divided by the sum of total mass of stoichiometric reactants. The value of RME varies from 0-100%. The larger number of RME is considered as better as it is the measure of “cleanness” of the reaction.

$\text{Reaction mass efficiency} = \text{mass of product} / \Sigma(\text{mass of stoichiometric reactants}) \times 100$

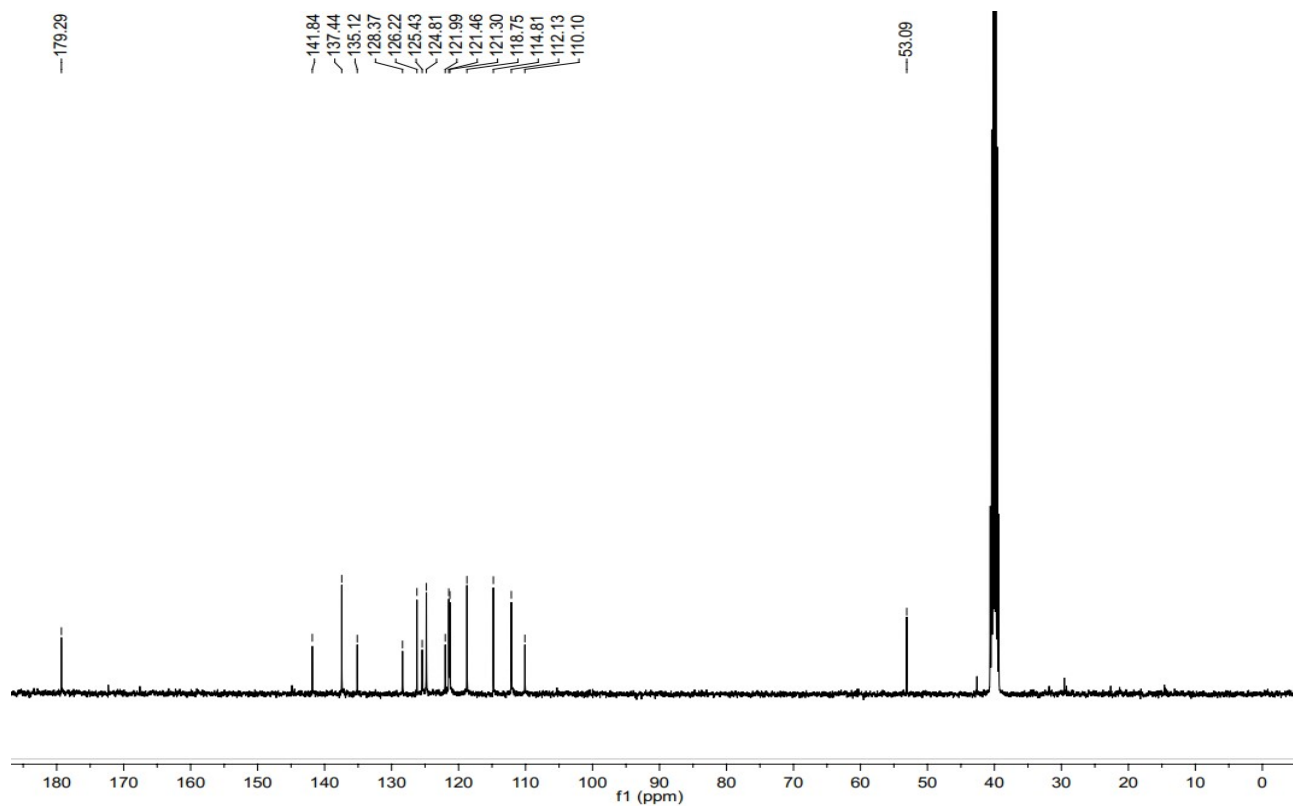
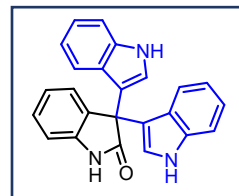
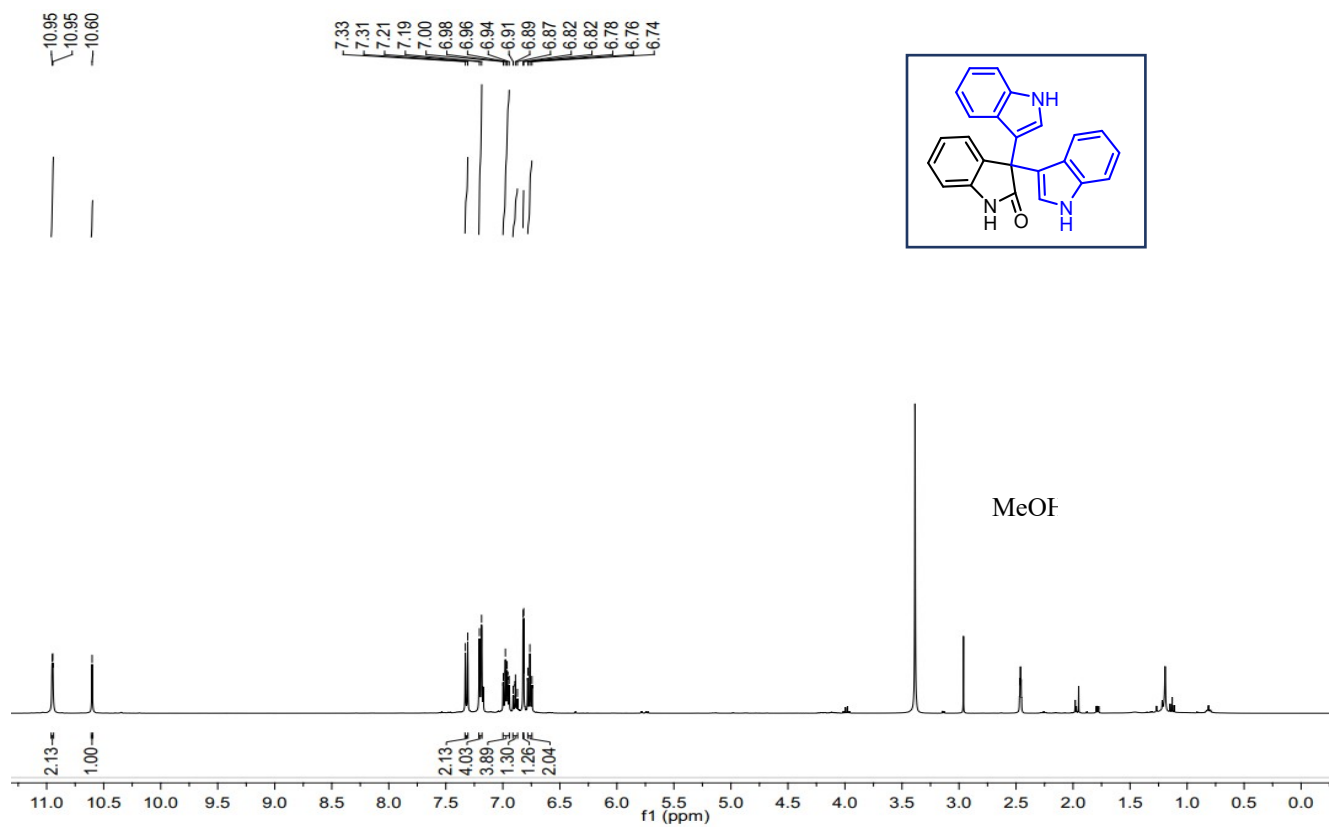
Mass of product (3a) = 0.987g

Total mass of reactants (1a+2a) = (159.15 mg x 3.1) + (117.15 mg x 6.3) = 493.36 + 491.4 = 1231.4mg = 1.231 g

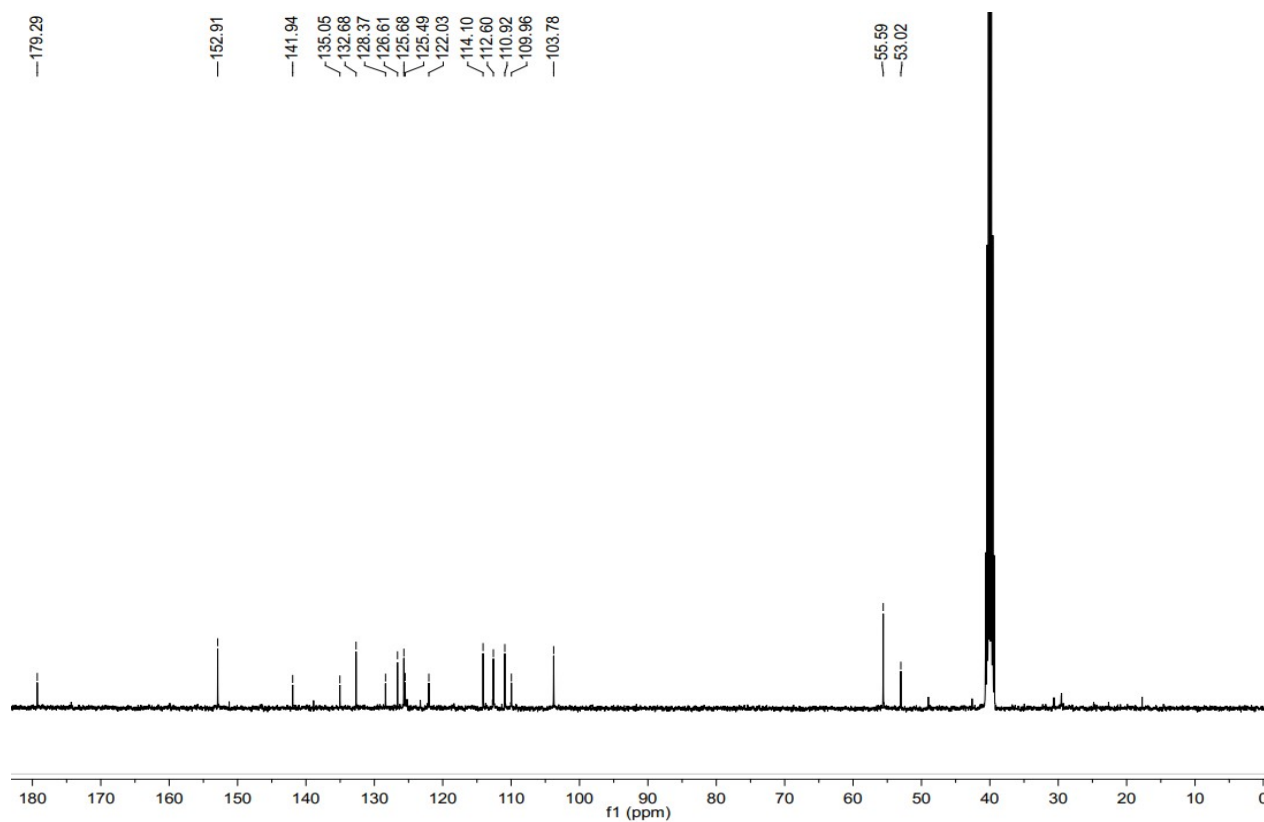
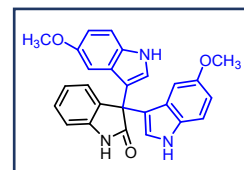
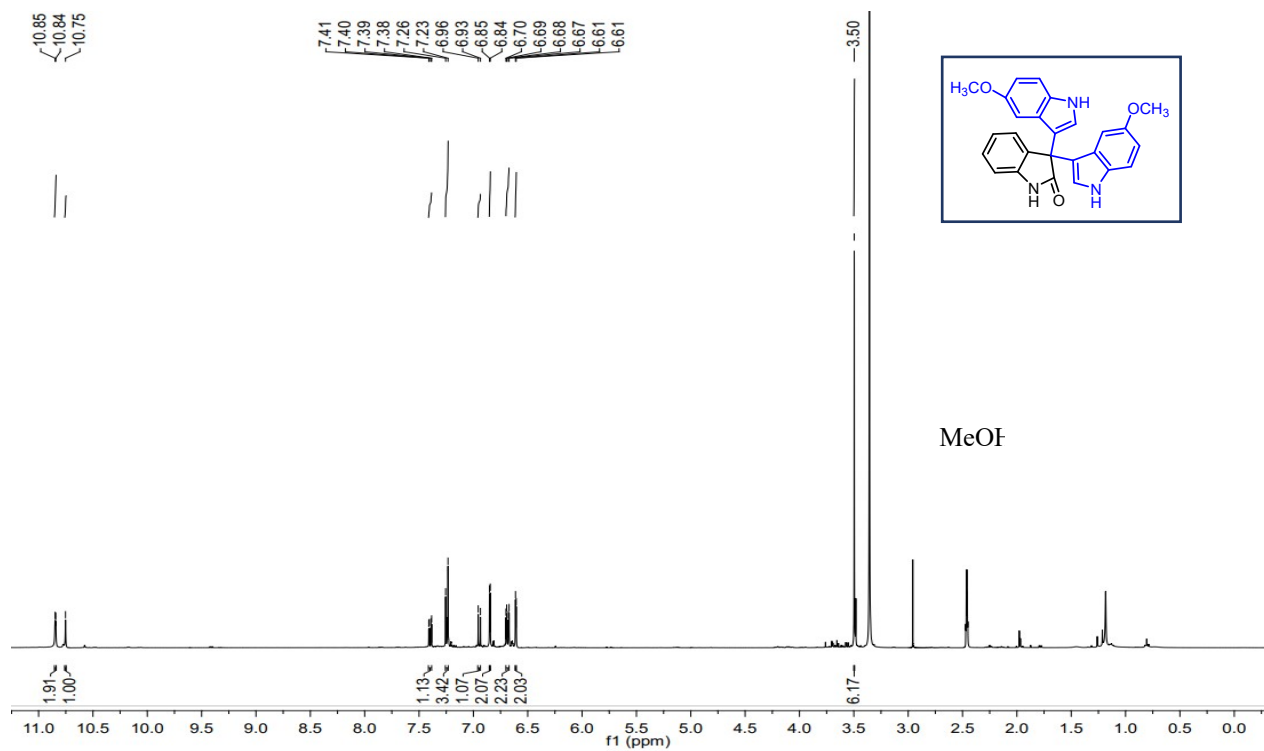
$RME = 0.987 \div 1.231 \times 100 = 80.1\%$

^1H and ^{13}C -NMR Spectra of Synthesized compounds (3a-3s)

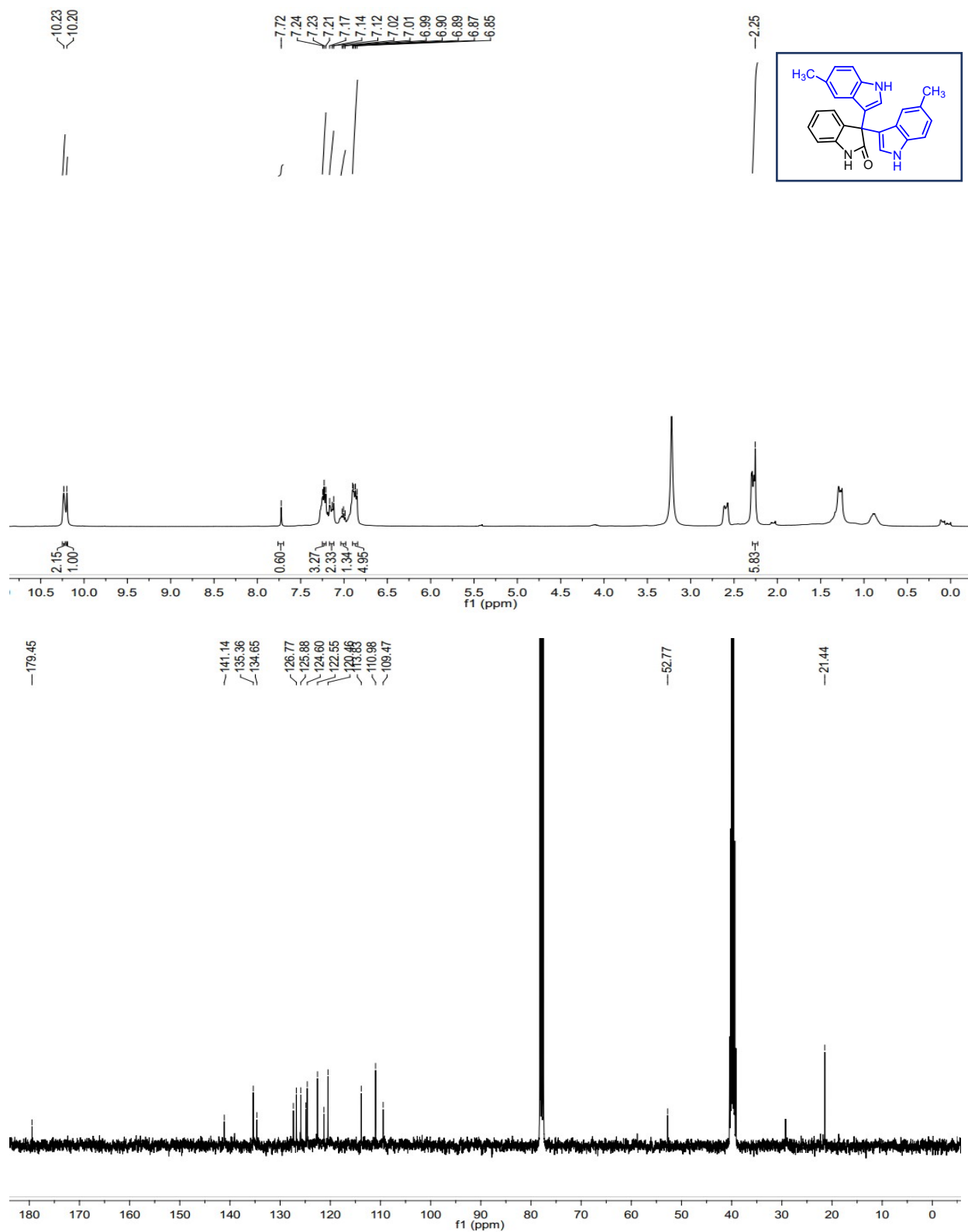
¹H and ¹³C NMR spectra of 3a



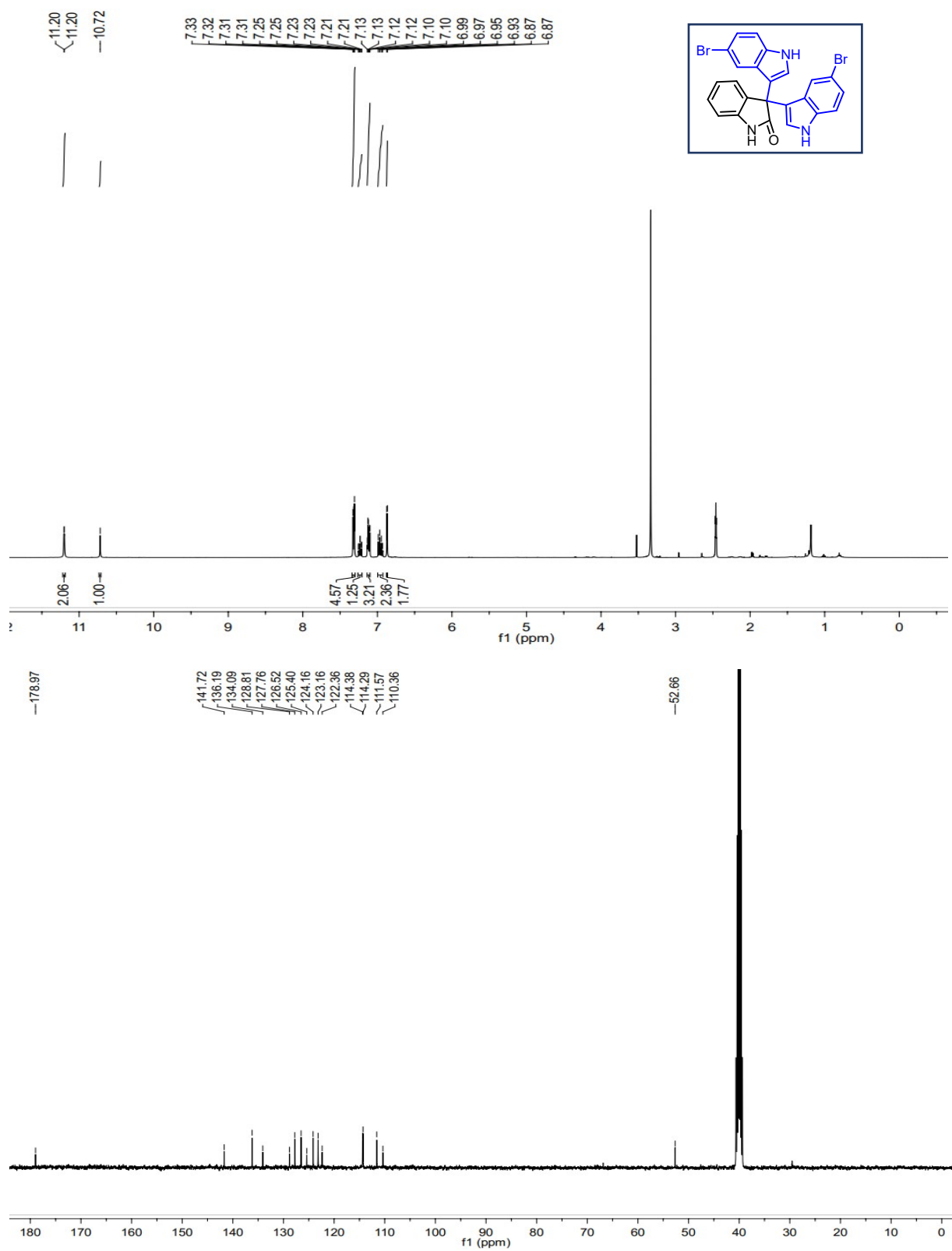
¹H and ¹³C NMR spectra of 3b



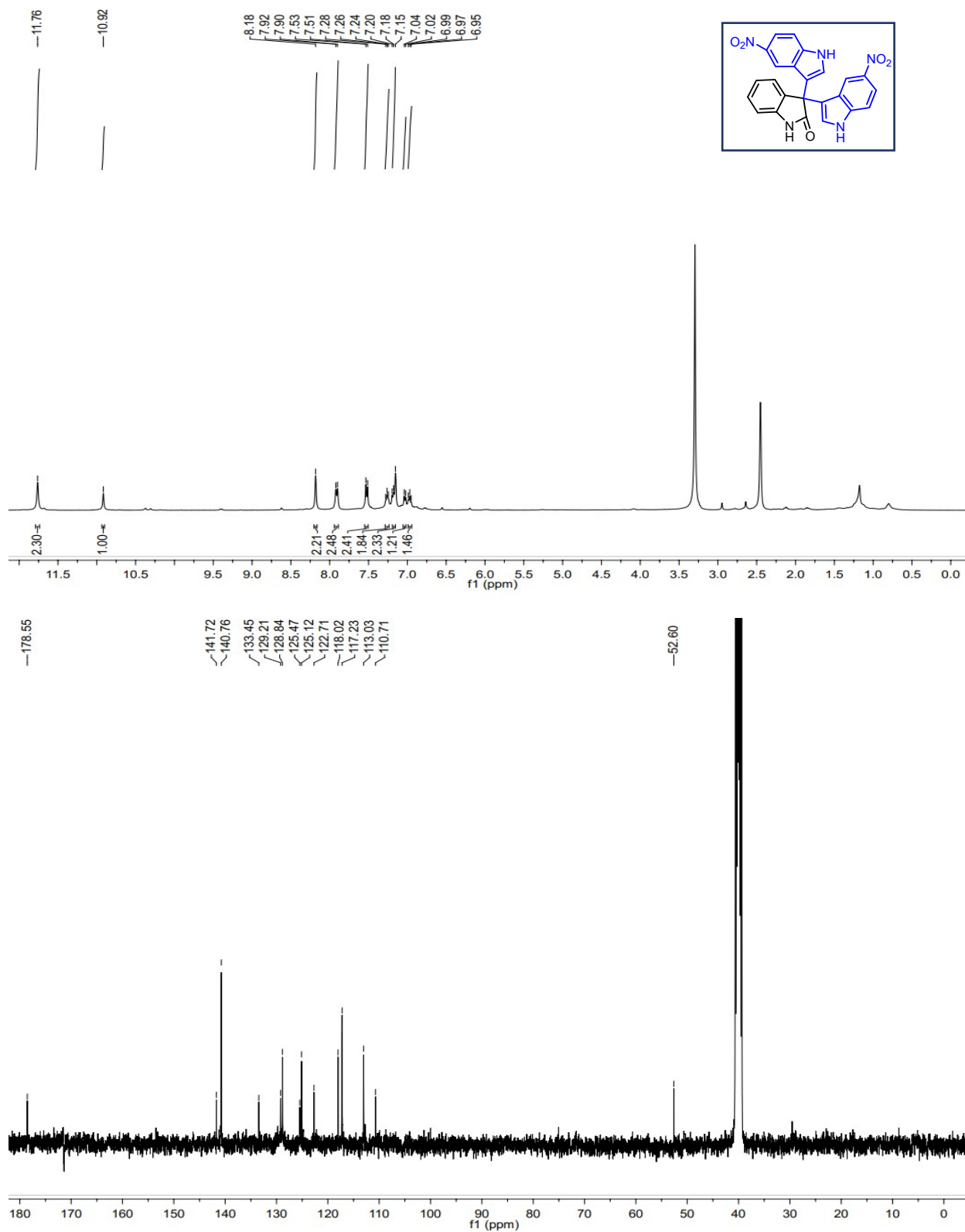
¹H and ¹³C NMR spectra of 3c



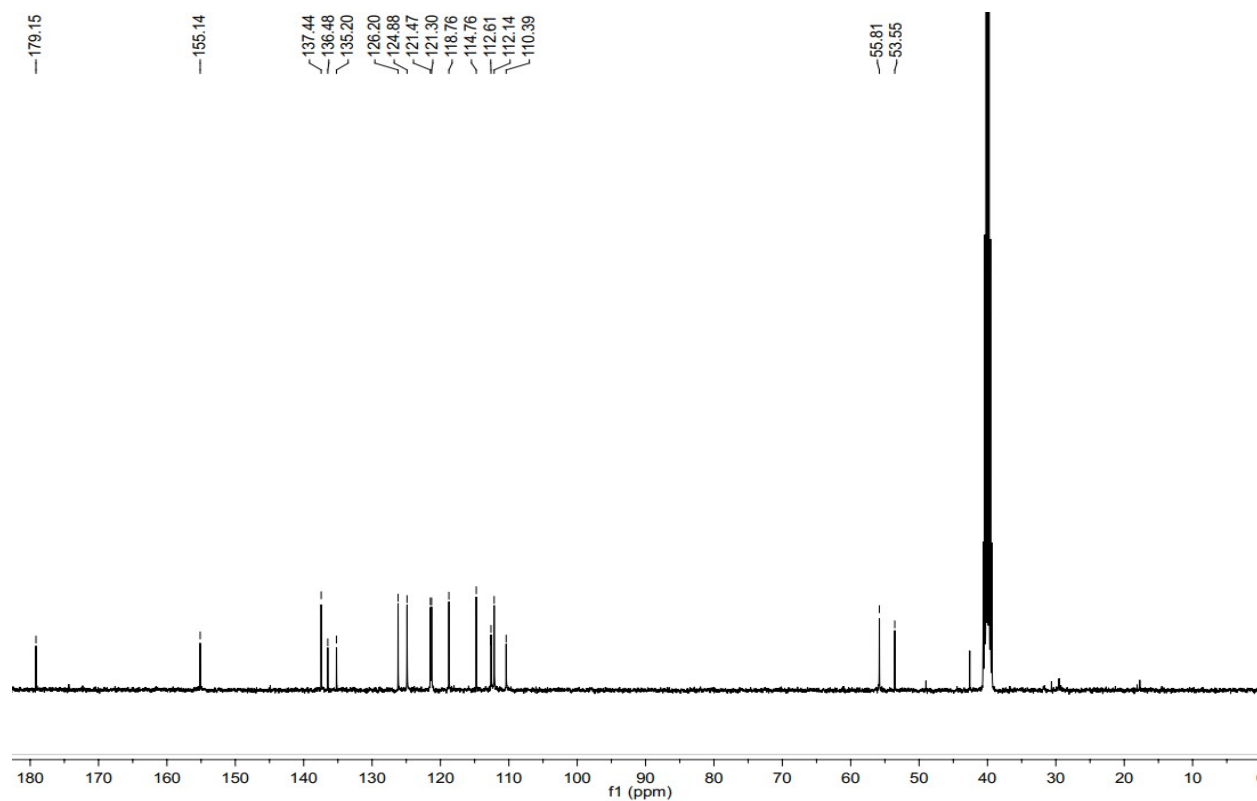
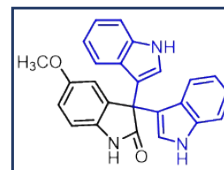
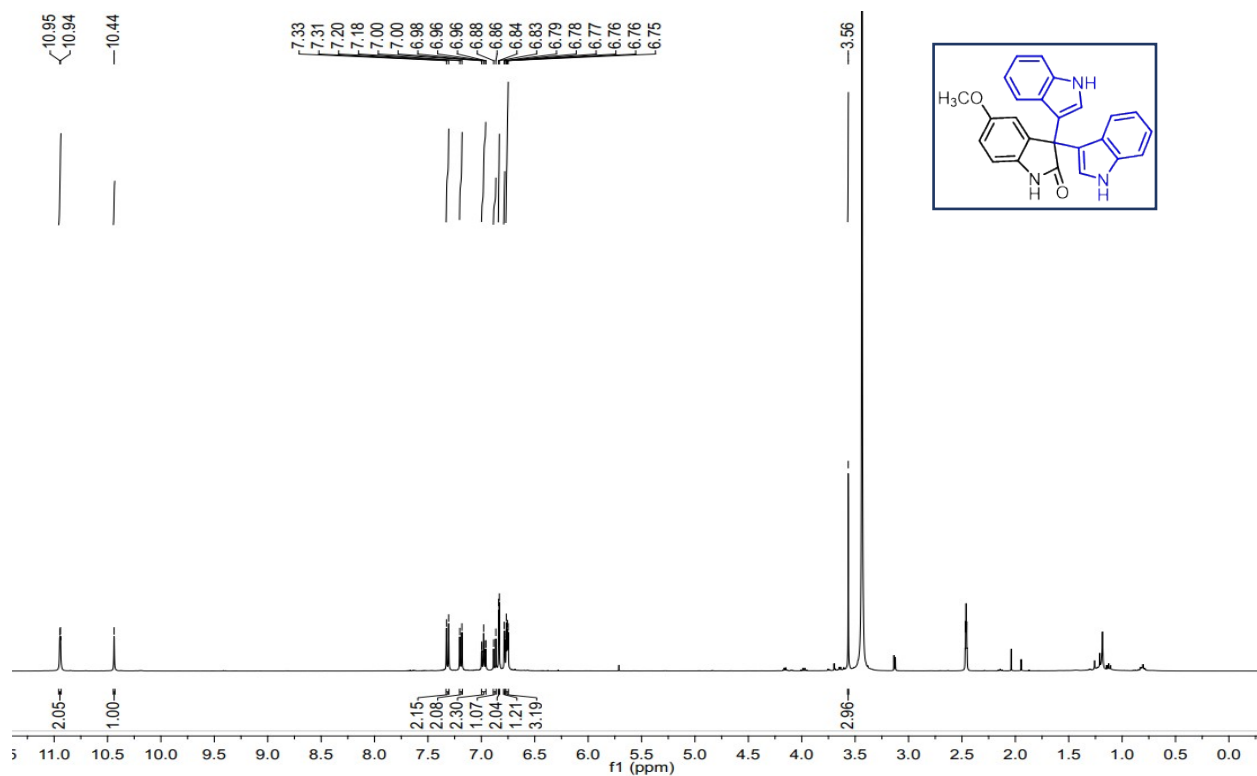
¹H and ¹³C NMR spectra of 3d



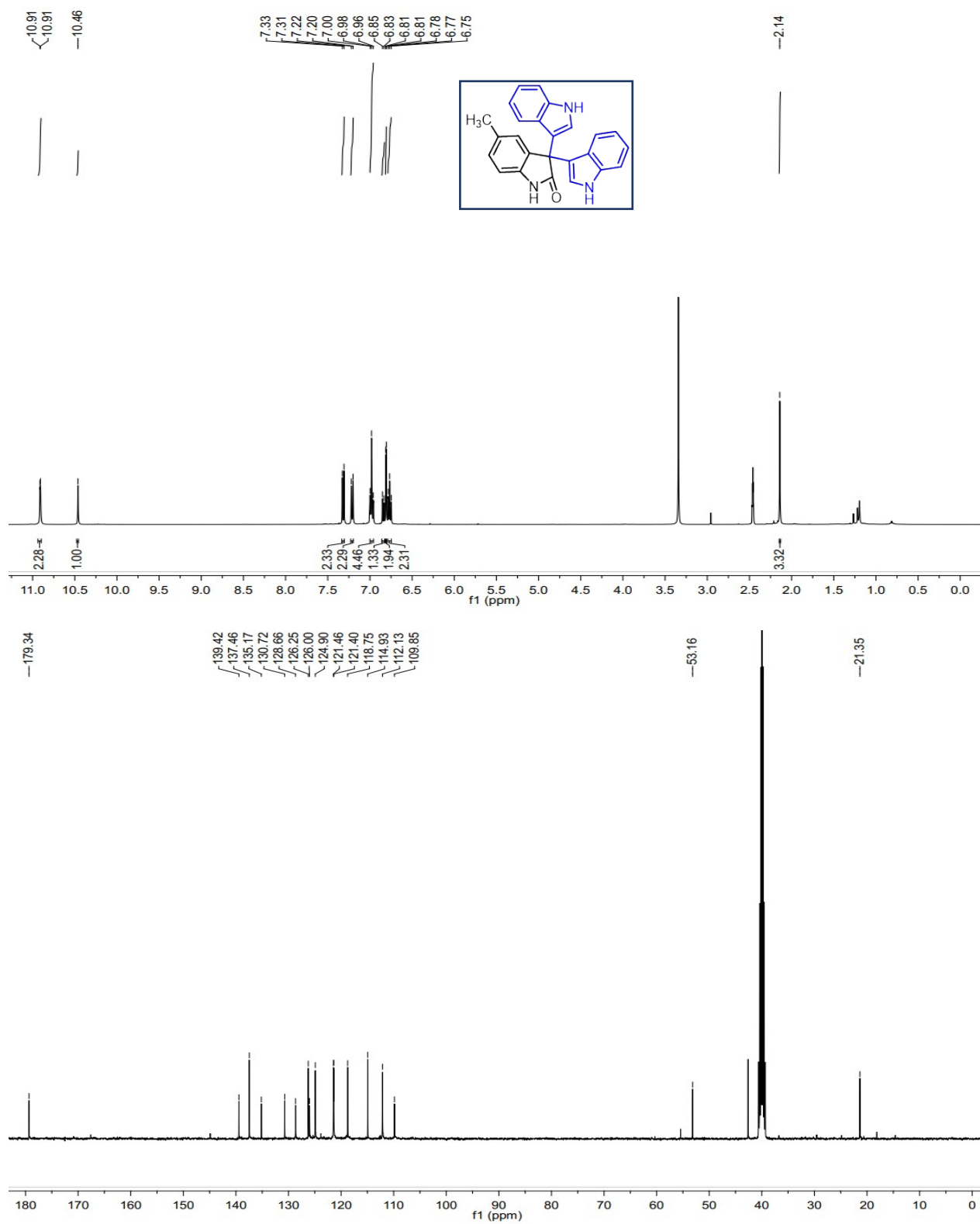
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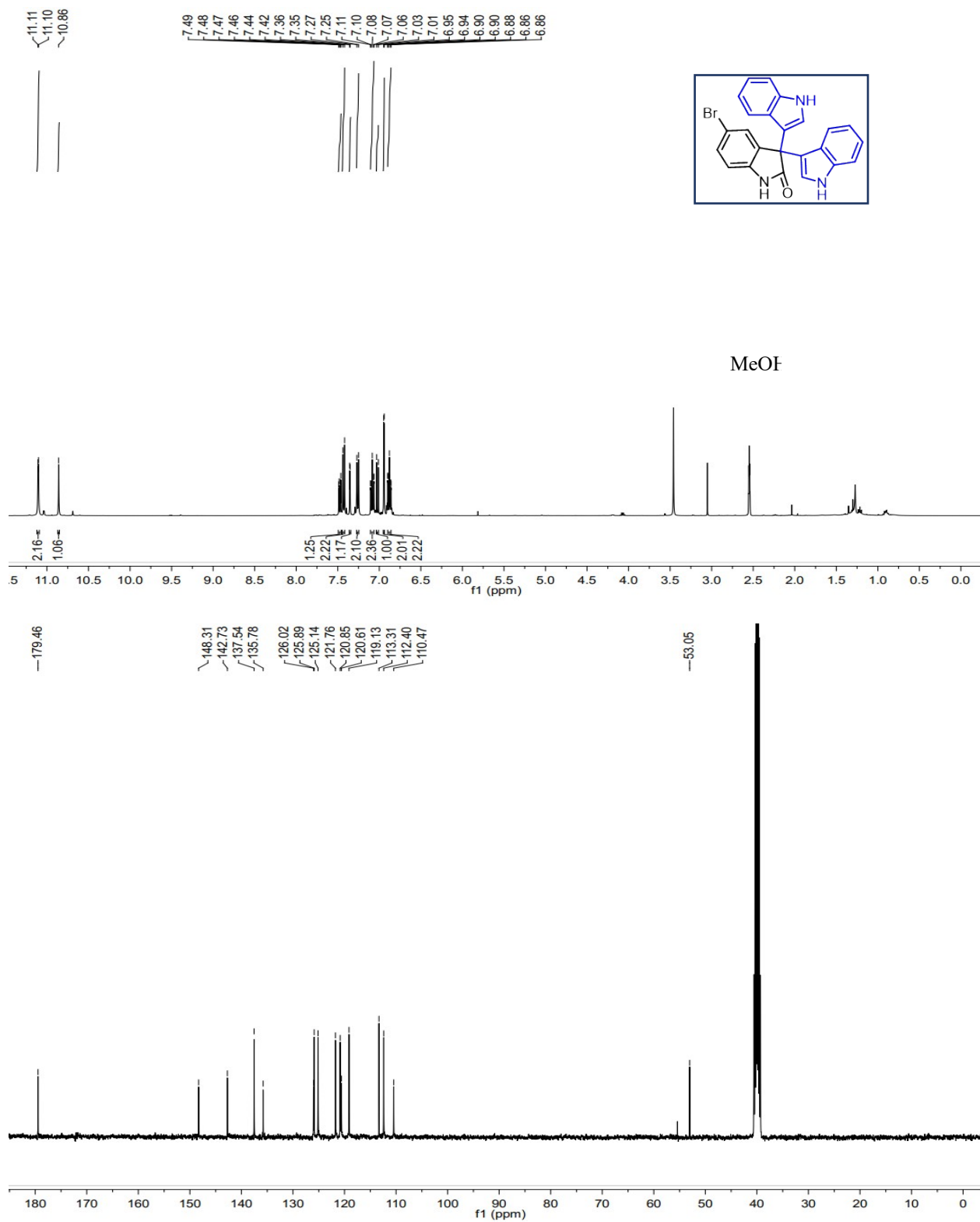
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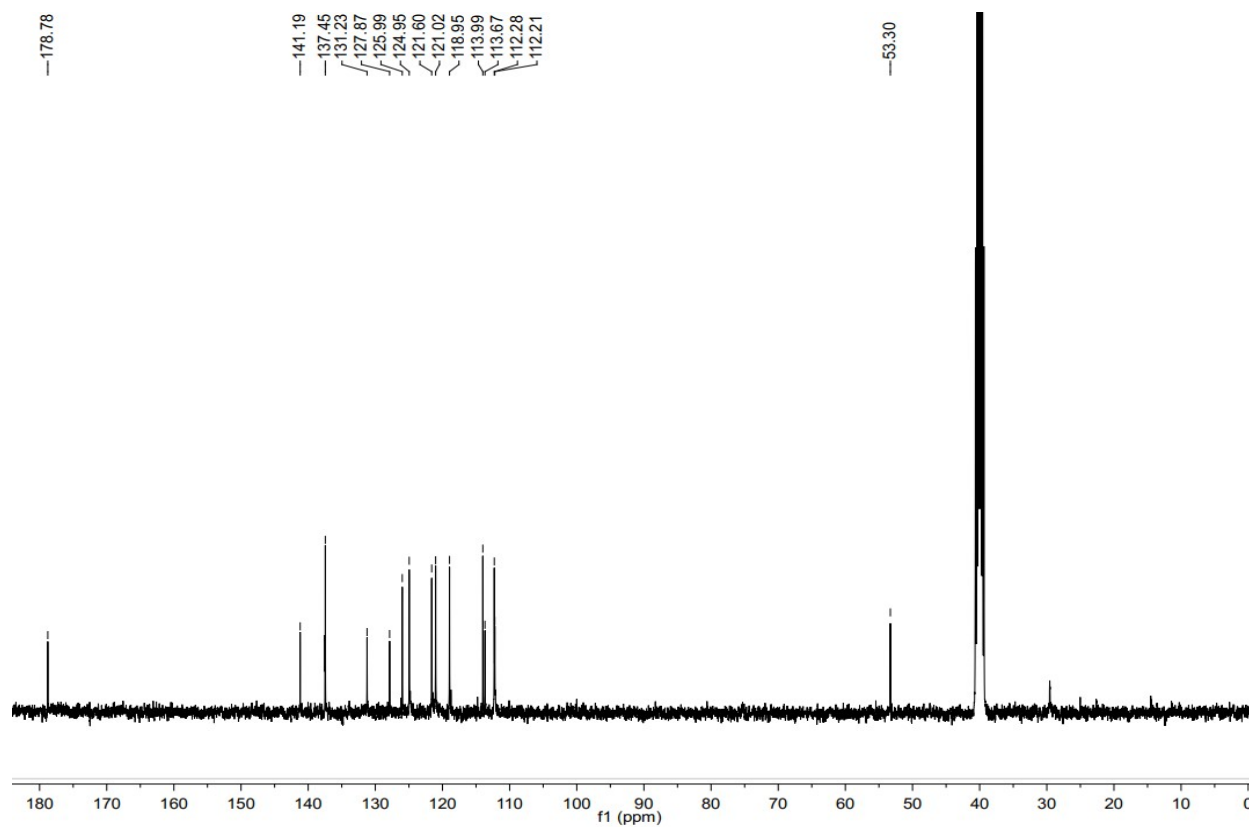
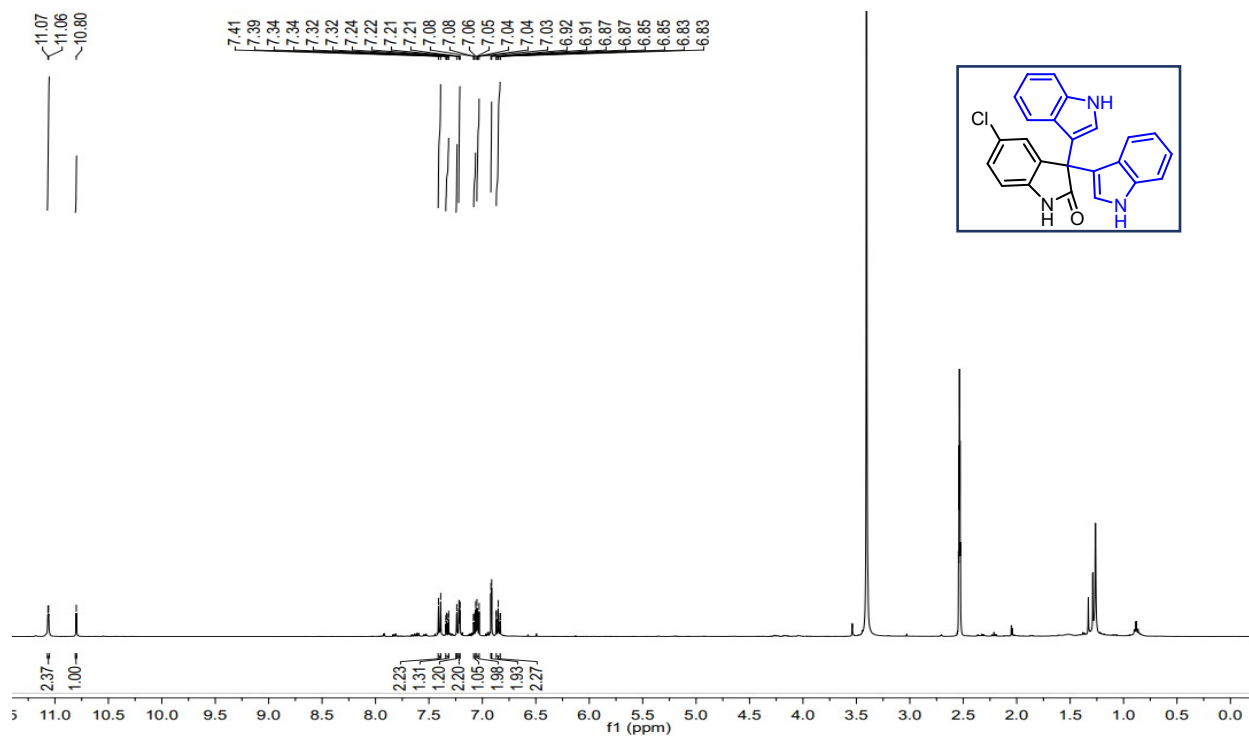
¹H and ¹³C NMR spectra of 3g



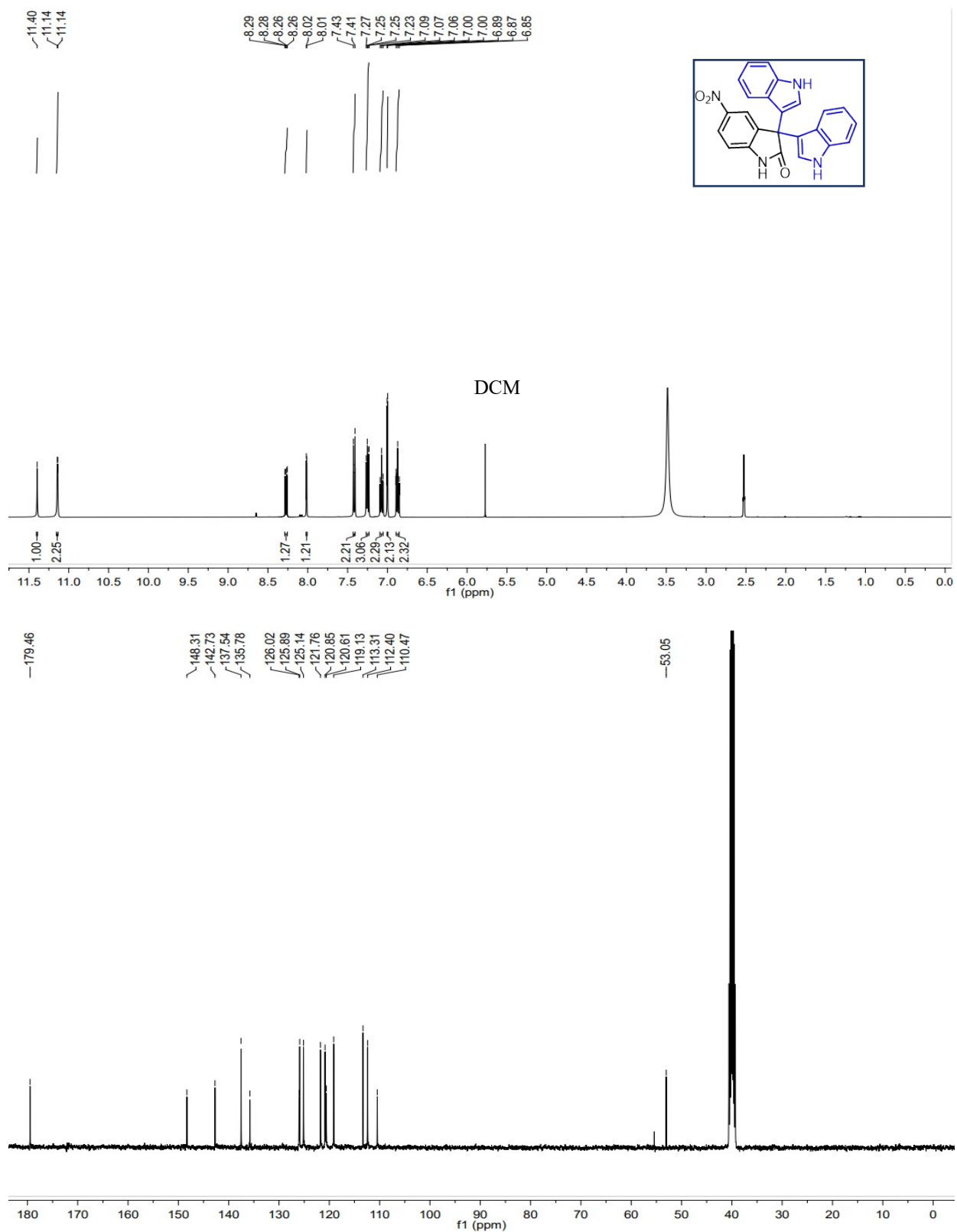
¹H and ¹³C NMR spectra of 3h



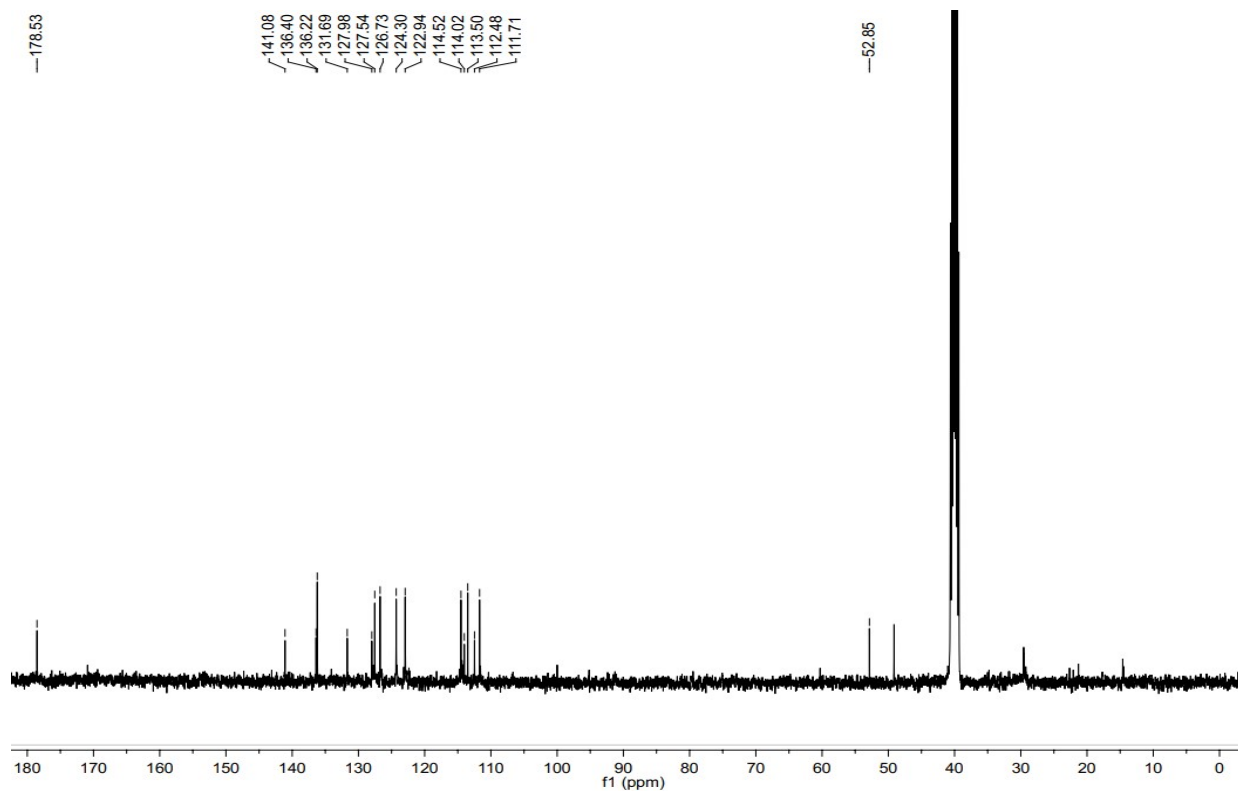
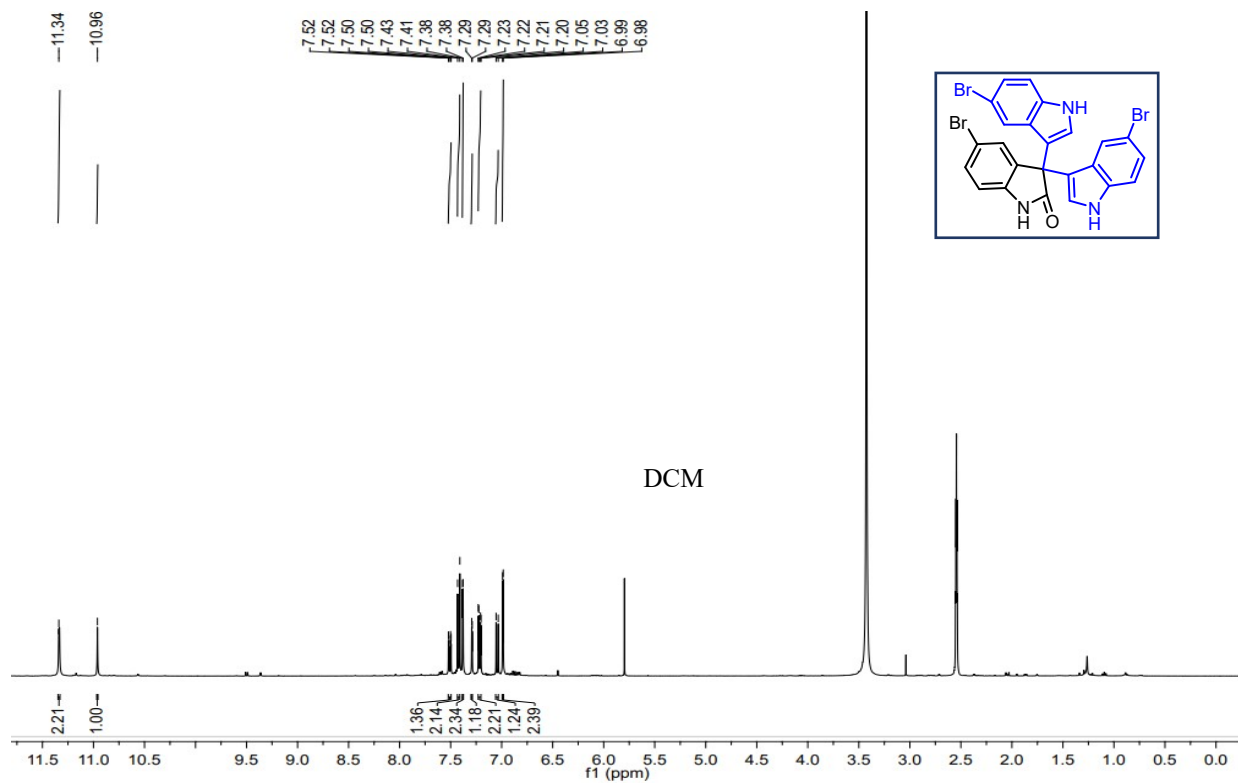
¹H and ¹³C NMR spectra of 3i



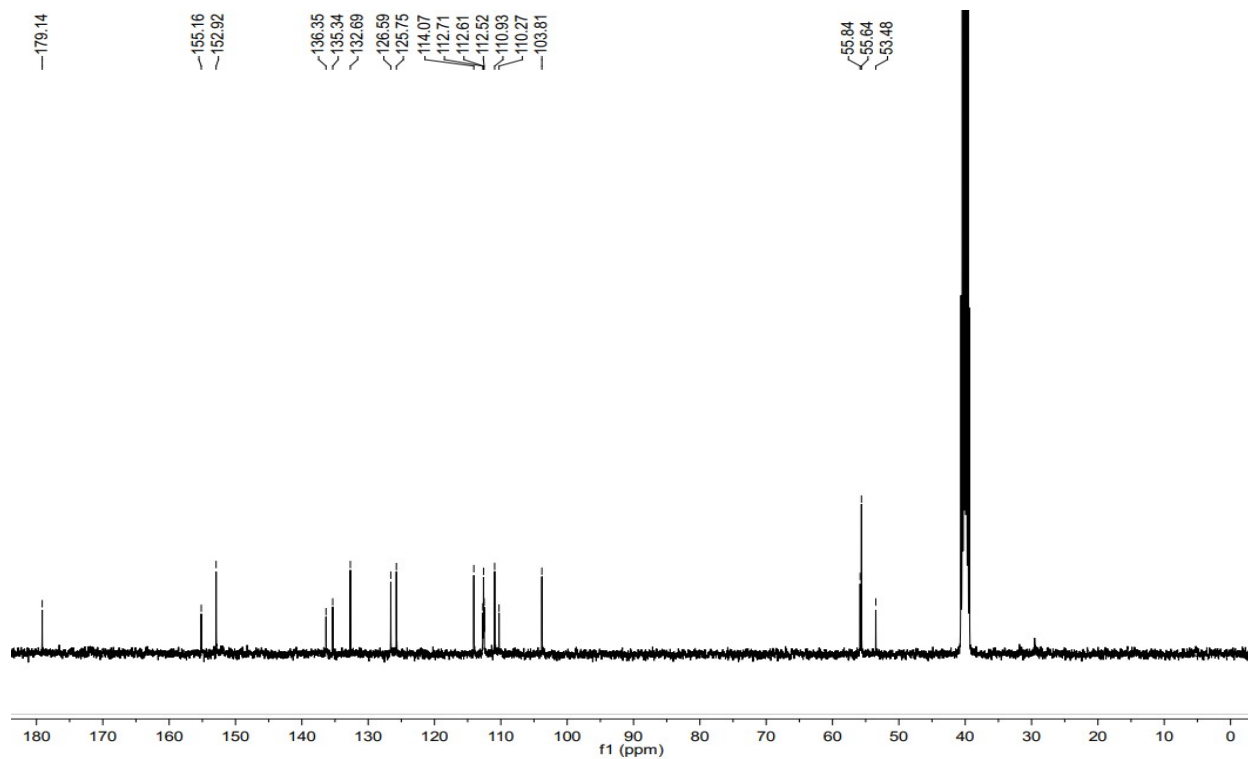
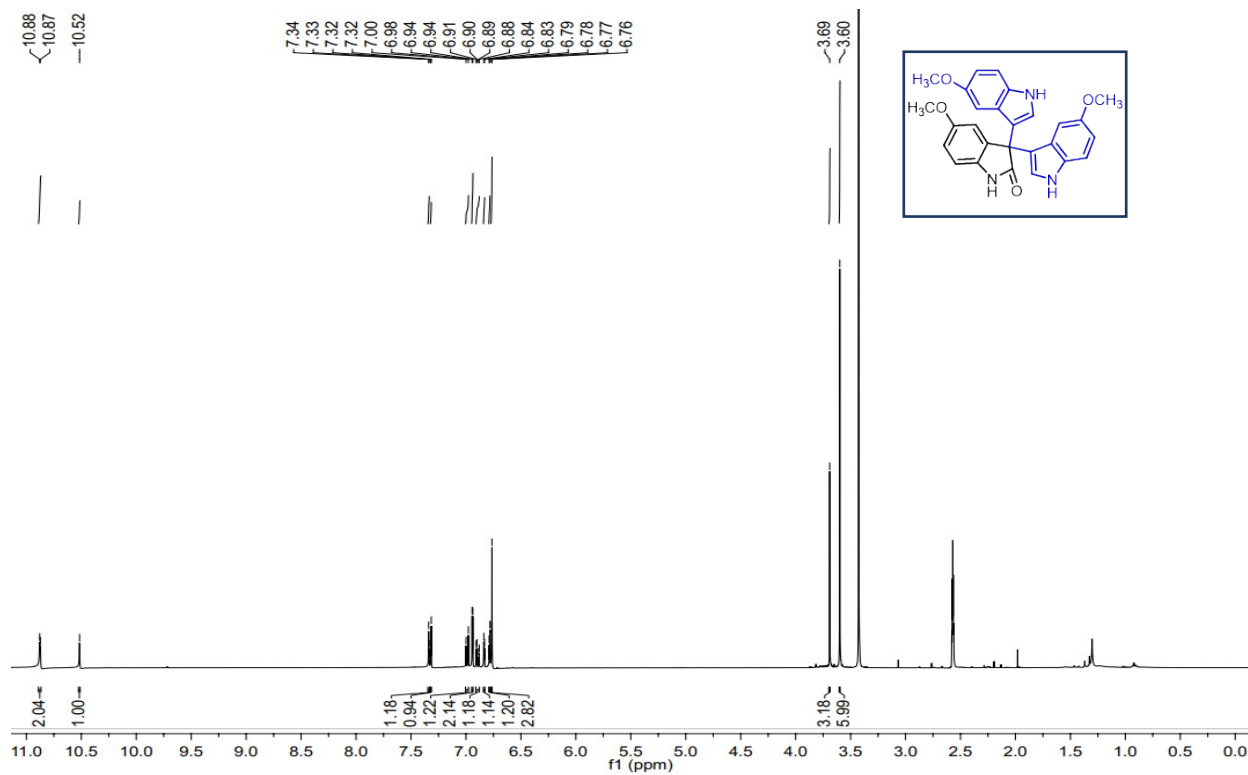
¹H and ¹³C NMR spectra of 3j



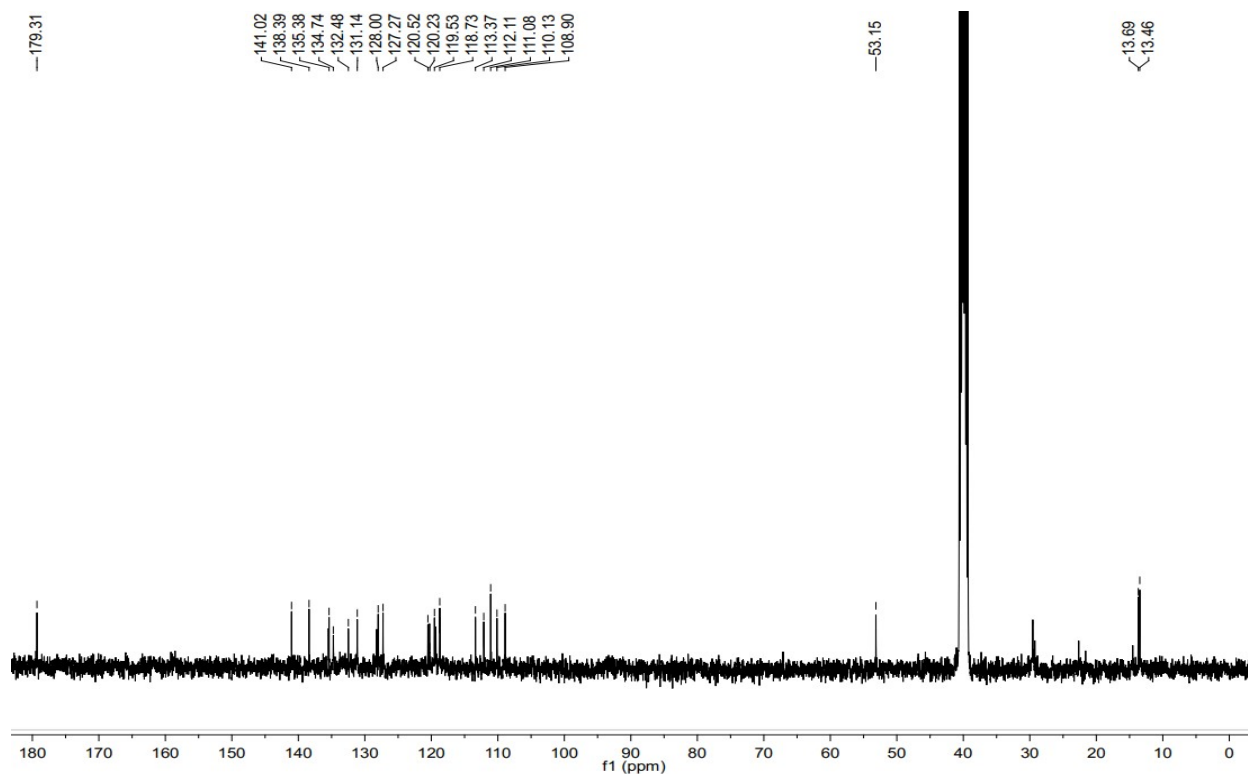
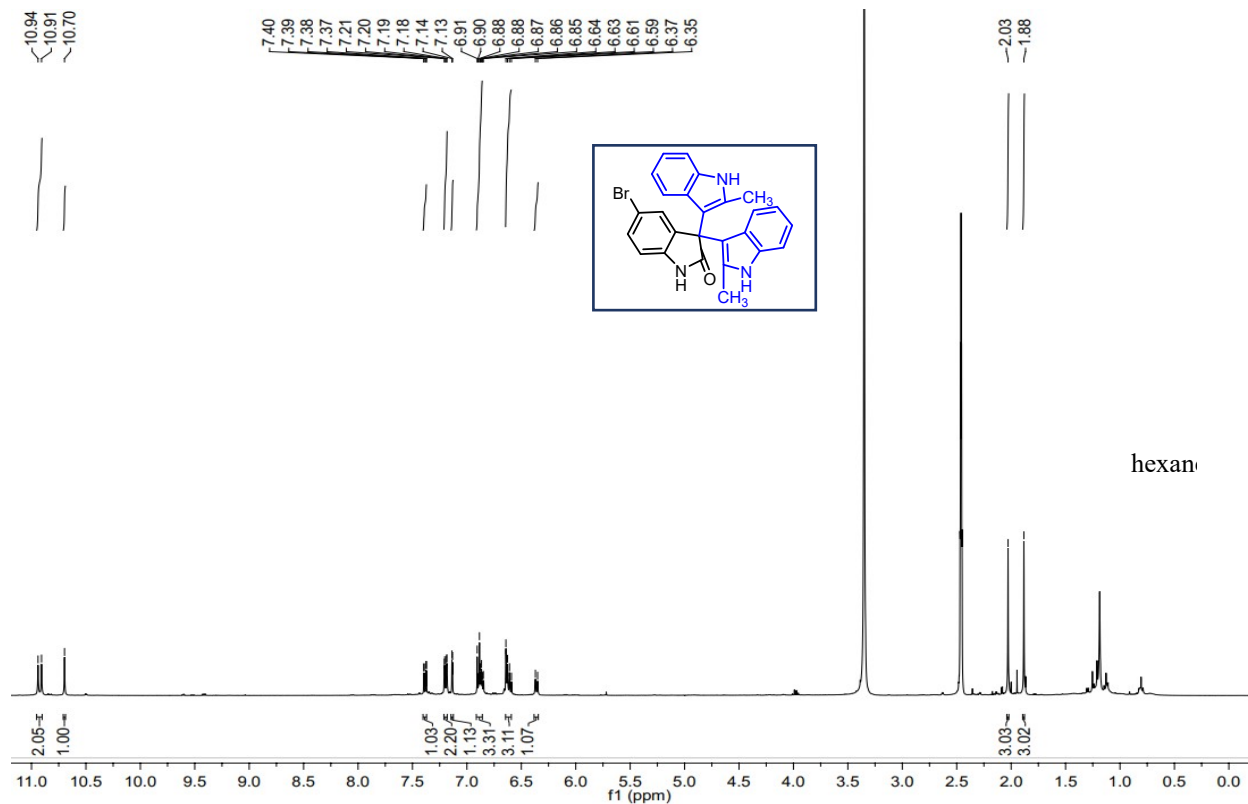
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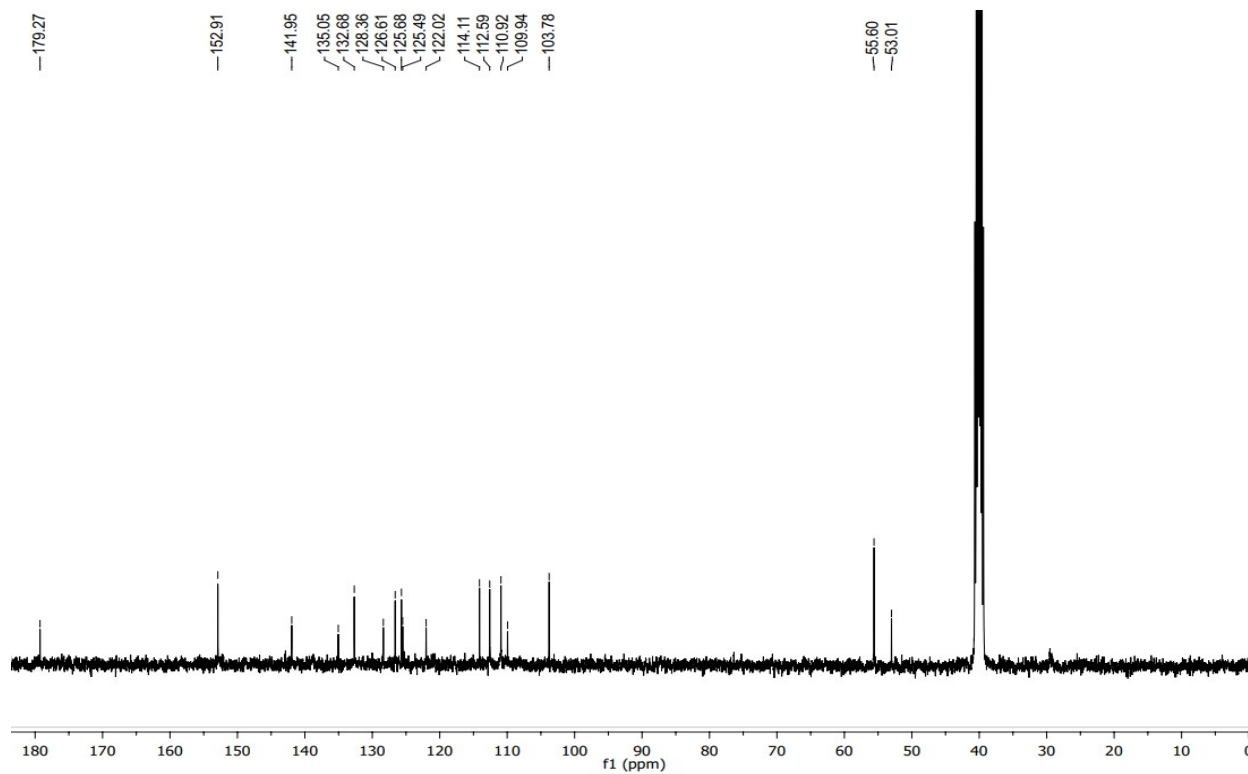
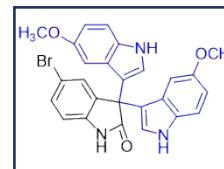
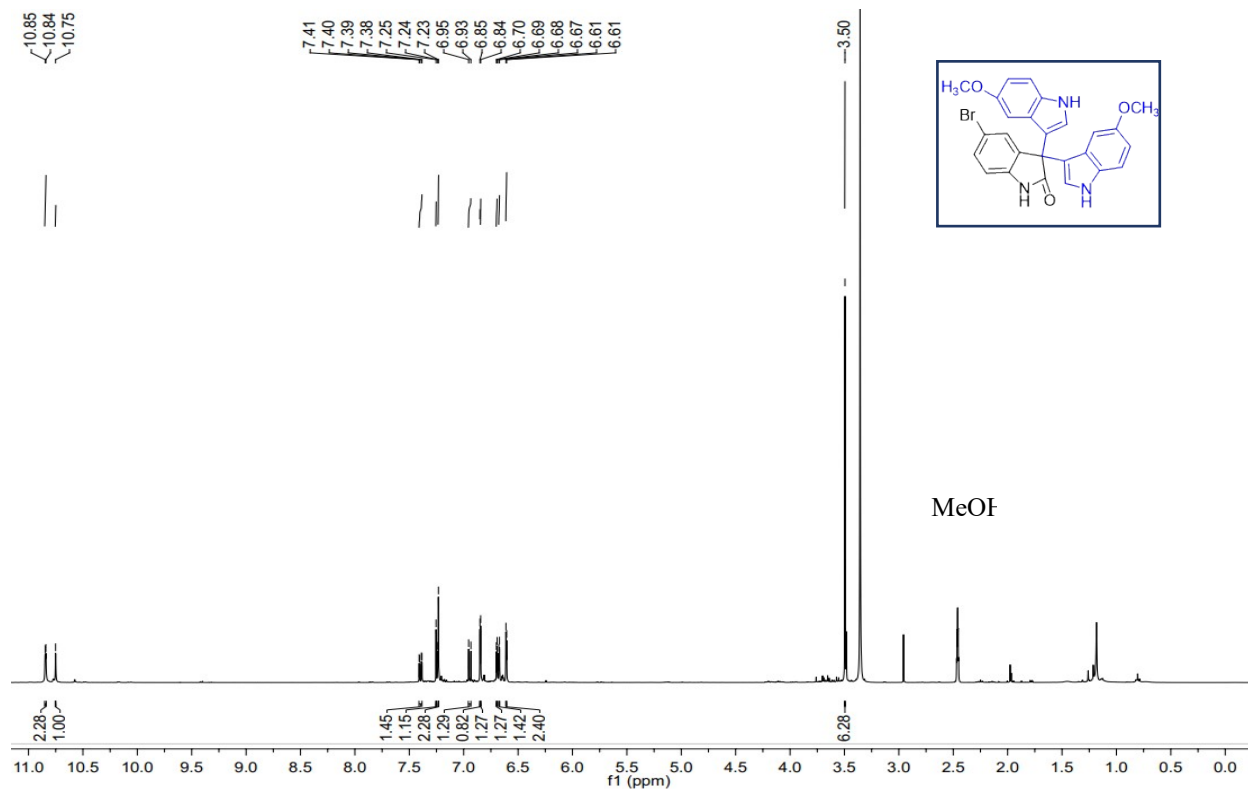
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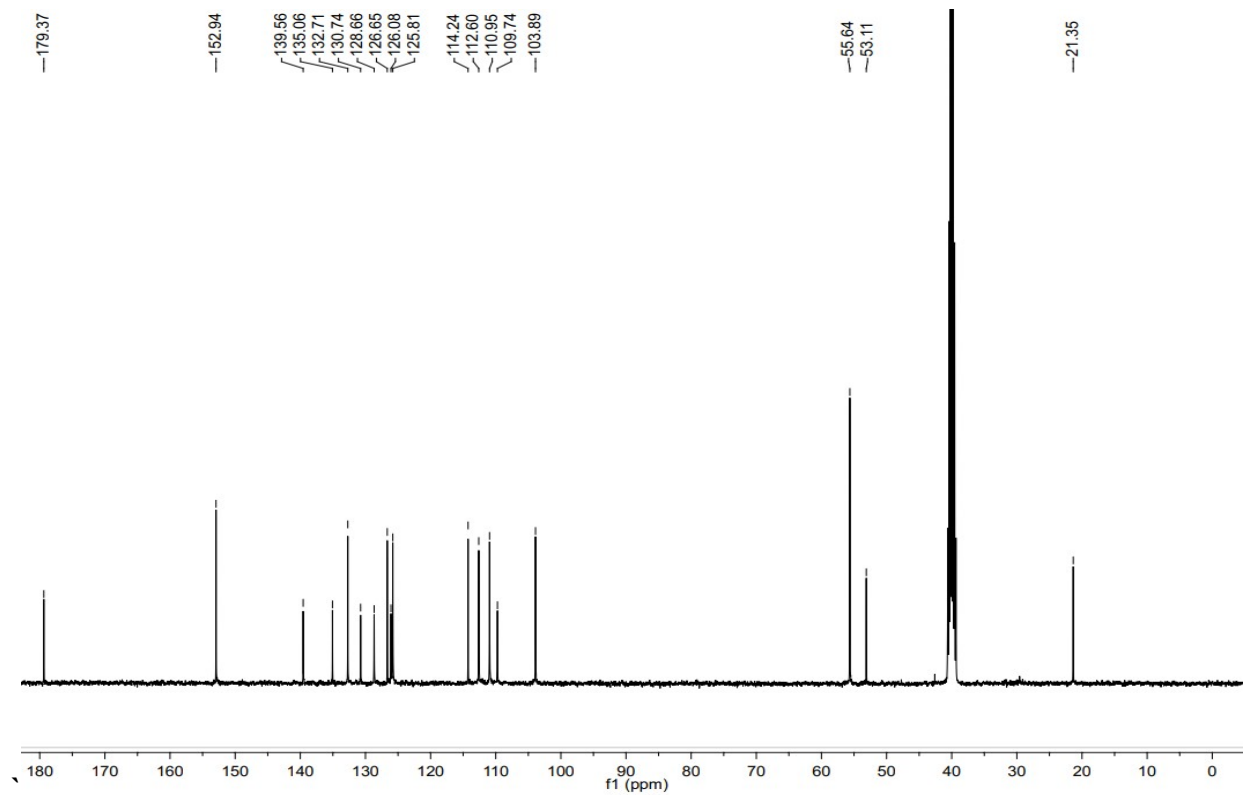
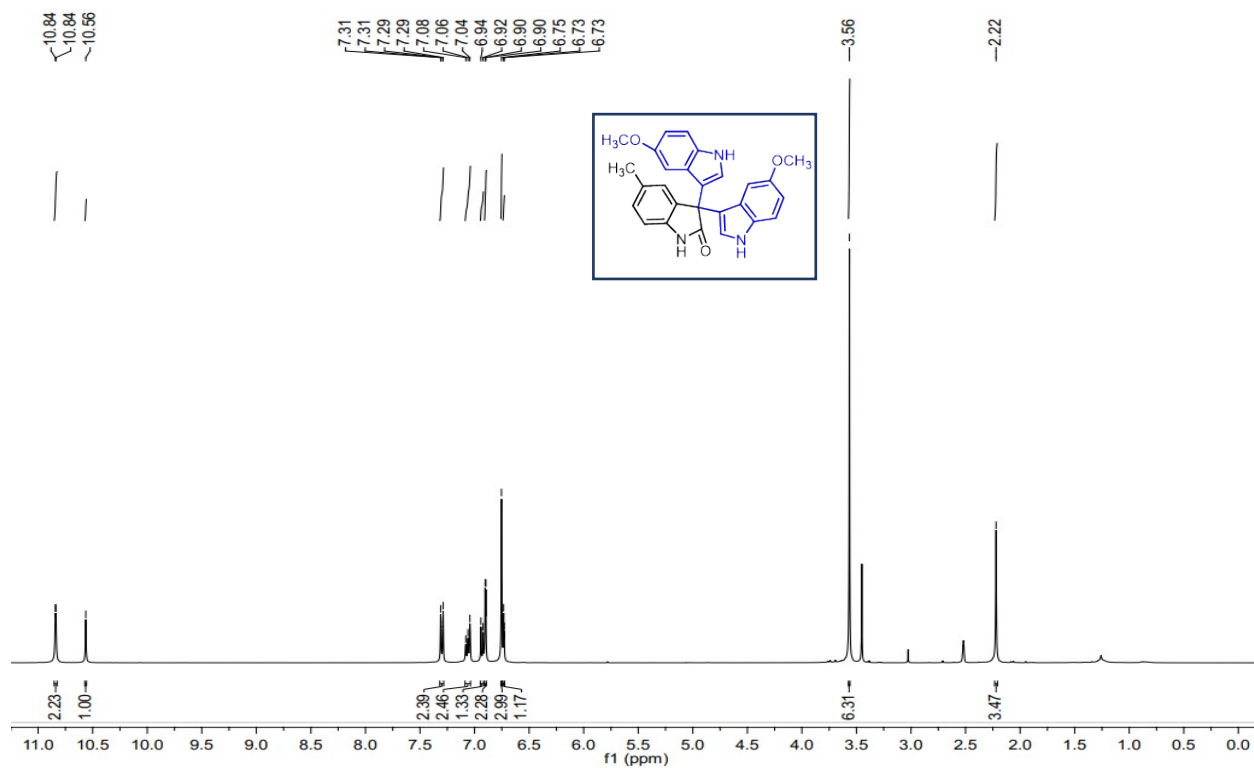
¹H and ¹³C NMR spectra of 3m



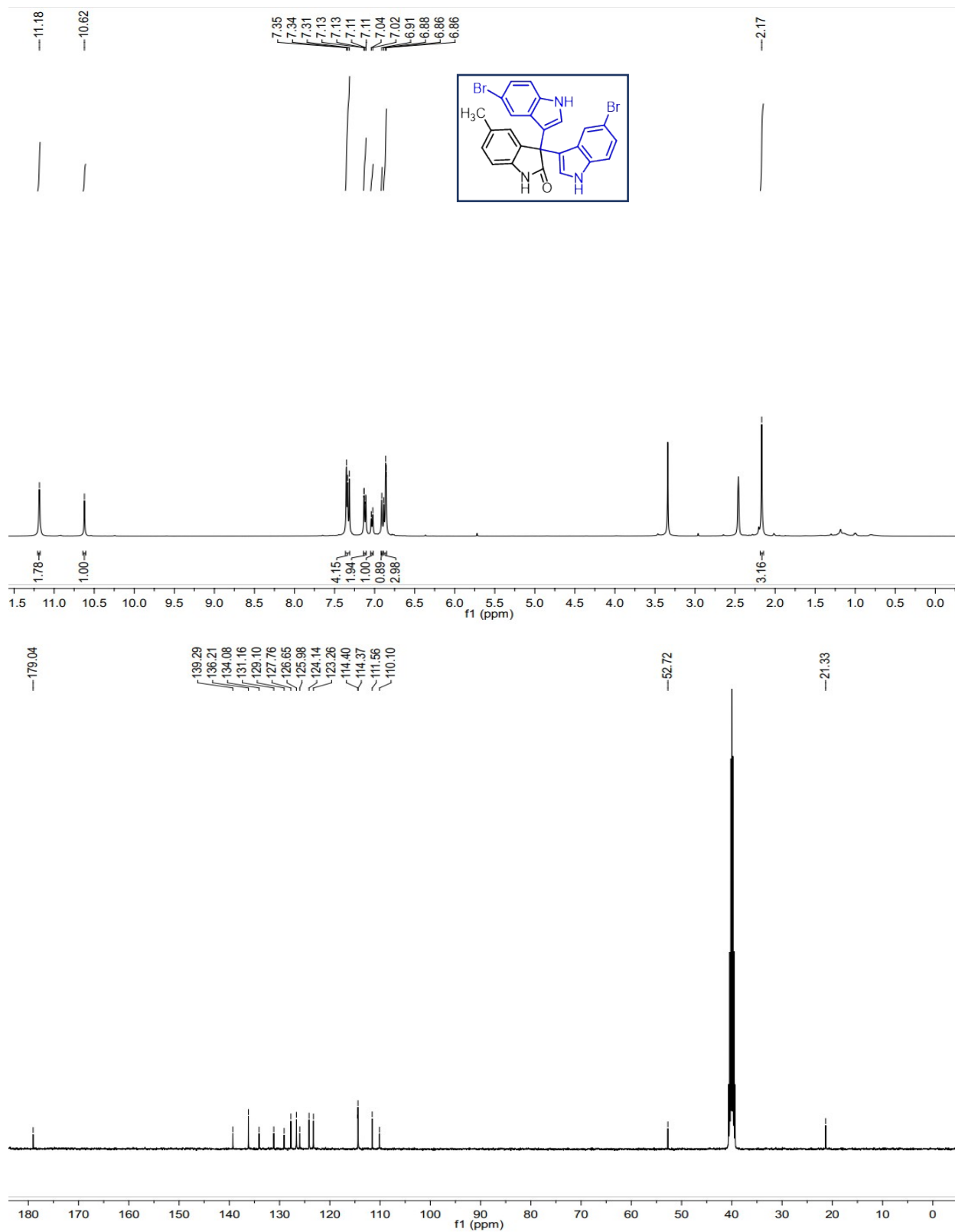
¹H and ¹³C NMR spectra of 3n



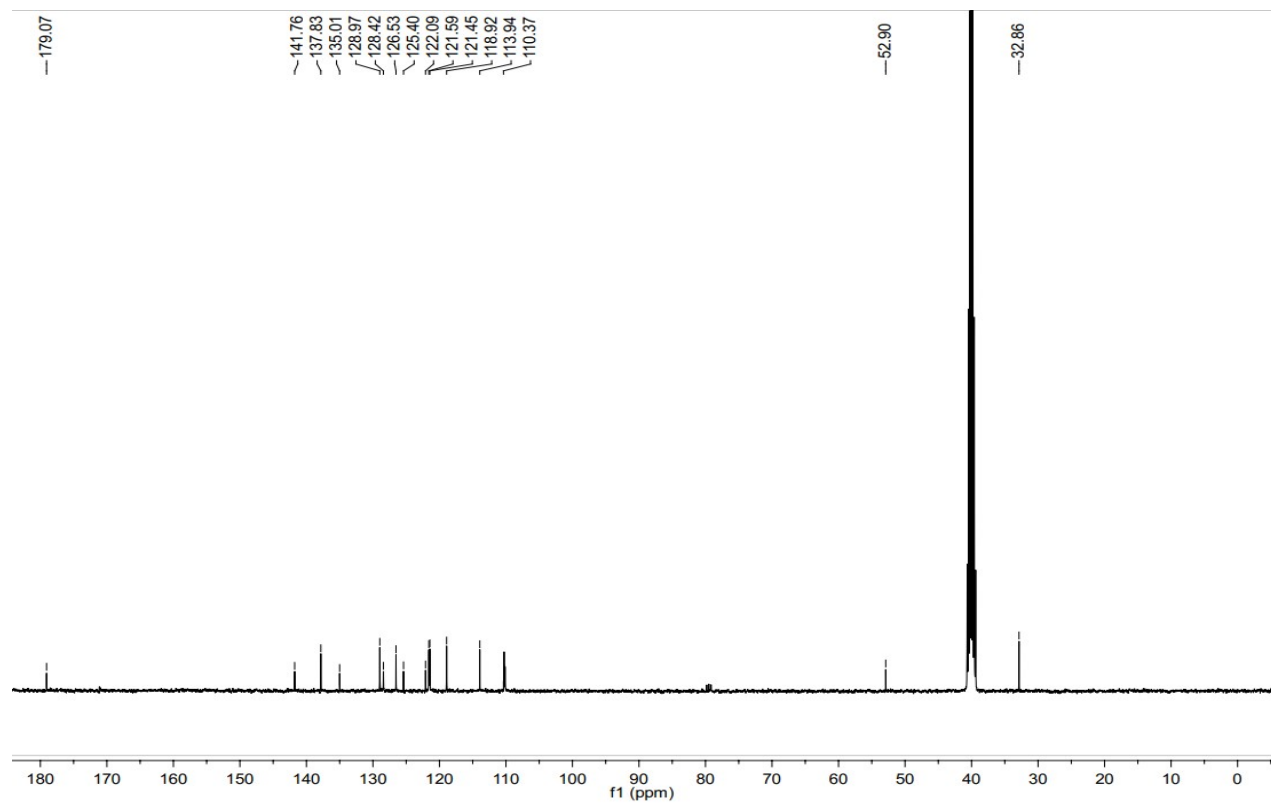
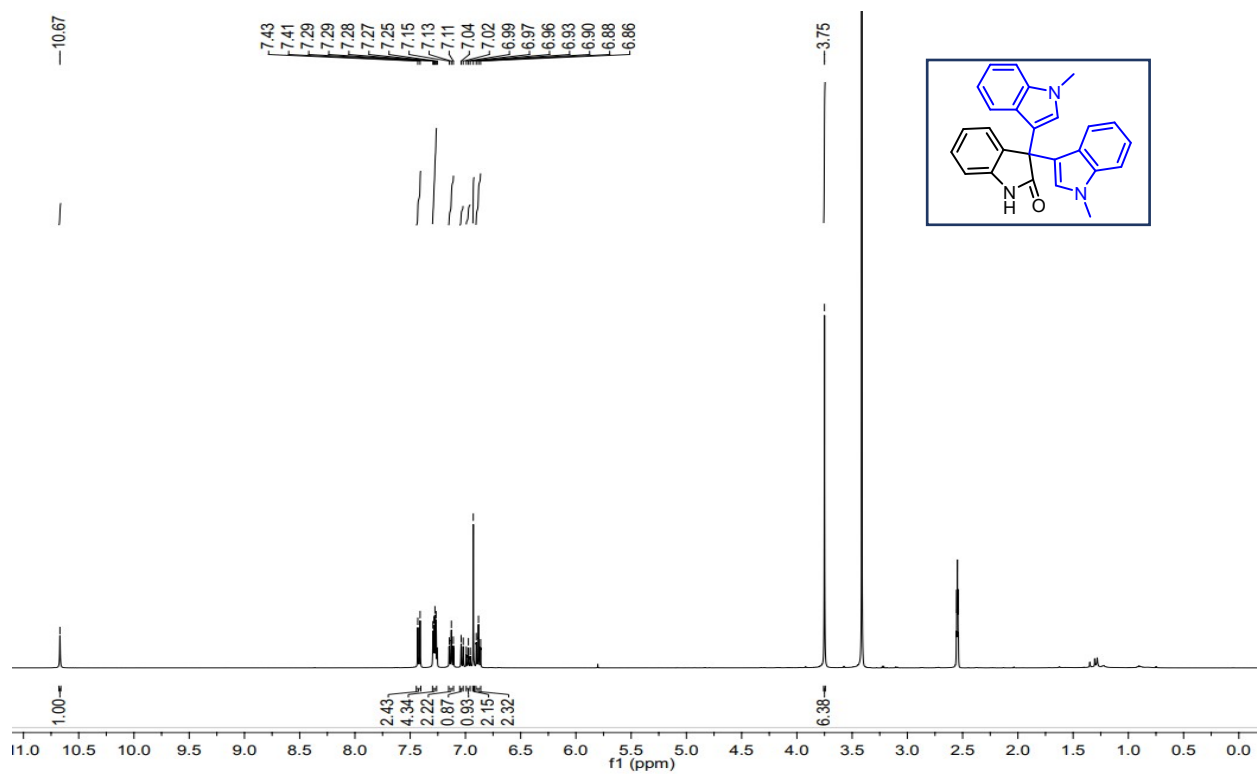
¹H and ¹³C NMR spectra of 3o



¹H and ¹³C NMR spectra of 3p



¹H and ¹³C NMR spectra of 3s



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