

Supporting Information

Copper(II)-Catalysed Direct C3-H Esterification of Indoles Assisted by an *N,N*-Bidentate Auxiliary Moieties

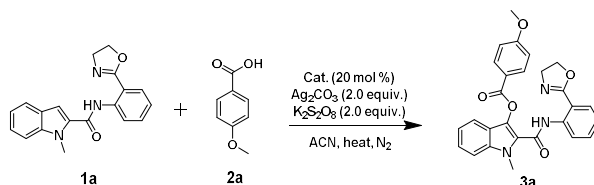
You-Lu Pan,^a Hai-Feng Xu,^a Xu-Yang Hu,^a Gang-Jian Li,^a and Jian-Zhong Chen^{a,*}

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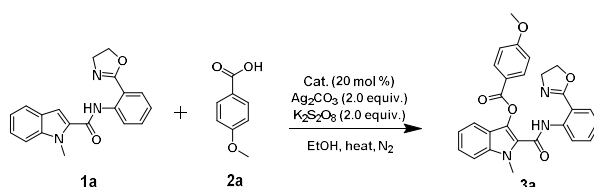
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Scheme S1. The reaction in different solvents



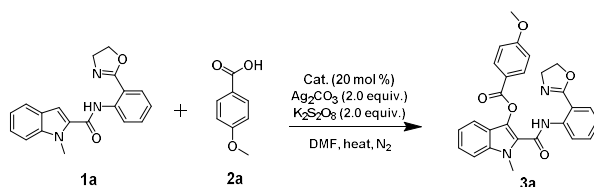
(1)

Firstly, we added **1a** (32.0 mg, 0.1 mmol), 4-methoxybenzoic acid (30.4 mg, 0.2 mmol), CuBr_2 (20% mmol), Ag_2CO_3 (55.2 mg, 0.2 mmol), $\text{K}_2\text{S}_2\text{O}_8$ (54.0 mg, 0.2 mmol), and dry ACN (3 mL) into 10 mL pressure tube at 80 °C for 10 hours under the N_2 . TLC (Pe/EtOAc=5/1) detected the no reaction occurred.



(2)

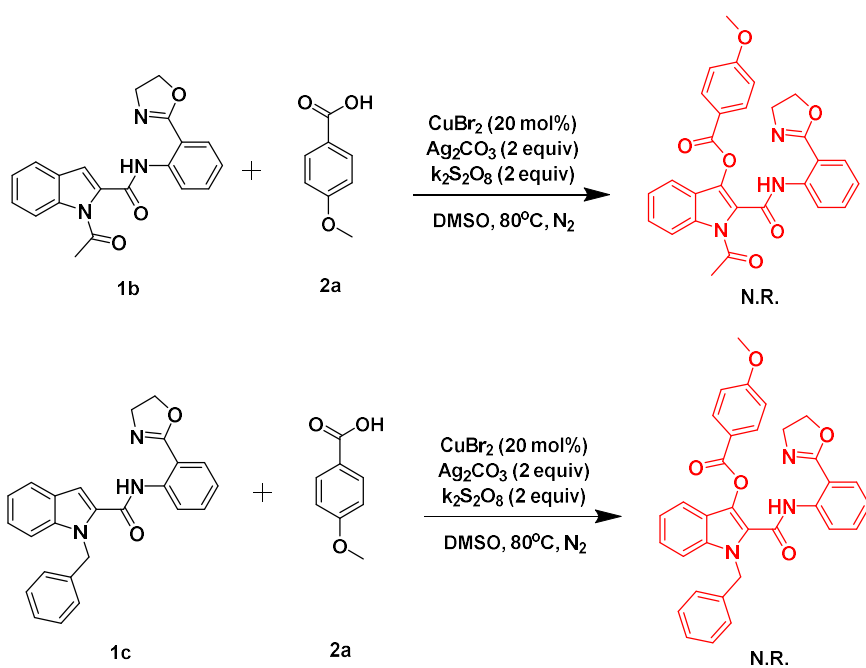
We added **1a** (32.0 mg, 0.1 mmol), 4-methoxybenzoic acid (30.4 mg, 0.2 mmol), CuBr_2 (20% mmol), Ag_2CO_3 (55.2 mg, 0.2 mmol), $\text{K}_2\text{S}_2\text{O}_8$ (54.0 mg, 0.2 mmol), and dry EtOH (3 mL) into 10 mL pressure tube at 80 °C for 10 hours under the N_2 . TLC (Pe/EtOAc=5/1) detected the no reaction occurred.



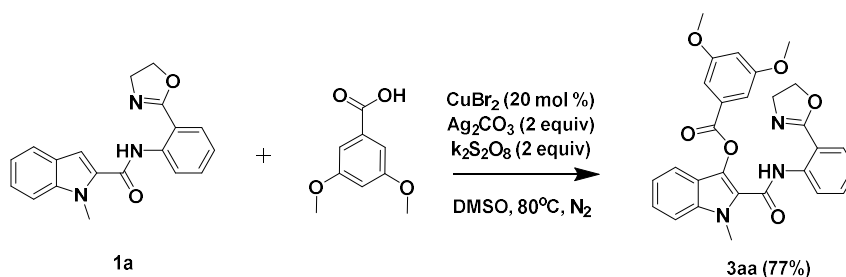
(3)

We added **1a** (32.0 mg, 0.1 mmol), 4-methoxybenzoic acid (30.4 mg, 0.2 mmol), CuBr_2 (20% mmol), Ag_2CO_3 (55.2 mg, 0.2 mmol), $\text{K}_2\text{S}_2\text{O}_8$ (54.0 mg, 0.2 mmol), and dry DMF (3 mL) into 10 mL reaction tube at 80 °C for 10 hours under the N_2 . TLC (Pe/EtOAc=5/1) detected the no reaction occurred.

Scheme S2. The reaction between **1b** or **1c** and 4-methoxybenzoic acid

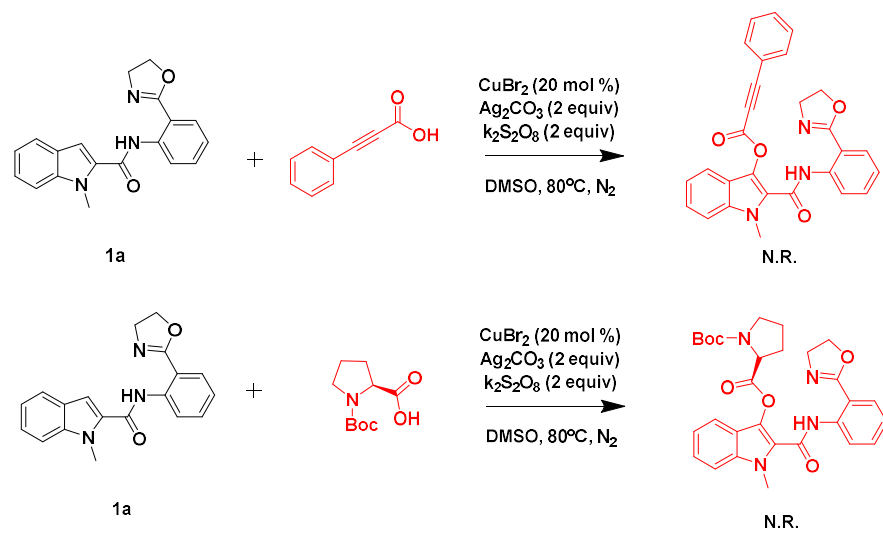


Scheme S3. A Large Scale of Substrate

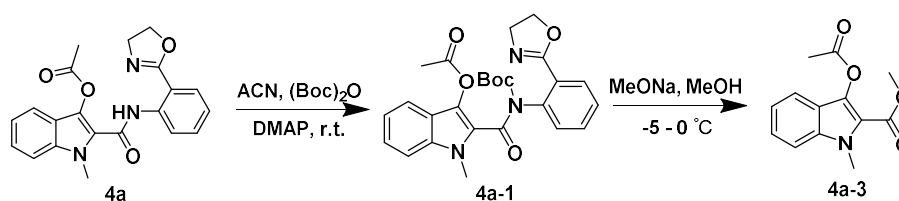


To a 25 mL reaction tube, we added amide **1a** (319.4 mg, 1 mmol), 3,5-dimethoxybenzoic acid (304.3 mg, 2 mmol), Ag_2CO_3 (551.5 mg, 2 mmol), $\text{K}_2\text{S}_2\text{O}_8$ (540.64 mg, 2 mmol), and DMSO (8 mL) under N_2 . The mixture was stirred at 80 °C for 10 hours. TLC detected the reaction completed. The reaction mixture was then cooled to room temperature and quenched by water. The aqueous phase was extracted with EtOAc (3 * 20 mL), and the combined organic layer was washed with saturated NaHCO_3 solution (2 * 10 mL). The organic phase was dried over Na_2SO_4 . After evaporation, the residue was purified by flash chromatography to afford the product as a colorless oil (380 mg, 77%).

Scheme S4. No reaction of **1a** with 3-phenylpropionic acid or Boc-*L*-proline



Scheme S5. The removal of OXA



The representative procedure for reaction a was followed: using **4a** (37.7 mg, 0.1 mmol, 1.0 equiv.), DMAP (4.0 mg, 30 mol %) and $(\text{Boc})_2\text{O}$ (33 mg, 1.5 equiv.) in ACN (3 mL). The resultant reaction mixture was stirred at room temperature about 12 h. The mixture was diluted with ethyl acetate (20 mL) and washed with 1N HCl solution. The combined organic layer dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The resulting residue was conducted for next step without further purification.

The resulting residue was dissolved in dry MeOH, and the MeONa (8 mg, 1.5 equiv.) under the $-10\text{ }^\circ\text{C}$. Then, the ice bath was removed, and the reaction was stirred at $-5\text{ }^\circ\text{C} - 0\text{ }^\circ\text{C}$ about 6 h. TLC detected the reaction completed and the ice water (5 mL) was added into the reaction. The mixture was diluted with ethyl acetate (15 mL) and washed with saturated NaCl solution. The combined organic layer was dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 8/1) to get the white solid **4a-3** (9.4 mg, 38% yield). The structure of **4a-3** was confirmed by $^1\text{H-NMR}$ (Figure S1) which is accordant with reported data¹.

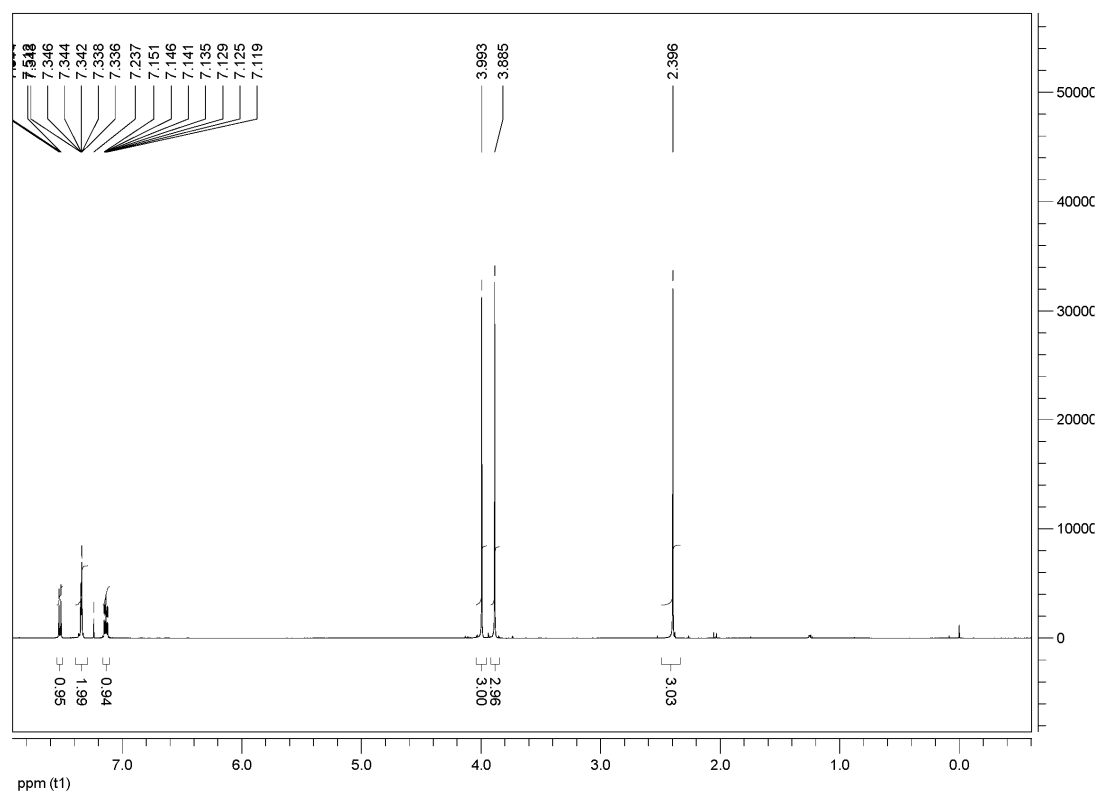
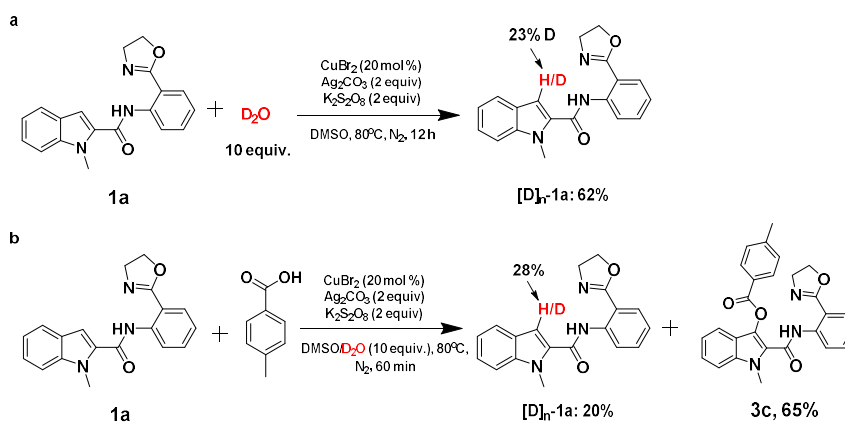


Figure S1. the $^1\text{H-NMR}$ of **4a-3**

Scheme S6. H/D scrambling experiment



The representative procedure for reaction a was followed: using **1a** (31.9 mg, 0.1 mmol, 1.0 equiv.), D₂O (10 equiv.), CuBr₂ (4.5 mg, 20 mol %), Ag₂CO₃ (55 mg, 0.2 mmol), K₂S₂O₈ (54 mg, 0.2 mmol) and in DMSO (1 mL). The resultant reaction mixture was stirred under N₂ atmosphere at 80 °C in a preheated oil bath for 60 min. The mixture was then cooled to room temperature, diluted with ethyl acetate (20 mL) and washed with saturated NaHCO₃ solution. The combined organic layer was dried over Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 10/1) to give [D]_n-**1a** (19.8 mg, 62%). The ¹H-NMR analysis of compound **1a** show 23% incorporation of deuterium at the C3 position (Figure S2).

The representative procedure for reaction a was followed: using **1a** (31.9 mg, 0.1 mmol, 1.0 equiv.), 4-methylbenzoic acid (27 mg, 0.2 mmol), D₂O (10 equiv.), CuBr₂ (4.5 mg, 20 mol %), Ag₂CO₃ (55 mg, 0.2 mmol), K₂S₂O₈ (54 mg, 0.2 mmol) and in DMSO (1 mL). The resultant reaction mixture was stirred under N₂ atmosphere at 80 °C in a preheated oil bath for 12 h. The mixture was then cooled to room temperature, diluted with ethyl acetate (20 mL) and washed with saturated NaHCO₃ solution. The combined organic layer was dried over Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (petroleum

ether/ethyl acetate = 12/1) to give [D]_n-**1a** (7 mg, 20%) and product **3c** (29.4 mg, 62%). The ¹H-NMR analysis of compound **1a** show 28% incorporation of deuterium at the C3 position (Figure S3).

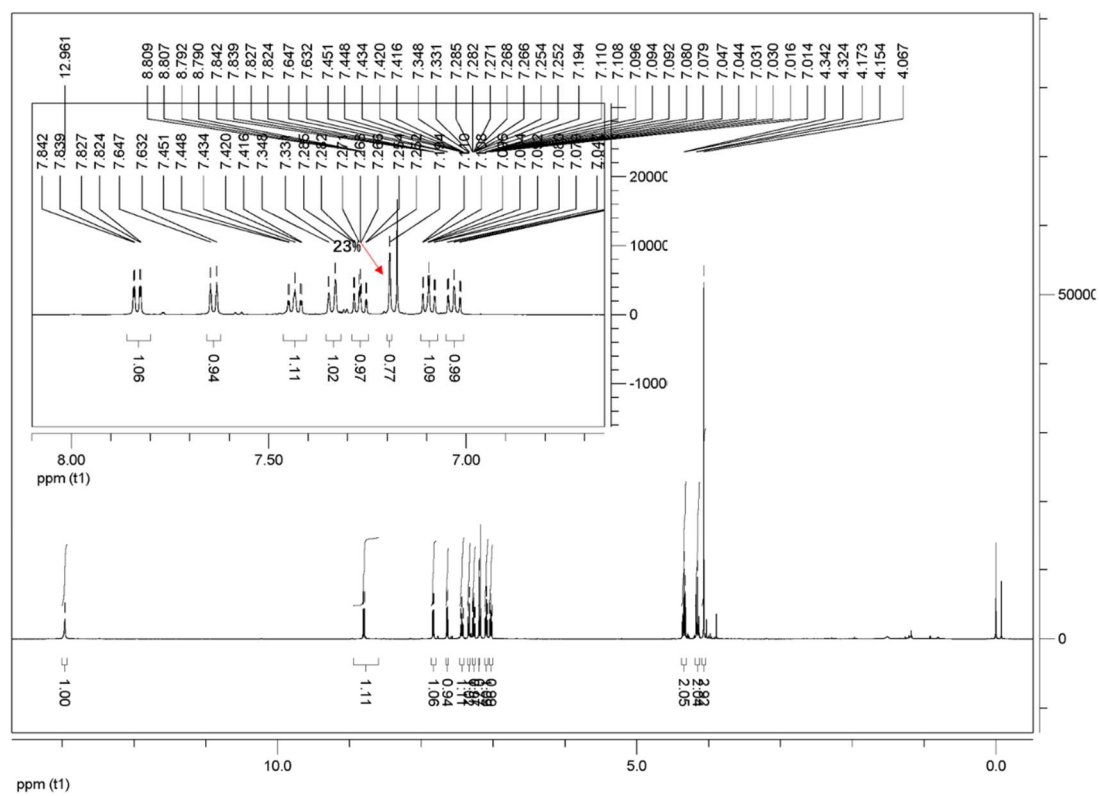


Figure S2. The $^1\text{H-NMR}$ of recovered **1a** after H/D scrambling experiment

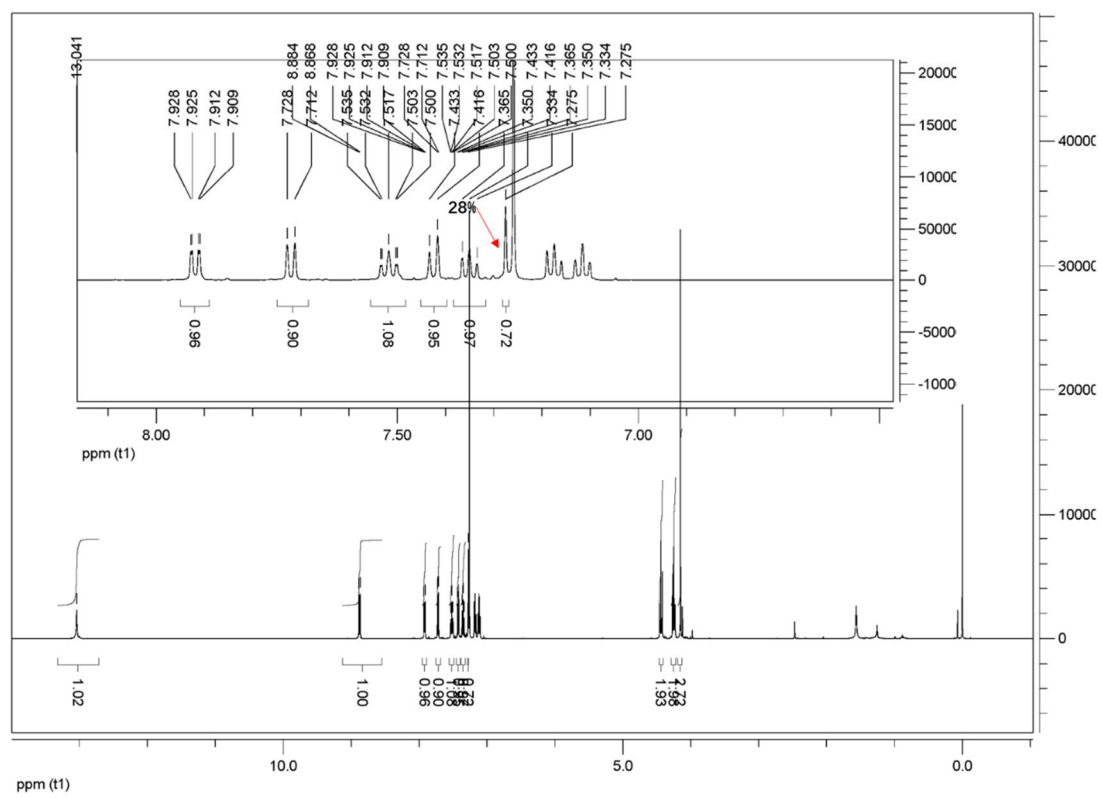
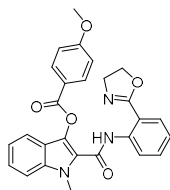


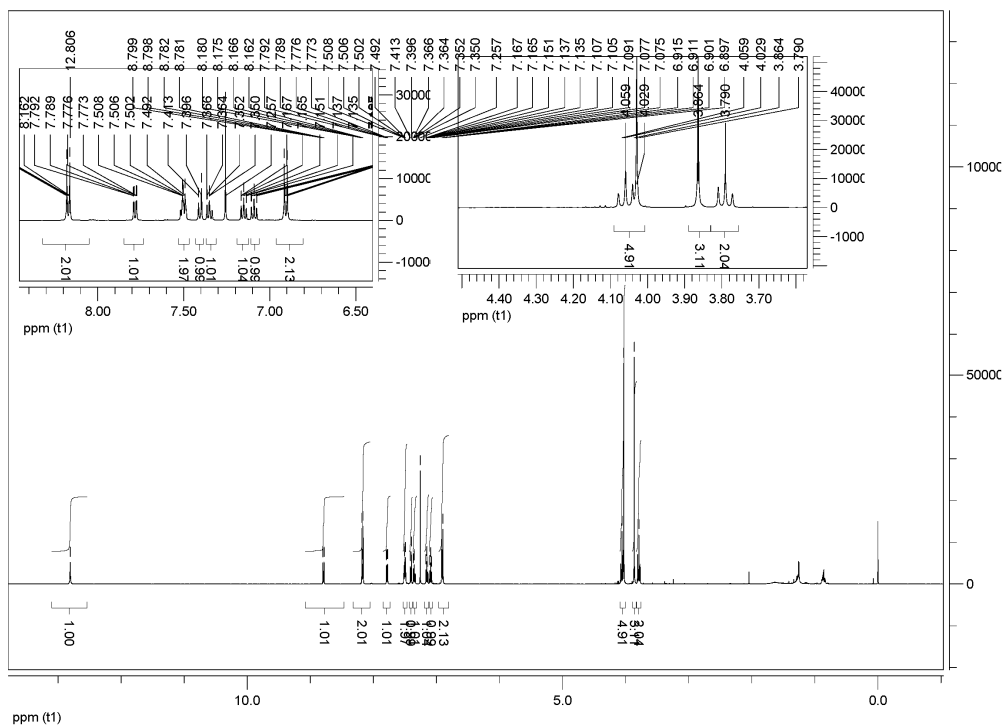
Figure S3. The $^1\text{H-NMR}$ of recovered **1a** after H/D scrambling experiment

Copies of ¹H-NMR and ¹³C-NMR Spectra

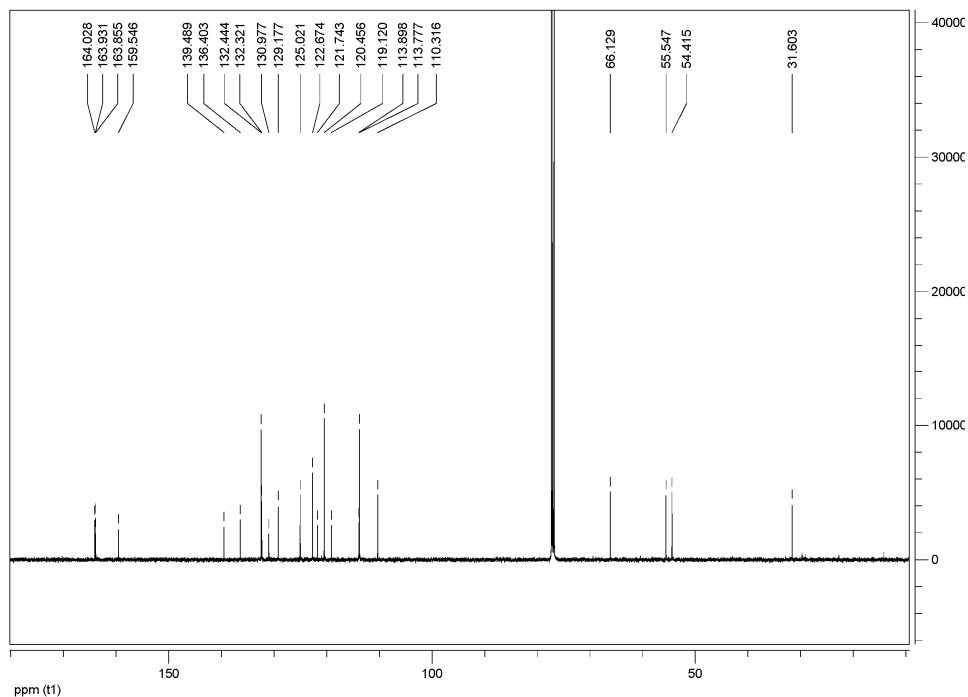


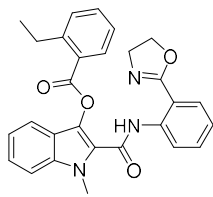
3a

¹H-NMR



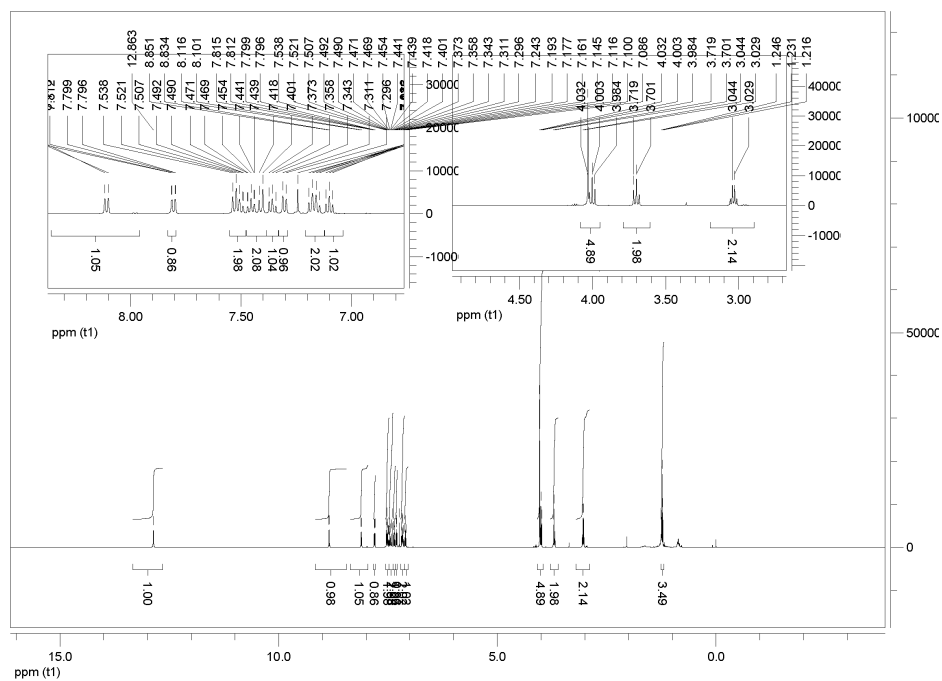
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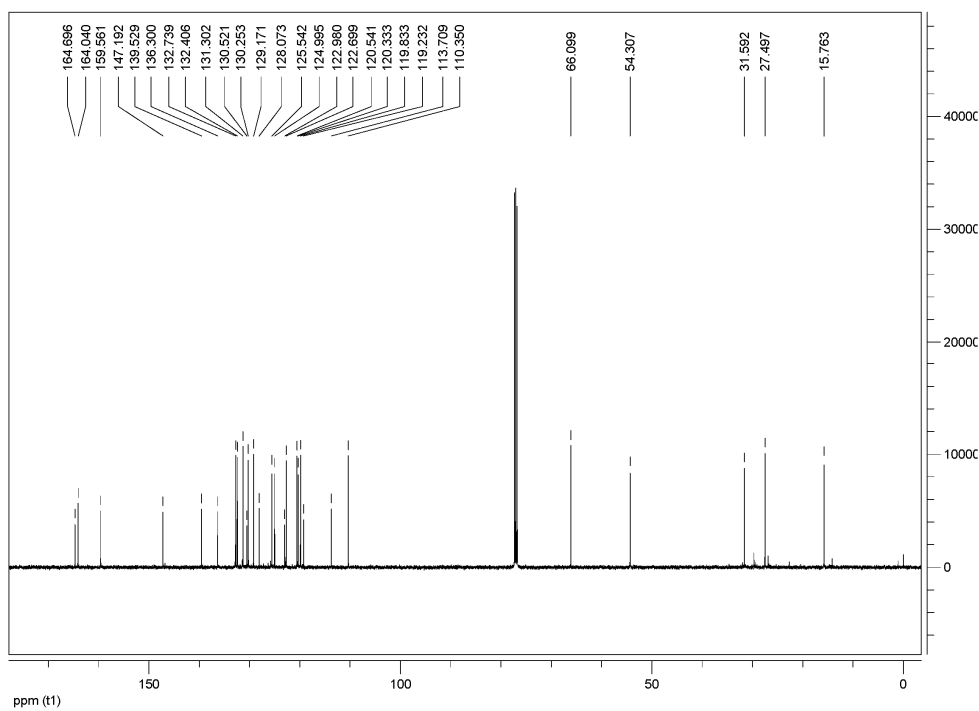


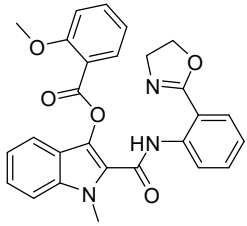
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¹H-NMR



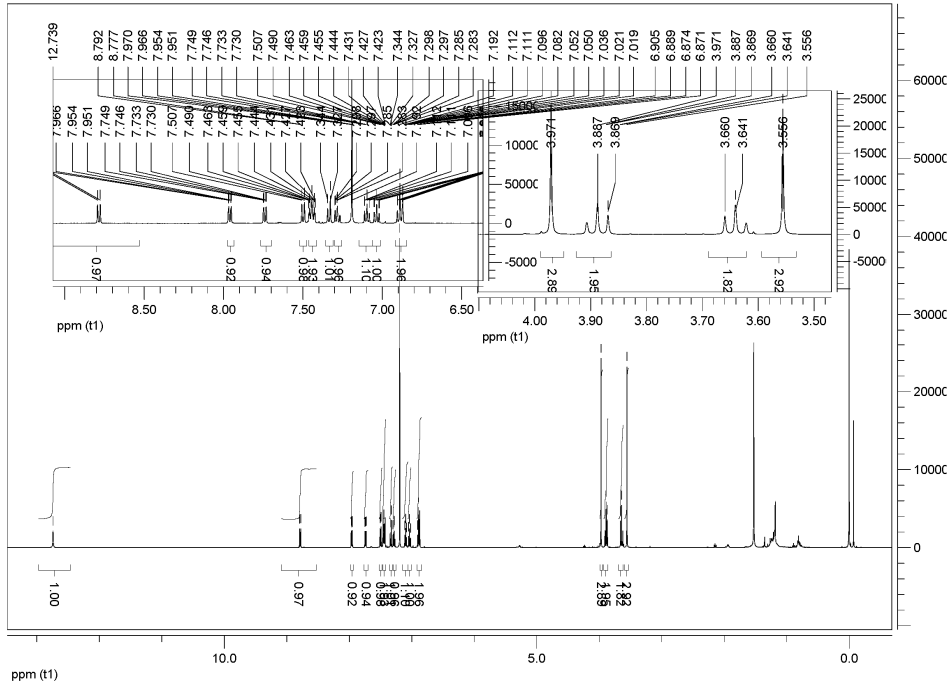
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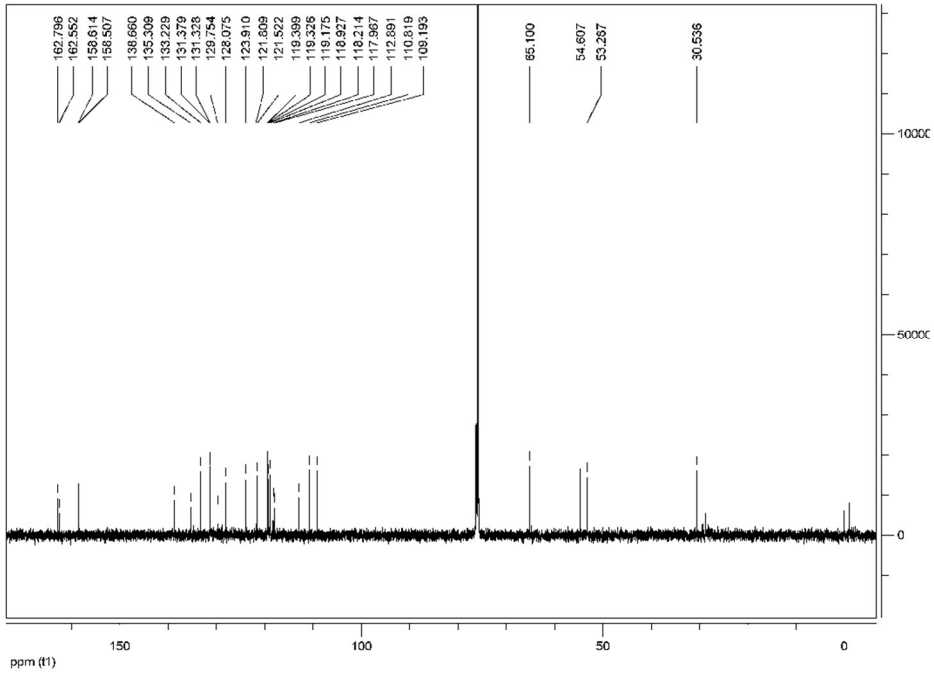


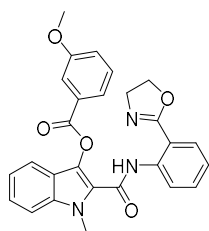
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¹H-NMR



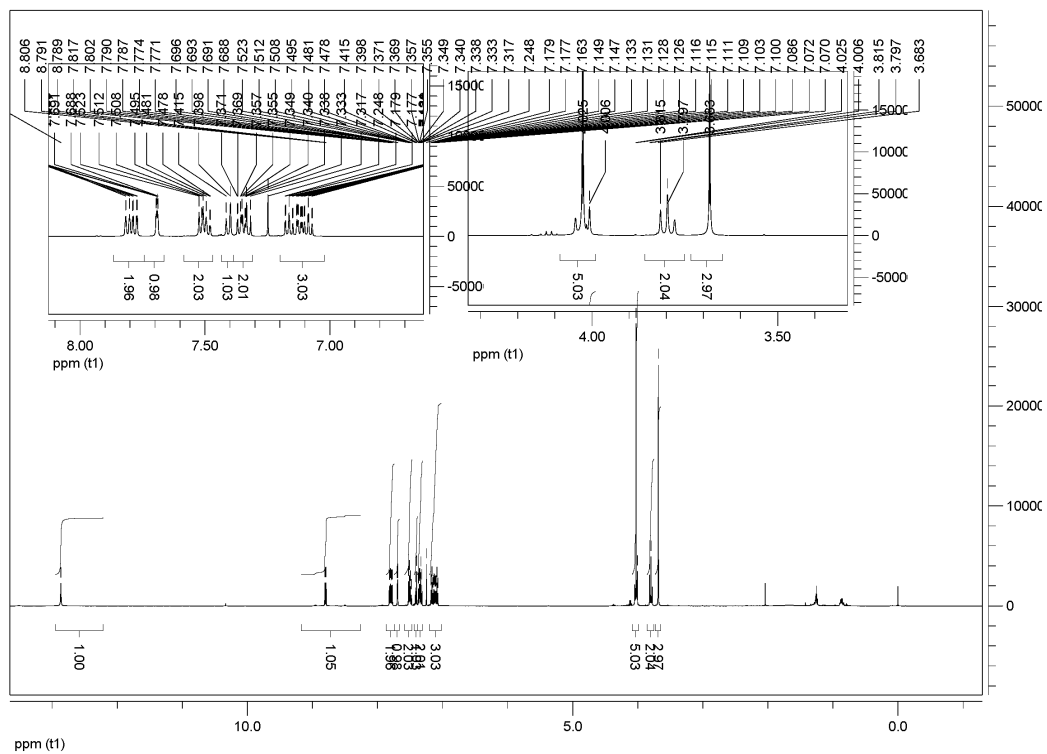
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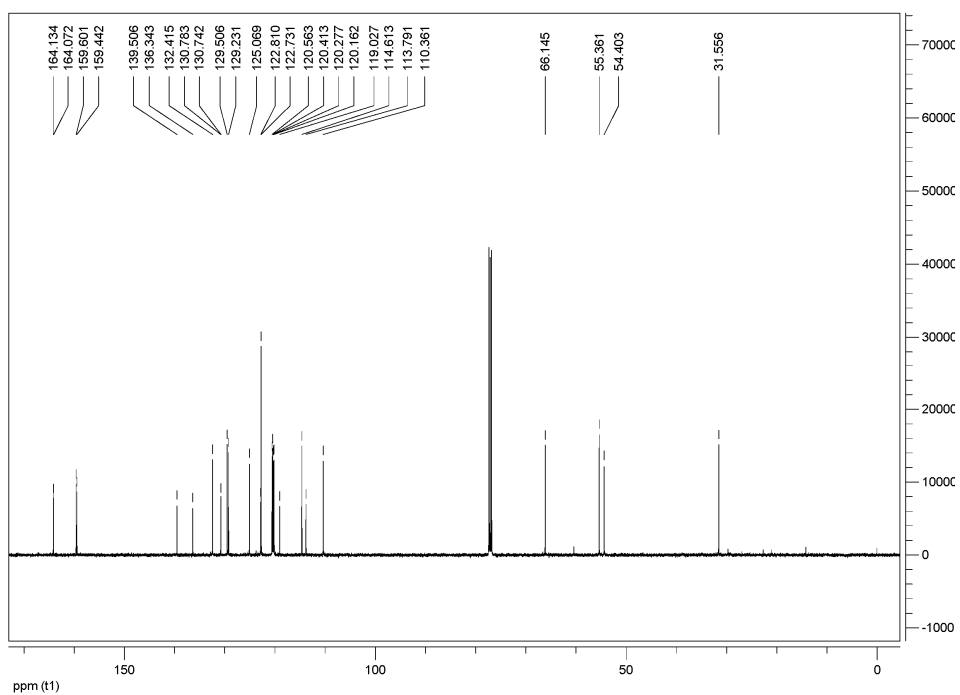


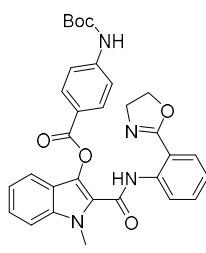
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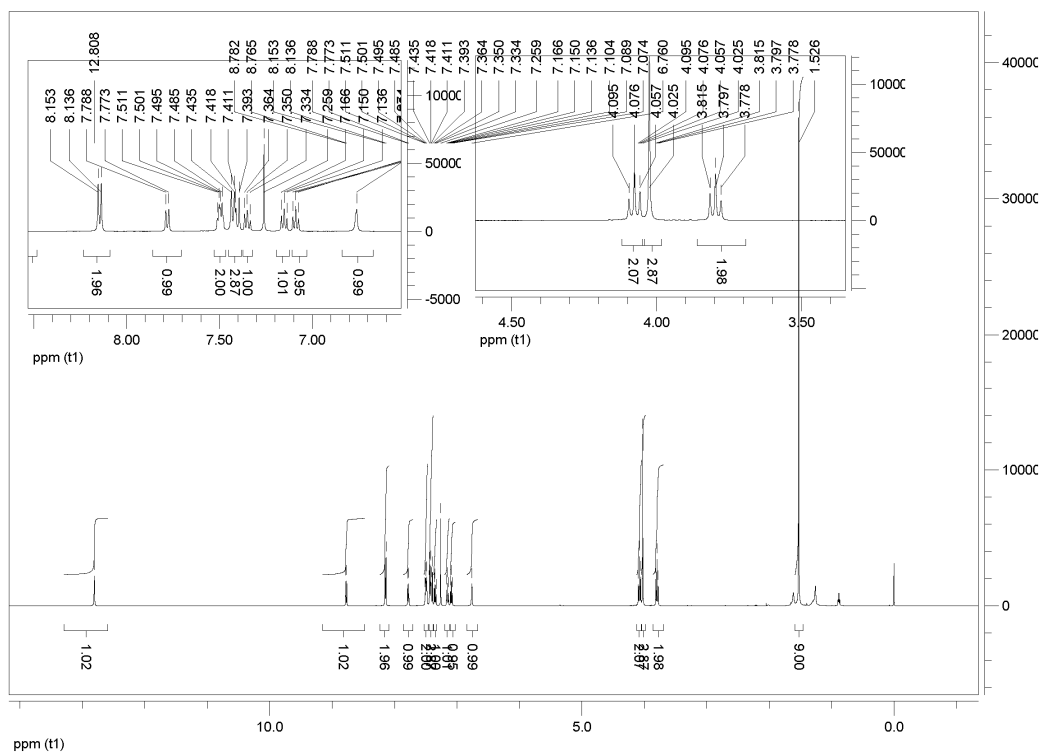


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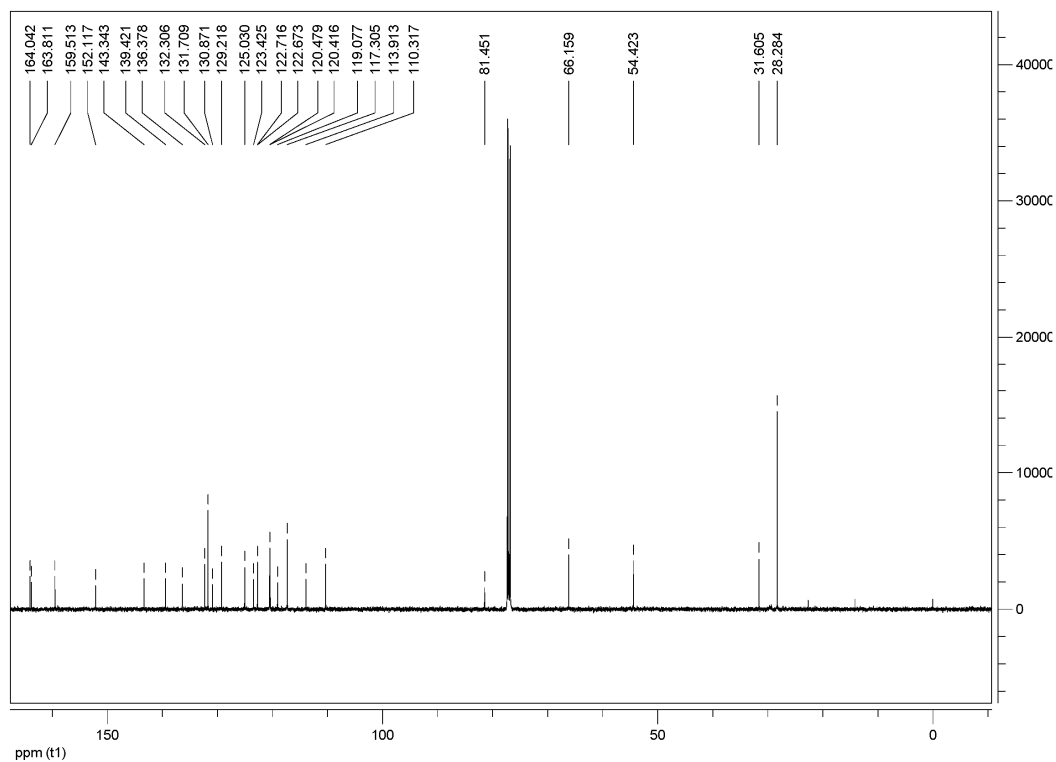


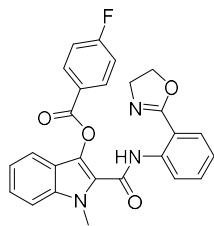


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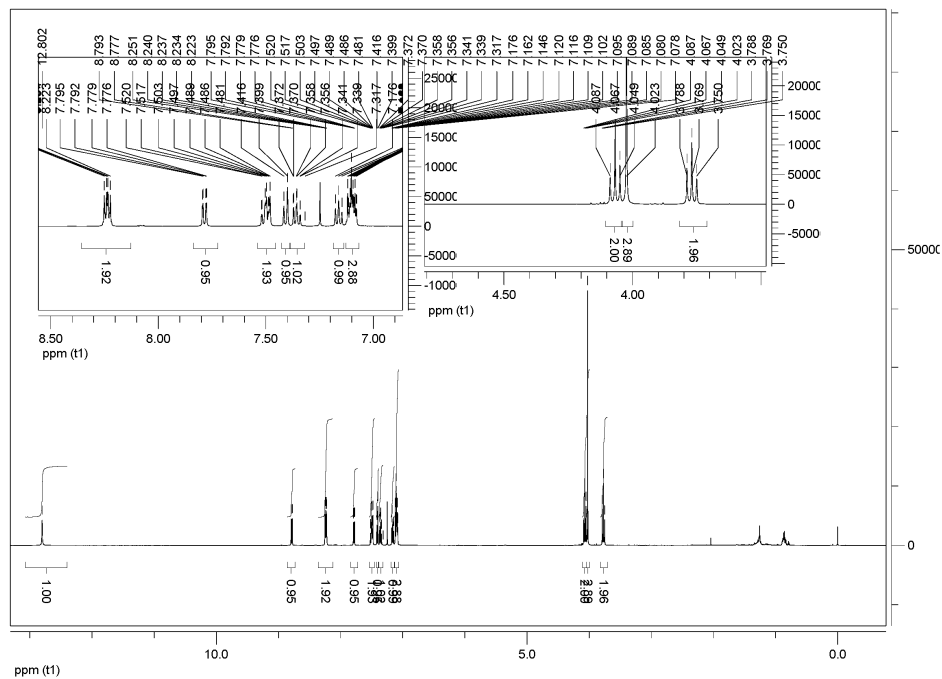
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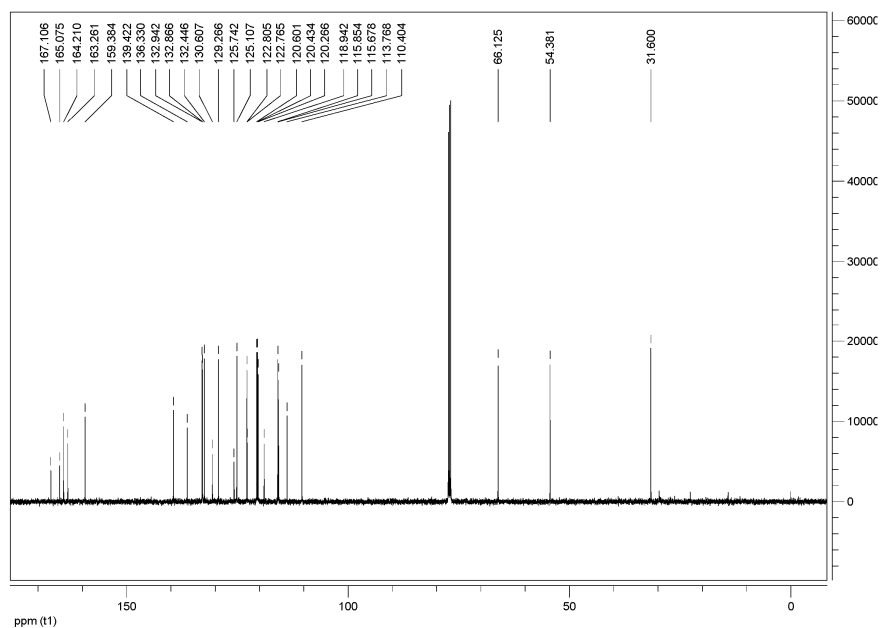


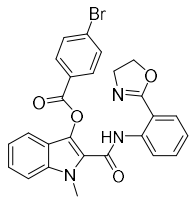
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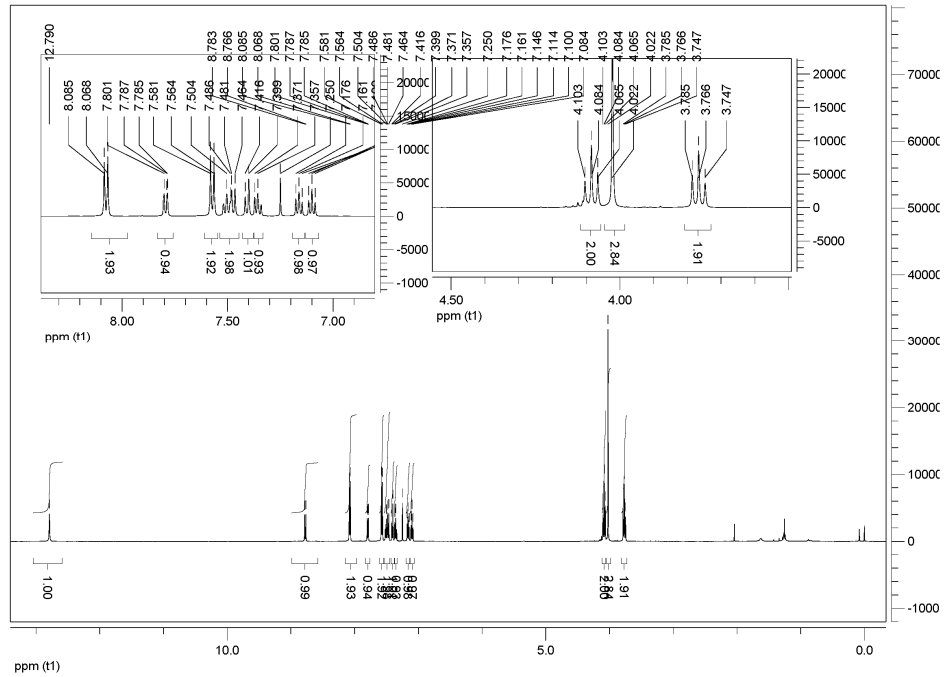
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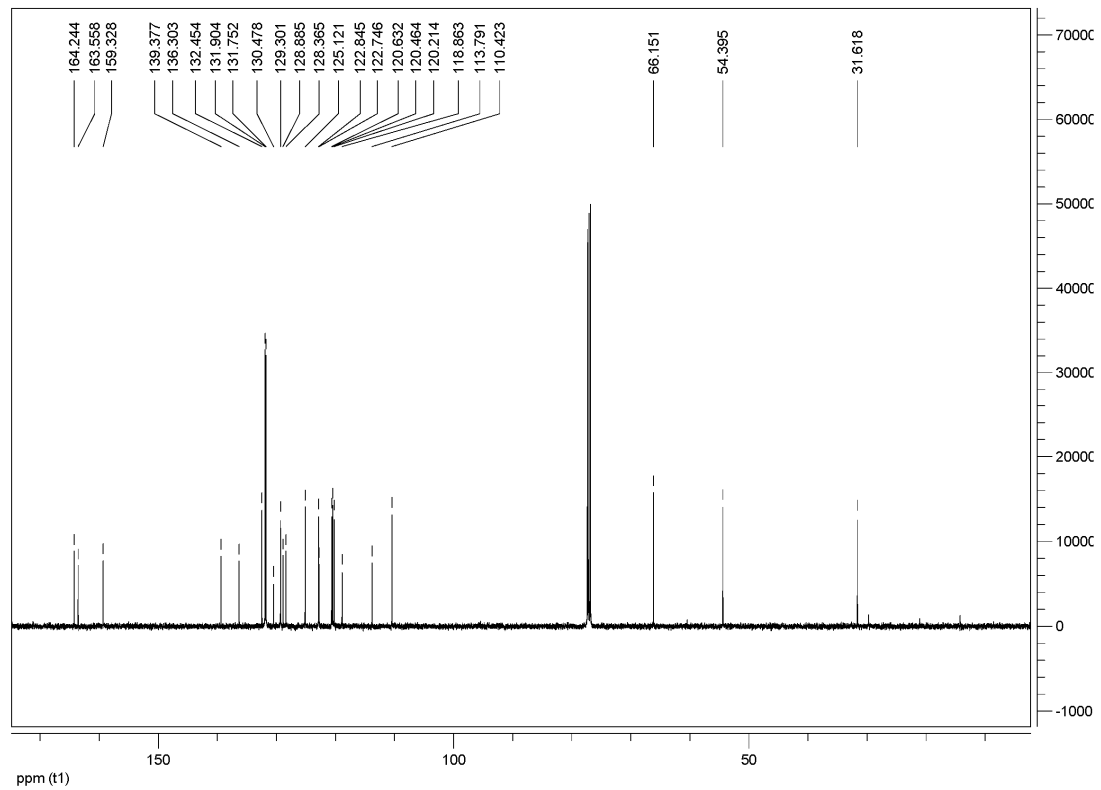


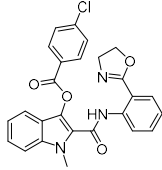
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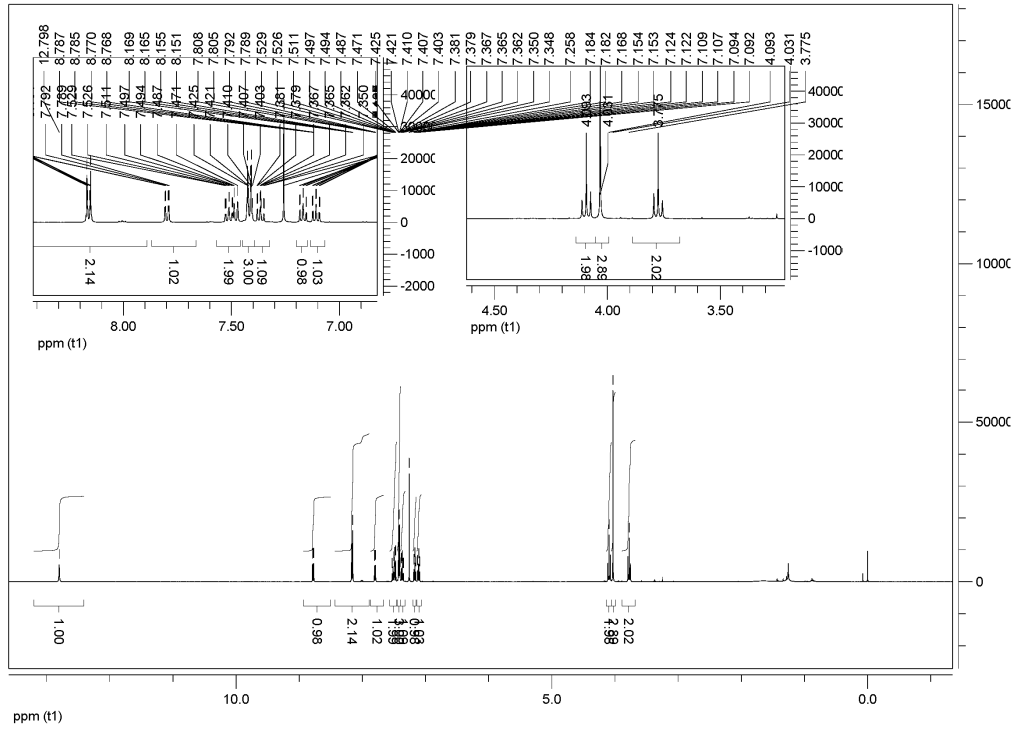
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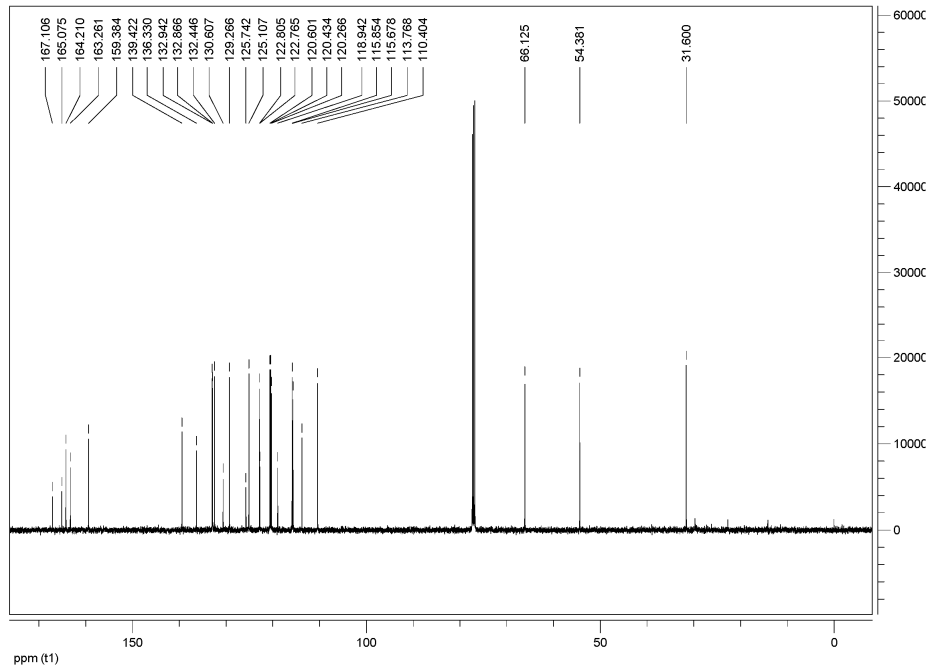


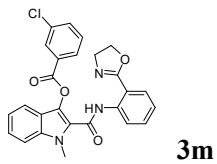
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¹H-NMR

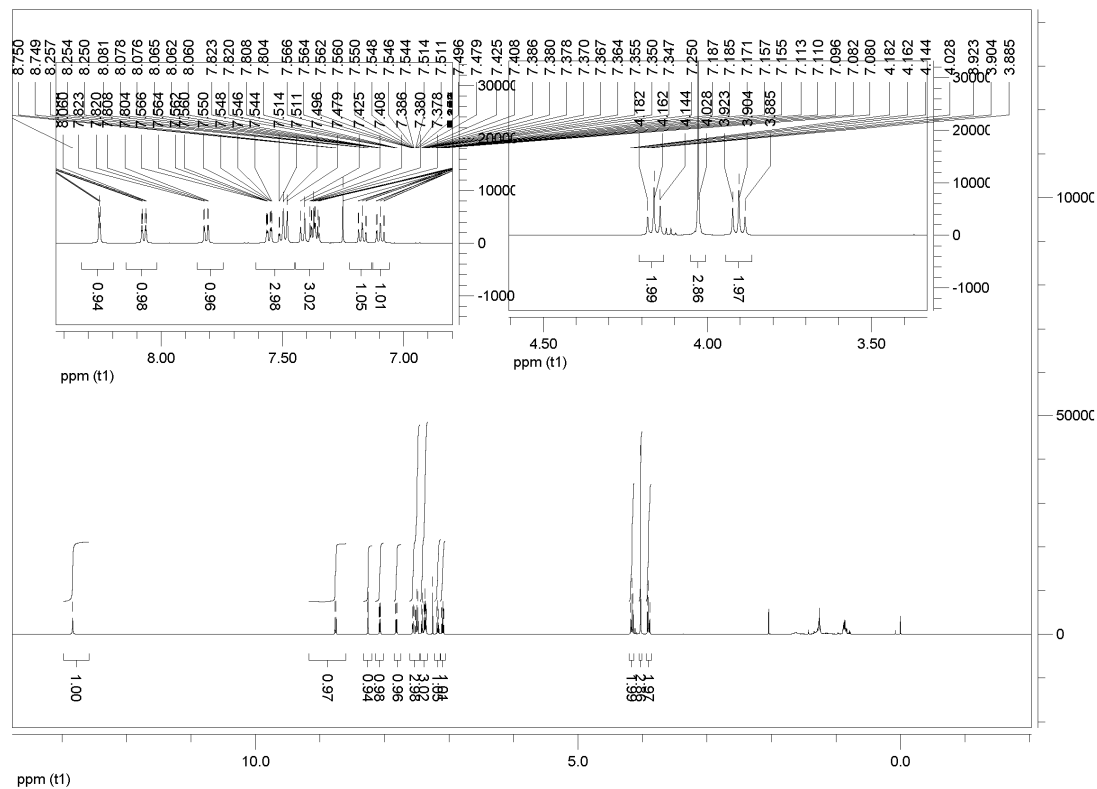


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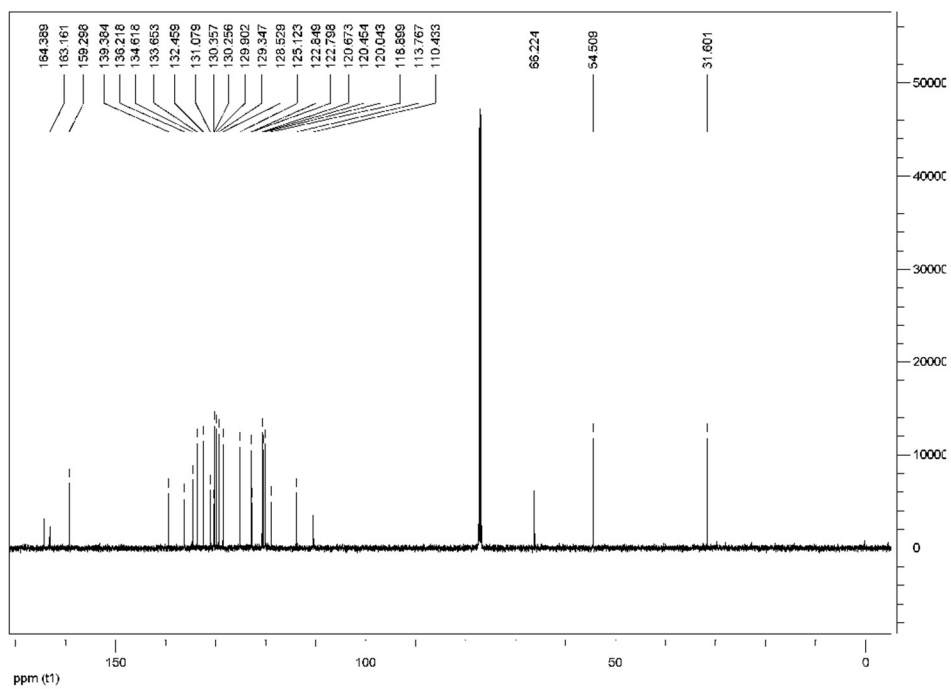


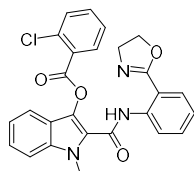


$^1\text{H-NMR}$



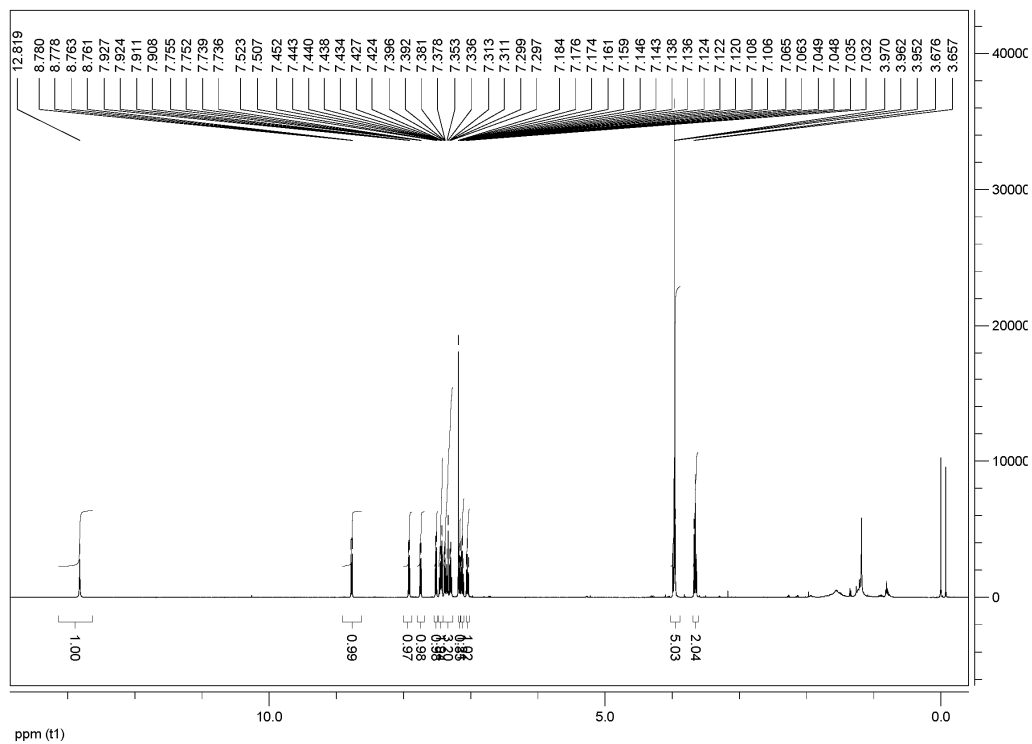
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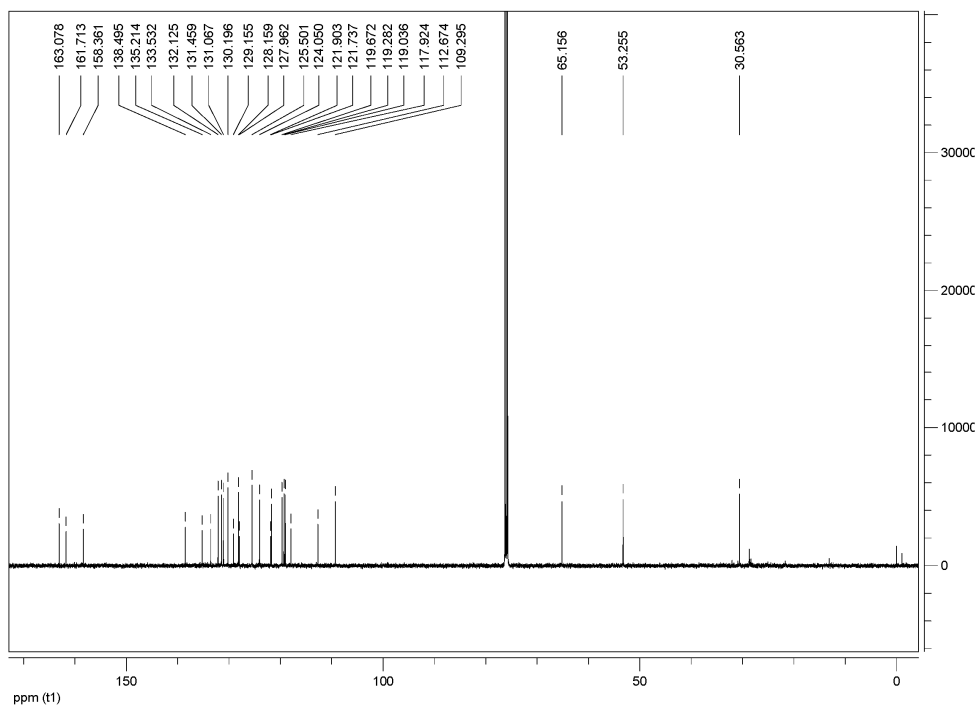


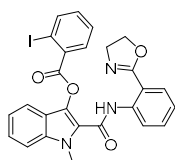
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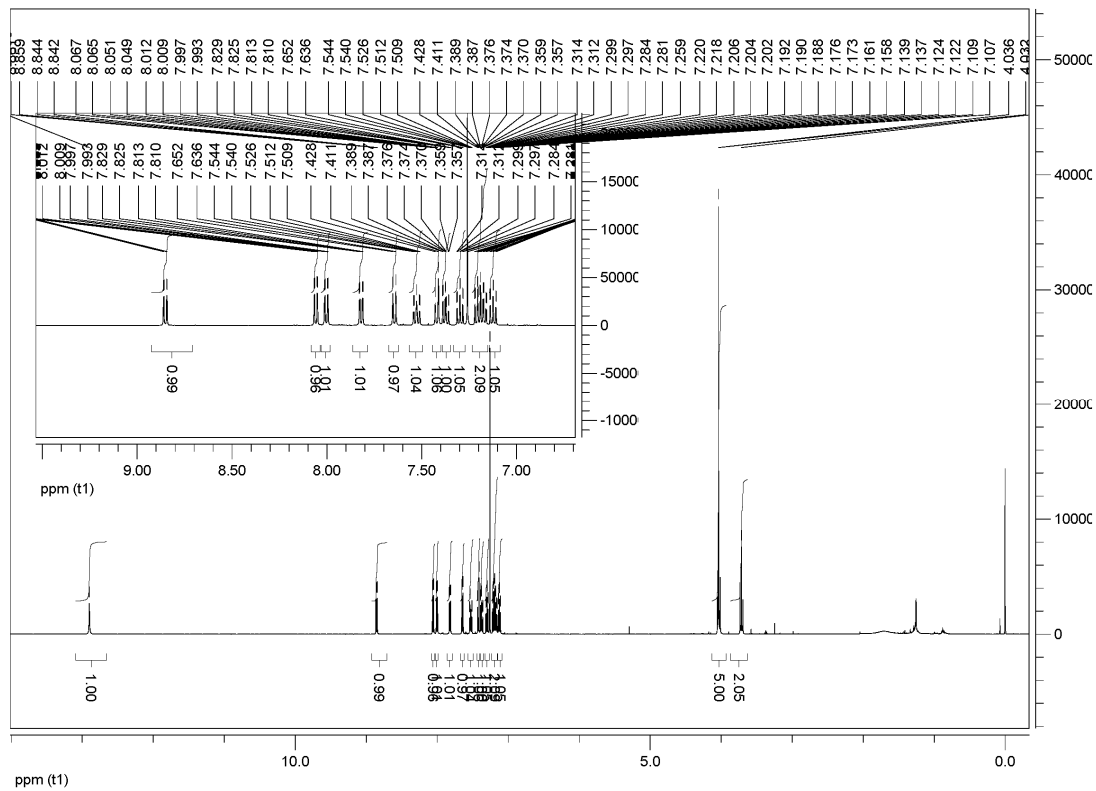
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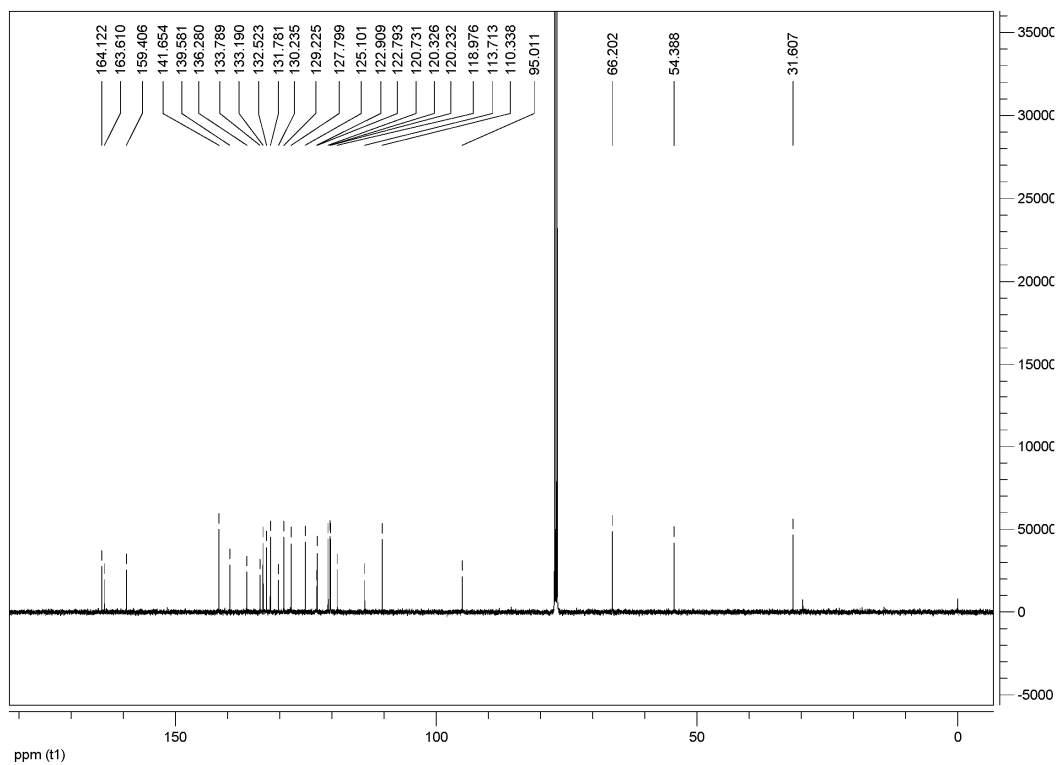


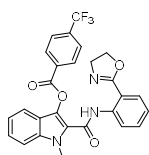
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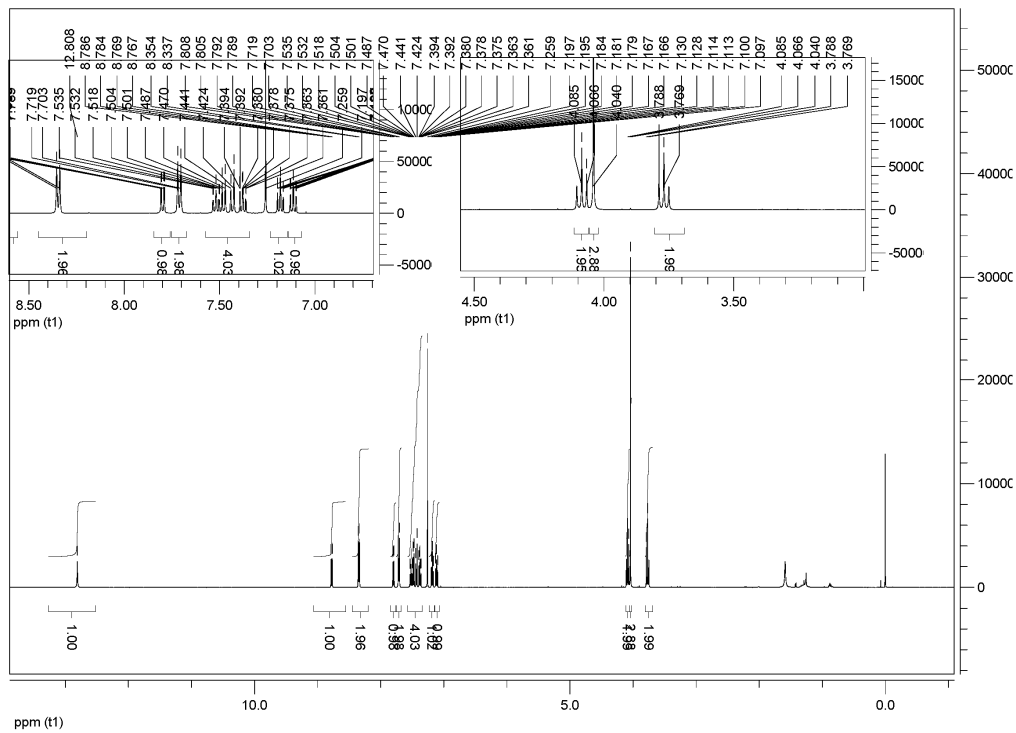
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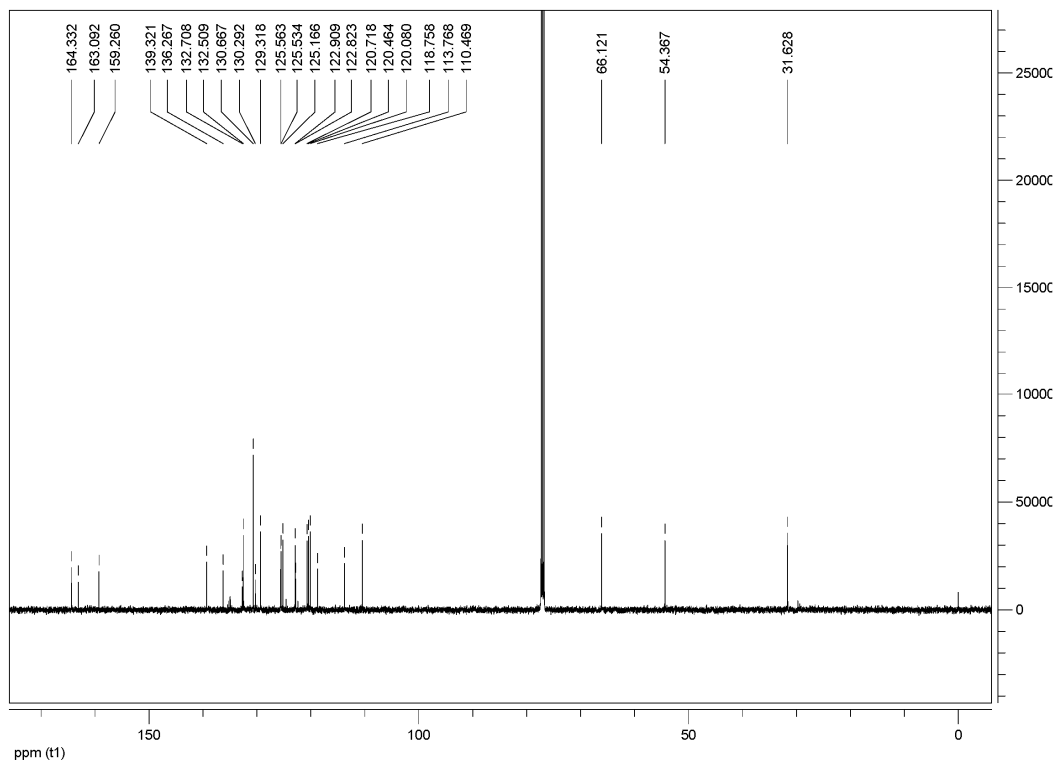


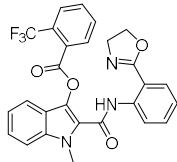
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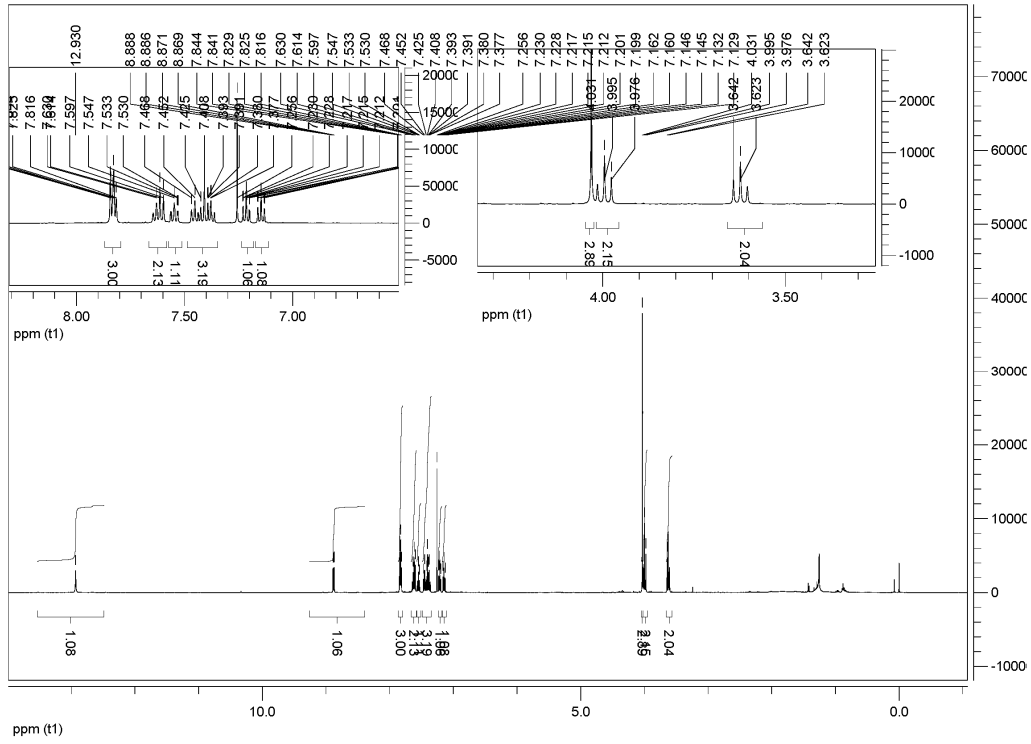
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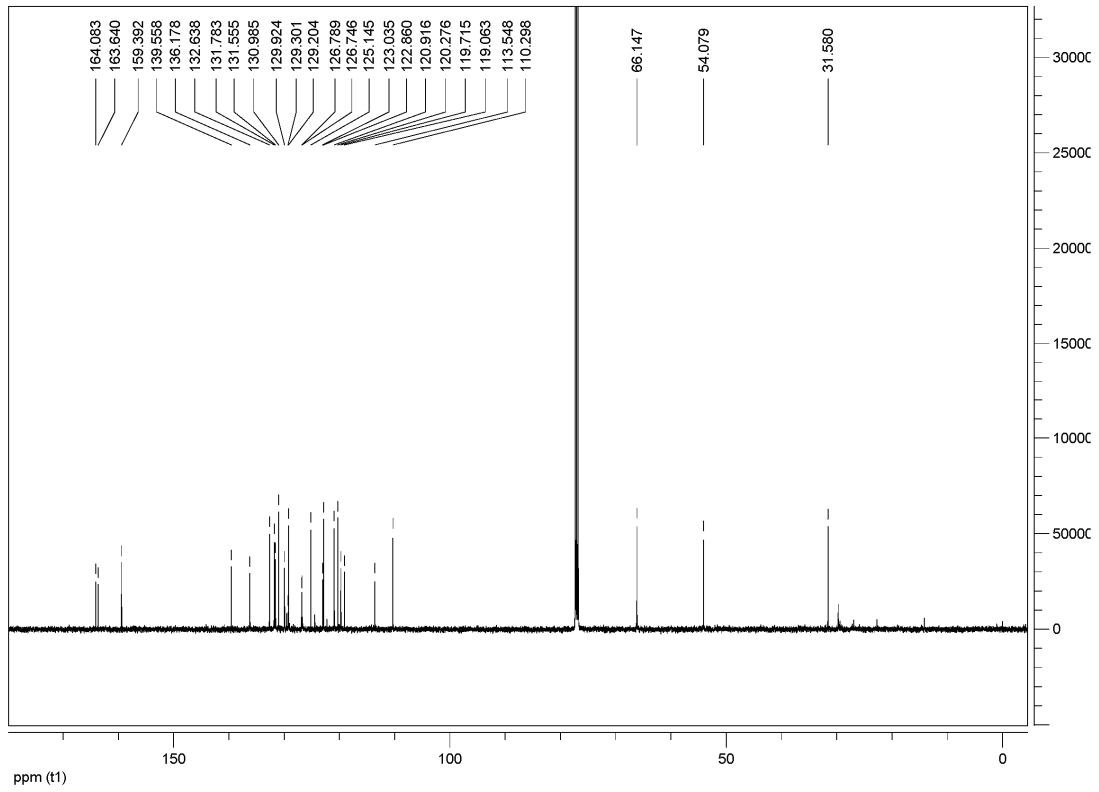


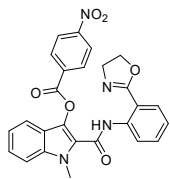
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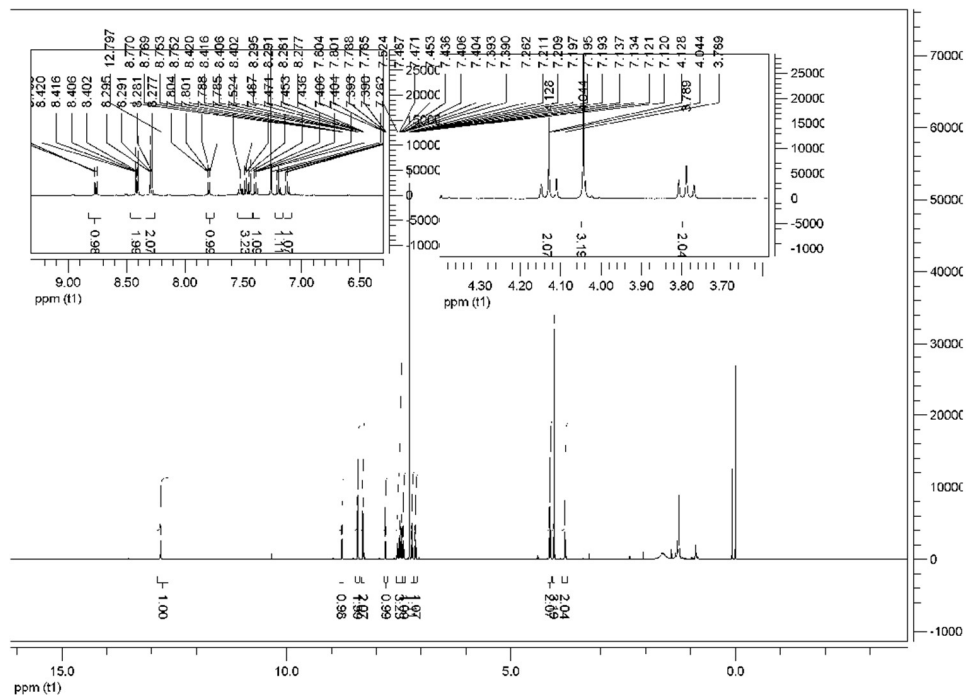
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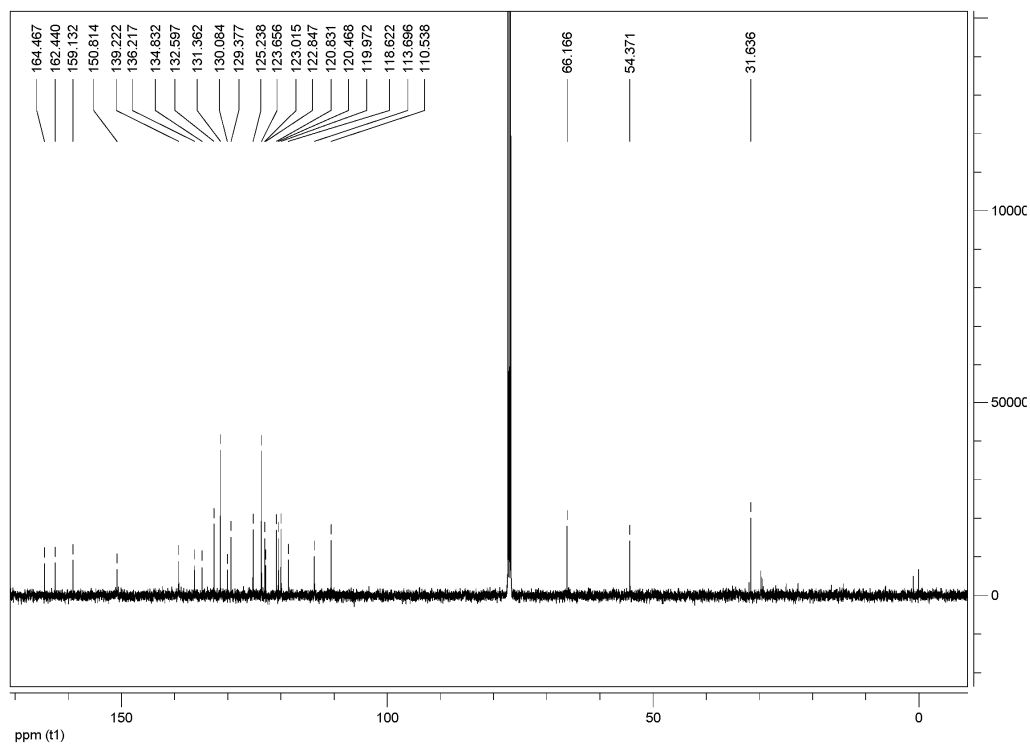


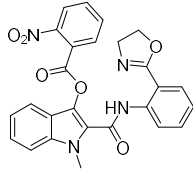
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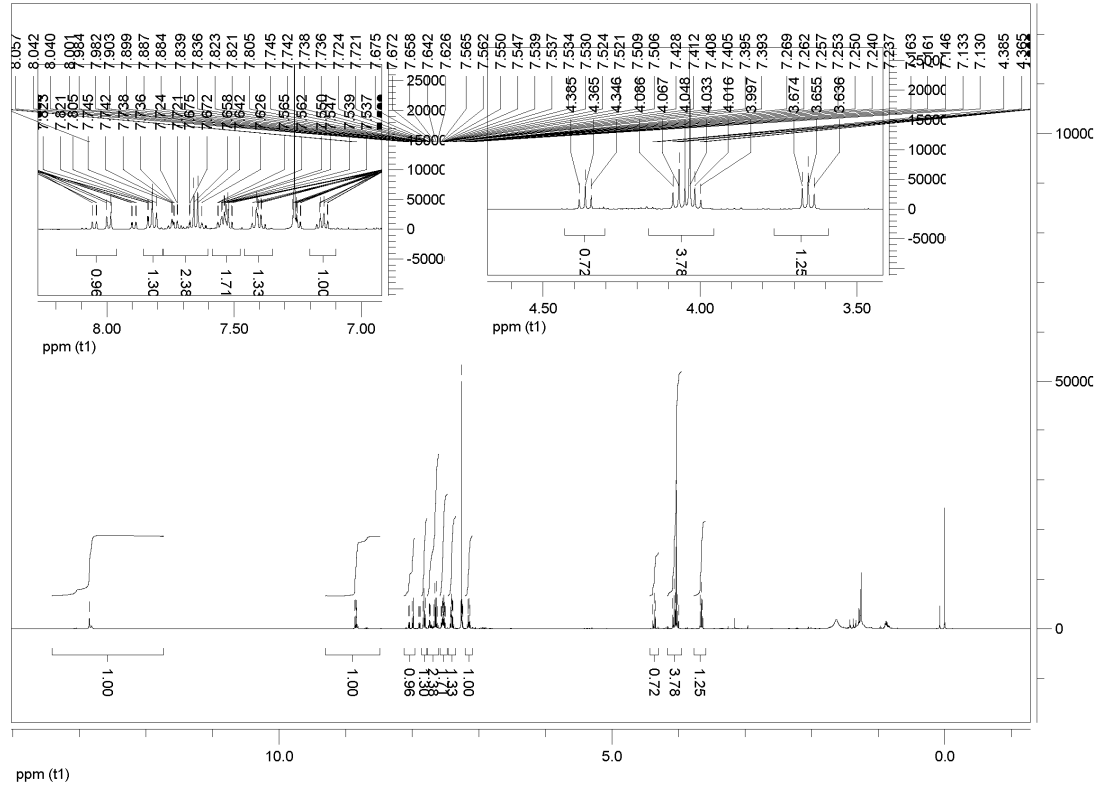
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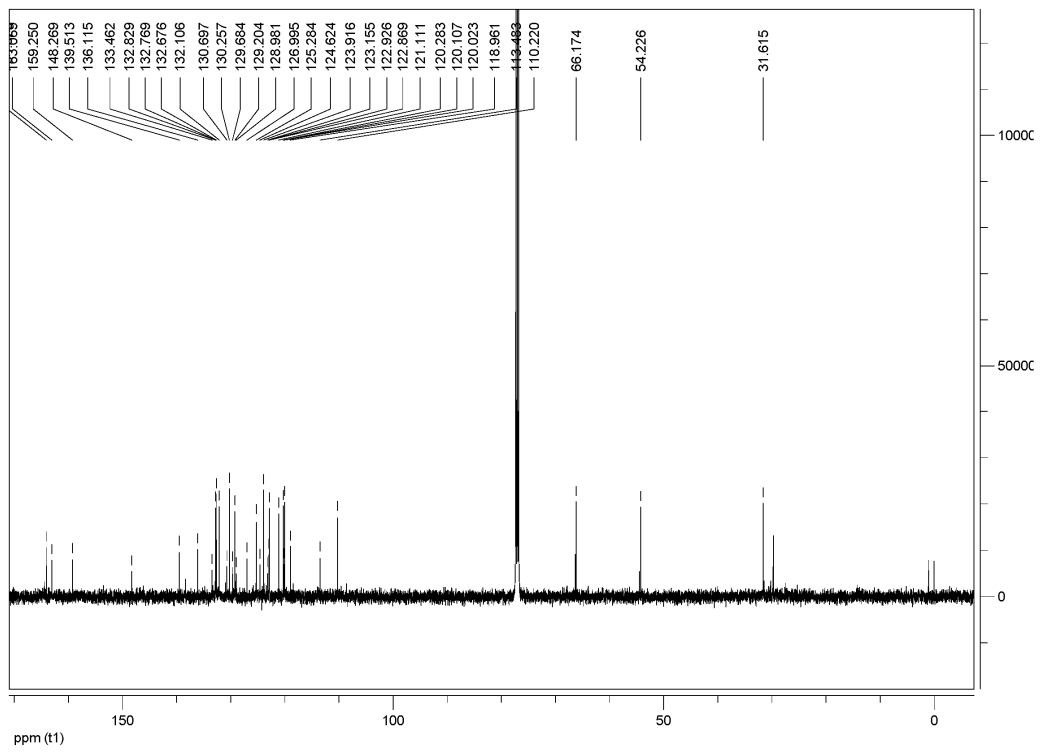


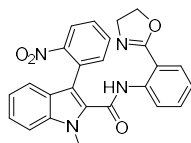
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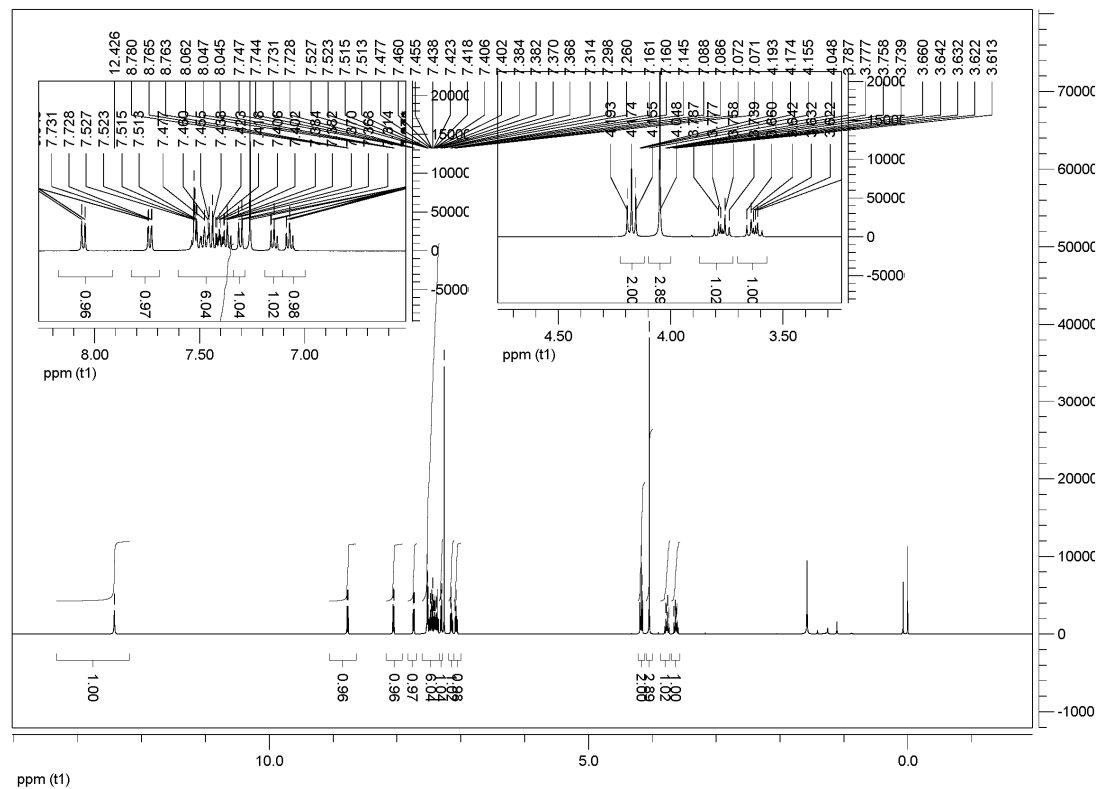
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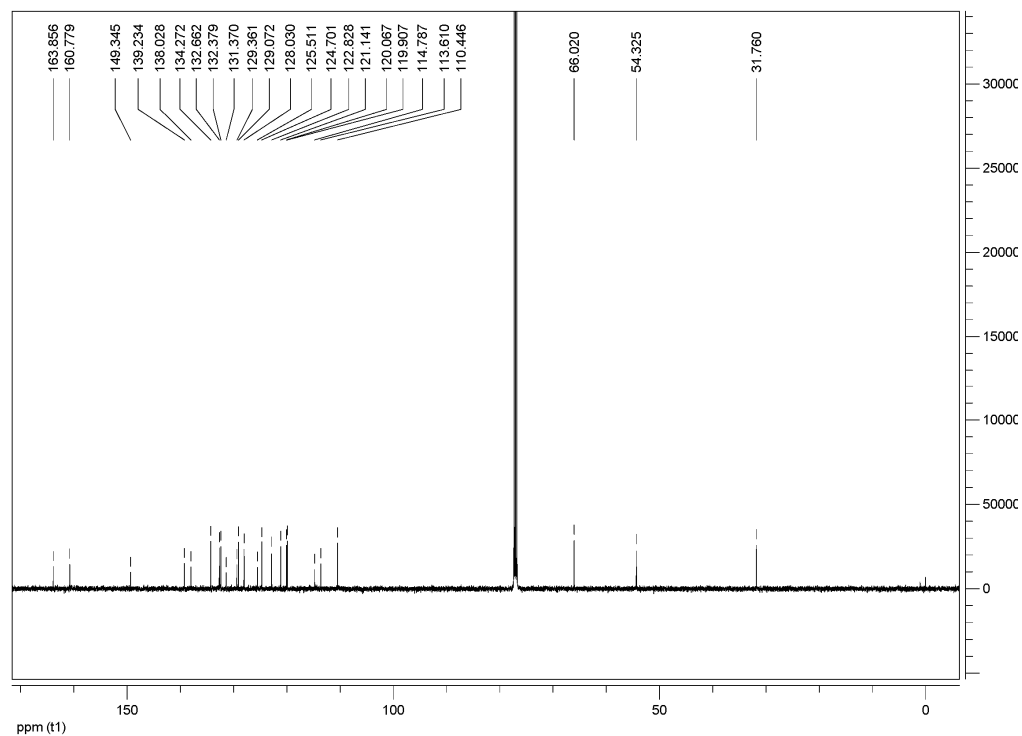


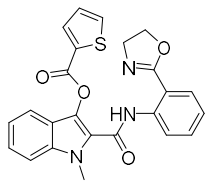
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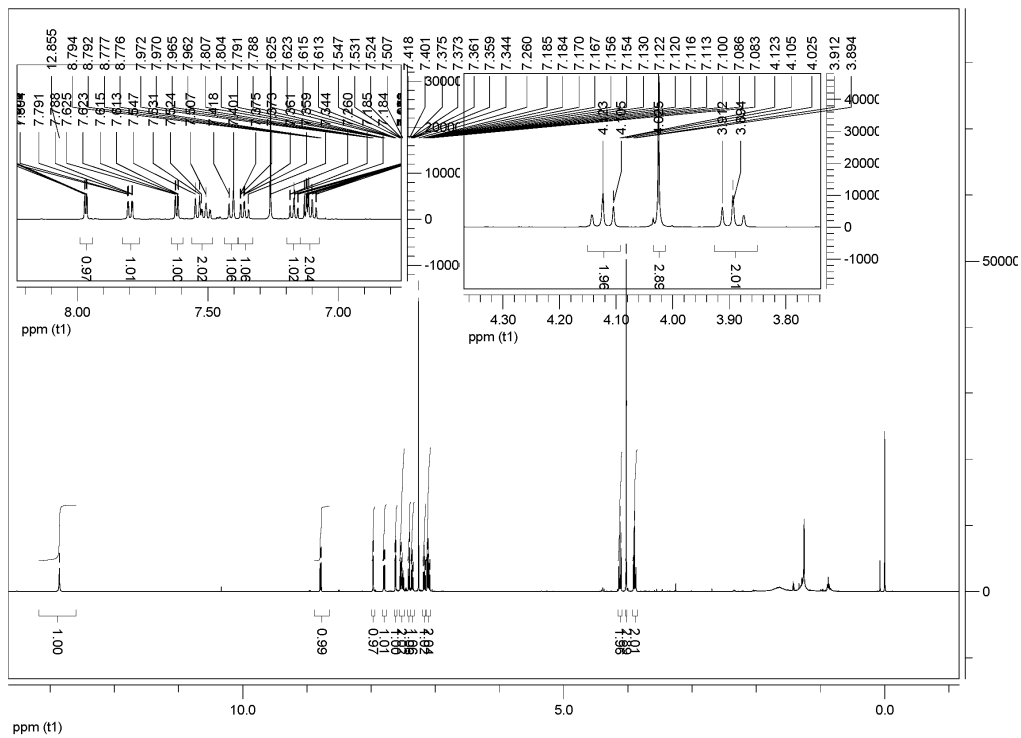
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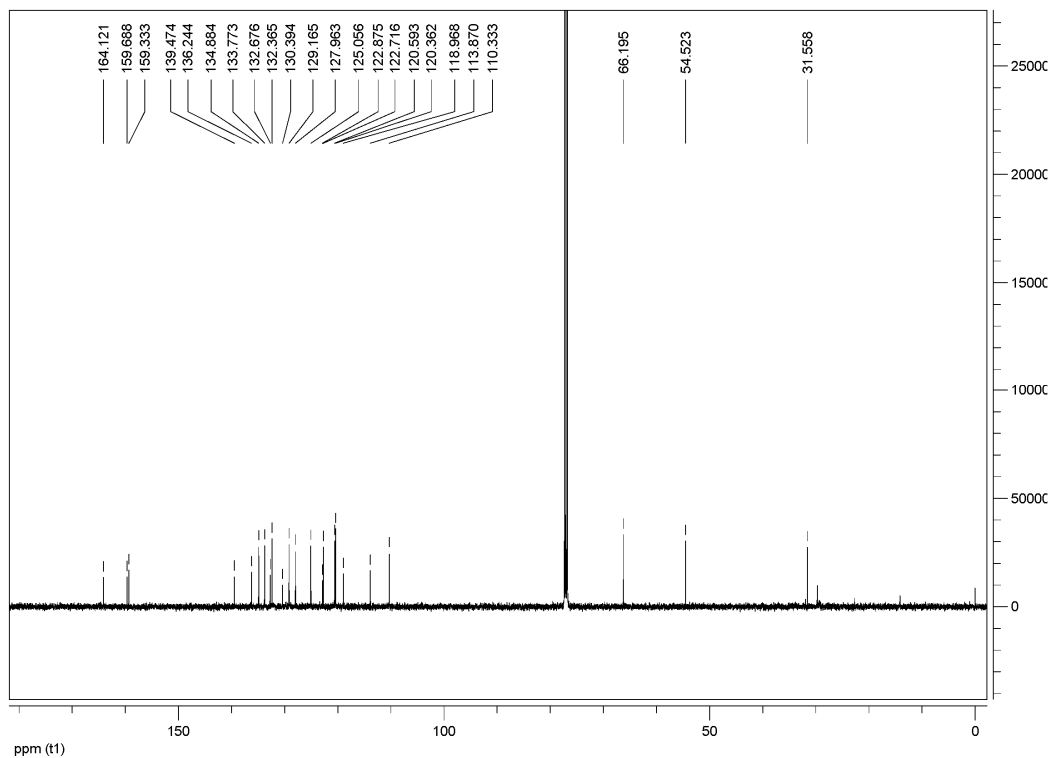


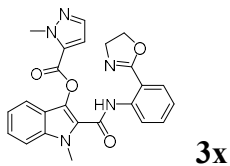
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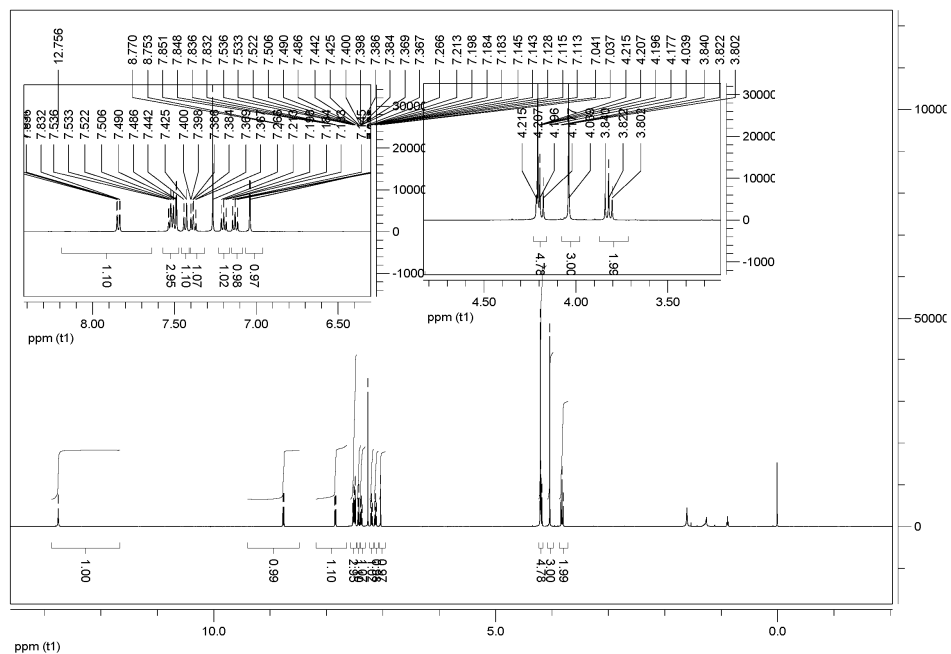


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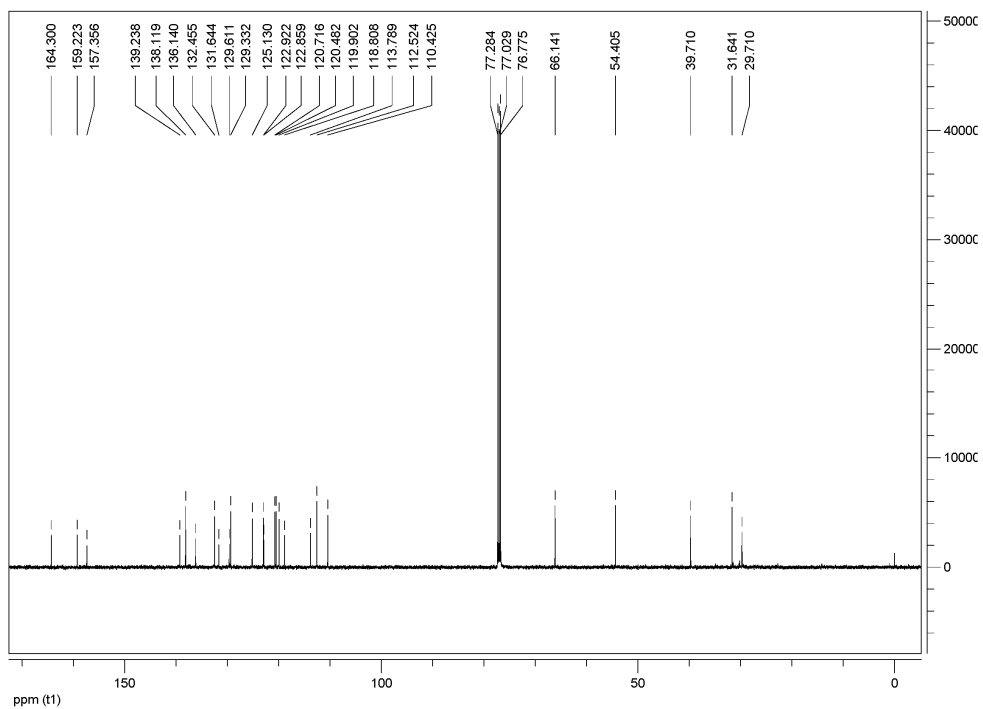


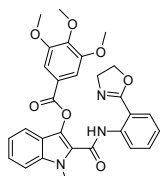


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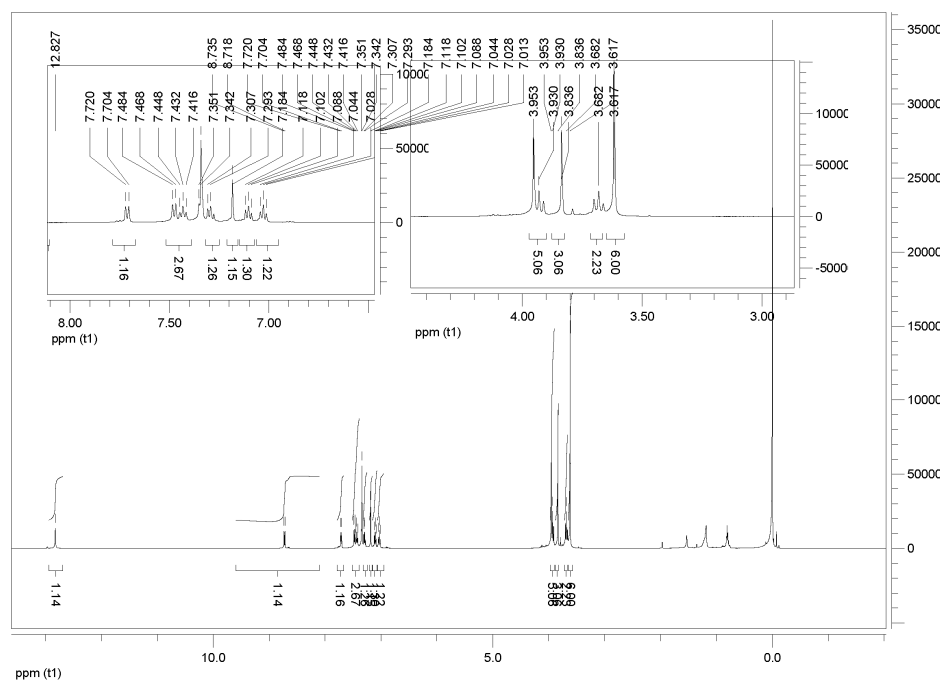
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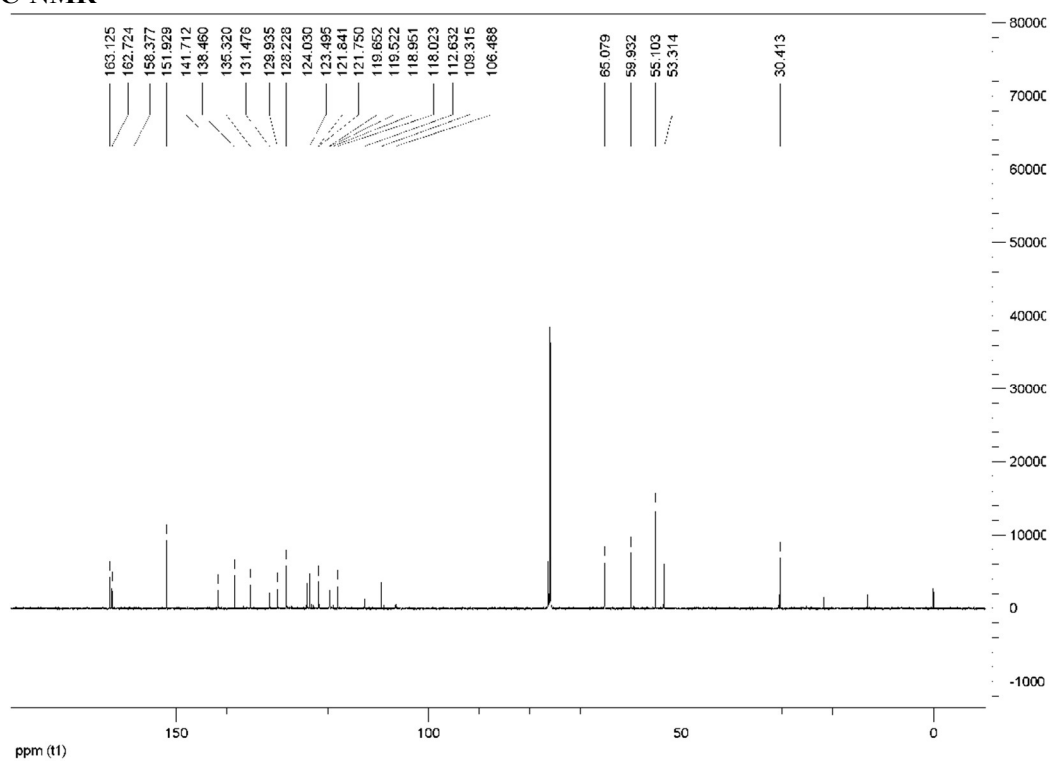


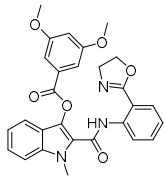
3z

¹H-NMR



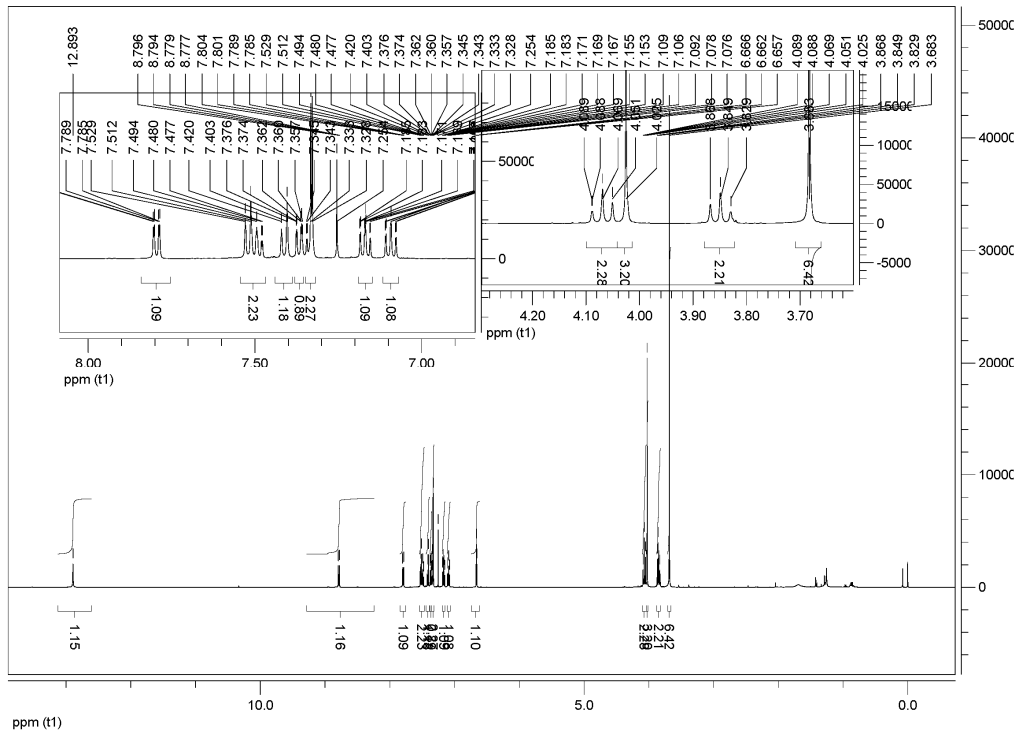
¹³C-NMR



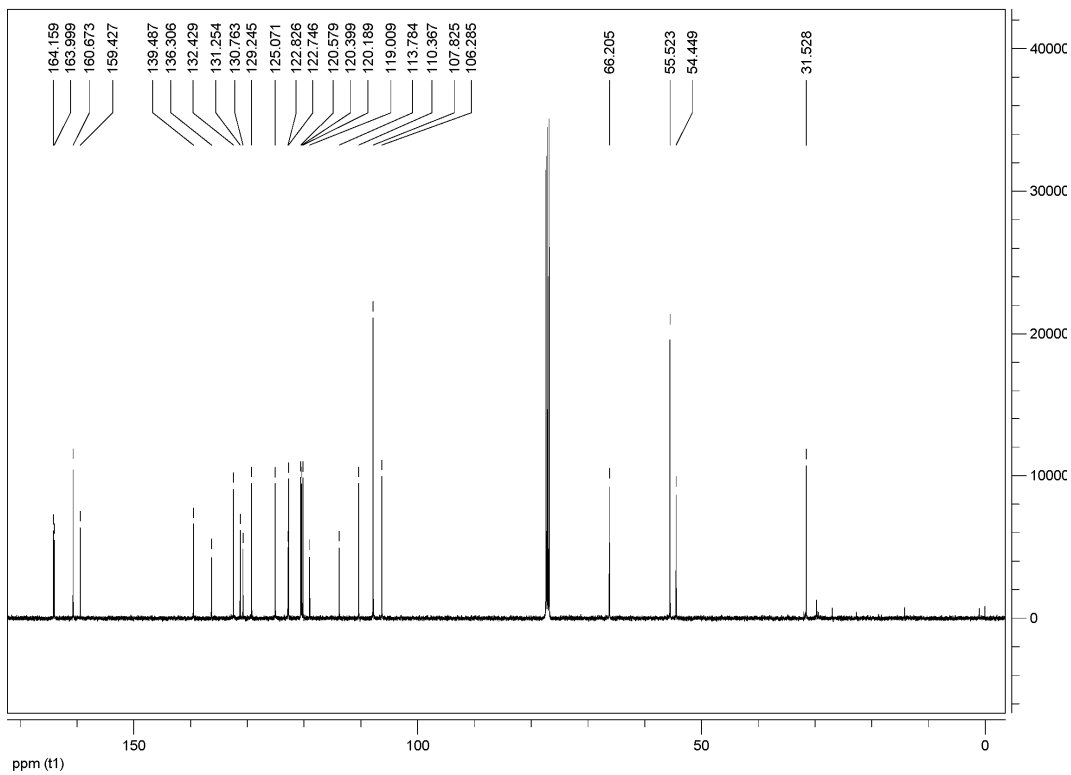


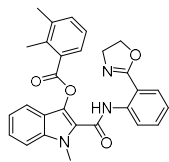
3aa

$^1\text{H-NMR}$



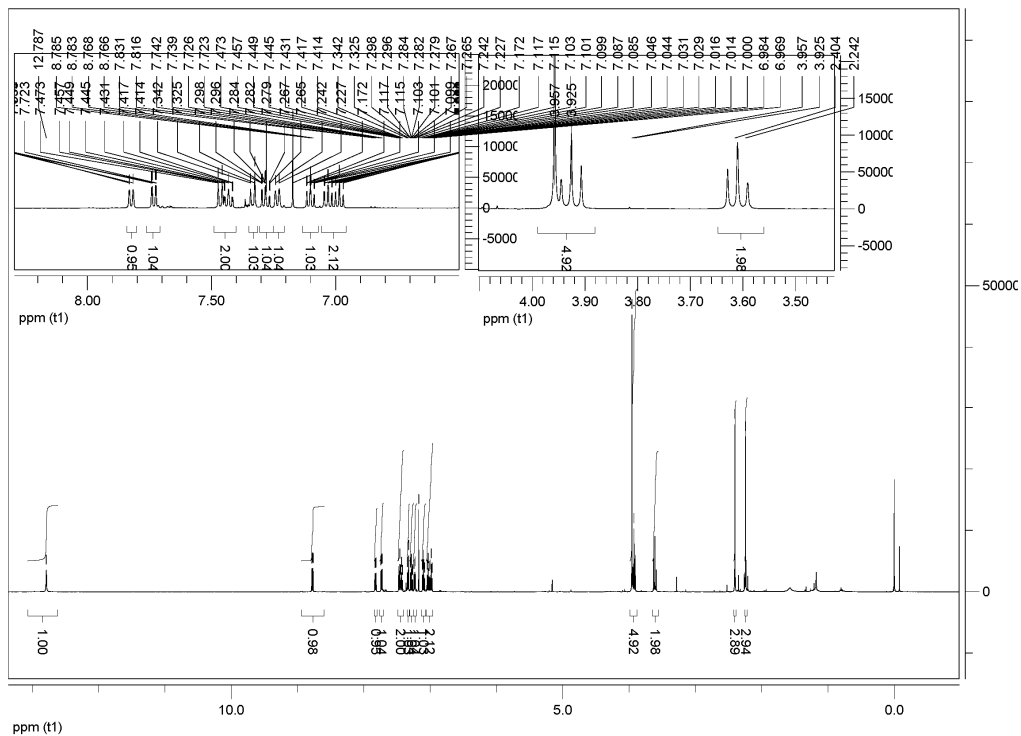
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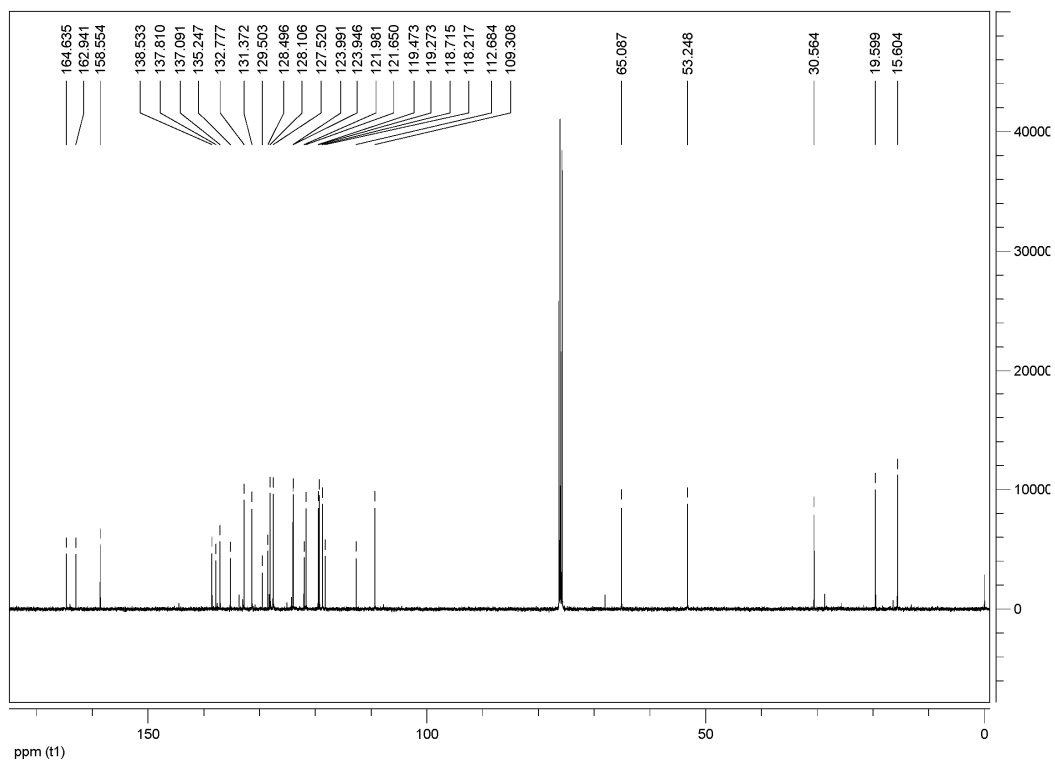


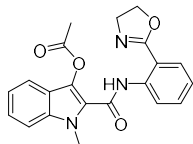
3ab

¹H-NMR



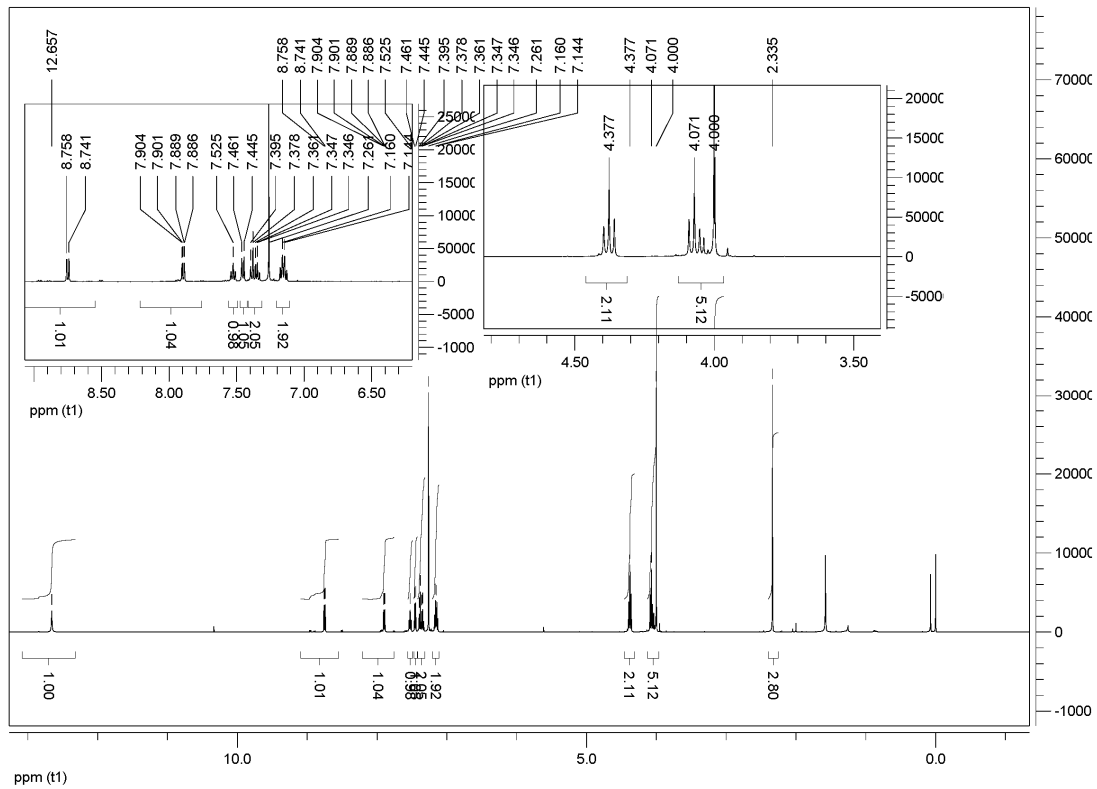
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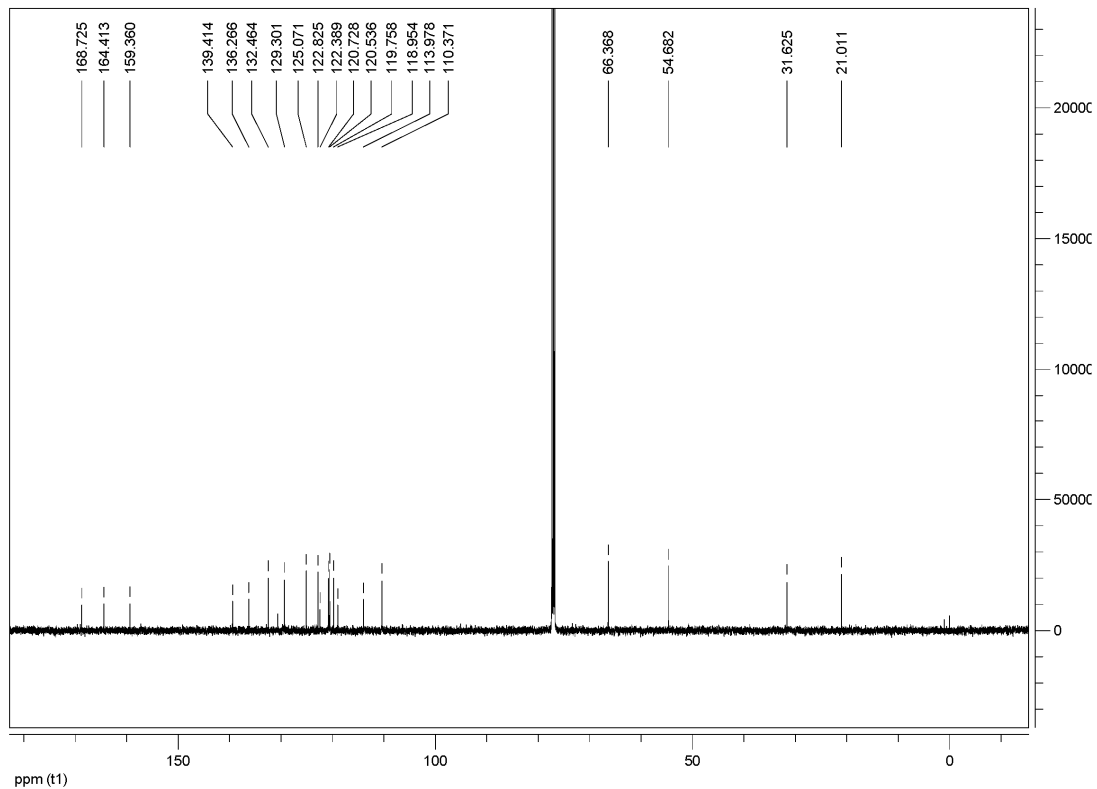


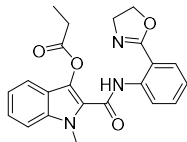
4a

¹H-NMR



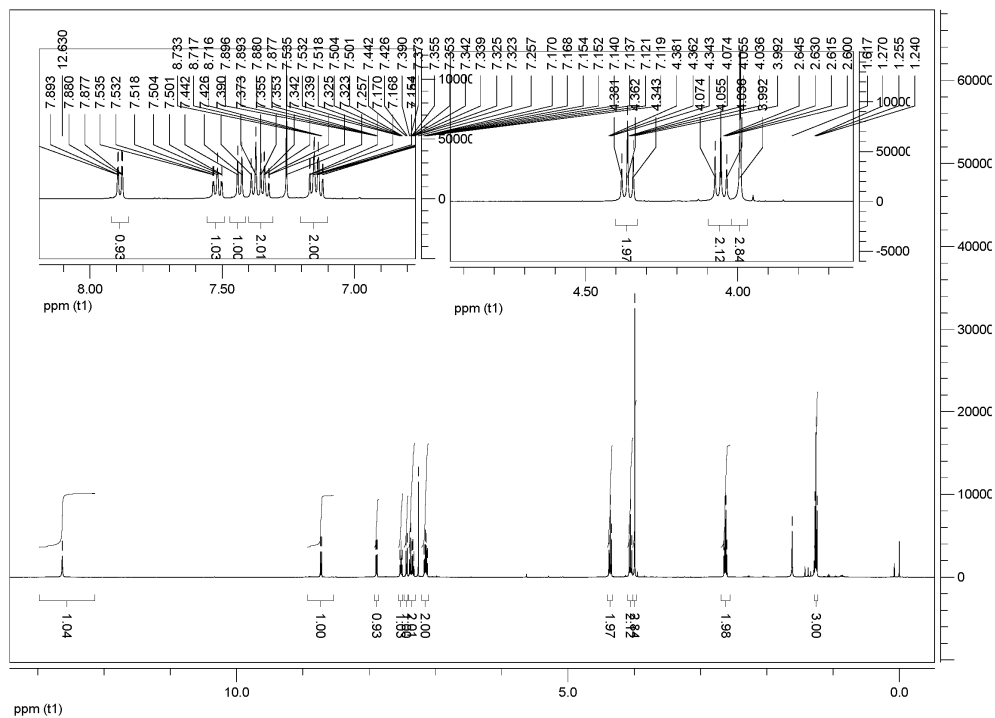
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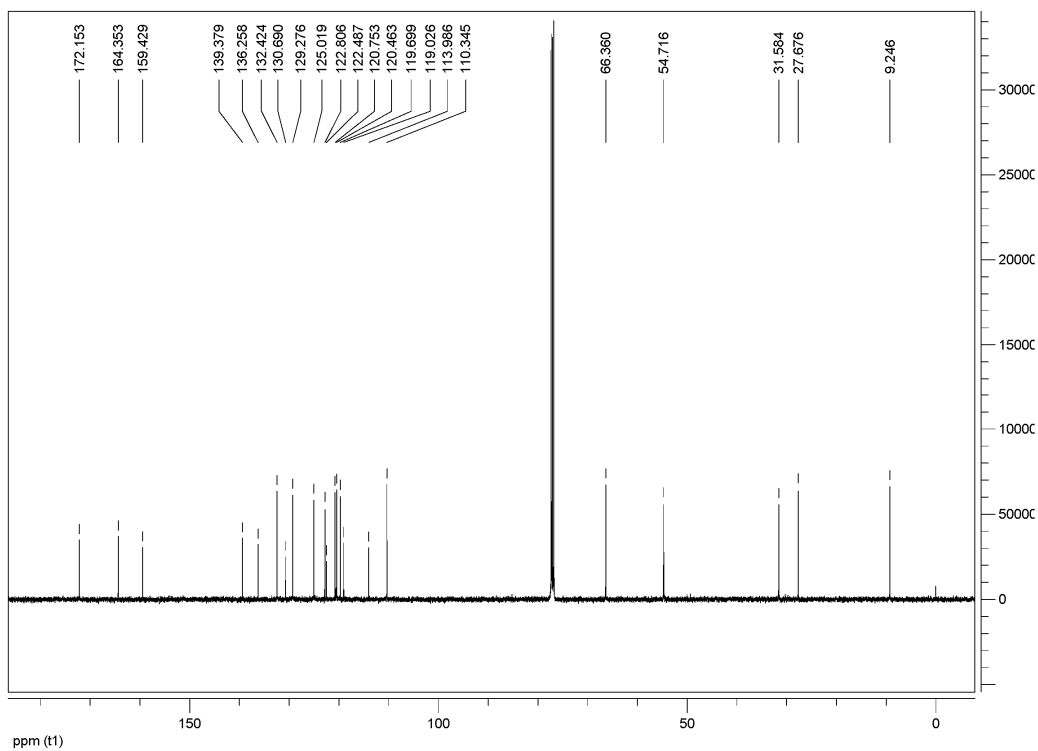


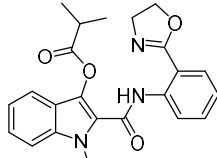
4b

¹H-NMR



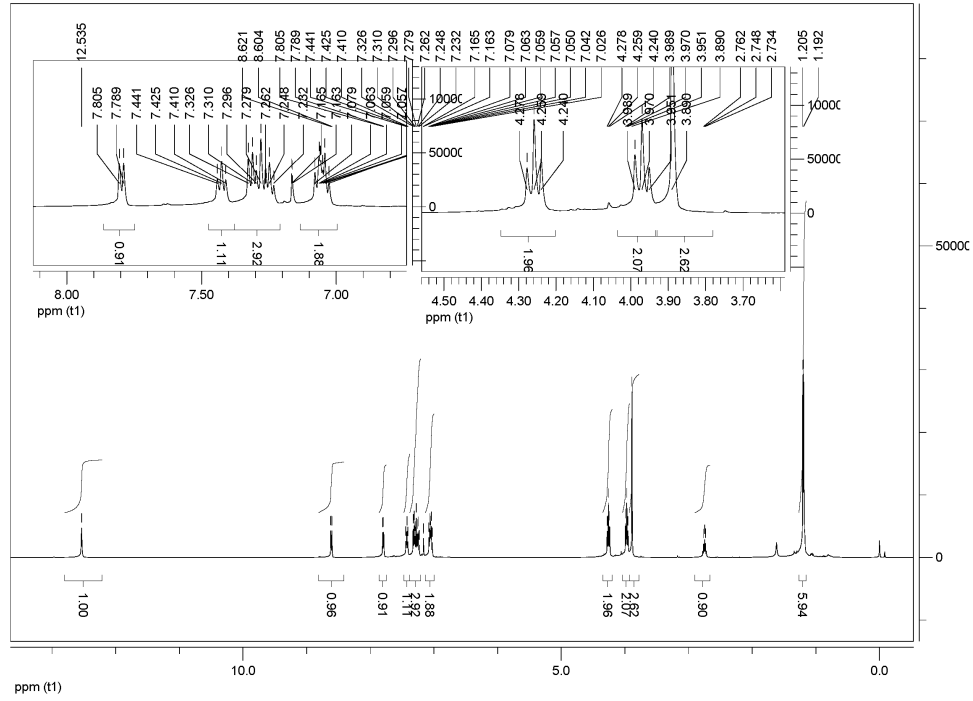
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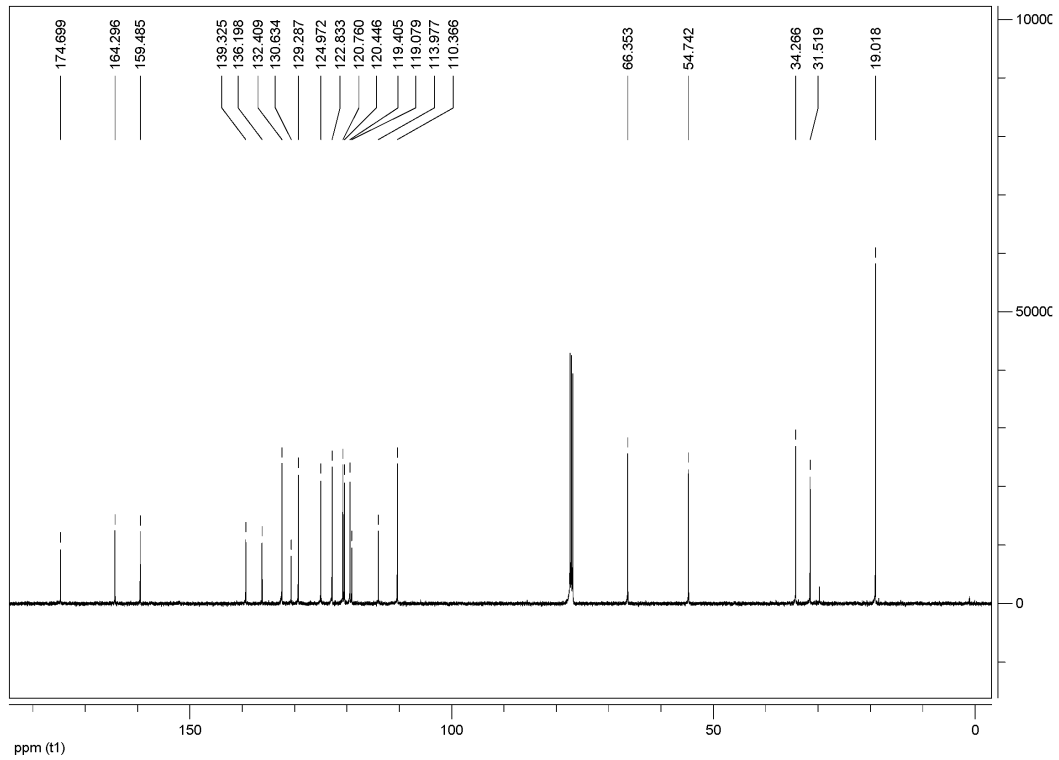


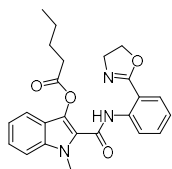
4c

¹H-NMR



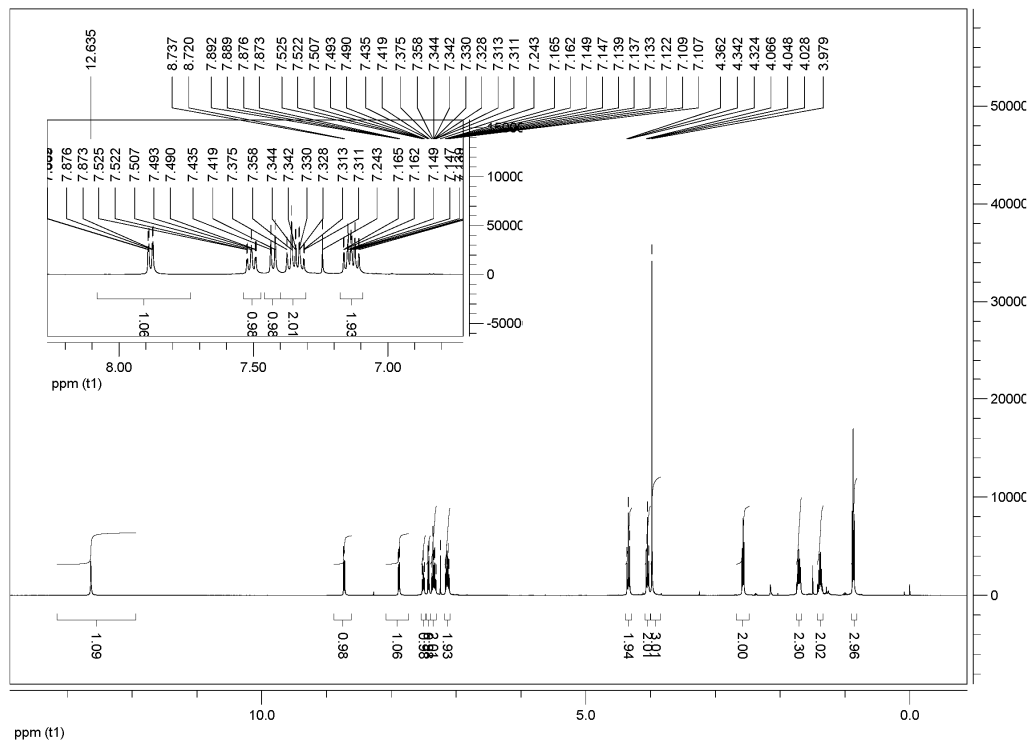
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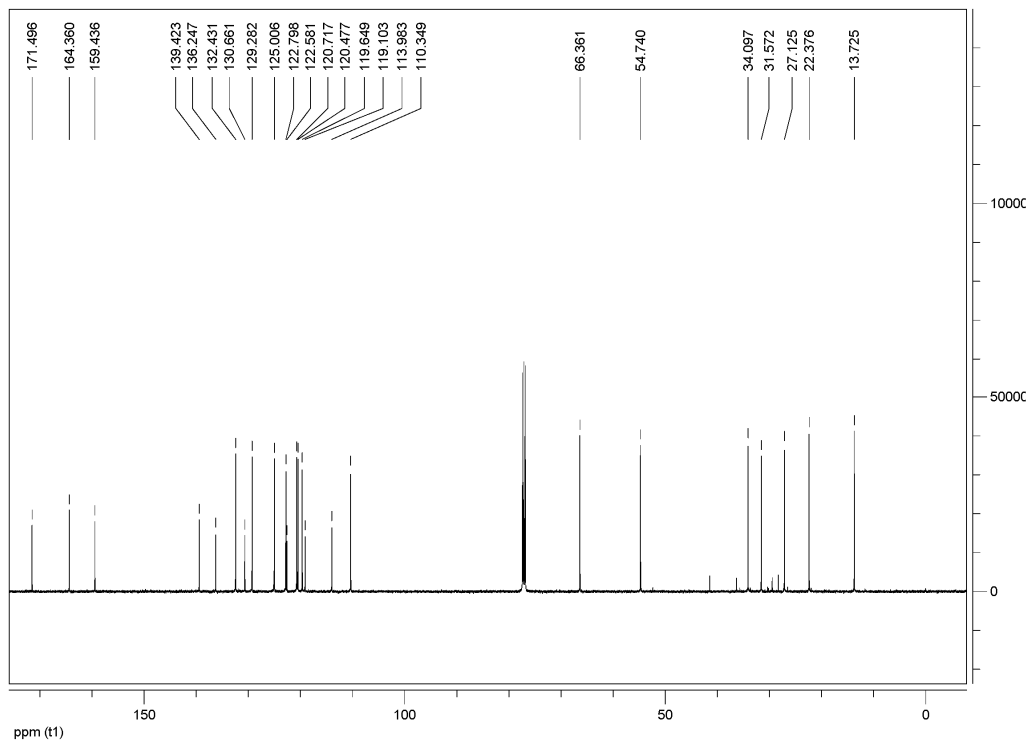


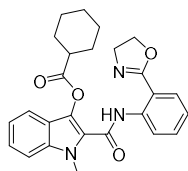
4d

¹H-NMR



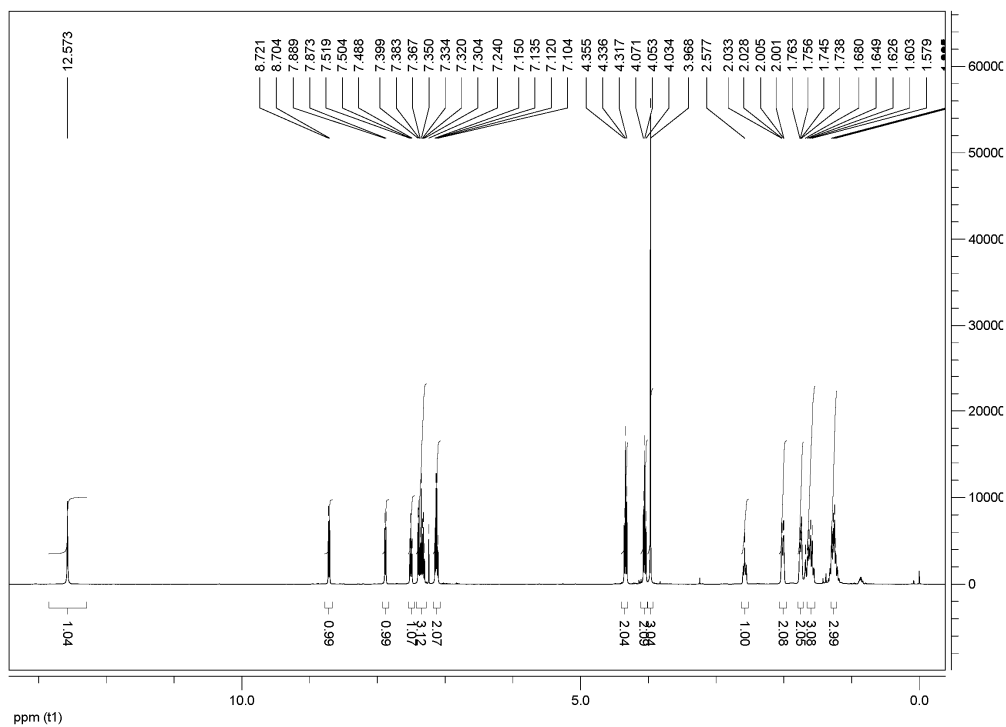
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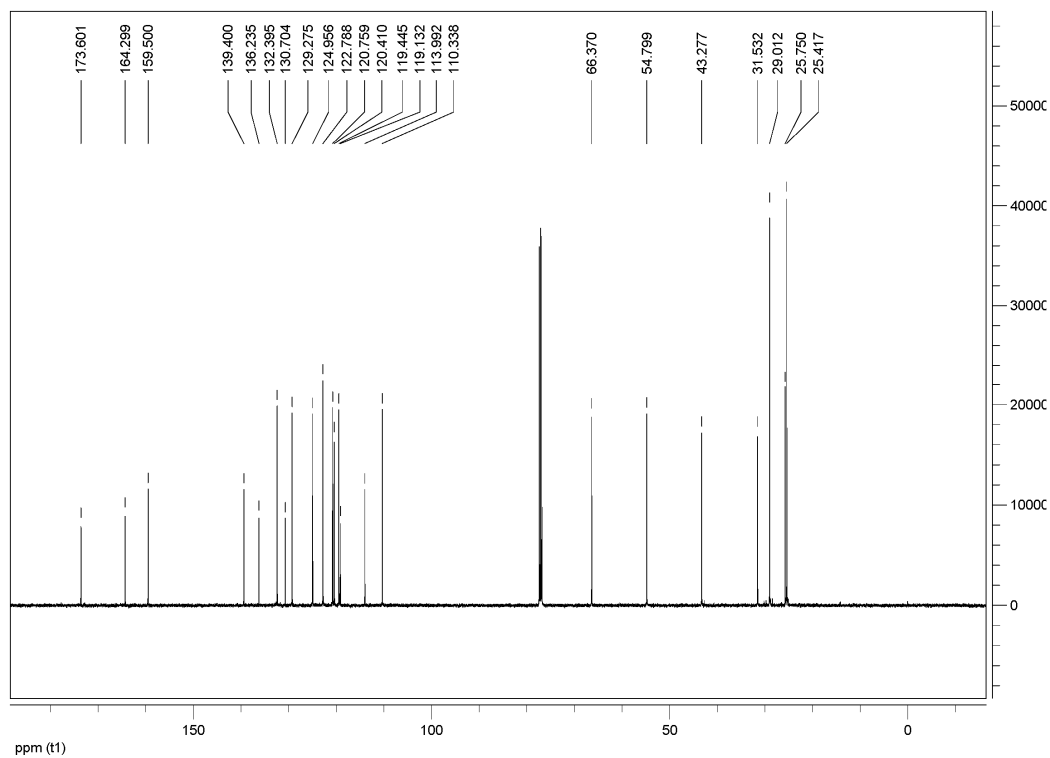


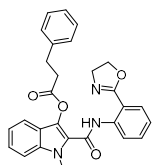
4f

¹H-NMR



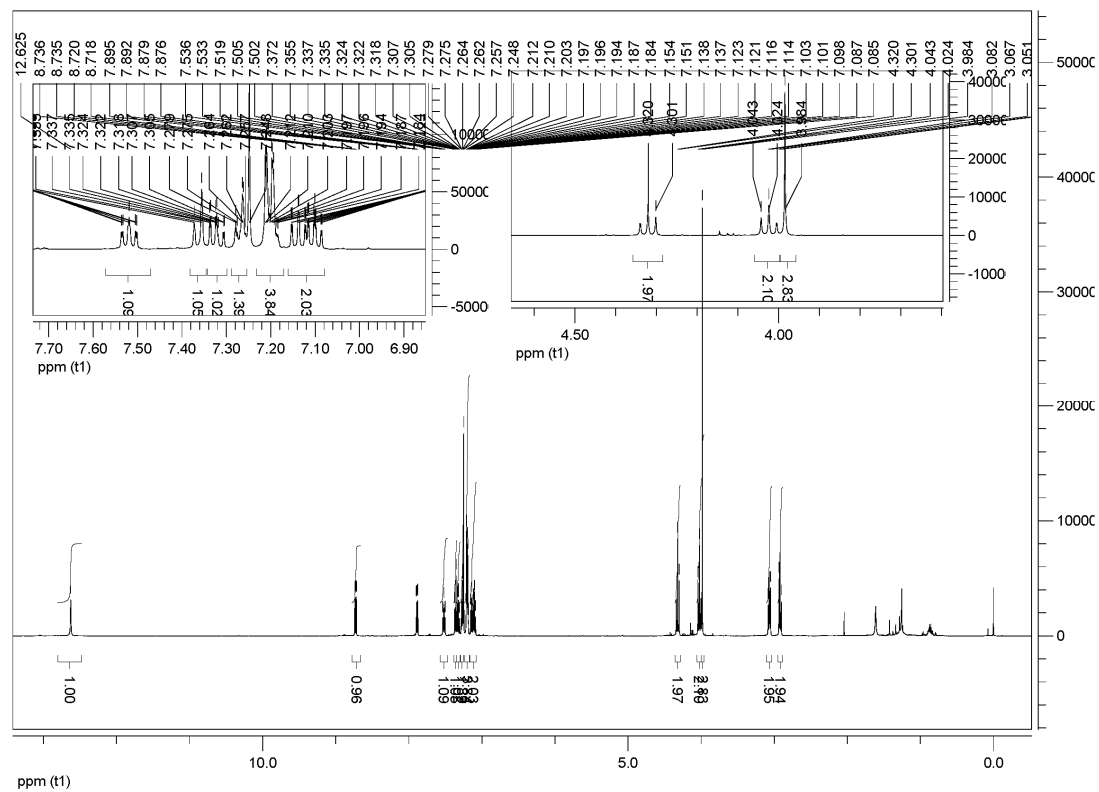
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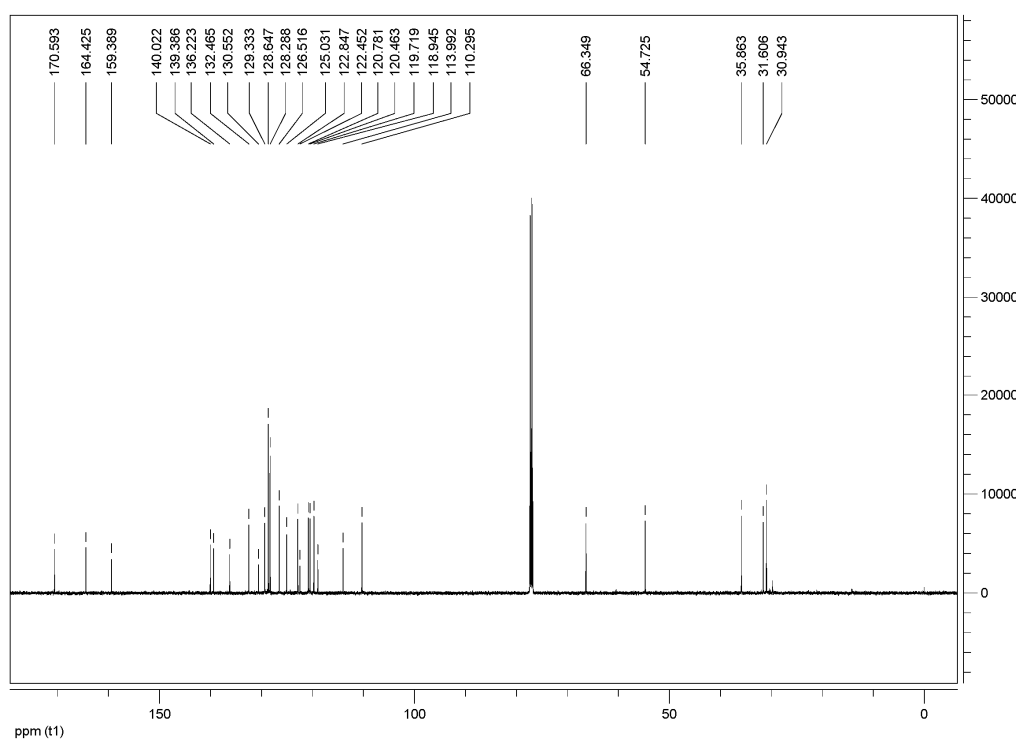


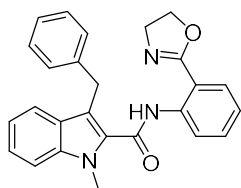
4g

¹H-NMR



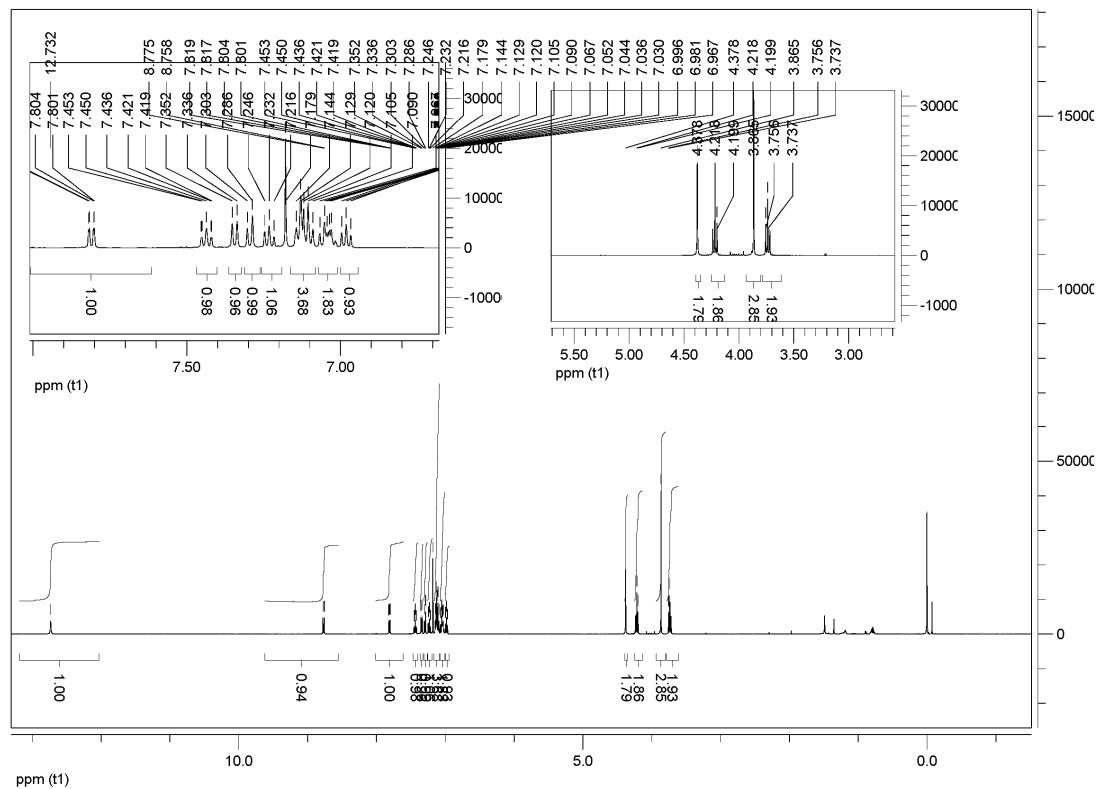
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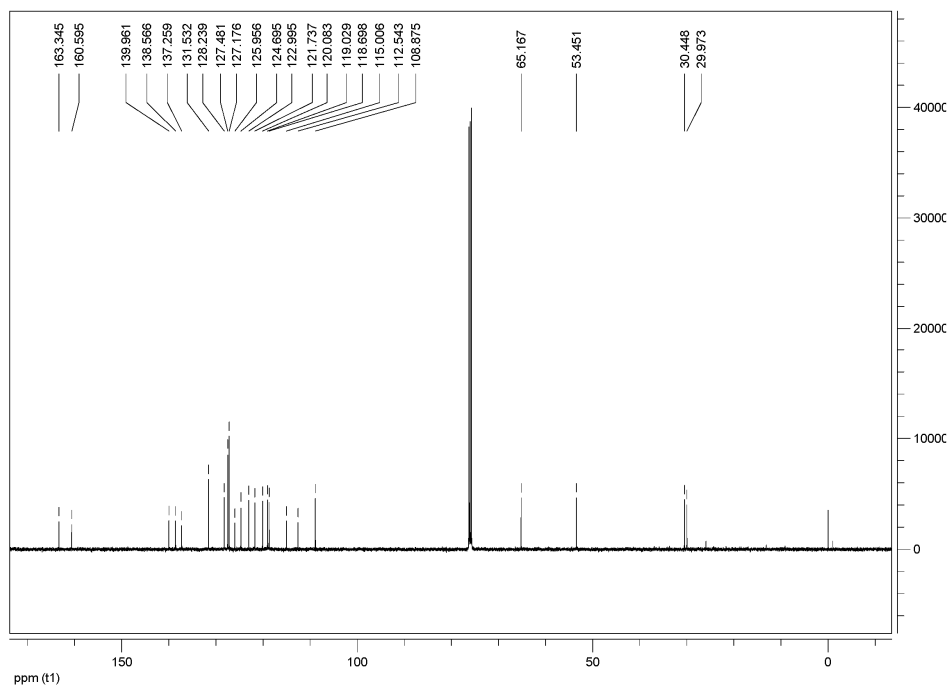


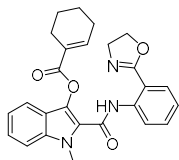
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¹H-NMR



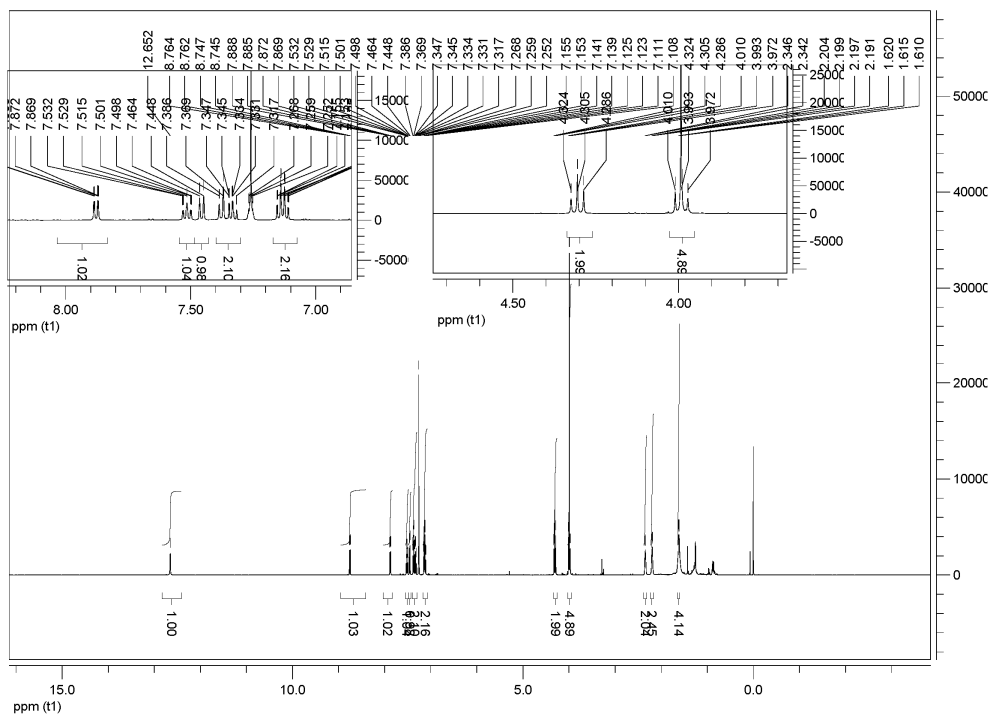
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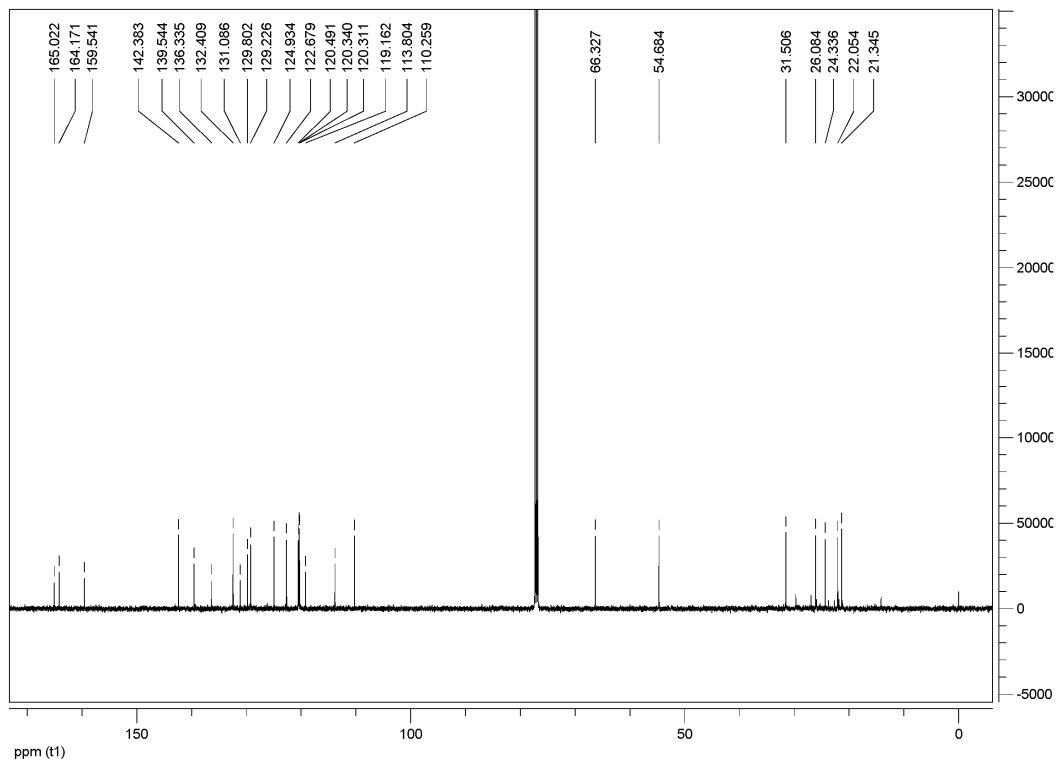


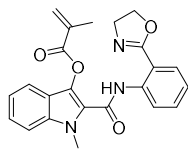
4i

¹H-NMR



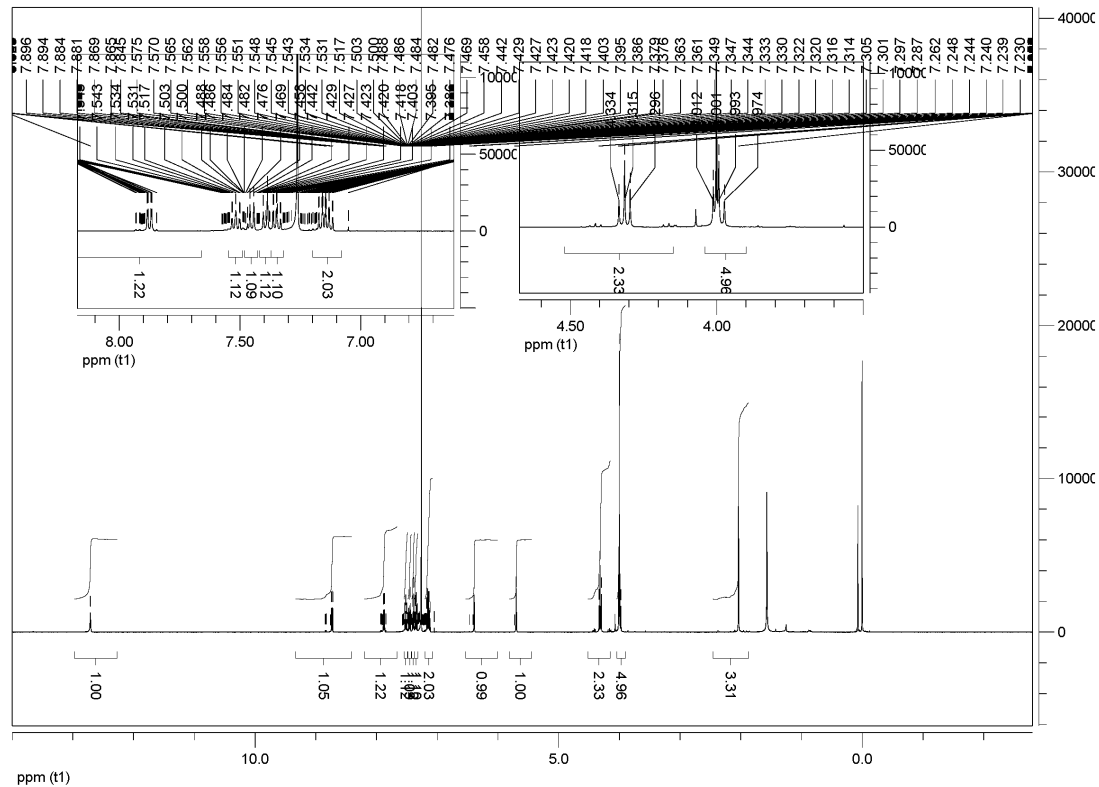
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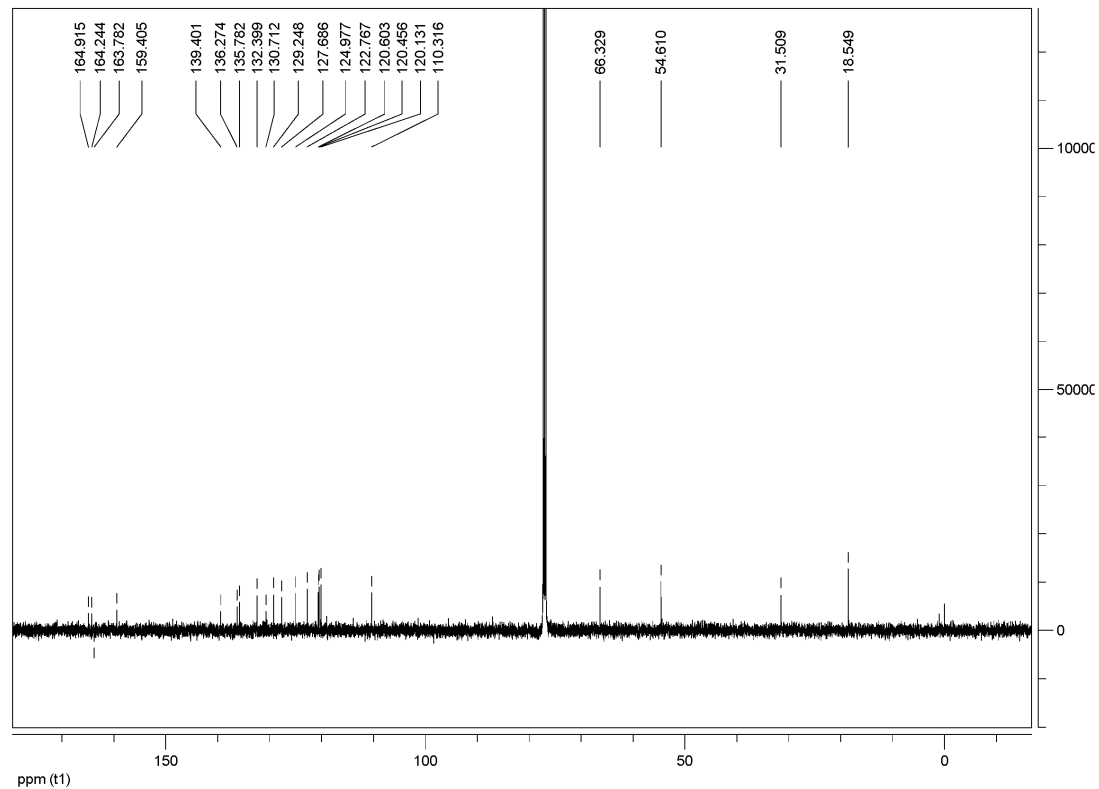


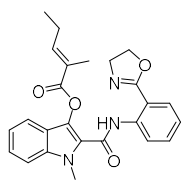
4j

¹H-NMR



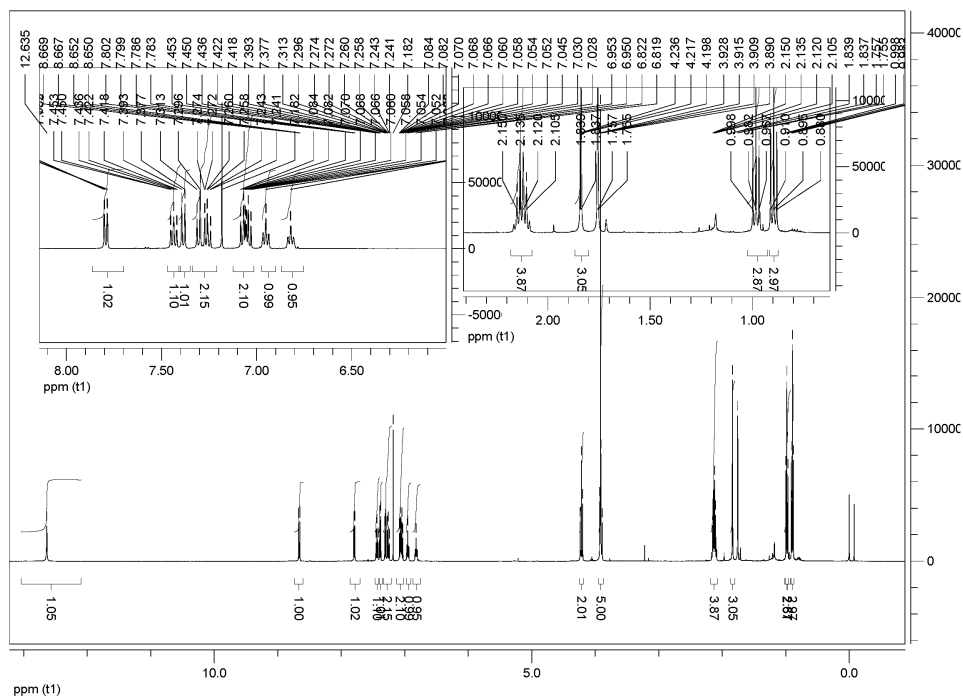
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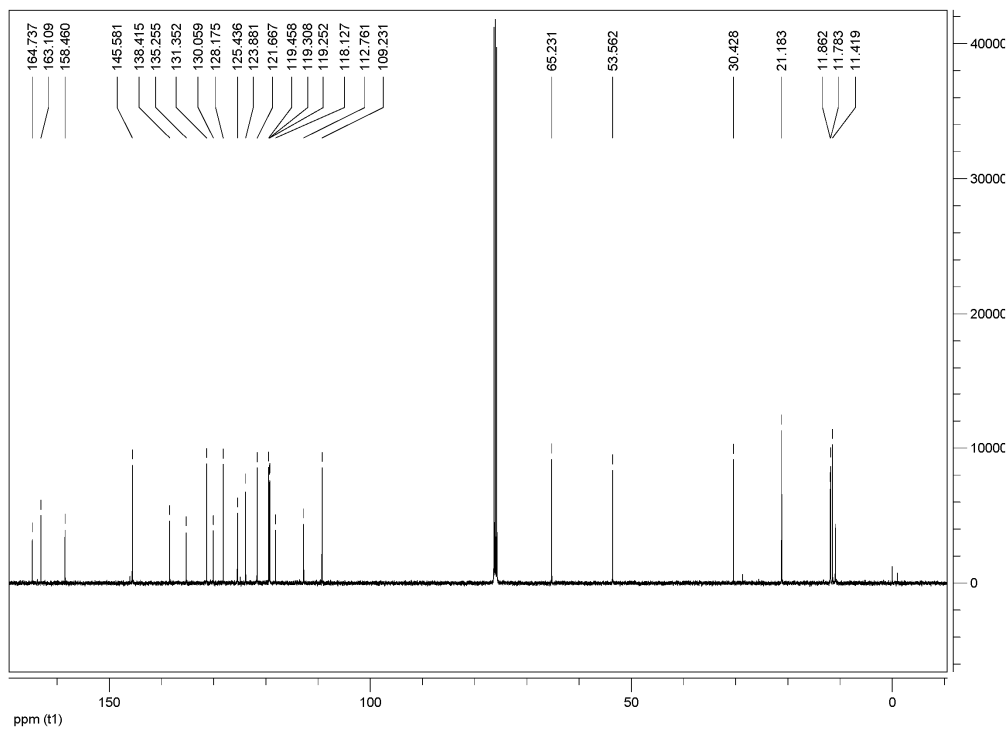


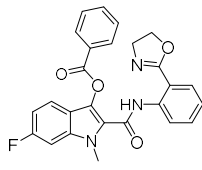
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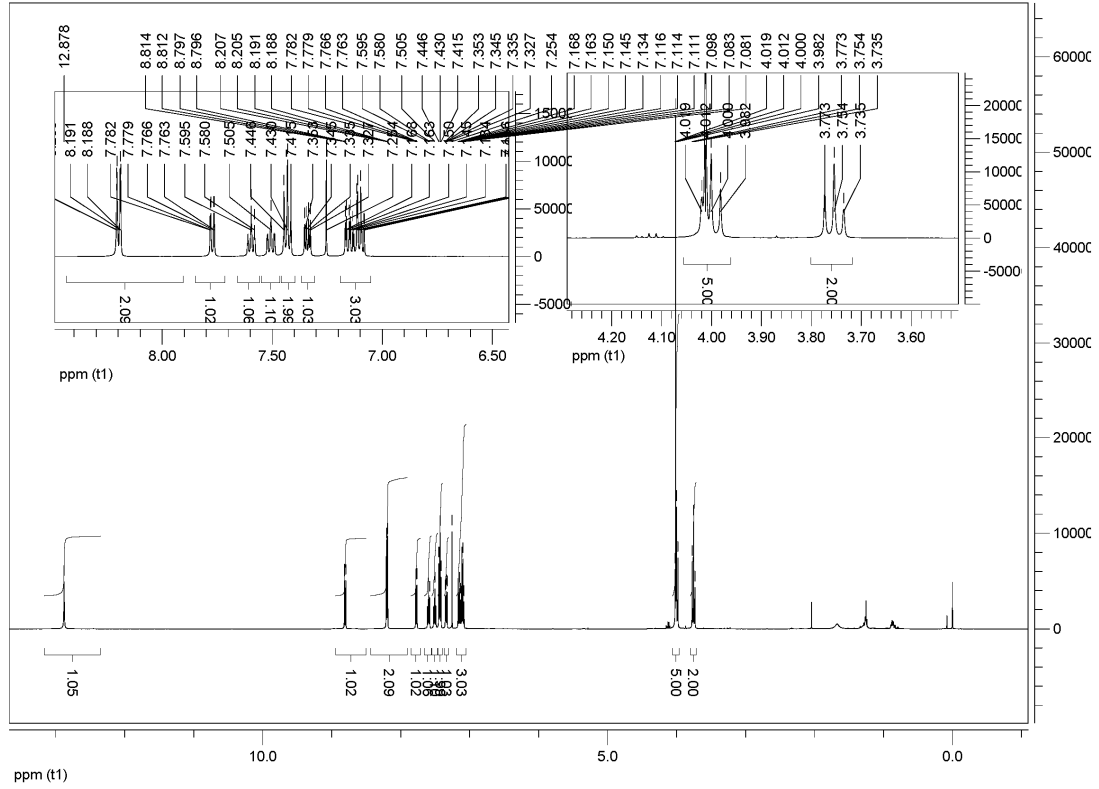
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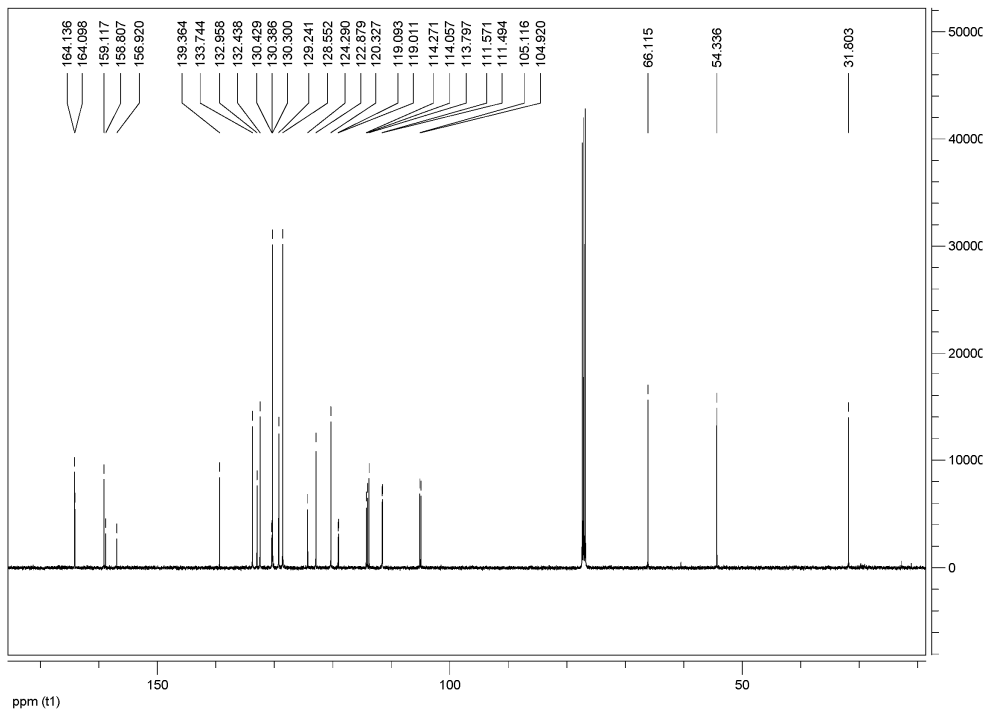


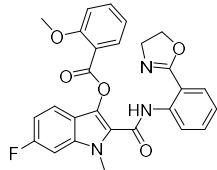
5a

¹H-NMR



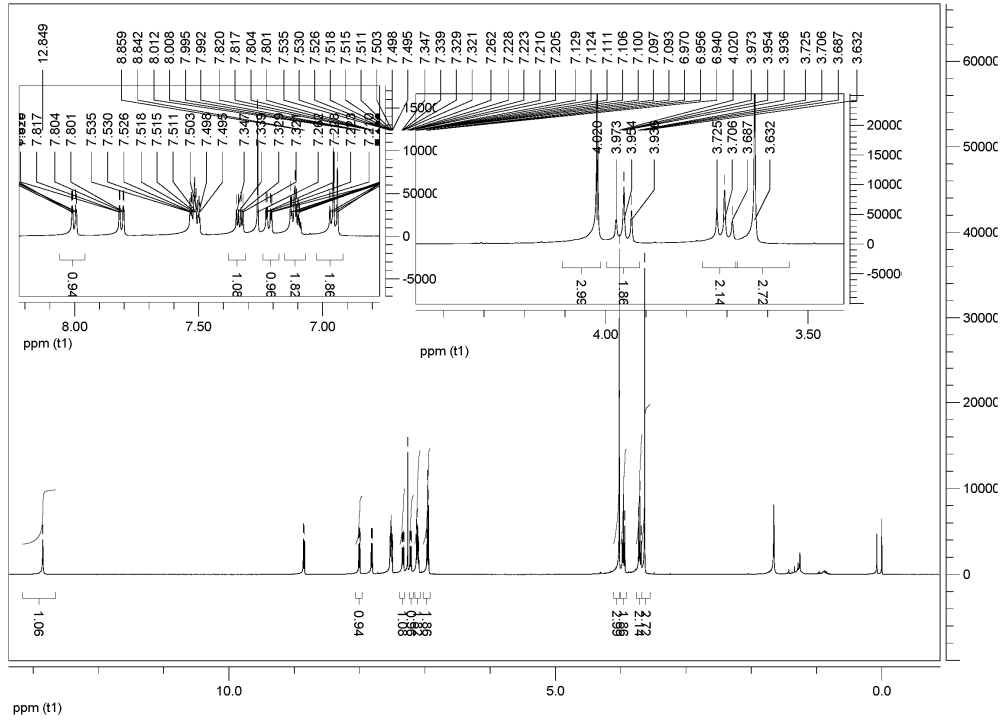
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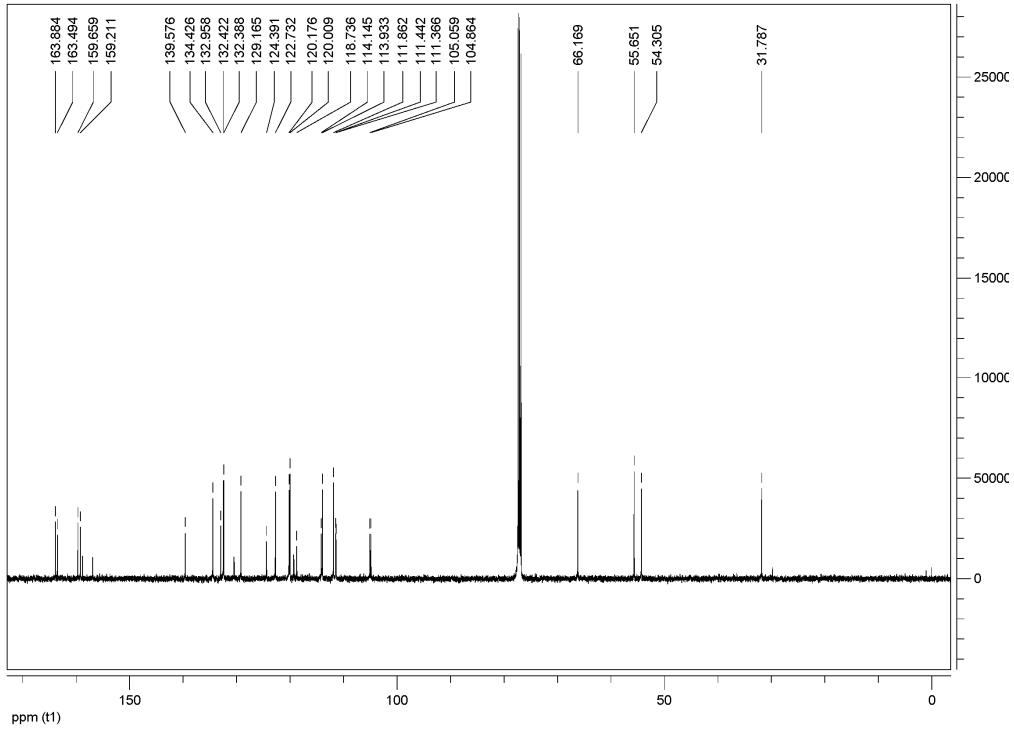


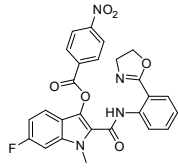
5b

¹H-NMR



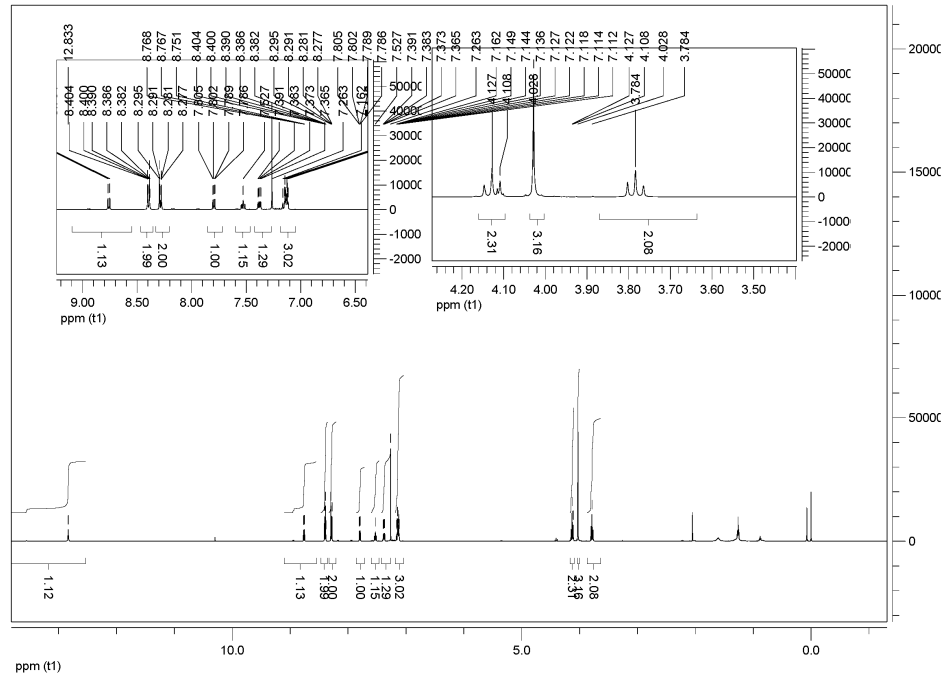
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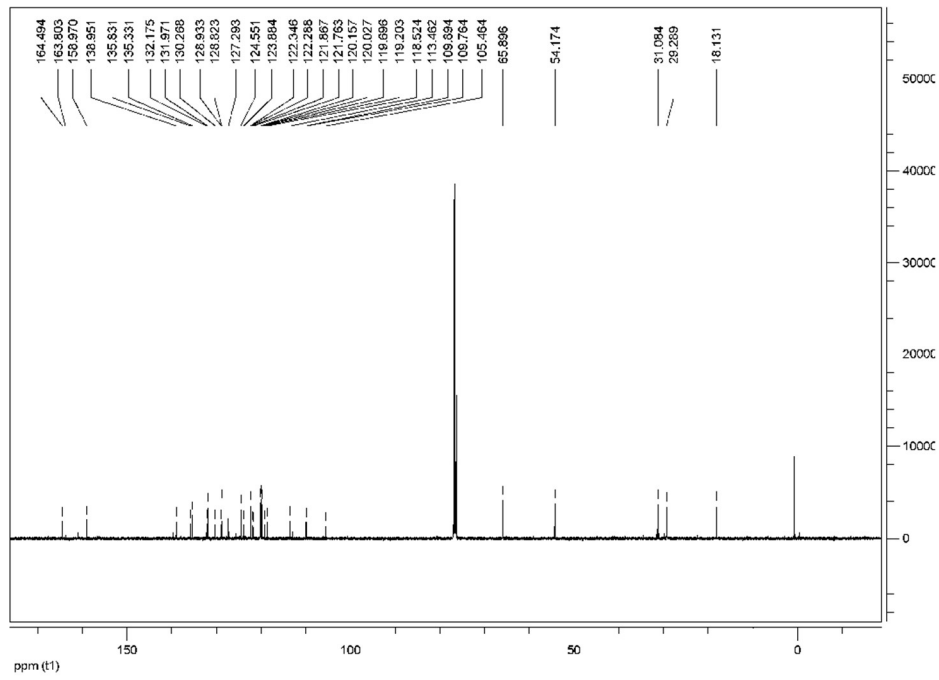


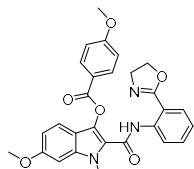
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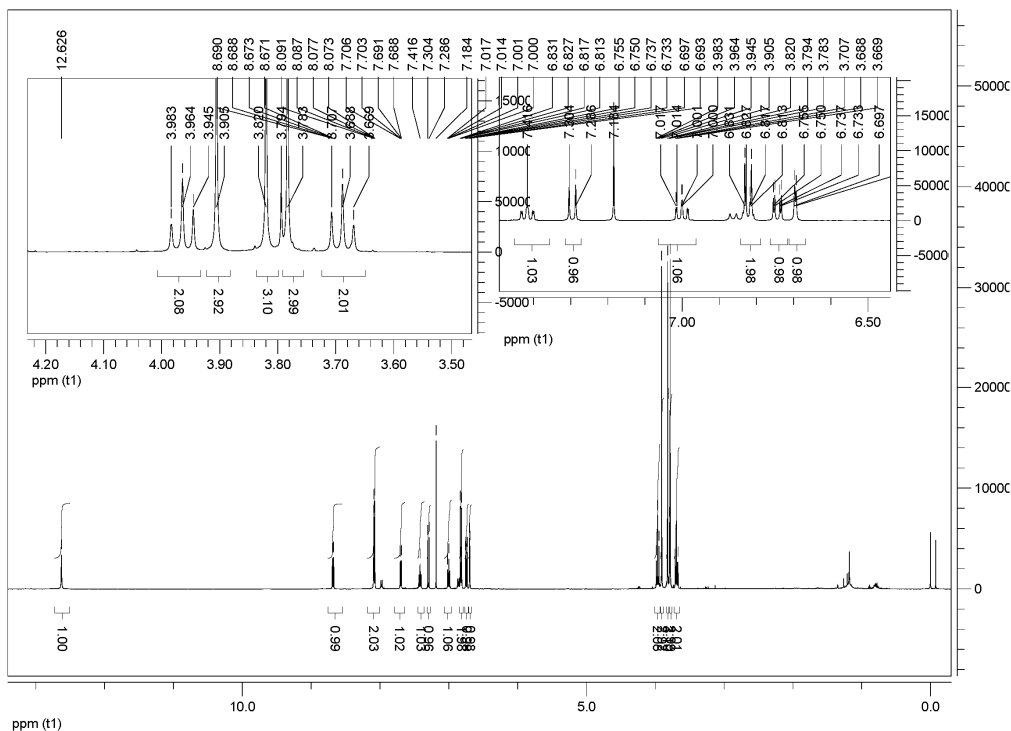
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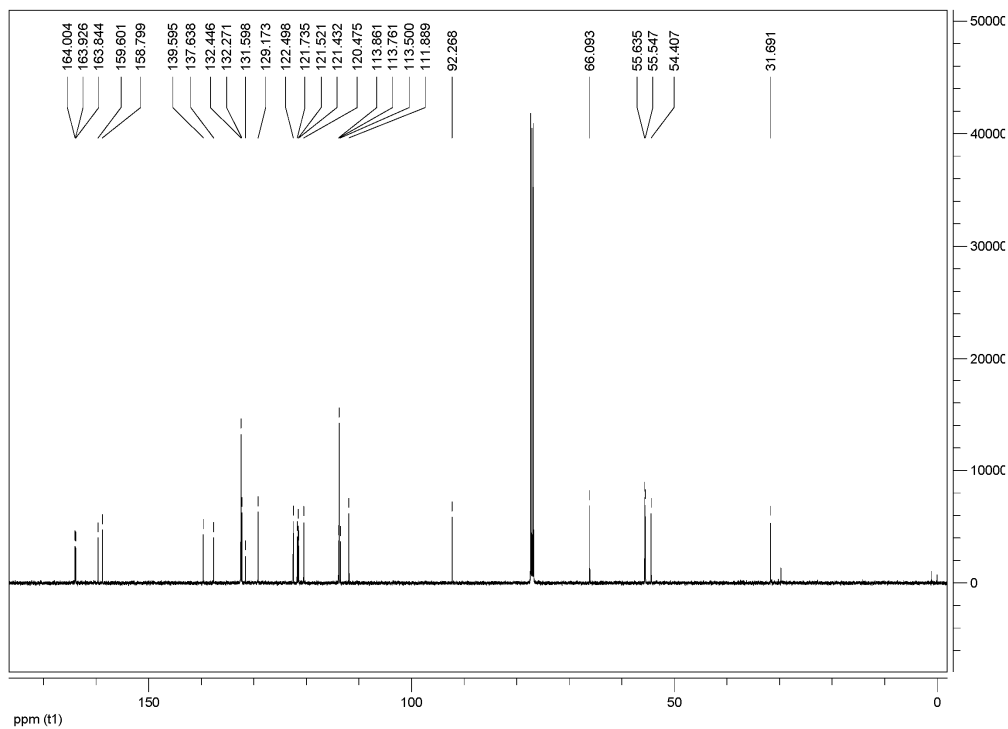


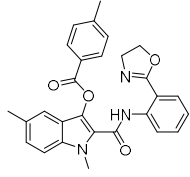
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¹H-NMR



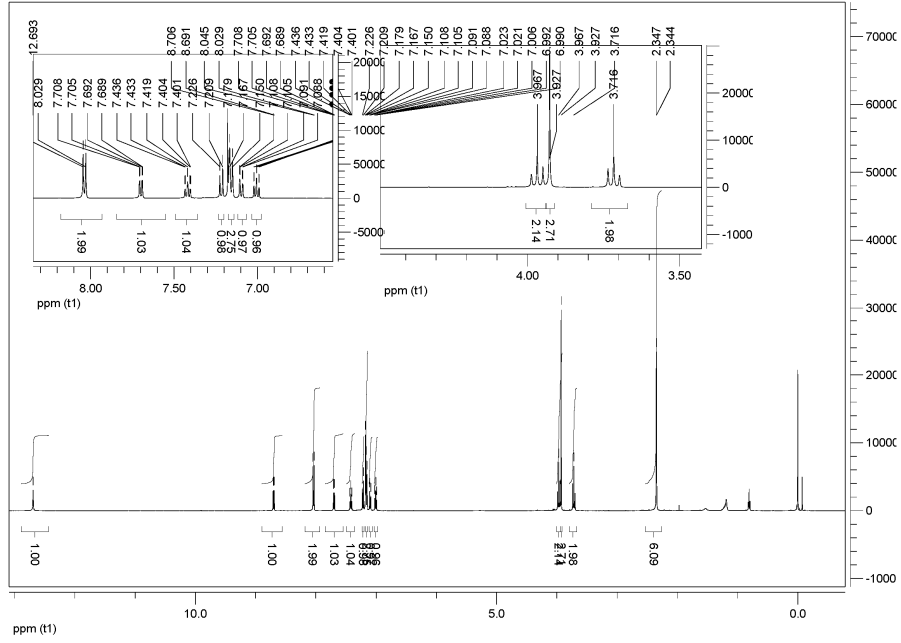
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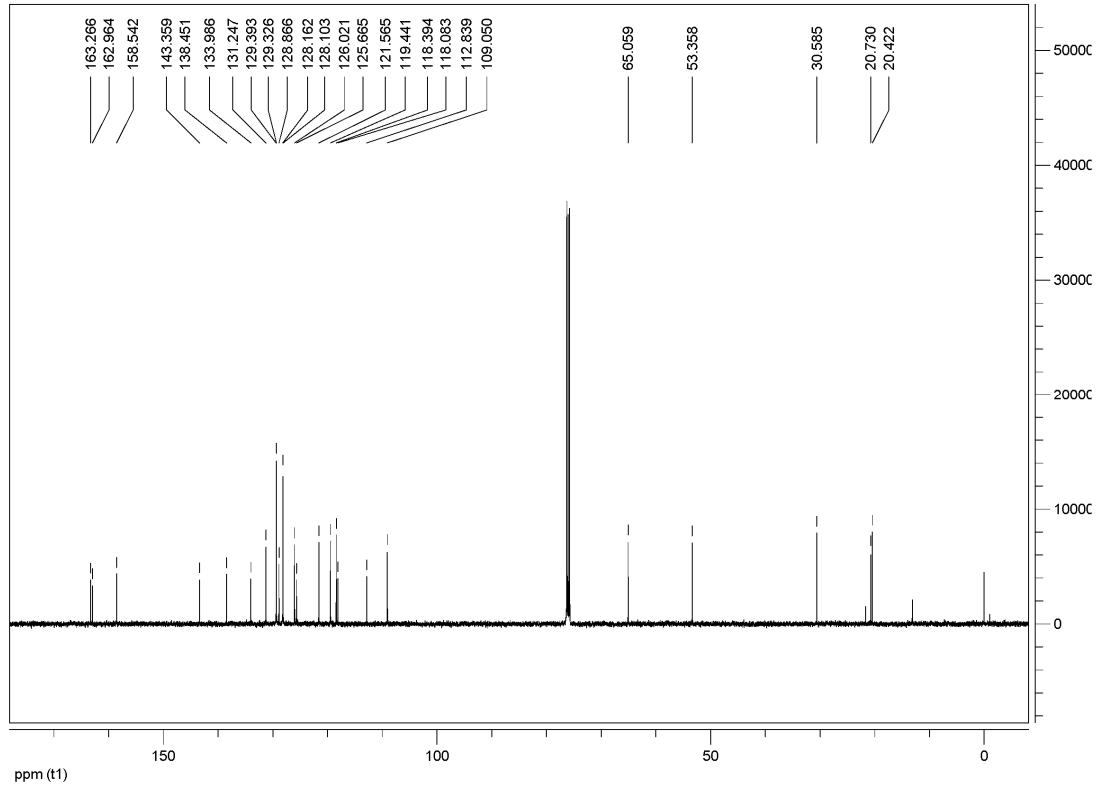


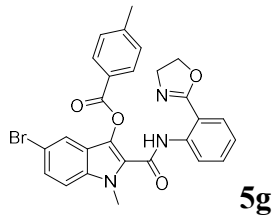
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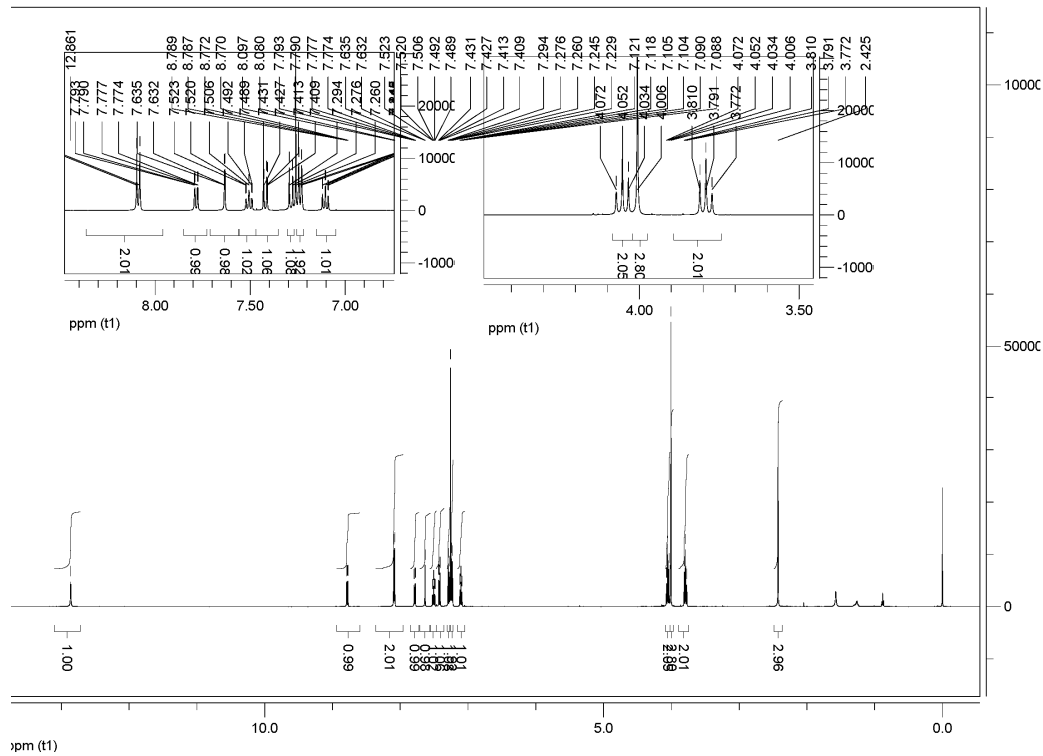


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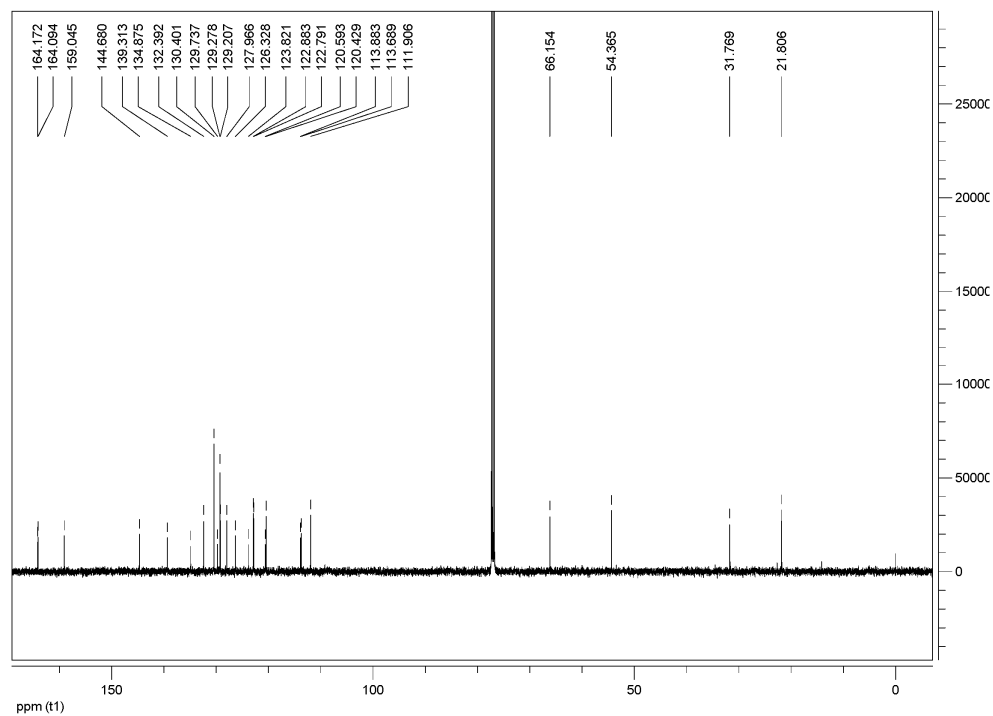


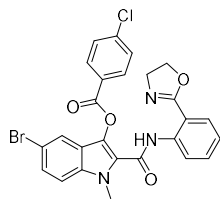


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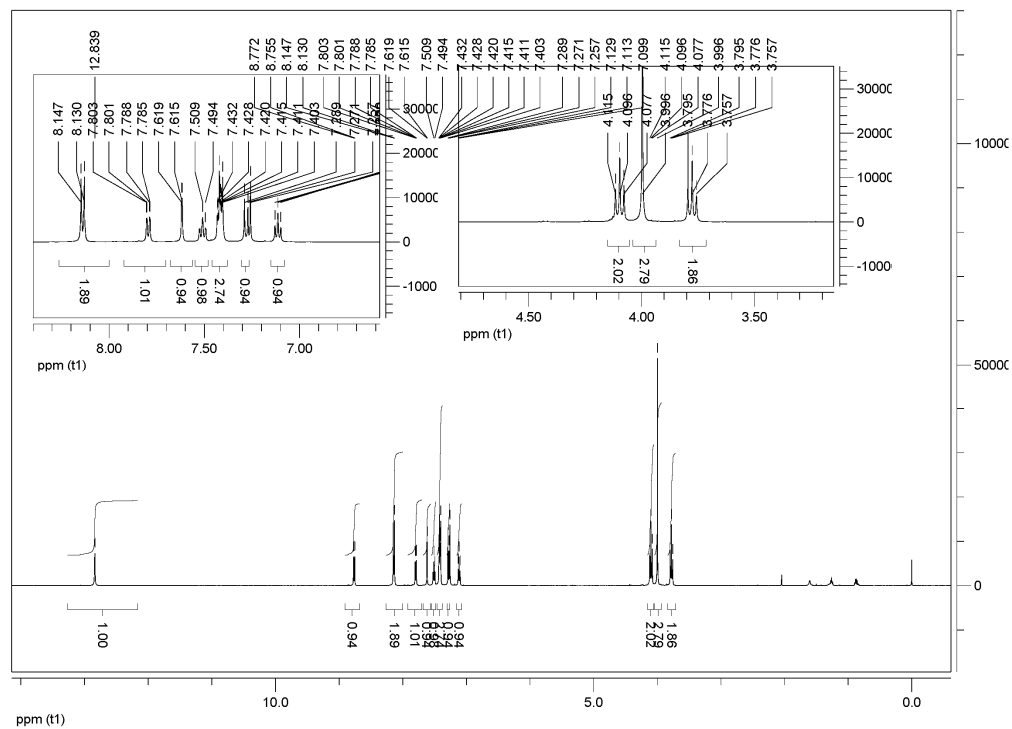
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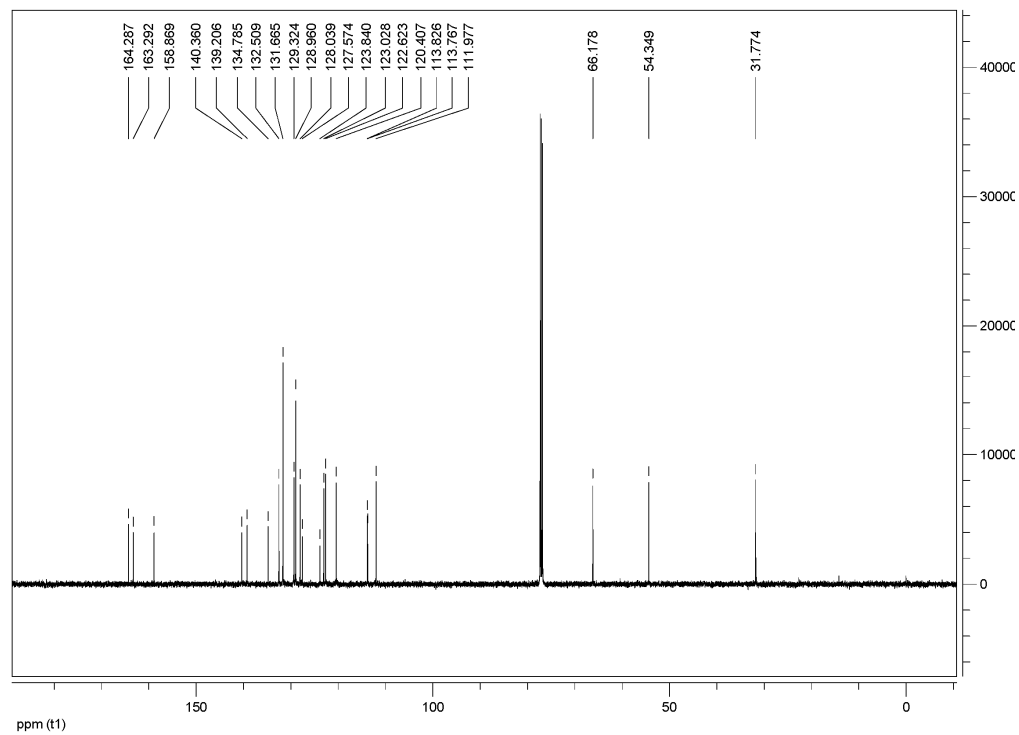


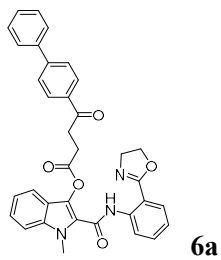
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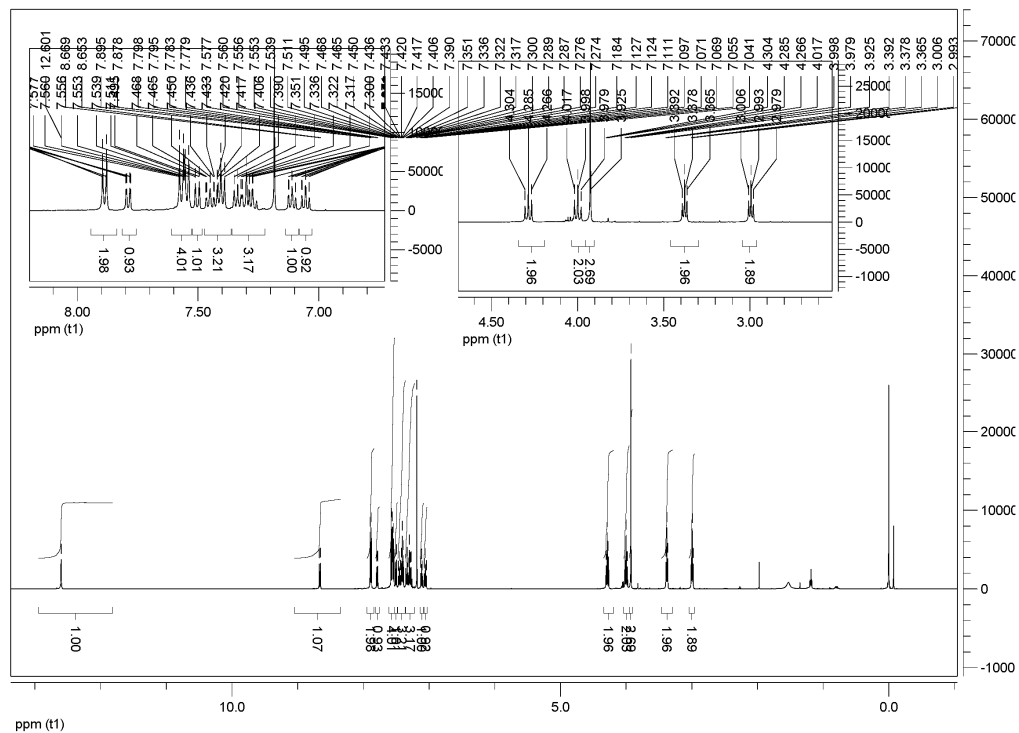


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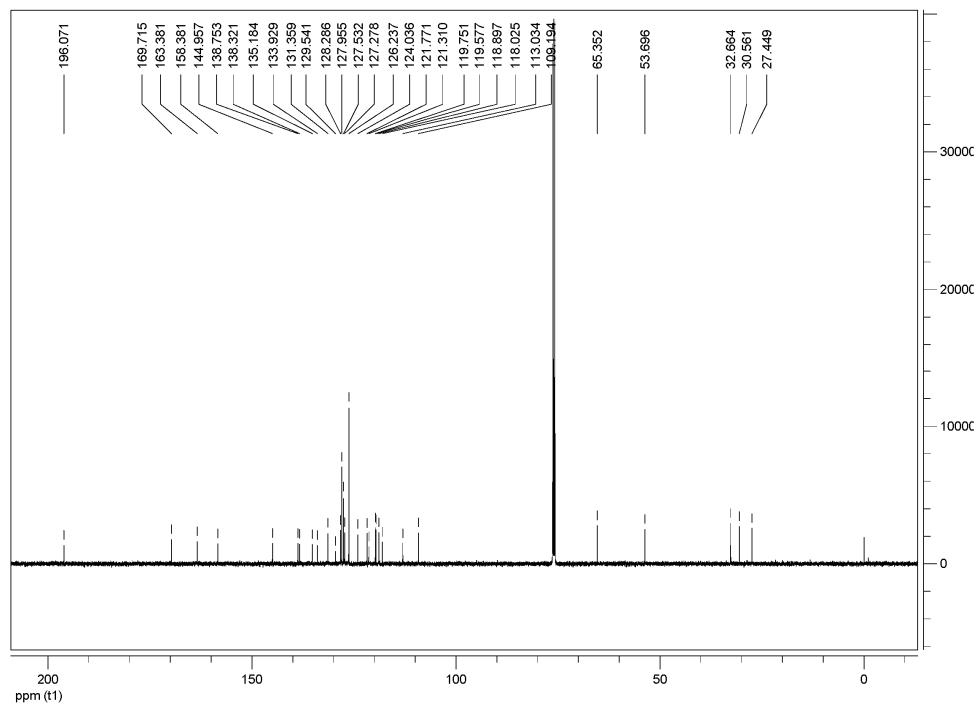


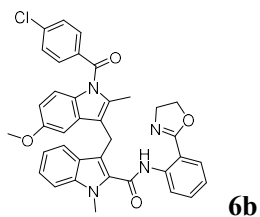


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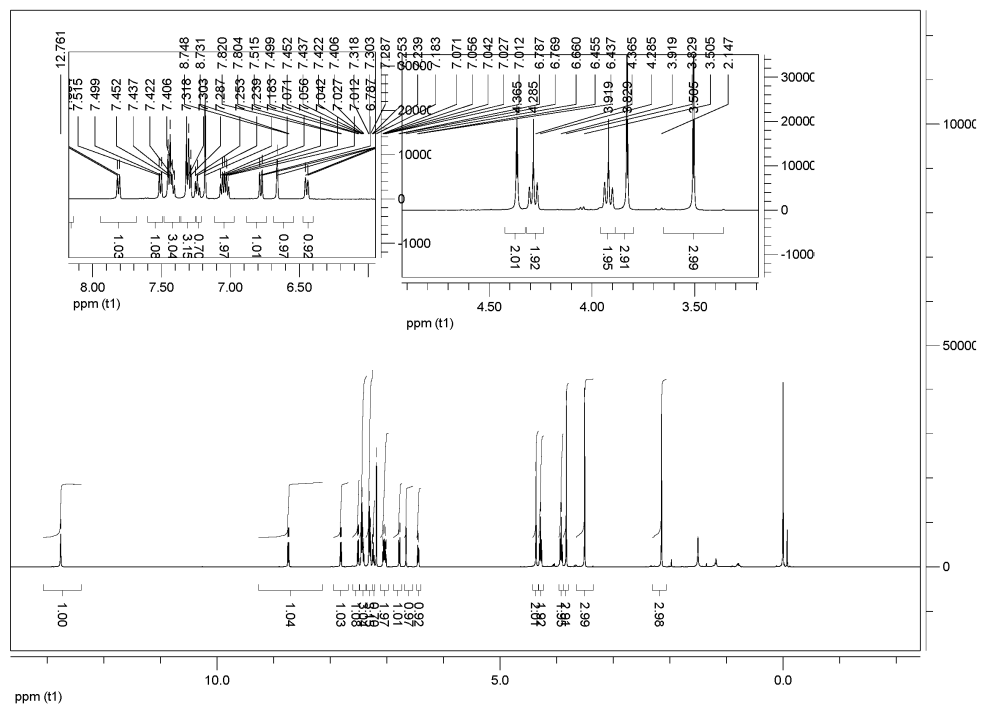


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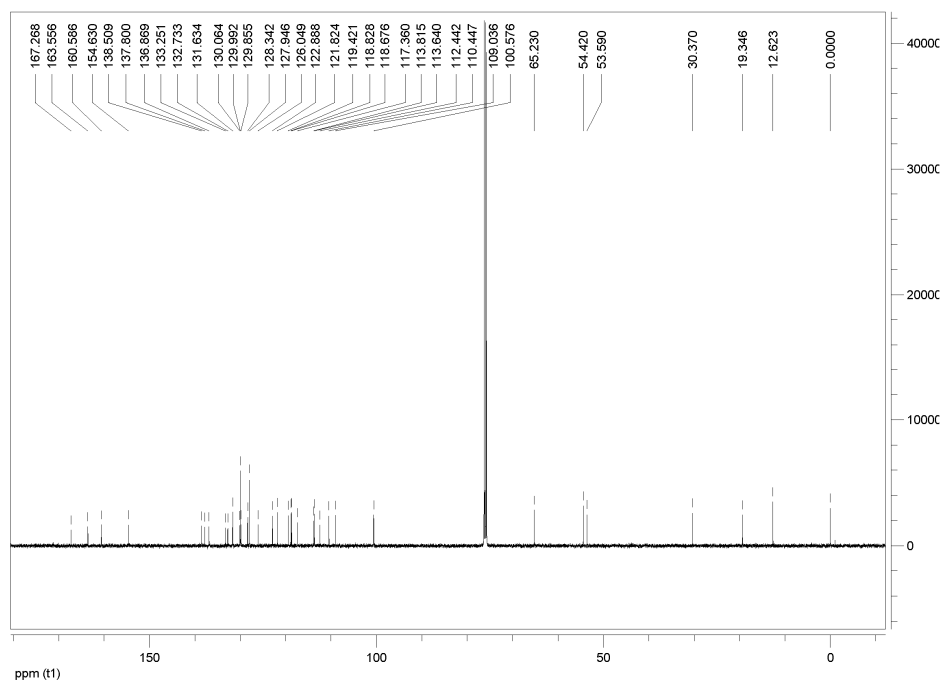




¹H-NMR



¹³C-NMR



Reference

1. I. Mutule, E. Suna, K. Olofsson and B. Pelcman, *The Journal of Organic Chemistry*, 2009, **74**, 7195-7198.