Supplementary information

Development and Assessment of 1,5-Diarylpyrazole/Oxime Hybrids Targeting EGFR and JNK-2 as Antiproliferative Agents: A Comprehensive Study Through Synthesis, Molecular Docking, and Evaluation

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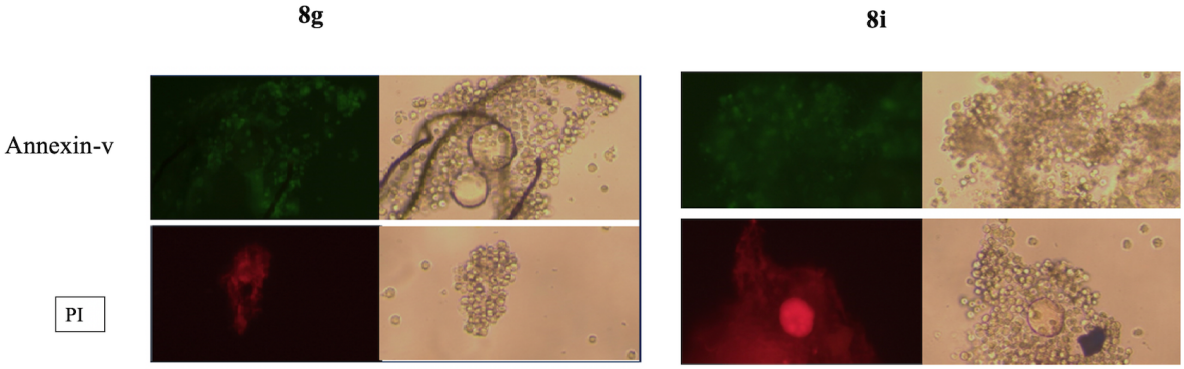


Figure S1. Microscopic examination of apoptosis and necrosis of compounds **8g** and **8i** using annexin-v and PI on Hela cell line. Treatment with 8 μM annexin-v and 16 μM PI for **8g**, and Treatment with 2.5 μM annexin-v and 1.5 μM PI for **8i**.

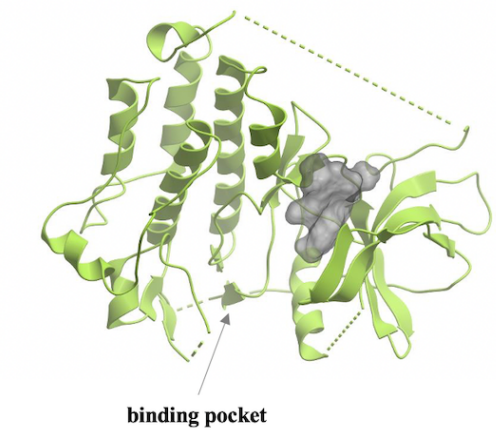


Figure S2. Ribbon representation of EGFR showing the binding pocket with a grey skin mesh (PDB ID: 4ZAU).

Table S1. Calculated binding properties of test compounds and sorafenib against EGFR.

Test compounds	Binding score	Hydrogen bonding energy (Kcal/mol)	Hydrophobic interaction energy (Kcal/mol)
Sorafenib	-38.13	-2.52	-7.12
8d	-32.33	-1.19	-7.97
8g	-16.46	-2.25	-7.62
8i	-12.98	-2.47	-7.50
10c	-23.74	-3.36	-7.35

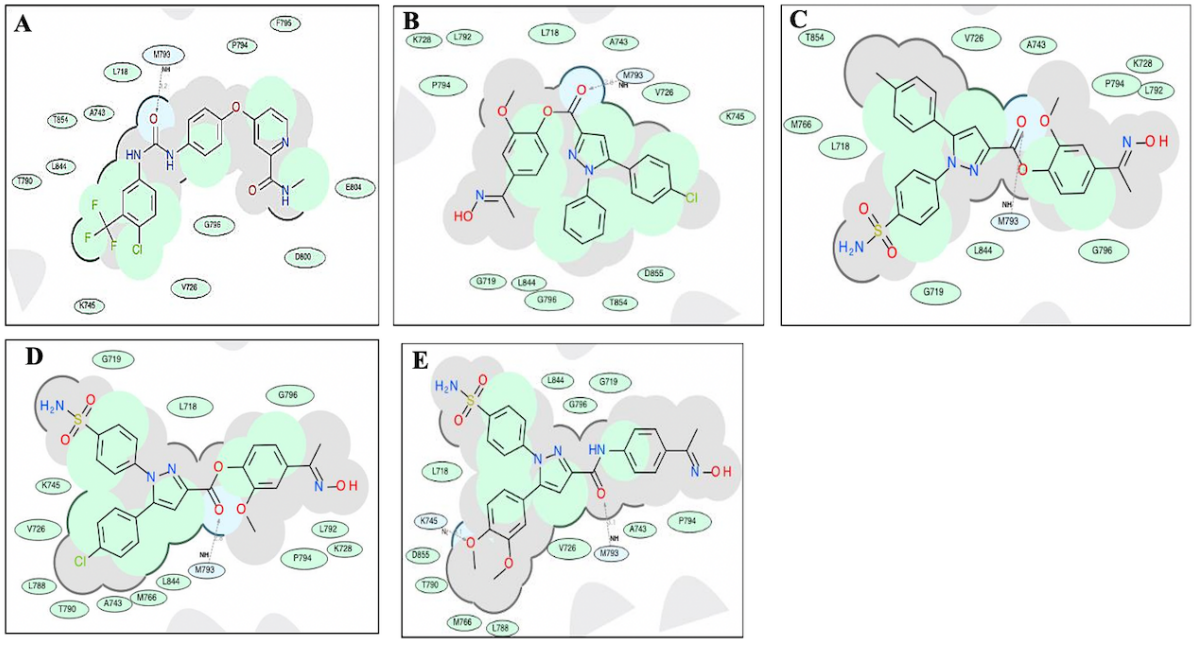


Figure S3. (A-E) Docking pose of sorafenib at the EGFR binding pocket.

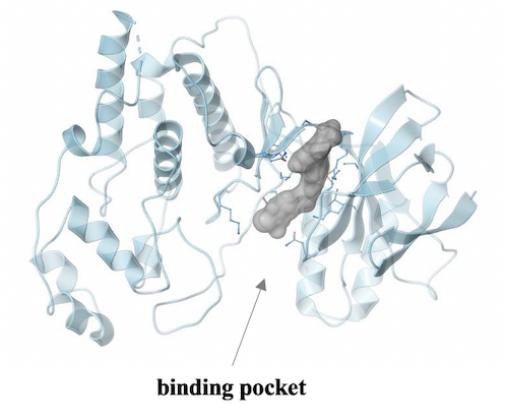


Figure S4. Ribbon representation of JNK-2 showing the binding pocket with a grey skin mesh (PDB ID: 3E7O) [15].

Table S2. Calculated binding properties of test compounds andsorafenib against JNK-2.

Test compounds	Binding score	Hydrogen bonding energy (Kcal/mol)	Hydrophobic interaction energy (Kcal/mol)	Van der Waals interaction energy (Kcal/mol)
Sorafenib	-21.48	-2.72	-8.46	-35.60
8d	-9.16	-0.99	-7.97	-33.70
8i	-12.00	-3.19	-7.66	-32.59

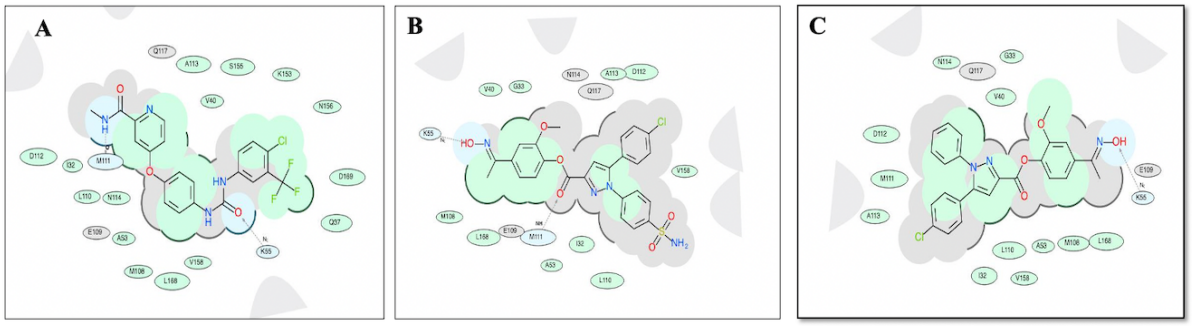
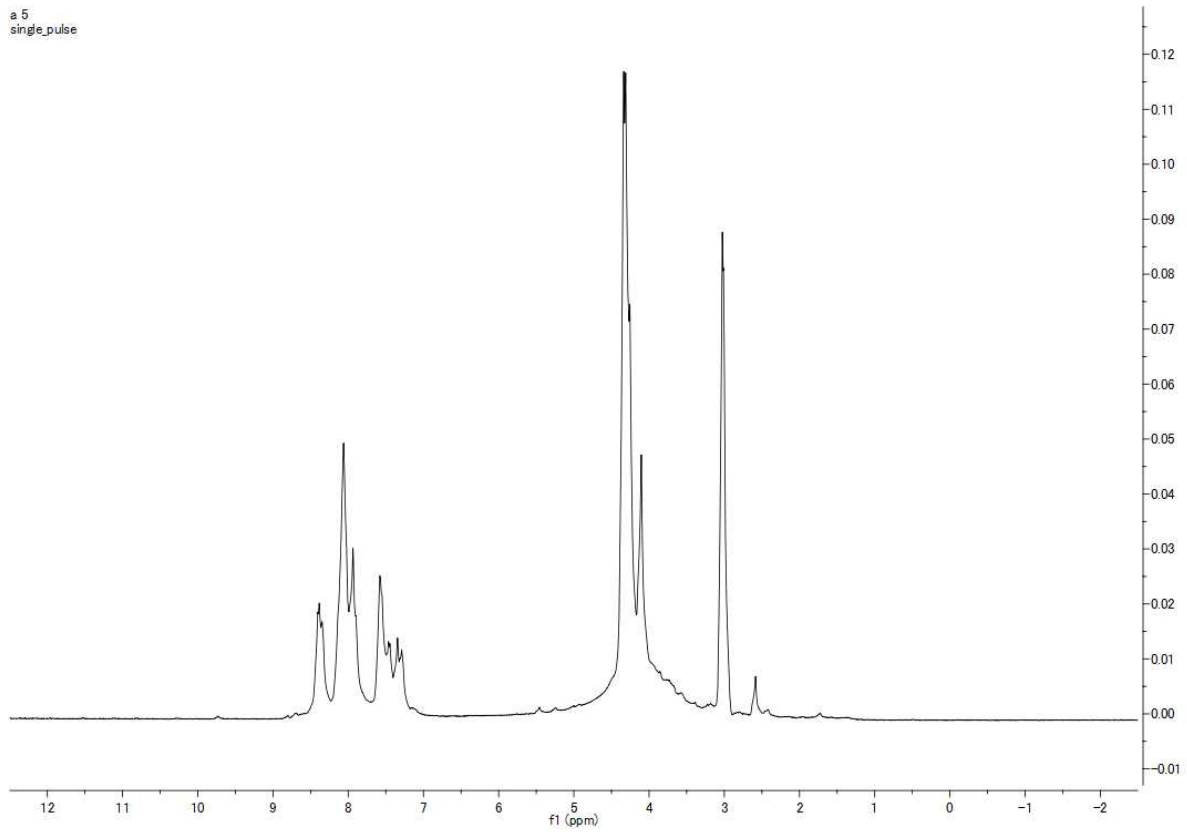
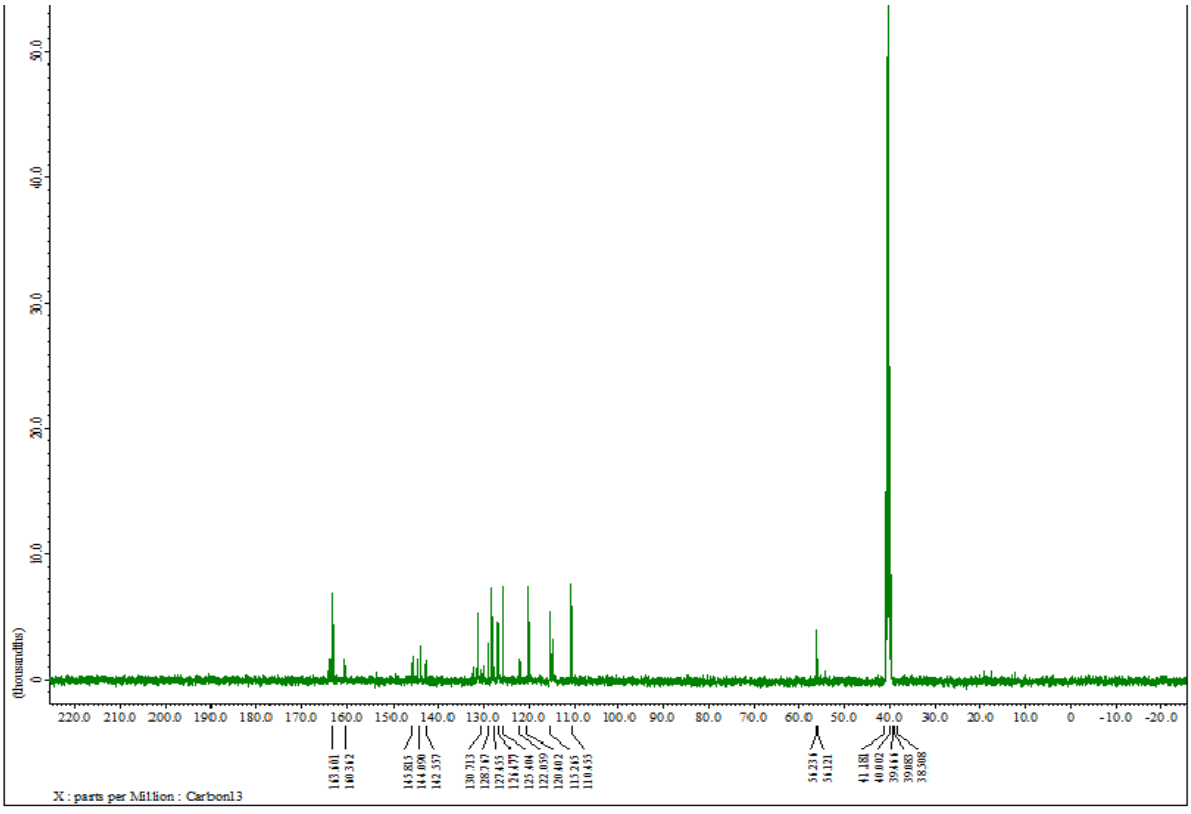


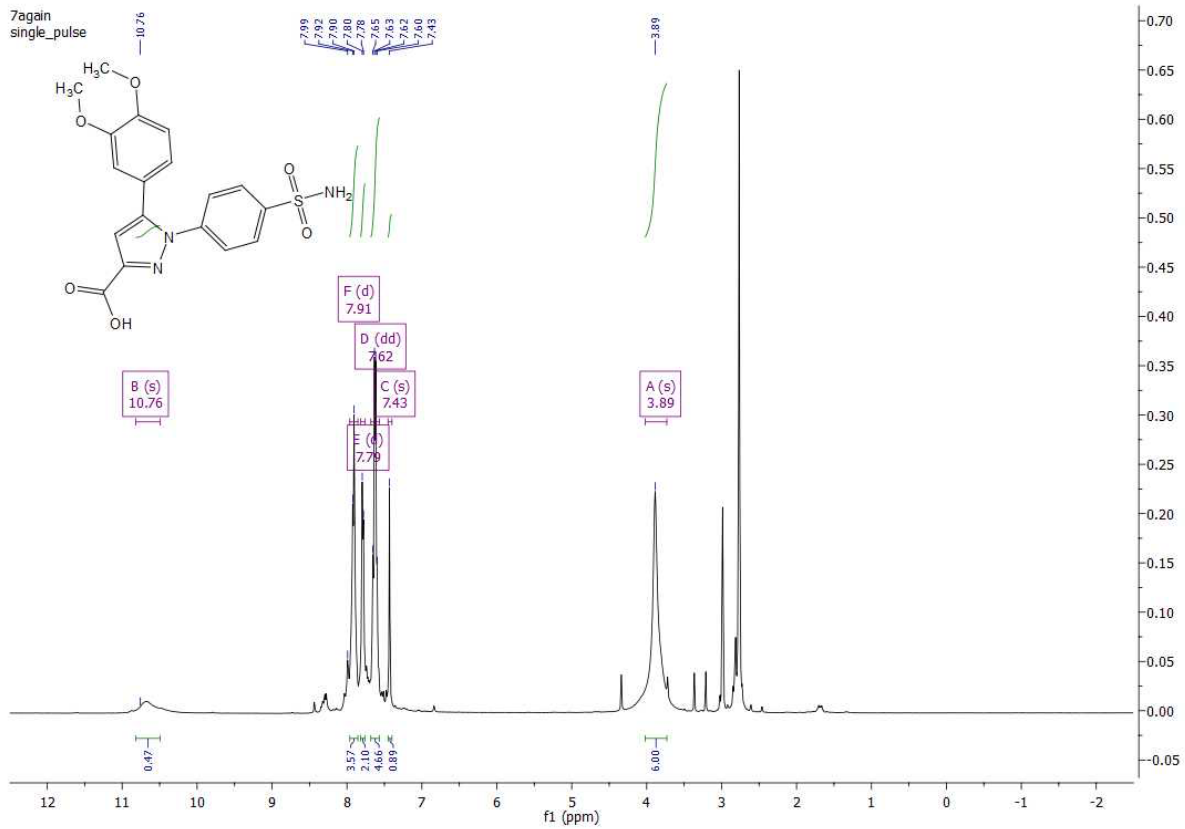
Figure S5. (A-C) Docking pose of sorafenib at the JNK-2 binding pocket.



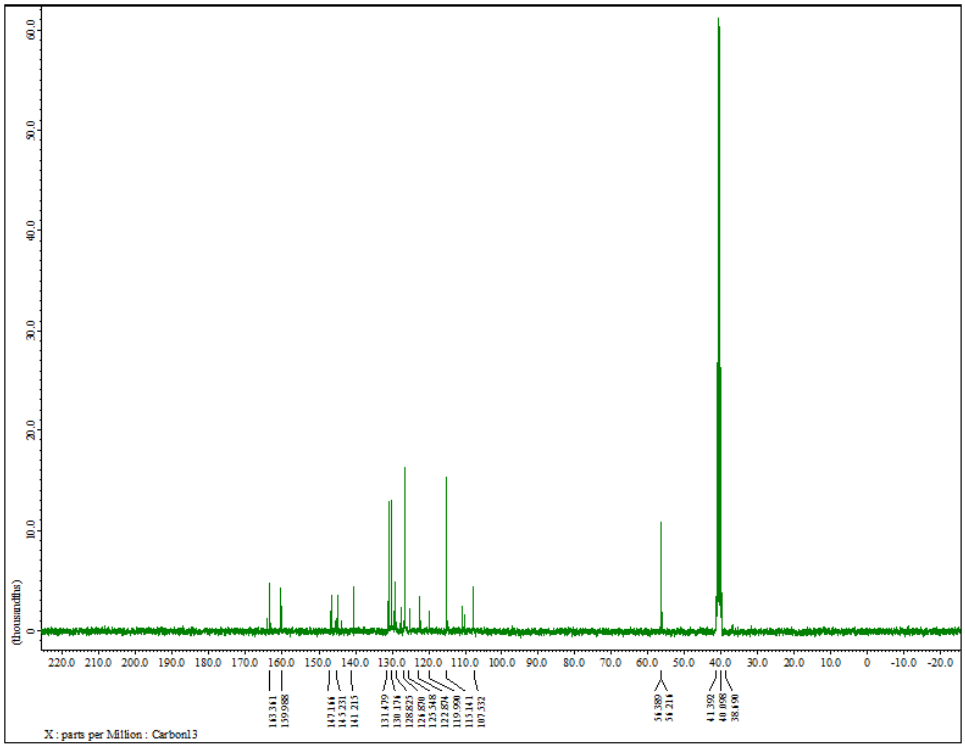
^{1}H-NMR of compound **6e** in DMSO-*d6*.



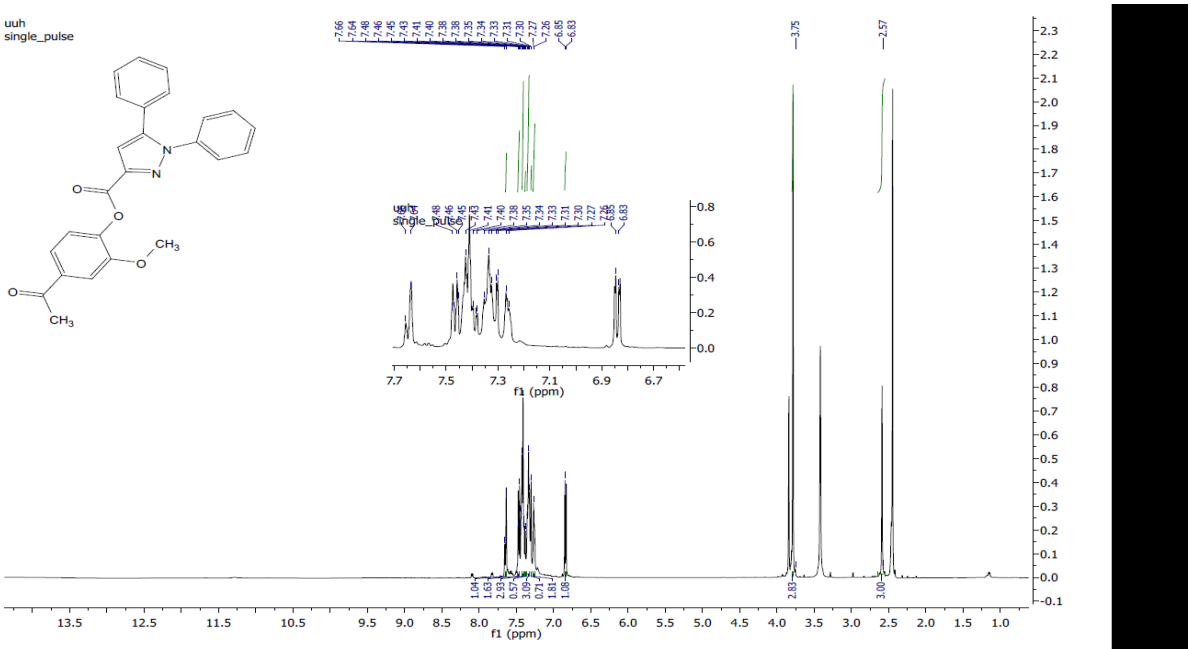
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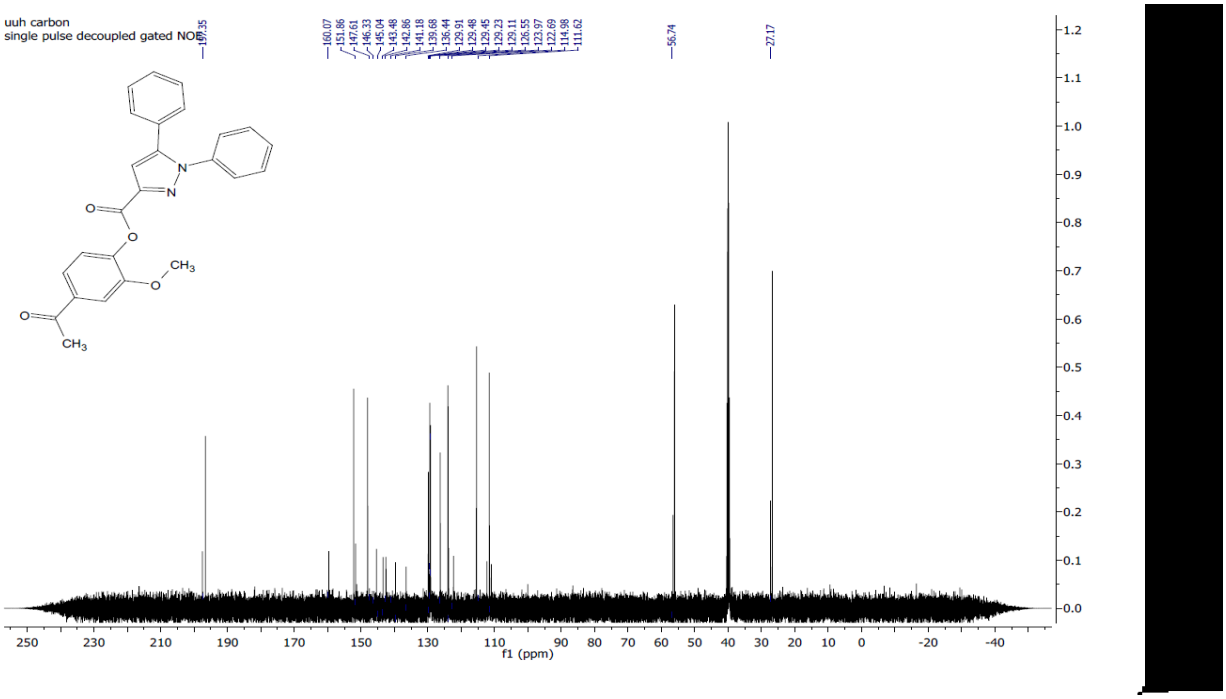
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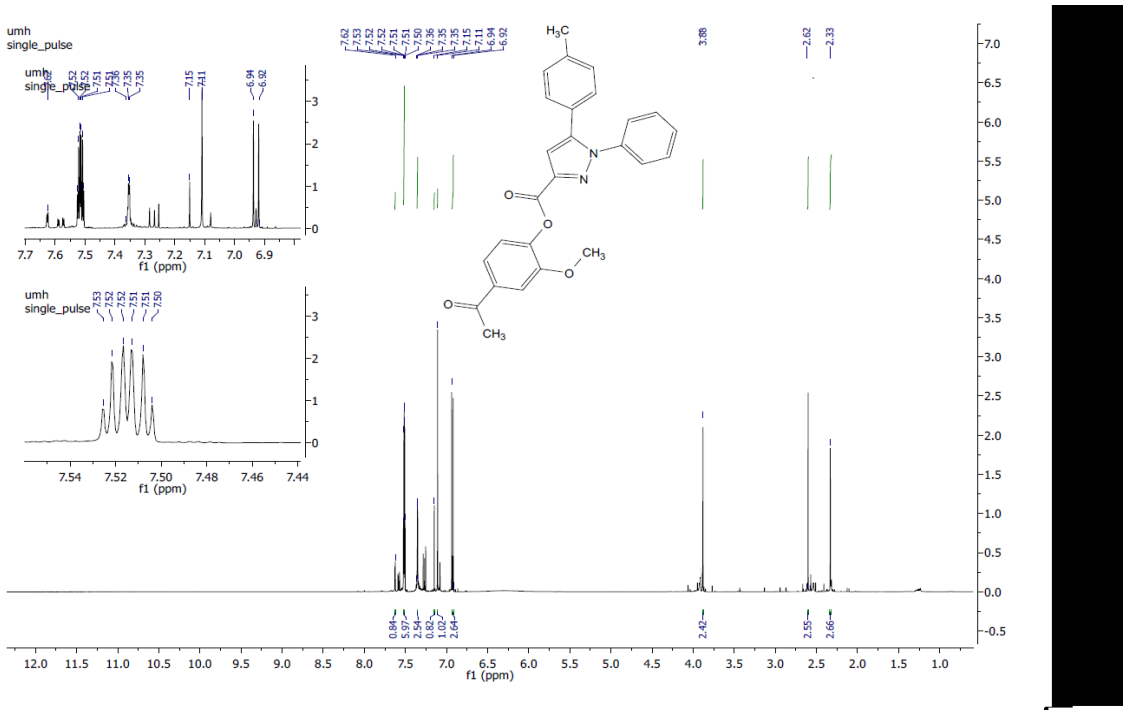
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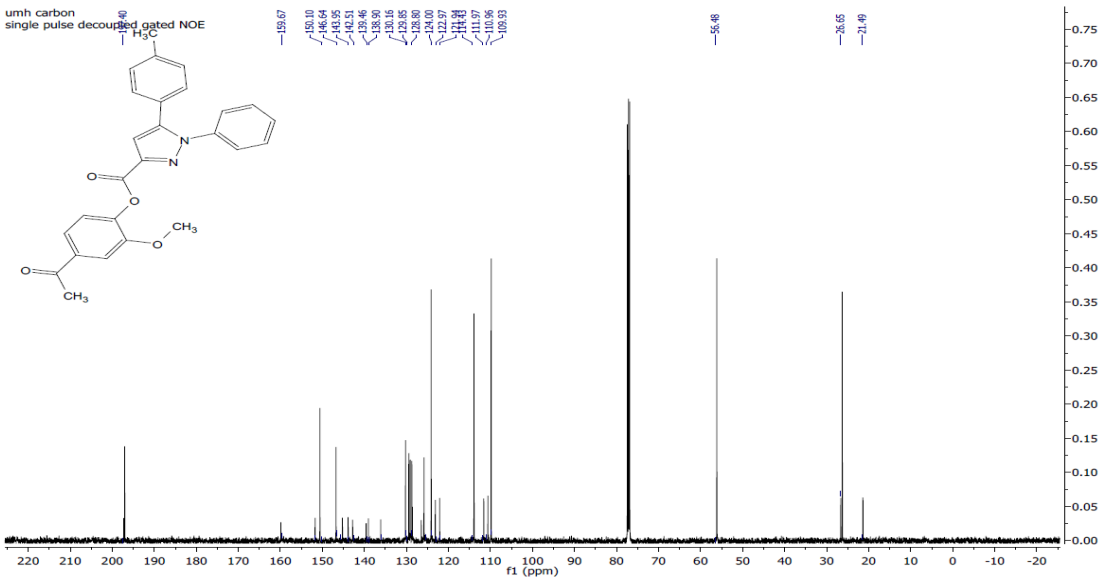
^{1}H-NMR of compound **7a** in DMSO-*d6*.



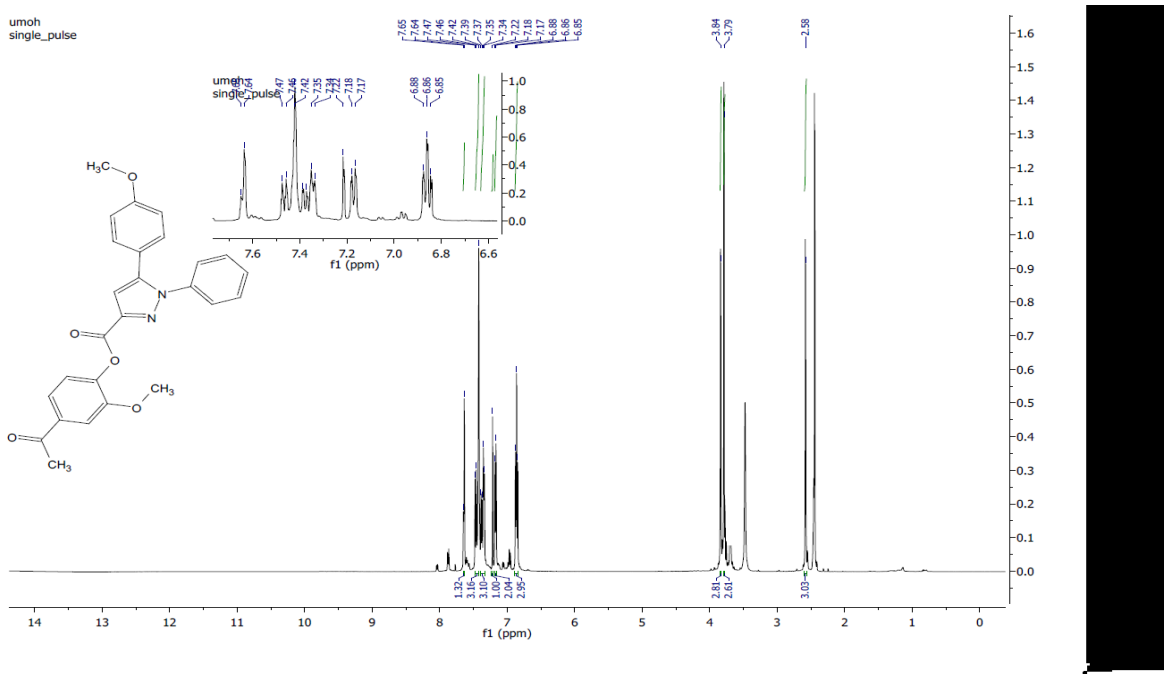
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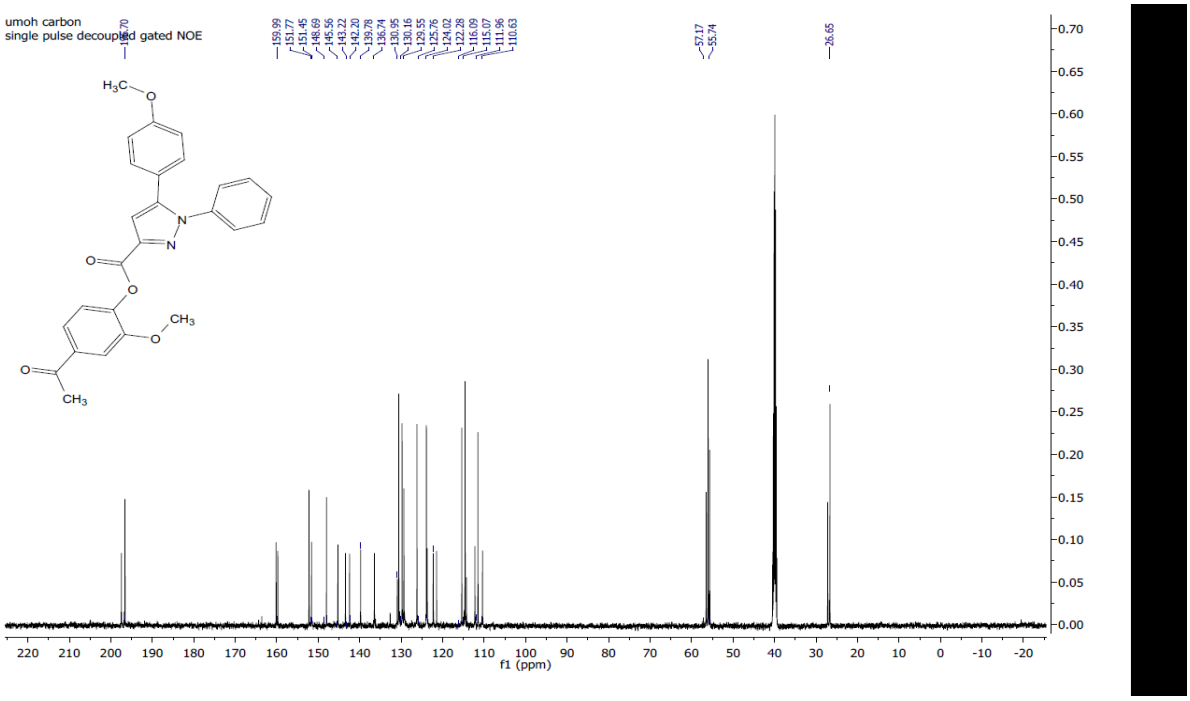
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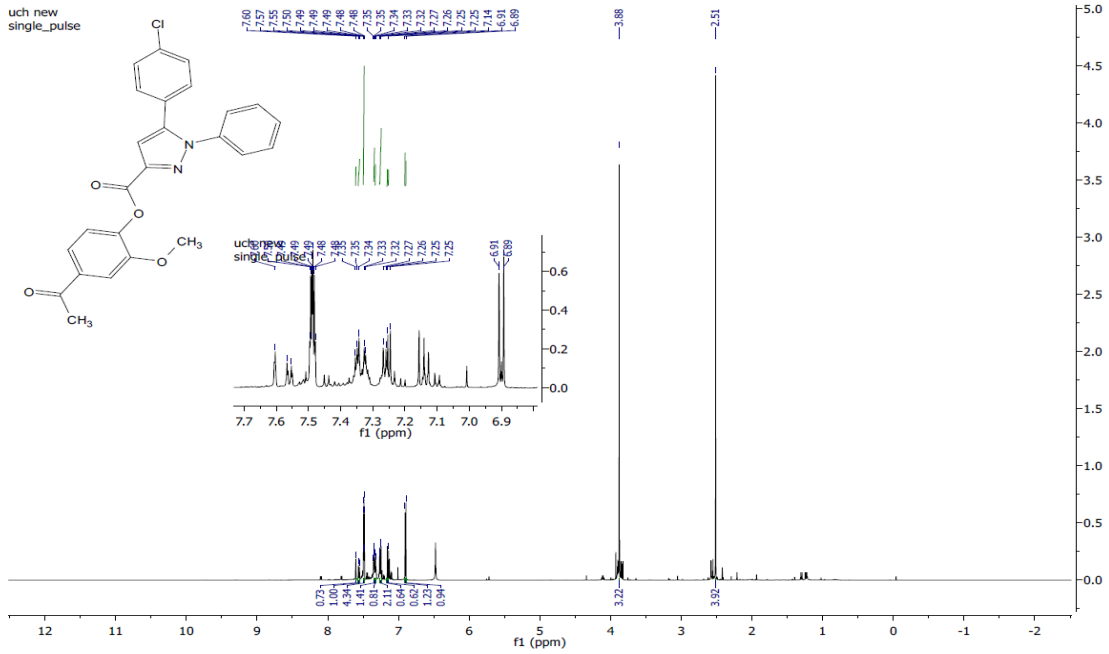
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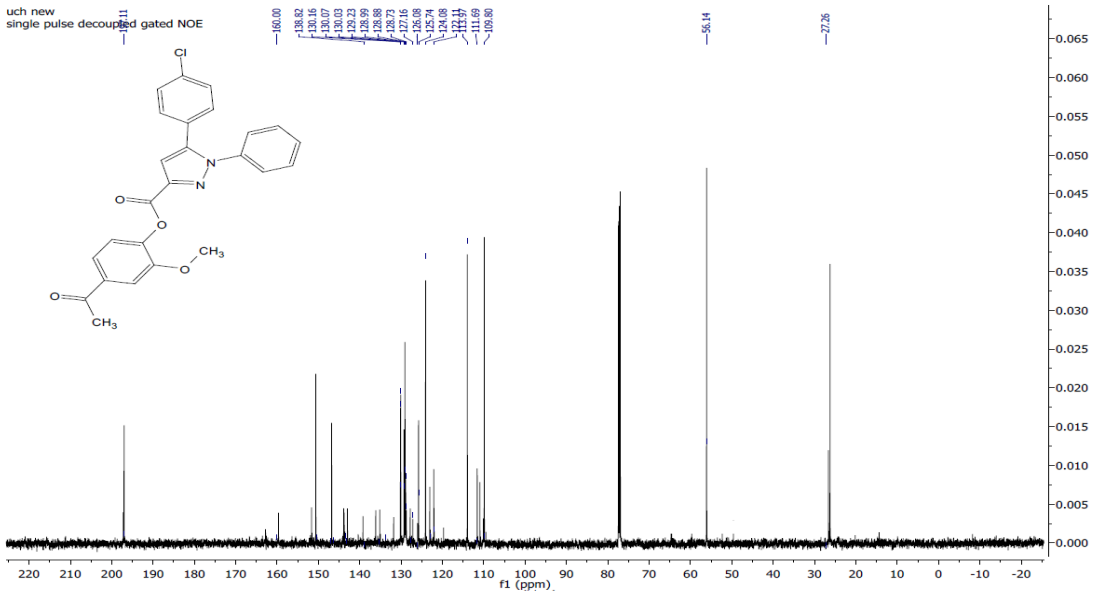
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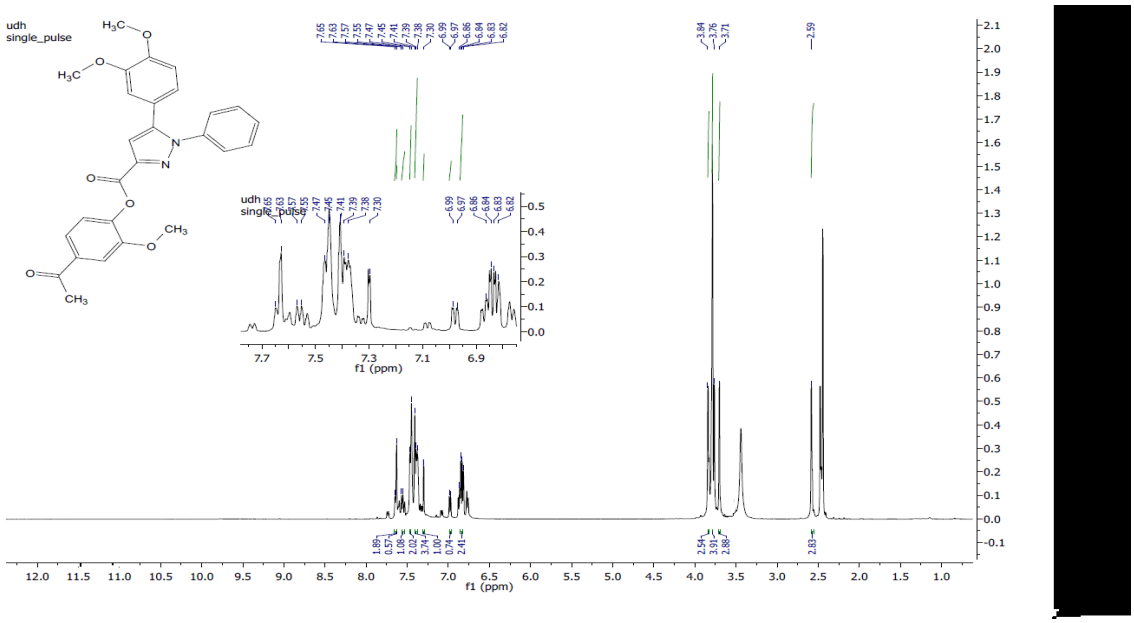
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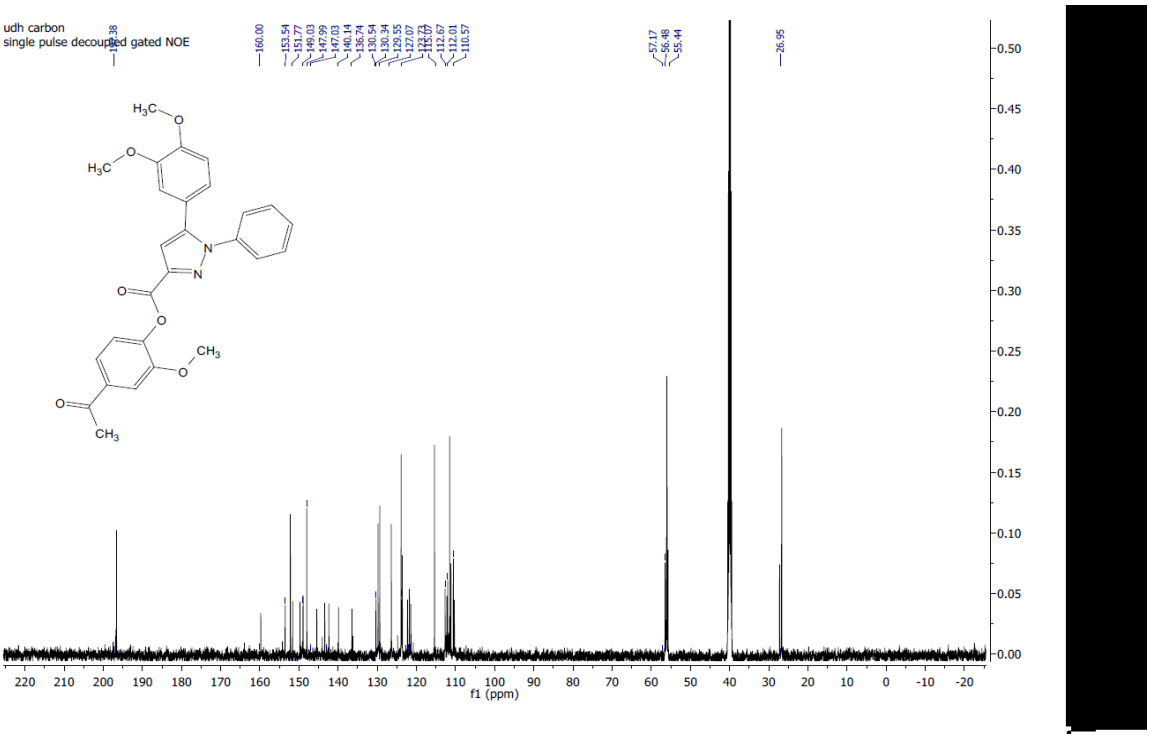
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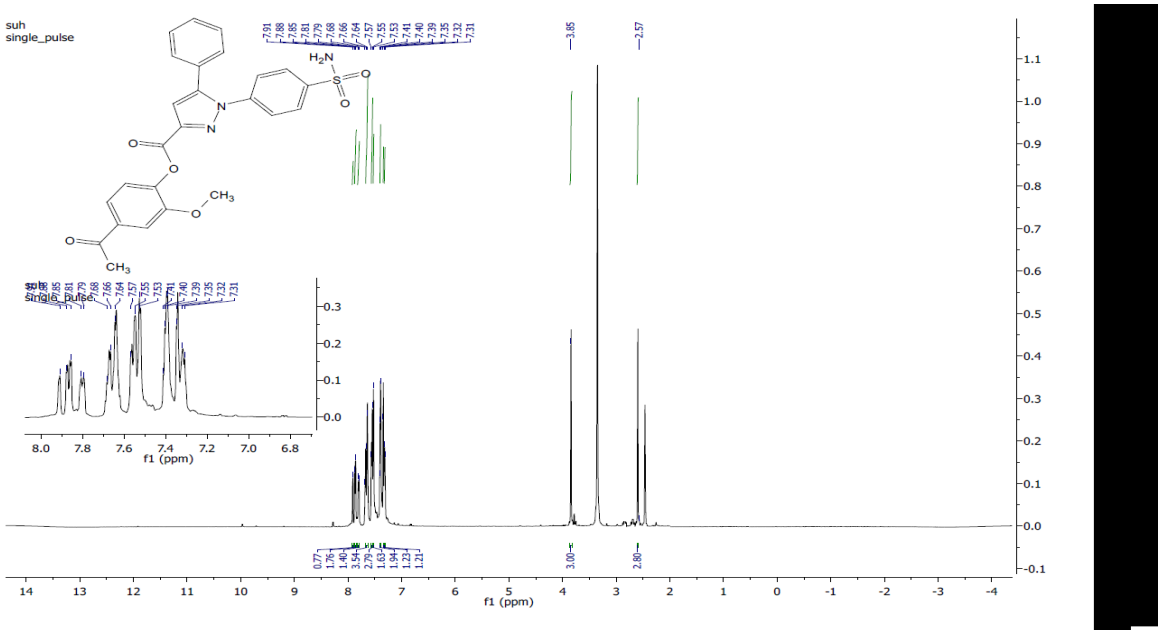
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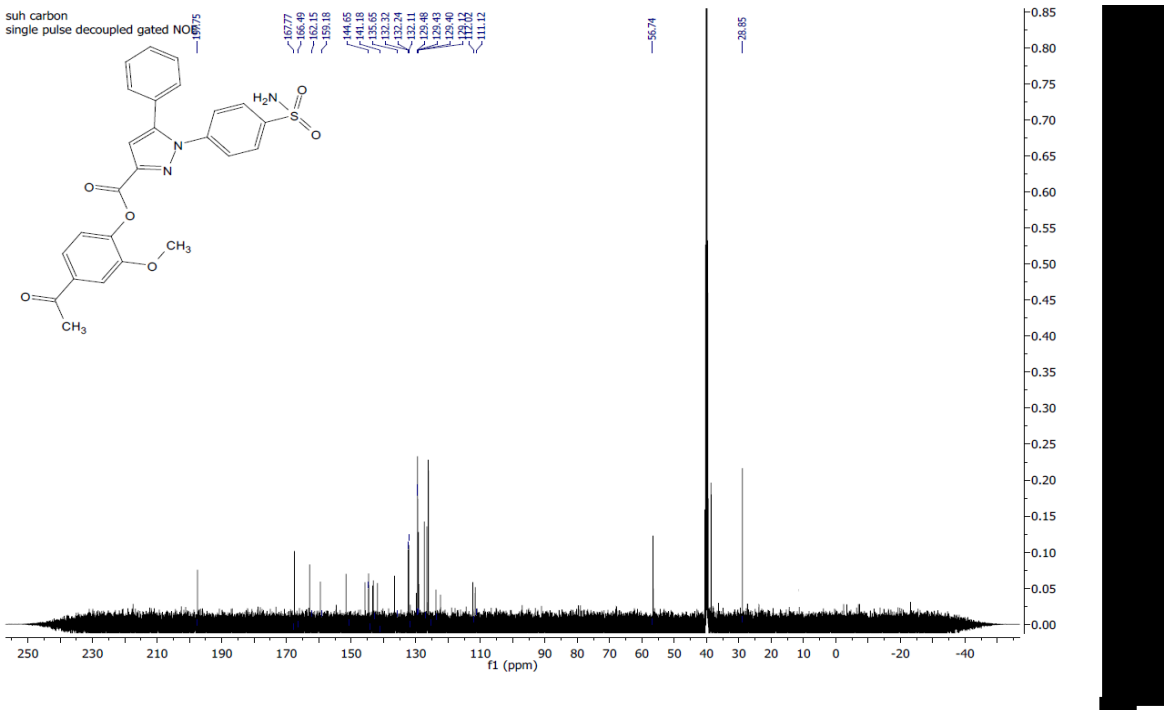
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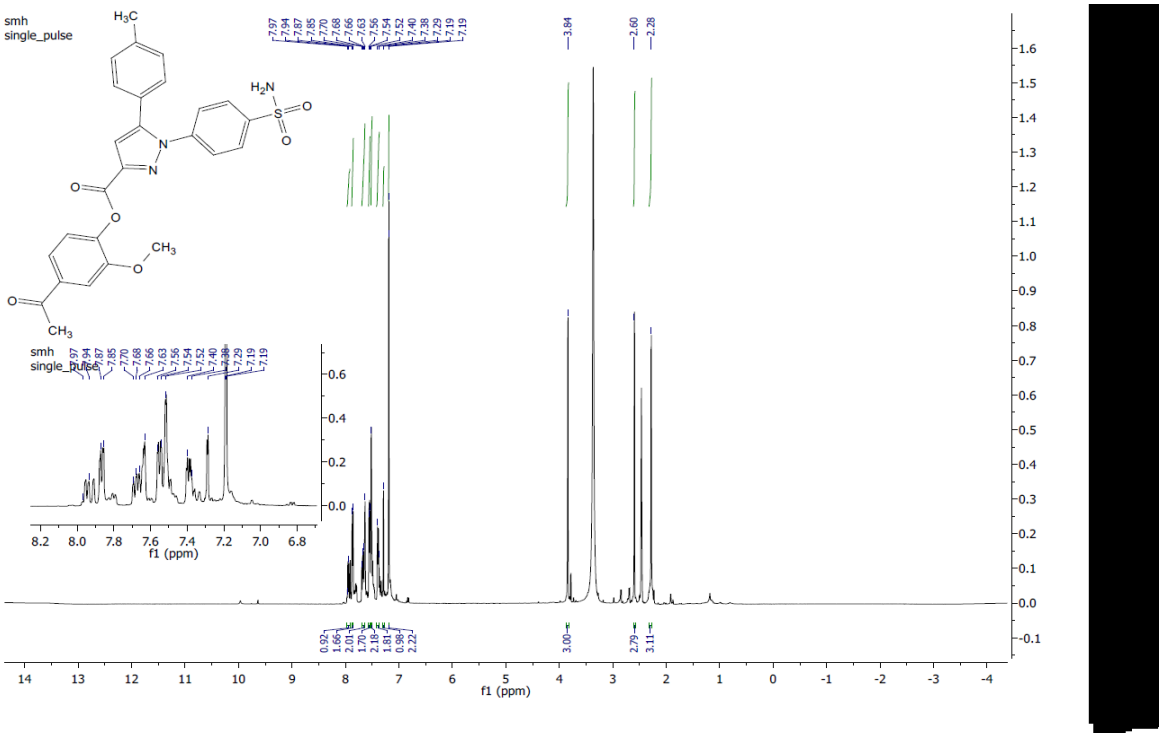
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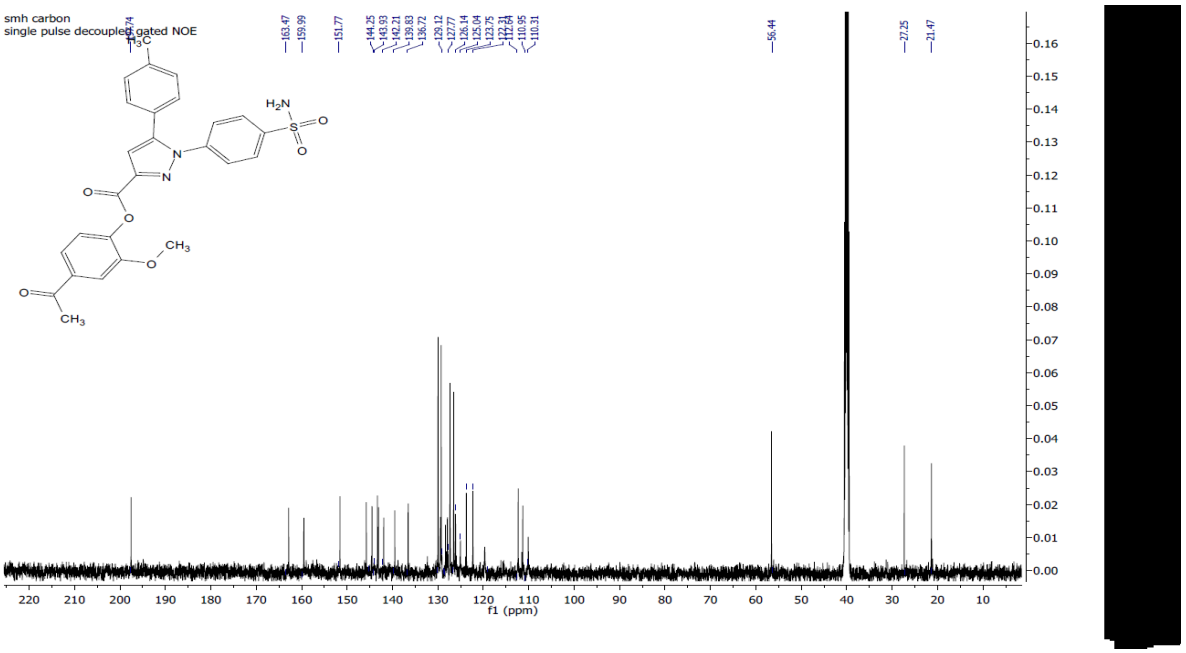
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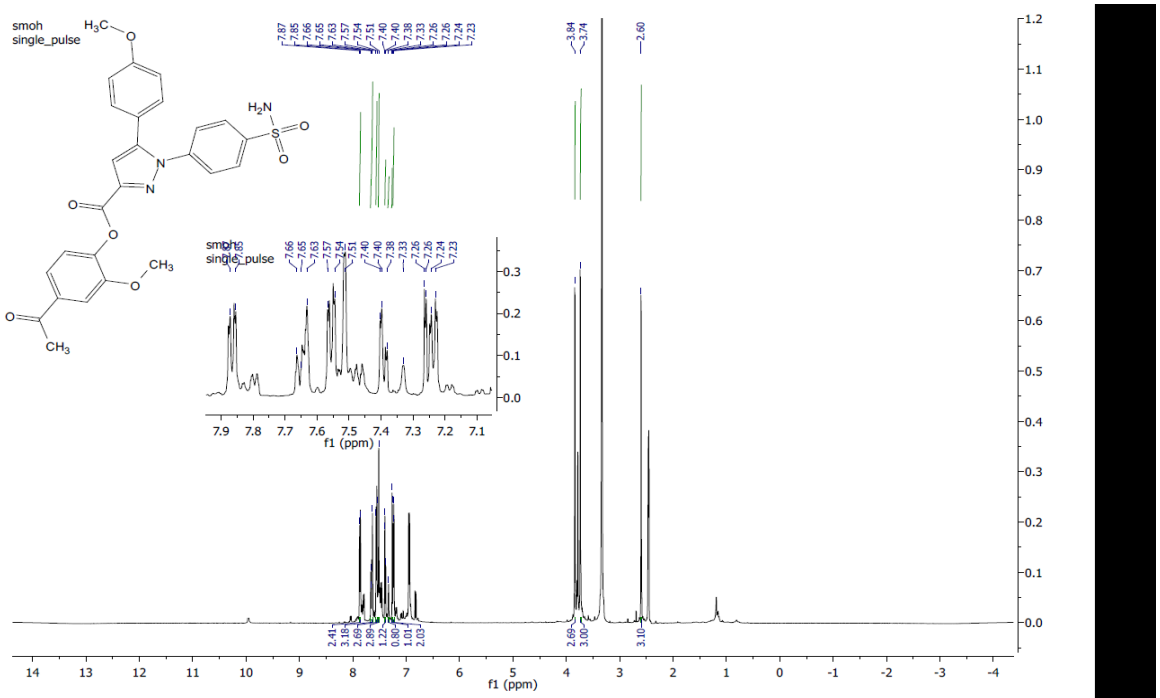
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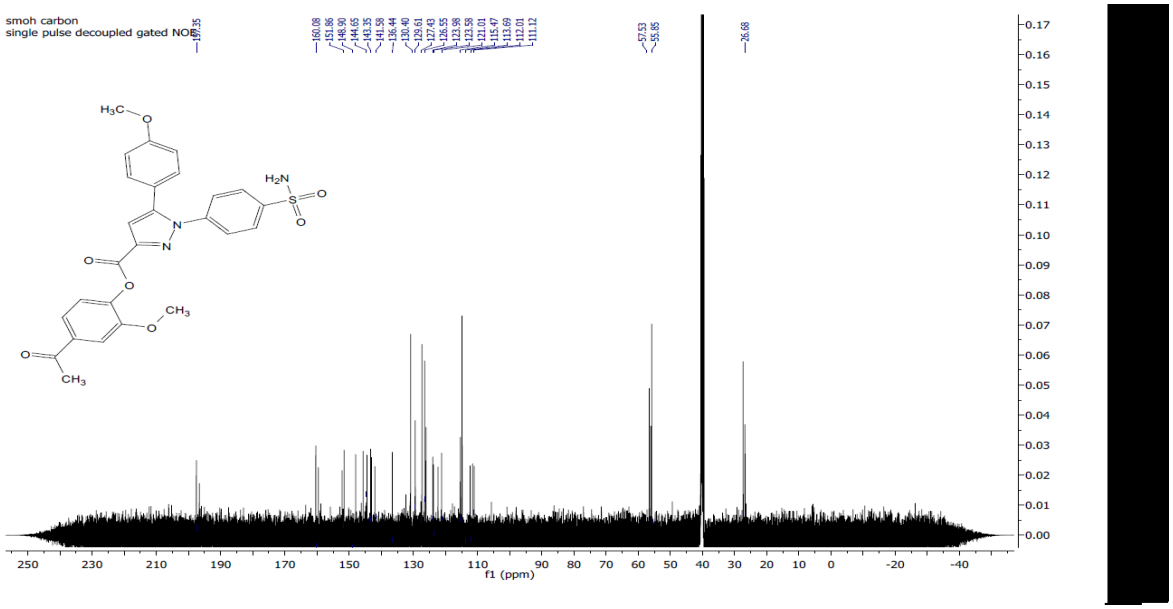
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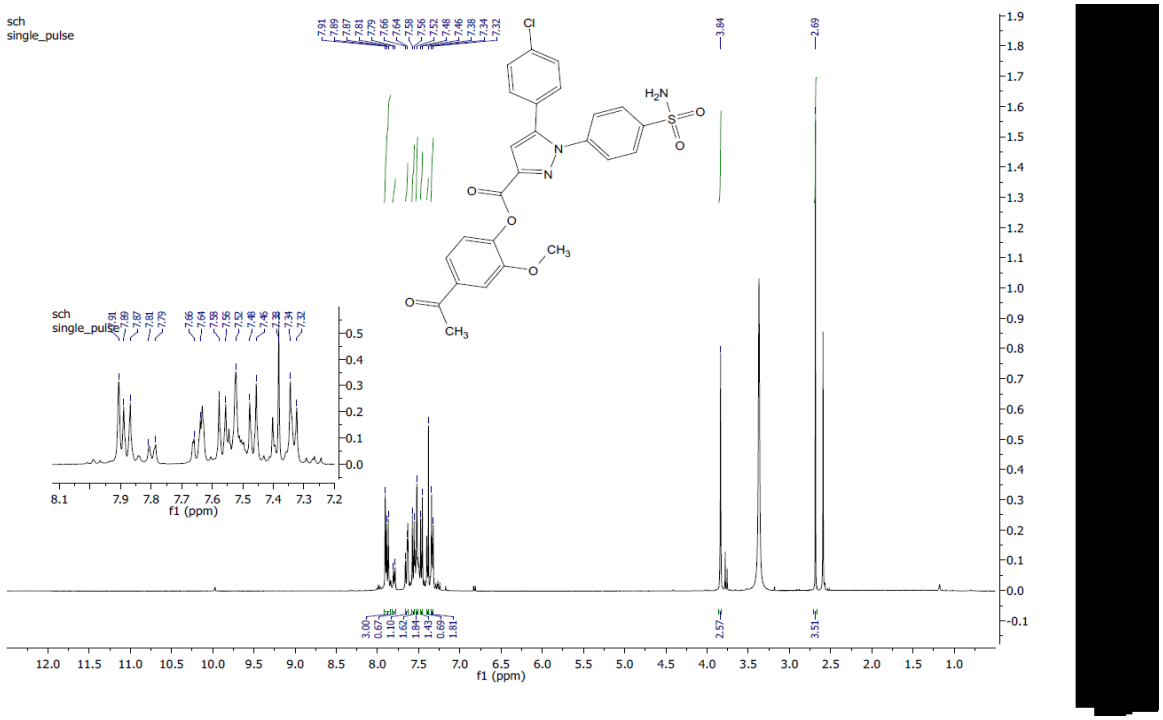
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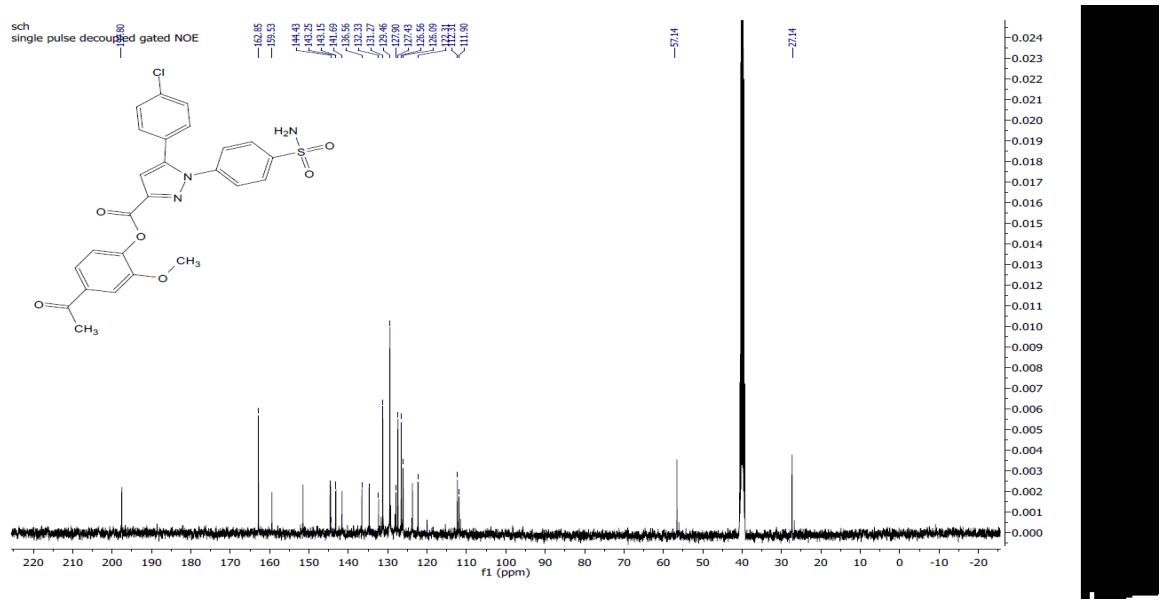
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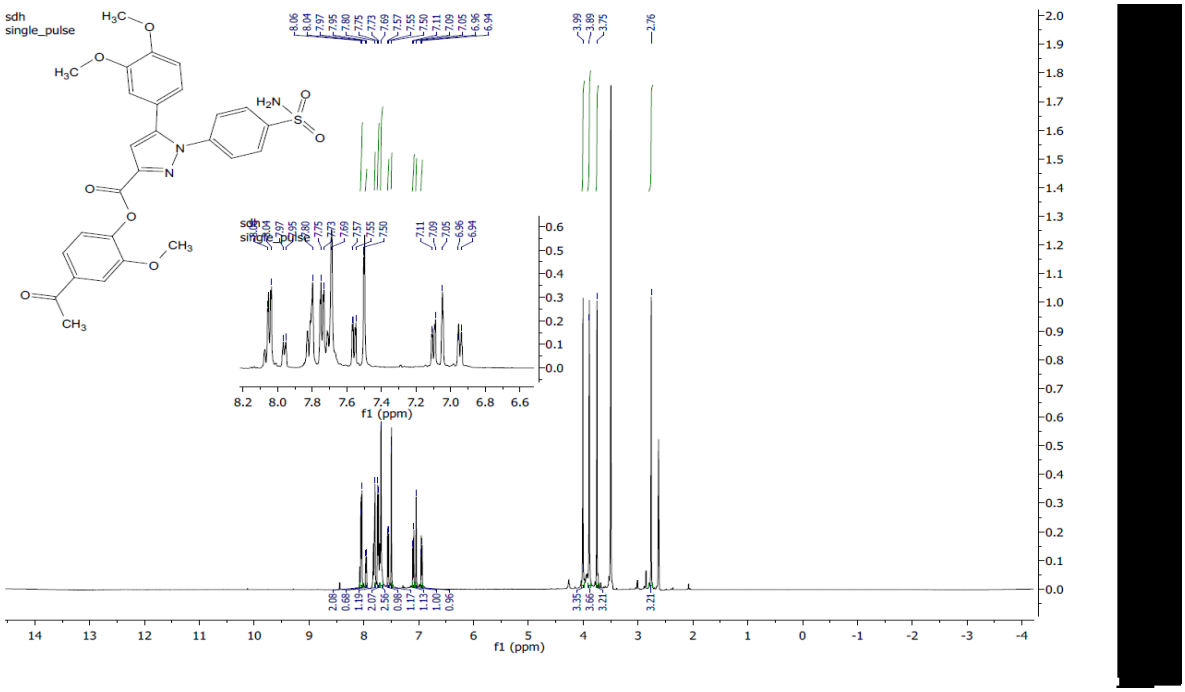
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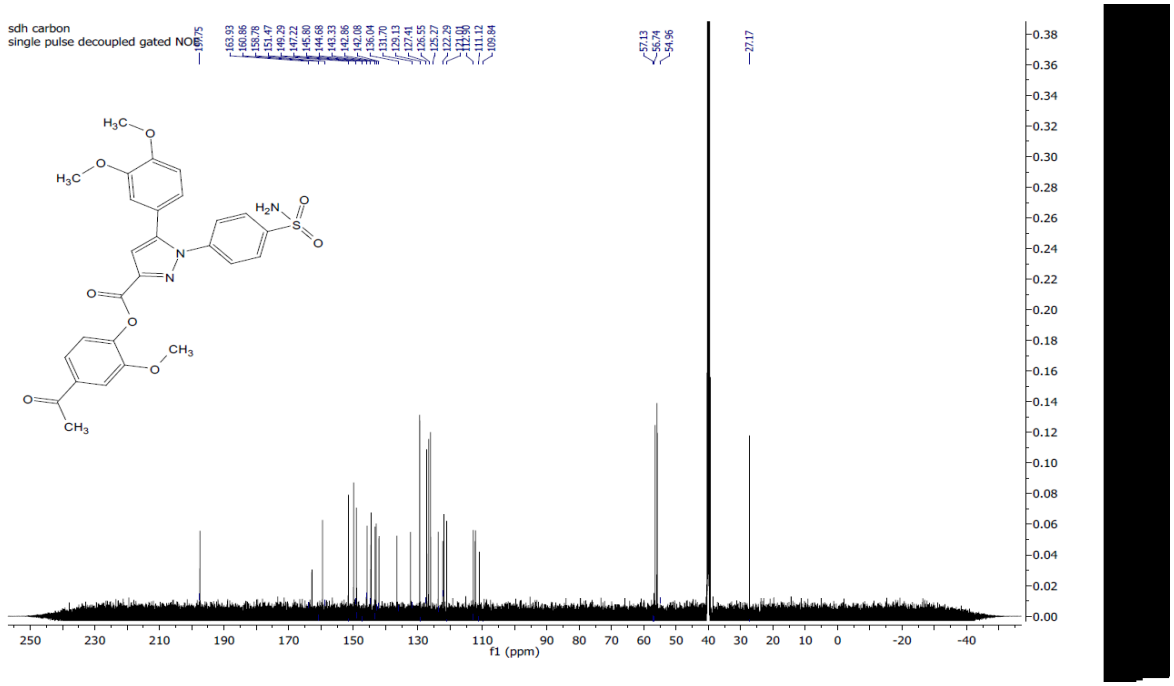
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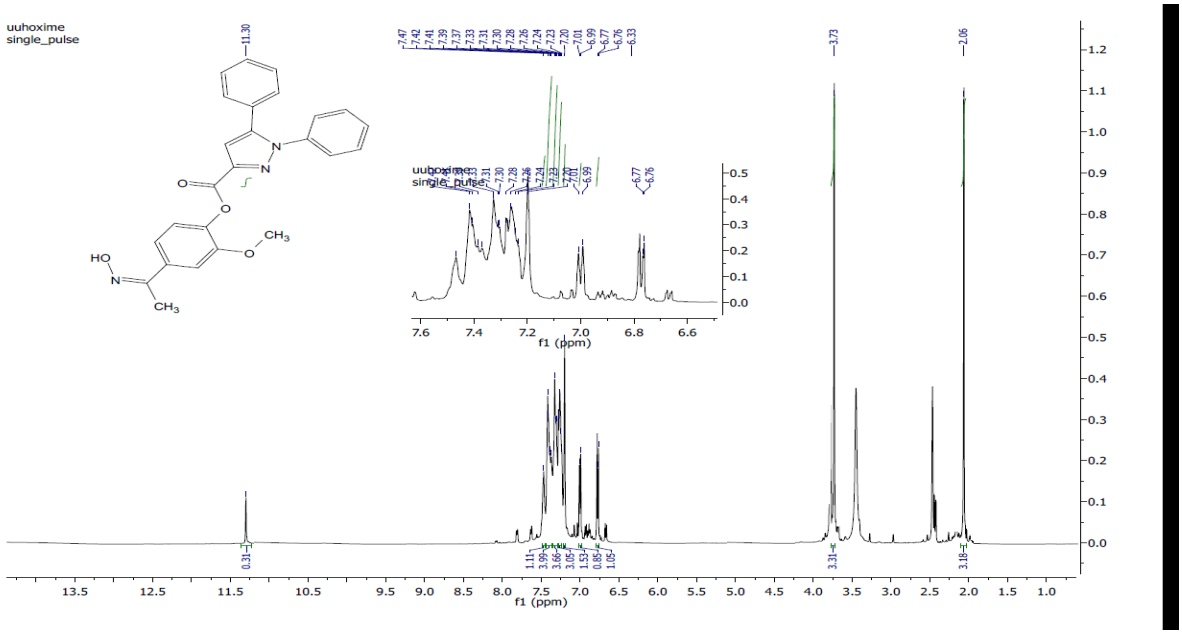
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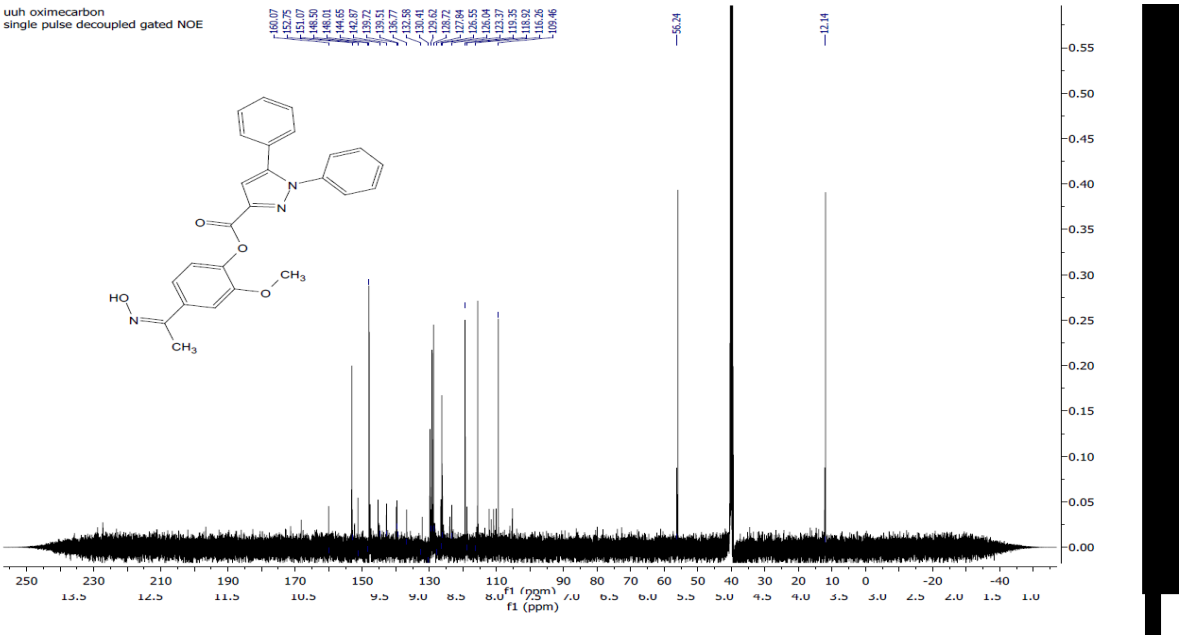
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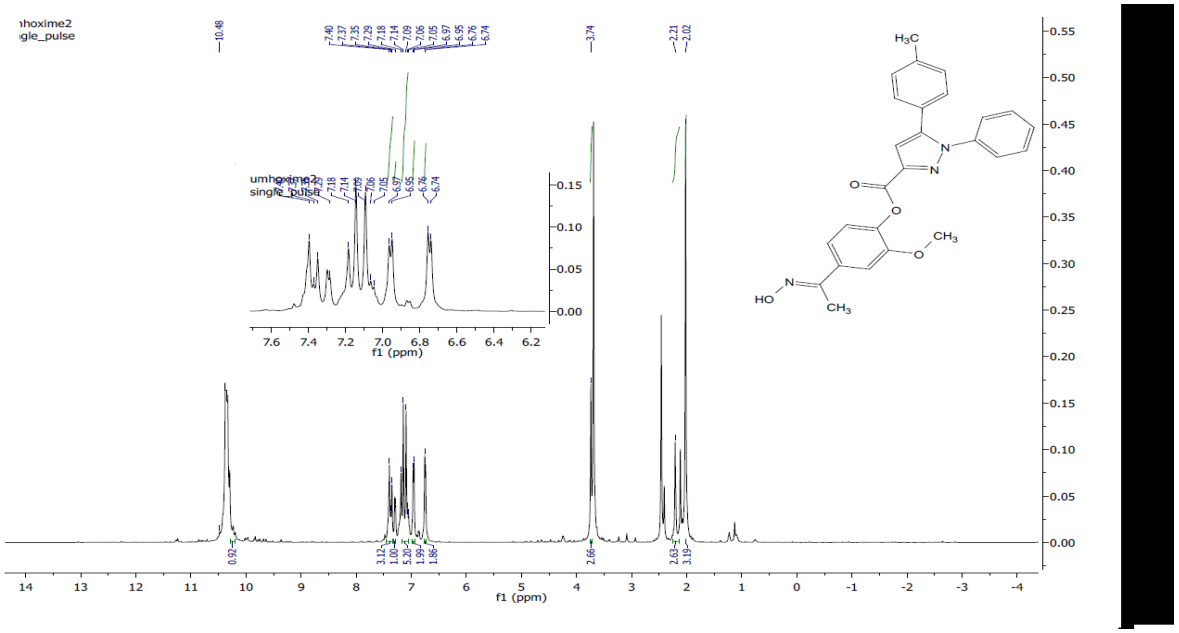
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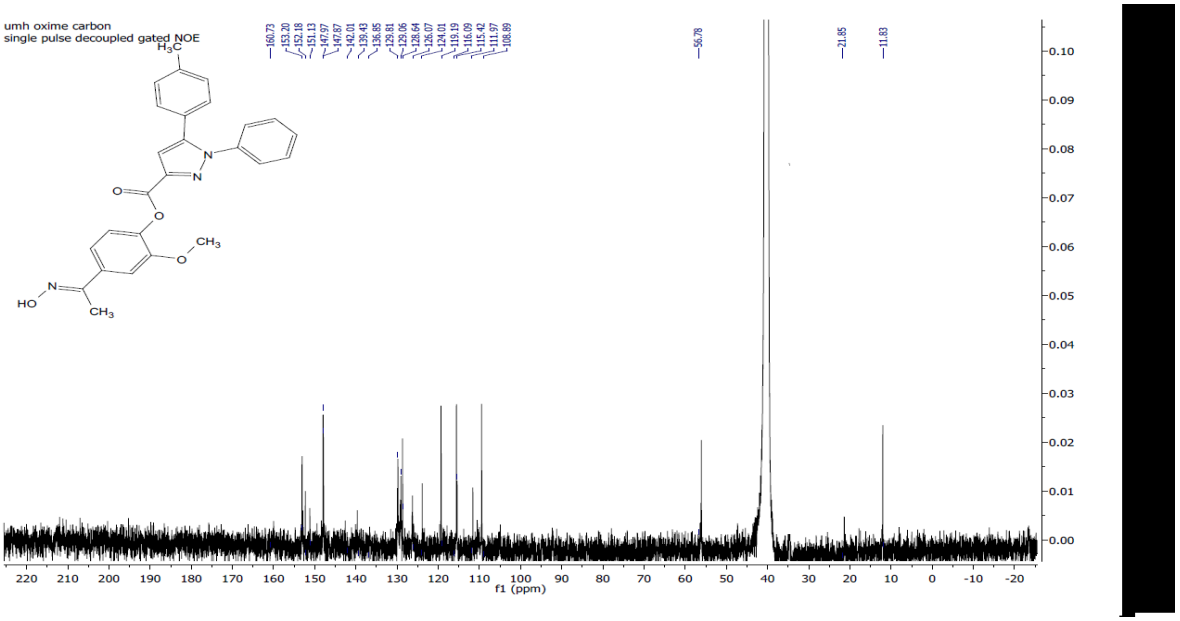
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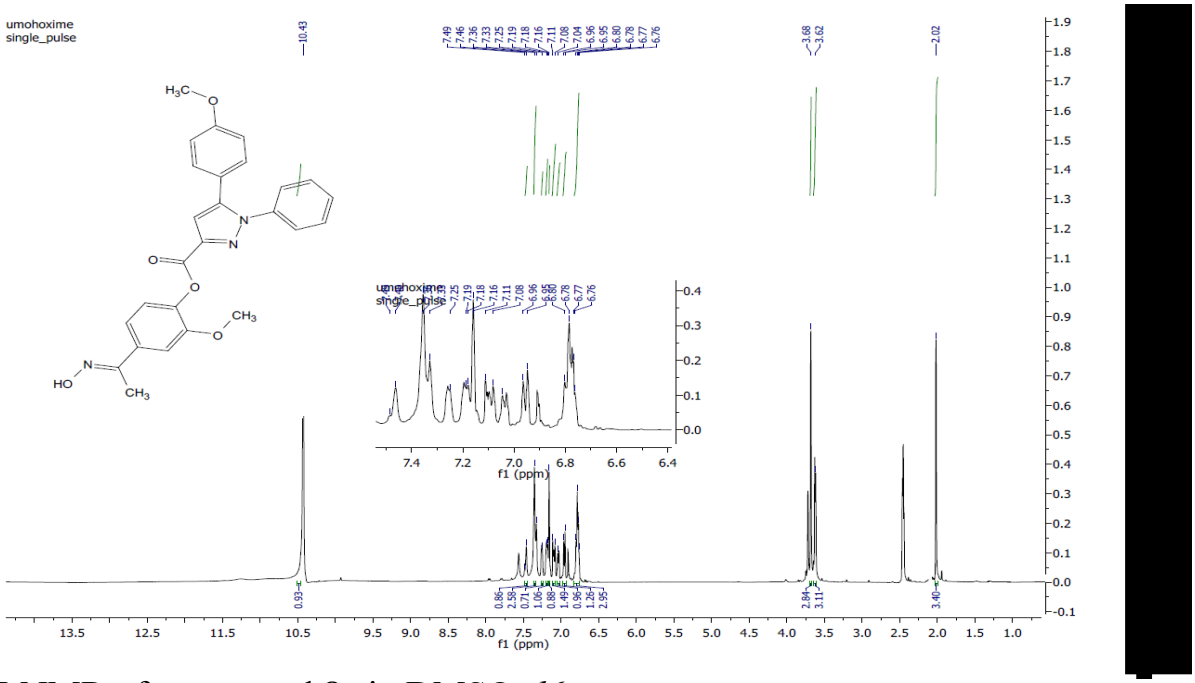
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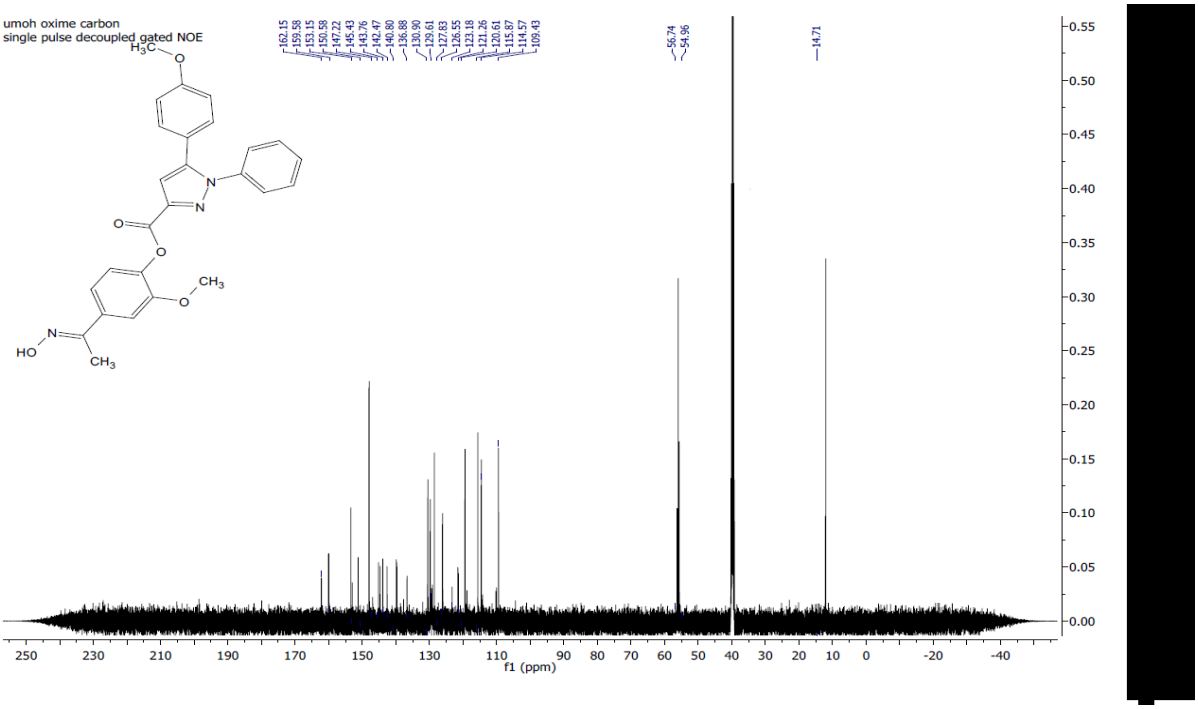
^{1}H-NMR of compound **8b** in DMSO-*d6*.



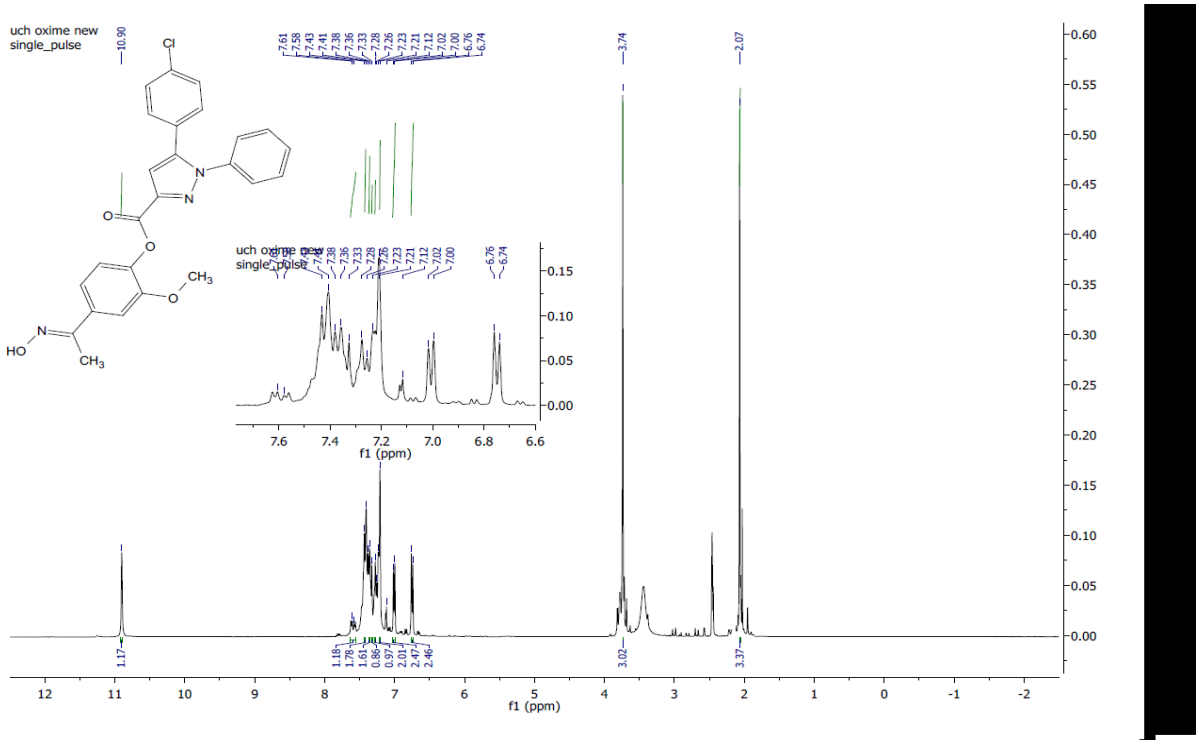
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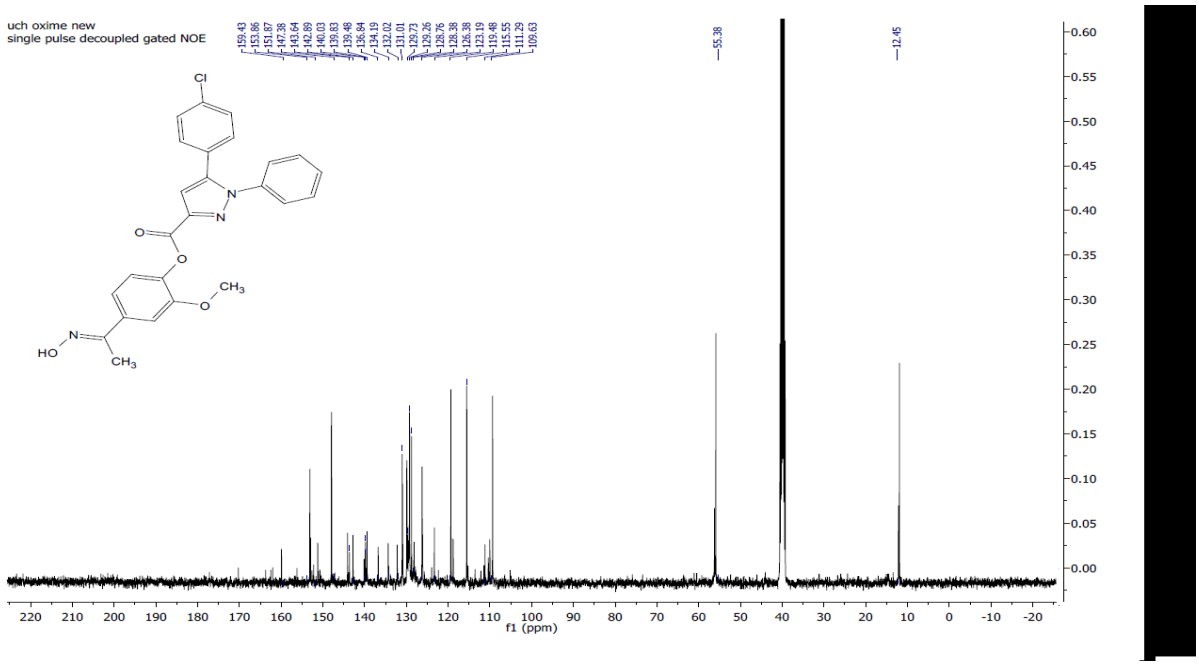
^{1}H-NMR of compound **8c** in DMSO-*d6*.



^{13}C-NMR of Compound **8c** in DMSO-*d6*.



^{1}H-NMR of compound **8d** in DMSO-*d6*.



^{13}C-NMR of Compound **8d** in DMSO-*d6*.

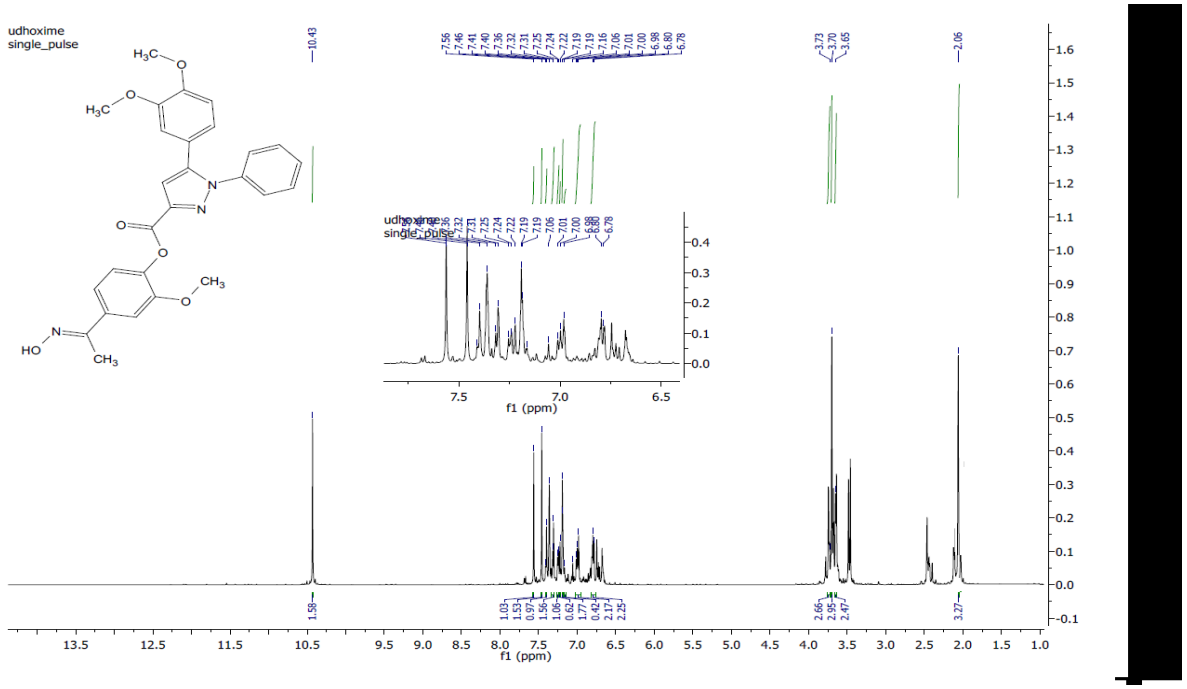
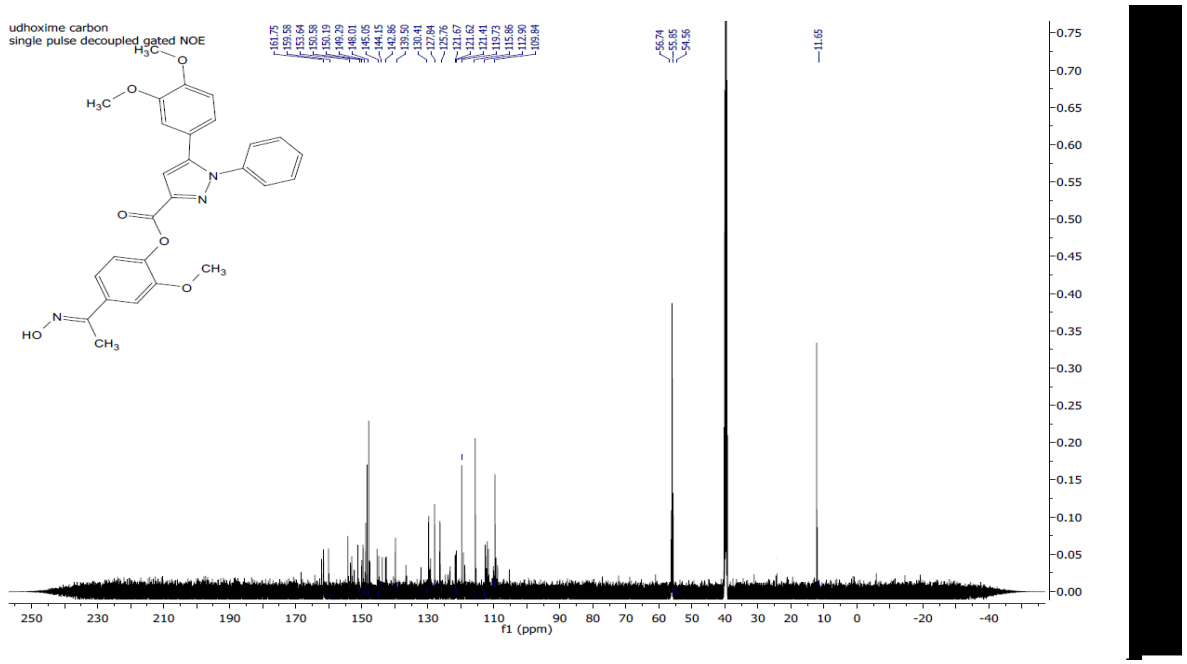


Fig. 49: ^{1}H-NMR of compound **8e** in DMSO-*d6*.



^{13}C-NMR of Compound **8e** in DMSO-*d6*.

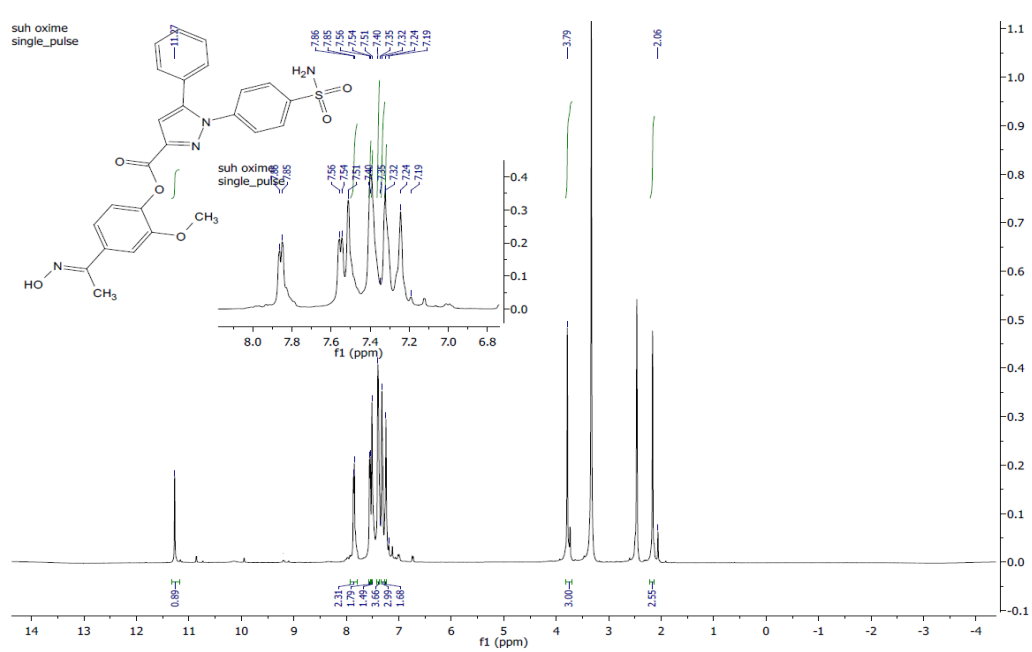
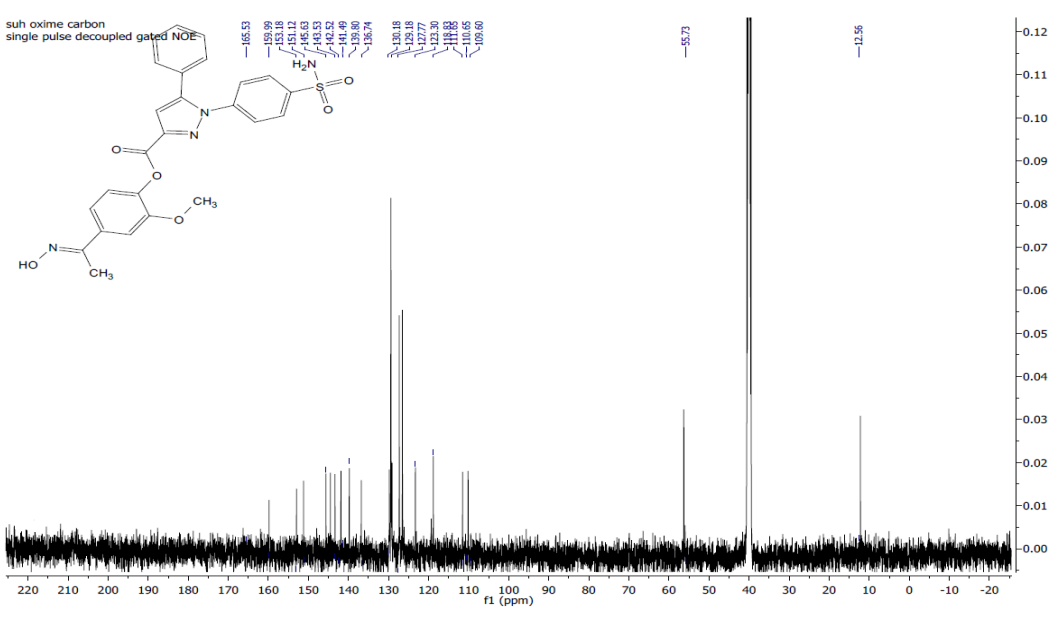
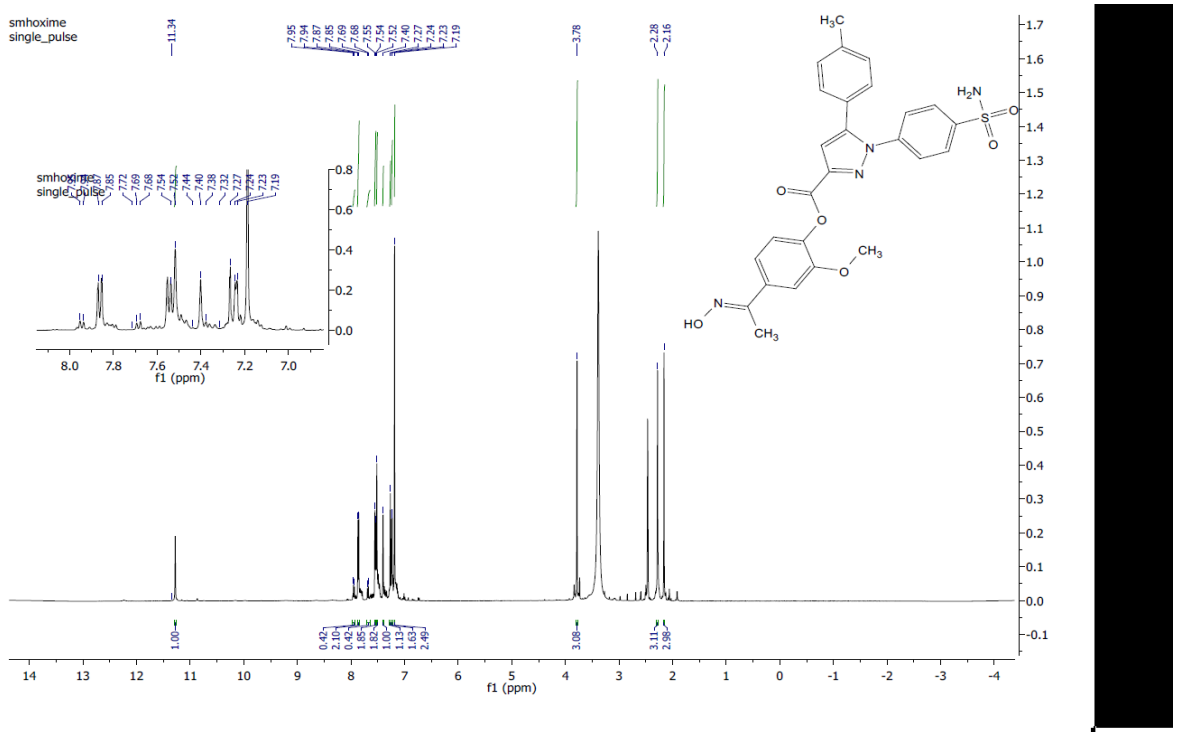


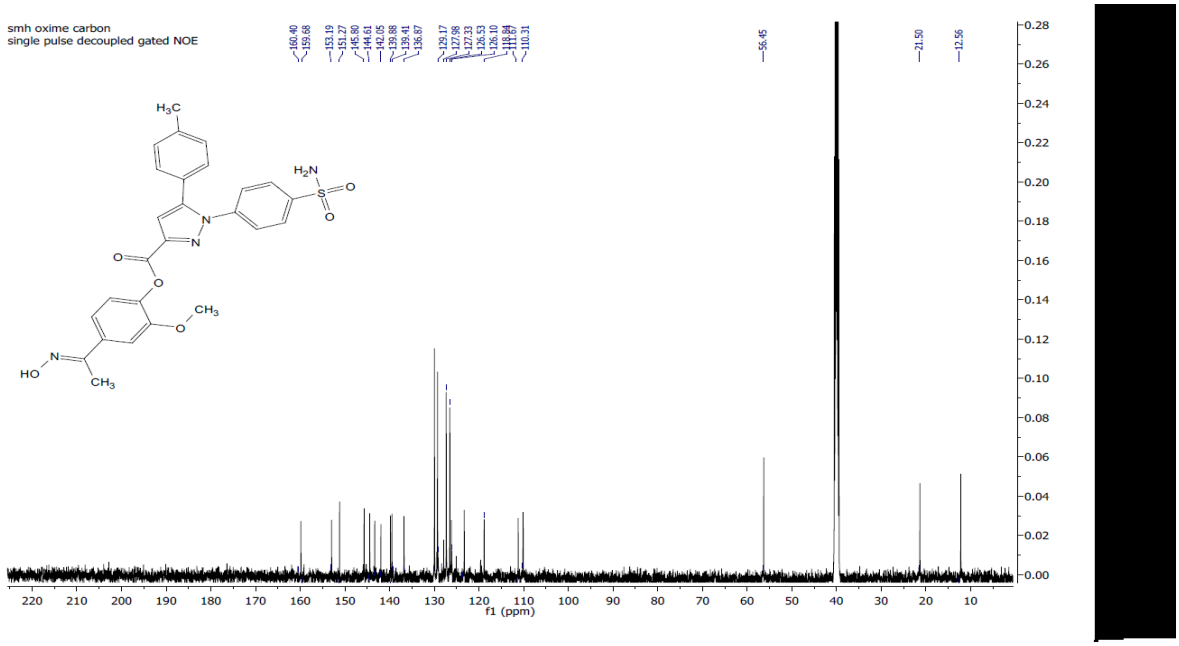
Fig. 52: ^{1}H-NMR of compound **8f** in DMSO-*d6*.



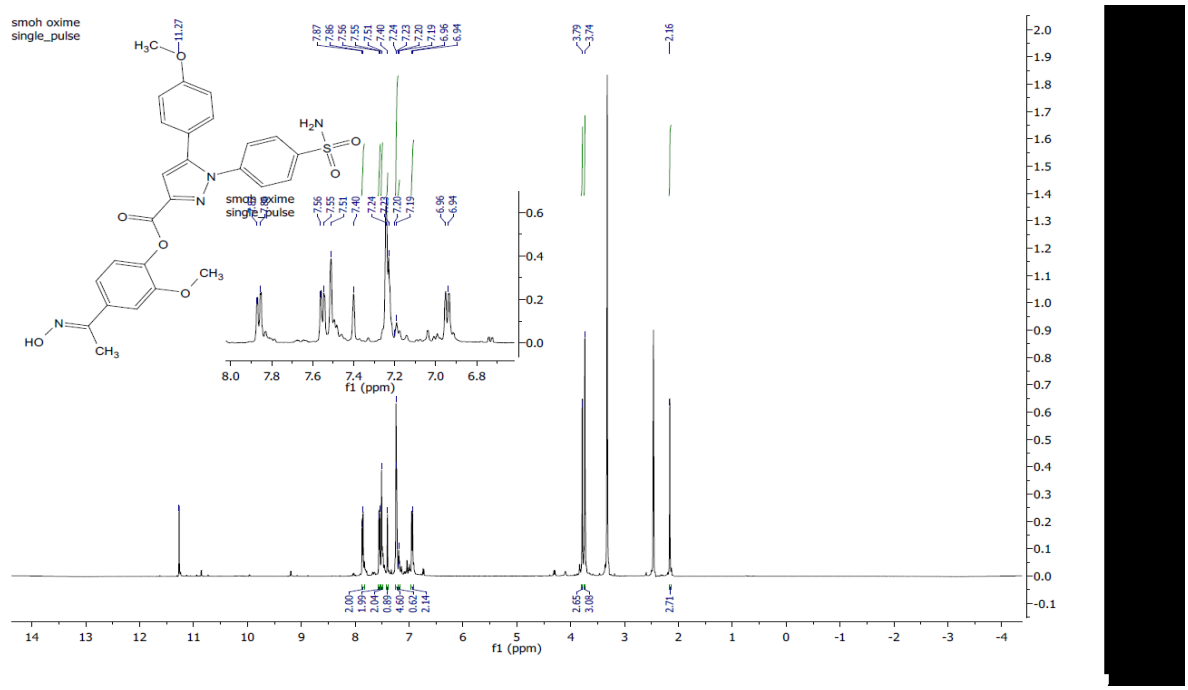
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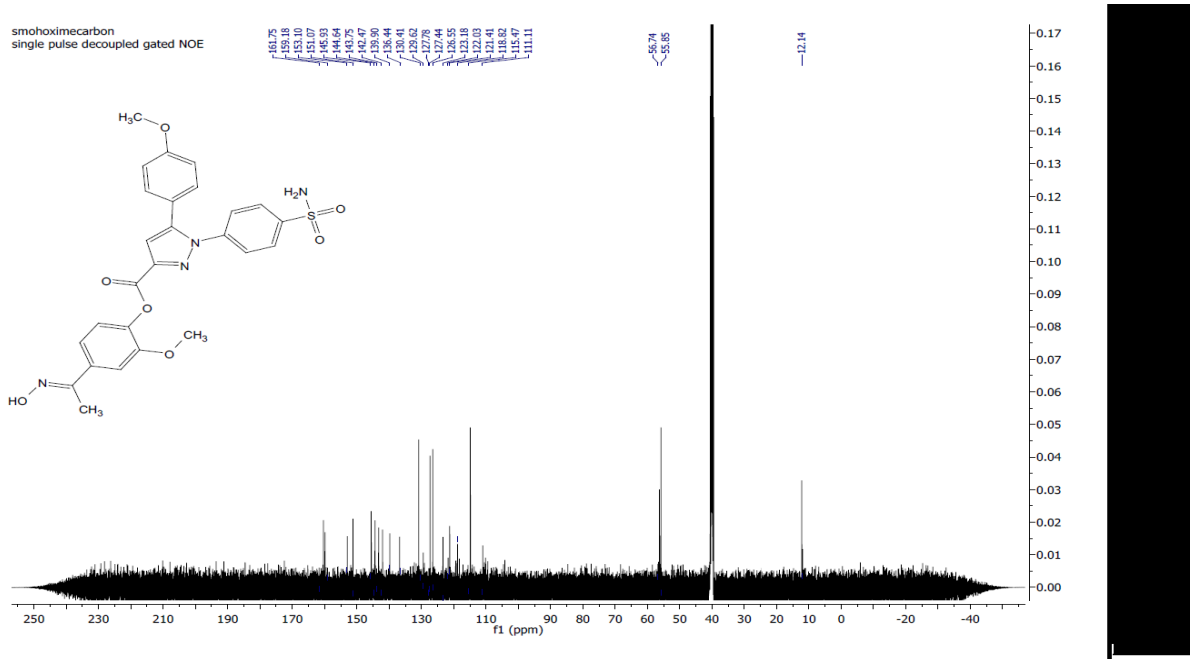
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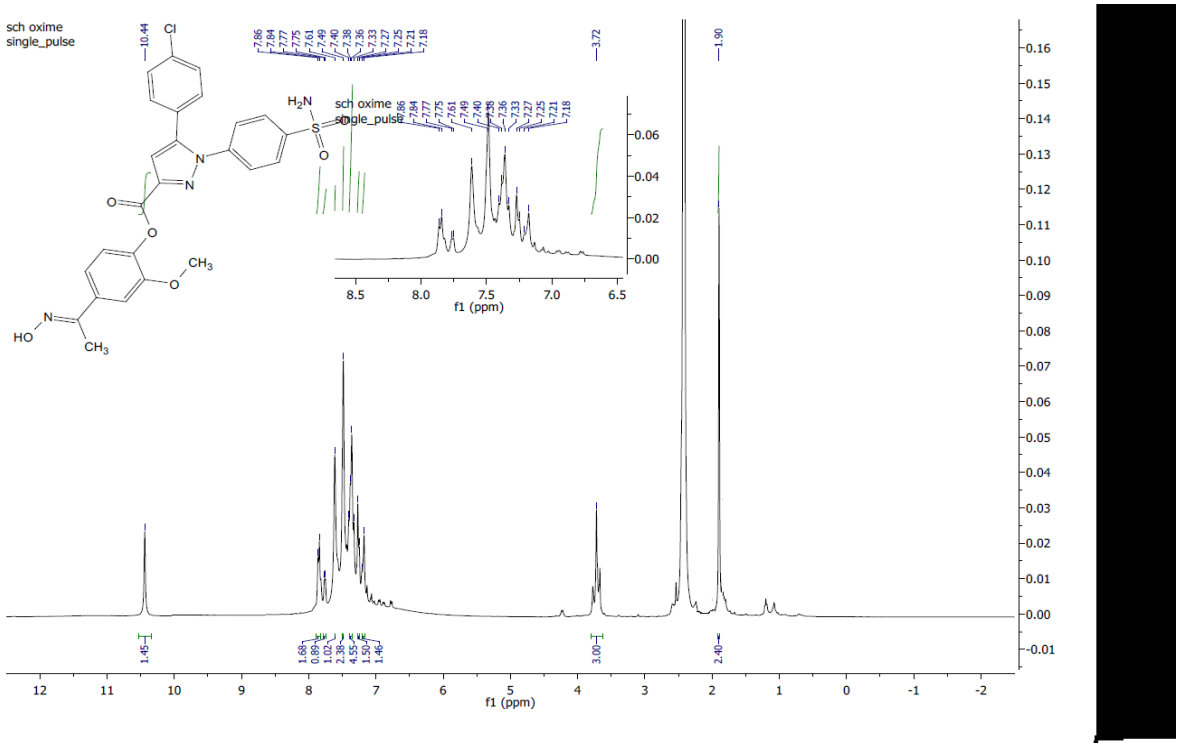
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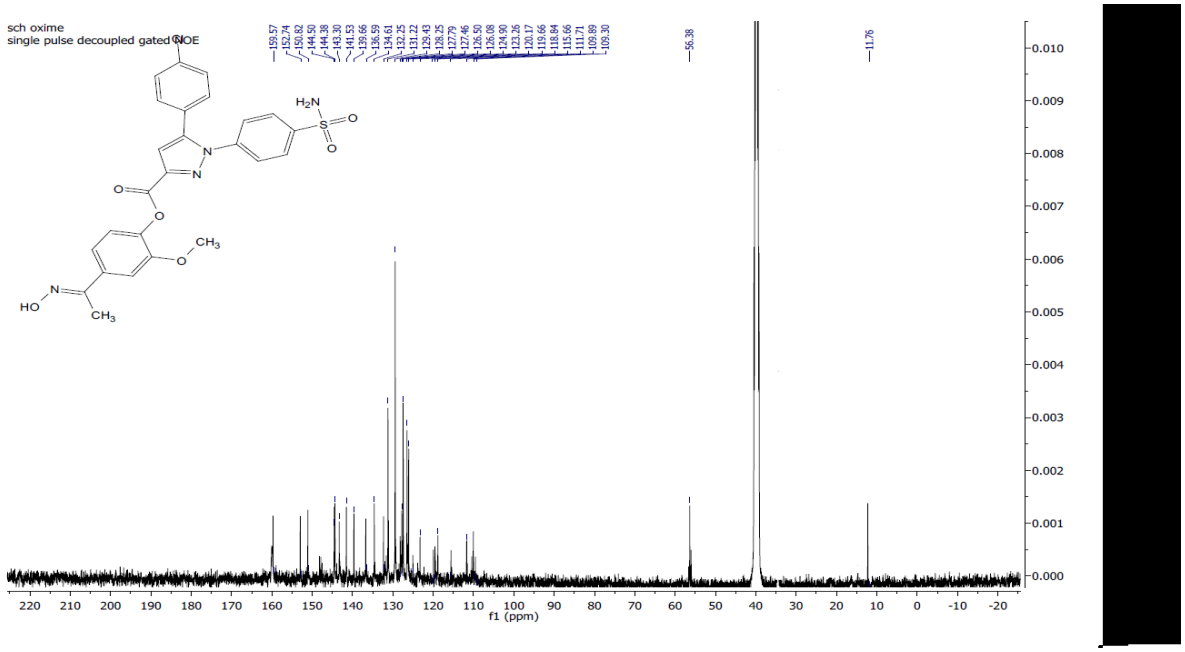
^{1}H-NMR of compound **8h** in DMSO-*d6*.



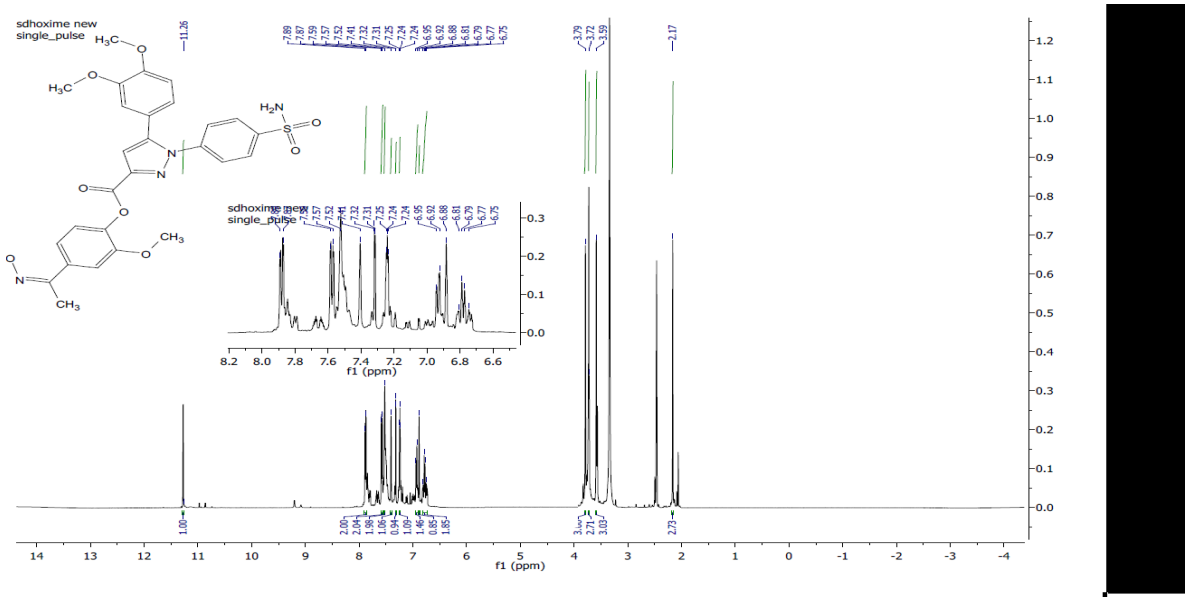
^{13}C-NMR of Compound **8h** in DMSO-*d6*.



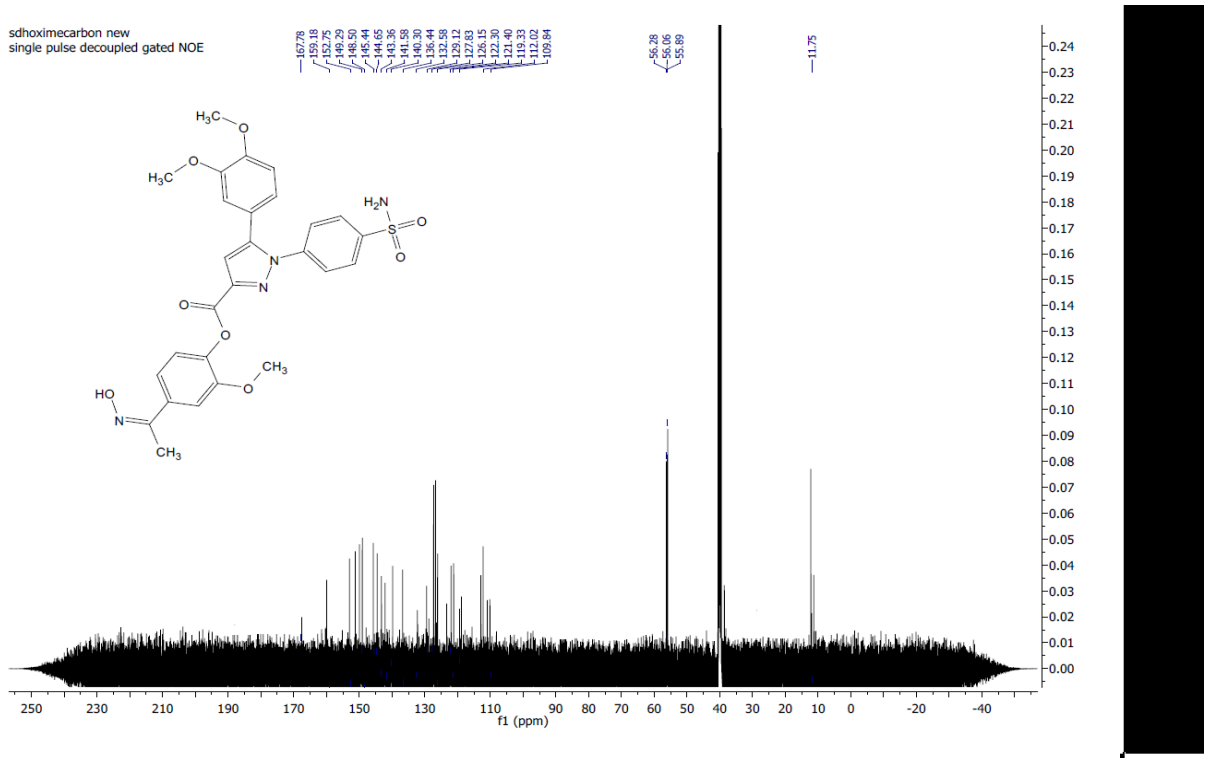
^{1}H-NMR of compound **8i** in DMSO-*d6*.



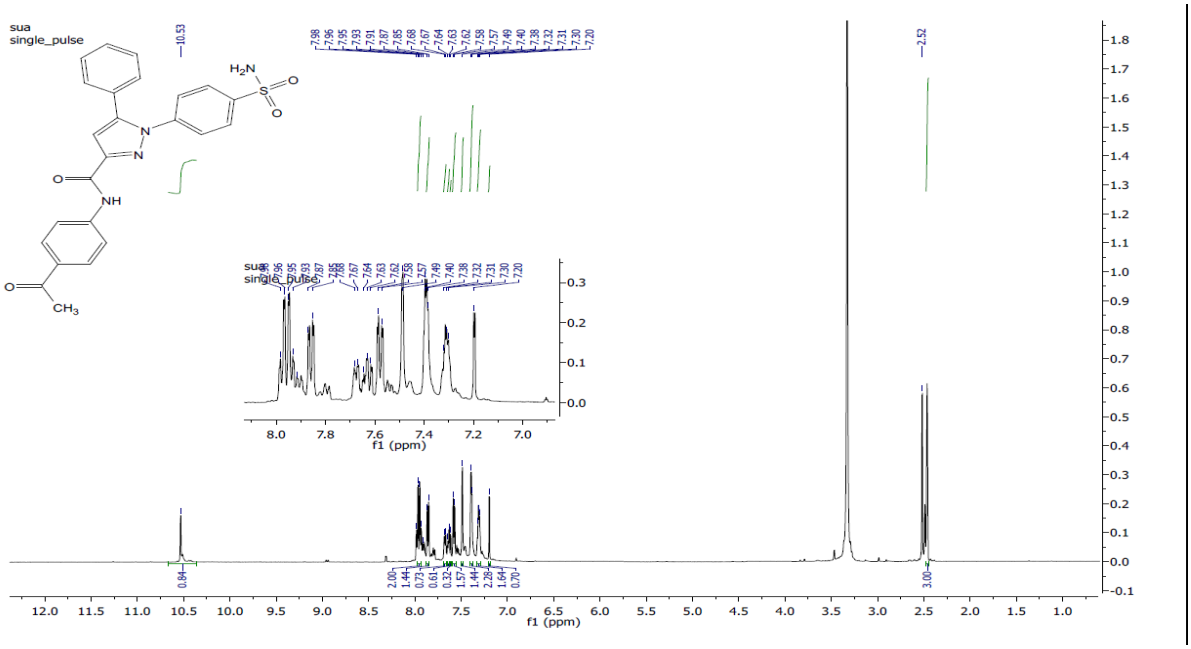
^{13}C-NMR of Compound **8i** in DMSO-*d6*.



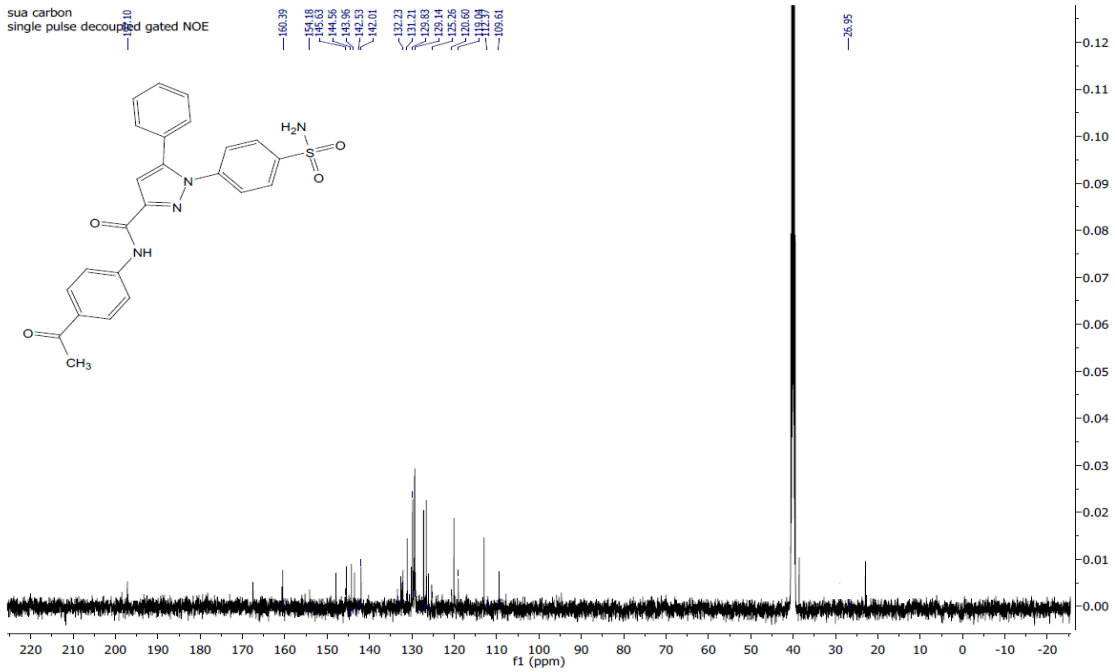
^{1}H-NMR of compound **8j** in DMSO-*d6*.



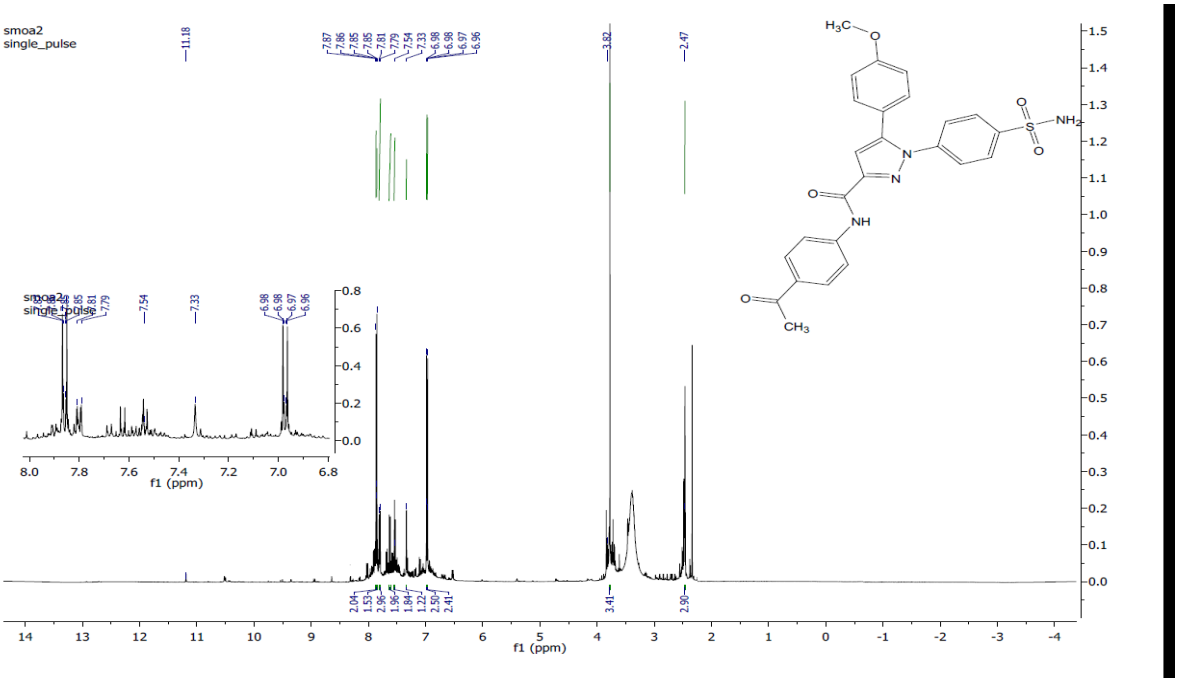
^{13}C-NMR of Compound **8j** in DMSO-*d6*.



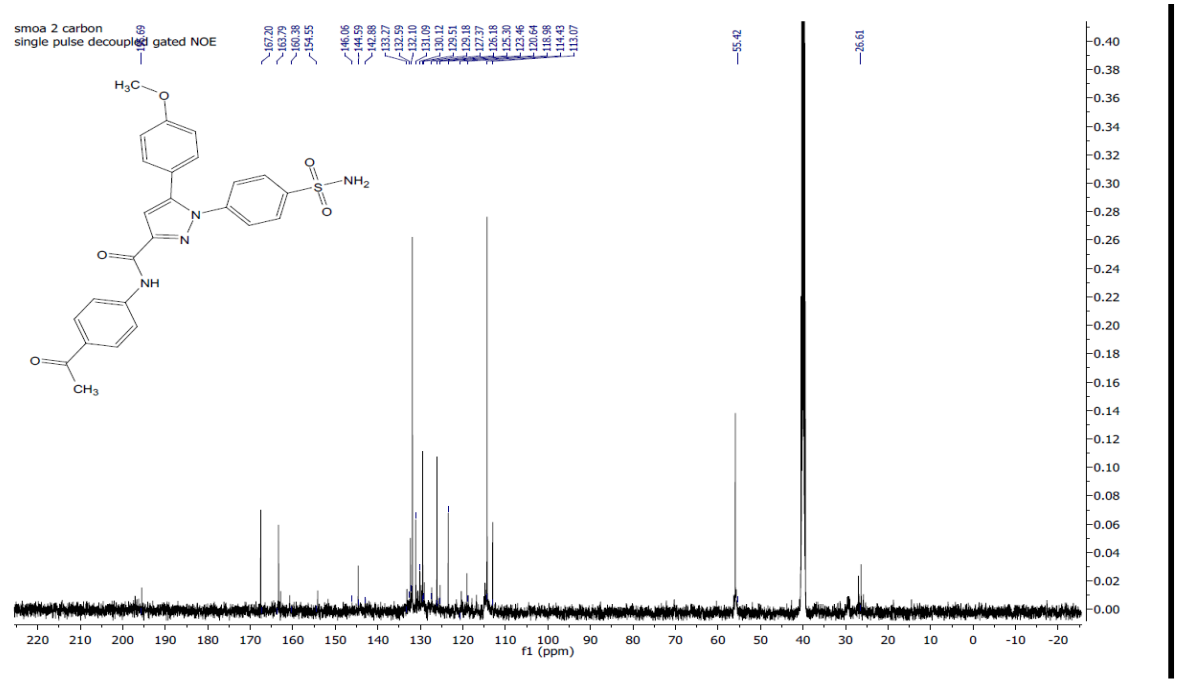
^{1}H-NMR of compound **9a** in DMSO-*d6*.



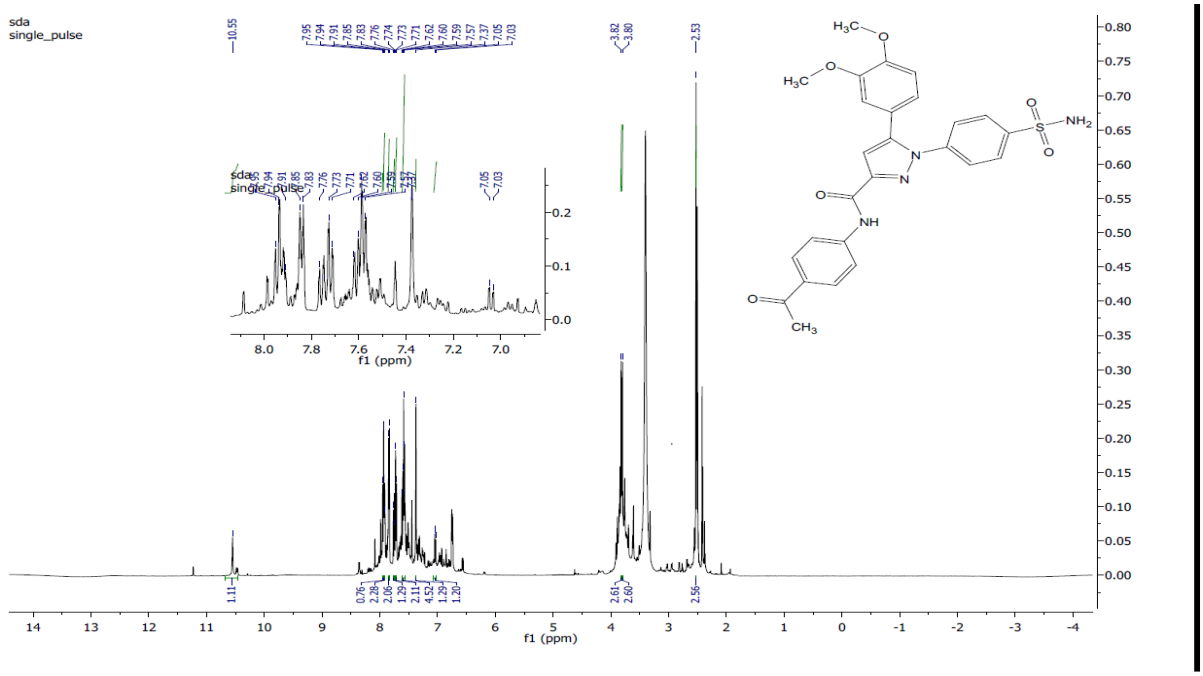
^{13}C-NMR of Compound **9a** in DMSO-*d6*.



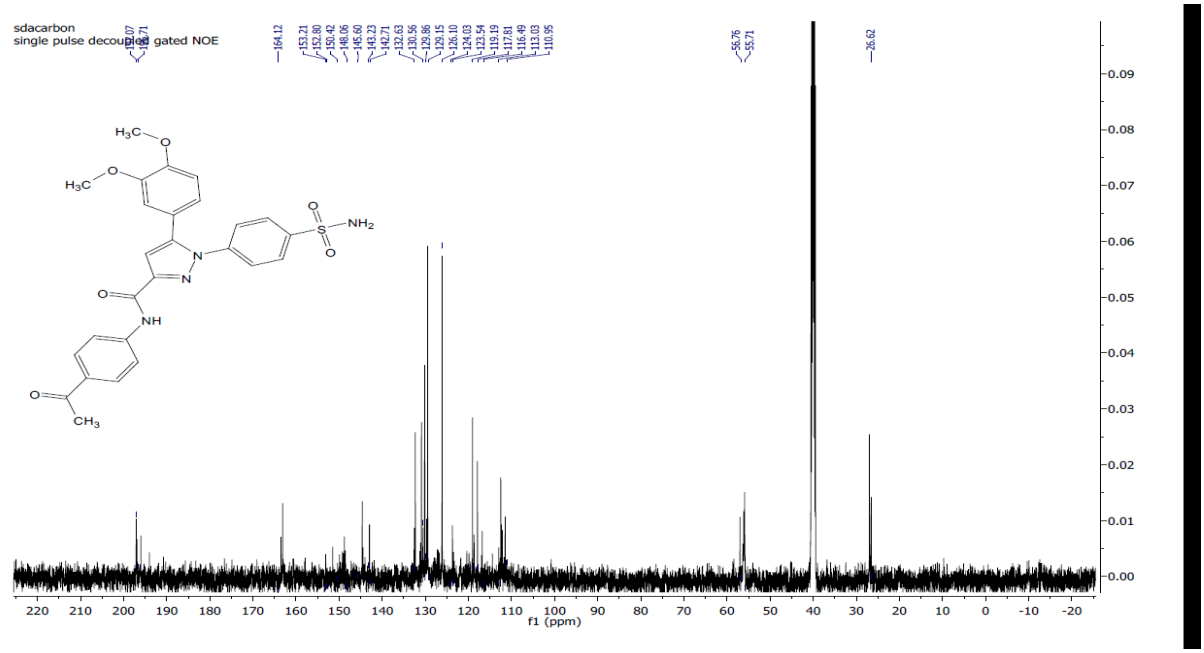
^{1}H-NMR of compound **9b** in DMSO-*d6*.



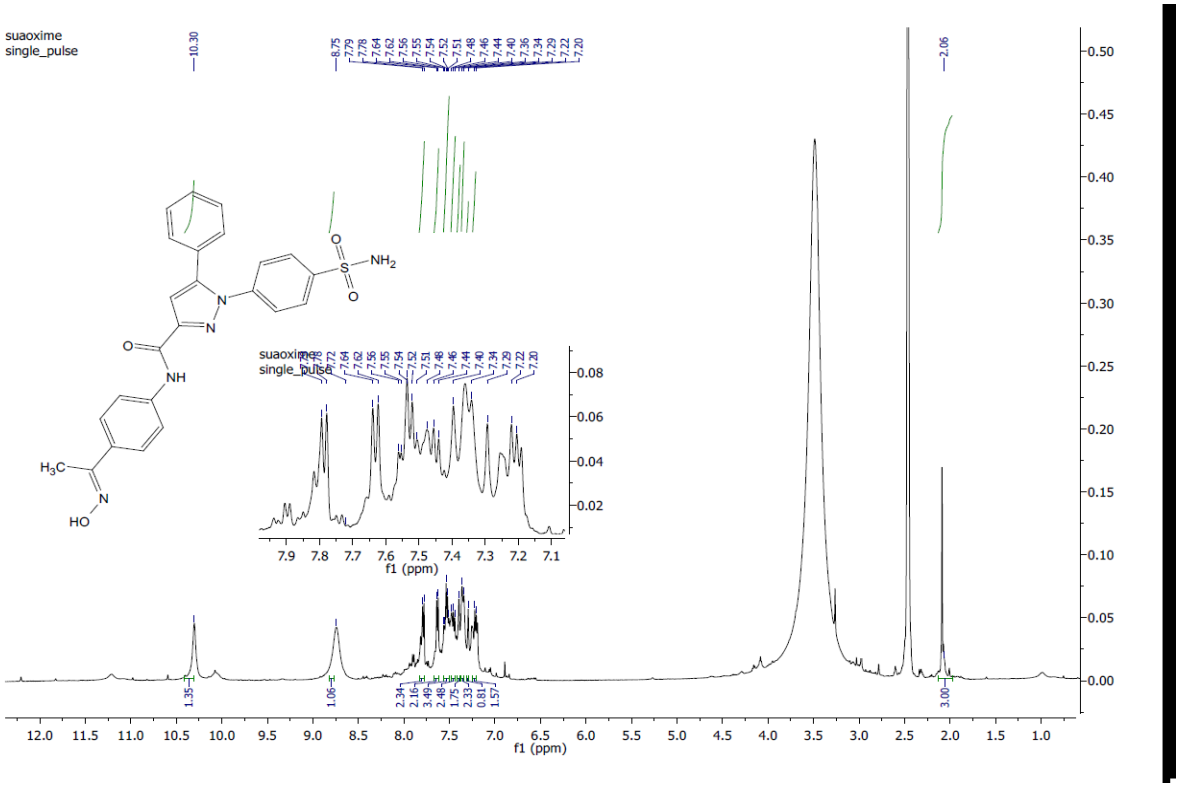
^{13}C-NMR of Compound **9b** in DMSO-*d6*.



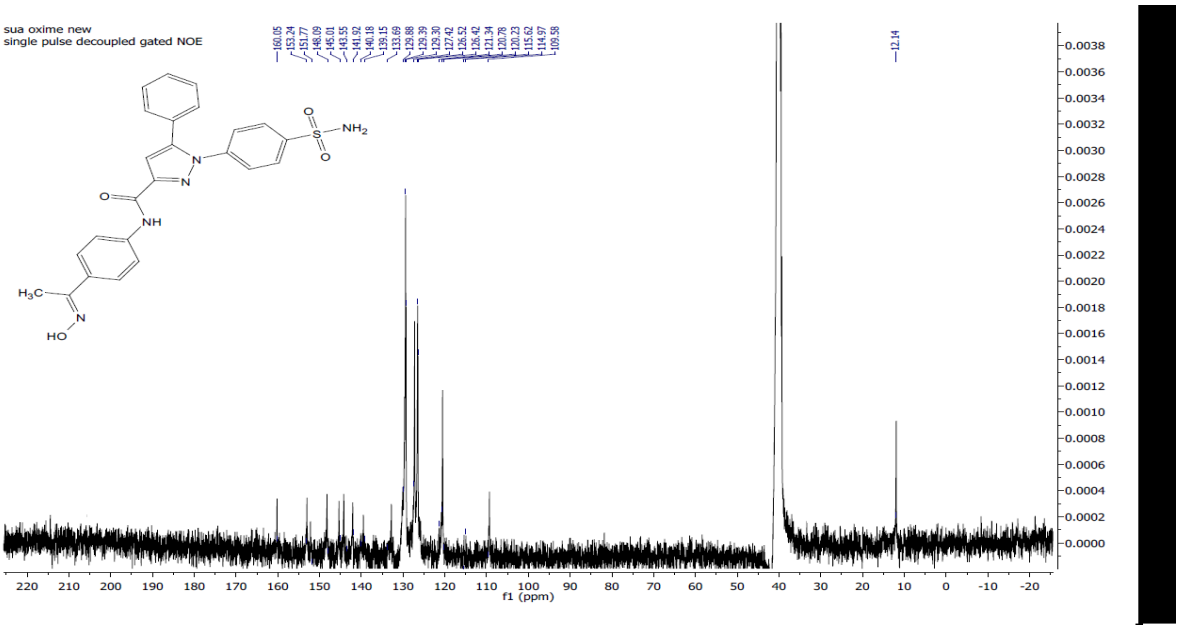
^{1}H-NMR of compound **9c** in DMSO-*d6*.



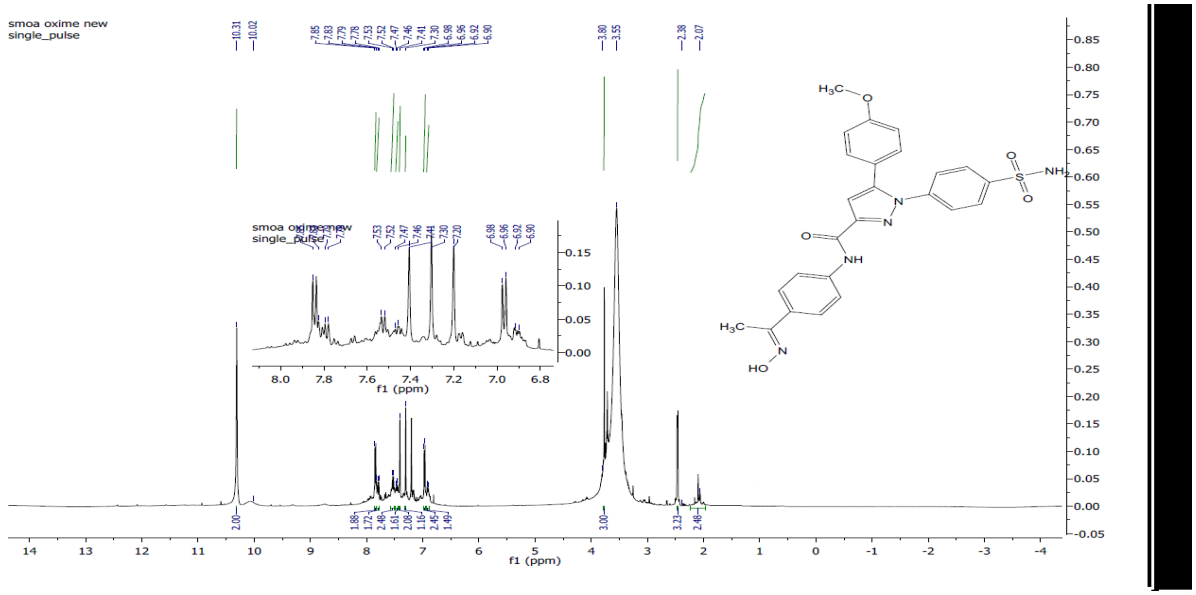
^{13}C-NMR of Compound **9c** in DMSO-*d6*.



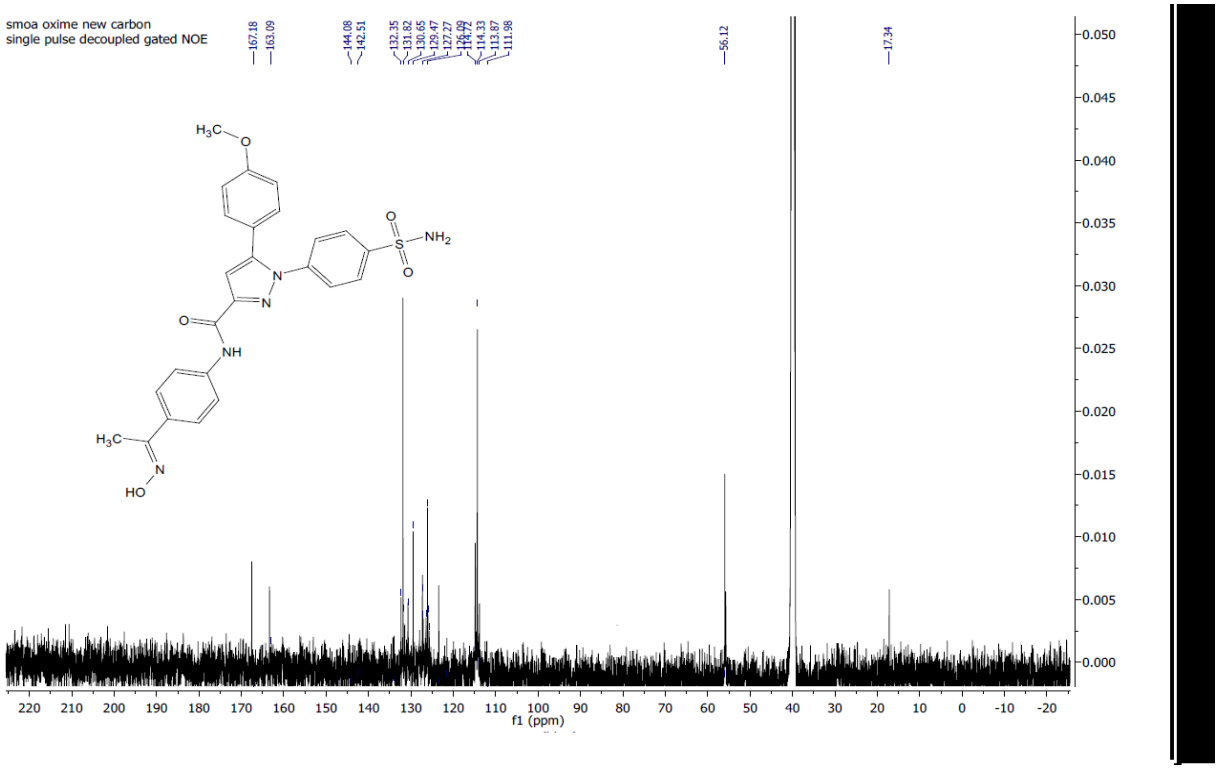
^{1}H-NMR of compound **10a** in DMSO-*d6*.



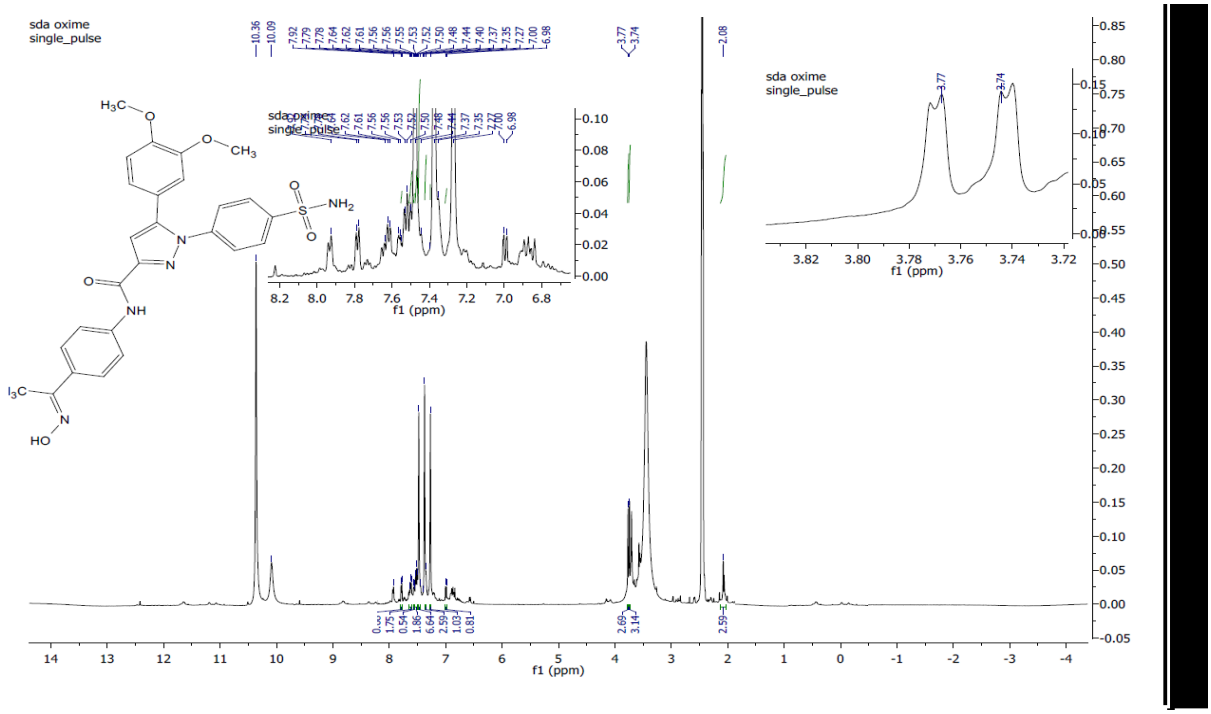
^{13}C-NMR of Compound **10a** in DMSO-*d6*.



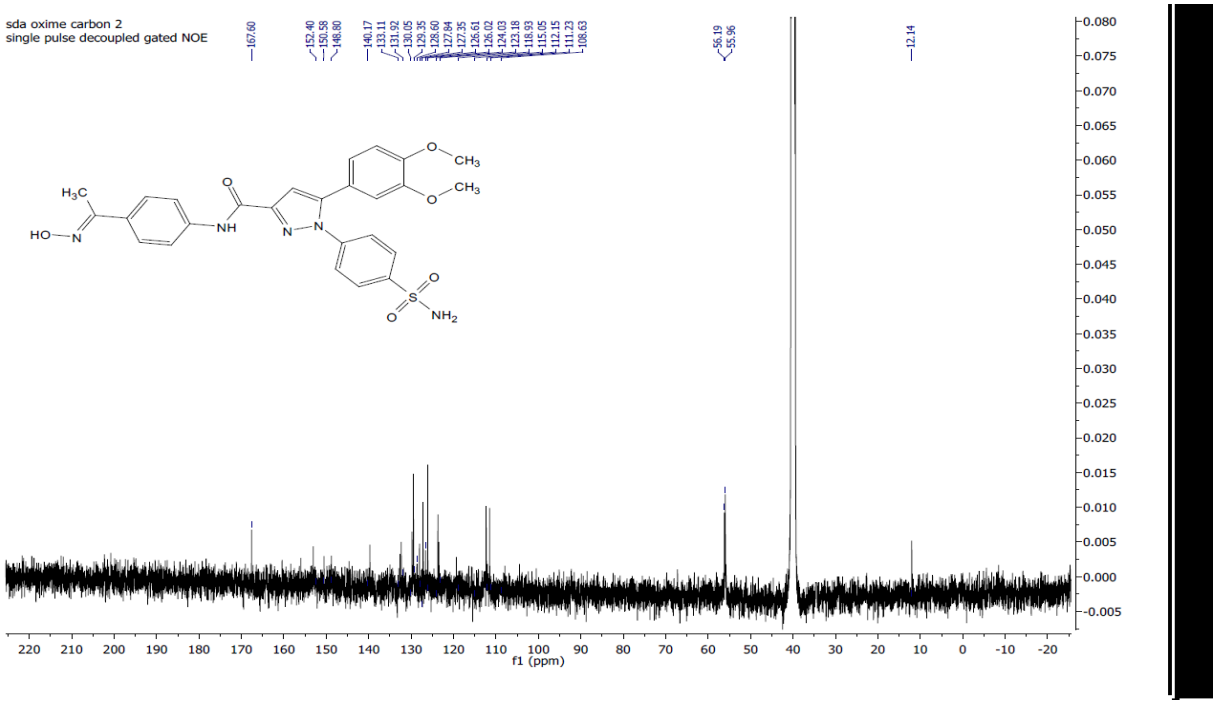
^{1}H-NMR of compound **10b** in DMSO-*d6*.



^{13}C-NMR of Compound **10b** in DMSO-*d6*.



^{1}H-NMR of compound **10c** in DMSO-*d6*



^{13}C-NMR of Compound **10c** in DMSO-*d6*.