

Supplementary Information

Design, synthesis and computational studies of new azaheterocyclic coumarin derivatives as anti-*Mycobacterium tuberculosis* agents targeting enoyl acyl carrier protein reductase (InhA)

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- Table S1. Antimycobacterial activity of tested compounds
- Table S2. Cytotoxicity of the selected compound 4c to human macrophages
- Table S3. Statistical analysis of the antibacterial effect of the selected compound 4c against tubercle bacilli located inside human macrophages.
- ¹HNMR and ¹³CNMR of the new compounds.

Table S1. Antimycobacterial activity of tested compounds.

compounds	Mtb - MIC [µg/mL]	M.abscessus - MIC [µg/mL]	IC50=L929 [µg/mL]	bactericidal concentration	IC50/MIC - Mtb
3	62.5	>125	ND	ND	ND
4a	62.5	>125	ND	ND	ND
4b	15	>125	31.25	ND	2
4c	15	>125	125	75	8
8a	>125	>125	ND	ND	ND
8b	62.5	>125	ND	ND	ND
8c	62.5	>125	ND	ND	ND
9a	31.25	>125	62.5	ND	2
9b	62.5	>125	ND	ND	ND
9c	62.5	>125	ND	ND	ND
10	>125	>125	ND	ND	ND
11	62.5	>125	ND	ND	ND
12	125	>125	ND	ND	ND
13	62.5	>125	ND	ND	ND
14	62.5	>125	ND	ND	ND
15	>125	>125	ND	ND	ND
16	>125	>125	ND	ND	ND
17	>125	>125	ND	ND	ND

ND – not determined, Mtb – *M. tuberculosis*, L929 – mouse fibroblasts cell line,

Table S2. Cytotoxicity of the selected compound 4c to human macrophages

concentration	2xMI C	4xMI C
compounds:	% cytotoxicity	
4c	32	34
media-control		
IMDM	0	
DMSO/2M	2	
DMSO/4M	11	

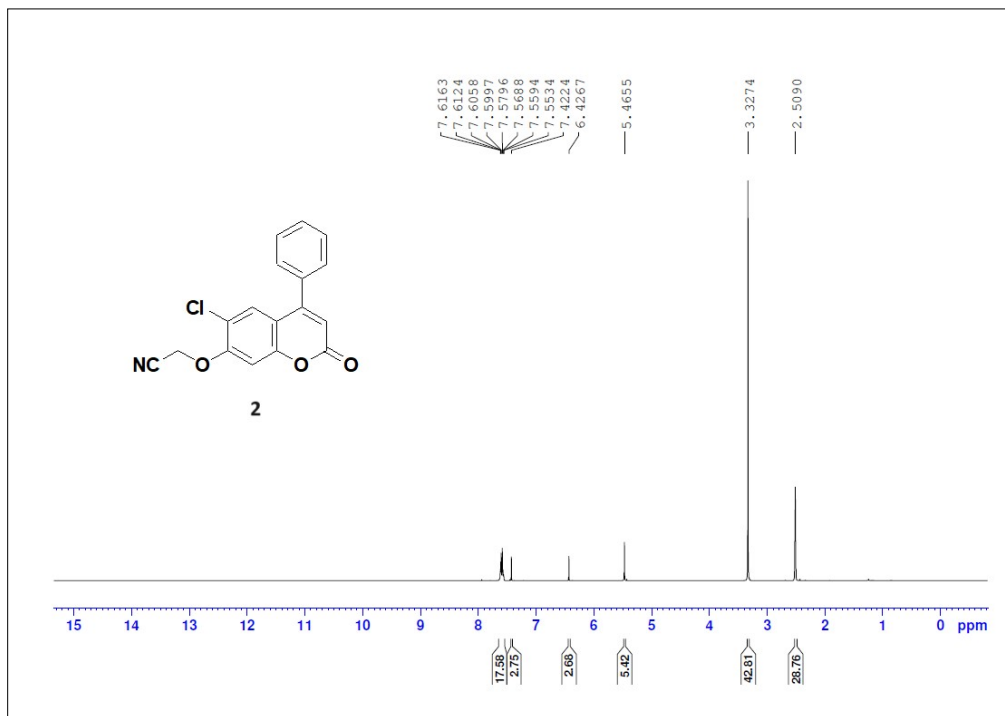
IMDM - media, DMSO/2M – xx, DMSO/4M - xx

Table S3. Statistical analysis of the antibacterial effect of the selected compound 4c against tubercle bacilli located inside human macrophages.

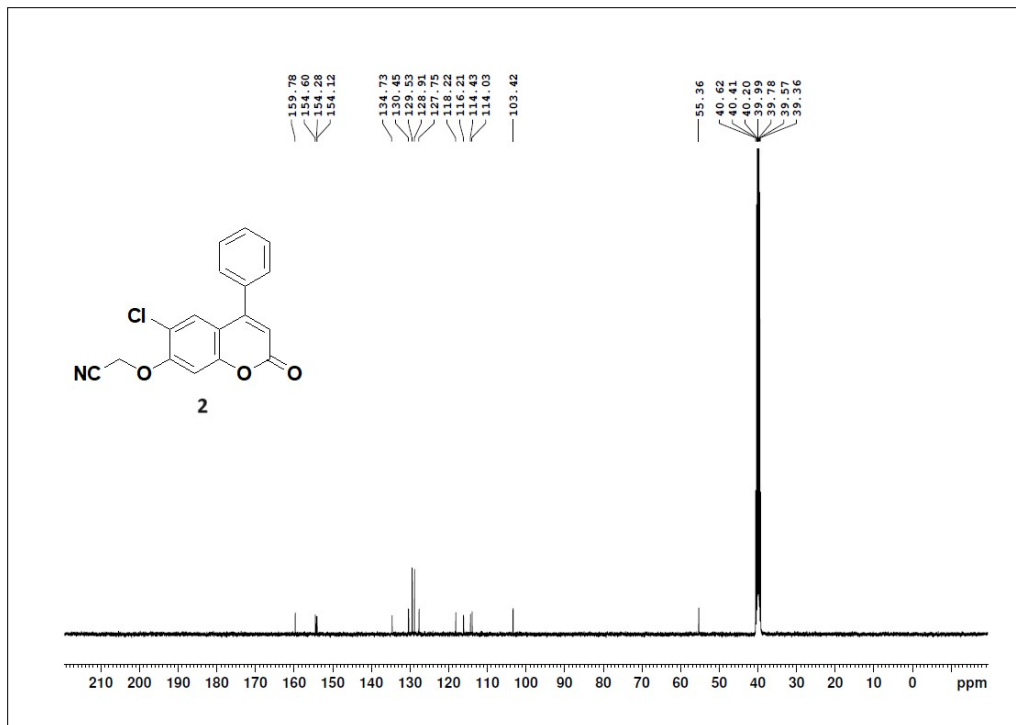
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value
control vs. 4c	70333	18988 to 121678	Yes	**	0,0041

Ordinary one-way ANOVA test was applied for all comparisons.

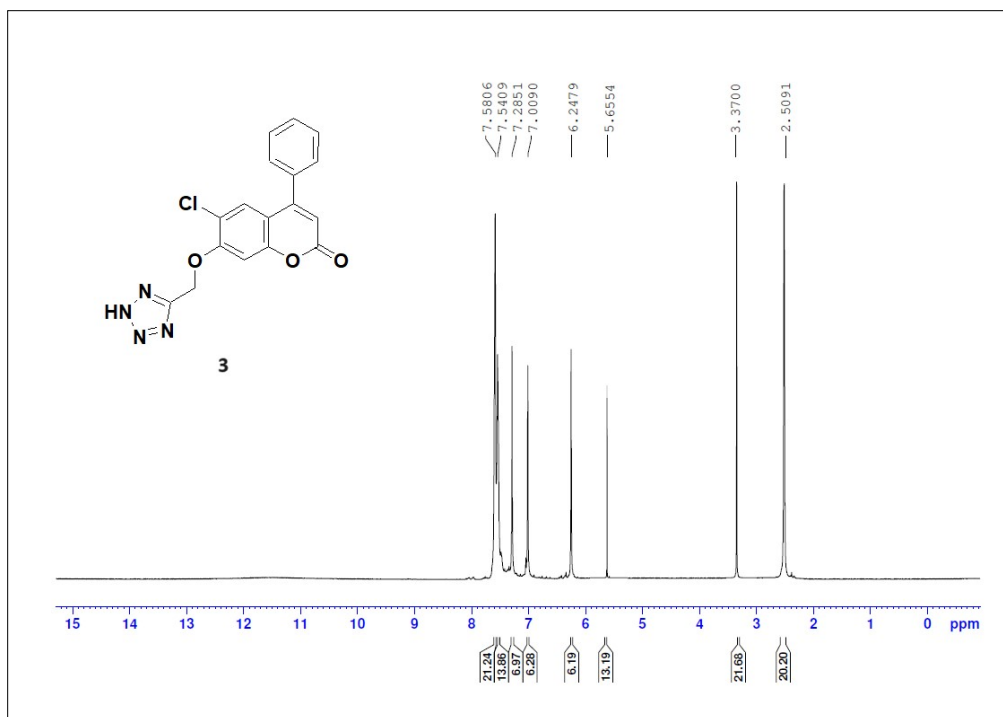
- ^1H NMR and ^{13}C NMR of the new compounds.**



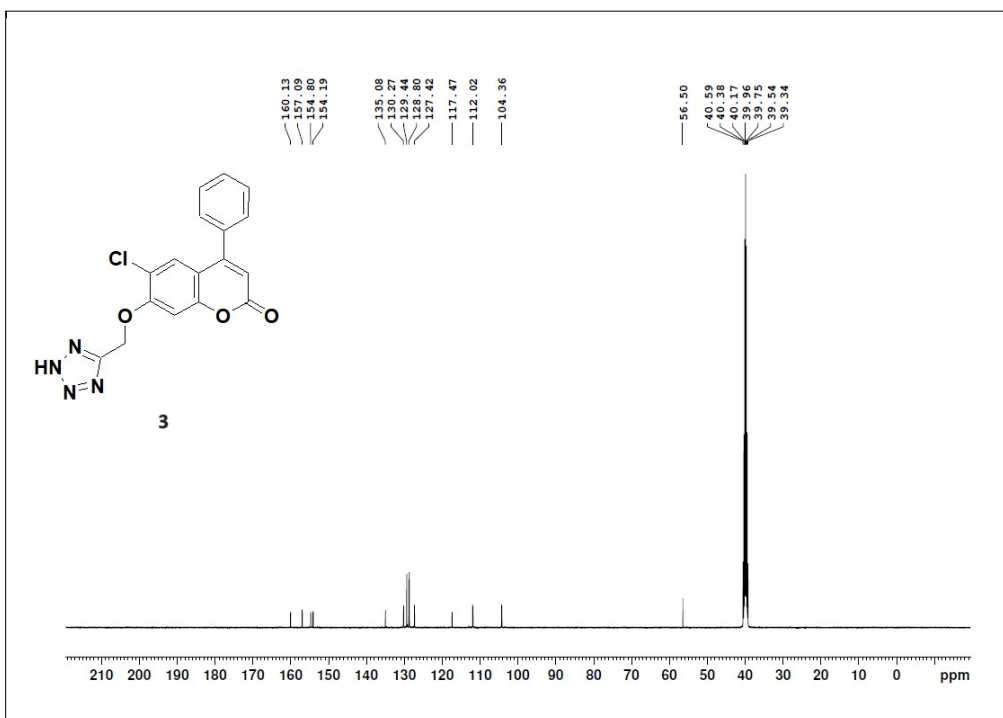
^1H NMR of compound 2



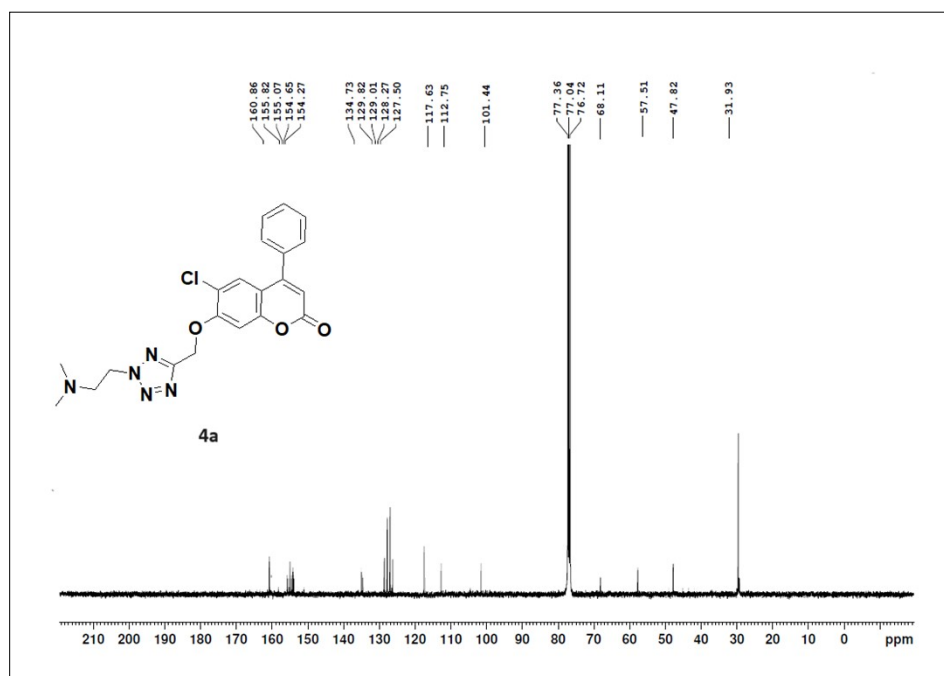
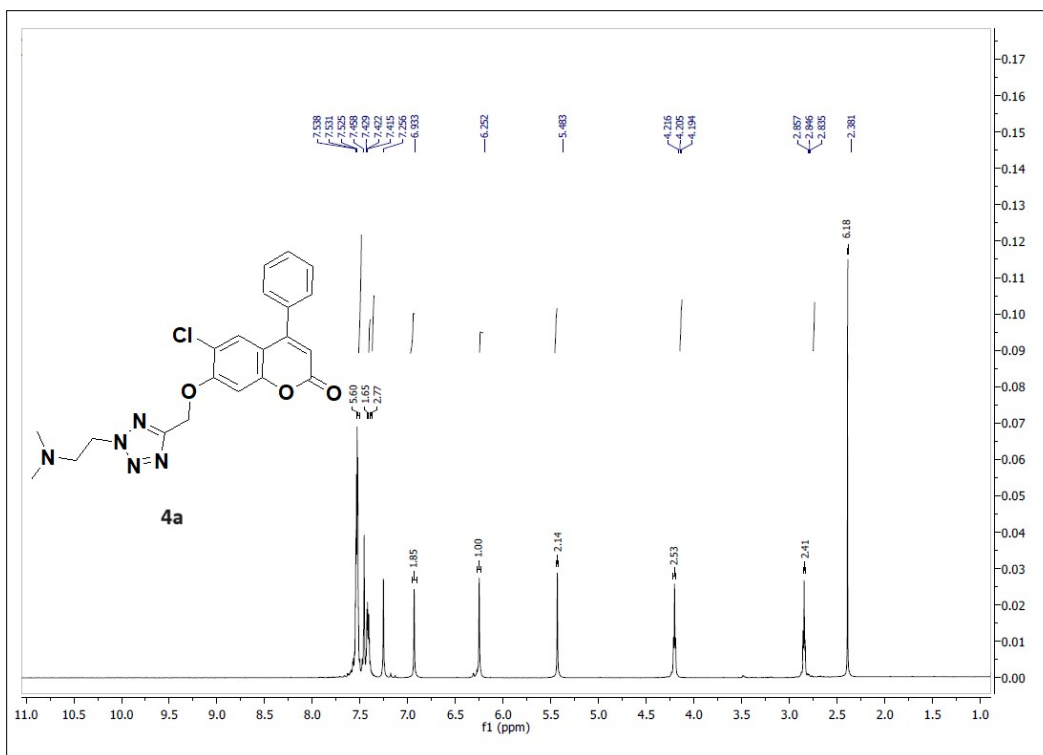
^{13}C NMR of compound 2

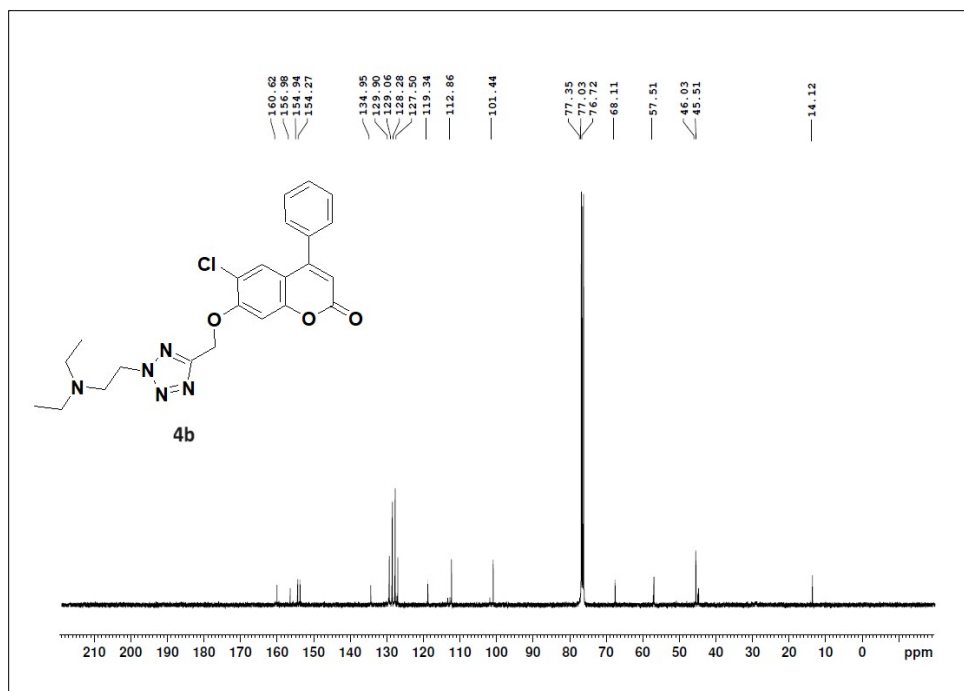


¹H NMR of compound 3

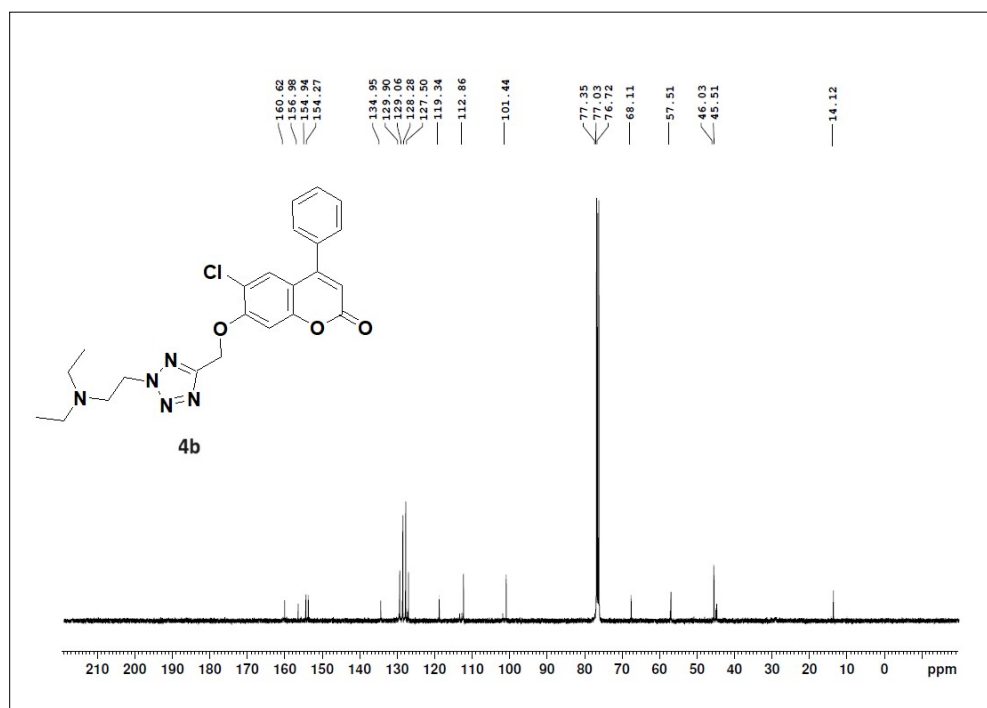


¹³C NMR of compound 3

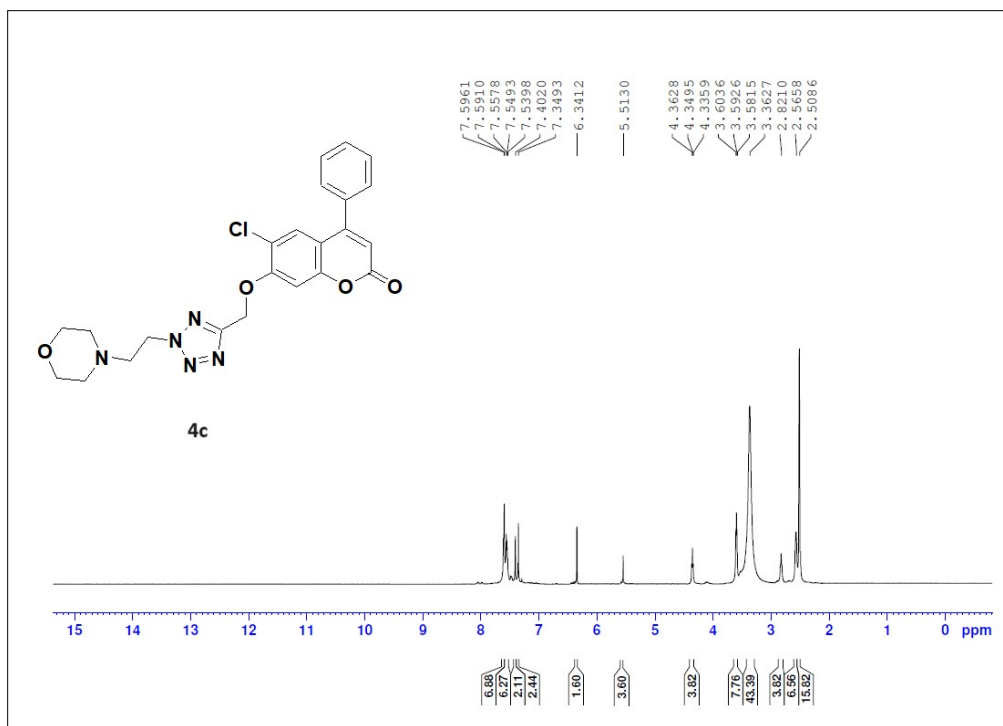




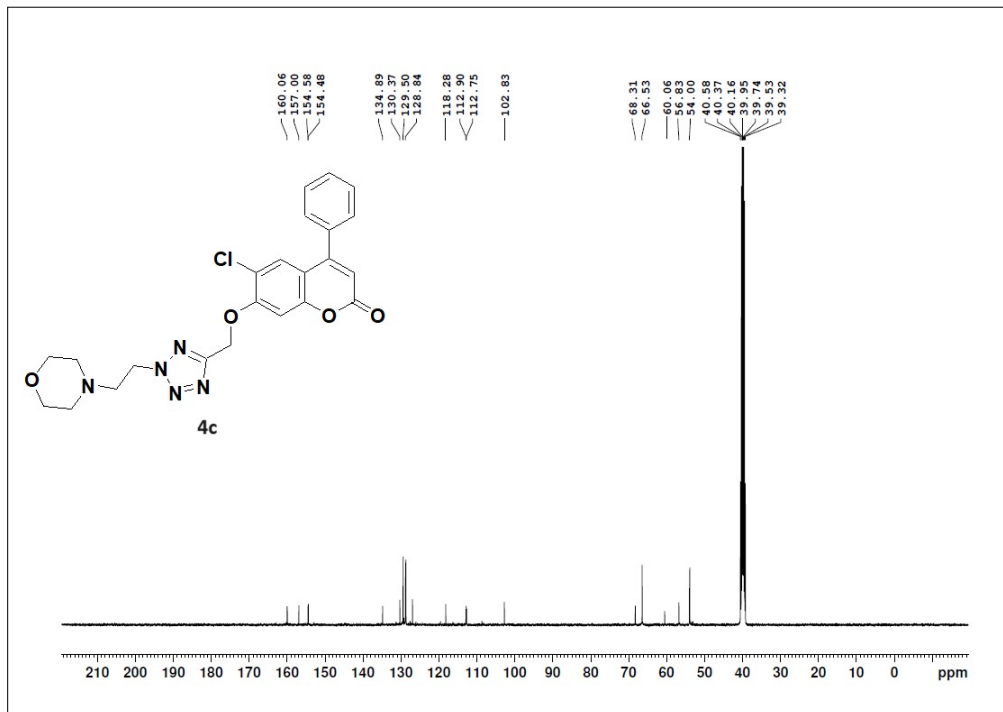
¹H NMR of compound 4b



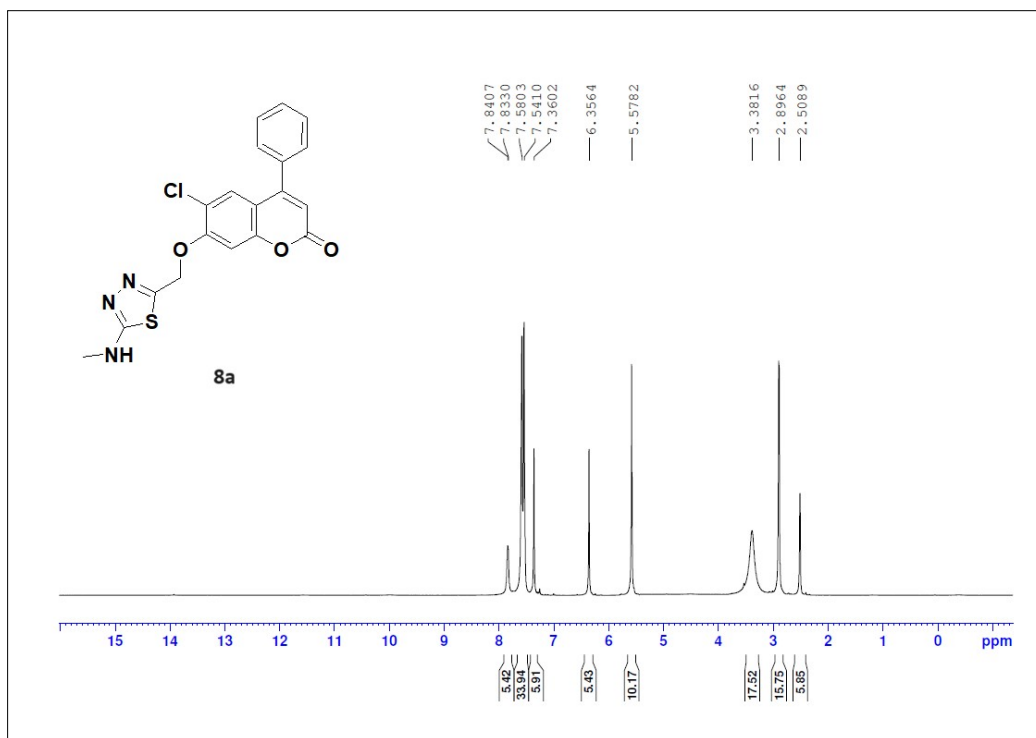
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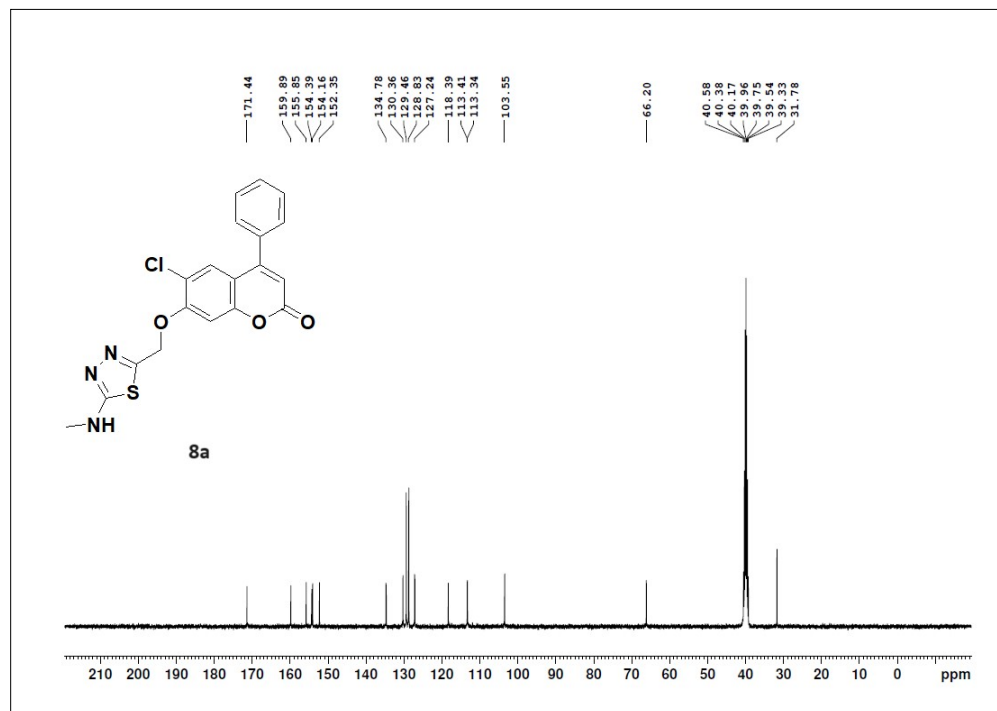
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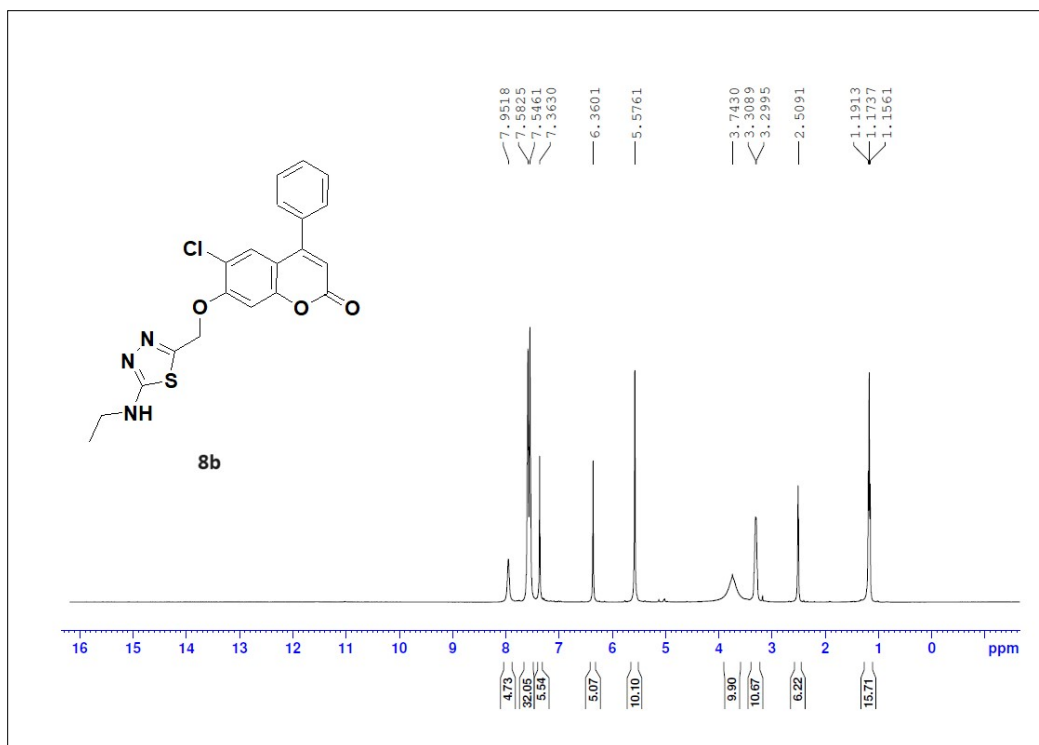
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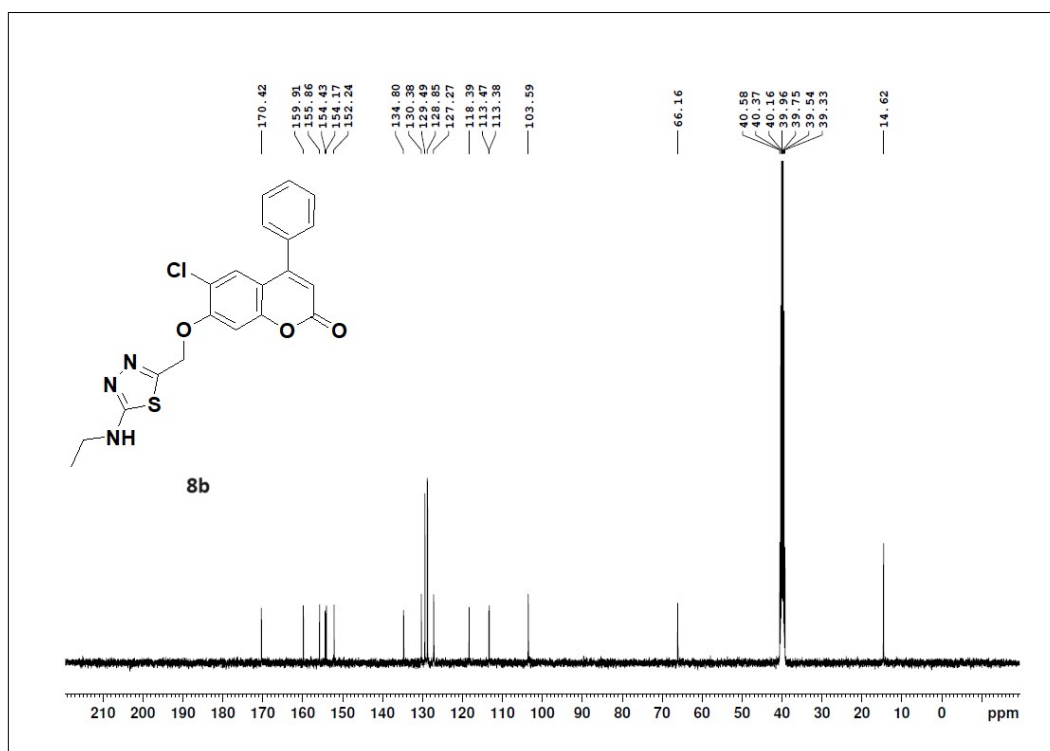
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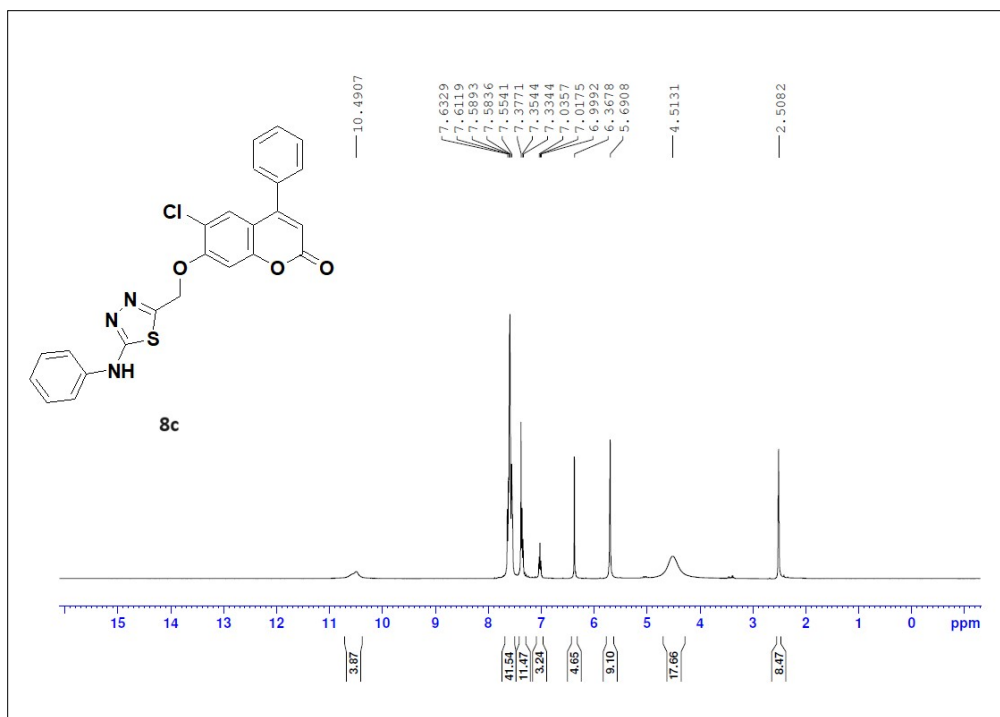
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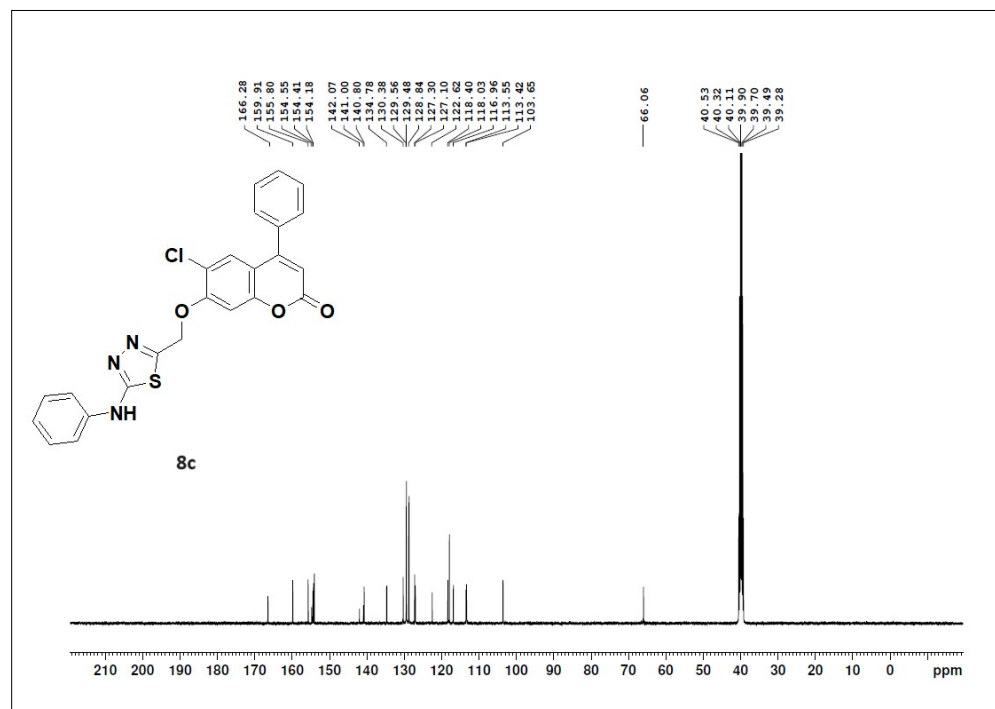
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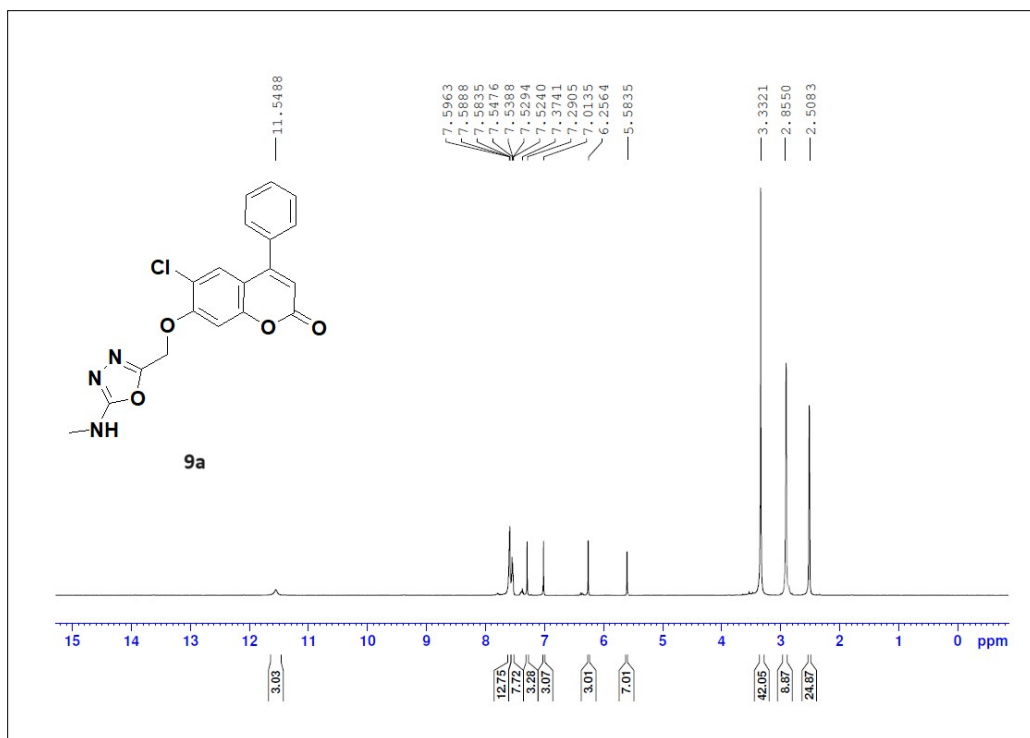
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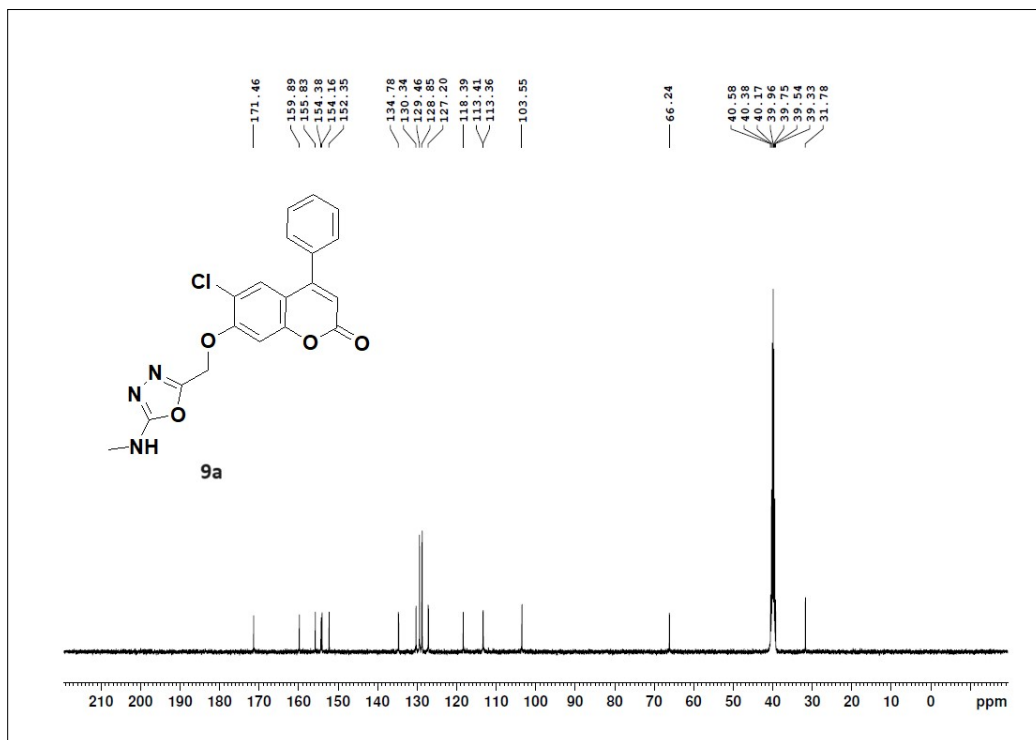
¹H NMR of compound 8c



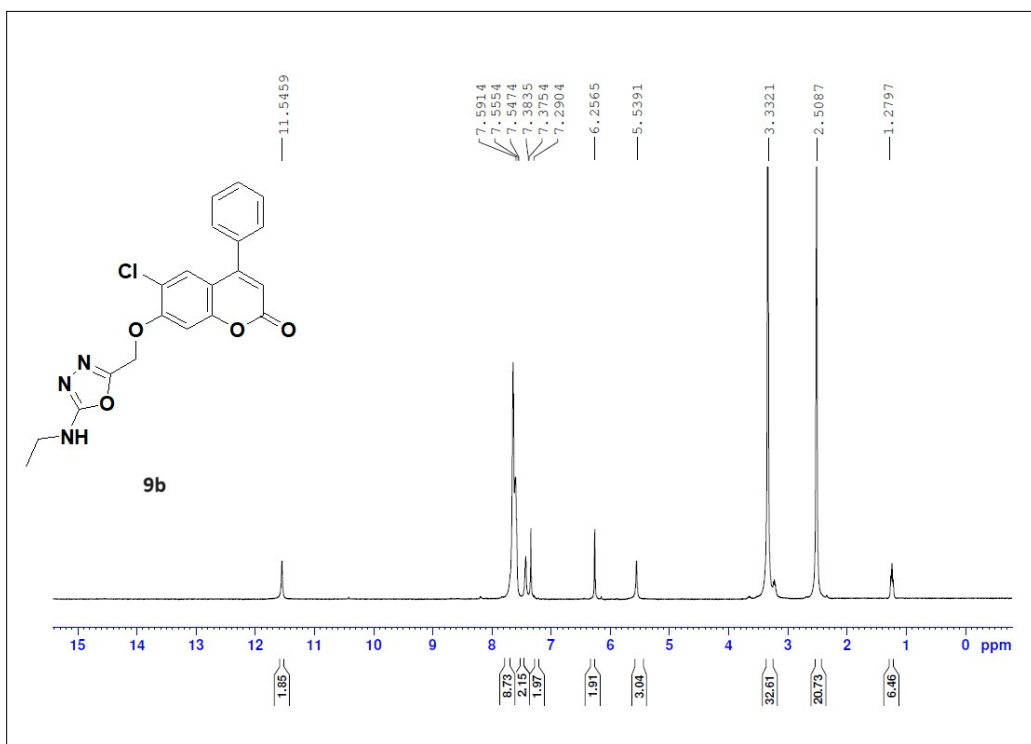
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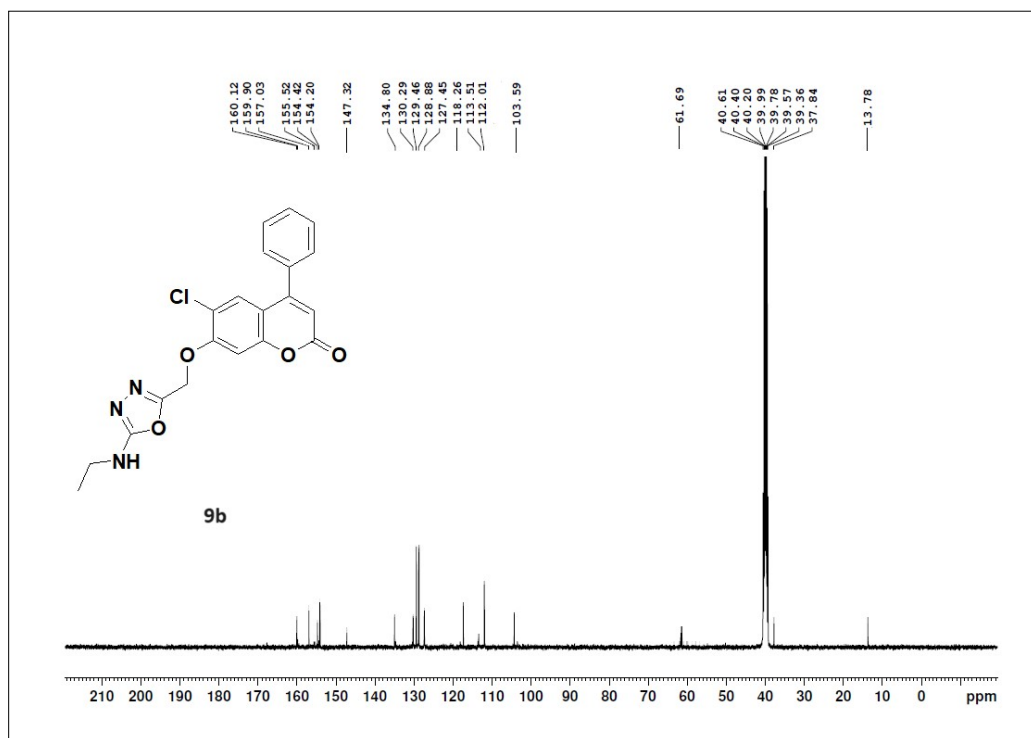
¹H NMR of compound 9a



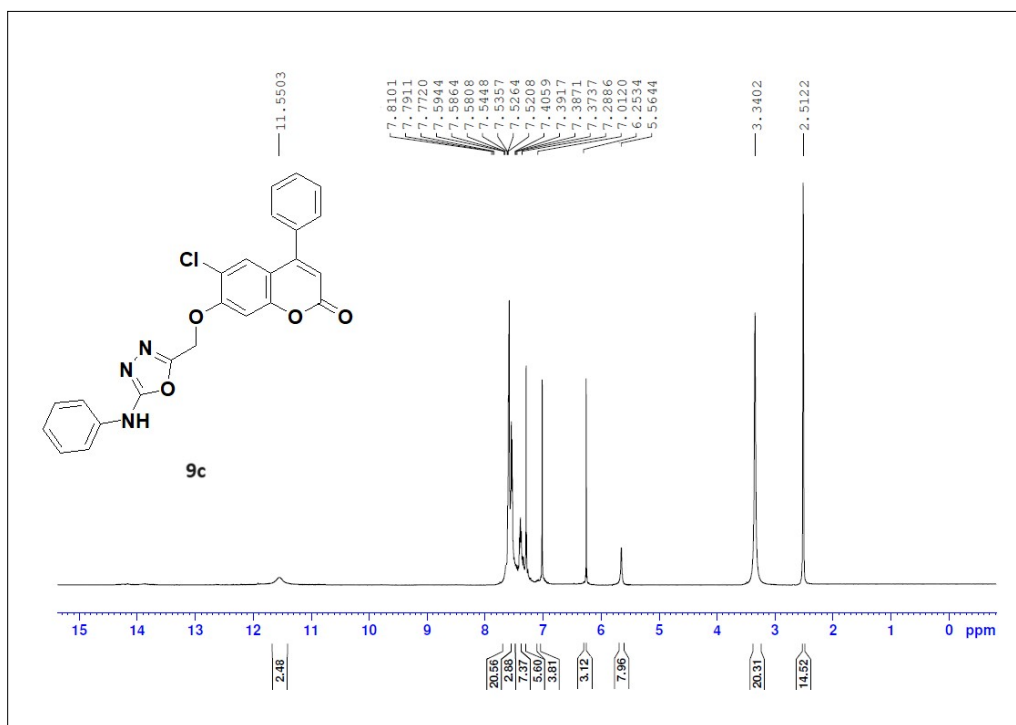
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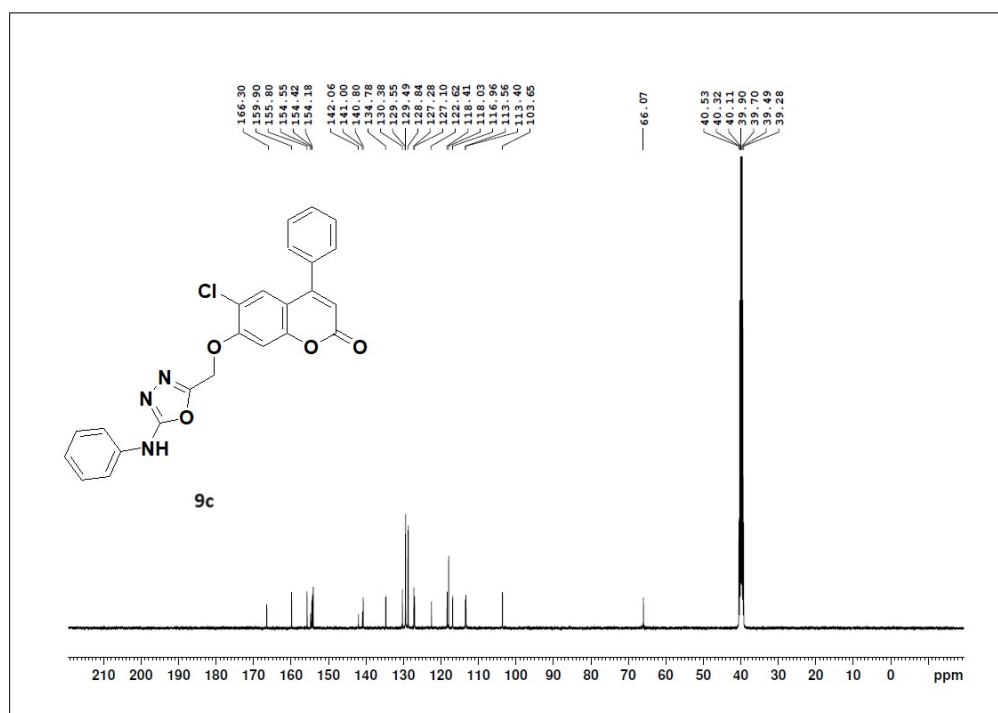
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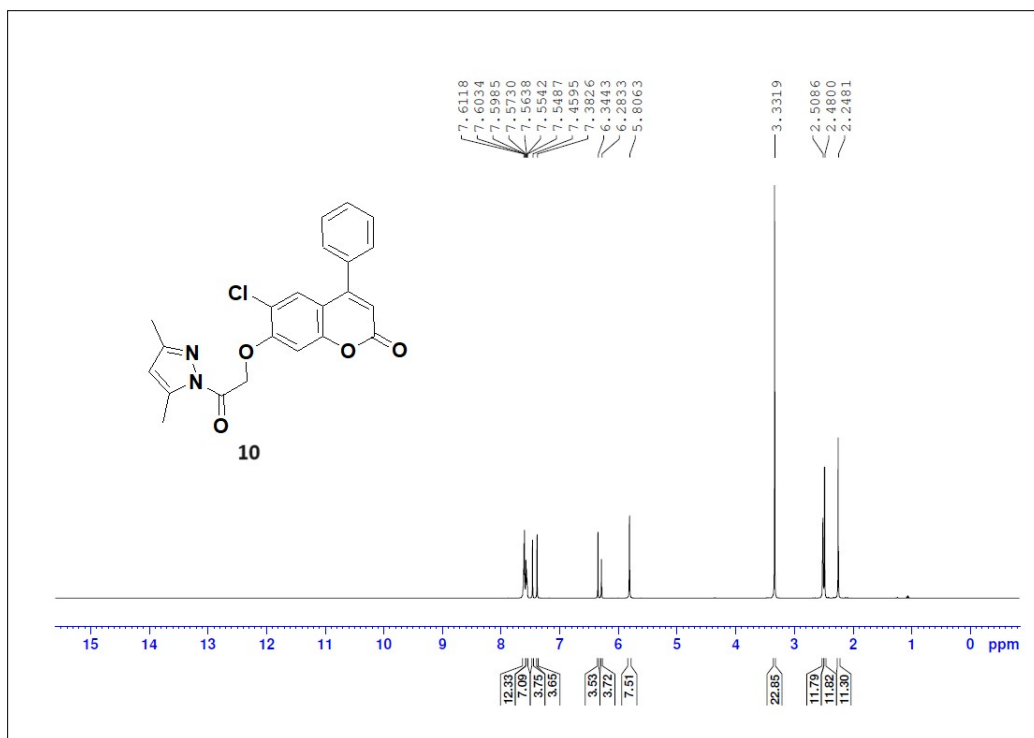
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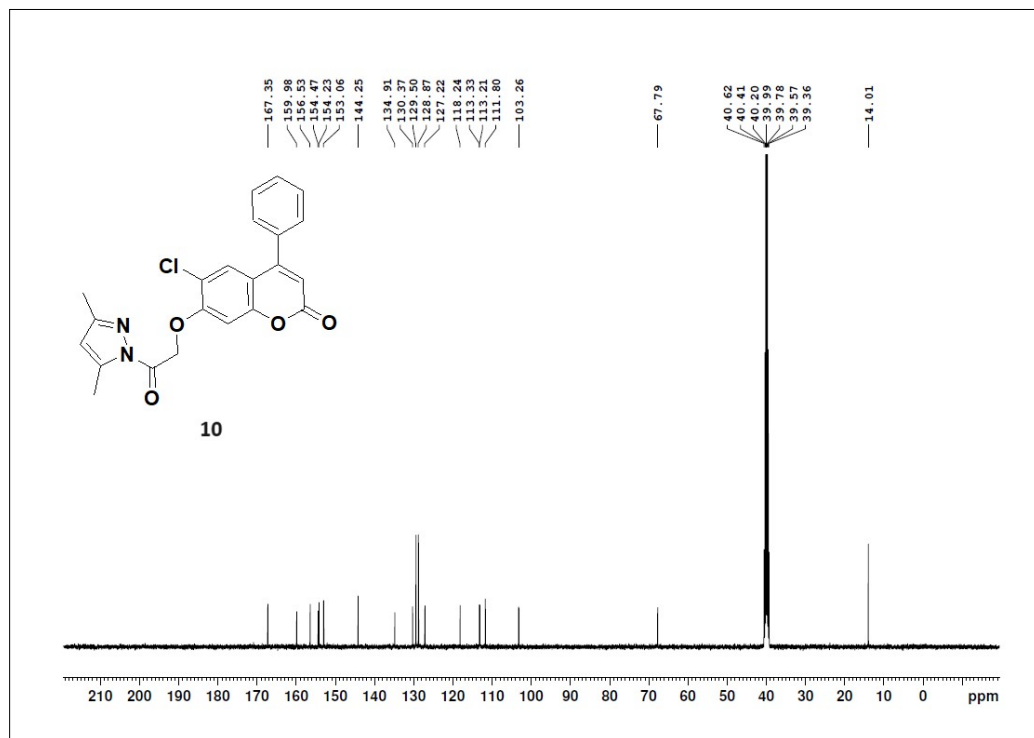
¹H NMR of compound 9c



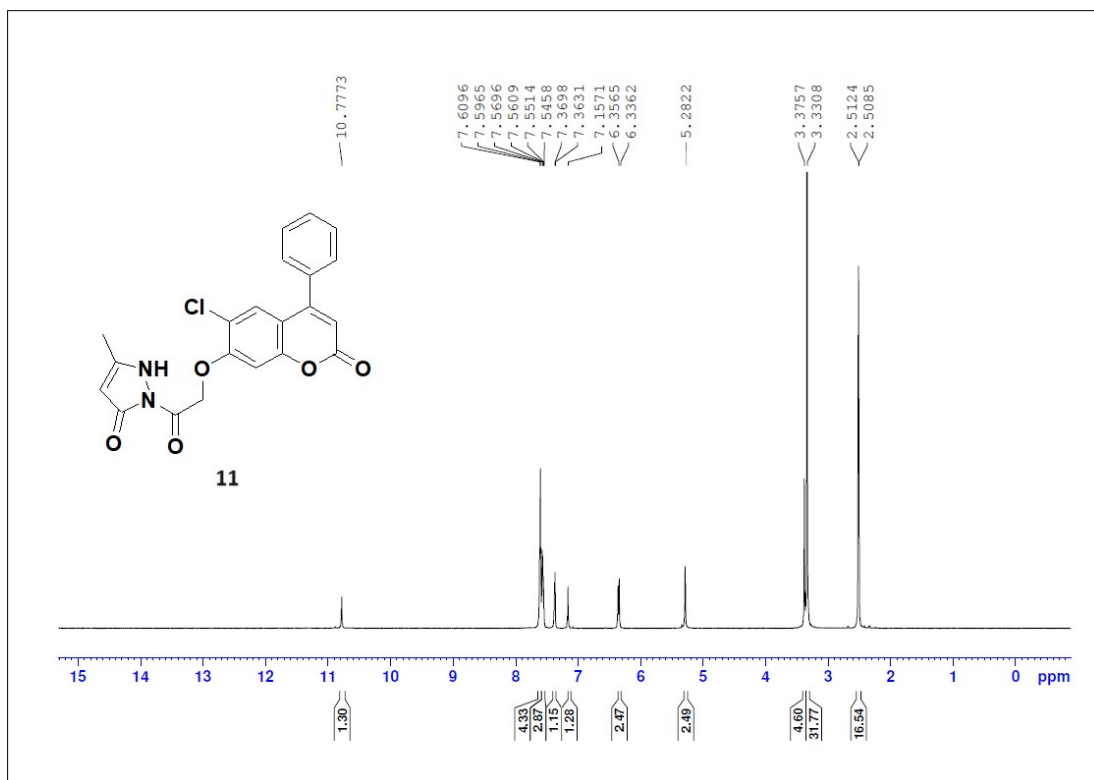
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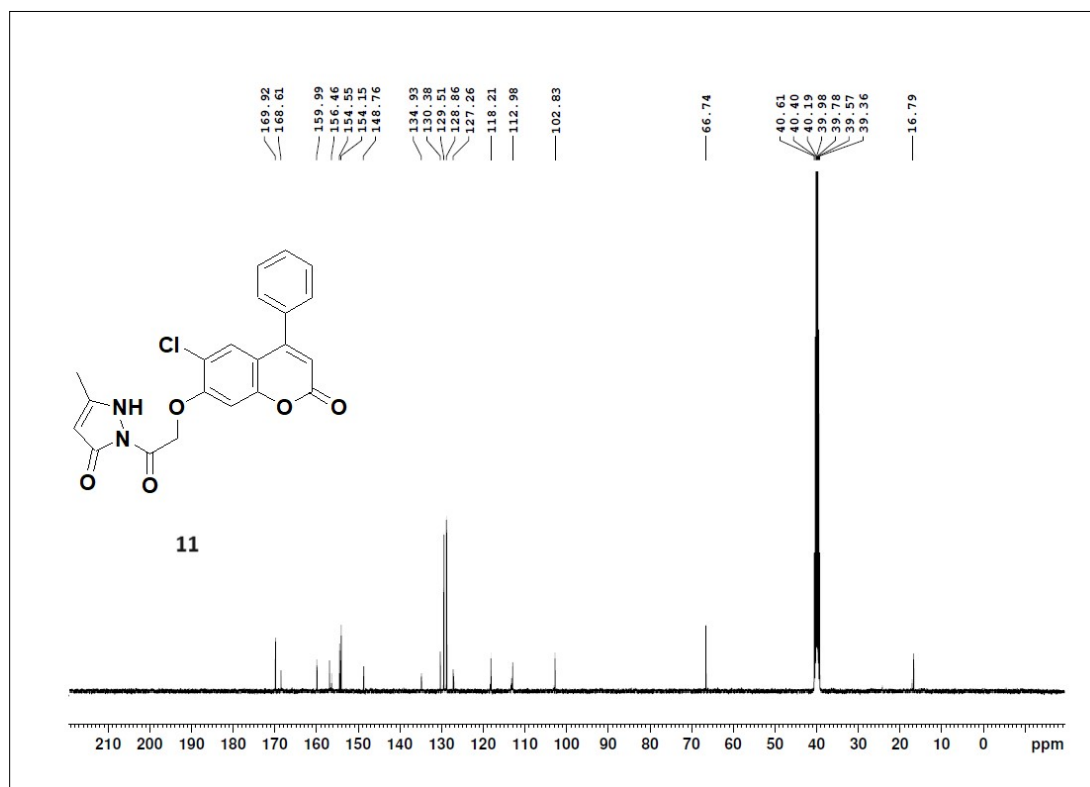
¹H NMR of compound 10



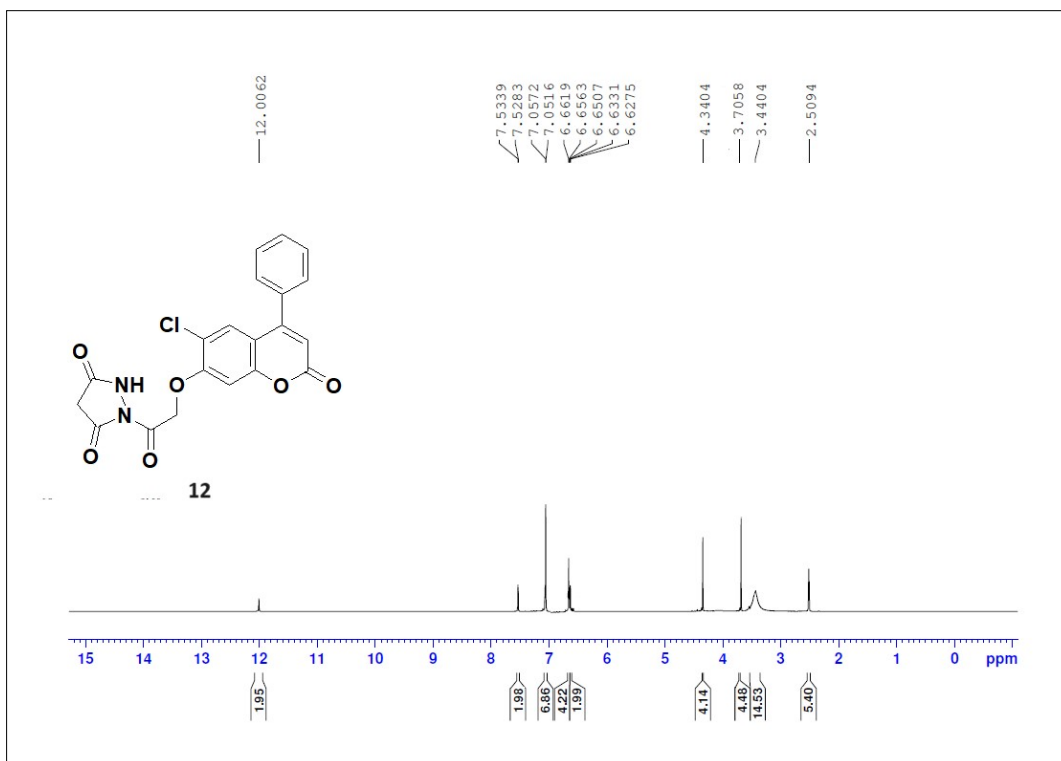
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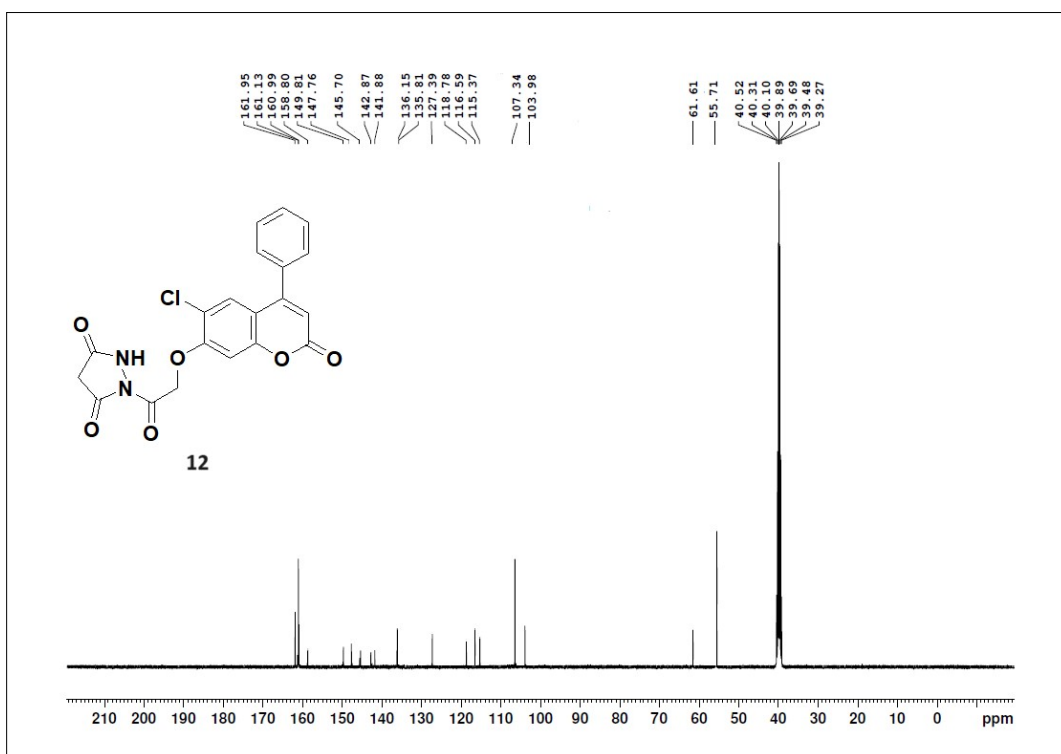
¹H NMR of compound 11



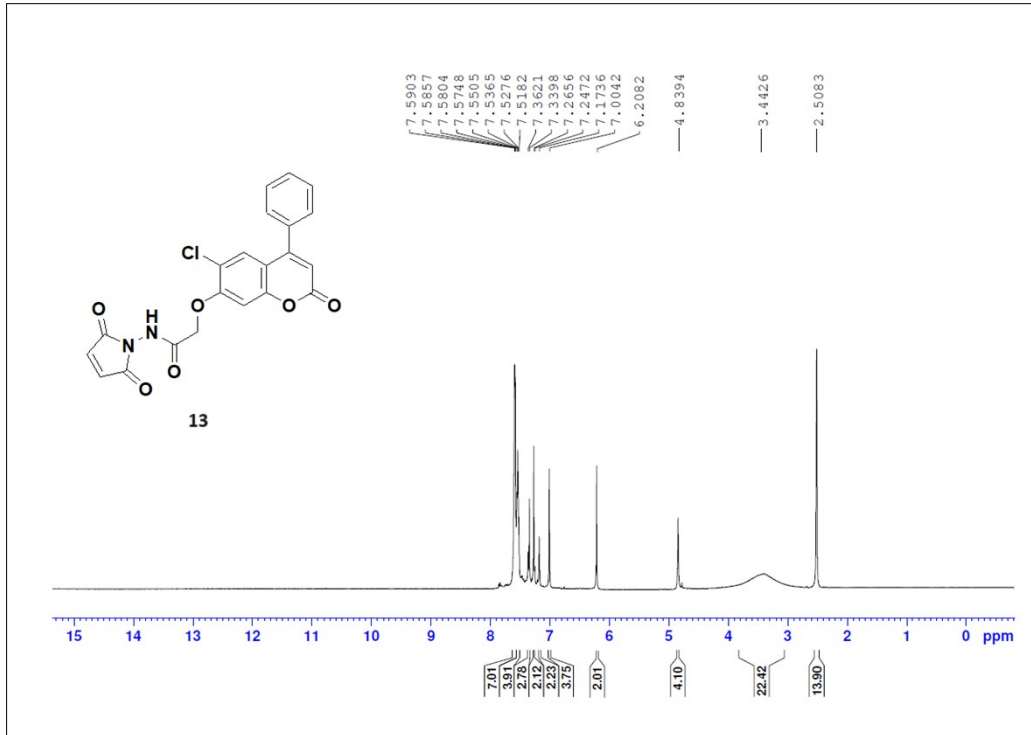
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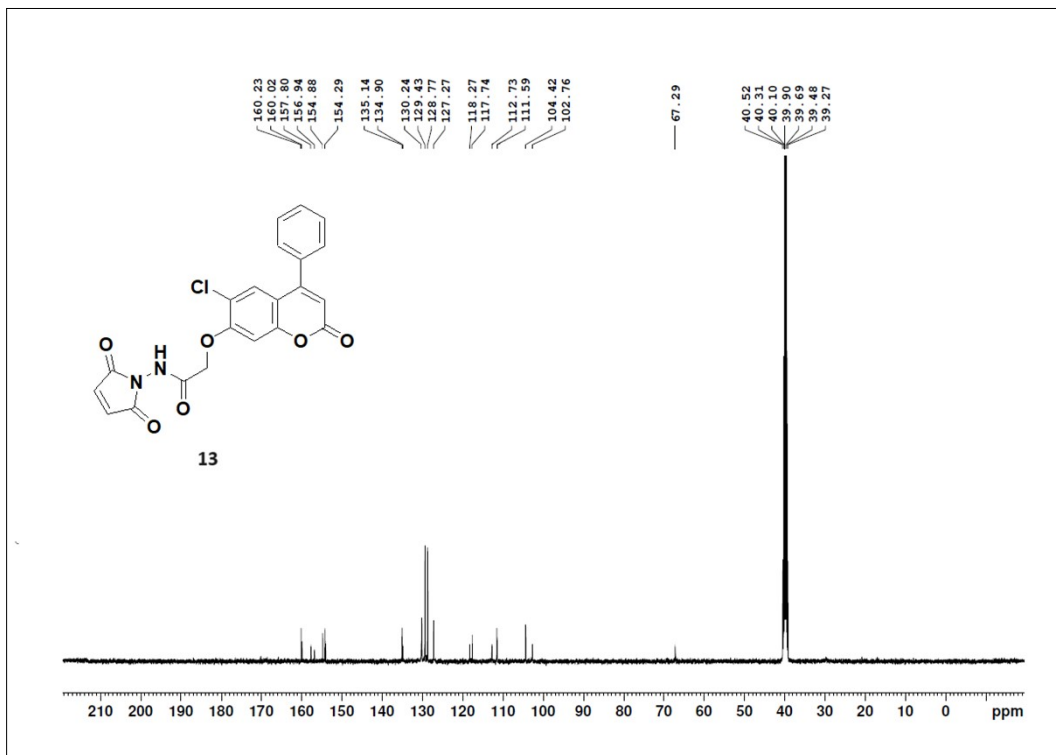
¹H NMR of compound 12



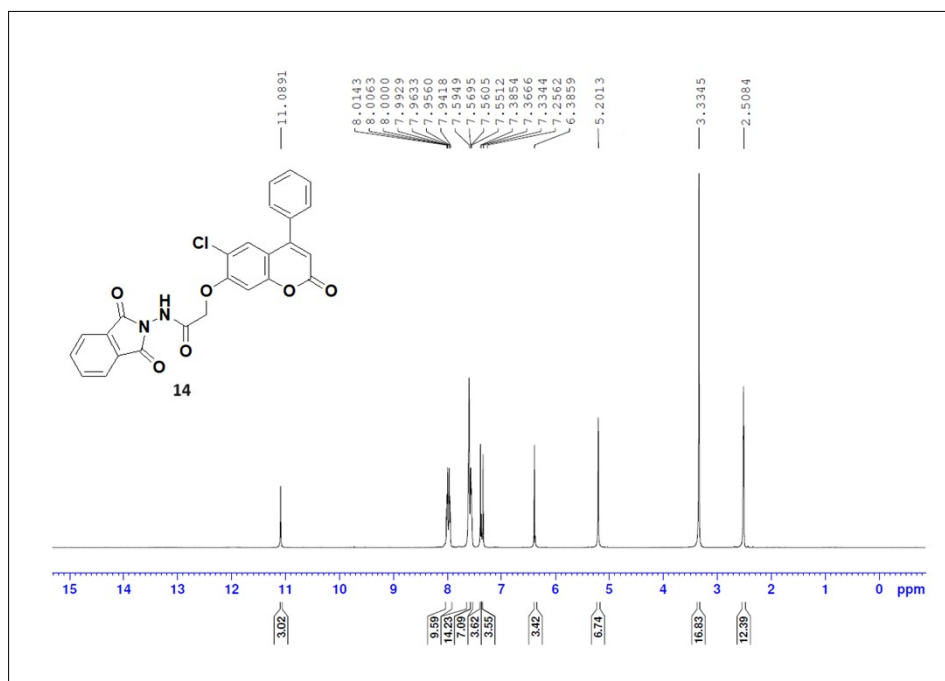
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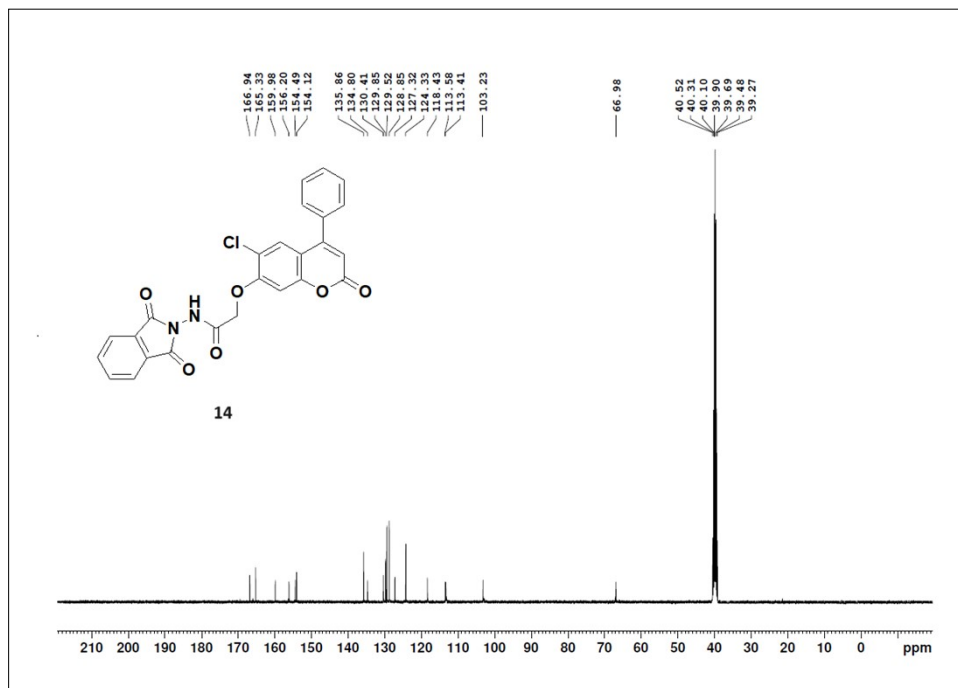
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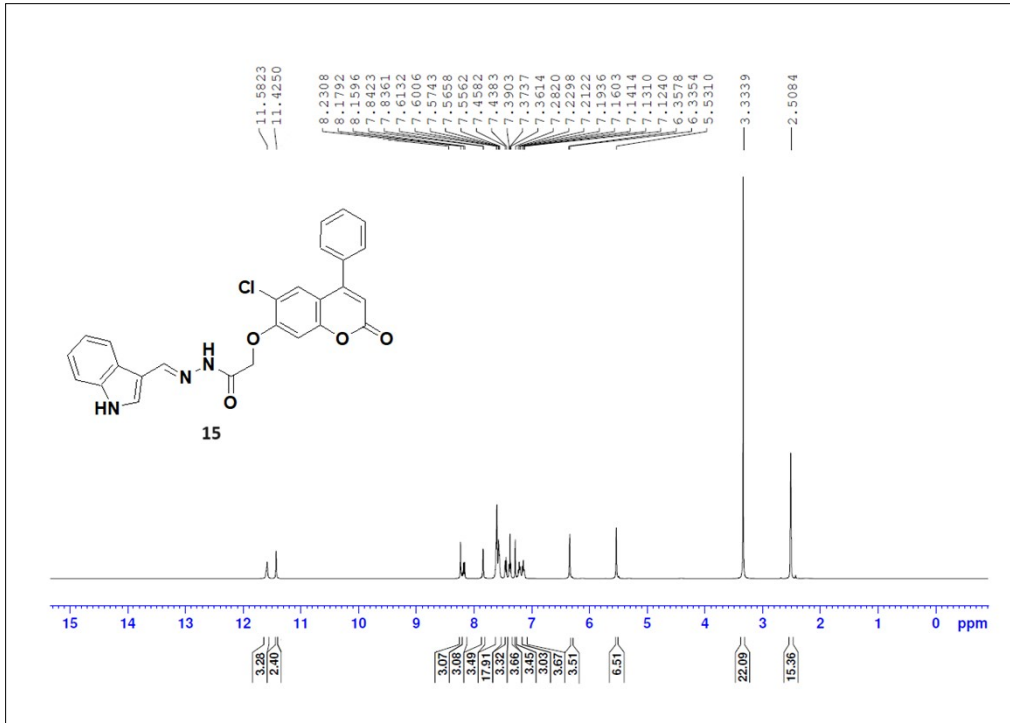
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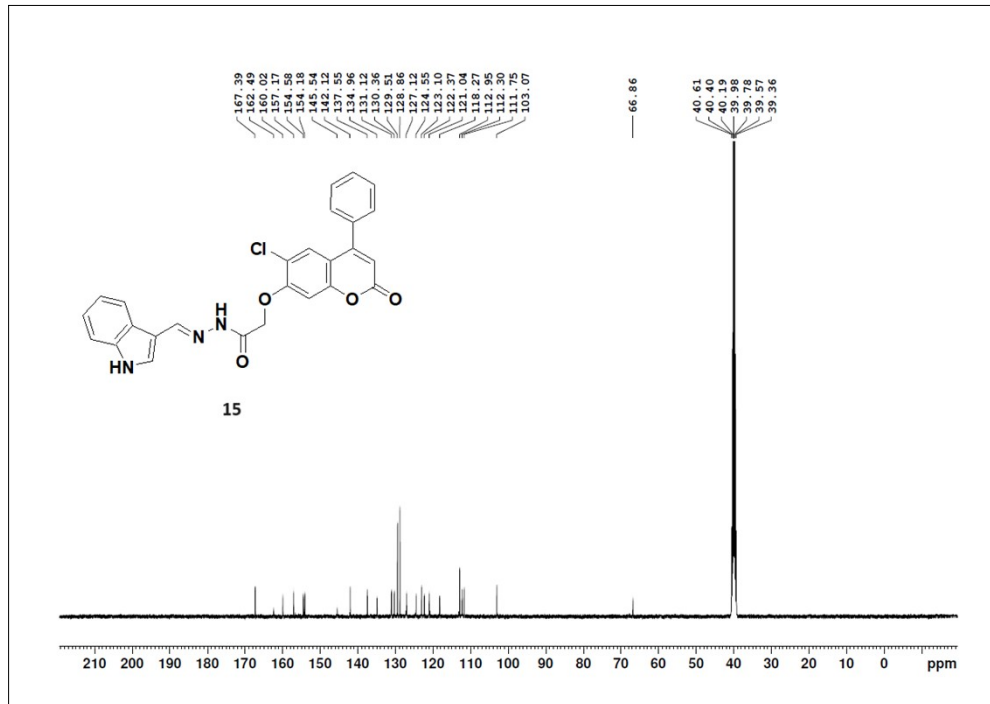
¹H NMR of compound 14



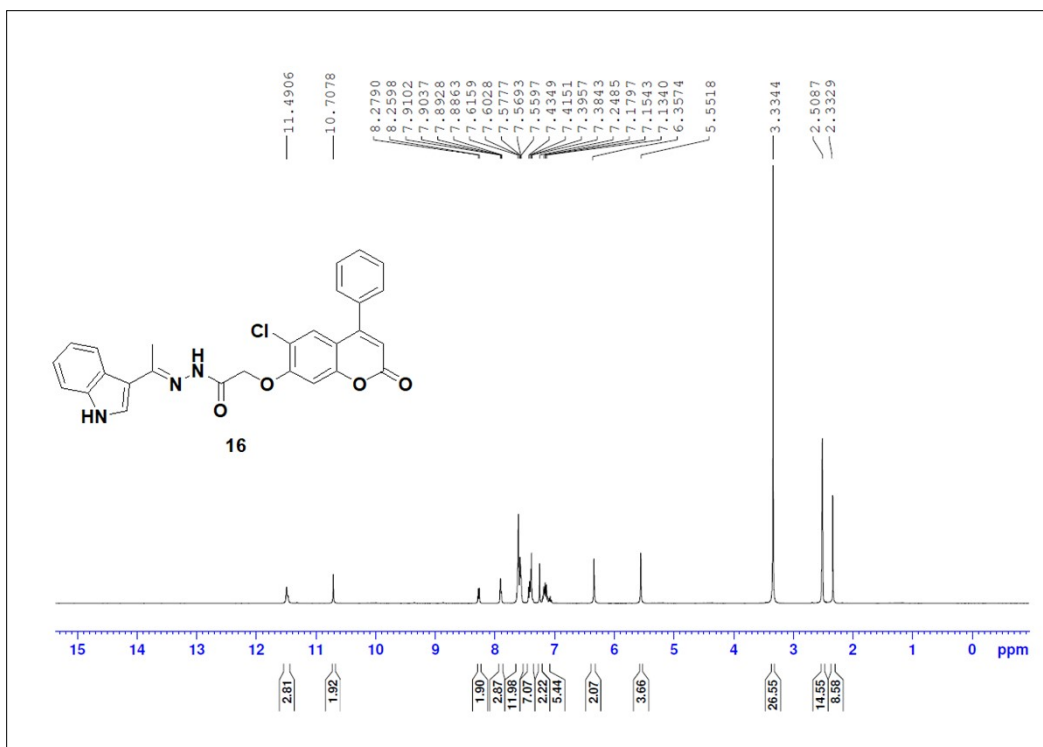
¹³C NMR of compound 14



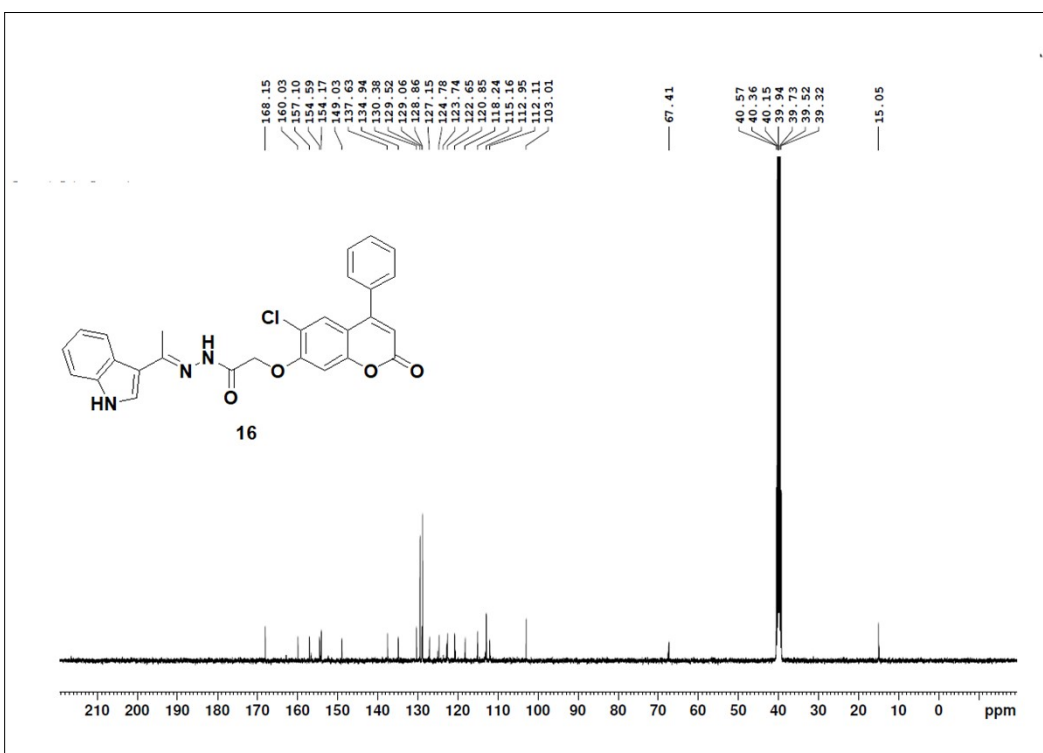
¹H NMR of compound 15



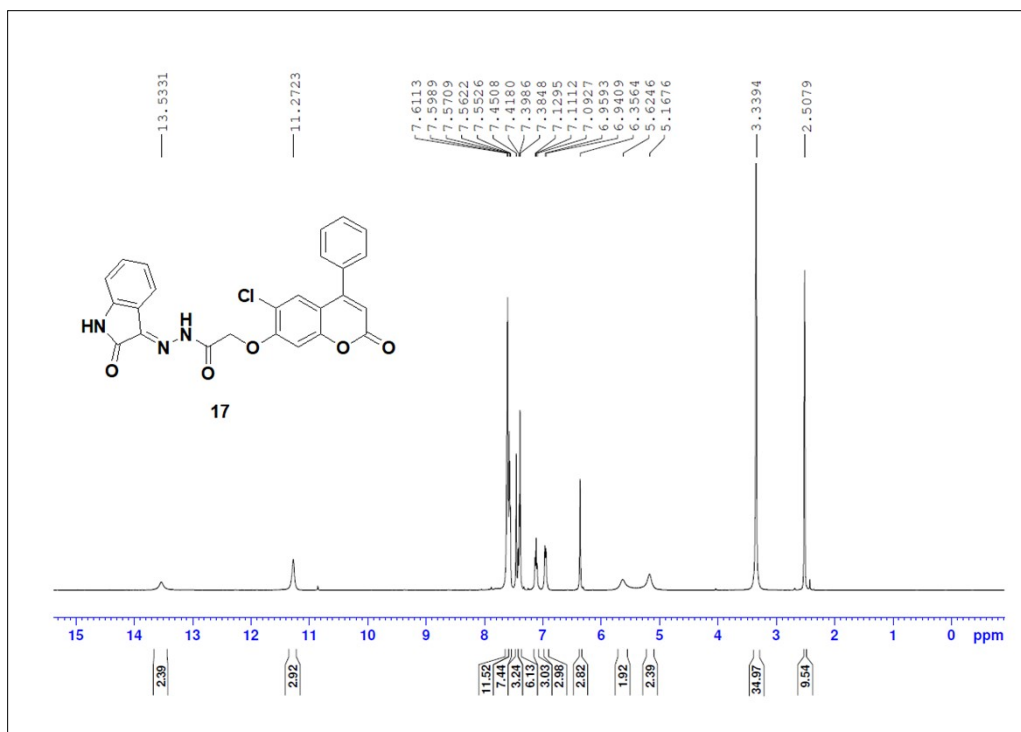
¹³C NMR of compound 15



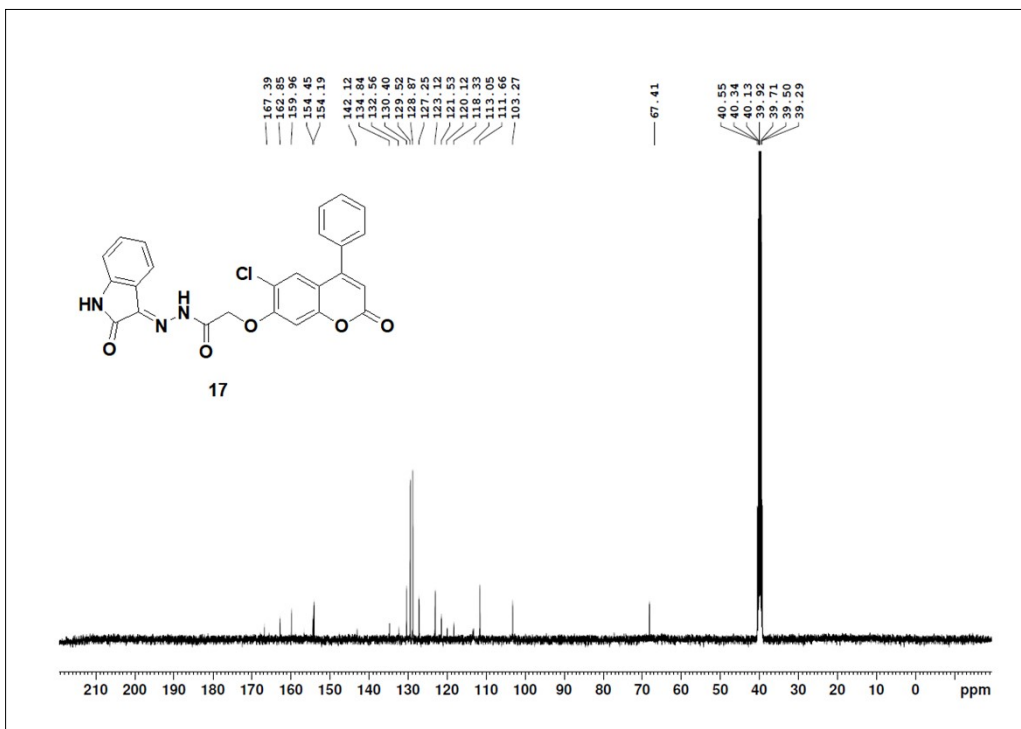
¹H NMR of compound 16



¹³C NMR of compound 16



¹H NMR of compound 17



¹³C NMR of compound 17