

# Supporting Information

## Newly Synthesized Pyrazolinone Chalcones as Anticancer Agents via Inhibiting PI3K/Akt/ERK1/2 Signaling Pathway

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<sup>2</sup> Department of Chemistry, Pure and Applied Chemistry Research Group, College of Sciences, University of Sharjah, Sharjah, 27272, UAE.

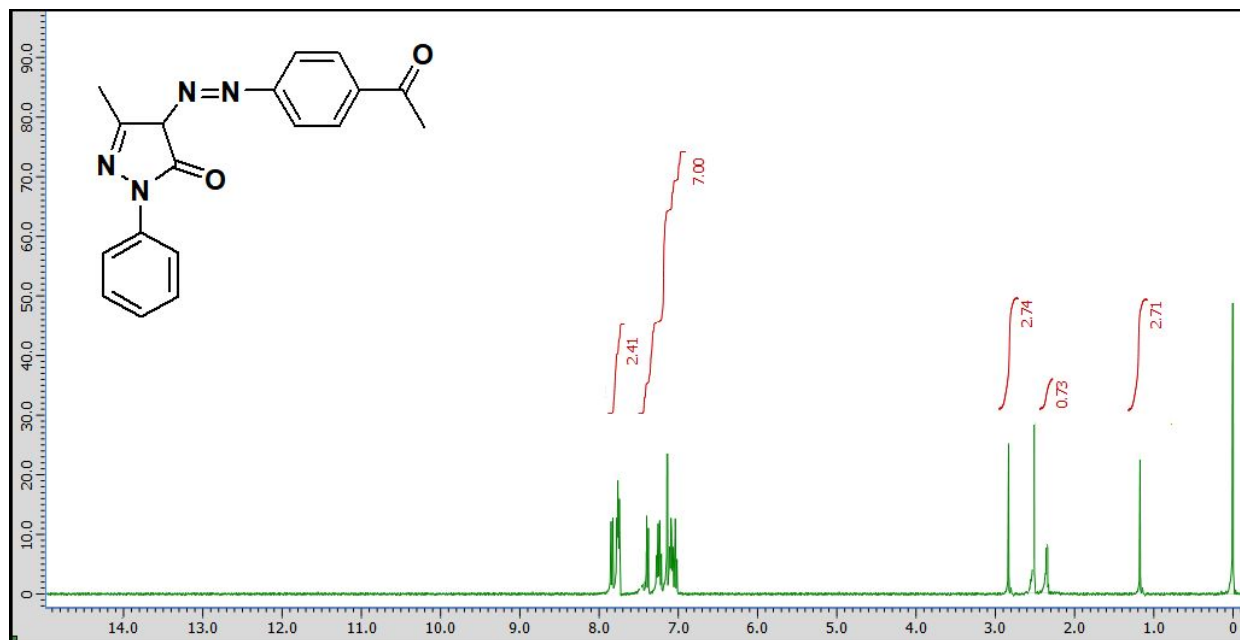
<sup>3</sup> Chemistry Department, Faculty of Science, South Valley University, Qena 83523, Egypt.

<sup>4</sup> Biochemistry Division, Chemistry Department, Faculty of Science, Tanta University, Tanta 31527, Egypt.

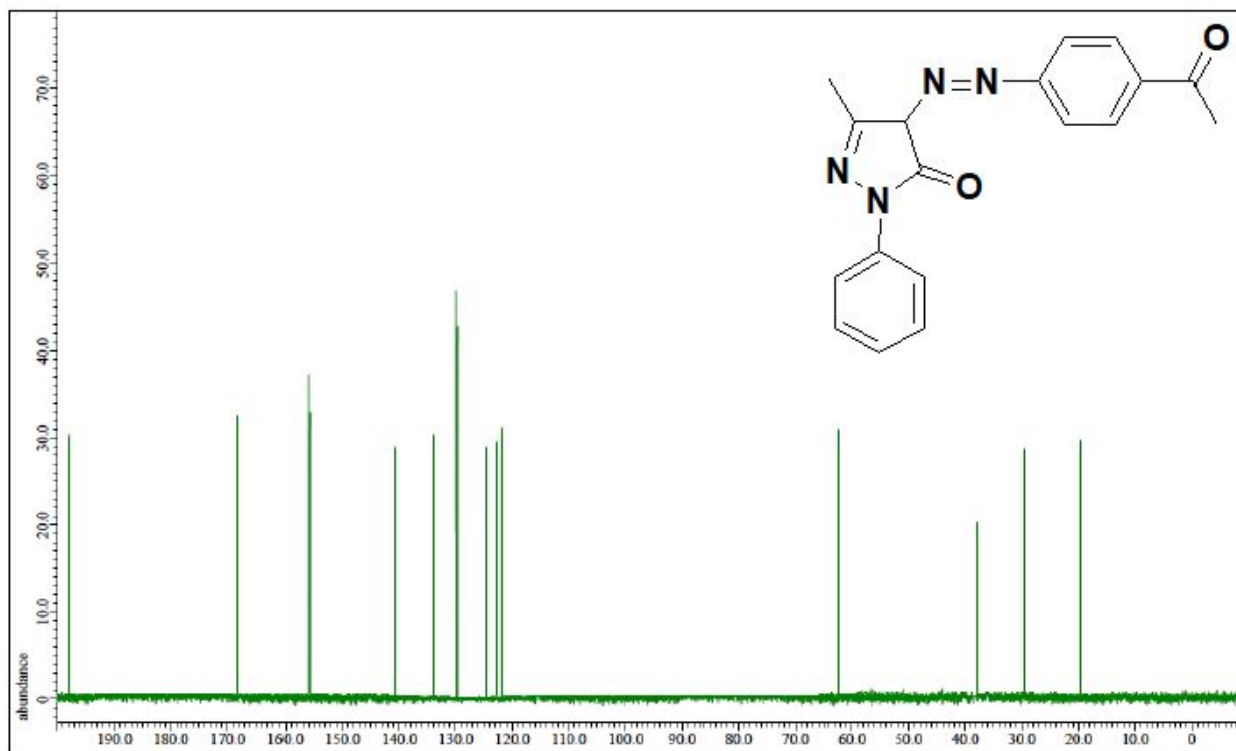
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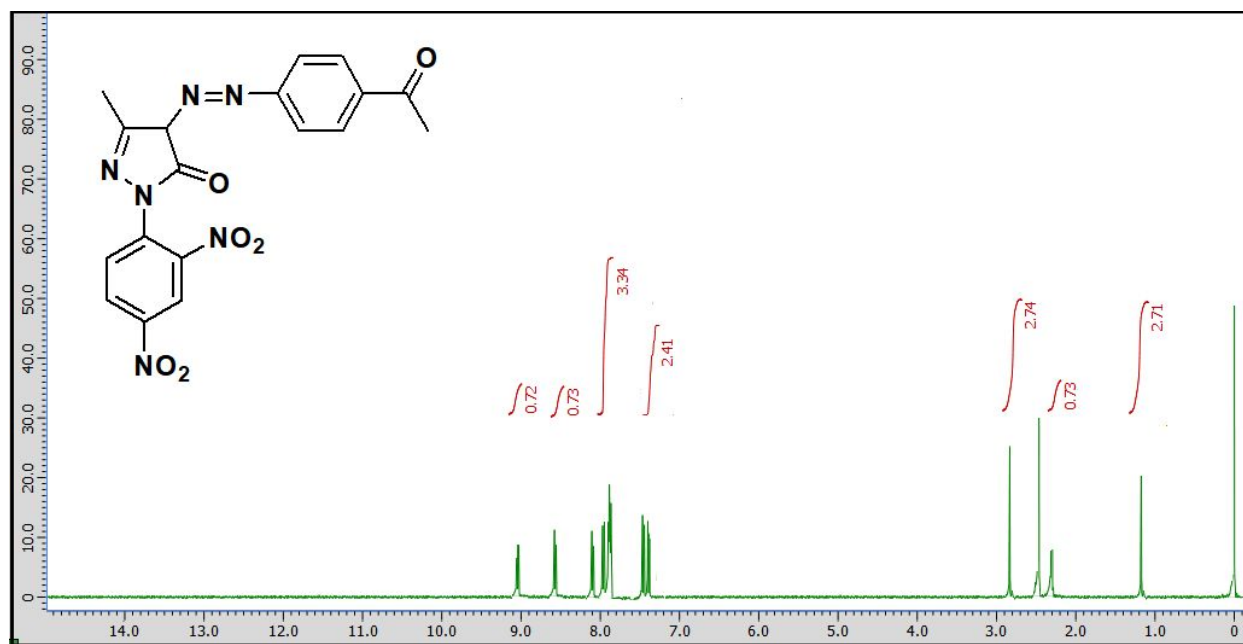
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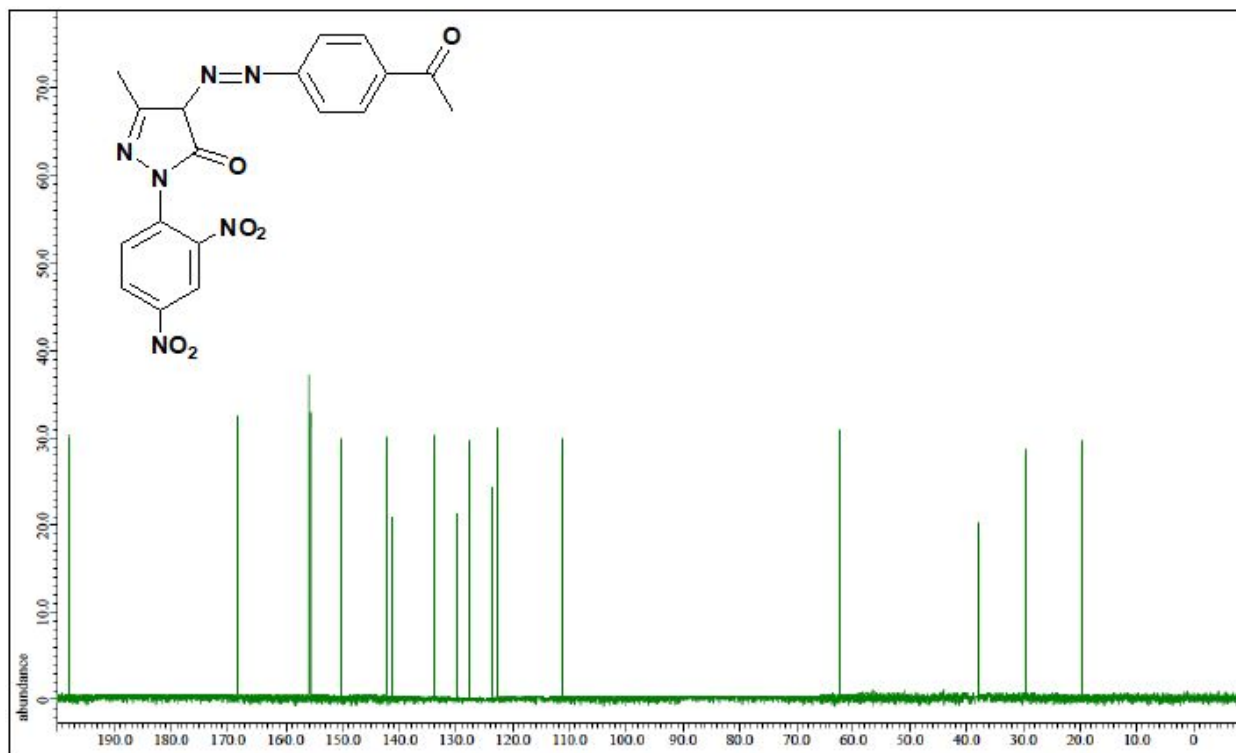
<sup>1</sup>H-NMR of compound 2b



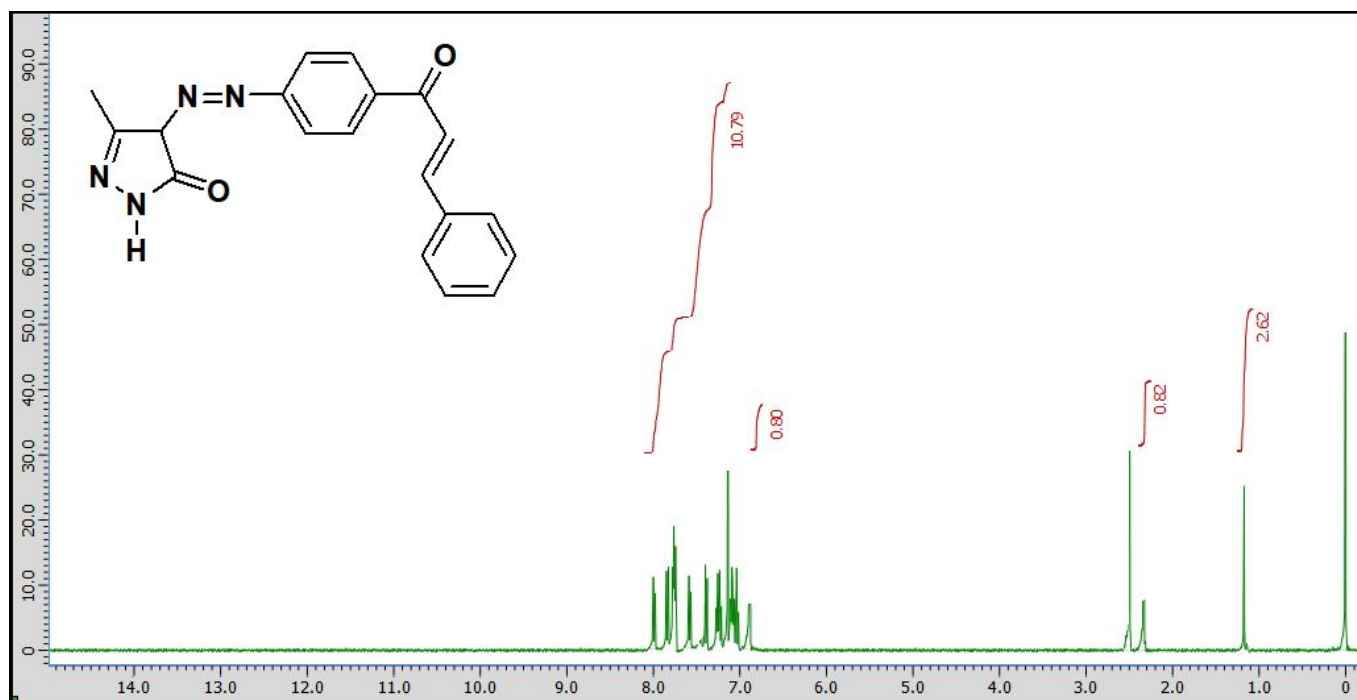
<sup>13</sup>C-NMR of compound 2b



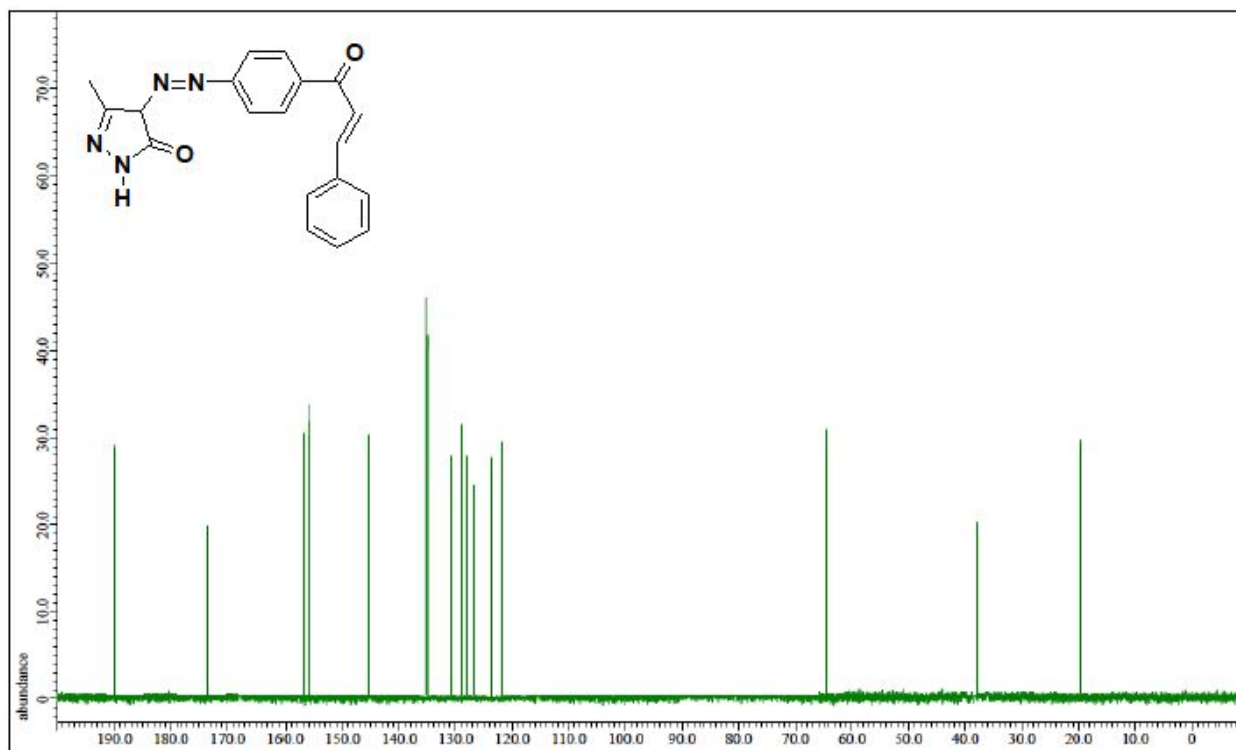
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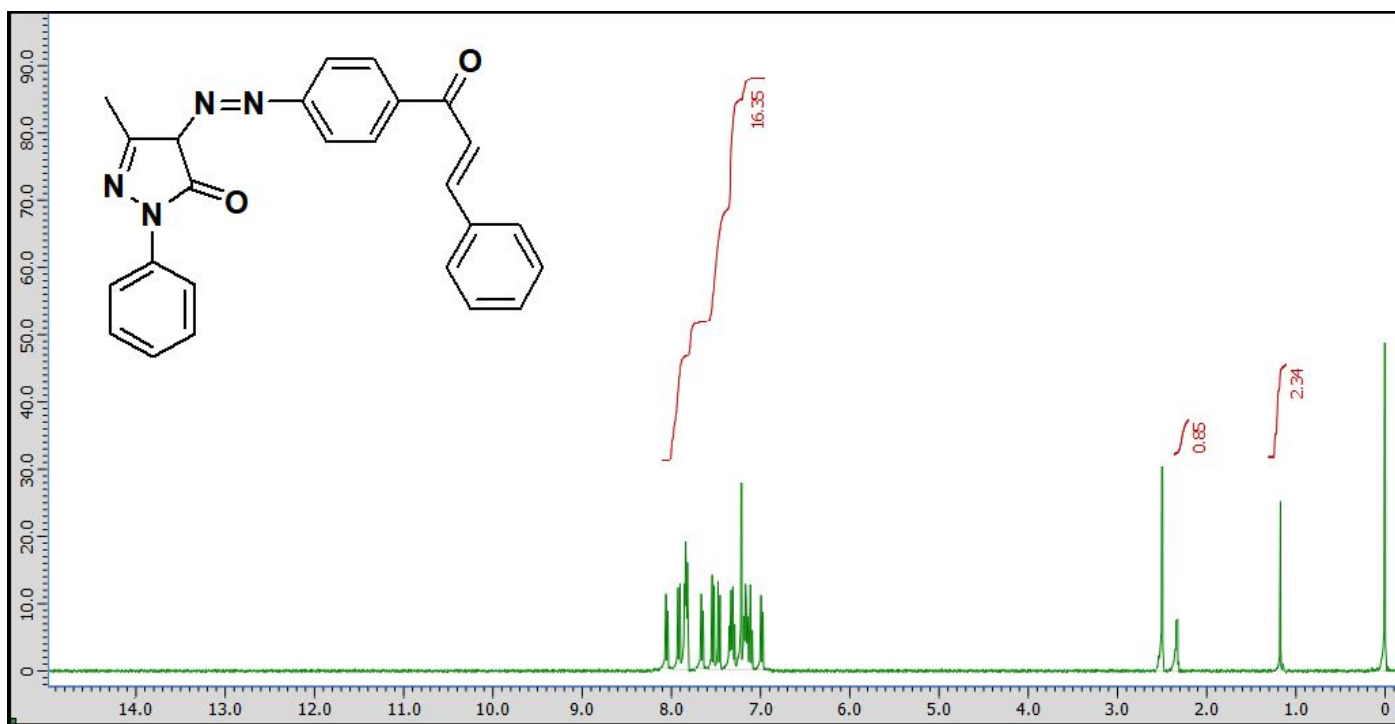
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<sup>1</sup>H-NMR of compound 3a

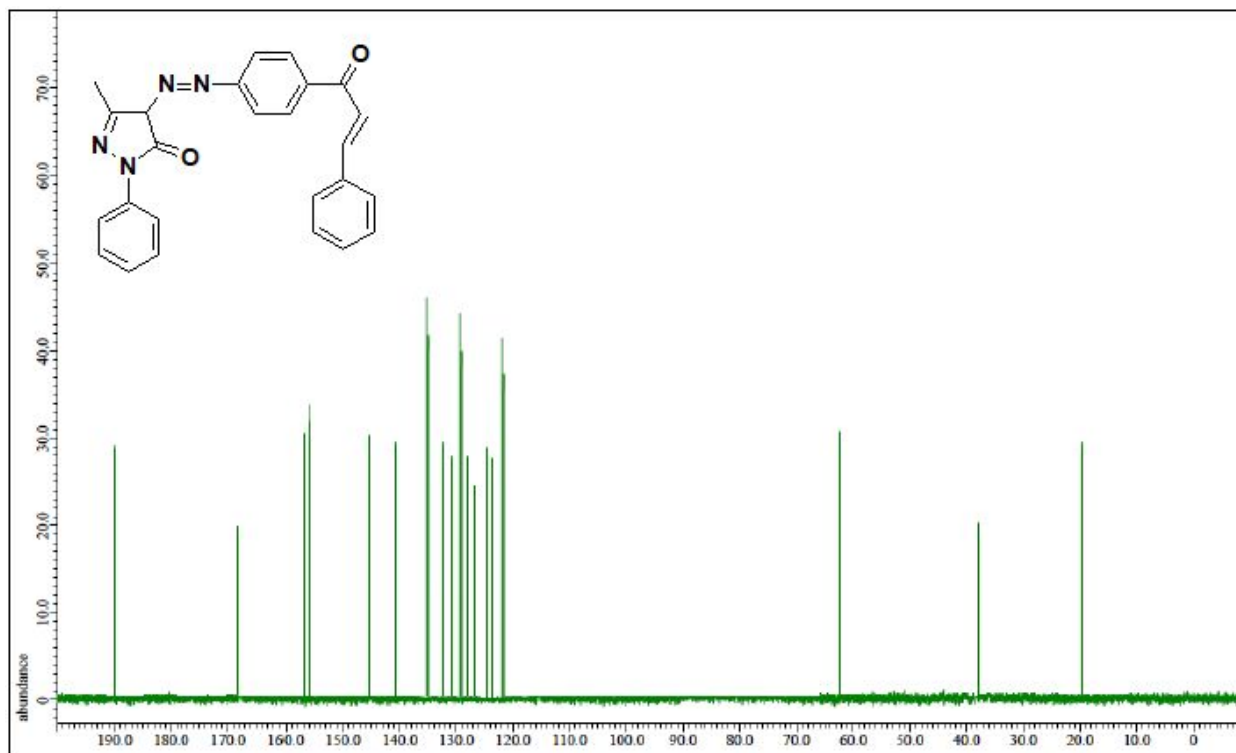


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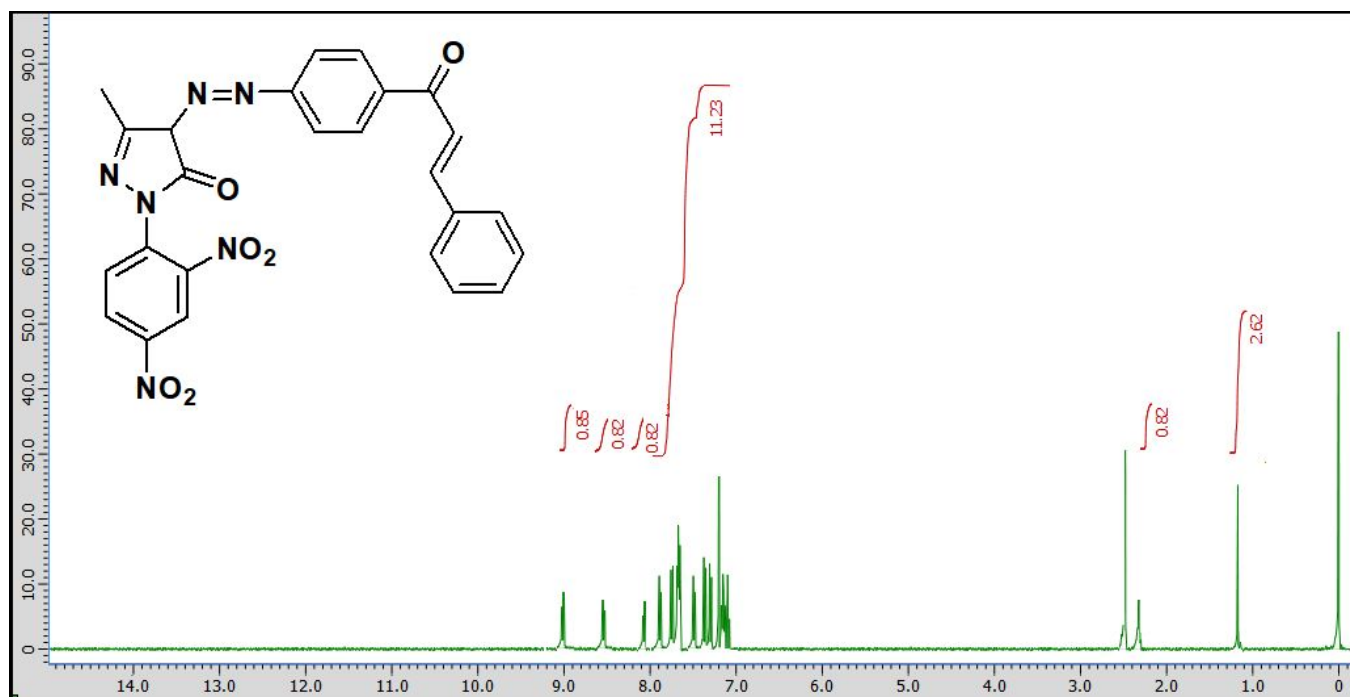


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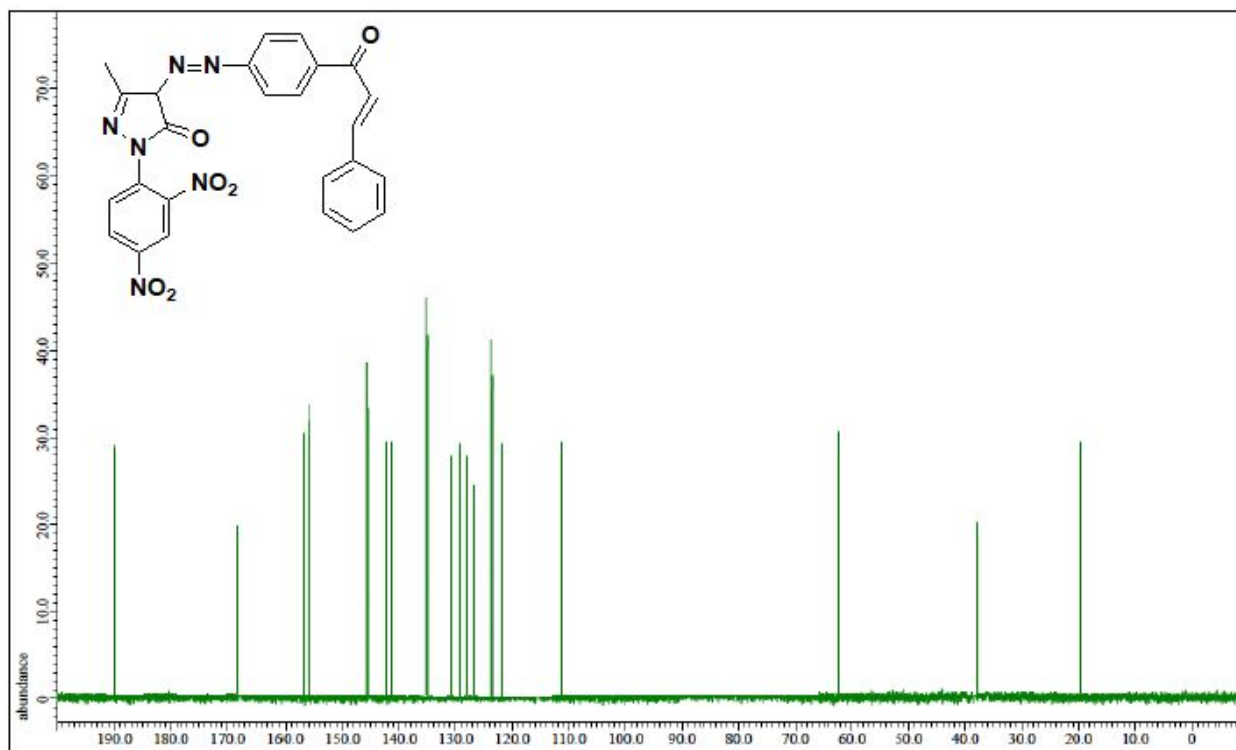




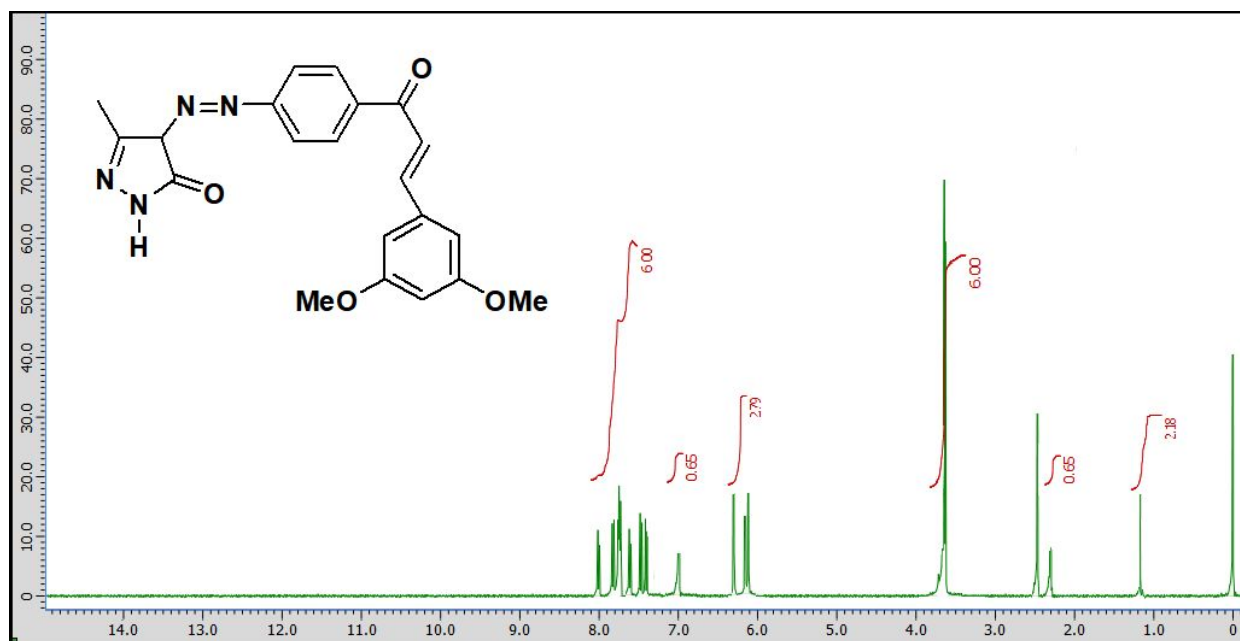
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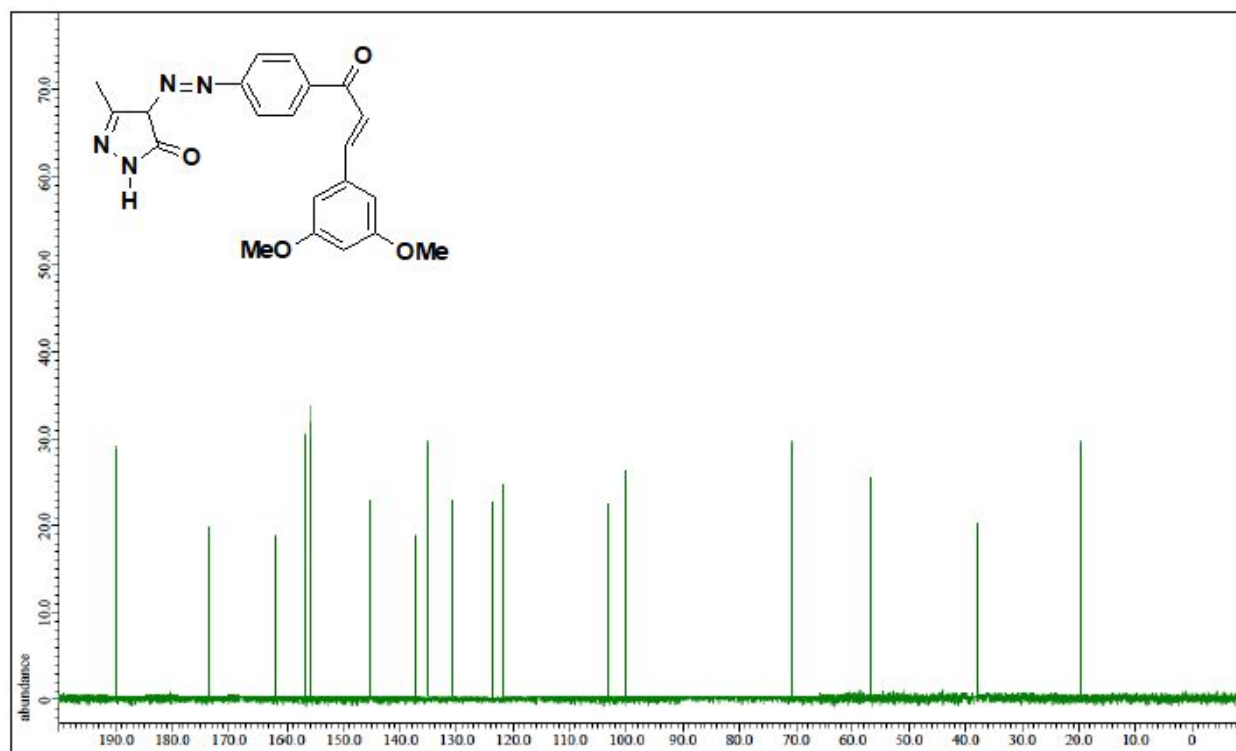
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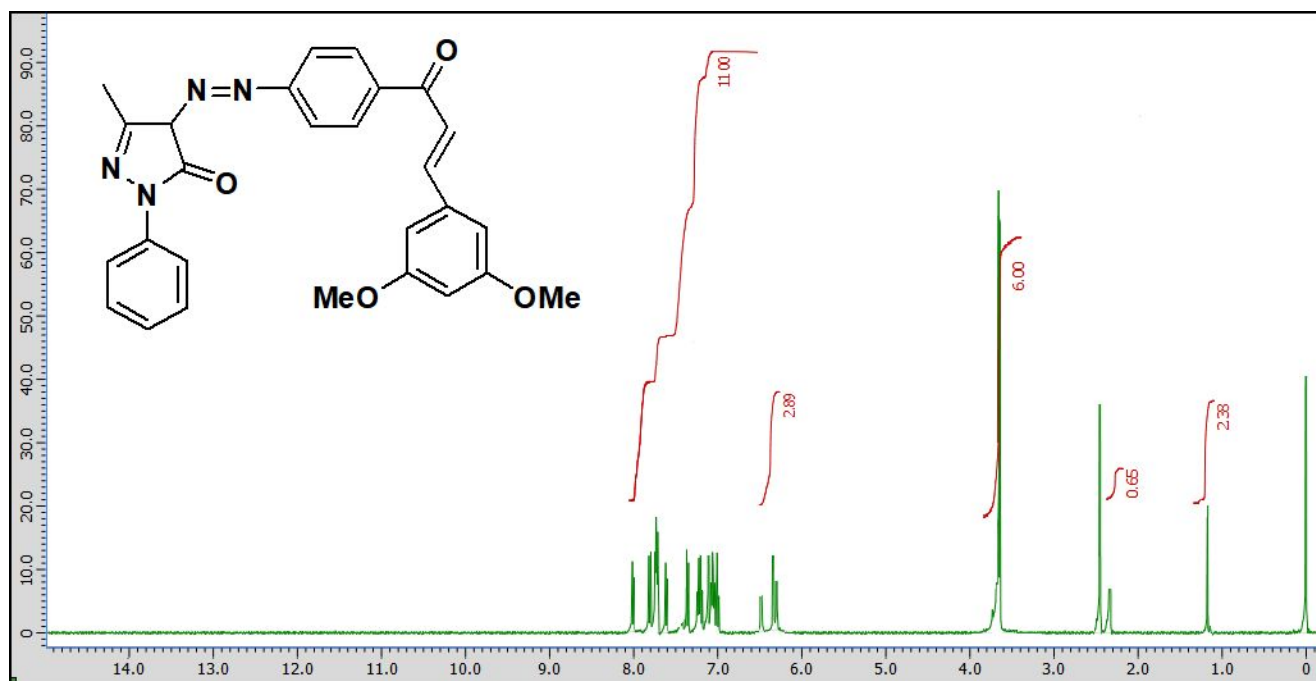
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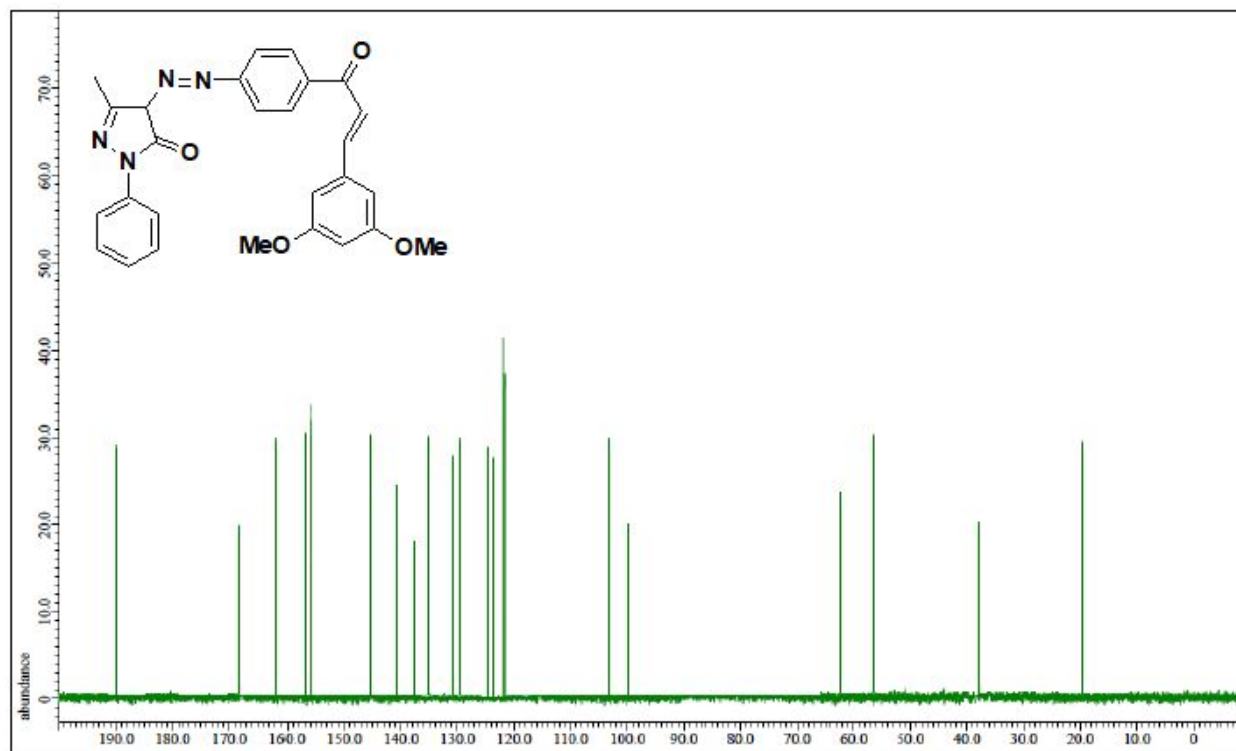
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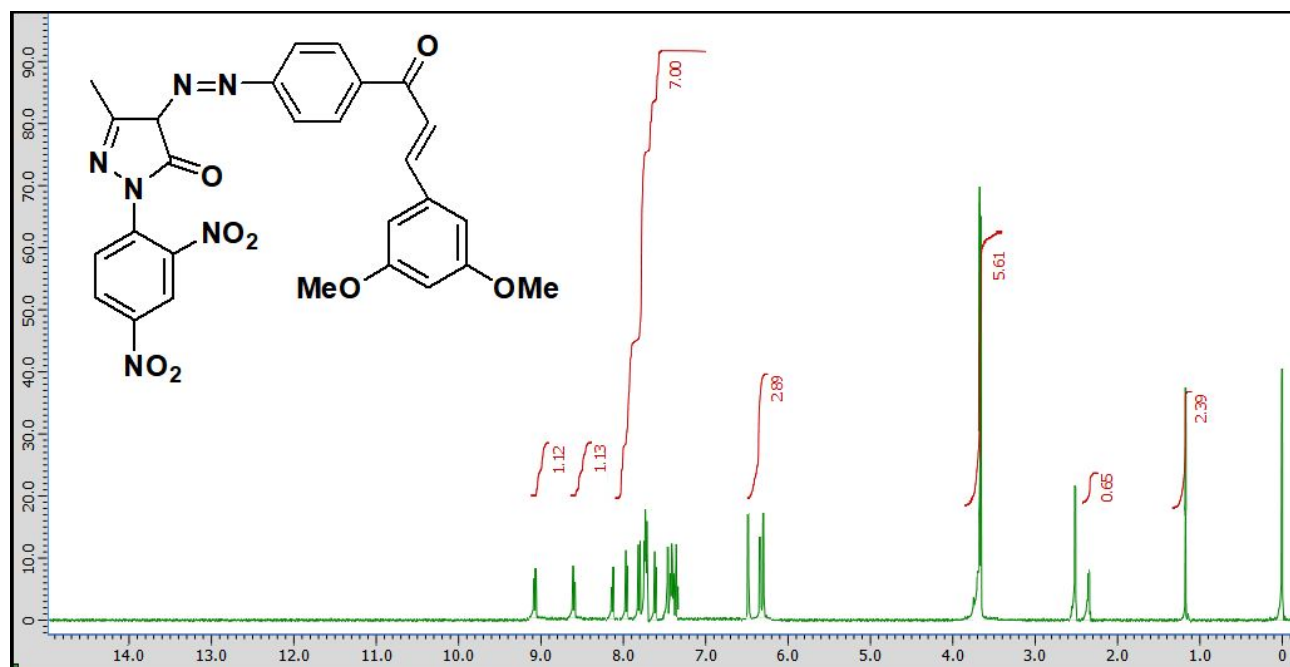
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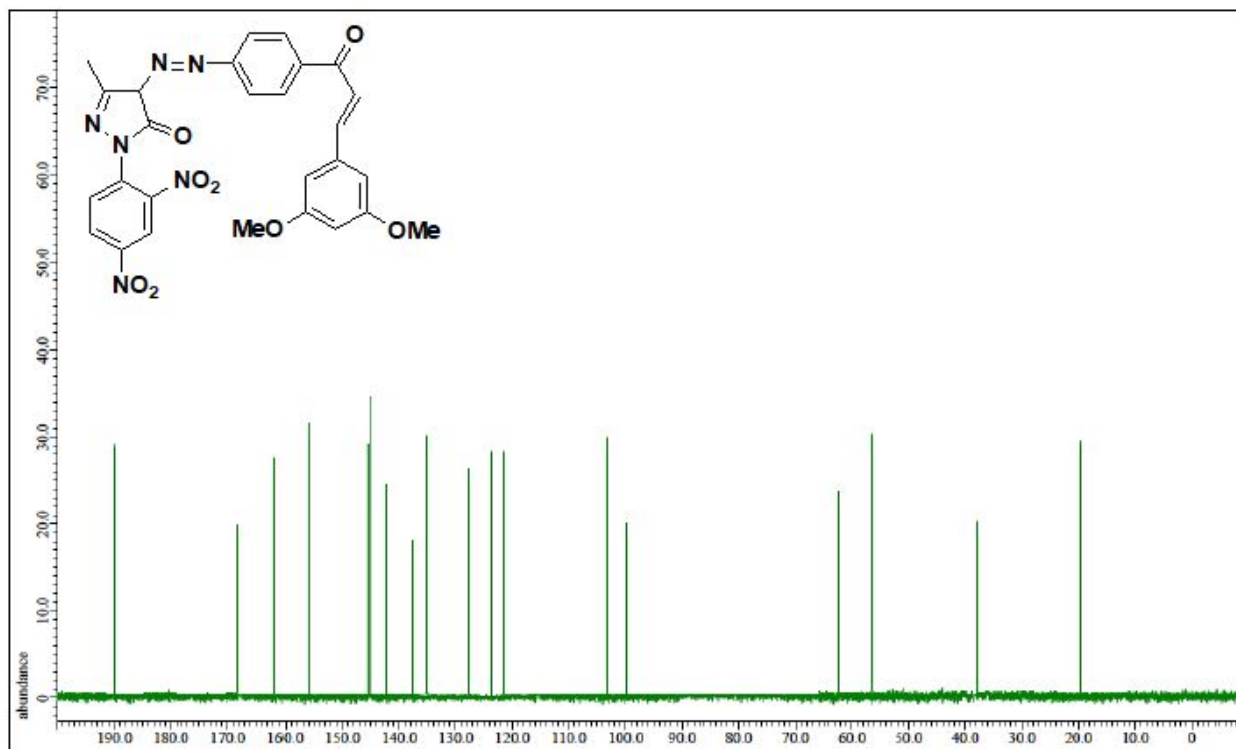


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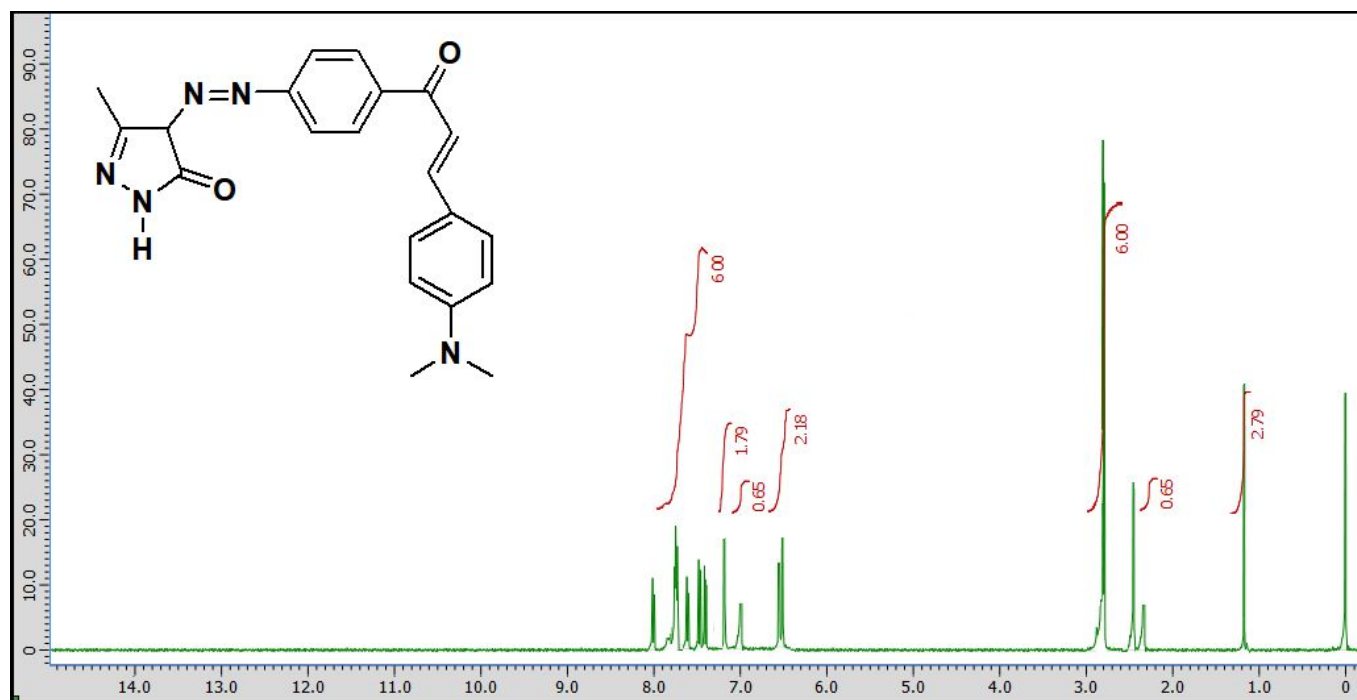


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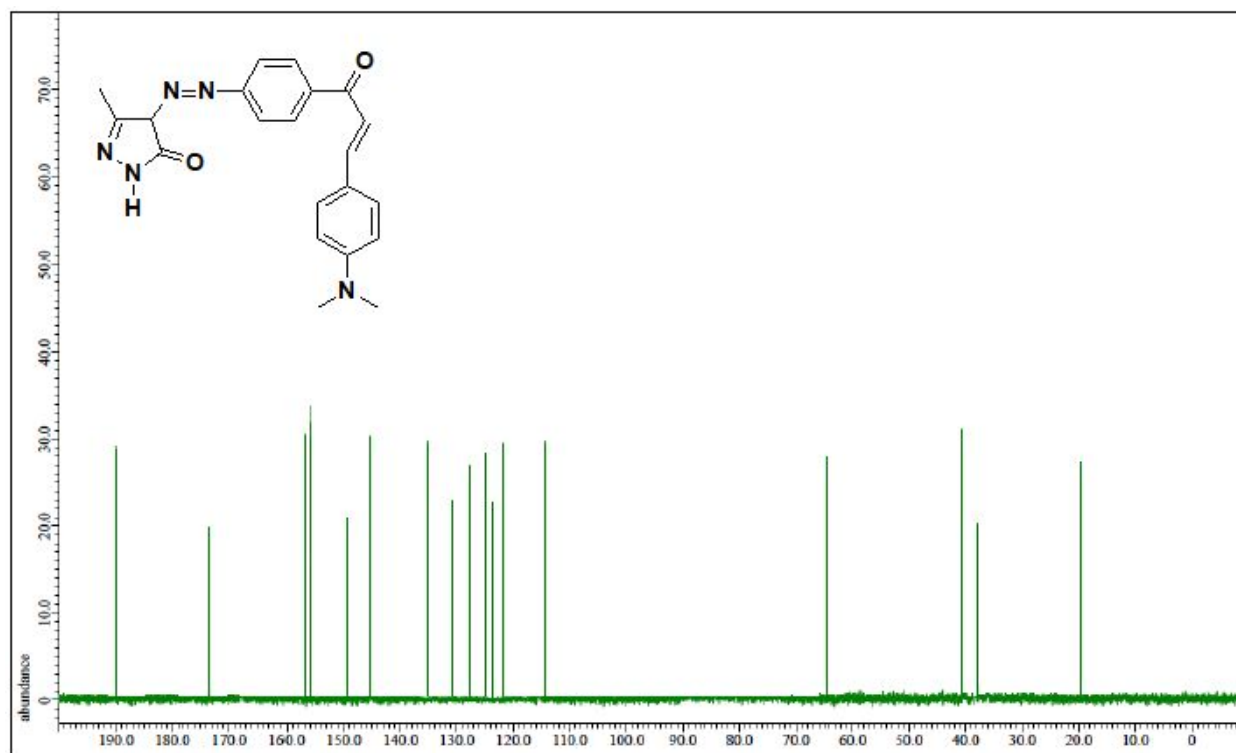




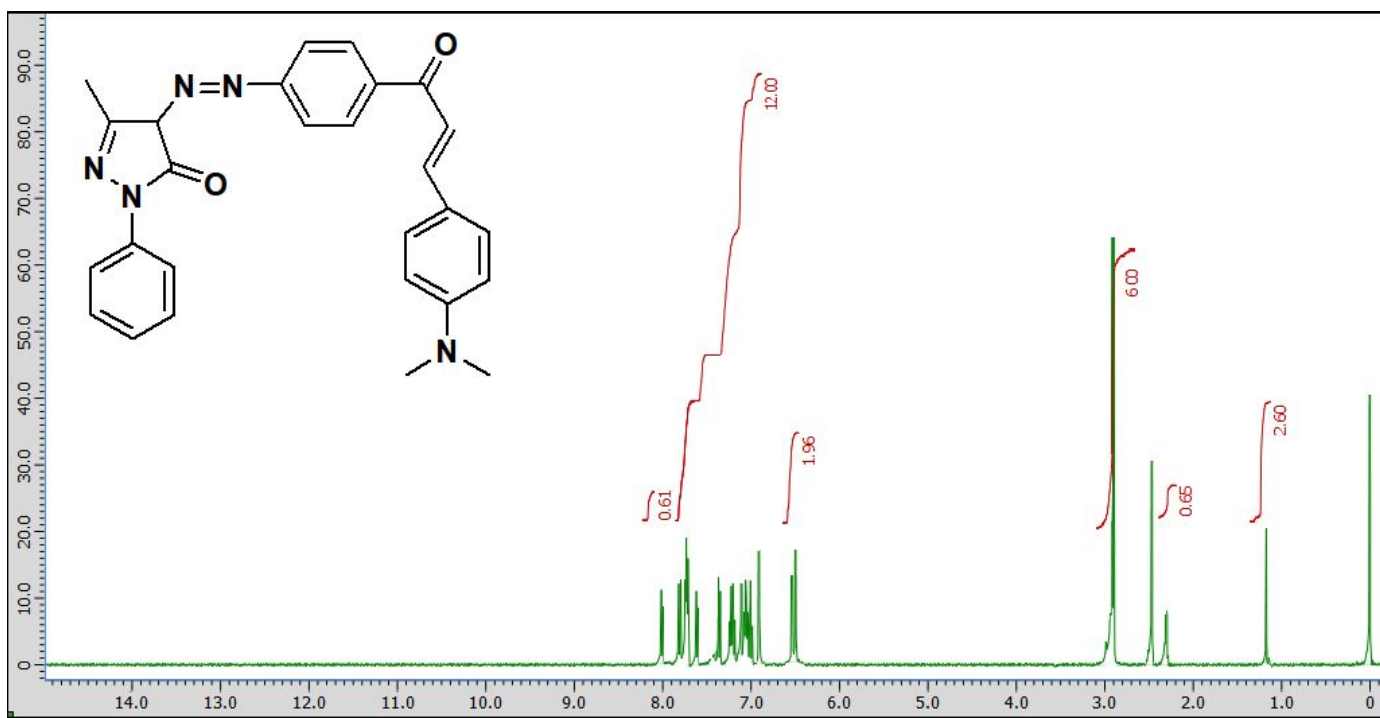
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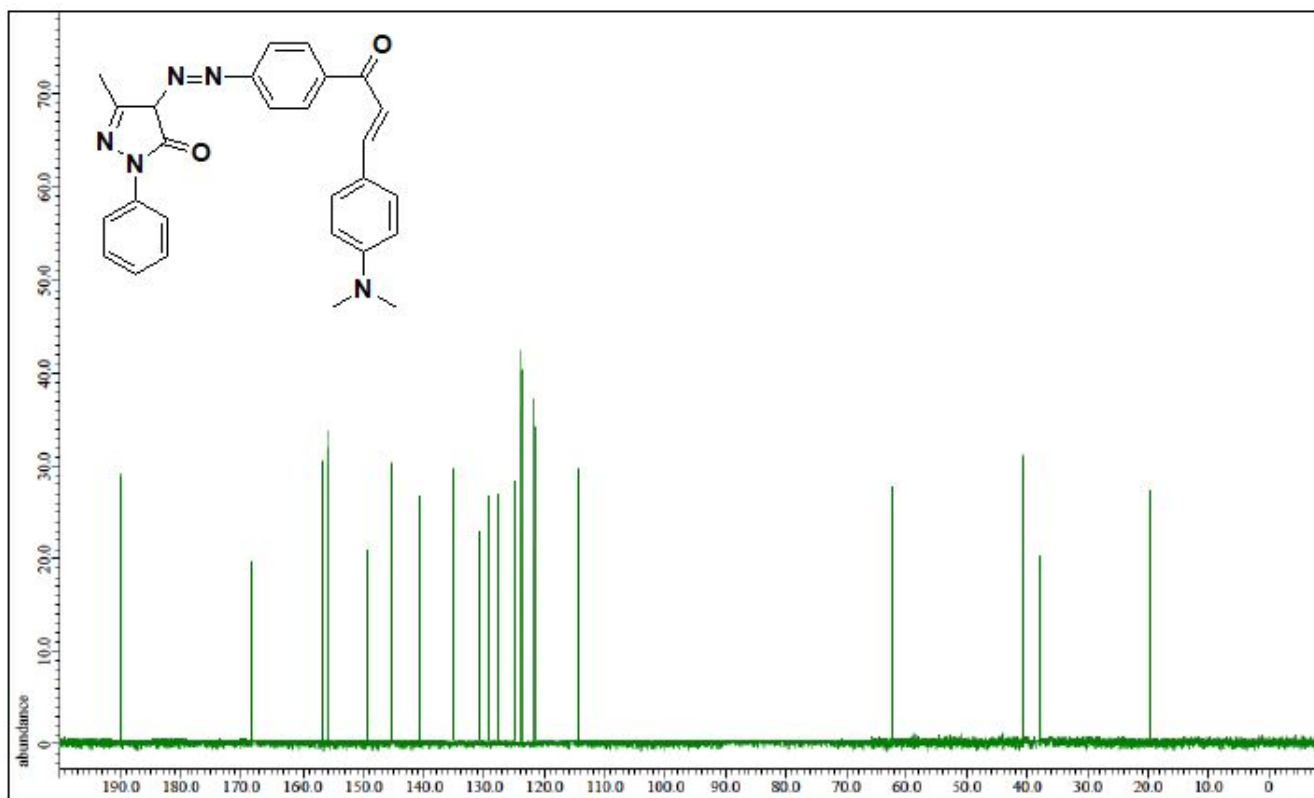
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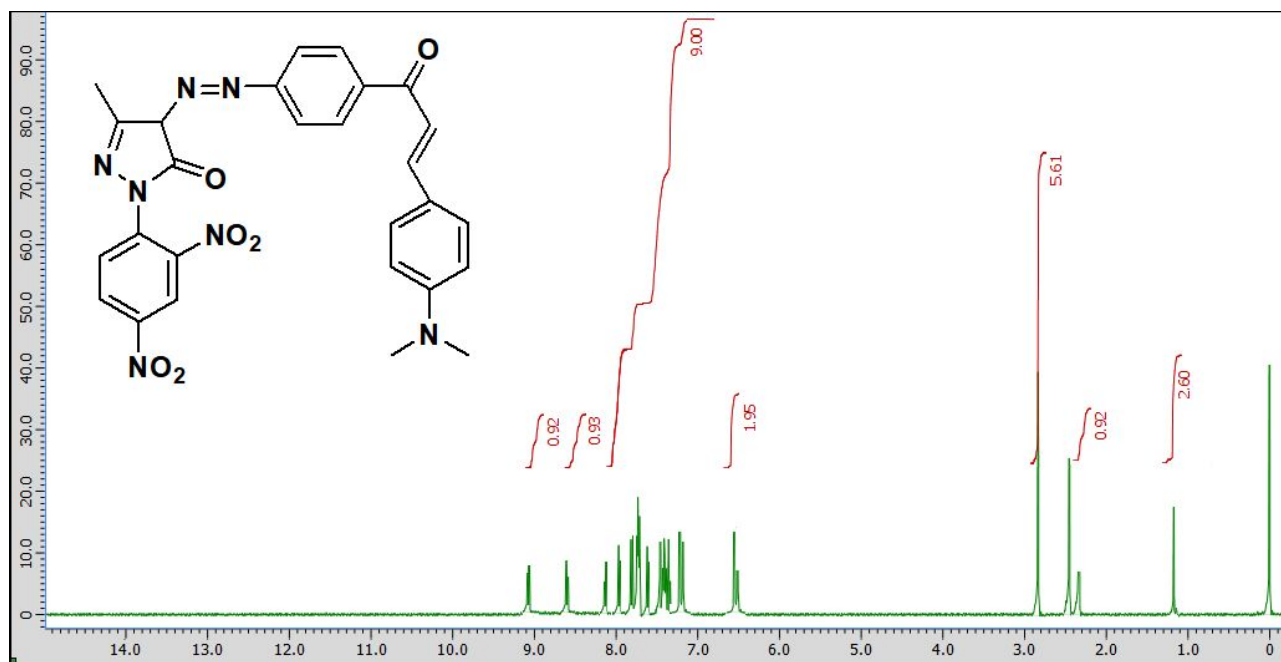
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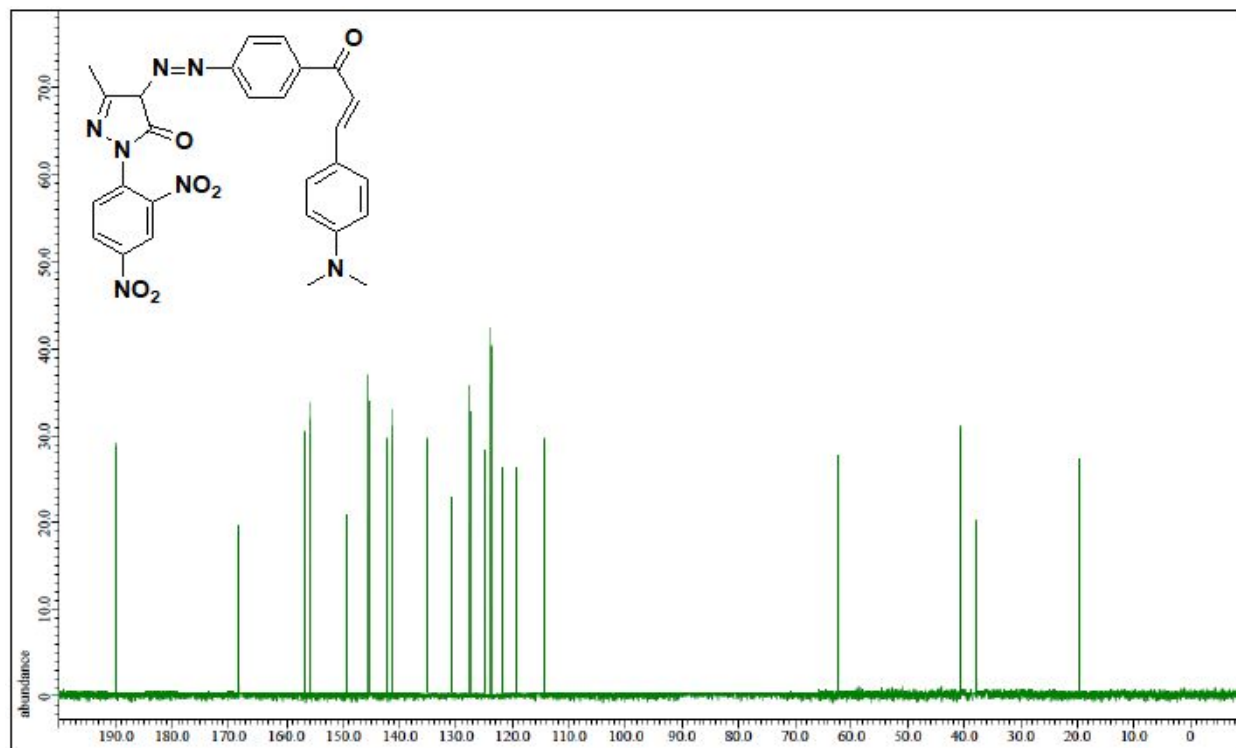
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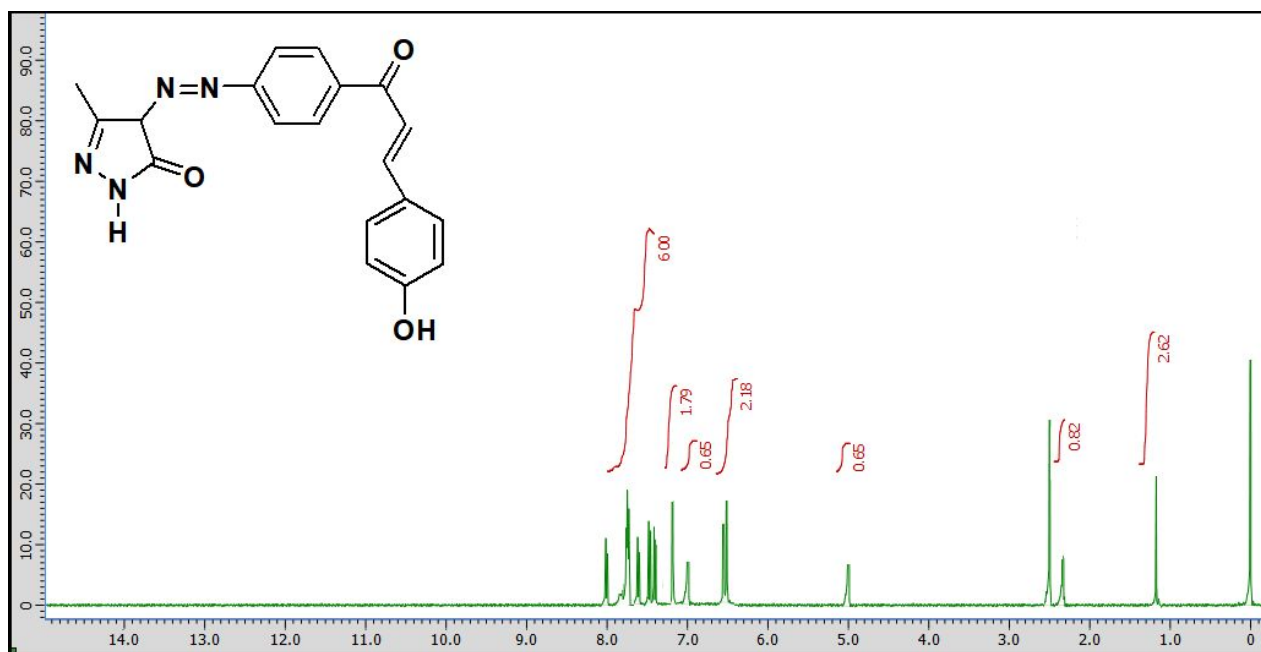
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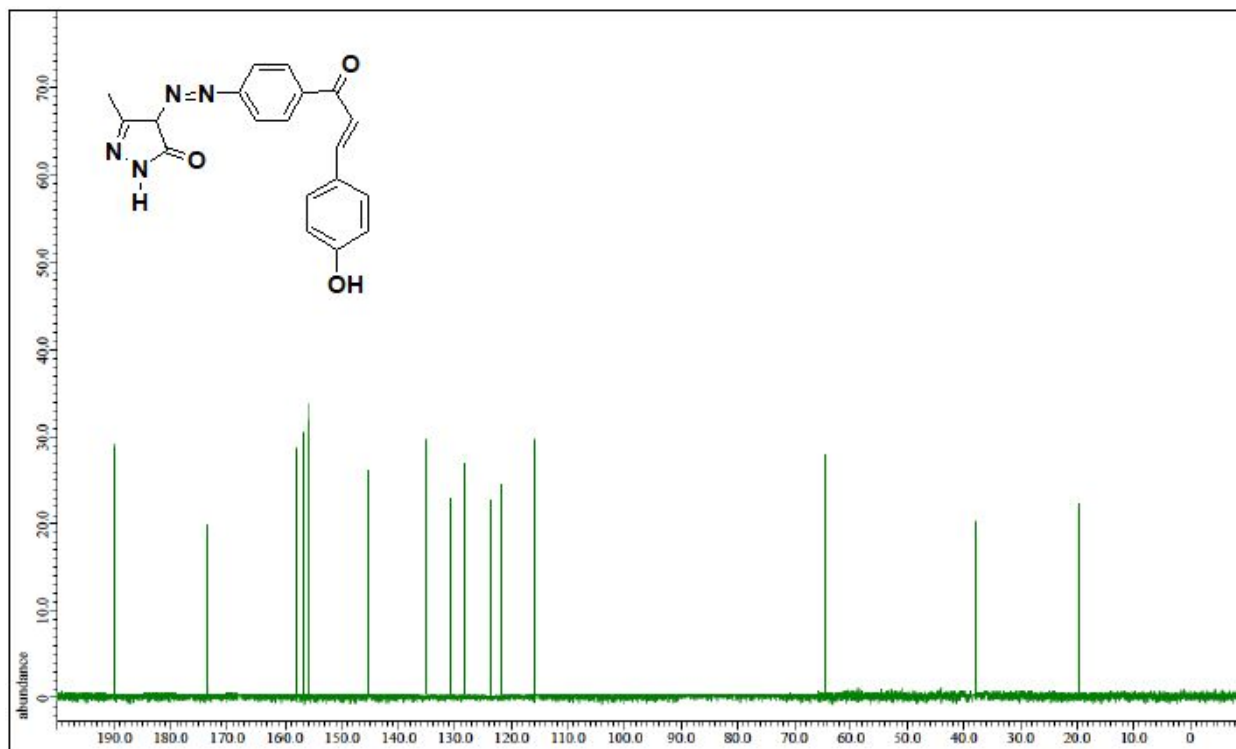


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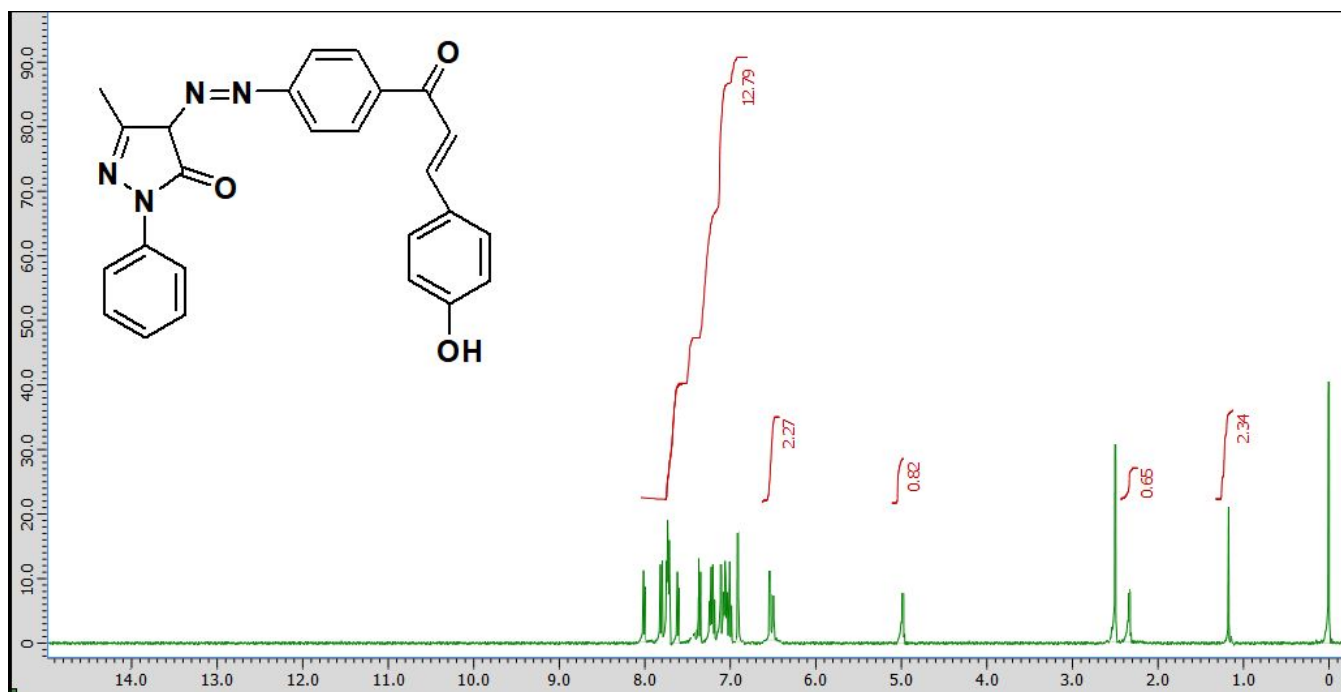


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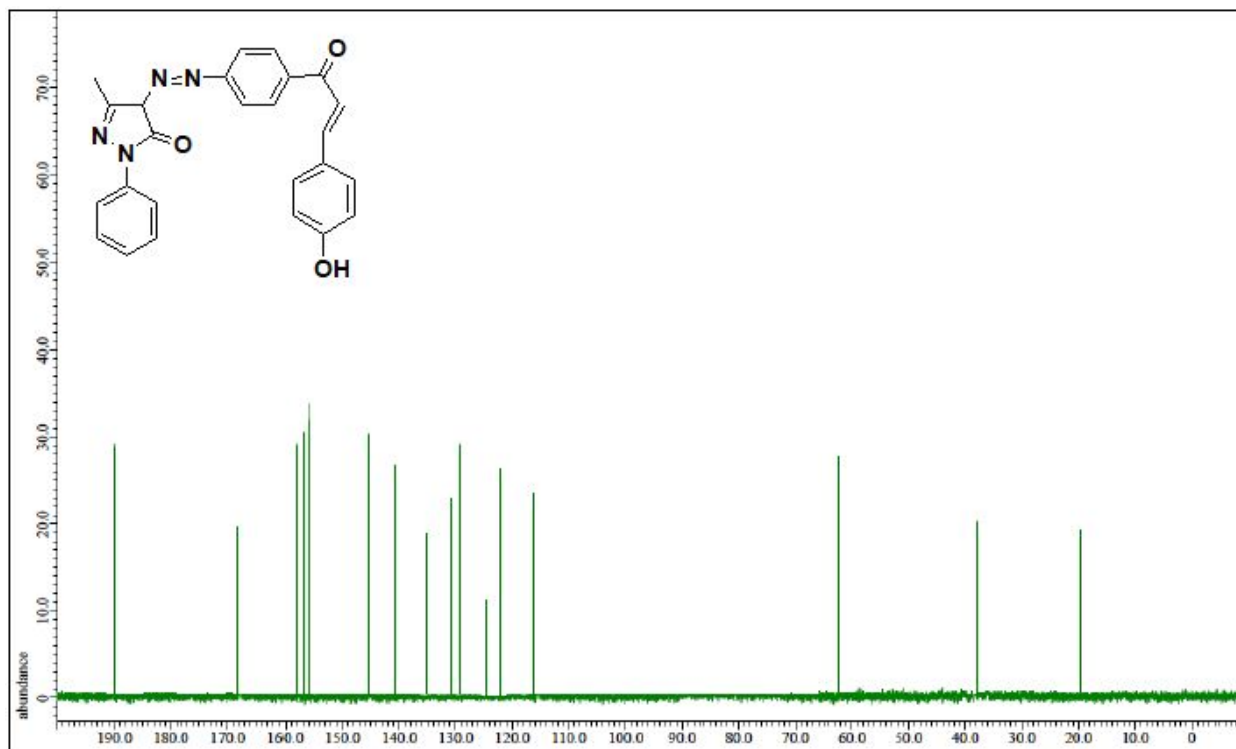




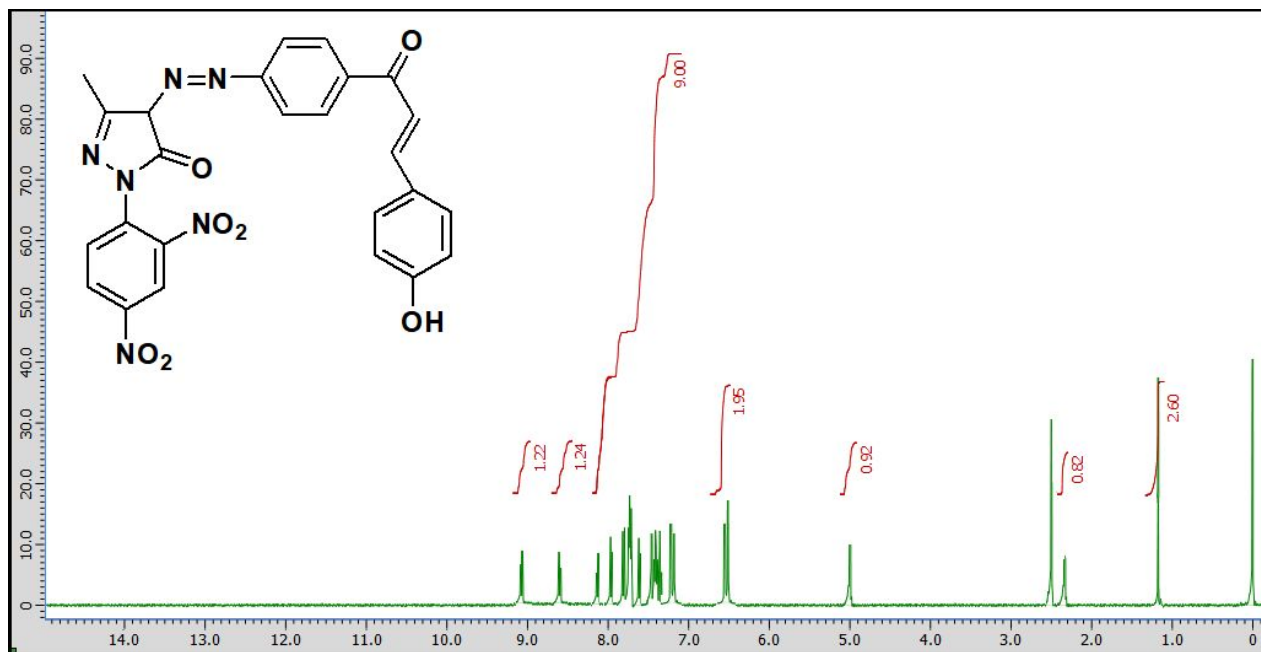
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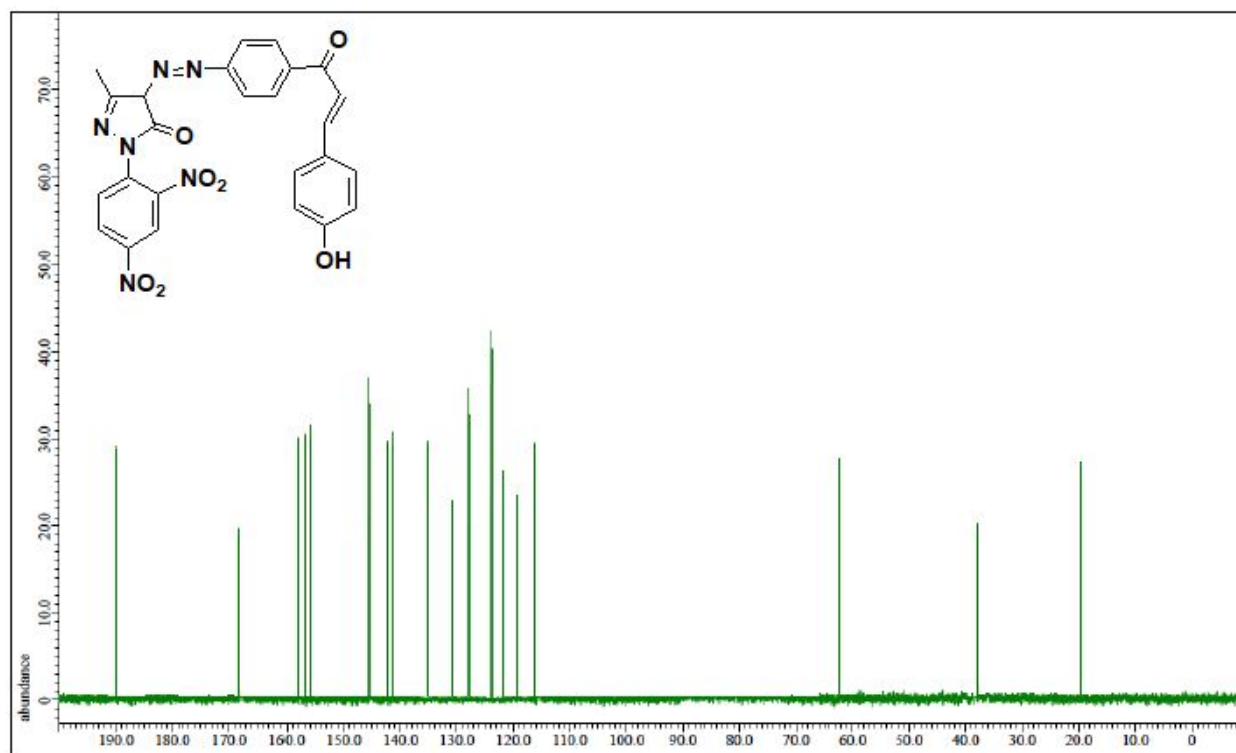
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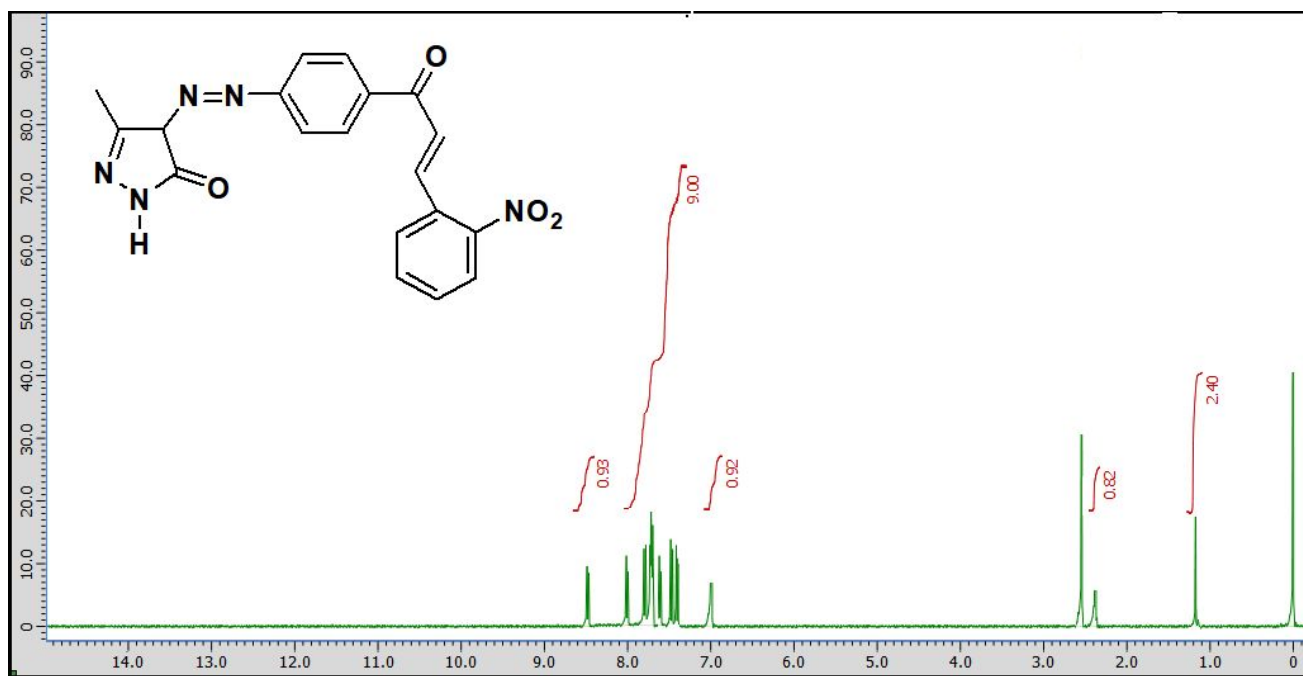
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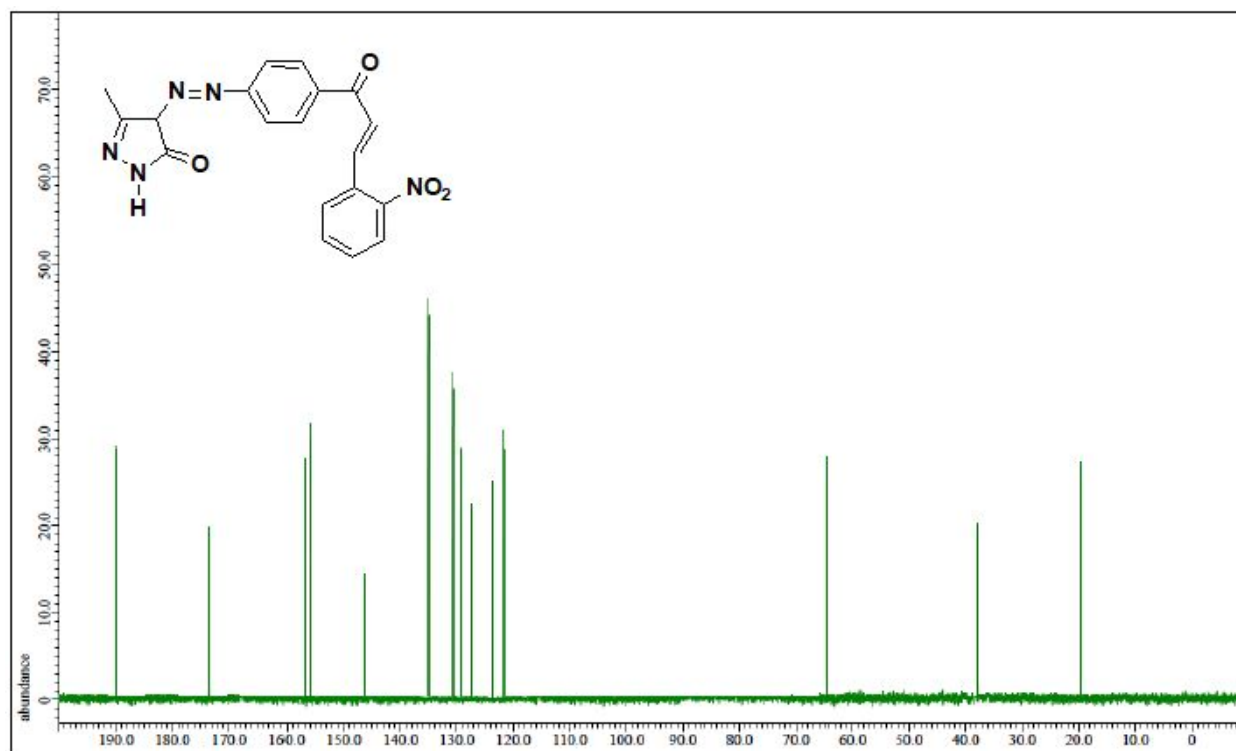
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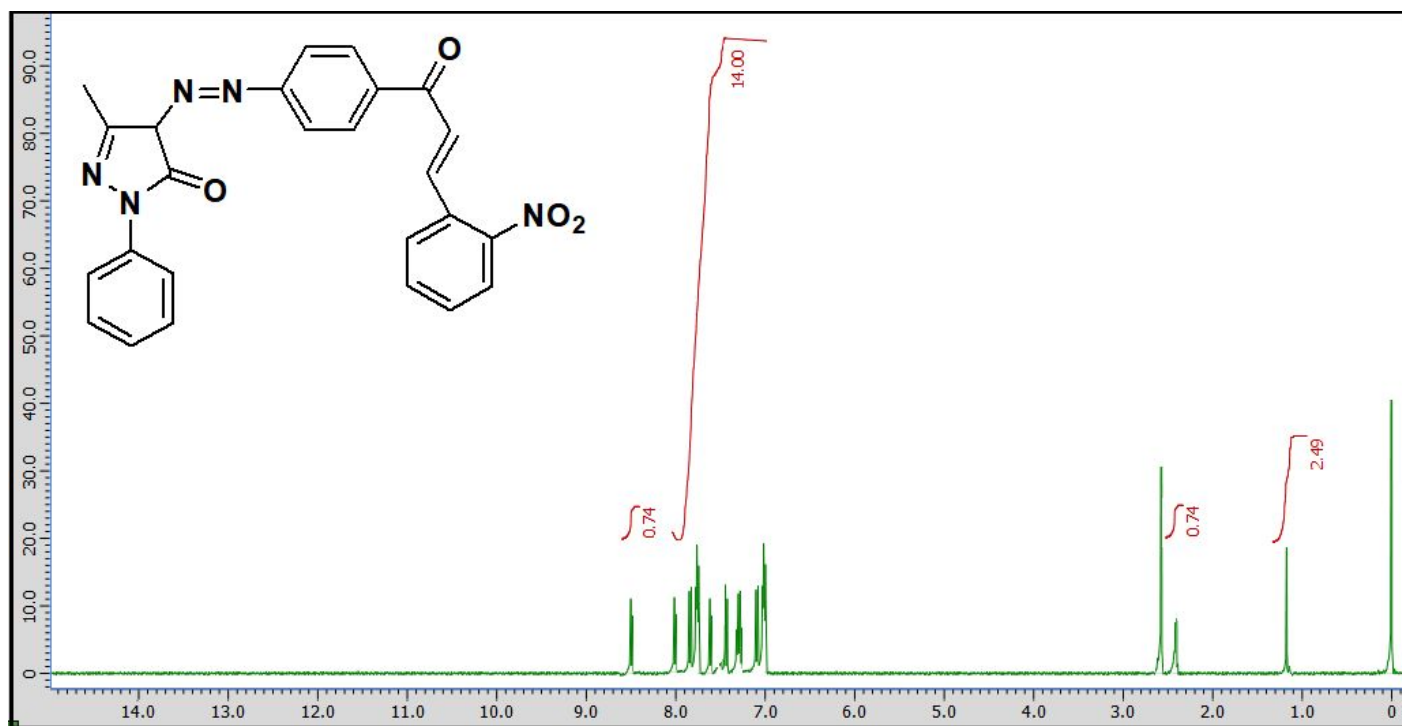
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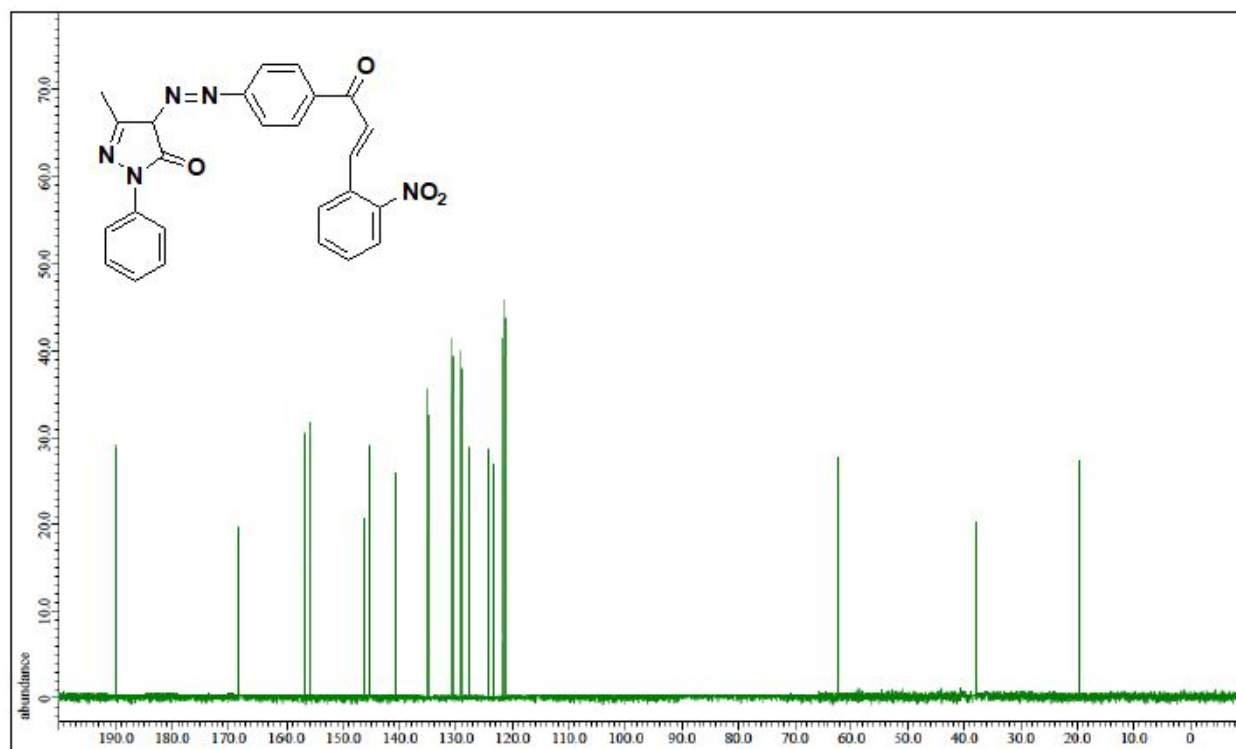


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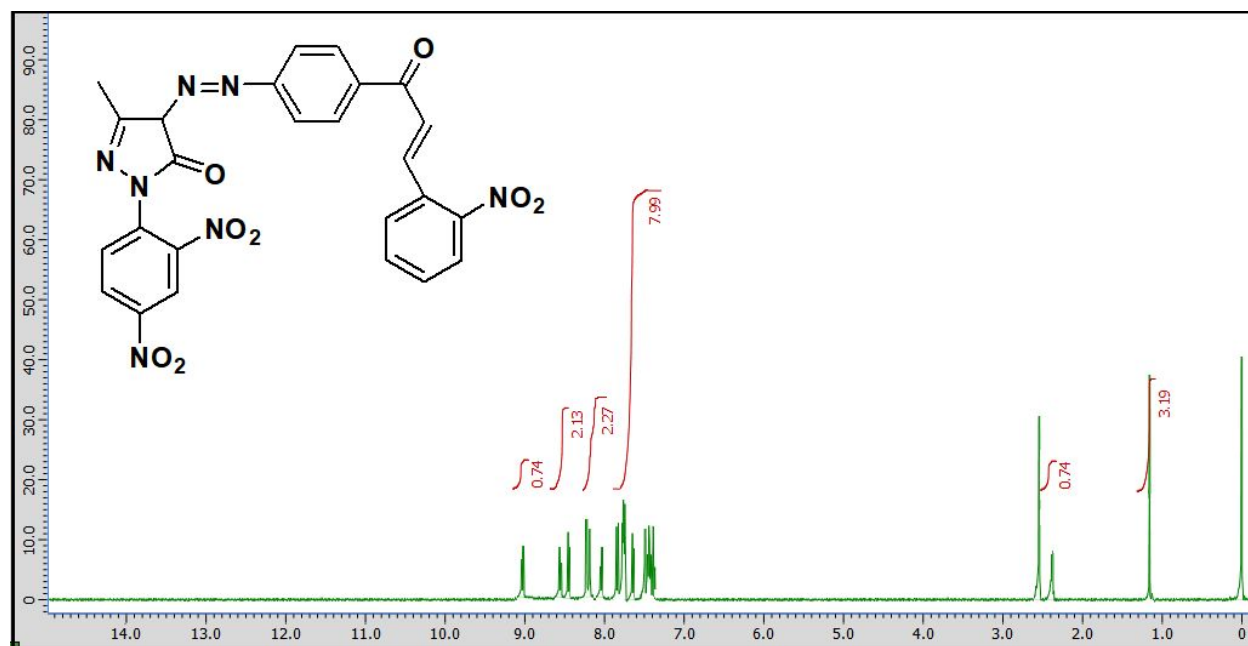


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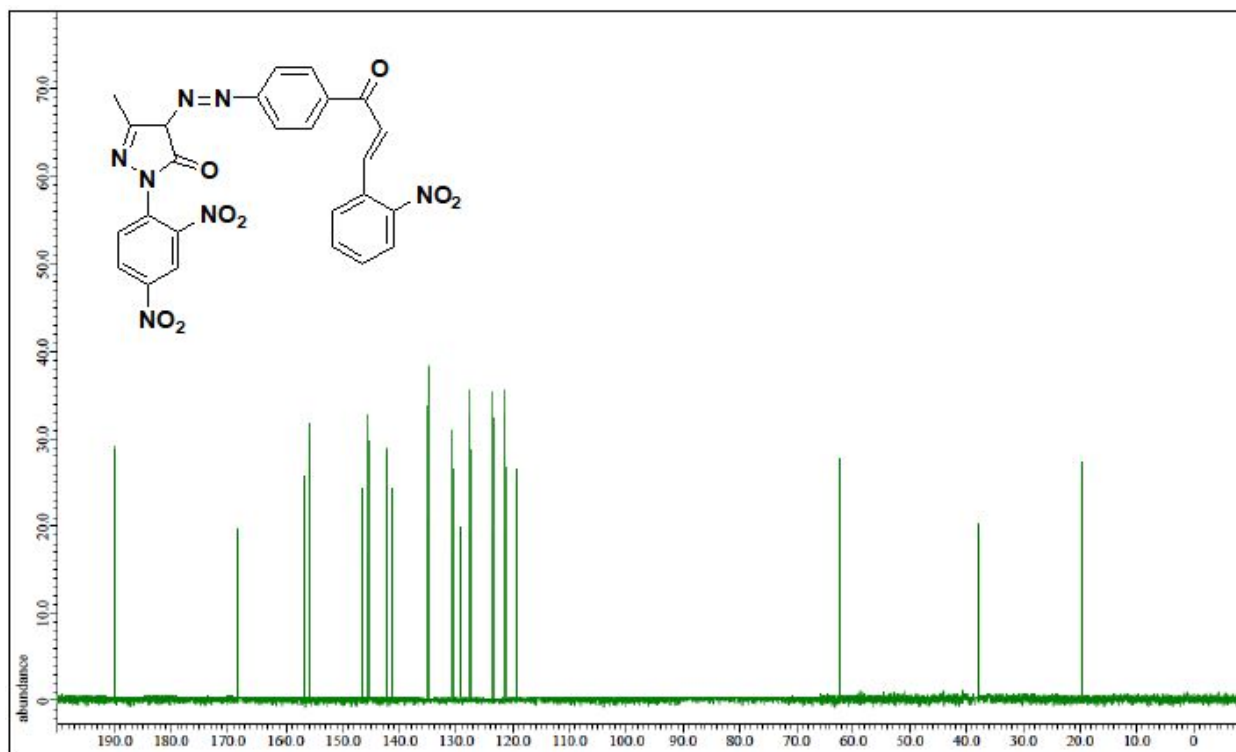




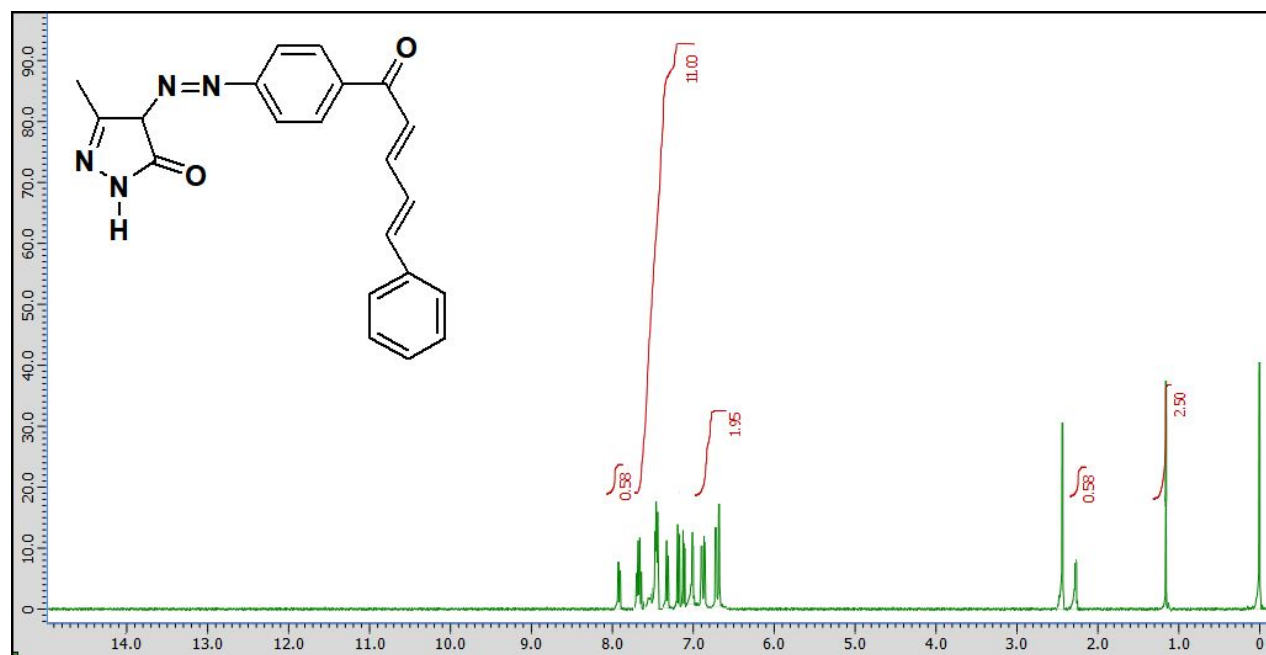
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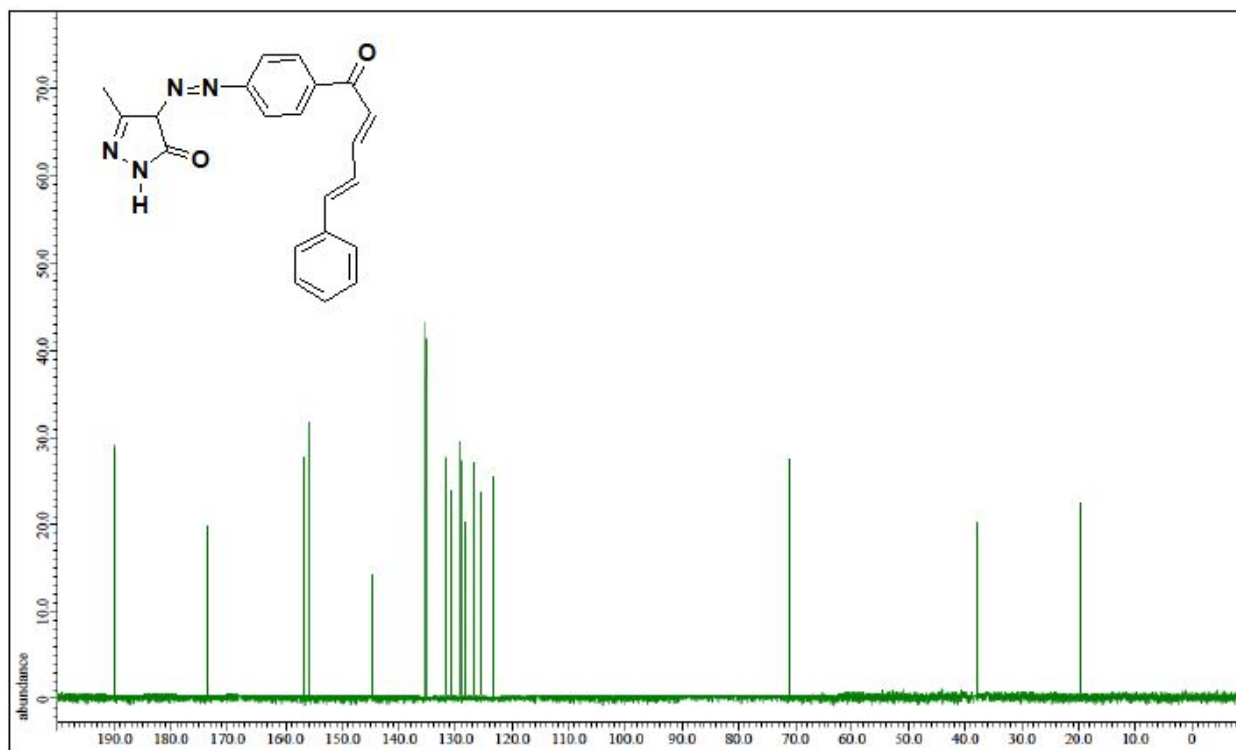
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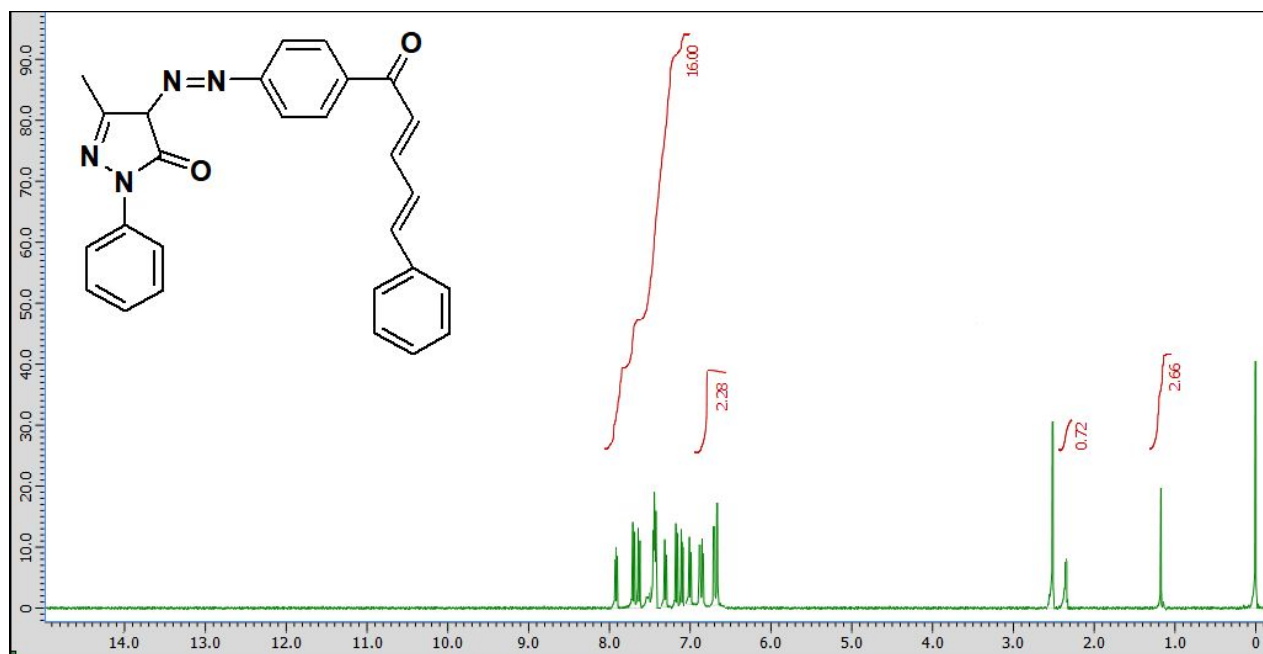
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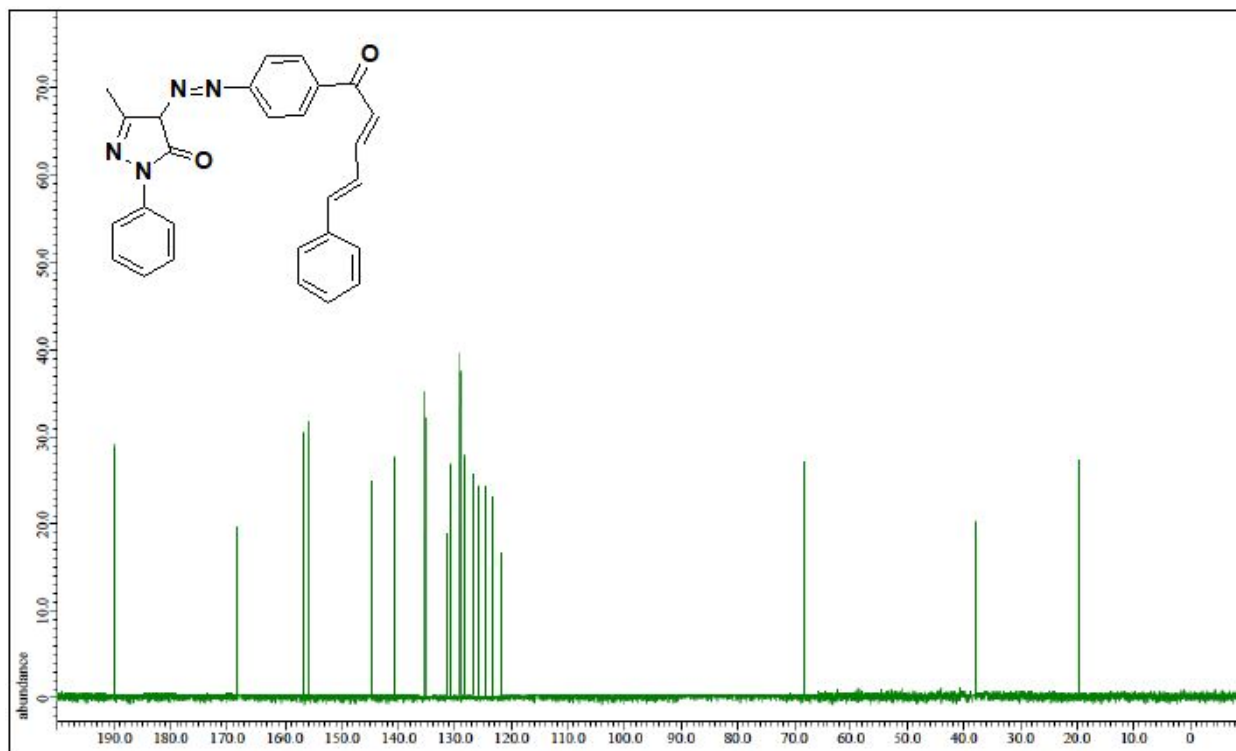
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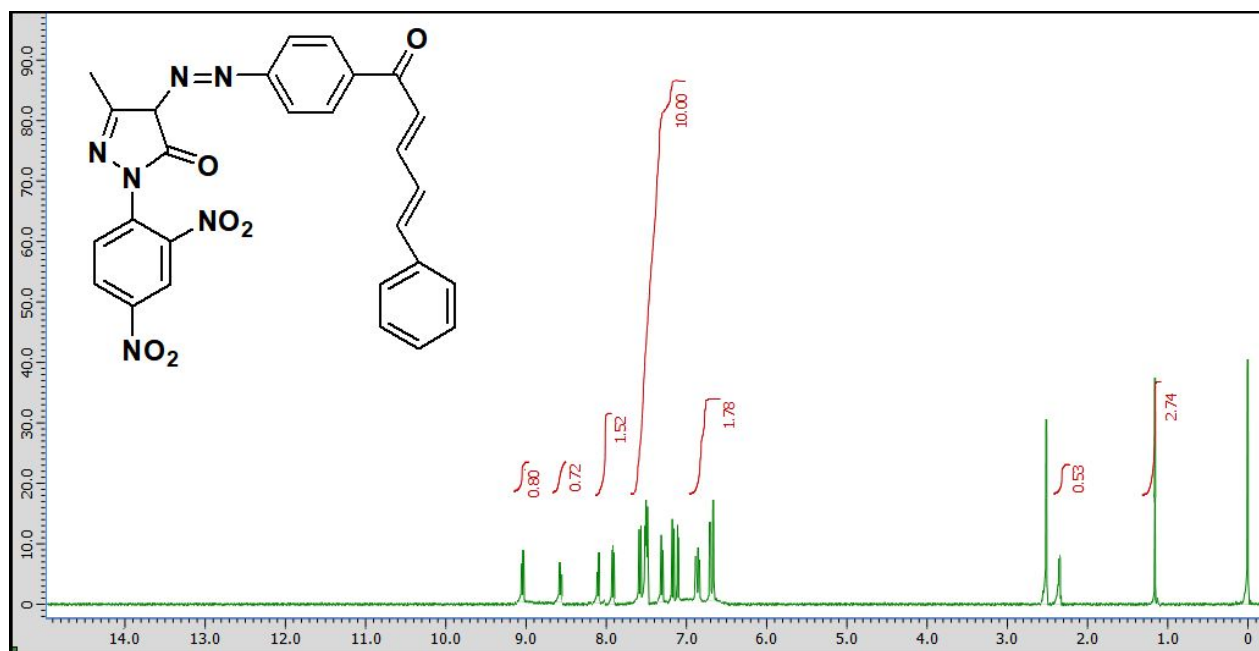
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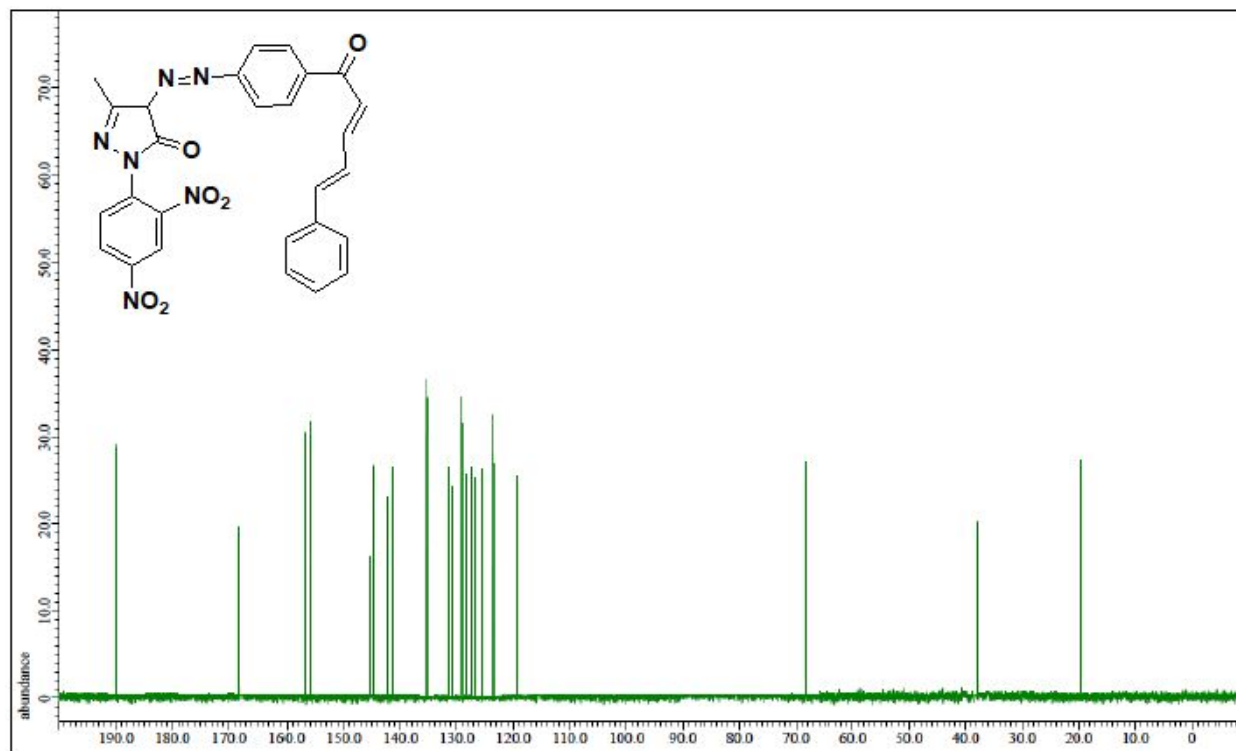


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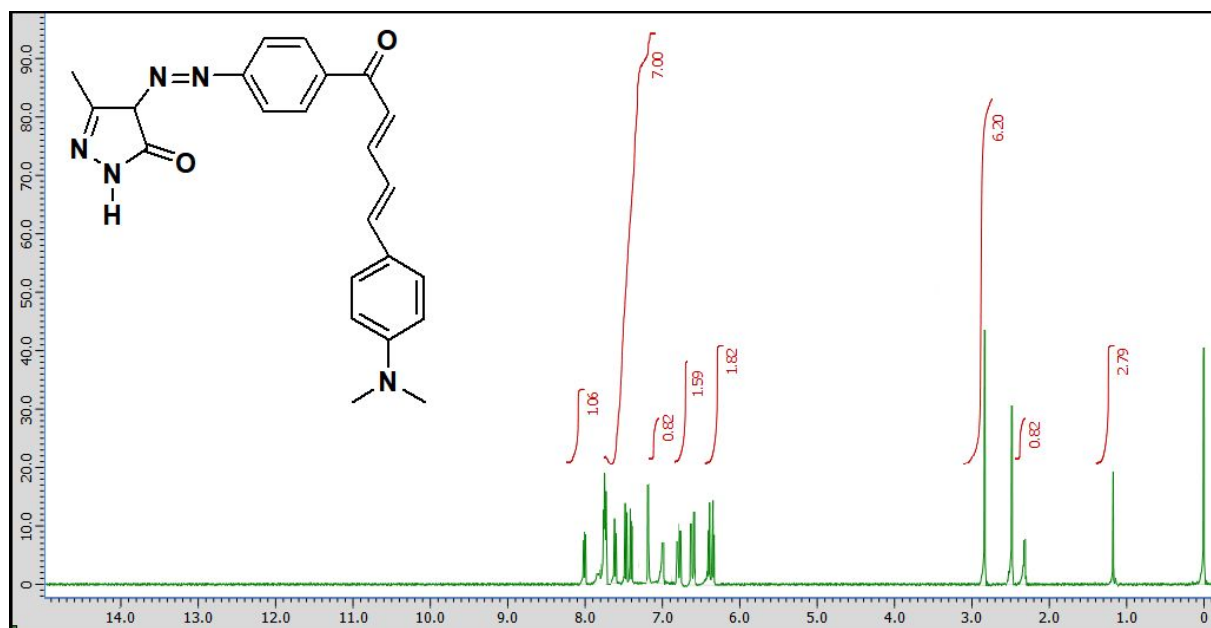


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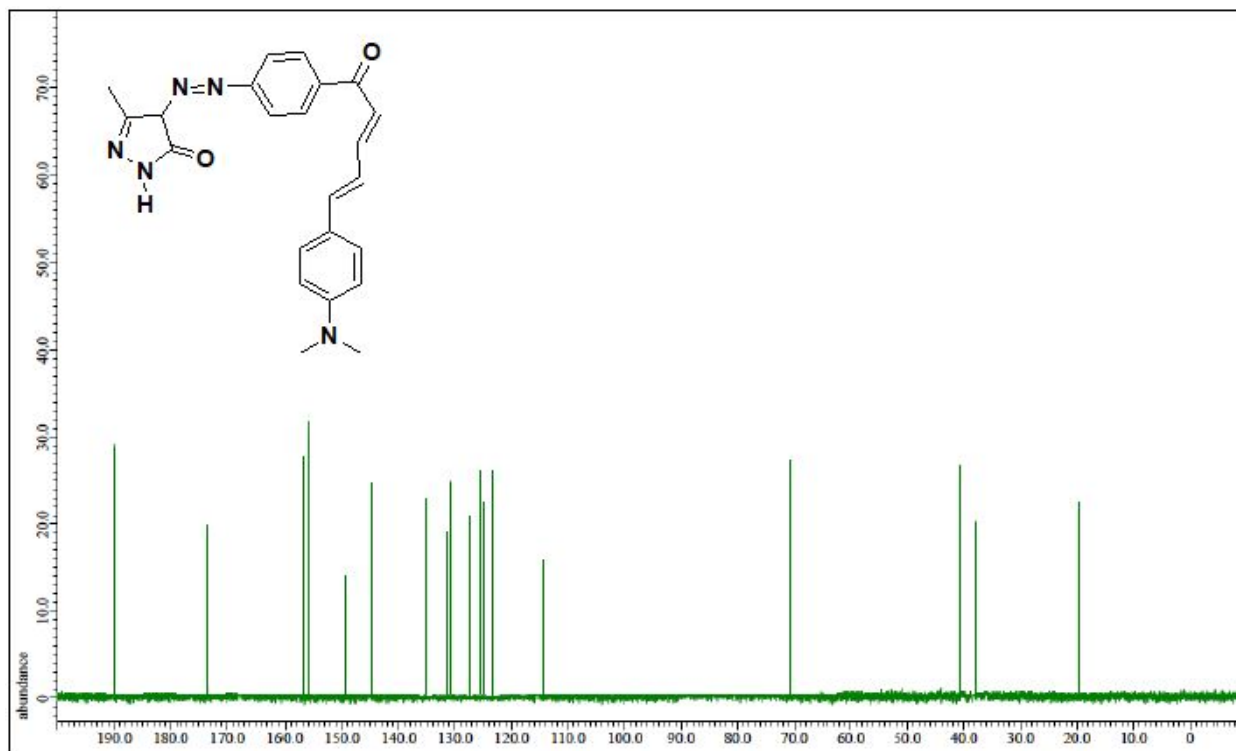




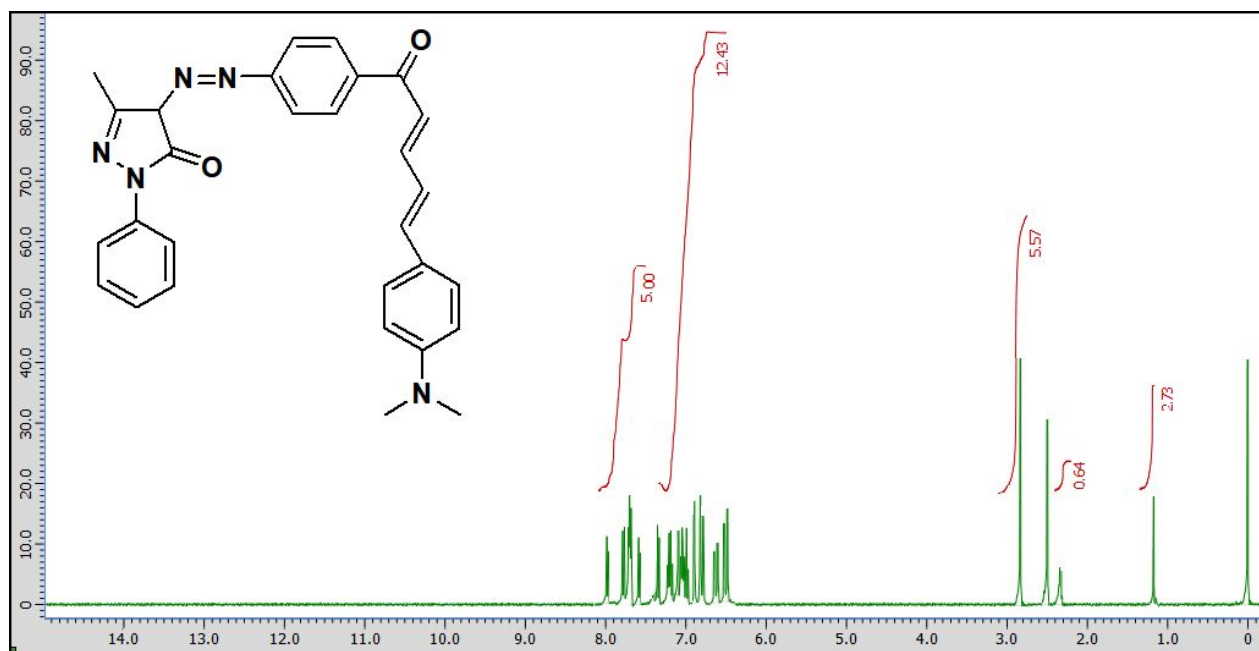
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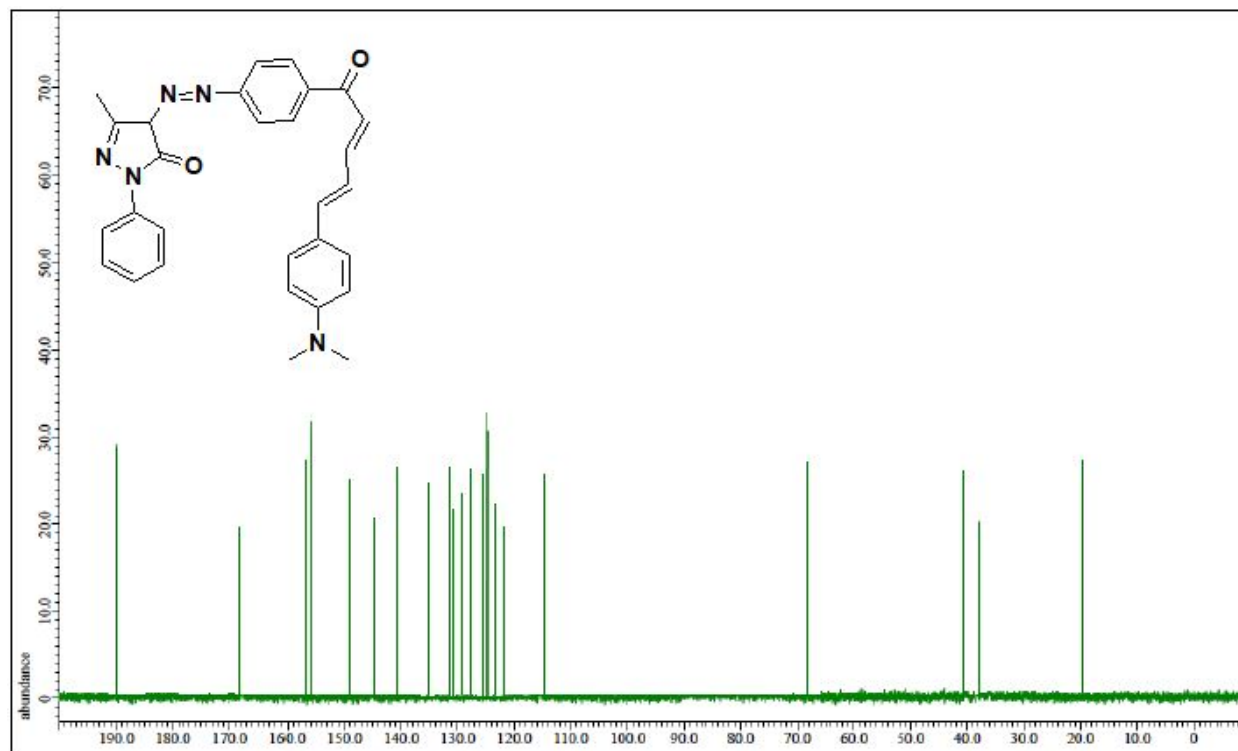
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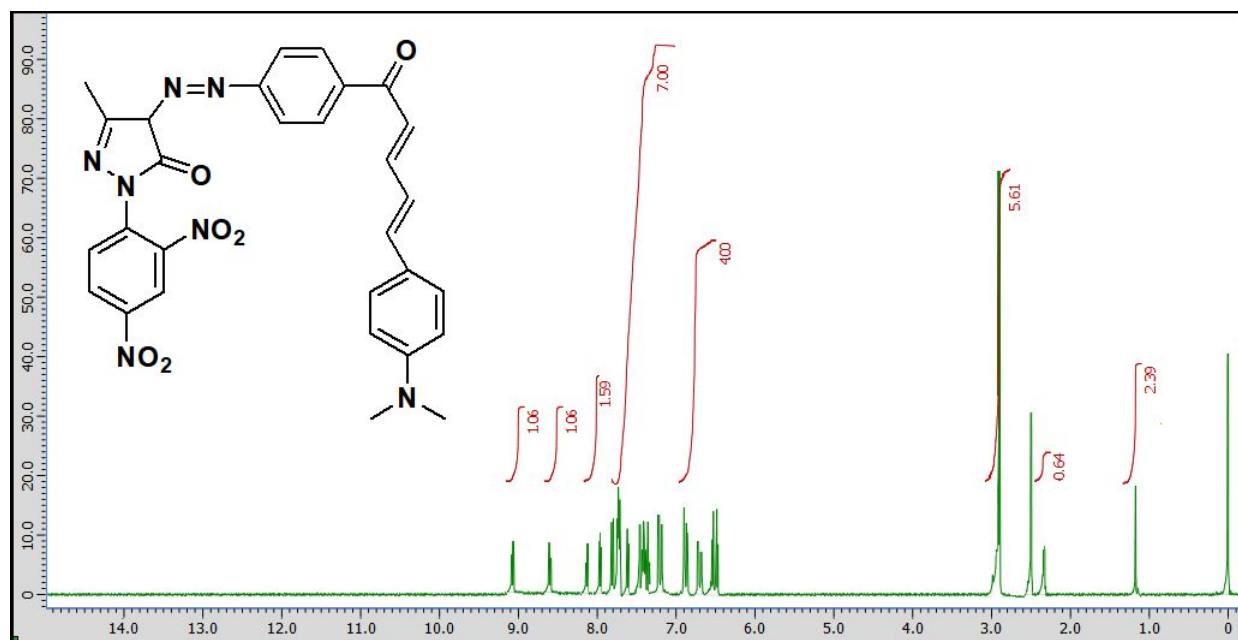
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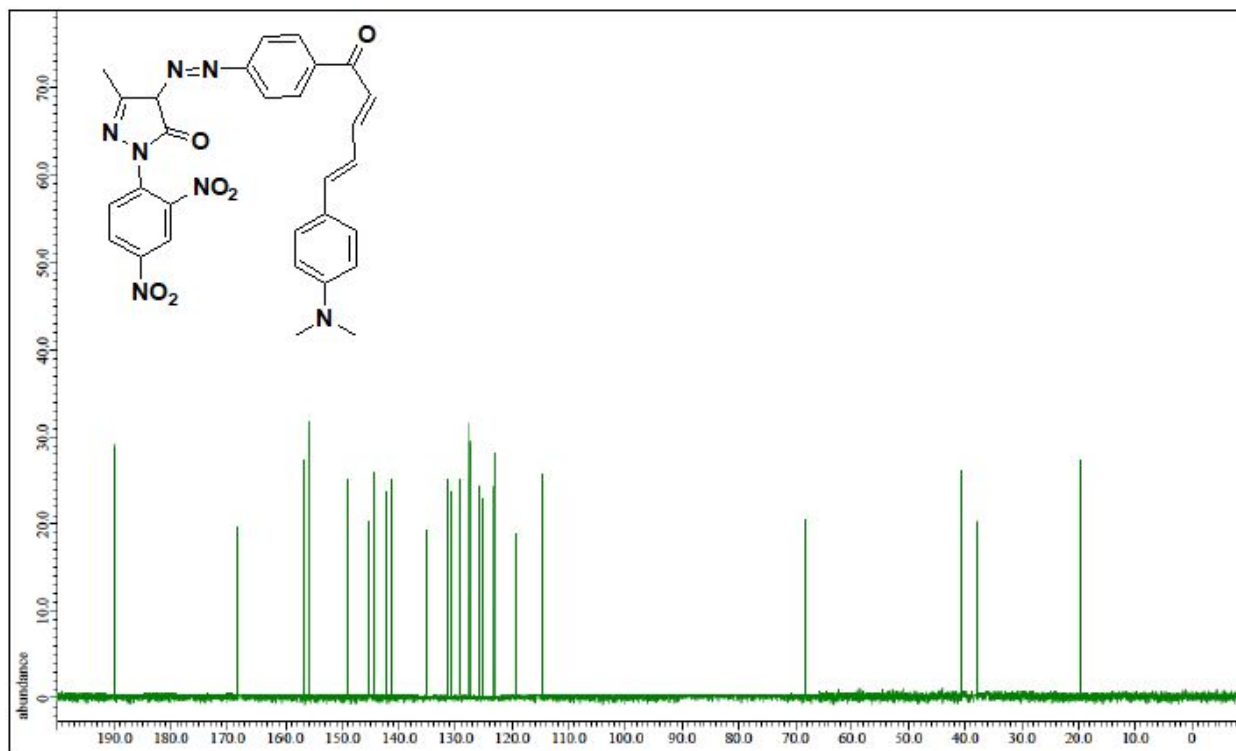
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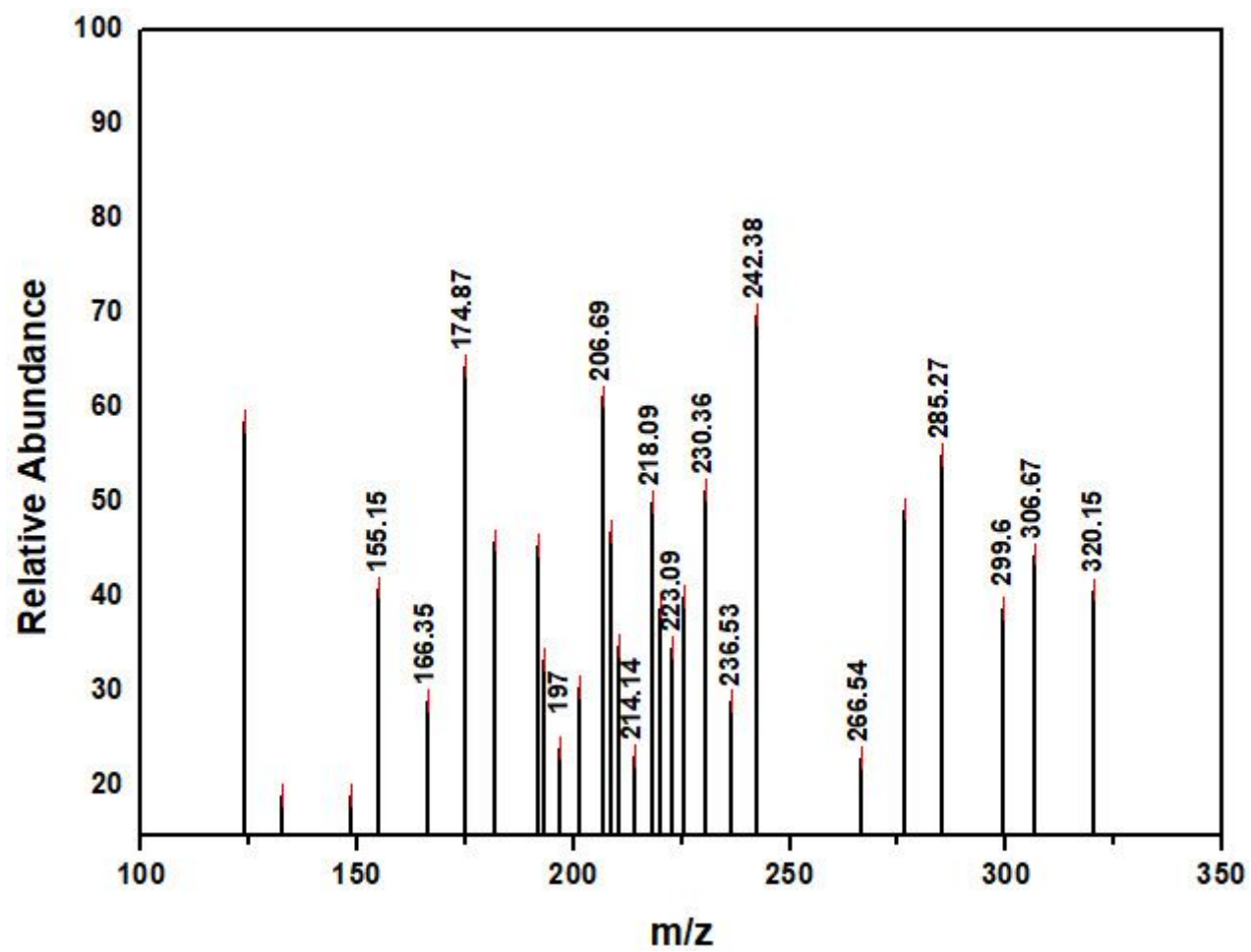
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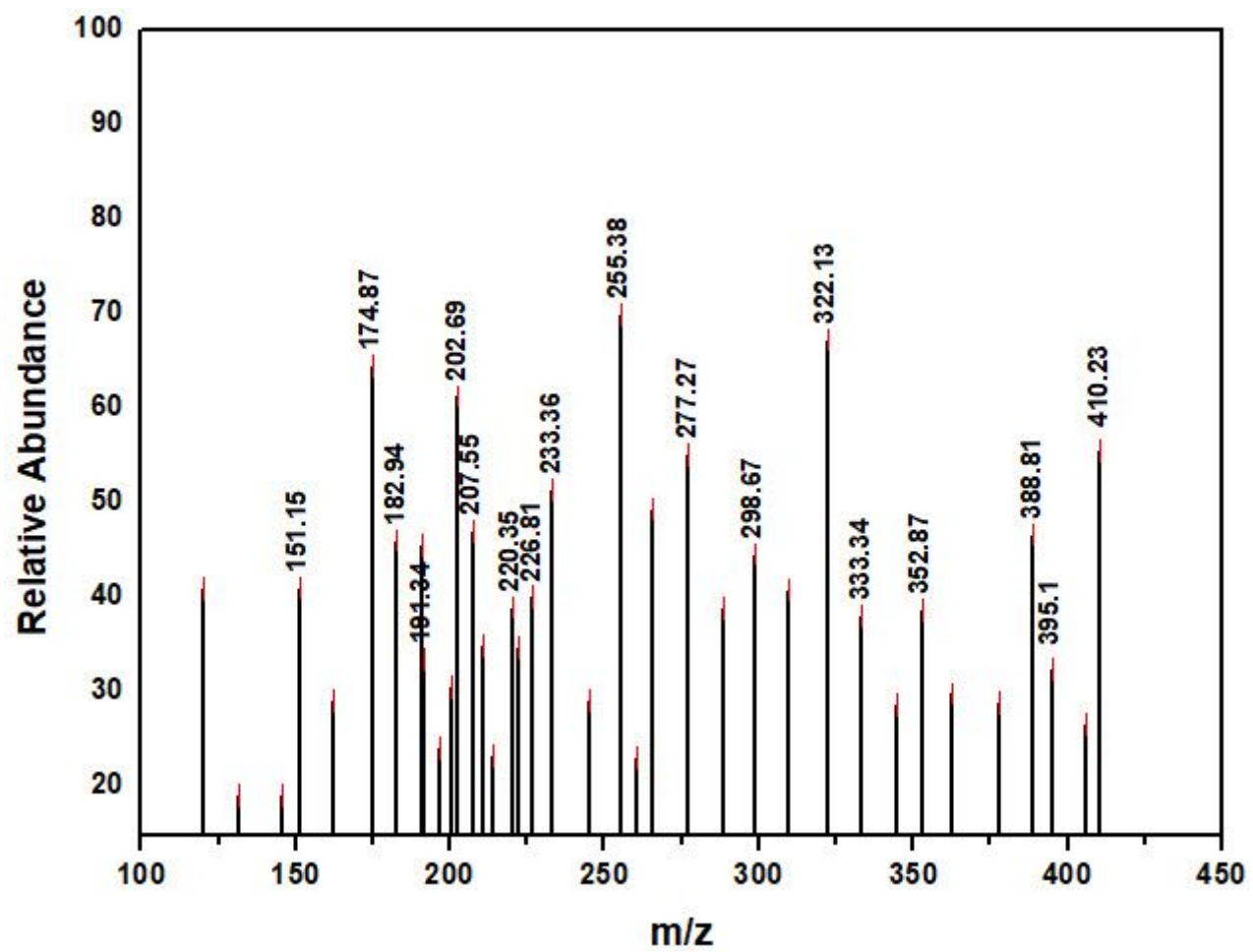


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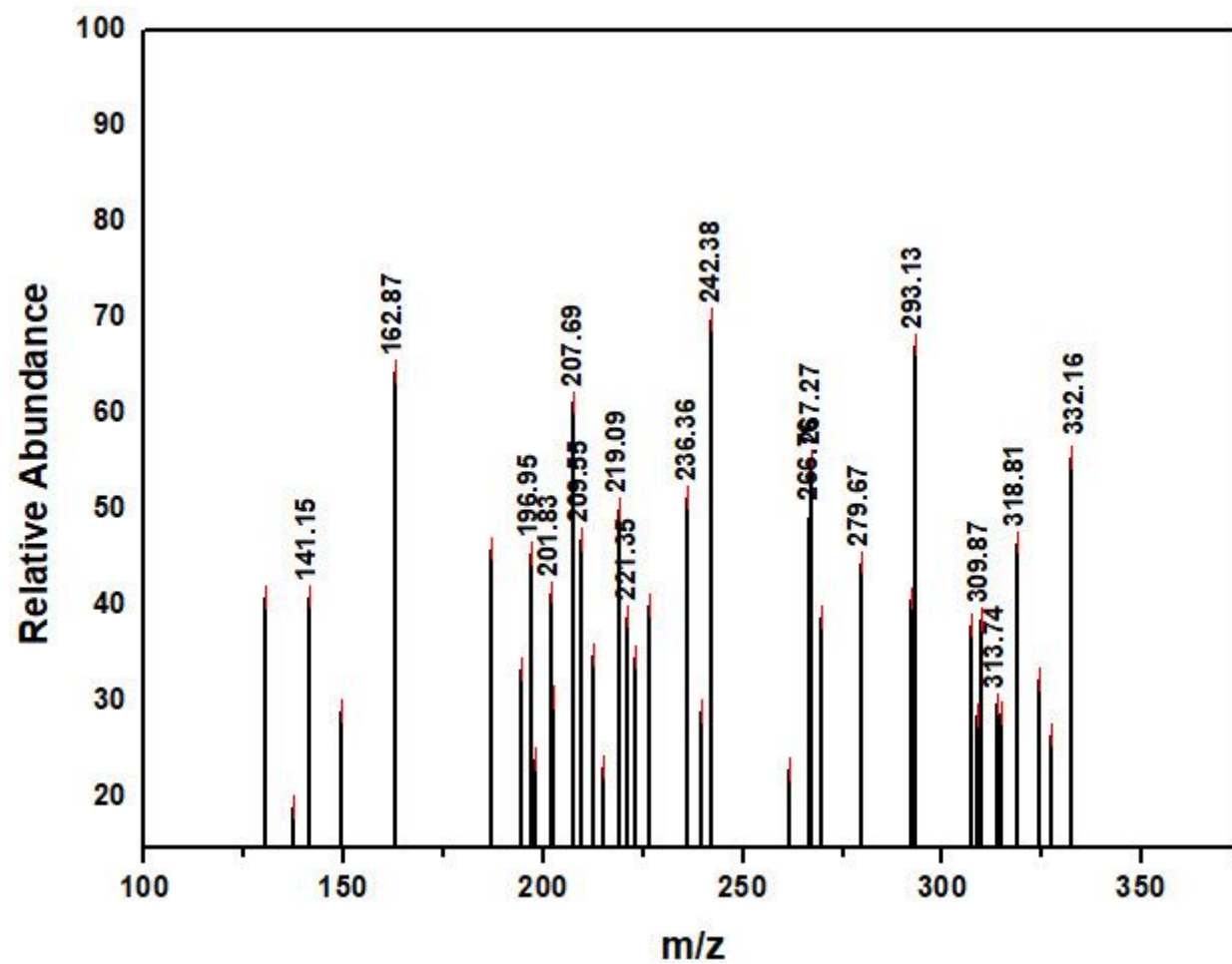


Mass spectra of compound 2b

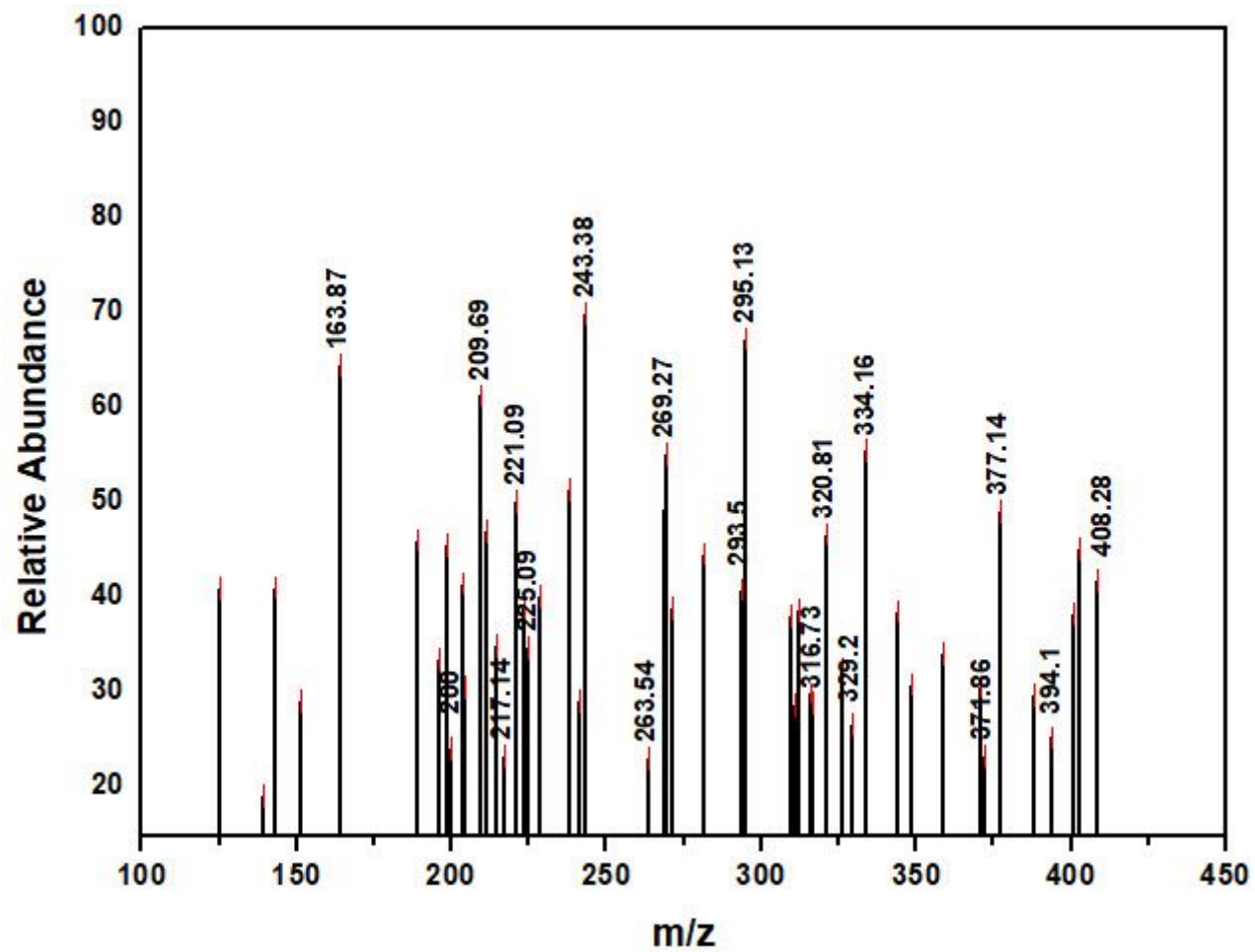




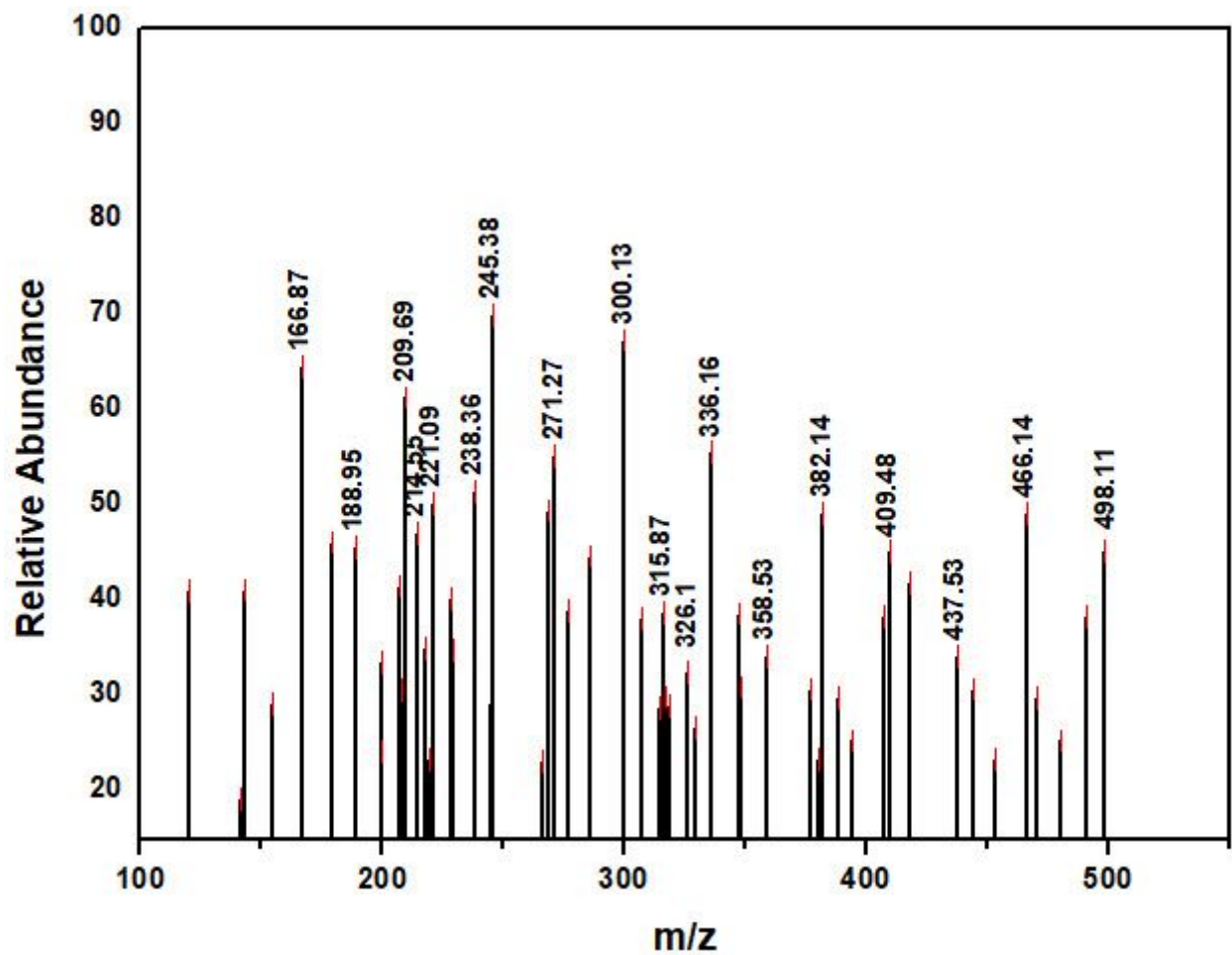
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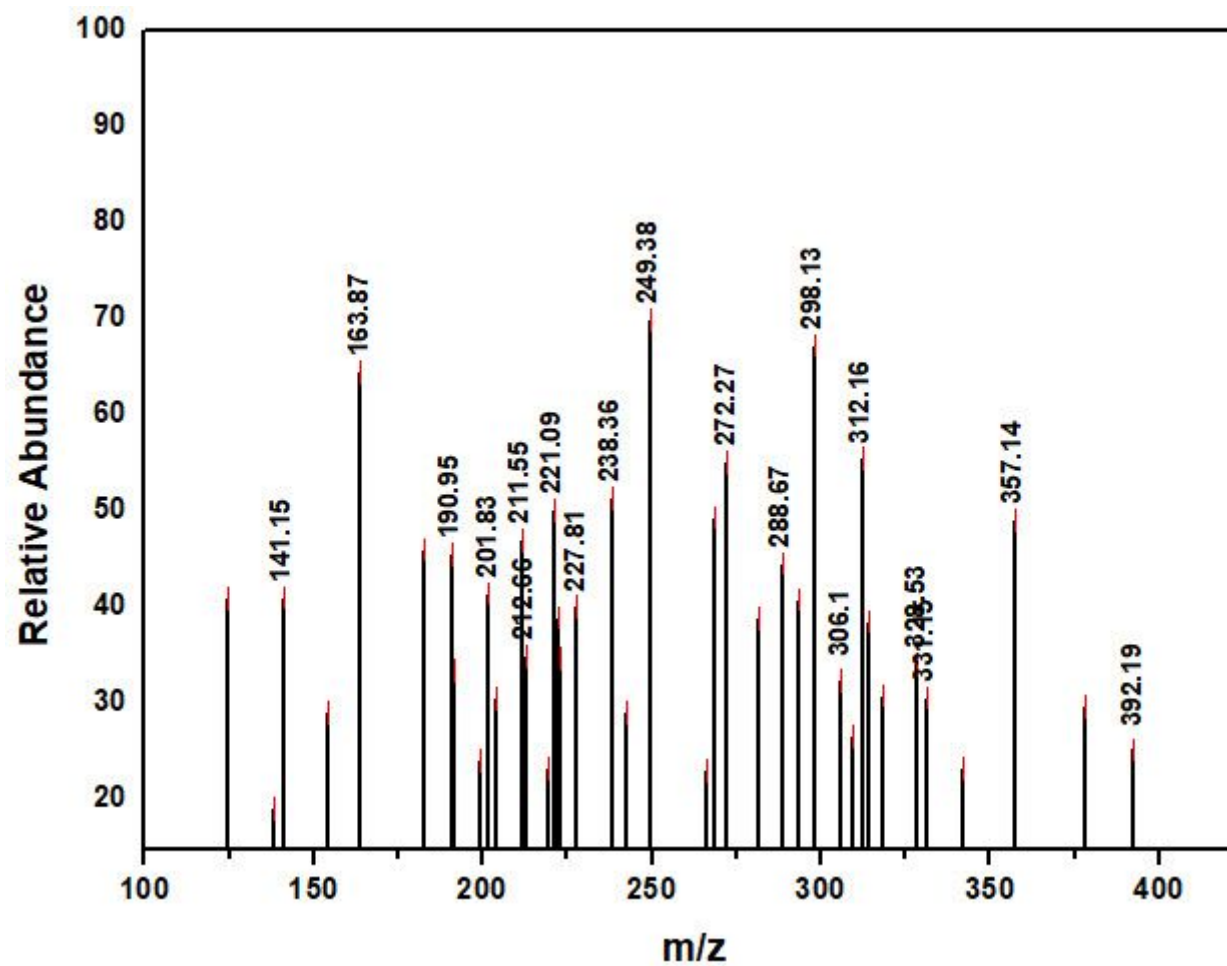
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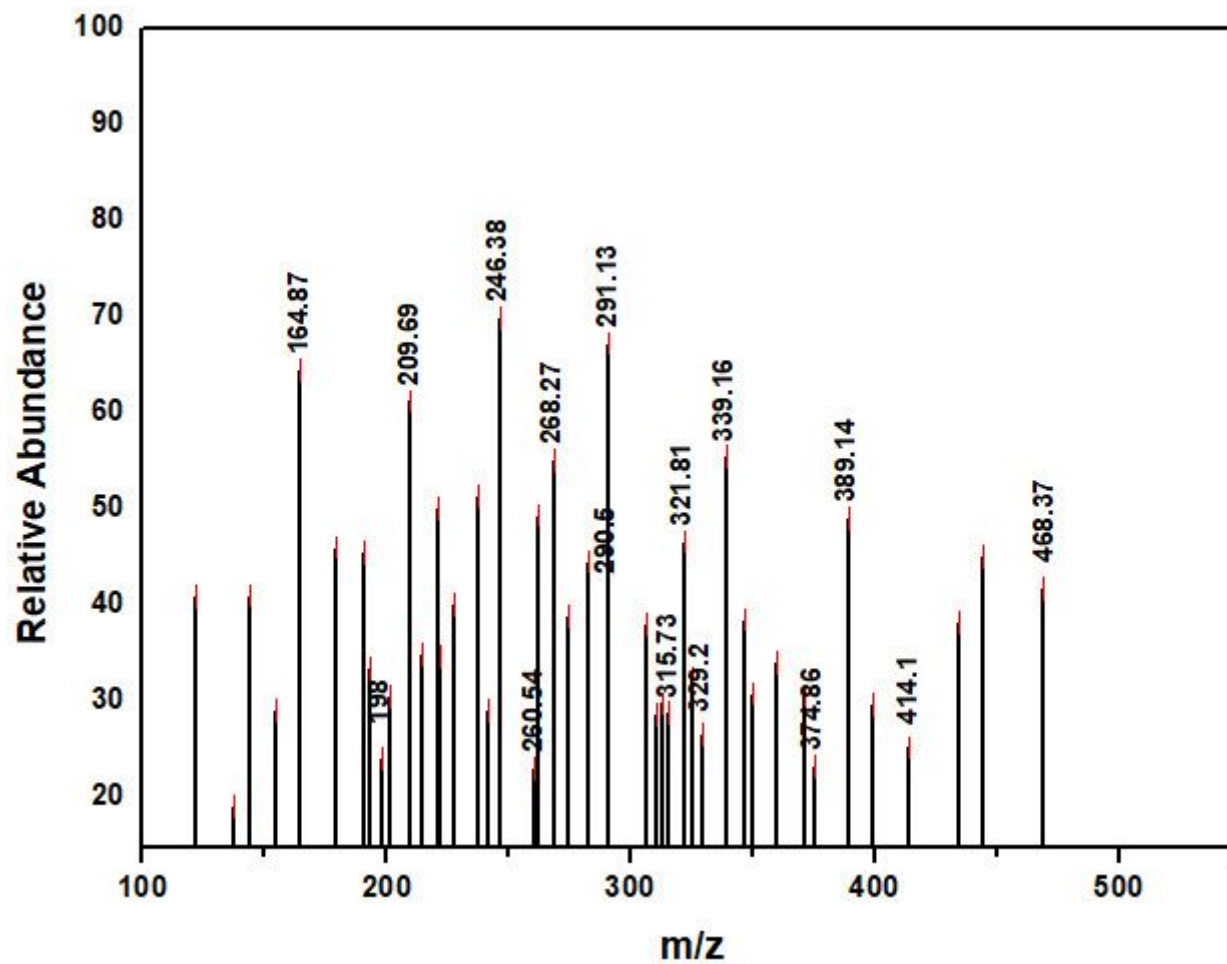
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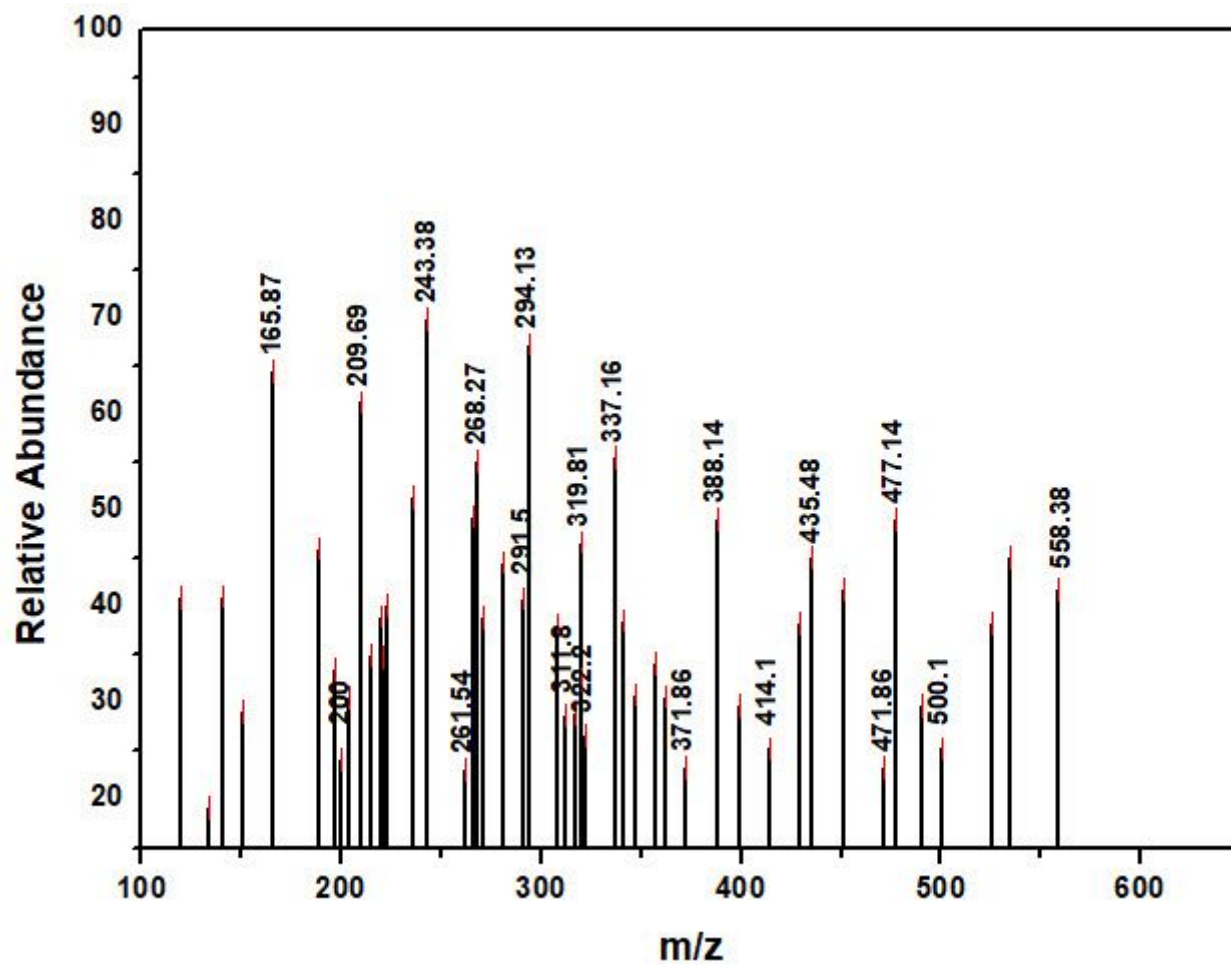
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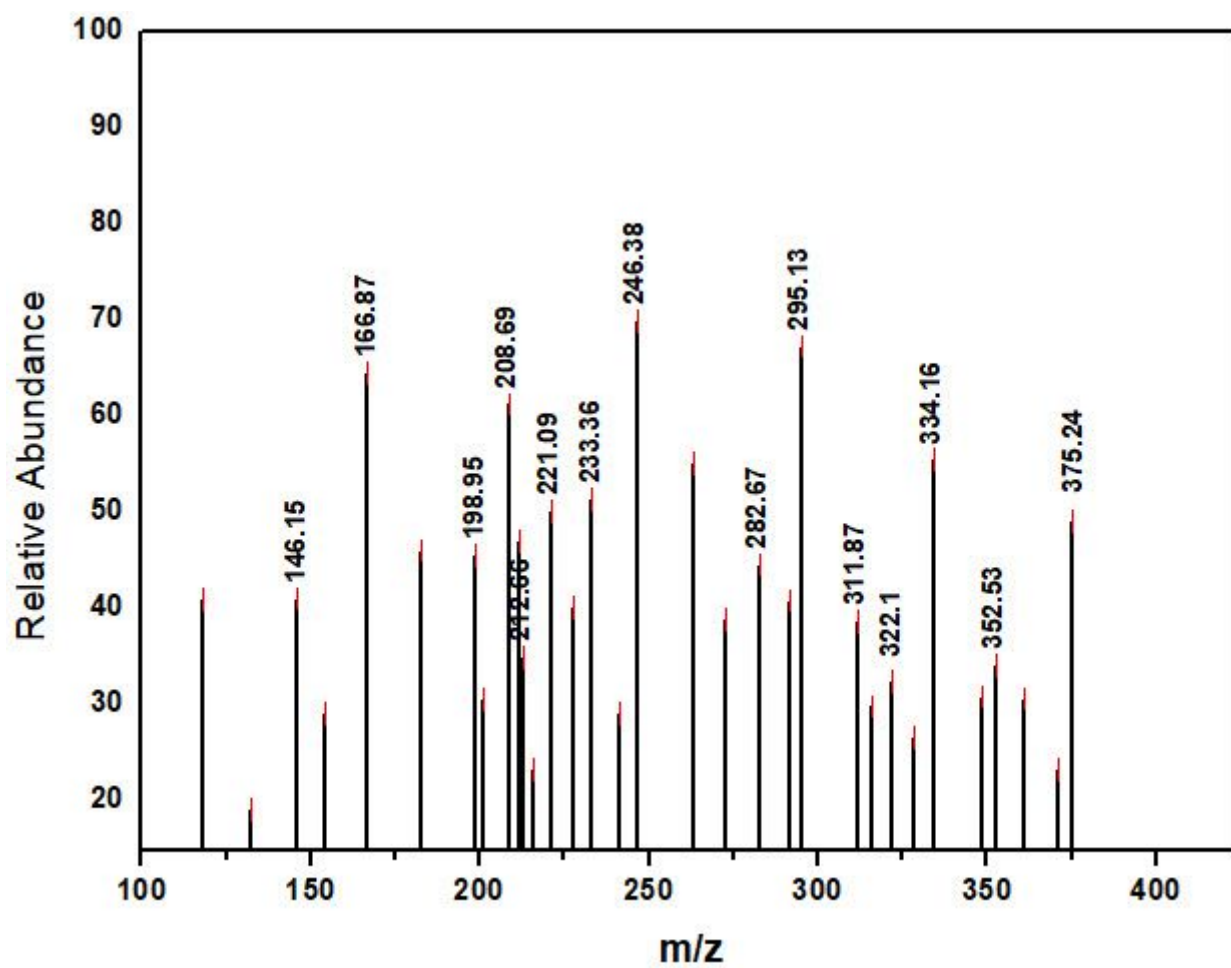
Mass spectra of compound 4a



Mass spectra of compound 4b

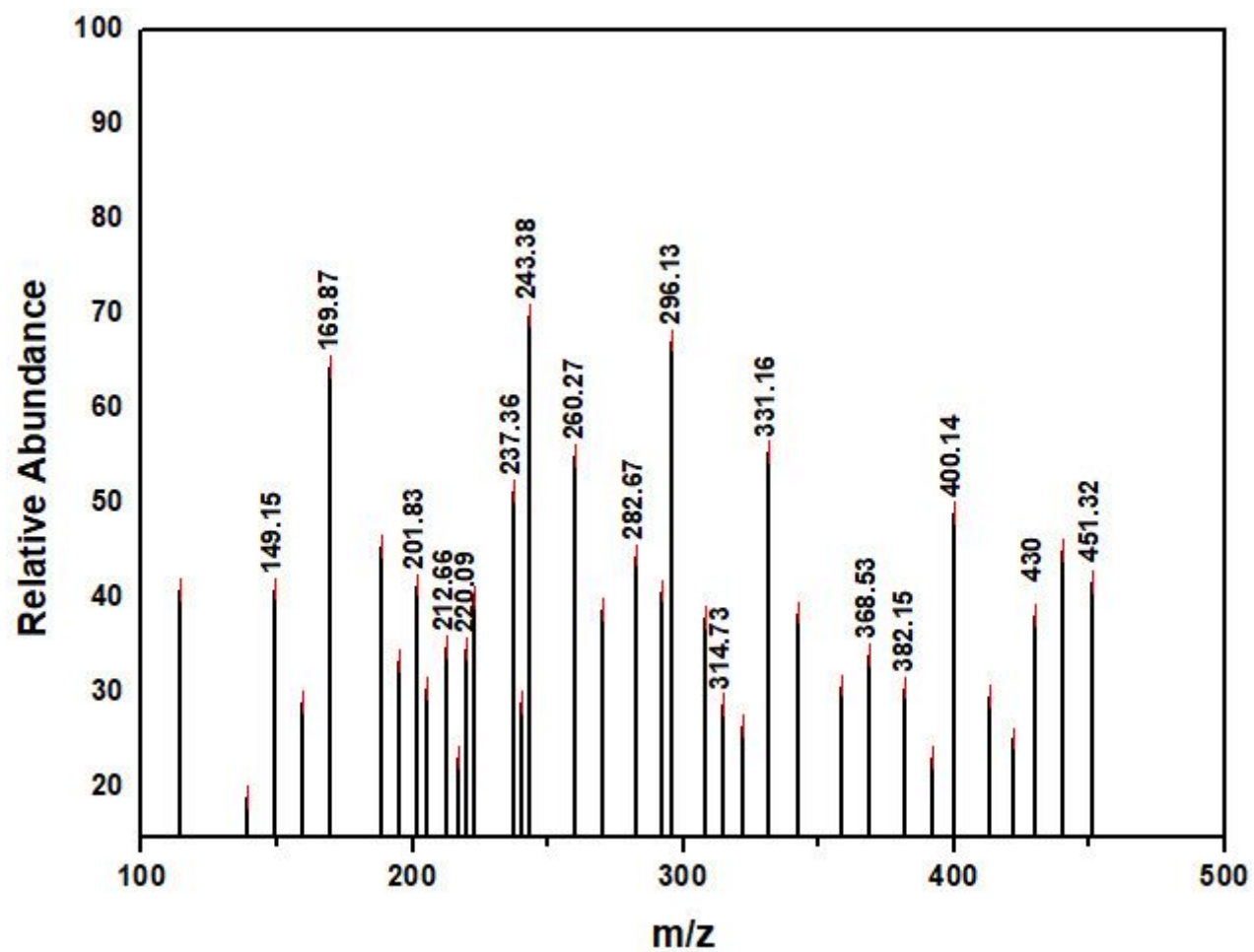


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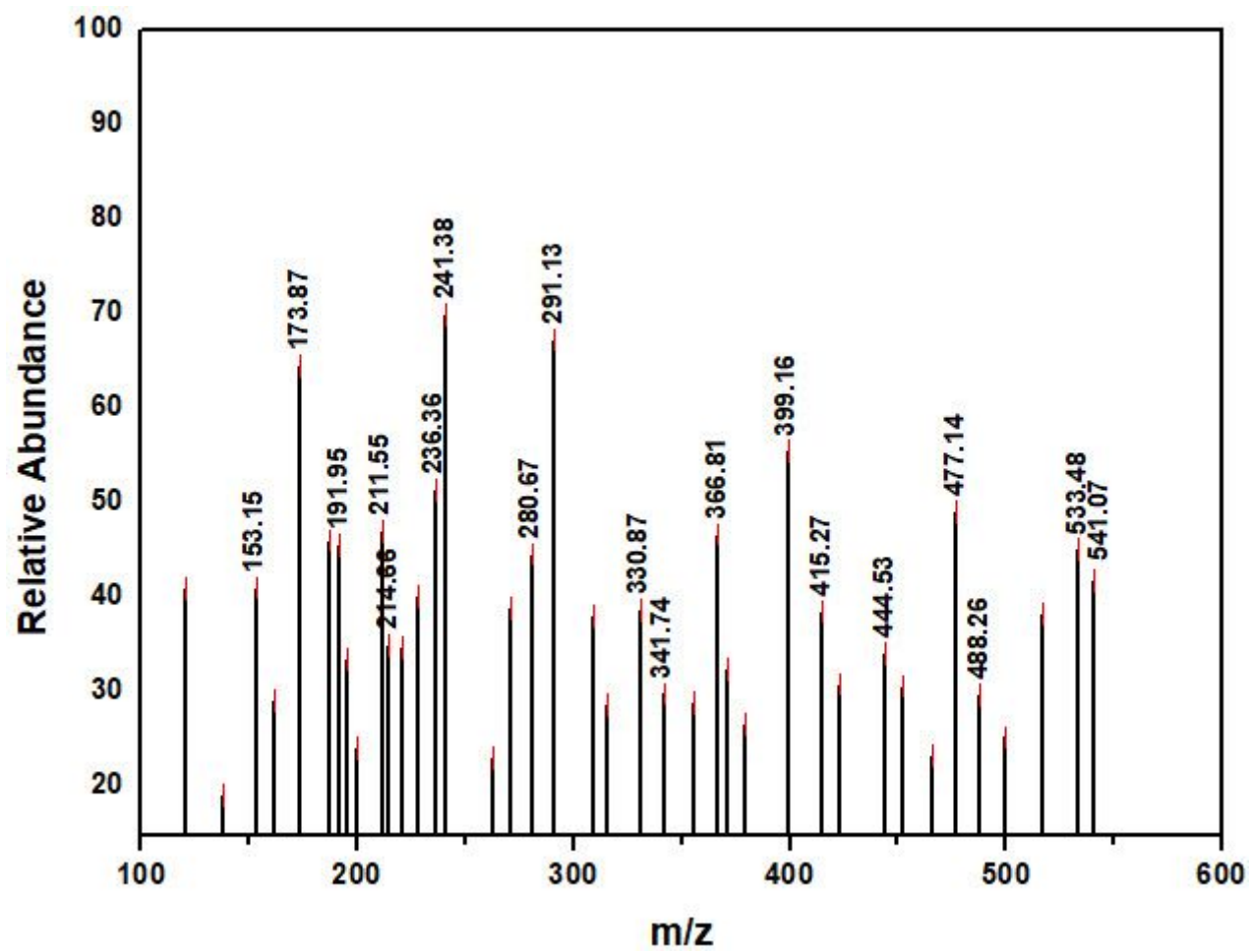


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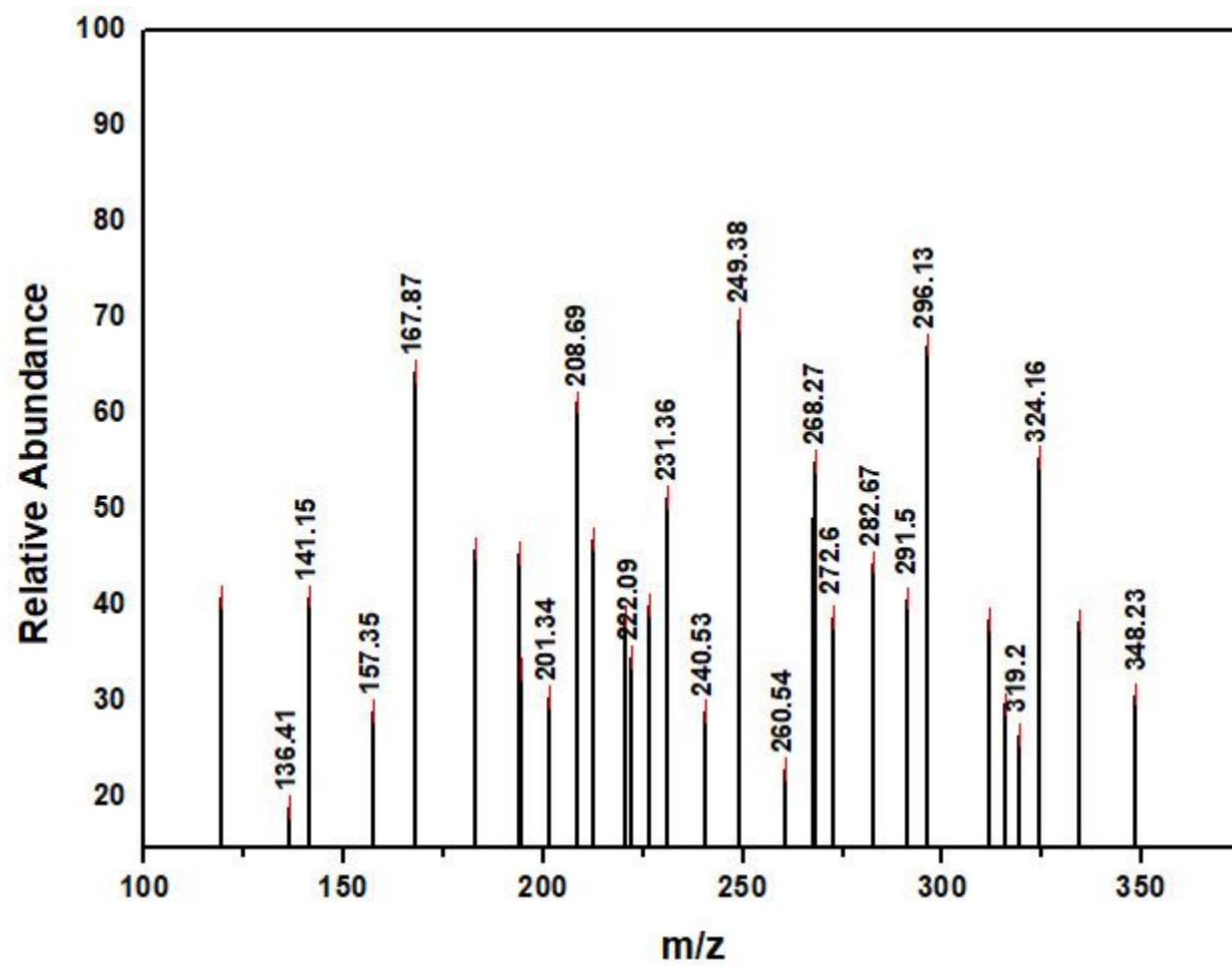




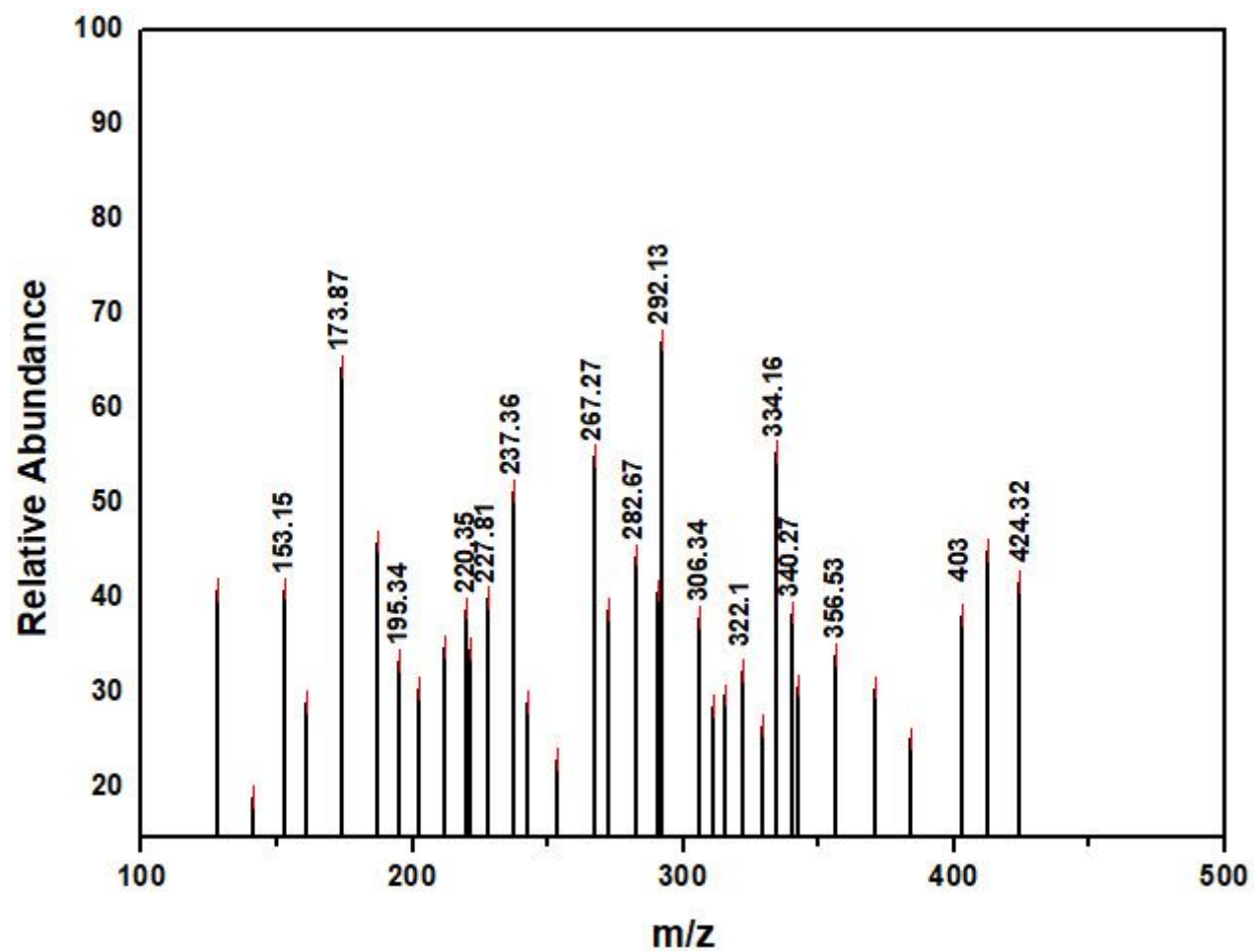
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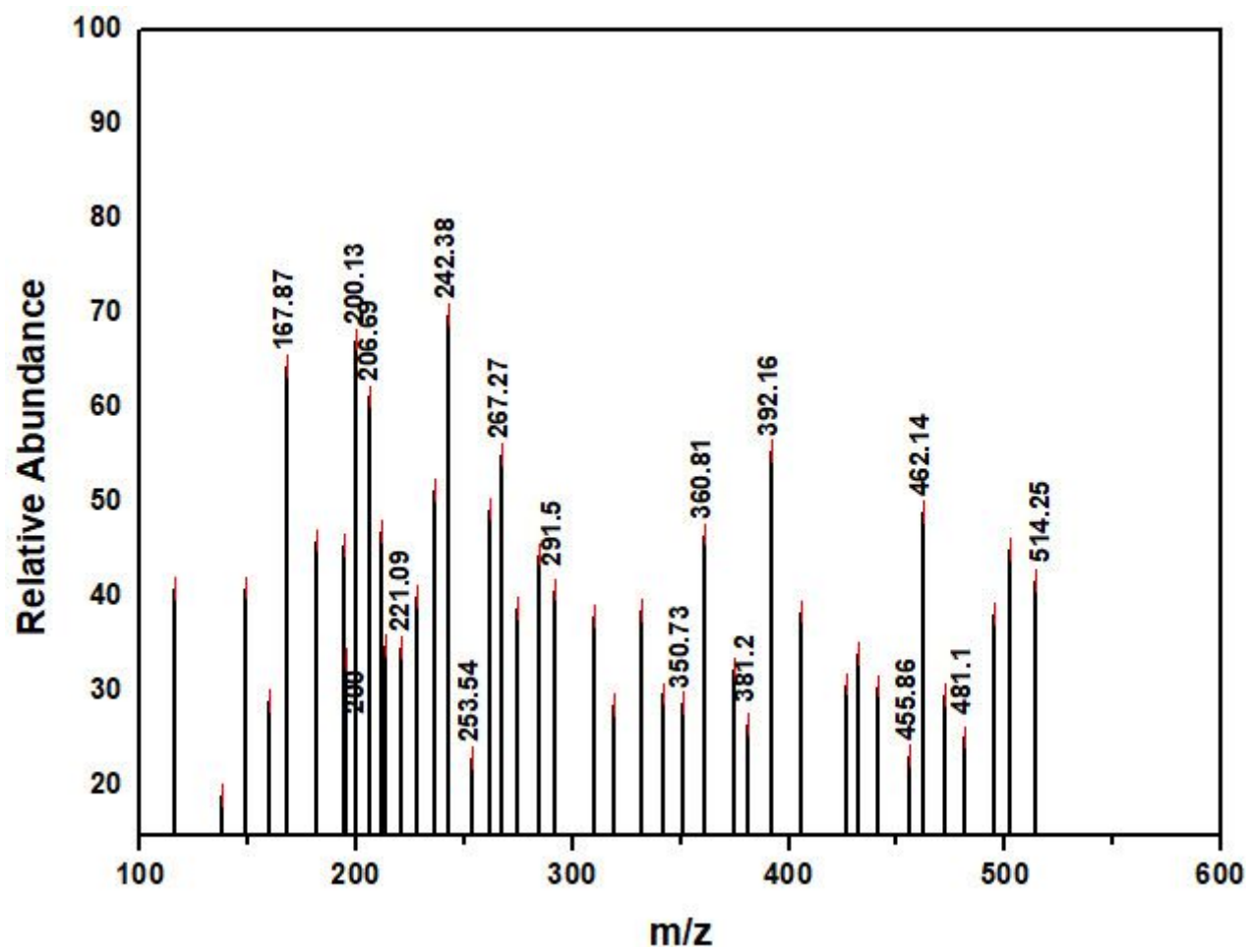
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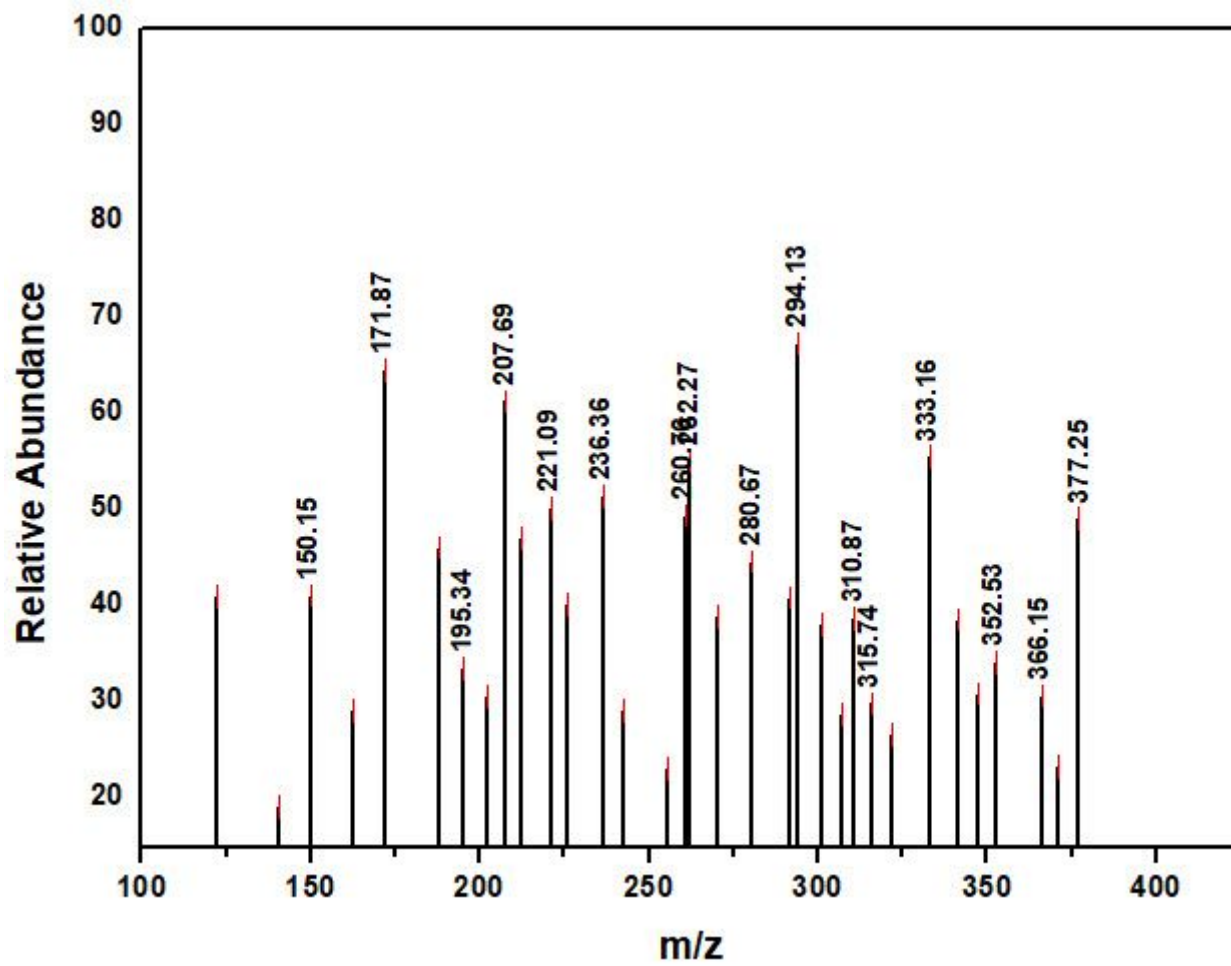
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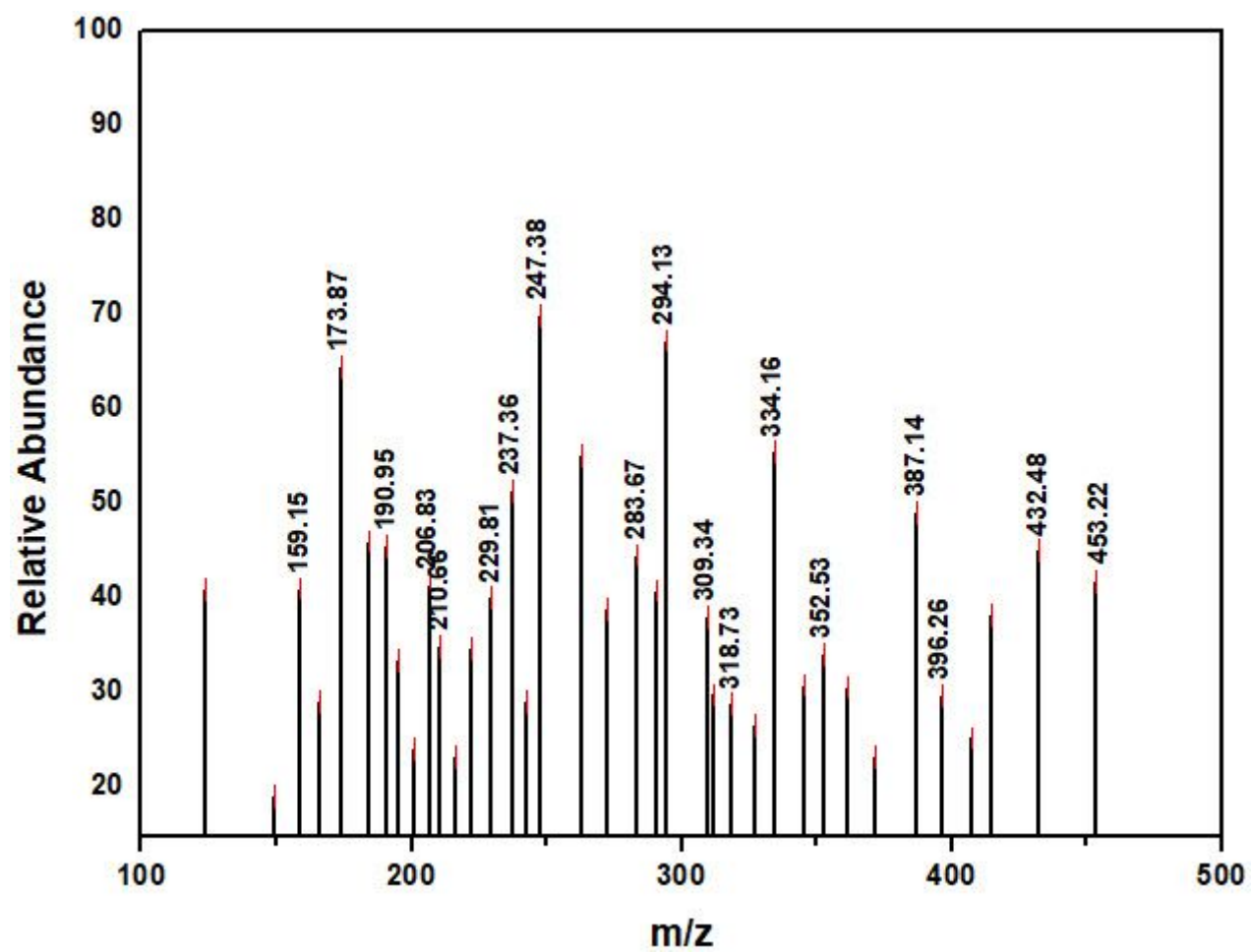
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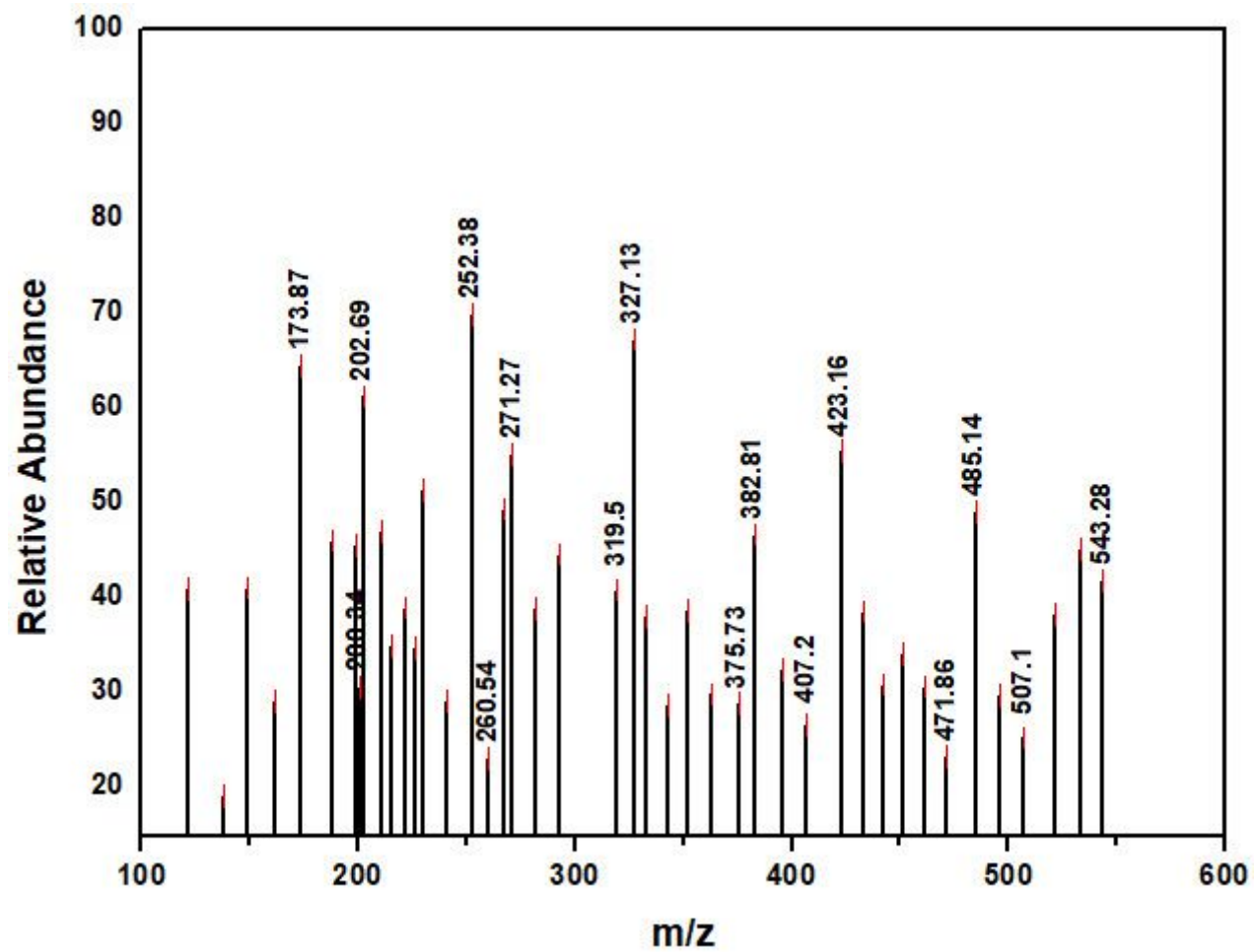
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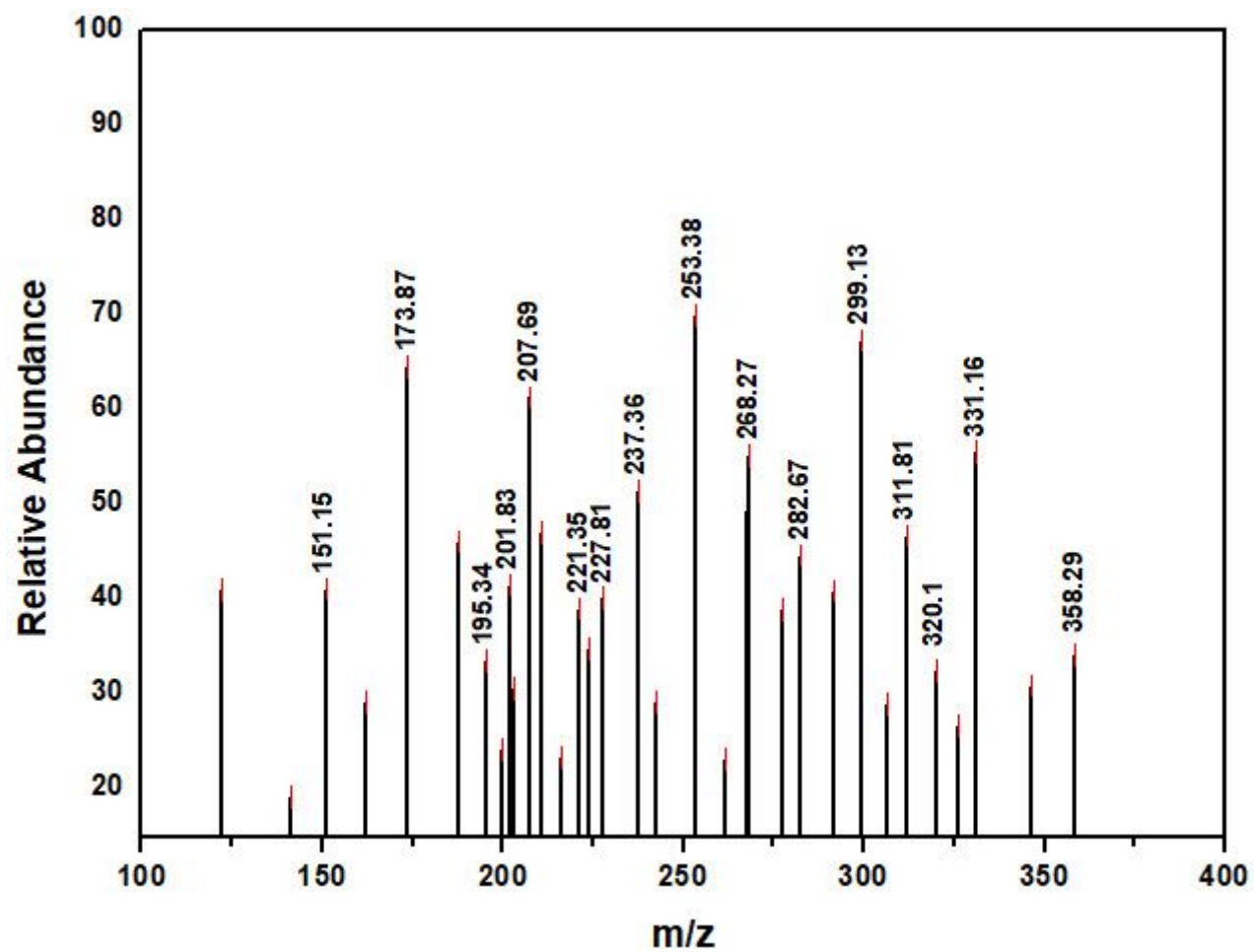


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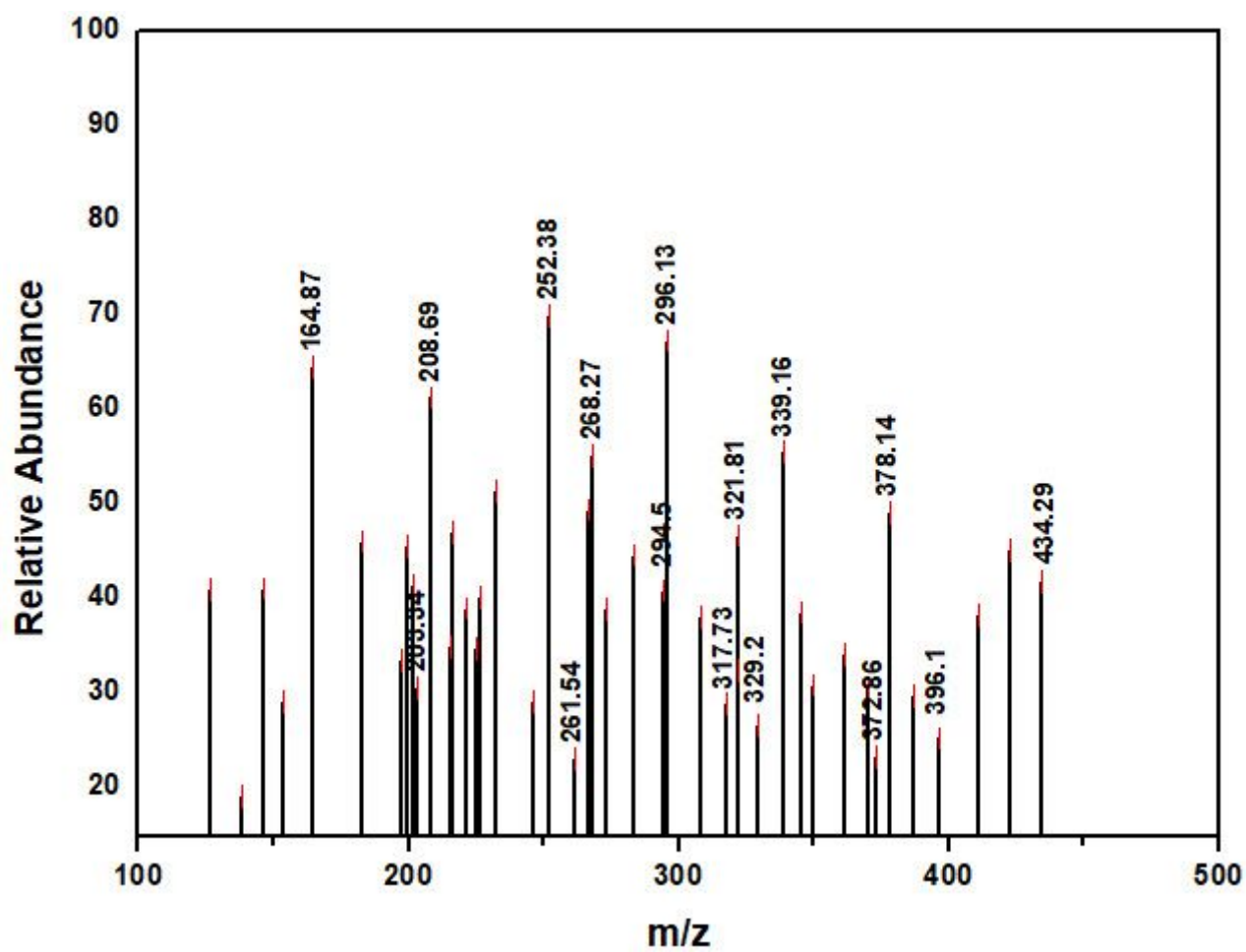


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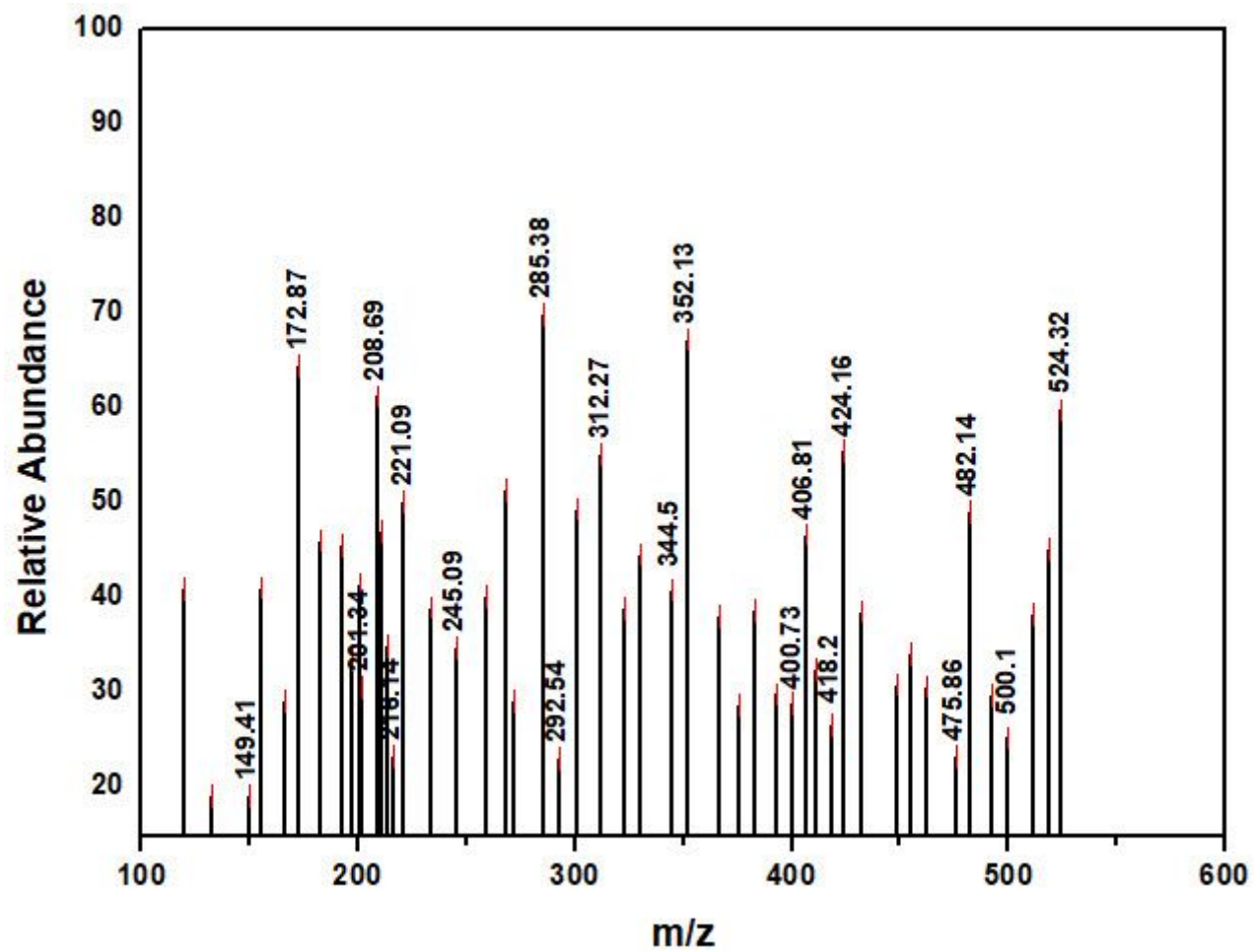




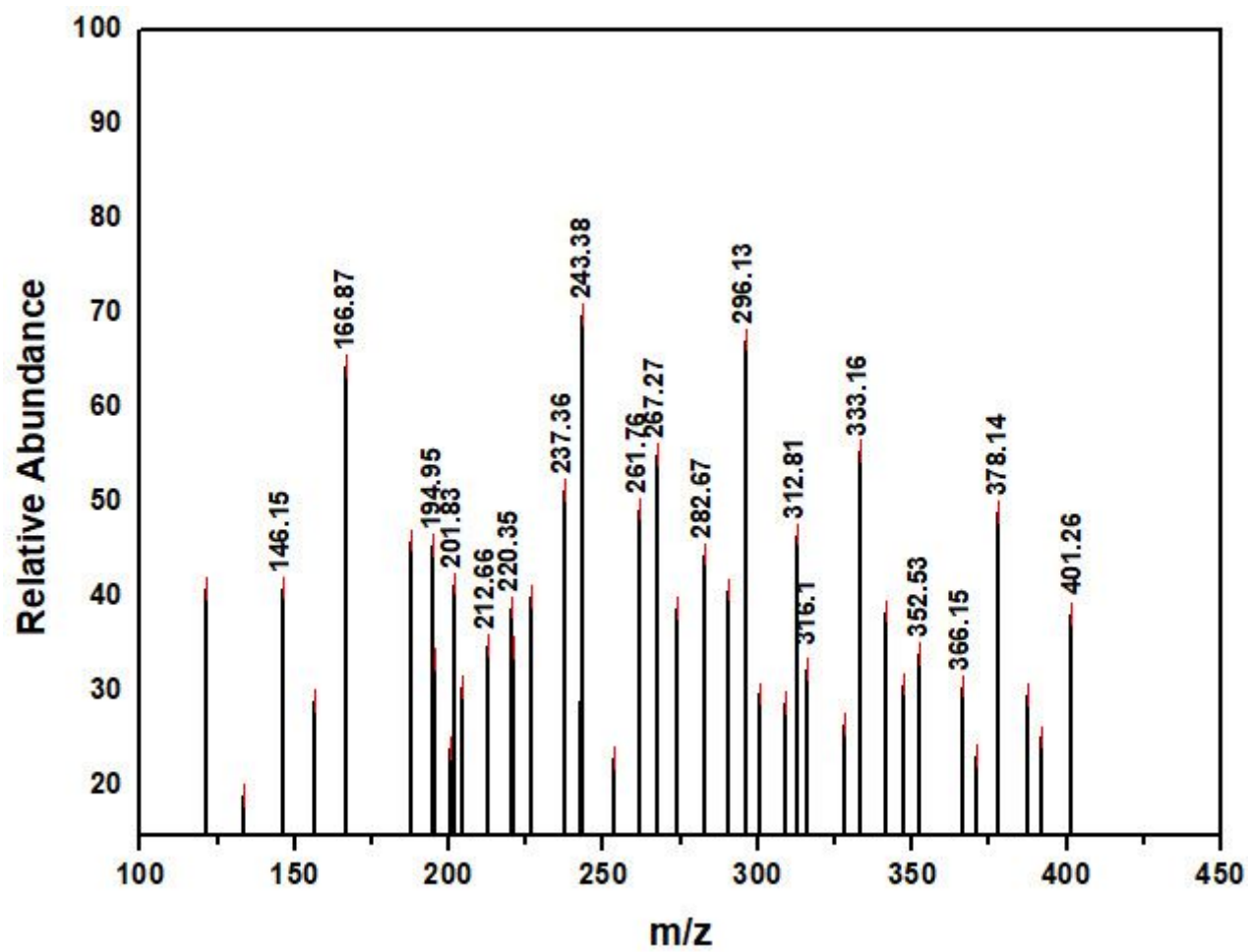
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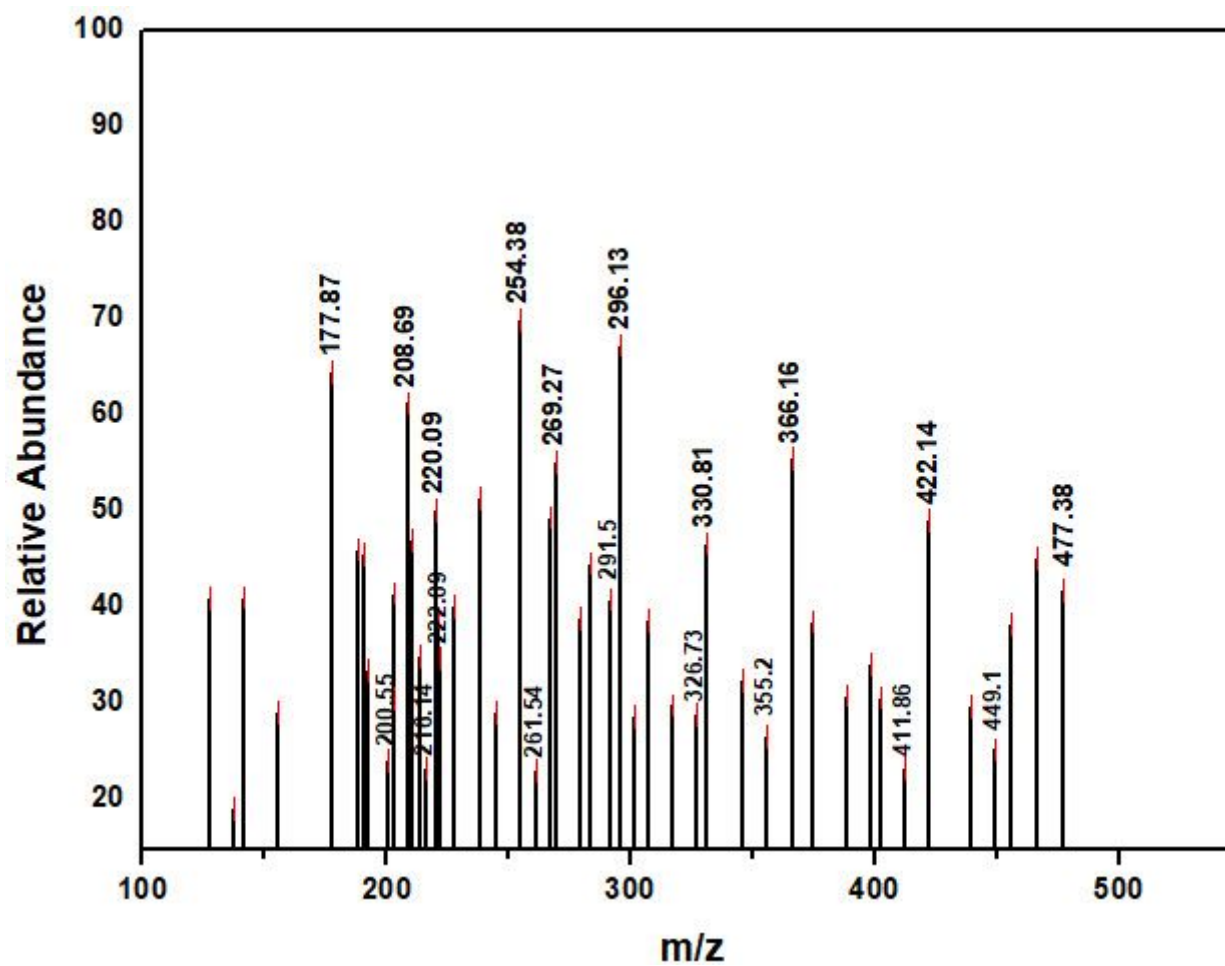
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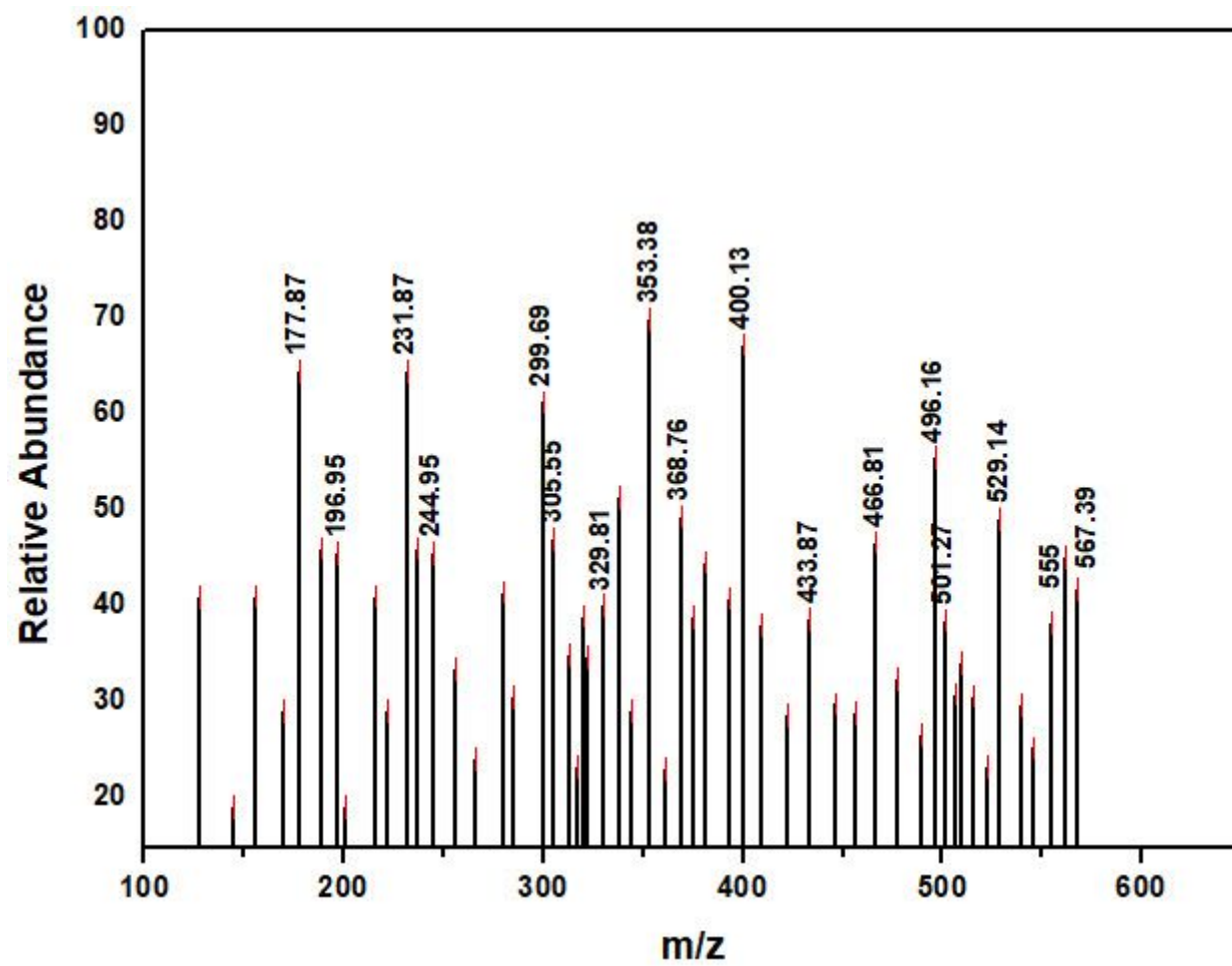
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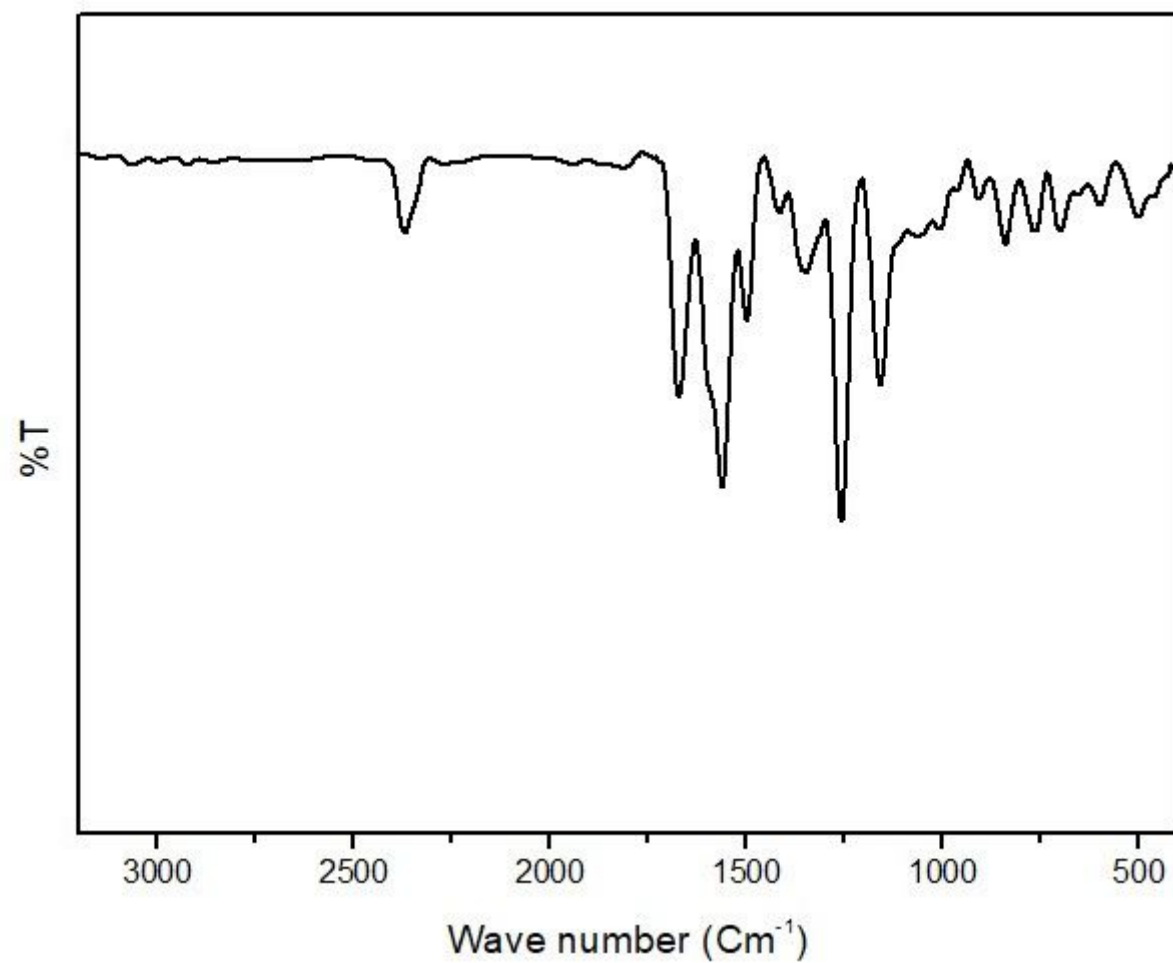
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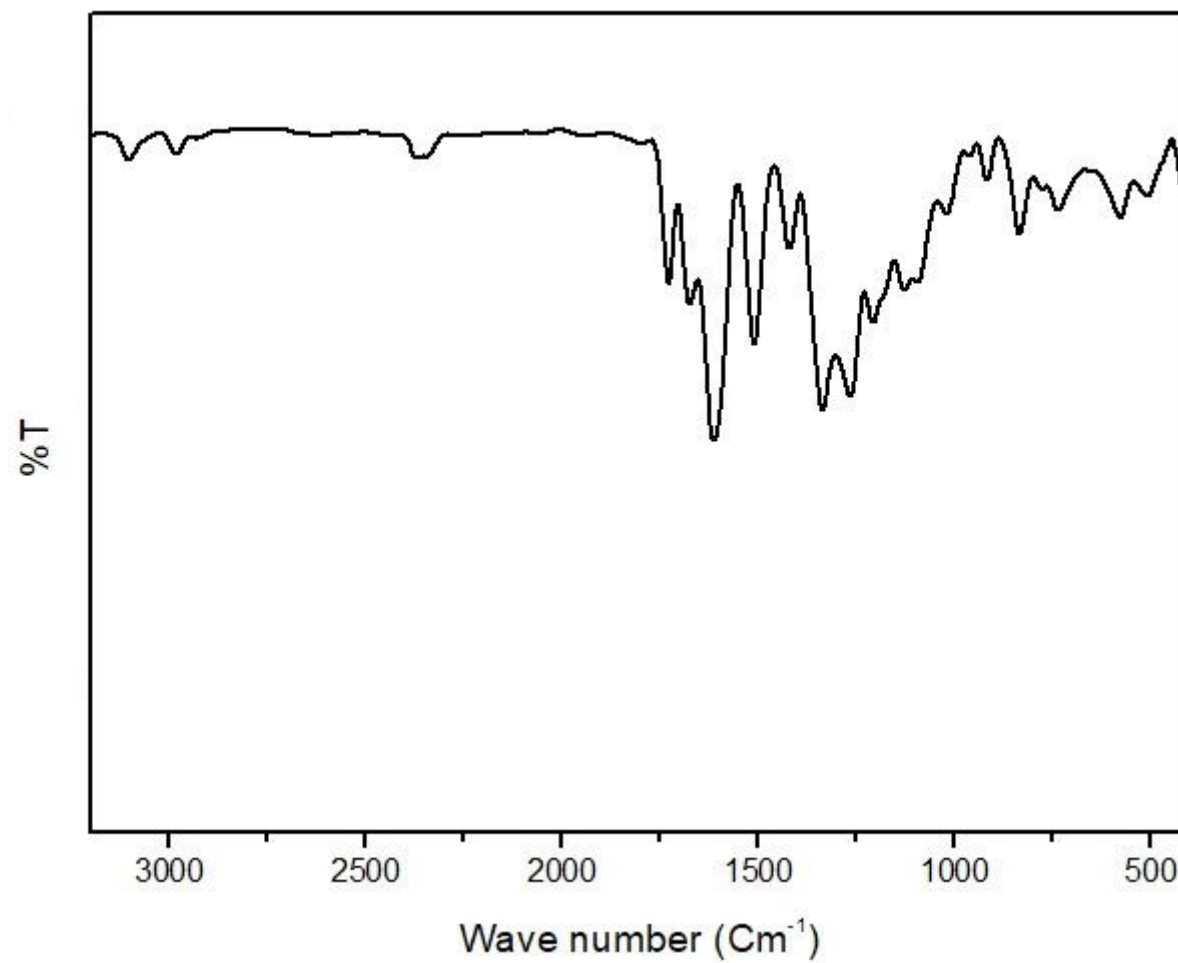
Mass spectra of compound 9b



Mass spectra of compound 9c

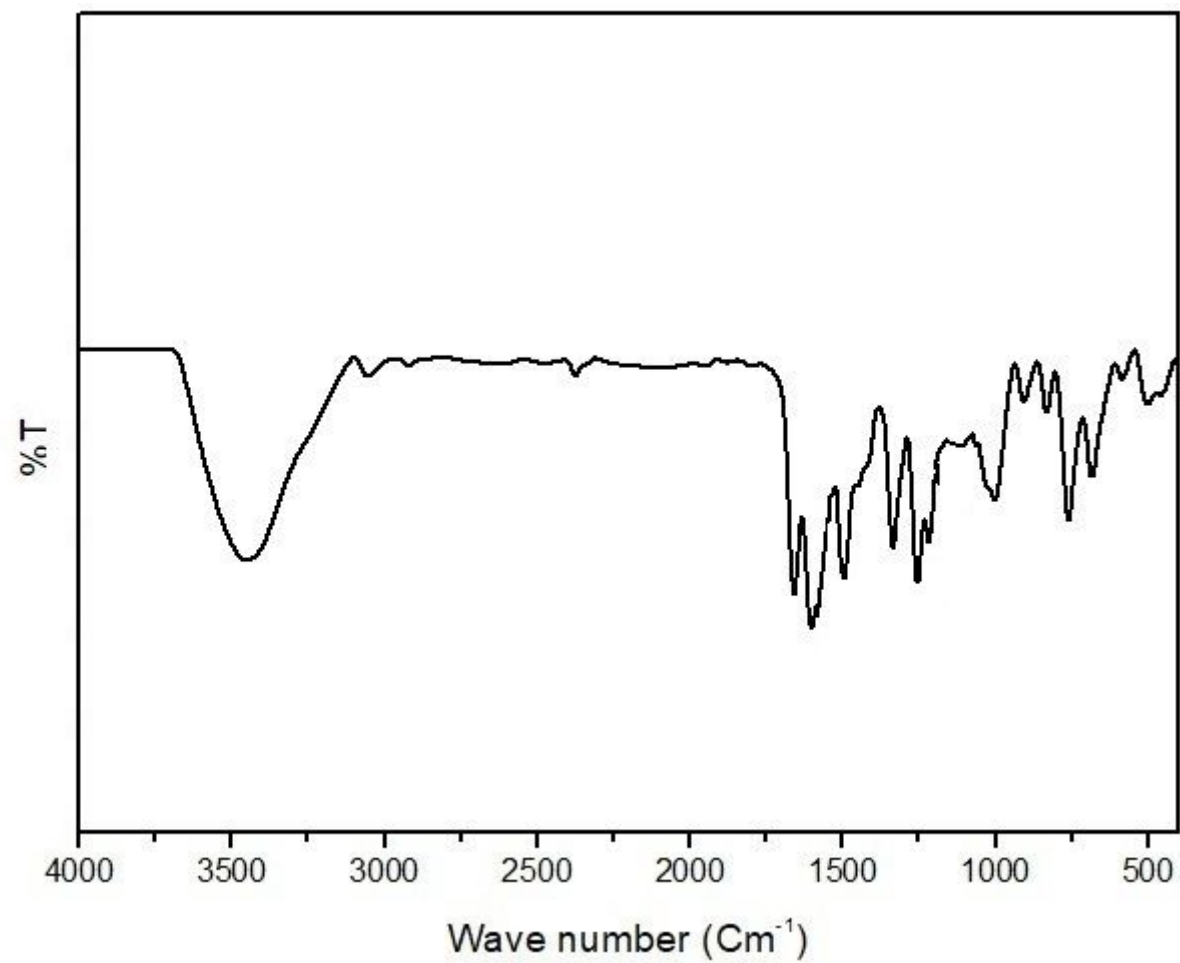


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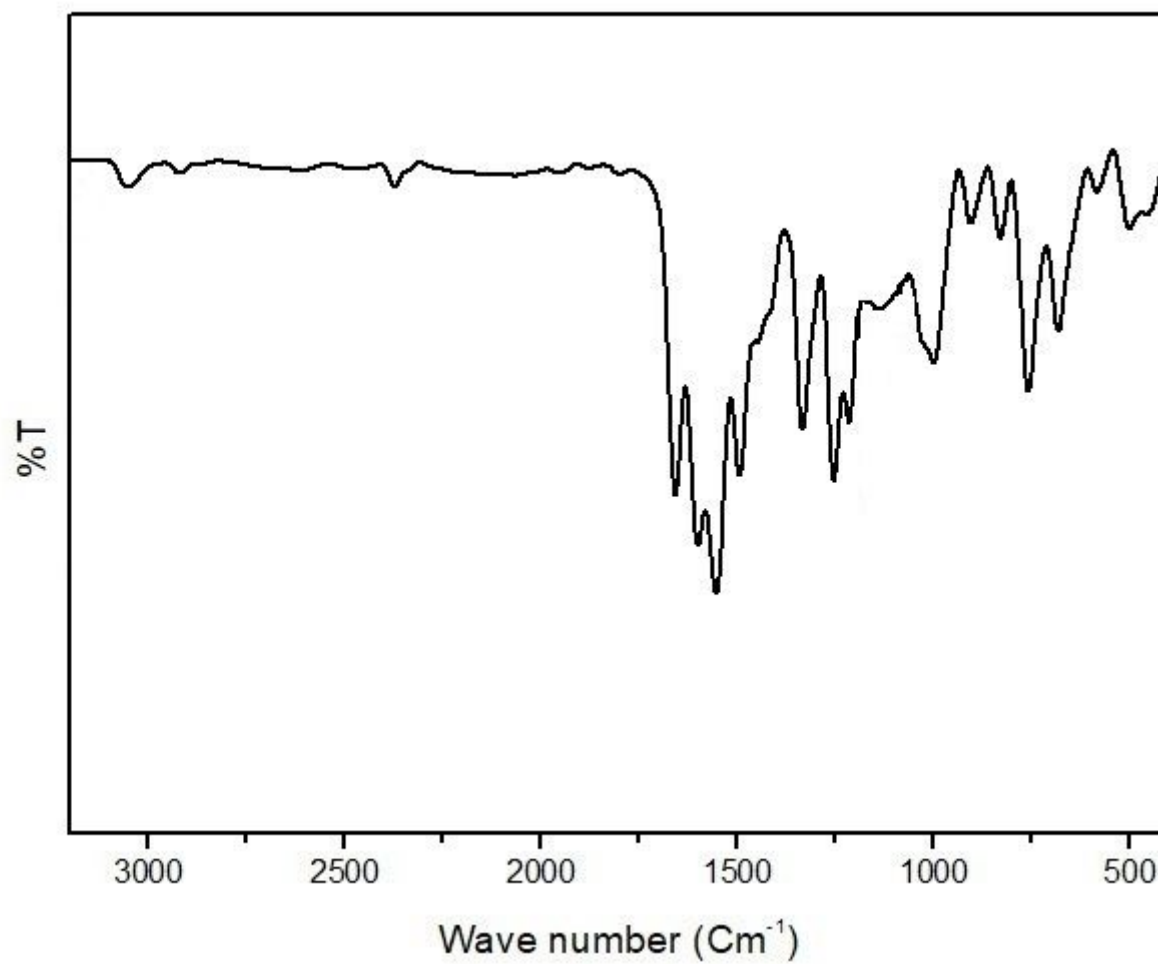


FT-IR spectra of compound 2c

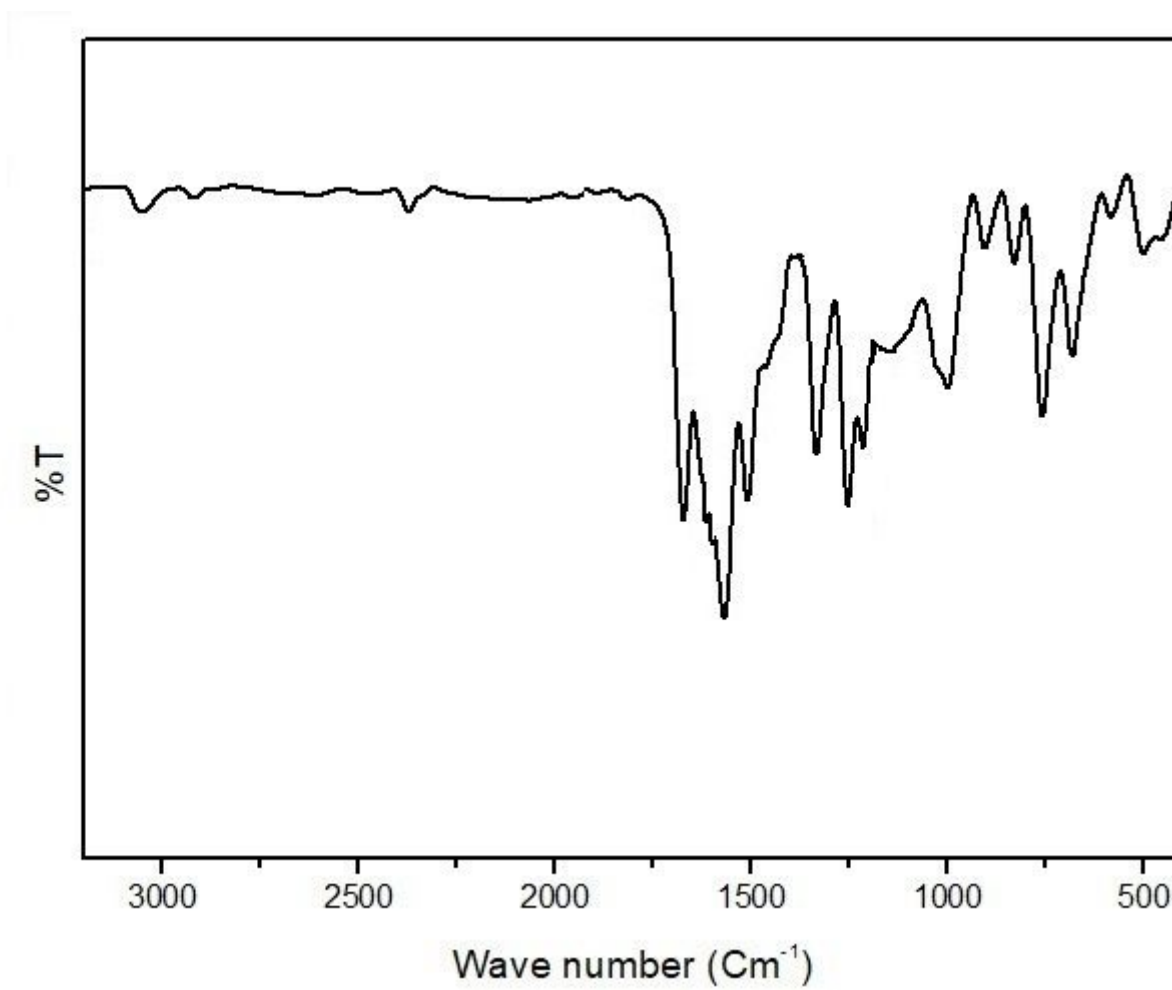




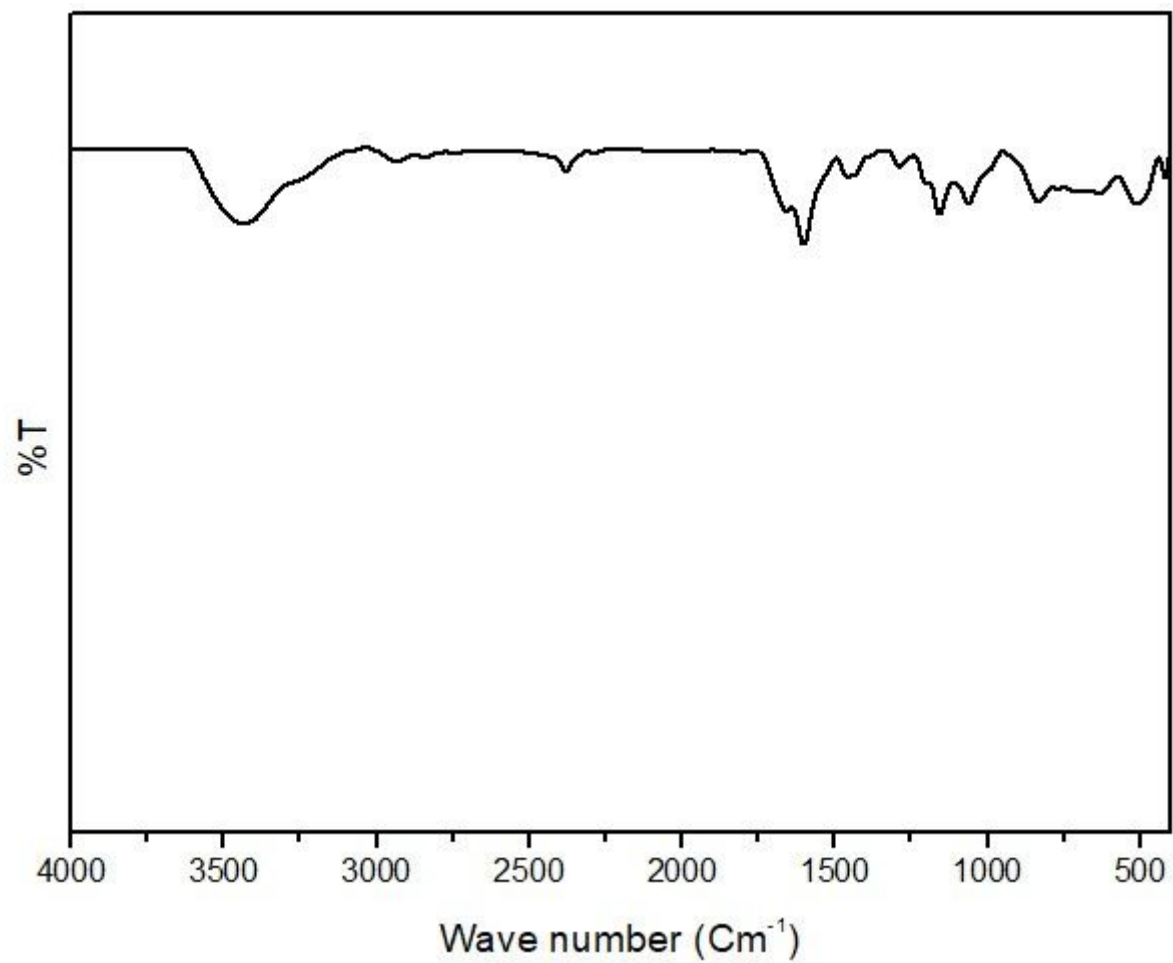
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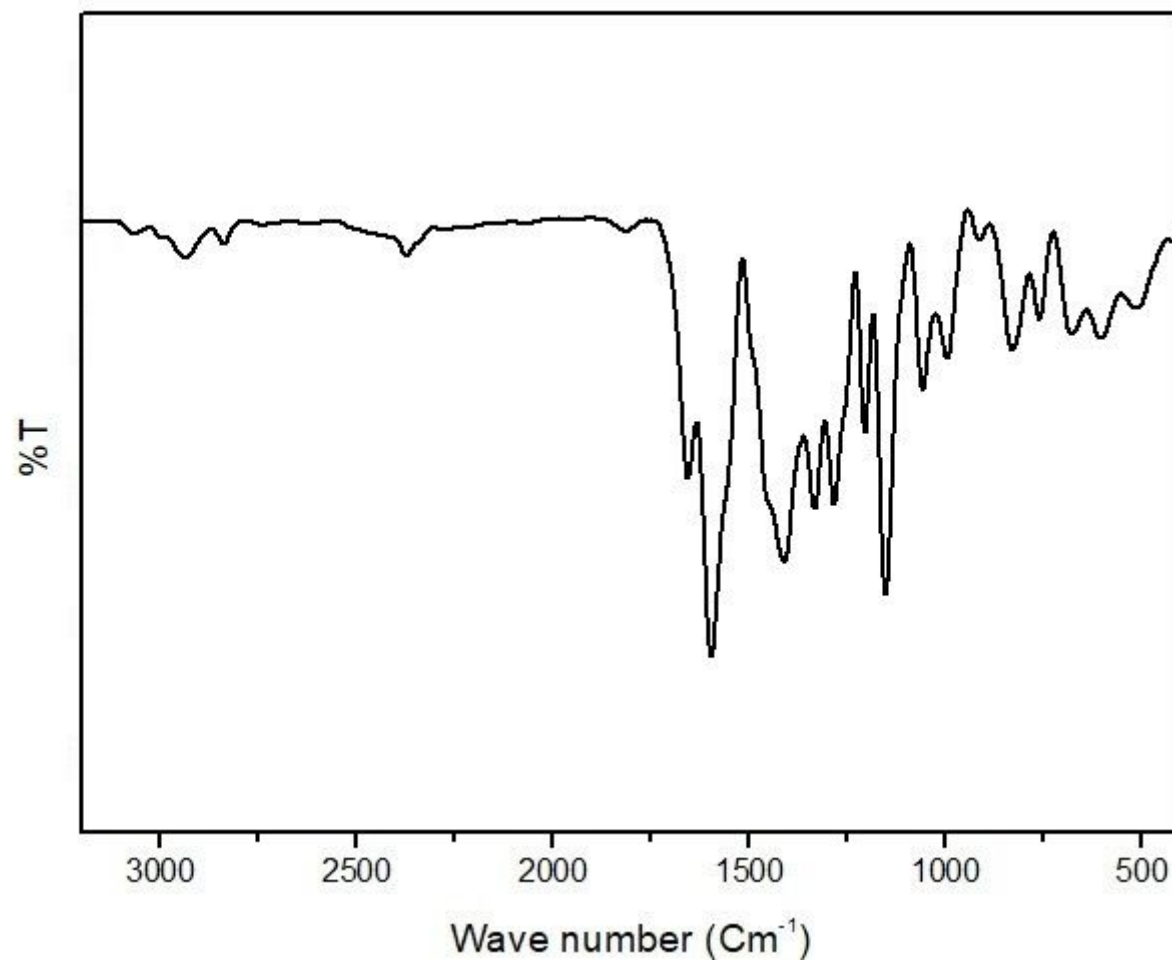
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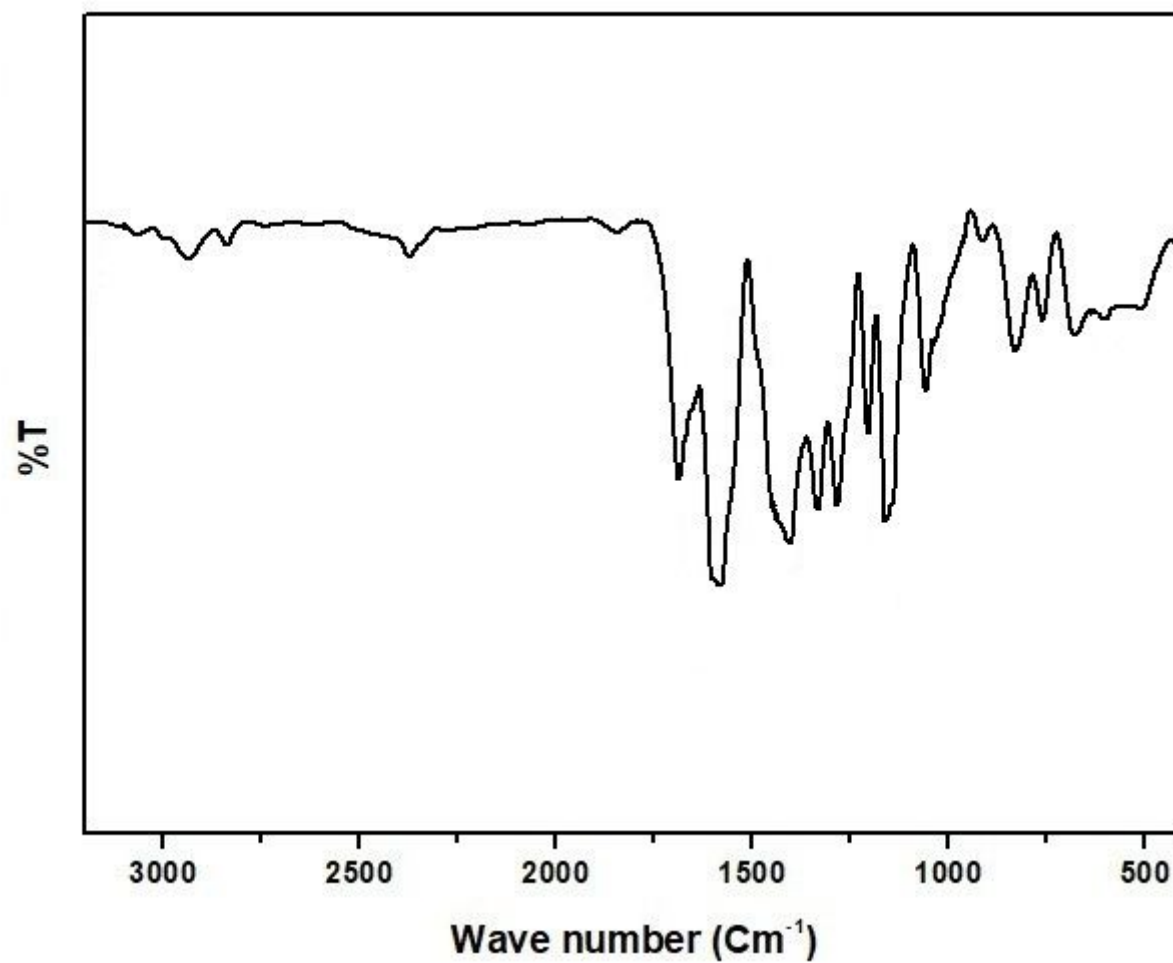
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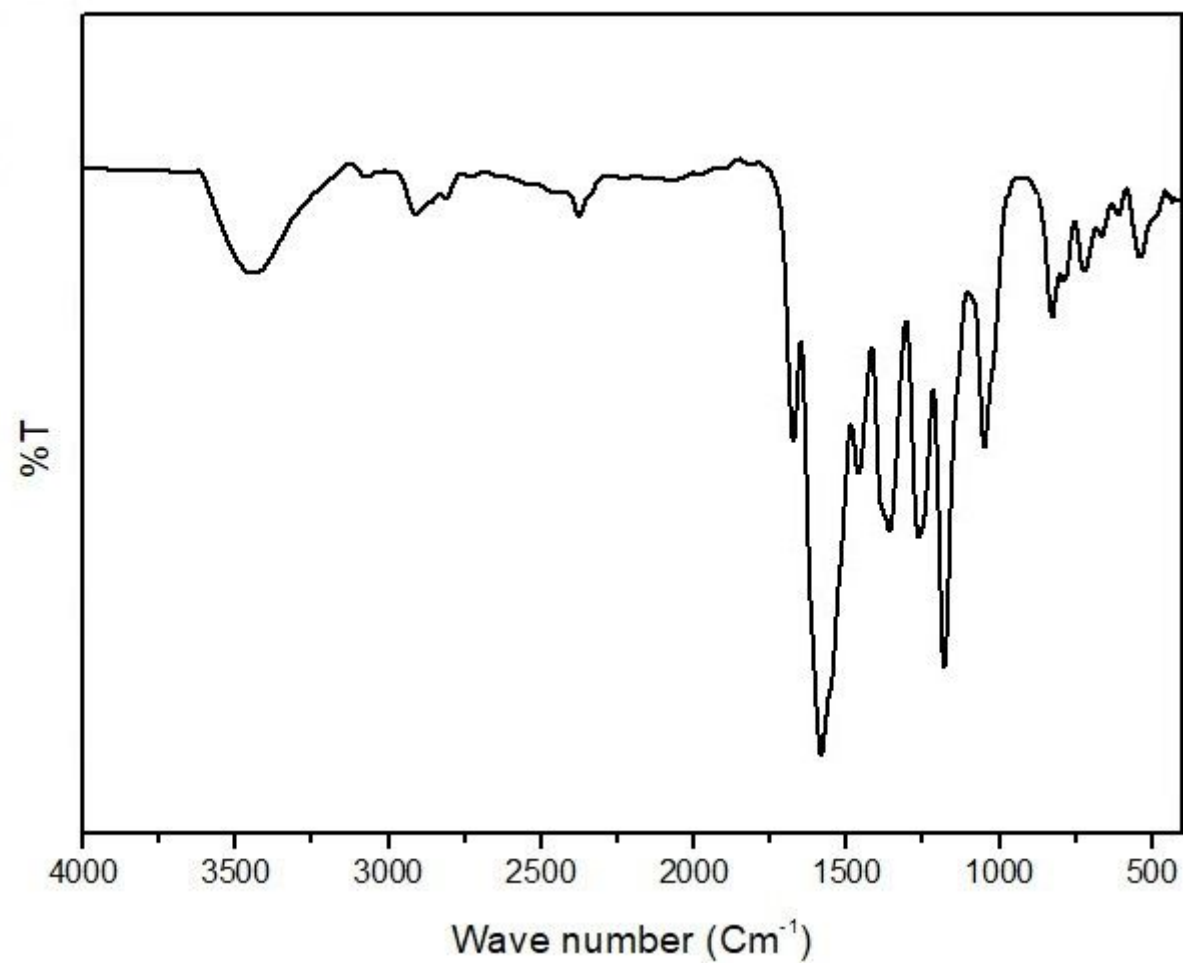
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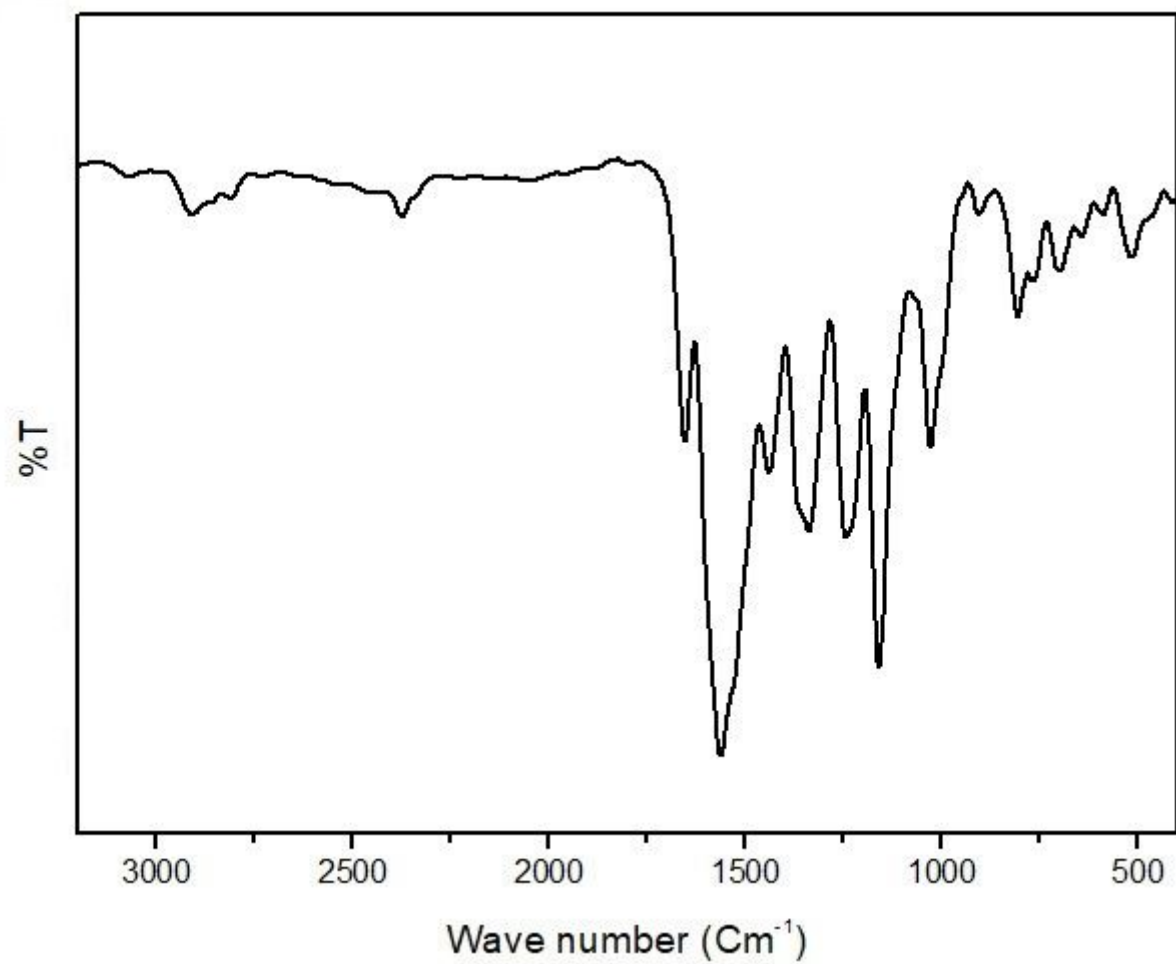
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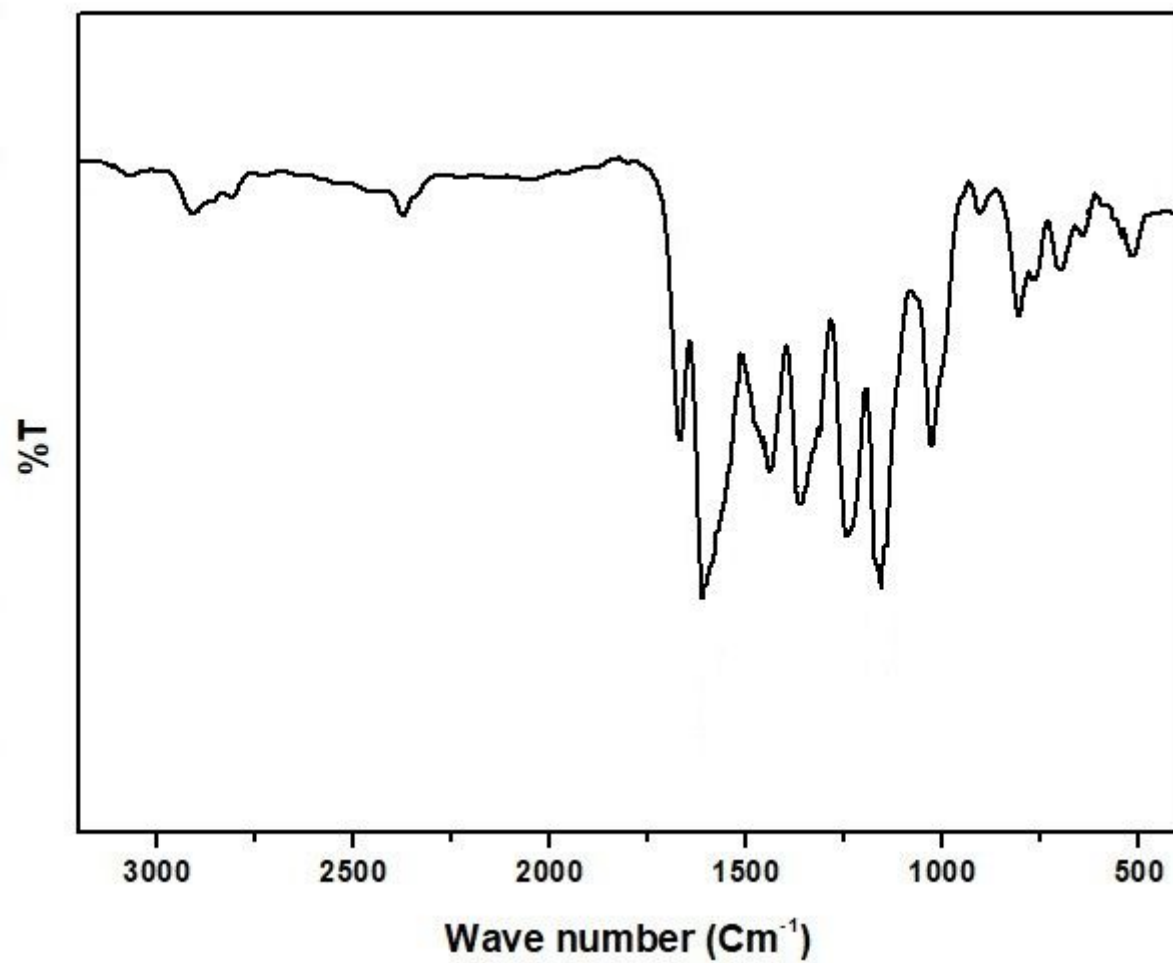


FT-IR spectra of compound 5a

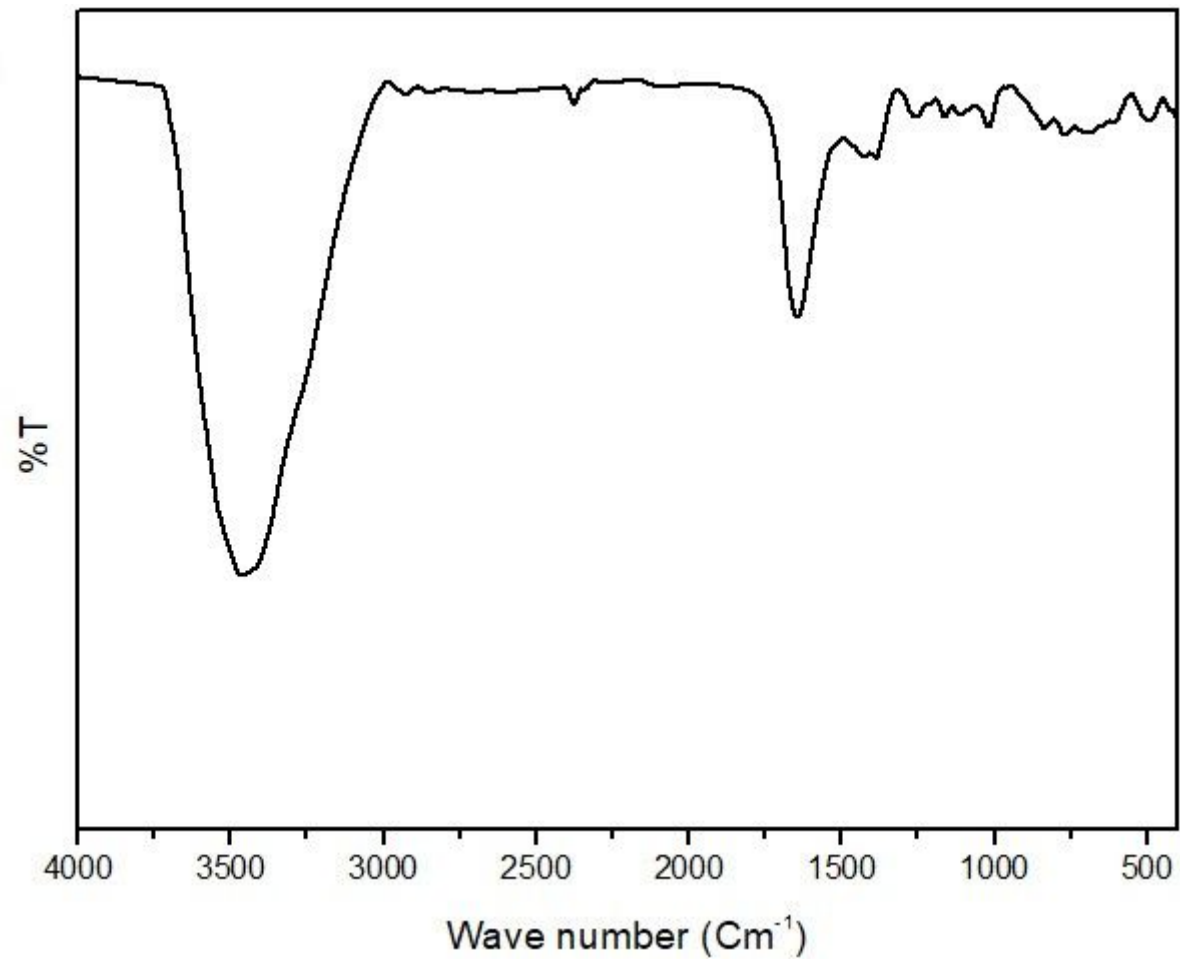


FT-IR spectra of compound 5b

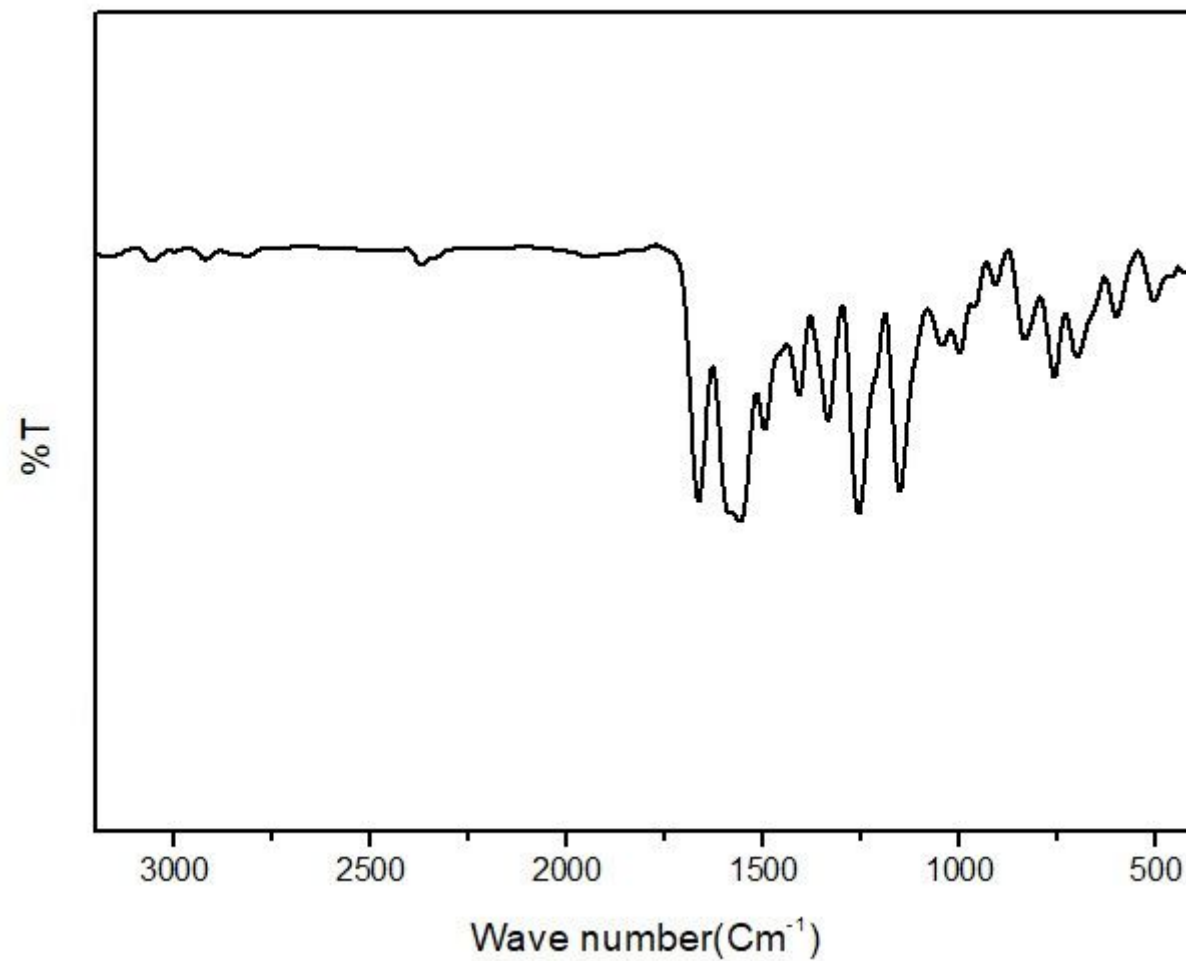




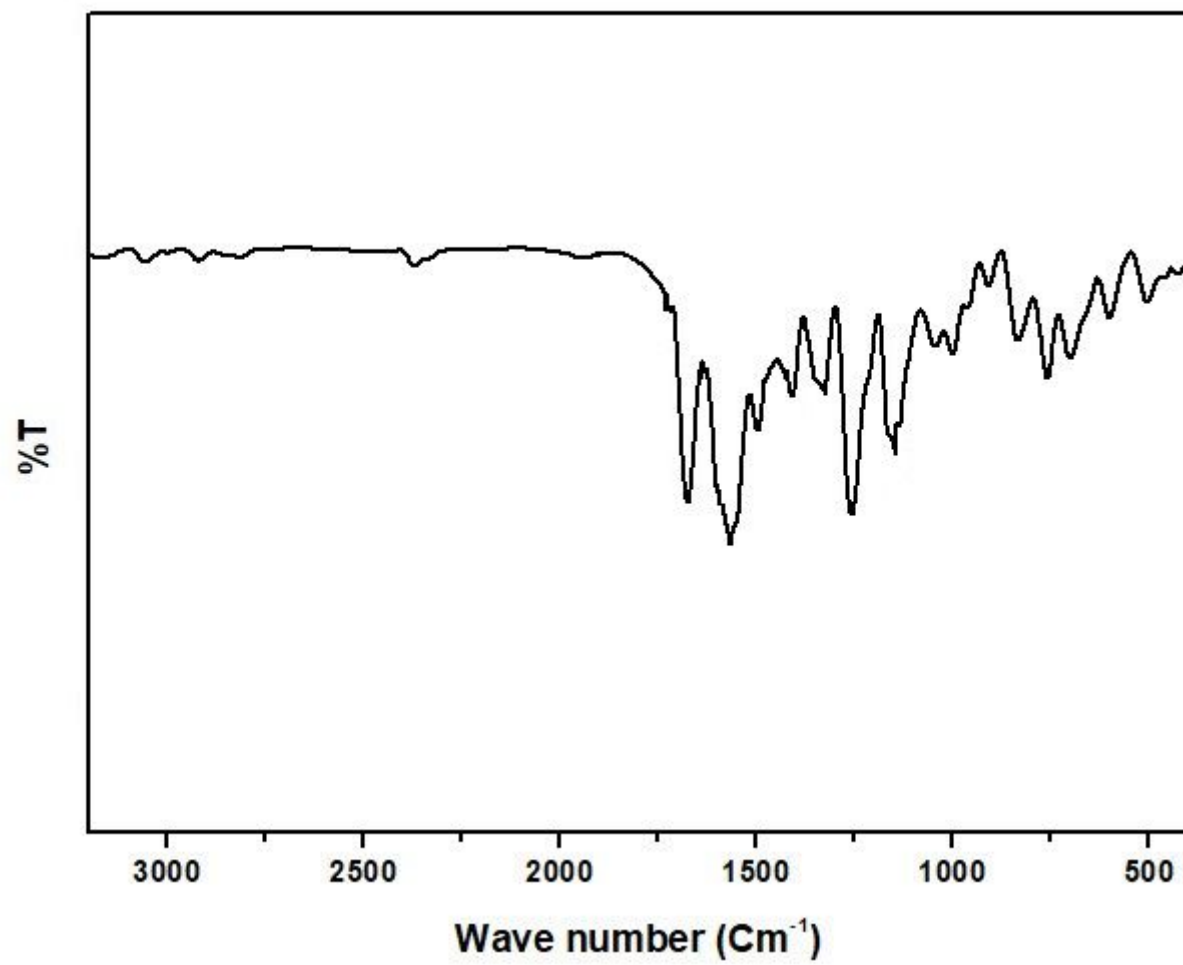
FT-IR spectra of compound 5c



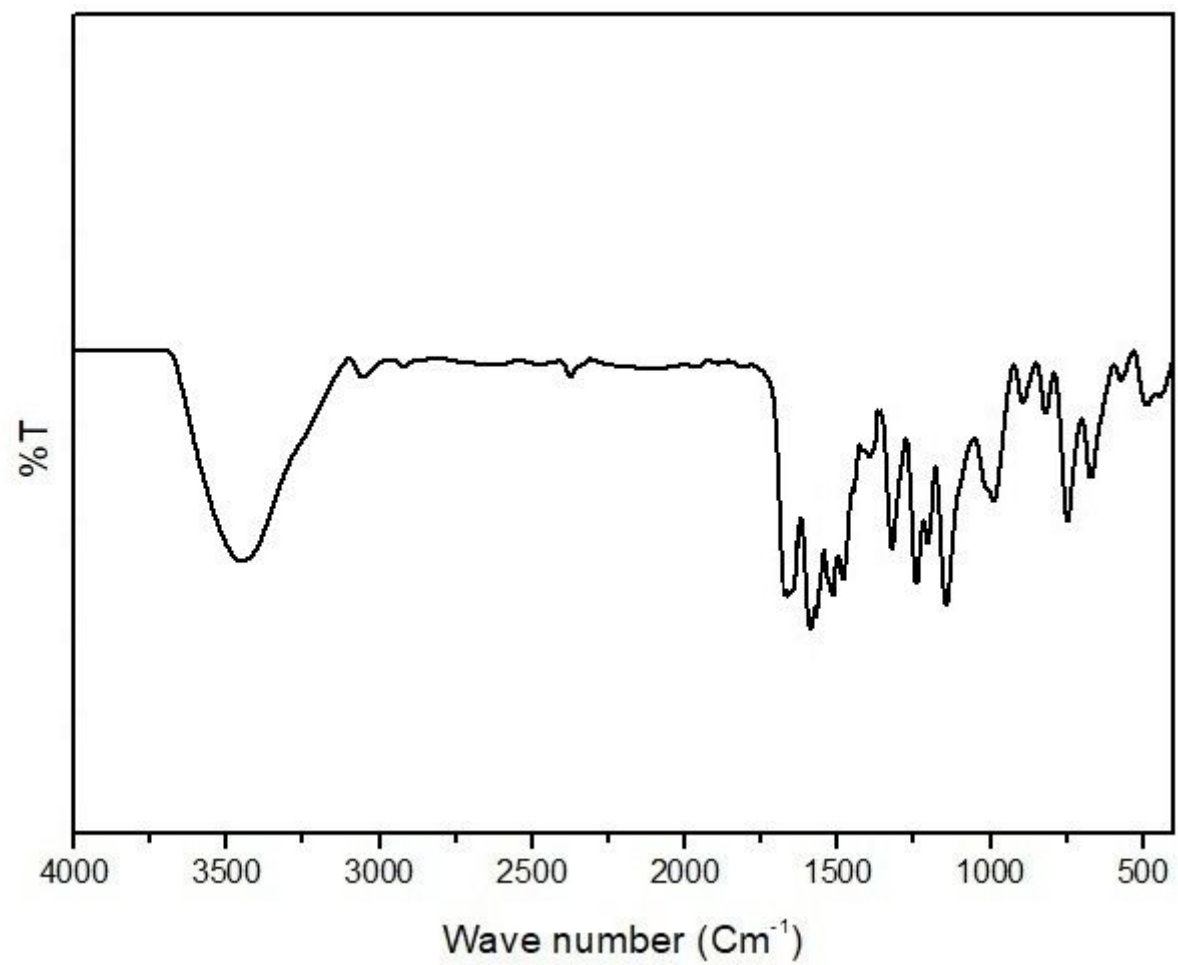
FT-IR spectra of compound 6a



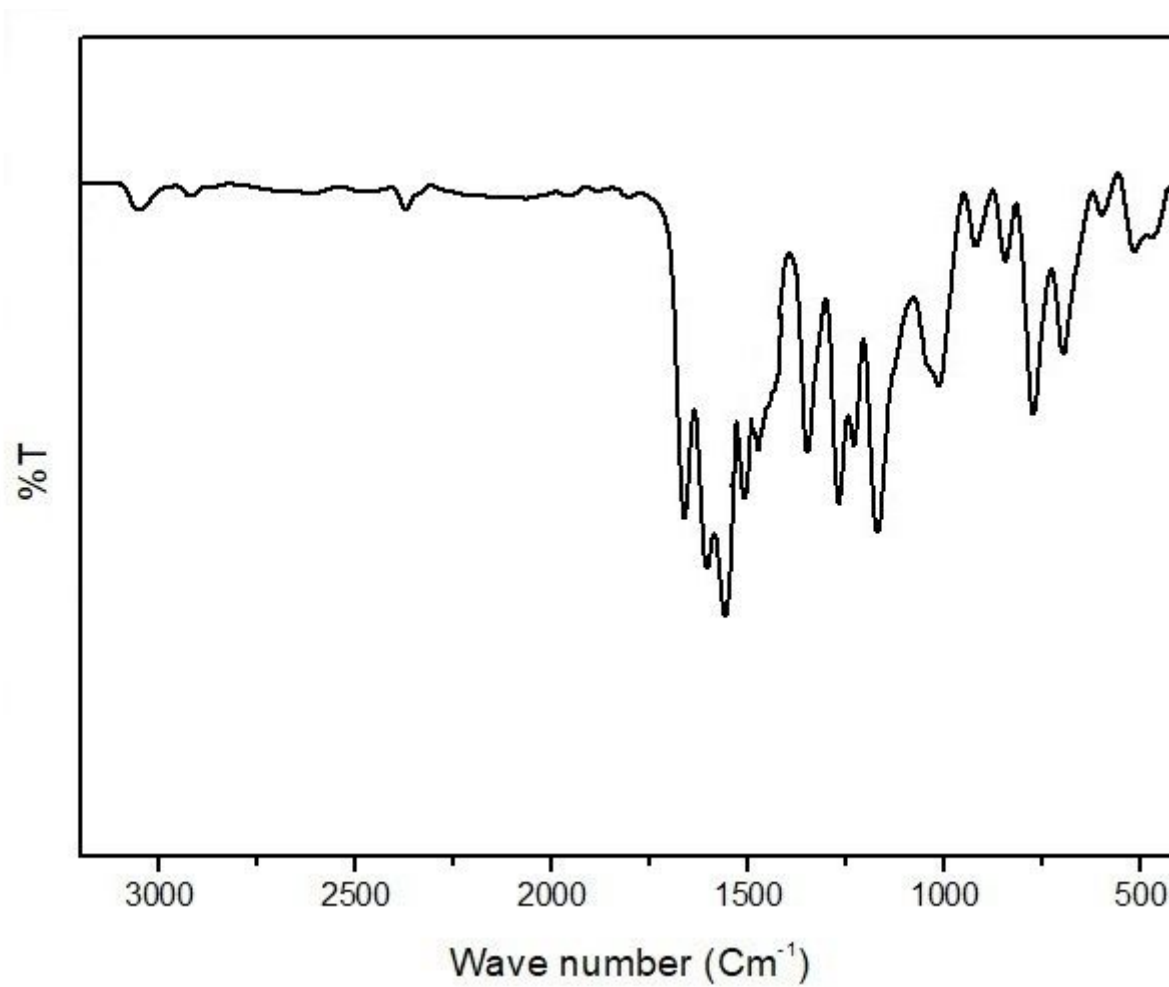
FT-IR spectra of compound 6b



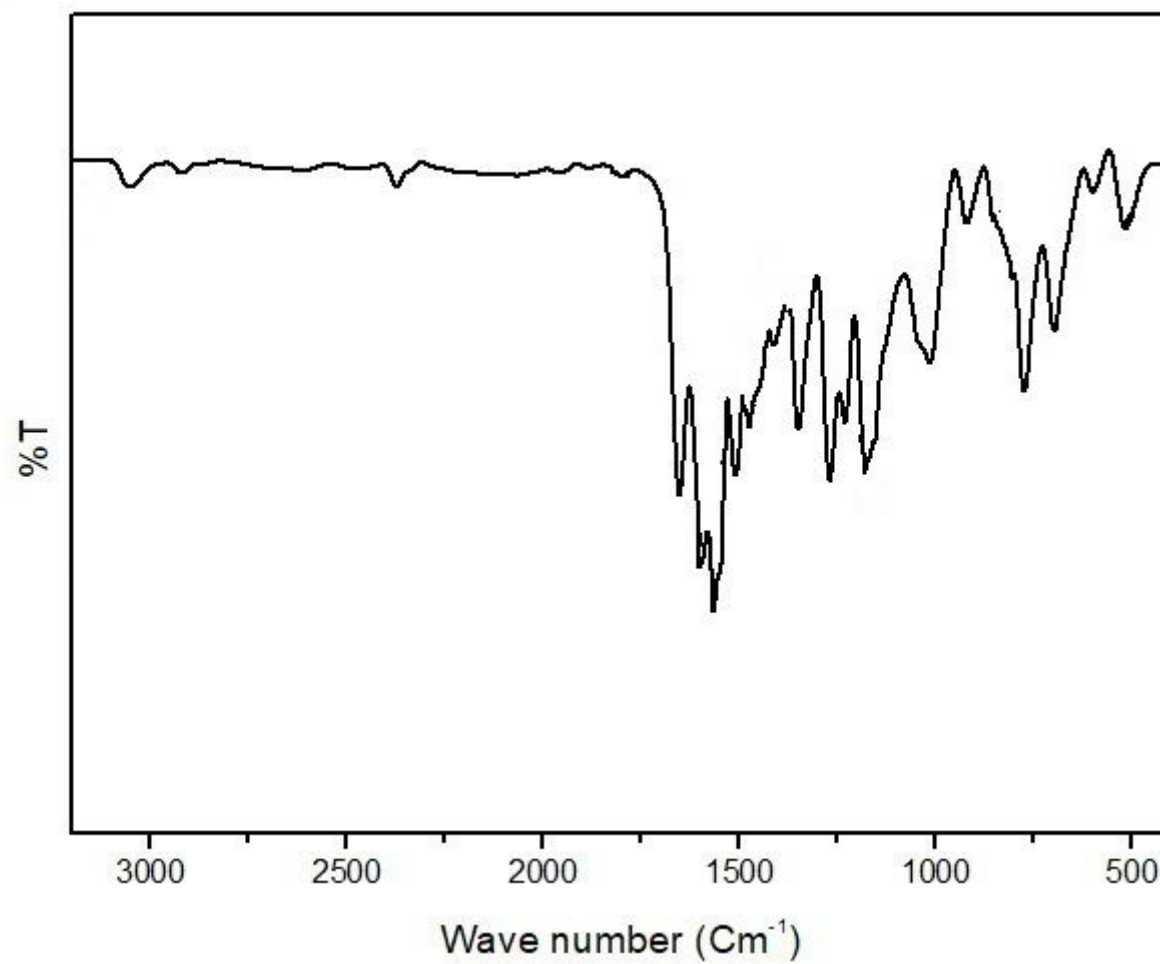
FT-IR spectra of compound 6c



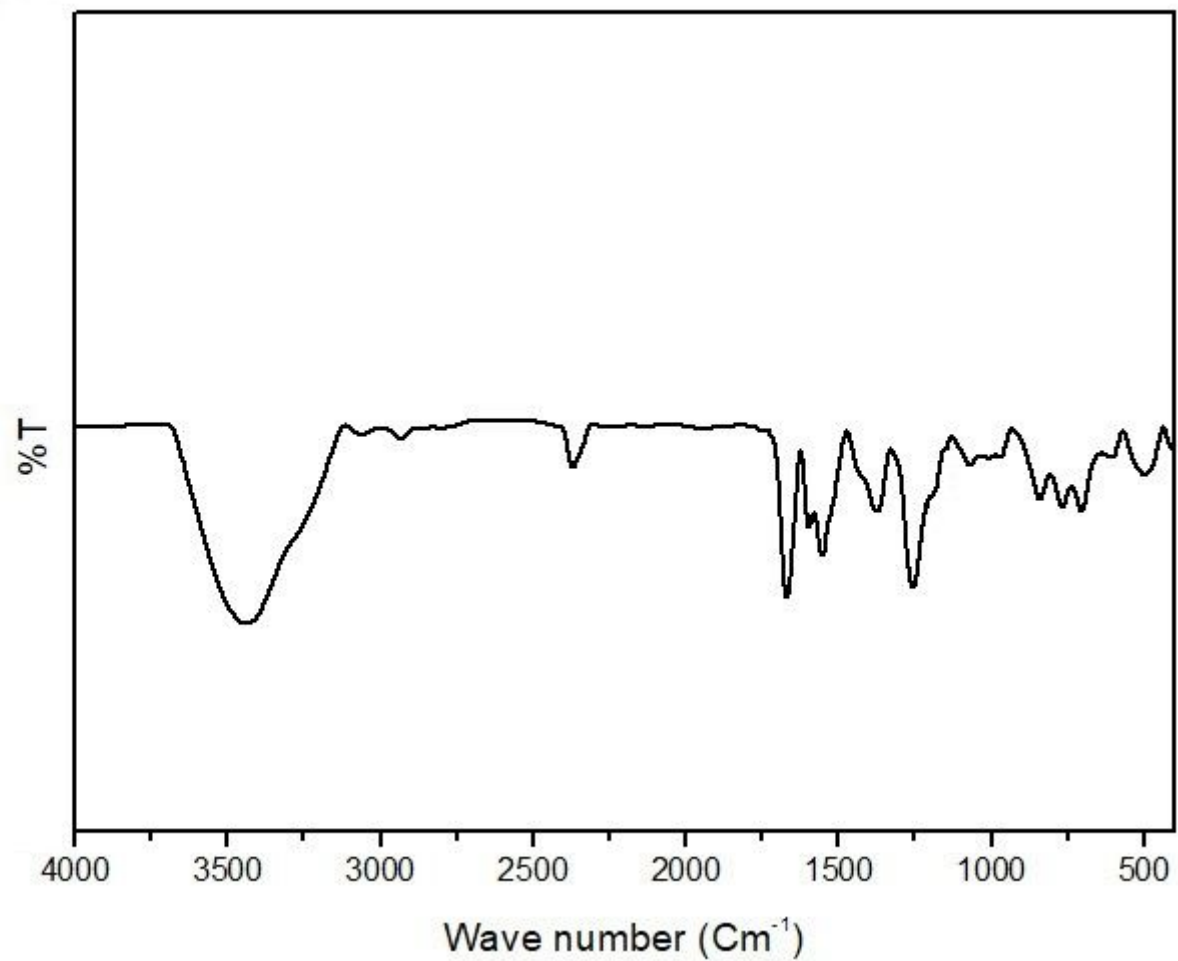
FT-IR spectra of compound 7a



FT-IR spectra of compound 7b



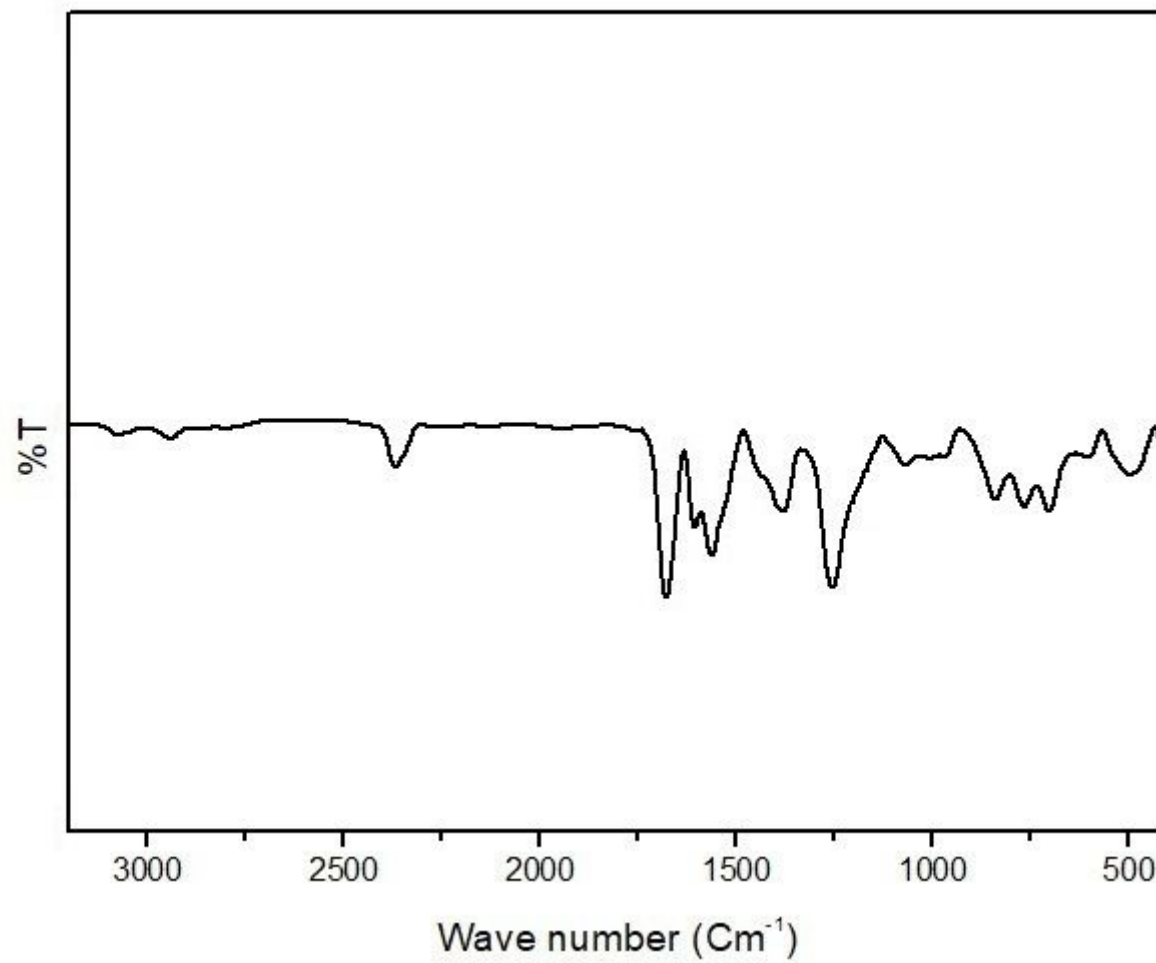
FT-IR spectra of compound 7c



FT-IR spectra of compound 8a

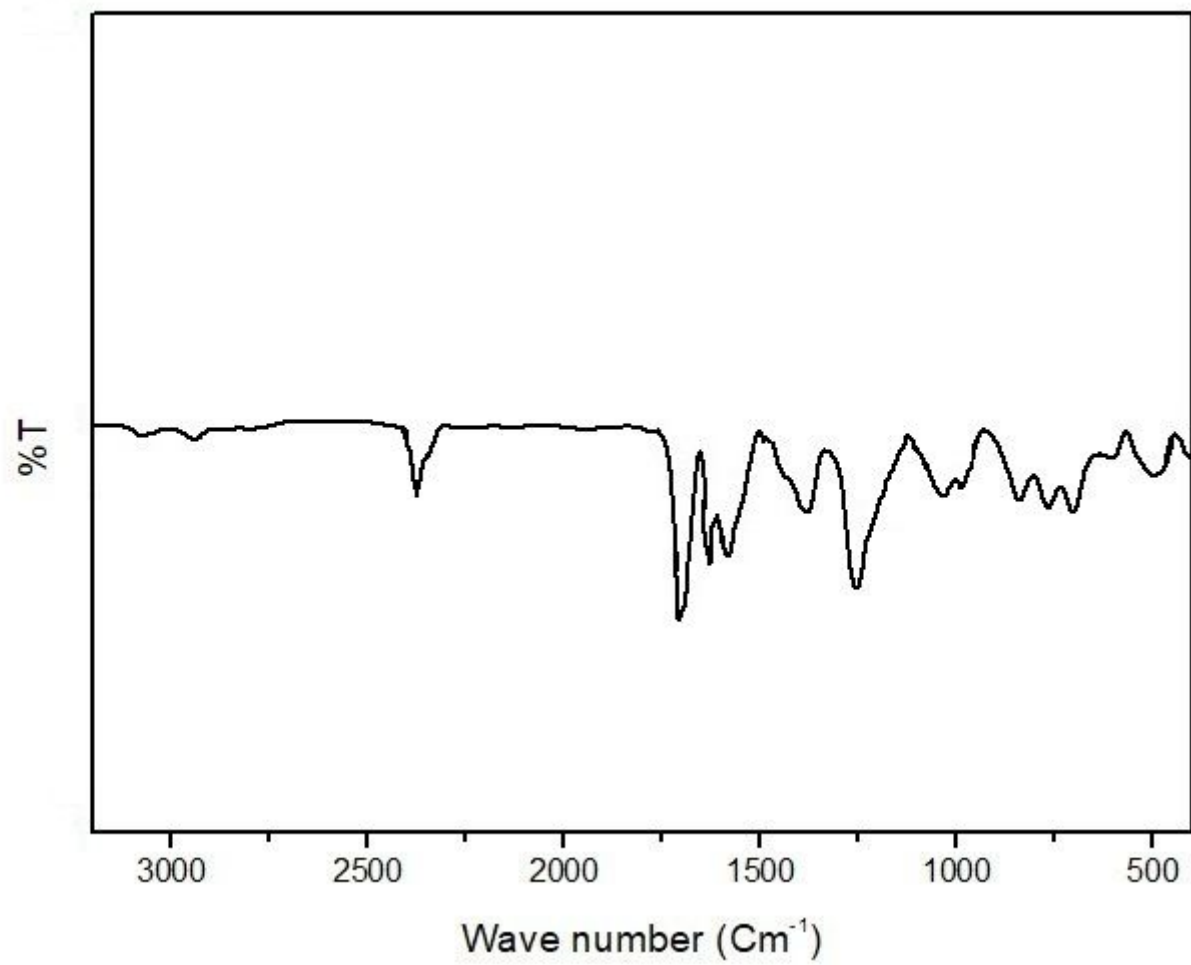
S-88





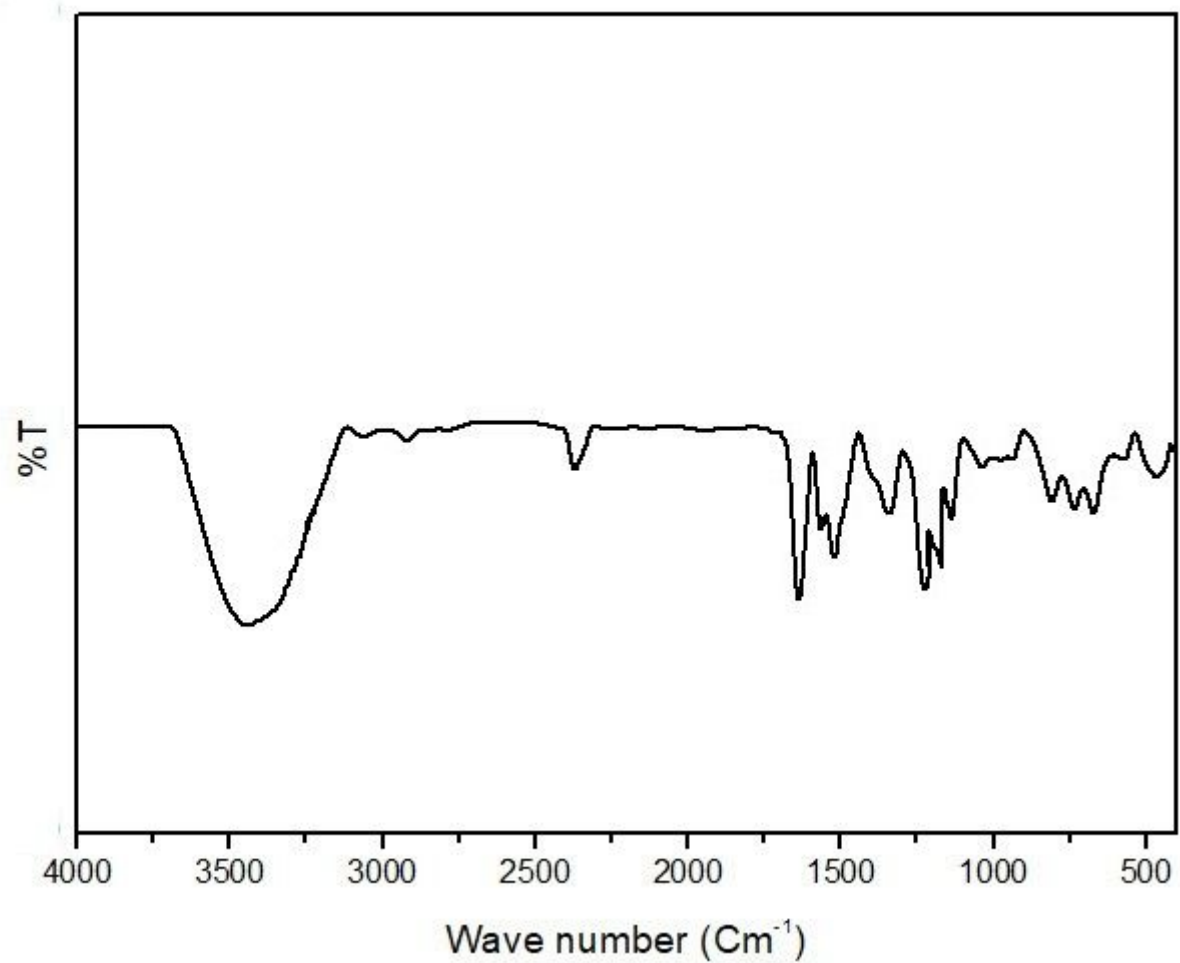
FT-IR spectra of compound 8b

S-89



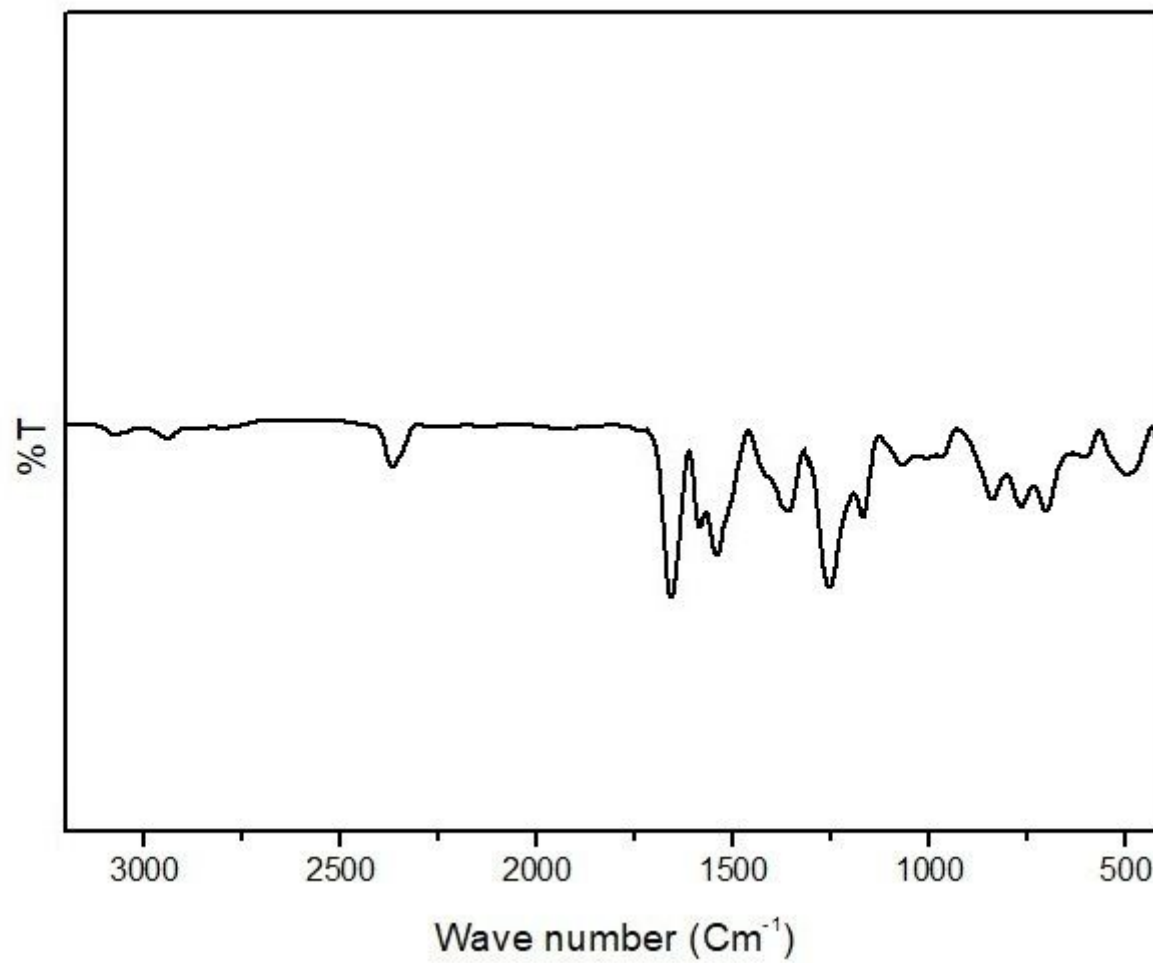
FT-IR spectra of compound 8c

S-90



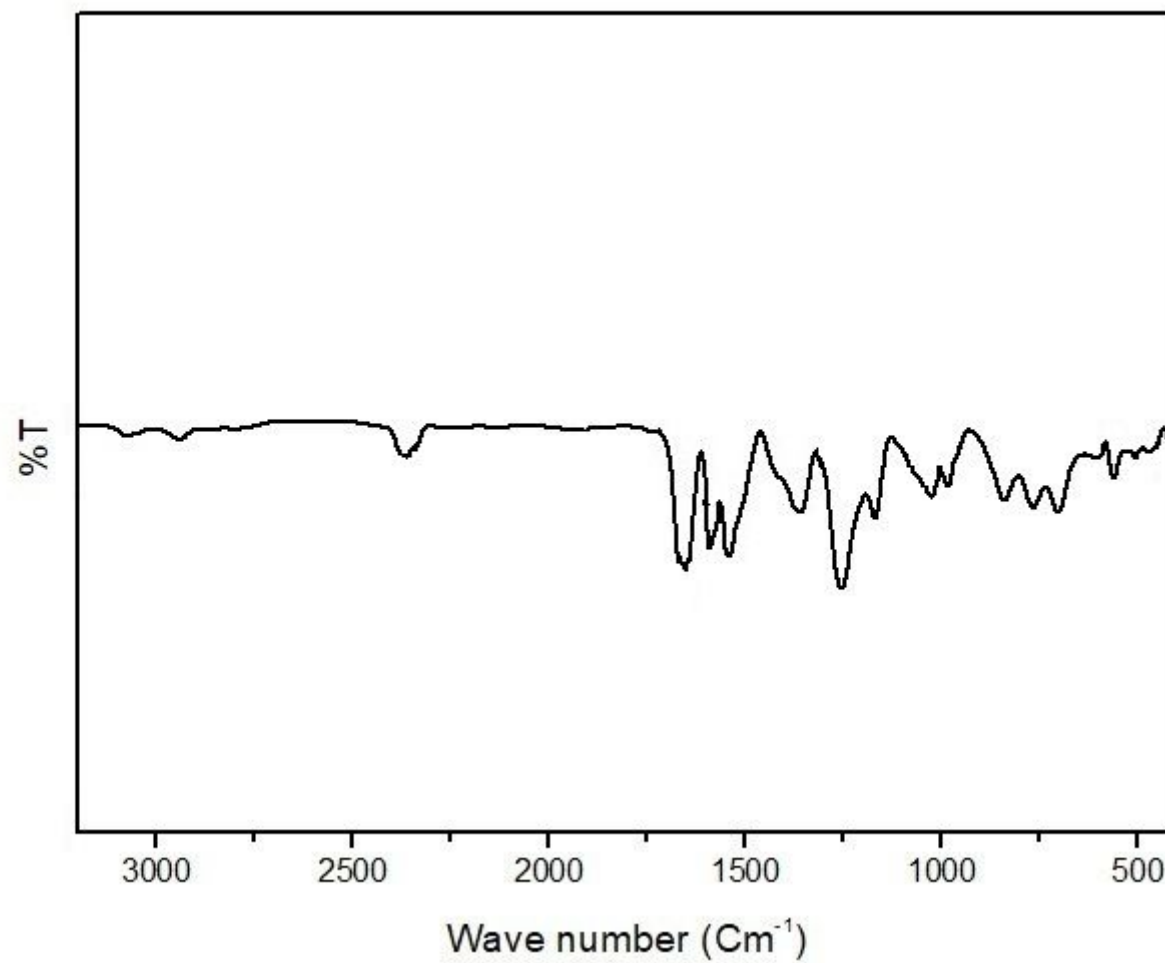
FT-IR spectra of compound 9a

S-91



FT-IR spectra of compound 9b

S-92



FT-IR spectra of compound 9c

Compd	PI3K			AKT		
	Docking Score ( $\Delta G_{\text{bind}}$ )	Docked complex (amino acid–ligand) interactions	Distance (Å)	Docking Score ( $\Delta G_{\text{bind}}$ )	Docked complex (amino acid–ligand) interactions	Distance (Å)
<b>3a</b>	-9.9	<b>H-bond</b> Glu259:OE2---compound 3a	2.48	-9.3	<b>H-bond</b> Gly162:N---compound 3a	2.85
		<b><math>\pi</math>-<math>\pi</math></b> His701---compound 3a	5.31		<b><math>\pi</math>-cation</b> Lys179:NZ---compound 3a	3.92
<b>3b</b>	-8.8	<b>H-bond</b> Asn756:ND2---compound 3b	2.99	-10.2	<b>H-bond</b> Lys158:N---compound 3b	2.99
		<b><math>\pi</math>-<math>\pi</math></b> Phe666---compound 3b	4.03		<b><math>\pi</math>-cation</b> Lys179:NZ---compound 3b	4.34
		<b><math>\pi</math>-cation</b> Lys271:NZ---compound 3b	5.13			
<b>3c</b>	-10.4	<b>H-bond</b> Gln630:NE2---compound 3c	3.00	-10.3	<b>H-bond</b> Lys179:NZ---compound 3c	3.00
		Cys838:N---compound 3c	2.89		Thr195:OG1---compound 3c	2.96
		Tyr836:O---compound 3c	2.99		Thr195:OG1---compound 3c	2.96
		Met811:O---compound 3c	2.00		Glu198:OE1---compound 3c	1.96
		Ser629:O---compound 3c	2.24			
		<b><math>\pi</math>-cation</b> Arg818:NH2---compound 3c	5.98			
<b>4a</b>	-8.3	<b>H-bond</b> Asn756:ND2---compound 4a	3.00	-8.6	<b>H-bond</b> Glu198:OE1---compound 4a	2.60
		Arg818:NH1---compound 4a	2.84			
		<b><math>\pi</math>-<math>\pi</math></b> Phe666---compound 4a	4.38			
		<b><math>\pi</math>-cation</b> Lys271:NZ---compound 4a	5.37			

<b>4b</b>	-9.1	<b>H-bond</b> Ser854:OG---compound 4b	2.76	-10.4	<b><math>\pi</math>-cation</b> Lys179:NZ---compound 4b	4.23
<b>4c</b>	-8.9	<b>H-bond</b> Arg87:NH2---compound 4c Arg93:NH2---compound 4c Arg93:NH2---compound 4c Glu707:OE1---compound 4c <b><math>\pi</math>-<math>\pi</math></b> Arg115---compound 4c <b><math>\pi</math>-cation</b> Arg87---compound 4c	2.98 2.99 3.00 2.36 4.10 5.15	-10.0	<b>H-bond</b> Thr195:N---compound 4c Thr195:OG1---compound 4c Thr195:OG1---compound 4c	2.98 5.79 2.12
<b>5a</b>	-9.5	<b><math>\pi</math>-<math>\pi</math></b> Phe666---compound 5a <b><math>\pi</math>-cation</b> Arg662:NH2---compound 5a <b><math>\pi</math>-sigma</b> Arg662:CG---compound 5a	4.26 5.88 3.93	-9.1	<b>H-bond</b> Lys179:NZ---compound 5a	2.97
<b>5b</b>	-8.7	<b>H-bond</b> Tyr272:N---compound 5b <b><math>\pi</math>-<math>\pi</math></b> Phe666---compound 5b <b><math>\pi</math>-cation</b> ARG818:NH1---compound 5b ARG818:NH2---compound 5b	2.99 3.80 5.65 5.72	-10.5	<b><math>\pi</math>-cation</b> Lys179:NZ---compound 5b	4.18
<b>5c</b>	-9.2	<b>H-bond</b> Asn170:ND2---compound 5c Ser275:OG---compound 5c Ser275:OG---compound 5c Ser275:OG---compound 5c	2.92 2.98 3.00 2.32	-10.3	<b>H-bond</b> Lys158:N---compound 5c Thr195:N---compound 5c Thr195:OG1---compound 5c Thr195:OG1---compound 5c	2.15 2.97 2.66 2.42

		Asn756:ND2---compound 5c Asn756:ND2---compound 5c Asn756:ND2---compound 5c	2.87 3.00 2.95			
<b>6a</b>	-8.8	<b>H-bond</b> Gln643---compound 6a	2.65	-9.2	<b>H-bond</b> Gly159:N---compound 6a Gly162:N---compound 6a Thr195:N---compound 6a Thr195:OG1---compound 6a Thr195:OG1---compound 6a Thr291:OG1---compound 6a <b><math>\pi</math>-cation</b> Lys179:NZ---compound 6a Lys179:NZ---compound 6a	2.14 2.65 1.98 3.00 2.54 2.13 4.13 4.58
<b>6c</b>	-9.5	<b>H-bond</b> Asn114:ND2---compound 6c Val125:N---compound 6c Cys126:N---compound 6c Ser690:OG---compound 6c Glu78:OE1---compound 6c <b><math>\pi</math>-cation</b> Arg140:NH1---compound 6c Arg693:NH2---compound 6c	3.06 3.06 2.98 2.71 2.44 5.86 4.17	-10.4	<b>H-bond</b> Thr195:OG1---compound 6c Thr195:OG1---compound 6c Thr195:OG1---compound 6c Ala230:N---compound 6c Glu228:O---compound 6c <b><math>\pi</math>-cation</b> Lys179:NZ---compound 6c	2.72 2.80 2.85 2.70 2.60 4.27
<b>7a</b>	-9.1	<b>H-bond</b> Tyr836:OH---compound 7a Val851:N---compound 7a Asn853:N---compound 7a Ser854:N---compound 7a Ser854:OG---compound 7a Ser854:OG---compound 7a	2.75 3.08 3.03 2.78 3.03 3.06	-9.3	<b>H-bond</b> Lys179:NZ---compound 7a Gly294:N---compound 7a Glu198:OE1---compound 7a <b><math>\pi</math>-cation</b> Lys179:NZ---compound 7a	2.35 2.40 2.19 4.10

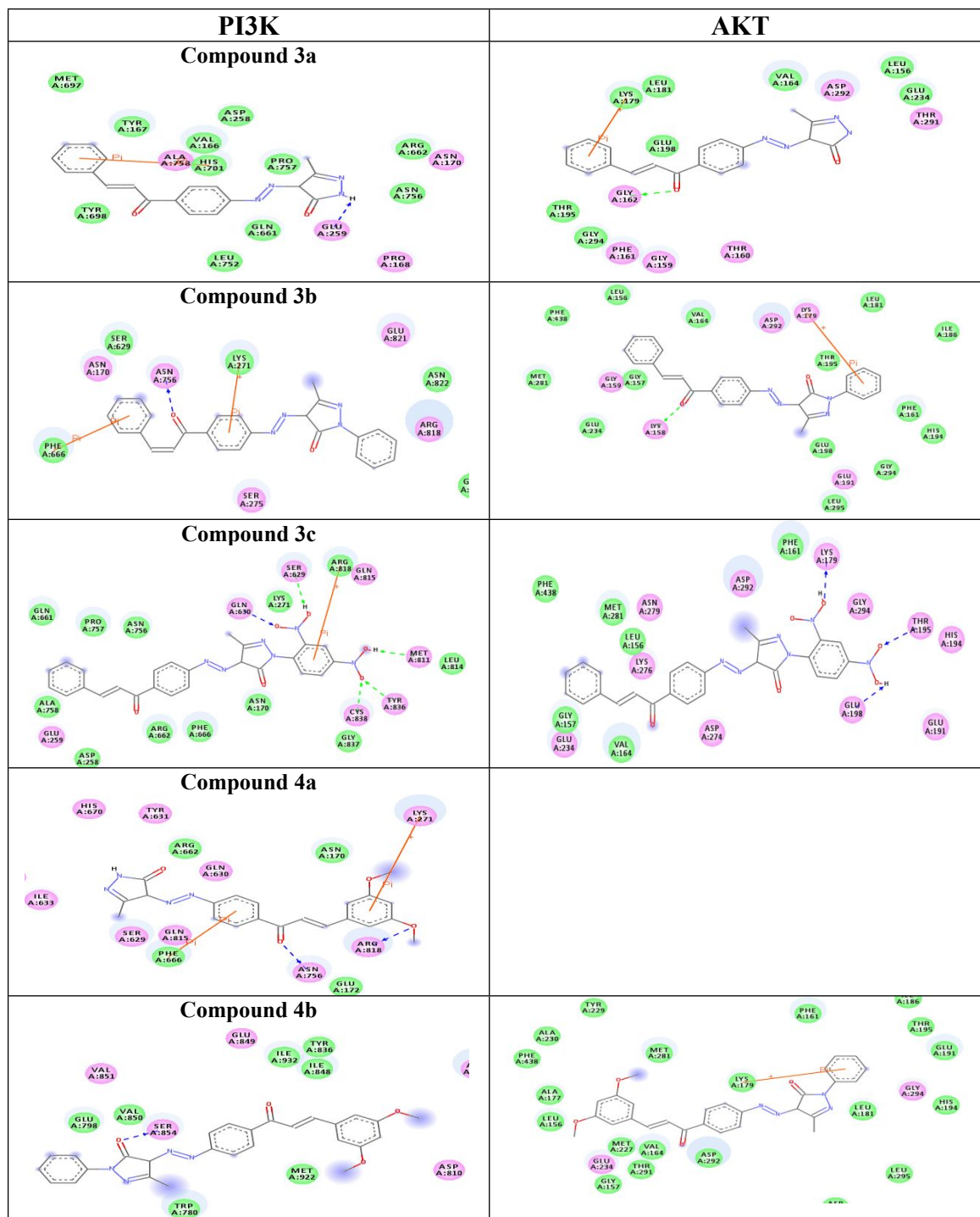


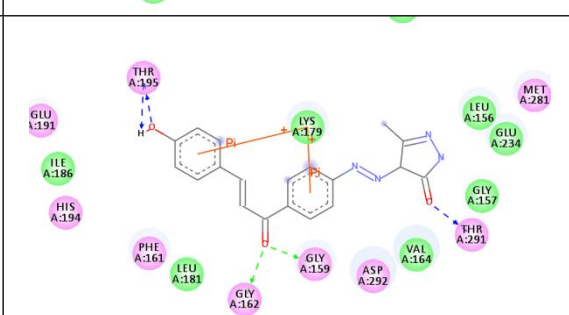
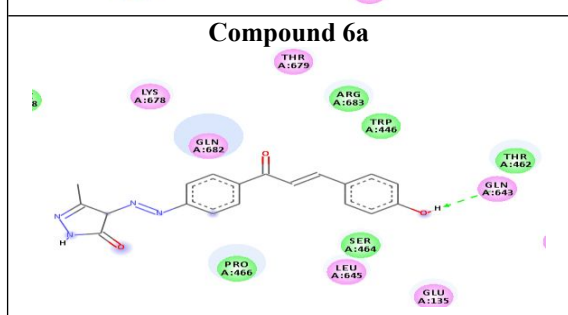
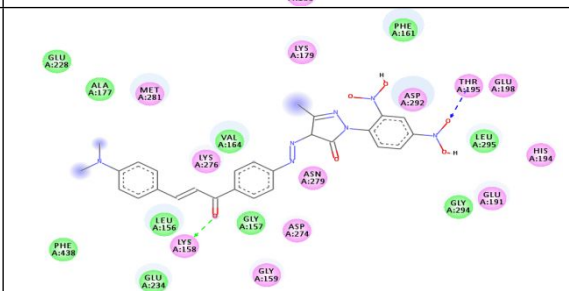
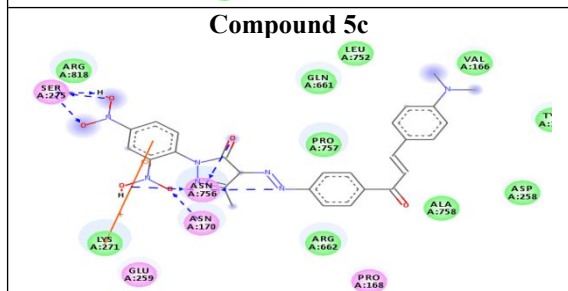
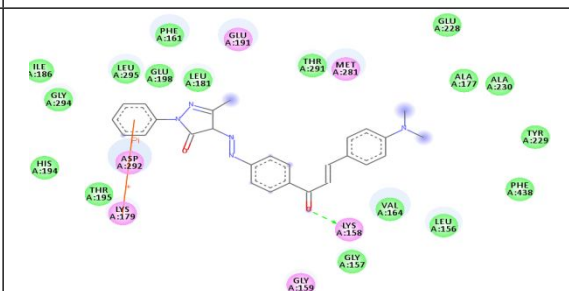
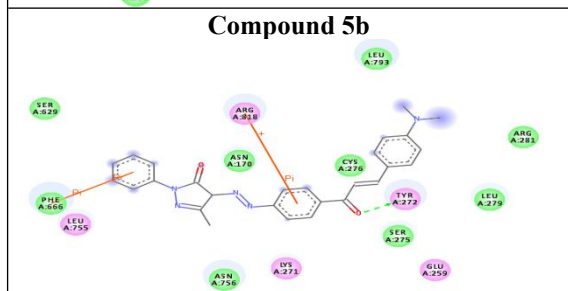
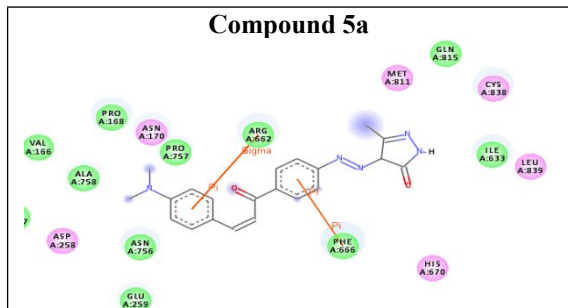
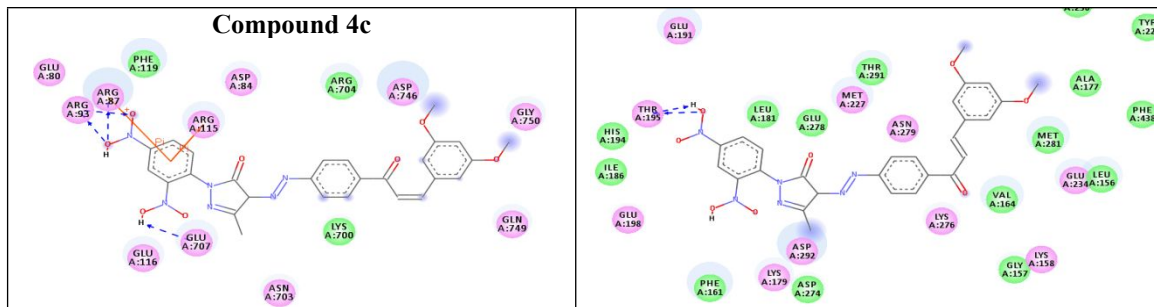
		Asp810:OD2---compound 7a	2.45			
<b>7b</b>	-9.4	<b>H-bond</b> Asn796:ND2---compound 7b Asn853:ND2---compound 7b Ser854:OG---compound 7b Ser854:OG---compound 7b Asn796:OD1---compound 7b Glu798:OE2---compound 7b <b><math>\pi</math>-cation</b> Arg852:NH2---compound 7b	3.00 2.98 3.00 2.90 2.85 2.36 5.68	-10.4	<b>H-bond</b> Lys179:NZ---compound 7b Thr291:OG1---compound 7b Asp292:OD2---compound 7b <b><math>\pi</math>-cation</b> Lys179:NZ---compound 7b	2.45 2.14 2.98 4.33
<b>7c</b>	-10.1	<b>H-bond</b> Gln661:O---compound 7c Arg662:N---compound 7c Arg818:NE---compound 7c	2.12 2.95 2.93	-10.5	<b>H-bond</b> Lys179:NZ---compound 7c Thr195:N---compound 7c Thr195:OG1---compound 7c Thr195:OG1---compound 7c Asp292:N---compound 7c Asp292:OD1---compound 7c Phe293:N---compound 7c Gly294:N---compound 7c <b><math>\pi</math>-cation</b> Lys179:NZ---compound 7c	2.33 2.47 2.63 2.47 2.79 2.88 2.98 2.97 4.15
<b>8a</b>	-9.5	<b>H-bond</b> Asn170:ND2---compound 8a Met811:O---compound 8a Cys838:O---compound 8a <b><math>\pi</math>-cation</b> Arg818:NH2---compound 8a Arg662:NH2---compound 8a <b><math>\pi</math>-sigma</b>	2.98 3.00 2.38 5.44 5.76	-9.5	<b>H-bond</b> Glu191:OE1---compound 8a	2.11

		Pro168:CD---compound 8a	3.89			
<b>8b</b>	-9.2	<b>H-bond</b> Asn853:ND2---compound 8b Ser854:OG---compound 8b Ser854:OG---compound 8b Ser854:OG---compound 8b Ser854:O---compound 8b <b><math>\pi</math>-cation</b> Arg852:NH1---compound 8b Arg852:NH2---compound 8b <b><math>\pi</math>-sigma</b> Met922:CE---compound 8b	3.02 2.99 2.86 3.07 2.98 5.88 5.36 3.50	-10.3	<b>H-bond</b> Lys179:NZ---compound 8b <b><math>\pi</math>-cation</b> Lys179:NZ---compound 8b	2.14 4.10
<b>8c</b>	-9.6	<b>H-bond</b> Cys838:N---compound 8c His670:NE2---compound 8c <b><math>\pi</math>-<math>\pi</math></b> Phe666---compound 8c <b><math>\pi</math>-cation</b> Arg818:NH1---compound 8c Arg818:NH2---compound 8c	2.89 2.81 4.08 5.43 4.99	-10.1	<b>H-bond</b> Thr195:OG1---compound 8c Leu295:N---compound 8c Thr195:OG1---compound 8c Glu198:OE1---compound 8c <b><math>\pi</math>-cation</b> Lys179:NZ---compound 8c	2.45 2.35 2.10 2.18 4.05
<b>9a</b>	-8.8	<b>H-bond</b> Met811:O---compound 9a Met811:O---compound 9a Cys838:O---compound 9a <b><math>\pi</math>-cation</b> Arg818:NH1---compound 9a Arg818:NH2---compound 9a Arg818:NH2---compound 9a <b><math>\pi</math>-sigma</b>	2.95 2.49 2.98 4.71 4.08 5.35	-9.2	<b>H-bond</b> Glu228:O---compound 9a Glu228:O---compound 9a <b><math>\pi</math>-cation</b> Lys179:NZ---compound 9a <b><math>\pi</math>-sigma</b> Thr291:CG2 ---compound 9a	1.97 2.43 3.50 3.92

		Arg662:CG---compound 9a	3.97			
<b>9b</b>	-8.7	<b>H-bond</b> Tyr836:OH---compound 9b Asp933:N---compound 9b	2.83 2.99	-9.6	<b><math>\pi</math>-cation</b> Lys179:NZ---compound 9b	3.95
		<b><math>\pi</math>-cation</b> Lys802:NZ---compound 9b	4.85			
<b>9c</b>	-9.2	<b>H-bond</b> Asn170:ND2---compound 9c Cys838:N---compound 9c His670:NE2---compound 9c	2.88 2.89 2.95	-9.5	<b>H-bond</b> Lys179:NZ---compound 9c Glu234---compound 9c	2.31 2.54
		<b><math>\pi</math>-<math>\pi</math></b> Phe666---compound 9c	4.24		<b><math>\pi</math>-cation</b> Lys179:NZ---compound 9c	3.97

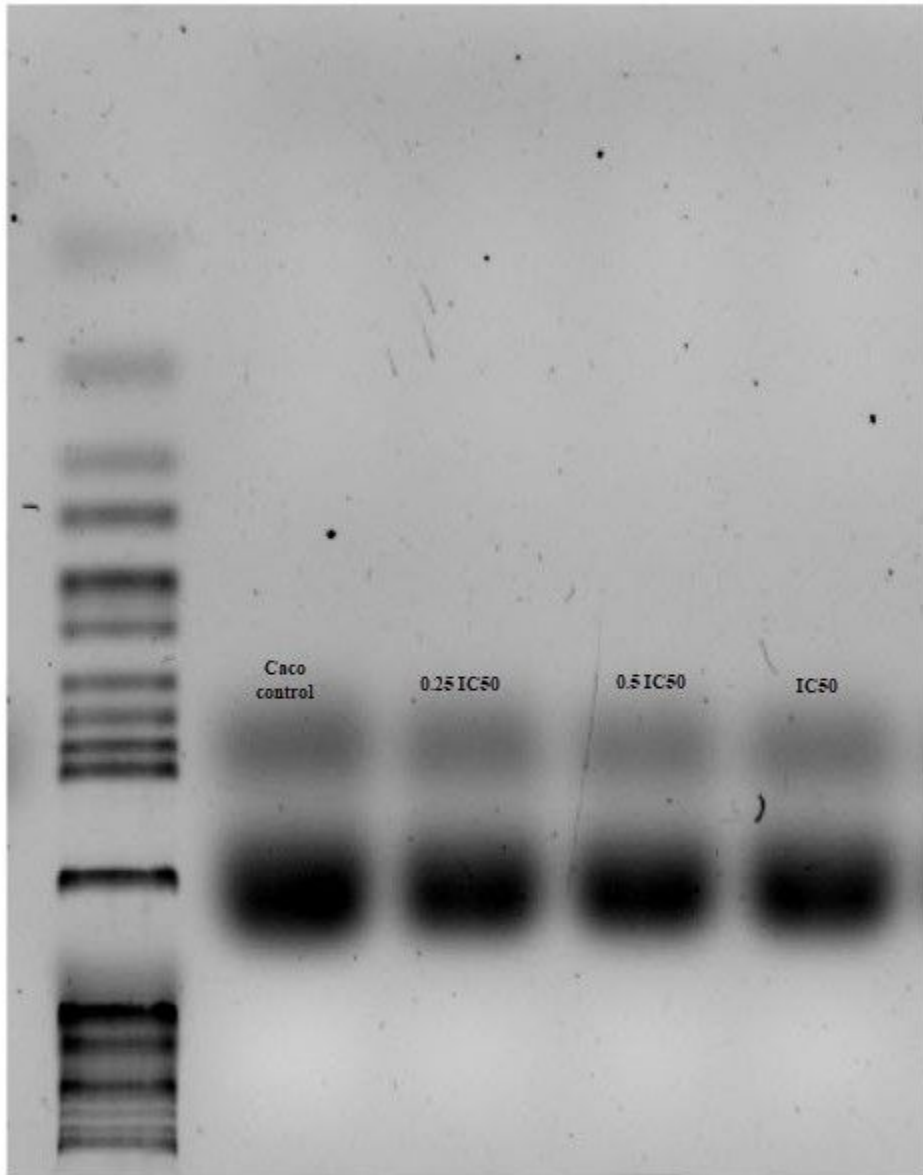
**Table S1.**





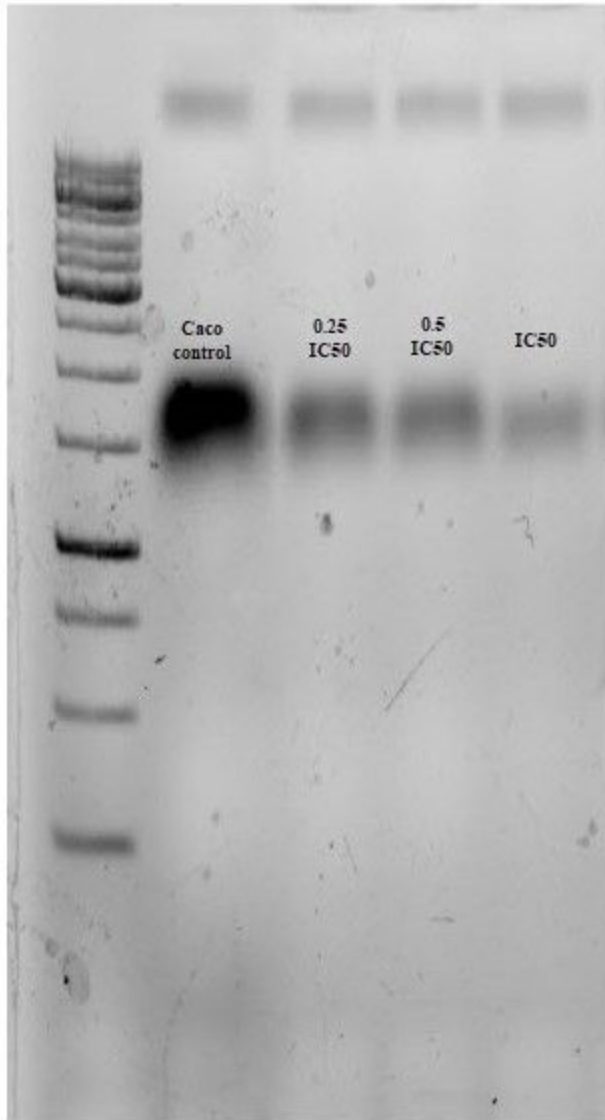




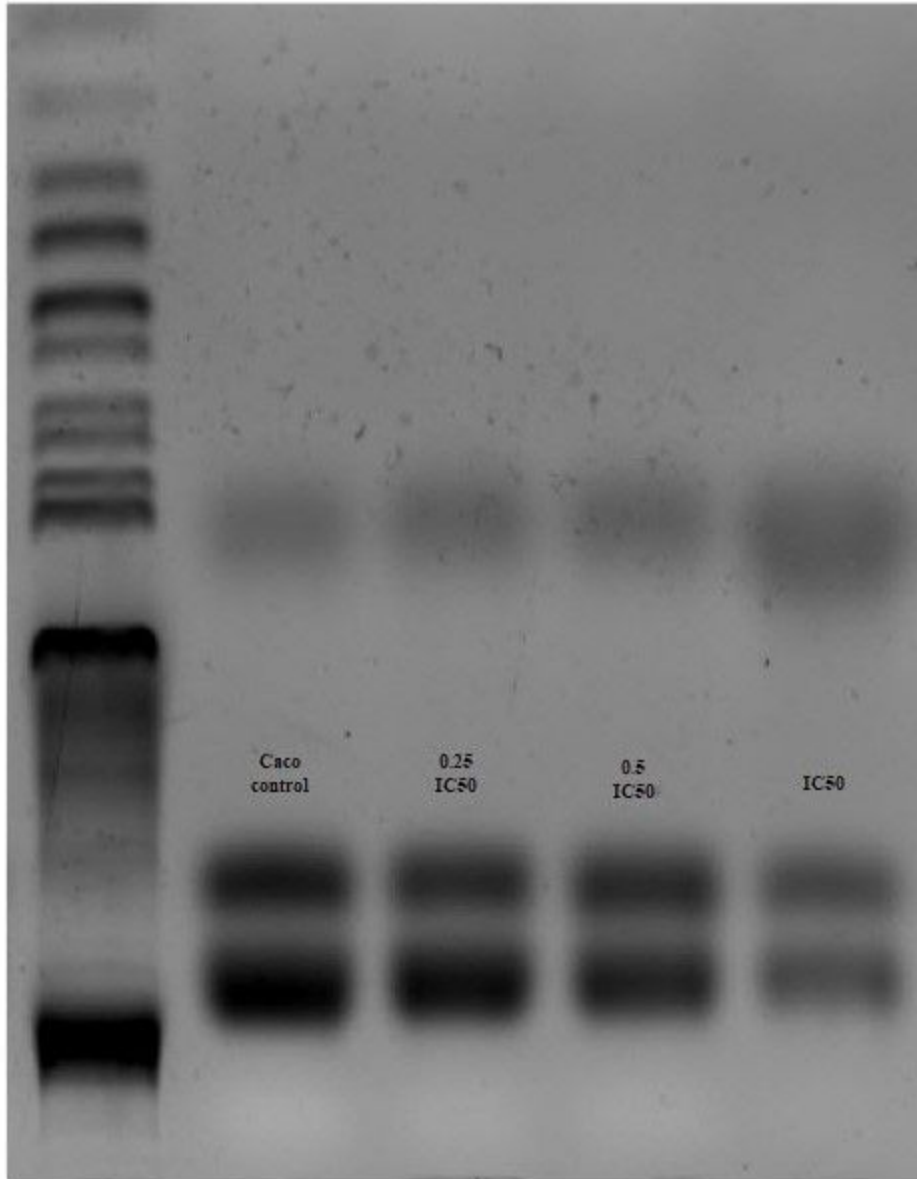


$\beta$ -actin western blot raw data

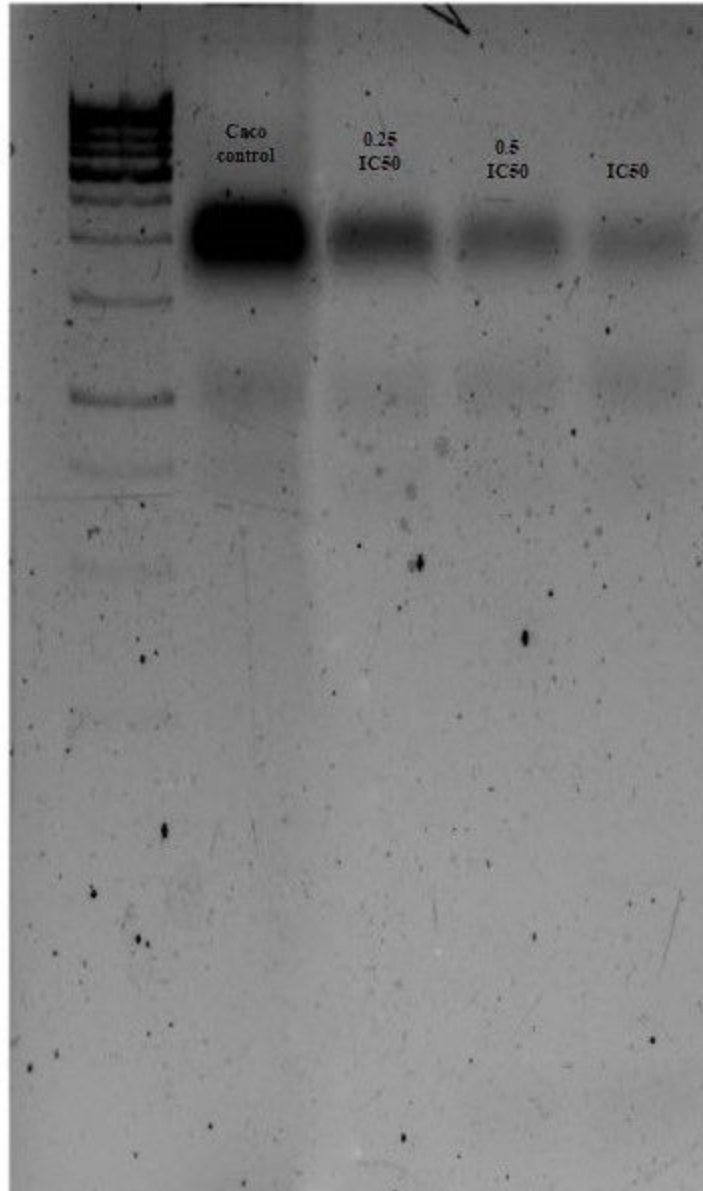




p-Akt western blot raw data



p-ERK1/2 western blot raw data



p-PI3K western blot raw data