

Supporting information

Article

Synthesis and Bioactivity of Hydrazone-hydrazones of 1-Adamantyl-carbonyl Moiety

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Scheme 1. Synthesis of hydrazide hydrazones **4a-i** and **5a-k**

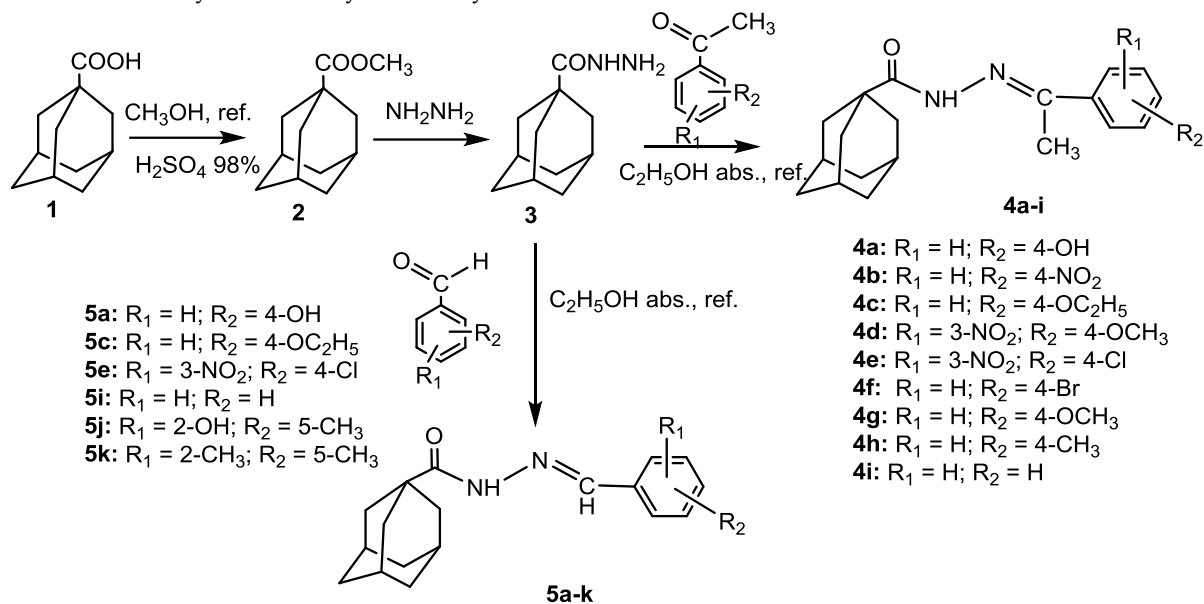


Table 1. Crystal solvent (Cryst. Solv.), melting point (m.p), yield (%), molecular formulae, molecular weight (Mol. Wt.) and Rf of hydrazide-hydrazones **4a-i** and **5a-k**.

Comp. No.	R1	R2	Cryst. Solv.	m.p (°C)	Yield (%)	Molecular Formular (Mol. Wt.)	TLC* (Rf)
4a	H	4-OH	EtOH	252.5-254.1	30.6	C ₁₉ H ₂₄ N ₂ O ₂ (312.41)	0.36
4b	H	4-NO ₂	EtOH	226.0-227.6	60.5	C ₁₉ H ₂₃ N ₃ O ₃ (341.41)	0.58
4c	H	4-OC ₂ H ₅	EtOH	159.5-160.6	32.2	C ₂₁ H ₂₈ N ₂ O ₂ (340.47)	0.57
4d	3-NO ₂	4-OCH ₃	EtOH	182.0-184.1	33.0	C ₂₀ H ₂₅ N ₃ O ₄ (371.44)	0.44
4e	3-NO ₂	4-Cl	EtOH	188.2-189.3	26.2	C ₁₉ H ₂₂ ClN ₃ O ₃ (375.85)	0.56
4f	H	4-Br	EtOH	190.7-191.0	29.0	C ₁₉ H ₂₃ BrN ₂ O (375.31)	0.62
4g	H	4-OCH ₃	EtOH	171.6-173.0	30.0	C ₂₀ H ₂₆ N ₂ O ₂ (326.44)	0.52
4h	H	4-CH ₃	EtOH	179.5-180.4	37.3	C ₂₀ H ₂₆ N ₂ O (310.44)	0.66
4i	H	H	EtOH	174.4-175.2	54.5	C ₁₉ H ₂₄ N ₂ O (296.41)	0.59
5a	H	4-OH	EtOH	289.6 -290.5	44.0	C ₁₈ H ₂₂ N ₂ O ₂ (298.39)	0.33
5c	H	4-OC ₂ H ₅	EtOH	235.2-236.4	15.1	C ₂₀ H ₂₆ N ₂ O ₂ (326.44)	0.59
5e	3-NO ₂	4-Cl	EtOH	247.8-248.5	50.6	C ₁₈ H ₂₀ ClN ₃ O ₃ (361.83)	0.55
5i	H	H	EtOH	186.9-187.2	60.5	C ₁₈ H ₂₂ N ₂ O (282.39)	0.54
5j	2-OH	5-CH ₃	EtOH	247.6-248.8	60.4	C ₁₉ H ₂₄ N ₂ O ₂ (312.41)	0.57
5k	2-CH ₃	5-CH ₃	EtOH	283.5-284.0	35.5	C ₂₀ H ₂₆ N ₂ O (310.44)	0.45

Table 2. MIC of synthesized hydrazide-hydrazole **4a-i** and **5a-k**

Comp. No.	MIC of synthesized compounds (μM)						
	Gram (+)			Gram (-)			Fungus
	EF	SA	BC	EC	PA	SE	CA
4a	12.5	12.5	12.5	-	-	-	12.5
4b	25	25	25	-	-	-	25
4c	25	25	25	-	-	-	25
4d	12.5	50	100	-	-	-	6.25
4e	25	50	50	-	-	-	25
4f	50	50	50	-	-	-	12.5
4g	25	25	100	-	-	-	25
4h	25	25	50	-	-	-	12.5
4i	25	50	50	-	-	-	25
5a	12.5	25	25	-	-	-	12.5
5c	12.5	50	100	-	-	-	12.5
5e	25	25	25	-	-	-	25
5i	50	50	50	-	-	-	50
5j	50	50	50	-	-	-	25
5k	25	25	25	-	-	-	25
STM	256 $\mu\text{g/mL}$	256 $\mu\text{g/mL}$	128 $\mu\text{g/mL}$	32 $\mu\text{g/mL}$	256 $\mu\text{g/mL}$	128 $\mu\text{g/mL}$	NT
CHM	NT	NT	NT	NT	NT	NT	32 $\mu\text{g/mL}$

EF: *Enterococcus faecalis* (ATCC13124); SA: *Staphylococcus aureus* (ATCC25923); BC: *Bacillus cereus* (ATCC 13245); EC: *Escherichia coli* (ATCC25922); PA: *Pseudomonas aeruginosa* (ATCC27853); SE: *Salmonella enterica* (ATCC12228); CA: *Candida albicans* (ATCC10231); STM: streptomycine; CHM: Cycloheximide; NT: not tested; - : inactive

Table 3. IC₅₀ of synthesized hydrazide-hydrazole **4a-i** and **5a-k**

Comp. No.	IC50 of synthesized compounds (µM)						Fungus
	Gram (+)			Gram (-)			
	EF	SA	BC	EC	PA	SE	CA
4a	6.35	6.77	6.12	-	-	-	6.37
4b	11.56	11.45	12.56	-	-	-	12.78
4c	13.24	12.67	12.77	-	-	-	13.11
4d	6.88	25.45	52.11	-	-	-	3.56
4e	13.55	25.11	25.99	-	-	-	13.57
4f	24.79	13.44	25.33	-	-	-	6.77
4g	12.56	12.55	56.7	-	-	-	11.55
4h	13.22	13.45	23.88	-	-	-	6.45
4i	12.56	25.66	25.65	-	-	-	12.33
5a	6.73	12.33	12.37	-	-	-	6.25
5c	6.77	26.55	26.78	-	-	-	6.66
5e	13.25	12.67	12.33	-	-	-	13.22
5i	25.66	26.55	26.56	-	-	-	25.33
5j	24.58	24.56	24.33	-	-	-	11.45
5k	12.35	12.45	12.33	-	-	-	13.46

EF: *Enterococcus faecalis* (ATCC13124); SA: *Staphylococcus aureus* (ATCC25923); BC: *Bacillus cereus* (ATCC 13245); EC: *Escherichia coli* (ATCC25922); PA: *Pseudomonas aeruginosa* (ATCC27853); SE: *Salmonella enterica* (ATCC12228); CA: *Candida albicans* (ATCC10231); - : inactive.

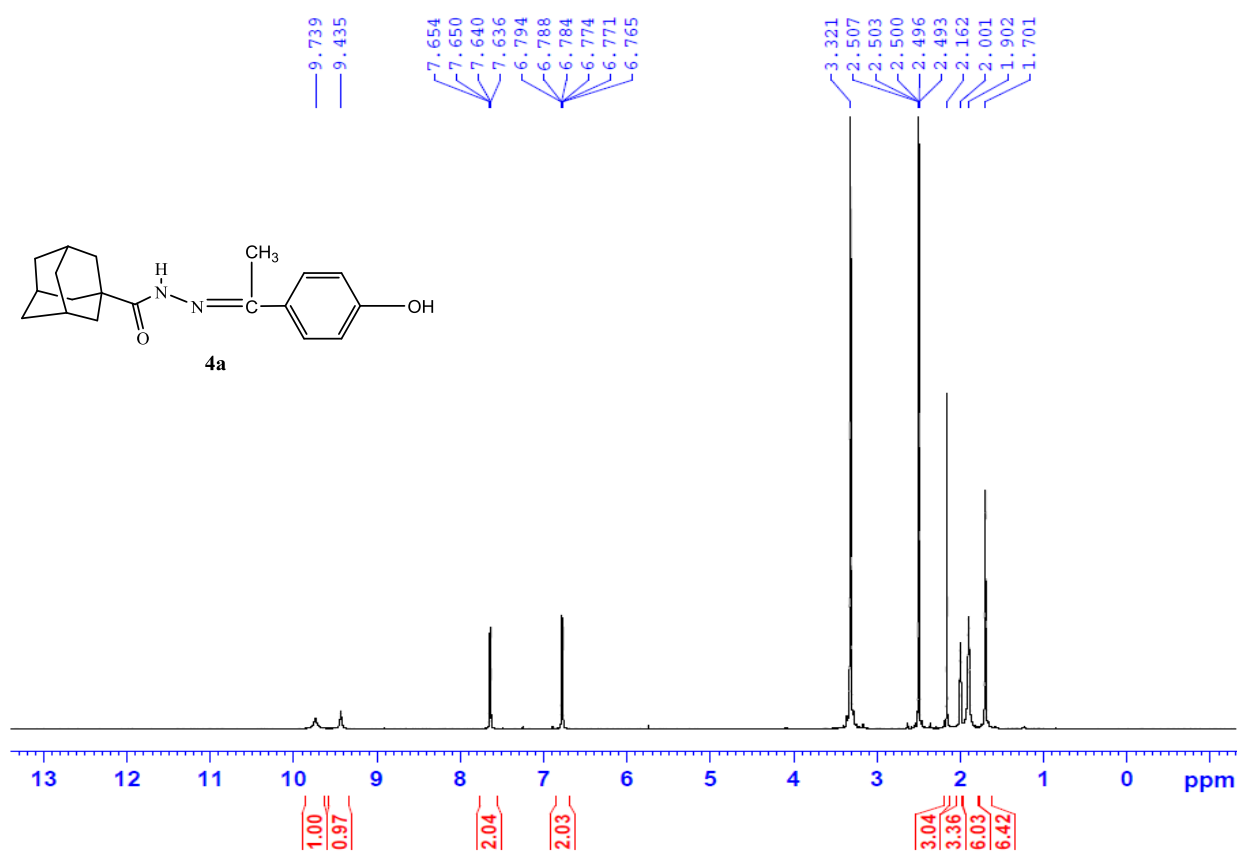
Table 4. The effect of newly synthesized hydrazide-hydrazole **4a-i** and **5a-k** on the viability of HeP3B, HeLa, A549 and MCF-7 cell after 48 h of incubation

Comp. No.	Conc.	Hep3B	HeLa	A549	MCF-7
4a	30µM	63.89 ± 0.69	73.09 ± 2.31	67.78 ± 0.26	63.28 ± 1.41
	100 µM	56.53 ± 1.32	66.87 ± 1.10	51.63 ± 0.81	58.60 ± 0.32
4b	30µM	66.83 ± 1.15	82.84 ± 1.37	66.89 ± 0.94	64.32 ± 2.92
	100 µM	56.49 ± 2.17	77.20 ± 0.90	62.26 ± 0.15	52.64 ± 2.02
4c	30µM	80.62 ± 1.25	93.64 ± 0.88	77.76 ± 1.51	79.36 ± 1.40
	100 µM	72.74 ± 2.00	90.51 ± 1.28	70.20 ± 0.13	67.78 ± 0.95
4d	30µM	96.80 ± 0.26	> 100	65.33 ± 1.28	90.20 ± 0.25
	100 µM	84.59 ± 2.39	86.34 ± 1.35	62.01 ± 2.37	78.82 ± 2.22
4e	30µM	94.59 ± 2.20	80.07 ± 1.87	64.43 ± 0.49	60.94 ± 1.39
	100 µM	55.91 ± 1.70	44.37 ± 1.39	38.51 ± 1.59	38.69 ± 1.20
4f	30µM	>100	88.26 ± 1.74	76.22 ± 0.98	94.68 ± 1.33
	100 µM	97.95 ± 2.43	83.18 ± 0.20	73.68 ± 1.03	91.27 ± 2.26
4g	30µM	91.63 ± 2.63	96.61 ± 1.98	87.40 ± 0.95	83.11 ± 2.86
	100 µM	77.00 ± 1.84	79.46 ± 1.28	70.61 ± 1.66	71.75 ± 1.71
4h	30µM	98.29 ± 2.46	> 100	78.42 ± 0.83	91.59 ± 2.29
	100 µM	75.83 ± 2.76	99.77 ± 1.89	68.99 ± 2.36	70.66 ± 2.57
4i	30µM	81.96 ± 1.67	88.70 ± 1.79	68.43 ± 1.72	59.77 ± 2.41
	100 µM	80.7 ± 2.17	87.75 ± 0.29	67.73 ± 1.89	57.24 ± 0.75
5a	30µM	87.03 ± 1.28	87.53 ± 0.21	69.08 ± 2.56	86.14 ± 0.49
	100 µM	68.89 ± 2.18	68.26 ± 2.02	50.78 ± 1.86	64.33 ± 1.76
5c	30µM	88.96 ± 0.91	89.07 ± 1.21	90.47 ± 2.23	70.30 ± 1.23
	100 µM	78.97 ± 1.82	85.41 ± 1.34	81.32 ± 1.20	65.62 ± 0.64
5e	30µM	57.77 ± 1.59	76.75 ± 1.07	36.42 ± 0.94	52.56 ± 0.75
	100 µM	37.78 ± 2.44	40.42 ± 0.38	19.62 ± 1.74	34.13 ± 2.22
5i	30µM	83.16 ± 1.19	89.12 ± 2.43	79.49 ± 0.94	71.53 ± 1.64
	100 µM	74.90 ± 1.34	84.28 ± 2.12	55.22 ± 1.63	65.31 ± 1.66
5j	30µM	92.80 ± 2.24	68.96 ± 2.38	78.71 ± 1.75	86.48 ± 2.08
	100 µM	85.71 ± 2.28	57.90 ± 1.35	59.18 ± 2.01	79.86 ± 2.13
5k	30µM	98.51 ± 0.38	82.96 ± 0.59	62.55 ± 0.59	91.80 ± 0.35
	100 µM	83.34 ± 1.65	74.27 ± 1.67	52.39 ± 1.54	77.66 ± 1.54
CPT*	0.1µg/mL	69.56 ± 1.27	57.06 ± 1.35	67.68 ± 1.88	56.68 ± 0.68
	5 µg/mL	37.65 ± 1.21	18.61 ± 0.56	26.74 ± 2.16	28.89 ± 1.07

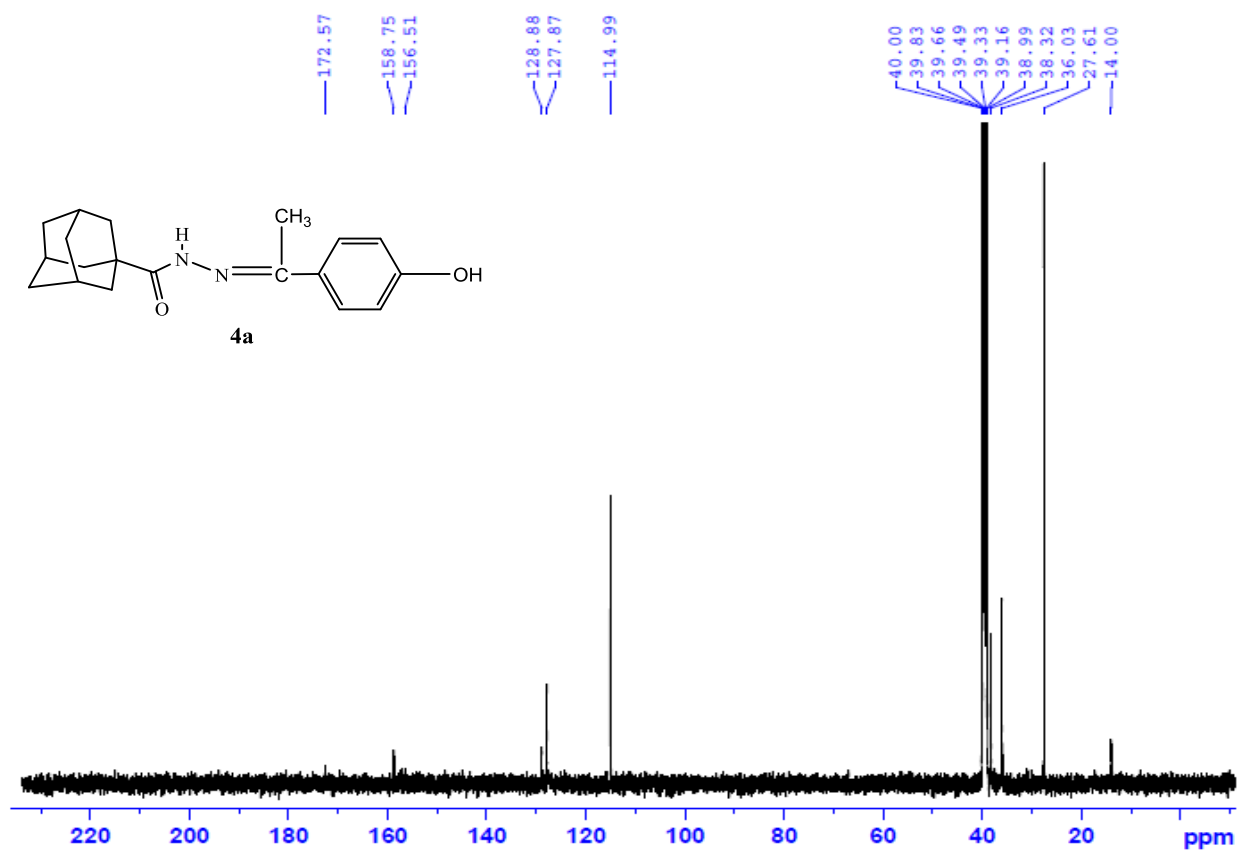
*Camptothecine.

Data is presented as percentage of the cell viability ± SD.

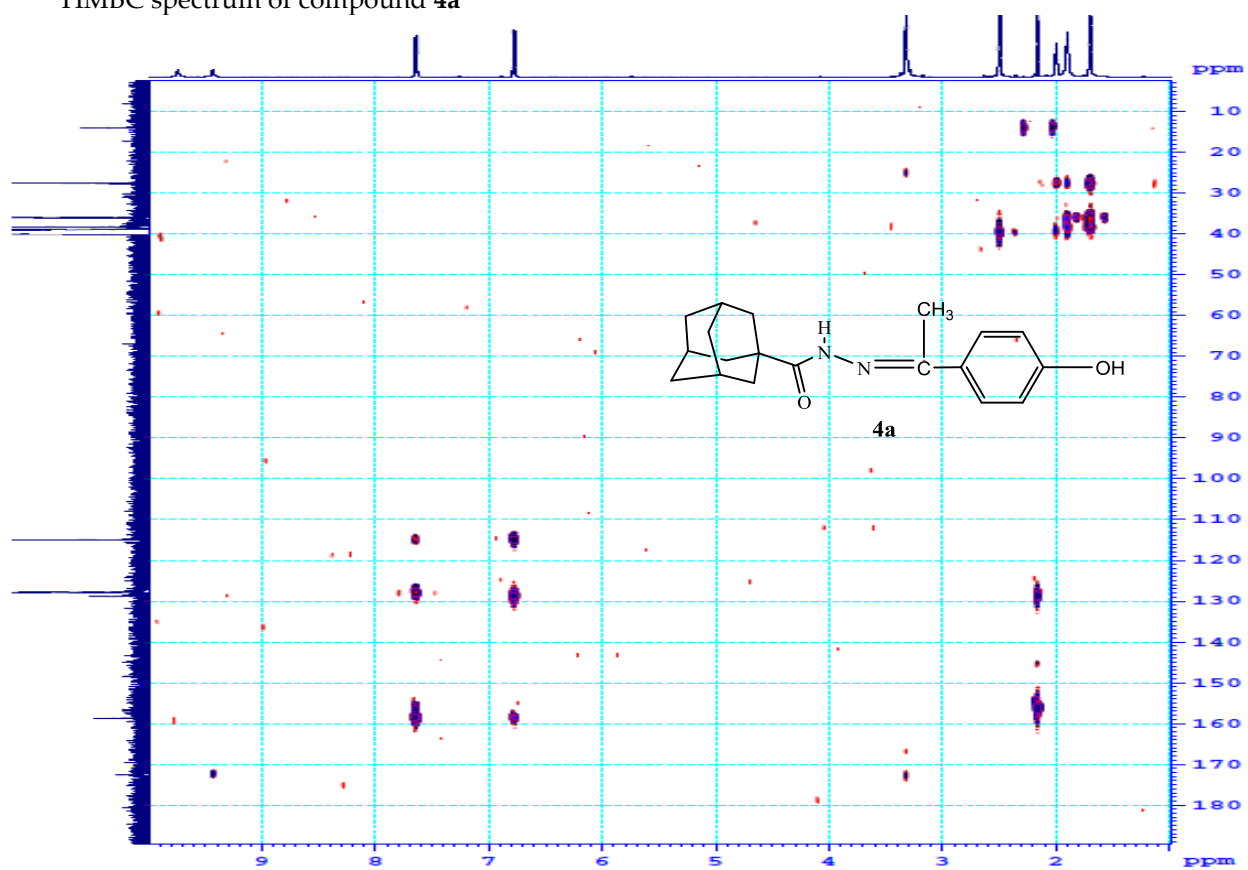
¹H-NMR spectrum of compound 4a



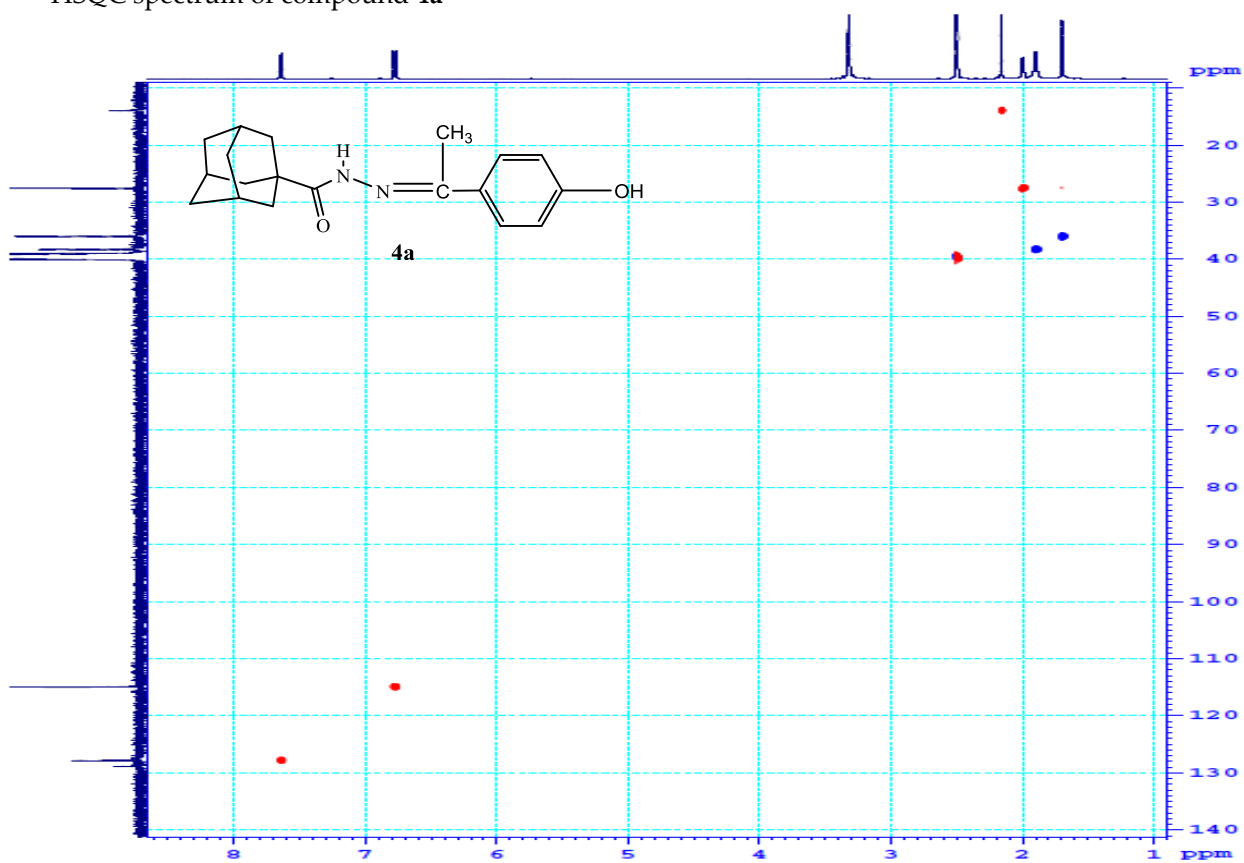
¹³C-NMR spectrum of compound 4a



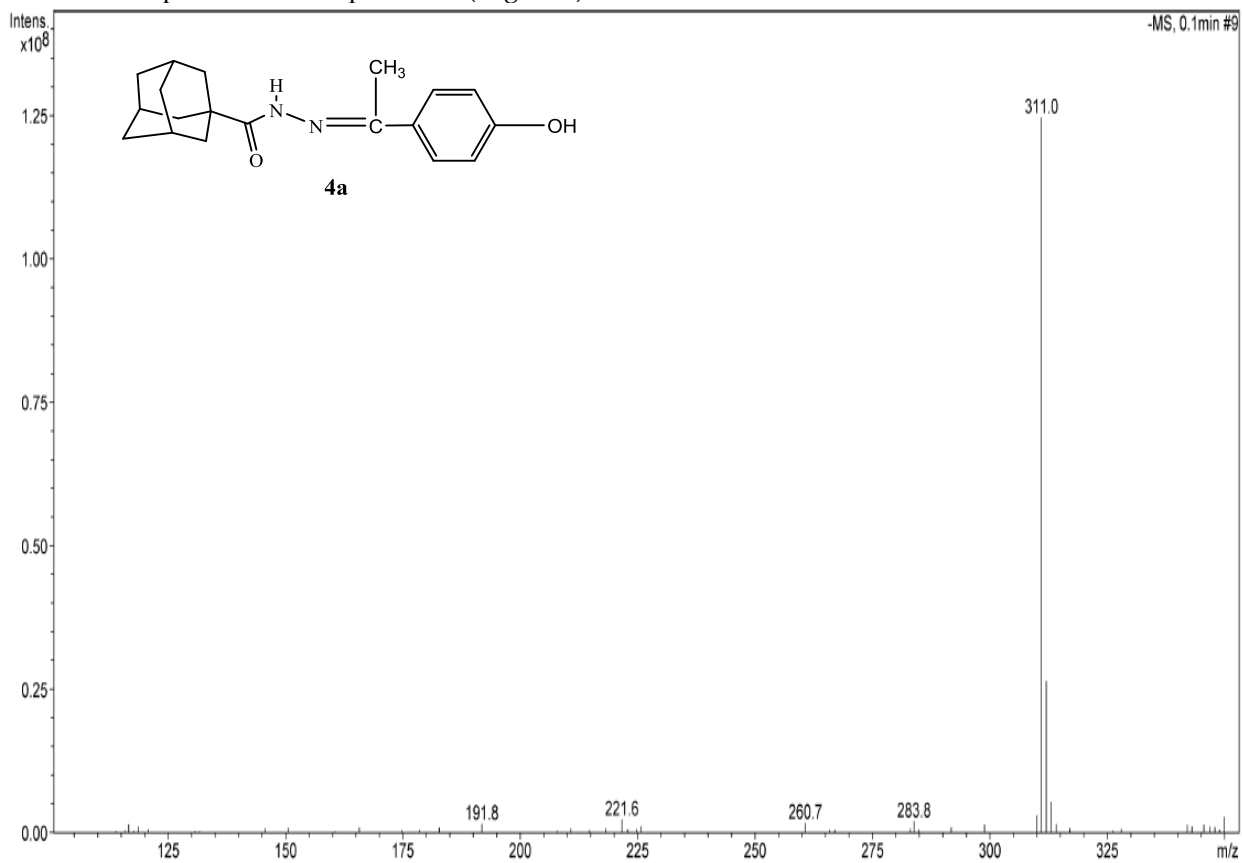
HMBC spectrum of compound 4a



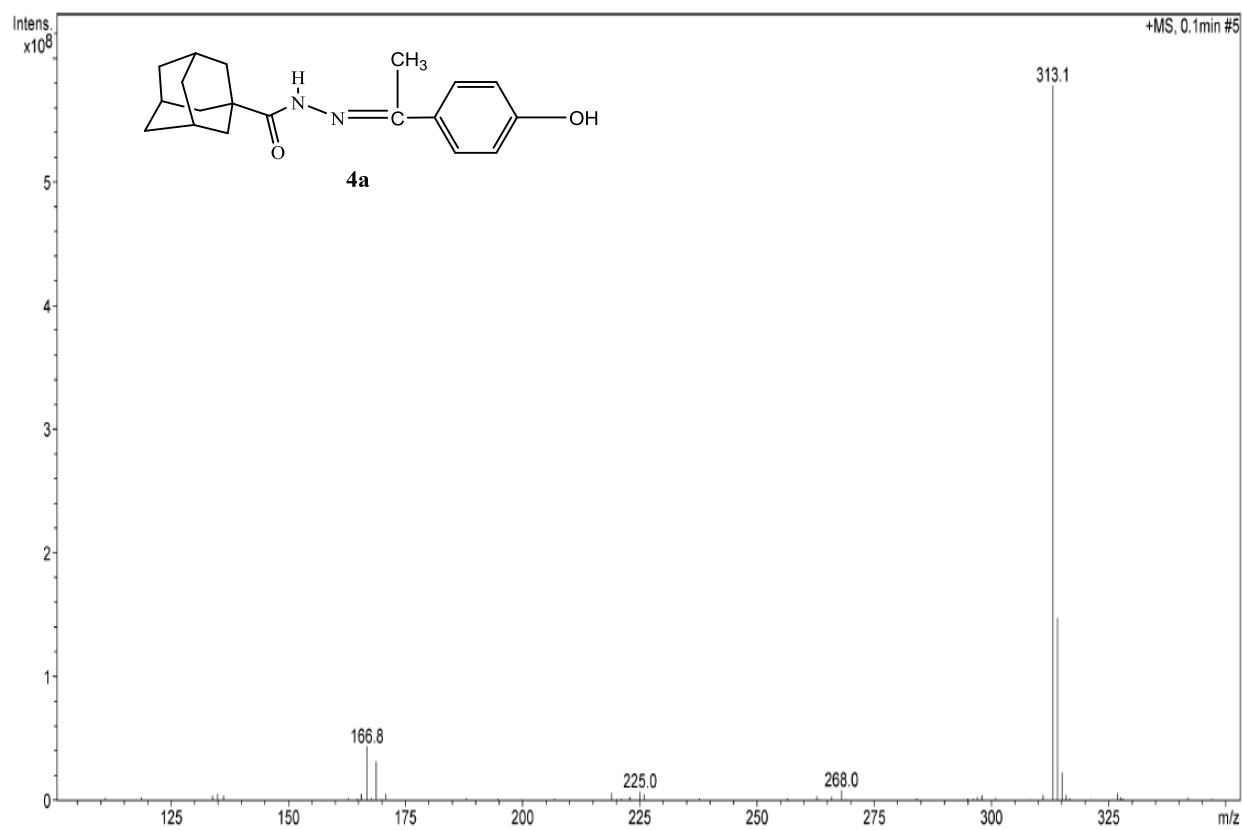
HSQC spectrum of compound 4a



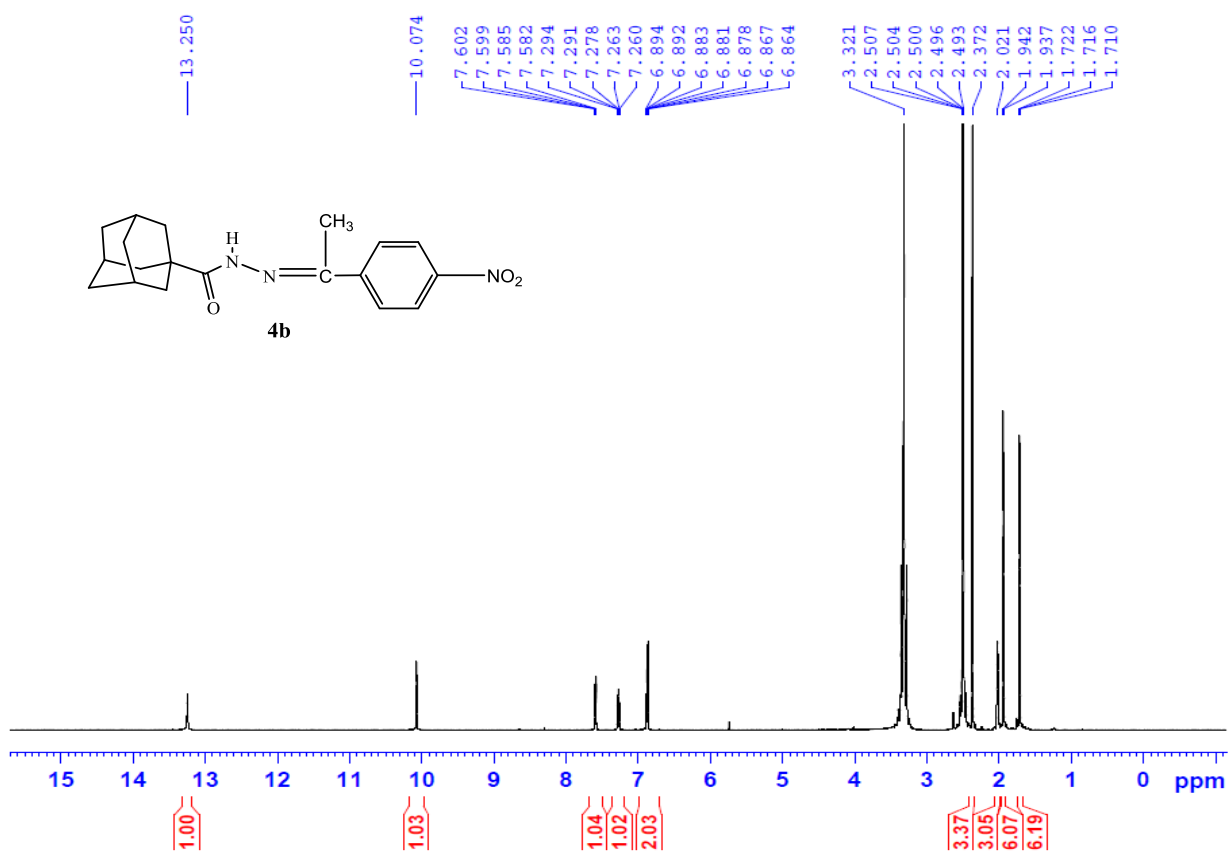
ESI-MS spectrum of compound **4a** (negative)



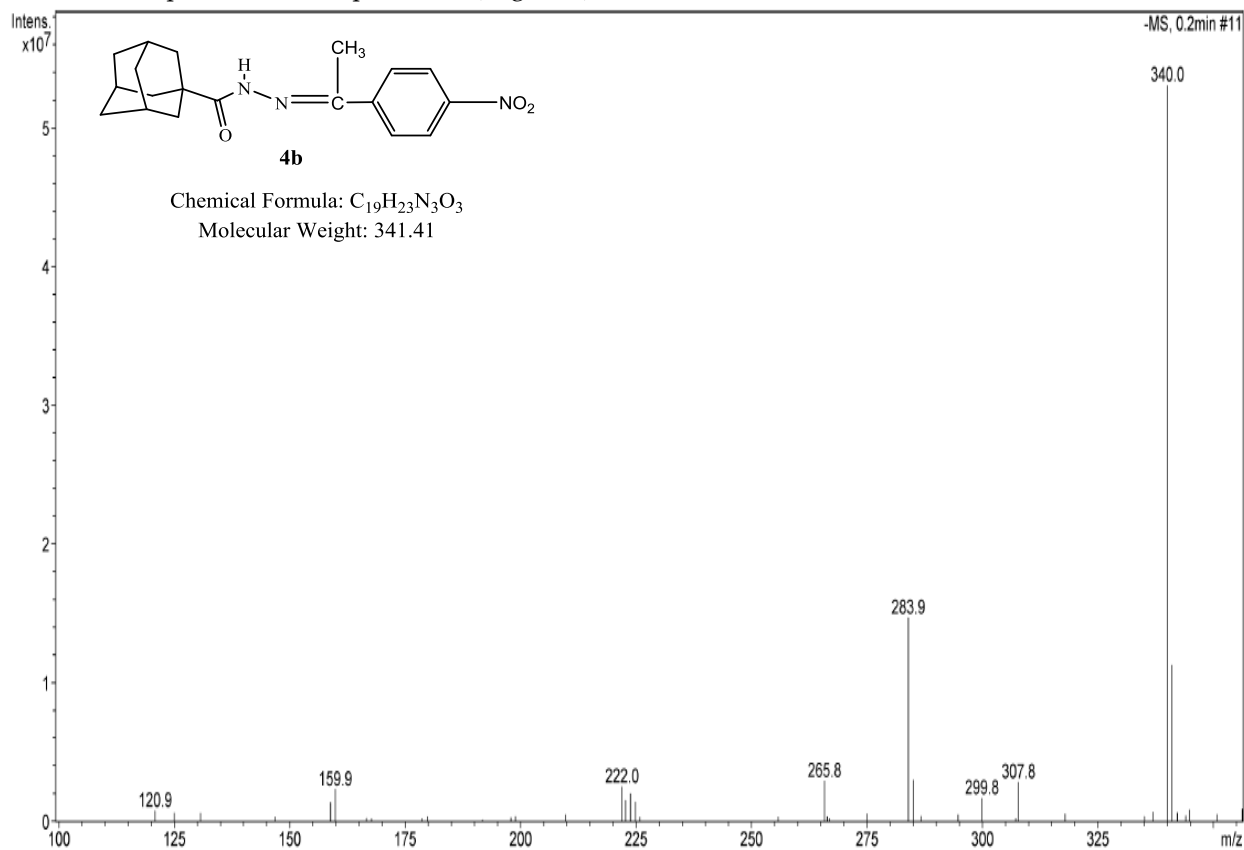
ESI-MS spectrum of compound **4a** (positive)



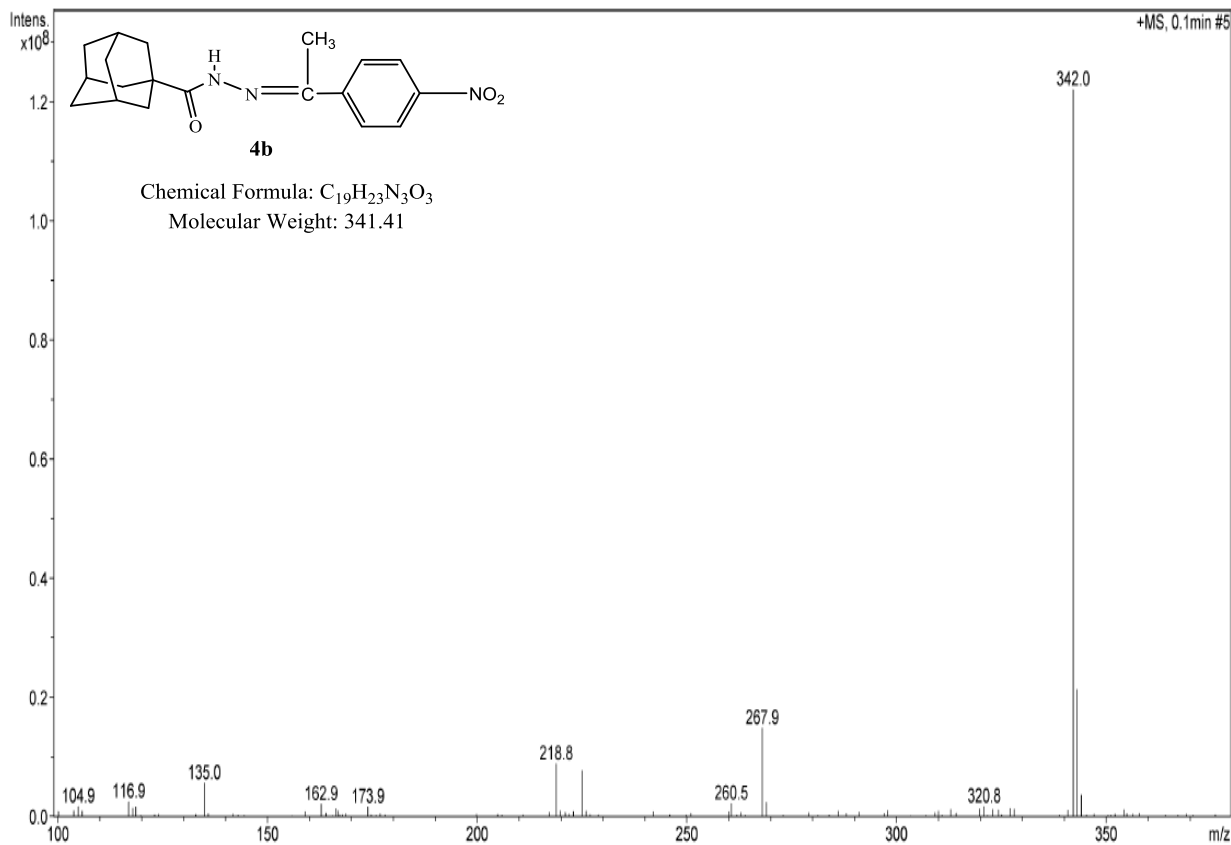
¹H-NMR spectrum of compound **4b**



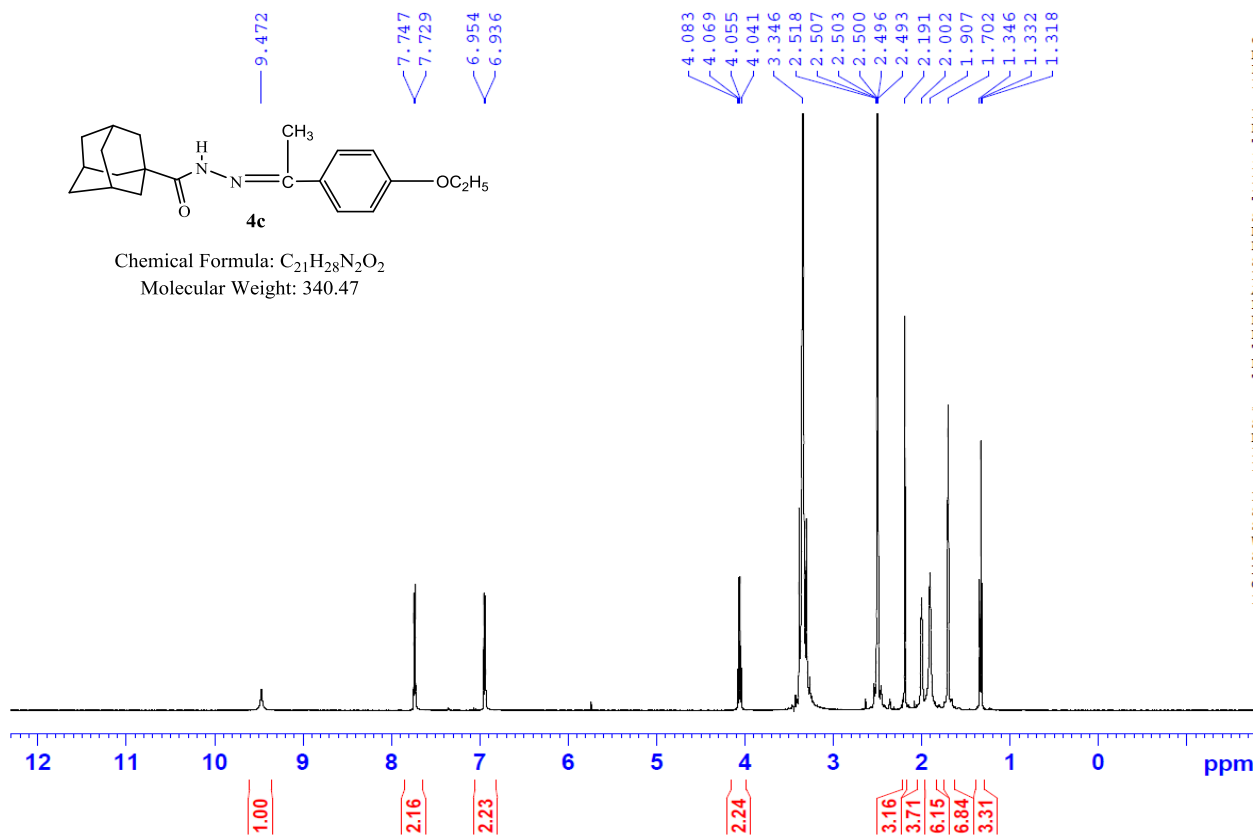
ESI-MS spectrum of compound **4b** (negative)



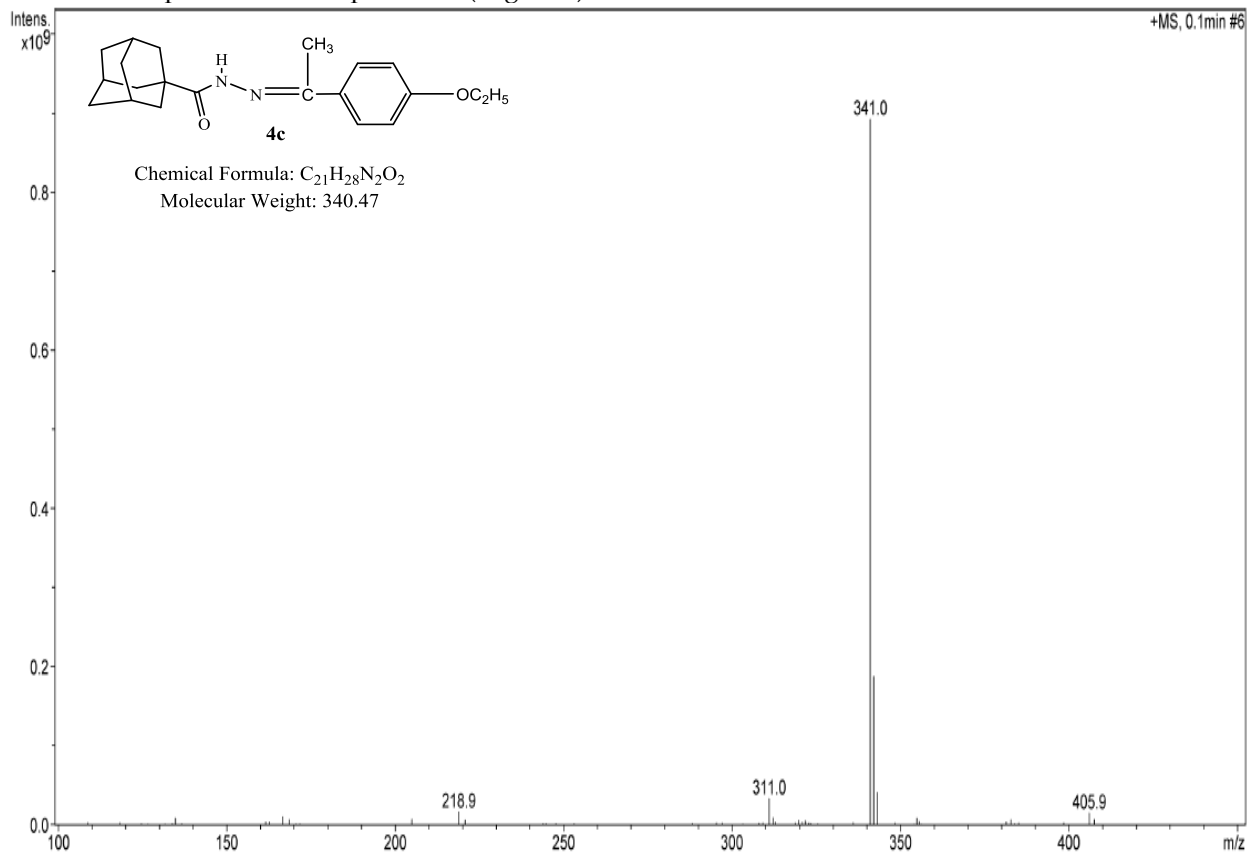
ESI-MS spectrum of compound **4b** (positive)



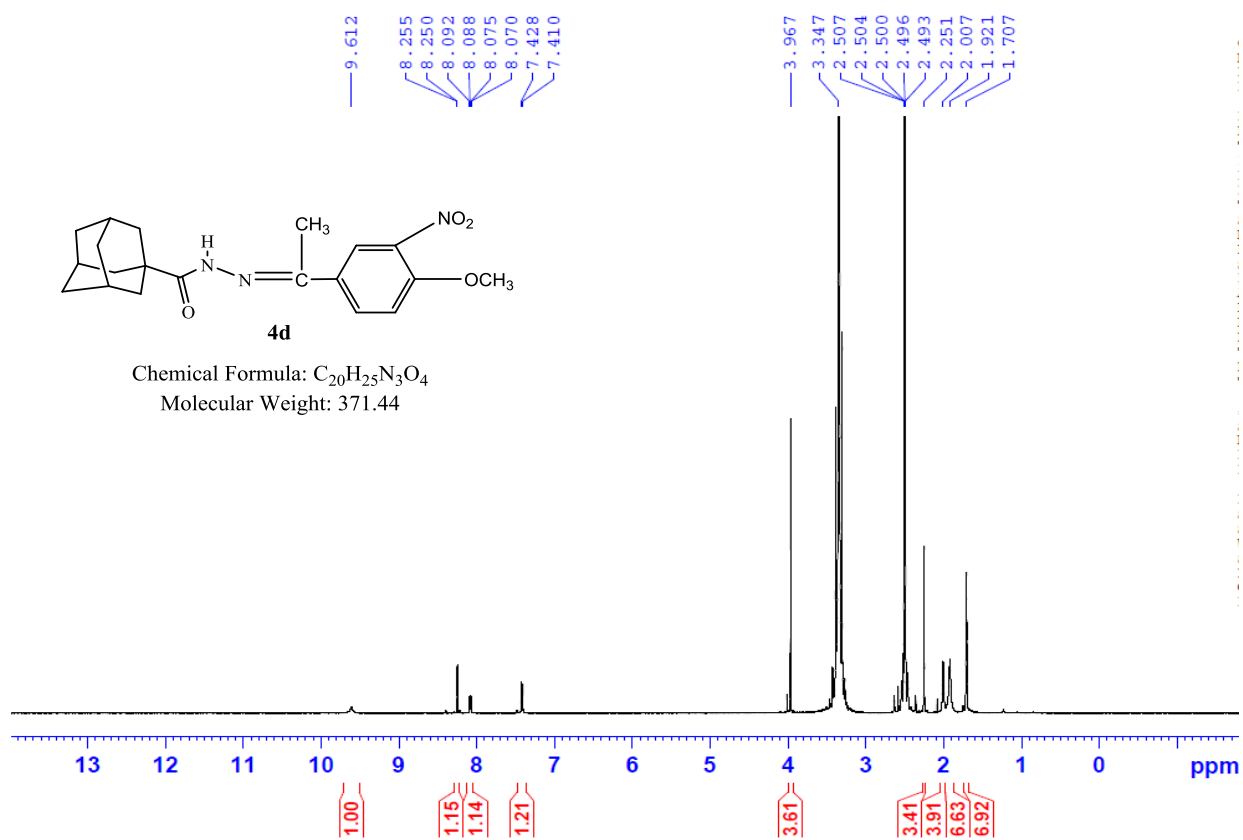
1H -NMR spectrum of compound **4c**



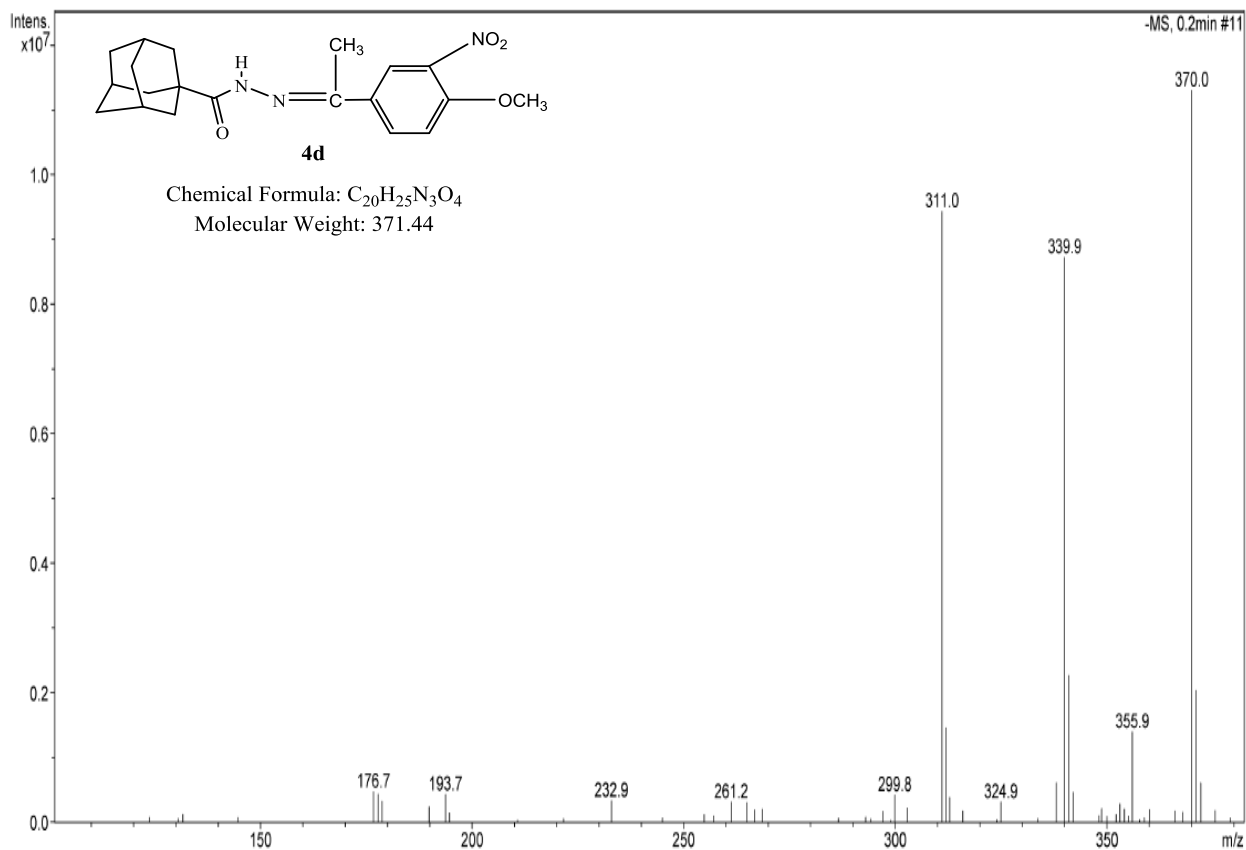
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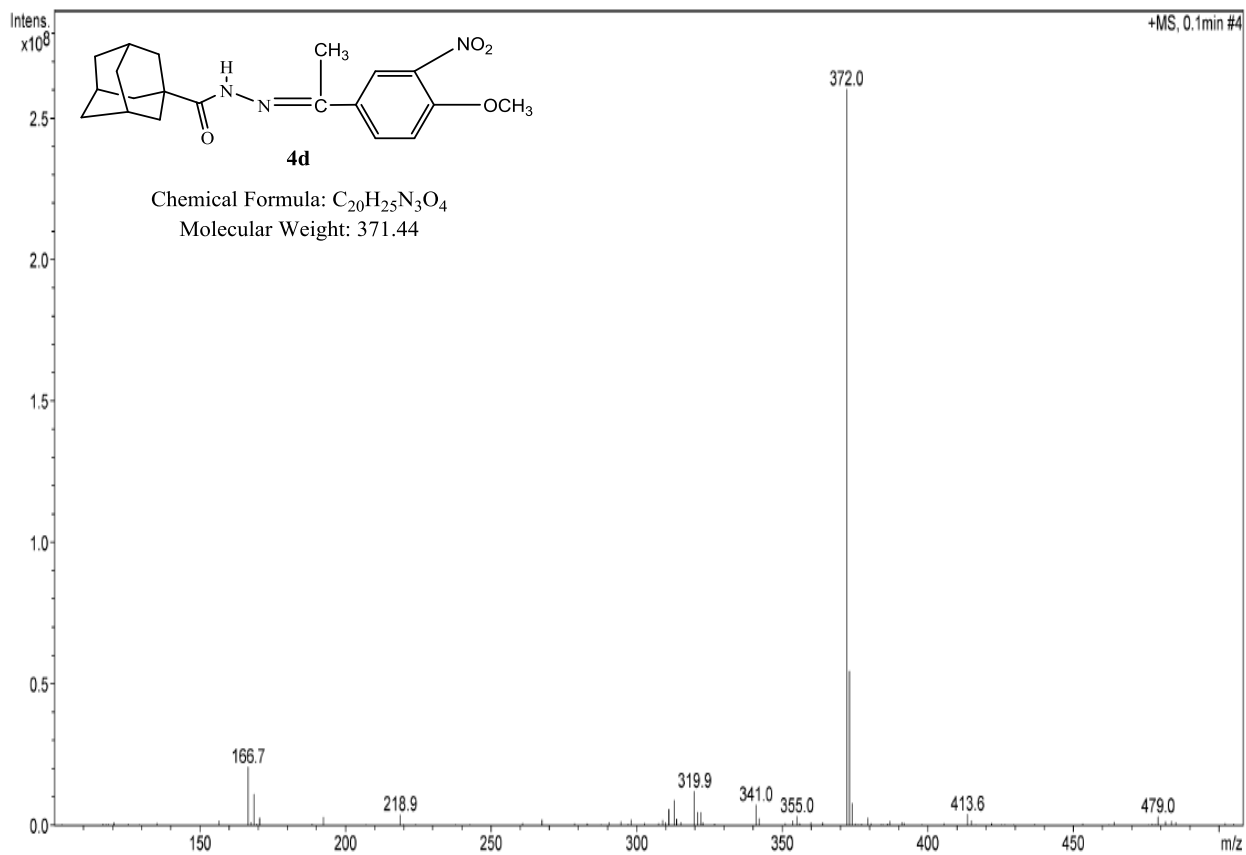
1H -NMR spectrum of compound **4d**



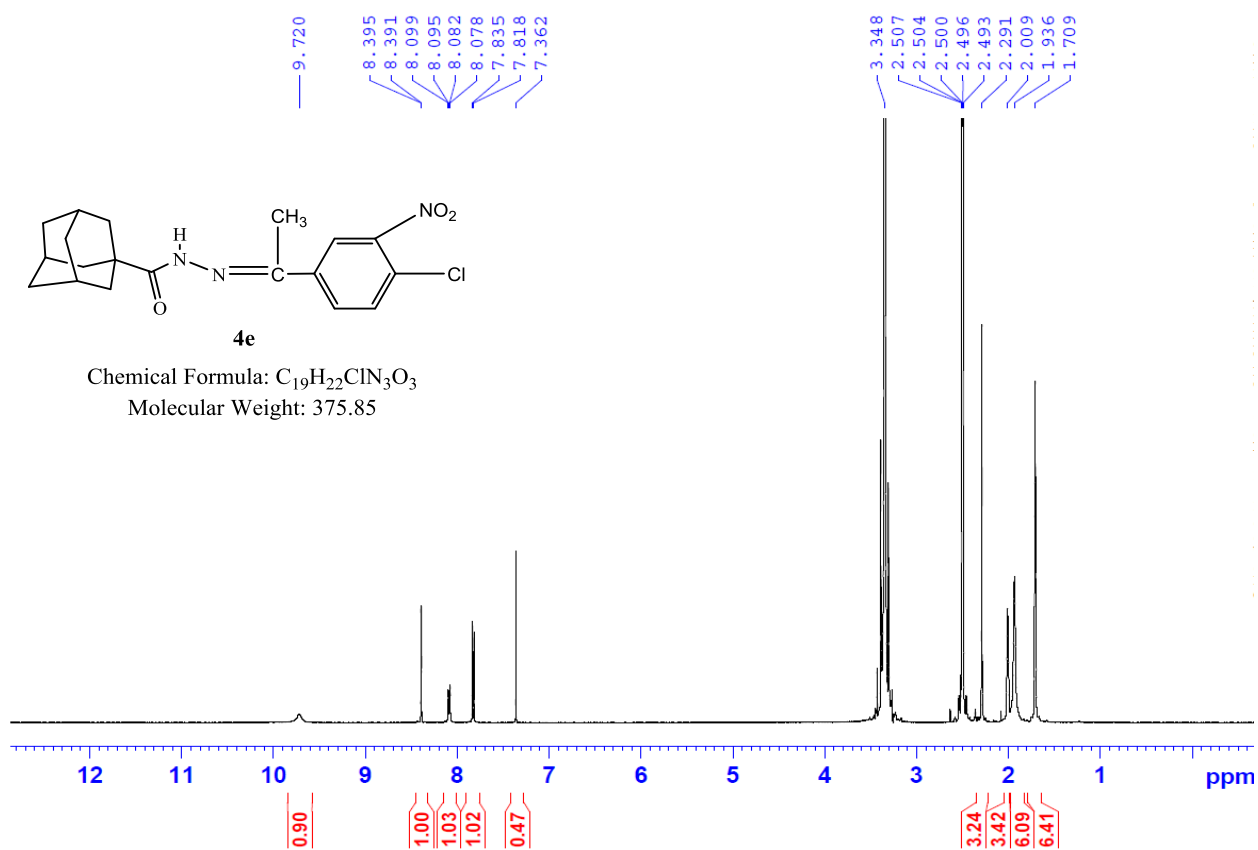
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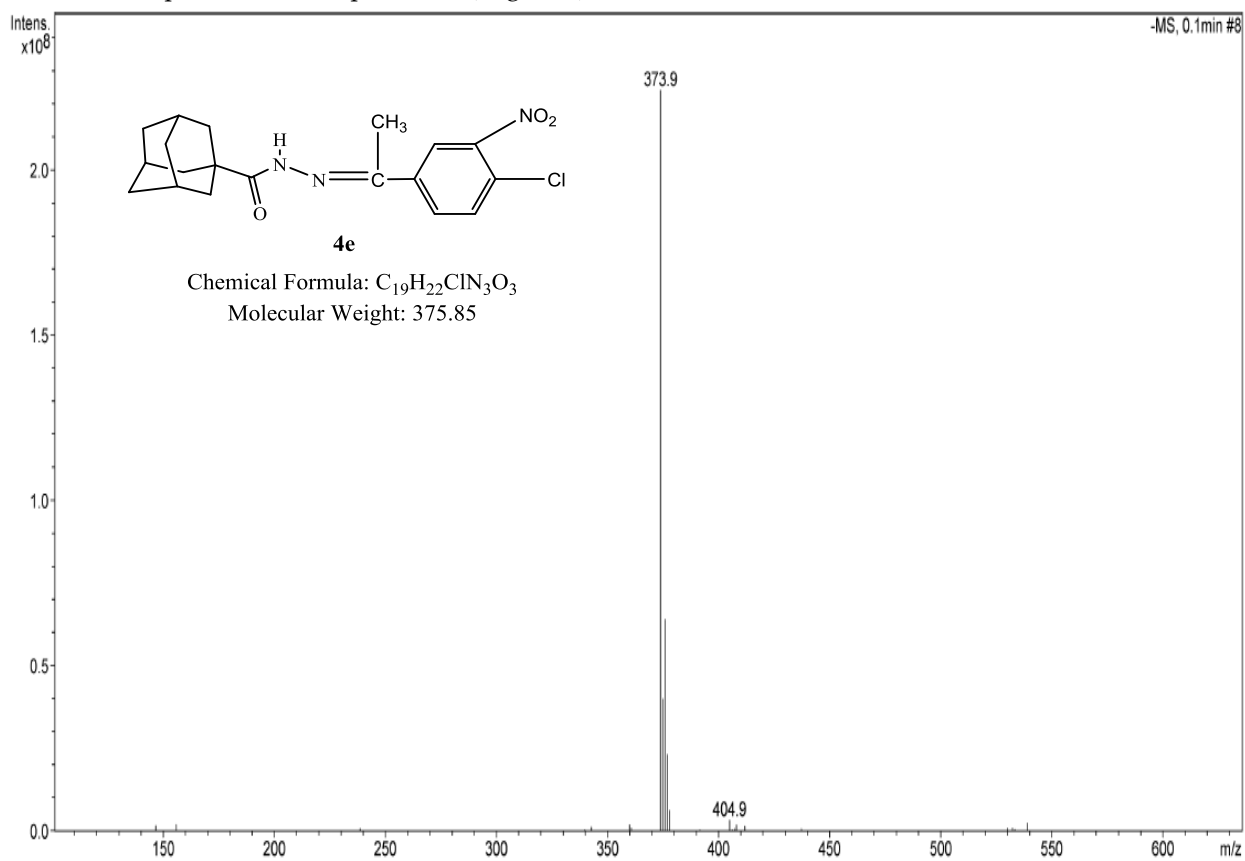
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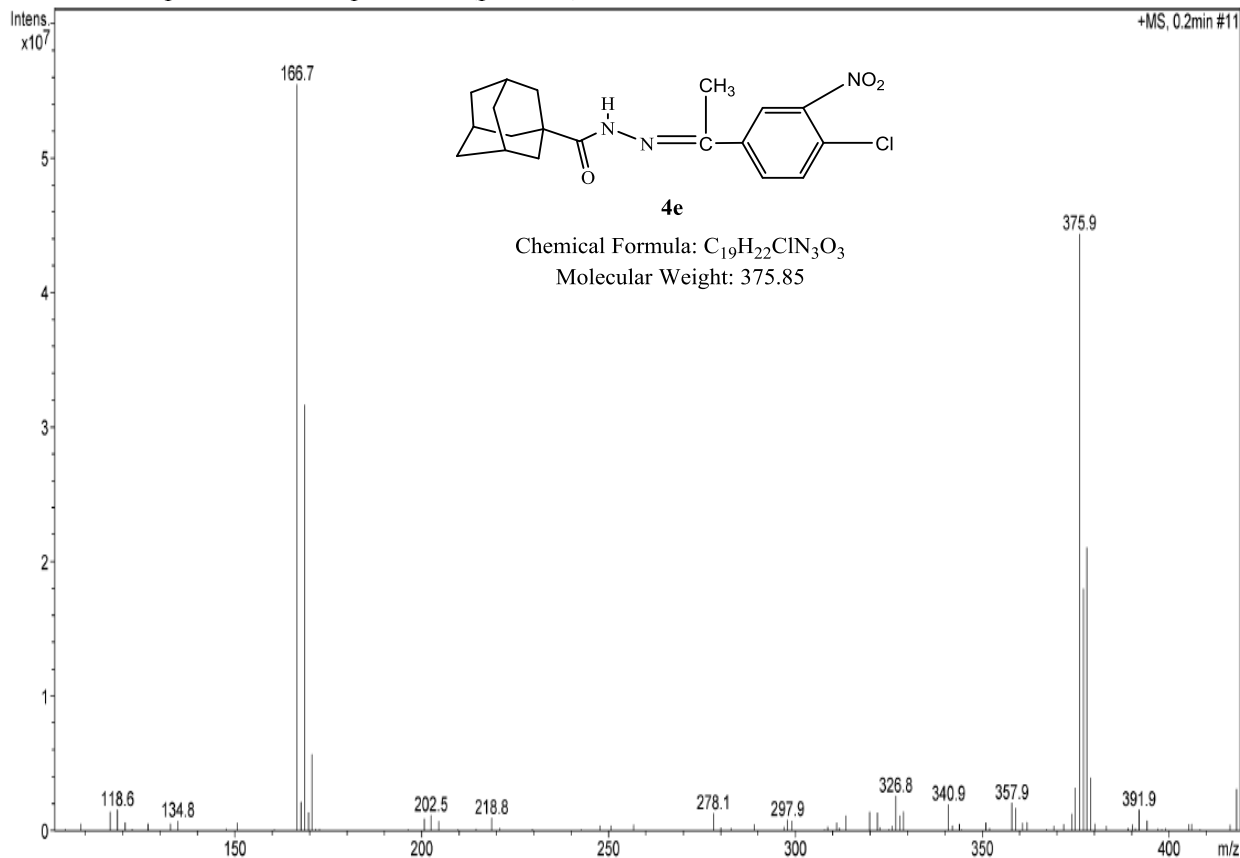
¹H-NMR spectrum of compound **4e**



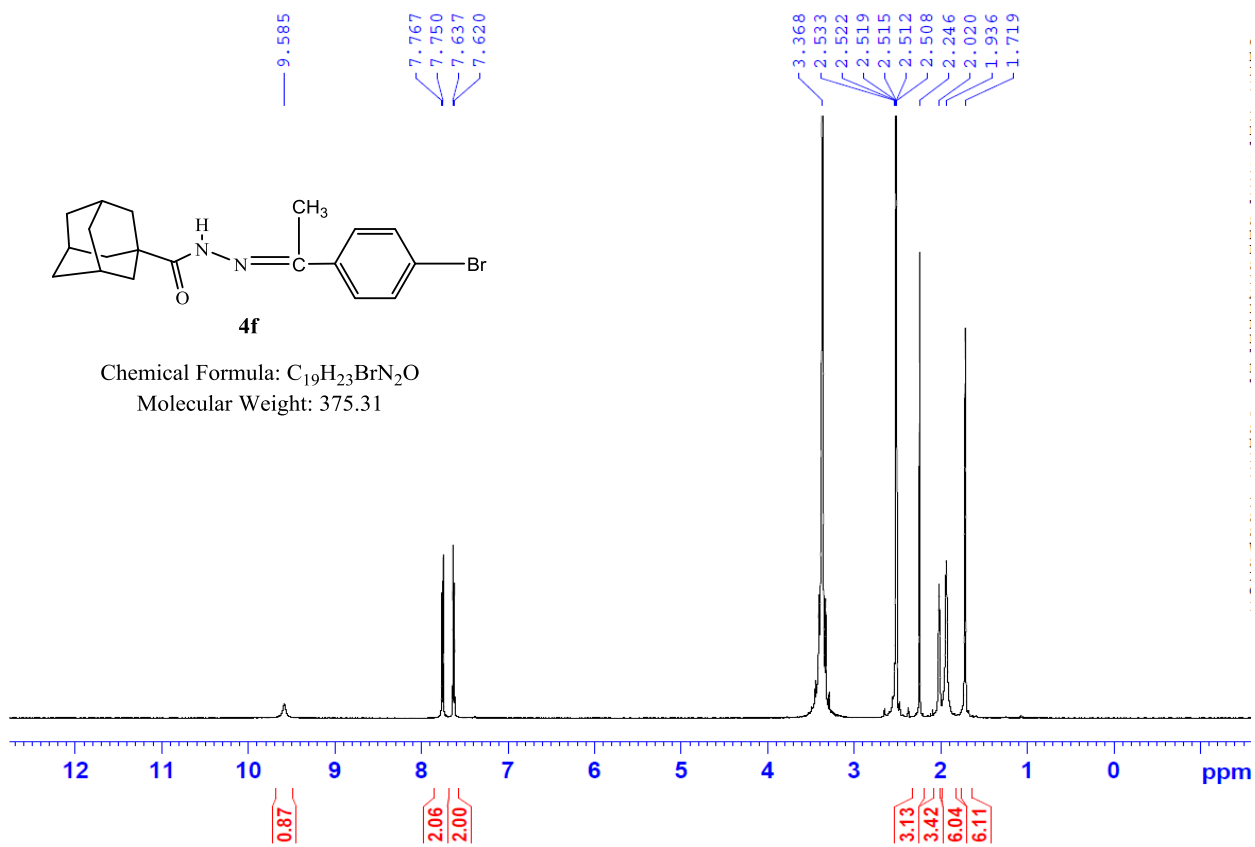
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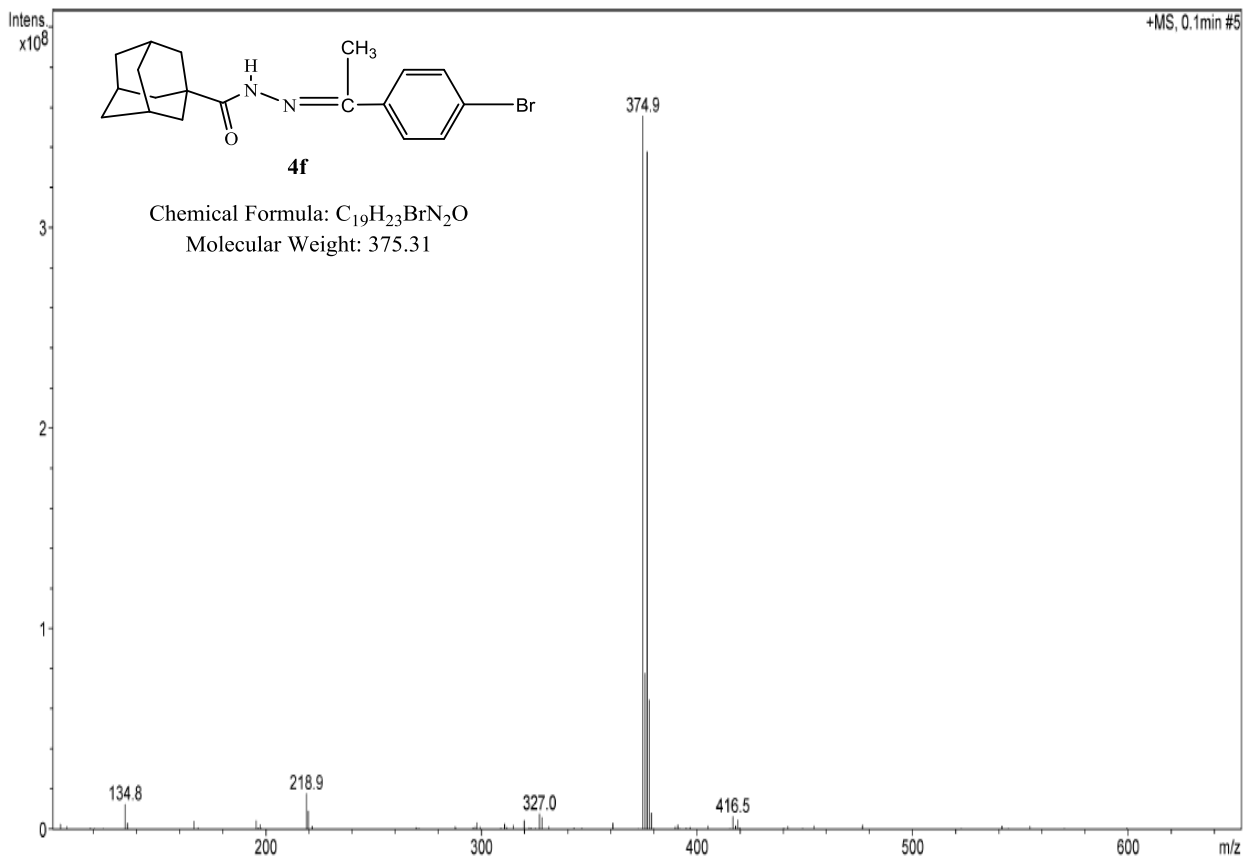
ESI-MS spectrum of compound **4e** (positive)



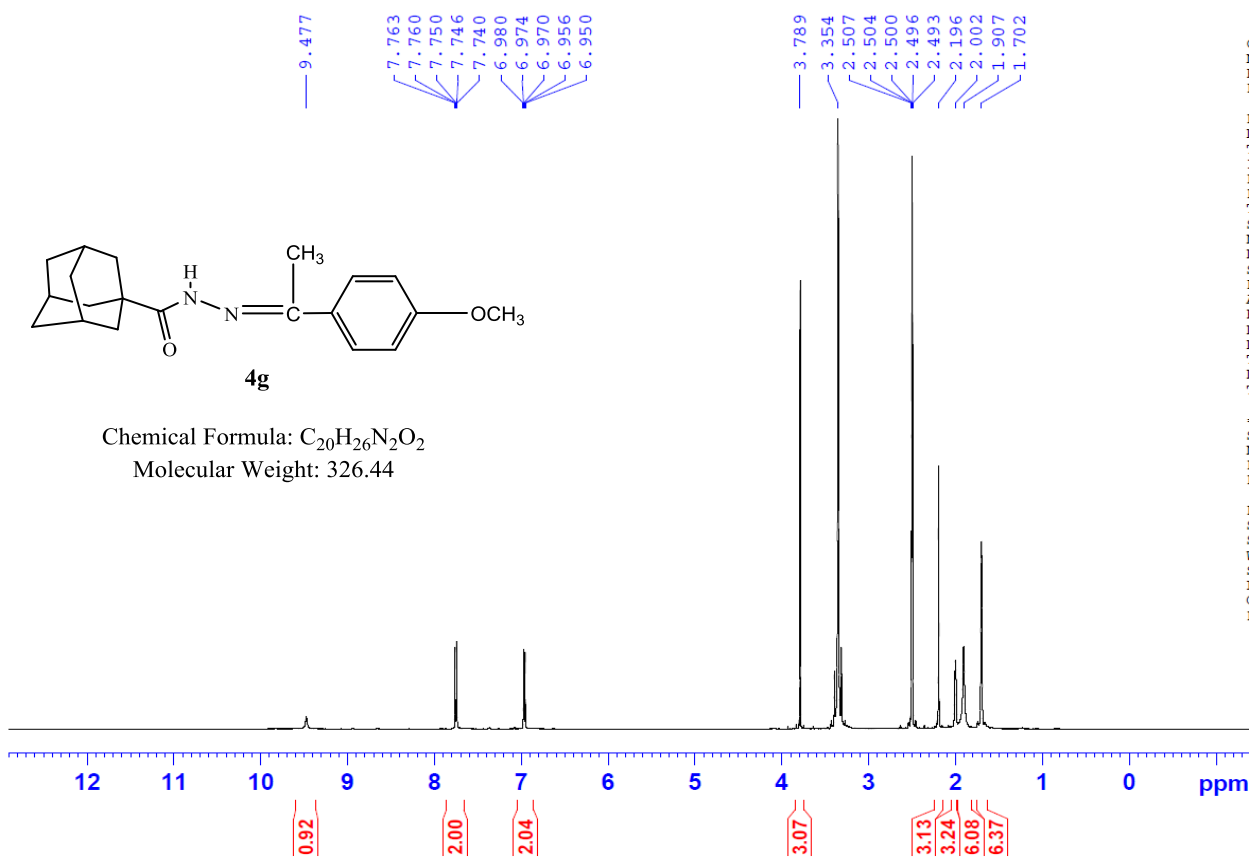
1H -NMR spectrum of compound **4f**



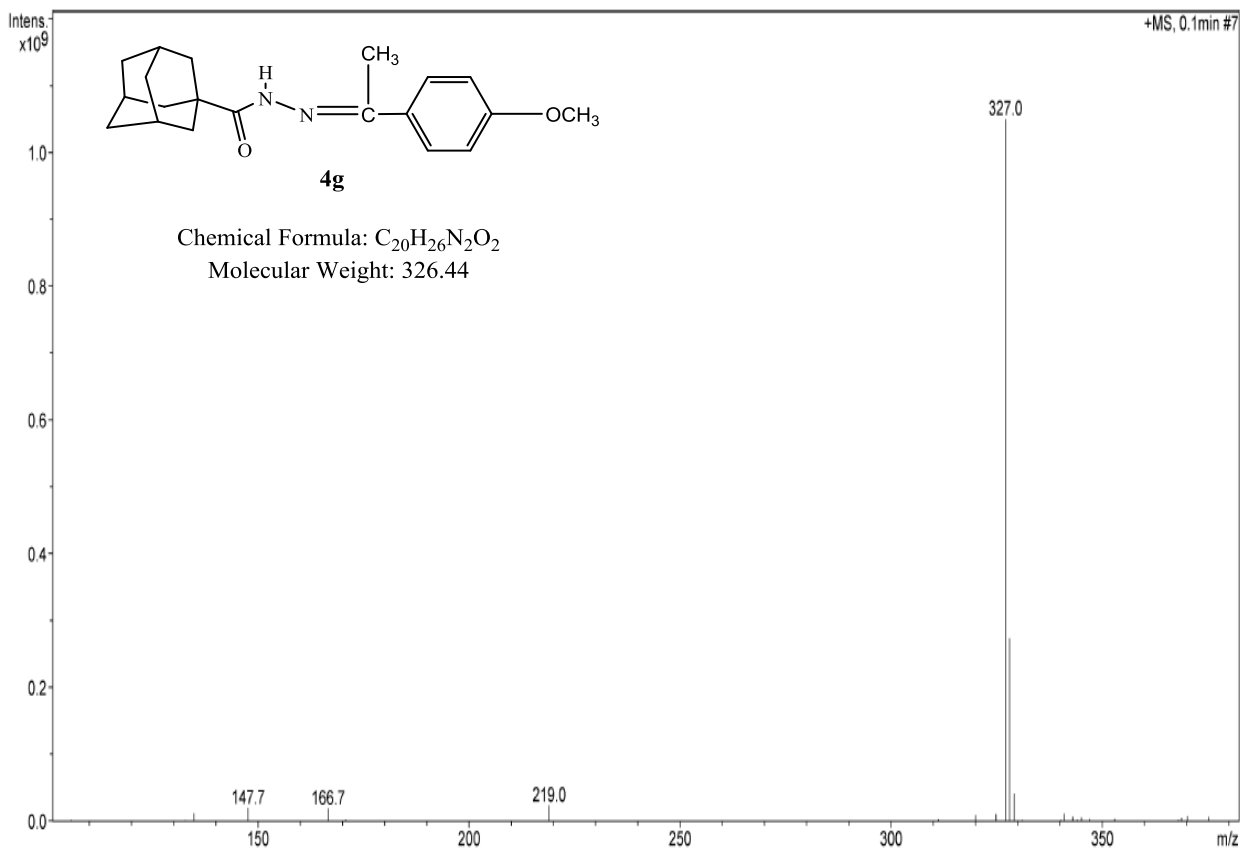
ESI-MS spectrum of compound **4f** (positive)



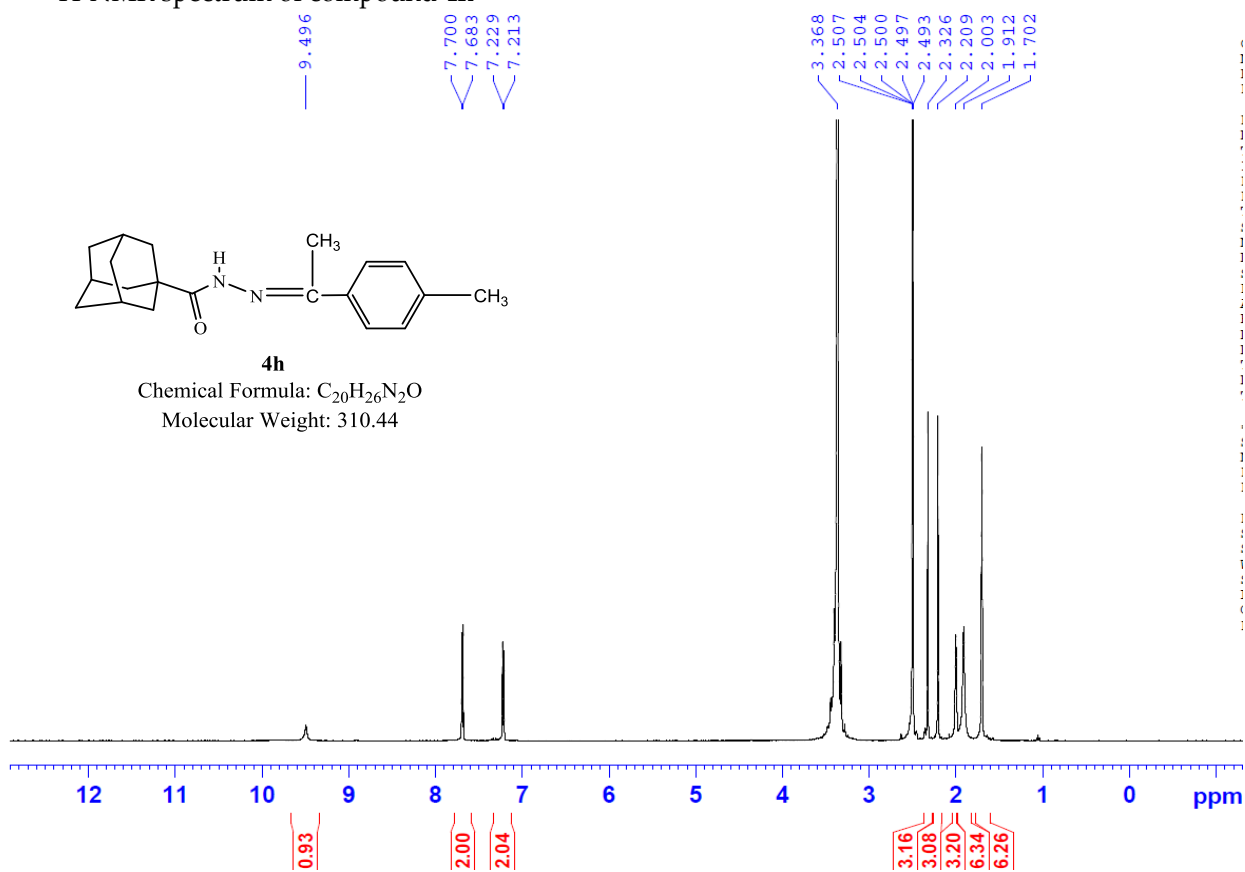
¹H-NMR spectrum of compound **4g**



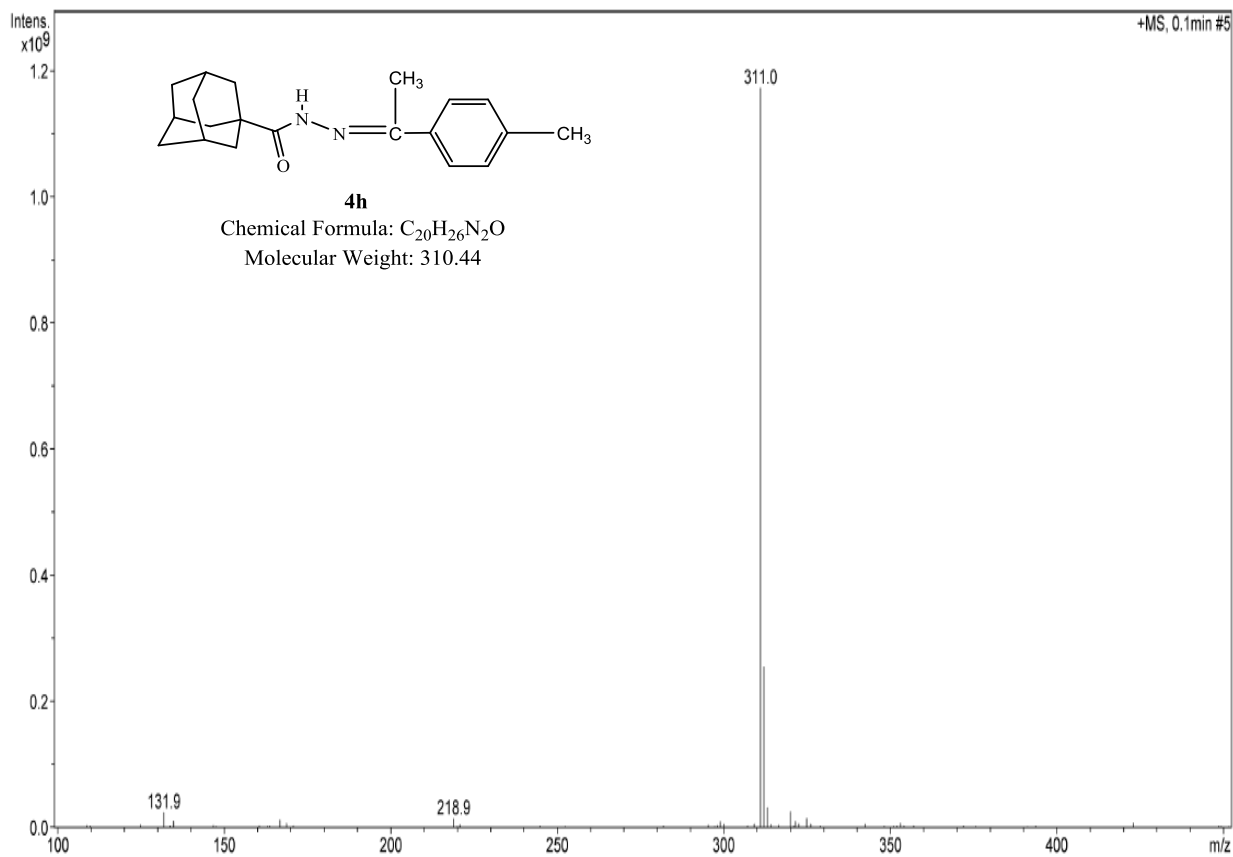
ESI-MS spectrum of compound **4g** (positive)



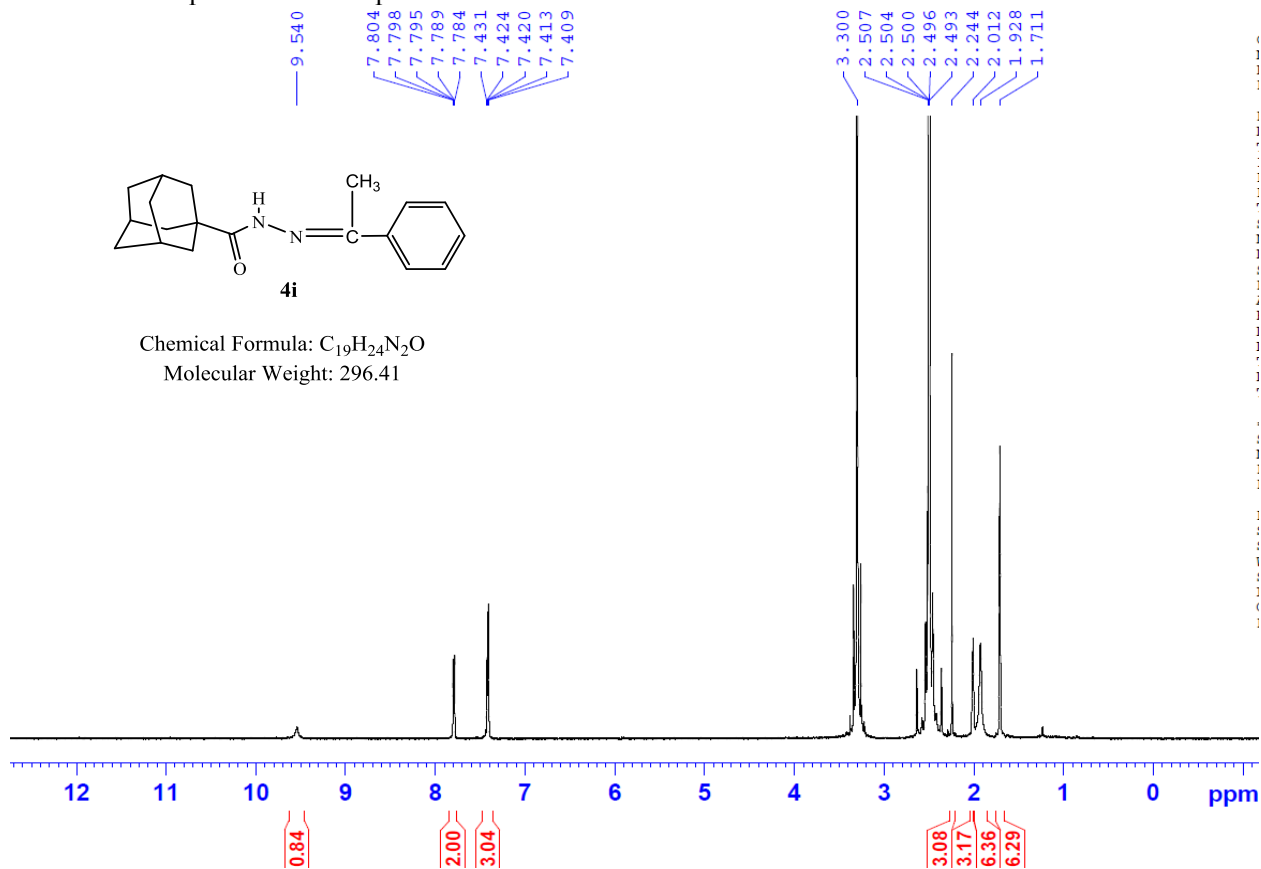
¹H-NMR spectrum of compound **4h**



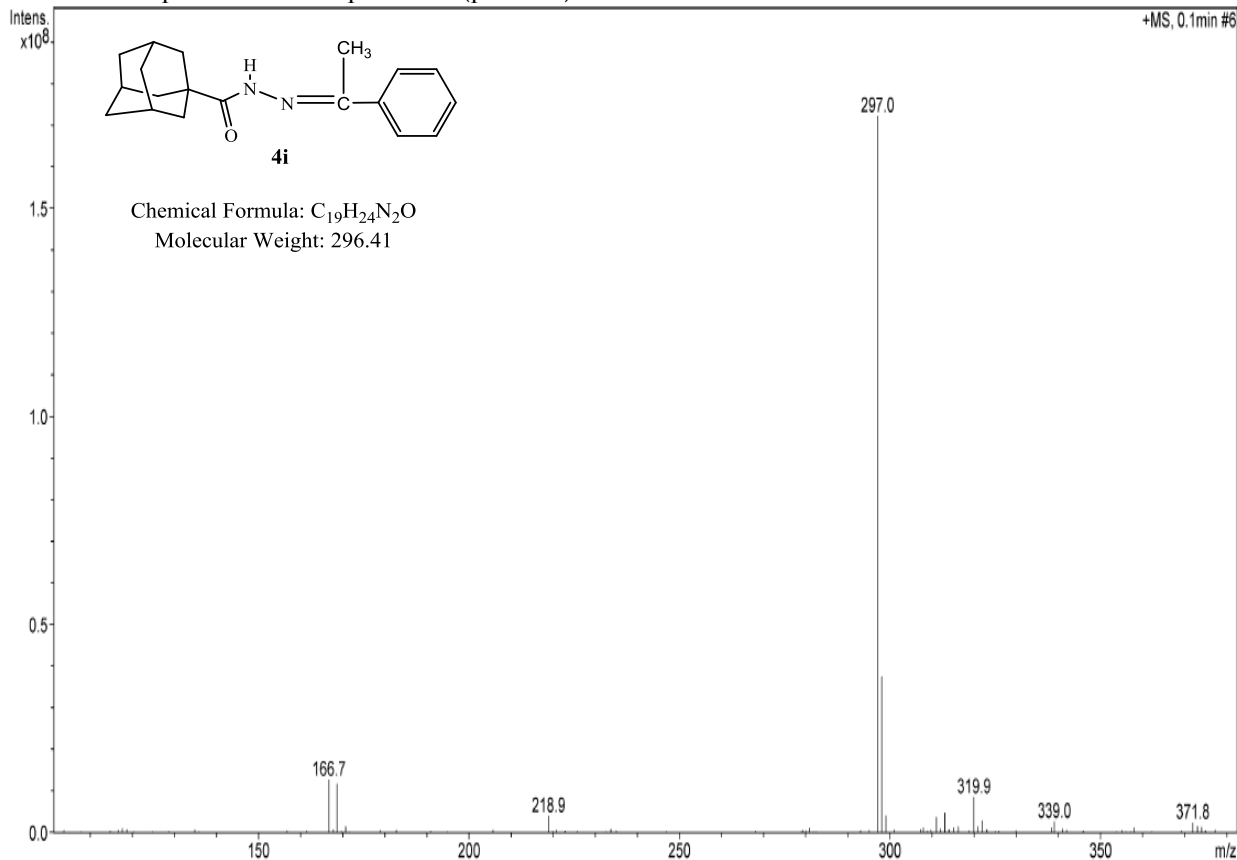
ESI-MS spectrum of compound **4h** (positive)



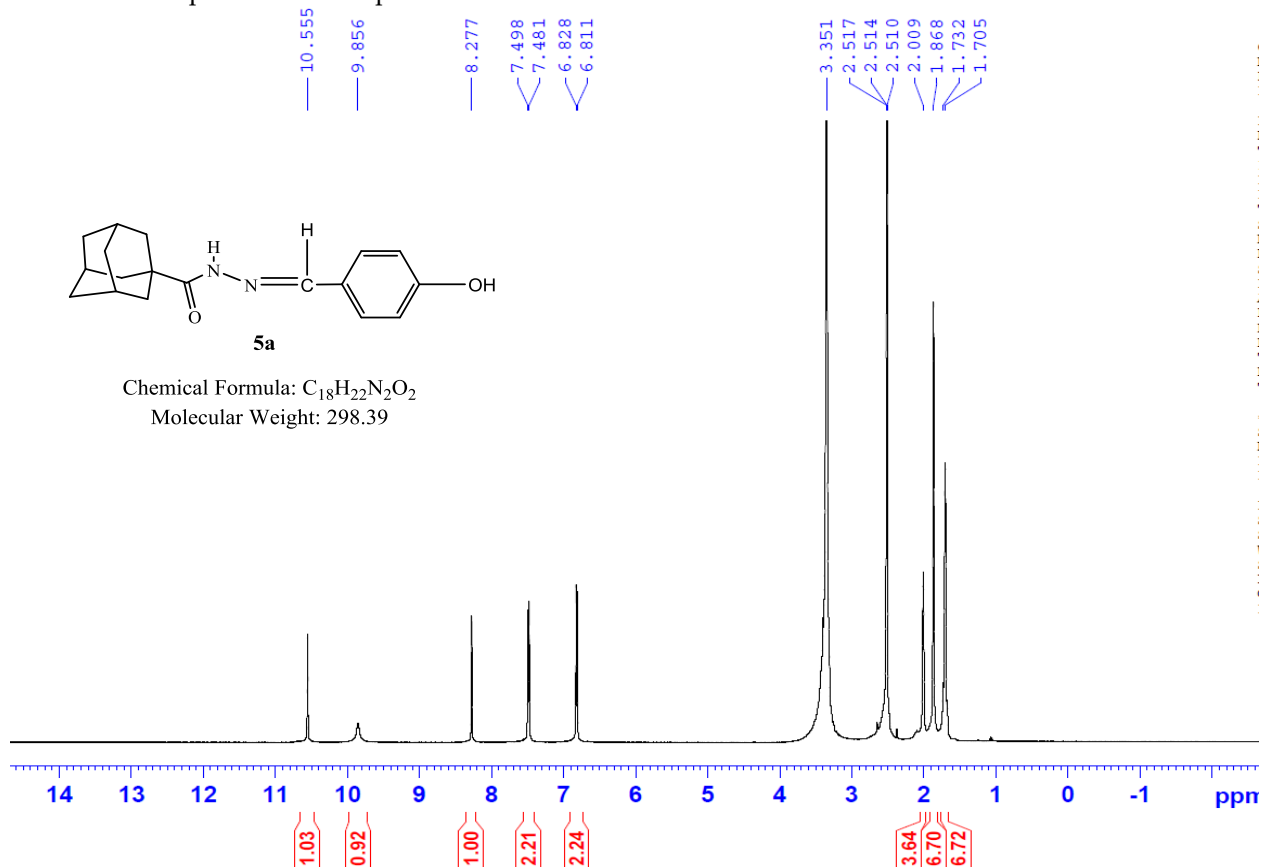
1H -NMR spectrum of compound **4i**



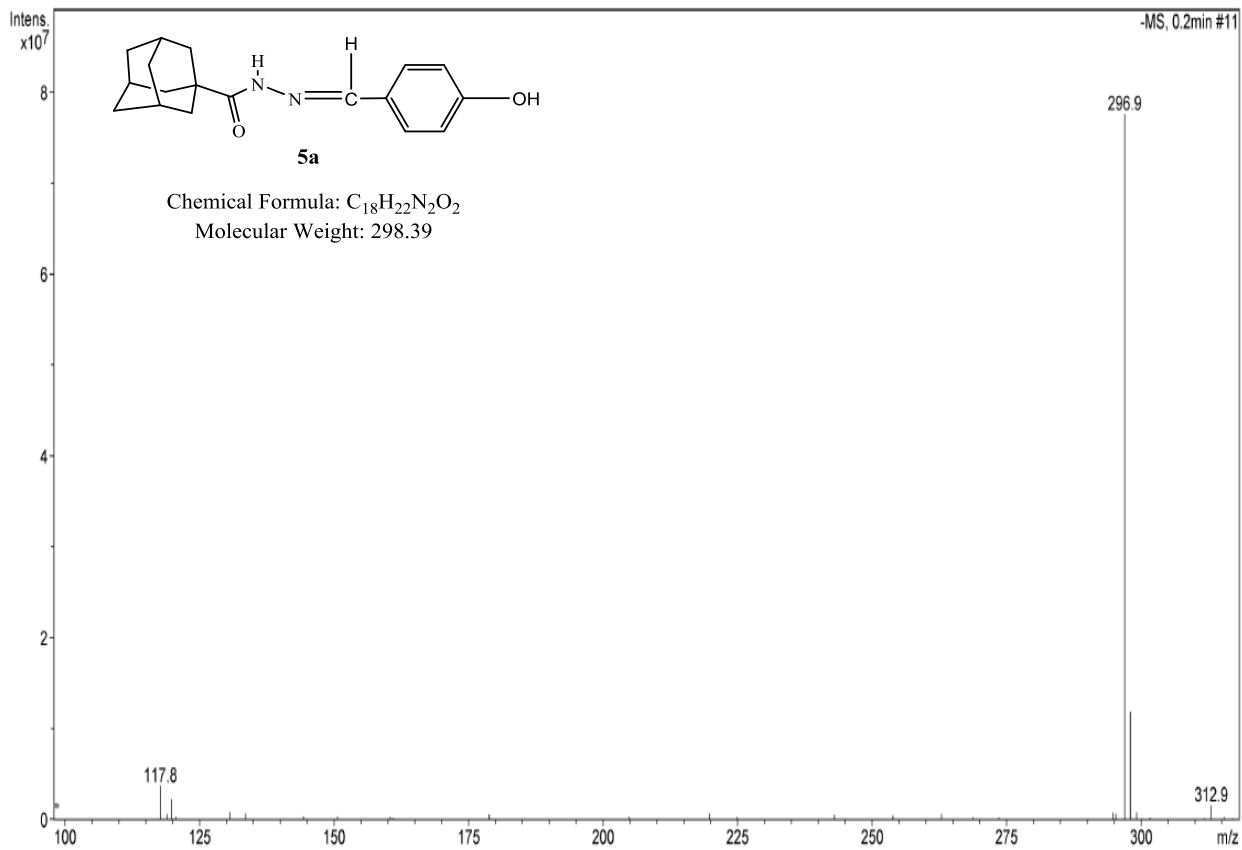
ESI-MS spectrum of compound **4i** (positive)



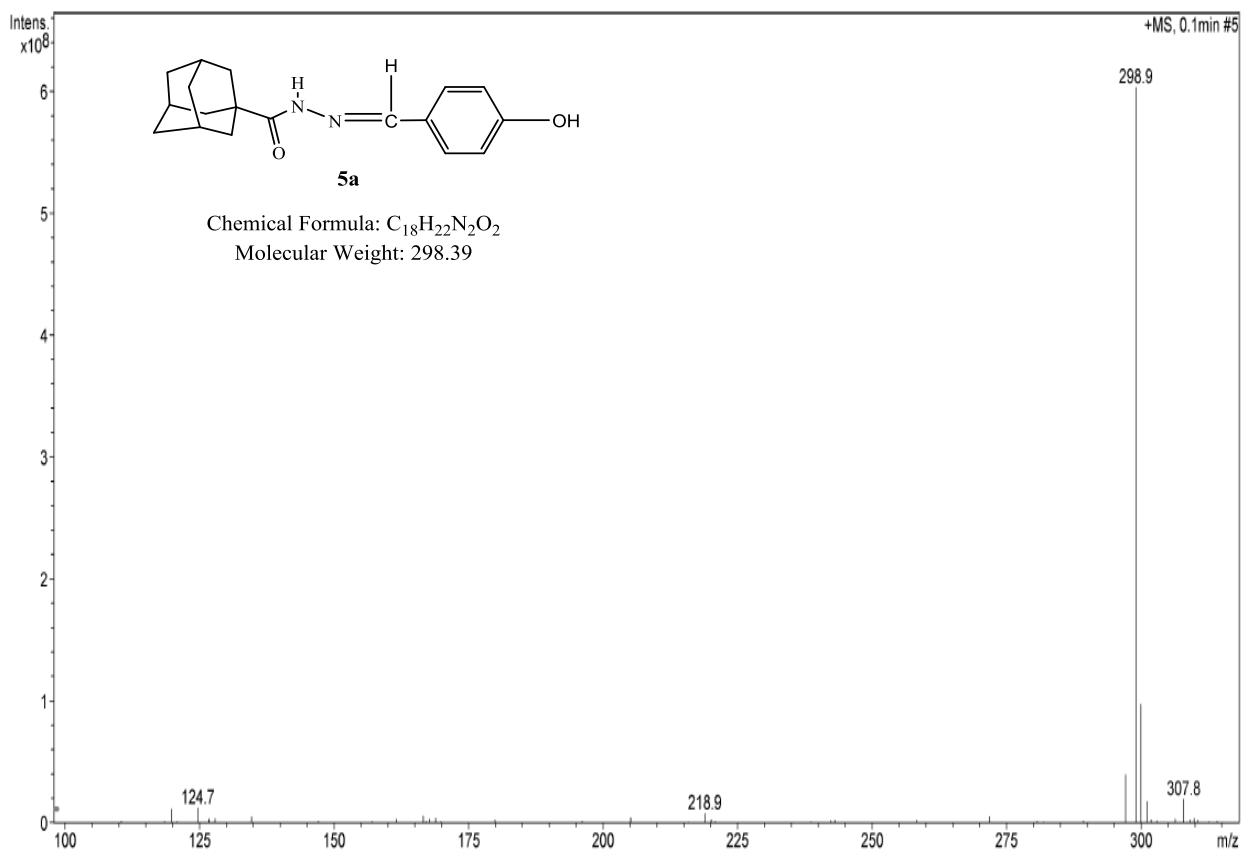
1H -NMR spectrum of compound **5a**



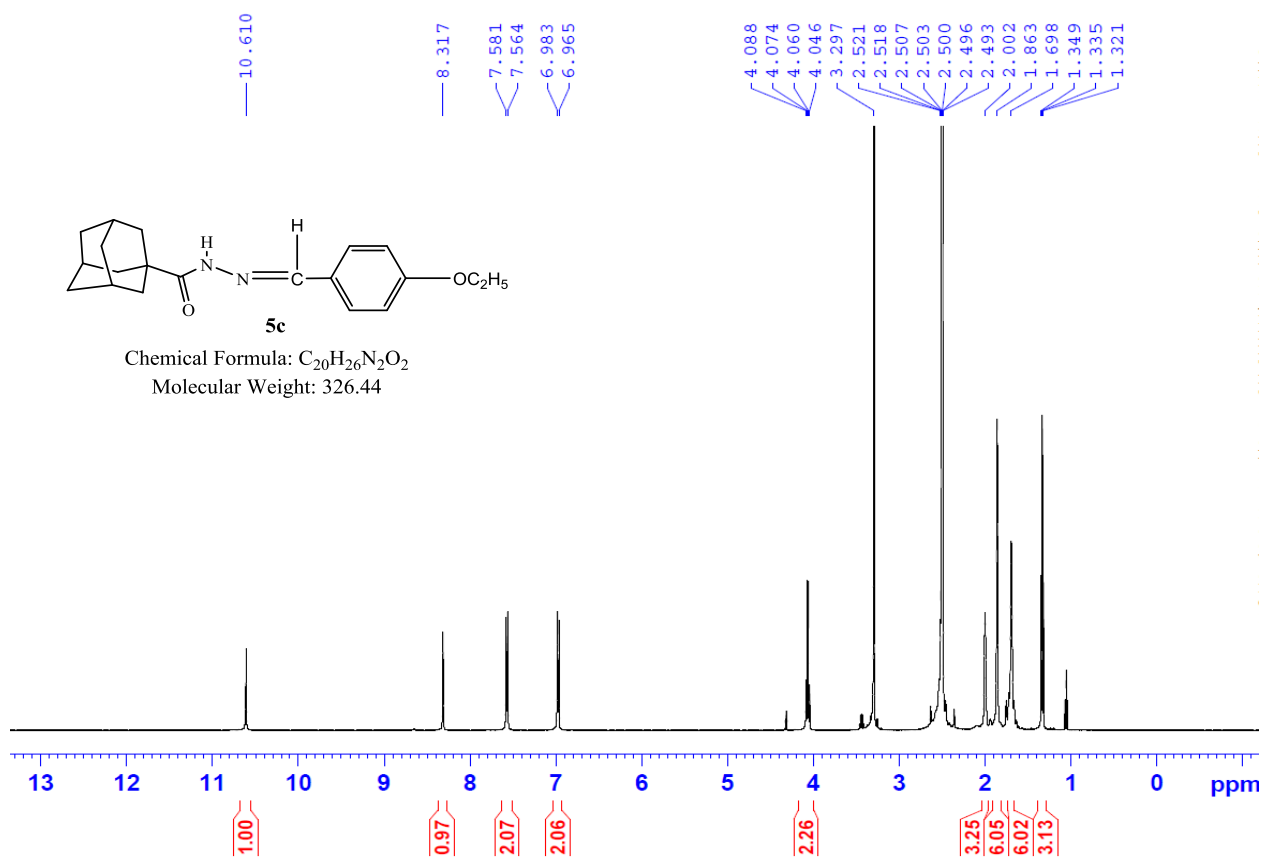
ESI-MS spectrum of compound **5a** (negative)



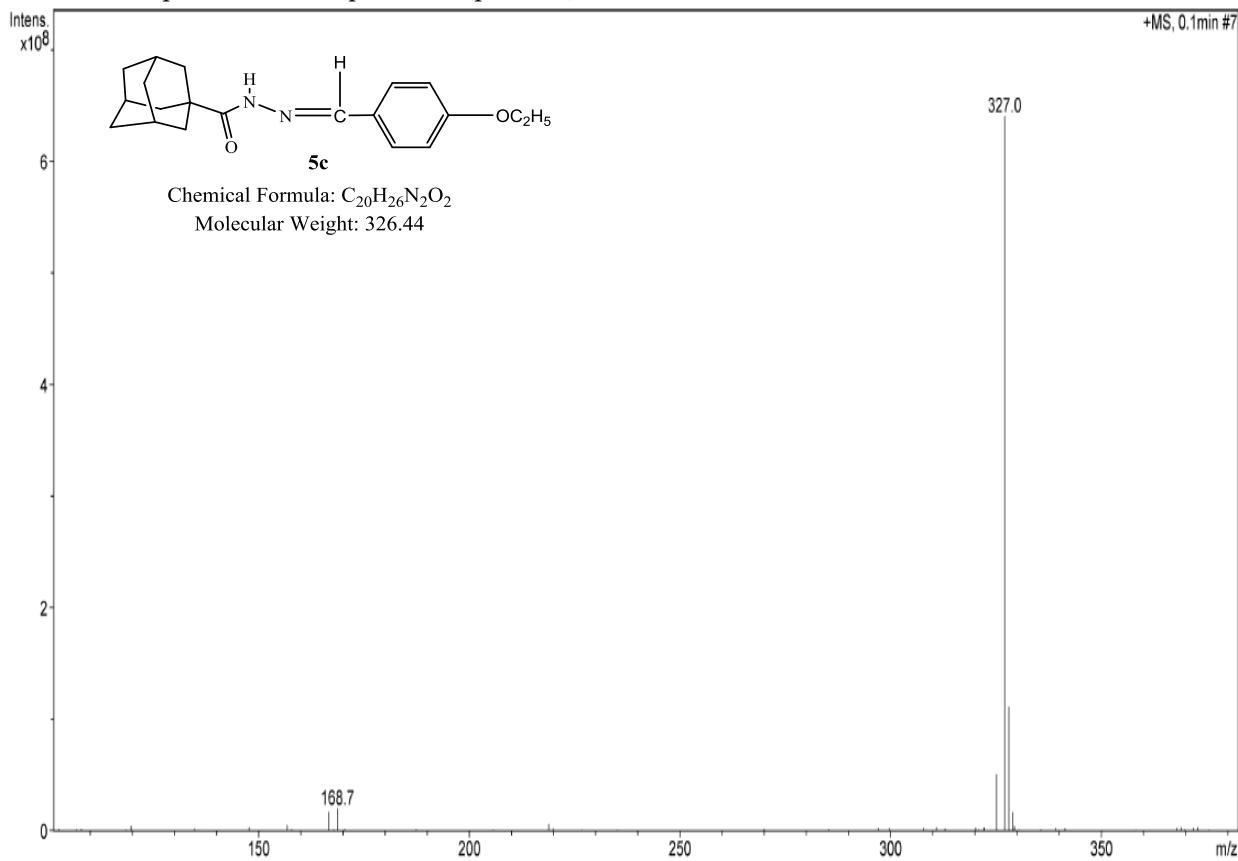
ESI-MS spectrum of compound **5a** (positive)



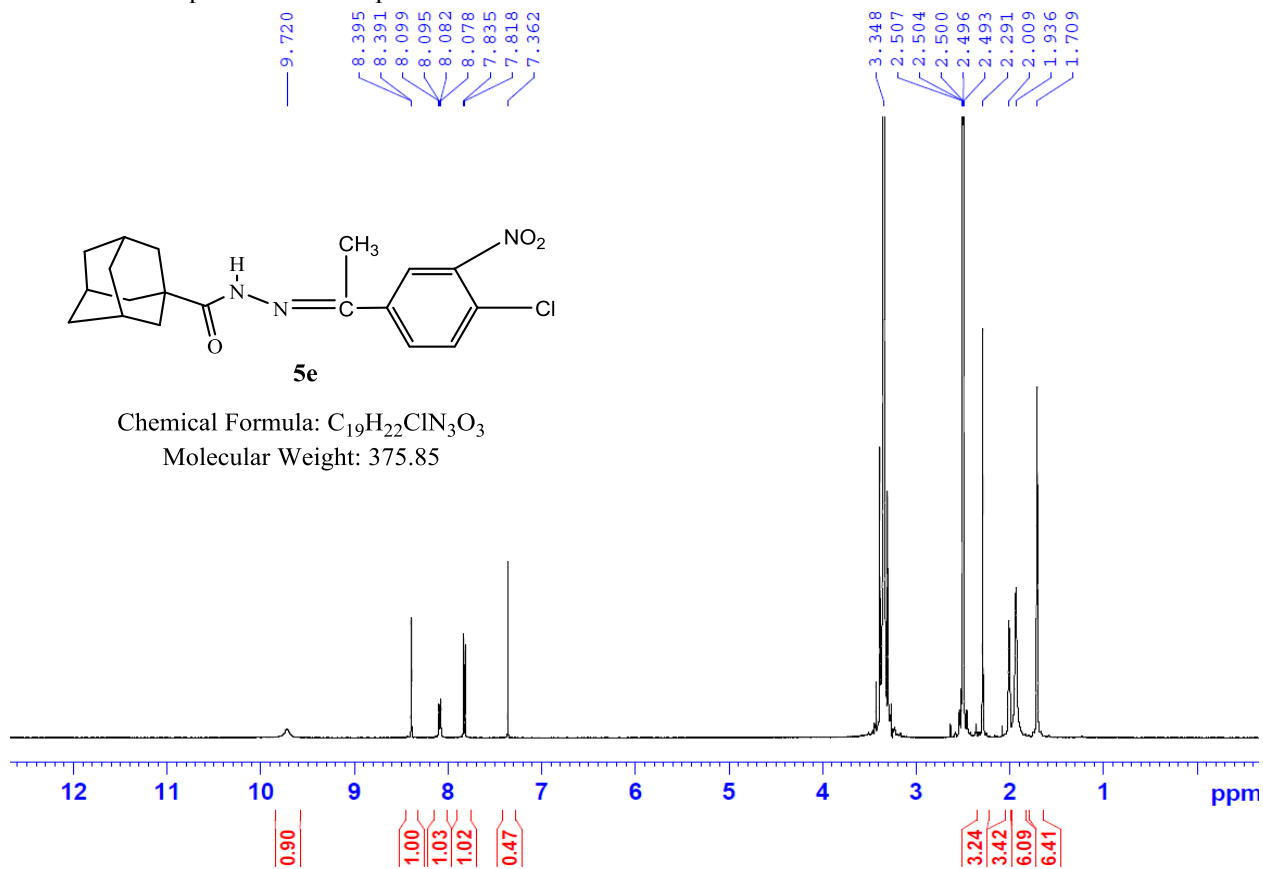
¹H-NMR spectrum of compound **5c**



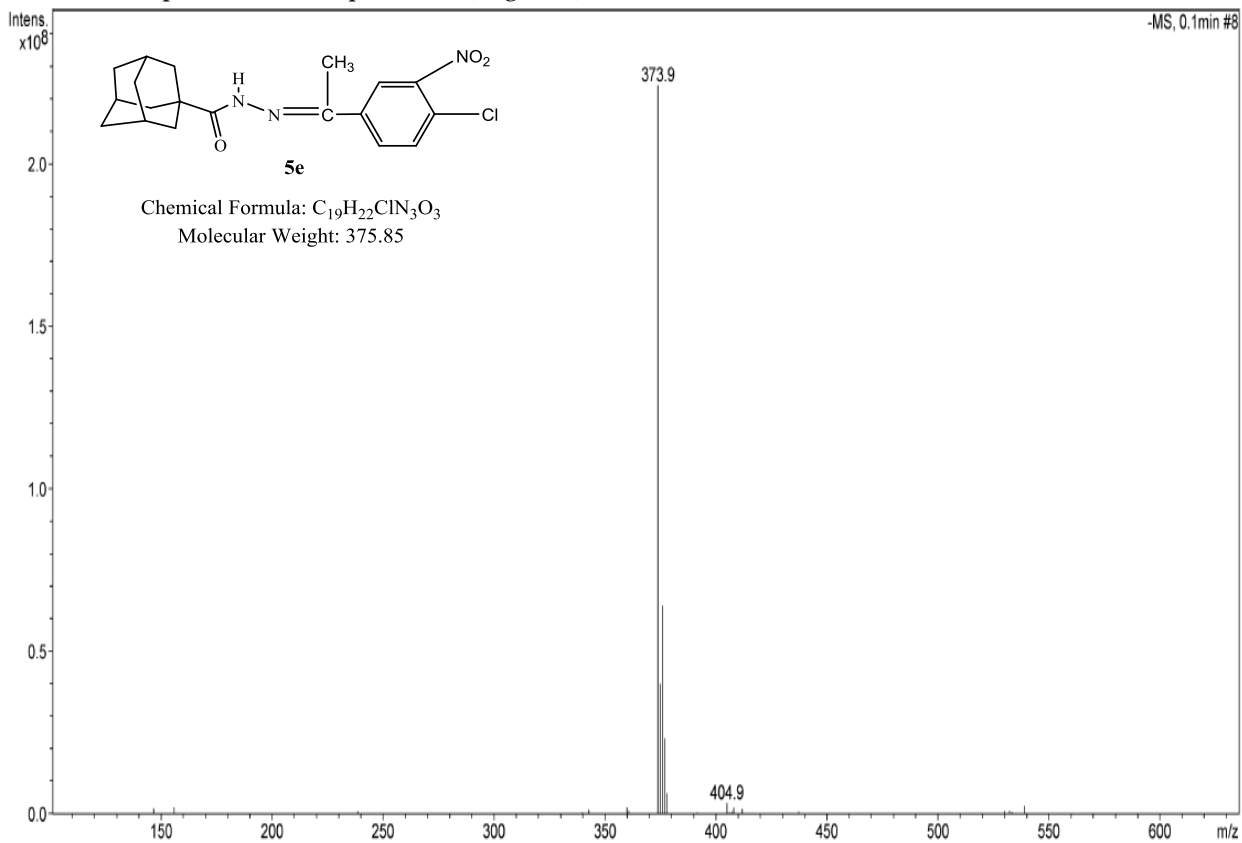
ESI-MS spectrum of compound **5c** (positive)



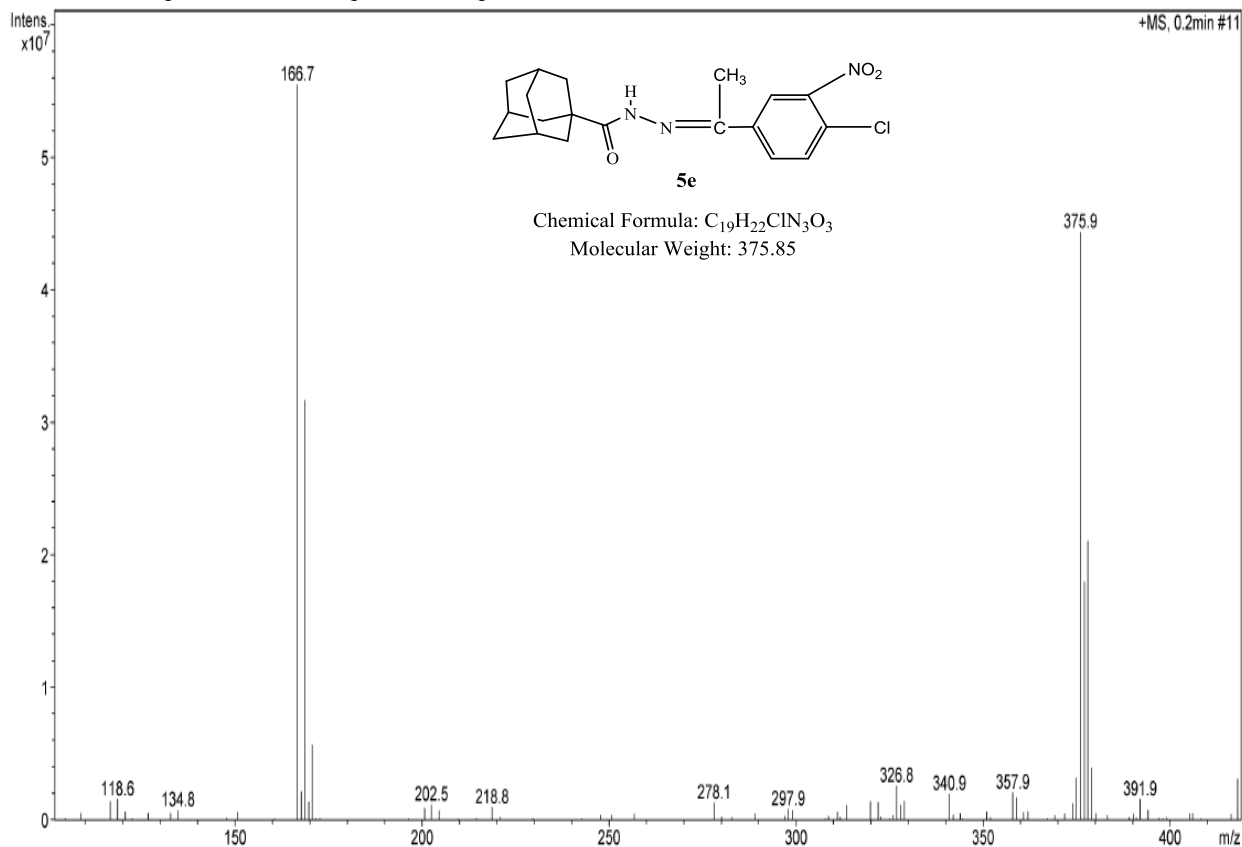
¹H-NMR spectrum of compound **5e**



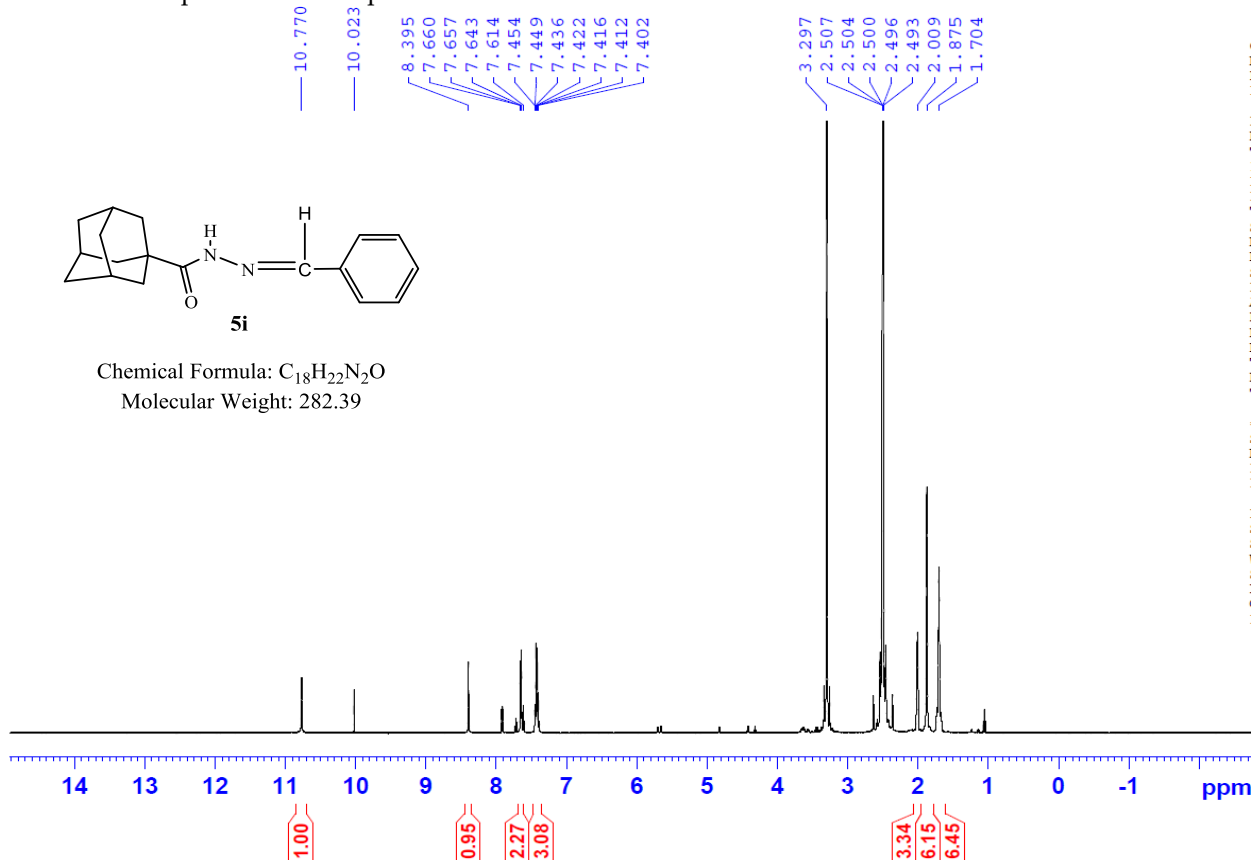
ESI-MS spectrum of compound **5e** (negative)



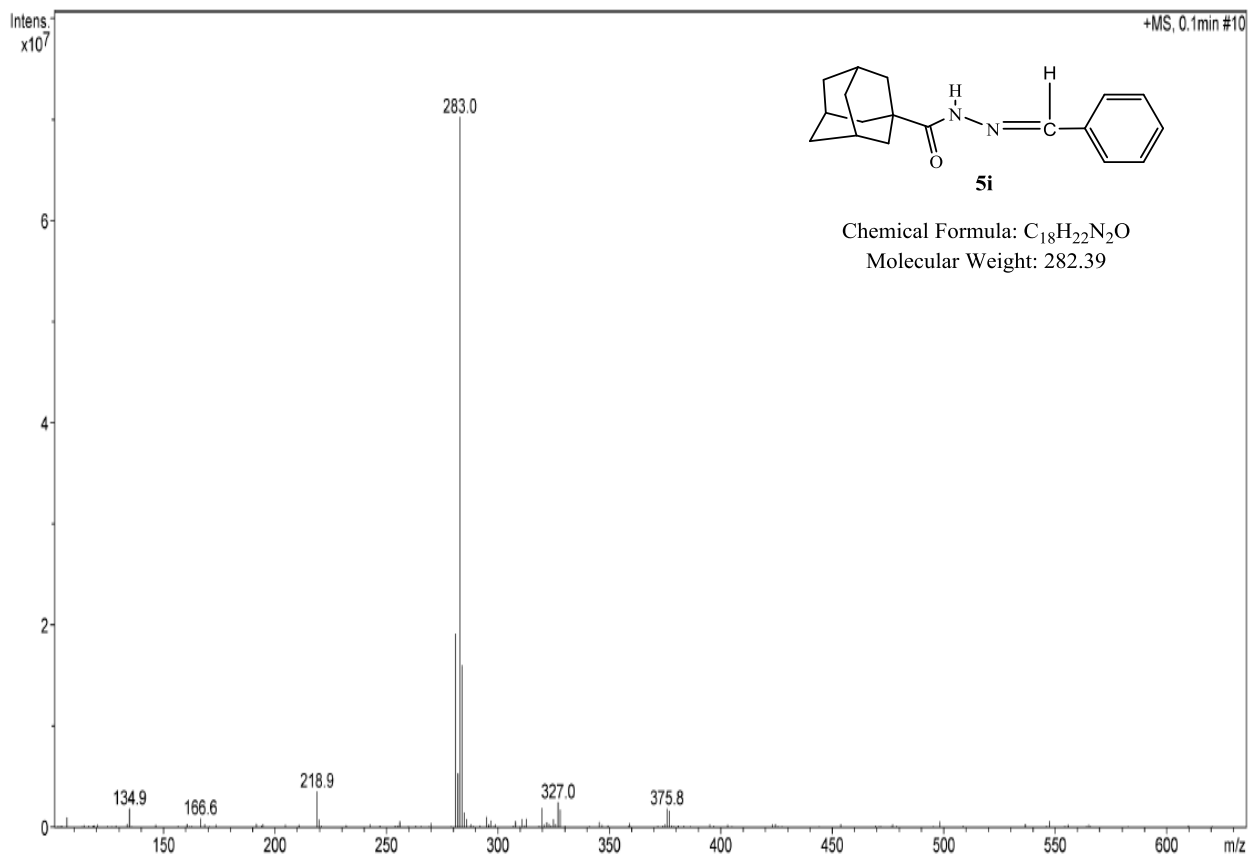
ESI-MS spectrum of compound **5e** (positive)



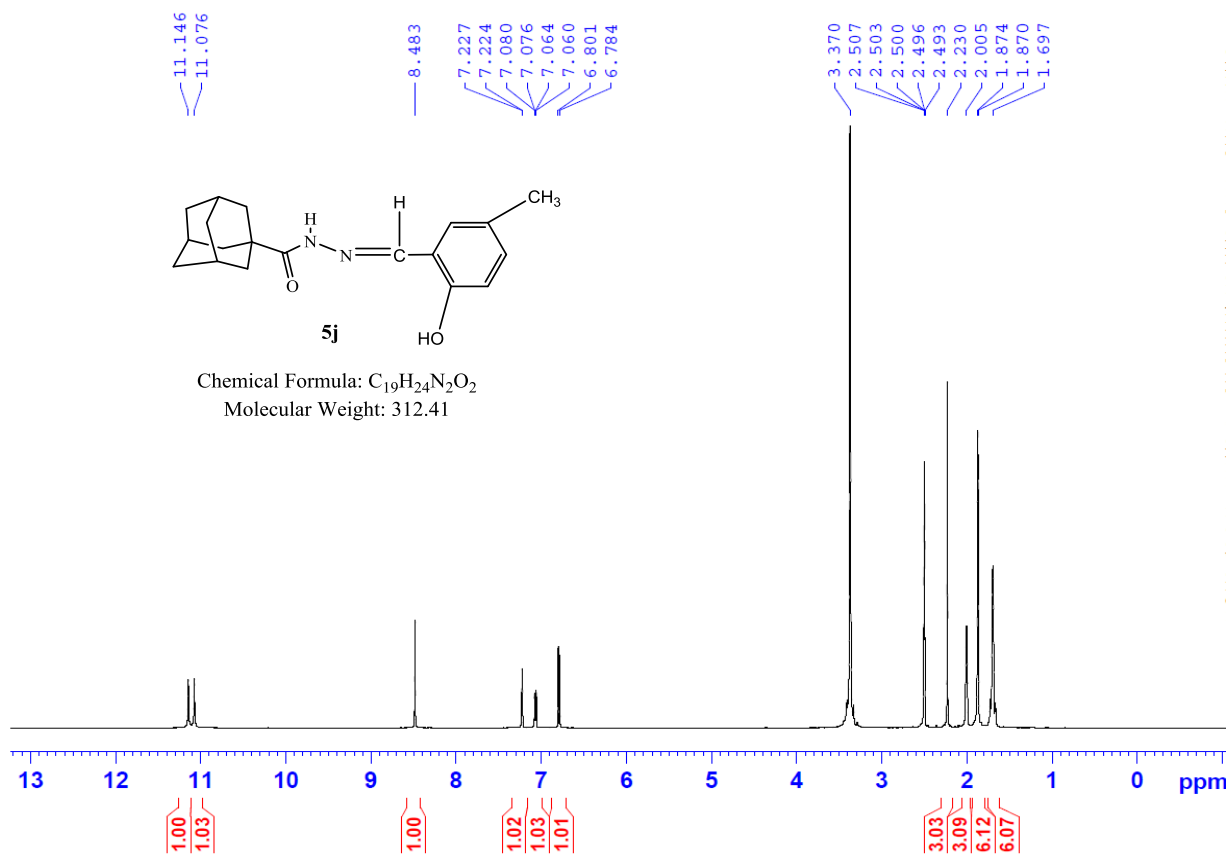
1H -NMR spectrum of compound **5i**



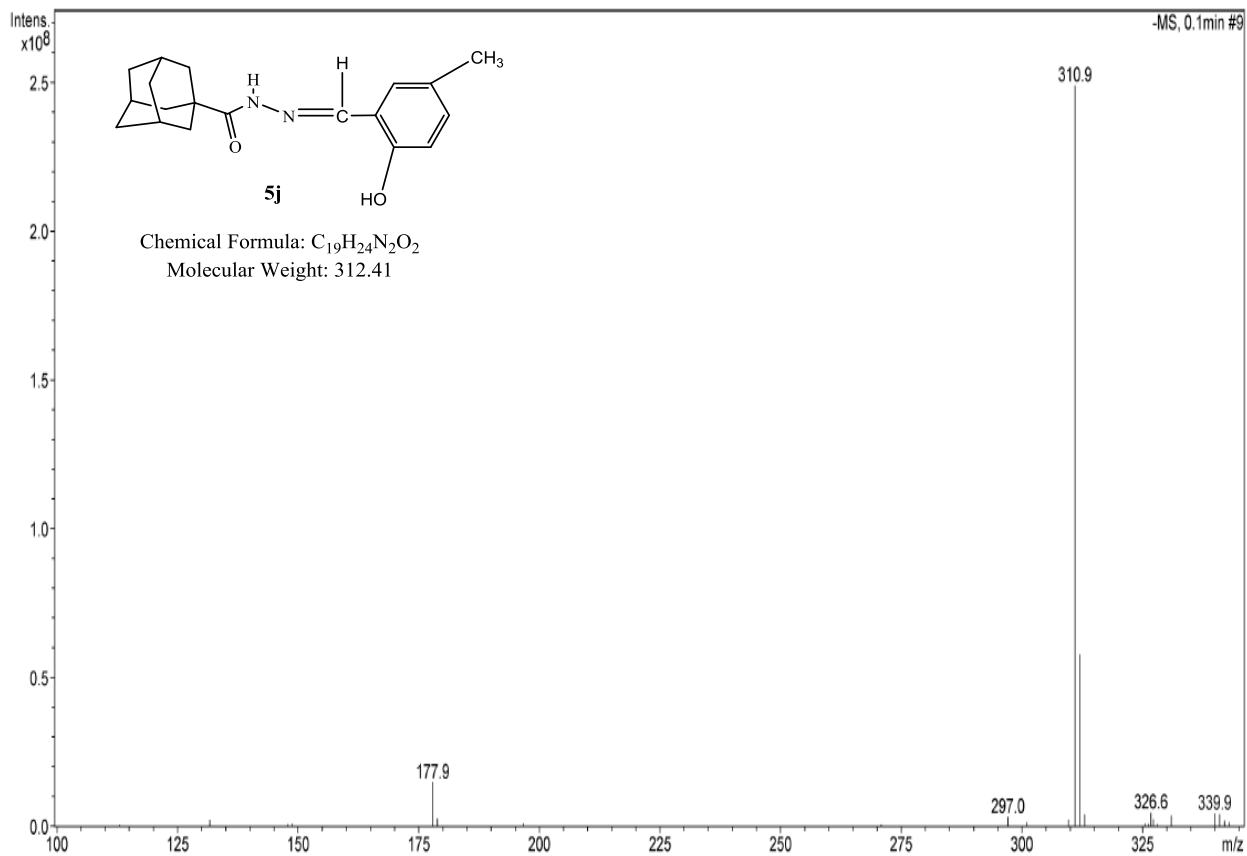
ESI-MS spectrum of compound **5i** (positive)



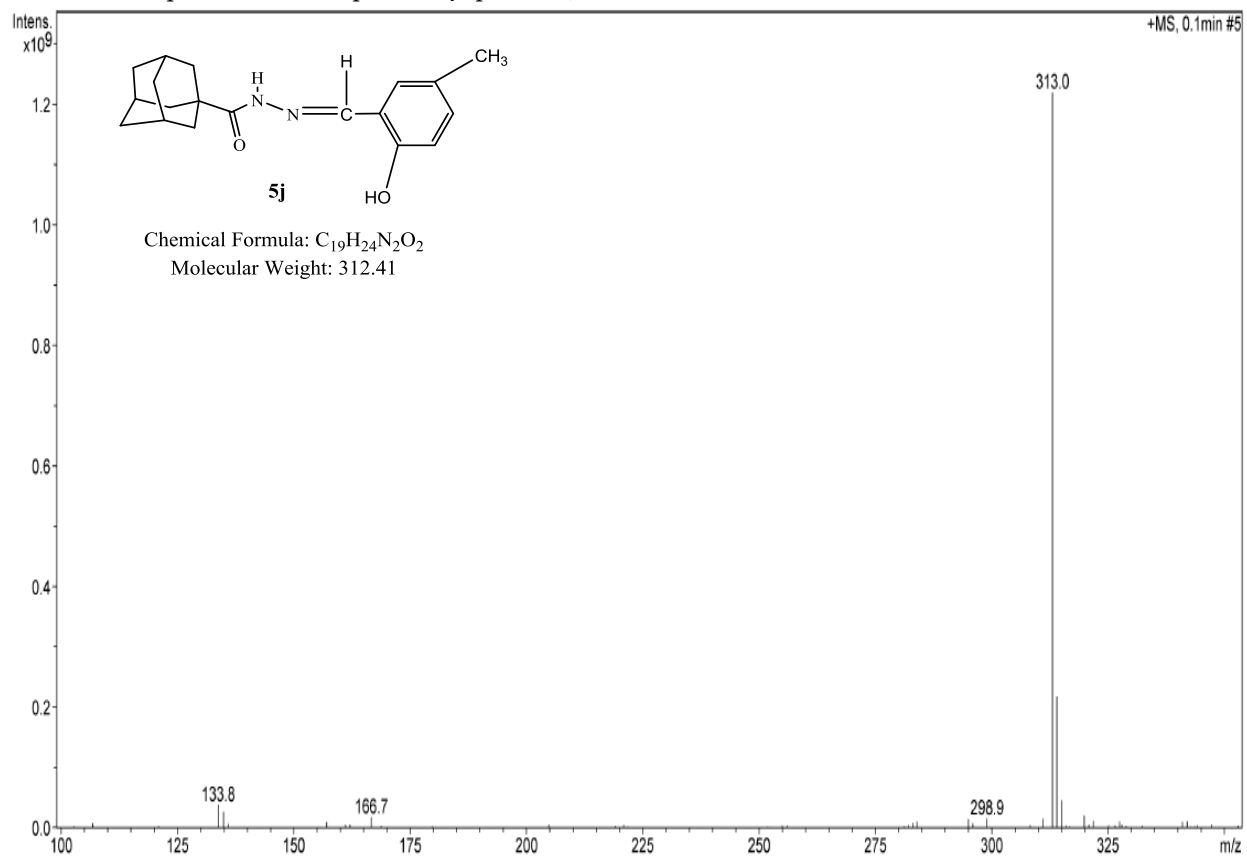
¹H-NMR spectrum of compound **5j**



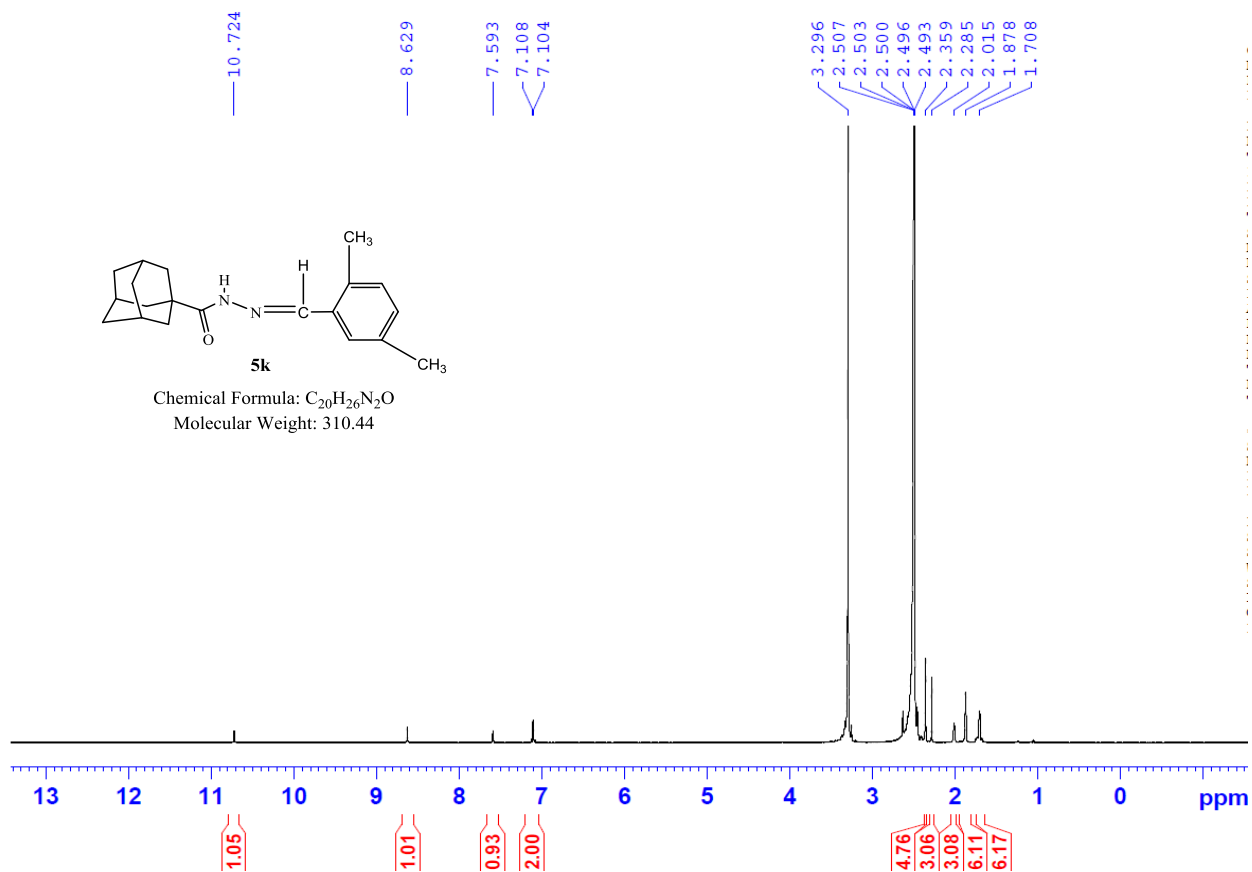
ESI-MS spectrum of compound **5j** (negative)



ESI-MS spectrum of compound **5j** (positive)



1H -NMR spectrum of compound **5k**



ESI-MS spectrum of compound **5k** (positive)

