of mass spectra of trisubstituted-2-thiohydantoins

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Síntesis, actividad biológica y espectros de masas de impacto electrónico de 2-tiohidantoínas trisubstituidas

Síntesi, activitat biològica i espectres de masses d'impacte electrònic de 2-tiohidantoïnes trisubstituïdes

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RESUMEN

Se prepara la 3-[1-(2-hidroxifenil)etilidenamino]-2-tiohidantoína (2) por ciclación de la tiosemicarbazona de la 2-hidroxiacetofenona (1) con cloroacetato de etilo en presencia de acetato sódico fundido. Se describe el comportamiento químico de 2 frente anhídrido acético, cloruro de arenodiazonio, aldehídos aromáticos e hidrato de hidrazina. Los espectros de masas con ionización por impacto electrónico de los compuestos 2 y 3 muestran el pico del ión molecular intenso, y el pico base a *m/z* 232 como resultado de la fragmentación. El ión molecular de los compuestos 4a, 4b y 8 es el pico base, a *m/z* 353, 387 y 288, respectivamente. En contraste, los compuestos 5a y 5b muestran el pico base a *m/z* 336 y 370 como resultado de la fragmentación. Los compuestos 6a,b y 7a,b presentan un patrón de fragmentación característico, con un fragmento muy estable a *m/z* 326 y 350, respectivamente. Algunos de los compuestos sintetizados exhiben además actividades antimicrobianas.

Palabras clave: **Tiohidatoína. Tiosemicarbazona. Espectros de masas. Actividades antimicrobianas.**

SUMMARY

3-[1-(2-Hydroxyphenyl)ethylideneamino]-2-thiohydantoin (2) was prepared via cyclization of 2-hydroxyacetophenone thiosemicarbazone (1) with ethyl chloroacetate in the presence of fused sodium acetate. The chemical behaviour of 2 towards acetic anhydride, arenediazonium chloride, aromatic aldehydes and hydrazine hydrate is described. The electron impact ionization mass spectra of compounds 2 and 3 show a strong molecular ion peak and a base peak of *m/z* 232 resulting from cleavage fragmentation. The molecular ion of compounds 4a, 4b, and 8 is a base peak of *m/z* 353, 387 and 288, respectively. In contrast, compounds 5a and 5b show a base peak at *m/z* 336 and 370 resulting from fragmentation. Compounds 6a,b and 7a,b give a characteristic fragmentation pattern with a very stable fragment of *m/z* 326 and 350, respectively. Some of the synthesized compounds also exhibited antimicrobial activities.

Key words: **Thiohydatoin. Thiosemicarbazone. Mass spectra. Antimicrobial activities.**

RESUM

Es prepara la 3-[1-(2-hidroxifenil)etilidenamino]-2-tiohidantoïna (2) per ciclització de la tiosemicarbazona de la 2-hidroxiacetofenona (1) amb cloroacetat d'etil en presència d'acetat sòdic fos. Es descriu el comportament químic de 2 front anhídrid acètic, clorur d'arendiazoni, aldehids aromàtics i hidrat d'hidrazina. Els espectres de masses amb ionització per impacte electrònic dels compostos 2 i 3 mostren el pic de l'ió molecular intens, i el pic base a *m/z* 232 com a resultat de la fragmentació. L'ió molecular del compostos 4a, 4b i 8 és el pic base, a *m/z* 353, 387 i 288, respectivament. En contrast, els compostos 5a i 5b mostren el pic base a *m/z* 336 i 370 com a resultat de la fragmentació. Els compostos 6a,b i 7a,b presenten un patró de fragmentació característic, amb un fragment molt estable a *m/z* 326 i 350, respectivament. Alguns dels compostos sintetitzats exhibeixen a més activitats antimicrobianes.

Mots clau: **Tiohidatoïna. Tiosemicarbazona. Espectres de masses. Activitats antimicrobianes.**

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1 - INTRODUCTION

Derivatives of 2-thiohydantoins have found application in clinical medicine as therapeutics[1-3] as well as fungicides and herbicides[4]. Among these compounds the pyridyl imidazolidinones were recently found to have strong activity virus (EV 71)[5,6] and the S-glucosylated hydantoins[7] exhibit properties against the herpes simplex virus[8] (HSV), the human immuno deficiency virus[9] (HIV). Keeping these in view, 3,5-disubstituted-2-thiohydantoins (2, 3, 4, 5, 6 and 7) was synthesized from 2-hydroxyacetophenone as key starting material. The electron Impact (EI) ionization mass spectral fragmentation of some synthesized 2-thiohydantoins derivatives was described.

2 - RESULTS AND DISCUSSION

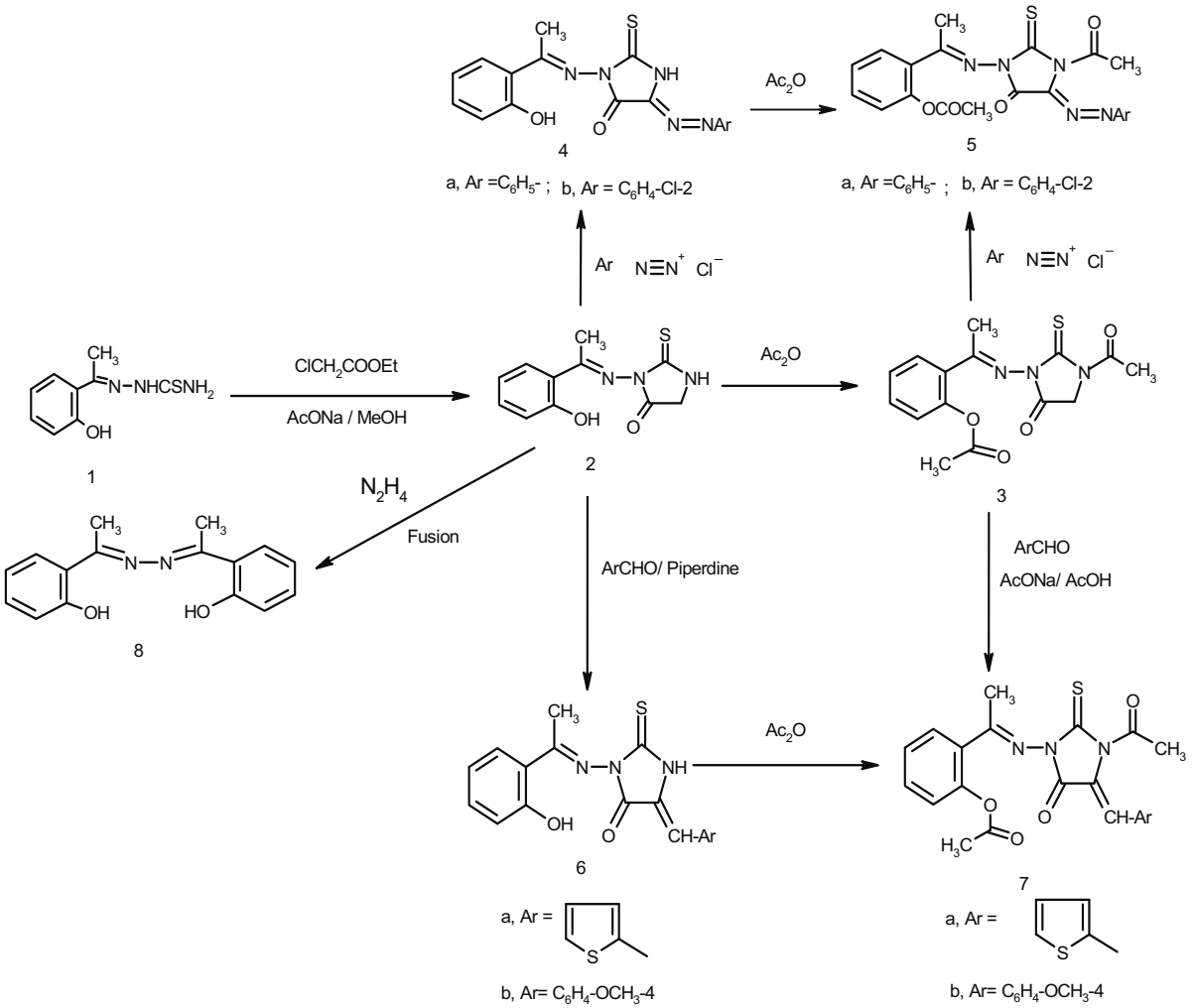
2.1. Chemistry

The synthetic pathways leading to the new 2-thiohydantoins derivatives are illustrated in scheme 1. The reaction of 2-hydroxyacetophenone with thiosemicarbazide in ethanol under reflux led to the corresponding 2-hydroxyacetophenone thiosemicarbazone (1). 3-[1-(2-hydroxyphenylethylidene) amino]-2-thiohydantoin (2) was prepared by reaction[10] of compound 1 with ethyl chloroacetate in the presence of fused sodium acetate in methanol. Acylation of 2-thiohydnatoin (2) with acetic anhydride under reflux led to the formation of 1-acetyl-3-[1-(2-acetoxyphenylethylidene) amino]-2-thiodantoin (3).

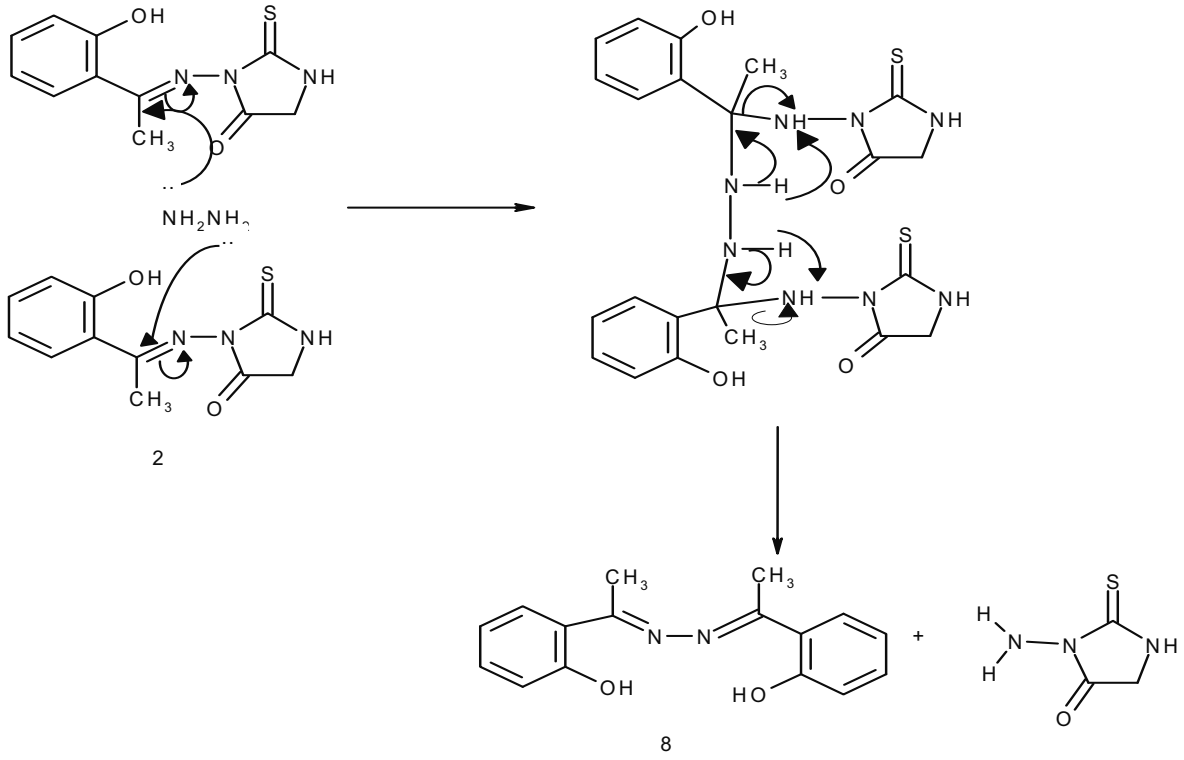
Diazotization[11-13] of aromatic amines (such as aniline and 2-chloroaniline) followed by coupling with sodium salt of 2-thiohydantoin (2) gave the corresponding to 5-arylazo-3-[1-(2-hydroxyphenylethylidene)-amino]-2-thiohydantoins (4a, b). Acylation of 4 with acetic anhydride under reflux afforded the corresponding 1-acetyl-3-[1-(2-acetoxyphenylethylidene)-amino]-5-arylazo-2-thiohydantoins (5a, b).

Condensation[14] of 2-thiohydantoin (2) with aromatic aldehydes (such as thiophene-2-carboxaldehyde and anisaldehyde) in the presence of piperidine under fusion led to the formation of 5-arylidene -3-[1-(2-hydroxyphenylethylidene)-amino]-2-thiohydantoins (6a, b). Acylation of compound 6 with acetic anhydride under reflux yielded the corresponding 1-acetyl-3-[1-(2-acetoxyphenylethylidene)-amino]-5-arylidene-2-thiohydantoins (7a, b). The compound 7 was obtained via another way with condensation of compound 3 with aromatic aldehydes under reflux in acetic acid with sodium acetate.

Hydrazonlysis[15] of 2-thiohydantoin (2) with hydrazine hydrate by fusion at 150ºC, gave the corresponding 1,2-bis(2-hydroxyacetophenone)-hydrazone (8), which may be formed by the nucleophilic attack at methylene carbon atom in 2 by hydrazine via the removal of 1-amino-2-thiohydantoin as shown in scheme 2.



Scheme 1.



Scheme 2.

2.2. Mass Spectrometry

The mass spectral decomposition modes[16-18] of the prepared 3,5-disubstituted-2-thiohydantoins containing 1-(2-hydroxyphenyl) ethylidene amino ring have been investigated.

Table 1 lists the *m/z* (relative abundance, %) values of the principle fragment of synthesized compounds. The mass spectrum of compound 2 (Fig. 1) showed an intense molecular ion peak at *m/z* 249, corresponding to the molecular formula $C_{11}H_{11}N_3O_5S$. The molecular ion of *m/z* 249 fragmented further involving two various pathways. The ion of *m/z* 249 underwent fragmentation via the pathway A to produce a stable peak at *m/z* 232 by losing hydroxyl group (OH). The loss of two molecules from hydrogen cyanide and thioformyl group (CHS) from the ion of *m/z* 232 resulted in an ion at *m/z* 133. The ion at *m/z* 133 underwent loss of nitrogen atom, methylene group, carbon monoxide and acetylene molecule to give peaks at *m/z* 119, 105, 77 and *m/z* 51, respectively. Accordingly, the same molecular ion of *m/z* 249 fragmented via the pathway B by cleavage of 2-thiohydantoin radical, has relatively low abundance to give the ion of *m/z* 134 which lost nitrogen atom to give the ion of *m/z* 120. The loss of formyl group from the ion with *m/z* 120 gave a torpylium ion at *m/z* 91, which lost acetylene molecule to give the ion of *m/z* 65.

From the mass spectrum of compound 3 (Fig. 2), it was concluded that the molecular ion was at *m/z* 333. The ion of *m/z* 333 underwent fragmentation to produce a peak at *m/z* 291 by losing CH_2CO molecule. The loss of CH2=C=O ketene molecule from the ion peak at *m/z* 291 gave a peak at *m/z* 249, corresponding to the molecular ion peak of compound 2. The ion of *m/z* 249 further broke via pathway similar to compound 2. The molecular ion of compound 2 and 3 fragmented further and involved two suggested pathways as illustrated in scheme 3.

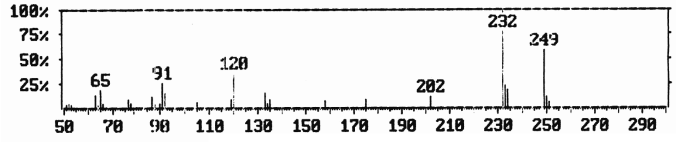


Figure 1.

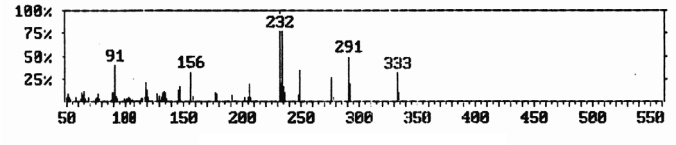
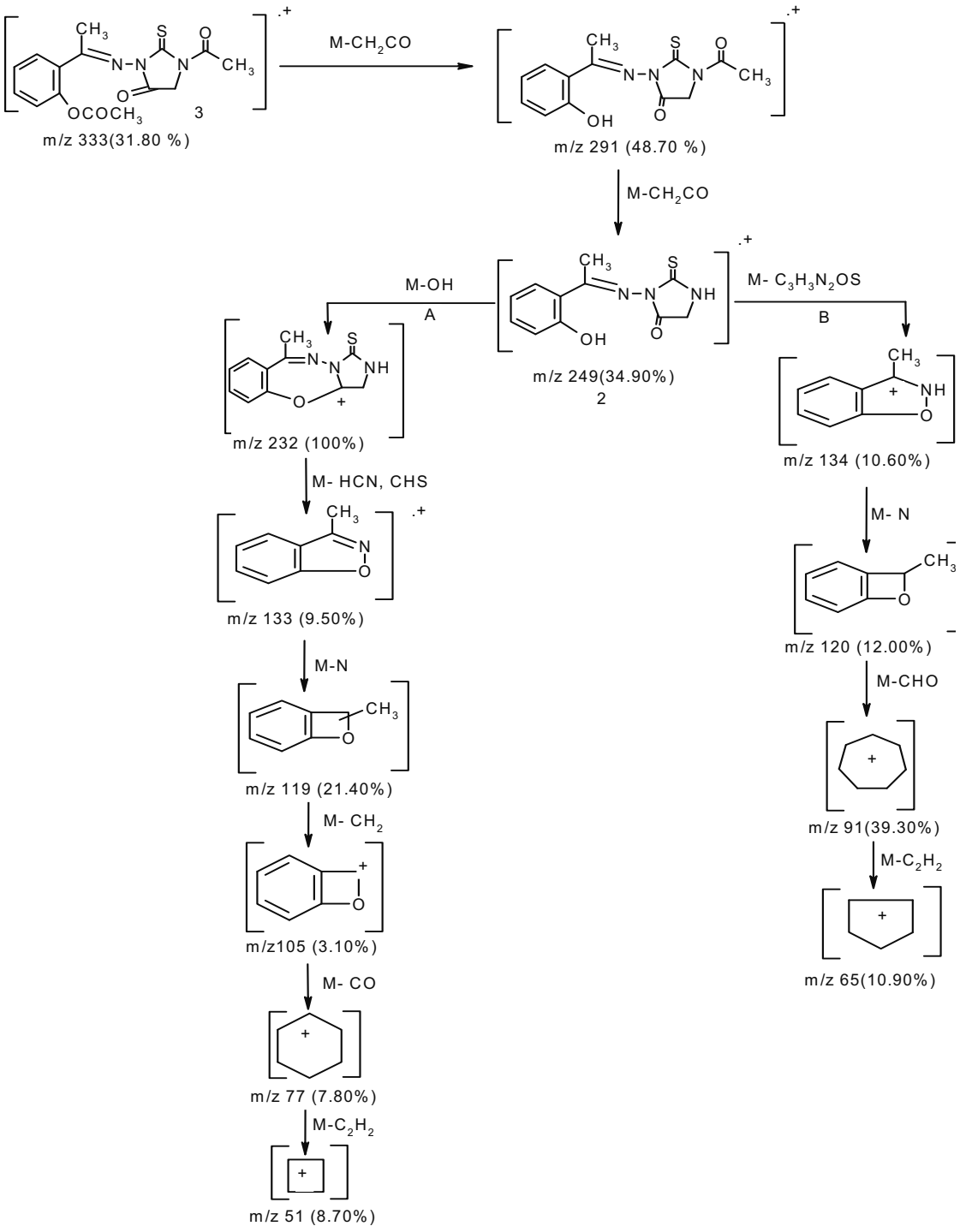


Figure 2.

The mass spectra of compounds 4a, b showed intense molecular ion peaks at *m/z* 353 and 387, consistent with molecular formula C17 H15 N5 O2 S and $C_{17}H_{14}ClN_5O_2S$, respectively. The molecular ion of compounds 4a and 4b underwent fragmentation via pathway A to produce peaks at *m/z* 336 and *m/z* 370 by losing hydroxyl group. The ions at *m/z* 336 and *m/z* 370 underwent fragmentation to give peak at *m/z* 161. The loss of CH = NH group from the ion with *m/z* 161 resulted in an ion at *m/z* 133. The ion at *m/z* 133 underwent loss nitrogen atom, methylene group, carbon monoxide and acetylene molecule to give peaks at *m/z* 119, 105, 77 and *m/z* 51, respectively. Also, the ions of *m/z* 336 and *m/z* 370 underwent broken to give an ions at 175 and m/z 209. The ions of *m/z* 175 and *m/z* 209 underwent loss of carbon monothioxoide (C = S), cyano group (CN) and nitrogen molecule (N_2) to give peaks at m/z 131, 105, 77 and *m/z* 165, 139, 111, respectively.



Scheme 3. Main fragmentation pathway of compds 2 and 3.

The molecular ions of compounds 4a and 4b were also found to undergo fragmentation via pathway B to produce the ion of *m/z* 276 by losing phenyl radical and/ or chlorophenyl radical. The loss of nitrogen molecule (N_2) from the ion with *m/z* 276 resulted in an ion at *m/z* 248. The ion at *m/z* 248 underwent loss of HCN-CO, CS, NH, N and CHO to give peaks at *m/z* 193, 149, 134, 120 and *m/z* 91, respectively. The molecular ion peaks of compounds 5a and 5b were observed at *m/z* 437 and *m/z* 471, corresponding to the molecular formula $C_{21}H_{19}N_5O_4S$ and $C_{21}H_{18}ClN_5O_4S$. The molecular ion of compounds 5a and 5b (*m/z* 437 and 471) had fragmented to give the ions of *m/z* 395 and 429. The loss of $CH_2 = C = O$ ketene molecule from the ion of *m/z* 395 and 429 gave peals at *m/z* 353 and *m/z* 387, corresponding to the molecular ion of compounds 4a and 4b. The ions of *m/z* 353 and 387 were broken via pathway in the same fragmentation processes which observed for compound 4. The mass spectra of compounds 4a, b (Fig. 3) showed the molecular ion peaks were found to be the base peak. The mass spectra of compounds 5a, b illustrated in scheme 4 (Fig. 4) showed the base peak at *m/z* 336 and *m/z* 370, respectively.

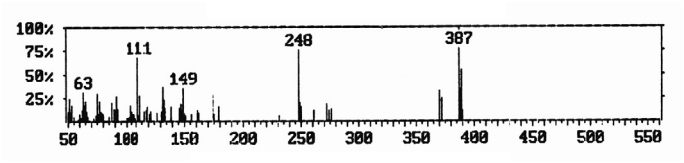


Figure 3.

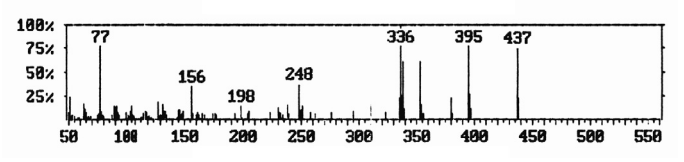
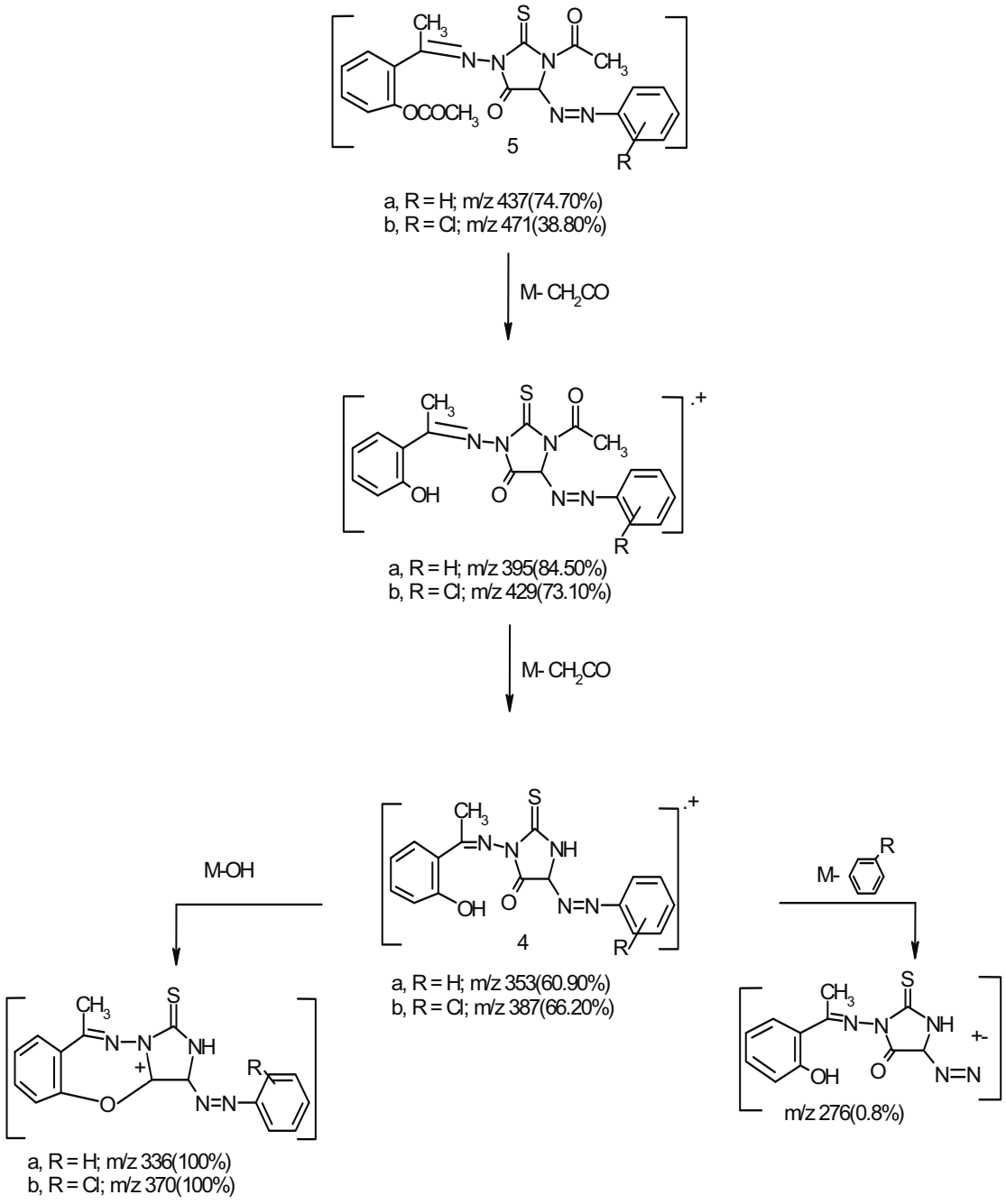


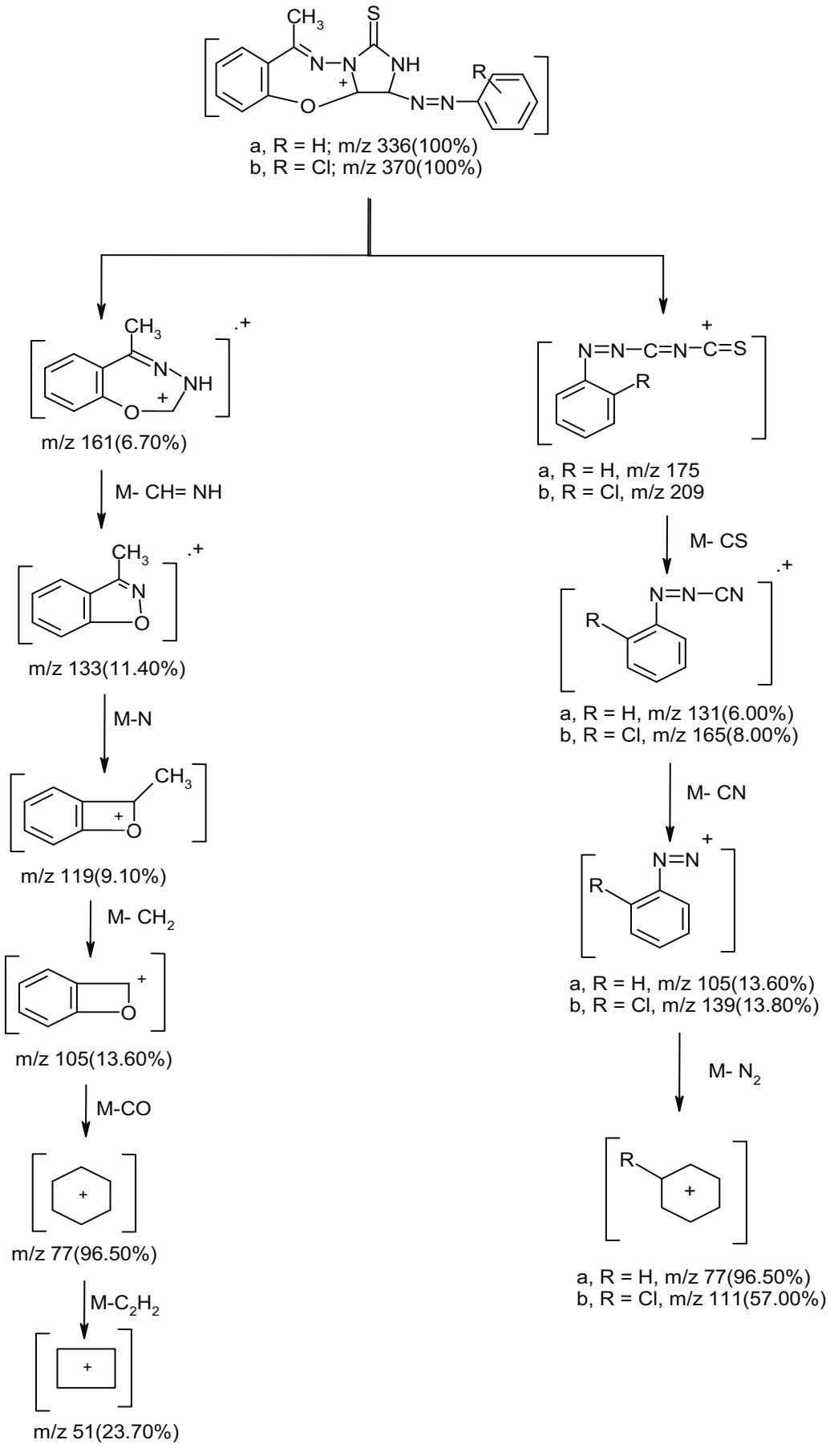
Figure 4.

The mass spectra of compounds 6a, b and 7a, b are fully consistent with the assigned structures. In most cases, intense molecular ion peaks were observed. Thus, compounds 6a, 6b, 7a and 7b showed intense molecular ion peaks at *m/z* 343, 367, 427 and *m/z* 451, consistent with the molecular formula $C_{16}H_{13}N_3O_2S_2$, $C_{19}H_{17}N_3O_3S$, $C_{20}H_{17}N_3O_4S_2$ and $C_{23}H_{21}N_3O_5S$, respectively. From a study of the mass spectra of compounds 6a, b and 7a, b, it was found that the molecular ion for all these compounds fragmented further and involved two various suggested pathways as illustrated by scheme 5.

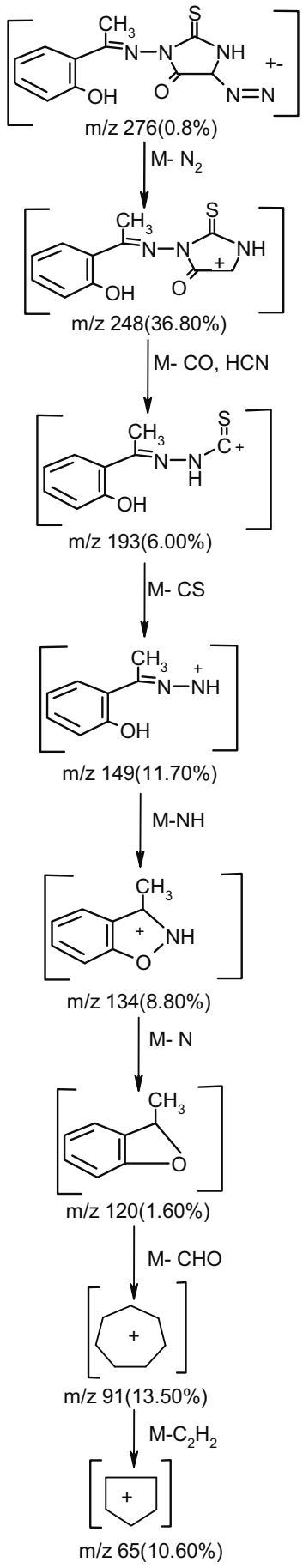
The molecular ion of compounds 6a and 6b had fragmented to stable ions of *m/z* 326 and *m/z* 350. This ions of *m/z* 326 and *m/z* 350 fragmented further and involved two various pathways as illustrated in Table I.



Scheme 4. Main fragmentation pathway of compds 4 and 5.



condt Scheme 4. Main fragmentation pathway of compds 4 and 5.



condt Scheme 4.

TABLE I

EI mass sprectra (70eV) of compounds 1-8, m/z (relative intensity, %).

Compd	M+	Pathway A		Pathway B		Other Ions
		-M	*m/z*	–M	*m/z*	
1	$[C_9H_{11}N_3OS]^+$ 209(63.40)	NH CHS NH N CHO C_2H_2	$[C_9H_{10}N_2OS]^+$ 194(100) $[C_8H_9N_2O]^+$ 149(26.10) $[C_8H_8NO]^+$ 134(16.20) $[C_8H_8O]^+$ 120(20.40) $[C_7H_7]^+$ 91(41.10) $[C_5H_5]^+$ 65(23.30)	NH_2 CHS N_2 CH_3 CO C_2H_2	$[C_9H_9N_2OS]^+$ 193(4.10) $[C_8H_8N_2O]^+$ 148(3.40) $[C_8H_8O]^+$ 120(20.40) $[C_7H_5O]^+$ 105(8.30) $[C_6H_5]^+$ 77(10.50) $[C_4H_3]^+$ 51(11.30)	210(M^++1,6.50), 208(M±1,3.80), 196(8.30) 195(11.60), 167(14.40), 166(10.10), 150(7.80), 145(7.80), 132(4.60), 122(7.20), 119(9.40), 118(4.40), 104(6.10), 103(4.70), 102(3.20), 92(12.60), 90(10.40), 89(4.00), 78(3.60), 76(5.20), 75(9.70), 66(4.40), 60(34.60), 59(3.90), 53(8.30), 52(2.90), 50(5.60)
2	$[C_{11}H_{11}N_3O_2S]^+$ 249(57.90)	OH 2(HCN), CHS N CH_2 CO C_2H_2	$[C_{11}H_{10}N_3OS]^+$ 232(100) $[C_8H_7NO]^+$ 133(14.90) $[C_8H_7O]^+$ 119(8.50) $[C_7H_5O]^+$ 105(5.80) $[C_6H_5]^+$ 77(8.20) $[C_4H_3]^+$ 51(3.30)	$C_3H_3N_2OS$ N CHO C_2H_2	$[C_8H_8NO]^+$ 134(4.70) $[C_8H_8O]^+$ 120(33.60) $[C_7H_7]^+$ 91(24.30) $[C_5H_5]^+$ 65(17.60)	250(M^++1,10.90), 234(18.70), 233(21.60) 202(10.90), 175(8.20), 158(7.30), 135(8.70), 92(14.90), 90(3.80), 88(4.90), 87(10.70), 78(4.70), 66(4.00), 64(3.60), 63(13.10), 53(3.60), 51(4.70)
3	$[C_{15}H_{15}N_3O_4S]^+$ 333(31.80)	CH_2CO CH_2CO OH 2(HCN), CHS N CH_2 CO C_2H_2	$[C_{13}H_{13}N_3O_3S]^+$ 291(48.70) $[C_{11}H_{11}N_3O_2S]^+$ 249(34.90) $[C_{11}H_{10}N_3OS]^+$ 232(100) $[C_8H_7NO]^+$ 133(9.50) $[C_8H_7O]^+$ 119(21.40) $[C_7H_5O]^+$ 105(3.10) $[C_6H_5]^+$ 77(7.80) $[C_4H_3]^+$ 51(8.70)	CH_2CO CH_2CO $C_3H_3N_2OS$ N CHO C_2H_2	$[C_{13}H_{13}N_3O_3S]^+$ 291(48.70) $[C_{11}H_{11}N_3O_2S]^+$ 249(34.90) $[C_8H_8N]^+$ 134(10.60) $[C_8H_8O]^+$ 120(12.00) $[C_7H_7]^+$ 91(39.30) $[C_5H_5]^+$ 65(10.90)	334(M^++1,10.10),292(18.70), 278(4.50), 276(26.90), 248(7.40), 236(10.30), 235(17.10), 234(86.20), 233(18.90), 207(4.50), 206(19.70), 205(3.90), 202(3.80), 191(6.60), 178(7.90), 177(9.60), 158(5.90), 156(32.20), 147(16.30), 146(12.30), 135(10.30), 132(4.30), 130(5.60), 12(4.30), 118(4.30), 104(4.00), 103(2.40), 102(3.20), 101(3.50), 92(5.50), 90(9.80), 89(9.50), 78(3.20), 76(4.00), 69(3.80), 66(3.40), 64(6.90), 63(9.90), 58(4.80), 52(3.70), 50(3.70)
4a	$[C_{17}H_{15}N_5O_2S]^+$ 353(100)	OH		$[C_{17}H_{14}N_5OS]^+$ 336(23.40)		C_6H_5 N_2 HCN, CO CS NH N CHO C_2H_2	$[C_{11}H_{10}N_5O_2S]^+$ 276(4.70) $[C_{11}H_{10}N_3O_2S]^+$ 248(39.00) $[C_9H_9N_2OS]^+$ 193(7.20) $[C_8H_9N_2O]^+$ 149(15.40) $[C_8H_9NO]^+$ 134(3.80) $[C_8H_8O]^+$ 120(3.20) $[C_7H_7]^+$ 91(13.50) $[C_5H_5]^+$ 65(13.10)	354(M^++1,25.10), 251(4.80), 250(6.70), 249(11.70), 238(8.30), 179(6.10), 177(2.70), 166(3.50), 162(3.50), 148(4.60), 147(7.20), 146(4.40), 132(19.50), 130(1.80), 121(8.10), 119(6.00), 118(4.30), 104(10.20), 92(10.00), 90(5.80), 89(7.60), 78(11.60), 76(4.80), 66(5.40), 64(9.30), 63(16.20), 53(7.90), 50(6.10)
		$[C_9H_8N_2O]^+$ 161(5.10)		$[C_8H_5N_3S]^+$ 175(4.30)				
		-M	*m/z*	–M	*m/z*			
		CH=NH N CH_2 CO C_2H_2	$[C_8H_7NO]^+$ 133(8.60) $[C_8H_7O]^+$ 119(6.00) $[C_7H_5O]^+$ 105(8.60) $[C_6H_5]^+$ 77(67.10) $[C_4H_3]^+$ 51(33.20)	CS CN N_2 C_2H	$[C_7H_5N_3]^+$ 131(3.90) $[C_6H_5N_2]^+$ 105(8.70) $[C_5H_3]^+$ 77(67.10) $[C_4H_4]^+$ 52(5.50)			

TABLE I (cont.)

EI mass sprectra (70eV) of compounds 1-8, m/z (relative intensity, %).

Compd	M+	Pathway A				Pathway B		Other Ions
		-M	*m/z*			–M	*m/z*	
4b	$[C_{17}H_{14}ClN_5O_2S]^+$ 387(100)	OH		$[C_{17}H_{13}ClN_5OS]^+$ 370(31.70)		C_6H_4Cl	$[C_{11}H_{10}N_5O_2S]^+$ 276(13.00)	389(M^++2,54.10), 372(23.20),
		$[C_9H_9N_2O]^+$ 161(11.50)		$[C_8H_7ClN_5S]^+$ 209(0.01)		N_2	$[C_{11}H_{10}N_5O_2S]^+$ 248(75.00)	274(10.70), 272(18.20), 261(11.70), 250(15.70),
		-M	*m/z*	–M	*m/z*	HCN	$[C_9H_9N_2OS]^+$ 193(0.20)	249(20.00), 231(6.30), 179(15.10), 175(7.30), 174(27.90), 162(9.10),
		CH=NH	$[C_8H_7NO]^+$ 133(21.90)	CS	$[C_7H_4ClN_3]^+$ 165(2.10)	CS	$[C_8H_9N_2O]^+$ 149(34.70)	156(7.00), 151(5.00), 150(8.90), 148(11.50), 147(17.70),
		N	$[C_8H_7O]^+$ 119(14.80)	CN	$[C_6H_4ClN_2]^+$ 139(14.80)	NH	$[C_8H_8NO]^+$ 134(14.60)	146(13.50), 132(35.70), 131(10.40), 122(9.70), 118(11.90),
		CH_2	$[C_7H_5O]^+$ 105(9.40)	N_2	$[C_6H_4Cl]^+$ 111(67.70)	N	$[C_8H_8O]^{\cdot+}$ 120(6.70)	106(7.10), 104(16.40), 103(4.10), 92(12.50), 90(11.40), 89(13.00),
		CO	$[C_6H_5]^+$ 77(20.30)	C_2H	$[C_6H_3]^+$ 75(29.20)	CHO	$[C_7H_7]^+$ 91(25.80)	87(19.20), 78(9.70), 76(7.50), 66(9.40), 64(16.40), 63(29.70),
		C_2H_2	$[C_4H_3]^+$ 51(23.50)		$[C_4H_2]^+$ 50(10.10)	C_2H_2	$[C_5H_5]^+$ 65(21.40)	62(11.20), 53(16.10), 52(8.60)
5a	$[C_{21}H_{19}N_5O_4S]^{\cdot+}$ 436(74.70)	CH_2CO		$[C_{19}H_{17}N_5O_3S]^{\cdot+}$ 395(89.50)		CH_2CO	$[C_{19}H_{17}N_5O_3S]^{\cdot+}$ 395(89.50)	438(M^++1,22.30), 397(11.40),
		CH_2CO		$[C_{17}H_{15}N_5O_2S]^{\cdot+}$ 353(60.90)		CH_2CO	$[C_{17}H_{15}N_5O_2S]^{\cdot+}$ 353(60.90)	396(25.80), 381(6.20), 380(21.70), 354(15.50), 339(11.50),
		OH		$[C_{17}H_{14}N_5OS]^+$ 336(100)		C_6H_5	$[C_{11}H_{10}N_5O_2S]^+$ 276(7.60)	338(60.60), 337(24.40), 335(21.70), 323(6.80), 310(5.30),
		$[C_9H_9N_2O]^+$ 161(6.70)		$[C_8H_5N_3S]^+$ 175(5.70)		N_2	$[C_{11}H_{10}N_3O_2S]^+$ 248(36.40)	295(8.10), 262(6.00), 251(13.60), 249(9.80), 238(15.10), 234(4.80),
		-M	*m/z*	–M	*m/z*	HCN, CO	$[C_9H_9N_2OS]^+$ 193(6.00)	231(6.70), 230(12.10), 223(7.70), 205(8.30), 204(5.60), 198(13.20),
		CH=NH	$[C_8H_7NO]^+$ 133(8.20)	CS	$[C_7H_5N_3]^{\cdot+}$ 131(3.50)	CS	$[C_8H_9N_2O]^+$ 149(8.10)	176(5.70), 167(3.90), 165(5.30), 162(3.90), 157(5.90), 156(39.30),
		H	$[C_8H_7O]^+$ 119(7.60)	CN	$[C_6H_5N_2]^+$ 105(13.60)	NH	$[C_8H_8NO]^+$ 134(8.80)	148(5.50), 146(9.60), 145(9.70), 132(15.60), 130(4.90), 121(3.30),
		N	$[C_7H_5O]^+$ 105(13.60)	N_2	$[C_6H_5]^+$ 77(96.50)	N	$[C_8H_8O]^{\cdot+}$ 120(1.60)	118(8.60), 104(8.50), 103(3.50), 92(6.80), 90(12.10), 89(13.70),
		CH_2	$[C_6H_5]^+$ 77(96.50)	C_2H	$[C_4H_4]^+$ 52(3.50)	CHO	$[C_7H_7]^+$ 91(13.50)	78(8.40), 76(5.50), 64(11.20), 63(17.70), 53(3.80), 50(6.70)
		CO	$[C_4H_3]^+$ 51(23.70)			C_2H_2	$[C_5H_5]^+$ 65(7.60)	
		C_2H_2						

TABLE I (cont.)

EI mass sprectra (70eV) of compounds 1-8, m/z (relative intensity, %).

Compd	M+	Pathway A				Pathway B		Other Ions
		-M	*m/z*			–M	*m/z*	
5b	$[C_{21}H_{19}N_5O_4S]^+$	CH_2CO	$[C_{19}H_{16}ClN_5O_3S]^+$			CH_2CO	$[C_{19}H_{16}ClN_5O_3S]^+$	
	471(38.80)		429(73.10)				429(73.10)	473(M^++2,20.60), 431(28.40),
		CH_2CO	$[C_{17}H_{14}ClN_5O_2S]^+$			CH_2CO	$[C_{17}H_{14}ClN_5O_2S]^+$	430(19.30), 416(11.80),
			387(66.20)				387(66.20)	415(12.80), 414(24.60),
		OH	$[C_{17}H_{13}ClN_5OS]^+$			C_6H_4Cl	$[C_{11}H_{10}N_5O_2S]^+$	389(37.60), 388(18.80),
			370(100)				276(10.80)	374(26.00), 373(29.50),
		$[C_9H_9N_2O]^+$	$[C_8H_7ClN_5S]^+$			N_2	$[C_{11}H_{10}N_3O_2S]^+$	372(80.40), 371(27.50),
		161(11.50)	209(0.01)				248(36.80)	369(11.70), 344(22.70),
		-M	*m/z*	–M	*m/z*	HCN, CO	$[C_9H_9N_2OS]^+$	316(13.30), 284(10.20), 274(16.20),
		CH=NH	$[C_8H_7NO]^+$	CS	$[C_7H_4ClN_3]^+$		193(3.30)	273(12.60), 272(26.40),
		H	133(11.40)		165(8.00)	CS	$[C_8H_9N_2O]^+$	259(10.20), 258(11.60),
			$[C_8H_7O]^+$	CN	$[C_6H_4ClN_2]^+$		149(11.70)	257(10.90), 233(7.90), 232(16.30),
		N	119(9.00)		139(13.80)	NH	$[C_8H_9NO]^+$	230(17.60), 227(10.10),
			$[C_7H_5O]^+$	N_2	$[C_6H_4Cl]^+$		139(4.80)	205(10.10), 197(3.80), 192(4.00),
		CH_2	105(5.00)		111(57.00)	N	$[C_8H_8O]^+$	191(6.50), 179(6.40), 177(8.30),
			$[C_6H_5]^+$	HCl	$[C_6H_3]^+$		120(6.80)	174(6.30), 148(4.00), 146(8.80),
		CO	77(11.40)		75(16.80)	CHO	$[C_7H_7]^+$	141(4.80), 140(5.80), 132(15.80),
			$[C_4H_3]^+$	C_2H	$[C_4H_2]^+$		91(12.10)	131(6.00), 128(30.20), 127(10.40),
		C_2H_2	51(13.70)		50(8.40)	C_2H_2	$[C_5H_5]^+$	118(13.30), 113(23.60),
							65(10.60)	104(13.70), 103(3.10), 90(20.60),
								89(20.40), 78(4.40), 76(8.30),
								64(10.70), 63(13.40), 52(7.80)
6a	$[C_{16}H_{13}N_3O_2S_2]^+$	OH	$[C_{16}H_{12}N_3OS_2]^+$			OH	$[C_{16}H_{12}N_3OS_2]^+$	
	343(45.70)		326(100)				326(100)	344(M^++1,14.40), 328(23.50),
		$C_8H_5N_2S_2$	$[C_8H_7NO]^+$			C_8H_7NO	$[C_8H_5N_2S_2]^+$	327(26.80), 300(3.70), 250(2.10),
			133(3.00)				193(2.10)	176(4.80), 175(4.20), 169(5.90),
		N	$[C_8H_7O]^+$			CN	$[C_7H_5NS_2]^+$	168(2.60), 146(3.50), 142(8.80),
			119(6.60)				167(6.50)	141(14.00), 139(5.10), 135(9.90),
		CO	$[C_7H_7]^+$			HCN	$[C_6H_4S_2]^+$	134(5.50), 120(3.50), 108(6.60),
			91(16.90)				140(74.30)	105(2.70), 104(2.90), 103(11.60),
		C_2H_2	$[C_5H_5]^+$			CS	$[C_5H_4S]^+$	97(8.40), 95(7.60), 92(5.30),
			65(13.70)				96(9.00)	90(2.70), 77(4.40), 64(6.60),
						S	$[C_5H_4]^+$	63(8.00), 52(2.60), 51(5.20),
							64(6.60)	50(2.90)

TABLE I (cont.)

EI mass sprectra (70eV) of compounds 1-8, m/z (relative intensity, %).

Compd	M+	Pathway A		Pathway B		Other Ions
		-M	*m/z*	–M	*m/z*	
6b	$[C_{19}H_{17}N_3O_3S]^{+}$ 367(52.70)	OH	$[C_{19}H_{16}N_3O_2S]^{+}$ 350(100)	OH	$[C_{19}H_{16}N_3O_2S]^{+}$ 350(100)	368(M^{+}+1,21.20), 352(21.10), 351(28.50), 175(4.20), 165(8.50), 150(5.30), 149(21.10), 91(1.70), 105(1.20), 92(1.20), 91(1.70), 89(3.30), 78(0.60), 77(1.40), 76(2.50), 63(4.20), 51(2.60), 50(3.00)
		$C_{11}H_8N_2OS$	$[C_8H_7NO]^{+}$ 133(2.00)	C_8H_7NO	$[C_{11}H_9N_2OS]^{+}$ 217(0.10)	
		N	$[C_8H_7O]^{+}$ 119(2.10)	CN	$[C_{10}H_9NOS]^{+}$ 191(5.10)	
		CO	$[C_7H_7]^{+}$ 91(1.70)	HCN	$[C_9H_8OS]^{+}$ 164(39.00)	
		C_2H_2	$[C_5H_5]^{+}$ 65(2.40)	CS	$[C_8H_8S]^{+}$ 120(0.30)	
				CH_2O	$[C_7H_6]^{+}$ 90(3.60)	
				C_2H_2	$[C_5H_4]^{+}$ 64(3.60)	
7a	$[C_{20}H_{17}N_3O_4S_2]^{+}$ 427(49.70)	CH_2CO	$[C_{18}H_{15}N_3O_3S_2]^{+}$ 385(35.00)	CH_2CO	$[C_{18}H_{15}N_3O_3S_2]^{+}$ 385(35.00)	428(M^{+}+1,21.60), 412(8.70), 387(7.60), 386(9.10), 370(26.60), 331(3.20), 330(16.50), 329(21.70), 328(84.00), 327(34.30), 300(17.90), 284(7.90), 252(5.70), 250(21.40), 182(1.10), 181(9.10), 178(7.40), 176(3.10), 175(4.40), 169(4.70), 168(2.50), 146(9.00), 141(11.00), 139(2.80), 135(8.40), 134(7.80), 121(2.30), 120(9.60), 108(9.10), 101(4.10), 97(6.70), 95(5.40), 92(3.40), 90(5.70), 75(2.00), 63(9.20), 52(2.50), 51(3.80), 50(2.80)
		CH_2CO	$[C_{16}H_{13}N_3O_2S_2]^{+}$ 343(9.40)	CH_2CO	$[C_{16}H_{13}N_3O_2S_2]^{+}$ 343(9.40)	
		OH	$[C_{16}H_{12}N_3OS_2]^{+}$ 326(100)	OH	$[C_{16}H_{12}N_3OS_2]^{+}$ 326(100)	
		$C_8H_5N_2S_2$	$[C_8H_7NO]^{+}$ 133(7.80)	C_8H_7NO	$[C_8H_5N_2S_2]^{+}$ 193(1.30)	
		N	$[C_8H_7O]^{+}$ 119(16.10)	CN	$[C_7H_5NS_2]^{+}$ 167(2.90)	
		CO	$[C_7H_7]^{+}$ 91(21.40)	HCN	$[C_6H_4S_2]^{+}$ 140(39.60)	
		C_2H_2	$[C_5H_5]^{+}$ 65(11.20)	CS	$[C_5H_4S]^{+}$ 96(16.20)	
				S	$[C_5H_4]^{+}$ 64(5.30)	
7b	$[C_{23}H_{21}N_3O_5S]^{+}$ 451(53.20)	CH_2CO	$[C_{21}H_{19}N_3O_4S]^{+}$ 409(39.50)	CH_2CO	$[C_{21}H_{19}N_3O_4S]^{+}$ 409(39.50)	452(M^{+}+1,22.50), 410(21.30), 407(3.50), 368(3.50), 366(4.20), 352(12.30), 351(72.30), 349(26.30), 285(2.30), 284(6.20), 250(1.30), 232(1.30), 216(1.60), 210(1.30), 205(2.20), 134(5.50), 132(2.50), 192(4.20), 190(1.10), 165(10.20), 163(8.50), 157(1.30), 156(12.30), 149(6.30), 148(4.00), 121(1.30), 105(2.30), 104(2.20), 93(2.10), 89(5.20), 77(11.60), 75(6.50), 52(3.50), 51(6.50)
		CH_2CO	$[C_{19}H_{17}N_3O_3S]^{+}$ 367(13.30)	CH_2CO	$[C_{19}H_{17}N_3O_3S]^{+}$ 367(13.30)	
		OH	$[C_{19}H_{16}N_3O_2S]^{+}$ 350(100)	OH	$[C_{19}H_{16}N_3O_2S]^{+}$ 350(100)	
		$C_{11}H_9N_2OS$	$[C_8H_7NO]^{+}$ 133(6.80)	C_8H_7NO	$[C_{11}H_9N_2OS]^{+}$ 217(0.30)	
		N	$[C_8H_7O]^{+}$ 119(17.20)	CN	$[C_{10}H_9NOS]^{+}$ 191(6.30)	
		CO	$[C_7H_7]^{+}$ 91(27.25)	HCN	$[C_4H_8OS]^{+}$ 164(43.30)	
		C_2H_2	$[C_5H_5]^{+}$ 65(7.20)	CS	$[C_8H_8O]^{+}$ 120(1.30)	
				CH_2O	$[C_7H_6]^{+}$ 90(7.60)	
				C2H_2	$[C_5H_4]^{+}$ 64(5.30)	

TABLE I (cont.)

EI mass sprectra (70eV) of compounds 1-8, m/z (relative intensity, %).

Compd	M+	Pathway A		Pathway B		Other Ions
		-M	*m/z*	-M	*m/z*	
8	$[C_{16}H_{16}N_2O_2]^+$ 268(100)	C_8H_8NO	$[C_8H_8NO]^+$ 134(40.50)	CH_3	$[C_{15}H_{13}N_2O_2]^+$ 253(82.80)	269(M^++1,20.0), 254(23.40), 252(10.40), 251(32.70), 212(10.10), 148(10.90), 133(24.90), 132(4.30), 131(3.30), 107(6.80), 106(5.60), 104(5.20), 102(4.40), 93(8.10), 92(12.00), 90(7.10), 89(4.60), 79(4.10), 78(6.80), 75(4.70), 66(5.80), 64(11.10), 63(15.20), 62(4.70), 55(4.40), 53(11.80), 52(6.10), 50(5.20)
		$C_{11}H_8N_2OS$	$[C_8H_8O]^+$ 120(19.70)	CH=CHOH	$[C_{13}H_{10}N_2O]^+$ 210(14.20)	
		N	$[C_7H_7]^+$ 91(49.00)	C_6H	$[C_8H_8N_2O]^+$ 149(11.70)	
		CO	$[C_5H_5]^+$ 65(43.50)	N	$[C_8H_9NO]^{+\cdot}$ 135(18.50)	
				CH_3	$[C_7H_5NO]^{+\cdot}$ 119(12.40)	
				N	$[C_7H_5O]^+$ 105(5.30)	
				CO	$[C_6H_5]^+$ 77(10.90)	
				C_2H_2	$[C_4H_3]^+$ 51(10.90)	

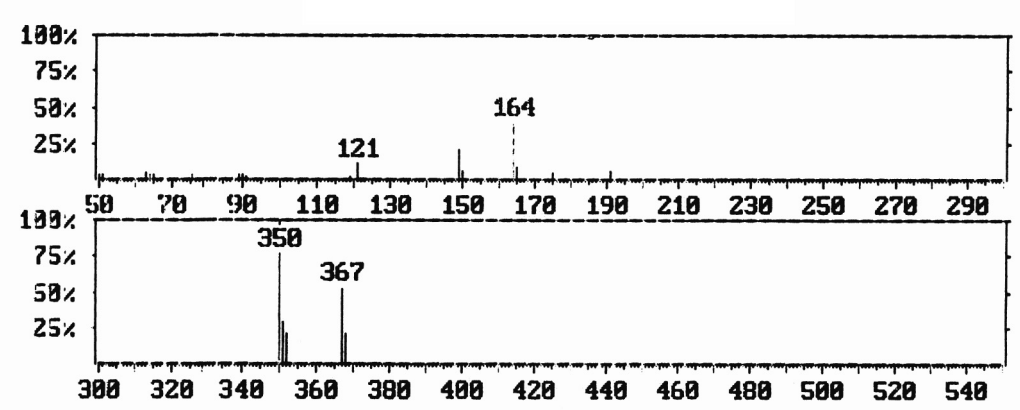


Figure 5.

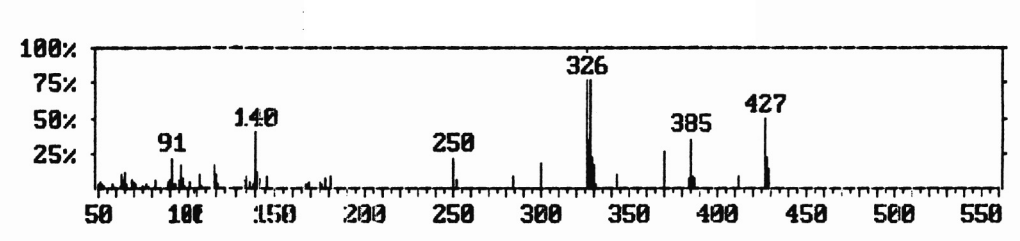


Figure 6.

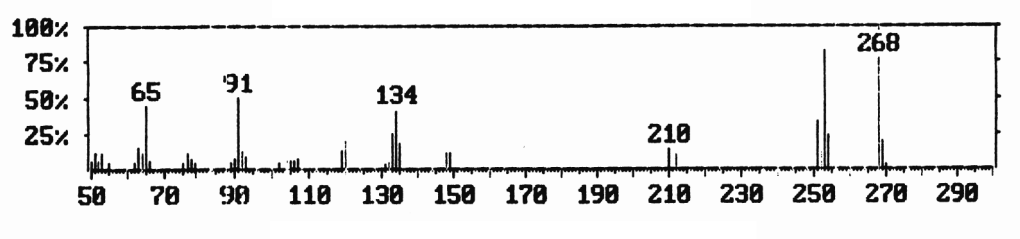
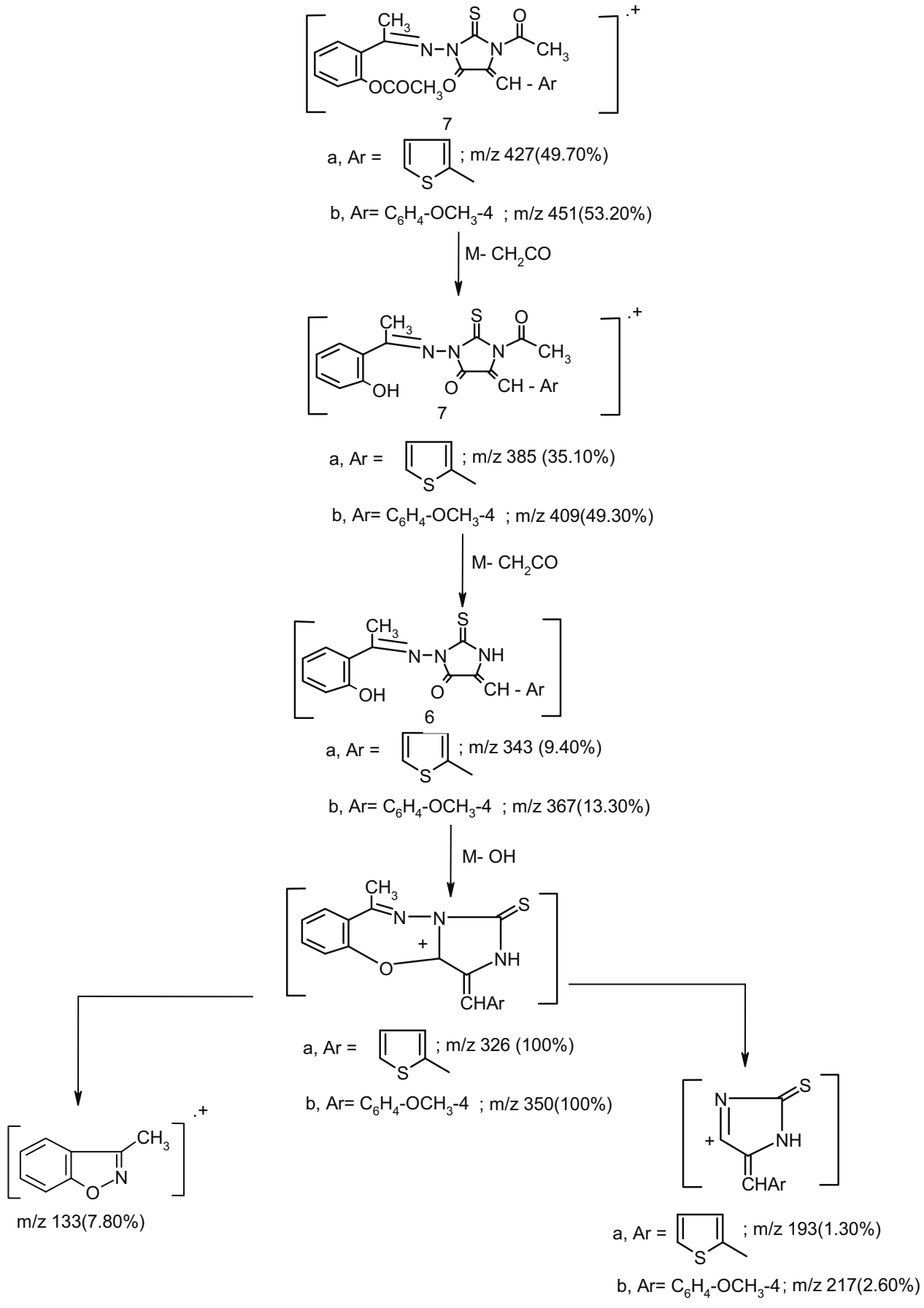
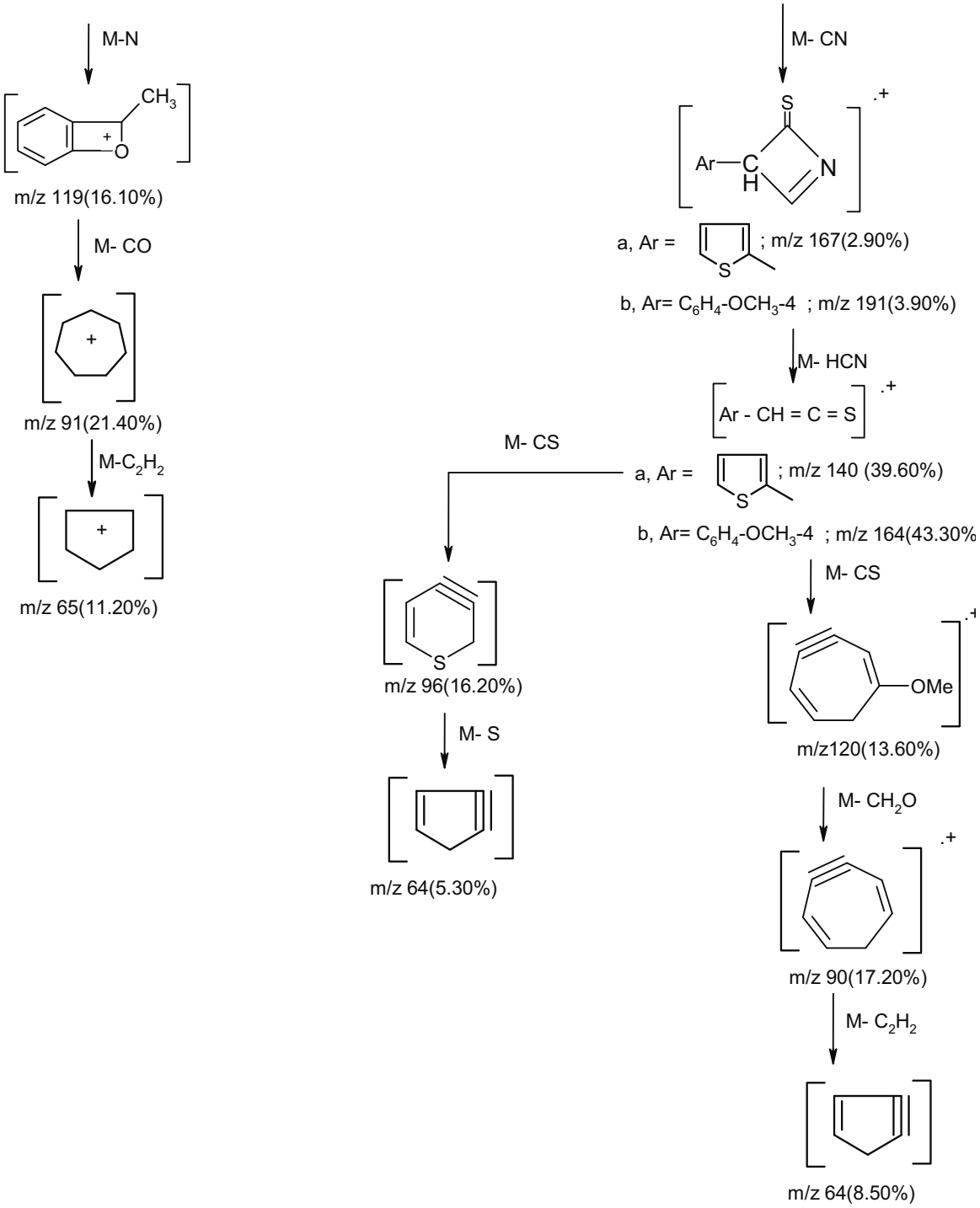


Figure 7.



Scheme 5. Main fragmentation pathway of compds 6 and 7.



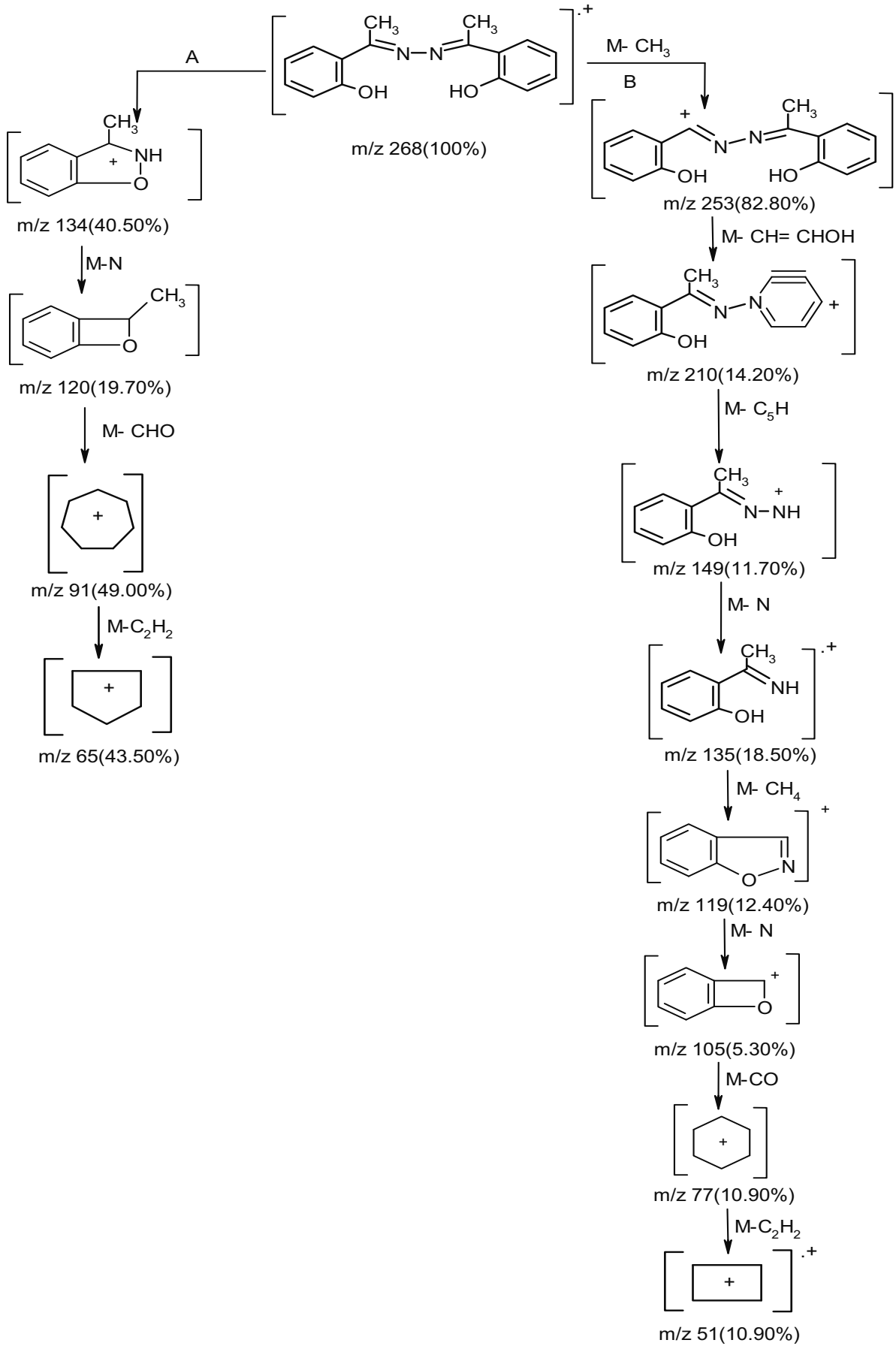
condt Scheme 5. Main fragmentation pathway of compds 6 and 7.

The ions of *m/z* 326 and *m/z* 350 fragmented via the pathway A and gave a fragmented ion of *m/z* 133 which further fragmented and gave a fragmented ion of *m/z* 119 by losing nitrogen atom. The loss of carbon monoxide from the ion of *m/z* 119 gave a peak at *m/z* 91.

Subsequently, the fragmented ions of *m/z* 326 and *m/z* 350 fragmented via pathway B to give fragmented ions of *m/z* 193 and *m/z* 217. This fragmentation led to other different ions, which depending on the nature of substituent in aromatic ring.

The molecular ions of compounds 7a, b (*m/z* 427 and 451) had fragmented to give the ion of *m/z* 385 and 409 by losing CH_2CO molecule. The loss of $CH_2 = C = O$ ketene molecule from the ions at *m/z* 385 and *m/z* 409 gave peaks at *m/z* 343 and *m/z* 367, corresponding to the molecular ion of compounds 6a and 6b. The ions of *m/z* 343 and *m/z* 367 were broken via pathway in the same fragmentation processes which observed for compound 6.

The mass spectra of compounds 6a, b (Fig. 4) and 7a, b (Fig. 5) showed the base peak at *m/z* 326 and *m/z* 350.



Scheme 6. Main Fragmentation Pathway of compound 8.

TABLE II

– No antimicrobial activity, + Mild activity, ++ Moderate activity, +++ Marked activity.

Compd No	Antibacterial Activity					Antifungal Activity	
	Gram Positive Bacteria			Gram Negative Bacteria			
	Bacillus Subtilis	Staphylococcus Aureas	Streptococcus Pneumonia	Escherichia Coli	Pseudomonas Solanarium	Aspergillus Nigaer	Penicillum
1	+	–	–	–	–	+	+
2	+	++	–	+	–	–	+
3	+++	+++	+	+	+	+	+++
4a	+	–	–	++	–	++	+
4b	++	+	–	+++	+	+++	+++
5a	+	–	+++	+	+++	+	+++
5b	–	+	+	+++	+++	+	–
6a	+	++	+++	+	+	+++	+
7a	+	++	+	+	+++	+++	+++
8	+	+	–	–	++	+++	+

The mass spectrum of compound 8 showed an intense molecular ion peak at *m/z* 268, corresponding to the molecular formula $C_{16}H_{16}N_2O_2$. The molecular ion peak was found to be the base peak (Fig. 6). The molecular ion of 8 (Scheme 6) underwent fragmentation via pathway A to produce peak at *m/z* 134. It further underwent loss of N, CHO and C_2H_2 to give peaks at *m/z* 120, 91 and *m/z* 65, respectively.

The molecular ion of compound 8 was also found to undergo fragmentation via the pathway B to produce the ion of *m/z* 253 by losing methyl group. This fragmentation led to *m/z* 210, 149, 135, 114, 105 and *m/z* 77, respectively.

3 - BIOLOGICAL ACTIVITY

Using paper disc agar diffusion technique[19, 20] all the newly synthesized compounds were tested in vitro for antibacterial activity against sever at strains of bacteria such as *Bacillus subtilis*, *Straphylocouus aureas*, *Streptococcus pneumonia*, *Escherichia coli* and *Pseudomonas solanarium*. Also these compounds were tested in vitro against some fungi such as *Aspergillus Nigar* and *Penicillium*. The compounds were tested at 100µg/ml concentration and the activity was determined by measuring Zone of inhibition. The screening results given in Table II indicated that all the compounds exhibited antibacterial and antifungal activities against one or the other type of bacteria and fungi.

4 - EXPERIMENTAL

Melting points were determined in capillaries with a Thomas-Hover Uni-Melt apparatus and are uncorrected. Infrared spectra were taken on a Perkin-Elmer 337 spectrophotometer using KBr wafers. Proton NMR spectra were obtained on a Varian EM 360 spectrometer using solutions in hexadeuteroiodimethyl sulfoxide with tetramethyl silana as the internal standard. Mass spectra were recorded on a VG Autspec GEI FAB$^+$ and a Hewlett Packard MS-Engine thermo spray and ionization by electron impact at 70 eV. The accelerating voltage was 6 kv, the temperature of the source was ~ 200oC, and the emission current ~100 mA. Microanalysis were conducted using on a Perkin-Elmer 2408 CHN analyzer.

2-Hydroxyacetophenone thiosemicarbazone (1)

A mixture of 2-hydroxyacetophenone (0.01 mole) and thiosemicarbazide (0.01 mole) in methanol (30 ml) was heated under reflux for 4 hr, and then cooled. The resulting solid was filtered off, washed with methanol, dried and recrystallized from methanol to give 1 as colourless, yield 76%, mp: 167 ºC, IR (KBr): 3398, 3213 (NH_2), 3270 (NH), 3430-2727 (br. OH), 1620 (C=N), 1605, 1581 (C=C), 1423 (C=S), 1238, 1107 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.21 (S, 3H, CH_3), 6.91 (S, 2H, NH_2), 7.12-7.83 (m, 4H, Ar H), 10.65 (s, 1H, NH), 11.98 (S, 1H, OH) ppm. Anal. Calcd for $C_9H_{11}N_3OS$: C, 51.67; H, 5.26; N, 20.10; S, 15.31. Found: C, 51.33; H, 5.02; N, 19.82; S, 15.11.

3-[1-(2-Hydroxyphenylethylidene)-amino]-2-thiohydantoin (2)

A mixture of 1 (0.01 mole) and ethylchloroacetate (0.01 mole) in methanol (50 ml) in the presence of fused sodium acetate (0.03 mole) was heated under reflux for 4 hr. The reaction mixture was cooled and poured into water. The resulting solid was filtered off, washed with hot water, dried and recrystallized from ethanol to give 2 as pale yellow crystals, yield 75%, mp: 225 ºC, IR (KBr): 3252 (NH), 3430-2590 (br. OH), 1701 (C=O), 1623 (C=N), 1612, 1562 (C=C), 1442 (C=S), 1161, 1026 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.38 (S, 3H, CH_3), 3.55 (S, 2H, COH_2-N), 6.91-7.71 (m, 4H, Ar H), 12.16 (S, 1H, NH), 12.61 (S, 1H, OH) ppm. Anal. Calcd for $C_{11}H_{11}N_3O_2S$: C, 53.01; H, 4.42; N, 16.87; S, 12.85. Found: C, 52.81; H, 4.19; N, 16.69; S, 12.59.

5-Arylazo-3-[1-(2-hydroxyphenylethylidene)-amino]-2-thiohydantoins (4a, b)

A solution of 2 (0.01 mole) in aqueous sodium hydroxide (5 ml, 10%) was chilled in ice to 0-5 ºC. A cold aqueous solution (0-5 ºC) of the diazonium salt (0.01 mole) was added dropwise with stirring during 45 min. After addition the

reaction mixture was stirred for further 30 min. and then left for 2 hr. in a refrigerator. The precipitated product was collected, washed with water, dried, and purified by recrystallization with ethanol to give 4. 5-phenylazo-3-[1-(2-Hydroxyphenylethylidene)-amino]-2-thiohydantoin (4a) as red crystals, yield 68%, mp: 286 ºC, IR(KBr): 3143 (NH), 3395-2588 (br. OH), 1716 (C=O), 1623 (C=N), 1612, 1580 (C=C), 1419 (C=S), 1122, 1072 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.24 (S, 3H, CH_3), 4.21 (S, 1H, COHN), 7.10- 8.01 (m, 9H, Ar H), 12.23 (S, 1H, NH), 13.27(S, 1H, OH) ppm. Anal. Calcd for $C_{17}H_{15}N_5O_2S$: C, 57.79; H, 4.25; N, 19.83; S, 9.07. Found: C, 57.52; H, 4.03; N, 19.71; S, 8.88.

5-(2-chlorophenylazo)-3-[1-(2-Hydroxyphenylethylidene)-amino]-2-thiohydantoin (4b) as deep orange crystals, yield 63%, mp: 279 ºC, IR (KBr): 3136 (NH), 3381-2557 (br. OH), 1716 (C=O), 1623 (C=N), 1612, 1589 (C=C), 1415 (C=S), 1118, 1056 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.34 (S, 3H, CH_3), 4.25 (S, 1H, COHN), 7.41-8.40 (m, 8H, Ar H), 12.18 (S, 1H, NH), 13.30 (S, 1H, OH) ppm. Anal. Calcd for $C_{17}H_{14}ClN_5O_2S$: C, 52.71; H, 3.62; N, 18.09; Cl, 9.04; S, 8.27. Found: C, 52.49; H, 3.43; N, 17.82; Cl, 8.79; S, 8.02.

5-Arylidene-3-[1-(2-hydroxyphenylethylidene)-amino]-2-thiohydantoins (6a, b)

A mixture of 2 (0.01 mole), aromatic aldehydes (such as thiophene-2-carboxaldehyde and 4-methoxybenzaldehyde (0.01 mole)) and piperidine (1 ml) was fused on a hot plate at 120-125 ºC for 1 hr. The reaction mixture was cooled and acidified with dilute hydrochloric acid (2%). The crude product was filtered off, washed with water, dried and purified by recrystallization from acetic acid to give compound 6. 5-(Thiophen-2-ylidene)-3-[1-(2-hydroxyphenylethylidene)-amino]-2-thiohydantoin (6a) as yellow crystals, yield 73%, mp: 256 ºC, IR (KBr): 3190 (NH), 3380-2480 (br. OH), 1701 (C=O), 1626 (C=N), 1612, 1589 (C=C), 1415 (C=S), 1203, 1053 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.81(S, 3H, CH_3), 6.80-8.11(m, 8H, Ar H, olefinic proton and thiophene-H), 12.17 (S, 1H, NH), 12.76 (br. S., 1H, OH) ppm. Anal. Calcd for $C_{16}H_{13}N_3O_2S_2$: C, 55.98; H, 2.99; N, 12.24; S, 18.66. Found: C, 55.67; H, 2.78; N, 12.03; S, 18.39.

5-(4-Methoxy)benzylidene-3-[1-(2-Hydroxyphenylethylidene)-amino]-2-thiohydantoin (6b) as yellow crystals, yield 79%, mp: 263 ºC, IR (KBr): 3210 (NH), 3440-2750 (br. OH), 1712 (C=O), 1620 (C=N), 1605, 1508 (C=C), 1446 (C=S), 1164, 1026 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.61 (S, 3H, CH_3), 3.98 (S, 3H, OCH_3), 6.81-7.91 (m, 9H, Ar H, olefinic proton), 12.10 (S, 1H, NH), 12.81 (S., 1H, OH) ppm. Anal. Calcd for $C_{19}H_{17}N_3O_3S$: C, 62.13; H, 4.63; N, 11.44; S, 8.72. Found: C, 62.01; H, 4.34; N, 11.21; S, 8.51.

1-Acetyl-3-[1-(2-acetoxyphenylethylidene)- amino]-5-substituted-2-thiohydantoins (3,5 and 7)

A solution of 2, 4 and/ or 6 (0.01 mole) in acetic anhydride (25 ml) was heated under reflux for 2 hr, then cooled and poured into ice-water. The solid formed was filtered off, washed with water, dried and recrystallization from benzene to give 3, 5 and 7.

1-Acetyl-3-[1-(2-acetoxyphenylethylidene)-amino]-2-thiohydantoin (3) as pale yellow crystals, yield 53%, mp: 120 ºC, IR (KBr): 1759, 1724 (C=O), 1625 (C=N), 1612, 1592 (C=C), 1415 (C=S), 1191, 1010 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.11 (S, 3H, $COCH_3$), 2.24 (S, 3H, $COCH_3$), 3.35 (S, 3H, CH_3), 4.23 (S, 2H, NCH_2CO), 7.11-7.78 (m, 4H, Ar H) ppm. Anal. Calcd for $C_{15}H_{15}N_3O_4S$: C, 54.05; H, 4.50; N, 12.61; S, 9.61. Found: C, 53.82; H, 4.33; N, 12.28; S, 9.34.

1-Acetyl-3-[1-(2-acetoxyphenylethylidene)-amino]-5-phenylazo-2-thiohydantoin (5a) as pale red crystals, yield 51%, mp: 165 ºC, IR (KBr): 1753, 1732 (C=O), 1625 (C=N), 1604, 1582 (C=C), 1411 (C=S), 1188, 1010 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.21(S, 3H, $COCH_3$), 2.31 (S, 3H, $COCH_3$), 3.35 (S, 3H, CH_3), 4.25 (S, 2H, NCH_2CO), 7.12-8.10 (m, 9H, Ar H) ppm. Anal. Calcd for $C_{21}H_{19}N5$ O4 S: C, 57.66; H, 4.35; N, 16.02; S, 7.32. Found: C, 57.35; H, 4.22; N, 15.87; S, 7.02.

1-Acetyl-3-[1-(2-acetoxyphenylethylidene)-amino]-5-(2-chloro)phenylazo-2-thiohydantoin (5b) as orange crystals, yield 58%, mp: 175 ºC, IR (KBr): 1753, 1735, 1711 (C=O), 1623 (C=N), 1605, 1578 (C=C), 1418 (C=S), 1200, 1015 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.12(S, 3H, $COCH_3$), 2.22 (S, 3H, $COCH_3$), 3.35 (S, 3H, CH_3), 4.21 (S, 2H, NCH_2CO), 7.12-7.98 (m, 8H, Ar H) ppm. Anal. Calcd for $C_{21}H_{18}ClN_5O_4$ S: C, 53.50; H, 3.82; N, 14.86; Cl, 7.43; S, 6.79. Found: C, 53.28; H, 3.67; N, 14.58; Cl, 7.17; S, 6.41.

1-Acetyl-3-[1-(2-acetoxyphenylethylidene)-amino]-5-thinylidene-2-thiohydantoin (7a) as yellow crystals, yield 56%, mp: 142 ºC, IR (KBr): 1753, 1720, 1705 (C=O), 1625 (C=N), 1612, 1587 (C=C), 1418 (C=S), 1210, 1078 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.29 (S, 3H, $COCH_3$), 2.38 (S, 3H, $COCH_3$), 3.35 (S, 2H, NCH_2CO), 7.11-8.01(m, 8H, Ar H, olefinic proton and thiophene-H) ppm. Anal. Calcd for $C_{20}H_{17}N_3O_4S_2$: C, 56.21; H, 3.98; N, 9.84; S, 14.99. Found: C, 56.00; H, 3.68; N, 9.59; S, 14.71.

1-Acetyl-3-[1-(2-acetoxyphenylethylidene)-amino]-5-(4-methoxy)benzylidene-2-thiohydantoin (7b) as yellow crystals, yield 57%, mp: 152 ºC, IR (KBr): 1751, 1732, 1706 (C=O), 1623 (C=N), 1611, 1583 (C=C), 1417 (C=S), 1125, 1095 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.21 (S, 3H, $COCH_3$), 2.35 (S, 3H, $COCH_3$), 3.35 (S, 3H, CH_3), 3.98 (S, 3H, OCH_3), 7.01-8.10 (m, 9H, Ar H, olefinic proton) ppm. Anal. Calcd for $C_{23}H_{21}N_3O_5S$: C, 61.20; H, 4.66; N, 9.31; S, 7.10. Found: C, 61.02; H, 4.33; N, 9.07; S, 6.88.

Reaction of 3 with aromatic aldehydes: Formation of 7a, b

A mixture of 3 (0.01 mole), aromatic aldehydes (such as thiophene-2-carboxaldehyde and anisaldehyde(0.01mole)) and sodium acetate (0.03 mole) in acetic acid (50 ml) was heated under reflux for 4 hr. The reaction mixture was cooled and poured into water. The solid obtained was filtered off, washed with hot water, dried and recrystallized from acetic acid to give 7.

1,2-Bis(2-hydroxyacetophenone)-hydrazone (8)

A mixture of 2 (0.01 mole) and hydrazine hydrate (0.02 mole) was fused on a hot plate for 1 hr. The reaction mixture was added to boiling methanol (30 ml) and heated under reflux for 1 hr, then cooled and poured into dilute hydrochloric acid (2%). The solid formed was filtered off, washed with water, dried and purified by recrystallization with ethanol to give 8 as pale yellow crystals, yield 49%, mp. 178 ºC, IR (KBr): 3420 (OH), 1625 (C=N), 1608, 1562 (C=C), 1242, 1161 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.51 (S, 6H, 2×CH_3), 7.10-7.89 (m, 8H, Ar H), 12.30 (S, 2H, 2×OH) ppm. Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.64; H, 5.97; N, 10.45. Found: C, 71.33; H, 5.63; N, 10.26.

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