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Synthesis , Biological Activity and Mass Spectra Investigation of 1,2,4- Triazino- [2,1-a]- 1,2,4- triazine Derivatives

J.A. Hassanen , H .Kh Ashour and SH. A. Zkaria

Chemistry Department, Faculty of Science ,Suez Canal University, Ismailia,Eygpt.

ABSTRACT

*2-(Aminothiocarbonyl)-3-phenyl-5-benzylidene-1,2,4-triazin-6-one **(2)** was prepared via the condensation of oxazolinon **(1)** with thiosemicarbazide under reflux. Treatment of compound **2** with bromoethyl aryl ketons and ethyl chloroacetate in presence of fused sodium cetate yield the corresponding 1,2,4 triazino-[2,1-a]-1,2,4-triazine derivatives **(3and4)** .Acylation of triazino-[2,1-a]-1,2,4-triazines **(3 and4)** with acetic anhydride afforded the corresponding N-acetyl derivatives **(5and6)**.Condensation of compound **4** with aromatic aldehydes to give 2-arylidiene-4-thioxo-1,2,4-triazino-[2,1-a]-1,2,4-triazine-1,8-diones **(7a,b)**.The electron impact mass spectra of both of the above series of fused 1,2,4-triazine derivatives have also been recorded and their fragmentation pattern is discussed. The prepared fused 1, 2, 4- triazino -[2,1-a]-1,2,4-triazine derivatives also exhibited antimicrobial activity and anti-cancer evaluation.*

INTRODUCTION

1,2,4- triazine derivatives have been reported to possess a broad spectrum of biological activities, including antifungal[1,2] ,anti HIV[3], anticancer[4], anti-inflamatory[5], analgesic[6], and anti hypertensive[7] activities besides this ,triazines were used as herbicides , pesticides and dyes[8,9].This prompted us to synthesize 1,2,4- triazine via cyclocondensation of 3,1-oxazolinone **(1)** with thiosemicarbazide. It was found that 1,2,4- triazine **(2)** is converted into fused triazine by the action of 4-substituted phenacyl bromide and ethyl choloroacetate under reflux, has prompted us to report their synthesis and study their electron impact (EI) mass spectral fragmentation .

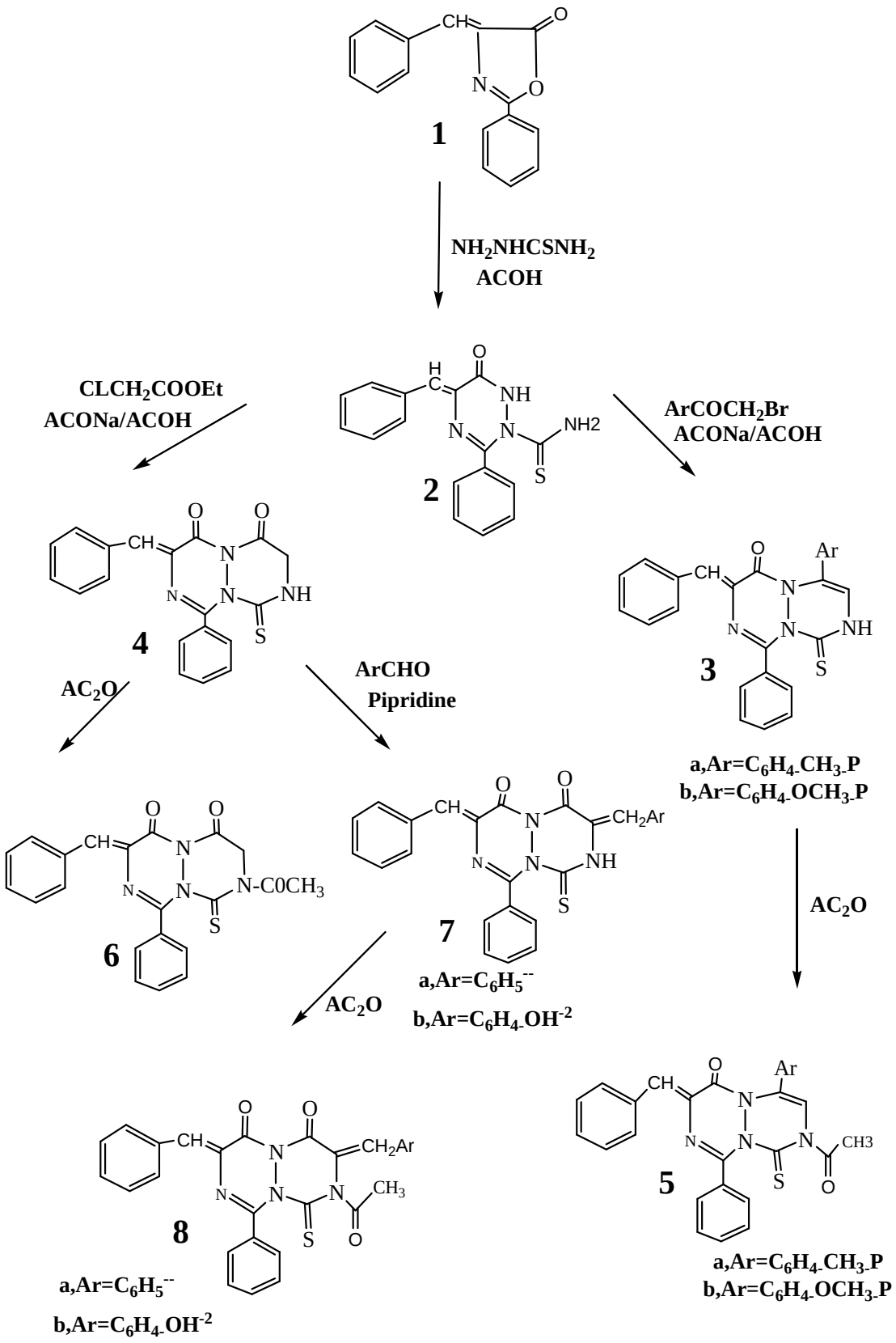
RESULT AND DISCUSSION

1-Chemistry

2-phenyl-4-benzylidene-5H-oxazol-5-one **(1)** was prepared via the reaction of hypuric acid with benzaldhyde in presence of fused sodium acetate and acetic anhydride under fusion.

Condensation [10,11] of 2-phenyl-4-benzylidene -5H-oxazlinone **(1)** with thiosemicarbazide in glacial acetic acid under reflux afforded the corresponding of 2-(amino thiocarbonyl)-3-phenyl-5- benzylidien-1,2,4-triazine-6-one **(2)**. Treatment of compound **2** with w-bromomethylaryl ketones (such as 4-methyl phenacyl bromide and 4- methoxy phenacyl bromide) and ethyl choloro acetate in presence of fused sodium acetate in acetic acid under reflux , yielded the corresponding to 1-aryl-4-thioxo- 5- phenyl-7-benzylidene-triazino -[2,1-a]-1,2,4-triazine-8-ones **(3a,b)** , and 4-thioxo-5-phenyl-7-benzylidene-triazino-[2,1-a]-1,2,4-triazine-1,8-dione **(4 , Scheme 1)**.

Acetylation [12]of compounds **3** and **4** with acetic anhydride under reflux led to the formation of 1-aryl-3-acetyl-4-thioxo-5-phenyl-7-benzylidene-triazino-[2,1-a]-1,2,4-triazine-8-ones **(5a,b)** , and3-acetyl-4-thioxo-5-phenyl-7-benzylidene -1,2,4-triazino-[2,1-a]-1,2,4-triazine-1,8,dione **(6)**.


1
NH2NHCSNH2
ACOH
2
CLCH2COOEt
ACONa/ACOH
ArCOCH2Br
ACONa/ACOH
4
3
AC2O
ArCHO
Pipridine
a,Ar=C6H4-CH3-P
b,Ar=C6H4-OCH3-P
6
7
AC2O
AC2O
a,Ar=C6H5--
b,Ar=C6H4-OH-2
8
5
a,Ar=C6H5--
b,Ar=C6H4-OH-2
a,Ar=C6H4-CH3-P
b,Ar=C6H4-OCH3-P

Scheme 1

Condensation of compound **4** with aromatic aldehydes (namely , benzaldhyde and 2-hydroxybenzaldhyde) in presence of pipridine under fusion yielded the corresponding to 2-arylidene-4-thioxo- 5-phenyl-7-benzylidien- 1,2,4-triazino-[2,1-a]-1,2,4-triazine-1,8-diones **(7a,b)**.

Acetylation of compound **7** with acetic anhydride under reflux led to the formation of 2-aryllidene -3-acetyl-4-thioxo-5-phenyl-7-benzylidene-1,2,4-triazino -[2,1-a]-1,2,4-triazine-1,8-diones **(8a ,b ;scheme 1)**

2-Mass spectrometry:

The mass spectra decomposition modes[13,14] of various fused1,2,4-triazines heterocyclic compounds have been investigated. The mass spectra of the synthesized compounds 2,3,4,5,6,7 and 8 showed intense molecular ion peaks at m/z 322 , 436 ,452 ,362 , 478 ,494 ,404 ,450 ,466 ,492 , and m/z 508,consistent with the molecular formula $C_{17}H_{14}N_4OS$, $C_{26}H_{20}N_4OS$, $C_{26}H_{20}N_4O_2S$, $C_{19}H_{14}N_4O_2S$, $C_{28}H_{22}N_4O_2S$, $C_{28}H_{22}N_4O_3S$, $C_{21}H_{16}N_4O_3S$, $C_{26}H_{18}N_4O_2S$, $C_{26}H_{18}N_4O_3S$, $C_{28}H_{20}N_4O_3S$, $C_{28}H_{20}N_4O_4S$, respectively.

Table 1. lists the m/z (relative abundance,%) values of the principal fragments of the prepared compounds **2 , 3 , 4 , 5 , 6 , 7 and 8** show relatively small molecular ions peaks typical of a cleavage and rearrangement process type fragmentation.

Compound 2

The molecular ion of compound **2 (Fig.1)** fragmented further and involved two possible pathways as illustrated in **scheme 2**. The molecular ion of m/z 322 fragmented via pathway A gave the fragment of m/z 306 by losing amino group (NH_2). The fragment of m/z 306, which fragmented to give the fragment of m/z 262 by losing thiocarbonyl group (C=S). the fragment of m/z 262 was broken to give an ion of m/z 234,which further broke to give a stable ion of m/z 117. The ion of m/z 117 underwent fragmentations led to the ion of m/z 91 and m/z 65, respectively.

Accordingly, the same molecular ion of m/z 322 fragmented via pathway B to give the ion of m/z 263 which lost (NH) group to give the ion of m/z 248, corresponds the 2-phenyl-5-benzylidene-4-oxo imidazolidinone. The fragment of m/z 248, which fragmented to give the fragment of m/z 144 by losing C7H6N .This fragmentations led to fragments of m/z 116, 90 and m/z 64, respectively.

Compounds 3 and 5

The molecular ion of compounds **3a** (m/z 436) and **3b** (m/z 452) Underwent fragmentation via pathway A to produce peak at m/z 248, corresponding 2-phenyl-5- benzylidene-4-oxo imidazolidinone . The loss of cyanobenzene from the fragment ion m/z 248 gave fragment at m/z 145, which further broke to give the stable ion of m/z 117 **(Fig 2a , 2b)**. It further underwent loss of hydrogen cyanid (HCN) and acetylene (CH≡CH) molecules to gives peaks at m/z 90 and m/z 64, respectively.

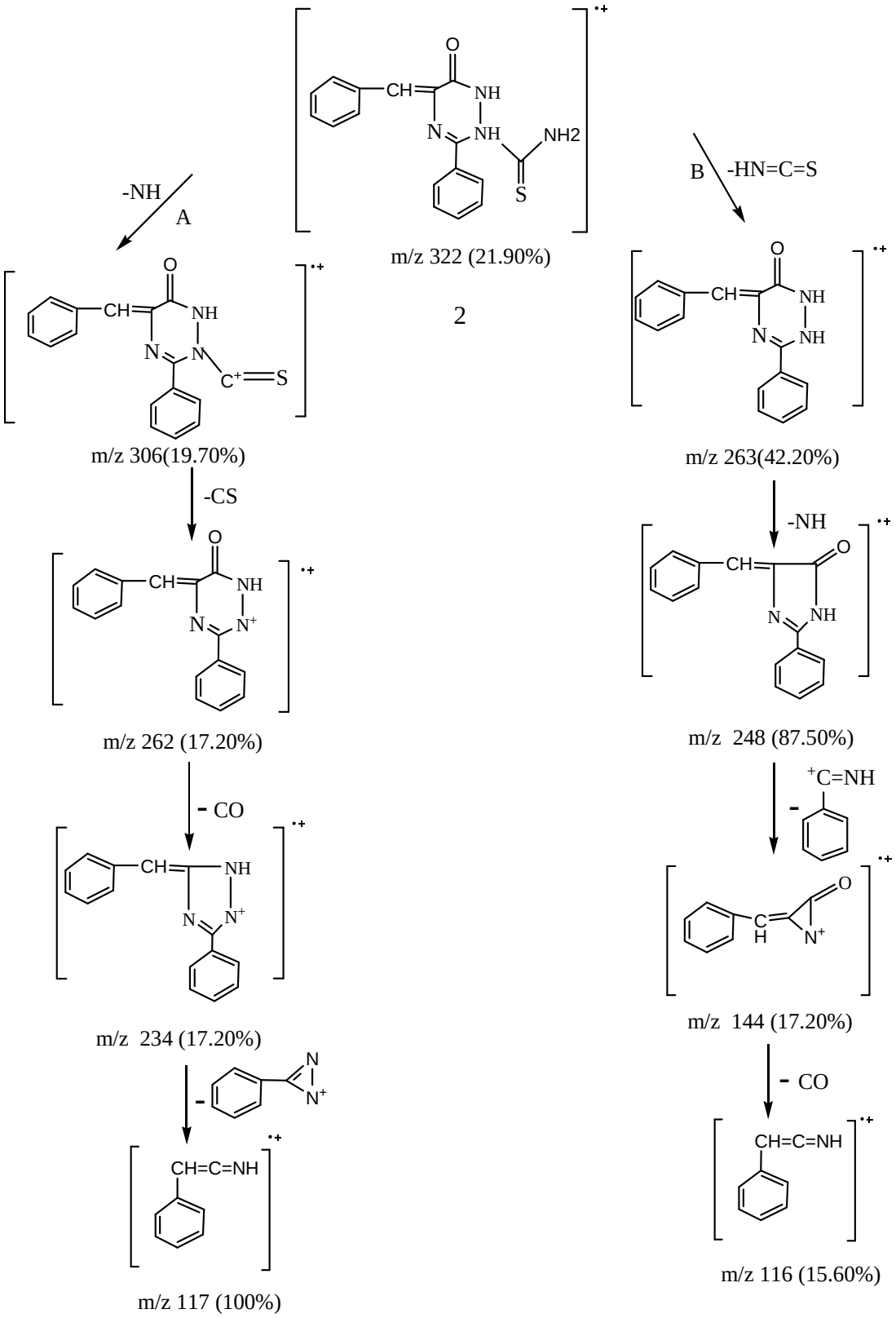
The molecular ion of compounds **3a** and **3b** were also found to undergo fragmentation via pathway B to produce peaks at m/z 188 and m/z 204 corresponding to the 4- substiruted-2-thioxo-imidazolidine. The loss of thiocarbonyl (C=S)from the fragments ion m/z 188 and m/z 204 gave fragments at m/z 144 and m/z 160, which further broke to gives the ion of m/z 117 an d m/z 133. This fragmentation led to fragments of m/z 103,77 and m/z 51,repectively **(scheme 3)**.

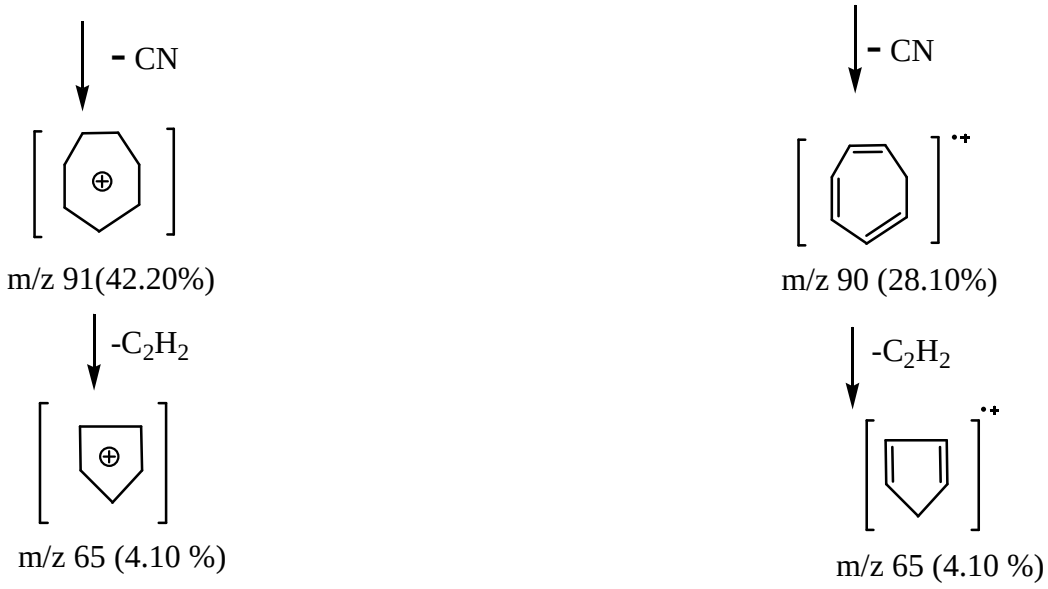
From the mass spectrum of compounds **5a** and **5b (Fig 3a and 3b)**, It were concluded that the m olecular ions were at m/z 478 and m/z 494. The ion of m/z 478 and m/z 494 underwent fragmentation to produce peaks at m/z 436 and mlz 452 by losing ketone molecule (CH_2CO), corresponding to the molecular ions of compounds 3a and 3b. the fragments of m/z 436 and m/z 452 further broke via pathway similar to compound **3 (Scheme 3).**

Compounds 4 and 6

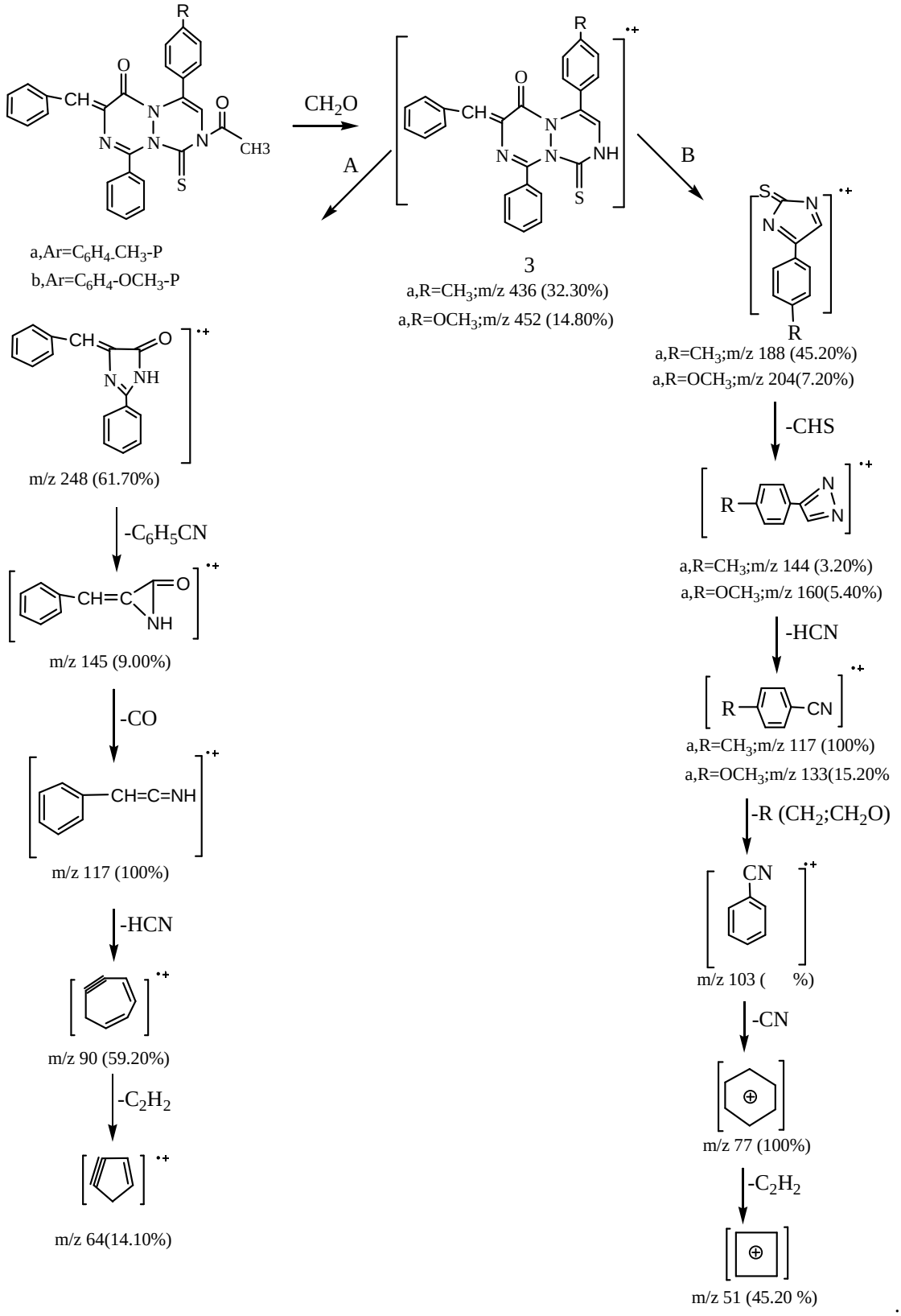
The molecular ion of compound **4 (scheme 4)** underwent fragmentation via pathway A to produce a peak at m/z 248 by lossing 2-thioxo imidazoline-4-one molecule.

The loss of cyanobenzene from the ion with m/z 248 resulted in an ion at m/z 117. The ion at m/z 117 underwent loss of hydrogen cyanide (HCN) and ethyne (CH≡CH) molecules to give peaks at m/z 90 m/z 64, respectively.

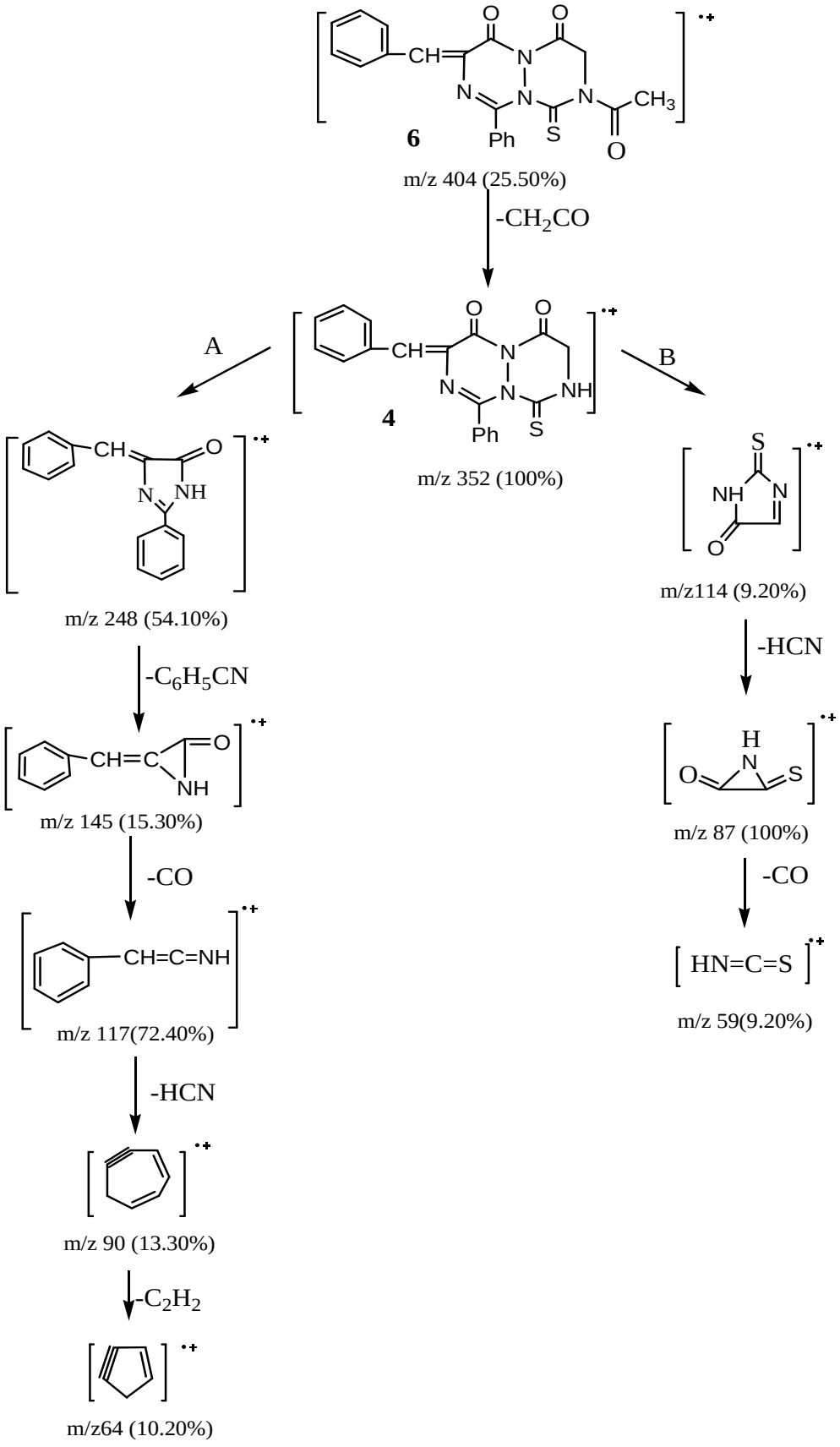

m/z 322 (21.90%)
2
-NH
A
B
-HN=C=S
m/z 306(19.70%)
m/z 263(42.20%)
-CS
-NH
m/z 262 (17.20%)
m/z 248 (87.50%)
- CO
+C=NH
m/z 234 (17.20%)
m/z 144 (17.20%)
- CO
m/z 117 (100%)
m/z 116 (15.60%)



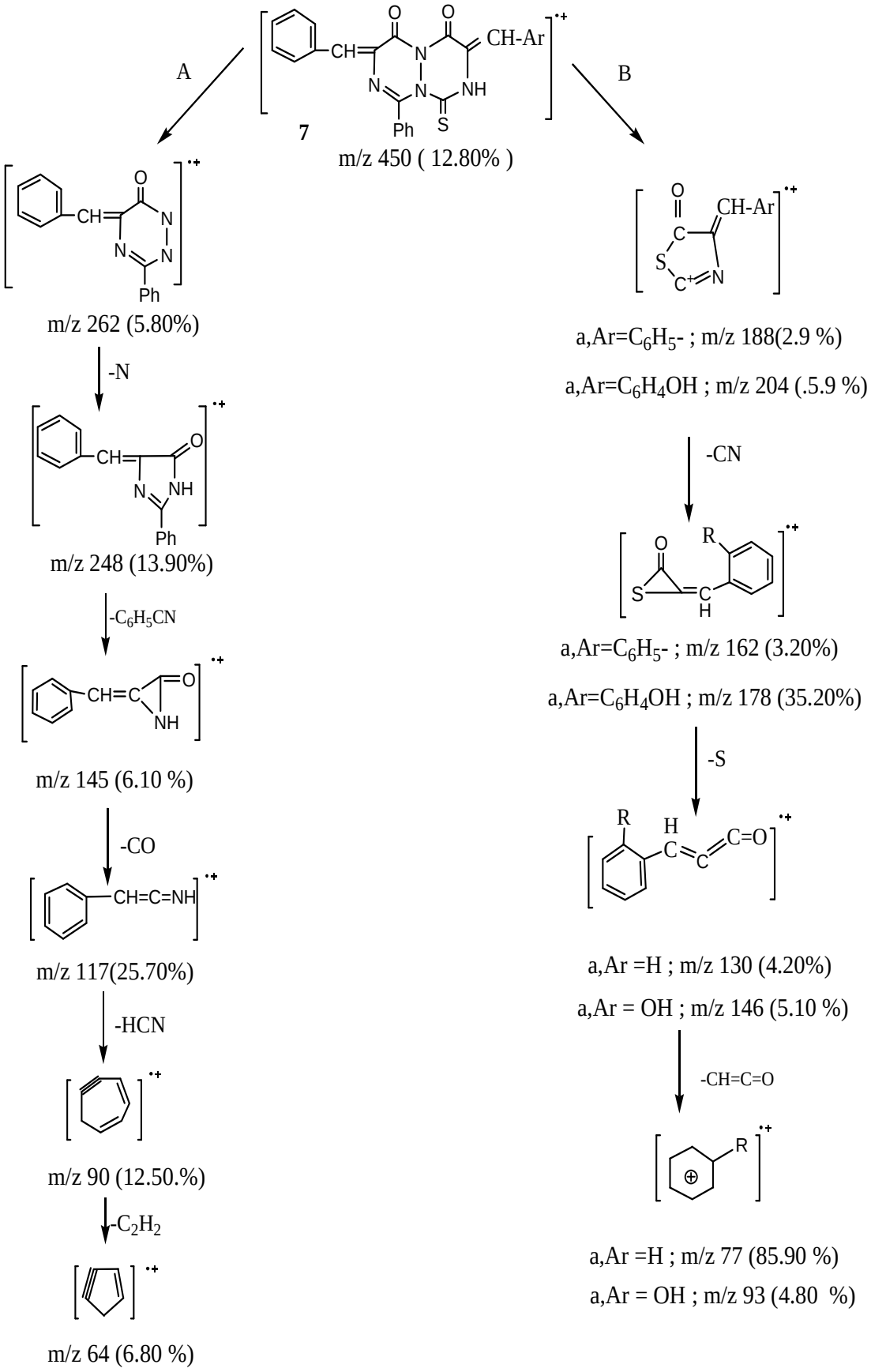
Scheme 2: Main fragmaintaion pathway of compound 2



Scheme 3: Main fragmentation pathway of compounds 3a ,b.



Scheme 4: Main fragmentation pathway of compounds 4 , 6.



Scheme 5:Main fragmentation pathway of compounds 7a and 7b.

Also the ion of m/z 362 underwent loss of 2-phenyl-5- benzylidene-4-oxoimidazolinone. via pathway B to give peak at m/z 114 the ion of m/z 114 underwent fragmentation to produce a stable ion at m/z 87 by losing hydrogen cyanide (HCN).the loss of carbon monoxide from the stable ion with m/z 87 resulted in an ion at m/z 59.

From the mass spectrum of compound **6 (Fig.4),** It was concluded that the molecular ion was at m/z 404. The ion of m/z 404 underwent fragmentation to produce a peak at m/z 362 by losing ketone (CH_2CO), corresponding to the base peak and molecular ion of compound **4 (Fig. 5)**. The stable fragment of m/z 362 further broke via pathway similar to compound **4 (Scheme 4).**

Compounds 7 and 8

The mass spectra of Compounds **7a, b** and **8a, b** show relatively small molecular ions and peaks typical of a cleavage and rearrangement processes type fragmentation. from the study of The mass spectra of Compounds **7a,7b, 8a** and **8b**, It was found that the molecular ion for all these compounds fragmented further and involved two various pathway are summarized in **table 1**.

3- Biologicl activity

3.1-Anti microbial activity

Mean zone of inhibition in mm ± Standard deviation beyond will diameter (6 mm) produced on arrange of envirommental and clinically

Table 1.EI mass spectra (70ev) of compounds 2-8 , m/Z(relative intensity,%)

Compound No.	M^+	Pathway A		Pathway B		Other ions
		-M	M/Z	-M	M/Z	
2	$[C_{17}H_{14}N_4OS]^{\cdot+}$ 322(21.90)	$-NH_2$ CS CO $C_7H_5N_2$ CN C_2H_2	$[C_{17}H_{12}N_3OS]^+$ 306 (19.70) $[C_{16}H_{12}N_3O]^+$ 262 (17.20) $[C_{15}H_{12}N_3]^+$ 234 (17.20) $[C_8H_7N]^{\cdot+}$ 117 (100) $[C_7H_7N]^+$ 91(42.20) $[C_5H_5]^+$ 65 (14.10)	-NHCS -NH $-C_7H_6N$ CO CN C_2H_2	$[C_{16}H_{13}N_3O]^{\cdot+}$ 363 (42.20) $[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (87.50) $[C_9H_6NO]^+$ 144 (17.20) $[C_8H_6N]^+$ 116 (15.60) $[C_7H_6]^{\cdot+}$ 90 (28.10) $[C_5H_4]^{\cdot+}$ 64 (25.10)	323 (M^{+}+1,7.80), 321 (MI1,14.10), 305 (29.70), 304 (7.80), 283 (3.10), 282 (7.80), 247 (50.00), 246 (20.30), 235 (14.10), 177 (12.50), 161 (12.50), 160 (10.90), 153 (10.90), 149 (32.80), 143 (12.50), 141 (12.50), 122 (12.50), 121 (12.50), 120 (15.60), 119 (84.40), 118 (31.30), 115 (21.90), 104 (31.30), 103 (26.8), 101 (28.10), 97 (21.90), 96 (14.10), 89 (18.80), 85 (15.60), 84 (17.20), 83 (21.90), 82 (15.60), 81 (10.90), 74 (21.90), 75 (4.70), 74 (9.40), 73 (28.10), 72 (17.20), 71 (25.00), 70 (25.00), 69 (26.60), 68 (14.10), 67 (15.60), 56 (21.90) .
3a	$[C_{26}H_{20}N_4OS]^{\cdot+}$ 436 (32.30)	$C_{10}H_8N_2S$ C_7H_5N CO HCN C_2H_2	$[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (41.90) $[C_9H_7NO]^{\cdot+}$ 145 (19.40) $[C_8H_7N]^{\cdot+}$ 117 (100) $[C_7H_6]^{\cdot+}$ 90 (54.80) $[C_5H_4]^{\cdot+}$ 64 (19.40)	$C_{16}H_{12}N_2O$ -CS -HCN $-CH_2$ -CN $-C_2H_2$	$[C_{10}H_8N_2S]^{\cdot+}$ 188 (45.20) $[C_9H_8N_2]^{\cdot+}$ 144 (3.20) $[C_8H_7N]^{\cdot+}$ 117 (100) $[C_7H_5N]^+$ 103 (38.70) $[C_6H_5]^{\cdot+}$ 77 (100) $[C_4H_3]^+$ 51 (45.20)	437 (M^{+}+1,1 8.20), 435 (M^{+}.1, 25.80), 249 (45.20), 247 (67.70), 140 (22.60), 189 (45.20), 148 (54.80), 147 (9.70), 119 (29.00), 118 (41.90), 116 (83.90), 115 (41.90), 104 (90.30), 102 (38.70), 91 (12.90), 89 (45.20), 88 (41.90), 82 (22.60), 81 (29.00), 80 (22.60), 76 (77.40), 75 (32.30), 73 (45.20), 69 (38.70), 66 (6.50), 65 (58.10), 62 (54.80), 61 (25.80), 50 (48.40) .

Cont…

Compound No.	M^+	Pathway A		Pathway B		Other ions
		-M	M/Z	-M	M/Z	
3b	$[C_{26}H_{20}N_4O_2S]^{\cdot+}$ 452(14.80)	$C_{10}H_8N_2OS$ C_7H_5N CO HCN C_2H_2	$[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (61.70) $[C_4H_7NO]^{\cdot+}$ 145 (9.00) $[C_8H_7N]^{\cdot+}$ 117 (100) $[C_7H_6]^{\cdot+}$ 90 (32.90) $[C_5H_4]^{\cdot+}$ 64 (3.00)	$C_{16}H_{12}N_2O$ -CS HCN CH_2O CN C_2H_2	$[C_{10}H_8N_2OS]^{\cdot+}$ 204 (7.20) $[C_9H_8N_2O]^{\cdot+}$ 160 (5.40) $[C_8H_7NO]^{\cdot+}$ 133 (15.20) $[C_7H_5N]^{\cdot+}$ 103 (70.70) $[C_6H_5]^+$ 77 (94.60) $[C_4H_3]^+$ 51 (52.70)	451 (M^{+} -1,13.20), 450 (3.00), 293 (6.60), 292 (3.00), 264 (5.4), 263 (8.40), 262 (6.00), 244 (12.60), 247 (46.70), 214 (4.80), 206 (13.80), 205 (5.40), 203 (9.5), 175 (6.60), 161 (6.00), 153 (4.80), 152 (5.40), 132 (6.60), 145 (9.00), 144 (10.20), 143 (6.00), 130 (6.60), 118 (21.60), 116 (35.30), 115 (13.20), 105 (34.10), 104 (86.80), 102 (32.90) 91 (18.00), 89 (31.70), 88 (13.20), 78 (12.60), 76 (50.30), 75 (19.20), 65 (4.20), 63 (14.40), 62 (12.00), 52 (15.60), 50 (43.10) .
4	$[C_{14}H_{14}N_4O_2S]^{\cdot+}$ 362 (91.20)	$C_3H_2N_2OS$ C_7H_5N	$[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (8.80) $[C_9H_7NO]^{\cdot+}$ 145 (2.00)	$C_{16}H_{12}N_2O$ HCN	$[C_3H_2N_2OS]^{\cdot+}$ 114 (9.20) $[C_2HNOS]^{\cdot+}$ 87 (100)	363 (M^{+}+1, 18.90), 361 (M^{+}.1, 20.0), 288 (1.00), 287 (1.00), 263 (0.90), 262 (1.00), 249 (1.80), 247 (5.80), 246 (2.30), 234 (1.00), 233 (0.70), 214 (11.90), 218

		CO HCN C_2H_2	$[C_8H_7N]^{\cdot+}$ 117 (18.60) $[C_7H_6]^{\cdot+}$ 90 (7.20) $[C_5H_4]^{\cdot+}$ 64 (4.20)	CO	$[CHNS]^+$ 59 (9.20)	(84.50), 217 (8.50), 205 (4.10), 204 (3.70), 203 (2.10), 202 (1.00), 178 (1.40), 177 (1.30), 176 (1.60), 161 (1.10), 160 (1.00), 148 (17.50), 144 (12.10), 143 (3.10), 132 (2.80), 131 (3.40), 130 (2.80), 118 (2.30), 116 (19.50), 115 (3.60), 105 (44.10), 104 (55.80), 103 (25.50), 102 (26.00), 91 (1.80), 89 (24.60), 86 (13.20), 77 (44.00), 76 (28.0), 75 (8.20), 65 (2.0), 63 (12.50), 62 (4.80), 52 (8.40), 51 (19.20), 50 (11.80) .

Cont…

Compound No.	M^+	Pathway A		Pathway B		Other ions
		-M	M/Z	-M	M/Z	
5a	$[C_{28}H_{22}N_4O_2S]^{\cdot+}$ 478 (22.00)	CH_2CO $C_{10}H_8N_2S$ C_7H_5N CO HCN C_2H_2	$[C_{26}H_{20}N_4OS]^{\cdot+}$ 436 (84.70) $[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (45.80) $[C_9H_7NO]^{\cdot+}$ 145 (15.30) $[C_8H_7N]^{\cdot+}$ 117(67.80) $[C_7H_6]^{\cdot+}$ 90 (42.40) $[C_4H_4]^{\cdot+}$ 64 (32.20)	CH_2CO $C_{16}H_{12}N_2O$ CS HCN CH2 CN C_2H_2	$[C_{26}H_{20}N_4OS]^{\cdot+}$ 436 (84.70) $[C_{10}H_8N_2S]^{\cdot+}$ 188 (5.30) $[C_9H_8N_2]^{\cdot+}$ 144 (11.90) $[C_8H_7N]^{\cdot+}$ 117 (67.80) $[C_7H_5N]^{\cdot+}$ 103 (37.30) $[C_6H_5]^+$ 77 (44.10) $[C_4H_3]^+$ 51 (44.10)	479 (M^++1, 13.60), 477 (M^+-1, 8.50), 455 (10.20), 454 (6.80), 437 (28.80), 435 (57.60), 434 (37.30), 340 (13.60), 347 (8.50), 306 (11.90), 305 (22.00), 243 (11.90), 292 (10.20), 286 (40.70), 285 (13.60), 263 (23.70), 262 (10.20), 244 (22.00), 247 (32.20), 205 (10.20), 204 (22.00), 190 (18.00), 189 (23.70), 187 (15.30), 175 (15.30), 163 (13.60), 162 (25.40), 161 (11.90), 160 (18.60), 148 (37.30), 147 (21.10), 146 (22.0), 119 (64.40), 118 (45.80), 116 (42.40), 115 (22.00), 114 (22.00), 105 (44.90), 104 (40.70), 102 (28.80), 101 (22.00), 94 (13.60), 93 (39.00), 91 (47.50), 89 (40.70), 78 (32.20), 76 (50.80), 75 (32.90), 65 (27.10), 63 (35.60), 52 (15.10), 50 (28.80) .
5b	$[C_{28}H_{22}N_4O_3S]^{\cdot+}$ 494 (23.50)	CH_2CO $C_{10}H_8N_2OS$ C_7H_5N CO HCN C_2H_2	$[C_{26}H_{20}N_4O_2S]^{\cdot+}$ 252 (23.50) $[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (11.80) $[C_9H_7NO]^{\cdot+}$ 145 (13.20) $[C_8H_7N]^{\cdot+}$ 117 (8.80) $[C_7H_6]^{\cdot+}$ 90 (17.60) $[C_5H_4]^{\cdot+}$ 64 (5.90)	CH_2CO $C_{16}H_{12}N_2O$ -CS HCN CH_2O CN C_2H_2	$[C_{26}H_{20}N_4O_2S]^{\cdot+}$ 452 (23.50) $[C_{10}H_8N_2OS]^{\cdot+}$ 204 (26.50) $[C_9H_8N_2O]^{\cdot+}$ 160 (23.50) $[C_8H_7NO]^{\cdot+}$ 133 (17.60) $[C_7H_5N]^{\cdot+}$ 103 (8.80) $[C_8H_5]^+$ 77 (100) $[C_4H_3]+$ 51 (14.70)	493 (M^+-1, 23.50), 453 (5.90), 451 (14.70), 370 (11.80), 347 (47.10), 335 (20.60), 326 (14.70), 282 (17.60), 281 (20.60), 263 (20.60), 262 (32.40), 247 (20.60), 233 (14.70), 218 (17.60), 206 (23.50), 191 (17.60), 189 (14.70), 169 (14.70), 163 (32.40), 161 (8.80), 159 (11.80), 157 (14.70), 150 (20.60), 136 (8.80), 135 (55.90), 121 (23.50), 119 (23.50), 118 (32.40), 115 (17.60), 109 (20.60), 108 (23.50), 107 (44.10), 106 (32.40), 104 (50.00), 93 (29.40), 92 (20.60), 91 (50.00), 78 (17.60), 74 (38.20), 71 (32.60), 70 (26.50), 65 (4.70), 63 (26.50), 61 (17.20), 53 (17.60), 52 (17.60) .

Cont…

Compound No.	M^+	Pathway A		Pathway B		Other ions
		-M	M/Z	-M	M/Z	
6	$[C_{21}H_{16}N_4O_3S]^{\cdot+}$ 404 (25.20)	CH_2CO $C_3H_2N_2OS$ C_7H_5N CO HCN C_2H_2	$[C_{19}H_{14}N_4O_2S]^{\cdot+}$ 362 (100) $[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (54.10) $[C_9H_7NO]^{\cdot+}$ 145 (15.30) $[C_8H_7N]^{\cdot+}$ 117(72.40) $[C_7H_6]^{\cdot+}$ 90 (13.30) $[C_5H_4]^{\cdot+}$ 64 (10.20)	CH_2CO $C_{16}H_{12}N_2O$ HCN CO	$[C_{19}H_{14}N_4O_2S]^{\cdot+}$ 362 (100) $[C_3H_2N_2OS]^{\cdot+}$ 114 (9.20) $[C_2HNOS]^{\cdot+}$ 87 (5.10) $[CHNS]^{\cdot+}$ 59 (9.20)	403 (M^+ -1, 21.40), 364 (16.30), 363 (14.4), 361 (69.40), 360 (10.20), 289 (8.20), 247 (46.90), 218 (29.50), 205 (10.20), 204 (12.20), 144 (26.50), 143 (9.20), 119 (18.40), 118 (20.40), 116 (44.40), 115 (21.40), 104 (33.70), 103 (56.10), 102 (31.60), 101 (21.40), 91 (13.30), 89 (5.10), 88 (16.30), 75 (9.20), 74 (7.10), 73 (11.30), 65 (7.10), 63 (3.10), 61 (11.20), 60 (16.30), 56 (11.20), 52 (8.20) .
7a	$[C_{26}H_{18}N_4O_2S]^{\cdot+}$ 450 (12.80)	$C_{10}H_6NOS$ N C_7H_5N	$[C_{16}H_{12}N_3O]^+$ 262 (5.80) $[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (13.50) $[C_9H_7NO]^{\cdot+}$	$C_{16}H_{12}N_3O$ CN S	$[C_{10}H_6NOS]^{\cdot+}$ 188 (2.90) $[C_9H_6OS]^{\cdot+}$ 162 (3.20) $[C_9H_6O]^{\cdot+}$	444 (M^+-1,1.90), 363 (7.40), 362 (27.30), 361 (15.80), 323 (2.40), 307 (4.50), 306 (2.30), 264 (2.60), 263 (5.50), 262 (5.80), 244 (11.60), 247 (10.00), 214 (7.40), 218 (31.20), 217 (17.40), 210 (2.30), 205

		CO HCN C_2H_2	145 (6.10) $[C_8H_7N]^{\cdot+}$ 117 (25.70) $[C_7H_6]^{\cdot+}$ 90 (12.50) $[C_5H_4]^{\cdot+}$ 64 (6.80)	CO C_2H C_2H_2	130 (4.20) $[C_8H_6]^{+}$ 102 (18.00) $[C_6H_5]^{+}$ 77 (85.90) $[C_4H_3]^{+}$ 51 (30.90)	(2.30) 204 (3.5), 203 (2.60), 178 (3.20), 165 (2.90), 144 (2.60), 148 (7.70), 144 (8.00), 143 (3.90), 135 (4.20), 134 (9.30), 118 (7.40), 116 (14.80), 106 (11.30), 105 (100), 104 (46.80), 103 (21.20), 102 (18.00), 91 (9.00), 89 (23.80), 88 (11.90), 87 (34.40), 78 (8.70), 77 (85.90), 76 (29.60), 65 (5.8), 63 (15.80), 62 (7.10), 52 (10.90), 50 (20.90).

Cont…

Compound No.	M^+	Pathway A		Pathway B		Other ions
		-M	M/Z	-M	M/Z	
7b	$[C_{26}H_{18}N_4O_3S]^{+}$ 466 (15.80)	$C_{10}H_{16}NO_2S$ -N $-C_7H_5N$ -CO -HCN $-C_2H_2$	$[C_{16}H_{12}N_3O]^{+}$ 262 (11.80) $[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (38.70) $[C_9H_7NO]^{\cdot+}$ 145 (13.30) $[C_8H_7N]^{\cdot+}$ 117(55.80) $[C_7H_6]^{\cdot+}$ 90 (29.50) $[C_4H_4]^{\cdot+}$ 64 (9.50)	$C_{16}H_{12}N_3O$ -CN -S -CO $-C_2H$ -O	$[C_{10}H_6NO_2S]^{\cdot+}$ 204 (5.90) $[C_9H_6O_2S]^{\cdot+}$ 178 (35.20) $[C_9H_6O_2]^{\cdot+}$ 146 (5.10) $[C_8H_6O]^{\cdot+}$ 118 (20.60) $[C_6H_5O]^{+}$ 93 (4.80) $[C_6H_5]^{+}$ 77 (100)	467 (M^++1,11.90), 465 (14.60), 449 (3.60), 448 (7.40), 447 (6.70), 392 (2.90), 391 (4.20), 390 (4.40), 374 (2.10), 373 (3.40), 355 (5.70), 354 (2.30), 304 (16.60), 303 (7.80), 289 (4.40), 288 (5.10), 287 (3.10), 263 (22.70), 261 (5.10), 244 (8.40), 247 (22.90), 246 (4.20), 219 (2.90), 218 (3.60), 217 (2.50), 205 (3.20), 203 (5.30), 179 (8.00), 177 (15.40), 176 (6.50), 150 (22.50), 144 (15.40), 146 (5.10), 144 (13.30), 134 (3.60), 133 (4.00), 131 (7.40), 132 (5.90), 121 (24.40), 119 (17.70), 102 (23.60), 91 (24.40), 89 (40.60), 78 (17.50), 76 (32.60), 75 (15.20), 65 (8.40), 63 (28.80), 62 (11.40), 52 (12.80), 50 (31.20) .
8a	$[C_{28}H_{20}N_4O_3S]^{\cdot+}$ 492 (12.5)	$-CH_2CO$ $C_{10}H_6NOS$ N C_7H_5N CO HCN C_2H_2	$[C_{26}H_{18}N_4O_2S]^{+}$ 450 (17.50) $[C_{16}H_{12}N_3O]^{\cdot+}$ 262 (13.50) $[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (63.00) $[C_9H_7NO]^{\cdot+}$ 145 (15.00) $[C_8H_7N]^{\cdot+}$ 117 (48.10) $[C_7H_6]^{\cdot+}$ 90 (11.10) $[C_5H]^{\cdot+}$ 64 (40.7)	$-CH_2CO$ $C_{16}H_{12}N_3O$ CN S CO C_2H C_2H_2	$[C_{26}H_{18}N_4O_2S]^{+}$ 450 (17.50) $[C_{10}H_6NOS]^{+}$ 188(11.50) $[C_9H_6OS]^{\cdot+}$ 162 (37.0) $[C_8H_6O]^{+}$ 130 (27.00) $[C_8H_6]^{+}$ 102 (33.50) $[C_6H_5]^{+}$ 77 (92.60) $[C_4H_3]^{+}$ 51 (40.70)	493(M^++1 , 7.20), 456 (18.50), 455 (18.50), 362 (51.90), 298 (18.50), 297 (11.10), 268 (48.10), 267 (14.50) ,261 (10.20), 255 (22.20) , 254 (33.30), 252 (29.60), 249 (63.00), 224 (17.00), 223 (25.90) , 210 (18.50), 181 (51.90), 179(29.60), 165 (37.00), 140(22.20), 139(22.20), 183 (14.80), 129 (37.00), 124 (29.60), 123 (14.6), 122 (59.20), 119 (29.60), 118 (33.30), 106 (40.70), 105 (100.00), 103 (33.30), 98 (22.10), 84 (40.70), 79 (34.00), 78 (25.90) ,76 (25.90) , 62 (22.20), 61 (29.60), 60 (44.40), 52 (14.40).

Cont…

Compound No.	M^+	Pathway A		Pathway B		Other ions
		-M	M/Z	-M	M/Z	
8b	$[C_{28}H_{20}N_4O_4S]^{\cdot+}$ 508 (5.20)	CH_2CO $C_{10}H_6NO_2S$ -N C_7H_5N -CO HCN C_2H_2	$[C_{26}H_{18}N_4O_3S]^{+}$ 466 (4.30) $[C_{16}H_{12}N_3O]^{+}$ 262 (6.90) $[C_{16}H_{12}N_2O]^{\cdot+}$ 248 (7.70) $[C_9H_7NO]^{\cdot+}$ 145 (8.20) $[C_8H_7N]^{\cdot+}$ 117 (15.90) $[C_7H_6]^{\cdot+}$ 90 (10.70) $[C_5H_4]^{\cdot+}$ 64 (6.40)	CH_2CO $C_{16}H_{12}N_3O$ CN -S CO C_2H -O	$[C_{26}H_{18}N_4O_3S]^{\cdot+}$ 466 (4.30) $[C_{10}H_{12}NO_2S]^{+}$ 204 (3.00) $[C_9H_6O_2S]^{\cdot+}$ 178 (6.00) $[C_9H_6O_2]^{\cdot+}$ 146 (7.20) $[C_8H_6O]^{\cdot+}$ 118 (8.20) $[C_6H_5O]^{+}$ 93 (6.90) $[C_6H_5]^{+}$ 77 (70.80)	504 (M^++1,3.95), 507 (M^+ -1,3.95), 464 (3.40), 359 (2.10), 358 (2.10), 336 (3.90), 323 (2.6), 322 (5.20), 321 (2.60), 289 (3.0), 288 (3.00), 287 (2.60), 263 (6.00), 244 (11.60), 247 (5.60), 234 (3.40), 235 (3.00), 205 (2.10), 203 (3.90), 187 (3.20), 177 (6.90), 165 (3.40), 161 (4.70), 144 (7.30), 144 (4.70), 132 (3.90), 131 (3.90), 131 (3.90), 121 (9.90), 119 (6.90), 116 (8.20), 106 (10.70), 105 (100), 104 (27.70), 103 (13.20), 92 (6.00), 91 (8.20), 87 (14.20), 76 (14.60), 75 (6.90), 65 (5.60), 63 (10.30), 62 (5.20), 57 (12.00), 56 (12.00), 52 (6.90), 50 (15.50) .

Table 2.Antibacterial activity of all compounds prepared (4-7).

Compound / Tested microorganism	3a	3b	4	5a	6	ST.(30 µg/ml)	
						Penicillin G	Streptomycin
Gram positive bacteria							
S.Aureus	21.7 ± 0.3	20.2 ± 0.07	16.5 ± 0.09	14.2 ± 0.3	23.2 ± 0.09	30.1±0.06	28.1±0.07
B-Subtilis	22.8± 0.04	21.4±0.2	20.7±0.3	14.7±0.04	24.3±0.3	31.6±0.05	29.7±0.06
Gram negative bacteria							
P.Aeruginosa	15.9±0.07	NA	NA	NA	17.5 ±0.09	28.3±0.08	25.2±0.09
E-Coli	18.3±0.06	9.2±0.05	15.5±0.06	13.8±0.2	20.9 ± 0.1	33.1 ± 0.09	29.7±0.07

NA:No activity.

Table 3.Antifungal activity of all compounds prepared (4-7).

Compound / Tested microorganism	3a	3b	4	5a	6	ST.(30 µg/ml)	
						Penicillin G	Streptomycin
ASP.Fumigatus	20.8± 0.08	17.5 ± 0.07	15.7 ± 0.2	11.4 ± 0.05	22.8 ± 0.1	27.4 ± 0.05	26.3 ± 0.08
G.Candidum	17.9 ± 0.3	15.4 ± 0.2	13.4± 0.09	9.4 ± 0.07	20.5 ± 0.07	24.2 ± 0.04	23.2 ± 0.03
G.albicans	14.3 ± 0.04	11.2± 0.09	10.2 ± 0.03	8.3 ± 0.2	17.8 ± 0.09	25.2 ± 0.07	20.8 ± 0.02
Syn.Racemosum	10.4 ± 0.06	NA	NA	NA	12.8 ± 0.09	23.9 ± 0.04	21.4 ± 0.05

NA:No activity.

Pathogenic microorganism using (10 mg/ml) concentration of tested compounds. The data are summarized in **table 2** and **table 3**.All compounds showed activity against bacteria, while compounds **3b**, **4**and **5a** did not exhibit any activity against Psedidomonas aeruginosa.

Also, All compounds were active against fungi ,except compounds **3b**, **4** and **5a** were no activity against Syncephalastrum racemosum .

3.2-Anticancer activity

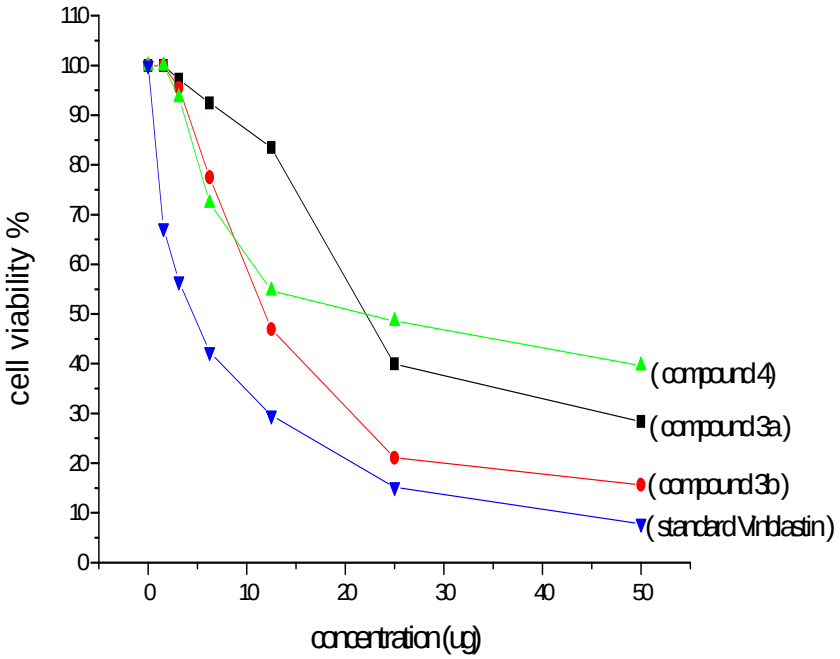
Compound **3a**, **b**, **4**, **5a**, **6** and **7a** were evaluated for their human tumor cell growth inhibitory activity against cell line MCF-7(breast adenocarcinoma). The measurment of cell growth and viability were Vijayenatal (2004).
Inhibitory activity against breast carcinoma cells (MCF-7 cell line) was detected by using different concentrations (0-50µg) of the tested compounds and Vinblastine drug as standard and viability cells (%) was determined by colorimetric method.

Also , inhibitory concentration fifty " IC_{50}" was calculated from **table 4** and **figures 7**, **8**.

Table 4. Evaluation of cytotoxicity of prepared compound against MCF-7 cell line.

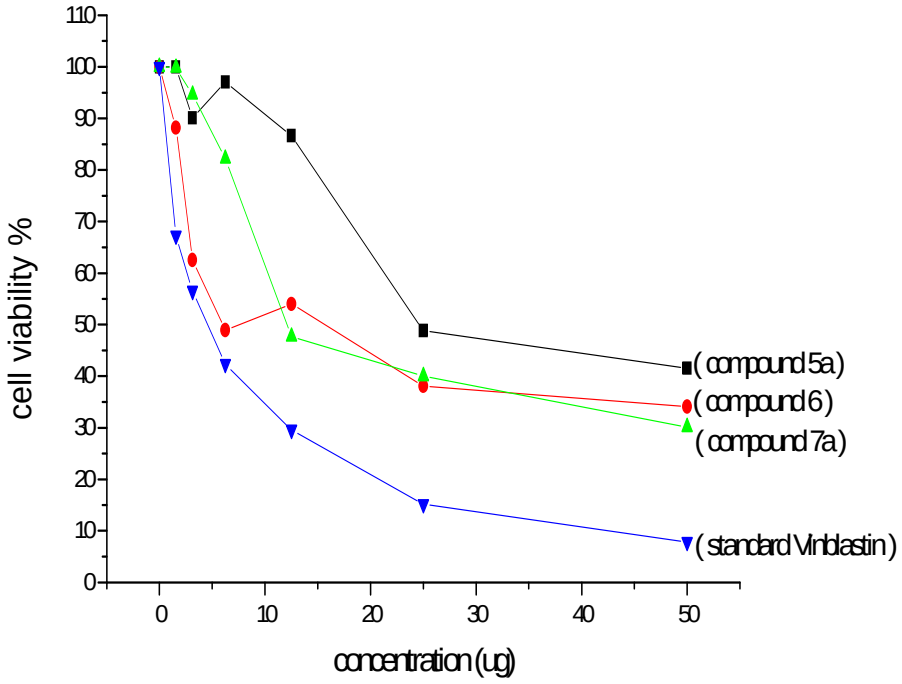
Sample No. / Sample conc. (µg)	Viability %						
	3a	3b	4	5a	6	7a	Standard Vinblastin.
50	28.36	15.64	39.62	41.54	34.10	30.13	7.82
25	39.93	21.07	48.59	48.85	38.08	40.00	15.18
12.5	83.49	46.93	54.74	86.67	54.00	47.69	29.6
6.25	92.43	77.50	72.31	97.05	48.97	82.18	42.33
3.125	97.21	95.50	93.59	90.10	62.56	94.62	56.54
1.56	100.00	100.00	100.00	100.00	88.21	99.84	67.24
0	100.00	100.00	100.00	100.00	100.00	100.00	100.00

MCF-2



Figuer 7

MCF-2



Figuer 8

The results of inhibitory concentration fifty (IC_{50}) data are summarized in **table 5**.

Table 5:- IC_{50} (µg) values of tumor cell lines after 72h continuous exposure to test.

Compounds	MCF-7 cell line
3a	19.40
3b	10.40
4	21.40
5a	24.50
6	6.10
7a	11.80
Vinblastine standard	4.60

IC_{50} is the concentration that induces 50% growth inhibition compared with untreated control cells.

In comparison with standard antitumor vinblastine , compound **6** found to be high active against MCF-7 than anthor tested compounds.

4- Experimental section

Meting points were uncorrected and determined in an open capillary tube. IR spectra were recorded On FTIR shimadzu spectrometer. ^{1}H-NMR spectra were recorded in DMSO-d_6 on Avance 300 MH_z spectrometer using TMS as an internal stand-ard. The mass spectra were recorded on EI-shimadzu-GC-MS spectrometer. Elemental analyses were performed on a Carlo Erba 106 Perkin-Elmer model 240 analyzer.

2-phenyl-4-benzylidene-5H-oxazolinon (1)

A mixture of hyperic acid (0.01 mole), benzaid hyde (0.01 mole), fused sodium acetate (0.03 mole) and acetic anhydride (3ml) was fused on a hot plate for 2-3min. the reaction mixture was heated on a water – bath for 2h, then cooled and poured into water. The resulting solid was filtered off, washed with hot water, dried and purified by recrystallization with benzene to give 1 as yellow crystal , yield 78% , m.p.153^{o}c IR (KBR): 1760 (C=O),1625(C=N),1605,1568 (C=C), 1225,1083 (C-O) cm^{-1} .Ms: m/z (%)=250 (M^+_{+1},3.60) ,249(M^+,13.30) ,116 (6.70), 107 (2.40),106 (10.90),105 (100) ,104(18.8), 103 (4.20), 90 (2.40), 89 (5.50) ,77 (57.00) ,76 (20.60) ,63 (5.50) ,58 (10.30) ,51 (20.60) ,50(15.20). Anal $C_{16}H_{11}NO_2$ for calcd:c,77.11;H;4.42;N;5.62.found: c,77.00;H,4.33;N,5.48.

2-(Amino thio carbonyl)-3-phenyl-5-benzylidene-1,2,4-triazin -6-one (2).

A mixture of compound **1** (0.01mole) and thio semi-carbazide (0.01mole) in glacial acetic acid (25ml) was heated under reflux for 3-4 hr, then cooled and poured into ice-water. The solid formed was filtered off, washed with water, dried and purified by recrystallization with ethanol to give 2 as pale yellow crystals, yield 73%,m.p.220^{o}c.IR (KBR):3443,3123 (NH_2),3271 (NH),1713 (C=O),1633 (C=O), 1449(C=S) cm^{-1}. ^{1}H-NMR (DMSO-d_6) :δ 7.20-8.01 (m,11H,Ar-H and olefinic-H) ,8.35 (S,2H,NH_2) , 10.02 (S,1H,NH) ppm. Anal. $C_{17}H_{14}N_4OS$. For calcd : c, 63.35 ; H , 4.35; N, 17.39. found: C, 63.21; H, 4.23; N, 17.17.

1-aryl-4- thioxo-5- phenyl -7- benzylidene - 1,2,4- triazino-[2,1-a] - 1,2,4- triazin -8- ones (3a,b)
4- Thioxo-5- phenyl -7- benzylidene -1,2,4- triazino-[2,1-a]- 1,2,4- triazin -1,8- doine (4).

A mixture of compound **2** (0.01mole), w-bromo methyl aryl ketones (such as 4-methyl phenacyl bromide and 4-methoxy phenacyl bromide) and ethyl chloroacetate (0.01mole) in acetic acid (25ml) in presence of fused sodium acetate (0.03mole) was heated under reflux 2hrs, then cooled and poured into water. The resulting solid was filtered off, washed with water, dried and purified by recrystallization from a suitable solvent to give **3** and **4**.

1-(P-methyl phenyl)-4- thioxo-5-phenyl-7 -benzylidene-1,2,4 – triazino-[2,1-a]-,1,2,4-triazin-8-one (3a) as yellow crystals , yield 71%, m.p.85^{o}c. IR (KBr): 3225 (NH), 1698(C=O), 1625 (C=N), 1605,1585 (C=C), 1398(C=S) cm^{-1}. ^{1}H-NMR (DMSO-d_6) :δ 2.30(S,3H,CH_3), 6.75- 8.20 (m,16H,Ar-H and olefinic -H), 10.20 (S,1H,NH) ppm. Anal. $C_{26}H_{20}N_4OS$ for calcd: C, 71.56; H, 4.59; N, 12.84. Found: C, 71.42; H, 4.33; N, 12.62.

1-(P-methoxy phenyl)-4 thioxo-5-phenyl-7 benzylidene-1,2,4 – triazino-[2,1-a]-1,2,4-triazino-8-one (3b) as yellow crystals , yield 73%, m.p.100^{o}c. IR (KBr):3257 (NH), 1698(C=O), 1630 (C=N), 1608, 1595(C=C), 1397(C=S) cm^{-1}. ^{1}H-NMR (DMSO-d_6) : δ 3.85(S,3H,OCH_3), 6.78-8.01 (m, 16H, Ar-H and olefinic -H), 10.31 (S,1H,NH) ppm. Anal . $C_{26}H_{20}N_4O_2S$ for calcd: C, 69.03, H, 4.42, N, 12.39. Found: C, 68.98; H, 4.31, N,12.11.

4-Thioxo-5-phenyl-7- benzylidene-1,2,4 - triazino[2,1-a]-,1,2,4-triazin-1,8-dione (4) as yellow crystals , yield 76%, m.p.195^{o}c. IR(KBr): 3231 (NH),1738, 1694 (C=O), 1630(C=N),1602, 1585 (C=C),1394 (C=S) cm^{-1}. ^{1}H-NMR

(DMSO-d_6) :δ 4.10 (S,2H,NCH_2CO), 7.24- 8.35 (m,11H,Ar-H and olefinic-H),10.35 (S,1H,NH) ppm. Anal . $C_{19}H_{14}N4O_2S$ for calcd: C, 62.98, H, 3.87, N, 15.47, S, 8.84. Found: c, 62.68; H, 3.69;H,3.69, N,15.29,S,8.63.

1-Aryl-3- acetyl -4-thioxo -5- phenyl -7- benzylidene – 1,2,4- triazino -[2,1-a] - 1,2,4- triazin -8- ones (5a,b)
3- Acetyl -4- thioxo -5- phenyl -7- benzylidene - 1,2,4- triazino [2,1-a] - 1,2,4- triazin -1,8- doine (6)
A solution of 3 and /or 4 (0.01mole) in acetic anhydride (15ml) was heated under reflux 2hr, then cooled and poured into ice-water. The solid obtained was filtered off, washed with water, dried and purified off, washed with water, dried and purified by recrystallization with benzene to give 5 and 6.
1-(P-methyl phenyl) -3- acetyl -4- thio xo-5-phenyl-7 benzyl-idene-1,2,4 – triazino-[2,1-a]-,1,2,4-triazin- 8- one **(5a)** as pale yellow crystals , yield 68% , m.p.95^{o}c . IR (KBr) : 1710 , 1695 (C=O) , 1624 (C=N) , 1605 , 1585 (C=C) , 1398 (C=S) cm^{-1} . Anal . C_{28} H_{22} N_4 O_2S for calcd : c, 70.29; H, 4.60; N, 11.71; S, 6.69.

1-(P-methoxy phenyl) - 3 –acetyl-4- thio xo -5- phenyl-7 -benzylidene-1,2,4 - triazino-[2,1-a]-,1,2,4-triazin-8-one **(5b**) as pale yellow crystals , yield 72%, m.p,65^{o}c. IR(KBr) : 1711, 1698 (C=O) , 1629 (C=N) , 1605 , 1588 (C=C) , 1395 (C=S) , 1210 , 1085 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6) :δ 2.21(S,3H,$COCH_3$), 3.85 (S,3H,OCH_3), 6.98 -8.12 (m, 16H, Ar-H and olefinic-H)ppm . Anal C_{28} H_{22} N_4 O_3S for calcd : C, 68.02
; H, 4.45 ; N, 11.34 ; S , 6.48 . Found : C, 67.98 ; H, 4.34 ; N, 11.22 ; S, 6.22.

3-Acetyl - 4 -thioxo-5-phenyl-7- benzylidene-1,2,4 – triazino-[2,1-a]-,1,2,4-triazin-1,8-dione **(6)** as pale yellow crystals , yield 65%, m.p,170^{o}c. ^{1}H-NMR (DMSO-d_6) :δ 2.14 (S,3H,$COCH_3$) , 3.2 (S,2H,NCH_2CO), 6.91- 8.40 (m, 11H, Ar-H and olefinic –H),ppm . Anal . C_{21} H_{16} N_4 O_3S for calcd : C, 62.38 ; H, 3.96; N, 13.86; S, 7.92 . Found; C, 62.17 ; H, 3.69; N, 13.66; S, 7.73.

2-Arylidene -4-thio xo-5-phenyl-7- benzylidene-1,2,4-triazino-[2,1-a]-,1,2,4-triazin-1,8-doines (7a,b).
A mixture of 4 (0.01mole), aromatic aldhydes (such as benzaldhyde and 2- hydroxy benzaldhyde) (0.01 mole) and piperidine (1ml) was fused on a hot plate at 120-125 ^{o}C for 1 hr. The reaction mixture was cooled and acidified with dilute hydrochloric acid (2N). the crude product was filtered off ,washed with water , dried and purified by recrystallization from ethanol to give **7**.

2,7- benzylidene 4 - thioxo -5- phenyl-7- benzylidene - 1, 2,4 -triazino - [2,1 -a] - , 1, 2,4 - triazin - 1,8-doine **(7a)** as yellow crystals , yield 74%,m.p,110^{o}c. IR (KBr)1722 ^{1}H-NMR (DMSO-d_6):δ 6.89-7.89 (m . 17 H , Ar-H and H-Olifinic), 10.35 (S ,1H ,NH) Anal. C_{26} H_{18} N_4 O_2S for calcd : C, 69.33; H, 4.00; N, 12.44; S, 7.11 . Found ; C, 69.18; H, 3.82; N, 12.22; S, 7.03.

2-(O- hydroxy benzylidene)-4- athioxo -5- phenyl -7 benzylidene -1,2, 4- triazino - [2,1 - a] -,1, 2,4- triazin -1,8-doine **(7b)** as yellow crystals , yield 72%,m.p,145^{o}c. IR(KBR) 1720. ^{1}H-NMR (DMSO-d_6):δ 6.89-7.89 (m, 16 H , Ar-H and H-Olifinic), 10.20 (S ,1H ,NH) ,10.75 (S , 1H , OH)PPm. Anal C_{26} H_{18} N_4 O_3Sb for calcd : C, 66.95; H, 3.86; N, 12.02; S, 6.87. Found ; C,66.79; H, 3.66; N, 11.98; S, 6.66.

2-Arylidene -3- acetyl -4- thio xo -5- phenyl -7- benzylidene - 1,2,4- triazino -[2,1-a] - 1,2,4- triazin -1,8- doines (8a,b).
A solution of 7 in acetic anhydride (15ml) was heated under refulx for 2hr, then cooled and poured into water. The resulting solid was filtered off, washed with water. The resulting solid was filtered off , washed with water , dried and purified by recrystallization from benzene to give **8**.

2,7- Dibenzylidene-3-acetyl -4-thioxo-5- phenyl-7- benzylidene_-1,2,4- triazino- [2,1-a]-,1,2,4 - triazin - 1,8-doine **(8a)** as yellow crystals , yield 63%,m.p,70 ^{o}c .IR(KBr):1722.^{1}H-NMR (DMSO-d_6); δ 2.35 (S,3 H , $COCH_3$) , 6.81 - 7.81 (m , 17 H, Ar-H and H-Olefinic) PPm .Anal. $C_{28}H_{20}N_4O_3S$ for calcd: C,68.29; H 4.06 ; N,11.38; S, 6.50.Found: C, 68.03; H, 3.89; N, 11.23; S, 6.33.

2-(O- hydroxy benzylidene)-3- acetyl -4- thio xo -5- phenyl-7-benzylidene-1,2,4-triazino-[2,1-a] - 1,2,4-triazin-1,8-doine **(8b)**. as pale yellow crystals, yield 63%, m.p.100^{o}c. IR (KBr) 1721. ^{1}H-NMR (DMSO-d_6); δ 2.35 (S, 3 H , $COCH_3$) , 6.83 -7.85 (m , 16 H, Ar-H and H-Olefinic) 10.39 (S,1H , OH) PPm .Anal $C_{28}H_{20}N_4O_4S$ for calcd; C, 66.14; H, 3.94; N, 11.02; S, 6.30.Found; C, 66.03; H, 3.79, N, 10.93; S, 6.08.

CONCLUSION

The series of nitrogen hetero cyclic were synthesized. In comparison the anti microbial and anticancer activity of these compounds with standard drug used. All compounds showed activity against antimicrobial except **3b , 4, 5a** did not exhibit any activity against (one kind of tested fungi and one kind of tested bacteria) , In comparison with antitumor vinblastine drug compound **6** found to be high active against MCF-7 than anthor tested compounds.

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