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Electron impact ionization mass spectra of 1, 2, 4-triazine derivatives with antimicrobial activity

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ABSTRACT

2– (Aminothiocarbonyl) -3- aryl – 5 – arylidene – 1, 2, 4-triazin – 6– ones **(3_{a-c})** were prepared via condensation of oxazolinones **(2_{a-c})** with thiosemicarbazide. 1-methyl – 3 – thioxo – 4 –aryl – 6– arylidene – triazolo – [2, 1–a] – 1, 2, 4 – triazin–7 – ones **(4_{a-c})** were obtained by refluxing compound **(3)** with acetic anhydride. Treatment of **(3)** with benzoyl chloride in acetic acid yielded the corresponding 2– (benzoylamine) thiocarbonyl–3–aryl–5 arylidene–1, 2, 4-– triazin–6–ones **(5)**. The electron impact ionization mass spectra of compounds **(3_b)**, **(4_a)**, **(4_b)**, **(5_a)** and **(5_b)** showed a weak molecular ion peak and a base peak of m/z 139 resulting from a cleavage fragmentation, but the compound **(3_a)** a base peak at m/z 138. The compounds **(3_c)** and **(5_c)** gave a characteristic fragmentation pattern with a very stable fragment at m/z 104, while the compound **(4_c)** was at m/z 119.

INTRODUCTION

Triazine derivatives have occupied a unique position in medicinal chemistry. Triazine derivatives have attracted considerable pharmaceutical interest due to their antitumor[1-5], anticonvulsant[6] and antileukemic[7,8] activities and cytotoxic effect[9]. Traiazine has been used to form many types of functional groups other than amines and heterocycles and used as protecting groups in natural product synthesis. Thus, they are reactive groups, which are adaptable to different synthetic transformations. The synthetic strategy of the compounds was outlined in the scheme 1. Synthesis of some substituted of 1, 2, 4- triazine derivatives was carried out by the condensation of 4-substituted-2- phenyl – 4H- oxazol–5-one and thiosemicarbazide in glacial acetic acid as a solvent.

RESULTS AND DISCUSSION

4- Substituted– 2– aryl– 4H – oxazol– 5–one **(2_{a-c})** were prepared via the reaction of N–aroylglycine **(1)** with aromatic aldehydes in presence of fused sodium acetate and acetic anhydride under fusion. Cyclocondensation[10-12] of oxazolinone derivatives **(2_{a-c})** with thiosemicarbazid in glacial acetic acid under reflux led to the formation of 2– (aminothiocarbonyl) – 3 – aryl –5– arylidene – 1, 2, 4- triazin – 6– ones **(3_{a-c})**, (scheme 1).

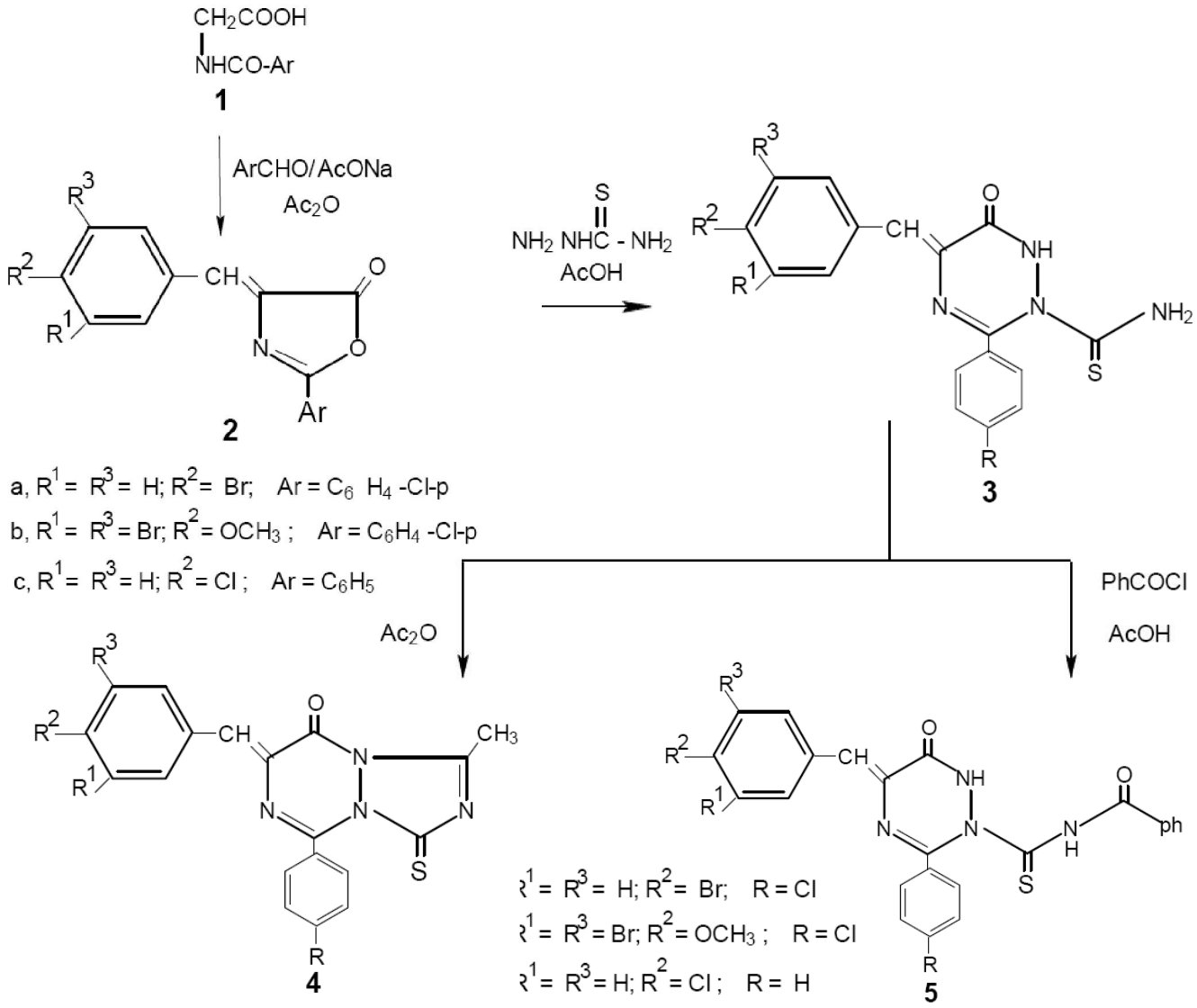
1–Methyl–3– thioxo– 4– aryl–6– arylidene–triazolo [2,1-a]– 1, 2, 4–triazin– 7 – ones **(4_{a-c})** were prepared by refluxing of 2– (aminothiocarbonyl)– 3, 5– substituted– 1, 2, 4–triazin–6–ones **(3_{a-c})** with acetic anhydride.

Treatment of 2– (aminothiocarbonyl)– 3,5–substituted– 1, 2, 4– triazin– 6– one with benzoylchloride in acetic acid yielded the corresponding 2– (benzoylamino) thiocarbonyl –3-aryl-5-arylidene-1,2,4-triazin–6-ones **(5_{a-c})**.

MASS SPECTROSCOPY

TABLE 1 list the m/z (relative abundance, %) val-

ues of the principle fragments of the studied 1, 2, 4– triazine derivatives.

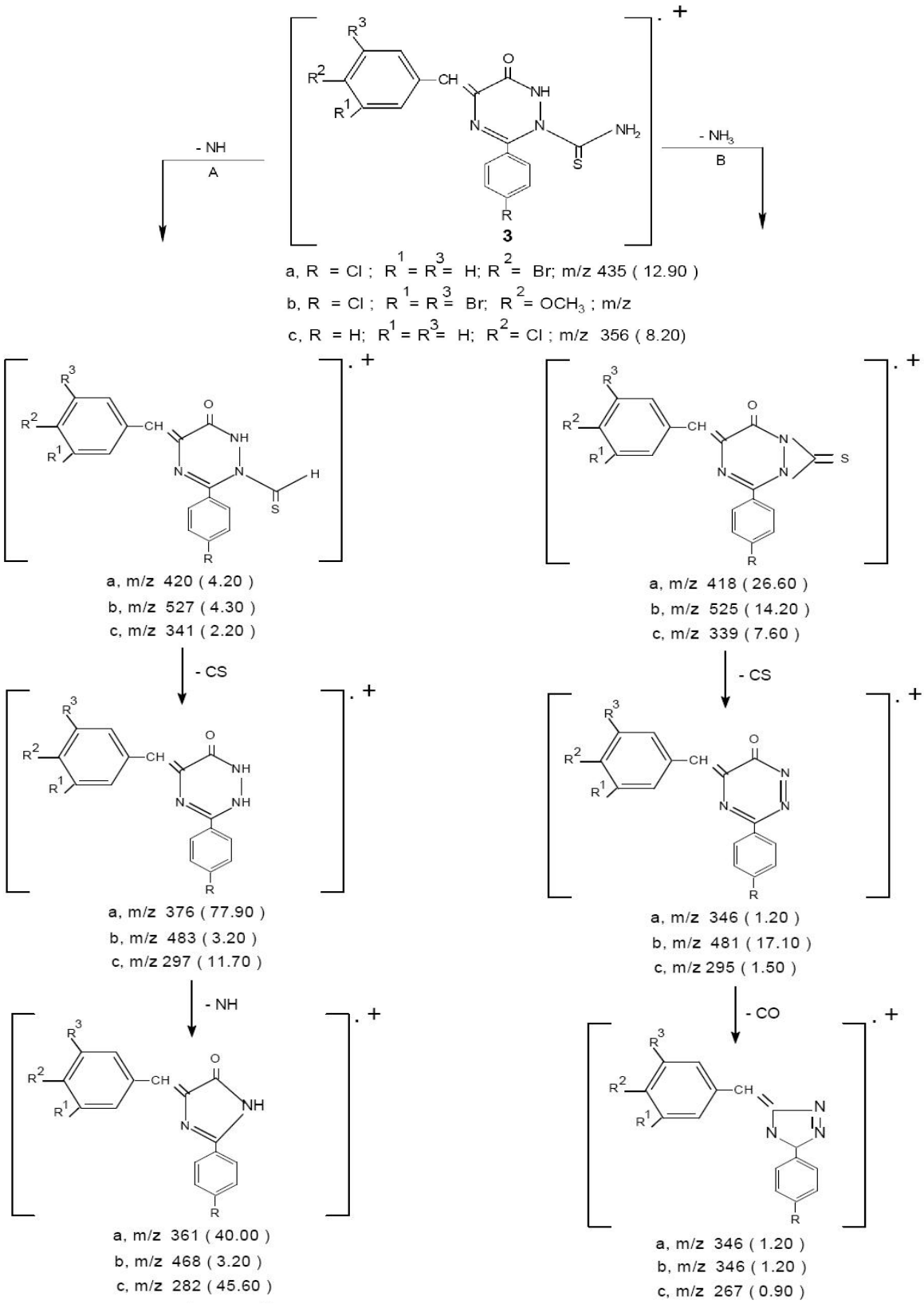


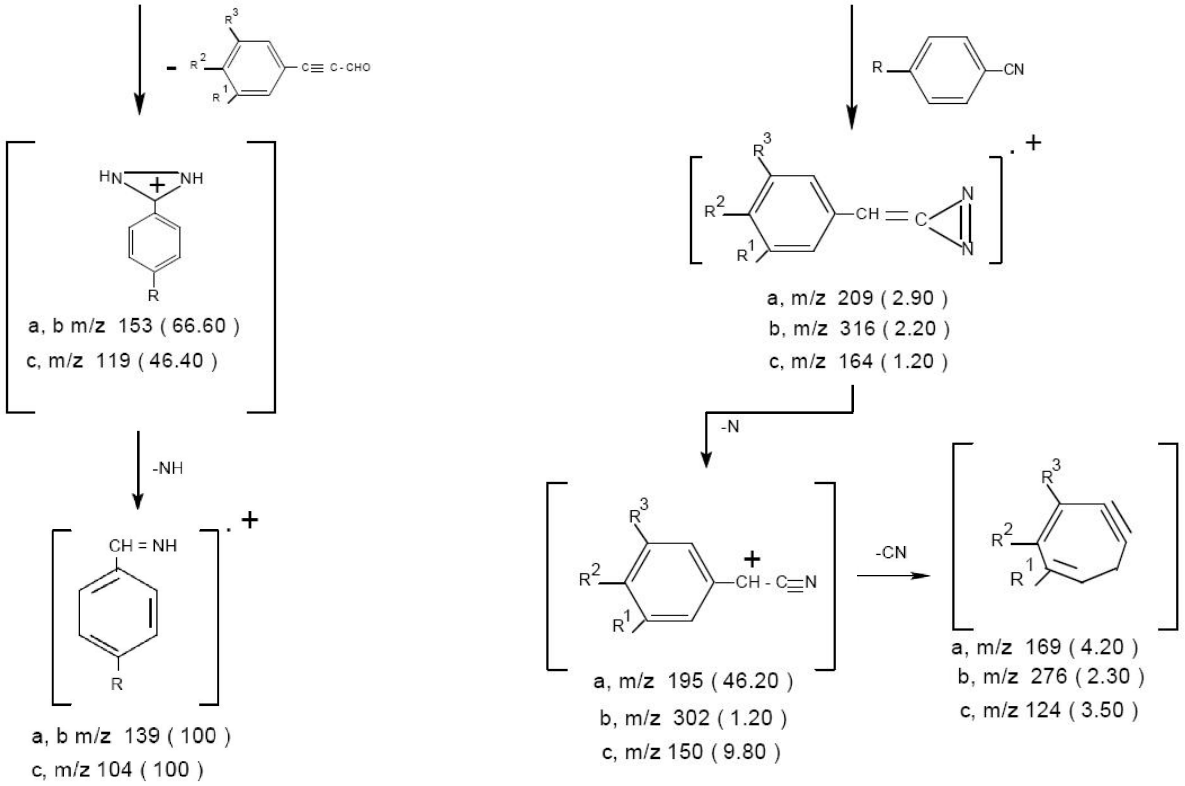
Scheme 1

The mass spectra (TABLE 1) of compounds **(3)**, **(4)** and **(5)** show relatively small molecular ions and peaks typical of a cleavage and rearrangement process[13,14] type fragmentation. The main fragmentation pathway of compound **(3)** was summarized in scheme 2. The detection of both complementary fragments of the cleavage and rearrangement processes was attributed to their comparable ionization potentials. From the study of the mass spectra of compound **(3_a)** (Figure l) and **(3_c)** (Figure 2). It was found that the molecular ions at m/z 435 and m/z 356 fragmented further involving two various pathways shown in scheme 2. The ions of m/z 435 and m/z 356 fragmented via the suggested pathway A and gave fragments of m/z 420 and m/z 341, which lost thiocarbonyl (CS) and gave a fragments of m/z 376 and m/z 297. The ions of m/z 376 and m/z 297 were broken and gave ions of m/z 361 and m/z 282 by losing NH group. The fragmentations of m/z 361 and m/z 282 underwent fragmentations and produced ions of m/z 153 and m/z 119, which further fragmented and gave a stable fragments of m/z 138 and m/z 104 by losing NH group. This fragmentation led to ions of m/z 111, 77 and m/z 75, 51, respectively.

Subsequently, the molecular ions of m/z 435 and m/z 356 fragmented via the suggested pathway B and gave a fragments to m/z 418 and m/z 339 by losing ammonia molecule. The fragments of m/z 418 and m/z 339 were broken and gave a fragments of m/z 374

and m/z 295, which lost carbon monoxide (C = O) and gave a fragments of m/z 346 and m/z 267. The fragments of m/z 346 and m/z 267 underwent fragmentations and produced peaks at m/z 209, m/z 164 and m/z 195, m/z 150 and 169, m/z 124 and m/z 89, respectively.





Scheme 2

TABLE 1 : EI mass spectra (70 ev) of compounds 3, 4 and 5 m/z (relative intensity %)

No.	M^+	Pathway A		Pathway B		Other ions
		M-	m/z	M-	m/z	
3a	$[C_{17}H_{12}N_4BrClOS]^{-+}$ 435 (12.90)	- NH	$[C_{17}H_{11}N_3BrClOS]^{-+}$ 420 (4.20)	$-NH_3$	$[C_{17}H_9N_3BrClOS]^{-+}$ 418 (26.60)	437 (M^+ + 2, 12.30), 434 (M^+ - 1, 12.20), 420 (22.00), 417 (24.20), 416 (8.10), 380 (2.00), 379 (7.40), 377 (19.40), 376 (17.90), 375 (13.50), 364 (12.50), 363 (11.80), 362 (40.80), 360 (36.90), 359 (30.70), 347 (1.30), 298 (2.00), 297 (1.20), 295 (2.70), 259 (2.70), 258 (2.00), 257 (2.70), 255 (1.70), 240 (2.70), 239 (1.56), 238 (3.40), 237 (1.50), 211 (2.00), 210 (2.20), 208 (1.70), 197 (39.10), 196 (36.40), 194 (36.90), 183 (5.20), 182 (6.10), 181 (7.60), 180 (6.40), 168 (2.70), 167 (2.50), 155 (27.00), 154 (23.80), 152 (17.90), 134 (58.50), 140 (32.20), 137 (74.00), 136 (18.20), 144 (4.40), 142 (3.70), 141 (12.80), 113 (27.80), 89 (38.60), 88 (16.00), 87 (11.30), 76 (64.40), 74 (26.30), 64 (51.70)
		-CS	$[C_{16}H_{11}N_3BrClO]^{-+}$ 376 (77.90)	-CS	$[C_{16}H_9N_3BrClO]^{-+}$ 374 (53.20)	
		-NH	$[C_{16}H_{10}N_2BrClO]^{-+}$ 361 (40.00)	-CO	$[C_{15}H_9N_3BrCl]^{-+}$ 346 (1.20)	
		C_9H_4BrO	$[C_7H_6N_2Cl]^{-+}$ 153 (66.60)	C_7H_4NCl	$[C_8H_5N_2Br]^{-+}$ 209 (2.90)	
		- NH	$[C_7H_5NCl]^{-+}$ 138 (100)	-N	$[C_8H_5NBr]^{+}$ 195 (46.20)	
		- HCN	$[C_6H_4Cl]^{+}$ 111 (71.50)	- CN	$[C_7H_5Br]^{-+}$ 169 (4.20)	
		- HCl	$[C_6H_3]^{-+}$ 75 (79.10)	- Br	$[C_7H_5]^{+}$ 89 (13.20)	
				$-C_2H$	$[C_5H_4]^{-+}$ 64 (14.20)	
3b	$[C_{18}H_{13}N_4Br_2ClO_2S]^{-+}$ 542 (11.00)	- NH	$[C_{18}H_{12}N_3Br_2ClO_2S]^{-+}$ 527 (4.30)	$-NH_3$	$[C_{18}H_{10}N_3Br_2ClO_2S]^{-+}$ 525 (14.20)	544 (M^+ + 2, 10.20), 526 (1.20), 524 (2.30), 484 (1.20), 482 (1.20), 480 (2.30), 470 (1.20), 469 (1.30), 455 (1.20), 454 (1.10), 452 (2.20), 317 (1.20), 315 (1.20), 303 (0.60), 296 (1.70), 289 (2.30), 286 (2.00), 285 (1.00), 270 (1.60), 232 (1.40), 216 (1.20), 215 (3.30), 144 (1.20), 196 (1.20), 195 (1.20), 170 (2.30) 169 (1.60), 168 (1.80), 141 (36.30), 140 (9.00), 138 (14.50), 136 (1.40), 115 (1.90), 113 (7.80), 112 (7.20), 103 (1.60), 102 (2.50), 88 (1.80), 78 (0.20), 76 (5.30), 701 (4.70),
		-CS	$[C_{17}H_{12}N_3Br_2ClO_2]^{-+}$ 483 (3.20)	-CS	$[C_{17}H_{10}N_3Br_2ClO_2]^{-+}$ 481 (17.20)	
		-NH	$[C_{17}H_{11}N_2Br_2ClO_2]^{-+}$ 468 (3.20)	-CO	$[C_{16}H_{10}N_3Br_2ClO]^{+}$ 453 (3.10)	
		$C_{10}H_5Br_2O_2$	$[C_7H_6N_2Cl]^{+}$ 153 (21.20)	C_7H_4NCl	$[C_9H_6N_2Br_2O]^{-+}$ 316 (2.20)	
		- N	$[C_7H_6NCl]^{-+}$ 139 (100)	-N	$[C_9H_6NBr_2O]^{+}$ 302 (1.20)	
		$-CH_2N$	$[C_6H_4Cl]^{+}$ 111 (21.90)	- CN	$[C_8H_6Br_2O]^{-+}$ 276 (2.30)	

No.	M^+	Pathway A		Pathway B		Other ions
		M-	m/z	M-	m/z	
3b		- HCl	$[C_6H_3]^{-+}$ 75 (15.80)	- Br	$[C_8H_6BrO]^+$ 198 (1.40)	64 (1.20), 63 (3.30), 62 (1.40), 51 (4.30), 50 (5.70)
				- Br	$[C_8H_6O]^{-+}$ 118 (1.20)	
3c	$[C_{17}H_{13}N_4ClOS]^{-+}$ 356 (8.20)	- NH	$[C_{17}H_{12}N_3ClOS]^{-+}$ 341 (2.20)	$-NH_3$	$[C_{17}H_{10}N_3ClOS]^{-+}$ 339 (7.60)	358 (M^+ + 2, 3.60),355 (M^4 – 1, 4.80), 343 (0.30), 340 (2.50), 338 (4.60), 298 (2.70), 284 (13.70), 281 (28.80), 280 (6.40), 238 (3.00), 237 (1.40), 204 (1.30), 203 (2.00), 178 (3.00), 177 (2.20), 176 (1.20), 165 (1.20), 163 (160), 161 (6.10), 153 (11.20), 152 (9.30), 151 (37.50), 138 (2.10), 136 (6.50), 125 (2.70), 123 (7.30), 120 (4.00), 118 (4.80), 116 (6.60), 105 (13.70), 103 (33.50), 88 (6.80), 87 (3.60), 78 (7.50), 76 (36.80), 75 (20.80), 65 (2.30), 63 (9.80), 62 (5.40), 50 (15.10)
		-CS	$[C_{16}H_{12}N_3ClO]^{-+}$ 297 (11.70)	-CS	$[C_{16}H_{10}N_3ClO]^{-+}$ 295 (1.50)	
		-NH	$[C_{16}H_{11}N_2ClO]^{-+}$ 282 (45.60)	-CO	$[C_{15}H_{10}N_3Cl]^{-+}$ 267 (0.90)	
		C_9H_4ClO	$[C_7H_7N_2]^+$ 119 (46.40)	C_7H_5N	$[C_8H_5N_2Cl]^{-+}$ 164 (1.20)	
		- NH	$[C_7H_6N]^+$ 104 (100)	-N	$[C_8H_5NCl]^+$ 150 (9.80)	
		-HCN	$[C_6H_5]^+$ 77 (89.50)	- CN	$[C_7H_5Cl]^{-+}$ 124 (3.50)	
		$-C_2H_2$	$[C_4H_3]^+$ 51 (34.10)	- Cl	$[C_7H_5]^+$ 89 (11.10)	
				- C_2H	$[C_5H_4]^{-+}$ 64 (18.50)	
4a	$[C_{19}H_{12}N_4BrClOS]^{-+}$ 458 (3.40)	- C_2NH	$[C_{17}H_{11}N_3BrClOS]^{-+}$ 420 (1.70)	C_2H_3N	$[C_{17}H_9N_3BrClOS]^{-+}$ 418 (4.70)	460 (M+ + 2, 3.30), 457 (1.40), 421 (1.80), 379 (1.50), 378 (1.90), 377 (5.50), 375 (4.60), 365 (2.30), 364 (2.30), 363 (8.10), 362 (6.60), 360 (4.10), 302 (0.60), 301 (1.50), 300 (1.20), 249 (1.30), 298 (1.00), 212 (1.30), 211 (1.30), 210 (1.20), 197 (3.00), 196 (2.10), 194 (2.30), 181 (2.00), 180 (2.10), 179 (1.40), 167 (1.10), 155 (4.00), 154 (3.20), 152 (18.06), 143 (1.10), 142 (3.50), 14 (34.80), 140 (31.40), 138 (17.10), 119 (2.70), 118 (3.60), 117 (3.80), 114 (4.50), 113 (10.70), 112 (4.50), 110 (9.20), 90 (1.50), 88 (5.40), 77 (4.70), 76 (13.70), 74 (10.80), 65 (1.40), 63 (5.60), 62 (6.10), 51 (11.70), 50 (14.00)
		-CS	$[C_{16}H_{11}N_3BrClO]^{-+}$ 376 (4.40)	-CS	$[C_{16}H_9N_3BrClO]^{-+}$ 374 (3.40)	
		-NH	$[C_{16}H_{10}N_2BrClO]^{-+}$ 361 (5.30)	-CO	$[C_{15}H_9N_3BrCl]^{-+}$ 346 (1.50)	
		C_9H_4BrO	$[C_7H_6N_2Cl]^{-+}$ 153 (10.00)	C_7H_4NCl	$[C_8H_5N_2Br]^{-+}$ 209 (1.80)	
		- N	$[C_7H_6NCl]^+$ 139 (100)	-N	$[C_8H_5NBr]^{-+}$ 195 (4.40)	
		$-H_2CN$	$[C_6H_4Cl]^+$ 111 (34.90)	-CN	$[C_7H_5Br]^+$ 168 (1.00)	
		-HCl	$[C_6H_3]^{-+}$ 75 (31.90)	- Br	$[C_7H_5]^+$ 89 (3.70)	
				- C_2H	$[C_5H_4]^+$ 64 (2.30)	
4b	$[C_{20}H_{13}N_4Br_2ClO_2S]^{-+}$ 566 (22.10)	$-C_2HN$	$[C_{18}H_{12}N_3Br_2ClO_2S]^{-+}$ 527 (2.30)	C_2H_3N	$[C_{18}H_{10}N_3Br_2ClO_2S]^{-+}$ 525 (1.30)	568 (M^+ + 2, 20.20), 565 (5.20), 528 (1.20), 526 (1.20), 524 (0.90), 484 (1.20), 482 (2.20), 480 (1.30), 470 (0.30), 469 (1.10), 467 (1.00), 454 (1.50), 452 (1.20), 317 (1.20), 315 (1.60), 392 (5.40), 391 (10.90), 373 (13.00), 366 (7.60), 365 (6.50), 362 (9.80), 361 (10.90), 373 (13.00), 366 (7.60), 365 (6.50), 362 (9.80), 361 (10.90), 3.28 (5.40), 270 (8.70), 269 (7.60), 253 (7.60), 252 (8.70), 247 (6.50), 242 (6.50), 230 (5.40), 229 (7.60), 215 (7.60), 214 (10.90), 213 (16.30), 199 (6.50), 198 (4.30), 178 (5.40), 152 (8.70), 141 (47.80), 138 (59.80), 119 (5.40), 117 (9.80), 114 (13.00), 113 (10.90), 110 (20.70), 105 (10.90), 104 (7.60), 103 (7.60), 101 (17.40), 76 (16.30), 74 (18.50), 63 (13.00), 61 (16.30)
		-CS	$[C_{17}H_{12}N_3Br_2ClO_2]^{-+}$ 483 (5.20)	-CS	$[C_{17}H_{10}N_3Br_2ClO_2]^{-+}$ 481 (3.30)	
		-NH	$[C_{17}H_{11}N_2Br_2ClO_2]^{-+}$ 468 (1.30)	-CO	$[C_{16}H_{10}N_3Br_2ClO]^{-+}$ 453 (2.10)	
		$C_{10}H_5Br_2O_2$	$[C_7H_6N_2Cl]^+$ 153 (9.60)	C_7H_4NCl	$[C_9H_6N_2Br_2O]^{-+}$ 316 (3.20)	
		- N	$[C_7H_6NCl]^+$ 139 (100)	-N	$[C_9H_6NBr_2O]^+$ 302 (2.20)	
		$-CH_2N$	$[C_6H_4Cl]^+$ 111 (50.00)	-CN	$[C_8H_6Br_2O]^+$ 276 (3.30)	
		-HCl	$[C_6H_3]^{-+}$ 75 (28.30)	- Br	$[C_8H_6BrO]^+$ 197 (4.40)	
				- Br	$[C_8H_6O]^+$ 118 (6.50)	
4c	$[C_{19}H_{13}N_4ClOS]^{-+}$ 380 (28.40)	C_2HN	$[C_{17}H_{12}N_3ClOS]^{-+}$ 341 (11.60)	C_2H_3N	$[C_{17}H_{10}N_3ClOS]^{-+}$ 339 (31.30)	382 (M+ + 2, 9.90), 381 (28.40), 340 (10.40), 338 (21.00), 299 (21.20), 298 (13.00), 296 (12.00), 281 (2.30), 280 (1.90), 279 (3.60), 262 (1.90), 216 (2.40), 204 (2.70), 202 (1.70), 163 (4.80), 162 (5.30), 161 (34.50), 153 (4.60),
		-CS	$[C_{16}H_{12}N_3ClO]^+$ 297 (48.90)	-CS	$[C_{16}H_{10}N_3ClO]^{-+}$ 295 (4.10)	
		-NH	$[C_{16}H_{11}N_2ClO]^+$ 282 (2.90)	-CO	$[C_{15}H_{10}N_3Cl]^{-+}$ 267 (1.50)	
		C_9H_4ClO	$[C_7H_7N_2]^+$ 119 (100)	C_7H_5N	$[C_8H_5N_2Cl]^{-+}$ 164 (5.30)	

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No.	M^+	Pathway A		Pathway B		Other ions
		M-	m/z	M-	m/z	
4c		-NH	$[C_7H_6N]^+$ 104 (20.50)	-N	$[C_8H_5NCl]^+$ 150 (3.60)	151 (5.80), 145 (3.60), 144 (2.70), 138 (8.70), 137 (5.50), 136 (17.30), 135 (7.00), 120 (11.80), 118 (15.20), 103 (15.20), 101 (18.60), 91 (4.60), 90 (2.20), 88 (4.30), 76 (10.60), 75 (10.80), 65 (3.10), 63 (2.40), 62 (3.10), 53 (2.90), 51 (11.20)
		-HCN	$[C_6H_5]^+$ 77 (6.70)	-CN	$[C_7H_5Cl]^+$ 124 (2.70)	
		$-C_2H_2$	$[C_4H_3]^+$ 51 (11.20)	-Cl	$[C_7H_5]^+$ 89 (4.10)	
				$-C_2H$	$[C_5H_4]^+$ 64 (1.50)	
5a	$[C_{24}H_{16}N_4BrClO_2S]^{-+}$ 538 (1.30)	C_7H_5NO	$[C_{17}H_{11}N_3BrClO_2S]^{-+}$ 420 (1.60)	C_7H_7NO	$[C_{17}H_9N_3BrClOS]^{-+}$ 418 (1.40)	540 (M^+ + 2, 1.30), 537 (0.90), 448 (1.10), 447 (0.90), 446 (1.20), 419 (1.40), 417 (0.30), 378 (1.60), 377 (1.60), 375 (1.30), 364 (1.30), 363 (4.90), 362 (4.90), 337 (2.50), 336 (1.40), 335 (2.00), 333 (1.60), 281 (0.70), 280 (1.80), 206 (1.30), 204 (1.30), 201 (1.30), 197 (3.40), 196 (2.00), 144 (1.60), 168 (3.40), 167 (1.10), 155 (3.30), 154 (6.10), 148 (1.30), 141 (32.00), 140 (10.70), 138 (13.20), 119 (1.30), 118 (1.80), 116 (4.00), 115 (4.90), 114 (4.30), 113 (10.20), 112 (7.80), 110 (5.60), 91 (2.70), 90 (5.40), 88 (5.10), 74 (6.10), 62 (1.80), 60 (3.30), 55 (2.40), 51 (1.30)
		-CS	$[C_{16}H_{11}N_3BrClO]^{-+}$ 376 (2.20)	-CS	$[C_{16}H_9N_3BrClO]^{-+}$ 374 (2.00)	
		-NH	$[C_{16}H_{10}N_2BrClO]^{-+}$ 361 (3.40)	-CO	$[C_{15}H_9N_3BrCl]^{-+}$ 346 (2.20)	
		C_9H_4BrO	$[C_7H_6N_2Cl]^{-+}$ 153 (6.10)	C_7H_4NCl	$[C_8H_5N_2Br]^{-+}$ 209 (1.40)	
		-N	$[C_7H_6NCl]^{-+}$ 139 (100)	-N	$[C_8H_5NBr]^+$ 195 (2.00)	
		$-CH_2N$	$[C_6H_4Cl]^{-+}$ 111 (26.60)	-CN	$[C_7H_5Br]^+$ 169 (2.70)	
		-HCl	$[C_6H_3]^{-+}$ 75 (21.50)	-Br	$[C_7H_5]^{-+}$ 89 (4.10)	
				$-C_2H_2$	$[C_5H_3]^{-+}$ 63 (4.90)	
5b	$[C_{25}H_{17}N_4Br_2ClO_3S]^{-+}$ 646 (1.30)	C_7H_5NO	$[C_{18}H_{12}N_3Br_2ClO_2S]^{-+}$ 527 (1.30)	C_7H_7NO	$[C_{18}H_{10}N_3Br_2ClO_2S]^{-+}$ 525 (1.20)	648 (M^+ + 1, 1.20), 645 (1.20), 529 (1.20), 528 (1.30), 526 (1.20), 524 (1.10), 482 (1.20), 480 (1.30), 470 (1.30), 469 (1.30), 455 (2.20), 454 (1.20), 392 (4.20), 366 (4.20), 365 (6.30), 284 (3.50), 239 (4.20), 238 (3.70), 237 (2.80), 224 (3.50), 212 (2.80), 199 (4.20), 196 (3.20), 195 (2.80), 181 (2.80), 180 (4.90), 157 (6.90), 156 (6.30), 155 (11.10), 142 (8.30), 141 (34.70), 140 (22.90), 138 (72.90), 137 (10.40), 114 (4.90), 113 (11.80), 112 (9.00), 110 (10.90), 105 (4.90), 104 (4.20), 103 (13.20), 102 (9.00), 90 (8.30), 89 (6.30), 77 (4.20), 76 (9.00), 74 (12.50), 73 (10.50), 68 (5.60), 60 (16.00), 51 (6.9), 50 (8.30)
		-CS	$[C_{17}H_{12}N_3Br_2ClO_2]^{-+}$ 483 (2.30)	-CS	$[C_{17}H_{10}N_3Br_2ClO_2]^{-+}$ 481 (2.20)	
		-NH	$[C_{17}H_{11}N_2Br_2ClO_2]^{-+}$ 468 (1.90)	-CO	$[C_{16}H_{10}N_3Br_2ClO]^{-+}$ 453 (3.30)	
		$C_{10}H_5Br_2O_2$	$[C_7H_6N_2Cl]^{-+}$ 153 (6.30)	C_7H_4NCl	$[C_9H_6N_2Br_2O]^{-+}$ 316 (2.30)	
		-N	$[C_7H_6NCl]^{-+}$ 139 (100)	-N	$[C_9H_6NBr_2O]^{-+}$ 302 (3.33)	
		$-CH_2N$	$[C_6H_4Cl]^{-+}$ 111 (34.60)	-CN	$[C_8H_6Br_2O]^{-+}$ 276 (1.70)	
		-HCl	$[C_6H_3]^{-+}$ 75 (71.40)	-Br	$[C_8H_6BrO]^{-+}$ 197 (4.20)	
				- Br	$[C_8H_6O]^{-+}$ 118 (3.50)	
5c	$[C_{24}H_{17}N_4ClO_2S]^{-+}$ 460 (12.20)	C_7H_5NO	$[C_{17}H_{12}N_3ClOS]^{-+}$ 341 (3.30)	C_7H_7NO	$[C_{17}H_{10}N_3ClOS]^{-+}$ 339 (6.70)	462 (M+ + 2, 5.60), 459 (1.30), 341 (0.40), 340 (1.80), 338 (3.60), 298 (7.20), 238 (4.20), 237 (1.20), 204 (1.70), 203 (2.20), 178 (4.10), 177 (3.30), 176 (1.60), 165 (1.70), 163 (1.30), 161 (5.60), 153 (13.20), 152 (10.30), 151 (36.20), 138 (1.40), 136 (7.20), 125 (3.30), 123 (8.10), 120 (3.90), 118 (14.60), 116 (7.30), 105 (71.20), 103 (63.20), 102 (10.20), 88 (6.30), 87 (4.60), 78 (8.20), 76 (31.20), 75 (18.20), 65 (18.20), 63 (11.20), 62 (01.20), 51 (13.20), 50 (21.20)
		-CS	$[C_{16}H_{12}N_3ClO]^{-+}$ 297 (10.30)	-CS	$[C_{16}H_{10}N_3ClO]^{-+}$ 295 (2.30)	
		-NH	$[C_{16}H_{11}N_2ClO]^{-+}$ 282 (14.60)	-CO	$[C_{15}H_{10}N_3Cl]^{-+}$ 267 (0.80)	
		C_9H_4ClO	$[C_7H_7N_2]^{-+}$ 119 (43.20)	C_7H_5N	$[C_8H_5N_2Cl]^{-+}$ 164 (2.30)	
		-NH	$[C_7H_6N]^+$ 104 (100)	-N	$[C_8H_5NCl]^{-+}$ 150 (11.30)	
		-HCN	$[C_6H_5]^{-+}$ 77 (87.20)	-CN	$[C_7H_5Cl]^{-+}$ 124 (4.50)	
		$-C_2H_2$	$[C_4H_3]^{-+}$ 51 (22.30)	-Cl	$[C_7H_5]^+$ 89 (12.30)	
				$-C_2H$	$[C_5H_4]^{-+}$ 64 (9.30)	

Compounds (4 and 5)

The molecular ion of compounds **(4)** (Figure 3, 4) and **(5)** (Figure 5) had fragmented and gave fragment ions of m/z 420, m/z 527 and m/z 341 via pathway A by losing C_2HN and C_7H_5NO groups. The fragments of m/z 420, 527 and m/z 341 were broken via pathway in the same fragmented processes which were observed

for compounds **(3_{a-c})**.

Also, the molecular ions of compounds **(4)** and **(5)** had fragmented via pathway B and gave the fragments of m/z 418, 525 and m/z 393 by losing methyl nitrile and benzamide molecules.

This fragments of m/z 418, 525 and m/z 393 underwent fragmentation via pathway B similar to compounds **(3_{a-c})**.

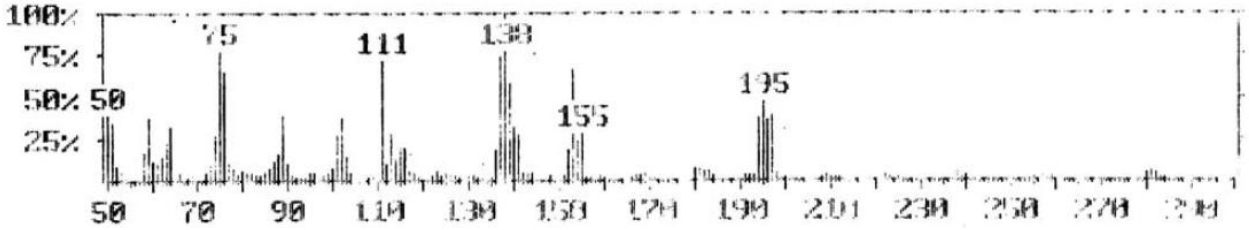

Figure 1 : Mass fragmentation of compound (3a)

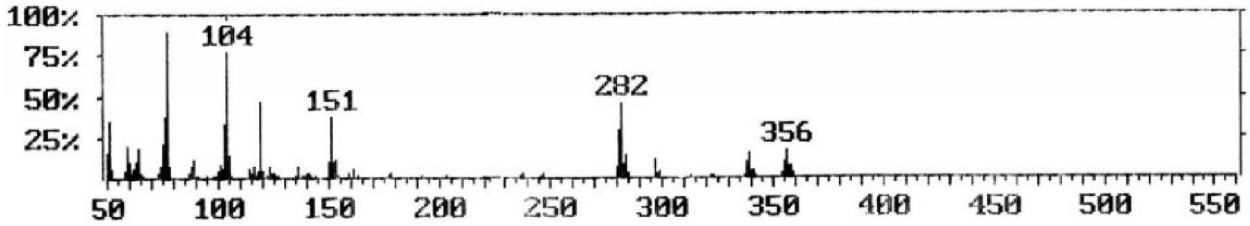

Figure 2 : Mass fragmentation of compound (3c)

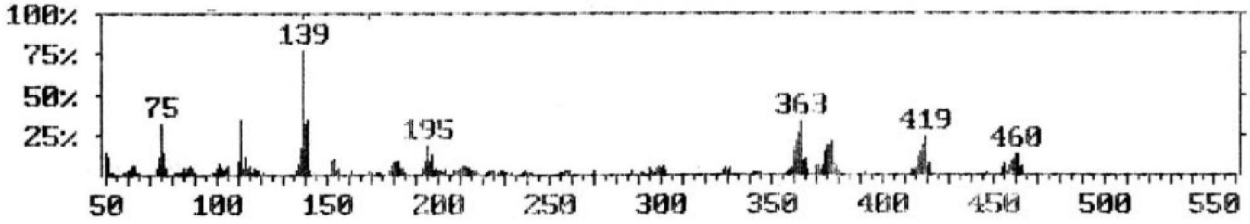

Figure 3 : Mass fragmentation of compound (4a)

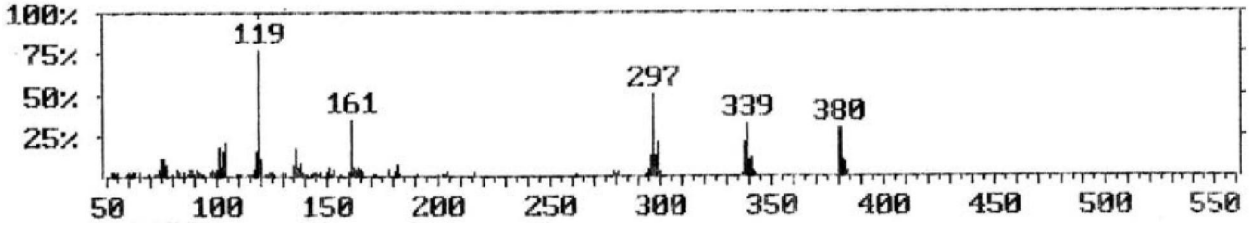

Figure 4 : Mass fragmentation of compound (4c)

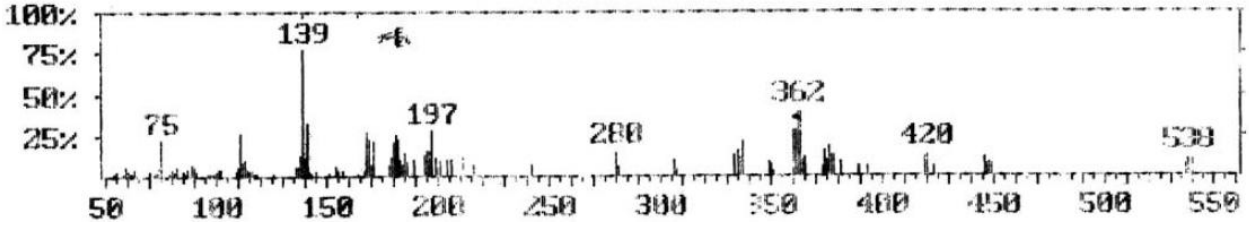

Figure 5 : Mass fragmentation of compound (5a)

EXPERIMENTAL

Melting points were determined in open capillary tubes with a Thomas Hoover apparatus and are uncorrected. Infrared spectra were recorded on a BOMEM DA-8FF-IR instrument and the frequencies are expressed in cm^{-1}.

NMR Spectra (90 MHz) were recorded on a Varian EM-390 spectrometer. Chemical shifts are

reported in ppm downfield from internal tetramethyl silane and are given on the δ scale. Mass spectral data were obtained with a JEOL D-300 (EI) mass spectrometer. Elemental analyses were carried out on a Heracus CHN-O-Rapid analyzer. All compounds gave satisfactory elemental analyses with in ± 0.5% of the theoretical values.

4-arylidene–2–aryl-4H-oxazol-5-ones (2_{a-c})

A mixture of N-Aroyl glycine (0.01 mole), aromatic aldehydes (0.01 mole), fused sodium acetate (0.03 mole) and acetic anhydride (0.03 mole) was fused on a hot plate for 2-3 min. The reaction mixture was heated on a water-bath for 2h, then cooled and poured into water. The solid formed was filtered off, washed with hot water, dried and purified by re-crystallization with benzene and gave **(2)**.

2-(p-Chlorophenyl)-4-(p-bromobenzylid-ene) – 3,1– oxazolin – 5 – one (2_a)

As yellow crystals, yield 78%, m.p. 168°C. IR(KBr); 1758 (C=O), 1625(C=N), 1605, 1585 (C=C), 1210, 1080 (C–O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 7.21- 8.01 (m, 9H, Ar-H and olefinic–H) ppm. Anal. $C_{16}H_9NBrClO_2$ for Calcd.: C, 53.18, H, 2.49, N, 3.88, Br, 21.88, Cl, 9.69. Found: C, 53.02, H, 2.33, N, 3.61, Br, 21.59, Cl, 9.52.

2– (P–Chlorophenyl)– 4 – (3, 5-dibromo–4–methoxybenzylidene) 3, 1– oxazolin– 5 –one (2_b)

As yellow crystals, yield 77%; m.p.180°C. IR (KBr): 1758 (C=O), 1625 (C=N), 1611, 1589(C=C), 1185, 1093 (C–O) cm^{-1}. ^{1}H-NMR(DMSO-d_6): δ 3.85 (s, 3H, OCH_3), 7.21 – 7.91 (m,7H, Ar-H and olefinic-H) ppm. Anal. $C_{17}H_{10}NBr_2ClO_3$ for Calcd.: C, 43.49; H, 2.13, N, 2.98, Br, 33.69, Cl, 7.46. Found: C, 43.27, H, 2.03, N, 2.69, Br, 33.43, Cl 7.21.

2– (phenyl)–4–(p–chlorobenzylidene) –3, 1–oxazolin–5–one (3_a)

As yellow crystals, yield 76%, m.p. 175°C. IR (KBr): 1755 (C=O), 1621 (C=N), 1605, 1598 (C=C), 1120, 1035 (C-O)cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 7.12 – 7.91 (m, 10H, Ar-H and olefinic-H) ppm. Anal. $C_{16}H_{10}NC1O_2$ for Calcd.: C, 67.84, H, 3.53, N, 4.95, Cl, 12.37. Found: C, 67.67, H, 3.35, N, 4.67, Cl, 12.22.

2-(Aminothiocarbonyl)–3-aryl-5-arylidene-1, 2, 4-triazin – 6–ones (3_{a-c})

A mixture of oxazolinone derivative **(2)** (0.01 mole) and thiosemicarbazide (0.01mole) in glacial acetic acid (30 ml) was heated under reflux for 3 - 4hr, then cooled and poured into water. The resulting solid was filtered off, washed with water dried and purified by recrystallization with ethanol and gave **(3)**.

2-(Aminothiocarbonyl)-3-(p-chlorophenyl)- 5- (4-bromobenzylidene) – 1, 2, 4 triazin–6–one (3_a)

As yellow crystals, yield 79%, mp. 210°C. IR (KBr): 3420, 3189 (NH_2), 3225 (NH), 1689 (C=O), 1621 (C=N), 1610, 1603, 1589 (C=C), 1389 (C=S)cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 6.20 (s, 2H, NH_2), 7.21 - 8.10 (m, 9H, Ar-H and olefinic–H), 10.35 (s,1H, NH) ppm. Anal. $C_{17}H_{12}N_4BrClOS$ for Calcd.: C, 46.89, H, 2.76, N, 12.87, Br, 18.16, Cl, 8.04, S, 7.36. Found: C, 46.69, H, 2.58, N, 12.66, Br, 18.09, Cl, 7.96, S, 7.22.

2-(Aminothiocarbonyl)-3-(p-chlorophenyl)- 5- (3, 5-dibromo-4-methoxybenzylidene)– 1, 2, 4- triazin – 6- one (3_b)

As yellow crystals, yield 76%, m.p.205°C. IK (KBr): 3401, 3195 (NH_2), 3220 (NH), 1693 (C=O), 1624 (C=N), 1605, 1588 (C=C), 1393 (C=S), 1205, 1085 (C–O)cm^{-1}. ^{1}H-NMR (DMSO-d_6): 3.89 (s, 3H, OCH_3), 6.42 (s, 2H, NH_2), 7.42 - 8.01 (m, 7H, Ar-H and olefinic–H), 10.39 (s, 1H, NH) ppm. Anal. $C_{18}H_{13}N_4Br_2ClO_2S$ for Calcd.: C, 39.70, H, 2.39, N, 10.29, Br, 29.04, Cl, 6.43, S, 5.88. Found: C, 39.69; H, 2.28, N, 10.03, Br, 28.88, Cl, 6.23, S, 5:66.

2- (Aminothiocarbonyl) -3- phenyl- 5 – (p-chlorophenyl)- 1, 2, 4- triazin–6–one (3_c)

As yellow crystals, yield 781, m.p 220°C, IR (KBr): 3415, 3185 (NH_2) 3250 (NH), 1689 (C=O), 1625 (C=N), 1605, 1589 (C=S), 1395 (C=S)cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 6.12 (s, 2H, NH_2), 7.12 - 7.98 (m, 10H, Ar-H and olefinic–H), 10.33 (S, 1H, NH) ppm. Anal. $C_{17}H_{13}N_4ClOS$ for calcd: C, 57.30, H, 3.65, N, 15.73, Cl, 9.83, S, 8.99. Found: C, 57.08, H, 3.46, N, 15.57, Cl, 9.66, S, 8.78.

1-Methyl-3-thioxo-4-aryl-6-arylidene-triazolo- (2, 1-a). 1,2, 4-triazin-7-ones (4_{a-c})

A solution of 3 (0.01 mol) in acetic anhydride (20ml)

was heated under reflux for 2-3 hr, then cooled and poured into ice-water. The solid obtained was filtered off, washed with water, dried and purified by recrystalization with ethanol and gave **(4)**.

1–Methyl–3–thioxo– 4 – (p-chlorophenyl)–6– (p-bromobenzylidene) – triazolo (2,1–a)–1, 2, 4-triazin – 7–one (4_a)

As yellow crystals, yield 68%, m.p.180°C. IR (KBr): 1695 (C=O), 1625 (C=N), 1608, 1585 (C=C), 1389 (C=S) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.31 (s, 3H, CH_3), 7.21 – 8.01 (m, 9H, Ar-H and olefinic-H) ppm. Anal. $C_{19}H_{12}N_4BrClOS$ for Calcd.: C, 49.78, H, 2.62, N, 12.22, Br, 17.2 H, Cl, 7.64, S, 6.98. Found: C, 49.64, H, 2.51, N, 12.00, Br, 17.03, Cl, 7.51, S, 6.79.

1-Methyl–3–thioxo–4–(p-chlorophenyl)–6–(3,5dibromo–4–methoxybenzylidene)–triazolo (2, 1-a)– 1, 2, 4– triazin–7–one (4_b)

As yellow crystals, yield 71%, m.p: 185°C. IR (KBR): 1693 (C=O), 1623 (C=N), 1610, 1593 (C=C), 1391 (C=S), 1210, 1083 (C–O) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 2.21 (s, 3H, CH_3), 3.89 (s, 3H, OCH_3), 7.21 - 8.01 (m, 7H, Ar-H and olefinic- H) ppm. Anal. $C_{20}H_{13}N_4Br_2ClO_2S$ for Calcd: C, 42.40, H, 2.30, N, 9.89, Br, 27.91, Cl, 6.18, S, 5.65. Found: C, 42.22, H, 2.15, N, 9.69, Br, 27.77, Cl, 6.02, S, 5.33.

1– Methyl– 3– thioxo– 4– phenyl– 6 – (p–chlrobenzylidene)– triazolo– (2, 1–a) –1, 2, 4–triazin–7–one (4_c)

As yellow crystals, yield 72%, m.p. 225°C. IR (KBr): 1692 (C=O), 1623 (C=N), 1608, 1587 (C=S), 1392 (C=S) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.22 (s, 3H, CH_3), 7.12 – 7.92 (m, 10H, Ar-H and olefinic -H) ppm. Anal. $C_{19}H_{13}N_4ClOS$ for Caled: C, 60.00; H, 3.42, N, 14.74, Cl, 9.21, S, 8.42 Found: C, 59.83, H, 3.22, N, 14.53, Cl, 9.02, S, 8.28.

2-(Benzolylamino)thicarbonyl–3–aryl–5–arylidene–1, 2, 4- triazin– 6–ones (5_{a-c})

A mixture of 3 (0.01 mole) and benzoyl- chloride (0.01 mole) in acetic and (25mL) was heated under reflux for 2-3hr. then cooled and poured into water. The resulting product was filtered off, washed with hot water, dried and purified by recrystallization with ethanol and gave **(5)**.

2– (Benzoylamino) thiocarbonyl– 3– (p–chlorophenyl) –5– (p-bromobenzylidene) – 1, 2, 4-triazin-6- one (5a)

As pale yellow crystals, yield 63%, m.p.435°C. IR (KBr): 3225 (NH), 1695 – 1688 (C=O), 1623 (C=N), 1603, 1593 (C=C), 1389 (C=S) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 7.12 – 7.98 (m, 14H, Ar-H and olefinic-H), 10–30 (s, 1H, NH), 11–20 (s,1H, NH) ppm. Anal. $C_{24}H_{16}N_4BrClO_2S$ for Calcd: C, 53.53, H, 2.97, N, 10.41, Br, 14.68, Cl, 6.51, S, 5.95. Found: C, 53.33, H, 2.83, N, 10.32, Br, 14.48, Cl, 6.35, S, 5.67.

2– (Benzoylamino) thiocarbonyl – 3 – (p–chlorophenyl) – 5– (3, 5 – dibromo – 4 – methoxybenzylidene) – 1, 2, 4– traizin– 6–one (5_b)

As pale yellow crystals, yield 63%, m.p 146°C. IR(KBr): 3235 (NH), 1700–1689 (C=O), 1624 (C=N), 1607, 1589 (C=C), 1389 (C=S), 1210, 1087 (C–O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.89 (S, 3H, OCH_3), 7.20 – 8.01 (m, 12H, Ar-H and olefinic-H), 1020 (s, 1H, NH), 11.20 (s, 1H, NH) ppm. Anal. $C_{25}H_{17}N_4Br_2ClO_3S$ for Calcd. S 46.44, H, 2.63, N, 8.67, Br, 24.46; Cl, 5.42, S, 4.95. Found: C, 46.23, H, 2.41, N, 8.52, Br, 24.33, Cl, 5.31, S, 4.73.

2–Benzoylamino) thiocarbonyl– 3 – phenyl – 5 – (p-chlorobenzylidene) – 1, 2, 4- triazin–6–one (5_c)

As pale yellow crystals yield 67%, m.p: 137°C. IR(KBr): 3257 (NH), 1698 – 1683 (C=O), 1622 (C=N), 1605, 1589 (C=C), 1389 (C=S). ^{1}H-NMR (DMSO-d_6): δ 7.11 – 7.98 (m, 15 H, Ar-H and olefinic-H), 10.11 (s, 1H, NH), 1091 (s, 1H, NH) ppm. Anal. $C_{24}H_{17}B_4ClO_2S$ for Calcd: C, 62.61, H, 3.69, N, 12.17, Cl, 7.61, S, 6.95. Found: C, 62.43, H, 3.52, N, 12.02, Cl, 7.38, S, 6.71.

ANTIMICROBIAL ACTIVITY

The antimicrobial activity of the synthetic compounds **(3_a)**, **(3_b)**, **(3_c)**, **(4_a)** and **(4_b)** were evaluated against Aspergillus Flavus and Penicillium Citrinum as stock cultures. After seeding of the solid medium by the microbial suspension (10 ml ≤ 250 medium), pouring to sterile plates, the cultures were incubated overnight for pre-germination, then 500 µl of each tested compound

was pipetted to the wells of the plate cultures. Blanks of dissolving solvent were made. The cultures were incubated for 4 days at 30 ^{0}C then the diameter of the inhibition growth zone, around each well, was measured. The antimicrobial activity was expressed by the diameter of inhibitory zone, comparing to griseofulvin as standard antifungal agents[15].

It is clearly observed from the data obtained in TABLE 2, compounds **(3a)**, **(3b)** and **(4b)** are the potent antifungal agent against Aspergillus Flavus comparing to Griseofulvin. However, these compounds have no inhibitory effect on the growth of penicillium sp. The negative antimicrobial effect reveals the feasibility of these compounds as growth elements and stabilizing factors for some metabolic pathways supporting the microbial growth.

TABLE 2 : Antimicrobial activity of the tested compounds expressed by the diameter of inhibition zone (cm) around the well.

Compound	Aspergillus Flavus	Penicillium sp
3a	+	-
3b	+	-
3c	-	-
4a	-	-
4b	+	-

- No antimicrobial activity (< 0.1 cm); + Slightly antimicrobial activity (0.1 – 0.8)

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