Synthesis, antimicrobial activity and Electron Impact of Mass Spectra of Phthalazine-1,4-dione Derivatives

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Síntesis, actividad antimicrobiana y espectros de masas de impacto electrónico de derivados de ftalazina-1,4-diona

Síntesi, activitat antimicrobiana i espectres de masses d'impacte electrònic de derivats de ftalazina-1,4-diona

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RESUMEN

Las reacciones de la 3-aminotiocarbonilftalazina-1,4-diona **(2)** con aldehídos aromáticos, cloruro de benzoílo, benzoína y ω-bromometilarilcetonas rinden las correspondientes 3-(amina substituida)tiocarbonilftalazina-1,4-dionas (**3**, **8** y **9**) y 4-aril-1-tioxo-1,2,4-triazino[1,2-*b*]ftalazina-5,10-dionas **(7)**. La acilación de **3b** con anhídrido acético da el correspondiente derivado diacetilado **(4)**. Se registran también los espectros de masas de las dos series de compuestos anteriores y se discute su patrón de fragmentación.

Palabras clave: Ftalazinona, impacto electrónico, actividad antimicrobiana.

ABSTRACT

Reactions of 3-aminothiocarbonylphthalazine-1,4-dione **(2)** with aromatic aldehydes, benzoyl chloride, benzoin and ω-bromomethylarylketones yielded the corresponding 3-(substituted amino)thiocarbonylphthalazine-1,4-diones (**3**, **8**, and **9**) and 4-aryl-1-thioxo-1,2,4-triazino[1,2-*b*] phthalazine-5,10-diones **(7)**. Acylation of **3b** with acetic anhydride gave the corresponding diacetyl derivative **(4)**. The electron impact mass spectra of both the above series of compounds have also been recorded and their fragmentation pattern is discussed.

Key words: Phthalazinone, electron impact, antimicrobial activity.

RESUM

Les reaccions de la 3-aminotiocarbonilftalazina-1,4-diona **(2)** amb aldehids aromàtics, clorur de benzoïl, benzoina i ω-bromometilarilcetones rendeixen les corresponents 3-(amina substituïda)tiocarbonilftalazina-1,4-diones (**3**, **8** i **9**) i 4-aril-1-tioxo-1,2,4-triazina[1,2-*b*]ftalazina-5,10-diones **(7)**. L'acilació de **3b** amb anhídrid acètic dóna el corresponent derivat diacetilat **(4)**. Es registren també els espectres de masses de les dues sèries de compostos anteriors i es discuteix el seu patró de fragmentació.

Mots clau: Ftalazinona, impacte electrònic, activitat antimicrobiana.

INTRODUCTION

Phthalazinone derivatives constitute an important class of hetero-cycles in medicinal chemistry because many derivatives have been identified as molecules which may interact with a broad range of biological targets[1-4]. In course of investigations, involving phthalic anhydride and thiosemicarbazide, it was found that 2-aminothiocarbonylphthalazine-1,4-dione (**2**) is converted into 2-substituted aminothio-carbonyl-phthalazine-1,4-diones (**3**, **4**, **8** and **9**) and substituted triazino- [1,2-b]-phthalazine-5,10-dione (**7**) by the action of aromatic aldehydes, benzoyl chloride, benzoin and ω-bromomethyl ketones under different conditions. The electron impact (EI) mass spectral fragmentation patterns of some synthesized phthalazinone derivatives are described.

RESULTS AND DISCUSSIONS

Chemistry

2-Aminothiocarbonyl-phthalazine-1,4-dione (**2**) was prepared via the reaction of phthalic anhydride with thiosemicarbazide under reflux in methanol. Condensation[5] of compound **2** with aromatic aldehydes (such as 2-hydroxybenzaldehyde and 5-bromo-2-hydroxybenzaldehyde) under reflux in acetic acid gave the corresponding 2-[(arylethylidene)amino]- thiocarbnyl-phthalazine-1,4-diones (**3a,b**; Scheme 1).

Acylation[6] of compound **3b** with acetic anhydride under reflux led to the formation of 2-[(2-acetoxy-5-bromophenylethylidene)amino]thiocarbon-yl-3-acetyl-Phthalazine-1,4-dione (**4**).

Bromination[7] of 2-(o-hydroxyphenylethylidene)aminothiocarbon-yl-phthalazine-1,4-dione **3a** with one mole bromine in glacial acetic acid at room temperature, followed by cyclization with removal hydrogen bromide led to the formation of 3-(o-hydroxyphenyl)-1-thioxo-1,2,4-triazolo[1,2-b]-phthalzine-4,9-dione (**5**).

Treatment of 2-aminothiocarbonyl-phthalzine-1,4-dione **2** with ω-bromo-methylarylketones (such as 4-methylphenacyl bromide and 4-chloro-phenacyl bromide) in methanol in presence of fused sodium acetate[8] gave the corresponding 4-aryl-1-thioxo-1,2,4-triazino[1,2-b]-phthalazine-5, 10-diones (**7a**, **b**), which does not give the expected structure of 2-(5\-aryl-thiazol-2\-yl)-phthalazine-1,4-diones (**6a**, **b**; Scheme 1).

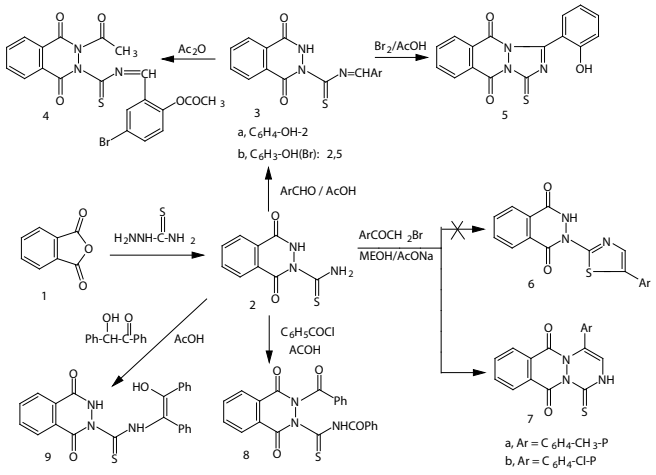
2-(Benzoylamino)thiocarbonyl-3-benzoyl-phthalazine-1,4-dione (**8**) was synthesized by a benzoylation of the 2-aminothiocarbonyl-phthalazine-1,4-dione **2** with two mole from the benzoyl chloride under reflux in acetic acid.

Condensation of compound **2** with benzoin under reflux in acetic acid formed the 2-[(1\-hydroxy-1\, 2\-diphenylethene-2\-yl)amino]- thiocarboyl-phthalzine-1,4-dione (**9**, Scheme 1).

Mass Spectrometry

As a part of structural investigation[9-11], mass spectra of five compounds 2, 3a, 3b, 4, 7a, 7b and 9 belonging to this series were recorded and all the spectra showed characteristic common fragmentation pathways, as shown in Schemes 2,

The mass spectrum of compound **2** (Figure 1) showed an intense molecular ion peak at m/z 221, corresponding to the molecular formula $C_9H_7N_3O_2S$.

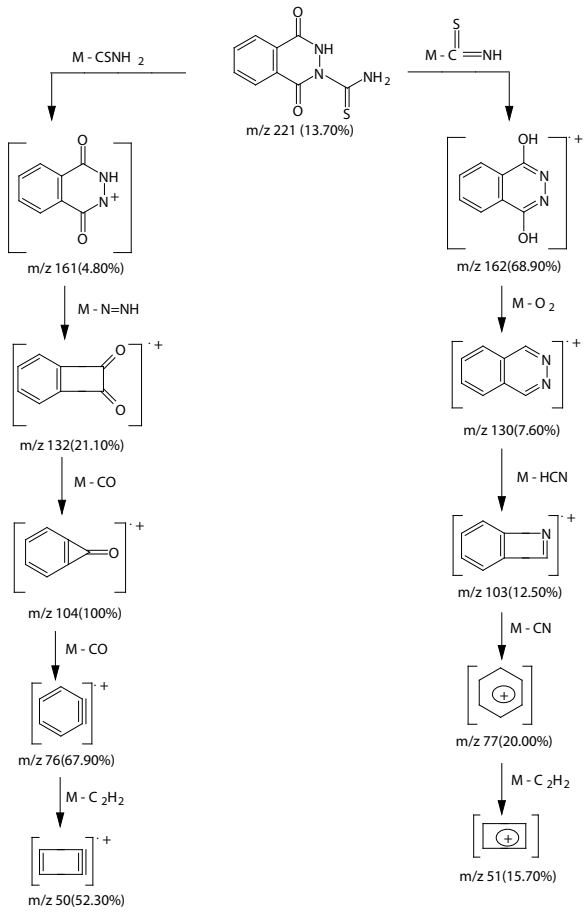


Scheme 1

The molecular ion of compound **2** (Scheme 2) underwent fragmentation to produce peak at m/z 161 by losing $CSNH_2$ group.

The loss of N=NH group from the ion with m/z 161 resulted in an ion at m/z 132. The ion at m/z 132 underwent loss of CO to give a stable peak at m/z 104. the base ion of m/z 104 underwent loss of CO and C_2H_2 molecules to give peaks at m/z 76 and m/z 50, respectively.

Also, the ion of m/z 221 underwent loss of S=C=NH group to give peak at m/z 162, corresponding to phthalazine-1,4-dione molecule. The loss of O_2 and HCN molecule from the ion with m/z 162 resulted in an ion at m/z 103. The ion at m/z 103 underwent loss of CN and C_2H_2 to give peaks at m/z 77 and m/z 51, respectively.



Scheme 2. Mass Fragmentation pattern of compound 2

The mass spectra of compounds **3a**,.**b** (Figure 2) are fully consistent with the assigned structures. In most cases, intense molecular ion peaks were observed. Thus, compound **3a**, **b** showed intense molecular ion peaks at m/z 325 and 403, consistent with the molecular formula $C_{16}H_{11}N_3O_3S$ and $C_{16}H_{10}N_3BrO_3S$, respectively.

The molecular ion of compounds **3a** and **3b** (Scheme 3) underwent fragmentation with rearrangement to produce peaks at m/z 195 and m/z 273, corresponding to the molecular ion of 5-substituted-2-hydroxy- benzaldehyde-thiosemicarbazone. It further underwent loss of NH_3 and NCS to give peaks at m/z 178, 256 and 120, 198, respectively.

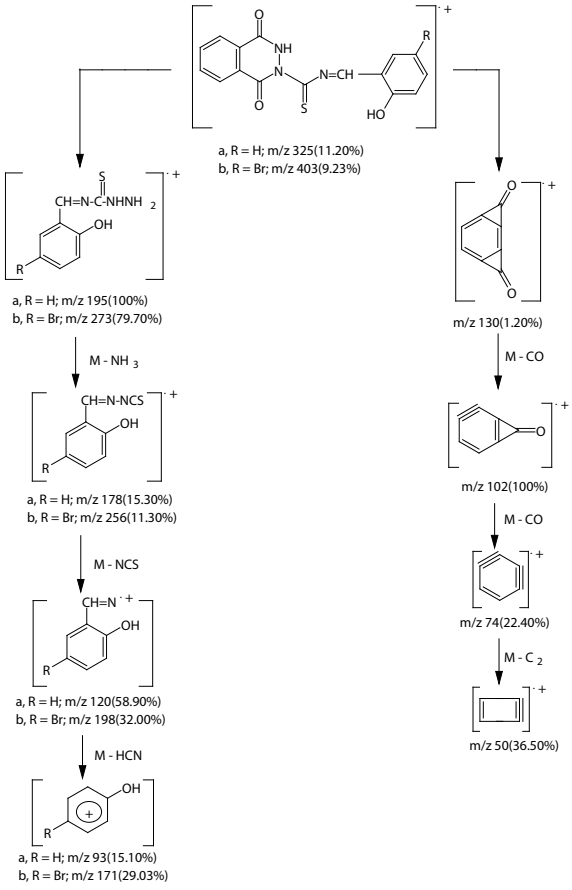
The molecular ions of compounds **3a** and **3b** were also found to undergo fragmentation to produce the ion of m/z 130. the ion of m/z 130 broke to give an ion at m/z 74 which lost two molecule from carbon monoxide.

From the mass spectrum of compound **4** (Figure 3), it was concluded that the molecular ion was at m/z 487. The ion of m/z 487 underwent fragmentation with rearrangement to produce peaks at m/z 357, corresponding to the molecular ion of 1-acetyl-4-(5-bromo-2- acetoxy)benzaldehyde-thiosemicarbazone.

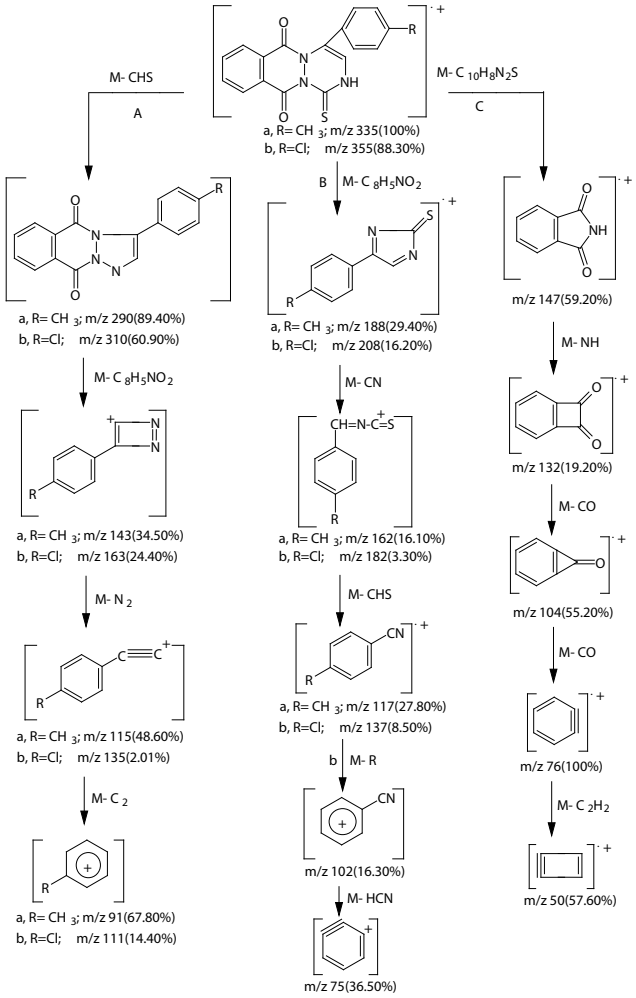
It further underwent loss of two molecule from CH_2CO to give peaks at m/z 315 and m/z 273, respectively. The fragment ion of m/z 273 further broke via pathway similar to fragmentation of m/z 273, which produced from the fragmentation of compound **3b** (Scheme 3). Base peaks at m/z 195 and 76, found in the MS of compounds **3a** and **4**, corresponding to the 4-(2-hydroxy)-benzaldehyde-thiosemicarbazone and benzyne ions, while the base peak of compound **3b** at m/z 60.

The mass spectra of the triazino[1,2-b]-phthalazine-5,10-diones **7a, b** (Figure 4) showed intense molecular ion peaks at m/z 335 and m/z 355, consistent with the molecular formula $C_{18}H_{13}N_3O_2S$ and $C_{17}H_{10}N_3ClO_2S$, respectively. The M+2 of compound **7b** was observed along with the molecular ion peak due to the presence of isotopes chlorine atom present in the compound. The molecular ion of compound **7a** and **7b** fragmented further and involved three pathways as illustrated in Scheme 4.

The molecular ion of m/z 335 and m/z 355 fragment via the pathway A give peak at m/z 290 and m/z 310 by lossing thioformyl group (CHS). The ions of m/z 290 and m/z 310 underwent fragmentation produce ions of m/z 143 and m/z 163 by losing phthalamide radical cation molecule. This fragmentation led to ions of m/z 115, 135 and ions of m/z 91, 111 respectively. Accordingly, the same molecular ion



Scheme 3. Mass fragmentation pattern of compounds 3a and 3b



Scheme 4. Mass fragmentation pattern of compound 7a and 7b

of m/z 335 and m/z 355 fragmented via pathway B by a cleavage phthalamide molecule to give the peak at m/z 188 and m/z 208 which lost cyano group to give the peak at m/z 162 and m/z 182, respectively. It further underwent loss of CHS and CH_3 or Cl to give peaks at m/z 117, 137 and m/z 102, respectively.

Subsequently, the molecular ion of compound **7a** and **7b** at m/z 335, m/z 355 fragmented via the pathway C by a cleavage of 4-(P-substituted phenyl)-imidazolidin-2-thione radical cation, to give peak at m/z 147, corresponding to the molecular ion radical of phthalamide.

It further underwent loss of two molecule from carbon monoxide to give the base ion peak at m/z 76. The molecular ion of compound **7a** is the base peak, while the base peak of compound **7b** is m/z 76.

The mass spectrum of compound **9** (Figure 5) showed an intense molecular ion peak at m/z 415, corresponding to the molecular formula $C_{23}H_{17}N_3O_3S$. The molecular ion of **9** (Scheme 5) underwent fragmentation to produce a peak at m/z 254 by losing phthalazine-1,4-dione cation radical. The loss of H_2O and NCS groups from the ion with m/z 254 resulted in an stable fragment ion at m/z 178. The ion of m/z 178 underwent loss of phenyl group and C_2 to give peaks at m/z 101 and m/z 77, respectively. Also the ion of m/z 415 underwent fragmentations to produce peak at m/z 161, corresponding to the molecular ion of phthalazine-1,4-dione cation radical. It further loss of NCO, NH and CO to give peaks at m/z 119, 104 and m/z 76, respectively.

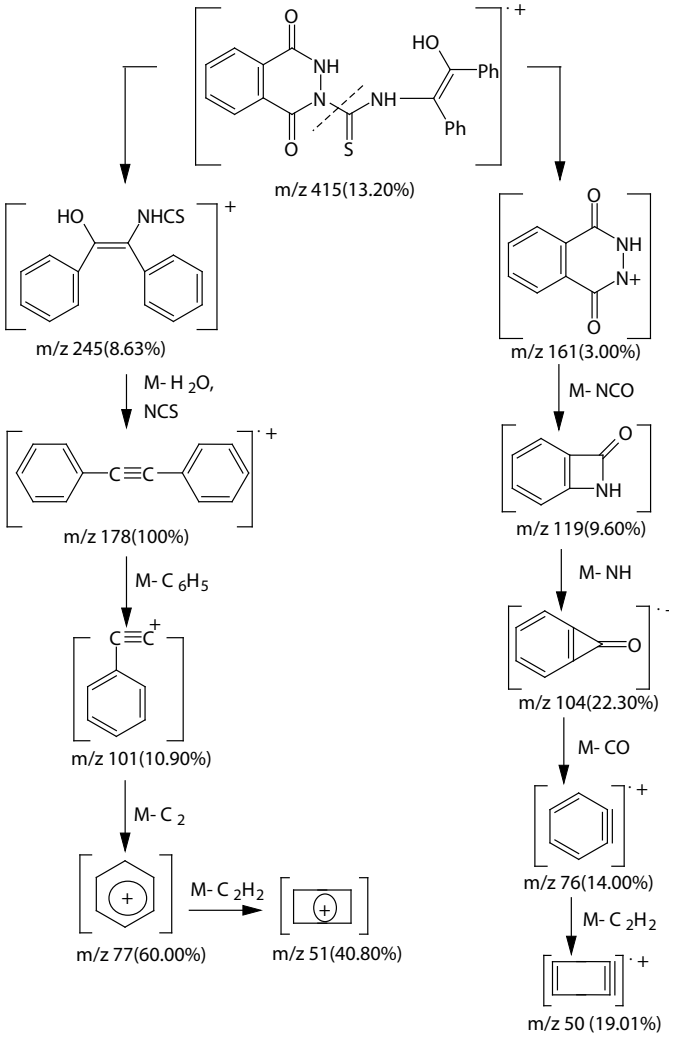
Antimicrobial activity

Antibacterial activity was measured by the following agar-diffusion technique[12] all the newly synthesized compounds were tested in vitro for against sever at strains of bacteria such as Bacillus Subtilis, Straphylocouus Aureas, Streptococcus Pneumonia, Escherichia Coli and Pseudomonas. All compounds showed 86 % 100 µg/ml concentration level. Also, antifungal activities activity against Aspergillus Nigaer and Penicillium Sp. using agar-plate diffusion technique[13] in DMF (75µL) has been screened. Most of the compounds showed about 83 % inhibition at the concentration of 100 µg/ ml. The antimicrobial activity of synthesized compounds is listed in Table 1.

- No antimicrobial activity, + Mild activity, ++ Moderate activity +++ Marked activity

Experimental

NMR spectra were recorded on a General electric QE 300 instrument and chemical shifts are given in δ (ppm) with TMS as internal references. IR spectra were recorded on a Perkin-Elmer 1420 and a Biorad FTS7 spectrometer in KBr pellets. Mass spectra were obtained on a Jeol JMS D-300 spectrometer operating at 70 eV. Microanalysis were conducted using a 1106 elemental analyzer. Melting points were determined on a Reichet Hot Instrument and are uncorrected.



Scheme 5. Mass fragmentation pattern of compound 9

3-Aminothiocarbonyl-phthalazine-1,4-dione (2)

A mixture of phthalic anhydride (0.01 mole) and thiosemicarbazide (0.01 mole) in methanol (50 mL) was heated under reflux for 3h., then cooled. The solid formed was filtered off, washed with methanol, dried and purified by recrystallization from acetic acid to give **2** as colorless crystals. Yield 87%, m.p. 185°C; IR(KBr): 3336, 3191(NH_2), 3264 (NH), 1685 (C=O), 1622, 1585 (C=C), 1393 (C=S)cm^{-1}. ^{1}H-NMR(DMSO-d_6): δ 3.92(s, 2H, NH_2), 7.36-8.06(m, 4H, ArH), 10.35(s,1H, NH). MS: m/z(%): 222(8.30), 221(M^+, 13.7), 204(4.90), 203(4.90), 187(8.80), 168(12.60), 167(9.60), 165(14.60), 164(12.50), 163(11.20), 162(68.90), 147(14.40), 146(15.80), 105(22.20), 104(100.00), 103(12.50), 102(5.50), 91(11.30), 77(20.00), 76(67.90), 75(16.90), 74(13.80), 65(4.30), 64(8.10), 63(9.70), 60(24.20), 59(12.10), 58(22.90), 52(9.40), 51(15.70), 50(52.30), Anal Found : C, 48.63; H, 3.09, N, 18.86; S, 14.24. $C_9H_7N_3O_2S$ requires; C, 48.87, H, 3.17; N, 19.00; S, 14.48.

2-[(Arylethylidene)amino]-thiocarbonyl-phthalazine-1,4-diones (3a, b)

2-[(1′-hyaroxy-1′,2′-diphenyl-ethene-2′-yl)amino]-thiocarbonylphth-alazine-1,4-dione (9).

A mixture of **2** (0.01 mole), aromatic aldehydes (such as 2-hydroxylbenzaldehyde and 5-bromo-2-hydroxybenzaldehyde) and benzoin (0.01 mole) in acetic acid (30 mL) was heated under reflux for 4h., then cooled and poured into water. The resulting solid was filtered off, washed with water, dried and purified by recrystallization from suitable solvent to give **3** and **9**.

2- [(2-hydroxy phenyl-ethylidene)amino]-thiocarbonyl-phthalzine-1, 4-dione (3a) as pale yellow crystals**,** Yield 76%, m.p. 220°C; IR (KBr): 3442 (OH), 3319 (NH), 1698 (C=O), 1620 (C=N), 1613, 1582 (C=C), 1405 (C=S), 1201, 1110, 1034 (C-O) cm^{-1}. ^{1}H-NMR(DMSO-d_6): δ 6.89-8.18(m, 8H, ArH), 8.42(s, 1H, CH=N), 9.89-10.11 (br, s, 1H, NH), 11.45 (s, 1H, OH). MS: m/z (%) 326 (M^++1, 2.30), 325 (M^+, 12.33), 324(9.23), 308(13.25), 263(14.50), 262(15.60), 146(8.40), 195(100), 194(8.40), 178(15.30), 164(6.40), 162(3.10), 161(5.40), 135(14.00), 122(8.90), 121(18.40), 120(58.90), 119(25.80), 118(3.80), 107(15.10), 106(8.20), 105(15.10), 102(19.40), 93(15.10), 92(17.60), 91(36.70), 90(9.90), 79(10.70), 78(20.70), 77(50.50), 76(46.20), 75(9.20), 74(10.20), 66(19.40), 65(34.90), 64(24.50), 63(24.50), 62(12.80), 60(42.60), 55(11.70), 53(15.60), 52(20.20), 51(31.90), 50(17.10). Anal. Found: C, 58.87; H, 3.19; N, 12.87; S, 9.63. $C_{16}H_{11}N_3O_3S$ requires; C, 59.07; H, 3.38; N, 12.92; S, 9.85.

2-[(5-bromo-2-hydroxyphenyl-ethylidene)amino]-thiocarbonyl-phthalazine-1,4-dione (3b) as pale yellow crystals, yield 79%, m.p. 225°C; IR(KBr): 3452 (OH), 3249(NH), 1642 (C=O), 1623 (C=N), 1607, 1544 (C=C), 1351 (C=S), 1262, 1122, 1077 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 6.82-8.17(m, 7H, ArH), 8.38(s, 1H, CH=N), 10.23 (s, 1H, NH), 11.42 (s, 1H, OH). MS: M/z (%) 405 (M^++2, 12.60) 403(M^+, 10.30), 402(M^+-1, 7.20), 277(7.80), 276(14.80), 275(75.10), 274(14.20), 273(79.70), 258(11.60), 256(11.40), 216(5.80), 215(9.20), 214(7.20), 213(6.40), 202(8.10), 201(14.90), 200(44.50), 199(45.30), 198(32.00), 197(27.60), 187(10.90), 186(10.20), 185(16.20), 172(11.10), 171(29.00), 170(14.90), 169(23.00), 145(10.90), 144(7.70), 143(17.80), 120(6.10), 119(11.80), 118(11.20), 117(6.70), 107(8.50), 105(16.60), 104(3.60), 102(26.60), 92(8.70), 91(13.40), 90(20.60), 89(10.50), 79(13.20), 78(27.60), 77(69.90), 76(70.30), 75(26.80), 74(22.40), 65(19.20), 64(29.70), 63(76.30), 62(33.50), 61(16.8), 60(100), 59(22.90), 53(32.10), 52(22.40), 51(49.70), 50(36.50). Anal. Found: C, 47.46; H,

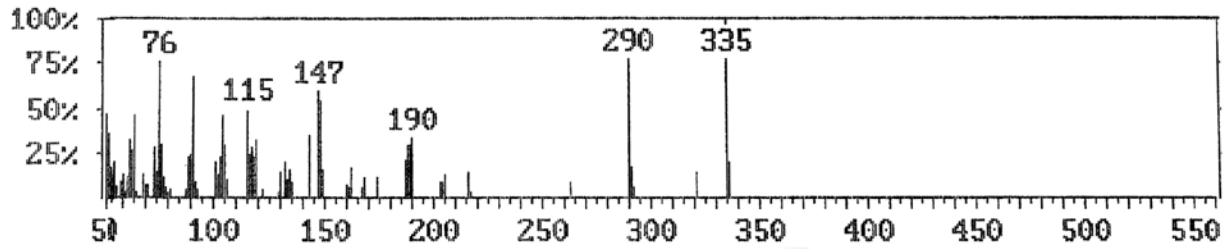


Figure 4a: 70 eV mass spectrum of compound 7a

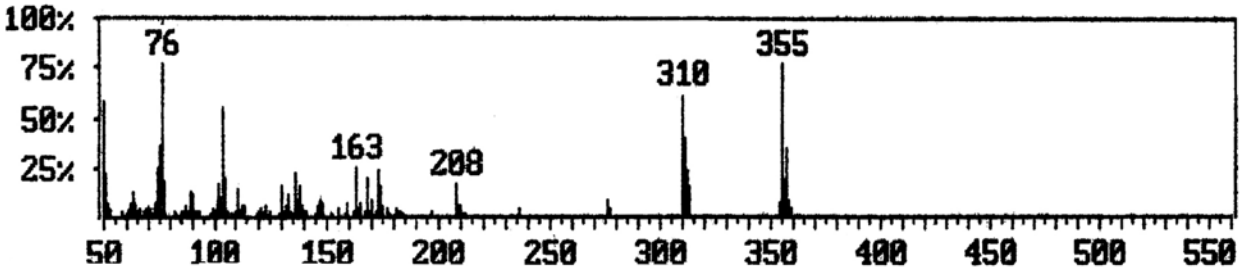


Figure 4b: 70 eV mass spectrum of compound 7b

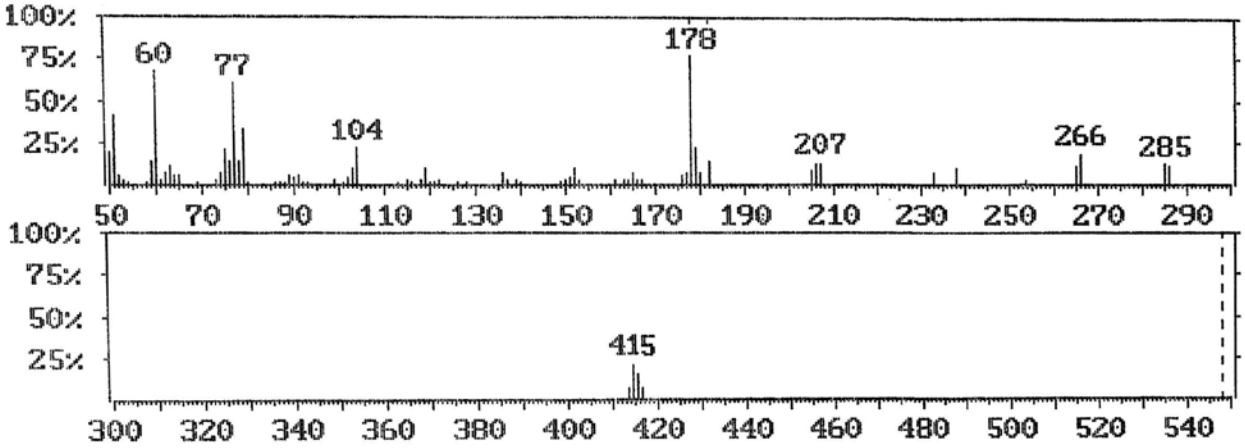


Figure 5: 70 eV mass spectrum of compound 9

2.28; N, 10.23; Br, 19.36; S, 7.62. $C_{16}H_{10}N_3BrO_3S$ requires: C, 47.64; H, 2.48; N, 10.42; Br, 19.60; S, 7.94.

2-[(1',2'-Diphenyl-1'-hydroxyethene-2'-yl)amino]-thiocarbonyl-phthalzine-1, 4-dione (9), as pole yellow crystals, yield 62%, m.p. 140°C, IR(KBr): 3410(OH), 3249, 3156(NH), 1679(C=O), 1602, 1582(C=C), 1391(C=S), 1265, 1070, 1028(C-O) cm^{-1}. ^{1}H-NMR (DMSO-d6): δ 6.82-8.12 (m, 14H, ArH), 9.23 (s, 1H, NH), 10.12 (s, 1H, NH), 11.23 (s, 1H, OH). MS: m/z(%) 416 (M^++1, 3.20), 415 (M^+, 13.20), 286(1.40), 285(1.60), 266(2.30), 265(1.40), 254(3.20), 238(1.20), 233(1.00), 207(1.60), 206(1.60), 205(1.10), 180(7.00), 179(21.90), 178(100), 177(7.20), 167(3.00), 166(2.50), 165(6.40), 163(3.20), 152(9.10), 151(3.80), 150(3.30), 137(2.90), 136(6.70), 120(2.10), 119(9.60), 118(2.80), 115(3.10), 104(22.30), 103(9.50), 102(4.60), 92(1.70), 91(5.60), 90(3.90), 89(5.40), 79(33.10), 78(14.30), 77(60.00), 76(14.00), 75(20.20), 74(7.60), 63(11.50), 62(6.90), 61(3.30), 60(66.90), 59(13.30), 51(40.80), 50(19.00), Anal. Found: C, 66.33; H, 4.00; N, 10.03; S, 7.48. $C_{23}H_{17}N_3O_3S$ requires: C, 66.51; H, 4.10; N, 10.12; S, 7.71.

2-[(2-Acetoxy-5-bromophenyl-ethylidene)amino]-thiocarbonyl-3-acetyl-phthalazine-1,4-dione (4)

A solution of **3b** (0.01 mole) in acetic anhydride (25 mL) was heated under reflux for 2h., then cooled and poured onto ice-water. The resulting product was filtered off, washed with water, dried and purified by recrystallization from benzene to give **4** as pale yellow crystals, yield 53%, m.p. 120°C. IR(KBr): 1766 (CO of ester), 1699 (C=O), 1622 (C=N), 1610, 1538 (C=C), 1367 (C=S), 1168, 1105, 1002 (C-O) cm^{-1}. ^{1}H-NMR(DMSO-d_6): δ 2.30(s, 3H, $COCH_3$), 2.62(s, 3H, $COCH_3$), 6.82-8.11 (m, 7H, ArH), 8.39(s, 1H, CH=N). MS: m/z (%) 489(M^++2, 6.83), 488(2.30), 487(M^+, 9.25), 486(3.20), 358(62.60), 357(28.30), 356(49.50), 317(30.10), 316(42.90), 315(35.90), 314(47.00), 300(18.90), 299(11.10), 298(18.40), 275(37.90), 274(26.00), 273(40.20), 272(17.40), 258(13.40), 257(32.30), 256(15.90), 255(17.20), 233(10.90), 231(21.00), 217(23.00), 216(18.40), 215(26.30), 200(25.80), 199(27.80), 198(30.80), 197(19.70) 187(23.50), 185(14.10), 177(11.90), 144(43.90), 120(9.10), 119(23.50), 118(45.50), 108(21.70), 107(7.10), 103(5.30), 102(39.90), 90(11.30), 85(38.10), 78(15.40), 77(33.60), 76(100), 75(28.30), 74(21.00), 65(12.60), 63(21.20), 62(11.90), 60(52.50), 59(12.60), 51(12.60), 50(20.20). Anal. Found: C, 49.02; H, 2.63; N, 8.47; Br, 16.01; S, 6.39. $C_{20}H_{14}N_3BrO_5S$ requires: C, 49.28; H, 2.87; N, 8.62; Br, 16.22; S, 6.57.

3- [(o-Hydroxyphenyl)-1-thioxo-1, 2,4-triazolo[1, 2-b]-phthalazine-4, 9-dione (5)

A solution of **3a** (0.01 mole) in acetic acid (30 mL) was heated at 25-35°C. a solution of bromine (0.01 mole) in acetic acid (10 mL) was added dropwise with stirring

Compd No	Antibacterial Activity					Antifungal Activity	
	Gram Positive Bacteria			Gram Negative Bacteria			
	Bacillus Subtilis	Staphylococcus Aureas	Streptococcus Penumonia	Escherichia Coli	Pesudomonas SP.	Aspergillus Nigaer	Penicillium SP.
2	+++	+	+++	+++	++	+++	+
3a	+	++	++	+++	+	++	+
3b	+ +	+	+	+	+++	++	+++
4	++	+++	+	-	-	+++	++
7b	-	++	+++	+	++	+	++
9	+++	+	+++	++	-	-	-

Table1. Antimicrobial activity of some synthesized compounds 2, 3, 4, 7 and 9

during 30 min. after addition the mixture was stirred for 2h. the reaction mixture poured into water. The resulting solid was filtered off, washed with water, dried and purified by methanol to give **5** as yellow crystals, yield 52%, m.p. 160°C. IR(KBr): 3413(OH), 1688(C=O), 1625(C=N), 1605, 1581(C=C), 1398(C=S), 1150, 1055(C-O) Cm^{-1}. ^{1}H-NMR(DMSO-d_6):δ 6.89-8.10(m, 8H, Ar-H), 11.41 (s, 1H, OH). MS: m/z (%) 315(M^++1, 6.80), 314(M^+, 17.90), 273(18.60), 272(17.50), 271(7.00), 230(15.70), 200(10.70), 199(15.50), 198(9.90), 171(9.40), 158(5.00), 157(6.80), 146(6.30), 143(5.70), 119(9.20), 116(11.80), 105(6.30), 104(7.70), 102(4.40), 90(7.40), 83(2.60), 82(100), 81(56.00), 80(99.40), 79(51.70), 77(14.20), 76(13.30), 74(19.30), 65(11.60), 64(35.00), 63(21.40), 62(10.90), 60(13.40), 59(11.60), 53(12.00), 51(14.50), 50(9.6). Anal. Found : C, 61.00; H, 2.59; N, 13.23; S, 10.03. $C_{16}H_9N_3O_3S$ requires: C, 61.15; H, 2.86; N, 13.37; S, 10.19.

4-Aryl-1-thioxo-1, 2, 4- triazino[1, 2-b]-phthalazine-5, 10-diones (7a, b).

A mixture of **2** (0.01 mole) and ω-bromomethylarylketones (such as 4-methylphenacyl bromide and 4-chlorophenacyl bromide) (0.01 mole) in methanol (50 mL) in presence of fused sodium acetate (0.03 mole) was heated under reflux for 4h., then cooled and poured into water. The product formed was filtered off, washed with water, dried and purified by recrystallization from ethanol to give 7.

4-(P-Methylphenyl)-1-thioxo-1, 2, 4-triazino[1, 2-b]- phthalazine-5, 10-dione (7a), as pale yellow crystals, yield 63%, m.p. 80°C. IR(KBr): 3320(NH), 1730(C=O), 1605, 1540(C=C), 1378(C=S)cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.25(s, 3H, CH_3), 6.81-8.12 (m, 9H, ArH and triazine ring), 10.35 (s, 1H, NH). MS: m/z (%) 336(M^++1, 20.00), 335(M^+, 100), 321(14.50), 292(6.30), 291(16.50), 290(89.40), 263(8.60), 217(3.50), 216(14.50), 205(12.20), 204(8.30), 203(9.00), 190(32.90), 189(29.40), 188(29.40), 187(20.40), 174(11.40), 168(11.00), 167(5.90), 162(16.10), 161(5.10), 160(7.10), 149(15.30), 148(54.10), 147(59.20), 143(34.50), 134(14.90), 133(9.40), 132(19.60), 130(14.50), 119(48.60), 118(22.70), 117(27.80), 116(23.90), 115(48.60), 105(29.40), 104(45.50), 103(21.60), 102(12.90), 101(19.60), 92(8.60), 91(67.80), 90(23.90), 89(22.40), 78(11.80), 77(29.40), 76(75.70), 75(14.50), 74(27.10), 69(12.90), 65(45.50), 64(25.90), 63(32.20), 62(11.00), 60(12.90), 56(18.80), 53(12.90), 52(17.30), 51(35.70), 50(47.10). Anal. Found: C, 64.29; H, 3.59; N, 12.42; S, 9.31. $C_{18}H_{13}N_3O_2S$ requires: C, 64.48; H, 3.88; N, 12.54; S, 9.55.

4-(P-Chlorophenyl)-1- thioxo-1, 2, 4-triazino [1, 2-b]-phthalazine-5, 10-dione (7b), as pale yellow crystals, yield 67%, m.p. 160°C. IR(KBr): 3114 (NH), 1738(C=O), 1605, 1588 (C=C), 1396 (C=S) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 7.21-8.12 (m, 9H, Ar.H and triazine ring), 10.37 (s, 1H, NH). MS: m/z (%) 357(M^++2, 34.50), 356(M^++1, 17.60), 355(M^+, 88.30), 354(M^+-1, 6.70), 313(15.00), 312(24.00), 311(40.20), 310(60.90), 277(4.80), 276(7.90), 236(4.70), 209(5.30), 208(16.20), 175(5.90), 174(15.30), 173(23.90), 169(3.50), 168(19.40), 165(7.30), 163(24.40), 139(6.30), 138(14.90), 137(8.50), 136(22.70), 133(11.30), 132(6.00), 130(15.70), 113(6.10), 111(14.40), 105(19.10), 104(55.20), 103(9.50), 102(16.30), 91(3.10), 90(11.80), 89(12.50), 77(18.50), 76(100), 75(36.10), 74(24.40), 64(7.30), 63(12.80), 62(7.30), 51(22.00), 50(57.60). Anal. Found: C, 60.72; H, 2.66; N, 11.59; Cl, 9.73; S, 8.88. $C_{17}H_{10}N_3ClO_2S$ requires: C, 60.84; H, 2.82; N, 11.83; Cl, 9.86; S, 9.01.

2- (Benzoylamino)-thiocarbonyl-3-benzoyl-phthalazine-1, 4-dione (8)

A mixture of **2** (0.01 mole) and benzoyl chloride (0.02 mole) in acetic acid (50 mL) was heated under reflux for 3h., then concentrated. The reaction mixture was cooled and the solid formed was filtered off, dried and purified by recrystallization with ethanol to give **8** as colourless crystals, yield 63%, m.p. 125°C. IR(KBr): 3225(NH), 1705, 1687 (C=O), 1605, 1580 (C=C), 1398 (C=S) cm^{-1}. ^{1}H-NMR(DMSO-d_6): δ 7.32-7.98 (m, 14 H, Ar-H), 10.23(br. s, 1H, NH). MS: m/z (%) 430 (M^++1, 3.50), 429(M^+, 7.85), 282(5.10), 281(16.20), 280(10.50), 253(16.40), 123(3.00), 121(12.60), 106(7.00), 105(100), 104(7.10), 78(5.60), 77(46.80), 76(12.00), 69(3.20), 51(13.70), 50(1.70). Anal. Found: C, 64.17; H, 3.22; N, 9.57; S, 7.31. $C_{23}H_{15}N_3O_4S$ requires: C, 64.34; H, 3.49; N, 9.79; S, 7.46.

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