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SOME REACTIONS ON 5-PHENYL-1,3,4-OXA(THIA)DIAZOLE-2-THIONES

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ABSTRACT

Reacting 5-phenyl-1,3,4-oxa(thia)diazole-2(3H)-thiones 1 with formaldehyde afforded the corresponding 3-hydroxmethyl derivatives 2 which on condensation with DEM and/or EAA gave 3 and 4, respectively. Treatment of 1 with maleic acid afforded the diacids 5 which on reacting with Ac_2O gave the anhydrides 6. Esterfication of 6 with MeOH and PhOH afforded the corresponding esters 7 and 8. Hydrazinolysis of 7 yielded 9 and 10. Treatment of 1 with p-benzoquinone, cyanogen bromide and phenacyl bromide afforded 11, 12 and 13, respectively. Thiation of 13 with P_2S_5 afforded 14. Reacting 1 with chloroacetyl chloride yielded 15 which on treatment with NH3 afforded the amide 16. Condensation of 1 with hydrazine hydrate afforded 17 which on treatment with phenacyl bromide gave 18. Cyclization of 18 with Ac_2O yielded 19. Treatment of 1 with phenylhydrazine gave 20 which on reacting with phenacyl bromide afforded 21. Some of the products were evaluated for their antibacterial activities.

INTRODUCTION

The chemistry of 1, 3, 4-oxa(thia)diazoles and their derivatives is the subject of various investigations in our laboratory[1-6] due to their importance and wide applications in biological as well as the *industrial* fields. A number of this class of compounds were found to have herbicidical properties [7,8]. Others are useful as dyestuffs[9]. Some are useful for their tubercluostatic activity[10] and intermediates in the manufacture of pharmaceuticals[11,12]. All these facts encouraged us to continue studying the chemistry of these type of compounds. Our results are reported in this article.

RESULTS AND DISCUSSION

It has been reported that 5-phenyl–1,3,4-oxa(thia)diazole-2-thiones 1a,b reacted with formaldehyde in absolute ethanol to give 3-(hydroxymethyl)-5-phenyl-1,3,4-oxa(thia)diazole-2(3H)-thiones 2a,b[1,2], which on treatment with diethyl malonate (DEM) and/or ethyl acetoacetate (EAA) in glacial acetic acid at r.t. afforded diethyl 2-{[5-phenyl-2-thioxo-1,3,4-oxa(thia)diazol-3(2H)-yl]methyl}malonates (3a,b) and ethyl 3-oxo-2-{[5-phenyl-2-thioxo-1,3,4-oxa(thia)diazol-3(2H)-yl]methyl}butanoates (4a,b), respectively. Compounds 1a,b reacted with

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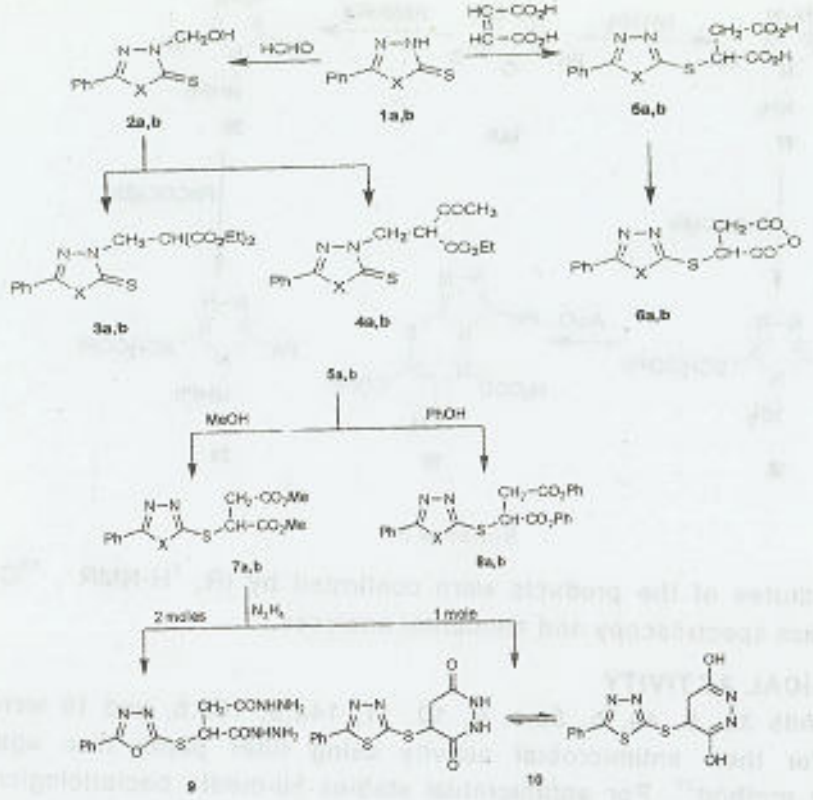
maleic acid in refluxing dioxane to yield 2-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio]succinic acids (5a,b)[3-5] which on treatment with boiling acetic anhydride gave 3-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio]-dihydrofuran-2,5-diones (6a,b). On heating compounds 5a,b with absolute methanol in the presence of H_2SO_4 and /or phenol in the presence of polyphosphoric acid (PPA) yielded dimethyl 2-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio]succinates (7a,b) and diphenyl 2-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio]succinates (8a,b), respectively. On reacting 1 mole of 7a with 2 moles of hydrazine hydrate in refluxing absolute ethanol afforded 2-(5-phenyl-1,3,4-oxadiazol-2-ylthio)succinohydrazide (9). While, refluxing equimoleculer amounts of 7b and hydrazine hydrate in absolute ethanol 4-(5-phenyl-1,3,4-thiadiazol-2-ylthio)piperazine-3,6-dione (10) was obtained (Scheme 1).

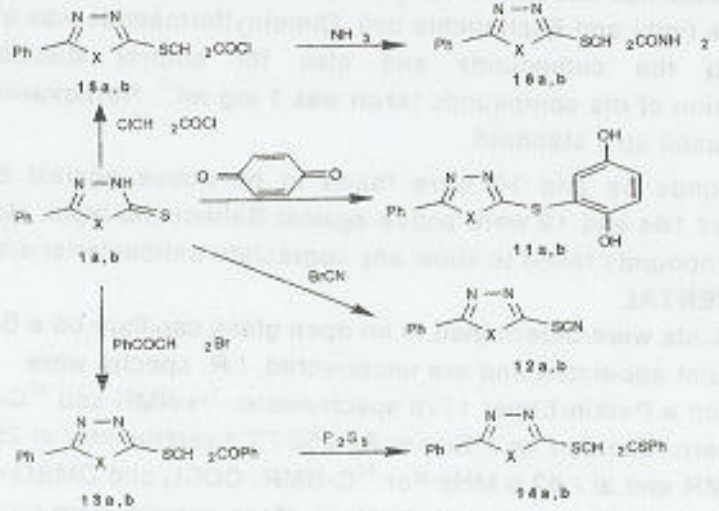
Compounds 1a,b reacted with p-benzoquinone and/or cyanogen bromide in anhydrous pyridine at r.t. to give 2-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio]benzene-1,4-diols (11a,b) and 2-phenyl-5-thiocyanato-1,3,4-oxa(thia)diazoles (12a,b), respectively.

Compounds 1a,b reacted with phenacyl bromide[13] in pyridine at room temperature and afforded 2-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio]-1-phenylethanones (13a,b) which could be thiated with P_2S_5 in refluxing xylene to give 2-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio]-1-phenyl-ethanethiones (14a,b). Treatment of compounds 1a,b with chloroacetyl chloride at r.t. in anhydrous benzene afforded 2-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio]acetyl chlorides (15a,b)[14,15] which on treatment with ammonia solution at r.t. gave 2-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio]acetamides (16a,b) (Scheme 2).

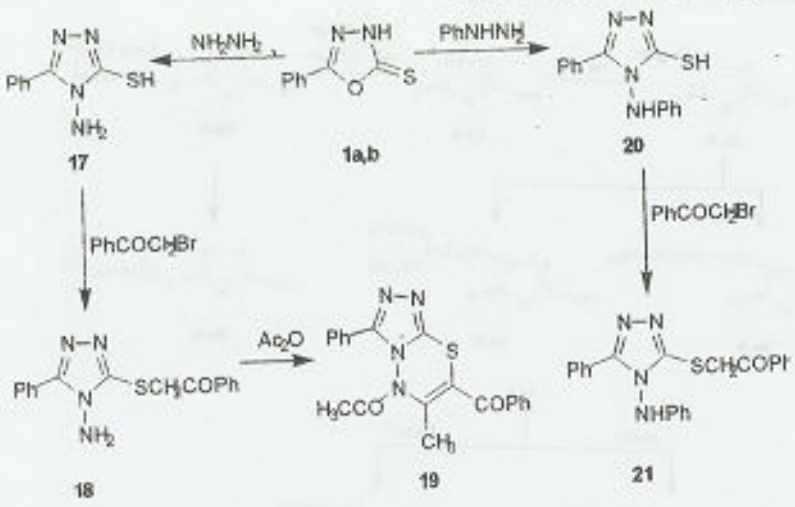
Condensation of 1a with hydrazine hydrate in boiling ethanol yielded 4-amino-5-phenyl-2-thioxo-1,2,4-triazole 17[16-19] which on treatment with phencayl bromide in anhydrous pyridine at r.t. afforded 2-[(4-amino-5-phenyl-4H-1,2,4-triazol-3-yl)thio]-1-phenylethanone (18).[6,20] Cyclization of 18 could be achieved on treatment with boiling acetic anhydride to give (5-acetyl-6-methyl-3-phenyl-5H-[1,2,4]-triazolo[3,4-b][1,3,4]- thiadiazin-7-yl)(phenyl)methanone (19). On the other hand, 4-anilino-5-phenyl-4H-1,2,4-triazole-3-thiol (20) reacted with phenacyl bromide in anhydrous pyridine at r.t. to afford 2-[(4-anilino-5-phenyl-4H-1,2,4-triazol-3-yl)thio]-1-phenylethanone (21) (Scheme 3).



Scheme 1



Scheme 2



Scheme 3

The structures of the products were confirmed by IR, ^{1}H-NMR , ^{13}C-NMR, mass spectroscopy and elemental analyses.

BIOLOGICAL ACTIVITY

Compounds 3a, b, 4a, b, 5a,b, 9, 10, 11, 14a,b, 16a,b, and 19 were tested for their antimicrobial activity using filter paper disc agar diffusion method[21]. For antimicrobial studies Hi-media bacteriological nutrient broth and bacteriological nutrient agar were used against Gram positive, Bascillus subtilis, Staphylococcus aureus and Gram negative Salmonella typhi and Escherichia coli. Dimethylformamide was used for solubilising the compounds and also for control studies. The concentration of the compounds taken was 1 mg ml^{-1}. Norfloxacin (1 mg ml^{-1}) was used as a standard.

Compounds 5a and 10 were found to be active against Bacillus subtilis and 16a and 19 were active against Salmonella typhi. However, rest of compounds failed to show any appreciate antibacterial activity.

EXPERIMENTAL

Melting points were determined in an open glass capillary on a Buchi melting point apparatus and are uncorrected. I.R. spectra were recorded on a Perkin-Elmer 1720 spectrometer ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker Ac 250 FT spectrometer at 250 MHz For ^{1}H-NMR and at /.62.9 MHz For ^{13}C-NMR. $CDCl_3$ and DMSO-d_6 as solvents using TMS as internal standard. Mass spectra were recorded using electron ionization (E.I.) on a varian Mat 311spectrometer.

3-(Hydroxymethyl)-5-phenyl-1,3,4-oxa(thia)diazole-2(3H)-thiones (2a,b)

A mixture of 1a,b (0.01 mole), formaldehyde (0.1 mole, 0.8 g) and absolute ethanol (20 ml) was refluxed for 6 hrs (tlc).On cooling, the separated solid was filtered off and recrystalized from ethanol to give 2a,b.

2a, yield 90%, m.p 132°C., lit (132 °C)[1].

2b, yield, 85%, m.p 105°C, lit (105°C)[1].

Diethyl-2-{[5-phenyl-2-thioxo-1,3,4-oxa(thia)diazol-3(2H)-yl] methyl} malonates (3a,b)

A mixture of 2a,b, (0.01 mole), and diethylmalonate (0.01 mole, 1.6 g), was stirred at r.t. in glacial acetic acid (10 ml) in the presence of triethylamine (0.5 ml) for 30 hrs (tlc). The reaction mixture was poured onto ice. The resulting solid was filtered off and recrystallized from ethanol to give 3a,b.

3a: I.R: 3140 cm^{-1} (CH), 1730 cm^{-1} (C = O). ^{1}H-NMR (DMSO): δ= 1.1 ppm (t, 6H, 2 x CH_3), 4.1 ppm (q, 4H, 2 x CH_2), 4.5 ppm, (d, 2H, CH_2), 5.7 ppm, (t, 1 H, CH), 7.5-8.5 ppm (m, 5H, aromatic protons). ^{13}C-NMR: δ = 13.66 ppm (CH_3), 49.07 ppm (CH_2), 61.59 ppm (CH), 122.36, 125.88, 129.24, 132.04 ppm (aromatic carbons), 160.31 ppm (C=O), 177.37 ppm (C=S). MS: M^+ at m/e = 350 (1.5%), m/e = 305 (M^+-OEt, 1%); m/e =278 (M^+-HCOOEt, 1.5%); m/e 178 (M^+-(CH_2=C(CO_2Et)$_2$), 100%); m/e = 118 (PhCNO, 74%); m/e = 103 (PhCN, 15%).

3b: I.R: 3096 cm^{-1} (OH), 1730 cm^{-1} (C = O). ^{1}H-NMR ($CDCl_3$): δ = 1.1 ppm (t, 6H, 2 x CH_3), 3.1 ppm (q, 4H, 2xCH2), 4.2 ppm, (d, 2 H, CH_2), 4.6 ppm (t, 1H, CH), 7.5 - 8.5 ppm (m, 5H aromatic protons). ^{13}C-NMR: δ = 13.82 ppm (CH_3), 45.70 ppm (CH2), 100.22 ppm (CH), 126.39, 128.54, 129.28, I31.35 ppm (aromatic carbons), 159.90 ppm (C=O), 187.52 ppm (C=S). MS: m/e = 292 (M^+-HCOOEt, 16%), m/e = 194 [M^+-(CH_2=C (COOEt)$_2$), 32%] ,m/e = 121 ($PhCS^+$, 28%), m/e = 103 (PhCN, 100%), m/e = 77 ($C_6H_5^+$, 37%).

Ethyl-3-oxo-2-{[5-phenyl-2-thioxo-1,3,4-oxa(thia) diazol- 3(2H)-yl] methyl} butanoates (4a,b)

A mixture of 2a,b (0.01 mole), and ethylacetoacetate (0.01 mole, 1.3 g) was stirred at r.t. in glacial acetic acid (10 ml) in the presence of triethylamine (0.5 ml) for 36 hrs (tlc). The reaction mixture was poured onto ice. The resulting solid was filtered off and recrystallized from methanol to afford 4a,b.

4a: I.R: 1730 cm^{-1}(C=O), 1186 cm^{-1} (C=S). ^{1}H-NMR (DMSO): δ = 1.00 ppm (t, 3H, CH_3), 2.40 ppm (s, 3H, CH_3), 4.2 ppm, (m, 3H, CH, CH_2), 4.5 ppm, (d, 2H, CH_2), and 7.5-8.5 ppm (m, 5H, aromatic protons). ^{13}C-NMR : δ = 13.6 ppm (CH_3 – CH_2), 29.49 ppm (CH_3-C=O), 61 .20 ppm (N - CH_2) 62.1, ppm (CH_2-CH_3),71.4 ppm (CH) 122.35, 125.94, 129.34 ,132.04 ppm (aromatic carbons), 160.30 ppm ($COCH_3$), 177.36 ppm (COOEt). 200.36 ppm (C=S). MS: M^+ at m/e = 320 (2%), m/e = 215 [M^+ (COOEt$^+$ COMe)] m/e = 178 (base, 100%), m/e 103 (PhCN, 14%), .

4b: I.R: 1770 cm^{-1} ($COCH_3$), 1737 cm^{-1} (COOEt). ^{1} H-NMR ($CDCl_3$): δ = 1.2 ppm (t, 3H, CH_3), 2.3 ppm (s, 3H, CH_3), 4.2 ppm, (q, 2H, CH_2), 4.5 ppm, (t, 1H, CH), 4.7 ppm (d, 2H, CH_2), 7.5-8.5 (m, 5H, aromatic protons).^{13}C-NMR: δ = 13.7 ppm (CH_3-CH_2), 29.32 ppm (CH_3-CO), 48.02 ppm ($CHCH_2$), δ = 56.6 ppm (CH_2CH_3), δ = 74.96 ppm (CH) l26.24, 126.4, 128.49, 129.31 ppm (aromatic carbons), 159.94 pprn (C=N), 159.97 ppm (COMe), 167.67 (COOEt), 200.63 ppm (C=S). MS: M^+ at m/e = 336 (3%), m/e = 293 (M^+-$COCH_3$), m/e = 291 (M^+-OEt,), m/e = 194 (base, 100%), m/e = 121 ($PhCS^+$, 14%), m/e=103 (PhCN, 14%), m/e =77 ($C_6H_5^+$, 28%).

2-[5-Phenyl-1,3,4-oxa(thia)diazol-2-ylthio]succinic acids (5a,b).

A mixture of 1a,b (0.01 mole) and maleic acid (0.01 mole, 1.16 g) , was refluxed in dioxane (10 ml) and triethylamine (1 ml) for 6 hrs (tlc). The reaction mixture was cooled, poured onto cold water. The resulting solid was filtered off and recrystallized from water to afford 5a,b.

5a: yield, 90%, m.p 169°C (Lit. 168°C) [3-5]

5b: I.R: 1710 cm^{-1} (C = O), 1524 cm-1(C=N). ^{1}H-NMR (DMSO): δ =3.0 ppm (d, 2 H, CH_2), 5.4 ppm (t, 1H, CH), 6.6 ppm (s, 2H, 2xOH), 7.5-8.0 ppm (m, 5H, aromatic protons). ^{13}C-NMR: δ = 45.54 ppm. (CH_2), 59.08 ppm (CH), 126.47, 126.06, 129.20, 134.02 ppm (aromatic carbons), 155.82 ppm (C=O), 166.12 ppm (C=O). 176.18 ppm (C=O) , 185.32 ppm (C-S-C). MS: M^+ at m/e = 310 (4%), m/e = 292 (M^+-H_2O, 84%), m/e = 276 (M^+- H_2O_2, 47%), m/e = 220 (M^+-$(COOH)_2$, 18%), m/e = 194 (base, 78%), m/e = 121 ($PhCS^+$, 20%), m/e = 103 (PhCN, 100%).

3-[5-Phenyl-1,3,4-oxa(thia)diazol-2-ylthio]-dihydrofuran-2,5-diones (6a,b)

A mixture of 5a,b (0.01 mole), and acetic anhydride (5 ml) was refluxed for 2 hrs (tlc). The reaction mixture was cooled, the resulting solid was filtered off and washed three times with petroleum ether 40/60°C to give 6a,b .

6a: yield, 90%, m.p 152°C (Lit. 153°C) [3-5].

6b: I.R: 1885 cm^{-1} (C=O), 1592 cm^{-1} (C=S). ^{1}H- NMR (DMSO): δ =3.2 ppm (d, 2H, CH_2), 6.0 ppm (t, 1H, CH), 7.5-8.0 ppm (m, 5H, aromatic protons). ^{13}C- NMR : δ = 45.86 ppm (CH_2), 59.53 ppm (CH), 127.59, 129.19, 132.02, 13.4.02 ppm (aromatic carbons), I66.05 ppm (N=C-S) 170.84 ppm (CH_2-C-O), 187.73 ppm. (S-CH-C-O).MS: M^+ at m/e = 292 (21%), at m/e = 248 (M^+-CO_2, 1%), m/e = 220 (M^+-(CO_2+CO), 6%), m/e = 194 (base, 100%), m/e = 118 ($PhCHN_2$, 48%).

Dimethyl-2-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio] succinates (7a,b)

A mixture of 5a,b (0.01 mole), and methanol (5 ml), was refluxed on a water bath in the presence of conc. H_2SO_4 (0.5 ml) for ½ hr (tlc) . The reaction mixture was cooled. The resulting solid was filtered off and recrystallized from ethanol to yield 7a,b.

7a: I.R: 1740 cm^{-1} (C=O), 1644 cm^{-1} (C=N). ^{1}H-NMR ($CDCl_3$): δ = 3.3. ppm (d, 2 H, CH_2), 3.8 ppm (s, 3H, CH_2COOCH_3), 3.9 ppm (s, 3H, $SCHCOOCH_3$), 5.8 ppm (d, 1H, CH) 7.5-8.0 ppm (m, 5H. aromatic protons). ^{13}C-NMR: δ = 33.8 ppm (CH_2), 52.21 ppm (OCH_3), 53.20 ppm (OCH_3), 56.86 ppm (CH), 121.92, 126.12, 128.39, 132.35 ppm (aromatic carbons), 159.18 (C=N), 167.01 (C-S-CH), 169.27 ($C=OCH_2$) and 176.88 (C=O-CH). MS: M^+ at m/e = 322 (26%), m/e =291 (M^+-OCH_3, 4%), m/e = 263 (M+-COOMe, 3%), m/e = 231 (M+-(CH_3OH + COOMe), 4%), m/e = 203 (M^+-(HCOOMe+COMe), 4%), m/e = 178 (base, 17%), m/e = 103 (PhCN, 27%).

7b: I.R: 1740 cm^{-1} (C=O), 1678 cm^{-1} (C=N). ^{1}H NMR ($CDCl_3$): δ = 3.3 ppm (t, 2H, CH_2), 3.8 ppm (s, 3H, CH_3), 3.9 ppm (s, 3H, CH_3), 6.3 ppm (d, ^{1}H, CH) , 7.5-8.5 (m, 14H, aromatic protons).^{13} C-NMR : δ = 33.87 ppm (CH_2), 52.16 (OCH_3), 53.09 ppm (OCH_3), 57.92 ppm (CH) 126.40, 128.34, 129.10, 132.39 ppm (aromatic carbons), 157.19 ppm(C=N), 167.51 ppm (C-S-CH), 176.94 ppm (CH_2-C=O), I 86.46 ppm (CH-CO). MS: M^+ at m/e =338 (100%), m/e = 307 (M^+ -OCH_3, 14%), m/e = 247 (M+ (CH_3OH + CH_3COO) 20%), m/e; 194 (base, 81%).

Diphenyl-2-[5-phenyl-1,3,4-oxa(thia)diazol-2-ylthio]succinates (8a,b)

A mixture of 5a,b (0.01 mole), phenol (0.01 mole, 1 g) and polyphosphric acid (5 g) was heated on a water bath for 24 hrs (tlc). The reaction mixture was cooled and extracted with boiling toluene (50 ml). The cooled toluene layer was washed three times with a saturated

solution of sodium bicarbonate to remove the unreacted phenol, followed by washing with water, then dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure. The resulting solid was recrystallized from ethanol to give 8a, b. 8a: I.R: 1756 cm^{-1} (C=O), 1666 cm^{-1} (C=N). MS: M^+ at m/e = 446 (21%), m/e= 353 (M^+- OC_6H_5, 100%), m/e = 231 (M^+- (2 COOPh), 3%), m/e = 104 ($PhC{=}NH^+$, 28%), m/e = 103 (PhCN, 7%), m/e 77 (C_6H_5+, 24%).

8b: I.R: 1759 cm^{-1} (C=O), 1068 cm^{-1} (C=N).

2-(5-Phenyl-1,3,4-oxadiazol-2-ylthio)succinohydrazide and 4-(5-phenyl-1,3,4-thiadiazol-2-ylthio)piperazine-3,6-dione (10).

A mixture of 7a and/or 7b (0.005 mole) and hydrazine hydrate (0.01 mole, 0.5 g) was refluxed in absolute ethanol (20 ml) in the presence of triethylamine (1 ml) for 3 hrs(tlc). The reaction mixture was cooled and the resulting solid was filtered off and crystallized from ethanol to give 9 and 10.

9: I.R: 2920 cm^{-1} (NH), 1676 cm^{-1} (C = O). ^{1}H-NMR ($CDCl_3$): δ = 2.9 ppm (d, 2H, CH_2), 4.3 ppm (t, ^{1}H, CH), 7.5-8.0 ppm (m, 5H, aromatic protons), 9.2 (bs, 2H, NH_2), 9.4 (bs, 2H, NH_2), 9.9 (bs, 1H, NH),10.1 (bs, ^{1}H, NH). ^{13}C-NMR: δ = 33.98 ppm (CH_2), 57.82, ppm (CH), 124.77, 127.35, 128.23, 132.19 ppm (aromatic carbons), 149.53 ppm (C=N), 162.83 ppm (C-S-CH), 165.74 ppm (CH_2-C=O), 168.65 ppm (CH-CO). MS: (M^+ -H) at m/e = 320 (1%), m/e = 260 (M^+ - $2NHNH_2$), m/e = 178 (base, 3%), m/e = 105 ($PhCO^+$, 100%), m/e = 77 ($C_6H_5^+$, 52%).

10: I.R: 2936 cm^{-1} (NH), 1696 cm^{-1} (C=O). ^{1}H-NMR($CDCl_3$): δ = 2.9 ppm (d , 2H, CH_2), 5.8 ppm (m, ^{1}H, CH), 7.5-8.0 ppm (m, 5H, aromatic protons), 9.2 ppm (s, 1H, NH or OH), and 9.5 ppm (s, 2H, NH or OH). ^{13}C-NMR: δ = 35.21 ppm (CH_2), 58.53, ppm (CH), 126.54, 128.22, 129.34, 131.69 ppm (aromatic carbons), 155.83 ppm (C-Ph), 166.12 ppm (C-S-CH), 167.49 ppm (CONH), 185.47 ppm (NHCO). MS: M^+ at m/e = 306 (29%), m/e = 247 (M^+- $CONHNH_2$ 14%), m/e =194 (base, 100%), m/e = 121 ($PhCS^+$, 17%), m/e = 118 ($PhCHN_2$, 74%), m/e = 104 ($PhC{=}NH^+$, 30%).

2-[5-Phenyl-1,3,4-oxa(thia)diazol-2-ylthio]benzene-1,4-diols (11a,b)

A mixture of 1a,b (0.01 mole) and p-benzoquinone (0.01 mole, 1.08 g), was stirred at r.t. in anhydrous pyridine (10 ml) for 1 hr (tlc). The reaction mixture was poured onto ice. The resulting solid was filtered off and washed three times with petroleum ether (40/60°C) to give 11a,b.

11a: yield, 83%, m.p. 110 °C (Lit. 111 °C) [9-11]

11b: I.R: 3265 cm^{-1} (NH), 1622 cm^{-1} (C=N). ^{1}H-NMR (CDCl3): δ = 7.0-8.0 ppm (m, 10H, aromatic protons), 8.2 ppm (S,1H, OH), 9.2 ppm (s, 1H, OH). ^{13}C-NMR: δ = 115.25, 117.48, 119.74, 120.64, 125.81, 126.34, 127.35, 128.46, 129.36 ppm. (aromatic carbons), 150.40 ppm (C-Ph), δ =168.49 ppm (C-S-C). M.S: M^+ at m/e = 302 (79%) , m/e= 285 (M^+,- OH, 100%); m/e = 268 (M^+,- 2OH, 13%); m/e = 194 (M^+- benzoquinone, 46%),m/e = 121 ($PhCS^+$, 45%).

2-Phenyl-5-thiocyanato-1,3,4-oxa(thia)diazoles (12a,b)

A mixture of 1a,b (0.01 mole) and cyanogen bromide (0.01 mole, 1.08 g) was stirred at r.t. in anhydrous pyridine (5 ml) for 30 min (tlc). The reaction mixture was poured onto ice and the resulting solid was recrystallized from ethanol. to give 12a,b.

12a: I.R: 2165 cm^{-1} (C≡N), 1658 cm^{-1} (C=N). ^{1}H-NMR (CDCl3): δ = 7.5-8.0 (m, 5H, aromatic protons). ^{13}C-NMR: δ = 122.68 ppm (CN) 126.96, 129.04, 132.40 ppm (aromatic carbons), 155.52 ppm (Ph-C=N), 167.81 ppm (C-S-CN). MS: m/e = 178 (M^+ -CN, 2%); m/e = 145 (M^+ - SCN, 100%); m/e = 105 ($PhCO^+$, 17%), m/e = 103 (PhCN, 11%) , m/e = 77 ($C_6H_5^+$, 49%).

12b: I.R: 2358 cm^{-1} (C≡N), 1677 cm^{-1} (C=N). ^{1}H-NMR ($CDCl_3$): δ = 7.5-8.0 (m,5H,aromatic protons). ^{13}C-NMR: δ = 126.62 ppm (CN), 127.95, 129.54, 131.64 ppm (aromatic carbons), 152.71 ppm (Ph-C=N) and 170.26 ppm. (C-S-CN). MS: M^+ at m/e = 219 (1%) , m/e = 194 (M^+- CN, 24%); m/e = 162 (M^+- SCN, 100%); m/e = 135 (PhNCS, 23%); m/e = 103 (PhCN, 17%).

2-[5-Phenyl-1,3,4-oxa(thia)diazol-2-ylthio]-1-phenylethanones (13a,b)

A mixture of 1a,b (0.01 mole) and phenacyl bromide (0.01 mole, 1.99 g) was stirred at r.t. in anhydrous pyridine (5 ml) for 30 min (tlc). The reaction mixture was poured onto crushed ice. The resulting solid was filtered off and recrystallized from ethanol to yield 13a,b.

13a: yield, 80%, m.p .160 °C (Lit.163 °C) [13]. 13b: yield, 80%, m.p. 121 °C (Lit. 122 °C) [13].

2-[5-Phenyl-1,3,4-oxa(thia)diazol-2-ylthio]-1-phenylethanethiones (14a,b)

A mixture of 13a,b (0.01 mole) and phosphorous pentasulfide (0.01 mole, 2.3 g) was refluxed in anhydrous xylene (10 ml) for 10 hrs (tlc).

The solvent was evaporated till dryness under reduced pressure . The resulting solid was recrystallised from ethanol and afforded 14a,b.

14a: I.R: 2358 cm^{-1} (C=S), 1677 cm^{-1} (C=N). ^{1}H-NMR ($CDCl_3$): δ = 5.10 ppm (s, 2H, CH_2), 7.5-8.5 ppm (m, 10H aromatic protons). ^{13}C-NMR: δ = 41.68 ppm (CH_2), 126.27, 127.36, 128.40, 129.39, 131.24, 133.81, 135.13 ppm (aromatic carbons), 164.53 ppm (N=C-Ph.), 167.93 ppm (C-S-CH_2) 192.58 ppm (C=S).

14b: I.R: 1677 cm^{-1} (C=N), 1120 cm^{-1} (C=S). ^{1}H-NMR ($CDCl_3$): δ = 4.4 ppm (s, 2H, CH_2), 7.0-8.0 ppm (m, 10H, aromatic protons). ^{13}C-NMR: δ = 45.38 ppm (CH_2), 125.95, 126.24, 126.41, 127.35, 127.67, 128.47, 129.12, 129.36, 131.32, 131.44, 132.12 ppm (aromatic carbons), 164.51 ppm (N=C-Ph), 168.94 ppm (C-S-CH_2), 187.6 ppm (C=S).

2-[5-Phenyl-1,3,4-oxa(thia)diazol-2-ylthio]acetyl chlorides (15a,b)

A mixture of 1a,b (0.01 mole) and chloroacetyl chloride (0.01 mole, 1.12 g) was stirred at r.t. in anhydrous benzene (10 ml) for 12 hrs (tlc). The resulting solid was washed three times with petroleum ether 40/60°C to give 15a,b.

15a: I.R: 1762 cm^{-1} (C=O). ^{1}H-NMR($CDCl_3$): δ =4.7 ppm (m, 2H, CH_2), 7.5-8.1 ppm (m, 5H, aromatic protons). ^{13}C-NMR: δ = 37.04 ppm (CH_2), 122.34, 125.88, 128.37, 132.06 ppm (aromatic carbons), 160.30 (N=C-Ph.), 164.80 ppm (C-S-CH_2), and 177.34 ppm (C=O). MS: M^+ at m/e=256, m/e = 178 (base, 100%); m/e = 119 (PhNCO, 8%), m/e = 105 (PhCO+, 12%).

15b: I.R: 1688 cm^{-1} (C=O), 1610 cm^{-1} (C=N). ^{1}H-NMR ($CDCl_3$): δ = 4.3 ppm (m ,2H,CH_2), 7.5-8.5 ppm (m, 5H, aromatic protons). ^{13}C-NMR: δ = 43.70 ppm (CH_2), 122.14, 125.78, 129.12, 131.97 ppm (aromatic carbons), 186.13 ppm (C=O).

2-[5-Phenyl-1,3,4-oxa(thia)diazol-2-ylthio]acetamides (16a,b)

A mixture of 15a,b (0.01 mole) and a solution of saturated methanolic ammonia (5 ml) was stirred at r.t. for 1 hr (tlc). The resulting solid was washed with water and recrystallized from ethanol to give 16a,b.

16a: yield, 80%, m.p, 180°C (Lit.182°C) [13].

16b: I.R: 3425 cm^{-1} (NH_2), 1688 cm^{-1} (C=O). MS: M^+ at m/e = 235. (58%), m/e = 192 (M^+- CONH, 55%); m/e = 187 (base, 2%); m/e = 145 (M^+-SCH_2CONH_2, 87%), m/e = 105 (PhCO, 95%).

Table: Experimental and physical data for compounds 3 – 21.

No.	M.P (°C)	Yield (%)	Formula (M. wt)	Analysis; calcd. / found % C	H	N	S
(3a)	115	70	$C_{15}H_{18}N_2O_5S$ (350.4)	54.8 54.0	5.1 5.1	8.0 7.7	9.2 9.1
(3b)	190	70	$C_{16}H_{18}N_2O_4S_2$ (366.5)	52.4 53.0	4.9 4.8	7.6 7.6	17.5 17.7
(4a)	200	76	$C_{15}H_{16}N_2O_4S$ (340.4)	56.2 56.3	5.0 5.2	8.7 7.4	10.0 10.0
(4b)	167	66	$C_{15}H_{16}N_2O_3S_2$ (336.4)	53.5 52.3	4.7 5.1	8.3 8.5	19.1 19.0
(5b)	180	90	$C_{12}H_{10}N_2O_4S_2$ (310.3)	46.4 46.3	3.5 3.6	9.0 9.8	20.6 20.6
(6b)	201	80	$C_{12}H_8N_2O_3S_2$ (292.2)	49.3 49.1	2.7 2.4	9.6 10.6	21.9
(7a)	95	60	$C_{14}H_{14}N_2O_5S$ (322.8)	52.2 52.7	4.4 4.3	8.7 8.7	9.9 9.9
(7b)	81	60	$C_{14}H_{14}N_2O_4S_2$ (338.8)	49.8 50.8	4.2 4.2	8.3 8.6	18.9 18.0
(8a)	155	40	$C_{24}H_{18}N_2O_5S$ (446.5)	64.6 64.9	4.1 4.0	6.3 6.4	7.2 7.1
(8b)	133	45	$C_{24}H_{18}N_2O_4S_2$ (462.5)	66.9 66.4	4.2 4.0	6.1 6.0	13.9 13.6
(9)	150	40	$C_{12}H_{14}N_6O_5S$ (322.3)	44.7 43.4	4.4 4.6	26.1 26.2	9.9 9.9
(10)	180	50	$C_{12}H_{10}N_4O_2S_2$ (306.4)	47.1 48.1	3.3 3.3	18.3 18.2	20.9
(11b)	190	80	$C_{14}H_{10}N_2O_2S_2$ (302.4)	55.6 56.6	3.4 3.6	9.3 9.4	21.2 21.1
(12a)	120	60	$C_9H_5N_3OS$ (203.2)	53.2 52.4	2.5 2.9	20.7 20.7	15.9 15.8
(12b)	119	80	$C_9H_5N_3S_2$ (219.3)	49.3 49.6	2.3 2.7	19.2 19.6	
(14a)	181	55	$C_{16}H_{12}N_2OS_2$ (312.4)	61.5 60.6	3.9 3.5	8.9 8.8	20.5 20.3
(14b)	185	43	$C_{16}H_{12}N_2S_3$ (328.5)	58.5 58.5	3.6 3.6	8.5 7.5	
(15a)	160	60	$C_{10}H_7CLN_2OS_2$ (271.1)	47.2 47.3	2.8 2.9	10.9 10.5	23.7 23.8
(15b)	215	57	$C_{10}H_8N_2OS_2$ (251.3)	44.3 44.4	2.6 2.5	10.3 10.1	
(16b)	150	70	$C_{10}H_7ClN_2O_2S$ (265.1)	47.8 47.9	3.6 3.5	16.7 16.6	25.5 25.6
(19)	173	65	$C_{20}H_{16}N_4O_2S$ (376.4)	63.7 63.5	4.3 4.3	14.8 14.3	8.5 8.4
(21)	155	80	$C_{22}H_{18}N_4OS$ (386.5)	68.4 68.5	4.7 4.7	14.5 14.4	8.4 9.4

5-Acetyl-6-methyl-3-phenyl-5H-[1,2,4]triazolo[3,4-b][1,3,4]-thiadiazin-7-yl) phenylmethanone (19)

A mixture of 18 (0.01 mole, 3.1g) and acetic anhydride (10 ml) was refluxed for 5 hrs (tlc). The reaction mixture was cooled and poured onto ice. The resulting solid was filtered off and recrystallized from ethanol to yield 19.

19: I.R: 1685 cm^{-1} (C=O), 1597 cm^{-1} (C=N). ^{1}H-NMR (DMSO): δ = 2.4 ppm (s, 3H, CH_3), 2.8 ppm (s, 3H, OCH_3), 7.5-8.5 (m, 10H, aromatic protons). ^{13}C-NMR: δ = 21.53 ppm (CH_3), 28.80 ppm (OCH_3), 127.48, 128.73, 128.58, 128.98, 131.56, 131.86 ppm (aromatic carbons), 140.94 ppm ($SCCH_3$), 146.77 ppm (SCCOPh) 146.78 ppm (N=C-Ph.), 152.76 ppm (C-S-CH_2), 166.57 ppm ($COCH_3$), 194.16 ppm. (COPh). MS: M^+ at m/e = 376 (15%), m/e = 334 (M^+ - CH_2CO, 25%); m/e = 292 (M^+ - $CH_3CONCCH_3$).100%); m/e = 105 ($PhCO^+$, 4%), m/e = 103 (PhCN, 11%).

2-[(4-Anilino-5-phenyl-4H-1,2,4-triazol-3-yl)thio]-1-phenylethanone (21)

A mixture of 20 (0.01 mole, 2.7 g) and phenacyl bromide (0.01 mole, 1.99g) was stirred at r.t. in anhydrous pyridine (5 ml) for 30 min(tlc). The reaction mixture was poured onto ice and the resulting solid was recrystallized from ethanol to give 21.

21: I.R: 3335 cm^{-1} (NH), 1778 cm^{-1} (C=O). ^{1}H.NMR (DMSO): δ = 5.0 ppm (s, 2H, CH_2) 7.3 – 8.0 ppm (m, 15H, aromatic protons), 9.7 ppm (s, 1H, NH). ^{13}C-NMR: δ = 41.37 ppm (CH_2), 114.70, 123.29, 126.54, 127.36, 127.43, 128.78, 129.17, 129.12, 130.95, 131.25, 131.57, 134.05, 134.74 ppm (aromatic carbons), I63.58 ppm (N=-C-Ph), 165.81 ppm (C-S-CH_2), I91.97ppm. (CO). MS: m/e = 296 (M^+-, NHPh, 8%), m/e =178 (base, 9%), m/e = 105 ($COPh^+$, 100%), m/e = 103 (PhCN, 8%), m/e = 91 ($NHPh^+$, 5%), m/e = 77 (Ph^+, 53%).

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بعض تفاعلات على ٥- فنيل ٤،٣،١ – أوكسا (ثيا) دايزول – ٣- ثيون

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شركة كفر الزيات للمبيدات والكيماويات – كفر الزيات – ج.م.ع

يتفاعل ٥- فنيل ٤،٣،١ – أوكسا (ثيا) دايزول (١) مع الفورمالدهيد ليعطي (٢) والذى يتفاعله مع المركبات المحتوية على مجموعة مثيلين نشطة يعطى المركبات ٤،٣ . معالجة (١) مع حمض المالميك يعطي (٥) والذى يعطي الأندريد المقابل (٦) بتفاعلة مع أندريد حمض الخليك دبا سترته مع المثيانول والفنيول يعطي ٨،٧ . بمعالجة(٧) بالهيدرازين يعطي ١٠،٩ . بمعالجة المركب (١) مع بارابنزو الكنيون – سيانوجين البروميد وفنياسيل البروميد يعطي ١١-١٣ . كبرتة (١٣) يعطي ١٤ . يتفاعل المركب (١) مع كلورو أستيايل الكلوريد ثم الأمونيا يعطي ١٦ . الذى يتكاثف مع الهيدرازين وفيناسيل البروميد وأندريد حمض الخليك على التوالي ولقد تم إختبار بعض النواتج بيولوجيا ضد بعض أنواع البكتريا ووجد لبعضها فاعلية متوسطه.