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STUDIES ON SOME 1,3,4-OXA(THIA)DIAZOLE DERIVATIVES

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ABSTRACT

Fusion of 2-chloro-5-phenyl-1,3,4-oxa(thia)diazoles (1a,b) with anthranilic acid gave the cyclized compounds 3a,b which on thiation afforded 2-phenyl-1-oxa(thia)-3,3a,9-triaza-cyclopenta[b]naphthalene-4-thiones (4a,b). Treatment of 1 with 4-chlorophenol and/or 4-chloro-aniline yielded compounds 5a,b and 5c,d, respectively. Condensation of 1a,b with 4-aminoacetophenone yielded 1-[4-(5-phenyl-[1,3, 4]oxa(thia)diazol-2-ylamino)-phenyl]-ethanones (6a,b) which on fusion with benzaldehyde afforded the corresponding chalcones 7. Reaction of compounds 7a,b with pentane-2,4-dione and hydrazine afforded compounds 8a,b and 9a,b, respectively. Refluxing 9 with Ac_2O afforded N-acetylated compounds (10a,b). Reaction of 2-amino-5-phenyl-1,3,4-oxa(thia)diazoles (11) with acyl bromides afforded 12a-d which on boiling with hydrogen bromide yielded 2,5-diphenylimidazo[2,1-b][1,3,4]oxadiazoles (13a,b). Fusion of 11a,b with 2-phenyl-4H-3,1-benzoxazin-4-one afforded 2-phenyl-3-(5-phenyl-[1,3,4]oxa(thia)diazol-2-yl)-3H-quinazolin-4-ones (14a,b). Condensation of 11a,b with benzoyl chloride gave 15a,b which on treatment with sodium azide yielded 5-phenyl-1-(5-phenyl-[1,3,4]oxa(thia)diazol-2-yl)-1H-tetrazoles (16a,b). Reacting 11a,b with phenylisothio-cyanate gave 17a,b which on condensation with malonic acid afforded 1-phenyl-3-(5-phenyl-[1,3,4]oxa(thia)diazol-2-yl)-2-thioxo-dihydro-pyrimidine-4, 6-diones (18a,b). Some of the compounds have been screened for their fungicidal activity.

Keywords: 1,3,4-Oxa(thia)diazoles, anthranilic acid, 4-aminoacetophenone, phenylisothiocyanate, 2-phenyl-2H-3,1-benzoxazin-4-ones.

INTRODUCTION

1, 3, 4-Oxa(thia)diazoles are important classes of compounds which are used as pharmacological agents.[1-3] Also, they act as fungicides, herbicides[4] and in the manufacture of dyes.[5] Due to their extraordinarily high stability, they can be used as bath liquids and solvents for highly fluorinated polymers.[6] In this report, we have studied the reaction of 2,5-disubstituted 1,3,4-oxa(thia)diazoles with different reagents to afford various new products. Some of the new products were tested for their activity as fungicides.

RESULTS AND DISCUSSION

2-Chloro-5-phenyl-1,3,4-oxadiazole (1a) was fused with anthranilic acid at 100 °C to afford the condensed 2-(5-phenyl-1,3,4-oxadiazol-2(3H)-ylideneamino)benzoic acid (2a) which was cyclized by refluxing in

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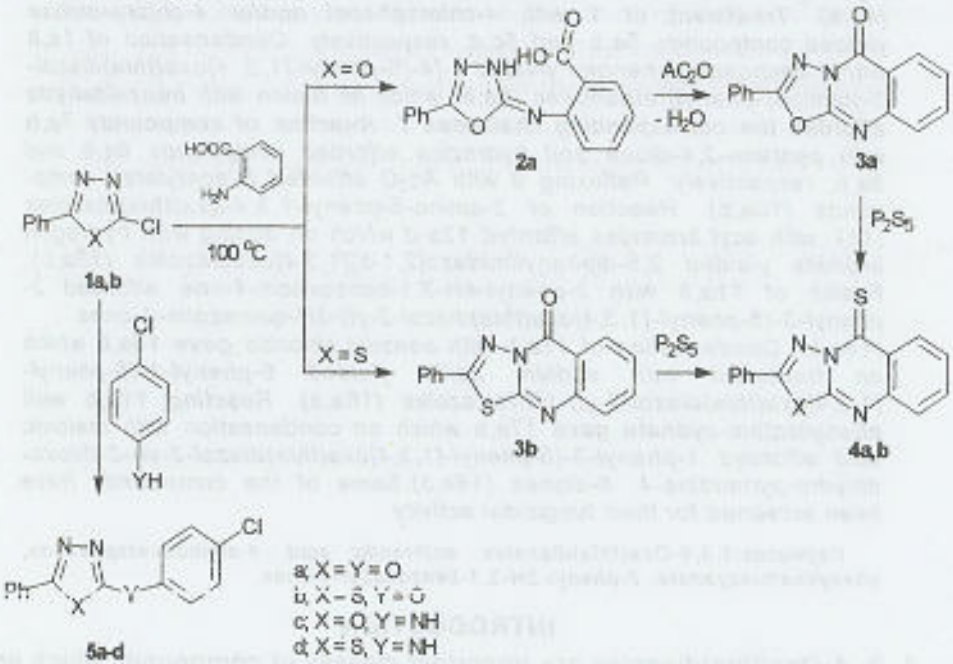
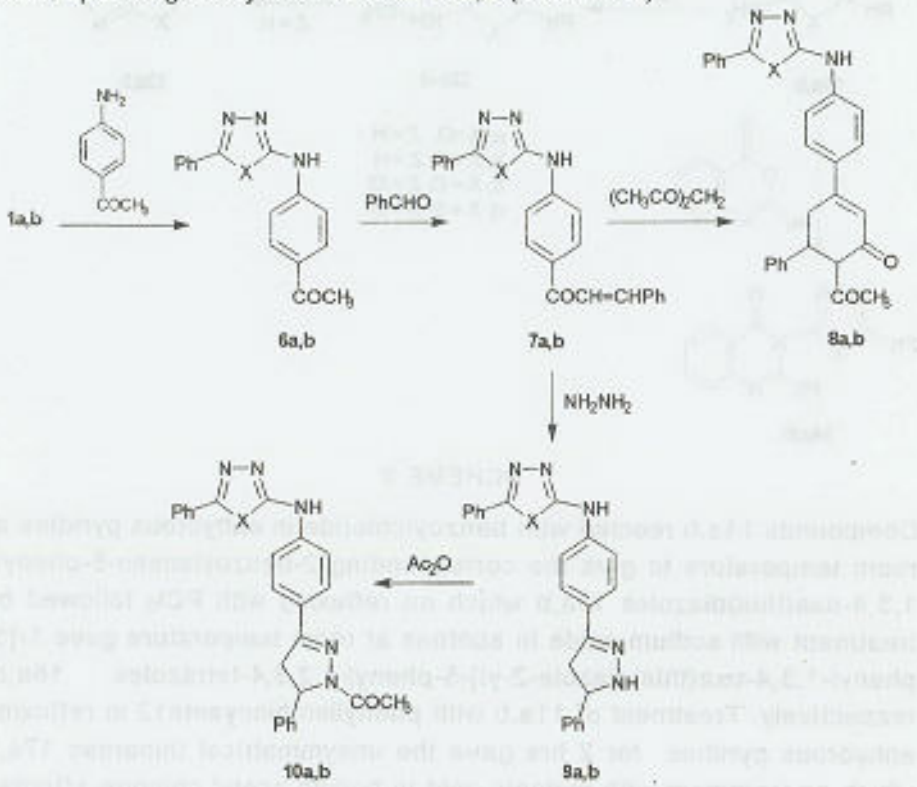
acetic anhydride to yield 2-phenyl-5H-[1,3,4]oxadiazolo[2,3-b]quinazolin-5-one (3a). While, 2-phenyl-5H-[1,3,4]thiadiazolo[2,3-b]quinazolin-5-one (3b) was formed directly by fusion of 1b with anthranilic acid. Compounds 3a,b were converted to their thiono derivatives by treatment with phosphorus pentasulfide in refluxing xylene to give 2 - Phenyl-1-oxa (thia) -3, 3a, 9-triazacyclopenta [b] naphthalene-4-thiones 4a, b, respectively. Compounds 1a, b reacted with 4-chlorophenol and/or 4-chloroaniline by fusion at 140 – 150°C to afford 2-(4-chlorophenoxy-5-phenyl-1,3,4-oxa(thia)diazoles 5a,b and/or 2-(4-chlorophenylamino) -5-phenyl-1, 3,4-oxa (thia) diazoles 5c,d, respectively (Scheme 1).



SCHEME 1

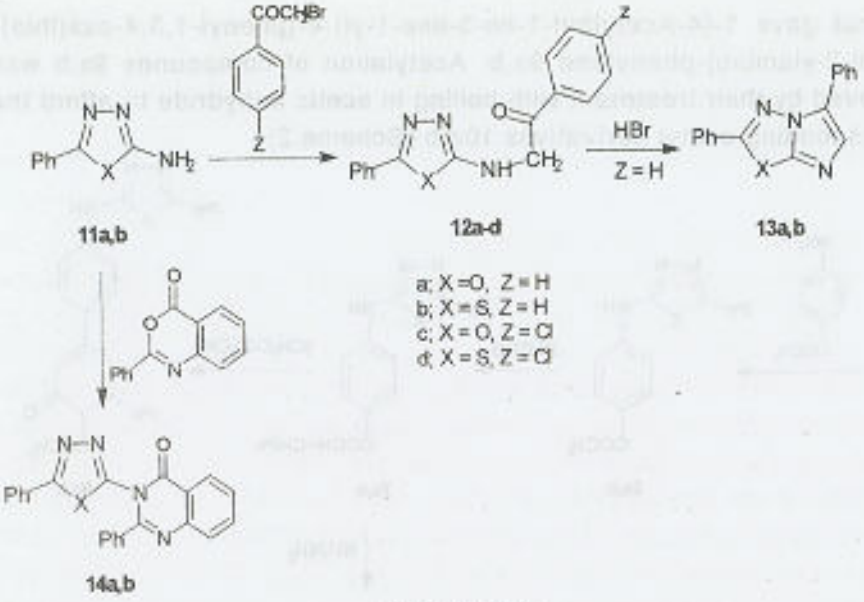
Compounds 1a,b reacted with 4-aminoacetophenone 8-10 by fusion at 150–160°C to give 2-(4-1-[4-(6-phenyl-1,3,4-oxa(thia)diazole-2-yloxy)-phenyl]-ethanone 6a,b, which on fusion with benzaldehyde at 160°C afforded 2-benzylidenyl-1-[4-(6-phenyl-1,3,4-oxa(thia)diazol-2-yloxy)-phenyl]-ethanone 7a,b. Refluxing 7a,b with pentane-2,4-dione in a mixture of sodium ethoxide in absolute ethanol yielded 1-(5-phenyl-4H-pyrazol-3-yl)-4-(5-phenyl-1,3,4-oxa(thia)-2-amino)-phenylene 8a,b. On the other hand, on treating 7a,b with hydrazine hydrate in refluxing

ethanol gave 1-(4-Acetylbut-1-en-3-one-1-yl)-4-(phenyl-1,3,4-oxa(thia)-diazol-2-ylamino)-phenylene 9a,b. Acetylation of compounds 9a,b was achieved by their treatment with boiling in acetic anhydride to afford the corresponding acetyl derivatives 10a,b (Scheme 2).



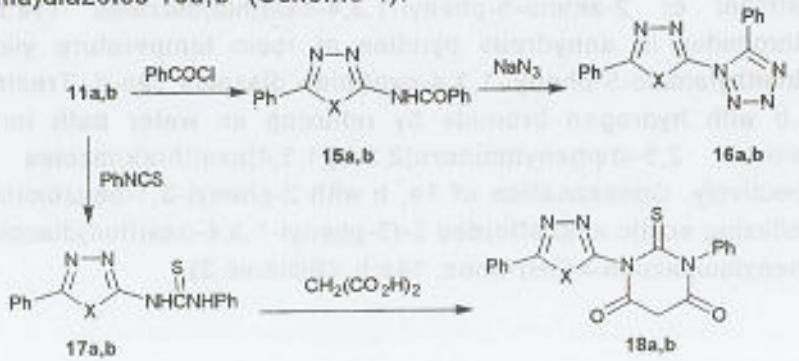
SCHEME 2

Treatment of 2-amino-5-phenyl-1,3,4-oxa(thia)diazoles 11a,b with acylbromides in anhydrous pyridine at room temperature yielded-2-acylmethylamino-5-phenyl-1,3,4-oxa(thia)- diazoles 12a-d. Treatment of 12a,b with hydrogen bromide by refluxing on water bath for 4 hrs furnished 2,5–diphenylimidazo[2,3-b][1,3,4]oxa(thia)diazoles 13a,b respectively. Condensation of 1a, b with 2-phenyl-3,1-benzoxain-4-one in refluxing acetic acid afforded 3-(5-phenyl-1,3,4-oxa(thia)diazole-2-yl)-2-phenylquinazolin-4(3H)-ones, 14a,b, (Scheme 3).



SCHEME 3

Compounds 11a,b reacted with benzoylchloride in anhydrous pyridine at room temperature to give the corresponding 2-benzoylamino-5-phenyl-1,3,4-oxa(thia)diazoles 15a,b which on refluxing with PCl_5 followed by treatment with sodium azide in acetone at room temperature gave 1-[5-phenyl-1,3,4-oxa(thia)diazole-2-yl]-5-phenyl-1,2,3,4-tetrazoles 16a,b, respectively. Treatment of 11a,b with phenylisothiocyante12 in refluxing anhydrous pyridine for 2 hrs gave the unsymmetrical thioureas 17a,b which on treatment with malonic acid in boiling acetyl chloride afforded 2-(3–phenyl-4,6,(3H,5H)dioxo–2H,3H)–thioxopyrimidin-1-yl)-1,3,4-oxa(thia)diazoles 18a,b (Scheme 4).



SCHEME 4

The structure of compounds 2-18 was confirmed by IR, ^{1}H-NMR, ^{13}C-NMR, mass spectroscopy and elemental analyses.

Fungicidal Activity

Compounds 3b, 4a,b, 7a,b, 13a,b, 14a,b 16a,b, and 18a,b were screened for their anti-fungal studies using Sabouroud`s dextrose broth and dextrose agar14 against Aspergillus fami-gatus, Aspergillus niger, Alternaria alternate and Penicillium chrysogenum. Dimethylformamide was used for solubilising the compounds and also for control studies. The concentration for the compounds taken was 1 mg mL^{-1}. Clotrimazole (1 mg mL^{-1}) was used as a standard.

The study revealed that compounds 4b, 14a and 16a were active against Alternaria alternate and compound 18b was active against Aspergillus fumigatus. The rest of compounds did not show any antifungal activity.

EXPERIMENTAL

Melting points were determined on a glass capillary on a Büchi 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 Brüker Ac 250 FT spectrometer at 250 MHz for ^{1}H NMR and at 62.9 MHz For ^{13}C-NMR. CDCl3 and DMSO as solvents using TMS as an internal standard. Mass spectra were recorded using electron ionization (EI) on a Varian Mat 311spectrometer.

2-(5-Phenyl-3H-[1,3,4]oxadiazol-2-ylideneamino)-benzoic acid (2)

A mixture of 1a (0.01 mole, 1.8 g) and anthranilic acid (0.01 mole, 1.4 g) was fused at 100°C in an oil bath for ½ hr. The temperature was raised to 160°C and heating was continued for 3 hrs (tlc). The resulting solid was recrystallized from ethanol to afford 2; yield 47%; m.p. 180°C; IR (KBr) ν = 3386 (NH), 3250 (OH) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ = 7.15-8.45 (m, 9H, H_{arom}) 9.20 (s, 1H, OH), 11.17 (s, 1H, NH) ppm; ^{13}C NMR (DMSO-d6) δ = 116.12, 120.32, 122.37, 125.84, 126.82, 128.33, 131.19 , 131.42, 132.69, 134.57 (Carom), 146.68 (N=C-Ph), 157.10 (N=C-NH), 167.32 (C=O) ppm; Ms, m/z: 280 (M^{+}, 46%), 235 (100%). Anal. Calcd. for $C_{15}H_{10}N_3O_3$: C, 64.1; H, 3.9; N, 14.9. Found: C, 64.9; H, 4.0; N, 14.1.

2-Phenyl-1-oxa-3,3a,9-triazacyclopenta[b]naphthalen-4-one (3a)

Compound 2 (0.01mole, 2.8g) was refluxed in acetic anhydride (10 mL) for 5 hrs (tlc). The solvent was evaporated till dryness under reduced pressure and the resulting solid was filtered off and

recrystallized from ethanol to give 3a, yield 60%; m.p.165°C.[14]

2-Phenyl-1-thia-3,3a,9-triazacyclopenta[b]naphthalen-4-one (3b)

A mixture of 1b (0.01 mole, 1.96 g) and anthranilic acid (0.01 mole, 1.4 g) was fused in an oil bath for 30 min. at 100°C, then temperature was raised to 160°C and heating was continued for 3 hrs (tlc). The resulting solid was recrystalized from ethanol to give 3b; yield 55%; m.p. 235°C.[14]

2-Phenyl-1-oxa(thia)-3,3a,9-triazacyclopenta[b]naphthalene-4-thiones (4a,b)

Compound 3a,b (0.01 mole) and phosphorus pentasulfide (0.01 mole, 2.2 g) was refluxed in anhydrous xylene (10 mL) for 10 hrs (tlc). The solvent was evaporated till dryness under reduced pressure. The residual solid was recrystallized from ethanol to yield 4a,b.

4a. Yield 55%; m.p. 203°C; IR (KBr) ν = 1613 (C=N), 1164 (C=S) cm-1; ^{1}H NMR (DMSO-d6) δ = 7.48-8.45 (m, 9H, Harom) ppm. Anal. Calcd. for $C_{15}H_9N_3OS$: C, 64.5; H, 3.2; N, 15.1; S, 11.5. Found: C, 64.5; H, 3.4; N, 15.3; S, 11.9.

4b. Yield 60%; m.p. 250°C; IR (KBr) ν = 1596 (C=N), 1174 (C=S) cm-1; ^{1}H NMR (DMSO-d6) δ = 7.46-8.23 (m, 9H, Harom); Ms, m/z: 295 (M+, 100%). Anal. Calcd. for $C_{15}H_9N_3S_2$: C, 61.0; H, 3.1; N, 14.2; S, 21.7. Found: C, 61.1; H, 3.0; N, 14.3; S, 21.8.

General procedure for synthesis of (5a-d)

A mixture of 1a,b (0.01 mole) and 4-chlorophenol (0.01 mole, 1.2 g) and/or 4-chloroaniline (0.01 mole, 1.3 g) was fused at 100 °C in an oil bath for 30 min. The temperature was raised to 160 °C and heating was continued for additional 3 hrs. The solid product that formed was filtered off and recrystallized from ethanol and dried to afford 5a-d.

5a. Yield 60%; m.p. 125 °C; IR (KBr) ν = 1608 (C=N), 1031 (C-O-C) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ = 7.52-8.05 (m, 9H, H_{arom}) ppm; ^{13}C NMR (DMSO-d_6) δ = 116.82, 123.90, 125.11, 127.27, 128.32, 128.97, 129.05, 131, 66 (C_{arom}), 153.70 (Ph-C=N), 156.22 (C-O-Ar) ppm. Anal. Calcd for $C_{14}H_9ClN_2O_2$: C, 61.7; H, 3.3; N, 10.3. Found: C, 61.6; H, 3.5; N, 10.4.

5b. Yield 50%; m.p. 160°C; IR (KBr) ν = 1634 (C=N), (C-S-C) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ = 7.53-8.21 (m, 9H, H_{arom}); ^{13}C NMR (DMSO-d_6) δ = 116.62, 126.40, 127.21, 128.82, 129.11, 129.32, 129.38, 131.24, 132.15 ppm (C_{arom}), 153.22 (Ph-C=N) 166.22 (C-O-Ar) ppm; Ms, m/z: 288 (M$^+$, 7%), 103 (100%). Anal. Calcd. for $C_{14}H_9ClN_2OS$: C, 58.2; H, 3.1; N, 9.7. Found: C, 57.3; H, 4.2; N, 10.4.

5c.Yield 65%; m.p. 223°C; IR (KBr) v = 3579 (NH), 1634 (C=N) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 7.35-8.22 (m, 9H, H_{arom}) δ = 10.30 (s, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6) δ = 119.99, 125.36, 127.45, 128.33, 128.49, 131.64, 132.46, 138.62 (C_{arom}) 155.44, (Ph-C=N), 166.44 (C-NH) ppm; Ms, m/z = 271 (M^+, 24%), 105 (100%). Anal. Calcd. for $C_{14}H_{10}ClN_3O$: C, 58.2; H, 3.8; N, 14.6. Found: C, 59.4; H, 4.6; N, 14.7.

5d. Yield 70%; m.p. 220°C; IR (KBr) v = 3436 (NH),1619 (C=N) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 7.42-8.05 (m, 9H, H_{arom}), 10.88 (bs, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6) δ = 118.98, 125.43, 126.72, 128.81, 129.I 4, 130.17, 139.36 (C_{arom}), 157.93 (C-Ph), 163.68 (C-NH) ppm; .Ms, m/z: 287 (M^+, 100%). Anal. Calcd. for $C_{14}H_{10}ClN_3S$: C, 61.1; H, 3.8; N, 9.3. Found: C, 61.5; H, 4.5; N, 9.2.

1-[4-(5-Phenyl-[1,3,4]oxa(thio)diazol-2-ylamino)-phenyl]-ethanones (6a,b)

A mixture of 1a,b (0.01 mole) and 4-aminoacetophenone (0.01 mole,1.2 g) was fused at 100°C in an oil bath for 30 min. The temperature was raised to 150°C and heating was continued for 3 hrs. The resulting solid was filtered off, recrystallized from acetic acid and dried to yield 6a,b.

6a: yield, 70%, m.p.117 °C.[8-10]

6b. Yield 70%; m.p. 133°C; IR (KBr) v = 3751 (NH), 1668 (C= O) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 2.51 (s, 3H, CH_3), 7.42-8.10 (m, 9H, H_{arom}), 10.98 (s, 1H, NH) ppm; ^{13}C NMR (DMSO-d6) δ = 26.17 (CH3), 116.53, 117.8, 126.64, 127.64, 129.11, 129.77, I29.96, 130.28 (C_{arom}), 144.34 (N=C-Ph), 163.18 (N=C-NH) , 195.96 (C=O) ppm; Ms, m/z = 295 (M^+, 100%). Anal. Calcd. for $C_{16}H_{13}N_3OS$: C, 63.6; H, 4.6; N, 14.8, S, 11.3. Found: C, 62.7: H, 4.5; N, 13.9, S, 11.1.

3-Phenyl-1-[4-(5-phenyl-[1,3,4]oxa(thia)diazol-2-ylamino)-phenyl]-propenones (7a,b)

A mixture of 6a,b (0.01 mole) and benzaldehyde (0.01 mole, 1.06 g) was fused at 140°C in an oil bath for 5 hrs (tlc). The resulting solid was recrystallized from ethanol to afford 7a,b.

7a: yield, 55%, m.p.115°C[8-10]

7b. Yield 63%; m.p. 252°C; IR (KBr) v = 3637 (NH), 3027 (CH) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 7.11-8.24 (m, 16H, H_{arom} and 2CH), 11.00 (bs. 1H, NH) ppm; Ms, m/z = 383 (M^+, 37%), 118 (100%). Anal. Calcd. for $C_{23}H_{17}N_3OS$: C, 72.1; H, 4.5; N, 10.9; S, 8.4. Found: C, 72.0; H, 4.6; N, 10.8; S, 9.4.

6-Acetyl-5-phenyl-3-[4-(5-phenyl-[1,3,4]oxa(thia)diazol-2-ylamino)-phenyl]-cyclohex-2-enones (8a,b)

A mixture of 7a,b (0.01 mole) and pentane-2,4-dione (0.01 mole, 1 g) was refluxed in sodium ethoxide (0.01mole) in absolute ethanol (20 mL) for 6 hrs. The reaction mixture was poured on ice/ cold water, the resulting solid was filtered off and recrystallized from ethanol to yield 8a,b.

8a: yield, 65%, m.p. 160°C.[8-10]

8b. Yield 65%; m.p. 230°C; IR (KBr) ν = 3434 (NH), 3051 (CH) cm^{-1}; ^1H NMR (DMSO-d6) δ = 1.32 (s, 3H, CH_3), 2.56 (m, 2H, CH_2), 4.2 (s, 1H, CH), 4.6 (m, 1H,CH), 7.4-8.2 (m, 18H, H_{arom}), 10.6 (s, 1H, NH); Ms, m/z = 465 (M^+, 94%), 383 (100%). Anal. Calcd. for $C_{28}H_{23}N_3O_2S$: C, 72.2; H, 5.0; N, 9.0; S, 6.9. Found: C, 72.3; H, 5.1; N, 8.5; S, 6.8.

[4-(5-Phenyl-4,5-dihydro-1H-pyrazol-3-yl)-phenyl]-(5-phenyl-[1,3,4]oxa(thia)- diazol-2-yl)-amines (9a,b)

A mixture of 7a,b (0.01 mole) and hydrazine hydrate (0.01 mole, 0.59 g) was refluxed in absolute ethanol (20 mL) in the presence of triethylamine (1 mL) for 6 hrs. The reaction mixture was cooled, the resulting solid was filtered off and recrystallized from ethanol to yield 9a,b.

9a: yield 70%, m.p.137°C[8-10]

9b:Yield 67%; m.p. 220°C; IR (KBr) ν = 3414 (NH),2964 (CH) cm^{-1};^1H NMR (DMSO-d_6) δ = 1.9 (d, 2H, CH2), 2.5 (t, 1H, CH), 7.0-7.6 ppm (m, I5H, H_{arom}), 8.4 (s, 1H, NH),12.2 (s, 1H, NH) ppm. Anal. Calcd. for $C_{23}H_{19}N_5S$: C, 69.5; H, 4.8; N, 17.7; S, 8.1. Found: C, 69.0; H, 4.6; N, 17.8; S, 8.0.

1-{5-Phenyl-3-[4-(5-phenyl-[1,3,4]oxadiazol-2-ylamino)-phenyl]-4,5-dihydro-pyrazol-1-yl}-ethanones (10a,b)

Compounds 9a,b (0.01 mole) were refluxed in acetic anhydride (10 mL) for 6 hrs (tlc). The reaction mixture was cooled and poured onto cold water (50mL) .The resulting solid was filtered off and recrystallized from ethanol to give 10a,b.

10a. Yield 45%; m. p. 146°C; IR (KBr) ν = 3441 (NH), 1772 (C=O) cm^{-1}; ^1H NMR (DMSO-d6) δ = 2.1 (s , 3H, CH_3), 2.5 (s, 2H, CH_2), 3.8 (s,1H, CH), 7.5-8.0 (m, 14H, H_{arom}) ppm. Anal. Calcd. for $C_{25}H_{21}N_5O_2$: C, 70.9; H, 5.0; N, 16.5. Found: C, 71.0; H, 5.0; N, 16.5.

10b. Yield 47%; m. p. 130°C; IR (KBr) ν = 3429 (NH) 1776 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 1.8 (s, 3H, CH3), 2.5 (s, 2H, CH_2), 3.5 (s, 1H, CH), 7.5-8.0 (m, 14H, H_{arom}), 8.3 (s, 1H, NH) ppm. Anal. Calcd. for

$C_{25}H_{21}N_5OS$: C, 68.3; H, 4.8; N, 15.9; S, 7.3. Found: C, 68.5; H, 4.7; N, 15.9; S, 7.2.

General procedure for synthesis of compounds (12a-d)

2-Amino-5-phenyl-1,3,4-oxa(thia)diazoles 11a,b (0.01 mole) and phenacyl bromide. (0.01 mole, 2.0 g) and/or 4-chlorophenacyl bromide (0.01 mole, 2.3 g) was stirred at r.t. in anhydrous pyridine (5 mL) for 30 min (tlc). The reaction mixture was poured onto ice/cold water. The resulting solid was filtered off and recrystallized from ethanol to yield 12a-d.

12a: yield, 65%, m.p.109°C.[11]

12b. Yield 67%; m.p. 174°C; IR v = 3249 (NH), 1659 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 4.9 (s, 2H, CH_2), 7.0-8.5 (m, 9H, H_{arom}), 14.3 (s, 1H, NH) ppm; ^{13}C-NMR (DMSO-d_6) δ = 23.66 (CH_2), 125.66, 127.00, 128.49, 129.95, 131.1, 132.44, 134.25, 138.56 ppm (C_{arom}), 157.7 (C-Ph), 167.0 (C-NH); 193.0 (C=O) ppm. Anal. Calcd. for $C_{16}H_{13}N_3OS$: C, 65.1; H, 4.4; N, 14.2; S, 10.9. Found: C, 65.4; H, 4.6; N, 14.3; S, 11.0.

12c. Yield 80%; m. p. 103°C; IR (KBr) v = 3275 (NH), 1679 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 4.9 (s, 2H,CH_2), 7.0-8.5 (m, 9H, H_{arom}), 14.5 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ = 40.01 (CH_2), 125.9, 128.8, 130.3, 134.3 (C_{arom}), 138.9 (C-Ph), 155.7 (C-NH), 192.9 (C=O); Ms, m/z = 329 (M^+, 20%), 139 (100%). Anal. Calcd. for $C_{16}H_{12}ClN_3O_2$: C, 64.1; H, 4.0; Found: C, 64.5; H, 4.5.

12d. Yield 83%; m.p. 115°C; IR (KBr) v = 3130 (NH), 1682 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 4.9 (s, 2H, CH_2), 7.0-8.5 (m, 9H, H_{arom} protons), 13.9 (S. 1H, NH). Anal. Calcd. for $C_{16}H_{12}ClN_3OS$: C, 58.3; H, 3.7; N, 12.7; S, 9.7. Found: C, 58.4; H, 3.8; N, 12.2; S, 9.4.

2,5-Diphenyl-imidazo[2,1-b][1,3,4]oxadiazoles (13a,b)

A mixture of 12c,d (0.01 mole) and hydrogen bromide (5 mL) was refluxed for 4 hrs(tlc). The reaction mixture was cooled and the resulting solid was filtered off and recrystallized from ethanol to afford 13a,b.

13a. Yield 61%; m.p. 103°C; IR (KBr) v = 1679 (C=N), 1469 (C=C) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 7.5-8.0 (m, 10H, H_{arom}) ppm. Anal. Calcd. for $C_{16}H_{10}N_3O$: C, 73.8; H, 3.8; N, 16.1. Found: C, 73.9; H, 3.9; N, 16.2.

13b. Yield 64%; m.p. 115°C; IR (KBr) v = 1618 (C=N), 1485 (C=C) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 7.5-8.0 (m, 10H, H_{arom}) ppm. Anal. Calcd. for $C_{16}H_{10}N_3S$: C, 69.5; H, 3.6; N, 15.2; S, 11.6. Found: C, 69.8; H, 3.5; N, 15.3; S, 11.5.

2-Phenyl-3-(5-phenyl-[1,3,4]oxa(thia)diazol-2-yl)-3H-quinazolin-4-ones (14a,b)

A mixture of 11a,b (0.01 mole), 2-phenyl-4H-3,1-benzoxazin-4-one. (0.01 mole, 2.2 g) and acetic acid (10 mL) was refluxed for 5 hrs (tlc). The resulting solid was filtered off and recrystallized from acetic acid to afford 14a,b.

14a. Yield 52%; m.p. 100°C; IR (KBr) ν = 1689 (C=O), 1643 (C=N) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 7.0-8.0 (m, 14H, H_{arom}) ppm. Anal. Calcd. for $C_{22}H_{14}N_4O_2$: C, 72.1; H, 3.9; N, 15.3. Found: C, 72.2; H, 4.0; N, 14.7.

14b. Yield 59%; m.p. 220°C; IR (KBr) ν = 1685 (C=O), 1597 (C=N) cm^{-1}; ^1H NMR (DMSO-d6) δ = 7.0-8.0 (m, 14H , H_{arom}). Anal. Calcd. for $C_{22}H_{14}N_4OS$: C, 69.1; H, 3.7; N, 14.7. Found: C, 69.0; H, 3.8; N, 14.5.

N-(5-Phenyl-[1,3,4]oxa(thia)diazol-2-yl)-benzamides (15a,b)

A mixture of 11a,b (0.01 mole) and benzoyl chloride. (0.01 mole, 1.5 g) was stirred at r.t. in anhydrous pyridine (5 mL) for 2 hrs (tlc). The reaction mixture was poured on ice/cold water (20 mL). The resulting solid was filtered off and recrystallized from ethanol to give 15a,b.

15a: yield, 65%, m.p.137°C[12].

15b::yield ,70%, m.p.210°C[12] .

5-Phenyl-1-(5-phenyl-[1,3,4]oxa(thia)diazol-2-yl)-1H-tetrazoles (16a,b)

A mixture of 15a,b (0.01 mole) and phosphorus oxychloride (5 mL) was refluxed for 1 hr at 150°C (tlc). The excess of $POCl_3$ was evaporated till dryness under reduced pressure and the resulting product was stirred with sodium azide (0.01 mole, 0.65 g) in acetone (10 mL) at r.t. for 2 hrs. The resulting solid was recrystallized from ethanol to give 16a,b.

16a. Yield 53%; m.p. 95°C; IR (KBr) ν = 1619 (C=N), 1025 (C-O-C) cm^{-1}; ^1H NMR (DMSO-d6) δ = 7.0-8.5 (m, 10H, Harom) ppm. Anal. Calcd. for C15H10N6O: C, 62.1; H, 3.5; N, 29.0. Found: C, 62.6; H, 3.5; N, 28.9.

16b. Yield 50%; m.p. 162°C; IR (KBr) ν = 1619 (C=N),1025 (C-O-C) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 7.5-8.0 (m, 10H, H_{arom}) ppm. Anal. Calcd. for $C_{15}H_{10}N_8S$: C, 58.8; H, 3.3; N, 27.4; S, 10.5. Found: C, 58.6; H, 3.6; N, 27.5; S, 10.6.

1-Phenyl-3-(5-phenyl-[1,3,4]oxa(thia)diazol-2-yl)-thioureas (17a,b)

A mixture of 11a,b (0.01 mole), phenylisothiocyanate (0.01 mole, 1.35 g) and anhydrous pyridine (5 mL) was refluxed for 2 hrs. The

reaction mixture was cooled and poured onto ice/cold water. The resulting solid was filtered off and recrystallized from ethanol to give 17a,b.

17a. Yield, 80%, m.p.109°C13.

17b. Yield 74%; m.p. 180°C; IR (KBr) v = 1685 (C=N), 1369 (C=S) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 7.5-8.0 (m, 10 H, H_{arom}), 9.9 (s, 1H, NH), 10.3 (s, 1H, NH) ppm; ^{13}C-NMR (DMSO-d_6) δ 125.8-129.2 (Carom), 132.0 (C-NH), 10.3 (C-Ph), 177.4 (C=S). Anal. Calcd. for C15H12N4S: C, 57.7; H, 3.9; N, 17.9; S, 10.3. Found: C, 57.8; H, 3.9; N, 18.2, S, 10.4.

1-Phenyl-3-(5-phenyl-[1,3,4]oxa(thia)diazol-2-yl)-2-thioxo-dihydro-pyrimidine-4,6-diones (18a,b)

A mixture of 17a,b (0.01 mole), malonic acid (0.01 mole, 1.04 g), and acetyl chloride (5 mL) was refluxed for 1 hr (tlc). On cooling, the resulting solid was filtered off and recrystallized from methanol to yield 18a,b.

18a. Yield 57% (MeOH); m.p. 222°C; IR (KBr) v = 1772 (C=O), 1332 (C=S) cm^{-1}; ^1H NMR (DMSO-d6) δ = 3.4 (s, 2H, CH_2), 7.5-8.0 (m, 10H, Harom) ppm. Anal. Calcd. for $C_{16}H_{12}N_4O_3S$: C, 59.3; H, 4.5; S, 9.3. Found: C, 59.6; H, 4.6; S, 9.2.

18b. Yield 61% (MeOH); m.p. 210°C; IR (KBr) v = 1759 (C=O), 1359 (C=S) cm^{-1}; ^1H NMR (DMSO-d_6) δ = 3.5 (s, 2H, CH_2), 7.05-8.0 (m, 10H, H_{arom}). Anal. Calcd. for $C_{16}H_{16}N_4O_2S_2$: C, 56.8; H, 3.2; N, 14.7; S, 16.9. Found: C, 55.4; H, 3.7; N, 14.8; S, 17.0.

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دراسات على بعض مشتقات ٤،٣،١ – أوكسا (ثيا) ديازولات

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شركة كفر الزيات للكيماويات والمبيدات الحشريه – كفر الزيات – ج.م.ع

عند معالجة ٢- كلورو-٥- فينيل ٤،٣،١- أوكسا (ثيا) ديازولات (١) مع حمض الأنثراليك يعطي (٢) الذى يمكن تحويله إلى المركب الحلقي (٣) بمعالجته بأندريد حمض الخليك. كبرتة المركب (٣) يعطى (٤) . عند تكاثف المركب (١) مع ٤- أمينو أسيتو الفينون يعطي المركب (٥) والذى بصهره مع البنزالدهيد يعطي الشالكون (٦) والذى بتفاعله مع بعض الكواشف يعطى المركبات ٨،٧ وبمعالجة الأخير باندريد حمض الخليك يعطي (٩). عند تفاعل (٨) مع بعض المشتقات الهالوجنية يعطي (١١) الذى بتفاعلة مع أستيل البروميد يعطي (١٢) والذى بغليانه مع بروميد الهيدروجين يعطي (١٣). تفاعل المركب (١١) مع أزيد الصوديوم وحمض المالونيك يعطي ١٦،١٥ . بعض النواتج تم إختبارها بيولوجيا ضد أنواع البكتيريا ووجد لها فاعلية مناسبه.