Synthesis and Evaluation of Anti-Microbial Activity of 2-(4-methylphenyl)-3-(5,5,7-trimethyl-4,5,6,7-tetrahydro-1,3-benzoxazol-2-yl)-1,3-oxazolan-4-one.

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Abstract: A new series of novel 2-(4-methylphenyl)-3-(5,5,7-trimethyl-4,5,6,7-tetrahydro-1,3-benzoxazol-2-yl)-1,3-oxazolan-4-one **9(a-j)** in good to excellent yield by the reaction of 4-amino-5-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-4*H*-1,2,4-triazol- 3-ylhydrosulfide with a variety of Aromatic aldehydes. The compounds of all the novel new compounds were confirmed by ^{1}H, IR,^{13}C-NMR, MS spectral and elemental data. The compounds **9(a-j)** were evaluated for their antibacterial activity against four human pathogenic bacteria *viz.Escherichiacoli, Klebseilla pneumoniae, Shigelladysentriae and shigellaflexnei.*Amongst all of them,compounds containing (4-methylphenyl) moiety **9b,**(4-methoxyphenyl) moiety **9c,**(4-chlorophenyl) moiety **9d,**(4-dichlorophenyl) moiety **9f,**showed efficient antibacterial activity, almost equal/more than the activity of the standard drug Streptomycin and anti fungal activity of all of them, compounds also evaluated anti fungal studies against *Candida albicans*, *Aspergillus fumigatus* and *Aspergillus niger*,*Rhizopus oryze*,Fungis compounds containing (4-methylphenyl) moiety **9b,** 4-chlorophenyl) moiety **9d** and [(2-thienyl) methylidene] moiety exhibit more potent activity then standared drug amphoterecin-I. Most of the compounds are novel compounds showed good activity against test bacteria and fungi.

Keywords: Synthesis,4-amino-5-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-4*H*-1,2,4-triazol- 3-ylhydrosulfide,6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4] triazolo[3,4-b][1,3,4]oxadiazine, Microbial activity.

1.Introduction

Heterocyclic rings bearing oxygen, Sulphur and thiadiazole moieties constitute the core structure of a number of biologically interesting compounds. The thiazole nucleus appears frequently in the structure of various natural products and biologically active compounds, notably thiamine, penicillin, antibiotics such as anticancer[1], antitumor[2], analgesic and hypothermic[3], local and spinal anesthetic[4], CNS stimulant[5], hypnotic[6], anti-HIV[7] and nematicidal[8],micrococcin[9], troglitazone[10] and many metabolic products of fungi and primitive marine animals, including 2-(aminoalkyl)oxazole-4-carboxylic acids[11]. Numerous thiazolidinone derivatives have shown significant pharmacological and biological activities[12] like sedative[13], anti-inflammatory[14], antibacterial[15], antifungal[16], anti tubercular[17].

Many biologically active products having thiazolidinones are used in medicine for the treatment of various diseases, *e.g.* Triglitazone and Rosiglitazone used as insulin sensitizing drugs for the treatment of type-2 diabetes. 2-Imino-4-oxazolidinones and proved to have interesting anti-inflammatory activity, anti-bacterial and anti-fungal activities [18-28].

The present work deals with the synthesis a new series of novel 2-(4-methylphenyl)-3-(5,5,7-trimethyl-4,5,6,7-tetrahydro-1,3-benzoxazol-2-yl)-1,3-oxazolan-4-one 9 (a-j) in good to excellent yield by the reaction of 4-amino-5-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-4*H*-1,2,4-triazol- 3-ylhydrosulfide with a variety of Aromatic aldehydes. The antimicrobial activities of the compounds 9(a-j) also have been investigated.

2. Materials and Instrumentation:

In this experiment all reagents are used analytical reagent grade obtained from Sigma-Aldrich, Merck, SD fine and avira chemicals.With using standard procedures we purified Water,methanol,acetone,ether etc. 6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4] triazolo[3,4-b][1,3,4]oxadiazine complexes ^{1}H NMR and ^{13}C NMR spectra of the

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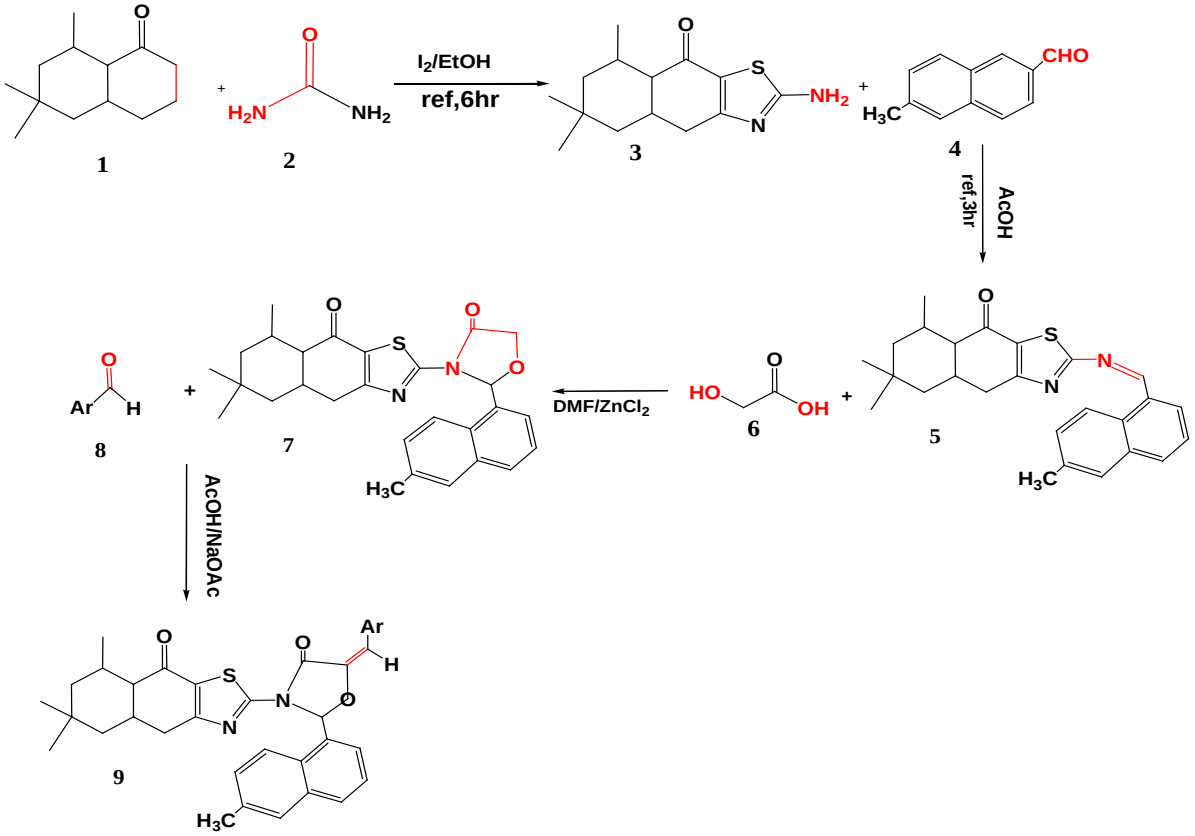
recorded on were recorded on Bruker 400 MHz NMR instrument using tetra methyl silane (TMS) as internal standard compound and coupling constants (*J*) are reported in Hz units.VG AUTOSPEC mass spectrometer. Electronic spectra of all compounds were recorded on Schimadzu UV–Vis 1601 spectrophotometer. ESI mass spectra were Melting points of the ligands and metal complexes decomposition temperature were determined on Polmon instrument (Model No. MP-102). IR spectra of the compounds were recorded using KBr pellets in the range 4000–600 cm^{1} on Perkin-Elmer Infrared model 337. The percentage composition of C, H, N of the compounds were determined by using micro analytical techniques on Perkin Elmer 240C (USA) elemental analyzer. All reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel F254 plates from Merck, and compounds visualized either by exposure to UV light. Chromatographic columns 60–120 mesh silica gel for separations were used. Elemental analyses (C, H, N) determined by means of a Perkin–Elmer 240 C,H,N and O elemental analyzer, were within ± 0.4% of Perkin–Elmer theory.

3. Result and Dissection:

The 2-amino-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one (**3)**, the key intermediate, has been prepared in excellent yield by cyclo condensation of compound **1** with diamino carbonyl (urea) in the presence of iodine in ethanol or propanol at reflux for 5 hrs, in 76% of yield. The condensation of compound **3**[29-30] with p-methylnapthalaldehyde in acetic acid in reflux condition for 4 hrs, furnished the (Z)-6,6,8-trimethyl-2-((6-methylnaphthaleneamino)-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one **5** in 74% yield.

The one-pot synthesis of 6,6,8-trimethyl-2-(2-(6-methylnapthalen-1-yl)-4-oxathiazolidin-3-yl)-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one ***(7)*** was carried out by the cyclization fallowed by condensation reaction between compound **5** and thio aceticacid in the presence of anhydrous $ZnCl_2$ in DMF solvent under reflux for 6 h, with 76% of yield.Further, compounds **7** on condensation with different aromatic aldehydes in the presence of anhydrous sodium acetate (NaOAc) in glacial AcOH at reflux condition $80^{0}C$ temperature for gave (Z)-2-(5-benzylidine-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one 9 (a–j) in 70-84% yields.In this investigation all the synthesized compounds shows good spectral data consistent with their skeleton structures.



9: Ar= (**a**)4-CH_3-C_6H_4; (**b**) 4-Cl-C_6H_4; (**c**) 4-NO_2-C_6H_4; (**d**) 3-NO_2-C_6H_4; (**e**) 3-OH-C_6H_4; (**f**) 2-OH-C_6H_4; (**g**) g=4-dimethylaminophenyl; (**h**) 4-OH-3-OMe-C_6H_4; (**i**) 2-Furyl; (**j**) 2- thienyl.

3.1. Antibacterial Activity

All the newly synthesized compounds **9(a-j)** were collected for their anti-bacterial activity against representative three Gram-negative bacteria *viz. Pseudomonas Aeruginosa*, *Klobsinella Aerogenes* and *Chromobacterium Violaceum* and three Gram-positive bacteria *viz. Bacillus Subtilis,Bacillus Sphaericus* and *Staphylococcus Aureus* by paper disc diffusion method. The mean inhibition zones were measured and compared with the standard drug Streptomycin and results are presented in **Table 1** and Graphical form presented in **Fig.1**

Table 1. Antibacterial Activity of Compounds **9 (a-j)**

Compound	Mean zone inhibition (MZI)[a] in 10 μg/mL					
	B. subtilis	***B. sphaericus***	***S. aureus***	***P. aeruginosa***	***K. aerogenes***	***C. violaceum***
9a	23	16	33	19	25	21
9b	34	26	34	22	28	27
9c	19	21	28	17	19	19
9d	35	28	36	18	29	16
9e	14	19	20	16	26	19
9f	29	17	24	18	26	15
9g	22	19	13	17	20	20
9h	21	25	29	17	28	22
9i	26	24	16	14	29	19
9j	32	26	30	25	27	24
Streptomycin	29	22	32	17	28	22

[a]Values are mean (n = 3).

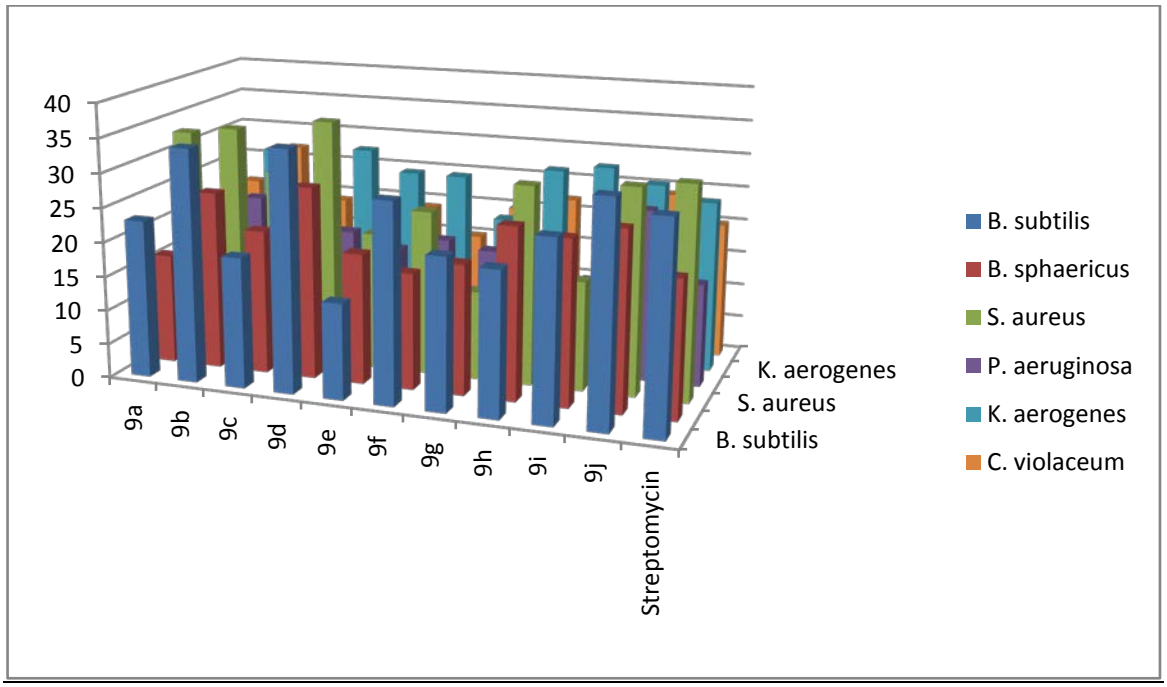


Fig1: Graphical chat of Antibacterial Screening**.**

3.2. Antifungal Activity

All the new compounds 9(a-j) were also evaluate their antifungal activity against *Candida albicans*, *Aspergillus fumigatus* and *Aspergillus niger*,*Rhizopus oryze*(Fungi) in dimethyl sulfoxide (DMSO) by paper disc difusion method. Amphotericin B was used as a standard drug and the mean inhibition zone (MZI) data were measured and compared with controls, the MZI values of the compounds evaluated are given in **Table 2** and graphical form presented in **Fig2.**

Table 2. Antifungal Activity of Compounds **9 (a-j)**

Compound	Mean zone inhibition (MZI)[a] in 100 μg/mL			
	C.albicans	***A.fumigatus***	***A.niger***	***R.oryze***
9a	12	18	12	19
9b	26	22	17	23
9c	16	20	18	18
9d	22	27	20	23
9e	15	20	17	20
9f	13	19	13	19
9g	14	13	16	20
9h	21	22	17	12
9i	18	14	18	20
9j	25	24	22	22
Amphotericin I	22	25	20	22

[a]Values are mean (n = 3).

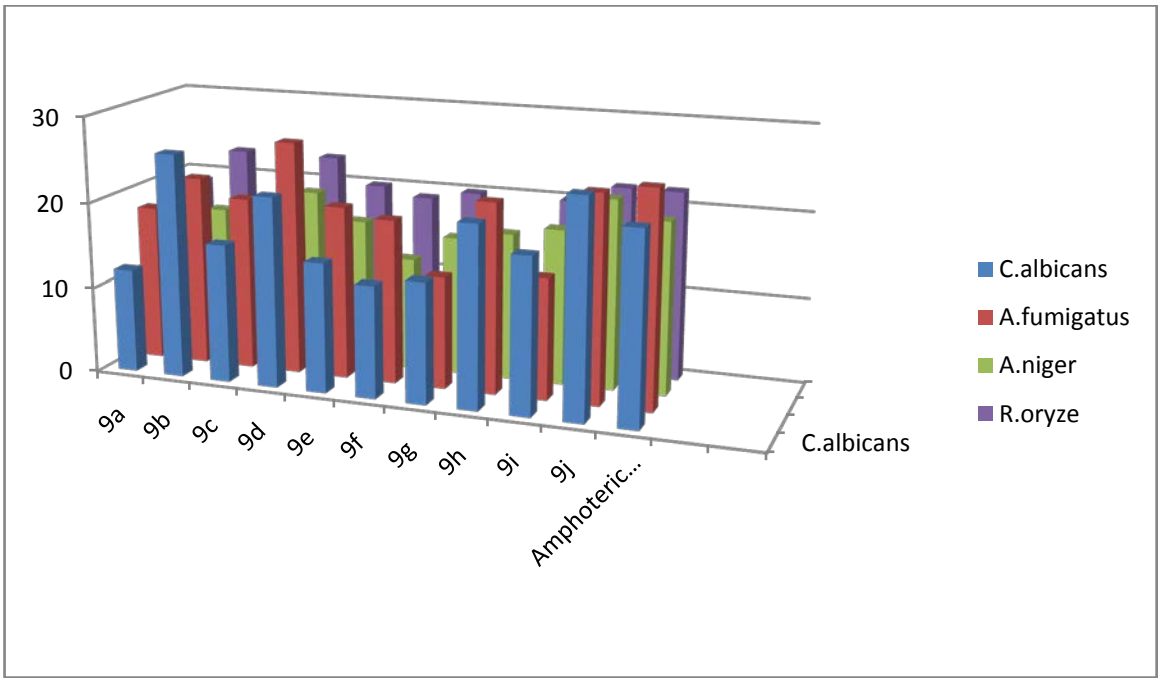


Fig2: Graphical chat of Antifungal Screening**.**

4.Conclusion

A series of (Z)-2-(5-benzylidine-2-(6-methylnaphthalen-1-yl)-4-oxoazolidin-3-yl)-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one **9(a-j)** have been prepared and evaluated for their antibacterial activity against Gram-positive, Gram-negative bacteria and also evaluted anti fungal character againist standard fungis. Most of the compounds showed a more potent antimicrobial activity. Amongst all of them, compounds containing [(4-chlorophenyl)methylidene] moiety **9b**, [(3-nitrophenyl)methylidene] moiety **9d** and [(2-thienyl) methylidene] moiety **9j** showed significant antimicrobial activity, almost equal/more than the activity of the standard drug streptomycin and Amphotericin.

5.Experimental

5.1.Synthesis of 2-amino-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one (**3**)

To a mixture of compound **1** (1.6g, 0.01 mol) in ethanol (20 mL), urea (2.75g, 0.03 mol) and iodine (2.77g, 0.01 mol) were added and heated under reflux for 5-6 hrs. Then the reaction mixture was then cooled to 18 ^{o}C and purified in water (70 mL). The purified mass was basified with liquid ammonia solution and extracted with ethyl aceto acetate (130 mL). The ethyl aceto acetate extract was then concentrated and the crude residue was purified by column chromato graphy using chloroform as eluent and silicagel (70-230 mesh) as solid phase. The pure fraction on concentration gave the pure compound **3** in 66% of yield, m.p. 65-67 ^{o}C.

IR (KBr): ν_{max} 3340-3235, 2857, 2864, 1575, 742 cm^{-1},**^{1}H NMR** ($CDCl_3$, 300 MHz): δ 2.63 (d,2H,CH_2),1.45(S,2H,CH_2),1.46(d,2H,CH_2),1.83(q,1H,CH),2.28(t,1H,CH),2.05(q,1H,CH),1.06(d ,3H,CH_3), 1.11(s,6H,2CH_3),4.0(s,2H,NH_2),**^{13}C NMR** ($CDCl_3$ 75 MHz): δ 21.7, 29.5, 31.3, 36.5, 47.0, 47.7, 128.6, 139.4, 156.5.**MS**: *m/z* 248 (M^+ +1).**Anal. Calcd.** for $C_{14}H_{20}N_2O_2$: C, 76.18; H, 10.21; N, 28.27. Found: C, 68.18; H, 10.21; N, 8.32.

5.2.Synthesis of *(Z)-6,6,8-trimethyl-2-((6-methylnaphthaleneamino)-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one*(**5**)

A combination of compound **3** (2.07 g, 0.02 mol), 4-methylnapthaldehyde (1.3 mL, 0.03 mol) and acetic acid (1 mL) were refluxed in presence non polar solvent like toluene for 4 h.Total this reaction progress checked by TLC by using toluene : butanol (3:2) as an eluent. After completion

of the reaction, solvent was removed by distillation to give solid, which was filtered, and recrystallized from ethyl alcohol to give pure compound **5** in 65% of yield, m.p. 150-152 ^{o}C.
IR (KBr) : ν_{max} 3153, 2952, 1598, 1605 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): δ 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45 (d, 4H, 2CH_2), 1.83 (t, 1H, CH), 2.04(t,1H,CH), 2.46(s,3H,CH_3),2.63(d,2H,CH_2), 7.18(m,*J* = 7.3 Hz, 1H, Ar-H),7.46 (m,*J* = 7.3 Hz, 1H,Ar-H),7.61(m,*J* = 7.3 Hz, 1H, Ar-H),7.92(m, *J* = 7.3 Hz, 2H, Ar-H),7.55(m, 7.3 Hz, 1H, Ar-H),7.88(m, *J* = 7.3 Hz, 1H, Ar-H),8.1(s,1H, CH=N),**^{13}C NMR** (DMSO-d_6 75 MHz): δ 18.9, 24.7, 25.0, 27.8, 27.9, 32.1, 32.5, 44.1, 46.7, 50.5,125.0, 125.4,126.2,127.6,128.1, 130.0, 132.2, 133.7,136.0, 148.9, 150.6,196.9,**MS**: *m/z:* 400 (M^+),**Anal. Calcd.** for $C_{18}H_{22}N_2S$: C, 72.44; H, 7.43; N, 9.39. Found: C, 72.44; H, 7.43; N, 9.32.

5.3.Synthesis of 6,6,8-trimethyl-2-(2-(6-methylnapthalen-1-yl)-4-oxathiazolidin-3-yl)-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one (7).

A combination of compound **5** (3.45g, 0.02 mol), hydraoxyaceticacid (3.2 mL, 0.03 mol) in *N*, *N*-dimethylformamide (30 mL) with a small amount of anhydrous $ZnCl_2$, was refluxed for 5-6 h, Total progress of reaction checked by TLC by eluent toluene: ethyl aceto acetate (3:2). The reaction mixture was cooled -18^{0}C and then poured into crussed ice. It was set-aside at room temperature for 12hrs. The solid was formed and thus separated with filtered, and purified by column chromatography on silica gel with benzene-ethyl aceto acetate as eluent and compound **7** is obtained in 70% yield; m.p. 160-162 ^{o}C.

IR (KBr): ν_{max} 3132, 1708, 1621, 1601, 1461 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): δ 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45(d, 4H, 2CH_2), 1.83 (t, 1H, CH), 2.04(t,1H,CH), 2.46(s,3H,CH_3), 2.63(d, 2H,CH_2), 3.38(s,2H,CH_2),7.18(m,*J* = 7.3 Hz, 1H, Ar-H),7.46 (m,*J* = 7.3 Hz, 1H, Ar-H),7.61(m,*J* = 7.3 Hz, 1H, Ar-H),7.92(m, *J* = 7.3 Hz, 2H, Ar-H),7.55(m, 7.3 Hz, 1H, Ar-H),7.88(m, *J* = 7.3 Hz, 1H, Ar-H). **^{13}C NMR** (DMSO-d_6 75 MHz): δ 18.9, 24.7, 25.0, 27.8, 27.9, 32.1, 32.5, 44.1, 46.7, 50.5,125.0, 125.4,126.2,127.6,128.1, 130.0, 132.2, 133.7,136.0, 148.9, 150.6,162.3,196.9,**MS**: *m/z:* 458 (M^+),**Anal. Calcd.** for $C_{28}H_{30}N_2O_2S$: C, 65.72; H, 6.78; N, 7.64. Found: C, 64.35; H, 7.53; N, 8.80.

5.4.Genral procedure for the synthesis of (Z)-2-(5-benzylidine-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one 9(a–j)

A combination of compound **7** (4.67g, 0.02 mol), corresponding different aromatic and hetero cyclic aldehydes **8** (0.02 mol) and sodium acetate (0.02 mol) in hydroxy acetic acid (10 mL), were refluxed for 5-6 hrs.The reaction mixture was cooled at -20^{0}C.Solids were obtained and separated,filtered and twice washed with water the crude product thus obtained was purified by column chromatography on silica gel with eluent as benzene-ethyl aceto acetate (3:2) to afford pure compounds **9(a-j)** in 70-84% yields. All the products were characterized by IR, ^{1}H, ^{13}C NMR, Mass and elemental analyses.

5.4.1.(Z)-2-(5-(4-methylbenzylidine-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl- 4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one(9a).

IR (KBr): ν_{max} 3102, 2962, 1674, 1603, 1596, 1432 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): δ 1.09(s,3H,CH_3),1.42(s,3H, CH_3),1.11(s,6H,2CH_3),1.45 (d, 4H, 2CH_2), 1.83 (t, 1H, CH), 2.04 (t,1H,CH), 2.48 (s,3H, CH_3), 2.63(d,2H,CH_2),5.3(s,1H,=C-H),5.56(s,1H,N-CH-S),7.18(m,*J* = 7.3 Hz, 1H, Ar-H),7.46 (m,*J* = 7.3 Hz, 1H, Ar-H),7.61(m,*J* = 7.3 Hz, 1H, Ar-H),7.92(m, *J* = 7.3 Hz, 2H, Ar-H),7.55(m, 7.3 Hz, 1H, Ar-H),7.88(m, *J* = 7.3 Hz, 1H, Ar-H),**^{13}C NMR** (DMSO-d_6 75 MHz): δ 18.9, 24.7, 25.0, 27.8, 27.9, 32.1, 32.5, 44.1, 46.7, 50.5, 125.0,125.1, 125.4,125.8, 126.2, 127.6, 128.1, 130.0,131.2, 132.2, 133.7, 134.6,136.0,137.7, 148.9, 150.6, 196.9,**MS**: *m/z:* 549.2 (M^+),**Anal. Calcd.** for $C_{36}H_{36}N_2O_3S$: C, 68.83; H, 6.38; N, 5.80. Found: C, 71.82; H, 6.21; N, 5.84.

5.4.2.(Z)-2-(5-(4-chlorobenzylidine-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl- 4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one (9b)

IR (KBr): ν_{max} 3098, 2973, 1702, 1625, 1462, 690 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): δ 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45 (d, 4H, 2CH_2), 1.83 (t, 1H, CH),2.40(t,1H,CH), 2.60(s,3H,CH_3), 2.63(d,2H,CH_2), 5.3(s,1H,=C-H), 7.18(s,*J* = 7.3 Hz, 1H, Ar-H),7.46 (s,*J* = 7.3

Hz, 1H, Ar-H),7.61(s,*J* = 7.3 Hz, 1H, Ar-H),7.92(d, *J* = 7.3 Hz, 2H, Ar-H),7.55(t, 7.3 Hz, 1H, Ar-H),7.88(d, *J* = 7.3 Hz, 1H, Ar-H),**^{13}C NMR** (DMSO-d_6 75 MHz): *δ* 19.9, 24.7, 25.4, 27.8, 27.9, 32.1, 32.5, 44.1, 46.7, 50.5,122.5,123.4,124,1, 125.0, 125.4, 126.2, 127.6, 128.1, 130.0,131.2, 132.2, 133.7,135.1,136.8, 148.9, 150.6,180.7,192.9,**MS**: *m/z:* 594 (M^+),**Anal. Calcd.** for $C_{35}H_{33}ClN_2O_3S$: C, 64.40; H, 6.60; N, 5.68. Found: C, 64.44; H, 5.78; N, 5.70.

5.4.3.(Z)-2-(5-(4-nitrobenzylidine-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one (9c)

IR (KBr): ν_{max} 3067, 2962, 1699, 1542, 1477, 1371 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): *δ* 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45 (d, 4H, 2CH_2), 1.83 (t, 1H, CH),2.04(t,1H,CH), 2.46(s,3H,CH_3), 2.63(d,2H,CH_2), 5.5(s,1H,=C-H),7.20(m,*J* = 7.3 Hz, 1H, Ar-H),7.46 (m,*J* = 7.3 Hz, 1H, Ar-H),7.61(m,*J* = 7.3 Hz, 1H, Ar-H),7.62(m, *J* = 7.3 Hz, 2H, Ar-H),7.67(m, 7.3 Hz, 1H, Ar-H),7.84(m, *J* = 7.3 Hz, 1H, Ar-H), **^{13}C NMR** (DMSO-d_6 75 MHz): *δ* 18.9, 24.7, 25.0, 27.8, 27.9,32.1,32.5,44.1,46.7,50.5,122.1,123.4,124.6,125.0,125.4,126.2,127.6,128.1,129.8,130.0,132.2, 133.7,136.0,140.2,147.6, 148.9, 150.6, 195.6,196.9,**MS**: *m/z:* 554 (M^+),**Anal. Calcd.** for $C_{35}H_{33}N_3O_5$: C, 63.14; H, 6.68; N, 9.42. Found: C, 63.11; H, 6.42; N, 9.38.

5.4.4.(Z)-2-(5-(3-nitrobenzylidine-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one(9d)

IR (KBr): ν_{max} 3069, 2972, 1694, 1541, 1477, 1374 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): *δ* 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45 (d, 4H, 2CH_2), 1.83 (t, 1H, CH),2.04(t,1H,CH), 2.46(s,3H,CH_3), 2.63(d,2H,CH_2), 5.3(s,1H,=C-H),7.18(s,*J* = 7.3 Hz, 1H, Ar-H),7.46 (m,*J* = 7.3 Hz, 1H, Ar-H),7.61(m,*J* = 7.3 Hz, 1H, Ar-H),7.92(m, *J* = 7.3 Hz, 2H, Ar-H),7.50(m, 7.3 Hz, 1H, Ar-H),7.67(m, *J* = 7.3 Hz, 1H, Ar-H),**^{13}C NMR** (DMSO-d_6 75 MHz): *δ* 18.9, 23.7, 25.0, 27.8, 27.9,32.1,32.5,44.1,46.7,50.5,121.3,122.4,123.5,125.0,125.4,126.2,127.6,128.1,130.0,132.2,133.7, 136.0,140.6,S147,6,148.9,167.6,196.9,**MS**: *m/z:* 554 (M^+),**Anal. Calcd.** for $C_{35}H_{27}N_3O_5$: C, 65.15; H, 5.95; N, 7.81. Found: C, 65.12; H, 6.34; N, 8.36.

5.4.5.(Z)-2-(5-(4-hydroxybenzylidine-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one (9e)

IR (KBr): ν_{max} 3342, 3071, 2975, 1695, 1616, 1478 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): *δ* 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45 (d, 4H, 2CH_2),1.57(s, 3H,CH_3), 1.83 (t, 1H, CH), 2.04(t,1H,CH), 2.46(s,3H,CH_3), 2.63(d,2H,CH_2),5.01(s.1H,b,-OH), 5.3(s,1H,=C-H),7.18(m,*J* = 7.3 Hz, 1H, Ar-H),7.46 (m,*J* = 7.3 Hz, 1H, Ar-H),7.61(m,*J* = 7.3 Hz, 1H, Ar-H),7.92(m, *J* = 7.2 Hz,2H, Ar-H),7.55(m, 7.3 Hz, 1H, Ar-H),7.88(m, *J* = 7.3 Hz, 1H, ArH), **^{13}C NMR** (DMSO-d_6 75 MHz): *δ* 18.9, 23.7, 25.0, 27.8, 27.9, 32.1, 32.5, 44.1, 46.7, 50.5,121.4,122.3,124.6,125.0, 125.4,126.2,127.6,128.1,130.0,132.2,133.7,136.0,140.3,142.5,148.9,150.6,181.6,190.9,**MS**: *m/z:* 578 (M^+),**Anal. Calcd.** for $C_{35}H_{34}N_2O_4S$: C, 66.12; H, 5.84; N, 5.76. Found: C, 67.54; H, 6.66; N, 5.73.

5.4.6. (Z)-2-(5-(2-hydroxybenzylidine-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one (9f)

IR (KBr): ν_{max} 3345, 3077, 2972, 1699, 1612, 1479 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): *δ* 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45(d,4H, 2CH_2),1.83(t,1H,CH),2.04(t,1H,CH), 2.46(s,3H,CH_3), 2.63(d,2H,CH_2),5.01(s,1H,OH),5.3(s,1H,=C-H),7.18(m,*J* = 7.3 Hz, 1H, Ar-H),7.46 (m,*J* = 7.3 Hz, 1H, Ar-H),7.61(m,*J* = 7.3 Hz, 1H, Ar-H),7.92(m, *J* = 7.3 Hz, 2H, Ar-H),7.55(m, 7.3 Hz, 1H, Ar-H),7.88(m, *J* = 7.3 Hz, 1H, Ar-H),**^{13}C NMR** (DMSO-d_6 75 MHz): *δ* 18.9, 24.7, 25.0, 27.8, 27.9, 32.1, 32.5, 44.1, 46.7, 50.5,121.2,122.4,123.6,124.8,125.0, 125.4,126.2,127.6,128.1, 130.0, 132.2, 133.7,136.0, 140.9,148.9, 150.6,196.9,**MS**: *m/z:* 578 (M^+),***Anal*. Calcd.** for $C_{35}H_{34}N_2O_4S$: C, 67.05; H, 5.87; N, 5.72. Found: C, 66.02; H, 5.78; N, 5.64.

5.4.7.(Z)-2-(5-(4-(dimethylamino)benzylidine-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one (9g)

IR (KBr): ν_{max} 3068, 2978, 1698, 1616, 1478 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): *δ* 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45 (d, 4H, 2CH_2), 1.83 (t, 1H, CH),2.04(t,1H,CH), 2.48(s,3H,CH_3), 2.67(d,2H,CH_2),4.32(s,6H,2CH_3),5.5(s,1H,=C-H), 7.20(m,*J* = 7.3 Hz, 1H, Ar-H),7.50 (m,*J* = 7.3 Hz, 1H, Ar-H),7.62(m,*J* = 7.3 Hz, 1H, Ar-H),7.92(m, *J* = 7.3 Hz, 2H, Ar-

H),7.55(m, 7.3 Hz, 1H, Ar-H),7.76(m, *J* = 7.3 Hz, 1H, Ar-H),**^{13}C NMR** (DMSO-d_6 75 MHz): δ 18.9, 24.7, 25.0, 27.8, 27.9, 32.1, 32.5, 44.1, 46.7, 50.5,121.2,122.4,123.7,124.4,125.0, 125.4,126.2,127.6,128.1, 130.0, 132.2, 134.7,136.0, 140.9,148.9, 150.6,181.3,196.9,**MS**: *m/z:* 604 (M^+).**Anal. Calcd.** for $C_{37}H_{38}N_3O_3S$: C, 69.17; H, 7.78; N, 8.54. Found: C, 68.13; H, 7.48; N, 9.41.

5.4.8.(Z)-2-(5-(4-hydroxy-3-mothoxybenzylidine-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one (9h)

IR (KBr): ν_{max} 3340, 3070, 2978, 1698, 1478, 1270 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): δ 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45 (d, 4H, 2CH_2), 1.83 (t, 1H, CH),2.04(t,1H,CH), 2.46(s,3H,CH_3), 2.63(d,2H,CH_2), 4.01(s,1H,-OH),5.3(s,1H,=C-H),7.20(s,*J* = 7.3 Hz, 1H, Ar-H),7.56 (s,*J* = 7.3 Hz, 1H, Ar-H),7.63(s,*J* = 7.3 Hz, 1H, Ar-H),7.89(d, *J* = 7.3 Hz, 2H, Ar-H),7.79(t, 7.3 Hz, 1H, Ar-H),7.98(d, *J* = 7.3 Hz, 1H, Ar-H),**^{13}C NMR** (DMSO-d_6 75 MHz): δ 18.9, 24.7, 25.0, 27.8, 27.9, 32.1, 32.5, 44.1, 46.7, 50.5,121.3,122.4,123.5,124.7,125.0, 125.4,126.2,127.6,128.1, 130.0, 132.2, 133.7,136.0, 140.9,148.9, 150.6,186.5,196.9,**MS**: *m/z:* 606 (M^+),**Anal. Calcd.** for $C_{36}H_{34}N_2O_5S$: C, 67.42; H, 6.25; N, 6.26. Found: C, 67.56; H, 6.73; N, 6.62.

5.4.9. (Z)-2-(5-furyl-2-ylmethylene-2-(6-methylnaphthalen-1-yl)-4-oxothioazolidin-3-yl)-6,6,8-trimethyl-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one(9i)

IR (KBr): ν_{max} 3103, 2872, 1702, 1621, 1490, 1102 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): δ 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45 (d, 4H, 2CH_2), 1.83 (t, 1H, CH),2.04(t,1H,CH), 2.50(s,3H,CH_3), 2.65(d,2H,CH_2), 5.7(s,1H,=C-H),7.20(m,*J* = 7.3 Hz, 1H, Ar-H),7.57 (m,*J* = 7.3 Hz, 1H, Ar-H),7.63(m,*J* = 7.3 Hz, 1H, Ar-H),7.68(m, *J* = 7.3 Hz, 2H, Ar-H),7.62(m, 7.3 Hz, 1H, Ar-H),7.98(m, *J* = 7.3 Hz, 1H, Ar-H),**^{13}C NMR** (DMSO-d_6 75 MHz): δ 18.9, 23.5, 25.0, 27.8, 27.9,32.1,32.5,44.1,46.7,50.5,121.3,122.4,123.7,124.7,125.0,125.4,126.2,127.6,128.1,130.0,132.2, 133.7,136.0,140.9,148.9,150.6,196.9,**MS**: *m/z:* 552 (M^+),**Anal. Calcd.** for $C_{33}H_{32}N_2O_4S$: C, 65.66; H, 4.63; N, 7.12. Found: C, 65.11; H, 6.70; N, 6.24.

5.4.10.(Z)-6,6,8-trimethyl-2-(2-(6-methylnaphthalen-1-yl)-4-oxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-4a,5,6,7,8,8a-hexahydronaphtho[2,3-d]oxazol-9(4H)-one (9j)

IR (KBr): ν_{max} 3154, 2905, 1673, 1678, 1482, 973 cm^{-1},**^{1}H NMR** (DMSO-d_6 300 MHz): δ 1.06(s,3H,CH_3),1.11(s,6H,2CH_3),1.45 (d, 4H, 2CH_2), 1.83 (t, 1H, CH), 2.04(t,1H,CH), 2.46(s,3H,CH_3), 2.63(d,2H,CH_2), 5.3(s,1H,=C-H),7.18(s,*J* = 7.3 Hz, 1H, Ar-H),7.46 (s,*J* = 7.3 Hz, 1H, Ar-H),7.61(s,*J* = 7.3 Hz, 1H, Ar-H),7.92(d, *J* = 7.3 Hz, 2H, Ar-H),7.55(t, 7.3 Hz, 1H, Ar-H),7.88(d, *J* = 7.3 Hz, 1H, Ar-H),**^{13}C NMR** (DMSO-d_6 75 MHz): δ 18.9, 24.7, 25.0, 27.8, 27.9, 32.1, 32.5, 44.1, 46.7, 50.5,121.3,122.4,123.6,124.7,125.0, 125.4,126.2,127.6,128.1, 130.0, 132.2, 133.7,136.0, 140.9,148.9, 150.6,181.5,196.9,**MS**: *m/z:* 564 (M^+),**Anal. Calcd.** for $C_{33}H_{32}N_2O_3S_2$: C, 65.54; H, 6.72; N, 8.65. Found: C, 64.50; H, 6.68; N, 5.75.

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