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Synthesis And Antimicrobial Activity Of Schiff Bases Of 1, 3-Oxazines

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Abstract : A new series of Schiff bases of 1, 3-oxazines were synthesized in three steps. In the first step, 4-bromoacetophenone and substituted aromatic aldehyde reacted in the presence of sodium hydroxide to give substituted chalcones (Claisen-Schmidt condensation). In second step, substituted chalcones reacted with urea to produce 4-(4-bromophenyl)-6-(substituted phenyl)-6H-1,3-oxazin-2-amine analogues. In third step, these compounds were reacted with substituted aromatic aldehydes to produce 4-(4-bromophenyl)-6-(substituted phenyl)- 2-{[(1E) (substituted phenyl) methylidenene]}-6H-1,3-oxazin-amine. The newly synthesized compounds were characterized with IR, NMR and screened for their antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli* and antifungal activity against *Candida albicans.* The study revealed that compounds exhibited excellent antibacterial as well as antifungal activity.
Keywords: Schiff bases, 1, 3-oxazines, antimicrobial activity.

INTRODUCTION

Antimicrobial research, too long, the poor relation of life style drug discovery, is once again a topic of heated discussion and cutting edge research. Reports of communally and hospital-acquired infection from multidrug-resistant microbes continue to make the news. The decline of antimicrobial research by many of the big pharmaceutical companies has led to a short fall in new and better agents to fight the present threat of drug resistance (1). The focus of much antimicrobial research has therefore, moved to the identification of novel chemical classes and novel microbial targets. Some heterocyclic compounds, such as 1,3-oxazines have been reported of wide range of biological activity. In light of the growing number of applications in recent years, there has been an enormous increase in the interest among biologists and chemists in their synthesis and bioactivity of 1,3-oxazine derivatives (2).

Nitrogen heterocycles are of special interest because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities. Investigation of the 1,3-oxazine heterocycles has shown that they possess varied biological properties such as antibacterial (3), analgesic (4), antitubercular (5), anticancer (6) and anticoagulant activity (7). Here we report synthesis and preliminary biological evaluation of Schiff bases of 1, 3-oxazines, showing antimicrobial activity.

MATERIALS AND METHODS

GENERAL PROCEDURE FOR SYNTHESIS OF SUBSTITUTED CHALCONES 1a-1f (8)

A solution of 22 gm of sodium hydroxide in 200 ml of water and 100 gm (122.5 ml) of ethanol was placed in 500 ml bolt hand flask provided with a magnetic stirrer (Remi- capacity 1 litre). The flask was immersed in a bath of a crushed ice poured in 52 gm (0.43 mol) of 4-bromoacetophenone then

stirring was started and 46 gm (44 ml,0.43 mol) of pure substituted benzaldehyde was added. The temperature of mix was kept at about 25^0 C and stirred vigorously until the mixture was so thick that stirring is no longer effective (2-3 hr). The stirrer was removed and reaction mixture was left in a refrigerator for overnight. The product was filtered with suction on stirred glass funnel and then washed with cold water until the washing are neutral to litmus then rinsed with 20 ml of ice-cold rectified spirit. The crude chalcone obtained was dried in air. It was recrystallised from rectified spirit.

GENERAL PROCEDURE FOR SYNTHESIS OF SUBSTITUTED 1,3-OXAZINE-2-AMINES 2a-2f (8)

A mixture of chalcone (0.02 mol) and urea (0.02 mol) was dissolved in ethanolic NaOH (10 ml) and stirred for about 2-3 hr with magnetic stirrer. Then 400 ml of cold water was poured into it with continuous stirring for 1 hr. and then kept in refrigerator for 24 hr. Then precipitate obtained was filtered and recrystallized from rectified spirit.

GENERAL PROCEDURE FOR SYNTHESIS OF SCHIFF BASES OF 1,3-OXAZINES 3a-3r (9)

Mixture of substituted aldehydes (0.1 moles) and 4-(4-bromophenyl)-6-(4-substitutedphenyl)-6*H*-1,3-oxazin-2-amine (0.1 moles) in acetonitrile were taken in round bottom flask separately and a few drops of sulphuric acid was added to reaction mixtures. The reaction mixture was refluxed for two hours on a water bath. The clear solution obtained was cooled and poured onto cold water. Pale yellow crystals immediately separated out. The solids separated on filteration were dried and recrystallized from acetic acid.

4-(4-Bromophenyl)-6-(4-chlorophenyl)-N-[(E)-(4-nitrophenyl) methylidene]-6H-1, 3- oxazin-2-amine (3a)

Yield: 71.46%, M.P.: 140-142^{0}C, IR (KBr, cm^{-1}): 3054.69, 944.94 (C-C-H), 1648.84 (C=N), 1563.99, 1342.21 (NO_2), 1224.58 (C-O), 1178.29 (C-N), 815.74 (C-Cl), 694.248 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.887-7.771 (m, 4H, Ar-Br), 7.633-7.533 (m, 4H, Ar-Cl), 7.297-7.245 (m, 4H, Ar-NO_2), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 1.612 (s, 1H, CH).

4-(4-Bromophenyl)-6-(3,4, 5-trimethoxy phenyl) -N-[(E)(4-nitrophenyl)methylidene]-6H-1,3-oxazin-2-amine (3b)

Yield: 68.43%, M.P.: 152-154^{0}C, IR (KBr, cm^{-1}): 3109.73, 934.83 (C-H), 1623.73 (C=N), 1523.25, 1333.33 (NO_2), 1212.55 (C-O), 1182.44 (C-N), 1093.28 (C-O), 667.55 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.965-7.787 (m, 4H, Ar-Br), 7.723-7.633 (m, 2H, Ar-$(OCH_3)_3$, 7.387-7.255 (m, 4H, Ar-NO_2), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 2.525-2.625 (s, 9H, OCH_3), 1.721 (s, 1H, CH).

4-(4-Bromophenyl)-6-(nitrophenyl)-N-[(E)(4-nitrophenyl)methylidene]-6H-1,3-oxazin-2-amine (3c)

Yield: 62.71%, M.P.: 140-142^{0}C, IR (KBr, cm^{-1}): 3052, 945 (CCH), 1646 (C=N), 1564, 1377 (NO_2), 1226, 1173 (C-N), 692 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.899-7.772 (m, 4H, Ar-Br), 7.387-6.99 (m, 8H, Ar-NO_2), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 1.612 (s, 1H, CH).

4-(4-Bromophenyl)-6-(N,N-dimethylaminophenyl)-N-[(E)(4-nitrophenyl)methylidene]-6H-1,3-oxazin-2-amine (3d)

Yield: 65.14%, M.P.: 172-174^{0}C, IR (KBr, cm^{-1}): 2918, 1440 (-CH_3), 1648 (C=N), 1564, 1343 (NO_2), 1223 (C-O), 1173 (C-N), 690 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.903-7.678 (m, 4H, Ar-Br), 7.564-7.454 (m, 4H, Ar-NO_2), 7.343-7.266 (m, 4H, Ar-N$(CH_3)_2$), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 1.569 (s, 6H, N-CH_3), 1.273 (s, 1H, CH).

4-(4-Bromophenyl)-6-(4-methoxyphenyl)-N-[(E)-(4-nitrophenyl)methylidene]-6H-1,3-oxazin-2-amine (3e)

Yield: 64.44%, M.P.: 130-132^{0}C, IR (KBr, cm^{-1}): 3198.83, 935.83 (C-H), 1694.94 (C=N), 1524.25, 1384.39 (NO_2), 1267.55 (C-O), 1183.42 (C-N), 1093.28 (C-O), 669.53 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.961-7.737 (m, 4H, Ar-Br), 7.713-7.663 (m, 4H, Ar-(OCH_3), 7.357-7.235 (m, 4H, Ar-NO_2), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 2.525-2.625 (s, 3H, OCH_3), 1.718 (s, 1H, CH).

2-[4-(4-Bromophenyl)-2-{[(1E)-(4-nitrophenyl)methylene]amino}-6H-1,3-oxazin-6- yl]phenol (3f)

Yield: 53.76%, M.P.:128-130^{0}C, IR (KBr, cm^{-1}): 3456.84 (OH), 1649.67 (C=N), 1544.74, 1343.83 (NO_2), 1223.78 (C-O), 1163.23(C-N), 638.92 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.983-7.773 (m, 4H, Ar-Br), 7.453-7.221 (m, 4H, Ar-(OH)), 7.357-7.235 (m, 4H, Ar-NO_2), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 4.231-4.442 (s, H, OH), 1.718 (s, 1H, CH).

4-(4-Bromophenyl)-6-(4-chlorophenyl)-N-[(E)-(4-chlorophenyl)-methylidene]-6H-1,3-oxazin-2-amine (3g)

Yield: 69.68%, M.P.:144-146^{0}C, IR (KBr, cm^{-1}): 3154.19, 954.44 (C-C-H), 1628.54 (C=N), 1224.58 (C-O), 1178.29 (C-N), 815.74, 824.34 (C-Cl), 694.24 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.876-7.745 (m, 8H, Ar-Cl), 7.867-7.754 (m, 4H, Ar-Br), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 1.687 (s, 1H, CH).

4-(4-Bromophenyl)-6-(3,4,5-trimethoxyphenyl)-N-[(E)-(4chlorophenyl)methylidene]-6H-1,3-oxazin-2-amine (3h)

Yield: 66.12%, M.P.: 148-150^{0}C, IR (KBr, cm^{-1}): 3154.19, 954.44 (C-C-H), 1628.54 (C=N), 1224.58 (C-O), 1178.29 (C-N), 815.74, 824.34 (C-Cl), 694.24 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.963-7.754 (m, 4H, Ar-Br), 7.871-7.743 (m, 4H, Ar-Cl), 7.723-7.633 (m, 2H, Ar-$(OCH_3)_3$, 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 2.538-2.485 (s, 9H ,OCH_3), 1.731 (s, 1H, CH).

4-(4-Bromophenyl)-N-[(1E)-(4-chlorophenyl) methylidene]-6-(4-nitrophenyl)-6H-1,3-oxazin-2-amine (3i)

Yield: 61.45%, M.P.:140-142^{0}C, IR (KBr, cm^{-1}): 3054.79, 987.14 (C-C-H), 1609.12 (C=N), 1274.09 (C-O), 1148.29 (C-N), 825.33, 846.04 (C-Cl), 664.24 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.887-7.699 (m, 4H, Ar-Cl), 7.876-7.769 (m, 4H, Ar-Br), 7.387-6.99 (m, 4H, Ar-NO_2), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 1.612 (s, 1H, CH).

4-(4-Bromophenyl)-6-(N,N-dimethylamino phenyl)-N-[(E)(4-chlorophenyl) methylidene]-6H-1, 3-oxazin-2-amine (3j)

Yield: 71.27%, M.P.: 170-172^{0}C, IR (KBr, cm^{-1}): 3254.19, 937.17 (C-C-H), 1611.13 (C=N), 1218.90 (C-O), 1128.79 (C-N), 875.04, 835.12 (C-Cl), 667.24 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.932-7.743 (m, 4H, Ar-Br), 7.864-7.754 (m, 4H, Ar-Cl), 7.343-7.266 (m, 4H, Ar-$N(CH_3)_2$), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 1.569 (s, 6H, N-CH_3), 1.189 (s, 1H, CH).

4-(4-Bromophenyl)-N-[(1E)-(4-chlorophenyl) methylidene]-6-(4-methoxyphenyl)-6H-1,3-oxazin-2-amine (3k)

Yield: 68.93%, M.P.: 126-128^{0}C, IR (KBr, cm^{-1}): 3084.89, 945.89 (C-C-H), 1657.97 (C=N), 1234.76 (C-O), 1158.29 (C-N), 834.74, 814.34 (C-Cl), 654.73 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.943-7.777 (m, 4H, Ar-Br), 7.857-7.735 (m, 4H, Ar-Cl), 7.773-7.643 (m, 4H, Ar-(OCH_3), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 2.575-2.653 (s, 3H, OCH_3), 1.518 (s, 1H, CH).

2-[4-(4-Bromophenyl)-2-{[(1E)-(4-chloro phenyl)methylidene]amino}-6H-1,3-oxazin-6-yl]phenol (3l)

Yield: 57.08%, M.P.: 128-130^{0}C, IR (KBr, cm^{-1}): 3194.19, 984.44 (C-C-H), 1638.54 (C=N), 1298.58 (C-O), 1147.29 (C-N), 825.74, 814.34 (C-Cl), 665.63 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.963-7.763 (m, 4H, Ar-Br), 7.857-7.735 (m, 4H, Ar-Cl), 7.431-7.217 (m, 4H, Ar-(OH)), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 4.431-4.2874 (s, H, OH), 1.764 (s, 1H, CH).

4-(4-Bromophenyl)-6-(4-chlorophenyl)-N-[(1E)-(4-methoxyphenyl)methylidene]-6H-1,3-oxazin-2-amine (3m)

Yield: 61.75%, M.P.: 140-142^{0}C, IR (KBr, cm^{-1}): 3054.69, 944.94 (C-C-H), 1648.84 (C=N), 1224.58, 1089.23 (C-O), 1178.29 (C-N), 825.74 (C-Cl), 684.48 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.876-7.745 (m, 4H, Ar-Cl), 7.867-7.754 (m, 4H, Ar-Br), 7.276-7.104 (m, 4H, Ar-OCH_3), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 2.543-2.647 (s, 3H ,OCH_3), 1.689 (s, 1H, CH).

4-(4-Bromophenyl)-6-(3,4,5-trimethoxyphenyl)-N-[(1E)(4-methoxyphenyl) methylidene]-6H-1, 3-oxazin-2-amine (3n)

Yield: 63.56%, M.P.: 150-152^{0}C, IR (KBr, cm^{-1}): 3209.73, 964.83 (C-H), 1633.73 (C=N), 1223.55, 1045 (C-O), 1182.44 (C-N), 697.27 (C-Br). ^{1}H NMR (300 MHz, TMS) δ : 7.965-7.787 (m, 4H, Ar-Br), 7.723-7.633 (m, 2H, Ar-$(OCH_3)_3$, 7.226-7.114 (m, 4H, Ar-OCH_3), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 2.535-2.413 (s, 3H ,OCH_3), 2.525-2.625 (s ,9H, OCH_3), 1.721 (s, 1H, CH).

4-(4-Bromophenyl)-N-[(1E)-(4-methoxy phenyl)methylidene]-6-(4-nitrophenyl)-6H-1,3-oxazin-2-amine (3o)

Yield: 63.86%, M.P.: 142-144^{0}C, IR (KBr, cm^{-1}): 3129.73, 984.83 (C-H), 1623.73 (C=N), 1543.15, 1338.31 (NO_2), 1212.55, 1097.13 (C-O), 1182.44 (C-N), 667.55 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.876-7.769 (m, 4H, Ar-Br), 7.387-6.99 (m, 4H, Ar-NO_2), 7.289-7.107 (m, 4H, Ar-OCH_3), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 2.543-2.453 (s, 3H, OCH_3), 1.612 (s, 1H, CH).

4-(4-Bromophenyl)-6-(N,N-dimethylamino phenyl)-N-[(1E)-(4-methoxyphenyl) methylidene]-6H-1, 3-oxazin-2-amine (3p)

Yield: 67.89%, M.P.: 172-174^{0}C, IR (KBr, cm^{-1}): 3018.41, 1470.57 (-CH_3), 1648.47(C=N), 1213.12,

1045.67 (C-O), 1143.67 (C-N), 693.12 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.903-7.678 (m, 4H, Ar-Br), 7.343-7.266 (m, 4H, Ar-N(CH_3)$_2$), 7.276-7.104 (m, 4H, Ar-OCH_3), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 2.593-2.476 (s, 3H ,OCH_3), 1.548 (s, 6H, N-CH_3), 1.283 (s, 1H, CH).

4-(4-Bromophenyl)-6-(4-methoxyphenyl)-N-[(1E)-(4-methoxyphenyl)methylidene]-6H-1,3-oxazin-2-amine (3q)

Yield: 65.13%, M.P.: 136-138^{0}C, IR (KBr, cm^{-1}): 3109.73, 984.83 (C-H), 1613.73 (C=N), 1233.27, 1041.34 (C-O), 1162.34 (C-N), 687.17 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.943-7.777 (m, 4H, Ar-Br), 7.781-7.693 (m, 4H, Ar-(OCH_3), 7.267-7.109 (m, 4H, Ar-OCH_3), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 2.583-2.478 (s, 3H, OCH_3), 1.514 (s, 1H, CH).

2-[4-(4-Bromophenyl)-2-{[(E)-(4-nitrophenyl) methylidene]amino}-6H-1,3-oxazin-6-yl] phenol (3r)

Yield: 68.93%, M.P.: 126-128^{0}C, IR (KBr, cm^{-1}): 3356.74 (OH), 1637.36 (C=N), 1303.07, 1037.83 (C-O), 1166.13 (C-N), 678.02 (C-Br). ^{1}H NMR (300 MHz, TMS) δ: 7.963-7.763 (m, 4H, Ar-Br), 7.476-7.211 (m, 4H, Ar-(OH), 7.273-7.114 (m, 4H, Ar-OCH_3), 6.3 (d, 1H, fifth CH oxazine), 6.12 (d, 1H, sixth CH oxazine), 4.486-4.2974 (s, H ,OH), 2.574-2.456 (s ,3H ,OCH_3), 1.764 (s, 1H, CH).

ANTIBACTERIAL ACTIVITY

Antibacterial activity of eighteen/title compounds was tested *in vitro* against gram-positive bacteria *Staphylococcus aureus* (NCIM-2079), gram-negative bacteria *Escherichia coli* (NCIM-2109) and fungal strain *Candida albicans* (NCIM-3471) by double dilution method (10), using dimethyl sulfoxide as solvent and ofloxacin and amphotericin-B as standard drugs. Minimum inhibitory concentrations (MIC) of all these compounds were determined and tabulated in Table 3.

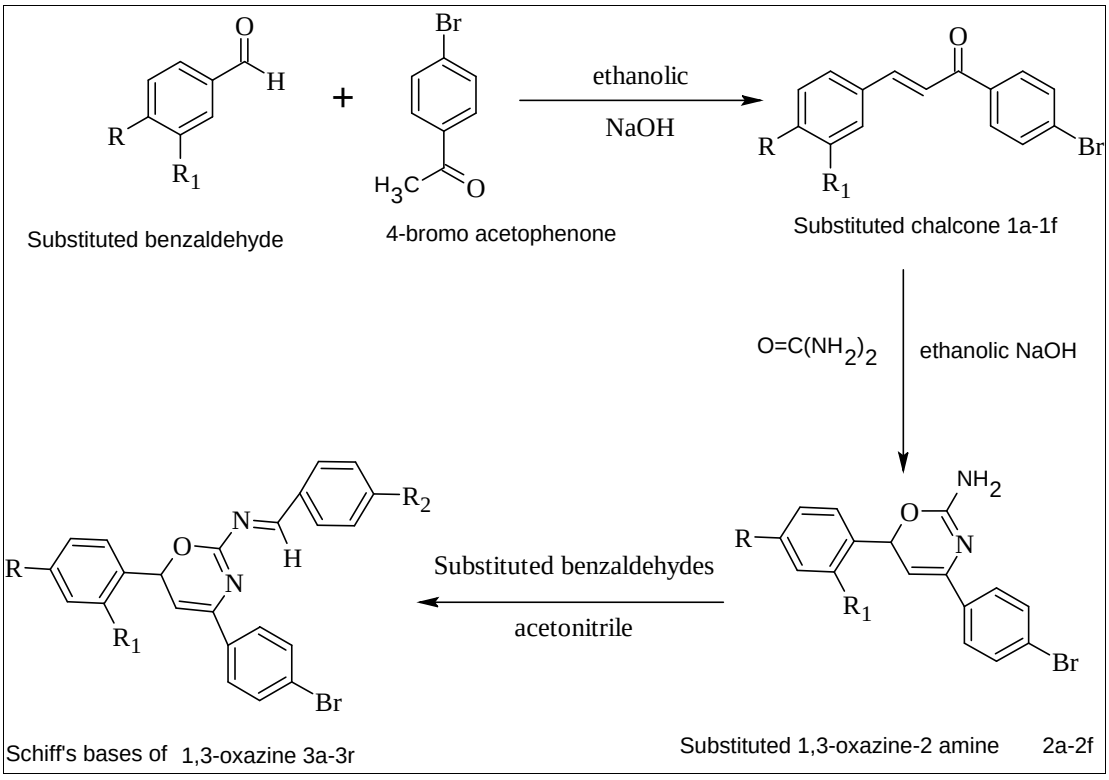

Figure 1: Synthesis scheme

Table 1. Various substituents used for Schiff's bases of 1,3-oxazine (3a-3r)

Compound	R	R_1	R_2
3a	Cl	H	NO_2
3b	$(OCH_{3)3}$	H	NO_2
3c	NO_2	H	NO_2
3d	$N(CH_3)_2$	H	NO_2
3e	OCH_3	H	NO_2
3f	H	OH	NO_2
3g	Cl	H	Cl
3h	$(OCH_3)_3$	H	Cl
3i	NO_2	H	Cl
3j	$N(CH_3)_2$	H	Cl
3k	OCH_3	H	Cl
3l	H	OH	Cl
3m	Cl	H	OCH_3
3n	$(OCH_3)_3$	H	OCH_3
3o	NO_2	H	OCH_3
3p	$N(CH_3)_2$	H	OCH_3
3q	OCH_3	H	OCH_3
3r	H	OH	OCH_3

Table 2. Physical data of synthesized compounds (3a-3r)

Compound	Molecular Formula	Molecular Weight	% Yield	M .P.^{0}C	R_f Value
3a	$C_{23}H_{15}BrClN_2O$	486.18	71.46	140-142	0.83
3b	$C_2\ H_{22}BrN_3O_6$	568.41	68.43	152-154	0.61
3c	$C_{23}H_{15}Br\ N_4O_5$	506.28	62.71	140-142	0.75
3d	$C_{25}H_{21}Br\ N_4O_3$	505.36	65.14	172-174	0.65
3e	$C_{25}H_{18}Br\ N_2O_4$	491.33	53.76	128-130	0.53
3f	$C_{23}H_{16}BrN_3O_4$	478.29	64.44	130-132	0.47
3g	$C_{23}H_{15}BrCl_2N_2O$	486.18	69.68	144-146	0.90
3h	$C_{27}H_{22}BrClN_2O_4$	540.83	66.12	148-150	0.58
3i	$C_{23}H_{15}BrClN_3O_3$	496.74	61.45	140-142	0.73
3j	$C_{25}H_{21}BrClN_3O$	494.81	71.27	170-172	0.69
3k	$C_{24}H_{18}BrClN_2O_2$	481.76	57.08	128-130	0.56
3l	$C_{23}H_{16}BrClN_2O_2$	467.74	68.93	126-128	0.51
3m	$C_{24}H_{18}BrClN_2O_2$	481.76	61.75	140-142	0.61
3n	$C_{28}H_{25}BrN_2O_5$	553.44	63.56	150-152	0.49
3o	$C_{24}H_{18}BrN_2O_4$	492.32	63.86	142-144	0.56
3p	$C_{26}H_{24}BrN_3O_2$	490.39	67.89	172-174	0.53
3q	$C_{25}H_{21}BrN_2O_3$	477.34	53.78	132-134	0.37
3r	$C_{23}H_{19}BrN_3O4$	478.29	65.13	136-138	0.29

Table 3. Antimicrobial activity (MIC) of title compounds (3a-3r)

Compounds	*S. aureus*	*E. coli*	*Candida aibicans*
Ofloxacin	8	8	-
Amphotericin B	-	-	1
3a	64	128	128
3b	64	64	64
3c	64	64	64
3d	64	1024	64
3e	256	64	64
3f	128	128	128
3g	128	1024	64
3h	64	64	64
3i	1024	16	1024
3j	8	16	4
3k	8	8	4
3l	8	8	8
3m	8	32	32
3n	16	8	16
3o	64	8	4
3p	256	1024	16
3q	32	32	64
3r	8	8	4

RESULTS AND DISCUSSION

Initially six compounds **(1a-1f)**, which are substituted chalcones were synthesized. Subsequently six compounds **(2a-2f)** were synthesized with substitution of 4-bromophenyl at 4^{th} position and phenyl substitution on 6^{th} position of 1,3-oxazine-2-amine. The Schiff bases **(3a-3r)** of 1,3-oxazine has been synthesized with formation of imine group with substituted phenyl ring at 2 position of 1,3-oxazine ring. Various substituents and physicochemical data of title compounds are tabulated in Table 1 and 2 respectively.

In the first step, 4-bromoacetophenone and substituted aromatic aldehyde reacted in the presence of sodium hydroxide to give substituted chalcones (Claisen-Schmidt condensation). In second step, substituted chalcones reacted with urea to produce 4-(4-bromophenyl)-6-(substituted phenyl)-6H-1,3-oxazin-2-amine analogues. In third step, these compounds was reacted with substituted aromatic aldehydes to produce 4-(4-bromophenyl)-6-(substituted phenyl)-2-{[(1E)-(substitutedphenyl)methylidenene]-6H-1,3-oxazin-amine.

Melting points of the synthesized compounds were determined in an open capillary tube and hence are uncorrected. The structures of the title compounds were established on the basis of spectral data. The IR spectra were recorded on a Jasco FTIR 4100 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian NMR 300 MHz spectrometer using $CDCl_3$ as solvent with TMS as an internal standard. Purity of the synthesized compounds was checked by silica gel G plate using benzene and methanol as mobile phase.

The antimicrobial screening reveals that the synthesized compounds exhibited significant activity against bacterial and fungal species. Compounds **3j, 3k, 3l, 3o, 3r** were found to be most active whereas compounds **3i, 3m, 3n, 3p, 3q** exhibited moderate to weak activity.

CONCLUSION

The present study concludes that compounds 4-(4-Bromophenyl)-6-(N,N-dimethylaminophenyl)-N-[(E)(4-chlorophenyl) methylidene]-6H-1, 3-oxazin -2-amine (3j); 4-(4-Bromophenyl)-N-[(1E)-(4-chlorophenyl)methylidene]-6-(4-methoxyphenyl)-6H-1,3-oxazin-2-amine (3k); 2-[4-(4-Bromo phenyl)-2-{[(1E)-(4-chlorophenyl)methylidene] amino}-6H-1,3-oxazin-6-yl]phenol (3l); 2-[4-(4-Bromophenyl)-2-{[(E)-(4-nitrophenyl) methylidene]amino}-6H-1,3-oxazin-6-yl] phenol (3r) are broad spectrum antimicrobials showing significant inhibition of bacterial and fungal strains.

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