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Research Article

Synthesis and Evaluation of Schiff Bases of 1,3,4-Thiadiazolidine Derivatives

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Abstract: In present study a new series of 5-substituted - 1, 3, 4-thiadiazolidine Schiff bases have been synthesized. The synthesis involves reaction between various aliphatic/arylaldehydes/ ketones with 5-substituted -2-amino -1, 3, 4-thiadiazolidines. The structures of synthesised compounds were established on the basis of IR, ^{1}HNMR spectral data. Insilco analysis was carried, aiming to present potential selective activities as ion channel modulator and enzyme inhibitors. These activities were suggested by the score values using molinspiration cheminformatics programme. In vitro antibacterial and antifungal activity were also evaluated and compared with standard drugs.
Keywords: Schiff bases, synthesis, antibacterial activity, antifungal activity, thiadiazolidines.

INTRODUCTION

Microbial diseases are very common all over the world. Infectious diseases can be the result of the colonization of the body by various microbes. There are many similar disease states that can arise from different causes, i.e., pneumonia can be caused by viruses, many types of bacteria, protozoa, and even fungi. Currently used anti microbial agents are not effective due to development of the resistant to antibacterial agents, it is vital to discover novel scaffold for the design and synthesis of new antimicrobial agents to help in the battle against pathogenic microorganisms. It is ongoing efforts for the synthesis of the new antimicrobial agents. Antimicrobial agents reduces or completely block the growth and multiplication of bacteria and are helpful in the treatment of various infectious diseases like meningitis, malaria, tuberculosis, pneumonia, AIDS, etc**.**

The synthesis and biological activities of Schiff bases derivatives occupy an important position in heterocyclic chemistry as well as in medicinal chemistry. The biological activity of a compound depends upon their molecular structure. There are number of five member heterocyclic compound containing nitrogen and sulphur atom, have turned out to be potential chemotherapeutic and pharmaco therapeutic agents. The biological profile of 1, 3, 4-Thiadiazole derivatives are very extensive. The compounds with azomethine linkages were also shown to possess an array of biological activities such as antifungal [1], antibacterial [2,3], antiinflammatory[4-6], antitubercular[7-8], anticancer, antiviral [9-10] and antiparkinsonism[11].

The scientific literature also states that antiviral and antibacterial of the thiourea derivatives are due to the presence of –NH-C(S)-NH function in the molecule and the change in the activity depends on the nature of the substituent[14].

EXPERIMENTAL:

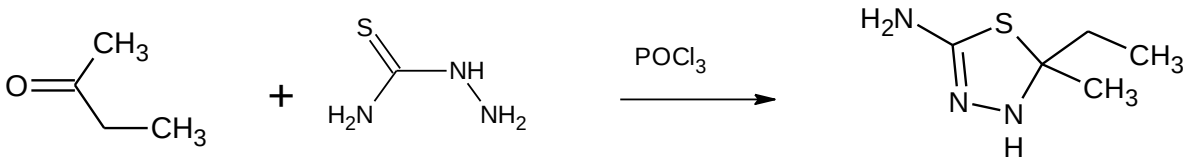
General details:

The chemicals used for the synthesis were supplied by LOBA chemicals. Purity of the compounds was checked on thin layer chromatography (TLC) plates (Silica Gel G) using the solvent systems ethyl acetate: hexane (1:1). The spots were identified in iodine chamber. Melting points were determined on GallenKamp (MFB-600) melting point apparatus and were uncorrected. The IR spectra of the compounds were recorded on a shimadzu FT-IR-8300 spectrometer as KBr disc. The ^{1}H-NMR and ^{13}C-NMR spectra (solvent DMSO-d6) were recorded on Bruker 400 MHz spectrophotometer using TMS as internal standard.

Synthesis of compounds ST-1 TO ST-17:SCHEME-1

Preparation of 5-ethyl-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-amine(ST-1)

A mixture of equimolar amounts of Thiosemicarbazide (0.01moles) and ethyl methyl ketone (0.01moles) in water and phosphorus oxy chloride was added drop by drop by continuous stirring until the product was obtained. The product was filtered, washed well with water and purified by recrystallization from methanol. The purity of compounds was validated by monitoring TLC.



butan-2-one

hydrazinecarbothioamide

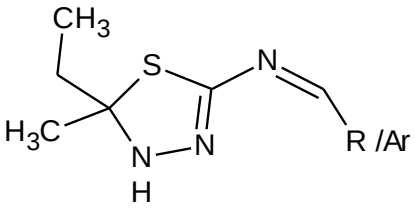
5-ethyl-5-methyl-4,5-dihydro-1,3,4 -thiadiazol-2-amine (ST - 1)

+

R -CHO /Ar -CHO

dil.HCl

Ethanol - NaOH

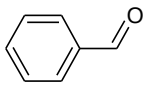


ST - 2 to ST -17

SCHEME-1

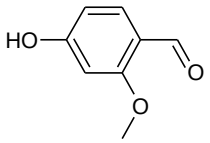
Aromatic aldehydes / Heterocyclic aldehydes

ST -2)



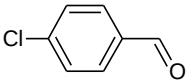
benzaldehyde

ST -3)



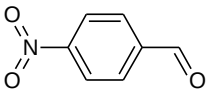
4-hydroxy-2-methoxybenzaldehyde

ST -4)



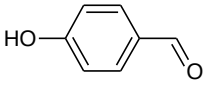
4-chlorobenzaldehyde

ST -5)



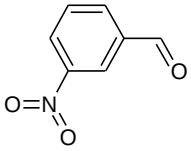
4-nitrobenzaldehyde

ST -6)



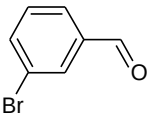
4-hydroxybenzaldehyde

ST -7)



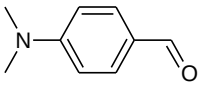
3-nitrobenzaldehyde

ST -8)



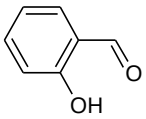
3-bromobenzaldehyde

ST -9)



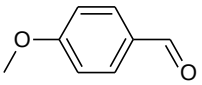
4-(dimethylamino)benzaldehyde

ST -10)



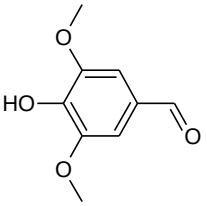
2-hydroxybenzaldehyde

ST -11)



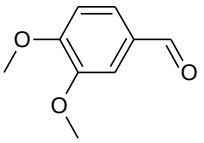
4-methoxybenzaldehyde

ST -12)



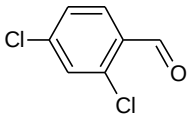
4-hydroxy-3,5-dimethoxy benzaldehyde

ST -13)



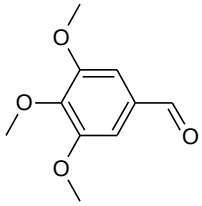
3,4-dimethoxybenzaldehyde

ST -14)



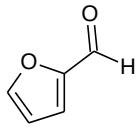
2,4-dichlorobenzaldehyde

ST -15)



3,4,5-trimethoxybenzaldehyde

ST -16)



furan-2-carbaldehyde

ST - 17)

formaldehyde

PreparationofN-(5-ethyl-5-methyl-4,5-dihydro1,3,4-thiadiazol-2yl)-1- phenylmethanimine : (ST2 -17)

A mixture of compound ST-1 with different aromatic/heterocyclic aldehydes in ethanol in presence of sodium hydroxide was stirred for 1 hour. The product was obtained by neutralisation with acid. The product was filtered, washed well with water and purified by recrystallization from methanol. The purity of compounds was validated by monitoring TLC. The physical and analytical data of the compounds are given in **Table 1**

Table 1: Physical and Analytical Data Of Synthesized Compounds

Code	Empirical formula	Molecular weight	Melting point	%Yield	R_f	Elemental analysis					
						C	H	N	S	O	X
ST-1	$C_5H_{11}N_3S$	145.23	69-70°C	83.8	`0.56	41.35	7.63	28.93	22.08	-	-
ST-2	$C_{12}H_{15}N_3S$	233.34	155-162°C	40.15	0.61	61.77	6.48	18.01	13.74	-	-
ST-3	$C_{13}H_{17}N_3O_2S$	279.36	185°C	13.5	0.46	55.89	6.13	15.04	11.48	11.45	-
ST-4	$C_{12}H_{14}ClN_3S$	267.78	196°C	56.17	0.55	53.82	5.27	15.69	11.97	-	13.24
ST-5	$C_{12}H_{14}N_4O_2S$	278.33	208°C	32.01	0.63	51.78	5.07	20.13	11.52	11.5	-
ST-6	$C_{12}H_{15}N_3OS$	249.33	198-200°C	10.4	0.43	57.81	6.06	16.85	12.86	6.42	-
ST-7	$C_{12}H_{14}N_4O_2S$	278.33	66-68°C	43.1	0.63	51.78	5.07	20.13	11.52	11.5	-
ST-8	$C_{12}H_{14}BrN_3S$	312.23	188-190°C	41.5	0.58	46.16	4.52	13.46	10.27	-	25.59
ST-9	$C_{14}H_{20}N_4S$	276.40	125°C	28.6	0.58	60.84	7.29	20.27	11.6	-	-
ST-10	$C_{12}H_{15}N_3OS$	249.33	198-202°C	48.19	0.55	57.81	6.06	16.85	12.86	6.42	-
ST-11	$C_{13}H_{17}N_3OS$	263.366	169-171°C	45.6	0.75	59.29	6.51	15.96	12.18	6.08	-
ST-12	$C_{14}H_{19}N_3O_3S$	309.39	Decomposition Point-270°C	30.9	0.63	54.35	6.19	13.58	10.36	15.51	
ST-13	$C_{14}H_{19}N_3O_2S$	293.392	178-182°C	43.34	0.63	57.31	6.53	14.32	10.93	10.91	-
ST-14	$C_{12}H_{13}Cl_2N_3S$	302.23	200-202°C	20.15	0.7	47.69	4.34	13.9	10.61	-	23.46
ST-15	$C_{15}H_{21}N_3O_3S$	323.41	187-189°C	60.68	0.53	55.71	6.54	12.99	9.91	14.84	-
ST-16	$C_{10}H_{13}N_3OS$	223.301	142°C	21.52	0.58	53.79	5.87	18.82	14.36	7.17	-
ST-17	$C_7H_{13}N_3S$	171.29	72°C	15.09	0.2	49.09	7.65	24.54	18.72	-	-

Spectral Data For Synthesized Compounds (ST-1TO ST-17):

5-ethyl-5-methyl-4, 5-dihydro-1, 3, 4-thiadiazol-amine (ST-1):

Reactiontime:10min;%yield:83.8;R_f:0.56(ethylacetate:hexane1:1);M.P(^{0}c):6970;IR(KBr,V_{max},Cm^1):3243,3184(NH_2),1362(C=S),2360(CH),1517(C=N).;^{1}HNMR(500MHZ,$CDCl_3$)1.6(s),0.87(t)(CH_3),2.31,2.10(CH_2(q)),8(CH(s)),5.17(NH(s));^{13}CNMR(125MHZ,$CDCl_3$):149.45,75.47,31.43,27.42,8.89. (basic ring carbons)

N-(5-ethyl-5-methyl-4,5-dihydro1,3,4-thiadiazol-2yl)-1-phenylmethanimine (ST-2):

Reaction time:90mins; %yield: 40.15% ;R_f:0.61(ethyl acetate:hexane1:1); M.P: 155-162^{0}C ;IR (KBr,V_{max}, Cm^{-1}): 3733 (NH), , 2810(CH_3), 1600(C=C Aromatic),1538(C=N)1362(C-S).;^{1}HNMR(500MHZ,$CDCl_3$):1.6(S),0.88(t)(CH_3),7.56(m),7.34(ddt) 50 , 2,2.18 (CH_2(q)),7.71(CH(t)),6.82(NH(s));^{13}C(125MHZ,$CDCl_3$):162.34,160.40,136.34,130.55,129.19,128.97,73.38,31.43,27.42,8.89(basic ring carbons).

4-{[(5-ethyl-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)imino]methyl}-2 methoxy phenol (ST-3):

Reaction time:90min; %yield: 13.7%;R_f:0.46(ethyl acetate:hexane1:1); M.P(^{0}c):185 ;IR(KBr,V_{max},Cm^1):3744(NH),2899(CH_3),1600(C=CAromatic),1510(C=N),1743(OCH_3)1362(C^{1}HNMR(500MHZ,$CDCl_3$):1.6(S),0.88(t)(CH_3),6.87(m)(C=C),2.9,2.20(CH_2(q)),7.73(CH(t)),6.67(NH(s));^{13}CNMR(125MHZ,$CDCl_3$):162.34,160.40,153.94,147.97,129.19,124.97,112 7.42,8.89(basic ring carbons).

1-(4-chlorophenyl)-N-(5-ethyl-5methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2yl) methanimine (ST-4):

Reaction time:90min; %yield: 56.1% ;R_f:0.55(ethyl acetate:hexane1:1); M.P(^{0}c):196; IR

(KBr,V_{max},Cm^1):3744(NH),2899(CH_3),1600(C=CAromatic),1517(C=N),810(Cl),1362(CS).;^{1}HNMR(500MHZ,$CDCl_3$):1.16(S),0.88(t)(CH_3),7.84(m),7.74(t),7.46(m)(C=C),2.49,2.12(CH_2(q)),7.73(CH(t)),6.73(NH(s));^{13}CNMR(125MHZ,$CDCl_3$):162.40,162.34,136.51,135.01,129.31,121.94,73.38,31.43,27.42,8.89.(basic ring carbons).

N-(5-ethyl-5methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2yl)-1-(4-nitrophenyl) methanimine (ST-5):
Reaction time:90min; %yield: 32.10% ;R_f:0.63(ethyl acetate:hexane1:1); M.P(^{0}c):208; IR (KBr,V_{max},Cm^1):3744(NH),,2899(CH_3),8(t)(CH_3),m),7.77(d),7.59(m),(C=C),2.18,2.06(CH_2(q)),7.73(CH(t)),7.18(NH(s));^{13}CNMR(125MHZ,$CDCl_3$):162.34,160.40,148.56,138.65,128.65,124.33,73.38,31.43,27.42,8.89.(basic ring carbons).

4-{[(5-ethyl-5methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2-yl) imino] methyl} phenol (ST-6):
(ST-5) Reaction time:90min; %yield: 10.4% ;R_f:0.43 (ethyl acetate:hexane1:1); M.P(^{0}c):198200;IR(KBr,V_{max},Cm^1):3744(NH),,2899(CH_3),1600(C=CAromatic),1517(C=N),3650(OH),1362(CS).;^{1}HNMR(500MHZ,$CDCl_3$):1.57(S),0.86(t)(CH_3),7.33(m),6.85(C=C),2.49,2.12(CH(q)),7.73(CH(t)),6.23(NH(s)),9.89(OH),;^{13}CNMR(125MHZ,$CDCl_3$):162.40,162.34,149.96,131.18,130.97,115.40,73.38,31.43,27.42,8.89.(basic ring carbons).

N-(5-ethyl-5methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2-yl)-1-(3-nitrophenyl) methanimine (ST-7):
Reaction time:90min; %yield: 43.1% ;R_f:0.63(ethyl acetate:hexane1:1); M.P(^{0}c):67-68; IR (KBr,V_{max},Cm^1):3744(NH),,2899(CH_3),1600(C=CAromatic),1515(C=N),1362(CS),2160(CN).;^{1}HNMR(500MHZ,$CDCl_3$):1.16(S),0.88(t)(CH_3),8.33(m),7.77(d),7.59(m)(C=C),2.49,2.12(CH_2(q)),7.73(CH(t)),7.18(NH(s));^{13}CNMR(125MHZ,$CDCl_3$):162.40,162.34,148.56,138.65,128.65,124.33,73.38,31.43,27.42,8.89.(basic ring carbons).

1-(3-bromophenyl)-N-(5-ethyl-5methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2-yl) methanimine (ST-8):
Reaction time:90min; %yield: 56.1% ;R_f:0.55(ethyl acetate:hexane1:1); M.P(^{0}c):196; IR (KBr,V_{max},Cm^1):3744(NH),,2899(CH_3),1600(C=CAromatic),1517(C=N),673.25(Br),1362(CS).;^{1}HNMR(500MHZ,$CDCl_3$):1.16(S),0.88(t)(CH_3),7.84(m),7.74(t),7.46(m)(CH_2protons),2.49,2.12(CH_2(q)),7.73(CH(t)),6.73(NH(s));^{13}CNMR(125MHZ,$CDCl_3$):162.40,162.34,136.51,135.01,129.31,121.94,73.38,31.43,27.42,8.89.(basic ring carbons).

4-{[(5-ethyl-5methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2-yl) imino] methyl} N, N-dimethylaniline (ST-9):
Reaction time:90min; %yield: 28.6% ;R_f:0.58(ethyl acetate:hexane1:1); M.P(^{0}c):125; IR (KBr,V_{max}, Cm^{-1}): 3744(NH), ,2899(CH_3), 1600(C=CAromatic),1517(C=N),(Br),1362(C-S),1650(NH).;^{1}HNMR(500MHZ,$CDCl_3$):1.16(S),0.88(t)(CH_3),7.84(m),7.74(t),7.46(m)(C=C),2.49,2.20(CH_2(q)),7.73(CH(t)),6.58(NH(s));^{13}CNMR(125MHZ,$CDCl_3$):162.40,162.34,151.81,130.45,127.61,111.57,73.38,31.43,27.42,8.89.(basic ring carbons).

2-{[(5-ethyl-5methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2-yl) imino] methyl} phenol (ST-10):
Reaction time:90min; %yield: 48.6% ;R_f:0.55(ethyl acetate:hexane1:1); M.P(^{0}c):198-200; IR(KBr,V_{max},Cm^1):3744(NH),,2899(CH_3),1600(C=CAromatic),1517(C=N),3648(OH),1362(CS).;^{1}HNMR(500MHZ,$CDCl_3$):1.16(S),0.88(t)(CH_3),7.31(m),7.16(t),6.99(dd)(C=C),2.49,2.12(CH_2(q)),7.73(CH(t)),6.66(NH(s))7.91(OH);^{13}CNMR(125MHZ,$CDCl_3$):165.03,162.34,161.21,132.31,132.69,117.30,119.09,
73.38,31.43,27.42,8.89.(basic ring carbons).

N-(5-ethyl-5-methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2-yl)-1-(4-methoxyphenyl) methanimine (ST-11):
Reaction time:90min; %yield: 45.6% ;R_f:0.75(ethyl acetate:hexane1:1); M.P(^{0}c):169-171; IR (KBr,V_{max}, Cm^{-1}): 3744(NH), ,2899(CH_3), 1600(C=CAromatic),1517(C=N), 1362(C-S).1055.9(OCH_3);^{1}HNMR(500MHZ,$CDCl_3$):1.58(S),0.88(t)(CH_3),7.73(m),7.34(t),7.04(m)(C=C),2.49,2.12(CH_2(q)),7.73(CH(t)),6.63(NH(s));^{13}CNMR(125MHZ,$CDCl_3$):162.40,162.34,131.51,131.27,114.69,73.38,31.43,27.42,8.89.(basic ring carbons).

4-{[(5-ethyl-5-methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2-yl) imino] methyl}-2, 6-dimethoxyphenol (ST-12):
Reaction time:90min; %yield: 30.69% ;R_f:0.63(ethyl acetate:hexane1:1);
M.P(^{0}c):decompositionpoint202;IR(KBr,V_{max},Cm^1):3744(NH),,2899(CH_3),1600(C=CAromatic),1517(C=N),3648(OH),1112.5(OCH_3),1362(CS).;^{1}HNMR(500MHZ,$CDCl_3$):1.16(S),0.88(t)(CH_3),7.84(m),7.74(t),7.46(m)(C=C), 2.49,2.12(CH_2(q)), 7.73(CH(t)), 6.73(NH(s)), 9.89(OH),. ^{13}C NMR (125MHZ,$CDCl_3$): 162.40, 162.34, 136.51, 135.01, 129.31, 121.94, 73.38, 31.43,27.42,8.89.(basic ring carbons).

1-(3, 4-dimethoxyphenyl)-N-(5-ethyl-5-methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2yl) methanimine (ST-13):
Reaction time:90min; %yield: 43.34% ;R_f:0.63(ethyl acetate:hexane1:1); M.P(^{0}c):178-182; IR (KBr,V_{max}, Cm^1):3744(NH),,2899(CH_3),1600(C=CAromatic),1509(C=N),1016.2(OCH_3
),1362(CS).;^{1}HNMR(500MHZ,$CDCl_3$):1.16(S),0.88(t)(CH_3),7.84(m),7.74(t),7.46(m)(C=C),2.49,2.09(CH_2(q)),7.74(CH(t)),6.73(NH(s));^{13}CNMR(125MHZ,$CDCl_3$):162.34,160.72,150.27,148.90,123.72,110.12,73.38,31.43,27.42,8.89.(basic ring carbons).

1-(2,4-dichlorophenyl)-N-(5-ethyl-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)metha nimine (ST-14):
Reaction time:90min; %yield: 20.17% ;R_f:0.7(ethyl acetate:hexane1:1); M.P(^{0}c):200-202; IR(KBr,V_{max},Cm^1):3744(NH),,2899(CH_3),1600(C=CAromatic),1517(C=N),820.64(Cl),1362(CS).;^{1}HNMR(500

MHZ,$CDCl_3$):1.16(S),0.88(t)(CH_3),7.84(m),7.74(t),7.46 (m)(C=C),2.49,2.12(CH_2(q)),7.73(CH(t)),6.73(NH(s));[1] [3]CNMR(125MHZ,$CDCl_3$):162.40,162.34,136.51,135.0 1,129.31,121.94,73.38,31.43,27.42,8.89.(basic ring carbons).

N-(5-ethyl-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)-1-(3,4,5-trimethoxyphenyl)meth animine (ST-15):
Reaction time:90min; %yield: 60.67% ;R_f:0.53(ethyl acetate:hexane1:1); M.P(^{0}c):187-189; IR (KBr,V_{max}, Cm^{-1}): 3744(NH), ,2899(CH_3), 1600(C=C Aromatic),1507(C=N), 1058.11(OCH_3),1362(CS).;[1]HNMR(500MHZ,$CDCl_3$):1 .16(S),0.88(t)(CH_3),7.84(m),7.74(t),7.46(m)(C=C),2.49, 2.12(CH_2(q)),3.75,3.85(OCH_3(s)),7.73(CH(t)),6.73(NH(s));[13]CNMR(125MHZ,$CDCl_3$):162.40,162.34,136.51,13 5.01,129.31,121.94,73.38,31.43,27.42,8.89.(basic ring carbons).

N-(5-ethyl-5-methyl-4, 5-dihydro-1, 3, 4-thiadiazol-2-yl)-1-(furan-2yl) methanimine (ST-16):
Reaction time:90min; %yield: 56.1% ;R_f:0.55(ethyl acetate:hexane1:1); M.P(^{0}c):196; IR (KBr,V_{max}, Cm^{-1}): 3744(NH), ,2899(CH_3), 1600(C=C Aromatic),1520(C=N),755.9(C-O), 1362(CS).;[1]HNMR(500MHZ,$CDCl_3$):1.16(S),0.88(t)(C H_3),7.84(m),7.74(t),7.46(m)(CH_2protons),2.49,2.12(CH $_2$(q)),7.73(CH(t)),8.40(NH(s));[13]CNMR(125MHZ,CDCl $_3$):167.58,143.82,142.19,112.29,99.61,73.38,31.43,27.4 2,8.89.(basic ring carbons).

N-(5-ethyl-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)methanimine (ST-17):
Reaction time:90min; %yield: 15.09% ;R_f:0.2(ethyl acetate:hexane1:1); M.P(^{0}c):72; IR (KBr,V_{max},Cm^{-1}): 3744(NH), ,2899(CH_3), 1600(C=C Aromatic),1516(C=N),810(Cl),1362(C-S).;[1]HNMR(500MHZ,$CDCl_3$): 1.16(S), 0.88(t) (CH_3), 6.06,6.01(C=C), 2.49,2.12(CH_2(q)), 7.73(CH(t)),6.61(NH(s));[13]C NMR (125MHZ,$CDCl_3$): 164.10, 146.45, 73.38, 31.43, 27.42, 8.89. (basic ring carbons).

INSILICO ACTIVITY:

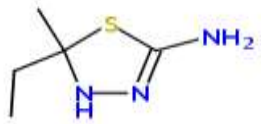
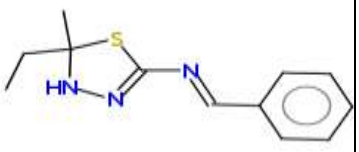
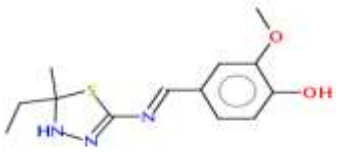
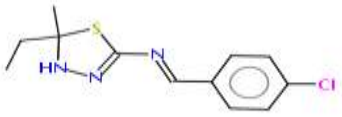
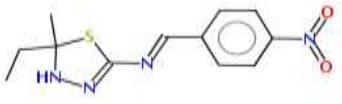
Molinspiration, web based software [12-13] was used to obtain parameter such as drug likeness and bioactive scores. Drug likeness may be defined as a complex balance of various molecular properties and structure features which determine whether particular molecule is similar to the known drugs following Lipinski rule of five. Calculated drug likeness score of each compounds and compared with the specific activity of each compound, and the results were compared with standard drug. For organic molecules the probability is if the bioactivity score is (>0) then it is active, if (-0.5-0.0) then moderately active, if (< -0.5) then inactive [14-15]. The drug likeness score, the calculated value of various parameters and bioactivity scores of the synthesised compounds (ST-1 to ST-17) are represented in **Table 2 and 3**.

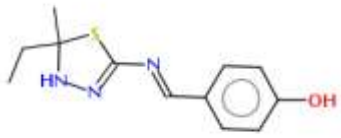
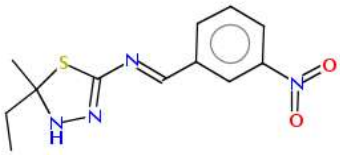
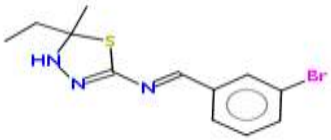
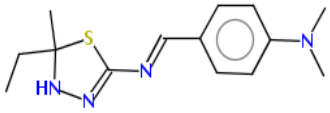
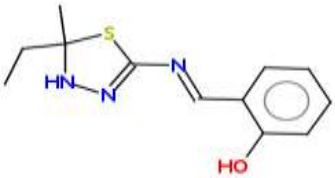
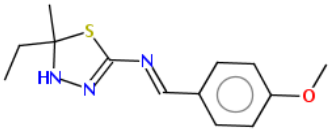
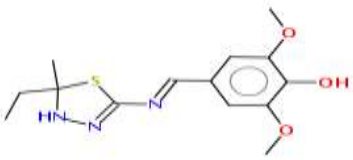
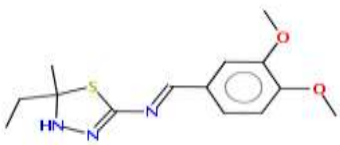
Table-2: Molecular Properties

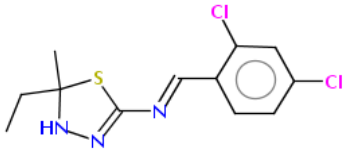
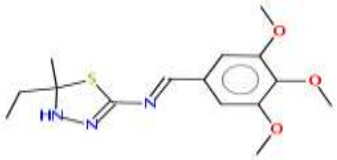
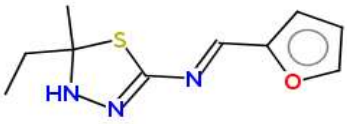
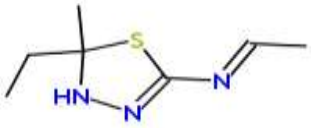
S.NO	Log p	TPSA	Natoms	M.w	NON	NOHNH	Nviolation	Nrotb	Volume
ST-1	1.08	50.414	9.0	145.231	3	3	0	1	133.3
ST-2	3.13	63.75	16	233.34	3	1	0	3	216.681
ST-3	2.469	66.217	19.0	279.36	5	2	0	4	250.244
ST-4	3.784	36.755	17.0	267.78	3	1	0	3	230.21
ST-5	3.088	82.579	19.0	278.337	6	1	0	4	240.015
ST-6	2.626	56.983	17.0	249.339	4	2	0	3	224.69
ST-7	3.088	82.57	19.0	278.337	6	1	0	4	240.015
ST-8	3.915	36.75	17.0	312.236	3	1	0	3	234.566
ST-9	3.232	39.993	19.0	276.409	4	1	0	4	262.58
ST-10	3.07	56.983	17.0	249.339	4	2	0	3	224.699
ST-11	3.186	45.989	18.0	263.366	4	1	0	4	242.227
ST-	2.485	75.451	21.0	309.39	6	2	0	5	275.79

12									
ST-13	2.776	55.22	20.0	293.392	5	1	0	5	267.77
ST-14	4.413	36.755	18.0	302.23	3	1	0	3	243.75
ST-15	2.761	64.457	22.0	323.418	6	1	0	6	293.318
ST-16	2.387	49.895	15.0	223.301	4	1	0	3	198.249
ST-17	1.911	36.755	11.0	171.269	3	1	0	2	161.8

Table-3: Bioactive Scores

S.NO	compound	GPCR ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
ST-1		-2.75	-1.93	-3.19	-3.59	-2.39	-2.20
ST-2		-0.94	-0.48	-1.16	-1.35	-0.96	-0.57
ST-3		-0.67	-0.44	-0.81	-0.91	-0.76	-0.40
ST-4		-0.84	-0.44	-1.05	-1.23	-0.91	-0.55
ST-5		-0.86	-0.45	-1.00	-1.09	-0.84	-0.55

ST-6		-0.77	-0.37	-0.96	-0.99	-0.82	-0.43
ST-7		-0.87	-0.47	-1.00	-1.10	-0.85	-0.58
ST-8		-0.99	-0.55	-1.14	-1.4	-1.04	-0.63
ST-9		-0.64	-0.41	-0.76	-0.94	-0.69	-0.42
ST-10		-0.80	-0.52	-1.01	-1.01	-1.07	-0.77
ST-11		-0.79	-0.50	-0.96	-1.09	-0.82	-0.51
ST-12		-0.56	-0.40	-0.64	-0.78	-0.58	-0.31
ST-13		-0.64	-0.47	-0.77	-0.92	-0.68	-0.43

ST-14		-0.79	-0.45	-0.96	-1.19	-0.85	-0.52
ST-15		-0.54	-0.44	-0.63	-0.84	-0.56	-0.39
ST-16		-1.18	-0.81	-1.62	-1.76	-1.16	-0.86
ST-17		-1.3	-0.75	-2.00	-2.15	-1.26	-0.93

ANTIMICROBIAL ACTIVITY

Antibacterial Activity

The antibacterial activity [16-17] was assayed by agar cup plate diffusion method at the different concentration. All synthesized compounds were tested in vitro against for their antibacterial activity against microorganisms such as *Bacillus subtilis*(NCIM-2063), *Eischerria coli* (NCIM-2345), *Proteus Vulgaris*(NCIM-2027), *Pseudomonas aeruginosa*(NCIM-2862).Each test compound was dissolved in dimethyl formamide (DMF) to get concentration of 5mg/mL. The agar medium was inoculated, previously seeded with 0.2mL of broth culture of each organism for 18hrs. Cultures of the test organism mentioned above aseptically into sterile Petri dishes and allowed to set at room temperature for about 30 minutes. The cups are made with the help of sterile metallic bore (8mm in diameter). The uniform volume of different concentrations of the test and standard solutions were added to the cups in the Petri plates. The solution was allowed to diffuse by leaving plates undisturbed for 90mins in a refrigerator. The plates were incubated at 37°C for 24 h and the inhibition zones were measured in mm.DMF and Benzyl penicillin as anti fungal reference standard. The results were representing in table- 4.

Anti Fungal Activity

The antifungal activity was assayed by potato dextrose agar media cup diffusion method at the different concentration [16-17]. All synthesized compounds were tested in vitro against for their antifungal activity against microorganisms such as *Aspergillus niger* (NCIM-1196); *Penicillium notatam* (NCIM-741).Each test compound was dissolved in dimethyl formamide (DMF) to get concentration of 5mg/mL. The potato dextrose agar medium was inoculated, previously seeded with 0.2mL of broth culture of each organism for 18hrs. Cultures of the test organism mentioned above aseptically into sterile Petri dishes and allowed to set at room temperature for about 30 minutes. The cups are made with the help of sterile metallic bore (8mm in diameter). The uniform volume of different concentrations of the test and standard solutions were added to the cups in the Petri plates. The solution was allowed to diffuse by leaving plates undisturbed for 90mins in a refrigerator. The plates were incubated at 22°C for 48 h and the inhibition zones were measured in mm.DMF and Fluconazole as anti fungal reference standard. The results were representing in table- 5.

Table-4: Results Of Antibacterial Activity Of Synthesized Compounds

code	Inhibition of zone diameter in mm															
	Bacillus subtilis				***Escherichia coil***				***Proteus Vulgaris***				***Pseudomonas aeruginosa***			
	50 µg	**100 µg**	**150 µg**	**200 µg**	**50 µg**	**100 µg**	**150 µg**	**200 µg**	**50 µg**	**100 µg**	**150 µg**	**200 µg**	**50 µg**	**100 µg**	**150 µg**	**200 µg**
ST-1	9	10	11	12	-	-	-	10	-	-	11	15	-	-	-	11
ST-2	11	12	13	15	8	10	11	12	11	12	13	14	9	9	10	12
ST-3	12	13	14	17	9	10	11	14	9	12	15	18	9	10	12	13
ST-4	12	13	14	15	9	11	12	14	9	12	13	14	13	14	14	15
ST-5	12	15	16	18	12	13	14	16	9	10	12	13	11	13	15	17
ST-6	12	12	14	14	9	11	14	16	8	9	10	11	8	12	13	14
ST-7	9	11	12	13	8	12	15	17	8	9	11	12	8	9	10	11
ST-8	11	12	14	15	11	12	13	14	12	15	18	20	9	12	14	15
ST-9	11	15	16	19	8	12	13	15	10	10	12	13	10	12	13	14
ST-10	9	12	13	14	10	11	12	12	9	14	16	18	8	9	10	12
ST-11	12	14	15	19	10	11	13	15	12	12	13	14	8	9	10	13
ST-12	13	14	15	16	8	10	12	14	-	-	-	-	-	-	-	-
ST-13	12	13	14	15	10	13	11	16	13	14	15	18	10	12	14	15
ST-14	11	12	13	14	10	14	16	13	10	13	14	18	12	14	15	16
ST-15	14	15	15	16	9	11	15	13	9	11	12	13	8	9	10	10
ST-16	12	14	15	16	10	11	13	15	11	12	14	15	12	13	14	15
ST-17	12	13	13	14	-	-	-	-	-	-	-	-	-	-	-	-
STD	15	17	18	16	14	16	18	18	15	16	17	19	14	17	16	18

Table-5: Antifungal Activity of Synthesized Compounds

code	Inhibition of zone diameter in mm							
	Penicillium notatam				***Aspergillus niger***			
	100 µg	**150 µg**	**200 µg**	**250 µg**	**100 µg**	**150 µg**	**200 µg**	**250 µg**
ST-1	-	-	-	13	-	-	-	-
ST-2	13	14	16	17	-	-	-	-
ST-3	14	14	16	17	-	-	-	-
ST-4	13	14	15	16	-	-	-	-
ST-5	12	13	16	17	-	-	-	-

ST-6	12	13	13	14	-	-	-	-
ST-7	15	16	18	19	-	-	-	-
ST-8	15	16	19	20	-	-	-	-
ST-9	13	14	15	17	20	21	22	25
ST-10	15	17	17	18	18	23	25	25
ST-11	13	12	14	15	-	-	-	-
ST-12	10	12	13	14	-	-	-	-
ST-13	12	14	16	18	18	22	24	25
ST-14	14	16	18	20	18	19	20	22
ST-15	10	13	15	16	-	-	-	-
ST-16	13	15	16	18	-	-	-	-
ST-17	8	9	10	11	-	-	-	-
STD	17	18	18	21	21	23	25	25

RESULT AND DISCUSSION

Insilico Activity:

All the compounds (ST-1 to ST-17) fulfil Lipinski's rule and show good drug likeness score (Table 2). Mlog P < 5. TPSA< 160 Å2, *n* violations = 0 it means compound easily bind to receptor, molecular mass <500, n rotb < 5, No. hydrogen bond donors ≤ 5 (The sum of OHs and NHs), No. hydrogen bond acceptor ≤ 10 (The sum of Os and Ns). The compounds showed good bioactive scores for compounds ST-6, ST-9, ST-12 for ionchannel modulator and ST-12 and ST-15 for enzyme inhibition activities on comparison with other compounds.

Antibacterial activity:

The anti bacterial activity was determined by the cup diffusion method at the different concentrations. All synthesized compounds were tested in vitro for their antibacterial activity against *Bacillus subtilis* (NCIM-2063), *Eischerria coli*(NCIM-2345), *Proteus Vulgaris*(NCIM-2027) , *Pseudomonas aeruginosa*(NCIM-2862), using Benzyl penicillin as standard antibacterial. The results were presented in table -2. All the compounds synthesised showed good anti bacterial activity . The 1,3,4- thiadiazoline derivatives of Schiff bases synthesised from 3,4,5-trimethoxybenzaldehyde,4-methoxybenzaldehyde, p-dimethylamino benzaldehyde and 4-hydroxybenzaldehyde are effective against *Bacillus subtilis* and Pseudomonas aeroginosa. The 1,3,4-thiadiazoline derivatives of Schiff bases synthesised from 3-nitrobenzaldehyde, 3,4,-dimethoxybenzaldehyde, 4-nitrobenzaldehyde, and 4-hydroxy benzaldehyde were effective against Escherichia coli and that the 1,3,4- thiadiazoline derivatives of Schiff bases synthesised from 3-bromobenzaldehyde good activity against *Proteus Vulgaris*.

Anti fungal activity:

The anti fungal activity was determined by the cup diffusion method at the different concentrations. All synthesized compounds were tested in vitro against for their antifungal activity against microorganisms such as *Aspergillus niger* (NCIM-1196); *Penicillium notatam* (NCIM-741 using fluconazole as standard antifungal. The results presented in table -3. All the compounds synthesised showed good anti fungal activity . The1,3,4-thiadiazoline derivatives of Schiff bases synthesised from 2,4-dichloro benzaldehyde, p-dimethyl-aminobenzaldehyde show good activity against *Penicillium notatam*. The 1,3,4- thiadiazoline derivatives of Schiff bases synthesised from 3,4,-dimethoxybenzaldehyde, p-dimethyl-aminobenzaldehyde, vanillin, salicyaldehyde show good activity against *Aspergillus niger*

CONCLUSION:

From the above results the derivatives containing strong to moderate ring activating groups such as –NH_2,-OH,-OCH_3, etc. showed significant rise in anti bacterial and anti fungal activity.

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