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Synthesis, characterization and antimicrobial activity of substituted N-benzhydrylpiperidin-4-amine derivatives

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ABSTRACT

As a part of systematic investigation of synthesis, characterization and biological activity of several new substituted N-benzhydrylpiperidin-4-amine derivatives (7a-7j) have been synthesized by reductive amination of Benzhydrylamine and N-Substituted 4-piperidone (3a-3e) as the starting material. . The structures of all the synthesized compounds have been determined by their spectral and microanalytical data. All the synthesized products were evaluated for their antibacterial activity against Bacillus substilis, Escherichia coli. Klebsiella pneumoniae and Streptococcus aureus bacteria and antifungal activity against Aspergillus niger, Aspergillus flavus, fungi respectively. Most of the synthesized compounds exhibited significant anti-bacterial and anti-fungal activities.

Keywords: Diphenylmethanamine, N-Boc-piperidin-4-amine, Reductive-amination, Grignard reagent, Sulphonamides, Antibacterial activity.

INTRODUCTION

Biphenyl methane and 4-aminopiperidine derivative are highly versatile ring systems and well established medicinally useful class of compounds, because of their wide range of therapeutic and pharmacological properties like Anti-microbial, Anti-fungal, Antihistaminic, Analgesic, Anti-tubercular, Anthelmintic activity and Antipsychotic agents[1-6]. Biphenylamines were developed by reaction of Benzonitrile and Grignard reagent[8,9] to form imine and resulting

imine was reduced to obtained secondary amine. Reductive amination of Biphenyl amines and N-Substituted 4-piperidone gives N-benzhydrylpiperidin-4-amine derivatives. Their chemical structure was confirmed by IR, ^{1}HNMR, Mass spectral and Elemental analysis. Sulphonamide derivative of N-Piperidine[7,10] were screened for their antibacterial activity against gram + Ve bacteria, gram - Ve bacteria, and anti-fungal activities by paper disc diffusion technique.

EXPERIMENTAL SECTION

The melting points were taken in open capillary tube and are uncorrected. The IR Spectra of the compounds were recorded on ABB Bomem FTIR spectrometer MB 104 with KBr pellets. The $_1$H-NMR (400 MHz) spectra were recorded on a Bruker 400 NMR spectrometer (with TMS as internal references). Mass spectra were recorded on Shimadzu GC MS QP 5000. The purity of the compounds was checked by TLC on pre-coated SiO2 gel (HF254, 200 mesh) aluminium plates (E Merk) using Ethyl acetate and Hexane visualized in UV light. The reagent grade chemicals were purchased from the commercial sources and purified by either distillation or recrystallisation before use.

General procedure for synthesis of (3a-3e)

1-(phenylsulfonyl)piperidin-4-one (3a): Piperidin-4-one hydrochloride (5.0g, 0.0332 mol) and Triethylamine (0.098 mol) were dissolved in Tetrahydrofuran (150 ml), under stirring Benzenesulfonyl chloride (0.359 mol) was added drop wise. The reaction mixture was stirred at room temperature and kept for 14-16 hr. After completion of reaction confirmed by TLC examination, the reaction mixture was diluted with water and product was extracted with ethyl acetate. Organic layer was dried over Na_2SO_4 and distilled out at reduced pressure to obtain product (**3a**) Yield 95%, Mp 284-288°C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 1.66-1.71 (m, 2H), 1.93-1.98 (m, 2H), 2.84-2.90 (m, 2H), 3.30-3.36 (m, 2H), 7.66-7.75 (m, 5H), MS *m*/*z* 240.06 (M + H+).

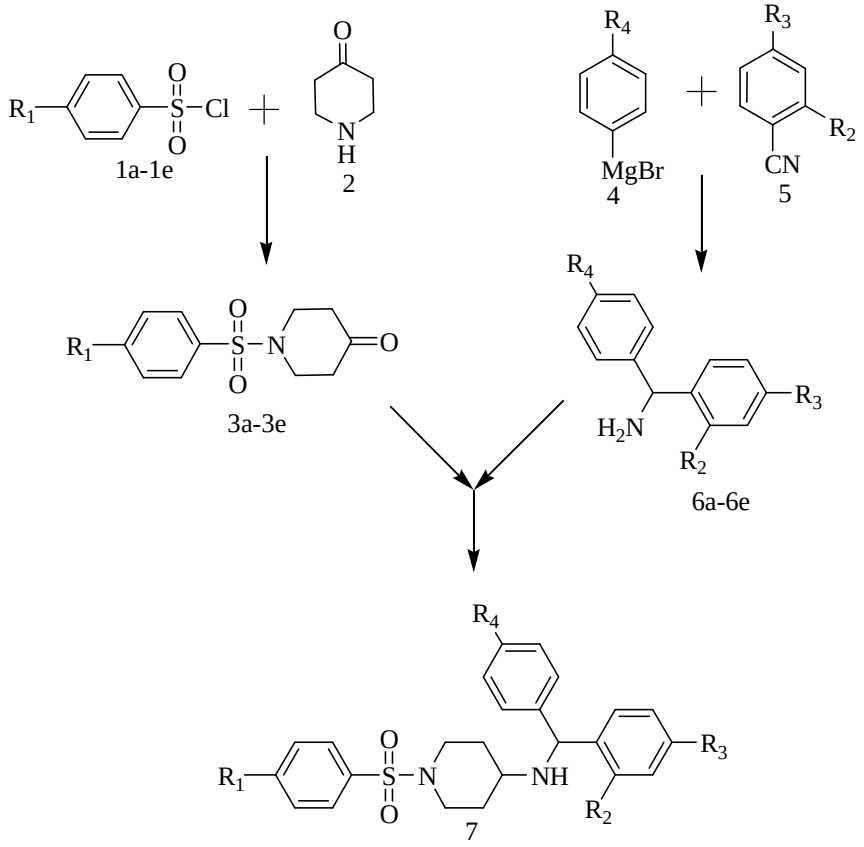
1-Tosylpiperidin-4-one (3b): Compound 3b was synthesized according to the procedure same as (3a) from 4-methylbenzene-1-sulfonyl chloride and Piperidin-4-one hydrochloride. Yield 92%, Mp 262-265°C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 1.66-1.71 (m, 2H), 1.93-1.98 (m, 2H), 2.29 (s, 3H), 2.84-2.90 (m, 2H), 3.30-3.36 (m, 2H), 7.69-7.77 (m, 4H). MS *m*/*z* 254.3 (M + H+).

1-(4-bromophenylsulfonyl)piperidin-4-one (3c) Compound 3c was synthesized according to the procedure same as (3a) from 4-bromobenzene-1-sulfonyl chloride and Piperidin-4-one hydrochloride. Yield 91%, Mp 255-261 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 1.66-1.71 (m, 2H). 1.93-1.98 (m, 2H), 2.84-2.90 (m, 2H), 3.30-3.36 (m, 2H), 7.55-7.57 (d, 2H), 7.73-7.75 (d, 2H), MS *m*/*z* 318.9 (M + H+).

1-(4-tert-butylphenylsulfonyl)piperidin-4-one (3d) Compound 3d was synthesized according to the procedure same as (3a) from 4-tert-butylbenzene-1-sulfonyl chloride and Piperidin-4-one hydrochloride. Yield 85%, Mp 275-277 °C.^{1}H NMR (400 MHz, DMSO-*d*6): 1.41 (s, 9H). 1.66-1.71 (m, 2H),1.93-1.98 (m, 2H), 2.84-2.90 (m, 2H), 3.30-3.36 (m, 2H), 7.55-7.57 (d, 2H),7.73-7.75 (d, 2H), MS *m*/*z* 296.1 (M + H+).

1-(4-methoxyphenylsulfonyl)piperidin-4-one (3e) Compound 3e was synthesized according to the procedure same as (3a) from 4-methoxybenzene-1-sulfonyl chloride and Piperidin-4-one hydrochloride. Yield 88%, Mp 280-285°C. ^{1}H NMR (400 MHz, DMSO-*d*6):, 1.66-1.71 (m, 2H), 1.93-1.98 (m, 2H), 2.84-2.90 (m, 2H), 3.30-3.36 (m, 2H), 3.61 (s, 3H), 7.54-7.56 (d, 2H), 7.71-7.73 (d, 2H), MS *m*/*z* 270.1 (M + H+).

Scheme



Where

R_1=a= H
b= CH_3
c= Br
d= $C(CH_3)_3$
e= OCH_3

R_2=H, CH_3, Cl
R_3=H, CH_3, Cl
R_4=H, CH_3, Cl

General procedure for synthesis of " (6a-6e)"

Diphenylmethanamine (6a).

To a solution of Benzonitrile (0.50 g, 3.30 mmol) in anhydrous THF (5 mL) at 0□C was added 1 M solution of phenyl magnesium bromide in THF (3.96 mL, 4.95 mmol) very slowly within 10 minutes, stirred for 30 minutes and the resulted mixture was warmed to room temperature. The reaction mixture was stirred at room temperature for 60 minutes followed by heated to 60^0C and stirred at same temperature for 4 hr. The formation of imine was monitored by TLC using Hexanes: EtOAc (5:5). After completion of the imine formation, the reaction mixture was cooled

to 0°C and added 5 mL of methanol very slowly followed by sodium borohydride (0.188 g, 4.90 mmol). The resulted mixture was warmed to room temperature and stirred overnight. The completion of the reaction was monitored by TLC using Hexanes: EtOAc (5:5) as a mobile phase. After completion of the reaction, the solvent was evaporated and added 10 mL of water in to the residue. The aqueous layer was extracted with ethyl acetate (3 * 40 mL), washed with brine (30 mL), dried over Na_2SO_4 and evaporated to obtained a crude product Diphenylmethanamine (0.311 g, 35.42%).^{1}H NMR (400 MHz, DMSO) δ 7.49-7.51 (d, 4 H), 7.37-7.40 (d, 2 H), 7.26-7.35 (m, 6 H), 5.29 (s, 1 H).

(4-chloro-2-methylphenyl)(4-chlorophenyl)methanamine (6b).
Compound 6b was synthesized according to the procedure same as (6a) using 4-chloro-2-methyl-benzonitrile and 1 M solution of 4-chloro phenyl magnesium bromide in THF..^{1}H NMR (400 MHz, DMSO) δ 7.49-7.51 (d, 1 H), 7.37-7.40 (d, 2 H), 7.26-7.35 (m, 3 H), 7.21-7.22 (d, 1 H), 5.29 (s, 1 H), 2.08 (s, 3 H).

(2,4-dimethylphenyl)(phenyl)methanamine (6c)
Compound 6c was synthesized according to the procedure same as (6a) using a solution of 2,4-dimethylbenzonitrile and 1 M solution of phenyl magnesium bromide in THF.

(4-chlorophenyl)(2,4-dimethylphenyl)methanamine (6d).
Compound **6d** was synthesized according to the procedure same as (6a) a solution of 2,4-dimethylbenzonitrile and 1 M solution of 4-chloro phenyl magnesium bromide (Yield 29.62 %). ^{1}H NMR (400 MHz, DMSO) δ 7.27-7.36 (m, 5 H), 6.97-6.99 (d, 1 H), 6.95 (d, 1 H), 5.18 (s, 1 H), 2.17-2.23 (d, 8 H).

(4-chloro-2-methylphenyl)(p-tolyl)methanamine (6e)
Compound 6e was synthesized according to the procedure same as (6a) a solution of 4-chloro-2-methyl-benzonitrile and 1 M solution of 4-Methyl phenyl magnesium bromide (Yield 29.62 %). ^{1}H NMR (400 MHz, DMSO) δ 7.27-7.36 (m, 5 H), 6.97-6.99 (d, 1 H), 6.91 (d, 1 H), 5.18 (s, 1 H), 2.17-2.22 (d, 8 H).

General procedure for synthesis of " (7a-7j)"

N-benzhydryl-1-(phenylsulfonyl)piperidin-4-amine(7a): To a solution of 1-(phenylsulfonyl) piperidin-4-one(**3a**): (1.25g, 1.0eq, 5.223mmol) in Dichloromethane (10.0 mL), Biphenyl methanamine (**6a)** (1.05g, 1.1eq, 5.741mmol) and 5- 10 drops of Concentrated Acetic acid were added at 0°C. The reaction mixture was stirred at 0°C for 2 hours, (white solid of imine appeared in reaction mixture) then Sodium borohydride (0.290g, 1.5eq, 7.832mmol) were added portion wise to reaction mixture and stirred at room temperature for 3 hours.. Completion of reaction was confirmed by TLC. Reaction diluted with water and washed with aqueous Sodium Bicarbonate solution. Product was extracted with Dichloromethane, organic layer was dried over sodium sulphate and removed in vacuum. The crude product was purified by column chromatography on silica gel using ethyl acetate: Hexane(1:3) as mobile phase to obtain title compound. Yield 87.6%. ^{1}H NMR (400 MHz, $CDCl_3$) 7.66-7.75 (m, 5H), δ 7.49-7.51 (d, 4 H), 7.37-7.40 (d, 2 H), 7.31-7.35 (m, 5 H), 5.29 (s, 1 H), 3.30-3.36 (m, 2H), 2.84-2.90 (m, 2H), 1.93-1.98 (m, 2H),1.66-1.71 (m, 2H) MS *m*/*z* 407.85 (M + H+).

N-benzhydryl-1-tosylpiperidin-4-amine(7b): Compound was synthesized according to the procedure same as (7a) Yield 89.7%. ^{1}H (400 MHz, $CDCl_3$) 7.64-7.72 (m, 4H), δ 7.49-7.51 (d, 4 H), 7.37-7.40 (d, 2 H), 7.31-7.35 (m, 5 H), 5.29 (s, 1 H), 3.30-3.36 (m, 2H), 2.84-2.90 (m, 2H), 2.23 (s, 3H), 1.93-1.98 (m, 2H),1.66-1.71 (m, 2H) MS *m*/*z* 421.25 (M + H+).

1-(4-bromophenylsulfonyl)-N-(phenyl(o-tolyl)methyl)piperidin-4-amine (7c): Compound was synthesized according to the procedure same as (7a) Yield 82.3.6%. IR(cm-1,KBr) ~3220(NH), 3092.5(Ar-CH-str),~1320(C-N),~1130(C=S). ^{1}H NMR (400 MHz, $CDCl_3$) 7.64-7.72 (m, 4H), δ 7.49-7.51 (d, 3 H), 7.37-7.40 (d, 2 H), 7.31-7.35 (m, 5 H), 5.29 (s, 1 H), 3.30-3.36 (m, 2H), 2.84-2.90 (m, 2H), 2.23 (s, 3H), 1.93-1.98 (m, 2H),1.66-1.71 (m, 2H) MS *m*/*z* 501.45 (M + 2H+).

1-(4-tert-butylphenylsulfonyl)-N-((4-chloro-2-methylphenyl)(4-chlorophenyl)methyl) piperidin-4-amine (7d): Compound was synthesized according to the procedure same as (7a) Yield 65.6%. IR(cm-1,KBr) ~3325(NH), 3092.5(Ar-CH-str),~1320(C-N),~1130(C=S) ^{1}H NMR (400 MHz, $CDCl_3$) 7.64-7.72 (m, 4H), δ 7.49-7.51 (d, 2 H), 7.37-7.40 (d, 2 H), 7.31-7.35 (m, 4 H), 5.29 (s, 1 H), 3.30-3.36 (m, 2H), 2.84-2.90 (m, 2H), 2.23 (s, 3H), 1.93-1.98 (m, 2H),1.66-1.71 (m, 2H), 1.35 (s, 9H). MS *m*/*z* 546.7 (M + H)+.

1-(4-methoxyphenylsulfonyl)-N-(phenyl(o-tolyl)methyl)piperidin-4-amine (7e): Compound was synthesized according to the procedure same as (7a) Yield 77.6%. IR(cm-1,KBr) ~3220(NH), 3092.5(Ar-CH-str),~1320(C-N),~1130(C=S). ^{1}H NMR (400 MHz, $CDCl_3$) 7.64-7.72 (m, 4H), δ 7.49-7.51 (d, 3 H), 7.37-7.40 (d, 2 H), 7.31-7.35 (m, 5 H), 5.29 (s, 1 H), 3.61 (s, 3H), 3.30-3.36 (m, 2H), 2.84-2.90 (m, 2H), 2.23 (s, 3H), 1.93-1.98 (m, 2H),1.66-1.71 (m, 2H) MS *m*/*z* 451.2 (M + H)+.

1-(4-tert-butylphenylsulfonyl)-N-((2,4-dimethylphenyl)(phenyl)methyl)piperidin-4-amine(7f): Compound was synthesized according to the procedure same as (7a) Yield 72.3.6%. IR(cm-1,KBr) ~3220(NH), 3092.5(Ar-CH-str),~1320(C-N),~1130(C=S) ^{1}H NMR (400 MHz, $CDCl_3$) 7.64-7.72 (m, 4H), δ 7.49-7.51 (d, 2 H), 7.37-7.40 (d, 2 H), 7.31-7.35 (m, 5 H), 5.29 (s, 1 H), 3.30-3.36 (m, 2H), 2.84-2.90 (m, 2H), 2.23 (s, 6H), 1.93-1.98 (m, 2H),1.66-1.71 (m, 2H), 1.35 (s, 9H). MS *m*/*z* 491.1 (M + H)+.

1-(4-tert-butylphenylsulfonyl)-N-((4-chlorophenyl)(2,4-dimethylphenyl)methyl)piperidin-4-amine (7g): Compound was synthesized according to the procedure same as (7a) Yield 61.6%. IR(cm-1,KBr) ~3220(NH), 3092.5(Ar-CH-str),~~1320(C-N),~1130(C=S),~748(C-Cl). ^{1}H NMR 400 MHz, $CDCl_3$) 7.64-7.72 (m, 4H), δ 7.49-7.51 (d, 2 H), 7.37-7.40 (d, 2 H), 7.31-7.35 (m, 4 H), 5.29 (s, 1 H), 3.30-3.36 (m, 2H), 2.84-2.90 (m, 2H), 2.23 (s, 6H), 1.93-1.98 (m, 2H),1.66-1.71 (m, 2H), 1.35 (s, 9H). MS *m*/526.4 (M + H)+.

N-benzhydryl-1-(4-tert-butylphenylsulfonyl)piperidin-4-amine(7h): Compound was synthesized according to the procedure same as (7a) Yield 69.6%. IR(cm-1,KBr) ~3220(NH),~ 3092.5(Ar-CH-str),~1320(C-N),~1130(C=S). ^{1}H NMR (400 MHz, $CDCl_3$) 7.66-7.75 (m, 5H), δ 7.49-7.51 (d, 4 H), 7.37-7.40 (d, 2 H), 7.31-7.35 (m, 5 H), 5.29 (s, 1 H), 3.30-3.36 (m, 2H), 2.84-2.90 (m, 2H), 1.93-1.98 (m, 2H),1.66-1.71 (m, 2H), 1.35 (s, 9H) MS *m*/*z* 466.1 (M + 1H)+.

1-(4-tert-butylphenylsulfonyl)-N-(phenyl(o-tolyl)methyl)piperidin-4-amine (7i): Compound was synthesized according to the procedure same as (7a) Yield 71.2%. IR(cm-1,KBr) ~3220(NH), ~1590(C=N),~1320(C-N), ~1130(C=S). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64-7.66 (d, 2H), 7.44-7.752 (m, 3H), 7.22-7.28 (m, 4H), 7.16-7.21 (t, 2H), 7.10-7.14 (t, 2H), 5.116 (s, 1H), 3.67-370 (d, 2H), 2.28-2.42 (m, 6H), 2.00-2.03 (d, 2H), 1.48-1.51 (d, 4H), 1.352 (s, 9H). MS ESI+ *m*/*z* 477.1 (M + H)+.

1-(4-tert-butylphenylsulfonyl)-N-((4-chloro-2-methylphenyl)(p-tolyl)methyl)piperidin-4-amine (7j): Compound was synthesized according to the procedure same as (7a) Yield 67.6%.IR(cm-1,KBr) ~3220(NH),~1320(C-N),~1130(C=S),~748(C-Cl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64-7.66 (d, 2H), 7.48-7.752 (m, 2H), 7.46 (s, 1H), 7.15-7.18 (t, 2H), 7.08-7.14 (m, 4H), 5.064 (s, 1H), 3.67-371 (q, 2H), 2.26-2.39 (m, 6H), 2.22 (s, 3H), 1.99 (bs, 2H), 1.46-1.52 (m, 3H), 1.352 (s, 9H).MS ESI+ *m*/*z* 526.5 (M + H)+.

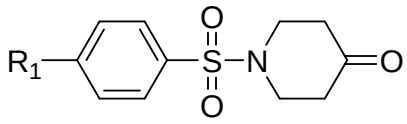
Anti-Microbial Screening

The anti-bacterial activity[11,12] of the synthesized compounds was tested against *Staphylococcus aureus (*ATCC 9144), *Escherichia coli (*ATCC 25922), *Pseudomonas aeruginosa* using nutrient agar medium (Hi-Media Laboratories, India). The antifungal activities[13] of the compounds were tested against *Aspergillus niger (* ATCC 9029) and *Aspergillus fumigatus* using Sabouraud dextrose agar medium (Hi-Media Laboratories, India).

***Paper disc diffusion technique*:** The Sterilized 78 (autoclaved at 120°C for 30min) medium (40-50°C) was inoculated (1mL/100mL of medium) with the suspension (105cfu mL-1) of the micro-organism (matched to McFarland barium sulphate standard) and poured into a petridish to give a depth of 3-4 mm. The paper impregnated with the test compounds (250µg/disc) was placed on the solidified medium. The plates were pre-incubated for 1 hr at room temperature and incubated at 37°C for 24 and 48 hrs for anti-bacterial and anti-fungal activities, respectively. Ciprofloxacin (100 µg/disc) and Fluconazole (100 µg/disc) were used as standard for anti-bacterial and anti-fungal activities, respectively.

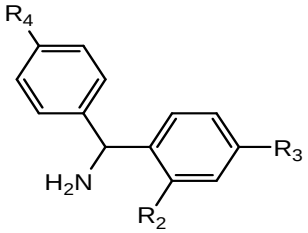
RESULTS AND DISCUSSION:

Table-1: Synthesis of 1-(phenylsulfonyl)piperidin-4-one (3a-3e)



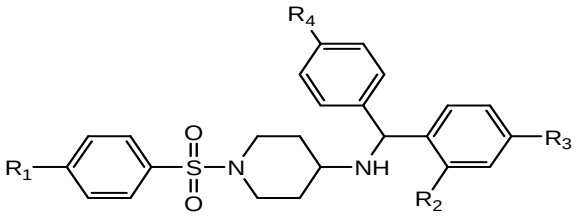
S. No.	Compound Name	R1	M.Wt.	M.Formula	Yield
1.	3a	-H	239.29	$C_{11}H_{13}NO_3S$	95%
2.	3b	$-CH_3$	253.32	$C_{12}H_{15}NO_3S$	92%
3.	3c	-Br	318.19	$C_{11}H_{12}BrNO_3S$	91%
4.	3d	$-C(CH_3)_3$	295.40	$C_{15}H_{21}NO_3S$	85%
5.	3e	$-OCH_3$	269.32	$C_{12}H_{15}NO_4S$	79%

Table-2: Synthesis of Diphenylmethanamine Derivatives (6a-6e)

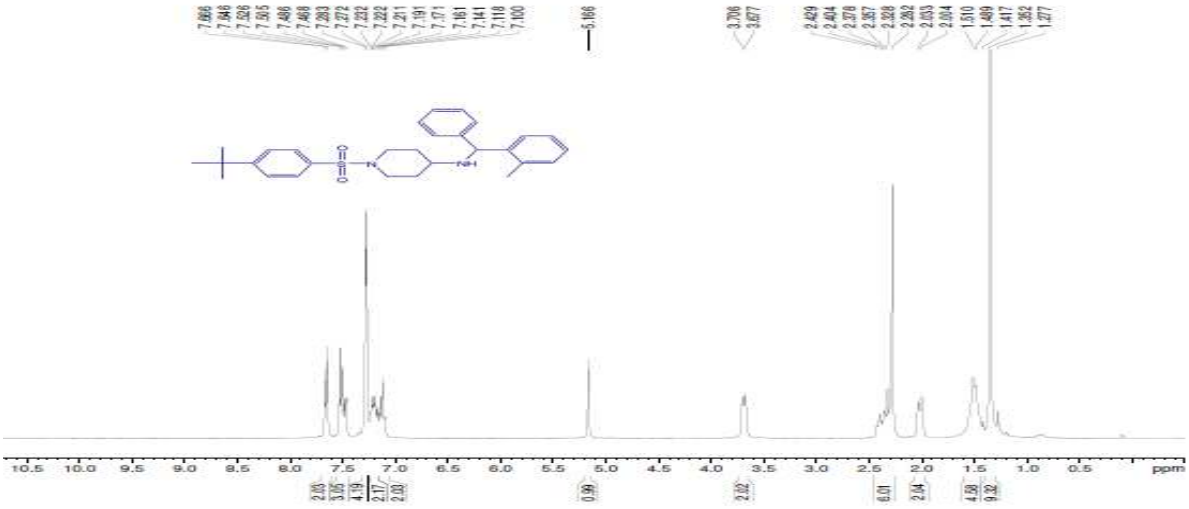


S. No.	Compound Name	R_2	R_3	R_4	M.Wt.	M.Formula	Yield
1.	6a	-H	-H	-H	183.25	$C_{13}H_{13}N$	67%
2.	6b	$-CH_3$	-Cl	-Cl	266.17	$C_{14}H_{13}Cl_2N$	32%
3.	6c	$-CH_3$	$-CH_3$	-H	211.30	$C_{15}H_{17}N$	51%
4.	6d	$-CH_3$	$-CH_3$	-Cl	245.75	$C_{15}H_{16}ClN$	45%
5.	6e	$-CH_3$	-Cl	$-CH_3$	245.75	$C_{15}H_{16}ClN$	69%

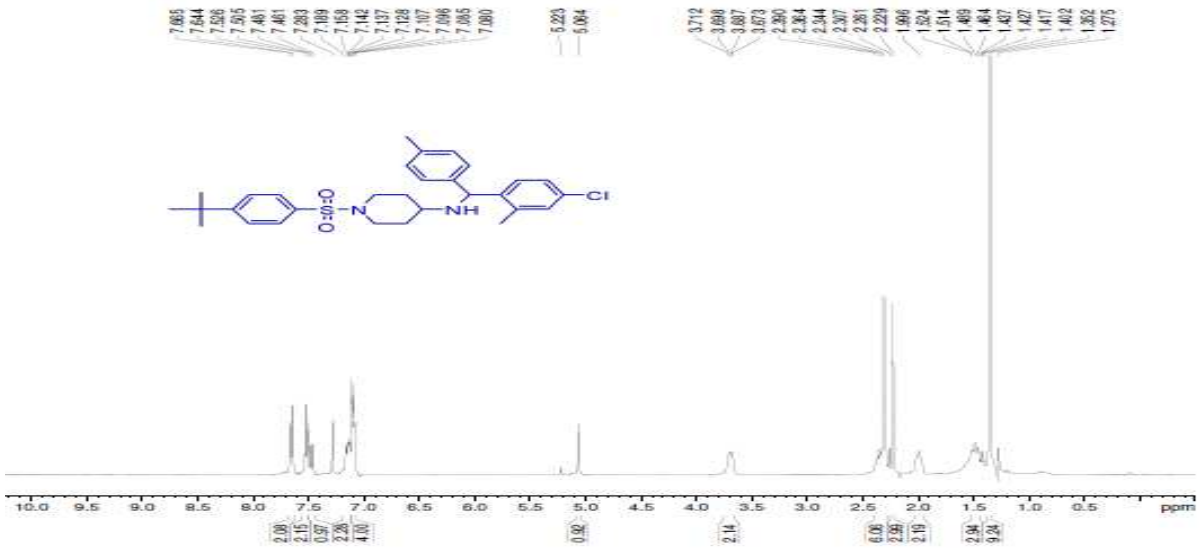
Table-3: Synthesis of N-benzhydryl-1-(phenylsulfonyl)piperidin-4-amine (7a-7j)



S. No.	Compound Name	R_1	R_2	R_3	R_4	M.Wt.	M.Formla	Yield %
1.	7a	-H	-H	-H	-H	406.54	$C_{24}H_{26}N_2O_2S$	87.6 %
2.	7b	$-CH_3$	-H	-H	-H	420.57	$C_{25}H_{28}N_2O_2S$	89.7 %
3.	7c	-Br	$-CH_3$	-H	-H	499.46	$C_{25}H_{27}BrN_2O_2S$	82.3 %
4.	7d	$-C(CH_3)_3$	$-CH_3$	-Cl	-Cl	545.56	$C_{29}H_{34}Cl_2N_2O_2S$	65.6 %
5.	7e	$-OCH_3$	$-CH_3$	-H	-H	450.59	$C_{26}H_{30}N_2O_3S$	77.6 %
6.	7f	$-C(CH_3)_3$	$-CH_3$	$-CH_3$	-H	490.70	$C_{30}H_{38}N_2O_2S$	72.3 %
7.	7g	$-C(CH_3)_3$	$-CH_3$	$-CH_3$	-Cl	525.14	$C_{30}H_{37}ClN_2O_2S$	61.6 %
8.	7h	$-C(CH_3)_3$	-H	-H	-H	462.65	$C_{28}H_{34}N_2O_2S$	67.6 %
9.	7i	$-C(CH_3)_3$	$-CH_3$	-H	-H	476.67	$C_{29}H_{36}N_2O_2S$	71.2 %
10.	7j	$-C(CH_3)_3$	$-CH_3$	-Cl	$-CH_3$	525.14	$C_{30}H_{37}ClN_2O_2S$	67.6 %



PMR of 7i (solvent $CDCl_3$)



PMR of 7j (solvent $CDCl_3$)

(B) Anti-Microbial Screening:

Table IV: Antibacterial Activity of the newly synthesized compounds

Compound Name	Zone of Inhibition (mm)				
	Antibacterial activity			Antifungal activity	
	Staphylococcus aureus	*Pseudomonas aeruginosa*	*Escherichia coli*	*Aspergillus niger*	*Aspergillus fumigatus*
7a	03	02	04	02	02
7b	08	09	07	02	03
7c	12	13	08	13	13
7d	18	18	20	10	11
7e	06	08	07	02	02
7f	10	09	09	04	03
7g	06	07	08	04	06
7h	08	08	07	05	05
7i	11	12	11	09	08
7j	16	18	19	12	11
Ciprofloxacin	22	20	23	---------	--------
Fluconazole	----------	----------	---------	22	24

**Concentration of standard Ciprofloxacin (100 µg/disc) and Fluconazole (100 µg/disc).*
**Concentration of Test Compounds 7a-7j (250µg/disc).*

Most of the synthesized compounds exhibited mild to moderate anti-microbial activity against the tested microorganisms. Compounds **7c, 7d,** and **7j** were found to possess significant anti-bacterial and anti-fungal activity when compared to standard drug (Ciprofloxacin and Fluconazole for anti-bacterial and anti-fungal respectively). Compounds **7b**, **7e, and 7f** displayed moderate anti-microbial activity where as the remaining compounds shown lesser activity.

CONCLUSION

We successfully synthesize more the 10 new substituted N-benzhydryl piperidin-4-amine derivatives. All compounds were characterized for their structure by 1HNMR and found correct. The entire synthesized compound exhibited better anti-bacterial activity than antifungal activity. In addition to that, many compounds are most active against gram '+'Ve bacteria than the gram '–'Ve one. The potent anti-microbial activity exhibited by **7c** and **7j** may be due to the 4-Bromo substitution. In conclusion, the present study highlights the importance Benzhydrylamine and Piperidine-Sulphonamide ring features responsible for the antimicrobial activities and therefore may serve as a lead molecule for further modification to obtain clinically useful novel entities.

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