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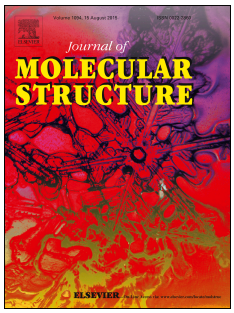

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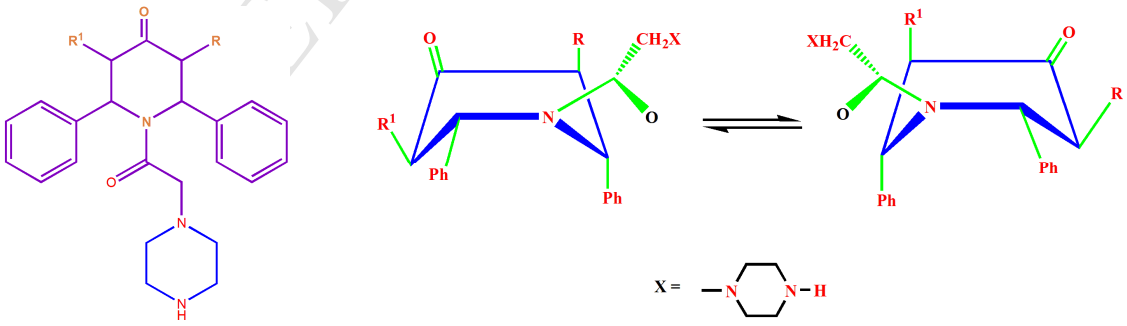
Graphical abstract

A series of *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones have been synthesized and their stereochemistry established. All the synthesized compounds have been evaluated for their antibacterial and antifungal activities and the results reveal a better structure – activity relationship.



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Abstract

Five new *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** have been synthesized and characterized using IR, ^{1}H, ^{13}C, DEPT & 2D NMR and mass spectral studies. The NMR spectral data indicate that the *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** prefer to exist in an equilibrium between **B1** and **B2** conformations. Furthermore, the antibacterial and antifungal studies were carried out. The results show that the piperazinoacetyl piperidin-4-ones **11-15** exhibit good activity against the selected bacterial and fungal strains.

Keywords: *N*-Piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones, NMR spectra, $A^{1,3}$-strain, stereochemistry, distorted boat conformation.

1. Introduction

Over the past decades, the incidence of systematic microbial infections has been increasing dramatically due to an increase in the number of immune-compromised hosts [1]. In recent years, there has been a growing interest pertaining to the synthesis of bioactive heterocyclic compounds in the field of medicinal chemistry. Piperazine nucleus is one of the most important heterocyclic moieties exhibiting remarkable pharmacological activities [1b].

The nitrogen atoms of the piperazine ring confer bioactivity to molecules and enhance favourable interaction with macromolecules [2,3]. Piperazinyl linked ciprofloxacin dimers are potent antibacterial agents against resistant strains, antimalarial agents and potential antiphychotic agents [4-6]. Piperazine derivatives containing tetrazole nucleus have been reported as antifungal agents [7]. Substituted benzamide piperazine derivatives have shown strong antagonistic activity while the substituted acetamide piperazine derivatives have better dopamine D4 receptor agonist activity [8,9].

Diphenylpiperazine derivatives possess broad pharmacological action on central Nervous System (CNS) especially on dopaminergic neurotransmission [10]. *N*-Sulfonamide derivatives of 1-(4-flurophenyl)-methylpiperazine exhibit potent antibacterial activity [11]. Most of the quinoline drugs, such as norfloxacin and ciprofloxacin having piperazine nucleus have shown broad spectrum activity against respiratory, urinary, gastrointestinal tract, skin and soft tissue infection caused by bacteria [12]. Various cyanopiperazine derivatives have been known for their use in the

synthesis of pharmaceutical intermediates, peptide analogues and antibacterial drugs [13-15].

The ring conformations of piperidin-4-ones have been changed drastically due to the attachment of nitroso and acyl functions at nitrogen. The relative influences of allylic strain, torsional strain, resonance energy due to delocalization of the lone-pair electrons of nitrogen with the hetero π electron systems have been studied on *N*- nitroso [16] and *N*-acyl [17-24] piperidin-4-ones and other related systems [23g-j].

The synthesis and stereochemistry of *N*-methylpiperazinoacetyl-2,6-diaryl-piperidin-4-ones were reported by Kabilan et al [24b]. They possess good antibacterial, analgesic and antipyretic activities against selected strains. In order to test the activity of piperazine moiety without a methyl group, some *N*-piperazinoacetyl-2,6-diphenyl-piperidin-4-ones have been synthesized and their antibacterial and antifungal activities evaluated.

2. Experimental

2.1 Materials, methods and instruments

The melting points reported in this work are uncorrected and measured using melting point apparatus. All IR spectra were recorded in SHIMADZU FTIR 8400S spectrometer and BRUKER - alpha model FTIR using KBr pellets. The ^{1}H and ^{13}C NMR spectra were recorded in a $CDCl_3$ solution using TMS as the internal standard in Bruker DRX 500 and 125 MHz Bruker AMX 400 and 100 MHz NMR spectrometers and the chemical shifts were referenced to TMS. A 0.05 M solution of the sample prepared in $CDCl_3$ was used for obtaining the 2D NMR spectra. The tubes used for recording the

NMR spectra were of 5-mm diameter. Electron impact mass spectra were recorded using a JEOL GS mate spectrometer. Unless otherwise stated, all the reagents and solvents were of high grade and purchased from Aldrich and Merck. All the solvents were distilled prior to use. The parent 2,6-diarylpiperidin-4-one **1-5** and *N*-chloroacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **6-10** were prepared by following the literature procedures [23-25].

2.2 General procedure for N-piperazinoacetyl-2,6-diphenyl-piperidin-4-ones 11-15

A mixture of *N*-chloroacetylpiperidin-4-ones **6-10** (1 mmol), piperazine (0.086 g, 1 mmol) and triethylamine (1 ml, 7.2 mmol) in anhydrous benzene (30 ml) was stirred at RT for 7 hours. The precipitated ammonium salt was filtered and the benzene solution was washed with water (4x10 ml). The resulting solution was passed through a short column of silica and concentrated. The pasty mass was purified by crystallization from benzene and pet-ether (60-80ºC) in the ratio of 95: 5. The analytical data of these compounds **11-15** are furnished in Table-1.

2.3 Antibacterial activity

All the synthesized *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones (**11-15**) were tested for their *in vitro* antibacterial activity against *Proteus mirabilis, Staphylococcus, E.Coli, Enterococcus faecalis* and *Klebsiella* using Muller-Hint agar medium by disc diffusion technique [26]. Sterile Muller-Hinton agar plates were prepared and the agar surface was inoculated with the bacteria. Compounds **11-15** were dissolved in 1mL of DMSO in various concentrations in separate tubes. Commercially available sterile discs were soaked in the preparation for half an hour. It

was then placed in empty petri plates for air-drying. Using sterile forceps, the discs were placed on the surface of the agar plates and gently pressed on to the agar surface. The culture plates were inverted and incubated for 24-48 hrs at 37°C. After incubation, zone of clearance was observed and its diameter measured using microscope. Zone of inhibition of extracts was compared with standard Chloramphenicol for antibacterial activity.

2.4 Antifungal activity

The *invitro* antifungal activity of compounds **11-15** was studied against the fungal strains *viz., Aspergillus niger, Aspergillus flavus, Aspergillus oryzae, Aspergillus fungigates* and *Tricoderma viride*. For antifungal, assays measuring inhibition of mycelia growth on agar media were used. Compounds **11-15** were dissolved in 1 ml of sterile Dimethyl sulfoxide (DMSO) serving as a stock solution. Then it was transferred it to 4 ml Sabouraud dextrose agar (SDA) growth media in separate tubes and autoclaved at 121℃ for 15 minutes. These tubes were allowed to cool to 50°C and non solidified SDA of each tube was loaded with various concentration of drug solution. Tubes were then allowed to solidify at room temperature. Then each glass tube was inoculated with 4 m diameter piece of inoculums removed from 7 days old culture of fungus [27,28]. All these tubes were incubated at 28±1℃ for 10 days. A relative humidity was maintained at 40-50% in the incubation room. Growth in the media was determined [29] by measuring linear growth (mm) of the compounds **11-15** and compared with chloramphenicol which was used as a standard reference.

3. Results and discussion

The *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** were synthesized by the reaction of piperazine on the corresponding *N*-chloroacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **6-10**. *N*-Chloroacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **6-10** were prepared by the action of chloroacetylchloride on the corresponding *r*-2,*c*-6-diphenylpiperidin-4-ones **1-5** in dry benzene using triethylamine as a catalyst [23a, Scheme-1]. The analytical data of the compounds are presented in Table-1.

In the IR spectra of the compounds **11-15**, the appearance of new N-H peak (Figure-1) around 3320 cm^{-1} (Table-2) confirms the formation of piperazine derivatives. Furthermore, in the ^{1}H NMR spectra of **11-15**, the shielding of signals of *N*–$COCH_2$ protons (**6-10**: 3.92-4.05 ppm [23a] due to the removal of chlorine and appearance of piperazine signals also confirm the formation of these compounds.

The preferred conformations of the *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** have been arrived at from the ^{1}H and ^{13}C NMR spectral data in comparison with those of the parent *r*-2,*c*-6-diphenylpiperidin-4-ones **1-5** [23a]. The *N*-chloroacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **6-10** prefer to exist in a conformational equilibrium between *syn* rotamer of boat conformation **B1** and *anti* rotamer of boat conformation **B2** [23a].

3.1 ^{1}H NMR spectra

The signals of ^{1}H NMR spectra of *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** are assigned based on their positions, multiplicities and in comparison with those of the parent amines **6-10**. In all these compounds the aromatic protons of **11-15** show signals around 7.53-6.96 ppm. The signals in the range of 6.56-4.93 ppm are due

to H_2 and H_6 protons of **11-15**. The piperazine protons of **11-15** appear in the range of 3.09-2.90 and 2.58-2.44 ppm (Figure-2). The complete assignments of all the ^{1}H NMR signals of **11-15** are presented in Table-3. The *cis* and *trans* vicinal coupling constants for the H_6 benzylic protons of **12-14** are extracted from their coupling partners H_{5a} and H_{5e}. The extracted coupling constant values of **12-14** are presented in Table-4. The vicinal coupling constant data are employed to calculate the dihedral angles between the vicinal protons by DAERM (Dihedral Angle Estimation by Ratio Method) [30].

3.2 ^{13}C NMR spectra

In the ^{13}C NMR spectra, the signals in the range of 128.8-122.6 ppm are due to aromatic carbons of **11-15**. The CO of *N*-$COCH_2$ carbon appears around 170.1-171.6 ppm for **11-15**. Similarly, the C=O group at C_4 of **11-15** appears around 203.5-211.1 ppm. The signals in the range of 60.0-63.0 and 53.9-63.0 pm are due to C_2 and C_6 carbons of **11-15**, respectively. The C_3 and C_5 carbons of **11-15** show signals around 31.5-58.1 and 44.2-52.4 ppm, respectively. The piperazine carbons of **11-15** appear in the range of 43.7-54.7 ppm (Figure-3). The unambiguous assignment of ^{13}C NMR signals of *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** has been made using their DEPT 135 and HSQC NMR (Figure-4) spectra and is presented in Table-5.

3.3 Orientation of >C=O group

The *N*-X=Y group can adopt either coplanar or perpendicular orientation to the dynamically averaged plane of the ring. The broadening of one of the benzylic protons signal of **11-15** at room temperature is due to existence of restricted rotation about *N*-

CO bond in the molecule, which could be possible only in the coplanar orientation with respect to C_2-N_1-C_6 plane of the piperidine ring system.

The coplanar orientation of the compounds **11-15** has been further confirmed from the following observations:

(i) Greater deshielding of benzylic protons compared to the parent piperidin-4-ones **1-5** in the ^{1}H NMR spectra (Table-6).

(ii) Greater shielding of benzylic carbons (C_2 & C_6) in the ^{13}C NMR spectra (Table-6), when compared to piperidin-4-ones **1-5**.

3.4 Preferred conformation of the ring

All the *N*-piperazinoacetyl compounds **11-15** have similar trend in the NMR spectral data compared to those of the parent *N*-chloroacetylpiperidin-4-ones **6-10**. Hence, compound **14** is taken as a representative example for the conformational analysis. The possible conformations for the *N*-piperazinoacetyl-*c*-3,*t*-3-dimethyl-*r*-2,*c*-6-diphenylpiperidin-4-one (**14**) with coplanar orientation of *N*-C=O group are depicted in Figure-5.

(i) Chair conformation with equatorial phenyl groups (**CE**)

(ii) Alternate chair conformation with axial phenyl groups (**CA**)

(iii) Boat conformation with equatorial phenyl groups (**BE**)

(iv) Boat conformation with axial phenyl groups (**BA**)

(v) Boat conformation **B1** & **B2**

In the chair conformation **CE** of *N*-piperazinoacetyl-*c*-3,*t*-3-dimethyl-*r*-2,*c*-6-diphenylpiperidin-4-one (**14**), the dihedral angles expected between H_6 benzylic proton

and H_{5e} & H_{5a} protons are around 60° and 180°, respectively, ($\phi_{cis} = \phi_{6a,\ 5e} \approx 60^o$ and $\phi_{trans} = \phi_{6a,\ 5a} \approx 180^o$). However, the observed *cis* coupling constant ($^3J_{6a,5e}$) value of 7.0 Hz for the compound **14** (Table-4) and the corresponding dihedral angle of 36° (Table-4) could not be explained using the **CE** conformation. In addition, the chair conformation **CE** with equatorial phenyl groups is destabilized by $A^{1,3}$-strain and the benzylic protons at C_2 and C_6 occupy axial orientations and are in out of plane region. The observed deshielding of H_2 and H_6 ($\Delta\delta$ = 0.03 and 0.15 ppm) from the parent **9** cannot be explained using the model proposed by Paulsen and Todt for the anisotropic effect of amides [31]. Hence, the possibility of chair conformation **CE** is ruled out. In order to alleviate $A^{1,3}$-strain, an alternate chair **CA** may be considered.

In the alternate chair conformation **CA** and boat conformation **BA** with axial phenyl groups, $A^{1,3}$-strain is relieved. But the two phenyl groups would exhibit 1,3-diaxial interaction which destabilizes the ring. The expected *cis* and *trans* coupling constants would be around 2-4 Hz. But the observed J value could not be used to explain the conformation **CA** & **BA**. Hence, the possibility of conformation **CA** & **BA** is ruled out.

The boat conformation **BE** is destabilized by the $A^{1,3}$-strain and bond eclipsing interaction. Expected vicinal coupling constant would be around 8 Hz and 4Hz, but the observed values eliminated the possibility of **BE** conformation.

The deshielding of benzylic protons and the observed higher value of the vicinal coupling constants similar to *N*-chloroacetyl-2,6-dipheylpiperidin-4-ones **6-10**, could only be explained by assuming the equilibrium between the boat conformation **B1** and **B2** with one axial and one equatorial phenyl groups. The shielding of C_2 and C_6 carbons

also supports the above conformation. The *N*-C=O group is coplanar to the C_2-N-C_6 plane of the piperidine ring causing γ-eclipsing interaction between C-O and N_1-C_2/N_1-C_6 bonds. This may be explained by considering a slight twist along N-C_2-C_3 bond. The slight twisting along N-C_2-C_3 bond would reduce the dihedral angle between *N*-C-O and C-N-C_2 Plane.

Hence, it is concluded that the *N*-piperazinoacetyl-*c*-3,*t*-3-dimethyl-*r*-2,*c*-6-diphenylpiperidin-4-one (**14**) prefers to adopt an equilibrium between the boat conformations **B1** and **B2** (Figure-5). Similarly all the *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** prefer to exist in an equilibrium between the boat conformations **B1** and **B2** (Figure-5).

3.5 Antibacterial activity

In general all the synthesized compounds exert a wide range of modest antibacterial activity against the tested organism except **11** (Table-7). Among the *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** the compounds **13** & **15** with isopropyl group at C_3 position and two methyl groups at C_3 & C_5 positions, respectively, have superior activity against all the organisms. The compound **12** containing ethyl group at C_3 position exhibits superior activity against *Proteus mirabilis, Staphylococcus,* and *Enterococcus faecalis.* The compound **12** shows better activity against *E.Coli* and *Klebsiella*. Furthermore, compound **13** with an isopropyl group shows better activity when compared to compound **12**. Compound **13** exhibits superior activity against *Proteus mirabilis, Staphylococcus, E.Coli, Enterococcus faecalis* and *Klebsiella*.

Introduction of another methyl group at C_3 position (Compound **14**) shows superior activity against *Proteus mirabilis,* better activity against *Staphylococcus* and *Klebsiella*, good activity against *E.Coli,* and better activity against *Enterococcus faecalis.* Similarly the two methyl groups at 3 and 5 positions in compound **15** increase the activity against all the organisms. It shows double the amount of activity against *Enterococcus faecalis, Klebsiella, Staphylococcus, Proteus mirabilis* and *E.Coli.* All the compounds exhibit significant antibacterial activity at 250µg/mL. The graphical representation of the antibacterial activity is presented in Figure-6.

The antibacterial activity of the *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** is comparable to that of *N*-methylpiperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones [24b] but it is found to be less when compared with that of compounds containing *p*-chlorophenyl piperidin-4-ones [24b].

3.6 Antifungal activity

Generally all the synthesized compounds exert a modest *in vitro* antifungal activity against all the tested organisms except **11** (Table-8). The compound **12**, containing ethyl group at C-3 position exhibits superior activity against *Aspergillus flavus, Aspergillus oryzae* and *Aspergillus fumigates* when compared to the standard chloramphenicol. Compound **12** shows better activity against *Tricoderma viride* and significant activity against *Aspergillus niger*.

Compound **13** obtained by the replacement of isopropyl group in place of ethyl group at C_3 in compound **12** shows superior activity against *Aspergillus flavus* and *Aspergillus fumigates* and good activity against *Aspergillus oryzae* and *Tricoderma*

Viride and significant activity against *Aspergillus niger*. Compound **14** obtained by the introduction of one more methyl group at C_3 position in compound **11** increases the activity against *Aspergillus oryzae* and a better activity against *Aspergillus fumigates* and good activity against *Aspergillus flavus* and *Tricoderma viride* and significant activity against *Aspergillus niger*.

Compound **15** containing two methyl groups at C_3 and C_5 position shows better activity against *Aspergillus oryzae, Aspergillus fumigates* & *Tricoderma viride* and good activity against *Aspergillus niger* & *Aspergillus flavus*. In general, all the compounds exhibit significant antifungal activity at 250µg/mL. The graphical representation of the antifungal activity is presented in Figure-7.

Thus the antifungal activity of the *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** is more compared to that of *N*-methylpiperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones [24b] but it is less when compared with that of compounds containing *p*-chlorophenylpiperidin-4-ones [24b].

Conclusion

Thus, in this work, five *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** have been synthesized and their stereochemistry studied with the help of ^{1}H, ^{13}C, DEPT and 2D NMR (^{1}H-^{1}H COSY and HSQC) spectral data. In addition mass spectra were also recorded. On the basis of NMR spectral data, it is concluded that the compounds **11-15** prefer to adopt an equilibrium between boat conformations **B1** and **B2**. Furthermore, the antibacterial and antifungal studies have been carried out. The results show the greater activity of all the compounds **11-15** against all the tested micro organisms when compared to the standard reference drug.

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Scheme caption:

Scheme 1:

Synthesis of *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15**

Figure captions:

Figure – 1

IR spectrum of compound **13**

Figure - 2

^{1}H NMR spectrum of compound **13**

Figure - 3

^{13} C NMR spectrum of compound **13**

Figure – 4

HSQC NMR spectrum of compound **13**

Figure – 5

Possible conformation of the compounds **11-15**

Figure – 6

Graphical representation of antibacterial activity for the compounds **11-15**

Figure – 7

Graphical representation of antifungal activity for the compounds **11-15**

Table captions

Table - 1

Analytical data for the compounds **11-15**

Table - 2

IR spectral data for compounds **11-15**

Table - 3

^{1}H NMR Chemical shift values (δ ppm) of *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15**

Table - 4

Coupling constant and dihedral angles for selected *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15**

Table - 5

^{13}C NMR Chemical shift values (δ ppm) of *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15**

Table - 6

Chemical shift differences between the *N*-piperazinoacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **11-15** and their parent *N*-chloroacetyl-*r*-2,*c*-6-diphenylpiperidin-4-ones **6-10**

Table - 7

Antibacterial activity for the compounds **11-15**

Table - 8

Antifungal activity for the compounds **11-15**

Table - 1

Compounds	Molecular formula	Melting point ℃	Yield %
11	$C_{24}H_{29}N_3O_2$ (391)	226-228	51.2
12	$C_{25}H_{31}N_3O_2$ (405)	220-222	64.1
13	$C_{26}H_{33}N_3O_2$ (419)	142-144	50.1
14	$C_{25}H_{31}N_3O_2$ (405)	108-110	49.3
15	$C_{25}H_{31}N_3O_2$ (405)	113-114	44.4

Table 2

Compounds	IR (cm^{-1})
11	3392(N-H), 3056-3030 (C-H Aromatic), 2935-2824 (C-H Aliphatic), 1715(C=O at C_4), 1642(C=O of *N*-$COCH_2$), 1453, 1079
12	3340(N-H), 3056-3030 (C-H Aromatic), 2944-2820 (C-H Aliphatic), 1711(C=O at C_4), 1634(C=O of *N*-$COCH_2$), 1496, 1024
13	3328(N-H), 3090-3030 (C-H Aromatic), 2968-2816 (C-H Aliphatic), 1702(C=O at C_4), 1631(C=O of *N*-$COCH_2$), 1498, 1017
14	3305(N-H), 3064 (C-H Aromatic), 2999(C-H Aliphatic), 1714(C=O at C_4), 1647(C=O of *N*-$COCH_2$), 1600, 1024
15	3326(N-H), 3087-3031 (C-H Aromatic), 2975-2819(C-H Aliphatic), 1716(C=O at C_4), 1635(C=O of *N*-$COCH_2$), 1585, 1016

Table – 3

Compound	H_2	H_3	H_{5a}	H_{5e}	H_6	Pip (a)	Pip(b)	NH	CH_2 of $NCOCH_2$	Aromatic protons	CH at C_3	CH_2 at C_3	CH_3 at C_3
11	6.57	a	2.80	a	6.11	3.04	2.52	2.16	a	7.53-6.99	-	-	1.07
12	6.28	2.87	3.03	2.70	5.81	2.91	2.44	1.71	3.17,3.03	7.38-6.85	-	1.28	1.06
13	6.56	2.80	2.84	2.75	5.70	2.91	2.47	2.14	3.27,2.95	7.36-6.96	2.03	-	1.04,1.13
14	6.20	-	b	2.92	5.59	3.02	2.54	4.93	b	7.34-6.65	-	-	1.32
15	4.93	c	c	c	4.93	3.12	2.58	5.46	c	7.35-7.11	-	-	1.03

a, b, c indicates merged with Piperazine (a) protons

Table – 4

Compound	$^{3}J_{5e,6a}$	$^{3}J_{5a,6a}$	$\Phi_{5e,6a}$	$\Phi_{5a,6a}$
12	3.0	7.0	47	167
13	6.50	8.0	32	152
14	7.0	10.0	36	156

Table – 5

Compound	C_2	C_3	C_5	C_6	Pip (a) carbons	Pip(b) carbons	*N*$COCH_2$	CO at C_4	CO of *N*$COCH_2$	Aromatic Carbons	*Ipso* carbons	CH at	CH_2 at	CH_3 at C_3
11	62.2	32.8	47.3	56.9	45.7	53.4	62.7	209.6	171.2	128.8-125.8	141.2,128.9	-	-	19.6
12	62.9	31.5	23.3	52.3	45.9	54.7	54.8	209.9	171.6	128.8-126.3	141.6,129.0	-	14.1	11.9
13	60.4	58.2	44.4	56.9	45.8	54.7	62.8	209.8	171.4	128.6-127.2	141.1,126.2	28.2	-	20.5,21.7
14	62.0	47.4	45.1	56.9	44.1	52.1	61.6	211.2	170.5	129.5-125.1	142.6,139.0	-	-	21.5,25.9
15	63.0	45.4	45.4	63.0	43.7	51.4	61.3	211.2	171.4	128.8-127.6	141.0,129.0	-	-	14.1

Table – 6

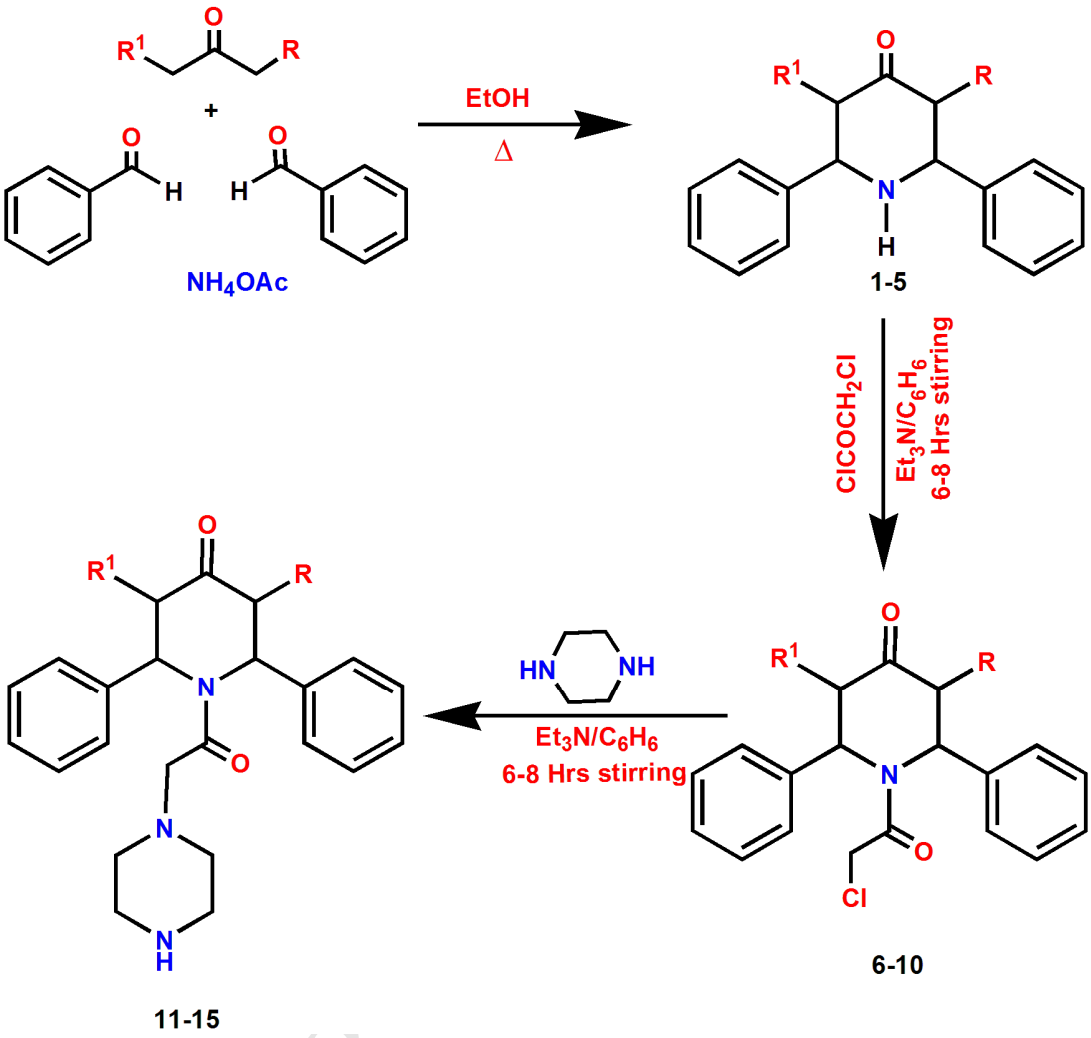
Compound	H_2	H_6	C_2	C_6
11	6.56	6.11	62.0	53.9
6	5.40	5.93	54.5	61.6
1	3.62	4.09	68.4	61.5
12	6.27	5.81	60.0	54.8
7	6.14	5.53	56.5	56.5
2	3.73	4.07	66.7	61.8
13	6.56	5.70	60.4	56.9
8	6.49	5.44	57.2	54.6
3	3.99	4.09	66.6	61.7
14	6.20	5.59	62.0	56.9
9	6.17	5.44	62.8	57.4
4	3.84	4.07	69.7	61.8
15	4.93		63.0	
10	5.49		61.1	
5	3.61		68.8	

Table - 7:

Sample (250 µg/disc)	Zone of inhibition (mm)				
	Proteus mirabilis	*Staphylococcus*	*E.Coli*	*E. faecalis*	*Klebsiella*
11	3	5	6	3	4
12	6	10	7	12	7
13	6	11	14	11	13
14	6	6	7	4	7
15	7	12	11	15	16
Chloramphenicol 250 µg/disc	5	7	9	6	8

Table - 8

Sample (250 µg/disc)	Zone of inhibition (mm)				
	A. niger	*A. flavus*	*A. oryzae*	*A. fumigatus*	*T.viride*
11	4	3	5	4	6
12	6	7	9	5	6
13	7	6	6	7	8
14	6	7	8	6	7
15	5	4	6	5	8
Chloramphenicol 250 µg/disc	6	5	7	6	8



	R	R^1		
1	Me	H	**6**	**11**
2	Et	H	**7**	**12**
3	*i*-Pr	H	**8**	**13**
4	$(Me)_2$	H	**9**	**14**
5	Me	Me	**10**	**15**

Scheme - 1

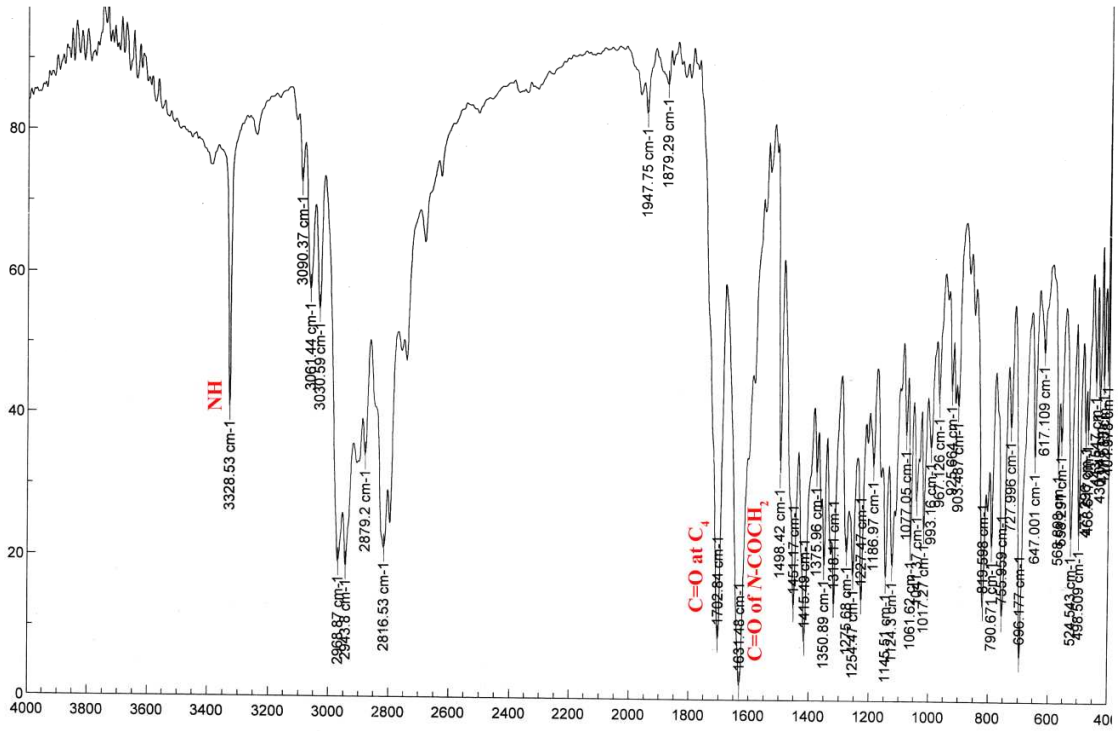


Figure - 1

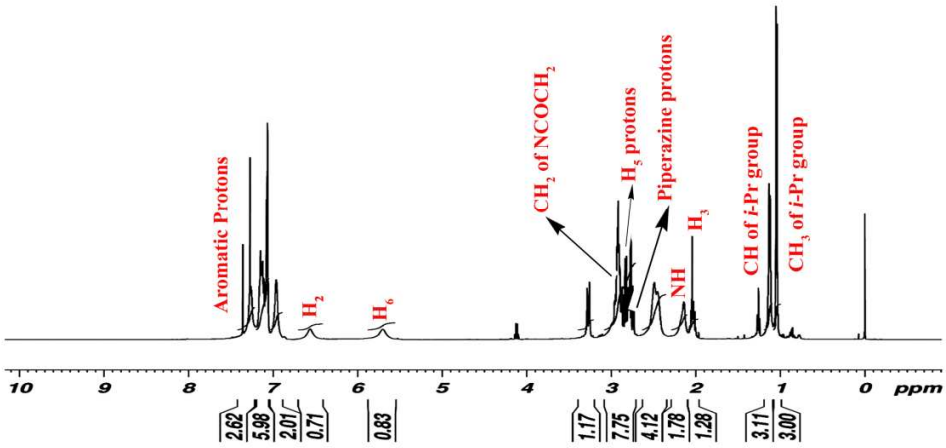


Figure – 2

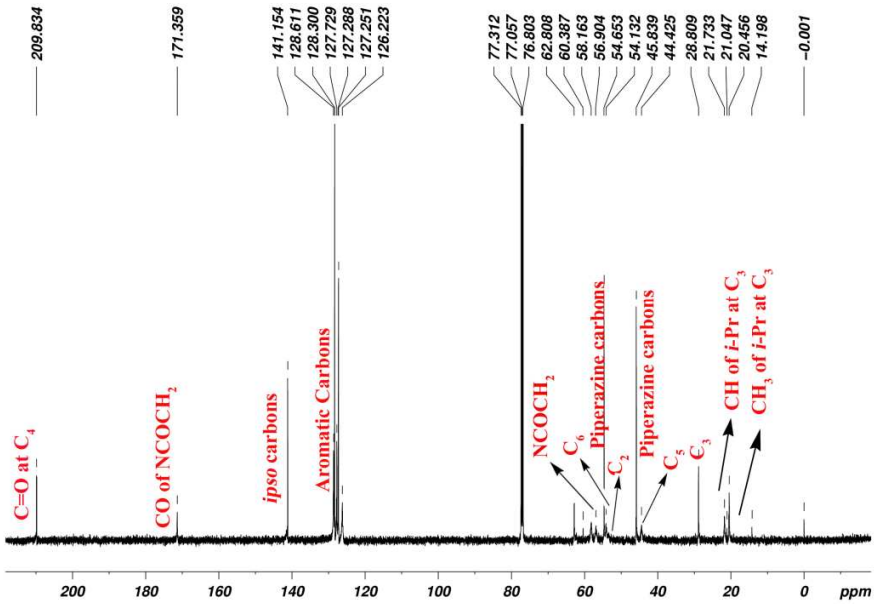


Figure – 3

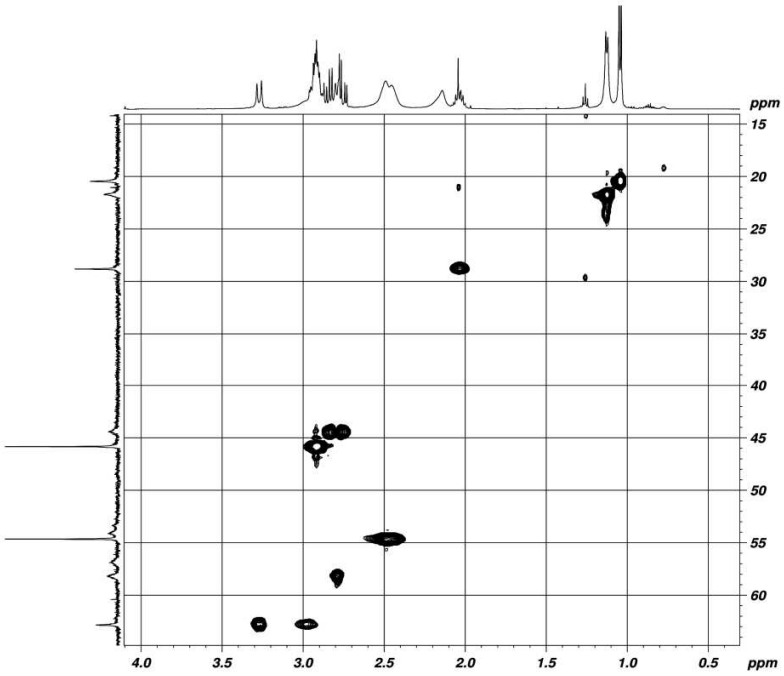
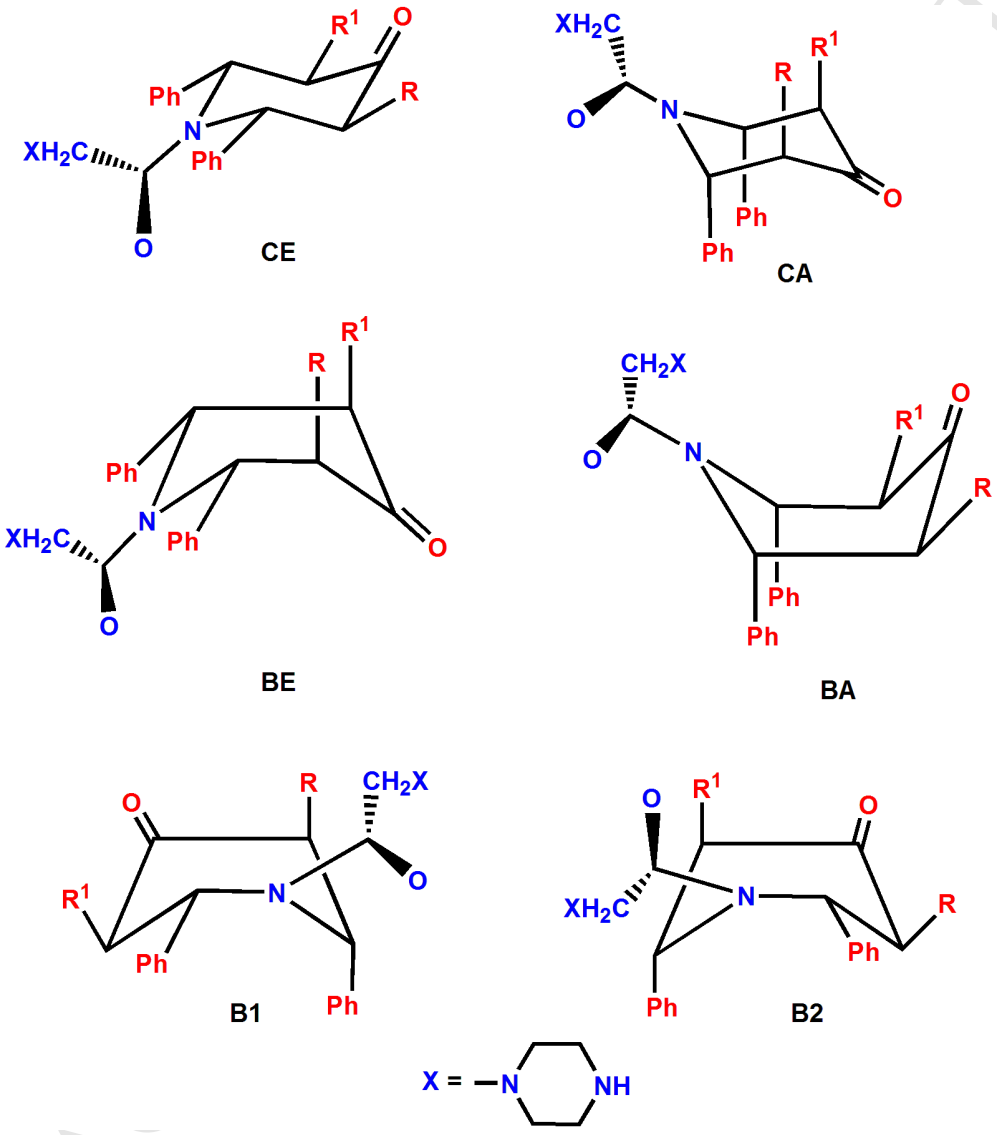


Figure - 4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XH2C
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R
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N
Ph
O
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CA
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R
Ph
N
XH2C
Ph
O
O
BE
CH2X
O
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O
N
R
Ph
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BA
R
CH2X
O
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N
R
Ph
Ph
B2
X = N NH

Figure-5

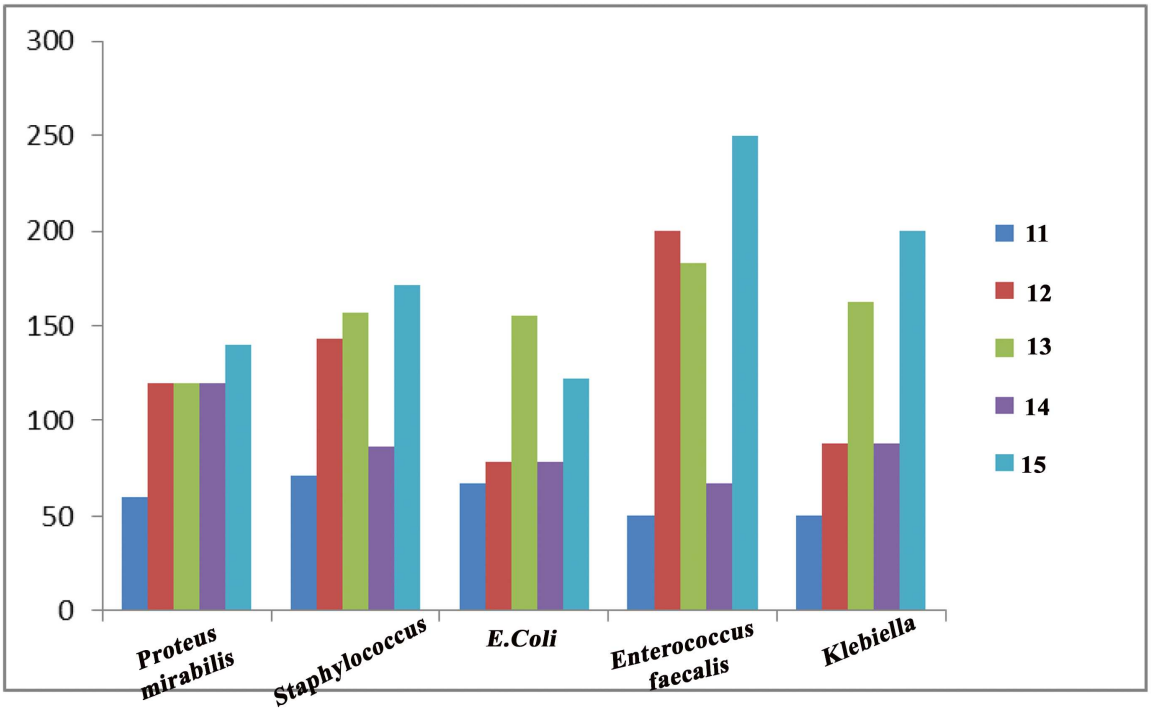

Figure – 6

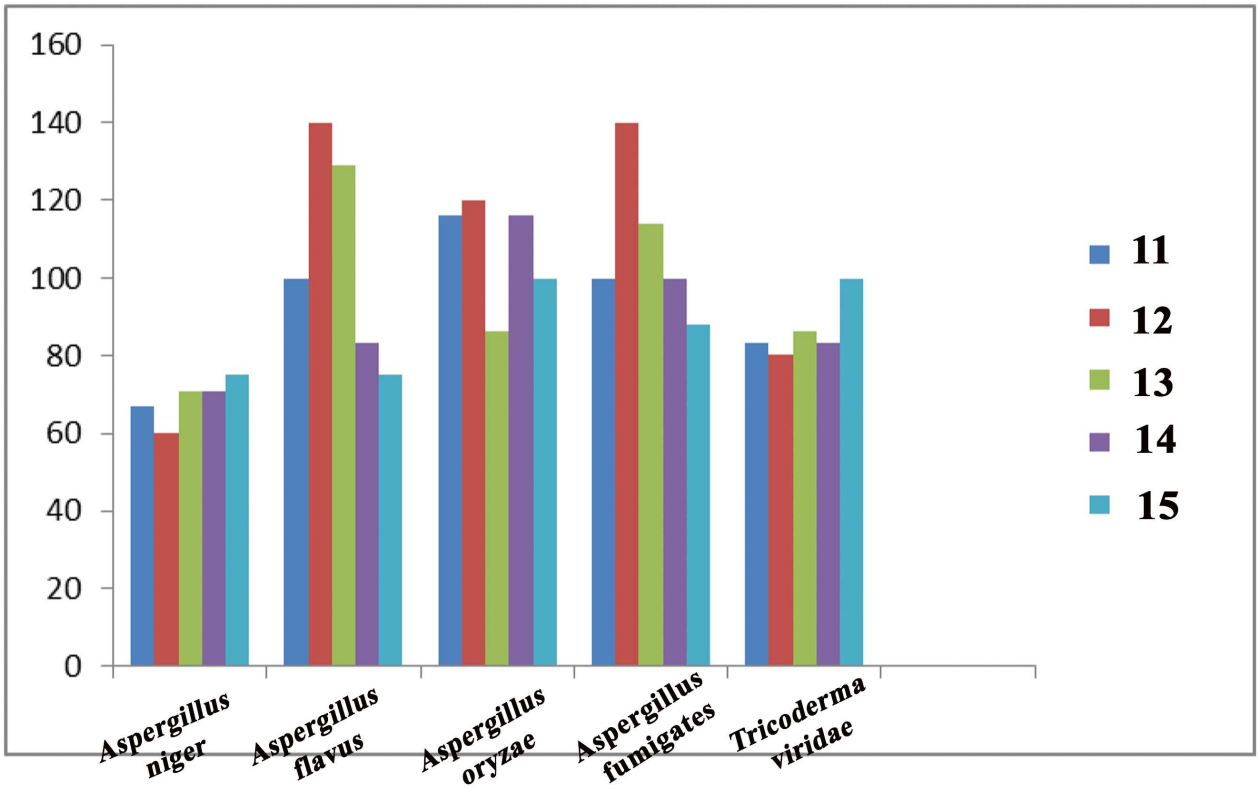

Figure – 7

Highlights

- Five piperidin-4-ones were synthesized and conformational analysis was carried out.
- Assignment of ^{1}H & ^{13}C NMR signals are made using 2D NMR spectra.
- All compounds prefer to exist in an equilibrium between **B1** and **B2** conformations.
- Antibacterial and antifungal studies were carried out for all the compounds.
- Compounds exhibit good activity against the selected bacterial and fungal strains.

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