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# Synthesis, Spectral Characterization and Biological Study of 3-of 3-Chloro-2,6-Bis-(4-Methoxy-Phenyl)-3-Methyl-Piperidin-4-One

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## *Abstract*

*Piperidin is an important class of heterocyclic compound which forms a part in many of the alkaloid compounds. Such compounds play a vital role in the field of medicinal chemistry. Several 2, 6-disubstituted derivatives of piperidin compounds are found to posses biological activities such as herbicidal, fungicidal, anticancer, anesthetic etc. In the present work a new piperidin -4-one with chloro and methyl substitution at 3-position have been prepared and characterized using IR, $^{1}$H NMR, $^{13}$C NMR and Biological studies.*

***Keywords***: *3-chloro-2;6-bis-(4-methoxy phenyl)-3-methyl-piperidin-4-one; IR, $^{1}$H NMR; $^{13}$C NMR; Biological studies.*

## 1. INTRODUCTION

Piperidin a heterocyclic amine, has a six membered ring. It is a colourless fuming liquid with an odour described as ammonical, pepper like. The name comes from the genus name piper, which is the Latin word for pepper. Piperidin is widely used as a building block and chemical reagent in the synthesis of organic compounds including pharmaceuticals.

Heterocyclic compounds are important class of compounds owing to their pharmacological, agrochemical and in brief, biological activities. The piperidin-4-one units are present in a variety of alkaloids which are occurring naturally. They find wide applications as drugs.

These aspects prompted us to take a study on the heterals, particularly on piperidinone chemistry. Literature report shows that a wide range of 2,6-as well as 3,5-disubstituted piperidinone-4-ones have been prepared, the substituents being alkyl, aryl and chloro groups[2-6]. There has been no report so for, on the chloro and methyl disubstitution of any on these positions. Keeping in view of this, it has been prepared chloro and methyl disubstituted piperidin-4-one at the third position. The compound has been analysed for its structural features and biological activity. The present study deals with synthesis of 3-chloro-2,6-bis-(4-methoxy phenyl) -3-methyl-piperidin-4-one. It is characterization by IR, $^{1}$H NMR, $^{13}$C NMR and biological studies.

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## 2. EXPERIMENTAL SECTION

### 2.1 Materials & Methods

#### *2.1.1 Synthesis of 3-Chloro-2, 6-Bis-(4-Methoxy-Phenyl)- 3-Methyl-Piperidin-4-One*

Dried ammonium acetate (4 gm 1 mol), 3-chloro-2-butanone (6 ml 0.03 mol) and 4-methoxy benzaldehyde (12 ml 2 mol) ethanol 10ml added are taken in RB flask.

Then the mixture is refluxed at 60-70 $^{o}$C in a water bath with shaking until the colour changes into red orange. The solution is cooled, then added ether (50 ml) and filter, solution is transferred into conical flask, con. HCl (5 ml) is added. White precipitate is formed.

The precipitate is washed with 5:1 ethanol : ether to remove the unreacted reactants and dried, added acetone (10 ml ), liquid ammonia (5 ml) and excess of coldwater to get the free base. Then the

product is recrystallised from ethanol. The melting point of compound is 125 $^{o}$C.

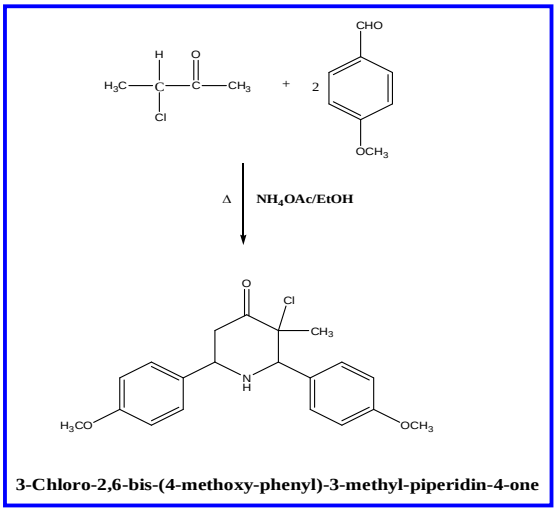


**Fig. 1: 3 – chloro – 2, 6 – bis - ( 4 - methoxy phenyl ) – 3 - methyl-piperidin – 4 – one. (3-chloro-2-butanone and ammonium acetate supplied by E.merk were used as such. 4 - methoxybenzaldehyde was supplied by BDH. Absolute alcohol of hayman is used as such. Silica gel.G supplied by BDH was used to prepare TLC plates.)**

## 3. RESULT & DISCUSSION

### Spectral characterization

IR (KBr): 3333 ($\upsilon_{N-H}$) 3023, 2926 ($\upsilon_{C-H}$ ), 1718 ($\upsilon_{C=O}$), 1543, 1448 ($\upsilon_{C=C}$), 758 ($\upsilon_{C-C1}$) cm-$^{1}$. $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.268 – 7.209 (d, 4H, ArH), 6.998-6.926(d,4H, ArH), 4.065-4.027 (d, 1H, Benzylic H), 3.935 (s, 1H, Benzylic-H), 3.857 (s,6H, methoxy protons), 3.458-3.394(t, 2H,$CH_2$), 2.545-2.503 (d,1H,NH), 1.698 (s,3H,$CH_3$). $^{13}$C NMR ($CDCl_3$, 100 MHz ): δ 201.7, 159.6, 158.7, 136.2,133.7,(128.4 & 128.1), 115.6, 114.9, 85.4, 65.4, 60.5, 56.6, 45.2, 21.9.

### 3.1 Anti-Microbial activities

The antimicrobial activities for the compound was carried out by Disc diffusion technique. The compound was tested against Gram positive bacteria (*Staphylococcus aureus & Klebsiella aerogenes*), Gram negative bacteria (*Escherichia coli & Pseudomonas aeruginosa*) and fungi (*Mucor & Aspergillusniger*). The test micro organisms were obtained from National Chemical Laboratory (NCL) Pune and maintained by periodical sub culturing on nutrient agar and sabour and dextrose medium for bacteria and fungi respectively.

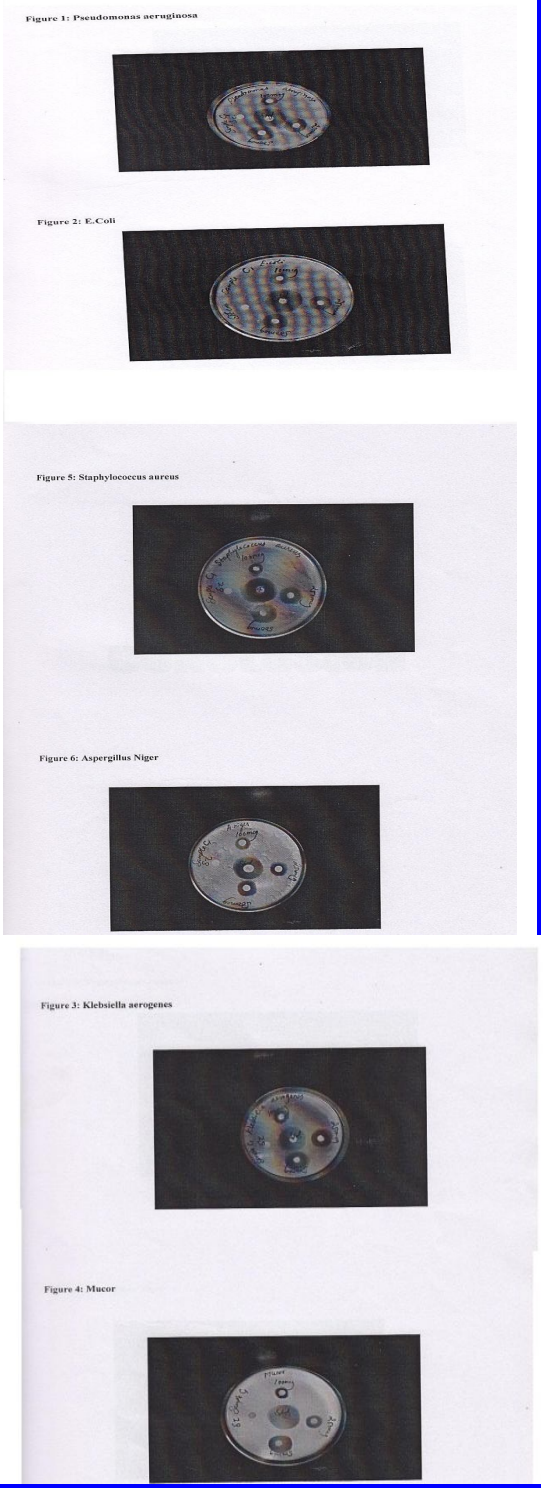


**Fig. 2: Showing zone of inhibition of antibacterial activity and anti fungal activity for 3-Chloro-2,6-Bis-(4-methoxy phenyl)3-methyl piperidin-4-one**

**Table 1. Standard – Ciprofloxacin 5 µ g/ disc for bacteria; Nystatin 100 units / disc for fungi. Solvent control (DMSO)**

| Sl.No | Name of the micro organisms | Diameter Zone of Inhibition in mm | | | | |
|---|---|---|---|---|---|---|
| | | Sample | | | Solvent Control | Standard |
| | | C1 100 µ | C1 250 µ | C1 500 µ | | |
| 1 | Staphylocous Aureus (NCIM 2079 ) | 13 | 20 | 24 | - | 35 |
| 2 | Klebsiella Aerogenes (NCIM 2098) | 16 | 20 | 25 | - | 30 |
| 3 | E.Coli (NCIM 2065) | 12 | 18 | 20 | - | 38 |
| 4 | Pseudomonas Aeruginosa (NCIM 2036) | 12 | 18 | 20 | - | 35 |
| 5. | Aspergillus Niger (NCIM 105) | 15 | 22 | 25 | - | 35 |
| 6 | Mucor (NCIM 108) | 18 | 26 | 30 | - | 32 |

Discs impregnated with known concentration of compound was placed on agar plate that had been inoculated uniformly over the entire plate with a culture of the micro organism to be tested. The plate was incubated for 24 hours at 37 $^{o}$C. During that period, the compound diffuses through the agar and prevent the growth of the organism. Effectiveness of the susceptibility is proportional to the diameter of zone of inhibition. The zone of inhibition was measured in mm and the activities were compared with Ciprofloxacin 5 µg/disc for bacteria and Nystatin 100 units/ager well for fungi as reference standard. It had been found that the compound possess appreciable antimicrobial activities against selected organism.

### 3.2 Anti-Bacterial activity

From the zone of inhibition, it is observed that 3-Chloro-2,6-Bis-(4-Methoxy Phenyl)3-Methyl Piperidin-4-One compared to the standard shows 69 % active against the bacteria *Staphylocous Aureus*. Similarly for the reference 82 % active against the bacteria *Klebsiella Aerogenes*. Similarly for thereference 53% active against the bacteria E.Coli. Similarly for the reference 56 % active against thebacteria *Pseudomonas Aeruginosa*. This compound value 82 % is higher. When compared to other values (69 %, 53 % & 56 % )

### 3.3 Anti-Fungal Activity

3 - Chloro - 2, 6 - Bis - (4-Methoxy Phenyl) 3-Methyl Piperidin-4-One compared to the standard shows 70% activity against the Fungai Aspergillus Niger. Similarly for the reference 95 % active against *Fungai Mucor*. This compound value is 95 % higher when compared to other value (70 %).

## 4. CONCLUSION

The compound 3 – Chloro - 2, 6 – Bis - (4-Methoxy Phenyl) 3 - Methyl Piperidin – 4 - One is prepared based on the procedure available in the literature. This compound analysis by IR, $^{1}$H NMR, $^{13}$C NMR and it is highly active against *Klebsiella Aerogenes* (Bacterial study) and highly active against Mucor (Fungai study).

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