

**SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL EVALUATION OF
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ABSTRACT

In an effort to establish new candidates with improved antimicrobial activity of N-(4-chlorophenyl)-2,6-bis(3-nitrophenyl)-4-oxopiperidine-3-carboxamide was synthesized, characterized and evaluated for antimicrobial activity. The desired compounds was synthesized by the condensation of 4-chloroacetoacetanilide, 3-nitrobenzaldehyde with ammonium formate. Compound was characterized by IR, ¹H-NMR, ¹³C- NMR and elemental analysis. They were also screened for antimicrobial activity against *Klebsiella pneumonia*, *Staphylococcus auerus*, *Shigellady sentaeriae*, *Escheria coli*, *Pseudomonous aeruginosa*, *Streptococcus pneumonia* and *Proteus vulgaris*.

KEYWORDS: 4-chloroacetoacetanilide, 3-nitrobenzaldehyde, Synthesis, Spectral studies and Antimicrobial activities.**INTRODUCTION**

Heterocycles form by far the largest of classical divisions of organic chemistry and are of immense importance biologically and industrially. The majority of pharmaceuticals and biologically active agrochemicals are heterocyclic while countless additives and modifiers used in industrial applications ranging from cosmetics, reprography, information storage and plastics are heterocyclic in nature. One striking structural features inherent to heterocycles, which continue to be exploited to great advantage by the drug industry, lies in their ability to manifest substituents around a core scaffold in defined three dimensional representations. For more than a century, heterocycles have constituted one the largest areas of research in organic chemistry. They have contributed to the development of society from a biological and industrial point of view as well as to the understanding of life processes and to the efforts to improve the quality of life. Among the approximately 20 million chemical compounds identified by the end of the second millennium, more than two-thirds are fully or partially aromatic and approximately half are heterocyclic.^[1]

Heterocyclic compound with a piperidone skeleton are attractive target for organic synthesis and there is found to be significant in compound possessing aromatic substitution in 2nd and 6th position in the piperidone rings.^[2-4] Piperidin-4-one was prepared in the laboratory based on the literature method.^[4-10] 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- substituted piperidinone-4-ones have been prepared, the substituents being alkyl, aryl and chloro groups.^[10-16] The compound has been analyzed for its structural features and biological activity. The present study deals with synthesis of N-(4-chlorophenyl)-2,6-bis(3-nitrophenyl)-4-oxopiperidine-3-carboxamide. It was characterized by IR, ¹H NMR, ¹³C NMR and biological studies.

MATERIALS AND METHODS

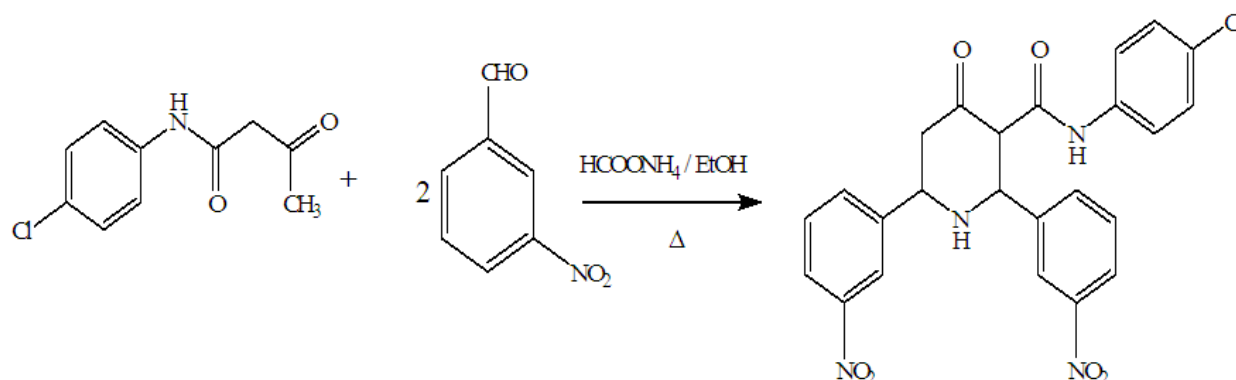
All the reagents and solvents used were of laboratory grade. The melting points of the compounds were determined by open capillaries on a Thomas Hoover apparatus and are uncorrected. The purity and homogeneity of compounds were checked using TLC technique. IR spectra were recorded using KBr pellets on Perkin Elmer 337 spectrophotometer, ¹H NMR were recorded on Bruker WH 500 spectrophotometer using CHCl₃ and DMSO as solvent.

EXPERIMENTAL METHODS

4-chloroacetoacetanilide (1.6g; 0.1mol), ammonium formate (4g; 0.1mol) and 3-nitrobenzaldehyde (3.02.gm; 0.03mol) were taken in a RB flask containing ethanol (10ml). The mixture was refluxed in a water bath with occasional shaking until the colour changed into red orange. The solution was cooled, and then ether (50ml)

was added. The filtered solution was transferred into conical flask and Con.HCl (5ml) was added. A white precipitate was formed. The precipitate was washed with 5:1 ethanol: ether mixture and dried. Acetone (10ml),

liquid ammonia (5ml), and excess of coldwater were added. The precipitate was formed, filtered and dried. Then the product was recrystallised with ethanol. The product was dried, m.p 220-222^oC.



SCHEME I: N-(4-CHLOROPHENYL)-2,6-BIS(3-NITROPHENYL)-4-OXOPIPERIDINE-3-CARBOXAMIDE.

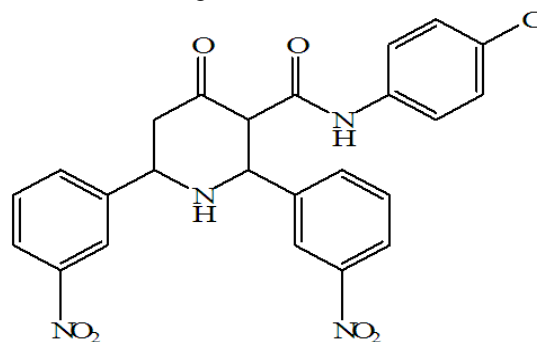
RESULTS AND DISCUSSION

Spectral characterization

N-(4-chlorophenyl)-2,6-bis(3-nitrophenyl)-4-oxopiperidine-3-carboxamide Yield: 86-92%; mp: 220-222^oC. FT-IR (KBr): 3406 (ν N-H), 3064 (ν aromatic-CH), 3030 (ν aliphatic-CH), 1714 (ν C=O), 704 (ν C-Cl), 1347 (ν C-N)cm⁻¹, ¹H NMR (500MHz, DMSO-d₆, δ in ppm); 7.97 (s, N-H, 2^o amide H); 7.09-7.55 (m, aromatic-H); 4.175 – 4.669 (d, benzylic-H at C₂); 3.363 – 3.892 (d, Methine H at C₃); 2.071(s, NH proton at ring). ¹³CNMR (500MHz, DMSO-d₆, δ in ppm): 201 (>C=O), 161,157,149,120.

N-(4-CHLOROPHENYL)-2,6-BIS(3-NITROPHENYL)-4-OXOPIPERIDINE-3-CARBOXAMIDE

Based on the above spectral data the compound is identified as and the given structure



BIOLOGICAL ACTIVITY

The obtained results are tabulated as following Table-I.

S.No	Name of the Micro Organisms	30 μ g/ml	35 μ g/ml	Solvent Control	Standard (Amoxycillin)
1	<i>Klebsiellapneumonia</i>	17	18	-	10
2	<i>Staphylococcus aureus</i>	16	20	-	9
3	<i>Shigelladysenteriae</i>	16	17	-	9
4	<i>Escherichia coli</i>	18	20	-	12
5	<i>Pseudomonas Aeruginosa</i>	15	19	-	11
6	<i>Streptococcus pneumonia</i>	20	18	-	11
7	<i>Proteus vulgaris</i>	16	18	-	8

Standard – Amoxylillin 10 μ g/disc for bacteria; Solvent – DMSO.

Followed by incubation at 37^oC for 24 Hrs and 25^oC for two days for bacteria and fungi were observed for zone of inhibition. The zone of inhibition was measured by using a standard scale. The diameter of the zone of inhibition directly proportional to the amount of active constituent present in the sample. The synthesized compound has high degree of inhibition towards *Klebsiellapneumonia*, *Staphylococcus aureus*, *Shigelladysenteriae*, *Escherichia coli*, *Pseudomonas*

Aeruginosa, *Streptococcus pneumonia* and *Proteus vulgaris*.

DISCUSSION

❖ The microorganism of *Klebsiellapneumonia* in microbial activity 30= 17mm, 35=18mm then standard 10mm.

- ❖ The microorganism of *Staphylococcus aureus* in microbial activity 30= 16mm, 35=20mm then standard 9mm.
 - ❖ The microorganism of *Shigelladysenteriae* in microbial activity 30= 16mm, 35=17mm then standard 9mm.
 - ❖ The microorganism of *Escherichia coli* in microbial activity 30= 18mm, 35=20mm then standard 12mm.
 - ❖ The microorganism of *Pseudomonas aeruginosa* in microbial activity 30= 15mm, 35=19mm then standard 11mm.
 - ❖ The microorganism of *Streptococcus pneumonia* in microbial activity 30= 20mm, 35=18mm then standard 11mm.
 - ❖ The microorganism of *Proteus vulgaris* in microbial activity 30= 16mm, 35=18mm then standard 8mm.
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CONCLUSION

A simple and elegant method for the synthesis of the compound described in this work. Nitrogen containing piperidine-4-ones are obtained, when more convenient ammonium formate is employed instead of the deliquescent ammonium acetate. The synthesized compound was characterized by FT-IR, ¹H-NMR, ¹³C-NMR and biological activity.

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