

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL STUDIES OF NOVEL HETEROCYCLIC COMPOUND

M. Sathyanarayanan, S. Mohamed Rabeek and M. Seeni Mubarak*

PG and Research Department of Chemistry, Jamal Mohamed College (Affiliated to Bharathidasan University), Tiruchirappalli - 620 020, Tamil Nadu, India.

Article Received on
29 March 2017,

Revised on 19 April 2017,
Accepted on 09 May 2017

DOI:10.20959/wjpr20176-8563

*Corresponding Author

M. Seeni Mubarak

PG and Research

Department of Chemistry,

Jamal Mohamed College

(Affiliated to Bharathidasan

University), Tiruchirappalli

- 620 020, Tamil Nadu,

India.

ABSTRACT

A novel, efficient and environmentally friendly method for the synthesis of 3-benzyl -2,6-bis-(1H-indol-3-yl)-piperidin-4-one. The compound has been derived by the condensation of 4-phenyl-2-butanone and Indole-3-carbaldehyde using ammonium acetate. The structure of the synthesized compound was elucidated by spectral studies such as IR, ¹H, ¹³C-NMR, Elemental analysis and Biological studies. The newly synthesized compound was screened by its antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, *Aspergillus niger*, *Klebsiella aerogenes* and *Candida albicans*.

KEYWORDS: 3-benzyl -2,6-bis-(1H-indol-3-yl)-piperidin-4-one, FT-IR, ¹H, ¹³C-NMR and Biological studies.

INTRODUCTION

The synthesis and structures of Mannich Bases have attracted much attention in biology and chemistry due to their model character and practical application. Mannich base piperidin-4-one has remained an important and popular area of research due to simple synthesis, adaptability and diverse range of applications. 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.^[1-3]

Literature reports shows that a wide range of 2,6 disubstituted piperidin-4-one.^[4-8] Among the piperidin derivatives, piperidones are important intermediates in several synthetic sections.^{[9-}

^{14]} Due to the known therapeutic properties of piperidones and the presence of keto functional

group that facilitates the introduction of other substituted derivatives of this class compounds have been found to possess biological activities such as herbicidal, insecticidal, fungicidal, anti-inflammatory, anesthetic, anti-virus and anti-cancer activity.

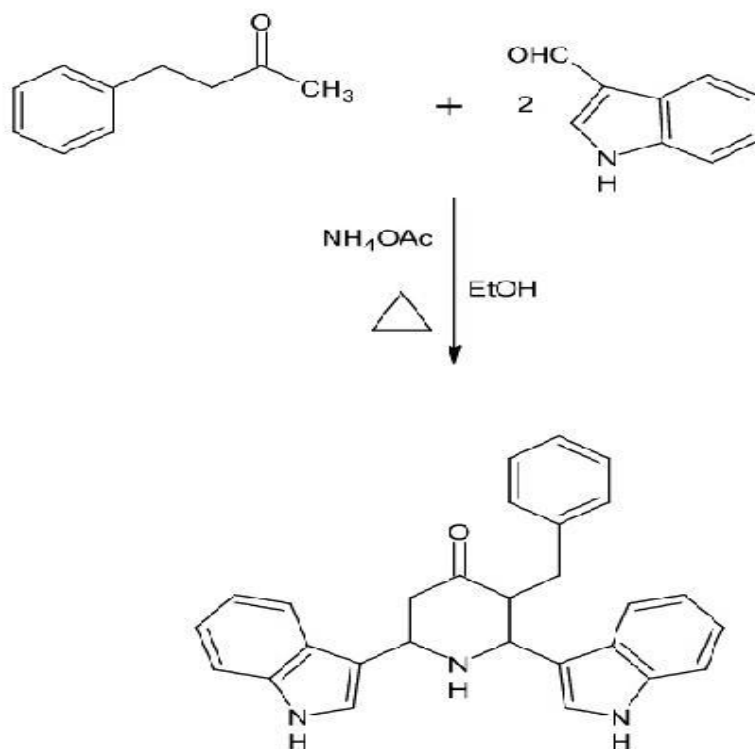
The antimicrobial activity was performed by the Disc diffusion technique method, using different concentrations (50mcg, 100mcg, 500mcg and 1000mcg). The sterile Muller hinton agar and Sabouraud dextrose agar were used for bacteria and fungi respectively. Two Gram positive, two Gram negative and two fungal strains were used to study the antimicrobial activity. All these strains were obtained from Pune. (NCIM-National collection of Industrial microbes). The Watt-man Number 2 filter paper of 6mm diameter was loaded with 100mcg of the diluted sample placed at equal intervals over the uniformly inoculated plate along with a standard disc Ciprofloxacin 5µg/disc for bacteria and Nystatin 100 units/disc for fungi were also placed along with sample to maintain quality control.^[15-18]

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-phenyl-2-butanone (1.48 ml; 0.1mol), ammonium acetate (4g; 0.1mol) and Indole-3-carbaldehyde (2.9 g; 0.02 mol) 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 (50 ml) was added. The filtered solution was transferred into conical flask and Con.HCl (5 ml) 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 cold water were added. The precipitate formed was filtered and dried. Then the product was recrystallised with ethanol. The product was dried, melting point 160-162⁰C.



3-BENZYL -2,6-BIS-(1H-INDOL-3-YL)-PIPERIDIN-4-ONE

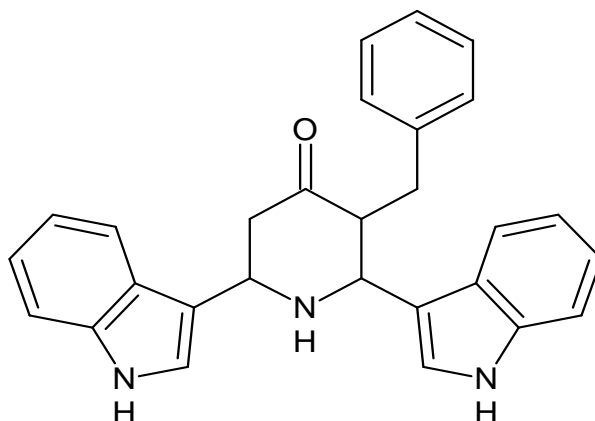
RESULTS AND DISCUSSION

Spectral Characterization.

3-benzyl -2,6-bis-(1H-indol-3-yl)-piperidin-4-one Yield: 87-94%; mp:160-162⁰C. FT-IR (KBr):3409 (ν N-H), 3054 (ν aromatic -CH), 2931 (ν aliphatic -CH), 1637 (ν C=O), 744 (ν C-C), 700 (ν C=C) cm^{-1} , ¹H-NMR (300MHz, DMSO-d₆, δ in ppm); 6.73-6.70 (t, 6H, aromatic H); 7.26-7.04 (m,12H, aromatic-H); 4.28-4.25 (d, 2H, benzylic-H (C₃ and C₅ protons)); 4.50-4.49 (d, 2H, benzylic-H (C₂ and C₆ protons)); 2.1 (s, 1H, NH); 10.1(indol N-H). ¹³C-NMR (100MHz, DMSO-d₆, δ in ppm): 206.4(>C=O), 158.09, 136.62, 130.0 -113.16, 66.01, 63.66, 54.81

Based on the above spectral data the compound is identified as

3-BENZYL -2,6-BIS-(1H-INDOL-3-YL)-PIPERIDIN-4-ONE and the given structure as



BIOLOGICAL STUDIES

The obtained results are tabulated as following Table: I

S.No.	Name of the Microorganisms	Zone of inhibition in mm					
		50mcg	100mcg	500mcg	1000mcg	Solvent control	standard
1	<i>Staphylococcus aureus</i> (NCIM2079)	16	18	20	20	-	35
2	<i>Basillus subtilis</i> (NCIM2063)	18	20	20	21	-	40
3	<i>Klebsiella aerogenes</i> (NCIM2098)	12	16	18	19	-	30
4	<i>Escherichia coli</i> (NCIM2065)	16	18	20	24	-	<u>38</u>
5	<i>Aspergillus niger</i> (NCIM2105)	16	18	18	20	-	35
6	<i>Candida albicans</i> (NCIM3102)	16	16	17	20	-	32

Standard-Ciprofloxacin 5µg/disc for bacteria: Nystatin 100units/disc for fungi.

Solvent-DMSO

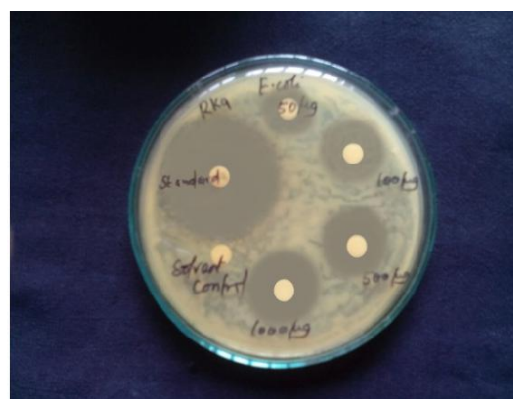
Fig-a: *S.aureus*Fig-b: *B. subtilis*Fig-c: *K.aerogenes*Fig-d: *E.coli*Fig-e: *A. niger*Fig-f: *C.albicans*

Figure-1: Zone of Inhibition

Antimicrobial activities of **3-BENZYL-2,6-BIS-(1H-INDOL-3-YL)-PIPERIDIN-4-ONE** Followed by incubation at 37⁰C for 24 Hrs and 25⁰C 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 compound were found to be effective against Gram positive (*Staphylococcus aureus* and *Basillus subtilis*). Among these two Gram positive the effect was found to be remarkable at low concentration (50 mcg) towards *Basillus subtilis* and more effective against Gram negative *Escherichia coli* and *Klebsiella aerogenes*. In the compound showed better response towards fungal strains *Aspergillus niger* and *Candida albicans*.

DISCUSSION

The micro organism of *Staphylococcus aureus* in microbial activity 50=16 mm, 100=18mm, 500=20mm, 1000=20mm then standard 35mm.

The micro organism of *Basillus subtilis* in microbial activity 50=18 mm, 100=20mm, 500=20mm, 1000=21mm then standard 40mm.

The micro organism of *Klebsiella aerogenes* in microbial activity 50=12mm, 100=16mm, 500=18mm, 1000=19mm then standard 30mm.

The micro organism of *Escheriachia coli* in microbial activity 50=16mm, 100=18mm, 500=20mm, 1000=24mm then standard 38mm.

The micro organism of *Aspergillus niger* in microbial activity 50=16mm, 100=18mm, 500=18mm, 1000=20mm then standard 35mm.

The micro organism of *Candida albicans* in microbial activity 50=16mm, 100=16mm, 500=17mm, 1000=20mm then standard 32mm.

CONCLUSION

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

ACKNOWLEDGEMENT

The Authors thanks the Principal and Management committee members, Jamal Mohamed College, Trichy- 620 020 for providing necessary facilities. We are very thankful to the

Sastra University, Thanjavur collected for NMR studies and also Periyar Maniyammai Pharmaceuticals College and Research Institute, Trichy for their help in antimicrobial susceptibility testing.

REFERENCES

1. Finer.I.L, "Organic Chemistry" ELBS, 1975; 2.
2. Noller.C and Baliah. V, J. Am. Chem. Soc., 1948; 70: 3853.
3. Baliah. V, Ekambaram A, Govindarajan T.S, Curr. Sci., 1954; 23: 264.
4. Baliah. V, Jeyaraman R, Chandrasekaran L. J. Am. Chem. Soc, Rev., 1983; 83: 379-423.
5. Baliah. V and Chandrasekaran. J, Indian Journal of Chemistry, 1977; 15B: 55S.
6. Baliah. V, Gopalakrishnan V, Jeyaraman R, Indian. J. Chem, Soc., Sec. B, 1978; 6B: 1065.
7. Baliah. V, Gopalakrishnan V, Jeyaraman R, Indian Journal of Chemical Society, Sec.B, 1978; 16B: 1065.
8. Fazal Mohamed M.I and Krishnapillay M, Indian. Chem. Soc., 1993; 70: 258.
9. Fazal Mohamed M.I and Krishnapillay M, Indian. J. Chem., 1997: 36B: 50.
10. Jeyaraman R and Avila S, Chem. Rev., 1981; 81: 1499.
11. Baliah. V and T.S. Govindarajan, Curr. Sce, 1954; 23: 91.
12. Baliah. V and A. Ekambaram, J. Indian. Chem. Soc., 1955; 33: 274.
13. Silverstein, Bassler and Morrill, Spectrometric Identification of Organic Compounds. 4th Edn. John Wiley and Sons.
14. Seenii Mubarak M, et al., Oriental J. Chem., 2011; 27(1): 333.
15. Ramani Devi R, Kathirvel R, Seenii Mubarak M, Mohamed Rabeek S, Fazal Mohamed M.I; International J.ITEE., 2014; 3: 1-4.