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Conventional Synthesis of Isonitroso Phenyl 2 Propanone and It's Screening for Antibacterial and Antifungal Activities

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Abstract- A new ketone Isonitroso phenyl 2 propanone (HINP2P) has been synthesized by the reaction of Benzyl magnesium chloride with cadmium chloride and acetyl chloride. On subsequent treatment of Phenyl 2 propanone with n- amyl nitrite gives Isonitroso Phenyl 2 Propanone. The structure of these compounds has been confirmed by physiochemical and spectral data. A preliminary screening of these compounds for biological activity against microorganisms has indicated that they are selective growth inhibitors.

I. INTRODUCTION

The title ligand Isonitroso phenyl 2 propanone (HINP2P) contain a reactive grouping —C(=O)—C(=NOH)— which determine the characteristic reactions of Isonitroso ketones1is The potential ambident ligands capable of forming metal complexes with different types of structure and bonding2. These compounds find several applications as sensitive and selective reagents in the detection and determination of various metal ions. In addition, many of these compounds possess a wide spectrum of biological activity3. The present paper deals with the preparation and characterization of the title ligand viz Isonitroso phenyl 2 propanone (HINP2P). Various physicochemical techniques such as elemental analysis, U.V., N.M.R., I.R. have been employed to assign the structures of the synthesized ligand. Their biological activity has been tested to find minimum inhibitory concentrations against microorganisms.

II. MATERIAL AND METHOD

The reaction was carried out with analytical reagent grade chemicals. The glasswares used were made of pyrex glass. The organic solvents were redistilled before use. Elemental analysis was done on Perkin Elemer elemental auto analyzer & CHNS thermoquest auto analyzer. I.R. spectra were recorded on Perkin Elemer RX1 Spectrophotometer in Nujolmull/KBr pellets. 1HNMR spectra were recorded on Brucker FT 300 at 300 MHz Nmr spectrophotometer at CDRI Lucknow. The chemical shifts were reported in δ units relative to TMS used as an internal standard. The antifungal and antibacterial activity of ligand INP2P is determined by disk diffusion method using various biological strains accoding to the method described elsewhere4.

III. SYNTHESIS OF PHENYL 2 PROPANONE

Benzyl magnesium chloride was prepared from a solution of 0.2 mol benzyl chloride in 100 ml. anhydrous ether and 0.2 mol magnesium turnings5. The clear dark solution was filtered. The solution of Grignard's reagent was diluted with ether so that the concentration was not greater than 0.2 mole per 300 ml and than cooled in an ice bath. Anhydrous cadmium chloride was added with vigorous stirring over 10-15 min. stirring was continued with cooling for 2 hrs. A solution of 0.1 mol acetyl chloride in 3 volumes anhydrous ether was added to the cold benzyl cadmium reagent over 5 min. The mixture was stirred in an ice bath for 1 hr., and hydrolyzed with 20% H2SO4. The ether layer was separated and the aqueous phase extracted twice with ether. The combined ether layer solutions were washed with water and 10% sodium bicarbonate and were allowed to stand without drying over night. The ether solution was then extracted with 10% sodium bicarbonate, and the combined aqueous extracts were extracted twice with ether, and all the pooled ether extracts were washed with water and dried over sodium sulphate. The ether was distilled off, and the residue was distilled to give phenyl 2- propanone.

Preparation of Isonitroso phenyl 2 propanone:

Isonitroso phenyl 2 propanone (INP2P) was synthesized as described. Dissolved 12 g of sodium in 250ml of absolute alcohol and to this solution, added in small portions, and with cooling, first 60 ml of n-amylnitrite and then 70 ml of Isonitroso phenyl 2 propanone. This mixture was allowed to stand for 2 days in a well-Stoppard bottle in a refrigerator. At the end of this time, the brown sodium salt was filtered and dried in air. The dried sodium salt was dissolved in a minimum quantity of ice cold water and treated with a calculated quantity of glacial acetic acid. Precipitated Isonitroso phenyl 2 propanone was then filtered through suction, and dried in vacuum. The crude product was recrystallised from benzene.

IV. RESULT & DISCUSSION

The melting point of INP2P was found to be 107o C (reported m.pt. 106-107oC). The results of chemical analysis are as follows:

Element	%C	%H	%N	%O
	66.01	5.36	8.32	19.34
	(66.23)	(5.56)	(8.58)	(19.61)

Electronic Spectra:

The electronic spectra of INP2P in DMSO show as intense band at 211nm. It splits into two strong bands 241nm and 250nm in NaOH solution. This can be explained by presuming that the symmetric π electron system cloud of INP2P becomes asymmetric by the dissociations of a proton.

Infrared Spectra:

The infrared spectrum of free ligand HINP2P shows a broad band around 3190.17 cm-1 is known to be lowered due to the hydrogen bonding6, 7. Therefore the absorption near 3190.17 cm-1 in HINP2P is assigned to the hydrogen bonded OH stretching. This assignment is further confirmed by the presence of new band at 2925.18 cm-1 in the spectrum of the HINP2P. In the spectrum of HINP2P many bands are observed in the region 1650-650 cm-1. Some of these bands are assigned on the basis of their position and intensity. HINP2P shows two picks at 1640.40 cm-1 and 1602.44 cm-1 which may be attributed to the ν C=O and ν C=N respectively. This is supported by the fact that they do not shift appreciably where as ethylacetoacetate is reported9 to show two ν C=O bands at 1738 cm-1 and 1717 cm-1. The lower peaks are probably due to hydrogen bonding. The peak at 1400-1450 cm-1 may possibly be due to - CH stretching. The ν N – O stretching frequency in simple oximes108 appear between 900-960 cm-1. But in quinone oximes it is observed at a slightly higher frequency 1000 cm-1 probably due to the increase in the double bond character. Patel109 has assigned the bands at 1000 cm-1 and 1200 cm-1 in isonitrosoacetylacetate (HINAA) to ν N – O stretching frequencies. The peak near 1047.75 cm-1 in HINP2P may therefore be attributed to ν N – O stretching modes, as expected these peaks are not shifted appreciably. Moreover, peaks due to the common group such as methyl are found at their respective positions reported in lliterature10.

NMR Spectra:

The nuclear magnetic resonance spectrum HINP2P in DMSO solution revels a peak around 8.30 δ due to =NOH group, aromatic ring are observed at 7.18 δ and for –CH2 group at 3.38 δ. The proton signal due to –CH group appears at 6.74 δ. It may be mentioned that the dioxime solutions of isonitrosoacetylacetone (HINAA) & Isonitrosoacetophenone99(HINAP) show =NOH resonance at 8.65 δ & 8.60 δ respectively. Similarly HIMAP show =NOH proton resonance at 8.64 δ.

Antimicrobial & Antibacterial test:

The synthesized ligand HINP2P was screened in vitro for antibacterial activities against Gram-positive S. aureus , B. subtillis, B. cereus and Gram-negative P. aeruginosa, E. coli and K.pneumonae as well as antifungal activities against C. albicans and A. niger by disk diffusion method. Gentamycin and miconazole were used as standard for antibacterial and antifungal activity respectively. The agar dilution method was performed using Mueller-Hinton agar (HiMedia) medium for antibacterial activity and Saburoud's dextrose agar (HiMedia) medium for antifungal activity.

It is observed that ligand INP2P is active aginst all the biological strains. But the synthesized compound does not show more activity as compared to standard drug.

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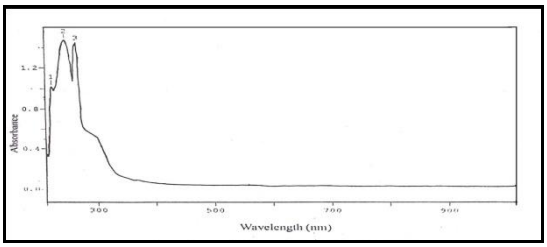
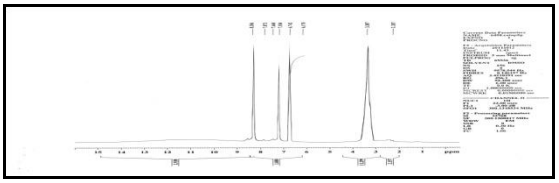
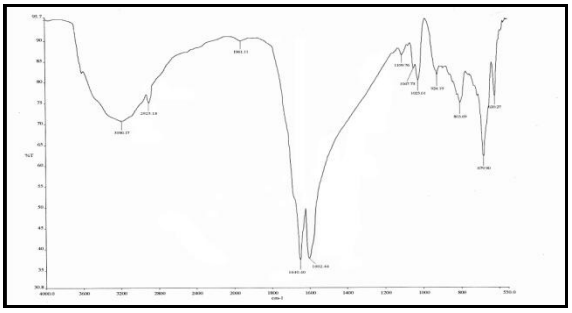
ABSORPTION SPECTRA OF HINP2P



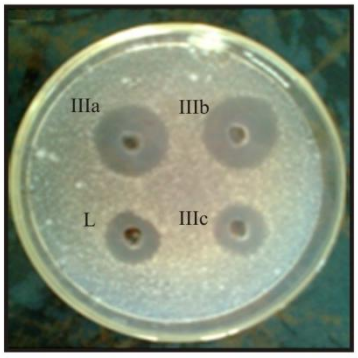
NMR SPECTRA OF INP2P



INFRARED SPECTRA OF INP2P



Photographs showing zone of inhibition by standard Gentamycin against bacteria E.coli



Photographs showing zone of inhibition by INP2P and complexes against bacteria E.coli