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Synthesis, growth, characterization, structure and molecular docking studies of 1-[(*E*)-{[4-(morpholin-4-yl)phenyl]imino} methyl] naphthalen-2-ol single crystal: A potential antimicrobial agent

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HIGHLIGHTS

- Asymmetric unit contains two crystallographically independent molecules in different orientations.
- Morpholine ring adopts *chair* conformation.
- Compound exhibits potent antimicrobial activities against *Gram-positive*, *Gram-negative* bacteria and yeast.
- Morpholine derivative exhibits good inhibition against anti-cancer protein Hsp90.

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ABSTRACT

High-quality single crystals of *1-[(E)-{[4-(Morpholin-4-yl)phenyl]imino}methyl]naphthalen-2-ol* were grown by slow evaporation method using ethylacetate solution at room temperature and the sample is characterized by FTIR, UV–visible, NMR and single crystal X-ray diffraction studies. The crystal structure was solved by direct methods and refined by full-matrix least-squares procedure to a final reliability value of 0.047. The asymmetric unit contains two crystallographically independent molecules in different orientations. The weak O--H···N and C--H···π interactions are responsible for the stability of the molecules in the unit cell. The antimicrobial activity of the compound was screened using different species of bacteria and for their ability to inhibit the heat shock protein 90(Hsp90). Molecular docking studies also supported the work.

1. Introduction

Morpholine and its derivatives possess diverse pharmacological and physiological activities such as antidiabetic [1,2], antiemetic [3,4], platelet aggregation inhibitors [1], antihyperlipoproteinemics [1], bronchodilators [5], growth stimulants [5] and antidepressants [1,5,6]. They are used in the treatment of inflammatory diseases, pain, migraine and asthma [4]. Morpholine have been widely investigated, due to their importance in the search of new therapeutically and biologically active compounds [7]. The molecule morpholine is a building block in the preparation of antibiotic and anticancer agents. Morpholine is used as an emulsifier and solubility aids for shellac, which is used as a wax for fruit coating [8].

Morpholine is a simple heterocyclic compound that has a wide range of industrial applications. Morpholine and its derivatives are used as rubber additives, corrosion inhibitors, solvents, optical brighteners, antioxidants and also in the manufacture of a number of drugs and herbicides. Consequently, morpholine occurs in industrial effluents and can be disseminated in the environment. The Schiff bases of 4-(4-aminophenyl)-morpholine possess potential antimicrobial properties [9]. 4-Phenyl morpholine derivatives are reported as anti-inflammatory [10] and central nervous system [11] activities.

In the present study, synthesis, growth, characterization, structure and antimicrobial activity of the compound 1-[(*E*)-{[4-(morpholin-4-yl)phenyl]imino}methyl]naphthalen-2-ol [MPIMN] was established. The structure analysis and tautomeric studies were carried out using FT-IR, ^{1}H NMR, ^{13}C NMR, UV–visible and

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X-ray crystallographic methods. Molecular docking study was also performed on MPIMN with the targeted protein Hsp90.

2. Experimental procedure

2.1. Synthesis of the compound

An ethanolic solution (20 ml) of 4-(4-aminophenyl) morpholine (10 mmol) was magnetically stirred in a round bottom flask followed by drop wise addition of 2-hydroxy-1-napthaldehyde (10 mmol). The reaction mixture was then refluxed for three hours and upon cooling to 0 °C, a red crystalline solid precipitates in the mixture. The solid is separated out, filtered, washed with ice cold ethanol and dried in vaccum over anhydrous $CaCl_2$. Single crystals suitable for X-ray diffraction studies were obtained by slow evaporation in ethyl acetate at room temperature (mp = 175–180 °C). The schematic diagram of the synthesis is shown in Scheme 1.

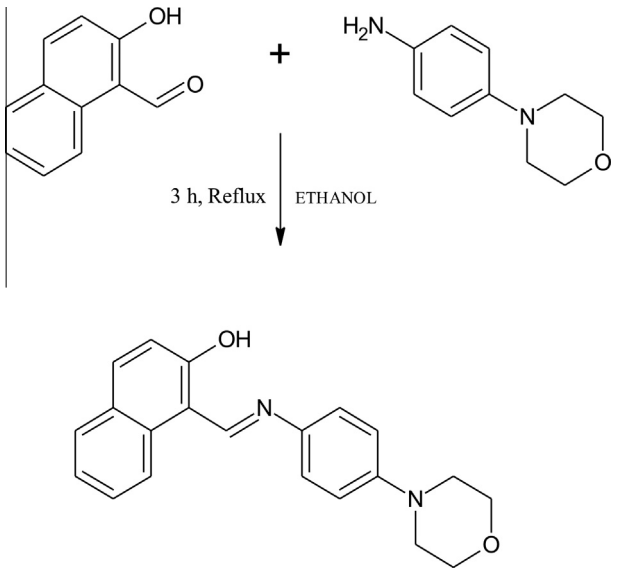
2.2. Crystal growth

The solubility of the compound is determined by adding the solvent to a known amount till it completely dissolved. A supersaturated solution was prepared by dissolving the sample in the ethylacetate at ambient temperature. The prepared solution was filtered, slightly warmed and allowed to evaporate slowly at room temperature, in a dust free atmosphere [12]. After about 3 days, good quality tiny crystals appeared and were allowed to grow to a maximum possible dimension and then harvested. The grown reddish transparent crystals are shown in Fig. 1.

3. Results and discussion

3.1. UV–visible spectral studies

The UV–visible spectrum was recorded using a LAMBDA 35 UV–visible spectrophotometer in the range 380–800 nm. The scanned spectrum is displayed in Fig. 2. The UV spectrum of MPIMN was recorded at room temperature. The maximum absorption takes place at a wavelength of 515 nm. The band observed around 389 nm is due to charge transfer from imine nitrogen to aromatic ring. The band is found at 515 nm which indicates the presence of conjugation linkage of C=C bond (hyper congregation).



Scheme 1. Synthesis of MPIMN.

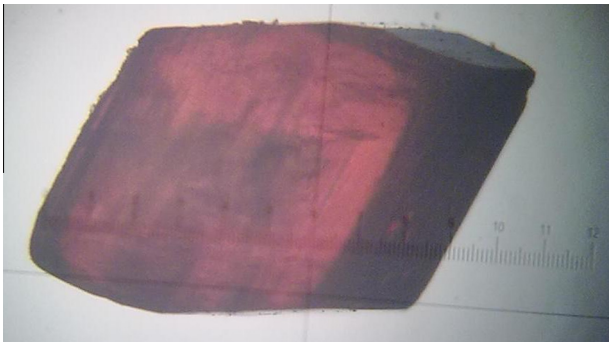


Fig. 1. Grown crystals of MPIMN.

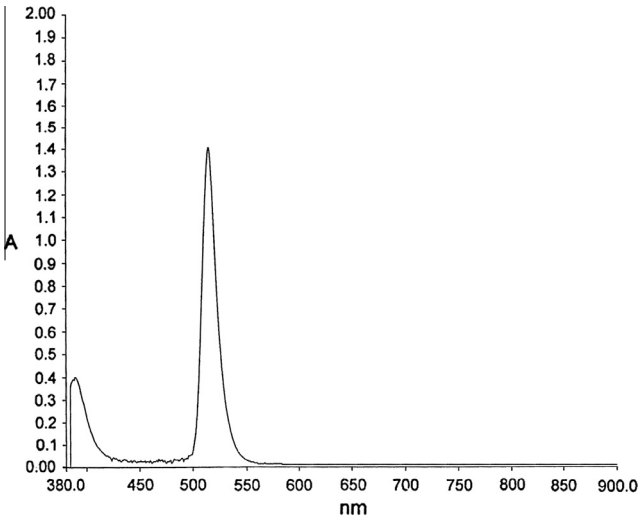


Fig. 2. UV spectrum of MPIMN.

3.2. FTIR spectral analysis

The FTIR analysis of MPIMN was carried out to investigate the presence of functional groups and their vibration modes, as shown in Fig. 3. FTIR spectrum was recorded in the range 400–4000 cm^{-1} at room temperature using SPECTRUM RXI FT-IR spectrophotometer. The bands appeared at 3430 cm^{-1} shows the presence of —OH group. The bands appeared at 1698 cm^{-1} and 1625 cm^{-1} correspond to C=N— functional groups. The band observed at

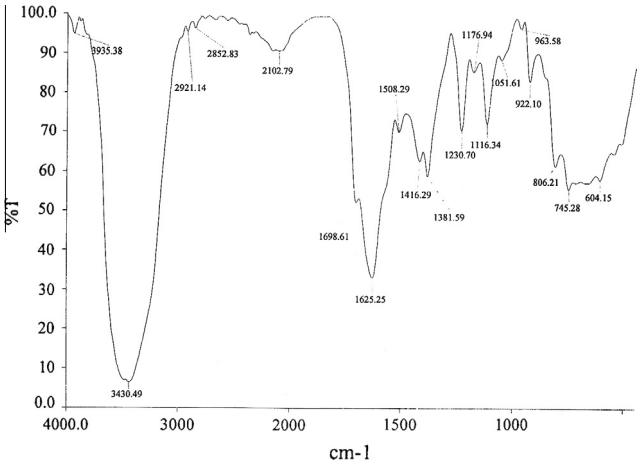


Fig. 3. FTIR spectrum of MPIMN.