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Research Article

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Synthesis, Structural Characterization and Molecular Modeling Studies of New Schiff Base Derived from Hydrazino benzoxazine and Vanillin

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ABSTRACT

A novel Schiff base ligand 3-(2-(4-hydroxy-3-methoxy benzylidene) hydrazinyl)-2H-benzo[b] [1,4]oxazin-2-one (HMB-HBO) was synthesized from Hydrazino benzoxazine and Vanillin and characterized by elemental analysis, IR, ^{1}H-NMR, LC-MS mass, electron absorption spectra and powder X-ray diffraction. 3D molecular modeling structure of the ligand was obtained by using Argus lab software. The Schiff base HMB-HBO is expected to behave as a multidentate chelating ligand, which can coordinate with the deprotonated phenolic oxygen, carbonyl oxygen and azomethine nitrogen atoms with different metals forming stable polymeric complexes possessing various biological activities.

Keywords: Hydrazino benzoxazine; Vanillin; Powder XRD; 3D modeling; multidentate chelating ligand.

INTRODUCTION

Schiff bases are widely used as chelating ligands in coordination chemistry [1] and are useful in catalysis, in medicine as antibiotics, antiallergic and antitumor agents [2]. The Schiff base metal complexes derived from heterocyclic compounds have been the center of attraction in recent years [3]. Schiff bases play important role in coordination chemistry as they easily form stable complexes with most transition metal ions [4]. Many biologically important Schiff bases have been reported in the literature possessing, antibacterial [5], antifungal [6], anti-inflammatory, antimicrobial, anticonvulsant, anti-HIV and antitumor activities [7]. A literature survey reveals that a Schiff base containing poly functional group can coordinate with transition metal ions forming metal complexes. Benzoxazines are an important class of N-containing heterocyclic compounds which exhibit a wide range of biological activity and are used as key structural motifs for the synthesis of various pharmaceutical agents. Benzoxazines show diverse biological activities including plant resistance factor against microbial diseases and insects, potassium channel modulators, anti-rheumatic and antihypertensive activity [8]. In view of the importance of such benzoxazines, in the present research article we described the synthesis and characterization of the Schiff base 3-(2-(4-hydroxy-3-methoxy benzylidene) hydrazinyl)-2H-benzo[b] [1,4]oxazin-2-one (HMB-HBO) which was characterized by elemental analysis, ^{1}H-NMR, mass, IR, UV-Vis spectral methods.

EXPERIMENTAL SECTION

2.1 Chemicals and Instrumentation

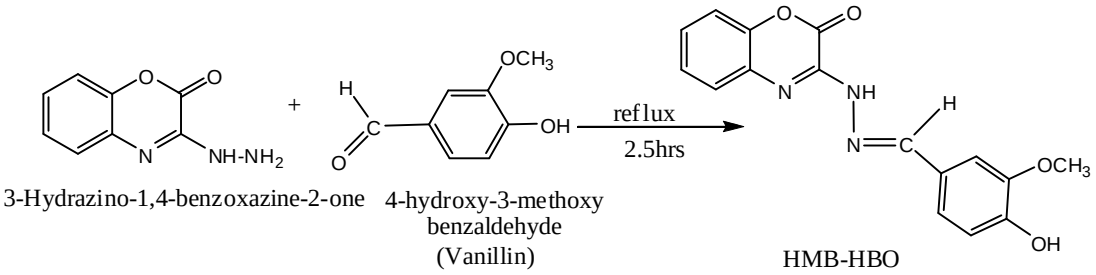
All the organic solvents of analytical grade were procured from Merck (India) and other chemicals (oxalyl chloride, o-amino phenol, o-dichloro benzene, Hydrazine hydrate, Vanillin) used were purchased from Sigma Aldrich company and were used without further purification. ^{1}H-NMR data was obtained on a Varian 400 MHz Mercury plus spectrometer using DMSO-d_6 at RT using TMS as internal standard. IR spectra was recorded in the region of 4000 - ≈ 400 cm^{-1} using KBr discs on Bruker optics Germany TENSOR 27 FTIR instrument. Far IR spectrum was recorded in the region of 750 - ≈ 250 cm^{-1} using IR Prestige-21 Shimadzu spectrophotometer. UV-3600 Shimadzu UV-Vis-NIR spectrometer was used to record Solid UV spectra. Using Thermo Finnigan Flash EA 1112 elemental

analyzer elemental analysis was performed. LC-MS mass spectrum was recorded on a Shimadzu Japan LCMS-2010 A spectrometer. Rigaku Miniflex diffractometer was used to record XRD in the range of 5° to 80° 2θ values. The possible geometry of the Schiff base was evaluated using molecular calculations with Argus lab software.

2.2 Preparation of the Schiff base HMB-HBO

HMB-HBO was prepared by a three-step process involving the synthesis of 1,4-Benzoxazine-2, 3-dione [9] and 3-Hydrazino-1, 4-benzoxazine-2-one (HBO) [10].

To HBO (1.77 g, 0.01 M) dissolved in 25 ml of hot distilled water, 4-hydroxy-3-methoxy benzaldehyde (Vanillin) (0.01M, 1.52 g) dissolved in minimum amount of hot water was added slowly. The contents were then refluxed on a heating mantle for two and half hours. The Schiff base was separated out as an off white solid. It was filtered while hot, washed thoroughly with small quantity of distilled water, recrystallized using acetic acid and dried in desiccator. Fig.1.



3-Hydrazino-1,4-benzoxazine-2-one 4-hydroxy-3-methoxy benzaldehyde (Vanillin) HMB-HBO

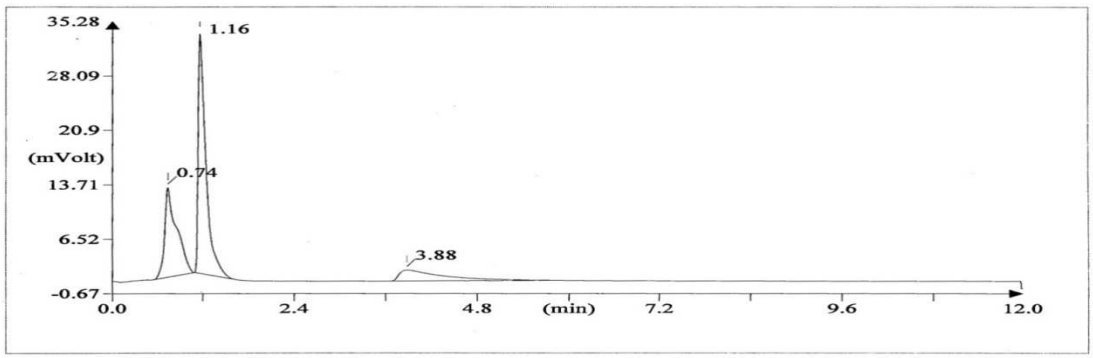
Fig.1 Preparation of HMB-HBO

2.3. Molecular Modeling Studies of HMB-HBO

The geometry of the Schiff base was evaluated using Argus lab software [11] and geometry optimization of the molecule was done by Quantum mechanics based AM1 approximation which was used for molecular orbital calculations of HMB-HBO

RESULTS AND DISCUSSION

The new Schiff base HMB-HBO is soluble in DMSO. The melting point was found to be 298-300 °C and the Yield obtained was 85 %. The molecular formula of the Schiff base is calculated as $C_{16}H_{13}N_3O_4$ based on the analytical data which is in close match with the expected structure. The data suggests 1:1 condensation of Vanillin with 3-hydrazino-1, 4-benzoxazine-2-one. Fig.2.



Element Name	Element %	Ret. Time
Nitrogen	13. 36	0. 74
Carbon	61. 85	1. 16
Hydrogen	4. 28	3. 88

Fig.2 CHN data of HMB-HBO

3.1. LC-MS spectrum of HMB-HBO

The M+1 peak observed at m/z 312 in the LC-MS mass spectrum is in good agreement with its molecular weight 311. Fig.3

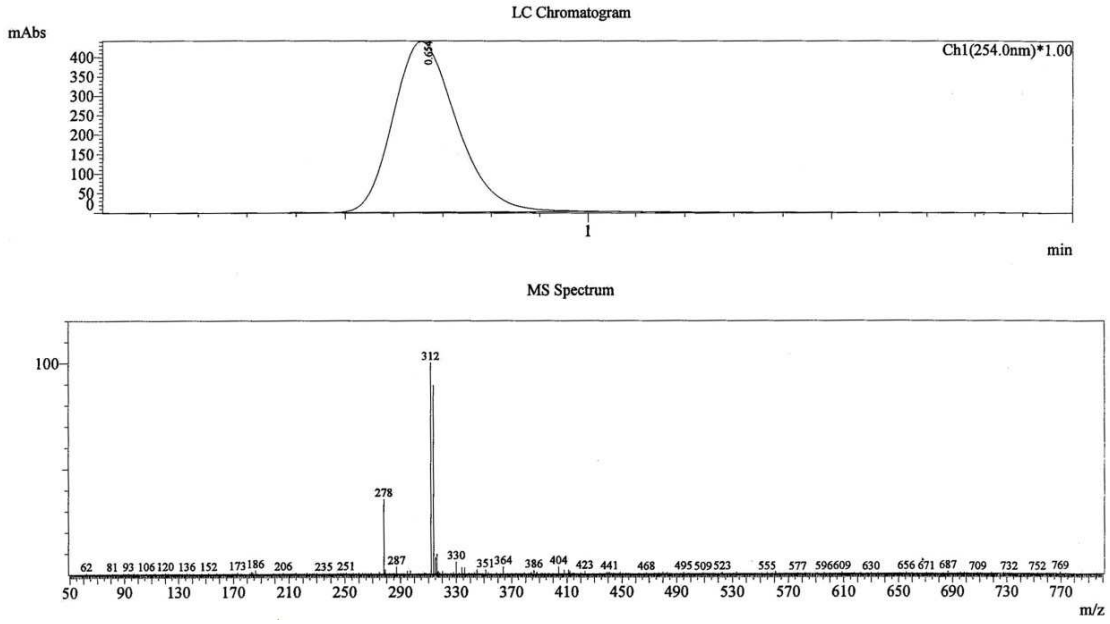


Fig.3 LC-MS Spectrum of HMB-HBO

3.2. ^{1}H-NMR Spectrum of HMB-HBO

^{1}H-NMR spectrum of HMB-HBO was recorded in DMSO-d6. The chemical shifts (δ) are given in ppm downfield from tetra methyl silane Fig.4. The spectrum showed exchangeable signals due to NH and phenolic OH. The spectrum has indicated signals in the range of 6.4δ to 7.5δ which can be attributed to aromatic protons of HMB-HBO. The methoxy protons resonated at 3.83δ (singlet) [12]. A signal at 8.47δ (singlet) can be attributed to the azomethine =CH proton [13]. The singlet at lower field 9.63δ can be assigned to NH proton [13]. The singlet at lower field 12.07δ can be assigned to phenolic OH proton. The three aromatic protons of vanillin group of Schiff base appear as two doublets at 6.85 and 7.09 δ and a singlet at 7.26 δ. The four aromatic protons of benzoxazine moiety show their appearance at 7.50δ as a doublet and a multiplet in the range of 6.45 – 6.75 δ, where the integration of each signal matches with the expected structure. ^{1}H-NMR spectral data is shown in Table 1.

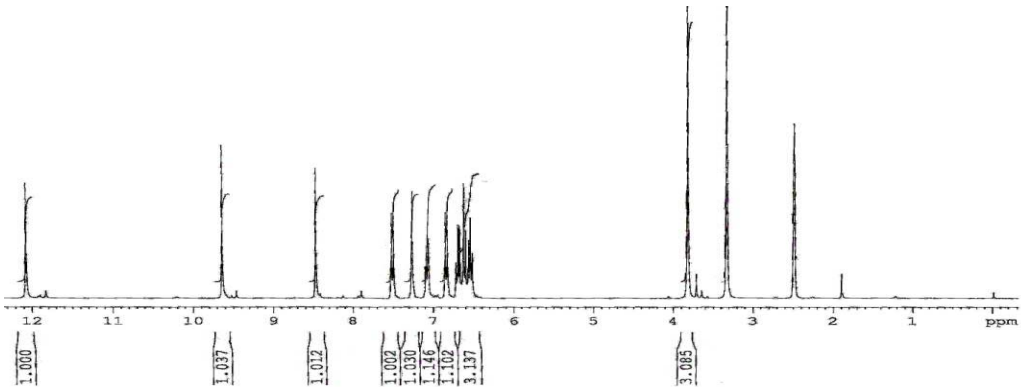


Fig.4 ^{1}H-NMR Spectrum of HMB-HBO

Table 1. ^{1}H-NMR spectral data of the HMB-HBO

Chemical shift (δ, ppm)	Multiplicity	Number of protons	Type of protons assigned
6.4-7.5	1(m), 3(d) and 1(s)	7	Aromatic protons
3.83	Singlet	3	-OCH3
8.47	Singlet	1	Azomethine =CH
9.63	Singlet	1	-NH
12.07	Singlet	1	-OH

3.3. IR spectrum of HMB-HBO

The IR spectrum of HMB-HBO presents a peak at 3501 cm^{-1} corresponding to ν OH (phenolic), a sharp peak at 3238 cm^{-1} can be assigned to ν NH. The ν C-O (phenolic) is observed at 1210 cm^{-1} [14, 3]. The strong band with a shoulder noticed at 1656 cm^{-1} can be attributed to ν C=O of lactone carbonyl group. The spectrum also presents sharp bands at 1603 cm^{-1} & 1512 cm^{-1} corresponding to ν C=N of free and ring azomethine groups. The stretching mode of ν N-N can be observed at 958 cm^{-1} [15]. It also shows bands due to aromatic and aliphatic stretching. 3038 cm^{-1} peak and a group of 3 peaks at 1475-1430 cm^{-1} corresponds to aromatic ν CH and ν C=C stretching modes respectively [16] and a band in the region 2750-2923 cm^{-1} may be given to the aliphatic -CH stretching of $–OCH_3$ in vanillin moiety Fig.5. The characteristic infrared frequencies are given in Table 2.

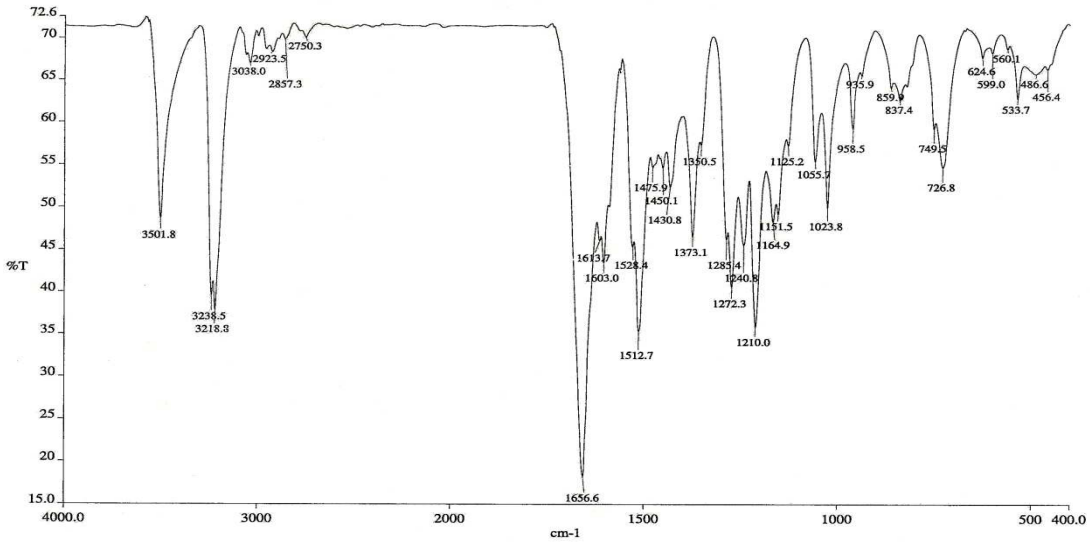


Fig.5 IR spectrum of HMB-HBO

Table 2. Characteristic infrared frequencies of HMB-HBO (cm^{-1})

ν OH	ν NH	ν C=O	ν C=N (free)	ν C=N(ring)	ν C-O	ν N-N
3501	3238	1656	1603	1512	1210	958

3.4. UV-Vis spectrum of HMB-HBO

The UV of solid sample of the Schiff base was recorded in the range of 200-1600 nm. The electronic spectrum exhibits several electronic bands corresponding to the expected structure summarized in Table 3. The bands observed at 49751- 44642 cm^{-1} are due to the π-π* transitions of substituted benzene moieties of the HMB-HBO [10]. The bands appearing at 38461 – 36764 cm^{-1} can be attributed to the n- π* transition of benzoxazine moiety [10] and hydrazine side chain. The band at 30959 cm^{-1} is due to the n-π* transition of phenolic group. The band observed at 30030 cm^{-1} is confined to transition of lactone carbonyl chromophore and bands at 29154 and 28985 cm^{-1} are due to π-π* and n-π* transitions of ring and free azomethine groups [12, 17]. Fig.6.

Table 3. UV-Vis spectral data of HMB-HBO

UV-Vis Bands (ν)cm^{-1}	Assignment
49751 - 44642	π-π* transitions of substituted benzene moiety.
38461 - 36764	n-π* of benzoxazine moiety and hydrazine side chain.
30959	n-π* transition of phenolic functional group.
30030	n-π* transition of lactone carbonyl group chromophore.
29154 & 28985	π-π* and n-π* transitions of ring and free azomethine groups.

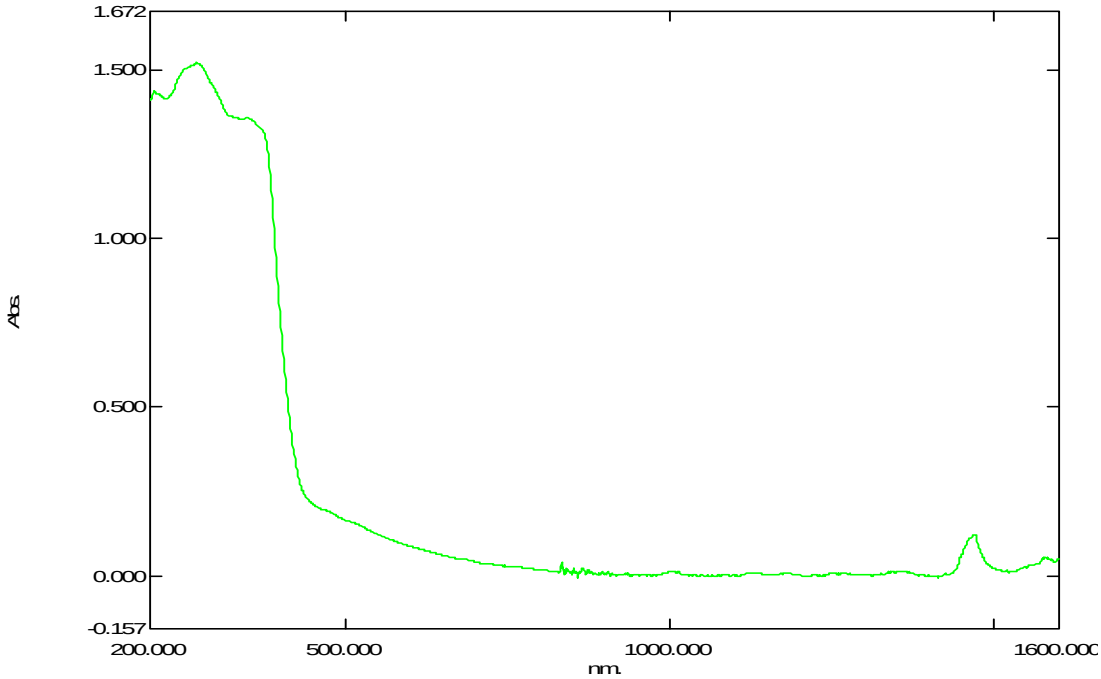
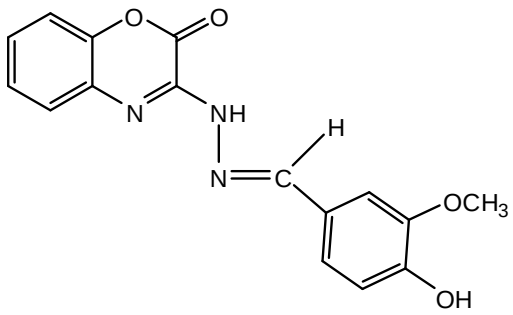


Fig.6 UV-Vis Spectrum of HMB-HBO

From the above obtained data the proposed structure of HMB-HBO is:



3.5. Molecular Modeling Studies of HMB-HBO

The geometry of the Schiff base was evaluated using Argus lab software [11]. Geometry optimization of the built molecule was done using molecular mechanics uniform force field (UFF) method. Quantum mechanics based AM1 (Austin Model 1) approximation was used to perform molecular orbital calculations for HMB-HBO and the electron density surfaces of highest occupied molecular orbitals (HOMO) and lowest unoccupied molecular orbitals (LUMO), generated from the calculations for the ground state are shown below. The Self consistent field (SCF) energy value and heat of formation ΔH_f for the optimized geometry are reported below. Figs.7, 8 & 9.

Final SCF Energy = -95158.5640 kcal/mol
Heat of Formation = -17.6953 kcal/mol

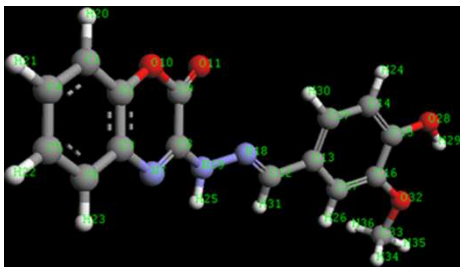


Fig.7 HMB-HBO

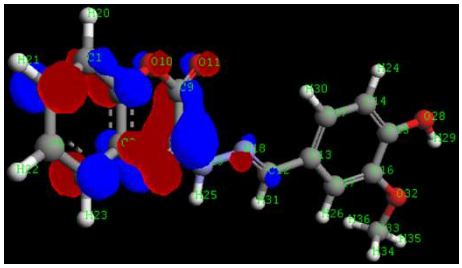


Fig.8 HMB-HBO (HOMO)

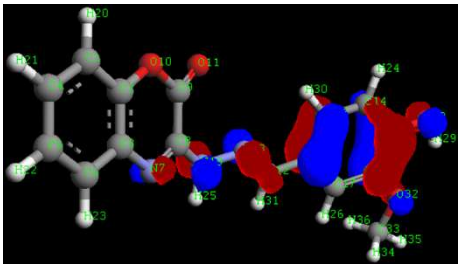


Fig.9 HMB-HBO (LUMO)

3.6. Powder X-Ray Diffraction Studies of HMB-HBO

Single crystal could not be prepared and hence powder diffraction data was obtained for structural characterization. The X-ray diffractogram was recorded in the range 5º to 80º 2θ values, which is shown in the Fig.10. The XRD pattern indicates that HMB-HBO has crystalline patterns with various degrees of crystallinity.

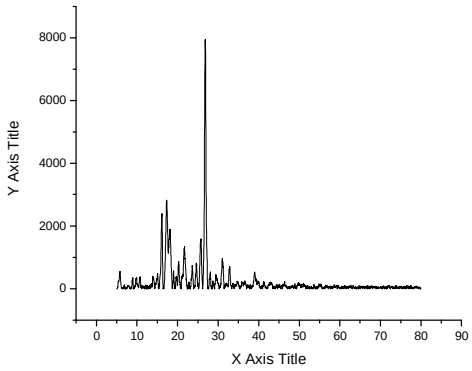


Fig.10 Powder XRD spectrum of HMB-HBO

CONCLUSION

In this study a novel Schiff base HMB-HBO has been synthesized and characterized. The Schiff base is of significant importance based on its chelation sites providing O & N atoms as donor sites for coordination with metals for effective metal binding reactions. The Schiff base HMB-HBO can behave as multidentate system producing polymeric complexes.

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