Synthesis, Physical Characterization, Antibacterial and Antifungal activities of a novel bis(3-((*E*)-1-(2-hydroxyphenyl)ethylideneamino)phenyl)methanone

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Abstract: Bis (3-((*E*)-1-(2-hydroxyphenyl) ethylideneamino) phenyl) methanone has been synthesized in this paper and its structure was confirmed by ^{1}H-NMR, ^{13}C-NMR, IR and Mass spectra. Its AM1 and B3LYP/6-31G* calculations to characterize the physical properties of this molecule has been also presented. Finally, the antifungal and antibacterial activities of this derivative have been evaluated.

Introduction
Particular attention has recently been paid to the synthesis and study of the diimino tetradentate Schiff bases and their complexes. This is due to their uses as biological models in understanding the structure of biomolecules and biological processes. The crucial role of Schiff bases in the biological function of bacteriorhodospin is proven. The retinal chromophore is bound covalently to the protein via a protonated Schiff base [1].Schiff-base ligands derived from 2-hydroxyacetophenone have been used as complexing agents [2]. In these ligands the electronic, steric and geometric effect of a methyl group on an imine carbon on asymmetric catalytic reactions can be investigated [3]. Salen type complexes are very well studied because this type of Schiff base ligands present suitable biometric properties that can mimic the structural feature of the active site[4].Based on these facts we decided to synthesize a new bis Schiff base derived from 2-hydroxyacetophenone.

Results and Discussion:
3,3'-Diaminobenzophenone **1** (0.212g, 1.00mmol) and 2-Hydroxyacetophenone **2** (0.272g, 2.00mmol) were dissolved in 10 mL of warm ethanol. The reaction mixture was refluxed for 10h and allowed to stand aside. The crystals were filtered off and washed with ethanol. The pure Schiff base **3** was recrystalized from ethanol as light yellow crystals. The IR spectrum showed the characteristic absorption of Schiff base C=N at 1612 cm^{-1}. The ^{1}H-NMR spectrum showed a multiplet for aromatic protons at 6.76-7.85 ppm. The OH group appeared as a singlet at 14.37 ppm. The ^{13}C-NMR spectrum showed C=N group at 162.23, C=O group at 196.97 and the CH$_3$ group at (18.48, 30.61). The mass spectrum showed the (M+1) peak at 449. The yield was 57%.
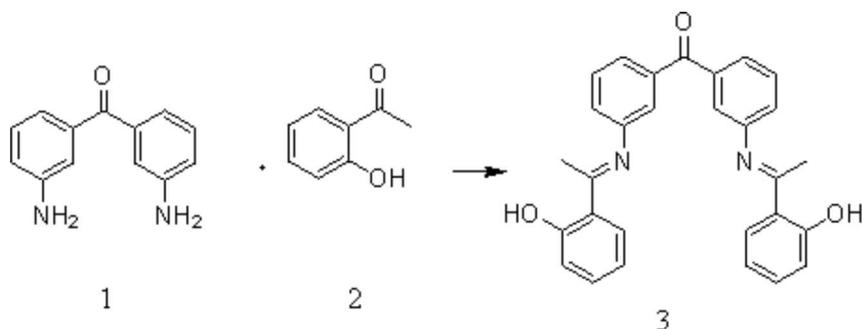
Melting point: 182-184 °C.

IR (KBr, cm^{-1}): 3248; 1716; 1612 cm^{-1}.

^{1}H NMR (250 MHz, CDCl$_3$): δ= 14.37 (OH); 7.85- 6.76 (Aromatic protons); 1.65 (s, CH$_3$).

^{13}C NMR (62.9 MHz, CDCl$_3$): δ= 196.97; 162.23; 148.62; 138.29; 117.67; 116.98; 114.34; 30.61; 18.48.

MS: 449 (M+1), 195, 120, 92, 65, 43.

All calculations in this work where carried out with the AM1 level of theory using the GAUSSIAN 03 [5] suite of programs. In addition we have carried very intense B3LYP/6-31G* optimizations and frequency calculations. More information about these methods is available elsewhere [6]. Figure 1 presents the optimized structure of the molecule with bond lengths and bond angles shown as well as the theoretical IR vibrational spectrum.
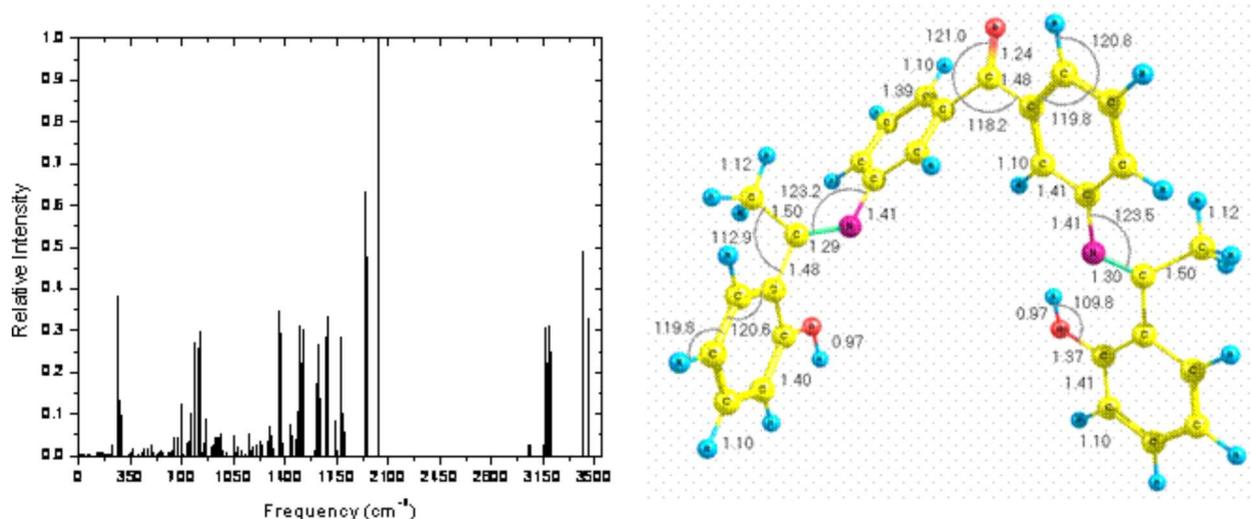

Figure 1. AM1 optimized structure and its theoretical IR vibrational spectrum for molecule **3**.

	Fitted Thermodynamic Equation (T/1000=t)	100 K	298.15 K	**1000 K**
C_p	$61.26809 + 1473.5495*t -123.39616*t^2 -341.74085*t^3 -0.0486*t^{-2}$	205.78	477.77	1077.52
S	$53.05624*\ln(t) + 1474.23257*t + 423.72982*t^2/2 -484.29762*t^3/3 -32.45372/(2*t^2) -3357.13221$	518.49	863.88	1807.1
ΔH	$89.57261*t + 1689.9106*t^2/2 -308.96521*t^3/3 -332.76221*t^4/4 + 0.78161/t -370.051$	13.13	80.56	670.35

Table 1: Thermodynamic properties of the molecule **3** in Figure 1, calculated at the AM1 level and B3LYP/6-31G* of theory, where C_p is the heat capacity in J mol^{-1} K^{-1}, S is the entropy in J mol^{-1} K^{-1}, and ΔH is the standard entha mol^{-1}. These where fitted to the Shomate equations which are implemented by the JANAF tables of the NIST data

These equations converged to an R^2 value of 0.999 on average.

Table 1 shows the thermodynamic properties for the where T (temperature in K), S (entropy in J mol-1 K-1), C molecule in Figure 1 capacity at constant pressure in kJ mol^{-1} K^{-1}), and $\Delta H = H° - H°298.15$ (enthalpy content, in kJ T1=100 K, T2=298.15 K, and T3=1000 K calculated AM1 and B3LYP/6-31G* frequencies. The fits were per according to the equations implemented by the National Institute of Standards and Technology (NIST) [7]. These eq have been very good at predicting physical properties of various molecules, as we have tested in the past [6-10].

Antibacterial and antifungal tests

Derivative **3** was evaluated for its *in vitro* biological properties against human pathogens [11]. This compound was found to possess no antifungal activities against *S. cerevisiae* (ATCC 28383) and no antibacterial activities against Gram-positive and Gram-negative bacteria even if a slight antibacterial activity against *S. aureus* (CIP 4.83) at a concentration of 100 µg/mL has been noticed (Table 2).

Sample CIP	Antimicrobial activity (MIC), µg/mL			
	S. cerevisiae (ATCC 28383)	S. aureus (4.83)	C. albicans (1180-79)	E. Coli (54127)
3	>100	100	>100	>100

Table 2: Antimicrobial activity of Schiff base **3**

Acknowledgment

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Sample Availability: Available from MDPI.