

Synthesis, Characterization, Electrochemical, Biological and Thermal Studies of Binucleating Tetradentate Schiff Base Derivative

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In this study, binucleating tetradentate Schiff base derivative was synthesized, characterized, screened for antibacterial activities on five bacteria and investigated of electrochemical behaviours. Electrochemical behaviours were investigated on the glassy carbon electrode surface with cyclic voltammetry. The Schiff base showed antibacterial activity using disc diffusion method.

Key Words: Schiff base, Synthesis, Antibacterial activity, Glassy carbon electrode, Thermal analysis.

INTRODUCTION

Azomethines are generally known as Schiff bases to honour Hugo Schiff, who synthesized such compounds. These are the compounds containing characteristic -C=N- group. In coordination chemistry, Schiff bases have a significant role as ligands still a century after their discovery^{1,2}. The importance of Schiff bases and their metal complexes are important as biochemical³, electrochemical⁴, analytical⁵, antiviral and antibacterial activities^{6,7}, redox catalysts⁸. Schiff bases with donors (N, O, S, etc.) have structural similarities with biological systems and imports in elucidating the mechanism of transformation and racemization reaction in biological systems due to presence of imine (-N=CH-) group⁹.

In the present work, we have synthesized binucleating tetradentate Schiff base ligand. The antibacterial activities of the synthesized Schiff base were reported *in vitro* using disc diffusion method against the bacteria: *B. cereus*, *E. coli*, *B. subtilis*, *S. mutans* and *S. aureus*. Electrochemical behaviours were investigated on the glass carbon electrode surface with cyclic voltammetry.

EXPERIMENTAL

All chemicals were of analytical-reagent grade from Fluka and Sigma-Aldrich and were used directly without further purification. Electrochemical experiments were carried out using a conventional three-electrode system. All solutions were prepared with 0.1 M TBATFB in DMSO at 1 mM concentration used in surface modification. A three-electrode cell was employed incorporating a glassy carbon

electrode (BAS Model MF-2012, 0.071 cm² diameter) as working electrode, Ag/Ag⁺ (0.01 M AgNO₃ in 0.1 M TBATFB) (BAS Model MF-2042) for non-aqueous media as reference electrode and a platinum wire (BAS Model MW-1032) as auxiliary electrode. Reference electrodes calibrated to the E_{1/2} of 1 mM ferrocene in 0.1 M TBATFB.

N,N'-tetrakis-(2,5-dihydroxy-benzylidene)-3,3'-diaminobenzidine (H₄L): A mixture of 3,3'-diaminobenzidine (0.107 g, 0.5 mmol) and 2,5-dihydroxybenzaldehyde (0.276 g, 2 mmol) in absolute ethanol was refluxed for 4 h, m.p. 303-304 °C. Elemental analysis (%): Found: C, 69.18; H, 4.38; N, 8.10. Calcd. for C₄₀H₃₀N₄O₈: C, 69.16; H, 4.35; N, 8.06. Some IR frequencies (KBr, ν_{max}, cm⁻¹): 3347 (O-H); 1275 (C-O); 1616 (C=N); 1503 (C=C). ¹H NMR (DMSO-*d*₆): 12.23 (d, 4H, *J* = 5.2), 10.17 (s, 2H); 10.05 (s, 2H) Ar-OH; 9.13 (s, 4H) HC=N; 8.95-6.80 (m, 18H) Ar-H ppm. LC-MS; C₄₀H₃₀N₄O₈ [m/z] calculated: 694.71, found: [M] = 695, [M⁺] = 696.

Antibacterial activity: The antibacterial activities of the Schiff base were tested *in vitro* using disc diffusion method¹⁰. Bacterial inoculums were prepared from overnight grown cultures (24 h) in Nutrient broth (Difco) and turbidity was adjusted equivalent to 0.5 McFarland units (*ca.* 10⁸ cfu/mL). Aliquots (100 μL) of inoculums were spread over the surface of Mueller Hinton Agar (Difco) plates with a sterile glass spreader. Sterilized paper discs (Oxoid, 6 mm diameter) were wetted with 10 μL of a solution of each compound to be tested, in the concentration of 0.02 g/mL (200 μg per disc) in DMSO. DMSO had no effect on the microorganism in the concentrations studied. The plates were then incubated 24 h at 37 °C.

RESULTS AND DISCUSSION

In this study, binucleating tetradentate Schiff base ligand was synthesized following the preparative route illustrated in Fig. 1. The compound was labeled as H₄L. The important IR absorption bands for the synthesized Schiff base, the strong band show at 1616 cm⁻¹ is assigned to the ν(C=N) stretching mode. In the IR spectrum, ligand exhibits broad band at 3347 cm⁻¹ corresponding to the stretching vibration of O-H groups. The band show at 1503 cm⁻¹ is assigned to the ν(C=C) stretching mode. This band proves the presence benzene^{11,12}. ¹H NMR spectrum of the H₄L exhibits a singlet at 9.13 ppm due to the imine protons. The spectra of the ligand shows multiplet signals at 6.80-8.95 ppm, integrated for the aromatic hydrogens of the phenyl rings. The ¹H NMR spectra of H₄L shows signals at 10.05-12.23 ppm characteristic of the aromatic O-H groups^{12,13}. The mass spectrum of H₄L showed base peak at m/z (%) = 695 (100.0 %), which corresponding to its molecular formula C₄₀H₃₀N₄O₈. The results of LC-MS and elemental analysis were found in good agreement with the calculated values.

H₄L give pattern two stages of decomposition within the temperature range 30-900 °C in the argon atmosphere. The TGA/DTA results are given in Table-1 (Fig. 2). Experimental mass losses are in a very good agreement with the TG/DTA results. Experimental weight losses are found in good agreement with the calculated values.

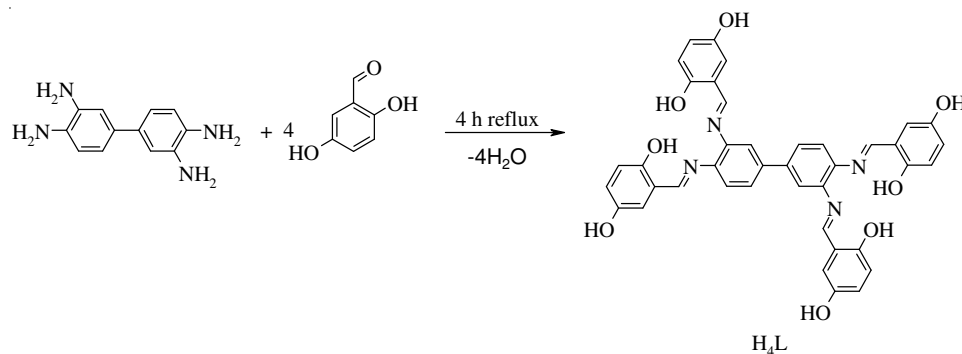


Fig. 1. Synthesis of *N,N'*-tetrakis-(2,5-dihydroxy-benzylidene)-3,3'-diaminobenzidine (H_4L)

TABLE-1
THERMAL ANALYSIS DATA FOR H_4L

Dissociation stages	TG results temp. range (°C)	DTA results temp. peak (°C)	Weight loss, Found (calcd.) (%)	Decomposition assignment
Stage I	50-274	103.94	15.01 (14.68)	The loss of C_8H_6
Stage II	274-638	517.32	17.58 (18.13)	The loss of $C_6N_4H_2$

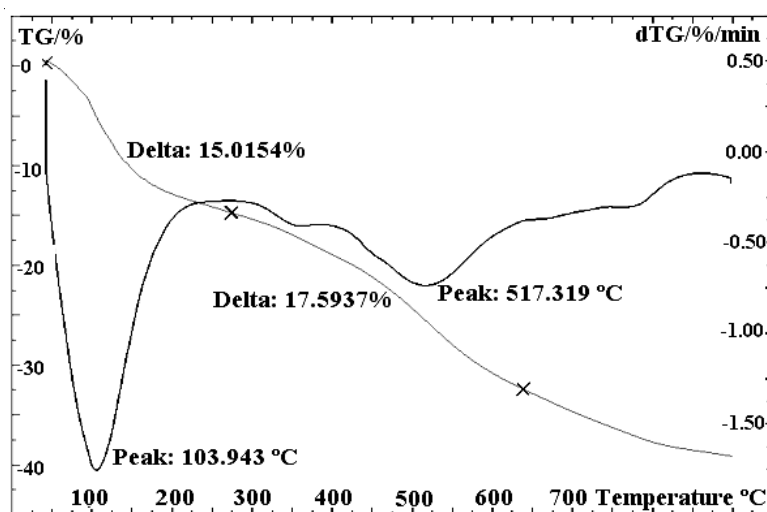


Fig. 2. TGA/DTA curve of H_4L

The first stage at 50-274 °C with a mass loss of 15.01 % (calculated; 14.68) corresponds to the loss of C_8H_6 . The second stage at 274-638 °C with a mass loss of 17.58 % (calculated; 18.13) corresponds to the loss of $C_6N_4H_2$. Endothermic peaks are showed by the DTA analysis. The endothermic peaks are observed at 103.94 and 517.32 °C. Endothermic peaks are generally connected with thermal decomposition and phase change¹⁴.

The antibacterial activities data are given in Table-2. The formed inhibition zones were measured in mm. DMSO was used as a control and cephalosporin was used as a standard. H₄L showed moderate activity against *E. coli*, *B. subtilis*, *S. mutans*, *B. cereus* and *S. aureus* because of the presence of phenyl rings and -OH groups. It is clear that H₄L has displayed maximum activity against *B. cereus*.

TABLE-2
ANTIBACTERIAL ACTIVITIES OF H₄L AGAINST SOME BACTERIAS

Compound	Zone of inhibition (mm)				
	<i>E. coli</i>	<i>B. subtilis</i>	<i>S. mutans</i>	<i>B. cereus</i>	<i>S. aureus</i>
H ₄ L	10	11	11	14	8
DMSO	–	–	–	–	–
Cephazoline	16	19	22	18	22

The electrochemical behaviour of H₄L on GCE surface were investigated using CV technique. 1 mM H₄L (in 0.1 M TBATFB) was prepared and used in the modification process. The modification of the ligand to the surface was performed in the 0.0 mV and + 1000 mV potential range using 100 mV s⁻¹ scanning rate with 30 cycles (Fig. 3a). Two different irreversible oxidation peaks were observed at 374 and 620 mV. When the voltammogram obtained in non aqueous media using ferrocene redox probe is overlaid with the voltammogram obtained for bare GCE, it is clear that the surface does allow electron transfer (Fig. 3b). Considering the structure of the ligand, -OH groups attached to the phenyl groups can be easily oxidized¹⁵, but the ligand doesn't modified to the GCE.

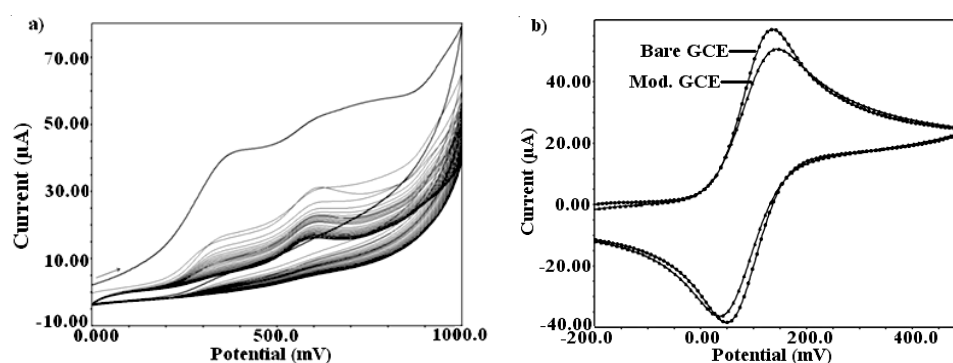


Fig. 3. (a) Cyclic voltammogram of 1 mM H₄L in 0.1 M TBATFB in DMSO, 0.0 mV and +1000 mV potential range using 100 mV s⁻¹ with 30 cycle, (b) surface characterization with ferrocene

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