

Research Article

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Synthesis and characterization of some sulfadruugs azodyes, potentiometric studies of the synthesized dyes and their Fe (III) complexes

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Abstract: New sulfa drugs azo dyes (HL₁, HL₂, HL₃, HL₄ and HL₅) were prepared by the coupling of 6-formyl-7-hydroxy-5-methoxy-2-methylbenzopyran-4-one with the sulfa drugs (sulfadiazine, sulfapyridine, sulfamethoxazole, sulfadimidine, sulfathiazole). The five prepared ligands were characterized by elemental analysis, infrared, mass spectra, and ¹H-NMR spectra. The ionization constants of the ligands and stability constants of their Fe (III) complexes were determined potentiometrically in ethanol-water media at 25°C. HL₁ ligand has two pKa values while the other ligands (HL₂, HL₃, HL₄ and HL₅) have one pKa value. All the ligands form 1:1 metal chelates.

Supporting information: ¹H-NMR, Mass spectra

Keywords: Azo dyes, sulfa drugs, benzoprane, potentiometry, Fe(III)

1. INTRODUCTION

Sulfonamides were the first effective chemotherapeutic agents to be employed systematically for the prevention and cure of bacterial infections where the metal sulphonamide complexes are found to be more effective than the parent sulphonamides [1]. Azo dyes have been widely used in various fields and technologies like textiles, leather, plastics, paper, laser liquid crystalline displays and ink jet printers [2-4]. Benzoprane are those compounds which contain γ -pyrane nucleus fused to benzene ring at the 5- and 6-positions. Benzoprane are important compounds having pharmacological activity. Some benzoprane have marked analgesic anti-inflammatory and antipyretic activities [5].

2. EXPERIMENTAL

All chemicals used were chemically pure grade from BDH. They included; ferric (III) nitrate, potassium dichromate, 10% sulphuric acid, hydrochloric acid, sodium chloride and 5-methoxy-2-methyl-furanochromone. The organic solvents used

in the study were obtained as grade materials from BDH. Doubly distilled water was always used.

2.1. Analysis and physical measurements

The carbon, hydrogen and nitrogen of the ligands were analyzed by standard microanalysis methods at the Microanalytical Center, Cairo University, Giza, Egypt. IR spectra of the ligands as KBr discs were recorded on a Shimadzu FTIR spectrometer. ¹H-NMR spectra of the ligand in DMSO-d₆, were recorded on a Varian 300 MHz NMR spectrometer at room temperature using TMS as an internal standard. Mass spectra were recorded on a Q 1000 EX GC-MS Shimadzu spectrometer at 70 eV and 100 μ A energy using a direct insertion probe at 90-110°C. Potentiometric titrations were carried out on Jenway 3010 pH-meter, UK. The temperature was kept constant at 25°C using Techne Tu-20D temp-unit (Ftu20de), UK.

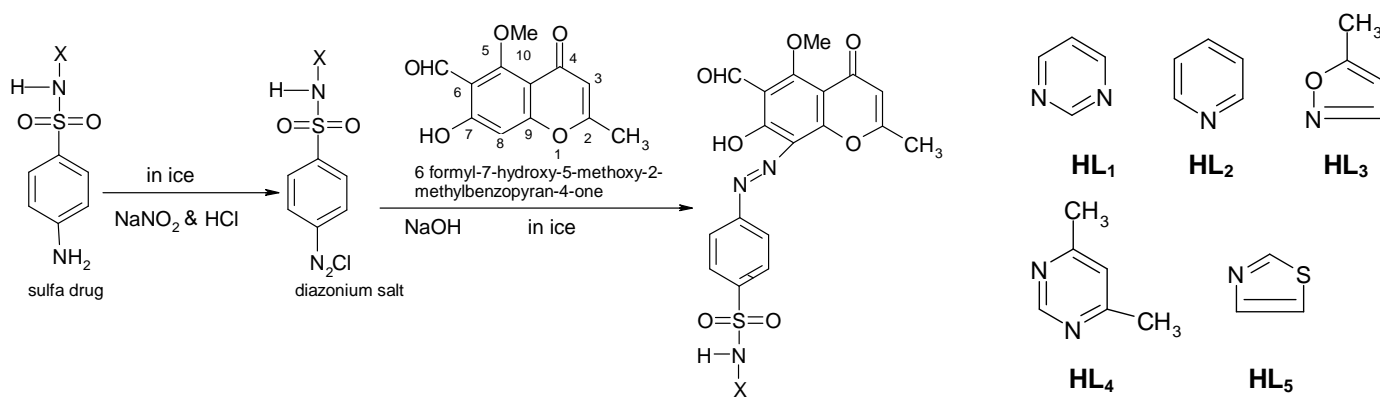
2.2 Synthesis of the ligands

The ligands were synthesized in two steps. The first step is the oxidation of 5-Methoxy-2-methyl-furanochromone as previously described [6]. The obtained white precipitate of 6-formyl-7-hydroxy-5-methoxy-2-methylbenzopyran-4-one is washed with distilled water then recrystallize from ethanol. The second step is the coupling of diazonium salt with 6-formyl-7-hydroxy-5-methoxy-2-methylbenzopyran-4-one (1.872 g, 0.016 mmol) which dissolved in NaOH (2 g in 100 ml distilled water) in ice bath. The diazonium salt was prepared by adding 12-20 ml HCl 50% (v/v) HCl-water mixture to nearly 2 g (0.016 mmole) of sulfa drug. The precipitated azo dye was stirred for 15 minutes then was kept in refrigerator till second day. The azo dye was filtered, washed with distilled water and crystallized from acetic acid for HL₁, HL₂ while for HL₃, HL₄, HL₅ were crystallized from ethanol. The prepared azo dyes were stored in dessicator. The resulting azodyes is represented in the scheme 1.

2.3 Potentiometric titrations

The following mixtures were prepared:

a: 3 mL 0.08 mol/L HCl +5 mL 1 mol/L NaCl +25 mL ethanol



Scheme 1: Synthesis of azodyes ligands

then complete to 50 mL with distilled water to obtain solutions containing 50% by volume of the organic solvent.

b: 3 mL 0.08 mol/L HCl + 5 mL 1 mol/L NaCl + 15 mL 10^{-3} mol/L ligand solution in the same solvent used in the mixture + 10 mL ethanol then complete to 50 mL with distilled water to obtain solutions containing 50% by volume of the organic solvent.

c: 3 mL metal 10^{-3} M solution dissolved in 0.08 mol/L HCl + 5 mL 1 mol/L NaCl + 15 mL 10^{-3} mol/L ligand solution in the same solvent used in the mixture + 10 mL ethanol then complete to 50 mL with distilled water to obtain solutions containing 50% by volume of the organic solvent. The above mixtures were titrated potentiometrically[7] against 0.2422 mol/L NaOH.

3. RESULTS AND DISCUSSION

The azo dyes were subjected to C, H and N elemental analyses. The elemental analysis data of the prepared azodyes are consistent with the calculated results from the empirical formula of each compound.

3.1. Characterization of the synthesized azo dyes

The IR spectra of all ligands show bands in the range of 3325-3634 cm^{-1} for phenolic OH stretching[8] and 3058-3065 cm^{-1} for NH stretching. Carbonyl group of benzopyran-4-one ring show bands in the range of 1625-1631 cm^{-1} [9,10]. All ligands show band at 1388 cm^{-1} which may be due to the bending vibration of CH_3 group in position two of benzopyran-4-one ring. The asymmetric and symmetric stretching vibrations of $\text{S}=\text{O}$ [9] group appear in the range of 1342-1361 cm^{-1} and 1135-1164 cm^{-1} , respectively in the IR spectra of all ligands. Table (1) shows the most important bands in the IR spectra of the ligands.

Mass spectra of HL₁, HL₂, HL₃, HL₄ and HL₅ exhibit the molecular ion peaks at $m/e=495$ (M), 494 (M), 498 (M), 523 (M) and 501 (M+1) confirming their formula weights are equal to their molecular weights. The molecular ion peaks are in good agreement with their empirical formula as indicated from elemental analysis.

¹H NMR data used to confirm the structures of the ligands are shown in Table 2. Due to solubility problems with ligands HL₁ and HL₄, the ¹H-NMR of HL₂, HL₃ and HL₅ in DMSO-d₆ were only performed. The ¹H-NMR of HL₂, HL₃ and HL₅ exhibit a singlet at 2.3-2.5 ppm with integration value equivalent to 3

Table 1: Important bands in IR spectra of the ligands(cm^{-1}).

Bands	HL ₁	HL ₂	HL ₃	HL ₄	HL ₅
$\nu\text{C}=\text{O}$ aldehyde	1645	1660	1662	1662	1658
$\nu\text{C}=\text{O}$ ketone	1631	1631	1625	1629	1630
$\nu\text{N}=\text{N}$	1461	1431	1431	1431	1431
$\nu\text{O}-\text{H}$	3550	3325	3600	3400	3633
$\nu\text{C}=\text{C}$	1589	1585	1581	1581	1581
$\nu\text{N}-\text{H}$	3058	3062	3060	3060	3065
$\nu\text{S}=\text{O}$ assymetric	1361	1346	1342	1342	1342
$\nu\text{S}=\text{O}$ symetric	1137	1141	1164	1164	1135
$\nu\text{C}-\text{O}$	1265	1288	1292	1288	1288
$\nu\text{C}-\text{O}$ symetric	1087	1083	1083	1083	1083
νCH_3 bending	1388	1388	1388	1388	1388
$\nu\text{C}-\text{H}$ bending	775	779	786	786	786
$\nu\text{C}-\text{H}$ aromatics	2947	2935	2962	2962	2925

Table 2: Proton NMR(in ppm) spectral data of the ligands HL₂, HL₃ and HL₅ in DMSO-d₆

HL ₂	HL ₃	HL ₅	Assignment
2.3	2.3	2.58	CH ₃
3.85	3.8	3.60	OCH ₃
11.93	11.90	12.8	OH
10.2	10.2	10.2	CHO
10.4	11.45	11.9	NH
6.60-8.11	6.70-7.94	6.64-7.84	Aromatic protons

protons, which assigned to the CH₃ protons in the benzopyran-4-one ring in position two[11]. The proton of CHO appears at 10.2 ppm for all the ligands. The OH signal of the benzopyran-4-one ring appears at 11.90-12.8 ppm. The NH signal of the sulfa drug moiety appears at 10.4-11.9. The multiple signals observed at 6.60-8.11 ppm can be assigned to the aromatic protons.

3.2 Determination of the proton-ligand ionization constants

The ionization constant of the ligands were determined potentiometrically using the Irving-Rossotti technique [12, 13] at constant temperature 25 °C. The values of the average number of protons associated with the ligands n_A at different pH values were calculated. The proton-ligand formation curves are obtained by plotting n_A versus pH at constant temperature. It was found from these that the maximum n_A value is 1.7 for HL₁ indicating that the ligand has two pKa values. The first dissociation constant, pKa₁ (3.94) is assigned to NH proton while the second dissociation constant, pKa₂ (11.55) is assigned to the phenolic OH proton. While the maximum n_A for HL₂, HL₃, HL₄ and HL₅ is 0.9 indicating that these ligands have one dissociable proton.

3.3 Determination of the stability constant of Fe(III) complexes with the ligands:

The stability constant of Fe(III) complexes are evaluated at constant temperature. The values of n (the average number of ligand molecules attached per metal ion) and pL (the free ligand exponent) for metal-ligand mixtures were calculated at different pH values[12,13].The formation curves for the metal-ligand complexes were obtained by plotting the relation between (n) versus (pL). The curves show that the maximum value for n is 1

Table 3: The pKa values of the ligands and log K of their Fe (III) complexes.

Ligands	pKa of ligands	Log K of complexes
HL ₁	3.94, 11.55	13.50
HL ₂	7.0	11.423
HL ₃	7.55	12.50
HL ₄	6.91	11.74
HL ₅	6.57	11.88

indicating that 1:1 metal chelates were formed. The formation constants (log K) of Fe (III) with the ligands were calculated by Interpolation at half n values method[12,13]. The values of formation constants of Fe (III) with the ligands and pKa values of the ligands are listed in Table 3.

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