

Binding Properties of Some Pyranopyridothiazole Derivatives in Acetonitrile

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ABSTRACT: The complexation properties of some pyranopyridothiazole derivatives L1-L4 towards alkali, alkaline earth, and some transition metal cations have been investigated in acetonitrile by means of UV spectrophotometry absorption and conductivity. Therefore, the stoichiometries of complexes formed are ML and their profiles of stability illustrate selectivities of L2 towards Sr²⁺ and Cu²⁺ and of L4 towards Na⁺.

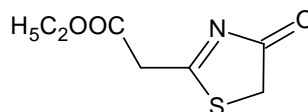
Keywords: Pyranopyridothiazole derivatives; Stoichiometries; Complexation; Stability constants and Cation binding properties.

INTRODUCTION: Heterocycles containing nitrogen atoms have common features integrated into the structures of many natural products and pharmaceutical compounds¹. Among these heterocycles, the pyranopyrazoles are fused heterocyclic compounds that possess many biological properties such as fungicides², bactericides^{3 & 4} and vasodilatory activity since they act as anticancer agents⁵. They were synthesized and used for applications such as pharmaceutical ingredients and biodegradable agrochemical⁶⁻⁹. The aminothiazole derivatives have several useful properties as anti-corrosive activities^{10 & 11}, antimicrobial, and antitumor¹². As detection of heavy metal, the aminothiazole materials have been reported with Hg (II)¹³ and other ions¹⁴. Besides, they have useful properties as therapeutic agents in the field clinic.¹⁵⁻¹⁷ They have been used as analgesics, anti-inflammatory, ulcerogenic, antibacterial¹⁸ antifongiques¹⁹⁻²⁰ antimalarials,²¹ antitumorales²² antioxidant²³, antiproliferative²⁴, antihypertensives²⁵, and hypnotic²⁶, vasodilatateurs²⁷⁻³⁰, antibacterial³¹⁻³² and inhibit rice³³. They have been widely used as drugs and biodegradable agrochemicals³⁴. Several works have been published describing multi process of synthesis of new pyranopyrazoles³⁵⁻⁴⁰.

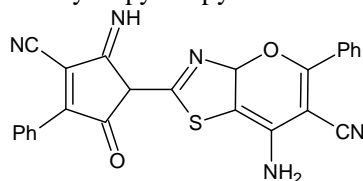
In recent work, the complexation properties of pyranopyridothiazole derivatives L1-L4 towards some transition and heavy metal cations have been investigated in methanol by means of UV spectrophotometry absorption and conductivity. The studies showed the

formation of complexes mononuclear in all case of systems metal/ligand and a low affinity in complexation. Moreover, compounds L2, L3 and L4 exhibit same affinity in extraction⁴¹ while ligand L1 its extraction affinity is very weak.

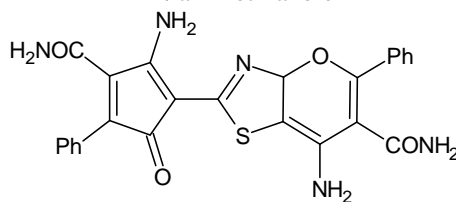
In this context we continue to report the binding properties of pyranopyridothiazole derivatives L1-L4 in acetonitrile. The studies have been followed by spectrophotometry UV-visible and conductivity in CH₃CN.



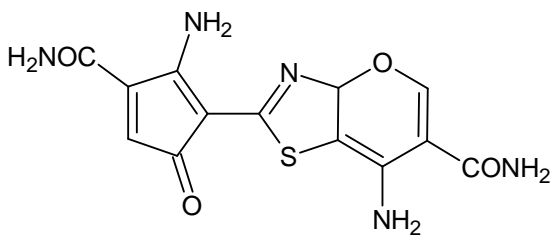
L1: cyanopyranopyridothiazole



L2: aminothiazole



L3: iminothiazole



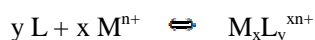
L4: phenyliminothiazole

Figure 1: Chemical structural of pyranopyridothiazole derivatives L1-L4.

MATERIAL AND METHODS:

Instrument and Materials: The UV spectra were recorded on Perkin Elmer Lambda 24 spectrophotometer. Acetonitrile (SDS for HPLC, 0.03% water content) and dichloromethane (Fluka, purum) were commercial and used without further purification. The supporting electrolyte used in the stability constant determinations was NET_4ClO_4 (Acros Organics). The metal salts chosen were perchlorates (Fluka, purum).

Stability Constant Measurements: The stability constants β_{xy} being the concentration ratios $[\text{M}_x\text{L}_y^{xn+}]/[\text{M}^{n+}]^x[\text{L}]^y$ and corresponding to the general equilibrium:



(where M^{n+} = metal ion, L = ligand) were determined in acetonitrile by UV-absorption spectrophotometry at 25°C.

The ionic strength has been maintained at 0.01 mol.L⁻¹ using Et_4NClO_4 . The concentration of ligand solutions is ranging between 10⁻⁴ and 2×10⁻⁴ mol.L⁻¹ and the UV spectra has been recorded between 220 nm and 350 nm. Generally the metal to ligand ratio R at the end of the titration did not exceed 15 and the equilibria were quasi-instantaneous for all the systems. The titration of the ligand by the metal solution induced spectra changes, large enough to allow the analysis of the resulting data using the program "Letagrop" [42]. The stability constants of the various species and their molar absorption coefficients are deduced from the best fit between the experimental and calculated UV spectra. The best fit is reflected by the lowest value of U (the sum of U values for all given lambda) corresponding to the square sum of a differences between experimental and calculated absorbances ($U = \sum (\text{Acal} - \text{Aexp})^2$). The β_{xy} values correspond to the arithmetic means of at least three independent experiments.

Conductimetric studies: While complexation by a neutral ligand is not expected to dramatically alter the molar conductivity of a cationic species, the diffe-

rences can usually be detected and so the measurement of conductance of a solution of a ligand into which a metal ion is added can be useful to establishing the stoichiometry of complexes. Therefore, this procedure was followed to obtain preliminary estimates of the metal: ligand ratio of the complexes formed during the titration of the heterocyclic amine.

RESULTS AND DISCUSSION:

Complexation followed by Spectrophotometry UV:

The complexation studies of ligands L1-L4 were followed with alkali, alkaline-earth and some transition metal cations. The variation of spectrum during the titration indicates generally the formation of a new species. In fact, the recording of a solution containing compounds L1-L4 separately and free illustrates the existence of a maximum of absorbance at around 270 nm and a shoulder between 300 and 320 nm. The titration by metal solution involves a decrease in absorbances and in some cases a hypsochromic shift as shown on the figure 2. The later is corresponding to the complexation of copper by compound L2 ($\Delta\lambda=4\text{nm}$). Moreover, two isobestic points appear at 255 and 296 nm respectively.

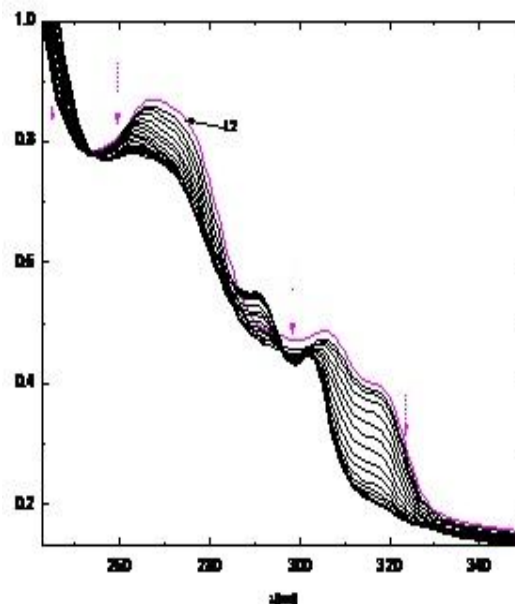


Figure 2: UV absorption spectra of the complexation of copper (II) by L2 in acetonitrile ($0 \leq R_{ML} \leq 2.5$) at 25°C.

The treatment of the UV spectra shows the formation of complexes ML in all cases of metal/ligand. The logarithms of stability constants $\log \beta_{xy}$ are given in TABLE 1. These values are the average of at least two independent experiments.

Table 1: Stability Constants $\log \beta_{11}$ of Complexes ML of L1, L2, L3 and L4 with alkali metal, alkaline earth and some transition metal cations in Acetonitrile at 25 °C, $I = 10^{-2}$ M, ($0.01 \leq \sigma_{n-1} \leq 0.16$).

	Li ⁺	Na ⁺	K ⁺	Rb ⁺	Cs ⁺	Mg ²⁺	Ca ²⁺	Sr ²⁺	Ba ²⁺	Co ²⁺	Ni ²⁺	Cu ²⁺
L 1	3.60	3.80	4.03	4.10	a	a	3.74	4.03	a	a	4.01	4.11
L 2	a	a	a	4.01	a	a	3.91	4.10	a	4.01	a	4.33
L 3	a	a	3.61	4.11	a	a	a	4.05	a	a	3.84	4.20
L 4	3.40	4.12	4.01	4.06	a	a	3.62	3.89	a	4.06	3.97	4.16

a: Absorbance changes too small to enable satisfactory fitting.

In the case of alkali metal cations, the stability constants vary between 3.40 and 4.12 logarithmic units. Small spectral variations are observed for cesium with all compounds and for lithium, sodium with ligands L2 and L3 and for potassium with ligand L2. Their interpretation by letagrop was not significant. As regards to the stability, the affinities of L1, L3 and L4 increase from lithium to rubidium. The values are so close to not allow the detection of important selectivity. Small favorite of L4 towards Na⁺ is detected however L1 and L3 show similar preference to rubidium. Figure 3 illustrates the profiles of stability of complexes ML formed by ligands L1-L4.

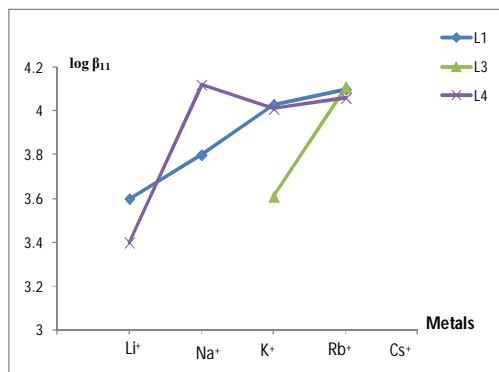


Figure 3: Profiles of stability of complexes ML with L1, L3 and L4.

For alkaline-earth cations, complexes ML were detected only in the case of Ca²⁺ and Sr²⁺. However, no affinity towards Mg²⁺ and Ba²⁺ were observed. The spectral changes are very small to enable their treatments. The stability constants shift between 3.62 and 4.10 logarithmic units. The four ligands exhibit almost same affinities towards calcium ($\log \beta_{11} \approx 3.8$) and strontium ($\log \beta_{11} \approx 4.0$), respectively.

Furthermore, in the first series of transition metal cation, only cobalt, nickel and copper were studied. The best values were obtained with Cu²⁺ and the stability of complexes ML with ligands L1-L4 is almost equal. This preference to Cu²⁺ makes us recall the Irving-Williams Rule [43] though the sequence of the transition metals studied is not complete. Moreover,

the stability of the complexes [Ni.L4]²⁺ and [Ni.L1]²⁺ are more stable than [Ni.L3]²⁺. Figure 4 illustrates the increase of affinity of L1, L3 and L4 from cobalt to copper.

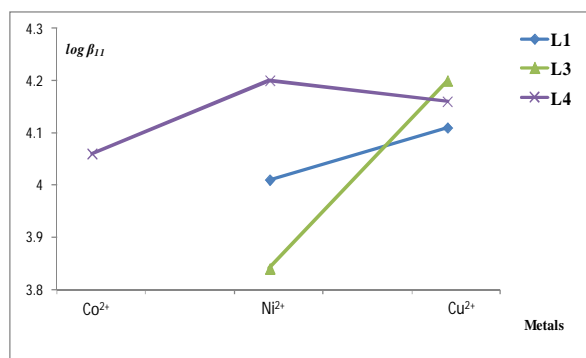


Figure 4: Profiles of stability of complexes ML of transition metal cations.

Complexation followed by conductivity: In order to check some stoichiometry, further studies of complexation properties were followed by conductivity in same condition of work (T, solvent, concentration). As a result, this technique allowed confirming the stoichiometries of 1:1 of complexes formed by ligands L1-L4. Figure 5 make evidence of the change of the slope in the ratio M/L equals to 1 which means the complex formed by compound L1 and Cu²⁺ is ML. This result is in agreement with the study followed by UV spectrophotometry.

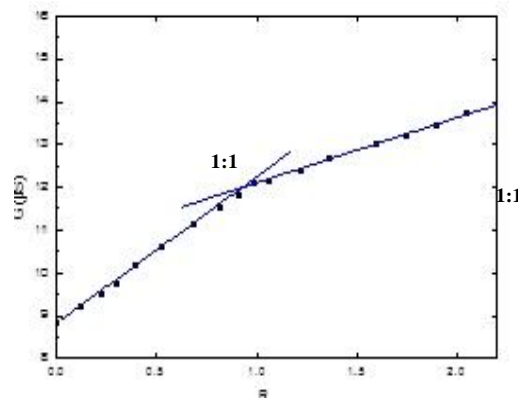


Figure 5: Conductometric titration of L1 by Cu²⁺.

CONCLUSION: The structures of these products were confirmed by their spectral data. The results show the formation of mononuclear species by ligand L1-L4 with metals studied. The four ligands exhibit almost same affinity towards alkali, alkaline-earth and transition metal cations. It could be explained by the presence of oxygen, nitrogen and sulfur, hard and soft atoms respectively, in the four ligands. The conductometric titration confirmed mainly the stoichiometries of the complexes formed in solution with L1-L4.

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