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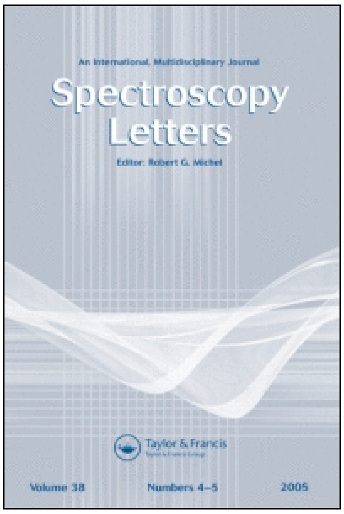

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SPECTROPHOTOMETRIC INVESTIGATION OF TERNARY COMPLEX FORMATION BETWEEN 1,8-DIHYDROXY-9,10-ANTHRAQUINONE AND IMIDAZOLE WITH Co^{2}, Ni^{2}, Cu^{2} AND Zn^{2} IN METHANOL AT 25°C

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SPECTROSCOPY LETTERS, 35(1), 31–42 (2002)

SPECTROPHOTOMETRIC INVESTIGATION OF TERNARY COMPLEX FORMATION BETWEEN 1,8-DIHYDROXY-9,10-ANTHRAQUINONE AND IMIDAZOLE WITH Co^{2+}, Ni^{2+}, Cu^{2+} AND Zn^{2+} IN METHANOL AT 25°C

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ABSTRACT

The complexation reaction between 1,8-dihydroxy-9,10-anthraquinone (DHAQ) and imidazole (Im) and Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+} are studied spectrophotometrically in methanol at 25°C. The possibility of complex formation between metal ions and ligands are illustrated by visible spectra at different M^{2+}:DHAQ:Im ratios. Computer fitting of experimental spectra to purposed chemical model using SQUAD program obtains the stability constants and stoichiometries of all resulting complexes. The species ML, ML_2 type ($L = DHAQ$) and MB, MB_2, MB_3 and MB_4 ($B = Im$) are

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obtained in binary systems. The species types detected in ternary systems are MLB, MLB_2, ML_2B_2.The higher stability of ternary systems over binary ones are discussed according to ΔLogX values.

Key Words: Complexation; Mixed ligands; Imidazole; Dihydroxy anthraquinones; Spectrophotometry; Stability constants; Nonaqueous solutions

INTRODUCTION

Anthracyclines constitute an important class of chemical compounds. These compounds recently gained more appreciation with the discovery that they could be used as drugs in the treatment of cancer[1–5]. Earlier studies[6,7] have shown that formation of metal complexes with these drugs greatly influences the toxicity imparted by them. There are several reports on the determination of acidity and formation constants of anthraquinones with several metal ions in non aqueous and mixed aqueous solutions[8–11].

The structure and bonding of mononuclear and homobinuclear chelates of 1,8-dihydroxy-9,10-anthraquinone (DHAQ) with Ni^{2+}, Cu^{2+}, Zn^{2+}, Mn^{2+} were studied in solid and liquid phases by the Tsipis and Christiunopoulou[11] and Tachibana and Iwaizami[12] research groups. Tipis and Christiunopoulou[11] have also obtained the structure and detailed configuration of mononuclear and homobinuclear complexes of DHAQ with Cu^{2+}. Recently Das, Saha and Mandal[13], have evaluated the acidity constants and complexing ability of 1,2-DHAQ with Cu^{2+}, and Ni^{2+} in aqueous media and obtained stoichiometries and the stability constants of 1,2-DHAQ with Cu^{2+} and Ni^{2+}, 1:3 (metal to ligand ratio), 3.44×10^{25} and 1:3, 5.13×10^{29}, respectively.

Despite the above mentioned reports on the complexation of mono- and dihydroxyanthraquinones, there are many vacancies on the metal-ligand solution equlibria data of these molecules. Thus in the present work we study the complexation between 1,8-dihydroxyanthraquinones, imidazole and transition metal ions as a ternary system. Since the solubility of the ligand (DHAQ) and their complexes are very sparse in aqueous media, methanol is selected as a suitable solvent. Because of ease of use and availability of a computerized scanning spectrophotometer and the lack of problems associated with a pH electrode in nonaqueous media, the spectrophotometric method was applied in this investigation.

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EXPERIMENTAL

The nitrate salts of copper, nickel, cobalt and zinc (all from Merck) were used as supplied and their stock solutions were standardized by EDTA in the presence of suitable indicator. 1,8-dihydroxy-9,10-anthraquinone (DHAQ, Fluka) was used after recrystalization from pure heptane and vacuum-drying. HPLC grade methanol (MeOH, Merck) and reagent grade imidazole (Im, Merck) were used as received.

The electronic spectra of solutions of DHAQ:M^{2+} and Im:M^{2+} systems (in the binary case) and DHAQ:Im:M^{2+} (in the ternary case) at various ratios in a double-walled cell were recorded on a GBC 911 microprocessor-controlled UV-Vis spectrophotometer. The digitized spectra were gathered and saved as an ASCII file by Scan Master software. The temperature of the cell was kept constant at 25°C ± 0.1°C by circulation of water with a Polystat CC3 thermostat (Huber Company). The ionic strength of the solutions used was maintained constant at 0.01 M using $NaClO_4$.

SQUAD[14,15] is a program with capability of refining the stability constants of a general complex $M_m M_l H_k L_n L_q$, where m, l, n, $q > 0$ and k is positive for protons and negative or zero for hydroxide ions. This software employs a linear least-squares approach. The data fed to SQUAD are absorption spectra, chemical composition (total concentration of M, M′, L, L′ and pH) and a chemical model to described the system. The residual sum (U) is calculated from the following equation.

$$U = \sum_{1}^{I} \sum_{1}^{NW} (A_{i,k}^{Calc} - A_{i,k}^{Obs})^2 \tag{1}$$

where the $A_{i,k}$ is the absorbance value of the i*th* solution at the k*th* wavelength, given a total of I solutions and a grand total of NW wavelengths.

RESULTS AND DISCUSSION

The photometric titration of DHAQ with Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+} was obtained from the titration of 5 mL of 5×10^{-5} ligand solution with 0.001 M of each metal ion solution in a stepwise increment of metal solution. In all cases the enormous change found in spectral characteristics of ligands, reveal the complexation reaction. The titration spectra of DHAQ with each metal ion are shown in Figs. 1 and 2.

The stability constants of resulting complexes are obtained from computer refinement of spectra at different ratios of metals to ligand. The

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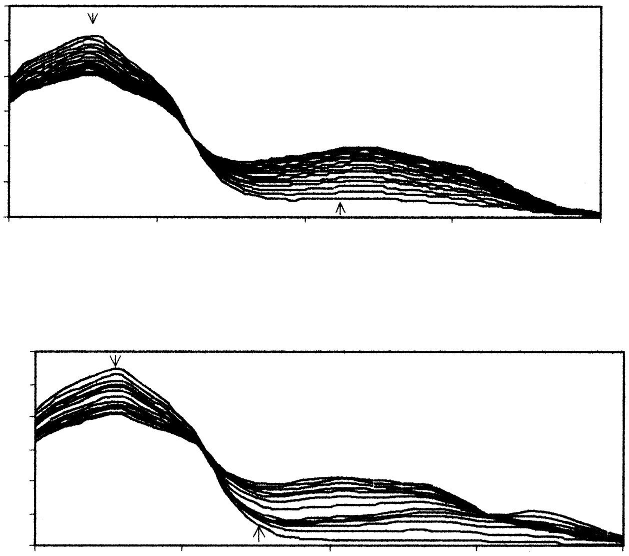

Figure 1. Titration spectra of DHAQ with Cu^{2+}(a) and Ni^{2+}(b) at different mole ratios; (a) – 1, 0.0; 2, 0.11; 3, 0.165; 4, 0.221; 5, 0.276; 60.331; 7, 0.387; 8, 0.442; 9, 0.497; 10, 0.553; 11, 0.608; 12, 0.663; 13, 0.774; 14, 0.884; 15, 0.995; 16, 1.070 (b) – 1, 0; 2, 0.054; 3, 0.109; 4, 0.169; 5, 0.219; 6, 0.274; 7, 0.384; 8, 0.449; 9, 0.609; 10, 0.714; 11, 0.824; 12, 0.934; 13, 1.043.

stability constants of binary systems (M^{2+}-DHAQ) are listed in Table 1. As can be seen from Fig. 1, that the titration spectra of DHAQ with Cu^{2+} has two clear isosbestic point at 450 and 560 nm, which indicates the existence of at least two equlibria between metal and ligand moieties.

The further evidence to this, is the variation of absorbance versus metal to ligand mole ratios, at several wavelengths, which show two distinct areas in their variations (Fig. 3). According to above comments the proposed equilibrium model for Cu^{2+}-DHAQ in MeOH is:

$$\mathrm{M} + \mathrm{L} \leftrightarrows \mathrm{ML} \quad K_1 = \frac{[ML]}{[M][L]}$$

$$\mathrm{ML} + \mathrm{L} \rightleftarrows \mathrm{ML_2} \quad K_2 = \frac{[ML_2]}{[ML][L]}$$

Tsipis and Christiunopoulou[11] and Tachibana and Iwaizami[12] also detected the ML and ML_2 species and unexpected M_2L_2 type of complexes and they

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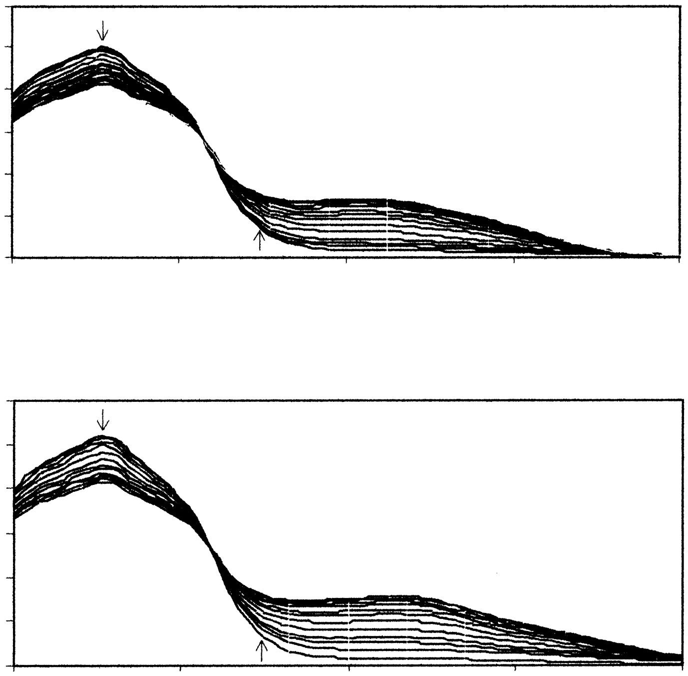

Figure 2. Titration spectra of DHAQ with Co^{2+}(a) and Zn^{2+}(b) at different mole ratios; (a)–1, 0.0; 2, 0.056; 3, 0.112; 4, 0.224; 5, 0.336; 6, 0.448; 7, 0.56; 8, 0.672; 9, 0.784; 10, 0.952; 11, 1.176; 12, 1.512; 13, 1.96; 14, 2.52 (b)–1,0.0; 2, 0.055; 3, 0.111; 4, 0.167; 5, 0.279; 6, 0.39; 7, 0.502; 8, 0.614; 9, 0.781; 10, 0.949; 11, 1.284; 12, 1.842.

proposed coordination structures of the Cu^{2+}-DHAQ complexes as shown in Fig. 4.

As indicated in Fig. 5 the addition of Ni^{2+} and Zn^{2+} solutions to DHAQ, shows similar trends in both systems. The titration spectra and mole ratio plots of these two systems reveal that the species ML and ML$_2$ are formed for Zn^{2+} and Ni^{2+} respectively. In the Co^{2+}-DHAQ system, however, the appearance of titration spectra shows only one isosbestic point, but the computer refinement of obtained spectra was fitted to the ML and ML$_2$ equilibrium model.

It is clear from Table 1, that the Cu^{2+}-DHAQ complex is more stable than Ni^{2+}-DHAQ and the Ni^{2+}-DHAQ complex in turn is stronger than Co^{2+}-DHAQ. This behavior corresponds to more general behavior of transition metal complexes toward conventional ligands (Irving-William's order[16]).

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Table 1. The Stability Constants of M^{2+}-DHAQ in Binary Systems

Equilibrium System	M	L	$\log\beta \pm \sigma$	$\log K$
Cu^{2+}-DHAQ	1	1	6.45 ± 0.05	6.45
	1	2	12.30 ± 0.05	5.85
Ni^{2+}-DHAQ	1	2	9.10 ± 0.02	9.10
Co^{2+}-DHAQ	1	1	5.60 ± 0.04	5.60
	1	2	10.29 ± 0.09	4.49
Zn^{2+}-DHAQ	1	1	5.80 ± 0.03	5.80

The titration spectra of mixed systems are obtained by titration of DHAQ solution with each M^{2+} metal ion until reach predetermined mole ratios (i.e. at least two or greater). The titration of the resulting solution was continued with Im solution. A sample of titration spectra for the ternary system is shown in Fig. 6.

It is evident from Fig. 6 that complexation reaction occurred between the species present in the ternary system. The quantity of spectral change during titration, is the measure of stability of the resulting complexes. To ascertain that, the spectral change is not due to the Im-DHAQ interaction (protolytic equlibria) in a separate experiment, a solution of DHAQ was

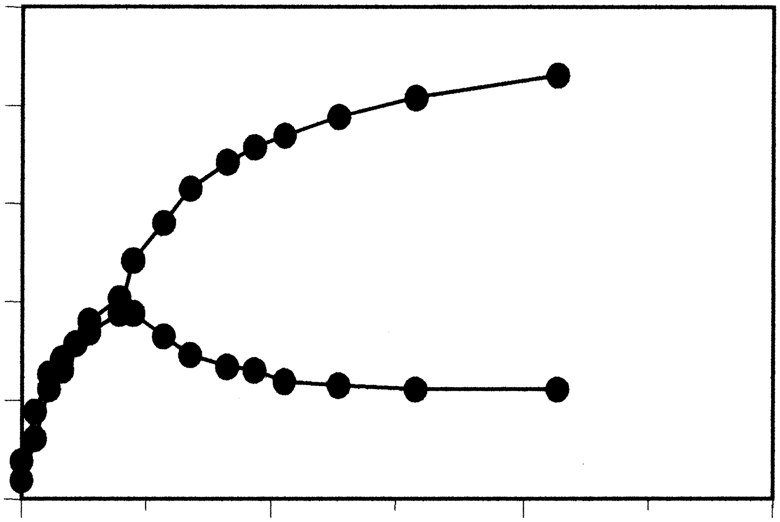

Figure 3. Mole ratio plots of DHAQ-Cu^{2+} at 505 and 570 nm.

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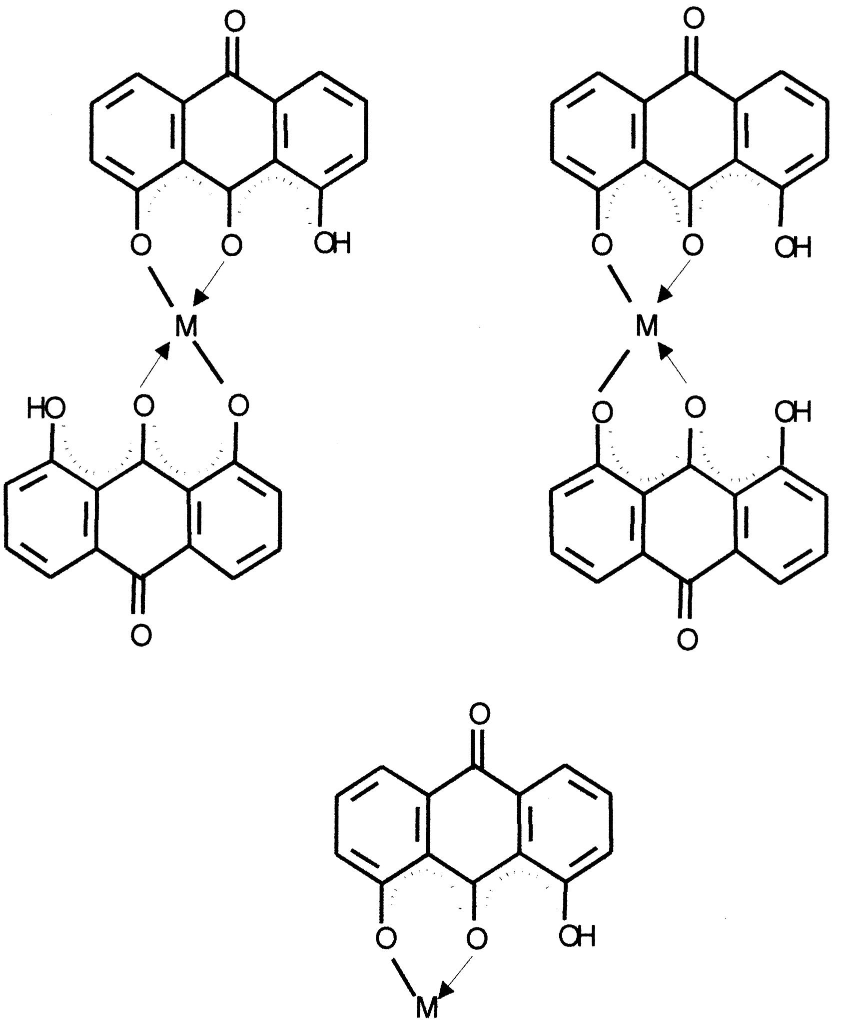

Figure 4. Proposed structures of M^{2+}-DHAQ system.

titrated with Im. It was found that the change in spectral characteristics was not measurable.

The stability constants of all binary and ternary complexes formed between DHAQ, Im and each metal ion obtained by computer refinement of the corresponding spectral data using SQUAD are listed in Table 2.

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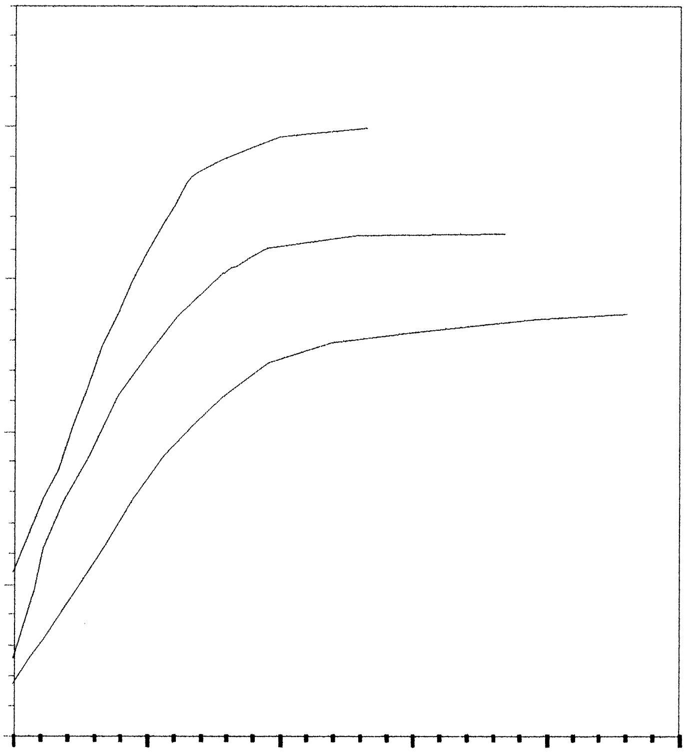

Figure 5. The mole ratio plots of DHAQ-Ni^{2+}, Co^{2+} and Zn^{2+} at λ_{max} of their complexes.

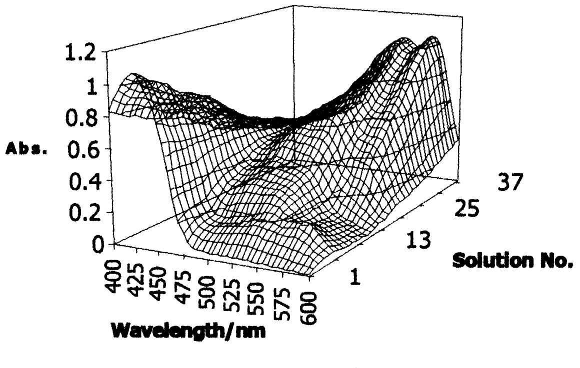

Figure 6. Titration spectra of DHAQ with Cu^{2+} (solution no. 1–12) and with Im (solution no. 13–37).

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Table 2. The Stability Constants of $\mathbf{M}^{2+}$-Im (A) and $\mathbf{M}^{2+}$-DHAQ-Im (B)[a]

(A)

System	M	L	log β ± σ	Log K
Cu^{2+}-Im	1	1	6.99 ± 0.04	6.99
	1	2	13.08 ± 0.09	6.09
	1	3	19.20 ± 0.09	6.12
	1	4	23.10 ± 0.08	3.90
Ni^{2+}-Im	1	1	5.54 ± 0.02	5.54
	1	2	9.75 ± 0.06	4.21
	1	3	15.13 ± 0.05	5.38
	1	4	18.79 ± 0.1	3.67
Co^{2+}-Im	1	1	4.60 ± 0.04	4.60
	1	2	8.90 ± 0.05	4.30
	1	3	13.07 ± 0.07	4.17
Zn^{2+}-Im	1	1	5.93 ± 0.06	5.93
	1	2	12.09 ± 0.02	5.16
	1	3	16.64 ± 0.04	4.55
	1	4	21.13 ± 0.12	4.49

(B)

System	m	l_1	l_2	log β ± σ	Δ log K	log X
Cu^{2+}-DHAQ-Im	1	1	1	13.89 ± 0.09	0.45	1.59
	1	1	2	20.44 ± 0.06	0.1	–
	1	2	1	20.13 ± 0.12	0.84	–
	1	2	2	25.91 ± 0.1	−0.28	–
Ni^{2+}-DHAQ-Im	1	1	1	10.95 ± 0.09	–	3.05
	1	1	2	16.02 ± 0.05	–	–
	1	2	1	14.36 ± 0.14	−0.28	–
	1	2	2	20.57 ± 0.06	1.27	–
Co^{2+}-DHAQ-Im	1	1	1	9.53 ± 0.05	−0.67	0.13
	1	1	2	14.95 ± 0.08	0.45	–
	1	2	1	15.28 ± 0.13	0.39	–
	1	2	2	20.00 ± 0.09	0.81	–
Zn^{2+}-DHAQ-Im	1	1	1	13.00 ± 0.08	1.27	–
	1	1	2	18.68 ± 0.07	0.79	–

[a] l, m, l_1, l_2 are stoichiometric coefficients of ligands and metal ions in complex.

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As shown in Table 2 the observed trend in stability constants of Im-M^{2+} more or less, resemble previously reported values[17–19]. To our knowledge this is the first report on the study of Im complexes in methanol solution via a competitive manner. The differences between these data and previously reports are due to different experimental conditions such as temperature and, more importantly, to solvent media.

In contrast with the stability of the binary complexes, the relative stability of the ternary ones can be expressed in several ways. The most common is the calculation of $\Delta \log K$, that is in fact the difference in stabilities for the addition of ligand B to the 1:1 MA complex and to the solvated metal ion as shown by the following equation:

$$\Delta \log \mathrm{K} = \log K^{MA}_{MAB} - \log K^{M}_{MA} = \log K^{MB}_{MBA} - \log K^{M}_{MB} \tag{2}$$

where A and B are first and second ligands which bond to the metal ion.

Another parameter generally used for indicating the stabilization of the ternary complexes relative to the binary ones is the disproportionation constant log X which is shown as:

$$\mathrm{MA_2} + \mathrm{MB_2} \Leftrightarrow 2\mathrm{MAB}$$

$$\mathrm{X_{MAB}} = \frac{[MAB]^2}{[MA_2][MB_2]} \quad \mathrm{Log\ X_{MAB}} = 2\log\beta_{\mathrm{MAB}} - (\log\beta_{\mathrm{MA2}} + \log\beta_{\mathrm{MB2}}) \tag{3}$$

On the statistical calculations[20], the positive $\log \mathrm{X}$ and less negative $\Delta \log K$ values, indicate the marked stability of the mixed complexes over the binary complexes. These statistical parameters are also obtained from the resulting stability constants and are shown in Table 2. These parameters are more positive than their theoretical (tabulated) values[21] which is indicative of the preferential formation of ternary complexes relative to binary parent complexes.

The concentration distribution diagram for all binary and mixed systems are obtained in terms of percent metal ions as a function pM. The concentration distribution diagram plots of M^{2+}-L-B's systems in which $M^{2+} = Co^{2+}$, Ni^{2+}, Zn^{2+} and Cu^{2+}, L = DHAQ and B = Im, are obtained and DHAQ-Im-Co^{2+} and DHAQ-Im-Cu^{2+} are shown in Figs. 7A and 7B. In some cases the concentration of mixed species rise up to 60%. Among mixed species formed in ternary systems, the MLB_2 has more concentration than the other mixed species and at high pM values the ML_2B_2 species have

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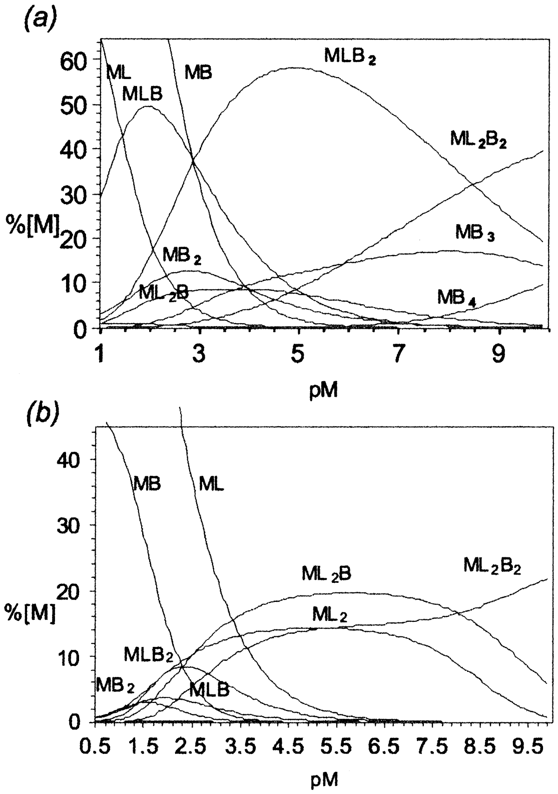

Figure 7. The concentration distribution diagram of species formed in DHAQ(L)-Im (B)-Cu^{2+} system (a) and DHAQ (L)-Im (B)-Co^{2+} system (b).

a marked concentration percent over other mixed species. As can be seen from distribution plots, formation of the B rich species are concentrated at low pM values and L rich ones at high pM values.

It is interesting to note that, percent species obtained for mixed components is by far higher than what is expected of statistical inferences. This also shows the higher stability of mixed species over parent binary ones.

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