



Binding properties of heterocyclic amines towards some metal cations

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ABSTRACT

The binding properties of a 2-aminobenzimidazole toward the alkali, alkaline earth cations, some transition, and heavy metals and some lanthanides have been investigated in acetonitrile and methanol, followed by UV Spectrophotometry Absorption and conductivity. Thus, the stoichiometries of complexes formed and their stability constants were determined by digital processing of data.

The results of liquid-liquid extraction show that the ligand extracted only a Mg^{2+} and Co^{2+} in the series of the picrate salts considered.

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KEYWORDS

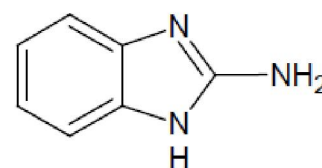
Inclusion properties;
Heterocyclic amine;
Stoichiometry;
Complexation;
Extraction;
Stability constants.

INTRODUCTION

Heterocyclic containing nitrogen atoms have common features integrated into the structures of many natural products and pharmaceuticals compounds. The multidentate ligands are widely used in coordination chemistry. Among these ligands some including derivatives of benzimidazole because of their biological importance as constituents of many biomolecules and drugs^[1].

Thanks to its properties and with no toxicity^[2], the 2-aminobenzimidazole is involved in the pharmaceutical, therapeutic, industrial, agricultural (as fungicide^[3,4]) and pharmacologic fields. Indeed, the structure aminobenzimidazole is commonly used in a large number of drugs^[5,6]. In addition, benzimidazole, being the nucleus of several drugs and its derivatives have several pharmacological activities importantes^[3] because they can act as anti-cancer, anti-parasitic and anti-hel-

minthic^[4] inflammatory^[7]. Some of these compounds show an anti-HIV^[7] and it was confirmed that they had a control activity against virus grippé^[7]. They also show activity antifongique^[2].



2-aminobenzimidazole

Similarly, aminobenzimidazole is an important structural motif in medicinal chemistry and can be found in some biologically actives^[8]. Heterocyclic amines exhibit a power in their complexing affinity with metallic cations^[7-10]. In some cases, structural and biological properties of organic ligands can be modified to improve the cation coordination^[11]. It was found that metal cations are the most studied transition metals^[7,10,3]. Given the

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above, recent studies of the coordination chemistry of compounds containing these heterocycles have been made^[12].

In search of new frameworks, the choice of 2-aminobenzimidazole was due to the fact that compounds containing this heterocyclic have shown a broad spectrum of pharmacological activities^[13].

In some cases, the coordination complexes formed from these organic compounds can improve the biological activities^[11]. Thus, a group of complex compounds of 2-aminobenzimidazole derivatives with some metals, such as cobalt, zinc and copper, showed anti-fungal and antibacterial activities, while complexes with ruthenium exhibited cytotoxic activity against the cells of human cancer cell lines^[13].

EXPERIMENTAL

Instrument and materials

The UV spectra were recorded on a Perkin Elmer Lambda 11 spectrophotometer. Methanol (Riedel-deHaën for HPLC), 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_4Cl and NEt_4ClO_4 (Acros Organics). The metal salts chosen were chlorides or perchlorates (Fluka, purum). The picrate salts employed in extraction were prepared as described in literature^[14].

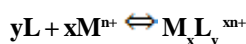
Extraction studies

The extraction experiments of alkali, alkali earth, transition metal picrate from water into dichloromethane were performed according to a procedure described in the literature^[15]. Equal volumes (5 mL) of neutral aqueous solution of alkali metal picrate ($2.5 \times 10^{-4} \text{ mol.L}^{-1}$) and CH_2Cl_2 solution (5 mL) of heterocyclic amines ($2.5 \times 10^{-4} \text{ mol.L}^{-1}$) were mixed and magnetically shaken in a thermo-regulated water bath at 25°C for 30 min and then left standing for 2 to 6 h in order to obtain a complete separation of the two phases. The concentration of metal picrate remaining in the aqueous phase was determined from the absorbance A at 355 nm. The percentage extraction (%E) was derived from the following expression in which A_0 is the absorbance of the aqueous solution of a blank experiment without heterocyclic amines:

$$\%E = 100(A_0 - A)/A_0$$

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 and methanol by UV-absorption spectrophotometry at 25°C .

The ionic strength was been maintained at 0.01 mol.L^{-1} using Et_4NClO_4 . The spectra of ligand solutions of concentrations ranging between 10^{-4} and $2 \times 10^{-4} \text{ mol.L}^{-1}$ and increasing concentration of metal ion were recorded between 220 nm and 320 nm. Generally the metal to ligand ratio R at the end of the titration did not exceed 20 and the equilibriums were quasi-instantaneous for all the systems. Addition of the metal salts to the ligand induced spectra changes large enough to allow the analysis of the resulting data using the program "Letagrop"^[16]. Best values for the formation constants β_{xy} of the various complex species and their molar absorptivity coefficients for various wavelengths, 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 differences 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 a useful rapid means of establishing the stoichiometry of a complex ion species. Thus, this procedure was followed to obtain preliminary estimates of the metal:ligand ratio in the complexes formed by the heterocyclic amine.

RESULTS AND DISCUSSION

Complexation of metal cations in methanol and acetonitrile

The logarithms of the stability constants $\log\beta_{xy}$ and

the stoichiometries for the different complexes formed by ligand with alkali metal, alkaline-earth metal, some transition metal and some lanthanide metal cations in methanol and acetonitrile are given in TABLES 1-2.

The profile of the spectrum of a ligand exchange with the solvent nature, both principal and secondary maxima is reversed in going from methanol to acetonitrile.

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TABLE 1 : Stability Constants $\log \beta_{xy}$ of the complexes of 2-aminobenzimidazole with Alkali and Alkaline earth cations (a) in Methanol and (b) in acetonitrile at 25 °C, $I = 10^{-2}M$.

M:L	Li ⁺	Na ⁺	K ⁺	Rb ⁺	Cs ⁺	Mg ²⁺	Ca ²⁺	Sr ²⁺	Ba ²⁺	
^a 2-aminbenz	1:1	4.10	3.93	4.18	3.21	4.28	3.54	3.00	3.41	4.08
^b 2-aminbenz	1:1	4.05	4.81	3.31	2.78	4.12	4.80	4.12	4.91	4.21

$$0.01 \leq \sigma_{n-1} \leq 0.16$$

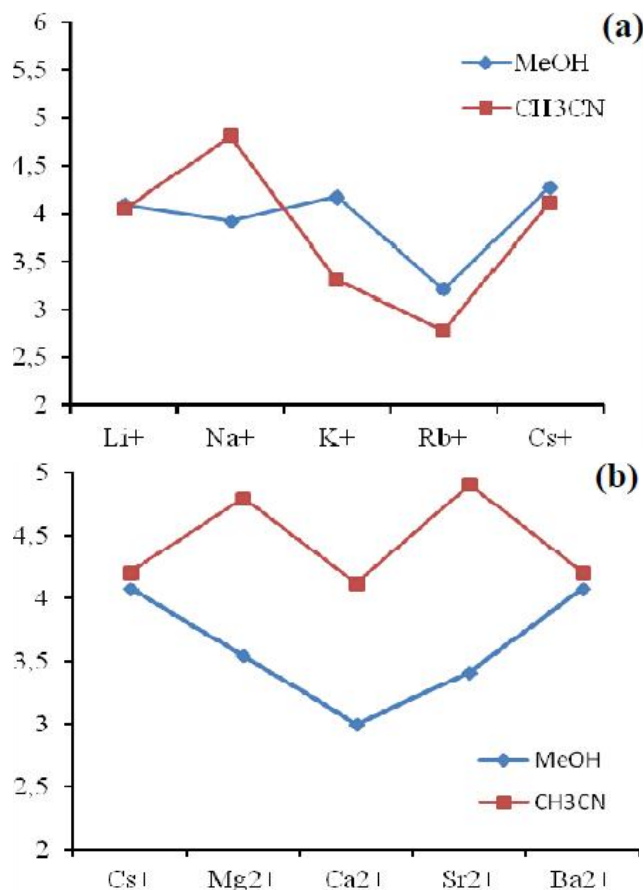


Figure 1 : Stability constants $\log \beta_{11}$ (determined in methanol and acetonitrile) for (a) alkali metals series; (b) alkaline earth metals series with 2-aminobenzimidazole.

The selectivity profile of the 2-aminobenzimidazole in the series of alkali cations, shows an affinity complexation of sodium in acetonitrile whereas this affinity is in favor of potassium in methanol. The solvent effect is not observed for complexes of lithium and cesium and their stabilities do not change with the change of solvent. Moreover, the variation profiles selectivities leaves suggest that the size of the cations is not a dominant factor in the phenomenon of complexation.

The selectivity profile of the 2-aminobenzimidazole in the series of alkaline earth cations shows a better stability of the complexes formed in acetonitrile compared to their counterparts formed in methanol with the exception of barium complex where the values of stability constants in the two solvents are almost equal. The stability of complexes formed in acetonitrile can be explained by a better solvation of the complexes in acetonitrile compared to that in methanol.

Unlike other cation families, stability of complexes formed with Ni²⁺ and Cu²⁺ shows greater stability in methanol compared with acetonitrile, indicating a different solvation of these cations in the solvents considered. However, the stability of the complexes is not supported solely by the size. Indeed, the ions of cobalt and copper, which have the same ionic radius, have different stability constants.

The complexes formed with the heavy metals and the 2-aminobenzimidazole are biligands, which implies an interaction between the metal and the ligand, in sandwich or linear polymer (1D polymer)^[17,3].

Regarding the lanthanum and neodymium complexes are formed in acetonitrile biligand species with improved stability for the complexes of lanthanum with respect to neodymium.

In the other hand, the 1:1 stoichiometry of the complexes with 2-aminobenzimidazole were confirmed by conductimetric studies (Figure 4)

Extraction of metal picrates

Extraction percentages (%E) of alkali, alkaline earth and transition metal cations by 2-aminobenzimidazole from Water into dichloromethane are given in TABLE 3.

The study of the extraction of metal picrates from water to dichloromethane with 2-aminobenzimidazole shows that the extraction percentages obtained are gen-

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TABLE 2 : Stability constants $\log \beta_{xy}$ of the complexes of 2-aminobenzimidazole with some transition, have and lanthanide metal (a) in methanol and (b) in acetonitrile at 25 °C, $I = 10^{-2}M$.

	M:L	Cr ²⁺	Co ²⁺	Ni ²⁺	Cu ²⁺	Zn ²⁺	Cd ²⁺	Pb ²⁺	Hg ²⁺	La ³⁺	Nd ³⁺
^a 2-aminobenz	1:2	11.40	10.43	10.10	11.57	10.04	9.04	7.70	8.99	-	-
^b 2-aminobenz	1:2	11.60	10.81	8.51	7.09	9.02	8.02	8.30	8.70	10.01	9.03

$$0.01 \leq \sigma_{n-1} \leq 0.16$$

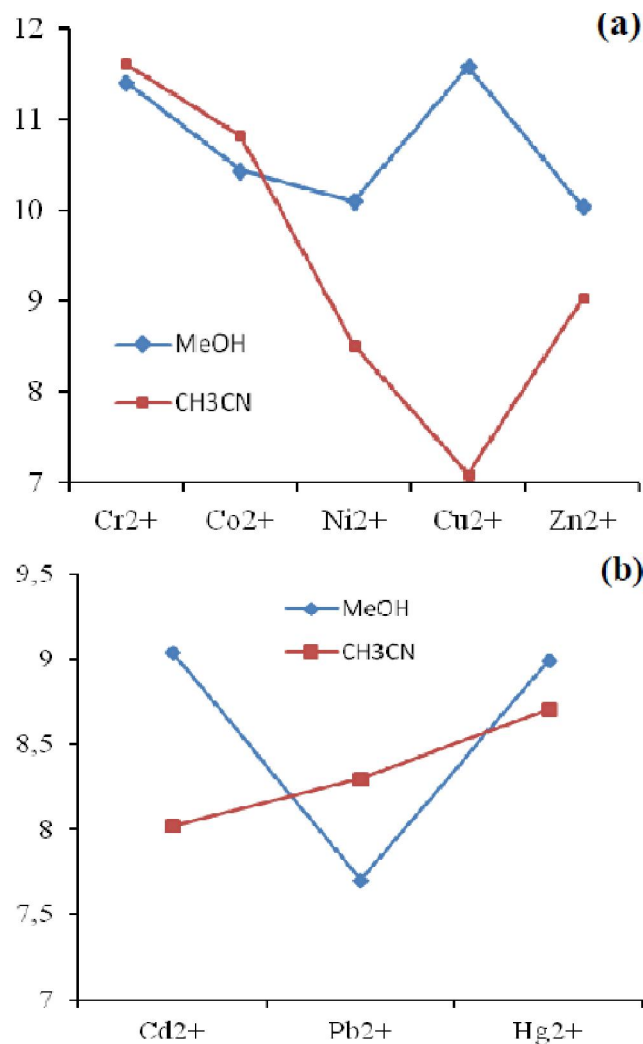


Figure 2 : Stability constants $\log \beta_{12}$ (determined in methanol and acetonitrile) for some (a) transition metals and (b) have metals series with 2-aminobenzimidazole.

erally low, with the exception of some cations such as Mg²⁺ and Co²⁺, where the extraction percentages exceed 10%. Indeed, the 2-aminobenz cation retrieves any of the series of alkali metals studied.

In the series of alkaline earth 2-aminobenzimidazole extracts notable Mg²⁺ with percentages of 58%.

The picrate of cobalt is the only extract in the series of transition metals studied by the ligand and this one only with a percentage of 45%.

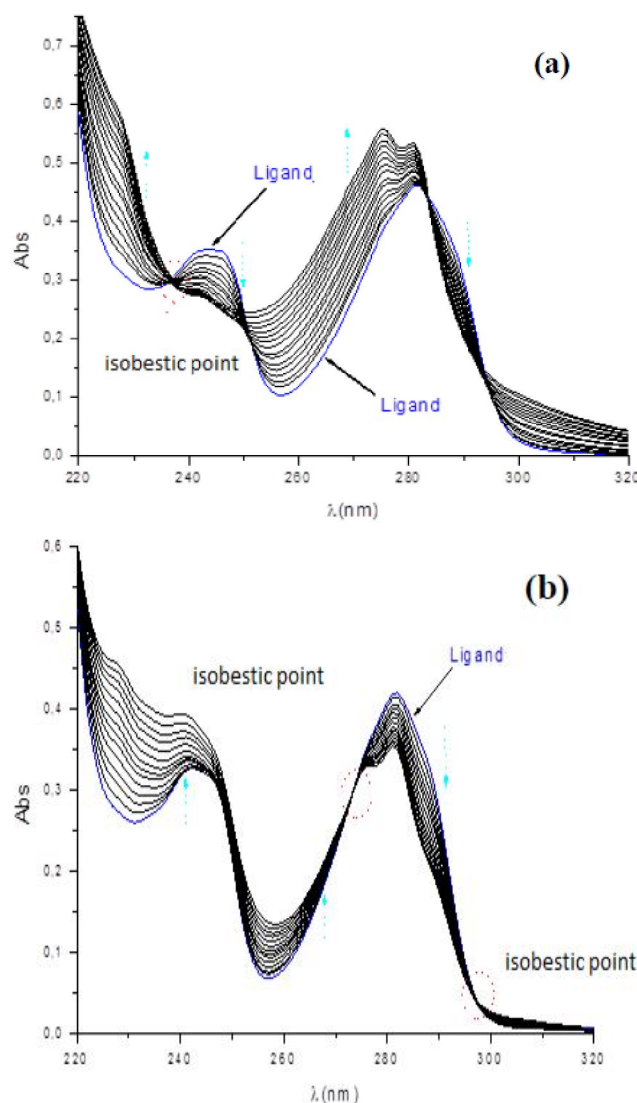


Figure 3 : UV absorption spectra on complexation of (a) Cu²⁺ and (b) Pb²⁺ with 2-aminobenzimidazole in methanol ($0 \leq R_{ML} \leq 2.3$) at 25°C.

However, 2-aminobenz show no affinity extraction towards the transition metals studied and lanthanide picrate.

Furthermore, we can deduce that the complexing 2-aminobenzimidazole is not the dominant factor in the extraction of metal cations as no cation is extracted by these two ligands, with the exception of Mg²⁺, where two ligands extract the metal cation.

Preliminary complexation studies of 2-aminobenzimidazole with $\text{Li}^+(\text{Pic}^-)$, $\text{Na}^+(\text{Pic}^-)$, $\text{Mg}^{2+}(\text{Pic}^-)_2$, $\text{Ca}^{2+}(\text{Pic}^-)_2$ and $\text{Ni}^{2+}(\text{Pic}^-)_2$ were monitored by means of $^1\text{H NMR}$. CDCl_3 solutions of 2-aminobenzimidazole ($10^{-3} \text{ mol L}^{-1}$) were reacted with the solid picrates (directly introduced in the NMR tube) until the spectra of the resulting solutions remained unchanged (7 days). The formation of a complex induced changes in the $^1\text{H NMR}$ patterns with the appearance of a singlet corresponding to the extracted picrate at 8.70–8.80 ppm.

The ratio of the extracted species to ligand in solution was estimated by calculating the integration ratio of

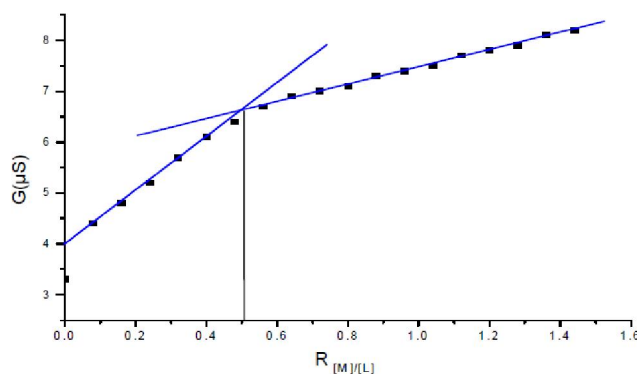


Figure 4 : Conductometric titration in the case of 2-aminobenzimidazole with Cu^{2+} .

TABLE 3 : Extraction percentages (%E) of metal picrates by 2-aminobenzimidazole from water into dichloromethane, at 25°C ($C_L = C_M = 2.5 \times 10^{-4} \text{ mol L}^{-1}$).

cations	Alkali cations				Alkaline earth cations				Transition metals cations					
	Li^+	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Ca^{2+}	Ba^{2+}	Co^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Hg^{2+}	Pb^{2+}
% E	≤ 1	≤ 1	≤ 1	5	2	58	15	≤ 1	45	8	5	≤ 1	≤ 1	≤ 1

the picrate proton resonances vs those of the protons of the ligand. Li^+ , Na^+ , Mg^{2+} , Ca^{2+} and Ni^{2+} induced changes of the spectrum of ligand with the formation of the following 1:1 complexes $\text{Li}^+(\text{Pic}^-)$, 2-aminobenzimidazole, $\text{Na}^+(\text{Pic}^-)$, 2-aminobenzimidazole, $\text{Mg}^{2+}(\text{Pic}^-)_2$, 2-aminobenzimidazole, $\text{Ca}^{2+}(\text{Pic}^-)_2$, 2-aminobenzimidazole and 1:2 complexes $\text{Ni}^{2+}(\text{Pic}^-)_2$, (2-aminobenzimidazole) $_2$.

CONCLUSION

The results show the formation of mononuclear species to a ligand complex with alkali metals and alkaline earth species biligands with transition metals, heavy metals and lanthanides. The conductometric titration and $^1\text{H NMR}$ solid-liquid extraction confirmed mainly stoichiometries of complexes formed in solution with 2-aminobenzimidazole determined by the UV Spectrophotometric study.

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