



Binding and Ionophoric Properties of Polythioamide Compounds. Ag(I) and Hg(II) Selectivities

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Abstract. The synthesis of tetrathiolactams and related di- and tetrathioamide compounds is described. The formation constants of their heavy-metal complexes are determined by using the strong UV absorption of the thioamide chromophore. Extraction and transport abilities of tetrathioamide ionophores show selectivities for Ag(I) and Hg(II) cations over alkali, alkaline-earth or other heavy metal cations including transition metals such as Co(II).

Key words: complexes, stability, extraction, transport, tetrathiolactams

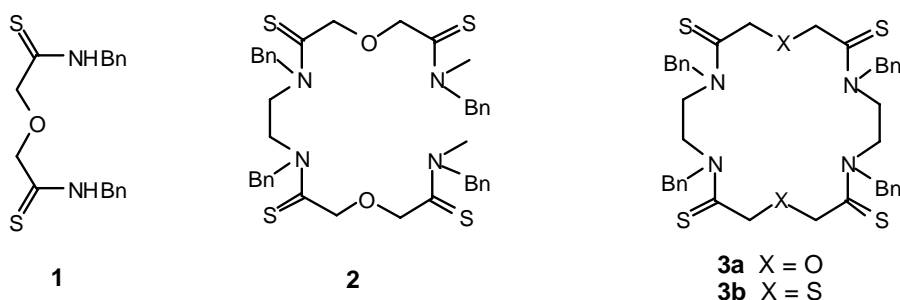
1. Introduction

Compounds with thioamide functions have been sparingly studied with regard to their ionophoric properties [1]. However, a recent paper [2] about cation complexation by thioamide derivatives of *tert*-butylcalixarenes prompted us to report on the binding and ionophoric properties of tetrathiolactams and related polythioamides.

Thioamide derivatives of calixarenes were found to be efficient extractants for Cu(II), Pb(II) and Ag(I) ions [2, 3] and, also, Ag(I), Pb(II) or Cd(II)-selective sensors for chemically modified field effect transistors (CHEMFETs) [1c, d]. None of the published data refer to Hg(II) ions which are promising targets for efficient and selective complexation by thioamide groups following Pearson's principle.

In a previous paper, we found [4] that tetralactams and tetramides are lead-selective ionophores. We examine here the dioxo- and dithiatetrathiolactams **3a** and **3b** and open-chain dithioamide **1** and tetrathioamide **2**. We determined spectrophotometrically their complex formation constants using, for the first time, the intense absorption of the thioamide chromophore and their extraction properties and transport abilities vs. various cations.

Selectivities for Ag(I) and Hg(II) ions were emphasized over alkali, alkaline-earth and other heavy metal ions.



2. Experimental

2.1. PREPARATION OF THE LIGANDS

The thioamide compounds **1–3** were derived from their amide analogs **1'–3'** which have been previously described [5–7].

General procedure for thionation of amide compounds. Lawesson's reagent (1.1 or 2.1 equiv.) was added to a solution of polyamide in dry toluene. The mixture was stirred at 110 °C under argon for 20 h. After filtration or evaporation a solid residue was obtained and purified by liquid chromatography on silicagel.

Dithioamide 1. Diamide **1'** [5] furnished dithioamide **1** as a white solid (86%), m.p. 132–134 °C (from dichloromethane/ethylacetate 99/1). Anal. calc. For $C_{18}H_{20}N_2O S_2$: C, 62.76; H, 5.85; N, 8.13. Found: C, 62.23; H, 5.80; N, 8.01. IR (KBr), ν 3213 (NH); 1538 (thioamide I). 1H NMR ($CDCl_3$), δ 4.4 (s, 4H, CH_2O); 4.85 (d, 4H, CH_2Ph); 7.25–7.36 (m, 10H, ArH); 8.24 (s, 2H, NH). ^{13}C NMR ($CDCl_3$), δ 43.7 (CH_2Ph); 71.2–72.4 (CH_2O); 130.3 (ArC); 132.0–132.8 (ArCH); 191.2 (C=S).

Tetrathioamide 2. Tetramide **2'** [6] furnished tetrathioamide **2** as a yellow solid (71%), m.p. 123–125 °C (from dichloromethane). Anal. calc. for $C_{40}H_{46}N_4O_2S_4$: C, 64.65; H, 6.24; N, 7.54. Found: C, 64.42; H, 6.20; N, 7.45. MS (DCI/ NH_3) m/z 743 (100%, $[M+H]^+$). IR (KBr), ν 1498 (thioamide I). 1H NMR ($CDCl_3$): δ 3.15–3.33 (s, 6H, CH_3); 4.12–4.22 (m, 4H, CH_2N); 4.58–4.65 (m, 8H, CH_2Ph); 4.85–5.29 (m, 8H, CH_2O); 7.05–7.35 (m, 20H, ArH). ^{13}C NMR ($CDCl_3$): δ 39.0, 42.7 (CH_3); 48.4–55.9 (CH_2N); 57.7, 58.5 (CH_2Ph); 76.8, 76.9, 77.4 (CH_2O); 126.7–129.1 (ArCH); 135.0, 135.1, 135.15, 135.5 (ArC); 197.1, 197.7, 198.3, 198.7 (C=S).

Dioxatetrathiolactam 3a. Dioxatetralthiolactam **3'a** [7] furnished dioxatetrathiolactam **3a** as a white solid (44%), m.p. > 200 °C (from dichloromethane/acetone 80/20). Anal. calc. for $C_{40}H_{44}N_4O_2S_4$: C, 64.83; H, 5.98; N, 7.56. Found: C, 64.81; H, 6.00; N, 7.42. MS (DCI/ NH_3) m/z = 741 (100%, $[M+H]^+$). IR (KBr), ν 1489 (thioamide I). 1H NMR ($CDCl_3$): δ 3.09 (m, 2H, CH_2N); 3.53 (m, 2H, CH_2N); 3.71 (m, 2H, CH_2N); 4.16 (m, 2H, CH_2N); 4.17–5.77 (m, 16H, CH_2Ph , CH_2O); 7.11–

7.4 (m, 20H, ArH). ^{13}C NMR (CDCl_3): δ 48.3–48.9 (CH_2N); 54.6–57.6 (CH_2Ph); 75.2–79.7 (CH_2O); 126.2–129.4 (ArCH); 134.6–135.8 (ArC); 197.1–201.0 (C=S).

Dithiatetrathiolactam 3b. Dithiatetralactam **3'b** [7] furnished dithiatetrathiolactam **3b** as a white solid (77%), m.p. > 200 °C (from dichloromethane/methanol 91/9). Anal. calc. for $\text{C}_{40}\text{H}_{44}\text{N}_4\text{S}_6$: C, 62.14; H, 5.74; N, 7.25. Found: C, 62.67; H, 5.80; N, 7.24. IR (KBr), 1496 (thioamide I). ^1H NMR (DMSO-d_6) δ 3.2–3.6 (m, 8H, CH_2N); 3.7–4.2 (m, 8H, CH_2Ph , CH_2S); 4.4–4.6, 4.9, 5.3 (m, 8H, CH_2Ph , CH_2S); 7.18–7.35 (m, 20H, ArH). ^{13}C NMR (DMSO-d_6) δ 42.0–45.3 (CH_2N); 47.8, 48.3, 48.8 (CH_2S); 51.6, 54.0, 55.3, 55.7, 56.4 (CH_2Ph); 126.1–129.0 (ArCH); 134.7–137.9 (ArC); 199.4 (C=S).

2.2. PREPARATION OF THE COMPLEXES

Mercuric perchlorates. One equivalent of mercuric perchlorate in acetonitrile (1 mL) was added to a 0.02 M chloroform solution (2 mL) of ligand. The complex was isolated by filtration, washed with ether and dried *under vacuum*.

2. Hg(ClO₄)₂. Anal. calc. for $\text{C}_{40}\text{H}_{46}\text{N}_4\text{O}_{10}\text{S}_4\text{Cl}_2\text{Hg}$: C, 42.05; H, 4.06; N, 4.90 Found: C, 41.93; H, 4.05; N, 5.00. IR (KBr), ν 1526 (thioamide I), 1175 (COC).

3a. Hg(ClO₄)₂·H₂O. Anal. calc. for $\text{C}_{40}\text{H}_{46}\text{N}_4\text{O}_{11}\text{S}_4\text{Cl}_2\text{Hg}$: C, 41.47; H, 4.00; N, 4.84 Found: C, 41.02; H, 3.78; N, 4.74. IR (KBr), ν 1525 (thioamide I), 1177 (COC).

Silver nitrate. One equivalent of silver nitrate in acetonitrile solution (1 mL) was added under argon in the dark to a 0.02 M solution in the same solvent (1 mL) of tetrathioamide **2**. A yellow solid product was obtained turning to dark brown by light exposure.

2. AgNO₃. ES⁺ MS (CH_3CN): $m/z = 851.1$ (100%, [**2**.Ag]⁺). IR (KBr), ν 1522 (thioamide I), 1157 (COC).

2.3. DETERMINATION OF THE FORMATION CONSTANTS

The overall apparent formation constants (β) of the heavy metal complexes were measured at 25 °C in acetonitrile solutions by UV-visible spectrophotometry using, for the first time, the thioamide absorbance. The thioamide function is characterized by a powerful chromophore associated to $\pi \rightarrow \pi^*$ or $n \rightarrow \sigma^*$ absorption bands [8]: $\epsilon = 25,000 \text{ M}^{-1}\cdot\text{cm}^{-1}$ at $\lambda_{\text{max}} = 268 \text{ nm}$ for dithioamide **1**, $\epsilon = 40,000$ at $\lambda_{\text{max}} = 280 \text{ nm}$ for tetrathioamide **2** and $\epsilon = 46,700$ at $\lambda_{\text{max}} = 287 \text{ nm}$ for tetrathiolactam **3a** in acetonitrile. Compound **1** in chloroform gives $\lambda_{\text{max}} = 271 \text{ nm}$ ($\epsilon = 25,100$) i.e. a bathochromic effect of 3 nm with respect to the more polar solvent

(acetonitrile) in agreement with a $n \rightarrow \sigma^*$ transition as previously found [9] for thioacetamide. These thioamide bands allow a direct determination of the formation constants of complexes in acetonitrile with metallic salts transparent in the UV range or slightly absorbing like perchlorates.

The evolution of the UV-visible spectra of ligands and complexes was monitored by adding aliquots of metal perchlorate so that $\rho = \text{metal/ligand}$ varied from 0 to 1–10. Plots of optical density as a function of the metal:ligand ratio gave a first indication of the number and stoichiometry of the complexes formed (Figures 1, 2). The STAR/FA program [10] was then used to confirm the number of different absorbing species in solution by factor analysis of the absorbance data matrix. Calculations of the formation constants were performed with the STAR program developed by Beltran [10] for studying ionic equilibria from spectrophotometric data. These calculations took into account the low absorption of perchlorates in acetonitrile. STAR is a non-linear regression program for the refinement of complex formation constants. The mass balance equations of the system were solved from the given model and the total concentrations of the components. The model took into account a set of complexes with fixed stoichiometry M_xL_y and variable (estimated) formation constants. STAR gives several statistical characteristic parameters to test the reliability of the regression process [10]. The most important parameter is the standard deviation of the absorbances (A) which must be compared to the instrumental error of the spectrophotometer ~ 0.002 . This program gave a good measure of the merits of different models M_xL_y used for complex stoichiometry, and the spectrophotometric data can be satisfactorily fitted with following equilibria:



Results as $\log \beta$ are gathered in Table I for ligands **1–3a** and their complexes with Pb(II), Cd(II), Hg(II), Zn(II) and Cu(II) cations. Wavelengths and extinction molar coefficients at the maximum of absorbance for the main bands and charge transfer bands of the complexes were also given by the STAR program.

2.4. EXTRACTION EXPERIMENTS

Two series of experiments were performed. One of them reproduces exactly the experimental conditions described in reference 4, i.e. in situ formation of picrate salts from picric acid (2×10^{-3} M or 10^{-3} M for di- and monovalent cations respectively) and excess of metallic nitrate (5×10^{-2} M) in the aqueous phase; extraction of the cation to a chloroform phase containing the ionophoric ligand (10^{-3} M). The second series takes into account the low solubility of the mercuric

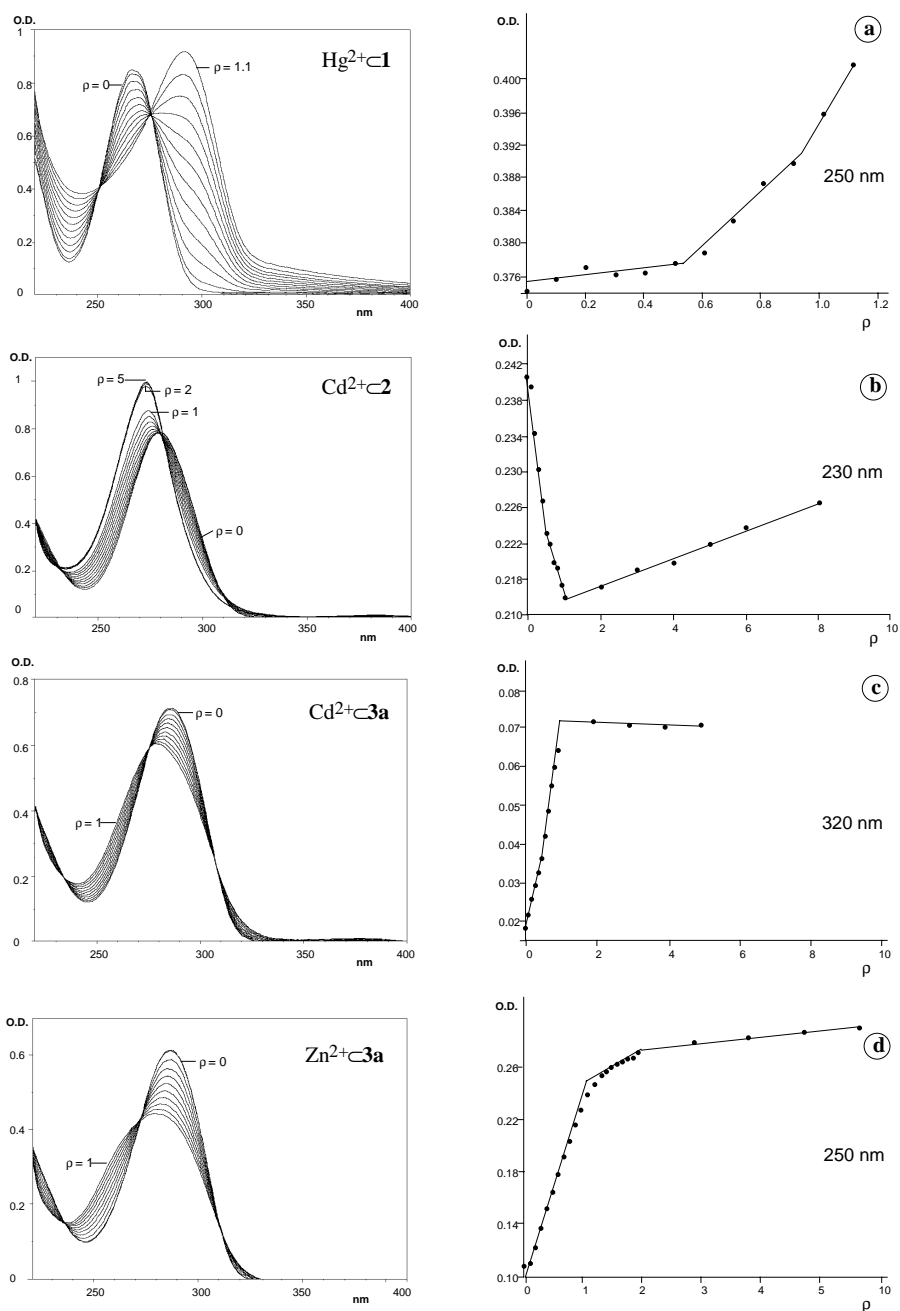


Figure 1. Evolution of the UV/visible spectrum of ligand **1** (a), **2** (b) or **3a** (c, d) upon addition in acetonitrile of Hg(ClO₄)₂ (a), Cd(ClO₄)₂ (b, c), Zn(ClO₄)₂ (d): [ligand] = 1.5–3.0 × 10⁻⁵ M. 0 ≤ ρ ≤ 1.1–10 and O.D. variation against ρ = [M(ClO₄)₂]/[ligand].

Table I. Formation constants^a (β), absorption maxima^b and molar absorption^c of cation complexes in acetonitrile at 25 °C

		Pb ²⁺			Cd ²⁺			Hg ²⁺			Zn ²⁺			Cu ²⁺			
		L	ML	ML ₂	M ₂ L	ML	ML ₂	M ₂ L	ML	ML ₂	M ₂ L	ML	ML ₂	M ₂ L	ML	ML ₂	M ₂ L
1	log β	–	d			5.7	10.7	–	5.8	10.7	–	e			5.9	–	10.6
	λ_{\max}	268				265	266	–	294	268	–				268	–	265
	ϵ_{\max}	25,000				26,700	49,500	–	33,700	50,400	–				20,200	–	22,200
2	log β	–	d			8.4 ^g	12.8	–	9.4 ^g	15.1	16.7	e			5.6	–	11.1
	λ_{\max}	280				274	284	–	286	279	270				281	–	279
	ϵ_{\max}	40,000				43,000	74,000	–	51,000	70,000	38,500				33,500	–	28,000
	$\lambda_{\text{ct}}^{\text{f}}$	–				–	–	–	–	–	395				–	–	390
	$\epsilon_{\text{ct}}^{\text{f}}$	–				–	–	–	–	–	3,200				–	–	11,300
3a	log β	–	7.0	11.8	12.2	6.7	11.6	–	7.3	12.5	14.0	6.4	11.4	11.1	6.1	–	12.3
	λ_{\max}	287	289	287	281	280	287	–	305	282	278	268	285	272	280	–	275
	ϵ_{\max}	46,700	39,000	89,000	42,000	38,000	92,000	–	54,000	78,000	39,000	33,000	83,500	22,000	33,000	–	25,500
	$\lambda_{\text{ct}}^{\text{f}}$	–	–	–	378	–	–	–	390	–	385	–	–	–	385	–	420
	$\epsilon_{\text{ct}}^{\text{f}}$	–	–	–	10,000	–	–	–	5,000	–	6,400	–	–	–	5,600	–	2,900

^a Uncertainties on log β values are around 5%. All the statistical tests [10] are satisfied.

^b λ_{\max} (nm).

^c ϵ_{\max} (M⁻¹ cm⁻¹).

^d no significant spectrum variation was observed.

^e not determined.

^f ct: charge transfer band.

^g more significantly, related to the experimental technique used, these values may be expressed as >8.

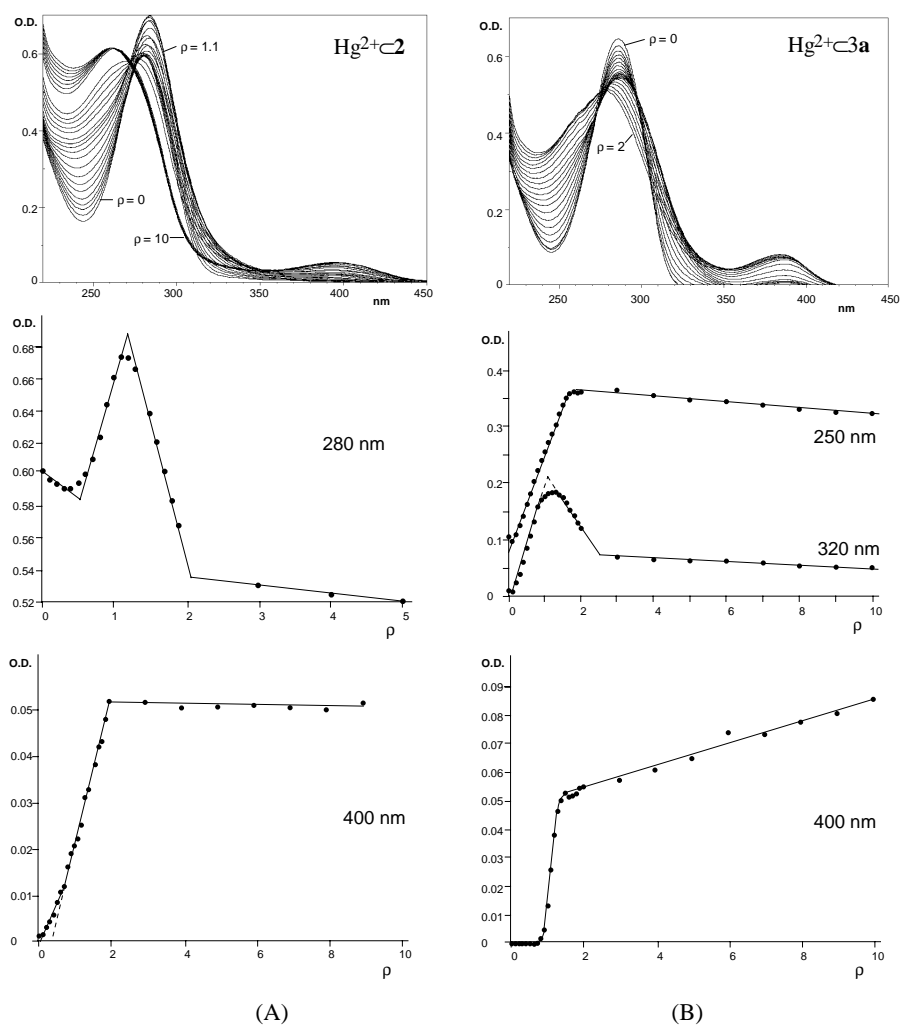


Figure 2. (A) Evolution of the UV/visible spectrum of ligand **2** upon addition of $\text{Hg}(\text{ClO}_4)_2$ in acetonitrile: $[\mathbf{2}] = 1.52 \times 10^{-5} \text{ M}$, $0 \leq \rho \leq 10$ and O.D. variation against $\rho = [\text{Hg}(\text{ClO}_4)_2]/[\mathbf{2}]$ at two wavelengths. (B) Evolution of the UV/visible spectrum of ligand **3a** upon addition of $\text{Hg}(\text{ClO}_4)_2$ in acetonitrile: $[\mathbf{3a}] = 1.35 \times 10^{-5} \text{ M}$, $0 \leq \rho \leq 10$ and O.D. variation against $\rho = [\text{Hg}(\text{ClO}_4)_2]/[\mathbf{3a}]$ at three wavelengths.

salts in aqueous medium. Thus, the concentrations were reduced to $[\text{picric acid}] = 2.5 \times 10^{-5} \text{ M}$, $[\text{metal nitrate}] = 10^{-3} \text{ M}$, $[\text{ionophore}] = 2.5 \times 10^{-4} \text{ M}$ as previously used by Nishimura [11].

In order to compare the results of extraction of heavy metals by the corresponding amides, four cations (Ag^+ , Hg^{2+} , Pb^{2+} , Cu^{2+}) were investigated at $2.5 \times 10^{-4} \text{ M}$ and all the studied cations apart from Hg^{2+} at 10^{-3} M .

2.5. TRANSPORT EXPERIMENTS

The instrumentation consisted of a thermostated cylindrical cell ($T = 25.0\text{ }^{\circ}\text{C}$) which is divided into three parts of 11 mL each separated by two Fluoropore membranes of $175\text{ }\mu\text{m}$ thickness. The three compartments were stirred independently and synchronously at 550 rpm. The ionophore, dissolved in CHCl_3 , was placed in the middle compartment and the aqueous phases were placed in the other parts. The transport rates gathered in Table III were calculated from the quantity of ion transported after 24 h into the aqueous receiving phase, which was determined by UV spectrophotometry.

Although very slightly extracted ($< 1\%$), picric acid is carried through the chloroform membrane so that isolated metal picrates were used for calcium, lead, cadmium and zinc but the nitrate was used for mercury.

The detection of this latter ion was performed by complexometric titration [12]. The dithizone was used with the usual cautions in buffered solutions (2 M glycine, $\text{pH} = 3.0$). A spectrophotometric calibration was carried out before each set of transport experiments. Measurements were realized at two wavelengths, 480 and 585 nm, on the aqueous receiving phase using titration curves.

3. Results and Discussion

3.1. STABILITY OF THE COMPLEXES

The UV-visible spectral variations of ligands as a function of the ratio of metallic picrate/ligand concentrations in the 220–450 nm interval (examples in Figures 1, 2) suggests the participation of several complexes (isosbestic points) and their stoichiometries (slope variations at given wavelengths) (Figures 1, 2, Table I).

For instance, ML complexes exist in all cases but ML_2 complexes are not observed for the Cu(II) cation probably related to the preferred tetracoordination of this atom in square planar or bipyramidal arrangements difficult to obtain in ML_2 complexes. On the other hand, M_2L complexes are not observed with Cd(II) whatever the ligand. This heavy metal cation is tetrahedrally coordinated in the tetrakis *N,N*-dimethylbenzenecarbothioamide/ $\text{Cd}(\text{ClO}_4)_2$ complex [13]. Thus, this structure and other structures (trigonal bipyramidal or octahedral) appear to be not adapted for M_2L units. The case of Hg(II), Zn(II) and Pb(II) ions is different since all three complexes were found, e.g. for **3a**. With the open-chain dithioamide **1** the M_2L complexes were not observed. A possible explanation is related to the fact that with only two thioamide soft coordinating sites these M_2L mercury or cadmium complexes are unlikely. It is not the case with Cu(II) where the ethereal oxygen atom can be coordinated as well as the thioamide sulfur atoms, aqueous molecules and perchlorate ions found, for instance, in the 2-formylpyridine thiosemicarbazone/ $\text{Cu}(\text{ClO}_4)_2$ complex [14]. In these ligands where oxygen and sulfur atoms are present, the structure of the complexes will be very dependent on Pearson's principle.

Other information can be extracted from these experiments: first, ML complexes induce either *hypsochromic effects* (CdC**1**, **2**, **3a**; Zn, CuC**3a**) or *bathochromic effects* (HgC**1**, **2**, **3a**). Hypsochromic effects agree with an increased $n \rightarrow \sigma^*$ transition energy according to the participation of sulfur atoms in the complexation which is confirmed by the I.R. analysis on the thioamide I band [15]. A spill-over effect [16], increasing the ν_{C-N} frequency near 1500 cm^{-1} by σ -type coordination between the sulfur atom and the metal ion, is observed: e.g. $\Delta\nu = 24\text{ cm}^{-1}$ (CdC**1**). Similar shifts are noticed for Hg(II) complexes: e.g. $\Delta\nu = 28\text{ cm}^{-1}$ (HgC**2**) or 36 cm^{-1} (HgC**3a**) supporting the involvement of sulfur atoms in the complexation. On the other hand, the bathochromic effect indicates a $\pi \rightarrow \pi^*$ perturbation which might be related to a thioamide function with an iminothiolate character in the formed complex; a greater effect obtained with dithioamide **1**, the only compound with secondary thioamide functions, is in favour of this hypothesis. Secondly, bands appear (Table I, Figure 2) in the 380–420 nm interval with ligands **2**, **3a** and Hg(II) or Cu(II) ions or even Pb(II)C**3a** with molar absorption coefficients in the range $2,900\text{--}11,300\text{ M}^{-1}\cdot\text{cm}^{-1}$. The O.D. variation against ρ shows that ML or M_2L complexes can be associated to these bands which are assigned to a $S \rightarrow Cu(II)$ ligand-to-metal charge transfer transition [17]. Koslowski et al. [18] describe such bands at 350 nm ($\epsilon = 6,000$) for tmet-NHMe or 361 nm ($\epsilon = 3,500$) for tleu-NHMe, thioamide analogs of methionine and leucine aminoacids and Ainscough et al. [14] at 385–435 nm for 2-formylpyridine thiosemicarbazone/Cu(II) complexes. Thirdly, the formation constants of the complexes as determined with the aid of the STAR program lead to the following comments: (i) dithioamide **1** gives ML complexes of the same strength ($\log \beta = 5.8$) with Cd^{2+} , Hg^{2+} and Cu^{2+} ions; (ii) the same ML complexes correspond to greater formation constants with dioxatetrathiolactam **3a** ($\log \beta = 6.1\text{--}7.3$) for all the five studied cations with a maximum value for Hg^{2+} ; (iii) a substantial increase with respect to **3a** is obtained with tetrathioamide **2** for Cd^{2+} and Hg^{2+} except for Cu^{2+} where a decrease of $\Delta\log \beta_{ML} = 0.5$ was calculated. With cadmium and mercury cations no macrocyclic effect was found. The greatest formation constants with the open-chain tetrathioamide might be correlated with a greater flexibility of this ligand which can better fit the metal ion around its coordination sphere. Similar results were obtained [6] for calcium complexes of tetramide vs. dioxatetrathiolactam, amide analogous of respectively **2** and **3a**.

3.2. LIQUID-LIQUID EXTRACTIONS

The extraction of cations from an aqueous phase to a chloroform phase was performed from picrates formed in situ using picric acid and an excess of metal nitrates following Nishimura [11]. When the extraction equilibrium was reached after about 15 h, the percentages (E) of cation extracted was measured spectrophotometrically by the absorption of the picrate anion in the aqueous phase and are reported for

Table II. Extraction^a percentages (E%) of metallic picrates at 25 °C from water to chloroform by thioamide ligands and, in brackets, by the corresponding amides^b

	Na ⁺	Ca ²⁺	Pb ²⁺	Cd ²⁺	Hg ²⁺	Zn ²⁺	Cu ²⁺	Co ²⁺	Ag ⁺	log P ^c
1	4	5	4 1*	4	– 26*	3	14 0*	6	– 12*	2.0
2	5 (0)	3(39)	4 (48) 2*	8 (2)	– 67*	3 (1)	44 (4) 22*	7 (4)	– 32*	5.2
3a	5 (5)	5 (1)	9 (72) 1*	4 (1)	– 68*	1 (0)	16 (2) 12*	14 (7)	– 50*	5.5
3b	–	–	– 2*	–	– 72*	–	–	–	– 66*	–

^a Conditions: aqueous phase [HPic] = 2×10^{-3} M or 2.5×10^{-5} M (*); $[M^{n+}(\text{NO}_3)_n] = 5 \times 10^{-2}$ M or 10^{-3} M (*); chloroform phase [ligand] = 10^{-3} M or 2.5×10^{-4} M (*).

^b Data and experimental procedure from ref. 4.

^c Lipophilicity measured by RPTLC technique [25].

thioamide compounds and their corresponding amides [4] at 10^{-3} M or 2.5×10^{-4} M (Table II).

A first examination indicates that (i) dithioamide **1** extracts poorly any cation except Hg(II) (26% at 2.5×10^{-4} M); (ii) Na⁺, Cd²⁺, Zn²⁺ and Co²⁺ are also poorly extracted with all the thioamide compounds and their corresponding amides; (iii) a striking difference is noticed with Ca²⁺, Pb²⁺ and Cu²⁺ extracted by amide (E_A) and thioamide (E_T) compounds, i.e. E_T/E_A = 3/39 (Ca²⁺ < **2**), 4/48 (Pb²⁺ < **2**), 9/72 (Pb²⁺ < **3a**), 44/4 (Cu²⁺ < **2**). (iv) Hg²⁺ and Ag⁺ are fairly (Hg²⁺ < **1**; Ag⁺ < **2**) or greatly (Hg²⁺ < **2, 3**; Ag⁺ < **3**) extracted at 2.5×10^{-4} M.

These results call for some comments: (i) the weak extraction with dithioamide **1** can be correlated to its low lipophilicity (log P = 2) and poor encapsulating power; (ii) the soft cations Hg²⁺ and Ag⁺ are extracted at high level with ligands containing sulfur atoms following the HSAB affinity principle [19]. Cd²⁺ which is also a soft cation is poorly extracted by thioamides **2–3** similar to some thioamide derivatives of calix[4]arenes [2]; opposite results in this latter series indicate an important sensitivity of the extraction process to the structure of the complexes. The increase of the extraction of Ag⁺ and Hg²⁺ is correlated to the number of sulfur ligating sites from 2 for compound **1** to 4 (tetrathioamides **2** and **3a**) and 6 (dithiatetrathioamide **3b**) due also in part, to the greater lipophilicity introduced by the substitution by sulfur of oxygen atoms. On the other hand a macrocyclic effect is noticed with Ag⁺ but not with Hg²⁺ (**2**→**3a**) indicating a possible better complementarity. In the calix[4]arene series, a compound where the phenoxy groups are substituted by *tert*-butyl-acetate groups presents also [11] a good extracting power for Ag⁺ (~60%) but a lesser one for Hg²⁺ (~50%); no data about Pb²⁺. In the *p-tert*-butylcalix[4]- and [5]-arene series, compounds with alkylthioamide substituents [2] give higher percentages for Ag⁺ (80–98%) but have also a great affinity

Table III. Transport rates $\times 10^7$ (mol/h) of thioamidic ligands^a and, in brackets, the corresponding amides^b at 25 °C

Carrier	Ca ²⁺	Pb ²⁺	Cd ²⁺	Hg ²⁺	Zn ²⁺
1	<0.1	<0.1	<0.1	0.8	<0.1
2	<0.1 (0.1)	<0.1 (1.7)	<0.1 (0.1)	1.7	<0.1 (<0.1)
3a	<0.1 (<0.1)	<0.1 (1.0)	<0.1 (1.0)	2.0	<0.1 (0.9)
3b	–	–	–	2.2	–

^a Conditions: aqueous phase I: 11 mL, guest picrate or nitrate (Hg(II)), 10^{-3} M; chloroform phase: 11 mL, host carrier, 10^{-3} M; aqueous phase II: 11 mL.

^b Data from ref. 4.

for Pb²⁺; no data about Hg²⁺. (iii) Pb²⁺ is extracted at high level with both amide (94–97%) and thioamide (32–96%) derivatives of these calixarenes where four or five phenolic oxygen atoms participate in the complexation [2] or with tetramide **2'** and tetralactam **3'a** [4], but less than 5% with the corresponding thioamide **2** and thiolactam **3a**. Pb²⁺ prefers to bind to a hard oxygen atom than to a softer sulfur atom taking into account its specificity as a hard-soft borderline element and its favourable hydration energy [21]. This result is in favour of either a weak or no participation of the ethereal oxygens of **1**, **2** and **3a** in the complexation. (iv) finally, tetrathioamide **2** and tetrathiolactams **3** are very good selective extractants for Ag⁺ or Hg²⁺ cations vs. alkali, alkaline-earth and other heavy metals including transition metals like Co²⁺.

3.3. CATION TRANSPORT ACROSS A LIQUID MEMBRANE

Transport of ions across a bulk membrane is widely used to characterize the ionophoric properties of ligands [22]. In our study, a 10^{-3} M aqueous solution of metal picrate (Pb²⁺, Cd²⁺, Zn²⁺, Ca²⁺) or nitrate (Hg²⁺) is brought to migrate across a chloroform membrane containing a 10^{-3} M solution of ionophore into a second aqueous phase. The results as transport rates measured after 24 h are gathered in Table III.

As shown in Table III, dithioamide **1**, tetrathioamide **2** and dioxatetrathiolactam **3a** carry poorly (<2%) calcium, lead, cadmium and zinc picrates; these results agree with extraction percentages (<9%) in the same concentration conditions. The mercuric nitrate is well carried taking into account the weaker lipophilicity of the nitrate anion. Moreover, the extraction of Hg(II) increases with the number of sulfur atoms contained in the ionophore: **1** (17%) < **2** (37%) < **3a** (43%) < **3b** (47%). Among the two open-chain and macrocyclic analogous tetrathioamide compounds (**2** and **3a**) with four sulfur atoms, **2** should be a better carrier than **3a** following their formation constants (**2**: $\log \beta_{ML} > 8$; **3a**: $\log \beta_{ML} \sim 7.3$ in acetonitrile); the inverse observed result might be rationalized using the optimal

stability constant concept. Following this concept [23] an optimal value of the stability constant exists above or below which the rate of transport decreases. Izatt et al. [24] estimate this logarithmic value between 5 and 7 in methanol for crown-ethers and cations such as alkali or alkaline-earth. A value of about 7 in acetonitrile might be optimum in the tetrathioamide series for Hg(II).

4. Conclusions

Stable complexes are formed in acetonitrile solutions between heavy metal ions and ligands bearing four thioamide functions with the preferential ML stoichiometry. Their formation constants are readily accessible by UV spectrophotometry using the strong absorption of the thioamide chromophore ($\lambda = 270\text{--}280\text{ nm}$, $\epsilon \sim 10,000$) and values ($\log \beta$) as high as 9 are observed for Hg(II)/tetrathioamide complexes.

The substitution of oxygen by sulfur atoms in open-chain or macrocyclic tetraamide derivatives led to marked differences in the extraction of several metallic salts. The polythioamide compounds display excellent extractabilities and selectivities for Ag(I) and Hg(II) cations while their corresponding polyamides extract selectively the Pb(II) ion.

The high selective transport of Hg(II) ions by these tetrathioamide ionophores confirms their extraction and affinity properties for this ion.

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