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Diaminoanthraquinone-Linked Polyazamacrocycles: Efficient and Simple Colorimetric Sensor for Lead Ion in Aqueous Solution

Elena Ranyuk,[†] Christiane Morkos Douaihy,[†] Alla Bessmertnykh,[†] Franck Denat,[†] Alexei Averin,[‡] Irina Beletskaya,[‡] and Roger Guilard*[,†]

Institut de Chimie Moléculaire de l'Université de Bourgogne (ICMUB),
UMR 5260 CNRS, 9 Avenue Alain Savary, BP 47870-21078 Dijon, France, and
Department of Chemistry, M. V. Lomonosov Moscow State University,
1-Leninsky Gory, Moscow, Russia

roger.guilard@u-bourgogne.fr

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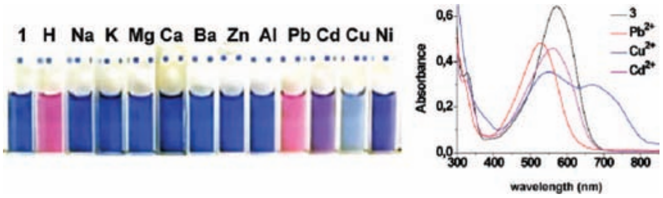
ABSTRACT



A new colorimetric molecular sensor based on a 1,8-diaminoanthraquinone signaling subunit exhibits efficient binding for lead ion in water and allows naked-eye detection.

Many works have been devoted to the design of new metal sensors for various applications such as clinical toxicology, environmental bioorganic chemistry, bioremediation, and waste management.[1] Lead ranks second in the list of toxic substances and is often encountered due to its wide distribution in the environment as well as its current and previous use in batteries, gasoline, pigments, and drinking water distribution systems.[2] Although numerous quantitative testing methods are available for lead, they are often cost demanding since atomic absorption spectroscopy (AAS) or inductively coupled plasma atomic emission spectroscopy (ICP-AES) are needed. In recent years, molecular sensors have been studied as new potential candidates for environmental monitoring.[3] Molecules capable of reversible target analyte-induced color changes are particularly attractive because they may be used as dip-stick sensors. Chromogenic sensors for lead ions have been described, but most of them operate in organic solvents, which limits their applications.[4] The development of water-soluble sensors is still progressing rather slowly because the synthesis of appropriate receptors is generally realized according to a multistep reaction and their solubility in aqueous medium is not easily predictable.

Anthraquinone derivatives have been described as important dyes for a long time,[5] but their use as a signaling subunit in chemosensors is limited due to their low solubility in aqueous media. To our knowledge, all chromogenic sensors containing this signaling subunit operate in organic solvents or in mixed organic−aqueous media.[6]

[†] Université de Bourgogne.

[‡] M.V. Lomonosov Moscow State University.

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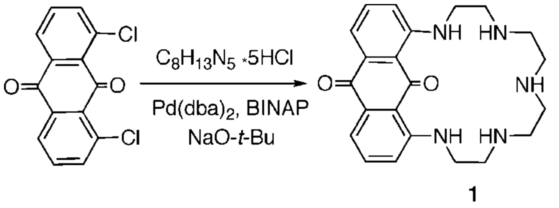
Recently, we have shown that the Buchwald−Hartwig amination reaction is a very efficient method for preparing polyazamacrocycles containing 1,5- and 1,8-diaminoanthraquinone moieties in the ring.[7] Such receptors have a priori a great interest for selective cation[8] or anion[9] detection. The presence of the anthraquinone fragment in close proximity to the cation-binding polyamine subunit induces the efficient participation of the anthraquinone moiety in metal binding and consequently gives an intensive optical response due to polarization, deprotonation,[8a,b] or conformation changes (which have not been yet exemplified for the anthraquinone-based chromogenic signaling subunits). Consequently, we have assumed that the polyazamacrocyclic backbone containing the anthraquinone unit incorporated into the macrocycle would be a good universal backbone for the development of selective sensors resulting from the simple attachement of additional coordination groups to this macrocycle. In order to illustrate this approach, we describe in this paper an efficient colorimetric sensor that allows a so-called "naked-eye" detection of lead ions in water. To achieve this goal, we have synthesized three 1,8-diaminoanthraquinone-based polyazamacrocycles **1**−**3** and studied their cation-binding affinity.

Initially, the parent receptor **1** was prepared according to the Buchwald−Hartwig reaction (Scheme 1).

Scheme 1. Synthesis of the Parent Compound **1**



We have shown that commercially available tetraethylenepentamine pentahydrochloride can be used as starting material when the heterocoupling reaction with 1,8-dichloroanthraquinone is carried out in the presence of a large excess of Cs_2CO_3. Pd(dba)$_2$/BINAP precatalyst is efficient under these conditions, and the target compound **1** was obtained in 41% yield.

A qualitative estimation of binding affinity of receptor **1** was performed visually and by UV−vis spectroscopy in a methanol−water solution (1:1, 80 mM, $\lambda_{max} = 562$ nm) since this compound was not soluble in aqueous media.

The addition of equimolar amounts of different metal analytes such as Na(I), K(I), Mg(II), Ca(II), Ba(II), Zn(II), Pb(II), Cd(II), and Ni(II) did not lead to color changes (Figure 1a). Complexation of Cu(II) ions has induced a red-shift of the absorption maximum (94 nm), and Al(III) ions led to a blue-shift (26 nm) (Figure 1a). The addition of an excess of metal ions had only a slight influence on the color change. Thus, chromoionophore **1** showed a good selectivity for Cu(II) and Al(III) ions but cannot be used in aqueous media.

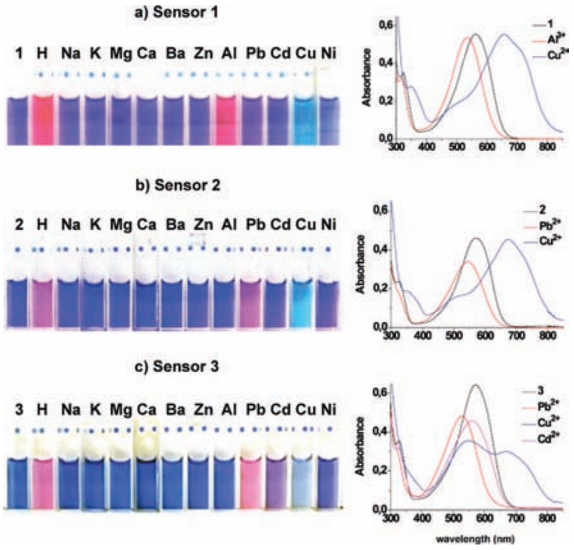


Figure 1. (Left panel) Solutions of the sensors **1**−**3** in the presence of the cation analytes (1 equiv). (Right panel) Examples of UV−vis spectra of sensors **1**−**3** and their complexes: (a) sensor **1** in MeOH/H_2O (1:1, 80 μM); (b) sensor **2** in DMSO/H_2O (1:1, 44 μM); (c) sensor **3** in water at pH = 7.4 (HEPES buffer (50 mM), 80 μM).

To improve Pb(II) affinity and solubility of receptor **1**, a simple structural modification of macrocycle **1** was done by the introduction of pendant arms possessing additional metal binding sites.

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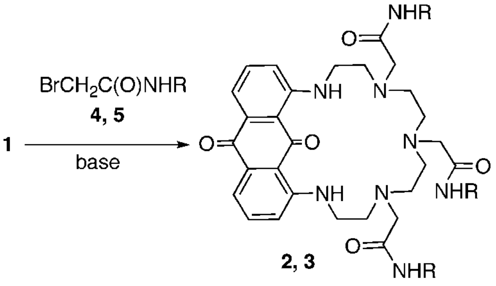
Two anthraquinone-based triamide receptors **2** and **3** have been synthesized by the reaction of the parent macrocycle **1** with bromoacetamide (**4**) and diethyl (bromoacetamido)-methylphosphonate (**5**), respectively (Scheme 2). It is interesting to note that the alkylation of compound **1** by bromide **5** proceeded smoothly in the presence of DIPEA in CH_2Cl_2 while the bromide **4** did not react with compound **1** under similar conditions. After numerous attempts, we have found that this alkylation reaction can be carried out only at higher temperature (150 °C) in DMF in the presence of K_2CO_3, and even under these conditions the desirable product **2** was obtained in modest 20% yield.

Scheme 2. Synthesis of Receptors **2** and **3**



2, 4 R = H (20%) **3, 5** R = $CH_2P(O)(OEt)_2$ (72%)

Low solubility of the triamide **2** in water (the absorbance of a saturated solution was only 0.032) and in the most protic solvents (MeOH, EtOH) limited interest of this compound. However, the color changes induced by metal analytes in $DMSO/H_2O$ solution (1:1, 44 μM, λ_{max} = 571 nm) were useful for Cu(II) and Pb(II) ion detection (Figure 1b). The color changed from violet to pink in the presence of Pb(II) (hypsochromic shift of 30 nm) and to blue (bathochromic shift of 103 nm) after the addition of Cu(II) ions. This sensor displayed a good selectivity for these ions. Alkali and alkaline earth metal ions did not disturb the determination even if added in 100-fold excess. Taken in equimolar amounts, Al(III), Zn(II), Ni(II), and Cd(II) do not change the color of the sensor solution. However, the 100-fold excess of these metals induced a color change from violet to lilac.

It is remarkable that (diethoxyphosphoryl)methyl groups crucially change the solubility of the sensor and compound **3** is perfectly soluble in most of organic solvents and in water. Since protonation usually disturbs a metal detection by a chromoionophore we first evaluated the influence of pH on the optical properties of receptor **3** in water solution. In fact, the protonation changes the solution color from violet to pink (Figure 1c). Thus, detailed studies were carried out at pH = 7.4 which was maintained with HEPES buffer (50 mM). Visual inspection of the solutions of sensor **3** (H_2O buffered with HEPES, 80 μM) before and after addition of 1 equiv of the metal salt showed a dramatic change of the color in the case of Pb(II) ions (Figure 1c). Such a change (blue-shift of 47 nm) suggests a strong binding of lead ion by the triamide **3**. The Cd(II)-induced spectral changes (a blue-shift of 44 nm) were similar but 4-fold excess of the Cd(II) analyte was needed to achieve the complete complexation. In the presence of only 1 equiv of metal analytes two solutions were simply discriminated by the naked eye (Figure 1c).[10]

The complexation of Cu(II) ions by receptor **3** was complete after addition of 1 equiv of the metal salt but led to a strong red-shift (97 nm) of the absorption band. This change allows a clear detection of this metal ion which can be easily distinguished from Pb(II) and Cd(II). Alkali and alkaline earth metal cations such as Na(I), K(I), Mg(II), Ca(II), Sr(II), and Ba(II) in 100-fold excess do not show substantial binding affinity to ionophore **3** and have a negligible influence on its optical properties, but the addition of 100-fold excess of Al(III), Zn(II) cations led to the change of the color to violet, whereas Ni(II), Cd(II) also taken in 100-fold excess gave pink solutions. The competitive binding experiments have shown that lead detection remains efficient in the presence of these metals including Al(III), Zn(II), and Cu(II) since the binding constant is significantly higher (Supporting Information).

UV−vis titration of receptor **3** with Pb(II) in aqueous solution without buffer and in HEPES buffer showed the same profile until the addition of 1 equiv of the metal analyte (Figure 2). Upon addition of increasing amounts of Pb(II), a gradual decrease in the absorption at 571 nm and an increase in the absorption at 524 nm were observed. A single isosbestic point at all receptor/Pb(II) ratios was observed which suggests that only one spectrally distinct complex was present. No changes in the spectrum were detected when the additional amount of the metal analyte was added to the water solution (this observation allows to indicate that the association constant for lead is higher than 10^8), while a gradual rise of the baseline was noted in HEPES buffer due to a partial precipitation of lead hydroxide at pH = 7.4. The naked eye detection limit of Pb(II) is 2−3 ppm (10−15 μM)

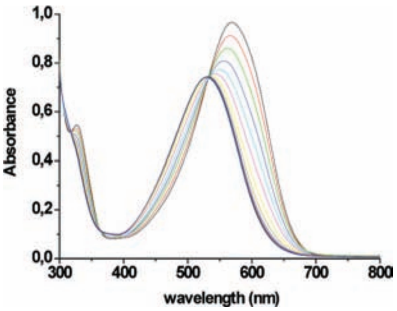


Figure 2. UV−vis titration of sensor **3** with $Pb(ClO_4)_2$. Each curve corresponds to addition of 0.125 equiv of $Pb(ClO_4)_2$ in water (pH = 7.4, HEPES buffer (50 mM)).

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[10] Other competitive metal ions were checked to prove the sensor **3** efficiency. No significant changes were observed in the UV−vis spectra upon addition of Ag(I) and Co(II). Hg(II) induced the solution color change, but after 4 days the color of this solution returned to blue, contrary to the solution containing Pb(II) ions (Supporting Information).

in solution. Using a conventional spectrometer, the detection limit is decreased to 21 ppb (0.1 μM) (Supporting Information). This low detection limit is due to the high stability of Pb(II) complex as well as the value of the molar absorption coefficient ($\epsilon = 4.9 \times 10^3$ L mol^{-1} cm^{-1}).

In accordance with this result, Job's plot based on UV−vis data showed maxima for a 0.5 M fraction which signifies that the host binds the cationic guest in a 1:1 ratio.

Accurate mass measurements were performed by electrospray ionization mass spectrometry (HRMS-ESI) (Supporting Information). The peak at *m*/*z* 611.1956 corresponding to $[M + Pb]^{2+}$ is observed when the peak corresponding to the free ligand **3** is absent. A comparison of IR spectra of compound **3** and its Pb(II) complex in the region 1600−1700 cm^{-1} clearly shows that carbonyl groups coordinate lead ion (Supporting Information). Based on NMR data, we can suggest that the complex exists in aqueous solution in at least two forms since three signals were observed in the ^{31}P NMR spectrum (Supporting Information). We suppose that for the major isomer all aliphatic nitrogen atoms as well as amide carbonyl oxygens bind the Pb(II) ion. As a lead ion favors a coordination number of 8, the two remaining sites might be occupied by an oxygen atom of carbonyl group or by the molecules of water. The hypsochromic shift of the absorption maximum observed in the spectrum of Pb complex suggests conformational changes of the macrocyclic backbone and a decrease of π-delocalization of the nitrogen atom lone electron pairs. The bathochromic shift observed in the presence of Cu(II) can be related to the deprotonation of the amino groups linked to anthraquinone backbone in the course of the metal complexation.[8] We are seeking now additional proof of these hypotheses.

We have also studied the fluorometric detection of different metal ions by ligand **3**. This area is of special interest since the recent discovery of anthraquinone fluorophores in metal sensors.[6] Unfortunately, the intensity of ligand **3** emission as well as its change in the presence of metal ions were too low to compete with previously described systems (Supporting Information).

In summary, anthraquinone-based receptor **3** is a remarkable colorimetric chemosensor for the selective recognition of Pb(II) in water solution at neutral pH. Our synthetic approach to chromogenic sensors based on a simple modification of a one-step available chromogenic macrocyclic backbone is particularly convenient for the development of selective sensors for different metal ions. In fact, by changing the nature and the number of side arms this backbone can be adapted to the nature of the metal analyte. In addition, the modification of solubility properties of the chosen receptor by the introduction of a neutral (diethoxyphosphosphoryl)methyl group is also interesting and can be widely applied for creating water-soluble receptors. Finally, chemosensor **3** can be used as an efficient organic precursor for inorganic−organic hybrid sensor materials since the immobilization of organophosphonates into inorganic metal oxide matrices is well-known in material chemistry.[11]

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Supporting Information Available: Experimental details for synthetic procedures, spectroscopic data, NMR spectra of **1**−**3**, and their complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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