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Crown Ether Benzoxazolyl-Alanines as Fluorimetric Chemosensors for the Detection of Palladium in Aqueous Environment †

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Abstract: Palladium has wide application in different contexts and, as a consequence, high levels of palladium in the environment have been reported, representing a risk to human health. Considering the interest to develop more selective and sensitive chemosensors for this analyte, two novel benzoxazolyl-alanine derivatives bearing a crown ether moiety were studied as potential fluorimetric chemosensors for palladium detection. Preliminary chemosensory studies for these unnatural amino acids in the presence of selected metal cations were performed in acetonitrile solution and in aqueous mixtures of sodium dodecyl sulfate (SDS, 20 mM, pH 7.5) solution with acetonitrile, 90:10 *v*/*v*. In acetonitrile solution, these probes had a fluorescence response for different cations but, most importantly, in SDS aqueous solution both compounds displayed a selective fluorescence response in the presence of palladium.

Keywords: fluorimetric chemosensors; metallic cations; palladium; unnatural amino acids

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1. Introduction

Palladium (Pd) is a transition metal extensively applied in several fields due to its special chemical and physical properties. For example, it is used in dental restorations, chemical catalysts, jewelry, electric equipment, automobile industry, among others [1,2]. As a consequence of its wide application, high levels of palladium in the environment have been reported, representing a risk to human health [3,4]. So far, a variety of small fluorescence probes have been successfully developed for Pd^{2+} detection [5], but there is an interest to design improved water-soluble probes for recognition of this metal in biological and environmental systems [1,6].

For the sensing of metallic cations, there are reports on fluorescent sensors based on amino acids containing different heterocyclic fluorescent and/or coordination units at the side chain [7–13]. Metal cations are known to be complexed through electron donor atoms at the main/side chains in amino acids, and the insertion of heterocycles at the side chain of natural amino acids yields novel unnatural amino acids with added functionality. In particular, the inclusion of crown ethers is largely used in the design of new chemosensors due to their unique ability to coordinate the cations of alkaline metals and they are also effective complexing reagents for alkaline-earth and transition metal ions [14,15].

Bearing these facts in mind, and considering the research group's experience on the design, synthesis and characterization of fluorescent chemosensors [7–12], we report herein the evaluation of two benzoxazolyl-alanine derivatives bearing a crown ether moiety as potential fluorimetric chemosensors for Pd^{2+} detection in aqueous media. Preliminary chemosensory studies for these unnatural amino acids in the presence of selected metal cations, with biological and environmental relevance, were performed in acetonitrile solution and in aqueous mixtures of SDS (20 mM, pH 7.5) solution with acetonitrile, 90:10 *v*/*v*.

2. Experimental Section

Methods and Materials

The synthesis and structural characterization of benzoxazolyl-alanine derivatives **1a-b** has been reported elsewhere [16]. For the photophysical characterization, UV-vis absorption spectra were obtained in acetonitrile solution (1.0×10^{-5} M) using a Shimadzu UV/2501PC spectrophotometer (Shimadzu Europa GmbH, Duisburg, Germany) and the fluorescence spectra were obtained using a Horiba FluoroMax-4 spectrofluorometer (HORIBA Europe GmbH, Darmstadt, Germany), using 9,10-diphenylanthracene in ethanol as fluorescence standard [7].

Evaluation of benzoxazolyl-alanine derivatives **1a-b** as fluorimetric chemosensors was carried out in the presence of several cations (Ag^{+}, K^{+}, Li^{+}, Hg^{2+}, Ca^{2+}, Co^{2+}, Pb^{2+}, Mn^{2+}, Fe^{2+}, Zn^{2+}, Ni^{2+}, Cd^{2+}, Cu^{2+}, Pd^{2+}, Fe^{3+} and Al^{3+}). Solutions of compounds **1a-b** (3.0×10^{-5} M) and of the ions under study (1.0×10^{-2} M) were prepared in acetonitrile and acetonitrile/water (75:25). Solutions of the compounds **1a-b** (1.0×10^{-5} M) and of the ions under study (1.0×10^{-2} M) were prepared in aqueous mixtures of SDS (20 mM, pH 7.5) solution with acetonitrile, 90:10 *v*/*v*. Preliminary studies were carried out by addition of up to 10 equivalents of each cation to the solution of compounds **1a-b** in acetonitrile and in mixture of acetonitrile/water. A similar study was performed by addition of up to 10 and 20 equivalents of each cation to the solution of compounds **1a-b** in aqueous environments using SDS. The solutions were analyzed in a CN15 viewing cabinet under UV lamp at 365 nm (Vilber Lourmat, Marne-la-Vallée, France).

3. Results and Discussion

Two benzoxazolyl-alanine derivatives bearing a crown ether moiety **1a-b** (Figure 1), previously synthesized, were characterized by UV-vis absorption and fluorescence spectroscopy. In both compounds, there is a protected benzoxazolyl-alanine core which is substituted at position 2 of the oxazole ring with a phenyl linked to a 15C5 azacrown ether moiety (**1a**) or a thiophene coupled to a 18C6 benzocrown ether (**1b**).

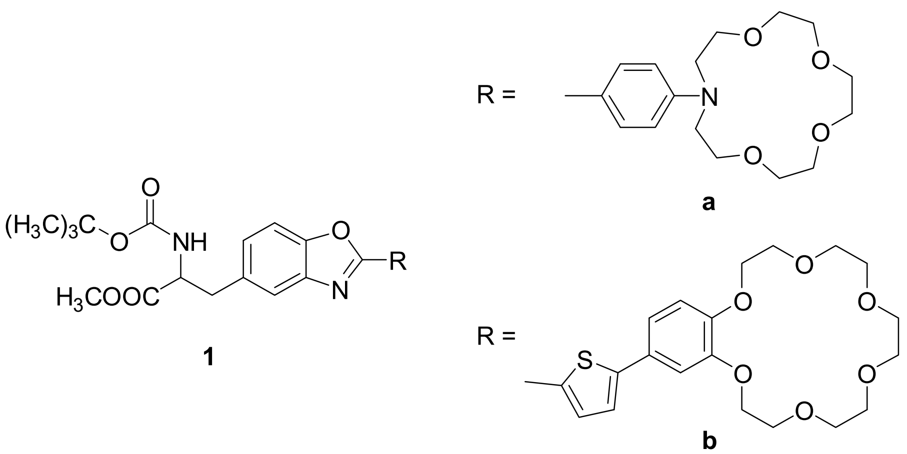

Figure 1. Crown ether benzoxazolyl-alanine derivatives (**1a-b**).

Solutions of crown ether benzoxazolyl-alanines **1a-b**, in acetonitrile (1.0×10^{-5} M), were analyzed and the wavelengths of maximum absorption and fluorescence, λ_{abs} and λ_{flu}, molar absorptivities at the absorption maximum, ε, relative fluorescence quantum yields, Φ_F, and Stokes' shifts were compiled in Table 1. Both compounds are highly fluorescent and the higher conjugation in compound **1b** is in agreement with the observed bathochromic shift in absorption and fluorescence, when compared to compound **1a**.

Table 1. UV-vis absorption and fluorescence data of crown ether benzoxazolyl-alanines **1a-b**, in acetonitrile (1.0 × 10^{-5} M).

Compound	UV-vis Absorption		Fluorescence		
	λ_{abs} (nm)	log ε	λ_{flu} (nm)	Φ_F	Stokes' shift
1a	334	4.04	395	0.82	61
1b	363	4.01	445	0.69	82

The novel benzoxazolyl-alanines **1a-b** were evaluated as fluorimetric chemosensors for the detection of metal cations, with biological and environmental relevance, through preliminary chemosensory studies.

Firstly, the fluorimetric behavior of compounds **1a-b** in the presence of selected cations was studied in acetonitrile, by addition of 10 equivalents of each cation. As expected, these probes had a different fluorimetric response for different cations: compound **1a** exhibited a remarkable fluorescence quenching upon interaction with Hg^{2+}, Pb^{2+}, Fe^{2+} and Pd^{2+} (Figure 2a), whereas compound **1b** interacted with Hg^{2+} and Pd^{2+} through a decrease of fluorescence and a complete quenching was seen in the presence of Fe^{3+} (Figure 3a). Considering the importance of water-soluble probes for recognition of metals in biological and environmental systems, the fluorimetric response of compounds **1a-b** to selected cations was tested in mixtures of acetonitrile/water (75:25). However, a relevant response was not observed in these conditions.

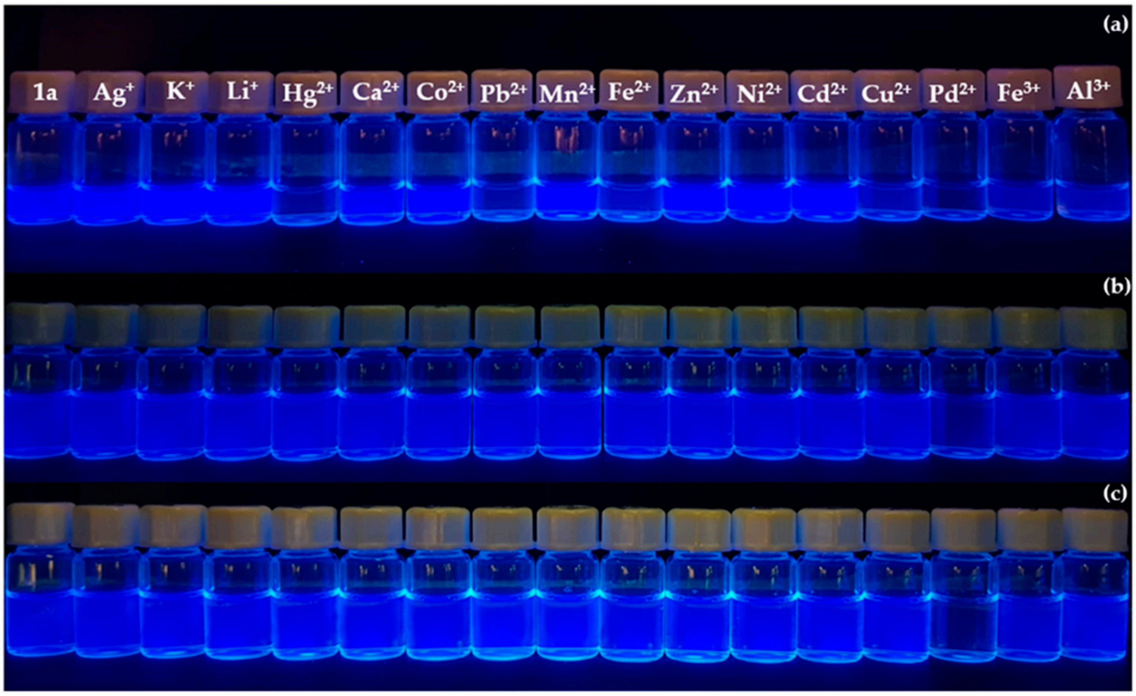

Figure 2. Preliminary chemosensing study of benzoxazolyl-alanine derivative **1a**: (**a**) in the presence of 10 equivalents of each cation, in acetonitrile (3.0 × 10^{-5} M); (**b**) in the presence of 10 equivalents of each cation, in SDS (20 mM, pH 7.5)-acetonitrile 90:10 (*v*/*v*) solution (1.0 × 10^{-5} M); (**c**) in the presence of 20 equivalents of each cation, in SDS (20 mM, pH 7.5)-acetonitrile 90:10 (*v*/*v*) solution (1.0 × 10^{-5} M).

Based on our previous experience, the use of an anionic surfactant such as sodium dodecylsulfate (SDS) was attempted to overcome this problem [17]. In fact, several authors reported that in aqueous environments using surfactants, selected binding sites and fluorophores can be arranged in micelles of surfactants allowing detection of metal cations in water by changes in fluorescence [18,19]. Taking this into account, solutions of compounds **1a-b** were prepared in aqueous mixtures of SDS (20 mM, pH 7.5) solution with acetonitrile, 90:10 *v*/*v*. SDS aqueous solutions of probes **1a-b** displayed a selective fluorescence quenching in the presence of 10 equivalents of Pd^{2+} (Figures 2b and 3b). Furthermore, further addition to 20 equivalents of each ion confirmed the selectivity of both crown ether benzoxazolyl-alanine derivatives **1a-b** for Pd^{2+} (Figures 2c and 3c).

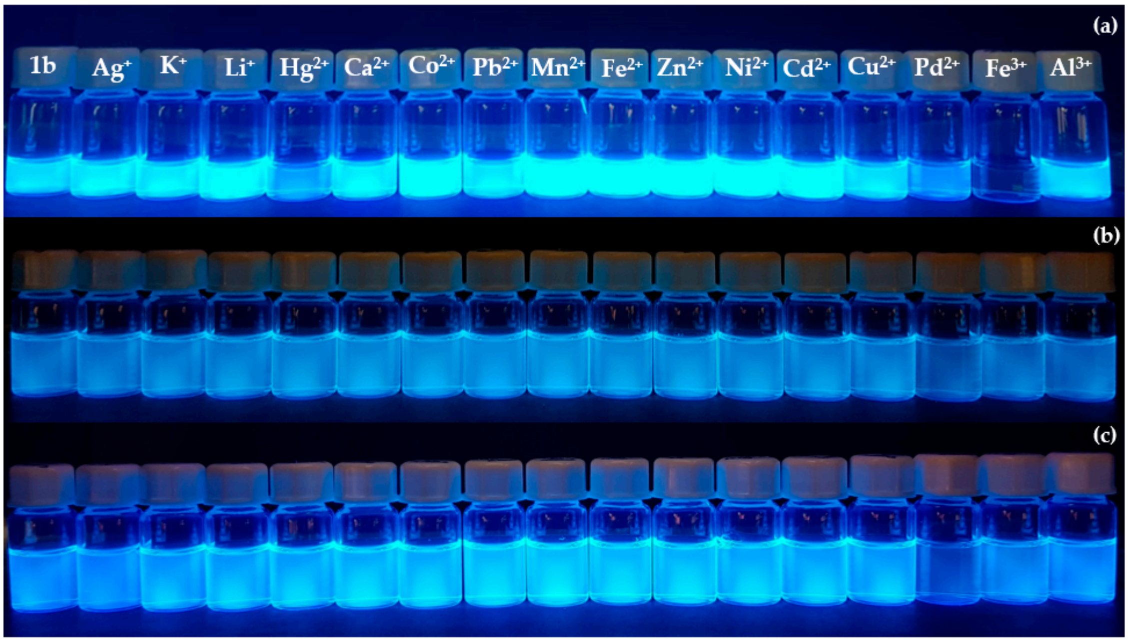

Figure 3. Preliminary chemosensing study of benzoxazolyl-alanine derivative **1b**: (**a**) in the presence of 10 equivalents of each cation, in acetonitrile (3.0×10^{-5} M); (**b**) in the presence of 10 equivalents of each cation, in SDS (20 mM, pH 7.5)-acetonitrile 90:10 (*v*/*v*) solution (1.0×10^{-5} M); (**c**) in the presence of 20 equivalents of each cation, in SDS (20 mM, pH 7.5)-acetonitrile 90:10 (*v*/*v*) solution (1.0×10^{-5} M).

4. Conclusions

In summary, two novel benzoxazolyl-alanines bearing a crown ether moiety **1a-b** were evaluated as fluorimetric chemosensors for several ions in acetonitrile and in mixtures of acetonitrile and aqueous SDS solution. As expected, these probes had a fluorimetric response for different cations in acetonitrile solutions but, most importantly, in aqueous mixtures using SDS anionic surfactant both crown ether benzoxazolyl-alanines displayed a selective fluorimetric quenching in the presence of Pd^{2+}. These results clearly indicated that probes **1a-b** could be used to detect the palladium cation in environmental and biological samples, with remarkable selectivity.

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Conflicts of Interest: The authors declare no conflicts of interest.

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