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Multi-Ion Analysis

Quadruple-Channel Sensing: A Molecular Sensor with a Single Type of Receptor Site for Selective and Quantitative Multi-Ion Analysis**

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Highly selective cation or anion sensing is imperative for many areas of technology, including environmental, biological, clinical, and waste management applications.[1] For heavy- and transition-metal ions (e.g. Pb^{2+}, Cd^{2+}, and Hg^{2+}; Cu^{2+} and Fe^{3+}), selective sensory protocols are particularly critical owing to their high toxicity and crucial role in biological systems.[2] Although various concepts in metal-ion sensing have been installed to enhance sensitivity, selectivity, and the dynamic working range,[3] the recognition of congregations of chemical species[4] and of multianalyte mixtures still poses a major challenge.[5] In this context, a "lab on a molecule" for the simultaneous, although only qualitative, detection of Zn^{2+}, H^+, and Na^+ by a logic-gate approach has recently been described.[4] However, even this innovative approach follows the paradigm that is still dominating traditional sensor design: one receptor site for one analyte.

As an alternative strategy, we and others[6] investigated a sensor molecule that operates on a single type of receptor unit for multi-ion analysis by using an array of detection methods. To obtain different metal-ion selectivities in the various sensing channels, the receptor, in our case an aza crown ether, should exhibit disparate conformational preferences depending on the detection method. This feature may be implemented by a nearby steric abutment, which prevents perfect overlap of the aza crown ether site and the π system used for spectroscopic investigation. Depending on the overlap and thus on the sensing method, compression of the aza crown ether ring against the steric abutment may thus modulate the available conformational space of the receptor (see Figure S8 in the Supporting Information). So far, steric perturbations and conformational constraints at binding sites have rarely been investigated[3d,7] and if so, then mostly with only one spectroscopic technique[8] thus precluding detection of different selectivities with distinct detection methods.

To explore the usefulness of the above concept, we turned our attention to ruthenium tris(diimine) complexes as their UV/Vis, photoluminescence (PL), electrogenerated chemiluminescence (ECL),[9] and redox properties are already well established[10] in the field of chemosensors, although never in a quadruple-channel sensing setup (Figure 1).[9,11] As a test case, complex **1** with aza crown ethers as the receptor units was designed and prepared from the corresponding phenanthroline ligands.[12] Owing to the 5,6-CH unit of phenanthroline acting as a steric abutment, the conformational space of the aza crown ethers is confined preventing a planar arrangement of the nitrogen with the ligand. To test the concept, the following array of metal ions was chosen throughout all four channels: Pb^{2+}, Hg^{2+}, Cd^{2+}, Zn^{2+}, Ag^+, Cu^{2+}, Ca^{2+}, Mg^{2+}, K^+, and Na^+ ions (see Figure 2).

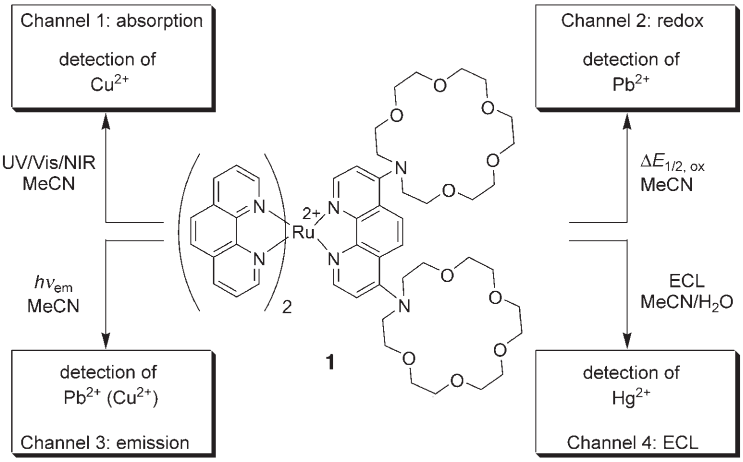

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Figure 1. Quadruple-channel sensing with ruthenium complex **1**. $\Delta E_{1/2}$: change in the redox potential of **1** ($Ru^{2+/3+}$) upon addition of metal ions.

The UV/Vis absorption of **1** in MeCN is dominated by a strong metal-to-ligand charge-transfer (MLCT) band at 429 nm ($\varepsilon = 2.43 \times 10^4\,\text{M}^{-1}\text{cm}^{-1}$). Studies in the presence of various metal ions indicated that only Cu^{2+} ions caused a notable response in the MLCT intensity, with the Pb^{2+} ions leading to minor effects and all other metal ions (Na^+, K^+, Mg^{2+}, Ca^{2+}, Zn^{2+}, Cd^{2+}, Ag^+, and Hg^{2+} ions) inducing negligible responses (Figures 2 and 3). Notably, with Cu^{2+} ions, a metal-to-metal charge-transfer (MMCT) absorption appeared in the near-IR (NIR) region at 1083 nm ($\varepsilon = 1.20 \times 10^4\,\text{M}^{-1}\text{cm}^{-1}$) allowing for unmistakable identification and quantification. Titration of **1** with Cu^{2+} ions at 429 nm revealed a one-step association sequence with $\log K_{\text{Cu}^{\text{II}}} = 10.7 \pm 0.2$[13] (see Figure S1 in the Supporting Information).

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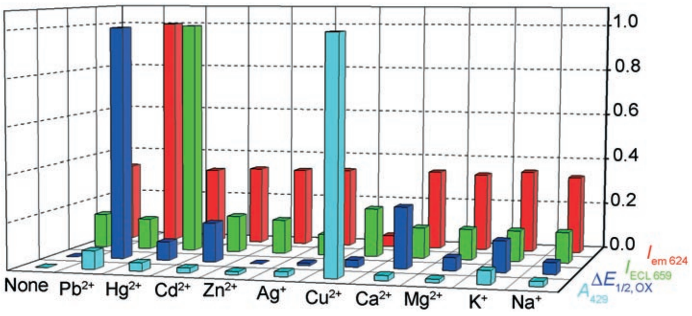

Figure 2. Plot of relative changes of UV/Vis, luminescence (both upon addition of 20 equivalents of metal ions), ECL (addition of 5.0 equivalents of metal ion), and redox potential (see text for details of metal ion addition) of **1**. $I_{em\,624}$: relative PL emission intensity at 624 nm; $I_{ECL\,659}$: relative ECL intensity at 659 nm; A_{429}: relative absorbance at 429 nm.

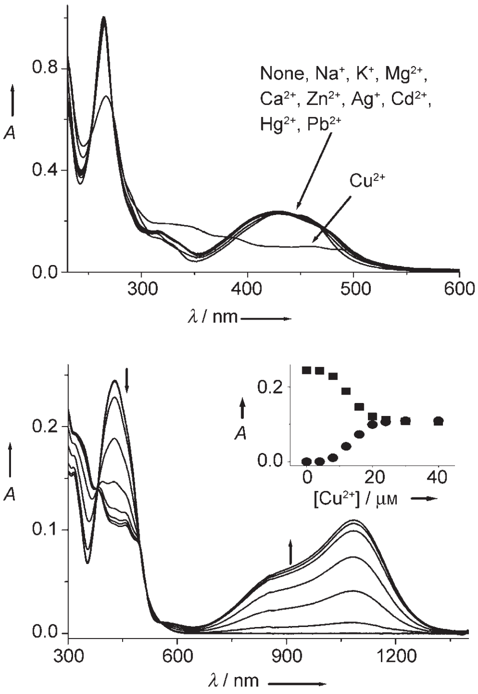

Figure 3. Top: UV/Vis absorption spectra of **1** (10 μM) in the presence of various metal ions (20 equiv) in MeCN. Bottom: UV/Vis/NIR titration of **1** (10 μM) with Cu^{2+} ions. The arrows indicat the direction of absorbance with increasing concentration of Cu^{2+} ions. Inset: Absorbance of **1** at 429 nm (black squares) and 1083 nm (black circles).

Cyclic voltammetry (CV) studies of complex **1** ($E_{1/2} = 0.56\,V_{Fc}$) at $100\,mV\,s^{-1}$ in acetonitrile revealed a fully reversible wave for the Ru^{2+}/Ru^{3+} transition. Upon addition of Pb^{2+} ions (20 equiv), the reversible wave shifted anodically by 180 mV, whereas only minute changes (< 50 mV) were noticed upon addition of Na^+, K^+, Mg^{2+}, Ca^{2+}, Zn^{2+}, Cd^{2+}, and Ag^+ ions (20 equiv) as well as Hg^{2+} and Cu^{2+} metal ions (2.0 equiv; Figure 2).[14] A linear correlation between the redox potential shift and the concentration of Pb^{2+} (see Figure S3 in the Supporting Information) allowed for facile quantification.

Complex **1**, as is the case for many related ruthenium complexes,[15] is also an intense luminophore with an emission band at 672 nm ($\lambda_{em} = 429$ nm). A survey of the photoluminescence in the presence of various metal ions (as their perchlorate salts, 20 equiv) in MeCN indicated that only the Pb^{2+} and Cu^{2+} ions induced marked changes in the emission of **1**, whereas Na^+, K^+, Mg^{2+}, Ca^{2+}, Zn^{2+}, Ag^+, Cd^{2+}, and Hg^{2+} ions exhibited basically no discernible changes at all (Figure 4). The addition of Pb^{2+} ions resulted in a 1.7-fold enhancement in the emission intensity along with a hypsochromic shift of $\lambda_{max\,em}$ from 672 nm to 624 nm. In contrast, Cu^{2+} ion addition (20 equiv) led to approximately 95 % quenching of the emission and showed a blue shift at high Cu^{2+} ion concentrations. The binding constants for Pb^{2+} ions to **1** were calculated to be $\log K_{1\,Pb^{II}} = 6.4 \pm 0.2$ and $\log \beta_{Pb^{II}} = 11.3 \pm 0.3$ from emission titration data.[13]

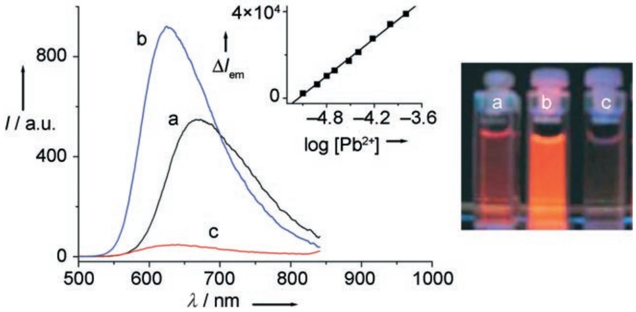

Figure 4. Luminescence ($\lambda_{em} = 429$ nm) spectra (left) and visible emission (right) of **1** (10 μM) in acetonitrile upon addition of 20 equivalents of different metal ions. a) **1** (blank), b) **1** + Pb^{2+}, and c) **1** + Cu^{2+}. Inset: Linear correlation of the integrated emission ΔI_{em} versus $\log[Pb^{2+}]$.

ECL has rarely been explored for metal-ion sensing[9] and virtually not at all in combination with other detection methods. Like $[Ru(bipy)_3]^{2+}$ and $[Ru(phen)_3]^{2+}$ ions (bipy = 4,4′-bipyridine, phen = 1,10-phenanthroline), **1** provided a notable ECL (at 659 nm) in aqueous MeCN buffer solution with tri-*n*-propylamine (TPrA) as a co-reactant (Figure 5). Negligible changes in the ECL spectrum were observed upon the addition of Na^+, K^+, Ca^{2+}, Ba^{2+}, and Pb^{2+} ions, whereas slight effects were detected upon the addition of Ag^+, Zn^{2+}, Cd^{2+}, and Cu^{2+} ions. Remarkably, a characteristic ECL enhancement ($I/I_0 = 8.2$) was found for Hg^{2+} ions, allowing detection of Hg^{2+} ions down to the ppm range in aqueous solution (see Figure 5 and inset) and in the presence of many other ions (see Figure 6). The only minor interference occurred in the presence of Ag^+ ions.

To further assess the value of **1** as a multi-ion sensor, additional competitive assays were investigated. The analysis of **1** in the presence of a 1:1:1 mixture of $Cu^{2+}/Hg^{2+}/Pb^{2+}$ ions clearly showed that Pb^{2+} was readily identified in the PL channel, whereas the Cu^{2+} ion was at first not visible in the UV/Vis channel, clearly owing to the higher binding constant of Pb^{2+} ions than that of Cu^{2+} ions. Nevertheless, the UV/Vis channel detection can be activated for the analysis of Cu^{2+} ions (see Figure S7 in the Supporting Information) after the

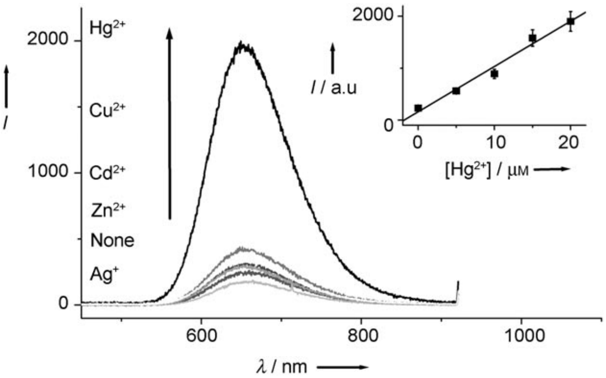

Figure 5. ECL spectra of **1** (10 µM) in 0.1 M tetra-*n*-butylammonium phosphate buffer solution (H_2O/MeCN = 9:1 v/v; pH 7.0) (50 mM TPrA as co-reactant) in the presence of various metal ions (50 µM). Inset: Linear correlation of the ECL intensity versus [Hg^{2+}].

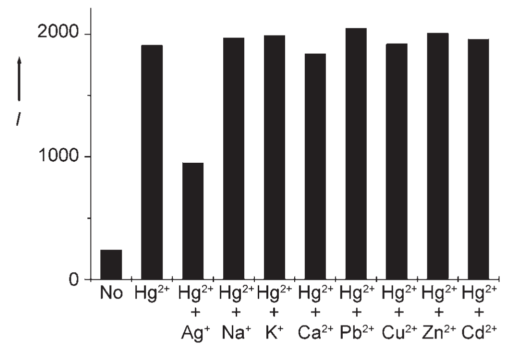

Figure 6. ECL intensity change profile of **1** (10 µM) in various mixtures of metal ions (Hg^{2+} and one other metal ion, both 20 µM) in 0.1 M aqueous tetra-*n*-butylammonium phosphate buffer solution (H_2O/acetonitrile = 9:1 v/v; pH 7.0; 50 mM TPrA as co-reactant).

addition of [18]crown-6, which traps Pb^{2+} ions through complexation. Electrochemical detection of Pb^{2+} ions was trouble-free as long as only small amounts of Cu^{2+} and Hg^{2+} ions were present. This, however, does not constitute a severe problem, as the concentration of Pb^{2+} ions can be determined by the PL channel. ECL detection of Hg^{2+} ions by **1** proved to be unperturbed by the addition of Cu^{2+} and Pb^{2+} ions.

In summary, a "lab on a molecule" for selective and quantitative multi-ion analysis was established for the first time. Complex **1**, containing only a single type of receptor site, is a chemosensor (Figure 2) for Pb^{2+} (CV, $h\nu_{em}$), Hg^{2+} (ECL), and Cu^{2+} ($h\nu_{em}$, A_{Vis}, A_{NIR}) by using quadruple-channel detection (UV/Vis, PL, ECL, CV). Depending on the sensing method, the conformational perturbation of the aza crown ether ring will result in a change in the cavity size and the availability of donor atoms. As can be derived from a comparison of the ECL of **1** with that of a related ruthenium system substituted with an aza crown ether,[9b] these effects are seen to materialize in distinct metal-ion selectivities. More detailed studies, however, are warranted to clarify the mechanism of operation and the scope of the concept.

Experimental Section

Metal ions were used as anhydrous perchlorate salts (Aldrich). Tri-*n*-propyl amine (TPrA) was purchased from Acros. As complex **1** contains two aza crown ether units, full loading may be achieved at 2 equivalents of metal ions.

The emission and UV/Vis measurements were carried out with a solution containing 10 µM of **1** in MeCN. The UV/Vis spectra were measured on a Varian Cary 100 Bio UV-Visible Spectrophotometer, and emission spectra were measured on a Varian Cary Eclipse Fluorescence Spectrophotometer with excitation and emission slit widths of 5 nm. All emission spectra were corrected. Emission and UV/Vis titration experiments were performed using 10 µM solutions in MeCN.

Electrochemical experiments were realized by using a standard three-electrode setup (Pt working and Pt auxiliary electrode, silver wire as reference electrode) connected to a Princeton Applied Research Model 362 potentiostat. Experiments were carried out on a 1.0 mM or 0.5 mM solution of **1** in acetonitrile with 0.1M tetra-*n*-butylammonium hexafluorophosphate as the supporting electrolyte. All potentials were measured at a scan rate of 100 mV s^{-1} and referenced to ferrocene (Fc) as the internal standard.

All ECL measurements were obtained with solutions containing 10 µM of **1** and 50 mM of TPrA in 0.1M tetra-*n*-butylammonium phosphate buffer solution (H_2O/acetonitrile = 9:1 v/v; pH 7.0). The three-electrode setup was the same as for the electroanalytical measurements. To generate ECL, the working electrode was swept between 0 to 1.5 V at a scan rate of 100 mV s^{-1}. The resulting emission spectra were obtained with a liquid-nitrogen-cooled CCD camera at approximately −130 °C (CCD 3000, Jobin Yvon—Spex Instruments S. A. Inc.) connected to a spectrometer 320 (Jobin Yvon—Spex Instruments S. A. Inc.).

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[13] Association constants and binding modes were evaluated using the computer program SPECFIT, Global Analysis system, Version 3.0.32.

[14] At higher amounts of Hg^{2+} or Cu^{2+} ions, no distinct Ru^{2+}/Ru^{3+} redox wave was observed in cyclic voltammetry, but the redox potentials could still be readily resolved by using differential pulse voltammetry (see Figure S4 in the Supporting Information).

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