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Optical Pd^{2+} sensing by rhodamine hydrazone ligands: different stoichiometries in aqueous/nonaqueous environments

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ABSTRACT

A series of rhodamine spiro-leuco compounds have been developed as fluorescence-enhanced sensors for optical sensing of palladium ion (Pd^{2+}). The initial rhodamine hydrazone derivatives, **RPd1-a**, **RPd1-b**, and **RPd1-c**, display a good coordination to Pd^{2+} inducing the spirolactam-open reaction with a significant fluorescence enhancement and color generation. Different stoichiometry results, 1:2 in EtOH/H_2O and 1:1 in MeOH/DCM were observed for Pd^{2+}/**RPd1-c** complexation.

In the past decades, considerable attention has been focused on the design and synthesis of fluorescent sensors for metal ions because of their significant importance in chemistry, cellular biology, and environmental science.[1] The analytes have mainly included the alkali metal ions,[2a] alkaline earth metal ions,[2b] heavy- (and inner-) transition-metal (HTM) ions,[2c] and precious metal ions,[3] such as gold ion, silver ion, and also platinum-group elements ions (especially Pt[4a] and Pd[4b–f]). Pd is one of the platinum-group elements (PGEs including Pd, Pt, Ru, Rh, Os, and Ir) which are widely used in various materials such as dental crowns, catalysts,[5a] fuel cells, and jewelry. Pd-catalyzed reactions, such as Buchwald–Hartwig, Heck, Sonogashira, and Suzuki–Miyaura reactions, are increasingly important because of their advantages in forming difficult bonds, thus play a pivotal role in the synthesis and development of drug molecules.[5b] However, even after several purification steps, a high level of residual palladium species are still often found in the final products which can be hazardous to human health,[5c] because Pd can bind to thiol-containing amino acids, proteins (casein, silk fibroin, and many enzymes), DNA or other macromolecules (vitamin B6) and thereby may disturb a variety of cellular processes.[5d] Therefore, analytical methods are urgently needed for the sensitive and selective detection of Pd in a high throughput fashion. The typically used analytical methods, such as atomic absorption spectrometry, inductively coupled plasma atomic emission spectrometry, solid-phase microextraction high-performance liquid chromatography, X-ray fluorescence, etc., all suffer from the high cost of instruments and their requirement of highly trained individuals.

Although colorimetric technique is frequently applied to the determination of Pd^{2+},[4b,4f] the fluorescent method would be more desirable because of the easy preparation, convenient operation, and also the nondestructive, quick, and sensitive detection of emission signals. Holdt et al., designed a fluorescence off–on Pd^{2+} sensor with a push pull dimercaptomaleonitrile moiety as the receptor which can also regulate the photoinduced electron transfer in their system.[6] Based on the Pd-catalyzed Tsuji–Trost allylic oxidative insertion reaction, Koide's group developed a fluorescein system as sensitive and selective fluorescent sensor for the residual Pd analysis in reaction vessels and in real samples of drug, rock, and soil.[7] Besides these Pd-catalyzed reaction mechanisms,[8] the rhodamine spirolactam framework[9] is also an ideal choice,[10] among which only Quah obtained the X-ray single crystal structure of the Pd^{2+}-sensor complex.[10e]

There have been several rhodamine hydrazone derivatives[10g] developed as fluorescence-enhanced sensors for Pd^{2+} detection. In our recent work, the rhodamine hydrazone derivatives (Scheme 1) with allylidene receptor (**RPd2** and **RPd3**)[10c] and tridentate PNO receptor (**RPd4**)[10f] were adopted for specific detection of Pd^{2+} over other PGEs ions and demonstrated their potential application for Pd-control and Pd-analysis in the environment. Actually, we found that the initial rhodamine hydrazone derivatives (**RPd1-a–c** in Scheme 1) also display good coordination to Pd^{2+} even without any additional modification. The cheap and commercially available starting materials make these sensors easy

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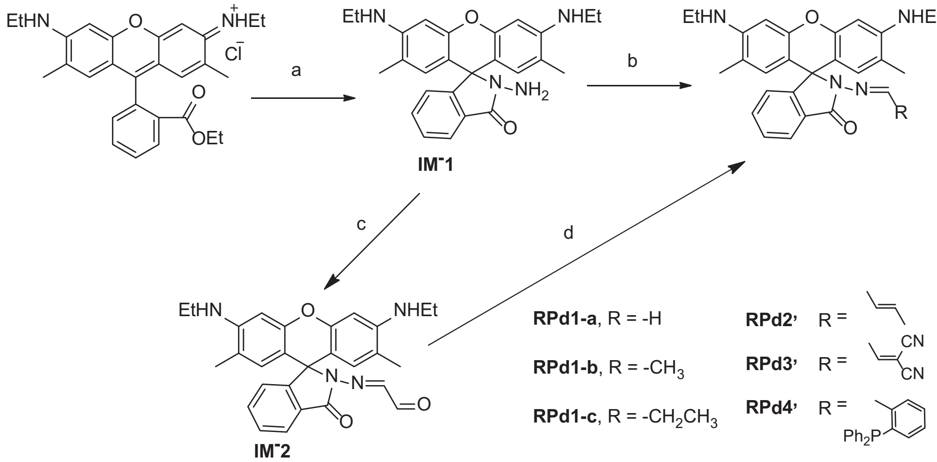


Scheme 1. The structures and synthetic routes of rhodamine hydrazone Pd sensors. (a) and (b) for **RPd1-a**, **RPd1-b**, **RPd1-c**, **RPd2**, **RPd4**, (a), (c) and (d) for **RPd3**. (a), Hydrazine, EtOH, refluxed, 88.5% for **IM-1**; (b), the aldehydes, EtOH, refluxed, 42.8% for **RPd1-a**, 62.3% for **RPd1-b**, 84.3% for **RPd1-c**, 85.2% for **RPd2**, 77.9% for **RPd4**; (c), glyoxal, EtOH, refluxed, 66.2% for **IM-2**; (d), malononitrile, CH_3CN, refluxed, 85.9% for **RPd3**.

to be obtained and may be developed as a common fluorescent reagent for Pd^{2+} sensing.

The rhodamine hydrazone derivatives **RPd1-a**, **b**, and **c** were synthesized by a reported procedure[12] in good yields (Scheme 1). All intermediates and products were purified by recrystallization that was much more convenient than column chromatography, and characterized by ^1H NMR, ^{13}C NMR, and TOF-MS. For **RPd1-c**, its X-ray crystal structure shows the characteristic spirolactam framework (Fig. 1, left). K^+, Ca^{2+}, Mg^{2+}, Zn^{2+}, Cd^{2+}, Ba^{2+}, Cr^{3+}, Pb^{2+}, Cu^{2+}, Hg^{2+}, Ag^+, Mn^{2+}, Ni^{2+}, Co^{2+}, La^{3+}, and NH_4^+ ions were used to evaluate the metal ion selectivity of **RPd1-a**, **b**, and **c** (10 μM) in 50% ethanolic water solution. Among these metal ions (2.0 equiv), the sensors **RPd1-a**, **b**, and **c** all showed a large fluorescence enhancement only with Pd^{2+} (Fig. 2), although Hg^{2+} induced a small portion of fluorescence enhancement. The addition of Pd^{2+} to these sensors solution induced both colorimetric and fluorometric responses that can be easily detected by the naked eye (Fig. 2 inset, e.g., **RPd1-c**). In the Pd^{2+} titration experiments, there are also new absorption peak centered at 540 nm and emission peak centered at 555 nm gradually generated on the absorption and emission spectra for all of the three sensors (Fig. 3 for **RPd1-c**, Supplementary Fig. S3 for **RPd1-a**, Supplementary Fig. S4 for

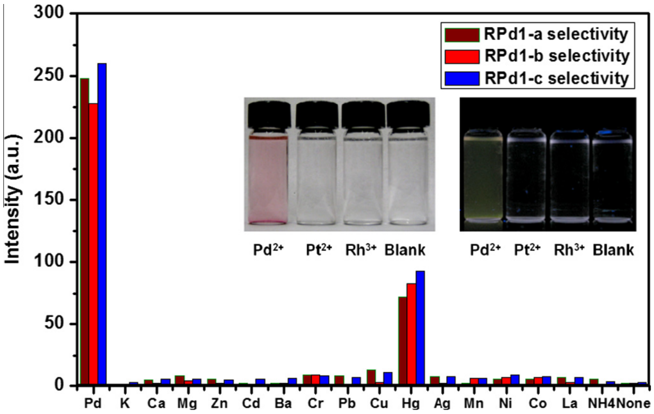


Figure 2. Fluorescence intensity (at 555 nm) of **RPd1-a** (dark red), **RPd1-b** (red), and **RPd1-c** (blue) samples with and without treatment of metal ions. Condition: 50% ethanolic aqueous solution, 10 μM for each sensor, 20 μM for each metal ion, $\lambda_{ex} = 505$ nm. Inset photos: photos of **RPd1-c** (10 μM) in 50% ethanolic water solution with and without 1.0 equiv of $PdCl_2$, $PtCl_2$, and $RhCl_3$ under sunlight (left) and UV light (right).

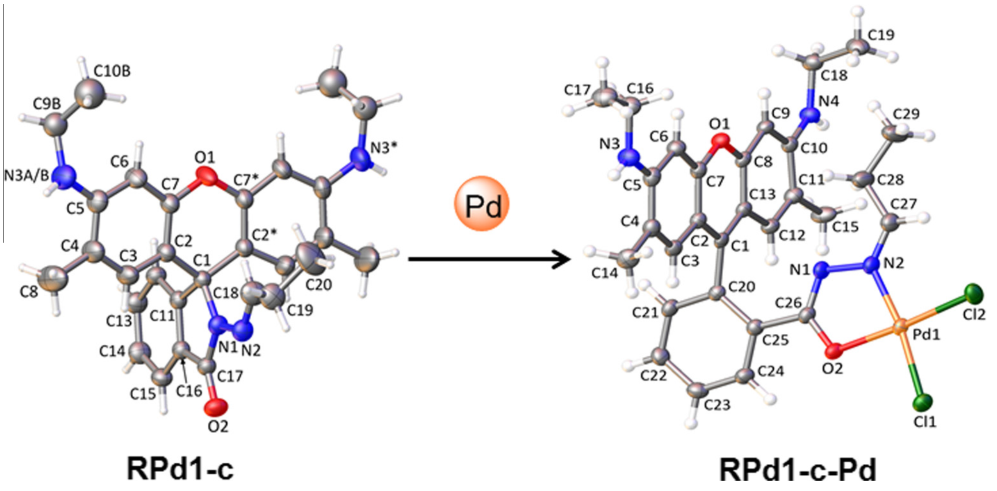


Figure 1. X-ray crystal structures of **RPd1-c** (left) and **RPd1-c-Pd** (right). Displacement ellipsoids are shown at the 30% probability level for **RPd1-c** and 60% probability level for **RPd1-c-Pd**.[11]

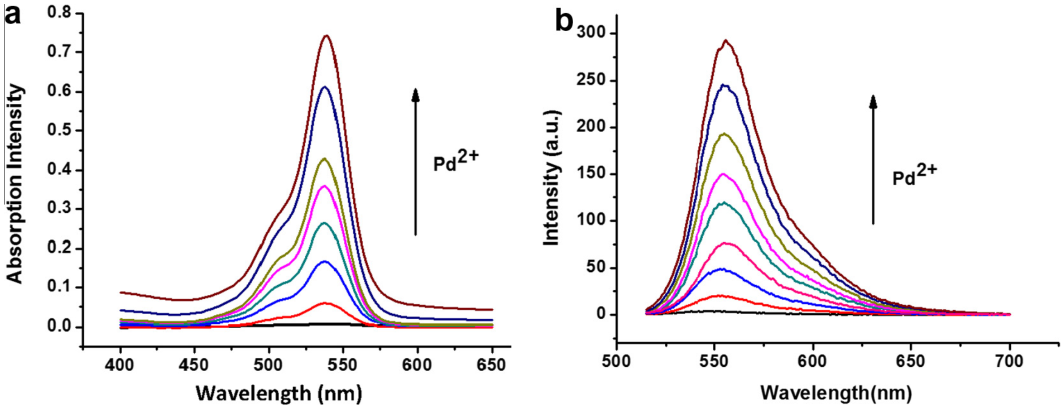


Figure 3. Absorption (a) and fluorescence (b) spectral changes of **RPd1-c** (10 μM) in 50% ethanolic water solution after addition of Pd^{2+} (0–50 μM). λ_{ex} = 505 nm.

RPd1-b, respectively). The coordination constant K_a of **RPd1-c-Pd** was $2.42 \times 10^6\,M^{-2}\,L^2$ (Supplementary Fig. S5b), inferred from the Hg^{2+} titration curves (Supplementary Fig. S5a).

Additionally, PGE salts such as $PdCl_2$, $PtCl_2$, $RhCl_3$, and $RuCl_3$ were adopted to check whether **RPd1-a**, **b**, and **c** could selectively detect the PGE ions. Supplementary Figure S6 shows the time course (0–60 min) of fluorescence intensities of these sensors treated with and without Pd^{2+}, Pt^{2+}, Rh^{3+}, and Ru^{3+}, respectively. It can be clearly observed that the selected PGE ions do not evidently enhance the fluorescence intensities, whereas Pd^{2+} leads to notable fluorescence signal enhancements. The inset photos in Figure 2 also display the visual detection of **RPd1-c** to Pd^{2+} over Pt^{2+} and Rh^{3+}. As shown in Supplementary Figure S7, the fluorescence of these sensors is pH independent at pH > 5. The resulting sigmoidal curves give pK_a of 3.70 for **RPd1-a**, 3.57 for **RPd1-b**, and 3.65 for **RPd1-c**, respectively, demonstrating that they can work in a wide physiological pH range.

In our previous work, we have figured out the mechanism that Pd^{2+}-coordination induced the ring-opening reaction of sensors **RPd2**, **3,** and **4** by Pd^{2+} titration experiment, TOF-MS result, and X-ray single crystal structure analysis. The hydrazone binding site has been considered as the key role in these sensors. In this work, the first evidence of the binding mode came from TOF-MS result of the complex **RPd1-c** and Pd^{2+} in 50% ethanolic water solution. The peak at *m*/*z* 521.2543 that corresponds to $[Pd(\mathbf{RPd1\text{-}c})_2]^{2+}$ (Fig. 4) was clearly observed to support the 1:2 stoichiometry for Pd(**RPd1-c**)$_2$ complexation. The same 1:2 stoichiometry was also obtained for Pd(**RPd1-a**)$_2$ and Pd(**RPd1-b**)$_2$ (see the TOF-MS results in Supplementary Figures S8 and S9). However, when 1.0 equiv of $PdCl_2$ was added into **RPd1-c** in nonaqueous solution of MeOH/DCM (1:1, v/v), the TOF-MS results showed the peak at *m*/*z* 619.1541 that corresponded to $[Pd\mathbf{RPd1\text{-}c}(HCOO^-)]^+$ cation (Supplementary Fig. S10) demonstrating a different stoichiometry of 1:1 between Pd^{2+} and **RPd1-c**. The different stoichiometry results were also observed by Job plots of **RPd1-c** in these two different systems (Supplementary Fig. S11).

The X-ray single crystal structure of **RPd1-c-Pd** complex (incubated in MeOH/DCM mixed solvents) also provided the coordination details. As can be seen clearly in Figure 1 right, two donor atoms that are provided by the lactam and hydrazone ligands, namely O_2, N_2, as well as two Cl atoms, describe a square–planar coordination sphere of Pd^{2+} and Pd^{2+} well within the mean plane that passes through the four donor atoms. The rhodamine part was present in the form of a ring-opened amide conformation to indicate the delocalized xanthene moiety, which shows the strong absorption and emission. Therefore, **RPd1-c** would prefer 1:1 coordination to Pd^{2+} in nonaqueous solution such as MeOH/DCM (1:1, v/v). The Pd^{2+}-coordination induced ring-opening reaction of **RPd1-c** with different stoichiometries of 1:2 in EtOH/H_2O and 1:1 in MeOH/DCM is shown in Scheme 2.

The partial fluorescence quenching[8a,8c] was also observed in **RPd1-c**-Pd^{2+} complex which was revealed by density functional theory (DFT) calculations (Fig. 5).[13] HOMO of **RPd1-c**-Pd^{2+} is localized on the Pd^{2+}-ligand moiety and its energy level locates just between the frontier molecular orbitals of the xanthene fluorophore (HOMO-5 and LUMO). Hence, the PeT (photo-induced electron

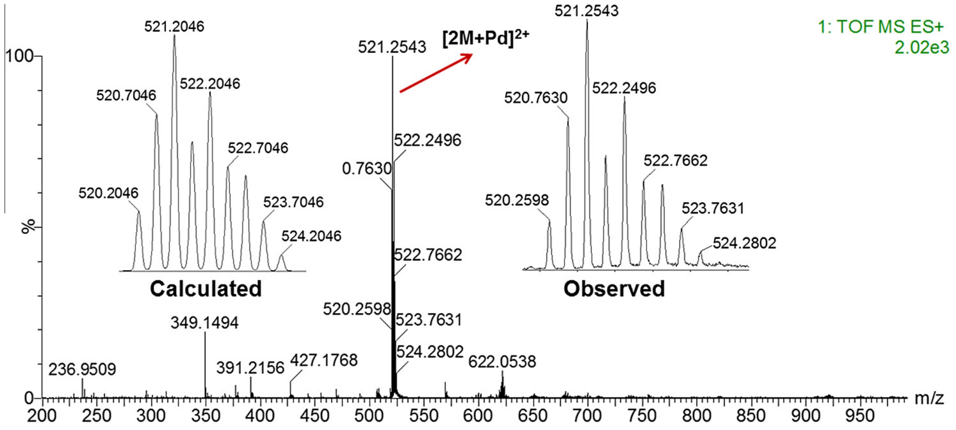
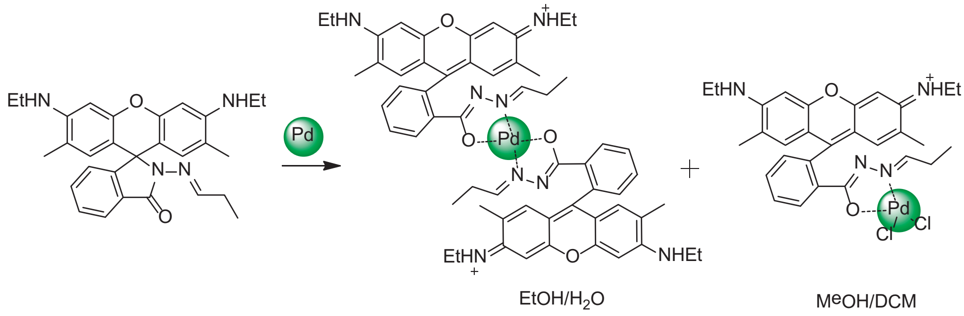


Figure 4. TOF-MS of **RPd1-c** (30 μM) in the presence of 1.0 equiv $PdCl_2$ in 50% ethanolic water solution. Insets: calculated (left) and observed (right) isotopic patterns for the $[Pd(\mathbf{RPd1\text{-}c})_2]^{2+}$ cation.



Scheme 2. Pd^{2+}-coordination induced ring-opening reaction of **RPd1-c** with different stoichiometries of 1:2 in $EtOH/H_2O$ and 1:1 in MeOH/DCM.

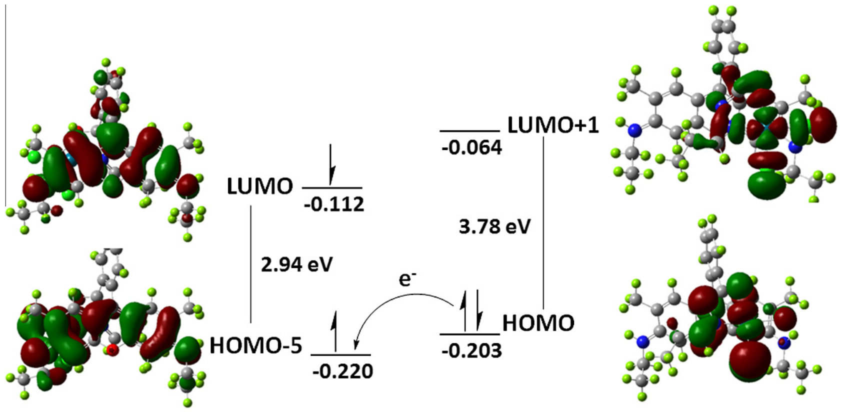


Figure 5. The calculated frontier molecular orbitals of **RPd1-c**-$PdCl_2$ and their energy levels.

transfer) quenching effect may occur from the Pd^{2+}-ligand moiety to the fluorophore.

In summary, we have developed a series of rhodamine spiro-leuco compounds as fluorescence-enhanced sensors for optical sensing of Pd^{2+}. The initial rhodamine hydrazone derivatives, **RPd1-a**, **RPd1-b**, and **RPd1-c**, display a good coordination to Pd^{2+} inducing the spirolactam-opening reaction with a significant fluorescence enhancement and color generation. The different stoichiometries (based on TOF-MS and X-ray single crystal structure) of **RPd1-c**/Pd^{2+} were obtained in $EtOH/H_2O$ and MeOH/DCM, demonstrating the different coordination patterns in aqueous/non-aqueous solutions. Moreover, these sensors can be easily synthesized from the cheap and commercially available starting materials by convenient purification process and in good yields, which all make them easy to be developed as common fluorescent reagents for Pd^{2+} sensing.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.05.094.

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11. CCDC 921199 & 921200 contain the supplementary crystallographic data for this Letter. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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