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Fluorogenic and Chromogenic Detection of Palladium Species through a Catalytic Conversion of a Rhodamine B Derivative

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ABSTRACT

A simple yet efficient detection method for palladium species is developed based on a molecular sensing system that undergoes a palladium-catalyzed oxidative addition. A rhodamine B derivative thus developed undergoes the catalytic process triggered by palladium insertion and gives both turn-on fluorescence and color changes. A usefulness of the sensing system is demonstrated by determining the residual palladium contents in a purified sample prepared through a palladium-catalyzed reaction.

Detection of palladium species with a fluorescence sensing system is drawing current research interest as an easy and sensitive method for determining the palladium contents in the drug intermediates synthesized by palladium catalysis or in mining ores, etc. Detection of palladium contents in those samples is usually carried out using analytical tools such as atomic absorption/emission spectrophotometry, ion-coupled plasma emission-mass spectrometry, and X-ray fluorescence spectroscopy.[1] These conventional methods, however, require large and expensive instruments as well as sophisticated experimental procedures such as complex sample pretreatments and precautions of cross-contamination from the prior analysis. In contrast, the fluorogenic detection method can be performed with a hand-held fluorimeter through relatively simple analysis protocols. Moreover, the chromogenic detection with the naked eye does not require any instruments, albeit less sensitive than the fluorescence method. Many fluorescent sensing systems for metal ions and small molecular anions have been developed, but still highly selective and "turn-on" type systems are desired. To achieve high selectivity and sensitivity, the reaction-based fluorescent sensing approach is attractive.[2]

Recently, Koide and co-workers reported a turn-on fluorescent sensing system for palladium based on the palladium-catalyzed Tsuji−Trost allylic addition reaction:[3] an allylated fluorescein, which is nonfluorescent, undergoes the catalytic deallylation reaction with Pd(0) generated in situ from the Pd(II) species to regenerate the fluorecein, a highly fluores-

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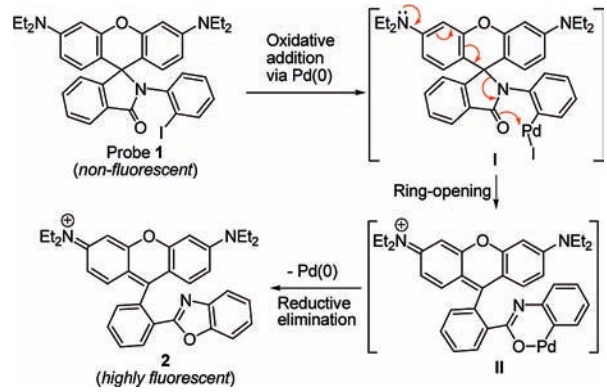
cent compound. A typical palladium species, $PdCl_2$, is thus detected with high selectivity and sensitivity in the presence of triphenylphosphine, tris(2-thiopenyl)phosphine (TFP), or TFP-$NaBH_4$. They have shown that the sensing system and subsequent more elaborate ones[4] are promising for the detection of palladium as well as platinum species in several samples.

We have developed some reaction-based fluorescent sensing systems for anions and metal cations,[5] including rhodamine dye-based ones.[5b,e] Spirolactam derivatives of rhodamine dyes are useful sensing platforms because the spirolactam ring-opening process leads to a turn-on fluorescence change.[2b] An additional advantage of such a rhodamine-based sensing system is that the ring-opening process is also accompanied by a vivid color change from colorless to pink, thus enabling detection simply with the naked eye. Herein, we wish to report an iodophenyllactam derivative of rhodamine B as an efficient fluorogenic and chromogenic sensing system for palladium species. Our rationale in the probe design is depicted in Scheme 1: A palladium intermediate **I** once generated by the oxidative insertion of Pd(0)[6] species to probe **1** may undergo spirolactam ring opening as the carboxamide oxygen coordinates to the corresponding Pd(II) intermediate. A subsequent reductive elimination process will lead to benzoxazole **2**, which is expected to be highly fluorescent because of a conjugated nature of the 6-amino-xanthen-3-ylidene-ammonium moiety. An apparent color change is also expected in addition to the turn-on fluorescence change. During our study, Peng and co-workers reported a rhodamine-based probe that senses palladium through metal coordination rather than catalytic conversion. Such a coordination-based sensing system is sensitive to the metal ligands and consequently to the solvent used, an obvious drawback.[7]

Probe **1** was synthesized from rhodamine B in 87% yield ($POCl_3$, 1,2-dichloroethane, reflux for 4 h; 2-iodoaniline, Et_3N, acetonitrile, 25 °C for 5 h).[8] Interestingly, the ^{13}C NMR spectrum of probe **1** showed 24 separate peaks for the 24 aromatic carbons, owing to atropisomerism: the iodophenyl group seems to experience hindered rotation with respect to the amide group at room temperature and thus causes the peak splitting.

Scheme 1. Spirolactam Ring-Opening Process Triggered by Pd(0)-Catalyzed Insertion, Which Gives a Turn-on Fluorescence Change



A solution of probe **1** in acetonitrile is colorless and nonfluorescent. To detect the Pd(II) species such as $PdCl_2$ according to the mechanism depicted in Scheme 1, a reducing agent is required to convert it to the Pd(0) species. We have found that $[(t\text{-Bu})_3PH]BF_4$ converts $PdCl_2$ into the Pd(0) species, which readily undergoes the oxidative insertion to the iodophenyl group at 85 °C.[9] When a solution of probe **1** in acetonitrile (10 μM) was treated with $PdCl_2$ (0.1 equiv to the probe) and $[(t\text{-Bu})_3PH]BF_4$ (2−4 equiv to the $PdCl_2$),[10] the colorless solution became pink (absorption λ_{max} = 520, 560 nm), and its fluorescence was turned on, from dark to bright orange (emission λ_{max} = 580 nm; excitation wavelength = 540 nm) (Figure 1a). This catalytic turn-on process under the dilute conditions required an initiation step for ~25 min and then proceeded readily within 1 h (Figure 2b). The results indicate that the palladium-catalyzed insertion reaction indeed triggers the spirolactam ring opening, as we intended in the probe design. Efforts to isolate the product **2** were

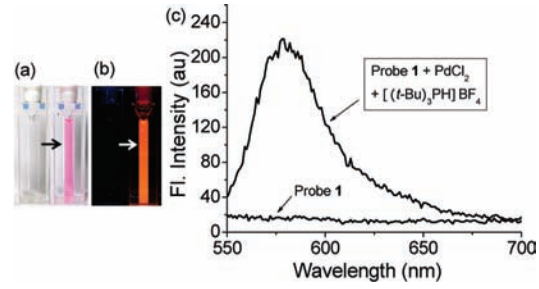


Figure 1. Photos that show (a) color and (b) fluorescence changes for a solution containing probe **1** (10 μM), $PdCl_2$ (1.0 μM), and $[(t\text{-Bu})_3PH]BF_4$ (4.0 μM) in acetonitrile, taken after 30 min at 85 °C. (c) Fluorescence spectral changes of probe **1** upon treatment with $PdCl_2$ (0.1 μM) and $[(t\text{-Bu})_3PH]BF_4$ (0.4 μM) in acetonitrile, measured after 1 h at 85 °C (excitation at 540 nm).

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(8) See the Supporting Information.

not successful because of its instability during silica gel chromatography; however, its formation was supported by in situ NMR analysis for the reaction mixture.[8]

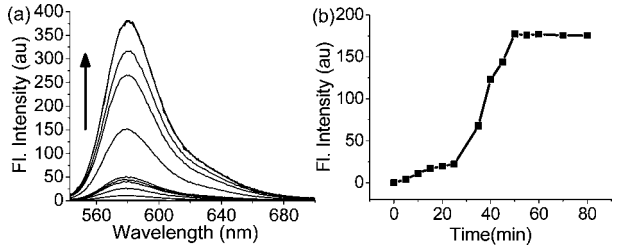

Figure 2. (a) Time-dependent fluorescence spectral changes of probe **1** (10 μM) upon treatment with $PdCl_2$ (1.0 μM) and [(*t*-Bu)$_3$PH]BF_4 (4.0 μM) in acetonitrile at 85 °C (excitation at 540 nm). (b) A plot of the fluorescence intensity change versus the reaction time.

Next, we investigated the sensing behavior of probe **1** toward various other metal chlorides under the established conditions: the catalytic turn-on process occurs only in the case of the palladium species, and other metal species such as Pt(II), Fe(II), Fe(III), Ni(II), Mn(II), Cu(II), Mg(II), Cr(II), and Co(II) do not cause any noticeable fluorescence changes (Figure 3). The palladium sensing is not interrupted in the presence of the other metal species including Zn(II) and Al(III) or acidic compounds such as acetic acid (5 equiv to $PdCl_2$).[8] Notably, the present system does not respond to Pt(II), which coexists with Pd(II) speices in ores and also competes with Pd(II) in the sensing studies.[4a]

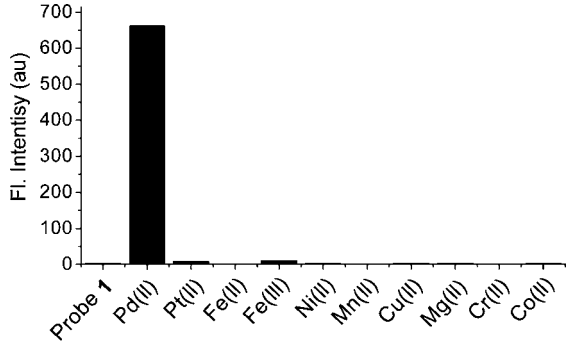

Figure 3. Fluorescence enhancement data of probe **1** (10 μM) toward various metal species (1.0 μM, as the chloride salt) in the presence of [(*t*-Bu)$_3$PH]BF_4 (4.0 μM) in acetonitrile, measured after 1 h at 85 °C (excitation at 540 nm).

The excellent selectivity observed should be originated from the metal-specific catalytic reaction. The present Pd(0)-catalyzed oxidative addition process does not occur with Pt(II), whereas the Tsuji−Trost allylic addition (Koide's system) seems to occur with both the metal catalysts.[3] Therefore, the present sensing protocol can be used for the selective detection of palladium in the presence of various other metal species as well as Pt(II). Furthermore, we can detect palladium species simply with the naked eye.

The present sensing protocol also applies to other palladium species such as $Pd(OAc)_2$ and Pd_2dba_3, which behaved similarly to $PdCl_2$ under the detection conditions.[8]

Sulfur-containing compounds may interfere with the palladium sensing.[3a,b] We examined the sensing of $PdCl_2$ described above in the presence of *N*-acetyl-L-cysteine (5 equiv to $PdCl_2$), but there was no change in the fluorescence enhancement.[8]

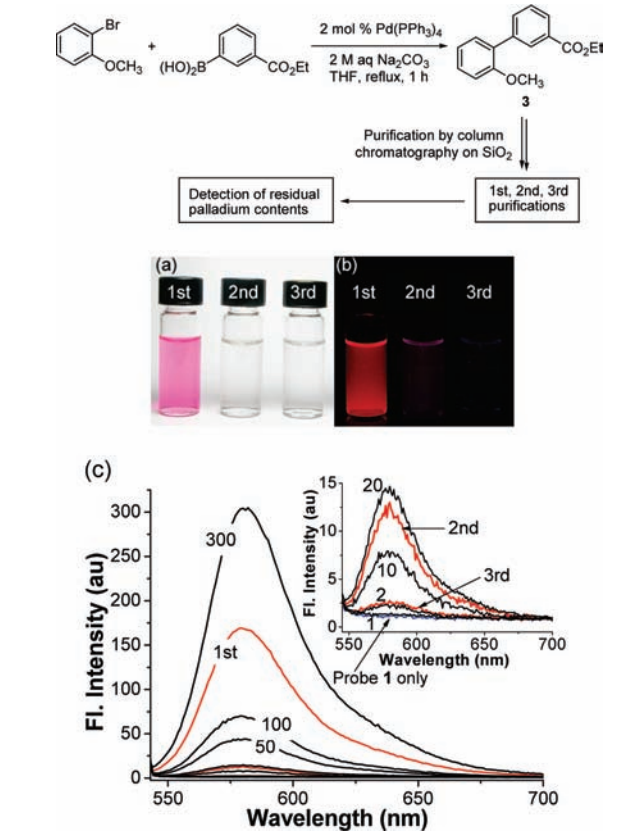

Figure 4. Determination of residual palladium contents in the compound **3** that is synthesized by a palladium-catalyzed reaction and purified by column chromatography. Photos that show both (a) color and (b) fluorescence changes for the purified **3**, after treatment with probe **1** (50 μM) and [(*t*-Bu)$_3$PH]BF_4 (50 μM) in acetonitrile at 85 °C for 1 h. (c) Fluorescence spectra taken for the purified **3** (in red) and for the reference samples containing a known amount of the palladium catalyst [$(Ph_3P)_4$Pd], after treatment with probe **1** under the same conditions (excitation at 540 nm): Arabic numbers on the spectra are in parts per billion units and indicate the amount of the palladium catalyst in each reference sample; the "1st", "2nd", and "3rd" indicate the samples of product **3** that are purified by column chromatography on silica gel once, twice, and three times, respectively. Inset: an expanded plot for the region of 1−20 ppb of the catalyst.

To demonstrate a potential usefulness of probe **1** for the detection of residual palladium contents in the chemical

(9) PPh_3 also caused the insertion but much less efficiently.
(10) 2−4 equiv of [(*t*-Bu)$_3$PH]BF_4 can be used.

products produced by palladium-catalyzed reactions, we carried out a known palladium-catalyzed reaction and analyzed the residual palladium content in the product depending on the number of purifications by column chromatography on silica gel (Figure 4). Thus, the Suzuki−Miyaura coupling reaction was carried out between 2-bromoanisole (300 mg, 1.6 mmol) and (3-ethyloxycarbonyl)benzene boronic acid (342 mg, 1.8 mmol) in the presence of 2 mol % of [$(PPh_3)_4Pd$] (37 mg, 0.03 mmol). The coupled product, (2′-methoxy)biphenyl-3-carboxylic acid ethyl ester, was isolated by standard extractive workup with ethylacetate, dried over anhydrous magnesium sulfate, and purified by column chromatography on silica gel (30 g; eluent, EtOAc/*n*-hexane = 1/4, by volume) to give **3** in 92% yield. This "1st-purified" product was analyzed by fluorimetry using probe **1** (50 μM) under the established conditions to determine the residual palladium content in it.

A solution of the first-purified sample showed bright pink (Figure 4a) as well as orange fluorescence (Figure 4b), indicating that a significant amount of palladium remains in the sample. In comparison with the fluorescence spectra obtained for the samples of known amounts of the palladium catalyst, we were able to determine the palladium content in the first-purified sample (3.84 mg) to be 10.2 ppm.[11] By purifying the first-purified sample again (second purification) through column chromatogrphy (silica gel, 30 g), the palladium content became 960 ppb, and after the third purification (silica gel, 30 g) the content became 110 ppb.[8] These results clearly demonstrate that probe **1** is potentially useful as an easy and sensitive method for determing the residual palladium content in chemical products produced by various palladium-catalyzed reactions. The allowed content of heavy metals in drug chemicals is below 10 ppm,[12] which indicates that we can readily monitor the residual palladium content in drug intermediates using the present sensing system. The palladium content in persons with amalgam fillings and metallic dental appliances is 10.6 ± 7.4 ppm from samples of morning saliva.[13]

In summary, we have developed a novel fluorogenic and chromogenic sensing system for palladium species based on the metal-catalyzed oxidative insertion reaction. The iodophenylspirolactam derivative of rhodamine B thus undergoes the palladium-catalyzed insertion reaction and triggers spirolactam ring opening, which accompanies both turn-on fluorescence and color changes. The catalytic ring-opening process is specific toward palladium species, and thus the sensing system can be used for the detection of palladium among various other metal species.

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Supporting Information Available: Synthesis and characterization of probe **1** and the fluorescence data mentioned. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) The weight of the solvent used and the weight percentage of palladium in the catalyst are accounted for in the calculation of the palladium content. See the Supporting Information for details.

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