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Short communication

A near-infrared and colorimetric fluorescent probe for palladium detection and bioimaging

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ABSTRACT

A near-infrared (NIR) and colorimetric fluorescent probe was developed for palladium species *via* a palladium catalyzed deallylation reaction. In this probe, 6-hydroxy-2,3-dihydro-xanthene-indolium (**CyH**) was acted as the signal unit and an allyl carbonate group was acted as the recognition unit. This non-fluorescent probe molecule can release the relevant fluorophore after interaction with palladium. The sensing mechanism was investigated by optical spectrum and NMR spectra. The probe can be used for "naked-eye" detection of palladium, and exhibited high selectivity to palladium over various other metal ions. Furthermore, the probe can be applied to imaging intracellular palladium ions in living HeLa cells, indicating its great potential for in *vivo* bioanalytical applications.

1. Introduction

Palladium (Pd) as a precious metal was widely used in various materials and pharmacy such as catalytic converters, fuel cells, jewelry, dental crowns and so on [1–3], which led to high level of residual palladium in the final product [4–6], thus resulting in fearful environmental and health problems because it can bind to biomolecules like proteins, DNA, thiol-containing amino acids and disturb cellular processes [7–9]. Therefore, development of efficiency methods for detective and imaging palladium species is important for environment safe and human health.

Up to now, there are many traditional methods reported for the detection of palladium species [10–13], such as inductively coupled plasma atomic emission spectrometry (ICP-AES), solid-phase microextraction high performance liquid chromatography (SPME-HPLC), X-ray, atomic absorption spectroscopy (AAS), *etc* [14–17]. However, they suffer from complicated sample preparation procedures, complicated instrumentation and the requirement for highly-trained individuals [18–20]. Compared with above technologies, fluorometry is more attractive due to excellent sensitivity, high selectivity, low detection limit and operational simplicity [21–24].

In the past few years, several fluorescent probes have been reported for the detection of palladium. For example, M. Kumar et al. design a fluorescent probe detection of palladium based on hydroxyphenyl-benzothiazole [25]. And Liu et al. prepared a "*turn-on*" fluorescent probe for palladium using rhodamine as the signal group [26]. However, these probes need the ultraviolet or visible light to excite, which severely limits in biological applications because the fluorescence imaging in the visible region would be easily disturbed by cell auto-fluorescence in living systems [27–32]. Therefore, it is consequential to develop the near infrared fluorescent probes for the detection of palladium [33]. Recently, Wang's group has design a near-infrared fluorescent probe for palladium, which exhibits high sensitivity and selectivity toward both Pd(0) and Pd(II). But this probe has a main drawback of poor water solubility, which is a disadvantage for bioimaging application [34]. Zhang' group reported a fluorescent probe for palladium. Although this probe emit in the red light region, it cannot be used for monitoring palladium in living cells due to the need high proportion of organic solvents [35]. Until now, the fluorescent probe based on near-infrared dyes for imaging intracellular palladium is very rare. In addition, colorimetric method has also draw much attention in terms of practical application due to its low-cost and convenient operations [36]. As a consequence, it is still urgently demanded to develop a novel NIR and colorimetric fluorescent probe for sensing palladium species in biological sample.

Based on above consideration, we choose heptamethine cyanine

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derivative (**CyH**) as the chromophore due to its NIR-emission, excellent water solubility, easily synthetic and predictable colour change in the solution after modification [37,38]. Herein, we designed and synthesized a new NIR and colorimetric fluorescent probe, 6-((allylcarbonyl)oxy)-2,3-dihydro-xanthenes-indolium (**CyPd**) detection of palladium. The probe is composed of **CyH** as the fluorophore and the allyl carbonate group as the recognition unit (in Scheme 1). In absence of any analyte, the free **CyPd** has almost no fluorescence due to the intermolecular charge transfer (**ICT**) possess from the fluorophore to the allyl carbonate group. Upon addition of palladium, the depropargylation reaction occurs and thus the protected hydroxyl group on the **CyPd** is liberated, which lead to the significant enhancement of fluorescence. Indeed, the synthesized probe showed many advantages as follow: high selective and sensitive to palladium; emission in the NIR light region (λ_{em} = 721 nm); excellent water solubility; simple synthesis; "naked-eye" detection for palladium; the capability of monitoring palladium in living cells. All of these performances make it appropriate for potential application in biology.

2. Experimental sections

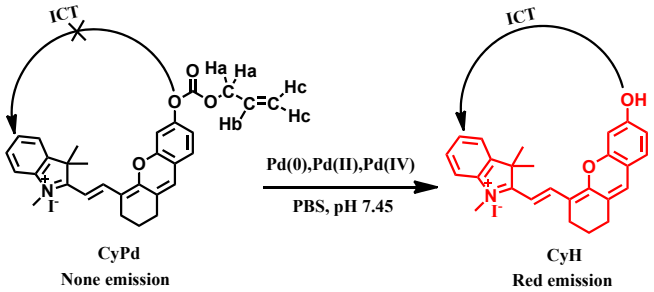
2.1. Reagents and apparatus

2,3,3-trimethyl-3H-indole, cyclohexanone, phosphoryl chloride, sodium acetate, resorcinol, potassium carbonate, triethylamine, allyl carbonochloridate, $Pd(PPh_3)_4$ (Pd(0)), $PdCl_2$ (Pd(II)) and $(NH_4)_2PdCl_6$ (Pd(IV)) were purchased from Energy Chemical. Acetonitrile (ACN), Chloroform, Dimethyl formamide (DMF), Dichloromethane (DCM), Dimethyl sulfoxide (DMSO), and Acetic anhydride were obtained from Sinopharm Chemical Reagent Company. All chemicals used in this work were of analytical grade and without further purification. Double distilled water was used in this work.

Electrospray mass spectrometry (ESI-MS) spectra were acquired on a ZQ2000 mass spectrometer (Manchester, UK). ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AVB-500 spectrometer using TMS as an internal standard. UV–vis spectra were recorded on a UV-2450 spectrophotometer (Shimadzu). Time dependent fluorescence spectra were recorded at 37 °C on a QM40 fluorescence spectrophotometer (PTI, Canada), and other fluorescence spectra were recorded at room temperature using an F-7000 fluorescence spectrophotometer (Hitachi Co., Japan) with the excitation and emission slit widths at 5 nm.

2.2. Synthesis of compounds

The synthetic route of **CyPd** is shown in Scheme 2. The resulting compounds were characterized by conventional ESI-MS, ^1H NMR, and ^{13}C NMR spectroscopy (see Fig. S1–S8).



Scheme 1. Recognition mechanism of **CyPd** toward palladium.

2.2.1. Synthesis of compound *1*

Compound 1 was synthesized on the basis of the procedures reported in the literature [39]. A mixture of dimethylformamide (40 mL) and methylene chloride (40 mL) was chilled in an ice bath for 30 min. Then phosphorus oxychloride (37 mL, 0.41 mol) and cyclohexanone (10.0 g, 0.10 mol) was added dropwise to the above mixture solution with stirring. The mixture solution was refluxed for 3 h, cooled, poured onto 300 g of ice, and stand to overnight. The yellow solid was collected with a yield of 7.8 g (44.5%).

2.2.2. Synthesis and characterization of *Cy-7*

2,3,3-trimethyl-3H-indole (3.66 g, 11.66 mmol), compound 1 (0.96 g, 5.44 mmol) and sodium acetate (0.47 g, 5.44 mmol) were dissolved in 30 mL acetic anhydride under nitrogen atmosphere. The mixture solvent was stirred for 2 h at room temperature. Then the mixture solvents were removed under vacuum. The residual were washed with ether to obtain 3.2 g of pure green solid (91%). ^1H NMR (500 MHz, $CDCl_3$): δ 8.31 (d, J = 14.1 Hz, 2H), 7.40–7.33 (m, 4H), 7.24–7.14 (m, 4H), 6.18–6.15 (s, 2H), 3.72 (s, 6H), 2.70 (t, J = 6.1 Hz, 4H), 1.97–1.88 (m, 2H), 1.69 (s, 12H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 172.90, 150.67, 144.38, 142.75, 140.89, 128.84, 127.65, 125.36, 122.15, 110.88, 101.60, 77.40, 77.15, 76.90, 49.25, 32.69, 29.66, 28.08, 26.73, 20.68.

2.2.3. Synthesis and characterization of *CyH*

A stirred solution of resorcinol (220 mg, 2.0 mmol) and K_2CO_3 (276 mg, 2.0 mmol) in 15 mL ACN at room temperature under nitrogen atmosphere, stirred for 20 min, a solution of ACN (10 mL) contain compound 2 (610 mg, 1.0 mmol) was added to the above mixture solution *via* a syringe. The mixture solution was heated for 4 h at 50 °C. The solvent was evaporated under reduced pressure, the crude product was purified by silica gel column chromatography (CH_2Cl_2/CH_3OH = 50:1), contain the desired **CyH** as a blue-green solid (373 mg, yield 73%). ^1H NMR (500 MHz, DMSO-d_6): δ 8.15 (d, J = 13.9, 1H), 7.56 (s, 1H), 7.53 (d, J = 7.3, 1H), 7.37 (t, J = 9.3, 2H), 7.28 (d, J = 7.9, 1H), 7.17 (t, J = 7.4, 1H), 6.59 (d, J = 8.9, 1H), 6.44 (s, 1H), 6.01 (d, J = 13.8, 1H), 3.55 (s, 3H), 2.64 (d, J = 17.9, 2H), 2.63 (t, J = 5.6 Hz, 2H), 1.79 (s, 2H), 1.66 (s, 6H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 169.76, 159.61, 143.83, 140.60, 138.46, 135.96, 130.38, 128.76, 123.96, 123.22, 122.60, 119.65, 115.88, 115.59, 110.42, 102.75, 98.32, 48.34, 40.50, 40.34–40.09, 40.00, 39.84, 39.67, 39.50, 31.25, 28.34, 28.01, 24.37, 21.10. MS (EI) m/z: 384.23 (M^+).

2.2.4. Synthesis and characterization of *CyPd*

To a stirred solution of **CyH** (102.2 mg, 0.2 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added triethylamine (Et_3N, 56 μL, 0.4 mmol, 2.0 equiv) and allyl chlorocarbonate (42.42 μL, 0.4 mmol, 2.0 equiv) at 0 °C under nitrogen atmosphere. Stirred for 30 min, the mixture was heated to room temperature and stirred overnight. the reaction mixture was concentrated under reduced pressure to give crude solid, then purified by silica gel column chromatography (CH_2Cl_2/CH_3OH = 50:1) to afford desired probe **CyPd** as a blue solid (51 mg, yield 43%). ^1H NMR (500 MHz, DMSO-d_6): δ 8.56 (d, J = 15.3 Hz, 1H), 7.78 (d, J = 7.4 Hz, 1H), 7.74 (d, J = 7.9 Hz, 1H), 7.58 (t, J = 10.1 Hz, 3H), 7.51 (t, J = 7.3 Hz, 1H), 7.38 (s, 1H), 7.22 (dd, J = 8.4, 2.2 Hz, 1H), 6.66 (d, J = 15.3 Hz, 1H), 6.03 (ddd, J = 22.8, 10.7, 5.7 Hz, 1H), 5.44 (dd, J = 17.2, 1.5 Hz, 1H), 5.34 (dd, J = 10.5, 1.2 Hz, 1H), 4.78 (d, J = 5.6 Hz, 2H), 3.94 (s, 3H), 2.75–2.70 (m, 2H), 2.68 (t, J = 5.9 Hz, 2H), 1.87–1.80 (m, 2H), 1.75 (s, 6H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 179.40, 158.85, 152.93, 152.76, 152.65, 145.51, 142.85, 142.64, 132.07, 130.56, 130.33, 129.33, 128.76, 128.23, 123.13, 120.20, 119.65, 119.04, 114.61, 114.26, 109.97, 107.37, 69.60, 51.25, 33.62, 29.15, 27.42, 24.01, 20.27. MS (EI) m/z: 468.20 (M^+).