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A simple and highly selective fluorescent sensor for palladium based on benzofuran-2-boronic acid

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ABSTRACT

Benzofuran-2-boronic acid could be used as a fluorescent sensor for the detection of Pd^{2+} because it was rapidly converted to highly fluorescent derivative after mixing with Pd^{2+} under basic condition at room temperature. We found that dimerization of benzofuran was occurred to form fluorescent derivative by the catalytic activity of palladium. The fluorescence intensity at 360 nm increased with increasing the concentration of Pd^{2+}. The excellent selectivity for Pd^{2+} was demonstrated among other metal ions. Based on this findings, we successfully applied benzofuran-2-boronic acid to develop a microplate-based assay for high-throughput measurement of Pd^{2+}. The detection limit (blank + 3SD) for Pd^{2+} of the proposed assay was 9.8 nM.

Introduction

Palladium (Pd) is a platinum group element and one of the most useful transition metal. It is widely used in various applications such as jewelries, coating materials, dental crowns and catalysts.[1,2] Especially, Pd catalyzed C—C cross-coupling reactions have been recognized as efficient and useful tools for the synthesis of organic compounds including pharmaceutical compounds.[3,4] However, an adverse influence of Pd on human health has been concerned because Pd ions can bind to thiol-containing proteins (e.g. casein and silk fibroin), DNA or other biomolecules (e.g. vitamin B_6, etc.) due to their high nucleophilicity.[5,6] The palladium residues in pharmaceutical compounds or in environment may cause considerable hazard. According to the European Medicines Agency (EMA) and the United States Pharmacopeia (USP), the permitted daily exposure of Pd in pharmaceutical products for oral formulations is less than 100 μg per person per day.[7] Therefore, development of a selective and sensitive analytical method for the determination of Pd should be important to evaluate possible adverse health effects of Pd residues.

Several instrumental analytical methods such as inductively coupled plasma mass spectroscopy (ICP-MS),[8] ICP optical emission spectrometry (ICP-OES)[9] and flame atomic absorption spectrometry (FAAS)[10] have been developed as effective methods to determine Pd. However, these methods require expensive, sophisticated instruments and complicated sample pre-treatment procedures. In contrast, fluorescent sensor based assays have advantages in terms of simplicity, high sensitivity, rapidness and cost effectiveness. Consequently, various fluorescent sensors for the detection of Pd^{2+} such as rhodamine spirolactam derivatives have been developed (Table 1).[2,6,11–20] However, these fluorescent sensors still have drawbacks and limitations such as low sensitivity,[11,13,15–17,19,20] slow response,[11–14] and necessity of heating at high temperature.[13,14] In addition, the availability of several sensors is low because the synthetic process of sensor is complicated.[2,6,11,12,14–20] Therefore, the demand for the development of new fluorescent sensor is still growing. On the other hand, it is well known that Pd can be used as an effective catalyst for the Suzuki-Miyaura coupling, which is the coupling reaction between an arylboronic acid and an aryl halide.[21] However, until now, boronic acid based fluorescent sensor has not been developed for the detection of Pd^{2+}.

Herein, we utilized benzofuran-2-boronic acid as a new fluorescent sensor for the selective detection of Pd^{2+}. Although the fluorescence of benzofuran-2-boronic acid was extremely weak, the fluorescence drastically increased by addition of Pd^{2+} under basic condition. We found that the intense fluorescence was attributed to the conversion of benzofuran-2-boronic acid to benzofuran dimer by the catalytic activity of Pd. Since the fluorescence intensity increased with increasing the concentration of Pd^{2+}, benzofuran-2-boronic acid could be used for the quantitative determination of Pd^{2+}. Benzofuran-2-boronic acid has several advantages as a fluorescent sensor for Pd^{2+} because benzofuran-2-boronic acid is stable compound and the fluorescence enhancement reaction with Pd^{2+} proceeds rapidly even at room tempera-

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Table 1
Comparison of LOD, reaction time and temperature obtained of various fluorescent sensors for the detection of Pd^{2+}.

Sensor	LOD, nM	Reaction time, min	Reaction temperature, °C	Reference
Benzofuran-2-boronic acid	9.8	5	Room temperature	Current work
Benzothiazole with phenyl allyl ether	5.2	5	25	6
Naphthyl propargyl ether	5.3×10	60	37	11
Phenylfluorone allyl ether	7.3	60	45	12
9-Bromophananthrene	5.0×10	120	70	13
Benzoxadiazole with allyl carbonate	1.1	120	55	14
Coumarine with allyl carbonate	1.7×10	30	37	15
GCTPOC with allyl carbonate	6.9×10^2	6	Room temperature	16
Hemicyanine with allyl carbonate	1.2×10	10	Room temperature	2
Heptamethine cyanine with allyl carbonate	2.2×10	30	37	18
Rhodamine spirolactam	2.4	Not discussed	Not discussed	19
Rhodamine spirolactam	35×10^3, 4.6×10^3	1	Room temperature	20

ture. Moreover, benzofuran-2-boronic acid is commercially available. Therefore, benzofuran-2-boronic acid is expected to overcome the limitations of previous fluorescent sensors. In this study, the spectral characteristics of benzofuran-2-boronic acid after the reaction with Pd^{2+} were investigated, and the selectivity for the detection of Pd^{2+} was evaluated. Finally, we applied benzofuran-2-boronic acid to develop a microplate-based assay for high-throughput measurement of Pd^{2+}.

Results and discussions

UV–vis and fluorescence spectral changes of benzofuran-2-boronic acid after addition of Pd^{2+}

To investigate the spectral changes of benzofuran-2-boronic acid after addition of various concentration of Pd^{2+}, absorption and fluorescence spectra were measured. As shown in Fig. 1, the absorption at 258 nm decreased with increasing Pd^{2+} concentration, while the absorptions at 320 and 340 nm increased. This bathochromic shift suggested an extension of the conjugation of benzofuran-2-boronic acid. Meanwhile, the fluorescence intensity at 360 nm increased with increasing the Pd^{2+} concentration although benzofuran-2-boronic showed extremely weak fluorescence (Fig. 2). It was suggested that benzofuran-2-boronic acid

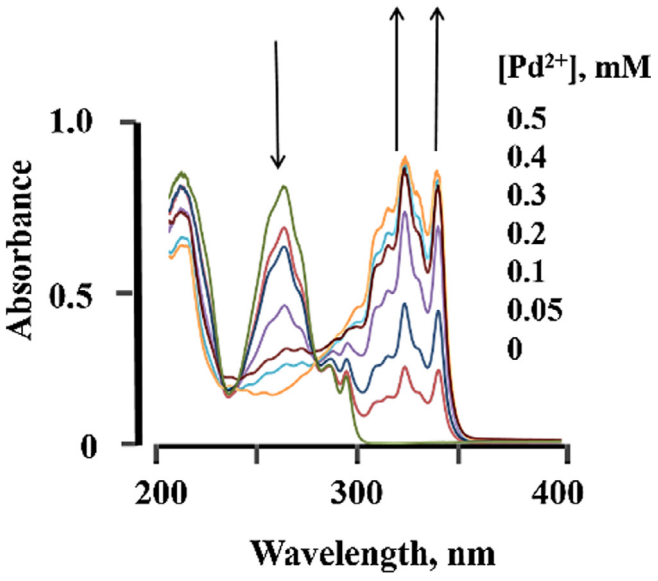

Fig. 1. The UV–vis absorption spectra of benzofuran-2-boronic acid (10 μM) in acetonitrile upon addition of different concentrations of Pd^{2+} (0, 0.050, 0.10, 0.20, 0.30, 0.40 and 0.50 mM) in acetonitrile.

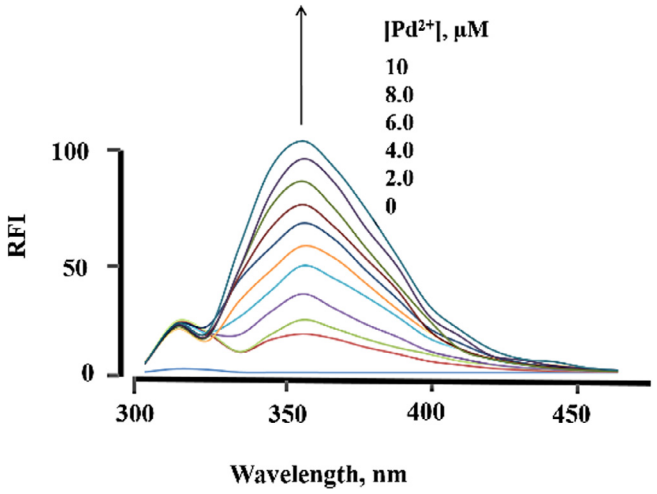

Fig. 2. The fluorescence spectra of benzofuran-2-boronic acid (10 μM) in acetonitrile upon addition of different concentration of Pd^{2+} (0, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0 and 10 μM) in acetonitrile; λ_{ex} = 315 nm.

was converted to highly fluorescent derivative after the reaction with Pd^{2+} under basic condition.

In addition to benzofuran-2-boronic acid, we measured the fluorescence of several types of arylboronic acids including phenylboronic acid, naphthalene-1-boronic acid, *N*-methyl-4-pyridine boronic acid and benzothiophene-2-boronic acid after the reaction with Pd^{2+}. However, the significant fluorescence enhancement was not observed from these arylboronic acids except for benzothiophene-2-boronic acid. Although the reaction mixture of benzothiophene-2-boronic acid emitted fluorescence at 370 nm under excitation at 315 nm, the fluorescence intensity was 25 times lower than that of the reaction mixture of benzofuran-2-boronic acid. Therefore, we concluded that benzofuran-2-boronic acid should be most suitable for fluorescent sensing of Pd^{2+}.

Confirmation of the structure of the fluorescent derivative

To elucidate the structure of the fluorescent derivate, the synthesized derivative was analyzed by EI-MS (JMS-DX 303 electron impact mass spectrometer, JEOL, Tokyo, Japan) and ^{1}H NMR (JNM-AL 400, JOEL Tokyo, Japan). The highest molecular ion peak in the EI-MS was observed at m/z = 234, and the results of ^{1}H NMR (400 MHz, $CDCl_3$) were as follows: δ, ppm = 7.63 (d, J = 7.2 Hz, 2H), 7.55 (d, J = 8.0 Hz, 2H), 7.41–7.26 (m, 4H), 7.17 (s, 2H). These results were in accordance with the previously reported data of benzofuran dimer.[22] It is known that the dimerization of arylboronic acid can be occurred by homo-coupling reaction in