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SHORT COMMUNICATION

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Push–Pull-Type Purine Nucleoside-Based Fluorescent Sensors for the Selective Detection of Pd^{2+} in Aqueous Buffer

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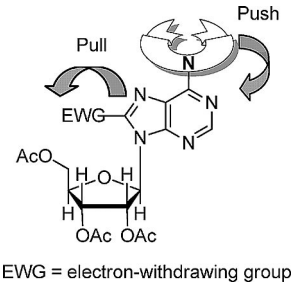
Push–pull-type purine nucleoside-based fluorescent sensor **L1** bearing a chelating *N*,*N*-bis(2-pyridylmethyl)amine group at the C6 position was designed and synthesized. Sensor **L1** showed clear and selective detection of Pd^{2+} in aqueous buffer, and it is the first "on–off"-type purine nucleoside-based fluorescent sensor for Pd^{2+}.

Introduction

Fluorescence technology is widely used to explore the structure, dynamics, and recognition of biomolecules,[1] and this has led many researchers to investigate the design of various fluorescent sensors. With the aim to apply fluorescent sensors in vivo, biological compatibility is important and favorable for an excellent fluorescent sensor.[2] Purine nucleosides are ubiquitous in RNA and DNA and possess outstanding biological compatibility.[3] However, owing to their weak fluorescent properties, purine nucleosides are difficult to use as fluorescent sensors.[4] Thus, we developed an efficient and novel way to enhance their fluorescent properties by a push–pull strategy.[5] In this new type of fluorescent sensor, the purine part functioned as the chromophore; an electron-donating amino derivative was directly incorporated into the C6 position of the purine to have a push effect, and an electron-withdrawing aryl group was attached to the C8 position of the purine to increase the conjugated system and exert a pull influence. Through this push–pull effect, electrons were able to flow into the fluorescent sensor, and the fluorescent properties of the purine nucleosides were simultaneously enhanced (Scheme 1).



Scheme 1. Push–pull-type purine nucleoside-based fluorescent sensors.

Nowadays, the development of fluorescent sensors for heavy-metal and transition-metal ions is a hot investigative topic.[6] Recently, palladium has attracted considerable attention owing to its extensive use in many catalytic reactions and industrial applications.[7] The use of such catalysts creates ultimate products often containing a high level of residual palladium, which can lead to the pollution of the environment, and furthermore, this metal is detrimental to health.[8] Therefore, searching for an efficient fluorescent sensor for the selective detection of Pd^{2+} is highly desirable.[9] In our push–pull-type purine nucleoside-based fluorescent sensors, if a chelating group is introduced into the C6 position of adenosine, this type of fluorescent sensor may show high selectivity towards metal ions including Pd^{2+} (Scheme 1). Herein, we wish to report new push–pull-type purine nucleoside-based fluorescent sensors for the selective detection of Pd^{2+}.

Results and Discussion

Initially, we chose the 4-nitrobenzyl group as the electron-withdrawing group attached to the C8 position of adenosine to form a push effect and incorporated *N*,*N*-di-

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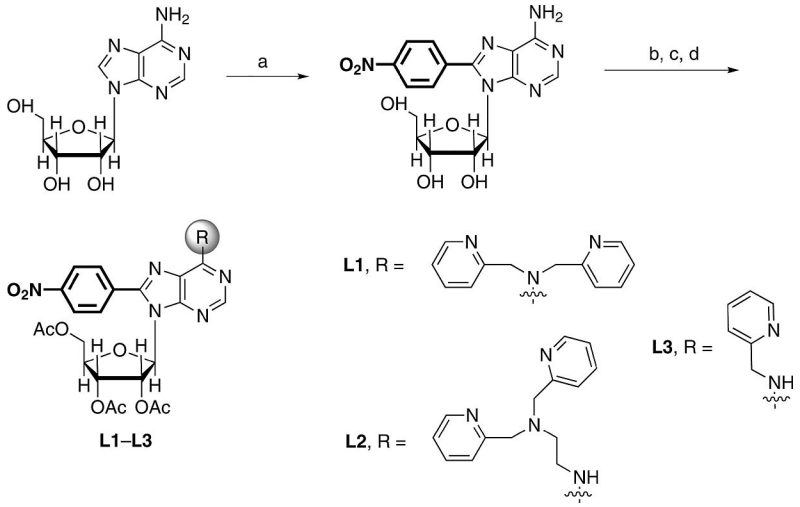

Scheme 2. Synthesis route of **L1**–**L3**. Reagents and conditions: (a) 1-iodo-4-nitrobenzene, $Pd(OAc)_2$, CuI, piperidine, DMF, 120 °C, 24 h; (b) Ac_2O, 4-(dimethylamino)pyridine, pyridine, r.t., 4 h; (c) isoamyl nitrite, $CHBr_3$, 65 °C, 3.5 h; (d) RH, EtOH, reflux.

(2-pyridylmethyl)amine (DPA) and similar amines[10] as the chelating groups in our purine nucleoside-based fluorescent sensors (Scheme 2, **L1**–**L3**). It was expected that the electron density of the conjugating system would be redistributed upon coordination to specific metal ions, which would give rise to a clear change in the emission spectra.

Subsequently, the photophysical properties of **L1**–**L3** were studied (Figure 1). According to the equation of fluorescence quantum efficiency,[5d,11] the emission intensity of sensor **L1** is more than 3 times stronger than that of sensor **L2** and about 1.5 times stronger than that of sensor **L3**. With respect to the luminous properties, the structural difference of the electron-donating groups at the C6 position resulted in a distinction in the fluorescence intensity, and modification by the DPA group was clearly favored over the other amine groups. Moreover, the molar absorptivity of sensor **L1** was 8.83×10^3 L mol^{-1} cm^{-1} and the quantum yield of sensor **L1** was 0.011; the fluorescence quantum yield was determined relative to known standards such as tryptophan in H_2O (λ_{ex} = 286 nm, λ_{em} = 355 nm, Ø = 0.13).

To evaluate the selectivity of **L1**–**L3**, the fluorescence spectra of **L1**–**L3** (6.0 μM) in the presence of different metal ions (4.0 equiv.) were recorded in aqueous buffer (10% DMSO, v/v, pH 7.3). As shown in Figure 2 (a), the fluorescence of **L1** was strongly quenched upon the addition of Pd^{2+}, and the presence of other metal ions including Zn^{2+}, Pb^{2+}, Cd^{2+}, Cr^{3+}, Co^{2+}, Cu^{2+}, Fe^{3+}, Ni^{2+}, Mn^{2+}, Hg^{2+}, and Ag^{+} resulted in negligible fluorescence intensity changes under identical conditions. However, for **L2** there were no distinctive fluorescence changes upon the addition of different metal ions (Figure S1b, Supporting Information), and the fluorescence of **L3** increased to different extents,

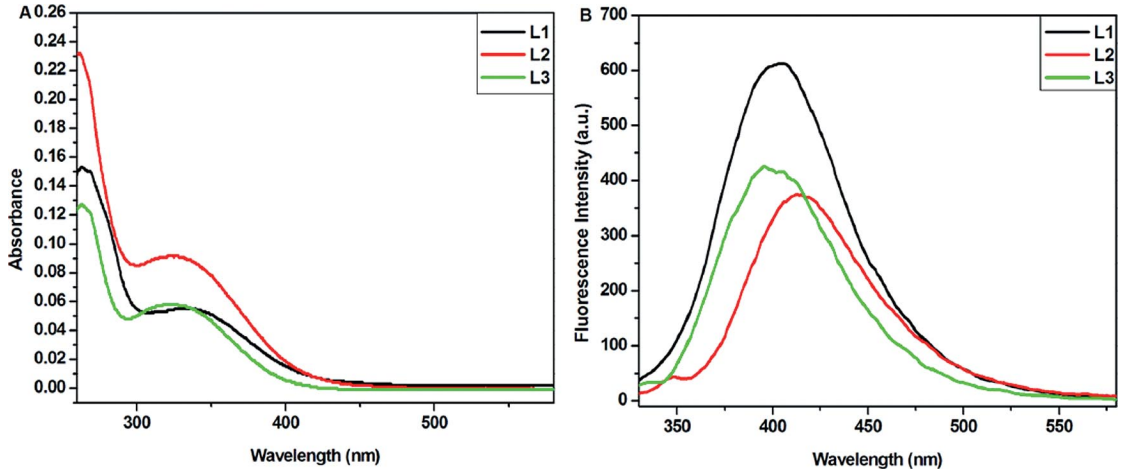

Figure 1. Absorption spectra and fluorescence spectra of **L1**–**L3** (6.0 μM) in 50.0 mM aqueous Tris-HCl buffer (10% DMSO, v/v, pH 7.3). Excitation wavelength of **L1** and **L2** was 310 nm. Excitation wavelength of **L3** was 300 nm.

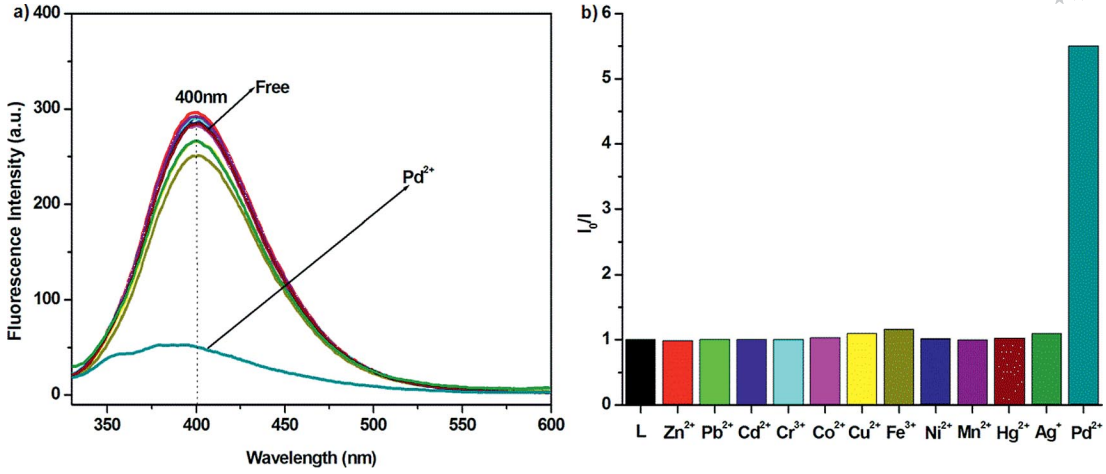

Figure 2. (a) Fluorescence responses of **L1** toward various metal ions (4.0 equiv.). (b) Fluorescence response of **L1** (6.0 μM) upon the addition of different metal cations (4.0 equiv.), and the bars are relative fluorescence intensities (I_0/I). All the experiments were performed in aqueous Tris-HCl buffer (10% DMSO, v/v, pH 7.3, λ_{ex} = 310 nm).

except for Pd^{2+} (Figure S1c, Supporting Information). The effect of metal ions on the fluorescence intensity of **L1** is shown in Figure 2 (b), which suggests that the selectivity of **L1** toward Pd^{2+} over other metal ions is extremely high. To our delight, this high selectivity of the fluorescence probe towards Pd^{2+} has not been found in other probes with a DPA receptor.

To understand the coordination effect of sensor **L1** with Pd^{2+} in detail, fluorescence titration experiments of **L1** with Pd^{2+} were performed at room temperature in aqueous Tris-HCl buffer (10% DMSO, v/v, pH 7.3). As shown in Figure 3 (a), with an increase in the amount of Pd^{2+}, a clear change in the fluorescence spectrum of **L1** took place. The intensity of the fluorescent band of **L1** centered at 400 nm decreased progressively, and the fluorescence was almost quenched completely upon the addition of 6.0 equiv. Pd^{2+}. Moreover, the fluorescence intensity of **L1** is linearly proportional to the concentration of Pd^{2+} in the range from 0 to 1.8 equiv. (Figure 3, b, c). The detection limit of sensor **L1** for Pd^{2+} was estimated to be 6.47×10^{-7} M; consequently, **L1** can be used for Pd^{2+}-polluted analysis in drugs according to the World Health Organization specified threshold limit for palladium content in drug chemicals [4.7×10^{-5} M (5.0 ppm) to 9.4×10^{-5} M (10.0 ppm)].[8e,12] Besides $Pd(OAc)_2$, other Pd^{2+} sources such as $PdCl_2$ could also be detected, which demonstrates the potential applications of Pd^{2+} sensor **L1** (Figure S2, Supporting Information).

Then, competition experiments were conducted to evaluate the selectivity of the binding event between **L1** and Pd^{2+}

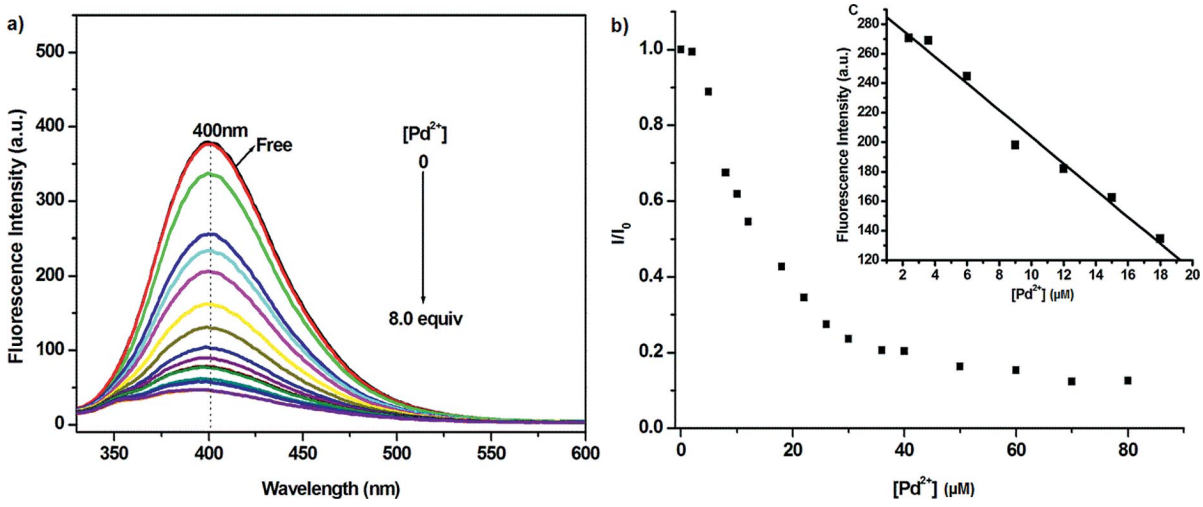

Figure 3. (a) Fluorescence spectra of **L1** (10.0 μM) upon the addition of various concentrations of Pd^{2+} (0, 0.2, 0.5, 0.8, 1.0, 1.2, 1.8, 2.2, 2.6, 3.0, 3.6, 4.0, 5.0, 6.0, 7.0, 8.0 equiv.) in aqueous buffer (10% DMSO, v/v, pH 7.3). (a) Relative fluorescence intensities (I/I_0) as a function of the concentration of Pd^{2+} in aqueous buffer (10% DMSO, v/v, pH 7.3). (c) Fluorescence intensities of **L1** versus Pd^{2+} concentration. Excitation wavelength was 310 nm.

(Figure 4). The results embodied that the Pd^{2+}-induced fluorescence was unaffected in the presence of competitive metal ions, which could be ascribed to the tight coordination of the DPA chelator to Pd^{2+}. Thus, **L1** can function as a fluorescence sensor for the selective detection of Pd^{2+}.

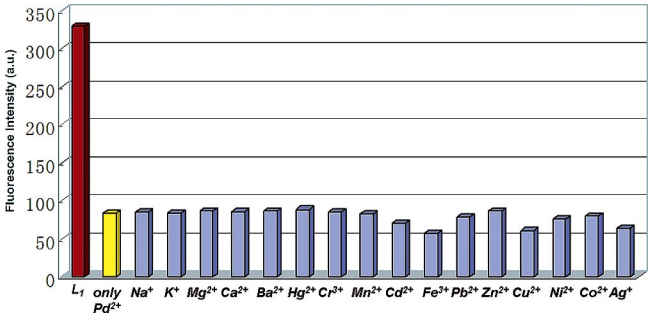

Figure 4. Fluorescence responses of **L1** (6.0 μM) toward Pd^{2+} (30.0 μM) in 50.0 mM aqueous Tris-HCl buffer (10% DMSO, v/v, pH 7.3) after the addition of other competitive metal ions (30.0 μM). Red bar represents the emission intensity of **L1** (6.0 μM). Yellow bar represents the emission intensity of **L1** (6.0 μM) in the presence of Pd^{2+} (30.0 μM). Blue bars represent the emission intensities that occurred upon the subsequent addition of Pd^{2+} (30.0 μM) to the mixed solutions of **L1** (6.0 μM) toward 30.0 μM other competitive metal ions (Na^+, K^+, Mg^{2+}, Ca^{2+}, Ba^{2+}, Hg^{2+}, Cr^{3+}, Mn^{2+}, Cd^{2+}, Fe^{3+}, Pb^{2+}, Zn^{2+}, Cu^{2+}, Ni^{2+}, Co^{2+}, and Ag^+). Emission intensities were recorded at 400 nm, and the excitation wavelength was 310 nm.

Subsequently, the mechanism of the fluorescent sensor for the selective detection of Pd^{2+} was investigated.[13] As mentioned above, after adding various metal ions, the fluorescence intensity of **L3** increased to different extents (Figure S1c, Supporting Information). However, the addition of Pd^{2+} to the solution of **L3** demonstrated a negligible effect on the fluorescence. Thus, we confirmed that (1) Pd^{2+} was not an inherent fluorescent quencher and (2) the N atom of the purine skeleton probably did not interact with Pd^{2+} to quench the fluorescence of **L1**. More importantly, the clearly comparative results indicated that the DPA moiety of **L1** played a key role in the selective binding with Pd^{2+}.

Next, S^{2-} titration experiments of the **L1**-Pd^{2+} system were used to test the coordination between **L1** and Pd^{2+}. If an excess amount of S^{2-} was added to a solution of **L1**-Pd^{2+}, the fluorescence of **L1** recovered gradually (Figure 5). This suggested that the binding of Pd^{2+} with **L1** was the reason for the fluorescence quenching. To our delight, the binding process was reversible, and thus, **L1** is the first "on–off"-type purine nucleoside-based fluorescent sensor for Pd^{2+} (Figure 6).

Moreover, this hypothesis was supported by HRMS experiments. The appearance of a clear peak at *m*/*z* = 837.1113 was assigned to [**L1** + Pd^{2+} + Cl^-]$^+$ (Figure 7, a). On the basis of the overall consideration of all the various evidence, a clear binding mode of Pd^{2+} with **L1** was proposed as shown in Figure 7 (b).

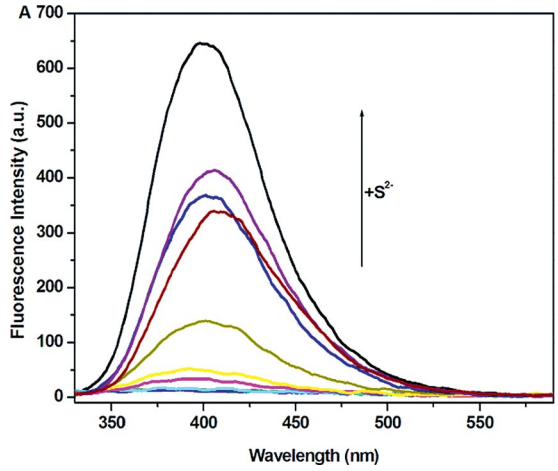

Figure 5. Fluorescence spectral changes of **L1**–Pd^{2+} mixed solution (6 μM for **L1**, [Pd^{2+}]/[**L1**] = 6) upon increasing the concentration of S^{2-} in aqueous buffer. Excitation wavelength is 310 nm.

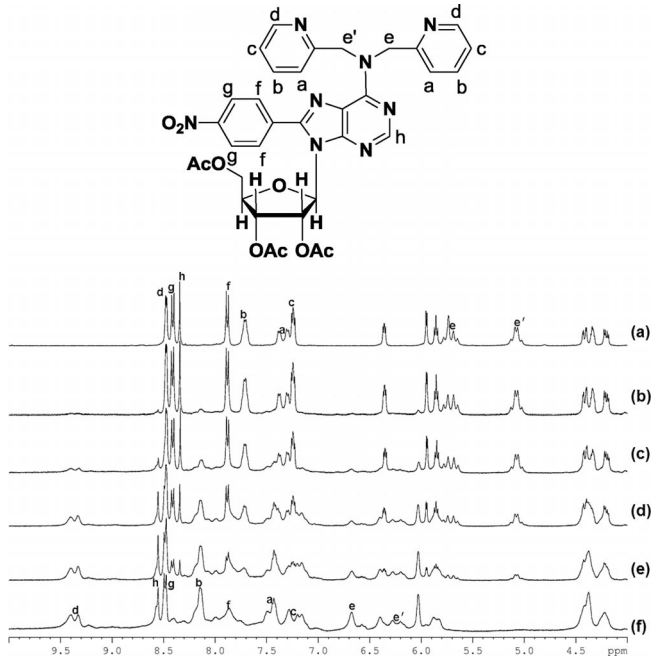

Figure 6. Partial ^{1}H NMR (400 MHz) spectra of **L1** in [D_6]DMSO. (a) [Pd^{2+}]/[**L1**] = 0 equiv., (b) [Pd^{2+}]/[**L1**] = 0.3 equiv., (c) [Pd^{2+}]/[**L1**] = 0.5 equiv., (d) [Pd^{2+}]/[**L1**] = 0.7 equiv., (e) [Pd^{2+}]/[**L1**] = 1.0 equiv., and (f) [Pd^{2+}]/[**L1**] = 2.0 equiv.

Conclusions

In conclusion, push–pull-type purine nucleoside-based fluorescent sensor **L1** possessing a DPA moiety as the binding unit was designed and synthesized. Sensor **L1** displays specific selectivity and sensitivity toward Pd^{2+} with a low detection limit in aqueous buffer, and it therefore has potential application in vivo and industrial analyses. To the best of our knowledge, this is the first "on–off"-type purine

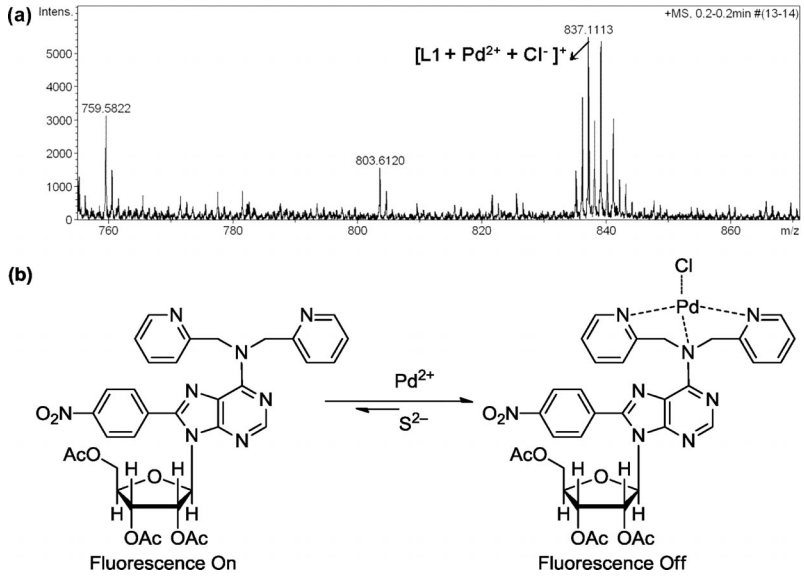

Figure 7. (a) HRMS spectra of **L1** in the presence of $PdCl_2$ (2.0 equiv.) in CH_3CN. (b) Proposed interaction model between **L1** and Pd^{2+}.

nucleoside-based fluorometric sensor for Pd^{2+} that exhibits remarkable fluorescent quenching. Further application of fluorescent sensor **L1** is currently underway.

Experimental Section

Stock solutions (1.0 mM) of each metal salt, **L1**, **L2**, and **L3** (0.1 mM) in CH_2Cl_2 were prepared. Test solutions were prepared by placing 0.2–1.0 mL of the probe's stock solution into a test tube, and then CH_2Cl_2 was removed. Subsequently, the test sample was dissolved by adding the appropriate amount of DMSO solution, and an appropriate aliquot of each metal stock solution was added. Then, the solution was diluted to 5.0 mL with 50.0 mM aqueous Tris-HCl buffer (pH 7.3) to give the final concentration. After complete mixing, UV/Vis absorption and fluorescent emission measurements were performed by using spectrophotometers with a 1.0 cm standard quartz cell.

Supporting Information (see footnote on the first page of this article): Synthesis, characterization data, and copies of the ^1H NMR and ^{13}C NMR spectra.

Acknowledgments

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[13] Because the absorption spectra of **L1** are similar to the absorption spectra of Pd^{2+}, no significant changes in the absorption spectra were observed, so that the Job's plot was not created.

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