Supporting Information

A Depropargylation-Triggered Spontaneous Cyclization Based Fluorescent “Turn-On” Chemodosimeter for the Detection of Palladium Ions and Its Application in Live-Cell Imaging

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Materials and methods

All the solvents were of analytic grade. NMR experiments were carried out on a Bruker AV-400 NMR spectrometer with chemical shifts reported in ppm (in CDCl₃ or TMS as an internal standard). Mass spectra were measured on an Agilent 1290 LC-MS spectrometer. All pH measurements were made with a Sartorius basic pH-Meter PB-10. Fluorescence spectra were determined on a PerkinElmer LS55 Fluorescence spectrophotometer. Absorption spectra were collected on a Shimadzu UV 2501(PC)S UV-Visible spectrophotometer. All the cation solutions were prepared from AlCl₃, CdCl₂, CrCl₃, CuCl₂, FeCl₂, FeCl₃, CsCl, HgCl₂, MgCl₂, ZnCl₂, Pb(OAc)₂, and PdCl₂ in distilled water, with a concentration of 1 mM, respectively. The excitation and emission widths for SPd1 were all 3/5.
Synthesis and characterization

Scheme S1 Synthesis of SPd1: (a) 3-bromopropyne/K₂CO₃, acetone, reflux, 12 h, 93%; (b) Et₃N, EtOH, rt, 12 h, 65%; (c) PdCl₂, THF-H₂O (1:1), rt, 3 h, 72%.

4-(diethylamino)-2-(prop-2-yn-1-lyloxy)benzaldehyde (2): 4-(diethylamino)-2-hydroxybenzaldehyde (0.50 g, 2.6 mmol) and potassium carbonate (1.07 g, 7.8 mmol) were dissolved in acetone (8 mL) under nitrogen atmosphere, then 3-bromoprop-1-yne (0.22 mL, 2.6 mmol) was added and the solution was refluxed for 12 h until all starting material got consumed which was monitored by TLC analysis. Water (50 mL) was then added to the solution, and the reaction mixture was extracted with DCM (3 × 20 mL). The extract was washed with brine (60 mL), dried over sodium sulfate and then concentrated under vacuum. The product was purified by flash chromatography using petroleum ether/ethyl acetate (5:1, v/v) as eluant to give 2 (0.56 g, 93%) as a pale yellow gum. ¹H NMR (400 MHz, Chloroform-d) δ 10.10 (s, 1H), 7.69 (d, J = 9.0 Hz, 1H), 6.30 (dd, J = 9.0, 2.2 Hz, 1H), 6.19 (d, J = 2.2 Hz, 1H), 4.77 (d, J = 2.4 Hz, 2H), 3.40 (q, J = 7.1 Hz, 4H), 1.20 (t, J = 7.2 Hz, 6H).
2-(benzo[d]thiazol-2-yl)acetonitrile was synthesized according to the literature.\textsuperscript{1} \textsuperscript{1}H NMR (400 MHz, Chloroform-\textit{d}) \( \delta \) 8.02 (d, \( J = 8.2 \) Hz, 1H), 7.86 (dd, \( J = 8.2, 1.3 \) Hz, 1H), 7.56-7.46 (m, 1H), 7.47-7.37 (m, 1H), 4.22 (s, 2H).

\textbf{3(Spd1)}

2-(benzo[d]thiazol-2-yl)-3-(4-(diethylamino)-2-(prop-2-yn-1-ol)phenyl)acrylonitrile (3, Spd1): 2-(benzo[d]thiazol-2-yl)acetonitrile (174 mg, 1.0 mmol) and 2 (231 mg, 1.0 mmol) were dissolved in ethanol (5 mL) under nitrogen atmosphere, then triethylamine (0.14 mL, 1.0 mmol) was added and the solution was stirred at room temperature for 12 h until all starting material got consumed which was monitored by TLC analysis. The precipitate was filtered and washed with cold ethanol to give 3 (250 mg, 65\%) as a red solid.

\( R_f = 0.45 \) (DCM);
M.p. = 151-152 °C;
\textsuperscript{1}H NMR (400 MHz, Chloroform-\textit{d}) \( \delta \) 8.52 (s, 1H), 8.44 (d, \( J = 9.1 \) Hz, 1H), 8.02 (d, \( J = 8.2 \) Hz, 1H), 7.84 (d, \( J = 8.0 \) Hz, 1H), 7.50-7.43 (m, 1H), 7.34 (t, \( J = 7.6 \) Hz, 1H), 6.41 (dd, \( J = 9.2, 2.3 \) Hz, 1H), 6.30 (d, \( J = 2.3 \) Hz, 1H), 4.84 (d, \( J = 2.3 \) Hz, 2H), 3.45 (q, \( J = 7.2 \) Hz, 4H), 1.25 (t, \( J = 7.1 \) Hz, 6H).

\textsuperscript{13}C NMR (100 MHz, Chloroform-\textit{d}) \( \delta \) 165.64, 159.20, 153.86, 152.35, 140.78, 134.42, 130.50, 126.30, 124.82, 122.78, 121.25, 118.60, 109.96, 105.63, 94.63, 78.14, 56.13, 44.97, 12.70.
HR-MS (TOF-ESI): Calcd. for ([M])\textsuperscript{+}, 388.1484; Found, 388.1480.
3-(benzo[d]thiazol-2-yl)-N, N-diethyl-2-imino-2H-chromen-7-amine (4): 3 (20 mg, 0.05 mmol) and PdCl₂ (40 mg, 0.23 mmol) were dissolved in THF (25 mL, containing 50% H₂O) and the solution was stirred at room temperature for 3 h. The solvent was pumped off and then water (10 mL) was added. The mixture was then extracted with DCM (3 × 5 mL). The extract was washed with brine (15 mL), dried over sodium sulfate and then concentrated under vacuum. The product was purified by flash chromatography using DCM/ethyl acetate (5:1, v/v) as eluant to give 4 (13 mg, 72%) as a red solid.¹ ¹H NMR (400 MHz, Chloroform-d) δ 8.40 (brs, 1H), 8.01 (dd, J = 8.3, 3.3 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.45 (td, J = 7.8, 3.0 Hz, 1H), 7.34 (td, J = 7.6, 3.0 Hz, 1H), 7.24 (m, 1H), 6.42 (dd, J = 7.3, 4.3 Hz, 1H), 6.35 (s, 1H), 3.36 (q, J = 6.9 Hz, 4H), 1.18 (t, J = 6.9 Hz, 6H).
Photophysical properties of SPd1

Table S1 Photophysical properties of the probe.

<table>
<thead>
<tr>
<th>entry</th>
<th>$\lambda_{ab}$ (nm)</th>
<th>$\lambda_{em}$ (nm)</th>
<th>$\Phi$</th>
<th>$\varepsilon / M^{-1} \text{cm}^{-1}$</th>
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<tbody>
<tr>
<td>SPd1</td>
<td>474</td>
<td>542</td>
<td>0.004</td>
<td>53918</td>
</tr>
<tr>
<td>SPd1+Pd$^{2+}$</td>
<td>474</td>
<td>542</td>
<td>0.023$^b$</td>
<td>40571</td>
</tr>
</tbody>
</table>

(a) The quantum yield ($\Phi$) of SPd1 and SPd1-Pd$^{2+}$ system were determined according to the literature.$^3$ (b) $\Phi$ was determined in the present of 10.0 equiv. of Pd$^{2+}$.

$$\Phi_{\text{Sample}} = \frac{\Phi_{\text{QS}} \cdot A_{\text{QS}} \cdot F_{\text{Sample}} \cdot \lambda_{\text{ex QS}} \cdot \eta_{\text{Sample}}^2}{A_{\text{Sample}} \cdot F_{\text{QS}} \cdot \lambda_{\text{ex Sample}} \cdot \eta_{\text{QS}}^2}$$

Where $\Phi$ is quantum yield; $A$ is absorbance at the excitation wavelength; $F$ is integrated area under the corrected emission spectra; $\lambda_{ex}$ is the excitation wavelength; $\eta$ is the refractive index of the solution; the Sample and QS refer to the sample and the standard, respectively. We chose Rhodamine 6G in EtOH as standard, which has the quantum yield of 0.95.$^4$
Additional spectroscopic data

**Fig. S1** The ratio of UV-vis absorption of SPd1 (20.0 μM) at 555 and 474 nm as a function of Pd^{2+} concentration (0-200.0 μM) in PBS buffer solution (10 mM, pH 7.4, containing 50% EtOH).
**Fig. S2** Fluorescence response of different solvents on the SPd1 (10.0 μM) alone and the reaction of SPd1 (10.0 μM) with Pd^{2+} (100.0 μM) (λ<sub>ex</sub> = 510 nm).
Fig. S3 Fluorescent intensity of SPd1 (10.0 μM) at 542 nm as a function of Pd\(^{2+}\) concentration (0-150.0 μM) in PBS buffer solution (10 mM, pH 7.4, containing 50% EtOH) (λ\(_{ex}\) = 510 nm).
**Fig. S4** The changes of fluorescent intensity of SPd1 (10.0 μM) at 542 nm as a function of Pd$^{2+}$ concentration (0-70.0 μM) under the same condition as the Pd$^{2+}$ titration.
**Fig. S5** The comparison of fluorescent spectra of probe SPd1, SPd1+Pd$^{2+}$ system, and compound 4 in 10 mM PBS buffer solution, pH 7.4, containing 50% EtOH, $\lambda_{ex} = 510$ nm.
**Fig. S6** Kinetic plot of fluorescent emission intensity at 542 nm of the pseudo-first order reaction of SPd1 (10.0 μM) to Pd^{2+} (100.0 μM), using excitation wavelength at 510 nm. The slope of the plot corresponds to observed reaction rate of $2.4 \times 10^{-2}$ min$^{-1}$. 

<table>
<thead>
<tr>
<th>Equation</th>
<th>$y = a + bx$</th>
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<tbody>
<tr>
<td>Adj. R-Square</td>
<td>0.99784</td>
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<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Standard Error</th>
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<tbody>
<tr>
<td>L Intercept</td>
<td>-0.14448</td>
<td>0.00658</td>
</tr>
<tr>
<td>L Slope</td>
<td>-0.02409</td>
<td>4.2384E-4</td>
</tr>
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</table>
Fig. S7 Fluorescence responses of SPd1 (10.0 μM) with 10.0 equiv. of metal ions in PBS buffer solution (10 mM, pH 7.4, containing 50% EtOH). Metal ions include Na⁺, K⁺, Ag⁺, Co²⁺, Mn²⁺, Al³⁺, Cd²⁺, Cr³⁺, Cs⁺, Cu²⁺, Fe²⁺, Fe³⁺, Hg²⁺, Mg²⁺, Zn²⁺, Pb²⁺, and Pd²⁺, (λₑₓ = 510 nm).
**Fig. S8** Fluorescence responses of SPd1 (10.0 μM) in the presence of 10.0 equiv. of metal ions (Na+, K+, Ag+, Co2+, Mn2+, Al3+, Cd2+, Cr3+, Cs+, Cu2+, Fe2+, Fe3+, Hg2+, Mg2+, Zn2+, Pb2+, and Pd2+) in PBS buffer solution (10 mM, pH 7.4, containing 50% EtOH), followed by 10.0 equiv. of Pd2+ (λex = 510 nm).
Fig. S9 Effect of the pH on the fluorescence emission of SPd1 (10.0 μM) alone and SPd1 (10.0 μM) reacted with Pd^{2+} (100.0 μM) (λ\text{ex} = 510 nm).
**Fig. S10** The $^1$H NMR spectra of SPd1, SPd1-Pd$^{2+}$ (with 1 equiv of Pd$^{2+}$, after 30 min incubation) solution, and compound 4 (in CD$_3$COCD$_3$).
**Fig. S11** Fluorescence responses of \textbf{SPd1} to various Pd (including 1: probe; 2: PdCl$_2$, 3: Pd(CF$_3$COO)$_2$, 4: Pd(OC$_4$H$_4$)$_2$, 5: K$_2$PdCl$_6$, and 6: Pd(PPh$_3$)$_4$). (The addition of 3.0 equiv. of the appropriate Pd to a 10.0 $\mu$M solution of \textbf{SPd1}, in PBS buffer solution, 10 mM, pH 7.4, containing 50% EtOH, $\lambda_{ex} = 510$ nm, slit 3/3).
**Cell lines and imaging experiments**

HeLa cells were cultured in DMEM (Invitrogen, Carlsbad, CA), supplemented with 10% fetal bovine serum in a humidified atmosphere of 5% CO$_2$ at 37 °C. For imaging experiments, exponentially growing cells (at a density of 20000-40000 cells per well, respectively) were seeded in 24-well plate. Cells were cultured at 37 °C in a 5% CO$_2$ atmosphere for 24 h before they were exposed to reagents. After the staining steps as described in figure captions, the images were collected upon excitation using the corresponding filters for DAPI (purple).

**Fig. S12** Cell viability of HeLa cells treated with different concentration of SPd1 for different time periods. No cytotoxic effect was observed for the cells incubated with SPd1 at 10 μM even for 24 h.
The characterization data of SPd1

$^{1}H$ NMR of 2

$^{1}H$ NMR of 2-(benzo[d]thiazol-2-yl)acetonitrile

$^{1}H$ NMR of 2-(benzo[d]thiazol-2-yl)acetonitrile
$^1$H NMR of 3 (SPd1)

$^{13}$C NMR of 3 (SPd1)
$^1$H NMR of 4
References