

Fluorescent Phosphane Selenide As Efficient Mercury Chemodosimeter

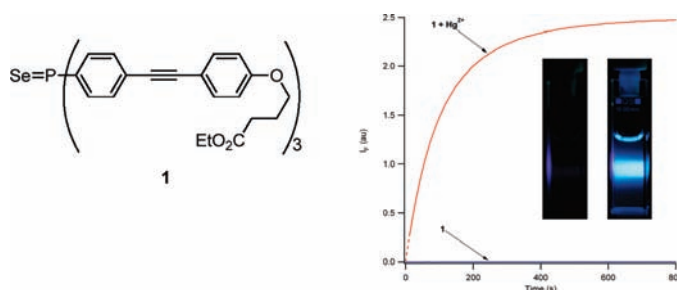
Issa Samb,[†] Jérémy Bell,[‡] Patrick Y. Toullec,[†] Véronique Michelet,^{*,†} and Isabelle Leray^{*,‡}

E.N.S.C.P., Chimie ParisTech, UMR 7223, Laboratoire Charles Friedel 11 rue P. et M. Curie, 75231 Paris Cedex 05, France, and PPSM, ENS Cachan, CNRS, 61, avenue du Président Wilson 94230 Cachan, France

veronique-michelet@chimie-paristech.fr; icmleray@ppsm.ens-cachan.fr

Received January 10, 2011

ABSTRACT



The synthesis and photophysical properties of a novel fluorescent sensor are described. The phosphorus–selenium moiety allowed a selective mercury salt complexation, followed by the formation of phosphane oxide, which leads to a turn-on of the fluorescence. The sensibility and selectivity toward mercury cations were evaluated (0.18 ppb) and found to be in complete adequation with the targeted level of the World Health Organization, which makes the dye an efficient dosimeter for mercury cations.

Heavy metal ions such as mercury represent highly toxic pollutants to the environment and are extremely dangerous for human health.¹ A wide variety of symptoms including digestive, cardiac, kidney, and especially neurological diseases result from a series of biological effects.^{1,2} Thus, the level of this detrimental ion is the object of several official norms; the World Health Organization established in 2004 a guideline for drinking water quality which included a mercury maximal value of $1 \mu\text{g} \cdot \text{L}^{-1}$.³ Whereas a wide set of analytical methods including inductively coupled plasma spectroscopy, atomic absorption, atomic emission, and electrochemical detection have been

developed, the development of new, inexpensive, and real-time monitoring methods for the detection of Hg^{2+} still instigates interest. In this context, optical methods based on chromogenic and fluorogenic molecular chemosensors have attracted ever increasing attention.⁴ The chalcogenophilicity of mercury⁵ has been extensively exploited by

(4) (a) Valeur, B.; Leray, I. *Coord. Chem. Rev.* **2000**, *205*, 3–40. (b) Nolan, E. M.; Lippard, S. J. *Chem. Rev.* **2008**, *108*, 3443–3480. (c) deSilva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515–1566. (d) Nolan, E. M.; Lippard, S. J. *Chem. Rev.* **2008**, *108*, 3443–3480. (e) Leray, I.; Valeur, B. *Eur. J. Inorg. Chem.* **2009**, 3525–3535.

(5) Melnik, J. G.; Yurkovich, K.; Parkin, G. *J. Am. Chem. Soc.* **2010**, *132*, 647–655.

(6) For selected examples of fluorescent chemodosensors exploiting the thiophilicity of mercury, see: (a) J Ros-Lis, J. V.; Marcos, M. D.; Martinez-Manez, R.; Rurack, K.; Soto, J. *Angew. Chem.* **2005**, *44*, 4405–4407. (b) Yang, Y.-K.; Yook, K.-J.; Tae, J. *Am. Chem. Soc.* **2005**, *127*, 16760–16761. (c) Liu, B.; Tian, H. *Chem. Commun.* **2005**, 3156–3158. (d) Song, K. C.; Kim, J. S.; Park, S. M.; Chung, K. C.; Ahn, S.; Chang, S. K. *Org. Lett.* **2006**, *8*, 3413–3416. (e) Shi, W.; Ma, H. M. *Chem. Commun.* **2008**, 1856–1858. (f) Lee, M. H.; Lee, S. W.; Kim, S. H.; Kang, C.; Kim, J. S. *Org. Lett.* **2009**, *11*, 2101–2104. (g) Tian, M. Q.; Ihmels, H. *Chem. Commun.* **2009**, 3175–3177. (h) Yoon, S.; Albers, A. E.; Wong, A. P.; Chang, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 16030–16031. Lin, W. Y.; Cao, X. W.; Ding, Y. D.; Yuan, L.; Long, L. L. *Chem. Commun.* **2010**, *46*, 3529–3531.

[†] E.N.S.C.P., Chimie ParisTech.

[‡] PPSM, ENS Cachan.

(1) (a) Hutchinson, T. C.; Meena, K. M. In *Lead, Mercury, Cadmium and Arsenic in the Environment*; John Wiley: New York, 1987. (b) Scoullos, G. H.; Vonkeman, M. J.; Thornton, L.; Makuch, Z. In *Mercury, Cadmium, Lead: Handbook for Sustainable Heavy Metals Policy and Regulation (Environment and Policy)*, V. 31; Kluwer Academic: Norwell, MA, 2001. (c) Koester, C. J.; Moulik, A. *Anal. Chem.* **2005**, *77*, 3737–3754. (d) Richardson, S. D.; Temes, T. A. *Anal. Chem.* **2005**, *77*, 3807–3838.

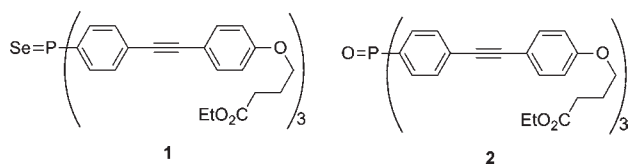
(2) (a) Clarkson, T. W.; Magos, L.; Myers, G. J. *N. Engl. J. Med.* **2003**, *349*, 1731–1737. (b) Carvalho, C. M. L.; Chew, E.-H.; Hashemy, S. I.; Lu, J.; Holmgren, A. *J. Biol. Chem.* **2008**, *283*, 11913.

(3) *Guidelines for drinking-water quality*, 3rd ed.; World Health Organization: Geneva, 2004; p 188.

synthetic chemists to design “OFF–ON” fluorescent chemodosimeters.^{6,7} Considering the stability of HgSe and some naturally occurring detoxification systems based on selenium,⁸ we hypothesized that selenide phosphane would be a suitable template for the capture of mercury cations. In line with our recent investigations regarding the use of phosphane oxides and phosphane sulfides bearing polyphenylethynyl fluorophores as highly selective and sensitive sensors,⁹ we therefore engaged in a study of phosphane selenide as potential candidates for the detection of mercury ions. In this paper, we report the synthesis, the spectroscopic properties, and a thorough investigation of cation-induced photophysical changes of a new fluorescent dosimeter.

In order to make a comparison between phosphane oxide and phosphane selenide push–pull fluorescent sensors, we engaged in the synthesis of the polar phosphorus derivatives **1** and **2**. The corresponding phosphane oxide derivative **2** was used as a comparison for the spectroscopic measurements (Scheme 1).

Scheme 1. Fluorescent Phosphane Selenide Chemodosimeter **1** and Phosphane Oxide **2**



The preparation of **1–2** was realized according to previous methodologies.⁹ Reaction of the Grignard derivative of 4-bromotrimethylsilylphenylacetylene **3** with PCl_3 afforded the corresponding triarylphosphane (Scheme 2). Treatment with an equimolar amount of selenium gave the corresponding phosphine selenide **4** in 44% yield over two steps. Desilylation was accomplished using K_2CO_3 in a $\text{CH}_3\text{OH}/\text{CH}_2\text{Cl}_2$ (2:1) solvent mixture to give phosphane

(7) For two recent examples of fluorescent chemodosimeters exploiting the selenophilicity of mercury, see: (a) Tang, B.; Ding, B.; Xu, K.; Tong, L. *Chem.—Eur. J.* **2009**, *15*, 3147–3151. (b) Chen, X.; Baek, K.-H.; Kim, Y.; Kim, S.-J.; Shin, I.; Yoon, J. *Tetrahedron* **2010**, *66*, 4016–4021.

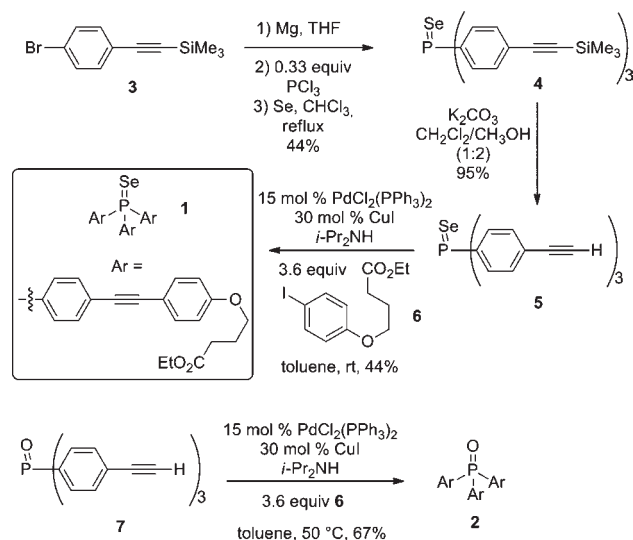
(8) (a) Miksa, I. R.; Buckley, C. L.; Carpenter, N. P.; Poppenga, R. H. *J. Vet. Diagn. Invest.* **2005**, *17*, 331–340. (b) Arai, T.; Ikemoto, T.; Hokura, A.; Terada, Y.; Kunito, T.; Tanabe, S.; Nakai, I. *Environ. Sci. Technol.* **2004**, *38*, 6468–6474.

(9) (a) Ha-Thi, M. H.; Souchon, V.; Hamdi, A.; Metivier, R.; Alain, V.; Nakatani, K.; Lacroix, P. G.; Genet, J. P.; Michelet, V.; Leray, I. *Chem.—Eur. J.* **2006**, *12*, 9056–9065. (b) Ha-Thi, M. H.; Penhoat, M.; Michelet, V.; Leray, I. *Org. Lett.* **2007**, *9*, 1133–1136. (c) Ha-Thi, M. H.; Souchon, V.; Penhoat, M.; Miomandre, F.; Genet, J. P.; Leray, I.; Michelet, V. *Lett. Org. Chem.* **2007**, *4*, 185–188. (d) Ha-Thi, M. H.; Penhoat, M.; Drouin, D.; Blanchard-Desce, M.; Michelet, V.; Leray, I. *Chem.—Eur. J.* **2008**, *14*, 5941–5950. (e) Ha-Thi, M. H.; Penhoat, M.; Michelet, V.; Leray, I. *Org. Biomol. Chem.* **2009**, *7*, 1665–1673.

(10) (a) Chinchilla, R.; Najera, C. *Chem. Rev.* **2007**, *107*, 874–922. (b) Doucet, H.; Hierso, J.-C. *Angew. Chem., Int. Ed.* **2007**, *46*, 834–871.

(11) Hajduk, P. J.; Sheppard, G.; Nettesheim, D. G.; Olejniczak, E. T.; Shuker, S. B.; Meadows, R. P.; Steinman, D. H.; Carrera, G. M., Jr.; Marcotte, P. A.; Severin, J.; Walter, K.; Smith, H.; Gubbins, E.; Simmer, R.; Holzman, T. F.; Morgan, D. W.; Davidsen, S. K.; Summers, J. B.; Fesik, S. W. *J. Am. Chem. Soc.* **1997**, *119*, 5818–5827.

Scheme 2. Synthesis of Phosphane Selenide **1** and Oxide **2**



selenide **5** in 95% yield. Sonogashira coupling¹⁰ between **5** and the aryl iodide **6**¹¹ was performed in the presence of 15 mol % of $\text{PdCl}_2(\text{PPh}_3)_2$ and 30 mol % CuI in the presence of diisopropylamine in toluene at room temperature and led to the phosphane selenide **1** in 44% isolated yield. The phosphane oxide analogue **2** was prepared starting from known compound **7**⁹ according to the same cross-coupling methodology and was isolated in 67% yield.

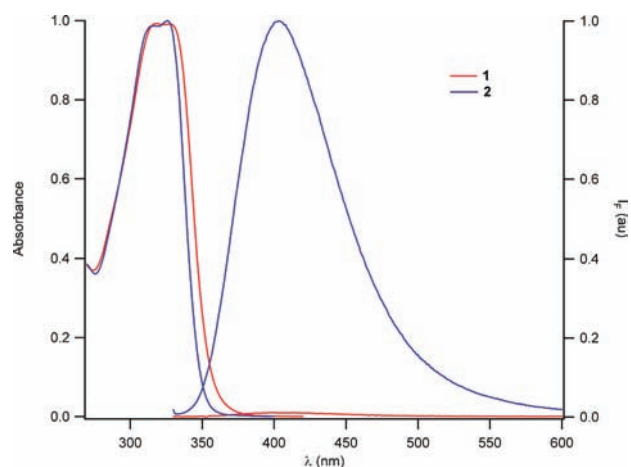


Figure 1. Absorption spectra and corrected normalized emission spectra of phosphane selenide **1** and phosphane oxide **2** in $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ 80:20 at $\text{pH} = 7$ (MES-NaOH buffer, 50 mM).

The absorption and fluorescence spectra of the phosphane selenide **1** and oxide **2** ligands are shown in Figure 1, and their photophysical characteristics are summarized in Table 1. The fluorophore **1** shows an intense absorption band in the near-UV region, and the absorption maximum of **1** is blue-shifted by comparison of the phosphane oxide

Table 1. Photophysical Properties of Phosphane Selenide **1** and Oxide **2** Derivatives in CH₃CN/H₂O 80:20^a

product	$\lambda_{\text{abs}}/\text{nm}$	$\epsilon/10^4 \text{ M}^{-1} \text{ cm}^{-1}$	$\lambda_{\text{em}}/\text{nm}$	Φ_{F}^b
1	319	13.5	405	2×10^{-3}
2	326	8.0	406	0.20

^a Maxima of the absorption λ_{abs} (nm) and of steady-state emission λ_{em} (nm), molar absorption coefficient ϵ ($10^4 \text{ M}^{-1} \text{ cm}^{-1}$), and fluorescence quantum yield Φ_{F} . ^b With 10% error.

derivative **2** which means that the electron-withdrawing character of the phosphane is reduced in the case of **1**. A significant difference of the fluorescence quantum yield between **1** and **2** was observed, 0.002 for **1** versus 0.2 for **2**.

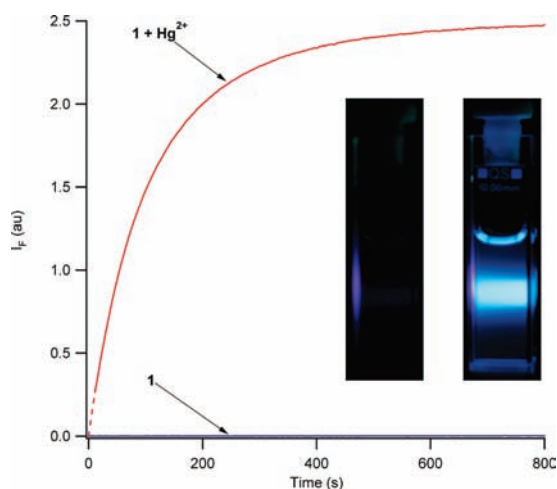
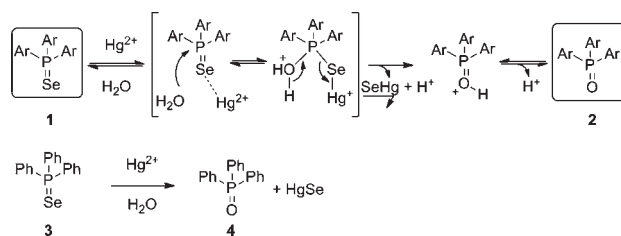


Figure 2. Time evolution of the fluorescence of **1** alone and after addition of 1 equiv of mercury under the same conditions ($[\text{I}] = 0.74 \mu\text{M}$ CH₃CN/H₂O 80:20, 40 °C, pH = 7, $\lambda_{\text{exc}} = 330 \text{ nm}$).

Upon addition of mercury salt to a solution of **1** in CH₃CN/H₂O 80:20 at pH = 7 (MES-NaOH,¹² 50 mM) a 100-fold enhancement of the fluorescence is observed as displayed in Figure 2. The inset of Figure 2 illustrates the increase of the fluorescence upon addition of Hg²⁺. Such an effect can be explained by a mercury-induced irreversible deselenization reaction (Scheme 3), which leads to the formation of the fluorescent phosphane oxide derivative ($\Phi_{\text{F}} = 0.2$). The proposed mechanism is in full agreement with various spectroscopic and analytical data such as ³¹P NMR spectra and HRMS data. To further probe the chemical transformation of phosphane selenide to oxide, we prepared the known triphenylphosphane selenide **3**¹³ and submitted this derivative to mercury salt. As anticipated we easily detected by ³¹P NMR spectroscopy the formation of phosphane oxide **4**. The reaction of phosphane selenide **3** in the presence of 1.2 equiv of mercury

Scheme 3. Deselenation Reaction Proposed Mechanism of **1** with Hg²⁺



perchlorate in an acetonitrile/water mixture at pH = 7 afforded the corresponding oxide in 4 h in 99% yield (Scheme 3).

After optimization of the conditions, the evolution of the fluorescence upon addition of increasing quantities of Hg²⁺ is displayed in Figure 3.

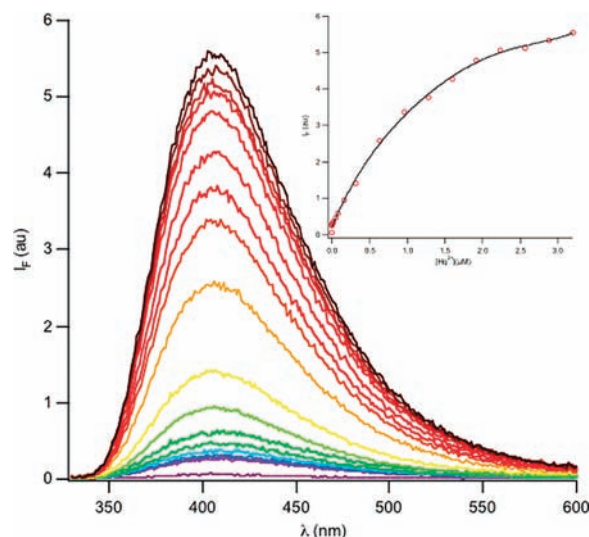


Figure 3. Corrected emission spectra of **1** (3.2 μM) in the presence of increasing concentration of Hg²⁺ in CH₃CN/H₂O 80:20 at pH = 7 at 40 °C after 20 min of equilibrium time. $\lambda_{\text{exc}} = 330 \text{ nm}$. Inset: Calibration curve as a function of mercury concentration.

The variation of the fluorescence intensity versus the mercury complexation is shown in the inset of figure 3. A linear response of the fluorescence intensity as a function of mercury concentration was observed from 0 to 0.8 μM . The detection limit calculated as three times the standard deviation of the background/noise ratio was found to be 0.9 nM (0.18 ppb) which to the best of our knowledge corresponds with one of the lowest reported sensitive systems for the detection of mercury.^{4d,14}

(12) MES: 2-(*N*-morpholino)ethanesulfonic acid.

(13) Gulyas, H.; Bacsik, Z.; Szollosy, A.; Bakos, J. *Adv. Synth. Catal.* **2006**, *348*, 1306–1310 and references cited therein.

(14) (a) Ye, B. C.; Yin, B. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 8386–8389. (b) Wegner, S. V.; Okesli, A.; Chen, P.; He, C. *J. Am. Chem. Soc.* **2007**, *129*, 3474–3475. (c) Nolan, E. M.; Racine, M. E.; Lippard, S. J. *Inorg. Chem.* **2006**, *45*, 2742–2749.

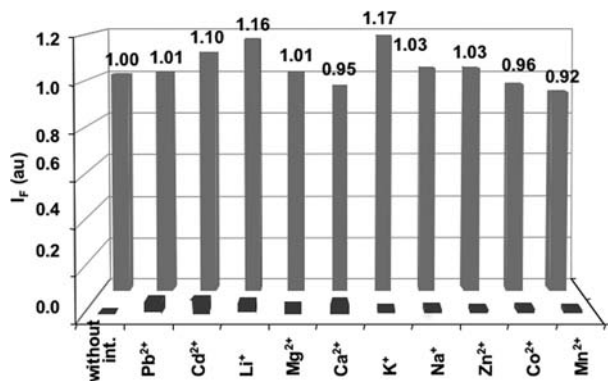


Figure 4. (Dark gray) Fluorescence intensity at 406 nm of **1** (1 μ M) toward interfering metal ions (10^{-3} mol·L⁻¹ for Pb²⁺, Cd²⁺, Li⁺, Mg²⁺, Ca²⁺, Zn²⁺, Co²⁺, Mn²⁺; 10^{-4} mol·L⁻¹ for Na⁺, K⁺). (Light gray) Response toward interfering ions (same concentration as that for part a) plus mercury (1 μ M) ($\lambda_{\text{exc}} = 330$ nm). Spectra were acquired in CH₃CN/H₂O 80:20 at pH = 7 at 40 °C in MES buffer.

Having in hand a highly sensitive derivative, we examined the selectivity of **1** for Hg²⁺ with respect to other cations such as K⁺, Na⁺, Ca²⁺, Li⁺, Mg²⁺, Zn²⁺, Pb²⁺, and Cd²⁺. As shown in Figure 4, no significant changes of the fluorescence is observed upon addition of interfering

cations at much higher concentrations. The selectivity diagram displayed in Figure 4 shows that the addition of interfering cation does not alter the fluorescence response of **1**.

In conclusion, we have synthesized and characterized a simple and efficient mercury dosimeter. The phosphorus-selenide moiety incorporated in a push-pull chromophore was found to be a selective complexation template for mercury salt. We showed that the complexation was accompanied by the chemical transformation of phosphane selenide to phosphane oxide, which leads to a turn-on of the fluorescence. The sensibility and selectivity toward mercury were evaluated (0.18 ppb) and found to be in complete adequation with the targeted level of the World Health Organization.

Acknowledgment. This work was supported by the National Research Agency program CP2D "FLUOSEN-SIL". I.S. and J.B. are grateful to the National Research Agency for their grants (2009-2011) and (2009-2012), respectively.

Supporting Information Available. Experimental procedure and full analyses of **1** and **2**. This material is available free of charge via the Internet at <http://pubs.acs.org>.