

# Isothiouronium-modified gold nanoparticles capable of colorimetric sensing of oxoanions in aqueous MeOH solution

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**Abstract**—Isothiouronium-modified gold nanoparticles **1** with an average diameter of 5.8 nm were synthesized from bis(5-(*N,N'*-dimethyl-*S*-isothiuronio)pentyl) disulfide **2**. The surface plasmon band at 524 nm in 10% (v/v) H<sub>2</sub>O–MeOH showed a selective red shift upon adding anions, making this potentially useful as a new anion sensor material.

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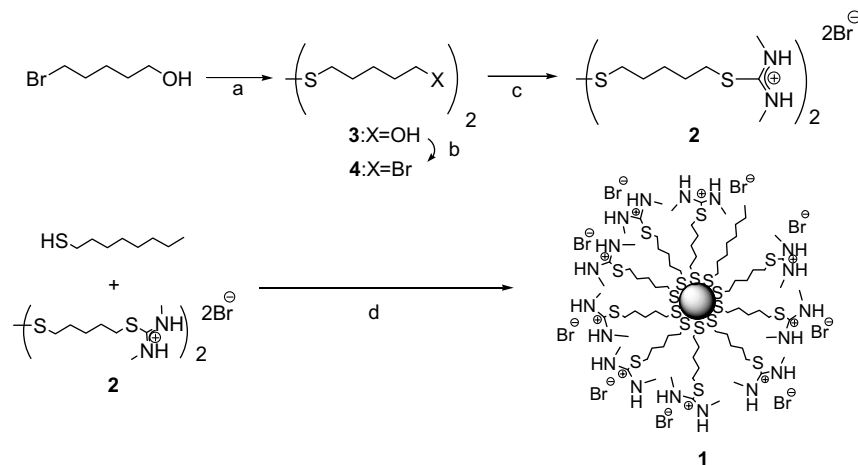
The development of molecular sensors for detecting chemically and biologically important species of anions has become a major research project in supramolecular chemistry.<sup>1</sup> It is still a challenge to find and study materials capable of recognizing and sensing anions in aqueous media, since water molecules surrounding the anions interfere with the desired host–guest interaction, resulting in low sensitivity to anions. Thus systems able to overcome this problem are needed.<sup>2</sup> In our laboratory, we have concentrated on the isothiuronium group as a suitable anion binding unit, because it has a high NH acidity for action as an ionic hydrogen bonding donor.<sup>3</sup> Accordingly, we fabricated an isothiuronium-organized monolayer to interact with anions at an air–water interface and proposed that an isothiuronium-assembled structure would be a feasible detection of oxoanions in aqueous solution.<sup>3</sup> Based on this strategy, we decided to synthesize gold nanoparticles stabilized with isothiuronium units, **1**, since nanosize controlled metal nanoparticles not only offer functional monolayer-protected surfaces but also have unique optical properties due to the surface plasmon band.<sup>4</sup> Indeed, Mirkin–Letsinger<sup>5</sup> and Alivisatos–Schultz<sup>6</sup> groups have pioneered functionalization of gold nanoparticles with oligonucleotides. DNA-driven aggregation of the nanoparticles led to develop a new colorimetric technique based on the sensitivity of surface plasmon band. In this

way, the extremely high extinction coefficient in the visible region and the strongly distance-dependent optical properties allow the nanoparticles to be utilized as excellent color reporting groups.<sup>7</sup> An isothiuronium-assembled gold surface should therefore interact with anions efficiently, even in aqueous media, so as to induce an aggregation to signal the detection of anions through color change. Our motivation in this study is due to the fact that the exploration of nanoparticles capable of sensing anions by means of the surface plasmon band in aqueous media is still in its infancy;<sup>8</sup> nevertheless nanoparticles can serve as a versatile scaffold for molecular recognition events because of the easy introduction of chemical functionality.<sup>9</sup> As described below in detail, **1** showed a selective colorimetric response to anions in 10% (v/v) H<sub>2</sub>O–MeOH solution. In particular, dicarboxylate-induced color change is of analytical importance, because dicarboxylates are critical components of numerous metabolic processes, such as the citric acid cycles.<sup>10</sup>

In developing an isothiuronium-modified surface installed on an Au cluster, a disulfide bearing isothiuronium moiety **2** at terminal position was synthesized as shown in Scheme 1. The starting materials, 5-bromopentanol, was converted to **3** through the reaction with thiourea and then oxidation under a basic condition in 63% yield. It was followed by the reaction with CBr<sub>4</sub> in the presence of PPh<sub>3</sub> to give the corresponding dibromo derivative **4** in 47% yield. And then **4** was allowed to react with *N,N'*-dimethylthiourea to give **2**<sup>11</sup> in 44% yield. The target **1** could be prepared using

**Keywords:** Isothiuronium; Anion sensor; Nanoparticle.

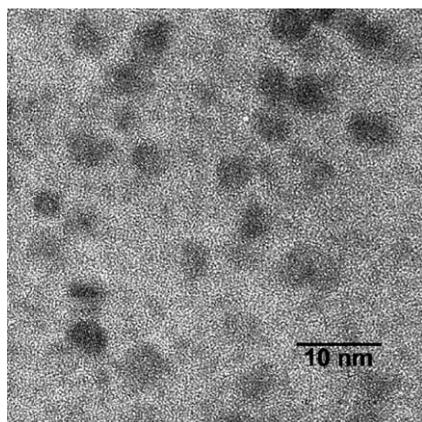
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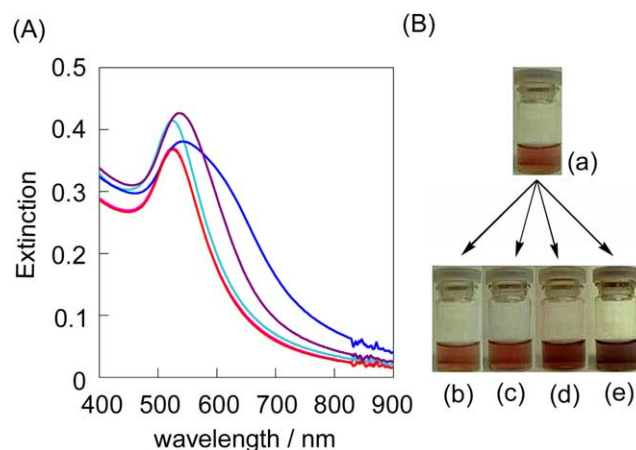
**Scheme 1.** Reagents and conditions: (a)  $\text{S}=\text{C}(\text{NH}_2)_2$ , dry EtOH, and then excess NaOH; (b)  $\text{CBr}_4$ ,  $\text{PPh}_3$ , dry THF; (c)  $\text{S}=\text{C}(\text{NHMe})_2$ , dry EtOH; (d)  $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$  in the presence of TOAB (tetra-*n*-octylammonium bromide), and then  $\text{NaBH}_4$ .

a slight modification of the procedure of Kamat et al.<sup>12</sup> (synthetic detail, see [Supplementary information](#)). A FT-IR measurement of **1** showed the vibration bands of isothiuronium unit (3400, 1612, 1522, and 1039  $\text{cm}^{-1}$ ), suggesting binding of the units to the gold surface. [Figure 1](#) shows the Transmission Electron Microscopic (TEM) image. The particles appear to be spherical and the average radius is  $2.9 \pm 0.51$  nm. Combined with the data from elemental analyses (C, 13.56; H, 3.06; N, 3.92; S, 9.03; Au, 60.41), this gives the average ratio of Au atoms to thiol ligands as 2.16; thus, the number of molecules attached to one Au particle is approximately 2800 ([isothiuronium unit]/[1-octanethiol] = 70). The MeOH solution of **1** is red, showing the surface plasmon band at 526 nm, and the molecular extinction coefficient is  $1.0 \times 10^7 \text{ M}^{-1} \text{ cm}^{-1}$ . In this way, a highly isothiuronium-organized surface was successfully fabricated on a gold cluster suitable for the recognition of anions.

We investigated whether the resulting **1** would serve as an anion sensor material; [Figure 2](#) shows the colorimetric response of **1** ( $3.4 \times 10^{-8} \text{ M}$ ) upon adding 600  $\mu\text{M}$  ([anion]/[isothiuronium unit on **1**] = 6.45) of putative anions ( $\text{Cl}^-$ ,  $\text{AcO}^-$ ,  $\text{HPO}_4^{2-}$ , and malonate) in 10% (v/v)

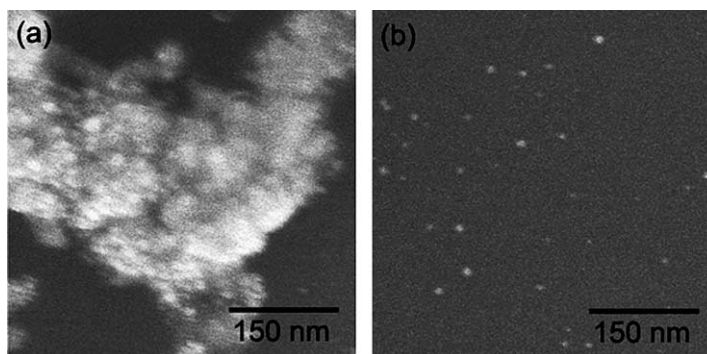


**Figure 1.** TEM image of **1**. The scale bar corresponds to 10 nm.



**Figure 2.** (A) UV/vis spectra of **1** ( $3.4 \times 10^{-8} \text{ M}$ ) in the presence of 600  $\mu\text{M}$  of anions as sodium salts in 10% (v/v)  $\text{H}_2\text{O}$ –MeOH at 25  $^\circ\text{C}$ : (a) **1** (■); (b) **1** +  $\text{Cl}^-$  (■); (c) **1** +  $\text{AcO}^-$  (■); (d) **1** +  $\text{HPO}_4^{2-}$  (■); (e) **1** + malonate (■). (B) Photographs of the solutions corresponding to (a)–(e).

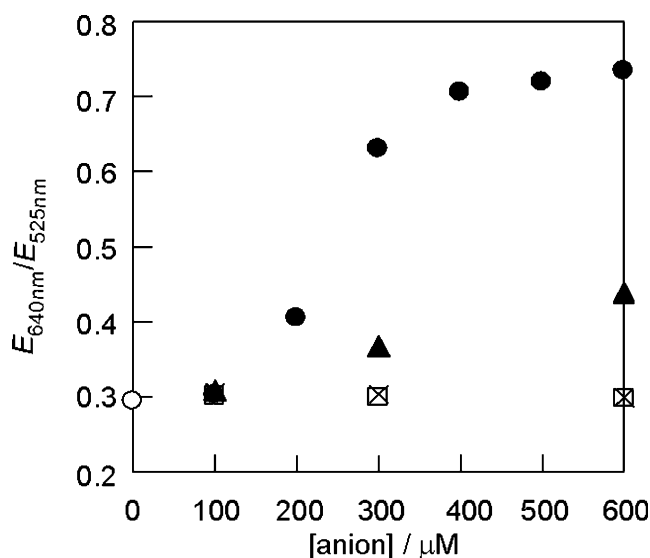
$\text{H}_2\text{O}$ –MeOH. Although there is no change in the UV/vis spectra in the presence of  $\text{Cl}^-$ , the presence of oxo-anion ( $\text{AcO}^-$  or  $\text{HPO}_4^{2-}$ ) induced a change in the plasmon band. In particular, when adding  $\text{HPO}_4^{2-}$ , a red shift of 13 nm was obtained with increasing intensity of extinction, the color of the solution changing from red to red-dish-violet. The red shift might be due to an aggregation with reduced interparticle distance as a result of interaction with  $\text{HPO}_4^{2-}$  at the surface of **1**, stemming from the higher basicity of  $\text{HPO}_4^{2-}$ . The most striking feature arose by upon adding malonate to the solution, which induced a dramatic color change to bluish-violet, generating a wide range of the plasmon band. This color change, detectable by the naked eye, is ascribed to the appearance of a shoulder peak at ca. 640 nm, possibly stemming from a stable aggregation of **1** in which malonate acts as a bridged ligand between the particles since the terminal carboxylate segments can bind to isothiuronium groups at the surface.<sup>13</sup> The Field Emission-Scanning Electron Microscope (FE-SEM) image of the



**Figure 3.** FE-SEM images of (a) **1** aggregated by adding malonate as disodium salt (500  $\mu\text{M}$ ) to the 10% (v/v)  $\text{H}_2\text{O}$ –MeOH solution (b) **1**;  $[\mathbf{1}] = 3.4 \times 10^{-8} \text{ M}$ . The scale bars correspond to 150 nm.

solution after adding malonate (Fig. 3a) clearly indicates a macroscopic aggregate structure, whereas the FE-SEM image of malonate-free **1** indicates well-isolated homogeneous nanoparticles without any aggregation (Fig. 3b). This fact strongly supports the notion that the interparticle distance is reduced sufficiently to cause the red shift of the plasmon band.<sup>14</sup> The colorimetric response occurred almost instantaneously, but the aggregation stage is relatively stable since there was no sedimentation for ca. 1 h after adding the anion. This phenomenon is a valuable property in a sensor.

To estimate the anion selectivity based on colorimetry, we noticed the malonate-induced wide range extinction ranging from 500 to 750 nm, which seems to be sensitive to aggregate formation. Consequently, semi-quantification of anion selectivity came from monitoring of the ratio of extinction at the plasmon peaks at 525 and 640 nm. A higher ratio is associated with aggregated nanoparticles of bluish violet color. Figure 4 summarizes the titration results based on the ratiometric method. Although the sigmoidal curve observed with malonate addition suggests that aggregation had



**Figure 4.** Changes in the extinction ratio (Ext. at 640 nm/Ext. at 525 nm) upon adding an incremental amount of anions as sodium salts into 10% (v/v)  $\text{H}_2\text{O}$ –MeOH solution of **1** ( $3.4 \times 10^{-8} \text{ M}$ ) at 25 °C: (○) **1**; (×)  $\text{Cl}^-$ ; (□)  $\text{AcO}^-$ ; (▲)  $\text{HPO}_4^{2-}$ ; (●) malonate.

scarcely taken place at low concentrations of the anion, a high ratio of the color change was obtained when adding 600  $\mu\text{M}$  of malonate, corresponding to a malonate-to-isothiuronium ratio of 6.5. The value ( $E_{640 \text{ nm}}/E_{525 \text{ nm}} = 0.735$ ) is larger than those with other anions under similar conditions by a factor of 1.7 for  $\text{HPO}_4^{2-}$ , 2.5 for  $\text{AcO}^-$ , and 2.5 for  $\text{Cl}^-$ , respectively. Employed the ratiometric method, we can read-out the recognition of anion species dissolved in aqueous media.

In conclusion, the isothiuronium-assembled surface on **1** allowed for a new nanoparticle-based colorimetric sensor of anions, as a result of selective anion-induced aggregation. Particularly, it is noteworthy that it exhibits real-time sensing for oxoanions in aqueous media. This finding suggests a promising way to design artificial chromogenic systems in anion recognition.

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### Supplementary data

Supplementary data associated with this article can be found, in the online version at [doi:10.1016/j.tetlet.2005.04.074](https://doi.org/10.1016/j.tetlet.2005.04.074).

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