

Reaction-Based Fluorescent Sensing of Au(I)/Au(III) Species: Mechanistic Implications on Vinylgold Intermediates

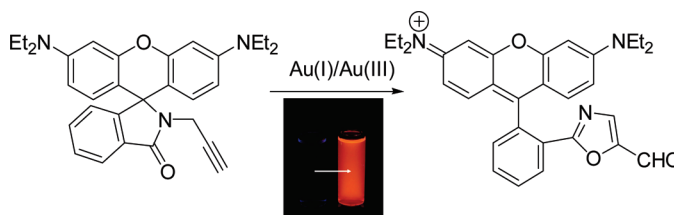
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Received October 19, 2009

ABSTRACT



A rhodamine-derived alkyne shows turn-on fluorescence change only toward Au(I)/Au(III) species among various other metal species examined. A formylloxazole compound is formed as the major product in aqueous media, presumably via a vinylgold intermediate, which casts new mechanistic implications on vinylgold intermediates.

Gold chemistry has experienced a renaissance in the last years because of unique and interesting properties of supported gold nanoparticles¹ and catalytic² and biological activities³ of gold complexes. Investigation of efficient gold-catalyzed reactions is an emerging field of organic chemistry.

Determination of trace levels of gold species can be carried out by spectroscopic (atomic absorption/emission spectroscopy with various atomizers), mass, and electrochemical (anodic stripping voltammetry) analysis methods.⁴ So far, however, little is known about fluorogenic or chromogenic

sensing systems for gold ions, which would provide simpler detection methods with high sensitivity and selectivity.

Catalytically active gold complexes have common oxidation states of +1 and +3. Typical AuCl or AuCl₃ has strong “alkynophilicity” and thus activates alkynes toward nucleophiles such as oxygen, nitrogen, or even carbon-based ones.² The characteristic behaviors of the gold species may be explored for the development of reaction-based fluorogenic and chromogenic probes for them, which can be used for the determination of gold species in certain circumstances.⁵ To this end, we have designed probe **1** for the fluorescent and colorimetric sensing of the gold species. We reasoned that the coordination ability of a Au(I)/Au(III) species to the acetylenic group in probe **1** would trigger a ring opening of the spiro-lactam with a concomitant intramolecular attack by the amide oxygen to the acetylenic group, forming heterocyclic compounds **2a/2b** through a vinylgold intermediate **1a** (Scheme 1). This ring-opening event would lead to “turn-on”

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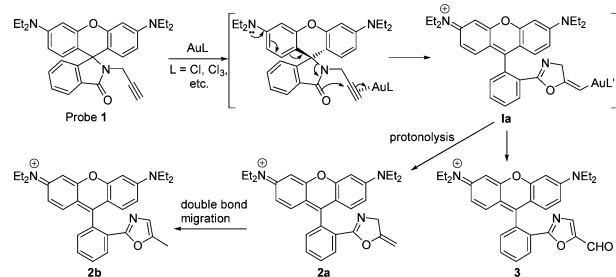
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Scheme 1. Au(I)/Au(III)-Promoted Spirolactam Ring Opening of Probe **1** to Give Fluorescent Compounds **2** and **3**



type fluorescence and color changes, owing to an electron delocalization in the diamino-xanthene moiety of compounds **2** and **3**.

A related but different ring-opening reaction has been used for the development of a fluorogenic and chromogenic sensing system for silver ions by us.⁶ To our surprise, 2-formyloxazole **3** also forms in addition to **2** depending on reaction media. Described here are fluorescent titrations of probe **1** toward the gold species and characterization of the reaction products.

The rhodamine derivative **1** is thus synthesized from rhodamine B through a simple two-step procedure (POCl₃, ClCH₂CH₂Cl, 80 °C, 6 h; 1.2 equiv of propargylamine, THF, 25 °C, overnight) in 70% yield.

Spirolactam **1** dissolved in 1:1 CH₃CN/PBS buffer (pH = 7.2) shows little color and fluorescence. However, upon addition of Au(I) or Au(III) species, the probe solution immediately becomes pink ($\lambda_{\text{max}} = 563 \text{ nm}$) and also gives strong orange fluorescence ($\lambda_{\text{max}} = 582 \text{ nm}$),⁷ suggesting that the ring-opening process takes place indeed. We have investigated the photo-physical behavior of probe **1** toward the typical gold species, AuCl and AuCl₃, and also an air-stable cationic Au(I) species (Ph₃PAuCl–AgNTf₂)⁸ in the aqueous media. When probe **1** (10 μM) was treated with an equimolar amount of AuCl in the aqueous media at 25 °C, the fluorescence increased rapidly up to 20 min and slowed down (Figure 1a). The fluorescence

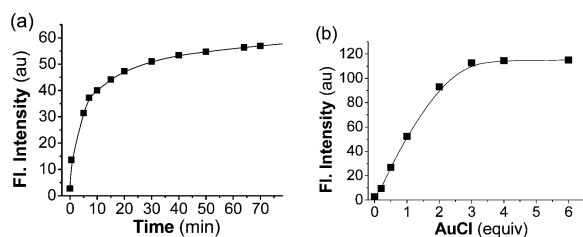


Figure 1. (a) Time-dependent fluorescence change acquired for an equimolar mixture of probe **1** (10 μM) and AuCl, measured in 1:1 CH₃CN/PBS buffer (pH = 7.2). (b) Change in the fluorescence intensity depending on equiv of AuCl with respect to probe **1**, measured after 20 min. In both cases, $\lambda_{\text{ex}} = 530 \text{ nm}$.

enhancement depending on the equivalent of AuCl, measured after 20 min for each sample, shows a saturation behavior at three equivalents (Figure 1b).

AuCl undergoes a disproportionation into Au(III) and Au(s) species in aqueous media [$3\text{Au(I)(aq)} \rightarrow \text{Au(III)(aq)} + 2\text{Au(s)}$].⁹ Thus, the saturation behavior observed with AuCl prompted us to evaluate the emission behavior of probe **1** toward AuCl₃. When probe **1** (10 μM) was treated with an equimolar amount of AuCl₃ in the aqueous media at 25 °C, the fluorescence increased more slowly than in the case of AuCl.⁷ Interestingly, again the fluorescence change with respect to the equivalent of AuCl₃ does not show a saturation behavior at the equivalent point but at about four equivalents. The nonstoichiometric saturation behaviors observed in both cases suggest that the vinylgold intermediate **Ia** follows additional reaction pathway(s) further, which is the case indeed (see below).

The stable cationic gold species, Ph₃PAuCl–AgNTf₂, also reacted with probe **1** to give fluorescence enhancement but with a much slower rate: a complete reaction of probe **1** with the stable Au(I) species required more than two days.

Next, we have compared fluorescence change of probe **1** in the aqueous media toward various metal species such as Mg(II), Ba(II), Cr(II), Mn(II), Fe(II), Fe(III), Co(II), Ni(II), Pd(II), Cu(II), Ag(I), Zn(II), Cd(II), Hg(II), Pb(II), Au(III), and Au(I) (as their chloride salts except for AgNO₃). As shown in Figure 2, probe **1** responds only toward the gold

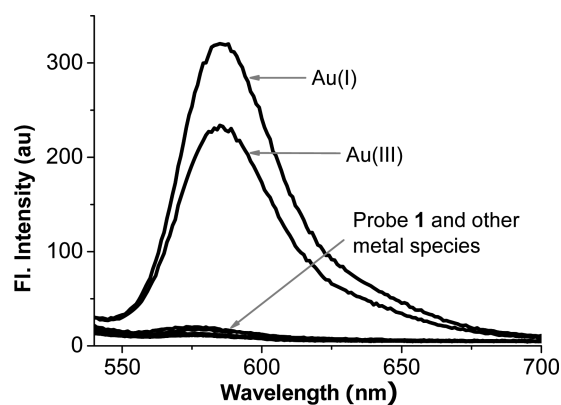


Figure 2. Comparison of fluorescence response of probe **1** (10 μM) toward various metal ions, obtained for each metal species (1 equiv) after 3 h [other metal species examined: Mg(II), Ba(II), Cr(II), Mn(II), Fe(II), Fe(III), Co(II), Ni(II), Pd(II), Cu(II), Ag(I), Zn(II), Cd(II), Hg(II), and Pb(II); as chloride salts except for AgNO₃] in 1:1 CH₃CN/PBS buffer (pH = 7.2), $\lambda_{\text{ex}} = 530 \text{ nm}$.

species among the metal species examined. Also, the fluorescence enhancement observed in the case of AuCl is not altered by the presence of all the nonreacting metal species.⁷

Probe **1** shows a large fluorescence enhancement in the case of AuCl (140 times) compared to the case of AuCl₃

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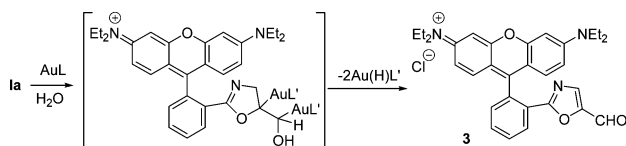
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(100 times). The excellent selectivity of probe **1** toward the gold species among other metal species demonstrates the special alkynophilicity of the gold species toward the triple bond.

The fluorescence response of probe **1** toward AuCl was linear in the range of 2–50 μM AuCl. On the basis of the signal-to-noise ratio of three,⁷ the detection limit of probe **1** for AuCl was estimated to be 0.4 ppm.

To identify the reaction products, we carried out the reaction between probe **1** and AuCl or AuCl₃ at higher concentration (~ 0.1 M of substrates in the aqueous media). Surprisingly, ¹H NMR analyses for the crude reaction mixtures, which contain highly fluorescent compounds, indicated that the major product is neither **2a** nor **2b**. The major product is identified to be 5-formyloxazole **3**, being judged from its ¹H/¹³C NMR as well as MS data.⁷ Formyloxazole **3** can also be isolated in 70% yield by treatment of probe **1** with the stable cationic Au(I) species in the aqueous media for four days at 25 °C. The formation of formyloxazole **3** is an unexpected result because so far vinylgold intermediates are merely assumed to undergo protonolysis in aqueous media to give the corresponding alkenes.² Formyloxazole **3** is likely to be formed from the vinylgold intermediate **1a**, possibly through the gold-promoted hydration followed by double “reductive elimination” processes (Scheme 2). A further study is required to warrant the reaction mechanism.

Scheme 2. Mechanism Suggested for the Formation of Formyloxazole **3** in the Aqueous Media



Although vinylgold species are assumed to be intermediates in many gold-catalyzed reactions of alkenes and alkynes, they are poorly characterized,¹⁰ and furthermore, their chemistry remains elusive at this stage. According to our explanation, the formation of formyloxazole **3** requires water

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molecules as the nucleophile. To get additional information on the reaction pathway, we carried out the titration experiments between probe **1** and AuCl or AuCl₃ in dry acetonitrile. In nonaqueous media, the hydration of vinyl gold intermediate **1a** is not possible during the progress of reaction; therefore, the final products would result from the competition between the protonolysis and the hydration-elimination process for the intermediate **1a** upon exposure to water at the final quenching stage. Under the nonaqueous conditions, among fluorescent compounds, methyloxazole **2b** is found to be the major product along with formyloxazole **3** as the minor component. The exomethylene compound **2a** seems to undergo the double-bond migration to give more stable methyloxazole **2b**.¹¹ The relative ratio of the two compounds **2b/3** determined by ¹H NMR analysis for the crude reaction mixtures obtained in acetonitrile varied from 2:1 to 9:1 in the cases of AuCl and AuCl₃, respectively. The results support that vinylgold **1a** is a common reaction intermediate, which leads to **2b** or **3** depending on the reaction media.

In summary, a fluorescence sensing system for Au(I)/Au(III) species has been developed for the first time based on their alkynophilicity. A rhodamine-derived alkyne probe undergoes a spirolactam ring opening and concomitant heterocycle formation upon coordination with the gold species, resulting in both the color and turn-on fluorescence changes. The probe shows remarkably high selectivity over other metal species. A major reaction product presumably produced from a vinylgold intermediate casts new mechanistic implications on vinylgold intermediates. This work provides a basis for the development of an efficient fluorescent sensing system for gold species, a hitherto unexplored area.

Acknowledgment. This work was supported by grants from the EPB Center (R11-2008-052-01001).

Supporting Information Available: Synthesis and characterization of probe **1** and the reaction products and the fluorescence titration data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL902395X

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