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# Triarylcarbinol functionalized gold nanoparticles for the colorimetric detection of nerve agent simulants



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# ABSTRACT

Gold nanoparticles functionalized with a triarylcarbinol derivative have been used as colorimetric molecular probes for the naked-eye detection of the nerve agent simulants DCNP and DFP. The detection process is based on the compensation of charges at the surface of the nanoparticles which triggers their aggregation in solution with the resulting change in their plasmon band.

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The detection of chemical warfare (CW) through a simple colorimetric method is an area of increasing interest. Among CW, nerve agents have received a lot of interest in the last few years since they are especially dangerous species and poisoning may occur through inhalation or consumption of contaminated liquids or foods.<sup>1</sup> Chemically, nerve agents are highly toxic phosphonic acid esters, structurally related to the larger family of organophosphorous compounds. The extreme toxicity of these compounds is due to their ability to bind primarily and rapidly to acetylcholinesterase in the neuromuscular junction of the central nervous system.<sup>2</sup>

Detection protocols for nerve agents are mainly based on enzymatic assays and physical measurements.<sup>3</sup> However, these protocols usually have limitations such as a certain level of complexity, high cost, and low portability. In the last years, the detection systems based on fluorogenic and chromogenic sensors have gained interest to overcome many of the previous limitations.<sup>4</sup> Colorimetric detection is particularly appealing because it uses low-cost, widely available instruments and the presence of the analyte can be detected by the naked eye.

Functionalized gold nanoparticles (AuNPs) have recently attracted interest in sensor applications.<sup>5</sup> The sensing strategy is based on the color change that arises from the interparticle Plasmon coupling that occurs during the aggregation of AuNPs or

the dispersion of AuNPs aggregates. The red color of dispersed nanoparticles turns to dark blue upon aggregation and the color change can be observed by the naked eye even at low concentrations.<sup>6</sup>

Our research group has recently reported a new approach for the direct colorimetric detection of the nerve agent simulant DCNP (Fig. 1) using thioctic acid capped AuNPs functionalized with pyridine ligands. Upon reaction with DCNP, positive charges are generated on the surface of the dispersed anionic nanoparticles triggering their aggregation with the resulting change in the color of the solution.<sup>7</sup>

On the other hand we have recently developed a new family of reagents for the chromogenic detection of nerve agent simulants DCNP and DFP based on the use of triarylcarbinols. Triarylcarbinols can be converted into their corresponding carbocations in the presence of nerve agent simulants resulting in strong color changes (Fig. 2, bottom).<sup>8</sup>

Herein, we want to extend these studies toward the direct colorimetric detection of DCNP and DFP simulants using thioctic acid capped AuNPs functionalized with a triarylcarbinol derivative. Thus, the reaction of the anionic AuNPs with the nerve agent simulants should generate positive charges on the surface of the nanoparticles inducing their aggregation (Fig. 2, top). This should produce a change in the surface Plasmon resonance absorption of the AuNPs and consequently a change in their color. It is noteworthy that despite the growing interest in the use of functionalized AuNPs as sensors, only few articles have been published on the detection of organophosphorus compounds, always via an indirect



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Figure 1. Chemical structures of nerve agents and the simulants used in this study.



**Figure 2.** Paradigm of the sensing mechanism using functionalized anionic AuNPs: reaction of the terminal ligands with the simulant produces positive charges which can compensate the negative charges of the nanoparticles inducing their aggregation (top). Colorimetric sensing using triarylcarbinols: The hydroxyl group undergoes phosphorylation, followed by elimination to generate the corresponding colored carbocation (bottom).

process.<sup>9</sup> Therefore we believe that this is a field that requires deeper study.

Triarylcarbinol **1** (Scheme 1) was synthesized from 2-(4-bromophenoxy)ethanol, 4-(dimethylamino)benzophenone, and BuLi in THF. The carbinol was obtained in a 50% yield after column chromatography. In order to attach the triarylcarbinol to the surface of the AuNPs, taking advantage of the strong affinity of gold for disulfide groups, the less hindered primary alcohol was esterified with thioctic acid in the presence of DCC and DMAP<sup>10</sup> to yield ligand **L**. The chemical structure and purity of **L** were confirmed by spectroscopic techniques (see SI). The absence of absorption bands in the visible region of the UV–vis spectrum is noteworthy, indicating the absence of carbocation from dehydration reactions.



Scheme 1. Ligand L to be attached to the AuNPs and synthesis of triarylcarbinol 1.

The corresponding triaryl carbonium ion, which was generated by the addition of concd HCl to DMF or acetonitrile solutions of the ligand, showed a broad UV-vis absorption band centered at 520 nm (5  $\times$  10<sup>-5</sup> M in DMF).

The functionalized gold nanoparticles were synthesized by a two-step procedure. First citrate-stabilized nanoparticles were prepared by reducing tetrachloroauric acid with trisodium citrate in boiling water.<sup>11</sup> Monodisperse citrate-stabilized nanoparticles were obtained with an average size of 13 nm, as determined by TEM, and with a Z-potential value of -72.6 mV. The surface plasmon peak appeared at 526 nm. The initial concentration of the citrate capped AuNPs was calculated to be  $3.4 \times 10^{-9}$  M according to the Lambert-Beer's Law from an estimated molar extinction coefficient of  $\varepsilon$  = 2.47 × 10<sup>8</sup> M<sup>-1</sup> cm<sup>-1</sup> (obtained from the plot of  $\varepsilon$  vs nanoparticle size previously reported).<sup>7</sup> In a second step, in a ligand-exchange reaction the citrate was replaced from the surface of the nanoparticles by a mixture of thioctic acid and ligand **L**, in an optimized ratio of 1:2. The pH of the aqueous solution was previously adjusted to 9.0 by addition of NaOH. The functionalized AuN-Ps (NP1) were then centrifuged and re-dissolved in DMF. These nanoparticles were neither stable in water nor in aqueous buffer solutions probably due to a slow dehydration of the carbinols leading to aggregation processes. This item was confirmed by studying the behavior of the free ligand L in buffer aqueous solution by UVvis spectroscopy. The appearance of a new band at 510 nm corresponding to the triaryl carbonium ion could be observed within minutes.

DMF solutions of the triarylcarbinol functionalized AuNPs (**NP1**) exhibited the characteristic surface plasmon resonance (SPR) band at 526 nm in the UV–vis spectrum. As expected, the presence of DCNP or DFP promoted a decrease in the intensity of this peak and the appearance of a new peak at around 640 nm indicating the formation of AuNP clusters. These results are consistent with the phosphorylation of the tertiary alcohol followed by an elimination reaction to generate the corresponding carbocation as shown in Figure 2.

Figure 3 shows the results of UV–vis titration studies performed with DMF solutions of our material in the presence of increasing amounts of DCNP and DFP. These changes in the spectra are concomitant with a change in the color of the solution from red to dark blue.

The variation of the ratio of the absorbance intensities of **NP1** at 640 nm and 526 ( $A_{640}/A_{526}$ ) versus DCNP or DFP concentration is also presented (insets of Fig. 3). A very significant increase in the  $A_{640}/A_{526}$  ratio was observed as the concentration of stimulant was increased. The limits of detection (LODs) expressed in ppm (v/v) obtained from these plots were 560 for DCNP and 465 for DFP.

To achieve a better understanding of the reaction, kinetic studies on the reactivity of the nanoparticles **NP1** in the presence of DFP were carried out in DMF solutions by using an excess of the simulant. The changes in the absorbance intensity of the aggregation band ( $A_{640}$ ) in the UV–vis spectra versus the reaction time are shown in Figure 4. As expected, an increase in the absorbance with time is observed until a plateau is reached at about 9 min of reaction.

It is well known that cyanide anions are capable of dissolving metals such as Au and Ag in the presence of oxygen upon the formation of soluble metal-cyanide complexes.<sup>12</sup> In order to evaluate if the cyanide which is released upon the reaction of our material with DCNP has influence in the obtained results, we studied the behavior of DMF solutions of **NP1** in the presence of an excess of KCN.

TEM studies proved that there had been a gradual dissolution of the gold nanoparticles due to the etching by cyanide, reaching an average size of ca. 4–6 nm, which was not observed for solutions of **NP1** exposed to DCNP (Fig. 5). Additionally, the UV–vis spectra



**Figure 3.** Color change observed in the solution of **NP1** in DMF upon addition of the simulants (top). UV-vis spectra of the triarylcarbinol functionalized AuNPs on addition of increasing amounts of DCNP (middle) and DFP (bottom) expressed mg/m<sup>3</sup>. Insets: Plots  $A_{640}/A_{526}$  versus DCNP and DFP concentration, respectively.



**Figure 4.** Changes in the aggregation absorbance band ( $A_{640}$ ) versus reaction time for **NP1** in DMF upon addition of excess DFP (8 mM).

in DMF showed a slight bathochromic displacement of the Plasmon band to 540 nm which can be attributed to the corresponding change in the nanoparticle size. These results confirm that the



Figure 5. TEM images of NP1 upon addition of excess DCNP (left) and upon addition of excess KCN (right) at a resolution of 200 nm.

behavior of **NP1** in the presence of DCNP or excess cyanide is clearly different.

In order to demonstrate the selectivity of the system, studies were undertaken which confirmed that **NP1** only showed modest responses (or no response at all) in its UV–vis spectra with some of the interference agents that may be present in a military or civilian settings such as some pesticides (malathion, dyfonate, 4,4'–DDD, 4,4'-DDE), gasoline, and diesel fuel at concentrations of 2.4 mM in DMF solution (see Fig. S4). No changes in the color of the solutions could be observed with any of these interferents, the gold nanoparticles remaining stable as a red monodispersion.

In summary, we have synthesized triarylcarbinol functionalized gold nanoparticles **NP1** for the colorimetric detection of DCNP and DFP nerve agent simulants. The detection process is based on the compensation of charges at the surface of the nanoparticles, which triggers their aggregation resulting in a bathochromic shift in the Plasmon resonance band.

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## Supplementary data

Supplementary data (General synthetic procedures. Synthesis and spectroscopic data of compounds **1** and **L**. Copies of <sup>1</sup>H and <sup>13</sup>C NMR and HRMS spectra. Interference studies.) associated with this article can be found, in the online version, at http://dx.doi.org/ 10.1016/j.tetlet.2014.03.139.

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