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Highly sensitive chiral sensing by calix[4]arene-modified silver nanoparticles via dynamic light scattering

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ABSTRACT

The reasonable chiral discrimination has been achieved using silver nanoparticles technique while improving the sensitivity of chiral recognition is essential and remains a challenging task. Dynamic light scattering (DLS), is expected to be a feasible method for improving the sensitivity of analyte discrimination. In this article, by capping Ag NPs with a novel chiral R-mandelic acid-derived calix[4]arene (R-MAC4), the intriguing optical and other properties of the structures can be modified via self-assembly. A method of dynamic light scattering (DLS) was used to recognize the N-Fmoc-D/L-aspartic acid (D/L-FAA). Using this dynamic light-scattering technique, the detection sensitivity was improved almost 500-fold, with detection limit of 5.0×10^{-8} M, compared with Ag NPs methods.

1. Introduction

Chiral analysis continues to receive considerable attention. Enantiomers of chiral drugs often differ in their pharmacological activity and pharmacokinetic profile because the molecules they interact with in biological systems are also optically active. One enantiomer may have the desired medicinal activity, while the other may be inactive or show a qualitatively different effect or quantitatively different potency and/or lead to toxic effects [1,2]. Amino acids are important bioactive substances. Research on enantiomeric recognition of amino acids can provide important information leading to a better understanding of chiral recognition in biological systems and furthering the development of useful molecular devices in biochemical and pharmaceutical studies [3]. Currently, the approaches that are typically employed for the determination of the enantiomeric contents of chiral compounds rely on high-performance liquid chromatography (HPLC), fluorescence, capillary electrophoresis (CE), and gas chromatography (GC) [4–7]. However, these methods are usually time-consuming and quite expensive as a result of requirement for sophisticated instrumentation. As a consequence, simple, inexpensive, convenient techniques and also high sensitivity for this purpose are still in demand [8,9].

Recent years have witnessed the development of a colorimetric assay utilizing silver nanoparticles (AgNPs) as a sensing element based on its unique surface plasmon resonance properties, which can induce to analyte-induced aggregation of nanoparticles [10]. By capping Ag NPs with a selection of chiral ligands have attracted attention, and application to chiral technologies is an interesting perspective. The considerable effort has been devoted to the synthesis and characterization of chiral, optically active ligand coated with silver nanoparticles [11]. For example, Graham and coworkers have reported that Oligonucleotide-silver nanoparticle conjugates enable detection of a lower concentration of a specific DNA sequence [12]. Ye also demonstrated that nucleotide-capped Ag nanoparticles (AgNPs) can be used as ultrahigh efficiency enantio-separation and detection platform for D- and L-cysteine [13]. As far as we know, the visual detection limit for Ag NPs only reached 10^{-7} M lever, which limited a practical analysis. Thus, a way to further improve the sensitivity of Ag NPs-based chiral recognition is a fascinating task in the practical analytical application.

Dynamic light scattering, also known as photon correlation spectroscopy (PCS), is a well-established noninvasive technique for measuring the size of particles in the range from 0.5 nm to 10 μm. DLS is an absolute measurement and is a powerful tool for determining small changes in the size of particles [14,15]. Chiral calixarenes, as a potential host, have been broadly exploited in many areas because of their efficient inclusion ability and easy derivatization of the upper and lower rims by functional groups [16]. Our group has reported chiral calix[4]arene may significantly improve sensitivity of chiral discrimination of mandelic acid using

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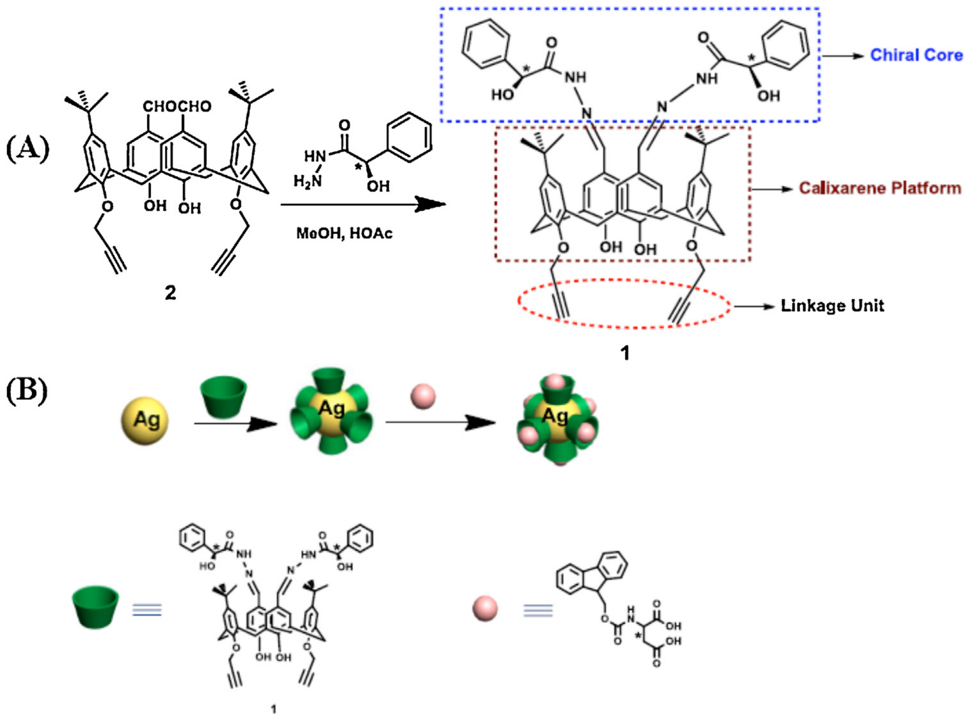

Scheme 1. (A) The synthesis of calix[4]arene R-mandelic acid derivatives 1. (B) Schematic representation of Ag NPs coated with Calix[4]arene 1 for detecting N-Fmoc-D/L-aspartic acid.

a DLS technique [17]. However, to the best of our knowledge, Ag nanoparticle based on DLS chiral sensing was not largely explored.

Herein, in this article, we presented the synthesis of a novel R-mandelic acid derivative of chiral calix[4]arene **1** by classic Schiff-base reaction. In the meantime, Ag NPs coated with chiral calix[4]arene R-mandelic acid derivatives may dramatically distinguish chiral D/L-FAA via DLS. Make most we delighted is the detection sensitivity via DLS improved almost 500-fold compared with that of Ag NPs method.

2. Experiment

2.1. Chemicals and materials

Unless otherwise stated, all chemicals used are of analytical grade and all solutions were prepared with double-distilled, deionized water. $AgNO_3$ was purchased from Aldrich (Milwaukee, WIS, USA). Sodium borohydride ($NaBH_4$, 98%) was obtained from Tianjin Chemical Reagent Plant. N-Fmoc-D/L-aspartic acid was purchased from Tokyo Chemical Industry Co., Ltd. Various concentrations of N-Fmoc-D/L-aspartic acid solutions were prepared by diluting the stock solutions of (1.0×10^{-3} M, in water) serially with deionized water.

2.2. Characterization

The morphology of the new synthesized R-MAC4-Ag NPs was characterized by transmission electron microscopy (TEM) by a JEOL-JEM 2010 transmission electron microscope operated at 200 kV. UV–vis absorption spectra were acquired on a UV-2501 UV–vis spectrometer (SHIMADZU CORPORATION). The infrared (IR) spectra were collected on a Thermo Nicolet NEXUS IR spectrometer in the wavenumber range 400–4000 cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian Mercury VX400 spectrometer at ambient temperature with TMS as the internal standard. MALDI-TOF MS were obtained on a Bruner BIFLEXIII mass spectrometer.

2.3. Synthesis of R-MAC4 and R-MAC4-Ag NPs

Most common amino acid receptors utilize their binding sites to form hydrogen bonds such as thiourea, urea, amide, peptide, etc. Herein, we designed and synthesized a chiral calixarene derivative including mandelic acid by Schiff-base reaction (Scheme 1A). The two chiral mandelic acid groups may bind with D/L-FAA through hydrogen bonds, while calixarene sever as schaffolds, and lower edge of alkynes in calixarene act as linkage unit. This construction may make the complexation more stable. As described below, in a 50 mL flask, calix[4]arene **2** was dissolved in ethanol (20 mL) under an argon atmosphere. Mandelic acid hydrazine (0.12 g, 0.51 mmol) was added. The solution was stirred for 30 min at ambient temperature and then catalytic amount of AcOH was added. The mixture was stirred for 10 h. After evaporation of the solvent, the crude product was dissolved in CH_2Cl_2, washed with brine for three times, and dried over with anhydrous Na_2SO_4. The residue was subject to column chromatography, yielding calix[4]arene R-mandelic acid derivatives **1** as a white powder (0.13 g, 65%).

R-MAC4-Ag NPs were prepared by the reduction of silver nitrate with sodium borohydride. In brief, 100 mL aqueous solution of $AgNO_3$ (1 mL, 0.1 mM) was first mixed with R-MAC4 (1 mL, 1.0×10^{-3} M) under vigorous stirring at room temperature for about 20 min, then fresh sodium borohydride solution (($NaBH_4$, 1 mL, 4.5 mg/mL) was added dropwise until a vivid yellow colored solution produced [18]. Finally, the silver colloidal solution was stirred for another 2 h to ensure self-assembly of the R-MAC4 onto the surface of silver nanoparticles.

3. Results and discussion

3.1. Characterization of R-MAC4-Ag NPs

R-MAC4-Ag NPs were characterized by transmission electron microscopy (TEM) and IR Spectra. In comparison with the IR spectrum of R-MAC4 and R-MAC4-Ag NPs indicates that R-MAC4 was