Decoration of Gold Nanoparticles by a Double-Armed Calix[4]pyrrole: A Receptor-Decorated Nanoensemble for Anion Sensing and Extraction

Punidha Sokkalingam,^[a] Seong-Jin Hong,^[a] Abdullah Aydogan,^[b] Jonathan L. Sessler,^{*[b]} and Chang-Hee Lee^{*[a]}



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Abstract: Gold nanoparticles decorated with a double-armed, deep-cavity calix-[4]pyrrole were prepared and fully characterized. Transmission electron microscopy imaging revealed that the average diameter of the particles was approximately 4 nm both before and after attachment of the receptor to the surface. The calix[4]pyrrole-functionalized nanoparticles exhibited highly elevated sensing behavior (approximately 1000 times in dichloromethane) relative to its monomeric congener while maintaining its guest selectivity. The receptor-nanoparticle conjugate (nanoreceptor) showed significant aggregation upon addition of the biphenolate anion, an effect ascribed to anion-

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mediated interparticle linking. The receptor-nanoparticle conjugate is also capable of extracting the fluoride anion (as its tetrabutylammonium salt) from an aqueous layer to an organic medium. Control experiments revealed that this extraction is not possible when using the analogous monomeric receptor.

Introduction

The importance and ubiquity of anions in a wide range of chemical and biological processes, including sensing, extraction, and catalysis, have encouraged intensive research in the area of anion recognition chemistry.^[1] As a subset of this effort, the covalent attachment of anion receptors to solid substrates has gained significant attention in recent years because of the enhanced binding affinity towards anionic guests that can be achieved using this approach as compared to the use of analogous monomeric entities.^[2] Gold nanoparticles (AuNPs) are of special interest as supports because of their large, highly exposed surface area, and the fact that they can be modified both in terms of surface functionality and particle size.^[3,4] The high molar absorptivity of AuNPs in the visible region also makes them attractive as potential optical nanoprobes for anionic species. These considerations provide an incentive to prepare anion-receptor-functionalized AuNPs.

Among the better studied anion-binding receptors are calix[4]pyrroles, a class of tetrapyrrolic nonaromatic macrocycles that are characterized by their simple molecular design and extremely convenient synthesis.^[5] Whereas the use of calix[4]pyrroles for the selective recognition of anions in organic media is well developed,^[6] their utility in polar competitive media, such as water, remains limited. Recently, significant progress has been made in improving the anion-

[a] Dr. P. Sokkalingam, S.-J. Hong, Prof. C.-H. Lee Department of Chemistry Kangwon National University Chun Cheon 200-701 (Korea) Fax: (+82)33-253-7582 E-mail: chhlee@kangwon.ac.kr Homepage: http://www.cc.kangwon.ac.kr/~chhlee

[b] A. Aydogan, Prof. J. L. Sessler Department of Chemistry and Biochemistry University of Texas at Austin Austin, TX 78712-0165 (USA) E-mail: sessler@mail.utexas.edu

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binding affinity and selectivity of calix[4]pyrroles. These efforts have mostly focused on polymeric scaffolds, wherein the calix[4]pyrrole receptor is tethered to a polymer backbone, either during polymerization or on a preformed polymeric support.^[2a,7] However, attractive as these systems are for extraction of certain anions, they generally fail to produce an appreciable change in optical signature when exposed to various anions. One potential way to overcome this limitation would be to attach the calixpyrrole subunit to a gold nanoparticle (AuNP). Because of the known toxicity of fluoride ions,^[8] we remain interested in developing so-called chemosensors for this Lewis basic species.^[9-12] We recently demonstrated that a calix[4]pyrrole that bore cis-bis(4fluorophenyl) pickets (compound 4) displayed a remarkable



binding affinity for fluoride anion salts and selectivity over other anions in organic media.^[5] However, the receptor exhibited an almost negligible binding affinity for the fluoride anion in aqueous media. We envisioned that by attaching the same receptor to the surface of AuNPs, not only would the affinity towards the fluoride anion be enhanced, a viable optical sensing system might also be achieved. The change in overall system polarity that would likewise accrue from this attachment led to the further consideration that calix[4]pyrrole-functionalized AuNPs might have a role to play as anion extractants.

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Results and Discussion

As detailed below, we have now proof-of-concept support for these postulates. Specifically, we have prepared and characterized calix[4]pyrrole-functionalized AuNPs based on **5** (i.e., Au·[**1**]_{*n*}) and show their use in colorimetric/fluorescence-based fluoride anion binding and sensing. These systems bind the fluoride anion effectively and with high selectivity. Moreover, and in marked contrast to the corresponding monomeric receptor, organic solutions of the nanoreceptor Au·[**1**]_{*n*} are capable of extracting fluoride anions from aqueous solution (Scheme 1). To the best of our knowledge, this is the first example of calix[4]pyrrole receptor-coated AuNPs and the first supported calixpyrrole system that can carry out both dual-mode sensing (i.e., both colorimetric-



Scheme 1. Schematic representation of probe-bound receptor attached to AuNPs. Also shown is the monitoring of guest recognition through fluor-escence dye displacement.

and fluorescence-based) and function as a carrier for aqueous-organic fluoride anion extraction.

With a view to attaching the calix[4]pyrrole subunit to an AuNP center $[Au(SC_{12}H_{25})_n,$ core diameter $\approx 4 \text{ nm}$] effectively, an effort was made to incorporate three design considerations. First, a calix[4]pyrrole with two thiol-bearing alkyl chains was used; this was expected to provide for a stable but flexible double anchoring of the anion recognition subunit to the nanocore. Second, the AuNPs were further decorated with a corona of polyethylene glycol so as to increase the solubility of the nanoparticles^[13] (since initial attempts to produce functionalized AuNPs using only alkyl-chain substitution yielded nanoparticles that were not dispersible in organic solvents). Finally, the basic substitution pattern on the calix[4]pyrrole subunit previously demonstrated to enhance fluoride anion recognition was retained.

Preparation of the thiol group, double-armed calix[4]pyrrole scaffold 1 began with the synthesis of a functionalized calix[4]pyrrole monomer 10 that featured cis-bis(p-fluorophenyl) groups and hydroxy linkers, which can be directly coupled to carboxyl-terminated thiol-protected moiety 14 (Scheme 2). The initial precursor that led to 10 (i.e., the dipyrromethane ethyl ester 8) was synthesized by means of the acid-catalyzed condensation of ethyl-3-(4-fluorobenzoyl)propionate with pyrrole. The calix[4]pyrrole intermediate 9 was then obtained by condensing 8 with acetone in the presence of a catalytic amount of BF₃. The desired hydroxyl-terminated calix[4]pyrrole 10 was prepared in 70% yield from 9 through NaBH₄ reduction. To obtain the other key precursor, 14, the thiol group present in compound 12 (prepared through a literature procedure)^[14] was subject to protection using the pyridine disulfide to afford 13. Saponification in aqueous lithium hydroxide then gave the carboxylterminated thiol-protected moiety 14. Compound 11 was then obtained by coupling a slight excess amount of 14 (2.5 equiv) with 10 in the presence of appropriate coupling agents, namely, 1,3-diisopropyl carbodiimide (DIPC) and 4-(N,N'-dimethylamino)pyridinium-4-toluenesulfonate

(DPTS).^[15] Finally, dithiothreitol (DTT) was employed to remove the pyridine-containing protecting group. This gave the target receptor system **1**. All new compounds were char-



Scheme 2. Synthesis of target compounds.

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acterized by standard spectroscopic methods and were found to give data consistent with the proposed structures (see the Supporting Information).

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With receptor **1** in hand, the synthesis of the receptorfunctionalized AuNPs, Au·[**1**]_{*n*} could be completed. It was found that the key attachment chemistry could be carried out using an exchange reaction. Specifically, an excess amount of **1** was mixed with dodecanethiol-functionalized AuNPs, Au(SC₁₂H₂₅)_{*n*}, in CH₂Cl₂. The nanoparticles prepared in this way were subject to analysis using TEM, SEM, ¹H NMR spectroscopy, and UV/Vis spectroscopy. Figure 1a



Figure 1. TEM images (and average sizes) of a) AuNPs ((3.97 ± 0.33) nm), b) Au·[1]_n ((3.90 ± 0.11) nm), c) Au·[1]_n after addition of TBAF ((3.90 ± 0.10) nm), and d) Au·[1]_n after addition of the 4,4'-biphenolate anion (as its TBA salt) 3 ((3.90 ± 0.10) nm). Scale bars are 20 nm.

shows a low-resolution TEM image of Au(SC₁₂H₂₅)_n. On the basis of this analysis, it was concluded that the average size of the particles was roughly 4 nm ((3.97 ± 0.33) nm). Importantly, TEM imaging of the final product, Au·[1]_n, revealed the presence of spherical particles of almost the same average size ((3.90 ± 0.11) nm; Figure 1b).^[3,15] The slight decrease in average size observed after functionalization is within the limits of experimental error. However, to the extent any such decrease occurs, it could reflect attachment of the bulky calix[4]pyrrole moieties to the AuNP core and the production of a less well-ordered surface structure. SEM images of Au·[1]_n are in agreement with the TEM results and reveal little gross change in structure and morphology (see the Supporting Information).

A comparison of the ¹H NMR spectra of the AuNPs before and after functionalization with receptor **1** showed the appearance of characteristic resonances for the pyrrole and aromatic protons. This latter finding provided initial support for the conclusion that the thiol-functionalized calix[4]pyrrole **1** was successfully attached to the surface of the AuNP (see the Supporting Information). More detailed analysis of the ¹H NMR spectrum allowed the degree of functionalization to be approximated. Since **1** has two free thiols and one calix[4]pyrrole functionality, each molecule of **1** would displace two of the original thiol-bound ligand sites

present on the $Au(SC_{12}H_{25})_n$ surface. Based on the integration of protons in the methylene directly adjacent to the terminal sulfur atom in the alkyl chains present in $Au(SC_{12}H_{25})_n$, as well as those for the β -pyrrolic protons, it proved possible to estimate the molar ratio of the dodecane thiol subunits to calix[4]pyrrole-appended thiols as 2:1:1 (see the Supporting Information).

As recorded in CH₂Cl₂, solutions of Au·[1]_n gave rise to UV/Vis spectra that were characterized by a highly intense absorption band at 228 nm that is considered diagnostic of the calix[4]pyrrole moiety.^[5] In addition, a weaker plasmon resonance band at 518 nm, which corresponds to the AuNPs,^[3] was observed. The combined observation of both these spectral features is taken as further support for the conclusion that Au·[1]_n was formed as per the synthetic design.

To estimate the number of calix[4]pyrrole molecules present on the $Au \cdot [1]_n$ surface, thermogravimetric analysis (TGA) was performed.^[15] As a control, $Au(SC_{12}H_{25})_n$ was analyzed to measure the amount of organic material (thiol ligands) present before the exchange that leads to $Au \cdot [1]_n$ was carried out. Previously it was reported, on the basis of TGA analyses, that 4 nm gold clusters contain approximately 1977 atoms $(M_{\rm Au}=390 \text{ kDa})^{[4a,e]}$ and that roughly 342 thiol ligands serve to cover their surface. In the case of decane thiol-based systems, this accounts for around 14.99% of the mass of the AuNPs. Using this same analysis, the composition of Au- $[1]_n$ was determined to be 38.26% organic and 61.74% metallic (i.e., Au). Since the molecular weight of the gold core is unchanged (i.e., 390 kDa), the total molecular weight of the organic shell is calculated to be 631 kDa. Assuming that approximately half of the dodecane thiol ligands (calculated from the ¹H NMR spectroscopic analysis discussed above) have undergone exchange with the thiols present in calix[4]pyrrole 1, the molecular weight of the calix[4]pyrrole moieties is 207 kDa. This corresponds to approximately 137 ligand sites. Therefore, we infer that there are approximately 69 receptor molecules per particle (see the Supporting Information for details of the analysis and calculations).

The anion-binding properties $Au \cdot [1]_n$ were analyzed using UV/Vis and fluorescence spectroscopic titrations. The addition of the fluoride anion (as its tetrabutylammonium (TBA) salt) to a solution of $Au \cdot [1]_n$ in CH_2Cl_2 resulted in dramatic changes in both absorption bands. Upon this addition, the absorption band at 228 nm underwent a 20-25 % enhancement with a slight redshift. Based on previous studies, such a finding is consistent with the complexation of an anion by the calix [4] pyrrole receptors.^[5] The intensity of the plasmon band at 518 nm was also found to decrease by 7-12%. The solution of $Au(SC_{12}H_{25})_n$ alone did not show any significant spectral change in the plasmon band upon exposure to anions including TBAF (see the Supporting Information). Thus, the changes in the absorption spectra associated with the addition of TBAF are ascribed to salt-receptor interactions, presumably anion binding to the calix[4]pyrrole subunits.

Anion binding to calix[4]pyrroles typically leads conversion from the less organized 1,3-alternate to the corresponding cone conformation. The decrease in molar absorptivity of the plasmon band is thus consistent with the proposed anion binding event; it would lead to an increase in local order and to a blocking of the nanoparticle interior. On the other hand, no appreciable change in the color of the nanoparticles (reflective of the plasmon band) was expected since the nanoreceptor–fluoride complex resides relatively far from the gold nanoparticle surface.

UV/Vis titrations of Au- $[1]_n$ with various anions (as their corresponding TBA salts) in CH₂Cl₂ revealed that the addition of TBAF produced the largest enhancement of the 228 nm absorption feature. For instance, addition of chloride or bromide (as the corresponding TBA salts) resulted in comparatively small enhancements in this band (see the Supporting Information). Only negligible changes were observed upon the addition of other anions (CN⁻, AcO⁻, NO₃⁻, HSO₄⁻, H₂PO₄⁻, and HP₂O₇³⁻, all as their TBA salts). These anions do not bind appreciably to monomer **4** and presumably the lack of spectroscopic changes seen with Au-[1]_n reflects the weak (or negligible) interaction between the anion and the receptor in these instances.

On the basis of the above comparisons and analysis, we suggest that the current nanohybrid receptor $Au \cdot [1]_n$ is selective for the fluoride anion. The calculated association constants,^[16] K, for the calix[4]pyrrole functionality present in Au- $[1]_n$ (effective concentration of 1 per nanoparticle = 1.01×10^{-8} M per molecule) and receptor 4 (1.01×10^{-5} M) for fluoride-anion binding in CH_2Cl_2 were $(1.43 \pm 0.16) \times 10^8$ and $(9.84 \pm 0.25) \times 10^{6} \text{ m}^{-1}$, respectively. These results provide support for the notion that attachment of the calix[4]pyrrole to the nanoparticles serves to enhanced the binding affinity increase the sensitivity in such a way that $Au \cdot [1]_n$ is capable of sensing fluoride anions at much lower effective concentrations ($\approx 10^{-8}$ M) than receptor 4 ($\approx 10^{-5}$ M). It is considered to be a manifestation of multivalency, and is thought to reflect the cooperative action of the individual subunits of receptor 1 assembled on the nanoparticle at a relatively high local concentration. Association constants for the other anions tested follow a similar trend. However, the binding interactions involved are substantially weaker even to the point of being below the limits of detection.

Further support for the strong interactions between Au-[1]_n and the fluoride anion came from ¹H NMR spectroscopic studies. Specifically, significant chemical-shift changes were seen for the pyrrole–NH proton signals (i.e., from δ = 7.2 to 12.6 ppm) upon the addition of TBAF. The final signal was also found to be split with a *J*=40.1 Hz coupling constant. Such changes (i.e., shifts and signal splitting) are typical of those associated with NH–F⁻ hydrogen bond seen for other calix[4]pyrrole systems (see the Supporting Information). The two signals that correspond to the β -pyrrolic protons, which initially appeared at δ =5.81 and 5.92 ppm, were shifted to δ =5.65 and 5.75 ppm, respectively. Two sets of phenyl protons also underwent upfield shifts from δ = 6.95 and 7.18 ppm to δ =6.61 and 6.80 ppm, respectively.

Taken in concert, these observations are fully consistent with the changes expected for anion binding to a calix[4]pyrrole subunit.

An effort was made to exploit the strong, selective binding of the fluoride anion to nanoreceptor $Au \cdot [1]_n$ for the purposes of sensing. Towards this end, the fluorescence dye displacement assay (FDDA) method, wherein a signaling fluorophore is released upon interaction with the targeted analytes, was explored. Fluorescence "turn-on" chemosensors based on the FDDA approach are often more sensitive than sensors based on other optical sensing techniques. Moreover, the use of a $Au \cdot [1]_n$ core for this purpose appeared particularly attractive given that the nanoparticle would be expected to quench the fluorescence of a fluorophore prior to analyte-induced displacement. This could make this system ideal for the detection of anions.^[5,17] To test this hypothesis, tetrabutylammonium-2-oxo-4-(trifluoromethyl)-2H-chromen-7-olate (2) was used as the fluorophore signaling agent. This dye is highly fluorescent in solution but, in accord with design expectations, became completely nonfluorescent upon binding to $Au \cdot [1]_n$. However, in the presence of the more strongly binding fluoride anion, displacement occurs, and 2 is released in its native, highly fluorescent form. Quantitative titrations of nanoreceptor Au $[1]_n$ with 2 in CH₂Cl₂ resulted in concentration-dependent quenching of the fluorescence centered at 500 nm. At 4.76 nm Au· $[1]_n$, nearly complete quenching (99%) was observed (see the Supporting Information). A significant enhancement in the absorption intensity at 228 nm and a decrease in that of the plasmon band at 518 nm were also observed. These optical changes were taken as evidence that fluorophore 2 binds to the nanoreceptor $Au \cdot [1]_n$ (see the Supporting Information).

The beneficial competitiveness of this assay was demonstrated by testing the efficiency of the FDDA with fluoride anions. The sequential addition of the fluoride anion (as the TBA salt) in CH₂Cl₂ resulted in a dramatic enhancement in the fluorescence intensity (Figure 2). The original fluorescence intensity of 2 was fully recovered at 51 nm fluoride (approximately 1000-fold enhancement relative to the quenched form, complex 2-Au- $[1]_n$; this permitted the direct visual detection of fluoride anions through the expected "turn-on" fluorescence produced as the result of anion displacement (Figure 3c). Gratifyingly, the fluorescence enhancement upon addition of fluoride anions was found to be linear at low concentrations $(0-41 \times 10^{-11} \text{ M})$; see the Supporting Information). The detection limit for $2 \cdot Au \cdot [1]_n$ was thus taken to be subnanomolar in concentration (Figure 4). This represents an approximately 500-fold increase in the effective limit of detection relative to receptor 4 (using the same fluorophore 2 and a similar FDDA assay) and an extremely low limit in absolute terms.

In an effort to establish whether the interactions that underlie the fluoride recognition and selectivity observed in chloroform would be retained in a more polar environment, $Au\cdot[1]_n$ was tested as a fluoride anion extractant. Towards this end, a D₂O solution of TBAF (14 mM) was mixed with a

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Figure 2. a) Changes in the fluorescence intensity of 2 (2.1 μ M) observed upon titration with receptor Au-[1]_n (4.76×10⁻⁹M) in CH₂Cl₂ at 25 °C (λ_{ex} =410 nm). The inset shows the corresponding Stern–Volmer plot of the associated fluorophore (2)-dependent fluorescence quenching (K_{SV} =2.36×10⁷). b) Recovery of fluorescence seen upon titration of complex 2-Au-[1]_n with fluoride anion (as the TBA salt, 0–5.13×10⁻⁸M) in CH₂Cl₂ (λ_{ex} =410 nm). Inset shows a plot of *I*/*I*₀ versus fluoride anion concentration. c) Photos of the solutions indicated in these figures under (top) ambient light and (bottom) upon irradiation with a UV lamp (λ_{ex} =365 nm).



Figure 3. UV/Vis spectroscopic titration curves corresponding to the interaction of Au·[1]_n with various anions (as the corresponding TBA salts) in CH₂Cl₂ at 25°C. The absorption changes were measured at 228 nm.

solution of $\operatorname{Au}\left[\mathbf{1}\right]_{n}$ (1.42 mm) in CDCl₃ and subjected to vigorous shaking. The organic phase was then analyzed by using ¹H NMR spectroscopy. Gratifyingly, this analysis revealed that both the anion (F-) and the counter cation (TBA+) were extracted into the organic phase as evidenced by the observation of a substantial downfield shift for the pyrrole-NH resonance ($\Delta \delta \approx 2.73$ ppm) and the appearance of new signals that correspond to the methylene in the TBA counter cation (at $\delta = 3.15$ ppm) that were not present in the original solution of $Au \cdot [1]_n$ in CDCl₃. These results stand in sharp contrast to the lack of spectral changes seen when a solution of the monomeric molecular receptor 4 (4.61 mm in CDCl₃) was contacted with an aqueous solution of TBAF in D₂O. These disparate findings (nanoreceptor versus free receptor) are taken as further evidence that attachment of the receptor to the NPs served to enhance the recognition efficacy of the calix[4]pyrrole subunits, even to the point where different operational results were obtained (i.e., effective TBAF extraction with $\operatorname{Au}\left[\mathbf{1}\right]_n$ but not **4**). As above,

these improvements in application-related function are ascribed to multivalency, namely, the presence of multiple receptors within a localized environment.

As a final test of the features of $\operatorname{Au}[\mathbf{1}]_n$, it was treated with the 4,4'-biphenolate dianion, **3** (as the TBA salt). This study was undertaken because it was envisioned that the nanoreceptor **1** would react with appropriately chosen bisanionic guests to create a linked dimeric nanoparticle ensemble.^[18] In fact, adding **3** to a solution of $\operatorname{Au}[\mathbf{1}]_n$ in dichloromethane gave rise to a higher level of aggregation as inferred from TEM measurements (see Figure 1).

The nanoreceptor Au- $[1]_n$ was also exposed to the fluoride anion under identical conditions. However, no evidence of aggregation was seen, even at high fluoride anion concentrations (Figure 1c,d). These results provide support for the notion that polyanions, such as **3**, can be used to crosslink calixpyrrole-functionalized gold nanoparticles. In due course, this feature could be exploited to create even more selective receptors and sensors.



Figure 4. Estimation of the detection limit of complex 2-Au- $[1]_{\nu}$ for F⁻. a) Fluorescence spectral change (λ_{ex} =410 nm) of the solution of Au·[1]_n (effective concentration of calix[4]pyrrole functionality per nanoparti $cle\!=\!4.76\!\times\!10^{-9}\text{m}$ upon addition of 2 (2.1 $\mu\text{m})) upon addition of TBAF$ $(0-41 \times 10^{-11} \text{ m})$ in CH₂Cl₂. b) Plot of the emission intensity ($\lambda_{em} = 500 \text{ nm}$) versus TBAF concentration. Error bars represent standard deviations of three experiments. Note that (for this experiment only) an emission slit width of 15 nm was used for more sensitive detection.

Conclusion

We have synthesized calix[4]pyrrole-functionalized AuNPs that permit the sensitive recognition of fluoride anions in organic media. The system shows both a chromogenic and a "turn-on" fluorogenic response upon exposure to TBAF. Moreover, it does so with a level of sensitivity that is greatly enhanced relative to the corresponding monomeric receptor. Under biphasic aqueous-organic conditions, $Au \cdot [1]_n$ acts as an effective extractant for TBAF, something that is not observed (within applicable error limits) for the corresponding control system, 4. Aggregation of the functionalized nanoparticles of this report was seen upon exposure to the biphenolate anion, thus demonstrating the potential for controlling the size, and perhaps the properties, of receptor-mediat-

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ed nanoparticles. The potential for recognition, sensing, and extraction leads us to suggest that receptor-substituted nanoparticles, such as $Au \cdot [1]_n$, could have a role to play in various practical applications in which the effective and selective binding of the fluoride anion is required.

Experimental Section

Compound 1: Dithiothreitol (DTT; 59 mg, 0.38 mmol) was added to a solution of 11 (0.3 g, 0.17 mmol) in 3:1 anhydrous DMF/CH₂Cl₂ (16 mL). The reaction mixture was then stirred at room temperature for 3 h. The absence of starting material as inferred from TLC analysis was taken to indicate complete removal of the pyridine moiety. The reaction was quenched by subjecting the reaction mixture to a threefold dilution with dichloromethane followed by two water extractions to remove DMF. The crude product was purified by column chromatography over silica gel using a mixture of CH2Cl2/CH3OH=9.9:0.1 as eluent to afford pure product 1 as a colorless viscous liquid. Yield: 0.14 g (52%); ¹H NMR (600 MHz, CDCl₃, 25 °C, TMS): $\delta = 7.13$ (brs, 4H; pyrrole-NH), 7.08-7.06 (m, 4H; aryl-H), 6.95-6.92 (m, 4H; aryl-H), 5.90-5.89 (m, 4H; pyrrole-H), 5.80-5.79 (m, 4H; pyrrole-H), 4.11 (s, 4H; -COCH₂O-), 4.05 (t, J=6.52 Hz, 4H; -OCH₂), 3.72-3.70 (m, 4H; -OCH₂), 3.68-3.67 (m, 4H; -OCH₂), 3.65-3.61 (m, 20H; -OCH₂), 3.58-3.56 (m, 4H; -OCH₂), 3.44 (t, J=6.80 Hz, 4H; -OCH₂), 2.54-2.50 (m, 4H; -SCH₂), 2.27-2.24 (m, 4H; -CH₂), 1.61-1.56 (m, 18H; -CH₂+-CH₃), 1.44 (s, 6H; -CH₃), 1.38-1.36 (m, 4H; $-CH_2$), 1.34–1.27 ppm (m, 24H; $-CH_2$); ¹³C NMR (150 MHz, CDCl₃, 25 °C, TMS): $\delta = 170.39$, 162.23, 160.69, 140.01, 138.69, 134.93, 129.78, 129.74, 114.60, 114.46, 106.43, 103.01, 71.55, 70.95, 70.63, 70.58, 70.51, 70.06, 68.58, 64.84, 48.12, 36.91, 35.04, 34.05, 29.65, 29.57, 29.50, 29.07, 28.38, 28.18, 26.10, 24.88, 24.66 ppm; MALDI-MS: m/z (%) calcd for $C_{84}H_{126}F_2N_4O_{14}S_2$: 1516.87; found: 1539.83 (100) [*M*+Na].

5,15-(4-Fluorophenyl)-5,15-(ethylpropionate)-10,10,20,20-

tetramethylcalix[4]pyrrole (9): BF3. OEt2 (0.73 mL, 5.88 mmol) was added to a solution of compound 8 (1.0 g, 2.94 mmol) in acetone (60 mL), and the mixture was stirred for 12 h at room temperature. The reaction mixture was quenched through the addition of triethylamine (1.76 mL, 12.6 mmol). Excess amounts of acetone were removed under reduced pressure, and the mixture was combined with water and extracted with CH_2Cl_2 (100 mL \times 2). The organic layer was dried over anhydrous Na2SO4, and the solvent was removed under vacuum. Column chromatography on silica gel afforded a clear separation of the two isomers. The first fraction that contained the trans isomer (0.18 g, 8%) was collected using a mixture of 9.6:0.4 CH₂Cl₂/EtOAc as an eluent. The second fraction that contained the required cis isomer 9 was collected by using a mixture of 9.4:0.6 CH₂Cl₂/EtOAc as the eluent; it was obtained in the form of a light yellow solid. Yield: 0.20 g (9%); ¹H NMR (400 MHz, CDCl₃, 25°C, TMS): δ=7.14-7.11 (m, 8H; aryl-H+pyrrole-NH), 6.97-6.92 (m, 4H; aryl-H), 5.91-5.89 (m, 4H; pyrrole-H), 5.83-5.82 (m, 4H; pyrrole-H), 4.05 (q, J=7.10 Hz, 4H; -OCH₂), 2.59-2.55 (m, 4H; -CH₂), 2.26–2.22 (m, 4H; $-CH_2$), 1.56 (s, 6H; $-CH_3$), 1.44 (s, 6H; $-CH_3$), 1.20 ppm (t, J=7.10 Hz, 6H; -CH₃); ¹³C NMR (100 MHz, CDCl₃, 25°C, TMS): $\delta = 173.95$, 173.83, 163.19, 160.74, 139.99, 139.96, 139.19, 134.86, 134.38, 130.17, 130.09, 129.91, 115.58, 115.37, 115.16, 114.95, 107.95, 106.90, 106.28, 103.41, 60.90, 48.50, 48.38, 35.75, 35.59, 35.45, 34.91, 31.26, 31.15, 30.06, 29.67, 28.71, 14.57 ppm; MALDI-MS: m/z (%) calcd for $C_{46}H_{50}F_2N_4O_4$: 760.38; found: 761.47 (100) [*M*+1].

Nanoreceptor Au-[1], Dodecanethiol-functionalized gold nanoparticles $Au(SC_{12}H_{25})_n$ (10 mg) were taken from a stock solution in toluene and dried on a rotary evaporator at 45°C. The dried particles were then dissolved in dichloromethane (1 mL). Compound 1 (50 mg, 33 mol) was dissolved in dichloromethane (2 mL). After purging both solution with nitrogen for 30 min, they were mixed together and stirred for approximately 3 d at room temperature. The solvent was removed under vacuum, and the crude product was then dissolved in DMF and placed in a 10 kDa regenerated cellulose membrane filter. The sample was purified by ultracentrifugation at 3000 rpm for 15 min. The solution was then concentrat-

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ed under vacuum and precipitated from hexane to give Au-[1]_n (30 mg). ¹H NMR (600 MHz, CDCl₃, 25 °C, TMS): δ = 7.10–7.06 (m; pyrrole-NH+ aryl-H), 6.95–6.92 (m, 4H; aryl-H), 5.91–5.90 (m, 4H; pyrrole-H), 5.80– 5.79 (m, 4H; pyrrole-H), 4.11 (s, 4H; –COCH₂O–), 4.06 (t, *J* = 6.42 Hz, 4H; –OCH₂), 3.72–3.70 (m, 4H; –OCH₂), 3.69–3.67 (m, 4H; –OCH₂), 3.65–3.61 (m, 20H; –OCH₂), 3.58–3.56 (m, 4H; –OCH₂), 3.44 (t, *J* = 6.80 Hz, 4H; –OCH₂), 2.54–2.50 (m, 4H; –SCH₂ of 1), 2.27–2.24 (m, 4H; –CH₂), 2.04–2.01 (m, 2H; –SCH₂ of Au(SC₁₂H₂₃)_n), 1.62–1.55 (m, 44H; –CH₂ of Au(SC₁₂H₂₅)_n), 1.45 (s, 6H; –CH₃), 1.38–1.36 (m, 6H; –CH₂), 1.34–1.26 ppm (m, 43H; –CH₂+–CH₃); ¹³C NMR (150 MHz, CDCl₃, 25 °C, TMS): δ = 170.39, 160.69, 140.00, 138.66, 134.90, 129.78, 129.74, 114.60, 114.46, 106.44, 103.01, 71.55, 70.95, 70.63, 70.58, 70.50, 70.05, 68.58, 64.84, 48.12, 36.89, 35.04, 34.05, 31.93, 29.65, 29.57, 29.51, 29.25, 29.07, 28.55, 28.38, 28.16, 26.10, 24.87, 24.66, 22.69, 14.12 ppm.

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FULL PAPER



Decorate and ye shall receive: Gold nanoparticles decorated with a doublearmed, deep-cavity calix[4]pyrrole produced so-called nanoreceptors with an average diameter of approximately 4 nm (see figure). These constructs could be used to sense the fluoride anion with high selectivity and efficacy in organic media.

Nanoparticles

Decoration of Gold Nanoparticles by a Double-Armed Calix[4]pyrrole: A Receptor-Decorated Nanoensemble for Anion Sensing and Extraction



Gold Nanoparticles Calix[4]pyrroles, a class of tetrapyrrolic nonaromatic macrocycle, are known to selectively bind anions in organic media. In their Full Paper on page ■■ ff, J. L. Sessler, C.-H, Lee et al, have shown that when gold nanoparticles are decorated with these macrocycles, the resulting conjugate exhibits enhanced sensing ability with similar selectivity compared to the monomeric macrocycle. Furthermore, in biphasic media, the conjugates are able to extract fluoride anion from the aqueous phase into the organic phase.