Redox-Modulated Recognition of Flavin by Functionalized Gold Nanoparticles

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Received February 19, 1999

Molecular systems provide a direct method for the miniaturization and mass production of devices. Considerable effort has been devoted to the development of switches,[1] wires[2] and logic gates,[3] biosensors,[4] and receptors.[5] One significant challenge to the efficient application of this methodology, however, is the interfacing of molecular and mesoscopic processes, including issues of immobilization, ordering, and addressing.

Colloids functionalized with self-assembled monolayers (SAMs) are inherently nanoscopic entities that provide a building block for microscale constructs.[6] Colloidal systems have been used to create nanowires,[7] organized arrays,[8] and ultrasensitive, nonisotopic bioprobes.[9] SAM-functionalized colloids also provide a scaffold for the attachment of molecular devices, providing a unique platform for the construction of functional nanoscopic systems.[10] In recent studies, we have established that the recognition of the flavin−diaminopyridine dyad can be increased through reduction of $\mathbf{Fl_{ox}}$ to the corresponding radical anion $\mathbf{Fl_{rad}}^-$ (Scheme 1),[11] providing an electrochemically controlled molecular switch. We report here the extension of this methodology to the direct control of host−guest interactions at the colloid−solution interface.

To provide a system for exploring colloid−solution interfacial recognition, we prepared the diacyldiaminopyridine-functionalized colloid **DAP**−**Au** (Scheme 2). After purification via sequential precipitation, the **DAP**−**Au** colloids were characterized by NMR, X-ray photoelectron, and UV−vis spectroscopies; end-group analysis demonstrated that the ratio of receptor to octanethiol was ∼1:7 and the colloids were ca. 2 nm in diameter.[12] For the typical nanoparticle, with ca. 90 thiols, there are 12 available recognition elements capable of host−guest interactions with flavins (Figure 1).[13]

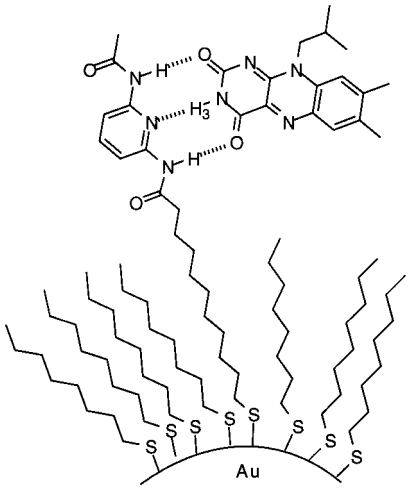
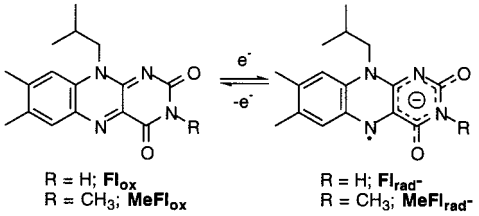
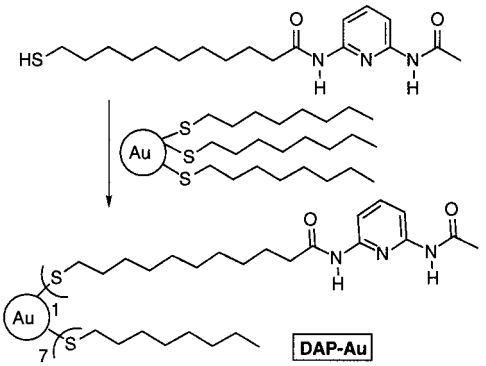


Figure 1. Recognition of flavin by **DAP**−**Au**.

Scheme 1



Scheme 2



Recognition between flavin $\mathbf{Fl_{ox}}$ and **DAP**−**Au** was established via NMR titration.[14] The downfield shift of the flavin N(3) proton upon addition of **DAP**−**Au** cleanly fits a 1:1 binding isotherm (Figure 2), providing an association constant (K_a) of 196 ± 8 M^{-1}. This result is consistent with the values previously observed (K_a = 193−537 M^{-1})[15] for diacyldiaminopyridine recognition of flavin $\mathbf{Fl_{ox}}$.

Shifts in guest reduction potential are directly related to redox-induced modulation of host−guest interactions, allowing changes in recognition to be quantified voltammetrically.[14] Addition of aliquots of **DAP**−**Au** to $\mathbf{Fl_{ox}}$ resulted in a steady positive shift in the flavin redox couple (Figure 3).[16] The maximum observed shift of 81 mV corresponds to a stabilization of the radical anion of 1.85 kcal/mol.[10] In contrast, the reduction potential of $\mathbf{MeFl_{ox}}$ is

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10.1021/ja9905288 CCC: $18.00
Published on Web 05/07/1999

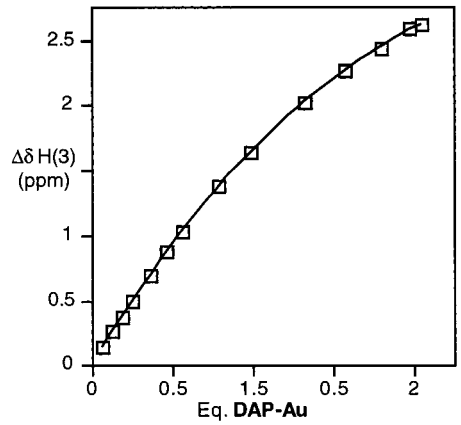

Figure 2. Change in the chemical shift of $\mathbf{Fl_{ox}}$ H(3) during the addition of **DAP**−**Au**. Equivalents **DAP**−**Au** is the effective equivalents of diaminopyridine receptor; $[\mathbf{Fl_{ox}}] = 4.0$ mM, line represents curve fit to 1:1 binding isotherm

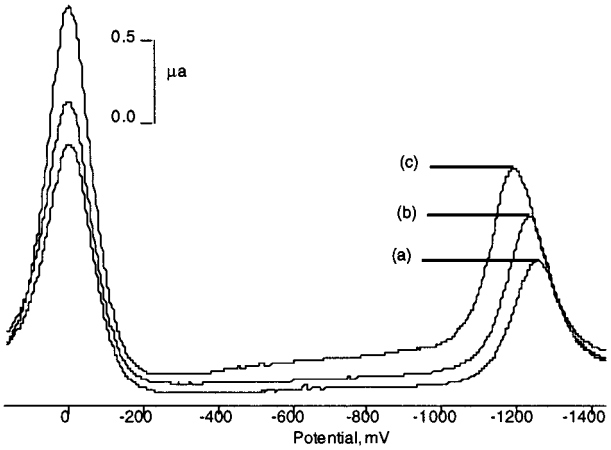

Figure 3. Change in $\mathbf{Fl_{ox}}/\mathbf{Fl_{rad}}^-$ redox couple upon addition of **DAP**−**Au**. Trace (a): 0 equiv **DAP**−**Au**, $E_{1/2}$ $\mathbf{Fl_{ox}} = -1260$ mV; (b): 83 equiv **DAP**−**Au**, $E_{1/2}$ $\mathbf{Fl_{ox}} = -1222$ mV; (c): 96 equiv **DAP**−**Au**, $E_{1/2}$ $\mathbf{Fl_{ox}} = -1184$ mV. $[\mathbf{Fl_{ox}}] = 0.05$ mM; CH_2Cl_2 with 0.1 M Bu_4NClO_4; internal ferrocene reference, period = 400 ms., $T = 23$ °C.

unaffected by the presence of **DAP**−**Au** (Supporting Information), demonstrating that the stabilization observed for $\mathbf{Fl_{rad}}^-$ arises from specific hydrogen bonds between the flavin and diaminopyridine moieties of **DAP**−**Au**.

Examination of the thermodynamic cycle for the host−guest redox process provides

$$K_a(\text{red})/K_a(\text{ox}) = \exp[(nF/RT)(E_{1/2(\text{bound})} - E_{1/2(\text{unbound})})] \quad (1)$$

Using this equation, we can establish that the binding of flavin

(16) The change in the amount of current passed during the electrochemical experiment is likely a result of colloids becoming physiadsorbed to the electrode. For previous electrochemical investigations of SAM-covered gold colloids, see: (a) Hostetler, M. J.; Green, S. J.; Stokes, J. J.; Murry, R. W. *J. Am. Chem. Soc.* **1996**, *118*, 4212. (b) Ingram, R. S.; Hostetler, M. J.; Murry, R. W.; Schaaff, T. G.; Khoury, J. T.; Whetten, R. L.; Bigioni, T. P.; Guthrie, D. K.; First, P. N. *J. Am. Chem. Soc.* **1997**, *119*, 9272.

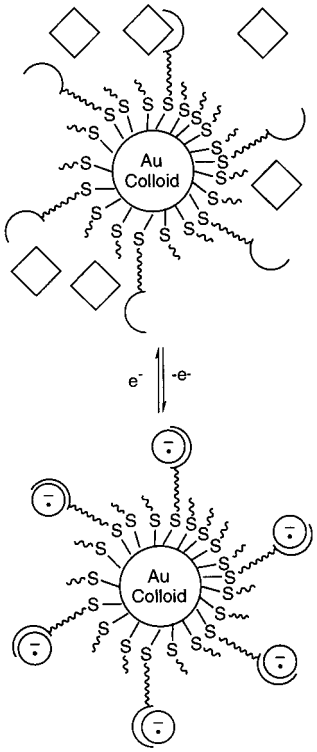

Figure 4. Illustration depicting increased binding of flavin to **DAP**−**Au** upon reduction.

increases greater than 20-fold upon reduction of $\mathbf{Fl_{ox}}$ to $\mathbf{Fl_{rad}}^-$.[17] This control of recognition provides a direct electrochemical switch for the control of the surface substitution of colloidal particles (Figure 4).

In summary, we have demonstrated the creation of a colloidal system where surface functionality can be varied through noncovalent host−guest complexation. The extent of this surface modification is electrochemically controlled, providing a prototypical platform for the generation and electrochemical control of multifunctional SAMs. Application of this methodology to the creation of colloidal arrays and to the combinatorial assembly of nanodevices is currently underway and will be reported in due course.

Acknowledgment. This research was supported by the National Science Foundation (CHE-9528099, MRSEC instrumentation), the Petroleum Resarch Fund of the ACS (PRF 33137-AC4,5), and the National Institutes of Health (GM 59249-0). VR acknowledges support from the Alfred P. Sloan Foundation, Research Corporation, and the Camille and Henry Dreyfus Foundation.

Supporting Information Available: Full synthetic and characterization data for all of the intermediates and **DAP**−**Au** and full description of electrochemical experiments (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA9905288

(17) Since we were unable to reach a limiting shift in potential, this value represents the lower limit for the redox enhancement of recognition.