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Noncovalent assembly of ferrocene on modified gold surfaces mediated by uracil–adenine base pairs

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ABSTRACT

Redox-active ferrocene was assembled on gold surfaces through the hydrogen bonding interactions between adenine-substituted ferrocene and a uracil-terminated organothiol monolayer. The surface coverage of ferrocene Γ could be varied from ca. 4×10^{-11} to 2.0×10^{-10} mol cm^{-2} by diluting the thiol-modified uracil derivative with inert 1-octanethiol. A decrease in the apparent electron transfer rate constant for ferrocene, k_{app}, from ca. 50 to 10 s^{-1} was observed upon increasing Γ.

1. Introduction

Due to the attractive electrochemical characteristics exhibited by ferrocene (i.e. fast electron-transfer rate, low oxidation potential, and stability), its covalent grafting onto conducting surfaces including doped semiconductors, metals and carbonaceous materials has been largely reported [1]. The main objective focused on the development of electrocatalytic and biosensing devices, electrically "wired" enzyme electrodes and two-bit molecular memories. In this regard, a wide variety of reactions including well-known organothiol self-assembly [2], hydrosilylation reaction [3], aryldiazonium [4], carbodiimide [5] and "click" [3d,6] chemistries, have been used to produce ferrocene-terminated monolayer films. These robust and structurally well-defined redox-active interfaces have been extensively used for the kinetic and thermodynamic studies of electron transfer, for the evaluation of the properties of the electrical double-layer, and the micro-environmental effects on long-range interfacial electron transfer kinetics [1–3,5]. Compared with the large number of reports devoted to the covalent binding of ferrocene on surfaces, the anchoring of this electroactive molecule using noncovalent interactions has been much less developed [7].

Herein, we demonstrate the noncovalent assembly of ferrocene on gold surfaces driven by hydrogen bonding of complementary nucleobases. As nucleobases exhibit a tendency to self-associate through Watson–Crick and Hoogsteen base-pairing modes, we decided to exploit this type of self-assembly for the preparation of ferrocene-modified surfaces [8]. For this purpose we used the hydrogen bonding interactions between a ferrocenyl conjugate of adenine [9] and a uracil-terminated monolayer-modified gold surface (Scheme 1). Interestingly, the surface coverage of ferrocene could be controlled by diluting the thiol-modified uracil derivative (**1**) with the inert 1-octanethiol (**2**). Co-reaction with 1-octanethiol allows the exposed pyrimidine lactam groups of the bound uracil moieties to protrude above the plane of terminal methyls. This has the beneficial effects of minimizing the disruption of the organic chain packing in the monolayers and allowing access to the uracil group by the adenine-substituted ferrocene.

2. Experimental

3-(6-Amino-9H-purin-9-yl)-1-ferrocenylpropan-1-one (**3**) was synthesized as reported in Ref. [9]. 3-Tritylsulfanyl-propionic acid and 1-(2-aminoethyl)uracil were prepared as described in Refs. [10] and [11], respectively. Synthesis of uracil derivative (**1**): a solution of 3-tritylsulfanyl-propionic acid (0.1 g, 0.287 mmol) in dry dichloromethane (20 mL) was cooled to 0 °C and HOBt (*N*-hydroxybenzotriazole) (0.046 g, 0.344 mmol) was added, followed by addition of

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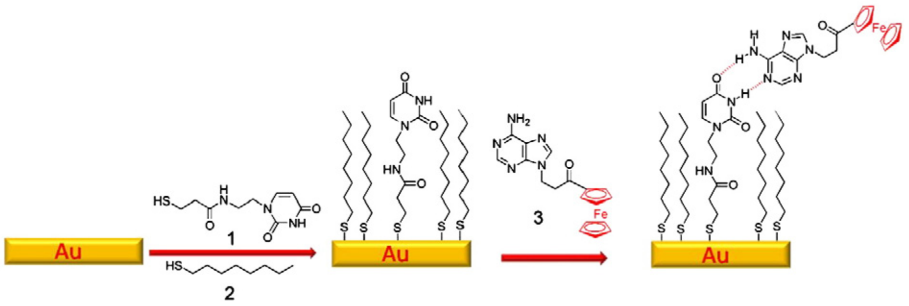

Scheme 1. Preparation of single-component or mixed uracil monolayers deposited on gold surfaces and further grafting of adenine-substituted ferrocene through hydrogen bonding.

EDC × HCl [1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride] (0.066 g, 0.344 mmol). After 1 h the mixture was allowed to reach room temperature and then 1-(2-aminoethyl) uracil (0.048 g, 0.316 mmol) dissolved in N,N′-dimethylformamide was added, followed by addition of diisopropylethyl amine (0.2 mL, 1.147 mmol). The reaction mixture was stirred for 24 h. The solvent was evaporated under high vacuum and dichloromethane (50 mL) was added to the crude solid and washed with 1 M $KHSO_4$ solution, 5% $NaHCO_3$ solution and finally with saturated brine solution. The collected organic layer was dried over anhydrous sodium sulphate and the solvent was evaporated under vacuum to get the crude compound. The crude product was further column chromatographed on silica gel (60–120) using (CH_3OH:CH_2Cl_2) as eluants to give pure trityl-protected compound 1 as a white solid (0.1 g) in 72% yield. Rf = 0.50 (10% CH_3OH:CH_2Cl_2). LC-MS: m/z 243.2 $[M\text{-trityl}]^+$. FT-IR: 3414, 3294, 3154, 1660, 1633, 1595, 1541 cm^{-1}. ^1H NMR (300 MHz) ($CDCl_3$): 1.98 (*t*, *J* = 6.9 Hz, 2H, CH2); 2.53 (*t*, *J* = 6.9 Hz, 2H, CH_2); 3.45 (*q*, *J* = 6.0 Hz, 2H, CH_2); 3.85 (*t*, *J* = 7.2 Hz, 2H, CH_2); 5.42 (dd, *J*1 = 7.8 Hz, *J*2 = 2.1 Hz, 1H, ArH (uracil); 5.81 (*t*, *J* = 7.2 Hz, 2H, CH_2); 7.15 (*d*, *J*1 = 7.8 Hz, 1H, ArH (uracil); 7.20–7.42 (*m*, 15H, ArH (trityl). ^{13}C NMR (75 MHz) ($CDCl_3$): 27.79, 35.24, 38.42, 48.40, 66.89, 101.73, 126.82, 127.98, 129.54, 144.54, 145.85, 151.31, 163.78, 172.02. The trityl-protected uracil derivative (0.13 g, 0.267 mmol) was dissolved in 10 mL of CH_2Cl_2:TFA (1:1), followed by addition of triisopropyl silane as a scavenger. The reaction was stirred for another 4 h at room temperature under Ar atmosphere. The solvent was evaporated under vacuum and crude product was triturated with diethylether to remove the traces of acid. The crude product was further column chromatographed on silica gel (60–120) using (CH_3OH:CH_2Cl_2) as eluants to give pure product 1 as a white solid (0.052 g) in 80% yield. Rf = 0.25 (10% CH_3OH:CH_2Cl_2). ^1H NMR (300 MHz) (DMSO-d_6:$CDCl_3$, 1:1): 1.22 (*t*, *J* = 8.1 Hz, 1H, SH); 1.98 (*t*, *J* = 6.6 Hz, 2H, CH_2); 2.27 (*q*, *J* = 6.9 Hz, 2H, CH_2); 2.96 (*q*, *J* = 5.4 Hz, 2H, CH_2); 3.35 (*t*, *J* = 6.0 Hz, 2H, CH_2); 5.05 (dd, *J*1 = 7.8 Hz, *J*2 = 2.1 Hz, 1H, ArH (uracil); 6.82 (*d*, *J*1 = 7.8 Hz, 1H, ArH (uracil); 5.81 (*t*, *J* = 7.2 Hz, 2H, CH_2). ^{13}C NMR (75 MHz) (DMSO-d_6:$CDCl_3$, 1:1): 19.20, 36.76, 38.60, 46.84, 100.28, 144.28, 150.18, 163.28, 170.31.

2.1. Preparation of gold surfaces modified with a uracyl-terminated monolayer and further grafting of adenine-substituted ferrocene

A gold-coated silicon piece (ca. 1 × 1 cm^2, 1000 Å coating, from Aldrich) was sonicated for 10 min successively in acetone (MOS electronic grade, Carlo-Erba), ethanol (VLSI electronic grade, Carlo-Erba) and ultrapure 18.2 MΩ cm water. It was then cleaned in 3:1 v/v 96–97% H_2SO_4/30% H_2O_2 (VLSI semiconductor grade, Riedel-de-Haën) at 80 °C for 2 min, followed by copious rinsing with ultrapure water and drying under an argon stream. Caution: the concentrated H_2SO_4:H_2O_2 (aq) piranha solution is very dangerous, particularly in contact with organic materials, and should be handled extremely carefully. The cleaned surface was then immersed for one day in argon-deaerated 1:1 (HPLC grade, VWR Prolabo) toluene/ethanol solvent mixture containing ca. 4 mM of **1** alone or diluted with **2** (98.5%, Aldrich) at 4 mM total thiol concentration ($x_1 = 0.02$, 0.1 or 0.2), previously sonicated for 15 min. The uracil-modified surface was then rinsed copiously with ethanol and acetone, and dried under an argon stream. The noncovalent attachment of ferrocene units on gold was performed by immersing the single-component or mixed uracil monolayer-modified gold surface in a deaerated toluene solution containing ca. 2 mM of **3** (previously sonicated for 10 min) at room temperature, under gentle stirring for one day. The ferrocene-modified surface was rinsed with distilled dichloromethane and dried under an argon stream.

2.2. Electrochemical characterizations

Cyclic voltammetry measurements were performed with an Autolab electrochemical analyzer (PGSTAT 30 potentiostat/galvanostat from Eco Chemie B.V.) equipped with the GPES software in a self-designed three-electrode Teflon cell. The working electrode was pressed against an opening in the cell bottom using a FETFE (Aldrich) O-ring seal (area: 0.1 cm^2). All reported potentials are referred to SCE. Tetra-*n*-butylammonium hexafluorophosphate Bu_4NPF_6 was purchased from Fluka (puriss, electrochemical grade). All electrochemical measurements were carried out at room temperature (20 ± 2 °C) and under a constant flow of argon.

3. Results and discussion

In the first step, a cleaned gold surface was dipped under argon in a 1:1 toluene/ethanol mixture containing **1** alone or diluted with **2** (molar fraction x_1 of **1**, corresponded to 0.02, 0.1 or 0.2). Ferrocene was then anchored on the gold surface through the hydrogen bonding between the adenine groups of the ferrocenyl derivative (**3**) and the uracil headgroups.

The X-ray photoelectron spectroscopy (XPS) analysis of the single-component and mixed uracil monolayer-modified gold surfaces reveals characteristic peaks from the gold substrate itself (Au $4f_{7/2}$ at 84.0 eV, which is used as a reference for binding energies) and from the C 1s, O 1s, N 1s and S 2p core levels of the attached molecules. The high-resolution C 1s peak can be decomposed into four components at 284.6 ± 0.1, 286.0 ± 0.1, 287.7 ± 0.1 and 289.0 ± 0.1 eV (Fig. 1). The first corresponds to unresolved contributions from both uracil and alkyl chain C–C bonds, and thiolate headgroups linked to the substrate [12]. The other peaks are attributed by order of increasing binding energies to heteroelement-bound carbons (*C*–N), amide carbons (*C*(O)NH) and pyrimidine carbonyl (N*C*(O)N), respectively. The peak areas are consistent with the structure of **1**. As expected, the peak area ascribed to C–C carbons increases as the molar fraction of **1** in the initial mixture of two thiols is decreased (Fig. 1B).