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SHORT COMMUNICATION

A conjugated hydrogen bond receptor for attachment to gold

Christian Glockner · Ulrich Lüning

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Abstract A fully conjugated host molecule (in order to allow conductivity) with a hydrogen bonding motif for molecular recognition (six hydrogen bonds in the Hamilton receptor array) on one end and a sulfur unit for immobilization on gold at the other end has been synthesized and its binding to gold clusters has been investigated by fluorescence spectroscopy.

Keywords Colloidal gold · Gold surface · Hydrogen bond · Molecular recognition · Nanoparticles · Thiol

Introduction

The strength of the sulfur–gold bond [2] between thiols and this precious metal is exploited when gold surfaces or gold nanoparticles are to be functionalized. Due to the excellent conductance of gold, functionalized gold can be incorporated into microelectronic devices. During the last years, nanowires have been functionalized and used as field effect transistors (FETs) for detection of molecular species like certain amino acids [3], for example. An inherent disadvantage with the FET concept, however, is that the desired molecules must be charged to allow detection. An alternative might be the use of nanoscopic gold wires which contain many nanoscopic gaps and are thus different from what is usually referred to as a "nanowire". Such gaps can be created easily during the production process of the nanowire in a thin-film crack [4–6].

A molecular recognition reaction could be used to bridge the nanoscopic gaps (at least partially). Immobilization of host molecules within the nanogaps should provide a change in electric resistance of the whole nanowire via partial bridging of the gaps, based on electron hopping and tunneling. After the addition of suitable guest molecules and formation of host–guest complexes in these gaps, conductivity should increase even more due to further bridging (see Fig. 3).

With this approach, unlike the FET concept, it should be possible not only to detect charged but also neutral molecules, and a carefully chosen recognition site shall allow to detect guest molecules selectively. Furthermore, nanowires with nanogaps have an even higher surface-to-volume ratio than "classic" nanowires and should therefore in general provide even higher sensitivity.

In order to be able to change the conductivity of such a nanowire by molecular recognition, a respective host molecule has to be attached to a conducting moiety which itself is able to bind to the surface of gold nanoclusters. As an electrically conducting linker, an arylethyne backbone was chosen [7] which carries a sulfur atom at one end and can be coupled to the recognition site at the other terminus for instance by a Sonogashira reaction (see Fig. 1).

One of the aryl rings in **1** carries a methyl group, as described [7], hopefully increasing solubility. A V-shaped "Hamilton receptor" [8] for barbiturates such as **2** and related molecules was chosen as the recognition site. This host molecule recognizes its counterpart by formation of six hydrogen bonds (Fig. 1, hydrogen bond donor and acceptor atoms are printed bold). With a non-conjugated linker, such a system has already been connected to a gold surface by a thiol linkage [9].

Multiple hydrogen bonds, Part 7. Part 6: see [1].

C. Glockner · U. Lüning (✉)
Otto-Diels-Institut für Organische Chemie,
Christian-Albrechts-Universität zu Kiel,
Olshausenstr. 40, 24098 Kiel, Germany
e-mail: luening@oc.uni-kiel.de

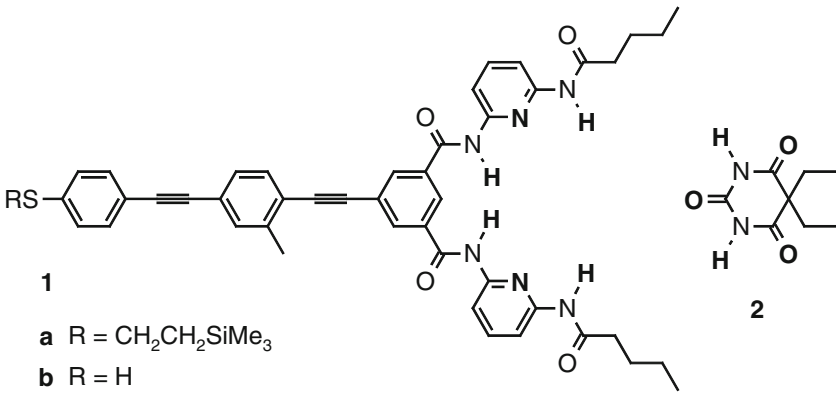

Fig. 1 Sulfur terminated arylethyne analog of a "Hamilton receptor" **1** in protected (**1a**) and deprotected form (**1b**) for immobilization on gold, and diethylbarbiturate (**2**) which can be recognized via six hydrogen bonds

Experimental

The arylethyne linker was synthesized as described [7], thus containing the thiol unit protected as a trimethylsilylethyl thioether. The Hamilton receptor was synthesized as its 5-iodo derivative as described by Brammer [10]. These two fragments were joint by Sonogashira coupling, and the resulting receptor **1a** (Fig. 1) was isolated from the product mixture by chromatography besides the Glaser homocoupling product of the ethyne. **1a** was fully characterized, and its host properties were controlled by ^{1}H NMR titration in chloroform at 298 K giving an association constant between **1a** and diethylbarbiturate (**2**) of 40000 M^{-1}.

Next, the interaction of the new Hamilton receptor with gold surfaces was investigated. It is a well known fact [11] that gold surfaces can quench the fluorescence of adsorbed molecules, so we have used fluorescence spectroscopy to prove that **1**, which is a fluorophore, can bind to nanoscopic gold. In this work, a commercially available colloidal gold solution in toluene (diameter of the gold clusters according to vendor: 3–6 nm) has been used. In a first set of measurements, we investigated the adsorption of **1a** onto gold clusters (Fig. 2a), in a second set of experiments we deprotected the sulfur unit by reaction of **1a** with tetra-*n*-butylammonium fluoride (TBAF) to give the free thiol **1b** (Fig. 2b). Fluorescence spectra were recorded of both mixtures in concentrated and diluted form.

When the solution of **1a** was mixed with gold clusters, fluorescence in the resulting spectrum decreased significantly. This shows that binding of **1a** to gold surfaces is possible even in the protected form, which is predicted for other thioethers by literature [12]. In the following experiment, the mixture was diluted to one-third of its concentration. If the molecules were bound strongly to the surface, one would expect that fluorescence intensity decreased to nearly one-third. This is not the case, consequently, **1a** is only physically adsorbed on gold nanoclusters and desorbs upon dilution.

But when the sulfur function in **1a** was deprotected by addition of TBAF to give the free thiol **1b**, fluorescence decreased upon dilution (Fig. 2).

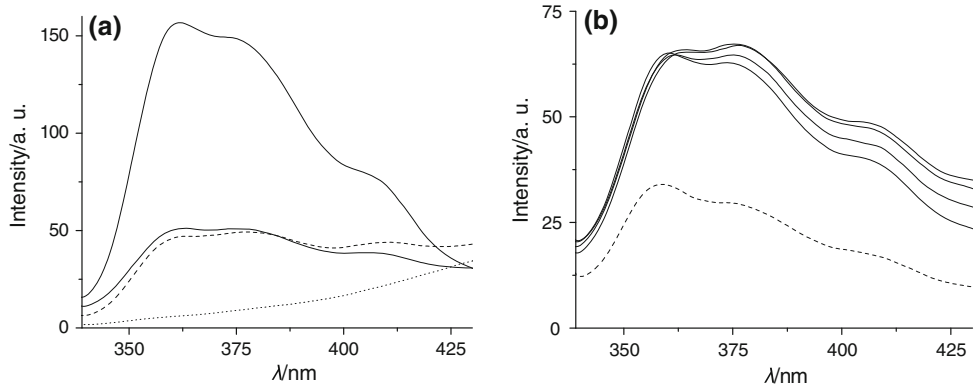

Fig. 2 Fluorescence spectra: **a** *straight curve* (top): **1a** (120 nmol L^{-1} in toluene), *dotted curve*: colloidal gold solution (0.005 % in toluene), *dashed curve*: 1:1 mixture of **1a** and gold solution (at least 70 surface gold atoms per host molecule available), *straight curve* (bottom): mixture diluted to one-third (toluene). **b** *straight curves* (from top to bottom): diluted mixture of the first measurements (a) after the addition of 1 mg of TBAF after 15 min, 40 min, 2 h, 15 h; *dashed curve*: dilution again to one-third (toluene, after 15 h)

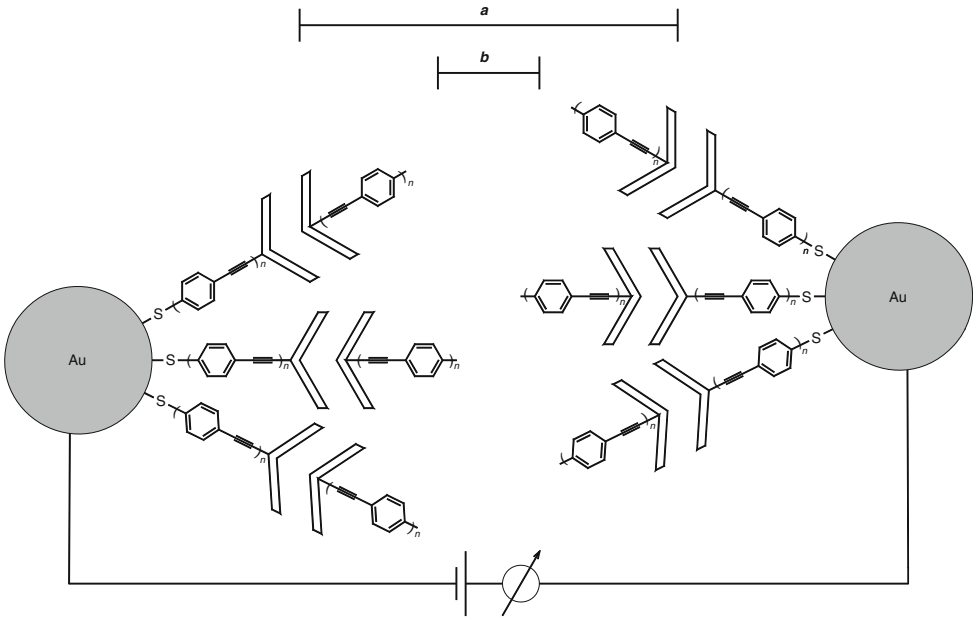

Fig. 3 Schematic representation of a single nanowire gap in a conductivity measurement setup. The distance ***a*** after attachment of conducting host molecules to the gold clusters (*in grey*) is considerably larger than the remaining distance ***b*** when conducting guests are bound. The recognition domains are shown schematically

Results and Discussion

As a conclusion, we have synthesized a molecule **1** with a conjugated π-system allowing molecular recognition of cyanurates or barbiturates (*e. g.* **2**). Its binding to gold clusters in solution has been shown, next, it shall be attached to gold clusters in nanowire gaps for conductivity measurements (Fig. 3).

Synthesis and characterization of 5-(2-Methyl-4-{4-[2-(trimethylsilyl)ethylsulfanyl]phenylethynyl} phenylethynyl)-*N,N*′-bis(6-valeroylaminopyrid-2-yl) isophthalic acid diamide **1a**

5-Iod-*N,N*′-bis(6-valeroylaminopyrid-2-yl)isophthalic acid diamide[10] (46.6 mg, 72.6 µmol), bis(dibenzylideneacetone)palladium(0) (4.1 mg, 7.1 µmol), triphenylphosphine (10.5 mg, 40.1 µmol) and copper(I) iodide (2.5 mg, 13 µmol) were dissolved in dry *N,N*-dimethylformamide (20 mL) and dry diisopropylamine (10 mL) under an atmosphere of nitrogen and hydrogen (1:1). 1-Ethynyl-2-methyl-{[4-(2-(trimethylsilyl)ethylsulfanyl]phenylethynyl}benzene (21.3 mg, 61.2 µmol) in dry *N,N*-dimethylformamide (5 mL) was added and the mixture was heated for 4 d to 70 °C. After the addition of chloroform (50 mL) and aqueous sodium bicarbonate (0.6 N, 50 mL), the layers were separated, and the aqueous layer was extracted with chloroform (2 × 40 mL). The combined extracts were dried with sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, cyclohexane/ethyl acetate, 3:2) to yield 12 mg (23%) of **1a**. M.p. 95 °C. (Found: C, 68.1; H, 6.3; N, 9.6; S, 3.6. Calc. for $C_{50}H_{54}N_6O_4SSi\bullet H_2O$: C, 68.15; H, 6.4; N, 9.5; S, 3.6.). IR (KBr) $\tilde{\nu}u/cm^{-1}$ = 3409, 3276, 2959 (aliph. CH), 2207 (C ≡ C), 1676 (CONH), 1585 (C = O), 1499 (C = C), 1448, 1261, 1086, 800. ^{1}H NMR (600 MHz; $CDCl_3$): δ/ppm = 0.06 (9 H, s, $SiMe_3$), 0.92–0.98 (8 H, m, $SiCH_2$, aliph. Me), 1.41 (4 H, m_c, $CH_2CH_2CH_2Me$), 1.72 (4 H, m_c, $CH_2CH_2CH_2Me$), 2.40 (4 H, t, J = 7.8 Hz, $CH_2CH_2CH_2Me$), 2.49 (3 H, s, arom. Me), 2.99 (2 H, m_c, SCH_2), 7.22–7.25 (2 H, m, Ar″-2,6-H), 7.31–7.34 (1 H, m, Ar′-6-H), 7.39 (1 H, m_c, Ar′-3-H), 7.41–7.45 (3 H, m, Ar′-5-H, Ar″-3,5-H), 7.73 (2 H, t, J = 8.2 Hz, Pyr-4-H), 7.91 (2 H, br s, *n*BuCONH), 7.97 (2 H, d, J = 8.4 Hz, Pyr-5-H), 8.00 (2 H, d, J = 8.2 Hz, Pyr-3-H), 8.16 (2 H, d, J = 1.9 Hz, Ar-4,6-H), 8.35 (1 H, t, J = 1.7 Hz, Ar-2-H), 8.53 (2 H, br s, ArCONH). ^{13}C NMR (150 MHz; $CDCl_3$): δ/ppm = −1.74 [q, $Si(Me_3)_3$], 13.78 (q, aliph. Me), 16.69 (t, $SiCH_2$), 20.63 (q, arom. Me), 22.34 (t, $CH_2CH_2CH_2Me$), 27.42 (t, $CH_2CH_2CH_2Me$), 28.94 (t, SCH_2), 37.52 (t, $CH_2CH_2CH_2Me$), 89.34 (s, Ar′C*C*Ar″), 91.03 (s, Ar*C*CAr′), 91.34 (s, Ar′*C*CAr″), 92.42 (s, ArC*C*Ar′), 109.71 (d, Pyr-5-C), 110.31 (d, Pyr-3-C), 119.71 (s, Ar″-1-C), 121.75 (s, Ar′-4-C), 124.07 (s, Ar′-1-C), 125.17 (d, Ar-2-C), 125.36 (s, Ar-5-C), 127.82 (d, Ar″-3,5-C), 128.89 (d, Ar′-5-C), 131.93 (d, Ar′-6-C), 132.06 (d, Ar′-3-C), 132.57 (d, Ar″-2,6- C), 133.36 (d, Ar-4,6-C), 135.16 (s, Ar-1,3-C), 138.87 (s, Ar″-4-C), 140.52 (s, Ar′-2-C), 140.97 (d, Pyr-4-C), 149.15 (s, Pyr-6-C), 149.86 (s, Pyr-2-C), 163.73 (s, ArCONH), 171.83 (*n*BuCONH). ESI (MeOH): m/z = 863 (M^++H, 21%), 879 (4, M^++H + O).

Fluorescence measurements

All spectra have been recorded with a Perkin–Elmer LS 22 spectrometer. Excitation wavelength for all measurements was 320 nm.

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