Two-dimensional self-assembly of disulfide functionalized bis-acylurea: a nanosheet template for gold nanoparticle arrays†

Jong-Uk Kim,[a] Ki-Hyun Kim,[b] Niko Haberkorn,[a] Peter J. Roth,[a] Jong-Chan Lee,[b] Patrick Theato[a] and Rudolf Zentel*[a]

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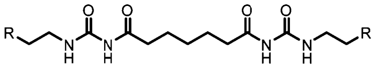
A new functional bis-acylurea molecule allows a two-stage self-organization process. It self-organizes—at first—into 2D nanosheets with disulfide groups at the surface, which act—in the second stage—as a template for gold nanoparticle arrays.

Self-assembly of low molecular mass organic molecules has been a fascinating subject for understanding the nature of molecular recognition. At the same time, it is a useful strategy to generate various supramolecular structures, due to its superiority in controlling the organization at a molecular level.[1] As the organization usually occurs on a nanometre scale, researchers have made many successful attempts to utilize self-organization for fabricating nanostructures such as fibers, vesicles, tubules, helixes, or platelets.[1]

Recently, hybrid inorganic–organic nanoobjects have attracted growing attention.[2] They are constructed by using self-assembled organic components to coordinate the inorganic nanophases to produce discrete integrated objects or higher-order structures. In fact, this two-stage self-assembly and the resulting hybrids are the basic concepts underlying bio-inspired (or bio-mimetic) materials chemistry. The most prominent example for this is biomineralization,[3] in which—at first—lipids self-assemble into membranes with the proper head groups, which then act as a template for the crystallization of the inorganic component (mostly $CaCO_3$). The results are found in bones, sea-shells or the skeletons of different microorganisms. The resulting inorganic/organic hybrid structure combines toughness with mechanical hardness in a very superior way. Another system, in which two types of self-assembly are combined, is liquid crystals gelled reversibly by gelator molecules, which self-assemble into fiber or platelet-like structures.[4–7]

Two-dimensional (2D) hybrid inorganic–organic materials have been realized using 2D multimetric proteins such as bacterial S-layer proteins,[8] ferritin,[9] and heat-shock proteins,[10] due to potential applications in biotemplating as well as their interesting structures of biomimicry. However, some issues about the biomolecule-based hybrid structures, such as low yields, lack of long-range order, narrow operating conditions (temperature, solvent) limit their uses in various applications.[11] Therefore, it is of great interest to devise artificial (synthetic) 2D self-assembled organic systems, which can serve as host materials for hybridization with inorganic guest components. Such functional nano-architectures would broaden the application range and enable more complex setups on a nano-scale.



R =	
$-C_2H_5$	**BuC5Bu**
-S-Trt	**1**
-SH	**2**
$-S-SCH_3$	**SSC5SS**

Recently, we reported a class of bis-acylurea derivatives showing an unusual self-assembling behavior.[12] The derivatives, **BuC*n*Bu**, contain bis-acylurea (CO–NH–CO–NH) moieties separated by a $(CH_2)_n$ spacer and butyl (**Bu**) groups at each end. They self-organize into 2D molecular sheets when they are gelatinized in solvents. As the self-complementary hydrogen bonds of these bis-acylureas are exceptionally strong, the 'odd–even effect' of the spacer,[13] which is one of the usual characteristics of most 1D fibrous organogelators, is not prominent. Even ultrasonication of several minutes does not destroy the 2D organization of the supramolecular structures. The resulting 2D nanostructures are several tens of μm wide, but only some tens of nm high. They are molecularly flat (height of individual molecule: 2.3 nm) over distances of 200 nm. Therefore, we believed the bis-acylurea derivatives could serve as robust building blocks for 2D nanosheets exhibiting various functionalities.

In this communication, we present a new route to gold nanoparticle arrays on a nanosheet template by a two-stage self-assembly process. For this we synthesized a new functionalized bis-acylurea **SSC5SS** with reactive methyl disulfide moieties at both ends. This bis-acylurea self-assembled—at first—into 2D nanosheets, which can serve—later on—as a 2D template for gold nanoparticles.

At the beginning of this work, we anticipated 2D nanosheet structures of thiol containing bis-acylurea, **2**, since thiols are highly versatile functional groups in nano- and biochemistry and strongly bind to metal surfaces. The synthesis of **2** was achieved in two steps; trityl-protected bis-acylurea, **1**, was synthesized through the reaction of Trt-*S*-mercaptoethylurea and pimeloyl chloride in the presence of base, and deprotection of **1** under acidic conditions afforded thiol containing bis-acylurea **2**. However, we could not control the self-organization of **2**, as it had various crystalline structures, *i.e.*, irregular shapes or leaflets (ESI†). Additionally, upon heating in solvents, **2** formed a brownish precipitate, probably

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[a] *Institute of Organic Chemistry, Johannes Gutenberg University Mainz, Duesbergweg 10-14, 55099, Mainz, Germany. E-mail: zentel@uni-mainz.de*
[b] *School of Chemical Engineering, Seoul National University, Shilim-9-Dong, Gwanak-Gu, Seoul 151-744, Korea*

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due to an oxidative dimerization of thiols. Hence, an alternative functional group was investigated.

A derivative of **2** with disulfide moieties instead of thiols (**SSC5SS**) was found to have a 2D morphology regardless of the disulfide end groups, which are an equally strong ligand for various metals (*e.g.* Au) as thiols.[14] **SSC5SS** was derived from **2** by simply stirring it with an excess amount of *S*-methyl methanethiosulfonate in ethanol. The methyl disulfide groups were stable during the synthesis and upon heating up to 80 °C, as was confirmed by ^{1}H NMR.

Two-dimensional multilayered structures formed spontaneously upon cooling of a hot solution of **SSC5SS** in ethanol. Scanning electron microscopy (SEM) and atomic force microscopy (AFM) analyses were used to characterize the supramolecular structure (Fig. 1a and 1b). The aspect ratio of the nanosheets was 20–100, as their widths and thicknesses were several micrometres and 100–200 nm, respectively. The mean thickness of each layer was determined to be 2.4 nm by AFM, which agreed well with the *d*-spacing (24.0 Å) recorded in a powder X-ray diffraction (XRD) measurement. The 2D organization of **SSC5SS** was studied using the XRD pattern of the wide angle region. **SSC5SS** has reflections at 4.49 Å and 3.51 Å, which are also found in the XRD pattern of **BuC5Bu** nanosheets (ESI†). Since these two reflections correspond to the (020) and the (117) planes, respectively, of the **BuC5Bu** 2D crystal,[12] it can be assumed that the crystalline structure of **SSC5SS** is very close to that of **BuC5Bu** (Fig. 1c).

We examined **SSC5SS** as a template for 2D arrays of gold nanoparticles. Immobilizing gold nanoparticles in a controlled manner offers many opportunities in optoelectronics[15] and for biosensors.[16] In particular, closely spaced colloidal gold nanoparticles enhance Raman scattering of absorbed materials on the surface (SERS).[15a] Therefore, it is considered to be of great interest to prepare 2D arrays of nanoparticles on functionalized substrates. To this goal, many attempts have been reported on flat substrates like polished silicon wafers,[15a,17] alumina,[18] self-assembled layer on graphite,[19] or gold nanosheets,[20] whereby the surfaces of these substrates have sometimes been modified by layer-by-layer[21] films to increase the interaction with the nanoparticle. Generally it is possible to assemble the nanoparticles on these surfaces and to vary the coverage up to a dense, but mostly amorphous packing. For self-assembled nanostructures, on the contrary, little work has been done as far as we are aware. In one report,[22] the binding of the nanoparticles to the edges or inclined steps of organic nanosheets was described.

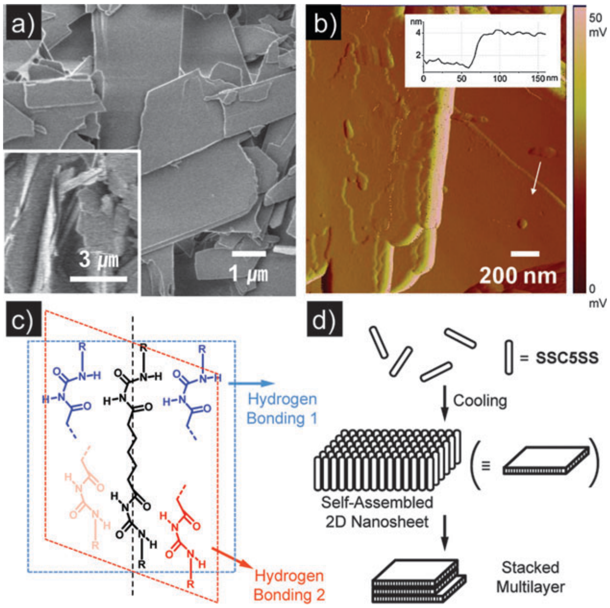

Fig. 1 Two-dimensional nanosheet structure of **SSC5SS**. (a) SEM image. The thicknesses of the nanosheets were determined by SEM images as shown in the inset. (b) AFM image shown in amplitude mode. The height profile along the arrow is shown in the inset. The layer thickness is 2.4 nm, which agrees well with the XRD result (length of molecule). (c) Proposed supramolecular structure of bis-acylureas stabilized by biaxial hydrogen bonding. (d) Schematic illustration for the self-assembly of **SSC5SS** upon cooling from a hot homogeneous solution.

We succeeded in immobilizing gold nanoparticles (AuNPs, 19 ± 3 nm) onto **SSC5SS** nanosheets by adding an aqueous gold colloid solution into a dispersion of **SSC5SS** nanosheets in H_2O followed by vigorous shaking. The gold colloid solution was prepared by the typical citrate reduction method as reported by others.[23] Prior to the immobilization reaction, the gold colloid solution was adjusted to pH 10 in order to prevent aggregation between AuNPs. The originally wine-red colored mixture, (λ_{max} = 520 nm) turned—in contact with the nanosheet suspension—within hours into bluish purple (λ_{max} = 650 nm), which indicated the formation of superlattices of AuNPs.[15] With an increased AuNP concentration, the absorbance band at 650 nm increased, implying that the number of attached gold nanoparticles increased. SEM images of the purified sample showed that AuNPs were attached onto the surface of **SSC5SS** nanosheets (Fig. 2a and b, ESI†), and the number of the tethered AuNPs increased with an increasing dose of AuNPs. We believe that the AuNPs are bound to the surface functional groups chemically rather than by physisorption, as the chemical binding between AuNPs and disulfide-terminated surfaces was reported in the literature.[14b,24] To further investigate the surface chemistry, we performed a similar experiment except that nanosheets of **BuC5Bu** were used. Provided that the binding occurs mainly by physisorption, AuNPs should be adsorbed on the surfaces of **BuC5Bu** nanosheets as well. But even after a week, no color change of the white solids (nanosheets) was observed, implying that no considerable amount of binding of AuNPs onto the surfaces of the nanosheets occurred. Because of this control experiment, we assume that AuNPs are attached to the surface of the **SSC5SS** nanosheets by covalent bonding with the functionality. When an excess amount of AuNPs was added in order to obtain more densely covered nanosheets, a fully covered monolayer in combination with multilayers of AuNPs was observed (ESI†). Presumably, trace amounts of **SSC5SS** dissolved in H_2O, then interlinked the AuNPs to form the multilayers. Thus the self-assembled organic nanosheets can be used for the further assembly of inorganic nanoobjects and their performance for this task is like those of modified macroscopic surfaces.[15–20] So far, we could not yet achieve perfect and homogeneous monolayers over larger sheets. Our

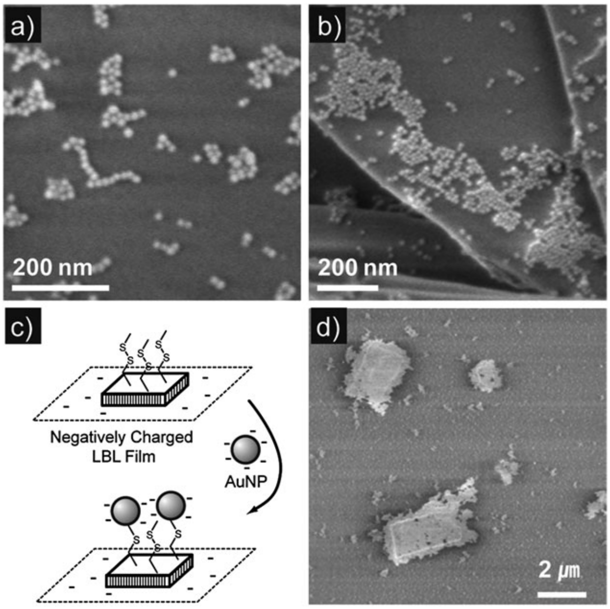

Fig. 2 (a) and (b) SEM images of AuNP-immobilized nanosheets. **SSC5SS** nanosheets were dispersed in an aqueous colloid solution of gold nanoparticles, stabilized by citrate anions. (c) Schematic illustration of AuNP immobilization onto **SSC5SS** nanosheets, which were attached to a negatively charged LBL film. (d) SEM image of AuNPs attached onto **SSC5SS** nanosheet islands on an LBL film. AuNPs were found mostly on the surface of **SSC5SS**, while aggregated AuNPs were also observed at the edges of the nanosheets.

next efforts will focus on defining the mechanism of the binding process and improving the stability.

In a different experiment, we examined the immobilization of AuNPs onto **SSC5SS** nanosheets that had been attached to a glass substrate using a layer-by-layer (LBL) film (Fig. 2c, ESI†). **SSC5SS** nanosheets were transferred onto a negatively charged LBL thin film on a glass substrate, followed by annealing at 80 °C. After thoroughly rinsing with water, the glass substrate was immersed into a AuNP colloid solution. SEM images showed that AuNPs had been immobilized onto the 2D nanosheets, and only a small portion of AuNPs were attached to the negatively charged surface (Fig. 2d). Apparently, discrete islands of AuNP arrays were fabricated on a substrate, which might be utilized in bioassay devices.

In conclusion, we prepared organic nanosheets having disulfide functional groups at the surface by self-assembly, and examined the nanosheets as templates for AuNP arrays in a second self-assembly process. We hope this report will stimulate researchers' interest to fabricate hybrid inorganic–organic nanostructures using self-organized organic templates in a biomimetic way.

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