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Surface Chemistry

Dynamic Microcrystal Assembly by Nitroxide Exchange Reactions**

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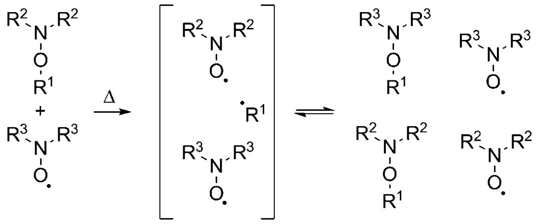
The synthesis, modification, and controlled self-assembly of hybrid nanomaterials are areas of great interest and a promising growing research field.[1] Nano- or microscopic inorganic building blocks can be assembled through covalent reactions with suitable functionalities to generate large functional materials with tuneable size and morphology.[2] The beauty of this approach is that single inorganic building blocks can be connected in such a way that they can keep their individual properties but in addition, through controlled assembly, generate new functions not present in the separate components. This approach also allows the generation of novel materials with individual nano- or macroscopic properties, such as anisotropy or polarizability, that can be translated into macroscopic properties. The controlled organization of length, properties, and geometry of nano- or micro-objects through "soft" linkers could lead to new classes of hybrid systems, which are potential materials for electronic and optical devices, as biomaterials for sensors, or as scaffolds for tissue or bone regeneration.[3]

The choice of suitable systems for ordering crystals by controlled assembly still remains a difficult task. This is due to the fact that the objects often do not have ideal surfaces, their functionalization can not be easily controlled, and the insertion of chemical groups in spatially resolved areas in order to allow the specific geometric growth is extremely hard. Moreover, for larger building blocks, weak intermolecular forces are not sufficient for the desired assembly process. However, weak interactions and hence reversibility of the assembly is essential for creating more sophisticated materials.

Herein we report a new approach for the assembly of organic–inorganic hybrid microcrystals by using nitroxide exchange reactions. Thermal radical nitroxide exchange reactions have been successfully used for synthesis and functionalization of polymers and polymer brushes.[4] In these processes, thermal C–O bond homolysis in alkoxyamines leads to transient carbon-centered radicals and persistent nitroxide radicals. Diffusion of these radicals out of the solvent cage is followed by trapping with the nitroxide radicals to reform alkoxyamines.[5] If homolysis of an alkoxyamine is performed in presence of an additional nitroxide radical, scrambling is observed and the thermodynamic product will be obtained (Scheme 1).



Scheme 1. Thermodynamic product formation in homolysis of an alkoxyamine in presence of an additional nitroxide radical.

In this study, we use the advantages of the nitroxide exchange process, namely reversibility and dynamic character of the reaction, to assemble zeolite L crystals. It is important to note that reversible covalent bond formation has been intensively used in supramolecular chemistry.[6] We now extend this concept to microsystems, and introduce the possibility to control the length, symmetry, and geometry of the assembled materials.

We chose zeolite L crystals because of their defined morphology, their optical transparency, the possibility to tune their size over a wide range (from 30 nm to 10 μm[7]), and the possibility to selectively functionalize their internal and external surfaces.[8] Zeolites are crystalline aluminosilicates in which corner-sharing SiO_4 and AlO_4 tetrahedra create a negatively charged three-dimensional channel network. The negative charge of the framework is compensated by exchangeable cations present inside the channels. These ions can be exchanged by positively charged small molecules or ions.[9] The ability to selectively functionalize channel entrances[10] of the crystals offers various possibilities for the assembly of these micro-objects.

Dye-loaded zeolite L crystals with a length of about 1 μm were site-selectively functionalized either with alkoxyamines or nitroxide radicals at the pore entrances (Scheme 2). Alkoxyamines of this type have weak C–O bonds[11] and should therefore be well-suited for thermal nitroxide exchange reactions (the synthesis of the chemically modified zeolites is discussed in the Supporting Information). In order to obtain asymmetric assemblies, we prepared alkoxyamine-functionalized zeolites loaded with the green dye pyronine and nitroxide-terminated zeolites with the red dye oxazine.

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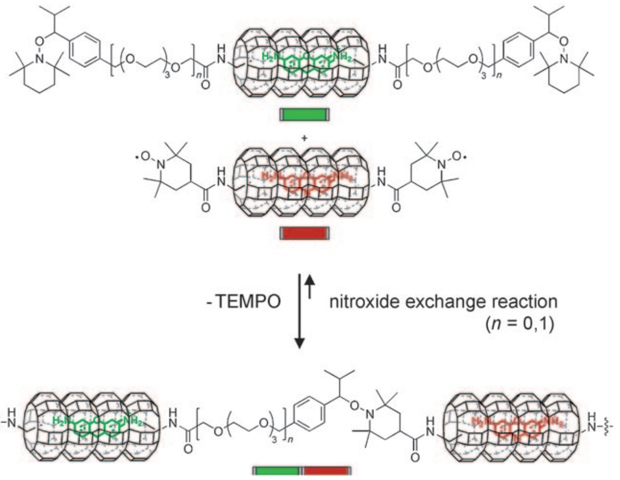

Scheme 2. Nitroxide exchange reaction of alkoxyamine-functionalized zeolite L crystals (green zeolites) with nitroxide-modified crystals (red zeolites) to form ordered zeolite chains.

For alkoxyamine-modified systems, two crystal series were prepared in which the length of the spacer between the alkoxyamine moiety and the channel entrance was varied (see Scheme 2).

Initial experiments were conducted with alkoxyamine-functionalized zeolites that did not contain the tetraethylene glycol (TEG) spacer ($n=0$). These crystals were mixed with the red nitroxide-functionalized zeolites in a 1:1 mass ratio and were stirred for 24 hours at 125 °C in dichloroethane (DCE). The sample was centrifuged and supernatant solvent was removed. An assay was taken up in toluene and ultrasonicated, and a drop of the suspension was placed on a microscope slide. Toluene was used because we have seen in earlier studies that there is no self-assembly resulting from drying effects when this solvent is used. Crystal assembly was then investigated by using SEM and fluorescence microscopy (Figure 1 a, b). The resulting ordering was not efficient and resulted in chains of only two to three crystals of alternate colors, along with many unassembled single crystals. This finding can probably be attributed to the rough surfaces of the crystals,[12] which prevent an efficient chemical reaction between the terminal groups.

To overcome this weakness and generate longer crystal chains, we included a TEG spacer group in the alkoxyamine-modified crystals, as the spacer should facilitate the chemical bridging between crystals with rather large surface roughness. Assembly experiments were conducted as described above. As expected, the images showed a great improvement of the assembly process, which we attribute to the introduction of the spacer group (Figure 1 c, d). Even with nonideal crystals, we were able to generate zeolite assemblies of up to 15 units aligned in chains strictly alternating in color, thus underlining the effectiveness of our approach and hence validating the concept.

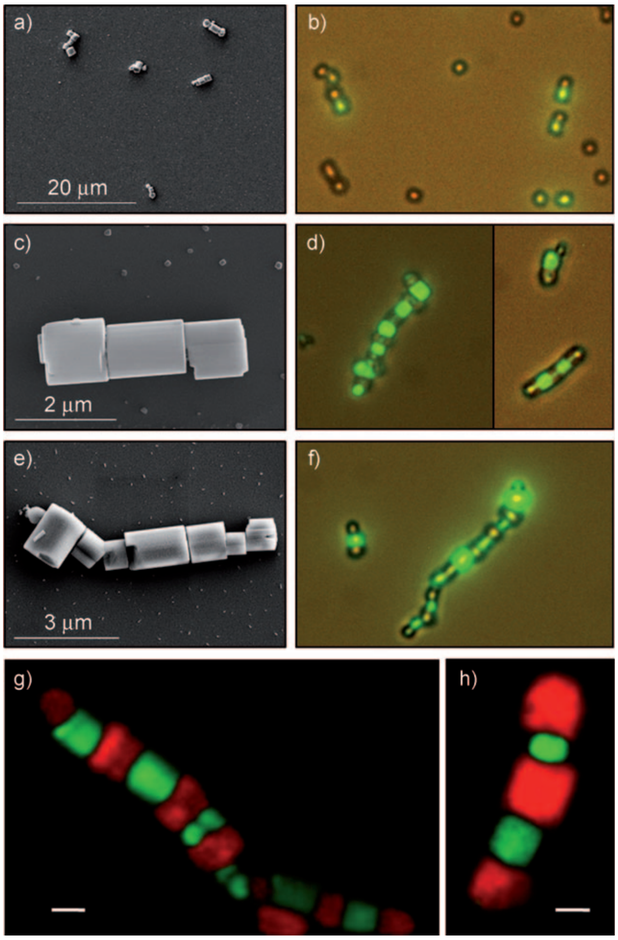

Figure 1. a, b) SEM and fluorescence microscopy images of the assembly of functionalized zeolites without spacer in the alkoxyamine group. c, d) SEM and fluorescence microscopy images of the assembly of functionalized zeolites using a TEG spacer in the alkoxyamine moiety. e, f) SEM and fluorescence microscopy images of the assembly of functionalized zeolites using a TEG spacer in the alkoxyamine moiety after reaction at room temperature for 2 h. g, h) Confocal micrographs of the assembly of functionalized zeolites using a TEG spacer in the alkoxyamine moiety after reaction at room temperature for 2 h (scale bars: 1 µm).

Importantly, similar results were obtained by conducting the exchange experiments at room temperature (see Figure 1 e–h). This observation was very surprising since nitroxide exchange reactions with alkoxyamines of this type generally occur at higher temperature. We believe that the reason for this unusual behavior could lie in a combination of several effects. One important aspect is the enhanced rate of C−O bond homolysis of alkoxyamines in polar environments.[11,13] More importantly, it has also been reported that inter- and intramolecular hydrogen bonding in alkoxyamines that bear appropriately positioned OH groups also accelerates the C−O bond cleavage of alkoxyamines.[11,14] The high number of surface silanol groups of the zeolite crystals that are able to interact with the surface-bound alkoxyamine moieties is therefore likely to play a major role in the experimentally observed nitroxide exchange at the zeolite surface at room temperature.

To further investigate this phenomenon, we applied a rhodamine-conjugated nitroxide derivative for the nitroxide exchange reaction at the surface of alkoxyamine end-functionalized zeolite crystals at room temperature. Fluorescence and confocal microscopy images after the exchange reaction at room temperature clearly showed the presence of the rhodamine dye at the bases of the crystals (see Figure S9 in the Supporting Information for images). Another aspect is the high density of reaction sites at the surfaces of the two crystals. After the initial exchange reaction of a few molecules at the bases of the two crystals, the proximity of the neighboring reaction sites at the bases will result in an enhanced exchange rate for entropic reasons.

In both cases (high-temperature and room-temperature experiments) we observed that assembly occurred mainly at the bases of the crystals as programmed by the channel entrance modification of the crystals. However, for few assemblies, we could also observe some zeolites that were connected through the sides (or coats) of the crystals (see Figure 1 e). This behavior is due to the fact that "base" selectivity in the initial zeolite chemical modification was not perfect and some alkoxyamines were therefore also bound to the coats of the crystals.

To further verify the success of the crossover reaction and to exclude accidental assembly of the crystals, we performed several control experiments. As an initial experiment, we repeated the assembly study by using either zeolites functionalized only with nitroxide radicals (red) or alkoxyamines (green). From fluorescence microscopy images, we could clearly see that crystal chain formation did not occur and, therefore, the assembly discussed above could clearly be attributed to result from nitroxide exchange reactions at zeolite surfaces (see Figures S4 and S5 in the Supporting Information for images). In a second control experiment, we mixed the two zeolite types (green with TEG spacer and red) in toluene. After just 2 minutes reaction time, which was not sufficient to allow any covalent bond formation, the mixture was centrifuged and analyzed, and chain formation was not observed. We can therefore exclude that regular assembly observed above was caused by drying effects during sample preparation (see Figure S6 in the Supporting Information). In addition, we can state that the nitroxide exchange process requires a longer reaction time (> 5 min at room temperature).

To study the reversible nature of chain formation, we added zeolites of one color (either nitroxide (red) or alkoxyamine (green) with TEG spacer) to a sample containing preformed assemblies of alternating red and green crystals. The assemblies underwent a modification so that the length decreased and chains were mostly terminated with the zeolite type present in excess (see Figure S9 in the Supporting Information for images). Moreover, we investigated zeolite assembly by using one crystal type (red or green) in large excess (10:1 by mass). Fluorescence microscopy images showed that chains generated were significantly shorter compared to those obtained by using a 1:1 mixing ratio. Importantly, the zeolite type present in lower concentration was always surrounded at both ends by the zeolite type present in excess, since they would react only with the complementary units. Hence, all chains were terminated with either only red or only green zeolites, depending on the mixing ratio. Upon changing the concentration from 10:1 to 2:1 by adding either red or green zeolites, the chain lengths significantly increased to result in chains terminated with both green and red zeolites (see Figure S7–S8 in the Supporting Information for images). To further investigate the dynamic nature of the assembly, we exposed preformed alternating zeolite chains to a large excess of a small-molecule nitroxide radical (2,2,6,6-tetramethylpiperidin-*N*-oxyl, TEMPO). Exchange with TEMPO at the connecting sites of the crystal assemblies should lead to a disassembly process (see Scheme 2 for the reaction mechanism). Indeed, disassembly of the longer chains was obtained upon TEMPO addition, as shown in Figure 2.

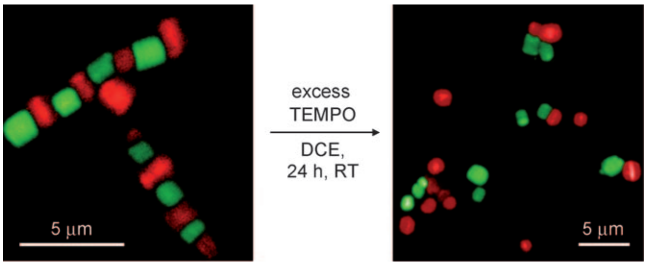

Figure 2. Confocal microscopy images showing the reversibility of the chain formation. Addition of excess TEMPO at room temperature led to disassembly.

In summary, we have shown that nitroxide exchange reactions are well-suited for controlled assembly of zeolite L crystals. The reactions are reversible and the assembly can be conducted under mild conditions. We believe that the approach presented herein is general and should find application for assembly of micro- and nanoparticles of various types. Moreover, the alkoxyamine-functionalized external surface of the zeolite crystals could be used as a synthesis platform to conjugate interesting nitroxide-containing functional molecules at the pore entrances for biological and photonic applications by surface nitroxide exchange reactions. Further experiments in this area are underway.

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