

Amino Acid Silica Hybrid Materials with Mesoporous Structure and Enantiopure Surfaces**

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Stereochemistry and in particular chirality is of crucial importance both for basic scientific research and application purposes. Proteins, representing the most important operating entity in organisms, are composed of stereochemically pure and specified amino acids. That is why the applications of chemical products in biological context are often associated directly with the ability to allocate them in an enantiomerically pure form. In an extreme case the same compound can either be a drug or a toxin depending on the enantiomeric form. Enantioselective synthesis has reached a profound stage of development.^[1] However, as long as the enantiomeric excess of catalytic reactions is below 100 % further improvement of the reactions and additional purification of the products is necessary.^[2]

The idea to equip a nanoporous material with chiral interfaces is tempting.^[3] The interaction of confined guests with the pore walls can be triggered by the adjustment of pore size and the target-oriented variation of surface functional groups. Such materials are valuable in chiral separation technology. Furthermore, they could eventually act as a stereo-directing reaction field.^[4] It has been documented that higher values of enantiomeric excess can be achieved when the reaction is conducted in a chiral matrix through indirect stereochemical induction.^[5] Chiral groups can be attached to the walls of mesoporous silica materials such as MCM-41 or SBA-15 by grafting,^[6] or through the condensation of terminal organosilanes $R^*Si(OR')_3$ (R^* = chiral, organic group) with surface-bound silanol groups ($Si-OH$) resulting in a stable $Si-O-Si$ linkage.^[7] Examples exist for amino acids and short peptide sequences.^[8] Aida and co-workers reported a different, highly interesting method.^[7,9] A triblock surfactant, the so-called lizard template, containing an alkoxysilane head group covalently bound to an amino acid group attached to a long alkyl chain together with approximately 90 % of a source for unmodified SiO_2 was employed for the one-pot synthesis of a mesoporous material with ordered porosity.^[9] However, the inherent disadvantage of the described methods is that the

porous materials contain the chiral entity only in minor amounts, typically in the range 5–15 mol %.^[7] There is an alternative approach to equip mesoporous silica materials with a higher content of organic functionality. Periodically ordered mesoporous organosilica materials (PMOs) are prepared by pure and undiluted silsesquioxane precursors possessing a bridging organic group $(R'O)_3Si-R-Si(OR')_3$.^[10] Because the composition of the resulting mesoporous network can be described as RSi_2O_3 , the interfacial accessibility of the organic group is maximized.^[11] The PMO field has been described recently in excellent review articles.^[7,12] Examples for real PMOs (ca. 100 % organic modification) in which chiral building blocks have been used are rare. Our group applied enantioselective catalytic hydroboration to the precursor $(EtO)_3Si-CH=CH-Si(EtO)_3$ to give a chiral PMO with “ $Si-C^*H(OH)-CH_2-Si$ ” entities embedded in the walls.^[13] Thomas and co-workers used a chiral hydroboration agent directly instead of a stereoselective catalyst.^[14] Froeba and co-workers could prepare a PMO with chiral benzylic ether bridges in 88 % *ee* also by enantioselective catalysis.^[15]

The synthesis of a stable, nanoporous matrix that is exclusively made from a chiral building block is difficult. This high goal was first reached in the field of metal–organic framework solids (MOFS) containing chiral linkers.^[16] Even for MOFS there are only limited reports describing amino acids as linker groups.^[17] Furthermore, similar to other crystalline, microporous materials, it is difficult to extend the pore size beyond 2 nm. As a consequence, it is challenging to use an enantiomerically pure compound from the natural pool as a bridging entity in a respective silsesquioxane precursor for PMO synthesis. Herein, we present a novel solid material constructed by the controlled assembly of amino acid derivatives into a well-defined mesoporous structure possessing above $600\text{ m}^2\text{ g}^{-1}$ of internal chiral surface.

We previously reported a PMO material (UKON2a) containing a bridging benzoic acid function along the pore walls (Figure 1 a).^[18] The benzoic acid groups in the pore walls are accessible for chemical modifications. The mesoporous organosilica UKON2a was treated with $H_2N-Ala-OMe$ (Ala = alanine) to give the material denoted UKON3a or with the “dipeptide” $H_2N-Ala-Asp-(OMe)_2$ (Asp = asparagine) to give UKON3b (see the Experimental Section in the Supporting Information). The modification of the benzoic acid groups can be monitored by NMR spectroscopy (spectra shown in the Supporting Information) and small-angle X-ray scattering (SAXS; Figure 1 b). The ^{13}C -MAS NMR spectra of UKON3a and UKON3b are markedly different from that of UKON2a, which is characterized by the signals for the $COOH$ group ($\delta = 173\text{ ppm}$) and the aromatic carbon atoms

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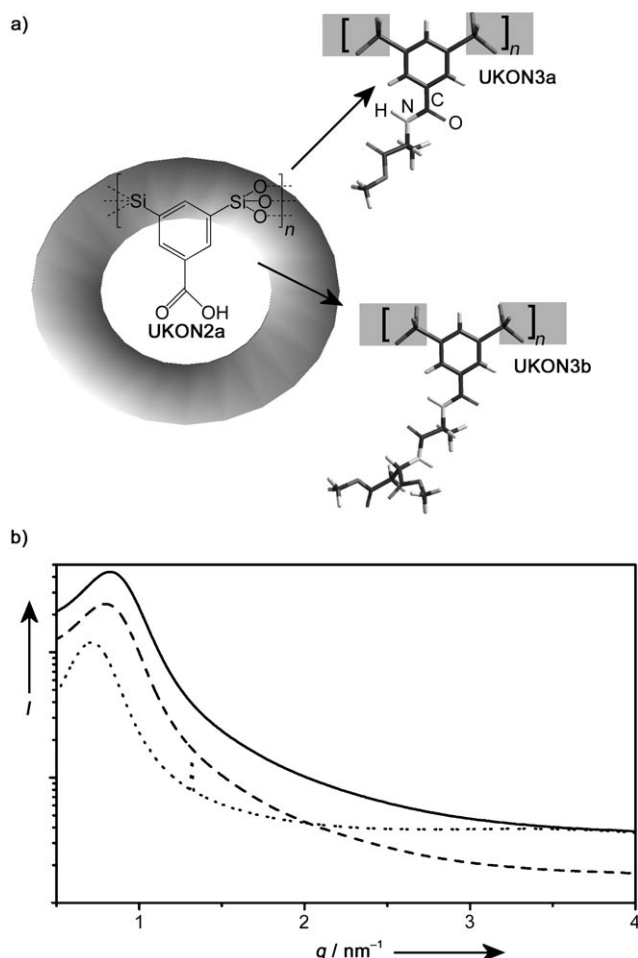
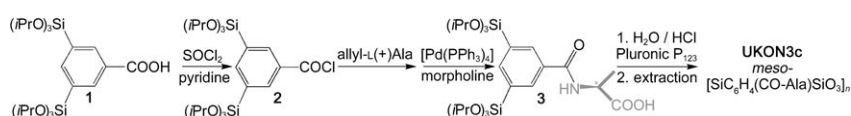


Figure 1. a) Synthesis of the PMO materials UKON3a,b by post-modification of the PMO UKON2a. b) SAXS patterns recorded for UKON2a (.....), UKON3a (-----), and UKON3b (—).

($\delta = 141, 135$ ppm).^[18] The former spectra are in good agreement with known data for classical amino acid compounds. For example, the three signals at $\delta = 19.5, 35.0$, and 53.5 ppm in the spectrum of UKON3b correspond to alanine CH_3 , asparagine CH_2 , and amino acid $\text{CH/O}-\text{CH}_3$ groups, respectively. The main reflection observed in SAXS shifts from 0.715 nm^{-1} for UKON2a to 0.801 nm^{-1} for UKON3a or 0.832 nm^{-1} for UKON3b. Because the latter two materials originate from the “parent” material UKON2a, it is unlikely that the grafting of amino acids changes the periodicities of the pore system to such extent ($\Delta d_{\text{UKON2a} \rightarrow \text{UKON3a}} = -0.943\text{ nm}$ and $\Delta d_{\text{UKON3a} \rightarrow \text{UKON3b}} = -0.293\text{ nm}$). The shift of the diffraction maximum in SAXS can be rationalized if one considers that, because of the amino acid groups at the surfaces (Figure 1a), UKON3a and UKON3b can no longer be regarded as strict two-phase systems (solid pore wall and empty pores). The latter assumption is also supported by the Porod behavior of the scattering patterns at high angles. The curves for UKON3a/3b decay significantly slower than that of UKON2a ($\propto q^{-4}$).^[19] Although the described grafting method (Figure 1a)



Scheme 1. Synthesis of a PMO material with L-(+)-alanine embedded in the pore wall.

is successful, it can not be excluded that not all the benzoic acid groups present in UKON2a react. For example, in the ^{13}C NMR spectrum of UKON3a two signals seem to be superposed in the spectral region typical for the $-\text{COX}$ function ($\delta_1 = 167\text{ ppm}$; $\delta_2 = 173\text{ ppm}$) indicating that the composition of the materials has to be described as $[\text{SiC}_6\text{H}_3\text{COOAlaOMeSiO}_3]_n[\text{SiC}_6\text{H}_3\text{COOHSiO}_3]_m$. The same argument accounts for UKON3b.

Consequently, it would be better to ensure that the entire material contains exclusively the desired amino acid entities. This is only possible by the bottom-up construction from a new bridged silsesquioxane precursor shown in Scheme 1. Activation of the $-\text{COOH}$ group in **1** can be achieved by conversion of **1** into the benzoyl chloride derivative **2**. The latter reacts with an allyl ester protected alanine, and after cleavage of the protecting group the desired compound **3** can be isolated. The compounds **2** and **3** were unambiguously characterized by NMR, IR, UV/Vis, and circular dichroism (CD) spectroscopy, as well as electron impact mass spectrometry (EI-MS) (see the Supporting Information). Precursor **3** was used for the preparation of a PMO material using a liquid crystalline phase of an amphiphilic block copolymer as a template. Template removal was achieved by liquid–liquid extraction. The resulting material UKON3c was characterized by transmission electron microscopy (TEM), SAXS, and nitrogen physisorption measurements, as well as solid-state NMR, FTIR, UV/Vis, and CD spectroscopy.

Four reflexes ($q_{100} = 0.62\text{ nm}^{-1}$, $q_{110} = 1.03\text{ nm}^{-1}$, $q_{200} = 1.23\text{ nm}^{-1}$, and $q_{210} = 1.66\text{ nm}^{-1}$) can be observed in SAXS, and in TEM a cylindrical, hexagonally aligned channel structure can be seen (Figure 2a and Supporting Information). The prepared PMO is well-ordered and possesses an average pore size of 5.2 nm and a BET surface area of $633\text{ m}^2\text{ g}^{-1}$, as determined from N_2 physisorption measurements (see the Supporting Information). From these results

and those from the SAXS and TEM analysis it can be concluded that the pore walls are rather thick (ca. 4.5 nm). The molecular composition of UKON3c was analyzed by ^{13}C -MAS NMR spectroscopy (Figure 2b). In the ^{13}C -MAS NMR spectrum, only the signals related to the phenyl-Ala entity can be observed. Comparison with the spectrum of the precursor reveals that the alkoxy-silane groups ($\delta = 64.8, 24.3\text{ ppm}$) have been cleaved in the course of the sol–gel process. The carbonyl–amide bond ($\delta = 170.4\text{ ppm}$) as well as the amino acid function were fully retained. ^{29}Si -MAS NMR spectroscopy proves that the carbon–silicon bond is also stable under the chosen conditions (see the Supporting Information). Only the three signals typical for monosubstituted organosilica materials $\text{RSi}(\text{OH})_2(\text{OSi})$ ($\delta = -69.5\text{ ppm}$), $\text{RSi}(\text{OH})(\text{OSi})_2$ ($\delta = -78.1\text{ ppm}$), $\text{RSi}(\text{OSi})_3$ ($\delta = -87.3\text{ ppm}$) are found.

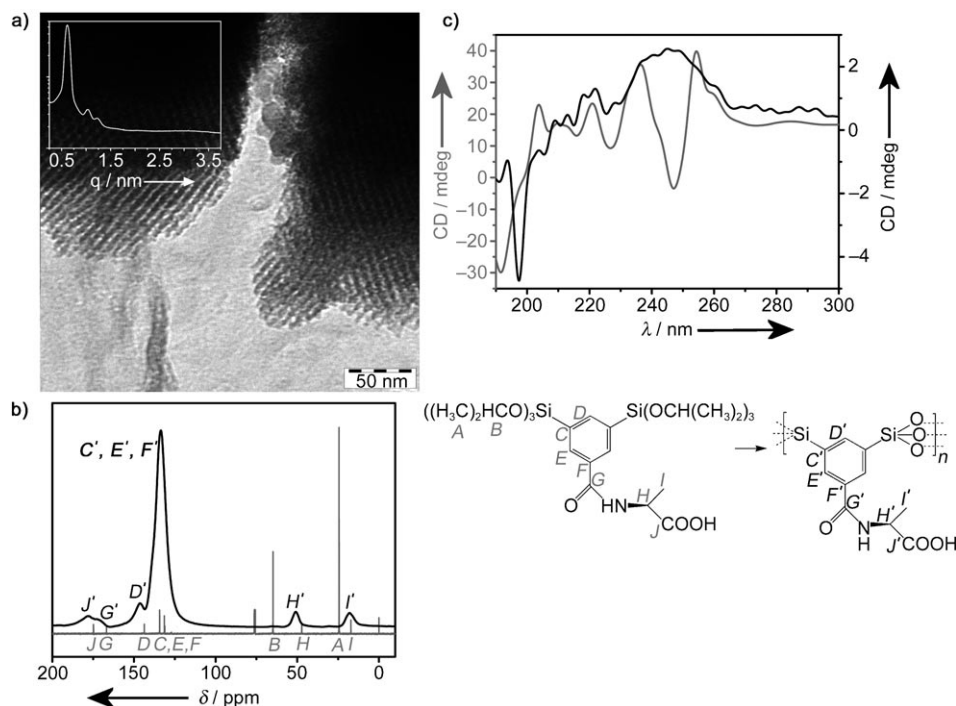


Figure 2. Selected analytical results for UKON3c: a) TEM micrograph and SAXS pattern (inset). b) ^{13}C NMR spectra of the mesoporous solid (black; solid state) and the precursor **3** (gray; recorded in CDCl_3) as a reference. c) CD spectra of a thin mesoporous film (black) and the precursor **3** (gray; measured in solution) as a reference.

Therefore, the composition of UKON3c can be described as $[\text{SiC}_6\text{H}_4\text{COAlaSiO}_3]_n$.

Furthermore, UKON3c is optically active. A transparent film thin enough to allow CD measurements was prepared by spin coating on a quartz plate. UKON3c gives a complicated CD spectrum. A solution of precursor **3** was measured as a reference and both spectra are compared in Figure 2c. It can be concluded that the formal composition and stereochemistry of UKON3c is L-(+)-AlaC₆H₄Si₂O₃. The essential question remaining is if the internal surfaces of UKON3c possess chiral properties. Recording physisorption data using chiral gases is potentially able to answer this question. To the best of our knowledge our results presented below are the first proof of the chirality of surfaces using physisorption measurements.

Propylene oxide was selected as a chiral gas because of its low boiling point, sufficient stability, and ready availability of both enantiomers in pure form. Adsorption isotherms recorded at 313.15 K are shown in Figure 3. UKON3c adsorbs significant amounts of propylene oxide over the entire pressure range. (*R*)-Propylene oxide is markedly less adsorbed than the *S* enantiomer. The differences are more pronounced at low pressures. This result is reasonable, since the strongest effects are expected for low coverage, which occurs at low pressure.

The surfaces of UKON3c are covered with (chiral) carboxylic groups. It could be interesting also to prepare an analogous material with surfaces characterized by chiral, alkaline groups. The linkage of the precursor backbone to an

amino acid through the -COX function of the latter requires a new starting compound, 3,5-bis(triisopropoxysilyl)aniline (**4**) as indicated in Scheme 2.

Compound **4**, which is reported herein for the first time, could be prepared by Pd-catalyzed coupling of 3,5-bis(triisopropoxysilyl)bromobenzene and zinc bis(trimethylsilyl)amide (see the Supporting Information). It should be noted that **4** itself can be converted into an interesting PMO material. However, the latter aspect is beyond the scope of the current manuscript and will be reported elsewhere. Herein, we concentrate on the possibility of attaching N-protected amino acids to **4** to obtain new, amino-terminated precursors **5** (see the Experimental Section in the Supporting Information).

Then, the synthesis of the corresponding PMO UKON3d proceeds in analogy to that of UKON3c using Pluronic P123 (see Scheme 1) as structuring agent in an acidic medium. The resulting mesoporous organosilica was analyzed by the same analytical techniques (see the Supporting Information). The

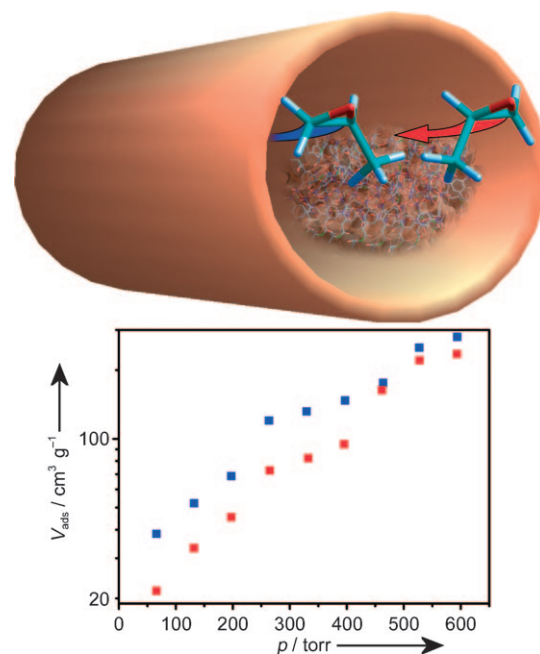
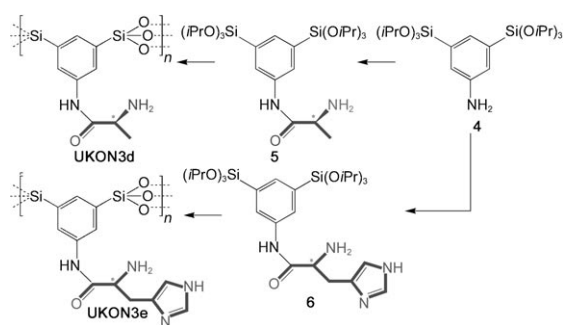


Figure 3. Top: Adsorption of the two enantiomers of propylene oxide on the chiral surfaces of the UKON3c material. Bottom: Adsorption data recorded at $T = 313.15 \text{ K}$. *R* enantiomer: red; *S* enantiomer: blue.



Scheme 2. Preparation PMO materials characterized by surfaces containing amino-terminated alanine or histidine.

TEM and SAXS results (main reflection at $q = 0.61 \text{ nm}^{-1}$) are consistent with a wormhole pore system. The ^{13}C -MAS NMR spectrum of UKON3d is given in Figure 4a. The signals at $\delta = 20 \text{ ppm}$ and 52 ppm are typical for the CH_3 and CH group in alanine. The peak at $\delta = 172 \text{ ppm}$ indicates that the CON bond is still intact. Similarly to the spectrum of UKON3c, the ^{29}Si -MAS NMR spectrum of UKON3d is also characterized

by the signals typical for T-linked silicon centers (see the Supporting Information). One further advantage of 3,5-bis(triisopropoxysilyl)aniline (**4**) is that alternative, more functional natural amino acids can be attached. Therefore, a new sol-gel precursor containing histidine (**6**) and the corresponding organosilicate (UKON3e) was prepared as a proof of concept (see Scheme 2). A comparison of the ^{13}C NMR spectrum of the precursor in CDCl_3 with that of the resulting $(\text{C}_6\text{H}_4\text{NH-His})\text{Si}_2\text{O}_3$ product is shown in Figure 4b. The corresponding ^{29}Si -NMR spectrum is given in the Supporting Information. SAXS (see the Supporting Information) reveals one reflection at $q = 0.62 \text{ nm}^{-1}$, indicating the expected *meso* order.

Summarizing, two methods have been discussed for the preparation of mesoporous materials containing enantiomerically pure amino acids located at the internal surfaces. The precursor approach allows the preparation of a PMO material composed exclusively of the amino acid building block. Pore walls terminated with carboxylic acid or amino groups could be generated. The chirality of the surfaces was probed by applying a unique experiment, namely, the measurement of adsorption of a chiral gas on the mesoporous solids.

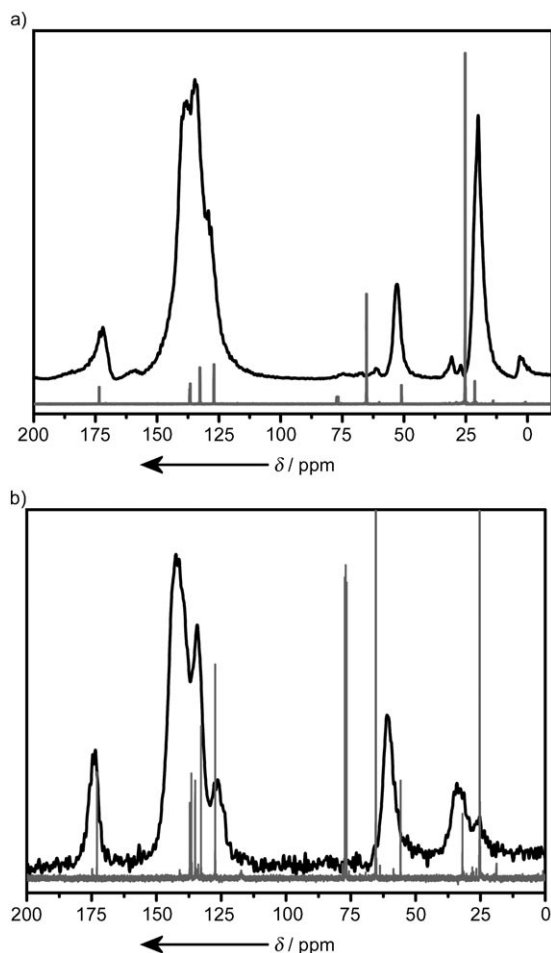


Figure 4. a) ^{13}C -MAS NMR spectrum of UKON3d (black) compared with the ^{13}C NMR spectrum of the precursor **5** (gray); b) ^{13}C -MAS NMR spectrum of UKON3e (black) compared with the ^{13}C NMR spectrum of precursor **6** (gray).

Experimental Section

A detailed description of the preparation and characterization of all compounds and materials discussed herein is given in the Supporting Information.

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