Organic Zeolites

Dipeptides as Microporous Materials**

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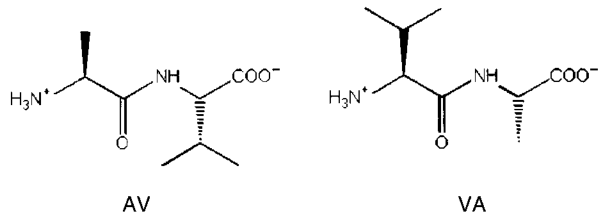
The synthesis and characterization of hydrophobic porous frameworks designed for a variety of applications has attracted significant research efforts over the last few years.[1] The key idea in such studies is to design building elements which allow for controllable assembly and disassembly, and which may be extensively replaced and modified to give porous frameworks with various topologies and functions. The natural world often provides excellent examples of how to proceed with the design of materials; for example, the initial experiences with natural zeolites has led to very successful efforts to produce a wide variety of industrially relevant synthetic materials.[2] Recently, supramolecular architectures based upon weaker interactions have motivated a number of studies;[3] polypeptides that can build tubular and helical structures, frequently referred as nanotubes, have attracted considerable attention because of their biological relevancy as ion channels, membrane pores, etc.[4] These naturally occurring and artificially created materials reveal a sophisticated complexity and are often difficult to characterize in detail. Thus, the lower oligomeric peptides, being both simpler model systems and cheaper, would appear to be useful as practical porous materials, especially since some dipeptides demonstrate the ability to host small organic molecules.[5] Moreover, the ability of single crystals of the dipeptides to sustain guest solvent exchange and removal was reported.[5d] Herein we examine the structure and sorption properties of the two closely related dipeptides L-alanyl-L-valine (AV) and L-valyl-L-alanine (VA; Scheme 1), and show that these lower oligomers have considerable promise as novel porous materials. Moreover, the wide variety of amino acids available should allow the assembly of materials with quite diverse structural motifs containing significant void space.



Scheme 1. Dipeptides studied.

The two dipeptides AV and VA are microporous crystalline materials. Hexagonal prisms of the dipeptides were grown from water and characterized by single-crystal X-ray diffraction (XRD) analysis at room temperature (Table 1).[6–8]

Table 1: Single-crystal XRD analysis of guest-free AV and VA.

Compound	AV	VA
temperature [K]	293	293
empirical formula	$C_8H_{16}N_2O_3$	$C_8H_{16}N_2O_3$
formula weight	188.2	188.2
crystal system, space group	hexagonal, $P6_1$	hexagonal, $P6_1$
a [Å]	14.462(2)	14.461(2)
c [Å]	10.027(1)	10.083(1)
V [Å^3]	1816.2(4)	1826.1(4)
Z	6	6
total data collected	21480	15948
data unique ($I > 2\sigma(I)$)	2189	1954
refined parameters	142	122
calculated density [g cm^{-3}]	1.033	1.027
final $R1$ ($I > 2\sigma(I)$)	0.048	0.057
$wR2$ ($I > 2\sigma(I)$)	0.103	0.116
max peak and hole [e Å^{-3}]	+0.17, −0.15	+0.15, −0.14

Both crystals are hexagonal with a $P6_1$ space group and lattice parameters that are nearly identical. Each dipeptide assembles through hydrogen bonds as a 6_1 spiral to form a channel (Figure 1). Mapping out the channel diameter along the z axis (Figure 2) shows that the channels have a smooth, constant-diameter shape similar to that of urea[10] (a well-known and extremely versatile host material) with an average diameter of 5.13 and 4.90 Å for AV and VA, respectively. A feature that distinguishes AV and VA from most other tubulates, however, is that their channels are essentially chiral.[11] The center of the channel is displaced from the 6_1 axis by 0.60 and 1.05 Å for AV and VA, respectively, and rotates around the axis in a right-handed fashion (Figure 3). It should be noted that chiral sorbents are important and challenging targets in crystal engineering. While researchers resort to subtle strategies to induce chirality into novel, artificially created porous materials,[12] the peptides form an endless source of naturally chiral building blocks ideally suited to this task.

Another distinction of the materials studied is the remarkable stability of their porous frameworks. The majority of hosts known to date collapse into a dense form once the stabilizing guest template is removed; only a few may exist in a porous form as a result of their kinetic stability with respect to the dense, thermodynamically stable polymorph.[13] To check for possible polymorphism, AV and VA samples were obtained from different commercial sources, and were

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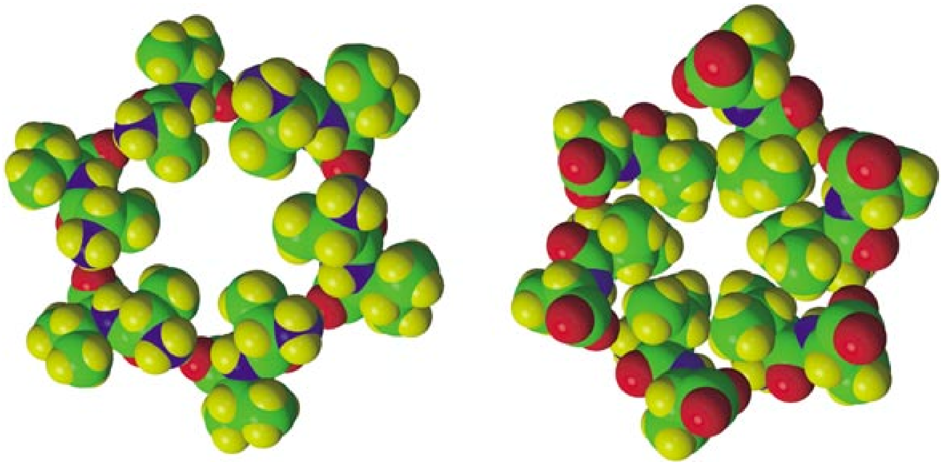

Figure 1. Spiral assembly of AV (left) and VA (right) dipeptide molecules that form a channel (van der Waals dimensions).

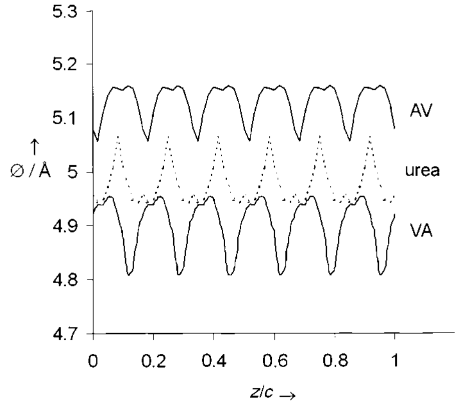

Figure 2. Channel diameter (∅) along the z axis in AV ($c = 10.027$ Å), VA ($c = 10.083$ Å), and urea ($c = 11.017$ Å).

Figure 3. The channel shape in AV (left) and VA (right) shown as a set of inscribed disks threaded on a sixfold screw axis. Two c-translation periods are shown for each dipeptide.

examined both as received and after recrystallization under a variety of conditions.[6] Only the porous forms of the materials were obtained in every case, as determined by powder XRD (PXRD). This observation reflects the fact that the structural motifs are governed by strongly directional H-bonding interactions rather than close packing. Therefore, dense forms of the materials are not easily obtained, or may not exist at all.

As materials that have permanent void space, it is worthwhile comparing AV and VA with the many varieties of zeolites—a large family of covalently bonded aluminosilicates assembled from a limited number of basic structural units.[14] Zeolites are kinetically stable with respect to the thermodynamically stable dense form, and they are widely used as sorbents, with porosities varying from about 18% (8 $cm^3 g^{-1}$) for analcime to about 53% (28 $cm^3 g^{-1}$) for faujasite.[2a] The porosity of the dipeptide materials was determined by comparing the density measured by He pycnometry with the density calculated from XRD unit cell measurements.[15] According to these determinations the volume fractions in the materials accessible to He gas were 11.7(3)% and 11.3(2)% for AV and VA, respectively. Similar values (11.4% and 10.4%) were calculated from the XRD results.[16] Taking into account the much lower density of the dipeptides, the capacity of the materials of about 11 $cm^3 g^{-1}$ falls into the range of values observed in practically useful zeolite materials.

A well-utilized property of zeolites is their ability to behave as molecular sieves, that is, they can distinguish between sorbate molecules differing in size as a result of the characteristic apertures that define the access to the internal void space. The channels in AV and VA, with average diameters of 5.13 and 4.90 Å, possess rather minor surface irregularities and are essentially hydrophobic, and therefore may exhibit a molecular-sieving effect. Since the materials displayed a high affinity towards Xe gas, we used it as the sorbate species to investigate the sorption behavior of the dipeptide materials.

The Xe adsorption isotherms were measured at room temperature for both AV and VA by using a combination of standard volumetric techniques and ^{129}Xe NMR spectroscopy.[17] It is quite remarkable that the two materials with such similar channel sizes show markedly different behavior towards Xe gas (Figure 4). Although the calculated sorption capacities are very similar (0.525(9) and 0.525(8) mol Xe per mol dipeptide for AV and VA, respectively), the sorption constants differ by a factor greater than four (0.120(5) and 0.52(2) bar^{-1} for AV and VA, respectively). The difference, in this case, should be attributable to a tighter binding between the host channel and the guest atom. With a van der Waals diameter of 4.4 Å, a Xe atom can interact more efficiently with the smaller channel in VA (4.90 Å) than with the larger channel of AV (5.13 Å). Although this size difference seems rather minor, it clearly has major consequences, and represents an example of molecular recognition based primarily on size-matching between the host and guest.

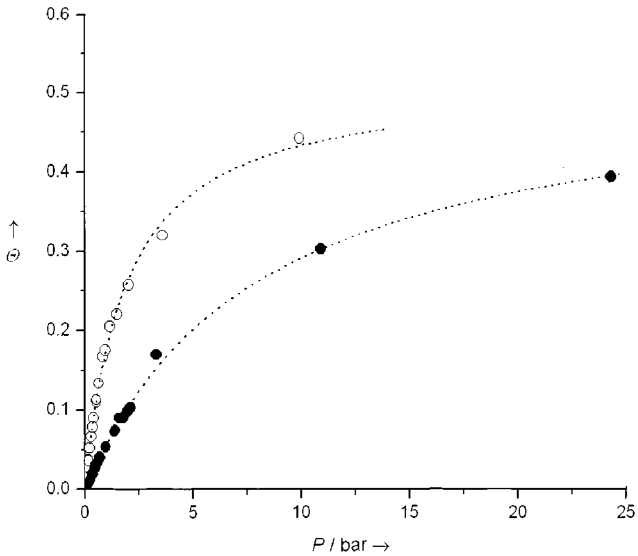

Figure 4. The sorption isotherms (298 K) of Xe in AV (solid circles) and VA (open circles) crystalline materials. Θ is the Xe/dipeptide molar ratio. The best-fit curves are drawn using a Langmuir equation.

The observed sorption capacity implies ideal compositions of AV$\supset$0.5Xe and VA$\supset$0.5Xe, that is, three Xe atoms per unit cell, or three Xe atoms per one *c*-translation. Taking the volume of a Xe atom to be 44.6 Å^3, the packing efficiency of the Xe atoms in the channels are 64.6 and 70.4 % for AV and VA, respectively. The total gas storage capacity of the materials is about 60 mL g^{-1}. For comparison, the gas storage capacity of a variety of recently designed metal-organic and organic sorbents is 9–52 mL g^{-1}.[18]

The studied materials showed significant thermal stability, as demonstrated by differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) experiments.[19] The dipeptides showed no decomposition, phase transitions, or mass loss up to their melting points of 238 °C (AV) and 213 °C (VA), followed by quantitative evaporation up to 270 °C.

Other potential applications of the current and related materials assembled from lower peptides are connected to their relevance to biological materials. Surprisingly, very few molecules, such as urea, gossypol, and deoxycholic acid, amongst the vast number of compounds utilized as hosts are known to arise from living organisms.[20] Dipeptides may be generated to form the entire family of bioorganic hosts and microporous solids:[5,21] The peptide materials are nontoxic and may be used in biological and medical contexts, such as in chiral recognition/separation or preservation/storage of drugs. Also, they may be extensively utilized to model, for example, transmembrane pores and ion channels,[4d] or the NMR spectroscopic signals of laser-polarized noble gases in proteins and living tissues.[22]

In conclusion, the dipeptides studied in this work have robust porous frameworks with a high capacity and the capability of preferential sorption, even towards chemically inert species such as Xe. Moreover, the new sorbents studied are constructed from natural organic materials and pose no environmental problems. This study suggests that a diverse variety of lower peptides with a propensity for forming frameworks with voids of different geometry should be considered as a promising new class of materials for potential applications where selective sorption/release or gas storage is important.

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[6] Crystallizations of AV and VA were performed from distilled water without using a template. Crystals suitable for single-crystal XRD analyses were obtained by evaporation of 0.3 M solutions at 60 °C. PXRD analyses indicated a total correspondence between the bulk products and the samples studied. The same single-crystal phase for each dipeptide, as confirmed by PXRD, was observed for the as-received samples (Sigma and ICN), solid products of fast crystallizations (evaporation in seconds at RT; evaporation over 2 h at 60 °C), very slow crystallizations (evaporation over 2 months at RT), and for crystals exhaustively equilibrated with their supernatant aqueous solutions (8 months at RT).

[7] Single-crystal XRD analyses: Bruker SMART CCD diffractometer, $\mathrm{Mo}_{K\alpha}$ radiation ($\lambda = 0.7107$ Å), crystal size $0.5 \times 0.07 \times 0.07$ mm (similar for AV and VA). The structures were solved with the SHELXTL programs (direct methods) and refined with full-matrix least-squares on F^2. CCDC-238397 (AV) and CCDC 238398 (VA) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

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[14] The diversity of zeolite structures results from the 16 identified “secondary structural units” which must be fitted together to give the combinations of channels and cavities which yield the repeat unit of the zeolite structures; see W. Meier, D. H. Olson, *Atlas of Zeolite Structure Types 2nd ed.*, University Press, Cambridge, **1987**; (the list of the units is given on p 5 therein).

[15] He pycnometry experiments were performed on an AccuPyc 1330 gas pycnometer (Micromeritics). Three samples (from different sources) of each dipeptide were measured several times (10 runs for each) till the results became stable. Typically, the first two measurements gave lower densities presumably because of blockage of the isolated channels by impurities (likely water in trace quantities; from TGA, the mass of possible absorbed sorbates was lower 0.5%). Average densities found for the “peptide framework body” were 1.169(4) $\mathrm{g\,cm^{-3}}$ and 1.157(3) $\mathrm{g\,cm^{-3}}$ for AV and VA, respectively (27 °C). Calculations performed as described in Ref. [1d] gave the following values (AV/VA): pore volume per unit cell, 212(6)/206(4) Å^3; pore volume fraction, 11.7(3)/11.3(2)%; average cross-section area of the channel, 21.2(5)/20.4(4) Å^2; average diameter of the channel, 5.2(1)/5.1(1) Å.

[16] The channel volumes were calculated from single-crystal XRD results by integration of the spatial figure composed of discs having diameters corresponding to the maximum-sized sphere that could be inscribed in the channel and centered on a given level along the crystallographic z axis.

[17] The intensity of the ^{129}Xe NMR signal in a known amount of material was monitored as a function of gas pressure and compared with that of a standard xenon sample to give the absolute amount of adsorbed xenon. The T_1 relaxation times of adsorbed xenon in the materials studied were found to be in the range of 50 to 80 s and care was taken to set the delays in the NMR experiments sufficiently long to ensure quantitative results. Equilibrium was reached typically in 2 h and the data were highly reproducable both when approaching equilbrium in the sorption or desorption modes. The sorption isotherms were approximated by a Langmuir equation, and the maximum sorption capacity and sorption constants were calculated as described in Ref. [1h].

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[19] DSC experiments were run on a TA 2920 calorimeter. Samples of approximately 4 mg were sealed in aluminum pans and heated at a rate of 5° $\mathrm{min^{-1}}$. TGA experiments were performed on a TA 2050 analyzer under flow of a N_2 at 50 $\mathrm{mL\,min^{-1}}$. Sample sizes were approximately 8 mg; heating rate 5° $\mathrm{min^{-1}}$.

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