**Permselective Crystals**

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# Dipeptide Crystals as Excellent Permselective Materials: Sequential Exclusion of Argon, Nitrogen, and Oxygen**

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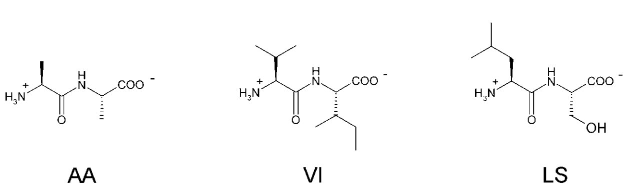
Gas storage and gas separation using porous solids are important technologies that have attracted great attention because of their environmental and energetic applications. Highly porous materials, such as zeolites, silicate, and carbon-based materials,[1] have long-established specific applications. The key for new applications is the development of new frameworks. Advances in gas sorption capacities were achieved through the synthesis of materials such as metal–organic frameworks (MOFs), organic polymers, and microporous organic crystals.[2] Recently, crystals formed by dipeptides were tested as adsorbents[3] with significant results in hydrogen absorption and methane purification from carbon dioxide.[3b]

Dipeptides can form microporous materials with channels of tunable size. Although the dipeptides self-assemble through a net of hydrogen bonds, the crystal matrix is conserved upon exchange of guest molecules. Moreover, crystalline dipeptides show a very high density of single-size micropores with very low tortuosity, which makes them excellent materials for storage or selective separation purposes. Finally, there is the remarkable feature that pores of crystalline dipeptides are perfectly aligned (along the crystallographic *c* axis), which indicates that they are excellent candidates for use as permeation-selective barriers.

Herein, we report for the first time the use of dipeptide crystals as permselective materials. Although this looks like an obvious engineering application for the kind of porous topology present in the crystals, there are issues that call for experimental support: 1) potential crystal defects, such as twinning or fractures, may greatly diminish their actual selectivity; and 2) the potential lack of rigidity of the crystal structure allows the pores to adapt to some extent to the size of the guest molecules. The dynamic behavior of the matrix of peptide crystals has already been observed by He picnometry and $^{129}$Xe NMR methods.[4]

We envisage the selective permeation of argon, nitrogen, and oxygen (the main components of air) through dipeptide crystals. This is a highly relevant industrial separation process and is also a very ambitious one given the similarity of the molecular sizes of the individual components.[5] The dipeptide crystals that were tested as single-crystal membranes were L-leucyl-L-serine (LS) (Scheme 1), L-valyl-L-isoleucine (VI), and L-alanyl-L-alanine (AA) crystals.



*Scheme 1.* Dipeptides used in this study.

The peptides were crystallized and their structures determined by X-ray diffraction (Figure 1). The structures of all three peptides had been resolved previously.[6] The VI crystal packing has hexagonal symmetry with molecules forming helices with six dipeptides per turn. LS crystals have a unique crystal packing with the inner walls formed by leucine side chains and with right-handed helicity. AA packs in the tetragonal space group *I*4 and the crystal arrangement is characterized by the segregation of the hydrophobic methyl groups into columns.

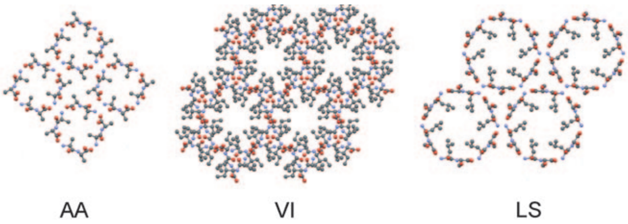


*Figure 1.* Crystal structures of the dipeptides viewed along the crystallographic *c* axis.

The calculated void volumes in the three crystal structures that are accessible to He, the molecule with the smallest kinetic diameter (2.6 Å), are shown in Figure 2.[7] LS and VI contain nanochannels while AA should be considered nonporous. The average channel diameters of LS and VI are displayed in Table 1.

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***Figure 2.*** Void volumes of the crystal structures of AA, VI, and LS that can hold a spherical "probe" with a diameter of 2.6 Å.

***Table 1:*** Dipeptide crystal permeabilities and selectivities towards He, $O_2$, $N_2$, and Ar.

| Dipeptide | Channel diameter [Å][a] | Permeabilities [Barrer] | | | | Selectivities[b] | | |
|---|---|---|---|---|---|---|---|---|
| | | He | $O_2$ | $N_2$ | Ar | $\alpha(O_2/N_2)$ | $\alpha(O_2/Ar)$ | $\alpha(O_2/He)$ |
| LS | 4.9/4.3 | $1.7\times10^7$ | $9.5\times10^6$ | $1.1\times10^7$ | $1.2\times10^7$ | 0.86 | 0.79 | 0.56 |
| VI | 3.7/3.0 | $2.8\times10^4$ | $2.7\times10^3$ | $2.2\times10^3$ | n.d.[c] | 1.2 | $>135$[c] | 0.096 |
| AA | –/– | 19 | 31 | n.d.[c] | n.d.[c] | $>124$[c] | $>124$[c] | 1.6 |

[a] Calculated from the crystal structure/reported in reference [4] based on He pycnometry. [b] Calculated from single-crystal monocomponent permeation experiments. [c] Not detected. The minimum permeate flow rate that can be accurately measured in the setup is ca. 0.0005 $mm^3\,h^{-1}$, which corresponds to permeabilities of 0.25 Barrer (AA crystals) and 20 Barrer (VI crystals).

The LS, VI, and AA single-crystal permeabilities towards $O_2$, $N_2$, Ar, and He were determined at room temperature (Table 1). The LS crystals are permeable to all the gas molecules and the respective selectivities are low, probably because the channel size is much bigger than the van der Waals diameter of the guest molecules.

Thus, we decided to test VI crystals because they display narrower channels. We observed that VI crystals are permeable to $O_2$ and $N_2$ but not to Ar (Table 1). However, the selectivity achieved for the $O_2/N_2$ (1.2) separation is too low to be of any practical significance, which prompted us to search for dipeptides forming smaller pores. The lower limit of pore diameters of dipeptide crystals is approximately 3 Å.[4,8] Still, we decided to study the AA crystals. Despite the fact that the pores are too small, the dynamics of the crystal matrix had never been investigated.

Remarkably, it was observed that the AA crystals are permeable to $O_2$ but not to $N_2$ or Ar (Table 1). The permeability of the AA crystals towards the smaller He molecules is lower than that towards $O_2$, which indicates that the host crystal matrix seems to respond individually to each particular guest molecule.

The unexpected penetration of guest molecules into too narrow pores had already been noticed in three other dipeptide crystals and attributed to the flexibility of the crystal framework.[4] Moreover, the experimental determination of the porosity of eight crystalline dipeptides (AV, VA, AI, VV, IA, IV, VI, and LS) showed that two, AV and VA, undergo pore-size expansion upon gas sorption.[4] It was suggested that in the VA class, there are backbone vibrational modes that contribute to the pore permeability.[9]

Despite the fact that irreversible changes were found with AV, VA, and AI crystals,[10] the flexibility of the AA packing seems to be reversible. The AA crystals remained non-permeable to $N_2$ after the $O_2$ experiments, and there was full retention of the crystal structure after 2 months of permeation experiments. Interestingly, traces of oxygen molecules are found in the channels at a pressure of 8.5 bar of pure oxygen (Figure 3).

There are four symmetry-equivalent positions for oxygen molecules in each vacancy void volume. The transport may be described in terms of hopping diffusion along the vacancy void volumes that are limited by the four methyl groups (Figure 3). The total $O_2$ occupation per void volume (0.018) can be obtained from the adsorption isotherm.

Adsorption isotherms of the penetrating gas species were measured at room temperature (Figure 4). LS shows negligible sorption selectivities towards Ar, $N_2$, and $O_2$, thus confirming that the channels are too large to discriminate between the species. In the case of VI, the $O_2/N_2$ selectivity is already noticeable, which corroborates the fact that the channel size closely matches the size of the gas molecules. The $O_2$ adsorption capacity of AA is marginal, thus reflecting the small void volume of the crystals.

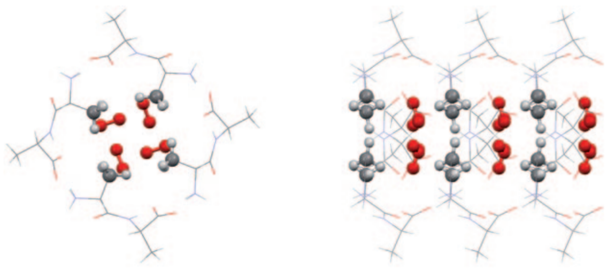

***Figure 3.*** Crystal structure of AA with $O_2$ viewed along the *c* axis (left) and along the *b* axis (right). Highlighted are the oxygen molecules trapped inside the pores and the Ala side chains that form the pore constrictions.

Although it is known that the Knudsen model does not apply to micropores,[11] it is interesting to observe that the measured gas flow through the LS channels significantly exceeds Knudsen diffusion predictions (see the Supporting Information). Very fast air flow rates had already been observed through 1.6 nm carbon nanotubes and was attributed to the smoothness of the carbon pore walls.[12] Apparently, the weak nature of the interactions produced by the methyl groups that decorate the LS channel walls also allows high gas flow rates.

A breakdown in the mass transport rate arises from the size matching between the guest molecules and channel diameters, as shown by the drastic decline of the VI and AA permeabilities (Table 1). The decrease in the gas sorption

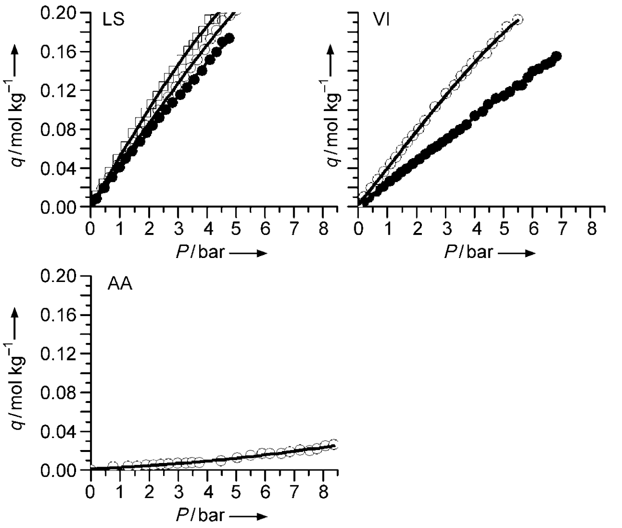

*Figure 4.* Adsorption isotherms of argon (□), nitrogen (●), and oxygen (○) in LS, VI, and AA at 295 K.

equilibrium, in particular for AA, and the reduction in the gas diffusivities certainly combine to produce such a strong drop in the permeabilities.

In conclusion, separations of practical significance are primarily obtained by size exclusion, and crystalline dipeptides are indeed able to behave as excellent permselective materials. In this work, we discovered that AA crystals show extremely high $O_2/N_2$ selectivities, well above those of polymeric[13] and carbon-based materials.[14] The variety of dipeptides available may find potential application in many important gas separation processes, including that of light gases with very similar molecular sizes. This class of materials can be very useful in the fabrication of gas sensor devices and microreactors. Moreover, the incorporation of the dipeptides in bulk materials for industrial membrane gas separations should not be overlooked.

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