Journal of the American Chemical Society is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

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COMMUNICATIONS

Chiral Permselectivity in Surface-Modified Nanoporous Opal Films

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The past decade has seen an increasing interest in the preparation of enantiomerically pure compounds, including chiral drugs.[1] Despite impressive advances in stereoselective synthesis, separation of racemic mixtures (e.g., by crystallization or chromatography) is presently the most widely used method of producing single enantiomers in industry, but it is labor, material, and energy intensive. Membrane separations provide an attractive alternative as they can potentially alleviate all three of these shortcomings. Presently used chiral membranes usually consist of a nonselective porous support coated with a chiral polymer.[2]

To be practical, chiral membranes require high molecular flux and high selectivity. Nanoporous opal membranes may provide an ideal medium for chiral separations. Recently, we reported surface-modified opal films characterized by high cation permselectivity and high molecular throughput.[3,4] To demonstrate that an opal film can work as a chiral permselective membrane, we modified the surface of the silica spheres comprising the film with a chiral selector moiety[5] (**1**) and studied transport of chiral molecules through the resulting chiral opal films.

Electrochemical methods allow characterizing permselectivity in films deposited on an electrode surface by measuring the molecular flux as a function of the film structure.[6] Recently, such a technique has been applied to investigating the chiral selectivity of a polyelectrolyte film.[7] To apply cyclic voltammetry to the investigation of the chiral permselectivity in opal films, we assembled thin opal films on the surface of glass-shrouded 25 μm diameter Pt microelectrodes as previously described.[3] We used a 1.5 wt % colloidal solution of monodisperse 200 nm silica spheres (Figure SI1),[8] which resulted in 7 μm films containing ca. 35 layers of silica spheres (Figure 1). Chiral opal films **2** were prepared[9] by first modifying the silica sphere surfaces with amines using (3-aminopropyl)triethoxysilane,[3] followed by treatment with the dry THF solution containing chiral selector **1**[5] (Scheme 1). The surface coverage of the silica spheres modified with the chiral selector moiety in a colloidal solution under the conditions used for the opal film modification[9] was determined by UV spectroscopy (after dissolving the modified silica spheres[9]) to be ca. 7 chiral moieties per nm^2. This value, which is 2 times higher than the typical number of hydroxyl groups on silica surface,[10] likely reflects the formation of a thin polymeric film during the amine modification of the silica spheres.[3]

To probe the permselectivity of the chiral opal films, we prepared both *R* and *S* enantiomers of three ferrocene derivatives (**3**−**5**, Chart 1) following the published procedure.[11] We then measured the flux of these chiral molecules across the opal films in quasi-steady-state voltammetric experiments. Figure 2 shows the overlay of voltammetric responses at the dichloromethane solutions of **3R** and **3S** (0.1 mM) and 0.1 M tetrabutylammonium hexafluorophosphate (TBAFP) as supporting electrolyte for the opal electrode before and after its modification with **1R** or **1S**.

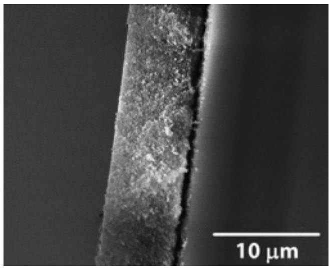


Figure 1. SEM image of the cross-section of the opal film prepared from 200 nm diameter silica spheres deposited on a glass slide under the conditions used to produce the opal film electrodes.[9]

Scheme 1

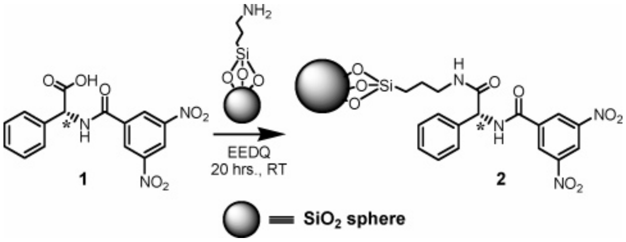
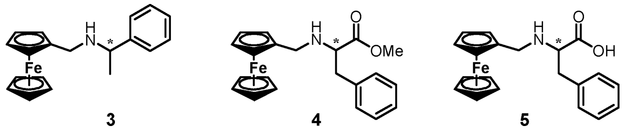


Chart 1



3 **4** **5**

The voltammetric response of the Pt electrode coated with unmodified opal film for each enantiomer of **3** (Figure 2A) displays a sigmoidal shape characteristic of radial transport to a microelectrode.[12] The limiting current (i_{lim}) corresponding to the one-electron reduction of **3R** and **3S** is virtually identical for both enantiomers and is only ~50% smaller compared to that for the bare Pt microelectrode. This drop in the limiting current is due solely to geometrical effects of the tortuous path the molecules take when diffusing through the opal lattice, and its magnitude clearly demonstrates the high molecular throughput in the opal film. Amine modification of the opal films did not reduce the limiting current further,[3] nor did it introduce permselectivity.

Chiral permselectivity is readily apparent in the voltammetric response of the opal electrode after covalent attachment of **1R** to the amine-modified silica spheres.[9] The voltammetric limiting current, i_{lim}, is diminished for both **3R** and **3S** (Figure 2A), but i_{lim} for the one-electron oxidation of **3R** is ca. 2 times smaller compared to that of **3S** (Figure 2B). This result is consistent with both *R* and *S* enantiomers strongly interacting with the chiral selector moieties on the silica spheres' surface, but to a different extent, leading to selective transport of the *S* enantiomer through the chiral opal film compared to the *R* enantiomer. The selectivity observed for **3** is comparable to that reported for transport of enantiomers in antibody-modified nanotube membranes[13] and higher than selectivity reported for optically active polyelectrolyte membranes.[7] We obtained a

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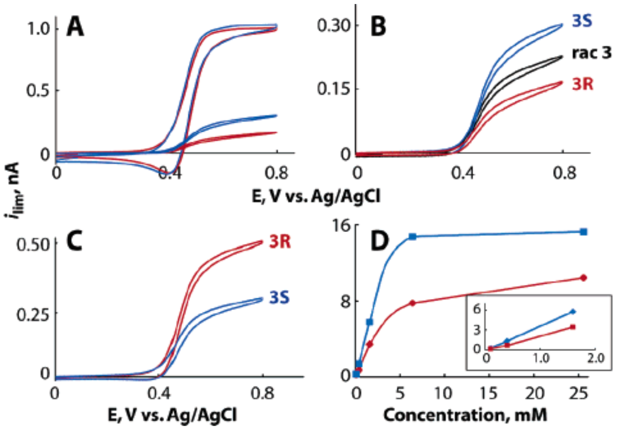

Figure 2. (A) Overlay of voltammetric responses of a Pt electrode for **3S** (blue) and **3R** (red) after opal film assembly (top) and after its modification with **1R** (bottom). (B) Expanded overlay for the opal film electrode modified with **1R**. (C) Expanded overlay for the opal film electrode modified with **1S**. (D) Limiting current as a function of concentration of **3S** (blue) and **3R** (red) for an opal film electrode modified with **1R**.

Table 1. Selectivities of the Chiral Opal Electrodes for Chiral Probes **3**−**5**

probe	$i_{lim}(S)/i_{lim}(R)$	
	1R opal film	**1S** opal film
3	2.16 ± 0.34	0.58 ± 0.01
4	1.33 ± 0.20	0.82 ± 0.11
5	2.01 ± 0.69	0.84 ± 0.04

similar selectivity for enantiomers of **3** using opal films assembled from 440 nm diameter silica spheres and modified with **1R** (Figure SI2).

To further confirm that the chiral permselectivity results from stereospecific interactions with the surface-bound chiral selector moieties, we modified opal films with the *S* enantiomer of **1**, which led to a reversed selectivity, where the limiting current for **3S** became smaller than that for **3R** (Figure 2C, Table 1). Opal films modified with racemic **1** showed no selectivity for **3R** and **3S** with the limiting current reduced equally for both enantiomers. Finally, the limiting current for racemic **3** was the average of the limiting currents for **3R** and **3S** (Figure 2B). We repeated the above experiments with six different electrodes, obtaining semiquantitative reproducibility in the absolute and relative changes in $i_{\rm lim}$ following deposition of the opal and chiral modification of the silica surface (Table 1), while selectivity for a given electrode remained virtually identical after storing electrodes for a month.

We investigated the transport through the chiral-modified opal film for two more chiral molecules (**4** and **5**) and, in both cases, found chiral permselectivity that was reversed with the reversal of the surface chirality (Table 1), although the selectivities of *R*- and *S*-modified opal films were not equal, a phenomenon that has been reported for chiral stationary phases used in liquid chromatography.[14]

To gain an insight into the mechanism of chiral permselectivity in opal films, we studied the dependence of the flux and selectivity on the concentration of **3** in the 0.1−25 mM range. We found that at low concentrations the molecular flux increases linearly with the concentration of **3** and flattens at higher concentrations (Figure 2D). This suggests that permselectivity in the chiral opal films is governed by surface transport in a way similar to that demonstrated in polymer membranes[7,15] and surface-modified nanotubes.[13] Such permselectivity relies on the noncovalent binding between the chiral permeant molecules and the surface receptors, which results in a stronger bound enantiomer moving faster through the chiral medium. According to the facilitated surface transport theory,[16] the highest selectivity is expected at the lowest permeant concentrations. Indeed, the chiral permselectivity in the opal film remains nearly constant (ca. 2.0) at low concentrations and decreases to 1.5 at the highest concentration.

The limiting current of ferrocene for the opal electrode decreases by ca. 75% upon opal film modification with **1R** (Figure SI3). Assuming that there is little interaction between ferrocene and the chiral selector moieties,[14] this drop in $i_{\rm lim}$ may be attributed to the nanopore size reduction as a result of surface modification. Using the relationship between the limiting current and opal void fraction,[12,17] and straightforward geometrical considerations,[18] the nanopore size inside the chiral opal film can be estimated, based on the $i_{\rm lim}$ decrease, as 6.4 nm, compared to 16 nm for the unmodified opal film. The relatively small pore size, combined with a polymeric film containing the chiral selector moieties on the silica sphere surfaces, makes surface-facilitated transport a likely mechanism. Chiral opal films described in the present work are only 7 μm thick, which leads us to believe that their chiral permselectivity is enhanced by the tortuous pathway within the opal and by the high surface area of the modified spheres.

The above preliminary experiments demonstrate two properties of opal-based chiral membranes that are important in enantioselective separations: (i) high chiral selectivity and (ii) high molecular throughput. We are presently working on further elucidating the chiral selectivity mechanism and on applying the chiral opal membranes to electrochemical resolution of enantiomers at a preparative scale, as well as chiral separations using suspended opal membranes.[19]

Acknowledgment. This work was supported by the ACS Petroleum Research Fund. I.Z. is grateful to the Camille and Henry Dreyfus Foundation for a New Faculty Award.

Supporting Information Available: Details of experimental procedures and electrochemical measurements. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) http://www.fda.gov/cder/guidance/stereo.htm (accessed April 2006).
(2) *Chiral Separation Techniques. A Practical Approach*; Subramanian, G., Ed.; Wiley-VCH: New York, 2001.
(3) Newton, M. R.; Bohaty, A. K.; White, H. S.; Zharov, I. *J. Am. Chem. Soc.* **2005**, *127*, 7268−7269.
(4) Newton, M. R.; Bohaty, A. K.; White, H. S.; Zharov, I. *Langmuir* **2006**, *22*, 4429−4432.
(5) Pirkle, W. H.; House, D. W.; Finn, J. M. *J. Chromatogr.* **1980**, *192*, 143−158.
(6) Redepenning, J.; Anson, F. C. *J. Phys. Chem.* **1987**, *91*, 4549−4553.
(7) Rmaile, H. H.; Schlenoff, J. B. *J. Am. Chem. Soc.* **2003**, *125*, 6602−6603.
(8) Ströber, W.; Fink, A.; Bohn, E. *J. J. Colloid Interface Sci.* **1968**, *26*, 62−69.
(9) See Supporting Information.
(10) Jal, P. K.; Patel, S.; Mishra, B. K. *Talanta* **2004**, *62*, 1005−1028 and references therein.
(11) Hess, A.; Sehnert, J.; Weyhermueller, T.; Metzler-Nolte, N. *Inorg. Chem.* **2000**, *39*, 5437−5443.
(12) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods: Fundamentals and Applications*, 2nd ed.; Wiley: New York, 2001.
(13) Lee, S. B.; Mitchell, D. T.; Trofin, L.; Nevanen, T. K.; Söderlund, H.; Martin, C. R. *Science* **2002**, *296*, 2198−2200.
(14) Pirkle, W. H.; Pochapsky, T. C. *Chem. Rev.* **1989**, *89*, 347−362.
(15) Farhat, T. R.; Schlenoff, J. B. *J. Am. Chem. Soc.* **2003**, *125*, 4627−4636.
(16) Lakshmi, B. B.; Martin, C. R. *Nature* **1997**, *388*, 758−760.
(17) Cussler, E. L. *Diffusion. Mass Transfer in Fluid Systems*, 2nd ed.; Cambridge University Press: New York, 1997.
(18) Schepelina, O.; Zharov, I. *Langmuir*, submitted for publication.
(19) Bohaty, A. K.; Zharov, I. *Langmuir*, accepted for publication.

JA062672G