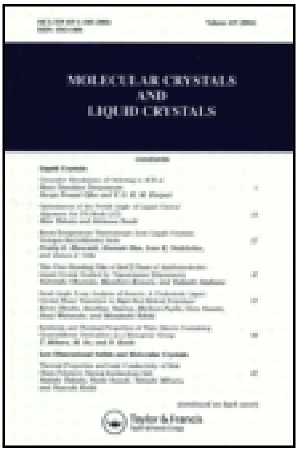

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Molecular Imprinting in Crosslinked Polymers - The Role of the Binding Sites

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MOLECULAR IMPRINTING IN CROSSLINKED POLYMERS - THE ROLE OF THE BINDING SITES

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Abstract Highly selective microcavities are formed in crosslinked polymers by polymerizing around a molecule that acts as a template and subsequently removing this template. The function of the binding sites within the cavities is discussed more in detail.

INTRODUCTION

Molecular recognition plays an important role in biological activity, e.g. in receptors, enzymes, and antibodies. Chemists have also tried to prepare systems with high selectivity. In many cases, low molecular weight ring or cage systems such as crown ethers, cryptates, cyclodextrins, cyclophanes or concave molecules are used.[1] Using a conceptually simpler process, similar cavities can be formed in synthetic polymers. With the aid of template molecules specific micro-cavities are created by an imprinting technique in crosslinked polymers.[2-5]

In this case, polymerizable binding-site groups are bound by covalent or noncovalent interactions to a suitable template molecule (see Fig. 1). This template monomer is copolymerized in the presence of a high amount of cross-linking agent. After splitting off of the template molecule from the polymer, microcavities are obtained having a shape and an arrangement of functional groups corresponding to an imprint of the template. If there is sufficient cross-linking, the polymer chains are in a fixed arrangement and the cavities retain their structure. The binding sites in this polymer are located at quite different points along the polymer chain, and they are held in a fixed spatial relationship with respect to one another by the cross-linking.

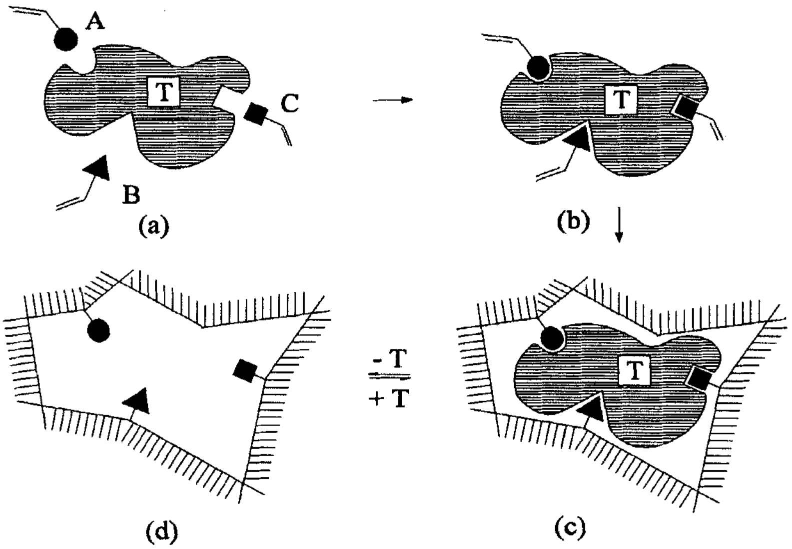
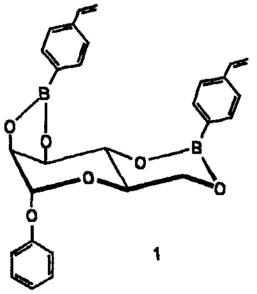


FIGURE 1 The preparation of defined functional cavities by an imprinting approach.

An Example of the Imprinting Procedure

As an example of the preparation of cavities with a defined arrangement of binding-site groups and with a predetermined shape, the polymerization of **1** is considered.



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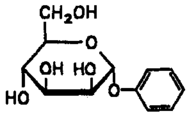

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Phenyl-α-D-mannopyranoside (**2**) acts as the template. Two molecules of 4-vinylphenylboronic acid are bound to the template molecule by esterification with each pair of hydroxyl groups. The boronic acid was chosen as the binding-site group because it undergoes an easily reversible interaction with diol groupings. The template molecule **2** is chiral and optically active, and for this reason the cavities produced should be chiral as well. Therefore, after cleavage of the original template, the accuracy of the steric arrangement of the binding sites in the cavity could be tested by the ability of the polymer to resolve the racemate of the template. The monomer **1** has been extensively used for the optimization of the imprinting method.

The monomer **1** was copolymerized by free-radical initiation in the presence of an inert solvent (porogenic agent) with a large amount of a bifunctional cross-linking agent. Under these conditions, macroporous polymers possessing a permanent pore structure and a high inner surface area were obtained. These polymers therefore exhibited good accessibility and low swelling characteristics and hence a limited mobility of the polymer chains.

The template can be split off by water or methanol to an extent of up to 95% (see Fig. 2). When this polymer is treated with the racemate of the template in a batch procedure under equilibrium conditions, the enantiomer that has been used as the template for the preparation of the polymer is taken up preferentially. If the specificity is expressed by the separation factor α, which is the ratio of the distribution coefficients of D- and L-forms between solution and polymer, α values ranging from 1.20 to 6.0 were obtained, depending on the equilibrium conditions and the polymer structure. Values of α as high as 6.0 result in the simple batch procedure with a maximal enrichment of the D-form at the polymer to the extent of 70-80 %ee.

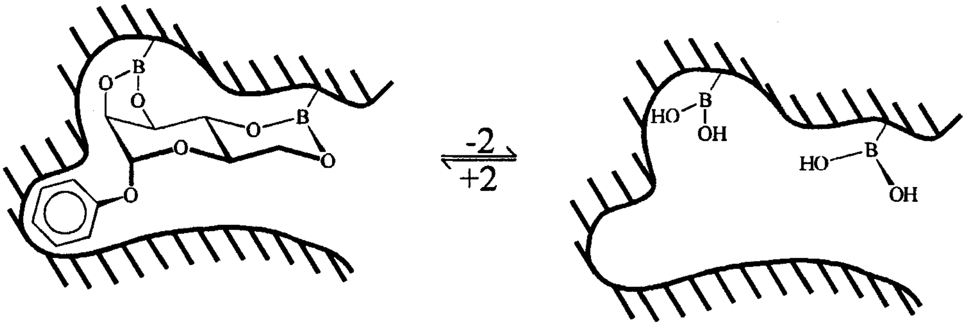

FIGURE 2 Schematic representation of a cavity obtained by polymerization of **1**. Removal of the template by water or methanol yields free cavities.

Polymers obtained by this procedure can be used for the chromatographic separation of the racemates of the template molecules.[6,7] The selectivity of the separation process is fairly high (separation factors up to $\alpha = 4.6$) and at higher temperature with gradient elution, resolution values of $R_S = 4.2$ with base line separation have been obtained (see Fig. 3). These sorbents can be prepared conveniently and possess excellent thermomechanical stability. Even when used at 80°C under high pressure for a long time, no leakage of the stationary phase nor decrease of selectivity during chromatography was observed.

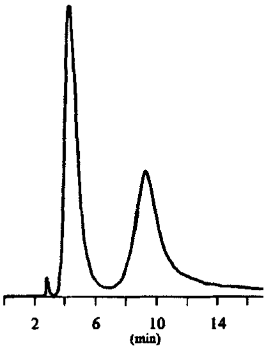

FIGURE 3 Chromatographic resolution of D,L-**2** on a polymer imprinted with **1**.

Apart from using sugar derivatives as templates with this method amono acids, hydroxy carboxylic acids, diols and other racemates have been separated.[5] Furthermore it has been possible to localize two amino groups in a defined distance at the surface of silica with this method.[5] These materials bind strongly by a cooperative binding dialdehydes or diacids in those cases where the functional groups have the correct distance from each other.

Other research groups in the meanwhile have also been working on molecular imprinting in crosslinked polymers.[5,8-10] By using a variety of different templates and binding site groups the scope of the method has been enlarged. The group led by Mosbach[8,10] concentrated on non-covalent interactions during polymerization and chromatography. In this way they were able to completely resolve derivatives of amino acid racemates.

The Role of the Binding Sites

In the imprinting procedure the binding groups have several functions.[5] On the one hand, the bond between the template and the binding group should be as strong as possible during the polymerization. This enables the binding groups to be fixed by the template in a definite orientation at the polymer chains during the cross-linking polymerization. It should then be possible to split off the templates as completely as possible. A very important function is then the interaction of the binding groups with the substrates to be bonded, for example, with the compound that acted as the template. This interaction should take place as rapidly and reversible as possible, so that the chromatographic process or catalysis will be rapid. Thus, although a high activation energy is desirable for the first function, it should be as low as possible for the two other functions. Interactions can be covalent or noncovalent. Covalent interactions have the advantage that the binding groups are precisely fixed in space during the polymerization. If it is possible to split off a high percentage of the templates and to strongly accelerate the interactions with substrates by catalysis, covalent interactions are very suitable. The same is true for templates fixed by metal coordination interaction. With noncovalent interactions, a considerable excess (usually four-fold) of binding groups is required in the polymerization mixture so that the binding sites in the template are completely saturated at equilibrium. In this way, a considerable proportion of the binding groups are incorporated randomly. On the other hand, the template is usually very easy to split off, and the reversible interactions with substrates are in principle rapid. The structure of the template molecule determines which interactions are the most favorable in the specific case. When producing chromatographic materials, noncovalent interactions are usually favorable, as the materials are more readily obtainable, and an excess of binding groups does apparently not have a detrimental effect on the selectivity of separations. For the construction of catalysts, the orientation of the binding groups and catalytically active groups in the cavity are of greater significance, so that covalent interactions should be more advantageous here.

CONCLUSION

Generation of imprinted sites in polymers and other materials including surfaces has now reached a high degree of sophistication. The applications of these materials are becoming more and more interesting. Such materials could in the near future find application as artificial antibodies, chemosensors, and catalysts. Practical application is particularly evident in the chromatographic resolution of racemates. The following problems are in the forefront of investigation today:

1. When high molecular weight biopolymers such as proteins, glycoproteins etc. have to be used as templates, special methods must be used. Surface imprinting is likely to be a useful solution here.
2. To enable a broader range of substrates to be used for imprinting, a wider array of binding groups must be developed which are specific for interaction with particular functional groups.

3. In spite of considerable improvement of the mass transfer in imprinted polymers, an acceleration of the attainment of equilibrium in the embedding of the substrate in cavities with two-point bonding is desirable.
4. It would be very useful if the selectivity differences between individual cavities ("polyclonality") could be further minimized.
5. For preparative chromatography, it is important to further increase the capacity of the columns. For this, it is important, if noncovalent interactions are used for the imprinting, to significantly increase the proportion of cavities that can be refilled.
6. An important simplification of the chromatographic process would be achieved if compounds could be directly separated without first forming derivatives.
7. When imprinted polymers are used as chemosensors, extremely sensitive methods are required fro the detection of substances bound to the imprinted membrane.

REFERENCES

1. See e.g. F. Vögtle, Supramolecular Chemistry (Wiley, New York, 1991); J.-M. Lehn, Supramolecular Chemistry (VCH, Weinheim, 1995).
2. G. Wulff, A. Sarhan, and K. Zabrocki, Tetrahedron Lett., 4329 (1973).
3. G. Wulff, W. Vesper, R. Grobe-Einsler, and A. Sarhan, Makromol. Chem., 178, 2799 (1977).
4. G. Wulff and S. Schauhoff, J. Org. Chem., 56, 395 (1991).
5. For comprehensive reviews see: G. Wulff, in Polymeric Reagents and Catalysts, edited by W. T. Ford (ACS Symp. Ser., 308, Washington, 1986), p.186. G. Wulff, Angew. Chem., 107, 2018 (1995); Angew. Chem. Int. Ed. Engl., 34, (1995), in press.
6. G. Wulff and M. Minárik, J. High Resolut. Chromatogr. Chromatogr. Commun., 9, 607 (1986).
7. G. Wulff and M. Minárik, J. Liqu. Chromatogr., 13, 2987 (1990).
8. B. Sellergren, M. Lepistö, and K. Mosbach, J. Am. Chem. Soc., 110, 5853 (1988).
9. K. J. Shea, Trends Polym. Sci., 2, 166 (1994).
10. K. Mosbach, Trends Biochem. Sci., 19, 9 (1994).