Use of Polymeric Catalysts in the Pore-Size-Specific Functionalization of Porous Polymers

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*Received April 22, 1993; Revised Manuscript Received July 19, 1993**

ABSTRACT: The size-restricted access of molecules to cavities of different sizes has been used in the demonstration of size-selective modification of a porous material. The epoxide functionalities of macroporous poly(glycidyl methacrylate-*co*-ethylene dimethacrylate) beads are hydrolyzed to diol groups in the presence of an acid catalyst. While sulfuric acid catalyzes hydrolysis of all epoxide groups, bulkier catalysts such as poly(styrenesulfonic acid) only cause hydrolysis to occur within pores large enough to accommodate them. As a result, porous materials containing two types of functionalities segregated respectively in pores larger and smaller than the catalyst are obtained. Similar size-specific functionalization has been achieved with macroporous beads containing benzylidene or tetrahydropyranyl ether groups.

Introduction

Size specificity is one of the leading principles of nature. Therefore, cell membranes allow the permeation of small molecules in and out of the cell body while large molecules cannot cross the interface. The principle of size exclusion has been adopted in numerous processes from sieving to advanced membrane technologies. Size exclusion is also employed in chromatographic separations, with a first report of gel filtration, now known as size-exclusion chromatography (SEC), appearing in 1959.[1] Further progress in SEC came in 1964 with the introduction of rigid macroporous poly(styrene-*co*-divinylbenzene) beads by Moore.[2] Meanwhile, SEC has become a universal tool for the separation of molecules according to their hydrodynamic sizes and is used extensively in chemistry, biology, bioengineering, medicine, etc.[3]

In general, porous polymers are prepared by the copolymerization of only a very small number of monomers such as styrene, vinylpyridine, acrylamide, or glycidyl methacrylate and cross-linking agents such a divinylbenzene, ethylene dimethacrylate, or bis(acrylamide). This is due to two main reasons: the lack of commercial availability of most other functional monomers and the fact that changes in polymer composition during copolymerization may drastically affect the physical properties of the copolymers that are obtained. While the monomers and cross-linkers listed above are not immune to composition changes during their copolymerization if their reactivity ratios and monomer feed are not perfectly matched, much is known on the physical properties of the resulting copolymers.[4] Therefore, access to a broad spectrum of pore surface chemistries is usually achieved through the chemical modification of a few standard copolymers.

The classical chemical modification of an insoluble porous polymer is typically controlled by kinetics factors, such as the concentration of the reagent, the reaction time and temperature, the rate of diffusion, the existence of neighboring group effects, etc.[4] It is not generally possible to direct the reaction to specific sites or selected regions of a porous polymer. Although reactions of groups exposed in the most readily accessible parts of the porous polymer are preferred, the modification process only stops after all available groups are consumed.

* Abstract published in *Advance ACS Abstracts*, September 1, 1993.

Table I. Properties of Uniformly Sized Porous Poly(glycidyl methacrylate-*co*-ethylene dimethacrylate) Beads

	bead		
	G-1	G-2	G-3
partizle size, μm	10	10	10
epoxide groups, mmol/g	2.7	2.1	2.0
specific pore volume,[a] mL/g	1.1	1.0	1.0
median pore diameter,[a] nm	13.8	7.0	
median pore diameter,[b] nm	10.9	6.4	4.6
polystyrene exclusion limit[a] (MW)	240 000	77 000	31 000
specific surface area,[b] m^2/g	114	26	>1

[a] Determined from inverse size-exclusion chromatography results.[9] [b] BET measurement.

Almost all porous polymers are characterized by a relatively broad pore size distribution. Typically,[3] they contain micropores smaller than 2 nm in diameter, mesopores with sizes in the range from 2 to 50 nm, and macropores with diameters larger than 50 nm. The pores are, in fact, irregular voids between clusters of globules (macropores), voids between globules in a cluster (mesopores), or voids inside a globule (micropores). All pores in such a porous material are typically interconnected.[4] Access to the different pores is controlled by the hydrodynamic volume of the dissolved molecules. Molecules will only penetrate those pores that are able to accommodate their size, while smaller pores remain inaccessible for steric reasons. This concept is also at the basis of the technique of size-exclusion chromatography.[5]

The size-restricted access of molecules to porous structures may be used in the design and preparation of a new generation of porous materials[6] in which functionalization of the pore surfaces is carried out in a size-specific manner that allows the introduction of different surface chemistries within well-defined areas of a single porous object. This report describes the use of polymeric catalysts with defined molecular sizes in the size-specific modification of porous materials.

Experimental Section

Polymer Beads. Three different samples of uniformly sized 10-μm porous 60:40 vol % glycidyl methacrylate–ethylene dimethacrylate copolymers (resin I; samples G-1, G-2, and G-3) each with a different but controlled pore size distribution were prepared by a modified shape template swelling and polymerization method described in detail elsewhere.[7] Table I lists the characteristics of the various porous beads. The specific surface

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Table II. Percentage of Remaining Epoxide Groups in Porous Poly(glycidyl methacrylate-*co*-ethylene dimethacrylate) Beads after Hydrolysis Catalyzed by Various Acids[a]

catalyst	M_w	M_w/M_n	% epoxide remaining G-1	G-2	G-3
sulfuric acid	100		0	0	0
4-toluenesulfonic acid	172		8	6	11
PSSA 5[b]	5 000	1.09	45	57	68
PSSA 47[b]	47 300	1.05	64	81	88
PSSA 400[b]	400 000	1.1	81	96	97
PSSA 1200[b]	1 200 000	1.1	89	98	97
PSSA 8	7 800	1.22	40	55	62
PSSA 141[c]	141 000	1.7	65	83	90

[a] Reaction conditions: beads, 200 mg; catalyst solution, 10 mL (0.1 mol/L of H_2SO_4, 0.1 mol/L of 4-toluenesulfonic acid, or 1 wt % poly(styrenesulfonic acid) in water); 48 h at room temperature. [b] Data reported by the manufacturer (Scientific Polymer Products, Inc.). [c] Molecular weight reported by the manufacturer (Polyscience) is 70 000.

areas were calculated from a BET isotherm of nitrogen sorption and desorption (combined BET sorptometer and mercury porosimeter, Porous Materials Inc., Ithaca, NY). Epoxide group contents were determined by volumetric titration as follows: the beads were dispersed in a 0.1 mol/L tetraethylammonium bromide solution in acetic acid and titrated with a 0.1 mol/L perchloric acid solution in acetic acid until the crystal violet indicator indicated the blue–green end point.[8]

Polymeric Catalysts. The characteristics of the poly(styrenesulfonic acids) (PSSA) used in this work are summarized in Table II. PSSA 8 was prepared by polymerization of styrenesulfonic acid butyl ester followed by a base-catalyzed hydrolysis.[9] Styrenesulfonic acid butyl ester was prepared by the reaction of styrenesulfonic acid chloride with 1-butanol. The molecular weight distribution of the butyl ester was determined by size-exclusion chromatography calibrated with polystyrene standards in THF using three Polymer Laboratories columns (500 Å, 50 Å, and mixed gel), a refractive index detector, and THF at a flow rate of 1 mL/min. PSSA 141 with a broader molecular weight distribution was purchased from Polyscience, and its molecular weight distribution was determined after esterification to poly(styrenesulfonic acid butyl ester). Sodium salts of PSSA narrow molecular weight distribution standards were obtained from Scientific Polymer Products, Inc. (Ontario, NY). Prior to their use, the PSSA sodium salts were converted to the free acids by an ion exchange process using a AG 50W-X strong acid cation exchanger (Bio Rad, Richmond, CA).

Polymer Bead Modifications. Hydrolysis. Total hydrolysis of the epoxide groups of **I** into vicinal diol groups proceeds under catalysis with mineral acid.[10] Resin **I** (10 g) was suspended in 50 mL of a 0.1 mol/L aqueous sulfuric acid, stirred occasionally, and kept at 60 °C for 10 h to afford diol resin (**II**) used for further modifications.

Acetalization. Diol resin **II** (10 g) was suspended in 200 mL of toluene containing 13.4 g of benzaldehyde (3-fold excess over the theoretical amount of hydroxyl groups) and 0.18 g of 4-toluenesulfonic acid. The mixture was heated to reflux for 48 h while water produced during the acetalization reaction was continuously removed using a Dean–Stark head. After cooling to ambient temperature, the product was washed with toluene, acetone, and methanol and dried at 60 °C in vacuum to afford resin **III**.

Etherification. Diol resin **II** (0.5 g) was suspended in 10 mL of 2,3-dihydro-4*H*-pyran containing 0.08 g of 4-toluenesulfonic acid as a catalyst. The mixture was heated at reflux for 8 h and then cooled. After filtration, washing with dioxane, acetone, and methanol, followed by drying at 60 °C in vacuo, afforded resin **IV**.

Pore-Size-Specific Hydrolytic Reactions. Pore-size-specific hydrolysis of the reactive groups contained in resins **I**, **III**, and **IV** was catalyzed with 0.1 mol/L sulfuric acid, 0.1 mol/L 4-toluenesulfonic acid, or a 1 wt % aqueous solution of poly(styrenesulfonic acid) of a specific molecular weight or molecular weight range containing 0.054 mol/L sulfonic groups.

The epoxide resin **I** (200 mg) was placed in a 50-mL beaker, 10 mL of aqueous catalyst solution was added, and the beaker was sealed with Parafilm. The dispersion was stirred magnetically at ambient temperature for 48 h. The modified beads were then filtered off on a fritted glass filter and washed with water until neutral. After washing with acetone and drying in vacuo at room temperature, the residual epoxide content was determined volumetrically using the method described above.

The resins containing benzylidene acetal groups **III** or tetrahydropyranyl ether groups **IV** (200 mg) were suspended in 5 mL of a 1:1 dioxane–0.1 mol/L sodium sulfate mixture, and 10 mL of the catalyst solution was added. The mixtures were refluxed for 60 and 30 h, respectively, and cooled, and the beads were worked up as in the previous case.

The kinetics experiments were run under the conditions shown in the figure captions. In each case the extents of the hydrolytic reactions were monitored by IR spectroscopy.

Aminolysis of Epoxide Groups. The resin containing epoxide groups (1.5 g) was placed in a 50-mL round-bottom flask, and 20 mL of diethylamine was added. The mixture was heated to reflux (55 °C) for 6 h, and the resin was filtered and washed with water. The remaining unreacted epoxide groups were hydrolyzed in 20 mL of 0.1 mol/L sulfuric acid at 60 °C for 4 h. The beads were filtered, washed with water and then with methanol, and dried.

A slightly modified procedure was used for the aminolysis of beads containing epoxide groups using octadecylamine. The beads (1 g) were admixed to 5 g of molten octadecylamine at 70 °C, and the mixture was stirred for 16 h. The reaction mixture was then diluted with 20 mL of 1,4-dioxane, stirred for 30 min, and filtered. The resulting beads were washed with dioxane, water, and methanol and dried.

The amino group content of the beads was determined by elemental analysis of nitrogen as well as by an acid–base titration.

IR Spectroscopy. IR spectra were recorded on a Nicolet FT-IR spectrometer from KBr pellets. Quantitative data were calculated from the ratio of the areas of the hydroxyl band at 3100–3800 cm^{-1} and the carbonyl band at 1600–2000 cm^{-1} using a calibration curve obtained from measurements of various known mixtures of beads modified to the maximum degree of substitution and unmodified beads.

High-Performance Liquid Chromatography. The properties of polymers prepared in this study were determined by inverse size-exclusion chromatography carried out in a 150 mm × 4.6 mm i.d. stainless steel column using a commercial HPLC chromatograph (IBM–Nicolet ternary gradient liquid chromatograph LC 9560) equipped with a Rheodyne 7125 loop injector and a Hewlett Packard 1050 UV detector. The inverse size-exclusion chromatography was performed in THF with benzene and narrow polystyrene standards with molecular weights ranging from 1250 to 2 950 000 (Polymer Laboratories). The exclusion limits were determined from calibration curves,[5] while the specific pore volume and median pore diameter were calculated according to the literature.[11]

Protein Recovery. The plasma protein recovery from the beads packed in a 150 mm × 4.6 mm i.d. column was obtained upon isocratic elution in a 20 vol % acetonitrile solution in a 0.2 mol/L phosphate buffer solution (pH 7.0) at a flow rate of 1 mL/min and ambient temperature. The initial concentration of bovine plasma (Sigma) was 70 mg/mL, and the volume injected was 20 μL. Recovery was calculated as the percentage of protein peak area leaving the column under standard chromatographic conditions with respect to the peak area of the same amount of the protein injected into a system from which the column was removed, and the inlet and outlet capillaries were connected with an empty column tube having a volume similar to the void volume of the packed column.

Results and Discussion

Characterization of the Starting Polymer Beads. Three different batches of uniformly sized 10-μm polymer beads were prepared from glycidyl methacrylate and ethylene dimethacrylate by a modified shape template swelling and polymerization method.[7] The process used in this preparation maintains the size uniformity of the

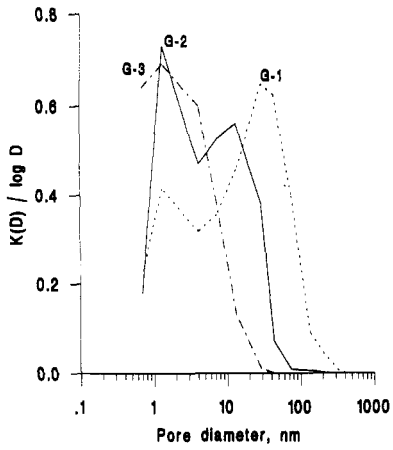


Figure 1. Pore size distribution curves of bead samples G-1, G-2, and G-3 calculated from chromatographic retention volumes of polystyrene standards in THF according to ref 11.

template particles while enlarging them and introducing macroporosity. Monodisperse polystyrene shape templates were prepared by emulsifier free emulsion polymerization[12] and swollen with a mixture of monomers and porogenic solvents. Batch G-1 was prepared with cyclohexanol and dodecanol as porogenic solvents, while for batches G-2 and G-3, butanethiol was added in order to shift the pore size distribution toward small pores.[13] Table I documents that the three batches of beads differ in their pore size distribution and related properties, such as specific surface areas and molecular size exclusion limits. In contrast, the particle size, overall composition of the polymerization mixture, and specific pore volume as determined from chromatographic measurements remain constant for all beads. The data obtained for the median pore diameters of beads G-1 and G-2 by two different techniques, inverse SEC and BET, correlate well despite the fact that the former involves measurement on a polymer immersed in THF while the latter is obtained from the dry polymer. This confirms that almost no volume change takes place in beads G-1 and G-2 after immersion of the dry polymer in THF. Figure 1 shows the pore size distribution curves obtained from the size-exclusion chromatography measurements. Beads G-1 have a bimodal pore size distribution typical for all macroporous polymers.[14] They contain a considerable volume of both macropores (over 50 nm) and mesopores (2–50 nm), while micropores (less than 2 nm) only account for a minor proportion of the total pore volume. In beads G-2 the bimodal character of the distribution curve is still retained but the maxima are shifted toward smaller pore sizes and the amount of micropores exceeds that of mesopores and macropores. Beads G-3 represent an extreme as they contain only a small amount of mesopores, no macropores, and a high proportion of micropores. The apparent discrepancy between the low value of the specific surface area and the volume of micropores is caused by the unusual morphology of the beads G-3. They consist of a highly cross-linked matrix with pores filled with a gellike polymer that generates porosity by swelling only when immersed in a solvent.[13]

Preparation of Polymer Beads Containing Acetal Groups. In order to fully test the concept of pore-size-specific functionalization, several polymers containing reactive groups that can be modified by acid-catalyzed hydrolysis were prepared.

Scheme I shows the preparation of resin **III** containing benzylidene acetal groups and resin **IV** containing tetrahydropyranyl ether groups, respectively. In a first step

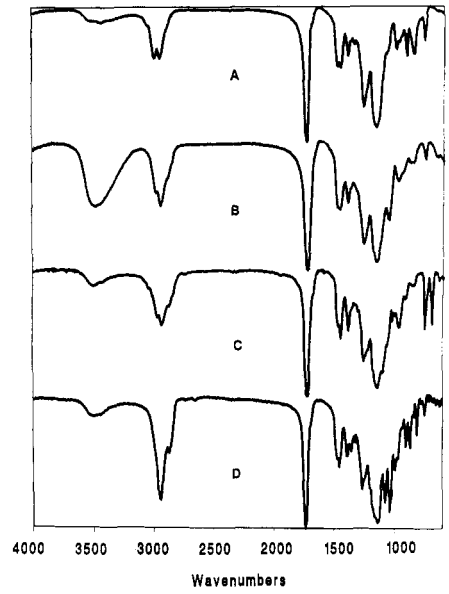
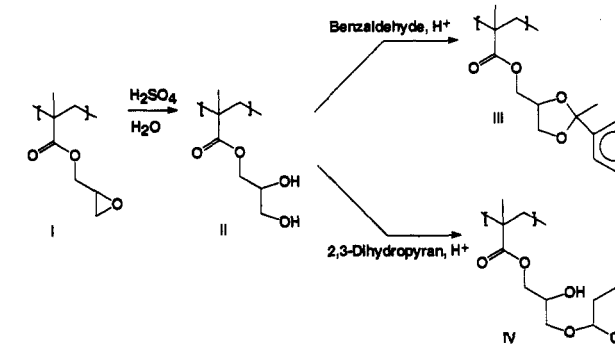


Figure 2. IR spectra of poly(glycidyl methacrylate-*co*-ethylene dimethacrylate) (A), totally hydrolyzed poly(glycidyl methacrylate-*co*-ethylene dimethacrylate) (B), benzylidene acetal (C), and a tetrahydropyranyl ether derivative (D).

Scheme I



the epoxide groups of resin **I** are completely hydrolyzed by treatment with dilute sulfuric acid as confirmed by IR spectrometry and by volumetric analysis. Introduction of the acetal groups is readily achieved by treatment of the diol resin **II** with the appropriate reagent, benzaldehyde or dihydropyran, in the presence of a catalytic amount of 4-toluenesulfonic acid under dehydrating conditions. Analysis of polymers **III** and **IV** by infrared spectroscopy (Figure 2) confirms that the acetalization reaction, though not complete, proceeded to a large extent. Polymers having structures **I**, **III**, and **IV** were used in a subsequent pore-size-specific modification study.

Pore-Size-Specific Functionalization. The principle of size exclusion can easily be coupled to the inherent reactivity of the functional groups on polymer matrices to achieve pore-size-specific functionalization of a porous material.

This concept is shown schematically in Figure 3 where the structure of a porous material is depicted as a combination of interconnected large and small cavities. In the case of resin **I**, these cavities are covered with epoxy groups, that are susceptible to acid-catalyzed hydrolysis to afford diol polymer **II**. In instances where the acid catalyst is itself a large molecule such as a polymer, its ability to catalyze reaction of the functional groups contained in the various cavities will be controlled by the relative size of the catalyst molecule and the cavity (Figure 3).

Pore-Size-Specific Hydrolysis of Epoxide Polymers. As demonstrated earlier, if the catalyst molecule

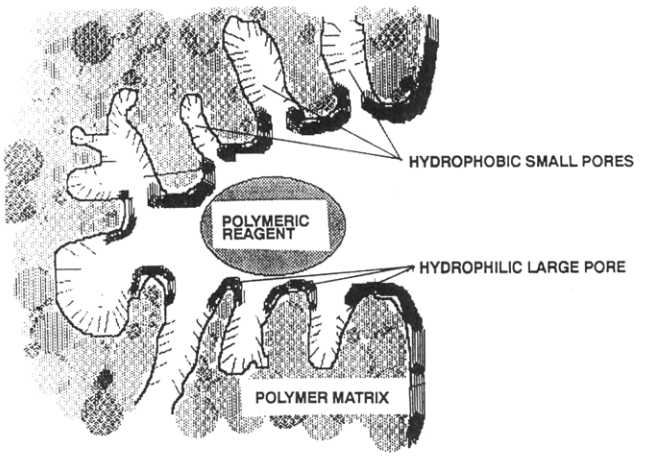


Figure 3. Schematic view of pore-size-specific functionalization.

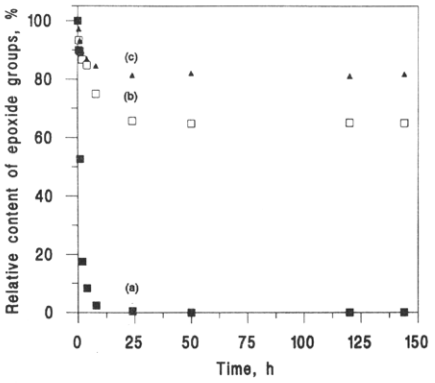


Figure 4. Kinetic curves of pore-size-specific hydrolysis of epoxide groups in beads G-1 and G-2 using catalysts with different molecular volumes. Curve a: G-1, sulfuric acid. Curve b: G-1, PSSA 141. Curve c: G-2, PSSA 141. Reaction conditions: beads, 1 g; aqueous acid solution, 10 mL; temperature, 20 °C.

is very small, for example, sulfuric acid, all the cavities of the porous material are easily penetrated and complete hydrolysis is obtained (Figure 4, curve a). In contrast, a polymeric acid such as poly(styrenesulfonic acid) will only hydrolyze the epoxide groups of cavities large enough to accommodate it (Figure 4, curves b and c).

Table II shows the percentages of epoxide groups remaining in resin **I** after acid hydrolysis using a variety of different catalysts from sulfuric acid to a poly(styrenesulfonic acid) with a molecular weight well over 1 million.

The influence of the size of the catalyst on the extent of reaction is clearly demonstrated as full hydrolysis is achieved with sulfuric acid while only 11% hydrolysis is observed for the highest molecular weight catalyst tested, PSSA 1200. It is interesting to note that size specificity is already observed with 4-toluenesulfonic acid which cannot penetrate the smallest cavities of any of our test porous materials G-1, G-2, and G-3.

While most of the polymeric catalysts used had narrow molecular weight distributions (PSSA 5, 47, 400, and 1200), the use of polydisperse catalysts is also possible. In this case, however, it is the smallest polymer molecules present in the overall distribution that will determine the threshold size of the pores that will be modified. This is demonstrated with PSSA 141 with a weight-average molecular weight of 141 000 and a polydispersity of 1.7. This polymer, which contains a significant low molecular weight fraction, behaves similarly to PSSA 47 with a more highly controlled polydispersity. Overall, control of the molecular size of the catalyst can be achieved through the use of polymers

Scheme II

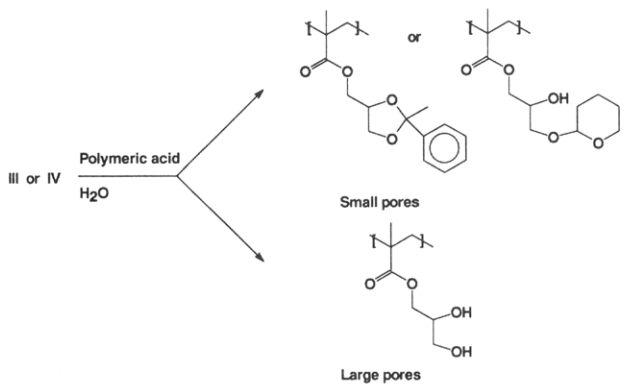


Table III. Percentage of Remaining Benzylidene Acetal and Tetrahydropyranyl Ether Groups in Modified Porous Poly(glycidyl methacrylate-*co*-ethylene dimethacrylate) Beads after Hydrolysis Catalyzed by Various Acids[a]

	remaining groups, %			
	benzylidene acetal		tetrahydropyranyl ether	
catalyst	G1	G2	G-1	G-2
sulfuric acid	0	0	0	0
4-toluenesulfonic acid	0	0	0	0
PSSA 5	7	22	18	29
PSSA 47	15	48	25	51
PSSA 400	24	89	33	88
PSSA 1200	47	95	53	96

[a] Reaction conditions: beads (200 mg) suspended in 5 mL of a 1:1 dioxane–0.1 mol/L sodium sulfate mixture, catalyst solution of 10 mL (0.1 mol/L H_2SO_4, 0.1 mol/L 4-toluenesulfonic acid, or 1 wt % poly(styrenesulfonic acid) in water), refluxed for 60 h (benzylidene acetal) or 30 h (tetrahydropyranyl ether).

with very narrow distribution or simply by fractionation of a polymer sample to remove the low molecular weight species below the desired size threshold.

Table II also shows the effect of pore structure on the extent of modification. For example, PSSA 5 can catalyze the hydrolysis of 55% of all pores in beads G-1 that contain a high proportion of large pores, while only 32% of the pores are accessed for beads G-3 that contain a fewer large pores. The same finding is made with all polymeric catalysts including polydisperse PSSA 141 as confirmed in Figure 4.

Pore-Size-Specific Functionalization of Acetalized Polymers. The observations made in the acid-catalyzed hydrolysis of the epoxide groups of resin **I** also apply to the acid hydrolysis of the acetal groups of **III** and **IV** (Scheme II). However, Table III shows that the extent of hydrolysis obtained for resins **III** and **IV** is significantly higher than that for the parent epoxide resin **I**. This is due to the incomplete acetalization of diol resin **II** catalyzed by 4-toluenesulfonic acid that cannot penetrate all pores (Table II) and leaves unreacted diol groups in the acetalized polymers during this preparation. These unreacted groups are largely localized in the smallest pores, and therefore the percentage of "hydrolysis" achieved with a polymer catalyst is skewed in comparison to the hydrolysis of the parent resin **I**. The largest acid catalyst cannot penetrate beads G-2 that contain a high proportion of small pores.

Figures 5 and 6 show the kinetics of the hydrolysis process with acids of different molecular weights. A comparison with Figure 4 reveals that the hydrolysis is slower than that of epoxide groups, with equilibrium being reached after 48 h at 100 °C (resins **III** and **IV**) versus 24 h at room temperature (resin **I**).

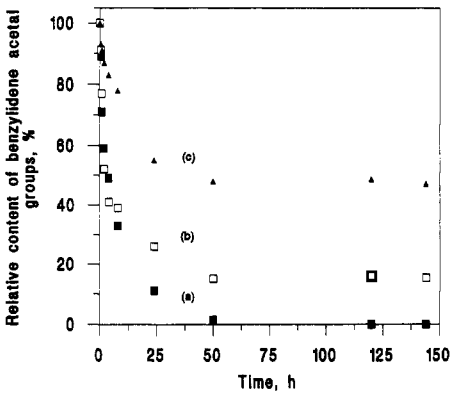


Figure 5. Kinetic curves of pore-size-specific hydrolysis of benzylidene acetal groups contained in beads G-1 using catalysts with different molecular volumes. Curves a: sulfuric acid. Curve b: PSSA 47. Curve c: PSSA 1200. Reaction conditions: beads, 1 g; aqueous acid solution, 10 mL; temperature, 70 °C.

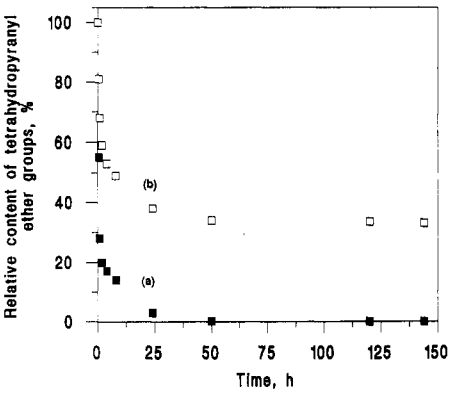


Figure 6. Kinetic curves of pore-size-specific hydrolysis of tetrahydropyranyl ether contained in beads G-1 using catalysts with different molecular volume. Curve a: sulfuric acid. Curve b: PSSA 400. Reaction conditions: beads, 1 g; aqueous acid solution, 10 mL; temperature, 70 °C.

Table IV. Effect of the Extent of Pore Surface Benzylidene Derivatization Controlled by the Size of the Hydrolytic Catalyst on Recovery of the Bovine Plasma Proteins from Beads G-2

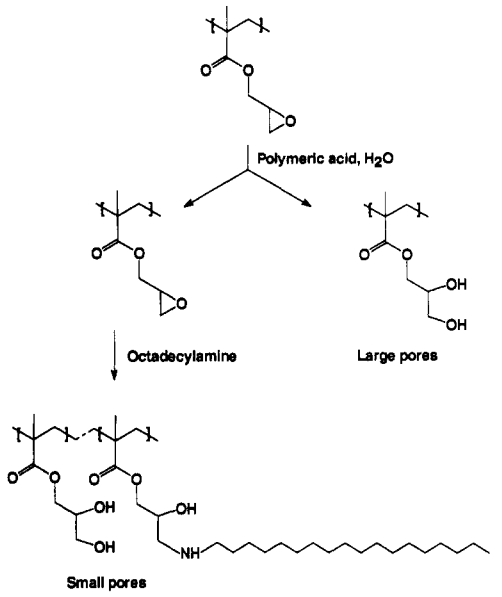
catalyst	protein recovery, %	catalyst	protein recovery, %
a	27	PSSA 47	98
PSSA 1200	51	PSSA 5	100
PSSA 400	78	sulfuric acid	99

[a] Beads after derivatization with benzylaldehyde.

Proteins are good probes for the determination of surface polarity. Typically, they are adsorbed by hydrophobic surfaces in porous materials. Obviously, proteins will only be adsorbed in pores of a size large enough to accommodate them. Hence, one measure of the effectiveness of the pore-size-specific method of modification may be protein recovery from HPLC columns in which only pores large enough to accommodate proteins are modified. Table IV illustrates the plasma protein recoveries from beads prepared by pore-size-specific hydrolysis of benzylidene resin **III** catalyzed by PSSA with narrow molecular weight distribution and by sulfuric acid (Scheme II). The effect of the molecular size of the catalyst is remarkable. For example, the recovery of injected protein from the unmodified beads of resin **III** was only 27%, while the beads treated with a solution of PSSA 47 or any other acid catalyst with molecular weight lower than 47 000 did not adsorb plasma proteins at all.

Pore-Size-Specific Introduction of Both Hydrophilic and Hydrophobic Functionalities in a Porous Medium. The pore-size-specific chemistry described above is not restricted to the preparation of porous materials in which the only largest pores have been modified. Further modification of the small pores can be carried out by selecting chemical processes that only affect their reactive groups. For example, we have prepared a porous material containing hydrophilic large pores and hydrophobic small pores by the very simple two-stage modification shown in Scheme III. Following modification of the large pores of resin **I** in the presence of a polymeric catalyst, octadecylamine is added to modify the remaining epoxide groups located in pores smaller than the polymeric catalyst. Modification with octadecylamine is both sluggish and only partial. This is due in part to the bulkiness of the reagent itself which does not penetrate the smallest pores and also to steric shielding of the epoxide groups by octadecyl-functionalized neighboring sites. For example, beads G-1 partly hydrolyzed with PSSA 141 still contain 1.7 mmol/g of epoxy groups. After reaction with octadecylamine the polymer contains 0.35 mmol/g of nitrogen, suggesting a conversion of only 20–25% of these epoxide groups. However, this degree of functionalization is sufficient to confer significant hydrophobic character to the smaller cavities of the modified porous material as demonstrated in a HPLC experiment. The chromatogram shown in Figure 7 documents the separation ability of the modified beads packed in a HPLC column and used for a truly bimodal separation of a mixture of proteins and aromatic hydrocarbons in the size-exclusion mode and in the reverse-phase mode. The various components of the complex mixture are injected together but are separated sequentially simply by changing the composition of the mobile phase during the chromatographic process which results in a change in the chromatographic mode. Following initial injection, the proteins are separated within large pores by SEC while the hydrocarbons are retained within the hydrophobic small pores. Once the proteins have eluted, the solvent composition is changed to initiate elution of the hydrocarbons, displacing them from the small pores by addition of an organic displacing solvent. The excellent separation of proteins and hydrocarbons confirms that both hydrophilic and hydrophobic functionalities are segregated in different size pores and do not interfere with each other. The separation shown in Figure 7 cannot be achieved with beads prepared by a simple modification of beads G-1 with octadecylamine.

Scheme III



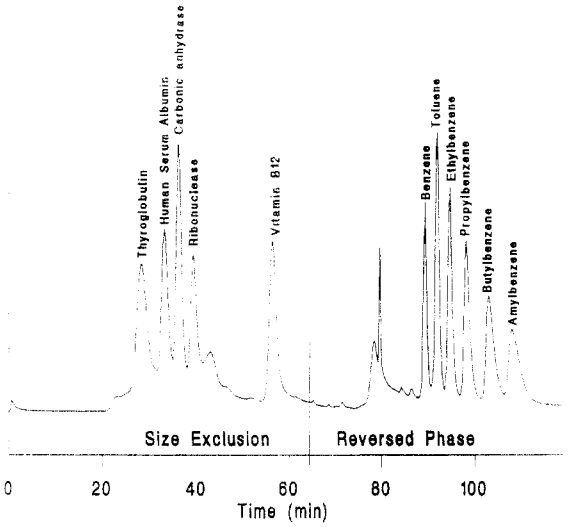


Figure 7. Bimodal HPLC separation of proteins and alkylbenzenes. Column, 300 mm × 7.8 mm i.d.. Size-exclusion mode: mobile phase, 0.1 mol/L phosphate buffer solution containing 0.15 mol/L NaCl, pH 7; flow rate, 0.2 mL/min. Reverse-phase mode: mobile phase, 0.1 mol/L phosphate buffer solution (pH 7)–acetonitrile (65/35, v/v) mixture; flow rate, 1 mL/min. UV detection.

More details of the chromatographic behavior of these new materials will appear elsewhere.

Further demonstration of the two-step pore-size-specific modification approach is provided by a similar process in which diethylamine is substituted for octadecylamine. In this instance beads G-2 with fewer large pores were tested. The starting beads contained 2.5 mmol/g of epoxide groups as determined by titration. Following treatment with aqueous PSSA 5, 1.4 mmol/g of epoxide remained. Subsequent reaction with diethylamine affords a final product with 1.3 mmol/g of nitrogen. In this instance, the smaller size of the modifying agent allowed the reaction to proceed, with 92% conversion being measured. The final product is a porous material containing diol functional groups in large pores and tertiary amino groups in small pores. Once again, these materials are being tested as novel dual-mode HPLC chromatographic media.

Conclusion

The use of polymeric catalysts for the pore-size-specific modification of porous polymers is a novel and versatile method of polymer modification. As the size of the catalyst may vary within a broad range, the fraction and size of the pores undergoing modification may be specifically controlled. The method allows the preparation of porous materials with pores modified according to their size with no overlap of the different functionalities. A suitable combination of reaction steps with carefully chosen catalysts may even result in particles with more than two types of different groups localized separately in pores of different sizes.

The pore-size-specific functionalization is well suited for the preparation of beads with functionalities separated in pores according to the pore size. They may be used as separation media, catalysts, or carriers containing at least a dual function for use in processes such as multimodal HPLC. We are currently testing pore-size-specific modified beads in the direct injection separation of plasma proteins and drugs and in bimodal HPLC.

Though the concept is documented on reactions of polymer beads, it is in no way restricted to any particular shape of the porous material. The most important characteristic of the materials is in this case their pore size distribution.

Acknowledgment. Support of this research by a grant from the National Institutes of Health (GM 44885-04) is gratefully acknowledged. This work also made use of MRL Central Facilities supported by the National Science Foundation under Award No. DMR-9121654.

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