Design and synthesis of macroporous polymeric separation media based on substituted phenols

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The suspension copolymerization of several *t*-butoxycarbonyl (*t*-BOC) protected 4-vinyl phenols with divinylbenzene has been studied to produce high porosity 10 μm bead materials with surface areas of 200–300 m^2/g for use as separation media. The choice and amount of porogen is critical for the control of porosity and surface area while particle size and size distribution is controlled by other reaction variables. The *t*-BOC protecting groups of the polymers are easily removed by thermolysis and the deprotected beads are useful in the separation of amines. The relationship between polymer structure and separation ability in h.p.l.c. has been explored and the effect of alkyl substituents located *ortho* to the phenolic groups is discussed.

(Keywords: suspension polymerization; porogen; separation media; macroporous poly(vinylphenol))

INTRODUCTION

H.p.l.c. columns containing polymeric resins have become have become increasingly popular because these columns have chemical stability that cannot be achieved with silica columns. Though silica gel columns are still by far the most widely used due to their desirable characteristics[1], their lack of stability in basic media[2] and the presence of residual acidic silanol groups on their surface restricts their use in some applications[3].

Separation media based on porous polymers are usually produced by suspension polymerization, and gradual improvements in reactor design and suspension polymerization methodology[4] have allowed the production of smaller and smaller polymeric beads. For example, the Hamilton Company (USA) introduced almost ten years ago a spherical macroporous 10 μm styrene-divinylbenzene copolymer designated as PRP-1 that is stable over a pH range of 0–14 and that can be used for the separation of a variety of organic molecules[5]. Other products were developed from this new material, such as PRP-X100, a high capacity and high efficiency anion exchanger which is prepared from PRP-1 by chemical modification[6]. Polymeric h.p.l.c. resins based on methacrylate polymers have also been produced[7].

In spite of the chemical instability of silica in basic media, it still remains the most popular h.p.l.c. adsorbent because its uniform pore structure leads to columns having much greater efficiencies than polymeric columns which have somewhat irregular pore structures[2]. The most recent trend in the area of polymeric h.p.l.c. columns has been to produce pellicular polymeric packings[8,9], which consist of thin layers of polymers chemically attached to the outer surface of small (3–5 μm), non-porous, spherical polymer beads. The short diffusion paths present in the outer layer leads to columns having very high efficiencies in addition to their inherent good chemical stability.

Our interest in functional polymers has led us to study the possibility of designing new polymer-based separation media containing phenolic functionalities of varying accessibilities. Polymeric resins containing phenol moieties were also chosen because their acidic hydrogens can form strong hydrogen bonds with basic compounds such as amines, which are frequently difficult to separate effectively, and because this bonding, which mirrors that occurring between organic molecules and the acidic silanol groups of silica adsorbents, can be modified by changes in steric environment. This paper describes a series of polymer-based chromatographic adsorbents in which both the acidity of the phenolic hydrogens and their steric environment has been changed systematically in order to study the effect of these variables on the separation ability of the various polymers. These adsorbents were prepared by suspension copolymerization of the appropriate vinyl monomers with commercial divinylbenzene, with the aim of producing small (10 μm), rigid, spherical, macroporous beads with good chemical and mechanical properties. The target structures shown in *Figure 1*, polymer **1a–c**, all contain 4-hydroxystyrene moieties with or without alkyl substituents in positions *ortho* to the phenolic hydroxyls.

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RESULTS AND DISCUSSION

The preparation of polymers 1a–c and their *t*-BOC protected precursors 5a–c is shown schematically in *Figure 2*.

In order to optimize the porosity and particle size of our phenolic resins, a systematic series of suspension polymerization experiments was carried out to prepare polymer 5a under a standard set of reaction conditions as follows. In each experiment, the monomer mixture consisted of 50 wt% of commercial divinylbenzene (an almost equimolar mixture of monomers 3 and 4) and 50 wt% of *p*-*t*-butoxycarbonyloxystyrene (monomer 2a). This monomer[10] was chosen for two reasons: first because the polymerization of unprotected vinyl phenols gives irregular and low molecular weight products[11] which may be too soft for practical use in h.p.l.c. and also because the *t*-BOC protecting groups can be easily thermolysed to yield the desired phenolic functionality[10]. Each experiment was run at 80°C for 16 h using a Büchi BEP 280 autoclave with AIBN as the initiator and a 2% solution of poly(vinyl alcohol) as the aqueous phase. Porosity was controlled by varying the amount and thermodynamic characteristics of the porogen used in the polymerization mixture, while particle size was controlled by changing the stirring speed and the relative ratio of the aqueous and organic phases.

Control of bead porosity

Table 1 lists the surface areas, solvent regains, and per cent porosities of the polymers obtained in the various suspension copolymerizations using a variety of solvents as porogens. As can be seen in this table, changing the thermodynamic characteristics of the porogens results in the formation of resins having a wide range of porous properties. For example, an organic phase containing 50% 1-butyl acetate gives a resin with a surface area $<1\,m^2/g$, while 50% cyclohexanol affords a resin with $190\,m^2/g$. *Table 1* also shows how the porosity can be varied greatly by simply changing the vol% of porogen used in the polymerization mixture. For example, with 1-butanol as the porogen, the porosity increases steadily as the percentage of 1-butanol is increased from 30% to 70%. This result is expected because the pore volume can generally be related to the amount of porogen used in the polymerization mixture. The variation in the surface area is less easily predicted as it increases from $<1\,m^2/g$ with 30% 1-butanol to $143\,m^2/g$ with 60% 1-butanol, then drops again to $26\,m^2/g$ with 70% 1-butanol. *Figure 3* shows the differential mercury porosimetry curves for the polymers prepared using 50%,

Table 1 Control of surface area and pore volume in the copolymerization of *p*-*t*-BOC-styrene and divinylbenzene

Porogen (volume %)	Surface area (m^2/g)	Solvent regain (ml/g)	% Porosity[a]
1-Butyl acetate (50%)	<1	0.43	30
1-Butanol (50%)	4.8	0.60	38
Benzyl alcohol (50%)	71	1.33	57
Cyclohexanol (40%)	<1	0.52	34
Cyclohexanol (50%)	190	0.92	48
Cyclohexanol (60%)	227	1.64	62
1-Heptane (50%)	197	1.03	51
1-Butanol (30%)	<1	0.12	11
1-Butanol (40%)	1.3	0.43	30
1-Butanol (50%)	4.8	0.60	38
1-Butanol (60%)	143	1.36	58
1-Butanol (70%)	26	1.85	65
1-Butanol (60%)	143	1.36	58
1-Pentanol (60%)	145	1.75	64
1-Heptanol (60%)	136	1.91	66
1-Octanol (60%)	93	1.95	66
1-Decanol (60%)	44	2.10	68

[a] Porosity represents the percentage porosity of each sample, which is calculated by the following equation: % Porosity $=100V_s/(V_s+V_p)$ where V_s is the volume of cyclohexane taken up by 1 g of the polymer, which can be determined from the solvent regain values. V_p is the volume of 1 g of polymer beads. This volume is taken as 1.0 ml in each case because the density of this polymer matrix was determined to be *c.* 1.0 g/ml from the value of its balanced density slurry

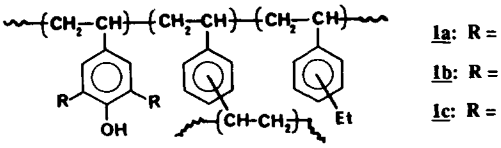

Figure 1 Structure of the bead polymers

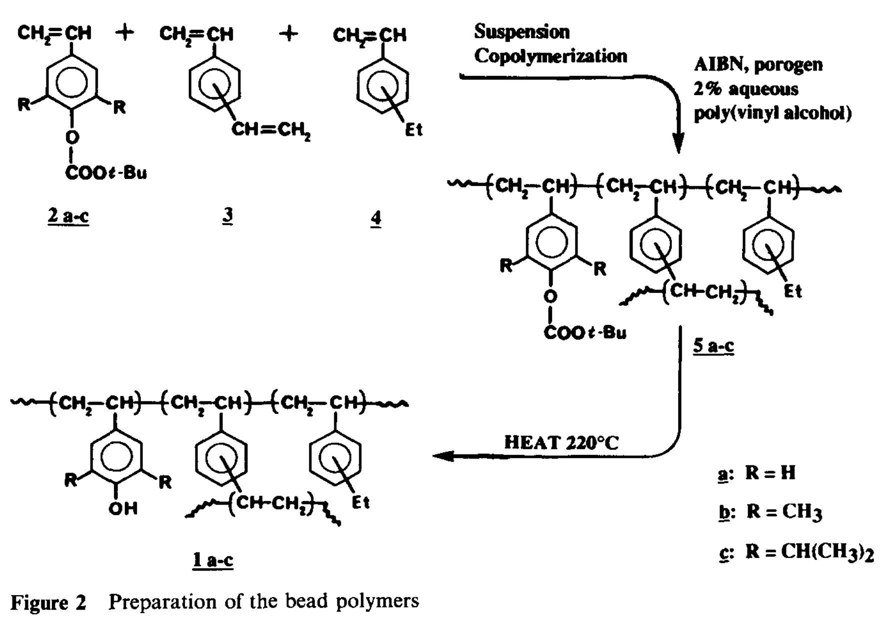

Figure 2 Preparation of the bead polymers

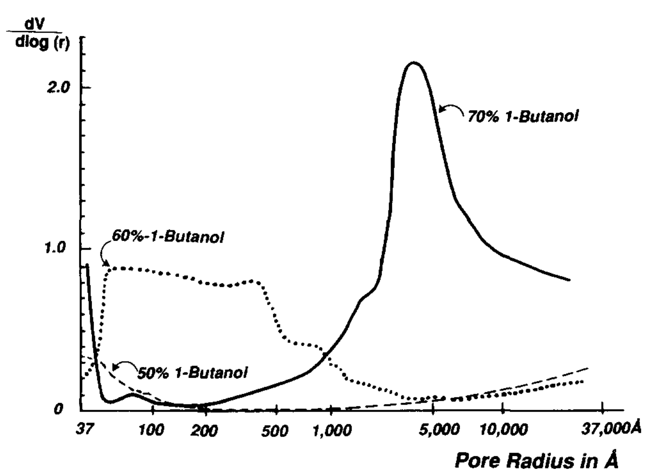

Figure 3 Porosity of the polymers obtained using an organic phase containing 50–70% 1-butanol as porogen

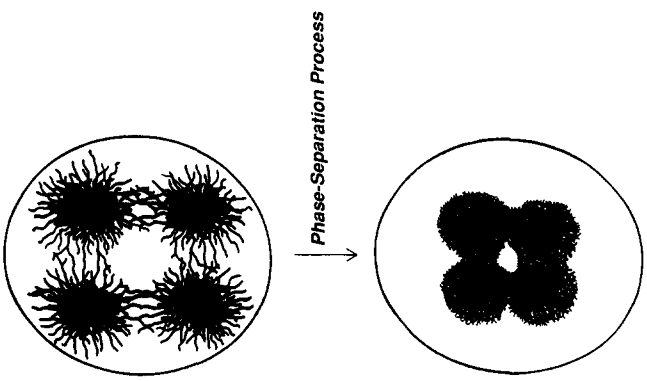

Figure 4 Phase separation process in the formation of pores

60%, and 70% 1-butanol which explain partially these results. Note that the pore radius data is plotted logarithmically because of the wide range of pore radii involved. Clearly, the polymer beads prepared using 50% 1-butanol as porogen have a low surface area because they contain very few pores, small or large. The polymer beads prepared using 60% 1-butanol as porogen have a high surface area because most of their porosity is contained in pores of less than 1000 Å. As the percentage of 1-butanol is increased to 70% the pore size increases and therefore the surface area drops as the beads now have virtually no small pores; most of their porosity is due to pores which are larger than 1000 Å.

The theory of pore formation in macroporous resins has been reviewed in great detail by Guyot and Bartholin[12] following extensive earlier studies[13–15]. These studies, which involved mainly the styrene–divinylbenzene system, showed that completely different porous structures are obtained depending on whether solvents or non-solvents of polystyrene are used as porogens. Guyot and coworkers[12–15] noted that styrene–divinylbenzene resins are inhomogeneous because the divinyl components of this mixture (*p*- and *m*-divinylbenzene) are incorporated into the polymer resin much faster than the monovinyl components (styrene, *p*- and *m*-ethylstyrene). This gives rise to regions of high crosslink density, termed 'nodules', which are connected by the less highly crosslinked molecules formed at a later stage of the polymerization. This is depicted in the top part of *Figure 4*. When the porogen is a solvent for the polymer molecules, such as toluene, the situation is very simple. If the amount of porogen is too low, the distance between the nodules will be very small and there will not be enough available volume for the polymerization to proceed to completion without complete coalescence or overlap of the nodules. As a result, a gel-like resin with no measurable surface area or pore volume will be produced. When the amount of porogen passes a critical threshold value and the distance between the nodules becomes greater, because of a dilution effect, some empty space or small pores will remain between the nodules at the completion of the polymerization, resulting in the production of a resin with a high surface area and a sharp pore size distribution. As the percentage of porogen is increased beyond this threshold value, the surface area and pore volume increase steadily. Because the porogen is a good solvent for the polymer molecules, there is no phase separation, and the result is a resin with a very uniform distribution of small pores[12].

When the porogen is a non-solvent for the polymer molecules, the situation is much more complex. This applies to our system in which 1-butanol is used as a porogen because alcohols are poor solvents for styrenic polymers[16,17] In the early stages of polymerization, the diluent mixture consists of the porogen and unreacted monomers. As the polymerization proceeds, the monomers are incorporated into the polymer and the composition of the diluent mixture shifts towards a higher percentage of the porogen, which is a non-solvent for the polymer. When the percentage of porogen in the diluent mixture becomes large enough, a phase separation occurs, in which most of the porogen is exuded from the regions between the polymer molecules. Two phases are created, one containing a high concentration of polymer molecules, and the other containing mostly porogen. The volume occupied by the exuded porogen corresponds to the very large pores seen in the pore size distributions of resins prepared using non-solvents as porogens[12–15]. This process is depicted in *Figure 4*.

The discussion presented above can be used to help explain the mercury porosimetry curves shown in *Figure 3*. When the porogen is 50% 1-butanol, there is simply not enough available volume in which the nodules can grow without coalescing because the percentage of diluent is relatively low. This leads to the production of a resin with no small or large pores and very little surface area or pore volume. There are probably no large pores because the percentage of 1-butanol may be too low to cause a phase separation. When 70% 1-butanol is used as the porogen, a resin with only very large pores is obtained. Phase separation occurs at a relatively early stage in this polymerization because of the large amount of non-solvent present. The nodules do not shrink very much when the porogen is exuded from this initial region because it contains highly crosslinked molecules. However, the molecules connecting adjacent nodules are much less crosslinked, and they do collapse to a large extent upon exudation of the porogen. As a result, the empty volume that lies between adjacent nodules is reduced considerably. Because the phase separation occurs very early in the polymerization, the nodules will grow to a considerable extent through polymerization of the remaining monomers and will eventually overlap and coalesce. No small pores remain upon completion of polymerization; only the large pores formed by the exudation of the solvent remain. As a result, a resin with a small surface area and a large pore volume is obtained. When 60% 1-butanol is used as the porogen, the phase separation which leads to a concentrated polymer phase occurs much later in the polymerization because there is less non-solvent present in the polymerization mixture. The nodules continue their growth after phase separation, but they do not grow as much as in the previous case because a large percentage of the polymerization has occurred before phase separation. Therefore, the nodules will not be completely coalesced upon completion of polymerization and many of the small pores remain, while larger pores formed by exudation of the solvent will also be present[12-15]. Therefore, a resin with both a large surface area and a large pore volume is obtained.

Table 1 also reports the surface areas, solvent regains, and per cent porosities of the polymers obtained in the suspension copolymerization of *p*-*t*-BOC-styrene 2a and commercial-divinylbenzene (3+4) using a variety of n-alcohols as porogens. The surface area is high when the lower molecular weight alcohols are used as porogens, but drops drastically when the higher molecular weight alcohols, such as 1-decanol, are used as porogens. The mercury porosimetry curves shown in *Figure 5* help to explain this data. These curves show the pore size distributions for the polymers prepared using 60% 1-butanol, 60% 1-heptanol, and 60% 1-decanol as porogens. When 1-butanol is used, the resin that is obtained has a rather broad pore size distribution containing both large and small pores. When 1-decanol is used as the porogen, most of the smaller and intermediate size pores disappear; only large pores (>1000 Å) and a few small pores (<100 Å) can be seen. This shift in the pore size distribution towards the larger poles accounts for the decrease in surface area and the increase in pore volume when the higher alcohols are used as porogens. When 1-heptanol is used as the porogen, the pore size distribution seems to lie between the distributions obtained with 1-butanol and 1-decanol.

The shift in pore size distribution which occurs when the porogen is changed from 60% 1-butanol to 60% 1-decanol is very similar to that which is observed when the porogen is changed from 60% 1-butanol to 70% 1-butanol. In the latter case, this shift occurred because a mixture of 70% 1-butanol and 30% monomers has much more precipitating power than a mixture containing 60% 1-butanol and 40% monomers, and the phase separation which is known to occur in these polymerizations occurs much earlier when the diluent mixture has more precipitating power. In the former case, this shift occurs for the same reason; that is, 1-decanol is a stronger precipitant for styrenic polymers than 1-butanol[17,18].

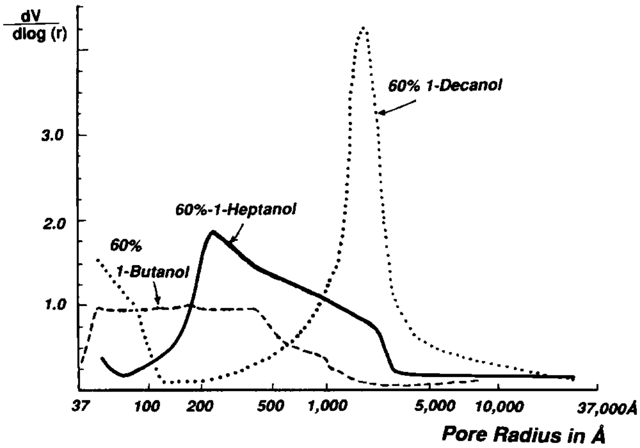

Figure 5 Porosity of the polymers obtained using an organic phase containing 60% 1-alkanol as porogen

Table 2 Control of particle size in the copolymerization of *p*-*t*-BOC-styrene and divinylbenzene by variation of the stirring speed

Porogen (vol%)	rpm	Volume ratio aqueous/organic	Mean particle size (s.d.)[a]
Cyclohexanol (60%)	725	4/1	13.77 μm (5.81)
Cyclohexanol (60%)	800	4/1	10.18 μm (4.42)
Cyclohexanol (60%)	850	4/1	8.25 μm (3.43)
Cyclohexanol (60%)	925	4/1	6.81 μm (3.13)

[a] s.d. = standard deviation

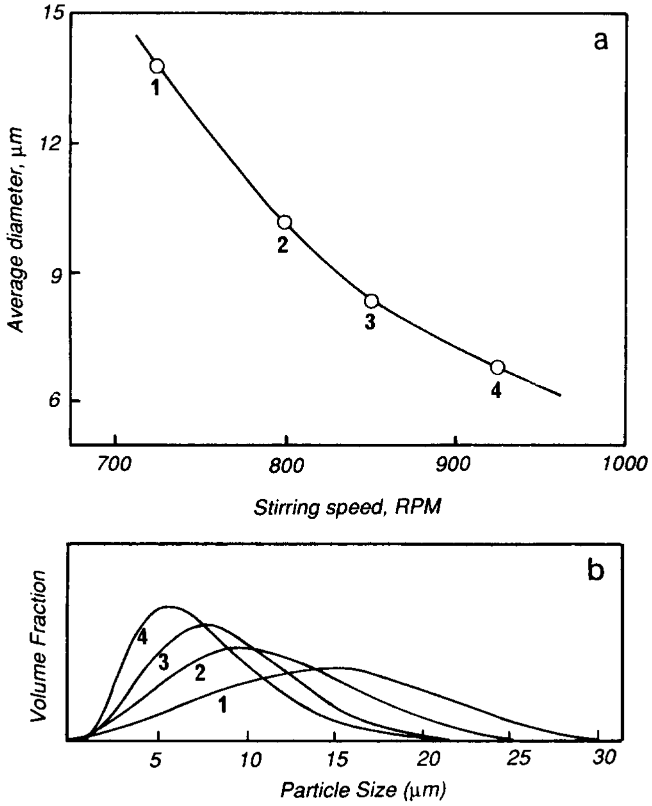

Figure 6 (a) Influence of stirring speed on mean particle size and (b) particle size distribution during the suspension polymerization of polymer 5a. Curve 1 725 rpm; curve 2 800 rpm; curve 3 850 rpm; curve 4 925 rpm

Control of particle size

A formulation using 40% monomers and 60% cyclohexanol was chosen for all the remaining experiments of this study as this affords resins having both a high surface area and a high percentage porosity, which is ideal for the chromatographic separation of small molecules. The percentage of commercial divinylbenzene was kept at a high level (50 wt%) because this leads to resins which have the rigidity which is needed to withstand the high pressures of liquid chromatography. High stirring speeds, high concentrations of suspension stabilizer and large ratios of aqueous to organic phase were used as such conditions favour the formation of small beads[19].

Table 2 contains details of the conditions used to produce small beads in the *p*-*t*-BOC-styrene–divinylbenzene system. The resulting particle size distribution curves are shown in *Figure 6*. By changing the stirring speed from 725 rpm to 925 rpm, beads with a mean particle size ranging from 13.8 to 6.8 μm could be produced. After isolation, the beads were tested as separation media without sizing due to the difficulties involved in sizing small amounts (10 g) of polymer beads. For our purpose, polymers with a particle size distribution centred around 10 μm were judged to be ideal. Distributions with a smaller average particle size led to high column back pressures in the h.p.l.c. experiments because of the large fraction of 'fines' in these samples. All remaining polymerizations were performed with the aim of producing a distribution with an average particle size of about 10 μm.

Preparation of the functionalized monomers

The synthetic scheme used to prepare more hindered analogues of 4-*t*-BOC-hydroxystyrene is shown in *Figure 7*. The first step involves formylation of the appropriate 2,6-dialkylphenol (6b–c) using hexamethylenetetramine and trifluoroacetic acid according to the procedure of Smith[20]. This gave a 70% yield of 7b with 2,6-dimethylphenol and 87% yield of 7c for the diisopropyl analogue. In the second step of this synthesis, the phenolic hydroxyls are protected as their *t*-butyl carbonate derivatives (8b–c) using di-*t*-butyl dicarbonate in a modification of the procedure of Houlihan *et al.*[21]. When this reaction was performed on 3,5-dimethyl-4-hydroxybenzaldehyde, a 90% isolated yield of 8b was obtained after overnight stirring. A similar reaction on the diisopropyl analogue gave an 87% yield of 8c, but required a few days to reach completion due to the additional steric constraints. Finally, conversion of the formyl groups to vinyl groups via a Wittig reaction gave 3,5-dimethyl-4-*t*-butoxycarbonyloxystyrene 2b and 3,5-diisopropyl-4-*t*-butoxycarbonyloxystyrene 2c in 81% and 86% yield, respectively.

Preparation of hindered vinyl phenol bead polymers

The techniques developed earlier for beads containing 4-hydroxystyrene as the active monomer were applied to the preparation of a series of small (10 μm) porous beads containing phenolic moieties with different acidities and steric environments. All of the polymerizations were run for 16 h at 80°C using AIBN as the initiator and a 2% solution of poly(vinyl alcohol) as the aqueous phase. The volume ratio of the aqueous phase to the organic phase was 4:1. The polymerizations were run at 800 rpm and 60 vol% of cyclohexanol was used as the porogen. The weights of the monomers used in each of the three polymerizations were adjusted so that each of the three formulations would contain approximately the same mole fraction of the protected vinyl phenol monomer. The physical characterization data for these polymer beads is reported in *Table 3*, which shows that success was obtained in the preparation of a series of resins having small particle sizes (10–12 μm) and high surface areas (200–300 m^2/g). *Table 3* also shows the thermolysis temperature for the *t*-BOC group of each polymer and the per cent weight loss upon heating from 50 to 300°C. The mole fraction of protected phenolic units in each sample was calculated from these weight losses.

Deprotection of the bead polymers

Cleavage of protecting groups on very small polymer beads can, in theory, be accomplished readily with chemical reagents, but in practice, the physical form of the polymer beads presents a special problem. Excess reagents, solvents, and reaction by-products are usually removed from insoluble polymer beads by filtration. However, filtrations done with very small polymer beads are quite difficult because these small particles can easily clog filtration media, and this leads to extremely long and inefficient filtration processes. To avoid filtration

Table 3 Physical data for polymers 5a, 5b, and 5c

Polymer	5a	5b	5c
Mean particle size	10.18 μm	10.42 μm	12.00 μm
(s.d.)	4.42	4.34	5.75
Surface area	232 m^2/g	313 m^2/g	262 m^2/g
Thermolysis temperature (°C)	190.8	210.8	215.8
% Weight loss	23.4	23.6	21.6
Mole fraction of *x* units in the polymer	0.39	0.43	0.45

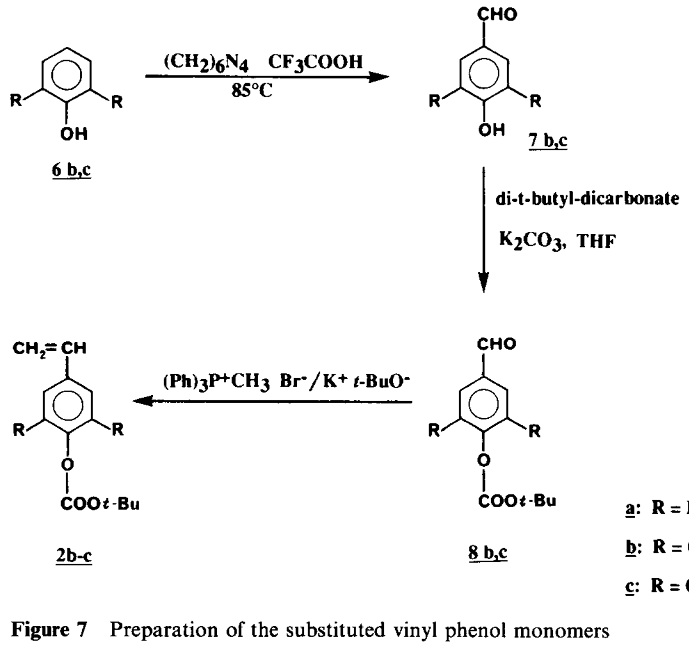

Figure 7 Preparation of the substituted vinyl phenol monomers

problems, these types of small particles are best washed through a series of decantations with the appropriate wash solvents. This is a lengthy procedure which may require several weeks because of the need to allow time for the wash solvent to fully penetrate the beads and for the impurities to diffuse out of the beads.

The *t*-BOC protecting group was used in this research because it is easily and cleanly removed by thermolysis in a process which affords only gaseous by-products. Therefore, it can be removed in a solid-state reaction that does not require any subsequent tedious washing procedure to isolate the beads. In a typical experiment the polymer beads 5a–c containing the *t*-BOC protected phenolic groups are placed in a round-bottom flask and heated to the appropriate temperature under a flow of inert gas or under a high vacuum. The by-products of this reaction are carbon dioxide and isobutylene[10], which are gases at the temperatures used for the cleavage of these protecting groups and are therefore easily removed. Once the cleavage reaction is complete, the deprotected polymer beads 1a–c are ready to be packed into h.p.l.c. columns. No reaction workup is necessary and the long washing times associated with chemical cleavage are avoided.

Another advantage of the *t*-BOC protecting group is that its thermolytic removal is not affected by the steric effects which may be quite important in normal chemical deprotection processes. For example, we found that the *t*-BOC group of 5a could be cleaved easily and quantitatively by heating the polymer beads overnight in a 5% solution of NaOH/MeOH at 65°C. In contrast, the *t*-BOC group of 5c was more difficult to cleave under these conditions because the bulky isopropyl groups shield the carbonate group from attack by chemical reagents. Even after seven days of heating 5c at 65°C in a 5% solution of NaOH/MeOH, a significant amount of the *t*-BOC group remained. This problem does not arise in the case of the thermolytic deprotection of 5c which only requires a few minutes of heating at 230°C as accessibility of the reactive sites is not a factor in this reaction.

Chromatographic properties of the resins

The polymer beads prepared above were packed into 15 × 0.46 cm stainless steel h.p.l.c. columns at 3000 psi of solvent pressure using methanol as the mobile phase and a balanced density slurry[22] of methanol and carbon tetrachloride. Columns having plate counts (N) of approximately 18 000 N/m were obtained with unsized resins such as 1a and 1b having a mean particle size near 10 μm. This plate count is considered to be quite good for a column packed with an unsized polymer sample.

A large number of chromatographic separations were carried out using columns packed with polymers 1a–c. In view of the design of the column packings, this testing was carried out entirely with a variety of amines which are generally very difficult to separate with silica-based separation media[23]. In general, elutions required the use of a solvent containing a polar component (e.g. hexane-ethyl acetate 9:1) because pure hexane was ineffective due to the formation of strong hydrogen bonds between the stationary phase and the amines to be eluted. *Figure 8* shows that aniline, 2,6-dimethylaniline, 2,6-diethylaniline, 2,6-diisopropylaniline, and 2,4,6-tri-*t*-butylaniline are all easily separated from one another by polymer 1a. The most hindered molecule, 2,4,6-tri-*t*-butylaniline, elutes with the column dead volume because it is too hindered to hydrogen bond to the phenol, while the least hindered molecule, aniline, shows the most retention because it can most easily form hydrogen bonds with the phenolic resin.

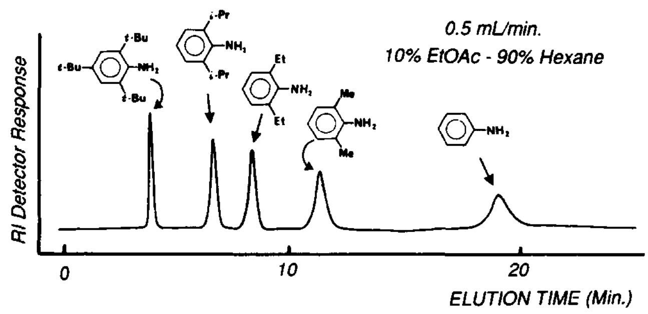

Figure 8 Separation of amines using polymer 1a

A potential application of these hindered phenol polymers lies in the separation of aliphatic amines which are much more basic than pyridines and anilines. We found that, as was the case with silica columns, it is virtually impossible to achieve any meaningful separation of aliphatic amines using polymer 1a. The phenol moiety has a pKa of approximately 10 (in aqueous solution), while the pKa of the conjugate acid of most aliphatic amines lies between 9 and 10 (refs 25 and 26). In this region of pKa values, proton exchange can occur between a phenol and an amine in addition to the formation of very strong hydrogen bonds. As a result, an attempted separation of 1-phenylethylamine and 2-phenylethylamine using polymer 1a required the use of a very polar solvent, methanol, to achieve elution of these aliphatic amines which were strongly absorbed to the resin and therefore the resulting chromatographic peaks were so broad that they virtually disappeared in the baseline.

2,6-Dimethylphenol and 2,6-diisopropylphenol are reported to have pKa values of 10.6 and 11.1 respectively[25,26], which means that they are much less acidic than the unhindered phenol moiety and should form weaker hydrogen bonds with aliphatic amines. In addition, the H-bonds which are formed may also be lengthened and weakened because of the steric interference between the *ortho* alkyl groups of the hindered phenol and the substituents of the molecule to which the phenol is hydrogen bonding[27]. Both of these factors could lead to the formation of a relatively weak hydrogen bond between the aliphatic amines and the 2,6-diisopropylphenol moiety of resin 1c. *Figure 9* shows a good separation with little tailing of benzylamine, 2-phenylethylamine, and 4-phenylbutylamine using 1c and a mobile phase consisting of 4:1 methanol–water.

A more extensive report of the chromatographic characteristics and properties of columns derived from polymers 1a–c will be published elsewhere.

EXPERIMENTAL

All suspension copolymerizations were performed in a Büchi BEP 280 autoclave (Büchi AG, Uster, Switzerland). This reactor has a motor which provides overhead stirring, a semi-cylindrical 250 ml round bottom glass reaction vessel with an outer water jacket, a circular water-cooled condenser, and a stainless-steel anchor-type stirrer. The polymer beads were packed into h.p.l.c.

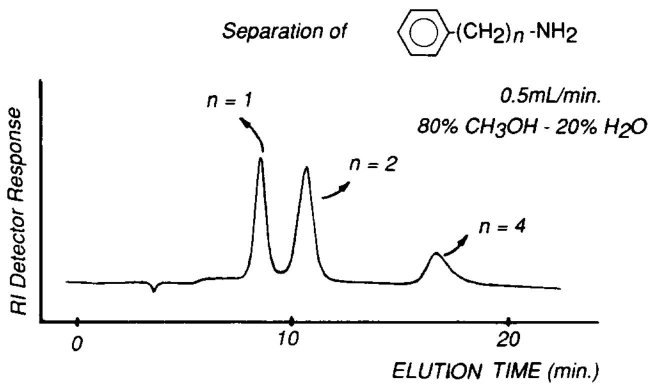

Figure 9 Separation of primary amines using polymer 1c

columns with a Chromatem slurry packing instrument for h.p.l.c. columns, purchased from Touzart and Matignon (France), using stainless-steel columns (15×0.46 cm i.d.) and stainless-steel frits. The analytical h.p.l.c. equipment used included a Perkin-Elmer Sigma 15 Chromatography Data Station, a Perkin-Elmer Series 10 Liquid Chromatograph, a Perkin-Elmer LC-25 Refractive Index Detector, and a Rheodyne 7125 Sample Injector equipped with a 6 μl sample loop. Plate/meter efficiencies of the columns were calculated from the half-width height of a pentane peak using methanol as the mobile phase at a flow rate of 0.5 ml/min. A Waters 500 Preparative h.p.l.c. instrument with two 500 g silica gel columns was used in monomer purifications. A sixteen-channel particle size analyser, Coulter Counter Model TA II (Coulter Electronics, Luton, England) was used to measure particle size distributions of bead samples. Calibration was performed with standard poly(styrene-divinylbenzene) latexes; a 1% NaCl solution served as the electrolyte. The orifice tube used had an aperture of 70 μm. The numerical results, in the form of the volume distribution, were transformed into a particle size distribution curve using a model distribution function that can be expressed in both the integral [I(x)] and differential dI/dx form[28]. All of the measurements of particle size and all of the calculations of the mean and standard deviation were performed at the Institute of Macromolecular Chemistry, Prague, Czechoslovakia.

Surface areas of polymer beads were obtained by the method of dynamic desorption of nitrogen using a Quantasorb Sorption System. The data was transformed into specific surface areas by way of the Brunauer–Emmett–Teller theory[29]. Mercury porosimetry measurements were made with a Carlo Erba Model 225 Hg porosimeter (Carlo Erba Strumentazione, Italy) at the Institute of Macromolecular Chemistry in Prague, Czechoslovakia. Solvent regains were measured by the centrifugation technique of Pepper[30] using disposable Centrex microfilters purchased from Mandel Scientific.

A Nicolet 10-DX *FT*i.r. spectrometer was used to obtain infrared spectra. Solid samples were run as KBr pellets. Liquids were run by spreading a thin film of the liquid on top of a KBr pellet. Nuclear magnetic resonance spectra were obtained on Varian CFT-80, and XL-300 spectrometers. $CDCl_3$ was used as the solvent and tetramethylsilane (TMS) was used as the internal standard. For ^{1}H n.m.r. spectra, δ values are reported in ppm from TMS. Abbreviations used are: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Thermogravimetric analyses were done with a Mettler TA 3000 at a heating rate of 10°C/min in a nitrogen atmosphere.

The monomer *p*-*t*-butoxycarbonyloxystyrene was prepared as previously reported[10]. Divinylbenzene was purchased from Polysciences Inc. (USA). Prior to polymerization, it was washed three times with 5% NaOH and three times with water, dried over $CaCl_2$, filtered, and then distilled at 50°C under reduced pressure (0.5 mm of Hg). Poly(vinyl alcohol) was purchased from Wacker Chemie (Polyviol 25/140, 86–89% hydrolysed, with molecular weight *c.* 80 000, DP = 1600).

Formylation of 2,6-dimethylphenol and 2,6-diisopropylphenol

A 1 l round-bottom flask equipped with a water-cooled condenser was charged with 480 ml of trifluoroacetic acid and 44.8 g (0.319 moles) of hexamethylenetetramine, followed by 39.04 g (0.319 moles) of 2,6-dimethylphenol. This mixture was stirred at 85°C for 13 h under nitrogen. A t.l.c. taken at this time indicated that there was no starting material remaining. Most of the trifluoroacetic acid was removed by evaporation and the crude product was poured into 500 ml of ice water. After stirring for five minutes, the mixture was neutralized by gradual addition of a 5% solution of sodium carbonate. The aqueous phase was then extracted three times with 500 ml portions of diethyl ether, and then most of the ether was removed on a rotavapour. At this point, the product has a dark brown colour which can be removed by shaking three times with 200 ml of 1N HCl. The clear, red ether solution was then washed three times with 300 ml portions of water, dried over magnesium sulphate and evaporated to dryness. For both monomers, the crude products were purified by recrystallization from a chloroform/hexane mixture; 3,5-dimethyl-4-hydroxybenzaldehyde and 3,5-diisopropyl-4-hydroxybenzaldehyde were isolated in 70 and 78% yield respectively.

For 3,5-dimethyl-4-hydroxybenzaldehyde: (7b). Elemental Analysis; found: C, 71.77, H, 6.65; calculated: C, 71.98, H, 6.71. ^{1}H n.m.r.: 9.73 (s, 1H, H-aldehyde); 7.47 (s, 2H, H-aromatic); 6.35 (broad absorption, 1H, OH); 2.30 (s, 6H, H-methyl). *FT*i.r.: 3234 (OH stretch): 2838 (aldehyde CH stretch); 1664 (aldehyde C=O stretch); 1595 (aromatic C=C ring stretch).

For 3,5-diisopropyl-4-hydroxybenzaldehyde: (7c). Elemental Analysis; found: C, 75.43, H, 8.82; calculated: C, 75.69, H, 8.79. ^{1}H n.m.r.: 9.83 (s, 1H, H-aldehyde); 7.57 (s, 2H, H-aromatic); 5.82 (broad 1H, OH); 3.19 (m, 2H, CH-isopropyl); 1.30 (d, 12H, CH_3-isopropyl). *FT*i.r. 3243 (OH stretch); 1665 (aldehyde C=O stretch); 1605, 1580 (aromatic C=C stretch).

Protection of the phenolic groups of 3,5-dimethyl-4-hydroxybenzaldehyde and 3,5-diisopropyl-4-hydroxybenzaldehyde as their t*-BOC derivatives*

In a typical experiment, a 3-neck, 1 litre flask equipped with overhead mechanical stirring was charged with 15 g (0.1 moles) of 3,5-dimethyl-4-hydroxybenzaldehyde, 27.64 g (0.2 moles) of finely ground anhydrous potassium carbonate and 400 ml of dry THF. The suspension was cooled to 5°C using an ice bath and then a solution of 21.83 g (0.1 moles) of di-*t*-butyl dicarbonate in 50 ml of THF was added to it. The mixture was stirred at 5°C for 1 h and then at room temperature for 48 h. A t.l.c. taken at this time indicated that there was very little starting material remaining. The solid phase was filtered off and the material in the filter was washed twice with ethyl acetate. The solvents were evaporated on a rotavapour and the resulting viscous, orange liquid was dried overnight in a vacuum oven. Any unreacted di-*t*-butyl dicarbonate was removed easily by raising the temperature in the vacuum oven to 60°C for a few hours. Although the crude product could be used directly in the next step of the synthesis, it was purified by preparative h.p.l.c. using 10% EtOAC/hexane. The yields of pure 3,5-dimethyl-4-*t*-butoxycarbonyloxybenzaldehyde and 3,5-diisopropyl-4-*t*-butoxycarbonyloxybenzaldehyde obtained after h.p.l.c. were 89.5% and 87% respectively.

*For 3,5-dimethyl-4-*t*-butoxycarbonyloxybenzaldehyde:* (8b). Elemental Analysis; found: C, 66.99, H, 7.31; calculated: C, 67.18, H, 7.24. ^{1}H n.m.r.: 9.93 (s, 1H, aldehyde); 7.60 (s, 2H, H-aromatic); 2.27 (s, 6H, H-methyl); 1.57 (s, 9H, H-*t*-butylcarbonate). *FT*i.r.: 2725 (aldehyde CH stretch); 1757 (carbonate $C{=}O$ stretch); 1698 (aldehyde $C{=}O$ stretch); 1600 (aromatic $C{=}C$ stretch).

*For 3,5-diisopropyl-4-*t*-butoxycarbonyloxybenzaldehyde:* (8c). Elemental Analysis; found: C, 70.46, H, 8.56; calculated: C, 70.56, H, 8.55. ^{1}H n.m.r.: 9.98 (s, 1H, aldehyde); 7.71 (s, 2H, aromatic); 3.13 (m, 2H, CH-isopropyl); 1.57 (s, 9H, *t*-butylcarbonate); 1.29 (d, 12H, CH_3-isopropyl). *FT*i.r.: 2715 (aldehyde CH stretch); 1758 (carbonate $C{=}O$ stretch); 1698 (aldehyde $C{=}O$ stretch); 1586 (aromatic $C{=}C$ stretch).

*Wittig reaction of 3,5-dimethyl-4-*t*-butoxycarbonyloxybenzaldehyde and 3,5-diisopropyl-4-*t*-butoxycarbonyloxybenzaldehyde*

In a typical experiment, a 0.5 l 3-neck flask equipped with magnetic stirring was immersed in an ice bath and charged with 31.31 g (0.087 moles) of methyltriphenylphosphonium bromide, 150 ml dry THF and stirred; 9.84 g (0.087 moles) of potassium *t*-butoxide were then added to the flask and the suspension was stirred for 20 minutes during which time the bright yellow-coloured ylide formed.

A solution of 19.92 g (0.080 moles) of 3,5-dimethyl-4-*t*-butoxycarbonyloxybenzaldehyde in 50 ml of THF was added dropwise from a dropping funnel, the ice bath was removed, and the resulting mixture was allowed to stir at room temperature for 5 h. The crude product was poured into 500 ml of ice water and this aqueous phase was then extracted 3 times with 500 ml of ethyl acetate. Some of the ethyl acetate was removed on a rotavapour, and then the ethyl acetate layer was back washed 3 times with 500 ml of water, dried over magnesium sulphate, and evaporated to dryness. The triphenylphosphine oxide by-product was removed with hexane prior to purification of the product by preparative h.p.l.c. The yields of 3,5-dimethyl-4-*t*-butoxycarbonyloxystyrene and 3,5-diisopropyl-4-*t*-butoxycarbonyloxystyrene obtained were 81 and 86%, respectively.

*For 3,5-dimethyl-4-*t*-butoxycarbonyloxystyrene:* (2b). Elemental Analysis; found: C, 72.72, H, 8.21; calculated: C, 72.55, H, 8.11. ^{1}H n.m.r.: 7.07 (s, 2H, H-aromatic); vinyl group with characteristic ABX pattern ($J_{AX}=18$ Hz, $J_{BX}=11$ Hz); 2.18 (s, 6H, H-methyl); 1.56 (s, 9H, H-*t*-butylcarbonate). *FT*i.r.: 3083 (vinylic CH stretch); 1755 (carbonate $C{=}O$ stretch); 1633 (vinylic $C{=}C$ stretch); 1601 (aromatic $C{=}C$ stretch).

*For 3,5-diisopropyl-4-*t*-butoxycarbonyloxystyrene:* (2c). Elemental Analysis; found: C, 74.91, H, 9.37; calculated: C, 74.96, H, 9.27. ^{1}H n.m.r.: 7.10 (s, 2H, H-aromatic); vinyl group with characteristic ABX pattern ($J_{AX}=18$ Hz, $J_{BX}=11$ Hz); 3.00 (m, 2H, CH-isopropyl); 1.53 (s, 9H, H-*t*-butylcarbonate); 1.22 (d, 12H, CH_3-isopropyl). *FT*i.r.: 3086 (vinylic CH stretch); 1751 (carbonate $C{=}O$ stretch); 1633 (vinylic CH stretch); 1599, 1589 (doublet, aromatic $C{=}C$ stretch).

Suspension copolymerization of p-t-*BOC-styrene* (*or its substituted analogues*) *with commercial divinylbenzene: Preparation of polymers* 5a–c

In a typical experiment, a 2% solution of poly(vinyl alcohol) was poured into the Büchi BEP 280 autoclave through a long-stemmed funnel and nitrogen was bubbled through this solution for 15 min. Nitrogen was bubbled through the organic phase for 10 min, and it was then poured into the reactor on top of the aqueous phase. The reactor was flushed with nitrogen and sealed, and then the suspension was stirred at room temperature for 25 min at the appropriate stirring speed. It was then heated with stirring at 80°C for 16 h, and then allowed to cool while stirring for an additional 30 min. For experiments which produced larger beads, the particles were taken into 500 ml of water and filtered through fine cloth. The polymer beads were then washed 10 times with 1 l of water, 10 times with 200 ml of methanol, 10 times with 100 ml of toluene, and 10 times with 200 ml of methanol, followed by drying overnight in a vacuum oven at 40°C. For experiments which produced smaller beads ($<15\ \mu$m), the milky-white suspension was poured into a 2 l beaker and diluted to a volume of 1 l with water. The beaker was placed in an ultrasonic bath and sonicated for 30 min. This process is used to break up the aggregates of the polymer beads that have formed by electrostatic interactions. This separates the 'fines' from the larger particles and allows the fines (which have a tendency to clog the frits in h.p.l.c. columns) to be removed in the decantation procedure. The beaker was removed from the ultrasonic bath and the particles were allowed to settle overnight.

After 24 h, the supernatant was removed by siphoning, and another 1 l of water was added. This sonication and siphoning procedure was carried out five more times with 1 l portions of water. This slow process is necessary both in view of the size of the particles and to allow the excess poly(vinyl alcohol) suspension stabilizer to diffuse out of beads and into the aqueous phase. The particles were then washed as above, allowing time for settling of particles and removing the wash liquid via siphoning, with five 500 ml portions of methanol, five 200 ml portions of toluene, and five 200 ml portions of methanol. The beads were then dried overnight in a vacuum oven at 40°C. The relevant experimental data is given in *Tables 4* and 5.

Thermal cleavage of the t-*BOC groups of polymers* 5a, 5b, *and* 5c

In a typical experiment, the polymer beads were placed in a 100 ml flask evacuated to 0.2 mm of Hg. The flask was then immersed in an oil bath preheated at 220–230°C and the polymer was heated in this temperature range for 30–90 minutes depending on the size of the sample to be deprotected. The *FT*i.r. spectra of the polymers after thermolysis showed that complete removal of the *t*-BOC groups had been achieved in each case.

Determination of pore volumes by the solvent regain method

Centrex disposable centrifugal microfilters were used for the determination of solvent regains. This apparatus consists of three pieces: a rubber cap, a plastic receiver tube which collects centrifuged solvent, and a plastic filter tube which is fitted with a Nylon membrane (0.2 μm pore size). In a typical experiment, the weight of the empty filter tube was recorded, a small amount of polymer beads was added (200 mg), and the filter tube was then reweighed. Four ml of cyclohexane were added and the tube was sealed with a rubber cap. The filter tube was then placed in a larger beaker of cyclohexane for 24 h. This step prevents the cyclohexane from draining through the membrane overnight. After the 24 h equilibration period had elapsed, the receiver tube was connected to the filter tube and the excess cyclohexane was removed by centrifugation (without the rubber cap) at high speeds for 5 min. The filter tube was then weighed quickly. The amount of cyclohexane absorbed by the sample, (a), was calculated from the increase in weight of the filter tube. In each experiment, an empty filter tube was also filled with cyclohexane and centrifuged. The weight of cyclohexane retained by the membrane, (b), was calculated from the increase in weight of this tube. The solvent regain of the polymer was then calculated using the following equation:

$$R_s = [(a-b)d]/w$$

where d = density of cyclohexane (0.78 ml/g), w = weight of polymer used in the experiment.

Table 4 Suspension copolymerization[a] of *p*-*t*-BOC-styrene and commercial divinylbenzene: experimental conditions for control of porosity

Porogen	Monomers[b] (ml)	Yield (%)	Surface area (m^2/g)	Solvent regain (ml/g)
1-Butanol (5.1 ml)	11.9	74	<1	0.12
1-Butanol (6.8 ml)	10.2	76	1.3	0.43
1-Butanol (8.5 ml)	8.5	78	4.8	0.60
1-Butanol (10.2 ml)	6.8	80	142.6	1.36
1-Butanol (11.9 ml)	5.1	76	26.1	1.85
Cyclohexanol (10.2 ml)	6.8	66	226.9	1.64
Cyclohexanol (8.5 ml)	8.5	76	189.5	0.92
Cyclohexanol (6.8 ml)	10.2	73	<1	0.52
1-Pentanol (10.2 ml)	6.8	80	145.1	1.75
1-Heptanol (10.2 ml)	6.8	87	136.3	1.91
1-Octanol (10.2 ml)	6.8	82	93.4	1.95
1-Decanol (10.2 ml)	6.8	81	44.0	2.10

[a] Aqueous phase: 60 ml of a 2% solution of poly(vinyl alcohol). Stirring speed: 350 rpm

[b] Monomers: Equal weights of *p*-*t*-BOC-styrene and divinylbenzene were weighed out and mixed together. To this was added 1.86 wt% of AIBN (based on the combined weight of the two monomers)

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Table 5 Experimental conditions for the suspension copolymerization of *p*-*t*-BOC-styrene and its substituted analogues with commercial divinylbenzene

Polymer	5a	5a	5a	5a	5b	5c
Volume of 2% PVA (ml)	90	90	90	90	90	90
Weight of monomer[a] (g)	4.50	4.50	4.50	4.50	4.82	5.00
Weight of DVB (g)	4.50	4.50	4.50	4.50	4.28	3.62
Weight of AIBN (g)	0.167	0.167	0.167	0.167	0.159	0.135
Total volume of monomers (ml)	9.0	9.0	9.0	9.0	9.0	9.0
Volume of cyclohexanol (ml)	13.5	13.5	13.5	13.5	13.5	13.5
Stirring speed (rpm)	800	725	850	925	800	800
Yield %	86	89	84	87	79	80
Mean particle size (μm)	10.2	13.8	8.3	6.8	10.4	12.0
(Standard deviation)	(4.42)	5.81	3.43	3.13	(4.34)	(5.75)
Surface area (m^2/g)	232	204	254	237	313	262

[a] For polymers 5a–c the monomers used were, respectively: *p*-*t*-BOC-styrene, 3,5-dimethyl-4-*t*-butyloxycarbonyloxystyrene, and 3,5-diisopropyl-4-*t*-butyloxycarbonyloxystyrene

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