Journal of Chromatography, 504 (1990) 97–112
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 22 222

High-performance liquid chromatography separation media based on functional polymers containing phenolic hydroxyls

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(First received August 29th, 1989; revised manuscript received December 15th, 1989)

SUMMARY

New separation media based on highly cross-linked porous-bead polymers containing pendant phenolic groups have been prepared. The steric environment and acidity of the phenolic groups have been varied systematically to provide access to a new family of separation media useful in the separation of aromatic as well as aliphatic amines. The bead polymers with 10 μm average size are prepared by suspension polymerization of 4-*tert.*-butyloxycarbonyl (t-BOC) derivatives of 4-hydroxystyrene or analogues with alkyl substituents in positions 3 and 5, with divinylbenzene under conditions which afford polymers with surface areas of more than 200 m^2/g. The t-BOC groups are removed from the bead polymers by a thermolysis process which greatly facilitates bead processing. The unclassified polymers gave high-performance liquid chromatography columns with approximately 18 000 plates per meter and were found to be very effective in the separation of amines.

INTRODUCTION

In the last decade there has been a large increase in the number of polymer-based high-performance liquid chromatography (HPLC) columns available for difficult separations. This increase has come about even though the plate counts of the best of these materials cannot match those of most of the silica-based separation media. The latter have enjoyed immense popularity because silica-based separation media can be produced inexpensively with small particle sizes, narrow particle size distributions, very uniform pore structures and with enough mechanical stability to easily withstand the high pressures of modern HPLC[1]. These properties result in columns which have high plate counts and very high resolution. In addition, the reactive silanol groups on the silica surface can be reacted with a variety of organic moieties to give separation media with a wide range of polarities[1], some of which may, for example, be useful in the resolution of stereoisomers[2]. A significant draw-

0021-9673/90/$03.50

back of the silica columns is their lack of stability in basic media[3]. Their use under basic conditions leads to dissolution of the silica matrix with formation of large void volumes, which limits the kinds of separations that can be performed. In spite of recent efforts to shield the silica with bulky silanizing reagents[4] or thick layers of polymer[5], none of the currently available silica-based materials is truly stable over the entire pH range.

This pH instability has sparked interest in new materials such as polymeric HPLC resins because many of these offer pH stability over the entire pH range, which places fewer limitations on the kinds of separations that can be performed. The first resins prepared by suspension polymerization were rather large particles, 50–100 μm, which were not very useful for HPLC[6]. Gradual improvements in reactor design and suspension polymerization methodology[7] have allowed the reproducible large-scale preparation of resins with an average particle size of 5 μm. One of the first high-resolution polymeric HPLC columns was packed with the PRP-1 resin, introduced in 1980 by the Hamilton company[8]. This spherical, 10-μm macroporous resin is a copolymer of styrene and divinylbenzene, which is stable from pH 0 to 14 and can be used for the separation of a wide variety of organic molecules. Many other unique polymeric HPLC columns have since been introduced, including ion exchangers[9], unique reversed-phase columns[10] and a new graphitized carbon column[11]. Other developments in this field include the seeded polymerization technique introduced by Ugelstad and co-workers[12,13], which allows the production of monodisperse polymeric resins, thereby avoiding the time-consuming size classification which is necessary with conventional suspension polymerized resins. The newest innovation has been the pellicular polymeric resins[14], which have efficiencies approaching those of the silica-based materials in certain applications and are likely to see further advances in the near future.

This paper describes the chromatographic properties of a series of macroporous polymeric resins containing reactive phenolic functionalities. The design and synthesis of the monomers and polymers used in this study is described in detail elsewhere[15–17]. Substituted phenol resins were selected since the phenol moiety contains an acidic hydrogen atom that can form strong hydrogen bonds to basic compounds such as amines, as demonstrated previously[18] in the removal of ε-caprolactam from aqueous solutions by using large particles of a cross-linked poly(hydroxystyrene) resin. In our research, a series of 10-μm, rigid, spherical, macroporous beads (Fig. 1, structures **1–3**) were prepared, in which the acidity of the phenolic hydrogen and the steric environment around the phenolic hydrogen was changed systematically in order to observe the influence of structure on separation ability.

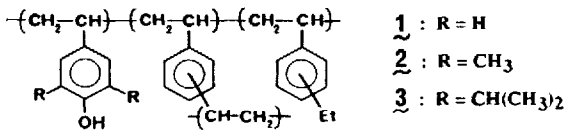

Fig. 1. Structure of the cross-linked bead polymers **1–3**. Et = Ethyl.

EXPERIMENTAL

Polymer beads were packed into HPLC columns with a Chromatem slurry packing machine for HPLC columns purchased from Touzart and Matignon. For a typical experiment, 1,5 g of polymer beads were suspended in 15 ml of slurry solvent (a balanced-density mixture as described in the section below) with the aid of sonication. This suspension was poured into the column packing tube and packed for 1 h at 3000 p.s.i. by using methanol as the packing solvent. The analytical HPLC 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 (RI) detector, and a Rheodyne 7125 sample injector equipped with a 6-μl sample loop. Stainless steel columns (15 cm × 0.46 cm I.D.) were purchased from Mandel Scientific, and all stainless-steel frits were purchased from P.M. Instruments (Toronto, Canada). Plate/meter efficiencies of the columns were calculated from the half-width height of a pentane peak by using methanol as the mobile phase at a flow-rate of 0.5 ml/min. All solvents used were HPLC grade and all of the solutes injected on the columns were purchased from Aldrich. Thermogravimetric analyses were done with a Mettler TA 3000 at a heating rate of 10°C/min and under a nitrogen atmosphere. Detailed experimental procedures for monomer synthesis and suspension polymerizations, as well as procedures for porosity and particle size analysis, can be found elsewhere[15,16].

Determination of the balanced-density slurry

A balanced-density solvent mixture is a mixture of two solvents, one having a higher density and the other a lower density than the polymer beads[19], and the overall density matching that of the polymer beads. The quantities of the two solvents are adjusted so that the beads do not rise or fall in the slurry solvent mixture. This helps to give a more homogeneously packed column because the larger and heavier polymer beads will not tend to settle to the bottom of the column while the slurry is in the column packing apparatus; this is especially important for an unsized sample of polymer beads. In order to determine the balanced-density slurry, a small amount of polymer beads (enough to fit on the tip of a spatula) was placed in a 10-ml vial and 2 ml of carbon tetrachloride (density = 1.594 g/ml) were added. In this solvent the polymer beads float up to the top of the vial. Methanol (density = 0.791 g/ml) was then added to the vial from a buret in 0.1-ml increments, and the direction of travel of the polymer beads was observed after the addition of each increment. The addition of methanol was stopped when the particles began to sink towards the bottom of the vial because the balanced density of the slurry was reached at this point. For polymers **1** and **2**, the balanced-density slurry composition was methanol–carbon tetrachloride (1.2:1.0, v/v), while for polymer **3** it was methanol–carbon tetrachloride (1.4:1.0, v/v).

*Thermal cleavage of the t-BOC groups of **9**, **10** and **11***

These reactions were done in 100-ml round-bottom flasks equipped with adapters connecting the flasks to a high-vacuum pump. The flask containing the polymer beads were immersed in an oil bath preheated to 220–230°C and left for time periods adjusted according to the sample size. Our previous work with t-BOC-protected phenolic polymers[17,20] has shown that deprotection times can be reduced drastically to a few minutes by decreasing the size of the polymer sample or by using a slowly rotating

system for which heat transfer is greatly improved. Fourier transfrom infrared (FT-IR) spectra confirmed the complete removal of the t-BOC groups after the thermolysis reaction (loss of strong t-BOC carbonyl band centered near 1760 cm^{-1}).

RESULTS AND DISCUSSION

Design and synthesis of the resins

The conditions used in the synthesis of our series of substituted phenolic resins are outlined schematically in Fig. 2. Suspension copolymerization of the appropriate alkyl-substituted *p*-t-BOC styrene monomer (**4–6**) with commercial "divinylbenzene" (55% of **7** and 45% of **8**) at 80°C in the presence of a porogen gave a series of rigid, spherical, macroporous substituted phenolic resins (**9–11**). High stirring speeds (800 rpm) and high concentrations of suspension stabilizer [2% poly(vinyl alcohol) in water] were used as these conditions favor the formation of small beads. Cyclohexanol (60% of the total organic phase) was used as the porogen as it gave resins with high surface areas and porosities. Monomers **4–6**, containing the t-BOC protecting group, were chosen because the t-BOC group can easily be thermolyzed once the polymer beads have been prepared to yield the desired phenolic functionality[17].

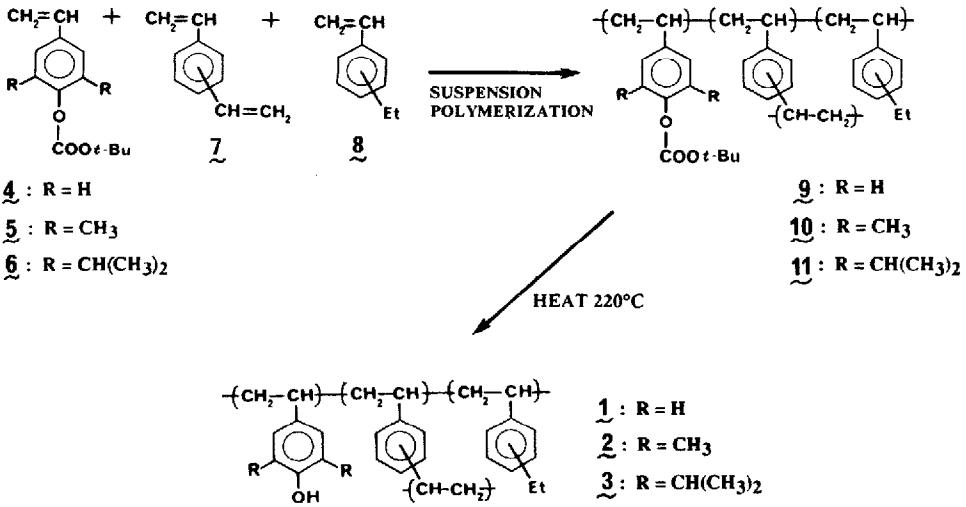

Fig. 2. Preparation of polymers **1–3**. Et = Ethyl; *t*-Bu = *tert.*-butyl.

Because of the small scale of the polymerization reaction no attempts were made to size the resin beads, but instead, conditions were optimized to produce batches with relatively narrow size distributions. Fig. 3 shows an example of a batch with an average particle size of about 10 μm, which was best suited for our study as distributions with a smaller average particle size led to high column back pressures because of the large percentages of fines in these samples. The physical data for polymers **9–11** are reported in Table I, which shows that we were successful in pro-

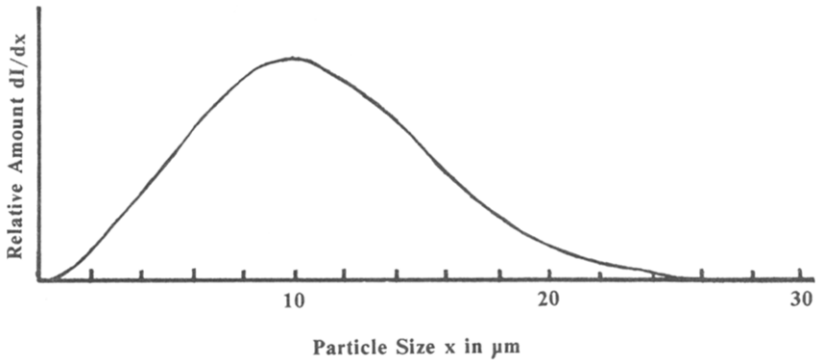

Fig. 3. Particle size distribution for polymer **9** prepared by suspension polymerization.

ducing a series of resins having small average particle sizes (10–12 μm) and high surface areas (200–300 m^2/g). This table also shows the thermolysis temperature for the t-BOC group of each polymer and the percentage weight loss upon heating from 50 to 300°C. In all cases, loss of the t-BOC groups upon thermolysis was confirmed by FT-IR monitoring as the strong carbonyl band near 1760 cm^{-1}, which is characteristic of the t-BOC groups, was absent after thermolysis. The mole fraction of protected phenolic units incorporated in each sample could be calculated from these weight losses. Fig. 4 contains the thermogravimetric analysis trace for **9**, demonstrating that the t-BOC protecting group can be removed cleanly and quantitatively simply by heating the resin to the appropriate temperature; similar curves were obtained in the thermolysis of polymers **10** and **11**. Fig. 5 shows the cumulative mercury porosimetry curve for polymer **9**. Most of the porosity can be found in pores below 1000 Å, which accounts for the high surface area of this polymer. The rise of this curve above 5000 Å is an artifact of the mercury porosimetry technique and represents the filling of the spaces between the beads by mercury; similar curves were obtained for **10** and **11**.

TABLE I

PHYSICAL DATA FOR POLYMERS **9**, **10** AND **11**

Parameter	*Polymer*		
	9	***10***	***11***
Mean particle size (μm)	10.20	10.42	12.00
(Standard deviation)	(4.4)	(4.3)	(5.7)
Surface area (m^2/g)	232	313	262
Thermolysis temperature (°C)	191	211	216
% Weight loss	23.4	23.6	21.6
Mole fraction of phenolic units	0.39	0.43	0.45

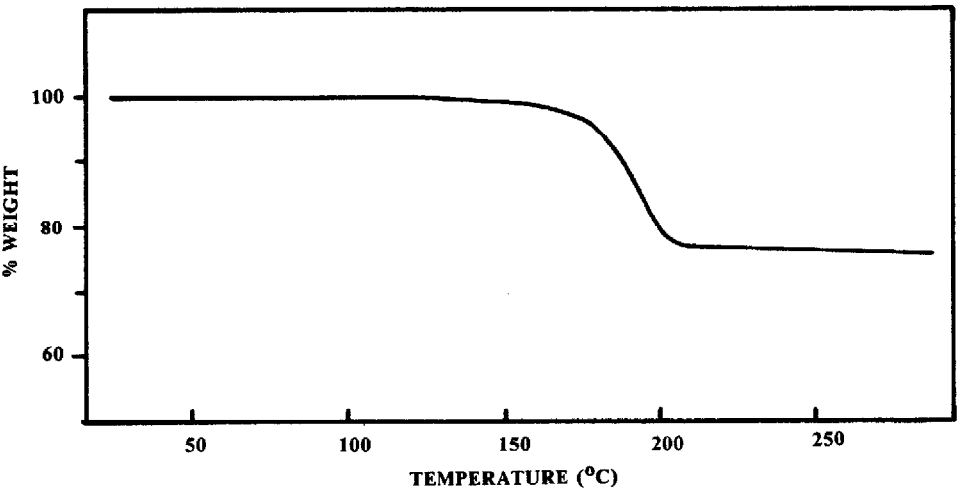

Fig. 4. Thermogravimetric analysis data recording the loss of t-BOC protecting group upon heating of polymer **9**.

Ease of processing of the bead products resulting from the thermal cleavage of the t-BOC group

The cleavage of protecting groups in HPLC-size polymer beads though easily conceived in terms of chemistry, is in fact a demanding and time-consuming operation due to the physical form of the polymer beads, which presents a special problem. While excess reagents, solvents and reaction by-products are usually removed from insoluble polymer beads by filtration, it is extremely difficult to filter very small polymer beads as small-size particles can easily clog filtration media leading to exceedingly long filtration times. To avoid these problems, it is convenient to wash the small beads through a series of decantations with appropriate solvents. This is a lengthy procedure that may typically require up to four weeks because one must allow the solvent to fully penetrate the beads and the impurities to diffuse out of the highly porous beads.

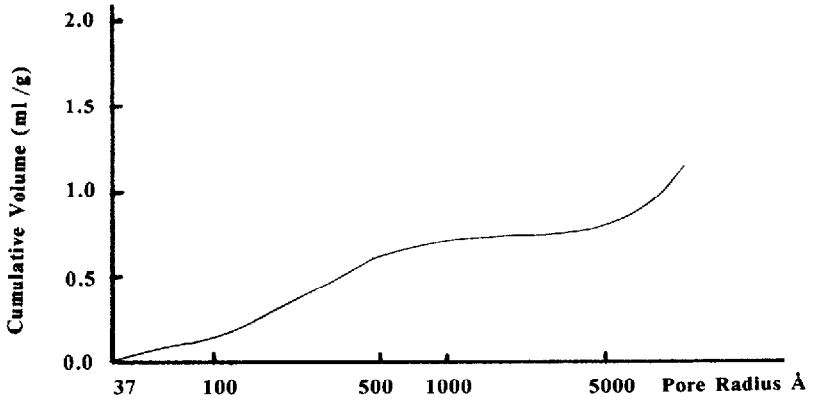

Fig. 5. Cumulative pore volume for polymer **9**.

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 procedures to isolate the purified beads. In our process, the polymer beads containing the t-BOC-protected phenolic groups were placed in a round-bottom flask and heated to the appropriate temperature under a flow of inert gas or under high vacuum. The by-products of this reaction — carbon dioxide and isobutylene[17] — are gases at the temperatures used for the cleavage reaction and are therefore easily removed. Once the cleavage reaction is complete, the beads are ready to be packed into HPLC columns without further work-up or washing. It is interesting to note that the thermolysis of the t-BOC groups of polymer **9** results in an apparent decrease in the surface area of the beads (from *ca.* 230 to *ca.* 150 m^2/g) as the flexibility of the more lightly cross-linked portions of the beads increase during the heating process and some temporary collapse is observed. However, the original surface area of the beads is regained (to *ca.* 225 m^2/g) after deprotection if the beads are again suspended in hexane, allowed to equilibrate and dried *in vacuo*.

Another advantage of the thermal reaction is that it is free from the steric inhibition effects which may be observed in the deprotection of the more hindered phenolic polymers used in this study. For example, we have found that the t-BOC group of **9** could be cleaved easily and quantitatively by heating to 65°C overnight a suspension of the polymer beads in a 5% solution of sodium hydroxide in methanol. In contrast, the t-BOC group of **11** proved much more resistant to cleavage under these conditions because the bulky isopropyl groups shield the carbonate group from attack by chemical reagents. Even after seven days of reaction at 65°C a significant amount of the t-BOC group remained. In contrast, the t-BOC group of **11** can be removed thermolytically in a few minutes by heating **11** at 200–230°C; accessibility of reactive sites is clearly not a factor with the thermolysis reaction.

Chromatographic properties of the resins

The polymer beads prepared above were packed *without prior sizing* into 15 cm × 0.46 cm I.D. stainless-steel HPLC columns at a solvent pressure of 3000 p.s.i. by using methanol as the mobile phase and a balanced-density slurry[19] of methanol and carbon tetrachloride. Polymers **1** and **2** gave columns with approximately 18 000

TABLE II

CALCULATION OF HEIGHT EQUIVALENT TO A THEORETICAL PLATE (HETP) FOR HPLC COLUMNS

Calculated from: $N = (t_{R_p}/W_{1/2})^2 \cdot 5.545$ and HETP = L/N, where N = number of plates, t_{R_p} = retention time for pentane (min), $W_{1/2}$ = width of pentane peak at half-height (min) and L = length of HPLC column (150 mm). HETP is measured by injection of 6 μl of a 2% solution of pentane in methanol by using 0.5 ml/min methanol as the mobile phase.

Polymer	t_{R_p}	$W_{1/2}$	N	N/m	*HETP* (μm)
1	4.85	0.220	2690	17 900	55.6
2	5.06	0.225	2800	18 700	53.5
3	5.51	0.330	1550	10 300	97.0

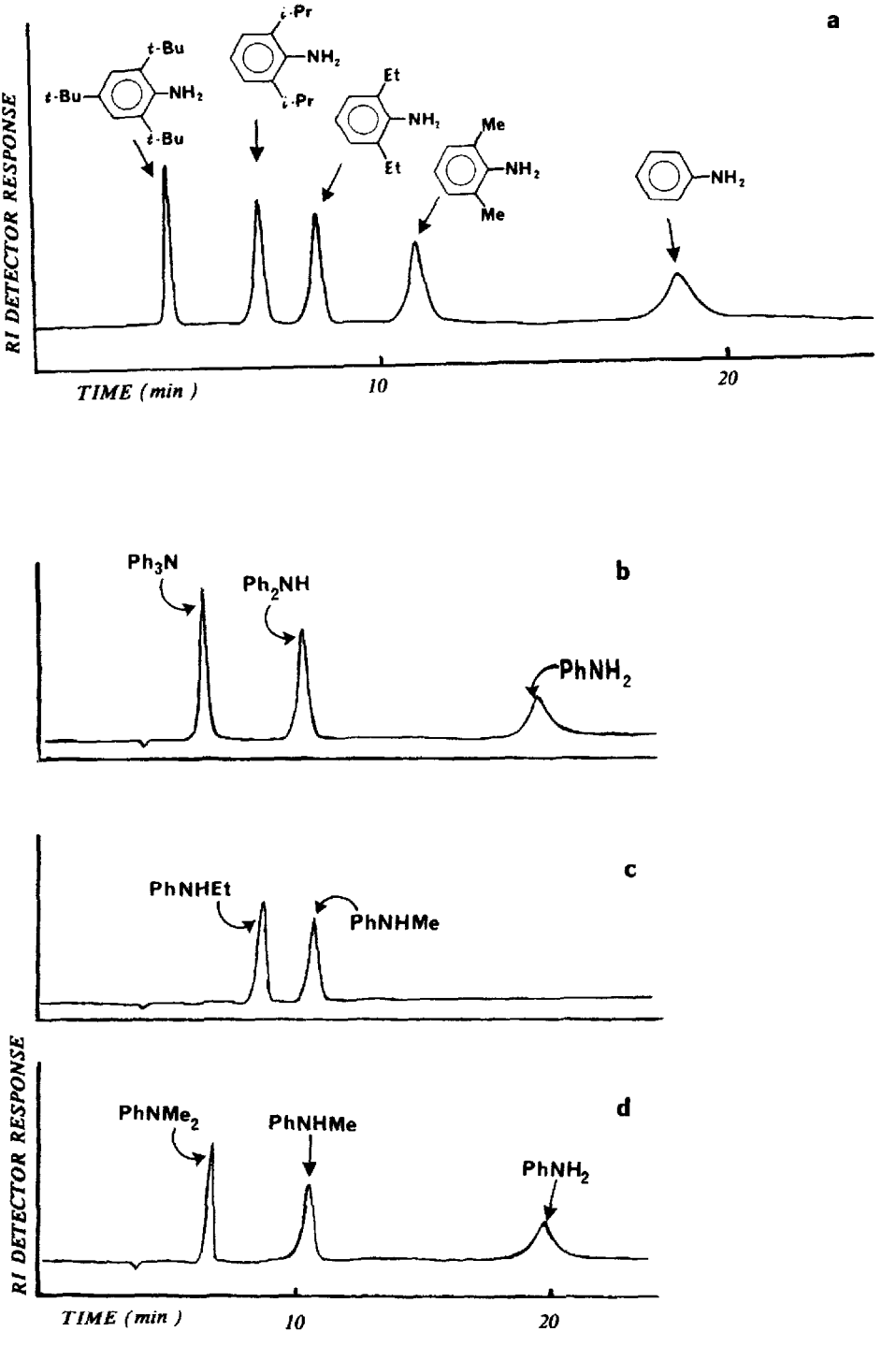
a
t-Bu
t-Bu
NH2
t-Bu
i-Pr
NH2
i-Pr
Et
NH2
Et
Me
NH2
Me
NH2
RI DETECTOR RESPONSE
TIME (min)
10
20
b
Ph3N
Ph2NH
PhNH2
c
PhNHEt
PhNHMe
d
PhNMe2
PhNHMe
PhNH2
RI DETECTOR RESPONSE
TIME (min)
10
20

Fig. 6.

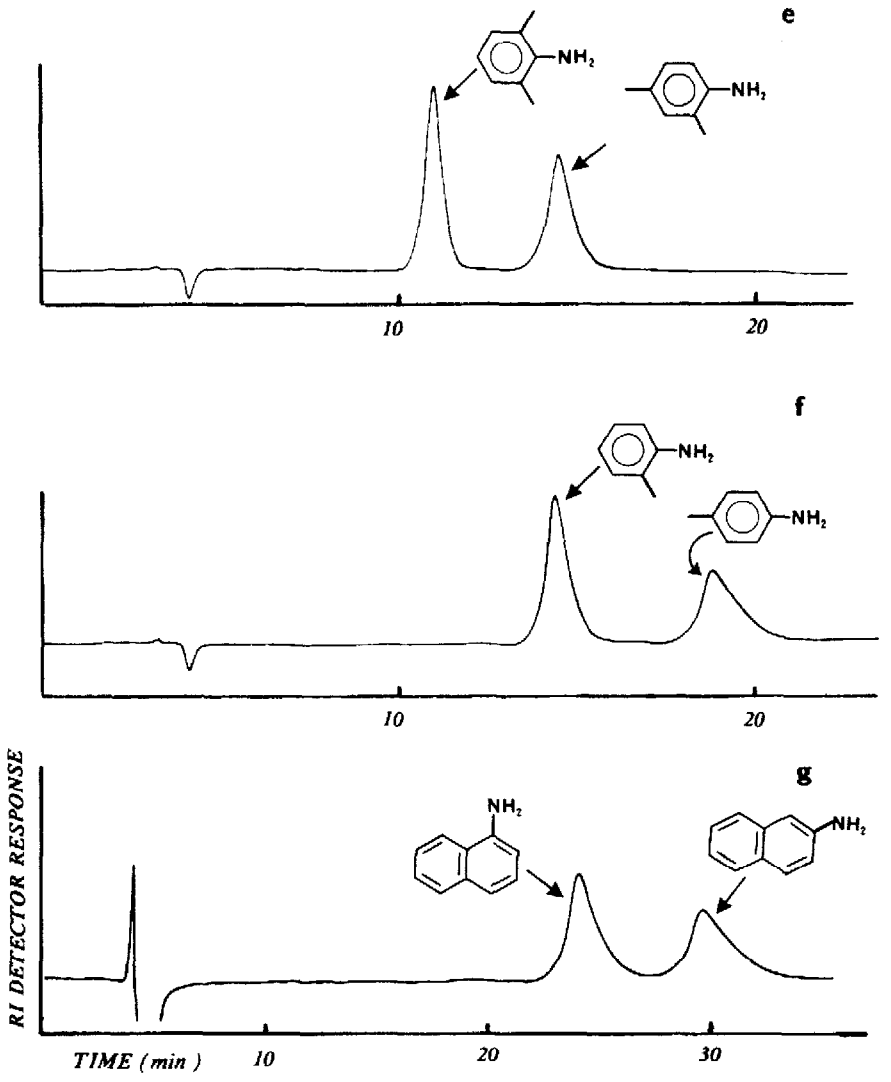

Fig. 6. Separation of aromatic amines on a 15-cm column of polymer **1** by using ethyl acetate–hexane (10:90, v/v) at 0.5 ml/min. Et = Ethyl; *i*-Pr = isopropyl; Me = methyl; Ph = phenyl; *t*-Bu = *tert.*-butyl. See text and Table III.

plates/m, as seen in Table II, while polymer **3** gave a column with approximately 10 000 plates/m; these values are considered to be very good for *unsized* polymer samples. Mobile phases ranging in polarity from methanol to hexane could be used with these columns without appreciable back pressure (about 1000 p.s.i.) and with retention of column efficiency as long as the flow-rates were not raised above 1.5 ml/min. Column dead volume times, t_0, were taken as the retention time for a heptane peak by using ethyl acetate–hexane (1:10, v/v) as the mobile phase.

A number of separations of a variety of aromatic amines performed by using polymer **1**, the unhindered phenol, are displayed in Fig. 6a–g; the corresponding

TABLE III

CHROMATOGRAPHIC DATA FOR SEPARATIONS DONE WITH 1

$k' = (t_R - t_0)/t_0$, t_R = retention time, t_0 = retention time of an unretained component (heptane) and $\alpha = k'_2/k'_1$. Both t_R and t_0 are in min.

Compound	t_R	t_0	k'	α
2,4,6-Tri-*tert.*-butylaniline	3.9	3.5	0.1	–
2,6-Diisopropylaniline	6.6	3.5	0.8	8.1
2,6-Diethylaniline	8.3	3.5	1.4	12.7
2,6-Dimethylaniline	11.2	3.5	2.2	20
Aniline	18.9	3.5	4.4	40
Triphenylamine	6.1	3.5	0.7	–
Diphenylamine	9.8	3.5	1.8	2.6
Aniline	18.9	3.5	4.4	6.3
N-Ethylaniline	8.2	3.5	1.3	–
N-Methylaniline	10.3	3.5	1.9	1.5
N,N-Dimethylaniline	6.4	3.5	0.8	–
N-Methylaniline	10.3	3.5	1.9	2.4
Aniline	19.0	3.5	4.4	5.5
2,6-Dimethylaniline	11.3	3.5	2.2	–
2,4-Dimethylaniline	14.3	3.5	3.1	1.4
2-Methylaniline	14.8	3.5	3.2	–
4-Methylaniline	18.7	3.5	4.3	1.3
2-Methylpyridine	12.1	3.5	2.4	–
4-Methylpyridine	14.7	3.5	3.2	1.3
2,6-Dimethylpyridine	10.9	3.5	2.1	–
2,5-Dimethylpyridine	13.6	3.5	2.9	1.4
2,4-Dimethylpyridine	15.6	3.5	3.4	1.6
1-Aminonaphthalene	23.7	3.5	5.7	–
2-Aminonaphthalene	29.5	3.5	7.4	1.3

chromatographic data are given in Table III. The term "α", which is the relative retention of one solute with respect to another, is obtained by dividing the capacity factors (k') of the solutes; the larger the value of α, the better the separation[21]. All of the values of α reported in Table III are determined relative to the first component of each mixture. Elution of these aromatic amines was possible by using a small percentage (10%) of a polar solvent, ethyl acetate, mixed with a non-polar solvent, hexane. The various amines could not be eluted from this column by using pure hexane as the mobile phase because of the relatively strong hydrogen bonds which are formed between the amines and the phenolic hydroxyl. Low flow-rates were used with the columns of unsized beads since higher flow-rates (>1.5 ml/min) caused excessive pressure drops.

Fig. 6a shows that aniline, 2,6-dimethylaniline, 2,6.diethylaniline, 2,6-diisopropylaniline and 2,4,6-tri-*tert.*-butylaniline are all easily separated from one another by polymer **1**. The most hindered molecule, 2,4,6-tri-*tert.*-butylaniline, elutes with the

column dead volume because it is too hindered to form hydrogen bonds with the phenol, while the least hindered molecule, aniline, shows the most retention because it can most easily form hydrogen bonds with the phenol. Fig. 6b illustrates the separation of triphenylamine, diphenylamine and aniline; Fig. 6c shows a good separation of N-methylaniline and N-ethylaniline, while Fig. 6d confirms that this column can easily separate primary, secondary and tertiary amines. Fig. 6e–g shows good separations for aromatic amine isomers, namely 2,6- and 2,4-dimethylaniline, 2- and 4-methylaniline and 1- and 2-aminonaphthalene. In each case, the least sterically hindered amine shows the greatest retention on the column.

Fig. 7a and b shows that excellent separations are obtained on resin **1** with some alkyl pyridine isomers, 2- and 4-methylpyridine, as well as 2,4-, 2,5- and 2,6-dimethylpyridine. For the separation of pyridines, which are generally more basic than anilines[22], a more polar mobile phase, ethyl acetate–hexane (90:10, v/v), was required to achieve retention times similar to those of the aromatic amines. At this point, it should be pointed out that these types of separations are normally very difficult to carry out on *any type* of silica-based separation media because of the severe hydrogen bonding and the ion-exchange type of interactions which occur between the amines and the residual silanol groups on the silica surface[23]; such interactions generally lead to badly shaped chromatographic peaks.

The separations discussed above were then performed on polymers **2** and **3**

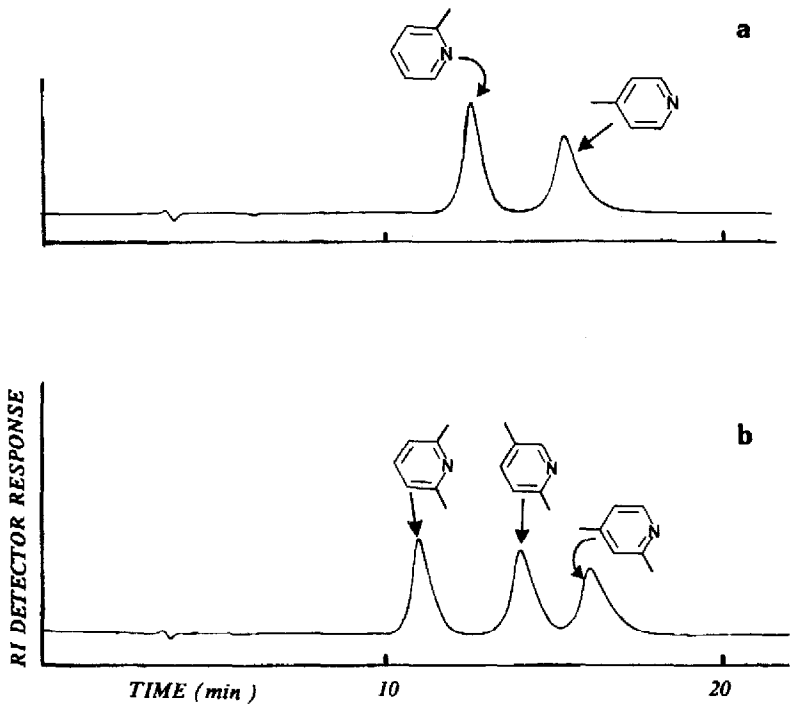

Fig. 7. Separation of substituted pyridines by using polymer **1**. A 15-cm column was eluted with ethyl acetate–hexane (90:10, v/v) at 0.5 ml/min.

under the conditions used with **1**; typical results are shown in Fig. 8. While baseline resolution of 2,6- 2,5- and 2,4-dimethylpyridine can be achieved by using the unhindered phenol polymer, **1**, the separation becomes progressively worse as the steric hindrance around the phenolic hydroxyl is increased. It is not surprising to see that the pyridines have less retention on the hindered phenol columns because the hindered phenols are less acidic than the unhindered phenol[24] and would be expected to form weaker hydrogen bonds with nitrogen containing compounds. In these cases, the decreased acidity and increased steric hindrance in **2** and **3** do not help to improve the selectivity of the separations. An aditional example of the differences which are observed in the separation of substituted pyridines with columns packed with polymers **1–3** is shown in Fig. 9. It is seen in this figure that some advantage may be taken of the differences in retention between the three types of packing materials. The

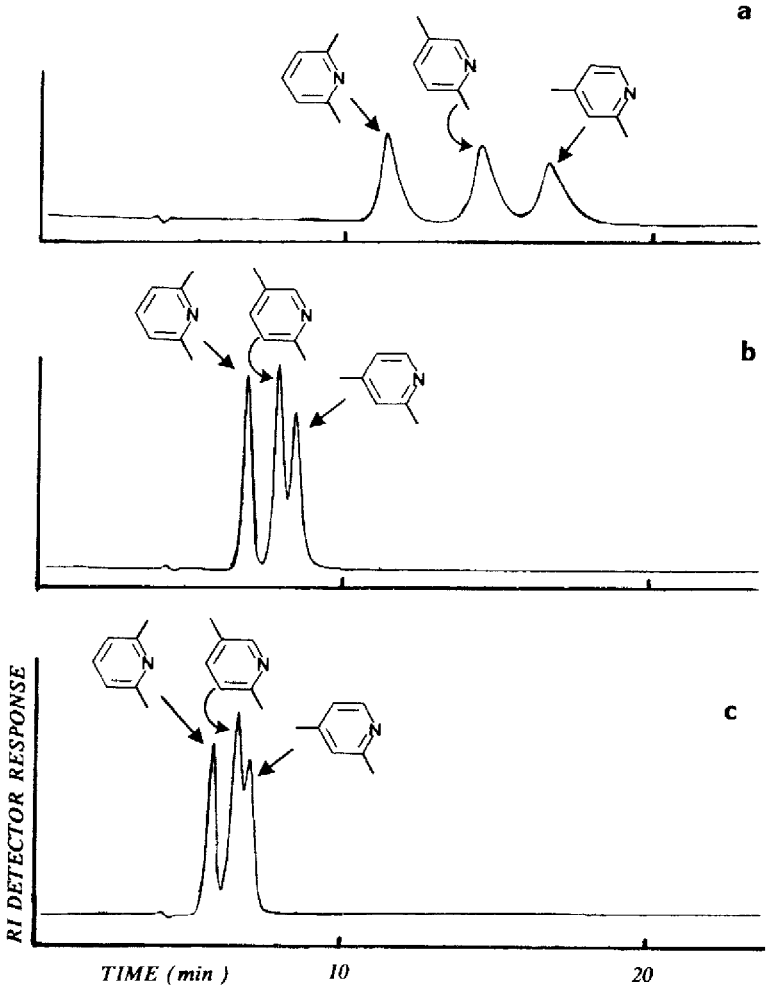

Fig. 8. Separation of substituted pyridines on 15-cm columns of (a) polymer **1**, (b) polymer **2**, and (c) polymer **3**, by using ethyl acetate–hexane (90:10, v/v) at 0.5 ml/min.

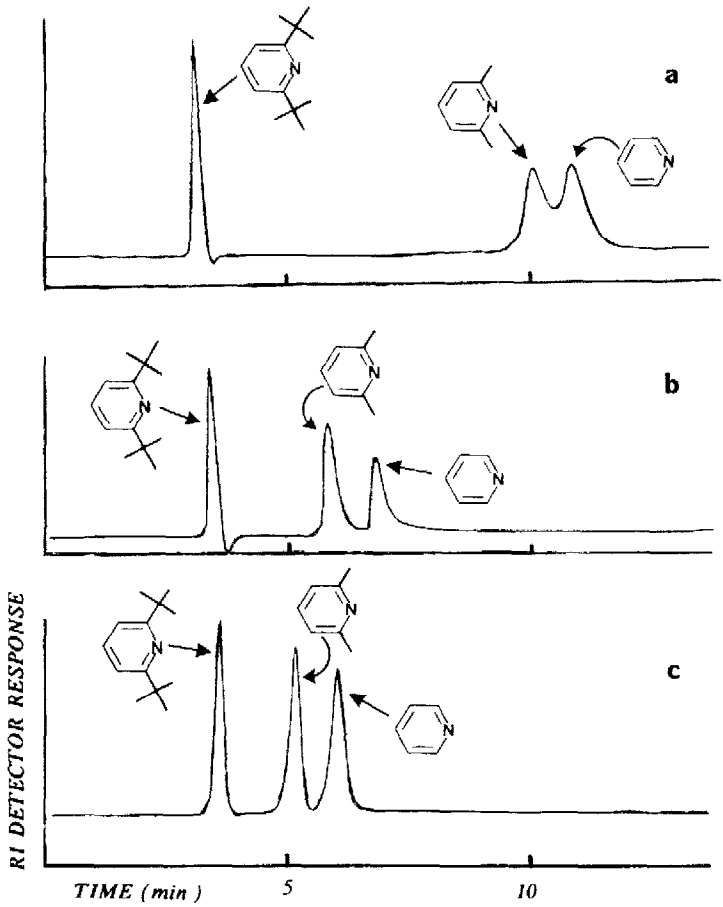

Fig. 9. Separation of substituted pyridines on 15-cm columns of (a) polymer **1** (Fig. 9a), (b) polymer **2**, and (c) polymer **3**, by using ethyl acetate–hexane (90:10, v/v) at 0.5 ml/min.

improved separation characteristics observed with columns packed with **2** or **3** likely result from the increased steric demands of these two polymers; it is noteworthy that columns packed with **2** or **3** also provide faster elution times.

It was expected that the hindered phenolic polymers **2** and **3** might prove even more versatile for the separation of aliphatic amines, which are much more basic than pyridines and anilines. As can be seen in Fig. 10a it is virtually impossible to achieve any meaningful separation of aliphatic amines by using polymer **1**. The phenol moiety of **1** has a pK_a of approximately 10 (in aqueous solution), while the pK_a of the conjugate acid of most aliphatic amines lies between 9 and 10 (ref. 24). In this region of pK_a values, proton exchange can occur between a phenol and an amine in addition to very strong hydrogen bonding. The separation attempted in Fig. 10a involved 1-phenylethylamine and 2-phenylethylamine on a column packed with polymer **1**; in this separation a very polar solvent, methanol, was required to achieve elution of the aliphatic amines. It can be seen that both of these amines adsorb so strongly onto **1**

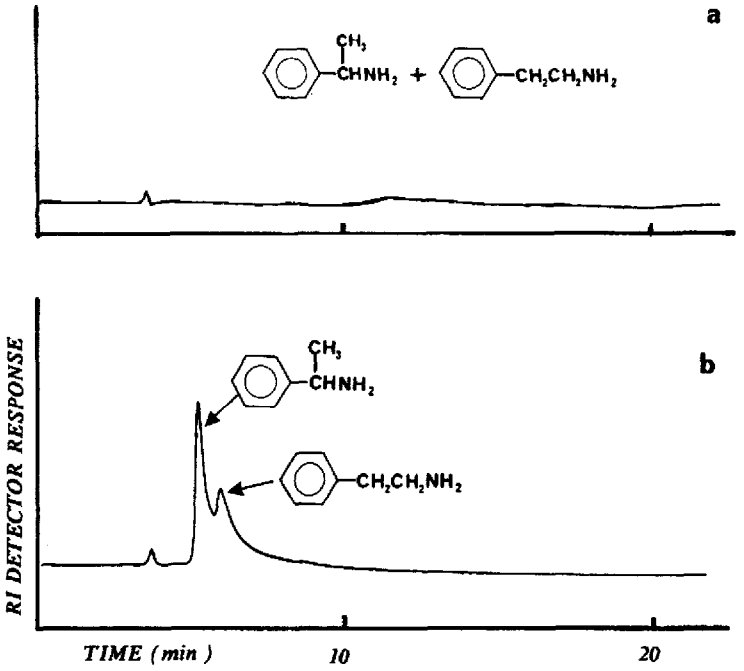

Fig. 10. Attempted separation of isomeric aliphatic amines by using 15-cm columns packed with (a) polymer **1**, and (b) polymer **3**, by using methanol at 0.5 ml/min.

that the resulting chromatographic peaks are so broad as to virtually disappear in the baseline.

2,6-Dimethylphenol and 2,6-diisopropylphenol are reported to have pK_a values of 10.6 and 11.1 respectively[24], which means that they are significantly less acidic than the unhindered phenol moiety and therefore should form weaker hydrogen bonds with aliphatic amines. Fig. 10b shows that more "normal" chromatographic peaks can be obtained with polymer **3** for a mixture of 1- and 2-phenylethylamine. Both the reduced acidity of **3** and the sterically congested environment of its phenolic group contribute to weaken the strength of the hydrogen bonds to the amino groups. This effect has been quantified previously with low molecular weight analogues[25]. Fig. 11a shows that the separation of these two compounds can be further improved by using methanol–water (80:20, v/v) as the mobile phase; Fig. 11b shows a similar separation of benzylamine, 2-phenylethylamine and 4-phenylbutylamine by using **3** as the separation medium and methanol–water (80:20, v/v) as the mobile phase.

Here again the ability of **3** to separate aliphatic amines is important in terms of potential practical applications since silica-based adsorbents are generally not suitable for the separation of such systems. In a recent article[26], procainamide, which contains a tertiary aliphatic amine group, showed very bad tailing on an octadecyl silica gel because of interactions, with residual silanol groups, which have been reported to have pK_a's ranging from 5 to 10 (ref. 27). In addition, our columns can operate both with aqueous as well as non-aqueous mobile phases, while bonded silica columns tend to be unstable[3] above pH 7.

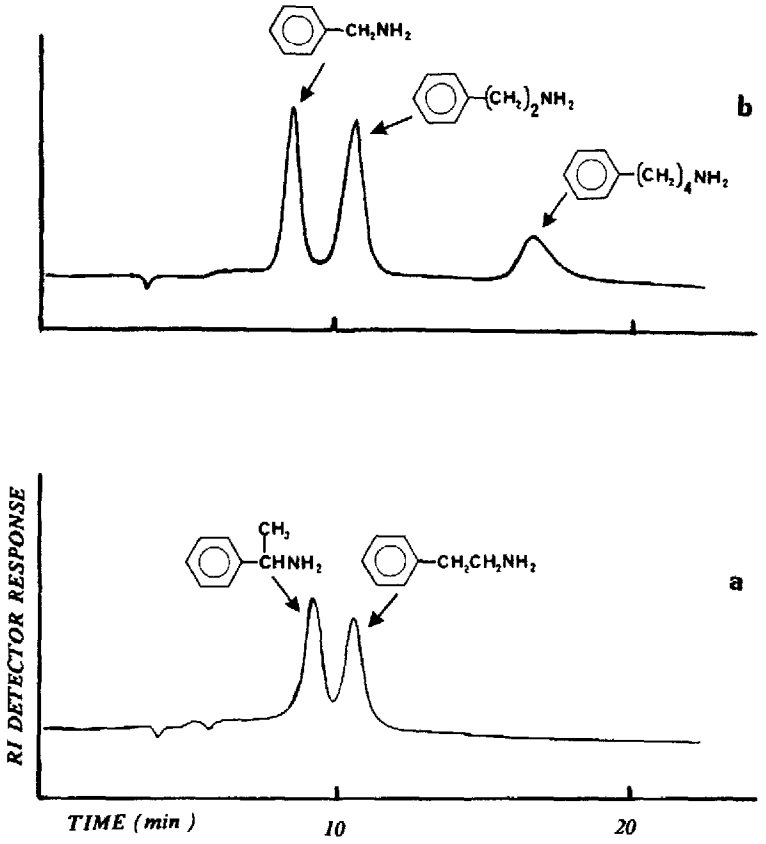

Fig. 11. Separation of aliphatic amines on a 15-cm column of polymer **3** by using methanol–water (80:20, v/v) at 0.5 ml/min.

CONCLUSION

This work demonstrates that the versatility of functionalized polymers can be applied to the preparation of HPLC separation media. The porous polymers can be used in both organic and aqueous media and their adsorption properties can be tuned to accommodate a variety of organic separations. In the case of our poly(hydroxystyrene) resins, both the steric environment and the pK_a of the phenolic groups are important variables which control the ultimate HPLC properties of the polymers. While suspension polymerization may be used effectively to prepare highly porous high-surface area resins, other techniques which can be used to produce porous but uniformly sized resins may provide another dimension to the approach. Our current work is also directed towards novel, monodispersed, non-porous, small-diameter beads with a high density of surface functionalities.

ACKNOWLEDGEMENTS

Financial assistance of this research on novel polymeric materials by IBM Corporation (Materials and Processing Sciences Program) and by the Natural Sciences and Engineering Research Council of Canada, is gratefully acknowledged.

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