

Poly(*p*-acetoxystyrene) resin: a prospective new support for combinatorial synthesis

Hervé Deleuze^a and David C. Sherrington^{*,b}

^a *Laboratoire de Chimie Organique et Organometallique, URA 35 – CNRS, Université Bordeaux I, 351 Cours de la Liberation, 33405 Talence, France*

^b *Department of Pure & Applied Chemistry, University of Strathclyde, 295 Cathedral Street, Glasgow, UK G1 1XL*

A range of spherical particulate resins have been prepared in high yield by suspension polymerisation of mixtures of *p*-acetoxystyrene (AS), styrene (S) and divinylbenzene. The particle size is typically 100–400 μm . The functional group content has been varied from *ca.* 15–60% and the degree of cross-linking from *ca.* 2–20%. Macroporous and gel-type species have been identified. Hydrazinolysis offers a facile and high conversion hydrolysis route to the free phenolic function independently of overall functional group loading, with the phenol content of resins being quantified by two independent methods. Further chemical modification of the phenol functions has been examined. Reaction with bromine is essentially quantitative, and attachment of dichlorotriazine residues occurs specifically by a single linkage even for heavily loaded resins. Subsequent displacement of chloride from the triazine residues by 2-aminomethylpyridine is again essentially quantitative.

These transformations suggest that *p*-acetoxystyrene-based resins offer an attractive complementary support to chloromethylated resins for exploitation in, *e.g.*, the combinatorial synthesis of libraries of organic compounds.

Introduction

The synthesis of spherical particulate polymer resins utilising *p*-acetoxystyrene as a functional comonomer has already been described by Ledwith *et al.*^{1,2} and the phenolic resins derived therefrom applied as supports by Kenner *et al.*^{3,4} in the solid-phase synthesis of oligopeptides. Epton and his co-workers^{5,6} have also exploited a phenolic resin in this context, and in this case the phenol function was introduced using *N*-[2-(4-hydroxyphenyl)]ethylacrylamide as a comonomer during resin synthesis. Whereas Kenner utilised resins with relatively low levels of phenol functionality (*ca.* 10 mol% of pendant groups), in keeping with conventional solid-phase synthesis methodology, Epton deliberately designed and exploited gel resins with a high loading of phenolic groups in order to facilitate the synthesis of larger quantities of oligopeptide. In each of these investigations the functional comonomer had to be synthesised initially and this, coupled with other factors, meant that these approaches have not been further developed.

Today the commercial availability of *p*-acetoxystyrene from Hoechst–Celanese⁷ now makes the synthesis and exploitation of phenolic-based supports a much more attractive proposition, and with the current wave of interest in combinatorial chemistry using supports,⁸ such resins might provide a versatile alternative precursor to chloromethylated resins. With this in mind therefore we have now synthesised a number of relatively highly loaded resins from *p*-acetoxystyrene, and examined how readily the resin can be chemically modified using a number of key reactions.

Experimental

Materials

The monomers *p*-acetoxystyrene (AS) (Hoechst–Celanese), styrene (S) (Dow Chemical Co.) and technical divinylbenzene (DVB) (Aldrich, *ca.* 55% *p*- and *m*-DVB, *ca.* 45% *p*- and *m*-ethylstyrenes) were used as supplied. The suspension stabilisers Biozan Gum R, Cellosize (Hercules Powder Co.) and poly(vinyl alcohol) (Aldrich, 100% hydrolysed, *M* \approx 110 000) were also used as received. The porogens 2-ethylhexanol (Fisons) and

toluene (Fisons, distilled over Na) and the reagents azoisobutyronitrile (AIBN) (Janssen Chemica, 98%), hydrazine hydrate (Aldrich), trichloroacetyl chloride (Aldrich, 99%), tributylamine (Fisons, 99%), cyanuric chloride (Lancaster Synthesis, 98%) and 2-aminomethylpyridine (Aldrich, 99%) were used without purification. The remaining solvents and chemicals were general purpose species.

Suspension polymerisations

These were performed in a parallel-sided flanged glass reactor already described in the literature.^{1,9} Typically the organic comonomer mixture was suspended with continuous stirring in an aqueous phase containing a dissolved suspension stabiliser. Two stabilising systems were employed, one using a mixture of Biozan Gum R and Cellosize, and the other a 2 wt% solution of poly(vinyl alcohol). Full experimental details of the former formulation have already been published.¹⁰

In a typical reaction a mixture of comonomers (15 cm³) and porogen (15 cm³) (usually 2-ethylhexanol; one preparation used toluene) were suspended in 240 cm³ of aqueous phase (aqueous:organic ratio = 8:1). AIBN (100 mg) was used as the free-radical source, and polymerisations were carried out at 80 °C for 6 h. After cooling the reaction mixture, the polymer beads were collected by filtration and then washed copiously with water and ethanol before being dried under vacuum at 60 °C for 24 h. The dry beads were sieved and four fractions collected (> 425 μm ; 425–212 μm ; 212–106 μm ; < 106 μm). ν_{max} (KBr)/cm⁻¹ 1760 (C=O), 1650 (aromatic C=C); elemental microanalysis (%): Found (Calc.): C, 86.9 (87.1); H, 7.0 (7.3); O, 6.1 (5.6) (by difference) for resin IB.

The data in Table 1 show representative examples of the resins synthesised.

Physical characteristics of the resins

The surface area of some of the (dry) resins was determined using the N₂ BET technique. The instrument employed was a Micromeritics Accusorb 1100E. Computer calculations were made using the Micromeritics 2100 SA program. The data are shown in Table 2.

The porosity of some of the resins was also assessed in terms of the levels of solvent imbibed. Typically polymer resin (*ca.* 2 g) was placed in a measuring cylinder (10 cm³) and solvent added in excess. The resin was stirred manually to remove trapped air bubbles and the resin left to equilibrate for 1 h. Excess solvent was then removed by gentle suction filtration and the solvent-imbibed resin re-weighed. The data expressed as g of solvent imbibed per g dry polymer are also shown in Table 2.

Solution synthesis of linear *p*-acetoxystyrene–styrene copolymer

p-Acetoxystyrene (1.0 g, 6.16 mmol) and styrene (0.49 g, 4.70 mmol) were dissolved in toluene (1.63 g) along with AIBN (20 mg). The solution was heated at 80 °C under N₂ for 3 days. The viscous solution which formed was cooled and poured dropwise into 150 cm³ of cold stirred methanol. The precipitated copolymer was collected by filtration, resolubilised in toluene (10 cm³) and again precipitated by addition to methanol. After filtration and vacuum drying a fine white powder (1.2 g, 81%) was obtained.

δ_{H} (250 MHz; CDCl₃) 1.0–2.1 (–CH₂–CH–), 2.2–2.3 (CH₃–C=O), 6.1–7.4 (C₆H₅ and C₆H₄). Appropriate integration showed the mole fraction of acetoxystyrene residues to be *ca.* 0.58 (theoretical, 0.57).

Hydrolysis of poly(*p*-acetoxystyrene) resins (Scheme 1)

The procedure used was adapted from that described by Ledwith *et al.*¹ The polymer resin (**I**) (1.0 g) was suspended in dioxane (50 cm³) with overhead mechanical stirring. Hydrazine hydrate (0.32 mol, 10 cm³) was added at room temperature, then the solution heated gently to 50 °C and kept at this temperature for 24 h. After cooling to room temperature, aqueous HCl (2 mol dm⁻³, 25 cm³) was added. The beads were then filtered off and washed successively with water, dioxane and ethanol. They were then placed in a Dean and Stark apparatus with toluene (50 cm³) and the solvent removed slowly over 24 h before vacuum drying. The recovery of **II** was 0.9 g. ν_{max} (KBr)/cm⁻¹ 3440 (OH), 1651 (aromatic C=C) [absorption band (1760 cm⁻¹) due to C=O almost completely absent]; elemental microanalysis (%): Found (Calc.): C, 87.2 (88.1); H, 8.0 (8.1); O, 4.8 (3.8) (by difference) for resin **II**B.

Quantitative analysis of poly(*p*-hydroxystyrene) resins

Analysis of **II** was undertaken (i) by neutralisation with aqueous NaOH and (ii) by reaction with trichloroacetyl chloride, followed by elemental microanalysis for Cl.

(i) **Acid/base reaction.** Polymer **II** (known weight *ca.* 500 mg) was placed in a 100 cm³ round-bottomed flask. Aqueous NaOH (25 cm³, 0.097 mol dm⁻³) was added and the flask reweighed. The water was then carefully evaporated and the flask placed in a vacuum oven overnight (10 °C, 20 mmHg). After cooling, distilled water was added until the original (total) weight was re-established. The suspension was stirred at room temperature for 30 min and then centrifuged (1000 rpm) for 20 min. The liquid phase was collected and titrated with aqueous HCl (0.016 mol dm⁻³) to estimate the amount of unchanged NaOH from which the phenol content of the resin was calculated. The results are shown in Table 3.

(ii) **Reaction with trichloroacetyl chloride (Scheme 1).** Polymer **II** (known weight *ca.* 1 g) was suspended in pyridine (20 cm³) under an N₂ atmosphere. Trichloroacetyl chloride (1.81 g, 10 mmol) was added dropwise. The suspension was heated with stirring at 80 °C overnight. After cooling of the reaction mixture in an ice-bath, the excess of the acid chloride was hydrolysed with water (20 cm³). The beads were filtered off and washed thoroughly with water and ethanol before being vacuum dried (50 °C, 10 mmHg) for 24 h. The chlorine content

was determined by a routine microanalytical method. The results are shown in Table 3. ν_{max} (KBr)/cm⁻¹ 1780 (C=C) (no OH band 3440).

Bromination of poly(*p*-hydroxystyrene) resins (Scheme 1)

Resin **II**B (1.0 g, *ca.* 1.8 mmol OH) was suspended in carbon tetrachloride (40 cm³) in a 100 cm³ three-necked round-bottomed flask fitted with a condenser and a dropping funnel. Tributylamine (1.67 g, 9 mmol) was added dropwise with stirring followed by bromine (1.62 g, 10 mmol). The flask was protected with aluminium foil and the mixture heated to reflux overnight. The red solution was cooled, and the beads collected by filtration. They were washed successively with 10% aq. thiosulfate solution, water, ethanol and then carbon tetrachloride. Finally, they were dried in a vacuum oven (50 °C, 10 mmHg) overnight. The recovery of beads was essentially quantitative. ν_{max} (KBr)/cm⁻¹ 3480 (OH), 1600 (C=C), 1466, 1274 (Ar), 850, 776, 737 (C–Br) (Found: Br, 22.1% \equiv 1.35 mmol Br g⁻¹ resin. Calc. for Br based on structure **IV** and original comonomer ratio = 24.2% \equiv 1.50 mmol Br g⁻¹ resin) (91% conversion).

Reaction of poly(*p*-hydroxystyrene) resins with cyanuric chloride (Scheme 1)

Resins **II**B and **II**F were first converted into their phenolate salts as follows. The resin (1.0 g, 1.8 mmol OH) was suspended in water (10 cm³) containing NaOH (80 mg, 2 mmol). The water was slowly evaporated off and the beads dried under vacuum (50 °C, 10 mmHg) for 2 days to yield the phenolate form (1.1 g).

Cyanuric chloride (368 mg, 2 mmol) was dispersed in acetone (10 cm³) and the solution cooled to *ca.* 0 °C. The solid resin (1.1 g) was added dropwise and the suspension stirred at 0 °C for 8 h and then at room temperature for 2 days. The polymer was recovered by filtration and washed successively with cold water and acetone, and then dried under vacuum (50 °C, 10 mmHg) for 2 days. The mass of recovered beads was 1.25 g. ν_{max} (KBr)/cm⁻¹ 3438, 3022, 2980, 1523, 1217, 706 (absorption band at 1750 cm⁻¹ due to cyanuric acid was absent) [Found for **VB**: C, 78.3; H, 5.6; Cl, 4.5; N, 2.8; O (by difference), 8.75. Found for **VF**: C, 71.5; H, 5.1; Cl, 6.7; N, 4.2; O (by difference) 12.3%].

Residues **V** predict an N:Cl mass ratio of 0.60; the experimental values for **VB** and **VF** are 0.61 and 0.63, respectively. The corresponding functional group resin loading data are summarised in Table 4.

Reaction of resins **V** with 2-(aminomethyl)pyridine (Scheme 1)

Resin **VB** (or **VF**) (0.5 g, 0.34 mmol triazine residues) was suspended in dioxane (20 cm³) in which 2-aminomethylpyridine (108 mg, 1 mmol) had been dissolved. The reaction mixture was stirred and heated at 60 °C for 3 days. The beads were filtered from the cooled solution and washed successively with dioxane–water (50:50 v/v) and acetone before being vacuum dried (50 °C, 10 mmHg) for 2 days. A grey product was obtained (*ca.* 0.58 g). ν_{max} (KBr)/cm⁻¹ 3438, 2365, 1625, 1523, 1242, 706 (absorption band at 1750 cm⁻¹ due to cyanuric acid was absent) [Found for **VIB**: C, 77.4; H, 6.8; Cl, 0.3; N, 5.4; O (by difference), 10.4%]. This corresponds to a loading of 3.9 mmol N per gram of resin, equivalent to 0.55 mmol of residue **VI** per gram of resin.

Similarly, the analytical data for **VIF** were: C, 74.7; H, 6.5; Cl, 0.3; N, 8.1; O (by difference) 10.4%. This corresponds to a loading of 5.8 mmol N per gram of resin, equivalent to 0.83 mmol of residue **VI** per gram of resin.

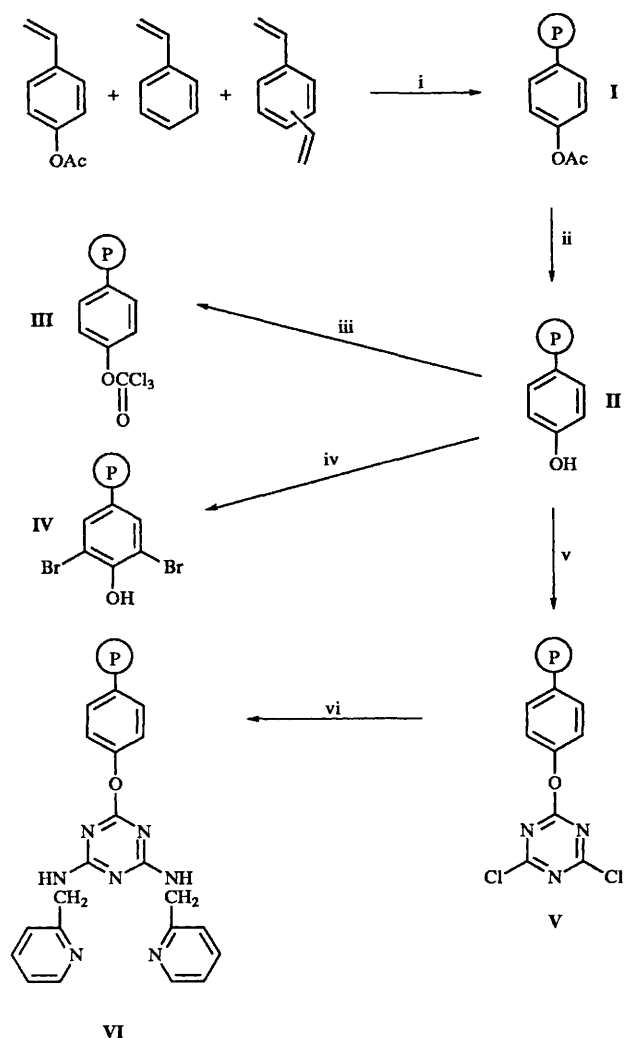
Instrumentation

¹H NMR spectra were recorded on a Bruker WM250 MHz instrument. FTIR spectra were recorded on a Unicam Mattson

Table 1 Synthesis of resins based on *p*-acetoxy styrene (AS)

Resin ^a	Monomer composition (AS/S/DVB) ^a	Stirrer speed (rpm)	Yield %	Particle size (μm) distribution (%)				Appearance ^b
				> 425	425–212	212–106	< 106	
IA	25/35/40 ^{c,e}	800	88	100	—	—	—	agglomerates
IB	25/35/40 ^{c,e}	1300	85	7	10	54	29	opaque beads, some aggregation
IC	25/35/40 ^{d,e}	1300	78	7	38	44	11	transparent beads
ID	60/0/40 ^{c,e}	800	91	100	—	—	—	aggregated beads
IE	60/0/40 ^{c,e}	1000	95	86	13	1	—	aggregated beads
IF	60/0/40 ^{c,e}	1300	83	16	32	32	20	opaque beads
IG	60/0/40 ^{c,f}	1300	90	100	—	—	—	opaque beads
IH	15/45/40 ^{c,e}	1300	89	23	38	18	21	opaque beads
II	96/0/4 ^{c,e}	1300	82	NR	—	—	—	opaque beads

^a AS = *p*-acetoxy styrene; S = styrene; DVB = technical divinylbenzene (mol%). ^b Optical microscope X16. ^c 2-Ethylhexanol porogen. ^d Toluene porogen. ^e Biozan/Cellulsize stabiliser. ^f Poly(vinyl alcohol) (2Wt%) stabiliser (see the Experimental section for further details). NR = not recorded.



Scheme 1 Synthesis and chemical modification of *p*-acetoxy styrene resins: i, AIBN, 80 °C, 6 h; ii, $\text{NH}_2\text{NH}_2 \cdot 1.5\text{H}_2\text{O}$, 50 °C, 24 h; iii, Cl_3COCl -pyridine, 80 °C, 12 h; iv, Br_2 - Bu_3N , 50 °C, 12 h; v, NaOH, cyanuric chloride, 0 °C, 2 days; vi, 2-(aminomethyl)pyridine, 50 °C, 3 days

1000 Spectrometer and elemental microanalyses were determined using a Perkin-Elmer 2400 Series II Elemental Analyser. Surface areas were assessed using a Micromeritics Accusorb 1100E as described earlier.

Results and discussion

Synthesis and analysis of *p*-acetoxy styrene based resins

Suspension polymerisations produced high yields of beaded products (Scheme 1) once suitable stirring conditions were established (Table 1). Typically in our apparatus a speed of *ca.* 1300 rpm was required to avoid aggregation of the beads. This figure would be expected to vary with the precise geometry, *etc.* of the reactor, stirrer and flanges. Yields were typically in excess of 85% of the monomer feed, and the losses were mainly in handling. Bead diameters are in the normal range for suspension polymerisation *ca.* 100–400 μm but interestingly the product formed using poly(vinyl alcohol) was rather large in diameter > 425 μm. Avoiding the use of inorganic stabilisers also eliminated the need for the prolonged washing/decantation procedure reported previously for the clean-up of the beads. In general, however, our results agree with the observations reported by Ledwith *et al.*¹ In the present work, the *p*-acetoxy styrene content of the resins has been varied over a much wider range 15–96%, the earlier work having focused on a figure of *ca.* 10%. In the latter resins, the divinylbenzene content was also restricted to *ca.* 1.4%, whereas we have now shown that resin DVB contents of *ca.* 4–40% (*i.e.*, degree of cross-linking *ca.* 2–20%) can be used and no doubt higher levels are readily achievable. To ensure accessibility in our resins we have utilised 2-ethylhexanol as a porogen in a volume ratio of 1:1 relative to total comonomer. The beads obtained in this way are somewhat opaque whereas replacing this alcohol with toluene as the porogen produces a transparent product. We have not pursued a full morphological study, but superficially at least it seems that the beads produced using 2-ethylhexanol as the porogen are 'macroporous'¹¹ with modest internal surface areas of *ca.* 50–85 m² g⁻¹ (Table 2). The product using toluene as the porogen (IC) seems much more 'gel-type' in nature¹¹ and the surface area in the dry state is < 10 m² g⁻¹. Interestingly the dry resins show a good response to various solvents with the uptake of toluene, ethanol and even water being very significant (Table 2). This is optimistic behaviour in terms of achieving good levels of chemical modification of these resins under a variety of reaction conditions.

In order to provide a baseline for molecular structural characterisation of the cross-linked resins, a linear copolymer of *p*-acetoxy styrene and styrene was prepared from a comonomer mixture of mole fraction 0.57 in *p*-acetoxy styrene. Appropriate analysis of the ¹H NMR spectrum of the product indicated an average incorporation of *p*-acetoxy styrene residues of *ca.* 0.58, *i.e.*, within the experimental error the comonomer and copolymer compositions are identical. This concurs well with the reactivity ratio data reported by Ledwith *et al.*¹ and Danusso *et al.*¹² ($r_1 = 1.2$, $r_2 = 0.88$; $r_1 = 1.35$, $r_2 = 0.85$,

Table 2 Physical characteristics of resins

Resin ^a	Nominal cross-link ratio	N ₂ BET Surface area/m ² g ⁻¹	Solvent uptake/g g ⁻¹ resin		
			Toluene	Ethanol	Water
IB ^b	20	75	2.12	1.73	0.45
IC ^c	20	< 10	0.91	0.31	0.12
IE ^b	20	59	NR	NR	NR
IF	20	65	2.02	1.64	0.41
IG ^b	20	49	NR	NR	NR
IH ^b	20	95	NR	NR	NR
II ^b	2	NR	2.35	0.81	0.33

^a Particle size 106–425 μm . ^b 2-Ethylhexanol porogen. ^c Toluene porogen. NR = not recorded.

respectively) showing *p*-acetoxystyrene (r_1) to be slightly the more reactive but with the copolymer composition being essentially random and controlled primarily by the comonomer feed composition. This provides some confidence that the proportion of *p*-acetoxystyrene residues in the cross-linked resins is likely to be very close to the comonomer ratios used in their syntheses (Table 1).

Hydrolysis of poly(*p*-acetoxystyrene) resins and analysis of poly(*p*-hydroxystyrene) resins so formed

The FTIR spectrum of hydrolysed resin shows essentially complete loss of the C=O absorption band, and so at least superficially the hydrazinolysis procedure is very efficient. Ledwith *et al.*^{1,2} also reported this to be so but surprisingly gave little quantitative data. In addition, the functional group content of their resins was rather low.

Neutralisation of resins **IIB**, **IIF** and **IIH** with excess NaOH, followed by back-titration with HCl, allowed the accessible phenolic content to be quantified. The results are shown in Table 3. Assuming *p*-acetoxystyrene residues are incorporated into the resins in accordance with the comonomer composition, ca. 85% of these are hydrolysed or at least ca. 85% are accessible as free phenol functions. This figure remains remarkably constant with a range of nominal acetoxy group contents (15–60%), and hence it is tempting to suggest that the copolymer composition of resins **I** may indeed be rather lower in acetoxy function than expected but there is no independent structural data to confirm this.

Conversion of the accessible phenolic groups to trichloroacetate yields the data also shown in Table 3. In this case the apparent conversion is down to ca. 76% based on the comonomer ratios. If, however, the acid/base titration data is taken as the baseline, the conversion of accessible phenol groups is ca. 90% over the range of resin compositions. No doubt further optimisation is possible.

Chemical modification of poly(*p*-hydroxystyrene) resins

Bromination of **II** would be expected to be facile yielding 2,6-dibromophenol residues, and this indeed seems to be the case. The conversion is ca. 91% based on the original comonomer ratio of resin **IB**, but based on the phenol content from acid/base titration it is ca. 105%. A figure in excess of 100% is possible if free radical bromination of the tertiary carbon on the polystyrene backbone occurs. The reaction flask was protected from light to avoid this possible side reaction, but low levels of free radical reaction cannot be totally discounted.

Resin **IV** and its chloro analogue would be expected to have significant antimicrobial activity against appropriate organisms, although we have not yet pursued this avenue of investigation.

The reaction of resin **II** with cyanuric chloride was also investigated because the latter moiety offers considerable potential in terms of sequential addition of groups to the resin. This arises from the well-known stepwise progressive

deactivation of the three chloride residues as each is reacted with a nucleophile.¹³ Increasingly harsh reaction conditions are required to displace each chloride and so chemical attachment to the phenolic resin by a single linkage (structure **V**) seemed possible. Resins functionalised with triazine residues have been described before by Kondo *et al.*¹⁴ In the latter case the synthetic strategy involved the use of 2,4-dichloro-6-(*p*-vinylphenyl)-1,3,5-triazine which had to be prepared specifically for the polymer synthesis. In our approach using moderate reaction conditions (0–20 °C) resin **VB** was obtained with N and Cl contents of 2.8 and 4.5%, respectively. This corresponds to ca. 0.66 mmol of residue **V** per gram of resin and a conversion of phenol of ca. 45% based on the comonomer composition. Since the N:Cl mass ratio is 0.61 and the theoretical figure for **V** is 0.60, it seems that few, if any, of the triazine residues are attached to the resin by more than a single linkage. Resin **VE** from **IIIE** contains 4.2% N and 6.7% Cl, an N:Cl mass ratio of ca. 0.63, again close to the theoretical for **V**. Thus increasing the density of phenol groups from ca. 15% of sidechain residues in **IIB** to ca. 60% in **IIF** does not appear to encourage attachment of the triazine residue to the resin by more than a single linkage. Why, however, the usage of phenol groups is rather low is unclear. Attempts to increase the content of triazine residues by raising the temperature (30–50 °C) failed to do so, but did give rise to di-attachment of these. Indeed, elemental microanalyses suggested that almost complete di-attachment was possible.

Exhaustive reaction of resins **VB** and **VF** with 2-(aminomethyl)pyridine led to resins **VIB** and **VIF** respectively, showing a substantial loss of chlorine in their elemental analysis data. For **VIB** the rise in N content to 4.5%, *i.e.*, 3.9 mmol of N per gram of resin, corresponds to a loading of residues **VI** of ca. 0.55 mmol per gram of resin (Table 4). The usage of original phenol function is ca. 40% (based on comonomer composition), but the conversion from dichlorotriazine **V** is ca. 90%. The data for resin **VIF** is very comparable and shows good reproducibility, independent of overall phenol content in the range 25–60% of polymer-pendent groups.

Summary and prospects

The commercial availability of *p*-acetoxystyrene now makes the wider chemical exploitation of phenolic polymer supports a much more attractive proposition than previously. A range of resins can be synthesised readily by suspension polymerisation and the products show good response to solvents of widely different polarity (toluene and water). Facile hydrolysis of the acetoxy protecting groups makes the phenol function available in very high conversions and likewise further chemical modification can be achieved with very useful efficiencies. These resins offer a complementary starting point to chloromethylated polystyrene resins for those interested in exploiting them, *e.g.*, in combinatorial chemistry. The range of peptide chemistry developed by Kenner *et al.*⁴ and Epton *et al.*^{5,6} might be readily exploited, but perhaps equally

Table 3 Accessible phenol content of resins

Original resin	Monomer composition ^a (AS/S/DVB)	Phenol content of II/mmol g ⁻¹			Trichloroacetate content of III/mmol g ⁻¹		
		Theoretical ^b	Found ^c	%	Theoretical ^b	Found ^b	%
IB	25/35/40	2.1	1.8	86	1.6	1.25	78
IF	60/0/40	3.4	2.8	82	2.9	2.2	76
IH	15/45/60	1.3	1.1	85	1.0	0.75	75

^a AS = *p*-acetoxystyrene; S = styrene; DVB = technical divinylbenzene (mol%). ^b Calculated from monomer composition. ^c Calculated from NaOH titration and expressed as a percentage of theoretical phenol content. ^d Calculated from Cl elemental microanalytical data and expressed as a percentage of theoretical phenol content.

Table 4 Reaction of poly(*p*-hydroxystyrene) resins with cyanuric chloride followed by amination

Original resin	Monomer composition ^a (AS/S/DVB)	Loading of V/mmol g ⁻¹			Loading of VI/mmol g ⁻¹			
		Theoretical ^b	Found	%	Theoretical ^b	Found ^d	%	% ^f
IB	25/35/40	1.6	0.67 ^d 0.65 ^e	45	1.4	0.55	39	91
IF	60/0/40	2.5	0.9 ^d 1.0 ^e	40	2.1	0.85	38	90

^a AS = *p*-acetoxystyrene; S = styrene; DVB = technical divinylbenzene (mol%). ^b Calculated from theoretical phenol content. ^c Average experimental content expressed as % of theoretical phenol content. ^d Calculated from N elemental microanalytical data. ^e Calculated from Cl elemental microanalytical data. ^f Expressed as a percentage of the content of cyanuric chloride residues.

importantly these resins seem to offer a very stable and useful basis for developing the combinatorial approach to other DiversomerTM15 libraries. We are currently developing our ideas in this context, but would welcome collaboration with other groups who have specific targets in mind where these resins might facilitate their approach.

Acknowledgements

We are grateful to Hoechst-Celanese for the gift of *p*-acetoxystyrene and H. D. acknowledges warmly the receipt of a Royal Society Fellowship which allowed him to spend a sabbatical leave in the UK.

References

- 1 R. Arshady, G. W. Kenner and A. Ledwith, *J. Polym. Sci., Polym. Chem.*, 1974, **12**, 2017.
- 2 A. Ledwith, M. Rahnema and P. K. Sen Gupta, *J. Polym. Sci., Polym. Chem.*, 1980, **17**, 2239.
- 3 D. Hudson and G. W. Kenner, *Int. J. Biol. Macromol.*, 1980, **2**, 63.
- 4 R. Arshady, A. Ledwith and G. W. Kenner, *Makromol. Chem.*, 1981, **182**, 41.
- 5 R. Epton, P. Goddard, G. Marr, J. V. McLaren and G. J. Morgan, *Polymer*, 1979, **20**, 1444.
- 6 R. Epton, D. A. Wellings and A. Williams, *Reactive Polym.*, 1987, **6**, 143.
- 7 *p*-Acetoxystyrene Monomer Product Bulletin, Hoechst-Celanese, 1250 West Mockingbird Lane, P.O. Box 569320, Dallas, Texas 75356-9320, USA.
- 8 M. A. Gallop, R. W. Barrett, W. J. Dower, S. P. A. Fodor and E. M. Gordon, *J. Med. Chem.*, 1994, **37**, 1233.
- 9 D. C. Sherrington, in *Polymer-supported Reactions in Organic Synthesis*, eds. P. Hodge and D. C. Sherrington, Wiley, Chichester, 1980, Appendix p. 470.
- 10 P. M. van Berkel and D. C. Sherrington, *Polymer*, in press.
- 11 A. Guyot, in *Syntheses and Separations using Functional Polymers*, eds. D. C. Sherrington and P. Hodge, Wiley, Chichester, UK, 1988, ch. 1, p. 1.
- 12 F. Danusso, P. Ferruti and C. Gazzaniga Marabelli, *Chim. Ind. (Milan)*, 1965, **47**, 585.
- 13 J. M. E. Quirk, in *Comprehensive Heterocyclic Chemistry*, Vol. 3, eds. A. R. Katritzky and C. W. Rees, Pergamon Press, NY, 1984, pp. 457-530 and references cited therein.
- 14 S. Kondo, T. Yamamoto, M. Mase, H. Mikami, H. Kunisada and Y. Yuki, *Reactive Polym.*, 1994, **22**, 75.
- 15 R. M. J. Liskamp, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 633.

Paper 5/04125B

Received 26th June 1995

Accepted 19th July 1995