Novel Route to Sulfonated Polyphosphazenes: Single-Step Synthesis Using "Noncovalent Protection" of Sulfonic Acid Functionality

Alexander K. Andrianov,* Alexander Marin, Jianping Chen, Jonathan Sargent, and Nathan Corbett

Parallel Solutions Inc., 763D Concord Avenue, Cambridge, Massachusetts 02138

Received February 6, 2004; Revised Manuscript Received March 2, 2004

ABSTRACT: A single-step approach for the synthesis of polyphosphazenes containing sulfonic acid functionalities is developed. Polyphosphazene "sulfonation" is conducted via the direct replacement of chlorine atoms of the macromolecular precursor, poly(dichlorophosphazene), PDCP with a sulfonic acid containing nucleophile—hydroxybenzenesulfonic acid. The method makes use of "noncovalent" protection of the sulfonic acid functionality with a hydrophobic ammonium ion, such as the dimethyldipalmitylammonium ion, which then can be easily removed after the completion of the reaction. ^{1}H, ^{31}P, and ^{13}C NMR and size-exclusion HPLC studies revealed no macromolecular byproducts or noticeable degradation of the polyphosphazene backbone under the conditions of the synthesis. Both sulfonated polyphosphazene homopolymers and mixed substituent copolymers containing 4-ethylphenoxy side groups were synthesized and characterized.

Introduction

Polyphosphazene sulfonic acids offer a peculiar combination of unique inorganic backbone, high ionic density, and unprecedented structural diversity. Out of these features stems their potency as biologically active and advanced industrial materials. Recently published data on their methanol and water retaining properties brought them to the front of the most promising materials for the development of direct methanol fuel cell.[1,2] Powerful immunostimulating properties, side-group dependent biodegradation, and versatile microencapsulating characteristics of polyphosphazene polyelectrolytes has advanced them as some of the most desirable macromolecular choices for biomedical applications.[3−6] Further development of polyphosphazene sulfonates in these areas dictates the need for their simple and well-defined synthesis.

Introduction of sulfonic acid functionalities into the polyphosphazene structure poses however significant synthetic challenge. To date sulfonated polyphosphazenes have been produced via a "post-substitution" methodology. This includes synthesis of the reactive macromolecular reagent, poly(dichlorophosphazene) (PDCP), its chemical derivatization using nucleophilic organic compounds to replace chlorine atoms with stable organic side groups, and then sulfonation of such poly(organophosphazene)s (Scheme 1, parts a and b).[7−10] Methods of sulfonation vary as to the chemistry of sulfonating agent or type of polymeric side group to be sulfonated. These reactions, however, introduce significant irregularities in the polymer structure, suffer from severe heterogeneity of the reaction mixture, and allow little or no control over the position and degree of sulfonation. Moreover, sulfonation conditions are often detrimental for a variety of "application-critical" side groups or even the phosphazene backbone itself and thus put severe restriction on one of the main advantages of polyphosphazene chemistry—its structural diversity.

* To whom correspondence should be addressed. E-mail: aandrianov@parallelsolutionsinc.com.

So far there has been little success in the development of methods allowing single-step direct "sulfonation" through the replacement of chlorine atoms of the macromolecular precursor with sulfonic acid containing nucleophile (Scheme 1c). A reported synthesis of a mixed substituent copolymer revealed fundamental problems associated with the reactions of the sulfonic acid group with poly(dichlorophosphazene), leading to unstable derivatives.[11]

In this paper, we report a new single-step substitution method utilizing "noncovalent protection" of sulfonic acid groups with hydrophobic ammonium salts. This methodology has been applied to the synthesis of both homopolymers and mixed substituent copolymers of sulfonated polyphosphazenes.

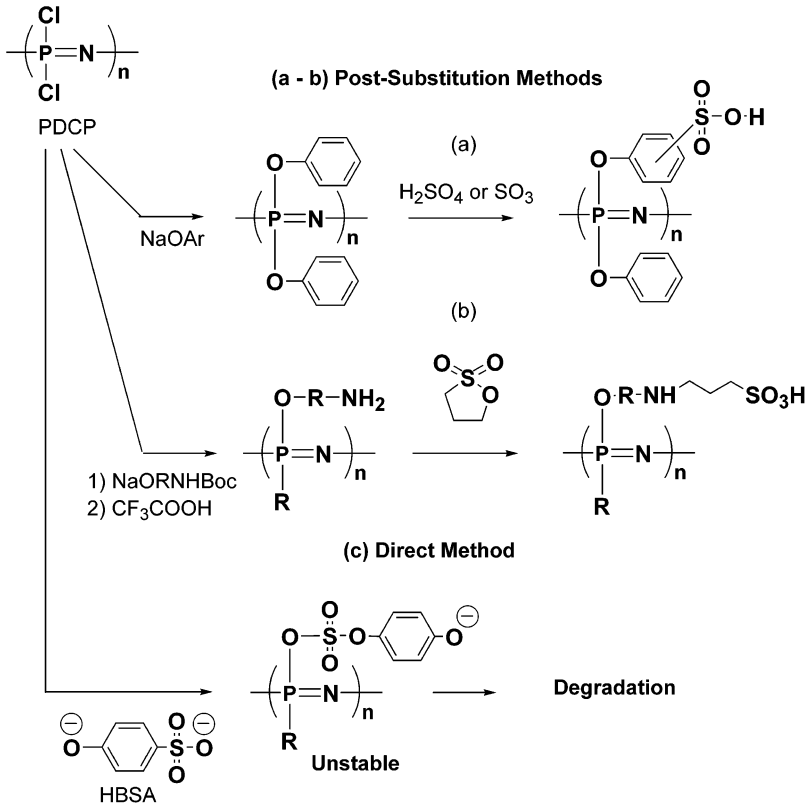
Experimental Section

Materials. Hexachlorocyclotriphosphazene (Nippon Fine Chemicals) was used as received. PDCP was synthesized using ring-opening polymerization of hexachlorocyclotriphosphazene in the titanium pressure reactor as described previously.[12] Propyl 4-hydroxybenzoate, 99+%; benzenesulfonic acid, sodium salt, 98%; and 4-hydroxybenzenesulfonic acid, sodium salt dehydrate, 98% (Aldrich Chemical Co., Inc., Milwaukee, WI) were dried prior to use in a vacuum oven at 80 °C for 8 h. Chlorobenzene, anhydrous; diglyme (methoxyethyl ether), anhydrous; methyl alcohol, 99.9%; methyl sulfoxide, 99.9%; 2-propanol, 99+% (Aldrich Chemical Co., Inc., Milwaukee, WI); dimethyldipalmitylammonium bromide, 97+% (TCI America, Portland, OR); *N*,*N*-dimethylacetamide, 99.9% (OmniSolv, Gibbstown, NJ); and tetra-*n*-butylammonium bromide, 98% (Alfa Aesar, Ward Hill, MA) were used as received.

Analytical Methods. Molecular weight of water-soluble poly[diphenoxyphosphazenedisulfonic acid] was determined by aqueous GPC analysis.[12,13] The polymer was characterized using an Ultrahydrogel Linear column (Waters, Milford, MA) with UV (Waters 486 tunable UV/visible absorbance detector, Waters, Milford, MA) and refractive index detection (Waters 410 RI detector, Waters, Milford, MA). A mixture of a phosphate buffered saline, PBS (pH 7.4), and methanol (9:1 ratio) was used as a mobile phase. GPC analysis of mixed substituent copolymers was performed in *N*,*N*-dimethylacetamide containing 0.1% tetra-*n*-butylammonium bromide using Waters Styragel HMW 6E column (Waters, Milford, MA) with

10.1021/ma049736x CCC: $27.50
Published on Web 04/23/2004

Scheme 1. Synthetic Pathways to Sulfonated Polyphosphazenes



refractive index detection (Waters 410 RI detector, Waters, Milford, MA).[12] Molecular weights were calculated using Waters Millennium software (Waters, Milford, MA) and sodium poly(styrenesulfonate) standards (Scientific Polymer Products, Inc., Ontario, NY) for aqueous system, poly(styrene) (Polysciences, Inc., Warrington, PA) standards for organic system.

^{31}P, ^{1}H, and ^{13}C NMR spectra were recorded using Varian UnityINOVA 400 MHz spectrometer.

Automated Synthetic Method Development. Automated parallel synthesis was performed using Quest 205 synthesizer containing a series of 10 100-mL Teflon reaction vessels (Argonaut Technologies, San Carlos, CA). Each reaction vessel is equipped with vertical oscillating agitation, temperature control, and filtration system. Synthesizer was used to investigate the effect of the reaction conditions and phase transfer reagents on the reaction of PDCP with sodium hydroxybenzenesulfonate. Total reaction volume was limited to 60 mL. Typically, 0.1 g of PDCP solution in 40 mL of diglyme was placed in the reaction vessel under nitrogen atmosphere, to which 1.4 g of sodium 4-hydroxybenzenesulfonate was added. Solvents, reactant ratios, reaction temperatures, and phase transfer reagents were varied. A total of more than 2000 reactions were performed. Upon completion of the reaction, reaction mixture was analyzed by GPC for the presence of macromolecular compounds. If precipitate was formed in the reaction mixture, it was separated, treated with water or aqueous potassium hydroxide solution and also analyzed by GPC.

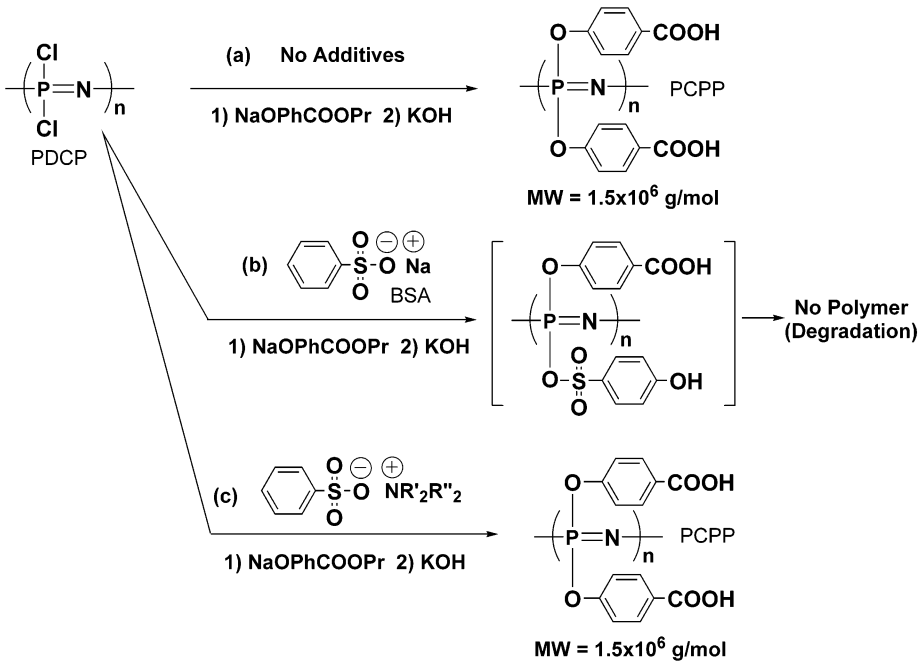
Synthesis of the Dimethyldipalmitylammonium Salt of 4-Hydroxybenzenesulfonate (DPSA). 5 g (0.0087 M) of dimethyldipalmitylammonium bromide (DMDPA) was mixed with 5 mL of methanol, and to this suspension was added 300 mL of deionized water. The mixture was then stirred until a clear solution was obtained. A 10 g (0.0042 mol) sample of 4-hydroxybenzenenesulfonic acid sodium salt was dissolved in 100 mL of aqueous solution containing 1.63 g (0.004 mol) of sodium hydroxide. This solution was then added to the solution of DMDPA; the mixture was stirred for 30 min and left at ambient temperature for 120 min. The resulting precipitate of DPSA was filtered and dried under vacuum (yield 4.6 g, 98%).

Synthesis of Poly[diphenoxyphosphazenedisulfonic acid], PDSA. 35 g (0.03 M) of DPSA, prepared as described above, was dissolved in 470 mL of anhydrous monochlorobenzene, placed in a 1 L flask equipped with stirrer, and kept under nitrogen. Then, 1.18 g (0.01 mol) of PDCP in 30 mL of diglyme was added dropwise to the flask at 100 °C with constant stirring. The reaction temperature was then increased to 120 °C and the reaction continued at this temperature for 5 h. The reaction mixture was then cooled to 70 °C and to this mixture 25 mL of ethanol and 32 mL of 12.7 N aqueous potassium hydroxide (0.41 M) were added. The mixture was stirred for an additional 1 h and cooled, and polymer was isolated by precipitation in 1500 mL of methanol. The precipitate was redissolved in 210 mL of 0.6 N aqueous potassium hydroxide (0.13 M) upon stirring at 50 °C for 1 h and precipitated with 650 mL of methanol. Polymer precipitation was repeated one more time. Polymer was then converted in the acid form by dissolving in 220 mL of 1 N aqueous hydrochloric acid and precipitating in 1200 mL of methanol. The resulting polymer was dried under vacuum to yield 2.8 g (70%). Polymer structure and purity were determined by ^{31}P, ^{1}H, and ^{13}C NMR, elemental analysis (sulfur), and size exclusion HPLC with photodiode array detection (200−600 nm). Polymer purity was determined to be in excess of 99%.

Synthesis of Mixed Substituent Copolymers. A typical procedure for the synthesis of mixed substituent copolymers is described below. First, 8.7 g of 4-ethylphenol (0.065 M) was reacted with 1.49 g of sodium (0.065 mol) in 30 mL of diglyme, and the resulting solution was added slowly to a reaction flask containing 4.69 g (0.04 M) of PDCP in a mixture of 45 mL of diglyme and 95 mL of monochlorobenzene at 50 °C. The temperature was then increased to 90 °C and the reaction was stirred for another 60 min.

Then, 35.3 g of DPSA (0.03 M) in 250 mL of monochlorobenzene was added slowly to the reaction mixture. The reaction mixture was stirred at 90 °C for 20 h and then cooled to 70 °C. Then, 25 mL of ethanol and 30 mL of 12.7 N aqueous potassium hydroxide solution were added; the mixture was

Scheme 2. Ability of Sulfonic Acid to Interfere with Substitution Reactions of PDCP Demonstrated for the Reaction of Poly[di(carboxylatophenoxy)phosphazene]: (a) PCPP Synthesis; (b) Addition of BSA to the Reaction Mixture Leading to a Complete Degradation of the Polymer; (c) Conversion of BSA into a Dimethyldipalmitylammonium Salt Completely Eliminating Degradation



stirred for additional 1 h and then polymer was recovered by precipitating in 1300 mL of 2-propanol. The polymer was redissolved in a mixture of 500 mL of dimethyl sulfoxide and 10 mL of 12.7 N aqueous potassium hydroxide upon stirring at 50 °C for 1 h and then precipitated in 2-propanol. The precipitation was repeated two more times. Polymer was converted to an acid form by dissolving it in dimethyl sulfoxide and adding 20 mL of 8 N aqueous hydrochloric acid and precipitating with 2000 mL of water. The polymer was dried under vacuum. The yield was 7.7 g (60%).

Substitution Reaction of PDCP with Sodium Propyl-4-hydroxybenzoate. PDCP derivatization using a model nucleophilic compound—sodium 4-hydroxybenzoate—is described below. First 0.65 g of 4-hydroxybenzoate and 0.07 g of sodium were reacted in 20 mL of diglyme. The obtained solution was then added to the three-neck reaction flask charged with 0.058 g (0.0005 M) of PDCP solution in 25 mL of diglyme while stirring. The reaction mixture was refluxed for 2 h under nitrogen and then cooled to 95 °C. Then, 10 mL of aqueous 13 N potassium hydroxide (0.13 M) was slowly added with vigorous stirring to the reaction mixture to bring about the hydrolysis and subsequent precipitation of poly[di(carboxylatophenoxy)phosphazene], PCPP. The liquid organic layer was decanted and the precipitate was dissolved in 300 mL of 15% aqueous sodium chloride solution and then reprecipitated by addition of 600 mL of deionized water. The aqueous layer was decanted, and the precipitate was redissolved in 150 mL of deionized water and finally precipitated by addition of 150 mL of ethanol. The PCPP precipitate was filtered, dried, and analyzed by aqueous GPC as described above. The effect of sodium benzenesulfonate was studied by the introduction of 0.6 g of this reagent to the reaction mixture immediately following the addition of propyl 4-hydroxybenzoate.

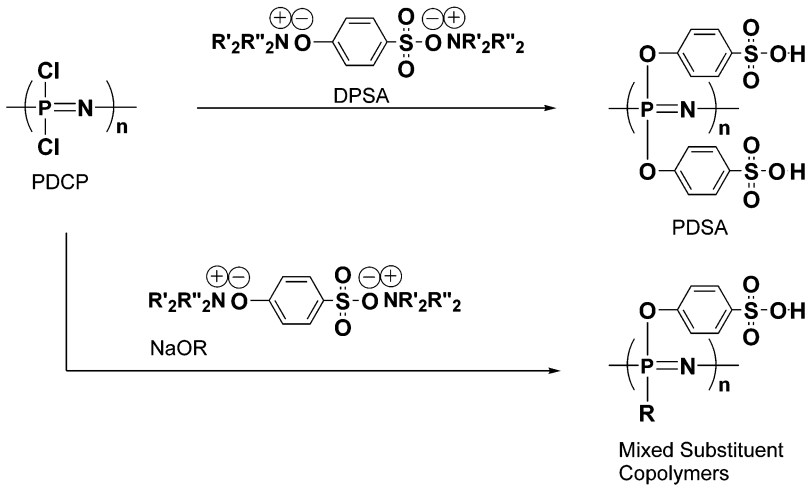
Results and Discussion

Reactions of Disodium 4-Hydroxybenzenesulfonate with PDCP. Direct replacement of chlorine atoms of PDCP with nucleophiles containing sulfonic acid functionalities (Scheme 1b) is a desirable single-step route to sulfonated polyphosphazenes, which in the case of its successful development can provide an unprecedented control over polymer composition and allow co-introduction of other important functionalities in the polymer structure. In an attempt to synthesize sulfonated polymers using this approach we investigated the reaction of the polyphosphazene precursor PDCP with disodium 4-hydroxybenzenesulfonate (HBSA). Since our initial experiments failed to yield detectable quantities of sulfonated polymer, we conducted comprehensive method development study using parallel synthesis approach and automated synthetic equipment.

A total of several hundreds of experiments were carried out in which we varied solvents (chlorobenzene, diglyme, THF, dioxane, toluene, and their mixtures), reaction temperatures (40−120 °C), and reaction lengths (2−48 h) and investigated the effects of phase transfer reagents (phenyltrimethylammonium bromide, *n*-dodecyltrimethylammonium bromide, or tetra-*n*-butylammonium bromide) and concentrations of PDCP and HBSA. In these studies, we were unable to detect any macromolecular products that were sufficiently stable for their analysis by GPC and NMR.

Effect of Benzenesulfonates on the Reactions of PDCP with Other Nucleophiles. (i) Sodium Benzenesulfonate. The failure of the PDCP−HBSA reaction to produce a macromolecular product may be caused by the low reactivity of the nucleophile in the substitution process or by the formation of an unstable substituted polymer, which degrades in the course of the reaction. The latter is supported by the previously reported data on the formation of unstable P−O−S bonds in the reaction of PDCP with 2-hydroxyethanesulfonic acid.[11] We evaluated the ability of sulfonates to interfere with the reaction of PDCP with nucleophiles by adding monofunctional arylsulfonate−sodium benzenesulfonate (BSA) to the reaction of PDCP with sodium 4-hydroxypropylbenzoate (Scheme 2). This reaction was thoroughly investigated and was chosen here because of its simplicity, high level of control and reproducibility.[12] As expected, when no sodium BSA was added to the reaction, polymer with the weight-average

Scheme 3. Synthesis of PDSA and Mixed Substituent Copolymers Using the Noncovalent Protection Method

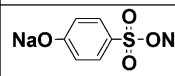
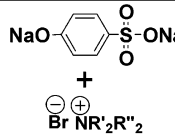
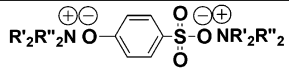


molecular weight in excess of 10^6 g/mol was produced (Scheme 2a—PCPP synthesis). Addition of sodium BSA to the reaction mixture resulted in a complete degradation of the polymer, which indicates high reactivity of BSA toward PDCP despite its low solubility in the reaction mixture. Thus, sodium sulfonate was able to compete effectively with highly reactive nucleophile leading to an unstable substitution product and complete degradation of the polymer (Scheme 2b).

(ii) Dimethyldipalmitylammonium Benzenesulfonate. In our attempts to suppress reactivity of arylsulfonates against PDCP, we focused on their hydrophobic ammonium salts. We anticipated, that introduction of hydrophobic bulky counterions can lead to significant steric hindrances for the reaction of sulfonic acid group with chlorine atoms of PDCP. In addition, it was expected that such hydrophobic salts will show improved solubility in the reaction mixture. We investigated the effect of dimethyldipalmitylammonium salt of benzenesulfonate on the reaction of PCPP synthesis described above. Sodium benzenesulfonate was converted to a hydrophobic ammonium salt by reacting it with dimethyldipalmitylammonium bromide in water with subsequent drying of the precipitated salt under vacuum. Contrary to the sodium salt, this hydrophobic quaternary ammonium salt was completely soluble in the reaction mixture, but showed no interference with the reaction of PCPP synthesis (Scheme 2c). ^{31}P NMR studies displayed no sign of any additional side groups in the structure of PCPP obtained in the presence of hydrophobic ammonium salt of BSA. It was assumed that due to the attractive interactions of the hydrophobic quaternary ammonium group with BSA, the concentration of the reactive sulfonate ions was negligibly low to produce interactions with PDCP. On the basis of these results, we investigated the use of ammonium salts for the noncovalent protection of the sulfonic acid functionality in the synthesis of sulfonated polyphosphazenes.

Synthesis of Dimethyldipalmitylammonium Salt of Hydroxybenzenesulfonate. Preparation of dimethyldipalmitylammonium salt of hydroxybenzenesulfonic acid (DPSA) included (a) converting sodium HBSA into its disodium salt using sodium hydroxide and (b) precipitating it in aqueous solution using the excess of dimethyldipalmitylammonium bromide (DMDPA) with subsequent drying under vacuum. ^{1}H NMR analysis of the resulting precipitate showed complete substitution of sodium ions, both in the sulfonate and hydroxyl group functionalities. This salt composition was independently confirmed by spectrophotometric titration of soluble HBSA in mixtures of HBSA and DMDPA with variable molar ratios.

Table 1. Reactions of PDCP with Salts of Hydroxybenzene Sulfonic Acid

Reaction No.	Reagent	MWx10^{-3}, g/mol
1		No polymer
2		85
3		1200

Synthesis of Sulfonated Polyphosphazene Using Hydrophobic Ammonium Salt of 4-Hydroxybenzenesulfonate—"Noncovalent Protection" Method. Use of DPSA as a substitution agent for PDCP led to a complete solubilization of both the nucleophile and the macromolecular product in their reaction mixture with PDCP. No precipitation of polymer was observed in the course of the reaction. The reaction (Scheme 3) was conducted at 120 °C, and the substitution was completed in 5 h based on the ^{31}P NMR data. The protective groups were removed by treating polymer with potassium hydroxide and precipitating it in methanol. The deprotection was monitored by ^{1}H NMR and two precipitations were usually sufficient to remove ammonium groups completely.

As seen from Table 1, the reaction yielded high molecular weight product indicating the absence of degradation processes in the system. Synthesis utilizing in situ produced salt (DMDPA was added to the reaction mixture) also generated polymeric product; however, low yield and a steep decrease in the molecular weight were observed as compared with the premade salt. This can be explained by the degradation of polymer due to the presence of sodium sulfonate groups (incompleteness of the salt formation reaction under these conditions). ^{31}P NMR analysis of the high molecular weight sulfonated polyphosphazene demonstrated only one type of substituent with no signs of structural irregularities, such

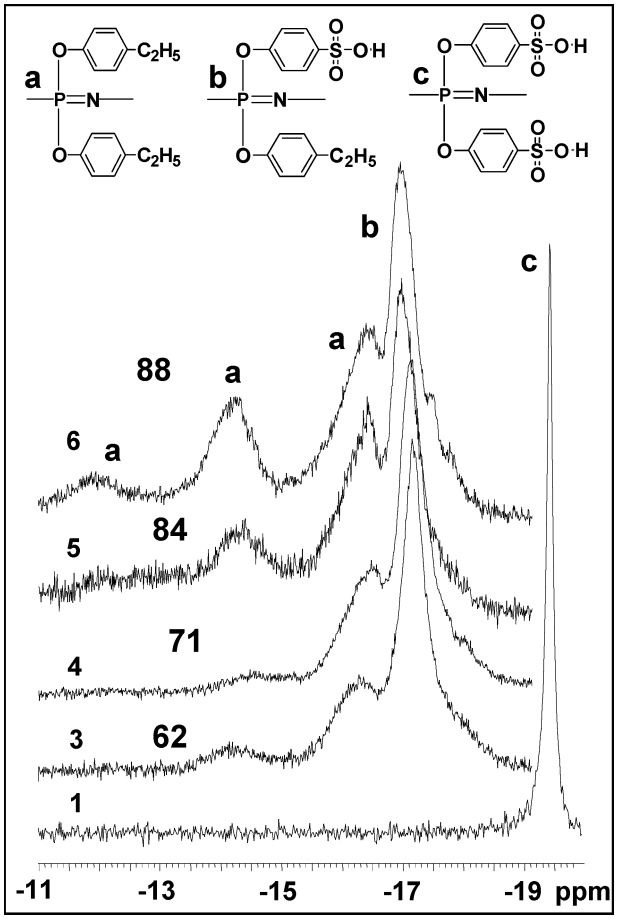


Figure 1. ^{31}P NMR spectra of PDSA in D_2O (**1**) and its mixed substituent copolymers containing *p*-ethylphenoxy side groups in DMF (polymers **3**−**6**). See Table 2 for the detailed composition of the copolymers and ^{1}H NMR data.

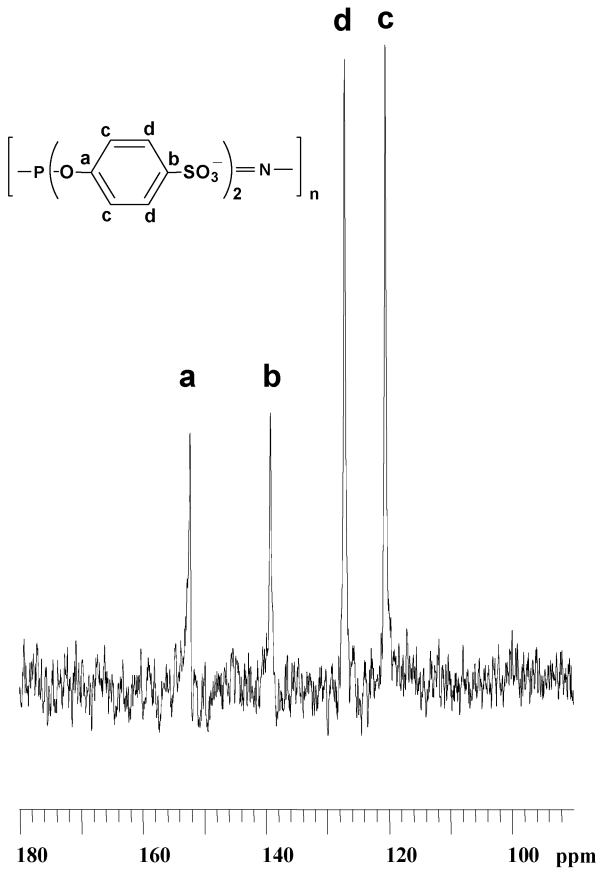


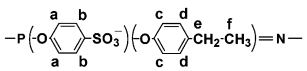
Figure 2. ^{13}C NMR spectra of PDSA in D_2O.

as side group attached through sulfonic acid functionality (Figure 1, curve 1). Both ^{1}H NMR (Table 2) and ^{13}C NMR (Figure 2) data confirm the structure of the poly[diphenoxyphosphazenedisulfonic acid], PDSA (with no indication of other side groups present in the polymer).

These results indicate that the direct route to the synthesis of sulfonated polyphosphazenes can be effectively performed without noticeable side reactions and byproducts. The hydrophobic ammonium protective groups are easy to remove and are not detected in the final product. Interestingly, the dimethyldipalmitylammonium-activated hydroxyl group of HBSA possessed high nucleophilicity in the reaction with PDCP.

Mixed Substituent Copolymers Containing Sulfonic Acid Groups. A series of copolymers containing sulfonic acid and 4-ethylphenoxy groups were prepared using the methodology described above (Scheme 3). As with the homopolymer, DPSA was employed, and reactions were performed by sequential addition of sodium

Table 2. Characterization of Sulfonated Polyphosphazenes[a]

Polymer	$[-P(R_1)_x(R_2)_y=N-]_n$ R_1  x, % mol.	R_2  y, % mol.	Mw • 10^{-3}, g/mol	^{1}H NMR 
1	100	0	600$^+$	6.5 (a), 7.3 (b)
2	58	42	800$^\pm$	0.92 (f), 2.3 (e), 6.7 - 7.0 (a,c,d)*, 7.4 (b)
3	38	62	800$^\pm$	1.0 (f), 2.4 (e), 6.7 - 7.1 (a,c,d)*$^+$, 7.5 (b)
4	29	71	1100$^\pm$	1.0 (f), 2.4 (e), 6.7 - 7.1 (a,c,d)*, 7.5 (b)
5	16	84	490$^\pm$	1.0 (f), 2.4 (e), 6.8 - 7.1 (a,c,d)*, 7.5 (b)
6	12	88	460$^\pm$	1.1 (f), 2.4 (e), 6.8 - 7.1 (a,c,d)*, 7.5 (b)

[a] Key: (*) This region of the spectrum consists of envelope of overlapping peaks. (+) Based on poly(styrenesulfonic acid) standards. (±) Based on poly(styrene) standards.

4-ethylphenoxide and DPSA in variable ratios. Protective groups were removed using aqueous potassium hydroxide using procedure similar to the described above. As seen from Table 2, all reactions produced high molecular weight polymers, and their structure and compositions were proved by ^{31}P NMR (Figure 1) and ^{1}H NMR (Table 2). Polymer compositions calculated based on ^{1}H NMR data are shown in Table 2 (correlates with ^{31}P NMR with an error not exceeding 5%).

As mentioned above, the ^{31}P NMR spectrum of the sulfonated homopolymer consisted of a sharp peak at −19.6 ppm (phosphorus c in Figure 1). No evidence was found from the ^{31}P NMR spectra indicating presence of detectable quantities of P−Cl or P−SO_3^- units. Spectra of the mixed substituent copolymers showed multiple resonances. Copolymers **3** and **4** containing 62% and 71% of the *p*-ethylphenoxy groups (calculated based on ^{1}H NMR data) had three distinct resonances: large relatively narrow peak at −17.2 ppm (phosphorus b in Figure 1) and two smaller broad peaks in the ranges −15.5−16.5 and −13.5−15 ppm, which might be attributed to phosphorus with ethylphenoxy groups (Figure 1, atoms a). Both of these peaks became larger as the content of ethylphenoxy groups in the copolymers increased to 84 and 88% (copolymers **5** and **6**) which support the identification as *p*-ethylphenoxy-substituted units. In addition, copolymers **5** and **6** display additional broad resonances in the range of −11−12.5 ppm. The presence of multiple resonances for the same type of phosphorus is not unusual and is explained by the variations in the surrounding units (substitution pattern). Repeating units may be flanked by others of the same kind, by units with mixed substituents, or by both of them.[14] Moreover the presence of cis- or trans-substituted neighbors may further complicate the picture.[14]

Conclusions

Studies on the reactivity of sulfonates in the reactions with PDCP supported previous findings on the formation of unstable intermediates, which can cause degradation of polyphosphazene backbone. We demonstrated that this undesirable effect can be completely eliminated by converting sulfonate into a hydrophobic ammonium salt, which is not reactive against PDCP. Such protective groups can be easily removed after the completion of the reaction. Interestingly, the conversion of sodium phenoxide into a hydrophobic ammonium salt did not change its reactivity against PDCP, which explains the success of the substitution reaction. Such a fascinating distinction in the behavior of sulfonic and phenoxide salts is clearly a result of the differences in their solubility and dissociation in the reaction mixture. We believe that the reported "noncovalent protection" methodology in polyphosphazene chemistry has a significant potential both for the development of novel functionalized structures and for the establishment of better synthetic control in the existing systems.

References and Notes

(1) Guo, Q.; Pintauro, P. N.; Tang, H.; O'Connor, S. *J. Membr. Sci.* **1998**, *154*, 175−181.
(2) Fedkin, M. V.; Zhou, X.; Hofmann, M. A.; Chalkova, E.; Weston, J. A.; Allcock, H. R.; Lvov, S. N. *Mater. Lett.* **2002**, *52*, 192−196.
(3) Andrianov, A. K.; Payne, L. G. *Adv. Drug Deliv. Rev.* **1998**, *34*, 155−170.
(4) Andrianov, A. K.; Payne, L. G. *Adv. Drug Deliv. Rev.* **1998**, *31*, 185−196.
(5) Andrianov, A. K.; Payne, L. G. In *Microparticulate Systems for the Delivery of Proteins and Vaccines*; Cohen, S., Bernstein, H., Eds.; Marcel Dekker: New York, Basel, Switzerland, and Hong Kong, 1996; pp 127−147.
(6) Andrianov, A. K.; Chen, J.; Payne, L. G. *Biomaterials* **1998**, *19*, 109−115.
(7) Montoneri, E.; Gleria, M.; Ricca, G.; Pappalardo, G. C. *J. Macromol. Sci.—Chem.* **1989**, *A26*, 645−661.
(8) Allcock, H. R.; Fitzpatrick, R. J.; Salvati, L. *Chem. Mater.* **1991**, *3*, 1120−1132.
(9) Wycisk, R.; Pintauro, P. N. *J. Membr. Sci.*. **1996**, *119*, 155−160.
(10) Allcock, H. R.; Klingenberg, E. H.; Welker, M. F. *Macromolecules* **1993**, *26*, 5512−5519.
(11) Ganapathiappan, S.; Chen, K.; Shriver, D. F. *Macromolecules* **1988**, *21*, 2299−2301.
(12) Andrianov, A. K.; Chen, J.; LeGolvan, M. P. *Macromolecules* **2004**, *37*, 414−420.
(13) Andrianov, A. K.; LeGolvan, M. P. *J. Appl. Polym. Sci.* **1996**, *60*, 2289−2295.
(14) Allcock, H. R. *Chemistry and Applications of Polyphosphazenes*; John Wiley & Sons: Hoboken, NJ, 2003; p 227.

MA049736X