Polycations. III. Synthesis of Polyphosphonium Salts for Use as Antibacterial Agents

Valeryi Shevchenko* and Robert Engel

Department of Chemistry and Biochemistry, Queens College of the City University of New York, 65-30 Kissena Boulevard, Flushing, NY 11367

Received 22 September 1997; revised 20 November 1997

ABSTRACT: *Several series of polyphosphonium salts have been prepared. These include those in which the cationic sites are located at regular intervals along a linear chain of defined length ("strings") and those in which the cationic sites are in linkages arrayed in branching arms about a central focus unit ("balloons"). Similarly, polyphosphonium balloon arrays have been attached to a polystyrene backbone providing a material that can serve as an anionic exchange resin. Several of the resultant materials have demonstrated antibacterial activity, in systems analogous to those previously reported for simple functionalized polystyrene species, and continue to be investigated.* © 1998 John Wiley & Sons, Inc. Heteroatom Chem 9:495–502, 1998

INTRODUCTION

Prior efforts of other laboratories [1–4] have demonstrated the ability of water-insoluble polyionic species to serve as antibacterial agents toward both gram-positive and gram-negative bacteria. In these earlier studies, cationic sites, either quaternary ammonium or quaternary phosphonium, were generated at surface-reactive sites of water-insoluble poly-

mers (polystyrene derivatives). Each polymer molecule thus bore numerous monocationic pendant sites. It was noted that the antibacterial activity of the polymers bearing surface-bound quaternary *phosphonium* sites was significantly greater than similar polymers with quaternary *ammonium* sites.

In an earlier report from this laboratory [5], we have noted the synthesis of *water-soluble* polyammonium species that have exhibited significant antibacterial activities against *E. coli* [6]. These polyammonium species, of analytically defined structure (as opposed to "polymeric" structures), bear from 2 to 10 quaternary ammonium ion sites regularly spaced in a linear array (cationic "strings"). The extent of antibacterial activity observed for these species depends upon both the number of cationic sites and the spacing between them in the linear array.

Given these observations, it became of interest to synthesize analytically defined polyphosphonium salts that might be anticipated to exhibit even more intense antibacterial activities than do the related polyammonium compounds. Our stepwise synthetic approach for the preparation of polyphosphonium string species involves the initial diquaternization of a suitable α, ω-bis(diphenylphosphino)alkane.

Depending on the quaternization agent, several categories of polycationic species can be produced. When an ω-haloalkyl-1-(diphenyl)phosphine oxide is used, the product bisphosphonium salt generated also bears tertiary phosphine oxide sites at each end. "Balloon" polyphosphonium species can be con-

Correspondence to: Robert Engel. Fax: (718) 997-5531; E-mail: robert__engel@qc.edu
*Permanent address: National Academy of Sciences of the Ukraine, Institute of Organic Chemistry, 5, Murmanskaya str., Kiev 94, 253660, Ukraine.

structed using a focus unit in which more than two tertiary phosphine sites are present. Finally, using reagents developed by the above-mentioned approaches, hexacationic balloon units can be attached to the surface of cross-linked chloromethylated polystyrene.
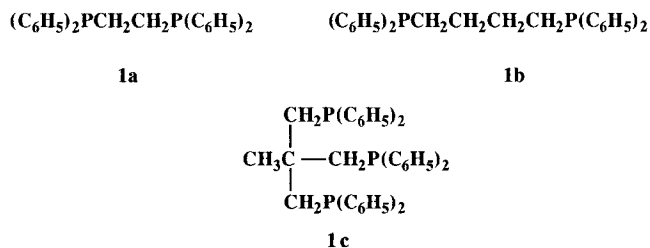
RESULTS AND DISCUSSION

The fundamental approach to the preparation of the polyphosphonium salts presented herein begins with a focus unit bearing two or more identical functional groups suitable for elaboration. For the construction of polyphosphonium species, as is the interest here, these functional groups are tertiary phosphines. Elaboration to generate polycationic strings proceeds by quaternization of each of the tertiary phosphine functional groups using an alkyl halide also bearing a distal functional group suitably protected for subsequent conversion into a further functionalizable site, that is, into new tertiary phosphine sites. In the present work, phosphine oxide functional groups have been used for this purpose, capable of being reduced to tertiary phosphine linkages under a variety of conditions. Once the new tertiary phosphine sites have been generated, continued elaboration by a repetition of the previously mentioned steps is possible. In this manner, highly defined polycationic species may be constructed (as opposed to that produced using standard linear polymerization approaches).

Verification of the structures of the synthesized materials relies heavily on NMR techniques. As with prior efforts in the synthesis of polycationic (ammonium) string species [5], "counting" of unique carbon sites using ^{13}C NMR is an important tool. However, both structural verification and determinations of purity of products is simplified in the present effort through the use of ^{31}P NMR techniques. The need for extended reaction time and product cleanup is readily determined through examination of the ^{31}P NMR spectra. Determination of the elemental composition, a standard procedure of synthetic organic chemistry, is particularly useful here for evaluation of the degree of hydration of the product salts.

Several multiphosphine reagents have been used as focus units in this work for the construction of the polyphosphonium species. These include two α, ω-bis(diphenylphosphino)alkanes, 1,2-bis(diphenylphosphino)ethane (**1a**), also known as "DIPHOS," and 1,4-bis(diphenylphosphino)butane (**1b**). The focus unit **1a** leads to polyphosphonium species in which the central phosphonium sites are separated
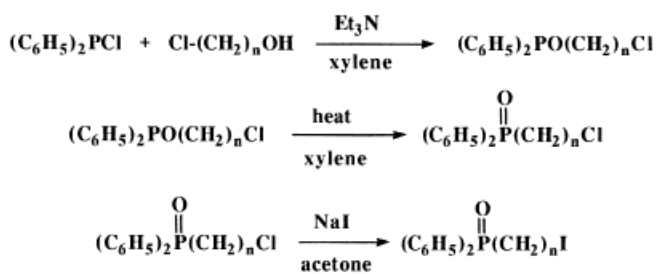
by two methylene groups, whereas **1b** provides species with a separation of four methylene groups.

$$(C_6H_5)_2PCH_2CH_2P(C_6H_5)_2 \qquad (C_6H_5)_2PCH_2CH_2CH_2CH_2P(C_6H_5)_2$$

1a **1b**

$$CH_3\overset{\overset{\displaystyle CH_2P(C_6H_5)_2}{|}}{\underset{\underset{\displaystyle CH_2P(C_6H_5)_2}{|}}{C}}\!\!-\!CH_2P(C_6H_5)_2$$

1c

The two tertiary phosphine sites of **1a** have been quaternized in several ways using ω-halo-1-substituted alkanes. One type of reagent applied to this end, useful for the further elaboration of polyphosphonium strings, is the ω-iodoalkyl-1-(diphenyl)phosphine oxide system (**2**). Such reagents are synthesized by a three-step route as illustrated in Scheme 1. As previously reported [7], diphenylchlorophosphine is esterified in a standard manner using an ω-halo-1-alcohol followed by Michaelis–Arbuzov reaction to generate the ω-chloroalkyl-1-(diphenyl)phosphine oxide. As the resultant chlorides were quite sluggish in the subsequent quaternization process, increased susceptibility toward displacement by a tertiary phosphine was accomplished by halide exchange to generate the ω-iodoalkyl-1-(diphenyl)phosphine oxide (**2**).

Reaction of the species **2** with the bis-tertiary-phosphine **1a** results in the formation of a tetraphosphorus string **3** in which the two central phosphorus atoms constitute quaternary phosphonium sites, and the more distant phosphorus atoms are tertiary phosphine oxide sites. This reaction produces **3** as the diiodide salt. Conversion to the dichloride salt was performed prior to subsequent chemical conversions.

An experimental advantage in the construction of polycationic *phosphorus* strings as compared to polycationic *nitrogen* strings is the relative ease of observation and analysis of the transformations. The

$$(C_6H_5)_2PCl + Cl\text{-}(CH_2)_nOH \xrightarrow[\text{xylene}]{Et_3N} (C_6H_5)_2PO(CH_2)_nCl$$

$$(C_6H_5)_2PO(CH_2)_nCl \xrightarrow[\text{xylene}]{\text{heat}} (C_6H_5)_2\overset{\overset{\displaystyle O}{\|}}{P}(CH_2)_nCl$$

$$(C_6H_5)_2\overset{\overset{\displaystyle O}{\|}}{P}(CH_2)_nCl \xrightarrow[\text{acetone}]{NaI} (C_6H_5)_2\overset{\overset{\displaystyle O}{\|}}{P}(CH_2)_nI$$

SCHEME 1

use of ^{31}P NMR allows facile tracking of reaction progress and the conversions of phosphorus sites. These analyses are significantly more difficult with non-phosphorus systems. Here, each new incorporation of phosphorus or transformation at a phosphorus site is easily monitored through the ^{31}P NMR spectrum. The pertinent ^{31}P NMR data for all compounds of interest in this work are summarized in Table 1.

The two tertiary phosphine oxide sites in **3** can be reduced using hexachlorodisilane to generate a tetraphosphorus species **4** in which the central two phosphorus atoms are phosphonium sites and the more distant phosphorus atoms are tertiary phosphine sites, the latter subject to quaternization for extension of the polycationic string as illustrated in Scheme 2 to generate **5**. All attempts at reduction of the P=O linkages of **5**, a prerequisite for continued elaboration, resulted in decomposition of the chain.

Several other polyphosphonium string species were generated by alkylation of the α, ω-bis(diphenylphosphino)alkanes, as illustrated in Scheme 3. The degree of alkylation can be controlled by the proper choice of solvent system for the alkylation.

The monoalkylated species **6** has been of particular use for the construction of an insoluble polymer-bound polyphosphonium species (Scheme 4) that, in addition to being a candidate for enhanced antibacterial activity in analogy with those materials previously studied [1–4], also serves as an anion exchange material. After initial functionalization of an insoluble chloromethylated copolymer of divinylbenzene and styrene (Merrifield's peptide resin) to provide sites for attachment, the phosphine/phosphonium species **6** was used for the introduction of cationic sites in high density with a balloon-type structure. The resultant fine powder exhibited an exchange capacity of 1.2 meq/g for monoanionic species. The triphosphine focus unit

TABLE 1 ^{31}P NMR Data

Compound	^{31}P Chemical Shift (δ, 85% H_3PO_4 reference)
2a	32.77
2b	31.83
3	33.95; 29.78
4	30.35; −17.91
5	33.78; 28.95; 28.37
6	30.63; −11.90
7	30.40
8	30.41
9	27.90
10	34.94; 26.52

1,1,1-tris(diphenylphosphinomethyl)ethane (**1c**) has also been used for the generation of tridirectional balloon polycationic species, as shown in Scheme 5.
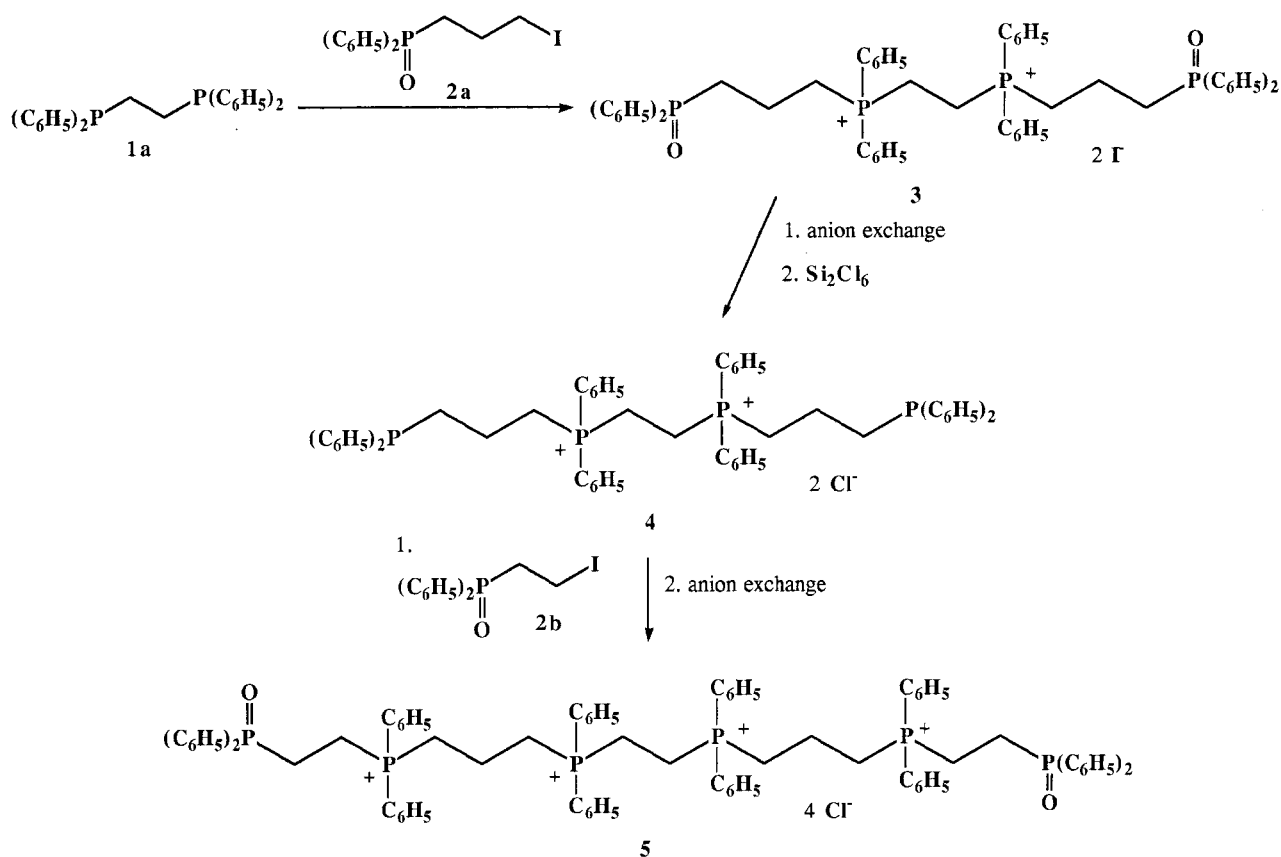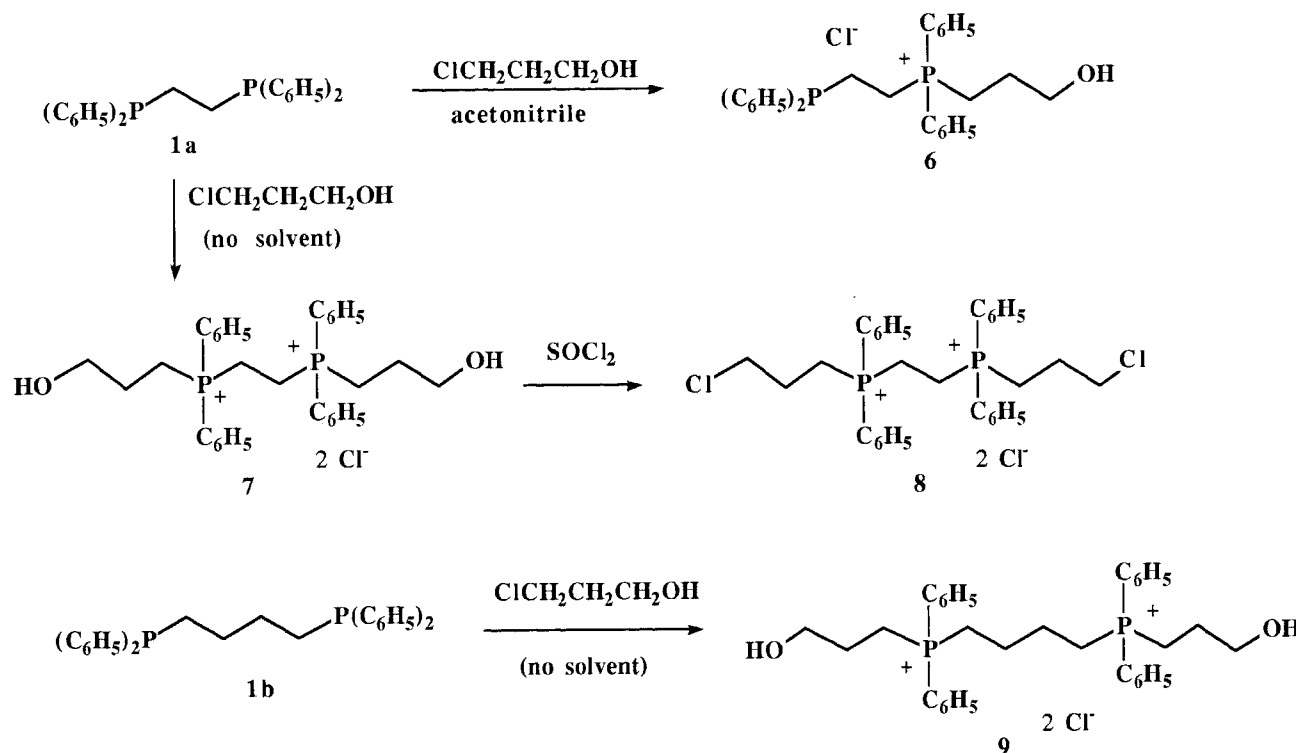
EXPERIMENTAL

General

All chemicals used in syntheses, purification, and comparison analyses were of commercial reagent quality and were used without purification. 3-Chloropropyl(diphenyl)phosphine oxide and 2-chloroethyl(diphenyl)phosphine oxide were prepared as previously reported [6]. All NMR spectra were measured using a Brüker 400 MHz DPX400 instrument. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, NY.

Preparation of 3-Iodopropyl(diphenyl)phosphine Oxide (**2a**). A mixture of 3-chloropropyl(diphenyl)phosphine oxide (5.92 g, 20.5 mmol) and sodium iodide (6.15 g, 41 mmol) dissolved in acetone (130 mL) was heated at reflux for 12 hours. After evaporation of the volatile materials under reduced pressure, the oily residue was washed with water (500 mL) upon which the insoluble organic material crystallized. The solid was washed with water and dried under vacuum to give pure 3-iodopropyl(diphenyl)phosphine oxide (7.50 g, 98.8% yield) of mp 103–104° that exhibited NMR spectra and elemental analyses in accord with the proposed structure. ^{1}H NMR (δ CDCl$_3$) 2.20 (2H, m), 2.42 (2H, m), 3.26 (2H, m), 7.47–7.75 (10H, m). ^{13}C NMR (δ CDCl$_3$—decoupled) 135.88, 134.50, 133.35, 131.31, 33.57, 28.12, 10.10. ^{31}P NMR (δ CDCl$_3$—decoupled) 32.77. Anal. C$_{15}$H$_{16}$POI requires: C, 48.67%; H, 4.36%. Found: C, 48.64%; H, 4.17%.

Preparation of 2-Iodoethyl(diphenyl)phosphine Oxide (**2b**). A mixture of 2-chloroethyl(diphenyl)phosphine oxide (11.0 g, 41.6 mmol) and sodium iodide (12.5 g, 83.1 mmol) dissolved in acetone (260 mL) was heated at reflux for 24 hours. After evaporation of the volatile materials under reduced pressure, the oily residue was washed with water (500 mL) upon which the insoluble organic material crystallized. The solid was washed with water and dried under vacuum to give pure 2-iodoethyl(diphenyl)phosphine oxide (14.0 g, 94.6% yield) of mp 135–136° that exhibited NMR spectra and elemental analyses in accord with the proposed structure. ^{1}H NMR (δ CDCl$_3$) 2.98 (2H, m), 3.32 (2H, m), 7.50–7.76 (10H, m). ^{13}C NMR (δ CDCl$_3$—decoupled) 130.38, 129.28, 128.89, 126.78, 34.05, 34.66. ^{31}P NMR (δ CDCl$_3$—de-

SCHEME 2

coupled) 31.83. Anal. $C_{14}H_{14}POI$ requires: C, 47.21%; H, 3.96%. Found: C, 47.46%; H, 3.98%.
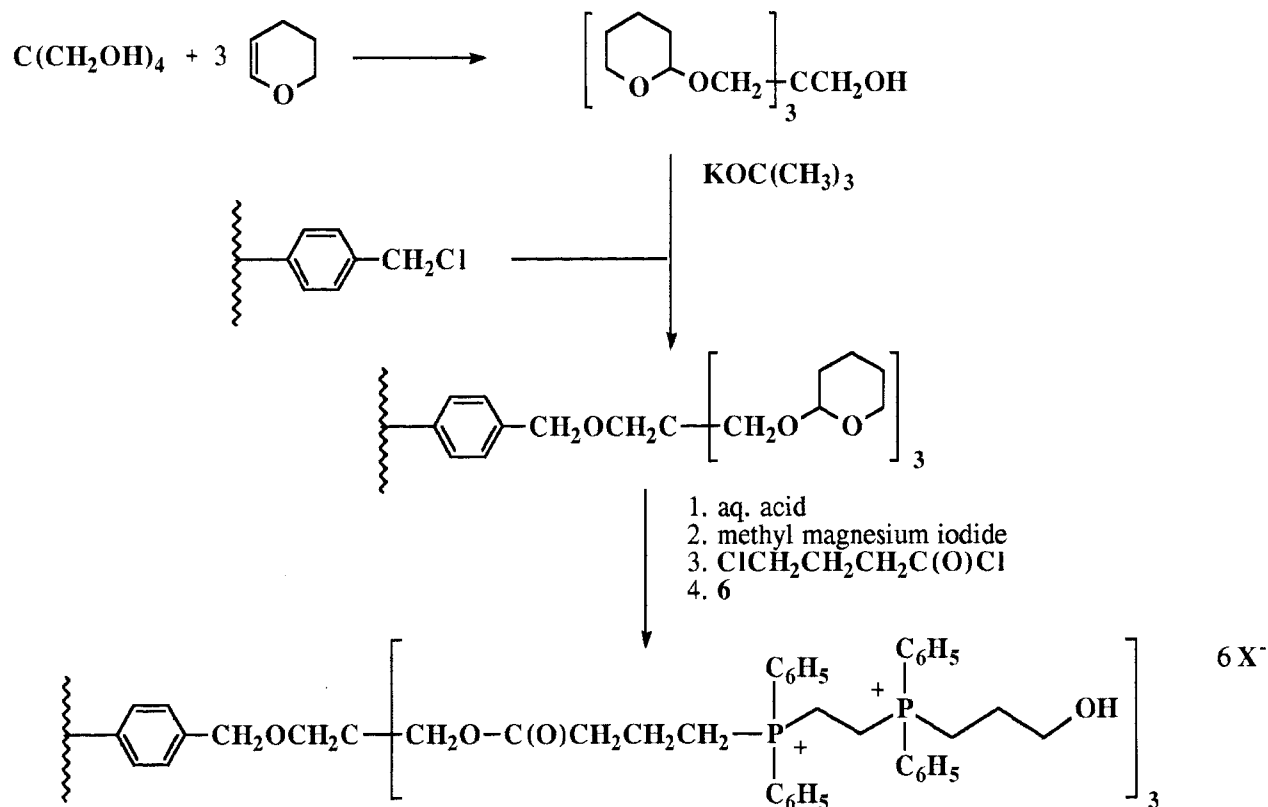
Preparation of 1,2-bis([3'-Diphenylphosphoryl-propyl]diphenylphosphonio)ethane Diiodide (**3**). A mixture of **2a** (5.60 g, 15.1 mmol) and **1a** (2.0 g, 5.0 mmol) dissolved in acetonitrile (40 mL) was heated in a sealed tube at 125° for 5 hours. After cooling to ambient temperature, a white precipitate formed that was collected by suction filtration, washed with anhydrous diethyl ether (200 mL), and dried under high vacuum to give **3** (5.60 g, 97.9% yield) as a mildly hydroscopic solid that exhibited NMR spectra and elemental analyses in accord with the dihydrate of the proposed structure. ^{1}H NMR (δ DMSO-d_6) 1.63 (4H, m), 2.64 (4H, m), 3.44 (4H, m), 3.86 (4H, m), 7.52–7.88 (40H, m). ^{13}C NMR (δ DMSO-d_6—decoupled) 135.89, 134.11, 133.65, 132.66, 1331.19, 130.97, 129.63, 117.47, 29.11, 20.14, 15.65, 13.56. ^{31}P NMR (δ DMSO-d_6—decoupled) 33.95, 29.78. Anal. $C_{56}H_{56}P_4O_2I_2 \cdot 2(H_2O)$ requires: C, 57.25%; H, 4.96%. Found: C, 57.30%; H, 5.14%.

Preparation of 1,2-bis([3'-Diphenylphosphinopropyl]diphenylphosphonio)ethane Dichloride (**4**). A
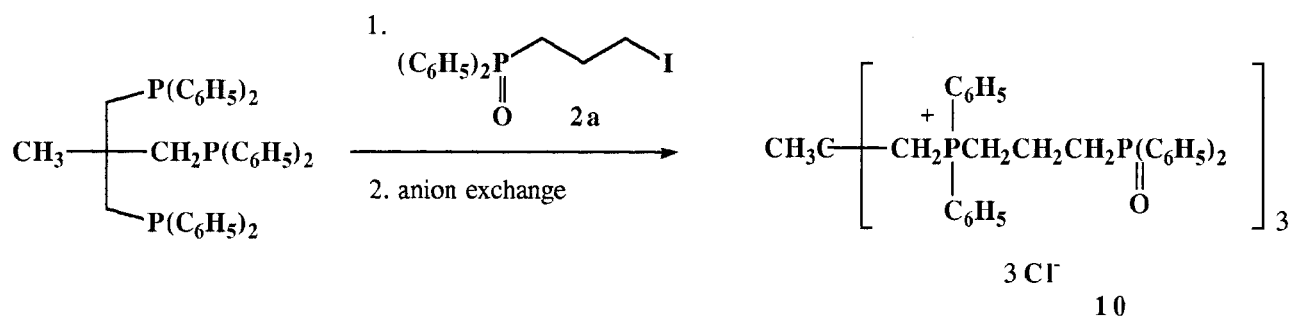
sample of **3** was converted to the dichloride salt by dissolution in water/methanol and eluting through a column of DOWEX™ 1-X8 in the chloride anion form, followed by evaporation of the solvent under reduced pressure. The resultant dichloride salt (1.70 g, 1.77 mmol) was dissolved in acetonitrile (20 mL), and to the solution was added dropwise an excess of Si_2Cl_6 (3 mL). The resultant solution was heated at 80° for 1 hour. After cooling to ambient temperature, volatile materials were removed under high vacuum. To the amorphous residue was added water (100 mL), and upon stirring at ambient temperature for 12 hours, there resulted a white precipitate that was collected by suction filtration and dissolved in methanol (200 mL). After removal of the volatile materials under reduced pressure, acetonitrile (10 mL) was added to the reside and stirred until the amorphous solid crystallized. The solid was collected by suction filtration and dried under high vacuum to give **4** (1.40 g, 85.6% yield) as a mildly hydroscopic solid that exhibited NMR spectra and elemental analyses in accord with the monohydrate of the proposed structure. ^{1}H NMR (δ CDCl$_3$) 1.35 (4H, m), 2.23 (4H, m), 3.71 (4H, m), 3.94 (4H, m), 7.25–8.08 (40H, m). ^{13}C NMR (δ CDCl$_3$—decoupled) 135.20, 132.85,

$(C_6H_5)_2P$—CH$_2$CH$_2$—$P(C_6H_5)_2$

1a

ClCH$_2$CH$_2$CH$_2$OH / acetonitrile

ClCH$_2$CH$_2$CH$_2$OH (no solvent)

6

7   2 Cl$^-$

SOCl$_2$

8   2 Cl$^-$

$(C_6H_5)_2P$—CH$_2$CH$_2$CH$_2$CH$_2$—$P(C_6H_5)_2$

1b

ClCH$_2$CH$_2$CH$_2$OH (no solvent)

9   2 Cl$^-$

SCHEME 3

$C(CH_2OH)_4$ + 3

$\left[\text{OCH}_2\right]_3CCH_2$OH

KOC(CH$_3$)$_3$

—CH$_2$Cl

—CH$_2$OCH$_2$C—[CH$_2$O—]$_3$

1. aq. acid
2. methyl magnesium iodide
3. ClCH$_2$CH$_2$CH$_2$C(O)Cl
4. **6**

—CH$_2$OCH$_2$C—[CH$_2$O—C(O)CH$_2$CH$_2$CH$_2$—P—CH$_2$CH$_2$—P—OH]$_3$ 6 X$^-$

SCHEME 4

SCHEME 5

131.61, 130.74, 128.40, 126.73, 126.43, 114.75, 26.20, 19.07, 16.46, 12.76. ^{31}P NMR (δ CDCl$_3$—decoupled) 30.35, -17.91. Anal. C$_{56}$H$_{56}$P$_4$Cl$_2$·(H$_2$O) requires: C, 71.41%; H, 6.21%. Found: C, 71.67%; H, 6.12%.

Preparation of 1,2-bis([[2″-Diphenylphosphoryl-ethyl]-3′-diphenylphosphoniopropyl]diphenylphos-phonio)ethane Tetrachloride (**5**). A mixture of **4** (1.27 g, 1.37 mmol) and **2b** (1.47 g, 4.12 mmol) in acetonitrile (15 mL) was heated at 125° in a sealed tube for 48 hours. After cooling to ambient temperature, volatile materials were removed under high vacuum. To the amorphous residue was added methanol (40 mL), and the mixture was cooled to 0°. On standing, a white precipitate formed that was collected by suction filtration. This material was converted to the tetrachloride salt by dissolution in water/methanol and eluting through a column of DOWEX™ 1-X8 in the chloride anion form, followed by evaporation of the solvent under reduced pressure. There was in this manner isolated a precipitate that was dried under high vacuum to give **5** (0.96 g, 48.8% yield) as a hydroscopic white solid that exhibited NMR spectra and elemental analyses in accord with the trihydrate of the proposed structure. ^1H NMR (δ CDCl$_3$) 1.71 (4H, m), 2.75 (4H, m), 3.10 (4H, m), 3.71 (4H, m), 4.21 (4H, m), 4.34 (4H, m), 7.27–8.05 (60H, m). ^{13}C NMR (δ CDCl$_3$—decoupled) 132.87, 132.74, 131.85, 131.21, 130.33, 129.22, 129.12, 128.79, 128.46, 127.75, 115.13, 115.41, 20.30, 18.50, 16.74, 14.91, 13.37, 12.48. ^{31}P NMR (δ CDCl$_3$—decoupled) 33.78, 28.95, 28.37. Anal. C$_{86}$H$_{84}$P$_6$O$_2$Cl$_4$·3(H$_2$O) requires: C, 66.99%; H, 6.02%. Found: C, 67.09%; H, 6.38%.

Preparation of 1-Diphenylphosphino-2-(3′-hy-droxypropyl)diphenylphosphonioethane Chloride (**6**). A mixture of **1a** (6.0 g, 15 mmol) and 3-chloro-1-propanol (1.42 g, 15 mmol) in acetonitrile (500 mL) was heated at reflux for 72 hours. After cooling to ambient temperature, volatile materials were evaporated under reduced pressure. To the viscous residue was added toluene (100 mL) to dissolve any unreacted starting materials. The undissolved residue was dissolved in water (100 mL) and the aqueous solution extracted with methylene chloride (100 mL). The organic layer was dried over anhydrous sodium sulfate, and volatile materials were evaporated under reduced pressure to give **6** (4.5 g, 60.6% yield) as a hydroscopic amorphous white solid that exhibited NMR spectra and elemental analyses in accord with the pentahydrate of the proposed structure. ^1H NMR (δ CDCl$_3$) 1.35 (2H, m), 2.13 (2H, m), 2.81 (2H, m), 3.43 (2H, m), 3.64 (2H, m), 7.08–7.63 (20H, m). ^{13}C NMR (δ CDCl$_3$—decoupled) 133.57, 131.64, 131.55, 129.36, 129.27, 128.29, 126.87, 115.51, 58.84, 28.56, 23.56, 18.08, 17.17. ^{31}P NMR (δ CDCl$_3$—decoupled) 30.63, -11.90. Anal. C$_{29}$H$_{31}$P$_2$OCl·5(H$_2$O) requires: C, 59.74%; H, 7.09%. Found: C, 59.83%; H, 6.92%.

Preparation of 1,2-bis[(3′-Hydroxypropyl)di-phenylphosphonio]ethane Dichloride (**7**). A mixture of **1a** (0.54 g, 1.35 mmol) and 3-chloro-1-propanol (0.50 g, 5.2 mmol) was heated without solvent at 130° for 48 hours. Volatile materials were evaporated under high vacuum to give **7** (0.73 g, 99.0% yield) as a mildly hydroscopic white crystalline solid that exhibited NMR spectra and elemental analyses in accord with the hemihydrate of the proposed structure. ^1H NMR (δ D$_2$O) 1.53 (4H, m), 2.92 (4H, m), 3.04 (4H, m), 3.47 (4H, m), 7.02–7.93 (20H, m). ^{13}C NMR (δ D$_2$O—decoupled) 140.43, 135.57, 135.13, 119.28, 48.66, 28.78, 22.19, 18.52. ^{31}P NMR (δ D$_2$O—decoupled) 30.40. Anal. C$_{32}$H$_{38}$P$_2$O$_2$Cl$_2$·1/2(H$_2$O) requires: C, 64.43%; H, 6.59%. Found: C, 64.54%; H, 6.51%.

Preparation of 1,2-bis[(3′-Chloropropyl)diphen-ylphosphonio]ethane Dichloride (**8**). To a heterogeneous mixture of **7** (0.75 g, 1.39 mmol) and chloroform (10 mL) was added an excess (0.6 g, 5.0 mmol) of thionyl chloride. The resultant mixture was heated at reflux for 2 hours, after which time volatile

materials were evaporated under high vacuum. The solid residue was dissolved in chloroform (10 mL) and insoluble solids removed by filtration. The volatile materials were evaporated from the solution under reduced pressure to give **7** (0.49 g, 61.2% yield) as a mildly hydroscopic crystalline solid that exhibited NMR spectra and elemental analyses in accord with the hemihydrate of the proposed structure. ^{1}H NMR (δ D$_2$O) 1.78 (4H, m), 3.04 (8H, m), 3.52 (4H, m), 7.61–7.80 (20H, m). ^{13}C NMR (δ D$_2$O—decoupled) 138.24, 135.41, 132.89, 117.13, 46.50, 26.63, 20.05, 16.72. ^{31}P NMR (δ D$_2$O—decoupled) 30.41. Anal. C$_{32}$H$_{36}$P$_2$O$_2$Cl$_4 \cdot$ 1/2(H$_2$O) requires: C, 60.71%; H, 5.89%. Found: C, 60.44%; H, 5.84%.

Preparation of 1,4-bis[(3'-Hydroxypropyl)diphenylphosphonio]butane Dichloride (**9**). A mixture of **1b** (1.00 g, 2.34 mmol) and 3-chloro-1-propanol (1.00 g, 10.6 mmol) was heated without solvent at 130° for 48 hours. Volatile materials were evaporated under high vacuum to leave a crude residue that was then dissolved in water (20 mL). Insoluble material was removed by filtration after which volatile materials were evaporated under high vacuum to give **9** (1.20 g, 83.3% yield) as a hydroscopic white crystalline solid that exhibited NMR spectra and elemental analyses in accord with the pentahydrate of the proposed structure. ^{1}H NMR (δ D$_2$O) 1.45 (8H, m), 1.52 (8H, m), 2.74 (4H, m), 7.56–7.70 (20H, m). ^{13}C NMR (δ D$_2$O—decoupled) 142.24, 138.83, 137.76, 124.24, 67.83, 30.84, 29.11, 26.90, 24.75. ^{31}P NMR (δ D$_2$O—decoupled) 27.90. Anal. C$_{34}$H$_{42}$P$_2$O$_2$Cl$_2 \cdot$ 5(H$_2$O) requires: C, 57.87%; H, 7.41%. Found: C, 57.55%; H, 7.29%.

Preparation of 1,1,1-tris[(3'-Diphenylphosphorylpropyl)diphenylphosphoniomethyl]ethane Trichloride (**10**). A mixture of **1c** (1.00 g, 1.60 mmol) and **2a** (2.66 g, 7.18 mmol) dissolved in acetonitrile (10 mL) was heated in a sealed tube at 130° for 48 hours. After cooling to ambient temperature, volatile materials were evaporated under reduced pressure, and the residue was washed with diethyl ether (100 mL) to leave a crystalline solid. This solid was dissolved in water/methanol, and the solution was eluted through a column of DOWEX™ 1-X8 in the chloride anion form. The eluted water/methanol solution was evaporated under reduced pressure, and the white solid residue dried under high vacuum to give **10** (1.30 g, 81.2% yield) as a hydroscopic solid that exhibited NMR spectra and elemental analyses in accord with the decahydrate of the proposed structure. ^{1}H NMR (δ CDCl$_3$) 1.41 (3H, s), 1.83 (6H, m), 2.38 (6H, d), 3.99 (6H, m), 4.38 (6H, m), 7.25–7.83 (60H, m). ^{13}C NMR (δ CDCl$_3$—decoupled)—although the

proposed structure contains eight unique carbon atoms in the aromatic rings, only six signals could be clearly resolved in the aromatic region of the spectrum—131.73, 130.96, 130.60, 128.69, 128.58, 115.62, 38.75, 38.31, 29.39, 28.71, 21.99, 17.59. ^{31}P NMR (δ CDCl$_3$—decoupled) 34.94, 26.52. Anal. C$_{86}$H$_{87}$P$_6$O$_3$Cl$_3 \cdot$ 10(H$_2$O) requires: C, 62.94%; H, 6.57%. Found: C, 62.60%; H, 6.20%.

Preparation of 2,2,2-tris(2'-Tetrahydropyranyloxymethyl)ethanol (**11**). Finely powdered pentaerythritol (8.00 g, 58.7 mmol) was dissolved in dry dimethylformamide (160 mL) with warming to 35°. After allowing the solution to cool to ambient temperature, an excess of 3,4-dihydro-2*H*-pyran (16.0 g, 190.2 mmol) was added with stirring. Upon addition of *p*-toluenesulfonic acid monohydrate (0.1 g) as catalyst, an exothermic reaction occurred. The temperature was maintained below 35° using a cooling bath until the exotherm had subsided, and the reaction mixture was then allowed to stir for an additional 48 hours. At this time, triethylamine (1 mL) was added to neutralize the acid, and volatile materials were evaporated under reduced pressure. The residue was poured into water (100 mL) and the resultant solution extracted with diethyl ether (3 × 100 mL). The organic layer was dried over KOH and filtered, and volatile materials were evaporated under reduced pressure. The crude product was purified by passage through a column of basic alumina (W200) eluting with hexane:ethyl acetate (1:5). In this manner was isolated **11** (7.40 g, 32.4% yield) as a viscous oil, which was shown to be a mixture of diastereoisomers by the complexity of the ^{13}C spectrum. ^{1}H NMR (δ CDCl$_3$) 1.51–1.81 (18H, m), 3.43–3.53 (6H, m), 3.75–3.87 (8H, m), 4.53 (3H, m). Anal. C$_{20}$H$_{36}$O$_7$ requires: C, 61.83%; H, 9.39%. Found: C, 61.66%; H, 9.42%.

Construction of the Polyphosphonium Anion Exchange Material. To a solution of **11** (6.00 g, 15.4 mmol) in dry tetrahydrofuran (30 mL) was added potassium *t*-butoxide (1.80 g, 16.0 mmol) with stirring under a nitrogen atmosphere. To the resultant solution was then added Merrifield's resin (6.0 g; 2% cross-linked chloromethylatedstyrene/divinylbenzene copolymer—~1 meq Cl/g). The mixture was stirred with heating at reflux under a nitrogen atmosphere for 62 hours, after which the solid was recovered by suction filtration. The recovered solid was then hydrolyzed to remove the tetrahydropyranyl protecting groups by refluxing in a mixture of ethanol (20 mL), water (10 mL), and concentrated hydrochloric acid (5 mL) for 24 hours. There was recovered by suction filtration and subsequent dry-

ing under vacuum 6.60 g of the substituted resin. The substituted resin thus isolated (1.00 g) was then treated with an excess (50 mL) of a solution of methyl magnesium iodide in diethyl ether. After evolution of methane ceased, the reaction mixture was filtered with suction under a dry nitrogen atmosphere to recover the further converted resin. The converted resin (magnesium salt stage) was then treated with an excess of a solution of 4-chlorobutanoyl chloride (1.00 g) in acetonitrile (30 mL), stirring at ambient temperature for 24 hours. At the end of this time, the solid was recovered by suction filtration, washed with water and diethyl ether, and dried under high vacuum to give 1.2 g of the further converted resin. The entire amount of this material was then heated at reflux in acetonitile (20 mL) with an excess of **6** (1.5 g, 3.0 mmol) and sodium iodide (0.1 g) for 48 hours. After this time, the solid material was recovered by suction filtration followed by washing with 10% aqueous sodium chloride (100 mL), water (100 mL), and diethyl ether (100 mL) and dried under high vacuum to yield 1.71 g of dried modified resin. The anion exchange capacity of the powdery resin was measured by first washing the resin with an excess (200 mL) of 1 *M* sodium chloride solution followed by water until no further traces of chloride ion were eluted (testing with aqueous silver nitrate solution). The resin (chloride ion form) was then washed with 1 *M* aqueous sodium nitrate solution (100 mL, to remove the chloride ion and convert the resin to the nitrate ion form), and aqueous silver nitrate was added to the eluent to precipitate silver chloride. The silver chloride was recovered by suction filtration, dried under high vacuum protected from the light, and quickly weighed. In this manner, the anion exchange capacity of the powdery resin was estimated at 1.2 meq/g.

REFERENCES

[1] A. Kanazawa, T. Ikeda, T. Endo, *J. Polym. Sci., Part A-1, 31,* 1993, 335.
[2] A. Kanazawa, T. Ikeda, T. Endo, *J. Polym. Sci., Part A-1, 31,* 1993, 1441.
[3] A. Kanazawa, T. Ikeda, T. Endo, *J. Polym. Sci., Part A-1, 31,* 1993, 1457.
[4] A. Kanazawa, T. Ikeda, T. Endo, *J. Polym. Sci., Part A-1, 31,* 1993, 3031.
[5] J. Fabian, T. October, A. Cherestes, R. Engel, *Synlett,* 1997, 1007.
[6] B. E. Tropp, L. Lin, T. Shimizu, N. Lau, R. Engel, unpublished results of this laboratory.
[7] (a) R. S. Cooper, U.S. Patent 3,035,096, 15 May 1962; (b) M. I. Kabachnik, T. Y. Medved, Y. M. Polikarpov, K. S. Yudina, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk,* 1962, 1584.