Polyphosphazenes with Glucosyl and Methylamino, Trifluoroethoxy, Phenoxy, or (Methoxyethoxy)ethoxy Side Groups

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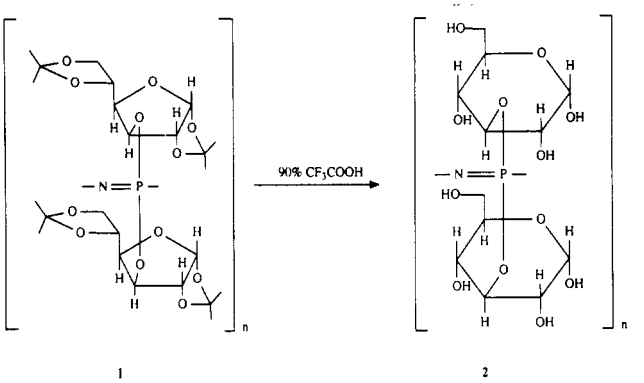
ABSTRACT: Four new types of polyphosphazenes have been synthesized that bear α-D-glucosyl side groups together with methylamino, trifluoroethoxy, phenoxy, or (methoxyethoxy)ethoxy cosubstituent groups. The formulas are $[NP(Gl)_x(NHMe)_y]_n$, $[NP(Gl)_x(OCH_2CF_3)_y]_n$, $[NP(Gl)_x(OPh)_y]_n$, and $[NP(Gl)_x(OCH_2CH_2OCH_2CH_2OCH_3)_y]_n$, where Gl = α-D-glucosyl, $x + y = 2$, and $n \approx 15\,000$. The syntheses were accomplished by the following sequence of reactions. First, the sodium salt of diacetone D-glucose or the cosubstituent nucleophile was allowed to react with poly(dichlorophosphazene) to generate an intermediate of formula $[NP(di\text{-}A\text{-}Gl)_xCl_y]_n$ or $[NPCl_x(OR)_y]_n$, with the ratio of x to y being determined by the ratio of the reactants. Second, the cosubstituent (NHR, OR, or di-A-Gl) was introduced by replacement of the remaining chlorine by reaction with methylamine or the appropriate alkoxide or aryl oxide. Finally, the protecting groups on the glucosyl residues were removed by treatment with acid. A wide range of ratios of x to y was explored, and the resultant polymers were studied with respect to solubility in water, hydrophilicity or hydrophobicity, cross-linking by γ-radiation or chemical reagents, and stability to hydrolysis. The new macromolecules offer a range of possibilities for utilization in membranes, hydrogels, biomaterials, and bioerodible polymers.

Polymers that bear sugar residues as side groups are of interest for use in membrane research or oligosaccharide synthesis, as matrices for the controlled delivery of pharmaceutical agents, and as hydrophilic or amphiphilic biomaterials. In an earlier publication, we described the synthesis of a single-substituent α-D-glucosyl phosphazene polymer by the reaction of the sodium salt of diacetone D-glucose with poly(dichlorophosphazene).[1] In this paper, we discuss an extension of these studies to polyphosphazenes that bear both glucosyl side groups and a second type of side group. The four cosubstituent groups employed were methylamino, trifluoroethoxy, phenoxy, and (methoxyethoxy)ethoxy units. Like the glucosyl groups, the methylamino and (methoxyethoxy)ethoxy side groups are water-solubilizing units. Trifluoroethoxy and phenoxy side groups are hydrophobic: hence the use of these cosubstituents offered the possibility that amphiphilic polymers could be synthesized.

In this work, we have attempted to answer the following questions. (1) For the glucosyl/trifluoroethoxy and the glucosyl/phenoxy mixed-substituent polymers, what ratio of glucosyl to hydrophobic substituent is required to generate hydrophilic surface character or solubility in water? (2) In the second halogen replacement step, does the introduction of the second organic substituent bring about displacement of the protected sugar residue? (3) Is the sugar deprotection step accompanied by any backbone cleavage or reaction of the cosubstituent groups? (4) In what ways do the changes in cosubstituent groups and side-group ratios influence changes in the polymer properties? (5) To what degree are the protected or deprotected polymers sensitive to water? (6) What conditions are required to bring about chemical or radiation cross-linking?

Results and Discussion

Limits to the Synthesis of α-D-Glucosyl Polyphosphazenes. The synthesis of polyphosphazenes that bear two diacetone D-glucosyl groups attached to every phosphorus atom along the chain (1) is limited by the steric hindrance effects associated with the bulky diacetone D-glucosyl groups. Thus, as halogen replacement takes place along a poly(dichlorophosphazene) chain, the remaining



1 2

P–Cl bonds become increasingly shielded by the organic units. Replacement of the last 10–15% of the chlorine atoms is exceedingly difficult. If the P–Cl units are left unreacted, their subsequent hydrolysis in aqueous media will lead to chain cleavage and to general breakdown of the polymer. Even if protected from hydrolysis, residual P–Cl bonds would be capable of generating cross-links by reaction with the glucosyl hydroxyl groups formed by deprotection. Replacement of the remaining chlorine atoms by diacetone D-glucosyl units can be accomplished by the use of forcing conditions (high temperatures, use of high-boiling solvents, prolonged reaction times, and the use of a pressurized reactor), but such conditions could lead to thermal depolymerization to low molecular weight polymers or oligomers or may favor a rearrangement of the alkoxy side units.[2-5] The use of unprotected glucosyl units would lead to extensive cross-linking. For these reasons the synthesis of high molecular weight $[NP(Gl)_2]_n$ (2) polymer is a challenging and somewhat unpredictable process.

To avoid this problem, we have developed a sequential synthesis route to mixed-substituent polyphosphazenes that contain α-D-glucosyl units and a second, less hindered side group (6). The approach involved an initial introduction of either the bulky diacetone D-glucosyl units to yield polymers of formula $[NP(di\text{-}A\text{-}Gl)_xCl_y]_n$ (4) or the cosubstituent, OR, to give polymers of formula $[NPCl_x(OR)_y]_n$ (7) in which the ratio of x to y was varied over the range 1:9 to 8:2. The remaining chlorine atoms were then replaced by reaction with the second nucleophile. Finally,

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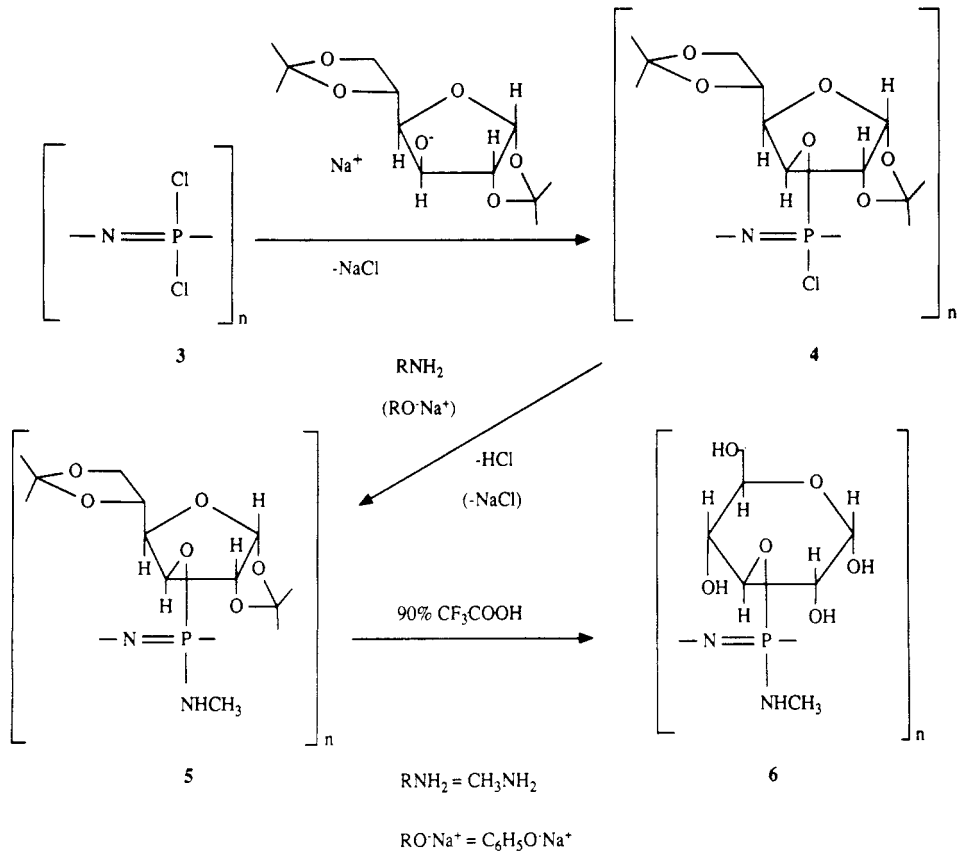
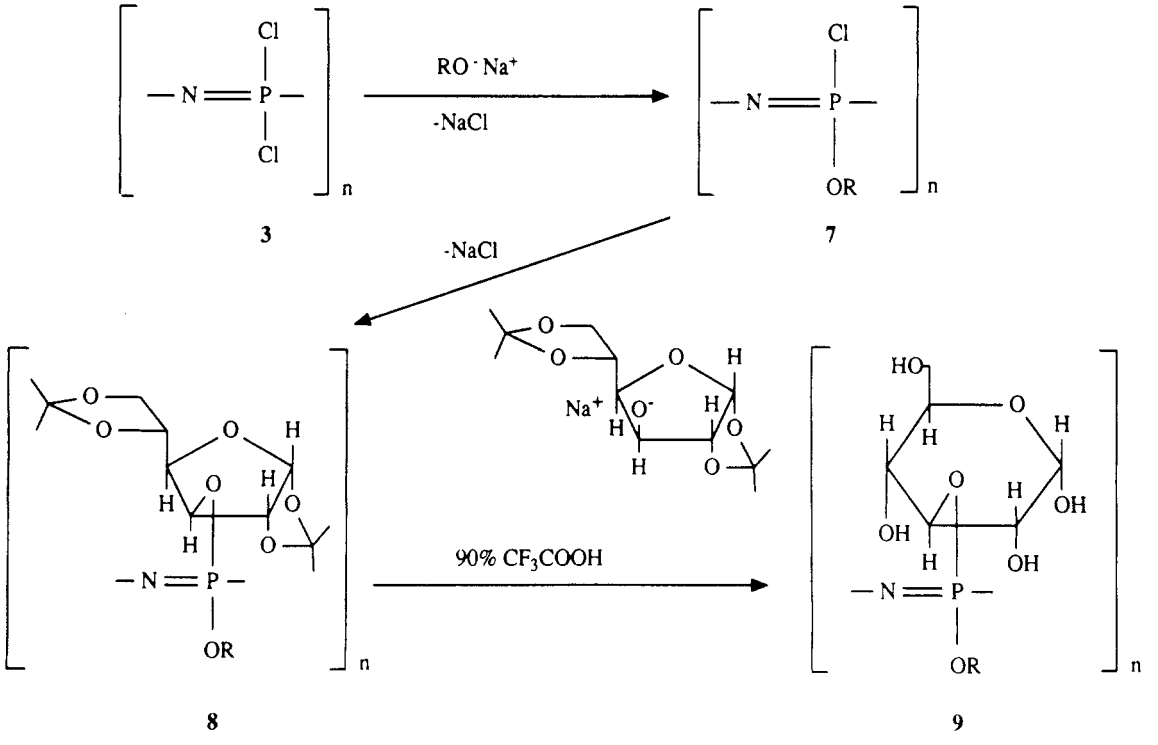
Scheme I



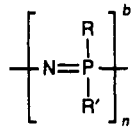
Scheme II



the glucosyl units were deprotected by treatment with trifluoroacetic acid.[6] The overall process is illustrated in Schemes I and II, which represent the special case of a 1:1 side-group ratio and an idealized nongeminal substitution pattern. The polymers synthesized are listed in Table I and in Chart I. The structures shown in Chart I are again idealized formulas for the special case of nongeminal side-group arrangements and a 1:1 substituent ratio.

A significant observation was that, over the whole range of substituent ratios studied, the remaining chlorine atoms in 4 can be replaced by methylamino, trifluoroethoxy, or (methoxyethoxy)ethoxy units. However, the phenoxy side

Table I
Substituent Ratios and Compound Identification Numbers[a]



compd	R	R′	compd	R	R′	R″
10	di-A-Gl (10%)	$NHCH_3$ (90%)	**30**[c]	di-A-Gl (10%)	OC_6H_5 (80%)	Cl (10%)
11	di-A-Gl (25%)	$NHCH_3$ (75%)	**31**	di-A-Gl (25%)	OC_6H_5 (58%)	Cl (17%)
12	di-A-Gl (50%)	$NHCH_3$ (50%)	**32**	di-A-Gl (43%)	OC_6H_5 (40%)	Cl (17%)
13	di-A-Gl (68%)	$NHCH_3$ (32%)	**33**	di-A-Gl (50%)	OC_6H_5 (23%)	Cl (27%)
14	di-A-Gl (79%)	$NHCH_3$ (21%)	**34**	di-A-Gl (63%)	OC_6H_5 (9%)	Cl (28%)
15	Gl (10%)	$NHCH_3$ (90%)	**35**	Gl (10%)	OC_6H_5 (80%)	Cl (10%)
16	Gl (25%)	$NHCH_3$ (75%)	**36**	Gl (25%)	OC_6H_5 (58%)	Cl (17%)
17	Gl (50%)	$NHCH_3$ (50%)				
18	Gl (68%)	$NHCH_3$ (32%)	**37**	di-A-Gl (36%)	OC_6H_5 (39%)	$NHCH_3$ (25%)
19	Gl (79%)	$NHCH_3$ (21%)	**38**	Gl (36%)	OC_6H_5 (39%)	$NHCH_3$ (25%)
20	di-A-Gl (10%)	OCH_2CF_3 (90%)	**39**	di-A-Gl (40%)	$OCH_2CH_2OCH_2CH_2OCH_3$ (60%)	
21	di-A-Gl (25%)	OCH_2CF_3 (75%)	**40**	di-A-Gl (60%)	$OCH_2CH_2OCH_2CH_2OCH_3$ (40%)	
22	di-A-Gl (50%)	OCH_2CF_3 (50%)	**41**	Gl (40%)	$OCH_2CH_2OCH_2CH_2OCH_3$ (60%)	
23	di-A-Gl (68%)	OCH_2CF_3 (32%)	**42**	Gl (60%)	$OCH_2CH_2OCH_2CH_2OCH_3$ (40%)	
24	di-A-Gl (79%)	OCH_2CF_3 (21%)				
25	Gl (10%)	OCH_2CF_3 (90%)				
26	Gl (25%)	OCH_2CF_3 (75%)				
27	Gl (50%)	OCH_2CF_3 (50%)				
28	Gl (68%)	OCH_2CF_3 (32%)				
29	Gl (79%)	OCH_2CF_3 (21%)				

[a] d-A-Gl = diacetone D-glucosyl, Gl = α-D-glucosyl. [b] This structure represents only the special case of a 50:50 side-group ratio and a nongeminal substitution pattern. [c] Side-group ratios in polymers **30–36** are the best estimates determined from ^1H NMR and elemental analysis data.

Table II
(Diacetone D-glucosyl)/Methylamino Polyphosphazene Characterization Data

polym		elem anal.[a] % C	% H	% N	% Cl	^{31}P NMR[b]	M_w[a]	T_g, °C
10	calcd	33.42	7.35	25.99	0	5.7	1.2×10^6	49
	found	33.36	7.37	25.57	0.03			
11	calcd	41.00	7.11	15.94	0	4.8, 1.9	1.3×10^6	69
	found	40.80	7.07	15.87	0.15			
12	calcd	46.70	6.95	9.22	0	1.0, −8.4	3.1×10^6	70
	found	46.48	6.94	8.97	0.08			
13	calcd	48.87	6.87	5.51	0	−0.2, −6.7	2.2×10^6	72
	found	48.60	6.92	5.65	0.19	−9.3		
14	calcd	49.81	6.84	4.31	0	−0.2, −8.8	2.0×10^6	77
	found	49.67	6.61	4.34	0.30			

^1H NMR: 1.2 (3 H, s), 1.3 (3 H, s), 1.4 (3 H, s), 1.6 (3 H, s), 2.5 (3 H, s), 3.5–4.5 (6 H, m), 5.9 (1 H, d) ppm
Infrared analysis: N–H, 3300 cm^{-1}; P=N/P–O, 1210 cm^{-1}; C–O, 1090 cm^{-1}; *gem*-CH_3, 1385 cm^{-1}

[a] Obtained by Galbraith Laboratories, Knoxville, TN. [b] 85% H_3PO_4 internal standard. [c] Calibrated with known molecular weight polystyrene standards.

group is sufficiently bulky that replacement of all the chlorine atoms did not occur for any ratios of the diacetone D-glucosyl to chlorine, including those in which 90% of the side groups were chlorine.

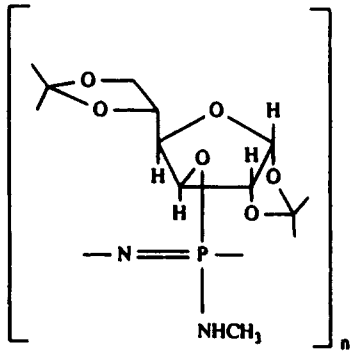
Synthesis and Characterization of α-D-Glucosyl/Methylamino Polyphosphazenes. Poly(dichlorophosphazene) (**3**) was first treated with different amounts of the sodium salt of diacetone D-glucose in order to replace 10%, 25%, 50%, 68%, and 79% of the chlorine atoms by diacetone D-glucosyl units (Scheme I). These macromolecular intermediates were not isolated, but were used directly in the next step. Each of the five polymers (**10–14**) was then treated with methylamine to generate polymers **15–19**. These species were isolated and purified (see Experimental Section) and were characterized by a combination of ^{31}P NMR and ^1H NMR (in $CDCl_3$) spectroscopy, infrared analysis, gel permeation chromatography (for molecular weight estimation), differential scanning calorimetry (for T_g values), and elemental analysis. These data are summarized in Table II.

The polymers were then deprotected by treatment with 90% trifluoroacetic acid. The reaction times for deprotection were changed for the different loading of diacetone D-glucosyl units on each polymer: higher loadings required longer deprotection times. In each case, the reaction conditions were chosen to provide complete deprotection without interference from side reactions such as cleavage of the phosphazene skeleton. The reaction mixtures were then neutralized, and the polymers were isolated and purified. Details are given in the Experimental Section.

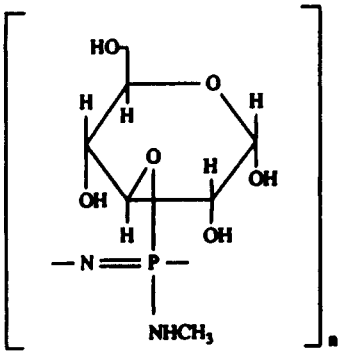
The macromolecules synthesized in this way are shown as structures **15–19** (Chart I and Table I). All these polymers were soluble in aqueous media, although each polymer precipitated initially during neutralization and then redissolved. The purified polymers in the solid state were colorless glasses. The characterization data are given in Table III.

Synthesis and Characterization of α-D-Glucosyl/Trifluoroethoxy Polyphosphazenes. In these syntheses

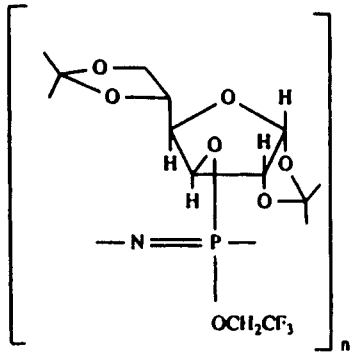
Chart I



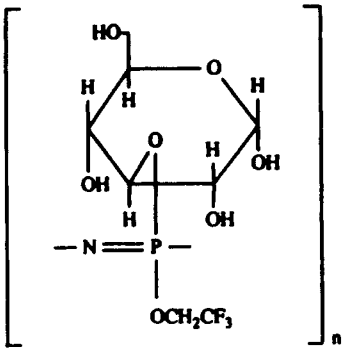
10-14



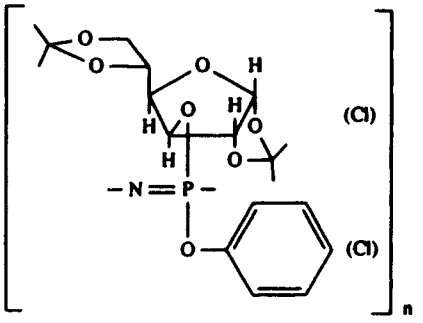
15-19



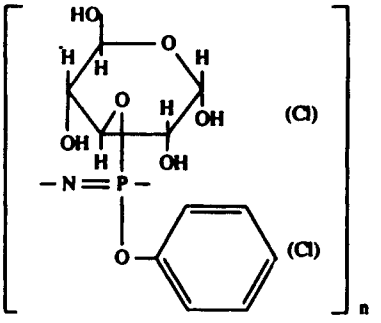
20-24



25-29



30-34



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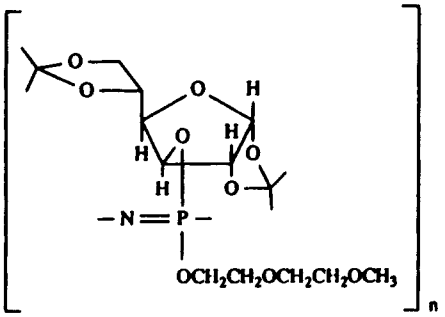

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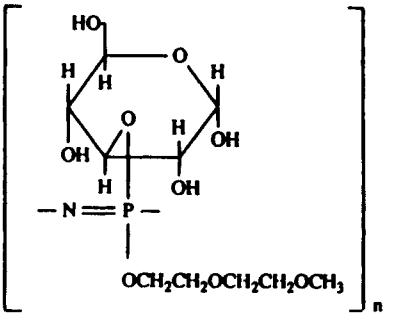

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the trifluoroethoxy groups were introduced first (Scheme II) in order to avoid the possibility that the trifluoroethoxide ion might displace diacetone D-glucosyl units already present.

Thus, poly(dichlorophosphazene) was allowed to react with sodium trifluoroethoxide to replace 90%, 75%, 50%, 32%, and 21% of the chlorine atoms by trifluoroethoxy groups. These polymers were then treated with sodium

Table III
α-D-Glucosyl/Methylamino Polyphosphazene Characterization Data

polymer		elem anal.[a] % C	% H	% N	% Cl	^{31}P NMR[b]	M_w[c]	T_g, °C
15	calcd	26.71	7.02	29.08	0	6.7	2.0×10^5	59
	found	26.40	6.97	28.91	0.04			
16	calcd	30.09	6.45	19.50	0	6.5, 5.6	1.7×10^5	71
	found	29.96	6.40	19.45	0.10			
17	calcd	33.07	5.95	11.02	0	5.1, -3.4	3.2×10^5	73
	found	32.99	5.96	11.10	0.06			
18	calcd	34.33	5.74	7.38	0	-1.7, -5.5	1.5×10^5	74
	found	34.60	5.75	7.29	0.20			
19	calcd	34.90	5.64	5.84	0	-5.2, -7.4	6.7×10^5	79
	found	35.01	5.68	5.79	0.32			

^{1}H NMR: 2.5 (3 H, s), 3.4–4.6 (11 H, m) ppm
Infrared analysis: N–H/O–H, 3420 cm^{-1}; P=N/P–O, 1220 cm^{-1}; C–O, 1100 cm^{-1}

[a] Obtained by Galbraith Laboratories, Knoxville, TN. [b] 85% H_3PO_4 internal standard. [c] Calibrated with known molecular weight poly(ethylene oxide) standards.

Table IV
(Diacetone D-glucosyl)/Trifluoroethoxy Polyphosphazene Characterization Data

polymer		elem anal.[a] % C	% H	% N	% Cl	^{31}P NMR[b]	M_w[c]	T_g, °C
20	calcd	26.19	2.71	5.09	0	-8.2	4.4×10^6	-63
	found	25.94	2.91	5.09	0.14			
21	calcd	33.45	3.90	4.34	0	-7.9	2.2×10^6	8
	found	33.31	3.81	4.29	0.07			
22	calcd	41.69	5.25	3.47	0	-8.1	1.2×10^6	44
	found	41.50	5.29	3.51	0.04			
23	calcd	45.85	5.93	3.04	0	-9.6	1.5×10^6	66
	found	45.98	5.94	3.09	0.03			
24	calcd	47.92	6.27	2.82	0	-11.2	3.5×10^6	68
	found	47.82	6.29	2.81	0.12			

^{1}H NMR: 1.2 (3 H, s), 1.3 (3 H, s), 1.4 (3 H, s), 1.5 (3 H, s), 3.5–5.0 (8 H, m), 6.0 (1 H, d) ppm
Infrared analysis: P=N/P–O, 1170 cm^{-1}; C–O, 1080 cm^{-1}; *gem*-CH_3, 1380 cm^{-1}; C–F, 885, 844 cm^{-1}

[a] Obtained by Galbraith Laboratories, Knoxville, TN. [b] 85% H_3PO_4 internal standard. [c] Calibrated with known molecular weight polystyrene standards.

Table V
α-D-Glucosyl/Trifluoroethoxy Polyphosphazene Characterization Data

polymer		elem anal.[a] % C	% H	% N	% Cl	^{31}P NMR[b]	M_w[c]	T_g, °C
25	calcd	22.65	2.26	5.41	0	-8.5	1.7×10^6	-57
	found	22.02	2.18	5.47	0.21			
26	calcd	25.45	3.03	4.95	0	-8.4	1.7×10^6	34
	found	25.37	2.98	5.13	0.12			
27	calcd	29.37	4.05	4.34	0	-7.8	7.9×10^5	56
	found	30.08	4.08	4.40	0.07			
28	calcd	32.21	4.65	3.98	0	-7.5	9.7×10^5	73
	found	32.02	4.52	3.94	0.23			
29	calcd	33.53	4.97	3.79	0	-7.7	6.9×10^5	74
	found	33.48	4.86	3.54	0.26			

^{1}H NMR: 3.5–5.0 (13 H, m) ppm
Infrared analysis: O–H, 3430 cm^{-1}; P=N/P–O, 1170 cm^{-1}; C–O, 1080 cm^{-1}; C–F, 880, 843 cm^{-1}

[a] Obtained by Galbraith Laboratories, Knoxville, TN. [b] 85% H_3PO_4 internal standard. [c] The molecular weights of polymers **25** and **26** were estimated by GPC calibrated with known molecular weight polystyrene standards. The molecular weights of polymers **27–29** were estimated by GPC calibrated with known molecular weight poly(ethylene oxide) standards.

diacetone D-glucoxide (in 100% excess relative to the P–Cl bonds present). The resultant polymers (**20–24**) had properties that varied with the ratios of the two substituents. Species **20** and **21**, with 10% and 25% diacetone D-glucosyl side groups, were tough, elastomeric materials. Polymer **22**, with 50% of both side groups, was a white, leathery material, while those polymers (**23** and **24**) with 68% and 79% of the diacetone D-glucosyl groups were colorless glasses.

These polymers were characterized by a combination of ^{31}P and ^{1}H NMR (in $CDCl_3$) spectroscopy, infrared analysis, GPC, DSC, and elemental microanalysis. The characterization data are given in Table IV.

Deprotection of the sugar residues was then accomplished by treatment with 90% trifluoroacetic acid. Again, the conditions for deprotection were chosen to balance the time required to deprotect the sugar residues present against the need to avoid cleavage of the phosphazene backbone. In general, longer times were needed for the deprotection of these polymers than for the methylamino cosubstituent polymers discussed earlier. The reaction mixtures were then neutralized with base. Species **25** and **26** (10% and 25% glucosyl units) could be purified by precipitation from THF into water. Polymers **27–29**

Table VI
(Diacetone D-glucosyl)/Phenoxy Polyphosphazene Characterization Data

polymer		elem anal.[a] % C	% H	% N	% Cl	^{31}P NMR[b]	M_w[c]	T_g, °C
30	calcd	59.96	4.88	5.30	0	-18.6	2.4×10^6	-2
	found	46.89	5.84	3.59	5.76			
31	calcd	57.96	5.45	4.46	0	-19.6, -16.5	2.3×10^6	10
	found	52.71	5.00	5.06	3.93			
32	calcd	54.41	6.09	3.53	0	-15.2, -14.4	2.2×10^6	59
	found	45.44	5.93	3.89	4.18			
33	calcd	52.96	6.40	3.06	0	-12.5	2.6×10^6	74
	found	48.05	6.11	3.77	3.96			
34	calcd	52.25	6.56	2.83	0	-11.9	2.5×10^6	80
	found	45.54	4.54	5.77	4.10			

^{1}H NMR: 1.3 (3 H, s), 1.35 (3 H, s), 1.4 (3 H, s), 1.6 (3 H, s), 3.8–4.5 (6 H, m), 5.9 (1 H, d), 7.3 (5 H, m) ppm
Infrared analysis: Ar–H, 3010 cm^{-1}; P=N/P–O, 1165 cm^{-1}; C–O, 1070 cm^{-1}; *gem*-CH_3, 1375 cm^{-1}

[a] Obtained by Galbraith Laboratories, Knoxville, TN. [b] 85% H_3PO_4 internal standard. [c] Calibrated with known molecular weight polystyrene standards.

Table VII

α-D-Glucosyl/Phenoxy Polyphosphazene Characterization Data

polymer		elem anal.[a] % C	% H	% N	% Cl	^{31}P NMR[b]	M_w[c]	T_g, °C
35	calcd	58.02	4.55	5.64	0	-19.9, -15.3	4.0×10^5	6
	found	52.08	4.50	5.62	3.43			
36	calcd	52.56	4.78	5.11	0	-19.2, -14.4	1.5×10^5	35
	found	46.93	4.71	5.61	1.68			

^{1}H NMR: 3.5–4.8 (11 H, m), 7.4 (5 H, m) ppm
Infrared analysis: O–H, 3250 cm^{-1}; Ar–H, 3020 cm^{-1}; P=N/P–O, 1210 cm^{-1}; C–O, 1070 cm^{-1}

Protected and Deprotected Glucosyl/Phenoxy/Methylamino Polyphosphazene Characterization Data

polymer		elem anal.[a] % C	% H	% N	% Cl	^{31}P NMR[b]	M_w[c]	T_g, °C
37	calcd	51.60	6.22	6.33	0	-5.9, -12.4	1.0×10^6	68
	found	51.24	5.58	5.60	0.67	-13.5		
38	calcd	42.49	5.33	7.83	0	-3.8, -6.7	6.0×10^5	80
	found	41.96	5.10	6.90	0.10	-13.1		

^{1}H NMR: polymer **37**, 1.2 (3 H, s), 1.3 (3 H, s), 1.4 (3 H, s), 1.5 (3 H, s), 2.5 (3 H, s), 3.6–4.5 (6 H, m), 5.9 (1 H, d), 6.9 (5 H, m) ppm
polymer **38**, 2.5 (3 H, s), 3.8–5.2 (11 H, m), 7.0 (5 H, m) ppm
Infrared analysis: polymer **37**, N–H, 3300 cm^{-1}; Ar–H, 3100 cm^{-1}; *gem*-CH_3, 1385 cm^{-1}; P=N/P–O, 1200 cm^{-1}; C–O, 1080 cm^{-1}
polymer **38**, N–H/O–H, 3200 cm^{-1}; Ar–H, 3100 cm^{-1}; P=N/P–O, 1205 cm^{-1}; C–O, 1090 cm^{-1}

[a] Obtained by Galbraith Laboratories, Knoxville, TN. [b] 85% H_3PO_4 internal standard. [c] Calibrated with known molecular weight polystyrene standards.

(50%, 68%, and 79% glucosyl units) were soluble in water and could be purified by dialysis.

In physical properties the polymers ranged from white elastomers (**25**) (10% glucosyl), through white, leathery materials (**26**) (25% glucosyl), to colorless glasses (**27–29**) (50–79% glucosyl). The characterization data are summarized in Table V.

Synthesis and Characterization of α-D-Glucosyl/Phenoxy Polyphosphazenes. Attempts to replace the chlorine atoms in poly(dichlorophosphazene) (**3**) by both diacetone D-glucosyl groups and phenoxy groups always yielded polymers (**30–34**) with unreacted P–Cl bonds, irrespective of the side-group ratios introduced. This is in spite of the fact that two different substitution sequences were investigated. In the first, the initial reaction of $[NPCl_2]_n$ with diacetone D-glucoxide was followed by treatment with an excess sodium phenoxide (Scheme I). In the second approach, the phenoxy side groups were introduced in the initial reaction, and the products were then allowed to react with diacetone D-glucoxide (Scheme II). Typically, after both substitutions, 15–25% of the side groups were residual chlorine atoms. This inability to replace all the chlorine atoms by the two organic groups was ascribed to the steric shielding of the chlorine atoms by the bulky diacetone D-glucosyl and phenoxy groups. Structures **30–34** (Table I) reflect the compositions of the five polymers synthesized in this phase of the study. Characterization data are listed in Table VI.

Deprotection of these polymers was attempted with 90% trifluoroacetic acid. Those species with a high phenoxy group content (90% and 75%) (**30** and **31**) underwent deprotection of the diacetone D-glucose units without significant attack on the P–Cl bonds and without detectable skeletal cleavage. Presumably, this is a further consequence of shielding of the remaining P–Cl by the phenoxy units. However, these polymers with a lower phenoxy group content (high diacetone D-glucose ratios) usually decomposed within 3–6 h of exposure to the acidic deprotection medium. It seems likely that, in these polymers, the residual P–Cl bonds were hydrolyzed to P–OH side units, species that are known to sensitize polyphosphazenes to hydrolytic skeletal cleavage. The two polymer systems that survived the deprotection treatment (**35, 36**) were characterized by the same methods as described before, and the data are summarized in Table VII.

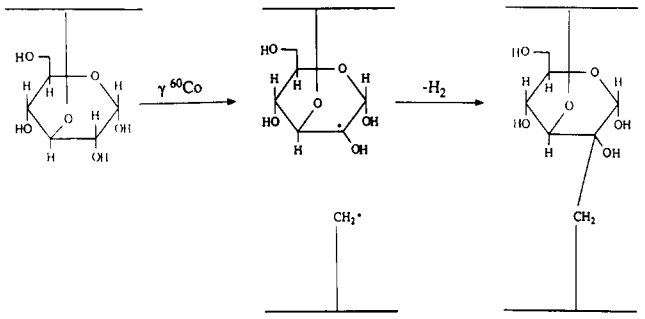
Table VIII
(Methoxyethoxy)ethoxy Cosubstituent Polyphosphazene Characterization Data

protected polymer		elem anal.[a] % C	% H	% N	% Cl	^{31}P NMR[b]	M_w[c]	T_g, °C
protected polymer								
39	calcd	45.17	6.85	3.39	0	−8.1	1.5×10^6	2
	found	45.51	6.57	3.77	0.33			
40	calcd	47.56	6.80	3.16	0	−9.0	2.1×10^6	39
	found	47.47	6.67	3.33	0.34			
deprotected polymer[d]								
41	calcd	37.01	6.28	4.00	0	−8.3	2.6×10^5	31
	found	37.48	6.57	3.96	0.03			
42	calcd	36.54	5.98	3.80	0	−8.5	9.5×10^5	58
	found	36.90	6.67	4.05	0.03			

^{1}H NMR: polymers **39**, **40**, 1.2 (3 H, s), 1.3 (3 H, s), 1.4 (3 H, s), 1.5 (3 H, s), 3.0–4.8 (17 H, m), 5.9 (1 H, d) ppm
polymers **41**, **42**, 3.1–4.8 (22 H, m) ppm
Infrared analysis: polymers **39**, **40**, P=N/P–O, 1220 cm^{-1}; *gem*-CH_3, 1385 cm^{-1}; C–O, 1070 cm^{-1}
polymers **41**, **42**, O–H, 3250 cm^{-1}; P=N/P–O, 1210 cm^{-1}; C–O, 1080 cm^{-1}

[a] Obtained by Galbraith Laboratories, Knoxville, TN. [b] 85% H_3PO_4 internal standard. [c] Calibrated with known molecular weight polystyrene standards. [d] The molecular weights of the deprotected polymers were estimated by GPC calibrated with known molecular weight poly(ethylene oxide) standards.

Scheme III



It should be noted that, in spite of the unreactivity of the last 25% of the P–Cl bonds to replacement by phenoxy or diacetone D-glucosyl units, replacement of the remaining chlorine was possible by treatment of the 50% (diacetone D-glucosyl)/50% phenoxy polymers with methylamine (see Experimental Section). By ^{1}H NMR spectroscopy, it was found that ca. 25% of the side groups were methylamino units. This trisubstituent polymer (**37**) was deprotected by treatment with 90% trifluoroacetic acid without detectable cleavage of the skeleton. The purified polymer was a colorless glass-forming material (**38**) (see Table VII).

Synthesis and Characterization of α-D-Glucosyl/(Methoxyethoxy)ethoxy Polyphosphazenes. Poly(dichlorophosphazene) (**3**) was allowed to react with sodium (methoxyethoxy)ethoxide, followed by treatment with sodium diacetone D-glucoside (Scheme II). Two side-group ratios were investigated—40:60 (diacetone D-glucosyl):(methoxyethoxy)ethoxide (**39**) and a 60:40 ratio (**40**) of the two substituents. All the chlorine atoms were replaced. The first of these polymers was a beige elastomer. The second was a brown glass, and the characterization data are given in Table VIII.

Deprotection was accomplished with 90% trifluoroacetic acid, and the reaction mixture was neutralized with base. Both polymers (**41**, **42**) were soluble in water and could be purified by dialysis. The polymer with 40% α-D-glucosyl units was a brown, leathery material, while the product with 60% of the sugar residues was a brown glass. Characterization data for the deprotected species are shown in Table VIII.

Solubility of the Polymers. Solubility in water or surface hydrophilicity (see later) were properties of particular interest in the design of these polymers. However, in addition to solubility in water, the solubility in other solvents such as hexane, dimethyl sulfoxide (DMSO), dimethylformamide (DMF), tetrahydrofuran (THF), acetone, diglyme, toluene, or ethanol was of interest.

The 10% (diacetone D-glucosyl)/90% methylamino substituted polymer was soluble in water, but the other polymers in this series were not. However, all were soluble in DMSO, THF, acetone, diglyme, and DMF. All the α-D-glucosyl/methylamino polymers were soluble in water and in DMSO. In this series, the solubility in DMF and diglyme decreased as the ratio of glucosyl to methylamino groups increased. All polymers in this series were partially soluble in ethanol.

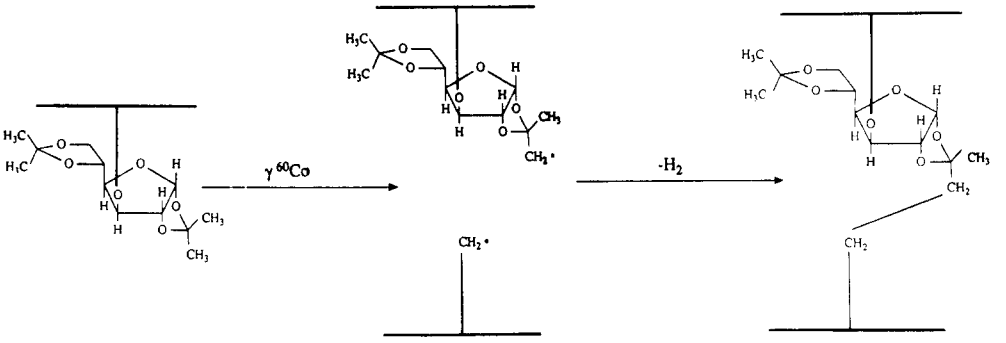
None of the (diacetone D-glucosyl)/trifluoroethoxy phosphazene polymers were soluble in water, but all were soluble in DMF, THF, acetone, and diglyme. Those polymers with a trifluoroethoxy content of 50% or less were also soluble in DMSO and toluene. After deprotection of the glucosyl groups, polymers with 50% or less trifluoroethoxy side groups became soluble in water and retained their solubility in DMSO and ethanol, but lost their solubility in THF, DMF, toluene, and acetone. Those polymers that contained 90% and 75% of the side groups as trifluoroethoxy units retained their solubility in THF and acetone, but lost solubility in DMF and diglyme.

The (diacetone D-glucosyl)/phenoxy phosphazene polymers were insoluble in water but were soluble in DMF, THF, acetone, and toluene. Solubility in diglyme increased with increasing diacetone D-glucosyl content. After deprotection, the polymers with 90% and 75% phenoxy side groups were still insoluble in water but retained their solubility in THF, DMF, acetone, and toluene. The α-D-glucosyl/phenoxy/methylamino phosphazene polymer discussed earlier was partially soluble in water and in THF but was soluble in DMSO.

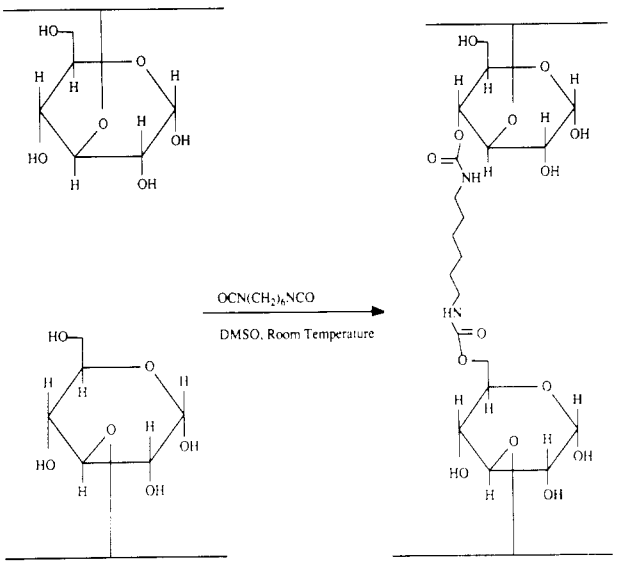
The two (diacetone D-glucosyl)/(methoxyethoxy)-ethoxy phosphazene polymers were partially soluble in water but were soluble in THF, DMF, acetone, and DMSO. The deprotected polymers were completely soluble in water, DMSO, and ethanol. Deprotection reduced the solubility in THF, acetone, and DMF.

Film-Forming Properties and Surface Characterization. Thin films (0.02 mm) of all the polymers were solvent cast on glass plates. The film-forming properties depended critically on the ratios of the two cosubstituents. For example, in the methylamino cosubstituent series, a high loading of methylamino groups generated

Scheme IV



Scheme V



film-forming properties, whereas a high loading of diacetone D-glucosyl or α-D-glucosyl units imparted glassy properties. In the trifluoroethoxy cosubstituent series also, the polymers with the highest trifluoroethoxy group content (90% and 75%) were flexible, film-forming materials with excellent membrane-forming characteristics. However, those with 50% trifluoroethoxy and 50% diacetone D-glucosyl or α-D-glucosyl were inflexible materials. Species with higher concentrations of the protected or deprotected sugar units were glasses. The same pattern was repeated in the (diacetone D-glucosyl)/phenoxy series. Polymers with a high loading of phenoxy groups formed good, flexible films, whereas those with high concentrations of the protected sugar units were brittle. Finally, in the (methoxyethoxy)ethoxy series, those species with 60% of the alkyl ether side group were flexible and elastomeric polymers that formed excellent membrane-type films. Those polymers with only 40% of the same cosubstituent group were glasses. We speculate that the presence of high concentrations of diacetone D-glucosyl or α-D-glucosyl side groups reduces the material's flexibility by steric hindrance and/or by hydrogen bonding.

The behavior of the films of the polymers to immersion in buffered water at pH 7.4 at room temperature for 5 months was also studied. Films from polymers in which 90% or 75% of the side groups were trifluoroethoxy or phenoxy units retained their flexibility and integrity throughout the experiments. The (diacetone D-glucosyl)/(methoxyethoxy)ethoxy (40:60 ratio) polymer dissolved slowly after 2 weeks, and the α-D-glucosyl analogues after 3 days. Additional data are presented in Table IX.

Surface contact angles to deionized water were measured for a number of the best film-forming materials, and the results are summarized in Table X. The values measured for these new polymers should be compared with those of the single-substituent polymers, $[NP(OCH_2CF_3)_2]_n$ and $[NP(OPh)_2]_n$ (100°) and $[NP(NHCH_3)_2]_n$ (39°). Three observations are of special interest. First, the incorporation of even low concentrations of diacetone D-glucosyl or α-D-glucosyl side groups into polymers that contained trifluoroethoxy or phenoxy cosubstituent groups lowered the contact angle significantly (in other words, raised the hydrophilicity). Moreover, it was apparent that no significant difference was brought about by the deprotection of the sugar residues. Second, the diacetone D-glucosyl units raised the contact angle of the methylamino cosubstituent polymer (9:1 ratio). Finally, the lowest contact angle found for any of the polymers was for the (methoxyethoxy)ethoxy cosubstituent species. Presumably this reflects the profound tendency of these side groups to hydrogen bond to water.

Cross-Linking Reactions: Radiation and Chemical Methods. γ-Irradiation has been shown in our previous work to provide a clean and efficient method for cross-linking a variety of solid poly(organophosphazenes).[7-9] The method works best if the polymer can be fabricated into a coherent film or fiber before irradiation. However, as discussed earlier, those polymers that contained high loadings of protected or deprotected sugar groups tended to generate brittle films or fibers. These polymers were, therefore, cross-linked in solution by chemical methods.

All the polymers synthesized in this work were exposed to 5 Mrad of ^{60}Co γ-radiation. It was known from earlier work that this radiation dose brings about cross-linking of polyphosphazenes that bear the (methoxyethoxy)ethoxy side group or methylamino units but does not induce cross-linking of phenoxy or trifluoroethoxy side groups.[7,8] Poly[bis(sol ketoxy)phosphazene] can be cross-linked with lower doses (2 Mrad) of γ-radiation.[9]

Strong evidence was obtained that the polymers synthesized in this work undergo radiation cross-linking through the diacetone D-glucosyl or α-D-glucosyl sites (Schemes III and IV). In the latter case, the cross-link sites are probably the C–H units on the pyran rings or the C–H groups on C-6. This assumption is supported by the work Stannett and co-workers,[10,11] who where able to radiation graft cellulose to vinyl monomers.

The experimental observations are as follows: All the polymers that contained methylamino cosubstituent groups underwent cross-linking. Within the diacetone D-glucosyl series, the behavior toward the potential solvents after cross-linking varied with ratios of the two cosubstituent groups. For example, the polymer with 10% diacetone D-glucosyl and 90% methylamino side groups swelled in water but swelled only slightly in organic solvents. A polymer with 25% diacetone D-glucosyl and 75% methylamino side groups swelled slightly in water and more so in organic solvents. Higher loadings of diacetone D-glu-

Table IX
Polymer Composition, Film Properties, and Water Solubility

compd	composition: % hydrophilic	composition: % hydrophobic	water solubility[a]	film properties
10	90% methylamino	10% diacetone D-glucosyl	+	brittle
11	75% methylamino	25% diacetone D-glucosyl	†	brittle
12	50% methylamino	50% diacetone D-glucosyl	–	glass
13	32% methylamino	68% diacetone D-glucosyl	–	glass
14	21% methylamino	79% diacetone D-glucosyl	–	glass
15	90% methylamino 10% α-D-glucosyl		+	glass
16	75% methylamino 25% α-D-glucosyl		+	glass
17	50% methylamino 50% α-D-glucosyl		+	glass
18	32% methylamino 68% α-D-glucosyl		+	glass
19	21% methylamino 79% α-D-glucosyl		+	glass
20		90% trifluoroethoxy 10% diacetone D-glucosyl	–	elastomeric
21		75% trifluoroethoxy 25% diacetone D-glucosyl	–	elastomeric
22		50% trifluoroethoxy 50% diacetone D-glucosyl	–	brittle
23		32% trifluoroethoxy 68% diacetone D-glucosyl	–	glass
24		21% trifluoroethoxy 79% diacetone D-glucosyl	–	glass
25	10% α-D-glucosyl	90% trifluoroethoxy	–	elastomeric
26	25% α-D-glucosyl	75% trifluoroethoxy	–	brittle
27	50% α-D-glucosyl	50% trifluoroethoxy	+	glass
28	68% α-D-glucosyl	32% trifluoroethoxy	+	glass
29	79% α-D-glucosyl	21% trifluoroethoxy	+	glass
30[b]		90% phenoxy 10% diacetone D-glucosyl	–	elastomeric
31[b]		75% phenoxy 25% diacetone D-glucosyl	–	elastomeric
32[b]		50% phenoxy 50% diacetone D-glucosyl	–	glass
33[b]		25% phenoxy 75% diacetone D-glucosyl	–	glass
34[b]		10% phenoxy 90% diacetone D-glucosyl	–	glass
35[b]	10% α-D-glucosyl	90% phenoxy	–	elastomeric
36[b]	25% α-D-glucosyl	75% phenoxy	–	brittle
37	25% methylamino	36% diacetone D-glucosyl 39% phenoxy	–	glass
38	25% methylamino 36% α-D-glucosyl	39% phenoxy	†	glass
39	60% (methoxyethoxy)ethoxy	40% diacetate D-glucosyl	†	elastomeric
40	40% (methoxyethoxy)ethoxy	60% diacetone D-glucosyl	†	brittle
41	60% (methoxyethoxy)ethoxy 40% α-D-glucosyl		+	brittle
42	40% (methoxyethoxy)ethoxy 60% α-D-glucosyl		+	glass

[a] Symbols: +, water soluble; –, water insoluble, †, partially water soluble. [b] Polymer possesses residual phosphorus–chlorine bonds.

Table X
Surface Contact Angles to Water of Selected Polyphosphazene Films

polymer composition	contact angle,[a] deg
$[NP(OCH_2CF_3)_{1.8}(OC_{12}H_{19}O_5)_{0.2}]_n$ (**20**)	86 (68)
$[NP(OC_6H_5)_{1.8}(OC_{12}H_{19}O_5)_{0.2}]_n$ (**30**)[b]	78 (64)
$[NP(NHCH_3)_{1.8}(OC_{12}H_{19}O_5)_{0.2}]_n$ (**10**)[c,d]	53 (34)
$[NP(OCH_2CF_3)_{1.8}(OC_6H_{11}O_5)_{0.2}]_n$ (**25**)	84 (64)
$[NP(OCH_2CH_2OCH_2CH_2OCH_3)_{1.2}(OC_{12}H_{19}O_5)_{0.8}]_n$ (**39**)[d]	43 (31)

[a] Measurement listed first was taken within 10–20 s of drop application; measurement in parentheses was taken after 5 min. [b] The polymer possessed residual phosphorus–chlorine bonds. [c] The polymer was glassy. [d] The surface of the film began to dissolve after 5 min of drop application.

cosyl groups yielded materials that did not swell in water but did swell in THF. In the α-D-glucosyl/methylamino series, all polymers swelled in water to form hydrogels but were unaffected by organic solvents.

Radiation cross-linking also occurred with those polymers that contained trifluoroethoxy cosubstituent groups. On the basis of previous studies, it seemed clear that the protected or deprotected sugar residues were the only cross-link sites available. Within the diacetone D-glucosyl series, radiation cross-linking generated materials that were insoluble and unswelled in water but that swelled in organic media without dissolving. In the α-D-glucosyl series, polymers with 10% or 25% α-D-glucosyl groups and 90% or 75% trifluoroethoxy were unaffected by water but swelled, without dissolving, in organic media. As the α-D-glucosyl content increased beyond this point, the irradiated polymers swelled in water to form hydrogels but became insoluble in organic media and did not swell. Those polymers that contained diacetone D-glucosyl and phe-

noxy cosubstituent groups behaved, after irradiation, in a similar manner to the polymers with trifluoroethoxy side groups.

Radiation cross-linking occurred readily with all the polymers that contained (methoxyethoxy)ethoxy cosubstituent groups. This side group is known to provide high concentrations of cross-link sites.[7] The irradiated polymers with diacetone D-glucosyl cosubstituent groups swelled slightly in water and swelled extensively in organic solvents, such as THF, acetone, and ethanol. Deprotection to yield α-D-glucosyl groups markedly increased the propensity for swelling in water to generate hydrogels but decreased the ability of the polymers to absorb organic solvents.

Chemical cross-linking was also investigated for the α-D-glucosyl polymers, via reactions of the pendent hydroxyl groups with hexamethylene diisocyanate (Scheme V). Those α-D-glucosyl polymers that contained 50%, 68%, and 79% sugar residues plus methylamino or trifluoroethoxy cosubstituent groups were studied. Treatment of these polymers in DMSO with the diisocyanate resulted in cross-linking and gelation in all cases (Scheme V). The degree to which these polymers swelled in water to form hydrogels depended on the ratio of diisocyanate to pendant hydroxyl groups in the system: a stoichiometric deficiency of diisocyanate yielded hydrogels with swelling ratios of more than 3. Larger amounts of diisocyanate reduced the ability of the system to imbibe water. No detectable decomposition of the hydrogels occurred during 5 months in contact with an aqueous buffer solution at pH 7.4 at 25 °C.

Hydrolytic Behavior of Un-Cross-Linked α-D-Glucosyl Polyphosphazenes. In earlier work we showed that poly(diglycerylphosphazene) and several amino acid ester polyphosphazenes are hydrolytically unstable and are excellent candidates for us as erodible biomaterials.[9,12-14] In the present study, we have carried out a preliminary examination of the hydrolysis behavior of the α-D-glucosyl/methylamino cosubstituent polyphosphazenes. At 100 °C, in aqueous buffer solutions (pH 6, 7, and 8), the polymers decomposed during 24–96 h. The decomposition was monitored by ^{31}P NMR spectroscopy in which the growth of a peak at 0 ppm indicated the formation of phosphate. At human body temperature (37 °C) and pH 7.4, the hydrolysis is much slower, with half-lives in the range 165–175 h being estimated. Further work on this aspect is needed, but we presume on the basis of earlier studies[12,15] that the hydrolysis products are phosphate, glucose, ammonia, and methylamine. This last product may be biomedically unacceptable; hence future studies may require the use of biologically acceptable cosubstituents such as amino acid ester[12] or ethoxy units.[3]

The biomedical applications of α-D-glucosyl polyphosphazenes are of considerable interest. Pharmaceutical agents or peptides could be linked to the polymers or to a hydrogel through the hydroxyl groups of the glucosyl units. In vivo hydrolysis would release the glucose-bound bioactive agents. Variations in the cosubstituent ratios would allow a sustained release of the bioactive agent over a controlled period of time. Thus, these polymers provide an alternate approach to existing polymers for use in controlled-release technology, biomaterials, and membrane research.[16,17]

Experimental Section

Reagents and Equipment. All reactions were carried out under an atmosphere of dry nitrogen (Liquid Carbonic) using standard Schlenk line techniques. Tetrahydrofuran (THF) (Omnisolv) was distilled from sodium–benzophenone ketal under a dry nitrogen atmosphere. 2,2,2-Trifluoroethanol (Aldrich) and 2-(2-methoxyethoxy)ethanol (Aldrich) were distilled and stored over 4-Å molecule sieves. Phenol (Aldrich) was dried by azeotroping from freshly distilled toluene immediately before use. Diacetone D-glucose (Sigma, Lancaster synthesis) was recrystallized from hot hexane/methylene chloride 3 times and then dried under vacuum. Trifluoroacetic acid (Aldrich), sodium metal (Aldrich), methylamine (Matheson), and hexamethylene diisocyanate (Aldrich) were used as received. Dimethyl sulfoxide (Fisher) was distilled from calcium hydride and stored over 3-Å molecular sieves. Hexachlorocyclotriphosphazene (Ethyl Corp.) was obtained from a trimer–tetramer mixture by two sublimations (30 °C/0.2 mmHg) and one recrystallization from hot hexane. Poly(dichlorophosphazene) was prepared by a published procedure.[18] All ^{31}P NMR (36.23 MHz) spectra were obtained with a JEOL FX-90Q spectrometer. Chemical shifts are reported in ppm relative to 85% H_3PO_4 at 0 ppm. High-field ^1H NMR spectra were obtained with a Bruker 200-MHz and a Bruker 360-MHz spectrometer. Glass transition temperatures were obtained with a Perkin-Elmer DSC 7 and TAS-7 software. A Perkin-Elmer Model 1710 Fourier transform spectrometer was used to obtain all infrared spectra. Molecular weights of the water-insoluble polymers were estimated by gel permeation chromatography with use of a Hewlett-Packard 1090 liquid chromatography unit, using a polystyrene stationary phase. Polystyrene standards of known molecular weight were used to calibrate the columns. Sample concentrations were ca. 1.5% (w/v) in THF. The molecular weights of the water-soluble polymers were estimated by gel permeation chromatography using a Waters 150-C ALC/GPC with Waters Ultrahydrogel 2000 and Ultrahydrogel 120 columns. Poly(ethylene oxide) standards of known molecular weight were used to calibrate the columns. Sample concentrations were ca. 0.15% (w/v) in deionized/distilled water. Elemental analyses were obtained by Galbraith Laboratories (Knoxville, TN).

Synthesis of $[NP(NHCH_3)_x(OC_{12}H_{19}O_5)_y]_n$ (10–14). These reactions were carried out in a similar manner. The procedure for the synthesis of polymer **12** is given as a typical example. A solution of diacetone D-glucose (22.36 g, 0.086 mol) in THF (100 mL) was allowed to react with sodium metal (2.024 g, 0.088 mol) in dry THF (100 mL) under nitrogen to prepare the sodium salt. The salt solution was then added to a solution of poly(dichlorophosphazene) (**3**) (10.0 g, 0.086 mol) in THF (500 mL) via an addition funnel under nitrogen. The reaction proceeded for 96 h at reflux. An excess of methylamine (100 mL, 2.3 mol) was condensed (−78 °C, dry ice/acetone) into THF. The cooled polymer solution was then added to the solution of the amine. Stirring was maintained for 8.5 h. The solution was then concentrated and precipitated into hexane (3×) and deionized water (3×). Polymer **10** was precipitated into hexane (2×), dissolved in deionized water, and dialyzed with cellulose tubing (12 000–14 000 molecular weight cutoff) against deionized water (72 h) and methanol (48 h).

Deprotection of $[NP(NHCH_3)_x(OC_{12}H_{19}O_5)_y]_n$ (10–14). All deprotections were carried out in a similar manner. The following procedure is for polymer **12**. Polymer **12** (1.0 g) was dissolved in 90% (v/v) trifluoroacetic acid (10 mL) and was allowed to react for 4.5 h. The ^{31}P NMR spectrum was monitored throughout the reaction to check for reaction completion and the survival of the polymer chain. The mixture was neutralized with aqueous sodium bicarbonate solution (125 mL) and was dialyzed for 72 h in cellulose tubing (12 000–14 000 molecular weight cutoff) against deionized water and against methanol (48 h). Polymer **17** was isolated by removal of the solvent under reduced pressure.

Synthesis of $[NP(OCH_2CF_3)_x(OC_{12}H_{19}O_5)_y]_n$ (20–24). The following typical procedure is for the synthesis of polymer **22**. A solution of trifluoroethanol (8 mL, 0.103 mol) in THF (25 mL) was allowed to react with sodium (1.98 g, 0.086 mol) in dry THF (100 mL). This nucleophile was added to a solution of poly(dichlorophosphazene) (**3**) (10.0 g, 0.086 mol) in THF (500 mL) via an addition funnel. The reaction was allowed to proceed for 24 h. A solution of diacetone D-glucose (53.7 g, 0.206 mol) in THF (100 mL) was allowed to react with sodium metal (3.956 g, 0.172 mol) in THF (150 mL). After the salt had formed, the second nucleophile was added to the partially substituted polymer via an addition funnel. The reaction mixture was maintained at reflux for 72 h. The product solution was concentrated and then

isolated and purified through precipitation into water (3×) and hexane (2×) from THF.

Deprotection of $[NP(OCH_2CF_3)_x(OC_{12}H_{19}O_5)_y]_n$ (20–24). All these reactions were carried out in a similar manner. The deprotection of polymer **22** is given as an example. Polymer **22** (1.0 g) was dissolved in 10.0 mL of 90% (v/v) trifluoroacetic acid and was allowed to react for 4.75 h. The ^{31}P NMR was followed to monitor reaction completion and the onset of chain decomposition. The acidic solution was neutralized with 125 mL of aqueous sodium bicarbonate solution and was dialyzed in cellulose tubing (12 000–14 000 molecular weight cutoff) against deionized water (72 h) and methanol (48 h). Polymer **27** was isolated by removal of the solvent under reduced pressure.

Synthesis of $[NP(OC_6H_5)_x(OC_{12}H_{19}O_5)_y]_n$ (30–34). All the syntheses in this series followed a similar procedure. The procedure for polymer **32** is given as an example. A solution of diacetone D-glucose (23.36 g, 0.086 mol) in THF (75 mL) was allowed to react with sodium (2.024 g, 0.088 mol) in dry THF (75 mL). This nucleophile was then added to a solution of poly(dichlorophosphazene) (**3**) (10.0 g, 0.086 mol) in dry THF (500 mL) via an addition funnel. This reaction was maintained at reflux for 72 h. A solution of phenol (19.4 g, 0.206 mol) in THF (100 mL) was added dropwise to sodium (3.96 g, 0.172 mol) suspended in THF (150 mL). The sodium phenoxide solution was added dropwise to the partially substituted polymer solution over a period of 0.5 h. One mole percent of *n*-butylammonium bromide was added to facilitate the substitution process. The reaction mixture was heated at reflux for 72–96 h. The solution was concentrated and was purified by precipitation into deionized water (3×), ethanol (2×), and hexane (2×).

Deprotection of $[NP(OC_6H_5)_x(OC_{12}H_{19}O_5)_y]_n$ (30–34). The following procedure for the deprotection of polymer **30** is typical. This polymer (1.0 g) was dissolved in 90% (v/v) trifluoroacetic acid (10.0 mL). The reaction was monitored by ^{31}P NMR and was terminated after 5.75 h. The acidic polymer solution was then neutralized with 125 mL of aqueous sodium bicarbonate solution. The polymer precipitated immediately. The polymer was dissolved in THF and precipitated into hexane (2×) and deionized water (2×) to yield species **35**.

Synthesis of $[NP(OC_6H_5)_x(OC_{12}H_{19}O_5)_y(NHCH_3)_z]_n$ (37). A solution of diacetone D-glucose (2.6 g, 0.01 mol) in THF (25 mL) was allowed to react with sodium (0.198 g, 0.0086 mol) in dry THF (25 mL). The nucleophile was then added to a solution of poly(dichlorophosphazene) (**3**) (1.0 g, 0.0086 mol) in THF (100 mL). The nucleophile was allowed to react for 72 h at reflux. Phenol (3.4 g, 0.036 mol) was allowed to react with sodium (0.69 g, 0.0301 mol) in THF (100 mL). After the addition of the second nucleophile, the reaction was refluxed was 120 h. The reaction mixture was then cooled to room temperature. Methylamine (100 mL, 2.3 mol) was condensed (−78 °C, dry ice/acetone) into THF (300 mL). The reaction mixture was then transferred to the condensed amine solution. This reaction proceeded for 8 h. The reaction solution was concentrated and precipitated into hexane to yield a white powder. The product was further purified by successive precipitations into hexane (3×) and deionized water (3×).

Deprotection of $[NP(OC_6H_5)_x(OC_{12}H_{19}O_5)_y(NHCH_3)_z]_n$ (37). Polymer **37** (1.0 g) was dissolved in trifluoroacetic acid (10 mL at 90% (v/v)). The reaction was monitored by ^{31}P NMR to ensure that no backbone cleavage occurred and was terminated after 7.5 h. The acidic reaction mixture was neutralized with aqueous sodium bicarbonate solution (125 mL). The polymer precipitated during neutralization. The polymer was purified by precipitated into hexane (1×) and deionized water (2×) from THF.

Synthesis of $[NP(OCH_2CH_2OCH_2CH_2OCH_3)_x(OC_{12}H_{19}O_5)_y]_n$ (39, 40). The following procedure for polymer **39** is typical. (Methoxyethoxy)ethanol (3.5 mL, 0.026 mol) was allowed to react with sodium (0.67 g, 0.029 mol) in dry THF (75 mL). The nucleophile was then added to a solution of poly(dichlorophosphazene) (**3**) (3.0 g, 0.026 mol) in THF (150 mL). The nucleophile was allowed to react with the polymer for 72 h in warm (35 °C) THF. A solution of diacetone D-glucose (20.2 g, 0.078 mol) in THF (50 mL) reacted with sodium (1.84 g, 0.080 mol) in THF (50 mL). After the addition of the second nucleophile, the reaction mixture was refluxed for 96 h. The solution was concentrated and purifid by precipitation into hexane (3×) and into deionized water (3×) to give polymer **39**.

Deprotection of $[NP(OCH_2CH_2OCH_2CH_2OCH_3)_x(OC_{12}H_{19}O_5)_y]_n$ (39, 40). The following procedure for the deprotection of polymer **39** is typical. Polymer **39** (1.0 g) was dissolved in trifluoroacetic acid (10.0 mL at 90% (v/v)). The ^{31}P NMR spectrum was monitored during the course of the reaction. After 6.5 h, no chain decomposition was detected by ^{31}P NMR spectroscopy. The acidic polymer solution was neutralized with aqueous sodium bicarbonate solution (125 mL). The polymer remained soluble in aqueous solution during neutralization. The neutral solution was dialyzed in celllulose tubing (12 000–14 000 molceular weight cutoff) against deionized water (72 h) and methanol (48 h). Removal of the dialysate gave purified polymer **41**.

Preparation of Films. Organic-soluble polymers were dissolved in a mixture of THF, dioxane, and toluene (4:1:1, respectively). Water-soluble polymers were dissolved in a mixture of water, DMSO, and acetone (4:1:0.5). The solutions were filtered and then cast, in a dust-free drybox, on clean glass plates. The plates were loosely covered to ensure slow solvent evaporation. After 144 h, the films were removed from the drybox and placed in a vacuum oven at 60 °C for 48 h. Films were then removed from the glass plates and stored in hexane, in which they were insoluble.

Cross-Linking Reactions: Radiation Induced. Each polymer synthesized (0.4 g) was exposed to 5.0 Mrad (0.2 Mrad/h) of ^{60}Co γ-radiation at the Brazeale Nuclear Reactor at The Pennsylvania State University. Each sample was placed in a vial, dried under vacuum for 72 h, and then placed in an evacuated container before irradiation.

Cross-Linking Reactions: Chemical. The reactions involved the 50%, 32%, and 21% methylamino/glucosyl and trifluoroethoxy/glucosyl polymers. Each polymer (0.5 g) was dissolved in DMSO (2 mL). After the polymer had dissolved completely, 0.2–0.4 mL (2.4×10^{-3}–4.8×10^{-3} moles) of hexamethylene diisocyanate was added to the polymer solutions. The mixture usually became completely immobile within 3–8 h. The products were then dialyzed against deionized water for 96 h and dried under vacuum for 24 h. The samples were weighed and then immersed in deionized water. After 24 h of immersion, the weight of polymer and imbibed water was measured.

Contact Angle Measurements. All contact angle measurements were carried out on a Rame-Hart Model 100 contact angle goniometer equipped with an environmental chamber. The chamber was maintained at 100% relative humidity and at 20–25 °C during the measurements. Contact angles were determined after 10–20 s and after 5 min following the application of 1 mL of distilled, deionized water. Each reported value is an average of ten measurements taken at different portions of the film.

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