Synthesis of Models of Teichoic Acids by Ring-Opening Polymerization

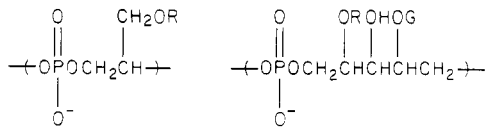
Paweł Kłosiński and Stanisław Penczek*

Center of Molecular and Macromolecular Studies, Polish Academy of Sciences, 90-362 Łódź, Poland. *Received February 16, 1982*

ABSTRACT: Models of simple teichoic acids were prepared by using a ring-opening polymerization. Thus a cyclic phosphite, 4-(acetoxymethyl)-2-oxo-1,3,2λ⁵-dioxaphospholane, was ionically polymerized under anhydrous conditions, giving the corresponding high molecular weight polyphosphite. The polyphosphite was directly oxidized, preferably with N_2O_4, to the corresponding poly(dialkyl phosphate) ($\bar{M}_n$ up to 10 000), having the structure of a simple model of a teichoic acid: poly[4-(acetoxymethyl)-2-hydroxy-2-oxo-1,3,2-dioxaphospholane] [poly(1-acetyl-2,3-glycerol phosphate)]. An alternative method, in which 4-(acetoxymethyl)-2-methoxy-2-oxo-1,3,2-dioxaphospholane was first polymerized to the corresponding polyester and then dealkylated to the polyacid, gave less promising results because of the incompleteness of the dealkylation step.

Introduction

Teichoic acids are polyesters of phosphoric acid. There is a large variety of these polymers, but their common feature is a phosphoryl unit in the backbone. Differences are due to the structure of the glycol constituent. Glycerol and ribitol derivatives are the most common ones existing in nature:[1]



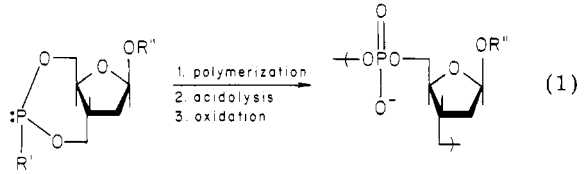
R = Ala or Ac, G = sugar

Teichoic acids are major components of cell walls, particularly in some bacteria, and are responsible for a number of biological functions, including flux of ions through the membranes.[2]

Stepwise chemical syntheses of teichoic acids have been described by Michelson[3] and Baddiley.[4] In both cases only relatively low molecular weight products were obtained ($(\bar{D}\bar{P})_n$ = 11 and $(\bar{D}\bar{P})_n$ = 5.6, respectively). Nevertheless, the product prepared by Michelson did have some immunological properties similar to the natural product extracted from a bacterial source (e.g., positive reaction with antibodies).[5] More recently, Vogt reported on the Mainz's group attempts directed toward preparation of poly(glycerol phosphate) by ring-opening polymerization of bicyclic glycerol phosphite.[6]

We first briefly described the preparation of models of teichoic acids at the IUPAC microsymposia in 1978[7] and then in 1979[8] as a part of our general program of synthesis of models of biopolymers by ring-opening polymerization. In the preparation of models of teichoic acids we use polymerization of cyclic monomers containing the required sequence of elements of the chain squeezed into the corresponding rings.

We have previously used the same approach in modeling nucleic acid backbones:[9]

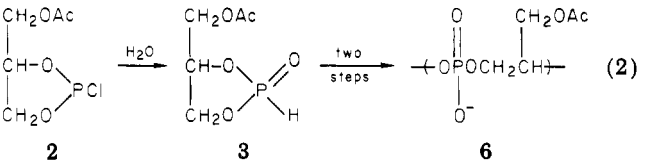


(1)

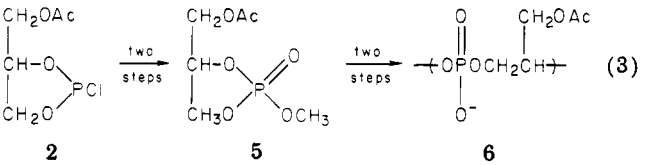
R′ = $(C_2H_5)_2N$

Results and Discussion

Two different ways of synthesis will be described in this paper, both leading to the simplest model of teichoic acid, namely, the "phosphite route" (eq 2) and the "ester route" (eq 3):



(2)



(3)

Synthesis of Monomers. 4-(Acetoxymethyl)-2-chloro-1,3,2-dioxaphospholane (**2**) was prepared by cyclization of glycerol acetate (**1**) (mostly a mixture of α and β monomers, which we did not attempt to separate) in reaction with PCl_3 and contained as major impurities 20–30 wt % of chlorodiacetoxypropanes and 5–10% of 5-acetoxy-2-chloro-1,3,2-dioxaphosphorinane.

4-(Acetoxymethyl)-2-oxo-1,3,2λ⁵-dioxaphospholane (mixture of cis and trans isomers) (**3**) was prepared by hydrolysis of **2** with less than the stoichiometric amount of H_2O, according to Nifant'ev.[10] Water used in excess caused a premature spontaneous polymerization of **3**; the use of amines to trap HCl in the cyclization step had the same effect. Spontaneous polymerization of 2-oxo-1,3,2λ⁵-dioxaphospholanes, which could not be stopped by using various inhibitors, is a known phenomenon.[11] We recently observed that stable monomeric compounds are easily obtained, provided that the described above requirements are met.

According to the $^{31}P\{^1H\}$ NMR spectrum of **3**, it contains, after several distillations, a few percent of two impurities, namely *cis*- and *trans*-5-acetoxy-2-oxo-1,3,2λ⁵-dioxaphosphorinanes (**3a** and **3b**), absorbing at −1.8 and 2.2 ppm (CH_2Cl_2). We determined the actual structures of **3a** and **3b** on the basis of $^1J_{PH}$ values. It is known that 1,3,2-dioxaphosphorinanes with axial oxygen have a larger $^1J_{PH}$ than when oxygen occupies an equatorial position.[12] Cis and trans isomers of **3** cannot be distinguished at the resolution of a 24.2-MHz apparatus. Both isomers are observed in ^1H NMR spectra on the basis of different

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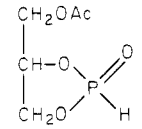
chemical shifts of H–P protons:

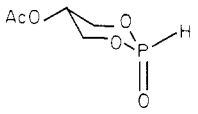


3

$^{31}P\{^1H\}$: δ 23.8 (both cis and trans)

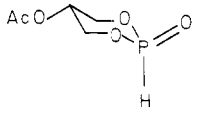
($^1J_{PH}$ = 727.5 Hz, $^1J_{PH}$ = 730.3 Hz)

^1H: δ 6.06 ($^1J_{PH}$ = 727 Hz)
δ 6.08 ($^1J_{PH}$ = 730 Hz)



3a

δ −1.8 ($^1J_{PH}$ = 726.6 Hz)

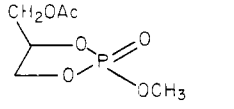


3b

δ 2.2 ($^1J_{PH}$ = 683.6 Hz)

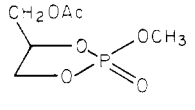
It is known that in 2-oxo-1,3,2λ⁵-dioxaphospholanes differences between $^1J_{PH}$ in both diastereoisomers are small; e.g., for 4-methyl-2-oxo-1,3,2λ⁵-dioxaphospholane Nifant'ev[10] observed ^{31}P NMR chemical shifts equal to δ 21.6 and 22.5 and $^1J_{PH}$ = 705 and 701 Hz, respectively. Usually, substitution in the ring causes an important decrease of differences between axial and equatorial $^1J_{PH}$.[12]

4-(Acetoxymethyl)-2-methoxy-2-oxo-1,3,2-dioxaphospholane (mixture of cis and trans isomers) (**5**) was prepared as shown in eq 3 from **2** through the intermediate 4-(acetoxymethyl)-2-methoxy-1,3,2-dioxaphospholane (**4**). The crucial step in these syntheses is separation of the isomeric structures due to the presence of derivatives of β-acetoxyglycerol, e.g., the undesirable six-membered isomeric dioxaphosphorinanes. This has been done at the stage of **4**, which was purified by spinning-band distillation. At the final stage of purification only two impurities were detected in **4**, namely, *cis*- and *trans*-5-acetoxy-2-methoxy-1,3,2-dioxaphosphorinanes in approximately 2% of **4**. Purity of **4** was determined on the basis of ^{31}P NMR spectra. Usually 95–98% **4** was used in the final step of oxidation, performed with N_2O_4 in 20% CH_2Cl_2 solutions. Final purification of thus-obtained **5**, after preliminary distillation, involved treatment with a Na mirror under vacuum. Again, as in the case of **3**, a mixture of cis and trans isomers was obtained, admixed with their six-membered isomers:



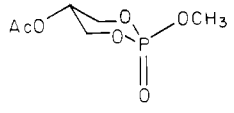
trans-**5**

$^{31}P\{^1H\}$: δ 16.8



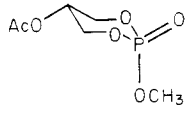
cis-**5**

δ 16.5



5a

δ −6.2



5b

δ −8.2 (lit.[13] δ −8.5)

Our assignments given for *cis*-**5** and *trans*-**5** are tentative and are based on the assumptions that the trans isomer of compounds like **4** predominates[14] and that oxidation of **4** proceeds with retention of the *P* configuration.[15]

Structures **3a,b** and **5a,b** are only postulated on the basis of the observed NMR spectra; none of these isomers have been isolated.

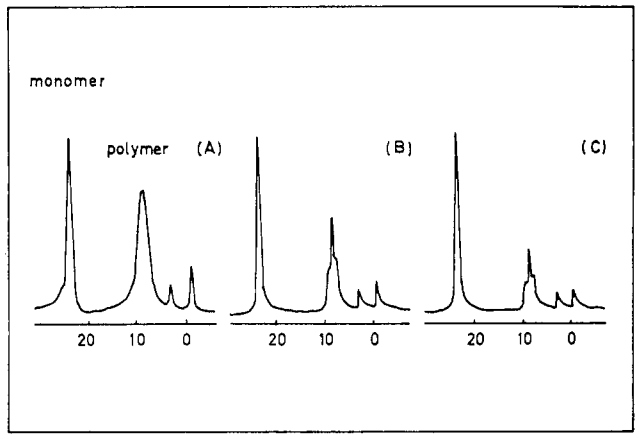


Figure 1. $^{31}P\{^1H\}$ NMR spectra of the polymerizing mixture of **3** at 40 (A), 80 (B), and 120 °C (C) in bulk; $[3]_0^{25}$ = 7.75 mol·L⁻¹, no initiator added. The two singlets at δ −0.8 and 3.0 correspond to six-membered isomers **3a** and **3b**, respectively.

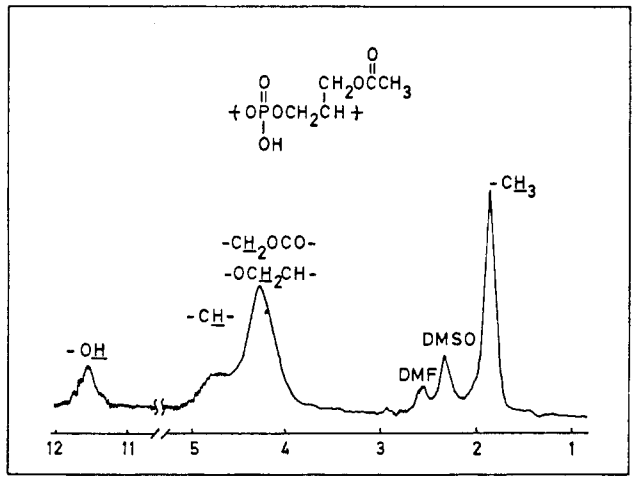
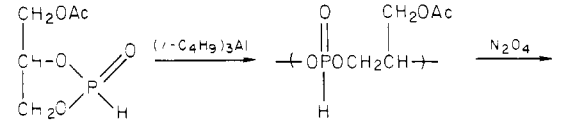


Figure 2. ^1H NMR spectrum of **6** in Me_2SO-d_6 (30% solution, 25 °C).

Polymerization and Conversion of Neutral Polymers into a Polyacid [Poly(dialkyl phosphate)]. Phosphite Route. Polymerization of **3** (mixture of cis and trans isomers) was conducted in CH_2Cl_2 solution; (i-$C_4H_9)_3Al$ was found to be the most versatile initiator. In a typical experiment **3** was dissolved in CH_2Cl_2 solvent (concentration 5.0 mol·L⁻¹) and polymerized with [(i-$C_4H_9)_3Al]_0$ = 0.5 mol·L⁻¹ at 25 °C for 3–6 h. After this time, 60% of **3** was converted into a polymer and the resulting mixture was directly oxidized. N_2O_4 was used as the oxidizing agent in the same way as described by us previously for poly(1,3-propylene phosphite).[16]

Thus this sequence of reactions is

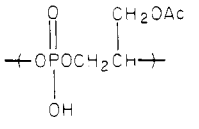


3

$^{31}P\{^1H\}$: δ 23.8

poly-**3**

δ 8.7



6

δ −2.3

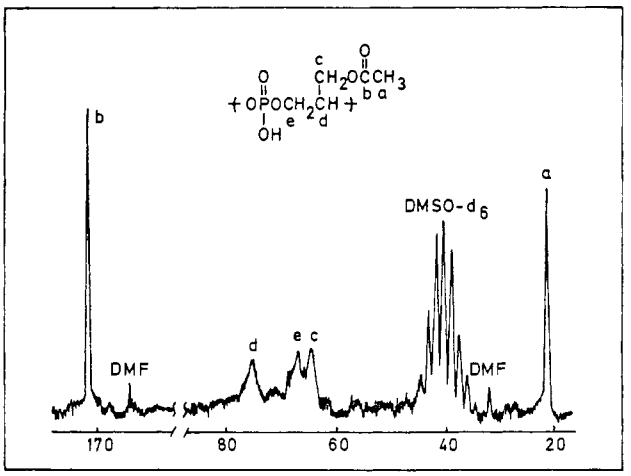


Figure 3. $^{13}C\{^1H\}$ NMR spectrum of **6** in Me_2SO-d_6 (30% solution, 25 °C).

A typical $^{31}P\{^1H\}$ NMR spectrum of the polymerizing mixture of **3** and poly-**3** is shown in Figure 1 for three different temperatures. In the $^{31}P\{^1H\}$ NMR spectra the proportions of monomer and polymer changing with temperature are clearly seen. The concentrations of impurities **3a** and **3b** (usually 5–10 mol %) did not change during polymerization, indicating that the six-membered monomers are much less reactive at the chosen polymerization conditions. In the purified polymer there are no signals that could be assigned to units derived from **3a** and **3b**. Thermodynamics of this reversible monomer–living polymer system was determined for bulk and without any initiator added. From the dependence of the equilibrium monomer concentration on the reciprocal of the absolute temperature, we found $\Delta H_{ls} = -5.4 \pm 0.7$ kJ·mol^{-1} (−1.3 ± 0.2 kcal·mol^{-1}) and $\Delta S_{ls} = -25.4 \pm 6.2$ J·mol^{-1}·deg^{-1} (−6.1 ± 1.5 cal·mol^{-1}·deg^{-1}).

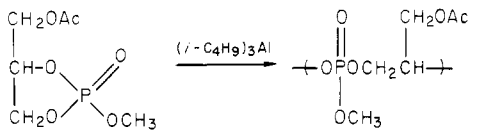
^1H and ^{13}C NMR spectra of **6** are shown in Figures 2 and 3, respectively. The assignments are given directly in the figures, indicating a good agreement with the assumed and expected structures. Multiplets observed for CH and both CH_2 carbon atoms in the ^{13}C NMR spectrum are, at least partially, due to C–P coupling. In the $^{31}P\{^1H\}$ NMR spectrum, only one singlet at δ −2.3 (Me_2SO) is observed. These spectra correspond to a polymer of $\bar{M}_n$(VPO in DMF solution) = 3.5×10^3. Polymers with $\bar{M}_n$ ranging up to 1.0×10^4 were prepared in the same way.

Thus it has been proven that high molecular weight models of teichoic acids can be prepared by polymerizing the corresponding cyclic monomers. Apparently, the ring-opening process proceeds in one way, producing exclusively head-to-tail regular structures. Otherwise single lines would not be observed for CH_2 in the ^{13}C and for >POO$^-$ in the $^{31}P\{^1H\}$ NMR spectra. Although the meso and racemic placements may result in polymerization and the iso- and syndiotactic units may be present in **6**, the NMR methods employed did not allow us to observe this chain isomerism. This is related both to broadening of the spectra because of the increased relaxation times and to insufficient sensitivity of the equipment used. However, we observed in 4-methyl-2-oxo-1,3,2λ^5-dioxaphospholane both ring openings proceeding with equal probability.

Ester Route. This route is based on our previous work, where poly(2-methoxy-2-oxo-1,3,2-dioxaphospholane) was converted into the corresponding polyacid by dealkylation of the side groups.[16]

Polymerization of **5** was usually performed with monomer of purity exceeding 95 wt % and with $(i\text{-}C_4H_9)_3Al$ as initiator in CH_2Cl_2 below 0 °C, as we described previously for various dioxaphospholanes unsubstituted in the ring.[17] Poly-**5** was precipitated from CH_2Cl_2 solution into benzene; **5** is soluble in this mixture. Purified polymer (prepared, e.g., at −20 °C, $[\mathbf{5}]_0 = 4.5$ mol·L^{-1}, and $[(i\text{-}C_4H_9)_3Al]_0 = 6.7 \times 10^{-2}$ mol·L^{-1} in CH_2Cl_2 solvent for 24 h) was a solid, transparent, elastic material, $\bar{M}_n = 2.5 \times 10^4$ (high-speed membrane osmometry in CH_2Cl_2 solution).

Conversion of monomer into polymer could be followed by $^{31}P\{^1H\}$ NMR:



$^{31}P\{^1H\}$: singlets at δ 16.8 and 16.5 (trans and cis)

multiplets from δ +0.9 to −2.6 ($CHCl_3$) (at least seven lines)

Judging from the the $^{31}P\{^1H\}$ NMR spectra of the polymerizing mixture, **5a** and **5b** were inactive in the polymerization of **5** and were removed during the workup of the poly-**5**.

We explain the multiplicity of the $^{31}P\{^1H\}$ NMR spectrum of poly-**5** by the possible presence of a number of configurational isomers due to chirality at the P atom and the C atom in the CH group. This assumption is substantiated by the observed simplification of the polymer spectrum when by the dealkylation process the methyl group is removed from the phosphoryl unit in the polymer chain and the triester is converted into a diester. Moreover, the ^1H and $^{13}C\{^1H\}$ NMR spectra also suggest the presence of isomeric structures. There are two doublets in the ^1H NMR spectrum in the region corresponding to methoxy groups (δ 3.52 and 3.54, $^3J_{POCH} = 10.7$ Hz and $^3J_{POCH} = 11.3$ Hz, respectively) and two close doublets in the $^{13}C\{^1H\}$ NMR spectrum (δ 53.6 and 54.4, $^2J_{POC} = 5.9$ Hz and $^2J_{POC} = 3.9$ Hz, respectively).

Conversion of poly-**5** into polysalts was performed by a number of dealkylation processes, namely, by using trialkylamines $(CH_3)_3N$ and $(C_2H_5)_3N$ or by using NaI in acetone solution. At present, the best results were obtained by the latter method. However, the extent of dealkylation did not exceed 80%. The same was observed in our work on dealkylation of poly(2-methoxy-2-oxo-1,3,2-dioxaphospholane) with trialkylamines.[16] We suspect that further approach of the dealkylating agents to the negatively charged macromolecules becomes difficult with increasing extent of dealkylation.

Some Properties of 6. Poly[4-(acetoxymethyl)-2-hydroxy-2-oxo-1,3,2-dioxaphospholane] prepared as described above and with $\bar{M}_n$ ranging from 3.5×10^3 to 1.0×10^4 is a white, solid, brittle material. This is in contrast to poly(2-hydroxy-2-oxo-1,3,2-dioxoaphosphorinane) [poly(1,3-propylene phosphate)], which we previously prepared as a solid, but highly elastic material, giving a transparent, elastic film when cast from, e.g., water solution.[16] Teichoic acids in the form of polysalts are also known to be fragile solids.[18] The oxidation of poly-**3** was found to be quantitative within the limits of accuracy of the $^{31}P\{^1H\}$ NMR spectra used for the polymer analyses.

Polyacid **6** is not stable in water solution. Dissolved in water it easily loses the acetoxy groups and can be converted into poly(glycerol phosphate).[19] A solution of **6** in the form of a polysalt, prepared by dissolution of solid **6** in aqueous Na_2CO_3, was found to be stable, at least over several days: the viscosity of water solutions did not change during this time, and no appreciable change was observed in either the $^{31}P\{^1H\}$ or the ^1H NMR spectra.

Experimental Part

^1H NMR spectra were measured at 60 MHz on a Perkin-Elmer R12B instrument with Me_4Si as an external standard. ^{31}P and ^{13}C NMR spectra were measured at 24.2 and 15.3 MHz on a JEOL-FX 60 apparatus with 85% H_3PO_4 as an external standard and Me_4Si as an internal standard, respectively. A Hewlett-Packard high-speed membrane osmometer, Model 502, or Hewlett-Packard vapor pressure osmometer, Model 302 B was used in determinations of $\bar{M}_n$. GLC analysis was carried out on a Varian Aerograph 2700 (fid detectors) with an LDC 308 computing integrator. Viscosity measurements were made in DMF solution for polyacid **6** and in H_2O for polysalts by using a suspended level Ubbelohde viscosimeter. All solvents and reagents were purified and dried by conventional methods. CH_2Cl_2 for the polymerization experiments was prepared by a known procedure.[20]

1-Acetoxypropane-2,3-diol (α-Monoacetin) (1). Acetic anhydride (283 mL, 3 mol) was added dropwise to a mixture of dry glycerol (276 g, 3 mol) and pyridine (242 mL, 3 mol) with vigorous stirring and cooling with cold water bath. The resulting mixture was kept overnight and then pyridine and acetic acid were distilled off under vacuum at room temperature. From the residue, distilled under vacuum, the fraction boiling at 104–110 °C (0.5 mmHg) (lit.[21] bp 129–131 °C (3 mmHg)) was collected (338.7 g, 84%, n_D^{23} = 1.4509, lit.[21] n^{20} = 1.4517). The product, a mixture of α- and β-monoacetin and -diacetins, was used for further synthesis without separation.

4-(Acetoxymethyl)-2-chloro-1,3,2-dioxaphospholane, a Mixture of Cis and Trans Isomers (2). The general procedure elaborated by Lucas et al.[22] was applied. Equimolar amounts of **1** (335 g, 2.5 mol) and PCl_3 (221 mL, 2.5 mol) were simultaneously added dropwise to vigorously stirred dry CH_2Cl_2 (500 mL), gaseous HCl being evacuated from the reaction flask at reduced pressure (water pump). After complete addition of all substrates, the solution was stirred under reduced pressure and solvent evaporated. The residue was distilled under vacuum and the fraction boiling at 60–70 °C (0.1 mmHg) was collected; yield 305.8 g. According to elemental analysis and ^1H NMR spectroscopy, the reaction product usually contained about 20–30% of chlorodiacetoxypropanes and about 5–10% of six-membered isomers. Then this mixture was fractionated on the spinning-band column under vacuum (~2 mmHg). The forerun (one-third of the total volume) and the main fraction (two-thirds of the total volume) were collected separately. According to the $^{31}P\{^1H\}$ NMR spectrum, there were only two impurities in this fraction, namely, 2% of six-membered cis and trans isomers.

4-(Acetoxymethyl)-2-oxo-1,3,2λ^5-dioxaphospholane, a Mixture of Cis and Trans Isomers (3). The product described in the preceding section and containing the known amount of **2** (39.7 g, 0.2 mol) was dissolved in dry CH_2Cl_2 (100 mL). Then a mixture of H_2O (3.24 g, 0.18 mol) with dioxane (25 mL) was added to this solution dropwise with stirring. Gaseous HCl was removed under reduced pressure (water pump). After complete addition, the resulting mixture was stirred and solvent was removed under reduced pressure. The resulting semiviscous residue was distilled under vacuum, and the major fraction boiling at 120–130 °C (0.03 mmHg) was collected: yield 25.3 g; ^1H NMR ($CHCl_3$, chemical shifts from $CHCl_3$ −7.25 ppm) δ 1.54 (s, 3 H), 3.4–4.7 (m, 5 H), 6.06 and 6.08 (2 d, $^1J_{PH}$ = 727 Hz and $^1J_{PH}$ = 730 Hz, respectively, 1 H), cis: trans isomer ratio = 1; $^{13}C\{^1H\}$ NMR (CD_3SOCD_3 in internal capilary) δ 19.6, 63.0, 66.5, 75.6, 170.1; $^{31}P\{^1H\}$ NMR (without solvent) δ 23.8. Anal. Calcd for $C_5H_9PO_5$: C, 33.33; H, 5.00; P, 17.22. Found: C, 33.46; H, 5.37; P, 16.87.

4-(Acetoxymethyl)-2-methoxy-1,3,2-dioxaphospholane, a Mixture of Cis and Trans Isomers (4). A mixture containing a calculated amount of **2** (99.25 g, 0.5 mol) was dissolved in dry benzene (200 mL). The solution was cooled to −5 °C and then a mixture of dry methanol (20.2 mL, 0.5 mol) and dry triethylamine (69.5 mL, 0.5 mol) was added dropwise with stirring and cooling. The temperature of the reaction mixture was maintained between −5 and 0 °C. After complete addition, the resulting mixture was stirred without cooling for 1.5 h. Then triethylamine hydrochloride was filtered off and the filtrate was concentrated. The residue was distilled under vacuum, and a fraction boiling at 60–66 °C (0.1 mmHg) was collected: yield 102.9 g of colorless liquid; $^{31}P\{^1H\}$ NMR (without solvent) δ 139.4, 133.7; 1:1.95 ratio. The product usually contained about 20–30% of chlorodiacetoxypropanes and 6–8% of six-membered isomers of **4**. This mixture fractionated on the spinning-band column gave a product containing less than 2% of six-membered isomers. Purity was determined by $^{31}P\{^1H\}$ NMR.

4-(Acetoxymethyl)-2-methoxy-2-oxo-1,3,2-dioxaphospholane, a Mixture of Cis and Trans Isomers (5). The product described in the preceding section (102.9 g) was dissolved in dry CH_2Cl_2 (200 mL) and this solution was stirred and cooled. When the temperature of the mixture reached −30 °C, a 15% solution of N_2O_4 in CH_2Cl_2 was added portionwise, keeping the temperature between −30 and −20 °C. A solution of N_2O_4 was added until the mixture turned blue. Then solvent was evaporated and the resulting residue distilled. The fraction boiling at 120–130 °C (0.1 mmHg) was collected; yield 66.7 g of colorless liquid. The product was purified by several distillations and by allowing it to stand over a Na mirror in vacuum vessels. GLC (2-m column, 10% OV 101, temperature programed from 70 to 280 °C (10 °C/min)) gave three peaks (retention time (s), percent of sample (assuming peak area proportional to the proportion): 732, 57.6; 746, 36.1; 772, 3.3. On the basis of the $^{31}P\{^1H\}$ NMR spectrum we calculated the following for this sample: *trans*-**5**, 61.7%; *cis*-**5**, 33.4%; **5a**, 1.5%; **5b**, 3.6%. Anal. Calcd for $C_6H_{11}PO_6$: C, 34.29; H, 5.24; P, 14.76. Found: C, 34.44; H, 5.48; P, 14.76. ^1H NMR ($CHCl_3$) δ 2.1 (s, 3 H), 3.8 (d, $^3J_{POCH}$ = 12 Hz, 3 H), 4.1–5.1 (m, 5 H); $^{31}P\{^1H\}$ NMR (without solvent) δ 16.8, 16.5; $^{13}C\{^1H\}$ NMR (CD_3SOCD_3) δ 19.9, 54.5 (d, $^2J_{POC}$ = 5.9 Hz), 54.8 (d, $^2J_{POC}$ = 3.9 Hz), 62.7 (d, $^3J_{POCC}$ = 9.8 Hz), 63.1 (d, $^3J_{POCC}$ = 3.9 Hz), 67.0, 75.7, 170.1.

Polymerization of **3** and **5** was carried out in ampules filled and sealed under vacuum. Monomer **3** was freshly distilled into the ampules immediately before polymerization. Initiator (i-$C_4H_9)_3Al$ was added in vials broken directly in the ampules in the monomer solution.

Poly-**5** was isolated and purified by several precipitations from CH_2Cl_2 solution into benzene and then dried under vacuum: yield, about 30–40% of transparent, colorless material; ^1H NMR ($CHCl_3$) δ 1.85 (s, 3 H), 3.52 and 3.54 (2 d, $^3J_{POCH}$ = 10.7 Hz and $^3J_{POCH}$ = 11.3 Hz, respectively, 3 H), 4.05 (broad signal, 4 H), 4.5 (broad signal, 1 H); $^{31}P\{^1H\}$ NMR ($CHCl_3$) δ 0.9, 0.3, −0.3, −1.0, −1.4, −2.2, −2.6; $^{13}C\{^1H\}$ NMR (CD_3SOCD_3) δ 20.1, 53.6 (d, $^2J_{POC}$ = 5.9 Hz), 54.4 (d, $^2J_{POC}$ = 3.9 Hz), 62.1, 66.1 (broad signal), 74.3 (broad signal), 169.9. Anal. Calcd for $C_6H_{11}PO_6$: C, 34.29; H, 5.24; P, 14.76. Found: C, 34.53; H, 5.24; P, 14.28.

Poly-**3** was not isolated but directly converted into a polyacid **6** by oxidation. Thus the polymerization mixture was diluted with dry CH_2Cl_2 and oxidized with an excess of N_2O_4 used as a 15% solution in CH_2Cl_2. Polyacid **6** was isolated and purified in two different manners, depending on the molecular weights of the polymers.

Method A. When the lower molecular weight polymer was oxidized, it did not precipitate from the oxidizing mixture. Thus the solution was evaporated and the residual product was purified by several precipitations from DMF solution into ethyl acetate. Purity of **6** was determined by $^{31}P\{^1H\}$ NMR spectroscopy.

Method B. Polyacid **6** precipitates from solution after and/or during oxidation as transparent, solid polymeric material. Solution was decanted, and the polymer was washed several times with CH_2Cl_2, dried on the vacuum line, and purified by precipitation from DMF solution into ethyl acetate. Decanted liquid was collected and worked up by method A to give a second fraction of the product. Solvents trapped in the polymer were removed from **6** on the vacuum line: yield, about 50% of colorless, brittle, hygroscopic material; ^1H and $^{13}C\{^1H\}$ NMR spectra are given in Figures 2 and 3, respectively; $^{31}P\{^1H\}$ NMR (Me_2SO) δ −2.3. Anal. Calcd for $C_5H_9PO_6$: C, 30.61; H, 4.59; F, 15.82. Found: C, 30.85; H, 5.12; P, 15.21.

Dealkylation of Poly-5. In the dealkylation process several dealkylating agents and procedures were tested.

1. Trimethylamine in water solution at room temperature after 2 days of reaction gave 60–70% dealkylation. About 70% of the acetic ester groups were removed.

2. Sodium iodide in acetone solution at room temperature after 2 days or under reflux after 2 h gave 70–75% dealkylation. No change in concentration of acetoxy groups in polymer samples was observed.

3. Trimethylsilyl bromide was used at room temperature in

CH_2Cl_2 solution. It was shown from the $^{31}P\{^1H\}$ NMR spectrum that this dealkylation agent is not selective for the side groups, as required, and reacts with the methoxy group as well as with a polymer chain.

Registry No. 1, 106-61-6; 2, 83999-29-5; 3, 83999-30-8; 4, 71638-12-5; 5, 71638-15-8; 5 (homopolymer), 83999-31-9; 5 (repeating unit), 84108-18-9; PCl_3, 7719-12-2; teichoic acid, 9041-38-7.

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Selective Ring-Opening Polymerization of 1,4-Anhydro-2,3-di-*O*-benzyl-α-D-xylopyranose and Synthesis of Stereoregular (1→5)-α-D-Xylofuranan

Toshiyuki Uryu,* Junichi Yamanouchi, Shuji Hayashi, Hidehiko Tamaki, and Kei Matsuzaki

Department of Industrial Chemistry, Faculty of Engineering, University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113, Japan.

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ABSTRACT: A new stereoregular polysaccharide, (1→5)-α-D-xylofuranan, was synthesized by selective ring-opening polymerization of 1,4-anhydro-2,3-di-*O*-benzyl-α-D-xylopyranose (ABXP) (1,5-anhydro-2,3-di-*O*-benzyl-β-D-xylofuranose) into 2,3-di-*O*-benzyl-(1→5)-α-D-xylofuranan and subsequent removal of the protective benzyl groups. Polymerizations of ABXP by boron trifluoride etherate catalyst gave 2,3-di-*O*-benzyl-(1→5)-α-D-xylofuranans with $[\alpha]_D$ values of +151 to +158° and number-average molecular weights of 26×10^3 ($(\bar{DP})_n = 83$) to 149×10^3 ($(\bar{DP})_n = 477$). Catalysts such as stannic chloride, silicon tetrafluoride, phosphorus pentafluoride, and niobium pentafluoride also gave poly(ABXPs) with high positive specific rotations. On the other hand, antimony pentachloride as catalyst provided poly(ABXPs) with mixed structures depending on the polymerization conditions. After debenzylation, stereoregular (1→5)-α-D-xylofuranan and xylofuranans with mixed structures consisting of (1→5)-α- and (1→5)-β-D-xylofuranosidic units were obtained. ^{13}C NMR spectra of a natural xylan consisting of (1→4)-β-D-xylopyranosidic units and of the synthetic xylans were measured to determine the structures of the xylans. The mechanism of the cationic ring-opening polymerization of ABXP is discussed.

Highly stereoregular polysaccharides of the dextran-type (1→6)-α-glycan have been synthesized by ring-opening polymerization of 1,6-anhydro sugars.[1,2] It has been possible to prepare a synthetic dextran with regioselective branching.[3] Furthermore, (1→6)-α-linked heteropolysaccharides were obtained by ring-opening copolymerization of different 1,6-anhydro sugars.[4,5] The chemical synthesis has also been attempted for the cellulose-type polysaccharide (1→4)-β-glycopyranose, which is the most naturally abundant polysaccharide, using the polycondensation of unsubstituted[6] and substituted saccharides,[7] though successful results have not been achieved.

Recently, we reported the first synthesis of a (1→4)-β-linked stereoregular polysaccharide by selective ring-opening polymerization of 1,4-anhydroribopyranose derivatives.[8] Since (1→4)-β-D-ribopyranan does not occur in nature, the physical properties and structure of the polysaccharide could not be compared with those of a natural polysaccharide of the same structure.

It is known that wood xylan, which is contained as the second most abundant polysaccharide next to cellulose in hardwoods and has the (1→4)-β-linked xylopyranose structure,[9] cannot be synthesized by the polycondensation of D-xylose.[10] However, the ring-opening polymerization of a 1,4-anhydro-α-D-xylopyranose derivative might provide a stereoregular synthetic (1→4)-β-D-xylopyranan if the selective opening of the 1,4-anhydro ring occurs during polymerization as in the case of 1,4-anhydroribopyranose.

Until now, only the ring-opening polymerization of 1,4-anhydro-α-D-glucopyranose,[11,12] -β-D-galactopyranose,[13] and -α-L-arabinopyranose[13] derivatives was investigated, resulting in the formation of nonstereoregular polysaccharide derivatives. Since 1,4-anhydro-α-D-glucopyranose can be regarded as 1,5-anhydro-β-D-glucofuranose, in which there are two possible ring-opening modes of 1,4- and 1,5-ring scissions, it is difficult to find monomer structures and polymerization conditions that will lead to the selective ring-opening polymerization. A model compound of the 1,4-anhydro sugar, 2,7-dioxabicyclo[2.2.1]heptane, has been polymerized by cationic catalysts to give a polymer with the backbone structure containing five-membered rings (furanose rings in the

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