

NEW POLYMERIZATIONS OF SPIRO ACYLOXYPHOSPHORANES

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Abstract - This paper describes new polymerizations using spiro acyloxyphosphoranes as starting monomers. First, syntheses of spiro acyloxyphosphorane monomers are mentioned. Then, polymerizations of these monomers are described by classifying the reaction type into four categories, i.e., i) Arbusov type ring-opening isomerization polymerizations (thermal reactions as well as reactions involving nucleophilic displacements such as Alcoholysis, Hydrolysis, and Aminolysis Polymerizations), ii) Polyphosphoranylations, iii) Deoxy-polymerizations, and iv) Deoxy-copolymerizations. Reactions of categories i) and ii) produced polymers having phosphorus in the main chain. Categories iii) and iv), on the other hand, gave polymers having α -ester unit, in which a phosphorus(III) component served as a deoxygenating agent from an α -keto acid component. All these polymerizations involved phosphonium type zwitterion intermediates. Polymerizations of category i) yielding polyphosphate derivatives constitute the major part in the present paper.

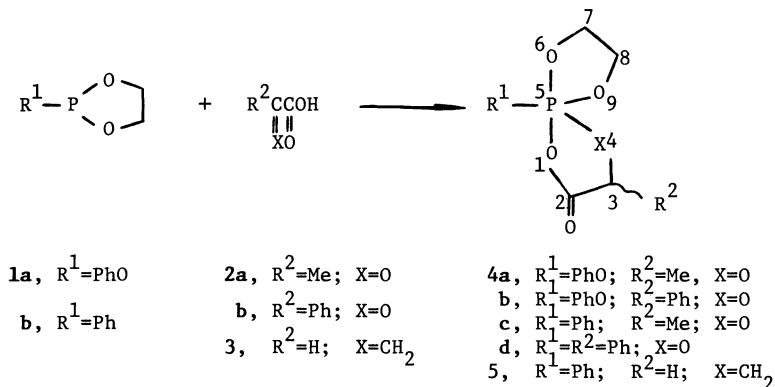
INTRODUCTION

Polymers containing phosphorus in the main chain have been prepared in various ways, i.e., ring-opening, condensation and radical polymerizations. Among these phosphorus-containing polymers, polyphosphates have attracted particular interest not only as a simple model of polynucleotides but also as physiologically active polymers (Refs. 1-6). We have recently found new methods to prepare polyphosphates, polyphosphonates, and polyphosphinates (Refs. 7-9). All these methods have been based on the ring-opening isomerization polymerizations of spiro acyloxyphosphoranes, a new class of pentacovalent phosphorus species having P-OC(O)-group, which have been prepared and isolated recently for the first time by us (Refs. 10-12). Related oxyphosphoranes have been studied extensively concerning synthetic utilities (Ref. 13) and reactions oriented to the biochemistry field (Ref. 14). The present paper focuses on the new reactions of polymer syntheses using spiro acyloxyphosphoranes as monomer. These polymerizations can be classified into four categories according to the type of reaction; i) Arbusov type ring-opening isomerization polymerization (thermal reaction and reaction involving nucleophilic displacement), ii) Polyphosphoranylation, iii) Deoxy-polymerization, and iv) Deoxy-copolymerization. Categories i) and ii) produce various phosphorus-containing polymers. Categories iii) and iv) give polymers having no phosphorus in the main chain, in which the starting phosphorus(III) component serves as a deoxygenating agent. All polymerizations of the above four categories proceed via zwitterion intermediates (Ref. 15). Polymerizations of category i) will be the major part in this paper.

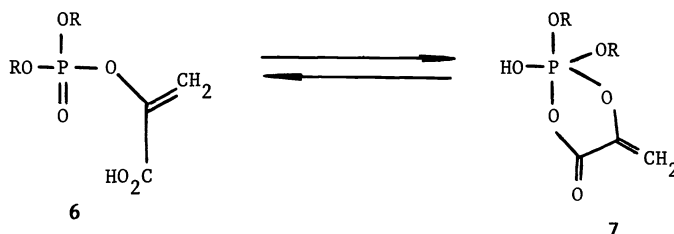
NEW MONOMERS OF SPIRO ACYLOXYPHOSPHORANES

The syntheses of monomers of spiro acyloxyphosphoranes (4 and 5) are based on the new reactions of cyclic phosphorus(III) compounds 1 with α -keto acid 2 (Ref. 10) or acrylic acids 3 (Ref. 11). 4 and 5 could be obtained as crystalline materials by the reaction below room temperature.

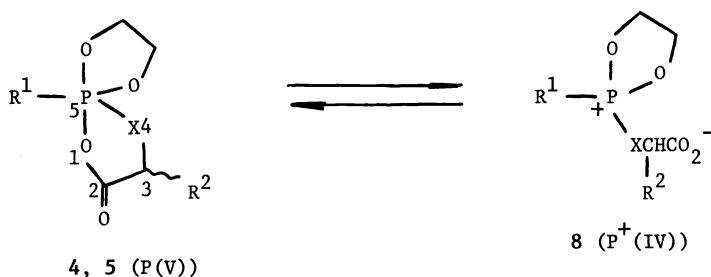
A typical example of the preparation of spiro acylpentaoxyphosphorane, 2-oxo-3-methyl-5-phenoxy-1,4,6,9-tetraoxa-5-phosphaspiro[4,4]nonane, 4a is given here. Into 20 ml of diethyl ether containing 3 mmol of 2-phenoxy-1,3,2-dioxaphospholane 1a was added 3 mmol of pyruvic acid 2a at 0°C under nitrogen and then the mixture was allowed to react at room temperature for 15 h. The mixture was further kept at -20°C for two weeks in order to crystallize the product. The crystalline material of 4a was separated to give 0.25 g (31% yield): mp 87°C, ³¹P NMR (DMF) -39.7 ppm (the higher magnetic field from external H₃PO₄ standard). The lower



isolated yield of **4a** was not due to the lower conversion of reaction but due to the relatively higher solubility of **4a** and the loss during separation procedures. Therefore, the yield will be improved. Actually, ^{31}P NMR of the reaction mixture showed that **1a** and **2a** completely disappeared and produced **4a** quantitatively after 3 h at $-30^\circ C$ (Ref. 16). Thus, the above reactions gave spiro acylphosphorane (**4a** and **4b**)-, acyltetraoxy (**4c** and **4d**)-, and acyltrioxy (**5**)-phosphoranes. More recently, new spiro diacyloxyphosphoranes have been obtained by using a cyclic acyloxyphosphonite as phosphorus(III) compound (Ref. 12). Spiro acyloxyphosphoranes are a new class of mixed anhydrides. Acylphosphorane derivatives, **4a** and **4b**, can be taken as "orthophosphates" of cyclic acyl phosphate, a high energy compound in biological metabolism (Ref. 17). A cyclic acyloxyphosphorane **7** is strongly implicated as an intermediate in the hydrolysis of phosphoenolpyruvate **6**. **4a** and **4b** may be good model compounds of **7**.



We have been studying the polymerizations as well as organic reactions of spiro acyloxyphosphoranes especially from the viewpoints of reactivities and stereochemistry. These investigations will be helpful for understanding the biologically related reactions. The most characteristic point of spiro acyloxyphosphoranes is probably the nature of equilibration between the phosphorane and the phosphonium-carboxylate zwitterion (**8**): $P(V) \rightleftharpoons P^+(IV)$. The $P(5) \rightarrow O(1)$ bond is very polarizable due to the strong electron-withdrawing ability of acyloxy group. At lower temperatures **4** and **5** could be isolated as crystalline materials

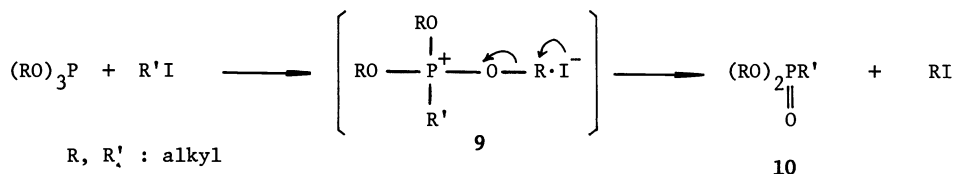


whereas at higher temperatures the zwitterion **8** becomes increased in concentration and operative in chemical reactions.

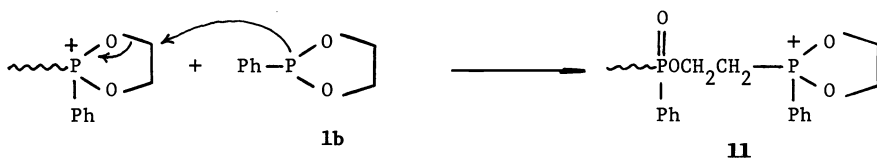
ARBUSOV TYPE THERMAL POLYMERIZATIONS

A typical Arbusov reaction is shown as follows (Ref. 18). Intermediate phosphonium iodide **9** is not stable when $R=$ alkyl group and nucleophilic attack of iodide onto the positively-charged carbon yields phosphinate **10** and alkyl iodide.

Cationic ring-opening polymerization of cyclic phosphorus(III) compounds such as **1b** is

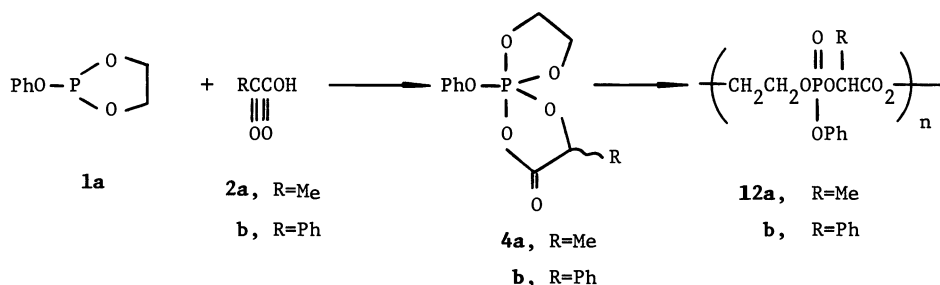


believed to proceed via the Arbusov type reaction (Ref. 19). The structure of the product polymer, however, did not consist of a simple phosphinate unit 11 but contained isomerized units due to side reactions.



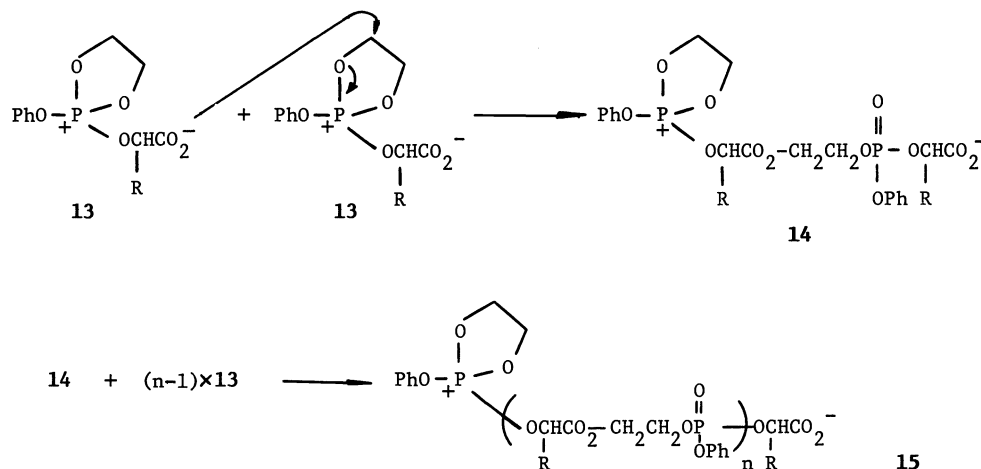
Polymerizations of spiro acyloxyphosphoranes mentioned in this part are induced thermally and proceed via the Arbusov type reaction involving ring-opening as well as isomerization. Zwitterion 8 in the polymerizations is corresponding to the intermediate 9 in the Arbusov reaction.

Spiro acylpentaoxyphosphoranes, 4a and 4b, were obtained from 1a and 2a or 2b. Isolated



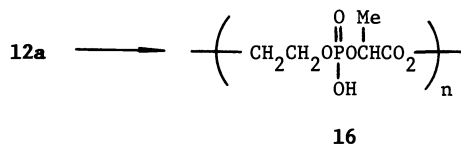
crystalline 4a was allowed to stand at 120°C for 24 h under nitrogen. Then, chloroform was added to the mixture and poured into a large amount of dry diethyl ether to precipitate polymeric materials. After drying, polyphosphate triester 12a was obtained quantitatively. The molecular weight of 12a was 4100 (Ref. 7). It was not necessary, however, to isolate "monomer" 4 for the production of polymer 12. Heating the 1:1 mixture of 1a and 2 in a solvent such as benzonitrile, toluene, or nitrobenzene, at 100–130°C gave 12 in good yields. 12 is an alternating copolymer of 1a and 2. During the copolymerization comonomer 1a was oxidized from P(III) to P(V) whereas the α -keto acid comonomer 2 was reduced to a unit of α -hydroxy acid ester in 12. Thus, it may well be termed as "oxidation-reduction copolymerization".

The reaction course for the production of 12 is explained by the following scheme. Under reaction conditions of higher temperatures 4 is in equilibrium with zwitterion 13. The reaction of two molecules of 13 via the Arbusov type reaction gives dimeric zwitterion 14.



Successive attacks of 13 onto 14 lead to the formation of macro-zwitterion 15, which is the product polymer 12.

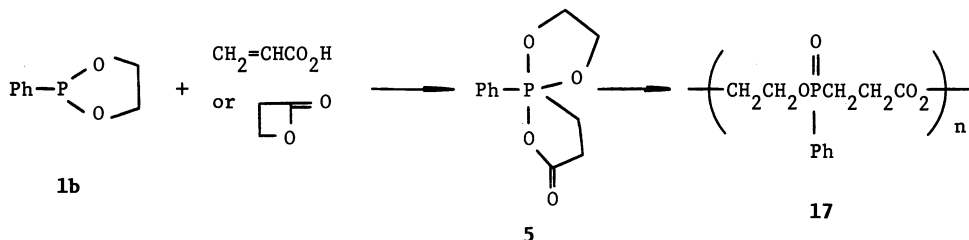
Polymer 12 has the structure of phosphoric acid triester. Some biopolymers such as polynucleotides are composed of phosphoric acid diester units. Several methods have been developed to prepare diester type polymers (Refs. 4-6). Therefore, the conversion of 12a to diester type polymer 16 was attempted by the hydrolysis and hydrogenolysis with platinum



catalyst. It is important to convert selectively the P-OPh group to P-OH without cleavage of the main chain. Various hydrolysis conditions were examined, i.e., sodium hydroxide, acetic acid, sodium acetate-acetic acid, imidazole-acetic acid, and pyridine-acetic acid in a methanol-water mixed solvent. Among these the pyridine-acetic acid system (at 70°C for 100 h) caused the complete hydrolysis of P-OPh to P-OH and gave 16 as a form of pyridinium phosphate. However, the hydrolytic cleavage of the main chain could not be excluded with this catalytic system.

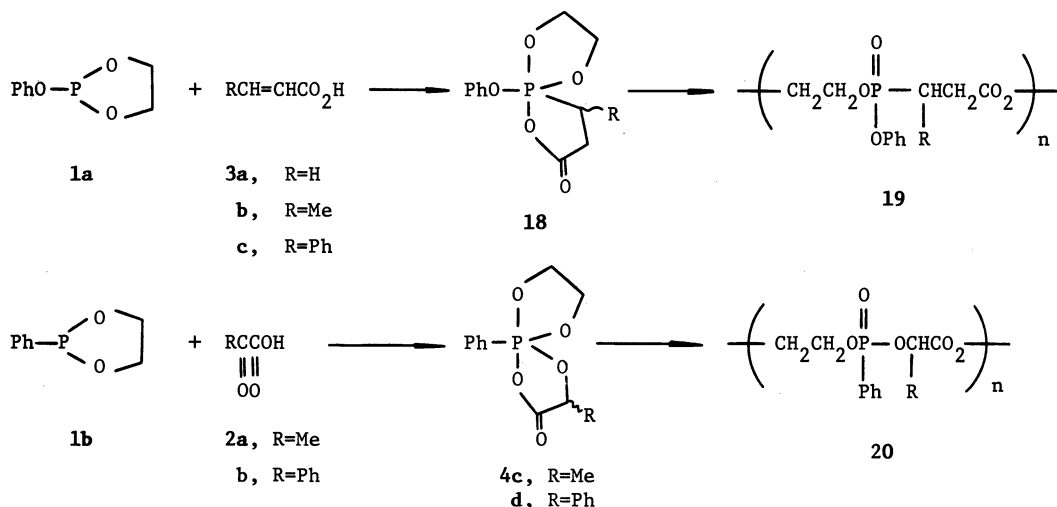
The hydrogenolysis with platinum oxide catalyst in acetic acid gave 16 having no phenyl group after 6 h at room temperature under atmospheric pressure of hydrogen gas. A small fraction of the main chain cleavage, however, was observed by this catalytic hydrogenolysis, i.e., the molecular weight of sample 12a was 2870 which decreased to 1000 (the calculated value was 1960).

Spiro acyltrioxyphosphorane 5, prepared from 1b and acrylic acid 3 or β -propiolactone, produced polyphosphinate 17 (Ref. 8). White crystalline 5 (mp 80°C) was heated at 160°C for 5 h without solvent gave 17 (MW=3430) in a quantitative yield. Polymer 17 was also

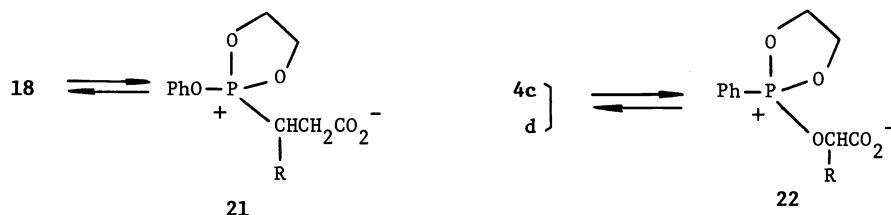


obtained by heating the 1:1 mixture of 1a and 3 or β -propiolactone in a dipolar aprotic solvent without isolating "monomer" 5. 17 is an alternating copolymer of 1b with 3 or β -propiolactone, in which 1b is a nucleophilic monomer and 3 or β -propiolactone serves as an electrophilic one.

Polyphosphonates (19 and 20) having one P-C bond have been obtained by alternating copolymerizations of two combinations of 1a-3 and 1b-2 (Ref. 9). Both copolymerizations involve

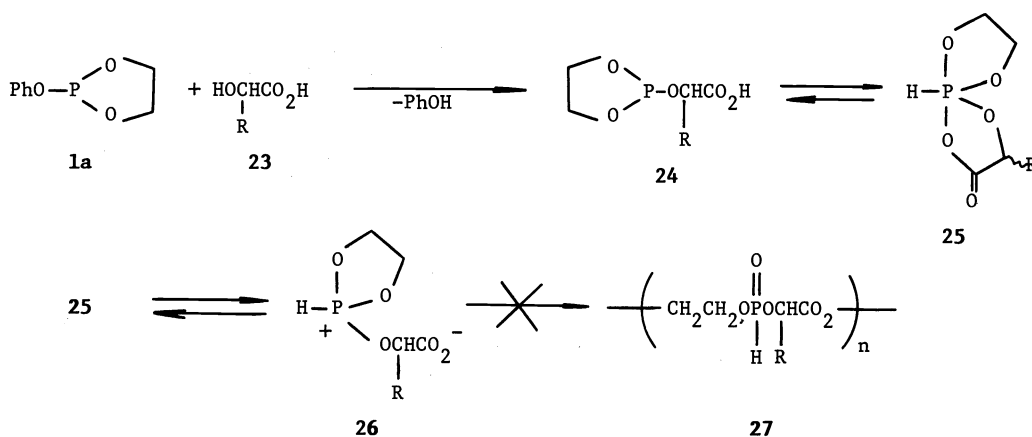


spiro acyltetraoxyphosphoranes, 18 and 4, respectively, the latter species being actually isolated (mp 4c; 56–58°C and 4d; 103–105 °C). Under the polymerization conditions of 100–120°C phosphoranes 18 and 4 were activated to form genetic zwitterions 21 and 22. The



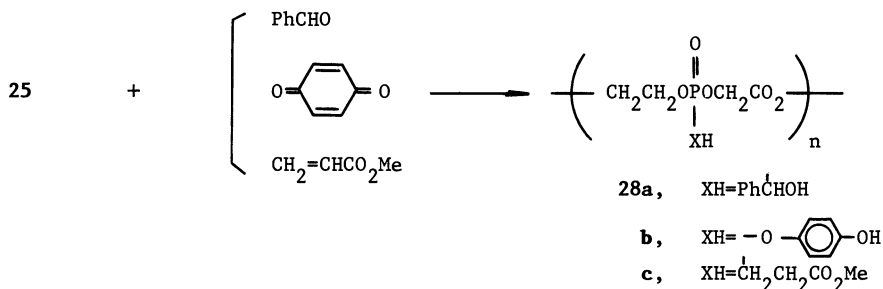
subsequent reactions of 21 and of 22 via the Arbusov type reaction yielded polyphosphonates 19 and 20.

Spiro acyloxyphosphoranes 25 having P-H bond have been made (Ref. 20). We have recently found the versatile preparation method of 25 and examined its polymerizability (Ref. 21). The reaction of 1a and α -oxy acids (23, R=H, Ph) gave 24 with liberation of phenol. At lower temperatures 24 isomerized to spiro phosphorane 25, probably a more stable form. If 25 can be in equilibrium with zwitterion form 26 as $4 \rightleftharpoons 8$, the production of polyphosphonate



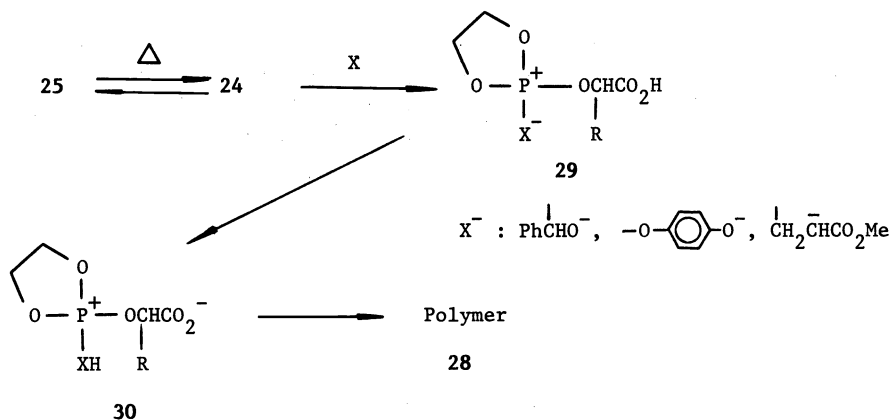
27 with P-H bond is expected. It turned out, however, that 27 was not produced. This result indicates that the nature of spiro phosphorane 25 with P-H bond is quite different, 25 being equilibrated rather with 24.

In order to achieve the polymerization of 25 it was necessary to modify the reactivity of 25. For this purpose we employed electrophiles such as benzaldehyde, p-benzoquinone, and methyl acrylate. Then, it became possible to obtain polymers 28. For example, a 1:1 mixture of 25 (R=H) and benzaldehyde was allowed to react at 130°C for 45h to give polymer 28a after



work-up procedures. 28a has a 1:1 composition of 25 and benzaldehyde. Its molecular weight was 5000.

The reaction course is given by the following scheme. At reaction temperatures, e.g., higher than 90°C, 25 exists in equilibrium with P(III) species 24 rather than with zwitterion 26. Electrophiles X have high reactivities toward P(III) compound 24 to form 29 followed by a proton-transfer to yield 30. Since 30 is genetic zwitterion like 8 subsequent



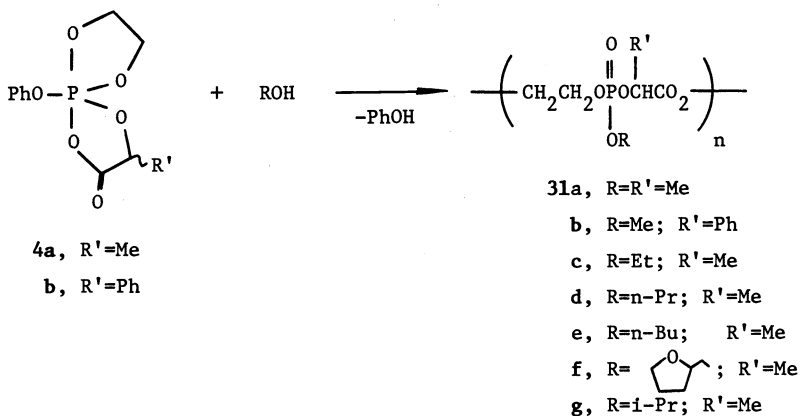
reactions of 30 lead to the formation of polymer 28.

ARBUSOV TYPE POLYMERIZATIONS INVOLVING NUCLEOPHILIC DISPLACEMENT AT SPIRO ACYCLOXY-PHOSPHORANES

In the course of the studies on the reactions of cyclic acyloxyphosphoranes we have found that they are reactive amphiphiles, i.e., they react with various kinds of both nucleophiles and electrophiles (Ref. 16). It is especially interesting that reactions of spiro acyl-pentaoxyphosphoranes having phenoxy group, 4a and 4b, with nucleophiles of alcohols, water, and amines give polyphosphate derivatives. During the polymerization nucleophiles are displaced with phenoxy group at the phosphorane.

Alcoholysis Polymerization


Primary and secondary alcohols. The reaction of 4 with primary and secondary "alcohols as nucleophiles" gave polyphosphate triesters 31 having alcohol components incorporated. Phenol was eliminated during the reaction (Ref. 22). The polymerization is a stoichiometric



reaction between 4 and an alcohol. First, 4a was prepared from 1a and 2a (3.0 mmol each) in 1 ml of benzonitrile at 0°C overnight. The reaction quantitatively gave 4a. To the mixture 3.0 mmol of methanol was added at room temperature. The reaction system was then kept at the same temperature for one day and at 120°C for 48 h. A usual work-up gave polymer 31a in 35% yield. The molecular weight of 31a was 4180 by vapor pressure osmometry.

The above polymerization was caused by the nucleophilic attack of alcohol, which was accompanied by the nucleophilic displacement of phenoxy group by alkoxy group. Therefore, we termed the reaction as Alcoholysis Polymerization of phosphorane 4. Alternatively, an alcohol is phosphorylated in this reaction and incorporated into polymer 31, and hence, a terminology of Polyphosphorylation of Alcohol was proposed. These results are given in TABLE 1.

TABLE 1. Alcoholysis polymerizations of 4^a

ROH	R'	Reaction			Polymer		
		Solvent	Temp. (°C) ^b	Time (h) ^b	Yield(%)	Structure	MW ^c
MeOH	Me	PhCN	120	48	35	31a	4180
MeOH	Ph	MeCN	100	30	16	31b	1780
MeOH	Me	PhCN	120	48	32	31c	4150
EtOH	Me	PhCN	100	240	49	31d	5160
n-PrOH	Me	PhCN	105	100	73	31e	2690
	Me	PhCN	100	200	80	31f	5660
i-PrOH	Me	CHCl ₃	90	73	65	31g	—

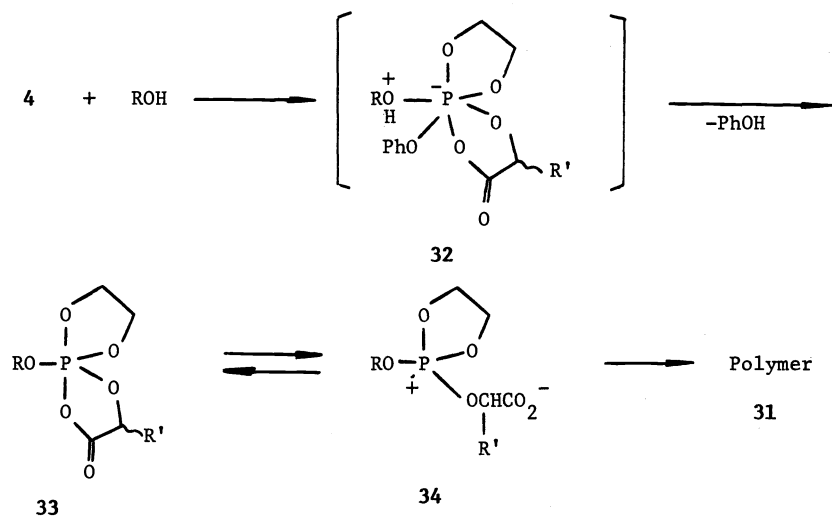
a. 4 prepared in situ = ROH = 3.0 mmol in 1 ml of solvent under nitrogen.

b. Indicating the value after the reaction of 4 with alcohol at room temperature for one day.

c. Determined by vapor pressure osmometry in chloroform at 35°C.

Primary alcohols gave polyphosphate triesters whose structures are given by 31a - 31f. A secondary alcohol i-propanol produced polymer consisting of two unit structures of triester 31g and diester 16. The latter unit was contained in about 30 molar percent and probably formed by the partial hydrolysis of P-O-i-Pr group of 31g during the work-up procedure.

Reaction mechanism. The reaction course of the alcoholysis polymerization is given as follows. The first step is a nucleophilic attack of an alcohol onto the central phosphorus atom to form a transient hexacoordinated species 32. A rapid proton-scrambling takes place on oxygen atoms in 32 and phenol is eliminated from 32 to give another spiro acyloxyphosphorane 33. The conversion of 4 to 33 is a new reaction of "transphosphorylation" in which

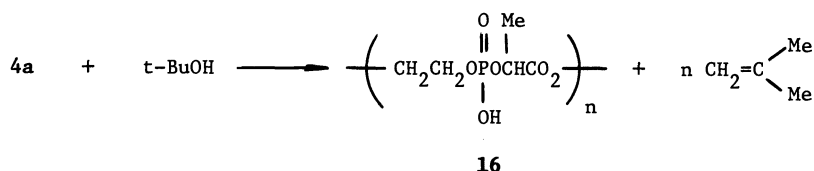


phenoxy group is displaced by alkoxy group since phenoxy is a better leaving group (Ref. 16). At polymerization temperatures higher than 90°C an equilibration of 33 with zwitterion 34 becomes important. Successive reactions of 34 via the Arbusov type lead to the formation of polymer 31. Phenol eliminated during the reaction does not interfere in the polymerization.

The mechanism above was also supported by the following observations. Spiro phosphorane 33 (R=R'=Me) was prepared from 2-methoxy-1,3,2-dioxaphospholane and pyruvic acid. Then,

heating of the phosphorane at 100°C for 100 h gave polymer having the same structure of 31a in 48% yield (MW=4680), indicating that 33 (R=R'=Me) is actually involved in the methanolysis polymerization of 4a. Thus, the alcoholysis polymerization provides a versatile one-pot synthetic method to prepare polyphosphate triesters having a variety of alcohol components from one kind of phosphorane 4; synthesis of 33 having a respective alkoxyl group being not necessary.

Tertiary alcohol. Tertiary alcohols such as t-butanol behaved differently. The reaction of 4a with t-butanol was very slow probably due to the steric hindrance of t-butyl group in the formation step of a hexacoordinated intermediate 32. The product polymer was polyphosphate consisting exclusively of diester unit 16 with liberation of phenol as well as isobutylene. Evolution of isobutylene was confirmed by GC analysis; t-butanol being

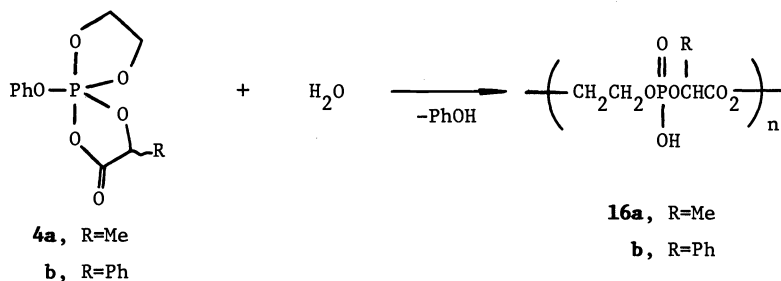


dehydrated by 4a (*vide infra*). The reaction of 4 with tertiary alcohols is another good way to produce polyphosphate diesters, which is compared with the method of the conversion of polymer 12 to 16.

Biological activity of polymers. Polyphosphate is an interesting material as a model of polynucleotides. One of possible applications of polyphosphates 31 is a utilization for pharmacologically active polymers or for a carrier polymer of pharmacologically active components. For such purpose a carrier polymer should be of very low toxicity (Ref. 23). Therefore, the acute toxicity of four polyphosphate triesters were examined. DMSO solution of polymer sample was intraperitoneally injected in 20 mice with an amount of 5 ml of DMSO solution / kg-mouse (DMSO itself did not show the toxicity at a dose rate of 10 ml/kg-mouse). The LD₅₀ values (mg/kg-mouse) obtained 14 days after the injection were as follows; 31c > 1000, 31d > 1000, 31f = ~1000, and 12a=420. The results indicate that these polyphosphate triesters are quite non-toxic and hence can be safely used as a carrier polymer. There are many pharmacologically active alcohols. They can be subjected to polyphosphorylation with 4 leading to polyphosphate triesters with the alcohol component as pendant group in the polymer. This is an attractive approach for developing new polymer drugs.

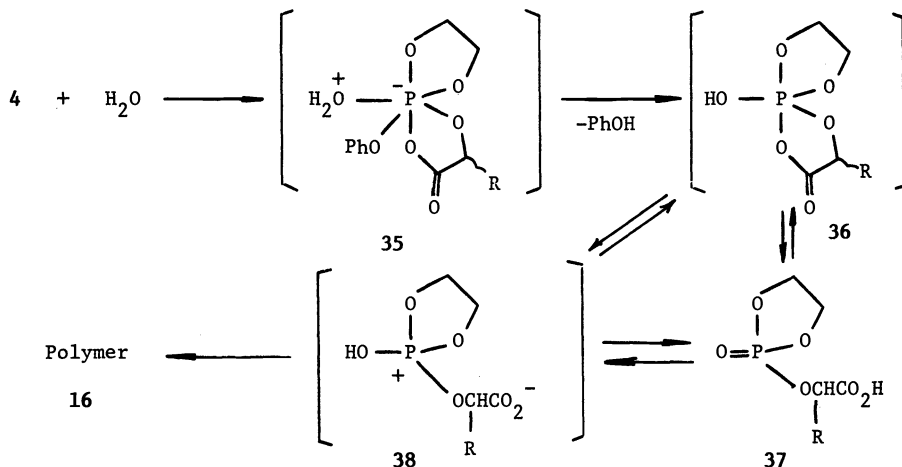
Hydrolysis Polymerization

Reaction with water. Water is a typical O-nucleophile like an alcohol. Spiro acylphosphorane 4 showed a high reactivity toward water at room temperature and produced polyphosphate diesters 16. This is a new polymerization induced by water, and therefore,



was termed as Hydrolysis Polymerization of 4 (Ref. 24). Some results are shown in TABLE 2. Polymers obtained were viscous liquid, powder, or rubbery materials depending on the molecular weight. They were soluble in water and highly polar organic solvents.

Reaction mechanism. The reaction course of the hydrolysis polymerization is understood as follows :

TABLE 2. Hydrolysis polymerization of 4^a

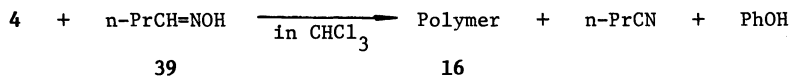
Phosphorane	Amount of water	Time	Polymer		
			Yield(%)	Structure	MW
4a	excess	50 hours	30	16a	2780
4a	equimol.	69 days	48	16a	7560
4b	excess	14 hours	30	16b	—
4b	equimol.	28 days	45	16b	5180

a. 4=3.0 mmol in 1.0 ml of acetonitrile at room temperature.

The nucleophilic reaction of water with 4 yields spiro hydroxyphosphorane 36 via a hexacoordinated intermediate 35. 36 exists as its isomeric phosphate form 37, a more stable species. 36 and/or 37 are probably equilibrated with a zwitterion of hydroxyphosphonium-carboxylate type 38. The formation of polymer 16 is well explained by considering 38 as a genetic zwitterion and its subsequent Arbuzov type reactions.

Significance of hydrolysis polymerization. The hydrolysis polymerization is a very convenient method for the production of diester type polyphosphate, which has not been obtained as a polymer of a clear-cut structure by converting 12 to 16. Furthermore, it should be emphasized that equimolar or excess amount of water induce the ionic polymerization of 4. In general, such amount of water inhibits ionic polymerizations (cationic, anionic as well as coordinate anionic) (Ref. 25).

Hydrolysis polymerization with aldoxime and tertiary alcohol. It has been found that other O-nucleophiles of aldoximes and tertiary alcohols also induced the hydrolysis polymerization (Ref. 26). Aldoxime 39 was allowed to react with an equimolar amount of 4. Then, polyphosphate diester 16, n-butyronitrile, and phenol were produced, in which 4 dehydrated 39 to the nitrile to give the hydrolysis polymerization product 16 (TABLE 3).

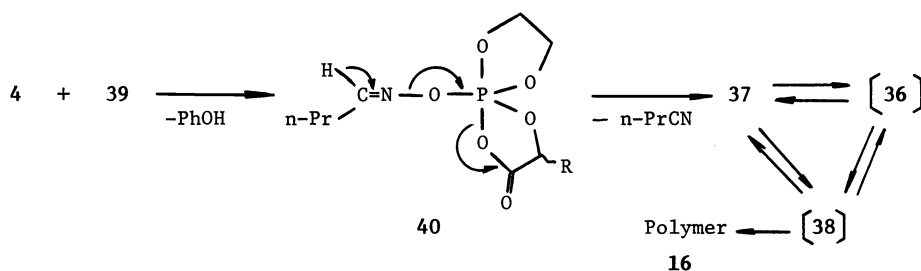


The reaction produces a displacement reaction product 40 which is not stable to decompose to n-butyronitrile and 37. The latter is a precursor "monomer" to lead to polymer 16.

Besides t-butanol, tertiary alcohols such as diphenylmethyl-, triethyl-, and phenylcyclohexyl-carbinols were dehydrated with 4 to give corresponding olefins whereas 4 gave polymer 16, the hydrolysis polymerization product (Ref. 26).

TABLE 3. Hydrolysis polymerization of 4 with 39

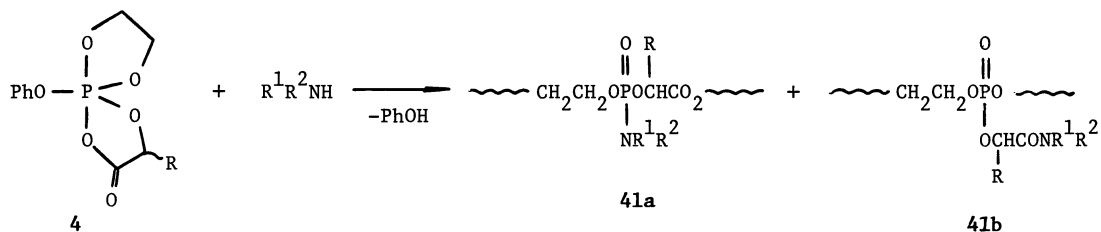
Phosphorane	Temp.	Time	Polymer yield(%)	MW	n-PrCN yield(%)	Phenol yield(%)
4a	r.t.	6 days	92	5160	95	94
4a	50°C	3 hr	84	3000	82	87
4b	r.t.	6 days	81	4650	100	87
4b	50°C	3 hr	83	3420	78	76



Aminolysis Polymerization

It has been explored recently that new reactions of spiro acylpentaoxyphosphoranes 4 with *N*-nucleophiles of aliphatic as well as aromatic amines and of ammonia produced polyphosphate derivatives (Aminolysis Polymerization) (Ref. 27).

Primary and secondary amines and ammonia. Stoichiometric reactions of 4 with primary and secondary amines took place even at room temperature and gave polyphosphate derivatives consisting of two kinds of unit, 41a and 41b.



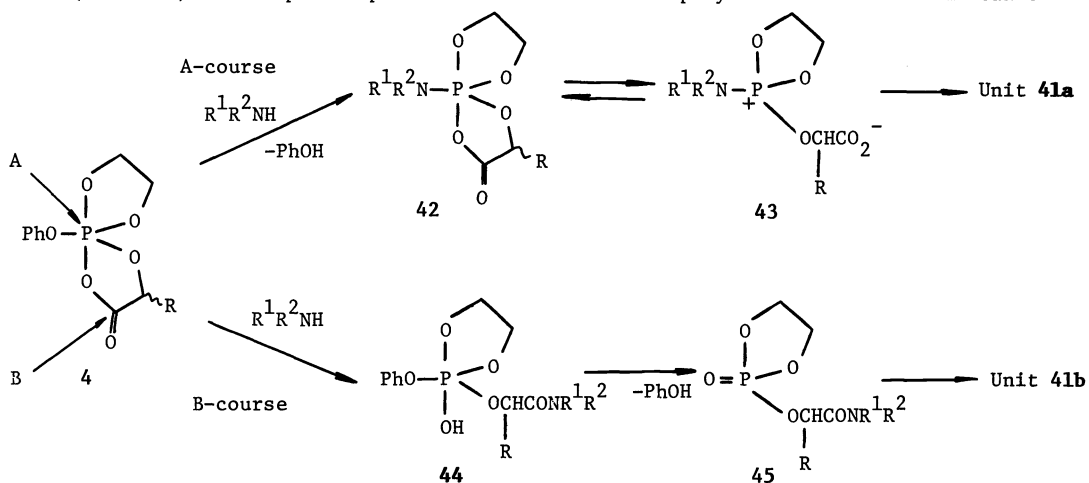
Determinations of polymer structure were made mainly by IR and ^{31}P NMR spectroscopy. Two signals of ^{31}P NMR were observed and assigned as follows: -7.7 ppm (up-field from H_3PO_4 external standard) for unit 41a and -2.7 ppm for unit 41b when diethylamine was used. Some results are shown in TABLE 4.

TABLE 4. Aminolysis polymerization of 4a with $\text{R}^1\text{R}^2\text{NH}$

Amine	Reaction			Polymer			
	Solvent	Temp.	Time (h)	Yield(%)	MW	Structure	
						41a (%)	41b (%)
Et_2NH	MeCN	100°C	70	32	3090	50	50
$\left(\text{C}_6\text{H}_5\right)_2\text{NH}$	MeCN	r.t.	100	57	1050	90	10
$\text{C}_6\text{H}_{11}\text{NH}$	MeCN	r.t.	288	31	2300	0	100
$n\text{-BuNH}_2$	MeCN	r.t.	288	58	1800	50	50
PhNH_2	MeCN	r.t.	100	59	1650	0	100
NH_3	$\text{C}_6\text{H}_6\text{-CH}_2\text{Cl}_2$	r.t.	3	61	1000	0	100

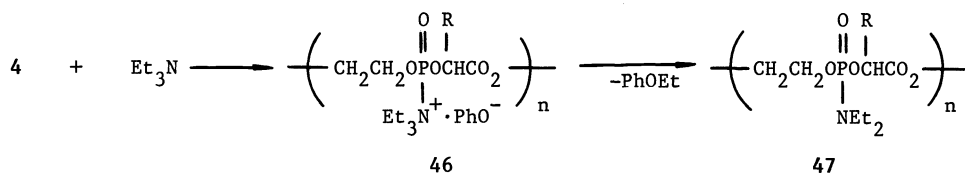
Ammonia also induced the polymerization of 4 giving rise to polymer consisting exclusively of unit 41b (Ammonolysis Polymerization) (TABLE 4).

Reaction mechanism. Aminolysis polymerizations of 4 with amines having N-H bond involve two reaction sites at the central phosphorus atom (A-course) and at the carbonyl carbon atom (B-course). It depends upon the nature of amine employed whether the amine takes

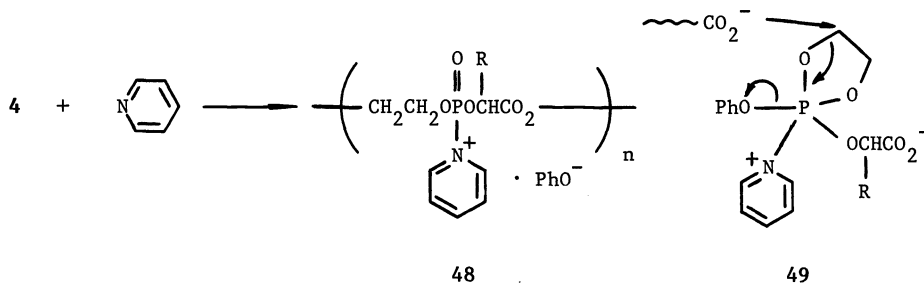


A- and/or B-course. A nucleophile of amine attacks the phosphorus atom to yield spiro acyloxyaminophosphorane 42 with liberating phenol probably through a hexacoordinated intermediate. 42 is unstable and produces a genetic zwitterion 43, whose Arbusov type ring-opening reaction with a nucleophile such as another 43 gives unit 41a. On the other hand, the attack of amine on the carbonyl carbon yields hydroxyphosphorane 44 which is quite unstable to give cyclic phosphate 45 with elimination of phenol. It is known that a cyclic phosphates is polymerized by anionic initiators such as amines (Ref.28). Therefore, 45 probably produces unit 41b under the basic reaction conditions containing amine. It should be mentioned that only amines with N-H bond took B-course in addition to A-course.

Tertiary amine. The reaction of 4 with triethylamine (1:1) in benzonitrile at 150°C for 78 h produced ionenetype polymer 46, which was not stable under reaction conditions and converted to 47 with the elimination of phenetole. Ultimately, polymer 47 was obtained in 78% yield (MW=4860).

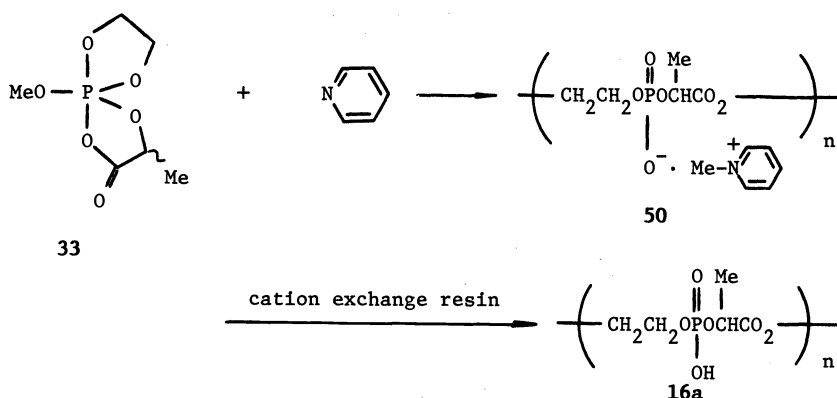


Aromatic amine. The combination of pyridine and 4 gave ionene polymer 48 which was quite stable under the reaction conditions. A typical example is given. An equimolar mixture of

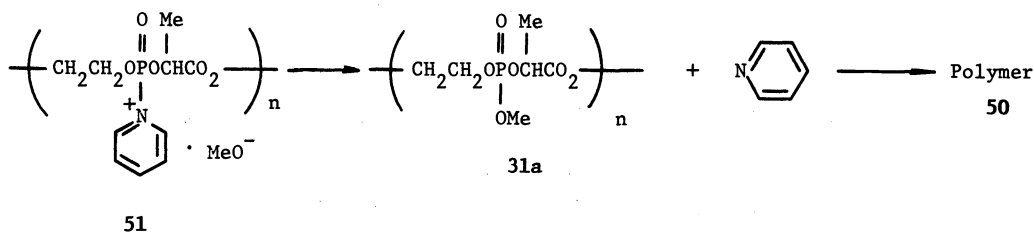


4a and pyridine in acetonitrile was kept at 90°C for 48 h and after a usual work-up powdery polymer 48 was obtained in 77% yield (MW=2370). Pyridinium-carboxylate type phosphorane 49 is postulated as a genetic zwitterion. The Arbusov type reactions of 49 lead to the production of 48.

The reaction of pyridine with spiro acyloxyphosphorane 33 having methoxyl group produced another ionene type polymer 50. The treatment of 50 with cation exchange resin gave polyphosphate diester 16a, the same type polymer prepared by the hydrolysis polymerization.



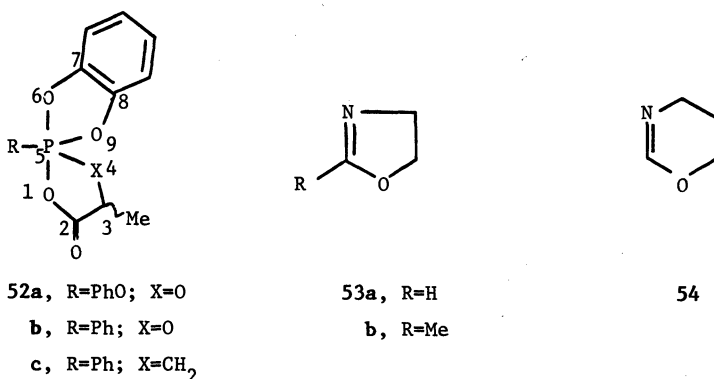
The production of 50 is explained as follows. From 33 and pyridine ionene polymer 51 was first formed. 51 was much less stable compared with 48, and hence isomerized to 31a and



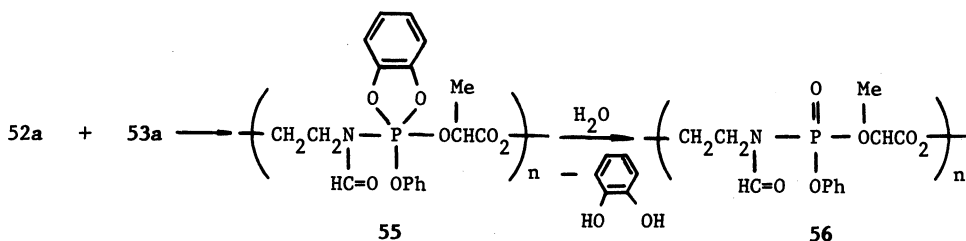
free pyridine. 31a is phosphate methyl ester and methylated pyridine to produce ionene polymer 50 as a stable product.

POLYPHOSPHORANYLATION

Polymerizations of spiro acyloxyphosphoranes mentioned above involved the ring-opening of a cyclic phosphonium zwitterion 8 by the attack of a nucleophile such as carboxylate anion onto the positively-charged carbon atom of the ethylene bridge. It is interesting, therefore, to examine chemical behavior of spiro acyloxyphosphoranes which do not allow the nucleophilic attack onto the bridge carbon. First, spiro acyloxyphosphoranes 52 were prepared, in which the attack onto carbon atoms of C(7) or C(8) is completely prohibited.

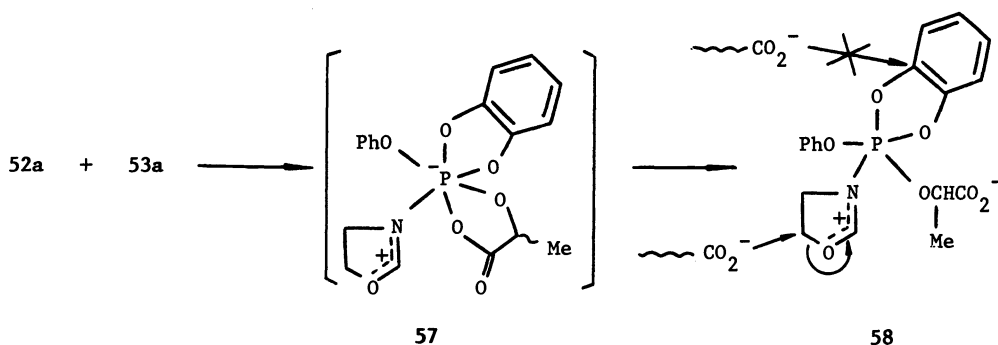


Since spiro acyloxyphosphoranes are reactive toward N-nucleophiles, copolymerizations of 52 with cyclic imino ethers such as 53 and 54 were attempted. It has been found that the copolymerization readily took place even at room temperature to give polymer 55 of phosphorane type, which was confirmed by ³¹P NMR of the reaction mixture. 55 was very sensitive toward moisture. During the work-up procedures 55 was hydrolyzed and the polymer was obtained as a form of 56. This copolymerization to produce polyphosphorane 55 was termed as Polyphosphoranylation (Ref. 29).



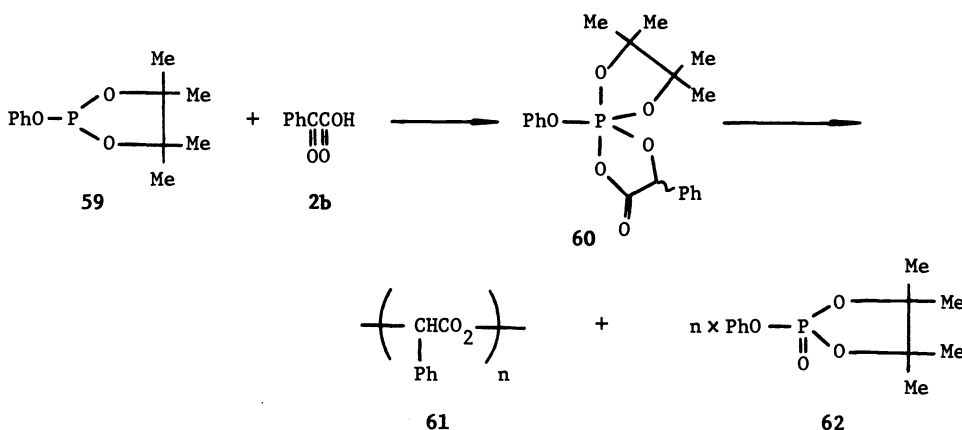
A mixture of pentaoxyphosphorane **52a** and 2-oxazoline **53a** (3.0 mmol each) in 3 ml of acetonitrile was kept at 50°C for 48 h. Then, the reprecipitation procedure of polymer was repeated three times. Polymer **56** was obtained in 72% yield (MW of **56**=4320). A similar reaction at room temperature for 58 h and work-up procedures gave **56** in 52% yield (MW of **56**=2840). Tetraoxy-(**52b**) and trioxy-phosphoranes (**52c**) were also copolymerized with **53** or 1,3-oxazine **54** to give polyphosphoranes.

In the copolymerization of **52a** with **53a** genetic zwitterion **58** is probably formed via a hexacoordinated intermediate **57**. Since the nucleophilic attack onto the aromatic carbon is impossible in **58**, carboxylate anion of another zwitterion attacks the oxazolinium ring to bring about the ring-opening as well as isomerization (Ref. 30) and gave rise to unit **55**.



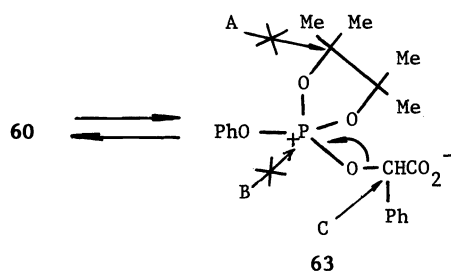
DEOXY-POLYMERIZATION

Into spiro acylpentoxyphosphorane **4b** four methyl groups were introduced to prepare **60**. The preparation of **60** was actually accomplished by the reaction of 2-phenoxy-4,4,5,5-tetra-methyl-1,3,2-dioxaphospholane **59** with phenylglyoxylic acid **2b**. The reaction of **60** in



acetonitrile at 100°C for 30 h yielded poly- α -ester **61** in 75% yield (MW of **61**=2380). During the reaction cyclic phosphate **62** was eliminated. In this polymerization the keto oxygen atom of **2b** was abstracted by **59** to yield α -ester unit **61**. Therefore, this new polymerization was called as Deoxy-polymerization (Ref. 31). This method of the preparation of poly- α -ester is compared with other methods e.g., the ring-opening polymerizations of anhydrosulphites of α -hydroxy-carboxylic acids (Ref. 32) and of intermediate α -lactones (Ref. 33).

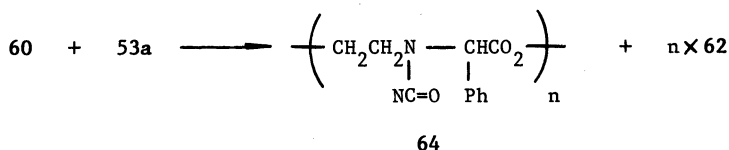
The formation of **61** is considered as follows. **60** is in equilibrium with zwitterion **63**.



Possible reaction sites of nucleophiles onto **63** are A, B, and C. The reaction at A is hindered by two methyl groups. The reaction at B is also sterically unfavored due to the presence of four methyl groups. Only C-course is possible. The carboxylate anion of zwitterions successively attacked at C and produced **61** and **62**.

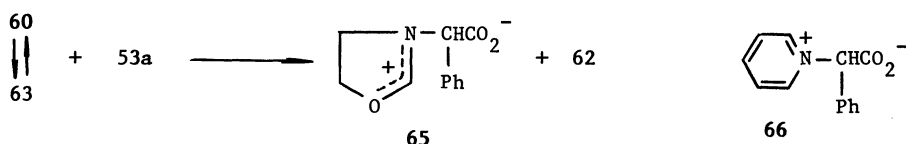
DEOXY-COPOLYMERIZATION

The fact that a nucleophile took a reaction course only at C in **63** prompted us to examine the copolymerization of **60** with cyclic imino ethers. The reaction of **60** with **53a** (3 mmol each) in acetonitrile at 50°C for 38 h produced polymer **64** in 71% yield (MW=1520). Cyclic



phosphate **62** was produced in an equal amount with unit **64**. Similar copolymerization also took place in the combination of **60** and **53b**. These reactions involve the deoxygenation of the keto oxygen atom by **59** to give α -ester unit and the copolymerization of the unit with cyclic imino ethers. Thus, Deoxy-copolymerization was suggested to name the reaction (Ref. 34).

In the deoxy-copolymerization between **60** and **53a** the first step is the formation of new zwitterion **65** and **62**. **65** was produced by the reaction of **53** probably at site C in **63** to cleave off the cyclic phosphate **62** as a good leaving group. So, **60** and/or **63** behaved as carriers of the α -ester unit in the reactions with nucleophiles. Once genetic zwitterion **65** was formed subsequent reactions led to the formation of dimeric and oligomeric zwitterions and gave macro-zwitterions of polymer **64**. As a model reaction of the copolymerization **60** was reacted with pyridine nucleophile. Then, new betaine **66** and **62** were produced in good yields.



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