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High-Molecular-Weight Poly(alkylene phosphate)s and Preparation of Amphiphilic Polymers Thereof

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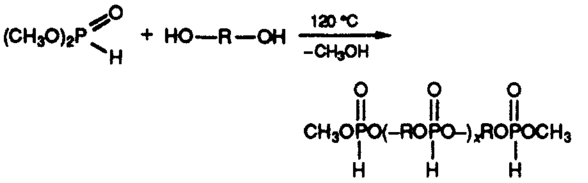
ABSTRACT: A new method of synthesis of polyphosphonates, based on transesterification of the short oligomers, ended with the methylphosphonate ester groups, afforded a series of polymers with either hydrophobic or hydrophilic chains. Thus, high-molecular-weight polymers with repeating units of desired length (i.e. $(-CH_2-)_n$) and a reactive group between them (–OP(H)(O)O–) were prepared. This function was used for further functionalization, and amphiphilic polymers were prepared with, e.g., a hydrophobic main chain and hydrophilic side chains or vice versa. Some of these polymers were shown to be able to self-organize, forming uniform spherical structures.

Introduction

In our previous papers[1,2] we described the successful preparation of high-molecular-weight poly(alkylene phosphate)s by polycondensation of dimethyl phosphonate with different diols, followed by transesterification. Thus, in the first stage, called the "low temperature stage", an excess of dimethyl phosphonate was used and short chains, with methyl ester end groups, were produced (eq 1).



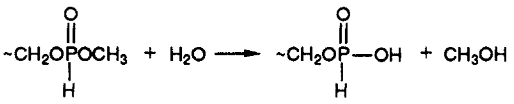
$$(CH_3O)_2P(O)H + HO{-}R{-}OH \xrightarrow[-CH_3OH]{120\,^{\circ}C} CH_3O\overset{O}{\underset{H}{P}}O(-RO\overset{O}{\underset{H}{P}}O-)_xRO\overset{O}{\underset{H}{P}}OCH_3 \qquad (1)$$

Reaction conditions are chosen in such a way (excess of dimethyl phosphonate, reaction time) that at the end of this stage the hydroxyl groups are reacted, as shown in eq 1. The polymerization degree x is in the range from 3 to 5. It is determined from the ^{31}P NMR spectra.[3]

Further transesterification, leading to high-molecular-weight products, requires higher temperatures. The same is true for the direct esterification. In the direct polyesterification process side reactions take place involving hydroxyl groups. Side reactions are eliminated in the transesterification.

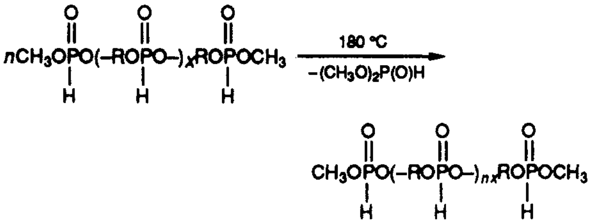
The main side reactions, proceeding with hydroxyl groups, are dehydration of the diol (eq 2) and formation of monoesters (eq 3).

$$\sim CH_2CH_2OH \longrightarrow H_2O + \sim CH{=}CH_2 \qquad (2)$$



$$\sim CH_2O\overset{O}{\underset{H}{P}}OCH_3 + H_2O \longrightarrow \sim CH_2O\overset{O}{\underset{H}{P}}{-}OH + CH_3OH \qquad (3)$$

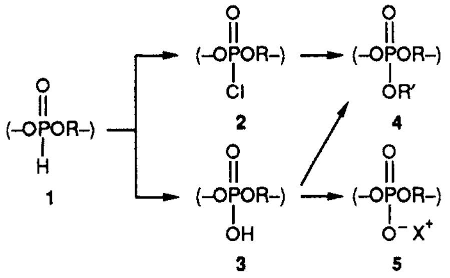
At the second stage, when a higher temperature is applied (>120 °C), the short chains (x in eq 1 from 3 to 5), formed according to eq 1, undergo a transesterification with elimination of dimethyl phosphonate (eq 4). In this way high-molecular-weight polymer is formed and side reactions are practically eliminated (for values of nx cf. Table I):



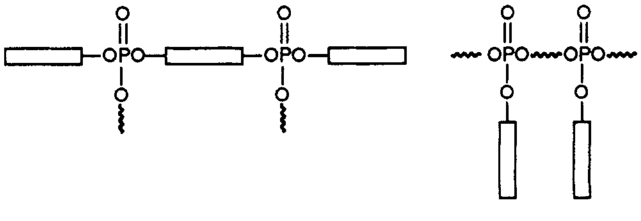
$$nCH_3O\overset{O}{\underset{H}{P}}O(-RO\overset{O}{\underset{H}{P}}O-)_xRO\overset{O}{\underset{H}{P}}OCH_3 \xrightarrow[-(CH_3O)_2P(O)H]{180\,^{\circ}C} CH_3O\overset{O}{\underset{H}{P}}O(-RO\overset{O}{\underset{H}{P}}O-)_{nx}RO\overset{O}{\underset{H}{P}}OCH_3 \qquad (4)$$

In this paper, polycondensation of dimethyl phosphonate with polymethylene diols is presented. The obtained poly(dialkyl phosphonate)s (polyphosphites) have further been converted into the corresponding poly(dialkyl phosphate)s, and the resulting polymers were characterized.

The polyphosphonates have also been used to prepare amphiphilic polymers either with a hydrophobic main chain and hydrophilic side chains or vice versa. Polymers with these structures were prepared from the corresponding polyphosphonate **1** in a two-stage process. In the first, **1** is converted into the polyphosphate **2** or **3** and in the second side groups (R′) are attached to the main chain.



An important feature of these polymers, related to phospholipids, is the exactly controlled length of hydrophobic and hydrophilic units:



where □ is a hydrophobic and ∼∼ is a hydrophilic unit.

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The phosphotriester bond stability toward hydrolysis can also be controlled by using required structures.

Experimental Part

Materials. Dimethyl phosphonate (Fluka) was purified as described previously.[1,2]

The following diols were used: 1,5-pentanediol (Aldrich), 1,6-hexanediol (Loba Chemie), 1,7-heptanediol (Aldrich), 1,8-octanediol (Fluka), 1,9-nonanediol (Aldrich), 1,10-decanediol (EGA Chemie), and 1,12-dodecanediol (Fluka). All diols were purified by vacuum distillation under reduced pressure. A small grain of sodium was added prior to distillation. Pyridine (POCh), tri-*n*-octylamine (Fluka), *n*-octyl bromide (Merck), octyl alcohol (Aldrich), epoxides (Aldrich), and diethylene glycol monomethyl ether (Aldrich) were dried and distilled before use.

Syntheses of Polymers. Polyphosphonates 1 were obtained from polycondensation of dimethyl phosphonate with corresponding diols as described in our previous papers for poly(ethylene glycol)s.[1,2]

Poly(alkylene chlorophosphate)s (2) were prepared by chlorination of 1. Dry Cl_2 was passed through a 10% solution of 1 in CH_2Cl_2 until a persistent yellow coloration appeared. Excess Cl_2 was then removed under vacuum until a colorless solution resulted. Solutions of 2 were used without polymer isolation.

Polyphosphates 3 were prepared by oxidation of 1. Dry N_2O_4 was passed through the 10% solution of 1 in CH_2Cl_2 at −15 °C until a persistent yellow coloration appeared. Then, the reaction mixture was kept for 24 h at room temperature. Product **3** precipitated gradually from the solution. After separation, **3** was washed several times with CH_2Cl_2 and *i*-PrOH and then dried under vacuum.

Polyphosphate 4-1. To a 20% solution of poly(chlorophosphate) **2** (R = PEG 200) in CH_2Cl_2 was added dropwise at 0 °C a solution of nonanol-1 and pyridine in CH_2Cl_2 (~20% solution), and the reaction mixture was kept for 24 h at 0 °C. Alcohol and pyridine were used in 10% excess. Pyridinium hydrochloride was removed by filtration, the filtrate, containing **4-1**, was concentrated to half of its original volume, and **4-1** was precipitated to 1:1 (vol) with a petroleum ether/C_6H_6 mixture. **4-1** was purified by dialysis in an EtOH/H_2O (1:1) system, until no more Cl^- was present (according to the $AgNO_3$ test).

Polyphosphates 4-2, 4-4, 4-6, and 4-7 were prepared in a manner similar to that described for **4-1**.

Polyphosphate 4-3. A sample of polyphosphate **3** was placed in a vacuum ampule. CH_2Cl_2 and a 5-fold excess of epoxide (ethylene, propylene, or 1,2-butylene oxide) were distilled into the ampule (CH_2Cl_2 to epoxide (v/v) ratio was equal to 1). The reaction mixture was kept for 48 h at 25 °C. During that time polymer **4-3** dissolved. At the end of the reaction CH_2Cl_2 and unreacted epoxide were removed in vacuo, and the polymer was dissolved in water and purified by dialysis in H_2O.

Polyphosphates 4-5, 4-8, and 4-9 were prepared in a manner similar to the synthesis of **4-3**.

Polyphosphate 5-1 was obtained by neutralization of polyphosphate **3** (R = PEG 600) with tri-*n*-octylamine in ethanol solution.

Polyphosphate 5-2 was prepared by neutralization of the polyacid **3** (R = PEG 600) with tetra-*n*-octylammonium hydroxide. Tetra-*n*-octylammonium hydroxide was obtained by quaternization of tri-*n*-octylamine with *n*-octyl bromide in boiling acetone in the presence of NaI.

$$n\text{-}C_8H_{17}Br + N(n\text{-}C_8H_{17})_3 + NaI \rightarrow (n\text{-}C_8H_{17})_4N^+I^- + NaBr$$

Tetra-*n*-octylammonium iodide was converted into the corresponding free hydroxide by passing an ethanol solution of the iodide through an anion-exchange resin Zerolit KMP (BDH).

Measurement. ^{31}P (81 MHz), ^{13}C (50 MHz), ^{1}H NMR (200 MHz) spectra were recorded with a Bruker AC 200 spectrometer. Molecular weights of polymers were measured by using a Hewlett-Packard 502 high-speed membrane or a Hewlett-Packard 302B vapor pressure osmometer. DSC diagrams were registered on a DSC V4.05 Du Pont 2000 apparatus. The optical microscopy observations were done using a CARL ZEISS JENA microscope.

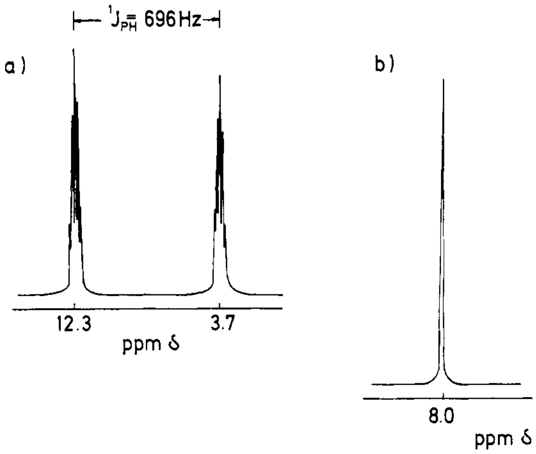


Figure 1. ^{31}P NMR (a) and $^{31}P\{^1H\}$ NMR (b) spectra of poly(decamethylene phosphonate) (1, x = 10) in $CDCl_3$.

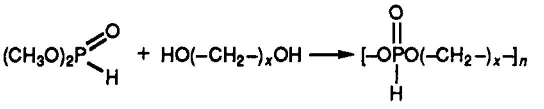
Table I
$\bar{M}_n$(vpo), η_{sp}, Chemical Shifts, and Coupling Constants in the ^{31}P NMR Spectra for Polyphosphonates 1

			^{31}P NMR[c]	
$(-CH_2-)_x$ x	$\bar{M}_n$ (osm)[a] in CH_2CH_2	η_{sp}[b]	δ, ppm	$^1J_{P-H}$, Hz
5	14 100	0.27	7.9	696
6	28 000	0.9	7.8	688
7	9 300	0.24	7.9	
8	13 100	0.27	7.9	697
9	9 700	0.34	7.8	
10	10 200 (21 300)	0.41	8.0	696, 699
12	9 900 (15 200)	0.25	7.8	691

[a] $\bar{M}_n$ corresponding to η_{sp} are given, except for values in parentheses. [b] Measured for 1% solutions in CH_2Cl_2, at 25 °C in an Ubelohde viscometer filled in vacuo. [c] Spectra recorded on a Bruker 200-MHz spectrometer for approximately 5% solutions in $CDCl_3$.

Results and Discussion

Synthesis of Polyphosphonates from Polymethylene diols (Poly(polymethylene phosphonate)s). Polyphosphonates of polymethylene diols were prepared in the two-stage polycondensation of dimethyl phosphonate with a selection of diols as described in eq 5, where x = from 2 to 10 and 12.



$$(CH_3O)_2P(=O)H + HO(-CH_2-)_xOH \longrightarrow [-OP(=O)(H)O(-CH_2-)_x-]_n \quad (5)$$

1

In the reaction of dimethyl phosphonate with ethylene glycol (x = 2) cyclic phosphonate and linear oligomers are obtained.[4] Condensation of 1,3-propanediol with dimethyl phosphonate leads almost exclusively to cyclic 2-hydro-2-oxo-1,3,2-dioxaphosphorinane.[5] In the case of 1,4-butanediol, under least at the applied conditions, the main reaction was formation of THF, in agreement with earlier observations of Vogt et al.[6] Higher diols (x = from 5 to 10 and 12) gave high-molecular-weight products. The high polymers are colorless solid materials. We observed that poly(alkylene phosphonate)s are hydrolytically unstable products. Thus, purification of the polymers at this stage and all measurements ($\bar{M}_n$, η, NMR spectra) require the use of anhydrous solvents. The ^1H, ^{31}P, and ^{13}C NMR spectra clearly indicate the structural uniformity of the polyphosphonates 1.

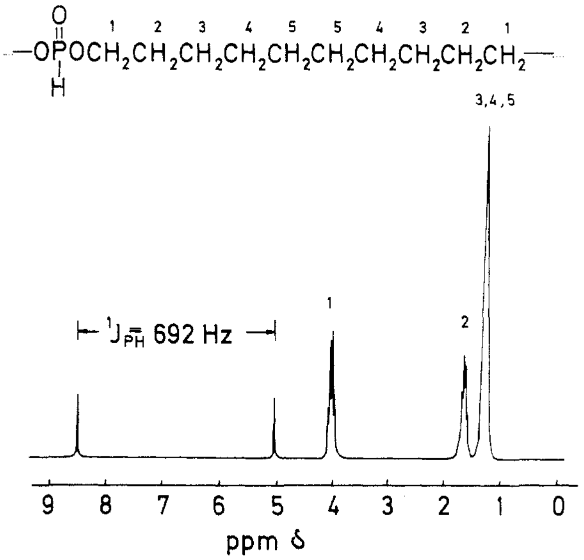


Figure 2. ^{1}H NMR spectrum of poly(decamethylene phosphonate) (1, $x = 10$) in $CDCl_3$.

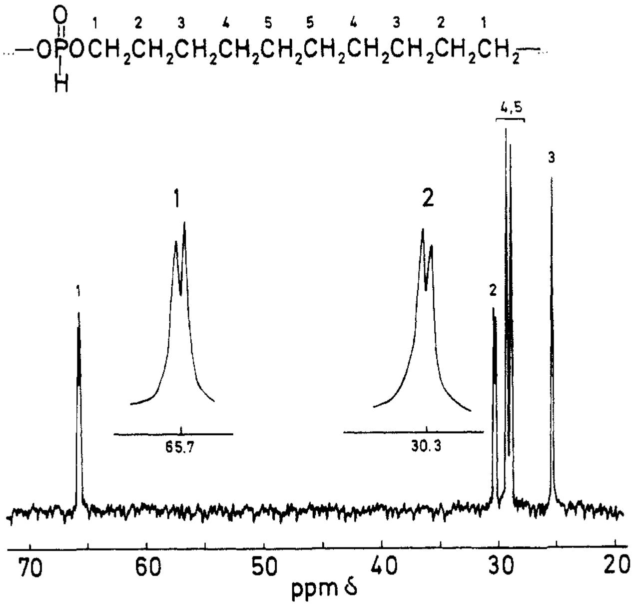
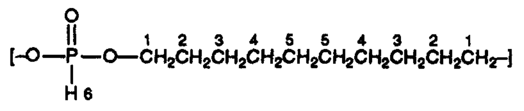


Figure 3. $^{13}C\{^1H\}$ NMR spectrum of poly(decamethylene phosphonate) (1, $x = 10$) in $CDCl_3$.

NMR Spectra of Poly(decamethylene phosphonate). In the ^{31}P NMR spectra of polyphosphonates 1 there are two quintets reduced to one sharp signal after decoupling from ^1H ($^{31}P\{^1H\}$ NMR). As an example the ^{31}P NMR spectrum of poly(decamethylene phosphonate) is shown in Figure 1.

Chemical shifts and coupling constants of selected polymers are given in Table I together with their specific viscosities, and $\bar{M}_n$.

Figures 2 and 3 show ^1H and ^{13}C NMR spectra of poly(decamethylene phosphonate), taken as a typical example of 1.



$$[-O-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle H6}{|}}{P}}-O-\overset{1}{CH_2}\overset{2}{CH_2}\overset{3}{CH_2}\overset{4}{CH_2}\overset{5}{CH_2}\overset{5}{CH_2}\overset{4}{CH_2}\overset{3}{CH_2}\overset{2}{CH_2}\overset{1}{CH_2}-]$$

1 ($x = 10$)

In the NMR spectra the following signals were observed. ^1H NMR: δ 1.27 (m, H_3, H_4, H_5), 1.66 (m, H_2), 4.01 and 4.05 (two t, H_1; $^3J_{PH} = 7.7$ Hz, $^3J_{HH} = 6.8$ Hz), 6.78 (d, H_6, $^1J_{PH} = 692.3$ Hz). $^{13}C\{^1H\}$ NMR: δ 25.41 (s, C_3), 29.01 and 29.31 (two s, C_4 and C_5), 30.34 (d, C_2, $^3J_{PC} = 5.5$ Hz), 65.72 (d, C_1, $^2J_{PC} = 5.3$ Hz). The assignments of the chemical shifts of carbon atoms for polymers have been based on the data published by Stothers[7] for the corresponding diols.

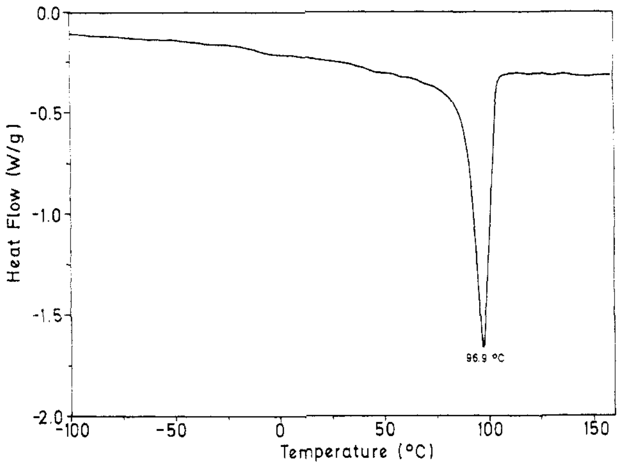


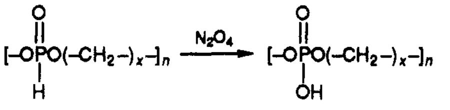
Figure 4. DSC thermogram of poly(decamethylene phosphate) (3, $x = 10$).

Table II
Values of T_g and T_m and the Elementary Analysis Data for Polyphosphates 3

			elemental analysis					
			theory, %			found, %		
$(-CH_2-)_x$ x	T_g, °C	T_m, °C	C	H	P	C	H	P
5			36.2	6.6	18.7	35.8	6.8	18.1
6	−20 to −6	68	40.0	7.2	17.2	39.0	7.2	16.1
7		65	43.3	7.7	16.0	41.9	7.8	15.2
8	−11 to −0.3	83	46.2	8.2	14.9	45.3	8.2	14.6
9	−35 to −31	78	48.6	8.6	13.9	47.5	8.6	13.5
10	−8 to −4	97	50.8	8.9	13.1	49.4	8.8	12.5
12[a]	−17 to −9	102	54.5	9.5	11.7	52.6	9.4	11.5

[a] Poly(dodecamethylene phosphate) has previously been prepared in the other laboratory.[9] A $\bar{M}_n$ of 1100 and $T_m = 40$ °C were reported. It was also claimed that this polymer exhibits LC properties.

Oxidation of Polyphosphonates into Polyphosphates. The polyphosphonates described in the previous section (eq 5) were converted into the corresponding polyphosphates using N_2O_4 in CH_2Cl_2 solution as an oxidizing agent.[8]



$$[-O\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle H}{|}}{P}}O(-CH_2-)_x-]_n \xrightarrow{N_2O_4} [-O\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle OH}{|}}{P}}O(-CH_2-)_x-]_n \qquad (6)$$

1 3

The resulting polyphosphates 3 precipitate from the reaction mixture.

Properties of Poly(polymethylene phosphate)s. Polyphosphates 3 are white, sparingly soluble powders. They were soluble in ethanol and butanol at 70 °C and are soluble in water when converted into salt forms. The melting and glass temperatures were measured by DSC, and Figure 4 shows a typical DSC graph of poly(decamethylene phosphate) (3; $x = 10$).

A summary of glass and melting temperatures, and the results of the elementary analysis are given in Table II.

All of the polyphosphates 3 collected in Table II show crystalline properties. A film of poly(decamethylene

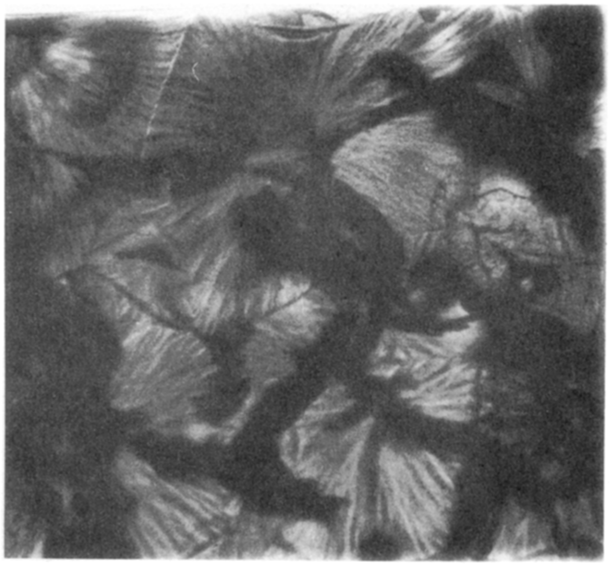


Figure 5. Spherolitic structures observed in crystalline poly(decamethylene phosphate).

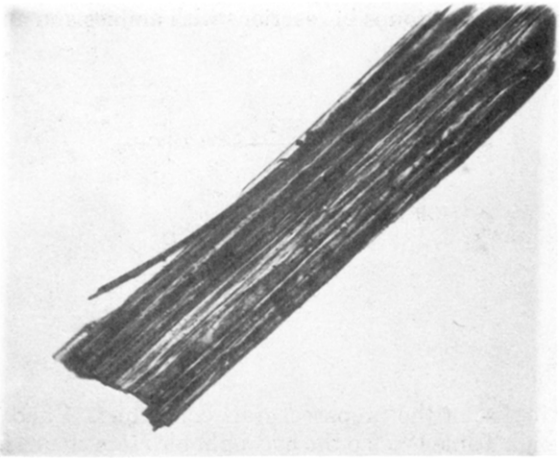
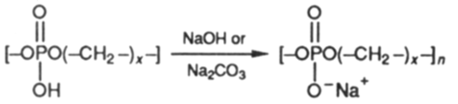


Figure 6. Oriented crystalline structure formed when the poly(decamethylene phosphate) sample was drawn from the melt.

phosphate) (**3**; $x = 10$), cast at 40 °C from ethanol solution, has clearly visible spherulites (Figure 5). The same sample gives an oriented structure when drawn from a melt (Figure 6).

The polyphosphates **3**, except **3** for which $x = 5$, are hydrophobic, apparently due to the association of the phosphate groups; however, these polymers are soluble in water, as indicated above, after conversion into the corresponding polysalts. Poly(pentamethylene phosphate) (**3**; $x = 5$) swells slowly in H_2O. It forms a gel-like material, after absorbing up to 1000% of H_2O and eventually it produces a metastable water solution.

Salts of Poly(polymethylene phosphate)s. Salts of polyphosphates were obtained by neutralization of the ethanol solution of the respective polyacids with Na_2CO_3 or NaOH. Excess base was removed by dialysis.



$$[-O\overset{\overset{O}{\|}}{\underset{\underset{OH}{|}}{P}}O(-CH_2-)_x-] \xrightarrow[Na_2CO_3]{NaOH\ or} [-O\overset{\overset{O}{\|}}{\underset{\underset{O^-Na^+}{|}}{P}}O(-CH_2-)_x-]_n \qquad (7)$$

3 **5**

The $\bar{M}_n$'s of polysalts **5** were measured osmometrically in 0.1 N NaCl solution. The $\overline{DP}_n$'s of polysalts were found to be very close to the $\overline{DP}_n$ of the starting polyphosphonates **1** (cf. Table III). In the ^{31}P NMR spectra of polysalts **5** signals related to the P–H group are absent. In $^{31}P\{^1H\}$ NMR spectra of polyphosphates **5** there is only one sharp signal at δ 0.0–1.0 ppm, which is slightly broadened in the ^{31}P NMR spectra. The $^1H\{^{31}P\}$ NMR spectrum of **5** is similar to the spectrum of **1** but the P–H doublet is absent. $^{13}C\{^1H\}$ NMR spectra of polysalts **5** are identical to the $^{13}C\{^1H\}$ NMR spectra of the corresponding **1**. Figure 7 shows a $^{13}C\{^1H\}$ NMR spectrum of the sodium salt of poly(decamethylene phosphate) (**5**; $x = 10$).

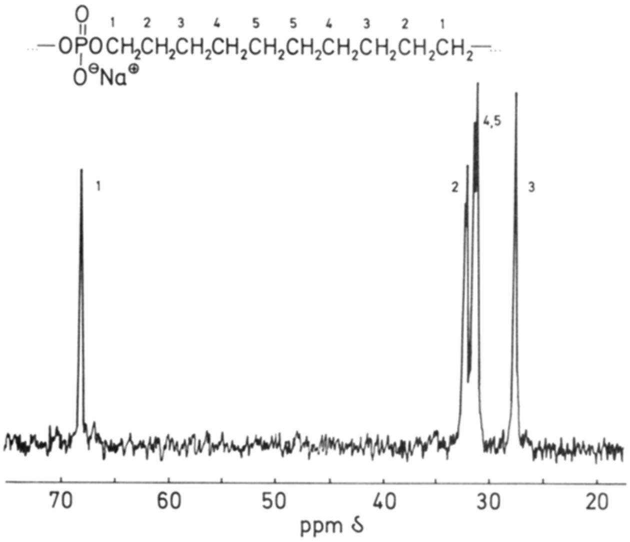
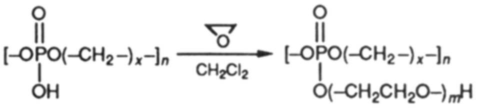


Figure 7. $^{13}C\{^1H\}$ NMR spectrum of poly(decamethylene phosphate) sodium salt (**5**, $x = 10$) in D_2O.

Reaction of Polyacids with Epoxides. Preparation of Graft Copolymers with Hydrophilic Side Chains. This reaction, converting polyacids into the electrically neutral products, allowed also the $\bar{M}_n$ of the polyacids to be checked, since it is known that $\bar{M}_n$ of polyelectrolytes, measured by osmometry, may provide erratic results.

Addition of ethylene oxide has been shown to be a quantitative process:



$$[-O\overset{\overset{O}{\|}}{\underset{\underset{OH}{|}}{P}}O(-CH_2-)_x-]_n \xrightarrow[CH_2Cl_2]{\triangledown_{O}} [-O\overset{\overset{O}{\|}}{\underset{\underset{O(-CH_2CH_2O-)_mH}{|}}{P}}O(-CH_2-)_x-]_n \qquad (8)$$

3 **4** ($m = 1, 2$)

As it has been shown in our laboratory, higher values of m can be obtained if an external acid is used as catalyst. In its absence oxyethylation stops when all of the acidic groups are consumed. This is because addition of an epoxide to the P–OH groups proceeds only when acid is present as a catalyst.[10,11]

Reaction of **3** with ethylene oxide was carried out in a heterogeneous system, namely in CH_2Cl_2 at 25 °C. A 5-fold excess of the epoxide was used. Reaction products **4** are soluble, complete conversion of the acidic groups is observed, and no side reactions are detected. This is evidenced from ^1H, ^{13}C, and ^{31}P NMR spectra. The length of the side chains (m in eq 8) was calculated on the basis of the integration ratio of the corresponding signals in the ^1H NMR spectrum. Figure 8 shows the $^{13}C\{^1H\}$ NMR spectrum of polyester **4** ($x = 10$) where the assignments are given directly in the figure.

$\bar{M}_n$'s of polymers prepared in the following reaction course, polycondensation → oxidation → esterification,

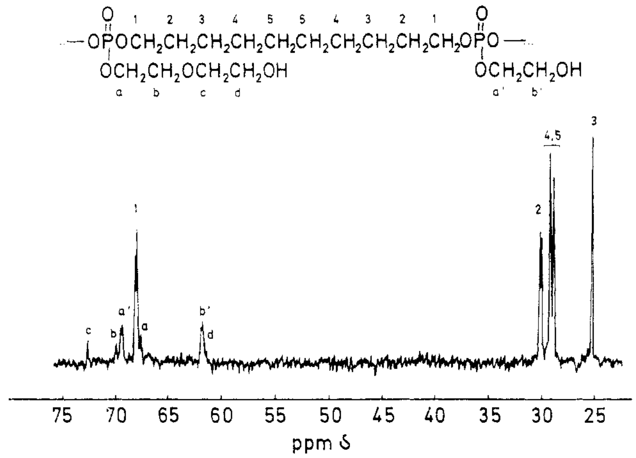
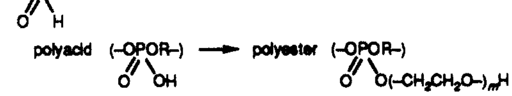
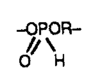
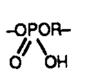
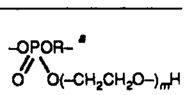


Figure 8. $^{13}C\{^1H\}$ NMR spectrum of poly(decamethylene phosphate) poly(hydroxyethylene) ester (4, $x = 10$) in $CDCl_3$.

Table III
$\overline{M}_n$ and $\overline{DP}_n$ of Polymers, Prepared in the Following Reaction Sequence



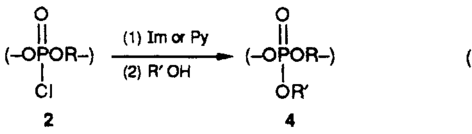
					 [a]	
R	$\bar{M}_n$(osm)	$\overline{DP}_n$	$\bar{M}_n$(osm)[b]	$\overline{DP}_n$	$\bar{M}_n$(osm)	$\overline{DP}_n$
$(-CH_2-)_5$	6 300	42	7800	47	8 200	37
$(-CH_2-)_8$	8 500	44	7750	37	7 600	30
$(-CH_2-)_9$	9 700	45	9500	41	8 300	30
$(-CH_2-)_{10}$	10 200	44	8000	32	13 200	44
	14 000	86	15000	84	16 200	70
$(-CH_2CH_2O-)_4$	12 700	57	14700	61	15 000	51
PEG 200[c]	12 500	51	9500	36	15 000	46

[a] $m = 1, 2$. [b] $\bar{M}_n$ measured in 0.1 N NaCl solution. [c] PEG 200 = poly(ethylene glycol) 200.

are presented in Table III. A slight decrease of $\overline{DP}_n$ results from the series of reactions leading to the oxyethylated polytriesters with oxyethylene units in the side chain.

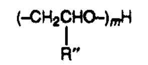
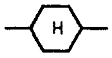
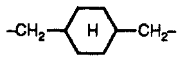
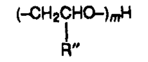
Synthesis of Amphiphilic Graft Copolymers with Poly(alkylene phosphate) Backbones. As it has already been mentioned in the Introduction, amphiphilic polyphosphates with a graft copolymer structure were prepared by transformation of the poly(alkylene chlorophosphate)s (2) and polyacids (3). 2 and 3 were obtained in the reaction of polyphosphonates 1 with Cl_2 and N_2O_4, respectively.[8,12]

Reactions with Poly(alkylene chlorophosphate)s (2). 2 were prepared from parent 1 by chlorination in CH_2Cl_2 solvent, as was described by us previously.[12] The P–Cl bonds in 2 reacted with corresponding alcohols in the presence of imidazole (Im) or pyridine (Py) (eq 9):



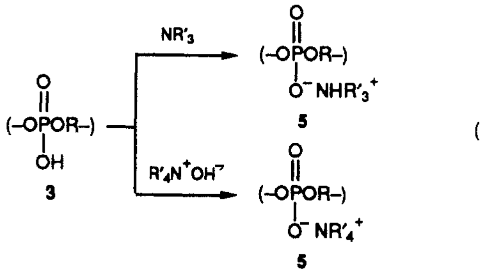
(9)

Table IV
List of the Prepared Graft Copolymers of the General Formula (–OP(O)(OR′)OR–)

	R	R′		no.
A	PEG 200[a]	$-n\text{-}C_9H_{19}$		**4-1**
	PEG 300	$-n\text{-}C_{16}H_{33}$		**4-2**
	PEG 200	 $(-CH_2\underset{R''}{CH}O-)_mH$	R″ = H, CH₃, C₂H₅ $\overline{m}$ = 1, 2	**4-3**
	PEG 600	$-^+NH(n\text{-}C_8H_{17})_3$		**5-1**
		$-^+N(n\text{-}C_8H_{17})_4$		**5-2**
B	$(-CH_2-)_6$	$-n\text{-}C_4H_9$		**4-4**
		$(-CH_2CH_2O-)_mH$	$\overline{m} = 1, 2$	**4-5**
		$(-CH_2CH_2O-)_{17}CH_3$		**4-6**
	$(-CH_2-)_{10}$	$(-CH_2CH_2O-)_2CH_3$		**4-7**
		$(-CH_2CH_2O-)_mH$	$\overline{m} = 1, 2$	**4-8**
		 $(-CH_2\underset{R''}{CH}O-)_mH$	R″ = H, CH₃ $\overline{m}$ = 1, 2	**4-9**

[a] PEG = poly(ethylene glycol). A, B = the backbones are hydrophilic and hydrophobic, respectively.

Reaction with Polyacids. Polyphosphates 3 give polyesters 4 in reaction with epoxides (ethylene, propylene, 1,2-butylene oxide) (eq 8) and polysalts (5) with long alkylene side groups in reactions with amines and amine hydroxides (eq 10).

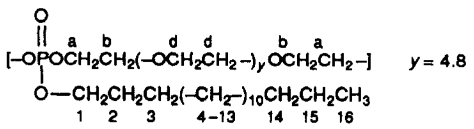


(10)

The list of the prepared graft copolymers 4 and 5 is given in Table IV. To the hydrophobic main chains have been attached hydrophilic side chains, whereas hydrophobic side chains have been attached to the hydrophilic backbones.

Polymers 4 and 5 were characterized by ^1H, ^{13}C, ^{31}P NMR spectroscopy. No defects were introduced during conversion of polyphosphonates 1 into polyphosphates 4 and 5. The ^{13}C NMR spectra of polymers 4-7 and 5-2 are presented as examples in Figures 9 and 10.

NMR Spectra. Chemical shifts in ^1H, ^{31}P, and ^{13}C NMR spectra of polymers 4-2, 5-2, and 4-7 are given below. Groups of atoms in the repeating unit of polymer 4-2, taken as an example, have been marked as follows:



$$[-O\overset{O}{\underset{O-\underset{1}{CH_2}\underset{2}{CH_2}\underset{3}{CH_2}(\underset{4-13}{-CH_2-})_{10}\underset{14}{CH_2}\underset{15}{CH_2}\underset{16}{CH_3}}{P}}O\overset{a}{CH_2}\overset{b}{CH_2}(-O\overset{d}{CH_2}\overset{d}{CH_2}-)_yO\overset{b}{CH_2}\overset{a}{CH_2}-] \qquad y = 4.8$$

4-2

In the ^{31}P NMR spectrum of 4-2 there is only one signal at $\delta = -1.81$ ppm. In ^1H NMR and ^{13}C NMR the following chemical shifts and multiplicities were observed. ^1H NMR: δ 0.83 (t, H_{16}, $^3J_{HH} = 5.6$ Hz), 1.21 (m, H_3–H_{15}), 1.62 (m, H_2), 3.59 (m, H_d), 3.65 (m, H_b), 3.98 and 4.00 (two t, H_1, $^3J_{PH} = 6.7$ Hz, $^3J_{HH} = 6.6$ Hz), 4.12 (m, H_a). ^{13}C NMR: δ 14.08 (s, C_{16}), 22.67 (s, C_{15}), 25.46 (s, C_3), 29.20–29.69 (m, C_4–C_{13}), 30.29 (d, C_2, $^3J_{PC} = 7.5$ Hz), 31.92 (s, C_{14}), 66.59 (d, C_a, $^2J_{PC} = 6.7$ Hz), 68.05 (d, C_1, $^2J_{PC} = 6.3$

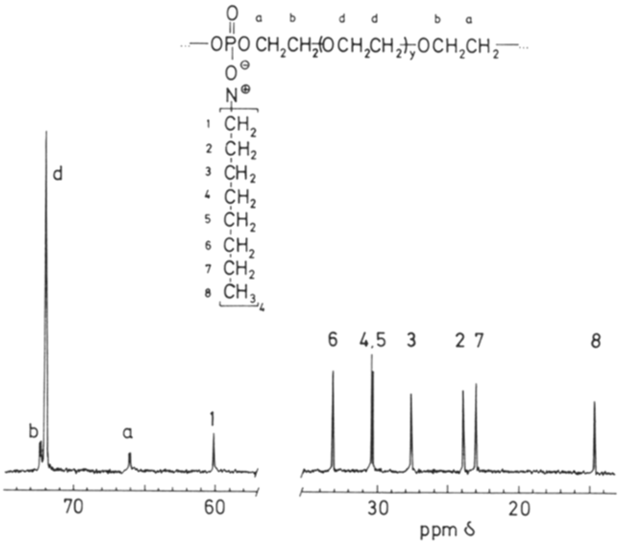
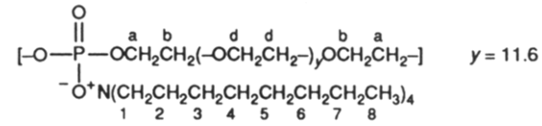


Figure 9. $^{13}C\{^1H\}$ NMR spectrum of polysalt **5-2** in CD_3OD.

Hz), 70.55 (d, C_b, $^3J_{PC}$ = 8.1 Hz), 70.61 (s, C_d).

The repeating unit of polymer **5-2** is



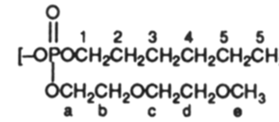
$$\left[-O-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle {}^{-}O^{+}N(\overset{1}{C}H_2\overset{2}{C}H_2\overset{3}{C}H_2\overset{4}{C}H_2\overset{5}{C}H_2\overset{6}{C}H_2\overset{7}{C}H_2\overset{8}{C}H_3)_4}{|}}{P}}-O\overset{a}{C}H_2\overset{b}{C}H_2(-O\overset{d}{C}H_2\overset{d}{C}H_2-)_yO\overset{b}{C}H_2\overset{a}{C}H_2-\right] \quad y = 11.6$$

5-2

In NMR spectra of **5-2** there are the following signals. $^{31}P\{^1H\}$ NMR: singlet at δ −1.00 ppm. ^1H NMR: δ 0.66 (s, H_8), 1.07–1.15 (m, H_3–H_7), 1.42 (s, H_2), 2.94 (s, H_1), 3.41 (s, H_d), 3.76 (s, H_b), 3.95 (s, H_a). $^{13}C\{^1H\}$ NMR: (Figure 9) δ 14.66 (s, C_8), 23.05 (s, C_7), 23.93 (s, C_2), 27.62 (s, C_3), 30.35 and 30.41 (two signals, C_4, C_5), 33.1 (s, C_6), 60.00 (s, C_1), 65.92 (d, C_a, $^2J_{PC}$ = 6.7 Hz), 71.89 (s, C_d), 72.23 (d, C_b, $^3J_{PC}$ = 8.1 Hz).

Polyphosphonate **1** (R = PEG 600) with $\bar{M}_n$ = 11 800 ($\overline{DP}_n$ = 18) was a starting material for polymer **5-2** ($\bar{M}_n$ = 18 600, $\overline{DP}_n$ = 16.5). According to the NMR spectra polysalt **5-2** includes no structural errors.

The repeating unit of polyester **4-7** has the following structure:



$$\left[-O\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O\overset{a}{C}H_2\overset{b}{C}H_2O\overset{c}{C}H_2\overset{d}{C}H_2O\overset{e}{C}H_3}{|}}{P}}O\overset{1}{C}H_2\overset{2}{C}H_2\overset{3}{C}H_2\overset{4}{C}H_2\overset{5}{C}H_2\overset{5}{C}H_2\overset{4}{C}H_2\overset{3}{C}H_2\overset{2}{C}H_2\overset{1}{C}H_2-\right]$$

4-7

The following chemical shifts are observed in NMR spectra of **4-7**. $^{31}P\{^1H\}$ NMR: δ = −2.01 (s). ^1H NMR: δ 1.22 (one signal, H_3–H_5), 1.60–1.63 (m, H_2), 3.31 (s, H_e), 3.46–3.54 (m, H_d), 3.58–3.72 (m, H_c, H_b), δ 3.94–4.00 (m, H_1), 4.07–4.13 (m, H_a). $^{13}C\{^1H\}$ NMR: (Figure 10) δ 25.49 (s, C_3), 29.21 and 29.51 (two peaks, C_4, C_5), 30.33 (d, C_2, $^3J_{PC}$ = 6.6 Hz), 59.08 (s, C_e), 66.48 (d, C_a, $^2J_{PC}$ = 5.2 Hz), 67.85 (d, C_1, $^2J_{PC}$ = 5.8 Hz), 70.15 (d, C_b, $^3J_{PC}$ = 6.9 Hz), 70.61 (s, C_c), 71.95 (s, C_d).

The starting material **1** (R = $(-CH_2-)_{10}$), $\bar{M}_n$ = 14 700 ($\overline{DP}_n$ = 67), has been used to prepare polymer **4-7**, $\bar{M}_n$ = 19 500 ($\overline{DP}_n$ = 58).

Several amphiphilic polymers, obtained as described above, have been used to prepare microspheres (plain or hollow).

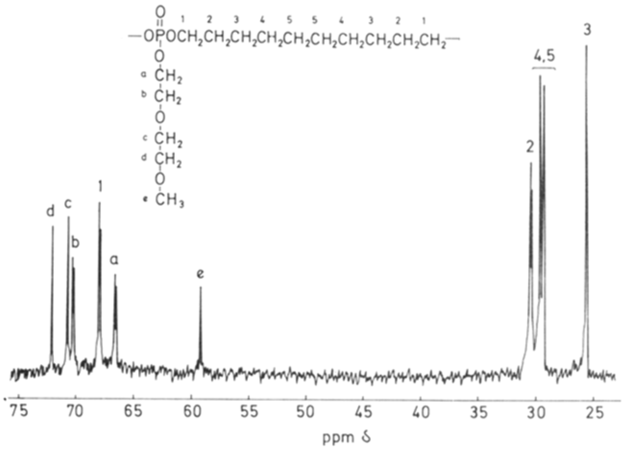


Figure 10. $^{13}C\{^1H\}$ NMR spectrum of polyester **4-7** in $CDCl_3$.

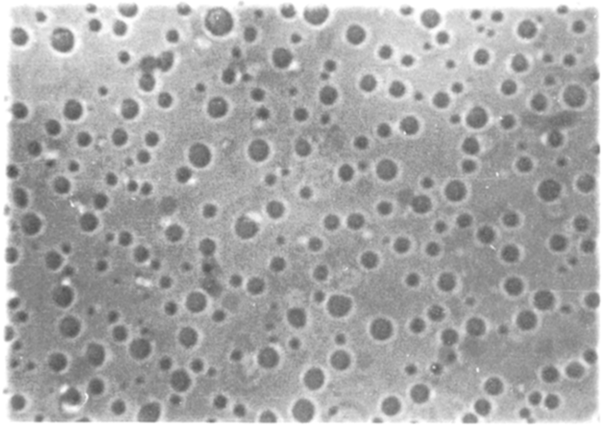


Figure 11. Self-organized microspheres prepared from the amphiphilic polymer **4-7**. The length of 5.5 mm in this figure corresponds to 10 μm in reality.

Polymers from amphiphilic polyphosphates **5-2** and **4-7** self-organize into microspheres when precipitated from the ethanol solution into water. Microspheres are visible in the optical microscope, and the water suspension of microspheres is stable for several months. In Figure 11 the photograph of microspheres prepared from polyester **4-7** and immobilized in the agar carrier is shown.

The self-organizing ability indicates that the core of the spheres is composed of the interpenetrating hydrophobic and hydrophilic domains or of the multilayer micellar structures with hydrophobic and hydrophilic layers. These structural problems and the ability of the here-described amphiphilic polymers to self-organize as the function of the length of the hydrophobic and hydrophilic segments will be published elsewhere.

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