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Inverse Micellar Catalysis of Phosphorylation of Hydroxybenzylated Polyethylenimines

E. P. Zhil'tsova, L. A. Kudryavtseva, G. A. Gainanova,
A. P. Timosheva, S. S. Lukashenko, and A. I. Konovalov

Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center,
Russian Academy of Sciences, Kazan, Tatarstan, Russia

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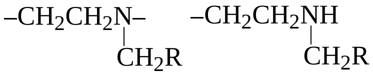
Abstract—The aggregation in polyethylenimine–chloroform and cetyltrimethylammonium bromide–polyethylenimine–chloroform systems is studied by dielcometric titration. Inverse micelles of cetyltrimethylammonium bromide catalyze the phosphorylation of hydroxybenzylated polyethylenimines in chloroform. The dependence of parameters of the micelle-catalyzed reaction on the structure and concentration of polyethylenimine and on the reaction temperature is studied. The inverse micelles affect the complexation of polyethylenimines with 4-nitrophenol.

An interest in systems based on polymers and surfactants is caused by their practical and theoretic importance. These systems are used in production of detergents, in cosmetic industry, and in the regeneration of oils. Furthermore, polymer-micellar solutions can serve as models of biological binding with the participation of biomembranes [1]. As a rule, studies in the field of polymer–colloid solutions concern the nature and structure of the associates. It was found that the polymer–micelle interaction depends on the structure of the polymer and on the chemical nature, geometry, and charge of the surfactant [1]. The presence of polymers in micellar solutions may affect the characteristics of micellar systems (critical micellization concentration, aggregation number, shape of aggregates), as well as the solubilizing power of micelles [1, 2]. At the same time, it is poorly understood how the formation of the polymer–micelle complex affects the reactivity of the polymer. Published papers in this field, as a rule, deal with aqueous solutions. For example, the effect of stuctural and concentration factors on the hydrolysis of phosphorus acid esters in the cationic surfactant–polyethylenimine–water system was examined in [3–7]. The dependence of the catalytic activity of the polymer–colloid complexes on their size, shape, and structure was revealed [7].

Our previous studies of phosphorylation of alkylated polyethylenimine in toluene micellar solutions of poly(ethylene glycol)-600 monolaurate showed that inverse micelles of a nonionic surfactant may both catalyze and inhibit this process, depending on the relative content of surfactant and polyethylenimine in solution [3].

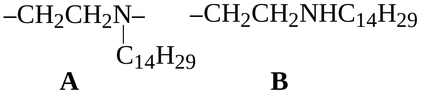
In this study we examined the effect of inverse micelles of a cationic surfactant, cetyltrimethylammonium bromide **I**, in chloroform on the reaction of 4-nitrophenyl bis(chloromethyl)phosphinate **II** with branched polyethylenimines **III**–**VI** containing *o*-hydroxybenzyl substituents at the tertiary and secondary nitrogen atoms.



$$-CH_2CH_2N(CH_2R)- \qquad -CH_2CH_2NH(CH_2R)$$

R = C_6H_4OH-*o* (**III**), C_6H_3(OH-*o*)(*i*-C_9H_{19}-*p*) (**IV**–**VI**).

The mean molecular mass of the monomeric unit of hydroxybenzylated polyethylenimines **III**–**VI** was 88, 77, 88, and 125, respectively. An increase in the molecular mass of the monomeric unit in the series **IV**–**VI** is indicative of an increase in the degree of substitution of the polymers. On the average, in **IV**–**VI** there was 0.12, 0.16, and 0.3 hydroxybenzylated fragment per unsubstituted monomeric fragment. The degree of substitution in **III** was 0.3. In alkylated polyethylenimine **VII** used for comparison and containing fragments **A** and **B** shown below, the molecular mass of the monomeric unit was 150, and the degree of substitution was 0.45.



$$-CH_2CH_2N(C_{14}H_{29})- \qquad -CH_2CH_2NHC_{14}H_{29}$$

A **B**

Micelle-forming properties of compound **I** in chloroform were studied previously by dielcometric

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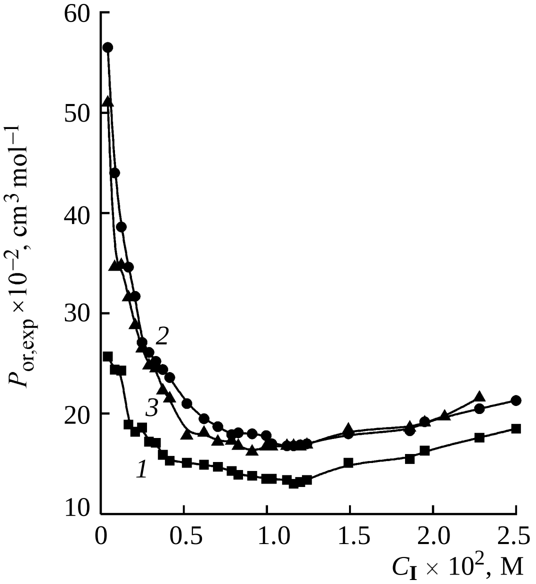

Fig. 1. Orientational polarization of cetyltrimethylammonium bromide solitions in chloroform (*1*) in the absence and (*2, 3*) in the presence of polyethylenimines (*2*) **III** and (*3*) **V**; 20°C, C_{PEI} 0.01 M.

titration and the kinetic method [8]. Formation of micellar aggregates of **I** in chloroform at 20–50°C proceeds in the concentration range 0.003–0.015 M. The aggregation behavior of **I** in the presence of polyethylenimines was studied by the dielcometric method. Figure 1 shows the concentration dependence of the orientational polarization ($P_{or,exp}$) of solutions of **I** in the absence and in the presence of **III** and **V**. In all the cases, in the initial part of the curve an increase in the concentration of **I** causes a decrease in the orientational polarization, which is followed by a flat minimum in the concentration range 0.003–0.005 M and certain increase beginning from the concentration of 0.012 M. Such a pattern, according to [9], is attributable to the formation of micellar aggregates and reconstruction of their structure at higher concentrations of the surfactant.

Inverse micelles of **I** formed in chloroform affect the reactivity of polyethylenimines toward phosphorus acid esters. The mechanism of nucleophilic substitution was studied by UV and ^{31}P NMR spectroscopy. Elimination of 4-nitrophenol, detected spectrophotometrically in the reactions of **III**–**VI** with phosphinate **II**, suggests the formation of phosphorylated polyethylenimines. However, polymers **III**–**VI** contain two functional groups, NH and phenolic hydroxyl, reactive toward **II**, and the reaction may occur at both reaction centers. ^{31}P NMR data show that the product formed by phosphorylation of polyethylenimines **III**–**VI** is characterized by the signals at 22.7, 22.9, 22.3, and 23.9 ppm, respectively. The product of phosphorylation of alkylated polyethylenimine **VII** containing no OH groups gives in chloroform the signal in the same range, 23.7 ppm. These facts indicate that compounds **III**–**VI** are phosphorylated at NH groups, with the formation of products **VIII**–**XI**, respectively.

$$\underset{\textbf{III–VI}}{\rangle NH} + \underset{\textbf{II}}{(ClCH_2)_2P(O)OC_6H_4NO_2\text{-}p}$$

$$\longrightarrow p\text{-}NO_2C_6H_4OH + \underset{\textbf{VIII–XI}}{\rangle NP(O)(CH_2Cl)_2}.$$

In the absence of surfactant **I**, the dependence of the observed rate constant (k_o) of the reaction of polyethylenimines **III**–**VI** with phosphinate **II** on the concentration of the nucleophile is linear (Fig. 2) and is described by the following equation:

$$k_{o,0} = k_{2,0}C_{PEI}.$$

For **III**–**VI** at 25°C, $k_{2,0}$ 0.85, 0.16, 0.33, and 0.66 $l\,mol^{-1}\,s^{-1}$, respectively. The value of $k_{2,0}$ for **III** is somewhat higher than for hydrophobized compound **VI** with the same degree of substitution. This is evidently associated with the unfavorable steric effect of hydrocarbon radicals of **VI**. In the series of compounds **IV**–**VI**, the relative content of the reactive N–H groups decreases, which should cause a decrease in the observed rate constants of the process. However, actually $k_{2,0}$ increases, which may be caused by the self-association; its occurrence is confirmed by dielcometric titration. The concentration dependences of the dielectric permittivity ε of solutions of **III**–**VI** in chloroform contain the clearly and weakly pronounced inflections (Fig. 3, Table 1). Inflections of the first type are caused by deceleration of the growth of ε and flattening-out of the dependence. Inflections of the second type are associated with a sharp increase in the dielectric permittivity at a high content of the polymers in solutions. According to [9], inflections of the first type may be caused by the appearance of symmetric sites due to self-association of polyethylenimines through intramolecular interactions in the polymeric chain. The presence of two inflections in the range of low concentrations of **III** and **IV** (Fig. 3) suggests the possibility of formation of associated structures of different types in solution. Increase in the concentration of the polymer favors the appearance of supramolecular associates due to the intermolecular hydrogen bonding and dipole–dipole interactions. Formation of large and apparently unsymmertical aggregates should make the system as a whole more asymmetric, causing an increase in the

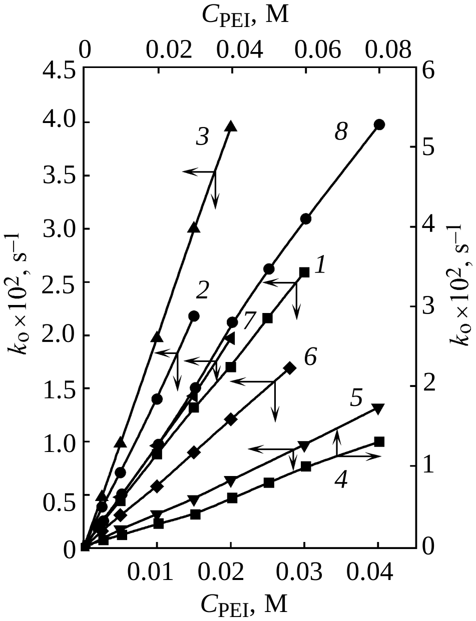

Fig. 2. Observed rate constant of the reaction of polyethylenimines (*1*–*3*) **III**, (*4*) **IV**, (*5*–*7*) **V**, and (*8*) **VI** with phosphinate **II** in chloroform (*1, 4, 5, 8*) in the absence and (*2, 3, 6, 7*) in the presence of surfactant **I** as a function of the concentration of polyethylenimines; 25°C, C_I, M: (*1, 4, 5, 8*) 0, (*2, 6*) 0.025, and (*3, 7*) 0.25.

effective values of the dielectric permittivity of the solutions.

In micellar solutions of cetyltrimethylammonium bromide, the dependence of the rate constant on the polyethylenimine concentration remains linear (Fig. 2) and is described by the following equation:

$$k_{o,S} = k_{2,S}C_{PEI}.$$

The values of $k_{2,S}$ for **III** and **V** at 25°C and 0.025 M concentration of **I** are 1.3 and 0.6 l mol^{-1} s^{-1}, and at 0.25 M concentration of **I**, 2.0 and 0.94 l mol^{-1} s^{-1}, respectively.

Figure 4 shows the dependence of the observed rate constant of phosphorylation of **III**–**VI** on the concentration of **I**. An increase in the content of cetyltrimethylammonium bromide in solution is accompanied by an increase in the rate constant of the process. A specific feature of the concentration dependences (Fig. 4) is their tendency to flatten out (in the surfactant concentration range 0.05–0.1 M) followed by an increase in the observed rate constant. We observed previously the latter trend in nucleophilic substitution in four-coordinate phosphorus acid esters in micellar solutions in nonaqueos media [10] and attributed it to the possible rearrangement of the structure of nanoaggregates.

Treatment of the concentration dependences (Fig. 4) at [**I**] < 0.15 M using the equation given below, corresponding to the pseudophase model of micellar catalysis [11], allowed us to calculate the parameters of the micelle-catalyzed reaction (Table 2).

$$k_o = \frac{k_m K_b C_S + k_0}{1 + K_b C_S}.$$

Here k_m and k_0 are the rate constants of the reactions in the micellar phase and in the bulk of the solvent, respectively; K_b, constant of binding of the substrate

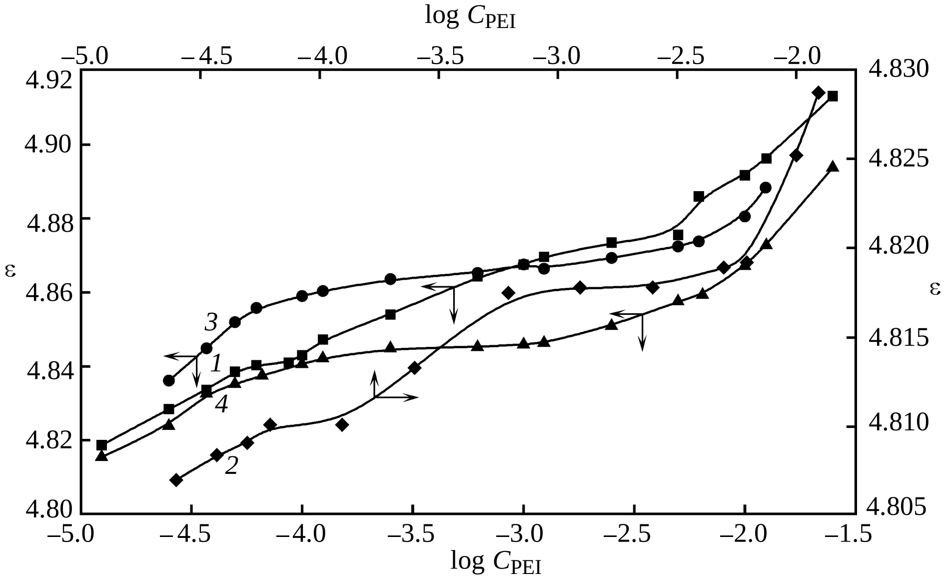

Fig. 3. Dielectric permittivity of solutions of (*1*) **III**, (*2*) **IV**, (*3*) **V**, and (*4*) **VI** in chloroform as a function of the logarithm of polyethyleneimine concentration at 20°C.

Table 1. Critical association concentrations corresponding to the inflections of the first and second types in the concentrational dependences of the dielectric permittivity of solutions of **III**–**IV** at 20°C

Comp. no.	Critical association concentration, M	
	type I inflections	type II inflections
III	7×10^{-5}, 1.2×10^{-3}	5×10^{-3}
IV	6.2×10^{-5}, 8×10^{-4}	6×10^{-3}
V	10^{-4}	8×10^{-3}
VI	2×10^{-4}	4×10^{-3}–10^{-2}

Table 2. Parameters of the reaction of polyethylenimines **III**–**VI** with phosphinate **II** in chloroform, catalyzed by micelles of cetyltrimethylammonium bromide

Comp. no.	PEI, M	T, °C	$k_m \times 10^2$, s^{-1}	K_b, l mol^{-1}	CMC $\times 10^3$, M
III	0.01	25	1.5	54	4.1
III	0.01	40	2.7	24	7.6
III	0.01	50	3.6	17	8.0
III	0.002	25	0.4	66	4.5
IV	0.01	25	0.3	186	2.9
V	0.01	25	0.87	90	2.5
V	0.002	25	0.16	67	8.8
VI	0.01	25	1.1	49	6.3

with the surfactant micelles, C_S, concentration of **I** in solution minus critical micellization concentration (CMC).

Table 2 shows that the rate constant in the micellar phase increases with the growth of the concentration of polyethylenimines and the reaction temperature. The constant of binding of substrates with micelles decreases with the growth of temperature and slightly depends on the concentration of polyethylenimines. Increase of the relative content of hydroxybenzyl substituents in the series of compounds **IV**–**VI** leads to an increase in the rate constant of the reaction in the micellar phase and to a decrease in the constant of binding of phosphinate **II** with micelles. Variation of the content of polyethylenimine **III** only slightly affects the micellization of cetyltrimethylammonium bromide. With an increase in the concentration of polyethylenimine **V** the critical micellization concentration of **I** decreases.

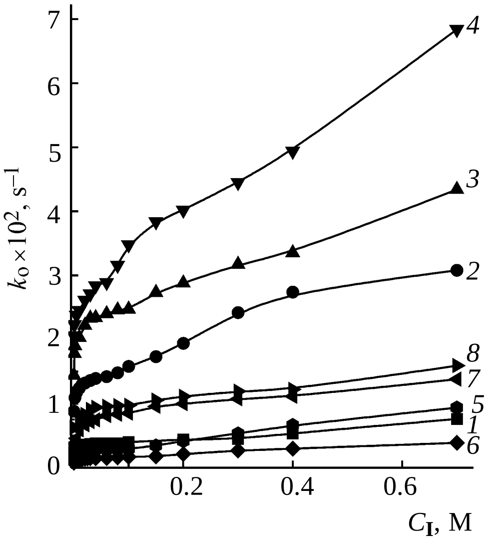

Fig. 4. Observed rate constant of the reaction of polyethylenimines (*1*–*4*) **III**, (*5*) **IV**, (*6*, *7*) **V**, and (*8*) **VI** with phosphinate **II** as a function of the concentration of **I** at (*1*, *2*, *5*–*8*) 25, (*3*) 40, and (*4*) 50°C. Concentration of polyethylenimines, M: (*1*, *6*) 0.002 and (*2*–*5*, *7*, *8*) 0.01.

Binding of polyethylenimines with inverse micelles of cationic surfactant **I** alters not only their reactivity, but also their complexing power toward 4-nitrophenol released by the nucleophilic substitution. Polyethylenimine forms a complex with 4-nitrophenol owing to the presence of NH groups in the polymer molecules. With an increase in the polymer concentration, the UV absorption band decreases in the intensity, and an absorption band appears in the visible range (Tables 3, 4). According to [12], this fact suggests the appearance in solution of hydrogen-bonded ion pair **XIII** along with free *p*-nitrophenol and hydrogen-bonded complex **XII**, with these species occurring in an equilibrium.

$$\begin{tikzcd}
p\text{-}NO_2C_6H_4OH + NR_3 \arrow[rr, shift left] \arrow[dr, shift left] & & p\text{-}NO_2C_6H_4OH\cdots NR_3 \arrow[ll, shift left] \arrow[dl, shift left] \\
& p\text{-}NO_2C_6H_4\text{–}O^-\cdots H\text{–}N^+R_3 \arrow[ul, shift left] \arrow[ur, shift left] &
\end{tikzcd}$$

XIII

It is known that the position of this equilibrium depends on the polarity of the medium [12]. In solvents with a low dielectric permittivity, it is shifted toward formation of the nonionic structure. This fact may be used for estimating the polarity of the microsurrounding of these molecules. In micellar solutions of cetyltrimethylammonium bromide in chloroform, 4-nitrophenol as well as its complex with polyethylenimine are bound with the micelles of **I**. This is confirmed by the bathochromic shift of the absorption band of 4-nitrophenol and hydrogen-bonded complex

Table 3. Optical density of the absorption bands of the polyethylenimine **III** or **IV**–4-nitrophenol complex in chloroform; 25°C, *d* 1 cm, 4-nitrophenol concentration 5×10^{-5} M

C_{III}, M	$D_{310\,nm}$	$D_{400\,nm}$	C_V, M	$D_{322.6\,nm}$	$D_{410\,nm}$
0	0.51	0	0	0.451	0
0.0005	0.459	0.161	0.002	0.249	0.5
0.001	0.396	0.278	0.005	0.224	0.613
0.002	0.358	0.397	0.01	0.171	0.671
0.005	0.293	0.5	0.015	0.182	0.691
0.01	0.253	0.597	0.02	0.163	0.708
0.015	0.23	0.627	0.03	0.123	0.744
0.02	0.219	0.648	0.04	0.106	0.774
0.03	0.208	0.701	0.05	0.098	0.82

Table 4. Optical density of the absorption bands of the polyethylenimine **V**–4-nitrophenol complex in the micellar solutions of surfactant **I** in chloroform; 25°C, *d* 1 cm, 4-nitrophenol concentration 5×10^{-5} M

C_V, M	C_I 0.025 M		C_I 0.25 M	
	$D_{322.6\,nm}$	$D_{424\,nm}$	$D_{322.6\,nm}$	$D_{430\,nm}$
0	0.54	0	0.56	0
0.0025	0.084	1.004	0.085	1.16
0.005	0.081	1.09	0.075	1.22
0.01	0.066	1.09	0.076	1.22
0.02	0.067	1.07	0.077	1.24
0.028	0.053	1.04	0.076	1.26

XII in the UV range of the spectrum and still greater shift of the absorption band in the visible range, belonging to ion pair **XIII** formed by *p*-nitrophenolate anion and protonated polyethylenimine (Table 5). Also, an increase in the concentration of **I** in chloroform leads to a decrease in the optical density of the absorption band of the complexes of polyethylenimines **III** and **V** with 4-nitrophenol in the UV part of the spectrum and to increase in the intensity of bands in the visible range (Fig. 5). This fact indicates that, in the polymer–micelle complex, the NH groups of polyethylenimine molecules are in a more polar microsurrounding, i.e., in the nuclei of the inverse micelles of the cationic surfactant.

Thus, the data obtained show that the binding of polyethylenimines with the inverse micelles of a cationic surfactant affects their reactivity and complexing properties. The extent and character of this effect depend on the content of surfactant in solution and on the structure and concentration of the polyethylenimine.

EXPERIMENTAL

Cetyltrimethylammonium bromide (Sigma) was purified by crystallization from acetone–ethanol mixture. 4-Nitrophenyl bis(chloromethyl)phosphinate was prepared according to [13]. Compounds **III**–**VI** were prepared from branched polyethylenimine (*M* 10 000) and *o*-dimethylaminomethylphenol or *o*-dimethylaminomethyl(*p*-isononyl)phenol (amine interchange) by refluxing for 5–10 h in *p*-xylene in the presence of a catalytic amount of *p*-toluenesulfonic acid with the subsequent removal of volatile products and keeping in a vacuum at 150°C to constant weight. Compound **VII** was prepared by the reaction of branched polyethylenimine (*M* 10 000) with tetradecyl bromide according to [14]. The sample of starting polyethylenimine (Aldrich) was used without additional purification. The mean molecular mass of monomeric units of polyethylenimines was evaluated by potentiometric titration [15]. The molecular mass of the monomeric unit of the starting unsubstituted polymer was 69. Chloroform was purified before use by a standard procedure [16].

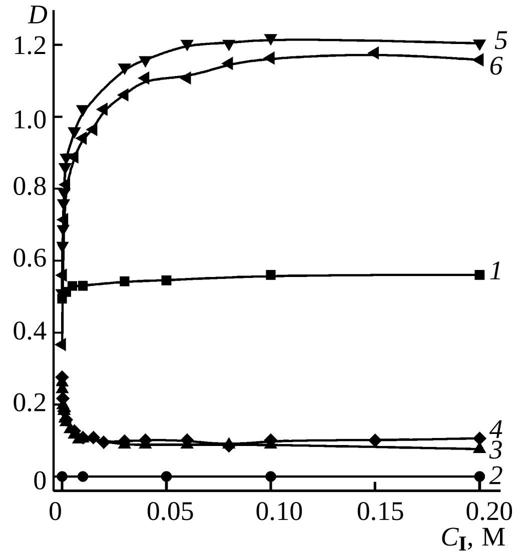

Fig. 5. Optical densities of the absorption bands of 4-nitrophenol at (*1*) 322.6 and (*2*) 400 nm and in the absorption maxima of 4-nitrophenol in the presence of polyethylenimines (*3, 5*) **III** and (*4, 6*) **V** in micellar solutions of surfactant **I** in chloroform in the (*3, 4*) UV and (*5, 6*) visible ranges, as functions of the concentration of **I**; 25°C, *d* 1 cm; (*1–6*) 4-nitrophenol concentration 5×10^{-5} M, (*3–6*) concentration of polyethylenimines 0.002 M.

Table 5. Positions of the band maxima in the absorption spectra of 4-nitrophenol and 4-nitrophenol–polyethylenimine **III, V** complex in the micellar solutions of surfactant **I** in chloroform; 25°C, 4-nitrophenol concentration 5×10^{-5} M

C_I, M	4-Nitrophenol	Complex **III**–4-nitrophenol		Complex **V**–4-nitrophenol (C_V 0.01 M)
		C_III 0.02 M	C_III 0,01 M	
0	310	400	400	402
0.002	312	412	410	412
0.01	316	415	418	416
0.02	–	418	420	417
0.03	318	420	–	417
0.06	–	425	423	423
0.1	321	427	424	423
0.2	322	428	425	426
0.4	322	428	428	432
0.7	323	428	429	432

The reaction kinetics were studied spectrophotometrically under pseudomonomolecular conditions by measuring the increase in the optical density of 4-nitrophenol at 400–435 nm on a Specord UV-Vis spectrophotometer. The reaction rate constants were evaluated from the first-order equation. The concentration of the substrate in the kinetic experiments was 5×10^{-5} M. The concentration of polyethylenimines **III**–**VI** (M) was calculated from the molecular weight of the monomeric unit.

The ^{31}P NMR spectra were measured on a Bruker MSL-400 spectrometer (162 MHz). Phosphinate **II** in chloroform gives a signal at 39.5 ppm. The starting concentration of substrate **II** was 0.02 M; that of **III**, **IV**, and **VI**, 0.15 M; and that of **V** and **VII**, 0.3 M.

Dielcometric titration was carried out according to [17]. The orientational polarization was calculated from the following equation:

$$P_{\mathrm{or,exp}} = 3 \times 10^3 C^{-1}[(\varepsilon_{12} - \varepsilon_1)/(\varepsilon_1 + 2)^2 - (n_{12}^2 - n_1^2)/(n_1^2 + 2)],$$

where C is the solute concentration, M; ε, dietectric permittivity; n, refractive index; indices 12 and 1 refer to the solution and solvent, respectively. The dielectric permittivity of solvents was measured on an installation consisting of an E12-1 device operating in the beat mode and a measuring cell, a temperature-controlled capacitor [18]. The refractive indices were measured on an IRF-23 refractometer.

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