

# Novel surface-active monomers containing phosphate group: synthesis, properties and application

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**Abstract** — *Polietilenglicol-containing maleate interaction with phosphorus (V) oxochloride has led to formation of a novel surface-active monomer with the terminal phosphate group. The polymerization ability of the synthesized monomer was studied in the processes of binary and tertiary copolymerization with peroxide-containing monomer 5-Tert-butylperoxy-5-methyl-2-hexene-3-yne (VEP) and N-vinyl pyrrolidone to form a surface-active copolymers. The possibility of using these copolymers as surface-active macroinitiators of emulsion polymerization of styrene and composites, to create polymeric substrates for tissue engineering was shown.*

Key words – surface activity, surface-active monomers, phosphates, organic surface-active copolymers.

## I. Introduction

Surface-active synthetic oligomers of different nature and polymer colloids based on them in recent years are increasingly being used in medicine and biology to make targeted drugs delivery [1], as carriers for genetic engineering [2], as modifiers of the surface of implants, of the materials for tissue engineering, and the interfacial surface of magnetic and gold colloid nanoparticles [3]. An effective method to obtain polymer colloids with functionalized interphase is traditional polymerization of functional monomers in the presence of surface-active monomers, called surfomers. Feature of surfomers is the presence in their structure of three units: hydrophobic, hydrophilic, which provide surface activity, and polymerization-able fragment with C = C bond. In the process of preparing an emulsion of monomers, surfomers, due to their surface activity localize mainly on the surface of monomer droplets and stabilize the monomer emulsion in water as usual surfactants [4].

During polymerization, the surfomer molecules, thanks to polymerization-able functions, form macromolecules together with monomer and localize mainly on the surface of polymer's particles because of the surface active fragments of surfomers [5]. The known surfomers usually contain as hydrophobic component the residues of higher aliphatic alcohols or acids, and as hydrophilic – preferably polyethylene glycol, carboxylate, sulfonate, phosphate or tetraalkylammonium group. Polymerization ability of surfomers is mainly determined by the environment of the polymerisation-able bond C = C, as

for usual monomers [5]. Today, a wide range of surfomers based on maleate [6], (meth) acrylate [7] and styrene [8] were synthesized. Changing the nature of polymerization-able units, we can adjust the activity of surfomers in polymerization reactions and thus the microstructure of copolymers.

Among these types of surfomers much attention is paid to maleate monomers because of the fact that they are hardly capable of homopolymerization and tend to form alternating copolymers [9]. Another advantage of maleate surfomers is a possibility to relatively simply adjust the hydrophilic-lipophilic balance in the molecule and, consequently, its colloid-chemical properties. It may be done by adding fragments of different nature to the carboxylic groups [10].

There are known surfactants of maleate type, which contain both hydrophilic polyethylene glycol units, or propane sulfonate tetraalkylammonium substituents as well as alkyl hydrophobic component and oligo siloxane fragments [11]. Surfomers may also contain other functional substituents in hydrophobic or hydrophilic parts of the molecule, which under certain conditions can act as anchor functions and provide interaction with substrates of different nature and biological objects [12].

Among the various substituents that can serve as anchor functions special attention deserves phosphate group. Phosphate groups provide anionic character of the surfactant, are also good anchor functions and provide effective immobilization of these compounds on positively charged surfaces, including magnetic particles and biopolymers etc.. Also phosphate groups show affinity for nucleotides. In addition, the presence of phosphate groups in the surfactant molecules facilitates their interaction with cell membranes. It is known that phosphate-containing surfactants of natural origin, the so-called phospholipids, are part of cell membranes and are also involved in the transport of fats, fatty acids and cholesterol in living organisms.

Recently conducted intensive research aimed at obtaining surfactants, including oligomers, that are capable to conjugate drugs of different nature, provide transportation and penetration through the cell membrane into the middle of the cells of living organisms. That's why there is an increased interest in the synthesis of compounds that are analogs or derivatives of natural phospholipids – typical structural lipids of biological membranes.

Therefore, in our view, it is perspective to receiving surfactant monomers containing a phosphate group, and a surfactant fosfatovmisnyh oligomers based on them.

Another area of application of various oligomers is their use for creation of polymeric substrates for tissue engineering. Hydroxy polyesters, especially polycaprolactone are often used for this purpose.

Polycaprolactone (PCL) is a biodegradable polymer widely used in a variety of biomedical application. However, applications of PCL might be limited because kinetics of degradation and resorption of PCL is considerably slower than other aliphatic polyester due to its hydrophobic character. One of the most popular modifying methods of PCL is hydrolysis, using NaOH

and amynolysis using 1,6-hexanediamine predominantly. These techniques provide a significant improvement in cell attachment and proliferation. Also, to improve the properties of polycaprolactone in tissue engineering, commonly used mixtures (composites, blends) with other polymers or inorganic substances.

## II. Objective

The main goal of this work is the synthesis of new maleate surfomer with phosphate groups, the study of its colloid-chemical properties and explore the possibility of obtaining the use of surface-active copolymers that contain units of the synthesized monomer.

## III. Experimental

### Initial Materials

Maleic anhydride, 1-butanol, triethylamine, styrene, phosphoryl chloride, N-vinylpyrrolidone were commercially available from Sigma-Aldrich and were additionally purified by distillation. Poly(ethylene glycol) 600 with average molecular weight 600 g/mol was also commercially available from Sigma-Aldrich and used without additional purification. Phosphorus trichloride was purchased from Merck and used without further purification. 5-Tert-butylperoxy-5-methyl-2-hexene-3-yne (VEP) was synthesized from 2-methylhex-5-en-3-yn-2-ol and tert-butyl hydroperoxide according to known technique [13] and purified by vacuum distillation. Polycaprolactone with average molecular weight 45000 was commercially available from Sigma-Aldrich. All solvents (hexane, dichloromethane, ethyl acetate, dioxane) were purchased from Sigma-Aldrich and purified according to known techniques [13] prior to use.

### Analysis

The presence of the phosphate groups was determined by potentiometric titration with 0.1N. sodium hydroxide in ethanol medium [14].

The structures of the obtained compounds were confirmed IR spectra, that were taken on the device Spectrod M80, 1H. NMR spectra were taken on the device Bruker 150 spectrometer at a working frequency of 300MHz in DMSO-d<sub>6</sub> (substance concentrations of 5 to 10%, internal standard-hexamethyldisiloxane).

The purity of synthesized compounds was additionally confirmed by elemental analysis.

### Surface tension

The characterization of surface activity of synthesized monomers and copolymers was characterized by surface tension measurements. These measurements were performed with a Du Nouÿ ring tensiometer at 20°C. The CMC values of the monomers as well as surface tension above CMC were determined from the inflection points on the surface tension isotherms.

The initial monomer **1** was obtained by successive reactions of maleic anhydride with 1-butanol, phosphorus trichloride and excess of polyethylene glycol (PEG-600) by the known method [13].

Phosphate **3**. To 3.37 g (0.022 mol) POCl<sub>3</sub> in 15 ml of dioxane at 0-5°C and vigorous stirring was added dropwise 3.32 g (0.0044 mol) of the monomer **1** and 0.6 g

(0.006 mol) of triethylamine in 10 ml of dioxane was stirred 2 h at 0-5°C. Triethylamine hydrochloride precipitate was filtered, the filtrate was distilled from excess POCl<sub>3</sub>, to the resulting residue was added 15 ml of dioxane and 1 ml (0.056 mol) of water and stirred at 0-5°C during a day. After distilling out the solvent and water the we gained 3.56 g (0.0044 mol) of the surfomer **3**. The yield is 90.6 %.

### Polymerization technique

Copolymerization reactions were carried out in ethyl acetate as a solvent under argon atmosphere in soldered dilatometers with volume from 15 to 50 ml and with 0.05 ml as scaling factor. No mixing was applied for the systems. As monomers we used n-vinylpyrrolidone (N-VP) and monomer 5-Tert-butylperoxy-5-methyl-2-hexene-3-yne (VEP). Concentration of monomers was varied in range from 1 to 4 mol/L.

Phosphate surfomer **3** copolymerization with N-VP and VEP was taken at molar ratio 1:5:5 at 70-75°C. The emulsion polymerization of styrene was carried out at molar ratio Water: styrene: copolymer 3:1:0.05 at 85°C.

Azobisisobutyronitrile at concentration 5\*10<sup>-2</sup> mol/L was used as initiator of polymerization. Obtained copolymers were isolated and purified by repeated precipitation by adding of excess of poor solvent (hexane) to a solution of copolymer in ethyl acetate. Isolated copolymers were dried under vacuum at ambient temperature to constant weight.

Emulsion polymerization was performed in thermostatic reactor equipped with stirrer and condenser under argon atmosphere. The conversion rate of monomers was determined by gravimetric technique [15]

### Particle size measurement

Particle size during emulsion polymerization was determined using light-scattering technique [15] in a plane-parallel cuvette in the wavelength range from 420 to 620 nm on photocolorimeter LMF-72M.

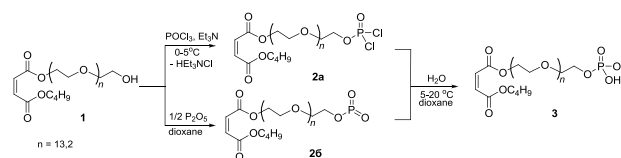
Preparation of films blending of PCL with surface active copolymer

2 g of PCL pelletes and corresponding amount of copolymer of surfmer with N-vinylpyrrolidone were dissolved in 20 mL of dichloromethane. The solution was cast onto glass substrate and the solvent was removed by evaporation at ambient temperature and in vacuum.

## IV. Results of discussion

### Surfmomers synthesis

Phosphate-containing monomer with terminal phosphate group **3** was obtained by the interaction of polyethylene glycol ester of maleic acid **1** with phosphorus (V) oxochloride or phosphorus(V)oxide and subsequent hydrolysis of the obtained intermediate phosphate **2a** or **2b**.



The reaction of compound **1** with phosphorus (V) oxochloride was carried out at 1:5 molar ratio of reactants in the presence of triethylamine as an HCl acceptor at 0-5°C in the solution of dichloromethane. The reaction intermediate **2a** was hydrolysed right after obtaining in dioxane at room temperature.

The target monomer **3** was also obtained by other means – with reaction of monomer **1** with phosphoric anhydride at stoichiometric ratio of reactants at 5-10°C in dioxane.

During carrying out the reaction at a higher temperature we obtained colored product. Hydrolysis of **2b** was carried out similarly as in the case of POCl<sub>3</sub>.

The structure of the synthesized monomer was confirmed by IR spectroscopy, elemental and functional analysis.

To study the colloidal properties of the monomer **3** the isotherms of the surface tension of aqueous solutions of it was taken. For comparison, also surface tension isotherm of aqueous solutions of the initial maleate **1** was taken too. These isotherms are shown at the Figure 1. CMC for monomer **1** was equal 0.7 mass %, and for phosphate-containing monomer **3** 0.6 mass%.

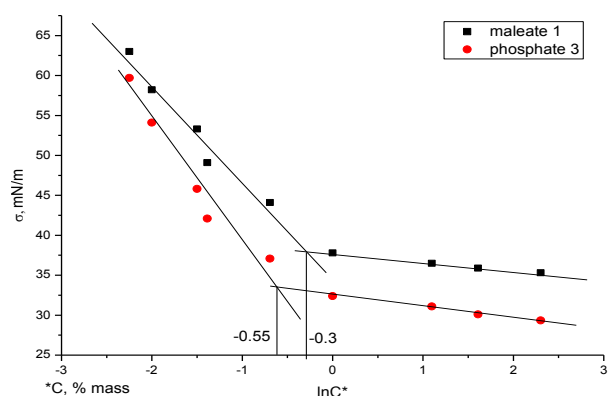


Fig. 1. The surface tension isotherm of maleate **1** and phosphate-containing surfomer **3**

As we can see from Fig. 1, studied monomers, as expected, show obvious surface-active properties. Due to the long polyethylene glycol hydrophilic the surfomers are readily soluble in water. Due to the presence of phosphate group, monomer **3** is more soluble in water and is more surface-active.

For the synthesis of surface-active oligomers the processes of free radical copolymerization of synthesized monomers was studied. A binary copolymerization of maleate surfomer **1** and phosphate-containing surfomer **3** with N-vinylpyrrolidone (N-VP). As the polymerization initiator used dinitryl azoizomaslyanoyi acid (SAC) at a concentration of  $5 \cdot 10^{-2}$  mol / l at 70-75°C.

The kinetic curves of binary copolymerization of synthesized surfactant monomers with N-VP are shown on Figure 2. These curves are typical for copolymerization of monomers this class and show that this process obeys the ordinary laws of radical polymerization. From these curves we can also see that polymerization goes to high degrees of conversion of monomers.

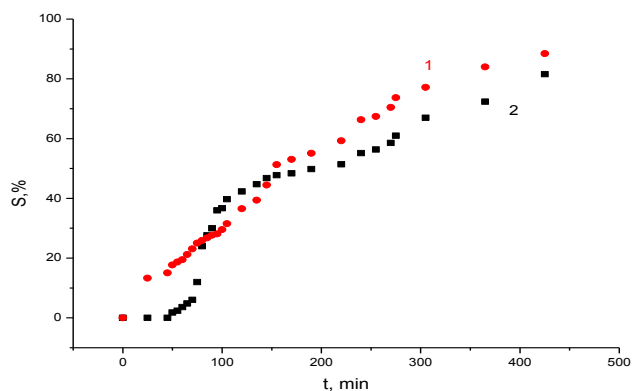


Fig. 2. The dependence of conversion degree of monomer mixture from time: 1-surfomer **1**-N-VP; 2 – surfomer **3**-N-VP

The next step was to conduct a ternary copolymerization of N-VP-surfomer **3** – VEP. Copolymerization was carried out in ethyl acetate at 70 ° C. As the polymerization initiator used dinitryl azoizomaslyanoyi acid (SAC) at a concentration of  $5 \cdot 10^{-2}$  mol / l. Polymerization also occurs to a high conversion of monomer mixture.

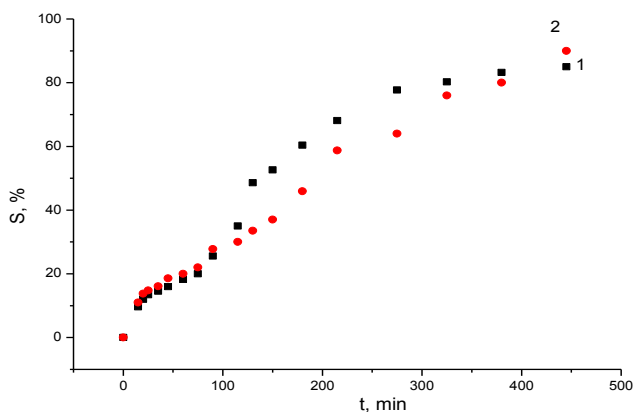


Fig. 3. The dependence of the degree of conversion of monomer mixture from time 1 – surfomer **1** – N-VP – VEP , 2 – surfomer **3** – N-VP-VEP

The synthesized new copolymers are water-soluble compounds and reduce the surface tension of aqueous solutions bordering air. In order to study their colloid-chemical properties we measured the value of the surface tension of aqueous solutions of the synthesized copolymers.

Binary copolymers of the surfomer **1** – N-VP – VEP and surfomer **3** – N-VP – VEP are very good soluble in water, for ternary copolymers value of the surface tension increases with increasing concentration of the surfomer.

Emulsion polymerization of styrene

Synthesized copolymer VEP-surfomer-VEP was used as a stabilizer and macroinitiators in styrene emulsion polymerization. The polymerization was carried out at 85°C and the weight ratio of water: styrene: copolymer 3:1:0.05.

We have prepared films with a mixture of polycaprolactone and copolymers surfomer **3** -N- VP, which contained 17% to 38% (by weight) of phosphate copolymer **3**.

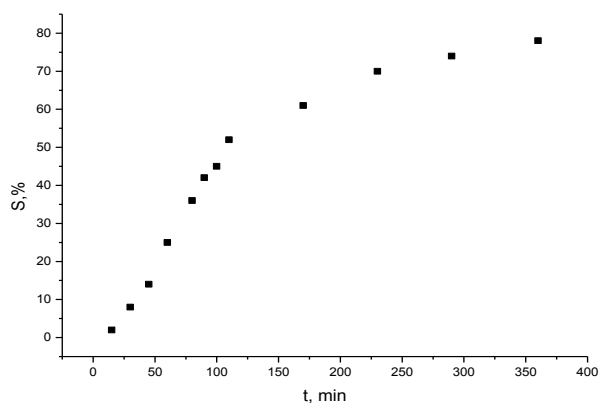


Fig. 4. The dependence of the degree of conversion of styrene in self-initiated water-dispersed copolymerization of mixtures of styrene – copolymer at 85°C

Also for comparison we obtained a hydrolyzed caprolactone film. For this, the film of caprolactone was kept 24 h in a 2N solution of NaOH, washed with distilled water and dried under vacuum to constant weight. Polycaprolactone is hydrophobic polymer and contact wetting angle of polycaprolactone films is 130–140°. We have measured the contact wetting angles of the films, made of a mixture of polycaprolactone and phosphate copolymer. The contact angle confirmed the excellent hydrophilicity of the surface. In case of film with 17% (blend 1) of polymer the value of c.a. was  $190 \pm 1.62^\circ$  and in case of film with 38% of polymer (blend B) the surface was too hydrophilic and so it was impossible to get the correct measurement of contact angle value. Such results could be explained by presence of three very hydrophilic units in polymer: PEG (polyethylene glycol), phosphate group and N-VP (N-vinylpyrrolidone). For comparison, contact angle of the film of hydrolyzed polycaprolactone was  $55.10 \pm 0.23^\circ$ .

The degradation of the received films in phosphate buffer solution was studied, the results of which are shown on the Fig. 5.

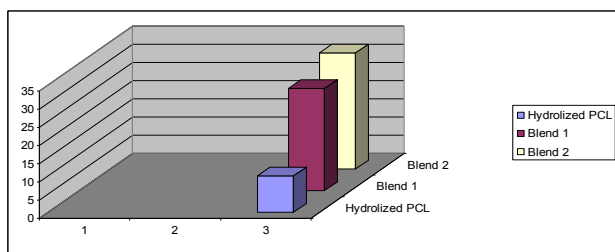


Fig. 5. The degradation of the received films in phosphate buffer solution

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