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Ethylene Oxide Homogeneous Heterobifunctional Acyclic Oligomers

Calin Jianu

Additional information is available at the end of the chapter

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1. Introduction

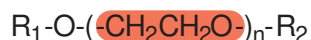
It is difficult, if not hazardous and partisan, to rank the top advances of organic chemistry in the last approx. 20 years for their role in the development of this science and adjacent, complementary others. It can, however, be said with certainty that the field of homogeneous (HOHAO) and heterogeneous heterobifunctional acyclic oligomers (HEHAO) [1] of ethylene oxide, through their diversity of macromolecular architectures and effects, turns out to be one of the most significant achievements. Their importance resides mainly in the resolve by affordable means of some fundamental problems of organic synthesis by the transfer to the same phase of reaction partners with different polarities (organic substrate and water-soluble, usually inorganic, reactant).

Pioneering attempts to structure homogeneous PEO chains with $n=3-20$ are recorded between the fourth and sixth decades of the XXth century and found in technical bulletins issued by large corporations (Hülles, Henkel, Union Carbide, Shell Oil etc.). For reasons of intellectual property protection (in the absence of patents) the technological information recorded within these publications are summary in terms of processing parameters, conversions, or secondary products.

Mulley, B.A. [2] has the merit of the first to de-centralize and systematize the efforts to structure the first proper homogeneous PEO chains in the true meaning of “homogeneous heterobifunctional acyclic oligomers of ethylene oxide” (HOHAO). The compounds reported by him are really just “homogeneous monofunctional acyclic oligomers of ethylene oxide”.

The material presented below introduces the reader to the field of homogeneous heterobifunctional acyclic oligomers of ethylene oxide (HOHAO).

HOHAO, “tailor-made macromolecules” (“designer macromolecules”) with the general structure (Figure 1), fall into the category of “niche” unitary organic compounds (derivatives of polyethylene glycols PEG_n).



n=homogeneous oligomerization degree (strictly monitored value); R₁, R₂=aliphatic, aromatic or mixed derivatization terminals

Figure 1. General structure of homogeneous heterobifunctional acyclic oligomers of ethylene oxide

Why have unitary polyoxyethylene chains PEO imposed themselves? On the one hand to eliminate the cumulative manifestation of the colloidal physico-chemical behavior of the group of chain homologues in the polydisperse heterogeneous structures (technical products) obtained by anionic polymerization; on the other hand to definitely delineate the colloidal physico-chemical competences of each homologue.

2. Ethylene oxide (EO) — Structure, properties, consequences

The origin of the steadily increasing interest that has fascinated for over a century the scientific effort of many researchers, laboratories and concerns for polyethylene glycols (PEG_n) and polyoxyethylene chains (PEO), is largely due to the specific structure and properties of ethylene oxide [3,4]. A slightly colored gas at 25°C, with a sweetish odor and taste characteristic of ethers particularly at concentrations above 500 ppm in air, it is readily soluble in water, ethanol and other organic solvents.

It is relatively thermally stable. In the absence of catalysts up to 300°C it does not dissociate, but above 570°C the major exothermic decomposition is recorded.

Union Carbide at the beginning of the 20th century inaugurated the first production plant of EO by the air oxidation of ethylene in the presence of catalytic metallic silver. Later Shell Oil Co. replaced air with high-purity oxygen and processed EO at 200-300°C and 1-3 MPa, respectively, with an oxidation yield between 63-75% and 75-82%.

The reactivity of the three-atom (two carbon, one oxygen) ether heterocycle (oxirane) (Figure 2a), also founded on the “ring tension theory”, favors the nucleophilic attack of organic compounds with hydroxyl, thiol, primary and/or secondary amine, etc., function with breaking of the C-O bond of the oxirane ring.

Its typical reactions are with nucleophiles, which proceed via the SN₂ mechanism, both in acidic (weak nucleophiles: water, alcohols) and alkaline media (strong nucleophiles: OH⁻, RO⁻, NH₃, RNH₂, RR'NH, etc.). The general reaction scheme is presented in Figure 2b.

Reactions of ethylene oxide with fatty alcohols proceed in the presence of sodium metal, sodium hydroxide or boron trifluoride and are used for the synthesis of surfactants.

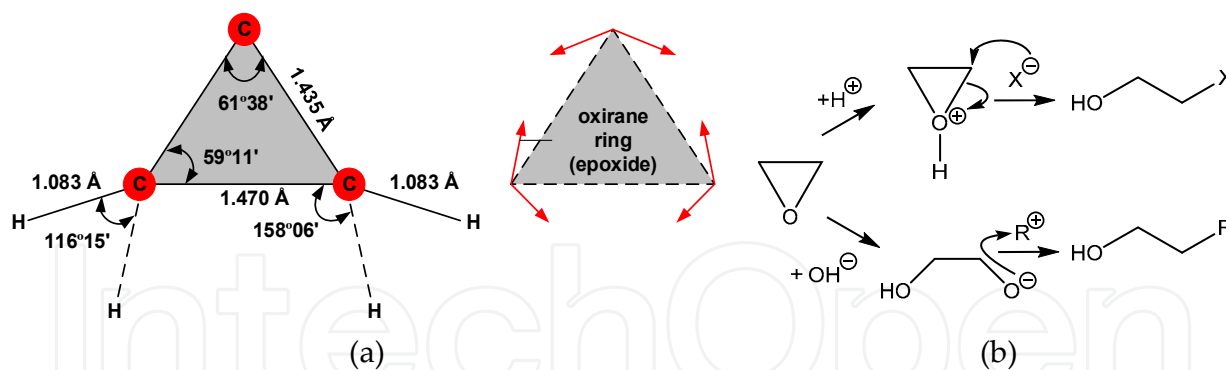


Figure 2. The detailed structural geometry of ethylene oxide (EO) [3,4]

The reaction is carried out in a special insulated reactor under inert atmosphere (nitrogen) to prevent the possible explosion of ethylene oxide. Finally, the reaction mixture is neutralized, degassed and purified.

A narrow-range ethoxylated alcohol also called “peaked ethoxylated” alcohol has a distribution curve that is narrower than the equivalent standard alcohol ethoxylate and a considerably lower content of unreacted alcohol. This gives the nonionic surfactant focused properties, a very low odor, even if based on a short-chain alcohol and avoids the formulation problems often associated with standard alcohol ethoxylates [3].

The lower the degree of ethoxylation, the higher the amount of free alcohol [3].

Polyethylene glycol is produced by the interaction of ethylene oxide with water, ethylene glycol, or ethylene glycol oligomers [5]. The reaction is catalyzed by acid or base catalysts.

The size distribution can be characterized statistically by its weight average molecular weight (M_w) and its number average molecular weight (M_n), the ratio of which is called the polydispersity index (M_w/M_n). M_w and M_n can be measured by mass spectrometry.

The different oligomeric and/or polymeric structures of ethylene oxide depend on the polymerization initiators. Ethylene glycol and its oligomers are preferable as starting materials (“lead compounds”) instead of water, because they allow the creation of polymers with low polydispersity (“narrow molecular weight distribution”) (NMWD).

A number of recent reviews [5,6] have also covered PEG_n chemistry and its applications in biotechnology and medicine, supported catalysis, aqueous two-phase systems in bioconversion, and solvent and phase transfer catalyst (PTC) in organic synthesis.

PEGylation [7] represents the covalent coupling of a PEG_n to a macromolecule (*e.g.*, lipids, therapeutic proteins, etc.). The effect of PEGylation is prolongation of the biological effect (produces a larger molecule with a prolonged half-life). PEGylation is similar to the structuring processes of heterogeneous heterobifunctional acyclic oligomers of ethylene oxide (HEHAO) (Figure 3).

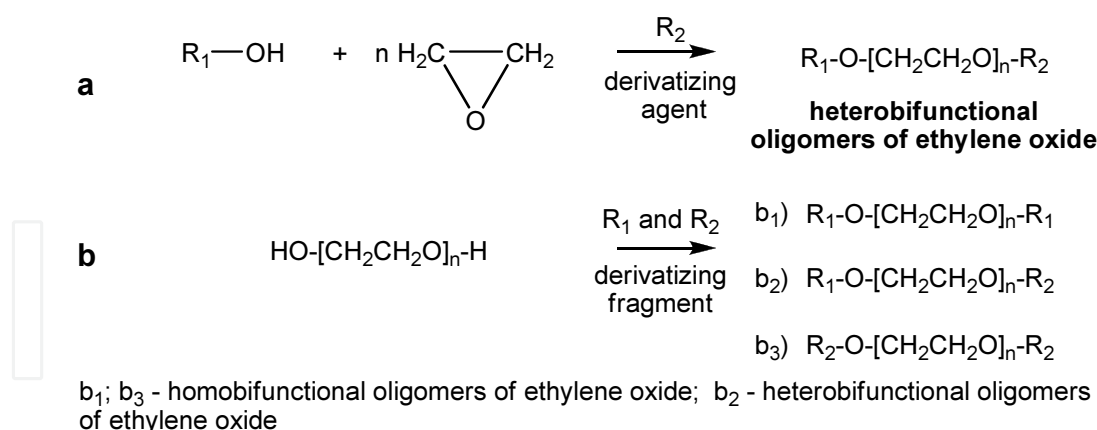


Figure 3. Synthetic methods for the preparation of heterogeneous heterobifunctional acyclic oligomers of ethylene oxide (HEHAO) a) direct preparation; b) end group derivatization of PEG_n diols

With the decision “no observed adverse effect level” (NOAEL) higher homologues PEG_n-1500 for doses of 600 mg/kg have also been advised.

PEG_n, PEO or POE refer to an oligomer or polymer of ethylene oxide. The three names are chemically synonymous.

Five concepts frequently accessed in the specialized literature on polyethylene glycols as such and/or derivatized have also cumulatively fueled the steadily increasing interest in homogeneous heterobifunctional acyclic oligomers of ethylene oxide (HOHAO):

- the particular physical properties of aqueous solutions of PEG_n;
- the unique solvent properties and the coordination competence of cations present in solution;
- the solvent competences of liquid low-molecular-weight PEG_n in chemical reactions;
- the employment of PEG_n as such and/or derivatized as alternative PTC (phase-transfer catalysis);
- the acceptance of aqueous biphasic reactive extraction (ABRE) as a present phenomenon in the development of alternative processes for wood pulping and green catalytic oxidation systems.

In addition to their own phase-transfer activity, PEG_n have also been employed as polymer support for other phase-transfer catalysts (PTCs). PEG_n have been modified with some typical PTCs such as crown ethers, ammonium salts, cryptands, and polypodants to enhance the phase-transfer in two-phase reactions.

After 1960 the coordination competences of alkali cations in the matrix of polyoxyethylene chains (PEO), as such and/or derivatized were also explicitly recognized. The striking analogy with crown polyethers could not fail to impose questions and provide answers pertinent to their capacity, stability and coordination geometry. Certainties that appeared after the series

of scientific speculations and subsequently of experimental evidence, preceded by several decades the conformational and geometrical interpretation of polyoxyethylene chains.

The infrared (IR) absorption characteristics of PEO-MY complexes differ from the individual species, but are similar to those seen in MY-cyclic polyethers systems reported earlier, thus suggesting that the coordination effect may be due to ion-dipole-type interactions in these systems.

This hypothesis becomes credible if the helical conformation (helix) of oligomeric PEO chains with minimum 7 units EO/coil and the electron-donor character (Lewis base) of the oxygen in the PEO chain are accepted.

3. Anionic polymerization of ethylene oxide

Heterogeneous polyoxyethylene chains obtained by the anionic polymerization of ethylene oxide ("anionic ring-opening polymerization") with a polydispersity degree $M_w/M_n < 1.1$ are hydrophilic, flexible (specific spatial conformation), biocompatible "bridges".

Generically, the term "oligomer", *oligos* being Greek for "a few", while *mer* with the meaning of primary structural unit (ethylene oxide) which is repeating, can be defined as a molecular assembly composed of a small number of monomeric units covalently grafted (ethylene oxide for HOHAO). Since ethylene oxide (EO) is accessed exclusively, the macromolecular structure formed is a homo-oligomer (homomer).

Oligomerization in the casuistry analyzed is a process of monitored attachment in a macromolecular architecture of (n) primary structural units of ethylene oxide. The demarcation of n between oligomerization and polymerization is undecided in the specialized literature. For HOHAO the range 3-20 is accepted compared to 10-100 in general. In the case of heterogeneous polyoxyethylene chains (polydisperse polymerization degree n_{average}) it is natural to assume the existence of homologous (mixtures of oligomers and/or polymers) oligomeric (polymeric) series with the same strictly defined structure, with molecular weights different from homogeneous oligomeric chains (definite oligomerization degree n).

For heterogeneous polyoxyethylene (PEO) chains the statistical distribution quantitatively expressed through the equations: Natta, Weibull/Nycander/Gold, Natta/Mantica, Poisson, etc., is accepted [8]

4. Homogeneous polyoxyethylene chains — Preparation, structure, competences

Although the structuring of homogeneous PEO chains represented a scientific challenge for more than six decades, today we still can not say that there is a single, rapid procedure for

their synthesis due to preparative difficulties, complex process flow diagrams for purification and characterization, consequently due to the high cost of processing in industrial quantities.

During our research the results obtained contributed decisively to the confirmation of the direct participation of PEO chains in nucleophilic addition reactions (cyanoethylation, amidoethylation) (Figure 10) of polyethoxylated higher alcohols purified of free higher alcohols, polyethylene glycols (PEG_n) and water, when the processing yields under similar conditions increase proportionally with the oligomerization degree, (n), of the PEO chain [9,10].

After almost a century of investigations, similar to other classes of macromolecular compounds for polyethylene glycols (PEG_n) and their derivatives (glyme, oligoglymes, PEGylated compounds), respectively, it can also be reasonably claimed that in addition to a primary structure there are a secondary (conformational) and a tertiary structure (micellar macromolecular architectures).

The main qualities of these tridimensional macromolecular architectures with consequences in the study of HOHAO are dimensional flexibility, transfer mobility, the existence of “meander”, “zig-zag”, and “helix” conformations of variable geometry, free coaxial C-C/C-O rotation, and the absence of “ring tensions” specific to rigid structures (crown polyethers).

With few exceptions, the preparation of homogeneous PEO chains as such and derivatized is reported with yields ranging between 60-80% for relatively small oligomerization degrees (n=3-6) [2]. The laborious, difficult to accomplish purification, associated with the presence of “neighboring effects” (“sympathy effects”) between two or more hydrophilic (polyoxyethylene) chain homologues with close physico-chemical constants, limited the extension of synthetic efforts [10].

The main colloidal characteristics of HEHAO and HOHAO, respectively, depend on their structure and heterogeneous or homogeneous composition. As mixtures with wide distribution of hydrophobic R₁, R₂ and hydrophilic PEO chain homologues, respectively, HEHAO manifest cumulatively through the individual colloidal behavior of each homologue present in the mixture, but also through mutual interdependences. That is why the experimental values of the main basic colloidal characteristics evaluated in the research carried out [9,10] were preliminarily only indicative, even though they were the result of the mathematical processing of a considerable number of measurements.

The actual distribution of the PEO chain homologues and hence of the oligomerization degrees (n_{average}) changes in the series $n_{\text{average}}=3-18$ from advanced symmetry for $n_{\text{average}} \leq 8$ to pronounced asymmetry for $n_{\text{average}}=9-18$.

The steadily increasing interest in the definite explanation of colloidal properties of heterogeneous (polydisperse) polyoxyethylene chains is evident in the literature after the sixth decade of the 20th century and by the research related to the obtaining, purification and characterization of homogeneous polyoxyethylene chains. Two types of PEO conformations are postulated during this period (“zig-zag” and “meander”) (Figure 4).

Today one can draw a unitary conclusion that would eliminate earlier partial speculative assumptions. Major contributions in this area were due to the accessing of modern instru-

mental methods: “short distance diffraction techniques”; “wide-angle-diffraction techniques” and “low-angle-diffraction techniques”.

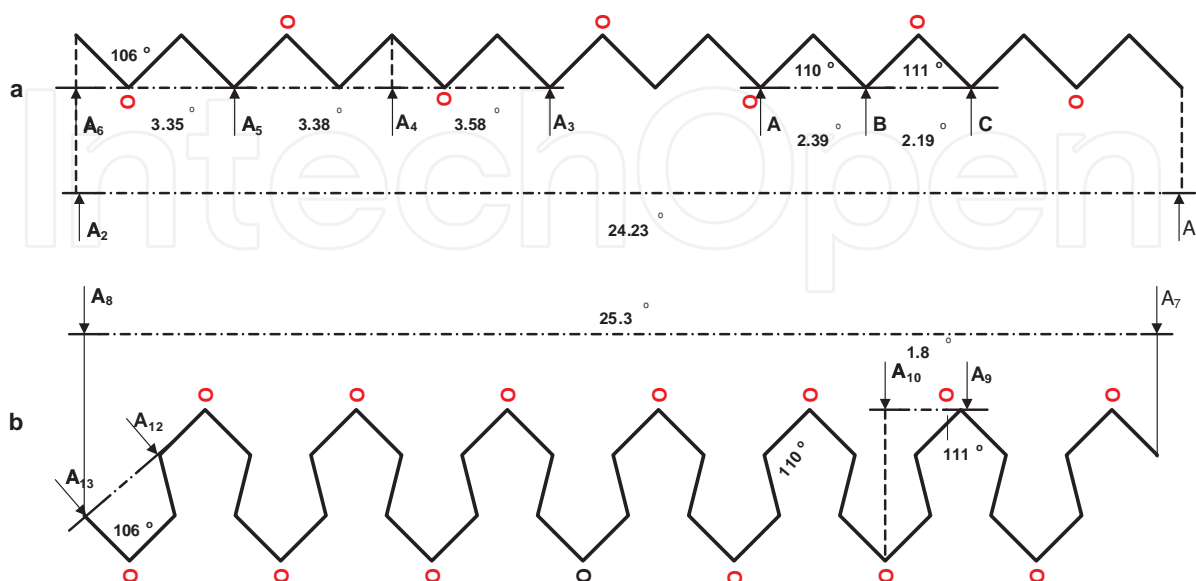


Figure 4. The “zig-zag” (a) and meander (b) conformations of the polyoxyethylene chain [11-15]

These constructive details about the PEO chain (“strain-free polyoxyethylene chain”) and the manner of “packing” in the “macromolecular lattice” are reasonably argued with the specifications:

- the “monoclinic unit cell” appears at four chain meanders;
- the meander has in its structure nine oxyethylene structural units ($-\text{CH}_2\text{CH}_2-\text{O}-$), *i.e.*, $4 \times 9 = 36$ total oxyethylene units in a “monoclinic unit cell”;
- the “repeat period” is identical (19.5 \AA);
- each oxyethylene unit is “twisted” to the neighboring structural unit, such that the main PEO chain returns to the original position at every tenth “lead/turn” (19.5 \AA);
- in the “meander” conformation one oxyethylene structural unit has a length of 1.9 \AA and a diameter of 4 \AA compared to the “zig-zag” conformation where the same geometrical parameters are 3.5 \AA and 2.5 \AA , respectively.

Today it is accepted that the “zig-zag” conformational form is specific to PEO with low oligomerization degrees, and the “meander” conformation to PEO chains with high oligomerization degrees.

Be mentioned that differences between some experimental results are due to the study of polyoxyethylene chains: in solution; in the solid state, in the range of average molecular weights between 2,400 and 100,000 ($n=55-2300$), and in the solid state, derivatized.

Experimental evidence favorable to the concepts expressed, associated with continuously developing advances in instrumental investigation, have decisively stimulated the theoretical and practical interest for the synthesis of HOHAO in general, and for mono- and diderivatized homogeneous and heterogeneous polyoxyethylene chains in particular.

The rediscovery of crown polyethers and their role as phase-transfer catalysts, and the pronounced mutual structural similarity constituted an additional major impetus for the theoretical and practical conformational study of acyclic PEO chains, suggested changes in terminology and their recognition as biomacromolecules with major physiological role.

The homologous series of dimethylated polyethylene glycols [$\text{CH}_3(\text{OCH}_2\text{CH}_2)_n\text{OCH}_3$; ($n \geq 3$)] also suggested the term *glyme* (oligoglyme) (*methylated glycols*). Although not yet widely accepted, there is a tendency to generalize this concept also to derivatized acyclic polyether (polyoxyethylene) chains.

From a simple working hypothesis (speculative nature) able to explain phenomena or processes, subsequent experimental studies based on X-ray investigations, electronic microscopy and diffraction confirmed their ability of intra- and interchain contraction, dependent on the structure and medium and the formation of “cavities” (“cage” of variable geometry) at oligomerization degrees (n , n_{average}) below and above nine ethylene oxide (EO) units, and “sandwich” below three structural units (EO), respectively [16].

The synergistic cumulation in a unitary structure of the conformational and colloidal qualities of homogeneous PEO chains with the possibility of controlled modification of the HLB (hydrophilic/hydrophobic balance) was and still is of wide theoretical and practical interest.

Technologies based on grafted PEG_n conjugates launched products of major biological importance, for research and diagnosis (PEG_n -modified proteins and liposomes, food, medical and analytical matrices), based on the accumulated knowledge on PEG_n and the prospects of PEG_n as biomaterial.

These considerations suggested the idea of structuring the HOHAO of the $\text{PEG}_n\text{-L(R';2R)}$ (2R';R) structured-lipids-type (Figure 5).

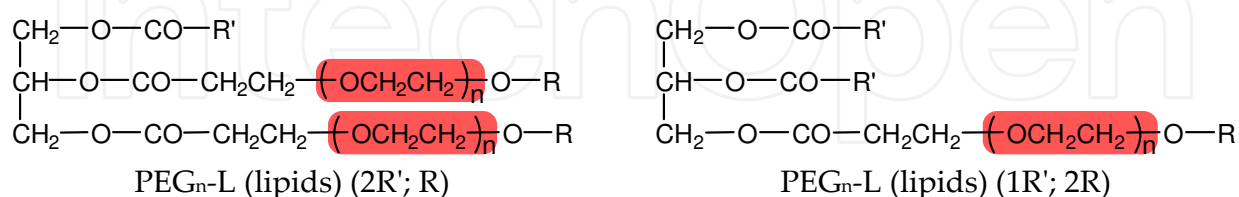


Figure 5. The structure of homogeneous heterobifunctional acyclic oligomers of ethylene oxide of the tailor-made-lipids type [10]

In Figures 6-9 are presented the main process flow charts which formed the basis of the synthesis of homogeneous polyoxyethylene chains in HOHAO. It is noted that in the stages with strongly ionic character were accessed PTC with homogeneous PEO chains, able to activate nucleophilic agents by coordinating the alkaline cation [9,10].

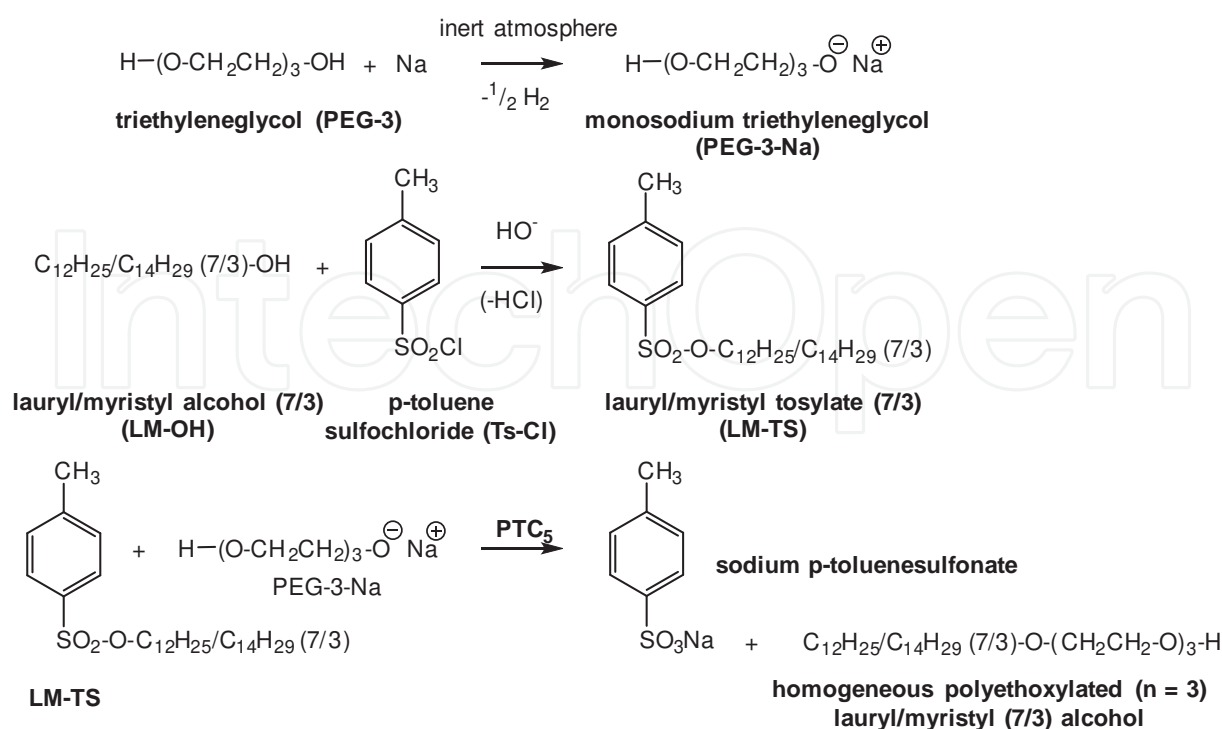


Figure 6. Reaction scheme for the production of homogeneous polyethoxylated ($n=3$) lauryl/myristyl (7/3) alcohol [LM(EO)₃H]

Homogeneous heterobifunctional acyclic oligomers of ethylene oxide (HOHAO) fall into the category of “niche” unitary organic compounds (derivatives of homogeneous polyethylene glycols PEG_n), whose synthesis, purification, chemical and physico-chemical characterization detaches from the classic heterodisperse character specific to the oligomerization and polymerization products of ethylene oxide (EO), through the unitary (homogeneous) structure of the polyoxyethylene chain (PEO) “constructed” through controlled successive covalent grafting of lower oxyethylene units, diethyleneglycol (DEO) or triethyleneglycol (TEO) (adapted Williamson synthesis), followed by the derivatization of the two terminals (“end groups”) with various fragments R₁, R₂ (Table 1) [9,10].

Aromatic sulphochlorides (tosyl chloride) react with higher alcohols (C₈-C₁₈), diols (PEG_n), and alkyl (C₈-C₁₂) phenols (NF), respectively, in the presence of a base, pyridine, forming sulpho-nate esters, effective alkylating agents (Figures 6, 7, 9). Higher alcohols (C₈-C₁₈), diols (DEO, TEO, PEG_n), and alkyl (C₈-C₁₂) phenols, respectively, react with thionyl chloride (SOCl₂) in the presence of pyridine as organic base, generating the corresponding chloro derivatives (PEG₂-2Cl; PEG₃-2Cl; PEG₆-2Cl) (Figures 8, 9). In order to direct (control) the course of the reaction in the direction of mono- or dichlorination, one hydroxyl terminal can be protected by acetylation (Ac) with acetic anhydride (Ac₂O) with the formation of PEG_n-Ac; PEG_n-2Ac; PEG_n-Ac,Cl [9,10].

Higher alcohols (C₈-C₁₈), alkyl (C₈-C₁₂) phenols and diols (DEO, TEO, PEG_n) also form under controlled inert atmosphere, without oxygen, CO₂ or traces of water (Figures 6, 9), alcoholates or phenolates (PEG₂-Na; PEG₃-Na; PEG₆-Na; PEG₉-Na; PEG₁₂-Na; PEG₁₈-Na), who subse-

quently participate in a directed manner (Figures 7-9) in the nucleophilic substitution of chloride in the mono-and/or dichloro derivatives (PEG₂-2Cl; PEG₃-2Cl; PEG₆-2Cl) for the elongation of the homogeneous PEO chain [9,10].

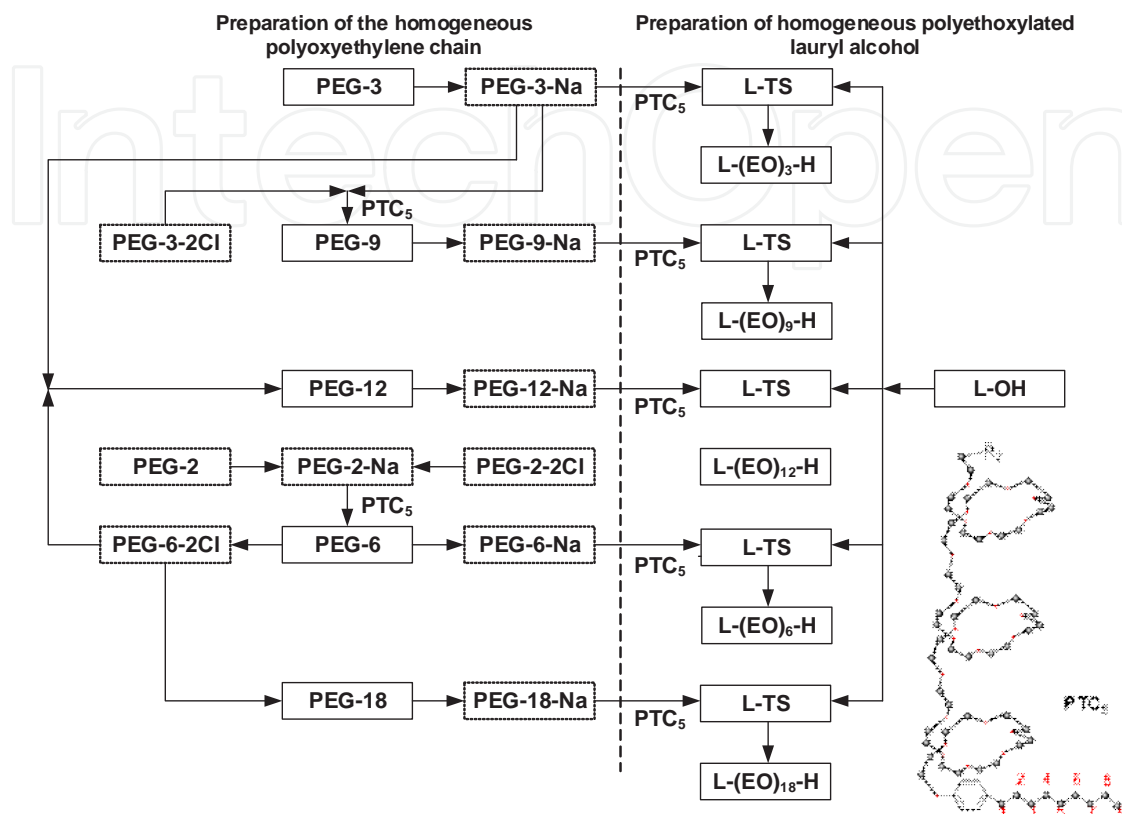


Figure 7. The preparation scheme of homogeneous polyethoxylated lauryl alcohol $n=3, 6, 9, 12, 18$ under phase-transfer catalysis conditions (PTC₅ – homogeneous β -nonylphenoxy polyethyleneoxy ($n=24$) methyl ether)

The process with a pronounced polar (ionic) character is additionally favored by the presence of micellar phase-transfer catalysts (PTC₁₋₅) (Figures 6-9, 13), which “sequester” the alkaline cation (sodium) in the “cavity” with flexible geometry of the homogeneous PEO chain’s helix for $n \geq 8-9$ (PTC₁, PTC₄, PTC₅) or in the interchain space (“sandwich” type) for $n \leq 3-4$ (PTC₂, PTC₃).

5. Homogeneous heterobifunctional acyclic oligomers of ethylene oxide

- a. Synthesis of homogeneous heterobifunctional acyclic oligomers of ethylene oxide from the category of surface-active compounds

An overview of the colloidal characteristics of two major categories of surface-active structures (ionic and nonionic) suggested the idea of creating a new class of hybrid surface-active compounds, of the nonionic-ionic type, with synergistically cumulated colloidal effects. After confirming the real possibilities of approaching the study it was decided upon the structuring

of HOHAO proper (Table 1). The common element of all the molecular architectures obtained was the directed synthesis of the homogenous polyoxyethylene chains (n) (Figure 7) ($n=3,6,9,12,18$), following the adapted Williamson variant [9,10]. Subsequently there was the monitored grafting (PEGylation) with fragments R_1 (Figures 7, 8), and the derivatization of the second hydroxyl terminal with fragments R_2 accessing a scheme of adapted classical reactions (Figures 10, 11). Literature reports similar structures of the nonionic-ionic type with heterogeneous polyoxyethylene chains ($n_{\text{average}}=3$) [9,10]. The study extends the range of HOHAO with surface-active competences using higher homogenous polyoxyethylene chains ($n=3-18$).

To facilitate the presentation of synthesized HOHAO (Figure 10) their chemical names have been encoded. The main organic functions were symbolized by the initials of the chemical names (*e.g.*: -propionitrile, PN; -primary ethylamine, EP; etc.), the homologues of the base hydrocarbon chain with the initials of the trivial names (*e.g.*: lauryl/myristyl, LM; cetyl/stearyl, CS) followed in parentheses by the ratio (7/3) signifying their mutual relative distribution. The hydrocarbon chains attached later by synthesis were symbolized by the number of carbon atoms contained (*e.g.*: in the cationic structure – EC-1.1.16., we find two methyl groups symbolized as (1.1.), and a hexadecyl chain indicated by the number (16.), respectively), and within the class in the natural order. For example: *N,N*-dimethyl-*N*-dodecyl (lauryl)-*N*- β -lauryl/myristyl (7/13) polyethyleneoxy ($n=9$) ethylammonium chloride has the symbol LM-(EO)₉-EC-1.1.12.

Similarly was done with the structures of structured lipids HOHAO (Figure 11) assimilated with PEG_{*n*}-L (lipids) conjugates.

Under equimolar AN/LM-OH conditions, increasing the temperature in the range 25-35°C determines the increase of the cyanoethylation yields, then between 40-60°C the yields drop. With excess acrylic monomer the evolution of yields follows the same trend. In these conditions between 25-40°C the amount of acrylic oligomers formed is below 1%, independently of the excess of monomer introduced, while between 40-60°C it increases dramatically. For cetyl/stearyl alcohol, under equimolar conditions or excess of monomer AN/CS-OH, increasing the temperature between 45-55°C (below this range the yields are low) favors the nucleophilic addition yields, the more so as the excess of acrylic monomer is higher. In the range 55-70°C the yields drop under the same conditions, and the content of acrylic oligomers is higher than in the case of lauryl/myristyl alcohol. At the cyanoethylation of homogeneous polyethoxylated ($n=3$) lauryl/myristyl alcohol under equimolar conditions or excess of acryl monomer, the addition yields increase between 25-35°C, then between 45-60°C decrease appreciably. The amount of acrylic oligomers formed follows roughly the same evolution as in the case of lauryl/myristyl alcohol over the entire temperature range. For homogeneous polyethoxylated ($n=3$) cetyl/stearyl alcohol under equimolar conditions or excess of monomer, the addition yields increase between 30-40°C then drop between 45-65°C. The content of acrylic oligomers increases in proportion to the temperature and excess of monomer. Compared with cetyl/stearyl alcohol it is noted that the cyanoethylation yields are higher at the same value of temperature even below 45°C. These suggest that the cyanoethylation reaction is reversible in character (Figure 12), the polyoxyethylene chain favors the addition, while increasing the hydrocarbon one reduces the yields.

No.	Structure $R_1-(\text{PEO})_n-R_2$			Name	Competences	References
	R_1	n	R_2			
	HO	3,6,9, 12,18	OH	homogeneous polyethylene glycols	controlled PEGylation structures	9,10
	Alk-O- Alk-Aryl- O-	3,6,9, 12,18	OH	monoderivatized homogeneous polyethylene glycols	homogeneous polyethoxylated (C_1 - C_{20}) alcohols	9,10
	Alk-O- Alk-Aryl- O-	3,6,9, 12,18	$-O-CH_2CH_2CN$	homogeneous β -alkyl (C_8 - C_{18})/alkyl (C_8 - C_{12}) aryl polyethyleneoxy propionitriles	PEGylation intermediates	9,10,17,28
	Alk-O- Alk-Aryl- O-	3,6,9, 12,18	$-O-CH_2CH_2CONH_2$	homogeneous β -alkyl (C_8 - C_{18})/alkyl (C_8 - C_{12}) aryl polyethyleneoxy propionamides	PEGylation intermediates	9,10,29
	Alk-O- Alk-Aryl- O-	3,6,9, 12,18	$-O-CH_2(CH_2)_mNH_2$ $m=1,2$	homogeneous β -alkyl (C_8 - C_{18})/alkyl (C_8 - C_{12}) aryl polyethyleneoxy ethyl/propyl amines	PEGylation intermediates	9,10,18
	Alk-O- Alk-Aryl- O-	3,6,9, 12,18	$-O-CH_2(CH_2)_m-N^+(CH_3)_2-Alkyl (C_1-C_{18})/Benzyl] Hlg^-$ ($m = 1,2$)	homogeneous N,N -dimethyl- N -alkyl (C_8 - C_{18})/benzyl- N - β -alkyl (C_1 - C_{18})/polyethyleneoxy ($n = 3$ -18) ethyl/propyl ammonium	flotation agents/phase-transfer catalysts	9,24
	Alk-O- Alk-Aryl- O-	3,6,9, 12,18	$-O-CH_2(CH_2)_mNH_3^+X^-$ ($m = 1,2$)	salified homogeneous β/γ -alkyl (C_8 - C_{18})/alkyl (C_8 - C_{12}) aryl polyethyleneoxy ethyl/propyl amines	micellar flotation agents	9,18,20
	Alk-O- Alk-Aryl- O-	3,6,9, 12,18	$-O-CH_2(CH_2)_m-\begin{array}{c} \text{C} \\ \parallel \\ \text{N} \\ \mid \\ \text{CH}_2 \end{array}-\begin{array}{c} \text{NH} \\ \mid \\ \text{CH}_2 \end{array}$ ($m = 1,2$)	homogeneous β -alkyl (C_8 - C_{18})/alkyl (C_8 - C_{12}) aryl polyethyleneoxy 2-imidazolines	structuring intermediates of amphoteric surface-active compounds	22,23,26
	Alk-O- Alk-Aryl- O-	3,6,9, 12,18	the structure is presented in detail on figure 5	glycerol esters containing carboxy ethyl/propyl polyethyleneoxy alkyl ether groups	tailor-made lipids, designer lipids, fat mimetics	10,21,35

Table 1. Homogeneous heterobifunctional acyclic oligomers $R_1-(\text{PEO})_n-R_2$ of ethylene oxide (selective exemplification)

These conclusions suggest a greater reactivity of the lauryl chain compared to the myristyl one with the increase of the homogeneous polyether chain.

In the cyanoethylation process of higher alcohols, the reaction time favors the formation of β -alkyl-oxy-propionitriles up to 180 minutes, and the oligomerization of the acrylic monomer throughout the process. After this period the cyanoethylation yields decrease, further confirming the reversible character of the nucleophilic addition under prolonged contact between reactants (Figure 12).

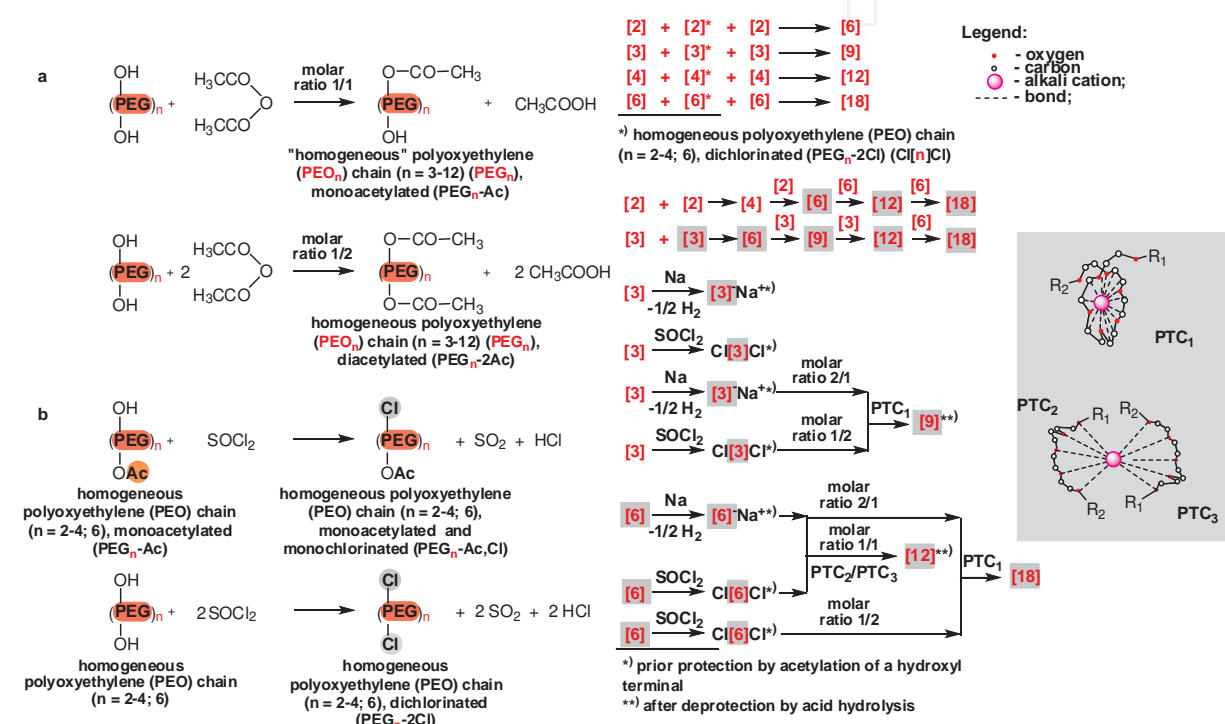


Figure 8. Operations flow chart of the monitored structuring of homogeneous polyoxyethylene (PEO) chains (n=6-18) as such accessing structural units of diethyleneglycol PEG₂ (DEO) (2), triethyleneglycol PEG₃ (TEO) (3) and/or homogeneous polyethylene glycols PEG_n (n). a) mono- and diacetylation, respectively, of the homogeneous chain (PEO) (n=3) (protection); b) mono- and dichlorination, respectively, of the PEO chains protected by acetylation; c) schemes of (directed) structuring of homogeneous polyoxyethylene (PEO) chains (n=6,9,12,18) by phase-transfer catalysis (PTC₁, PTC₂, PTC₃); PTC₁ – homogeneous dimethylglyme; PTC₂ – homogeneous β -alkyl (L/M) polyethyleneoxy (n=4) methyl ether; PTC₃ – dicyanoethyl triethyleneglycol.

Similar trends are observed in the cyanoethylation of nonylphenol and homogeneous polyethoxylated nonylphenols, respectively, for the entire series of homogeneous and/or heterogeneous PEO chain homologues.

In the series of homogeneous polyethoxylated lauryl/myristyl alcohols (n=3-18) the maximum value of the cyanoethylation yield is obtained at lower processing periods, which may suggest the favorable intervention of the polyoxyethylene chain in the cyanoethylation process (Figure 13).

On the overall process, increasing the reaction time up to approx. 180 minutes favors all reaction processes, including the formation of acrylic oligomers.

Increasing the amount of catalyst above the optimum value (4.5×10^{-3} mol/L) increases the alkalinity of the medium and the oligomerization reactions of the acrylic monomer. In the concentration range 15.50×10^{-3} mol/L, the content of homogeneous β -lauryl/myristyl (7/3) polyethyleneoxy ($n=3$) propionitrile decreases, in parallel with the sharp rise of the acrylic oligomers content. In the series of polyoxyethylene chain homologues, the maximum cyanoethylation yield is achieved at higher values of the catalyst concentration. At the same catalyst concentration, increasing the polyether chain determines a significant increase of the nucleophilic addition yields, but also a reduction in the amount of acrylic oligomers formed, probably due to the solvation of the acrylic monomer in the polyether chain [9,10].

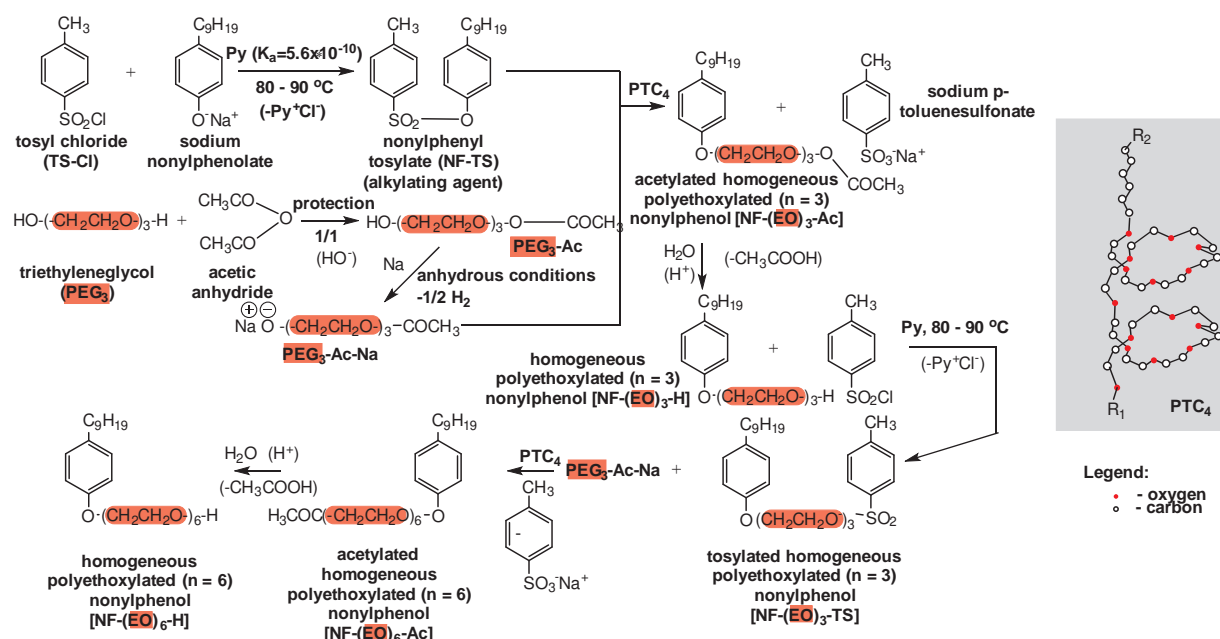


Figure 9. Flow chart of the processing and purification of homogeneous polyoxyethylene (PEO) chains ($n=3, 6$) mono-derivatized with nonylphenol (NF) by condensation of tosylated nonylphenol (NF-TS) with monosodium protected (acetylated) diethyleneglycol under phase-transfer catalysis conditions; PTC₄ – β -alkyl (L/M) polyethyleneoxy ($n=16$) ethylamine

The formation of acrylic oligomers was avoided by the introduction of ferrous cations, in the present case of anhydrous ferrous sulphate (FeSO_4), as polymerization inhibitors of the acrylic monomer. For 1%, the cyanoethylation yield of homogeneous lauryl/myristyl (7/3) alcohol increases by more than 10%, without the formation of acrylic oligomers. Similar results are obtained in the homologous series of homogeneous (C_{12} – C_{18}) polyethoxylated ($n=3$ – 18) alcohols, and also of nonylphenols as such and polyethoxylated nonylphenols, respectively, for the entire series of (PEO) chain homologues [9,10]. Increasing the length of the hydrocarbon chain, for the same size of the homogeneous polyoxyethylene chain, reduces the cyanoethylation yields through unfavorable steric effects.

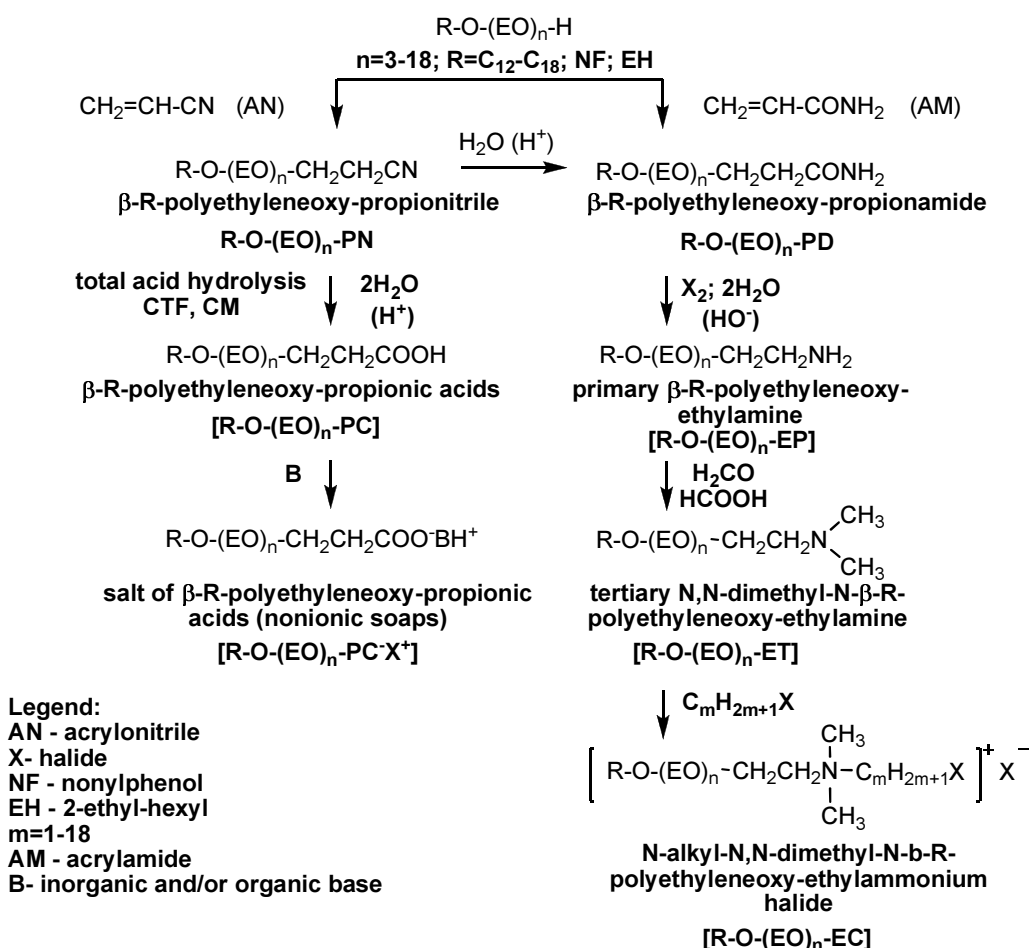
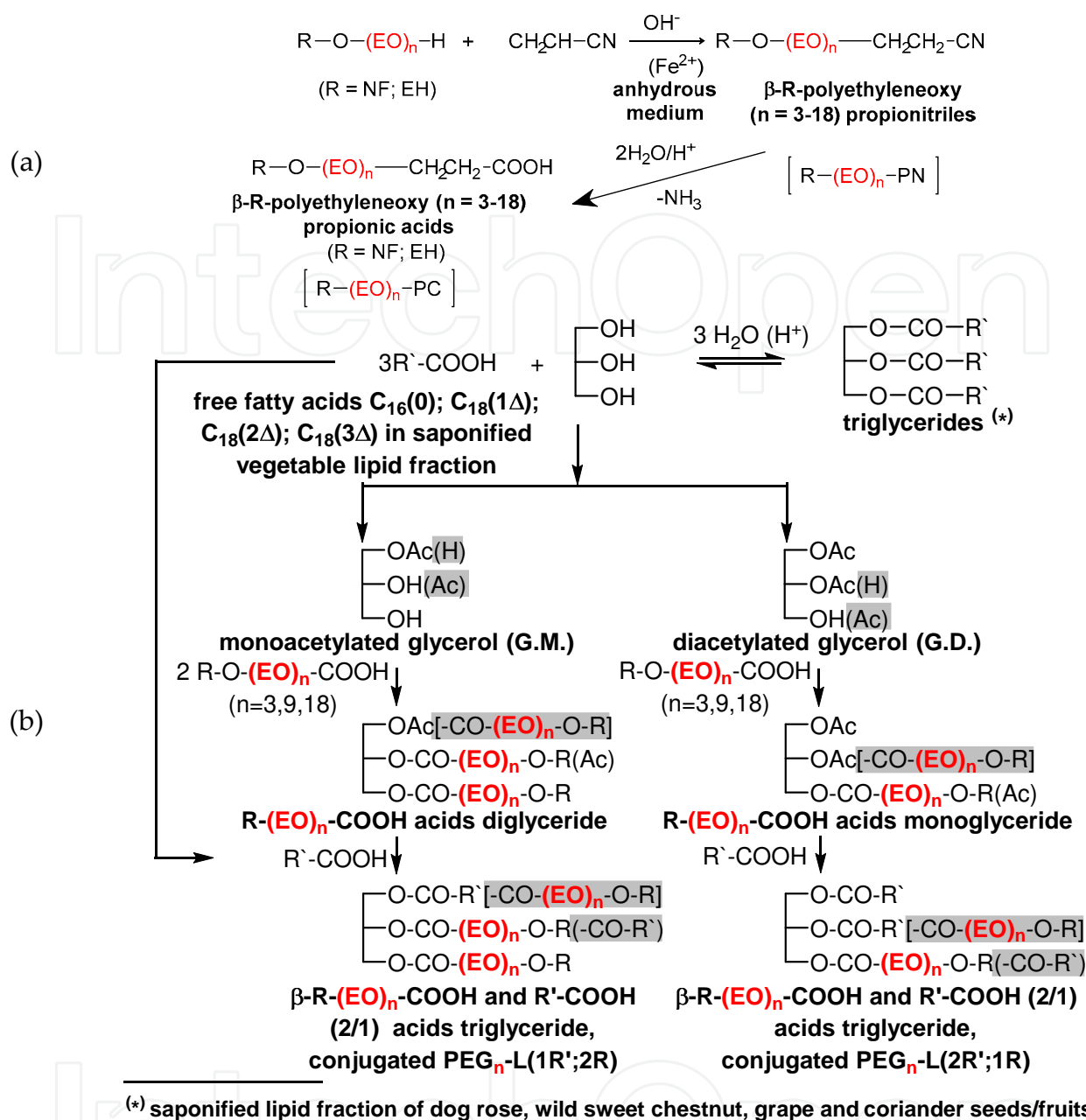


Figure 10. Reaction scheme of the processing of surface-active structures HOHAO [9,19]

The polyoxyethylene chain with its specific conformation interferes in the cyanoethylation process in non-polar reaction media (toluene, etc.) by activating the nucleophile, so that the cyanoethylation yields for higher polyethoxylated alcohols with the same hydrocarbon chain, but with a variable ($n=3-18$) polyoxyethylene chain increase.

The hydrocarbon chains in higher alcohols or in general β -R-oxy-propionitriles present in the process, through their length or tridimensional arrangement, respectively, generate “steric hindrance” phenomena (Figure 14), which reduce the overall rate the more so as the length is greater. The polyoxyethylene chains through their conformation favor the formation of non-solvated nucleophiles, which accelerates the cyanoethylation. For this reason cyanoethylation is also favored by the presence of phase-transfer catalysts which activate the nucleophile in the “reverse” micelle [9,25] medium system. Unprotected glymes, polyethylene glycols ($n=3-30$), in comparison with protected ones: dicyanoethylated homogeneous polyethylene glycols ($n=3,6,9,12,18$), homogeneous β -lauryl-polyethyleneoxy ($n=3,6,9,12,18$) propionitriles, together with the reaction rate increase the monomer consumption. The determination of the partial reaction order with respect to glymes allowed the indirect estimation of the size of the elementary coordination “cell” of the alkaline cation at the value of 8-9, and the thermody-



(a) controlled modification of homogeneous polyoxyethylene (PEO) chains (n=3, 6, 9, 12, 18), monoderivatized R(NF;EH) by cyanoethylation and total acid hydrolysis [R(EO)_nPC];
 (b) actual processing of conjugates PEG_n-L (2R';R) (R';2R)

Figure 11. Overall processing scheme of conjugates PEG_n-L(2R';R) (R';2R) [10]

namic expression of the rate constant did the same for the calculation of the “reverse” micelle-processing medium phase-transfer free energy [9].

A reversible reaction, cyanoethylation is influenced by temperature, time, excess reagent (monomer) and addition products. Secondary products existent in the unpurified technical raw materials (higher alcohols, polyethylene glycols, traces of water) and oligomers of AN affect the yields of nucleophilic addition in the synthesis of HEHAO through the consumption

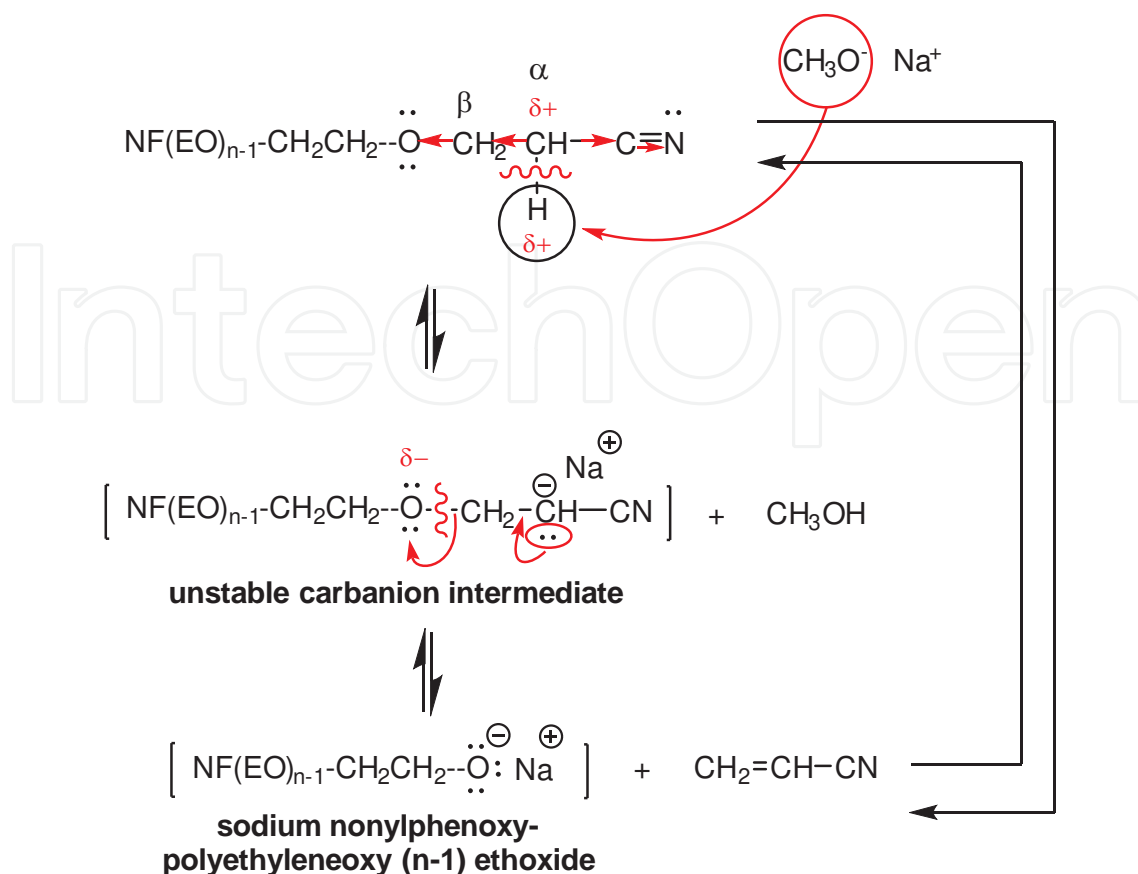


Figure 12. Mechanisms of the cleavage of the “ether bridge” formed in β -nonylphenoxypolyethyleneoxy ($n=3-18$) propionitriles under prolonged contact with the basic catalyst $[\text{CH}_3\text{O}^-\text{Na}^+]$

of monomer and further purification complications. The presence of oligomerization inhibitors favors the yields.

The partial hydrolysis of homogeneous β -R-polyethyleneoxy-propionitriles (HOHAO) is a heterogeneous process due to the limited solubility in water of homogeneous polyethyleneoxy ($n=0-18$) nitriles and their corresponding amides, respectively. The low reaction temperature along with the reduced solubility and the waxy, consistent appearance of homogeneous β -R-polyethyleneoxy ($n=0-18$) propionamides, constitute serious impediments in obtaining high hydrolysis yields. The use of large amounts of water or high reaction temperatures increase the total hydrolysis yields with the formation of the corresponding homogeneous β -R-polyethyleneoxy ($n=0-18$) propionic acids. In the research carried out it was proceeded to the partial hydrolysis of nitriles with 90% concentrated sulphuric acid in the temperature range $0-15^\circ\text{C}$.

Homogeneous β -R-polyethyleneoxy-propionic acids were also obtained through the acid-catalyzed exhaustive hydrolysis of homogeneous β -R-polyethyleneoxy-propionitriles. Depending on the processing conditions of the reaction products two classes of HOHAO are obtained: the free acids or their salts (soaps), $\text{R-(EO)}_n\text{-PC}$, with confirmed surface-active properties [19,22,23]. The evolution of the total hydrolysis yield is determined by the hetero-

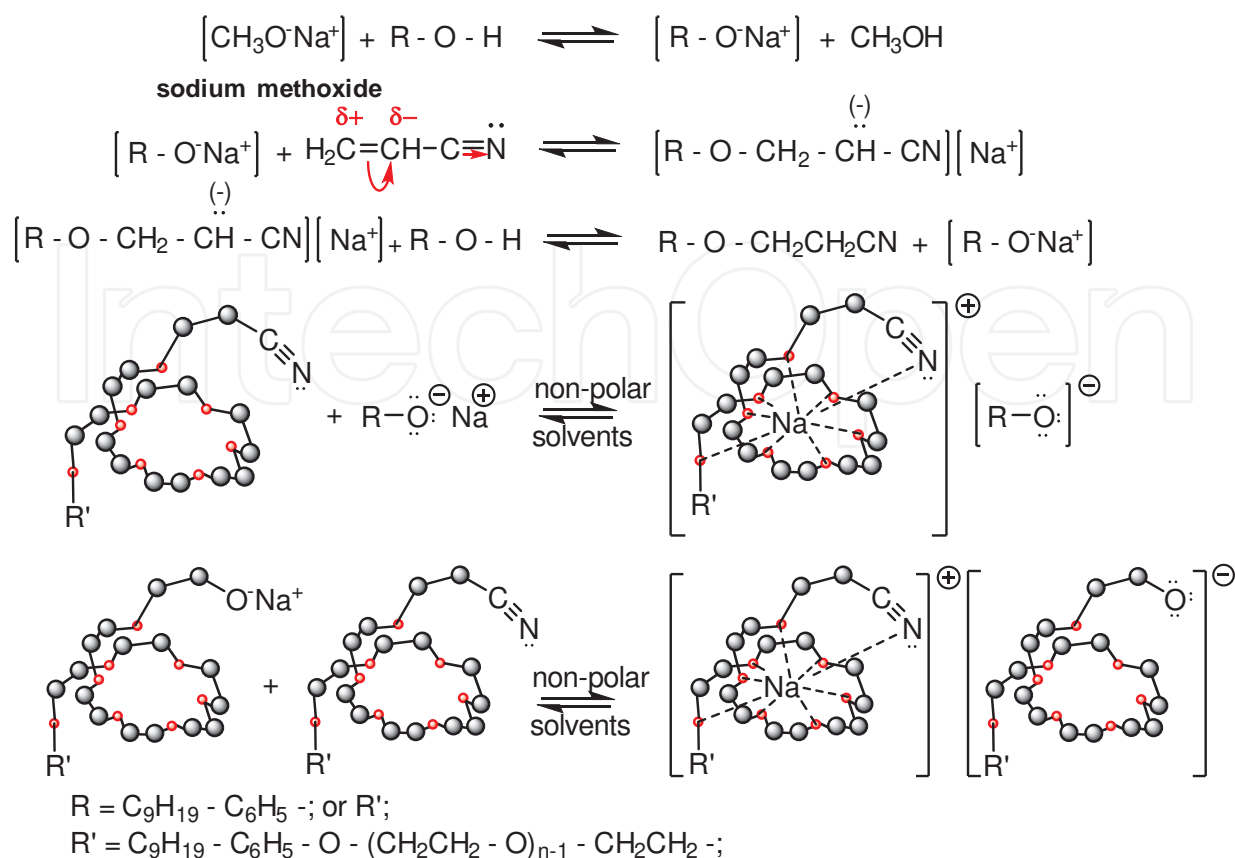


Figure 13. Scheme of the principle of coordination in non-polar solvents of alkali cations in the cavity of the polyoxyethylene chain with 8-9 oxygen atoms of β -R-polyethyleneoxy-propionitriles

geneity of the reaction medium (biphasic system); phenomena of micellar catalysis in emulsion or of phase-transfer play a major role in the development of the processes [22].

The nature of the acid catalyst (HY) $\text{Y}=\text{Cl}^-$; HOSO_3^- ; $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_3^-$, paratoluenesulphonic acid (TS); $\text{C}_{12}\text{H}_{25}\text{C}_6\text{H}_4\text{SO}_3^-$, dodecylbenzenesulphonic acid (DBSH), influences favorably the hydrolysis yields through the acid's strength. While in the presence of concentrated sulphuric acid at low temperatures are obtained predominantly homogeneous β -substituted propionamides, in the presence of hydrochloric acid above 80°C the corresponding propionic acids are formed. Under paratoluenesulphonic and/or dodecylbenzenesulphonic acid catalysis the yields in homogeneous β -R-polyethyleneoxy-propionamides increase at low temperatures for low molar ratios $\text{HY/R-(EO)}_n\text{PN}$, also on the account of the homogenizing effect of these structures with surface-active properties [22].

Increasing the temperature and the molar ratio HY/propionitrile favors the total hydrolysis yields. The amount of acid selectively influences the hydrolysis of nitriles. Thus, excess hydrochloric acid favors the formation of homogeneous β -substituted propionic acids, alongside their corresponding esters with higher alcohols either present as impurities or originating in the cleavage in acid medium of "ether bridges" formed in the cyanoethylation or amidoethylation process or existing initially in the homogeneous polyoxyethylene chain,

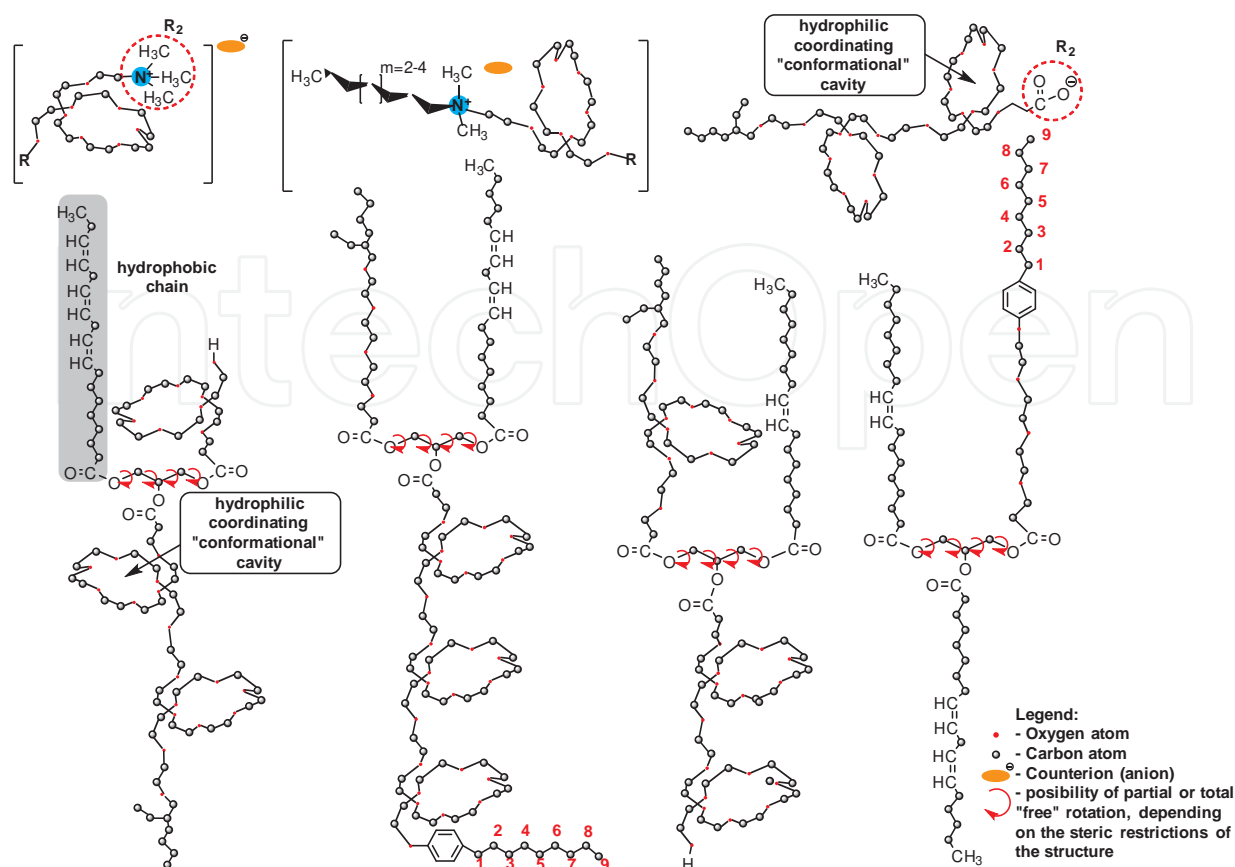


Figure 14. Three-dimensional conformation of HOHAO with structures generating difficulties of "packing" at hydrophilic and/or hydrophobic interfaces

while excess *n*-dodecylbenzenesulphonic acid favors preferentially the formation of propionamides and less of propionic acids, without the formation of the corresponding esters [28,29].

In all cases, above 80°C the content of homogeneous β -R-polyethyleneoxy ($n=0-18$) propionitriles decreases markedly regardless of the acid catalyst used and the presence of propionate esters is observed. Above 110°C in the presence of hydrochloric acid increasing amounts of higher alcohol are observed due to the cleavage of "ether bridges". Increasing the reaction time favors the total acid hydrolysis. At high temperatures (over 80°C) in the presence of hydrochloric acid, after approx. 60 minutes the β -substituted propionitrile disappears from the reaction mixture, and after 90 minutes also does the propionamide formed intermediately. In the presence of TS, at the same temperature and amount of water, propionitriles and propionamides can be found in traces even after 180 minutes and total conversions are generally not reached.

Hydrolysis of homogeneous β -R-polyethyleneoxy ($n=3-9$) propionitriles in the presence of free homogeneous polyethoxylated ($n=3-9$) higher alcohols ($C_{12}-C_{18}$) ensures the obtention of high yields of hydrolysis. In parallel the content of propionic ester is increasing, the more so as the length of the homogeneous polyoxyethylene chain in the homogeneous polyethoxylated ($n=3-9$) higher alcohol introduced is smaller.

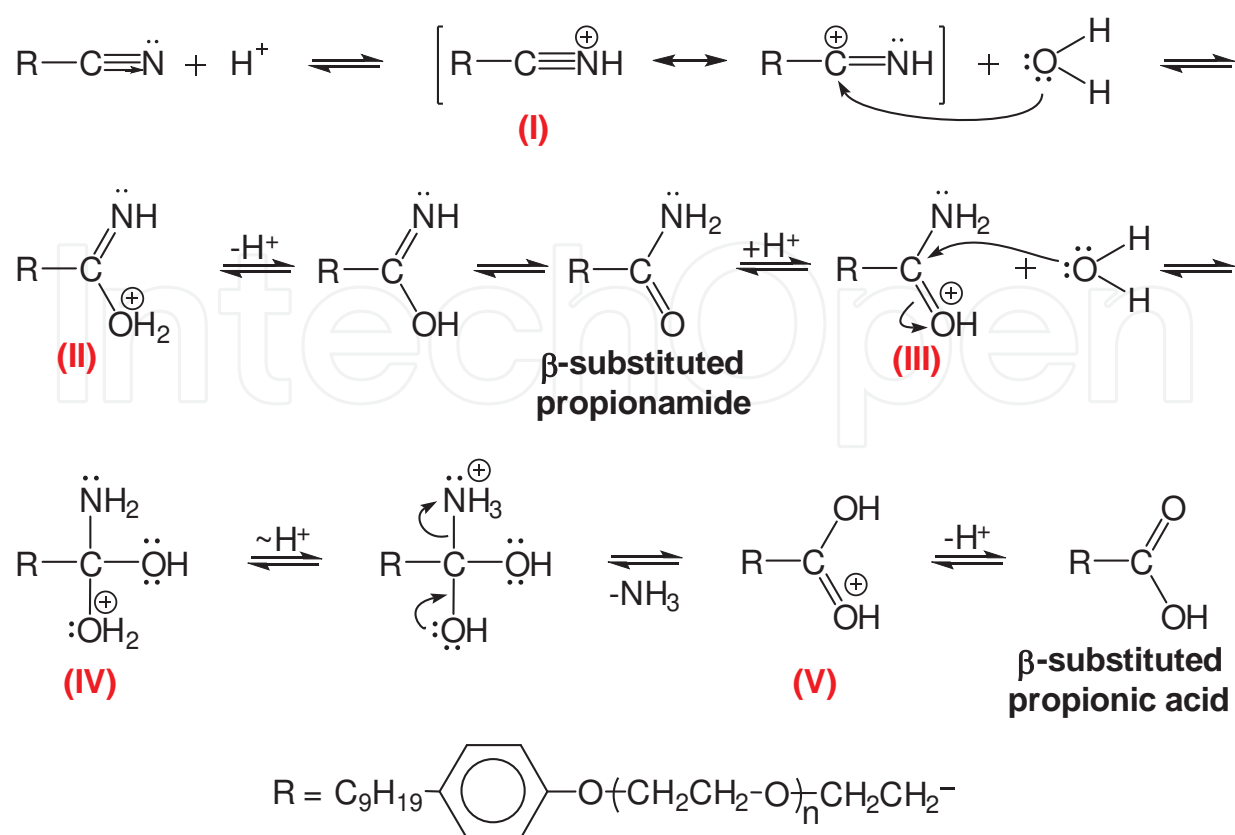


Figure 15. Probable mechanism for the exhaustive acid hydrolysis of β -nonylphenoxy polyethyleneoxy ($n=3-18$) propionitriles (β -substituted propionamide; β -substituted propionic acid) [22,23]

The favorable effect of homogeneous polyethoxylated ($n=3-9$) higher alcohols ($\text{C}_{12}-\text{C}_{18}$) with increasing polyoxyethylene chain on the process of total acid hydrolysis of propionitriles implies the existence of micellar catalysis ($n \geq 9$) or in emulsion phenomena (for $n=3-9$) [9].

Under the same conditions, increasing the homogeneous polyoxyethylene chain's length in the nitrile subjected to hydrolysis favors the yields, due to the stabilization effect on the hydrolysis intermediates. Increasing the hydrocarbon chain influences negatively, through its length, the total acid hydrolysis yield, probably due to steric reasons similar to cyanoethylation.

Because the hydrolysis of β -substituted propionitriles is a heterogeneous process which takes place both at the separation interface of the two phases (water/organic) and inside the two phases due to the mutual solubility of the two reagents, the use of the most diverse structures of the aforementioned phase-transfer catalysts in the class of the cationic HOHAO synthesized [*N,N,N*-trimethyl-*N*- β -lauryl/myristyl (7/3) oxy-ethylammonium chloride], LM-O-EC-1.1.1, determines the increase of total hydrolysis yields, without the cleavage of "ether bridges" even under mild reaction conditions [28,29].

- b. Synthesis of homogeneous heterobifunctional acyclic oligomers of ethylene oxide in the category of customized (structured) lipids.

In the series of efforts to diversify the macromolecular architectures HOHAO structured lipid similar to conjugates PEG_nL (Figure 5) were obtained with composition, physico-chemical and functional characteristics specific to the physiological benefits of cell membranes.

An adapted classical reaction scheme was accessed following these steps (Figure 14):

- synthesis, purification and characterization of the homologous series of homogeneous β -alkyl (EH) alkyl aryl (NF) polyethyleneoxy ($n=0-18$) propionic acids, HOHAO presented above R(EO)_nPC (Figure 10);
- solid/liquid extraction in petroleum ether (b.p.=30-60°C) of glycerides in the divided seed material of coriander (*Coriandrum sativum*, R'_{co}), grapes (*Vitis vinifera*, R'_s), dog rose (*Rosa canina*, R'_m), and nuts (fruits) of wild sweet chestnut (*Castanea vesca*, R'_{ca}), respectively.

In all the variants studied unsaturation in variable proportions is confirmed, by higher acids: oleic (C₁₈;1 Δ); linoleic (C₁₈;2 Δ) and linolenic (C₁₈;3 Δ).

The content of saturated higher acids, approx. 10.1% C₁₆ in grapes (s), 10.9% C₁₆ in wild sweet chestnut (ca), 3.18% C₁₆ in dog rose hips (m) and 2.7% C₁₆ in coriander (co), does not change the "fingerprint" of the vegetable lipid fractions rich in ω_3 acids of major interest in the composition of functional lipids reported in the last decades.

It is noted that in the saponified lipid fraction from grapes and dog rose hips predominate the acids C₁₈;2 Δ with a share of 57% and 83%, respectively. In continuation of the preparation scheme of PEG_n-L follow:

- separation of unsaponifiables, followed by the exhaustive acid hydrolysis (HCl) of free higher acids in R'_{co}; R'_m; R'_{ca}; R'_s, their purification and gas-chromatographic characterization;
- directed esterification of glycerol mono-and/or diprotected with R(EO)_nPC or free higher acids R'_{co}; R'_m; R'_{ca}; R'_s respectively.

c. Fundamental colloidal competences of surface-active HOHAO

Two basic surface-active properties were evaluated suggesting potential directions for the exploitation of synthesized HOHAO depending on the structural elements of the respective homologous series (hydrophilic-hydrophobic index, HLB, surface tension and critical micelle concentration, respectively) [33]. The determinations allowed the formulation of structure-surface activity correlations [30].

Surface tension as a form of free energy (expressed in N/m or dyne/cm) independent of the shape of the interface separating two phases in a system, is a function of temperature, time, and the structural characteristics of the HOHAO considered. Because the interface equilibrium is established within a short period, the existence of static and dynamic surface tension is accepted [34]. The latter manifests itself in aqueous floats of HOHAO and subsequently acquires great practical significance in the process of their actual use. Two aspects can be distinguished:

- the capacity of HOHAO to reduce the surface tension, expressed as the concentration required to achieve a certain effect of reducing the surface tension;

- the effectiveness of HOHAO, expressed by the minimum value which is capable of reducing the surface tension.

It will be proceeded to selectively comment some of the colloidal characteristics of the class. Following the evolution of the surface tension in the homologous series of cationic HOHAO synthesized, the following can be stated:

- for the same n and R_2 , $R_2 = -N(CH_3)_2 C_m H_{2m+1}$, $m = 1-18$, the capacity to reduce the surface tension increases in the series $LM < CS$, and the effectiveness of reduction decreases in the order $LM > CS$, as a result of the increase of the length of the hydrocarbon chain R_1 ;
- for the same n and R_1 , the capacity to reduce the surface tension decreases in the series of chain homologues R_2 , and the effectiveness of reduction increases with the R_2 chain's length due to the movement towards the center of the hydrophilic ionic polar group (Figure 14) ;
- for the same R_1 and R_2 , the effectiveness of reducing the surface tension increases in the order $(EO)_0 < (EO)_3 < (EO)_6 < (EO)_9 \dots < (EO)_{20}$, while the capacity to reduce the surface tension decreases in the same order: $(EO)_0 > (EO)_6 \dots > (EO)_{20}$, due to the increased hydrophilic (polar) character of the cationic structure and its solubility.

The most pronounced capacity to reduce the surface tension in the homologous series of *N,N*-dimethyl-*N*-alkyl (C_1 - C_4)-*N*- β -cetyl/stearyl (7/3) oxy-ethylammonium chlorides and *N,N*-dimethyl-*N*-alkyl (C_1 - C_4)-*N*- β -cetyl/stearyl (7/3) polyethyleneoxy ($n = 3-6$) ethylammonium chlorides, in comparison with *N,N*-dimethyl-*N*-alkyl (C_8 - C_{16})-*N*- β -lauryl/myristyl (7/3) oxy-ethylammonium chlorides and *N,N*-dimethyl-*N*-alkyl (C_1 - C_4)-*N*- β -lauryl/myristyl (7/3) polyethyleneoxy ($n = 3-18$) ethylammonium chlorides can be explained by the difference in the intensity of repulsion between the ionic and nonionic polar hydrophilic groups identically oriented at the separation interface [9]. In the first case the role of entropic factor lowers significantly on account of the increase of the micellization free energy, while in the second case it increases due to the reduction of the micellization free energy at the separation interface with the consequence of accumulation of increased numbers of surface-active cationic molecules (micelles). Another explanation can also be found in the relationship between the capacity to reduce the surface tension and the concentration of the surfactant at the liquid-air separation interface, the latter being decisively influenced by the free energy of the diffusion process from the aqueous float to the interface and the free energy of formation of cationic HOHAO micelles. The decrease of the micelle formation entropy corresponds to an advanced ordering in the micelle, that accumulates around it a greater number of water molecules as the polarity of the ionic hydrophilic group is higher.

The movement of the ionic polar group or the nonionic one towards the center of the cationic structure is followed by an advanced reduction of the entropic effect in solution (the effective length decreases along with the degree of "packing" at the interface), therefore of the capacity to reduce the surface tension [9].

In the homologous series of *N,N*-dimethyl-*N*-alkyl (C_1 - C_{16})-*N*- β -alkyl (C_{12} - C_{18}) polyethyleneoxy ($n = 0-20$) ethylammonium chlorides, the value of the critical micelle concentration (CMC) for the same environmental conditions is influenced by:

- the increase of the hydrocarbon chain's R_1 length (R_2 and n identical), which lowers the CMC value by reducing the solubility;
 - the increase of the hydrocarbon chain's R_1 length (R_2 and n identical) lowers the CMC value due to the reduction of the degree of "packing" at the interface;
 - the increase of the hydrocarbon chain's length (R_1 and R_2 identical) lowers the CMC value through the high hydrophilicity of the HOHAO structures.
- d. Fundamental colloidal competences and coordination (sequestration) competences of homogeneous heterobifunctional acyclic oligomers of ethylene oxide from the category of customized (structured) lipids

The numerous hopes of obtainment and technological implementation of the conjugates $PEG_n-L(2R';R)(R';2R)$ due primarily to their diversified structure, were based on their potential colloidal qualities: colloidal (micellar) solubility, interface phenomena, interfacial surface tension (σ), correlated with the critical micelle concentrations (CMC).

In the structure of customized lipids the independent variable, the homogeneous oligomerization degree (n), can provide in a homologous series the controlled modification of the hydrophilic/hydrophobic balance (HLB index), and implicitly the range of later practical applications.

From the evaluation of HLB values the following can be stated:

- increasing the homogeneous oligomerization degree (n) for the same hydrocarbon chain R and/or R' , either for the $PEG_n-L(R';2R)$ or $PEG_n-L(2R';R)$ conjugates, respectively, shows a more prominent increase of the HLB index for the first case regardless of the nature of R and/or R' ;
- increasing the share of hydrocarbon chain R' against R also determines the reduction of the HLB index value;
- modifying the chain $R(NF;EH)$ for the same structure of conjugate PEG_n-L and the same homogeneous oligomerization degree (n) causes variations in the HLB index due to the structural differences between the two chains;
- the modification of the hydrocarbon chain R' (R'_{ca} ; R'_s ; R'_m ; R'_{co}) for the same homologous series of conjugate PEG_n-L and homogeneous oligomerization degree (n) does not attract significant variations of the HLB index either for the same reasons;
- we find a good agreement between the HLB values determined [10] and calculated [30], which justifies the premises and operating colloidal strategies;
- in the series of the 48 conjugated PEG_n-L studied the overall range of variation of the HLB index is between 2.5-14, which allowed their indicative grouping in structures: $HLB=1-4$: lipophilic (insoluble in water) non-dispersible; $HLB=4-6$: partially dispersible (partially soluble in water); $HLB=6-8$: unstable microemulsions (after vigorous mechanical stirring); $HLB=8-10$: stable microemulsions (after gentle mechanical stirring); $HLB=10-13$: translucent (opalescent) to clear in the upper area of the domain; $HLB>13$: soluble, transparent).

Surface tension (σ) is a function of temperature, duration and structural characteristics also in the series of conjugates $\text{PEG}_n\text{-L}$ ($2\text{R}'$;1R) (R' ;2R).

The evaluation of this colloidal characteristic in close connection with the critical micelle concentration (CMC) sought to assess the ability of these structures to reduce the surface tension overall, and also the effectiveness of providing a minimum surface tension for a given concentration.

From the comparative interpretation of the experimental data the following correlations can be formulated:

- for the same homogeneous oligomerization degree (n) and the same hydrocarbon chain (R') the capacity to reduce the surface tension (σ) increases in the series $\text{R}(\text{EH}) \rightarrow \text{R}(\text{NF})$, while the effectiveness of reduction decreases in the order $\text{R}(\text{NF}) \rightarrow \text{R}(\text{EH})$, probably due to differences in chain length C_8 (EH) and C_{15} (NF), respectively;
- for the same homogeneous oligomerization degree (n) and the same hydrocarbon chain (R) the capacity to reduce the surface tension (σ) decreases significantly in the hydrocarbon chain series R' ($\text{R}'_{\text{co}} \geq \text{R}'_{\text{m}} > \text{R}'_{\text{ca}} > \text{R}'_{\text{s}}$), while the effectiveness of reduction of (CMC) increases in the same order, probably due to the movement of the hydrophilic polar groups towards the center of the structure of conjugates $\text{PEG}_n\text{-L}$ (Figure 14);
- for the same hydrocarbon chain R and R' the capacity to reduce the surface tension (σ) decreases with increasing the homogeneous oligomerization degree (n), while the effectiveness of reduction of (CMC) increases in the same homologous series of polyoxyethylene (PEO) chain ($n=3-18$), probably due to the intensification of the hydrophilic character of conjugates $\text{PEG}_n\text{-L}$, and of the solubility in the polar medium (water).

From the comparative interpretation of the experimental data on the coordination characteristics the following can be stated [10]:

- the sequestration (coordination) competences of the conjugates $\text{PEG}_n\text{-L}(2\text{R}'$;1R) (R' ;2R) depend on their concentration (below and/or above CMC) in the processing environment;
- the coordination competences in the homologous series of derivatized homogeneous polyoxyethylene (PEO) chains ($n=3,9,18$) studied can be correlated with the values of the main colloidal parameters: HLB index, cumulative homogeneous oligomerization degree (n_c), surface tension (σ);
- the coordination competences depend on the ionic radius (\AA) in the series of metal cations studied: $\text{Mg}^{2+}(0.65)$, $\text{Na}^+(0.95)$, $\text{Ca}^{2+}(0.99)$, $\text{K}^+(1.33)$ [10], below and above the CMC values of the respective conjugates $\text{PEG}_n\text{-L}(2\text{R}'$;1R) (R' ;2R); the premises formulated in the specialized literature on the similarity of the geometric coordinates of the conformational "host site" (diameter, radius, area etc.) of the homogeneous polyoxyethylene (PEO) chains ($n \geq 9$), with the geometric coordinates of the "guest" (ionic radius, diameter of metallic cations) are confirmed;
- the coordination competences follows the same trend in the case of coordination of transitional metal cations $\text{Ni}^{2+}(0.69)$, $\text{Co}^{2+}(0.72)$, $\text{Mn}^{2+}(0.80)$;

- the coordination competences can also be extrapolated through the structural parameter ionic radius (Å) to a coordination number (N.C.). The correlation relative to the sodium cation (centered cubic lattice with N.C.=6) took into account that in the case of transitional metal cations the evaluated interatomic distances are smaller due to the polarizability of the anions under the influence of proper metal cations, and that the atomic volume of alkali and alkaline-earth cations is larger than that of transitional cations;
- the preliminary study of the coordination competences for certain transitional metal cations (known promoters of lipid autooxidation) has technological importance in avoiding and/or eliminating autooxidation processes due to the high degree of unsaturation of the hydrocarbon chains (R'_{ca} ; R'_s ; R'_m ; R'_{co}) in conjugates $PEG_n-L(2R';1R)$ ($R';2R$);
- the phase-transfer competences assessed comparatively through the partition coefficient values K_D (1,2-dichloroethane) and/or K'_D (isooctane) suggest that the hydrophilicity of conjugates $PEG_n-L(2R';1R)$ ($R';2R$) favors the interphase distribution of the "host-guest" (PEO chain-metal cation) systems in industrial processing;
- because there are no significant differences between the K_D and K'_D values, the evaluated experimental data confirm the reality of the phase-transfer processes studied;
- the phase-transfer competences for the same cumulative homogeneous oligomerization degree (n_c) are lower for the conjugates $PEG_n-L(2R';1R)$ ($R';2R$) with hydrocarbon chains $R(EH)$ compared with $R(NF)$ due to differences in hydrophobicity [$EH(C_8) < NF(C_{15})$] and [$2EH(2C_8) < 2NF(2C_{15})$], respectively.

The comparative evaluation of the colloidal experimental data of conjugates $PEG_n-L(2R';1R)$ ($R';2R$) themselves revealed that not all the structures obtained offer directly potential colloidal and coordination competences due to the different degree of dispersibility in aqueous media (HLB=1-8) (increased lipophilicity).

Their exclusion from further tests does not represent the acceptable technical solution, which suggested two future work strategies:

- the study of cumulated colloidal competences in mixed systems $PEG_n-L(2R';1R)$ ($R';2R$) (HLB=1-8) with homogeneous polyoxyethylene chains ($n=9,18$), monoderivatized $R(EH;NF)$;
- the study of cumulated colloidal competences in mixed systems $PEG_n-L(2R';1R)$ ($R';2R$) (HLB=1-8) / $PEG_n-L(2R';1R)$ ($R';2R$) (HLB=9-13) (HLB>13).

In both variants it was counted on the cumulative properties recognized in the specialized literature, similar for mixtures with different proportions of colloidal (surface-active) compounds, but also of the structural units composing them. Thus, in order to shift the cumulative hydrophilic/hydrophobic balance (HLB_c) towards increasing hydrophilic character, it was originally resorted to homogeneous polyoxyethylene (PEO) chains ($n=3-18$) monoderivatized $R(EH;NF)$ with high HLB values ($HLB_{EH9}=15.35$; $HLB_{NF9}=12.86$; $HLB_{EH18}=17.37$; $HLB_{NF18}=14.24$). In this respect we can also admit the existence of a cumulated homogeneous oligomerization degree (n_c), exemplified randomly by $PEG_3-L(R_s;2NF)$ ($n_c=6$) or $PEG_{18}-L(R_s;2NF)$ ($n_c=36$).

Three categories of conjugates $\text{PEG}_n\text{-L}$ ($2\text{R}'$;1R) (R' ;2R) have been selected in the intervals $\text{HLB}=1\text{-}4$, $\text{HLB}=3\text{-}6$, $\text{HLB}=6\text{-}8$, respectively, each with eight representatives to which were controlledly added 1%, 10% and 20%, respectively, homogeneous polyoxyethylene (PEO) chain ($n=3\text{-}18$) monoderivatized $\text{R}(\text{EH};\text{NF})$, corresponding to the hydrocarbon chain R in the conjugates $\text{PEG}_n\text{-L}$ ($2\text{R}'$;1R) (R' ;2R) ($\text{HLB}=1\text{-}8$) evaluated. The HLB_c values (Pearson rule) experimentally verified by sampling led to results falling below the error limit of the confidence interval ($\pm 1\%$).

The typical colloidal characteristics were correlated and interpreted: surface tension (σ), critical micelle concentration (CMC), hydrophilic-hydrophobic balance (HLB), with the structural parameters for the 18 conjugates $\text{PEG}_n\text{-L}(2\text{R}'$;1R) (R' ;2R) nominated and subsequently associated in binary and ternary systems, overall finding that:

- increasing the homogeneous oligomerization degree (n) and the unsaturation in the chains R' ($\text{R}'_{\text{sr}}; \text{R}'_{\text{ca}}; \text{R}'_{\text{m}}; \text{R}'_{\text{co}}$) $1\Delta \rightarrow 2\Delta \rightarrow 3\Delta$ favors the hydrophilicity of conjugates $\text{PEG}_n\text{-L}(2\text{R}'$;1R) (R' ;2R);
- between the chains $\text{R}(\text{EH})$ and $\text{R}(\text{NF})$ differences in the colloidal behavior exist and manifest themselves sensibly in favor of increasing the hydrophobic character of conjugates [$\text{R}(\text{EH})(\text{C}_8) < \text{R}(\text{NF})(\text{C}_{15})$], due to the movement of the homogeneous polyoxyethylene (PEO) chains ($n=3\text{-}18$) towards the center of the structure of conjugates [$\text{R}(\text{NF})(\text{C}_{15}) < \text{R}(\text{EH})(\text{C}_8)$];
- the exclusive modification of the ratio R'/R affected the interface and transfer colloidal characteristics ($\text{R}' > \text{R}$ decrease $\text{R}' < \text{R}$ increase), probably due to “steric restrictions” adversely affecting “the degree of packing” of conjugates $\text{PEG}_n\text{-L}(2\text{R}'$;R) (R' ;2R) at interfaces;
- a high degree of unsaturation affects the colloidal characteristics, the more so as the share of higher unsaturated acids 2Δ and 3Δ is higher, due to their possibilities of spatial arrangement as geometric isomers, but also to the reduction of the capacity of free rotation (C-C) in the structure of conjugates $\text{PEG}_n\text{-L}(2\text{R}'$;R) (R' ;2R);
- the colloidal phenomena in the structural category of systems $\text{PEG}_n\text{-L}(2\text{R}'$;R) (R' ;2R) studied differ for concentration values below CMC [conformational competences are present exclusively due to the homogeneous polyoxyethylene (PEO) chains ($n=3,9,18$)] and values above CMC, both the conformational competences and the ones of micellar solubilization of homogeneous polyoxyethylene (PEO) chains ($n=3,9,18$) occur cumulatively and simultaneously;
- the gradual presence of homogeneous polyoxyethylene (PEO) chains ($n=9, 18$) monoderivatized $\text{R}(\text{EH};\text{NF})$ along with conjugates $\text{PEG}_n\text{-L}(2\text{R}'$;R) (R' ;2R) with $\text{HLB} < 6$ in binary and/or ternary associated systems favors the structuring of systems $\text{PEG}_n\text{-L}$ with $\text{HLB}' n_c \geq 8$, which widens the range of structural variants capable of interface and transfer phenomena, beneficial to the technological practice.

6. Conclusions and perspectives

Overall it can be stated that the obtainment and characterization for the first time of homogeneous heterobifunctional oligomers of ethylene oxide (HOHAO) as “niche” structures represents a “challenge” with real future perspectives.

The potential applications envisaged are based primarily on their structure but also their varied composition which allow the expression in perspective of colloidal phenomena [wetting, foaming/defoaming with the three components (strength, density, stability) [31,32], softening agent, micellar solubilization, controlled emulsification, adsorption at the interface in normal micelles (aqueous medium) and reverse micelles (non-aqueous media), cleaning in the most various hypostases (including resistance to hard water), chemical interface processes (chemisorption), coordination/sequestration and phase transfer, etc.]. The diversity of lipid conjugates and their competences recommends them as specialized structural units of the cell membrane walls.

Preliminary tests carried out and ongoing support these assertions.

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