

New Polydentate Sequestrants: Synthesis, Management and Potential Applications

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Nitrilotriacetic acid (NTA), a polydentate sequesterant, is accessed in fundamental and applied research for coordination processes of metal cations, generally of small entities. Practical interest determined also the diversification of the structural range by the synergistic cumulation of the sequestering competences of NTA with "homogeneous" ($n=3-18$) polyoxyethylene (PEO) chains, cyanoethylated and hydrolyzed exhaustively under acid catalysis in the presence of phase-transfer catalysts (PTC). This work aims to achieve, to formulate managerial considerations, potential applications and to characterize the series of "homogeneous" polyethoxylated ($n=3-18$) nitrilotripropionic acids, starting from triethanolamine (TEOA), "homogeneously" polyethoxylated ($n=3-18$) by the modified Williamson method, followed by cyanoethylation and exhaustive hydrolysis.

Keywords: Triethanolamine polyethoxylated, nitrilotripropionic acid, complexon, triethanolamine cyanoethylated

TEOA (fig. 1a) is an aminoalcohol, generator of mixed tetradentate chelates (GCTM) (fig. 1b), as it can coordinate small entities concomitantly through both the nitrogen and the oxygen atom as electron donors.

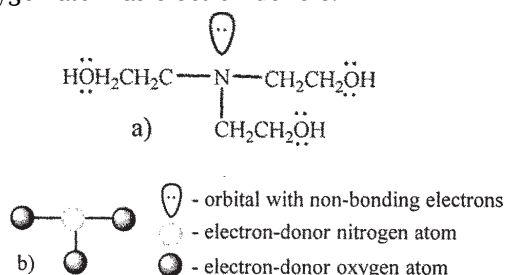


Fig. 1. The scheme of the structural arrangement of the electron-donating atoms (N; O) in the triethanolamine molecule (mixed tetradentate chelating agent)

In the GCTM category we find mainly complexon I (aminopolycarboxylic acids), dithioamine, bis-Schiff bases and templates macrocyclic compounds, respectively, etc. [1]. Nitrilotriacetic acid (H_3NTA), complexon I or Trilon A (fig. 2a) is found in solution in the betaine form (fig. 2b).

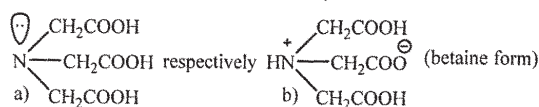


Fig. 2. Structural forms of nitrilotriacetic acid (NTA)

NTA coordinates metal ions generating five-membered cyclic structures [1,2] of the $[M^II(NTA)]^-$; $M^II = Mg, Ca, Sr, Ba, Fe, Mn, Co, Ni, Cu, Zn, Pb, Cd$, or $[M^III(NTA)_2]^{3-}$ type.

The knowledge and diversification of the range of structures able to coordinate (sequester) metal cations and small-size organic molecules has over the years concerned (reviews, monographs, patents etc.) a large number of researchers [3-6]. Under the requirements of management systems of food quality and safety, the

identification of new sources of multifunctional food additives represents a current priority [7,8].

Vegetable and animal products as raw materials, semi-finished or finished products contain: variable amounts (order of mg/100 g product) of various metal cations;

- variable amounts of the same order of magnitude of natural antioxidants: $\delta > \gamma > \beta > \alpha$ tocopherols; nordihydroguaiaretic acid (NDGA); gossypol etc.

The annihilation during preservation (storage) of the natural antioxidants above due to atmospheric oxygen determines the undesirable acceleration of lipid oxidation processes, with the consequence of accelerated degradation of nutritional utilities carriers in the chain of production-processing-food consumption.

Motivated also by the low toxicity, "no level effect" according to some sources, of polyoxyethylene (PEO) chains with various oligomerization degrees ($n=3-18$), based also on other encouraging preliminary experimental results, our interest extended towards the achievement and formulation of managerial considerations on new structures of the "homogeneously" polyethoxylated ($n=3-18$) nitrilotripropionic acids type (fig. 3).

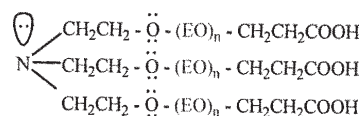


Fig. 3. Structure of polydentate sequesterant "homogeneously" polyethoxylated ($n=3-18$) nitrilotripropionic acids

Polyoxyethylene (PEO) chains as such and derivatized gained theoretical and practical interest at the beginning of the fourth decade of the last century, together with the synthesis of the first superficial-active products of condensation of higher acids with cu ethylene oxide (EO) and thereafter [9-11].

The rediscovery of crown polyethers and their role as phase-transfer catalysts (PTCs) [12] was the decisive impulse in the conformational study of acyclic POE chains.

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The behavioral similarity imposed a new terminology and the recognition of these structures as biomacromolecules with major physiological role (PEGylation compounds) [11,13-16].

After 1960 the coordination competences of alkali cations in the matrix of POE chains as such and derivatized are also explicitly recognized. The striking analogy to crown polyethers could not fail to impose questions and answers concerning their capacity, stability and coordination geometry. Certainties arose after the series of experimental evidence confirmed the wave of scientific speculations which preceded by several decades through conformational and geometric hypotheses the architecture of POE chains [13-16].

Today it is unanimously admitted that the geometry of the "coordination cavity" is flexible, mobile and dependent on the length of the POE chain and the geometry of the coordinated metal cations, respectively [29].

Experimental part

Materials, reagents (Sigma-Aldrich Germany): triethanolamine; triethyleneglycol; acetyl chloride; thionyl chloride; benzyltrimethylammonium hydroxide (40% methanolic solution); acrylonitrile (stabilized monomer).

Working protocols

Processing of exhaustively sodated triethanolamine [17,19-24]

Processing of "homogeneously" ($n=3-18$) polyethoxylated triethanolamine [17,19-24]

Processing of monoacetylated "homogeneous" ($n=3-18$) polyethyleneglycol [17,19-24]

Processing of monoacetylated "homogeneous" ($n=3-18$) chloro polyethyleneglycol [17,19-24]

Cyanoethylation of "homogeneously" ($n=3-18$) polyethoxylated triethanolamine (fluid products) [17,19-24]

Cyanoethylation of "homogeneously" ($n=10-18$) polyethoxylated triethanolamine (solid products) [17,19-24]

Exhaustive acid hydrolysis of cyanoethylated "homogeneously" ($n=3-18$) polyethoxylated triethanolamines [17,19-24]

Results and discussions

Triethanolamine has low basicity, but can form alkali aminoalkoxides by both classical methods, treatment with

alkali metals or hydroxides, in a perfectly dry reaction medium (controlled inert atmosphere free from traces of water, CO_2 and oxygen) [17,25-28].

Exhaustively sodated triethanolamine of controlled purity, processed with monochlorinated "homogeneous" polyethyleneglycols protected by monoacetylation, leads to polyoxyethylene ($n=3-18$) TEOA structures (fig. 4).

The processing yields indicated in the specified transformation sequence are decisively dependent on the purity of the raw materials used, particularly the water content, since being hydroxyl compounds they participate in cyanoethylation, or annihilate the alkoxides of polyethoxylated triethanolamine (alkalinity is necessary to catalyze the nucleophilic addition).

"Homogeneous" ($n=3-18$) polyoxyethylene (POE) chains (fig. 4) were accessed in order to specify the real, individual contribution of each oligomer and not the sum of the effects of statistical distribution as in the case of heterogeneous POE chains (from industrial processing).

In the conditions of a 3/1 TEOA(EO) $_{3n}$ /AN molar ratio, increasing the temperature in the 25-30°C range determines the increase of cyanoethylation yields, after which they drop in the 40-50°C range. In excess of acrylic monomer the yields follow the same trend. In these conditions in the 30-40°C range the amount of oligomers formed is below 1%, independently of the excess of monomer used, and between 50-60°C it increases markedly. This behaviour suggests that the cyanoethylation reaction has a reversible character, the polyethoxylated chain favors the addition (proportionally with the increase of the oligomerization degree " n ").

Preliminary cyanoethylation attempts of TEOA-(EO) $_n$; $n=3-18$ revealed in this case too that the oligomerization processes of the acrylic monomer, especially at temperatures above 40°C, hold a significant share. Nucleophilic addition yields decrease considerably, and the reaction tends to unfold violently, strongly exothermically, with the formation of reddish-brown resins soluble in polar solvents (water, acetone etc.), or yellow solid products, soluble in solvents with medium, low polarity [17].

The nature of the acid catalyst favorably influences the total hydrolysis yields through the acid strength. If in the presence of concentrated acid sulfuric at low temperatures are obtained mainly propionamides, in the presence of

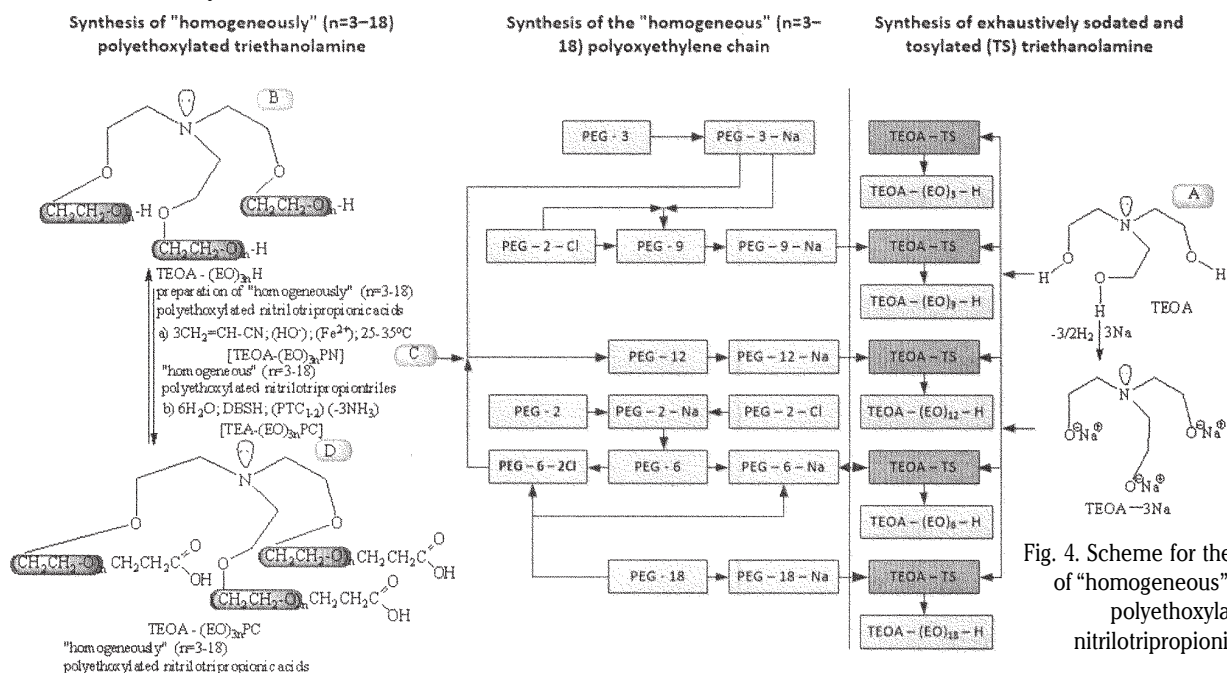


Fig. 4. Scheme for the preparation of "homogeneous" ($n=3-18$) polyethoxylated nitrilotripropionic acids

hydrochloric acid above 80°C substituted propionic acids are formed. In the presence of paratoluenesulfonic and dodecylbenzenesulfonic acid, the yields of β -alkyl-polyethyleneoxy-propionamides increase at low temperatures for small HA/TEOA - (EO)_{3n} PN molar ratios, also on the account of the homogenizing effect of these structures with surface-active properties.

In both stages of the hydrolysis process (partial and/or total) are encountered unstable intermediates (anionic and cationic species). Their stabilization along with the shift of the hydrolysis equilibrium to the right is favored by the presence of "homogeneous" ($n \geq 9$) polyoxyethylene chains through the coordination of the cationic species [10,17].

The stabilization of anionic species in the case of structures with "homogeneous" POE chains ($n \leq 8$) and the shift of the hydrolysis equilibrium to the right are also possible under phase-transfer catalysis (PTC) conditions [30-38]. In this work the following PTCs have been accessed [10,17]: PTC₁ - *N,N,N*-trimethyl-*N*- β -lauryl/myristyl (7/3) oxy ethylammonium chloride [10,17]; PTC₂ - *N,N,N*-trimethyl-*N*- β -lauryl/myristyl (7/3) polyethyleneoxy ($n=9$) ethylammonium chloride.

Increasing the temperature and the HA/nitrile molar ratio favours the total hydrolysis yields. The amount of acid selectively influences the hydrolysis of nitriles. Thus, the excess of hydrochloric acid favours the formation of propionic acids, alongside their esters with higher alcohols present as impurities or originating from the cleavage of ether bridges, while the excess of *n*-dodecylbenzenesulfonic acid favours more the formation of propionamides and less that of propionic acids, without forming also the corresponding esters.

Conclusions

The mixed tetradentate sequestrants of the "homogeneous" ($n=3-18$) polyethoxylated nitrilo-tripropionic acids type are "niche" structures which can be obtained in yields and with characteristics suitable for further applications of theoretical and practical interest. The series of experiments is required to be continued for the diversification and detailed knowledge of the colloidal and sequestration performances, if the preliminary sequestration tests conducted are deemed encouraging.

References

- MARCU GH., *Chimia compusilor coordinativi*, Editura Academiei Republicii Socialiste România, Bucuresti, 1984, p.64, p.68. (in Romanian)
- LITEANU C., HOPÎRTEAN E., *Chimie analitică cantitativă. Volumetria*, ed. VI, Ed. Didactică si Pedagogică, Bucuresti, 1972, p. 529-550 (in Romanian).
- DRĂGULESCU C., PETROVICI E., *Introducere în chimia anorganică modern*, Ed. Facla, Timisoara, 1973, p.217, p.226, p.272-277. (in Romanian).
- SĂRDULESCU D., *Manualul inginerului chimist*, I, Ed. Tehnică Bucuresti, 1972, p. 729. (in Romanian).
- BAILAR J., *The Chemistry of the Coordination Compounds*, Reinhold Publishing Corporation, New York, 1956, p.86, p. 184.
- DRĂGULESCU C., PETROVICI E., *Chimie structurală modernă. Chimia coordinaiei*, Ed. Academiei RSR, Bucuresti, 1977, p. 203. (in Romanian).
- *** EN ISO 22000:2005, Food safety management systems - requirements for any organisation in the food value chain (ISO).

- *** EN ISO 9001:2008, Quality Management System Standard. International Organization for Standardization (ISO).
- SCHICK M., *Nonionic surfactants*, Marcel Dekker Inc., New York, 1967, p. 158, p. 346.
- JIANU C., *Ethylene Oxide Homogeneous Heterobifunctional Acyclic Oligomers*. In: *Oligomerization of Chemical and Biological Compound*, Intech, Claire Lesieur (ed), Rijeka, 2014, p.103-132.
- YANAGIDA S., TAKAHASHI K., OKAHARA M., *Bull. Chem. Soc. Jpn.*, 50, 6, 1977, p.1386.
- PEDERSEN, C.J., *J. Amer. Chem. Soc.*, 89, 1967, p.7017
- HARVEY R.D., BARLOW D.J., DRAKE A.F., KUDSIOVA L., LAWRENCE M.J., BRAIN A., HEENAN R.K.: *J. Colloid. Interface. Sci.* **315**, 2007, p.648.
- GROZA I., TRĂSCĂ T.I., RIVIŞ A., RĂDOI B., *Rev.Chim. (Bucharest)*, **60**, no. 12, 2009, p.1347.
- YOKOYAMA Y., HIRAJIMA R., MORIGAKI K., YAMAGUCHI Y., UEDA K., *J. Am. Soc. Mass Spectrom.* **18**, 2007, p.1914.
- JACKSON A.T., SCRIVENS J.H., WILLIAMS J.P., BAKER E.S., GIDDEN J., BOWERS M.T., *Int. J. Mass Spectrom.* 238, 2004, p.287.
- JIANU I., *Aminoethers surfaceactive agents. Cationic surfaceactive agents*. PhD thesis. Polytechnic University; 1984 (in Romanian).
- JIANU C., JIANU I., *J. Food Agric. Environ.* 8, 3&4, 2010, p.148.
- JIANU C., NEDELEA G., LAZUREANU A., JIANU I., ADAMESCU A., *Bulletin UASVM Agriculture, Proceedings Paper*, 60, 2004, p.507.
- JIANU C., COCAN ILEANA, RUJESCU CRISTINA, JIANU I., *Commun. Agric. Appl. Biol. Sci.*, 78, 4, 2008, p.731.
- JIANU C., RINOVETZ A., CAZACU MIHAELA, ILIE A.C., *Rev. Chim. (Bucharest)*, **64**, no. 10, 2013, p.1072.
- JIANU C., *J. Food Agric. Environ.* 10, 1, 2012, p.10.
- JIANU C., *Chem. Cent. J.* 6, 2012, p.95, doi: 10.1186/1752-153X-6-95.
- *** SR ISO 2270:1995 Nonionic surface active agents. Polyethoxylated derivatives iodometrical determination of the oxyethylenic groups ISO 2270:1989.
- EDWARDS C.L., *Chemistry and Handling of Ethylene Oxide*. In: *Nonionic Surfactants: Organic Chemistry Science Series (Chapter 1)*, Marcel Dekker Inc., van Os N.M. (ed), New York, 1998, p.2
- EDWARDS C.L., *Polyoxyethylene alcohols*. In *Nonionic Surfactants: Organic Chemistry; Surfactant Science Series. 72*. Marcel Dekker Inc., van Os N.M. (ed), New York, 1998, p.87.
- NENIESCU C.D., *Chimie Organică ed. VI, Ed. Didactică si Pedagogică*, Bucuresti, 1966, p. 434, p. 501. (in Romanian).
- NENIESCU C.D., *Chimie general, Ed. Didactică si Pedagogică*, Bucuresti, 1966, p. 133-166. (in Romanian).
- ROSCH M., *Nonionic surfactants*, Marcel Dekker Inc., M.J. Schick (ed), New York, 1967, p.753.
- PAPAYOTOV I.M., PETROVA D.T., TSVETANOV C.B., *Makromol. Chem.*, 176, 1975, p.815.
- VÖGTLE F., WEBER, E., *Angew. Chem. Int. Edn.*, 13, 1974, p.814.
- FORNASIER R., MONTANARI F., PODDA G., TUNDO P., *Tetrahedron Lett.*, 1976, p.1381.
- CALZOLARI C., FAVRETTO L., PERTOLDI MARLETTA G., FAVRETTO GABRIELLI L., *Ann. Chim.*, 64, 1974, p.463.
- WEBER E., VÖGTLE F., *Tetrahedron Lett.*, 1975, p.2415.
- TRĂSCĂ I., POPOVICI A., CALAMAR POPOVICI D., RINOVETZ A., DOGARU D., *Rev. Chim. (Bucharest)*, **59**,no. 6, 2008, p. 669.
- IWAMOTO R., *Bull. Chem. Soc. Jpn.*, 46, 1973, p.1114, p.1118, p.1123, p.1127.
- TRĂSCĂ I., GROZA I., RINOVETZ A., RIVIŞ A., RĂDOI B.P., *Mat. Plast.*, **44**, no. 4, 2007, p.307.
- SOTOBAYASHI T., SUZUKI T., YAMADA K., *Chem. Lett.*, 1976, p.77

Manuscript received: 25.08.2014