ROMANIAN ACADEMY
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ABSTRACT HABILITATION THESIS

Nitroxyl radicals mediated functionalization of biopolymers: from synthesis to application

Domain: **Chemistry**

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CONTENT

Abstract

Polysaccharides along with oligosaccharides, the most abundant group of biopolymers, have been found to participate in many biological processes, such as cell–cell communication, embryonic development, infection of bacteria and/or virus, and tumoral and cellular immunity.[1,2] Therefore, polysaccharides together with polynucleotides, proteins, and lipids constitute the most important four biomacromolecules in life science. Although polysaccharides have been used for decades in various industrial applications, e.g. pharmaceuticals, biomaterials, food stuff and nutrition, and biofuels, growing understanding and deeper investigations of the importance of polysaccharides in life science are driving the development of polysaccharides for novel (biomolecular) applications.[3-5] Oxidation of cellulose is one of the most important modification methods to prepare value-added cellulose derivatives for further applications. For example, oxidized cellulose and regenerated cellulose are widely used as excellent hemostatic materials in various surgical operations and postsurgical adhesion prevention layers.[9] The last two decades represents a "*start line*" for the worldwide chemists, to develop new oxidizing methods, to replace the "old-fashion" ones, which are expensive, polluting, and proceed in harsh condition. One of the best candidates to be used, to satisfy the present global needs, is *N*-hydroyphthalimide (**NHPI**), which can be successfully used as a catalytic reagent in a wide range of organic transformations. NHPI proved its extraordinary powerful catalytic action, promoting the oxidation of a wide range of organic compounds with dioxygen in the presence of an cocatalyst, able to abstract a hydrogen atom, by a homolytic scission of the >N-O-H bond, to form the active species, phthalimide-*N*-oxy radical (**PINO**).[34-45] This thesis will present the most important achievements of the author in the field of the selective oxidation of polysaccharides, emphasizing on cellulose, by utilization for the first time in these processes of non-persistent nitroxyl radicals. At the same time, several applications of the functionalized polysaccharides (mainly cellulose and pullulan) we reported in the last few years are presented. The major accomplishments can be summarized as follow:

- Introduction for the first time of *N*-hydroxyphthalimide as mediator for the mild and selective oxidation of cellulose. The use of *N*-hydroxyphthalimide, to replace the well-established TEMPO, can avoid several issues linked with the decomposition (depolymerization) of the polymeric chain. Moreover the price of the NHPI is almost fifteen times lower than that of TEMPO.

- An exhaustive study of the catalytic activity exhibited by a series of non-persistent nitroxy radicals, which allows to control the degree of oxidation. Beside the use of NHPI, another three other compounds, like: 1-hydroxybenzotriazole, violuric acid, and *N*-hydroxy-3,4,5,6-tetraphenylphthalimide, able to in situ generate their corresponding nitroxyl radicals were introduced to oxidize the cellulose.

- Reporting a "*bromide free*" protocol for cellulose oxidation, which avoid the use of the harmful NaBr, as previously been extensively used. In the case of this new protocol, we tried to mimic natural oxidative processes in which enzymes are very effective. Copper enzymes are

extensively used as “*green methods*” for converting OH groups to carbonyl compounds. Therefore, the use of cupper salt in combination with NHPI allowed us to eliminate the presence of sodium bromide.

• The use of molecular oxygen as oxidizing agent in the presence of NHPI, a new environmentally friendly approach to cellulose selective oxidation. In terms of sustainability, O_2 is the ideal terminal oxidant. It is readily available and the only by-product after catalytic oxidation reaction is H_2O.

• The introduction of the oxidized polysaccharides (cellulose, pullulan) as efficient matrices for *hi-tech* application, such as nanoparticles encapsulation and heavy metals removal from waste water.

Polysaccharides (e.g. cellulose, starch) are naturally occurring macromolecules that make up a major proportion of the Earth's biomass. These biopolymers possess the greatest potential as renewable resources to replace traditionally made petroleum-based polymers (e.g. polyethylene) in many applications (e.g. automotive, aircraft industry). The forecast assumes that in the long term at least 33% of all demand for polymers can be adequately covered by the choice of bio-based resources. Nevertheless, the current projection for the year 2020 indicates that only between 1 - 4 % of the total polymer need will be met by the raw materials from renewable resources. Moreover, polysaccharides are used mainly as low complex and low value products and their exceptional properties are mostly neglected. The vision on polysaccharide usage therefore, should be translated to a better knowledge how these specific properties can be used more effectively in order to transfer these biopolymers into high value products, with applications starting with the already classical ones like the manufacturing of paper, textiles, membranes for water purification and/or biomedical applications up to more recent options such as magneto-responsive composites, bio-imaging materials or support for new catalysts.

The innovative findings of processability of cellulose and oxidized cellulose, are being translated into new processing technologies, cellulose functionalization methods and new cellulose materials, including blends, composites, fibers and ion gels. These materials can replace current analogues to overcome the environmental issues associated with petroleum-based products.