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From Plain Synthetic Chemistry to na approach of natural terpenes valorization

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António Manuel d'Albuquerque Rocha Gonsalves

Abstract: Rosin industry has a long tradition in Portugal and even a significant expression. Surprisingly, as a whole, it never reached an advanced level taking into consideration the dimension of the business. Basic research in chemical synthesis and catalysis can help reaching the desired target. Discussion of some studies centered on the primary stage of this objective will be presented.

DA SÍNTESE QUÍMICA BÁSICA A UMA PERSPECTIVA DE VALORIZAÇÃO DE TERPENOS

Sumário: A indústria de resinosos tem uma tradição relevante entre nós e até uma dimensão significativa. Genericamente nunca ultrapassou um estádio primário injustificável face à relevância atingida. Investigação básica em síntese química e catálise pode servir objectivos de modernização com utilidade para um salto qualitativo nessa indústria. Discussão de alguns estudos incidindo sobre a fase primária deste objectivo.

Chemical synthesis is the building of structures in the underworld of atoms and molecules, unities we only know through experimental data on their physical-chemical behavior and scientific rationalization of such observations. It is so justified that a potential architect came to become a synthetic chemistry researcher. Instead of handling with everyday objects building is made using materials of the microphysics world. Being so we need knowledge and understanding different from that of our daily experience.

To select and design a research topic it has always been our concern being focused in an area of up-to-dated basic research though it should be selected with the perspective of being able to have direct or indirect impact in solving problems of economic development and well-being.

Oxygen, the most abundant element in percentage by mass either in earth crust (mineral world) or in living matter, is involved in the most relevant chemical processes of the vital functions. Oxygen is a key element in chemical processes giving easy access to energy. Its involvement goes from the mild oxidations occurring in the cells to feed their work to the spectacular phenomenon of an open fire. In both cases the interaction of oxygen with other molecular structures liberates energy as a consequence of conversion of the original compounds in new structures. These, particularly those originating from mild reactions, may have important functions or uses. Products originating from fire are relatively uninteresting, directly useless even unsuitable or harmful. In actual fact the products from mild oxidations are interesting being important constituents of living structures or playing roles in vital and metabolic processes. Oxidation products obtained through classical laboratory reactions are widely used.

It must be emphasized that the oxygen molecule in its natural form is a kind of "jailed beast". Having the capacity to severally degrade molecular structures oxygen exists in its free state as a "dormant" form. It is this "mask" which allows that having oxygen the capacity to destroy everything in a free fire allows living creatures and oxidizable materials to survive in an oxygenated atmosphere while being an essential partner in the physical-chemical mechanisms of the cellular energetics.

The high temperatures required to start a fire and keep it ongoing generate the required highly reactive species developing a powerful oxidation process. However, the mild mechanism occurring inside the cells allows the controlled liberation of energy and the selective generation of products of different oxidation levels. Oxidations via classical chemical oxidations are in between those two.

In the case involving cytochrome P450, enzyme involved in many oxidation processes occurring in cells including elimination of toxic substances and activation of pharmaceutical drugs, the mechanism of oxygen incorporation includes two reductive steps before arrival to the peroxide stage required to oxidize the substrate as shown schematically in Fig. 1.

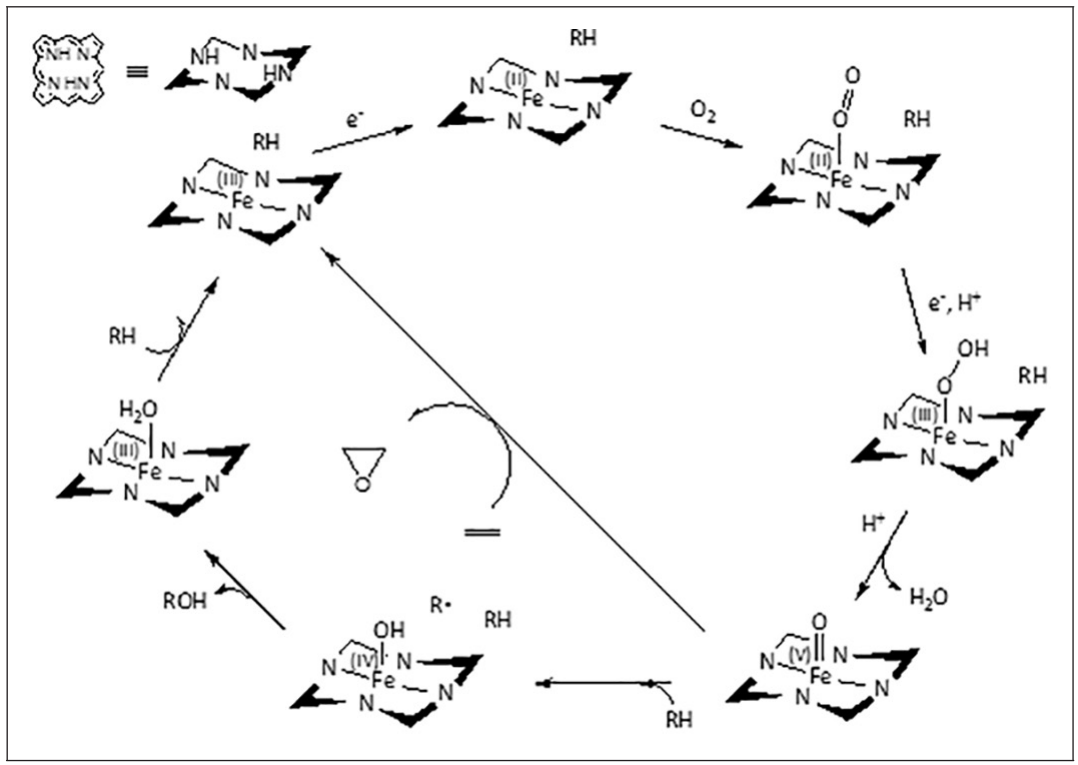


Figure 1
Simplified scheme of cytochrom P450 catalytic molecular oxygen oxidations

Emulate enzimatic oxidations in cells is certainly a chemist's aim attempting to obtain interesting and valuable compounds with economic interest through a more controlled and environmentaly efficient way.

There is more than one way to perform oxidation reactions replicating the "in vivo" approach: the most straightforward is the biotechnological one in which proper cells are used performing their

natural role to generate our desired compounds, this methodology only works well in some specific cases; since the efficiency of the chemical reactions occurring in the cells depends from the enzymatic catalysis, another approach involves isolation of the required enzyme the specific catalyst to be used in the reaction, a method which in the case of an enzyme reasonably stable leads to excellent results; a third approach involves the development and synthesis of a model of the enzyme using the physical-chemical knowledge of its structure, of the enzymatic activity and the knowledge of chemical synthesis to build a model adequate and efficient.

Our studies in the area of synthesis of porphyrins of simple but varied structures allowed:

1. the establishment of experimental conditions generalizing the applicability of the Rothemund reaction (Figure 2) making it work with a wide range of aldehydes and so generating different tetrapyrrolic macrocycles, not only porphyrins but others at different oxidation levels (Figure 3);

Figure 2
The original Rothemund reaction conditions were only satisfactory in the case where benzaldehyde was used.

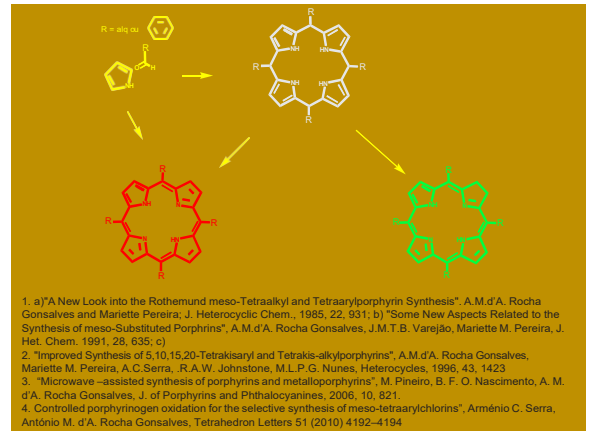


Figure 3
Experimental conditions established allowed to considerably extend the performance of the Rothemund approach to tetrapyrrolic macrocycles.

2. access to new or optimized experimental conditions to introduce different functional peripheral groups namely per-halogenation and particularly direct chlorosulfonylation, an unknown approach previously to our studies (Figure 4);

3. have an easy way to get tetrapyrrolic macrocycles having simple structures but modeled to be explored: for the preparation of Langmuir-Blodgett films with potential interest to be used in molecular electronics, as biomimetic catalysts, sensitizers for the diverse

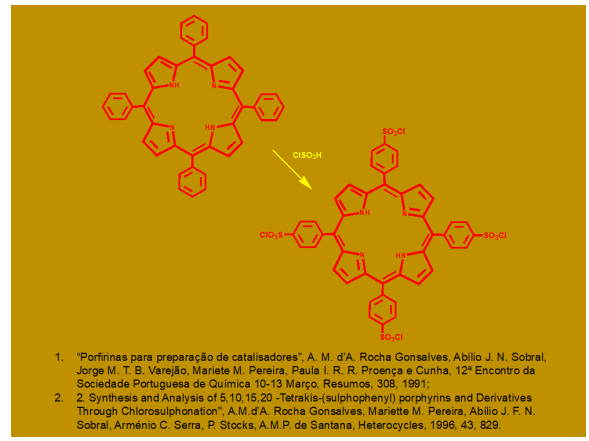


Figure 4
Direct synthesis of chlorosulfonylated tetra phenyl porphyrins.

photodynamic therapy applications or as diagnostic agents (1. a] "The small stones of Coimbra in the huge tetrapyrrolicchemistry building", António M.d'A. Rocha Gonsalves, Arménio C. Serra and Marta Piñeiro, *Journal of Porphyrins Phthalocyanines* 2009, 13: 429–445; b] "Chemical Synthesis in the Developmentof Therapeutics: Approach through analogies of natural structures and processes", António Manuel d'Albuquerque Rocha Gonsalves, Communication 1st of March 2012, *Memórias da Academia das Ciências de Lisboa*, Classe de Ciências, Tomo XLV, 323, 2018).

We saw (Figure 1) that in the oxidative cycle of cellular oxidations the characteristic blocking of the oxygen stationary state requires two reductive steps allowing its conversion to the peroxide state species having the capacity to promote the substrate oxidations. Fully replicate the enzymatic mechanism is difficult in an artificial simplified model. To start with, the coexistence of a reductive system is not compatible in the environment of the oxidative system particularly in an arrangement desired to be simple and operating continuously. An alternative is the use of an oxygen donor in which an oxygen atom is at a convenient oxidation state. The first and important approach was that introduced by Groves (2. J.T. Groves, T.E. Nemo and R. S. Myers, *J. Am. Chem Soc*. **101**. 1032, 1979). Groves used as enzyme

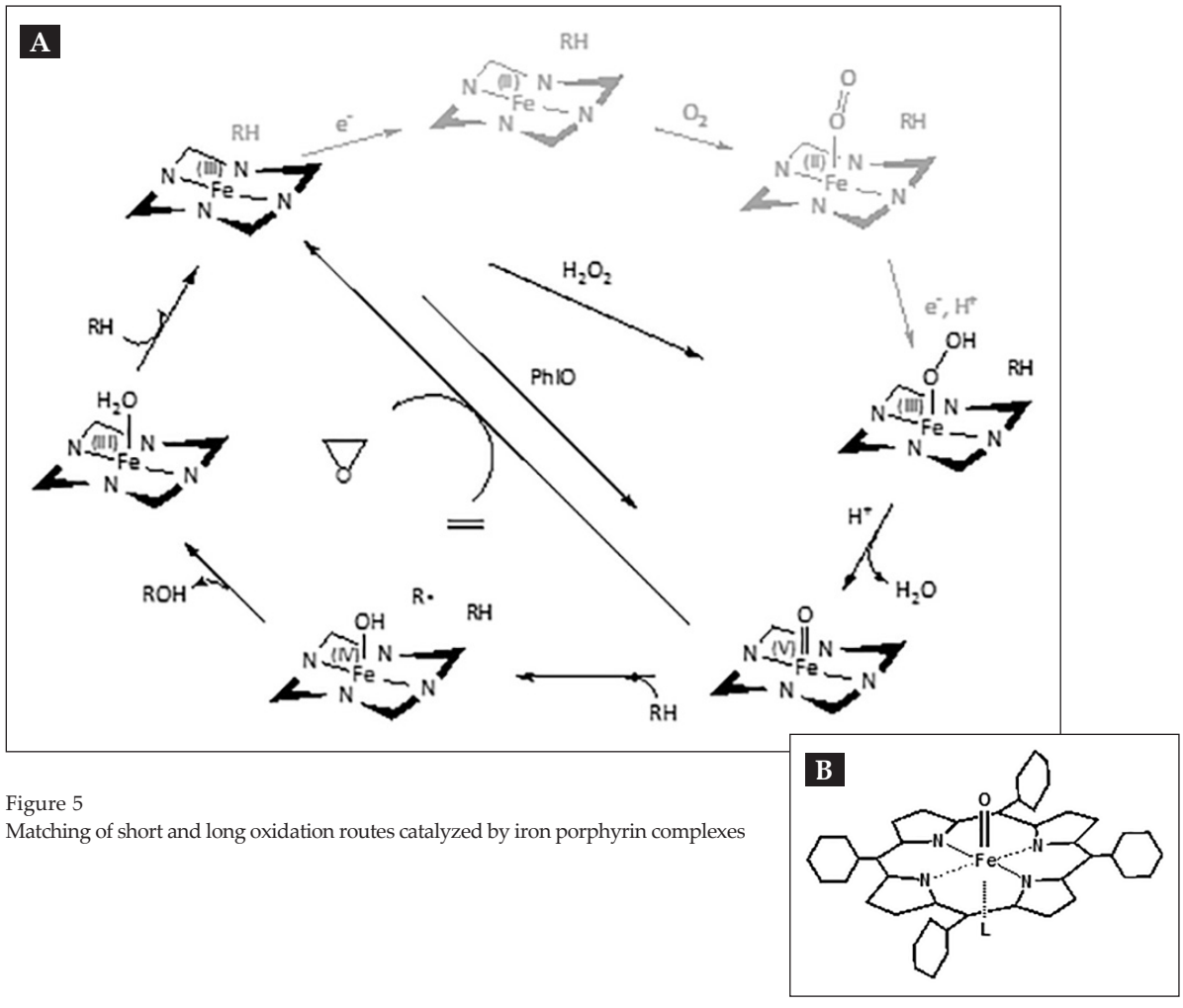


Figure 5
Matching of short and long oxidation routes catalyzed by iron porphyrin complexes

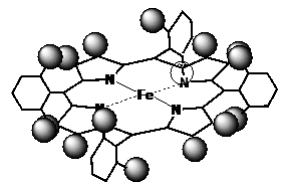
model the complex of iron tetraphenyl-porphyrin, FeTPP, and iodosylbenzene, PhIO, as oxygen source to generate directly the complex of iron(V) equivalent to that occurring in the cycle of enzymatic having the capacity to transfer oxygen to the substrate.

In Figure 5 we see a scheme of the simplified oxidation mechanisms using oxygen donors different of molecular oxygen overlapped on the enzymatic oxidation mechanism involving the oxygen molecule.

Groves found that the presence of an axial ligand opposite to the oxygen atom is required to assist the transfer of the oxygen to the substrate. On his first approach Groves used pyridine to perform this role. However, Groves approach having the great merit of being original and demonstrate de feasibility of developing a simple model of the oxidation enzyme was certainly a very preliminary approach. The oxygen donor is high-priced and not particularly convenient, the complex of TPP is not very stable, pyridine as ligand has the disadvantage of being oxidized under the reaction conditions and so consumed competing with the substrate during the process.

The difficulty in using molecular oxygen to perform biomimetic oxidations can be overcome using as oxidant a more convenient compound where oxygen is in a form similar to one of those existing in the enzyme catalyzed cycle. Hydrogen peroxide meets such characteristics being a natural candidate and raised our interest. Hydrogen peroxide can be labeled a "green reagent", being a low cost and also presently produced using a biological process particularly clean and efficient.

A second generation of catalysts following FeTPP firstly used by Groves used tetrapyrrolic macrocycles halogenated both in the phenyl-*meso* and in the β-positions (I). Such catalysts proved to be particularly more efficient and stable on reaction conditions (3. a] A. Robert, B. Meunier, *Tetrahedron Lett*. 1990, 1991; b]E. Samuel, R. Shuttleworth and T. Stevens., *J. Chem. Soc*., 145, 1967; c] H.J. Callot, *Bull. Chem Soc. France*, 1492, 1974; d] T.G. Taylor and S. Isuchiya, *Inorg. Chem*., 26, 1338, 1987).

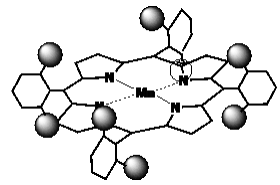


(I)

Our work addressed to the preparation of tetrapyrrolic macrocycles and various derivatives include significant improvements to the synthesis in a preparative scale of meso-phenyl porphyrins having halogen atoms in the *ortho*-positions of those phenyl groups, (4. a] A.M.d'A. Rocha Gonsalves, M.M. Pereira, *J. Heterocyclic Chemistry*, 22, 931, 1985; b] (A.M.d'A. Rocha Gonsalves, J.M.T.B.Varejão, M.M. Pereira, *J. Heterocyclic Chemistry*, 28, 635, 1991; c] A.M.d'A. Rocha Gonsalves, M.M. Pereira, A.C. Serra, R.A.W., Johnstone, M.L.P.G. Nunes, *Heterocycles*, 43, 1423, 1996), and the improvement in the halogenation conditions for β-halogenation of the tetrapyrrolic macrocycle. (5. a] A.M.d'A. Rocha Gonsalves, R.A.W., Johnstone, M.M. Shaw, and Abílio J.F. Sobral, *Tetrahedron Lett.*, 1335, 1991; b] ", A.M.d'A. Rocha Gonsalves, Mariette M. Pereira, Abílio J. F. N. Sobral, Arménio C. Serra, P. Stocks, A.M.P. de Santana, *Heterocycles*, 1996, 43, 829) .

The easy availability of the required macrocycles brought by preceding work allowed us to begin studies in the area of catalysis addressed to the problem of stability of the axial ligand and to the

reaction conditions of the catalytic oxidations. At the time it was important to overcome the difficulty brought by the use of pyridine or imidazole as axial ligands which being oxidized competes with the substrate loosing required ligand role. We paid attention on the problem of stability of the axial ligand for the catalyst MnTDCPP (II) in oxidations by hydrogen peroxide.



(II)

For these oxidations with hydrogen peroxide it was previously identified the need for the presence of a base, a requirement satisfied by the presence of the selected ligands (6. P. Battioni, J.P. Renaud, J.F. Bartoli, M. Reina-Artiles M. Fort, and D. Mansui, *J. Am. Chem. Soc.*, 110, 8462, 1988). Our approach replacing the original ligand and base for new ones correspond to reaction performed in homogeneous phase, dichloromethane/methanol, base and ligand ensured by the pair sodium acetate/di-isopropylamine-N-oxide.

Our studies addressed to the synthesis of derivatives of simpler tetrapyrrolic macrocycles allowed to perform the first direct chlorosulfonylation of tetra-chlorophenyl-porphyrins. This reaction proved to be an example of a high yield very simple process which opened the way to the preparation of a large number of new compounds and new solutions to a vast number of problems which in this way found convenient answer:

1. phenyl-*meso* groups of TPP and substituted derivatives are chlorosulfonylated very efficiently on treatment with chlorosulfonic giving a crystalline product and so very pure and easily isolated;
2. the regioselectivity of chlorosulfonylation in the case of having *meso*-phenyls with different degrees of deactivating substituents enables an easy purification of mixtures having structures of different symmetry relatively to the pattern of substituents of those phenyls;
3. use of more drastic conditions also allows the chlorosufonylation of the β-positions of the macrocycle;
4. the reactivity of the chlorosulfonyl group allows the easy preparation of other derivatives and linkage of the macrocycle to polymeric structures.

Making use of the chlorosulfonylation of the macrocycle in β, we obtained a particularly interesting result for oxidations with hydrogen peroxide which apparently occurs at the interface of a biphasic system liquid-liquid (7. a]"Sulphonamide Porphyrins in the Biometic Oxidation by H_2O_2. An Efficient Two Phase System", A.M.d'A. Rocha Gonsalves, M. M. Pereira, A.C. Serra, *Annales de Quimica*, Intern. Edit. 1996, 92, 375; b] "Metalloporphyrin Catalytic Oxidations of Hydrocarbons by H_2O_2", António M. d'A. Rocha Gonsalves and Arménio C. Serra, *J. Porphyrins Phtalocyanines*, 2000, 4, 599-604), as schematically shown in Figure 6.

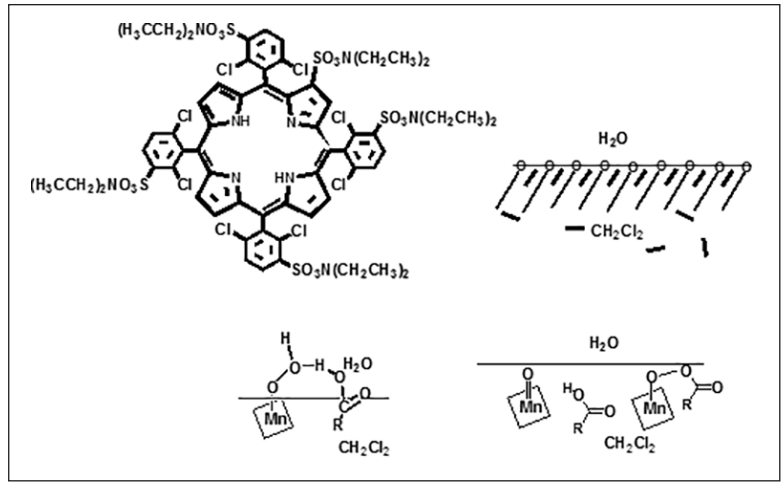


Figure 6
Schematic hydrogen peroxide oxidation in a biphasic system catalyzed by a manganese complex of a specific sulfonylated porphyrin.

Though significant progresses were obtained by us and other authors for catalytic oxidations by hydrogen peroxide, the possibility of performing oxidations with molecular oxygen is certainly still highly desirable. Activate molecular oxygen from its stationary state is possible in a different way from that of the enzymatic oxidation cycle via a photochemical mechanism. The molecule of oxygen in its natural form is photochemically activated to a different state which is able to react with the substrate providing a process extremely clean and efficient. Transition to the activated form of oxygen requires the presence of a sensitizer. This is a molecule having the capacity to absorb energy of the electromagnetic radiation to be converted in an activated state which is able to transmit such energy to the natural oxygen molecule which is converted to an electronic reactive state. In this activated state oxygen is able to interfere with substrates directly forming or evolving to the reaction product. The sensitizer works

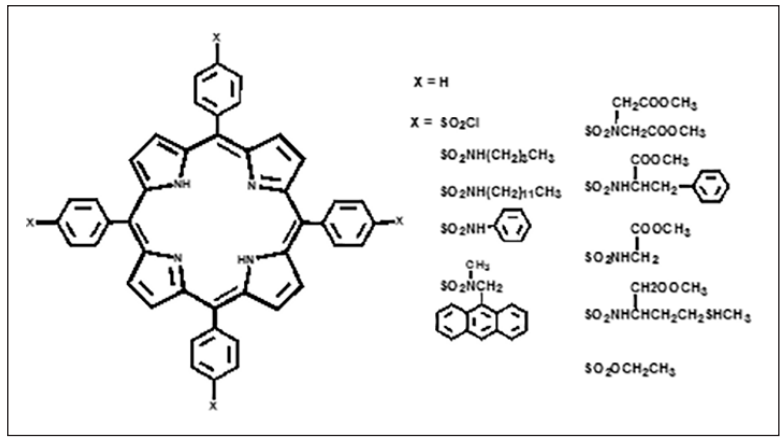


Figure 7
Examples of the first type of sulfonylated derivatives of porphyrins used in our first studies of applications in PDT.

therefore as a photochemical catalyst of the oxidation reaction. The mechanism of the photochemical activation is the same occurring in the photodynamic therapy technique discussed in our previous communication to this Academy (1. a).

Interestingly in our first studies of photodynamic therapy we used *meso*-phenyl-porphyrin derivatives with phenyl side chains having the sulfonyl group directly attached but replaced this type of porphyrins by other structures which proved more efficient for that particular purpose , Figure 7.

As also shown in that previous communication, for that purpose tetrapyrrolic macrocycle is usually used in the free form and not as metal complex. The specific structure of each macrocycle turns it more or less adequate or efficient to be used in each application particularly in the case of reactions performed inside leaving tissues. So, optimization and selection of a sensitizer is liable of modulation benefiting from expertise in the area of organic synthesis to implement appropriate solutions. In general terms the sensitizer has to obey the following characteristics:

1. be able to absorb electromagnetic radiation to jump from the single state to an excited state from where it can decay to a triplet state having an excess of energy of 115 kJ/mole, Figure 8;
2. lifetime of the triplet state must be as long as possible to optimize chance of oxygen triplet to be converted to singlet oxygen;
3. sensitizer must be stable to reaction conditions being also convenient the possibility of having the catalyst in a heterogeneous medium allowing its recovery and recycling at the end of reaction.

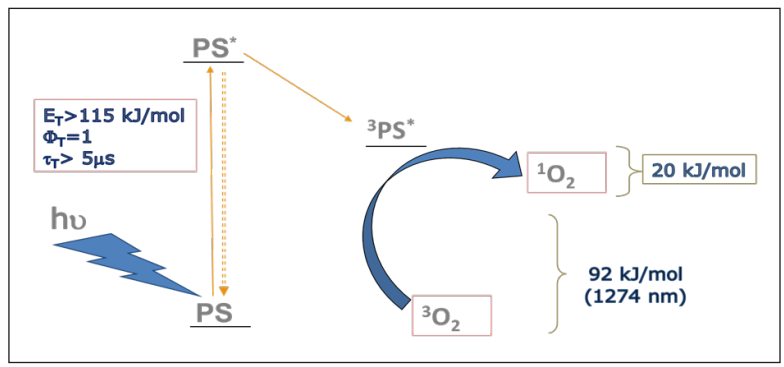
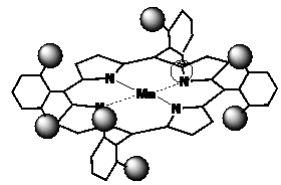


Figure 8
Transition of energy levels in sensitized conversion of oxygen triplet to singlet.

Looking at the stability of the macrocycles to reaction conditions, some of the characteristics of the structures we designed and synthesized to be used as biomimetic oxidation hydrogen peroxide catalysts also proved convenient for photodynamic therapy and for preparative photochemical oxidations though the role of the existing functionalities may be different in each case. This is particularly significant for the case of poly-halogenated macrocycles with different halogens. The chloro-sulfonylation of the TPP derivatives proved to be a reaction of broad value but different as an answer to each case.

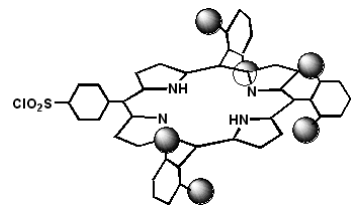
In a preliminary collaborative study photochemical conditions were established to be used in homogeneous medium photochemical oxidations with molecular oxygen (8. "Novel porphyrins and a chlorin as efficient Singlet Oxygen Photosensitizers for Photooxidation of Naphtol or Phenols to Quinones", D. Murtinho, M. Pineiro, M. M. Pereira, A. M. d'A. Rocha Gonsalves, L. G. Arnaut, M. Graça Miguel, H. Burros, *J. Chem. Soc.*, Perkin Trans. 2, 2000, 2441-2447).

The importance of many oxidation products of cheap readily available starting materials justified studies of development of heterogeneous catalysts allowing for the use of these oxidation processes cheap and clean. Classical chemical oxidation processes use expensive and polluting reagents making it highly desirable alternative approaches. In a first approach we decided to exploit our method of synthesis of chloro-sulfonylated derivatives of porphyrins using as catalyst a structure based on that of TDCPP but with one of the phenyls not having chlorine substituents, MTDCPPP, (III).



(III)

Using reaction conditions developed for totally symmetric porphyrins using a mixture of the corresponding di-chlorophenyl/phenyl-benzaldehyde in the proportions of 3:1 we cannot obtain pure MTDCPPP but a mixture where it is however the main component. The very high efficiency of our chlorosulfonylation method and regioselectivity favoring the phenyl group relatively to the phenyl having attached deactivating groups allows for a very easy and efficient purification of the required *meso*(chlorosulfonylphenyl-tridichlorophenyl)-porphyrin, CSPTDPP (IV).



(IV)

This new mono(chlorosulfonylated)porphyrin, CSTPDPP, proved useful for the preparation of catalysts supported on a polymeric matrix. In our case we used a Merrifield resin to which α, ω-diamines were previously attached to obtain amino alkylated polymers for easy attachment of the catalyst exploiting the reactivity of the chlorosulfonyl group. These supported catalysts proved able to generate singlet oxygen oxidizing substrates being the efficiency determined by the distance of the catalyst to the backbone of the polymer dependent of the chain length of the diamine used as spacer. Our catalysts

allow for additions of singlet oxygen of the type 4+2 to unsaturated systems such as in formation of ascaridole and conversion of naftols into naftoquinones, Figure 9 (9. "Covalently Immobilized Porphyrins as Photooxidation Catalysts", Sonia M. Ribeiro, A. C. Serra, A. M. d'A. Rocha Gonsalves, *Tetrahedron*, 63, 7885-7891, 2007).

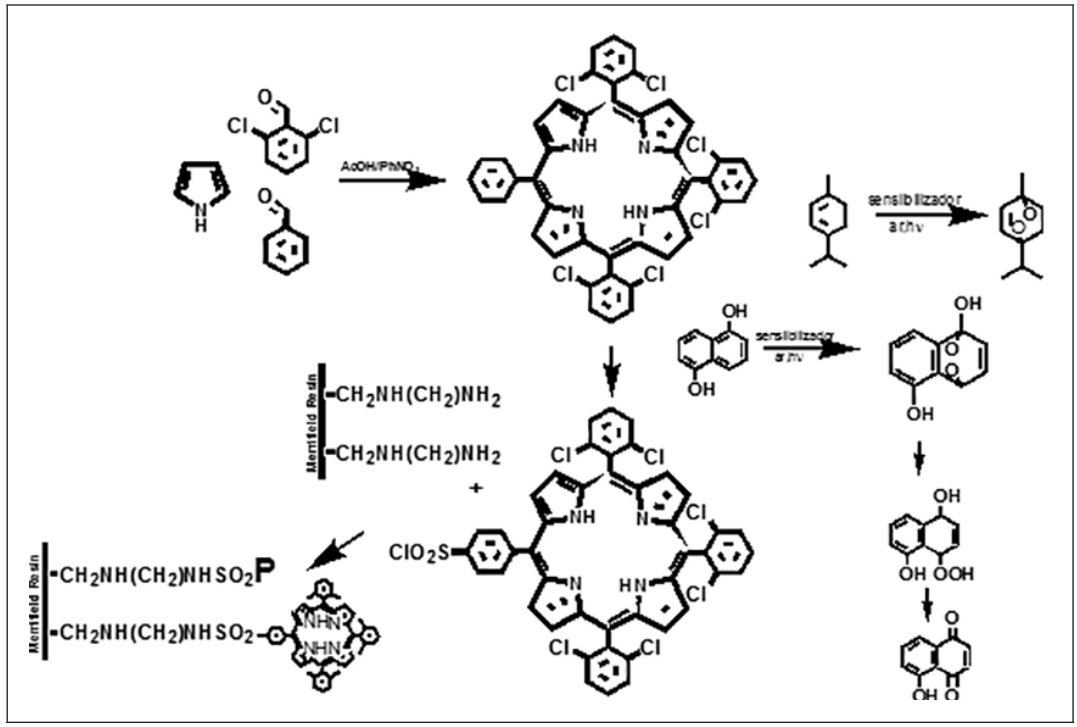


Figure 9
Porphyrin catalysis of photooxidations with molecular oxygen.

The preceding observations showed the potential of our approach to smooth efficient and clean oxidations over two groups of compounds of great practical and commercial interest. In drugs, aromas, food additives industries, and many others both terpenoids and quinones are particularly important chemicals. We intend to establish some connection between our basic research, the potential to exploit terpenes of our forest extractive products, industrial established capacities, market interest in this type of materials, and the need of bringing added value to them. In childhood we lived near what was then one of the first industrial facilities addressed to processing of national pine tree and this sounded then inquisitive to me. As a leader of a university research group I was asked consultancy to diversified industrial problems by industries using or exploiting terpenes. This gave us the opportunity to get some knowledge about this industrial and economic area. Broadly, the old Portuguese pine resin industry did not overcome a primary level and has to be considered as blocked. Partnership with international companies helped in some cases to a little progress but led also to cases of technical and business control truly appalling. During a large period, evolution of markets, selection of raw materials, and national forest exploitation led to almost full collapse of the old existing business with the survival of some structures under diverse frameworks,

though generally away of significant advances. At the moment there are some recovery attempts to exploit national raw materials, but we feel that many mentality handicaps persist. We still find many which we would classify as "old guard resin entrepreneurs". Looking for references of old university concerns addressed to industrial activity, namely in Vicente de Seabra book "Elementos de Chimica", (10. "Elementos de Chimica", Vicente Coelho de Seabra, Real Oficina da Universidade, M.DCCLXXXVIII), we see that over 200 years ago while interest was given to the novel developments of science attention was paid to the needs of the industry and economic developments of the time. However, the knowledge about resins and its derivatives revealed in that book is not relevant. Not much more than to mention resins containing drying or aromatic volatile oils and that these are able to get thick or hardened when in contact with a bit of oxygen citing namely the resin of common pine tree. The poor level of scientific knowledge at the time did not help a better development of this field in a sustainable durable way. But if we look at the job placements of those our now many graduates particularly PhD's, we find a distribution unique comparatively to what we find in advanced countries. In our case the vast majority is sheltered in public institutions whose productivity for development is we certainly know as not much fruitful. Unfortunately, we do not know any other similar situation elsewhere in advanced societies.

Without pretending to present a complete solution to the above referred problems we are going to focus in our scientific study which we believe to fall in the interests of productive activity of the chemical industry of terpenes. Some years from now a big project was devised when an entrepreneur from the pharmaceutical industry planned to build a plant addressed to exploit pine resin all the way from the tree to the production of aromas. The feasibility of such project required chemical technology optimization and expertise of fine chemistry, optimization of methods to reduce operating costs, environmental, and quality control. The work here presented is inserted in those objectives.

Being necessary restructuring the industry from the technological and scientific point of view in order to assure its feasibility and strengthening addressed to high value market products, one line of interest may be centered on the capacity to make terpenoids of high-value. Since these are often oxidation products of low value terpenes of natural origin, namely from pine resin, our preliminary results were certainly promising and deserved to be further exploited. After proving that the structures of simple porphyrins made available from our work could be easily attached to a polymeric matrix generating heterogenous catalysts able to promote photooxidation of a terpene by molecular oxygen, we extended our studies in order to obtain highly active and selective catalysts liable to good recovery and stability favoring recycling maintaining efficiency.

Silica gel was an attractive support for several reasons: material of low cost and stable, transparent to visible light, permeable to oxygen and to substrates since it is susceptible of modeling of dimension both of particle and porosity. The use of silica-gel to support catalysts was reported (11. A. Corma, H. Garcia, Adv. Synth. Catal. 348 (2006) 1391) including for the case of immobilizing photo-sensitizers. (12. a] H. Schmaderer, P. Hilgers, R. Lechner, B. Konig, Adv. Synth. Catal. 351 (2009) 163; b] T. Carofiglio, P. Donnola, M. Maggini, M. Rosseto, E. Rossi, Adv. Synth. Catal.350 (2008) 2815; c] K. Ishii, Y. Kikukawa, M. Shiine, N. Kobayashi, T. Tsuru, Y. Sakai, A. Sakoda, Eur. J. Inorg. Chem. (2008) 2975; d] H. Shimakoshi, T. Baba, Y. Iseki, A. Endo, C. Adachi, M. Watanabe, Y. Hisaeda, Tetrahedron Lett. 49 (2008) 6198;

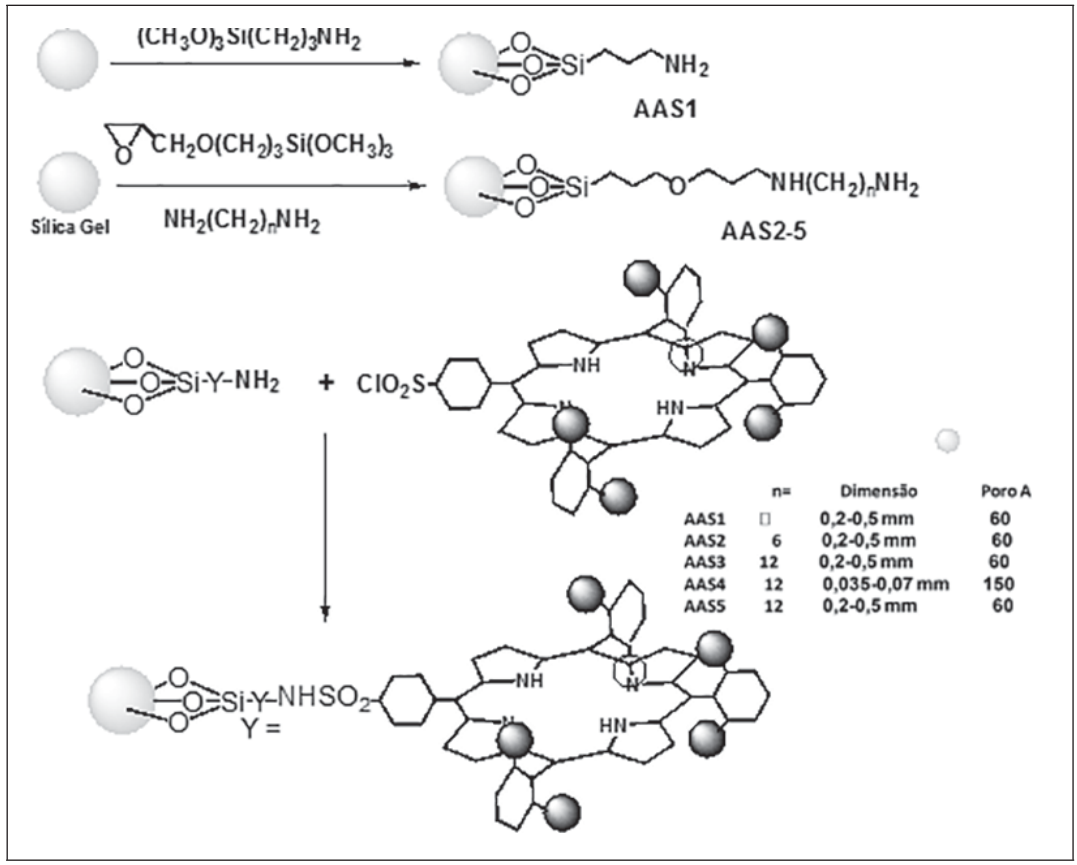


Figure 10
Scheme of attaching of the photocatalyst to a silica support

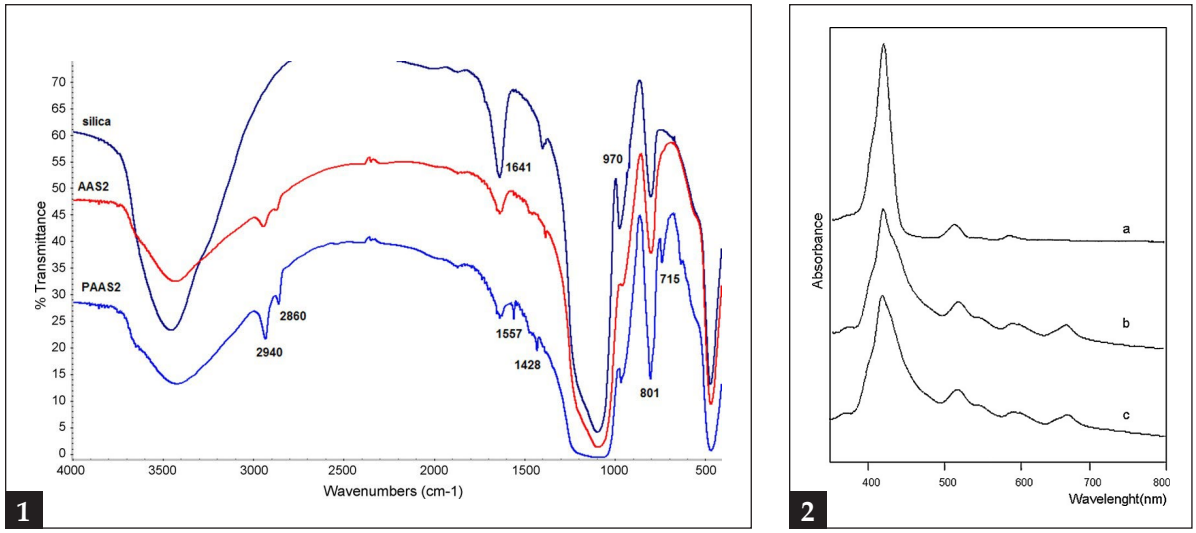


Figure 11
1) IR spectra of silica before and after attachement of the spacer, AAS2; **2)** Visible spectra of the free catalyst, P (a), and after attacchement to the support, PAAS (b, c).

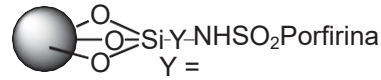
e] C. Cantau, S. Larribau, T. Pigot, M. Simon, M.T. Maurette, S. Lacombe, Catal. Today 122 (2007) 27; f] K. Feng, R.-Y. Zhang, L.-Z. Wu, B. Tu, M.-L. Peng, L.-P. Zhang, D. Zhao, C.-H. Tung, J. Am. Chem. Soc. 128 (2006) 14685; g] N. Kitamura, K. Yamada, K. Ueno, S. Iwata, J. Photochem. Photobiol. A: Chem. 184 (2006) 170; h] T. Hino, T. Anzai, N. Kuramoto, Tetrahedron Lett. 47 (2006) 1429). However, there was evidence of difficulties originating of suppression of singlet oxygen on silica surface. (13. a] C. Cantau, T. Pigot, N. Manoj, E. Oliveros, S. Lacombe, ChemPhysChem, 8 (2007) 2344; b] S. Jockush, J. Sivaguru, N.J. Turro, V. Ramamurthy, Photochem. Photobiol. Sci., 4 (2005) 403; c] K.-K. Iu, J.K. Thomas, J. Photochem. Photobiol. A: Chem. 71 (1993) 55).

Convenient conditions to insert spacers above referred allowed to exploit different spacers and types of silica-gel and we selected a lot of samples of silica with various particle and pore dimensions to which we attached different spacers starting from 3-(aminopropyl)tri-methoxysilane (14. T. Luts, W. Suprum, D. Hofmann, O. Klepel, H. Papp, J. Mol. Catal. A: Chem. 261 (2007) 16) and 3-(glycidyloxy-propyl)-trimetoxysylane, and 1,6-hexanodiamine, or 1,12-dodecanodiamine (15. D. Zois, C. Vartzouma, Y. Deligiannakis, N. Hadjiliadis, L. Casella, E. Monzani, M. Louloudi, J. Mol. Catal. A: Chem. 261 (2007) 306), following by connection to these one of our chlorosulfonylated porphyrins as sensitizer, PAAS (Figure 10). (16. "Covalently immobilized porphyrins on silica modified structures as photooxidation catalysts", Sónia M. Ribeiro, Arménio C. Serra, A.M.d'A. Rocha Gonsalves, Journal of Molecular Catalysis A, Chemical 326, 2010, 121–127).

The presence of the organic structures linked to the silica was confirmed by evidence trough the characteristic infrared bands not existing in the original silica (Figure 11-1). The presence of the sensitizer is easily detected from the visible spectra shown by the final catalyst spectra which also shows reasonable evidence of the catalyst transparency to visible light (Figure 11-2).

The incorporation of the porphyrin to the silica modified matrix is higher than that observed in the case of the modified Merrifield resin (17. M.S. Ribeiro, A.C. Serra, A.M.d'A. Rocha Gonsalves, J. Catal. 256 (2008) 331). In the case of a very short spacer that incorporation is comparatively low apparently due to the proximity of the amine group to the polymer impairing the reaction to the chlorosulfonyl group. Using previous experience and convenient adaptation we prepared various catalysts (Table 1).

Table 1

Aminoalkylated silica	**Amino group incorporation (mmol/g)**	**Catalyst**		**Incorporated Porphyrin (mmlo/g)**
AAS1	0,68	PAAS1	$-(CH_2)_3$	0,040
AAS2	0,38	PAAS2	$NH(CH_2)_6$ OH	0,142
AAS3	0,31	PAAS3	$NH(CH_2)_{12}$ OH	0,115
AAS4	0,29	PAAS4	$NH(CH_2)_{12}$ OH	0,158
AAS5	0,33	PAAS5	$NH(CH_2)_{12}$ OH	0,151

The above catalysts where used in photooxidations of α-terpinene as substrate in the ratio of 1:600 and 1:5000 leading to the production of ascaridole as principal product and also of some *p*-cymene (Figure 12 and Table 2).

Table 2

Entry	Photosensitizer	$R=n_{sens}/n_{sub}$	Time	5(%)a
1	1	1:600	1,5	93 (7)
2	1	1:5000	2,3	96 (4)
3	1b	1:5000	5	98 (2)
4	PAAS1	1:600	5	94 (6)
5	PAAS1	1:5000	8,5	90 (10)
6	PAAS2	1:5000	7,5	76 (24)
7	PAAS3	1:600	5,5	97 (3)
8	PAAS3	1:5000	7,5	86 (14)
11	PAAS4	1:5000	10,5	77 (23)
12	PAAS5	1:5000	13	76 (24)

a) Yield of isolated 5 (p-cymene)
b) Added silica to the homogeneous solution

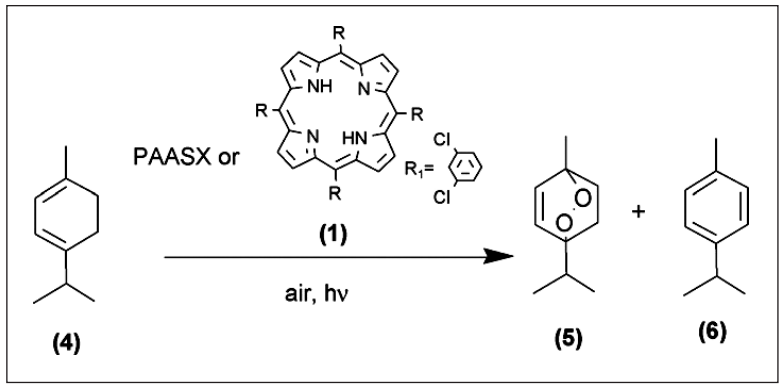


Figure 12
Photocatalytic oxidation of p-cymene.

After recovery from first reaction our catalysts proved to be recyclable as shown in Table 3.

Table 3
Oxidation of α-Terpinene, cat/subs 1:5000

Reuse	Photosensitizer	Time (h)	5 (%)
0	PAAS1	8,5	90 (10)
1st		8,5	78 (22)
2nd		12,5	50 (50)
0	PAAS2	7,5	76 (24)
1st		9,5	67 (33)
2nd		16	42 (58)
0	PAAS3	7,5	86 (14)
1st		11,5	83 (17)
2nd		11,5	85 (15)

Going to products of higher value we studied the capacity of our catalysts to oxidize citronellol, a necessary step to transform this compound into the high valuable rose oxide. In this case oxygen singlet through an *ene*-reaction attack to the substrate can lead to two products, Figure 13.

To generate rose oxide, isomer 8 must be favored.

In Table 4 we see that the various catalysts tend to generate almost equivalent quantities of 8 and 9 though the last is often favored. Eventual interaction of the citronellol hydroxy group with those on the silica surface has no favorable effect to desired prevalence of isomer 8. Only for the case of reaction performed in homogeneous medium in CCl_4 the formation of isomer 8 is relatively favored.

Under our reaction conditions we observed similar orientation relatively to the possible isomers for the photooxidation of linalool, regioselective reaction relatively to the two double bonds, Figure 14.

Our heterogeneous photooxidation catalysts on silica support allowed for high yield reactions in 4+2 and *ene*-reactions but having reaction times significantly larger then in the case of using the same catalyst as a free species.

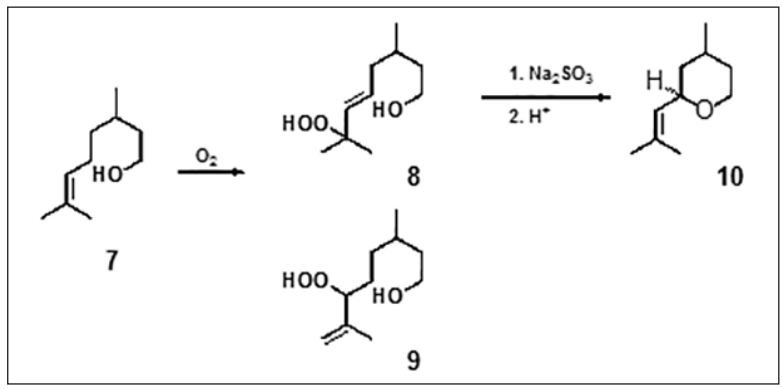


Figure 13
Scheme of conversion of citronellol to rose oil through photooxidation whit Porphyrin 1 or PAAS1-PAAS5.

Table 4
Results of photooxidation of citronellol with the various catalysts prepared

Entry	Photosensitizer	R=n_{sens}/n_{sub}	Time	Isolated(%)	8/9 (%)
1	1	1/600	1,5	99	49/51
2	1	1/5000	4	97	48/52
3	1a	1/5000	5	99	53/47
4	PAAS1	1/600	9	95	47/53
5	PAAS1	1/5000	45	99	34/66
6	PAAS2	1/5000	59	99	36/64
7	PAAS3	1/600	28	99	44/56
8	PAAS3	1/5000	44	99	35/65
9	PAAS3[a]	1/5000	47	99	45/55
10	PAAS4	1/5000	47	98	40/60
11	PAAS5	1/5000	71	99	39/61

a) Solvent CCl4

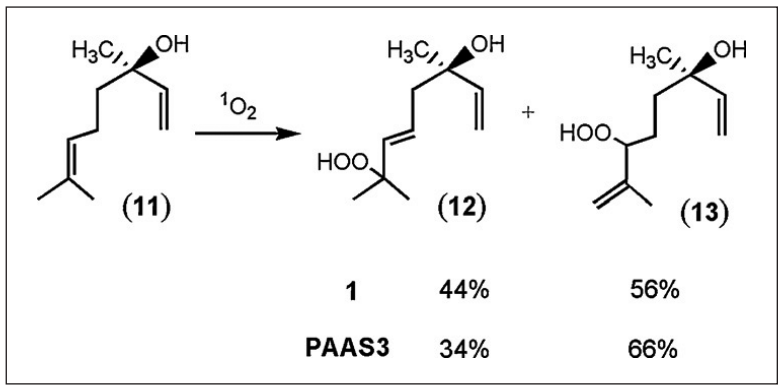


Figure 14
Selectivity of linalool photooxidation

Considering the above studies and aiming to find more convenient conditions, relatively to industrial improvements exploiting starting materials from pine resin, our studies followed with attempts to optimize the catalyst and reaction conditions from the energetic and environmental point of view (18. "Efficient Solar Photooxygenation with Supported Porphyrins as Catalysts", Sonia Ribeiro; Armenio C. Serra; and Antonio M. d' A. Rocha Gonsalves, ChemCatChem, 5, 134-137, 2013). An approach using the catalyst supported on a Merrifield resin seemed more convenient and so we tried to exploit alternative spacers to connect the catalyst to matrix. The alternatives are presented in scheme of Figure 15:

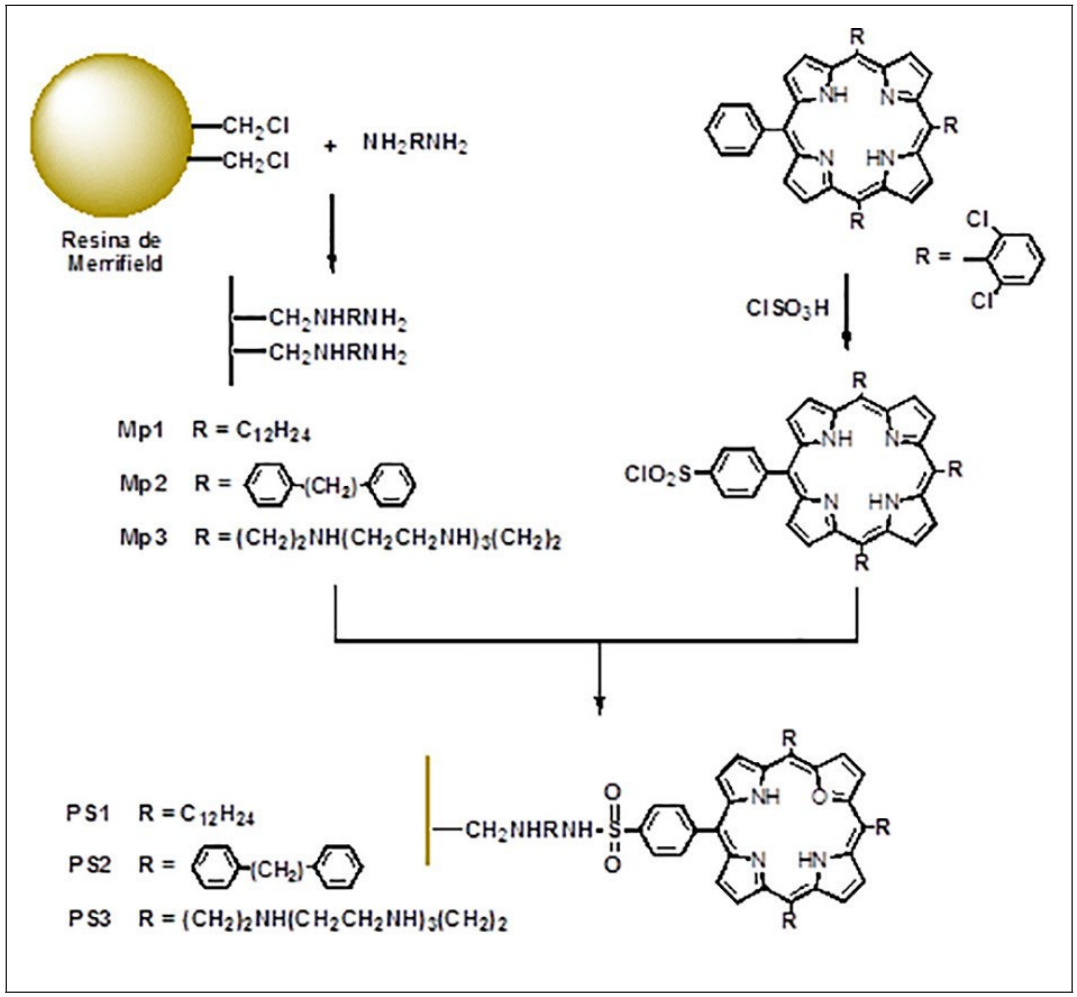


Figure 15
Spacers and scheme of preparation of catalysts supported on Merrifield resin.

The different spacers link the catalyst in different proportions but the higher catalyst proportion occurring with the di-aryl spacer does not correspond to the better performance as seen in Table 5.

Assembling a simple device built with laboratorial equipment we performed some trial experiments using only sunlight under a fluence measured as 45-55 W cm^2. In Figure 16 we see a scheme of the reactions studied. Results of such reactions performed in $CHCl_3$ are presented in Table 6.

Table 5
Nitrogen content of polymers MpX and PsX

Entry	Polymer	Nitrogen %	Polymer	Nitrogen %	Porphyrin incorporation (nmol/g)
1	Mp1	1.34	Ps1	1.54	0.0357
2	Mp2	1.18	Ps2	1.58	0.0714
3	Mp3	3.45	Ps3	3.65	0.0356

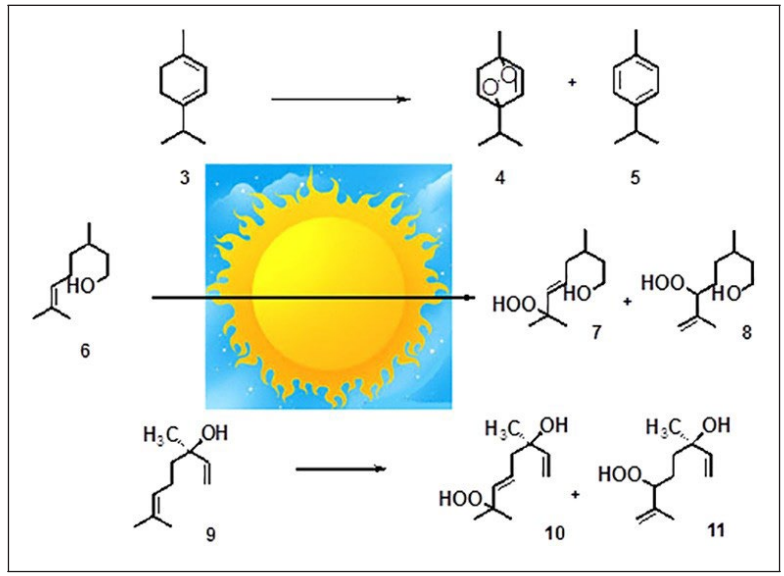


Figure 16
Photochemical catalytic sunlight conversions of natural terpenes.

Table 6
Sunlight photooxygenation with catalysts Ps1-Ps3

Entry	PsX	Substrate	n_{sens}/n_{sub}	Time (h)	Yield(%)	Selectivity (%)	
1	Ps1	3	1/10000	3	87	4 (84)	5 (16)
2	Ps1	3	1/30000	4	80	4 (61)	5 (39)
3	Ps1	3	1/30000	5	89	4 (71)	5 (29)
4	Ps1	3	1/60000	8	92	4 (31)	5 (69)
5	Ps1	6	1/10000	7	99	7 (47)	8 (53)
6	Ps1	9	1/10000	8	99	10 (47)	11 (53)
7	Ps2	3	1/30000	5	98	4 (70)	5 (30)
8	Ps2	6	1/10000	5	99	7 (42)	8 (58)
9	Ps2	9	1/10000	6	99	10 (42)	11 (58)
10	Ps3	3	1/10000	3	95	4 (87)	5 (13)
11	Ps3	3	1/30000	4	89	4 (87)	5 (13)
12	Ps3	6	1/10000	8	99	7 (48)	8 (52)
13	Ps3	9	1/10000	6	97	10 (52)	11 (48)
14	Free	3	1/10000	6	9	4 (9)	5 (91)

The conversions obtained are particularly high even in the case of a ratio catalyst/substrate 1:60,000 although not always with very favorable selectivities. In the case of linalool catalysis is regioselective. Only oxidation of the double bond more electron rich.

In Table 7 we can see the results obtained when catalysts PS1 and PS2 are recycled and used to convert substrate 3.

Table 7
Recycling of catalysts Ps1 and Ps2 on substrate 3

Entry	Ps1	Time	Yield, %	Selectivity, %	
1	Ps1	4	80	4 (61)	5 (39)
2	Ps1	5	86	4 (53)	5 (47)
3	Ps1	8	83	4 (50)	5 (50)
1	Ps2	4	89	4 (67)	5 (33)
2	Ps2	4.5	91	4 (66)	5 (34)
3	Ps2	4	91	4 (73)	5 (17)

Trying to eliminate the chlorinated solvent on grounds of environmental nature we decided to use ethanol though knowing that in such medium singlet oxygen has a shorter lifetime. But this approach proved particularly convenient. Results of photooxygenation with catalyst PS3 the catalyst which proved to be the preferred in previous experiments are shown in Table 8.

Table 8
Sunlight photooxygenation with catalyst Ps3 in ethanol

Entry	Substrate	n_{cat}/n_{sub}	Time (h)	Yield, %	Selectivity, %	
1	3	1/10000	1.5	94	4 (99)	5 (1)
2_a	3	1/30000	2.5	92	4 (99)	5 (1)
3_b	3	1/30000	3	86	4 (99)	5 (1)
4	3	1/30000	3.5	89	4 (99)	5 (1)
5	6	1/60000	6	90	4 (99)	5 (1)
6	9	1/10000	7	99	7 (49)	8 (51)

a) 1st recycling
b) 2nd recycling

It must be emphasized that the reactions are faster in ethanol than in chloroform and the rate of reaction compares with the one occurring with that observed when using a free catalyst in homogeneous phase. For the case of *a*-terpinene selectivity to the production of ascaridole has a spectacular increase being this even higher for the case of recycling experiments.

Oxidation of citronellol is also more efficient although without any increase of selectivity to any of the two possible products.

Our interpretation for the unexpected lower efficiency of the reactions performed in chloroform, where the lifetime of oxygen is longer than in ethanol, is based in the fact that chloroform competes with the substrate being oxidized giving a product which is decomposed liberating an acid which protonates the catalyst lowering its efficiency. This acid formed when using chloroform also assists the elimination of water favoring the formation of *p*-cymene.

Presenting this work as a study with interest for the qualitative development of the national terpenes industry we do not mean that it corresponds to a solution for all the difficulties that such development as experimented. But we have no doubt that it corresponds to a model of work and that some results and above all the concept presented can be used and adapted to the situation.

Having studied for example a reaction using sunlight irradiation does not mean that an industrial solution should necessarily adopt that source o radiation. An artificial source of radiation is probably a more adequate answer. But the experiment illustrates the potential and easy control of the method, fundamental aspects from the technological and economic points of view.

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na sessão de 16 de outubro de 2014)