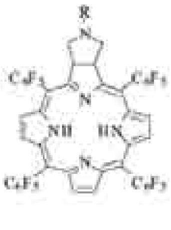
organic synthesis. new products with potential applications

organic chemistry research group

department of chemistry & QOPNA, university of aveiro



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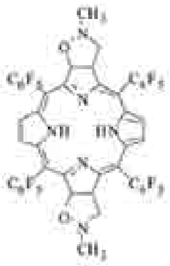

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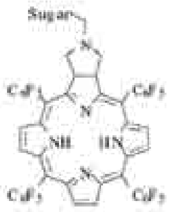

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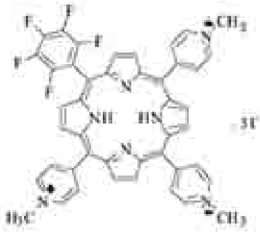

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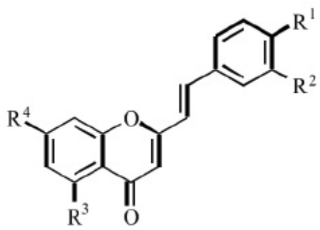
A) Structural features and amphiphilic properties are required for a new porphyrin derivative to be considered as a photosensitizer (PS) in photodynamic therapy (PDT). In such way chlorins and bacteriochlorins, as well as certain cationic and glycoconjugate derivatives, have been targets for several research groups.
We have been able to establish that certain porphyrin macrocycles can act as dienophiles or dipolarophiles in cycloaddition reactions; in such way novel chlorins and bacteriochlorins and some glycoconjugates and novel cationic derivatives can be obtained.
In collaboration with other groups the new products have been assessed as photosensitizing agents in PDT or in the photoinactivation of microorganisms. In particular, the action against antibiotic resistant bacteria, mainly the Gram (-) ones, is of great significance. It is also possible to photoinactivate microorganisms present in water samples, including sewage ones. Such potential applications have been patented.
B) Inflammatory processes are complex physiological responses, which involve an increase in vascular permeability as well as overproduction of reactive oxygen and nitrogen species. If these reactive species overcome host defense systems, damage in inflammatory sites can occur, contributing to chronic diseases. In order to control these diseases, anti-inflammatory substances possessing antioxidant properties need to be used. Polyphenols have important biological properties. The similarity of 2-styrylchromones with flavones and their known biological activities led us to develop new synthetic methods for this type of compounds and to design novel molecules presenting antioxidant, anti-inflammatory, and anti-norovirus activities. 2-Styrylchromones were starting materials, throughout cross-coupling reactions, for the development of a novel group of polyhydroxy-2,3-diarylxanthones, which already demonstrated potent antioxidant activities. Biological applications of these compounds gave rise to a European patent application.



R^1, R^2, R^3, R^4 = H or OH

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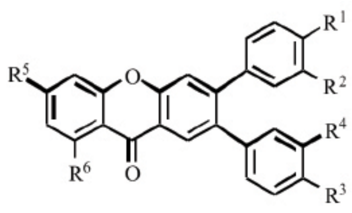

R^1, R^2, R^3, R^4, R^5, R^6 = H or OH

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mass spectrometry approaches to study breast cancer

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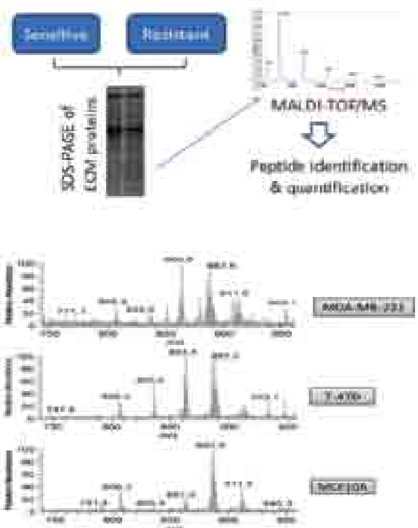
Breast cancer is the most common cancer in women and represents a major public health problem. Although early detection and recent advances in treatment have reduced the mortality rates, most breast cancers develop resistance to therapy. Therefore, it is necessary to identify novel therapeutic targets as well as markers of disease progression and resistance to therapy. Our lab is currently focused on two lines of research:
1) Extracellular matrix and estrogen signalling: Most breast cancers express estrogen receptors (ER) and depend on estrogen to grow. These cancers are treated with endocrine therapy, by blocking estrogen synthesis and ER action with antagonists. ERs are ligand activated transcription factors, subjected to a myriad of posttranslational modifications (PTMs) including phosphorylation.
Such modifications alter ER affinity for a ligand and ER transcriptional activity. In addition, hyperactive kinase pathways which target ER are often associated to endocrine resistance. Our aim is to identify modulators of such signalling pathways in the extracellular matrix (ECM) of endocrine sensitive and resistant tumours and associate their expression to ER PTMs. For this purpose, extracellular matrix proteins were extracted, separated by

SDS-PAGE and identified by MALDI-TOF/MS. In parallel, ER from the same tumours were purified using an E2 affinity column and PTMs will be identified by LC-MS/MS. Results from this work will allow identification of proteins with prospective use as markers and/or therapeutic target in endocrine resistant tumours.
2) The role of lipids in breast cancer has been largely understudied. Besides their contribution to the cell membrane mass, lipids regulate membrane fluidity, are an energy source and have roles in cell signalling; all processes altered in malignant progression. We used a lipidomic approach in which phospholipids were separated by thin layer chromatography and analyzed by ESI-MS/MS. Differences in the spectra of sphingomyelins and phosphoinositides – two PLs with roles in regulation of cell survival and motility – were found between non malignant and breast cancer cells with different degrees of aggressiveness. Presently, we are extending these studies to breast tumours with the aim to identify prospective biomarkers of disease progression.



an alternative to kinematic hardening in classical plasticity

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In metal forming, numerical simulations are very useful to optimize processes, and thereby, decrease development time and cost. Accurate results are achievable if sufficient consideration is paid to the choice of the numerical parameters, including type of mesh, boundary conditions and material constitutive behavior. In plasticity, multi-scale modeling has been instrumental for understanding the relationship between macroscopic properties and microstructural features at different scales and has been successfully applied for material design. Philosophically, multi-scale is a very comprehensive and interpretive approach to constitutive modeling. However, in many instances, it does not address very well the practical manufacturing needs, e.g., in the sheet forming industry when simple, yet accurate, material models with time-efficient implementations in commercial finite element (FE) codes are required. This is a domain where continuum descriptions are still very powerful.
Plasticity in metals is a phenomenon that is mainly controlled by dislocation glide on slip systems occupying weak or strong preferred orientations. The fields of dislocations dynamics and crystal plasticity have been very active over many decades to qualitatively and quantitatively understand the numerous mechanisms occurring during plastic deformation.
The effects of crystal plasticity have been roughly captured at the continuum level by the introduction of non-quadratic yield functions/plastic potentials.
These functions have been employed successfully in a number of examples where loading is nearly proportional. However, this is no longer the case when a material is subjected to cross-loading or stress reversal.
In this work, an approach is proposed for the description of the plastic behavior of materials subjected to multiple or continuous strain path changes. In particular, although it is not formulated with a kinematic hardening rule, it provides a reasonable description of the Bauschinger effect when loading is reversed. This description of anisotropic hardening is based on homogeneous yield functions/plastic potentials combining a stable, isotropic hardening-type, component and a fluctuating component. The latter captures, in average, the effect of dislocation interactions during strain path changes. For monotonic loading, this approach is identical to isotropic hardening, with an expanding isotropic or anisotropic yield surface around the active stress state. The capability of this constitutive description is illustrated with applications on a number of materials, namely, low carbon, dual phase and ferritic stainless steel samples.