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Dendrimers and Heterochemistry

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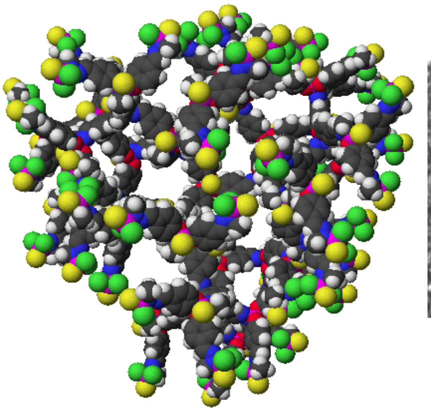
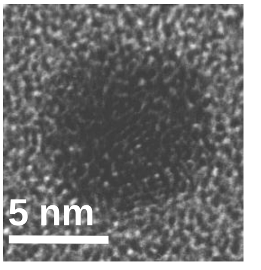
The major focus of our research is on the synthesis, the characterization, the reactivity, and the study of properties and applications of dendrimers and dendritic macromolecules. These hyperbranched and perfectly defined compounds are synthesized step-by-step from a central core, using in most cases the versatile reactivity of phosphorus derivatives .

Keywords: *Dendrimers – Heteroatoms – Organic synthesis – Reactivity – Phosphorus – Functionalization – Hyperbranched polymers – Homogeneous catalysis – Green chemistry – Chemistry in water – Nanomaterials – Nanobiotechnology – Electrochemistry –*

Synthesis of dendrimers

One of the method we develop allowed us to prepare the dendrimer of the highest generation well characterized known to date: generation 12 with more than 12,000 terminal functions and a molecular weight > 3,000,000. The following scheme illustrates the molecular modeling of a fifth generation dendrimer and its imaging by electron microscopy.





Our efforts are now focused on the search of new methods of synthesis, more straightforward., but also on the study of properties and uses of dendrimers.

Reactivity of dendrimers

Study of the reactivity of the surface, within the cascade structure and at the core of dendrimers is under active investigation. The presence of phosphorus at each branching point offers the possibility to perform a number of reactions: surface multifunctionalization, regioselective incorporation of functional groups, metals, charges within the cascade structure, formation of surface-block, layered surface-block and segment-block dendrimers all issued from the same original dendron etc. Highly sophisticated dendritic structures were obtained in this way.

A particular approach concerns now the synthesis of water-soluble compounds, bearing positively charged (ammoniums), negatively charged (carboxylates, phosphonates), or neutral (polyethylene glycol (PEG)) terminal groups.

Characterization of dendrimers

Due to their repetitive structure and their large size, the characterization of dendrimers is never trivial. Thanks to the presence of phosphorus at each layer of our dendrimers, ^{31}P NMR is particularly suitable for characterizing such compounds. Multinuclear NMR, UV-visible, IR, and fluorescence spectroscopy, as well as size exclusion chromatography and dynamic light scattering, are also very useful.

Applications of dendrimers

A variety of applications is presently developed in the group in collaboration with several research groups, in Toulouse, in France, in Europe, and worldwide. Among them, one can cite:

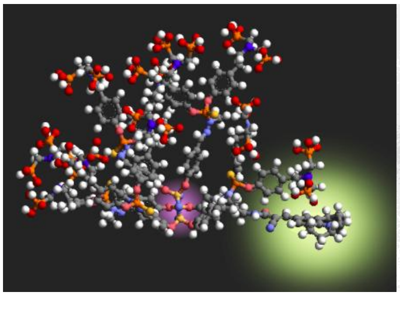
Dendrimers as catalysts:

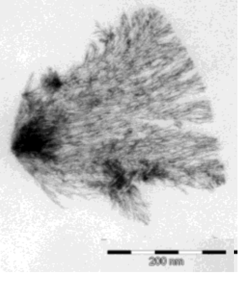
•Metalla dendrimers as homogeneous catalysts (Enantioselectivity, Use of cheap and non-toxic metals (Fe, Cu), In water, etc.)
•Organocatalysis
•Recyclability of dendritic catalysts

Dendrimers for (nano)materials

•Elaboration of thin films of dendrimers, via covalent or electrostatic interactions.
•Nanotubes of dendrimers and quantum dots in alternate layers, usable as bio-sensors.
•Microcapsules constituted of dendrimers layers.
•Nanoparticles elaborated in mild conditions with dendrimers.
•Hybrid organic-inorganic materials incorporating Si, Ti, Zr, Al or Ce, and dendrimers.
•Mesoporous materials incorporating dendrimers.
•Solid hydrogels (dendrimer < 1%, water > 99%)
•Electrodes modified by electroactive dendrimers, usable as electrochemical sensors.
•OLEDs with dendrimers as the emitting layer.
•Sensitive chemical sensors for the detection of phenols, or of various solvents.

The following images show the molecular modelling of a fluorescent dendrimers (*left*) and a dendritic network of Pt nanoparticles organized by a dendrimer (*right*, collaboration with R.M. Sebastian, Spain).





Dendrimers for (nano)biotechnology

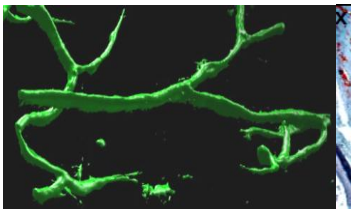
•Sensitive and reusable DNA-chips built from dendrimers; start-up Dendris created in 2009.
•Microstructured liposome array.
•Sensing layer for resonating piezoelectric membrane.
•AFM tip functionalization by dendrimers for biosensing

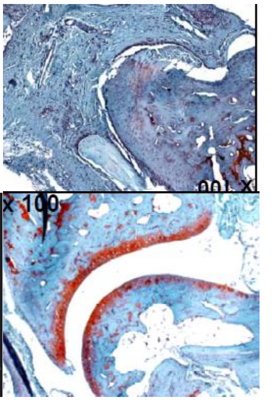
Dendrimers for biology

•Use of dendrimers as DNA transfecting agents.
•Anti- prion and anti-HIV activity.
•Influence on Alzheimer's peptides aggregation
•Dendrimers in immunology and oncology.
•Multiplication of human immune blood cells.
•Anti-inflammatory properties.
•Fluorescent dendrimers for biological imaging.

The following images show the vascular network of a living tadpole obtained with a fluorescent dendrimer (*left,* collaboration with Mireille Blanchard-Desce, Bordeaux), and the influence of a biologically active dendrimer on the joints of model mice of rheumathoid arthritis (*right*, collaboration with Rémy Poupot and J.L. Davignon, Toulouse;

upper part non-treated, *lower part* treated, published in *Sci. Transl. Med.* 2011).





Selected Recent Publications:

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•**Dendrimeric phosphines in asymmetric catalysis.** Caminade, A.M.; Servin, P.; Laurent, R.; Majoral, J.P. *Chem. Soc. Rev.* **2008**, *37*, 56-67.
•**Cooperative two-photon absorption enhancement via through-space interactions in covalent multichromophoric nanoassemblies.** Terenziani, F.; Parthasarathy, V.; Pla-Quintana, A.; Maishal, T.; Caminade, A.M.; Majoral, J.P.; Blanchard-Desce, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 8691-8694.
•**Nanostructuring polymeric materials by templating strategies.** Knoll, W.; Caminade, A.M.; Char, K.; Duran, H.; Feng, C.L.; Gitsas, A.; Kim, D.H.; Lau, A.; Lazzara, T.D.; Majoral, J.P.; Steinhart, M.; Yamee,n B.; Zhong, X.H. *Small* **2011**, *7*, 1384-1391.
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•**Dendrimers. Towards Catalytic, Material and Biomedical Uses.** Caminade, A.M.; Turrin, C.O.; Laurent, R.; Ouali, A.; Delavaux-Nicot, B. Eds. John Wiley & Sons, Chichester (UK), **2011,** pp 528. ISBN: 978-0-470-74881-7