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Review

Interactions gold/phosphorus dendrimers. Versatile ways to hybrid organic–metallic macromolecules

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ABSTRACT

Nanotechnology has the high capability to revolutionize many other technologies in many fields, due to the development of myriad nanodevices. Thus nanoparticles have been extensively studied over the last decade. Among all these, dendrimers pertain to the "nano-world" by virtue of their size (a few nanometers range). However, they are intrinsically different from classical 'hard' metallic nanoparticles because they are constituted exclusively of 'soft' organic matter (organic polymers). Their nanometric size effects can be observed and are reminiscent to those of the multivalent systems widely known in Nature. In this review we will report ways of incorporation of Au(I) or Au(III) selectively at the level of the core, within the cascade structure, regioselectively at a given generation, or on the outer shell of various phosphorus dendrimers. This can be achieved via the skeleton modification of these phosphorus dendrimers as well as with the selective incorporation of ligands as phosphine, thiol, iminophosphorane, thiophosphine, iminopyridine groups allowing complexation via formation of P—Au, S—Au, P=N—P=S—Au, or N—Au—N bonds. Original phosphorus dendritic structures as macromolecular asterisks, or onion peel dendritic structures allow to diversify the ways of obtaining either gold complexes or gold nanoparticles, some of them being used as chemical sensors. Finally, selected examples of applications of these gold nano-objects in nanomedicine for neuron activation or unprecedented anti-tumoral properties will be presented.

Contents

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1. Introduction

Dendrimers are macromolecules elaborated step by step (generation after generation) and constituted of branching units emanating radially from a central core. The different strategies used for the elaboration of dendrimers allow generally to build dendrimers up to generation 2–5 but high generations have been obtained in some cases: generation 9 for polyphenylene dendrimers [1], generation 10 for PAMAM dendrimers [2] and for polylysine dendrimers [3], generation 12 for phosphorhydrazone dendrimers [4], and recently generation 13 for triazine dendrimers [5]. In most cases, the internal structure has no specific function ready to use for further functionalizations, and all the terminal functions are identical. However, it is often desirable to have two (or more) types of functions present in a single dendrimer. Some examples of such multifunctional dendrimers have been displayed in a recent review, essentially centered on organic dendrimers [6].

Among the different types of dendrimers, those incorporating phosphorus in various positions in their structure, present undoubtedly the largest variety of tunable constitutive elements of the core, branching units, internal branches, backbones and surfaces due to the fascinating versatility of the organophosphorus chemistry by itself. The use of ^{31}P NMR technique, which represent a highly valuable tool for the characterization of these dendrimers, explains why a large number of synthetic procedures dedicated to the preparation of phosphorus dendrimers were proposed. Reactions are generally easy to perform under mild reaction conditions the by-products being removed without sophisticated technics (water and nitrogen are often the only by-products of the sequence of reactions), and the final compounds being obtained in high yields. As an example our first and main method of synthesis of phosphorus dendrimers [4,7] consists in the repetition of two quantitative reactions, the first step being the nucleophilic substitution of chlorine atoms by hydroxybenzaldehyde in basic conditions. The second step is the condensation of the aldehydes with the dichlorophosphothiohydrazide. This compound is also issued from the organic chemistry of phosphorus (substitution of one Cl of $P(S)Cl_3$ with methylhydrazine, at low temperature). The second step generates PCl_2 functions at the periphery of the dendrimer suitable to perform again substitutions with 4-hydroxybenzaldehyde (Scheme 1). Remarkably, this method has been carried out up to generation 12 from $P(S)Cl_3$ [4] and to generation 8 starting from $P_3N_3Cl_6$ [4c,7]. All the reactions are quantitative in most cases, using less than 5% excess of reagents.

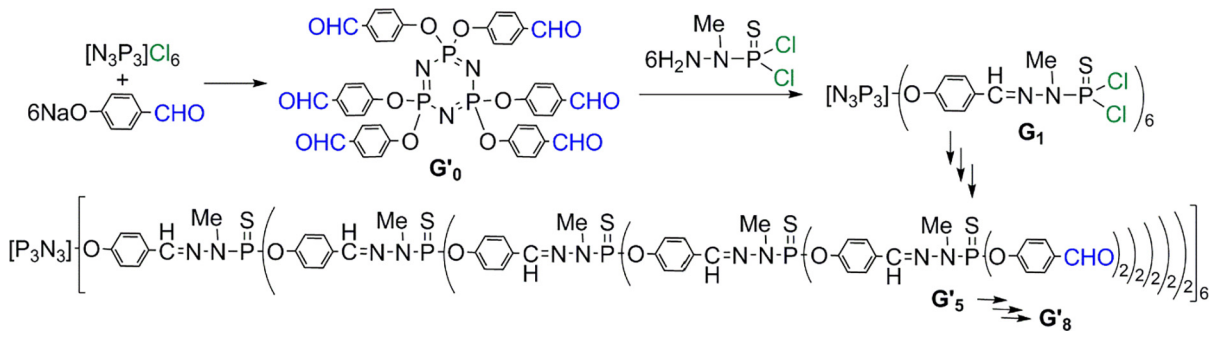
The presence of $P(S)Cl_2$ end groups on the outer shell of the dendrimers allows in particular the grafting of many types of functionalized phenols or amines and therefore the incorporation of various other functional groups instilling original properties. As a consequence, properties and applications of these nano-objects were intensively studied and successfully illustrated in different fields ranging from nanomaterials, biology, nanomedicine, catalysis, etc. They were used for the elaboration of materials incorporating the dendrimers in their structure, and for modifying the properties of the surface of the materials at the nanometric scale [8]. Very sensitive DNA chips were elaborated in this way [9]. Phosphorus dendrimers have also important biological properties: antiprions [10], anti HIV [11], anti-inflammatory [12], antitumoral [13] and ocular delivery [14] properties. Also they can be used against neurodegenerative diseases [15], for drug delivery using transfection [16] and can be administered via different routes [17].

Various organometallic phosphorus dendrimer complexes bearing Ru, Pt, or Cu were prepared and found to be able to catalyze various types of reactions, in diverse media including water, with good enantioselectivities, easy recycling of the dendritic catalyst, and excellent catalytic efficiencies in many cases [18]. In all of these examples the metal is grafted on the outer shell of the phosphorus dendrimer, therefore limiting *a priori* the possibilities of using these complexes in different fields. In this review we want to present the state of the art concerning the numerous possibilities to graft Au(I) or Au(III) on phosphorus dendrimers through complexation either on phosphorus, sulfur or nitrogen ligands located at different places at the core, within the cascade structure or on the surface of the dendritic structure. Design and stabilization of gold nanoparticles will be also illustrated as well as interactions of phosphorus dendrimers with gold clusters, gold nanoparticles or gold surfaces. Recent applications of these nanostructures will be briefly presented.

2. Complexation of Au(I) with phosphorus dendrimers

2.1. Au at the focal point

In a pioneering work Rengan and Engel reported in 1990 the preparation of a new category of cascade molecules in which the initiator core and subsequent branching points are quaternary phosphonium ion sites [19a]. Up to 40 phosphonium groups can be thus incorporated. One of the strategies consists of the



Scheme 1. Synthesis of polyphosphorhydrazone dendrimers.