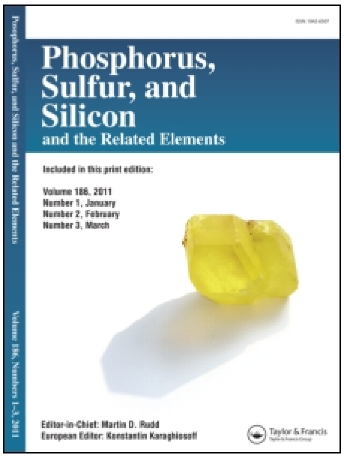

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ON THE SCENT OF SPHERICAL DENDRIMERS: CYCLOPHOSPHAZENIC DANDELION DENDRIMERS UP TO THE EIGHTH GENERATION

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Abstract Preparation of spherical dendrimers up to the eighth generation from D_{3h} cyclophosphazenic hexadangling cores (coded as sexapus) involves two repetitive steps: aminolysis of hexachlorocyclotriphosphazene, $N_3P_3Cl_6$ 0, by long-chain aliphatic diamines (such as 1,6-Diaminohexane and higher cousins) leading to sexapus cores with dangling diamino groups followed by a grafting of $N_3P_3Cl_5$ flagstones as 5-fold growing multipliers on these amino endings. Dendrimers of the first (compounds 1a, b) to the eighth (compounds 8a, b) are described. Dendrimer of the eighth generation, 8b, possesses 2,343,750 terminal (P-Cl) functions (molecular weight 228,977,179).

Dendrimers, the most highly branched functionalized molecules that exist, constitute a definite breakthrough into generations of new materials and they are attracting considerable attention in organic, supramolecular, and/or polymer chemistry [1]. Among these huge monomeric architectures, only few incorporate phosphorus [2] and only phosphorus dendrimers having charges within the cascade structure had been described [2] till the very recent past where two kinds of neutral phosphorus dendrimers were reported concomitantly by Majoral [3] and by ourselves [4]. Majoral's dendrimers have a cauliflower structure with $SPCl_3$ as the core and they possess 46 pentavalent phosphorus atoms and 48 terminal functions [aldehydic groups or phosphorus-chlorine bonds (molecular weight : 11268 or 15381)]. The synthesis of further generations having up to 384 functional groups (molecular weight 94146) was recently reported by Majoral's group [5].

Dendrimers from our own are **spherical** architectures which could be designed thanks to the previous skillful synthesis of D3h cyclophosphazenic cores. Indeed, we recently reported [4] on the neat synthesis of pure cyclophosphazenic hexapodanes (coded as **sexapus** by reference to an octopus with six tentacles) through a regiospecific peraminolysis of hexachlorocyclotriphosphazene, $N_3P_3Cl_6$ **0**, by long-chain diamines, $H_2N\text{-}(CH_2)_n\text{-}NH_2$ ($n \geq 6$), on **ALPOT [50:11]**, i.e. on alumina impregnated with a certain amount of potassium hydroxide [6]. These sexapus are **3-dimensional polyfunctional** cores suitable for generating cyclophosphazenic **spherical** (i.e. aesthetically similar to the structure of a **dry dandelion flower** and not of a **cauliflower**) dendrimers.

Amino endings of tentacles in **sexapus 1a** are accessible to further nucleophilic attacks. Our strategy for dendrimers design lies on a two-step process. The first step consists of the grafting of $N_3P_3Cl_5$ flagstones (**pentafunctional** fans) at the extremity of each tentacle (giving compounds **1b** or **first-generation**) and the second step results of a subsequent persubstitution of chlorine atoms from the $N_3P_3Cl_5$ flagstones by a new set of long-chain diamines, $H_2N\text{-}(CH_2)_n\text{-}NH_2$ ($n \geq 6$) as linkers (giving compounds **2a**). In other words, the linkage of such $N_3P_3Cl_5$ flagstones on **sexapus** cores leads to **first-generation** dendrimers, the number of linkers for further extension being **multiplied by five** with respect to the starting situation in $N_3P_3Cl_6$ itself. Thus, every two-step performance from **1b** yields a **new generation** and we reported recently on the synthesis of such generations up to the fifth one [7].

The present contribution reports on the synthesis and structural investigation of dendrimers elaborated to the eighth generation [8] which possesses 2,343,750 phosphorus chlorine bonds (molecular weight 228,977,179). Moreover, the preliminary study of the chemical properties of dendrimers of the first (**1b**) and second (**2b**) generations is under investigation in our Laboratory with the aim of knowing more about the point where steric congestion and/or loss of solubility would eventually prevent further growth of the dendrimer.

Every generation of dendrimers was obtained through a careful stepwise growth of successive phosphorus-containing layers. The synthesis of each generation necessitates two repetitive steps: aminolysis of hexachlorocyclotriphosphazene, $N_3P_3Cl_6$ **0**, by long-chain aliphatic diamines (such as 1,6-Diaminohexane and higher cousins) leading to cores with dangling diamino groups followed by a grafting of $N_3P_3Cl_5$ flagstones as 5-fold growing multipliers on these amino endings.

In each step, reactants are introduced quantitatively according to the suitable stoichiometry. The only by-products are hydrogen chloride and the related $Et_3N.HCl$ hydrochloride ! All the compounds of the generations (i.e. **1b** to **8b**) are stable and perfectly soluble in a wide variety of organic solvents (chloroform, ethyl ether, etc.). All the intermediate compounds (i.e. **2a** to **8a**) with amino groups at the periphery are no more soluble in the previous organic solvents but are rather soluble in water. All the dendrimers were characterized by NMR and IR spectroscopy, and elemental analysis. Mass spectrometry (FAB or Electrospray) was useful for dendrimers up to **2b**. Vapor Pressure Osmometry (VPO) was useful for dendrimers up to **3b**.

The **second-generation dendrimers 2b** are obtained through 1) a nucleophilic substitution of the 30 Cl atoms of the **first-generation 1b** by 30 diamino groups (leading to **2a**) and 2) a subsequent grafting of 30 $N_3P_3Cl_5$ moieties on the ends of the 30 new tentacles. We used the classical pathway where Et_3N was employed for scavenging HCl, a polar solvent such as Et_2O being used. Reactions take 48 h and yield light yellow syrupy oils which are actually Et_2O-clathrates. A magnetic stirring (one night) of these oils with large excess of n-heptane leads to the declathrated species as white powders.

Further **precursors** and **generations** of dendrimers from **sexapus** cores may be synthesized till the **eighth generation** [8], the amount of impurities (i.e. of non completely substituted species) increasing gently but steadily with the size of molecules. An efficient approach for circumventing this difficulty is based on the following remark: the three steps consisting into the successive graft of **n** linkers + **n** $N_3P_3Cl_5$ fans + 5**n** linkers are strictly identical, from a structural point of view, to the unique graft of **n** sexapus molecules ! Recent works illustrated this approach, compounds **5a**, which are precursors of **5b**, having been synthesized from compounds **3b** in this way [7]. Such a procedure decreases sharply the risk of generating impurities. Anyhow, single SiO_2 column chromatographies with n-hexane/ethyl ether (2:1) as the eluant lead to pure fourth to eighth generations which are now crystallizing.

The saga of dandelion dendrimers is currently going on and it seems that the chemical process for their design looks endless. These monomeric monsters, that we called previously UFO (Unsual Fascinating Objects) [7], will probably take the place of common polymers on the next century, both for *in vitro* and *in vivo* applications. Up-to-now, no clear technological use was evidenced in literature for such dendrimers, cauliflowers or dandelions, but Epistemology shows that Beauty leads always to Benefits for Mankind ...

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