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Synthesis and Structural Characterization of a Dendrimer Model Compound Based on a Cyclotriphosphazene Core with TEMPO Radicals as Substituents

Elena Badetti,[†,‡] Vega Lloveras,[†,‡] Klaus Wurst,[§] Rosa María Sebastián,[∥] Anne-Marie Caminade,[⊥] Jean-Pierre Majoral,[⊥] Jaume Veciana,[†,‡] and José Vidal-Gancedo*[,†,‡]

Institut de Ciència de Materials de Barcelona ICMAB−CSIC, Campus UAB, 08193 Bellaterra, Barcelona, Spain, and CIBER de Bioingeniería, Biomateriales y Nanomedicina, CIBER-BBN, Barcelona, Spain, Universitat Autònoma de Barcelona, Campus UAB, 08193 Bellaterra, Barcelona, Spain, Laboratoire de Chimie de Coordination − CNRS, Route de Narbonne 205, BP 44099, 31077 Toulouse cedex 4, France, and Institut für Allgemeine Anorganische und Teoretische Chemie, Universität Innsbruck, Innrain 52a, A-6020 Innsbruck, Austria

j.vidal@icmab.es

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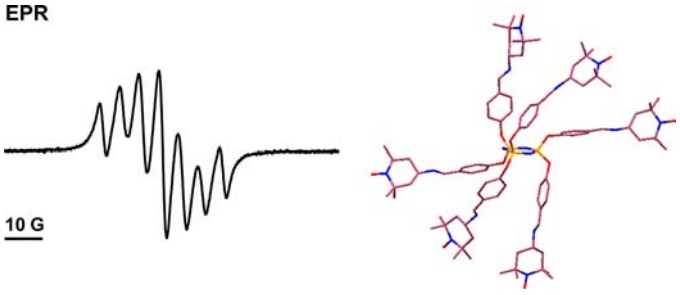
ABSTRACT



The synthesis of the $3Gc_0T$ zero generation dendrimer with a cyclotriphosphazene core functionalized with nitroxyl radicals in its six branches has been performed. The radical units have been used as probes to determine the orientation of the six branches in solution experimentally by Electron Paramagnetic Resonance (EPR) spectroscopy compared with the structure obtained in the solid state by X-ray diffraction. The orientation of the dendrimer branches is the same in solution as in the solid state.

Dendrimers,[1] in contrast to common linear polymers, enable full control over many of the molecular design parameters at the single molecular level such as molecule size, branching pattern, structure, and morphology. Therefore, they provide a new platform for obtaining functional materials with nanometer-scale precision. Most dendrimers are comprised of organic fragments although heteroatom-containing dendrimers and, in particular, phosphorus-containing dendrimers have also been reported becoming very promising molecules for Materials Science and Nanomedicine.[2] Some of us have described a new series of dendrimers built with a cyclotriphosphazene (N_3P_3) core with phosphorus atoms as branching points and with end

[†] Institut de Ciència de Materials de Barcelona ICMAB−CSIC.
[‡] CIBER-BBN.
[§] Universität Innsbruck.
[∥] Universitat Autònoma de Barcelona.
[⊥] Laboratoire de Chimie de Coordination − CNRS.

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groups that can be easily functionalized.[3] Currently, there is interest in determining the exact branching pattern and structure of this family of dendrimers.

There are few studies of different cyclotriphosphazene based dendrimers of zero generation by X-ray diffraction, IR, and RAMAN spectroscopy as well as few density functional theory (DFT) studies of vibrational spectra of this kind of dendrimer.[4] By X-ray analysis it has been demonstrated that three phenyl rings are situated above the cyclic phosphazene ring and the other three below.[5] However, there is still much controversy about the relative orientation of these six branches in solution. Here, we provide for the first time experimental data about the molecular structure in solution of the zero generation dendrimer of this family of dendrimers (Gc_0) with TEMPO radicals in its six branches (**3-Gc$_0$T**, Figure 1) demonstrating they have the same relative orientation as in the solid state.

The synthesis of the **3-Gc$_0$T** compound was based on the peripheral modification of dendrimer **1-Gc′$_0$**,[6] containing six aldehyde groups on its surface. This dendrimer was condensed with 4-amino-TEMPO **2** to obtain the corresponding hexaimine derivative **3-Gc$_0$T** in a 97% yield (Scheme 1).

We followed the conditions already reported for the condensation of different amines on dendrimers with aldehyde terminal groups,[3f] but the handling of radicals in solution was performed under dark conditions.

FT-IR allowed us to determine if the reaction had gone to completion by the disappearance of the aldehyde signal at 1695 cm^{-1} of **1-Gc′$_0$** as well as by ^1H NMR (9.9 ppm). Even though the signals of the ^1H NMR spectrum of **3-Gc$_0$T** were broad, due to the presence of the paramagnetic radical units, it was possible to establish the position of each group of protons of the molecule enabling the course of its preparation to be followed with this technique. On the other hand, the ^{31}P NMR signal of **1-Gc′$_0$** (δ = 4.9 ppm) and **3-Gc$_0$T** appearing at δ = 5.6 ppm (which was not too much affected by the presence of the radicals) permitted also the monitoring of the reaction and determination of the purity of the new dendrimer confirming that all the branches were substituted. Matrix-assisted laser desorption and ionization–time-of-flight (MALDI–TOF) mass spectrometry, employing a CIN (4-Hydroxy-3,5-dimethoxycinnamic acid) matrix, showed an isotopic distribution of peaks at an m/e of 1783 [M^+] confirming the identity of the **3-Gc$_0$T** dendrimer.

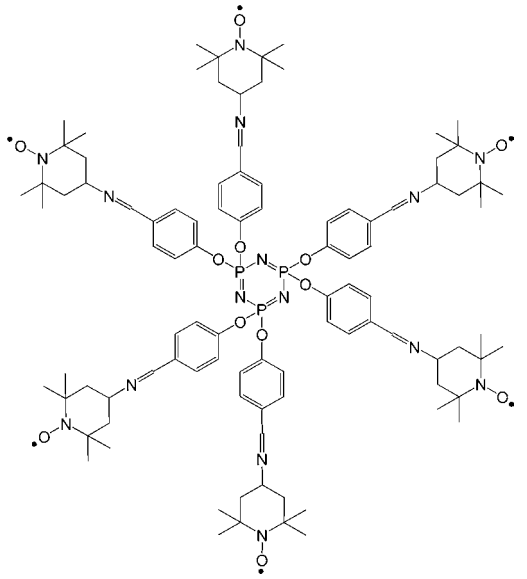
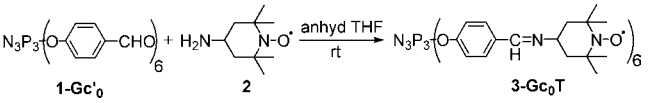


Figure 1. Molecular structure of the zero generation dendrimer with an N_3P_3 core functionalized with six TEMPO radicals (**3-Gc$_0$T**).

Scheme 1



The structure of compound **3-Gc$_0$T** was confirmed by X-ray diffraction analysis. Single crystals were grown from a slow evaporation of a toluene solution. Figure 2 shows a view of the asymmetric unit of **3-Gc$_0$T**.[7] The cyclotriphosphazene ring is nearly planar with slight puckering to a twisted boat conformation. Maximum deviation from the mean least-squares plane was detected at the N3 and P3 atoms, both 0.086(2) Å above and below the plane. This conformation is also observed in other solved structures of cyclotriphosphazene derivatives.[4,5,8] The most relevant feature is that there are three branches situated above the N_3P_3 ring, with the other three below it. The distances

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(7) **3-Gc$_0$T** crystallizes as a solvate together with three molecules of toluene for each molecule of the hexaradical (not shown in Figure 2).

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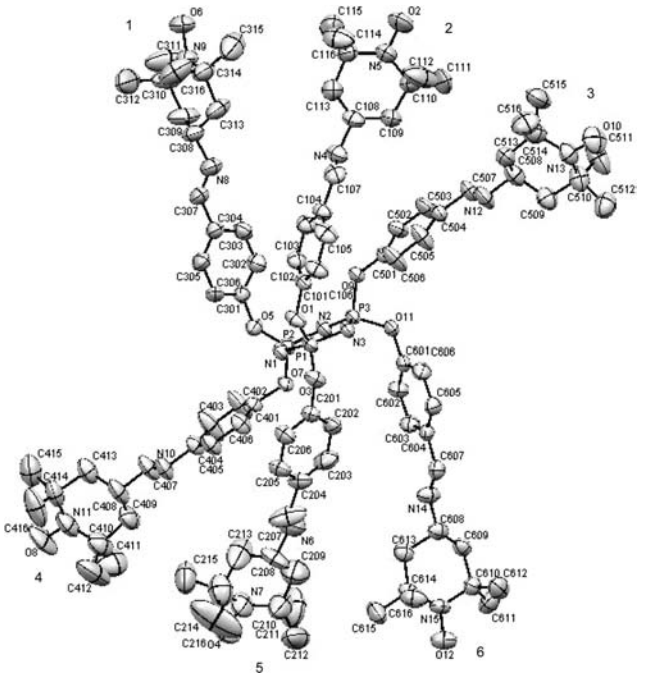

Figure 2. An ORTEP view of the molecular structure of compound **3-Gc$_0$T** showing the atom-labeling scheme in the asymmetric unit. Hydrogen atoms and toluene molecules have been omitted for clarity.

between atoms of the three branches are relatively close, with a distance between N_9 and N_5 of TEMPO 1 and 2 of 7.72 Å and between N_5 and N_{13} of TEMPO 2 and 3 of 8.45 Å; on the other side of the N_3P_3 ring, 7.71 and 7.87 Å are measured for $N_{11}-N_7$ and N_7-N_{15}. However, the distance between N atoms of TEMPOs located at the opposite sides of the N_3P_3 ring are 18.88, 21.91, and 18.47 Å between N_9-N_{11}, N_5-N_7, and $N_{13}-N_{15}$, respectively. It is also worth noting that this molecular conformation is stabilized by $C-H\cdots\pi$ stacking interactions between the benzene rings of the branches (see the Supporting Information). Full crystallographic data are listed in Tables S1–S6.[9]

The EPR spectrum of a 10^{-4} M solution of **3-Gc$_0$T** in a mixture of dichloromethane/toluene (1:1) at 350 K shows seven lines centered at $g = 2.0066$ and separated by *ca.* 5.0 G (Figure 3). This would fit with a spectrum generated by the interaction of three TEMPO radicals. However, the first, fourth, and seventh lines are more intense than those for the expected pattern. This result clearly suggests that the observed spectrum is in fact the sum of at least two different spectra. To understand this result it is essential to take into account the magnitude of the magnetic exchange interactions, J,[10] between the six radical units inside this molecule as well as the fact that these interactions may be not constant in solution because the units could be in movement under such conditions. Consequently, the EPR spectra should be dependent on the conformation and mobility of the dendrimer branches and, therefore, the shape of the spectra should depend on the temperature, viscosity, and nature of solvent (Figures S3 and S4). The influence of the exchange interaction J on the EPR spectra of polyradicals is complex and much less studied than for biradicals for which there are many reported examples studied in great detail.[11] In the case of a flexible N-containing biradical,[12] with only a through-space spin exchange mechanism between the two radicals, we may have two limited cases: (a) When radicals are too far and the magnitude of J is smaller than the hyperfine coupling constant with N nuclei, a_N, i.e. $|J| \ll |a_N|$, the spectrum of the biradical is similar to that of two independent monoradicals exhibiting three lines separated by the hyperfine coupling constant a_N with relative intensities of 1:1:1. (b) When radicals are closer and thereby $|J| \gg |a_N|$ the spectrum consists of a five-line hyperfine pattern with a 1/2 a_N separation and relative intensities of 1:2:3:2:1. At intermediate values, where $|J| \approx |a_N|$, the spectra are more complex and strongly dependent on the temperature and solvent since both conditions may influence the effective distance between the two radical moieties.

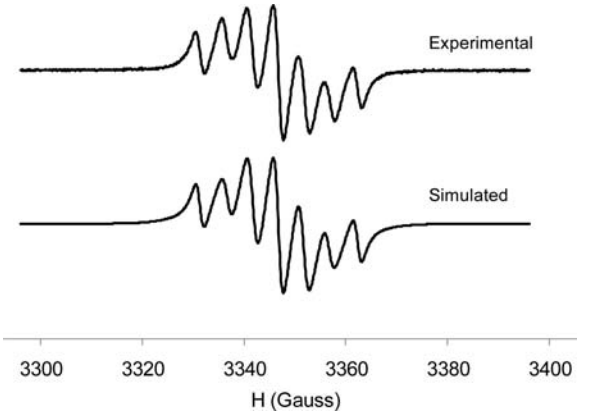

Figure 3. Experimental EPR spectrum of a 10^{-4} M solution of **3-Gc$_0$T** in dichloromethane/toluene (1:1) at 350 K and the simulated spectrum using data given in the text.

For a polyradical where only a through-space spin exchange mechanism between radical units is operative,

(9) CCDC-894232 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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the behavior should be similar although more complex than for biradicals.[13] Thus, in the case of a compound with three interacting N-containing radicals (Figure S5), when radicals are too far and $|J| \ll |a_N|$, the spectrum would be similar to that of three independent monoradicals exhibiting three lines separated by a_N with 1:1:1 relative intensities; whereas when radicals are close and $|J| \gg |a_N|$ it would give rise to a seven-line hyperfine pattern with a separation of 1/3 a_N and relative intensities of 1:3:6:7:6:3:1. Finally, in the case of a molecule with six radicals, when radicals are too far and therefore not interacting among them the spectrum would be similar to that of six independent monoradicals exhibiting three lines separated by a_N with relative intensities of 1:1:1, while when radicals interact strongly among them with equal J values being $|J| \gg |a_N|$, we expect to see a hyperfine pattern of 13 lines with a separation of 1/6 a_N. As already mentioned before, the spectrum of **3-Gc$_0$T** apparently looks like a superposition of two spectra, centered at the same g-value, one more intense with seven lines separated by *ca.* 5.0 G and another with three lines separated by *ca.* 15.5 G. Both spectra might correspond to two interconverting forms of the molecule, A and B, at slow interconverting rates which exist in different proportions. Form A could correspond to the compound with three equivalent radical units at each side of the molecule interacting strongly among them (and not with those at the other side of the molecule). The shape of the spectrum depends strongly on the temperature (Figure S3), showing an alternating line width effect due to the modulation of the spin exchange interaction.[14] To minimize this effect, we use the spectrum at 350 K. At this temperature, we observe a very small alternating line width effect because the spin exchange interaction is fast. Under these conditions, the main contribution to form A is the quartet state. Therefore, to simplify, we can only use such a quartet state in the simulation.[14] In form B the radical units are magnetically noninteracting among them. The stabilization by C−H$\cdots\pi$ stacking given in the solid state becomes weak in solution due to the increased mobility of the branches due to the effect, among other factors, of the temperature. This facilitates the existence of conformations in which the branches are arranged as in A but further apart (form B). In accordance with such an assumption, the spectrum at 350 K can be simulated as the sum of two contributions: One originated from form A (in conditions of fast exchange of a triradical) with a_N(3N) = 4.96 G and ΔH_{pp} = 2.8 G with a 96.5% molar abundance, and another from the B form with a_N(1N) = 15.6 G and ΔH_{pp} = 1.21 G with a 3.5% molar abundance. The good agreement between the experimental and simulated EPR spectra supports that **3-Gc$_0$T** has in solution the six branches organized into two groups of three, as occurs in the solid state.

In conclusion, the **3-Gc$_0$T** zero generation dendrimer based on a cyclotriphosphazene core with pendant nitroxyl radicals at its branches has been prepared for the first time. The structure of this compound in the solid state has been determined by single crystal X-ray diffraction analysis showing that three branches are situated above the cyclotriphosphazene ring and the other three below it. Experimental evidence has also been provided from the EPR spectra that this specific structure also occurs in solution.

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Supporting Information Available. Experimental procedure, collection of spectra, X-ray diffraction analysis, EPR spectra at different temperatures and solvents, and simulations of N-containing triradical systems. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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