Optimization of the geometry and calculation of the normal vibrations of the dendrimer with amine terminal groups

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Abstract. The structure of the first generation dendrimer $G_1$ constructed from a hexafunctional cyclotriphosphazene core with six branches –O–C$_6$H$_4$–CH=N–N(CH$_3$)$_2$–P(S)< and twelve 4-hydroxyphenethylamine end groups O–C$_6$H$_4$–(CH$_2$)$_2$–NH$_2$ was studied. Structural optimization and analysis of normal vibrations were performed for the G1 dendrimer. The G1 dendrimer molecule has a convex lens structure with flat –O–C$_6$H$_4$–CH=N–N(CH$_3$)$_2$–P(S)< fragments and a slightly nonplanar cyclotriphosphazene core. Full optimization shows that the conformation of terminal 4-hydroxyphenethylamine groups –O–C$_6$H$_4$–(CH$_2$)$_2$–NH$_2$ with dihedral angles C(13)–C(22)–C(23)–N(6) and C(22)–C(23)–N(6)–H(23): 63.7 and 46.8o is predominant. The flat and anisotropic form of the cyclotriphosphazene core determines the ability of dendrimers to pack with each other in the most likely disk-like form. The spatial distribution of electron density for the core and end groups allows estimating the magnitude of electrostatic interactions on the surface of the dendrimer in the guest-host complexes.

Keywords: dendrimers, spectroscopy, DFT, optimization, normal modes, geometry.

1 Introduction

Dendrimers are branched monodispersed macromolecular compounds [1-10]. The three structural components of dendrimers, namely, the inner core, the repeating branched units attached to the core, and the functional end groups can be adjusted. Phosphorus-containing dendrimers interact with biological systems and are used for drug delivery [10-19].

In this work, quantum chemical calculations are used to characterize a dendrimer constructed from a hexafunctional cyclotriphosphazene core with six branches –O–C$_6$H$_4$–CH=N–N(CH$_3$)$_2$–P(S)< and twelve terminal groups 4-hydroxyphenethylamine–O–C$_6$H$_4$–(CH$_2$)$_2$–NH$_2$ ($G_1$). We chose this dendrimer because it can be used as a medicine and in construction industry [20, 21].

Our goal was to combine the experimental results with DFT calculations to interpret the IR spectra of the dendrimer. Thanks to a complete optimization, we were able to find a conformer corresponding to the local minimum of the potential energy of the $G_1$ molecule and its IR spectrum using the DFT technique. We obtained the structural parameters of the $G_1$ dendrimer and compared them with the experimental values. We have tried to describe different structural elements of the dendrimer based on the analysis of its IR spectrum by the DFT method. The results obtained allow us to elucidate the relationship between the structural characteristics of the dendrimers and their vibrational spectra.

2 Materials and Methods

The production procedure and the main parameters of the dendrimer containing phosphorus $G_1$ have been described previously [20]. The $G_1$ dendrimer contains a cyclotriphosphazene (NP)$_3$ core, six branches –O–C$_6$H$_4$–CH=N–N(CH$_3$)$_2$–P(S)<, and twelve 4-hydroxyphenethylamine terminal groups –O–C$_6$H$_4$–(CH$_2$)$_2$–NH$_2$ (Figure 1). The $G_1$ dendrimer looked like a white powder.
The IR spectrum was calculated using the gradient-correlated theory with the exchange-correlated density functional PBE [22]. It was chosen because it satisfies the exact relationships for the exchange-correlation hole and does not contain adjustable parameters. A basis with three-exponential with two polarization functions (TZ2P) [22] was used. This basis was chosen to obtain the optimal ratio between precision and calculation time [22]. Its particularity is that a set of exponentials is used for all values of the angular momentum of atoms [23]. The PRIRODA program was used to perform calculations using the DFT method [23]. Program [24] was used to calculate the distribution of potential energy.

3 Results
The G1 dendrimer is an amorphous substance and has no long-range order in the condensed phase. The cyclotriphosphazene ring is almost flat [25]. The lengths of the chemically equivalent bonds are the same. Although the comparison between the structures in the gas and condensed phases is not very strict, there is a reasonable agreement between the theoretical calculation of G1 and the experimental data on X-ray diffraction for the crystalline phase of hexaphenoxycyclotriphosphazene and the phenethylamine derivative.

The complete optimization is provided by the conformer of the G1 molecule with a slightly nonplanar cyclotriphosphazene ring (Figure 2). The calculated dihedral angles of the cyclotriphosphazene ring are less than 30°. Our data are consistent with recent non-empirical calculations of phosphazenes. Most cyclotriphosphazene derivatives have a flat ring conformation.

It results from quantum chemical calculations that each branch \(-\text{O}–\text{C}_6\text{H}_4–\text{CH}=\text{N}–\text{N(CH}_3)_2–\text{P(S)}<\) is flat. The scanning of the potential energy surface for internal rotations shows that the dendrimer molecule mainly exists only in a single stable conformation of the branches.

The most stable is the conformer of the molecule G1 with calculated dihedral angles: 170.1 and 158.8°. The corresponding experimental angles are 174.7 and 172.8°. A complete optimization shows that the conformation of the 4-hydroxyphenethylamine terminal groups \(-\text{O}–\text{C}_6\text{H}_4–(\text{CH}_2)_2–\text{NH}_2\) with dihedral angles C(13)–C(22)–C(23)–N(6) and C(22)–C(23)–N(6)–H(23): 63.7 and 46.8° predominate.
Intramolecular interactions cause asymmetry in the arrangement of terminal groups.

The bond lengths calculated for $G_1$ (in Å) P(1)–N(3) (1.606), P(1)–O(1) (1.649) and C(1)–O (1) (1.388), are in good correspondence with the experimental values of 1.576, 1.585 and 1.401.

The shape of the dendrimer molecules can be characterized by the ratios $I_1/I_3$ and $I_2/I_3$ of the principal values of the gyration tensor. Their values of 0.22 and 0.98 correspond to the disk-shaped anisotropic form of the $G_1$ dendrimer molecules. Thus, the flat and anisotropic form of the cyclotriphosphazene core determines the ability of dendrimers to group in the most likely disk form.

The chemistry of the guest-host complex is generally based on the electrostatic interactions on the surface of the dendrimer. The spatial distribution of the electron density for the core and the terminal groups allows us to estimate the extent of these interactions. It follows from our calculations that the molecule $G_1$ comprises polar bonds P–N and P=S with Hirschfield charges on the atoms (in atomic units): N(1) (-0.31), P(1) (0.39), S(1) (-0.25) and P(4) (0.36). The charges on the atoms O(1) and O(2) are -0.12. Other atoms of the repeating unit and terminal groups are not charged. Thus, in the case of phosphorus-containing dendrimers, the macromolecules have a hydrophobic interior and active sites for reactions in the core of the dendrimer and the terminal groups.

Dipole moments can be used to characterize the structure of the dendrimers. The dipole moment of the molecule $G_1$ calculated in the gas phase is 4.17 D. Thus, $G_1$ dendrimer has a notable dipole moment, which can be attributed to the asymmetric distribution of the branches. The branches of this dendrimer inductively affect the core due to its isolation.

Lipophilicity is a very important molecular descriptor which is well correlated with the biological activity of chemical compounds and the solubility in water. Lipophilicity can be measured using logP, which shows the distribution between non-polar and polar bonds. In this work, we calculated logP for the molecule $G_1$ and obtained a fairly high value of 35.54. Thus, the first generation dendrimer has a high positive value for logP and is lipophilic. The lipophilicity of this dendrimer determines the geometry and the shape of the molecule in water. It follows from the results of our calculations that the internal structure of the dendrimer plays an important role in taking into account the biological properties.

4 Discussion
The theoretical IR spectrum of $G_1$ is illustrated in Figure 3.

![Theoretical (1) and experimental (2) IR spectrum $G_1$.](image)

**Figure 3.** Theoretical (1) and experimental (2) IR spectrum $G_1$.

Although the calculated absorption curve of an isolated molecule is much simpler than the experimental IR spectrum, the intensity of most the bands is reproduced by our calculations. Therefore, quantum chemical calculations can be used to interpret the spectra of the dendrimers. The band allocation has been made.

The band at 1687 cm$^{-1}$ was attributed to the stretching vibrations of the carbonyl groups of CF$_3$COOH, which formed during the synthesis of the dendrimer. The 1632 cm$^{-1}$ band is an NH$_2$ bending and has an average intensity in the IR spectra of $G_1$. The intense bands 1606 cm$^{-1}$ and 1505 cm$^{-1}$ were due to the CC$_{ar}$ stretching and the CCH deformation vibrations of the aromatic ring. The rather weak bands of 1469, 1441, 1429 cm$^{-1}$ in the IR spectrum of $G_1$ are associated with HCH deformation vibrations. The bands 1304 and 1368 cm$^{-1}$ in the IR spectrum are assigned to the NCH and CCH deformations.

The bands at 1164, 1181, 1198 cm$^{-1}$ belong to the C–O, P–N, and C–C stretching vibrations. The peak at 1017 cm$^{-1}$ has been attributed to the stretching vibrations of the C–N bonds. The 946 cm$^{-1}$ line was assigned to the P–O stretching vibrations. The 837 cm$^{-1}$ band in the IR spectrum of $G_1$ was connected with a symmetrical stretch of the COC.

The bands of 646 cm$^{-1}$ in the IR spectrum $G_1$ includes the contribution of the deformations CCC, CCH, and OCC. The band of 574 cm$^{-1}$ in the IR spectrum refers to the POC bending.

Thus, the core (NP)$_3$ of the dendrimer has a band of 1266 cm$^{-1}$ in the Raman spectrum $G_1$, attributed to the stretch P–N. The end groups are characterized by a band of 3436 cm$^{-1}$, assigned to the antisymmetric stretch NH$_2$. The 1577 cm$^{-1}$ line can be attributed to the $\nu$(C=N) of repeating units.
5 Conclusion

Structural optimization and normal mode analysis were performed for the $G_1$ dendrimer based on the DFT. The calculated geometric parameters and the harmonic vibration frequencies are predicted in good agreement with the experimental data.

It was found that $G_1$ has a concave lens structure with plane fragments $-O-C_6H_4-CH=N-N(CH_3)-P(S)<$ and slightly non-planar cyclotriphosphazene cores. The 4-oxyphenethylamino groups attached to different arms show significant deviations from a symmetrical arrangement. FTIR spectra of the first generation dendrimer $G_1$ built from the cyclotriphosphazene core, six arms $-O-C_6H_4-CH=N-N(CH_3)-P(S)<$ and twelve 4-oxyphenethylamino terminal groups $-O-C_6H_4-(CH_2)_2-NH_2$ $G_1$ have been recorded.

The experimental IR spectra of the dendrimer $G_1$ was interpreted using the potential energy distribution. Based on the DFT calculations, a complete vibration assignment is proposed. Thus, the used DFT method makes it possible to calculate the structure, the charges on the atoms and to reproduce the experimental IR spectrum of the dendrimer with a cyclotriphosphazene cores and 4-oxyphenethylamino terminal groups. The 4-oxyphenethylamino terminal groups are outside the plane of the repeating group. The calculated ratios of the principal moments of the gyration tensor reveal that the molecule $G_1$ has a very asymmetric shape.

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