Synthesis and Characterization of Bis-MPA Dendrimers via Positron Annihilation Spectroscopy

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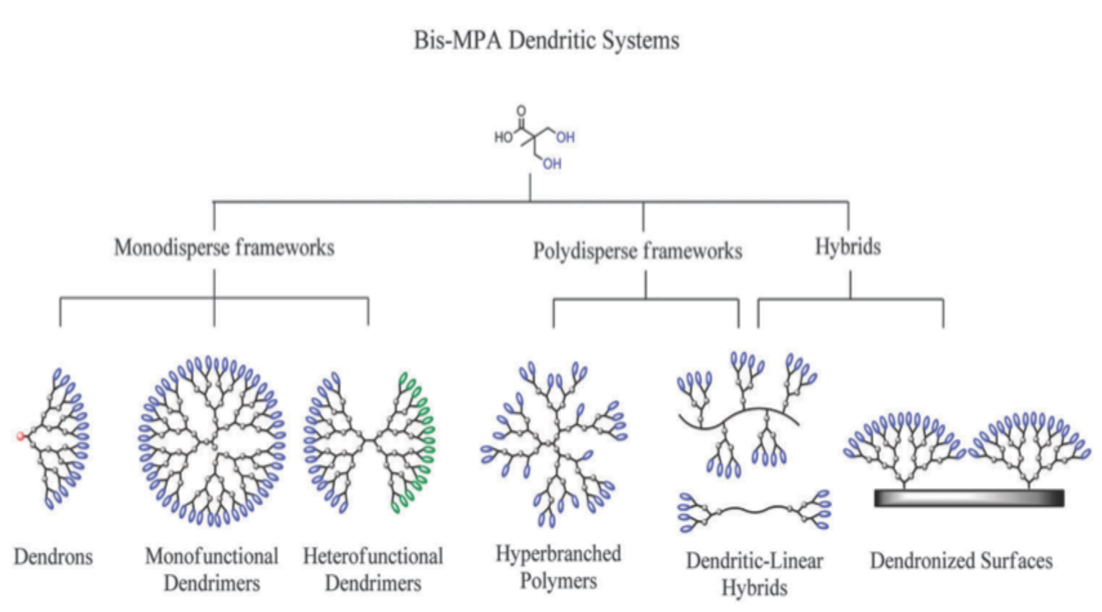
LA-SiGMA Louisiana Alliance for Simulation-Guided Materials Applications

Introduction

Dendritic synthesis based on 2,2-bis(methylol)propionic acid (Bis-MPA) was conducted for future analysis via positron annihilation spectroscopy. Using a monopentaerythritol core, these dendrimers were grown to the second generation. Proton NMR, Carbon NMR, and MALDI-TOF mass spectrometry were used to characterize the structures throughout synthesis in order to confirm the complete dendronization or deprotection of these molecules.

Background



[1] Figure 1

Recently, dendrimers based on 2,2-bis(methylol)propionic acid (Bis-MPA) have been of particular interest in both industry and academia.

Benefits of using Bis-MPA include:

- low cost (~$30/kg)
- non-toxicity
- stability, if kept dry
- biocompatibility [3]

Using Bis-MPA as a building block, several varieties of dendritic syntheses are possible. **Dendrimers** are branched molecules comprised of one or more concentric layers (generations), one or more branching arms, and functionalized end groups (Figure 2). My research focused on polyester dendrimers using monopentaerythritol as a core.

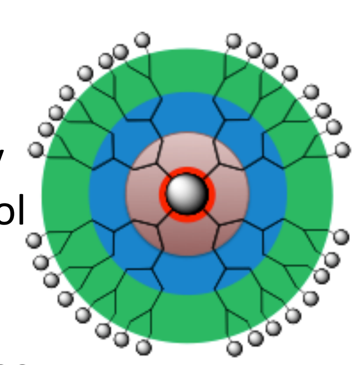
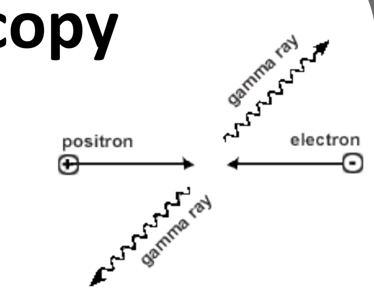


Figure 2

Through a series of deprotection and dendronization reactions (see Methods: Steps 2 and 3), these dendrimers can grown to larger and larger "generations". This study initially calls for a 2nd generation (G2) dendrimer to begin analysis via PAS.

About Positron Annihilation Spectroscopy

Positron Annihilation Spectroscopy (PAS) is an analytical technique capable of measuring the void spaces in polymers and other materials. PAS achieves this by calculating the size of the empty spaces in a given molecule by a function of the lifetime of positrons emitted. This process allows us to analyze the atomic interactions within and between different polymers.



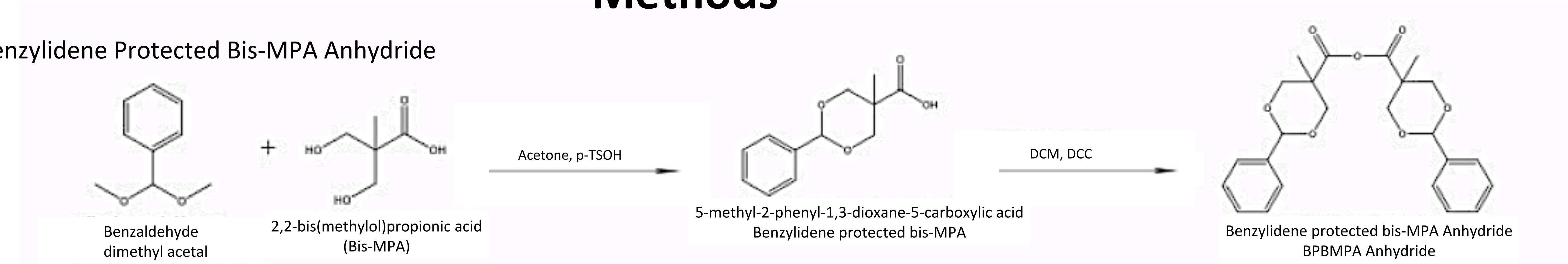
[2] Figure 3: PAS measures the radiation resulting from the collision of a positron with an electron.

Figure 1 above shows the diversity seen in bis-MPA dendritic systems alone. Each of these molecules pack "in bulk" (pure, without solvent) in different ways. For instance, linear polymers are able to pack together very tightly, whereas hyperbranched polymers pack more loosely due to their irregularity in shape. Following this trend, we expect dendrimers to resemble hard spheres, leaving a large amount of void space between molecules. The size and character of these voids can be established via PAS, affording us more information about the structure and properties of these materials.

By utilizing this unique technique*, we will be able to further understand how this molecular packing effects the properties of dendrimers.

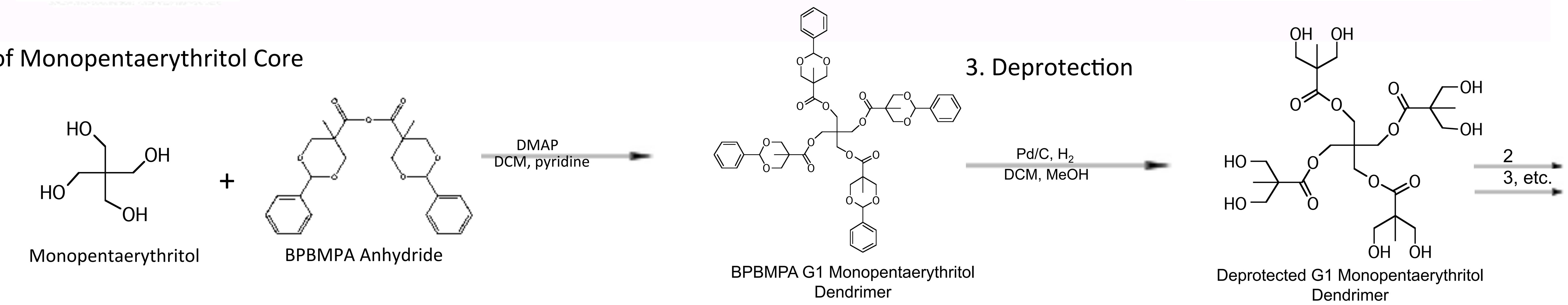
Methods

1. Synthesis of Benzylidene Protected Bis-MPA Anhydride



2. Dendronization of Monopentaerythritol Core

3. Deprotection



1. *P*-Toluene sulfonic acid was used as a catalyst for the initial esterification reaction. DCC was then used as a dehydrating agent to convert the acid into anhydride.
2. DMAP was used as a nucleophilic catalyst to form the BPBMPA G1. 3. Palladium on carbon was used as a catalyst to remove the benzylidene protecting groups to achieve our final product.

→This process of dendronization and deprotection can be repeated to achieve subsequent generations of dendrimers.

Analysis

Proton (^1H) and Carbon (^{13}C) NMRs were taken after each of the steps outlined above to ensure complete reactivity. As molecular weight increased, MALDI-TOF Mass Spectrometry was utilized to more accurately characterize the dendrimer products.

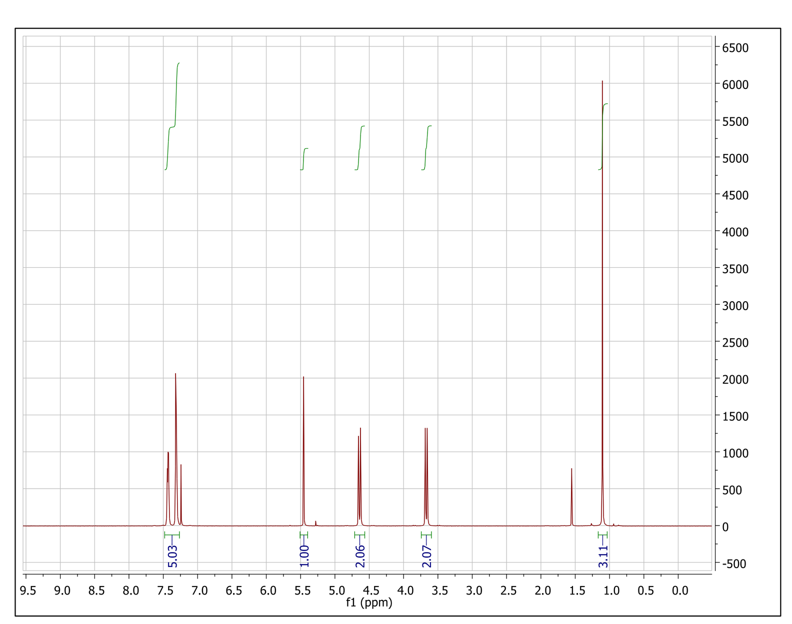


Fig. 3: ^1H NMR of BPBMPA Anhydride

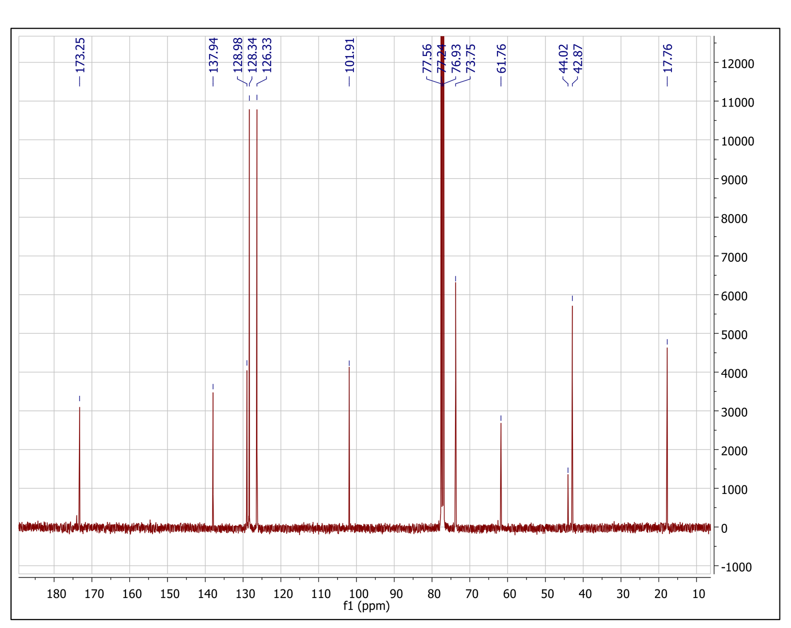


Fig. 4: ^{13}C NMR of a protected G1 dendrimer

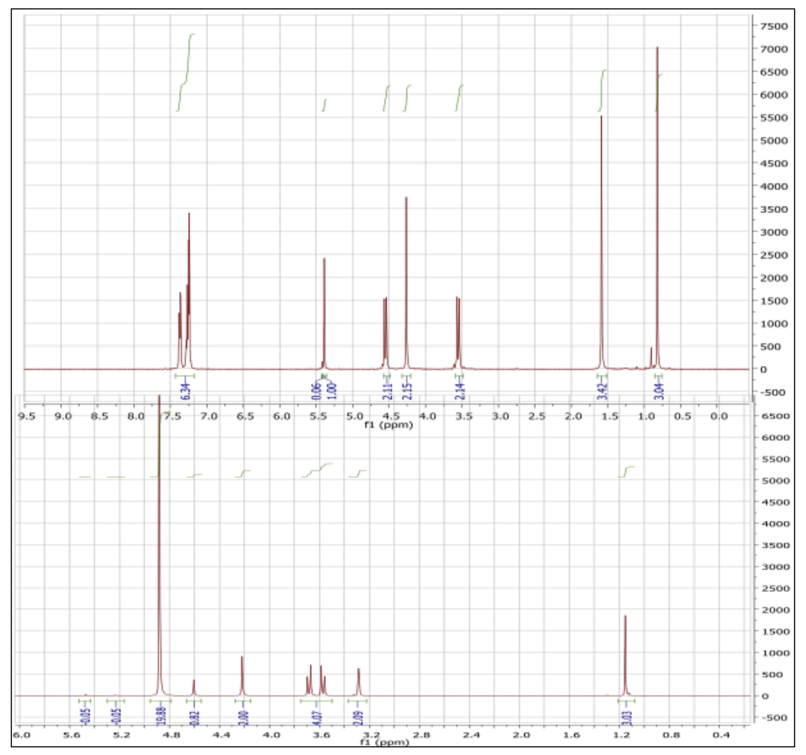


Fig. 5: ^1H NMR comparison of protected (top) vs. deprotected (bottom) G1 dendrimer.

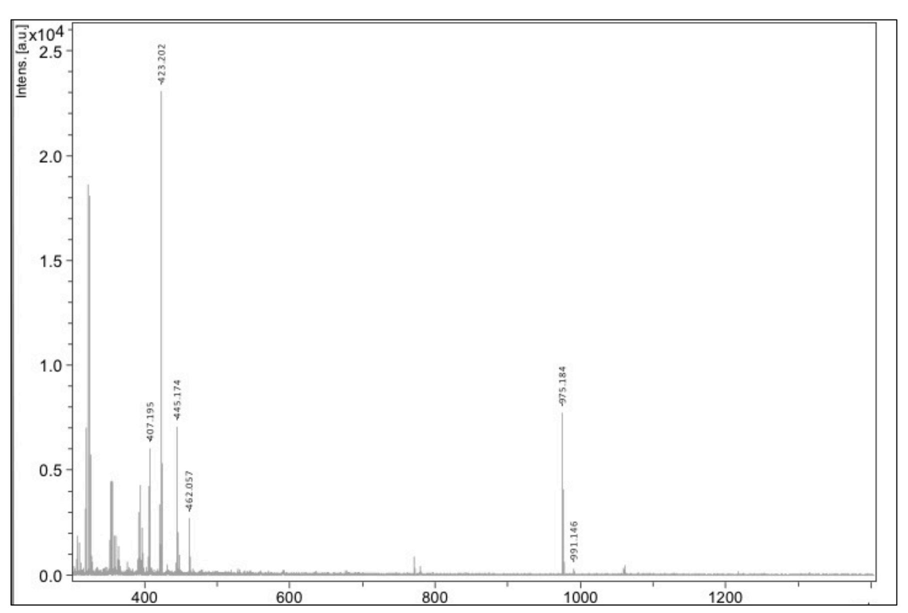


Figure 6: MALDI-TOF spectra of protected G1 dendrimers

Applications

As mentioned previously, one of the benefits of using bis-MPA is its biocompatible nature. This quality makes dendrimers promising drug delivery vehicles. End groups can be functionalized by replacing the hydroxyl groups with reactive intermediates, allowing for the attachment of a variety of structures.[4] A "large number of bioactive substituents have successfully been covalently attached to these scaffolds including carbohydrates, peptides, anticancer doxorubicin (DOX), and antibiotic penicillin derivative amoxicillin" (*Chem. Soc. Rev.*, 2013, 42, 5858).

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