Synthesis of generation 3-bisMPA dendrimers for nanotherapeutic drug delivery systems

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Abstract

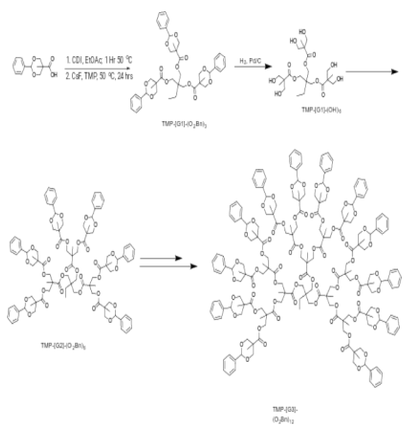
Stimuli Response Polymers (SRPs) are poised to make advances in nanotherapeutic drug delivery systems. In response to chemical, physical, or biological stimuli, SRPs can control the release of a drug into a system. The free polymers perform with a polydispersity that hinders their effectiveness in drug delivery, therefore we are using bis-MPA dendrimer as a core nucleation site for a precise assembly of these SRPs. This project involves the synthesis of nanomaterial consisting of a dendritic core, a ligand, and a stimuli response block co-polymer. The biocompatibility and monodispersity of bis-MPA dendrimers make them targets as potential drug delivery system platforms. To this end, the drug delivery potential of precisely defined materials made of stimuli response block co-polymers linked to the dendrimer core will be compared to that of free block co-polymers in solution.

This research highlights the synthesis of the dendritic core. The 2,2-bis(hydroxymethyl) propionic acid, (bis-MPA) is protected with benzaldehyde dimethyl acetal, and coupled with trimethylol propane (TMP), and then deprotected under acidic conditions to reveal hydroxy termini. The dendrimer core functions as an assembly site for stimuli response block co-polymers. A generation 1 dendrimer was produced and confirmed using ^{1}H NMR and MALDI-ToF. These reactions will be repeated in order to synthesize subsequent generations of bis-MPA dendrimer, with a final goal of synthesizing a generation 3 bis-MPA dendrimer.

Objectives

- Synthesize G1-tmp-[G1]-$(O_2Bn)_3$
- Analyze the G1 for purity using ^{1}H NMR and MALDI-ToF
- Repeat the procedure on larger bis-MPA generations for more precise drug delivery

Synthesis



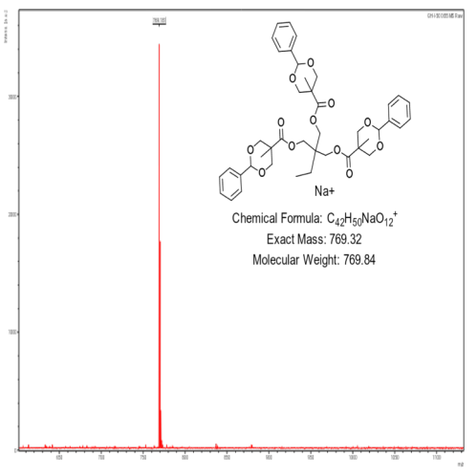


Figure 1: MALDI-ToF of TMP-[G1]-$(O_2Bn)_3$

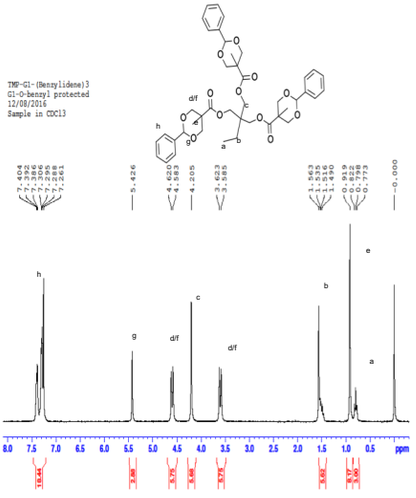


Figure 2: ^{1}H NMR spectra of TMP-[G1]-$(O_2Bn)_3$

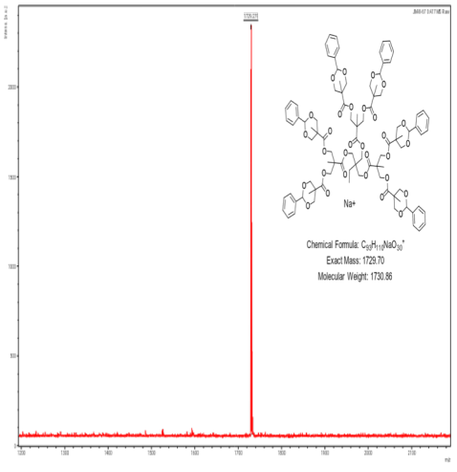


Figure 3: MALDI-ToF of TMP-[G2]-$(O_2Bn)_6$

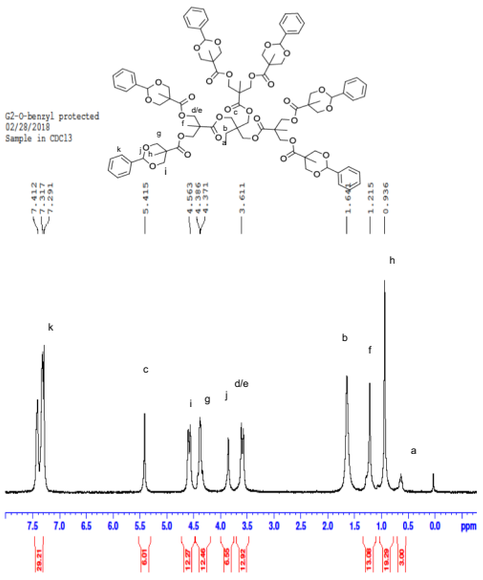
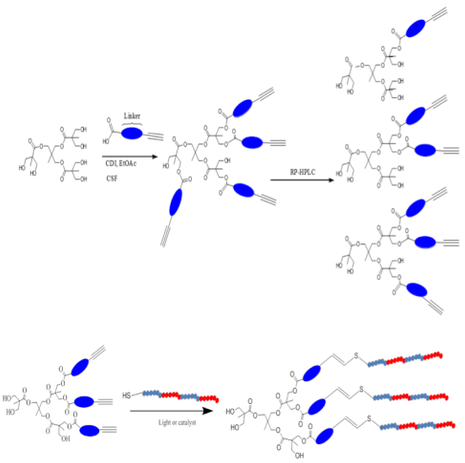


Figure 4: ^{1}H NMR spectra of TMP-[G2]-$(O_2Bn)_6$



Total Synthesis of SRP-Nanomaterial

Conclusions

- The ligand-dendrimer conjugates will be quantified and the populations will be isolated by HPLC.
- Each population will be attached to the SRP via thiolene or thiolyne click chemistry.
- The resulting precisely defined materials will be monitored by SR-ACOMP for the effects of varying numbers of SRPs per particle on drug delivery.

Acknowledgements

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