Synthesis and Analysis of Bis(methylol) propionic Dendrons

Lauren E. Luce[1], Jennifer L. Marple[2], Scott M. Grayson[2]

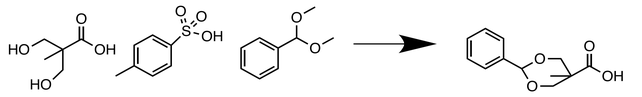
[1]Nicholls State University, 906 East 1st Street, Thibodaux, LA 70310

[2]Tulane University, 833 Maple Street, New Orleans, LA 70118

Introduction:

Small branched polymers are becoming widely used for drug delivery and gene therapy purposes but very little is known about the physical properties of these molecules, such as dendrimers, dendrons, and hyperbranched polymers. If their chemical reactivity is studied, it may lead to improvements of these polymers and could also broaden their applications. Bis-MPA, 3-hydroxy-2-(hyroxymethyl)-2-methylproponoic acid, was chosen as a building block for the synthesis of benzylidene anhydride because the two alcohols can be selectively protected, enabling ester formation with the carboxylic acid functionality. Dendrons with one, two, and three layers (referred to as generations) of these branched monomers will be synthesized from a methanol core using the benzylidene anhydride. Kinetic will be observed for the second and third generation dendrons and compared to the reactivity of hyperbranched polymers.

Synthesis of Benzylidene 2,2-Bis MPA (Anhydride) :



Molecular Weight: 222.24

Purification: The anhydride was dissolved in dichloromethane (DCM) and precipitated in hexanes stirring vigorously and refrigerated over night. Product was filtered but ^{1}H NMR showed DCU in it. It was then washed three times in water and precipitated using the previous method to yield a pure product.

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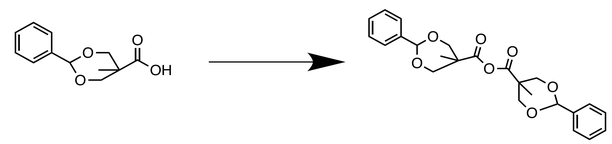
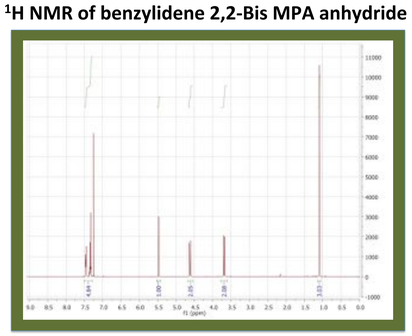
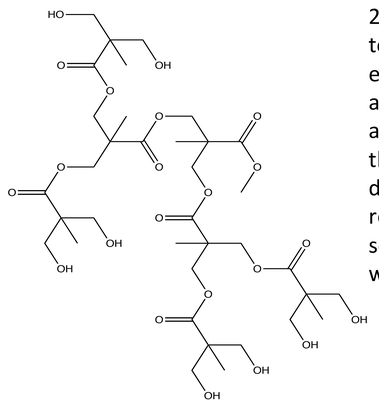


Molecular Weight: 426.46
m/z: 426.17 (100.0%), 427.17 (26.5%), 428.17 (4.7%)

^{1}H NMR of benzylidene 2,2-Bis MPA anhydride



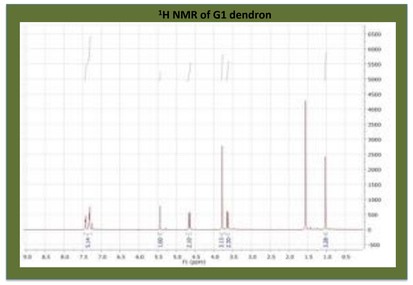
Synthesis of g1 Bis(methylol) propionic dendron:



G3 Bis(methylol) propionic dendron

The first generation, G1, Bis (methylol) propionic dendron was synthesized several times using different solvents and purification methods. The G1, with a molecular weight of 236 daltons, was too small to precipitate when attempting to in both hexane and methanol. The easiest and most effective synthesis was when using methanol in excess as a solvent and core. Methanol was used in a 40-50x excess and dichloromethane (DCM) was used to help dissolve the Benzylidene 2,2-bis MPA anhydride. DMAP, 4-dimethylaminopyridine, was used as a catalysis and reaction ran overnight. Four washes with $NaHCO_3$ solution, two washes with $NaHSO_4$ solution, and one wash with brine (NaCl) purified the dendron.

^{1}H NMR of G1 dendron



Deprotection of G1 Dendron:

The G1 dendron was deprotected using 10% w/w of palladium over dry carbon in a 1:5 ratio of DCM to methanol. It was stirred vigorously for over 24 hours under 10 atm of H_2 gas using a pressurized chamber informally known as “the Swedish soccer ball technique.”

Plans for the Future:

The second and third generations will be synthesized in a DCM or THF solvent after methanol is completely removed from the deprotected G1. Those generations should be large enough to purify by precipitating in hexane. They should also be large enough to be characterized by MALDI TOF. The G2’s kinetics will be studied to see the reaction rate of coupling more anhydride to each of the four alcohol groups. We know sterics will prevent the third and fourth groups from coupling as quickly, but the exact reaction rate has not been determined. The G3 dendron has the exact weight of a control sample of hyperbranched polymer prepared in our labs, so the reaction rate of coupling anhydride or another functional group will also be compared.

Acknowledgements:

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