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MacMillan-Type Reactions Using PAMAM Dendrimer Bound Catalysts

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Introduction

Abstract

Organocatalysts are a eco-friendly alternative to traditional catalysts, however they present challenges with their size, cost and efficiency. Dendrimers are hyper-branched macromolecules that are an attractive prospect for use as scaffolds for organocatalysts to overcome these problems. MacMillan-type asymmetric reactions would be a possible application of PAMAM dendrimer-bound catalysts in the hopes of increased recovery of product and recyclability of the organocatalyst. Terminal sites of generation 4 PAMAM dendrimers were functionalized with the MacMillan group's (2S,5S)-5-benzyl-2-tert-butyl-3-methyl- imidazolidin-4-one catalyst. These PAMAM dendrimer-bound catalysts show promising yield, enantioselectivity, and recoverability in MacMillan-type organocatalytic reactions.

PAMAM Dendrimers

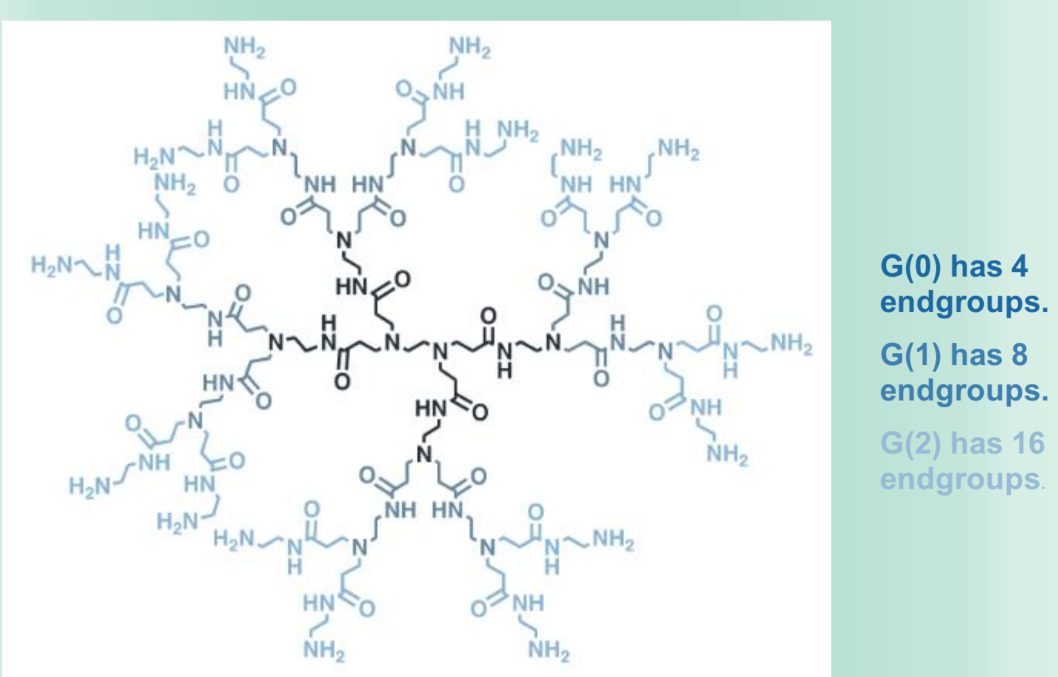


Figure 1: G(2) PAMAM Dendrimer

Polyamidoamine Dendrimers are convenient due to their ethylenediamine core and terminal amine groups[2]
G(4) PAMAM Dendrimers were utilized in this project
These have 64 endgroups with a total molecular weight of 14,215 amu

Catalyst Synthesis

Figure 2: Synthesis Scheme for Organocatalyst

- Synthesis completed by previous group members in this project
- Structure confirmed via NMR and MADLI-TOF MS
- Steps 1 and 2 were made 'greener' through DMSO as a solvent rather than DMF
- Resubmission of Step 3 was necessary before the catalyst was ready for use in synthesis
- Closing of ring in Step 3 was confirmed via NMR
- The total molecular weight of the catalyst is approximately 25000 amu.

Methods

Diels-Alder Screening Reaction

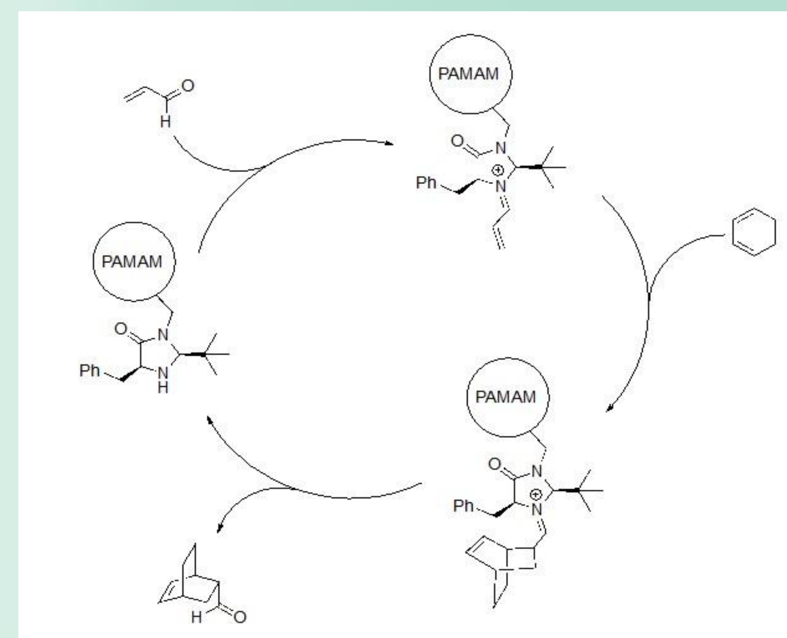


Figure 3: Diels-Alder Screening Reaction from MacMillan[1]

Catalyst Recovery

- Sephadex G50 Column
- 20/80 EtOH/H2O Solvent
- 30 0.25 mL Fractions collected
- Fractions dried on SpeedVac
- UV and NMR verification

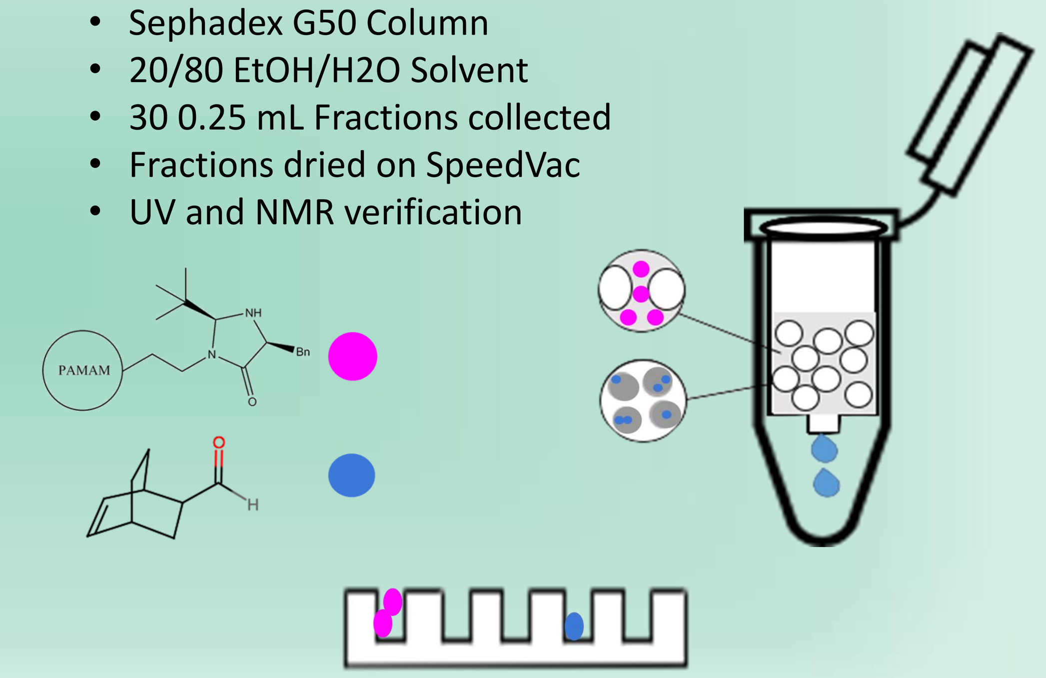


Figure 4: Recovery Apparatus

Results

Crude Reaction Yield

Table 1: Screening Reaction Analysis

Reaction Length	Average % Conversion
24hr	25
48hr	51
72hr	85
MacMillan @48hr	---
MacMillan @56hr	41

$$\frac{\int aldehyde}{\int aldehyde + (\int cyclohexadiene/2)}$$

Percent Conversion to product was determined through NMR peak integral ratios
Product identification was verified through NMR peaks

Separation of Catalyst

Table 2: Catalyst Recovery Analysis

Fractions	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Catalyst	-	-	-	C	C	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Product	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P

Use of SEC to recover the catalyst from product was extremely successful.
The catalyst repeatedly appeared within two small fractions widely separated from the product.

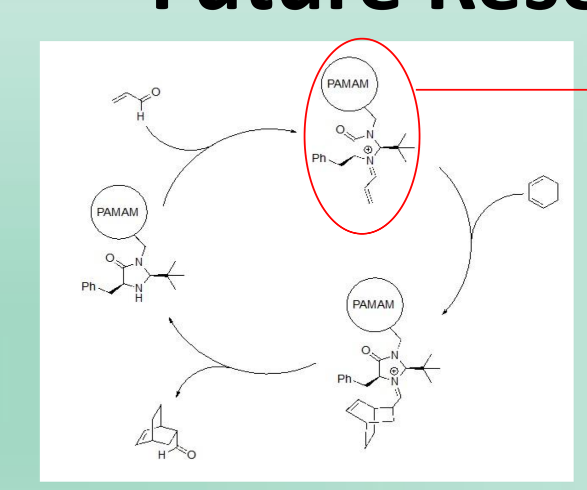
Recycling of the Catalyst

Only one trial of catalyst recycling was conducted thus far. It displayed successful production of product but analysis of exact yields is in progress.

Conclusions

- Synthesis of new PAMAM bound catalysts with G2,G3, and G4 PAMAM dendrimers was completed by earlier group members on this project.
- G4 PAMAM bound catalyst was utilized in the Diels-Alder reaction outlined by MacMillan.
- The dendrimer bound catalyst has shown higher yields than MacMillan's small molecule catalyst.
- Successful separation through SEC methods was achieved for the G4 PAMAM bound catalyst from the crude reactions.
- This recovered catalyst was successfully utilized to catalyze an additional Diels-Alder reaction.
- Further in-depth analysis of this recycled catalyst's efficiency is in progress.
- Replication of the recycling of this catalyst is the goal of this project, which will lead us to the analysis of its efficiency.

Future Research



Cyclohexadiene is the limiting reagent, therefore the catalyst stops at this phase in the catalytic cycle. This adds mass to the catalyst, making recovery calculations difficult.

Figure 5: Catalytic Cycle

- Replication of the Diels-Alder screening reaction to get a more accurate average percent product yield.
- Subjection of the catalyst to several cycles of reactions to produce a catalytic efficiency curve.
- Additional Screening Reaction; "One Pot" Cascade Synthesis developed by MacMillan where a single catalyst promotes sequential transformations.

Summary

- An eco-friendly organocatalyst, designed from MacMillan's original, was synthesized and characterized successfully in years past on this project.
- This new catalyst was used in a Diels-Alder Reaction to test it's efficiency. The new catalyst displayed much higher product yield than MacMillan's original.
- The catalyst was then successfully separated from the crude reaction via SEC methods.
- This recovered catalyst was then successfully recycled into a new reaction. However, full analysis of these results are still in progress and replication is necessary.

References

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