OLD DOMINION UNIVERSITY
IDEA FUSION

Design, Synthesis and Characterization of Glycolipids and Glycoclusters as Molecular Gelators

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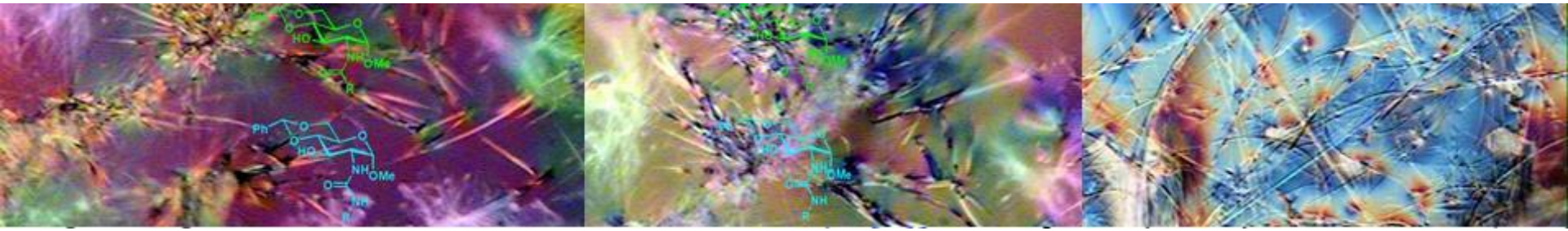
What are Molecular Gelators?

Glycolipids and Other Carbohydrate Based Self-Assembling Systems

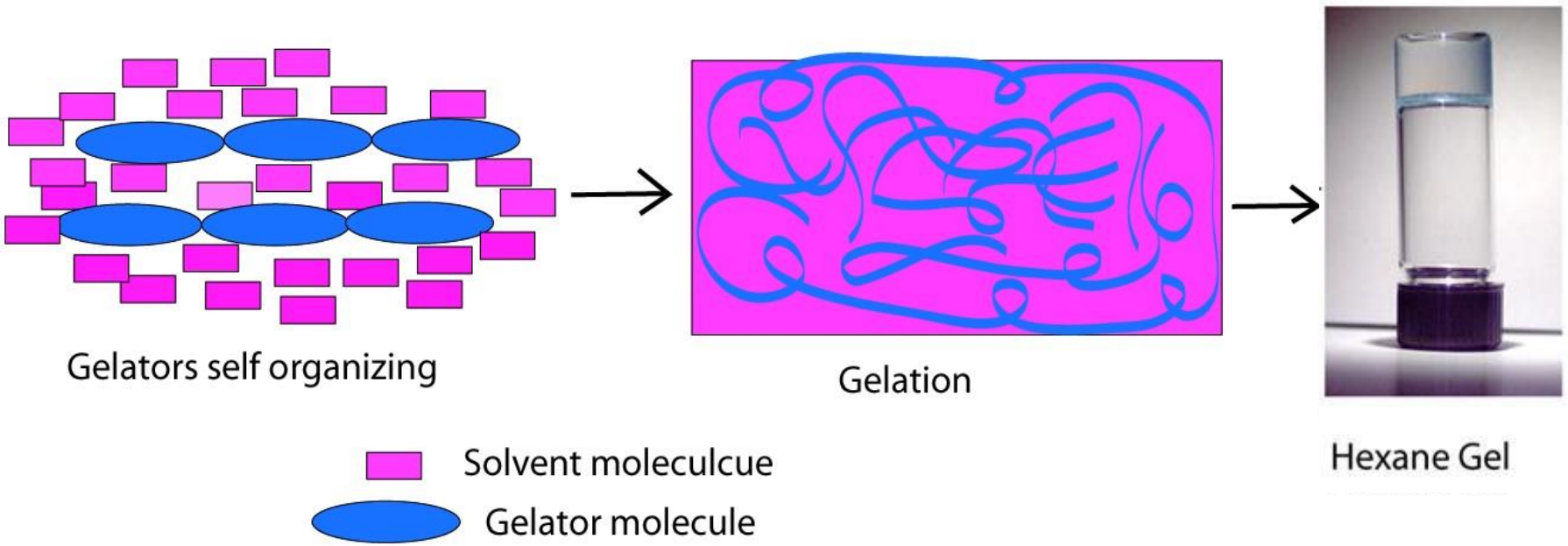
- D-Glucose based molecular gelators
- D-Glucosamine derivatives
- Photo-responsive functional gelators
- Other studies of glycoconjugates

Conclusions and Future Studies



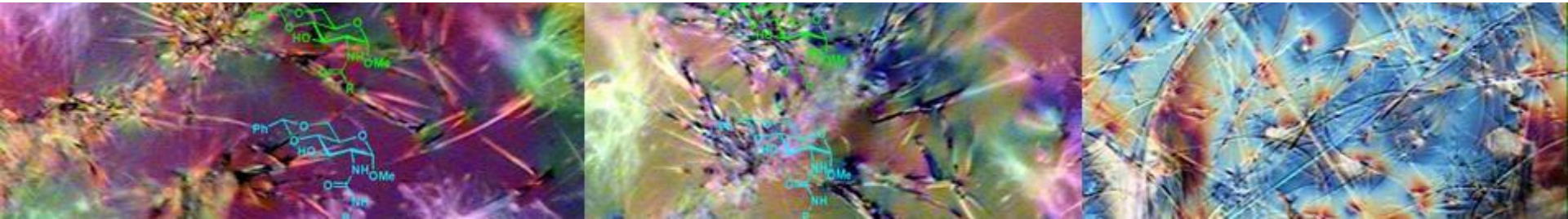
Low Molecular Weight Gelators (LMWGs)

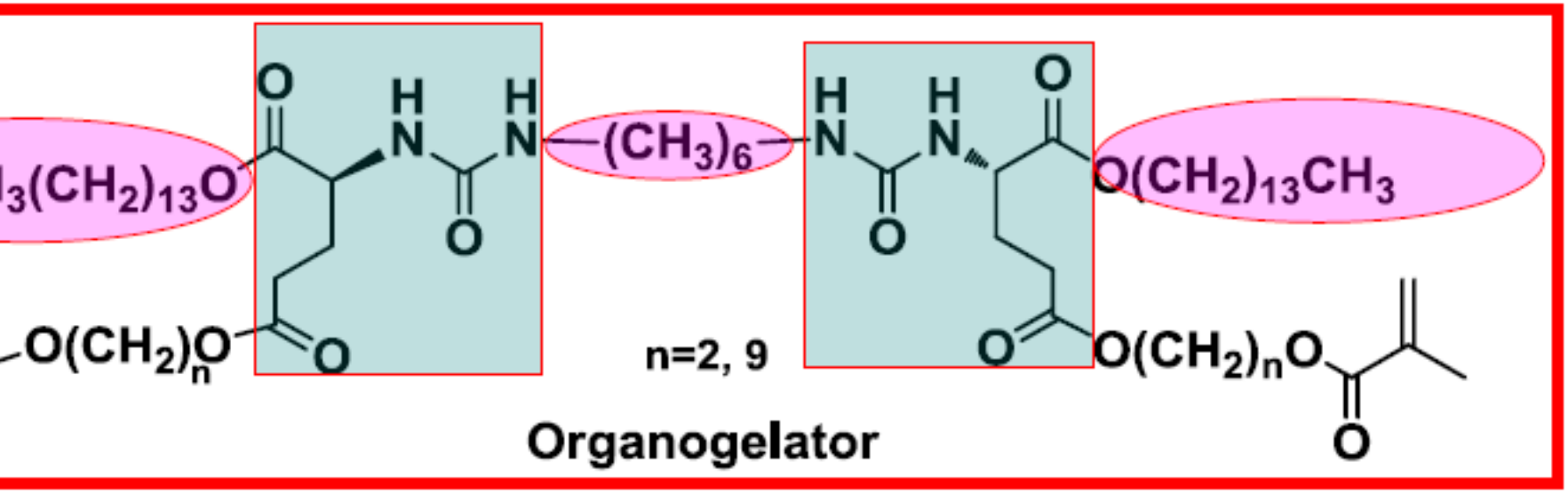
- A class of small molecules that can form gels in organic solvents or water, MW typically <1000.
- The driving forces are non-covalent forces such as hydrogen bonding, π-π stacking and van der Waals interactions.
- Preparations: dissolve compound (gelator) in a solvent, heat and/or sonicate to solution, leave at rt for 15 minutes.



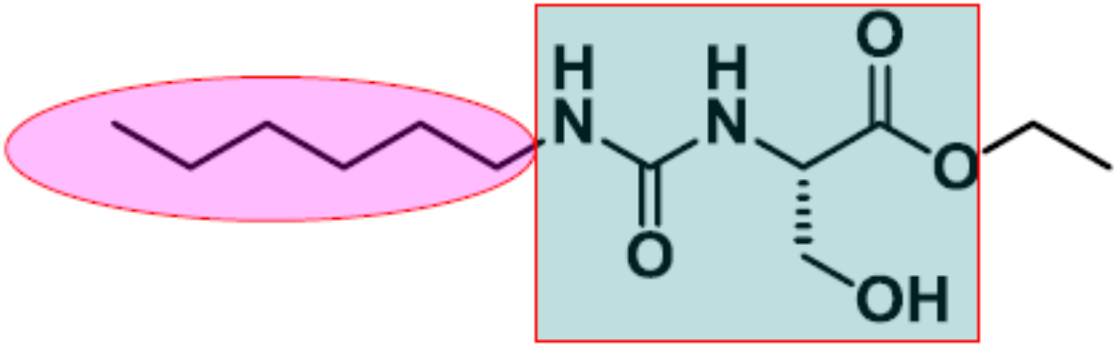
Carbohydrate Based Molecular Gelators

- Gels of biological and natural product origins are materials with potential biomedical applications.
- Hydrogelators can produce scaffolds for tissue engineering, drug delivery carriers, protein immobilization and separation.
- Carbohydrate based hydrogelators have intrinsic chirality, and the hydrogels thus formed are biocompatible and biodegradable



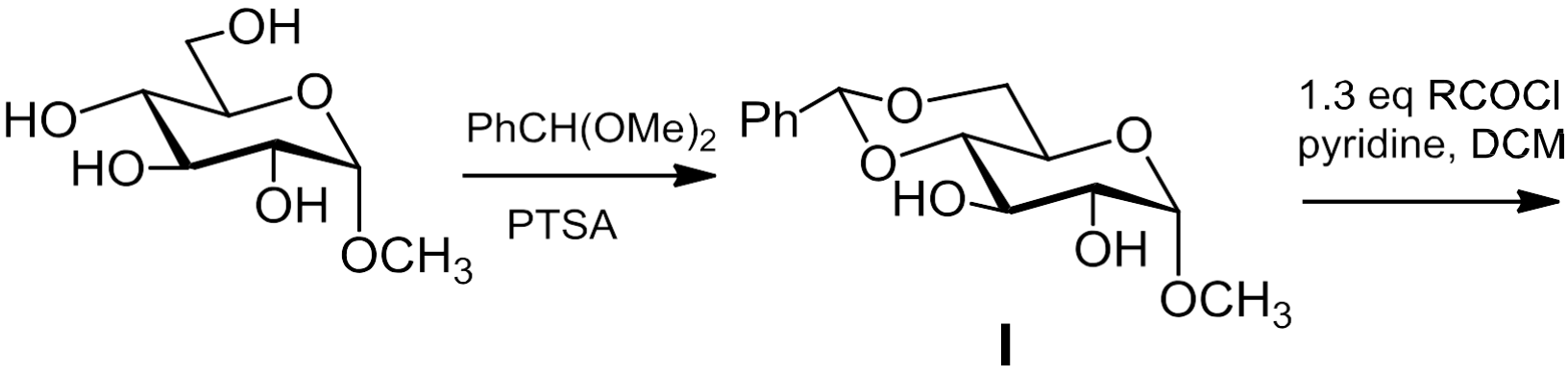


Organogelator

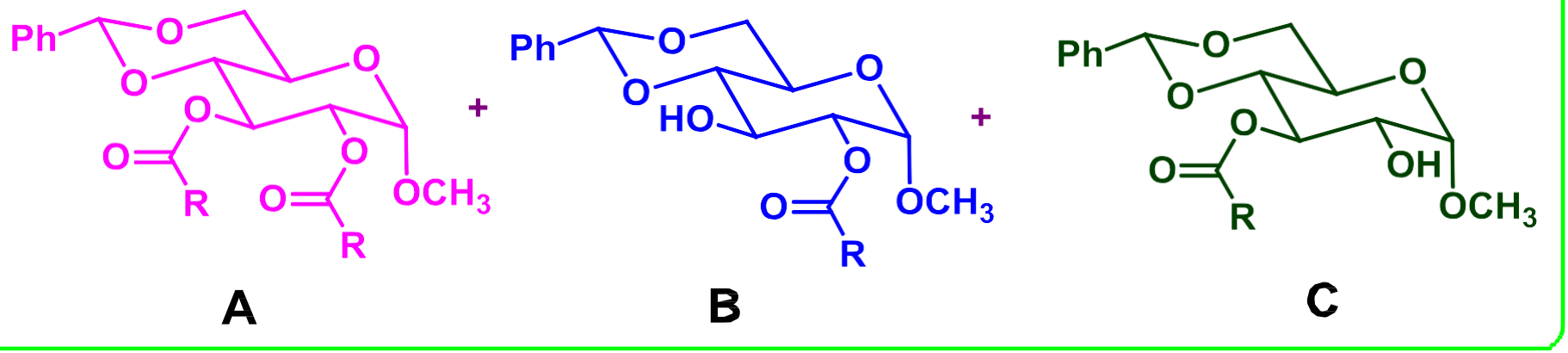


Hydrogelator

1. D-Glucose Based LMWGs: Esters and Carbamates



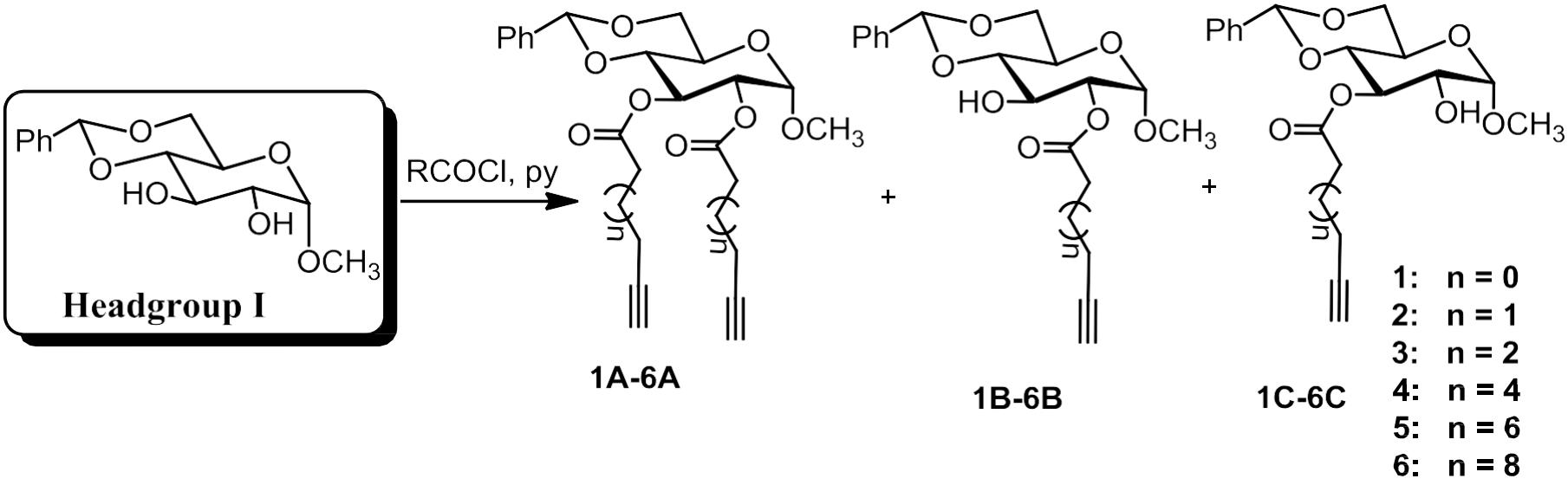
I



A B C

R = alkyl, aryl, total 68 compounds synthesized and tested

D-Glucose Derived Esters as Hydrogelators and Organogelators



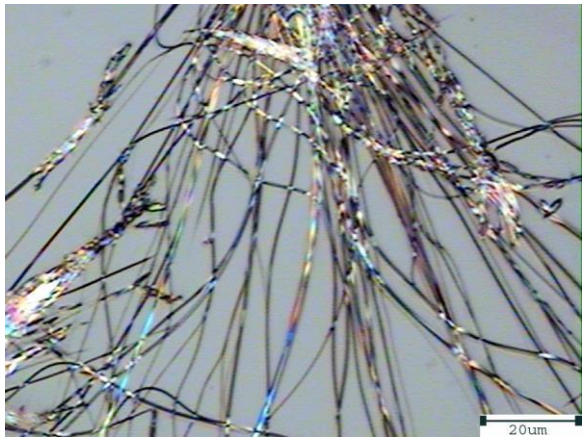
A: form gels in hexane and ethanol

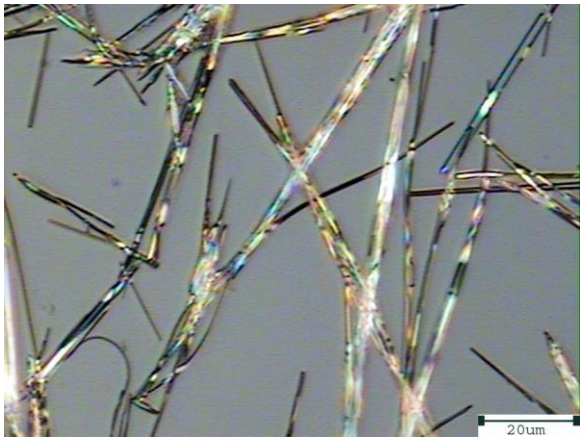
B: form gels in hexane and water

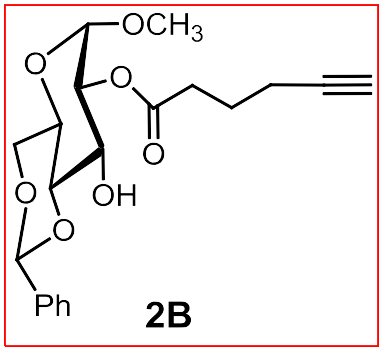
C: form gels in hexane and water

Wang, G.; Sharma, V.; Cheuk, S.; Williams, K.; Dakessian, L.; Thorton, Z. *Carbohydrate Res.* **2006**, *341*, 705-716.

Optical Micrographs of the Gels in Water and Hexane



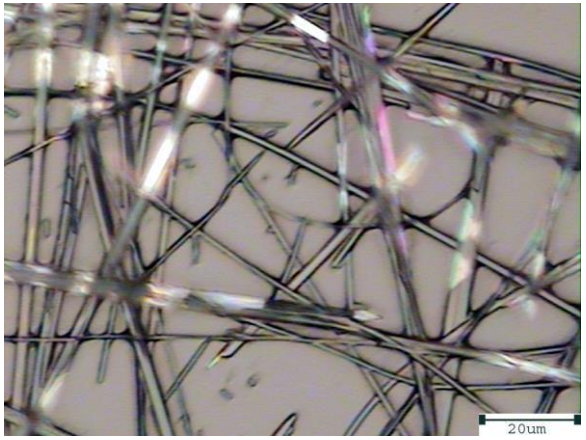


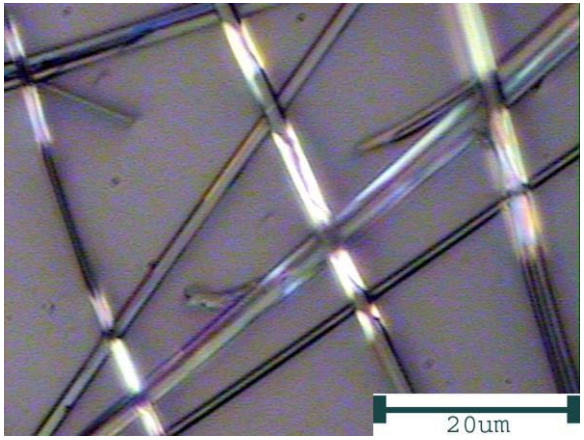


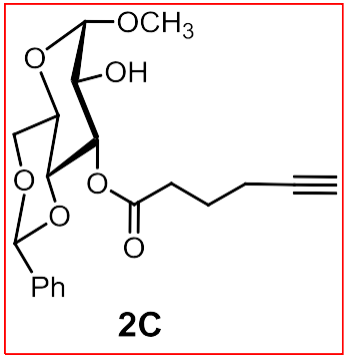
water

2B, 10mg/mL

2C, 10mg/mL







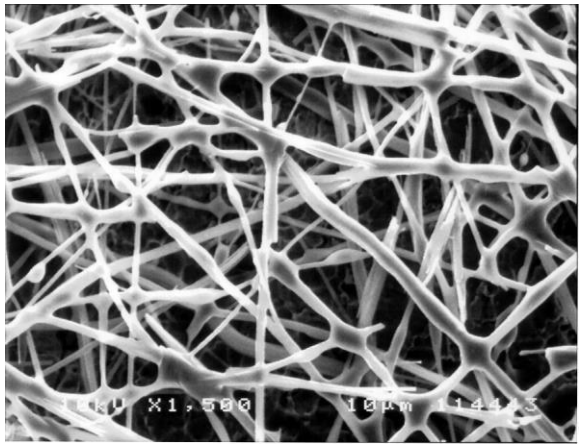
hexane

2C, 5 mg/mL

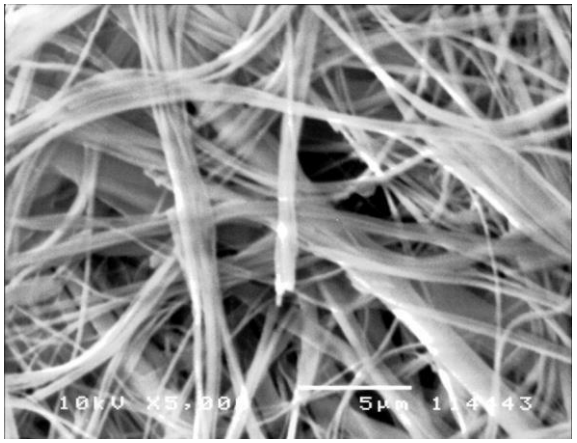
2C, 5 mg/mL

Wang, G.; Sharma, V.; Cheuk, S.; Williams, K.; Dakessian, L.; Thorton, Z. *Carbohydrate Res.* **2006**, *341*, 705-716.

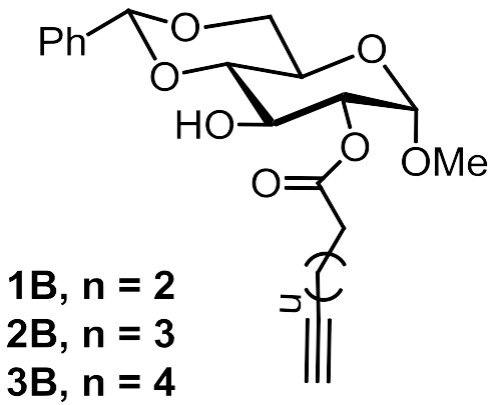
Scanning Electron Micrographs of the Hydrogels.



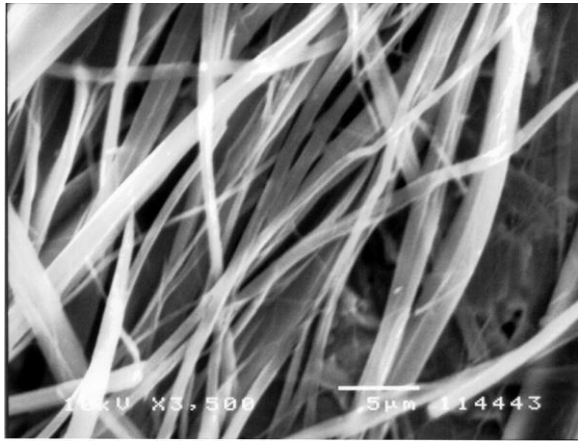
1B 5 mg/mL



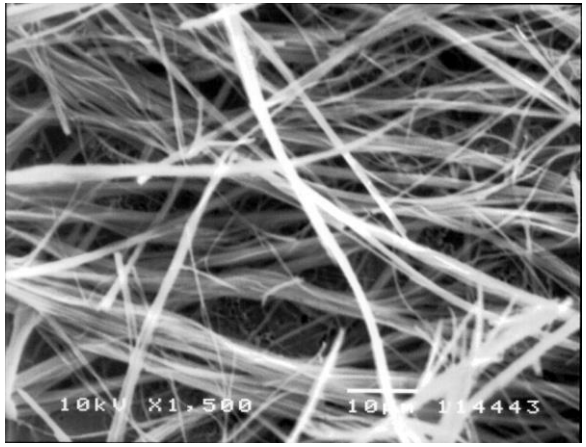
2B 10 mg/mL



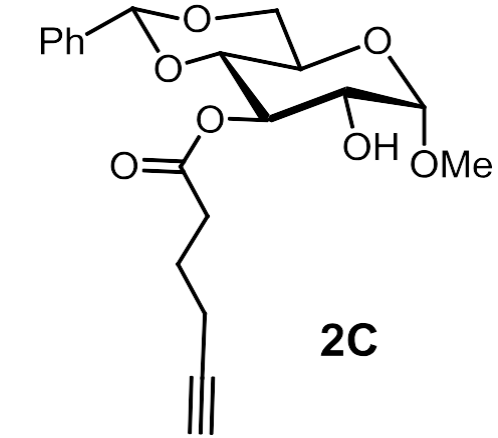
1B, n = 2
2B, n = 3
3B, n = 4



3B 10 mg/mL



2C 10 mg/mL

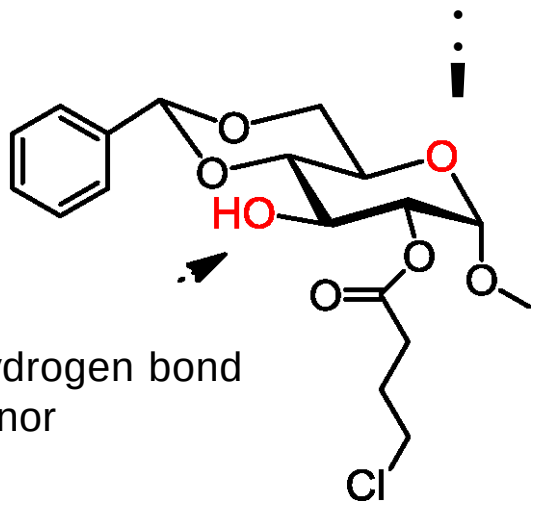


2C

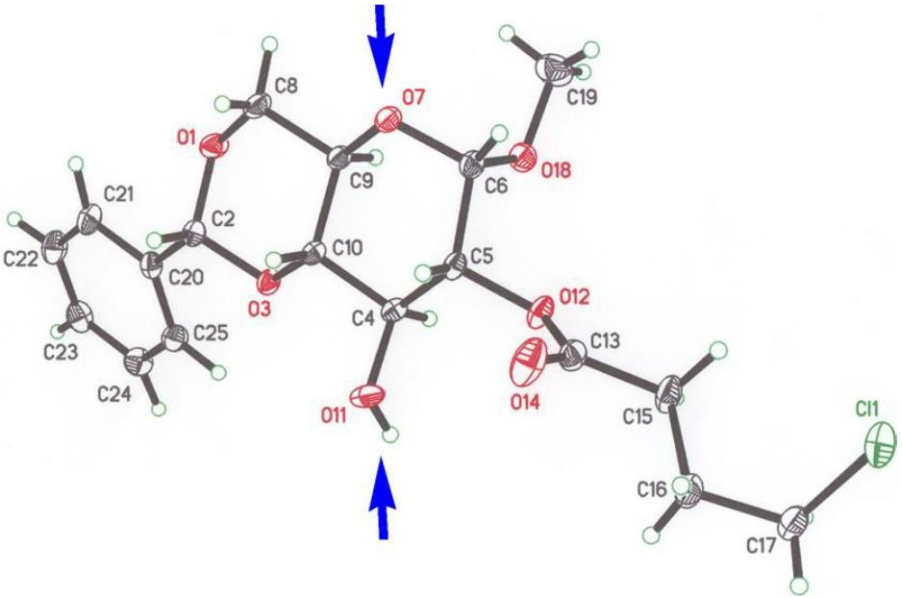
Wang, G.; Sharma, V.; Cheuk, S.; Williams, K.; Dakessian, L.; Thorton, Z. *Carbohydrate Res.* **2006**, *341*, 705-716.

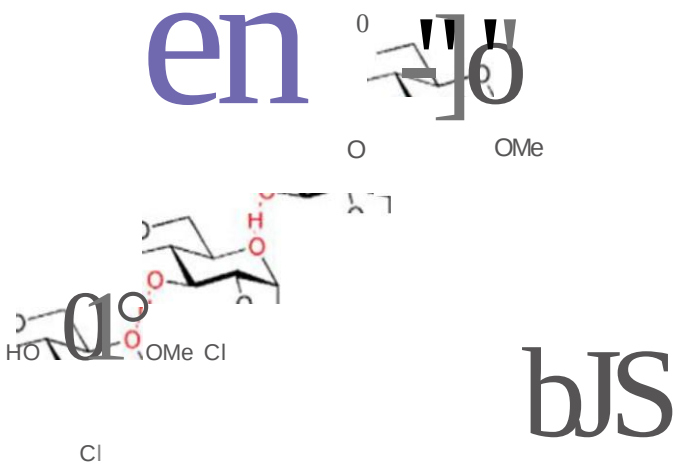
X-Ray Crystal Structure of 4-Chlorobutanoate.

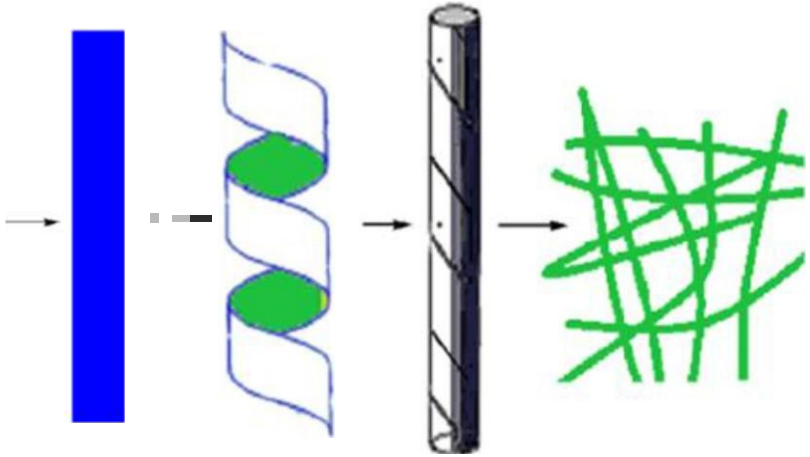
Hydrogen bond acceptor



Hydrogen bond donor

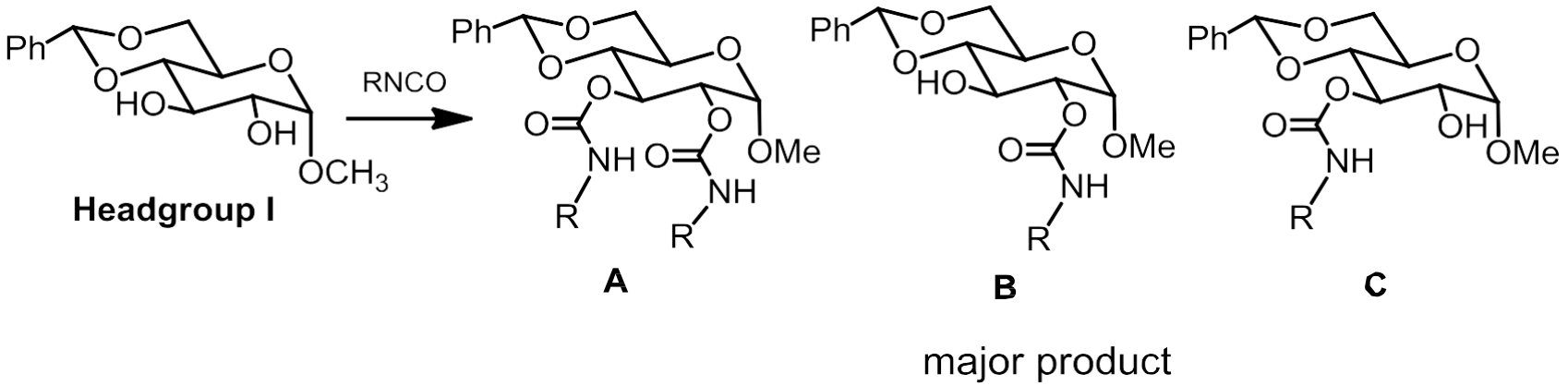




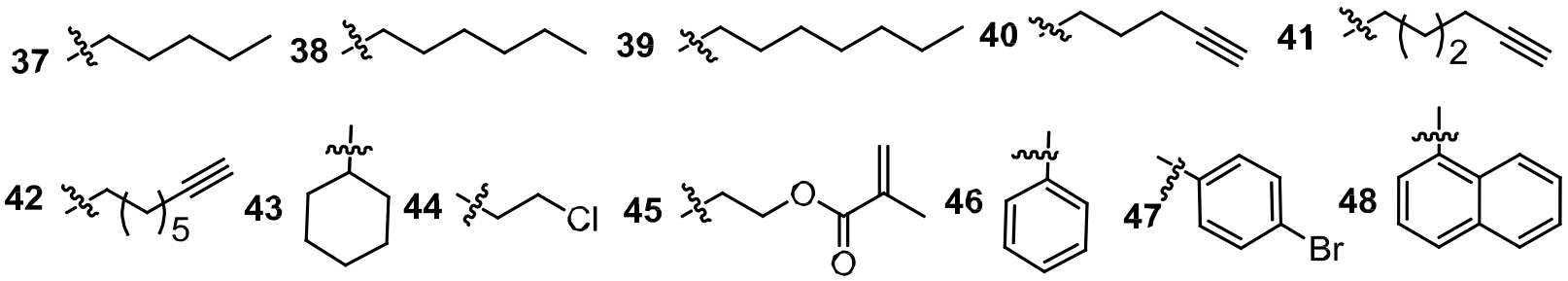


Effect of Additional Hydrogen Bond Donors

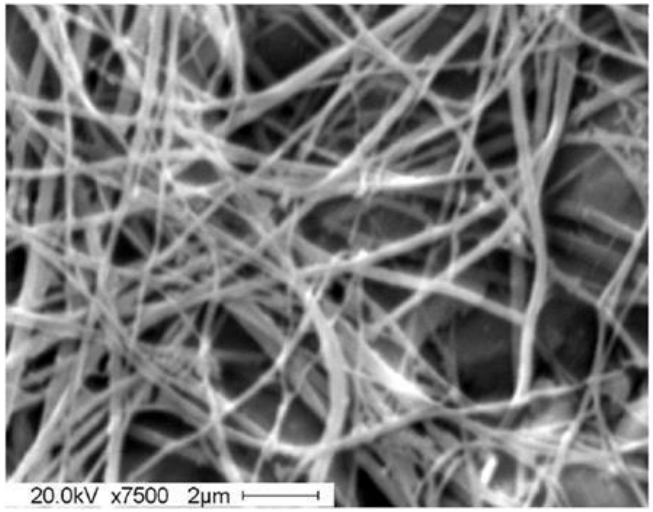
Synthesis of O-Linked Carbamates

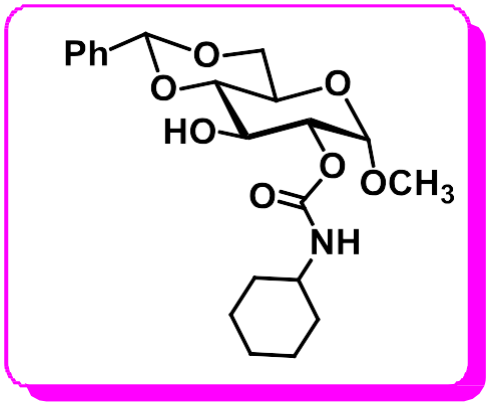


R =

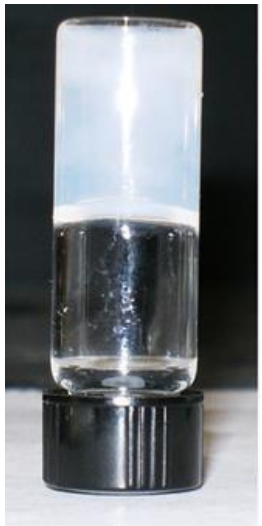


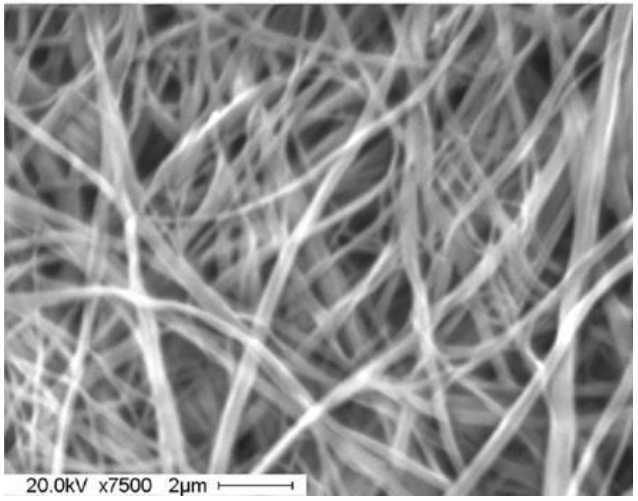
Characterization of Gels Formed by a Carbamate.

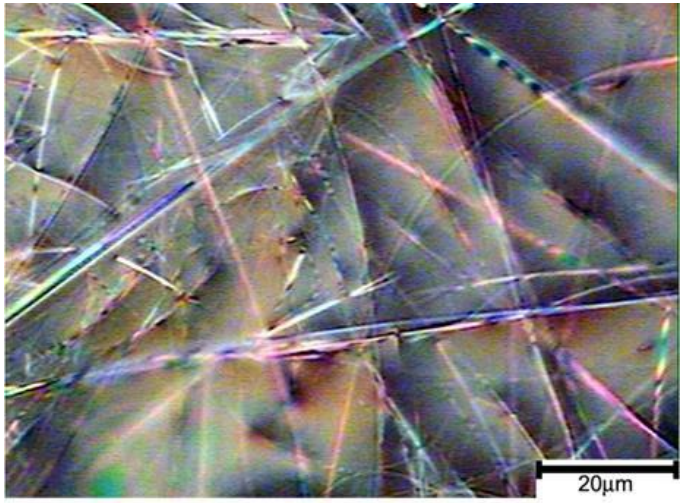




DMSO/H_2O (1:2) at 1.1 mg/mL



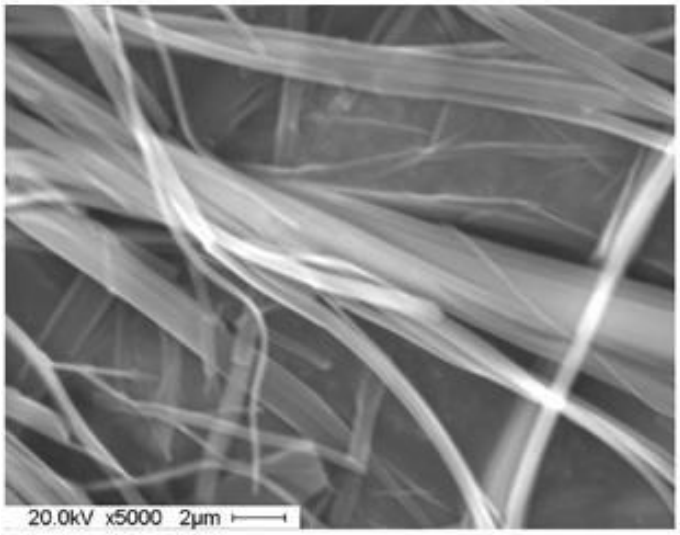


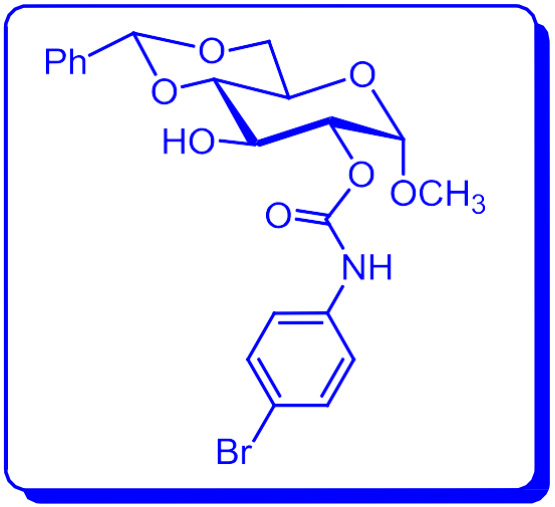


EtOH/H_2O (1:2) at 1.0 mg/mL

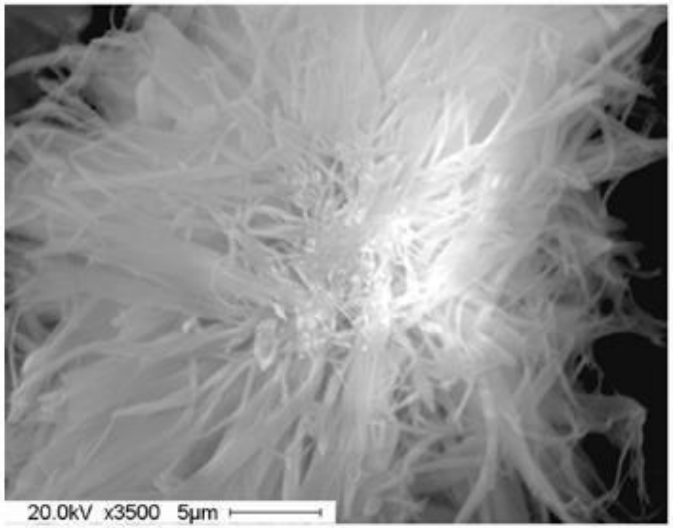
Wang, G.; Cheuk, S.; Yang, H.; Goyal, N.; Reddy, P. V. N. *Langmuir,* **2009**, *25*, 8696-8705.

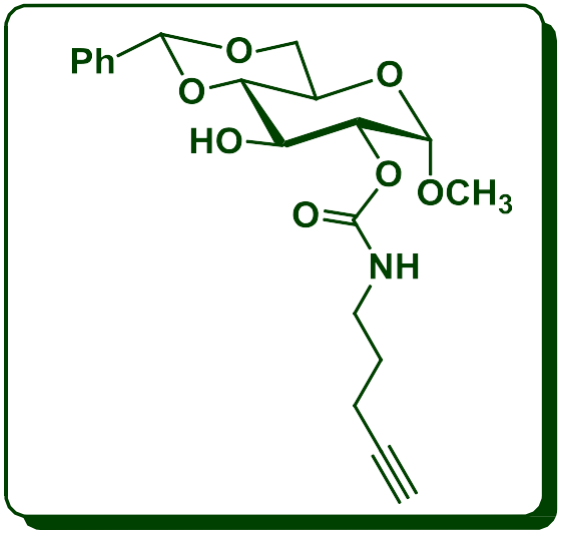
Scanning Electronic Micrographs of O-carbmate Gels





EtOH/H_2O (1:2) at 2 mg/mL

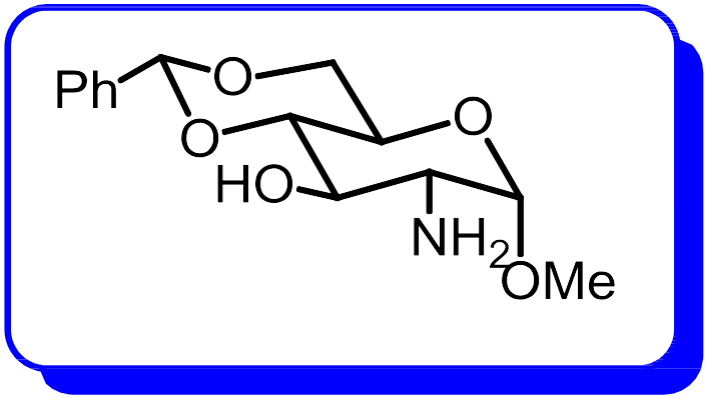




EtOH/H_2O (1:2) at 10 mg/mL

Wang, G.; Cheuk, S.; Yang, H.; Goyal, N.; Reddy, P. V. N. *Langmuir* **2009**, *25*, 8696-8705.

2. D-Glucosamine Derivatives as Low Molecular Weight Gelators

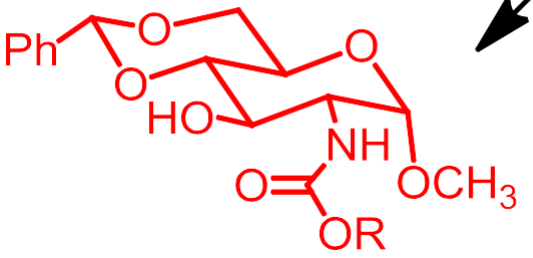


Headgroup II

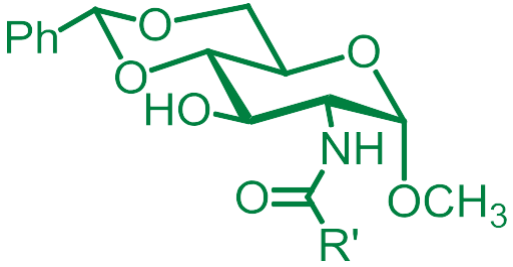
ROCOCl, py

R'COCl, py

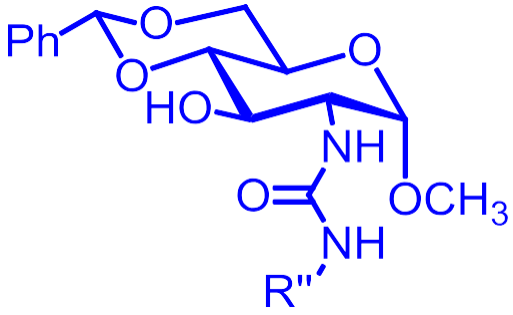
R''NCO



Carbamates

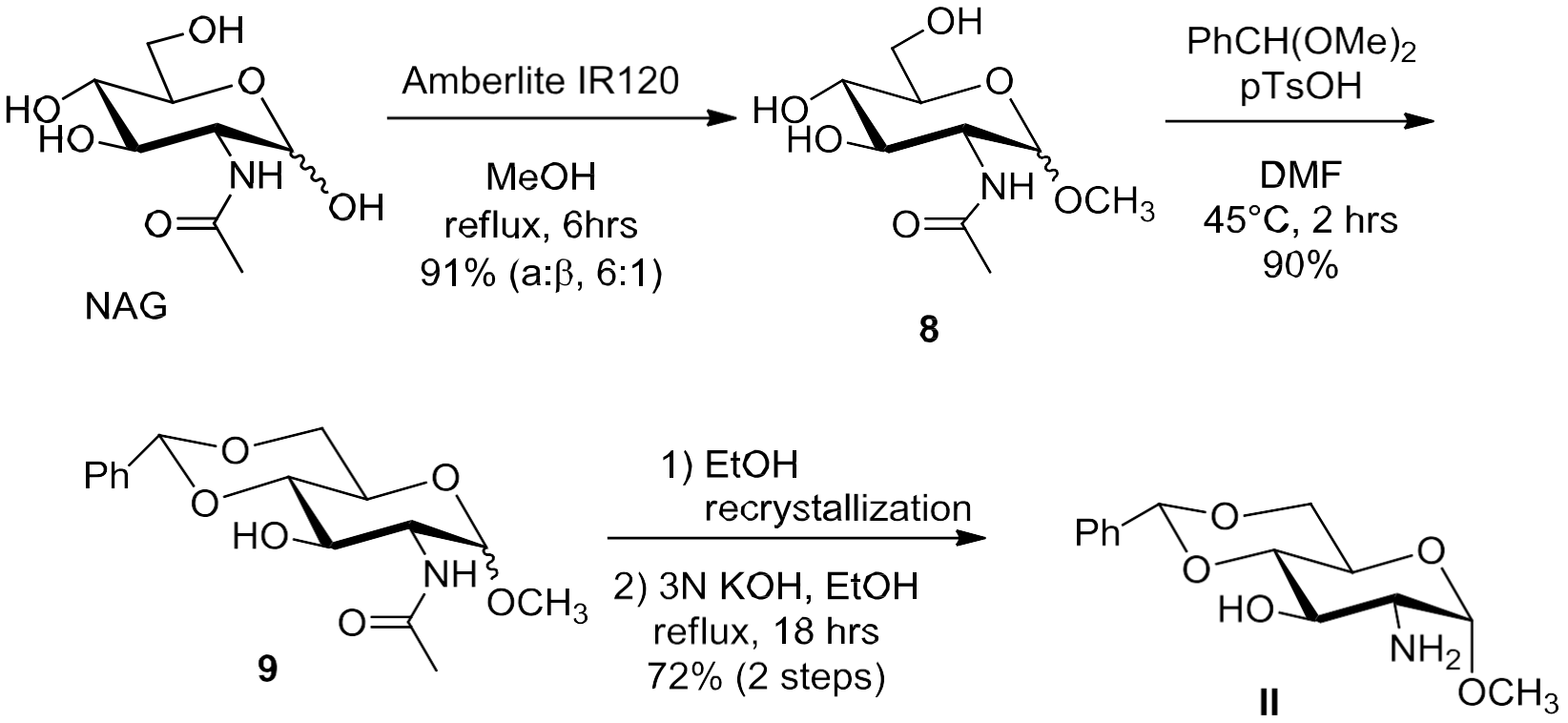


Amldes



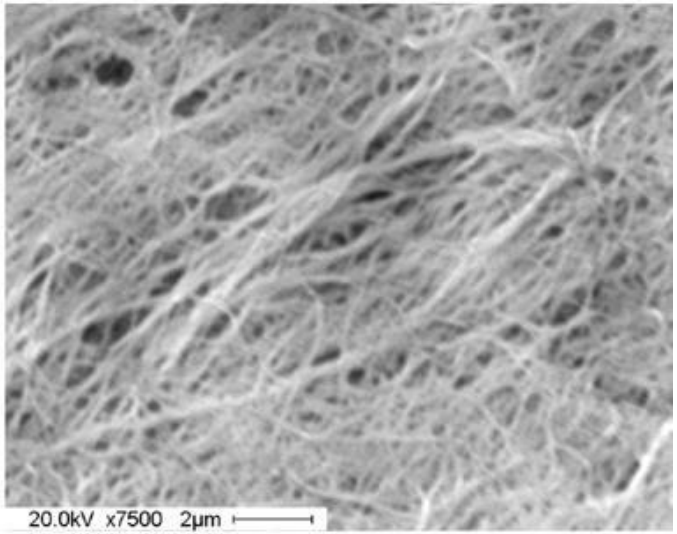
Ureas

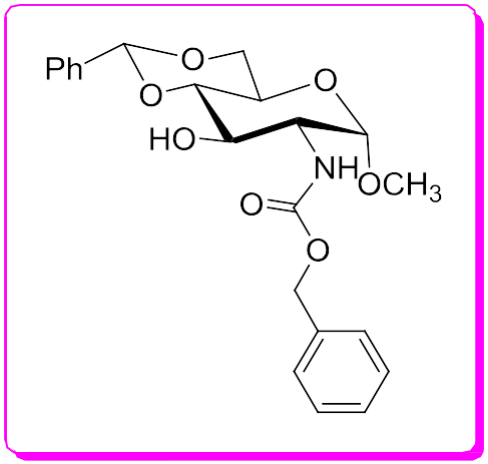
A General Synthesis of Headgroup II



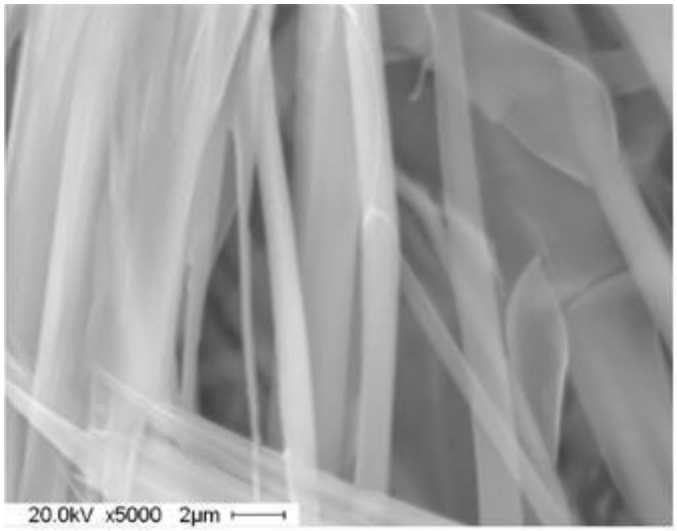
Goyal, N.; Cheuk, S.; Wang, G. *Tetrahedron* **2010**, *66,* 5962-5971.

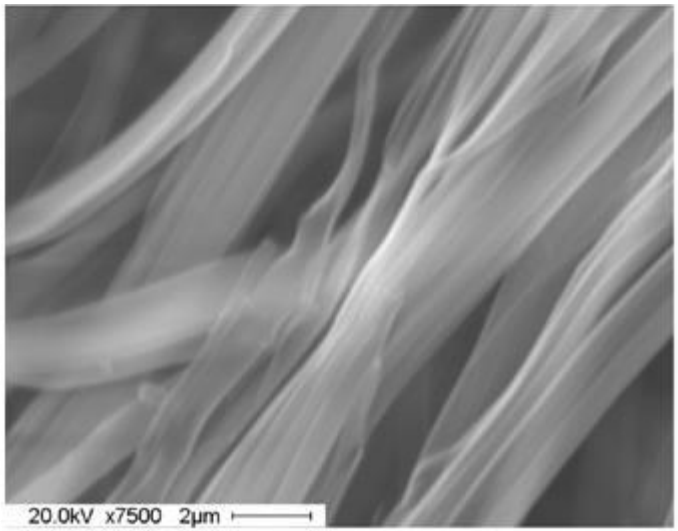
Scanning Electronic Micrographs of N-carbamate Gels

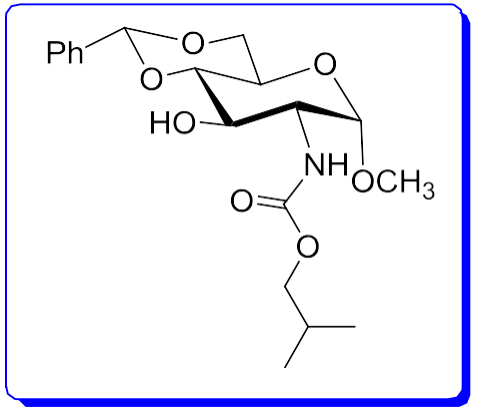




EtOH/H_2O (1:2) at 10 mg/mL



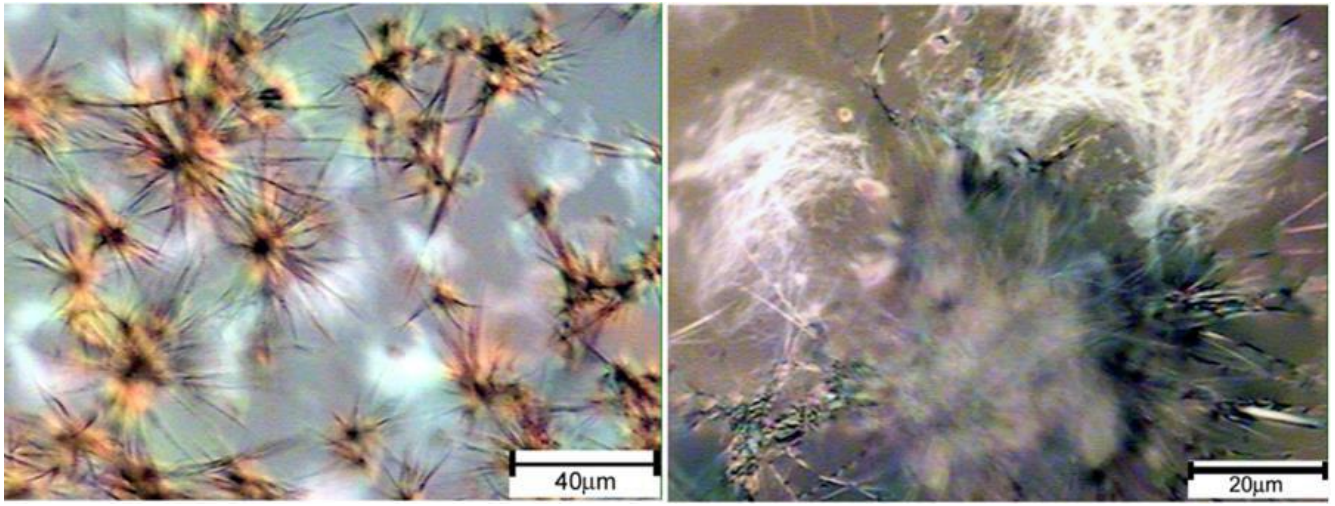




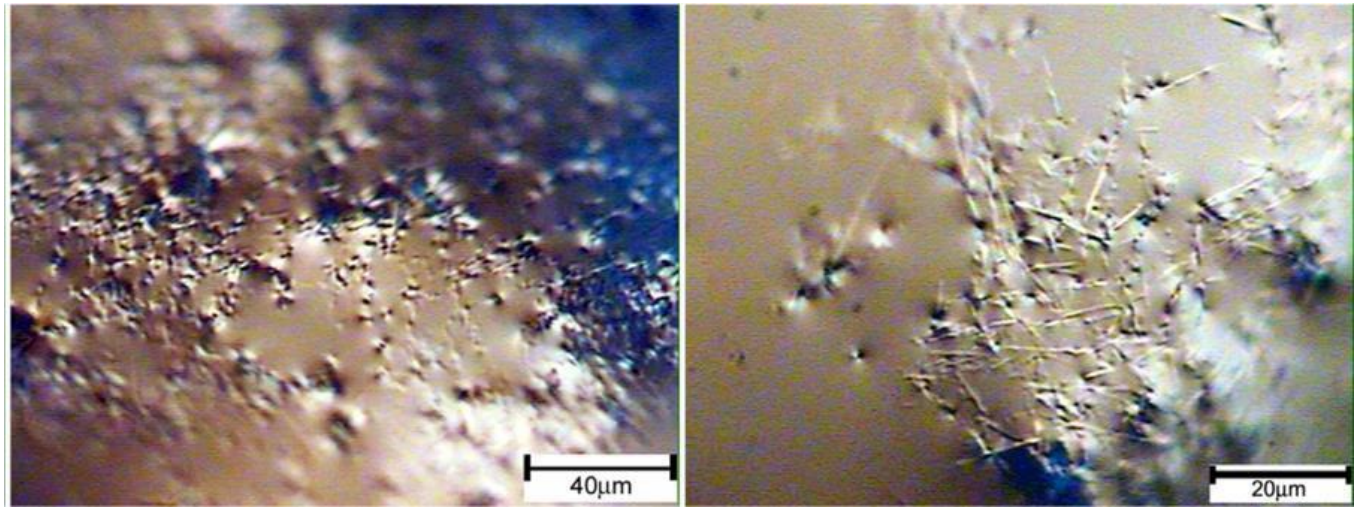
EtOH/H_2O (1:2) at 2.5 mg/mL

H_2O at 4.0 mg/mL

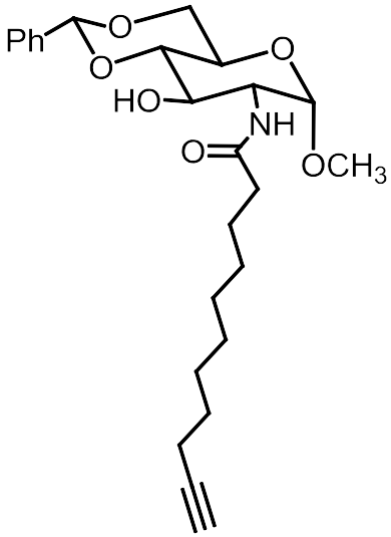
Optical Micrographs of the Gels of an Amide



EtOH/H_2O (1:2) at 3 mg/mL



DMSO/H_2O (1:2) at 2 mg/mL.

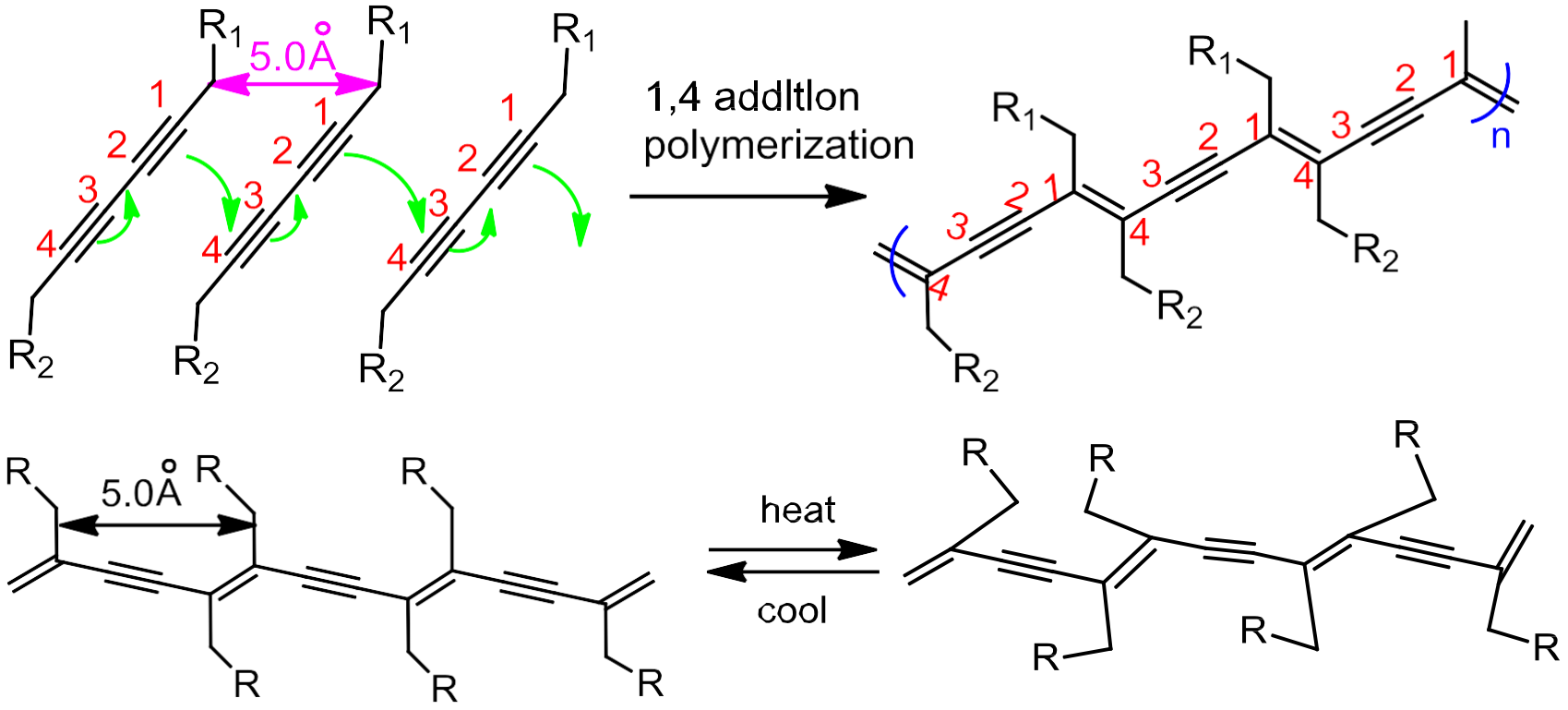


Goyal, N.; Cheuk, S.; Wang, G. *Tetrahedron.* **2010**, *66,* 5962-5971.

3. Diacetylene Containing Polymerizable Systems

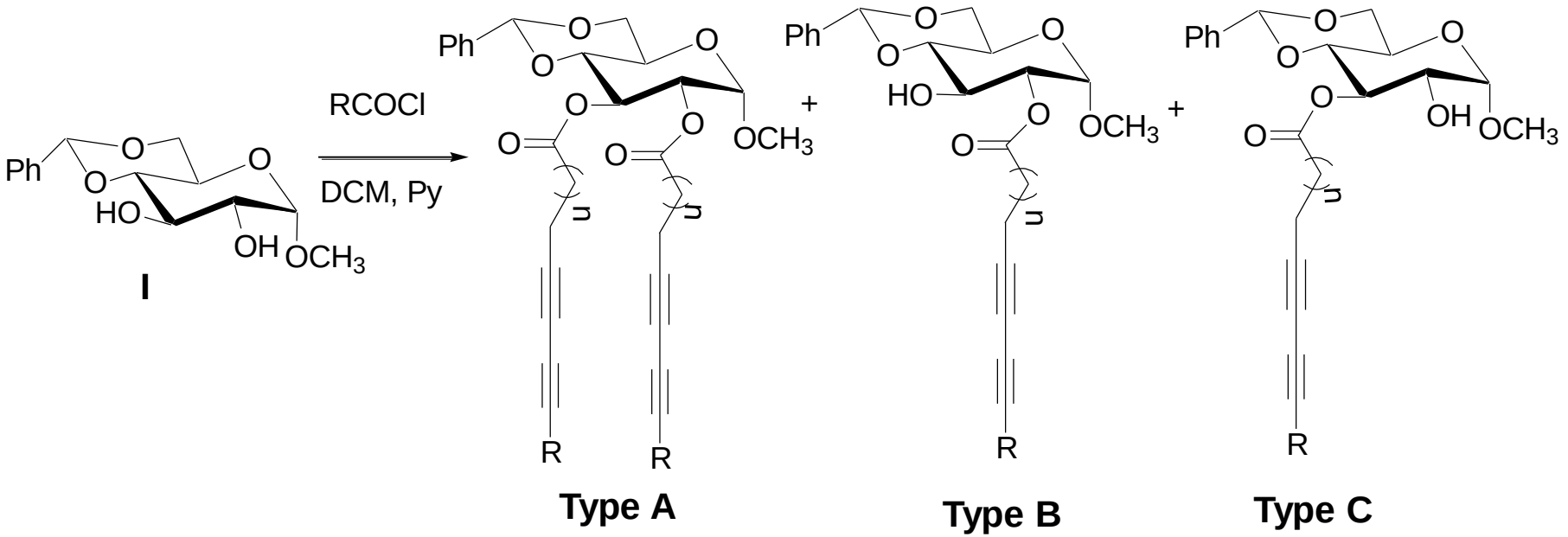
Polydiacetylenes (PDAs) exhibit a unique blue to red color transition in the presence of heat, mechanical stress, pH change and binding to biological agents. PDA containing gels are useful as biosensors or chemosensors.

The topochemical polymerization and the color transition mechanism.



Wang, G.; Hollingsworth, R. I. *Langmuir* **1999**, *15*, 3062-3069.

Synthesis of Diacetylene Containing Lipids Types A-C

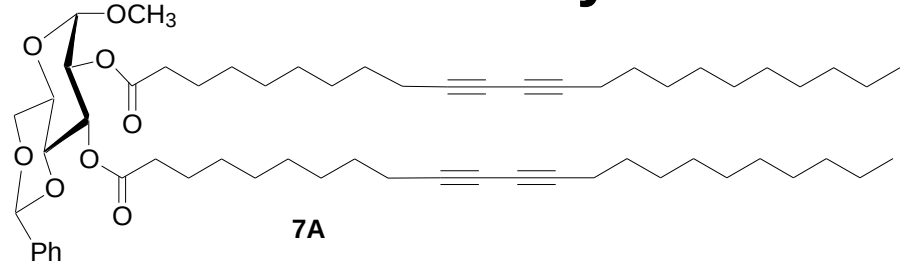


n = 2, 5, 7

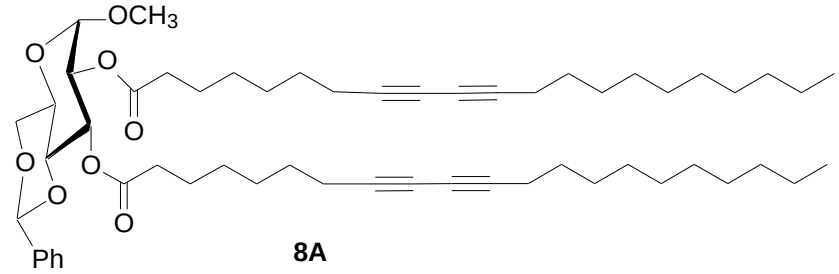
R = H, Ph, Et, CH_2CH_2Ph, $(CH_2)_7CH_3$, $(CH_2)_5CH_3$

Nie, X; Wang, G. *J. Org. Chem.* **2006**, *71,* 4734-4741.

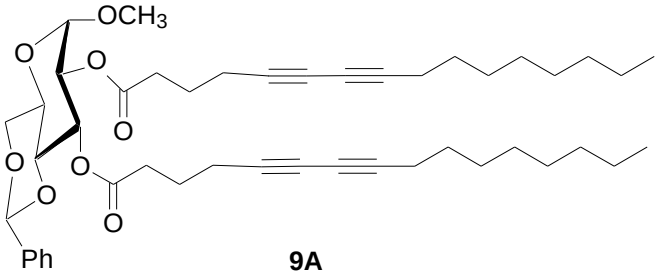
Structures of Diacetylene Compounds Synthesized



7A



8A



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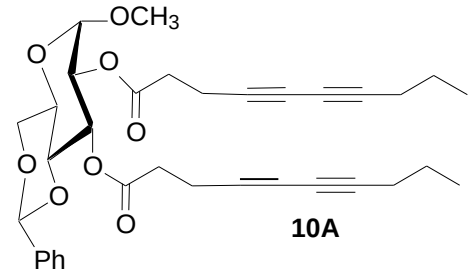

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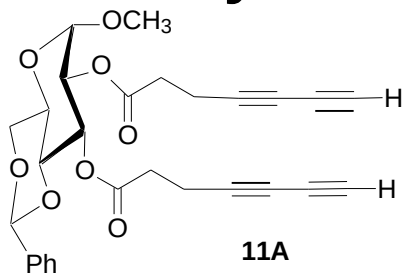

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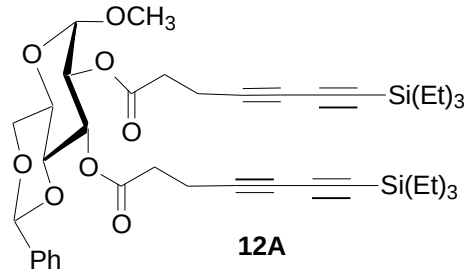

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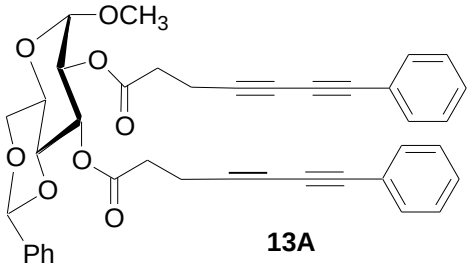

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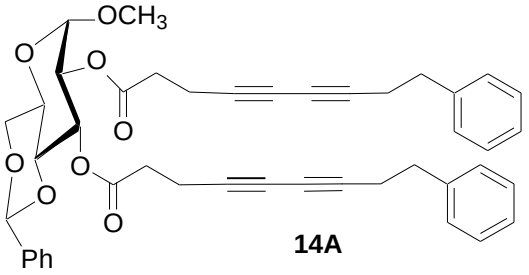
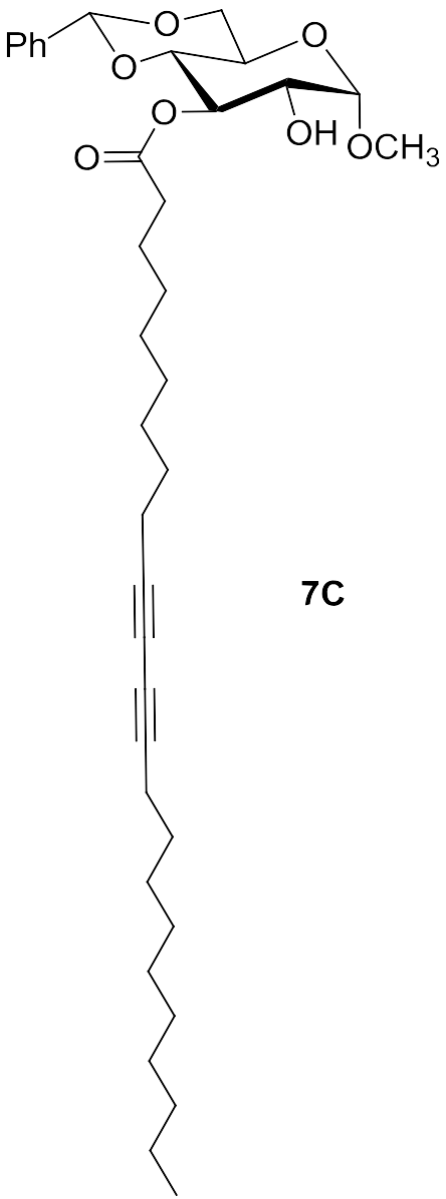


14A

Type B and C are analogs with only one fatty acyl chains

Polymerization of a Gel Formed by Compound 7C.



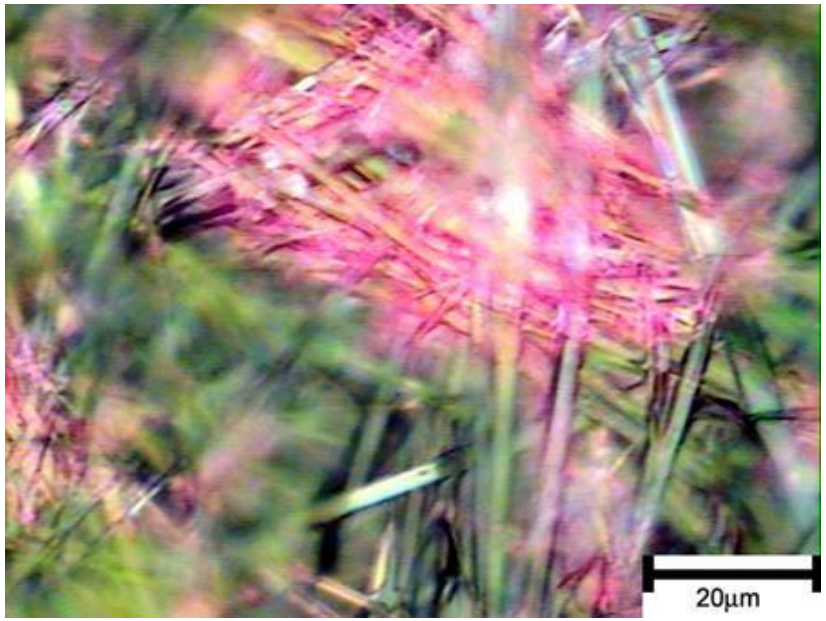
7C

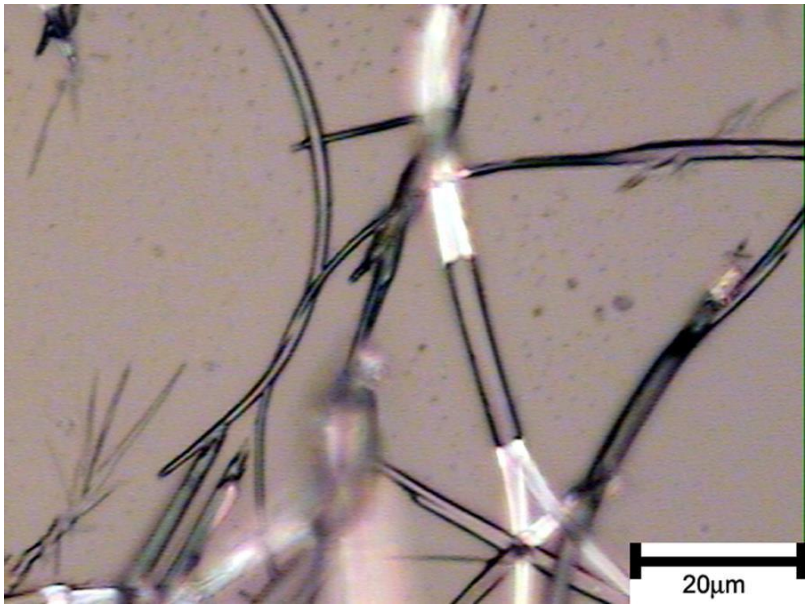
At r.t. **UV 3 min** **Heat <** 70 °C

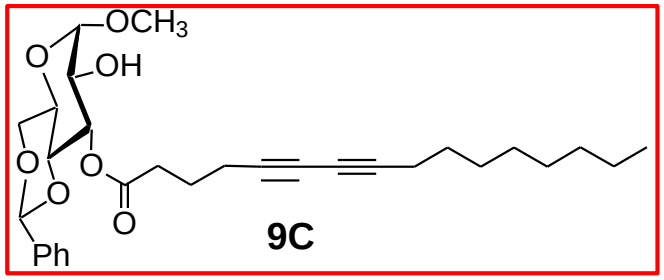
Ethanol 10 mg/mL

Nie, X; Wang, G. *J. Org. Chem.* **2006**, *71,* 4734-4741.

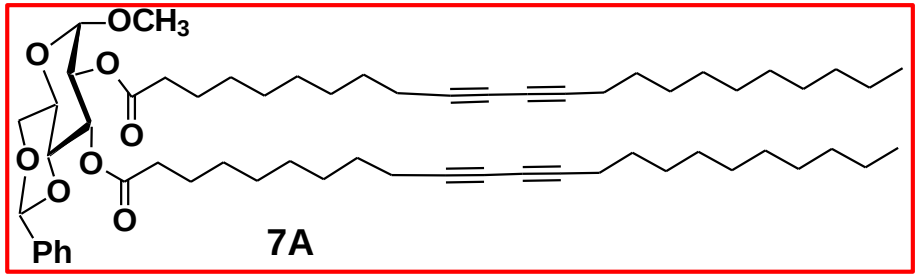
Optical Micrographs of Two Gels







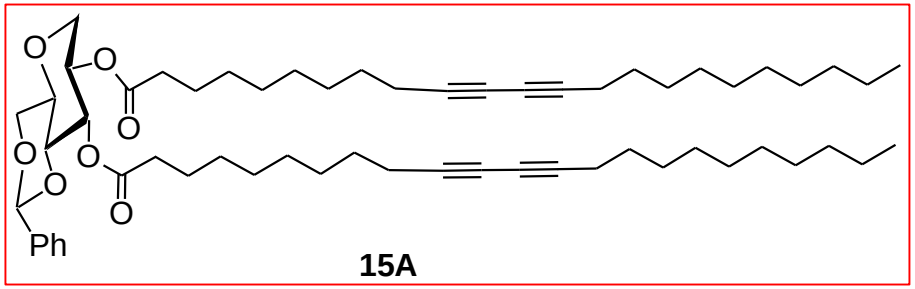
Partially polymerized



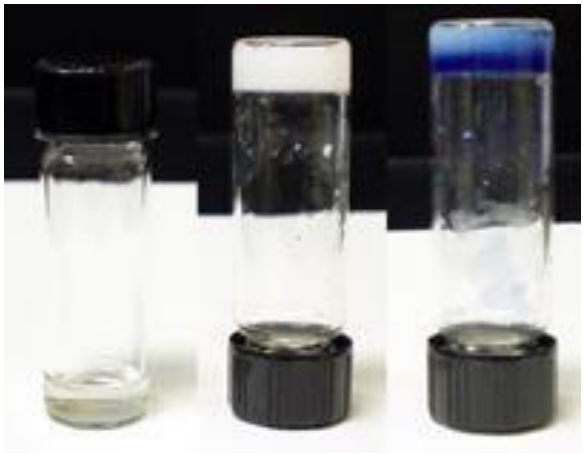
TLC lamp didn't cross link

Nie, X; Wang, G. *J. Org. Chem.* **2006**, *71,* 4734-4741.

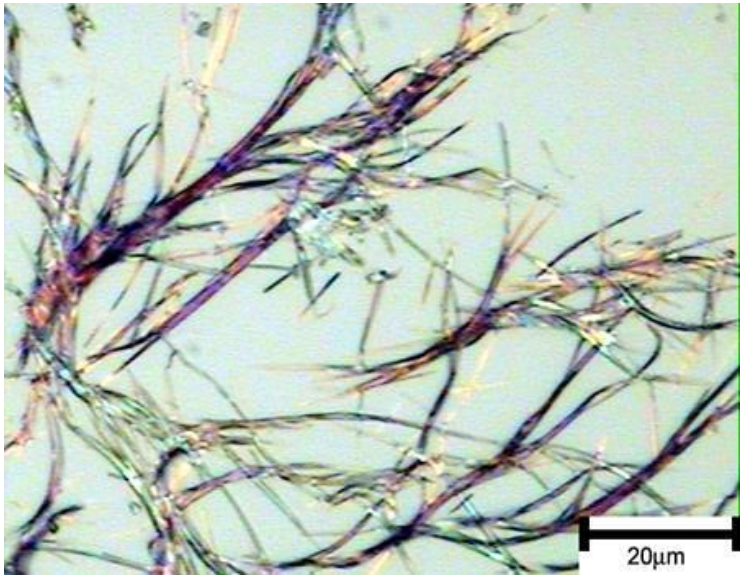
A Deoxy Sugar Diacetylene Lipid



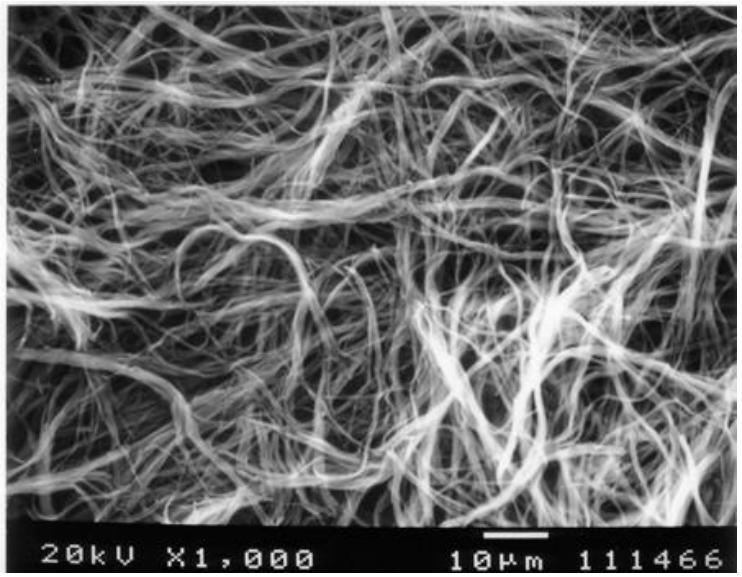
15A



Ethanol gel, 10 mg/mL

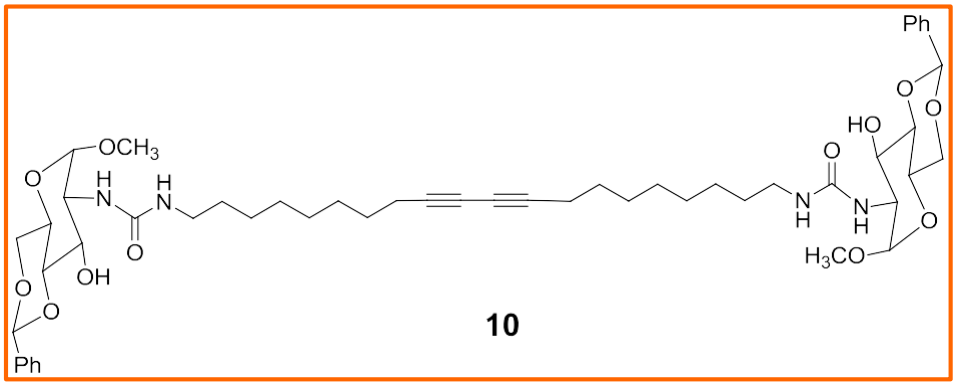


Optical micrograph



Scanning electron micrograph

Wang, G., Hao, Y., Cheuk, S. *Beilstein J. Org. Chem.* **2011**, *7***,** 234-242.



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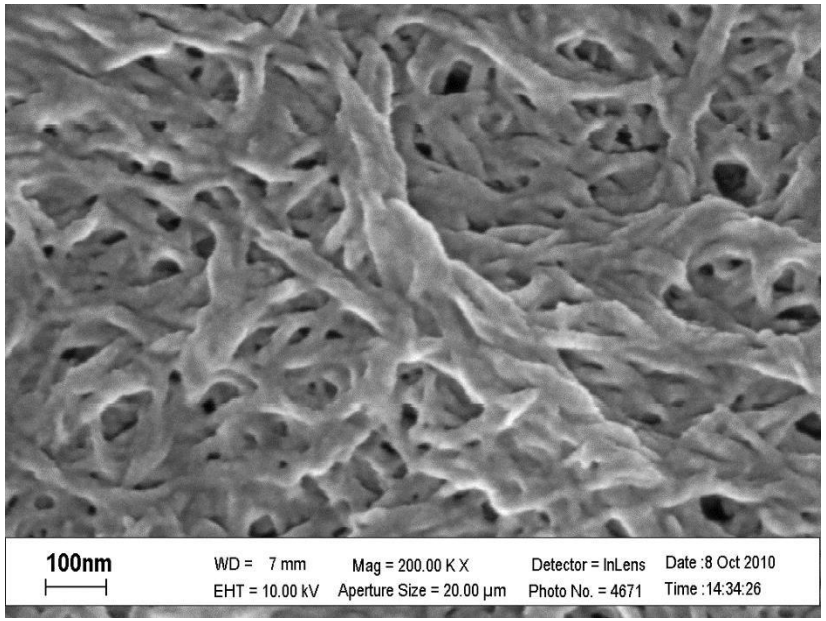
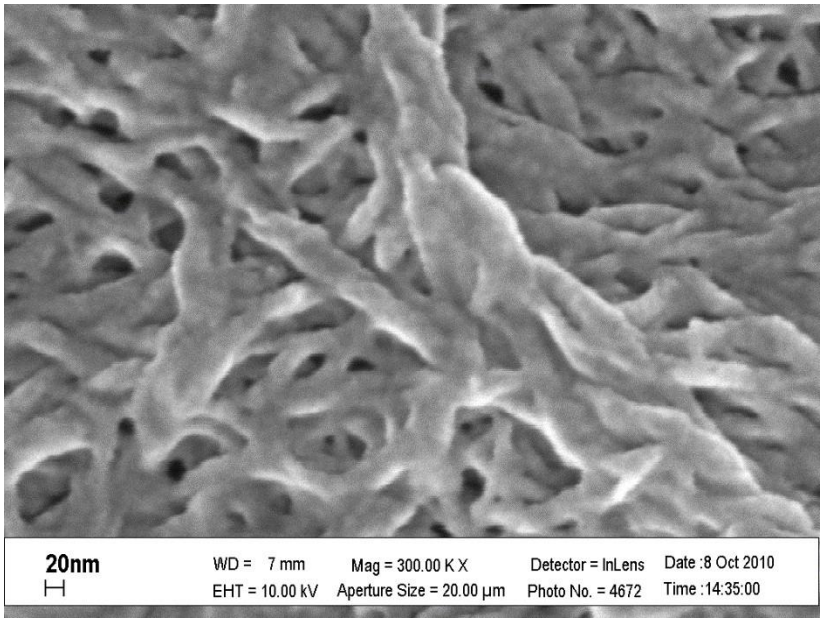




Field Emission SEM of compound 10, ethanol gel 1.2 mg/mL

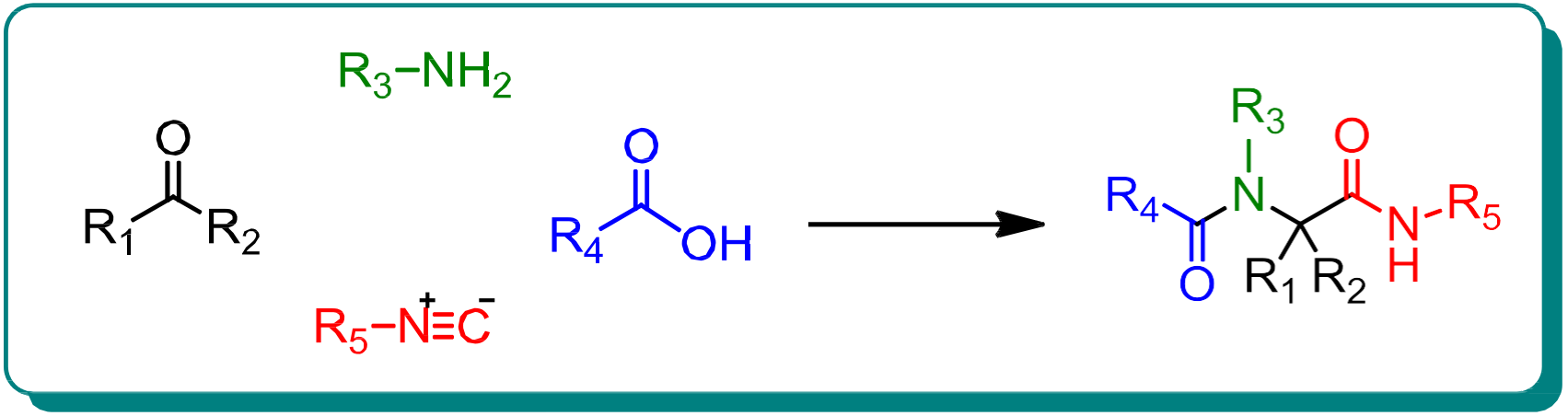
Wang, G.; Goyal, N.; Reddy, P. V. N. *J. Org. Chem.* **2015**, *80*, 733-743.

4. Other Studies of Glycoconjugates

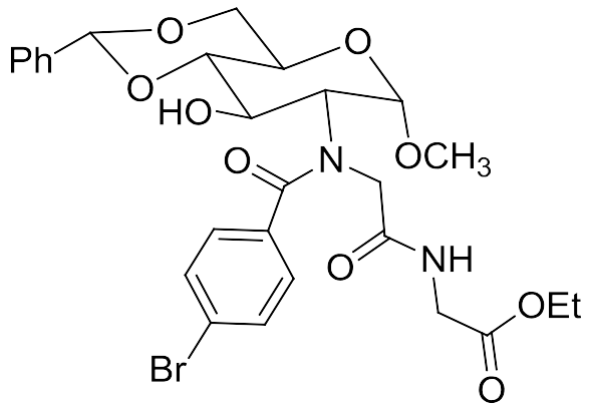
Glycopeptoids Synthesized by Ugi Reaction

Ugi one-pot four component reaction

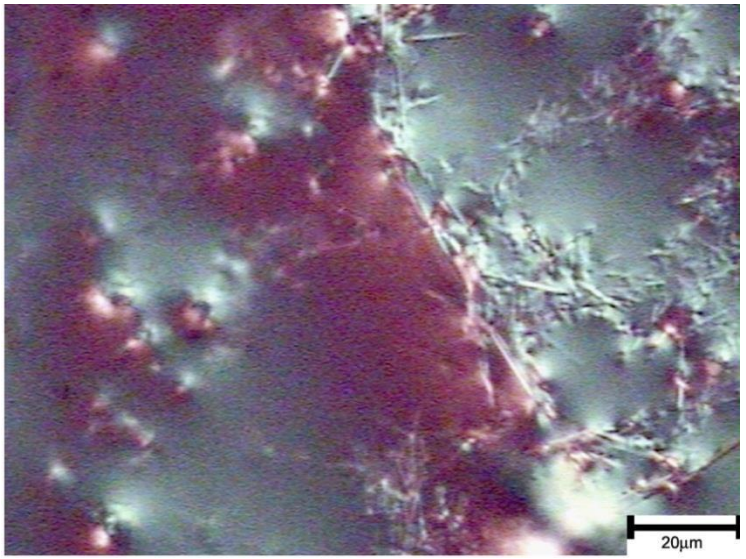
modular approach for structure diversity



Optical Micrographs of DMSO/Water Gels

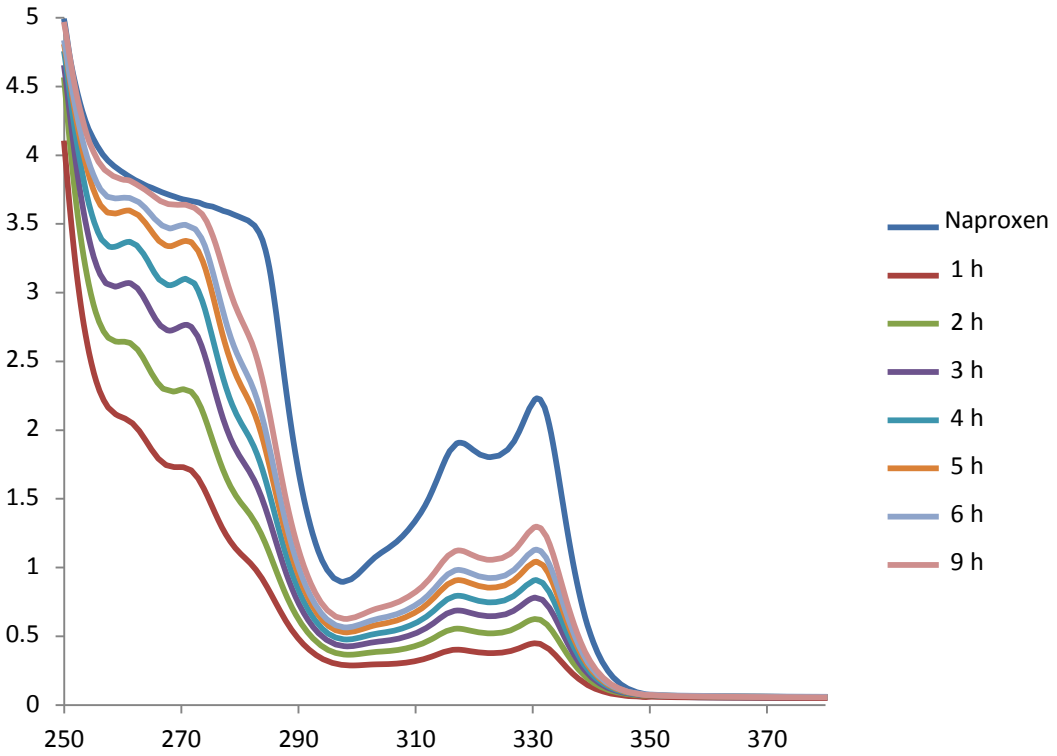


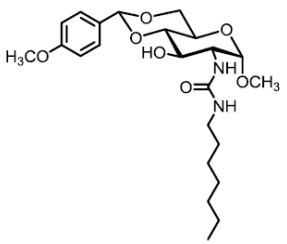
DMSO:H_2O (v 1:2), 10 mg/mL



Mangunuru, H. P. R.; Yang, H.; Wang, G. *Chem. Commun.* **2013**, *49*, 4489-4491.

Release Profile of Naproxen at Neutral Conditions



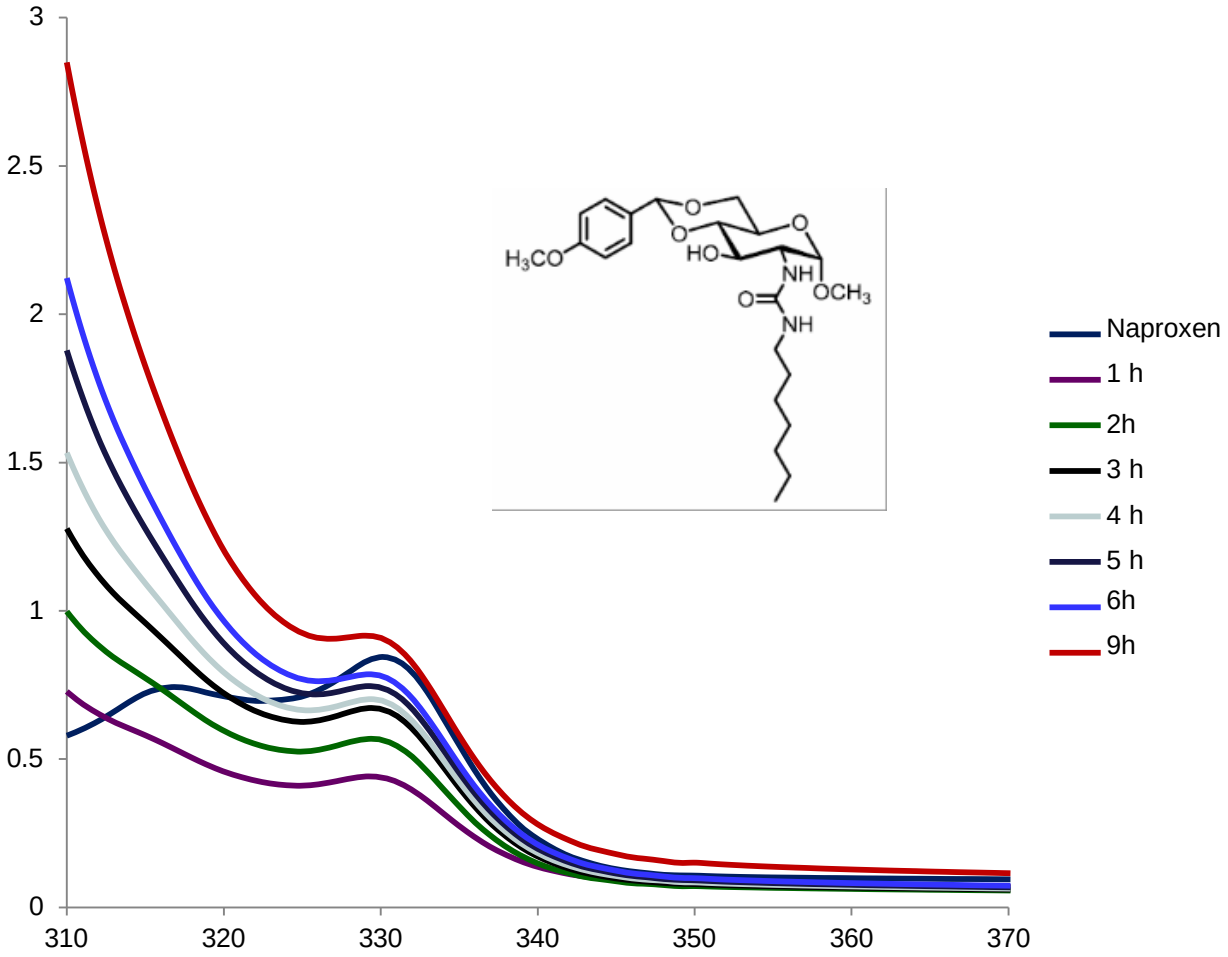


The UV-spectra of the gel in presence of water.

Compound (6mg) and Naproxen sodium salt (1.5 mg) were dissolved in 3 mL DMSO:H_2O (1:2).

Goyal, N.; Mangunuru, H.P.R.; Parikh, B.; Shrestha, S.; Wang, G. *Beilstein J. Org. Chem.* **2014**, *10*, 3111-3121.

Release Profile of Naproxen at Acidic Conditions



The UV-spectra of the gel in presence of 0.1 M of HCl solution.

Goyal, N.; Mangunuru, H.P.R.; Parikh, B.; Shrestha, S.; Wang, G. *Beilstein J. Org. Chem.* **2014**, *10*, 3111-3121.

Summary

- A systematic structure and gelation relationship study has been carried out for monosaccharide templates.
- Obtained functional diacetylene containing sugar gelators that can polymerize and exhibit desirable optical properties.
- Synthesis and characterization of stimuli responsive hydrogelators and organogelators, including light sensitive and pH sensitive systems.

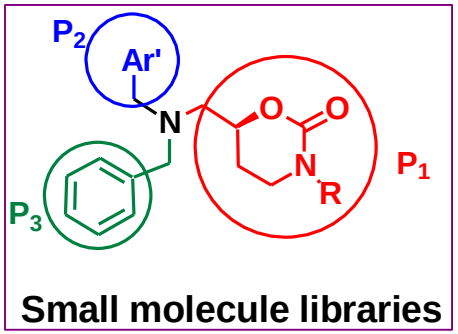
Future Research

- Synthesis of glycomimetics and study of their biological applications.
- Applications of the LMWGs as stimuli responsive smart materials in controlled release of drugs or biomolecules through collaborations.

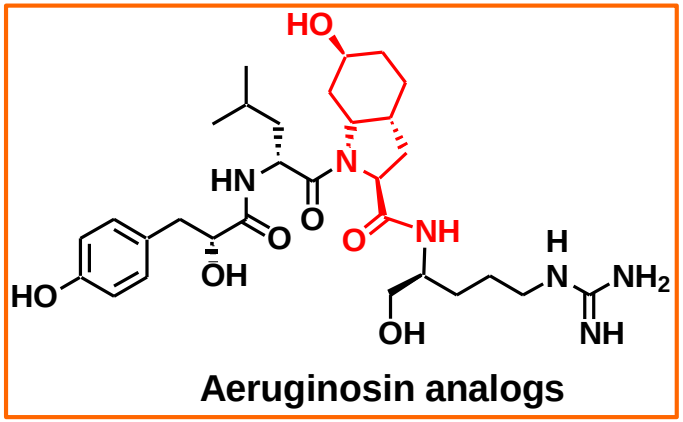
Brief Overview of Other Projects

Synthesis of chiral small molecules

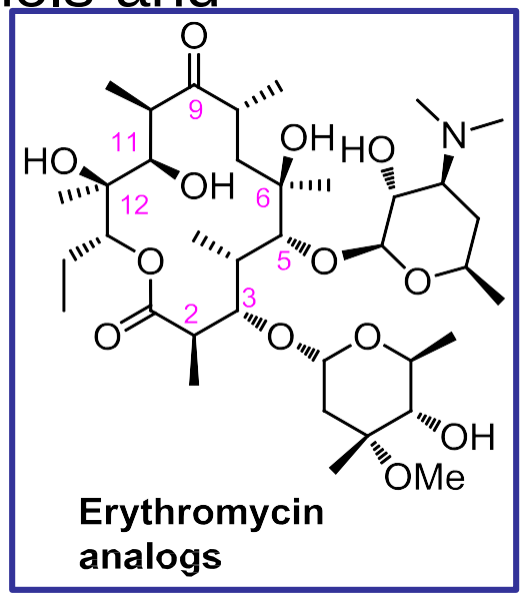
- Synthesis of chiral small molecules by chiral pool approach
- Asymmetric synthesis and synthetic methodology development and catalytic reactions
- Target compounds: chiral amino alcohols and heterocycles, unusual amino acids



Small molecule libraries



Aeruginosin analogs



Erythromycin analogs

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Graduate Students

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Navneet Goyal
Michal St. Martin
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Hari P. R. Mangunuru
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Anji Chen
Consuelo Garcia

Postdoctoral Associates

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Branden Hopkinson
Jennifer Vu
Sherman Coleman
Corey Hampton
Zeus Thornton
William Taylor
Andrew Allain
Sonu Shrestha
Sadia Akram
Kellie Mays
Angelo Espirito
Total 32 undergraduate students

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Professor Wang's Research Group, August 2014, Norfolk, VA

http://www.odu.edu/directory/people/g/g1wang