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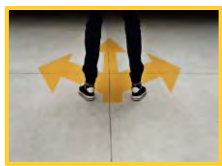

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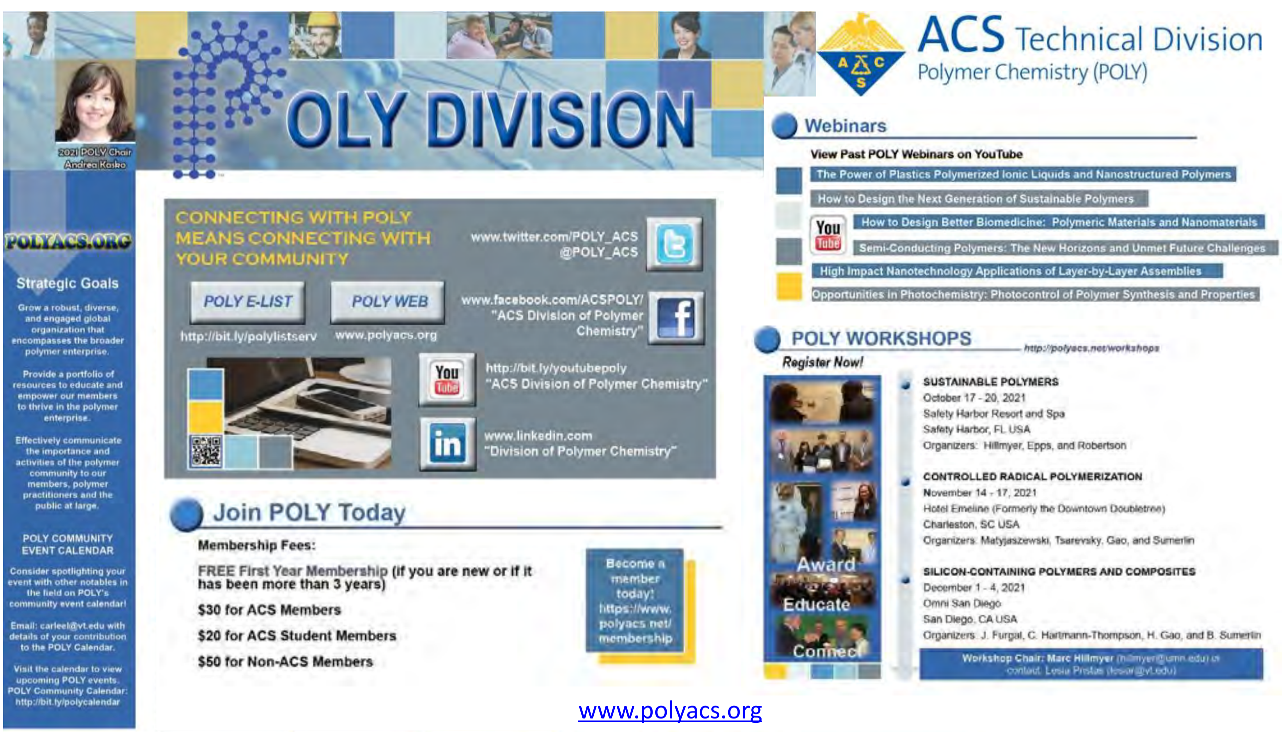

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Designing Around Structural Alerts in Drug Discovery

Date: Friday, September 17, 2021 @ 2-3:15pm ET
Speaker: Nick Meanwell, Bristol-Myers Squibb
Moderator: Deepak Dalvie, Crinetics Pharmaceuticals

Register for Free!

What You Will Learn:

- The identity of structural alerts that have been associated with problems in drug discovery and development
- The fundamental mechanistic organic chemistry subtending structural alerts that are subject to bioactivation
- Strategies and tactics to design around structural alerts

Co-produced with: ACS Division of Medicinal Chemistry, American Association of Pharmaceutical Scientists, and ACS Publications

Service Dogs in Your Chemistry Lab

Date: Wednesday, September 22, 2021 @ 2-3pm ET
Speakers: Patricia Redden, Saint Peter's University / Joey Ramp, Empower Ability Consulting, LLC / Ashley Neybert, Independence Science
Moderator: Partha Basu, Indiana University-Purdue University Indianapolis

Register for Free!

What You Will Learn:

- What does the Americans with Disabilities Act cover regarding access rights for service dogs
- How is a service dog selected for certain jobs or disabilities, and what type of training is required
- What types of service dogs exist and what is the process to obtain one

Co-produced with: Chemists with Disabilities (CWD) Committee, ACS Department of Diversity Programs, and ACS Diversity, Inclusion & Respect Advisory Board

Molecules to Manufacturing to Marketplace

3D Printing of Sulfonated Polyesters for Controlled Release

Date: Thursday, September 23, 2021 @ 2-3:15pm ET
Speakers: Timothy Long, Arizona State University and Michael Bortner, Virginia Tech
Moderator: Bryan Tweedy, American Chemical Society

Register for Free!

What You Will Learn:

- What is the impact of polyester ionomers and macromolecular architecture on processability and performance of 3D printed structures
- How to leverage rheology for predictive additive manufacturing system design and materials screening
- A snapshot of the topics and concepts captured in the ACS Polymer Chemistry: Principles and Practice short course held at Virginia Tech

Co-produced with: ACS Professional Education

www.acs.org/acswebinars

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ACS Chemistry for Life®

Co-produced with: POLY | ACS Division of Polymer Chemistry

Advancing Polymer Science with Organic Catalysts

FREE Webinar | TODAY at 2pm ET

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THIS ACS WEBINAR WILL BEGIN SHORTLY...

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ACS Chemistry for Life®

Advancing Polymer Science with Organic Catalysts

RACHEL LETTERI
Assistant Professor, Department of Chemical Engineering, University of Virginia

ROBERT WAYMOUTH
Robert Eckles Swain Professor in Chemistry, Stanford University

ANDREW DOVE
Professor, Sustainable Polymer Chemistry, University of Birmingham, UK

Presentation slides are available now! The edited recording will be made available as soon as possible.
www.acs.org/acswebinars

This ACS Webinar is co-produced with ACS Division of Polymer Chemistry.

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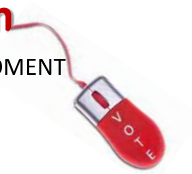
Audience Survey Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT



Do you have experience in using organic catalysis?

- Yes, I'm expert level!
- Yes, I have used them a lot
- Yes, but only a little
- No, I have never tried

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Advancing Polymer Science with Organic Catalysts

RACHEL LETTERI
Assistant Professor, Department of Chemical Engineering, University of Virginia

ROBERT WAYMOUTH
Robert Eckles Swain Professor in Chemistry, Stanford University

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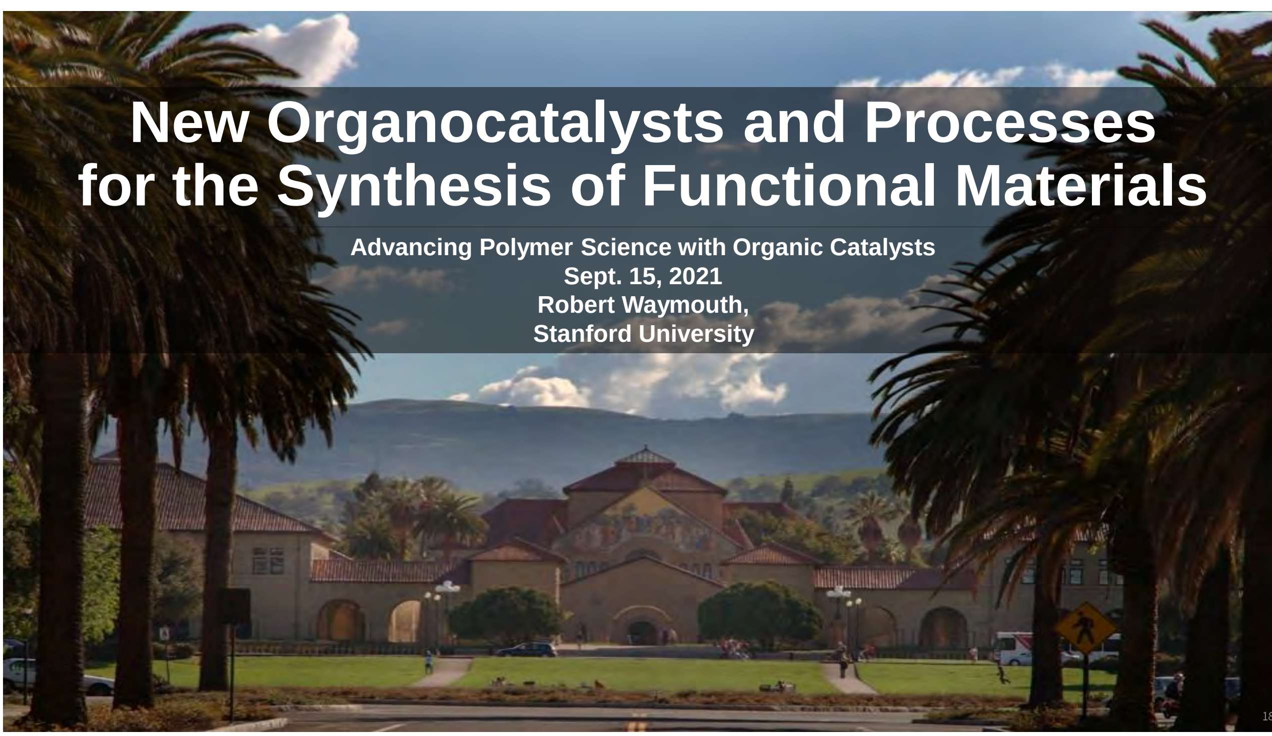
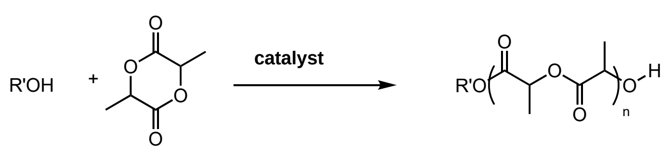


New Organocatalysts and Processes for the Synthesis of Functional Materials

Advances in Catalyst Design Continue to Drive Innovation in Polymer Science

Ring-Opening Polymerization of Lactones: Metal Catalysts

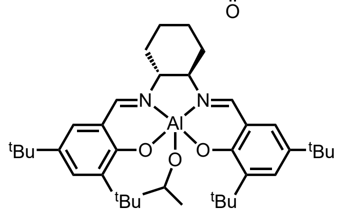


MOR, M = Li, Na, K

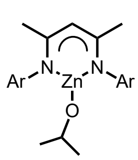
$Al(OR)_3$

$Sn(O_2CR)_2$

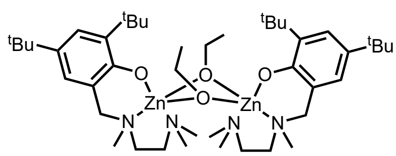
Kricheldorf, Jerome
Pencek, Duda



Spassky, Feijen

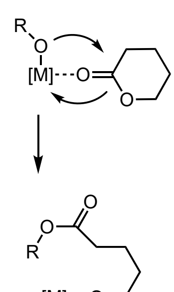


Coates

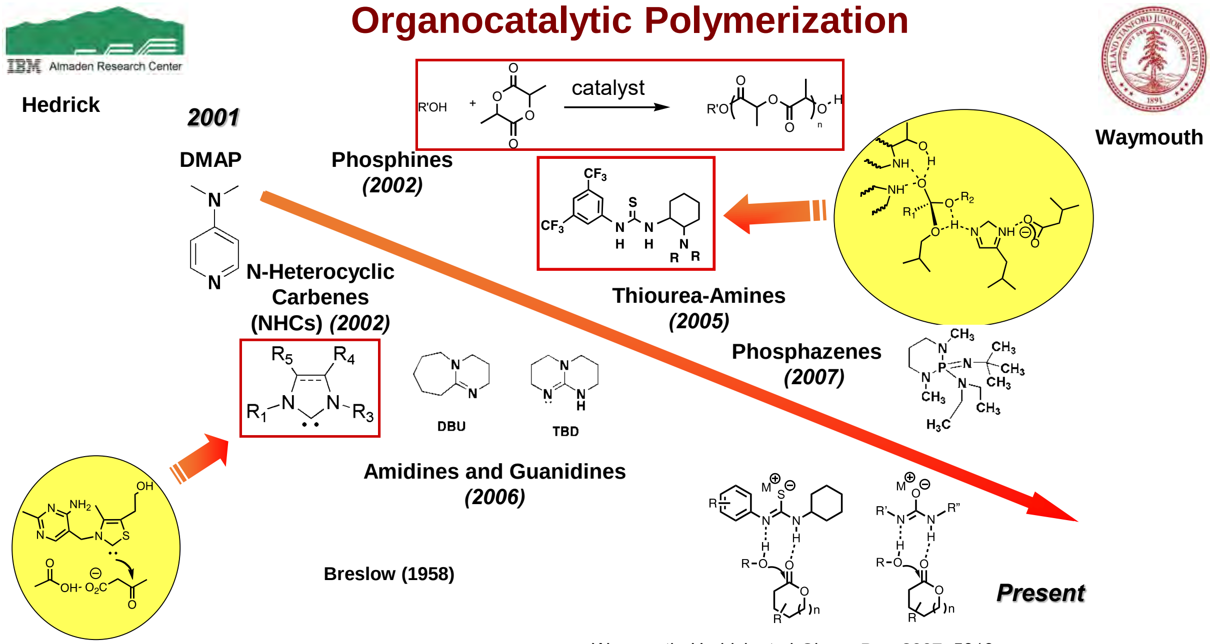


Tolman, Hillmyer

Proposed Mechanism



Organocatalytic Polymerization



Waymouth, Hedrick,et al *Chem. Rev.* **2007**, 5813
Zhang, Hedrick Waymouth, *Nat. Chem.* **2016**, 1047
Lin, Waymouth *JACS*, **2017**, 1645.

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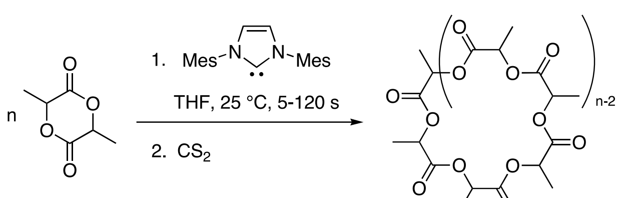
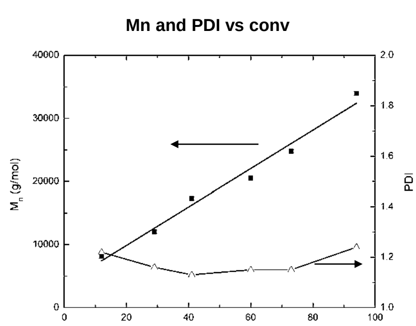
Synthesis of Cyclic Polyesters via NHC Catalysts



[lactide]$_0$ = 0.6 M

- ***Highly Active***
- ***Controlled***
  - ***–Mn tracks % conversion***
  - ***–Low PDIs***
- ***Forms large ring cyclics***



M_n (Da)	time (s)	M/Cat	conv (%)	PDI
28574	120	200	92	1.22
33957	120	100	94	1.24
28648	15	30	92	1.24
11742	12	200	30	1.14
12044	5	100	29	1.16
13566	5	30	29	1.11
5855	5	200	7	1.20

Mn tracks conversion, but non-zero intercept

Culkin,Szihony, Hedrick, Waymouth *ACIEE*, **2007**, 2627
Jeong, Waymouth, et.al, *JACS*, **2009**, 4884

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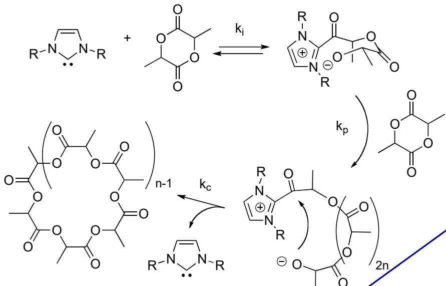
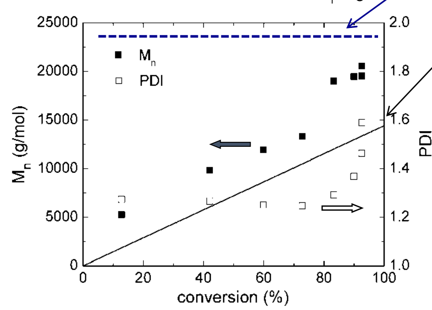
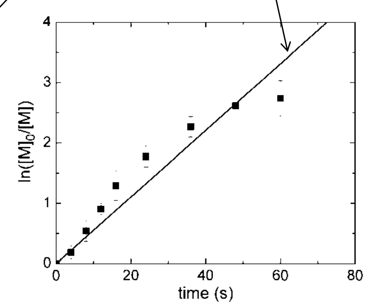
Mechanistic Anomalies: Zwitterionic Polymerization



(1) chain-growth with chain transfer
Mn constant with conv., PDI = 2.0

(2) "living"
Mn increase with conv., PDI = 1.x
first-order kinetics





Jeong, W.; Shin, E. Waymouth, R. M. *J. Am. Chem. Soc.*, **2009**, 4884.

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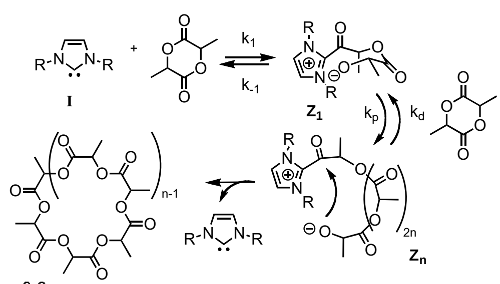
Kinetic Model of Zwitterionic Polymerization

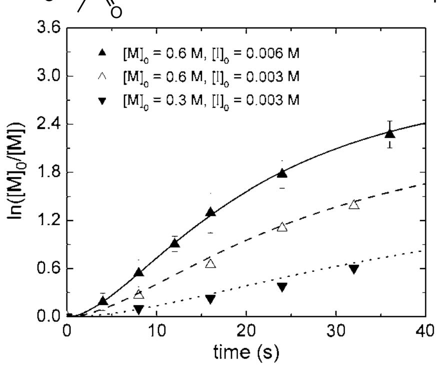


- **initiation: slow, second order in [M]**
- **propagation fast**
- **cyclization slow**

$$\frac{d[Z_1]}{dt} = \frac{k_1 k_2 [I][M]^2}{k_{-1} + k_2[M]} \gg \frac{k_1 k_2 [I][M]^2}{k_{-1}}$$

$$-\frac{d[I]}{dt} = k_i[I][M]^2 - k_c([Z_n])$$

$$-\frac{d[M]}{dt} = 2k_i[I][M]^2 + (k_p[M] - k_d)([Z_n])$$



k_p = 48.7 ($M^{-1}\cdot s^{-1}$)
k_i = 0.274 ($M^{-2}\cdot s^{-1}$)
k_c = 0.0575 (s^{-1})
k_d = 0.208 (s^{-1})

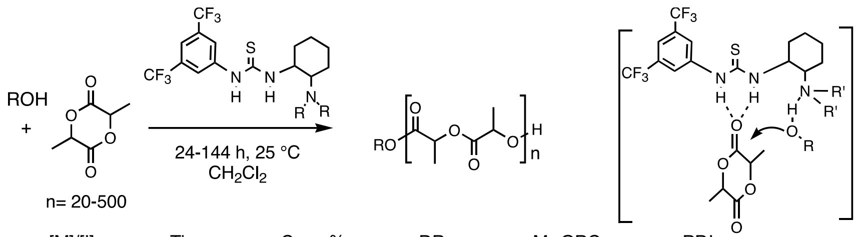
where

$$[Z_n] = ([I]_0 - [I])$$

Jeong, W.; Shin, E. Waymouth, R. M. *J. Am. Chem. Soc.*, **2009** 4884

24

Bifunctional Thiourea Catalysts for Lactide Polymerization



[M]/[I]	Time	Conv %	DP	M_n GPC	PDI
20	24 h	97	21	5200	1.08
50	32h	98	53	12300	1.05
100	48 h	97	103	23000	1.05
200	105h	98	215	42000	1.05
500	144	95	-[e]	- [e]	- [e]

[a] 5 mol% 1; [LA] = 1 M in CH_2Cl_2; [b] determined by 1H NMR; [c] degree of polymerization [e] not soluble in THF.

- Solvent Effect: Polymerization Observed in CH_2Cl_2, $CHCl_3$, toluene
  - No polymerization observed in THF, DMF

Dove, Pratt, Lohmeijer, Hedrick, Waymouth, *JACS*, **2005**, 13798

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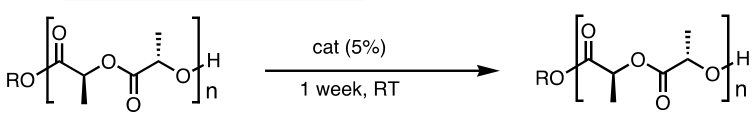
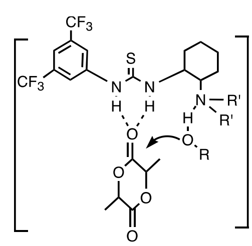
Chain Extension: No Transesterification

Minimal Transesterification

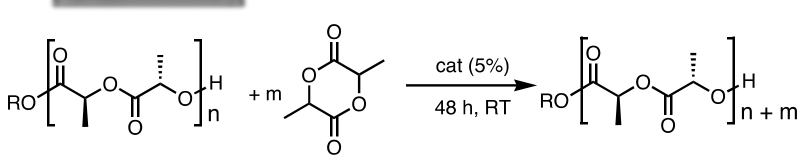




Mn = 21,300; PDI of 1.06

Mn = 20,900; PDI of 1.07

Chain extension



DP of 103 (PDI of 1.05)

additional 100 equiv of lactide

DP of 215 (PDI of 1.05)

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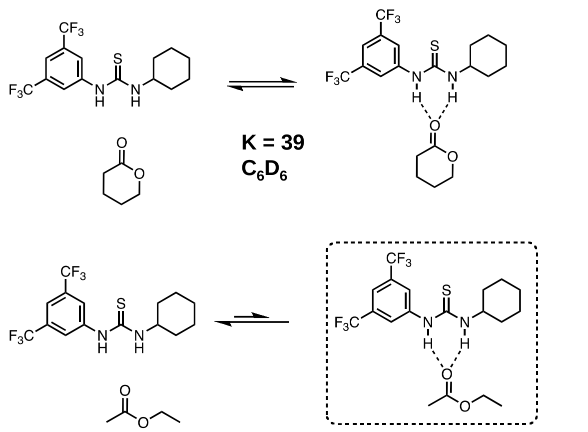
Origin of High Selectivity?

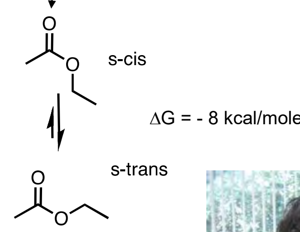


can't measure by ^{1}H NMR

K probably less than 5

Higher H-bond basicity
Laurence, *J. Med. Chem.* ***2009***, 4073.

Boxer,
Acc. Chem. Res. 2015, 998



Preston Hedrick
(high school junior)

DFT (Hans Horn, Julia Rice (IBM) Anthony De Crisci (Stanford)

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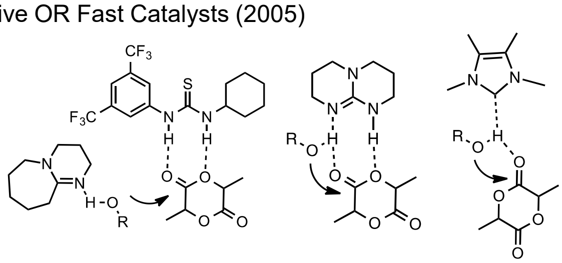
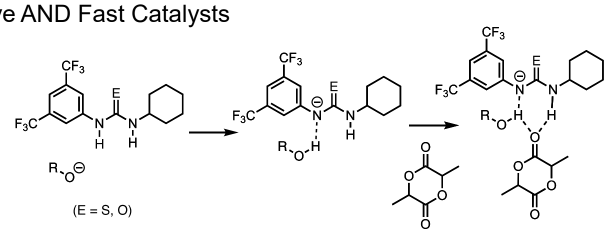
Development of Fast AND Selective Catalysts

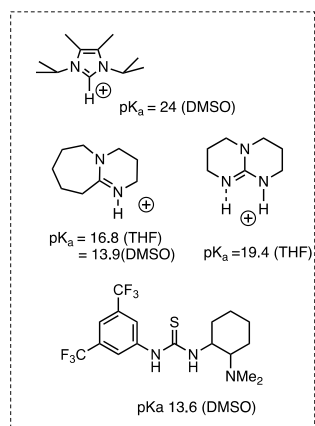
- Selective OR Fast Catalysts (2005)



Slow, but selective   Fast, but non-selective

- Selective AND Fast Catalysts





Zhang, X.; Jones, G. O.; Hedrick, J.L.; Waymouth, R. M. Nature Chem. **2016**, 8, 1047-1053.
Lin, B.; Waymouth, R. M. J. Am. Chem. Soc., **2017**, 1645–1652

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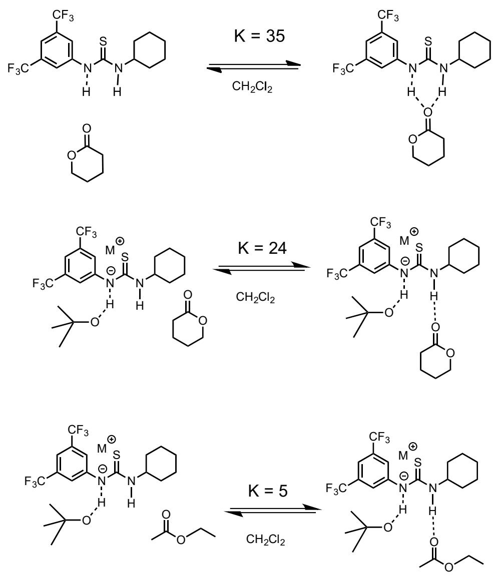
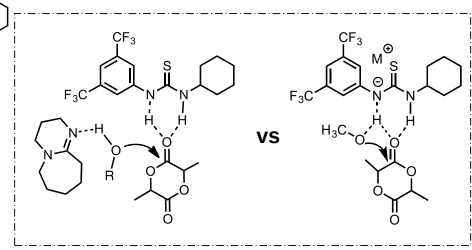
Origin of High Selectivity?

measured by ^{13}C NMR



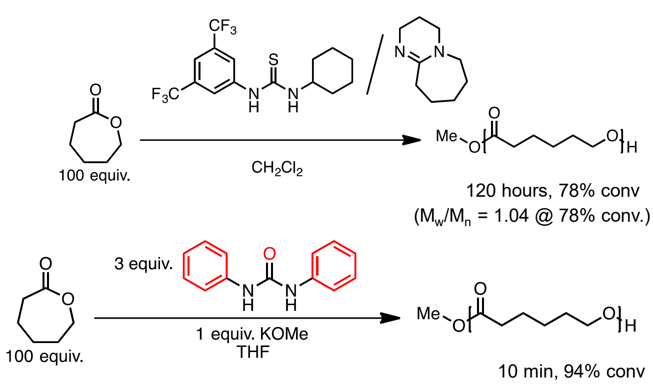


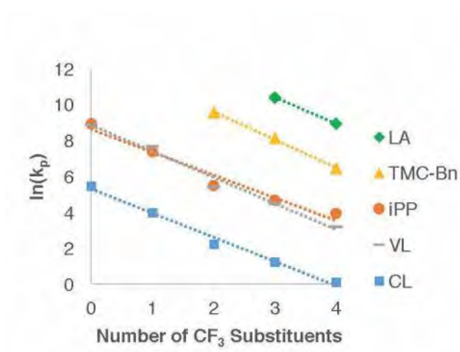
- **Higher Binding constant for s-trans lactones vs. s-cis esters:**
  - ***catalyst highly selective for opening lactone vs. transesterification***

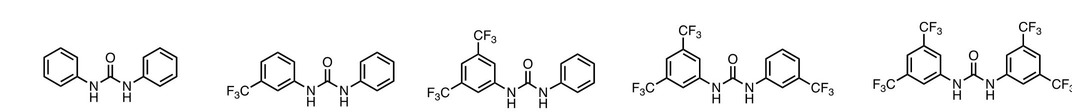
Xiangyi Zhang, Jones, Hedrick, Waymouth, *Nature Chem.* 2016

Urea Anions: Efficient Catalysts for Polymer Synthesis

Lohmeier, Hedrick Waymouth, Macro. 2006, 8574



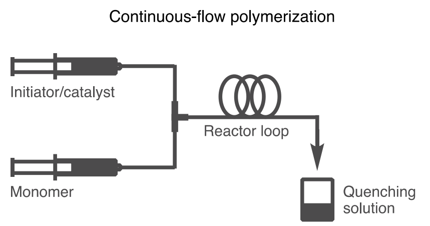


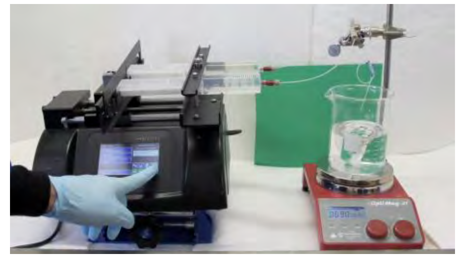


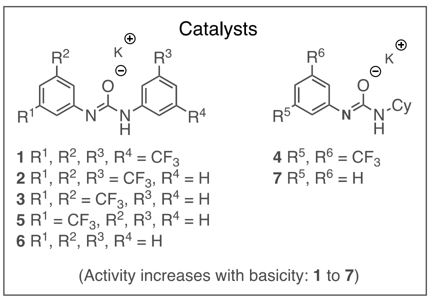
pKa (dmso) 18.7 | **16.1** | **13.8**

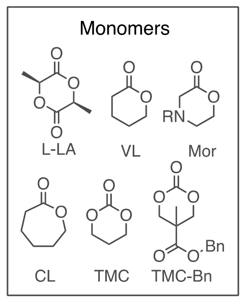
Lin, B.; Waymouth, R. M. J. Am. Chem. Soc., **2017**, 1645–1652

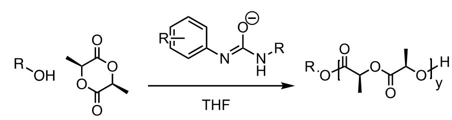
A New Catalyst Platform Tailored for Continuous Flow Processes











Movie: 16 grams PLA in 40 seconds!

Lin, Hedrick, Park, Waymouth, *J. Am. Chem. Soc.*, **2019**, *141*, 8921-8927.

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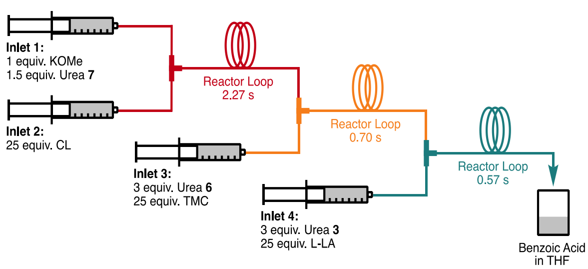
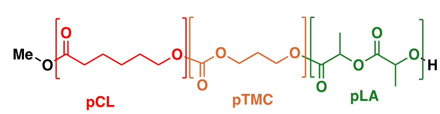
A New In-Flow Catalyst Switch for Rapid Generation of Multiblock Copolymers

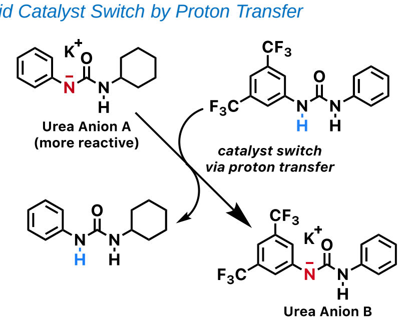


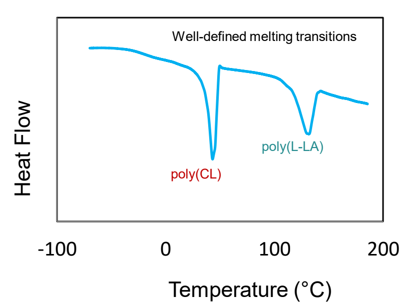


poly(CL)$_{25}$-block-poly(TMC)$_{25}$-block-poly(L-LA)$_{25}$

τ = 3.5 seconds, $M_{n\ GPC}$ = 12 kDa, Đ = 1.08.

Rapid Catalyst Switch by Proton Transfer





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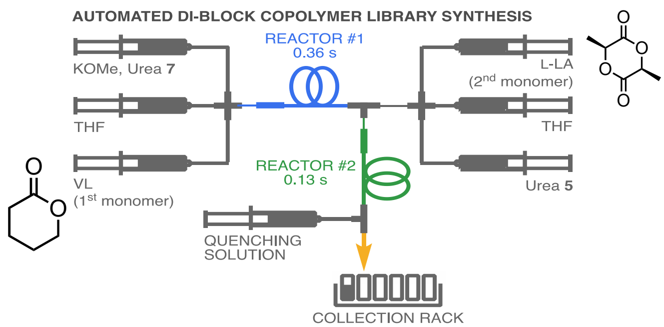
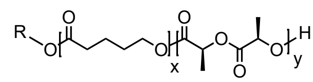
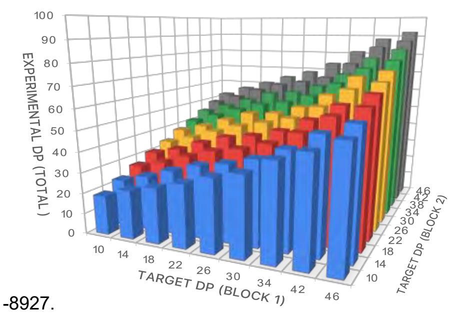
Programmed Library Generation in Flow Reactor





p(VL_x-b-LLA_y)

x, y = 10 – 46 in increments of 4



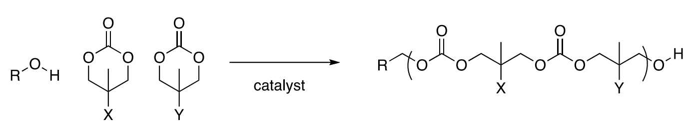
Automated, programmed generation of 100 separate VL-b-PLA diblock copolymers generated in 10 minutes

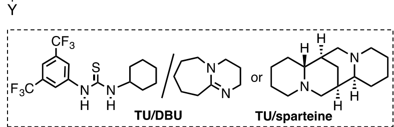
Length of each block ranging from 10 to 46 in increments of four monomer repeat units

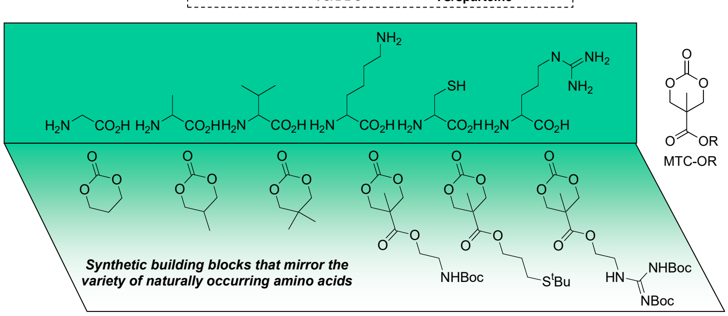
Lin, Hedrick, Park, Waymouth, J. Am. Chem. Soc., 2019, 141, 8921-8927.

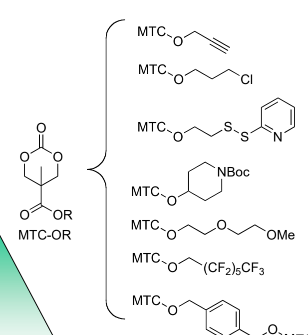
33

Polycarbonates: Synthetic Multifunctional Polymers







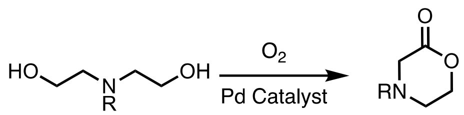


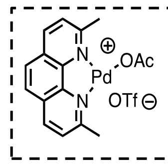
Pratt, R. C.; Nederberg, F.; Waymouth, R. M.; Hedrick, J. L. *Chem. Commun.* **2008**, 114-116.
Cooley, C. B.; Trantow, B. M.; Nederberg, F.; Kiesewetter, M. K.;
Hedrick, J. L.; Waymouth, R. M.; Wender, P. A. *JACS*, **2009**, 16401

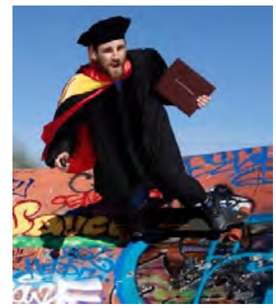
34

Degradable Polycations: Synthesis and Mechanism

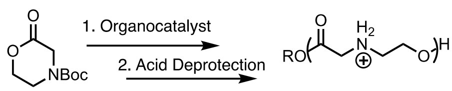
Chung, Blake, Waymouth,. et. al. *JACS*, **2013**, *135*, 7593-7602.

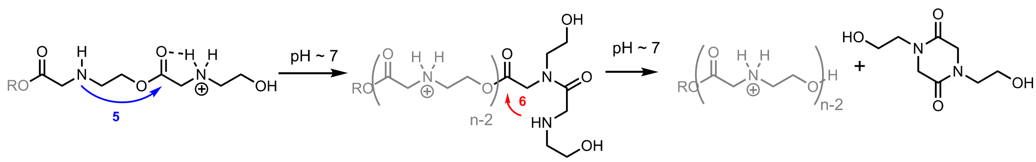






Blake, Waymouth *J. Am. Chem. Soc.* **2014**, 7593-7602.

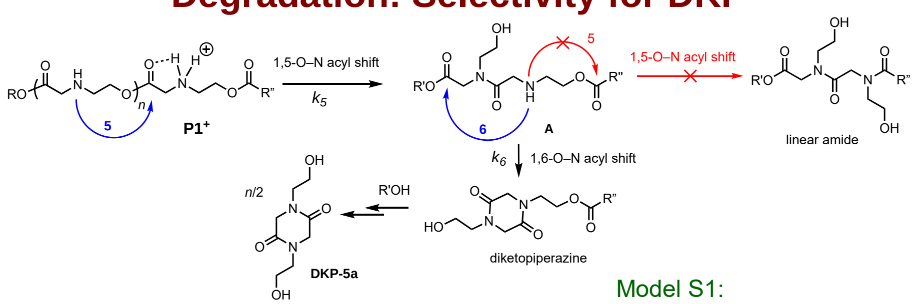


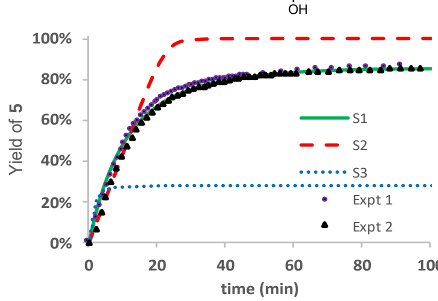


Blake, T. R.; Ho, W. C.; Turlington, C.R.; Zhang, X.; Huttner, M. A.; Wender, P. A.; Waymouth, R. M. "Synthesis and Mechanistic Investigations of Rapid Base-Triggered Immolative Cationic Polyesters" , *Chem. Sci*., **2020**, *11,* 2951.

35

Degradation: Selectivity for DKP





Model S1:
random at any point in chain;
$k_6/k_5 = 10^6$
$k_6 >> k_5 = 0.0412\ min^{-1}$

Model S2:
degradation from chain-end;
$k_6/k_5 = 10^6$
$k_6 >> k_5 = 1.44\ min^{-1}$

Model S3:
random at any point in chain;
$k_5 = k_6 = 0.483\ min^{-1}$

Blake, Ho, Turlington, Zhang, Huttner, Wender, Waymouth, "Synthesis and Mechanistic Investigations of Rapid Base-Triggered Immolative Cationic Polyesters" *Chem. Sci.*, **2020**, 2951

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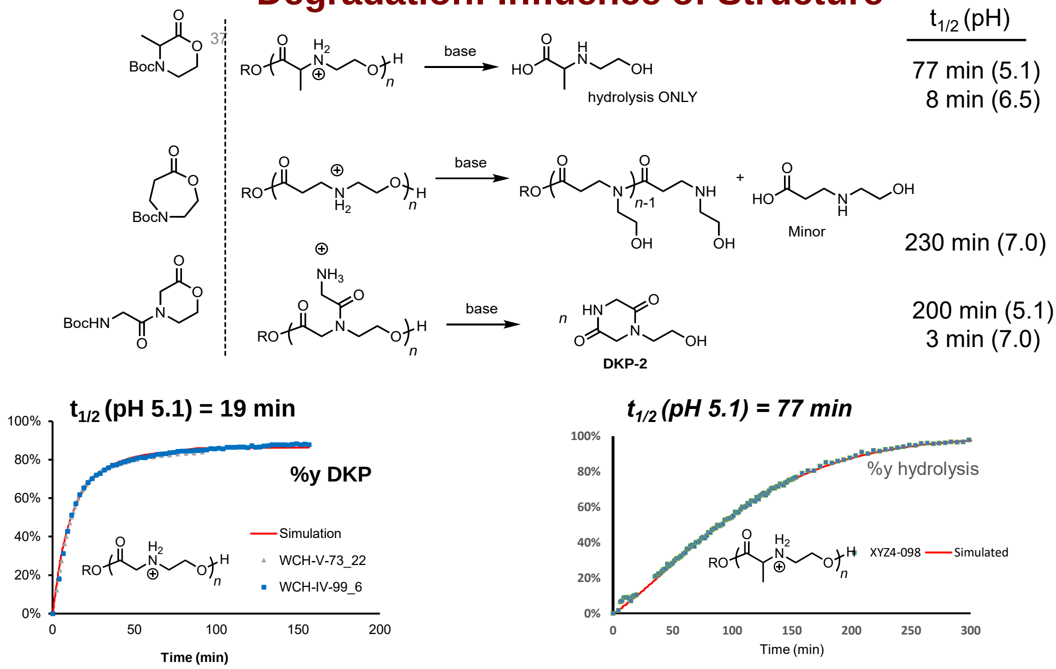
Degradation: Influence of Structure



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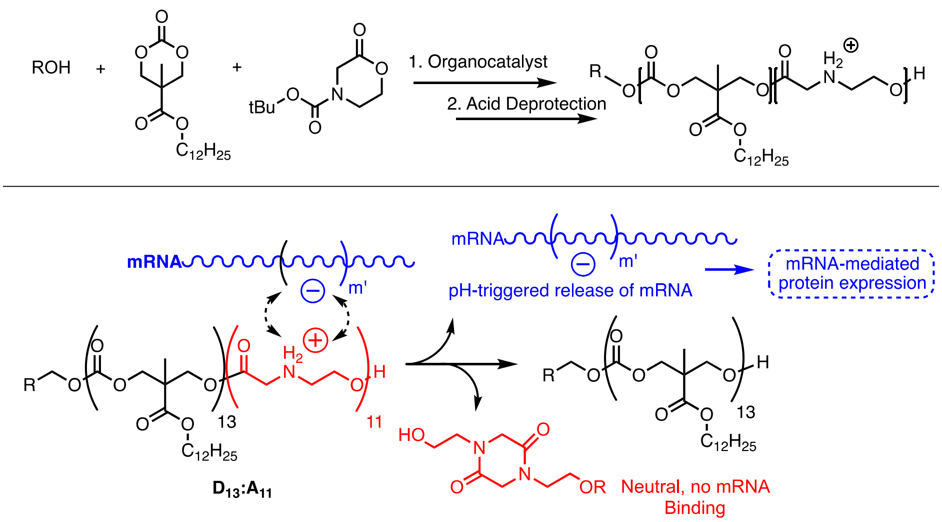
Degradable Polycations: A Mechanism of mRNA Release



McKinlay, Vargas, Blake, Hardy, Kanada, Contag, Wender, Waymouth, "Charge-altering Releasable Transporters (CARTs) for the delivery and release of messenger RNA in living animals" Proc. Natl. Acad. Sci., 2017, E448

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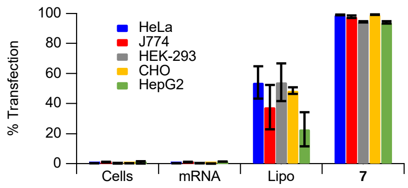
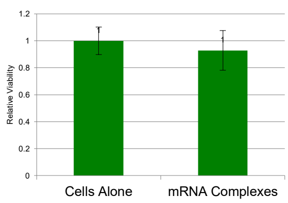
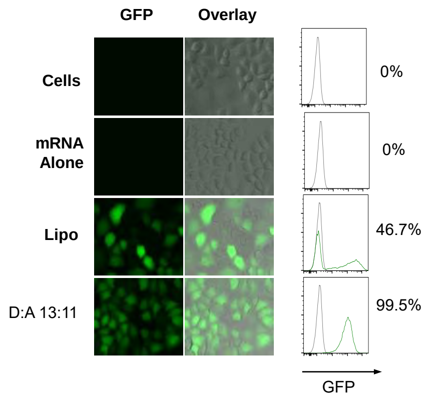
mRNA delivery: cell culture

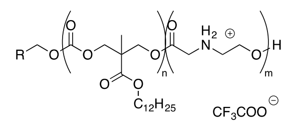
Using new amphipathic materials we were able to transfect mRNA and elicit the expression of Green Fluorescent Protein (HeLa cells)







D:A 13:11 (7)



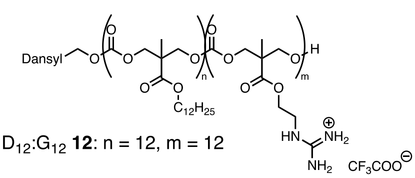
*Representative histograms of mRNA Transfection efficiency

- OROP and functionalized monomers allows for rapid screening for function
- Expression levels are higher than commercial Lipofectamine
- Non-toxic

McKinlay, Vargas, Blake, Hardy, Kanada, Contag, Wender, Waymouth, "Charge-altering Releasable Transporters (CARTs) for the delivery and release of messenger RNA in living animals" Proc. Natl. Acad. Sci., **2017**, E448

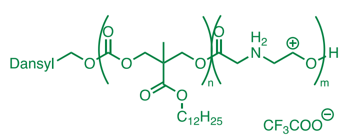
To Express mRNA, mRNA Must Escape Endosome

Confocal Microscopy
- Allows for independent imaging of transporter and cargo on a cell-by-cell basis

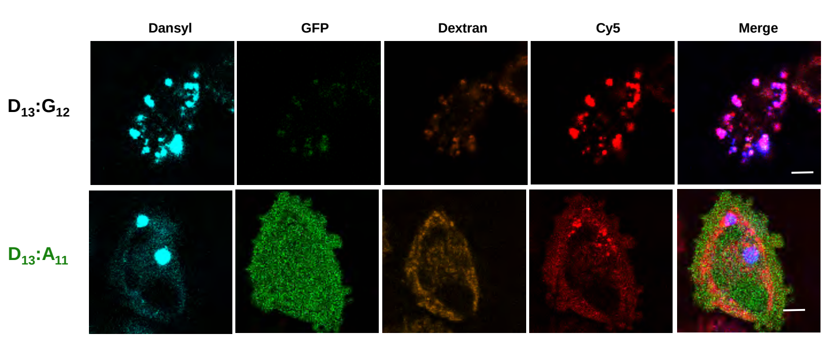


D_{12}:G_{12} **12**: n = 12, m = 12

Fluorophores
- Dansyl: attached to transporter
- GFP: indicates expression has occurred
- Dextran: stains endosomes
- Cy5: attached to mRNA

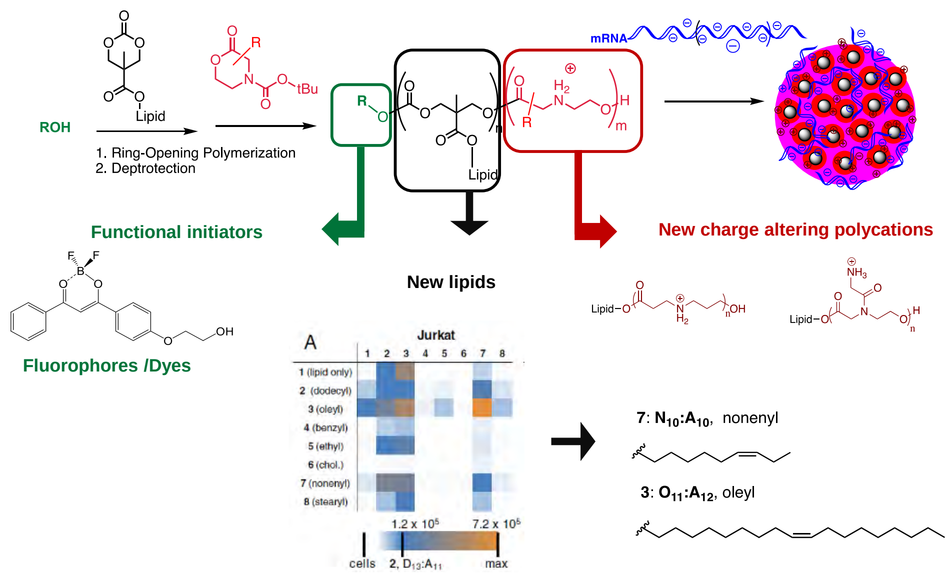


D_{13}:A_{11} **8**: n = 13, m = 11



Conditions: HeLa cells, 10:1 +/- charge ratio, 4 hours following treatment

Broad Chemical Space



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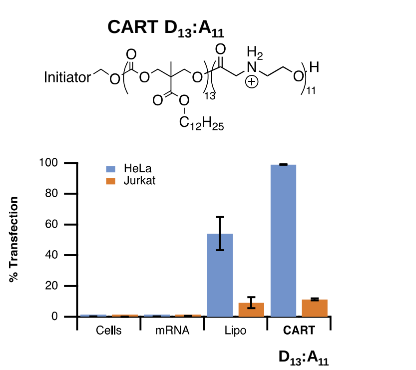
mRNA delivery with CARTs into *T lymphocytes*

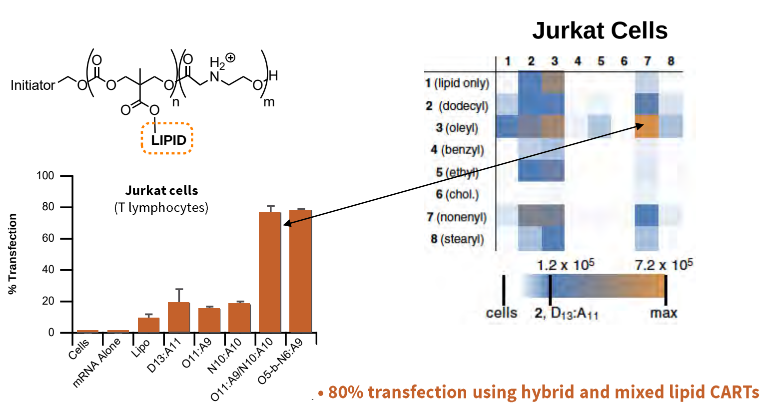
• **Combinatorial library: CART mixtures (2:1) High throughput screen**

Background



• >95% transfection efficiencies in many cultured cells types
• low lymphocyte transfection

McKinlay, C.; Vargas, J. *et at.* *PNAS* **2017**, *114*, E448



• **80% transfection using hybrid and mixed lipid CARTs**
• **8-fold increase over $D_{13}A_{11}$ and Lipo**

Lipid-mixed CARTs enhance mRNA delivery into:
•T cells and B cells (primary and immortalized)

McKinlay, C.; Benner, N. *et at.* *PNAS* **2018**, *115*, E5859

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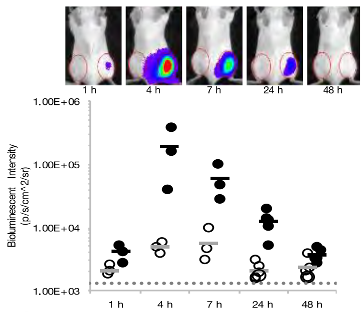
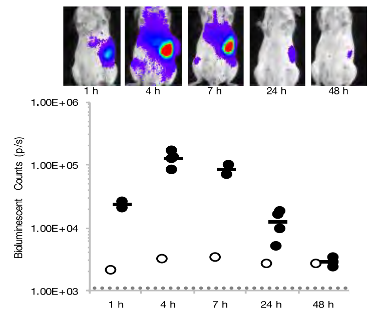
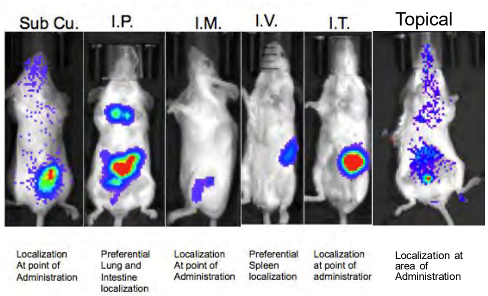
mRNA expression is effective via multiple routes of administration in vivo

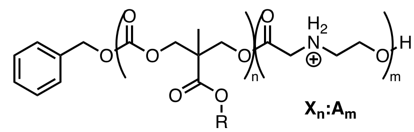
Intramuscular



Intravenous (tail-vein)

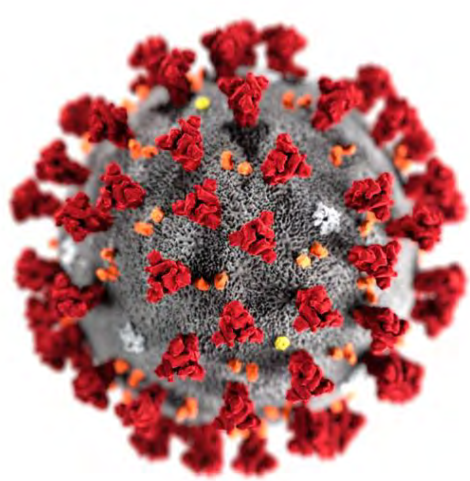






Biodistribution of mRNA expression influencedby mode of administration

The Plague Year

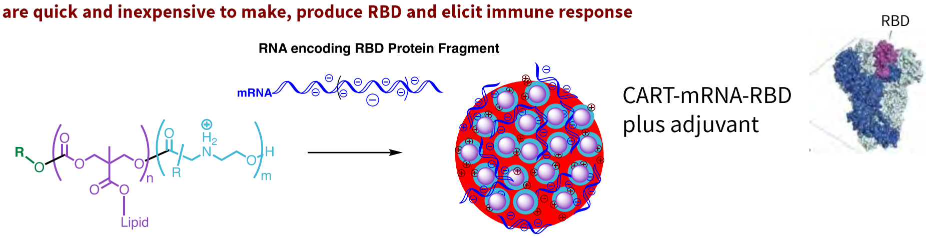


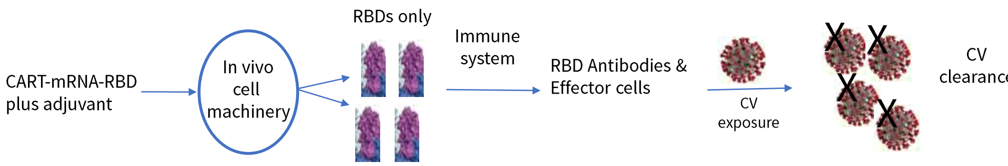
See: “the Plague Year”. Lawrence Wright, The New Yorker, Jan 4&11, 2021

The CART-mRNA Approach to COVID 19 Vaccination: Deliver the message, cells make the vaccine

Levy, Waymouth and Wender labs

mRNA vaccines are quick and inexpensive to make, produce RBD and elicit immune response





Haabeth, Lohmeyer, Sallets, Blake, Sagiv-Barfi, Czerwinski, Powell, Wender, Waymouth, Levy, An mRNA SARS-CoV-2 Vaccine Employing Charge-Altering Releasable Transporters with a TLR-9 Agonist Induces Neutralizing Antibodies and T Cell Memory y. *bioRxiv* 2021, 2021.04.14.439891, *ACS Central Science* **2021**,1191.

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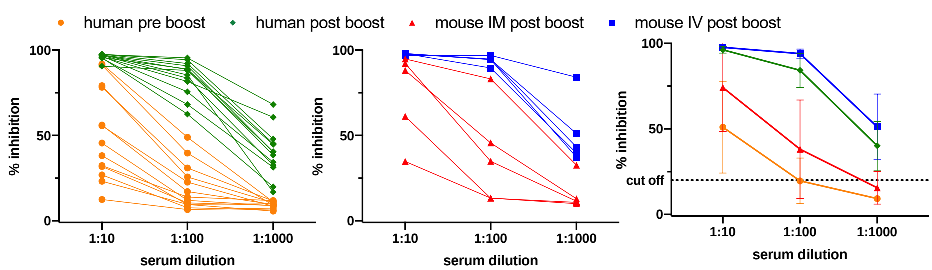
The CART-mRNA Approach to COVID 19 Vaccination:

Levy-Waymouth-Wender labs

CART-mRNA-RDB elicits a protective immune response



Sera from immunized mice (IM in red, IV in blue, n=5) was harvested on Day 28. Serum from blood donors (n=13) who were vaccinated with the Pfizer/ BioNTech mRNA vaccine was collected either within 7 days before (pre boost, black) or 15±4 days after the boost (post boost, green) was tested for the ability to inhibit RBD/ACE- 2 binding using a commercially available surrogate Virus Neutralization Test.

- Neutralizing antibody levels of immunized mice are comparable to those achieved in vaccinated humans

Haabeth, Lohmeyer, Sallets, Blake, Sagiv-Barfi, Czerwinski, Powell, Wender, Waymouth, Levy, An mRNA SARS-CoV-2 Vaccine Employing Charge-Altering Releasable Transporters with a TLR-9 Agonist Induces Neutralizing Antibodies and T Cell Memory y. *bioRxiv* 2021, 2021.04.14.439891, *ACS Central Science* **2021**,1191.

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New Organocatalysts and Processes for the Synthesis of Functional Materials

Advances in Catalyst Design Continue to Drive Innovation in Polymer Science

47

Dr. Tim Blake, Rebecca McClellan,
Keith Armstrong, Conor Galvin,
Summer Ramsay-Burroughs, Vince Pane,
Caleb Jadrich, Dan Marron,
Dr. Trevor Del Castillo, Dr. Blaine McCarthy
Jim Zhang, Yuan Jia, Isaac Appelbaum

Collaborators

Dr. James Hedrick (IBM)
Dr. Nathaniel Park (IBM)

Prof. Paul Wender (Stanford)
Prof. Ron Levy (Stanford)
Prof. Grant Rotskoff (Stanford)
Prof. Catherine Blish (Stanford)
Prof. Eric Kool (Stanford)
Dr. Ole Haalbeth (Stanford)

Prof. Jeff Glenn (Stanford)
Prof. V. Sebastiani (Stanford)

Prof. Dick Zare (Stanford)
Prof. Craig Criddle (Stanford)

National Science Foundation
National Institute of Health
Adelson Medical Research Foundation
The Leukemia and Lymphoma Society
NASA
IBM
EVONIK
Cancer TNT Program (Stanford)
SPARK Program (Stanford)
ChEM-H (Stanford)
Center For Molecular Analysis and Design
(Stanford Chemistry)

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Team Expertise and Background

Polymer synthesis Gene delivery

Prof. Robert M. Waymouth

Bob has pioneered the metal-free synthesis of biocompatible polymers, which are now used in many therapeutic Indications, including antimicrobials, gene and drug delivery agents

Drug and Gene delivery

Prof. Paul A Wender

Paul's work is directed at using chemistry and synthesis to address unsolved problems in medicine, including drug delivery, a cure for HIV/AIDS, cancer immunotherapy, Alzheimer's disease and antibiotic resistance

Clinical Oncology

Prof. Ronald Levy

Ron researches how the immune system can be harnessed to fight cancer. His work has led to personalized anticancer drugs, inventing an antibody-based drug, Rituxan, that is widely used to treat lymphoma

Stanford Team

Dr. Timothy R. Blake
Dr. Rebecca McClellan
Dr. Blaine McCarthy
Dr. Trevor Del Castillo
Dr. Ralph Lange
Summer Ramsay-Burrough
Yuan Jia
Isaac Applebaum

Dr. Colin McKinlay
Dr. Jessica Vargas
Dr. Nancy Benner
Harry Rahn
Zhijian Li
Gillian Sun
Dr. Steven Stanton

Dr. Ole A. W. Haabeth
Dr. Adrienne Sallets
Dr. Julian Lohmeyer
Dr. Idit Barfi
Dr. Stefano Testa

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UNIVERSITY OF BIRMINGHAM

Using organic catalysts for step growth polymerization and depolymerisation

Prof Andrew P. Dove

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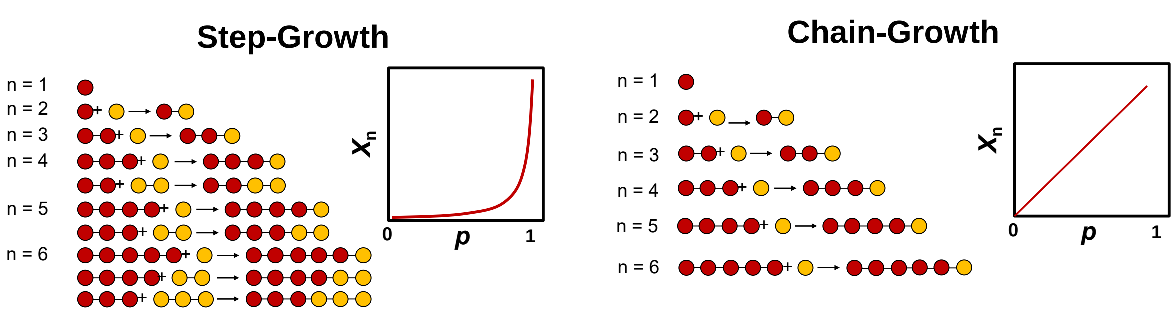
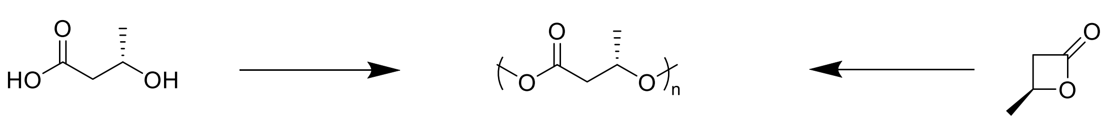
Step-Growth vs Chain Growth Polymerisation





Polymer structure is distinct from polymerisation process

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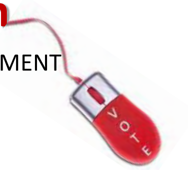
Audience Survey Question

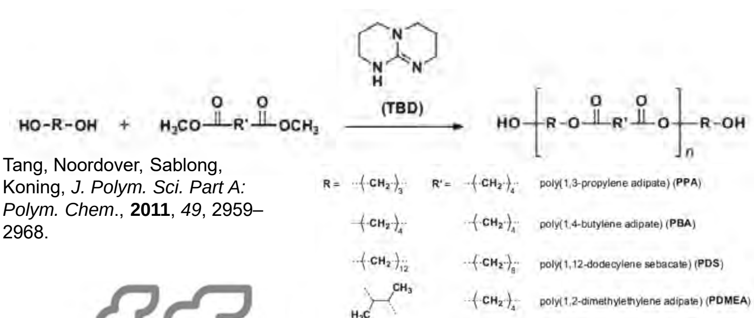
ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT



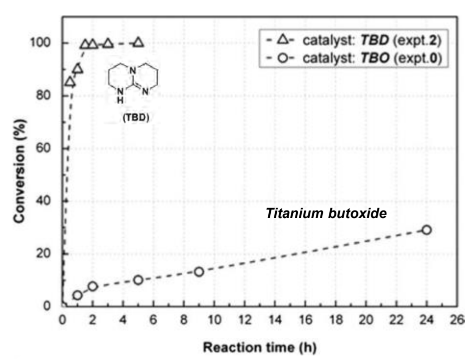
What do you think is the biggest remaining challenge to overcome for organic catalysis in polymer science?

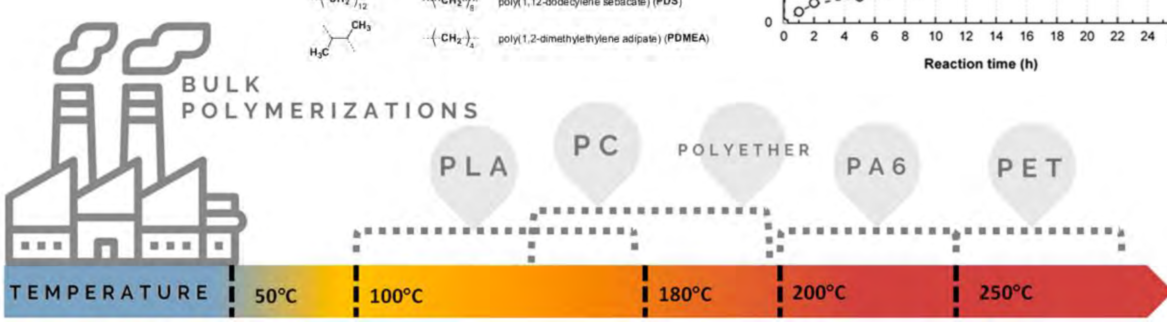
- Reaction scope
- Increasing reactivity
- High temperature operation
- Better stereoselectivity
- Other (Tell us more in the chat!)

Organocatalytic Polycondensation



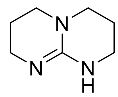
Tang, Noordover, Sablong, Koning, *J. Polym. Sci. Part A: Polym. Chem.*, **2011**, *49*, 2959–2968.





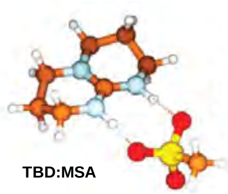
Basterretxea, Jehanno, Mercerreyes, Sardon. *ACS Macro Lett.* **2019**, *8*, 1055-1062

Thermal Stability is Commonly a Problem

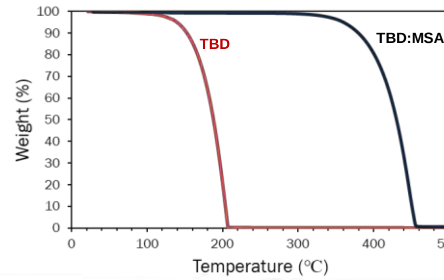


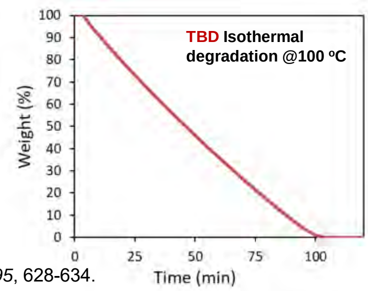
1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD)

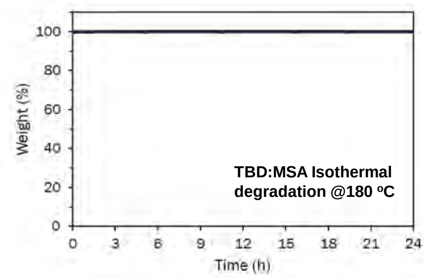
+ methane sulfonic acid (MSA)



37.4 kcal.mol^{-1} more stable than TBD and MSA







Mezzasalma, Dove, Coulembier, *Eur. Polym. J.* **2017**, *95*, 628-634.
Jehanno, Flores, Dove, Muller, Rupierez, Sardon, *Green Chem.*, **2018**, *20*, 1205-1212.

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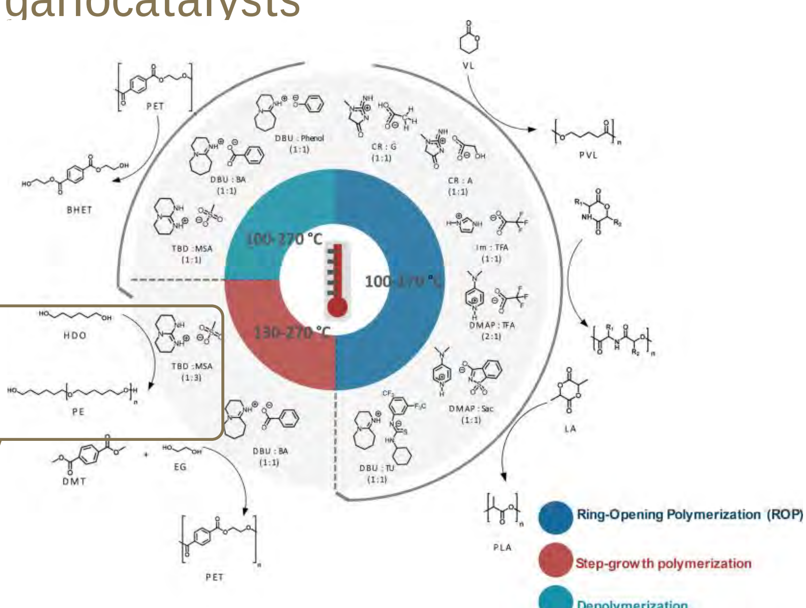
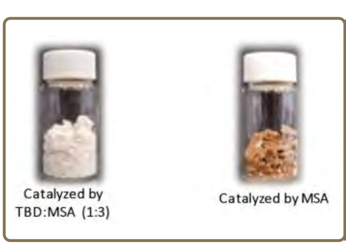
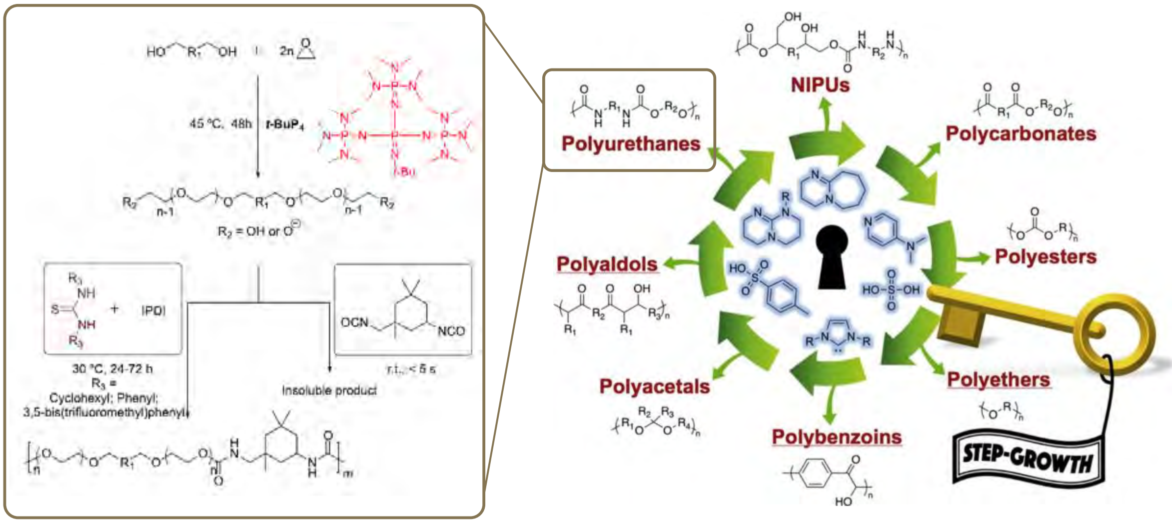
Thermally stable organocatalysts





Basterretxea, Jehanno, Mercerreyes, Sardon. *ACS Macro Lett.* **2019**, *8*, 1055-1062
Basterretxea, Gabirondo, Jehanno, Zhu, Flores, Muller, Etxeberria, Mecerreyes, Coulembier, Sardon, *ACS Sustainable Chem. Eng.* **2019**, *7*, 4103−4111

Lower Temperature Step-Growth



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Bossion, Heifferon, Meabe, Zivic, Taton, Hedrick, Long, Sardon. *Prog. Polym. Sci*. **2019**, *90*, 164-210

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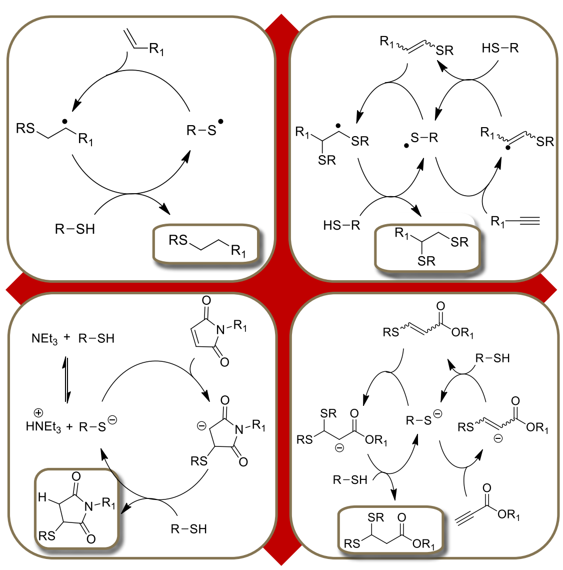
Thiol-ene Additions in Polymer Chemistry



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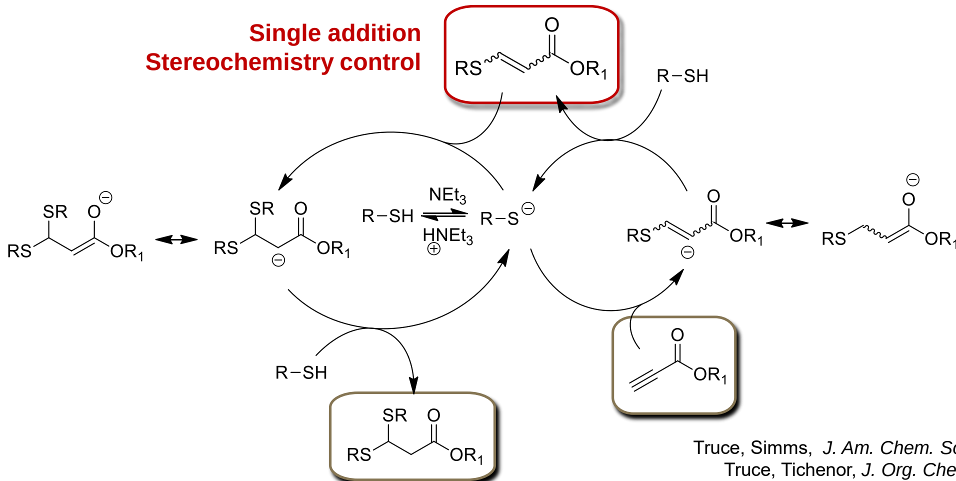
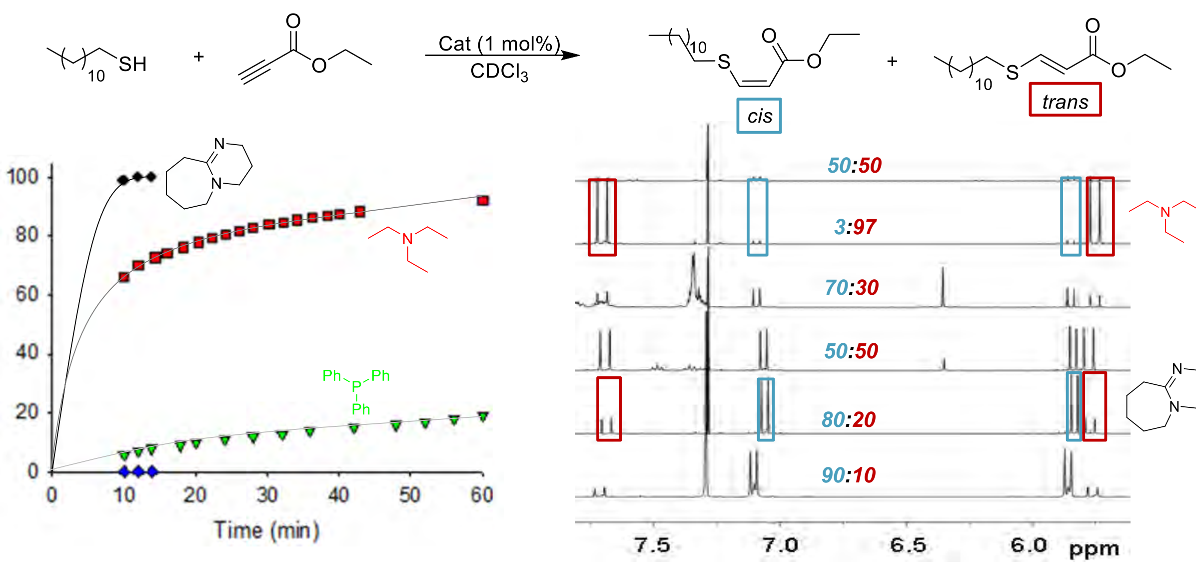
Nucelophilic Thiol-yne Addition



Truce, Simms, *J. Am. Chem. Soc.* 1956, *78*, 2756;
Truce, Tichenor, *J. Org. Chem.* 1972, *37*, 2391;
Halphen, Owen, *J. Org. Chem.* 1973, *38*, 3507.

Worch, Stubbs, Price, Dove, *Chem. Rev*. **2021**, *121*, 6744-6776.

Speed and Selectivity

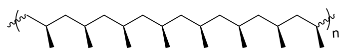


Truong, Dove, *Angew. Chem. Int. Ed.*, **2013**, *52*, 4132-4136

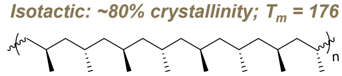
The Importance of Stereochemistry in Polymers

Optical Isomerism

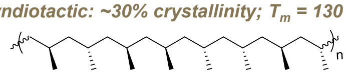
e.g. Polypropylene



Isotactic: ~80% crystallinity; T_m = 176 °C

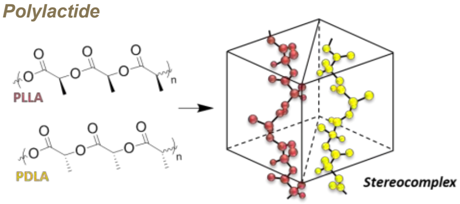


Syndiotactic: ~30% crystallinity; T_m = 130 °C



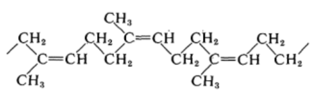
Atactic: amorphous, no defined T_m

or Polylactide

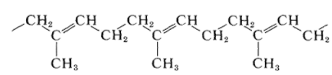


Homopolymer: T_m = 18(UTS = 4 *Stereocomplex: T_m = 240 °C UTS = 8 GPa*

Geometric Isomerism



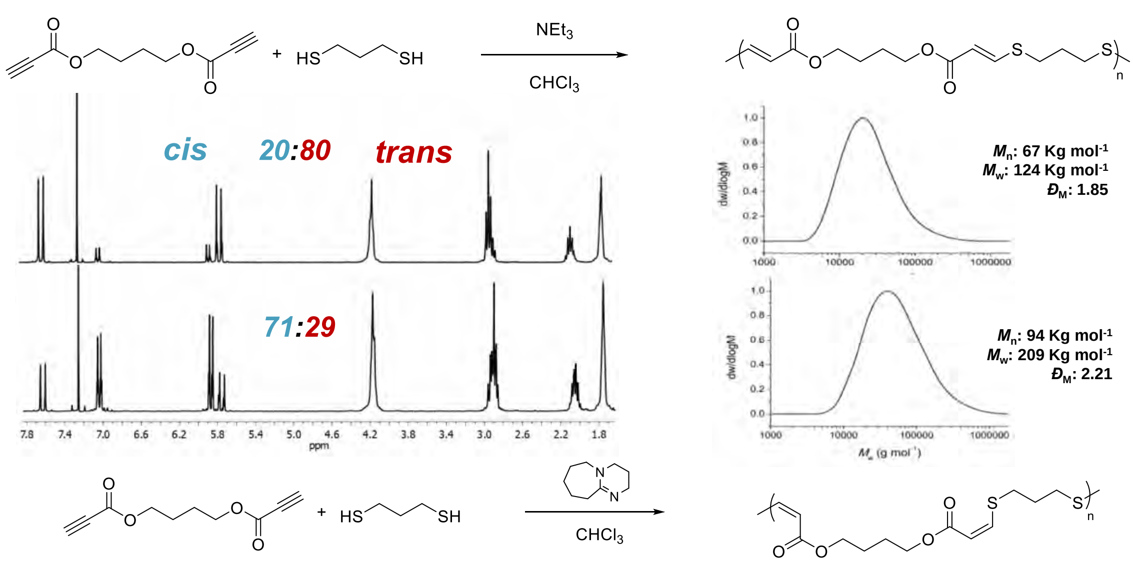
Natural rubber (cis-1,4-polyisoprene)
Elastic, E = 2 MPa



Gutta Percha (trans-1,4-polyisoprene)
Brittle, E = 80 MPa

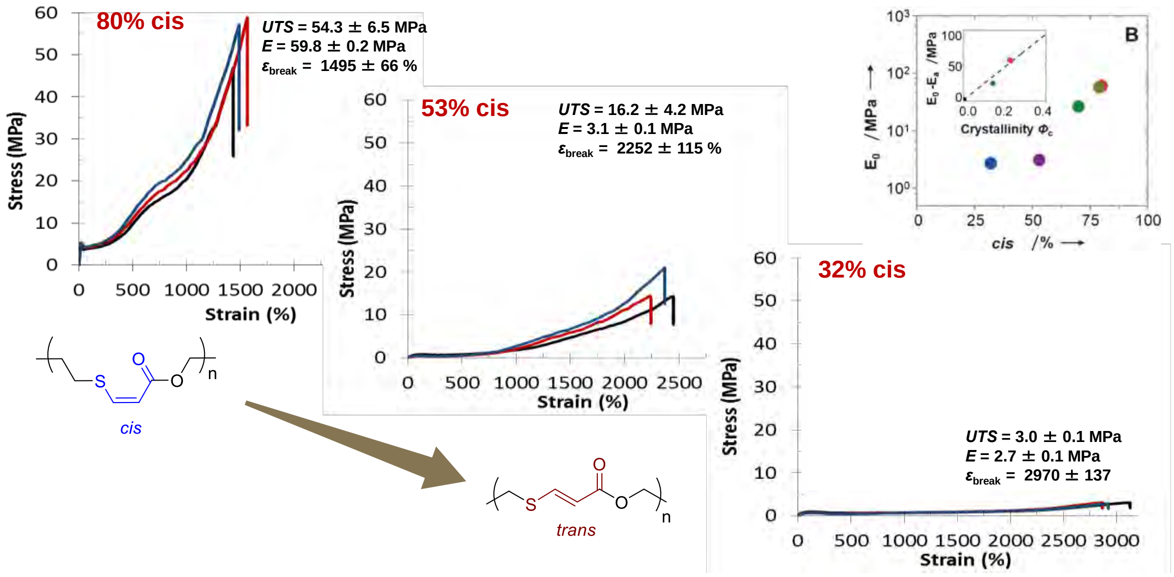
Worch, Prydderch, Jimaja, Bexis, Becker, Dove, *Nat. Rev. Chem.*, **2019**, *3*, 514-535.

Step-Growth Thiol-yne Addition



Bell, Yu, Barker, Truong, Cao, Dobrinyin, Becker, Dove, *Angew. Chem. Int. Ed.*, **2016**, *55*, 13076-13080.

Stereochemistry Dependent Mechanical Properties



Bell, Yu, Barker, Truong, Cao, Dobrinyin, Becker, Dove, *Angew. Chem. Int. Ed.*, **2016**, *55*, 13076-13080.

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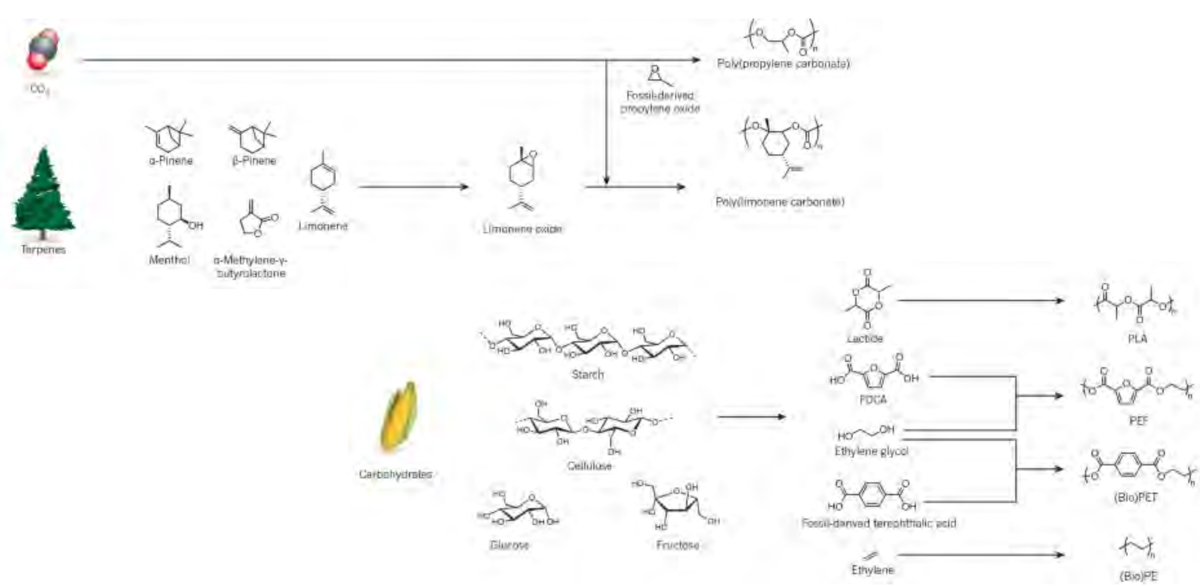
Stereochemistry in Naturally-Sourced Monomers



Zhu, Romain, Williams, *Nature*, **2016**, *540*, 354-362.

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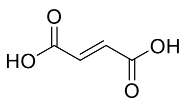
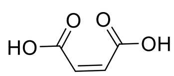
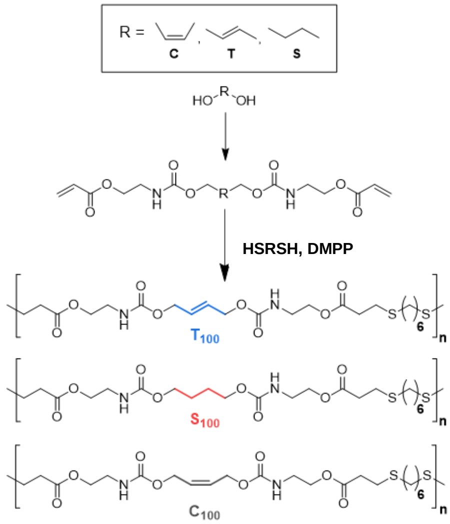
Organocatalytic Thiol-ene Step-Growth

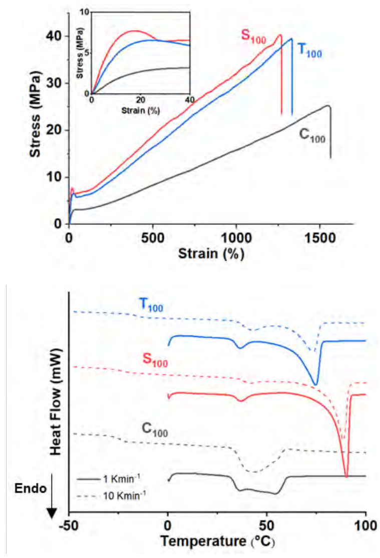


Fumaric Acid



Maleic Acid





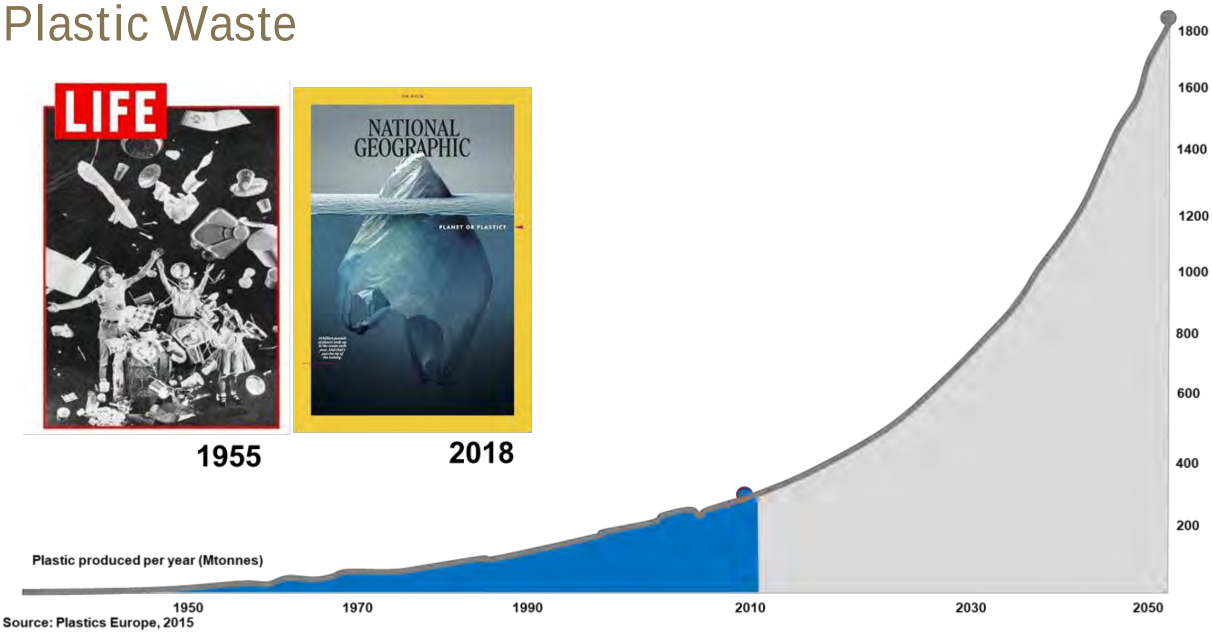
Stubbs, Worch, Prydderch, Becker, Dove, *Macromolecules*, **2020**, *53*, 174-181.

Organocatalytic Step-Growth Polymerisation

Mini-synopsis

- Organocatalysis can be used for a wide range of step-growth polymerisations – the frequently used ones and many more!
- Using organic salts, the thermal stability can be significantly increased to allow higher temperature operation for longer
- Using organocatalyzed nucleophilic thiol-yne addition chemistry, high levels of stereoselectivity can be obtained with which to control polymer properties.

Plastic Waste



Coates, Getzler. *Nat. Rev. Mater.* **2020**, *5*, 501-516 Worch, Dove, *ACS Macro Lett.*, **2020**, *9*, 1494-1506.

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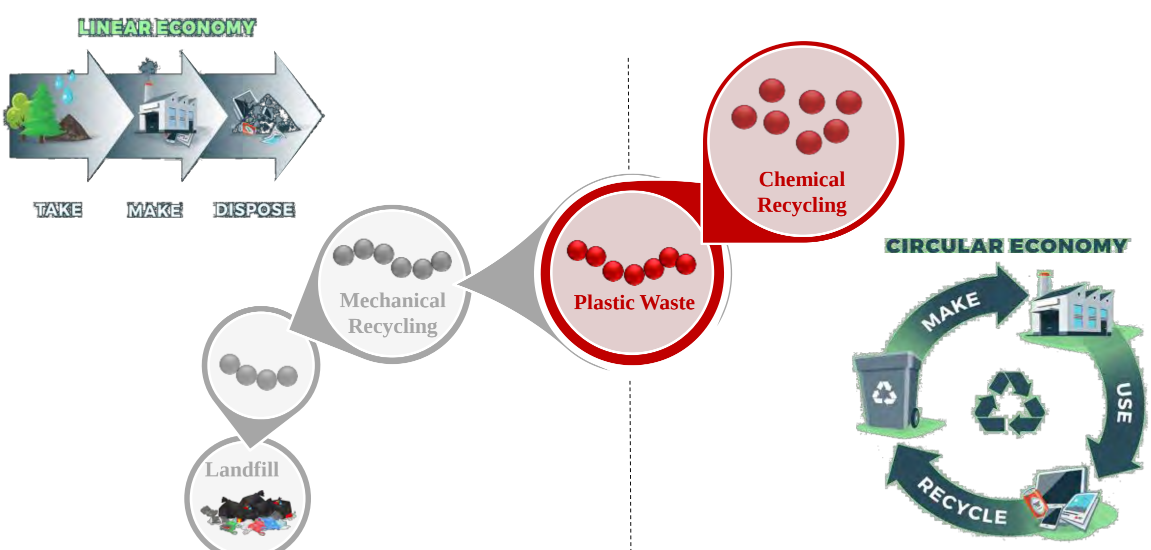
Overview of Plastic Recycling Options



Coates, Getzler. *Nat. Rev. Mater.* **2020**, *5*, 501-516

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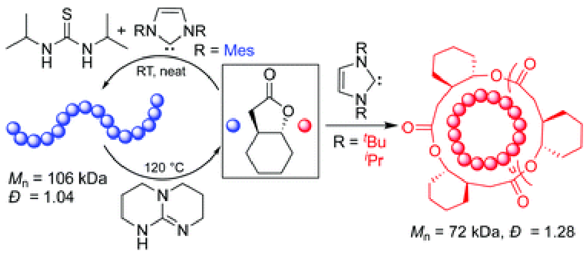
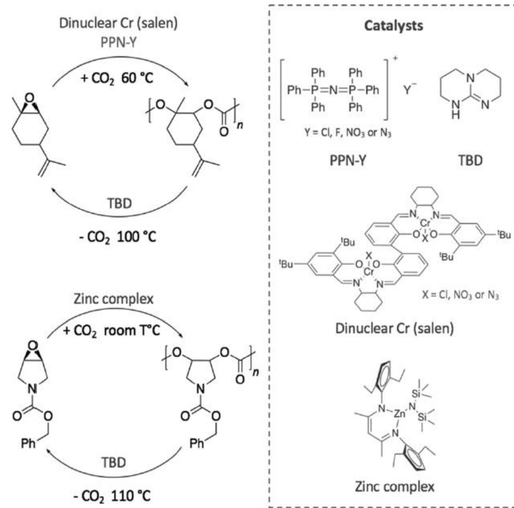
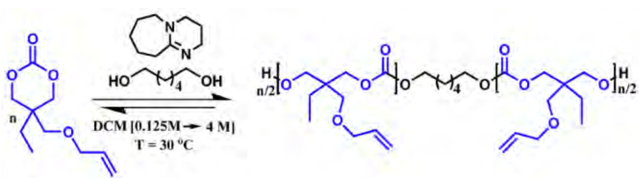
Organocatalytic Circular Economy Approaches



Cywar, Zhu, Chen. *Polym. Chem.* **2019**, *10*, 3097-3106





Olsen, Undin, Odelius, Keul, Albertsson, *Biomacromolecules* **2016**, *17*, 3995-4002

Liu, Zhou, Guo, Ren, Lu, *Angew. Chem. Int. Ed.* **2017**, *56*, 4862-4866.
Li, Sablong, van Benthem, Koning, *ACS Macro Lett*. **2017**, *6*, 684-688.

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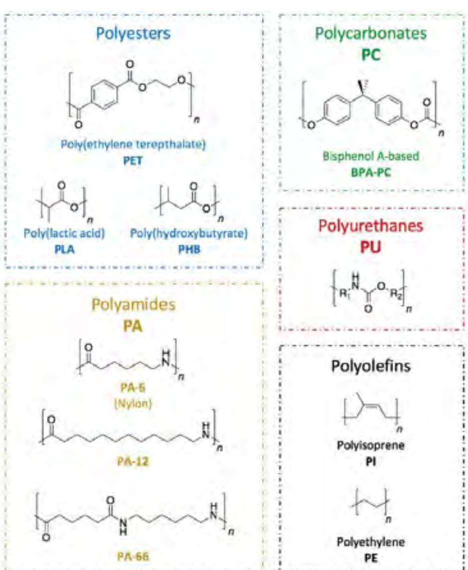
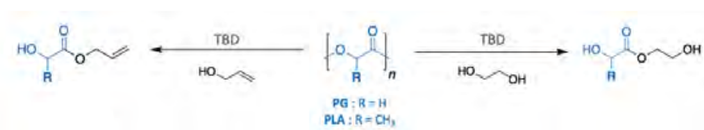
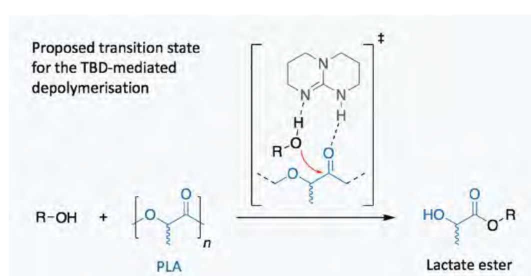
Organocatalytic Depolymerisation







Leibfarth, Moreno, Hawker, Shand, J. Polym. Sci., Part A: Polym. Chem., 2012, 50, 4814–4822.

Jehanno, Perez-Madrigal, Demarteau, Sardon, Dove. *Polym. Chem*. **2019**, *10*, 172-186

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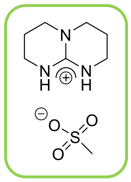
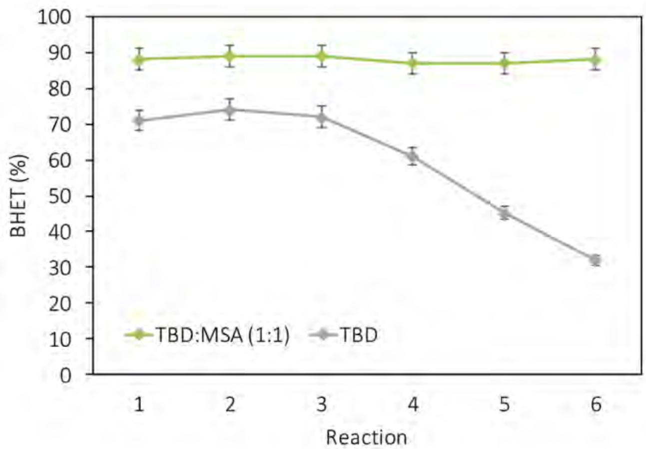
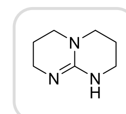
Higher Temperature Stability

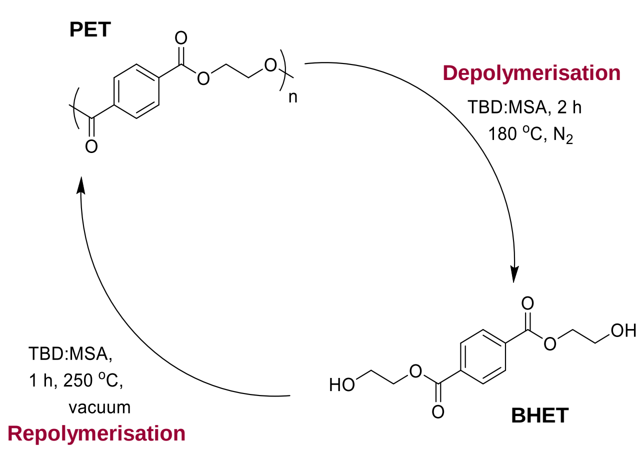


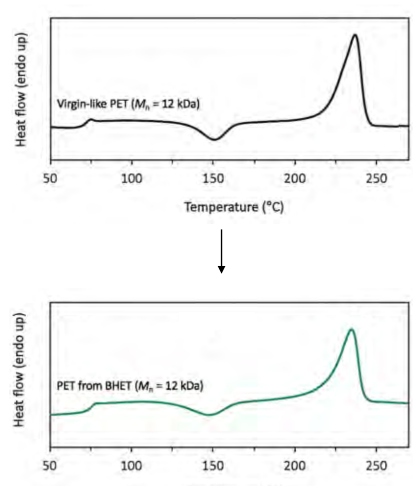




Jehanno, Flores, Dove, Muller, Rupierez, Sardon, *Green Chem.*, **2018**, *20*, 1205-1212.

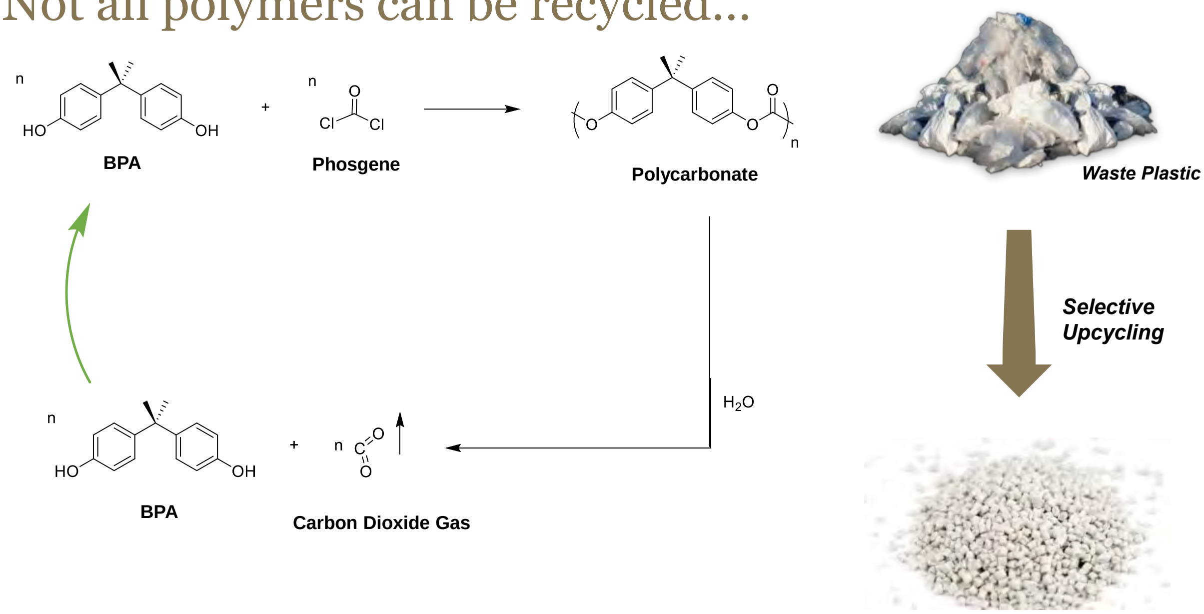
Depolymerise and Repolymerise



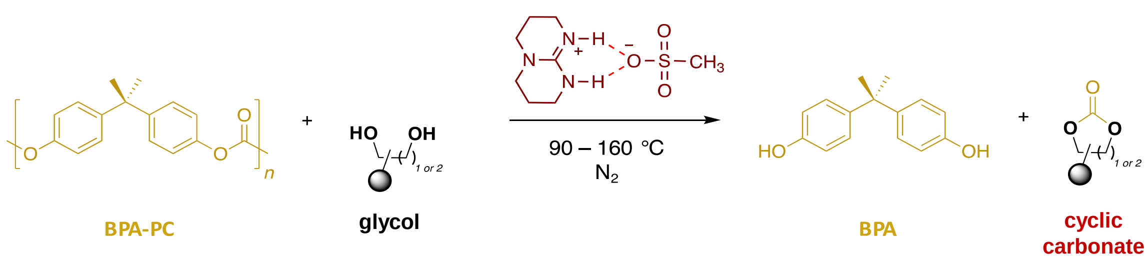


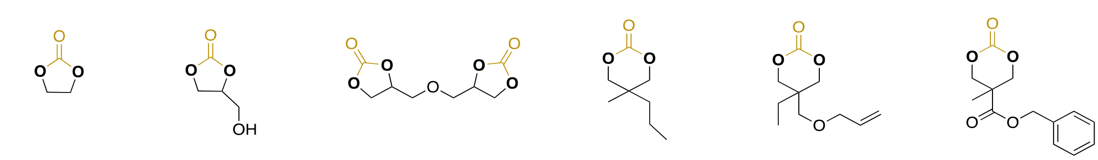
Jehanno, Flores, Dove, Muller, Rupierez, Sardon, *Green Chem.*, **2018**, *20*, 1205-1212.

Not all polymers can be recycled…



Upcycling to Aliphatic Polycarbonates

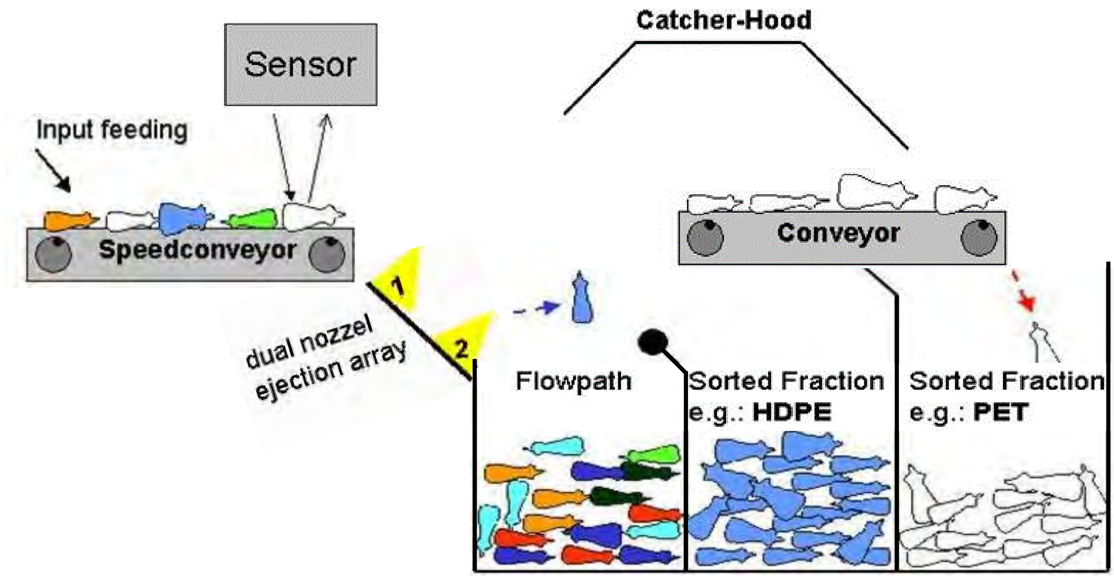




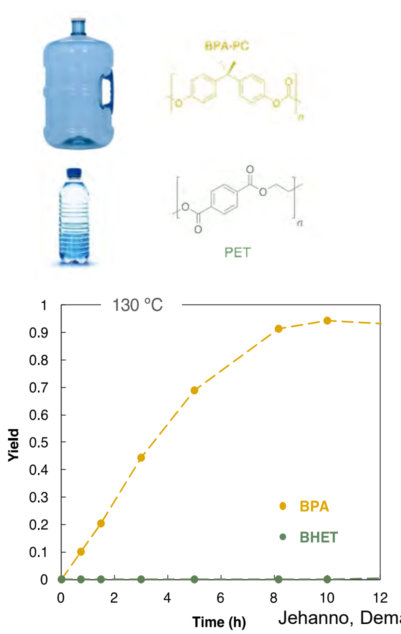
130 °C - 5h	160 °C - 2h	160 °C - 8h	130 °C - 3h	130 °C - 1h30	130 °C – 3h
83% (78%)	**90% (86%)**	**87% (84%)**	**77%**	**97% (88%)**	**96%**

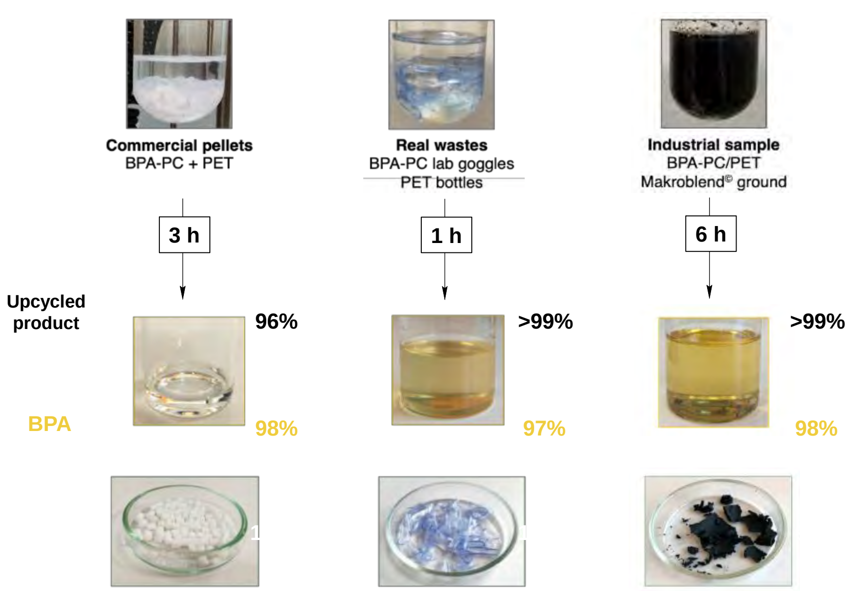
Jehanno, Demarteau, Mantione, Arno, Ruipérez, Hedrick, Dove, Sardon, *ACS Macro Lett.*, **2020** *9*, 443-447

Mixed Plastics



Selective Chemical Depolymerisation





Jehanno, Demarteau, Mantione, Arno, Ruipérez, Hedrick, Dove, Sardon, *Angew. Chem. Int. Ed.*, 2021 *60*, 6710-6717

Organocatalytic Depolymerisation

Mini-synopsis

- In the same way that organic catalysis offers excellent opportunities to create polymers, it offers excellent methods for depolymerisation of a wide range of polymers
- Thermally-stable catalysts offer a high activity alternative at high temperatures
- Leveraging kinetic differences in depolymerisation rate, different plastics can be selectively and sequentially depolymerised.

Acknowledgements

Co-workers
Dr Josh Worch
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Louisa Brenninkmeijer
Connor Stubbs

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Dr Vinh Truong (PDRA)
Dr Craig Bell (PDRA)
Dr Ian Barker (PDRA)

Key Academic Collaborators
Prof. Matthew Becker (Duke University, USA)
Dr Haritz Sardon (POLYMAT, Spain)

erc European Research Council
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Further Reading

Reviews

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Worch, Stubbs, Price, Dove, *Chem. Rev.* **2021**, *121*, 6744-6776.

Stereochemical enhancement of polymer properties.
Worch, Prydderch, Jimaja, Bexis, Becker, Dove, *Nat. Rev. Chem*., **2019**, *3*, 514-535.

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Chemically recyclable polymers: a circular economy approach to sustainability.
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Sustainable polymers from renewable resources.
Zhu, Romain, Williams, *Nature*, **2016**, *540*, 354-362.

Toward Catalytic Chemical Recycling of Waste (and Future) Plastics.
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Organocatalysis for depolymerisation.
Jehanno, Perez-Madrigal, Demarteau, Sardon, Dove. *Polym. Chem*. **2019**, *10*, 172-186

Original Research Articles

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Bell, Yu, Barker, Truong, Cao, Dobrinyin, Becker, Dove, *Angew. Chem. Int. Ed.*, **2016**, *55*, 13076-13080.

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Unsaturated Poly(ester-urethanes) with Stereochemically Dependent Thermomechanical Properties.
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Synthesis of Functionalized Cyclic Carbonates through Commodity Polymer Upcycling.
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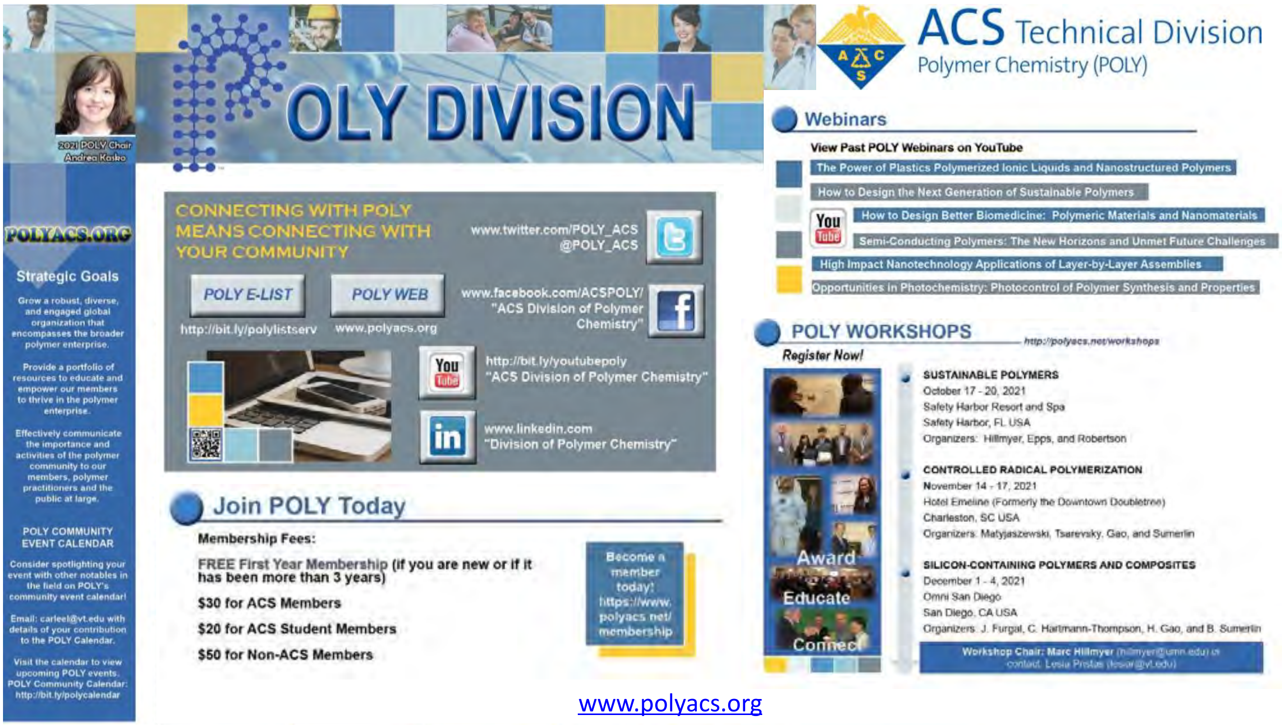

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Designing Around Structural Alerts in Drug Discovery

Date: Friday, September 17, 2021 @ 2-3:15pm ET
Speaker: Nick Meanwell, Bristol-Myers Squibb
Moderator: Deepak Dalvie, Crinetics Pharmaceuticals

Register for Free!

What You Will Learn:

- The identity of structural alerts that have been associated with problems in drug discovery and development
- The fundamental mechanistic organic chemistry subtending structural alerts that are subject to bioactivation
- Strategies and tactics to design around structural alerts

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Service Dogs in Your Chemistry Lab

Date: Wednesday, September 22, 2021 @ 2-3pm ET
Speakers: Patricia Redden, Saint Peter's University / Joey Ramp, Empower Ability Consulting, LLC / Ashley Neybert, Independence Science
Moderator: Partha Basu, Indiana University-Purdue University Indianapolis

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What You Will Learn:

- What does the Americans with Disabilities Act cover regarding access rights for service dogs
- How is a service dog selected for certain jobs or disabilities, and what type of training is required
- What types of service dogs exist and what is the process to obtain one

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Molecules to Manufacturing to Marketplace

3D Printing of Sulfonated Polyesters for Controlled Release

Date: Thursday, September 23, 2021 @ 2-3:15pm ET
Speakers: Timothy Long, Arizona State University and Michael Bortner, Virginia Tech
Moderator: Bryan Tweedy, American Chemical Society

Register for Free!

What You Will Learn:

- What is the impact of polyester ionomers and macromolecular architecture on processability and performance of 3D printed structures
- How to leverage rheology for predictive additive manufacturing system design and materials screening
- A snapshot of the topics and concepts captured in the ACS Polymer Chemistry: Principles and Practice short course held at Virginia Tech

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Date: Friday, September 17, 2021 @ 2-3:15pm ET
Speaker: Nick Meanwell, Bristol-Myers Squibb
Moderator: Deepak Dalvie, Crinetics Pharmaceuticals

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What You Will Learn:

- The identity of structural alerts that have been associated with problems in drug discovery and development
- The fundamental mechanistic organic chemistry subtending structural alerts that are subject to bioactivation
- Strategies and tactics to design around structural alerts

Co-produced with: ACS Division of Medicinal Chemistry, American Association of Pharmaceutical Scientists, and ACS Publications

Date: Wednesday, September 22, 2021 @ 2-3pm ET
Speakers: Patricia Redden, Saint Peter's University / Joey Ramp, Empower Ability Consulting, LLC / Ashley Neybert, Independence Science
Moderator: Partha Basu, Indiana University-Purdue University Indianapolis

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What You Will Learn:

- What does the Americans with Disabilities Act cover regarding access rights for service dogs
- How is a service dog selected for certain jobs or disabilities, and what type of training is required
- What types of service dogs exist and what is the process to obtain one

Co-produced with: Chemists with Disabilities (CWD) Committee, ACS Department of Diversity Programs, and ACS Diversity, Inclusion & Respect Advisory Board

Date: Thursday, September 23, 2021 @ 2-3:15pm ET
Speakers: Timothy Long, Arizona State University and Michael Bortner, Virginia Tech
Moderator: Bryan Tweedy, American Chemical Society

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What You Will Learn:

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