CAOS

THE 3RD
NCTU

CONFERENCE ON ADVANCED ORGANIC SYNTHESIS

TAMIO HAYASHI
TODD L. LOWARY
RONG-JIE CHEIN
CHIA-CHIH CHANG
RACHEL A. LETTERI

Room 210, Science Building II
National Chiao Tung University
December 3, 2020

3rd NCTU Conference on Advanced Organic Synthesis

December 3 (Thursday), 2020; Room 210, Science Building II, NCTU

Program Schedule		
Lecture 1 (online)	***Engineering Mirror Image Peptide Complexes as Dynamic, Biologically Interactive Elements of Polymer Biomaterials***	
09:30 – 10:00	Rachel A. Letteri (University of Virginia)	*Chair: Chia-Chih Chang*
10:00 – 12:00	Lab Tour & Graduate Student Research Discussion	*Chair: Shu-Pao Wu*
12:00 – 14:00	Lunch / Registration	
14:00 – 14:10	CAOS Short Speech by Ilhyong Ryu	
Lecture 2	***Synthesis of Complex Microbial Glycans***	
14:10 – 15:00	Todd L. Lowary (University of Alberta, Academia Sinica)	*Chair: Kwok-Kong Mong*
Lecture 3	***Designing Material Systems Featuring Mechanochemically Triggered Chemical Cascade***	
15:00 – 15:30	Chia-Chih Chang (National Chiao Tung University)	*Chair: Yoshito Tobe*
15:30 – 16:00	Coffee Break	
Lecture 4	***Recent Advances in Rhodium-Catalyzed Asymmetric Arylation***	
16:00 – 16:50	Tamio Hayashi (National Tsing Hua University)	*Chair: Ilhyong Ryu*
Lecture 5	***In Search of Treatment for COVID-19 – Synthesis of Remdesivir and Development of Antiviral Drugs***	
16:50 – 17:20	Rong-Jie Chein (Academia Sinica)	*Chair: Yen-Ku Wu*
17:20 – 17:30	Closing Remark	
18:00 – 20:00	Reception at Versailles – by invitation only	

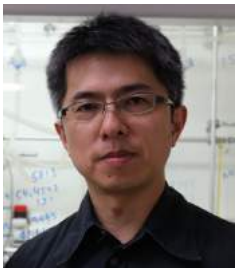
Invited Lecturers

Prof. Rachel A, Letteri (University of Virginia)

Prof. Todd L. Lowary (University of Alberta, Academia Sinica)

Prof. Chia-Chih Chang (NCTU)

Prof. Tamio Hayashi (NTHU)



Prof. Rong-Jie Chein (Academia Sinica)

Organizing Committee

Ilhyong Ryu	Kwok-Kong Mong	Yoshito Tobe	Wen-Sheng Chung
Chung-Ming Sun	Shih-Ching Chuang	Yen-Ju Cheng	Chien-Lung Wang
Yen-Ku Wu	Chia-Chih Chang	Hsueh-Ju Liu	Shu-Pao Wu

Sponsored by

Department of Applied Chemistry and Center for Emergent Functional Matter Science at National Chiao Tung University

Chairmen of CAOS-3

Ilhyong Ryu and Kwok-Kong Mong

Contact

Yen-Ku Wu (E-mail yenkuwu@nctu.edu.tw; Tel 03-5712121 #56505)

Engineering mirror image peptide complexes as dynamic, biologically interactive elements of polymer biomaterials

Rachel A. Letteri
Department of Chemical Engineering, University of Virginia
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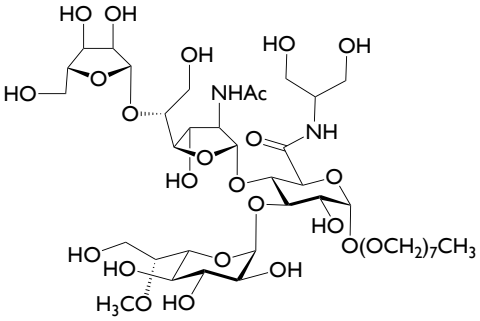
Towards capturing the highly specific, tunable properties of biological systems, we are developing mirror image peptide complexes, or 'stereocomplexes', as bio-interactive, transient junctions in synthetic polymer biomaterials. Building on findings that enantiomeric mixtures of stereoregular polymers or peptides exhibit enhanced stability and mechanical properties relative to the individual components, this talk will describe our group's research on mirror image peptide stereocomplexes as DNA- and coiled coiled peptide-mimetic components of polymer biomaterials. We use a combination of circular dichroism spectroscopy, isothermal titration calorimetry, nuclear magnetic resonance spectroscopy, rheology, and microscopy to connect peptide secondary structure to interactions between enantiomers, and rheology to connect stereocomplex strength to the properties of polymer- and peptide stereocomplex-containing biomaterials. For a series of model α-helical peptides, we investigated the effects of end groups and length on helicity for connection to interactions between enantiomers and the properties of polymer hydrogels cross-linked with these complexes. For β sheet-forming peptides, morphological transitions occurred upon mixing enantiomers that impact biomaterial mechanical properties. Going forward, we look forward to using peptide stereocomplexation to impart a myriad of biomimetic properties to polymer biomaterials, including self-healing and shear thinning behaviors, useful for 3D printing-based manufacturing processes and targeting biological proteins, among other applications.

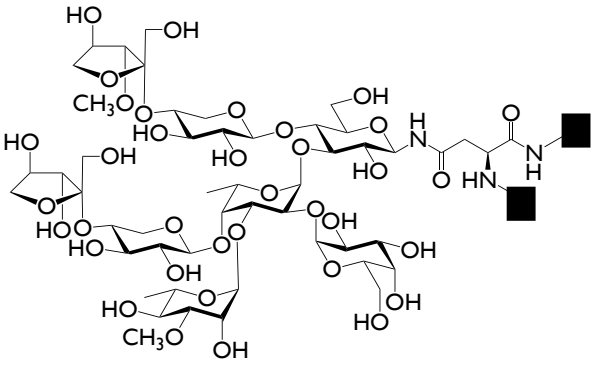
Bio: Rachel A. Letteri is an Assistant Professor of Chemical Engineering at the University of Virginia. She obtained a B.S. in Chemical & Biomolecular Engineering from the University of Notre Dame in 2010 and a Ph.D. in Polymer Science & Engineering from the University of Massachusetts Amherst in 2016. Her graduate research, under the direction of Professors Todd Emrick and Ryan Hayward, involved the synthesis and assembly of functional hydrophilic polymers. Rachel joined the laboratory of Professor Karen Wooley in the Department of Chemistry at Texas A&M University as a postdoctoral researcher in 2016, and investigated the impact of stereochemistry on the assembly of amphiphilic block polypeptides. At UVa, the Letteri group is engineering adaptive polymer-peptide composites that display a breadth of thermomechanical properties and promote productive interactions with biological systems. By leveraging the rich variety of polymer and peptide molecular interactions in solution and at interfaces, her lab will develop materials with shear-thinning, self-healing, shape-memory, and molecular recognition properties to enable 3D printing of regenerative scaffolds and new therapeutic strategies for Amyotrophic Lateral Sclerosis, multi-drug resistant bacterial infections, among other applications. Rachel serves as a member of the *ACS Biomaterials Science & Engineering* Early Career, the *Journal of Polymer Science*, and the *Polymer Chemistry* editorial advisory boards, and enjoys outreach activities with her research group to engage local students and the community in polymer science and engineering.

Synthesis of Complex Microbial Glycan Probes

Todd L. Lowary
Department of Chemistry, University of Alberta, Edmonton, Alberta Canada
Institute of Biological Chemistry, Academia Sinica, Nangang Taipei, Taiwan
E-mail: tlowary@gate.sinica.edu.tw, tlowary@ualberta.ca

Synthetic glycoconjugates are essential biological probes. This seminar will describe ongoing investigations focused on synthesizing two classes of complex glycans: 1) fragments of capsular polysaccharides from *Campylobacter jejuni* an important food borne pathogen (e.g., structure on the left) and 2) *N*-linked glycans from chlorella viruses (e.g., structure on the right).





Education

1989–1993	Ph.D., Chemistry, University of Alberta, Canada
1984–1988	B. A., Chemistry, University of Montana, USA

Professional Experience

2019–Present	Distinguished Research Fellow, Institute of Biological Chemistry Academia Sinica, Taiwan
2015–Present	R. U. Lemieux Professor of Carbohydrate Chemistry, Department of Chemistry, University of Alberta, Canada
2006–Present	Professor, Department of Chemistry, University of Alberta, Canada
2003–2006	Associate Professor, Department of Chemistry, University of Alberta, Canada
2002–2003	Associate Professor, Department of Chemistry, The Ohio State University, USA
1996–2002	Assistant Professor, Department of Chemistry, The Ohio State University, USA
1995–1996	Postdoctoral Fellow, Carlsberg Laboratory, Denmark
1993–1995	Postdoctoral Fellow, Department of Chemistry, University of Alberta, Canada

Designing material systems featuring mechanochemically triggered chemical cascade

Chia-Chih Chang
Department of Applied Chemistry, National Chiao Tung University
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Covalent polymer mechanochemistry offers many opportunities for constructing advanced material systems that are capable of stress-sensing, stress-strengthening and self-healing. Externally applied mechanical force can be exploited to promote selective chemical transformation in the overstressed region, resulting in the formation of new functional groups at the polymer chain scission point. Molecular engineering of mechanochemically responsive motifs provides a means for exploiting organic chemistry in the context of force-responsive materials. In this talk, we will discuss three material systems that can generate reactive chain ends, undergo retro-Diels-Alder reaction to unveil a highly fluorescent anthracene derivative, and delayed scission. Specifically, mechanochemical generation of isocyanates proves feasible through retro [2 + 2] cycloaddition of a 1,2-diazetidinone mechanophore; assessment of material damage is realized with retro [4 + 2] cycloaddition of a anthracene-maleimide mechanophore, and the concept for programmable polymer degradation is demonstrated by utilizing mechanically triggered ring-opening of a [4.2.0]bicyclooctene mechanophore that sets up a delayed, force-free cascade lactonization.

Chia-Chih Chang is an Assistant Professor of Applied Chemistry at National Chiao Tung University in Taiwan. Chia-Chih obtained a B.S in Chemistry from Colorado School of Mines and performed his Ph.D. studies under the guidance of Prof. Todd Emrick at the University of Massachusetts, Amherst in the U.S.A. His doctoral research focused on the development of interfacially active material platforms based on zwitterionic polymers with tailored functionalities for encapsulation and surface modification. He then moved to Duke University in 2016 and joined the research group of Prof. Stephen L. Craig as a postdoctoral researcher, where he began his adventure of designing mechanochemically active material systems.

Recent Advances in Rhodium-Catalyzed Asymmetric Arylation

Tamio Hayashi
Department of Chemistry, National Tsing Hua University
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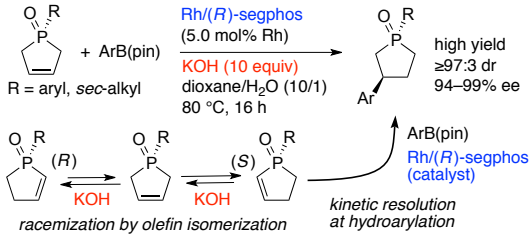
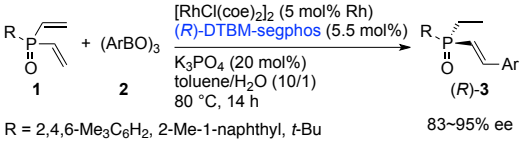
The rhodium-catalyzed asymmetric conjugate arylation of electron-deficient olefins with arylboron reagents has been recognized to be one of the most efficient and reliable methods of introducing aromatic groups with high enantioselectivity. The scope of olefinic substrate is very broad and the asymmetric arylation has been applied to the synthesis of a wide variety of enantioenriched compounds where the stereogenic center is at benzylic position. Here some of recent advances[1] in the rhodium-catalyzed asymmetric arylation will be presented, which include; 1) asymmetric hydroarylation of alkenyl sulfones and alkenylphosphine oxides, 2) asymmetric arylation/defluorination of 1-(trifluoromethyl)alkenes forming chiral 1,1-difluoro-alkenes, 3) desymmetrization of divinylphosphine oxides, and 4) asymmetric synthesis of SPINOLs by double arylation.

Dynamic kinetic resolution of phospholene oxides



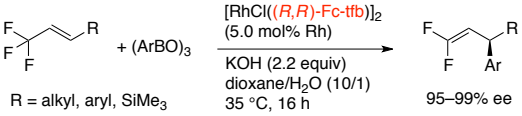
Lim, K. M.-H.; Hayashi, T. *J. Am. Chem. Soc.* **2017**, *139*, 8122.

Desymmetrization of divinylphosphine oxides



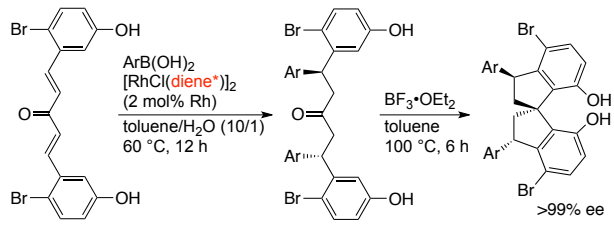
Wang, Z.; Hayashi, T. *Angew. Chem. Int. Ed.* **2018**, *57*, 1702.

Asymmetric arylation/defluorination



Huang, Y.; Hayashi, T. *J. Am. Chem. Soc.* **2016**, *138*, 12340.

Asymmetric synthesis of 3,3'-diaryl-SPINOLs



Lu, T.; Hayashi, T.; Dou, X. et al. *Angew. Chem. Int. Ed.* **2019**, *58*, 2474.

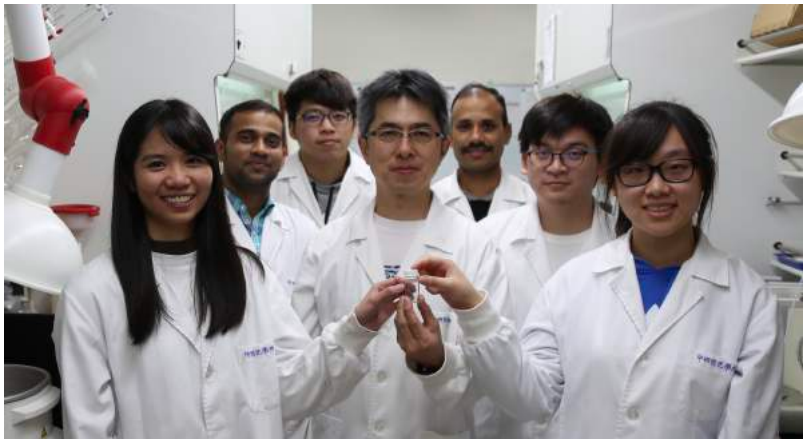
[1] Recent publications on Rh-catalyzed asymmetric arylation. (a) Chen, J.; Hayashi, T. *Angew. Chem. Int. Ed.* **2020**, *59*, 18510. (b) Yin, L.; Xing, J.; Wang, Y.; Shen, Y.; Lu, T.; Hayashi, T. Dou, X. *Angew. Chem. Int. Ed.* **2019**, *58*, 2474. (c) Xue, F.; Hayashi, T. *Angew. Chem. Int. Ed.* **2018**, *57*, 10368. (d) Wang, Z.; Hayashi, T. *Angew. Chem. Int. Ed.* **2018**, *57*, 1702. (e) Lim, K. M.-H.; Hayashi, T. *J. Am. Chem. Soc.* **2017**, *139*, 8122. (f) Huang, Y.; Hayashi, T. *J. Am. Chem. Soc.* **2016**, *138*, 12340. (g) Dou, X.; Lu, Y.; Hayashi, T. *Angew. Chem. Int. Ed.* **2016**, *55*, 6739.

2020–: Professor, National Tsing Hua University
2016–2019: Professor, Nanyang Technological University
2013–2016: Professor, National University of Singapore
2012–2016: Principal Scientist II, A*STAR, IMRE, Singapore
1994–2012: Professor, Graduate School of Science, Kyoto University
1989–1994: Professor, Catalysis Research Center, Hokkaido University
1976–1977: Postdoc, Colorado State University, USA
1975–1989: Assistant Professor, Faculty of Engineering, Kyoto University
1975: PhD, Faculty of Engineering, Kyoto University

In Search of Treatment for COVID-19 – Synthesis of Remdesivir and Development of Antiviral Drugs

Rong-Jie Chein
Institute of Chemistry, Academia Sinica
E-mail: rjchein@chem.sinica.edu.tw

Remdesivir is a broad-spectrum antiviral medication developed by the biopharmaceutical company Gilead Sciences and is currently the only registered drug for treating COVID-19 patients. As part of the search to make available potential remedies for the coronavirus, six of our group members in Academia Sinica started the Remdesivir Synthesis Project on February 6th of 2020 under the direction of President James C. Liao, completed the hundred-milligram-scale synthesis of Remdesivir in 2 weeks, and immediately followed by a 99% purity gram-scale synthesis in just 4 days. The project was started from scratch as acquiring the relatively rare starting materials was difficult during the pandemic, and as the result, the already complicated synthetic process had to be expanded from 11 to 20 steps. In this presentation, the development, mechanism of action, and large-scale manufacturing of Remdesivir are also discussed.



[1] M. L. Holshue et al., *N. Engl. J. Med.,* **2020**, *382*, 929-936.

[2] R. L. Mackman et al., *J. Med. Chem.,* **2017**, *60*, 1648-1661.

[3] R. Berisio et al. *Cell*, **2020**, *9*, 1267

[3] Z. Rao et al., *Science*, **2020**, *368*, 779–782.

Rong-Jie Chein (陳榮傑). National Chiao Tung University (Ph.D., 2005). Harvard University (Postdoc, E. J. Corey Lab, Jan. 2007 - June 2009). Academia Sinica (Assistant Research Fellow, July 2009 - April 2015, Associate Research Fellow, May 2015 -).
[Field of research] (1) Development of new synthetic strategies and methods. (2) Total synthesis and the study of the chemistry and biology of natural products and designed molecules.

CAOS-3