Asymmetric Organocatalysis: The Emerging Utility of α,β-Unsaturated Acylammonium Salts

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Date: 2018-10-29

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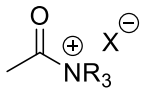
- **Education & Work Experience**
  B.A.： 1982-1986，Chemistry/Biology， Texas A&M
  Ph.D： 1986-1991，Colorado State University
  Post-Doctoral： 1991-1993，Harvard University (with Prof. Stuart L. Schreiber)
  Assistant Professor of Chemistry：1993-1999，Texas A&M
  Associate Professor of Chemistry：1999-2003，Texas A&M
  Professor of Chemistry：2003-2016，Texas A&M
  Baylor University: 2015-present

- **Research Interests**
  Research interests include total synthesis toward mechanism-of-action studies of natural products and methodology focused on novel organocascade processes.

Contents

1. Introduction

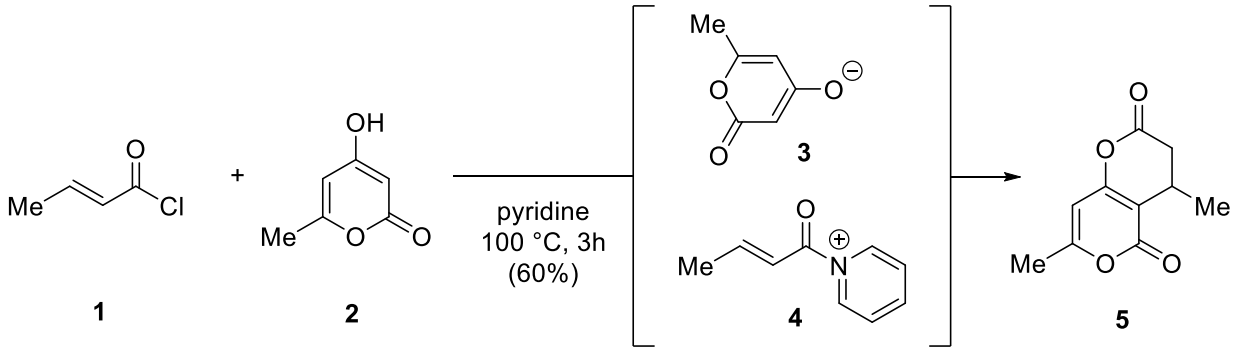
- **The seminal work of Wegler in 1932 demonstrated the potential of chiral acylammonium salts A for asymmetric acyl-transfer processes.**



acylammonium salts

A

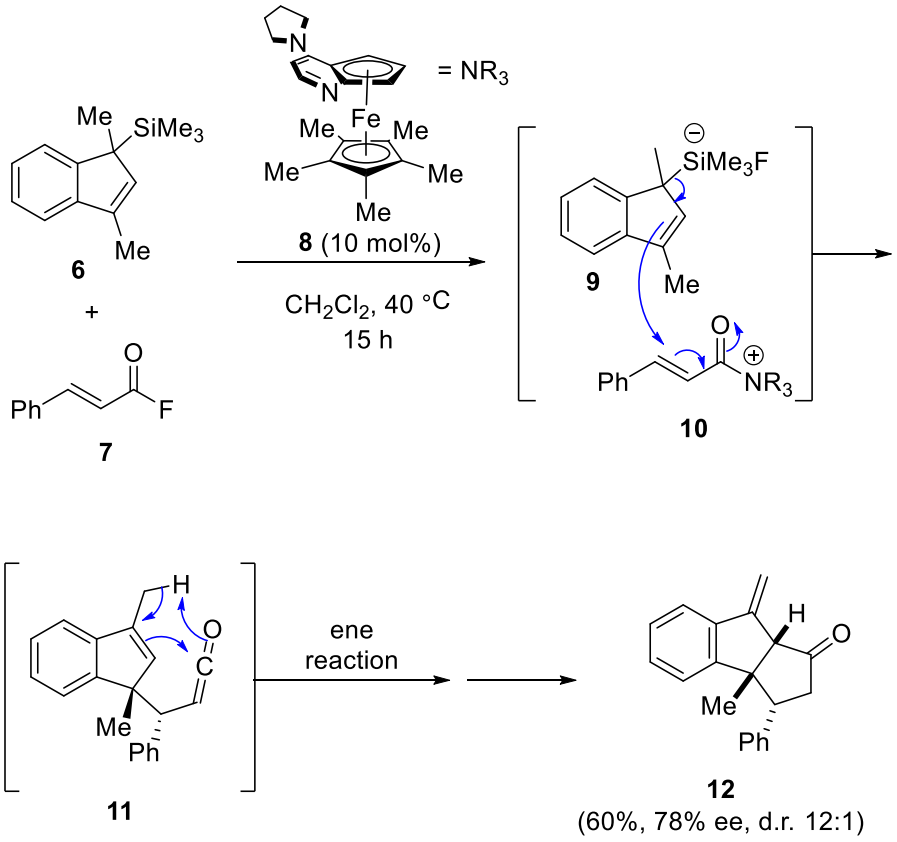
- **In the 1960s, Yamamura first studied α,β-unsaturated acylammonium salts for Michael reactions/lactonization reactions by employing pyridine as both a solvent and a Lewis base.**



*Chem. Commun.**1968,*** 324–325.

1. Introduction

- **In 2006, the group of Fu introduced the first use of chiral α,β - unsaturated acylammonium salts for an organocascade reaction.**

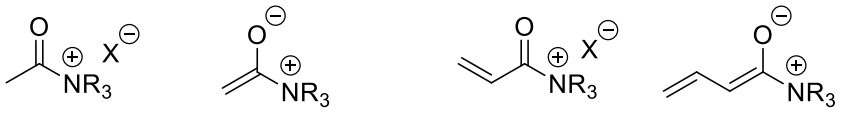


Chem. Commun. **2006,** 2604 –2606.

1. Introduction

- **These discoveries ultimately ushered in a new family of chiral intermediates for organocatalysis, the acylammonium family.**

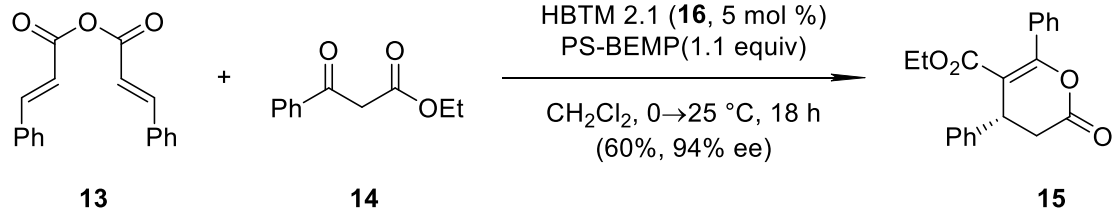
Acylammonium Family of Chiral Intermediates

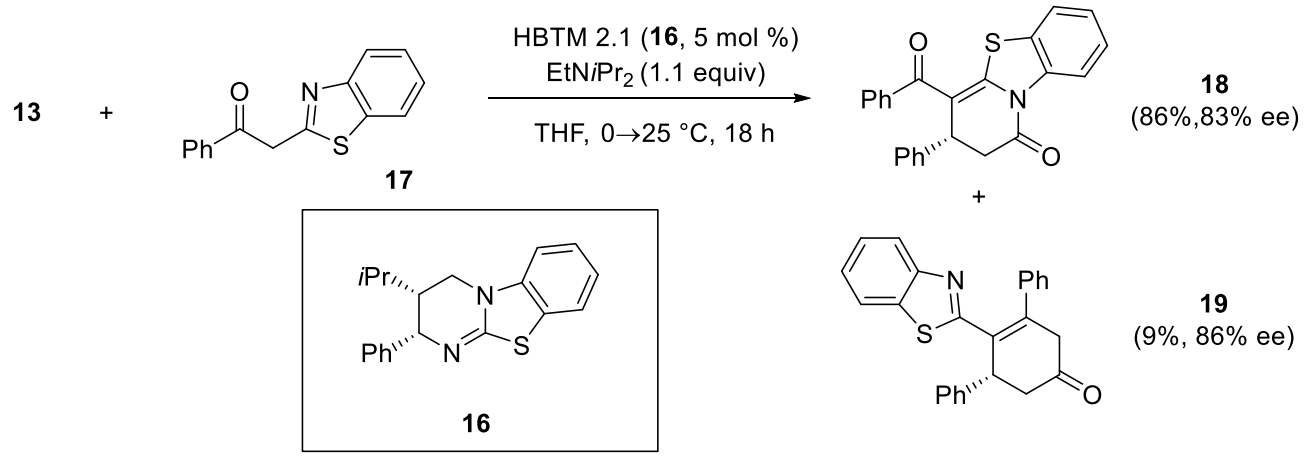


acylammonium salts	ammonium enolates	α,β-unsaturated acylammonium salts	ammonium dienolates
A	B	C	D

2.1 Conjugate Additions

Smith

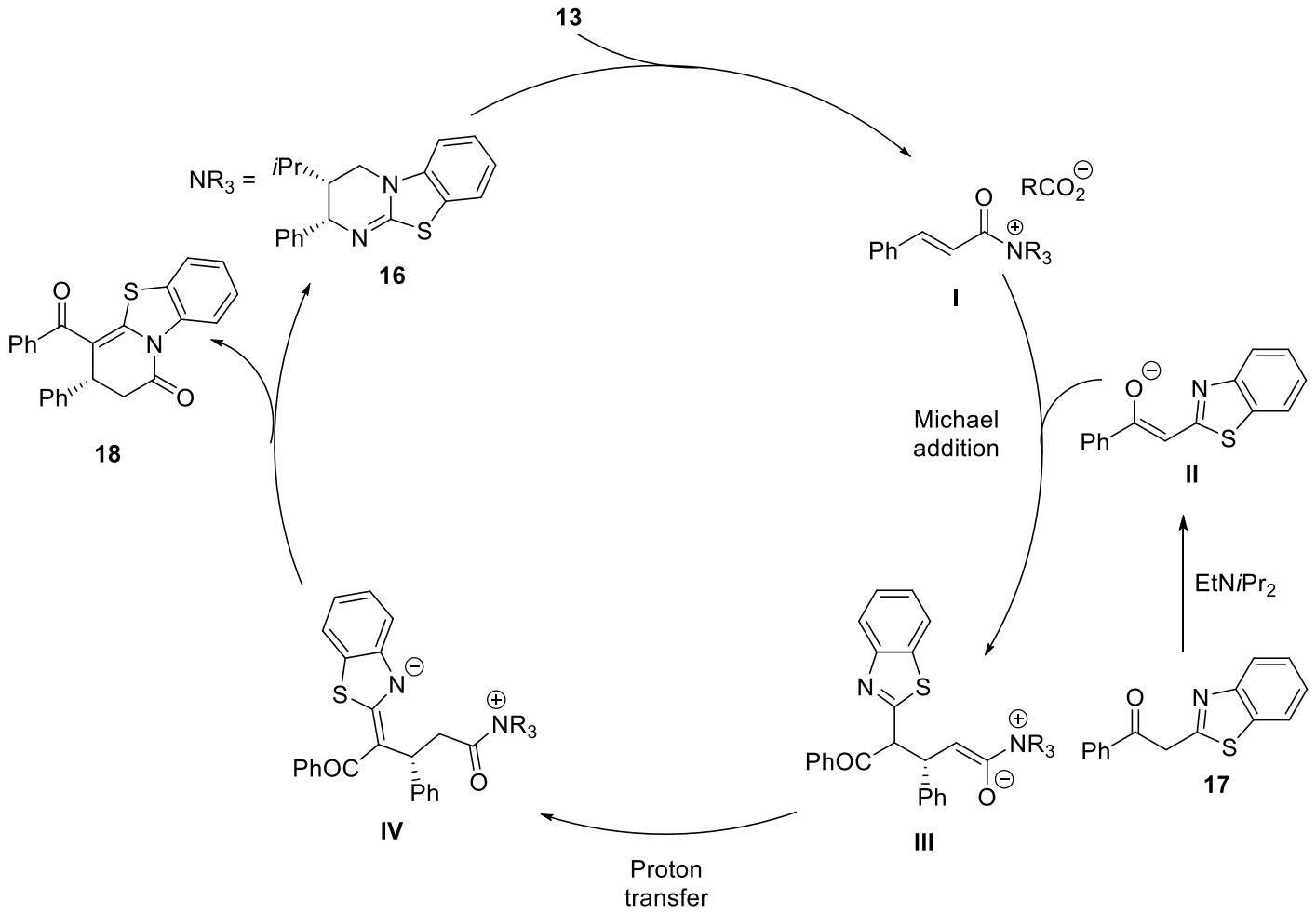




Tetrahedron Lett., **2006** 47, 4347–4350.

2.1 Conjugate Additions

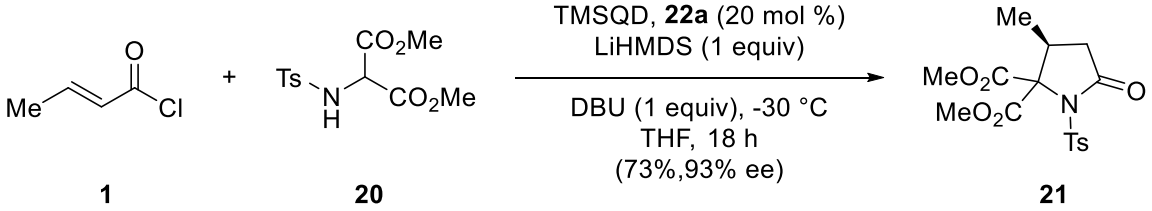
- **Catalytic cycle for the formation of lactam 18.**



2.1 Conjugate Additions

- **Michael reaction/proton transfer/lactamization organocascade with commodity acid chlorides.**

Romo



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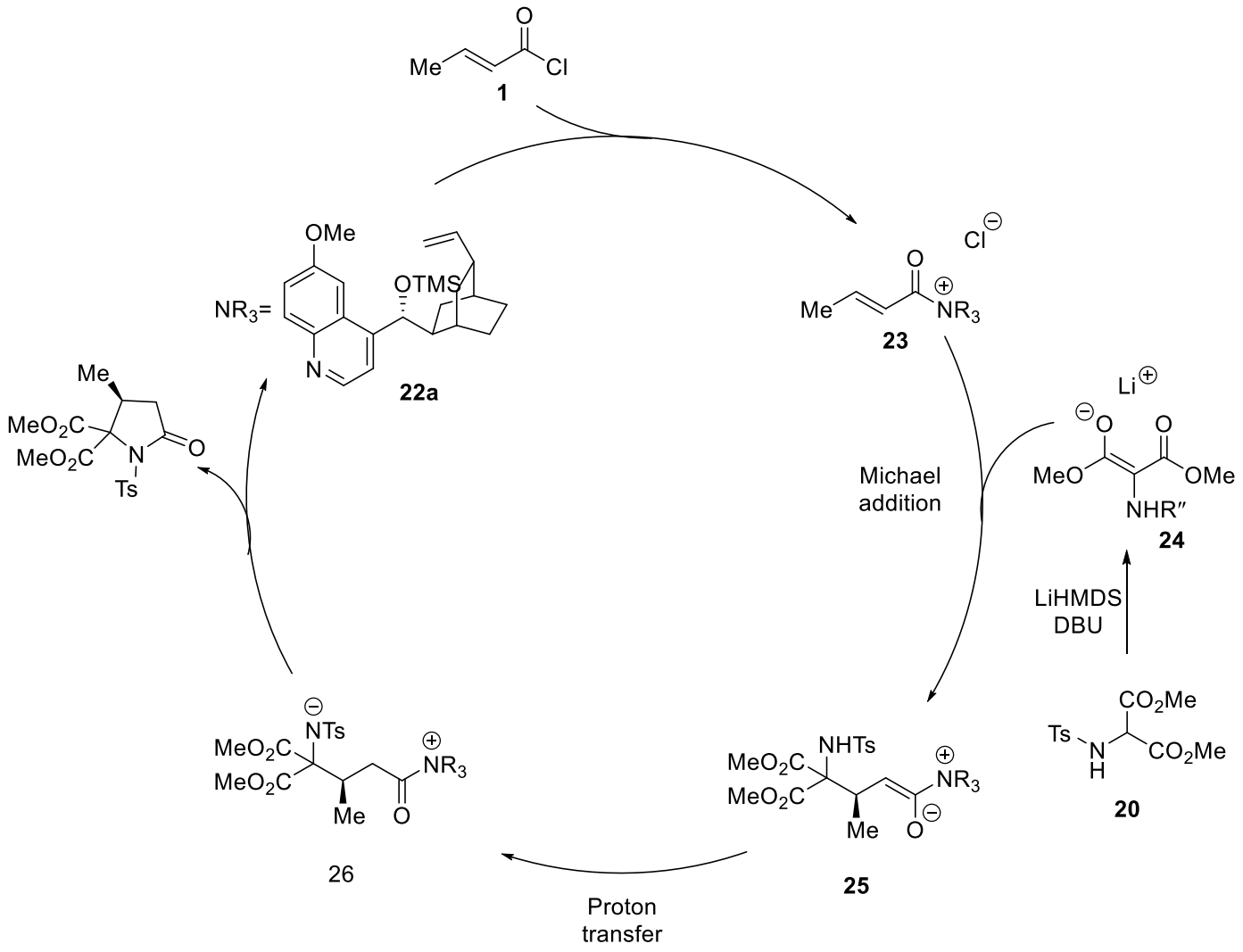
Angew. Chem. Int. Ed. **2013**,52, 13688–13693
Angew. Chem. **2013**, 125, 13933–13938.

2.1 Conjugate Additions

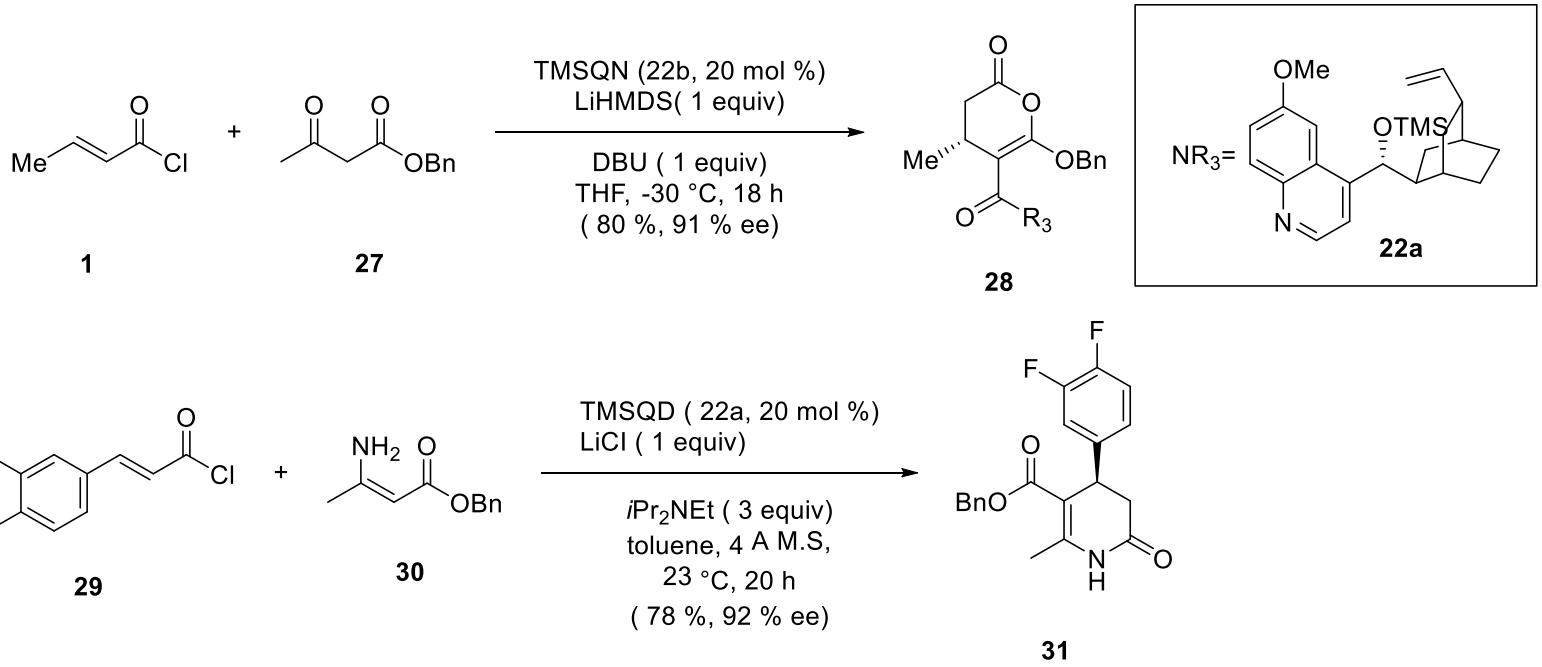
- **Proposed catalytic cycle for the organocascade.**



2.1 Conjugate Additions

- **Michael reaction/proton transfer/lactonization cascade with unsaturated acylammonium salts .**

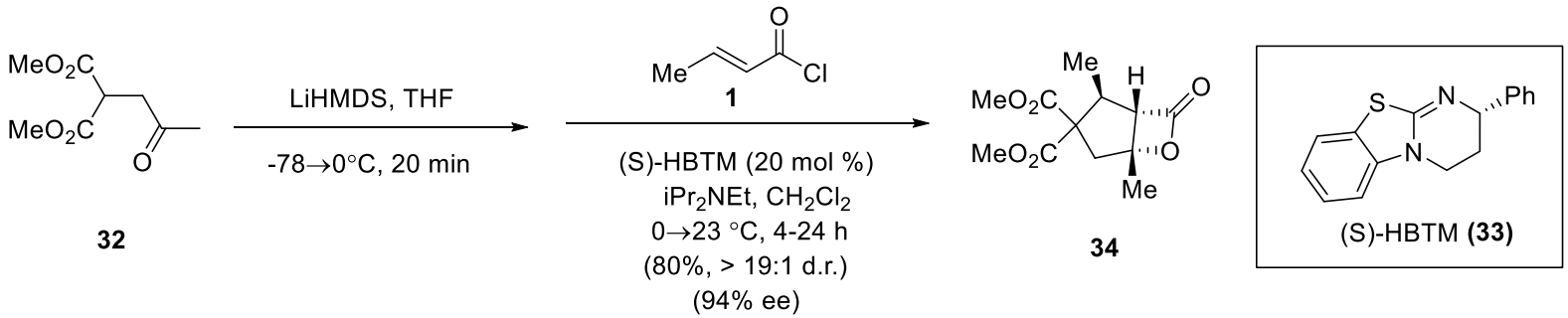
Smith



Med. Chem. Lett. **2000,** 10, 1625–1628.

2.1 Conjugate Additions

- **A aldol reaction/lactonization sequence led to the rapid construction of highly substituted cyclopentanes bearing fused β-lactone rings.**



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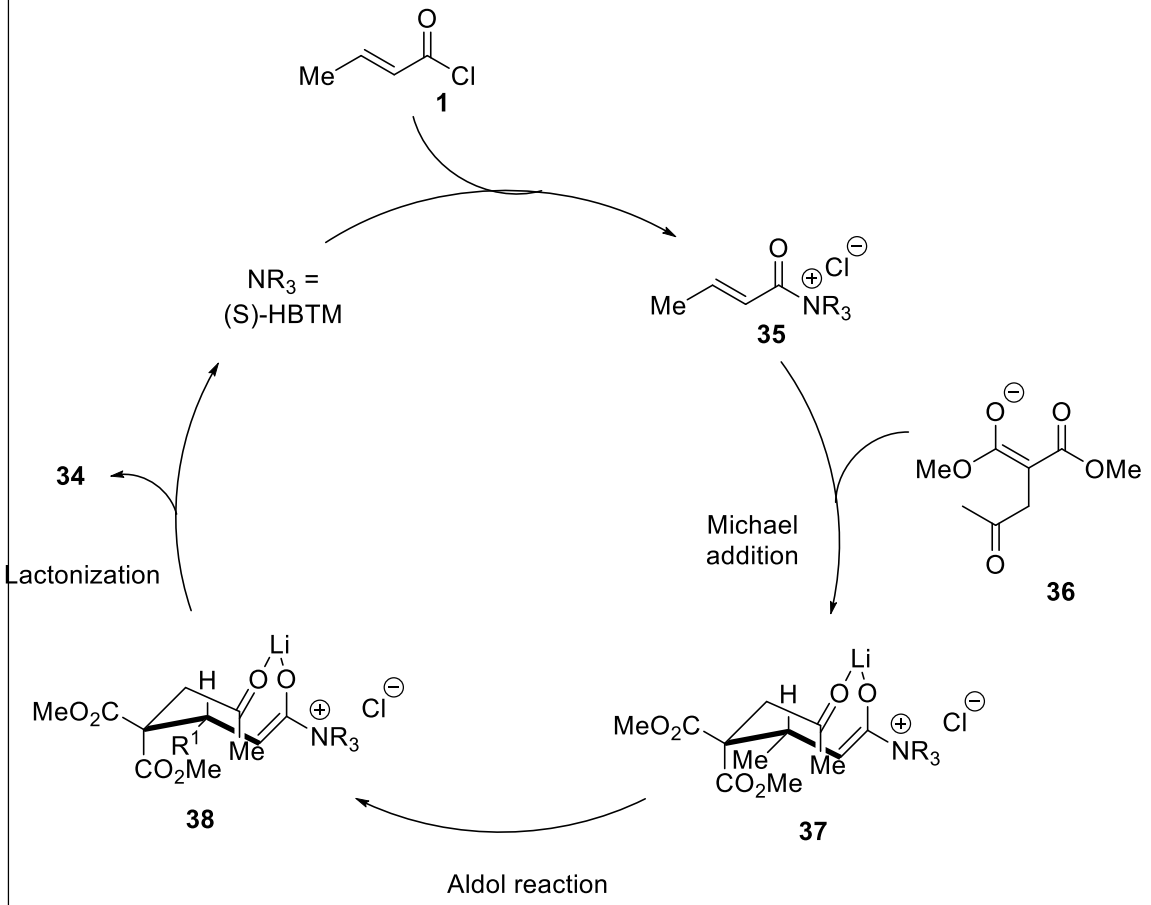
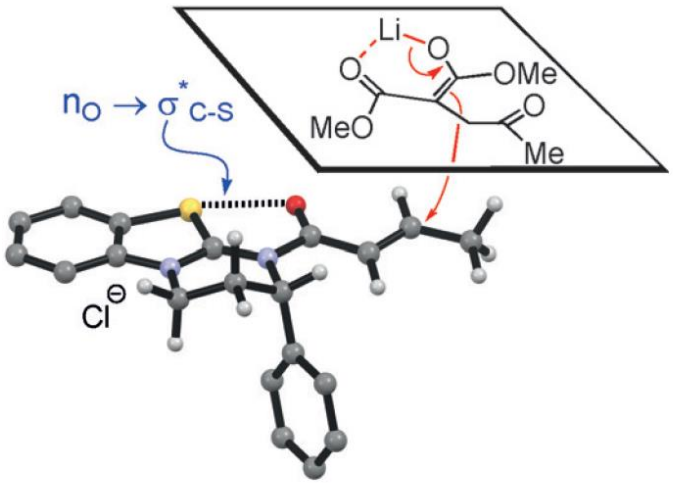
Nat.Chem. **2013**, 5, 1049–1057.

2.1 Conjugate Additions



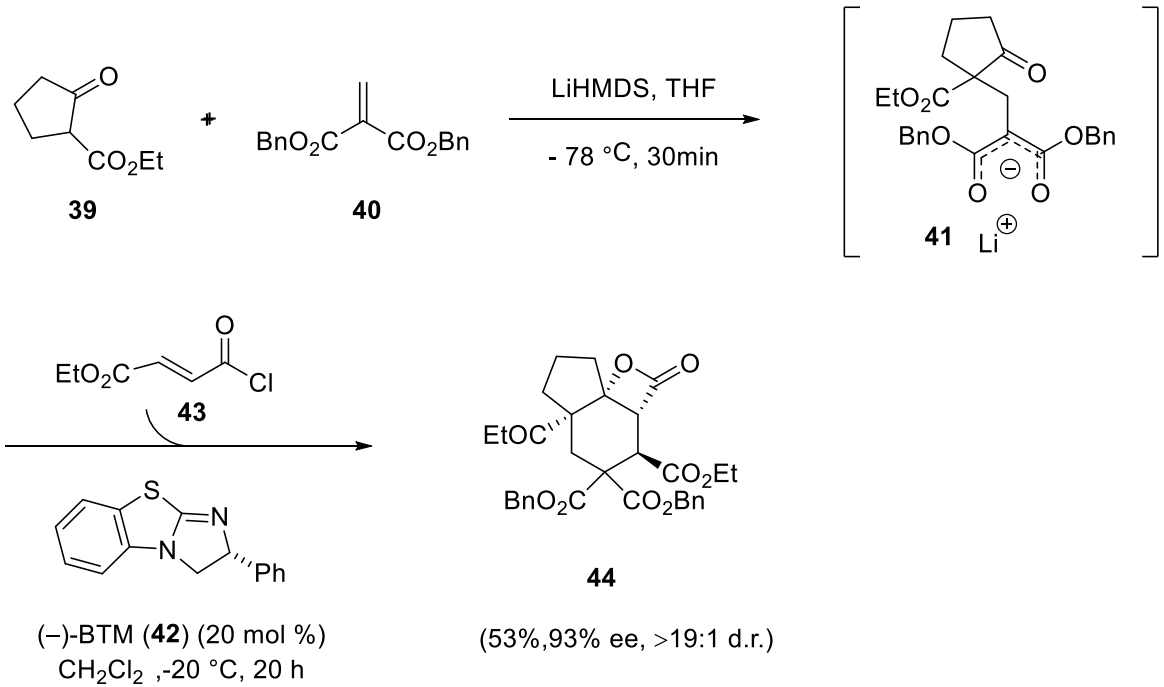


- **Nucleophile-catalyzed Michael reaction/aldol/lactonization (NCMAL) organocascade, proposed catalytic cycle, and rationalization of absolute configuration.**

2.1 Conjugate Additions

- **The first multicomponent organocascade involving unsaturated acylammonium salts also featuring a kinetic resolution of an in situ generated racemic malonate enolate (41).**

Romo

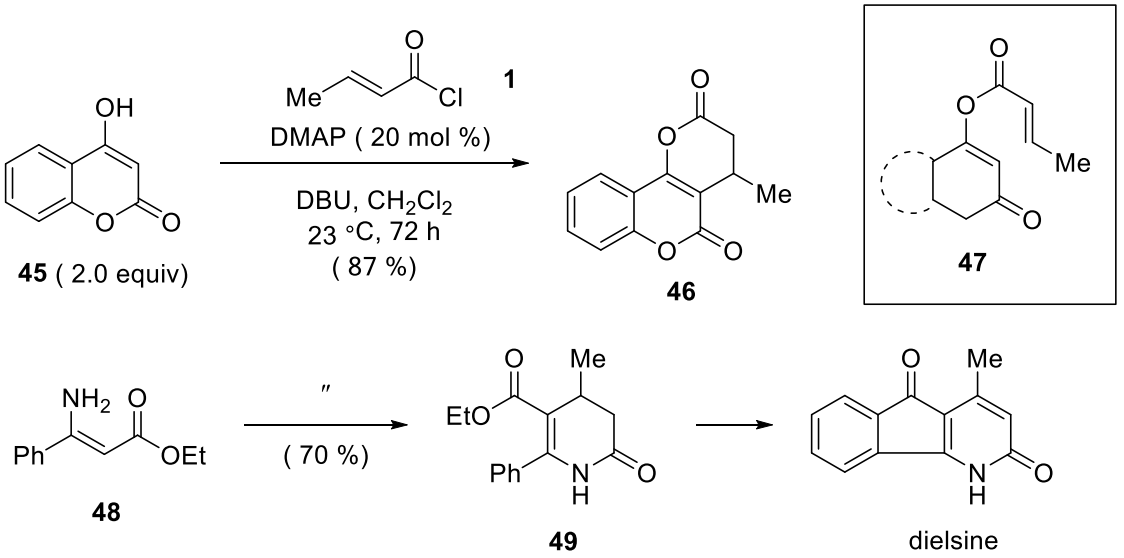


Nat.Chem. **2013**, 5, 1049–1057.

2.1 Conjugate Additions

- **Synthesis of polycyclic dihydropyranones (e.g. 46) and a dihydropyridone (49) through a Michael reaction/enol formation/lactonization/enamino lactamization organocascade.**

Romo

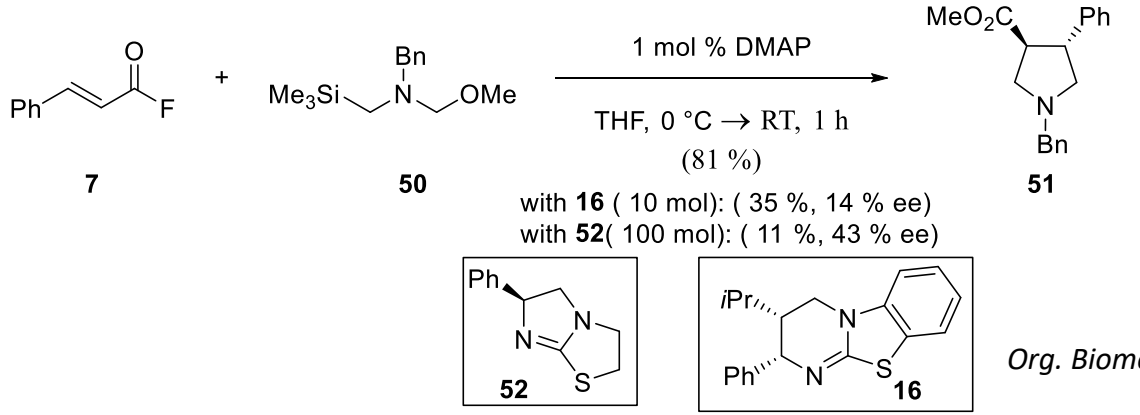


Tetrahedron Lett. **2015**, 56,3647–3652.

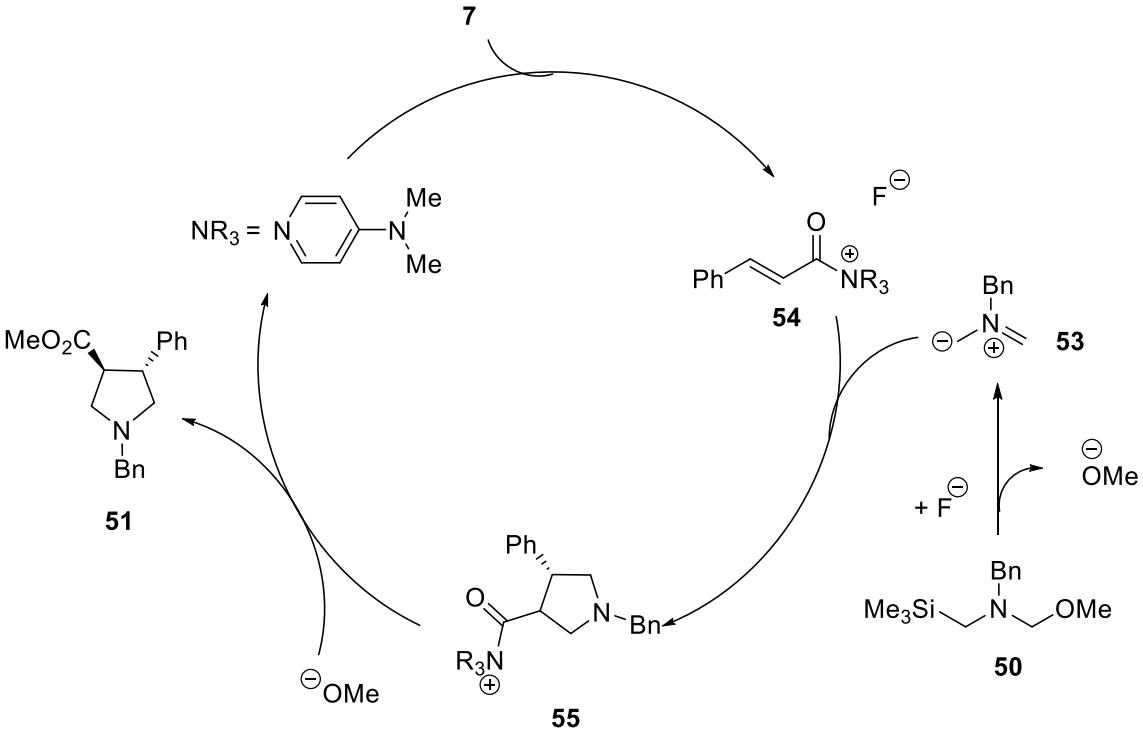
2.2. Cycloadditions

- **1,3-Dipolar cycloaddition of an unsaturated acylammonium salt with an azomethine ylide generated in situ from 50.**

Lupton



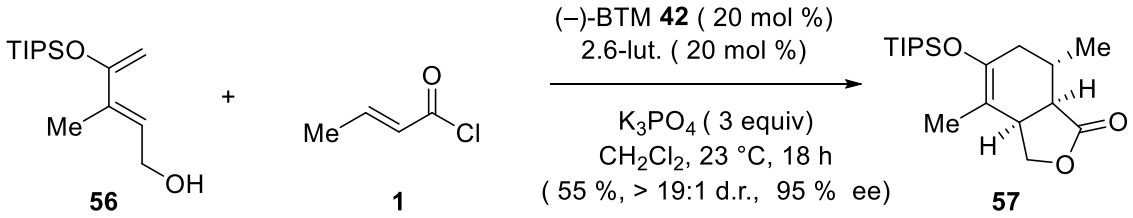
*Org. Biomol. Chem.***2012**, 10, 7903–7911.

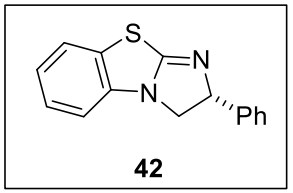


2.2. Cycloadditions

- **DAL organocascade, employing novel chiral unsaturated acylammonium dienophiles, and a proposed catalytic cycle.**

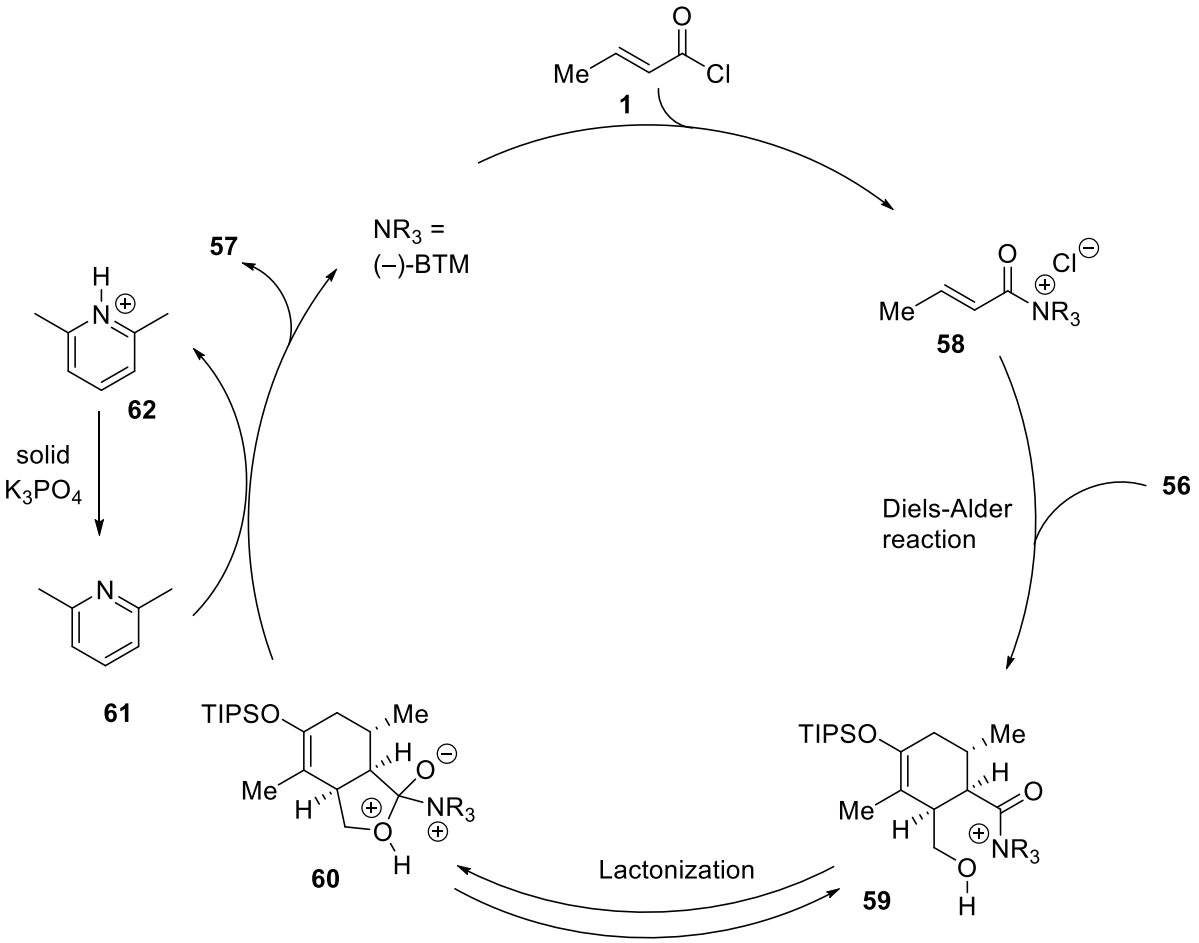
Romo





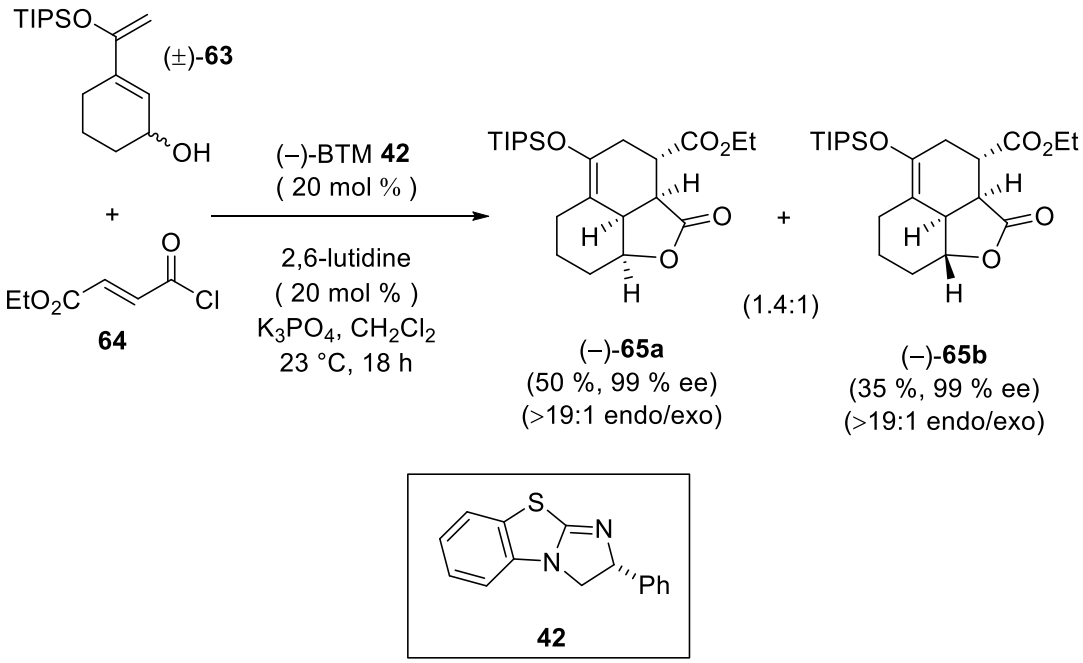
J. Am.Chem. Soc. **2014**, 136, 4492–4495.

2.2. Cycloadditions



2.2. Cycloadditions

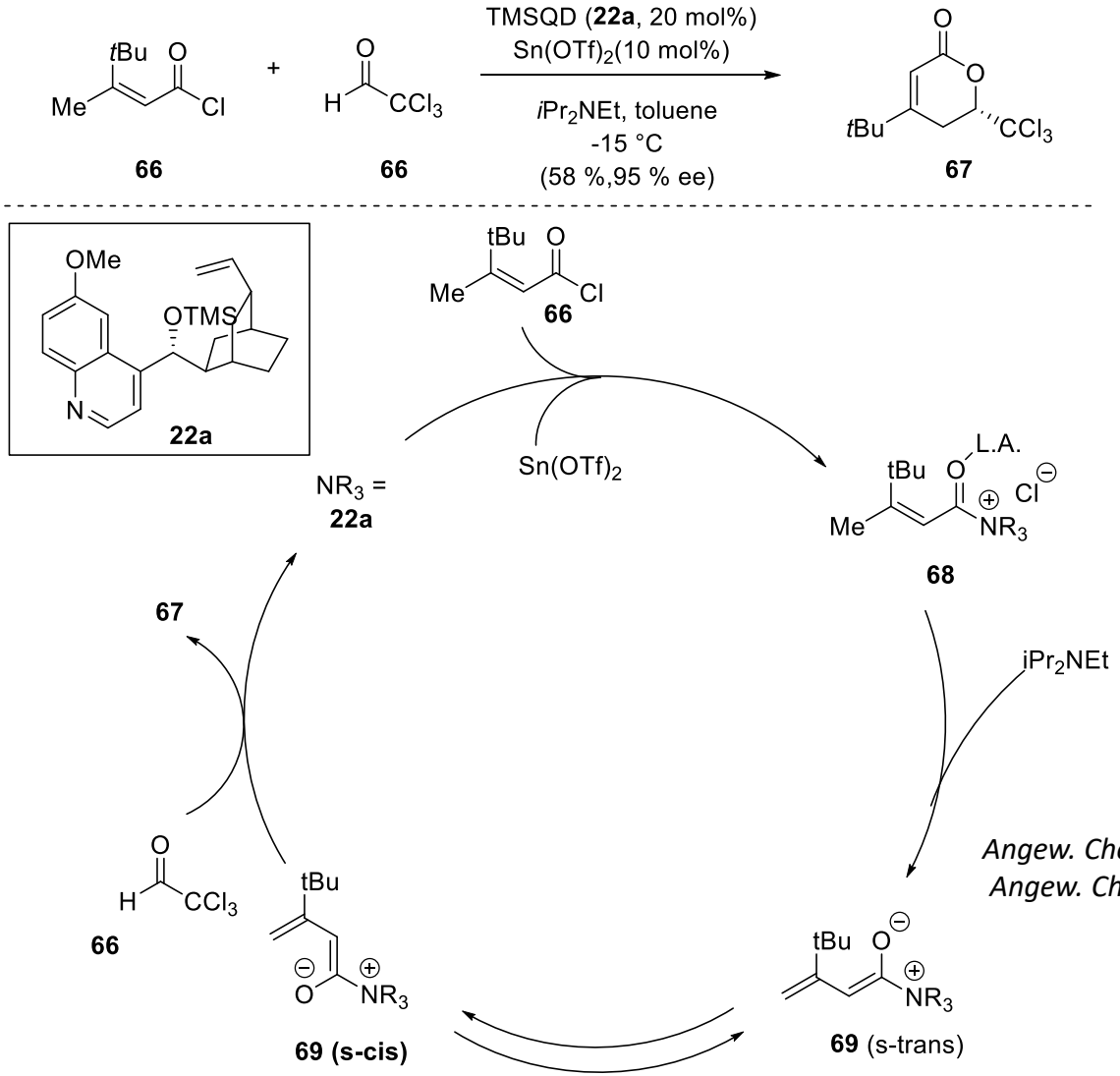
- **Stereodivergent DAL organocascades employing racemic diene 63 to deliver the complex and separable diastereomeric cycloadducts 65a,b.**



J. Am.Chem. Soc. **2014**, 136, 4492–4495.
Tetrahedron Lett. **1996**, 37, 1023.

2.3. Interplay of Unsaturated Acylammonium Intermediate and Ammonium Dienolate

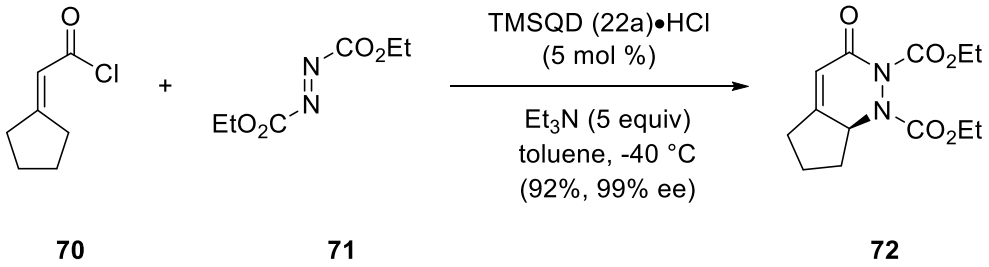
- **Generation of an ammonium dienolate and net [4+2]cycloaddition with chloral (66), and postulated catalytic cycle.**



Angew. Chem. Int. Ed. **2007**, 46, 5325 –5328
Angew. Chem. **2007**, 119, 5419–5422.

2.3. Interplay of Unsaturated Acylammonium Intermediate and Ammonium Dienolate

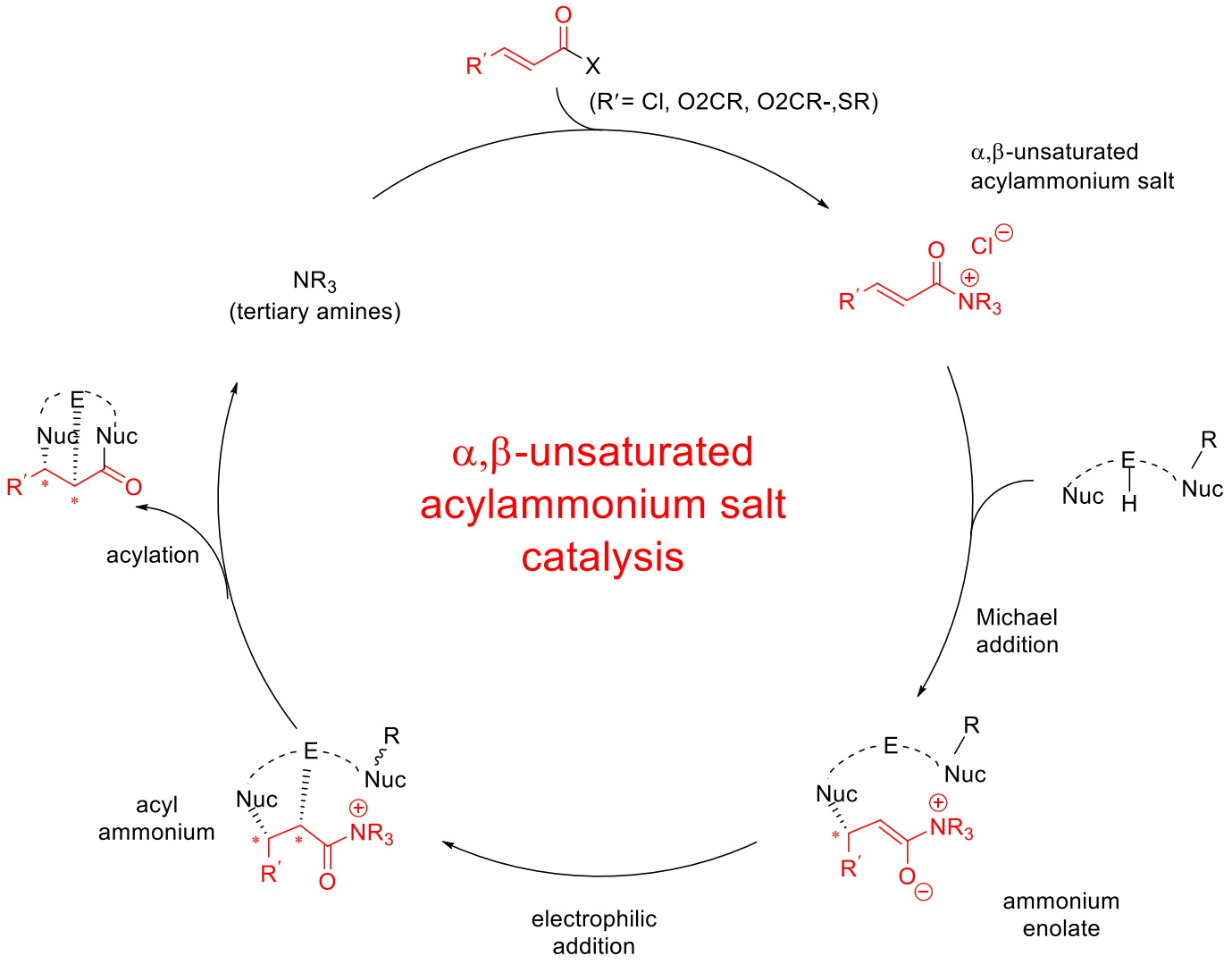
- **[4+2] Cycloaddition of ammonium dienolates and azo compounds leading to the net ϒ-amination of unsaturated acid chlorides.**



70 **71** **72**

J. Am. Chem. Soc. **2011**, 133, 15894 –15897.

3. Conclusion and Outlook



4. Acknowledgement

- **Prof. Huang**
- **Mr. Chen**
- **All members here**

Thanks for your attention!