Literature Report

Changbin Yu 2013-12-10 检查: 罗京

Organocatalytic Enantioselective Synthesis of 2,3-Allenoates by Intermolecular Addition of Nitroalkanes to Activated Enynes

Junliang Zhang and Jianwei Sun *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 18020

Prof. Jianwei Sun

Ph.D. in Organic Chemistry, University of Chicago (2008)

Assistant Professor of Chemistry

Hong Kong University of Science and Technology

Research Interests

- **Asymmetric nucleophilic catalysis (e.g., N- heterocyclic carbenes, chiral amines)**
- **Brønsted acid catalysis (e.g., chiral phosphoric acids)**
- **Lewis acid catalysis**
- **Synthesis of biologically active compounds and light-harvesting materials**

Prof. Junliang Zhang

Ph.D in Organic Chemistry SIOC, Supervisor: Prof. Shengming Ma (2002)

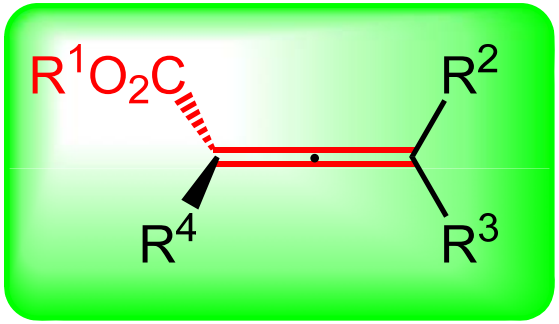
Professor of Chemistry

Department of Chemistry, East China Normal University

Research Interests

- **Developing new synthetic reactions of conjugated enynes and small rings such as cyclopropane, oxiranes and aziridines**
- **Design novel chiral ligand for gold, palladium, rhodium etc catalyzed reactions.**

Allenoates:

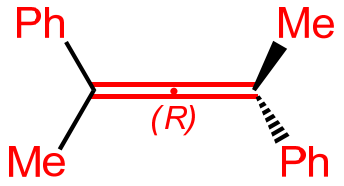


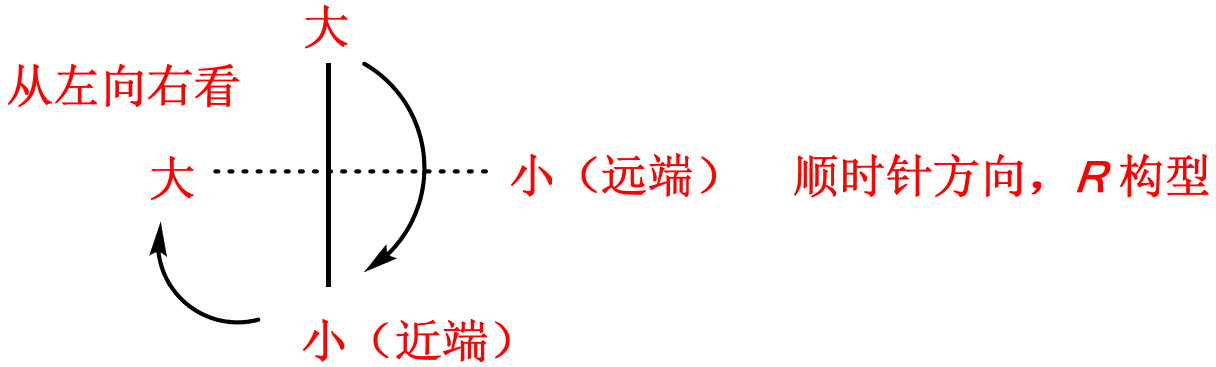
Asymmetric synthesis methods:

- **Enantioenriched substrates**
- **Stoichiometric amounts of chiral promoters/auxiliaries**
- **Catalytic asymmetric synthesis (a few)**

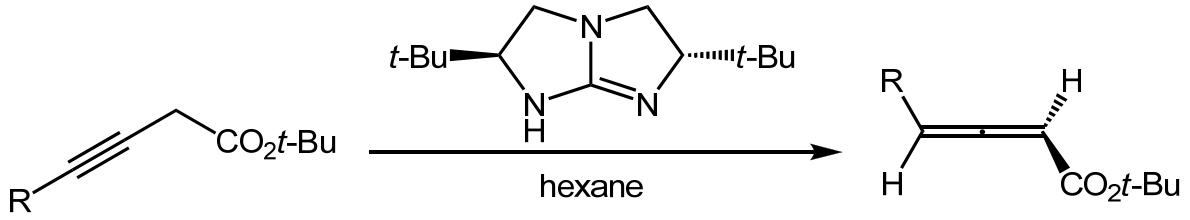
轴手性分子：

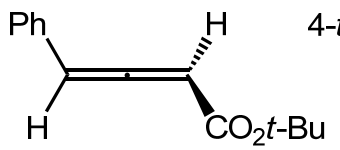
丙二烯型分子：



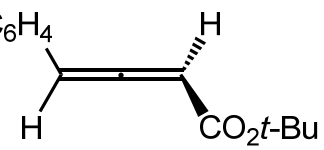


Enantioselective Synthesis of Chiral Allenoates by Guanidine-Catalyzed Isomerization of 3-Alkynoates

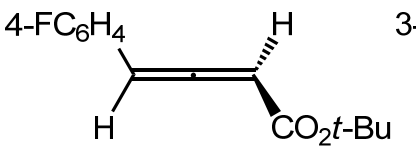




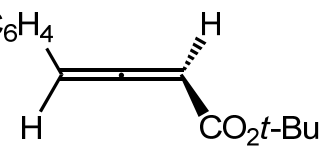
70% yield; 91% ee



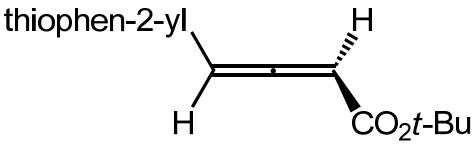
68% yield; 94% ee



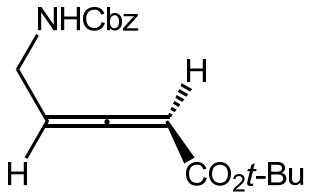
70% yield; 91% ee



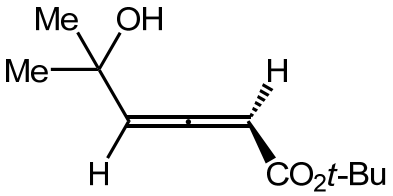
62% yield; 95% ee



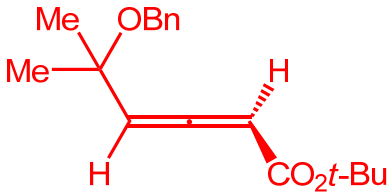
80% yield; 93% ee



65% yield; 91% ee



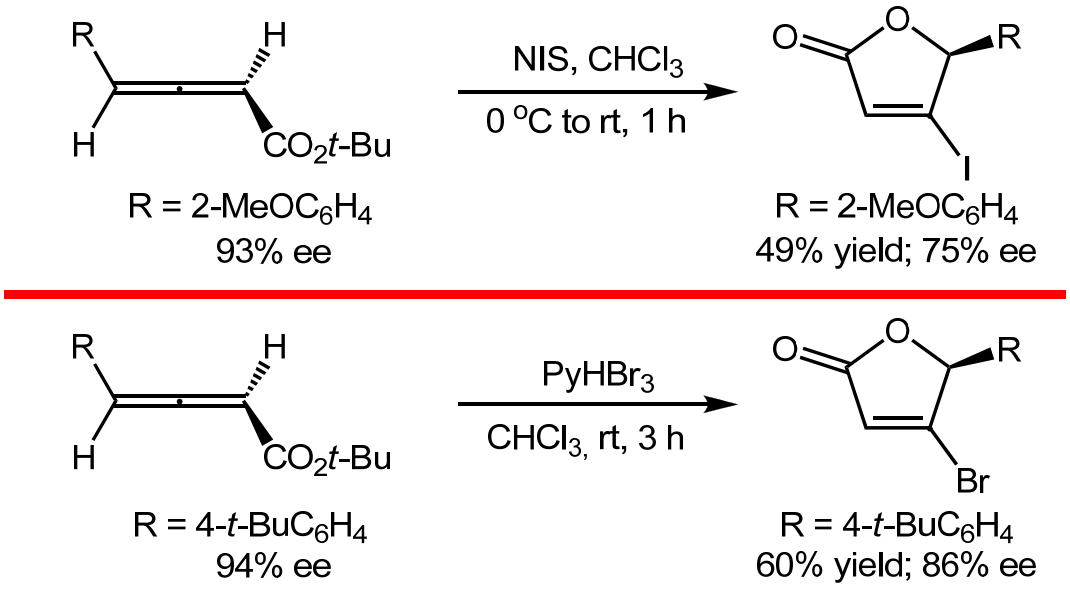
70% yield; 91% ee



79% yield; 95% ee

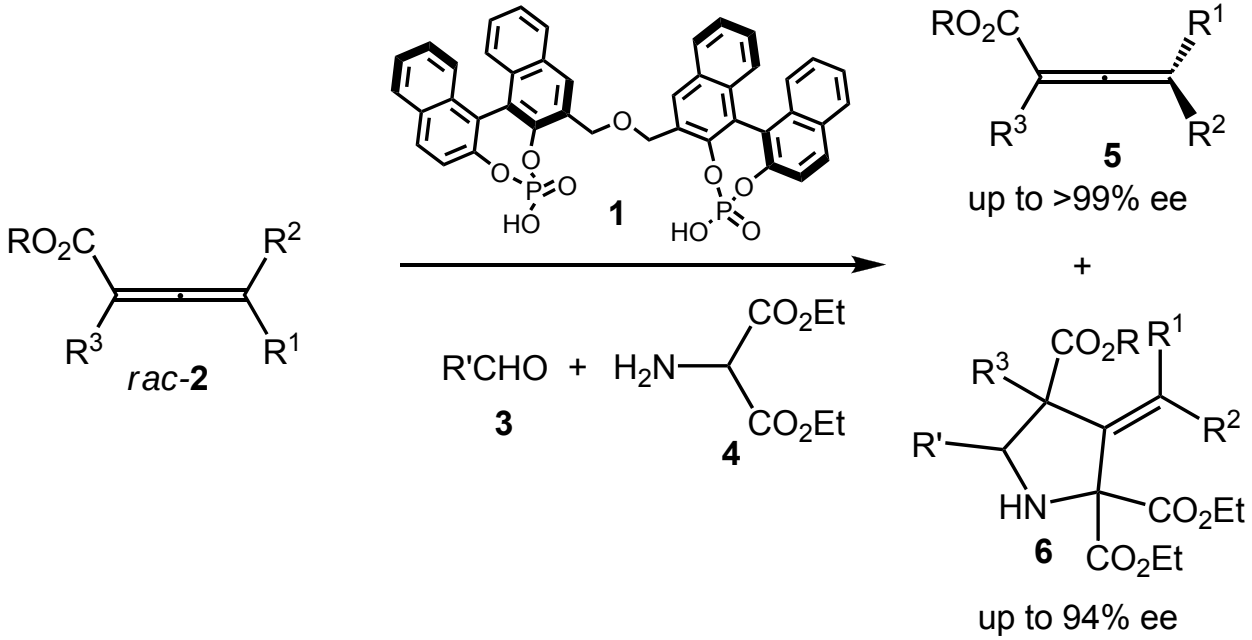
Choon-Hong Tan(陈俊峰) *et al*. *J. Am. Chem. Soc*. **2009**,*131*, 7212

Derivatization of the allenoates:



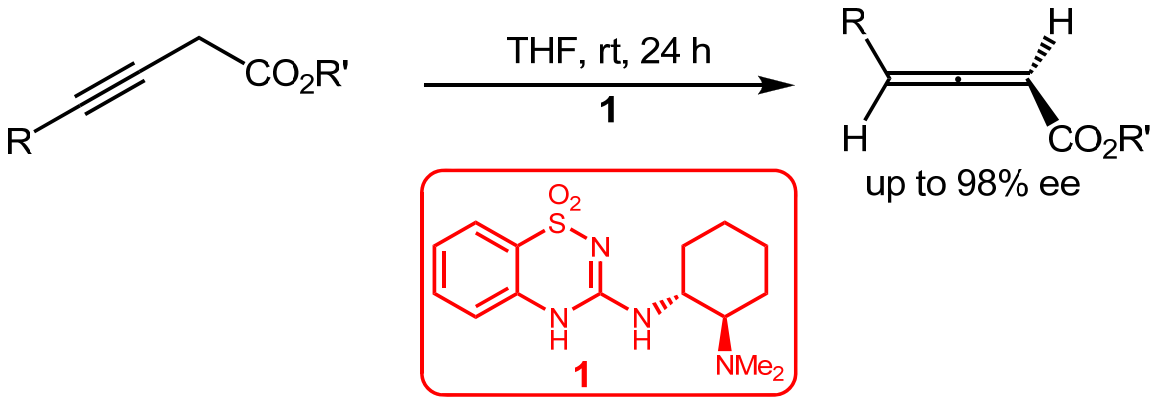
Choon-Hong Tan(陈俊峰) *et al*. *J. Am. Chem. Soc*. **2009**,*131*, 7212

Kinetic Resolution of Racemic 2,3-Allenoates by Organocatalytic Asymmetric 1,3-Dipolar Cycloaddition



Liu-Zhu Gong *et al*. *Org. Lett*. **2010**, *12*, 4050

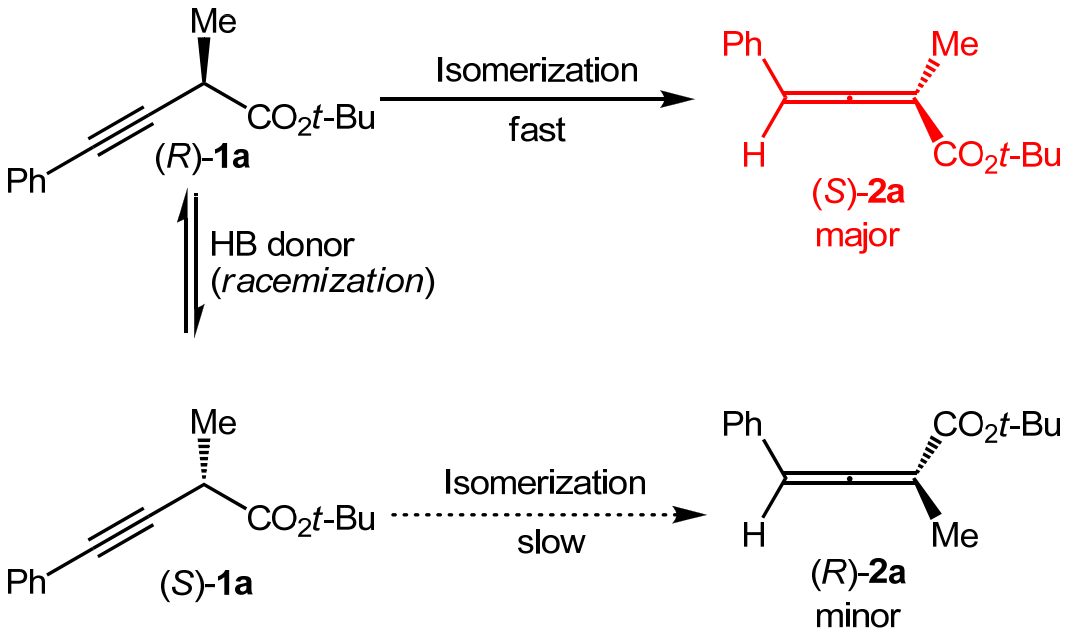
Bifunctional Hydrogen-Bond Donors That Bear a Quinazoline or Benzothiadiazine Skeleton for Asymmetric Organocatalysis



Yoshiji Takemoto *et al*. *Chem. Eur. J.* **2011**, *17*, 10470

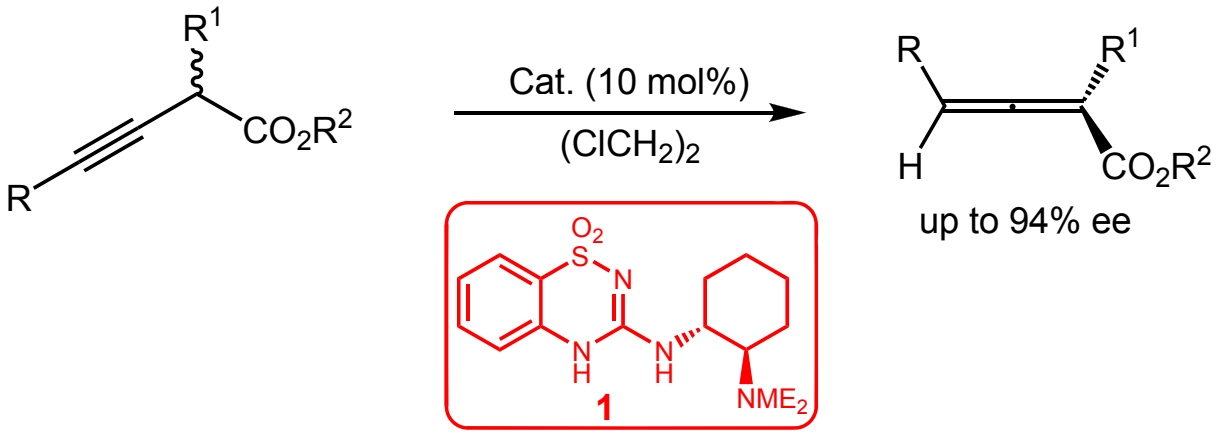
Organocatalyzed Isomerization of α-Substituted Alkynoates into Trisubstituted Allenoates by Dynamic Kinetic Resolution

Concept of this work:



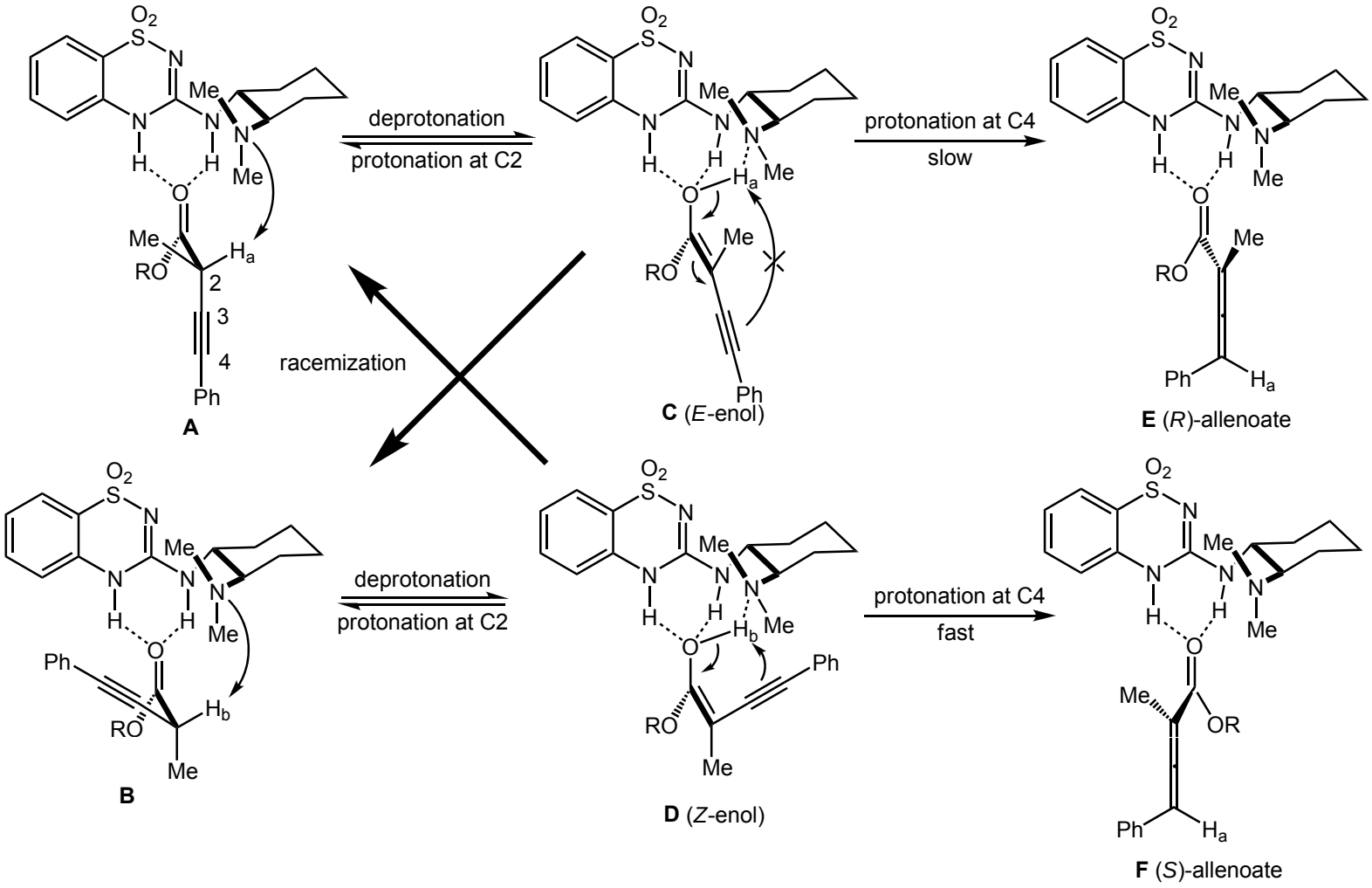
Yoshiji Takemoto *et al*. *ChemCatChem* **2012**, *4*, 983

The Substrate Scope:



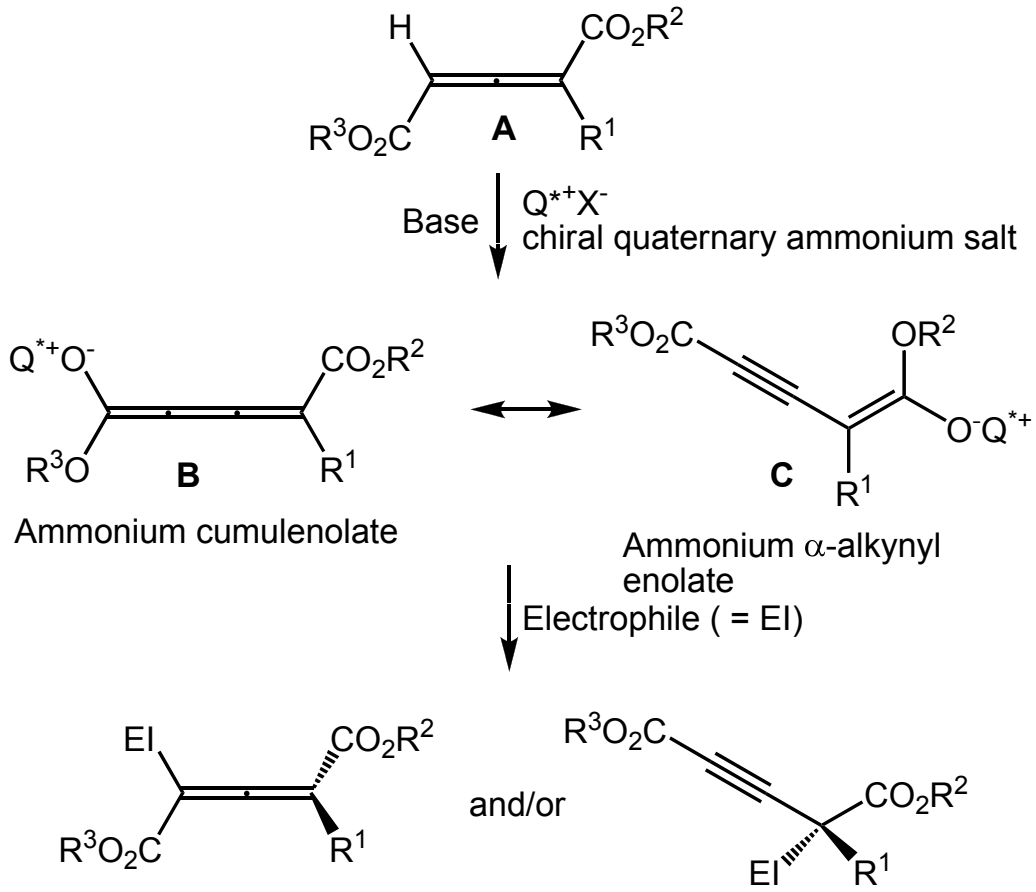
Yoshiji Takemoto *et al*. *ChemCatChem* **2012**, *4*, 983

Plausible reaction mechanism:



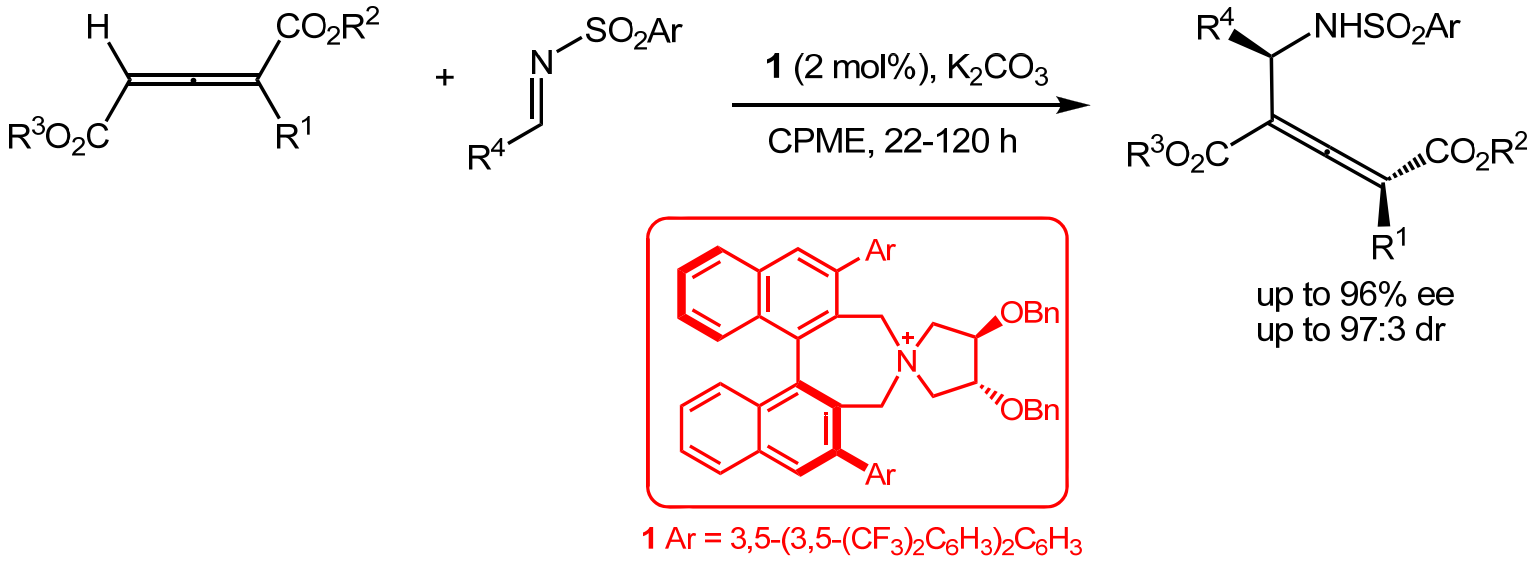
Yoshiji Takemoto *et al*. *ChemCatChem* **2012**, *4*, 983

Phase-transfer-catalysed asymmetric synthesis of tetrasubstituted allenes



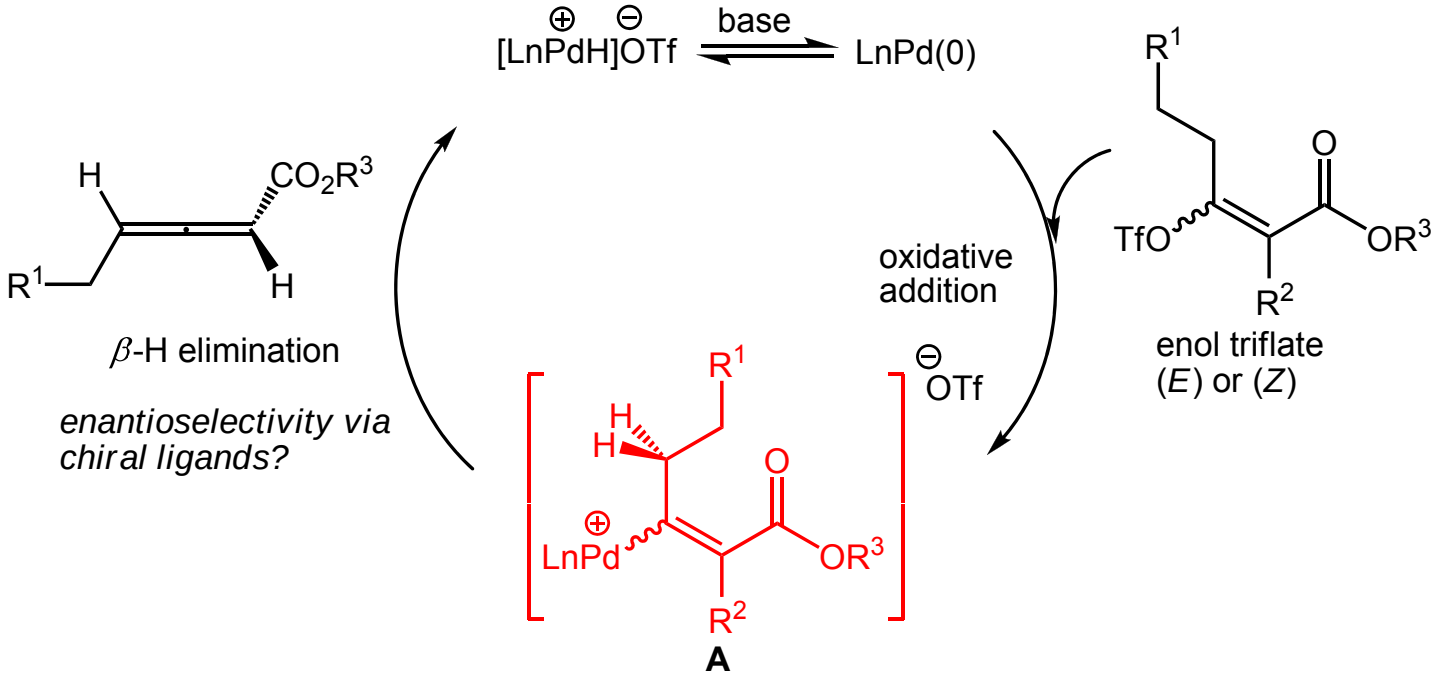
Keiji Maruoka *et al*. *Nature Chem.* **2013**, *5*, 240

Phase-transfer-catalysed asymmetric synthesis of tetrasubstituted allenes



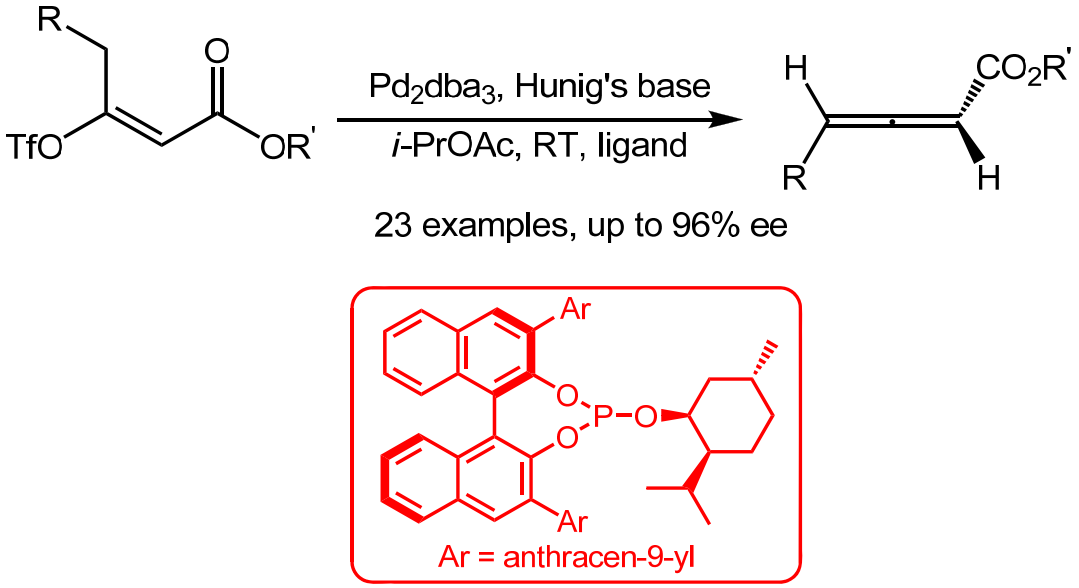
Keiji Maruoka *et al*. *Nature Chem.* **2013**, *5*, 240

Pd-Catalyzed Asymmetric β-Hydride Elimination en Route to Chiral Allenes



Doug E. Frantz *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 4970

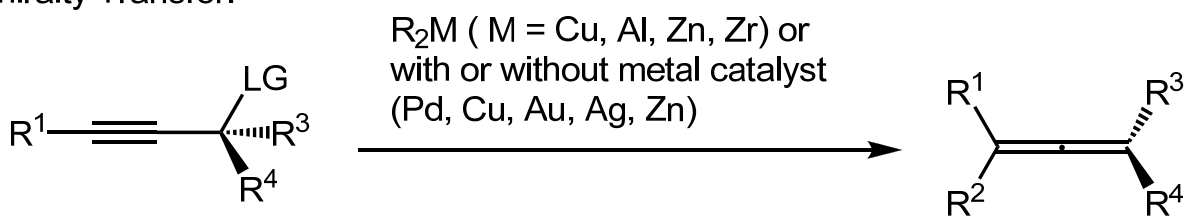
Pd-Catalyzed Asymmetric β-Hydride Elimination en Route to Chiral Allenes



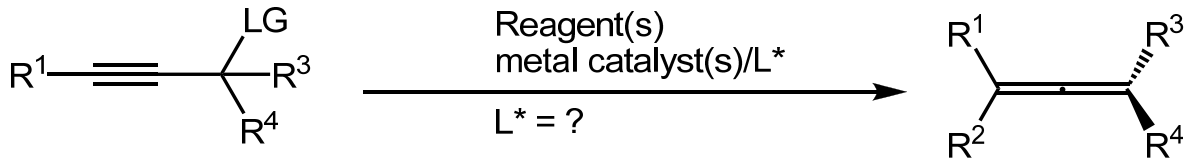
Doug E. Frantz *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 4970

A Room-Temperature Catalytic Asymmetric Synthesis of Allenes with ECNU-Phos

Chiralty Transfer:

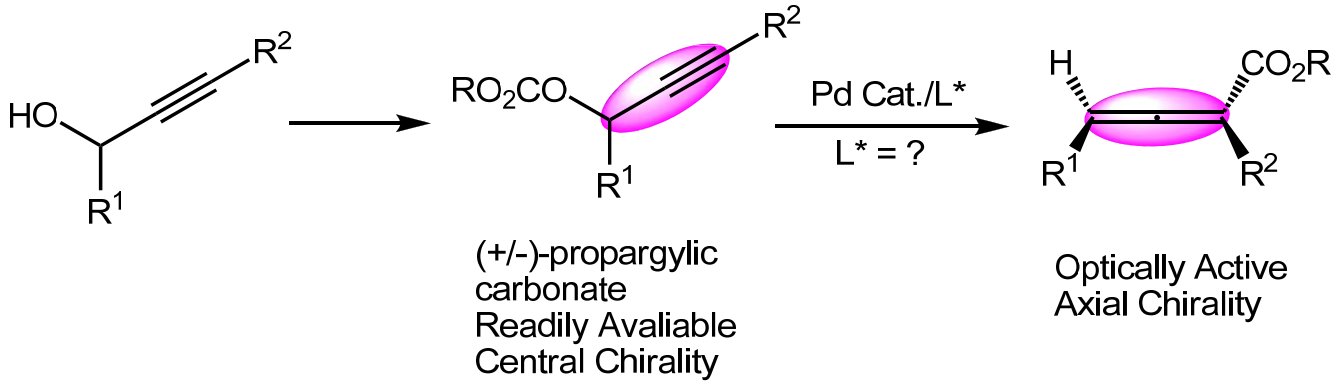


Our Concept:

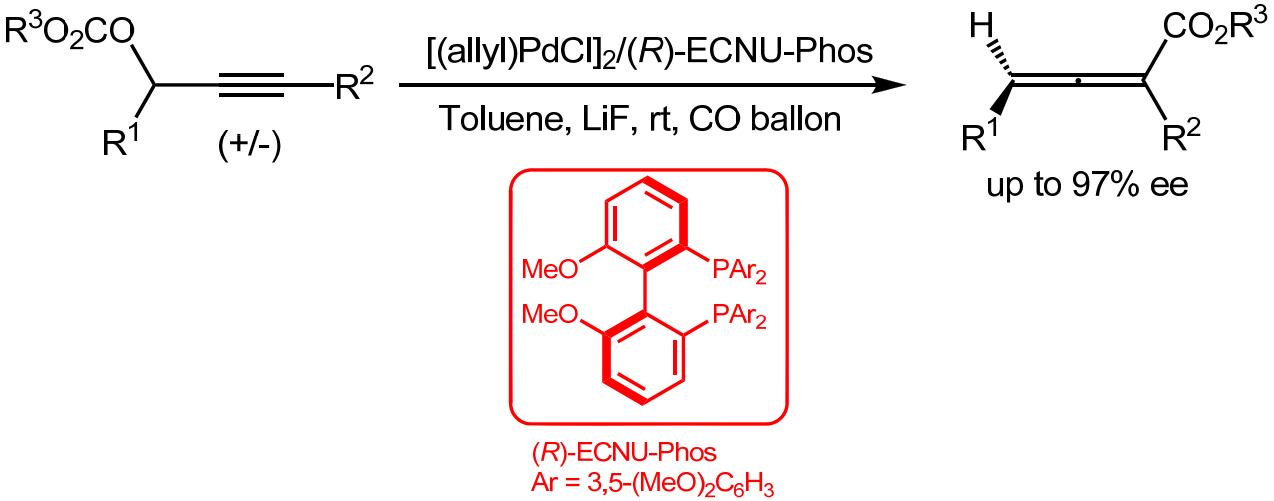


Shengming Ma *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 11517

Design of a Catalytic Approach to Synthesize Chiral 2,3-Allenoates:

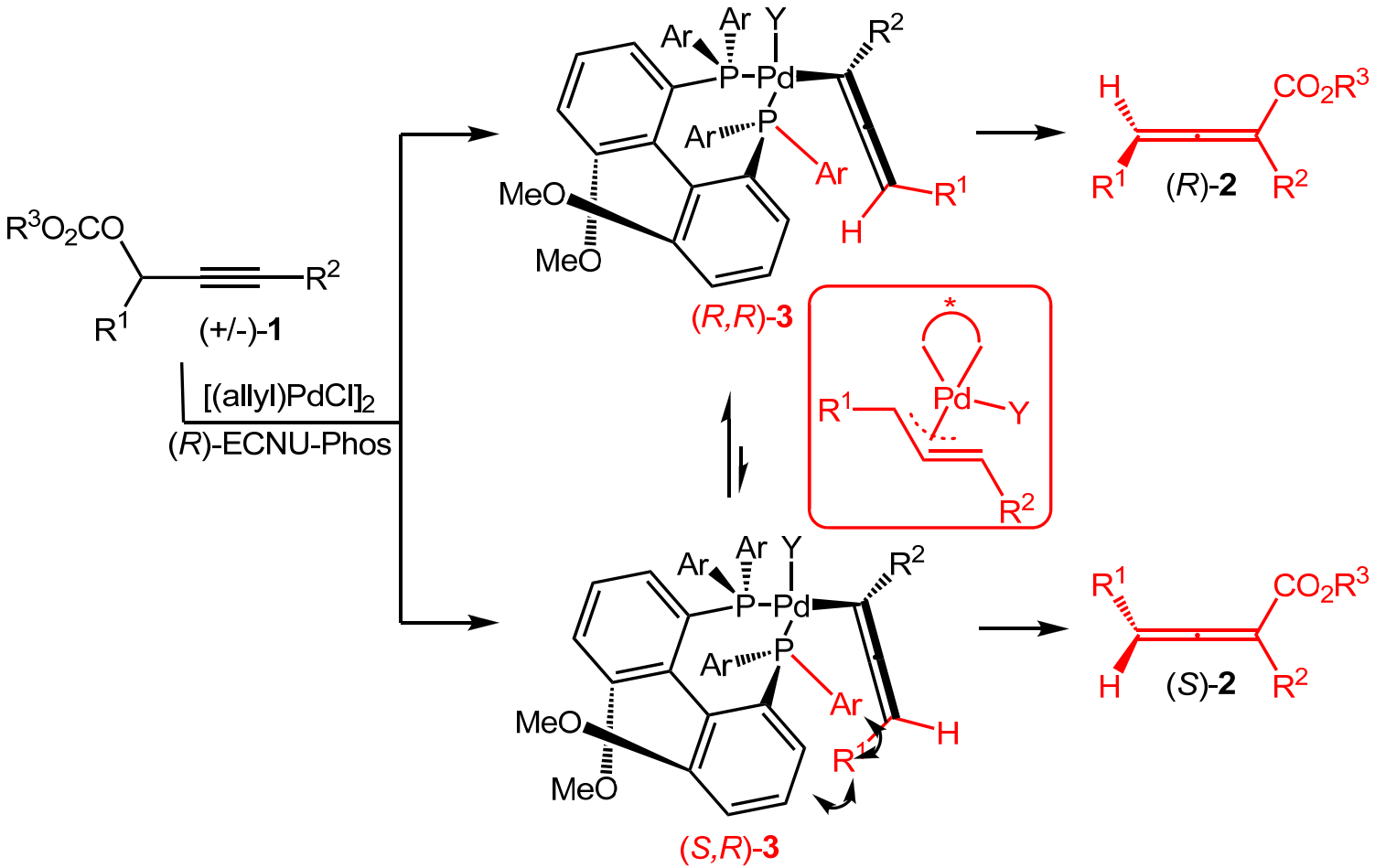


Shengming Ma *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 11517



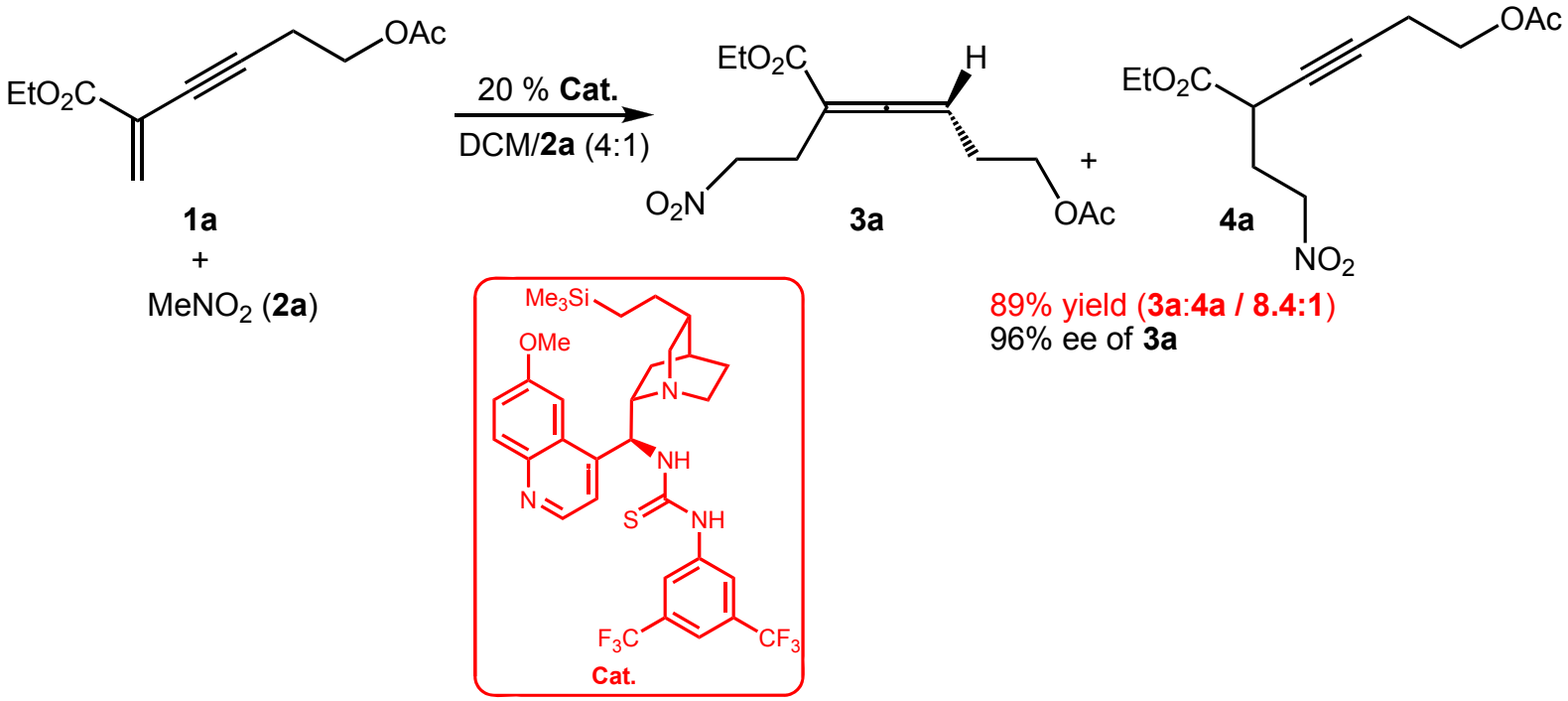
Shengming Ma *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 11517

Prediction of the Absolute Configuration of the Product:



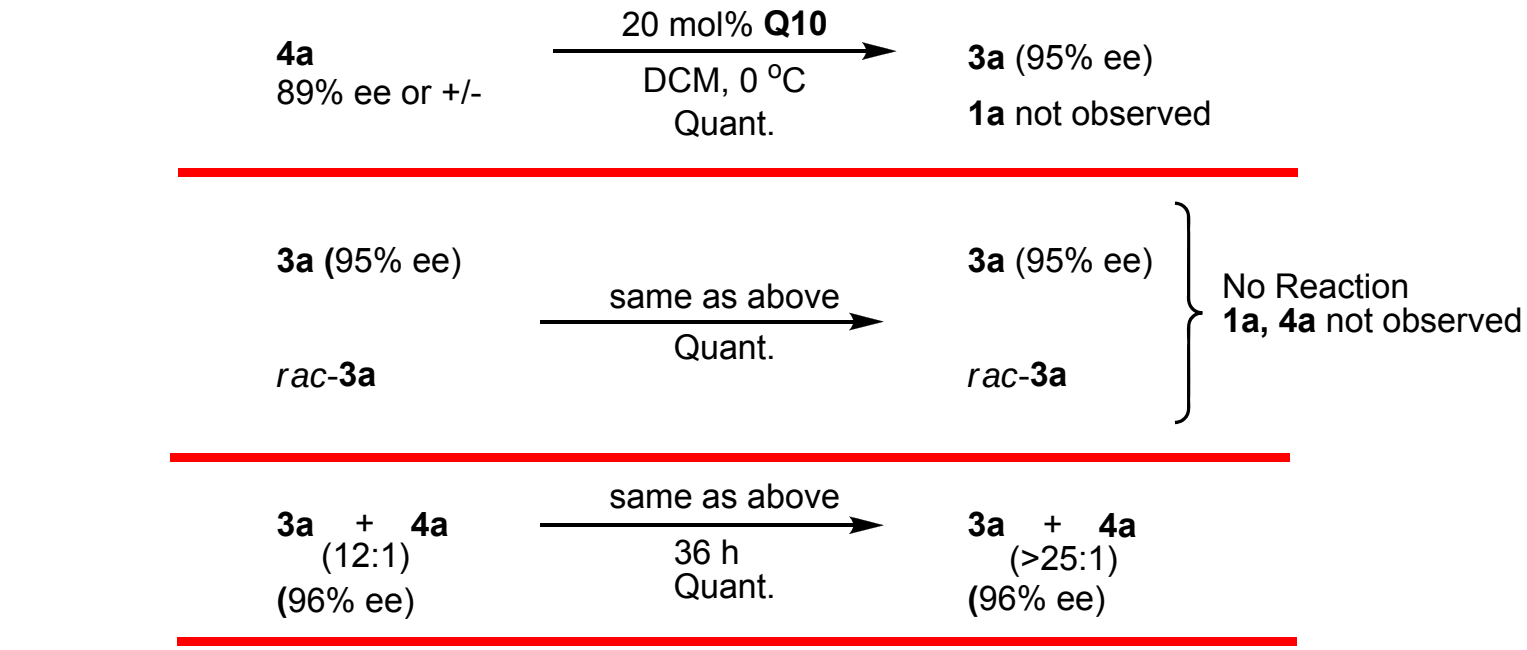
Shengming Ma *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 11517

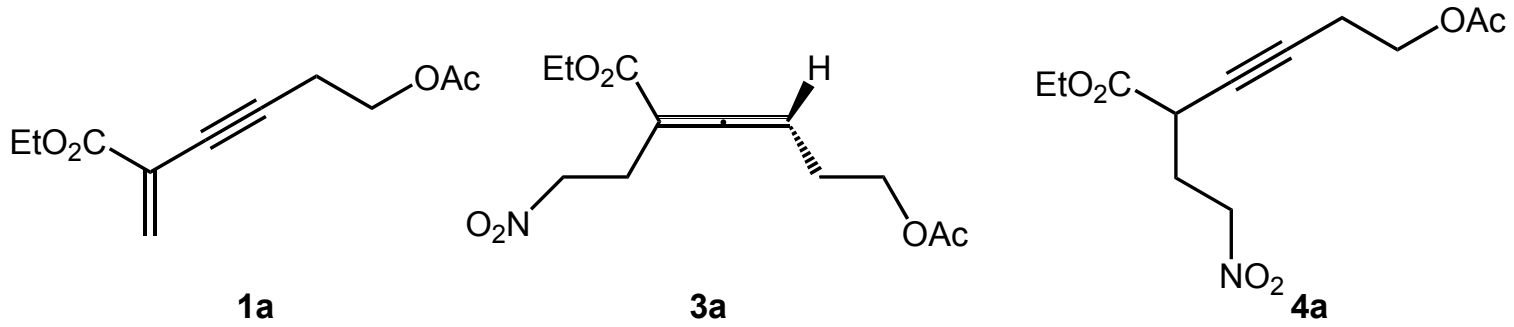
Organocatalytic Enantioselective Synthesis of 2,3-Allenoates by Intermolecular Addition of Nitroalkanes to Activated Enynes



Junliang Zhang and Jianwei Sun *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 18020

Control experiments:

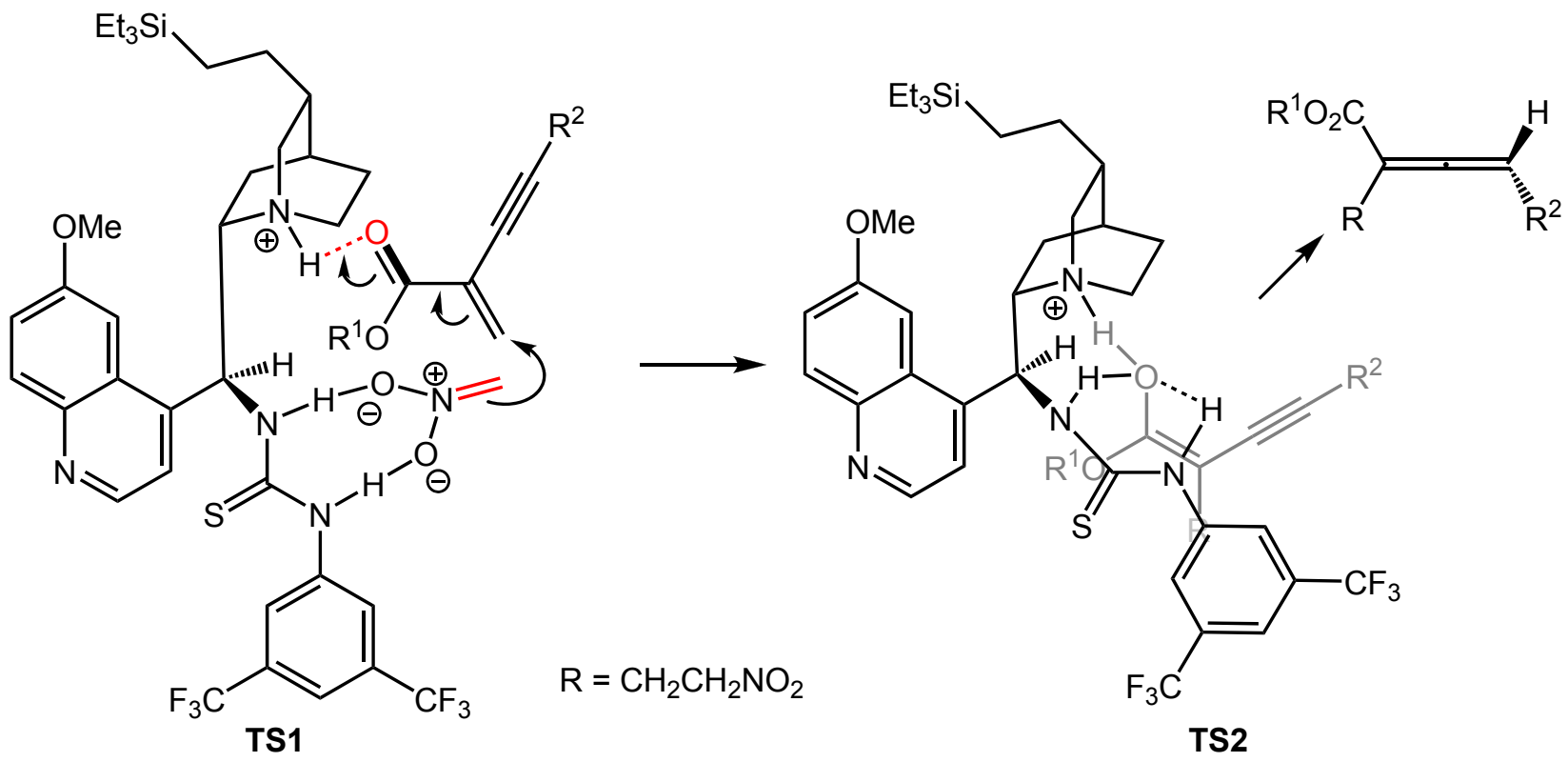




1a **3a** **4a**

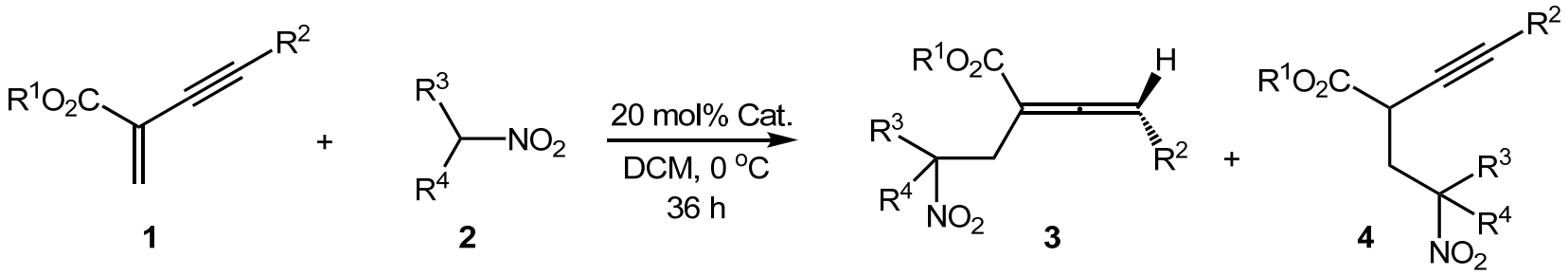
Junliang Zhang and Jianwei Sun *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 18020

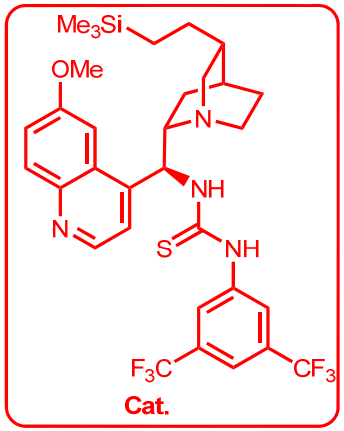
Plausible transition states:



Junliang Zhang and Jianwei Sun *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 18020

The Substrate Scope:

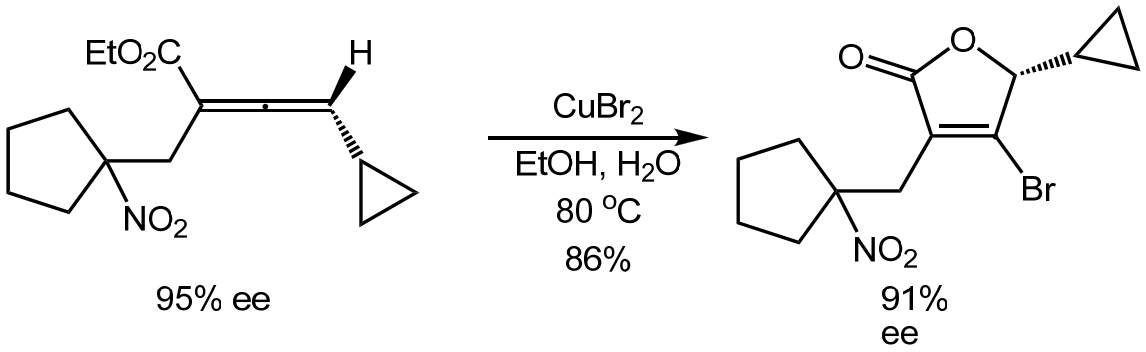




up to 96% ee
up to **3**/**4** > 25:1

Junliang Zhang and Jianwei Sun *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 18020

Derivatization of the allenoate:

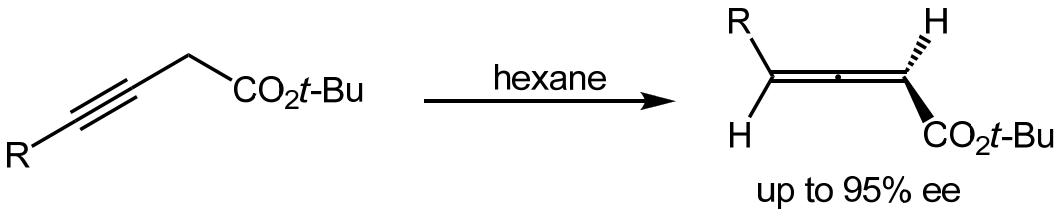


Junliang Zhang and Jianwei Sun *et al*. *J. Am. Chem. Soc*. **2013**, *135*, 18020

Summary:

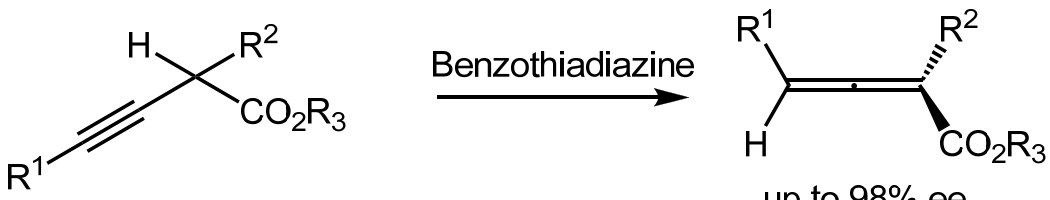
Isomerization by a chiral base:

Tan's work

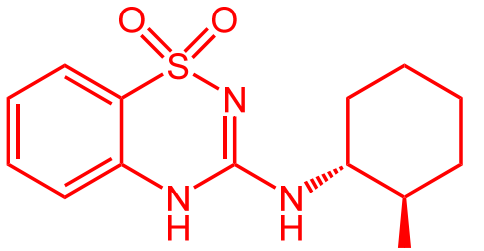


up to 95% ee

Takemoto's work



up to 98% ee

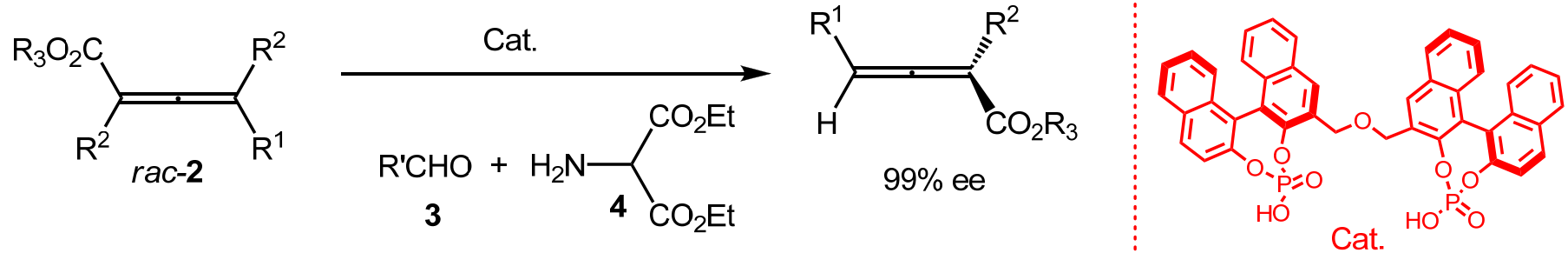


Benzothiadiazine

Summary:

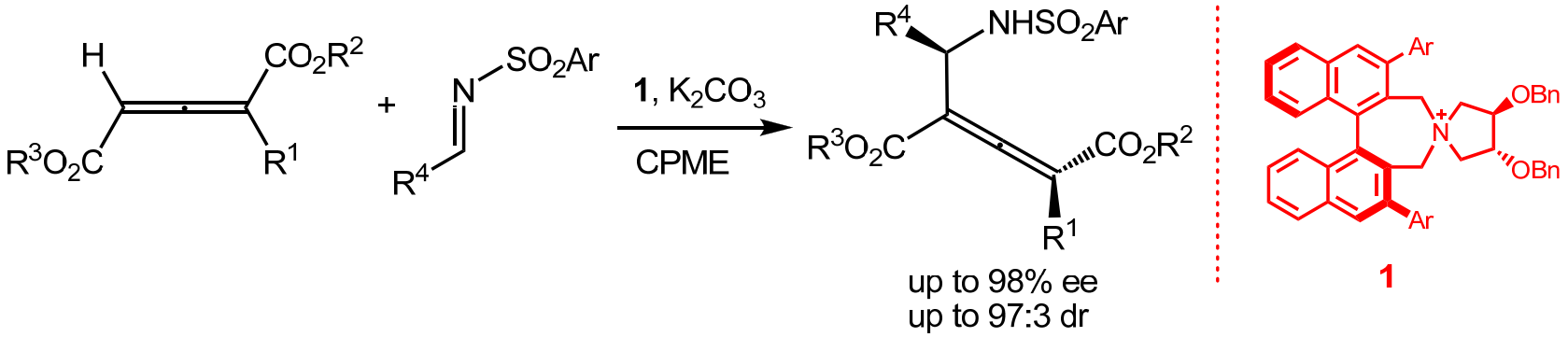
Kinetic resolution of racemic allenoates:

Gong's work



Phase-transfer catalyzed deprotonation:

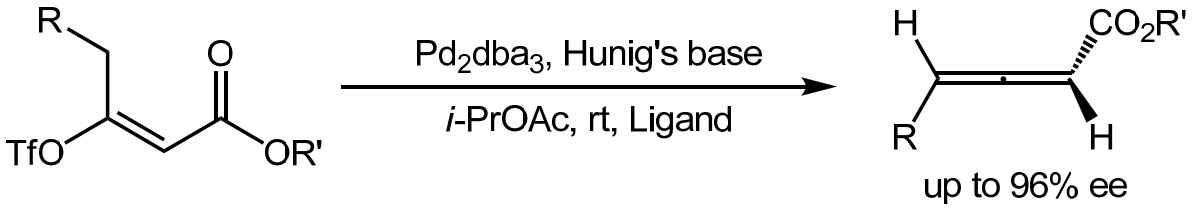
Maruoka's work

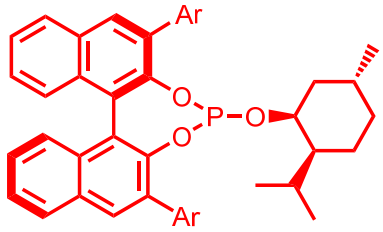


Summary:

Asymmetric *β*-hydride elimination of enoltriflates:

Frantz's work

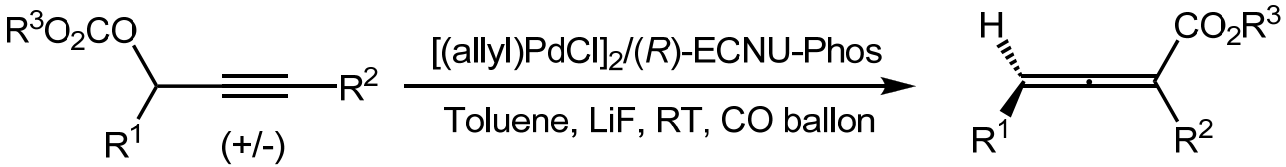


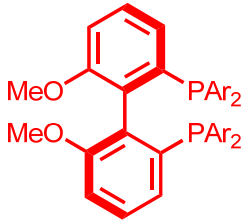


Ar = anthracen-9-yl

Asymmetric carbonylation of propargylic carbonates:

Ma's work





(*R*)-ECNU-Phos
Ar = 3,5-$(MeO)_2C_6H_3$

Asymmetric synthesis is fundamentally important in organic chemistry in view of the wide applications of enantioenriched materials. Over the past few decades, there has been significant progress in establishing central chirality and two-point axial chirality (e.g., BINAP). In sharp contrast, efficient generation of three-point axial chirality, such as that in allenes, has met with very limited success and still remains challenging today. On the other hand, enantioenriched allenes are tremendously important not only because of their wide occurrence in natural products and biologically active compounds as well as functional materials but also due to their versatility in organic synthesis as chiral building blocks and even chiral ligands/catalysts.

In summary, we have developed the first intermolecular asymmetric synthesis of 2,3-allenoates by bifunctional catalysis. It is a new addition to the small family of catalytic asymmetric syntheses of allenoates without using stoichiometric amounts of chiral reagents or starting materials. Enabled by the new bifunctional catalyst, the reactions between various nitroalkanes and activated enynes proceed efficiently under mild conditions with good functional group compatibility, and these trisubstituted allenoates were mostly obtained in excellent optical as well as chemical purity. The cinchona-based thiourea catalyst is crucial to the success because it not only provides a highly ordered transition state to promote the first C−C bond formation but also serves as an excellent proton shuttle in the second enantioselectivity determining step. Moreover, it can also function as an excellent isomerization catalyst for the conversion from racemic alkynoates to highly enantioenriched allenoates. These trisubstituted allenoates with a 2-nitroethyl α-substituent have been synthesized for the first time, and they are versatile synthetic intermediates toward other useful building blocks.

手性分子绝对构型的确定

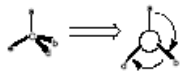
手性分子可以分为下面几种类型：中心手性分子，轴手性分子，平面手性分子及螺旋手性分子。

下面用 R/S 命名法依次对它们进行命名。

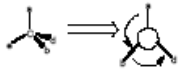
中心手性分子： 如果一个原子连接四个不同的基团，则称这个原子具有手性。常见的有 C, N, P, S, Si, As 等原子。

判断方法：先将与手性原子相连的四个原子（团）按次序规则进行排列，然后将次序最小的原子（团）放在距观察者最远的位置，再观察其他 3 个原子（团）的排列次序，若由大到小的排列次序为顺时针方向，则 R 为型，若为逆时针方向，则为 S 型.

假定原子的优先次序为 a > b > d > e



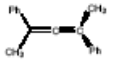
a → b → d 为顺时针方向，R 型



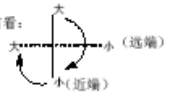
a → b → d 为逆时针方向，S 型

轴手性分子：四个基团围绕一根轴排列在平面之外的体系，当每对基团不同时，有可能是不对称的。轴手性分子可分为以下几种类型：

丙二烯型分子：

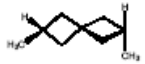


从左向右看：



逆时针方向，R 型

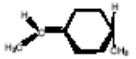
螺环型分子：



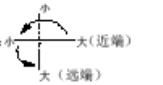
从左向右看：

逆时针方向，S 型

环外双键型分子：

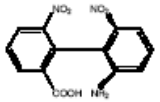


从左向右看：小

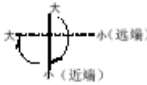


逆时针方向，S 型

联苯型分子：



从左向右看：



顺时针方向，R 型

判断方法：从左向右看，先看到的基团为近端，用实线表示，后看到的基团为远端，用虚线表示，然后从近端的大基团看到近端的小基团再看到远端的大基团（不看远端的小基团），若为顺时针方向，则为则 R 为型，若为逆时针方向，则为 S 型.

平面手性分子：平面手性通过对称平面的失对称作用而产生，其手性取决与平面的一边与另