

Literature Report 4

Organocatalytic Asymmetric Deoxygenation of Sulfones to Access Chiral Sulfinyl Compounds

Reporter: Qing-Xian Xie
Checker: Xiang Li

2023-4-24

Huang, S.; Yan, H.* *Nat. Chem.* **2023**, *15*, 185-193

CV of Prof. Hailong Yan



Research:

- Asymmetric axis chiral chemistry
 - Organocatalytic multicomponent reactions
 - Discovery and synthesis of chiral drug molecules
-

Background:

- **2000-2004** B.S., Northeastern University
- **2004-2007** M.S., Xinjiang Technical Institute of Physics and Chemistry
- **2007-2011** Ph.D., Sungkyunkwan University (Prof. Choong Eui Song)
- **2011-2012** Postdoc., Sungkyunkwan University (Prof. Choong Eui Song)
- **2012-2013** Postdoc., National University of Singapore (Prof. Yu Zhao)
- **2013-Now** Professor, Chongqing University

Contents

1 Introduction

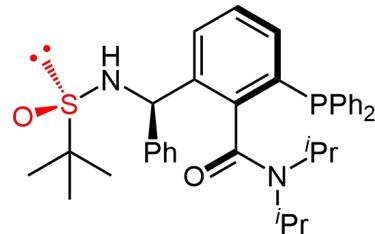
2 Main Strategies to Construct Chiral Sulfinyls

3 Deoxygenation of Sulfones to Access Chiral Sulfinyls

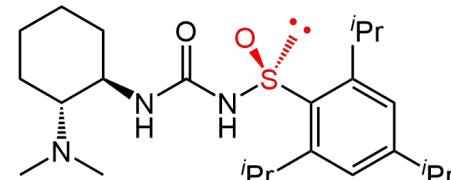
4 Summary

Introduction

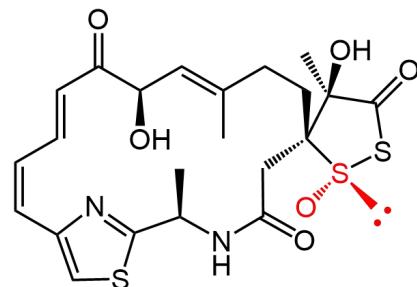
Potential Utility of Chiral Sulfinyl Compounds



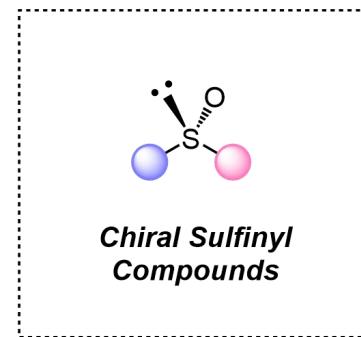
Chiral Organosulfur Ligand



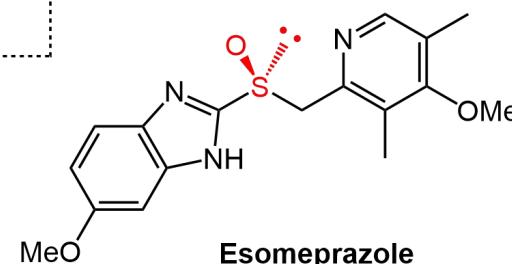
Organocatalyst



Leinamycin



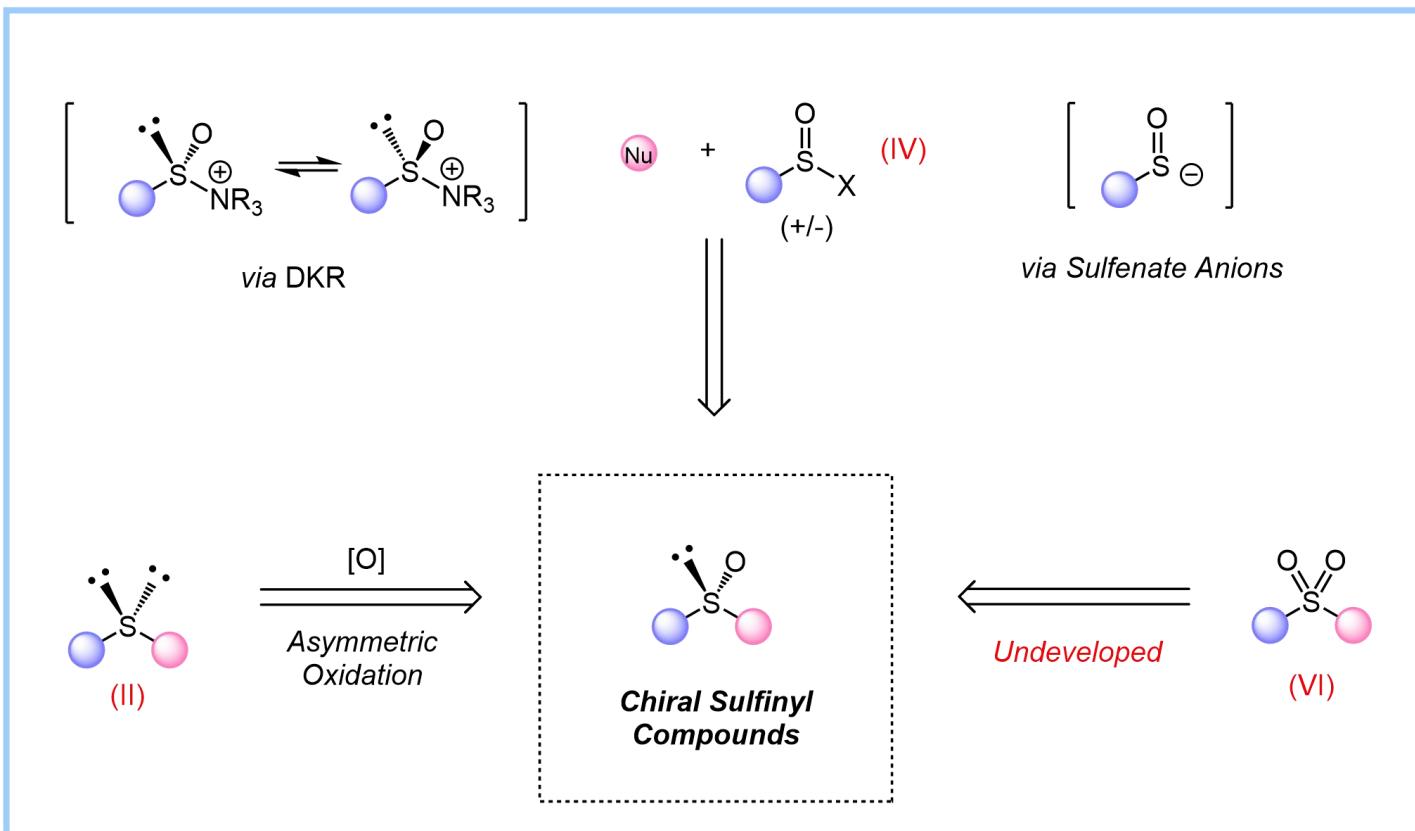
Chiral Sulfinyl Compounds



Esomeprazole

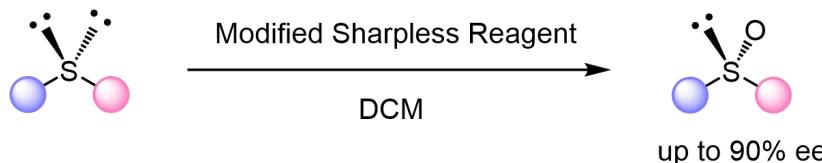
Introduction

Main Strategies to Construct Chiral Sulfinyl Compounds

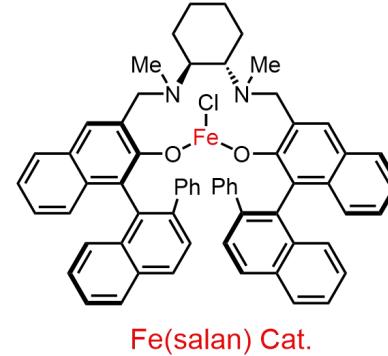
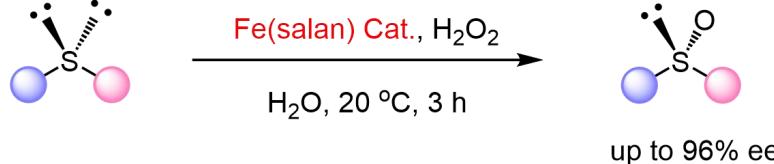


Asymmetric Oxidation from Divalent Sulfides

Sharpless and Jacobsen/Katsuki Type Asymmetric Oxidation



Modified Sharpless Reagent: Ti(O*i*Pr)₄/(*R,R*)-DET/TBHP/ H_2O (1:2:1:1)

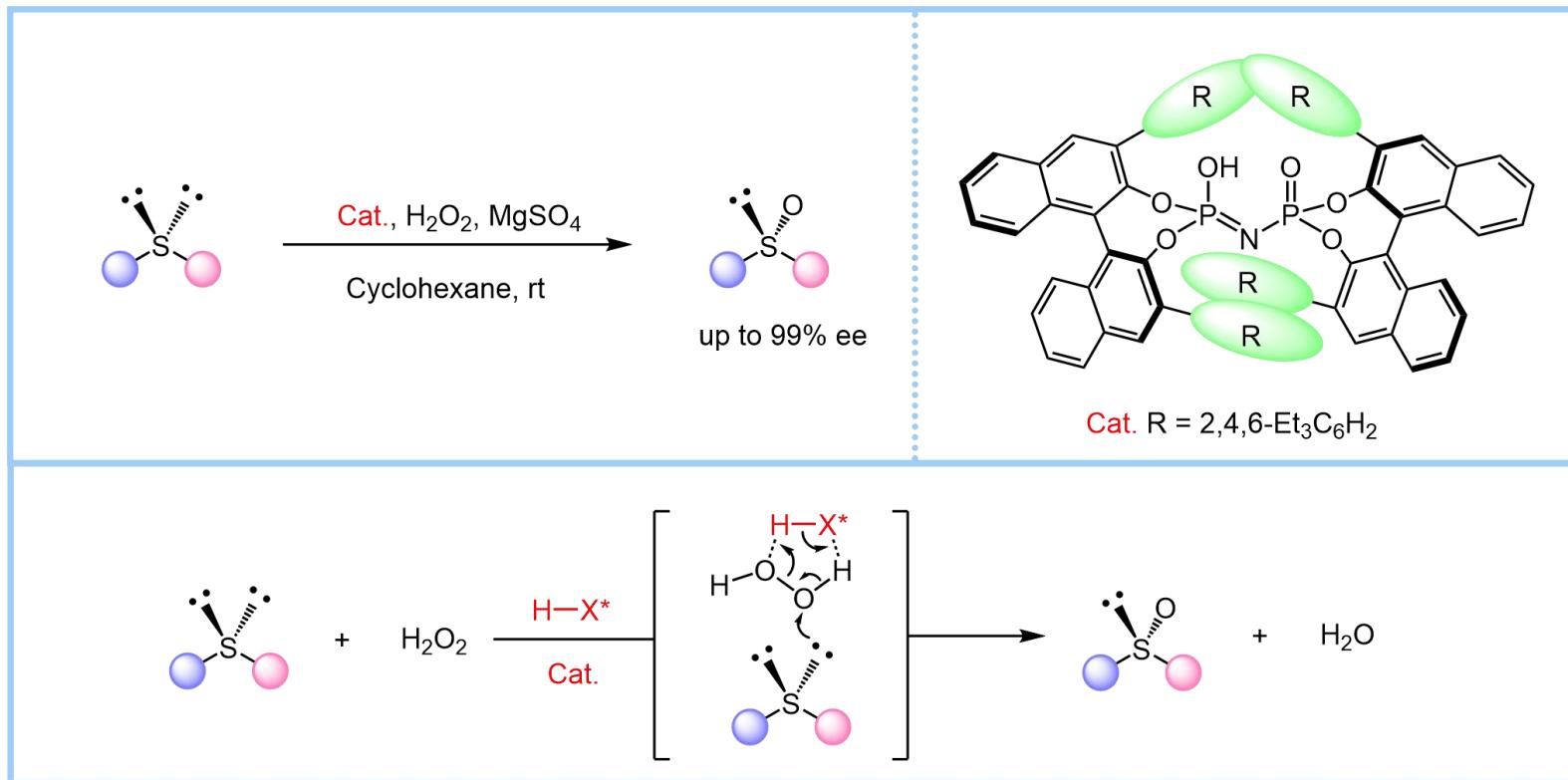


Pitchen, P.; Kagan, H. B.* *J. Am. Chem. Soc.* **1984**, *106*, 8188-8193

Egami, H.; Katsuki, T.* *J. Am. Chem. Soc.* **2007**, *129*, 8940-8941

Asymmetric Oxidation from Divalent Sulfides

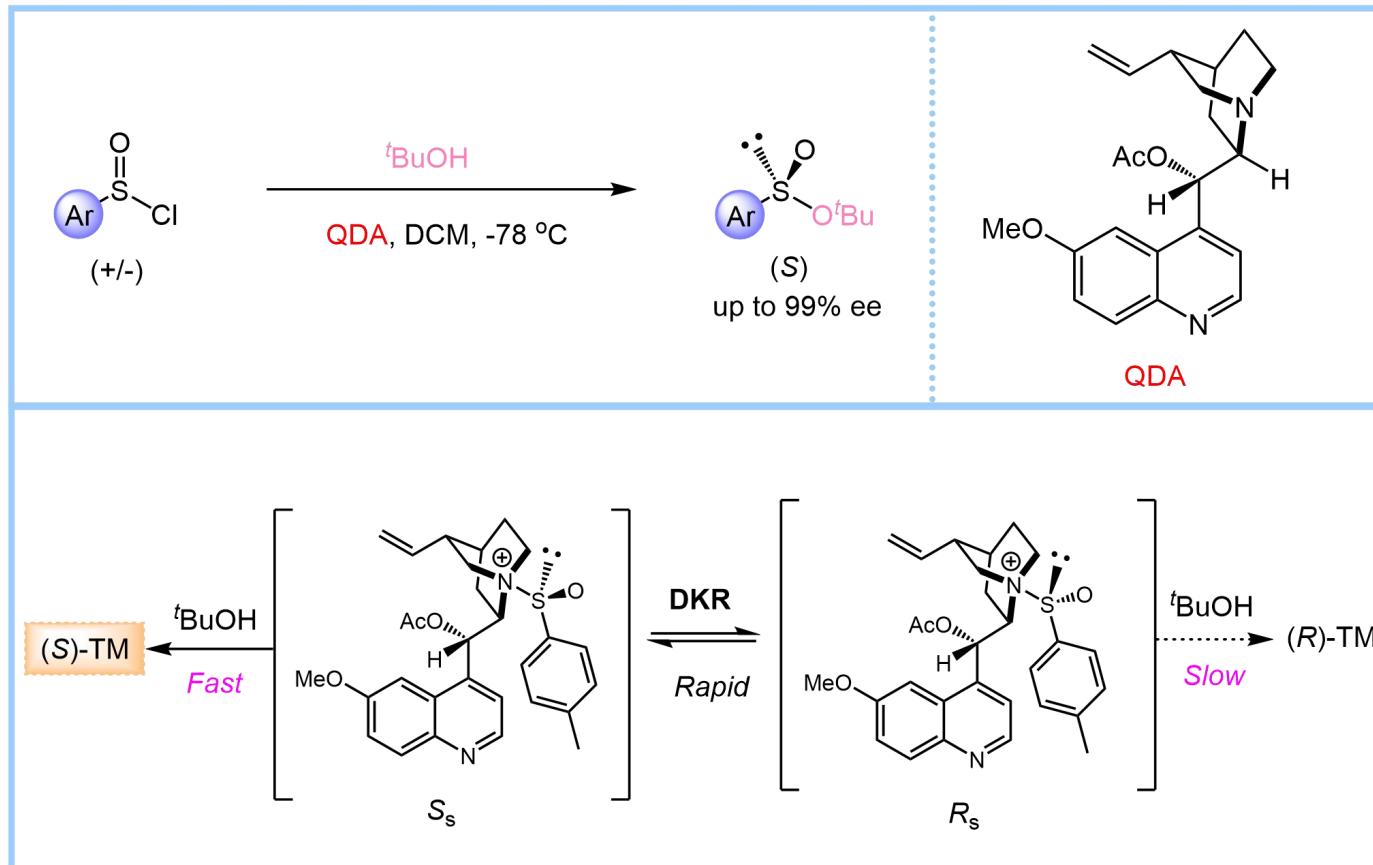
Organocatalytic Asymmetric Oxidation



Liao, S.; List, B.* *J. Am. Chem. Soc.* **2012**, 134, 10765-10768

Synthesis from Tetravalent Organosulfur Compounds

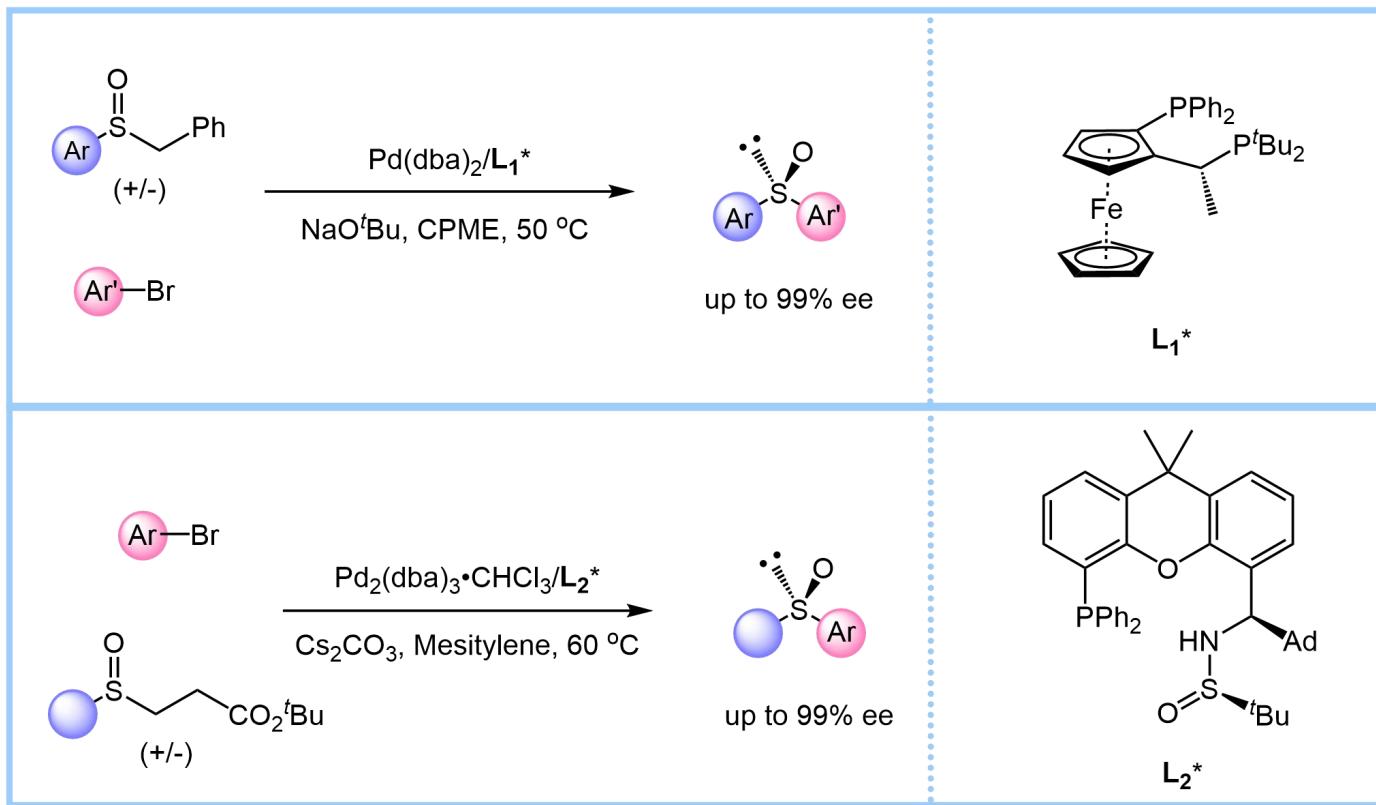
Organocatalytic Enantioselective Nucleophilic Substitution



Shibata, N.*; Toru, T.* *J. Am. Chem. Soc.* **2005**, 127, 1374-1375

Synthesis from Tetravalent Organosulfur Compounds

Transition-Metal-Catalyzed Arylations via Sulfenate Anions

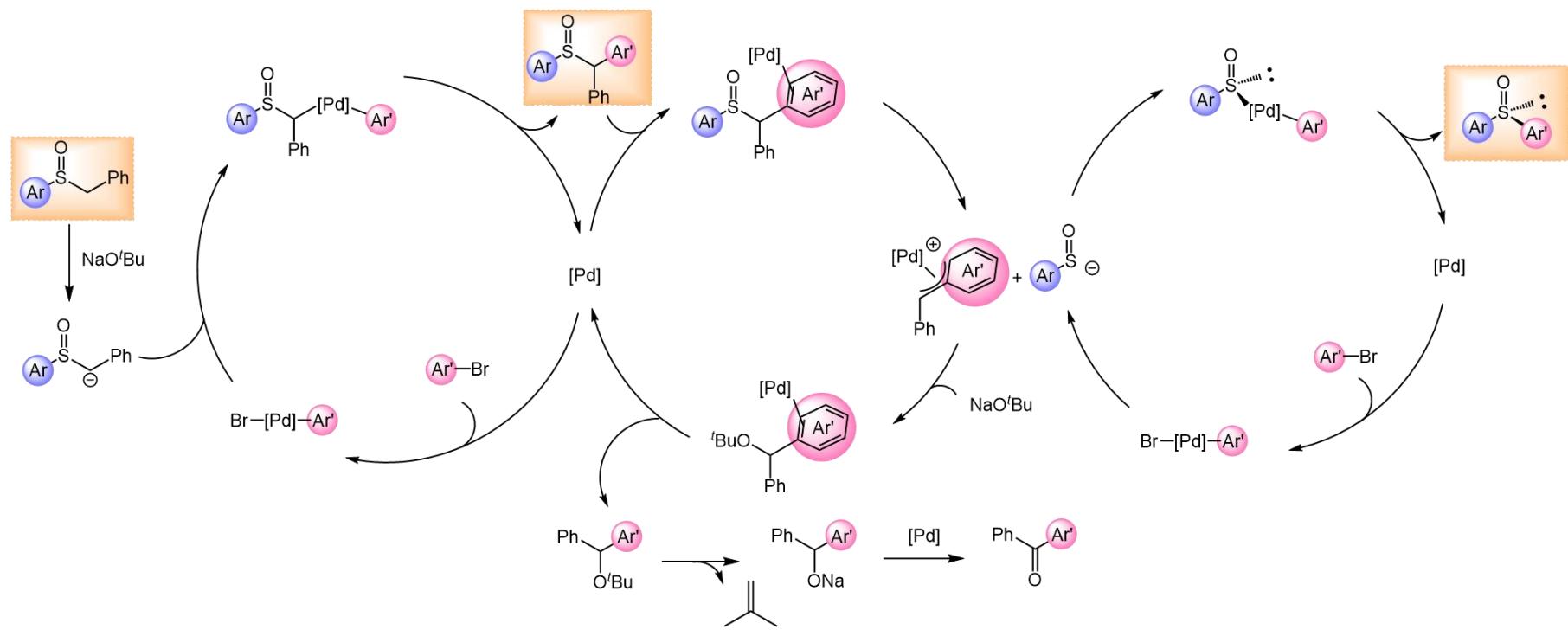


Jia, T.; Walsh, P. J.* *J. Am. Chem. Soc.* **2017**, *139*, 8337-8345

Wang, L.; Zhang, J.* *J. Am. Chem. Soc.* **2018**, *140*, 3467-3473

Synthesis from Tetravalent Organosulfur Compounds

Transition-metal-catalyzed Arylations via Sulfenate Anions

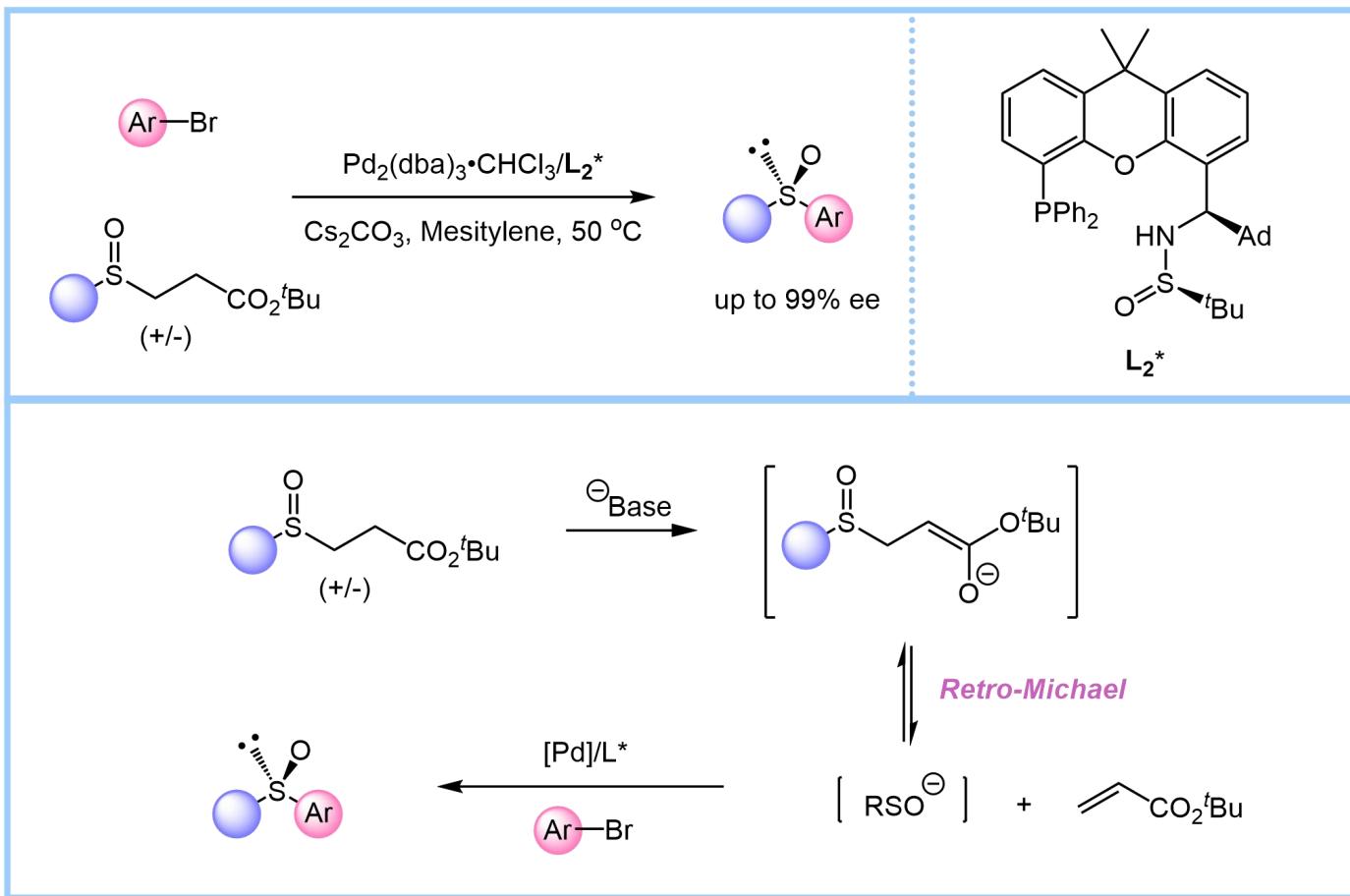


Jia, T.; Walsh, P. J.* *J. Am. Chem. Soc.* **2017**, *139*, 8337-8345

Jia, T.; Walsh, P. J.* *Angew. Chem. Int. Ed.* **2014**, *53*, 260-264

Synthesis from Tetravalent Organosulfur Compounds

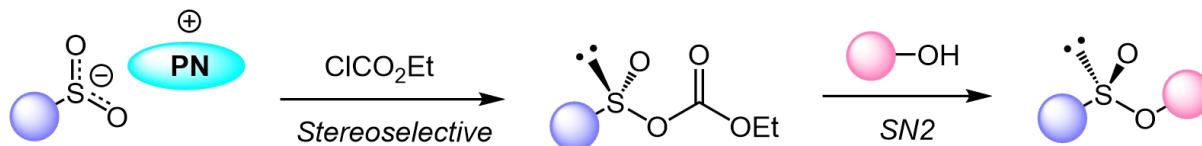
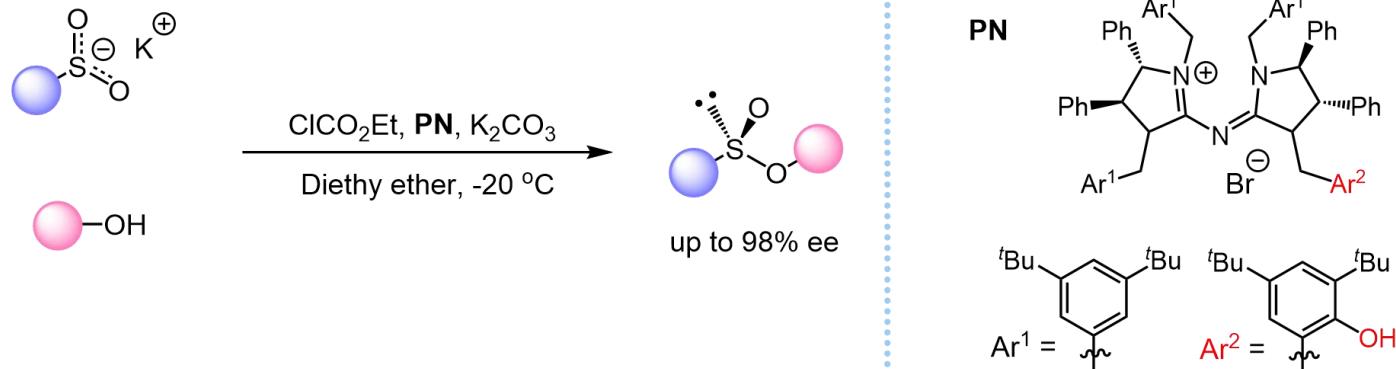
Transition-metal-catalyzed Arylations via Sulfenate Anions



Wang, L.; Zhang, J.* *J. Am. Chem. Soc.* **2018**, *140*, 3467-3473

Synthesis from Tetravalent Organosulfur Compounds

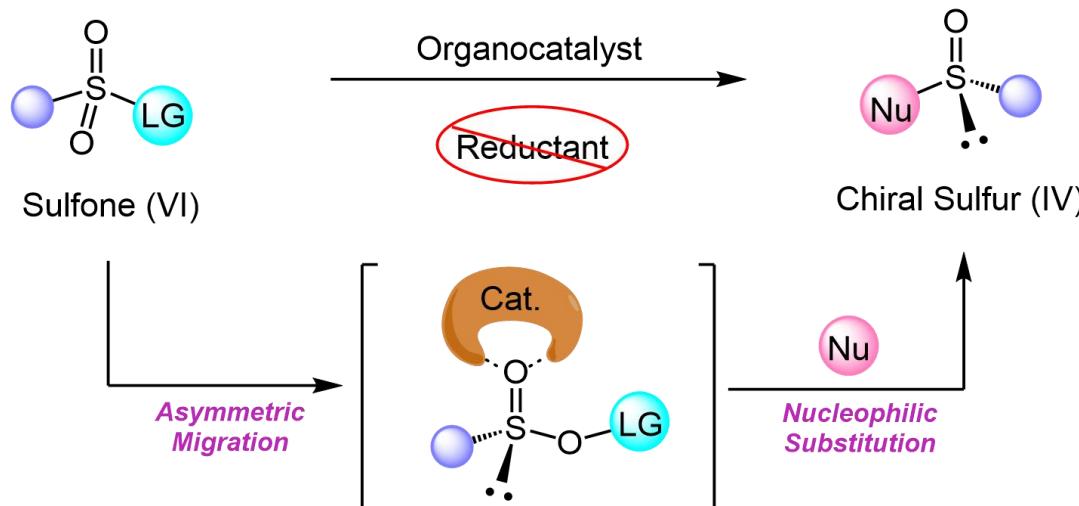
Synthesis of Chiral Sulfinic Esters by Asymmetric Condensation



Zhang, X.; Tan, C.-H.* *Nature* **2022**, *604*, 298-303

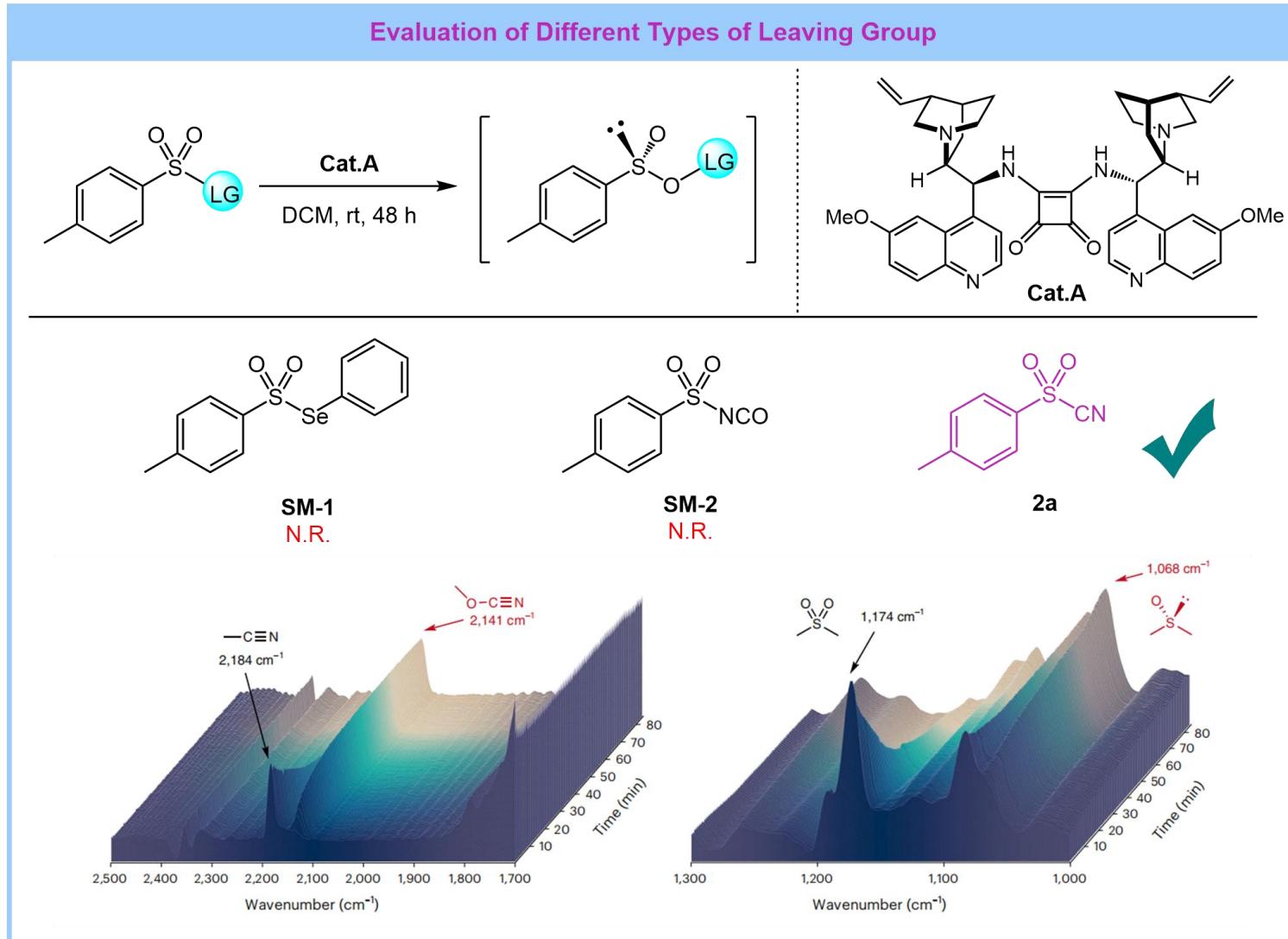
Project Synopsis

Organocatalytic Enantioselective Deoxygenation of Sulfones



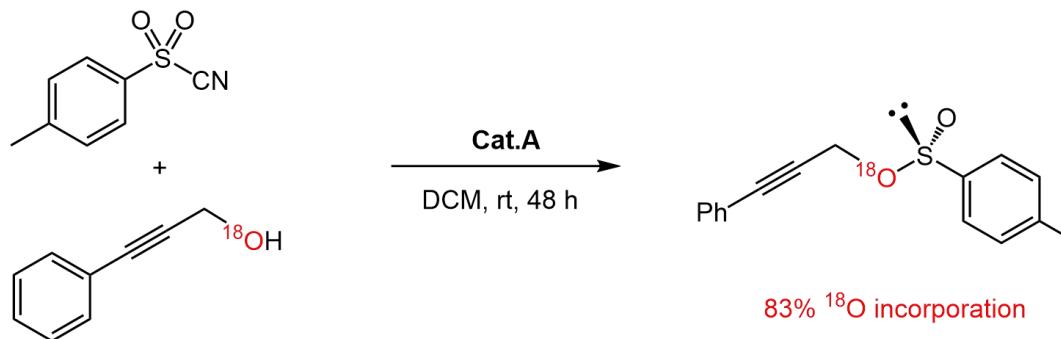
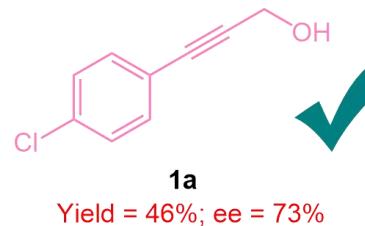
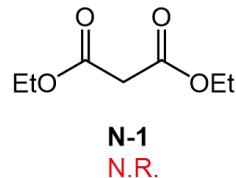
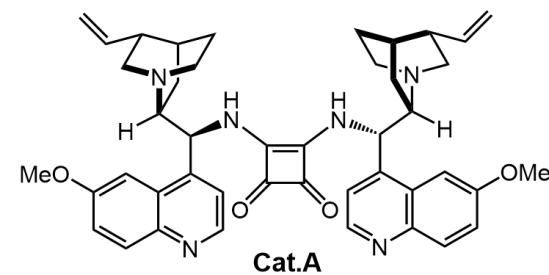
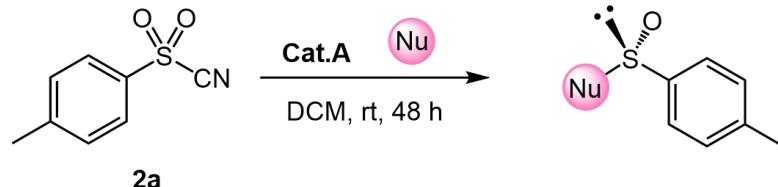
Huang, S.; Yan, H.* *Nat. Chem.* **2023**, 15, 185-193

Optimization of Reaction Conditions



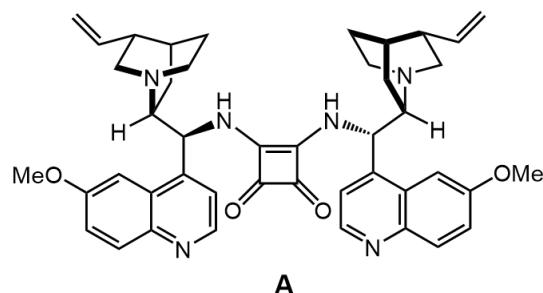
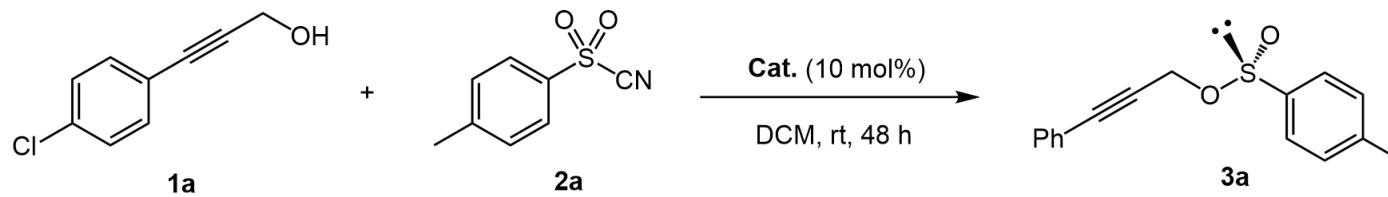
Optimization of Reaction Conditions

Trapped the Intermediate *in situ* with Nucleophiles

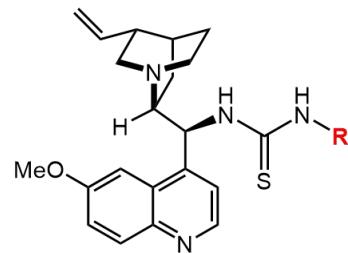


Optimization of Reaction Conditions

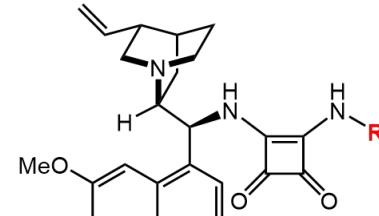
Initial Screening of Organocatalysts



46% yield; 73% ee

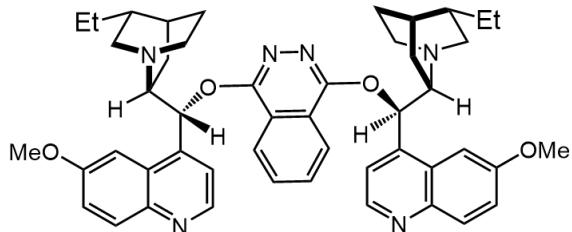


19% yield; 3% ee

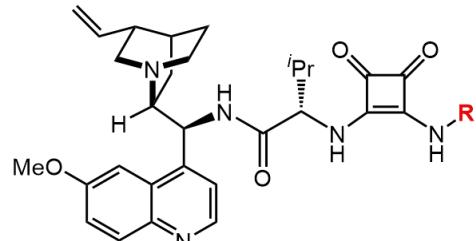


82% yield; 34% ee

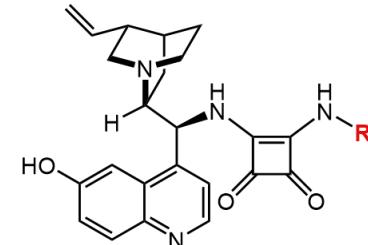
R = 3,5-(CF₃)₂-C₆H₃



55% yield; 20% ee



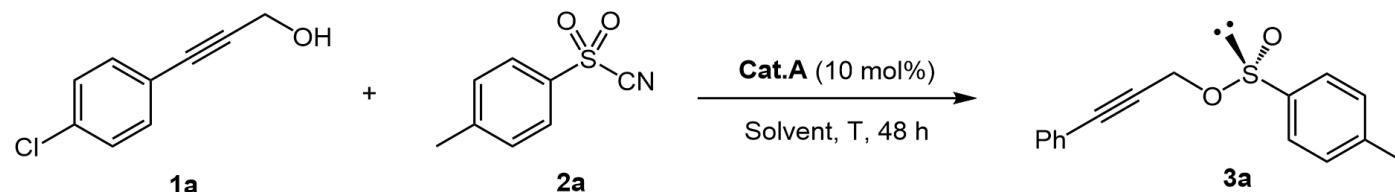
34% yield; 8% ee



56% yield; 30% ee

Optimization of Reaction Conditions

Further Optimization of Other Reaction Parameters

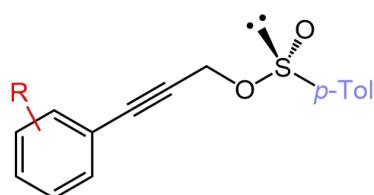
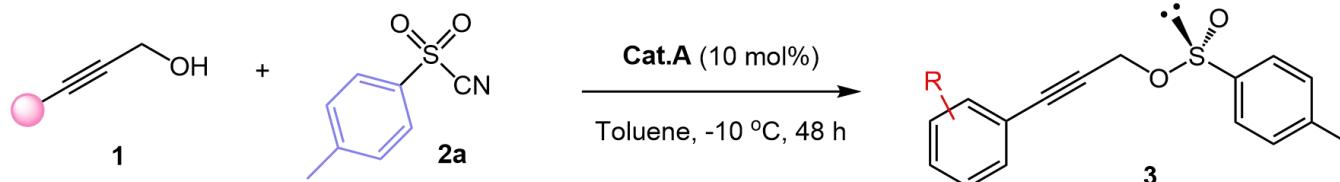


Entry ^a	Solvent	Temp. (°C)	Yield of 3a (%)	Ee of 3a (%)
1	DCM	rt	46	73
2	THF	rt	---	---
3	CH ₃ CN	rt	43	70
4	Toluene	rt	53	80
5	<i>m</i> -Xylene	rt	12	67
6	Toluene	0	61	87
6	Toluene	-10	67	91
6	Toluene	-20	63	89

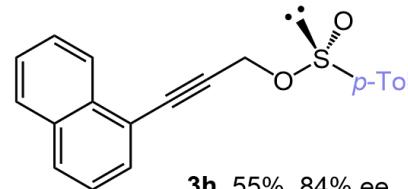
^aReaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.2 mmol, 1.0 equiv.) and **Cat. A** (10 mol%) in solvent (4.0 mL) were stirred at the corresponding temperature for 48 h.

Substrate Scope

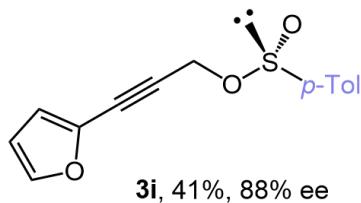
a) Substrate Generality of the Propargylic Alcohol



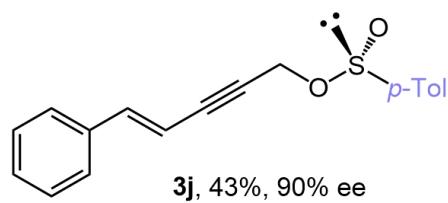
3a, $\text{R} = p\text{-Cl}$, 67%, 91% ee
3b, $\text{R} = p\text{-H}$, 43%, 90% ee
3c, $\text{R} = p\text{-Br}$, 47%, 90% ee
3d, $\text{R} = p\text{-OMe}$, 62%, 89% ee
3e, $\text{R} = o\text{-Cl}$, 46%, 88% ee
3f, $\text{R} = m\text{-Cl}$, 46%, 87% ee
3g, $\text{R} = 3,5\text{-(Me)}_2$, 59%, 82% ee



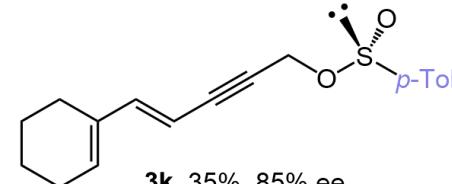
3h, 55%, 84% ee



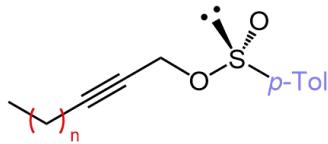
3i, 41%, 88% ee



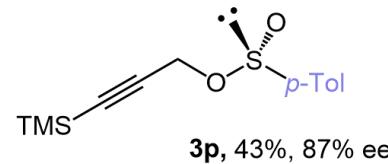
3j, 43%, 90% ee



3k, 35%, 85% ee



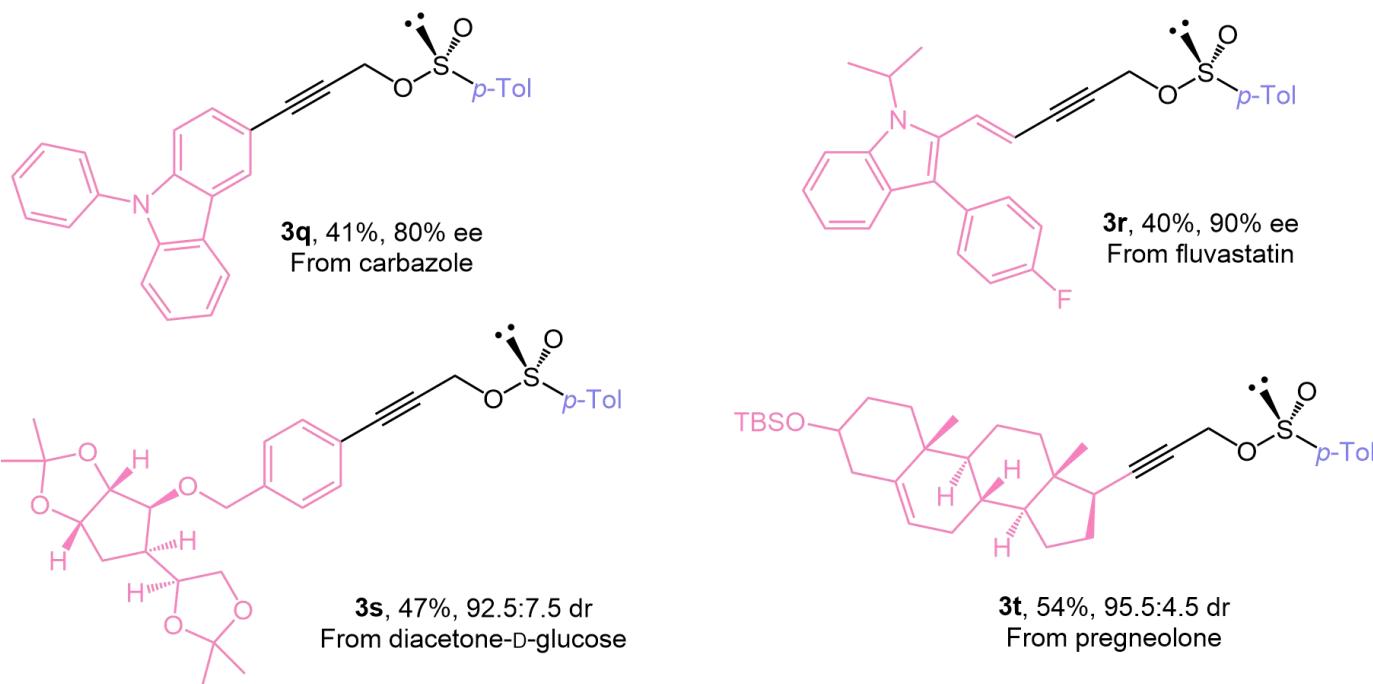
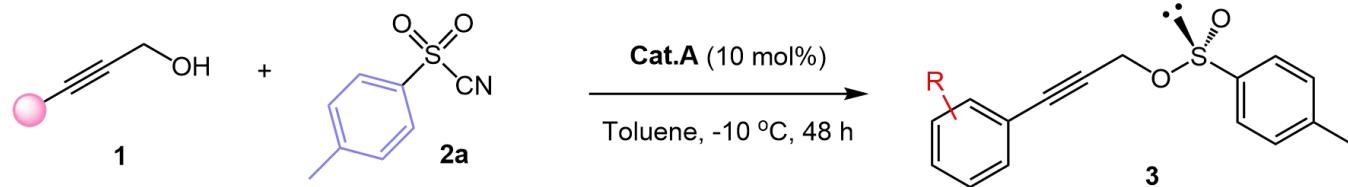
3l, $n = 0$, 32%, 90% ee
3m, $n = 2$, 31%, 94% ee
3n, $n = 4$, 55%, 94% ee
3o, $n = 6$, 48%, 87% ee



3p, 43%, 87% ee

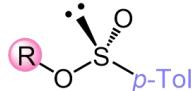
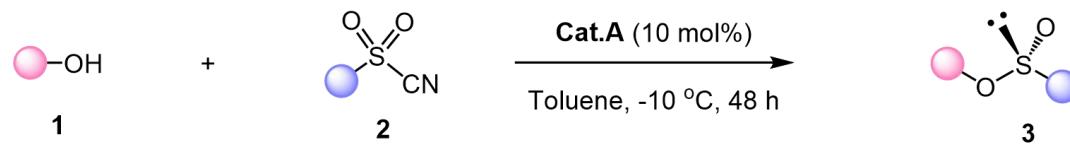
Substrate Scope

a) Substrate Generality of the Propargylic Alcohol



Substrate Scope

b) Other Alcohol Scope and Sufonyl Cyanide Scope



3aa, R = cinnamyl, 55%, 77% ee

3bb, R = benzyl, 31%, 80% ee

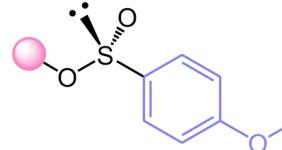
3cc, R = ethyl, 64%, 87% ee

3dd, R = octadecyl, 51%, 91% ee

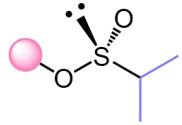
3ee, R = phenethyl, 67%, 90% ee

3ff, R = isopropyl, 47%, 88% ee

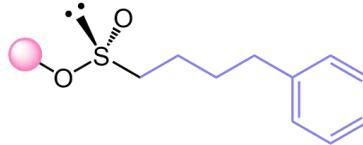
3ee, R = cyclohexyl, 44%, 88% ee



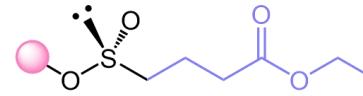
3ff, 46%, 89% ee



3gg, 44%, 87% ee

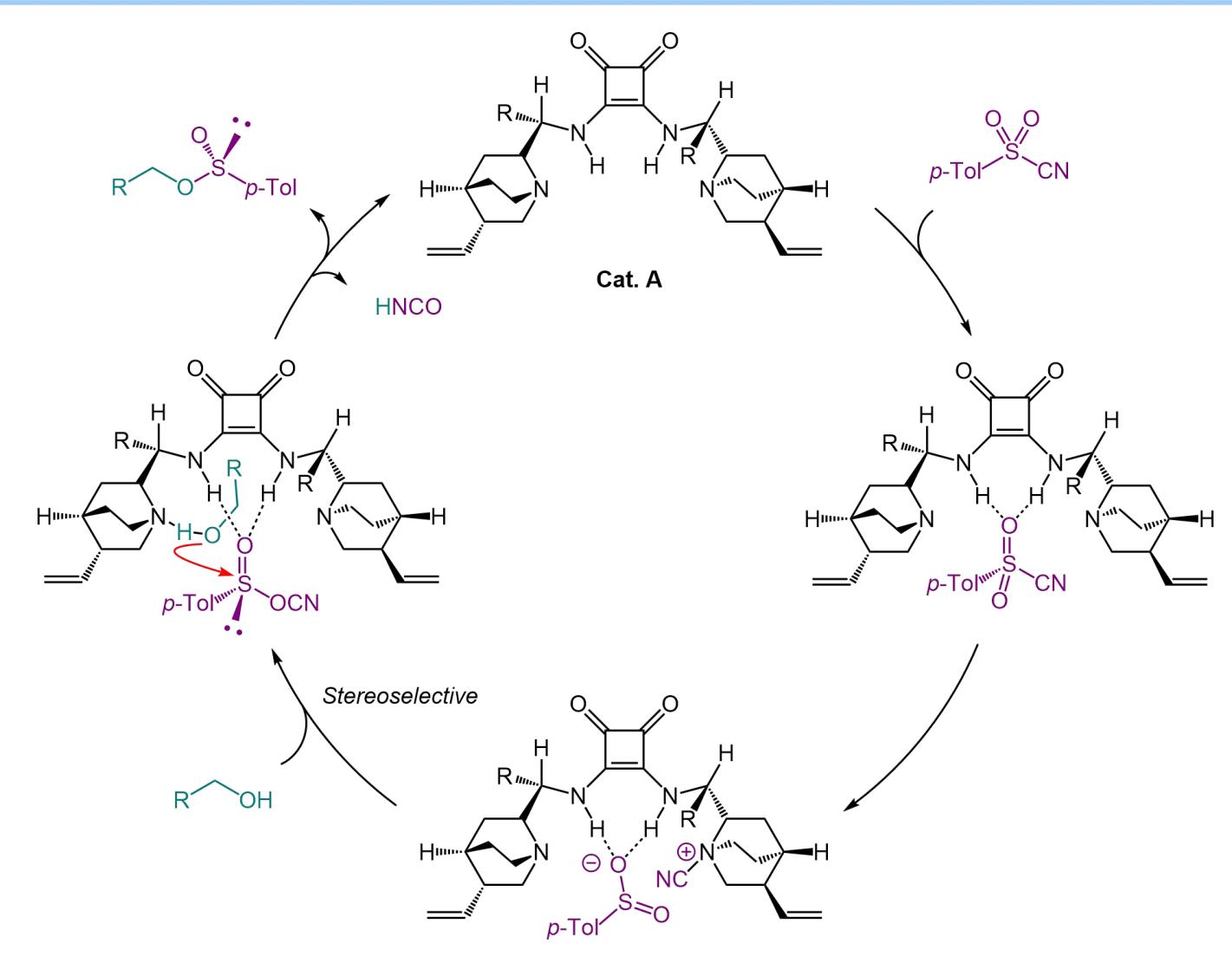


3gg, 54%, 80% ee



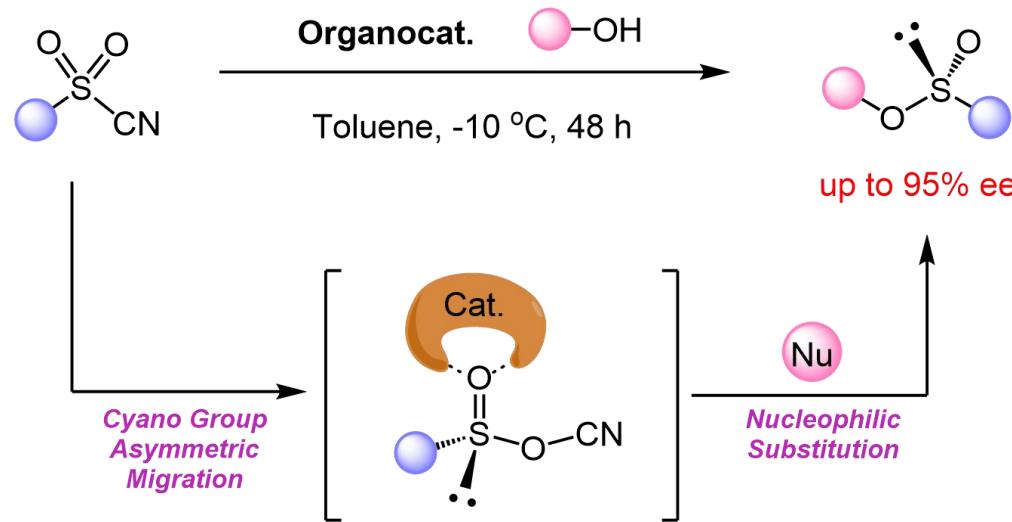
3hh, 46%, 58% ee

Proposed Mechanism



Summary

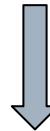
Organocatalytic Enantioselective Deoxygenation of Sulfones



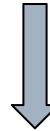
The First Paragraph

写作思路

四价硫立体中心化合物合成现状



介绍脱氧制备手性亚磺酰基化合物的策略及挑战

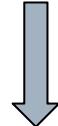


提出有机催化脱氧制备手性亚磺酰基化合物设想

The Last Paragraph

写作思路

总结工作：有机催化脱氧构建四价硫立体中心



关键机理：奎宁促进的氰基不对称迁移

Representative Examples

- …to access sulfinyl derivatives with sulfones as odourless, **easy-to-handle** and widely available raw material. (易于操控的)
- However, **looking at textbooks or reviews on the topic of** organosulfur chemistry, direct deoxygenation of sulfones has never emerged as a practical route to access chiral sulfinyl compounds. (用于提出全新研究方向)
- …the late-stage modification of drugs and bioactive natural products would **reveal the prospective utility of this protocol.**(揭示某种方法潜在价值)

Acknowledgement

Thanks for Your Attention