

Literature Report 6

Chiral Selenide/Achiral Sulfonic Acid Cocatalyzed Atroposelective Sulfenylation of Biaryl Phenols

Reporter: Han Wang

Checker: Qing-Xian Xie

Date: 2022.06.27

Luo, H.-Y.; Chen, Z.-M.* *J. Am. Chem. Soc.* **2022**, *144*, 2943.

CV of Dr. Chen Zhi-Min



Background:

- **2005-2009** B.S., Fuzhou University
- **2009-2014** Ph.D., Lanzhou University
- **2014-2017** Postdoc., Shanghai Jiao Tong University
- **2015-2017** Postdoc., The University of Utah
- **2017-now** Researcher, Shanghai Jiao Tong University

Research:

- ✓ **Chiral selenium chemistry and sulfur chemistry**
- ✓ **Asymmetric catalytic reactions**
- ✓ **Total synthesis of active natural products and drug molecules**

Contents

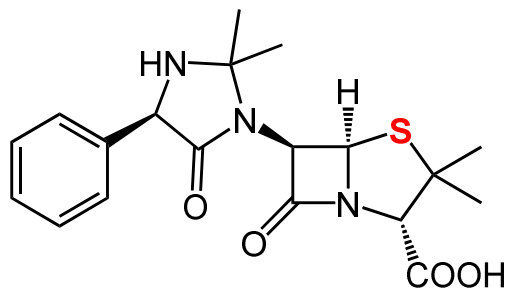
1 Introduction

2 Atroposelective Sulfenylation of Biaryl Phenols

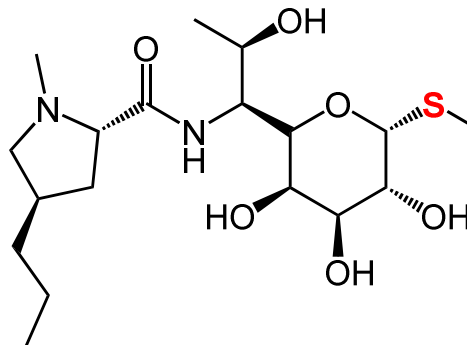
3 Summary

Introduction

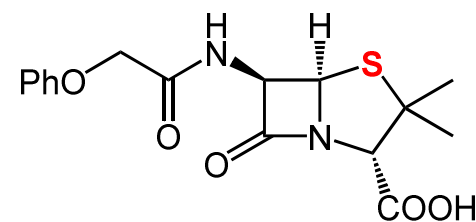
Chiral Sulfur-containing Drugs and Ligands



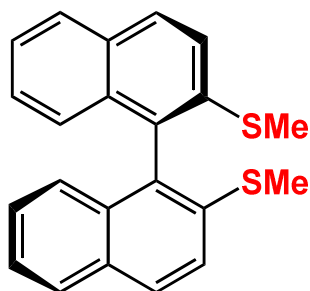
Hetacillin



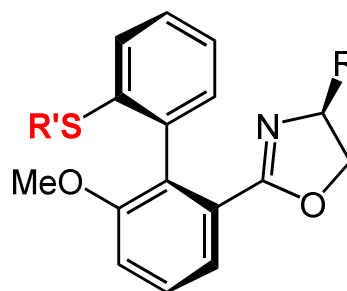
Lincomycin



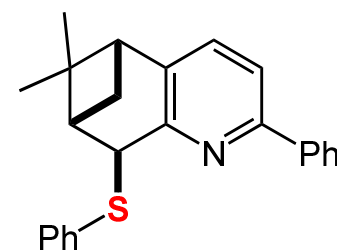
Penicillin V



Dithioether ligand



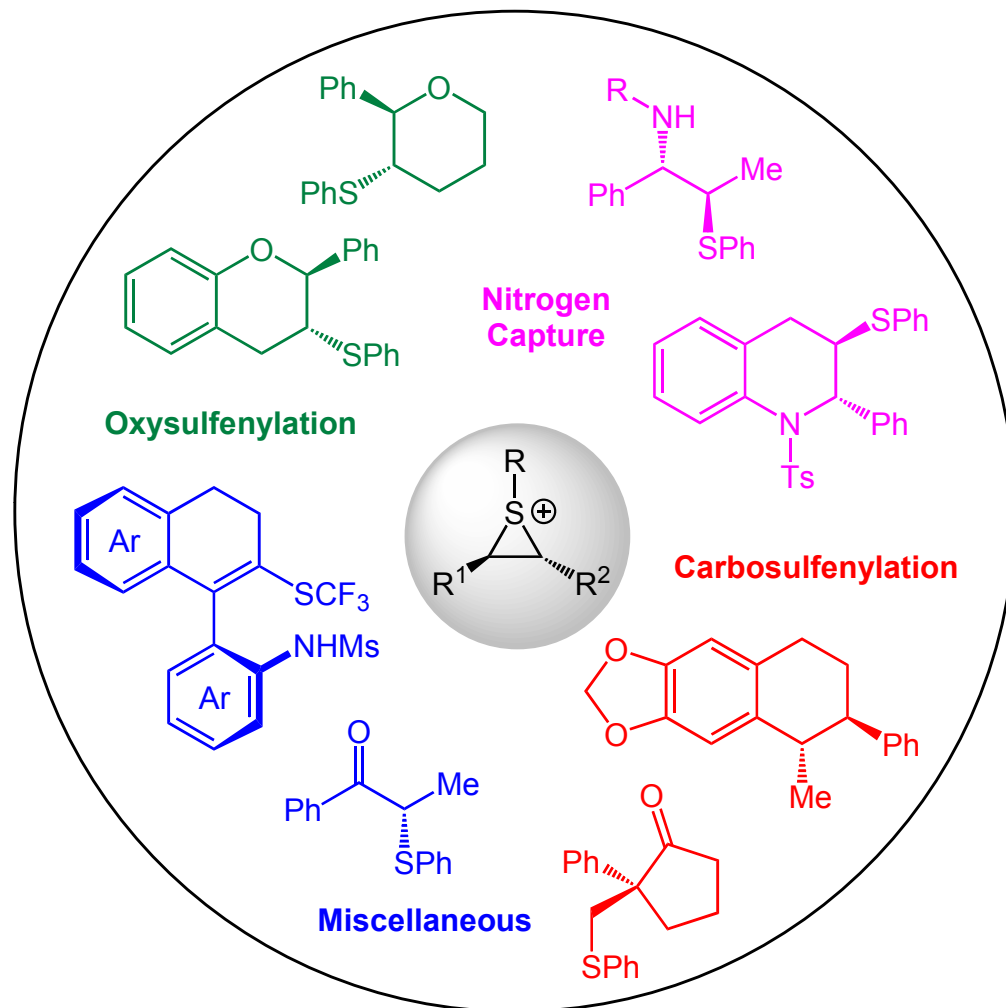
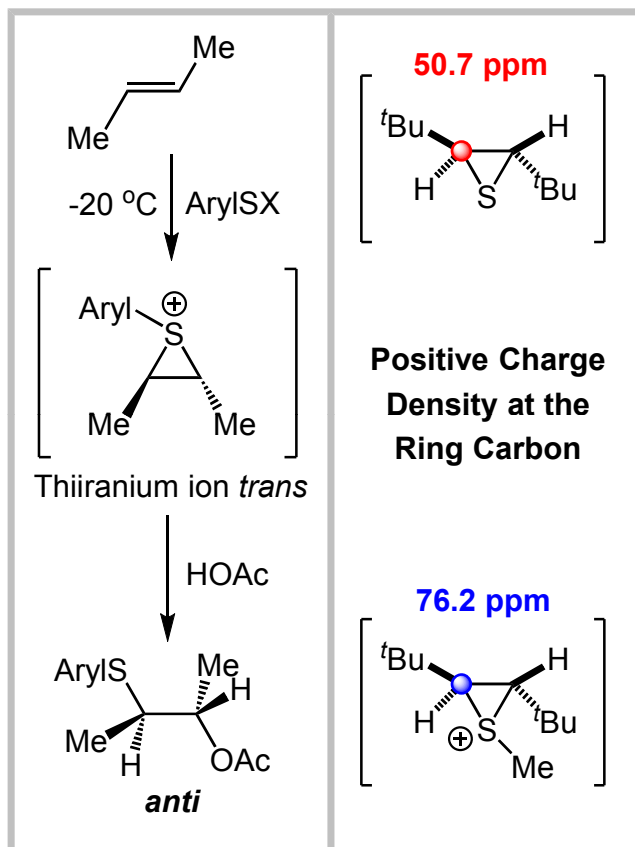
Thioether-oxazoline ligands



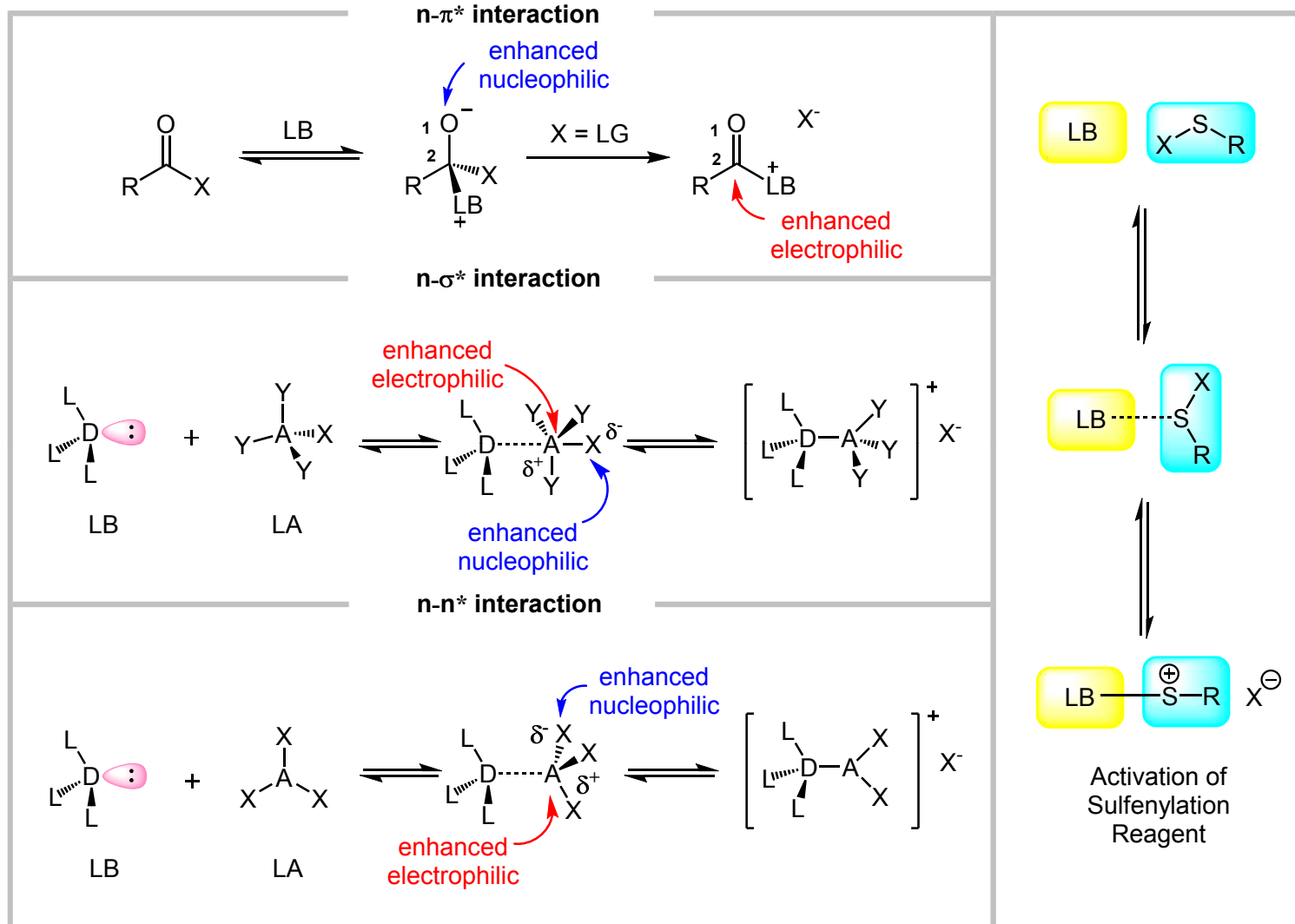
Thioether-pyridine ligands

Scott, K. A. *et al.* *Top. Curr. Chem.* **2018**, 376, 5.
Masdeu-Bultó, A. M. *et al.* *Coordin. Chem. Rev.* **2003**, 242, 159.

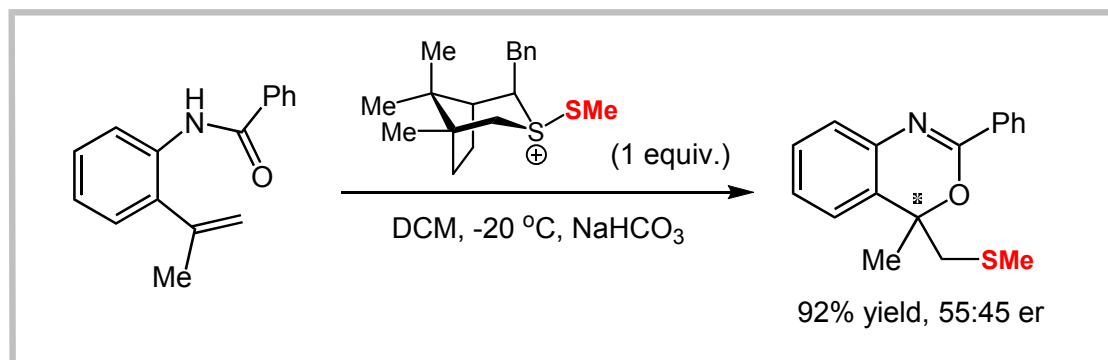
Introduction



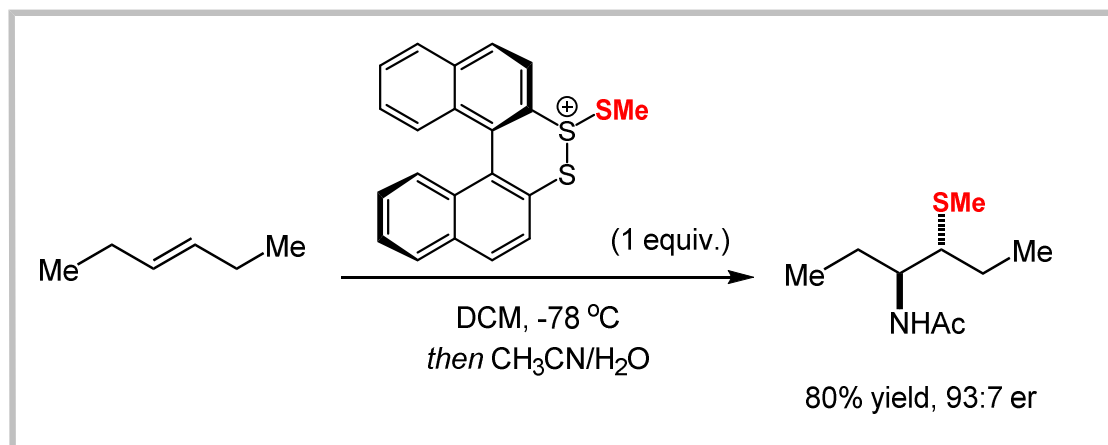
LB Activation of LA



Early Studies

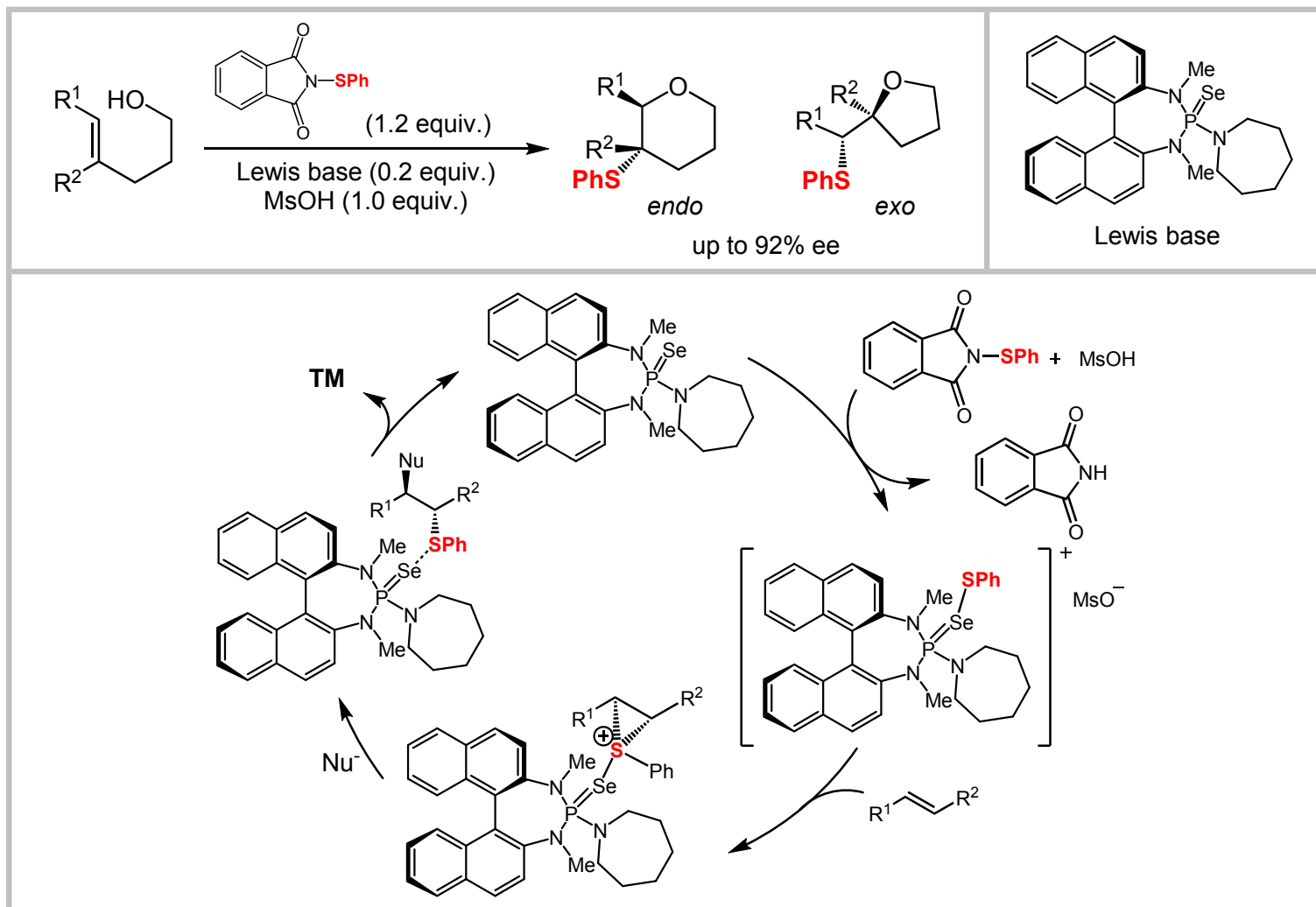


Rayner, C. M. *et al. Synlett.* **1994**, 32, 617.



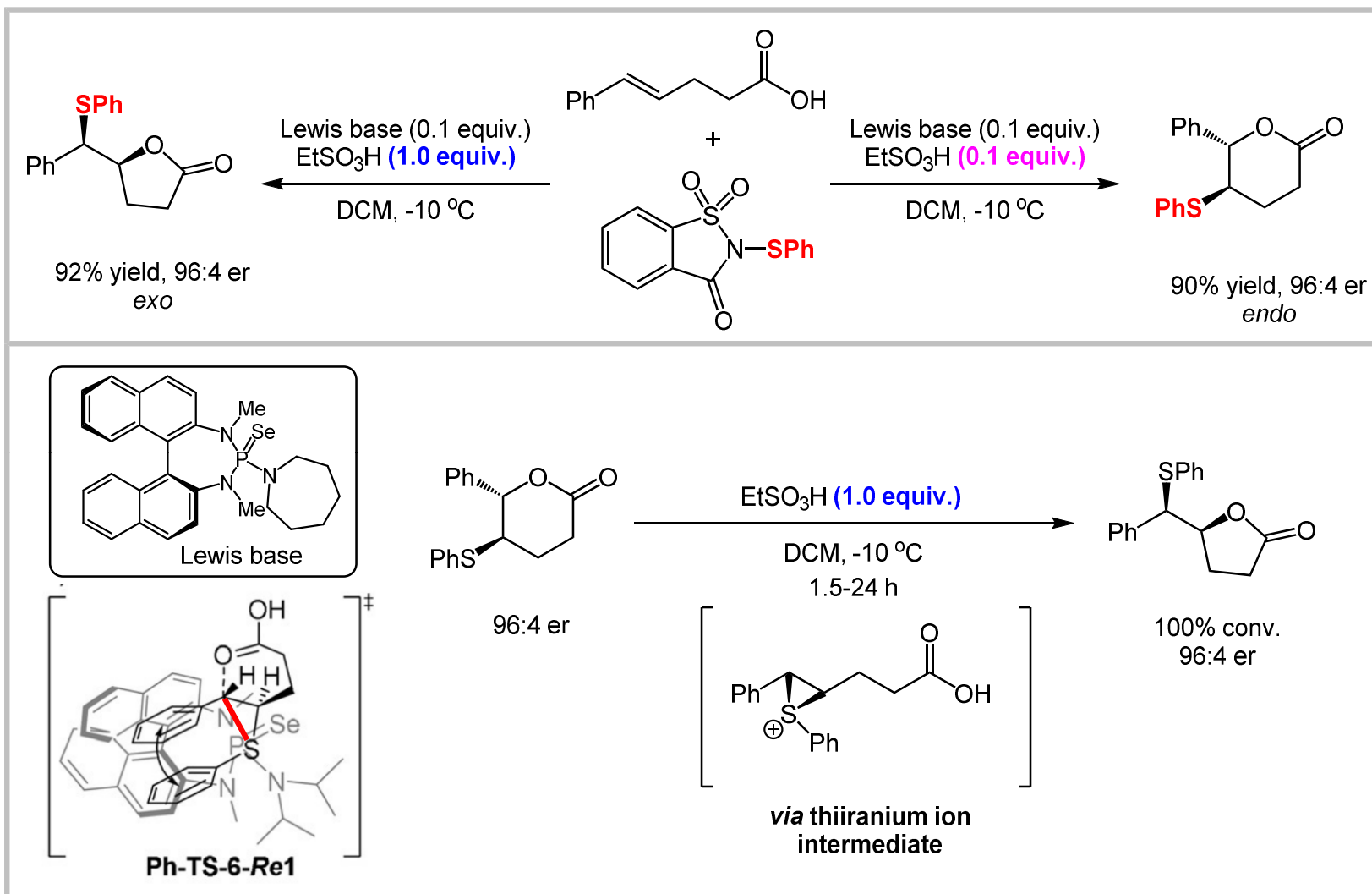
Pasquato, L. *et al. J. Chem. Soc. Chem. Commun.* **1994**, 1565.

Oxysulfenylation



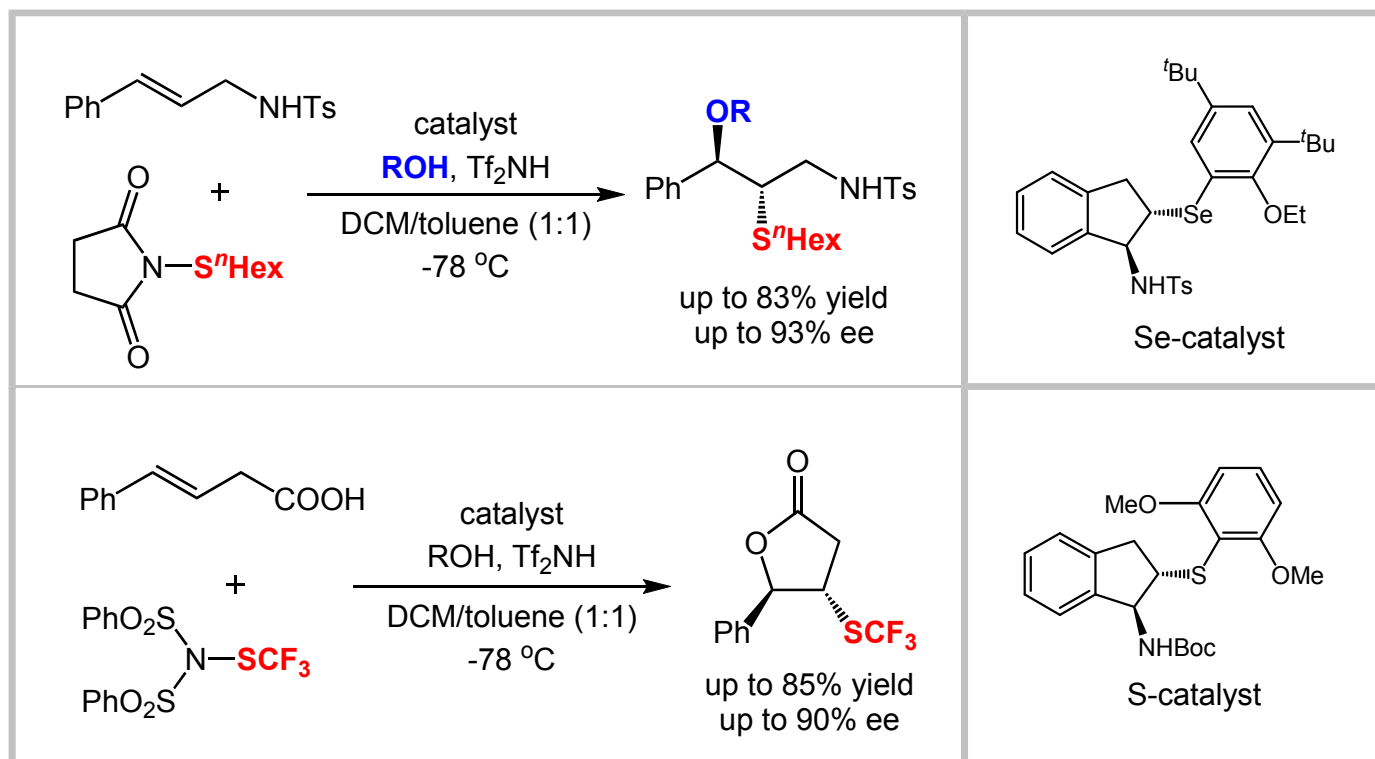
Denmark, S. E. *et al.* *J. Am. Chem. Soc.* **2011**, *133*, 15308.

Oxysulfenylation



Chen, Z. M. *et al.* *Chem. Eur. J.* **2019**, *25*, 15411.

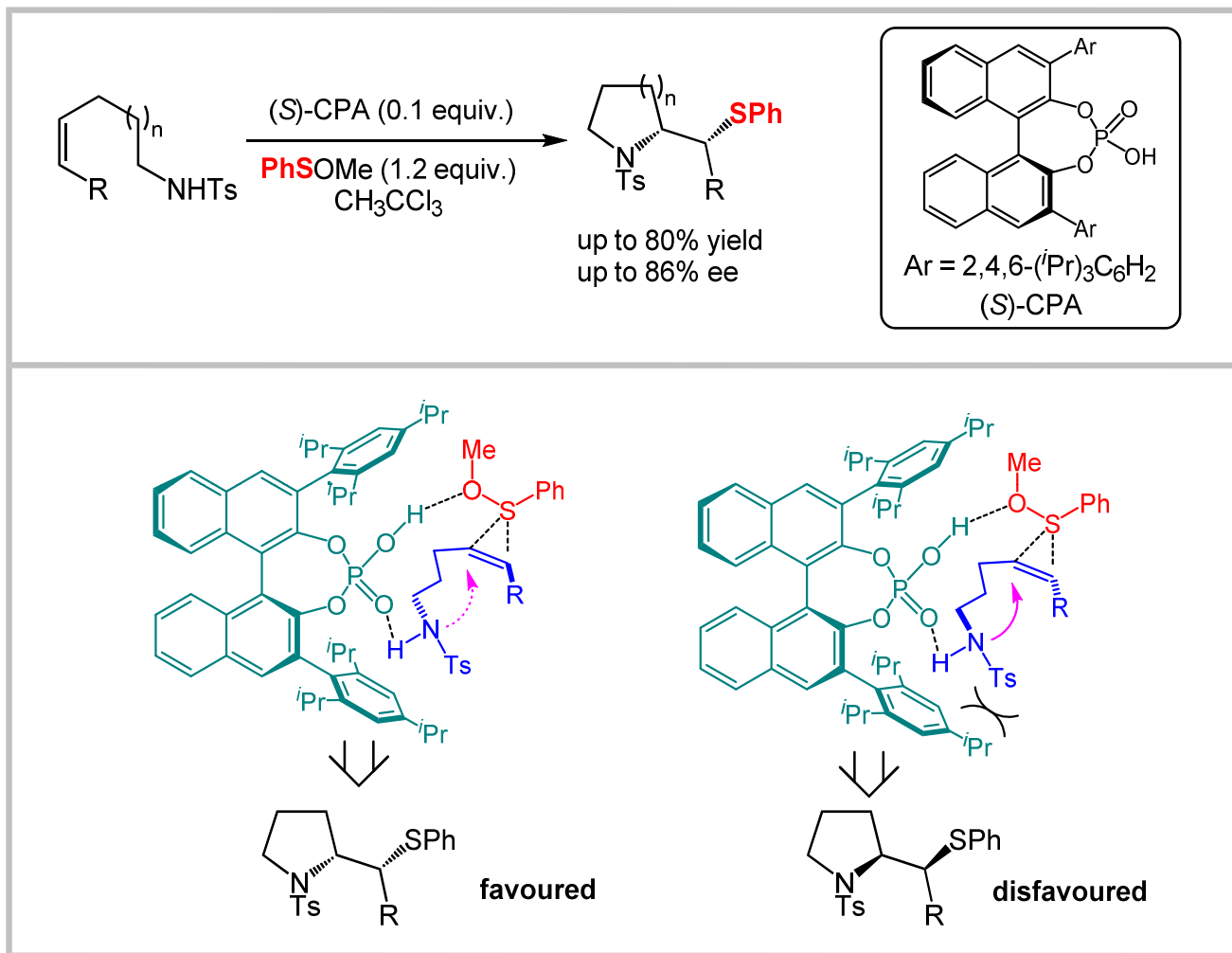
Oxysulfenylation



Zhao, X. *et al.* *Angew. Chem. Int. Ed.* **2016**, *55*, 5846.

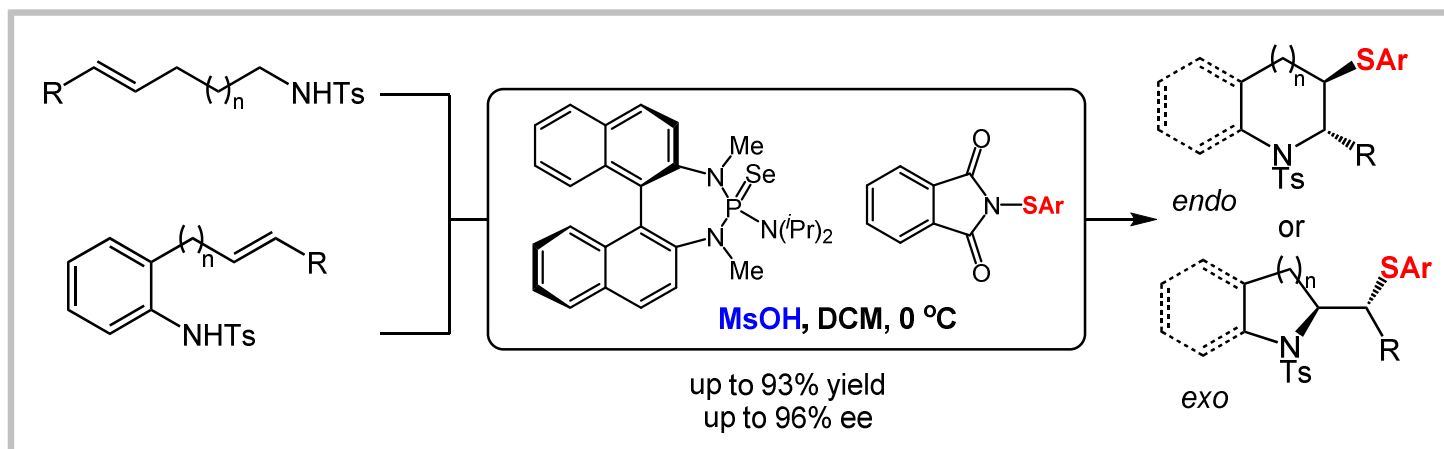
Zhao, X. *et al.* *ACS Catal.* **2019**, *9*, 6896.

Nitrogen Capture



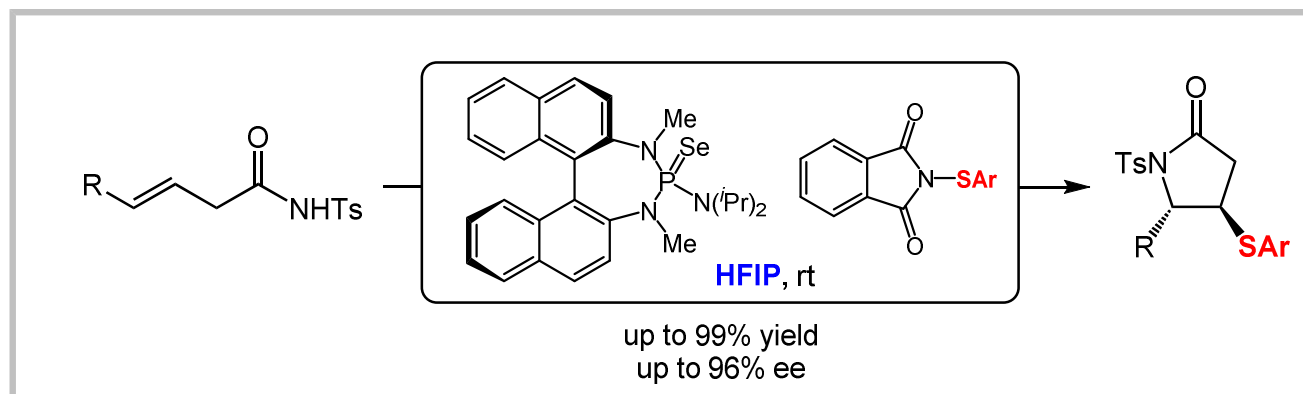
Shi, Y. *et al.* *RSC Adv.* **2013**, *3*, 4523.

Nitrogen Capture



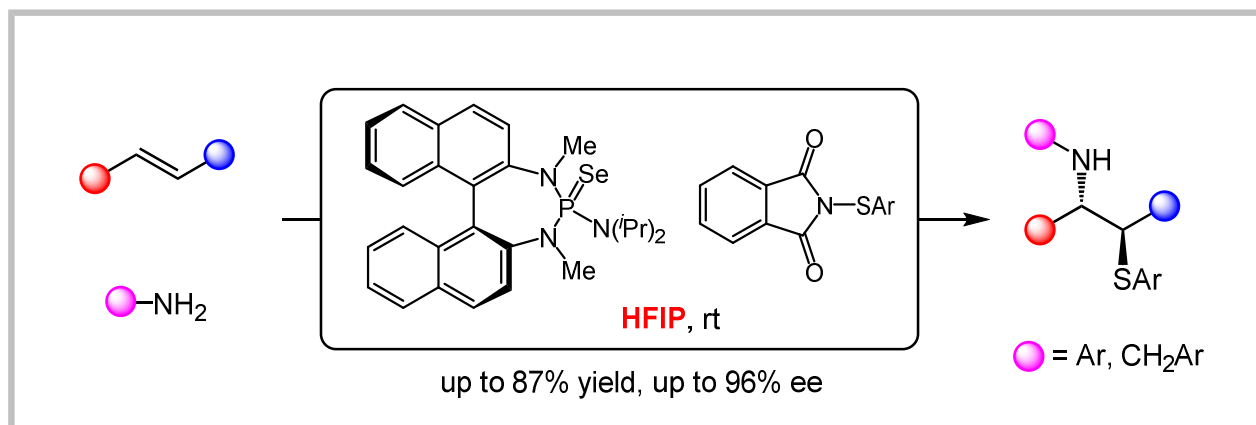
Denmark, S. E. *et al.* *J. Am. Chem. Soc.* **2014**, *136*, 8915.

Denmark, S. E. *et al.* *J. Org. Chem.* **2017**, *82*, 3826.

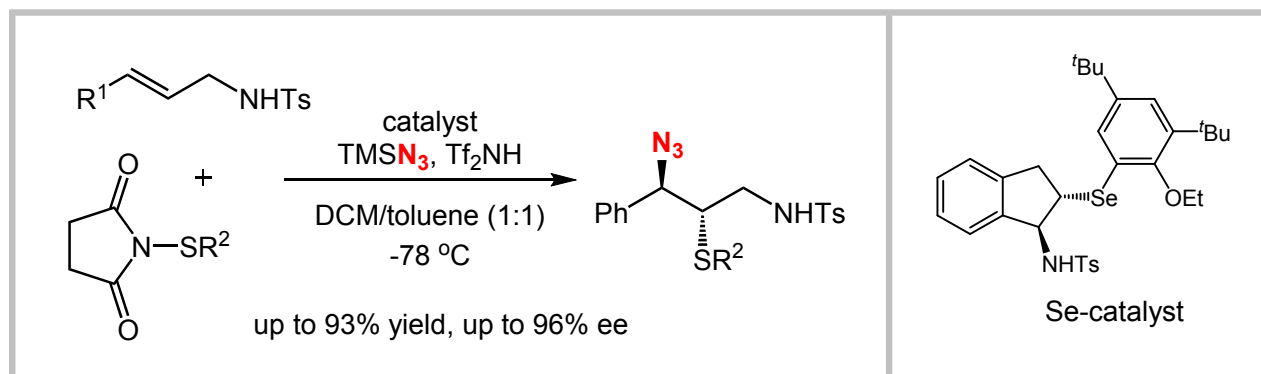


Denmark, S. E. *et al.* *Org. Lett.* **2020**, *22*, 2501.

Nitrogen Capture

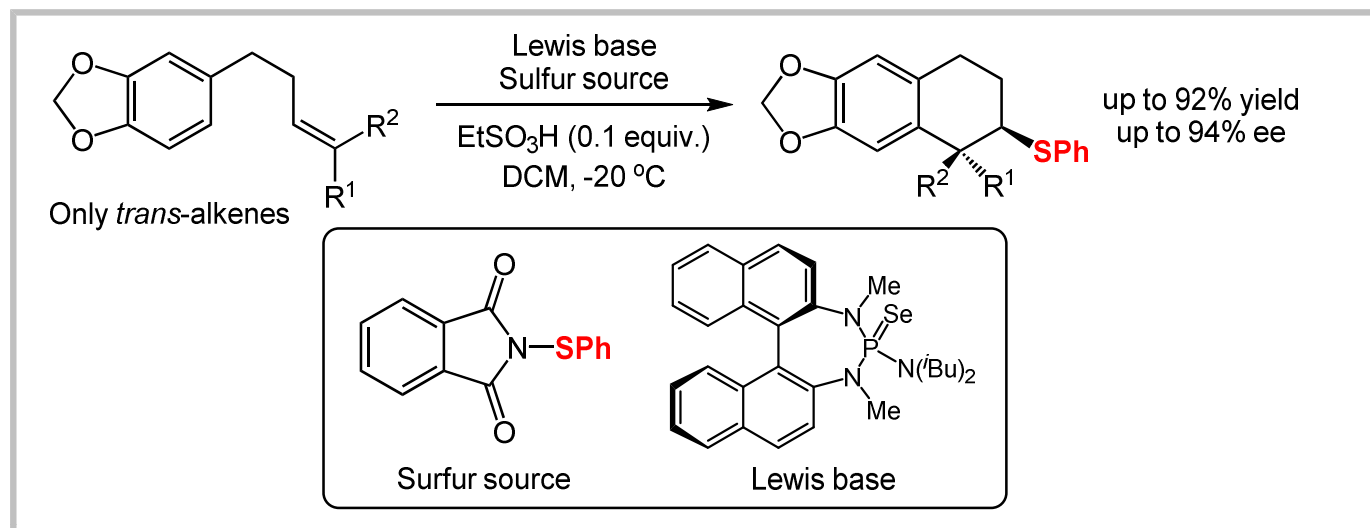


Denmark, S. E. *et al.* *J. Am. Chem. Soc.* **2019**, *141*, 13767.

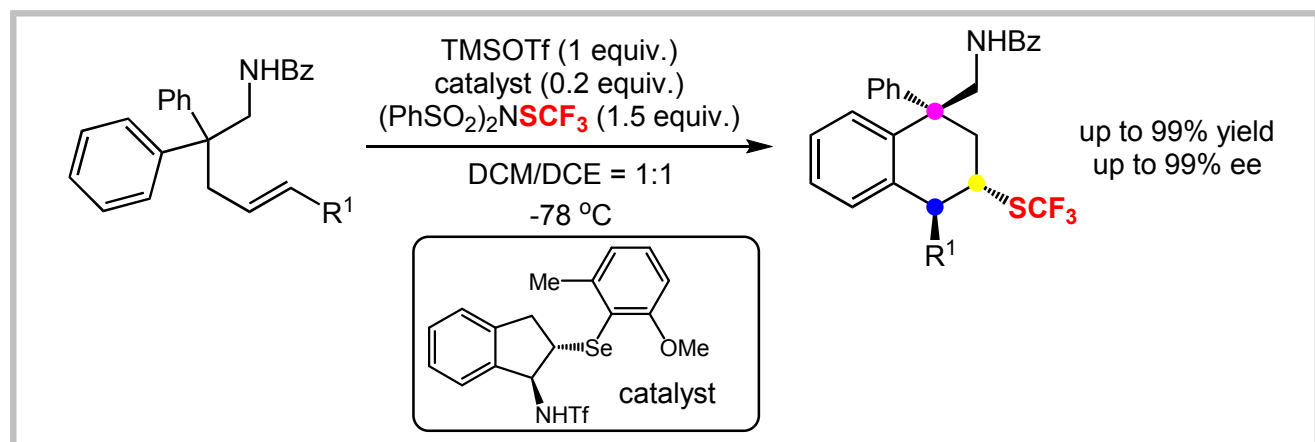


Zhao, X. *et al.* *ACS Catal.* **2019**, *9*, 6896.

Carbosulfenylation

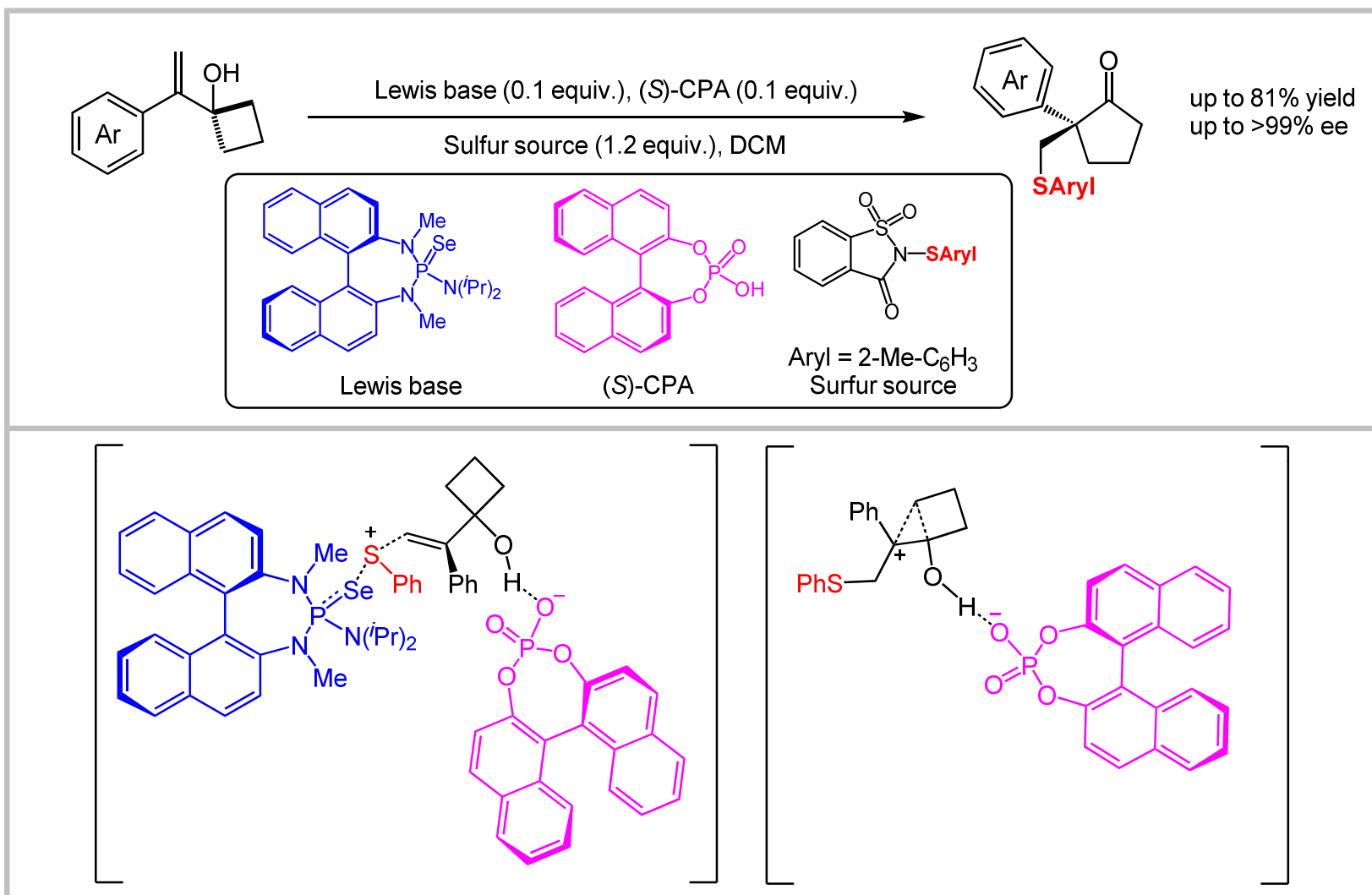


Denmark, S. E. *et al.* *J. Am. Chem. Soc.* **2013**, *135*, 6419.



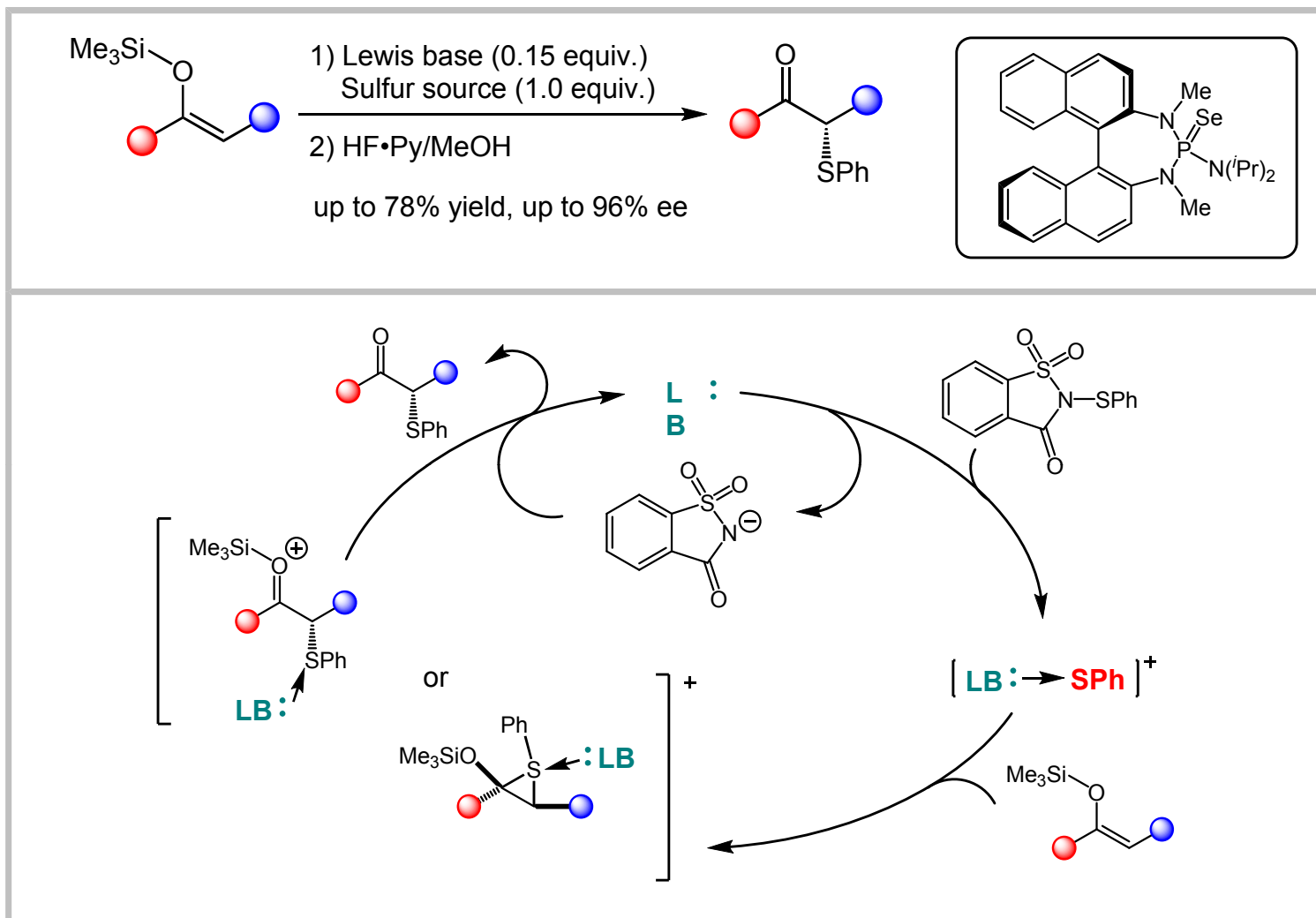
Zhao, X. *et al.* *Nat. Chem.* **2018**, *9*, 527.

Carbosulfenylation



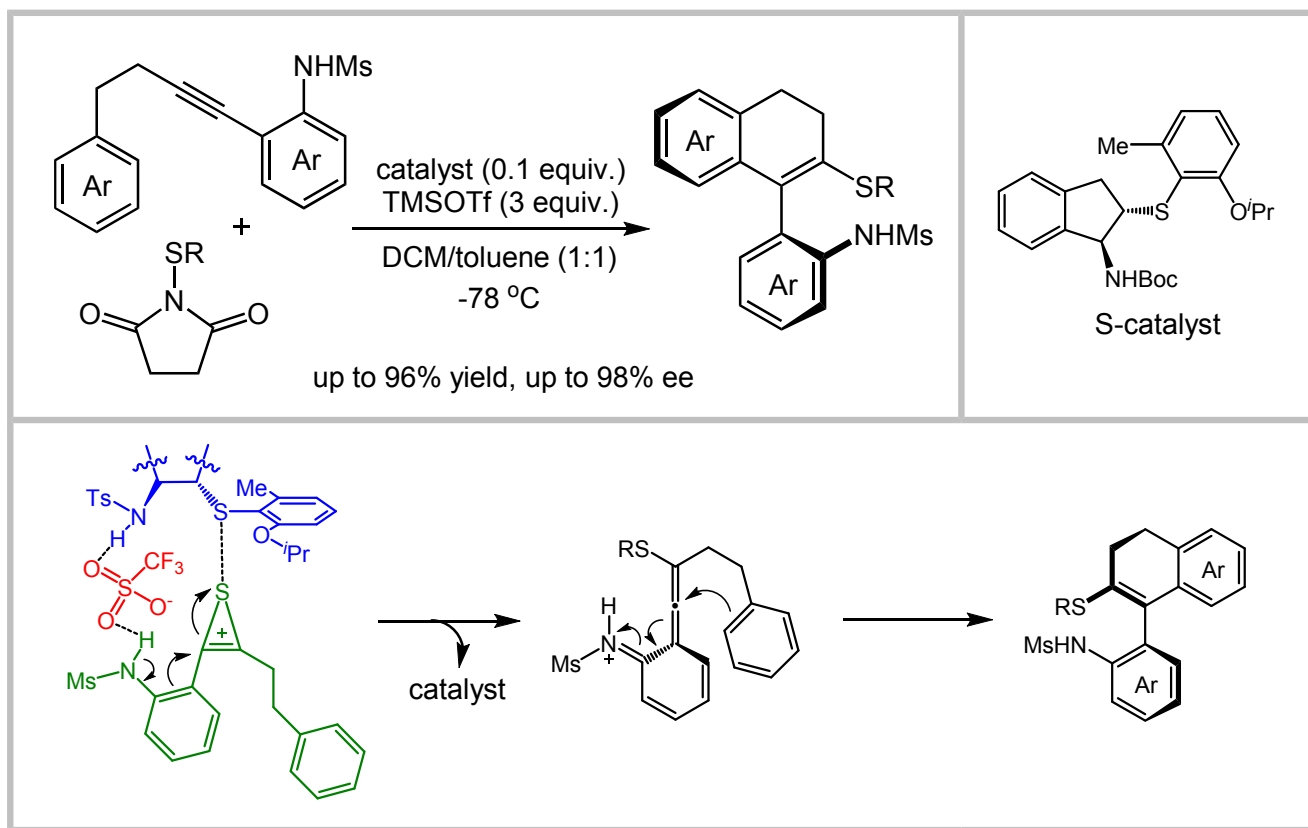
Chen, Z. M. *et al. Angew. Chem. Int. Ed.* **2019**, *58*, 12491.

Miscellaneous



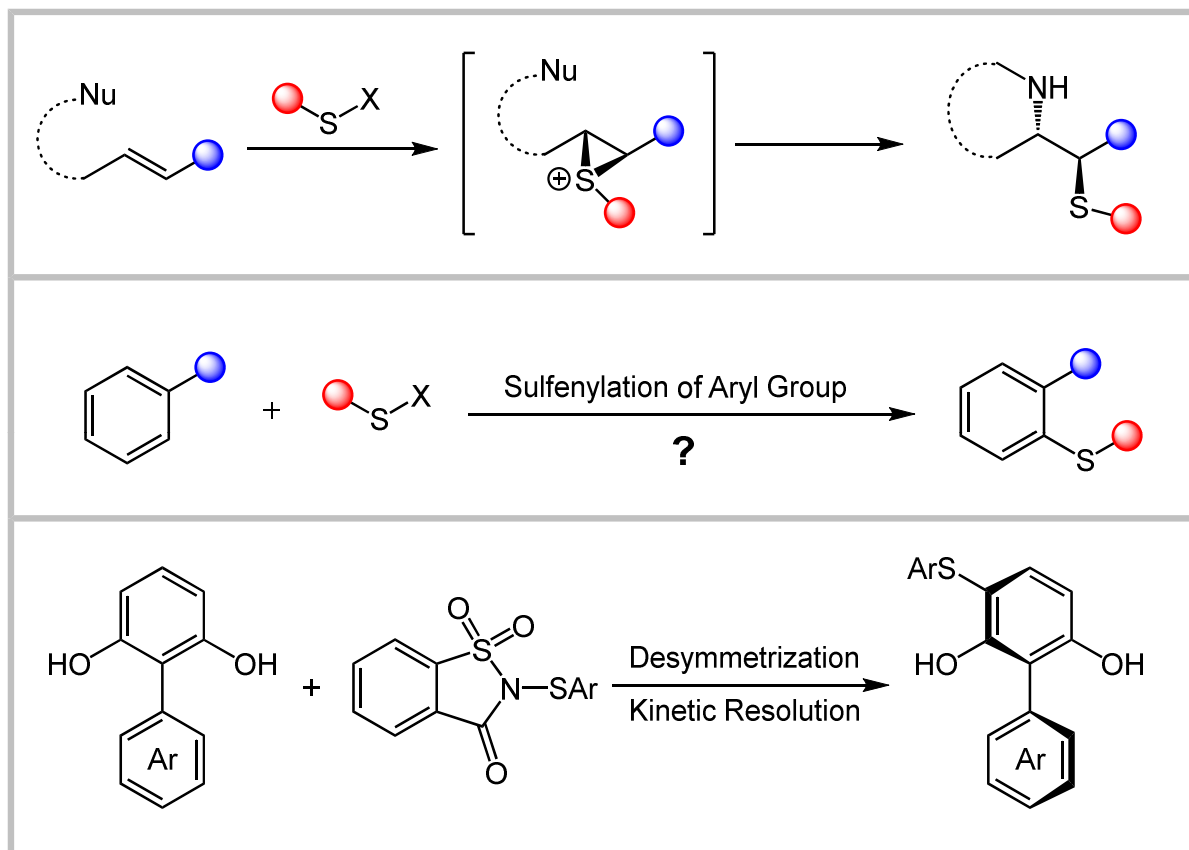
Denmark, S. E. *et al.* *J. Am. Chem. Soc.* **2014**, *136*, 13016.

Miscellaneous

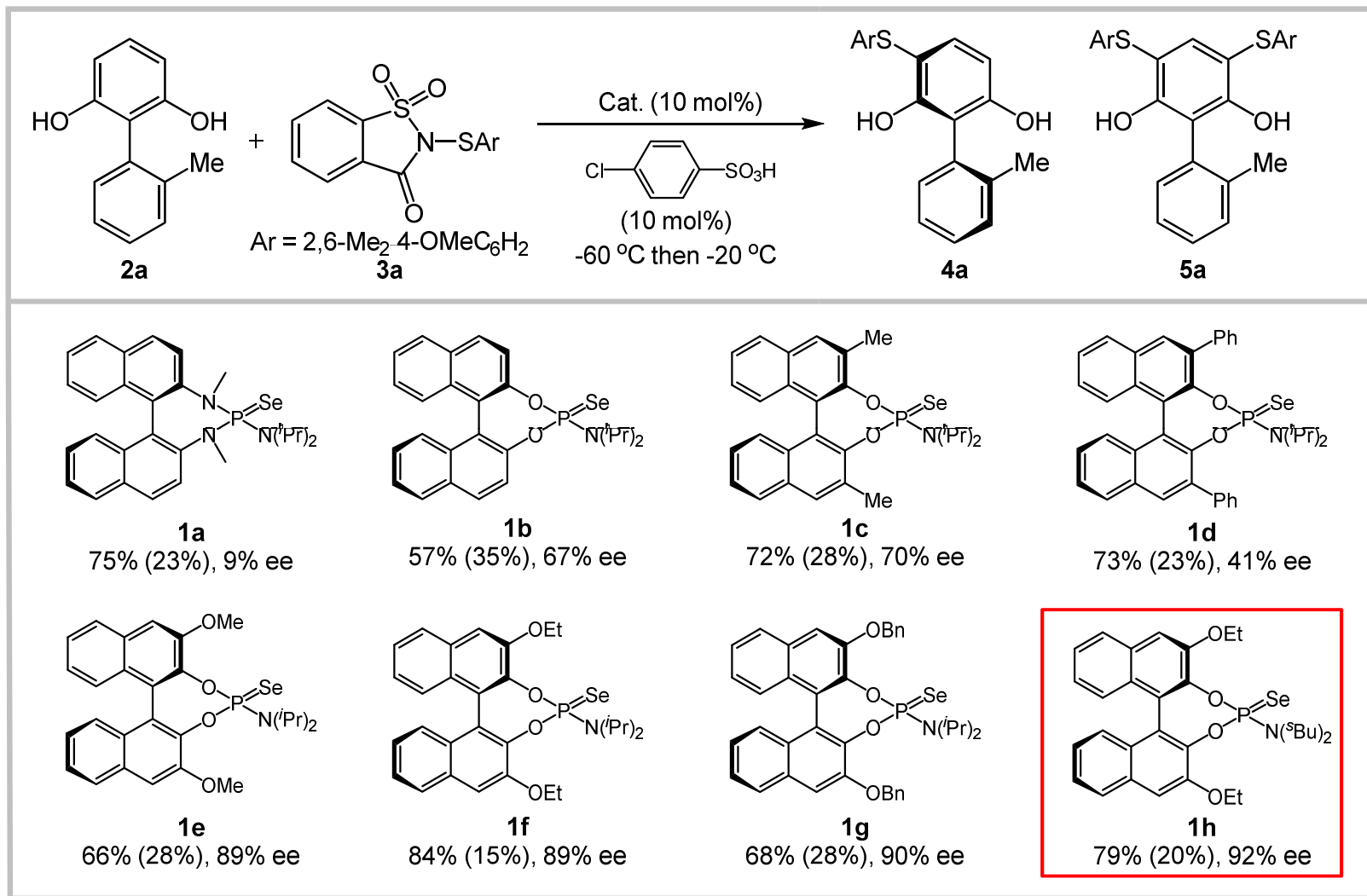


Zhao, X. *et al.* *Angew. Chem. Int. Ed.* **2020**, *59*, 4959.

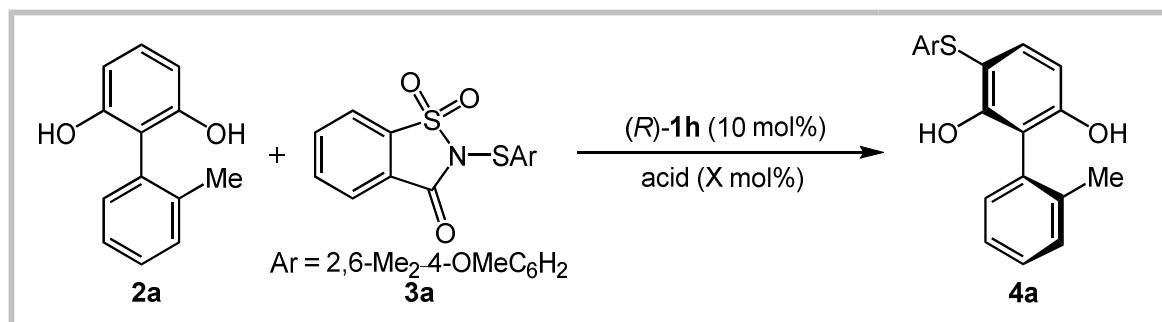
Summary and Proposition



Optimization of Reaction Parameters



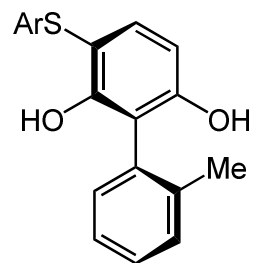
Optimization of Reaction Parameters



Entry ^a	Acid	X mol%	Yield [%]	Ee [%]	pKa
1	4-ClC ₆ H ₄ SO ₃ H	10	79	92	-0.8
2	none	0	67	0	-
3	4-ClC ₆ H ₄ SO ₃ H	5	99	83	-0.8
4	4-ClC ₆ H ₄ SO ₃ H	20	21	1	-0.8
5	4-ClC ₆ H ₄ SO ₃ H without (<i>R</i>)- 1h	10	37	0	-0.8
6	PTSA	10	71	90	-2.7
7	(PhO) ₂ P(O)OH	10	61	20	1.9
8	Benzoic acid	10	50	0	4.2

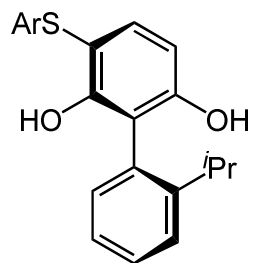
^a The reaction was conducted with **2a** (0.1 mmol), **3a** (0.15 mmol), (*R*)-**1h**. (0.01 mmol), and acid (0.01 mmol) in CDCl₃ (1 mL) at -60 °C for 24 h and then -20 °C for 5 h under Ar. Isolated yields are shown, and the data in parentheses is the yield of **5a**. The ee values were determined by HPLC.

Substrate Scope



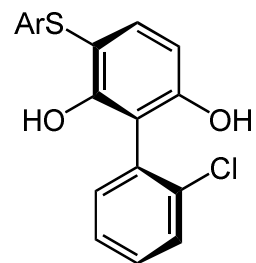
4a

79% (20%), 92% ee



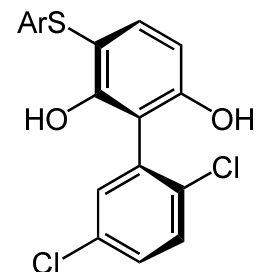
4b

72% (25%), 89% ee



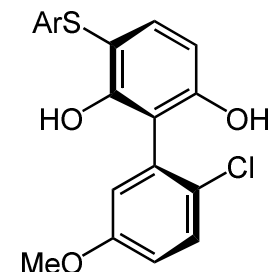
4c

74% (17%), 95% ee



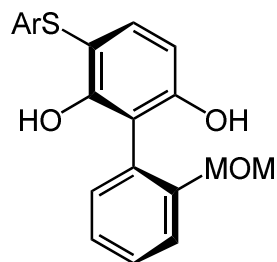
4d

71% (14%), 90% ee



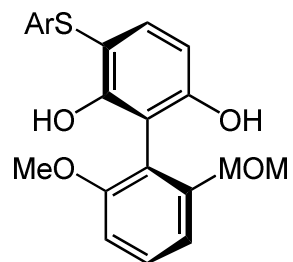
4e

68% (17%), 91% ee



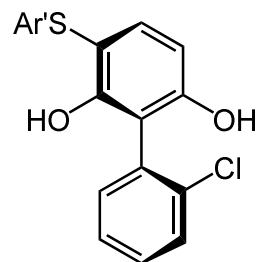
4f

66% (20%), 88% ee



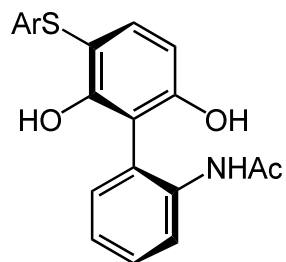
4g

61% (21%), 87% ee



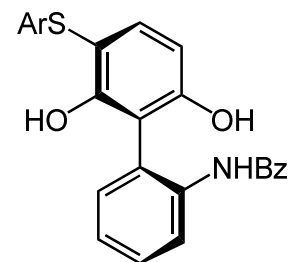
4h

Ar' = Mesitylene
85% (12%), 80% ee



4i

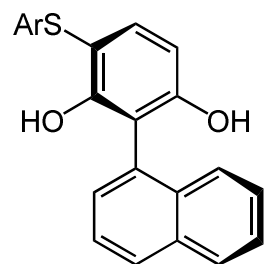
67% (8%), 76% ee



4j

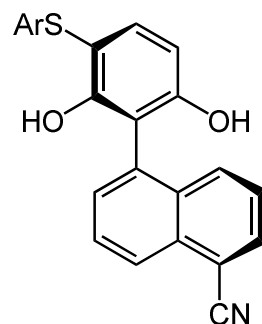
45% (17%), 22% ee

Substrate Scope



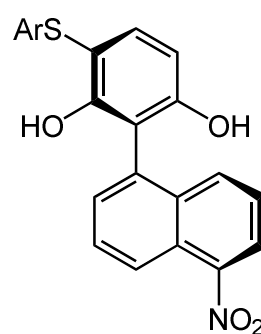
4k

84% (11%), 90% ee



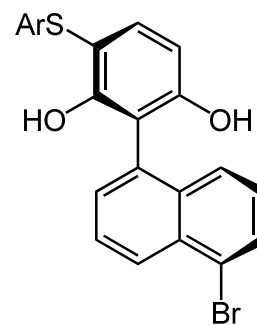
4l

82% (12%), 91% ee



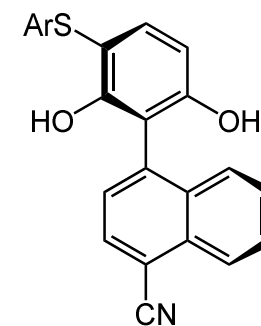
4m

65% (23%), 93% ee



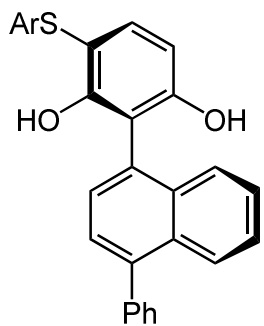
4n

70% (20%), 83% ee



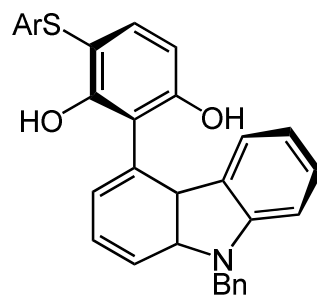
4o

80% (16%), 92% ee



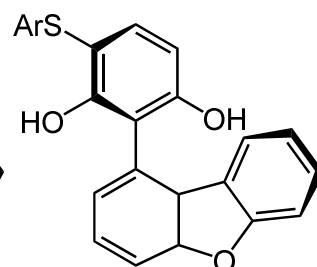
4p

75% (17%), 92% ee



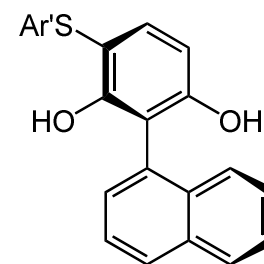
4q

90% (3%), 78% ee



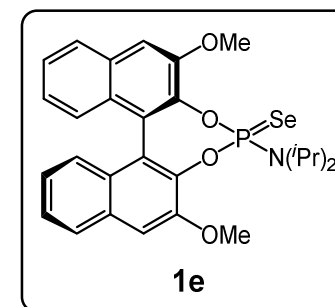
4r

79% (15%), 90% ee



4s

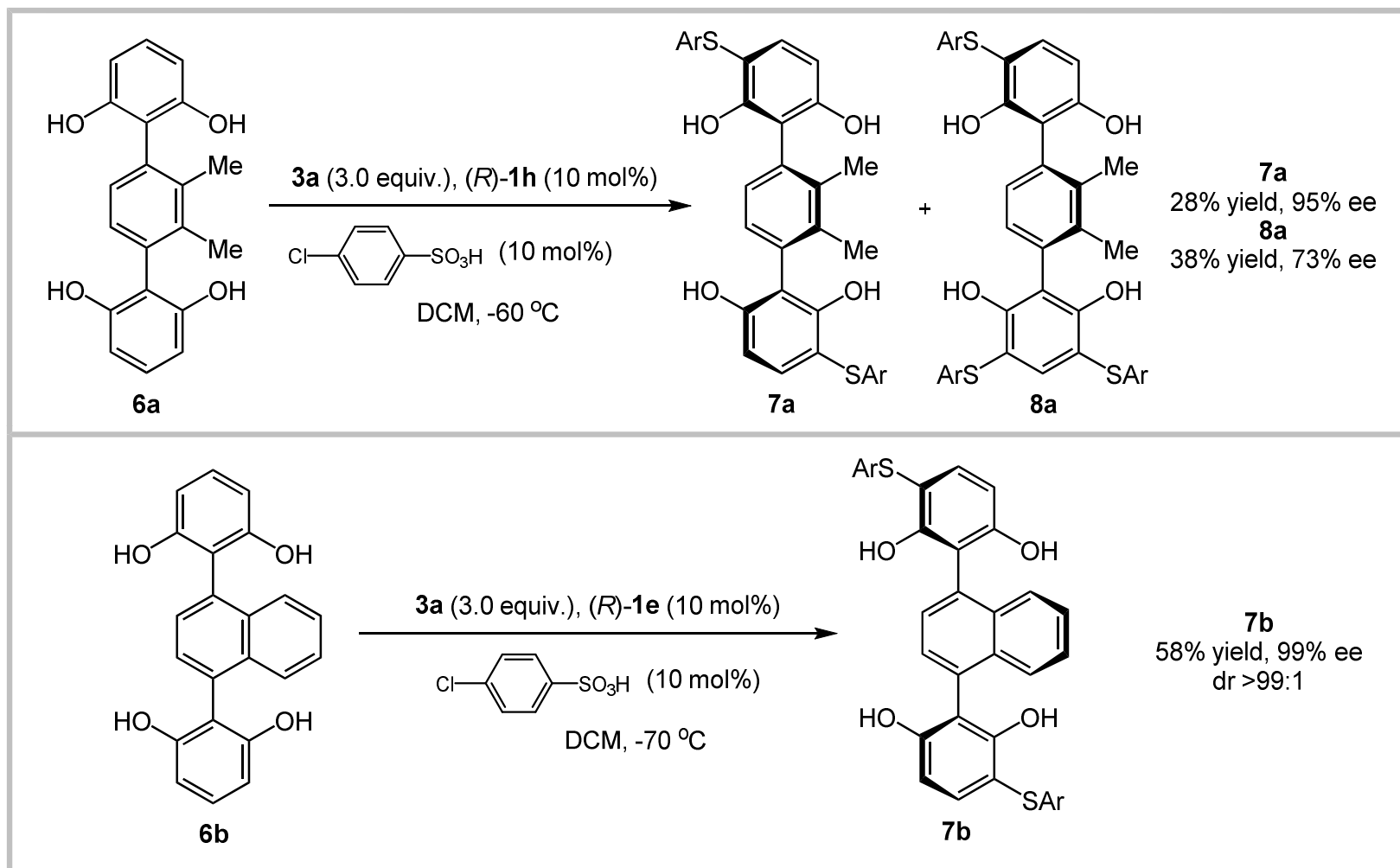
Ar' = Mesitylene
65% (22%), 81% ee



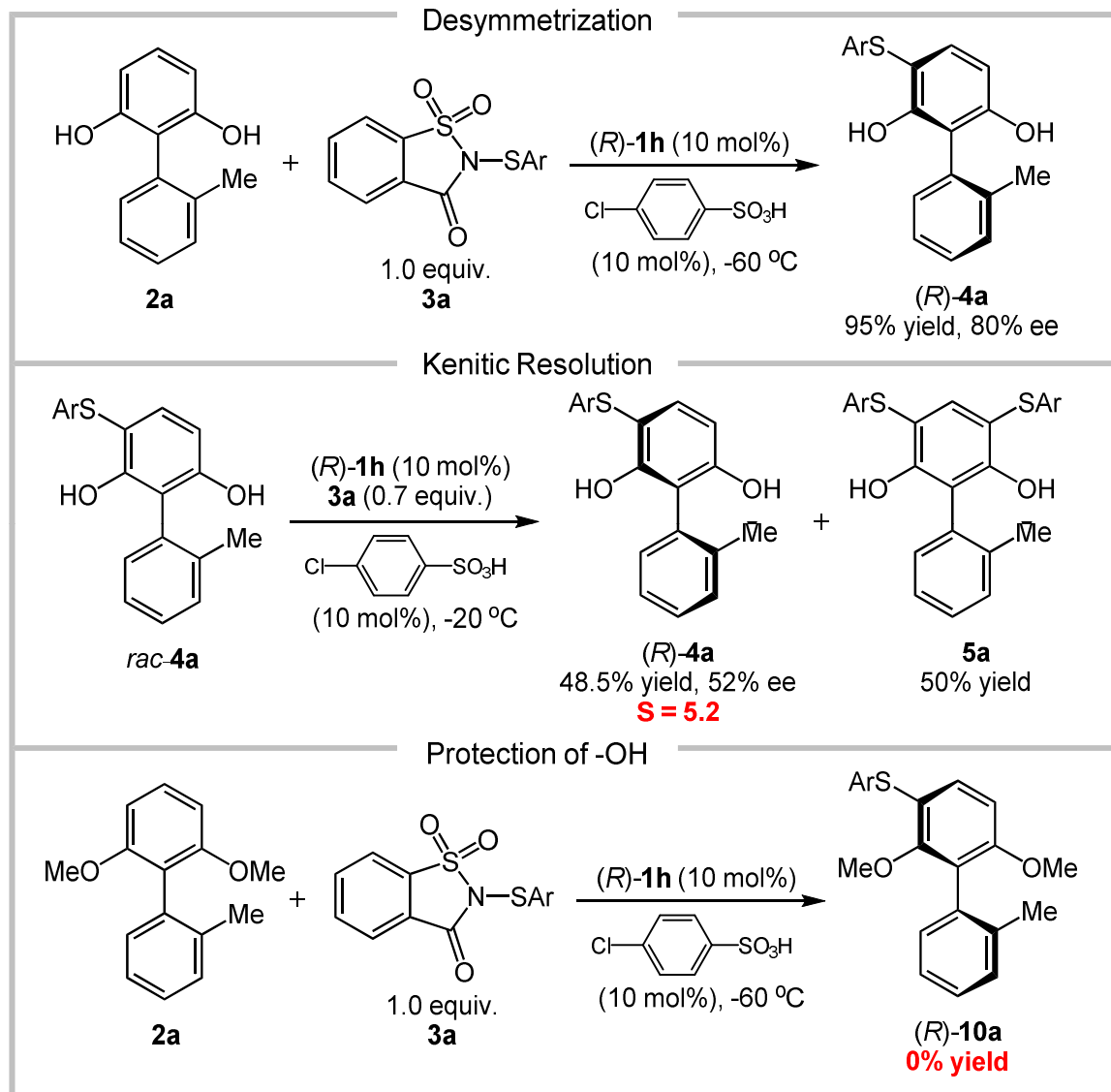
1e

(*R*)-**1e** instead of (*R*)-**1h**

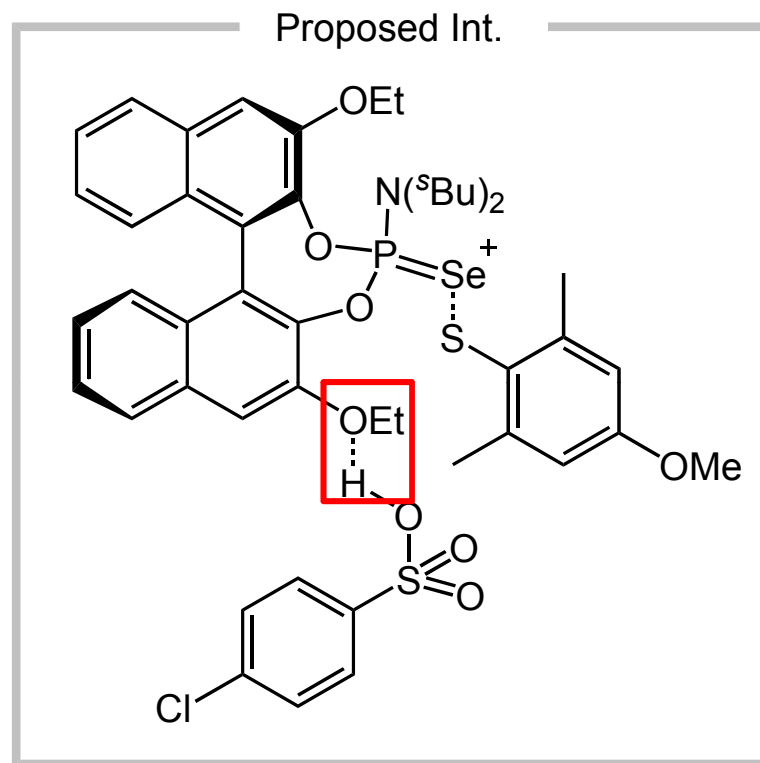
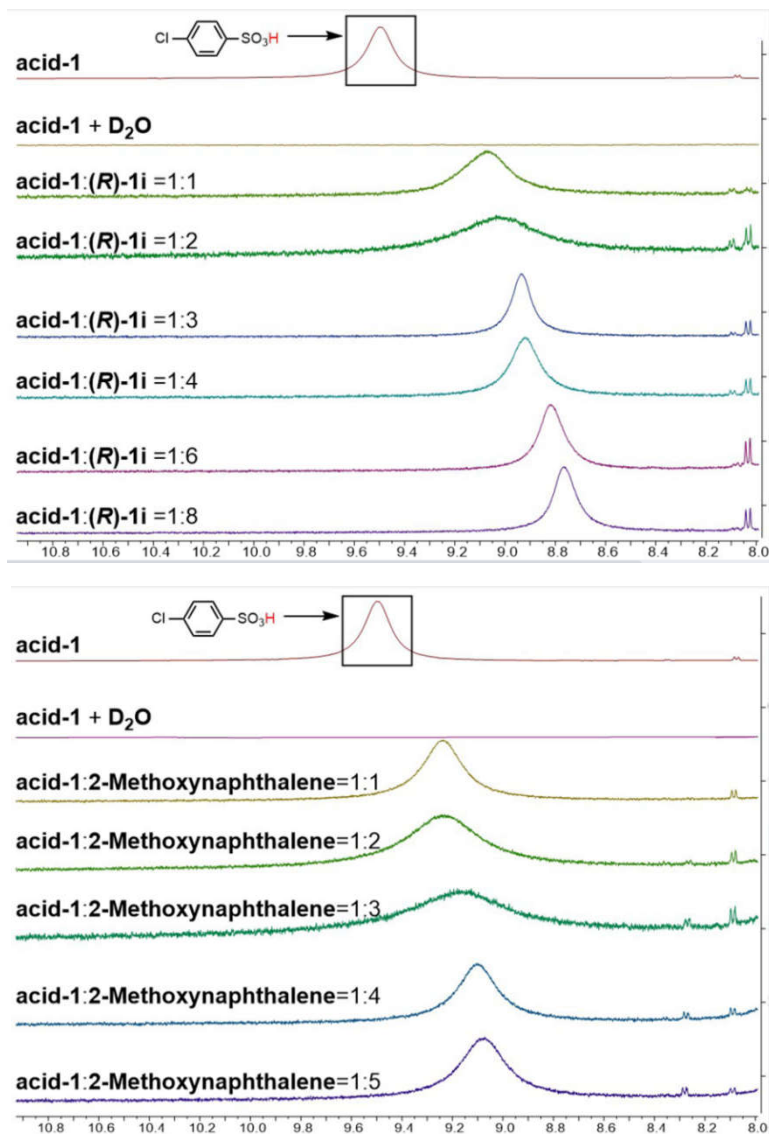
Substrate Scope



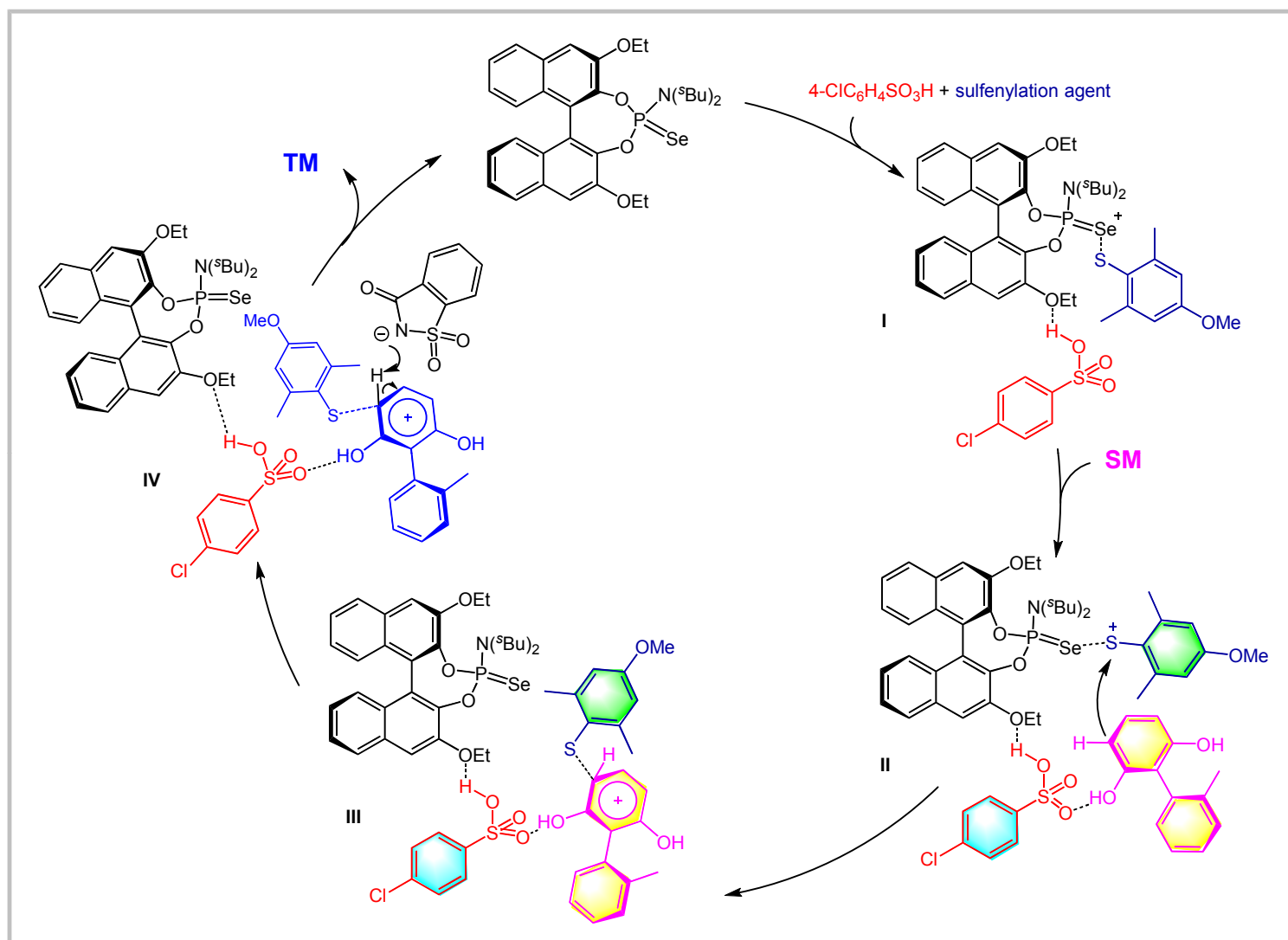
Control Experiments



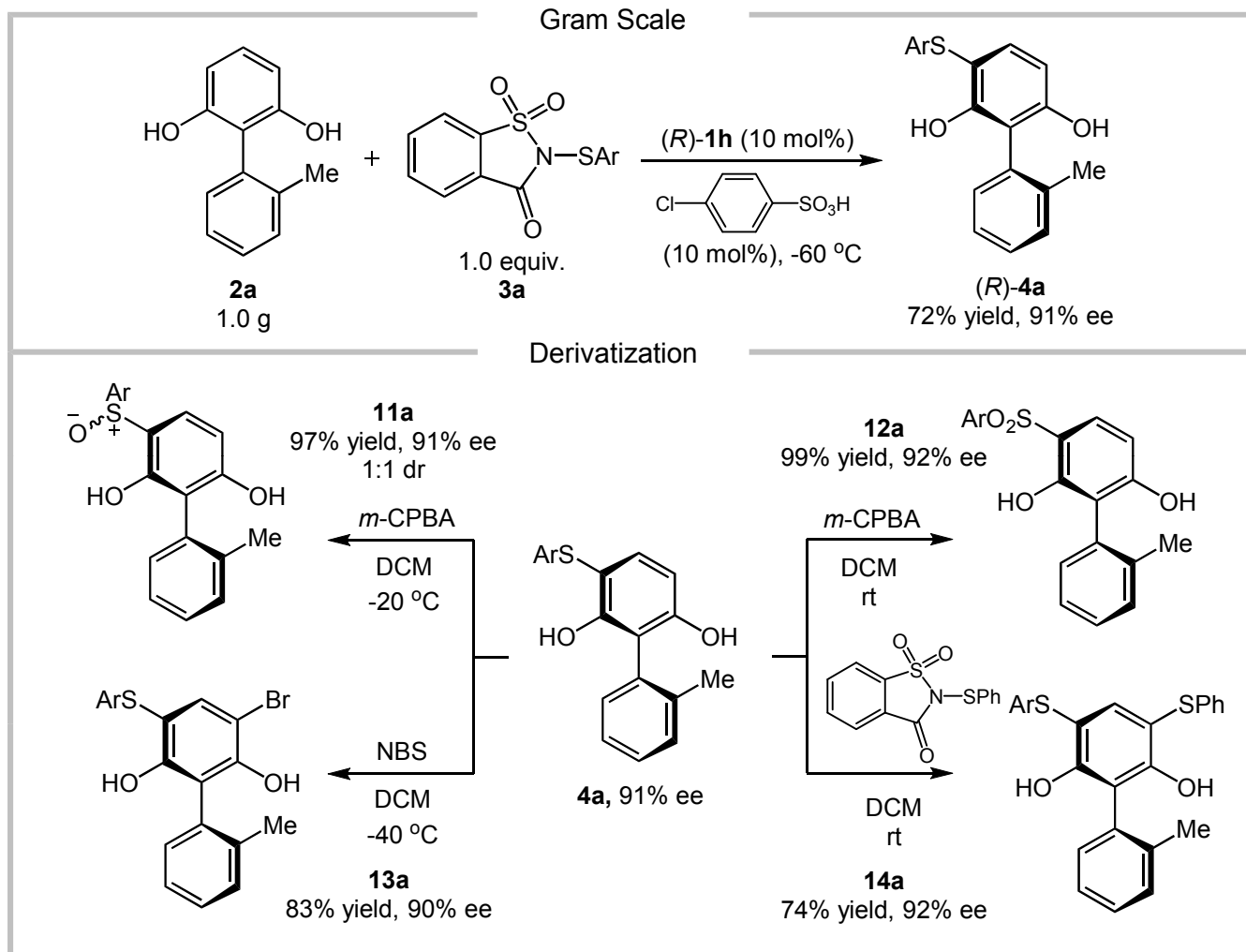
^1H NMR Titration



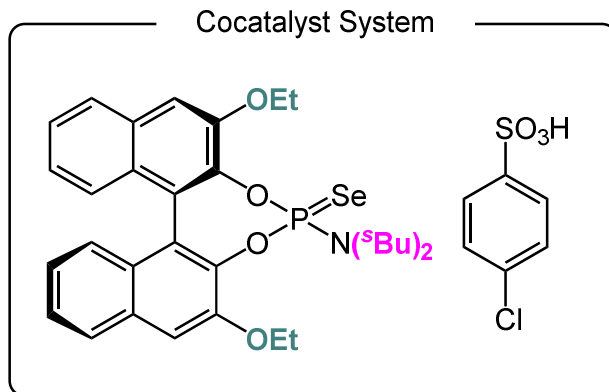
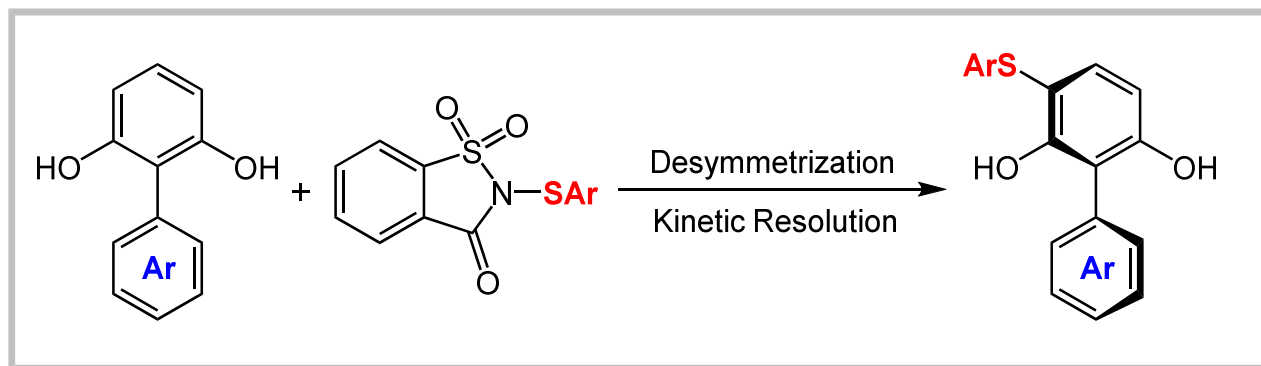
Proposed Mechanism



Gram Scale and Derivatization



Summary



- ✓ **New chiral selenide catalyst**
- ✓ **Multiple noncovalent interactions**
- ✓ **Good Substrate tolerance**

The First Paragraph

写作思路

手性含硫化合物重要性



构建手性C-S键方法



构建轴手性含硫化合物局限

The First Paragraph

Chiral organosulfur compounds are prevalent in a wide range of biologically active natural products and pharmaceuticals and are also employed as chiral catalysts and ligands. Given the importance of these compounds, considerable effort has been devoted to the development of enantioselective synthetic methodologies. Among these, the catalytic asymmetric electrophilic sulfenylation of alkenes is one of the most straightforward and efficient strategies for the preparation of chiral organosulfur compounds and so has recently attracted increasing attention. Denmark and co-workers first developed Lewis base catalysis for sulfenium ion transfer to alkenes and performed an array of pioneering studies of the catalytic enantioselective sulfenylation of alkenes.

The First Paragraph

Zhao's group also demonstrated various electrophilic sulfenylations of alkenes using novel indene derivatives as chiral bifunctional chalcogenide catalysts. However, these great advances focused primarily on the construction of centrally chiral organosulfur compounds. The catalytic enantioselective electrophilic sulfenylation syntheses of axially chiral sulfur-containing compounds are much less developed. In fact, only one successful example was documented by Zhao et al.

The Last Paragraph

写作思路

工作总结：阻转选择性磺基化构建含硫轴手性化合物



工作特点：手性Lewis碱/非手性Brønsted酸共催化



工作展望：构建更多含硫轴手性化合物

The Last Paragraph

In conclusion, we successfully developed a practical and modular method for the atroposelective synthesis of axially chiral biaryl derivatives through the electrophilic sulfenylation of biaryl phenols. This system involves tandem desymmetrization and kinetic resolution processes. Importantly, chiral two-axis sulfur-containing compounds could also be synthesized. A new 3,3'-disubstituted BINOL-derived selenide was explored as the Lewis base for the first time, and the asymmetric cooperative catalysis effect of a chiral selenide and an achiral sulfonic acid was discovered. Multiple noncovalent interactions between the cocatalysts and substrate were found to lead to high enantioselectivity and reactivity. The use of asymmetric cooperative catalysis to synthesize other useful chiral sulfur compounds is ongoing in our laboratory.

Representative Examples

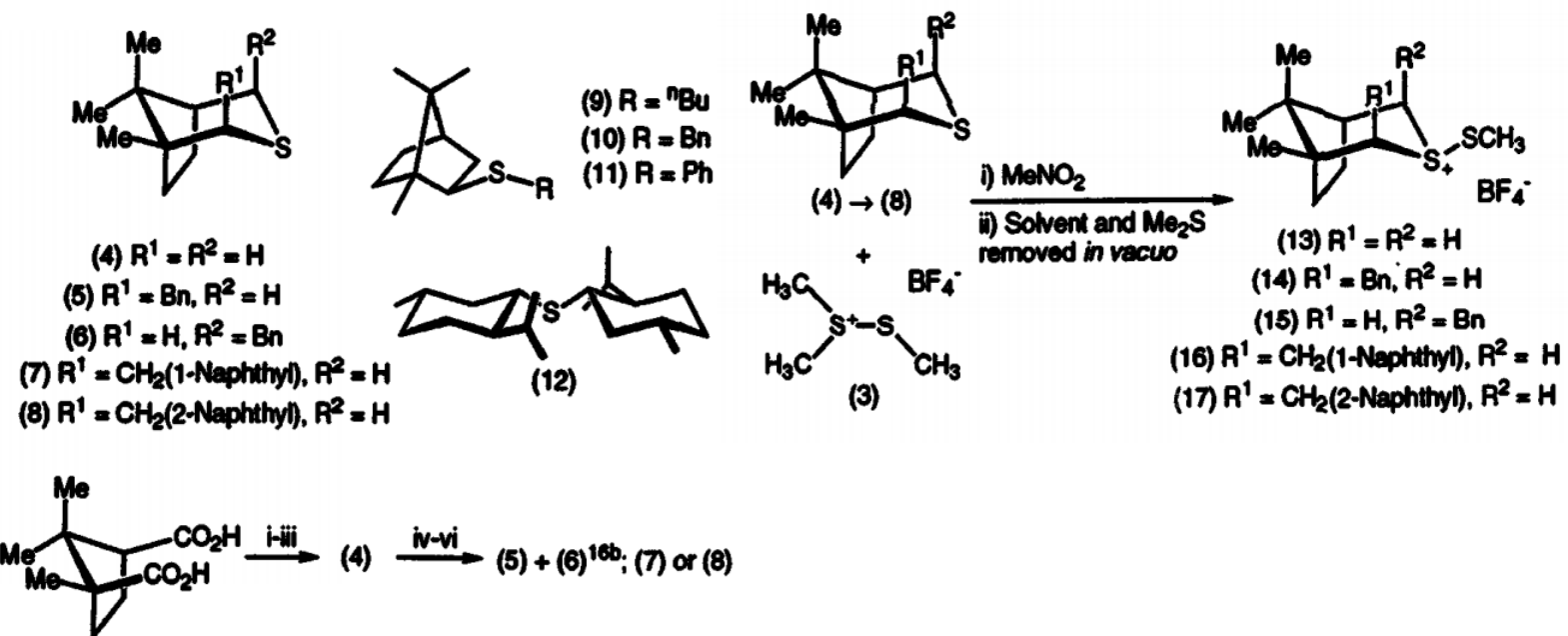
To gain mechanistic insights into this transformation, in particular the origin of the high enantioselectivity of the method, various control experiments were performed. (gain insight into 深入了解)

These results suggest that a suitable achiral acid catalyst is indispensable to the control of enantioselectivity... (必不可少的)

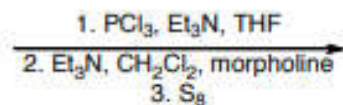
- Sulfenyl 亚磺酰基/硫基
- Sulfinyl 亚磺酰基
- Sulfonyl 磺酰基
- Chalcogenide 硫族元素

Acknowledgement

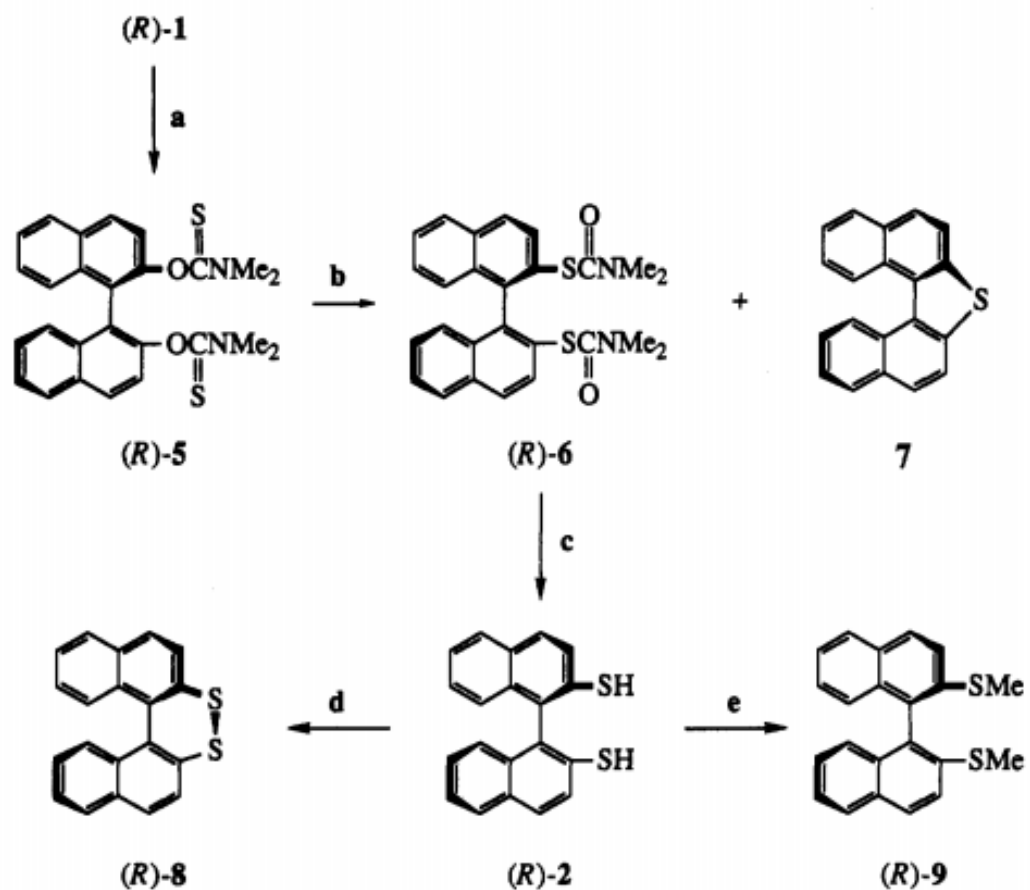
***Thanks
for your attention***



Reagents: i, BH_3 , THF, 93%; ii, TsCl, pyridine, 75%; iii, $Na_2S \cdot 9H_2O$, EtOH, 83%; iv, MCPBA, CH_2Cl_2 , 78%; v, MeLi, THF, $-78^\circ C$ then RX, see text; vi, AcCl, $SnCl_2$, 85-90%.



Scheme II^a



^a Key: (a) (i) NaH (oil dispersion), DMF, (ii) Me₂NC(S)Cl; (b) neat, 285 °C, 22 min; (c) LiAlH₄, THF; (d) I₂, CHCl₃; (e) Et₃N, MeI, MeOH.

