

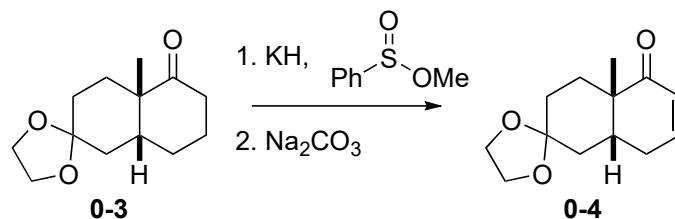
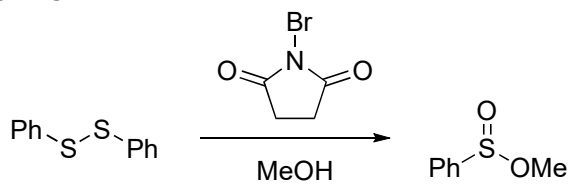
Problem Session (6) -Answer-

2025/09/13 Wataru Shigematsu

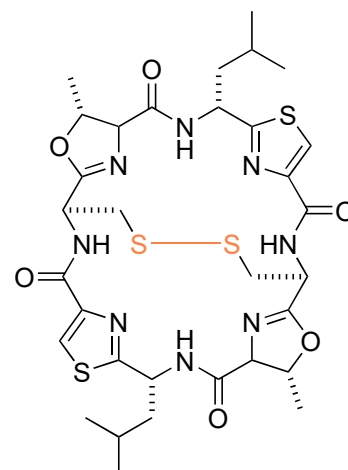
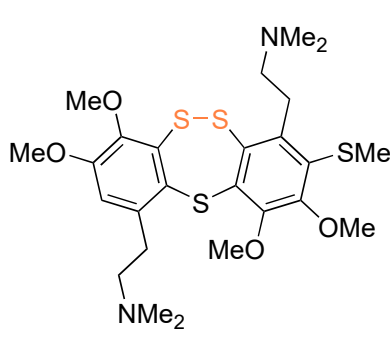
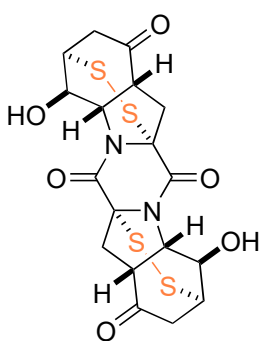
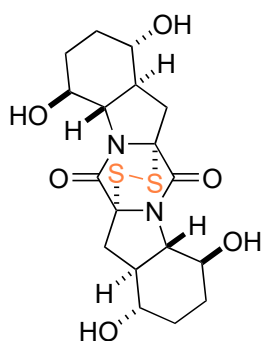
Topic: Use and synthesis of disulfide

0. Introduction

0-1. Use of disulfide ¹⁾



0-2. Disulfides in natural products



Rostratin A (**0-5**)

Epicoccin C (**0-6**)

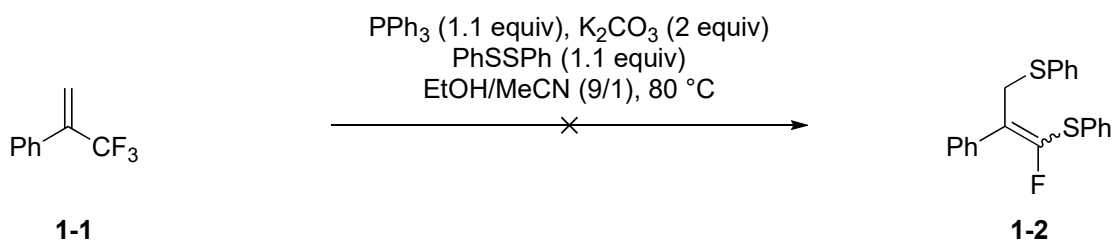
Lissoclibadin 5 (**0-7**)

Ulithiacyclamide (**0-8**)

Some natural products have disulfide moieties.

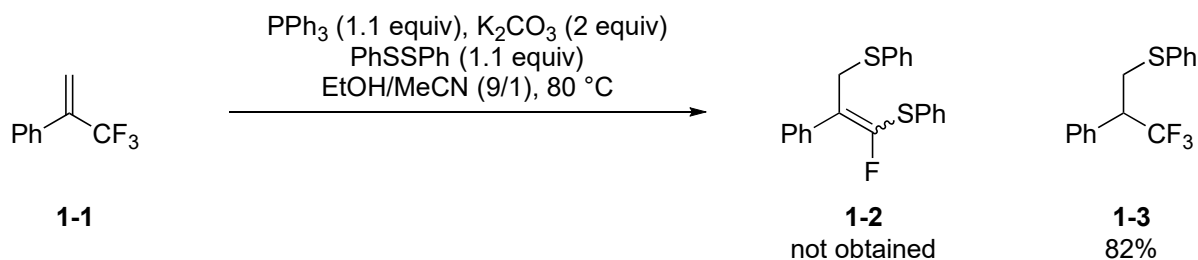
Disulfides are also used as a linker of ADC (antibody-drug conjugates).

1 In the conditions below, **1-2** wasn't obtained. Please make a minimum change to obtain **1-2**.

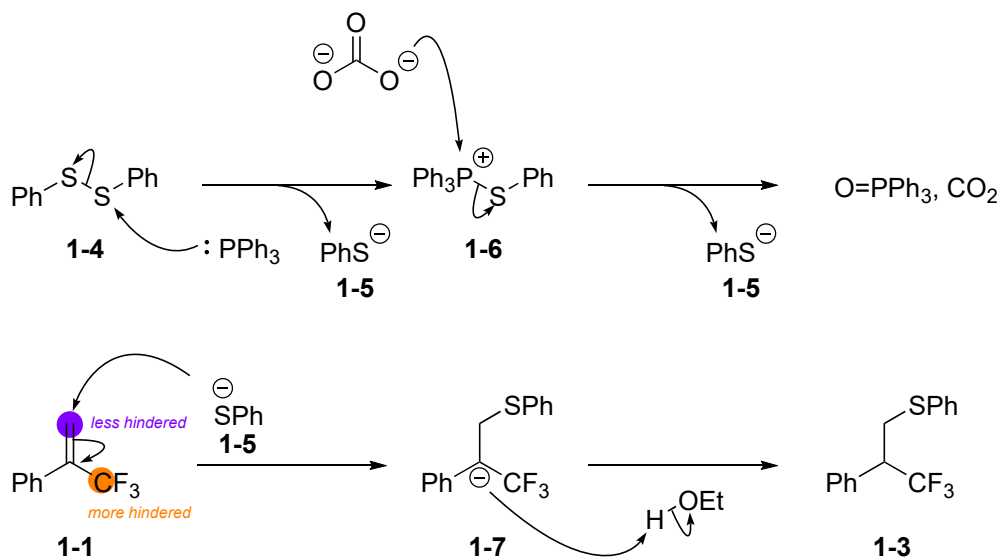


Huang, M.-Z.; Xiao, L.-X.; Zhang, X.-G.; Song, X.-F.; Tu, H.-Y. *Org. Lett.* **2025**, 27, 7137.

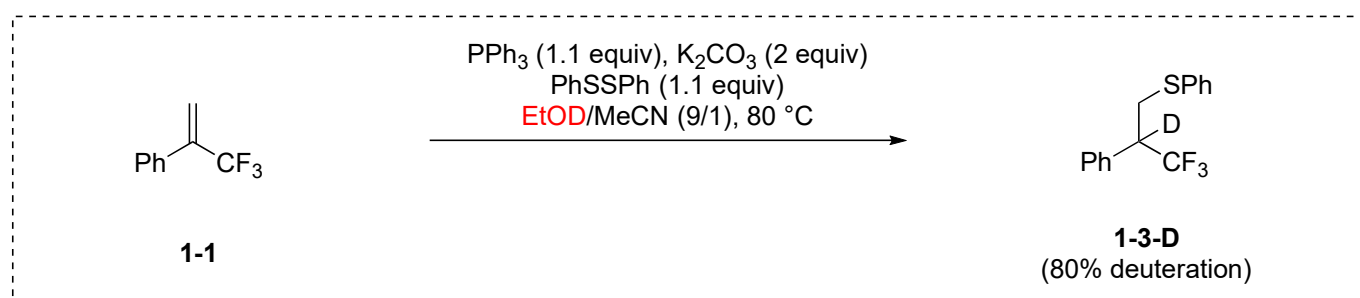
In this reaction, sulfide **1-3** was obtained.



1-1. Reaction mechanisms from 1-1 to 1-3

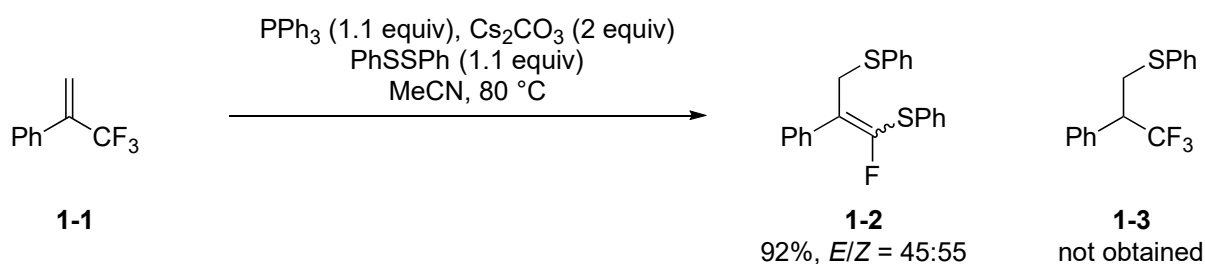


As **1-7** was protonated by EtOH , **1-3** was obtained instead of **1-2**. This mechanism is supported by the result that **1-3-D** was obtained in EtOD/MeCN .



1-2. Revised reaction conditions and reaction mechanisms

Revised reaction conditions



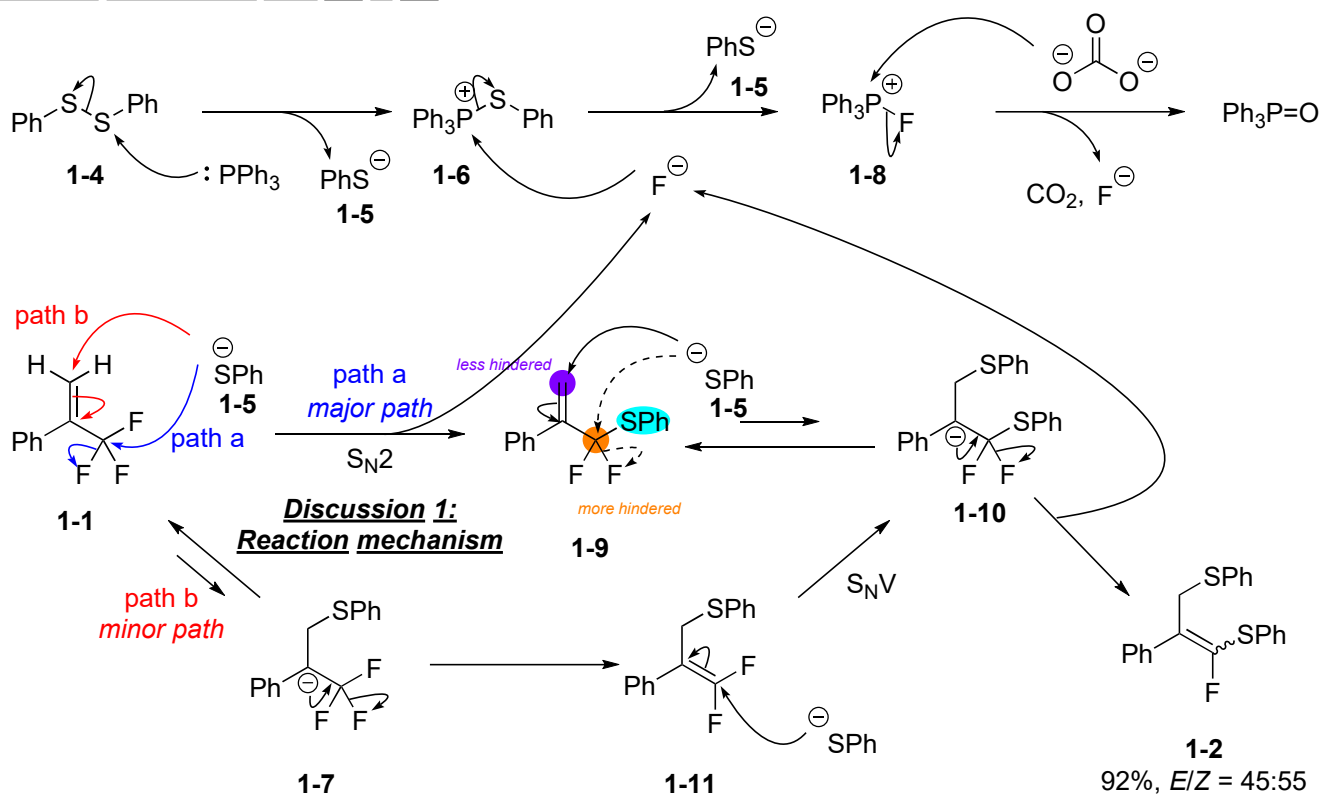
K_2CO_3 instead of Cs_2CO_3 will give **1-2** in good yield but only optimized conditions are shown in paper.

point 1. EtOH (and other protic solvent) shouldn't be used.

point 2. As 2 equiv of PhS^- will be generated from PhSSPh , the equivalent of PhSSPh don't have to be changed.

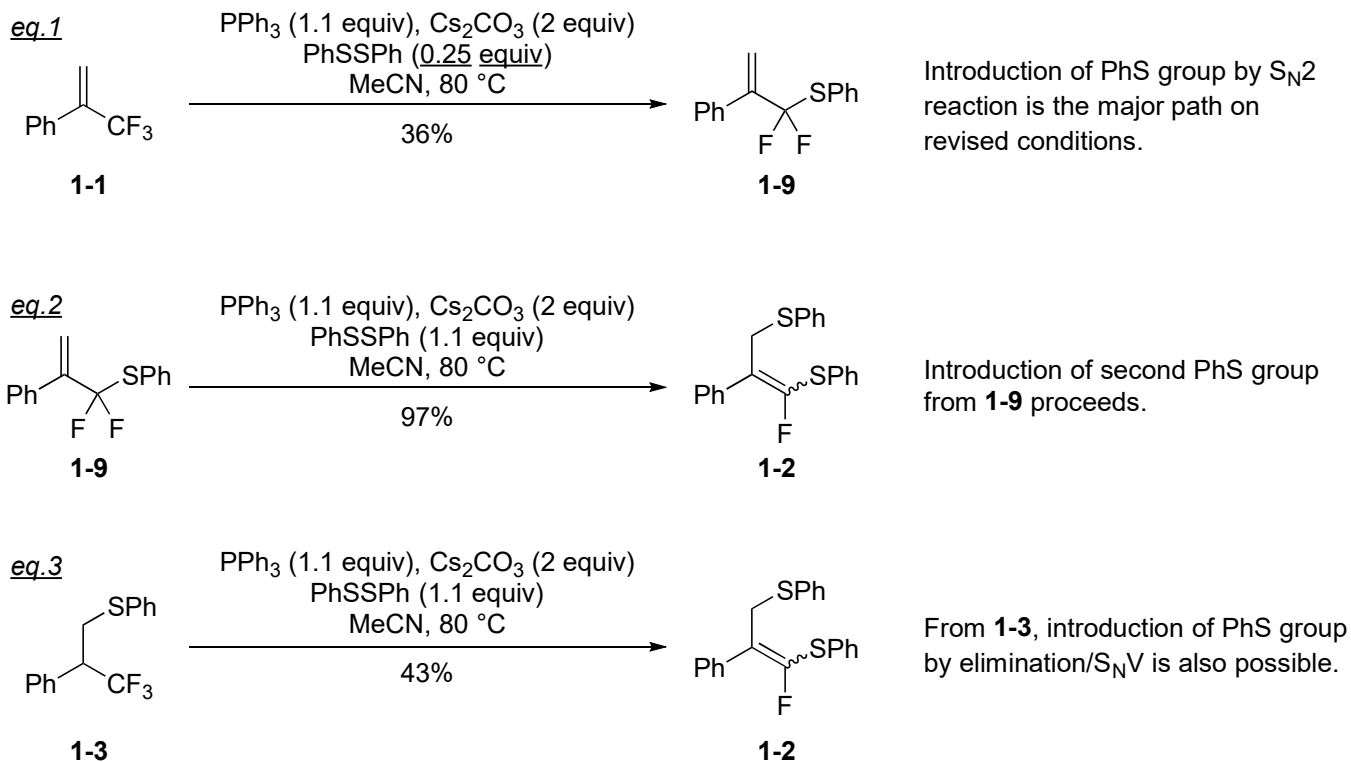
Before discussion in the seminar

Reaction mechanisms from 1-1 to 1-2



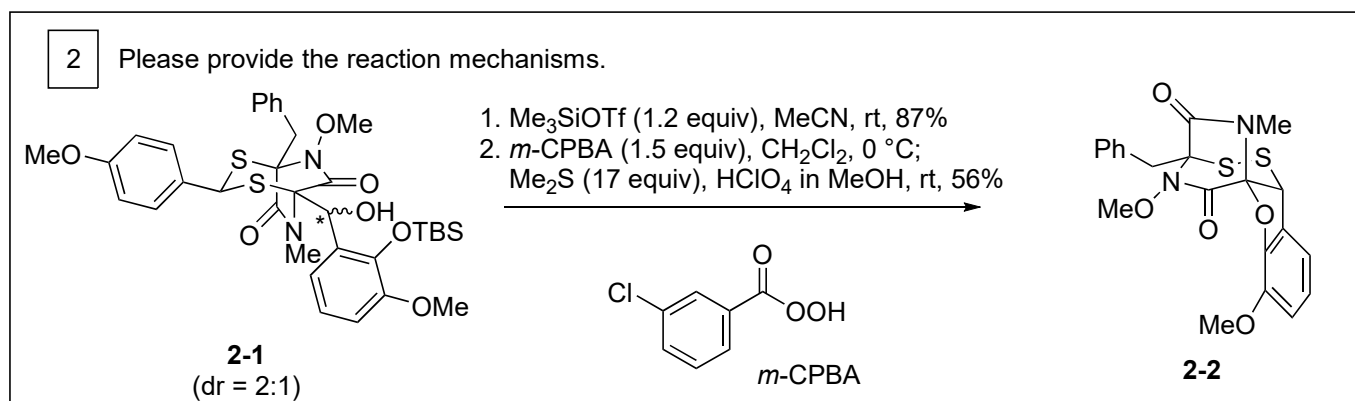
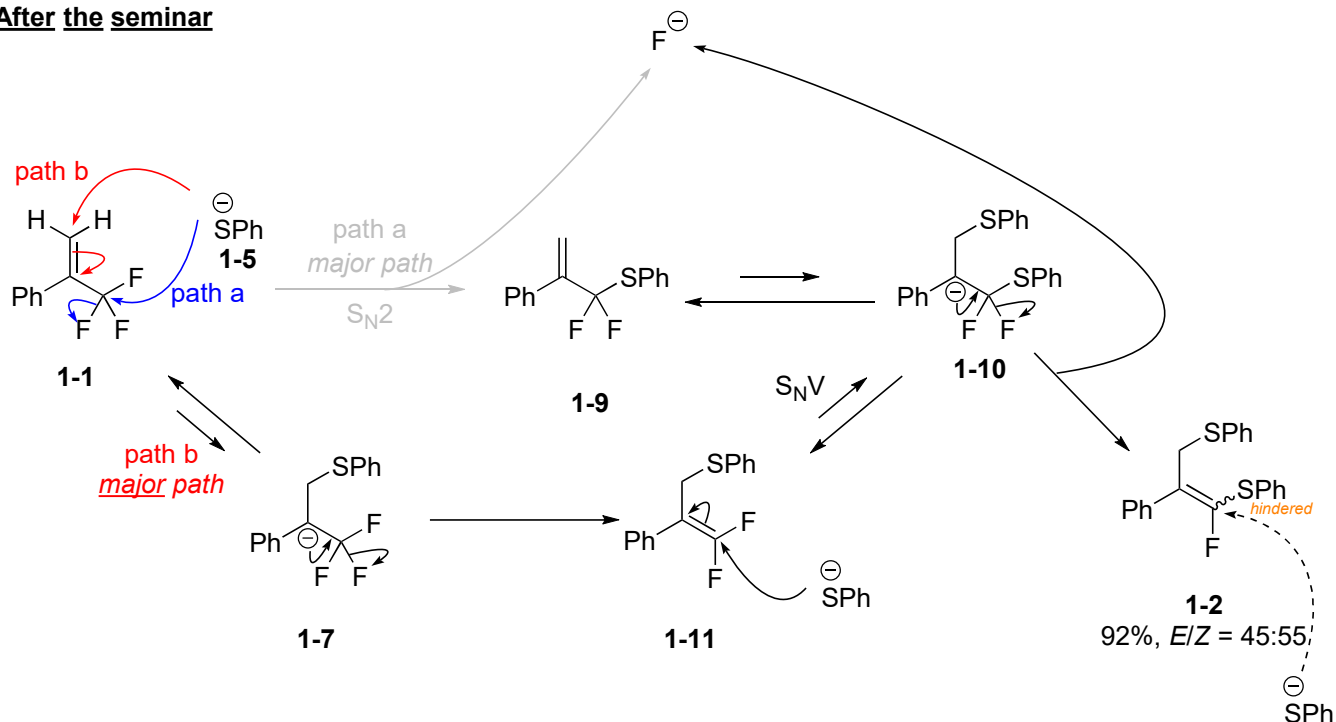
Discussion 1: Reaction mechanism on revised conditions

Mechanistic studies by authors

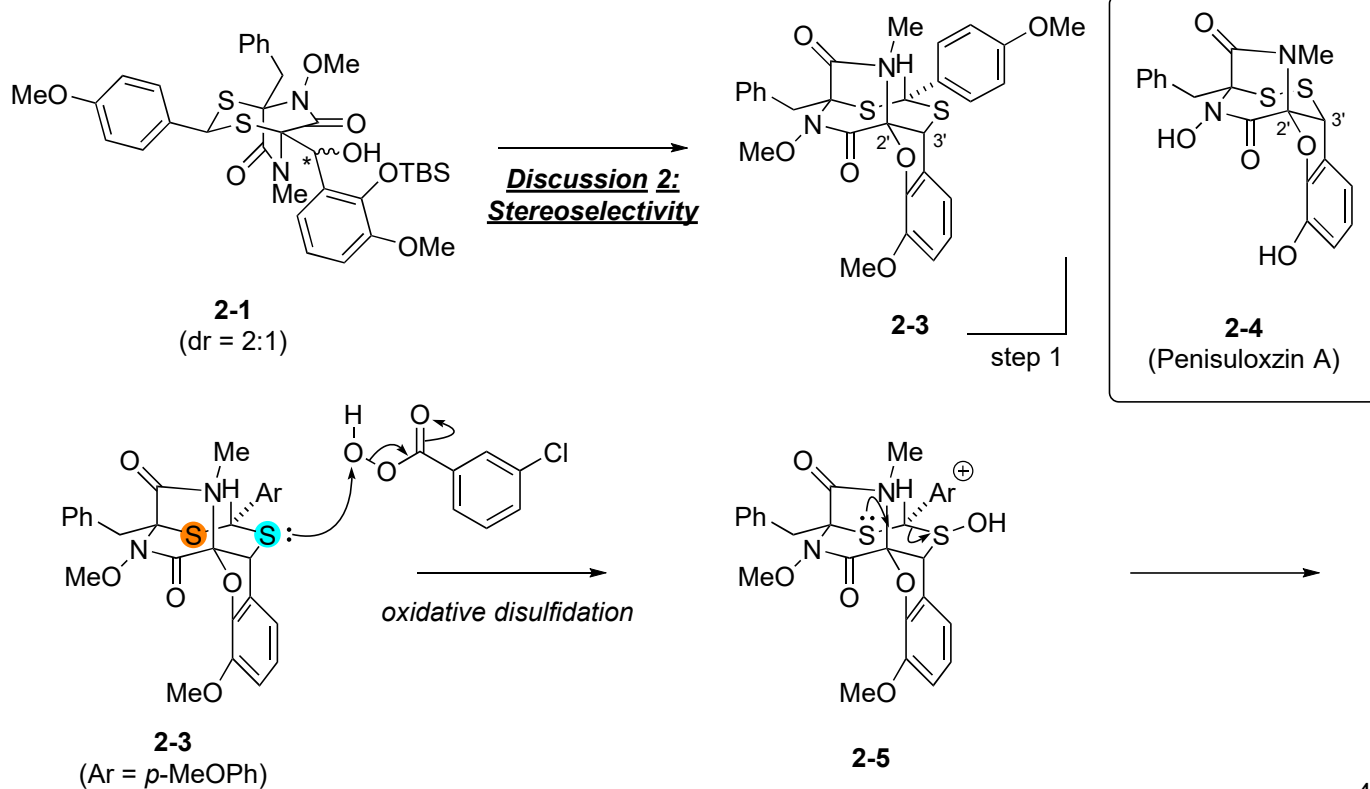


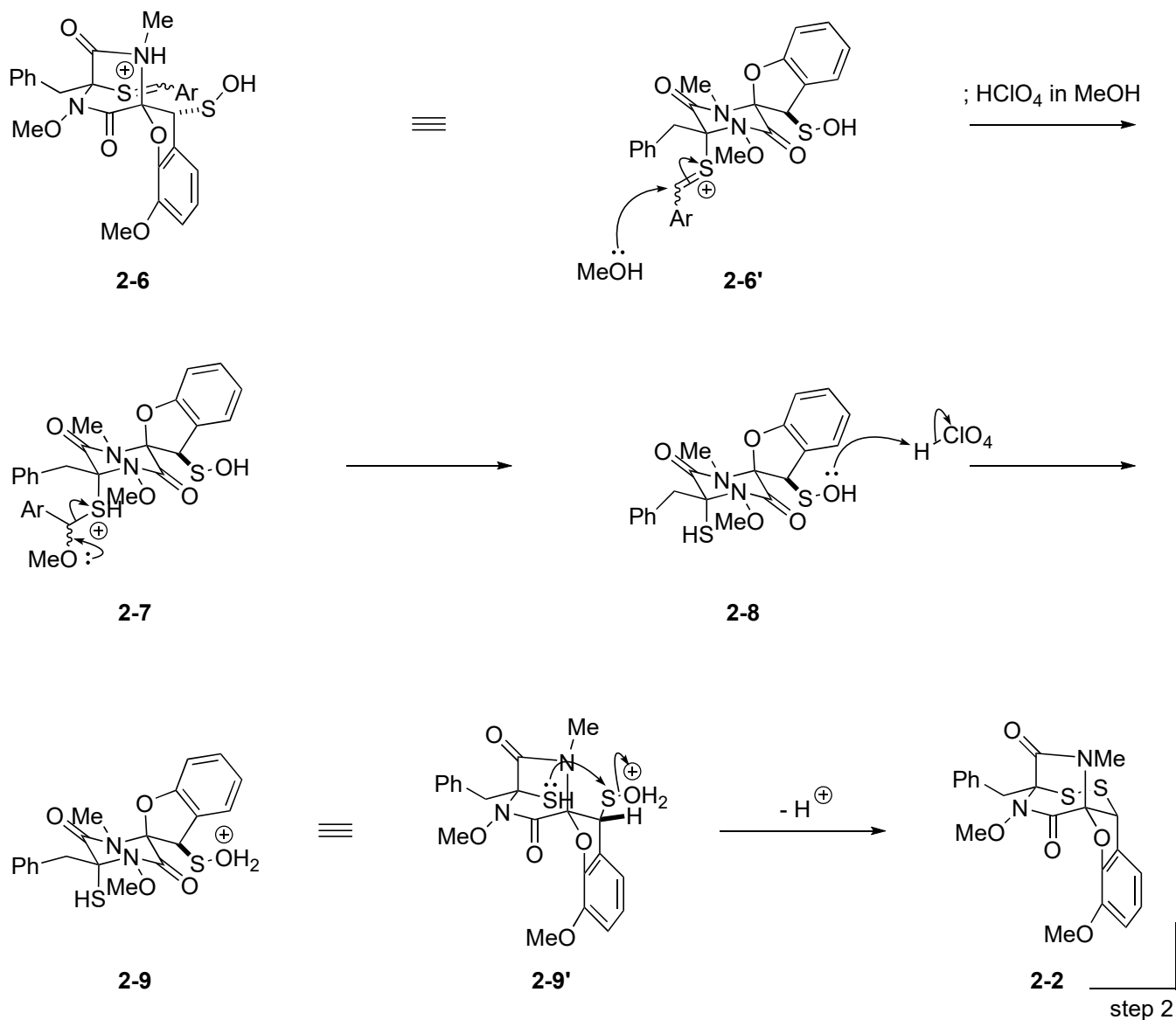
These mechanistic studies (especially eq.1) show that "path a" is the major path and "path b" can proceed as the minor path.

After the seminar



Mo, Z.; Wang, X.; Liu, L.; Tian, S.; Tang, Y. *Org. Lett.* **2025**, 27, 6001.





Discussion 2: Stereoselectivity on sulfur rearrangement

