

# 29<sup>th</sup> Symposium on Chemistry Postgraduate Research in Hong Kong

## Inter- and intramolecular (4+3) cycloadditions with epoxy allylsilanes as dienophiles

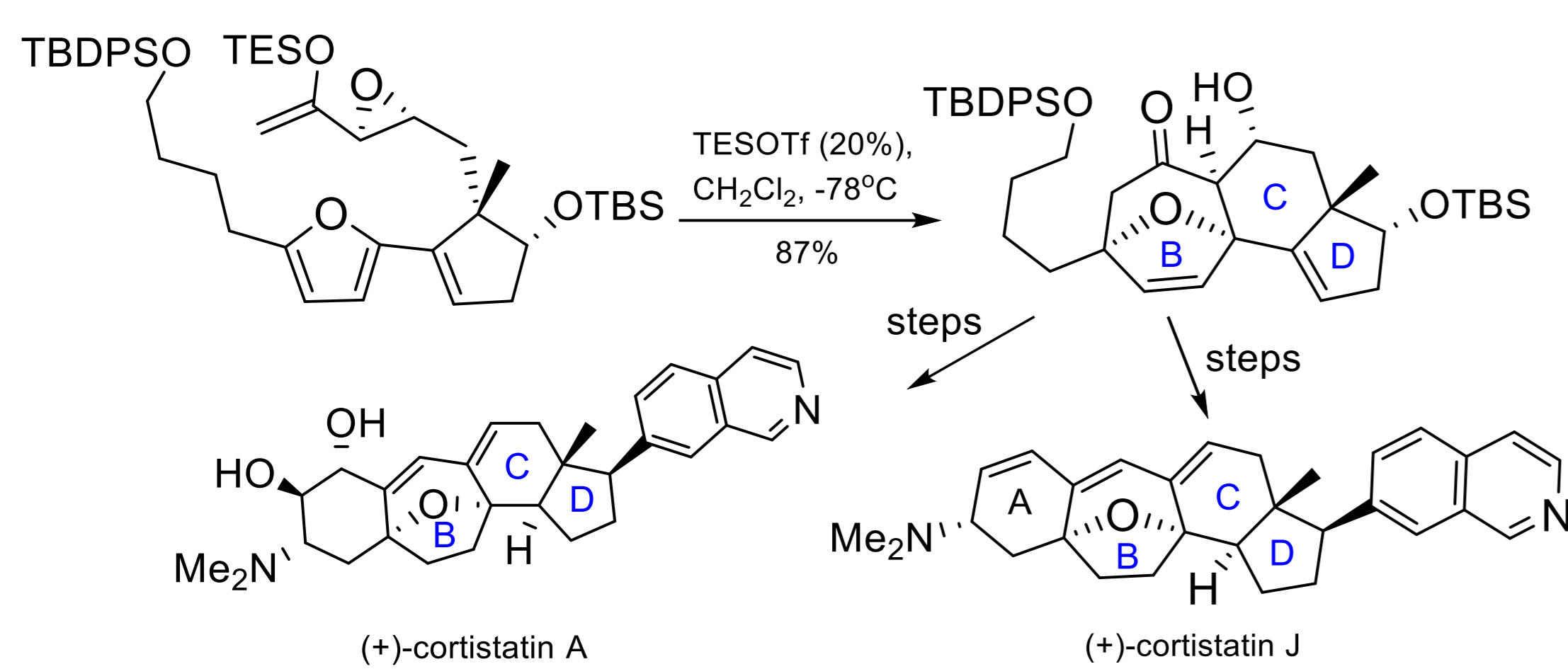


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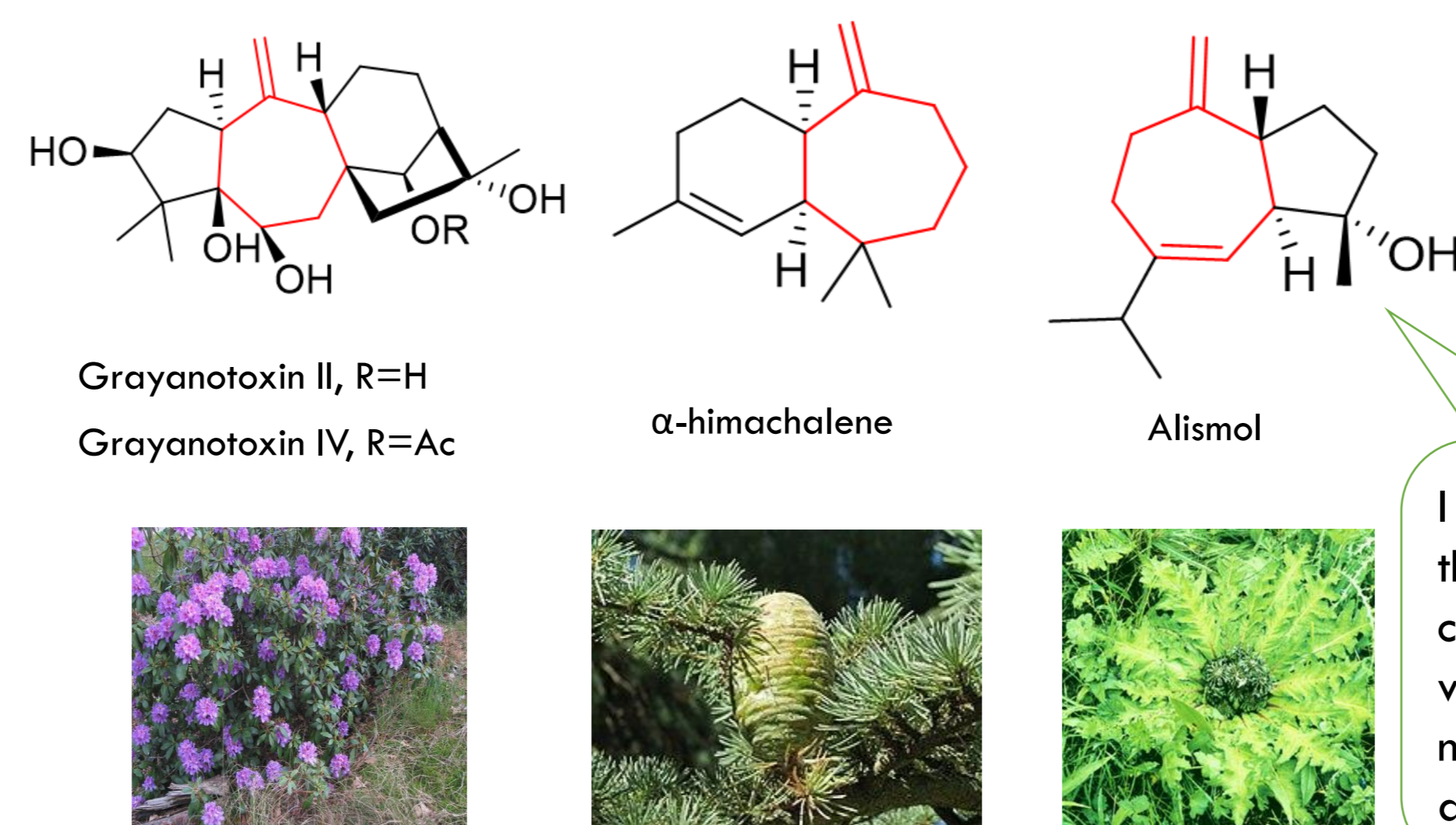
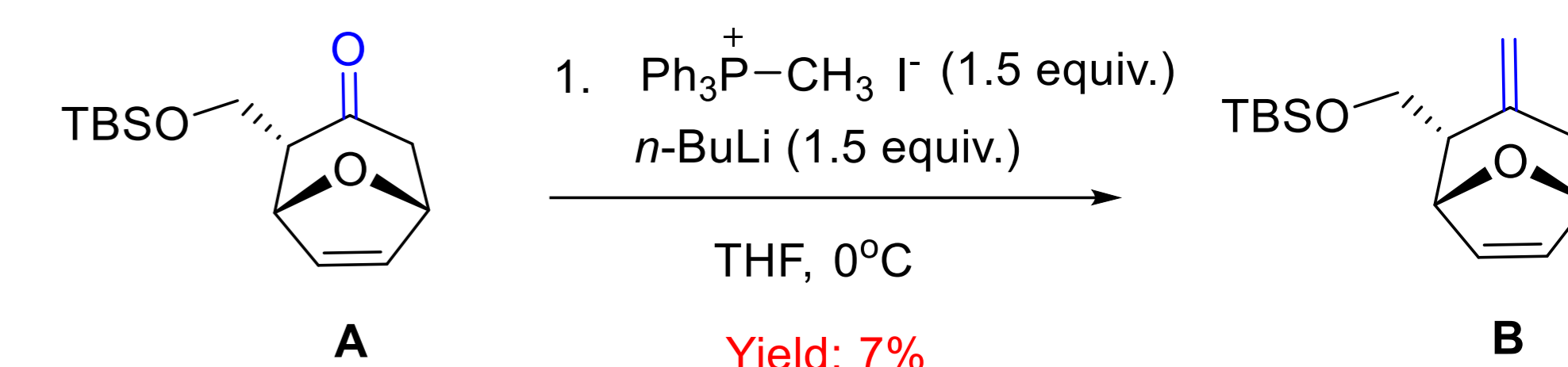
## INTRODUCTION

- The (4+3) cycloaddition reaction: A strategy that has been widely used to construct seven-membered carbocycles.<sup>1</sup>



Application of the methodology<sup>2</sup>:  
Construction of the rings of cortistatin during the total synthesis of (+) cortistatins A and J.<sup>3</sup>

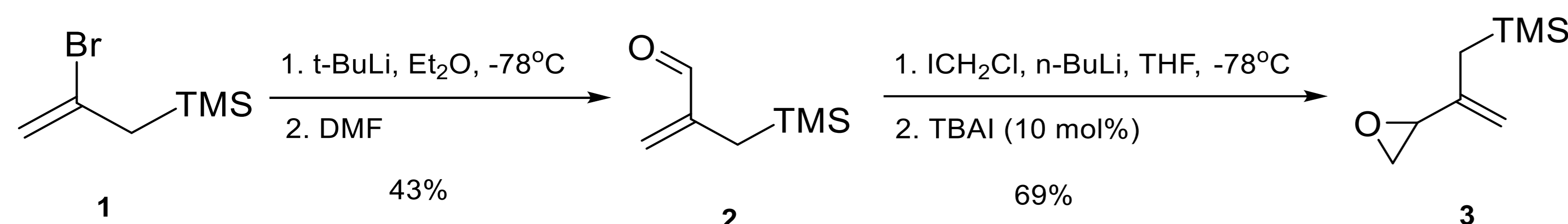
Scheme 1. Work done by our group.

Figure 1. Natural products with methylene cycloheptane frameworks<sup>5</sup>

Attempts to olefinate cycloheptanone **A** to methylene cycloheptane **B**:  
The Wittig reaction works poorly.

We are interested in developing a research methodology which utilizes epoxy allylsilanes to construct methylene cycloheptane frameworks.

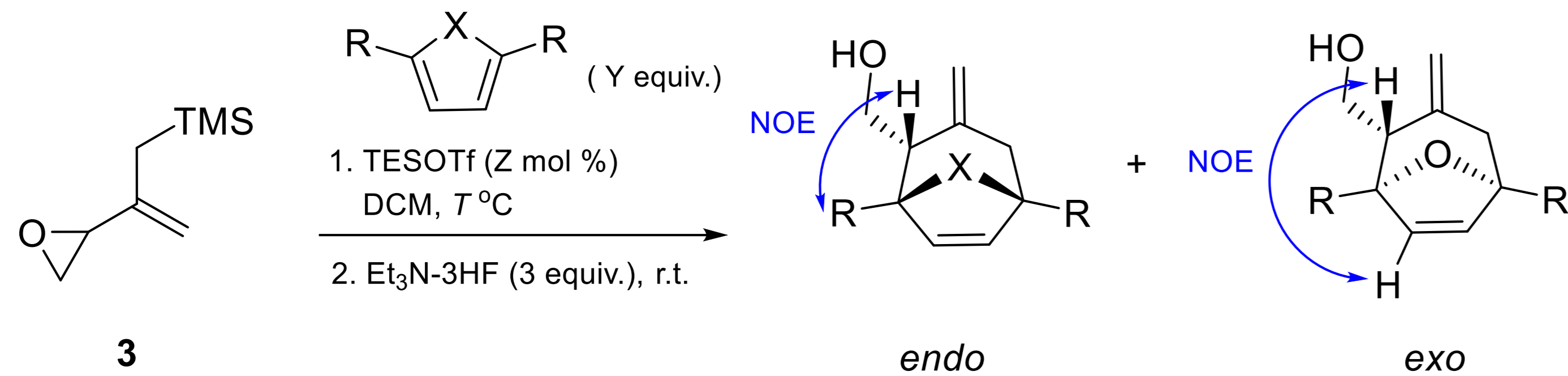
## INTERMOLECULAR CYCLOADDITION



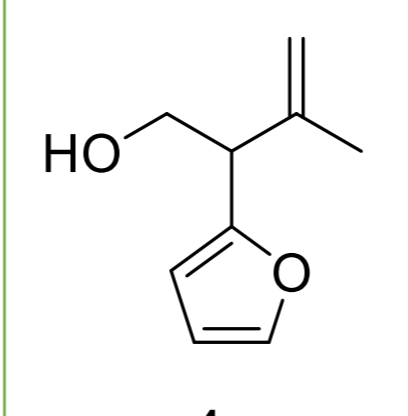
Ref: Trost, B.; Grese, T.; Chan, D. *J. Am. Chem. Soc.* **1991**, *113*, 7350-7362.

Yield of **2** diminished as **2** is volatile.  
b.p.: 156.3°C @ 760mmHg

Ref: Nguyen, M.; Imanishi, M.; Kurogi, T.; Smith, A. *J. Am. Chem. Soc.* **2016**, *138*, 3675-3678.

Scheme 2. Synthesis of dienophile **3**Table 1: Intermolecular cycloadditions of **3** with different dienes.

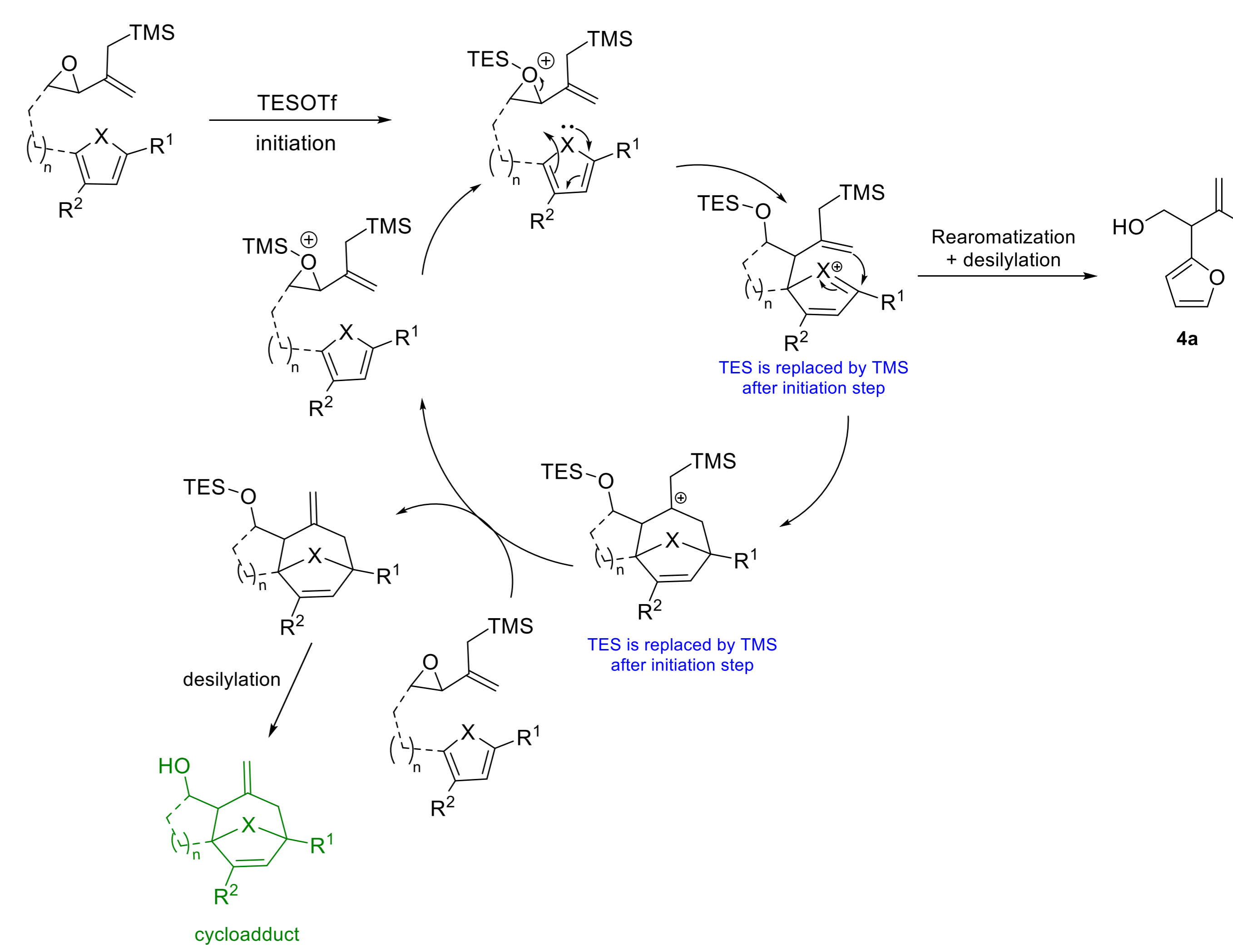
Side products:



entry	X	R	Conditions			yield	endo: exo
			diene (Y equiv.)	TESOTf (Z mol %)	T (°C)		
<b>1<sup>a</sup></b>	O	H	20	100	-94	43%	1:1.6
<b>2<sup>b</sup></b>	O	Me	20	100	-78	14%	6.7:1
<b>3</b>	CH <sub>2</sub>	H	10	20	-78	55%	1.2:1

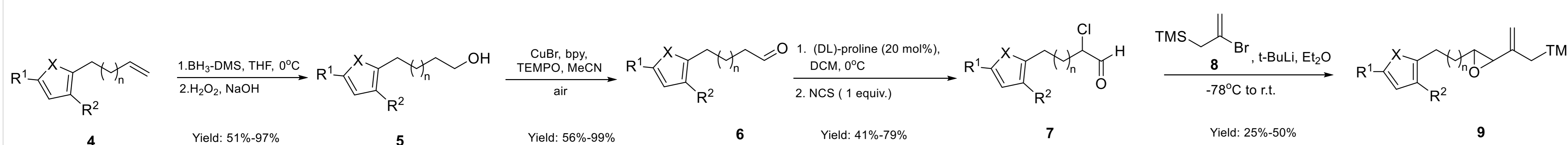
<sup>a</sup> **4a** (14%) also obtained. <sup>b</sup> **4b** (8%) also obtained.

## PROPOSED CATALYTIC CYCLE AND MECHANISM



Scheme 4. The formation of (4+3) cycloadducts and side products

## INTRAMOLECULAR CYCLOADDITION

Scheme 3. Synthesis of epoxy allylsilane precursor **9** (X=O, S; n=1, 2; R<sup>1</sup>=H, Me, CH<sub>2</sub>OTBDPS; R<sup>2</sup>=H, Me)Table 2: Intramolecular cycloadditions of **9**.

entry	X	n	R <sup>1</sup>	R <sup>2</sup>	Yield	endo: exo
<b>1</b>	O	2	H	H	93%	1.7 : 1
<b>2</b>	O	2	Me	H	90%	1.1 : 1
<b>3</b>	O	1	H	H	49%	1.4 : 1
<b>4</b>	O	1	Me	H	59%	2.9 : 1
<b>5</b>	O	2	CH <sub>2</sub> OTBDPS	H	47%	1 : 1
<b>6</b>	S	2	H	H	25%	1 : 1.8
<b>7</b>	S	2	H	Me	42%	exo only

## CONCLUSIONS

- The formation of methylenated bicyclic adducts was achieved by formal (4+3) cycloadditions of epoxy allylsilanes with different dienes.
- Epoxy allylsilane reacts with simple dienes in the presence of a catalytic amount of TESOTf results in the formation of intermolecular (4+3) cycloadducts with moderate yields.
- The epoxy allylsilane tethered to furan with TESOTf constructs cycloadducts with 6,7- and 5,7-fused bicyclic systems in excellent yields.
- Both *endo* and *exo* cycloadducts are formed in the cycloaddition reaction.

## REFERENCES

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